

Radical Germylzincation of Alkynes

Karen de La Vega Hernández

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SORBONNE UNIVERSITE

Ecole Doctorale de Chimie Moléculaire de Paris Centre – ED406 Institut Parisien de Chimie Moléculaire / Equipe ROCS

RADICAL GERMYLZINCATION OF ALKYNES

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Thèse de Doctorat de Chimie

Pour obtenir le grade de

Docteur de Sorbonne Université

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Devant un jury composé de :

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A mis padres...

A Manuel...

Y a mis abuelos... siempre los llevaré en mi corazón

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ABBREVIATIONS

AIBN	azobisisobutyronitrile
APCI	atmospheric pressure chemical ionization
aq	aqueous
BDE	bond dissociation energy
CCDC	Cambridge Crystallographic Data Centre
CCR	cross-coupling reaction
Conv.	conversion
CuTC	copper(I) thiophene-2-carboxylate
d.r.	diastereomeric ratio
dba	dibenzylideneacetone
DBU	1,8-diazabicyclo[5.4.0]undec-7-ene
DG	directing group
DIBAH	diisobutylaluminium hydride
DLP	dilauroyl peroxide
DMAP	N,N-dimethyl-4-aminopyridine
DMF	dimethylformamide
DMSO	dimethyl sulfoxide
DPAP	2,2-dimethoxy-2-phenylacetophenone
DTBP	di- <i>tert</i> -butyl peroxide
ETBP	4-ethyl-2,6,7-trioxa-1-phosphabicyclo[2.2.2]octane
equiv	equivalent
ESI	electrospray ionization
EWG	electron withdrawing group
НАТ	hydrogen atom transfer / H-atom transfer
HRMS	high resolution mass spectrometry
In•	radical initiation
IR	infrared
KHMDS	potassium bis(trimethylsilyl)amide

LDA	lithium diisopropylamide
M.W.	molecular weight
тСРВА	meta-chloroperoxybenzoic acid
Me-THF	2-methyltetrahydrofuran
MIDA	N-methyliminodiacetic acid
mp	melting point
MW	microwave heating
NBS	N-bromosuccinimide
NHC	N-heterocyclic carbene
NIS	N-iodosuccinimide
NMR	nuclear magnetic resonance
pin	pinacol
PRC	polarity-reversal catalysis
rt	room temperature
TBAF	tetra- <i>n</i> -butylammonium fluoride
TBDPS	tert-butyldiphenylsilyl
TBS	<i>tert</i> -butyldimethylsilyl
TCE	trichloroethylene
ТЕМРО	(2,2,6,6-tetramethylpiperidin-1-yl)oxyl
THF	tetrahydrofuran
TIPS	triisopropylsilyl
TLC	thin layer chromatography
ТМ	transition metal
TMEDA	tetramethylethylenediamine
TMS	trimethylsilyl
Ts	toluenesulfonyl or tosyl
UV	ultraviolet

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GENERAL INTRODUCTION

Germanium (Ge) is a group 14 chemical element located between silicon and tin in the periodic table. Likewise, Ge chemical reactivity often lays in between its group neighbors. For instance, the ability of group 14 elements to stabilize a positive charge at the β -position (the so-called β -effect)¹⁻³ has been determined to increase in the order Si < Ge < Sn,³ and numerous synthetic transformations based on this effect have been developed so far.^{4.5} However, not all the chemical properties of group 14 elements follow an anticipated trend. In this sense, the electronegativity of Ge (2.01) is slightly higher than the corresponding to Si (1.90) and Sn (1.96), probably as a consequence of the d-block contraction effect (due to the filled 3d¹⁰ shell of Ge), which causes an increase in the ionization potential of Ge as well as an atomic radius smaller than periodic trends would predict.⁶ Elemental Ge is mostly known for its properties as a semiconductor, with multiple applications in electronics.⁷⁻⁹

In the field of organic synthesis, **vinylgermanes**¹⁰⁻¹² (**Scheme GI-1**) have received attention from organic chemists for a long time. These reagents offer reactivity patterns related to those of vinylsilanes¹³ and vinylstannanes¹⁴ but, quite surprisingly, their application in synthesis is far less widespread than that of the more popular group 14 homologues. A higher cost,ⁱ as well as the limited commercial availability of organogermanium compounds until the early 2000s,¹¹ are certainly some of the causes. Yet, specific features such as increased stability toward protonolysis,¹⁵ facile halodegermylation,¹⁶⁻²³ the non-toxic nature of germanium at low doses,^{24-²⁷ and orthogonal reactivity with many other functional groups,^{23,28-30} make vinylgermanes a useful alternative to vinylsilanes and vinylstannanes when the latter meet flaws.^{18,20,21,23,31}}



SCHEME GI-1. Group 14 vinyl nucleophiles.

Notably, these intermediates have been involved as precursors in the key step of the stereoselective synthesis of natural products or pharmaceuticals (**Scheme GI-2**),^{21,23,32,33} thus demonstrating their potential as versatile building blocks. As a consequence, current interest in

ⁱ Prices from Sigma-Aldrich: Ph₃GeH (5 g) - 267.00 €; Ph₃SnH (5 g) - 83.10 €; Ph₃SiH (5 g) - 20.90 €; (Me₃Si)₃SiH (5 g) - 110.00 € (updated 17.06.2019).

this chemistry has raised considerably. Yet, a key requirement to generalize these applications is the regio- and stereochemically controlled preparation of the vinylgermane motif. To do so, several methodologies have been developed; however, the drawbacks encountered thus far have restricted the general preparation of structurally diverse vinylgermanes. Consequently, the regioand stereoselective synthesis of this scaffold is a field of intense ongoing research.



SCHEME GI-2. Selected examples of the use of vinylgermanes as key intermediates in the total synthesis of natural products and pharmaceuticals.

Nowadays, the major route for the direct synthesis of vinylgermanes relies on carbongermanium bond-forming addition reactions to alkynes. However, there are still limitations in these approaches. For instance, the general access to derivatives having two substituents distal to the position of the alkene germyl group is still beyond our reach. Filling in these gaps is the outermost goal of the work described hereafter. Elementometalation of alkynes^{34–36} (**Scheme GI-3**), i. e. the addition of element–metal bonds across the carbon-carbon triple bond of alkynes, is a conceptually appealing approach that allows the simultaneous creation of a $C(sp^2)$ –element bond and a $C(sp^2)$ –metal bond with orthogonal reactivity. The newly formed $C(sp^2)$ –metal bond can then be used as linchpin for *in situ* electrophilic substitution, whereas the $C(sp^2)$ –element bond can be later functionalized to access stereodefined alkenes.



SCHEME GI-3. Concept of elementometalation of alkynes.

Within this framework, the specific aim of this project was to develop a general approach for the germylzincation of alkynes as a straightforward route for the preparation of polysubstituted vinylgermanes.

The first part of this manuscript is devoted to a general literature overview of the chemistry of vinylgermanes in organic synthesis, with particular emphasis on their preparation from alkynes, as well as on the possibilities of post-functionalization of the vinylgermane template and its use as interesting building block for the construction of complex molecules. The radical approach for elementometalation reactions upon which our germylzincation strategy is built on will be also discussed.

In the second part, the germylzincation reaction of ynamides using a combination of a hydrogermane and Et_2Zn is studied, with special attention on mechanistic studies. Moreover, orthogonal functionalization of the newly formed C(sp²)–Zn bond and C(sp²)–Ge bond is explored to access elaborated di-, tri-, and tetrasubstituted vinylgermanes, and ultimately, alkenes of defined geometry. The extension of this approach to other α -heteroatom-substituted alkynes, as well as more challenging conventional alkynes, is then addressed in parts II-5 and II-6 (**Scheme GI-4**).



SCHEME GI-4. General outline of the work presented in this manuscript.

Furthermore, throughout the manuscript, the possibilities of performing direct hydrogermylation are succinctly covered. Also, some preliminary results offering perspectives to generalize the radical elementozincation approach to the silyl- and borylzincation of conventional alkynes are briefly commented.

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PART I. BIBLIOGRAPHIC OVERVIEW

The synthesis of vinylgermanes, in the spotlight of this thesis, has attracted increasing interest from the synthetic community. This structural motif has been prepared in several ways. The first part of this overview is devoted to describing the different methodologies to access vinylgermanes, with particular emphasis on the synthesis of vinylgermanes from alkynes by carbon–germanium bond-forming addition reactions. In the second part, a description of the possible functionalization of vinylgermanes is provided, along with some examples of their application in organic synthesis. Finally, in the framework of the elementometalation of alkynes, radical silylzincation of α -heteroatom-substituted alkynes is presented.



I-1. VINYLGERMANES IN ORGANIC CHEMISTRY

Vinylgermanes are attractive synthetic building blocks, representing one of the most useful germanium functionalities. This structural motif has encountered multiple applications in organic synthesis owing to the manifold of transformations they can undergo. In consequence, multiple efforts have been made toward the regio- and stereoselective synthesis of vinylgermanes. We will review them hereafter.

I-1.1. PREPARATION OF VINYLGERMANES

I-1.1.1. Overview of approaches for the preparation of vinylgermanes

Scheme I-1 offers a general overview of the main approaches reported to access vinylgermanes and evidences the sources of germanium engaged.

Electrophilic substitution of vinylmetals (generally vinyllithium and vinylmagnesium) with **halogermanes** (R₃GeX; X = Cl, Br) (Scheme I-1, A) is a first method that has been commonly applied to access vinylgermanes. This method offers the advantage of using the cheapest and more available germanium source, but the requirement for the preparation of the parent vinylmetals and issues associated to the loss of the stereochemical information are limitations often met. Furthermore, the approach was only scantily used to access α -substituted vinylgermanes.^{1–3}

Another highly useful and versatile source of germanium is **hydrogermanes** (R_3 GeH). They offer higher stability compared to halogermanes, ease of manipulation, and their commercial availability has recently increased. Vinylgermanes have been prepared from hydrogermanes following various C–Ge bond-forming reactions. Oshima reported the Pd(0)-catalyzed coupling of *tri(2-furyl)germane* with vinyl halides (X = I, Br)⁴ (Scheme I-1, B), a method that offered the advantage of preserving the stereochemical information enclosed on the starting vinyl halide. Alkenes have also been used as substrates to access vinylgermanes by reaction with hydrogermanes (Scheme I-1, C). In early work, Seki reported the stereoselective dehydrogenative germylation of styrene catalyzed by Ru₃(CO)₁₂.⁵ Later, in-depth investigations performed by Marciniec showed that RuHCl(CO)(PCy₃)₂ gave better results.⁶ Also related to this chemistry, the germylation of olefins with vinylgermanes in the presence of catalysts containing Ru–H bonds opened an effective catalytic route for the preparation of functionalized vinylgermanes.⁷ Notably, this methodology was applied to the synthesis of arylene-vinylene-germylene derivatives with interesting absorption and luminescence properties.⁸



SCHEME I-1. General approaches for the preparation of vinylgermanes (*Ge* = triorganogermyl).

Undoubtedly, the most frequent use of *hydrogermanes* to access vinylgermanes is the hydrogermylation of alkynes, that has been achieved *via* transition metal-catalysis, main-group Lewis acid-catalysis, or radical processes (Scheme I-1, H).ⁱ

Keeping with radical chemistry, Oshima as well disclosed a free radical substitution reaction for the conversion of vinylsulfides and vinylstannanes into vinylgermanes by using a combination of Ph_3GeH/Et_3B (Scheme I-1, D).⁹ However, the approach was limited by regioselectivity issues. By analogy, Wnuk reported later on the radical-mediated germyldesulfonylation of vinyl sulfones and (α -fluoro)vinyl sulfones with different *hydrogermanes* in the presence of AIBN

ⁱ These methods will be described in more detail in section I-1.1.2.

(azobisisobutyronitrile) as radical initiator (Scheme I-1, D).¹⁰⁻¹² This procedure found application for the synthesis of vinylgermane-containing nucleoside analogues.¹³

Compounds having **germanium–element** bonds represent another useful family of compounds that give access to vinylgermanes through their addition across alkynes.ⁱ The most common are germylstannation (Ge–Sn), digermylation (Ge–Ge), germylboration (Ge–B), and germylcyanation (Ge–CN) processes (Scheme I-1, H). In this context, a more recent and rather isolated approach to the synthesis of functionalized alkenylgermanes relies on the palladium-catalyzed *ortho*-germylation of aryl iodides/arylgermylation of oxanorbornadiene/retro-Diels–Alder domino reaction by using hexamethyldigermane (Ge–Ge) (Scheme I-1, E).¹⁴ However, despite the high yields obtained, this method is rather limited in terms of structural diversity of the final products.

The addition of **germanium–metal** bonds across alkynes has been also investigated but has remained so far restricted to a few reports on the germylcupration (Ge-Cu) of terminal alkynes and propiolates (Scheme I-1, H).ⁱⁱ

In addition to the abovementioned strategies that proceed through C–Ge bond formation, it is also important to mention that vinylgermanes can also be prepared through the transformation of substrates already containing a germanium moiety. **Alkynylgermanes** have been frequently converted into vinylgermanes through hydrometalation, as well as carbometalation processes (Scheme I-1, F). In the first case, hydroalumination,^{15,16} hydroboration,^{15,17} and hydrostannation¹⁸ reactions have been performed with (high) degrees of selectivity closely dependent on the nature of the metal and the characteristics of the substrate. In the second case, the carboalumination of germanium-substituted homopropargylic alcohols and their higher homologues was reported by Negishi.¹⁹ Another example of this chemistry came from the reaction of an alkynylgermane with allylborane and triethylborane via 1,1-allylboration or 1,1-ethylboration, respectively.²⁰ Also, intramolecular carbolithiation of alkynylgermanes has proved suitable for the preparation of vinylgermanes with high selectivity.^{21,22} Lastly, Takeda and Shindo also developed the highly Zselective olefination of **acylgermanes** with ynolates *via* torquoselective olefination (Scheme I-1, G).^{23,24} The stereochemical complementary approach was also achieved by stereoselective formation of lactone, followed by decarboxylation. Additionally, Takeda reported simultaneously the stereoselective synthesis of vinylgermanes utilizing cyclobutyl ketones (not shown).²³

ⁱ These methods will be described in more detail in section I-1.1.3.

ⁱⁱ These methods will be described in more detail in section I-1.1.4.

In brief, the complex landscape of methodologies analyzed up to now has common drawbacks, namely, the need for elaborated starting materials, limited scope, and lack of generality.

Undeniably, the **direct synthesis of vinylgermanes from alkynes by carbon–germanium bond-forming addition reactions** represents the most straightforward approach and has received the greatest attention (Scheme I-1, H, highlighted in red). Accordingly, we will detail it below.

I-1.1.2. Digging deeper into the hydrogermylation of alkynes

Arguably, the most efficient and atom-economical available approach for the direct synthesis of vinylgermanes relies on the hydrogermylation of alkynes, which is the addition of a Ge–H bond across C-C triple bonds. This addition reaction of hydrogermanes to alkynes has been revealed to occur through **transition metal-catalyzed**, **main-group Lewis acid-catalyzed**, or **radical processes**.

I-1.1.2.1. Transition metal-catalyzed hydrogermylation

Transition metal-catalyzed hydrogermylation is a long known reaction for which the control of the regio- and stereoselectivity has always been an issue.²⁵ Addition reactions between hydrogermanes and acetylenic compounds in the presence of a transition metal (TM) catalyst lead to the formation of four possible products, namely, α and β adducts and E or Z diastereomers (**Scheme I-2**). The relative ratio of the four isomers strongly depends on the catalytic system, the hydrogermane, and the acetylene/hydrogermane ratio.





Ru, Pt or Pd complexes^{15,26–32} have been commonly used to catalyze the hydrogermylation of terminal alkynes. For these reactions, the typical selectivity outcome is to obtain *E* stereoisomers with variable regioselectivity. As for other hydrometalation reactions (H–Met; Met = SiR₃, GeR₃, SnR₃), the *syn* delivery of the H–Met bond to the π system of a given alkyne is responsible for the observed stereoselectivity.

Long ago, Moreau reported the hydrogermylation of phenylacetylene catalyzed by Rh and Pt complexes (**Table I-1**).²⁶

	β R	+ R' ₃ GeH (1.0-1.5 equiv)	$\xrightarrow{\text{catalyst}} \begin{array}{c} R\\ R'_{3}Ge \end{array}$	$H + H + R'_{3Ge} + R + \beta, Z \text{ adduct}$	$\mathbf{R}_{\mathbf{GeR'}_{3}}$	
	Entry	R	R'3GeH	Catalyst	Yield	Ratio β,E:β,Z:α
	1	Ph	nBu₃GeH	(Ph ₃ P) ₃ RhCl	80%	85:14:1
	2	Ph	Ph₃GeH	(Ph ₃ P) ₃ RhCl	85%	82:15.5:2.5
Moreau,	3	Ph	<i>i</i> PrPh-1-NaphGeH	(Ph ₃ P) ₃ RhCl	70%	70:24:6
1972	4	Ph	<i>n</i> Bu₃GeH	cis-(Ph ₃ P) ₂ PtCl ₂	59%	73:7:20
	5	Ph	<i>n</i> Bu₃GeH	$H_2PtCl_6 \bullet 6H_2O$	68%	75:2:23
	6	Ph	Ph₃GeH	$H_2PtCl_6\bullet 6H_2O$	78%	70:0.5:29.5
Oshima, 1984	7	C10H21	Ph ₃ GeH	H ₂ PtCl ₆ •6H ₂ O	99%	75:0:25
	8	$C_{10}H_{21}$	nPr ₃ GeH	$H_2PtCl_6 \bullet 6H_2O$	93%	87:0:13

TABLE I-1. Hydrogermylation of terminal acetylenes catalyzed by Rh and Pt complexes.

In the presence of complex (Ph₃P)₃RhCl, the formation of the β adduct was largely favored, notwithstanding the stereocontrol was not excellent, being detrimental the more hindered the substitution was in the germyl group (Table I-1, entries 1-3). By contrast, the use of Pt complexes produced a noticeable increment in the formation of the α adduct, regardless of the nature of the hydrogermane (Table I-1, entries 4-6). A similar behavior was later observed by Oshima,¹⁵ when performing the hydrogermylation of 1-dodecyne with the same Pt catalytic system (H₂PtCl₆•6H₂O) (Table I-1, entries 7-8). Note however that in this case, the stereoselectivity of the β adduct was excellent, even if the regiocontrol was modest.

Regarding palladium catalysis for the *cis*-selective hydrogermylation of alkynes (**Scheme I-3**), the first example of this chemistry came from Oshima in 1987.²⁷ He showcased that $Pd(PPh_3)_4$ was essential for the reaction because Ph_3GeH was not able to reduce Pd(II) to the corresponding zerovalent palladium, which is the active catalyst. The reaction proceeded with excellent stereoselectivity (*Z* isomers not detected), but not always with perfect regioselectivity.

Afterwards, Maleczka applied Oshima's protocol for the preparation of *E*-vinyltributylgermanes from terminal acetylenes mostly decorated with an alcohol group (protected or unprotected).³⁰ However, the less hindered the propargylic position of the starting material, the poorer the regioselectivity. Later on, Blanchard developed a similar approach to access *E*-CF₃-vinylgermanes, resulting in a highly regio- and stereoselective addition, where no *Z* isomers were observed, and less than 5% of the α isomers were detected.^{31,32} Nonetheless, upon investigation of the scope of this transformation, only alkyl-substituted CF₃-alkynes were reactive, as the aryl-substituted counterparts remained unreacted even under forcing conditions (microwave, 100 °C).³²



SCHEME I-3. Pd(PPh₃)₄-catalyzed *cis*-hydrogermylation of alkynes.

It is important to mention that in the palladium-catalyzed examples showcased up to now, the hydrogermane is in equimolar ratio or just in slight excess with respect to the starting alkyne. What is surprising is the dramatic change in the outcome of the reaction when performing it in the presence of excess alkyne, as demonstrated by Oshima.^{28,29} By varying the alkyne/hydrogermane ratio from **1.0/(1.0-1.2)** to **3.0/1.0**, dienylgermane **1** was obtained as major product, together with the minor formation of dienylgermane **2**, which is arising from an initial α addition reaction to the alkyne (**Table I-2**, entry 1). The selectivity in favor of **1** was even higher when (2-furyl)₃GeH was used instead of Ph₃GeH (Table I-2, entry 2), while Et₃GeH did not provide any of the desired products under the same reaction conditions. After screening different catalytic systems, the best selectivity was obtained with [PdCl(η^3 -C₃H₅)]₂ as palladium source, combined with tris(2-*tert*-butylphenyl) phosphite (**4**) as ligand (Table I-2, entry 3). The optimized conditions also operated efficiently with propargyl alcohol (Table I-2, entry 4). By contrast, the selectivity for the dienylgermane was disappointing when performing the reaction with 1-trimethylsilylacetylene or *tert*-butylacetylene (Table I-2, entries 5-6), presumably as a consequence of the steric hindrance, as proposed by the authors. However, it is difficult to imagine that only steric factors can account for the difference between entries 5 and 6.

	$\beta \stackrel{\alpha}{\longrightarrow} R + R$ (3.0 equiv)	' ₃ GeH Pd H ₂ O, rt, 3 h	$R'_{3}Ge + R'_{3}Ge $	2 H +	R R' ₃ Ge 3	
Entry	R	R'₃GeH	Catalyst	Yield		
y			currently 50	1	2	3
1	nC_6H_{13}	Ph ₃ GeH	Pd(PPh ₃) ₄	69%	12%	-
2	<i>n</i> C ₆ H ₁₃	(2-furyl)₃GeH	Pd(PPh ₃) ₄	77%	11%	10%
3	<i>n</i> C ₆ H ₁₃	(2-furyl)₃GeH	$[PdCl(\eta^{3}-C_{3}H_{5})]_{2} - $	91%	8%	_
4	CH_2OH	(2-furyl)₃GeH	[PdCl(η ³ -C ₃ H ₅)] ₂ – 4	68%	8%	-
5	SiMe ₃	(2-furyl)₃GeH	[PdCl(η ³ -C ₃ H ₅)] ₂ – 4	60%	_	40%
6	<i>t</i> Bu	(2-furyl)₃GeH	$[PdCl(\eta^{3}-C_{3}H_{5})]_{2} - 4$	25%	-	71%

TABLE I-2. Formation of dienylgermanes by Pd(0)-catalyzed hydrogermylation of alkynes.

On the basis of these results, Oshima proposed a mechanism to account for the formation of both E vinylgermanes and dienylgermanes under Pd(0) catalysis (**Scheme I-4**).^{28,29}



SCHEME I-4. General mechanism for the Pd(0)-catalyzed hydrogermylation of alkynes: Formation of *E* vinylgermanes (**3**) and dienylgermanes (**1**).

The proposal involved first oxidative addition of R'_{3} GeH to Pd(0) providing **5**, followed by hydropalladation onto the alkyne (*syn* addition) (**6**). From there on two possible pathways were considered: direct reductive elimination to produce *E*-vinylgermane **3** and regenerate the Pd(0) catalyst (dashed pathway), or subsequent carbopalladation across a second molecule of alkyne (*syn* addition), followed by reductive elimination from dienylpalladium **7** to produce dienylgermane **1** and, once again, regenerate the Pd(0) catalyst (plain pathway).

Rh(I)-catalyzed regiodivergent hydrogermylation of terminal alkynes is also documented (**Scheme I-5**). Wada reported at an early point that the typical β adduct could be satisfactorily formed (with moderate *E* selectivity) by using RhCl(CO)(PPh₃)₂ as catalyst.³³ Significant improvement in the regio- and stereochemical outcome of this reaction was later observed by Spivey, attributable to the bulk of bis(naphtalen-2-ylmethyl) groups on the fluorous tagged germanium hydride used.^{34,35} Yet, to the best of our knowledge, Wada's report is also the only example concerning the somewhat selective formation of the α adduct from terminal alkynes in a *cis* fashion. In this regard, by switching from RhCl(CO)(PPh₃)₂ to Rh(hfa)(C₂H₄)₂ as catalyst, reversal of regioselectivity was observed during the hydrogermylation of phenylacetylene in the presence of *n*Bu₃GeH.³³ Reaction on deuterium-labeled phenylacetylene allowed to support a *syn* addition process. However, the origin of the α selectivity was not clarified, and generally, the regioselectivity was far from excellent. In most cases, a molar ratio [PhC=CH/*n*Bu₃GeH] of 10:1 was necessary in order to overcome β addition.



SCHEME I-5. Rh(I)-catalyzed regiodivergent hydrogermylation of terminal alkynes.

Less conventional *trans*-selective addition reactions, which disrupt the general trend of suprafacial delivery for hydrometalations, have been reported as well. The scant examples of this chemistry are basically limited to [Ru]-catalyzed processes. In this sense, Murakami developed a Markovnikov alkyne hydrogermylation catalyzed by a cationic ruthenium complex, [Cp*Ru(MeCN)₃]PF₆,³⁶ reminiscent of the known *trans*-hydrosilylation discovered by Trost.³⁷⁻³⁹ It was initially demonstrated that the reaction on deuterium-labeled phenylacetylene gave rise to the branched vinylgermane (Markovnikov addition, α regioisomer) (68%) with excellent *trans* selectivity. Further trials on symmetrical alkynes (**Table I-3**) uncovered the importance of the hydrogermane for the stereoselectivity: reaction with triethylgermane was highly *trans*-stereoselective (Table I-3, entries 1 and 3) while reaction with triphenylgermane resulted in the formation of an equimolar mixture of isomers (Table I-3, entry 2).

	R + R' ₃ G	eHRu	$\rightarrow \overset{R}{\underset{R}{\overset{CeR'_{3}}{\longrightarrow}}} + \overset{R}{\underset{(Z)}{\overset{COR'_{3}}{\longrightarrow}}} + \overset{R}{\underset{R}{\overset{COR'_{3}}{\longrightarrow}}} + \overset{R}{\underset{R}{\overset{COR'_{3}}{\longrightarrow}}} + \overset{R}{\underset{R}{\overset{R}{\longrightarrow}}} + \overset{R}{\underset{R}{\overset{R}{\to}} + \overset{R}{\underset{R}{\overset{R}{\to}}} + \overset{R}{\underset{R}{\overset{R}{{\to}}} + \overset{R}{\underset{R}{\overset{R}{{\to}}} + \overset{R}{\overset{R}{{\to}}} + \overset{R}{{\overset{R}{{\to}}} + \mathsf{$	H (E)	
Entry	Substrate	R' ₃ GeH	Catalyst	Yield	Z/E
1	<i>n</i> Pr	Et ₃ GeH	[Cp*Ru(MeCN)3]PF6	77%	>99:1
2	<i>n</i> Pr	Ph₃GeH	[Cp*Ru(MeCN)3]PF6	45%	50:50
3	Ph	Et₃GeH	[Cp*Ru(MeCN) ₃]PF ₆	25%	>99:1

TABLE I-3. [Ru]-catalyzed trans-hydrogermylation of symmetrical alkynes.

The high and rather unexpected *trans* selectivity of [Ru]-catalyzed hydrometalation of alkynes has deserved further exploration in the literature, mainly linked to hydrosilylation reactions. In this concern, Ojima reported an early mechanistic proposal for the apparent *anti* addition proceeding through initial *syn*-silylmetalation, and subsequent isomerization *via* a zwitterionic carbene complex prior to reductive elimination.⁴⁰ However, later on, Trost pointed out that the high selectivity for *anti* addition spoke against the possibility of a simple *syn* addition/isomerization mechanism.^{37,38} Alternatively, substantiated by extensive DFT calculations, they proposed a mechanism involving a direct three-component addition where the silane is activated through a σ -complex (**Scheme I-6**, A).^{39,41} It is reasonable to assume that a mechanism reminiscent of the one proposed by Trost could be operating in the [Ru]-catalyzed *trans*-hydrogermylation reported by Murakami.



SCHEME I-6. Mechanism for *trans*-selective [Ru]-catalyzed hydrosilylation of alkynes **(A)** and regioselectivity model for [Ru–Cl] catalysts in the presence of an alkyne bearing a protic functional group **(B)**.

Irrespective of the stereochemical outcome, hydrometalations of unsymmetrical nonterminal alkynes are usually confronted to regioselectivity problems. This is not the exception with [Cp*Ru(MeCN)₃]PF₆, where the regioselectivity is often poor with unsymmetrical substrates.

Fürstner and co-workers recently demonstrated that this problem can be solved upon switching to a catalyst containing a [Ru–Cl] bond, as long as the alkyne carries a protic functional group.⁴² The theory behind the regioselectivity control lies on the ability of the [Ru-Cl] bond to act as a hydrogen-bond acceptor for the protic functional group carried by the alkyne (Scheme I-6, B). The attractive force favors substrate binding, preorients the unsymmetrical alkyne within the coordination sphere of the catalyst, and probably increments the electronic bias of the acetylene linkage by polarization of the ligated triple bond. In order to prove the generality of their approach, they became interested in evaluating the steering effect of directing groups (DG) for the regioselective [Ru]-catalyzed trans-hydrogermylation of unsymmetrical alkynes (Table I-4). Firstly, they compared the chloride-free catalyst employed by Murakami in symmetrical substrates with [Cp*RuCl]₄ in the presence of an unsymmetrical propargylic alcohol (Table I-4, entries 1-2). In accordance with their working hypothesis, Et₃Ge-residue ended up at the proximal site of the propargylic alcohol when $[Cp*RuCl]_4$ was used (α isomer), while $[Cp*Ru(MeCN)_3]PF_6$ favors the distal regioisomer (β isomer). As expected, when protecting the OH (Table I-4, entry 3), the selectivity went back to the intrinsic one which inherently favored the distal addition, as proven in entry 1. OH group in homopropargylic position and sulfonamide also led to good results following the same principle (Table I-4, entries 4-5).

	$\beta \stackrel{\alpha}{\longrightarrow} \beta \stackrel{\alpha}{\longrightarrow} \beta \stackrel{\alpha}{\longrightarrow} \beta \stackrel{\beta}{\longrightarrow} + Et_3GeH$	Ru	$\rightarrow H \qquad $	$ \begin{array}{c} $	
Entry	Substrate	R' ₃ GeH	Catalyst	Yield	Ratio α/β^{a}
1	OH a	Et₃GeH	[Cp*Ru(MeCN) ₃]PF ₆	83%	24:76
2	β	Et₃GeH	[Cp*RuCl]4	78%	86:14
3	ο Me	Et ₃ GeH	[Cp*RuCl] ₄	88%	20:80
4	β ^α OH	Et₃GeH	[Cp*RuCl] ₄	96%	86:14
5	β α H CF ₃ N S O	Et ₃ GeH	[Cp*RuCl] ₄	78%	92:8

TABLE I-4. [Ru]-catalyzed trans-hydrogermylation of unsymmetrical alkynes.

^aThe selectivity for *anti* addition was \ge 95:5 in all cases.

Finally, there is also one example of transition metal-catalyzed alkyne hydrogermylation concerning the use of 3d transition metals instead of precious 4d and 5d metal complexes.
$CpFe(CO)_2(Me)$ proved to be a competent catalyst and hydrogermylation occurred with *trans* selectivity.²⁵ The reaction was efficient both for terminal and internal alkynes, as well as for different hydrogermanes, providing the corresponding *Z* adducts (**Scheme I-7**).



SCHEME I-7. CpFe(CO)₂(Me)-catalyzed *trans*-selective hydrogermylation of terminal and internal alkynes.

On the whole, transition metal-catalyzed hydrogermylation of alkynes has earned the welldeserved fame of regio- and stereoselectivity drawbacks. Despite of the advances made in recent years to overcome this limitation, there is still room for improvement.

I-1.1.2.2. Lewis acid-catalyzed hydrogermylation

Main-group Lewis acids also catalyze the hydrogermylation of alkynes in an efficient manner. Gevorgyan first reported the use of $B(C_6F_5)_3$ as catalyst for this transformation.⁴³ As it is shown in **Scheme I-8** (A), this approach leads to *Z*-vinylgermanes **8** in the case of nonactivated alkynes, whereas *E*-vinylgermanes **9** are obtained from propiolates. The reaction is high yielding, wide in scope, and occurs under mild reaction conditions. The functional group tolerance is high: methoxy, aryl halides (Br and I), furyl-containing alkyne, and pinacolborane moiety do not interfere with the hydrogermylation reaction. The regioselectivity is excellent and presumably largely electronically driven since it is fully controlled even in the case of alkynes having substituents with only slight electronic differences (Ph *vs* 4-MeO-C₆H₄ or Ph *vs* 4-CF₃-C₆H₄).



SCHEME I-8. B(C₆F₅)₃-catalyzed hydrogermylation of alkynes.

Concerning the stereocontrol of this reaction, the *anti* addition with electronically unbiased alkynes and the *syn* addition with biased $C \equiv C$ bonds (propiolates) suggested a different mechanistic rationale for the origin of stereoselectivity in each case. In this regard, the mechanism presented in Scheme I-8, A (left) was proposed in order to explain the *trans*-selective hydrogermylation of unbiased alkynes. Activation of the hydrogermane by $B(C_6F_5)_3$ and reversible

addition of the electrophilic germyl moiety **10** to the alkyne produces vinyl cation **11**, which is the regiodetermining step of the reaction. Subsequent hydride transfer from bulky $[HB(C_6F_5)_3]^-$ occurs from the less hindered side that is the opposite to the germyl group, thus providing the *anti* addition product and regenerating the catalyst. By contrast, in order to account for the *cis*-selective hydrogermylation observed with propiolates, the authors proposed the following rationalization: the reversible coordination of the ester-carbonyl group of propiolates to $B(C_6F_5)_3$ produces zwitterionic intermediate **12** which is converted to the corresponding allenolate **13** *via* hydride transfer from the hydrogermane to the cationic center of **12**. Trapping of **13** with germylium-type species occurs once again from the less hindered side (in this case, *cis* to the H), giving place to the *syn* addition product and the regeneration of the catalyst (Scheme I-8, A, right).

Later on, Oestreich reported the use of the same catalytic system to perform the hydrogermylation of alkenes with hydrogermane surrogates.⁴⁴ In this approach, the use of various cyclohexa-2,5-dien-1-yl-substituted germanes (**14**) was shown to deliver the *Ge*–H functional group serving as synthetic equivalents not only for the commercially available Et_3GeH but also for the gaseous and highly flammable Me_2GeH_2 and $MeGeH_3$ (fact that has discouraged the use of the latter in hydrogermylation reactions). In order to demonstrate the generality of the methodology, two model alkynes (electronically unbiased diphenylacetylene and biased phenylpropiolate) were also tested under the reaction conditions, yielding the corresponding products in a stereodivergent manner, as expected from previous results from Gevorgyan.⁴³ Mechanistically, *in situ* generation of ion pair comprising a germanium-stabilized Wheland complex or a benzene-stabilized germylium ion is obtained by hydride abstraction by $B(C_6F_5)_3$ from surrogate **14**, which eventually releases the hydrogermane along with benzene (Scheme I-8, B). Once the active species generated, the formation of the product follows the same rationale as proposed by Gevorgyan.

Aluminum-based catalysts have also been used as efficient Lewis-acid catalysts for hydrogermylation reactions (**Scheme I-9**). EtAlCl₂ catalyzed the presumably *trans*-hydrogermylation of 1-dodecyne on hydride-terminated Ge(100) surfaces⁴⁵ (Scheme I-9, A), while AlCl₃ catalyzed the *cis*-hydrogermylation of fluorinated alkyl propiolates⁴⁶ (Scheme I-9, B). The stereodivergent outcome of these two reports matches with the generalization observed in boron-catalyzed hydrogermylation reactions. However, these processes have been quite less investigated than the boron-catalyzed ones.



SCHEME I-9. Aluminum-catalyzed hydrogermylation of alkynes.

Altogether, the possibility to use diverse internal alkynes, the excellent regio- and stereoselectivity related to the nature of the alkyne, the high functional group tolerance, on top of the diversity of the substitution pattern of the hydrogermane are definitely assets of the Lewis acid-catalyzed hydrogermylation of alkynes.

I-1.1.2.3. Radical hydrogermylation

In a radical mechanistic framework, hydrogermylation of alkynes has been comprehensively studied. This approach has been grounded on the feasibility of generating germanium centered radicals from the parent hydrogermanes through a hydrogen abstraction process. Several studies have been devoted to determining the hydrogen donor abilities of hydrogermanes toward primary alkyl radicals.^{47–49} The values of the rate constants ($k_{\rm H}$, M⁻¹ s⁻¹) for this reaction have been summarized in **Figure I-1**. Given that the values come from different sources, they have been determined at different temperatures,^{47–50} but this factor has been taken into account for a more accurate analysis. The rate constant for the H-atom abstraction increases (~ 1 order of magnitude) along the substituent series:

Alkyl < Ph < Me₃Si

This is possibly linked to the relative stabilization of the unpaired electron by, respectively, inductive effects, mesomeric effects, or hyperconjugative effects with the Si–C β -bond.⁴⁹



FIGURE I-1. Rate constants for the H-atom abstraction of hydrogermanes by primary alkyl radicals.

Radical hydrogermylation reactions follow the general mechanism depicted in **Scheme I-10**. After initiation, germanium centered radicals **15** add across the C-C triple bonds of alkynes **16** to produce vinyl radical intermediate **17**. This radical then quickly reacts by H-atom transfer (HAT) with the hydrogermane to afford the corresponding *Z*-vinylgermane **18** along with R'₃Ge• (**15**) that propagates the radical chain.



SCHEME I-10. General mechanism for the radical hydrogermylation of alkynes.

The regioselectivity of the reactions is usually controlled by steric factors rather than electronic ones. For instance, in terminal alkynes, the regioisomer formed is the one with the germyl group bonded to the less hindered terminal sp² carbon (*anti*-Markovnikov, β selectivity). However, concerning the origin of the regioselectivity in internal alkynes, scant is known since there are barely any examples of that kind. Only the hydrogermylation of one symmetrical alkyl-substituted alkyne was reported⁵¹ (which evidently gives no insights about regioselectivity issues) and the other examples relied on electronically biased CF₃-alkynes. For the latter, the germyl radical attaches to the carbon in α position to the CF₃ moiety^{31,32} (*vide infra*).

Regarding the stereoselectivity, radical hydrogermylation typically delivers the *anti* addition product (kinetic product). This outcome is closely related to the geometry of the vinyl radical intermediates (**Scheme I-11**).



SCHEME I-11. Stereoselectivity model for the radical *trans*-hydrogermylation of alkynes.

It is well-documented that the geometry of vinyl radicals depends on the nature of the substituent in the α position of the radical center.^{52,53} There are two general cases:

- (i) *sp-hybridized radicals* that are radicals bearing π -type substituents. This substituent likely imposes a linear geometry in order to achieve maximum orbital overlap to stabilize the unpaired electron through resonance delocalization (π -substituted vinyl radical).
- (ii) sp^2 -hybridized radicals which bear σ -type substituents and possess a bent geometry with two diastereomeric structures rapidly interconverting (σ -substituted vinyl radical).

Focusing back into hydrogermylation reactions, in the presence of a linear radical (**17-linear**), the subsequent H-atom transfer process takes place from the less hindered side opposite to the bulky R'₃Ge group, yielding the *anti* addition product (*Z*-**18**) (Scheme I-11, bottom-left).

In the second case, the initially formed σ -bent *Z*-vinyl radical undergoes fast inversion yielding *anti/syn* diastereomers. One could expect that the rapidly equilibrating *E* form of the vinyl radical intermediate (*E*-**17-bent**) could give access to the *syn* addition product. However, due to steric hindrance owing to the presence of the bulky germyl group *syn* to the radical center, H-atom transfer to the *E*-vinyl radical is prevented. Therefore, *Z*-**17-bent** reacts by H-atom transfer with the hydrogermane to deliver the *anti* addition product (*Z*-**18**) as well (Scheme I-11, bottom-right).

In most cases, the presence of an added radical initiator is needed in order to initiate the radical chain. In particular, the reaction of alkynes with hydrogermanes in the presence of a

suitable radical initiation system has been known since the seminal work by Oshima and coworkers in 1987.⁵⁴ In this series of initial studies,^{54–56} Et₃B (in the presence of O₂) proved an efficient free radical initiator for the addition of Ph₃GeH or (2-furyl)₃GeH to terminal acetylenes at –78 °C (**Scheme I-12**, A-1, blue). This reaction easily occurred with terminal acetylenes but not with internal ones, as demonstrated by the non-competing addition to the internal C-C triple bond when tetradeca-1,8-diyne was employed as substrate. *Trans* selectivity was observed.

Importantly, however, when the reaction was performed at 60 °C, *syn* addition products were obtained (Scheme I-12, A-1, magenta). In this case, the kinetically controlled products (*Z*-**18**) isomerized into the *E*-vinylgermanes (*E*-**18**) under thermodynamic conditions. This isomerization reaction was explained by the authors as an addition-elimination sequence of the triorganogermyl radical (Scheme I-12, B).^{54,55}

The conditions developed by Oshima were applied later to the hydrogermylation of 5ethynyluracil nucleosides with Ph₃GeH (Scheme I-12, A-2).⁵⁷ The reaction occurred with excellent β regio- and Z stereoselectivity.



Conditions: 60 °C, in the presence of R'₃GeH and Et₃B

R'₃Ge

F-18

SCHEME I-12. Et₃B-induced radical hydrogermylation of terminal alkynes (A) and isomerization (B).

AIBN also proved an excellent initiator for the radical hydrogermylation of terminal acetylenes (**Scheme I-13**).⁵⁸ The reactions were highly regioselective, but stereoselectivity

R'₃Ge

Z-18

control was the main drawback and 1-germyl-1-alkenes were obtained as stereoisomeric mixtures in most cases.



SCHEME I-13. AIBN-mediated radical hydrogermylation of terminal alkynes.

Another radical initiator that has been successfully used for the efficient generation of germanium-centered radicals under oxidative conditions is ammonium persulfate. Notably, Blanchard developed the radical hydrogermylation of CF₃-alkynes as a stereocomplementary route to *Z*-CF₃-vinylgermanes (**Scheme I-14**).^{31,32} This inexpensive radical initiator mediated the hydrogermylation of both alkyl and aryl substituted trifluoromethylated alkynes using triphenylgermane, in aqueous acetonitrile (for alkyl substituted CF₃-alkynes) or DMF (for aryl substituted CF₃-alkynes).



 $\label{eq:scheme_scheme_scheme} Scheme I-14. Radical hydrogermylation of CF_3-alkynes.$

Radical hydrogermylation of alkynes facilitated by manganese catalysis was also developed (**Scheme I-15**). Oshima reported the radical addition of triphenylgermane to acetylenes in the presence of catalytic amounts of lithium tributylmanganate (II).⁵¹ Single-electron transfer (SET) from Li[Mn(nBu)₃] to triphenylgermane was considered to generate the triphenylgermyl radical in order to initiate the radical chain. To the best of our knowledge, this is the only case where a radical hydrogermylation has been done in an electronically unbiased nonterminal alkyne (6-

dodecyne). However, since the chosen substrate was symmetrical, this example did not provide any insight concerning regioselectivity issues with internal alkynes.

More recently, a visible-light-induced manganese-mediated activation of the Ge–H bond was also reported (Scheme I-15).⁵⁹ This protocol operates in terminal alkynes in the presence of nBu_3GeH with high regio- and stereoselectivity. Visible-light-induced Mn–Mn bond homolysis generates •Mn(CO)₅, which abstracts a hydrogen from nBu_3GeH to produce a germyl radical (that initiates the radical chain) along with HMn(CO)₅.



SCHEME I-15. Manganese-mediated radical hydrogermylation of alkynes.

Hydrogermylation of alkynes has also been achieved under thermal activation, leading to *Z*-vinylgermanes as major products.^{18,26,58,60} The desired alkenylgermanes are easily obtained either from terminal acetylenes^{26,58} or alkynylstannanes¹⁸ and triphenylgermane, or from phenylacetylene and tris(pentafluoroethyl)germane.⁶⁰ A radical mechanism has been proposed to explain the selective formation of *Z*-vinylgermanes under thermal conditions, based on the fact that the reaction has been inhibited in the presence of 1% of hydroquinone.²⁶ Other examples concerning microwave- or ultrasound-activated hydrogermylation have been also reported.⁵⁸ Despite no discussion about the mechanism of these physically-activated hydrogermylation reactions has been provided, the obtention of the *anti* addition product could suggest a radical pathway initiated by thermal-induced homolysis of the Ge–H bond of the hydrogermane.

Finally, *trans*-selective radical hydrogermylation of terminal acetylenes involving (Me₃Si)₃GeH proceeded smoothly at rt, even in the absence of deliberately added radical initiators.⁶¹ The authors proposed that "adventurous radicals" (perhaps generated by sunlight or traces of molecular oxygen) in the reaction mixture were enough to initiate the radical chain which was characterized for being very long. This fact is not surprising taking into account the

high rate constant for the H-atom abstraction of (Me₃Si)₃GeH, which makes it prone to react more efficiently than its trialkyl- or triaryl-substituted counterparts.

In summary, radical hydrogermylation has largely proven to be an efficient method for transselective addition of hydrogermanes across alkynes. However, the approach has been scantily applied with internal alkynes, owing likely to unfavorable steric factors.

 $\boldsymbol{\boldsymbol{\diamond}} \ \boldsymbol{\boldsymbol{\diamond}} \ \boldsymbol{\boldsymbol{\diamond}}$

Generally speaking, *hydrogermylation of alkynes* constitutes the most exploited route to access vinylgermanes. The main limitation of this approach is, however, the fact that it cannot provide access to derivatives with two substituents in the β position to the germyl group. To overcome this limitation, other approaches have been developed.

I-1.1.3. Germanium-element bond additions to alkynes

A first family of transformations suitable for this purpose is transition metal-catalyzed germanium–element additions across alkynes.⁶² This section will overview this field, organized by interelement bonds activated following the order: germanium-tin, germanium-germanium, germanium-boron, and germanium-carbon.

Germanium-Tin (Ge-Sn)

The palladium-catalyzed germylstannation of alkynes is known to provide access to vicinal germyl(stannyl)ethenes.^{63–66} These bimetallic species are effective precursors to stereodefined vinylgermanes after subsequent functionalization of the C(sp²)–Sn bond.

In 1987, Piers and co-workers reported that treatment of internal α,β -acetylenic esters with Me₃Ge–Sn(*n*Bu)₃ in the presence of a Pd(0) catalyst afforded a mixture of *Z* and *E* vicinal germyl(stannyl)ethenes (**Scheme I-16**, A).⁶³ It was suggested by the authors that the somewhat unexpected *E* configuration of the major product (β,E -**19**) could be explained by the thermal instability of the initially formed *Z* stereoisomer that isomerized upon warming. In an attempt to extend this approach to alkynes other than internal α,β -acetylenic esters, Mitchell reported the use of the same catalytic system [Pd(PPh₃)₄] for terminal alkynes (Scheme I-16, B).⁶⁴ In contrast to Piers' observations, here the addition only delivered *Z*-germyl(stannyl)ethenes (*Z*-**20**), in which the germyl group was bonded to the terminal sp² carbon. However, the product yields were lower than 50%, and in some of the few examples reported, as low as 7%. Evidently, this catalytic system was not efficient enough upon switching from acetylenic esters to the less reactive terminal alkynes.



A. Pd(PPh₃)₄-catalyzed addition of Sn–Ge bond across internal α,β -acetylenic esters (Piers, 1987)

B. Pd(PPh₃)₄-catalyzed addition of Sn–Ge bond across terminal alkynes (Mitchell, 1990)



C. Pd(dba)₂-P(OCH₂)₃CEt catalyzed addition of Sn–Ge bond across terminal alkynes (Nakano, 2000, 2001)



SCHEME I-16. General approaches to the palladium-catalyzed germylstannation of alkynes.

Seeking for a competent catalytic system to conduct this transformation, Nakano and coworkers carried out more in-depth studies with $Et_3Ge-Sn(nBu)_3$ as reagent (Scheme I-16, C).^{65,66} Under almost identical conditions to those developed by Mitchell, the reaction with phenylacetylene led to the desired product in only 5% yield, suggesting that the reactivity of $Et_3Ge-Sn(nBu)_3$ is lower than that of the Me₃Ge-Sn(nBu)₃. Nonetheless, by using Pd(dba)₂-PPh₃ as catalytic system in THF, promising results were obtained with an improved 32% yield, which was further improved by using P(OCH₂)₃CEt as ligand for the catalyst (91% yield). Under these conditions, a variety of *Z*-germyl(stannyl)ethenes (*Z*-**21**) were obtained with excellent regio- and stereoselectivities. Both electron-donating or electron-withdrawing substituted arylacetylenes, as well as heteroaryl-substituted alkynes and one alkynol were suitable substrates. However, limitations of the system were met when trying to perform the reaction with internal alkynes such as 2-butyn-1,4-diol or silyl-substituted phenylacetylenes, as well as when extending the approach to other alkynols such as 2-propyn-1-ol and 5-hexyn-1-ol. Neither of these substrates underwent germylstannation.

Further attention was then devoted to the transformation of these stereodefined germyl(stannyl)ethenes into the corresponding vinylgermanes through functionalization of the C(sp²)–Sn bond. In this regard, Piers reported the reaction of *E*-germyl(stannyl)ethenes with *n*BuLi followed by the alkylation or allylation of the vinyllithium intermediate, giving access to 4 examples of vinylgermanes with an ester moiety in the β position to the germyl group. This reaction proceeded with complete retention of configuration (**Scheme I-17**).⁶³



SCHEME I-17. Synthesis of vinylgermanes from *E*-germyl(stannyl)ethenes with *n*BuLi followed by alkylation/allylation.

On their side, Nakano and co-workers devoted further efforts to synthesize novel vinylgermanes bearing an allyl or an allenyl group starting from the corresponding *Z*-germyl(stannyl)ethenes through Stille-type cross-coupling reactions (**Scheme I-18**).^{65,67} In all cases, the C(sp²)–Sn bond functionalization occurred with excellent preservation of the double bond geometry. Firstly, the cross-coupling of vinylstannanes with an array of allyl halides was performed with a combination of Pd(dba)₂-CuI (Scheme I-18, path A). The reaction was equally efficient starting from *Z*-germyl(stannyl)ethenes bearing and aryl, 2-thienyl, or 1-hydroxyalkyl groups. In a similar fashion, crotyl halides also reacted under similar reaction conditions

producing the cross-coupled products with/without allylic transposition in the halide ($S_N 2$ and $S_N 2'$ type reactions). Remarkably, the allylation reaction also occurred in the absence of Pd(dba)₂. In this case, CuI-mediated reaction in DMSO/THF of *Z*-germyl(stannyl)ethenes with allyl halides took place at rt in high yields (Scheme I-18, path B). Finally, synthesis of vinylgermanes bearing an allenyl group was subsequently investigated by using propargyl bromide in the presence of a Pd(dba)₂-CuI catalyst (Scheme I-18, path C).



SCHEME I-18. Synthesis of allyl and allenyl vinylgermanes from *Z*-germyl(stannyl)ethenes.

Extensive access to *E*-vinylgermanes from *E*-germyl(stannyl)ethenes *via* Stille cross-coupling reaction was later developed by Duchêne. In this case, the starting *E*-germyl(stannyl)ethenes were prepared by either hydrogermylation of alkynylstannanes or hydrostannylation of alkynylgermanes under thermal activation. The scope was more thoroughly explored and the reaction gave place to a large variety of aryl or heteroaryl vinylgermanes, germyldienoic acids, and germyl α , β -enones.¹⁸

However, as a whole, the access to stereodefined vinylgermanes from alkynes through germylstannation chemistry requires (i) a two-step synthesis, (ii) the use of toxic tin compounds as well as (iii) the preparation of the corresponding [Ge]-[Sn] reagent (**Scheme I-19**).



SCHEME I-19. General procedure for the synthesis of vinylgermanes from alkynes through germylstannation chemistry (highlighted in red the drawbacks of the methodology).

Germanium-Germanium (Ge–Ge)

The addition of Ge–Ge bonds across C-C triple bonds (bis-germylation of alkynes) has been briefly investigated (Scheme I-20). Apropos of this approach, Tanaka reported the double germylation of acetylenes with ClMe₂Ge–GeMe₂Cl in the presence of Pd-catalysts.⁶⁸ Even if in the presence of phenylacetylene the reaction occurred with the expected *cis* selectivity, by switching to ethylene as substrate the major product was the *E* isomer. Since the *E* selectivity did not seem to be the intrinsic nature of the reaction, the authors suggested a Z-to-E isomerization under the reaction conditions, confirmed by diagnostic experiments. However, this reaction did not proceed with Me₃Ge–GeMe₃ as digermylating agent. Afterwards, Mochida and Yamamoto reported the digermylation of alkynes using diverse digermanes in the presence of platinum complexes as catalyst.⁶⁹ Reaction of phenylacetylene or (trimethylsilyl)acetylene with digermane Me₃Ge–GeMe₃ afforded the corresponding Z-1,2-bis(germyl)ethenes in moderate yields while other terminal alkynes, such as 1-hexyne or methyl propiolate, reacted with low yields. On the other side, internal alkynes proved unreactive under similar reaction conditions, and other digermanes, like ClMe₂Ge–GeMe₂Cl or Me₂PhGe–GePhMe₂, gave a complex mixture of germylation products or showed no reactivity at all. Later on, Mochida overcame this last limitation by switching to Pdcatalyzed insertion of ClR₂Ge–GeR₂Cl into phenylacetylene.⁷⁰ In general, the narrow scope of this approach, along with the impossibility of orthogonal functionalization of the two newly formed bonds, strongly limit the potentiality of these bisgermylvinyl compounds.



SCHEME I-20. Bis-germylation of terminal alkynes.

Germanium-Boron (Ge–B)

An isolated example concerning the germylboration of 1-hexyne was reported by Ito and coworkers while investigating the silaborative dimerization of alkynes catalyzed by nickel complexes.⁷¹ The analogous germylboration reaction occurred in the presence of Pt, Pd and Ni complexes to yield products **22** and **23** (Scheme I-21), in a ratio highly dependent on the metal catalyst used. In this context, Pt complex $[Pt(CH_2=CH_2)(PPh_3)_2]$ exclusively provided compound **22** in 87% yield with high E selectivity (E/Z = 91:9), whereas Pd complex [Pd(acac)₂/t-OcNC] gave a 1:1 mixture of **22** and **23**. The scenario diametrically changed when switching to Ni complex $[Ni(acac)_2/DIBAH]$ which promoted the germaborative dimerization of 1-hexyne selectively (23). Formation of these two products can be understood by taking a closer look at the mechanism of the reaction, which resembles the one already discussed for the Pd(0)-catalyzed hydrogermylation of alkynes with formation of either *E*-vinylgermanes or dienylgermanes (see Scheme I-4). After oxidative addition of the Ge–B bond onto the M(0) complex, intermediate 24 undergoes *cis*-selective borylmetalation into the alkyne with high regioselectivity. Subsequently, intermediate 25 can undergo either direct reductive elimination giving 22 along with the regeneration of the M(0) catalyst, or further insertion of 1-hexyne into the germyl-metal bond followed by reductive elimination from 26 leading to 23. The final product selectivities can be closely linked to the ease of complex 25 to undergo further insertion of a second alkyne molecule, which depends to a large extent on the nature of the germyl-metal bond of intermediate 25. Although this approach is highly appealing, taking into account the manifold of possibilities for the subsequent functionalization of **22** type-compounds, no further efforts have been devoted in this direction. Hence, the synthetic potential of this methodology (concerning substrate scope, functional group tolerance, *inter alia*) still remains unexplored.



SCHEME I-21. Transition metal-catalyzed germylboration of 1-hexyne (M = Pt, Pd, or Ni).

Germanium-Carbon (Ge–C)

A final example that remains rather specific is the introduction of Ge and CN groups through a germylcyanation of alkynes (carbogermylation). Palladium-catalyzed addition of Me₃GeCN to terminal alkynes occurred with high regio- and stereoselectivity, in which the germyl group was bonded to the terminal sp² carbon.⁷² The *syn* addition reaction gave access to several β -cyano vinylgermanes (*Z*-**27**) substituted by aryl or alkyl groups, tolerating functional groups such as methoxy, fluoro, chloro, cyano, etc. (**Scheme I-22**). The reaction did not occur when internal alkynes were used as substrates (4-octyne and diphenylacetylene).



SCHEME I-22. Germylcyanation of terminal alkynes.

*** * ***

In general terms, the *addition of germanium–element bonds* across the C-C triple bond of alkynes is rather restricted to terminal acetylenes, and hence it is not possible to obtain *gem*-substituted vinylgermanes, which strongly limits the applicability of the developed methodologies. Even though these reactions offer access to vinylgermanes with two substituents in the β position of the germyl group (overcoming the main limitation of hydrogermylation reactions, see section I-1.1.2), the access to tetrasubstituted vinylgermanes is totally constrained to internal propiolates, with scant examples in the literature, and the need of toxic tin reagents.

From the synthetic point of view, elementogermylation chemistry has not provided an efficient access to polysubstituted vinylgermanes up to now. In theory, the ideal process to achieve such a goal would rely on the germylmetalation of alkynes, where the simultaneous formation of a C(sp²)–Ge bond and a C(sp²)–metal bond that may be functionalized *in situ*, could provide the desired straightforward pathway to stereodefined vinylgermanes in a one-pot procedure.

I-1.1.4. Germylcupration of alkynes

Looking closer to this approach, we quickly grasped that examples of germylmetalation of alkynes are extremely scarce in the literature, in sharp contrast to silylmetalation and stannylmetalation chemistry.^{62,73,74}

In 1984, Oshima reported the germylcupration of terminal acetylenes with (tri*phenyl*germyl)– or (tri*ethyl*germyl)copper(I) reagents (**Table I-5**).⁷⁵ Excellent *cis* stereoselectivity was observed in all cases. However, the regioselectivity of the reaction either with (Ph₃Ge)₂Cu(X)Li (Table I-5, entries 1-8) or (Et₃Ge)₂Cu(X)Li (Table I-5, entries 9-12) was

highly dependent on the structure of the starting alkyne as well as the nature of the copper salt. As proposed by the authors, alkyl-substituted alkynes afforded as major product the α isomer (Table I-5, entries 1, 2, 9, 10), whereas substrates bearing aryl- or alkenyl-groups yielded the β isomer (Table I-5, entries 7, 8, 11, 12). Nevertheless, the very limited substrate scope of this protocol along with the variety of factors that can be influencing the regioselectivity (e. g. electronic effects of the substituent on the acetylene, the size of the germyl group, the nature of the additive, etc.) complicates the possibility of a generalization (as can be seen when comparing entries 5, 6 and 10).





Entry	CuX	Yield (28)	α/β	R	Entry	CuX	Yield (29)	α/β
1	CuCN	71% ^a	80:20	<i>n</i> C ₁₀ H ₂₁	9	CuBr∙SMe	2 81%	70:30
2	CuCN	$99\%^b$	70:30					
3	CuI	78% ^a	40:60					
4	CuCN, CuI or CuBr•SMe2	r 0% ^c	-					
5	CuCN	46% ^a	5:95	PhCH ₂ OCH ₂ CH ₂	10	CuBr∙SMe	2 91%	65:35
6	CuBr•SMe ₂	$82\%^b$	5:95					
7	CuCN	85% ^a	<5:>95	Ph	11	CuBr∙SMe	2 91%	15:85
8	CuBr•SMe ₂	98% ^a	1:99	CH ₂ =C(CH ₃)	12	CuBr∙SMe	2 95%	13:87

^{*a*}*n*BuOH. ^{*b*}*n*BuCHO. ^{*c*}No addition of *n*BuOH or *n*BuCHO, 1-dodecyne was recovered in >90%.

Regarding the copper reagent, superior regiocontrol was achieved with the (triphenylgermyl)cuprates than with the triethylgermyl analogues. However, when performing the germylcupration of alkynes with the (triphenylgermyl)copper(I) reagents, an additional problem was observed: in the absence of a proton donor source the reaction did not take place regardless of the nature of the copper salt (Table I-5, entry 4). In fact, unaltered starting material was recovered in more than 90% yield. Therefore, the coexistence of a proton donor such as *n*BuOH (Table I-5, entries 1, 3, 5, 7, 8), *n*BuCHO (Table I-5, entries 2, 6), or even water was essential for the formation of the corresponding vinylgermane, thus implying that the C(sp²)–Cu bond

formed was not available for subsequent elaboration. By contrast, germylcupration of alkynes with (trielthylgermyl)copper(I) reagent proceeded to completion without a proton donor, and therefore, the alkenylcopper intermediate (**30**) could be subsequently trapped with an electrophile. Conversely, due to the regiocontrol issues observed with (triethylgermyl)cuprates, only two examples of functionalization of the $C(sp^2)$ –Cu bond were reported and they were bounded to the phenylacetylene as starting material (**Scheme I-23**).



SCHEME I-23. Germylcupration of phenylacetylene followed by electrophilic trapping.

Later on, Piers briefly examined the use of novel (tri*methyl*germyl)copper(I) reagents for the addition to α,β -acetylenic esters (**Table I-6**).⁷⁶

	$Me \xrightarrow{\beta} CO_2Et \qquad Me_3GeCu \cdot W$ $THF, -78 °C$	$\begin{array}{c} H \\ Me_{3}Ge \\ Me \\ E-31 \end{array} + \begin{array}{c} Me_{3}Ge \\ He_{3}Ge \\ He_$	CO ₂ Et H Me 31
Entry	(Me₃Ge)Cu·W	Yield (31)	d.r. 31 (<i>E/Z</i>)
1	(Me3Ge)Cu• SMe 2	81%	>99:<1
2	(Me₃Ge)Cu• (CN)Li	90%	>99:<1
3	(Me3Ge)Cu• (GeMe3)Li	$90\%^a$	1.7:1
4	(Me₃Ge)Cu• (CN)(Me)Li 2	17% (E), 69% (Z)	1:3.9

 TABLE I-6. Germylcupration of ethyl but-2-ynoate.

^{*a*}Isolated as a mixture of E/Z isomers.

By contrast to Oshima's germylcupration of terminal acetylenes, in this case only one regioisomeric product was observed (β isomer), underscoring the determining role of the substituent on the acetylene group for the regioselectivity. Conversely, the stereoselectivity of the reaction was markedly affected by the nature of the copper ligands. A possible rationalization concerning the formation of these two isomers was proposed, as depicted in **Scheme I-24**. In this scenario, the *syn* addition of a (trimethylgermyl)copper(I) reagent to the triple bond of the alkyne

produces a vinylcopper intermediate **32**, that after protonation gives access to *E*-**31**. Alternatively, the authors proposed that isomerization of the vinylcopper intermediate to the allenoate species **33** followed by protonation could provide access to either isomer (*E* or *Z*), although the formation of the *Z* isomer should be favored due to the bulkiness of the Me₃Ge moiety.



SCHEME I-24. Rationalization of the stereoselectivity outcome of the germylcupration of ethyl but-2ynoate.

Surprisingly, no discussion about the possible reversibility of the reaction was addressed, despite the previous problems faced by Oshima, remaining unclear the necessity or not of a proton donor for accomplishing the reaction. Indeed, the formation of the $C(sp^2)$ –Cu bond was not confirmed by any experiment; no attempts to further functionalized the $C(sp^2)$ –Cu bond were done, and therefore the access to vinylgermanes with two substituents β to the germyl group was not demonstrated to be reachable by this methodology.

In conclusion, the reversibility issues encountered during the germylcupration of alkynes turned this approach into a blind alley to access polysubstituted vinylgermanes.

I-1.2. FUNCTIONALIZATION OF VINYLGERMANES: USE IN SYNTHESIS

Stereoselective transformation of vinylgermanes into stereodefined alkenes is a crucial stepping stone for the valorization of these synthons in organic chemistry. Several methods have been developed to do so, particularly focused on halodegermylation reactions to access vinyl halides, along with cross-coupling reactions to directly yield configurationally defined alkenes.

I-1.2.1. Halodegermylation reactions

Halodegermylation reactions have been mostly reported from trialkylvinylgermane derivatives (Scheme I-25, right), and several examples regarding their stereospecific transformation into vinyl halides were disclosed.^{13,15,43,57,77-82} Oshima firstly recognized that triethylvinylgermanes were transformed into the corresponding vinyl iodides or vinyl bromides upon treatment with iodine or N-bromosuccinimide (NBS), respectively, with retention of the double bond geometry.¹⁵ By contrast, treatment with bromine led to inversion of the configuration in a highly stereospecific reaction. One year later, Oshima and co-workers extended the scope of this transformation to cyclic vinylgermanes. Upon treatment with iodine, the corresponding iodides were obtained without difficulties.⁷⁷ It is worth mentioning that, in the course of these investigations, they pointed out that the substitution with halogens on a sp² carbon proceeded more easily for the germyl group than for the corresponding silyl group, together with improved stereochemical outcome and higher yields.¹⁵ Indeed, in the case of cyclic derivatives, vinylsilanes were shown unreactive under the same reaction conditions.⁷⁷ In 2005, Gevorgyan reported that *N*-iodosuccinimide (NIS) could be used as well, along with the previously reported NBS. Importantly, the reactions proceeded with perfect retention of the double bond geometry.⁴³ In 2010, Burke synthesized iodopolyenyl *N*-methyliminodiacetic acid (MIDA) boronates by stereospecific iododegermylations from the corresponding polyenylgermanium intermediates, in all possible stereoisomeric forms.82



SCHEME I-25. General approaches for the halodegermylation of vinylgermanes.

In a similar fashion, trimethylvinylgermanes have also proved suitable substrates for this transformation, even in more complex structural environments, as showcased mostly by Piers^{78–81} and Wnuk.⁵⁷ In addition, tributylvinyl-containing nucleoside analogues have been also

converted, with clean retention of the double bond geometry, into their valuable halovinyl counterparts.¹³

Interestingly, every single attempt to halodegermylate triphenylvinylgermanes has met with failure up to now (Scheme I-25, left).^{13,32} Extensive screening of reaction conditions by Blanchard showed that, even in the presence of iodine (in solution or neat), harsh reaction conditions, or ICl, the reaction was not accomplished in the case of CF₃-vinylgermanes.³² Obviously, the presence of a CF₃ group in the alkene could decisively contribute to this unfavorable outcome, since electron-poor double bonds are less reactive toward electrophiles. However, Wnuk also observed this lack of reactivity when trying to halodegermylate triphenylvinyl-containing nucleoside analogues: neither NBS nor NIS were suitable for this transformation.¹³

What is definitely a key point to demonstrate the synthetic potential of vinylgermanes as useful synthons in the construction of complex molecules is their application in total synthesis. In this context, Piers elegantly showed that stereoretentive and high-yielding iododegermylation of vinylgermanes is a crucial step in their proposed strategy for the total synthesis of diterpenoids,^{78,80,81} while Burke illustrated the potential of iododegermylation of polyenylgermanium species combined with iterative cross-coupling to build structurally and stereochemically complex polyene systems⁸² (**Scheme I-26**).



SCHEME I-26. Iododegermylation of vinylgermanes as key step in the total synthesis of natural products.

I-1.2.2. Palladium-catalyzed cross-coupling reactions of vinylgermanes

Cross-coupling reactions, which traditionally involve the metal-catalyzed coupling of an organic electrophile with an organometallic nucleophile, are nowadays crucial tools for the construction of carbon–carbon bonds.⁸³ Classical cross-coupling reactions are usually named on the basis of the nucleophile used. Hence, the reactions involving an organostannane as nucleophile are known as the Stille (or Stille–Migita–Kosugi) reaction,^{84–86} while reactions utilizing organosilanes as nucleophiles are called the Hiyama reaction⁸⁷ (or Hiyama-Denmark, depending on the nature of the organosilane).⁸⁸ However, the major drawback of the Stille reaction is the high toxicity of the tin starting materials and by-products,⁸⁹ while in the case of the Hiyama coupling the low reactivity of organosilanes requires the addition of an activator (typically fluoride ions), rendering this approach incompatible with some functional groups. Meanwhile, the modified Hiyama-Denmark reaction overcame this limitation but is somewhat restricted to organosilanols.⁹⁰

Organogermanes have received much less attention than organostannanes and organosilanes as possible carbanion surrogates in cross-coupling reactions, in spite of the privileged position of germanium between silicon and tin in the periodic table. The development of vinylgermanes as transmetalation reagents in palladium-catalyzed cross-coupling reactions has been probably hampered by the lower reactivity of tetracoordinated germanium species in comparison with tin analogues. Note however that, in some cases, this lower reactivity of vinylgermanes compared to the corresponding vinylstannanes has been advantageously employed in organic synthesis. For example, the construction of complex polyene scaffolds was initially based on the Sn-selective cross-coupling of Sn/Ge bis-metalated olefins.⁸²

Yet, successful cross-coupling reactions using vinylgermanes as nucleophiles have been reported (**Scheme I-27**). The first example of a Pd-catalyzed coupling comprising organogermanes was the reaction of trimethylvinylgermanes with aryldiazonium tetrafluoroborates to yield aryldegermylated products (Scheme I-27, A).⁹¹ However, the reaction was not highly regioselective. Faller later reported that alkenyl oxagermatranes underwent coupling with aryl iodides.⁹¹ The reaction was promoted by fluoride (Scheme I-27, B). Afterwards, Oshima found that vinyl-tri(2-furyl)germanes were also suitable under fluoride-activated reaction conditions (Scheme I-27, C): in a similar fashion to aryl-tri(2-furyl)germanes, the three furyl groups on germanium were likely cleaved by fluoride to form $(HO)_3Ge$ -derivatives or germanoxanes.²⁹ Nucleophilic hypervalent organogermanium species would have then undergone transmetalation from germanium to palladium. Later on, Spivey described the Pd(0)-catalyzed cross-coupling of photoactivated vinylgermanes with aryl bromides (Scheme I-27, D).³⁴ The germanes employed bore a C₈F₁₇-fluorous tag to facilitate the purification process. In addition,

bis(naphtalen-2-ylmethyl) substituents allowed photooxidative activation⁹² and thereby their smooth conversion into the corresponding alkenyldifluorogermanes that were immediately engaged in Pd(0)-catalyzed cross-coupling.³⁴ The reaction was highly stereoretentive. Finally, application of this reaction to the total synthesis of the C19 methyl ether of Aspercyclide A, a natural product with anti-asthmatic activity, was developed in parallel.³⁵ However, the need for fluoride-activation is certainly a drawback of these approaches.



SCHEME I-27. Palladium-catalyzed cross-coupling reactions of vinylgermanes.

To overcome this limitation, fluoride-free cross-coupling of intramolecularly activated vinylgermanes was also investigated. Shindo demonstrated that intramolecular donation from the carbonyl oxygen of a carboxylic acid to the germanium atom was a potent activation approach for the Pd-catalyzed cross-coupling of vinylgermanes under fluoride-free conditions (Scheme I-27, E).⁹³ The coupling reaction was found indeed to be more efficient with vinylgermanes than with the corresponding vinylsilanes. Importantly, this represents the first report of the use of vinylgermanes to access sterically congested tetrasubstituted alkenes. This remarkable feature was further exploited in the stereoselective synthesis of tamoxifen, an anticancer drug. Furthermore, a similar activation approach was described by Maleczka.³⁰ Tributylvinylgermanes having a proximal hydroxyl group cross-coupled with aryl halides under Stille and Heck conditions (Scheme I-27, F). In general, the reaction outcome was better under Heck conditions for the explored scope. However, regio- and stereoselectivity issues were commonly observed; after diagnostic experiments, an admixture of Stille and Heck mechanistic pathways was proposed.

Base induced activation conditions were further explored for the functionalization of vinylgermanes. Wnuk successfully showcased that vinyl tris(trimethylsilyl)germanes undergo Pd-catalyzed cross-coupling with aryl halides, alkenyl bromides, and aryl triflates in either aqueous (Method 1: $H_2O_2/NaOH/H_2O$) or anhydrous (Method 2: tBuOOH/KH) oxidative conditions in the presence of Pd(PPh₃)₄ (Scheme I-27, G).^{10,11} Additionally, (α -fluoro)vinyl tris(trimethylsilyl)germanes were also used as donors in Pd-catalyzed cross-coupling with aryl halides and alkenyl bromides under aqueous oxidative conditions to give stereoselectively access to fluoroalkenes and fluorodienes.¹² Apparently, hydrogen peroxide cleaved the Ge–Si bond to generate active germanol or germanoxane species, which subsequently underwent coupling.¹⁰⁻¹² reported the challenging functionalization of CF₃-substituted Finally, Blanchard triphenylvinylgermanes derivatives (that had proven unreactive for direct functionalization of the $C(sp^2)$ -Ge bond).^{31,32} The approach was to cleverly adjust the electron deficiency of the germanium atom by transformation into the vinyl trichlorogermanes or the bench stable sesquioxide derivatives. Both were later subjected to Pd-catalyzed cross-coupling reactions under the conditions reported by Fugami and Kosugi94,95 providing access to the stereoselective synthesis of Z- and E-trifluoromethylalkenes (Scheme I-27, H).^{31,32}

The regio- and stereoselectivity problems faced in some of the described methods deserve further clarification. In general, Pd(0)-catalyzed cross-coupling of vinylmetals with aryl halides are highly selective and provide *ipso*-products with retention of the regio- and stereochemistry of the starting vinylmetal employed. This is usually ascribed to a Stille-type pathway involving fast transmetalation to palladium, followed by reductive elimination (**Scheme I-28**, Stille pathway).⁸⁹

However, loss of stereochemical information and/or formation of the *cine*-products can also occur as result of a Heck-type mechanism⁹⁶ where a competition between *ipso* and *cine*-carbopalladation accounts for the selectivity outcome (Scheme I-28, Heck pathway), *cine*-products being formed *via* either a Kikukawa-type Pd–H elimination/readdition reaction^{97,98} (dashed pathway), or a Busacca-type Pd–carbene formation^{99–101} (not shown). Indeed, it is usually accepted that germyl-Stille pathway is governing the outcome of the reaction with vinylgermanes. Though, in some cases, Stille and Heck-type mechanisms can be operative simultaneously, therefore accounting for the regio- and stereoselectivity issues encountered thus far.



SCHEME I-28. Stille and Heck-type mechanisms possibly operative in the palladium-catalyzed crosscoupling reactions of vinylgermanes.

Overall, there are still plenty of stimulating challenges in this field. What becomes evident is the potential of vinylgermanes to act as organometallic nucleophiles in palladium-catalyzed crosscoupling reactions, which confers them an underexplored potentiality to complement the more popular group 14 vinyl nucleophiles.

I-2. A NEW CONCEPT FOR ELEMENTOMETALATION REACTIONS: *trans*-SELECTIVE RADICAL SILYLZINCATION

The stereoselective preparation of highly functionalized alkenes has attracted considerable attention since this structural motif is often present in biologically relevant molecules as well as industrially important compounds. Arguably, one of the most efficient and atom economical routes to synthesize polysubstituted alkenes is the **elementometalation of alkynes** (**Scheme I-29**).^{62,74,102–104} These reactions consist in the addition of element–metal bonds across the carboncarbon triple bond of alkynes to introduce two new functionalities in a single synthetic operation. This creates the opportunity for sequential selective and expeditious construction of molecular diversity on adjacent carbons. Elementometalations usually involve bimetallic reagents of the type R₃Si–MR_n or R₃Sn–MR_n, in which M = B, Al, Zn, Cu, Mg, Si or Sn.⁷⁴ Several reviews^{62,74,102,103} have been devoted to the extensive work developed in this field, mainly involving transition metal-catalyzed or anionic transfer addition processes. Both of these types of reactions usually follow *syn* addition courses and thus provide access to *cis*-elementometalated alkenes.



SCHEME I-29. Elementometalation of alkynes.

Recently, a new area of elementometalation reactions has emerged: the **radical approach**.¹⁰⁵⁻¹⁰⁷ In this context, our group initially developed the *trans*-selective radical silylzincation of terminal ynamides involving (Me₃Si)₃SiH and Et₂Zn (**Scheme I-30**).¹⁰⁵ Importantly, one-pot electrophilic substitution of the vinylzinc intermediate by Cu(I)-mediated C–C bond formation occurred with an array of carbon-centered electrophiles including allyl and propargyl bromides, methyl iodide, as well as aromatic, vinylic, or aliphatic acyl chlorides. This methodology provided modular access to 1,2-disubstituted or 1,2,2-trisubstituted silylenamides in an unprecedented *trans*-selective manner.



SCHEME I-30. *Trans*-selective radical silylzincation of terminal ynamides with (Me₃Si)₃SiH and Et₂Zn (*Si* = Si(SiMe₃)₃).

The radical-chain process proposed on the basis of diagnostic control experiments also accounts nicely for this unusual stereoselectivity (**Scheme I-31**).



SCHEME I-31. Mechanism for the *trans*-selective radical silylzincation of terminal ynamides with (Me₃Si)₃SiH and Et₂Zn.

Silicon-centered radical **35**, produced from (Me₃Si)₃SiH and ethyl radical **34**, adds across the C-C triple bond of terminal ynamides **36** to produce regio- and stereoselectively *Z*-configured vinyl radical intermediate **37**. This radical intermediate reacts with Et₂Zn by homolytic

substitution (S_H2) at the Zn atom to provide α -zincated β -silylenamide **38** along with ethyl radical **34** that propagates the radical chain. The homolytic substitution at the Zn atom is the stereodetermining step of this reaction. The presence of a Lewis basic group on the ynamide nitrogen activates the Et₂Zn reagent toward S_H2 by Lewis pair formation and in this way outcompetes the *Z*-to-*E* isomerization of the vinyl radical intermediate **37**. Therefore, *Z*-**38** is formed. It is also worth-mentioning that no competitive hydrosilylation reaction occurs, arising from the possible reaction of vinyl radical **37** with (Me₃Si)₃SiH by H-atom transfer.

Subsequently, our group also developed a stereodivergent approach for the silylzincation of nitrogen-, sulfur-, oxygen-, and phosphorus-substituted terminal alkynes by reaction with $(Me_3Si)_3SiH/Et_2Zn \ (Method \ A), \ [(Me_3Si)_3Si]_2Zn/Et_2Zn \ (Method \ B), or \ (Me_2PhSi)_2Zn \ (Method \ C)$ (Scheme I-32).^{106,107} The three protocols afforded exclusively β isomers but the stereoselectivity was tunable and dependent on the system employed: *trans*-selective with $(Me_3Si)_3SiH/Et_2Zn \ or \ [(Me_3Si)_3Si]_2Zn/Et_2Zn, and$ *cis* $-selective with <math>(Me_2PhSi)_2Zn$. In a similar fashion to the above-described *trans*-selective silylzincation of terminal ynamides with $(Me_3Si)_3SiH$ and Et_2Zn , the procedures involving $[(Me_3Si)_3Si]_2Zn \ and \ (Me_2PhSi)_2Zn \ can be combined as well, in a one-pot procedure, with subsequent Cu(I)-mediated electrophilic trapping of the vinylzinc intermediates, thus offering modular access to trisubstituted vinylsilanes decorated with heteroatom substituents with either double-bond configuration.$



SCHEME I-32. Stereodivergent silylzincation of terminal α -heteroatom substituted alkynes.

The difference of stereochemical outcome between the developed approaches is the result of mechanistic differences: Methods A and B involve the addition of silicon-centered radicals across the acetylene linkage, whereas Method C engages the polar transfer of a silicon anion proceeding through a conventional 1,2-addition mechanism.

It is worth-mentioning that for α -heteroatom-substituted alkynes other than ynamides, *trans*-selective radical silylzincation was more efficient with the system [(Me₃Si)₃Si]₂Zn/Et₂Zn than with (Me₃Si)₃SiH/Et₂Zn. This could be possibly ascribed to the higher reactivity of

[(Me₃Si)₃Si]₂Zn in comparison with (Me₃Si)₃SiH, along with more efficient radical chains when using [(Me₃Si)₃Si]₂Zn as organosilyl radical source. For this reagent, the regeneration of either ethyl radical **34** or directly silicon-centered radical **35** is achieved during the S_H2 step (**40** \rightarrow **41**) (Scheme I-33).



SCHEME I-33. Mechanism for the *trans*-selective radical silylzincation of terminal α -heteroatom-substituted alkynes with [(Me₃Si)₃Si]₂Zn and Et₂Zn.

On the whole, radical silylzincation opens the doors to a new way of approaching elementometalation reactions. By thoughtful selection of reaction conditions, limitless possibilities can be envisaged for the regio- and stereoselective preparation of elementometalated alkenes.

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PART II. RESULTS AND DISCUSSION

II-1. OPENING CONSIDERATIONS

II-1.1. SCIENTIFIC PROBLEM

Vinylgermanes have the potential for becoming important building blocks in organic synthesis as useful alternative to the more common (toxic) tin analogues as well as to vinylsilanes. Notably, the low toxicity and relative inertness to a wide range of reaction conditions makes them suitable for early installation in a synthetic sequence, while keeping the potential for a later selective transformation offered by the manifold of possibilities of functionalization of the C(sp²)– Ge bond. Yet, the lack of general broad-in-scope synthetic methods to access vinylgermanes hampers their development.

Undeniably, as indicated in **Part I**, the synthesis of vinylgermanes from alkynes with C–*Ge* bond formation is the main and more forthright route to access these reagents (**Figure II-1**).



FIGURE II-1. Reported synthesis of vinylgermanes from alkynes with C–*Ge* bond formation (*Ge* = triorganogermyl).

Hydrogermylation reactions have so far dominated the preparation of (1,1- or 1,2-)disubstituted and 1,1,2-trisubstituted vinylgermanes (see section I-1.1.2 and references therein), with only scattered compounds obtained with the germylcupration chemistry. The synthesis of **1,1-disubstituted** vinylgermanes is extremely restricted in examples (R = Ph^{1,2} or CO₂Et³). By contrast, the diverse methodologies for yielding **1,2-disubstituted** vinylgermanes, taken together, cover a wide scope. Regarding the **1,1,2-trisubstituted** analogues, internal propiolates have proven suitable substrates^{3,4} (here the alkyne linkage bearing an ester moiety strongly limits the structural diversity of the final compounds), whereas internal conventional alkynes have faced regioselectivity concerns.^{4,5} Thus, for the latter, except in a few cases,³ only symmetrical alkynes^{2,6,7} or electronically biased acetylenes^{4,8-10} were involved as substrates.

More generally, the synthesis of 1,2,2-trisubstituted and tetrasubstituted vinylgermanes suffers from several limitations. Concerning **1,2,2-trisubstituted** analogues, the available protocols rely fundamentally on *Ge*–Element bond addition reactions (*Ge*–Sn, *Ge*–Ge, *Ge*–B, *Ge*–CN).^{11–20} Only in the case of introduction of a tin moiety these protocols allow for broad-in-scope functionalization of the 2-position. In such a case however, access to the 1,2,2-trisubstituted vinylgermane target requires two synthetic steps. The limitations of these methodologies have already been discussed (*vide supra*, section I-1.1.3). With regard to the more challenging **tetrasubstituted** vinylgermanes, hardly anything has been described apart from Piers' early report on the germylstannation of internal propiolates.¹¹

Therefore, there is no direct and general solution available for the regio- and stereoselective preparation of 1,2,2-trisubstituted or tetrasubstituted vinylgermanes.

It is also important to underscore the fact that α -heteroatom-substituted alkynes have not been previously considered for any of the above-described methods in order to obtain valuable heteroatom-substituted vinylgermanes, and ultimately, interesting heteroatom-substituted alkenes.²¹

II-1.2. ANTICIPATED PLAN: **R**ADICAL GERMYLZINCATION AS THE PUZZLE MISSING PIECE TO SYNTHESIZE STRUCTURALLY DIVERSE VINYLGERMANES

To overcome this challenging problem, germylmetalation of alkynes appears definitely as a straightforward and conceptually appealing approach. Alkyne germylmetalation, i.e., the 1,2-addition of germanium–metal bonds across the carbon–carbon triple bond of alkynes, establishes in a single synthetic operation a C(sp²)–Ge bond and a C(sp²)–metal bond. The newly formed

reactive bond can then be used as linchpin for subsequent C–C bond formation in a one pot procedure following electrophilic substitution (**Scheme II-1**, General approach).



SCHEME II-1. General context of the present work (*Ge* = triorganogermyl).

In sharp contrast with the related silylmetalation and stannylmetalation chemistries that are prevalent approaches for the preparation of polysubstituted vinylsilanes²² and vinylstannanes,²³⁻

 26 germylmetalation reactions are almost unknown (as mentioned above^{8,27}). Furthermore, the approach has been plagued with reversibility issues, making it problematic for further functionalization of the C(sp²)–metal bond created (Scheme II-1, a).

In recent years, our group has developed a radical approach to the silylzincation of terminal α -heteroatom-substituted alkynes using a combination of (Me₃Si)₃SiH and Et₂Zn (Scheme II-1, b).^{28,29} In view of the feasibility of performing radical reactions with hydrogermanes, as largely demonstrated by the radical hydrogermylation of alkynes (Scheme II-1, c), our idea was to consider a related radical approach as indicated in Scheme II-1 (**this work**).

We reasoned, as shown in **Scheme II-2**, that after initiation (not shown in the scheme), germanium-centered radicals R"₃Ge[•], produced by H-atom transfer between the hydrogermane and ethyl radical **34**, should add readily across the C–C triple bond of alkynes **42** to provide regioselectively vinylic radicals **43** (**42** \rightarrow **43**). Radicals **43** would then react with Et₂Zn by homolytic substitution (S_H2) at the zinc atom (**43** \rightarrow **44**) to afford β -zincated vinylgermanes **44** along with ethyl radical **34** that would propagate the radical chain. Note however that for such a process to be possible, vinyl radical intermediate **43** would have to undergo Zn-atom transfer (**43** \rightarrow **44**) faster than competitive H-atom transfer from R₃GeH (**43** \rightarrow **45**). Otherwise, radical hydrogermylation would be the main reaction outcome and the Zn functionality would be lost. Another source of complications might be competitive carbozincation arising from the direct addition of ethyl radical **34** across the C–C triple bond of alkynes **42**.



SCHEME II-2. Anticipated radical approach to the germylzincation of alkynes.

The feasibility of this radical chain was further scrutinized by estimating the rate constants for each elementary step involved. It is generally admitted that for a radical chain to propagate in dilute solution, the rate for each elementary step has to be higher than $10^2 \text{ M}^{-1} \text{ s}^{-1.30}$

The possibility of generation of germanium-centered radicals from the parent hydrogermane has been largely demonstrated through the radical hydrogermylation reactions of alkynes.^{6,9,10,31-} ³⁶ As we already pointed out (see section I-1.1.2.3), the hydrogen donor abilities of hydrogermanes toward primary alkyl radicals have received noticeable attention.^{37–40} In a similar fashion to Figure I-1 (I-1.1.2.3), we have now summarized the values of the rate constants ($k_{\rm H}$, M⁻¹ s⁻¹) for the reaction of primary alkyl radicals with a variety of hydrogermanes and compared them with the more popularly used group-14 hydrides in radical chemistry, namely, (Me₃Si)₃SiH and Bu₃SnH (**Figure II-2**).^{37–41}



FIGURE II-2. Rate constants for the H-atom abstraction of group-14 hydrides by primary alkyl radicals.

In general, for a given substituent (R), the ease of H-atom abstraction, and thus of generation of group-14 centered radicals, follows the order:³⁸



This order is related to the trend of the BDE (bond dissociation energy) of the element–H bond.⁴²⁻⁴⁴

As we already discussed (*vide supra*, section I-1.1.2.3), for a particular metal hydride, the rate constant for H-abstraction increases (~ 1 order of magnitude) along the substituent series:³⁸

Essentially, as can be rationalized from Figure II-2, similar reactivity should then be expected between germanium hydrides and (Me₃Si)₃SiH, since their rate constants for the H-atom

abstraction are in the same order of magnitude, in the range of $10^{5}-10^{6}$ M⁻¹ s⁻¹ at ca. 25 °C (taking into account correction by variation of the temperature). This speaks in favor of the feasibility of the germylzincation reaction.

Furthermore, considerable empirical evidence is available to support the addition of germanium-centered radicals across triple bonds. However, the rate constant for these additions have not been determined.⁴⁵ It should nevertheless be of the same order of magnitude (though lower) than that for additions of silyl-centered radicals⁴⁶ ($1 \times 10^8 \text{ M}^{-1} \text{ s}^{-1}$ at 27 °C for the addition of the triethylsilyl radical across phenylacetylene).⁴⁵

Moreover, it is also important to emphasize that the rate of the addition of the ethyl radical across alkynes should be lower than $\sim 10^5 \,\text{M}^{-1} \,\text{s}^{-1}$, which is the rate for the addition of alkyl radicals across propiolates⁴⁵ (terminal alkynes with a strong electron-withdrawing substituent): consequently, direct ethyl radical addition leading to carbozincation products should be eluded.

Finally, the rate constant for the H-atom abstraction from Bu_3GeH by vinyl radical (HC•=CMe₂) has been reported to be $3.5 \times 10^7 M^{-1} s^{-1}.^{38,44,47}$ Therefore, for other hydrogermanes it should be in the same range (though higher). While little is known about the rate for the reaction between vinyl radicals and Et₂Zn, the previous work developed in our group on radical silylzincation demonstrates that for α -heteroatom-substituted vinylic radicals, the rate for S_H2 at the zinc atom is suitable for chain propagation and can outcompete H atom transfer from (Me₃Si)₃SiH.²⁸ Given that the rates for radical H-abstraction are in comparable ranges for R₃GeH and for (Me₃Si)₃SiH³⁸ (as we stated above), a similar situation would be expected here.

In conclusion, analysis of the rate coefficients for each elementary step involved in the anticipated radical germylzincation provided support for the feasibility of this approach.

If successful, radical germylzincation would become the puzzle missing piece for the preparation of a large variety of vinylgermanes: from simple disubstituted analogues to more complex and structurally diverse tetrasubstituted ones, which are unreachable by other methods (Scheme II-1, this work, **envisaged products**).

Therefore, the **main objective** of this doctoral thesis is to develop a general radical approach for the germylzincation of alkynes as a straightforward route for the preparation of polysubstituted vinylgermanes.

To do so, terminal and internal ynamides will be considered first taking into account their high and interesting reactivity. Other α -heteroatom-substituted alkynes will be next taken into consideration. Finally, more challenging conventional alkynes will be studied. In all cases, the possibility of functionalization of the C(sp²)–Zn bond will be examined, as a key requirement to

access vinylgermanes with two substituents in the β position to the germyl group, one of our core aims. Further functionalization of the C(sp²)–Ge bond will be investigated as well. To end with, perspectives to generalize the radical elementozincation approach to the silyl- and borylzincation of conventional alkynes will be preliminary examined.

II-2. GERMYLZINCATION OF TERMINAL YNAMIDES

The regio- and stereoselective addition of germanium and zinc across the carbon-carbon triple bond of terminal ynamides is described by reaction with a combination of hydrogermane and Et₂Zn. Deuterium-labeling experiments provided conclusive proof for the formation of vinylzinc intermediates. Diagnostic experiments supporting a radical-chain mechanism are comprehensively discussed. Possible competitive radical hydrogermylation is also investigated.



II-2.1. THE ABC OF YNAMIDES: MODEL SUBSTRATES FOR THE GERMYLZINCATION

Ynamides^{48–51} are nitrogen-substituted alkynes where the nitrogen atom bears an electronwithdrawing group (EWG) (**Scheme II-3**). As a result, the lone pair of the nitrogen is delocalized not only in the carbon-carbon triple bond of the alkyne but also in the electron-withdrawing group, translating into enhanced stability in comparison with ynamine analogues, while still retaining the polarization of the triple bond. As a plus, the electron-withdrawing group can also act as directing group or chiral auxiliary, modulating the versatile manifold of transformations that has starred this structural entity over the past decade.^{48,49,51-53}



SCHEME II-3. General structure of ynamines and ynamides.

The electronic bias imposed by the nitrogen on the acetylenic linkage results in a highly regioselective attack of this heteroatom-substituted alkyne by a variety of functional groups. As already shown in Scheme II-3, the electron-donating ability of the nitrogen onto the triple bond allows a keteniminium resonance structure, thus accounting for the typical α addition of nucleophiles due to the inherent polarized nature of this triple bond (**Scheme II-4**). By contrast, umpolung transformations (i.e. β addition) have been achieved by means of different strategies including metal-carbonyl (sulfonyl) chelation, radical addition, base-mediated addition, and ring strain factor.⁵³



SCHEME II-4. α vs β regioselectivity in nucleophilic additions to ynamides.

The high and interesting reactivity of ynamides was precisely the first feature that caught our attention when selecting them as model substrate for our study. This attribute, along with the known fact that unsymmetrical alkynes bearing a heteroatom (N, O, S) offered the potential for controlling the regioselectivity of elementometalation reactions through mesomeric, inductive, steric, or coordination effects,⁵⁴ influenced our selection of ynamides as starting material. Indeed, carbometalation^{53,55–61} and silylmetalation^{28,62–68} of ynamides have been the core of plethora of studies, evidencing high levels of regio- and stereocontrol. If we also consider that there has not been a single attempt to synthesize heteroatom-substituted vinylgermanes (as already discussed in the *Scientific Problem*), the ultimate decision of beginning our investigation from ynamides seemed justified.

II-2.1.1. Synthesis of substrates

The "ynamide boom" has been possible, to a large extent, due to the recent development of robust methodologies for their preparation.^{48–51} In this context, we prepared TIPS-protected ynamides according to Hsung's methodology⁶⁹ (**Scheme II-5**, left).



^aAlready available in the laboratory.



This general and mild procedure for the alkynylation of nitrogen nucleophiles with bromoalkynes gave us access to TIPS-protected *N*-alkynyl-carbamates **49–52** and *N*-alkynyl-sulfonamide **53** on gram scale with fair-to-excellent yields.

Desilylation of the TIPS-substituted ynamides was subsequently achieved by treatment with tetra-*n*-butylammonium fluoride (TBAF). The nucleophilic attack of the fluorine anion to the silicon atom led to pentacoordinated species that underwent fast cleavage of the C(sp)–Si bond to yield the desired terminal ynamides **54–58** (Scheme II-5, right). Good-to-excellent yields were obtained, and they could be prepared on gram scale and stored for months at room temperature without noticeable degradation.

II-2.2. STUDYING THE COMPETITION: HYDROGERMYLATION OF YNAMIDE 54

In order to check for the possibility that direct hydrogermylation could interfere in our system and lead to the desired β -germylenamides with loss of the metal functionality (see section II-1.2, Scheme II-2), we initially decided to study the reaction between hydrogermanes and ynamides. Furthermore, if achievable, this reaction could be interesting *per se* since there are no reports of hydrogermylation on this substrate class.

II-2.2.1. Preliminary experiments

We began our study with the reaction of model terminal ynamide **54** and Ph₃GeH, a wellestablished radical hydrogermylating reagent that is commercially available and easy-to-handle (**Table II-1**). The first experiment in *n*-hexane, a typical solvent for radical reactions, led to the exclusive formation of β -enamide **59** as single *Z* stereoisomer, with a satisfactory conversion (59%) (Table II-1, entry 1). The excellent *trans* selectivity of the addition was reasonably suggestive of a radical process, even if no radical initiator was deliberately added. Likewise, the high β regioselectivity was typical of radical additions across monosubstituted alkynes,⁴⁵ and presumably arose from steric factors. We also decided to test the reaction in THF, even if this solvent was not an obvious choice for radical reactions since it can undergo α -hydrogen abstraction,^{70,71} and thus hampers radical chains. Much to our surprise, a similar outcome than in *n*-hexane was observed in THF, and *Z*-**59** was obtained with excellent *trans* stereoselectivity, again indicative of a radical mechanism (Table II-1, entry 2). It is worth-mentioning that experiments carried out either in degassed or non-degassed solvents occurred without noticeable variation of the reaction outcome. Routinely, THF was degassed by 3 freeze-pump-thaw cycles while commercially available *n*-hexane was used without additional treatment.

			Ph ₃ GeH (n equiv) Conditions then NH ₄ Cl/NH ₃	Ph ₃ Ge		D + √N	н Н	
		54			Z -59	Ph ₃ Ge <i>E</i> -59		
Entry	Solvent	Ph₃GeH (equiv)	Additive	time	Т	Conversion (59/54) ^{<i>a,b</i>}	d.r. 59 (Z/E) ^a	Yield 59 (%) ^c [Z/E]
1	<i>n</i> -hexane	1.3	_	6 h	0 °C	59:41	>98:2	nc ^d
2	THF	1.3	-	3 h	0 °C	48:52	>98:2	nc ^d
3	THF	1.3	-	16 h	rt	80:20	96:4	80 ^e
4	THF	2.0	-	16 h	rt	98:2	96:4	93 [93:7] ^f
5	THF	2.0	-	4 h	40 °C	100:0	93:7	91 [93:7]
6	THF	1.3	Et ₂ Zn (10 mol%)	3 h	0 °C	80:20	91:9	nc ^d
7	THF	1.3	Et ₃ B (10 mol%)	3 h	0 °C	100:0	66:34	94 ^e
8	THF	1.3	Et ₃ B (10 mol%)	6 h	−78 °C	63:37	>98:2	nc^d
9	THF	1.3	Et ₃ B (100 mol%)	4 h	−78 °C	54:46	>98:2	nc^d
10	THF	1.3	Et ₃ B (10 mol%)	1 h	rt	100:0	<2:98	88 [<2:98]
11	<i>n</i> -hexane	1.3	Et ₃ B (10 mol%)	6 h	0 °C-rt	100:0	<2:98	nc^d

TABLE II-1. Optimization of the hydrogermylation of ynamide 54 with Ph₃GeH.

 \sim

^{*a*}Determined by ¹H NMR prior to purification. ^{*b*}Only β -germylated regioisomers were detected. ^{*c*}Isolated yield of **59** as a mixture of diastereoisomers. ^{*d*}Not calculated. ^{*e*}Yield estimated by ¹H NMR analysis of the crude reaction mixture using butadiene sulfone as internal standard. ^{*f*}Stereochemically enriched *Z* isomer [97:3] was isolated in 84% yield.

Further optimization of the reaction conditions was performed in THF. An increase of the temperature (from 0 °C to rt) together with the reaction time (from 3 h to 16 h) conducted to an improvement of the conversion (from 48% to 80%) with minimal erosion of the stereoselectivity (Table II-1, entry 3). By increasing the equivalents of Ph₃GeH (from 1.3 to 2.0 equiv), almost full conversion was achieved (98%) while preserving unaltered the stereoselectivity (Z/E = 96:4), and compound **59** was isolated in 93% yield. Further purification allowed isolation of *Z*-**59** with a faintly enriched stereoselectivity (Z/E = 97:3) (Table II-1, entry 4). While increase of the reaction temperature (to 40 °C) allowed for a decrease of the reaction time (to 4 h), an excellent isolated yield and a slight but still detrimental effect was observed on the stereoselectivity (Z/E = 93:7) (Table II-1, entry 5).

We also decided to test the effect of Et_2Zn (in sub-stoichiometric amount) on the initiation of the system. Indeed, the known generation of alkoxy or alkyl radicals arising from the oxidation of the dialkylzinc⁷²⁻⁷⁴ could abstract hydrogen from the Ph₃GeH, thus generating germaniumcentered radicals, and initiating the radical chain in a more efficient way. Higher conversion in comparison with entry 2 (from 48% to 80% at 0 °C) was indeed achieved (Table II-1, entry 6). However, a decrease in the stereoselectivity was also observed (from >98:2 to 91:9).

Next, and since Et₃B has proven an efficient initiator for the radical hydrogermylation of terminal acetylenes,^{31,32,35} we decided to test it in our reaction, in an endeavor to reduce the amount of Ph₃GeH necessary. Indeed, just 1.3 equiv of Ph₃GeH, along with 10 mol% of Et₃B, gave full conversion but with a substantial drop on the stereoselectivity (Table II-1, entry 7). Since similar observations had been made by Oshima,^{31,32} we then decided to try the reaction under the conditions he reported for the hydrogermylation of conventional alkynes with Ph₃GeH, i. e. at –78 °C. In a similar fashion to Oshima's results, outstanding *trans* selectivity was achieved, but in our case, the reaction was not complete (63% conversion). Passing from 10 mol% to 100 mol% of Et₃B did not improve the reaction conversion at –78 °C (Table II-1, entry 9). By contrast, at rt, not only full conversion was attained in a short reaction time, but also exceptional *cis* selectivity, and *E*-**59** was isolated in 88% yield (Table II-1, entry 10). Similar behavior was observed by switching to *n*-hexane, where also full conversion and total *E* stereoselectivity was observed (Table II-1, entry 11).

To put it briefly, balancing isolated yield with good stereoselectivity, optimized conditions for the *trans*-selective hydrogermylation of terminal ynamide **54** comprised 2.0 equiv of Ph₃GeH (THF, 16 h, rt) (Table II-1, entry 4), whereas *cis*-selective hydrogermylation could be achieved with 1.3 equiv of Ph₃GeH, and 10 mol% of Et₃B (THF, 1 h, rt) (Table II-1, entry 10).

In all cases, the geometry of the double bond was verified by ¹H NMR analysis of the crude reaction mixture (**Figure II-3**). The coupling constant (*J*) between vinylic protons allowed the determination of the relative *trans* or *cis* configuration. A coupling constant of 10.6 Hz, characteristic of a *cis*-vinyl coupling, was observed for the *Z* stereoisomer, while a coupling constant value of 17.5 Hz, typical of a *trans*-vinyl coupling, was noted for the *E* stereoisomer. It is also worth-mentioning that, in marked contrast to silylenamides, germylenamides were remarkably stable in CDCl₃. No isomerization was detected due to the possible presence of traces of HCl in the CDCl₃ (even under prolonged exposure to this solvent (weeks)), thus suggestive of the higher stability of vinylgermanes in comparison to vinylsilanes under acidic conditions.



FIGURE II-3. ¹H NMR of Z-59 and E-59: Zoom over the vinyl couplings.

II-2.2.2. Mechanistic considerations

Having developed conditions for either the *anti* or *syn* addition of Ph₃GeH to terminal ynamide **54**, we then focused on gaining some mechanistic insights for these reactions. Initially, since we anticipated a radical mechanism for the *trans*-stereoselective addition, we decided to perform experiments in the presence of TEMPO, a well-known radical scavenger. TEMPO (10–20 mol%) completely thwarted the reaction both at 0 °C and 40 °C in THF (**Table II-2**,ⁱ entries 2 and 4, respectively), thus providing clear evidence for the radical nature of this reaction.

ⁱ For the sake of simplicity, entries 2, 6 and 8 of **TABLE II-1** have been reproduced as entries 1, 3 and 5 of **TABLE II-2**, respectively.

		Ph ₃ GeH (r TEMF THF	n equiv) PO		D + Ph ₃		₃ C H ₃ C O TEMPO	-CH ₃ CH ₃
Entry	54 Ph3GeH (equiv)	TEMPO (mol%)	Et₃B (mol%)	z-59	Т	Conversion (59/54) ^{<i>a,b</i>}	d.r. 59 (Z/E) ^a	Yield 59 (%) ^c [Z/E]
1	1.3	_	-	3 h	0 °C	48:52	>98:2	nc ^d
2	1.3	10	-	3 h	0 °C	0:100 ^{e,f}	-	-
3	2.0	-	-	4 h	40 °C	100:0	93:7	91 [93:7]
4	2.0	20	-	4 h	40 °C	0:100 <i>e,f</i>	-	-
5	1.3	-	10	3 h	0 °C	100:0	66:34	94 ^{<i>f</i>}
6	1.3	10	20	3 h	0 °C	0:100 ^{e,f}	-	-

 TABLE II-2. Diagnostic experiments for the radical hydrogermylation of ynamide 54.

^{*a*}Determined by ¹H NMR prior to purification. ^{*b*}Only β -germylated regioisomers were detected. ^{*c*}Isolated yield of **59** as a mixture of diastereoisomers. ^{*d*}Not calculated. ^{*e*}>98% of starting ynamide **54** was recovered unaltered. ^{*f*}Yield estimated by ¹H NMR analysis of the crude reaction mixture using butadiene sulfone as internal standard.

Hence, a proposed mechanism for the *trans*-selective hydrogermylation of ynamide **54** is depicted in **Scheme II-6**, which basically follows the general mechanism already proposed for radical hydrogermylations of alkynes.



SCHEME II-6. Mechanism for the *trans*-selective radical hydrogermylation of ynamide 54.

In this context, germanium-centered radicals **60**, produced by hydrogen abstraction from the triphenylgermane, add across the carbon-carbon triple bond of terminal ynamide **54**, to afford regio- and stereoselectively *Z*-configured vinyl radical intermediate *Z*-**61**. This radical subsequently reacts with the triphenylgermane by H-atom transfer to provide the *anti* addition product *Z*-**59**. Since the vinyl radical intermediate should have a bent geometry, then we should expect this radical to exist in two equilibrating forms, being the equilibrium largely in favor of the *E* form (*E*-**61**) due to the unfavorable steric interaction between the triorganogermyl group and the oxazolidinone ring. However, subsequent H-atom transfer to *E*-**61** seems to be totally disfavored due to the steric hindrance imposed by the triphenylgermyl moiety, and only the *Z* radical reacts.

Concerning the initiation of the system, we conjectured that several pathways could be operational, including spontaneous- or light-induced homolysis of the Ge–H bond, as already proposed for other radical hydrogermylation reactions.³³ In fact, traces of molecular oxygen or sunlight have been suggested as the source of the so-called "adventurous radicals", that are enough to initiate the radical chain even in the absence of deliberately added radical initiators. Even if in some cases (typically the experiments performed in degassed THF), it could be expected that this hypothesis could be ruled out, we cannot exclude the possibility that oxygen is incorporated into the system during the addition of the reagents (for details, see Experimental Part). Regarding the contribution of the light to the initiation, we performed a control experiment in the dark to acquire some insights into this situation. As observed in **Scheme II-7**, the absence of light nearly halved the conversion to the desired product, thus suggesting that light definitely has a role in the initiation of the radical chain, even though other pathways should be simultaneously operating.



SCHEME II-7. Influence of light in the initiation of the radical chain for the *trans*-selective radical hydrogermylation of ynamide **54**.

The reason why in the presence of Et_3B the reaction gave reversed stereoselectivity was still something that concerned us. It is a fact that Oshima stumbled upon a similar situation when performing the hydrogermylation of terminal acetylenes in the presence of Et_3B at high temperatures (60 °C).^{31,32} In that case, the authors proposed that initial kinetically driven *trans*selective radical hydrogermylation was followed by radical isomerization through an additionelimination sequence of the triorganogermyl radical until the thermodynamic equilibrium was reached, thus accounting for the observed *E* stereoselectivity (for the proposed radical isomerization see Scheme I-12, Part I). To support this proposal he demonstrated that treatment of *Z*-1-triphenylgermyl-1-dodecene (*Z*-**62**) with *n*Pr₃GeH/Et₃B at 60 °C gave a mixture of *E*-1-triphenylgermyl-1-dodecene (*E*-**62**) and *E*-1-tripropylgermyl-1-dodecene (*E*-**63**) (*E*-**62**/*E*-**63** = 5:2), whereas treatment of *Z*-1-tripropylgermyl-1-dodecene (*Z*-**63**) with Ph₃GeH/Et₃B at 60 °C afforded the same reaction mixture (**Scheme II-8**). While this experiment sheds some light about the involvement of an addition-elimination sequence of the germyl moiety for the *Z*-to-*E* stereochemical scrambling of the vinylgermane, it does not necessarily imply a radical addition.



SCHEME II-8. Competition experiment performed by Oshima for demonstrating the addition-elimination sequence involved in the *Z*-to-*E* isomerization of vinylgermanes.

To gain additional understanding regarding this issue, we designed two experiments, our final goal being to determine whether the formation of the *E* isomer was attributable to (i) a primary formation of the *Z* isomer followed by isomerization, or (ii) the direct formation of the *syn* addition product. To this end, *in situ* NMR monitoring experiment of the Et₃B-induced hydrogermylation of terminal ynamide **54** was done (**Figure II-4**) under similar conditions to the ones already described in Table II-1, entry 8. As it has been already pointed out, chemical shifts (δ) and constant couplings of vinylic protons allowed the monitoring of the formation of both *Z*-**59** and *E*-**59** (see Figure II-3), along with completion of the reaction following the disappearance of the acetylenic proton of terminal ynamide **54** (δ 3.35 ppm in THF-*d*₈). However, three attempts to do so met with failure. To our surprise, the problem was that every time we set up the reaction and recorded the first ¹H NMR, the transformation was already completed, with the formation of a mixture of stereoisomers that did not evolve over time (in fact, the outcome observed is practically the same already obtained under these reactions conditions, i. e., full conversion with a *Z*/*E* = 68:32 (NMR monitoring) *vs* 66:34 (Table II-1, entry 8)). Therefore, it was not possible to discriminate between the two possibilities we were contemplating.



FIGURE II-4. *In situ* NMR monitoring experiment of Et₃B-induced hydrogermylation of ynamide **54**. In maroon: ¹H NMR of ynamide **54** in THF- d_8 (t₀ = 0 min); in blue-green: ¹H NMR of the reaction mixture (t₁ < 10 min).

Since the delay time between setting the reaction and obtaining the first FID was no less than 5–10 min, another method was required that allowed a real-time *in situ* monitoring of the reaction. Thus, secondly, we monitored these reactions by in situ IR (infrared) spectroscopy, since the starting ynamide 54 and both enamides Z-59 and E-59 have a carbonyl group in their structures. It is textbook knowledge that carbonyl stretching vibration peak is intense and is located in a unique wavenumber range, generally falling between 1800 and 1600 cm⁻¹. This attribute makes C=O stretches one of the easiest IR peaks to spot and assign. In our case we could determine the C=O stretch bands: 1786 cm⁻¹ (ynamide 54), 1768 cm⁻¹ (Z-59), and 1772 cm⁻¹ (E-**59**) (Figure II-5, A). As can be seen, starting ynamide **54** could be easily differentiated from products Z-59 and E-59; however, between enamides Z-59 and E-59 the bands were rather similar though still differentiable. We thus performed the *in situ* IR monitoring of the optimized conditions for the *trans*-selective hydrogermylation of terminal ynamide 54, as well as the Et₃Binduced *cis*-selective hydrogermylation. While in the first case it was possible to observe the somewhat slow direct formation of the Z isomer (completion of the reaction took around 16 h) (Figure II-5, **B**), in the presence of Et_3B was excitingly observed the extremely fast formation of the Z isomer, followed by equally fast isomerization (note that IR spectra were recorded every 15

s!) (Figure II-5, **C**). Even if we need to remain careful because the difference in the wavenumbers is small, this result strongly suggests that initial formation of the *Z* isomer followed by isomerization is accounting for the reversal of stereoselectivity observed in the presence of Et_3B .



B. Trans-selective hydrogermylation of terminal ynamide 54



C. Cis-selective hydrogermylation of terminal ynamide 54





FIGURE II-5. In situ IR monitoring experiments of the hydrogermylation of terminal ynamide 54.

Once established this point, we then turned our attention to confirm the radical character of the hydrogermylation reaction in the presence of Et_3B . Indeed, even if Et_3B/O_2 is widely recognized as an efficient radical initiator, we should not totally rule out the possibility that it could be acting as a Lewis-acid catalyst since boron-catalyzed hydrogermylations of alkynes have been reported as well.^{3,75} However, when the reaction was carried out in the presence of just 10 mol% of TEMPO, quantitative amount of starting ynamide **54** was recovered unchanged (Table II-2, entry 6).

Even though this experiment ratified the radical nature of the hydrogermylation reaction in the presence of Et_3B , we still needed to confirm the character (radical or not) of the isomerization step. To this end, we performed some experiments starting from the isolated *Z* stereoisomer (*Z*/*E* = 94:6) (**Table II-3**).

TABLE II-3. Isomerization of Z-59.



Entry	Ph₃GeH (equiv)	Et ₃ B (mol%)	TEMPO (mol%)	Т	Z/E crude
1	2.0	-	_	40 °C	94:6
2	_	10	_	0 °C	94:6
3	1.3	10	_	0 °C	<2:98
4	1.3	20	10	0 °C	5:95

What rapidly became evident for us was the fact that both, the hydrogermane and Et_3B , were necessary for the *Z*-to-*E* isomerization step (Table II-3, entries 1-3). Just the presence of Ph₃GeH, even in excess (2.0 equiv) and under heating (40 °C), did not alter the configuration of the starting material (Table II-3, entry 1), which was quite surprising taking into account that under these reaction conditions we should generate germyl radicals as already suggested the optimization of the hydrogermylation reaction. Even more unforeseen resulted the diagnostic experiment with TEMPO, as full isomerization was observed in THF at 0 °C (Table II-3, entry 4).

Such result suggests that radicals are not involved in the *Z*-to-*E* scrambling of the double bond geometry. Although we have to remain cautious, it is tempting to assume that activation of the Ph₃GeH by Lewis acidic Et₃B could render an electrophilic germyl moiety **64**, reminiscent of the one proposed by Gevorgyan.³ Taking into consideration the previously demonstrated involvement of an addition-elimination sequence in the isomerization step, the germyl entity could then undergo addition to the nucleophilic vinylgermane, generating a highly stabilized carbocation due to the β effect of two germyl groups (**65**). Free rotation followed by elimination would provide the thermodynamically more stable vinylgermane (*E* isomer) along with the regeneration of the activated germyl species that would undertake subsequent isomerization. However, further experiments have to be carried out in order to confirm this proposed mechanism (**Scheme II-9**).



SCHEME II-9. Proposed mechanism for the Et₃B-induced radical hydrogermylation of ynamide **54** followed by Lewis-acid-mediated isomerization.

In conclusion, radical hydrogermylation reaction is possible, meaning that competition could be expected during the germylzincation process. A thoughtful selection of the reaction conditions will be needed in order to overcome this side reaction. Since hydrogermylation was not our initial objective, no further attempts were done in order to explore the scope of this transformation, and we decided to devote our next efforts to find suitable conditions for the germylzincation of terminal ynamides.

II-2.3. GERMYLZINCATION OF TERMINAL YNAMIDES: OPTIMIZATION **STUDIES**

Based on our working hypothesis, we commenced our investigation of the germylzincation reaction under similar conditions to the previously reported radical silvlzincation of terminal ynamides,²⁸ i. e., 1.3 equiv of hydrogermane and 3.0 equiv of Et_2Zn at 0 °C in *n*-hexane (**Table II-4**).

	$\beta \stackrel{\alpha}{\longrightarrow} N \stackrel{\gamma}{\longrightarrow} O \qquad Ph_3GeH (1.3 equebra) \\ \frac{R_2Zn}{n-hexane} \\ 0 °C, 6 h \\ then NH_4CI/NH_2 \\ 54$	$\xrightarrow{\text{Ph}_3\text{Ge}} H$	0 + 0 + H Ph ₃ Ge <i>E</i> -59	D + N R 66a (R = E) 66b (R = if)	O it) Pr)
Entry	R2Zn (equiv)	Pre-contact ^a	Conversion [(59+66)/54] ^{b,c}	d.r. 59 (<i>Z/E</i>) ^c	66 (%) ^{b,c}
1	Et ₂ Zn ^d (3.0 equiv)	-	62:38	70:30	-
2	<i>i</i> Pr ₂ Zn ^{e,f} (3.0 equiv)	-	66:34	12:88	28
3	Et ₂ Zn ^d (3.0 equiv)	1 h	66:34	92:8	-
4	Et ₂ Zn ^d (1.0 equiv)	1 h	62:38	95:5	-
5	Et ₂ Zn ^d (6.0 equiv)	2 h	70:30	70:30	-

TABLE II-4. Initial experiments on the germylzincation of terminal ynamide **54** in *n*-hexane.

^aReaction time between ynamide **54** and Et₂Zn, before the addition of the Ph₃GeH. ^bOnly β -germylated regioisomers were detected. ^cDetermined by ¹H NMR prior to purification. ^dCommercially available Et₂Zn (1.0 M in *n*-hexane). *e*Commercially available *i*Pr₂Zn (1.0 M in toluene). */*Reaction time = 3 h.

In a first foray, we were pleased to find that the initial conditions led to the exclusive formation of the β -germylenamide **59** but as a mixture of stereoisomers (Z/E = 70.30) and the reaction was not complete (Table II-4, entry 1). We then considered that using a secondary dialkylzinc reagent would be more suitable for the reaction, since it should be more susceptible toward an S_{H2} step than Et₂Zn. However, with *i*Pr₂Zn, a totally reversed stereoselectivity was observed (from Z/E = 70:30 to 12:88), along with a highly competitive carbozincation process affording **66b**, finally resulting in an unfavorable yield of the desired product **59** (38%) (Table II-4, entry 3). Note however that iPr_2Zn is only commercially available as a 1.0 M solution in toluene: since the use of 3.0 equiv of dialkylzinc reagent accounted for an added volume of 0.75 mL of toluene (*vs* 2.0 mL of *n*-hexane), the amount introduced into the system is not negligible, and this can be definitely influencing the significant alteration observed in the outcome of the reaction (see below for a discussion of the solvent effect on the stereoselectivity).

Still to favor the S_H2 step, we then included a pre-contact between terminal ynamide **54** and Et_2Zn , prior to the addition of Ph_3GeH . Our idea was to force the coordination of Et_2Zn to the carbonyl group of the oxazolidinone ring (**Scheme II-10**, green pathway). The formation of such a complex could direct the attack of the Et_2Zn , thus facilitating the S_H2 step with the initially formed *Z*-configured vinyl radical (prior to the *Z*-to-*E* isomerization of the radical intermediate), and thereby providing enhanced *trans* stereoselectivity.



SCHEME II-10. Predicted outcomes for the germylzincation of ynamide **54** in *n*-hexane, under pre-contact with Et₂Zn.

In line with our hypothesis, a considerable improvement of the selectivity of the reaction was achieved (from Z/E = 70:30 to 92:8), even if the conversion remained essentially unchanged (62% *vs* 66%, respectively) (Table II-4, entry 4). This result was quite hopeful, and consequently we further explored this direction. However, either decrease or increase of the amount of Et₂Zn (to 1.0 or 6.0 equiv, respectively), did not make a significant difference in the conversion of the reaction (Table II-4, entries 5 and 6). Both 1.0 and 3.0 equiv of Et₂Zn furnished excellent *trans* stereoselectivity. By contrast, while using 6.0 equiv of Et₂Zn, a considerable drop on the stereoselectivity of the reaction was observed.

Moreover, one cannot lose sight of the fact that one is facing a double-edged sword: while the pre-contact might indeed render the desired and expected complex that would facilitate the transfer of alkylzinc group to the radical center, on the other edge, Et₂Zn could also deprotonate the starting terminal ynamide, thus substantially complicating the whole picture since an admixture of products could be formed (Scheme II-10). If we also consider that, as we already know, *trans*-selective radical hydrogermylation could be competing, it became necessary to perform deuterium-labeling studies to check for the formation of C(sp²)–Zn bonds (**Table II-5**).

β α Ν. 54	Et ₂ Z (n equ <i>n</i> -hexa 0 °C pre-con	n Pho niv) (1.3 ane n-he C 0 °C otact then NH or ND ₄ Cl	$\begin{array}{c} {}_{3}{\rm GeH} \\ {\rm equiv}) \\ \hline \\ {\rm exane} \\ {\rm C}, 6 h \\ {\rm H}_{4}{\rm CI/NH}_{3} \\ {\rm I/D}_{2}{\rm O/THF} \end{array}$	Ph ₃ Ge H/[H (<i>Z</i>) I/[² H]-I	P_{D} + $Ph_{3}Ge$ $Ph_{3}Ge$ Z		(E) II/[² H]-III	$ \begin{array}{c} $
Entry	Et2Zn (equiv)	Pre- contact ^a	Quench	I /[² H]- I ^b	II/[² H]-II	III/[² H]-III	IV /[² H]- IV	54 /[² H]- 54
1	1.0	1 h	Н	59	%	30	%	38%
2	1.0	1 h	D	41%/0%	3%/0%	0%/29%	-	20%/ <mark>7%</mark>
3	3.0	1 h	Н	61	%	50	%	34%
4	3.0	1 h	D	25%/6%	20%/7%	9%/14%	<mark>0%/2%</mark>	5%/12%
5	6.0	2 h	Н	49	%	21	%	30%
6	6.0	2 h	D	18%/20%	9%/6%	1%/21%	<mark>0%/</mark> 22%	3%/ <mark>0%</mark>

TABLE II-5. Deuterium-labeling experiments for selected reactions performed in *n*-hexane.

^{*a*}Reaction time between ynamide **54** and Et_2Zn , before the addition of the Ph₃GeH. ^{*b*}For the sake of simplicity, specific numbering has been assigned to the possible isotopomers of *Z*-**59** and *E*-**59**.

Unfortunately, direct hydrogermylation was responsible for the majority of the anti addition product obtained with either 1.0 or 3.0 equiv of Et_2Zn (Table II-5, compare entries 1–2 and 3–4). Basically, no trans-germylzincation was observed under these reaction conditions. Deprotonation of the starting material was irrelevant with 1.0 equiv of Et₂Zn, but switching to 3.0 equiv made the scenario totally different: hydrogermylation occurred with both terminal ynamide 54 and metalated **54** (which is undesirable for further functionalization of the C–Zn bond). Just when 6.0 equiv of Et₂Zn was used, germylzincation started to compete with hydrogermylation, but deprotonation of the ynamide was still an issue, and the stereoselectivity of the reaction was far from decent (Table II-5, entries 5 and 6). It is important to mention that cautious analysis of these results has to be done, since deuterium-labeling experiments were complicated by the necessary addition of THF during the quench. In the absence of THF, no trustable deuterium-incorporation values could be achieved, due to the immiscibility between this low-polarity solvent and D₂O. In fact, in the presence of THF, a considerable amount of the syn addition products was formed during the quench, which was not previously detected in the reactions with the standard quenching (NH₄Cl/NH₃). Despite this experimental issue, a data point is still clear and relevant: hydrogermylation reaction is outcompeting germylzincation, overcomplicated by the fact that Et₂Zn deprotonates the starting terminal ynamide, thus giving access to a variable mixture of 8 possible products. For further reaction optimization, it will be important to gain control over this scenario.

Given the complications observed in *n*-hexane, we decided to perform a survey of other solvents, since isolated clues suggested the decisive influence of this parameter in the reaction outcome (e. g. toluene and THF) (**Table II-6**).

	+	Ph ₃ GeH (1.3 e Et ₂ Zn (n equ	equiv) uiv)				D
		3 h <i>then</i> NH₄Cl/N	IH ₃ Ph ₃	H Ph ₃ Ge		Et	
Entry	Solvent	Et2Zn (equiv)	Т	Conversion [(59+66a)/54] ^{a,b}	d.r. 59 (<i>E</i> / <i>Z</i>) ^{<i>a</i>}	Yield 59 (%) ^c	Yield 66a (%) ^c
1	CH_2Cl_2	3.0	0 °C	50:50	70:30	37	nd ^d
2	Et ₂ O	3.0	0 °C	54:46	48:52	29	nd^d
3	Benzene	3.0	0 °C	85:15	57:43	nc ^e	nd^d
4	MTBE	3.0	0 °C	80:20	68:32	62	6
5	Me-THF	3.0	0 °C	>99:1	98:2	64	10
6	THF	3.0	0 °C	>99:1	>98:2	87 ^f	\mathbf{nd}^d
7	THF	1.8	0 °C	>99:1	90:10	nc ^e	nd^d
8	THF	1.2	0 °C	89:11	76:24	nc ^e	nd^d
9	THF	3.0	−78 °C	53:47	6:94	52	nd ^d
10	THF	3.0	rt	>99:1	>98:2	72	20

TABLE II-6. Optimization of the germylzincation of ynamide 54.

^{*a*}Determined by ¹H NMR prior to purification. ^{*b*}Only β -germylated regioisomers were detected. ^{*c*}Yield estimated by ¹H NMR analysis of the crude reaction mixture using butadiene sulfone as internal standard. ^{*d*}Not detected in the crude reaction mixture. ^{*e*}Not calculated. ^{*f*}Isolated yield of **59** as a mixture of diastereoisomers.

While no improvement of any kind was observed in CH_2Cl_2 and Et_2O , reactions in benzene and methyl *tert*-butyl ether (MTBE) provided improved conversion (~ 80%) (Table II-6, entries 1–4). Nevertheless, the stereoselectivity of the reaction was modest in all cases, and often in favor of the *E* isomer, in sharp contrast to the experiments performed in *n*-hexane. Additionally, competitive carbozincation was also detected in MTBE. In the end, full conversion and total stereocontrol, also in favor of the *E* isomer, were obtained using Me-THF and THF (Table II-6, entries 5 and 6). However, carbozincation of **54** occurred to some extent with the more hindered ether Me-THF (Table II-6, entry 5), and a better yield in **59** was obtained in THF (87% *vs* 64%).

The excellent *E* stereoselectivity obtained in THF was definitely unforeseen, and D-labeling experiments demonstrated that germylzincation (and not hydrogermylation) was taking place. Indeed, by quenching the reaction with ND₄Cl/D₂0, *E*-[²H]-**59** was recovered with an outstanding

97% deuterium incorporation at the α position, evidencing the formation of vinylzinc intermediate **67** (**Scheme II-11**).



SCHEME II-11. Deuterium-labeling experiment of the germylzincation reaction of terminal ynamide 54.

Next, the possibility to reduce the amount of Et_2Zn required for the reaction was also investigated. Despite a high conversion with either 1.8 or 1.2 equiv of Et_2Zn , the stereocontrol was lower (Table II-6, entries 7 and 8), likely because direct hydrogermylation affording the *Z* isomer was coming into play. More generally, it is also possible that the loss of stereoselectivity in other solvents arises from the same effect, i. e., competing germylzincation and direct hydrogermylation.

To round up our optimization studies, we then explored the influence of the temperature in the reaction outcome. At –78 °C, just the *Z* isomer was formed and the reaction was not complete (~ 50% conversion) (Table II-6, entry 9). The excellent *trans* selectivity is suggestive of direct hydrogermylation, comparable to the experiment we already performed at that temperature in the absence of Et₂Zn (see Table II-1, entry 9), or could also be owed to a slower interconversion rate of the vinyl radical intermediate, thus allowing subsequent reaction with Et₂Zn to outcompete *Z*-to-*E* isomerization of the vinyl radical. By contrast, when executed at rt, full conversion and total *E*-stereocontrol were observed, but competitive carbozincation became a significant reaction pathway (Table II-6, entry 10).

In conclusion, *cis*-selective germylzincation of terminal ynamides was achieved in THF by using a combination of Ph_3GeH and Et_2Zn at 0 °C. By careful selection of the reaction conditions (temperature, amount of Et_2Zn , solvent), it was possible to minimize or avoid either competitive hydrogermylation or carbozincation.

II-2.4. REACTION SCOPE AND LIMITATIONS

With the optimized conditions in hand, we examined the germylzincation of various terminal ynamides, considering in a first place the modification of the *N*-substitution (**Table II-7**).

	R ¹	Et ₂ Zn Ph ₃ Gel	(3.0 equiv) H (1.3 equiv)	N [_] EWG		WG GePh ₃ R ¹	N [_] EWG	
	β ^α N _{EWG}	ther	THF $0 ^{\circ}C$ γ quench A (E =	E H or D)	Ph ₃ Ge EWG	N R ¹ Et C (E =	E H or D)	
				eta/lpha > 98:2 : (unless oth	and <i>E/Z</i> > 98:2 nerwise noted)			
Entry	Substrate	time	Quench	Conv. ^a	Ratio A:B:C ^a	Product	Yield A (%) ^b	[² H] (%) ^c
1	<i>i</i> Pr NO	3 h	NH4Cl/NH3	97%	65:20:12		66 (E = H)	-
2	55	3 h	ND ₄ Cl/D ₂ O	99%	77:10:12	´ ⊑ Ph₃Ge 68 (E = H) [² H]-68 (E = D)	77 (E = D)	89d
3		3 h	NH ₄ Cl/NH ₃	93%	33:48:12 ^e		58 (E = H)	-
4		3 h	NH₄Cl/NH₃ (overnight)	90%	57:21:12		ndf	-
5		3 h	CuTC (1.0 equiv) NH4Cl/H2O	100%	88:0:12		70 (E = H)	_
6	56	3 h	NH ₄ Cl/H ₂ O ^g	100%	45:0:55	Ph ₃ Ge	30 ^{<i>h,i</i>} (E = H)	-
7	-	3 h	ND ₄ Cl/D ₂ O	95%	48:37:10	69 (E = H) [² H]-69 (E = D)	ndf	ndf
8		3 h	ND4Cl/D2O + MeOD (1 week)	90%	48:30:12		ndf	ndf
9		3 h	CuTC (1.0 equiv) ND4Cl/D2O	96%	84:0:12		66 (E = D)	99
10	Bn, N, O	16 h ^j	CuTC (1.0 equiv) NH4Cl/H2O	95%	83:0:12		70 (E = H)	-
11	57	16 h	CuTC (1.0 equiv) ND4Cl/D2O	100%	88:0:12	Ph ₃ Ge 70 (E = H) [² H]- 70 (E = D)	76 (E = D)	98
12	Bn N Ts 58	3 h	NH4Cl/NH3	Deco	mposition	-	_	_

Modification of the N-substitution.

^{*a*}Determined by ¹H NMR prior to purification. ^{*b*}Isolated yield of **A**-type compounds. ^{*c*}Percentage of deuterium incorporation estimated by ¹H NMR. ^{*d*}[²H] = 95% in the crude reaction mixture. ^{*e*}After 48 h, the ratio **A**:**B**:**C** = 54:27:12 in the crude reaction mixture. ^{*f*}Not determined. ^{*g*}CuTC (1.0 equiv) was added since the beginning of the reaction. ^{*h*}Yield estimated by ¹H NMR analysis of the crude reaction mixture using

butadiene sulfone as internal standard. ^{*i*}36% of Et addition product was formed, determined by internal standard. /With a reaction time of 3 h, just 50% conversion to the desired product was obtained.

Expecting that everything would go smoothly from here on, we faced the first problems when testing ynamide **55** (Table II-7, entry 1). In this case, besides the desired and expected *E*-**68**, small amounts (12%) of carbozincation adduct were detected in the crude reaction mixture, along with divinylzinc species (product of type **B**), likely formed by Schlenk equilibration of vinylzinc intermediates arising from germylzincation (**Scheme II-12**).



SCHEME II-12. Schlenk equilibrium of α -zincated β -germylenamides.

Even though divinylzinc complex was not obtained in substantial amounts, the eroded deuterium incorporation detected in the isolated compound in comparison with the one determined in the crude reaction mixture (89% *vs* 95%) (Table II-7, entry 2) could be ascribed to the hydrolysis of the divinylzinc complex yielding non deuterated **68** upon exposure to silica gel. However, isolated fractions still containing divinylzinc species speaks in favor of the remarkable stability toward hydrolysis of the C(sp²)–Zn bond of such complexes.

While with ynamide **55** the formation of divinylzinc complexes was not a major issue, the opposite occurred when turning to ynamide 56. Under typical quenching conditions, the divinylzinc species (product of type B) was formed in even higher amounts than the desired product 69 (Table II-7, entry 3). After 48 h, the ratio A:B changed in favor of A, due to slow hydrolysis of the divinylzinc complex. However, the problem was trickier than it looked at first sight since this was detrimental for the isolated yield in the desired product (58%), as divinylzinc complexes resisted protodemetalation even after column chromatography on silica gel! To overcome this limitation, we then decided to explore alternative quenching conditions that allowed for the protodemetalation of both vinylzinc intermediates and divinylzinc complexes, to deliver the full amount of the desired β -germylenamide. Initial attempts to subject our crude reaction mixture to the typical quenching conditions (i. e., NH_4Cl/NH_3) overnight, led to an increase of the ratio A:B in favor of A, but the hydrolysis of divinylzinc species (product of type B) was not complete and significant amounts of divinylzinc complexes were recovered in the crude (Table II-7, entry 4). Fortunately, addition of CuTC (copper(I)-thiophene-2-carboxylate) 5 min prior to the quenching with NH₄Cl/H₂O led to the exclusive formation of product *E*-69 (88%) and a nicely improved isolated yield of 70%, along with small amounts of ethylzincation product (12%) (Table II-7, entry 5). Apparently, the remarkably efficient transmetalation from Zn to Cu, allows for the hydrolysis of the vinylcopper intermediate and is responsible for this excellent outcome. To demonstrate that CuTC only intervenes for the quench, we performed an experiment wherein CuTC was added from the beginning of the reaction (Table II-7, entry 6). Here, carbozincation became the major reaction pathway. This is not totally surprising since it is well-known that copper can catalyze carbozincation reactions.^{76,77}

A similar situation was met during the deuterium-labeling experiments, where organometallic species of type **B** was not fully hydrolyzed with ND_4Cl/D_2O or MeOD (even upon exposure during 1 week!), leading to inconsistent D-incorporation values (Table II-7, entries 7 and 8). Efficient deuterio-demetalation of intermediate of type **B** was nevertheless achieved upon addition of CuTC prior to the reaction quench, and reliable (and outstanding) D-labeling data could be obtained (Table II-7, entry 9).

Next, ynamide **57** was subjected to the optimized reaction (and quenching) conditions, but the initial result after 3 h of reaction provided a poor 50% conversion. A simple increment of the reaction time furnished the desired product in 70% isolated yield (Table II-7, entry 10). Deuterium-labeling experiments occurred smoothly providing D-labeled enamide **70** with an excellent D-incorporation (Table II-7, entry 11).

Finally, *N*-tosyl ynamide **58** just led to degradation products (Table II-7, entry 12).

In general, modification of the substitution pattern α to the nitrogen atom of the oxazolidinone ring was well-tolerated and β -germylenamides **59**, **68–70** were isolated in good yields and as single *E* isomers.

Importantly, hydrogermanes other than Ph_3GeH were also investigated. To this end, we chose to explore the germylzincation reaction with commercially available nBu_3GeH and Et_3GeH , in addition to readily synthesized (2-furyl)₃GeH and (Me₃Si)₃GeH (**Table II-8**).


TABLE II-8. Reaction scope for the germylzincation of terminal ynamides: Hydrogermanes.

Entry	R ₃ GeH	R₃GeH (equiv)	time	Е	Product	Yield (%) ^a	d.r. (<i>E/Z</i>) ^b	[²H] (%) ^c
1	(2-furvl)3GeH	1.3	3 h	H ^d		72	>98:2	-
2	71			D ^d	(2-furyl)₃Ge 75 [² H]-75	83	>98:2	>99
3		1.3	3 h	Н		40 ^e	96:4	-
4	nBu₃GeH 72	2.0	16 h	Н	nBu₃Ge 76 [² H]-76	77	96:4	_
5				D		67	96:4	98
6	Et ₃ GeH	2.0		Н		76	95:5	-
7	73	2.0	16 h	D	Et ₃ Ge 77 [² H]-77	92	91:9	96
8	(Me₃Si)₃GeH 74	1.3	3 h	Н	(Me ₃ Si) ₃ Ge الطريم 78	81 ^f	35:65	_

^{*a*}Isolated yield as a mixture of diastereoisomers. ^{*b*}Determined by ¹H NMR prior to purification. ^{*c*}Percentage of deuterium incorporation estimated by ¹H NMR. ^{*d*}CuTC (1.0 equiv) was added before the reaction quench. ^{*e*}10% of Et addition product was detected. ^{*f*}Yield estimated by ¹H NMR analysis of the crude reaction mixture using butadiene sulfone as internal standard.

In view of the foregoing, we started the hydrogermane variation with (2-furyl)₃GeH (**71**) since its reactivity should be quite similar (if not higher) than Ph₃GeH, as elegantly showcased by Oshima.⁷⁸ We thus made **71** following the two-step procedure described by Oshima⁷⁸ (**Scheme II-13**). Firstly, treatment of furan with *n*BuLi and the cheapest germanium source (GeCl₄) provided tetra(2-furyl)germane **79** in 54% yield. Subsequently, reaction with lithium metal gave (2-furyl)₃GeH in 54% isolated yield after column chromatography on silica gel.



SCHEME II-13. Preparation of (2-furyl)₃GeH.

(2-furyl)₃GeH reacted smoothly under the optimized reaction conditions to provide stereopure *E*-**75** in 72% yield (Table II-8, entry 1). However, with *n*Bu₃GeH, the conversion was not complete (50%) and product **76** was obtained in a poorer 40% yield together with 10% of the carbozincation adduct (Table II-8, entry 3). This was not precisely unexpected since the rate coefficient for the reaction between trialkylgermanes and alkyl radicals is around 1 order of magnitude lower than for triarylgermanes,²⁸ making ethyl radical addition more competitive and the propagation of the radical chain less efficient. Nevertheless, with higher amounts of hydrogermane (2.0 equiv) and longer reaction times, both *n*Bu₃GeH and Et₃GeH provided **76** and **77**, respectively, in high yields with excellent stereoselectivities (≥95:5) (Table II-8, entries 4 and 6), and importantly, competitive ethylzincation was outcompeted. In all cases, the formation of vinylzinc intermediates upon reaction with R₃GeH/Et₂Zn was studied systematically by deuterium labeling experiments. Excellent D-incorporation (>96%) at the *α* position was observed in every case (Table II-8, entries 2, 5 and 7).

Finally, a last attempt was done with $(Me_3Si)_3GeH$ (74). However, its preparation turned trickier (Scheme II-14). Initially, the synthesis of tetrakis(trimethylsilyl)germane 80 was performed by the coupling of trimethylchlorosilane with germanium tetrachloride using lithium in THF at -78 °C, as described by Abdesaken.⁷⁹ A quite moderate yield was obtained (36%). However, subsequent preparation of tris(trimethylsilyl)germane 74 by cleavage of the tetrakis compound 80 using MeLi, followed by hydrolysis of the germyllithium reagent as already reported,⁷⁹ failed in our hands. Therefore, we changed the strategy, and starting once again from the tetrakis compound 80 we formed the tris(trimethylsilyl)germylpotassium 81 by reaction with potassium *tert*-butoxide, followed by simple hydrolysis with aqueous sulfuric acid to afford the respective germanium hydride 74⁸⁰ in 68% yield. Unfortunately, further attempts to reproduce this reaction were unsuccessful. Additionally, it is worth-mentioning that (Me₃Si)₃GeH is rather unstable, decomposing in a matter of days.



SCHEME II-14. Preparation of (Me₃Si)₃GeH.

Under the initially optimized reaction conditions, $(Me_3Si)_3GeH$ reacted with **54** to provide **78** in a reversed (and poorer) stereoselectivity (E/Z = 35:65) (Table II-8, entry 8). The loss in stereoselectivity was quite suggestive of a direct radical *trans*-selective hydrogermylation competing with a *cis*-germylzincation process. This would not be surprising since the rate constant for the H-atom abstraction of this hydrogermane is 1 order of magnitude higher than for triarylgermanes.²⁸

Overall, the trend of reactivity observed for the different hydrogermanes perfectly matched with what could be expected beforehand. However, not for that reason is less outstanding this unique feature, since the versatility of being able to use different types of substituents in germanium can pave the way to tailored post-functionalization of the C(sp²)–Ge bond.

II-2.5. MECHANISTIC CONSIDERATIONS

In mechanistic terms, as already discussed in section II-1.2, we anticipated the following radical mechanism (**Scheme II-15**).



SCHEME II-15. Proposed radical mechanism for the germylzincation of terminal ynamides.

Possibly, the most striking and unforeseen result so far, however, is the fact that our expected "radical" approach gave full *cis* selectivity, while typical radical additions across carbon-carbon triple bonds occur with *trans* selectivity. Therefore, confirming the mechanism of the germylzincation and clarifying this unorthodox stereochemical outcome were deemed a top priority.

II-2.5.1. Influence of metalation of terminal ynamide 54

The possible influence of metalation of the terminal ynamide in the reaction media during the germylzincation process was studied first. In the absence of Ph₃GeH, 43% deprotonation of **54** by Et₂Zn (3.0 equiv) was observed in THF after 3 h at 0 °C (**Scheme II-16**).



 $\label{eq:Scheme II-16.} Scheme II-16. Deprotonation of terminal ynamide 54 in THF by Et_2Zn.$

Yet, germylzincation under the same operating conditions on D-labeled ynamide [²H]-**54** led exclusively to E-[²H(β)]-**59** without loss of deuterium at the β position (**Scheme II-17**). Hence, deprotonation of **54** (neither by Et₂Zn nor by vinylzinc intermediates) does not take place during the germylzincation. Deuterium-labeling experiments starting from D-labeled ynamide [²H]-**54**

confirmed this point along with the fact that solely germylzincation reaction occurred, since excellent deuteration was observed at both the α and β positions.



SCHEME II-17. Germylzincation of [²H]-54 in THF.

All these results were easily analyzed by ¹H NMR spectroscopy. A zoom of the region of interest in the ¹H NMR spectra of **59**, $[{}^{2}H(\alpha)]$ -**59**, $[{}^{2}H(\beta)]$ -**59**, and $[{}^{2}H(\alpha), {}^{2}H(\beta)]$ -**59** (in all cases, E/Z > 98:2) is shown in **Figure II-6**.



FIGURE II-6. ¹H NMR of **59**, [²H(α)]-**59**, [²H(β)]-**59**, and [²H(α), ²H(β)]-**59**: Zoom over the region 6.7–3.9 ppm.

II-2.5.2. Radical character of the germylzincation reaction. Discrimination of radical vs radical/polar mechanism

Our next efforts were driven to gain evidence about the radical character of the germylzincation reaction. The presence of TEMPO completely stopped the germylzincation reaction (**Scheme II-18**): no conversion was observed when added at the beginning of the reaction with either 110 mol% or amounts as low as 10 mol%, and only 26% of *E*-**59** was formed upon addition after 5 min of reaction.

+	Et_2Zn (3.0 equiv) then Ph ₃ GeH (1.3 equiv) TEMPC			t₁ (min)	t ₁ (min) TEMPO (mol%)	
β Ň V	THF	THF		0	110	0:100
Ý 0	0 °C, t ₁ (min)	0 °C, 3 h	Ph ₃ Ge	0	10	0:100
54			59 (<i>E</i> / <i>Z</i> > 98:2)	5	10	26:74

SCHEME II-18. Diagnostic experiments in the presence of radical trapping agent TEMPO.

These experiments lend clear evidence of the radical nature of the germylzincation reaction. However, they do not discard a radical/polar scenario wherein Et_2Zn would react with the hydrogermane by a radical alkylzinc group-transfer process¹ and provide a germanium–zinc intermediate (e.g. **85**) that would subsequently react with the π -system of the triple bond of the ynamide in a polar *cis*-stereoselective way (**Scheme II-19**).



SCHEME II-19. Radical (left) *vs* polar (right) addition pathways (initiation of the radical chain has been omitted for the sake of simplicity).

ⁱ This process could be similar to the one involved in the formation of [(Me₃Si)₃Si]₂Zn from(Me₃Si)₃SiH and Et₂Zn, see Dobrovetsky, R.; Kratish, Y.; Tumanskii, B.; Botoshansky, M.; Bravo-Zhivotovskii, D.; Apeloig, Y. *Angew. Chem. Int. Ed.* **2012**, *51*, 4671–4675.

In fact, the reported formation of $(Ph_3Ge)_2Zn$ from Et_2Zn and Ph_3GeH in THF⁸¹ required to rule out this possibility. To do so, we performed an *in situ* ¹H NMR monitoring experiment to follow the depletion of Ph₃GeH upon contact with Et_2Zn in THF in the absence of ynamide (**Figure II-7**).



A. Evolution of the [8.0–5.3 ppm] region of the ¹H NMR spectra



B. Evolution of the concentration of Ph_3GeH (determined on the basis of the integration of the signal at 5.65 ppm of the ¹H NMR spectra)



FIGURE II-7. *In situ* ¹H NMR monitoring of the formation of germanium–zinc intermediate.

Some reaction was observed, but only 40% of the initial amount of Ph_3GeH disappeared after 3 h at 0 °C. Therefore, the rate of formation of a hypothetical germanium–zinc intermediate under these conditions seemed too slow to account conveniently for the germylzincation outcomes.

Yet, suspicion could still arise from this result, as a possible combination of mechanisms to some extent could be imagined. Further evidence to secure the mechanistic picture and discriminate between radical and radical/polar processes was sought by considering the reaction of Ph₃GeH/Et₂Zn with compound **86**²⁸ (**Scheme II-20**).



^aCombined yield of products isolated as mixtures after chromatography. ^bThe percentage of deuterium incorporation is indicated in brackets for each isomer.



In theory, radical 1,4-addition would deliver β -alkoxy radical **87** that would undergo a 5-*exodig* ring closure, whereas the alternative polar 1,4-addition would form a zinc enolate **88** prone to fragmentation. When **86** was subjected to Ph₃GeH/Et₂Zn in our reaction conditions, the sole formation of cyclized products **89** and **90** arising respectively from germyl and ethyl⁸² radical additions was observed. No products arising from the fragmentation of an intermediate zinc enolate were detected, thus ruling out a polar addition of germanium–zinc intermediates to **86**, and supporting a radical pathway.

II-2.5.3. Initiation

Having established the radical character of the germylzincation, the question of how the radical chain was initiated remained to be solved (Scheme II-15, dashed arrows), given that no radical initiator was deliberately added. What is important to underscore is that, as hydrogermylation, "spontaneous" initiation can be viable along several pathways, including oxygen or light-induced homolysis of the Ge–H bond.³³ Obviously, oxidation of diethylzinc by traces of molecular oxygen^{72,74} is an additional pathway that might also intervene. In spite of some experimentation, we were not however capable of identifying the radical initiator operating in our system.

II-2.5.4. The stereodiscriminating role of the SH2 step

The question that remained at that point was to explain why we were having *cis* stereoselectivity when radical addition to the triple bond of ynamides initially delivers a *Z*-configured vinyl radical intermediate. Consequently, more mechanistic work was called for. In this context, two possibilities can be easily visualized to obtain vinylzinc *Z*-**84** from vinyl radical *Z*-**83** (Scheme II-21).



SCHEME II-21. Possible pathways for the formation of vinylzinc Z-84 from vinyl radical Z-83.

The first one would be an initial *anti* addition to the substrate followed by *Z*-to-*E* isomerization of the double bond originally formed (red pathway).^{31,32} The second option could be *Z*-to-*E* isomerization of the vinylic radical **83** followed by a $S_H 2$ step from the *E*-configured vinyl radical intermediate (green pathway). Therefore, with the purpose of elucidating whether the isomerization of vinylzinc intermediate **84** or the isomerization of vinyl radical **83** was accounting

for the stereoselectivity outcome, we carried out an *in situ* ¹H NMR monitoring experiment of the germylzincation reaction of ynamide **54**.

Though, in order to perform a quantitative ¹H NMR experiment, it was crucial to ensure that all signals had fully relaxed between pulses. To guarantee this, it is recommendable to use a relaxation delay ("d1") of at least three times the T_1 of the slowest relaxing signal of interest in the spectrum. A major problem was that the relaxation times of the nuclei in the sample were not known. Thus, we firstly estimated the T_1 values for the ¹H nuclei of **54** with an inversion-recovery experiment (**Figure II-8**). This experience was recorded at 0 °C (273 K) in a mixture of THF- d_8 and *n*-hexane,¹ in the typical ratio involved in our system (2.7:1).



FIGURE II-8. Inversion-recovery experiment of terminal ynamide **54** in THF-*d*₈ / *n*-hexane (2.7:1) at 273 K (Zoom over the [4.55–3.0 ppm] region of the ¹H NMR spectra).

Since the slowest relaxing signal of terminal ynamide **54** was the one belonging to the acetylenic proton, with a T_1 of nearly 14 s, we then decided to use a d1 of 42 s (T_1 x 3). Having established all the compulsory parameters, we undertook the quantitative ¹H NMR experiment. As it is obvious from **Figure II-9**, exclusive and direct formation of *Z*-configured vinylzinc **91** was observed throughout the reaction, suggesting that the final geometric ratio was not the result of

ⁱ Note that *n*-hexane is introduced in our system because of the Et₂Zn, since it is commercially available as a 1.0 M solution in *n*-hexane.

isomerization. In fact, once formed, vinylzinc *Z*-**91** was configurationally stable and did not engage in secondary processes to any significant extent.



A. Evolution of the [8.0–3.0 ppm] region of the ¹H NMR spectra



B. Evolution of the concentration of 54, Ph₃GeH and Z-91





C. Signals in the ¹H NMR spectra used for the determination of the concentration of **54**, Ph_3GeH and Z-**91**

FIGURE II-9. *In situ* ¹H NMR monitoring of the reaction between Ph₃GeH/Et₂Zn and ynamide **54** in THF-*d*₈ at 273 K.

The NMR monitoring experiments thus allowed exclusion of the scenario involving isomerization of the intermediate vinylzincs **84** to account for the *cis* stereoselectivity of the germylzincation of terminal ynamides. Consequently, the S_H2 step was the stereodiscriminating step of the process and alkylzinc group transfer occurred from the *E*-configured vinyl radical (*E*-**83**). We ascribed this behavior to the fact that the *Z*/*E* equilibrium of vinyl radical **83** was essentially shifted toward the more stable *E* form ($K_{eq} \gg 1$) and hence the *Z* form was not significant in solution (**Scheme II-22**).



SCHEME II-22. Stereoselectivity model for the germylzincation of terminal ynamides.

II-2.5.5. Insights into the stereodivergent outcome of the germylzincation of terminal ynamides in *n*-hexane and THF

Once rationalized the *cis* selectivity for the germylzincation of terminal ynamides in THF, and having found during the course of our previous studies that the use of n-hexane as solvent mostly furnished the Z stereoisomer, both through radical pathways, we intended to clarify this remarkable solvent effect.

Making a parenthesis, the effect of substituents on the inversion energy barrier of vinyl radicals is worth discussing. In 1997, Galli and Mencarelli reported that the inversion barrier of the *Z* and *E* forms of vinyl radicals markedly increased as the electronegativity of the substituent in the α position to the radical center increases, with a quasilinear relationship (**Figure II-10**).⁸³ By contrast, the effect of substituents in the β position was greatly diminished.



FIGURE II-10. Inversion energy barriers (left) and inversion barrier *vs* electronegativity of the α -substituent (right) as obtained from DFT calculations (Source: Galli, C. *et al. J. Org. Chem.* **1997**, *62*, 4072).

In the light of the foregoing, we attributed the strong solvent effect to the complexation (or not) of Et_2Zn to the carbonyl group on the nitrogen atom (**Scheme II-23**). In this sense, the known coordinating ability of the THF toward Et_2Zn would prevent complexation of the Et_2Zn to the carbonyl group of the starting ynamide, and therefore, equilibration of **83** followed by S_H2 step could account for the *cis* stereoselectivity observed. By contrast, the possible formation of such a Lewis-pair in *n*-hexane could accelerate enough the S_H2 step to occur prior to *Z*-to-*E* isomerization of the vinyl radical **83** by means of (i) facilitating the alkylzinc group transfer due to the steering

effect of the coordination, or (ii) diminishing the electronic density of the nitrogen atom of the carbamate group and thus increasing the inversion energy barrier with the consequent decrease on the rate for *Z*-to-*E* interconversion of **83**.



SCHEME II-23. Solvent effect on the stereoselectivity outcome of the germylzincation reaction.

However, possible more subtle and general refinements awaited experimental testing. Therefore, *in situ* IR monitoring of Lewis-pair formation between ynamide **92** and Et_2Zn in *n*-hexane or THF was performed (**Figure II-11**). For these studies, since we were interested in evaluating the possible solvent-dependent coordination of Et_2Zn to the carbonyl fragment of the oxazolidinone ring, Ph-substituted internal ynamide **92** (for its preparation, see section II-3.1) was selected as model substrate instead of terminal ynamide **54**, in order to avoid complications associated with competing deprotonation of **54** by Et_2Zn .

Thus, the evolution of the system was initially monitored in *n*-hexane (Figure II-11, A and B). Ynamide **92** was introduced (t_0) and a suspension was obtained. After ~40 min, since most of the ynamide had dissolved and the system reached a steady state, Et₂Zn was subsequently added (t_1) and the turbid solution became clear. Outstandingly, a remarkable modification of the carbonyl absorption band of ynamide **92** upon addition of Et₂Zn was observed, thus suggesting the formation of a Lewis-pair in *n*-hexane. In striking contrast, when performed in THF, the addition of Et₂Zn only resulted in a dilution effect, and no modification of the carbonyl stretching was detected, thus confirming our initial hypothesis in which coordination of Et₂Zn by THF would prevent formation of a Lewis-pair between ynamide **92** and Et₂Zn (Figure II-11, C and D).



A. Selected IR spectra [1900–1500 cm⁻¹] region (experiment in n-hexane)



B. In situ IR monitoring [1900–1500 cm⁻¹] region (experiment in n-hexane)





C. Selected IR spectra [1900–1500 cm⁻¹] region (experiment in THF)

D. In situ IR monitoring [1900–1500 cm⁻¹] region (experiment in THF)



FIGURE II-11. *In situ* IR monitoring of Lewis-pair formation between ynamide **92** and Et₂Zn in *n*-hexane or THF.

Hence, unexplained at the time when this experiment was carried out, this result finally shed some light on what could have been considered turbid at first, namely, the reversal of stereoselectivity observed between the radical *trans*-silylzincation of terminal ynamides in *n*-hexane,²⁸ and the present *cis*-stereoselective germylzincation in THF.

II-2.5.6. *Cis*-germylzincation *vs trans*-silylzincation: further comments on the stereoselectivity

Notwithstanding, this point warrants a final remark. Since the *trans* selectivity for the silylzincation with $(Me_3Si)_3SiH/Et_2Zn$ was attributed (redundancy intended) to the formation, in *n*-hexane, of a Lewis pair between Et₂Zn and the carbonyl group on the nitrogen atom, where the

Zn-atom transfer step was accelerated and outcompeted *Z*-to-*E* interconversion of the α -amino vinyl radical; whereas, as evidenced with *in situ* IR experiments, THF prevented this Lewis-pair formation during germylzincation, thus exclusively providing the *E* stereomer, it is logical to expect that, if this assertion is in fact accurate, silylzincation of terminal ynamides with (Me₃Si)₃SiH/Et₂Zn **in THF** would deliver the *E* isomer. Therefore, as a final evidence, we were glad to find that this control experiment indeed proceeded with exclusive *cis* stereoselectivity in THF (**Scheme II-24**).



SCHEME II-24. Cis-silylzincation of ynamide 54 in THF.

II-2.6. PARTIAL CONCLUSIONS

In conclusion, we have also disclosed the first germylzincation reaction of terminal ynamides using a combination of a hydrogermane and Et₂Zn in THF at 0 °C.⁸⁴ Excellent levels of β -regio and *cis*-stereocontrol were achieved. In addition, the ready availability of the reagents, as well as the operational simplicity were important assets of this new protocol. Diagnostic experiments strongly supported a radical chain mechanism even if no deliberately added radical initiator was required. Moreover, deuterium-labeling experiments allowed us to confirm the (almost) exclusive formation of zincated vinylgermanes over possible competing hydrogermylation and carbozincation pathways. Importantly, this implies that the C(sp²)–Zn bond created remains available for subsequent elaboration. It is worthy of mention that a variety of hydrogermanes), appealing feature that could broaden the horizons for subsequent functionalization of the C(sp²)–Ge bond.

Notably, as part of this work, we have also developed the *trans*- and *cis*-selective radical hydrogermylation of model terminal ynamide **54**. This constitutes the first report of a hydrogermylation reaction on α -heteroatom-substituted alkynes. The reaction occurred with exceptional regio- and stereoselectivities, depending on the reaction conditions.

II-3. GERMYLZINCATION OF INTERNAL YNAMIDES

The regio- and stereoselective germylzincation of internal ynamides to access trisubstituted germylenamides is described. Deuterium-labeling experiments providing evidence for the exclusive formation of vinylzinc intermediates are presented. Lastly, a general rationalization for the stereoselectivity outcome of the germylzincation reaction is proposed.



During the course of the investigation on the radical silylzincation of ynamides,²⁸ it was found that the approach was not applicable with internal ynamides. For instance, reaction of ynamide **92** in either *n*-hexane or toluene at 0 °C using a combination of (Me₃Si)₃SiH and Et₂Zn rendered no conversion to the desired product (**Scheme II-25**). With these precedents in mind, we were very surprised to find that the above-developed conditions for the germylzincation of terminal ynamides did yield the product of germylzincation, albeit with low conversion.



SCHEME II-25. Silyl- vs germylzincation of internal ynamide 92: Preliminary results.

Encouraged by this finding, we decided to consider in more detail the germylzincation of internal ynamides.

II-3.1. SYNTHESIS OF INTERNAL YNAMIDES

Recent progress on the synthesis of ynamides has contributed to significantly improve their availability. Indeed, the marked interest on the reactivity of this scaffold has prompted the development of efficient tools for their preparation.^{48–51} Hence, versatile and structurally diverse ynamides can nowadays be obtained, and their preparation is not generally problematic anymore.

In the context of our work, three main methodologies were envisaged for the synthesis of internal ynamides: copper-catalyzed alkynylation of nitrogen nucleophiles with bromoalkynes (Hsung's procedure),⁶⁹ or *gem*-dibromoalkenes (Evano's procedure),⁸⁵ and oxidative alkynylation with alkynylcopper reagents (Evano's procedure).⁸⁶ The precursors required to apply these methods were prepared at first (**Scheme II-26**).



SCHEME II-26. Precursors for the synthesis of ynamides.

Alkynyl bromides **48**, **95–96** were easily prepared from the corresponding terminal alkynes in the presence of NBS and AgNO₃, and were used without further purification.⁸⁷ Regarding the *gem*-dibromoalkenes, they were prepared from the corresponding aldehydes,⁸⁸ rendering this approach significantly less expensive than starting from the corresponding alkynes. Moreover, owing to the remarkable number of aldehydes that are commercially available, the diversity of ynamides that could be potentially prepared from dibromoalkenes is broader than the ones that can be directly derived from alkynes or their derivatives. In general, 1,1-dibromo-1-alkenes **97– 104** were obtained in good-to-excellent yields, with few exceptions (**98, 102**). Finally, copper acetylide **105** was readily prepared by simply adding a terminal alkyne to a solution of copper iodide in a mixture of ammonia and ethanol.⁸⁶ The copper acetylide precipitated and was therefore simply obtained by filtration from the crude reaction mixture as a bench-stable yellow solid, storable for months without noticeable degradation.



With the precursors in hand, we then carried out the synthesis of internal ynamides (**Scheme II-27**).



The first envisioned methodology for the synthesis of internal ynamides was Hsung's methodology⁶⁹ (Scheme II-27, Method A), in a similar fashion as already described in section II-2.1.1. Ynamides 92, 107 and 119 were obtained in rather low yields, while internal N-alkynylsulfonamide 111 was obtained in an excellent 82% yield. In an effort to increase the yield of model internal ynamide 92, we turned our attention to the copper-catalyzed amination of gemdibromoalkenes (Scheme II-27, Method B), a route that has been efficiently applied to the synthesis of a varied range of ynamides.⁸⁵ Indeed, this reaction furnished an improved isolated yield in ynamide 92 (61%), and was consequently the method of choice for the majority of the ynamides synthesized (106, 108–110, 112–114, 117–118, 120). Moderate-to-excellent yields were obtained in these cases. The two main points left to mention are: a) the somewhat sluggish formation of acyclic *N*-alkynyl-carbamate **109** by using Method B, while no reaction (either in toluene or DMF) was observed from the corresponding alkynyl bromide (Method A) and b) the lack of reactivity of Ph-substituted tosylamine with (2,2-dibromovinyl)benzene 97 to afford compound **111** (Method B), despite the high reactivity exhibited toward the corresponding alkynyl bromide (Method A). Lastly, preparation of ynamide **116** was performed by oxidative alkynylation with copper acetylide⁸⁶ (Scheme II-27, Method C). However, the initial reaction with dimethyl-substituted oxazolidinone as nitrogen nucleophile failed (to access 115). Although this reaction has been reported with the non-substituted oxazolidinone, the simple introduction of two methyl groups completely thwarted the reaction, which could be possibly ascribed to the steric hindrance imposed by these added groups, since, as already reported by Evano,⁸⁶ the introduction of one substituent in this position of the oxazolidinone ring considerably dropped the yield of this transformation. We therefore decided to exactly reproduce the reaction with the non-substituted oxazolidinone, and the corresponding internal ynamide **116** was obtained in satisfactory yield. Unfortunately, substrate 121 that could had been useful for mechanistic studies was not formed under the tested reaction conditions.

Furthermore, preparation of unknown diynes **122** and **123** bearing an oxazolidinone moiety attracted our attention, since the reactivity of these ynamide derivatives has been barely explored (**Scheme II-28**). Thus, we performed a Pd-catalyzed C(sp)-C(sp) cross-coupling reaction, based on the report of Lei and co-workers,⁸⁹ but employing a 1-haloalkyne as the electrophile and a terminal ynamide as the nucleophile to construct the targeted unsymmetrical diynes. The major problem was the competitive formation of the homocoupled product, which was not unexpected since the use of PPh₃ as ligand was known to induce a non-negligible formation of this by-product. The literature solution to this problem is the use of the phosphine-electron deficient olefin ligand

L1.ⁱ However, its preparation required 3 synthetic steps!⁹⁰ and since our final goal was to obtain the desired diynes to assess their reactivity, commercially available PPh₃ was selected as ligand in detriment of the final yield, and no additional efforts were done to improve these results. Diynes **122** and **123** were finally obtained in 53% and 40% isolated yield, respectively.



SCHEME II-28. Synthesis of diynes 122 and 123.

In addition, capitalizing on Blanchard and Evano's oxidative trifluoromethylation of copper acetylides and terminal alkynes,⁹¹ we synthesized trifluoromethylated ynamide **124** from terminal ynamide **54**, using a copper-mediated oxidative cross-coupling with Ruppert–Prakash reagent (TMSCF₃) (**Scheme II-29**).



SCHEME II-29. Synthesis of trifluoromethylated ynamide 124.

By contrast, attempts to synthesize ynamide **125** as well as ynamides **127** and **128** met with failure (**Scheme II-30**).

Ligand L1	PPh ₂ Ligand L	1
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SCHEME II-30. Failed attempts to synthesize ynamides 125, 127–128.

In the first case, we intended to synthesize ynamide **125** by deprotonation of terminal ynamide **54** with KHMDS and subsequent reaction with iodine,⁹² but this approach led to a complex mixture. To access ynamides **127** and **128**, initial formation of dichloroenamide **126** from the corresponding oxazolidinone and trichloroethene (TCE) under mildly basic reaction conditions⁹³ was achieved in 44% yield. However, conversion of **126** to functionalized ynamides by reaction with *n*BuLi to form the lithiated ynamide, and subsequent trapping with electrophiles⁹⁴ were unsuccessful.

II-3.2. OPTIMIZATION STUDIES

In order to develop a protocol suitable for the germylzincation of internal ynamides, we first selected ynamide **92** as model substrate and conducted optimization studies (**Table II-9**).

	β α Ν C Ph 92	Ph ₃ GeH Et ₂ Zn (O solvent	(1.3 equiv) 3.0 equiv) , <i>time</i> , <i>T</i>	Ph Ph Ph ₃ Ge		NH₄CI/Nł O or ND₄CI/E 	H ₃ D ₂ O ► P Ph	94 (E = H) H]-94 (E = D)	
Entry	Solvent	Et2Zn (equiv)	time	Т	E	Conversion (94/92) ^{a,b}	d.r. 94 (<i>E/Z</i>) ^a	Yield 94 (%) ^c	[² H] (%) ^d
1	THF	3.0	6 h	0 °C	Н	21:79	>98:2	nd ^e	-
2	<i>n</i> -hexane	3.0	6 h	0 °C	Н	59:41	>98:2	nd ^e	-
3	THF	3.0	3 h	rt	Н	55:45	>98:2	nd ^e	-
4	<i>n</i> -hexane	3.0	3 h	rt	Н	72:28	>98:2	nd ^e	-
5	THF	3.0	3 h	40 °C	Н	75:25	>98:2	nd ^e	-
6	THF	3.0	3 h	40 °C	D	80:20	>98:2	nd ^e	98
7	<i>n</i> -hexane	3.0	3 h	40 °C	H	100:0	>98:2	92	-
8	<i>n</i> -hexane	3.0	3 h	40 °C	D	100:0	>98:2	88	98
9	<i>n</i> -hexane	_	3 h	40 °C	Н	0:100	_	_	_

TABLE II-9. Optimization of the germylzincation of internal ynamide 92.

^{*a*}Determined by ¹H NMR prior to purification. ^{*b*}Only β -germylated regioisomers were detected. ^{*c*}Isolated yield of **94**. ^{*d*}Percentage of deuterium incorporation estimated by ¹H NMR. ^{*e*}Not determined.

As stated previously, the reaction between 92, Ph₃GeH (1.3 equiv), Et₂Zn (3.0 equiv) in THF at 0 °C, yielded the product **94** with a low conversion (21%) (Table II-9, entry 1). Remarkably, full regio- and stereocontrol was observed, in favor of the β isomer and the *E* stereoisomer. Unexpectedly, reaction in *n*-hexane furnished even improved results (59% conversion) and an excellent cis stereoselectivity (Table II-9, entry 2), in sharp contrast to the trans selectivity observed with terminal ynamides. Subsequent performance of the reaction at rt resulted in an improved conversion in both solvents, being once again higher in *n*-hexane (Table II-9, entries 3 and 4). The sole formation of the desired product 94 was observed, and no competitive carbozincation was detected to any extent (by contrast with our observation with terminal ynamides). Further increase of the reaction temperature to 40 °C provided the targeted product as well. Even if in THF the conversion was good (75%) (Table II-9, entry 5), additional optimization of the reaction conditions in this solvent (higher temperatures, longer reaction times - not shown) did not lead to full conversion. By contrast, at that temperature, *n*-hexane provided full conversion and a nice 92% isolated yield (Table II-9, entry 7), and therefore was selected as solvent for further work. Bearing in mind the possibility of competitive hydrogermylation, we performed deuterium-labeling experiments in both solvents at 40 °C, and the excellent Dincorporation obtained (98%) (Table II-9, entries 6 and 8) allowed to confirm the exclusive

formation of vinylzinc intermediates. In fact, in the case of internal ynamide **92**, no direct hydrogermylation occurred in the absence of Et_2Zn at 40 °C (Table II-9, entry 9), probably as a consequence of the steric hindrance imposed by the Ph substituent. Here, it should be mentioned as already discussed in Part I, that previous examples of radical hydrogermylation of alkynes have been so far mostly restricted to terminal ones.

II-3.3. REACTION SCOPE AND LIMITATIONS

Having in hand these optimized conditions and a structurally diverse set of ynamides, we evaluated the scope of the germylzincation reaction, considering first aryl-substituted ynamides (Scheme II-31).

Starting with Ph-substituted ynamides, modification of the nitrogen-substituent was also well tolerated here, and the corresponding β -enamides **129–132** were obtained in 69–86% yields with a remarkable *E* stereoselectivity. Nicely, by contrast to our prior observations regarding the minor formation of carbozincation adducts with cyclic terminal ynamides, no competing ethyl radical addition was observed with internal ynamides. This is in agreement with the more difficult reaction of alkyl radicals with disubstituted alkynes than with monosubstituted ones.⁴⁵ Additionally, acyclic *N*-carbamate-substituted enamide **132** was isolated in 73% yield, even if a longer reaction time was needed (16 h). Unfortunately, both tosyl-ynamides **110** and **111** decomposed under the reaction conditions, and tosyl-enamides **133** and **134** were not detected in the crude reaction mixtures.

The scope concerning other hydrogermanes was next evaluated. Trifurylgermane **71** reacted well with **92** providing an excellent 88% yield. However, reaction with Et₃GeH was another matter: in spite of the decent yield (63%), almost no regioselectivity was observed. The absence of regiocontrol could be attributed, firstly and more importantly, to steric reasons, since the triethylgermyl group is sterically less demanding than the triphenylgermyl moiety. Yet, we cannot disregard the possibility that a polar effect could be contributing to this outcome. It is indeed accepted that germanium-centered radicals are nucleophilic,⁹⁵ due to the fact that the electronegativity of Ge is lower than the electronegativity of C (2.01 *vs* 2.55). Since triethylgermyl radicals have a more nucleophilic character than triphenylgermyl radicals, this could be favoring the reaction on the electrophilic center of the triple bond of the ynamide, i. e., the α position. Finally, (Me₃Si)₃GeH was tested, but no reaction was observed even after extended reaction times (24 h). The higher steric hindrance imposed by the three trimethylsilyl-substituents on the Ge

atom could be responsible for the frustrated addition step to the alkyne terminus now substituted by a phenyl ring.ⁱ



^aMeasured by ¹H NMR prior to purification.

SCHEME II-31. Reaction scope for the germylzincation of aryl-substituted ynamides.

Substitution of the phenyl ring had minor impact on the reaction outcome: both electrondonating and electron-withdrawing substituents were well tolerated regardless of the position of

ⁱ An additional attempt to perform the silylzincation of internal ynamide **92** under the optimized reaction conditions with (Me₃Si)₃SiH did not give any conversion to the desired silylenamide, probably for the same steric reasons.

the substituent in the aromatic ring (Scheme II-31). Accordingly, enamides **138** and **140** bearing electron-donor methoxy group in *para-* and *meta-*positions, respectively, as well as enamides **139** and **142** with *para-*chloro, and *ortho, ortho-*dichloro substituents, were all obtained in good-to-excellent yields (69–94%). In all cases, a noteworthy *E* selectivity was observed, being the only exception to this tendency enamide **141**, with an *ortho-*methoxy substituted phenyl ring. The loss of stereoselectivity in this particular case could be justified by the directing effect of the methoxy group, since its coordinating ability toward Et₂Zn could accelerate the alkylzinc group transfer step to the primarily formed *Z*-configured vinyl radical, as proposed in **Scheme II-32**.



SCHEME II-32. Rationalization for the loss of stereoselectivity in enamide **141**.

Noticeably, the germylzincation approach was not restricted to aryl-substituted ynamides (Scheme II-33).

Trisubstituted enamide **143** having an alkenyl-substituent β to the nitrogen atom was prepared in excellent yield, even if longer reaction time was needed to ensure full conversion. Notably, triphenylgermane proved highly alkynophilic in this case, and thus, the reaction showed a remarkable compatibility with an internal alkene. By contrast, reaction with TIPS-substituted ynamide **49** gave no conversion to the desired enamide **144** even after 24 h, probably due to the higher steric hindrance imposed by this substituent on the addition site to the alkyne by the bulky triphenylgermyl radical.



^aMeasured by ¹H NMR prior to purification. ^bIsolated yield. ^c13% of Et addition and 9% of an α isomer were detected.

SCHEME II-33. Reaction scope for the germylzincation of alkenyl-, TIPS-, alkynyl-, alkyl-, and CF₃- substituted ynamides.

We then investigated the reactivity with alkynyl-substituents at the alkyne terminus of the ynamide. Given that model internal ynamide **92** undergoes readily the addition of $Ph_3Ge \cdot \alpha$ to the Ph ring, control of the regioselectivity in the addition to dyine **122** did not appear as an obvious task. Indeed, a complex and inseparable mixture of products was obtained, most likely due to a lack of regioselectivity. With these caveats in mind, substrate **123** was deemed more appropriate, as we knew that no addition occurred in α position to a TIPS-substituted alkyne. Consistently, the TIPS-substituted carbon did not react and the conjugated enyne **146** was obtained in 45% yield.

Importantly, alkyl-substituted ynamides were also suitable for the germylzincation reaction, and trisubstituted enamides bearing either primary alkyl- (**147** and **148**) or secondary alkyl- (**149**) groups were obtained in good yields, even if the reactivity was lower and longer reaction times were necessary. Moreover, CF_3 -substituted ynamide **124** also furnished the corresponding product **150** in satisfactory yield, along with minor amounts of carbozincation and α -selective germylzincation. In the majority of cases, excellent *E* selectivity was obtained, but in the case of

cyclohexyl- and CF₃-substituted enamides **149** and **150**, inverse stereoselectivity was observed, and the *anti* addition products were isolated. These conclusions nicely agreed with a host of crystallographic data of products **130**, **132**, **147**, and **150** (Figure II-12).



FIGURE II-12. X-ray crystal structure of compounds 130, 132, 147, and 150.

Finally, D-labeled enamides were obtained in all cases on quenching with $ND_4Cl/D_2O/THF$ after reaction under the already determined best-suited conditions (**Scheme II-34**). The excellent deuterium incorporation in the final products confirmed the formation of vinylzinc intermediates upon germylzincation of internal ynamides, and ruled out any possibility of a competing hydrogermylation process, even in the face of doubtful products **149** and **150** arising from *anti* addition paths. This last one was particularly worrying, since Blanchard reported the *trans*-selective radical hydrogermylation of CF_3 -substituted alkynes.^{9,10} Once again, in the cases of **142** and **149**, quenching with a mixture of CuTC/ND₄Cl/D₂O/THF was essential to obtain reliable values for D-incorporation.



^{*a*}Measured by ¹H NMR prior to purification. ^{*b*}16 h reaction time. ^{*c*}CuTC (1.0 equiv) was added 5 min before the reaction quench. ^{*d*}Ph₃GeH (2.0 equiv). ^{*e*}13% of Et addition and 9% of an α isomer were detected.

SCHEME II-34. Deuterium-labeling experiments of the germylzincation of internal ynamides.

II-3.4. SELECTIVITY MODEL: RATIONALIZATION OF THE REGIO- AND STEREOSELECTIVITY FOR THE GERMYLZINCATION OF TERMINAL AND INTERNAL YNAMIDES

Yet, another feature of the germylzincation of terminal and internal ynamides merits a generalization: the regio- and stereoselectivity of the process. Remarkably, both terminal and internal ynamides lend themselves to highly regio- and stereoselective germylzincation whereby the R₃Ge-residue was faithfully delivered to the distal position to the *N*-substituent (β isomers). This was indeed totally consistent with previous reports on intermolecular radical additions to terminal and internal ynamides,^{96,97} including the direct hydrogermylation developed in section II-2.2.

In the case of terminal ynamides, we presumed that the excellent β regioselectivity was rooted in synergistic effects between steric factors, which usually accounts for the regioselectivity of radical additions across monosubstituted alkynes,⁴⁵ and the relative stability of the vinyl radical formed (**Scheme II-35**). Indeed, the marked difference of stability of the radical intermediate arising from α or β additions could be a major driving force, as the nitrogen substituent in α position to the radical center could stabilize the unpaired electron.⁹⁸



SCHEME II-35. Regioselectivity model for the germylzincation of terminal ynamides.

However, the rationalization of the regioselectivity with internal ynamides is not straightforward. The origin of the selectivity is actually difficult to estimate, since steric factors, stabilization of the vinyl radical by either the α -nitrogen atom or the R³ group, as well as dissimilar reactivity of the possible regioisomeric radicals in the subsequent alkylzinc group transfer step (S_H2) if the addition is reversible could intervene. In addition, even though germanium-centered radicals are generally considered to have a nucleophilic character, a possible electrophilic behaviour cannot be ruled out given that the reaction occurs exclusively on the nucleophilic sites of the ynamides. Notwithstanding, the β regioselectivity is significantly general and allows the site of germyl addition to be predicted, even though steric effects might synergize or counteract (like in the case of Et₃Ge-derivatives).

Finally, we would like to generalize our model concerning the stereoselectivity of the reaction. An initial brushstroke of information made clear the stereodiscriminating role of the $S_{H}2$ step, underlining that the final geometric ratio of vinylzinc intermediate was not the result of isomerization. Consequently, the Z/E ratio for the formation of vinylzinc **152** would depend on the relative stability of both isomers of vinyl radical **151** (K_{eq}), along with the relative ease of each diastereometric form to undergo the alkylzinc group transfer step ($k_Z vs k_E$) (Scheme II-36).



SCHEME II-36. Stereoselectivity model for the germylzincation of terminal and internal ynamides.

When R³ is a "small" substituent (H, aryl, primary alkyl), the position of the equilibrium is largely shifted in the direction of the more stable *E* form ($K_{eq} \gg 1$) and the formation of vinylzinc *Z*-**152** is favored. However, in a general scenario, radical *Z*-**151** would be expected to react more promptly than *E*-**151** with the Et₂Zn ($k_Z > k_E$), since the steric interaction of the Et₂Zn is less demanding with an R³ substituent than with a trisubstituted germyl moiety (R₃Ge). Hence, when R³ is a "larger" substituent (secondary alkyl or CF₃–which is similar in size to an *i*Pr group, with a van der Waals radius of 2.2 Å^{99–101}), the *E* form of the vinyl radical **151** becomes destabilized, thus lowering the K_{eq} , and the more favorable approach of the Et₂Zn from the less hindered side opposite to the bulky R₃Ge group ($k_z > k_E$) accounts for the reversal of stereoselectivity observed.

A final comment regarding this stereochemical model concerns the absence of solvent effect for internal ynamides. As previously discussed, in the case of terminal ynamides, the selectivity outcome was different in *n*-hexane and THF as a result of the presence or absence of Lewis pair formation that influenced the rate of interconversion of the intermediate vinylic radical. The absence of solvent effect for internal ynamides may be ascribed to the fact that the rate for S_H2 of the *Z* radical with Et_2Zn should be lower as a result of additional non-bonding interactions arising from the presence of $R^3 \neq H$ (Scheme II-36, general case). Hence, S_H2 does not outcompete *Z*-to-*E* interconversion even upon Lewis pair formation.

II-3.5. PARTIAL CONCLUSIONS

As closing remarks, radical germylzincation of internal ynamides was achieved⁸⁴ by slight modification of the reaction conditions already developed for terminal ynamides. This behavior is in sharp contrast to analogous radical silylzincation. The possibility of introducing a versatile substituent in the alkyne terminus of the ynamide considerably extends the scope of this approach, opening a concise gateway to structurally diverse trisubstituted germylenamides. Excellent levels of regio- and stereocontrol were achieved. Notably, no competitive hydrogermylation or carbozincation adducts were detected to any extent. In essence, deuteriumlabeled enamides suggested that the "inaccessible" tetrasubstituted vinylgermanes could be now within reach.

II-4. C(sp²)–Zn and C(sp²)–Ge Bond Functionalization

Functionalization of the $C(sp^2)$ –Zn bond is described, a unique feature of the radical germylzincation reaction offering access to elaborated tri- and tetrasubstituted vinylgermanes decorated with a nitrogen substituent β to the germanium atom. Installation of carbon and non-carbon substituents is achieved with complete retention of the double bond geometry by means of domino ynamide germylzincation/Cu(I)- or Pd(0)-mediated electrophilic substitution. Divinylzinc complexes arising from the germylzincation of terminal ynamides are isolated and characterized, including by X-ray crystallography. Specific possibilities of functionalization of the C(sp²)–Zn bond unlocked by these divinylzinc species are also discussed. Finally, the synthetic potential of the germylenamides prepared with the germylzincation chemistry are illustrated on the basis of diverse alternatives for the C(sp²)–Ge bond functionalization.


The core problem that initially brought us here was the **lack of a direct and general method for the regio- and stereoselective preparation of 1,2,2-trisubstituted or tetrasubstituted vinylgermanes (Scheme II-37)**.



SCHEME II-37. Our general approach for the synthesis of 1,2,2-trisubstituted and tetrasubstituted vinylgermanes (*Ge* = triorganogermyl).

To find a solution to this issue, we envisaged a two-step procedure in one-pot: germylzincation as the keystone to access β -zincated vinylgermanes, followed by *in situ* **electrophilic trapping**. We were already half way there.

II-4.1. C(sp²)–Zn BOND FUNCTIONALIZATION

Organozinc reagents are widely used organometallics in synthesis.¹⁰² Their recognized low reactivity allows the preparation of highly functionalized zinc reagents, but also implies that they are poorly reactive toward many organic electrophiles. However, this lack of reactivity can be easily overcome by transmetalation to another metal to generate a variety of new organometallics with enhanced reactivity toward plethora of organic electrophiles.¹⁰³

II-4.1.1. Domino ynamide germylzincation / Cu(I)-mediated electrophilic substitution

Especially interesting for synthetic applications has been the ability of zinc to transmetalate to copper, where the THF-soluble copper salt CuCN·2LiCl, popularized by Knochel,^{103,104} has been extensively used. Added in stoichiometric amount, it usually converts organozinc reagents into mixed zinc-copper reagents, with a reactivity pattern similar to organocopper species. We therefore decided to explore this pathway, and started by considering the functionalization of the β -zincated vinylgermanes arising from terminal ynamides using the optimized protocol employed in our group for the Cu(I)-mediated electrophilic substitution of β -zincated vinylsilanes.²⁸

Accordingly, *in situ* transmetalation to copper upon addition at -30 °C of CuCN·2LiCl, followed by reaction with different organic electrophiles readily provided access to vinylgermanes with two substituents β to the germanium atom (**Scheme II-38**).



SCHEME II-38. Domino terminal ynamide germylzincation/Cu(I)-mediated electrophilic substitution.

Allylation with allylbromide was performed under mild conditions, and afforded the substitution product **153** with complete retention of the double bond geometry in a remarkable 92% yield. Even though the typical procedure involved CuCN·2LiCl, commercially available CuTC could also be used with comparable results (**153**: 83%). Importantly, terminal tosyl-ynamide **58** also underwent the domino germylzincation/Cu(I)-mediated electrophilic allylation to furnish product **154** in 87% yield, despite the fact that, as already discussed in section II-2.4, the corresponding β -germylenamide arising from protodemetalation of the vinylzinc intermediate (E = H) decomposed during workup and could not be isolated. In addition, allylated product **155** was also obtained by reaction with a cyclic allylic bromide.

Benzoyl chloride was another competent carbon electrophile, providing functionalized α , β unsaturated ketone **156** in good yield. Moreover, the cross coupling reaction with alkynyl bromide offered an easy access to polyfunctionalized alkyne **157** in an excellent 94% yield. Finally, non-carbon electrophile phenyl phenylthio sulfone (PhO₂SSPh) furnished compound **158**, with the double bond bearing three different heteroatoms.

In general terms, the electrophilic substitution reactions occurred with high degree of *retention of the double bond geometry,* and were typically *high-yielding*. The configuration of the



double bond of compounds **153** and **156** was established by NOESY experiments, as shown in **Figure II-13**.

FIGURE II-13. NOESY spectra of compounds 153 and 156: Selected cross-peaks for the determination of the stereochemistry.

The configuration of functionalized products 154-155, 157-158 was assigned by analogy with 153 or 156. It is worthy to mention that the new substituent greatly influenced the chemical shift of the vinylic proton in relation to the corresponding disubstituted enamide 59 arising from *cis*-germylzincation, certainly due to additional conjugation (or not). By contrast, the methylene group of the oxazolidinone ring barely showed variation of the chemical shift with respect to β -

germylenamide **59** and this was really helpful as, in our experience, this signal presents a sufficiently large difference of chemical shifts between E and Z stereoisomers to allow for their easy identification.

Unfortunately, not all the electrophiles tested yielded the expected functionalized products (Scheme II-39).



SCHEME II-39. Unsuccessful electrophiles for the domino terminal ynamide germylzincation/Cu(I)mediated electrophilic substitution.

Methyl iodide was not a suitable electrophile for this transformation, neither benzyl bromide nor 3-iodocyclohexenone¹⁰⁵. Moreover, all our attempts to perform the stannylation of vinylzinc intermediates failed. Considering that the introduction of a nBu_3Sn group on the same side of the Ph₃Ge moiety could be hampered by steric interactions, we envisaged switching to smaller substituents on the heteroatoms. Unluckily, neither a change of Ph₃Ge by the smaller Et₃Ge nor a switch from nBu_3SnCl to Me₃SnCl provided the expected product to any extent. Only hydrolysis product was recovered in all cases, likely arising from protodemetalation of vinylmetal intermediates under workup conditions. Interestingly, here the products of protodemetalation were recovered as E/Z mixtures of isomers. This loss of stereochemical information was ascribed to the isomerization of the vinyl copper intermediates that are known to have a lower configurational stability than vinylzinc compounds.

In the quest for tetrasubstituted vinylgermanes, we then turned our attention to perform the domino germylzincation/Cu(I)-mediated electrophilic substitution with internal ynamides (Scheme II-40).



^aReaction performed at 1.0 mmol scale. ^bCuTC was used as Cu(I)-salt. ^cThe germylzincation was carried out with 2.0 equiv Ph₃GeH at rt for 24 h.

SCHEME II-40. Domino internal ynamide germylzincation/Cu(I)-mediated electrophilic substitution.

We were pleased to find that vinylzinc intermediates arising from initial germylzincation of internal ynamides were smoothly transformed into **diversely functionalized tetrasubstituted vinylgermanes 159–167** with defined geometry. Once again, allylbromide and bromo phenyl acetylene proved to be amenable electrophiles for this transformation, giving access to allylated vinylgermanes **159–163**, as well as alkynylated products **165–167**. The reaction could be even scaled up to 1.0 mmol without compromising its outcome.

Importantly, internal tosyl-ynamides **110** and **111** could be readily transformed into the functionalized products **162** and **163**, under milder reaction conditions (rt instead of 40 °C), by contrast with our initial unsuccessful trials to obtain the corresponding β -germylenamides by germylzincation followed by protodemetalation. Concerning the alkynylated products, it is worthmentioning the preparation of *trans*-enediyne **167** with our one-pot procedure, albeit in a low 20% yield. Methyl iodide performed well here, and the methylated vinylgermane **164** could be isolated in 45% yield. By contrast, a final attempt to use *n*Bu₃SnCl as electrophile met with failure.

Lastly, X-ray crystallographic analysis of alkynylated product **165** (**Figure II-14**) confirmed the expected *E* stereoselectivity, arising from an initial *cis*-germylzincation step and retention of the double bond geometry during the C(sp²)–Zn bond functionalization.



FIGURE II-14. X-ray crystal structure of compound 165.

II-4.1.2. Domino ynamide germylzincation / Cu(I)-mediated 1,4-addition

With the aim to broaden further the possibilities for $C(sp^2)$ –Zn bond functionalization, we also demonstrated that the intermediate β -germyl vinylzinc could participate in conjugate additions. Cyclohex-2-enone reacted in the presence of Me₃SiCl with the germylzincation adduct of **54** under similar conditions to the ones described by Knochel,¹⁰² to yield 67% of the Michael adduct **168** (Scheme II-41).



SCHEME II-41. Domino ynamide germylzincation/Cu(I)-mediated 1,4-addition.

II-4.1.3. Divinylzinc intermediates: synthesis and characterization

The excess of Et_2Zn necessary for the germylzincation step, complicated in certain cases clean $C(sp^2)$ –Zn bond functionalization, especially for halodezincation reactions where the control of the amount of the electrophile was a critical issue to obtain clean reactions. In order to address this shortfall, and since Et_2Zn is volatile, we envisaged the elimination of excess Et_2Zn by evaporation of the reaction mixture under reduced pressure before the electrophilic substitution step. As we had already observed the favorable formation of highly stable divinylzinc complexes arising from Schlenk equilibration of vinylzinc species (Scheme II-12) during the germylzincation of terminal ynamides, it seemed plausible to exploit these intermediates as precursors for the electrophilic substitution step. As anticipated, upon removal of Et_2Zn by evaporation following germylzincation of **54** and **55**, complete displacement of the Schlenk equilibrium resulted in the exclusive formation of divinylzincs **169** and **170** (Figure II-15).





FIGURE II-15. Synthesis and characterization of divinylzinc intermediates 169 and 170.

Remarkably, these complexes were even **isolated after column chromatography on silica gel!** NMR investigations allowed the structure of these complexes to be identified. Notably, the vinylic proton (green) and the carbon atom bonded to zinc (red) were easily characterized in the ¹H and ¹³C NMR spectra, respectively. These spectra typically evolved over time with formation of the protodemetalated products upon (slow) hydrolysis.

More importantly, the structures were confirmed beyond doubt when crystals of **169** and **170** that were suitable for X-ray crystallography were grown. We could therefore secure the *cis* geometry between zinc and germanium following germylzincation. Both crystal structures showed similar characteristics. An almost linear arrangement of the two carbon–zinc bonds was observed, as evidenced by bond angles around $165-170^{\circ}$ (**169**: C1–Zn–C26 = $170.8(3)^{\circ}$; **170**: C1–Zn–C27 = $165.5(3)^{\circ}$). Concerning the bond lengths, they were all in the expected range for diorganozinc compounds¹⁰⁶ (**169**: Zn–C1 = 1.995(8) Å, Zn–C26 = 1.985(8) Å; **170**: Zn–C1 = 1.989(7) Å, Zn–C27 = 2.009(7) Å). Remarkably, the zinc atom was also coordinated to the oxygen atoms of the carbonyl groups (**169**: O1–Zn1–O3 = $97.8(3)^{\circ}$; **170**: O1–Zn–O3 = $91.3(3)^{\circ}$), adopting an uncommon distorted seesaw shaped four-coordinate geometry.¹⁰⁷ The position of the phenyl rings of Ph₃Ge results also interesting. Even though there is no Zn–C_{*ipso*} contact, two of them sterically shield the central Zn atom and likely confer to these divinylzinc species the uncommon stability towards hydrolysis and oxidation.

II-4.1.4. C(sp²)–Zn bond functionalization *via* divinylzinc intermediate 169: further possibilities

Worried about the high stability of the divinylzinc intermediates we first decided to establish their reactivity as nucleophiles for Cu(I)-mediated allylation. Thus, we performed the germylzincation of model terminal ynamide **54** followed by evaporation of the volatiles (to obtain divinylzinc intermediate **169**), and addition of a THF-solution of CuCN·2LiCl and allylbromide (**Scheme II-42**). We were very pleased to find that allylated product **153** was obtained in comparable yield to our previous protocol, with the additional advantage of using a reduced amount of electrophile (2.5 equiv instead of 7.0 equiv). Remarkably, formation of **153** from **54** using *just* 10 mol% CuTC to promote the allylation step was also accomplished with an excellent 87% yield. Hence, an additional asset of the protocol involving divinylzinc intermediates is to enable the use of **catalytic amounts of Cu(I) salt**.



SCHEME II-42. Ynamide germylzincation/Cu(I)-mediated electrophilic allylation *via* divinylzinc intermediate **169**.

Encouraged by these results, halodezincation reactions were next investigated (Scheme II-43).



SCHEME II-43. C(sp²)–Zn bond functionalization *via* divinylzinc intermediate 169.

Commencing with iodine as halogen electrophile, reaction of intermediate **169** with 2.5 equiv for 16 h at rt in the presence of CuCN·2LiCl (conditions **A**) led to the formation of the desired product **172**, along with compounds of the type **171** in a 75:25 ratio. In fact, while we did not expect to observe competitive cleavage of the vinylic $C(sp^2)$ –Ge bond since triphenylvinylgermanes have largely proven unreactive toward halodegermylation, the loss of one or more phenyl groups from the Ph₃Ge moiety upon cleavage of aryl $C(sp^2)$ –Ge bonds was not surprising. Indeed, in the same vein, Blanchard reported the preferential reaction of various electrophiles on the phenyl substituent of the germanium *vs* the more electron-deficient (trifluoromethyl)alkene.⁹ The situation is also comparable to that observed in the reaction of triphenylvinylstannanes derivatives with I₂. In that case, it has been proposed by Hale that cleavage of the aryl–tin bonds becomes preferential if the alkene is too hindered as it prevents the approach of the electrophile.¹⁰⁸ A similar situation could be foreseen here, where hindered trisubstituted triphenylvinylgermane **172** undergoes the desired C(sp²)–Zn bond functionalization but also Ph–Ge cleavage by electrophilic substitution with iodine (**Scheme II-44**).



SCHEME II-44. Proposed mechanism for the formation of 171-type compounds.

Notwithstanding, taking into account the preferential reaction of iodine with the C(sp²)–Zn bond over competitive Ph–Ge cleavage, we thought that it could be feasible to overcome this unwanted side-reaction by careful selection of the reaction conditions (Scheme II-43). We therefore reduced the amount of iodine (2.0 equiv) and explored two sets of conditions: 1) transmetalation to copper at –40 °C followed by addition of the electrophile and quench after 20 min of reaction (conditions **C**) and 2) transmetalation to copper at –30 °C followed by addition of the electrophile and slow increase (over 16 h) of the reaction temperature to 0 °C (conditions **B**). While the first conditions only led to a low 11% of conversion to **172**, the last scenario exclusively delivered the desired product that was isolated in 66% yield. Furthermore, using this protocol, it was also feasible to perform the reaction with *N*-bromosuccinimide (NBS) as electrophile, and β -germylenamide **173** brominated in α position was obtained in moderate yield.

We next considered the more challenging electrophilic fluorination. In this sense, the classical source of electrophilic fluorine has been fluorine gas, which is highly toxic and a strong oxidizer.¹⁰⁹ Fortunately, a continuously growing commercially available portfolio of milder, safer and stable alternatives of electrophilic fluorinating reagents has emerged, mostly governed by N– F moiety-containing compounds. The choice of a fluorinating agent is mainly determined by its fluorinating power. In this context, we initially chose Selectfluor; however, despite its recognized reactivity, we obtained just a low 13% yield. We reasoned that other factors could be influencing the outcome of this transformation, namely, the low solubility of Selectfluor in most organic solvents (which compelled us to use a mixture of MeCN/THF for the functionalization step), as well as its steric size. Hence, we sought a compromise by switching to *N*-fluoropyridinium salts.

Indeed, we were aiming to reach a balance between good reactivity (though lower than Selectfluor), good solubility in common organic solvents (THF, CH₂Cl₂), and reduced size of the electrophile. The strategy met success and compound **174** was obtained in a more-than-satisfactory 59% yield.

Electrophilic trifluoromethylation using Umemoto's reagent was also achieved and enamide **175** was synthesized in 39% yield.

Divinylzinc intermediates arising from the germylzincation / Schlenk equilibration sequence underwent readily Cu(I)-mediated electrophilic substitution in THF, and this modified protocol offered further possibilities for C(sp²)–Zn bond functionalization with retention of the stereochemical integrity. However, not all was plain sailing and the approach also met limitations (**Scheme II-45**). Stannylation reactions remained elusive, and halodezincation attempts starting from internal ynamide **92** also failed.



SCHEME II-45. Failed domino ynamide germylzincation/Cu(I)-mediated electrophilic substitution *via* divinylzinc intermediates.

Finally, we also became interested in Negishi-type cross-coupling reactions (**Scheme II-46**), a versatile palladium-catalyzed coupling of organozinc compounds with organic halides that has found broad synthetic applications.¹¹⁰



SCHEME II-46. General scheme of the Negishi cross-coupling reaction.

In initial attempts, we considered the use of 1-iodo-4-nitrobenzene. Cross-coupling with **169** according to a slightly modified version of a procedure reported by Lam using $Pd_2dba_3/(2-Fur)_3P$ as catalytic system¹¹¹ did not deliver the expected product to any extent (**Scheme II-47**). Opportunely, a simple replacement of the electrophile by its analogue 1-bromo-4-nitrobenzene afforded arylated product **176** in 56% yield (along with 24% of product *E*-**59** coming from the hydrolysis of unreacted **169**). To underscore the significance of this result, it should be stressed that all the previous attempts of C(sp²)–Zn bond functionalization by these means without forming the divinylzinc intermediates had failed. This was also the case for the functionalization of vinylzinc intermediates arising from radical silylzincation.¹¹²



SCHEME II-47. Domino ynamide germylzincation/Pd(0)-catalyzed Negishi-type cross-coupling reaction *via* divinylzinc intermediate **169**.

To sum up, the versatile transformations of the $C(sp^2)$ –Zn bond unlock the access to vinylgermanes bearing two functionalities in β position to the germyl group. Altogether, our domino germylzincation/Cu(I)- or Pd(0)-mediated electrophilic substitution approach provides straight access to a large variety of stereodefined tri- and tetrasubstituted β -germylenamides.

Next, as part of our blueprint concerning this new germylzincation chemistry, illustrating the synthetic potential of the β -germylenamides prepared became the priority. With this in mind, we embarked on the study of the functionalization of the C(sp²)–Ge bond as a means to access stereodefined enamides.

II-4.2. C(sp²)–Ge BOND FUNCTIONALIZATION

Compared to the ubiquitous synthetic applications of vinylsilanes and vinylstannanes,^{22,26} the related transformations of vinylgermanes have been much less commonly investigated. In this regard, as already mentioned in Part I, the use of vinylgermanes in organic chemistry has been mostly focused on halodegermylation reactions to access vinyl halides (important coupling

partners), along with Stille-type cross-coupling reactions that yield directly (configurationally defined) alkenes. Our efforts to implement these two approaches are presented hereafter.

II-4.2.1. Germyl 1,2-migration: Unprecedented access to hemiaminal-type compounds

In general, *triphenyl*vinylgermanes undergo sluggishly, if at all, halodegermylation reactions, as discussed previously and as illustrated in prior literature reports.^{9,113} Hence, at the outset of our work, the halodegermylation of *triphenyl*germylenamides seemed challenging and, foreseeing a possible failure, we also developed the germylzincation reaction with hydrogermanes other than Ph₃GeH with the purpose that, if required, they could be used as back-up solution to achieve tailored transformations of the C(sp²)–Ge bond. *Triethyl*germylenamide **77** was thus brought back on stage since related *triethyl*vinylgermane derivatives are especially prone to undergo halodegermylation.

We began our study with the reaction between Br_2 and 77 (Scheme II-48).



SCHEME II-48. Reaction of β -germylenamides **77** and **59** with Br₂.

After 1 h at –78 °C plus 2 h at rt and evaporation of the volatiles as unique treatment, the anticipated compound **177**, expectedly formed through a typical electrophilic substitution reaction *via* bromonium intermediate **178** was not detected. On the contrary, clean and complete conversion to adduct **179** was observed, as shown in the ¹H NMR spectrum of the crude reaction mixture (**Figure II-16**, maroon). What turned out to be even more unpredictable was the isolation of stable hemiaminal **181** in 68% yield after column chromatography on silica gel (Scheme II-48). The ¹H NMR spectrum of the isolated compound **181** (Figure II-16, green) showed totally different

signals to the ones observed in the crude reaction mixture, its structure being unambiguously confirmed by X-ray crystallography (Scheme II-48). Interestingly, the same chemical reactivity was observed when commencing from *triphenyl*germylenamide **59** (that we had expected unreactive). The corresponding adduct **180** was observed after evaporation of the solvent (Figure II-16, blue), delivering once again compound **181** upon exposure to silica gel.



FIGURE II-16. ¹H NMR spectra of the reactions of β -germylenamides **59** and **77** with Br₂, prior (blue and maroon, respectively) and after column chromatography (green).

Revisiting the literature, Nakano observed an unprecedented 1,2-germyl migration during the protodestannylation of germyl(stannyl)ethenes^{16,114} (**Scheme II-49**). For those reactions, germyl group migration onto a neighboring carbon through the formation of a germacyclopropyl cation (**182**), followed by destannylation to form 1-aryl-1-germylethenes, was proposed.



SCHEME II-49. 1,2-germyl migration reported by Nakano during the protodestannylation of germyl(stannyl)ethenes.

A similar reaction pathway could be envisaged to explain the formation of adducts **179** and **180** (**Scheme II-50**). Initial addition of "Br+", followed by the formation of a transient germacyclopropyl cation (**183**), could then be selectively opened by subsequent addition of "Br-" (instead of bromodegermylation to reform the double bond).



SCHEME II-50. Proposed mechanism for the formation of adducts 179–180.

Subsequent transformation of adducts **179** and **180** into hemiaminal **181** seemed to occur by nucleophilic attack at the carbon adjacent to the nitrogen atom. This was further confirmed by exposing adduct **180** to methanol (**Scheme II-51**). After one hour of contact, we observed clean and complete conversion to the functionalized compound **184**, which was isolated in an excellent 87% yield, and proved remarkably stable. It is worth-highlighting that no similar hemiaminals (bearing two Br atoms in the adjacent carbon to the hemiaminal center) have been reported.



SCHEME II-51. Reactivity of adduct 180 toward MeOH.

However, how adducts **179** and **180** can be transformed into hemiaminal-type compounds **181** and **184** is still difficult to explain. Arguably, nucleophilic attack at the carbon adjacent to the nitrogen atom tacitly suggests the involvement of *N*-acyliminium ions, highly electrophilic intermediates (**Scheme II-52**). Typically, *N*-acyliminium ions are generated by having the lone pair on the nitrogen of an amide "driving out" a leaving group.¹¹⁵ However, the presence of a germyl group (which is not a leaving group) warns against this rationale, since no elimination from **179** and **180** should be expected. Investigation of the reaction mechanism involved in this transformation is compulsory in order to understand this reactivity pattern.



SCHEME II-52. Generation, structure and general reactivity of *N*-acyliminium ions.

Notwithstanding, the range of possibilities opened up by this unique reactivity profile is engaging (Scheme II-53). In advance, reactions of **179–180**-type adducts (or isolated hemiaminal **181**) with a variety of heteroatom and carbon nucleophiles under mild reaction conditions could provide access to highly functionalized *N*-substituted oxazolidinones. In addition, the presence of the *gem*-dibromo template might open the door to an orthogonal reactivity investigation, e.g. halogen–metal exchange reactions to provide access to functionalized metal carbenoids that could subsequently react with electrophilic or nucleophilic partners. Studies along these lines will be pursued in our team.



SCHEME II-53. Possibilities of functionalization of 179–180-type adducts.

II-4.2.2. Halodegermylation reactions

Wondering if the formation of adduct **185** with two different halides could be possible, reaction of *triphenyl*germylenamide **59** with ICl was then performed (**Scheme II-54**). This time, however, full conversion to iodoenamide **186** was obtained, with an outstanding 93% isolated yield.



SCHEME II-54. Iododegermylation reactions of disubstituted β -germylenamide **59**.

Furthermore, iodine was also suitable to obtain **186** from *triphenyl*germylenamide **59** with comparable results to ICl, although the reaction took longer to reach full conversion.

These outcomes are noteworthy because, to the best of our knowledge, this is the first time that *triphenyl*vinylgermane derivatives undergo such transformation. Encouraged by these results, we then investigated the reaction of sterically more crowded trisubstituted β -germylenamides **138**, **153** and **156** with Br₂ (**Scheme II-55**).



SCHEME II-55. Bromodegermylation reactions of trisubstituted β -germylenamides **138**, **153** and **156**.

Importantly, 1,2-germyl migration was not observed to any extent with neither of the considered substrates. Bromodegermylation yielded bromoenamides **187–189** with fair-to-quantitative yields (44–99%), in all cases with excellent degree of stereoselectivity. However, while trisubstituted β -germylenamides **187** and **188** reacted with retention of the double bond geometry, complete inversion of the configuration was observed from substrate **156**. This is not unprecedented since Oshima observed that triethylvinylgermanes were transformed into the corresponding vinyl halides with retention of the configuration upon treatment with iodine or NBS, whereas reaction with bromine led to inversion of the configuration.¹¹⁶

A possible rationalization for our stereoselectivity outcome is suggested in Scheme II-56.



SCHEME II-56. Proposed rationalization for the configuration obtained after bromodegermylation of β -germylenamides **153** and **156**.

In general, the mechanism of bromodegermylation involves the formation of a bromonium ion. Thus, both allylated product **153** and benzoylated product **156** have a common initial step: formation of **190**. From here on, two possible pathways are envisaged. In the case of allylated germylenamide **153**, the opening of bridged bromonium intermediate **190** generates carbocation **191**, stabilized by the β -effect of the germyl group. For subsequent bromodegermylation to occur, the C–Ge bond and the vacant p orbital must be aligned parallel in the conformation of the carbocation intermediate. To this end, rotation leading to **192** follows the least motion principle, and subsequent elimination provides the corresponding product **188** with retention of the configuration.

By contrast, inversion of configuration during bromodesilylation of vinylsilanes with Br₂ has been comprehensively explained through formation of a dibromide intermediate.¹¹⁷ A similar scenario could be envisaged here, since the opening of bridged bromonium intermediate **190** to form carbocation **193** in the case of benzoylated product **156** is perhaps less favorable, due to the destabilizing effect of the benzoyl substituent. Thus, nucleophilic bromide counterion opens intermediate **190** to give dibromide products **194** or **195** of *anti* addition. Whether the incoming bromide attacks β to the germyl group to provide **194** (path a) or α to it to afford **195** (path b) does not affect the final outcome. Since bromodegermylation is an *anti*-stereospecific process, subsequent rotation provides conformations **196** and **197**, from which elimination can take place. Both of these pathways lead to bromoenamide **189** with inversion of the configuration.

Finally, the more challenging halodegermylation of tetrasubstituted germylenamides **160** and **167** were explored (**Scheme II-57**). Unfortunately, treatment of both **160** and **167** with Br₂ furnished complex mixtures. Meanwhile, reaction of **160** with ICl or I₂ delivered the unreacted substrate intact.



SCHEME II-57. Failed halodegermylation reactions of tetrasubstituted β-germylenamides **160** and **167**.

II-4.2.3. Stille-type cross-coupling reactions

Stille-type cross-coupling reactions were then briefly investigated (**Scheme II-58**). As mentioned previously (see section I-1.2.2), Oshima demonstrated that *trifuryl*vinylgermanes could undergo Pd(0)-catalyzed cross-coupling with aryl iodides.⁷⁸ We thus selected di- and trisubstituted *trifuryl*germylenamides **75** and **135**. Under Oshima's conditions involving Pd₂(dba)₃·CHCl₃/(2-furyl)₃P/TBAF, our attempts met significant difficulties. Low conversion to the coupling product **200** was obtained starting from disubstituted **75**, along with unreacted starting material. With trisubstituted germylenamide **135**, no reaction was observed under these reaction conditions. Notwithstanding, the low but still exclusive formation of desired coupling product **200** offers promising perspectives for further optimization.



SCHEME II-58. Stille-type cross-coupling reactions on β -germylenamides **75** and **135**.

II-4.3. PARTIAL CONCLUSIONS

In summary, C(sp²)–Zn bond functionalization was feasible with an array of electrophiles, including carbon and non-carbon centered ones. The domino sequence concerning –both terminal and internal– ynamide germlyzincation/Cu(I)-mediated electrophilic substitution was generally high-yielding and occurred with complete retention of the double bond geometry. Importantly, exceptionally stable divinylzinc complexes were synthesized and fully characterized. These intermediates unlocked further and appealing possibilities of functionalization with halogen electrophiles, Umemoto's reagent, as well as direct Negishi-type cross-coupling reactions. As a

result, this approach offered modular access to a large variety of tri- and tetrasubstituted β germylenamides⁸⁴ not accessible thus far by other methods.

Notably, valorization of the accessible β -germylenamides was subsequently accomplished by means of functionalization of the C(sp²)–Ge bond. In this context, unexplored access to hemiaminal-type compounds from disubstituted germylenamides remains as an open door to access valuable and highly functionalized compounds (*unpublished results*). In addition, unprecedented and efficient halodegermylation reactions of *triphenyl*vinylgermane derivatives⁸⁴ are deemed to be of great strategic value for the future positioning of vinylgermanes in organic chemistry.

II-5. GERMYLZINCATION OF OTHER α -HETEROATOM-SUBSTITUTED ALKYNES

Germylzincation of α -sulfur-, oxygen-, and phosphorous-substituted alkynes is reported. Di- and trisubstituted vinylgermanes decorated with an arylsufide, arylsulfoxide, O-carbamate, and phosphonates β to the germanium atom are obtained with high degree of regio- and stereocontrol.



Heteroatom-substituted alkynes have attracted significant interest from the synthetic community due to the polarized nature of the triple bond that makes them privileged substrates in a wide range of chemical transformations.^{21,77,118,119} However, as indicated in the *Scientific Problem*, this substrate class has not been previously considered to access heteroatom-substituted vinylgermanes by any of the available methodologies. Since the radical germylzincation reaction proved highly successful with ynamides, this encouraged us to consider the possibility of extending our approach to other α -heteroatom-substituted alkynes, including sulfur-, oxygen-, and phosphorous-substituted alkynes (**Scheme II-59**).



SCHEME II-59. Envisaged substrate classes.

II-5.1. SYNTHESIS OF SUBSTRATES

Our first efforts were devoted to the synthesis of the required substrates.

Commencing with the preparation of alkynyl sulfides (**Scheme II-60**), deprotonation of terminal acetylenes **202** and **203** with *n*BuLi, followed by reaction with diphenyl disulfide **204**,¹²⁰ provided TIPS-protected alkynyl sulfide **205**, and alkyl-substituted alkynyl sulfide **207**, respectively. The TIPS-protected alkyne **205** was subsequently desilylated by treatment with TBAF to form the desired terminal alkyne **206** in 56% yield. On the other hand, phenyl-substituted alkynyl sulfide **210** was next targeted. However, initial methodology involving aerobic cross-dehydrogenative coupling of phenylacetylene **209** with thiophenol **208** catalyzed by Cu(I) using molecular oxygen as the oxidant¹²¹ did not provide product **210**. Only disulfide **204** was formed, conceivably through a dimerization pathway of copper thiolate in the presence of molecular oxygen. Since the initial attempted formation of product **210** was unrewarding, we chose to prepare alkynyl sulfide **210** via transition-metal-free catalyzed C–S coupling of 1,1-dibromo-1-alkene **97** with thiophenol **208**¹²² this time, the desired product was obtained in 41% yield.



SCHEME II-60. Synthesis of alkynyl sulfides.

Later oxidation of the resulting alkynyl sulfide **210** with *meta*-chloroperoxybenzoic acid (*m*CPBA) furnished alkynyl sulfoxide **211** in the crude reaction mixture (**Scheme II-61**). Unfortunately, attempts to isolate this compound led to its decomposition.



SCHEME II-61. Synthesis of alkynyl sulfoxides.

By contrast, terminal alkyne **214** substituted by a sulfoxide motif was obtained following a similar strategy than for the synthesis of **206**, this time using a Grignard reagent to perform the deprotonation, followed by reaction with **213**.¹²³ The silylated alkyne thus formed was hydrolyzed during chromatographic purification to produce compound **214** in 43% yield.

Switching to α -O-substituted alkynes (**Scheme II-62**), the synthesis of O-alkynyl carbamate **218** was accomplished in two steps.¹²⁴ Starting from acyl chloride **215** and alcohol **216**,

carbamate **217** was obtained in 78% yield. Subsequent treatment with LDA furnished O-alkynyl carbamate **218** in 72% yield.



SCHEME II-62. Synthesis of α -O-substituted alkynes.

However, preparation of ynol ethers remained elusive in our hands. Attempt to prepare **221** by means of copper-catalyzed cross-coupling¹²⁵ of 1,1-dibromo-1-alkene **97** with *m*-cresol **220** was unsuccessful, and only the self-condensation product **223** was observed, whereas *m*-cresol **220** was basically not engaged. An initial better result was obtained commencing from **219**; however, the desired ynol ether **224** was isolated together with byproduct **225**, and even a second treatment with *t*BuOK to complete elimination from **225** to yield **224** still resulted in the same mixture of products (this time enriched in **224**).

We finally turned our attention to the synthesis of alkynyl phosphonates (Scheme II-63).



SCHEME II-63. Synthesis of *α*-P-substituted alkynes.

Terminal alkyne **227** was readily synthesized by deprotonation of trimethylsilylacetylene **212** with a Grignard reagent, followed by reaction with diethyl chlorophosphate **226**.¹²⁶ Subsequent desilylation furnished the desired product in 26% yield. Alternatively, internal alkynyl phosphonate **230** was obtained in 86% yield *via* click-alkynylation of P-nucleophile **229** by oxidative cross-coupling with alkynylcopper reagent **228**.⁸⁶

In conclusion, a summary of the substrates that were next considered for the germylzincation reaction is shown in **Scheme II-64**.



SCHEME II-64. Final set of *α*-heteroatom-substituted alkynes selected for the germylzincation reaction.

II-5.2. GERMYLZINCATION OF α -S-SUBSTITUTED ALKYNES

Under the premise that α -heteroatom-substituted alkynes other than ynamides might qualify as substrates for direct preparation of vinylgermanes decorated with heteroatoms β to the triorganogermyl group, we became initially interested in the germylzincation of terminal alkynyl sulfide **206** (Scheme II-65).



SCHEME II-65. Germylzincation of terminal alkynyl sulfide 206.

In line with our expectations, **206** was converted into the corresponding vinylsulfide **232** bearing a germyl moiety, under the established conditions for terminal ynamides. The addition of germyl radicals to alkyne **206** took place on the less substituted carbon, offering the final product with an excellent β regioselectivity. In addition, formation of **232** occurred with remarkable *E* stereoselectivity. Finally, D-labeling experiments allowed to confirm the exclusive formation of vinylzinc intermediates, nicely mirroring the results obtained with ynamides.

By contrast, aryl-substituted alkynyl sulfide **210** did not have the same fate. When subjected to the optimized conditions for internal ynamides, the desired product **233** was not detected, and only alkynylgermane **234** was isolated after column chromatography (**Scheme II-66**).



SCHEME II-66. Germylzincation of aryl-substituted alkynyl sulfide 210.

We attributed the formation of alkynylgermane **234** to reversal of the regioselectivity of the radical addition step (α addition, **235**), followed by fragmentation of the corresponding β -sulfanyl radical **236** (**Scheme II-67**). The reversal of regioselectivity could be perhaps ascribed both to a lower bias of steric effects of the substituents on the triple bond, as well as to a lower difference in the stability of the vinyl radical intermediates arising from each of the addition pathways. This outcome was not totally unexpected since previous experiments performed in our laboratory in pursuit of the silylzincation of **210** met with similar behavior.¹¹²



SCHEME II-67. Proposed mechanism for the formation of alkynylgermane 234.

Switching to alkyl-substituted alkynyl sulfide **207** did not furnish any improvement (**Scheme II-68**). In this case, a complex mixture was obtained after workup. However, unlike aryl-substituted alkynyl sulfide **210**, substrate **207** was not prone to α addition followed by fragmentation, and alkynylgermane **234** was not detected to any extent in the crude reaction mixture.



SCHEME II-68. Germylzincation of alkyl-substituted alkynyl sulfide 207.

Next, alkyne **214** having a pendant sulfoxide group was subjected to the typical germylzincation conditions for terminal substrates (**Scheme II-69**). Vinylsulfoxide **238** was obtained as single *E* isomer with exclusive β regioselectivity, albeit in moderate yield. As for the alkynyl sulfides, the formation of D-labeled **238** upon quench with ND₄Cl/D₂O confirmed the formation of a C(sp²)–Zn bond.



SCHEME II-69. Germylzincation of terminal alkynyl sulfoxide 214.

To end with, terminal alkynyl sulfone **231** was also tested (**Scheme II-70**). In this case, a complex mixture of products was obtained. Nevertheless, the ratio of compounds **239** (germylzincation product) and **240** (carbozincation product) could be determined and was in favor of direct carbozincation.



SCHEME II-70. Germylzincation of terminal alkynyl sulfone 231.

In general, terminal alkynyl sulfides and sulfoxides were suitable substrates for the germylzincation reaction, whereas internal alkynyl sulfides and terminal sulfones rendered complex crude mixtures, as the consequence of lack of regioselectivity or competitive carbozincation.

II-5.3. GERMYLZINCATION OF α -O-SUBSTITUTED ALKYNES

The applicability of the germylzincation reaction to α -O-substituted alkynes was briefly surveyed. In this sense, O-alkynyl carbamate **218** served as starting point (**Scheme II-71**).



SCHEME II-71. Germylzincation of terminal O-alkynyl carbamate 218.

Here, the desired product **241** was isolated in a rather low 37% yield. The unfavorable outcome was related to the favored formation of terminal alkynylgermane **242**, again arising from an α -regioselective addition followed by fragmentation. In spite of the low yields, formation of vinylgermane **241** was exclusively owed to a germylzincation pathway, as confirmed by the excellent deuterium incorporation in [²H]-**241**.

II-5.4. Germylzincation of α -P-substituted alkynes

Finally, terminal alkynyl phosphonate 227 was considered (Table II-10).



TABLE II-10. Germylzincation of terminal alkynyl phosphonate 227.

Entry	Solvent	Pre- contact ^a	Т	time	E	Conversion (244/227) ^b	Yield 244 (%) ^c	α-[² H] (%) ^d	β-[²H] (%) ^d
1	THF	-	0 °C	3 h	Н	63:37	45	-	-
2	THF	-	0 °C to rt	16 h	Н	61:39	_	-	-
3	THF	-	0 °C to rt	16 h	D	nd ^e	-	>98	34
4	THF	1 h	0 °C to rt	16 h	Н	75:25	-	-	-
5	THF	1 h	0 °C to rt	16 h	D	nd ^e	-	>98	77
6	<i>n</i> -hexane	1 h	0 °C to rt	16 h	Н	77:23	70	-	-
7	<i>n</i> -hexane	1 h	0 °C to rt	16 h	D f	nd ^e	62	>98	>98

^{*a*}Reaction time between alkynyl phosphonate **227** and Et₂Zn, before the addition of Ph₃GeH. ^{*b*}Determined by ¹H NMR prior to purification. ^{*c*}Isolated yield. ^{*d*}Percentage of deuterium incorporation estimated by ¹H NMR. ^{*e*}Not determined. ^{*f*}THF (2.0 mL) was added upon quench with ND₄Cl/D₂O.

The optimized reaction conditions for terminal substrates exclusively yielded the expected product **244** with excellent regio- and stereoselectivity (Table II-10, entry 1) but without full conversion. Increasing the temperature and reaction time furnished similar results (Table II-10, entry 2). However, what in fact did complicate the situation was the initial results obtained by D-labeling experiments (Table II-10, entry 3): even though the excellent incorporation of deuterium in the α position (>98%) was a clear evidence of an exclusive germylzincation process, the simultaneous 34% of D-incorporation detected in the β position (di-deuterated compound), meant that deprotonation of **227** was occurring under the reaction conditions. Germylzincation was thus taking place not only across **227** but also across metalated **243**.

We therefore turned our attention to achieve full metalation of **227** before germylzincation befalls, in order to make this reaction synthetically useful for further possible functionalization. To do so, we decided to add 1 h of contact between terminal substrate **227** and Et₂Zn, followed by addition of the hydrogermane on the "already" metalated **227** (**243**) (Table II-10, entry 4). Preliminary experiments provided an enhanced conversion (75%), while the amount of product with deuterium at the α and β positions, simultaneously, represented an increased 77% of the total amount (Table II-10, entry 5). Since our previous experience with ynamides advocates in favor of *n*-hexane to promote the deprotonation step, we next switched to this solvent while keeping the pre-contact tactic. Surprisingly, the same conversion and identical regio- and stereoselectivity were achieved, and vinylphosphonate **244** was isolated in 70% yield (Table II-10, entry 6). More importantly, complete D-incorporation at both the α and β positions was attained upon quench with ND₄Cl/D₂O/THF (Table II-10, entry 7).

As a final point, internal alkynyl phosphonate **230** was subjected to the germylzincation reaction (**Scheme II-72**).



SCHEME II-72. Germylzincation of internal alkynyl phosphonate 230.

This reaction smoothly converted **230** into the desired trisubstituted vinylphosphonate **245** with good yield and, once again, exclusive β regioselectivity and *E* stereoselectivity. The geometry of the newly formed trisubstituted double bond was confirmed by X-ray crystallography (**Figure II-17**).





FIGURE II-17. X-ray crystal structure of compound 245.
II-5.5. PARTIAL CONCLUSIONS

In summary, we have outlined a useful extension of the germylzincation approach to other α -heteroatom-substituted alkynes.⁸⁴ Although often less efficient and general than for ynamides, this approach provides a firm basis for the synthesis of di- and trisubstituted vinylgermanes decorated with an arylsufide, arylsulfoxide, O-carbamate, and phosphonates β to the germanium atom (Scheme II-73), amenable to structural diversification.



SCHEME II-73. Summary of the synthesized vinylgermanes decorated with sulfur, oxygen and phosphorous.

II-6. GERMYLZINCATION OF CONVENTIONAL ALKYNES

The radical germylzincation of internal alkynes is addressed along this chapter. Extensive optimization for the stereoselective preparation of vinylgermanes arising from a variety of alkynes is described. (Aryl, alkyl)-substituted alkynes, diarylacetylenes, dialkylacetylenes, and aryl-, alkyl-, or TMS-substituted propargylic alcohols are suitable substrates for the germylzincation, as well as for a stereodivergent radical hydrogermylation approach. Finally, vinylzinc intermediates arising from the germylzincation are smoothly transformed into tetrasubstituted vinylgermanes by means of *in situ* Cu(I)-mediated electrophilic substitution, with excellent retention of the double bond geometry.



At this point of our study, one major challenge that remained to be tackled in order to turn our radical germylzincation approach into a broadly applicable synthetic methodology, was to achieve the transformation of conventional alkynes into carbon-substituted vinylgermanes. If successful, the underlying radical strategy would gain more relevance since it could be transferred to the synthesis of configurationally defined tri- and tetrasubstituted alkenes. However, the general arena for achieving this desired transformation did not look good at first and likely restricted to terminal alkynes, given the limited number of reports concerning the radical hydrogermylation^{6,9,10} as well as the transition metal-catalyzed silylzincation¹²⁷⁻¹³⁰ of internal alkynes, or the fact that radical silylzincation of these difficult substrates was not known. Typically, issues related to lower reactivity of electronically unbiased triple bonds, increased steric hindrance, and lack of regio- and stereocontrol have so far accounted for the failures met with these substrates.

II-6.1. PRELIMINARY EXPERIMENTS ON TERMINAL PHENYLACETYLENE DERIVATIVES: HYDROGERMYLATION BEATING GERMYLZINCATION

With this goal in mind, phenylacetylene seemed a convenient candidate as starting point to explore the feasibility of our prospect (**Table II-11**), since its radical hydrogermylation with Ph₃GeH was achieved with high degrees of regioselectivity (controlled by steric factors).^{33,36,131}

۶ 209 246	$\frac{\alpha}{\beta}$ $\frac{Ph_{3}GeH (1.3 equiv)}{Conditions}$ $\frac{Ph_{3}GeH (1.3 equiv)}{Conditions}$ $\frac{then NH_{4}CI/NH_{3}}{or ND_{4}CI/D_{2}O}$ $246 (R^{1} = OMe)$			H Ph ₃ Ge 247 (R 248 (R	H = H $1 = OMe$	+ Η Ph ₃ Ge [² H(α)]- 2 4 [² H(α)]- 2 4	D R^1 47 ($R^1 = H$) 48 ($R^1 = OMe$) 1	+ D. Ph ₃ ([² H(β)]- [² H(β)]-	247 (R ¹ = H) 248 (R ¹ = OMe)
Entry	R ¹	Solvent	time	Т	Quench	Product	Yield (%) ^{a,b}	d.r. (Z/E) ^c	Ratio I : II : III ^d
1	Н	<i>n</i> -hexane	16 h	40 °C	Н	247	56	68:32	-
2	Н	<i>n</i> -hexane	16 h	40 °C	D	247	nd ^e	nd ^e	35:21:44
3	OMe	<i>n</i> -hexane	3 h	0 °C	D	248	63 ^{<i>f</i>}	93:7	71:0:29
4	OMe	THF	3 h	0 °C	D	248	86 ^f	94:6	100:0:0

TABLE II-11. Preliminary experiments of the germylzincation of terminal phenylacetylene derivatives.

^{*a*}Only β -germylated regioisomers were detected. ^{*b*}Isolated yield as a mixture of diastereoisomers. ^{*c*}Determined by ¹H NMR prior to purification. ^{*d*}Ratio determined just for the major isomer (*Z*). ^{*e*}Not determined. /Yield estimated by ¹H NMR analysis of the crude reaction mixture using butadiene sulfone as internal standard. An initial experiment in *n*-hexane at 40 °C did yield vinylgermane **247**, but in a modest isolated yield, and with poor stereoselectivity (Z/E = 68:32) (Table II-11, entry 1). A more acute problem surfaced when performing D-labeling experiments: just 21% of the product obtained arose from the germylzincation process, the major compound being formed by direct hydrogermylation of phenylacetylene and also of the metalated starting material (Table II-11, entry 2). Discouraged by these results, we decided to use 2-ethynylanisole **246**, with the hope that a possible directing effect from the methoxy group could favor germylzincation. A preliminary screening of the reaction conditions, in both *n*-hexane and THF (Table II-11, entries 3 and 4), showed that by lowering the temperature, a marked increase of the stereoselectivity of the reaction was obtained. In fact, as we found out later, the erosion of stereocontrol observed with phenylacetylene at higher temperatures was due to the isomerization of the initially formed *Z*-vinylgermane. In any case, no germylzincation product [²H(α)]-**248** was observed in *n*-hexane at 0 °C. This was also the case in THF, despite the fact that deprotonation of the starting material could be avoided.

Although a setback, this outcome was understandable (Scheme II-74).



SCHEME II-74. Hydrogermylation *vs* germylzincation of phenylacetylene: Regio- and stereoselectivity rationalization.

After initial β addition of the germyl radical (favored by steric factors and by the higher stability of the vinyl radical intermediate formed (**249** *vs* **250**)), linear radical **250** is obtained (stabilized by delocalization of the unpaired electron in the aromatic system). Subsequent reaction with either Ph₃GeH or Et₂Zn should occur from the less hindered side opposite to the germyl moiety (*anti* addition). A hydrogen atom does not constitute a serious steric obstacle, and in such a case H-atom transfer from the hydrogermane is seemingly more favorable than S_H2 with Et₂Zn: hydrogermylation outcompetes germylzincation.

In retrospect, the precedents for radical hydrogermylation spoke in favor of the feasibility of the addition of germyl radicals to terminal acetylenes,^{6,31-33,35,36,131} a prerequisite for the germylzincation to be possible, but were also a warning about the possibility of facing competitive hydrogermylation, as we indeed did. Consequently, we decided to explore internal alkynes for which direct radical hydrogermylation had been scantily reported^{6,9,10} and appeared thus less favorable.

II-6.2. OUTCOMPETING HYDROGERMYLATION: SELECTION OF 1-PHENYL-1-PROPYNE AS MODEL SUBSTRATE

II-6.2.1. The proof of concept

Building on accumulated experimental evidence indicating that direct hydrogermylation of internal ynamides was a difficult process while germylzincation performed well, we decided to investigate 1-phenyl-1-propyne as substrate, with the hope that the methyl substituent in the alkyne terminus might hold back the H-atom transfer from the hydrogermane to the vinyl radical and thus favor germylzincation over hydrogermylation (**Scheme II-75**).



SCHEME II-75. General aspects that underpinned our selection of 1-phenyl-1-propyne as model substrate for the germylzincation reaction.

We were pleased to find out that our rationalization proved correct (Scheme II-76).



aromatic signals of the minor isomer.

SCHEME II-76. Initial assays of the germylzincation of 1-phenyl-1-propyne.

A first experiment involving THF as solvent at 40 °C provided compound **252** with an excellent β regioselectivity and *Z* stereoselectivity, albeit in moderate 40% yield. Most striking turned out to be the reversal of stereoselectivity observed by just switching the solvent to *n*-hexane, while still keeping the high regiocontrol. The structure of the products was confirmed by X-ray crystallography of the *E* isomer. More importantly, and what definitely provided the proof-of-concept for the project, was the high D-incorporation observed in both cases, thus demonstrating that the germylzincation pathway outcompeted the hydrogermylation process.

The excellent regioselectivity achieved with internal alkyne **251** (both in THF and *n*-hexane) is a particularly appealing asset of the radical approach since, unlike terminal alkynes that typically undergo elementometalation with high levels of regiocontrol,^{20,54,132,133} internal alkynes usually require the presence of specific substituents, e. g. $CO_2R^{8,11}$ or SiR_3 ,^{128,130} to achieve useful control. Once again, the difference of stability of the vinyl radical formed, as well as steric effects governing the initial radical addition step, can account for the high level of regioselectivity observed.

Regarding stereocontrol, we quickly conjectured that the difference in stereoselectivity in THF or *n*-hexane could arise from a possible isomerization (in *n*-hexane) of the kinetically formed *E* vinylzinc intermediate into the thermodynamically favored *Z* isomer (**Scheme II-77**). Similarly to the mechanism proposed by Oshima for the isomerization of vinylgermanes in radical

conditions, such isomerization should reasonably occur through addition of the triphenylgermyl radical to the vinylzinc intermediate *E*-**253**, followed by rotation around the carbon–carbon single bond, and subsequent elimination of the triphenylgermyl radical.



SCHEME II-77. Proposed isomerization mechanism of vinylzinc intermediates.

Since the configuration strongly determines the chemical and physical properties of an alkene motif, on top of the biological profile, it was of utmost importance to gain rigorous control over this structural feature. Hence, from this point onward, two different routes to **252** were pursued in order to obtain either of the stereoisomers.

II-6.2.2. In pursuit of kinetic stereocontrol

Starting from the preliminary reaction conditions that led to the formation of *Z*-**252** in THF (**Table II-12**, entry 1), we first undertook the quest for kinetic stereocontrol, i. e., the stereoselective preparation of the *Z* isomer through *trans*-selective germylzincation.

		α	Et ₂ Zn (3.0 equiv Ph ₃ GeH (n equiv	') /)				
		^в Ме 251	THF Conditions then NH ₄ Cl/NH ₃		$\begin{array}{cccc} & & & & & & & \\ & & & & & & \\ & & & &$			
Entry	c [M]	Ph₃GeH (equiv)	Radical initiator	MW	time	Т	Yield 252 (%) ^{a,b}	d.r. 252 (<i>Z/E</i>) ^c
1	0.09	1.3	-	-	24 h	40 °C	40^d	90:10
2	0.18	2.0	-	-	24 h	40 °C	59	81:19
3	0.18	2.0	-	-	1 h	80 °C	10	88:12
4	0.18	2.0	AIBN (10 mol%)	-	1 h	80 °C	53	51:49
5	0.18	2.0	AIBN (10 mol%)	Х	1 h	80 °C	60	39:61
6	0.18	2.0	AIBN (25 mol%)	-	1 h	80 °C	66	35:65
7	0.18	2.0	AIBN (50 mol%)	Х	1 h	100 °C	98	16:84
8	0.18	2.0	Dilauroyl peroxide (DLP) (10 mol%)	Х	1 h	80 °C	19	74:26
9	0.18	2.0	DPAP (50 mol%) ^e	-	1 h	rt	20 ^f	90:10

 TABLE II-12. Optimization of the germylzincation of 1-phenyl-1-propyne in THF.

 ${}^{a}\beta/\alpha > 95:5$ in all cases. b Yield estimated by 1 H NMR analysis of the crude reaction mixture using butadiene sulfone as internal standard. c Determined by 1 H NMR prior to purification. d Isolated yield. e The reaction was run in a UV reactor at 365 nm. f Complex mixture of products.

An increase of both concentration of the reaction medium and amount of hydrogermane provided a better 59% yield but with a slightly eroded stereoselectivity (Z/E = 81:19) (Table II-12, entry 2). Since kinetic stereocontrol is favored with shorter reaction times, we sought to find conditions to reduce the time necessary to achieve full conversion. Toward this end, we increased the temperature to 80 °C and, after 1 h, it was possible to prevent isomerization (Z/E = 88:12), but a low 10% yield was obtained (Table II-12, entry 3). We next considered using a better initiation system, since the low yield obtained even after long reaction times was suggestive of less efficient radical chains than for ynamides. We therefore added AIBN as radical initiator and kept the reaction temperature at 80 °C to ensure its decomposition. After 1 h of reaction, the yield was comparable to the one obtained after 24 h at 40 °C, but the stereocontrol was totally lost (Z/E = 51:49) (Table II-12, entry 4). Hence, conversion was increased, but isomerization also.

Since microwave (MW) heating is known to increase the rate of thermal dissociation of azo, peroxide or other initiators, and thus promote a faster initiation,¹³⁴ we then reproduced this last experiment under MW irradiation. However, the stereoselectivity was even poorer (Z/E = 39:61) (Table II-12, entry 5). Further increase of the loading of radical initiator in both oil bath (Table

II-12, entry 6) and MW, along with higher temperatures (Table II-12, entry 7), led to increasing yields and more extensive isomerization.

A final attempt to gain kinetic control over this reaction was focused on surveying other initiation systems. Firstly, we switched to dilauroyl peroxide as radical initiator (Table II-12, entry 8); nonetheless, low yield and poor stereoselectivity were the results of this approach. Indeed, since high temperatures could be detrimental for the stereocontrol, we therefore explored initiation systems that could operate at rt. The first choice was to use Et₃B; however, despite a really promising initial experiment affording 88% isolated yield and an excellent *Z* stereoselectivity (*Z*/*E* = 95:5), we never succeeded in reproducing this reaction (not included in the table). Finally, we tested DPAP, a radical photoinitiator that generates acyl and methyl radicals under UV radiation (λ_{max} = 365 nm) at rt (Table II-12, entry 9). However, once again, low yield of the desired product *Z*-**252** was obtained, in this case immersed in a complex reaction mixture.

Unfortunately, despite our efforts, we could not improve the initial result obtained in THF and this discouraged us to further explore this direction. Consequently, we decided to pursue the second route: to shift the E/Z equilibrium of the vinylzinc intermediates toward the Z isomer in order to access the E vinylgermane with synthetically useful levels of selectivity.

II-6.2.3. Tuning the system for *E* selectivity

As previously indicated, our first trials in *n*-hexane at 40 °C already rendered a 65% isolated yield with a good *E* stereoselectivity (E/Z = 88:12) (**Table II-13**, entry 1).

		β α Me 251	E Ph th or N	t_2Zn (n equ $_3GeH$ (n eq <i>Conditions</i> <i>en</i> NH ₄ Cl/N ND ₄ Cl/D ₂ O/	iv) uiv) H ₃ F THF	Me Ph ₃ Ge	E (F = H)	+ Ph ₃ 0	Ge Me -252	E	
				E-232 () E-[² H]-252 ()			(E = D)	Z-[² H]	-252	(E = D)	
Entry	c [M]	Solvent	Ph3GeH (equiv)	Et2Zn (equiv)	AIBN (mol%)	MW	time	Т	E	Yield 252 (%) ^{<i>a,b</i>}	d.r. 252 (<i>E/Z</i>) ^c
1	0.09	<i>n</i> -hexane	1.3	3.0	-	-	16 h	40 °C	Н	65 ^{<i>d</i>}	88:12
2	0.09	<i>n</i> -hexane	2.0	3.0	-	-	16 h	40 °C	Н	98	86:14
3	0.18	<i>n</i> -hexane	2.0	3.0	-	-	16 h	40 °C	Н	98	94:6
4	0.18	<i>n</i> -hexane	2.0	3.0	-	-	16 h	40 °C	D	90 ^e	90:10
5	0.25	<i>n</i> -hexane	2.0	3.0	-	-	16 h	40 °C	Н	94	91:9
6	0.18	heptane	2.0	3.0	10	-	16 h	100 °C	Н	>99	93:7
7	0.18	heptane	2.0	3.0	10	X	1 h	100 °C	H	97	96:4
8	0.18	heptane	2.0	3.0	10	X	1 h	100 °C	D	> 99 ^e	95:5
9	0.18	heptane	2.0	3.0	10	-	1 h	100 °C	Н	90	95:5
10	0.18	heptane	2.0	3.0	10	-	2 h	100 °C	H	93 ^d	95:5
11	0.18	heptane	2.0	3.0	10	-	2 h	100 °C	D	99 d,e	98:2
12	0.18	heptane	2.0	-	10	-	2 h	100 °C	Н	90 ^{<i>f</i>}	94:6
13	0.18	heptane	0.8	-	10	-	2 h	100 °C	Н	80 ^{<i>g</i>,<i>h</i>}	4:96
14	0.18	heptane	0.8	3.0	10	-	2 h	100 °C	Н	62 ^{<i>g</i>,<i>h</i>}	79:21

TABLE II-13. Optimization of the germylzincation of 1-phenyl-1-propyne in *n*-hexane or heptane.

 $a\beta/\alpha$ > 95:5. ^bYield estimated by ¹H NMR analysis of the crude reaction mixture using butadiene sulfone as internal standard. ^cDetermined by ¹H NMR prior to purification. ^dIsolated yield. ^e[²H] = 95%. ^f β/α = 93:7. $g\beta/\alpha = 94:6$. ^hBased on 1-phenyl-1-propyne.

Keeping *n*-hexane as solvent, further modification of the reaction conditions showed the effect that both the amount of hydrogermane and the concentration of the reaction medium had in the outcome of this protocol. Increasing the equivalents of hydrogermane led to a considerable improvement of the yield (from 65% to 98%) (Table II-13, entry 2), while increase of the concentration provided an enhanced stereoselectivity (from E/Z = 86:14 to 94:6) (Table II-13, entry 3). However, these reaction conditions did not provide totally reproducible results, as can be noticed from the D-labeling experiment (Table II-13, entry 4). Notwithstanding, the excellent D-incorporation detected in the crude reaction mixture indicated that we were on the right track.

Afterwards, an even higher increase of the concentration of the reaction medium to 0.25 M did not furnish any progress (Table II-13, entry 5). Therefore, we decided to add AIBN as radical initiator. To begin with, the temperature of the reaction was raised to 100 °C, and we thus decided to switch to the analogous higher boiling point solvent heptane (which is also less toxic) (Table II-13, entry 6). Quantitative yield and good stereoselectivity were achieved after 16 h of reaction time. By employing the same reaction conditions under MW irradiation for one hour, full conversion, even improved stereoselectivity, and totally reproducible results were obtained (Table II-13, entry 7). The excellent outcome while using a non-polar solvent with a low loss factor advocated for a "simple" MW-assisted heating process. Consistently, in the absence of MW, a high yield (even if not quantitative) and the same excellent stereoselectivity were achieved (Table II-13, entry 9). By just increasing the reaction time to 2 h (Table II-13, entry 10), comparable results to the ones obtained in MW were observed with conventional heating. In addition, the excellent D-incorporation observed in both cases confirmed the exclusive formation of the vinylzinc intermediate (Table II-13, entries 8 and 11). In conclusion, optimized reaction conditions for the cis-selective germylzincation of 1-phenyl-1-propyne involved 2.0 equiv of hydrogermane with 10 mol% AIBN in heptane at 100 °C, in either oil bath for 2 h or MW for 1 h. It is worthy to mention that, since the results for both protocols were basically the same, no specific effect of microwaves seems to be involved in this reaction.

To complete the picture, the reaction was then performed in the absence of Et_2Zn in order to evaluate a possible impact of direct radical hydrogermylation (that had not been described for internal arylacetylenes). Much to our surprise, the reaction provided vinylgermane **252** in high yield (90%) and with high *E* stereoselectivity (Table II-13, entry 12). Even more, when performed in default Ph₃GeH (0.8 equiv), similarly high yield was obtained with remarkable *Z* stereoselectivity! (Table II-13, entry 13). In point of fact, here the *Z*-to-*E* isomerization did not compete with the alkyne hydrogermylation process (the Ph₃Ge• radical does not react with the vinylgermane being formed while there is remaining 1-phenyl-1-propyne); the triphenylgermane simply run out before the isomerization could get even started. Hence, it is feasible to perform the hydrogermylation to yield both the kinetic product (in default Ph₃GeH) and the thermodynamic one (in excess Ph₃GeH) (**Scheme II-78**).





This prompted us to revisit the germylzincation in default of hydrogermane (Table II-13, entry 14), but unfortunately, here, isomerization of the vinylzinc intermediate occurred to a significant extent even in the presence of starting alkyne.

II-6.2.4. Mechanism

Hence, we propose the following reaction mechanism for the germylzincation of 1-phenyl-1propyne (**Scheme II-79**).



SCHEME II-79. Proposed reaction mechanism for the germylzincation of 1-phenyl-1-propyne.

After initiation by AIBN, germanium-centered radicals **60** add across the carbon-carbon triple bond of the starting alkyne to provide vinyl radical **255**. In theory, two possible radicals could arise from this addition step, specifically, with the germyl moiety in either the α (not shown) or β positions (**255**). Stabilization through conjugation with the phenyl ring makes radical **255** more stable and accounts for the highly favorable β addition. This step is regiodiscriminating. From here on, subsequent reaction of linear vinyl radical **255** with Et₂Zn affords exclusively *E*-**256**, as a result of the approach of Et₂Zn from the less hindered side opposite to the germyl group. Depending on the reaction conditions, *E*-**256** can isomerize to the thermodynamically more stable *Z*-**256**, likely through a reversible triphenylgermyl radical addition-elimination sequence involving intermediates **257** or **258**. Upon quench, *E*-**256** yields *Z*-**252** and *Z*-**256** delivers *E*-**252**.

The initiation process of the radical chain deserves further comment. Indeed, AIBN was remarkably efficient in comparison to the other radical initiators used. AIBN is an azo radical initiator that decomposes thermally by cleavage of two carbon–nitrogen bonds to produce nitrogen gas and two α -cyano-substituted alkyl radicals.¹³⁵ We suggest that the electrophilic character of radicals **254** contributes to the distinctive performance of AIBN, since subsequent hydrogen abstraction from the hydrogermane (**254** \rightarrow **60**) could benefit from favorable polarity-matching effects.

II-6.2.5. Reaction scope and limitations

With the optimized conditions in hand for the *cis*-selective germylzincation of 1-phenyl-1propyne, we then explored the scope of this transformation for other (aryl, alkyl)-substituted alkynes.

1-phenyl-1-butyne

To start with, commercially available 1-phenyl-1-butyne **259** was tested (**Table II-14**). The previously optimized conditions led to the formation of the desired product with a lower-thanexpected yield and stereoselectivity (64%, E/Z = 87:13) (Table II-14, entry 1). However, by just increasing the amount of AIBN (from 10 mol% to 25 mol%), excellent yield and improved stereoselectivity were obtained (Table II-14, entry 2), and subsequent reaction scale-up to 1.0 mmol was accomplished without deterioration of the reaction outcome (Table II-14, entry 3).

	β ^α Et 25	Et ₂ Zn (Ph ₃ GeH AIBN heptar 0. then N	Et ₂ Zn (3.0 equiv) Ph ₃ GeH (2.0 equiv) AIBN (n mol%) heptane, 100 °C 0.18 M then NH ₄ Cl/NH ₃ F-260				Ph ₃ Ge H Et Z-260		
Entry	Scale ^a	AIBN (mol%)	MW	time	Yield 260 (%) ^b	β/α^{c}	d.r. 260 (<i>E/Z</i>) ^c		
1	0.25 mmol	10	Х	1 h	64	95:5	87:13		
2	0.25 mmol	25	Х	1 h	94 (91) ^d	95:5	95:5		
3	1.00 mmol	25	-	5 h	98 (94) ^d	95:5	95:5		

 TABLE II-14. Germylzincation of 1-phenyl-1-butyne.

^{*a*}Based on 1-phenyl-1-butyne. ^{*b*}Yield estimated by ¹H NMR analysis of the crude reaction mixture using butadiene sulfone as internal standard. ^{*c*}Determined by ¹H NMR prior to purification. ^{*d*}Isolated yield is shown in parenthesis.

Propargylic alcohols

We then turned our attention to a substrate class that has gained noticeable attention due to their numerous applications in organic synthesis built on their dual functional groups: propargylic alcohols.^{108,135} Additionally, we were also interested in studying the influence of the hydroxy group on the regio- and stereoselectivity of the germylzincation.

To do so, we selected three examples: primary, secondary and tertiary aryl-substituted propargylic alcohols **261–263** (**Scheme II-80**). Primary and secondary propargylic alcohols **261** and **262** were commercially available, and tertiary propargylic alcohol **263** was readily prepared after deprotonation of phenylacetylene with *n*BuLi, and subsequent addition to camphor **264**.



SCHEME II-80. Aryl-substituted propargylic alcohols selected for the germylzincation reaction.

Accordingly, we then explored the germylzincation reaction of the targeted propargylic alcohols (**Table II-15**).

Treatment of **261** under the conditions previously described for 1-phenyl-1-butyne afforded clean conversion to a single vinylgermane (Table II-15, entry 1), which this time was the *Z* isomer (*Z*/*E* > 98:2). In order to shed some light into this situation, we performed the reaction in the absence of Et₂Zn. Similar high yield but opposite stereoselectivity (*Z*/*E* = 14:86) was obtained in this case *with excess Ph*₃*GeH* (thermodynamic product) (Table II-15, entry 2). We will return to this point later in the discussion of the reaction mechanism.

		Et ₂ Zn Ph ₃ G All	(0 <i>or</i> 3.0 equiv) GeH (2.0 equiv) BN (n mol%)		[+ $R^1 R^2$			
	HOR ¹ R ²	her the	otane, 100 °C 0.18 M n NH ₄ Cl/NH ₃	Ph_3Ge H HO R^2 T_2	+ HO Ph ₃ Ge	H			
Entry	Substrate	Et2Zn (equiv)	AIBN (mol%)	Product	Yield (%) ^a	β/α ^b	d.r. (Z/E) ^b		
1	но	3.0	25	Ph ₃ Ge H HO <i>Z-</i> 265	87 (87) ^c	>98:2	>98:2		
2	H0261	_	10	но н Ph ₃ Ge <i>E-</i> 265	84	>98:2	14:86		
3	HO Me 262	3.0	25	Ph ₃ Ge H HO Me Z-266	94 (83) ^c	>98:2	>98:2		
4	HO 263	3.0	25	Ph ₃ Ge H HO HO 267	0	_	_		

 TABLE II-15. Germylzincation and hydrogermylation reactions of aryl-substituted propargylic alcohols.

^{*a*}Yield estimated by ¹H NMR analysis of the crude reaction mixture using dimethyl sulfone as internal standard. ^{*b*}Determined by ¹H NMR prior to purification. ^{*c*}Isolated yield is shown in parenthesis.

Secondary propargylic alcohol **262** also performed well (Table II-15, entry 3). Excellent yield, regio- and stereoselectivities were obtained again in favor of the *Z* isomer. By contrast, tertiary propargylic alcohol **263** did not react at all (Table II-15, entry 4). This was not totally unexpected since the β carbon of **263** is highly sterically congested, and it is well-known that intermolecular radical additions are extremely susceptible to steric factors. For instance, previously reported

radical hydrostannation of tertiary propargylic alcohols gave rise to poor overall conversion, and substrates bearing complex branching adjacent to the tertiary OH often failed to react.^{108,136}

A final remark that deserves further highlight is the high stability of these germylated alcohols in column chromatography, in sharp contrast with the greater sensitivity of many stannylated alcohols toward protodestannylation on silica gel.^{108,137,138}

In light of the above-described results, a refined reaction mechanism for this substrate type was proposed (**Scheme II-81**).





The first detail to be underlined is the deprotonation of the alcohol function in the presence of Et_2Zn (**261** \rightarrow **268**). From here on, a similar mechanism to the already described for 1-phenyl-1-propyne is represented. After initiation (In[•]), regioselective addition of the germyl radical **60** to propargylic zinc alkoxide **268** renders vinyl radical intermediate **269**. Subsequent $S_{H}2$ step provides vinylzinc *E*-**270**, along with Et[•] radical that propagates the radical chain. The reason why no subsequent isomerization of vinylzinc *E*-**270** is observed may be found in the proposed structure of this intermediate: a metallacycle. The cyclometalated motif locks the configuration of the double bond and accounts for the final *Z* stereoselectivity observed (after protodemetalation). In line with this rationale, in the absence of Et_2Zn , direct hydrogermylation should give initial access, after H-atom transfer to vinyl radical intermediate **271**, to the *Z*-configured vinylgermane **265**, which unlocked, would then undergo isomerization to the thermodynamically more stable *E*-**265** in the presence of Ph₃Ge[•] radicals (excess Ph₃GeH).

Propargylic acetate

Simultaneously, we investigated the behavior of propargylic acetate **272** under hydrogermylation and germylzincation reaction conditions (**Scheme II-82**).



SCHEME II-82. Reactions of propargylic acetate **272** under hydrogermylation and germylzincation conditions.

As expected, in default Ph_3GeH , direct hydrogermylation yielded vinylgermane **273** with excellent *Z* stereoselectivity. This result ratifies, in conjunction with the experiment shown in Table II-15, entry 2, that either *trans*- or *cis*-selective radical hydrogermylation can be achieved in default or excess hydrogermane, respectively.

Surprisingly, under germylzincation conditions, the sole formation of allenylgermane **274** was observed in the crude reaction mixture. The only explanation we could find to account for the formation of this product would be to envisage the formation of Ge–Zn species (either $(Ph_3Ge)_2Zn$ or $Ph_3GeZnEt$), that could react with propargylic acetate **272** through a S_N2' mechanism, driven by the presence of acetate as leaving group (LG). This could be even fuelled by the Lewis acidity of Et_2Zn that could coordinate to the carbonyl oxygen of the acetyl group. However, why no radical germylzincation was occurring to any extent with this specific substrate is still an unanswered question.

(Aryl, TMS)-substituted alkyne

To end with, (phenyl, TMS)-substituted alkyne **275** was employed (**Scheme II-83**). Capitalizing on our previous experience with TIPS-substituted ynamides, it was not surprising that the formation of the β adduct was not detected. This could be attributed to the steric hindrance imposed by the TMS-group on the acetylenic carbon where the germyl addition usually takes place, or to the unfavorable polarization of the C(sp)–Si bond that renders this carbon more nucleophilic. However, reversal of regioselectivity in favor of the α addition was not observed either.



SCHEME II-83. Germylzincation reaction of trimethyl(phenylethynyl)silane 275.

II-6.3. FACING REGIOCONTROL CHALLENGES: FROM DIARYLACETYLENES...

Subsequently, we decided to explore diarylacetylene-type compounds.

II-6.3.1. Optimization studies

To avoid regioselectivity issues and focus initially on stereoselectivity, diphenylacetylene **277** was used as the point of departure. We began investigating the possibility to achieve E

selectivity (**Table II-16**) since this approach was most successful with (aryl, alkyl)-substituted alkynes.

				Et ₂ Zn Ph ₃ Ge Cor then N or ND ₄ 0	(3.0 e H (n e nditior NH ₄ Cl/ Cl/D ₂ C	quiv) quiv) ns NH ₃ D/THF	Ph ₃	Ge	E PI	n ₃ Ge	E	
		27	77				E- 2 E-[² H]- 2	78 (E 78 (E	= H) = D) Z-[²	<i>Z-</i> 278 (E H]-278 (E	= H) = D)	
Entry	c [M]	Solvent	Ph₃GeH (equiv)	AIBN (mol%)	MW	time	Т	E	Conversion (278/277) ^a	d.r. 278 (<i>E/Z</i>) ^a	Yield 278 (%) ^b	d.r. 278 (<i>E/Z</i>) ^c
1	0.09	<i>n</i> -hexane	1.3	-	-	16 h	40 °C	Η	82:18	40:60	64	40:60
2	0.09	<i>n</i> -hexane	1.3	-	_	16 h	40 °C	D	85:15	45:55	82	45:55

TABLE II-16. Optimization of the germylzincation of diphenylacetylene: the quest for *E* selectivity.

^{*a*}Estimated by ¹³C NMR analysis of the crude reaction mixture.^{*i*} ^{*b*}Isolated yield. ^{*c*}Determined by ¹H NMR after purification. ^{*d*}Not determined.

16h 100°C H

16h 120°C H

Η

1 h 100 °C

100:0

100:0

100:0

76:24

77:23

67:33

nd^d

nd^d

nd^d

nd^d

 nd^d

 nd^d

3

4

5

0.18 benzene

0.18 benzene

0.18 heptane

2.0

2.0

2.0

10

10

100

Х

_

An initial experiment in *n*-hexane at 40 °C (Table II-16, entry 1) provided comparable yield to 1-phenyl-1-propyne under identical reaction conditions (64% *vs* 65%) but with a lower stereoselectivity (E/Z = 40.60 vs 88:12). D-labeling confirmed the sole formation of vinylzinc intermediates, with excellent D-incorporation for both stereoisomers (Table II-16, entry 2). It thus became evident that harsher reaction conditions were required in order to shift totally the selectivity toward the *E* isomer. With this goal in mind, we then increased the concentration of the reaction medium, the amount of hydrogermane, the temperature, and AIBN was added as radical initiator while switching to a solvent of choice for radical reactions (despite its toxicity): benzene. Full conversion and improved selectivity in favor of the *E* isomer were obtained (Table II-16, entry 3), but still far from optimal (E/Z = 76:24). MW irradiation during 1 h afforded analogous results (Table II-16, entry 4), thus suggesting that perhaps the thermodynamic equilibrium was reached. Even harsher reaction conditions, this time in heptane (that has provided similar results to benzene with the advantage of a lower toxicity), together with a further increase of the amount of

¹ The stereoselectivity of the reaction in the crude mixture was estimated from the ¹³C NMR CH vinylic signals of both stereoisomers. The sequence used was not quantitative but, in general terms, a qualitative analysis was obtained and good correlations were found between the estimated stereoselectivity in the crude and the measured one by ¹H NMR of the isolated compound.

AIBN (from 10 mol% to 100 mol%), and temperature (to 120 °C) did not furnish any stereoselectivity improvement (Table II-16, entry 5).

Turning to hydrogermylating conditions, i.e. in the absence of Et_2Zn , a stereodivergent outcome was obtained under excess-triphenylgermane and default-triphenylgermane regimes (**Scheme II-84**). These results echo the stereodivergent hydrogermylation of (aryl, alkyl)-substituted alkynes. Good-to-excellent stereoselectivities were obtained with diphenylacetylene under both regimes, being worth-mentioning the complete isomerization observed toward the *E*-vinylgermane with excess triphenylgermane, by contrast with the germylzincation outcome.



SCHEME II-84. Stereodivergent hydrogermylation of diphenylacetylene under default- and excess-Ph₃GeH regimes.

This was rationalized on the basis of the equilibria between kinetic and thermodynamic products in both hydrogermylation and germylzincation reactions (**Scheme II-85**). In general, due to steric reasons, *E* alkenes are usually more stable than the corresponding *Z* alkenes. Control over product stereochemistry can be imposed by a sufficient size difference between substituents on the double bond. This seems to be the case under hydrogermylation conditions, where the favored formation of the *E* isomer under thermodynamic control can be probably justified by the steric bias. Note however that, when performing the germylzincation, vinylgermane **278** is no longer the intermediate that determines the *E*/*Z* ratio of the reaction. In this case, vinylzinc intermediates **279** are responsible for the stereoselectivity outcome, where the relative hindrance of the substituents determining the final composition of the mixture of stereoisomers is different than for vinylgermane **278**, and therefore, a different thermodynamic equilibrium could be expected. In addition, other factors, such as the ease of isomerization through additionelimination of germyl radicals to vinylzinc intermediates compared to vinylgermanes, should certainly play a role in the ultimate *E*/*Z* ratio observed.



SCHEME II-85. Kinetic *vs* thermodynamic product: Difference between hydrogermylation and germylzincation equilibria.

Germylzincation of diphenylacetylene **277** in non-polar solvents did not translate into a synthetically useful E/Z ratio in favor of the E isomer. Nevertheless, the noted lower ease for isomerization impelled us to consider the selective formation of the Z isomer (**Table II-17**).

TABLE II-17. Optimization of the germylzincation of diphenylacetylene: the quest for Z selectivity.

	Et ₂ Zn (3.0 equiv) Ph ₃ GeH (2.0 equiv)	Ph ₃ Ge	+
	THF	E	' K
	Conditions		Ph ₃ Ge
	or ND ₄ Cl/D ₂ O	\sim	
277	0/11040/020	Z- 278 (E = H)	<i>E-</i> 278 (E = H)
		Z-[² H]- 278 (E = D)	<i>E-</i> [² H]- 278 (E = D)

Entry	c [M]	AIBN (mol%)	MW	time	Т	Е	Conversion (278/277) ^a	d.r. 278 (Z/E) ^a	Yield 278 (%) ^b	d.r. 278 (Z/E) ^c
1	0.18	_	-	16 h	40 °C	Н	64:36	88:12	49	82:18
2	0.18	25	-	1 h	80 °C	Н	80:20	>98:2	67	92:8
3	0.18	25	-	1 h	80 °C	D	74:26	>98:2	71 [98% D]	92:8
4	0.18	25	Х	1 h	80 °C	Н	92:8	95:5	74	88:12
5	0.18	50	Х	1 h	80 °C	Н	100:0	87:13	nd ^d	nd^d
6	0.18	50	Х	1 h	70 °C	Н	87:13	91:9	nd ^d	nd^d
7	0.18	50	Х	0.5 h	80 °C	Н	94:6	92:8	nd ^d	nd^d
8	0.09	50	Х	1 h	80 °C	Н	80:20	96:4	nd ^d	nd^d
9	0.18	-	-	1 h	80 °C	Н	10:90	>98:2	nd ^d	nd^d

^{*a*}Estimated by ¹³C NMR analysis of the crude reaction mixture. ^{*b*}Isolated yield. ^{*c*}Determined by ¹H NMR after purification. ^{*d*}Not determined.

With THF as solvent of choice, initial reaction in the absence of radical initiators led to the isolation of the desired product in 49% yield and with *Z* selectivity (Z/E = 82:18) (Table II-17,

entry 1). Since long reaction times could increase the amount of the *E* isomer, we then performed the reaction just for 1 h at 80 °C with 25 mol% AIBN as initiator (Table II-17, entry 2). An improved 80% conversion was observed, together with an excellent stereoselectivity in the crude reaction mixture (Z/E > 98:2), which translated into a decent 67% isolated yield with Z/E = 92:8. Subsequent D-labeling experiment furnished a 71% isolated yield in [²H]-**278** with an excellent D-incorporation (98%) and identical stereoselectivity (Table II-17, entry 3). By switching from conventional heating to MW irradiation, an enhanced conversion was observed, delivering the desired product in 74% yield, but with lower stereocontrol (Z/E = 88:12) (Table II-17, entry 4). By adding more AIBN (50 mol%) full conversion was finally achieved, but it was detrimental for the stereoselectivity (Table II-17, entry 5). Further reduction of either the temperature (to 70 °C) (Table II-17, entry 6), reaction time (to 0.5 h) (Table II-17, entry 7), or concentration of the reaction medium (to 0.09 M) (Table II-17, entry 8) did not furnish improved results compared to entry 2. Finally, a last experiment under the optimized reaction conditions but in the absence of AIBN allowed us to confirm the radical character of this reaction, since a low 10% conversion was obtained (Table II-17, entry 9).

II-6.3.2. Reaction scope and limitations

Having established the optimized conditions for the *trans*-selective germylzincation of diphenylacetylene **277**, we then focused on exploring the scope of this transformation. To do so, a series of symmetrical and non-symmetrical diarylacetylenes were considered (**Scheme II-86**).



SCHEME II-86. Symmetrical and non-symmetrical diarylacetylenes selected for the germylzincation reaction.



Substrates **280–281**, **283** were commercially available. On the other hand, **282**, **284–286** were readily prepared *via* Sonogashira cross-coupling reactions as depicted in **Scheme II-87**.

SCHEME II-87. Synthesis of diarylacetylenes 282, 284–286.

Starting from symmetrical diarylacetylenes (**Scheme II-88**), both electron-donating and electron-withdrawing groups in *para*-positions were well tolerated. Accordingly, vinylgermane **287** bearing electron-donor *n*Bu group in *para*-positions, in addition to vinylgermanes **288** and **289** with *para*-bromo, and *para*-trifluoromethyl substituents, were all obtained in good yields (66–83%) with high *Z* selectivity (Z/E > 87:13). By contrast, vinylgermane **290** decorated with a Bpin substituent in *para*-positions decomposed in column chromatography and could not be isolated and characterized.



SCHEME II-88. Reaction scope for the germylzincation of symmetrical diarylacetylenes.

Subsequently, we decided to explore more challenging non-symmetrical diarylacetylenes (**Scheme II-89**), where the regioselectivity comes to play, and the presence of two substituents of the same chemical nature on the triple bond would definitely make its control highly challenging.



^aConfiguration of each isomer to be confirmed. ^bIsolated as mixture of regio- and stereoisomers. ^cMajor isomer isolated in 57% yield. ^dMajor isomer isolated.

SCHEME II-89. Reaction scope for the germylzincation of non-symmetrical diarylacetylenes.

A possible regiodiscrimination as a consequence of electronic effects was evaluated first by considering substrate **284** having an electron-donor methoxy-substituent on one side and an electron-poor trifluoromethyl-substituent on the other. A mixture of all possible isomers was obtained and they were only isolated as a mixture. Thus, it was not possible to determine the structure and configuration of the major isomer.

Subsequent experiments with (aryl, heteroaryl)-substituted alkynes did not furnish improved results. Vinylgermane **292** was isolated in almost quantitative yield but as a mixture of regioisomers. It is worth-mentioning that each regioisomer was formed as a single *Z* stereoisomer. Here, the major regioisomer could be isolated in a clean fraction and full characterization is in progress. Finally, alkyne **293** bearing a 2-pyridyl group was next considered, since the nitrogen in the 2-position could act as directing group. However, vinylgermane **293** was obtained with a lower stereoselectivity and the same regioselectivity than the analogue bearing a 3-pyridyl substituent, thus indicating that 2-pyridyl is not an efficient directing group here.

II-6.4. ... TO DIALKYLACETYLENES

Finally, the more challenging germylzincation of dialkylacetylenes was considered.

II-6.4.1. Optimization studies

Again, to avoid regioselectivity issues, we began our study on a model symmetrical dialkylacetylene: 4-octyne **294** (**Table II-18**). Since achieving either *Z* or *E* selectivity had proven to be dependent on the substrate type, we first surveyed different conditions with the purpose of determining the feasibility of controlling the stereoselectivity in either direction.

	//,	nPr Ph ₃	Zn (3.0 equiv) GeH (n equiv) _ → Ph₃G	n e	Pr	<i>n</i> Pr	nPr	. ₊ Ph₃Ge	<i>n</i> Pr	
n	Pr ///	(the	Conditions		n Pr	E .	Ph ₃ Ge	6		nPr	ePh ₃
	294	or	ND ₄ Cl/D ₂ O	Z-2 Z-[² H]-2	Z-295 (E = H)E-295 (E = H)E-296Z-[2H]-295 (E = D) $E-[^2H]-295 (E = D)$						
Entry	c [M]	Solvent	Ph₃GeH (n equiv)	AIBN (mol%)	MW	time	Т	E	Yield 295 (%) ^a	d.r. 295 (Z/E) ^b	Yield 296 (%) ^{a,c}
1	0.09	<i>n</i> -hexane	1.3	-	-	16 h	40 °C	Н	30	91:9	4
2	0.18	heptane	2.0	10	-	16 h	80 °C	Н	45	90:10	14
3	0.18	heptane	2.0	10	-	16 h	80 °C	D	47 [94% D]	nd ^d	14
4	0.18	heptane	2.0	50	Х	1 h	100 °C	Н	53	75:25	32 (32) ^e
5	0.18	THF	2.0	10	-	16 h	80 °C	Н	30	94:6	<1
6	0.18	THF	2.0	25	-	1 h	80 °C	Н	31	93:7	<1
7	0.18	THF	2.0	25	-	16 h	80 °C	Н	46 (37) ^{e,f}	90:10	1
8	0.18	THF	2.0	100	-	1 h	80 °C	Н	46	92:8	1
9	0.18	THF	2.0	100	-	16 h	80 °C	Н	62	89:11	3
10	0.18	THF	2.0	100	X	1 h	80 °C	H	72 (58) ^{e,g}	91:9	4
11	0.18	THF	2.0	100	X	1 h	80 °C	D	77 (62) ^e [94% D]	89:11	4
12	0.18	THF	2.0	100	Х	1 h	100 °C	Н	71	85:15	4
13	0.18	THF	2.5	100	Х	2 h	100 °C	Н	83	87:13	6

TABLE II-18. Optimization of the germylzincation of 4-octyne.

^{*a*}Yield estimated by ¹H NMR analysis of the crude reaction mixture using butadiene sulfone as internal standard. ^{*b*}Determined by ¹H NMR prior to purification. ^{*c*}E/Z > 98:2. ^{*d*}Not determined. ^{*e*}Isolated yield is shown in parenthesis. ^{*f*}Isolated as stereochemically enriched *Z* isomer (95:5). ^{*g*}Isolated as stereochemically enriched *Z* isomer (96:4).

The reaction of **294** with Et_2Zn (3.0) and Ph_3GeH (1.3) in the absence of AIBN in *n*-hexane at 40 °C for 16 h led to the formation of vinylgermane **295** in a low 30% yield, but with a marked *trans* selectivity (Z/E = 91:9) (Table II-18, entry 1). This result evidenced the lower reactivity of dialkylacetylene compounds in comparison with diarylacetylenes and (aryl, alkyl)-substituted alkynes, as well as a lower tendency of vinylzinc intermediates to isomerize. To our surprise, this was also the first time that bisgermylated byproduct of type **296** was detected (its structure was confirmed by X-ray crystallography), albeit in a low 4% yield. Increasing the concentration of the reaction medium, the amount of triphenylgermane, the temperature, and adding AIBN in heptane furnished an improved 45% yield and similar stereoselectivity, but an also increased 14% yield of byproduct **296** (Table II-18, entry 2). D-labeling confirmed the formation of vinylzinc

intermediates with a nice 94% of D-incorporation (Table II-18, entry 3). Subsequent increase of AIBN loading and reaction temperature while switching to MW irradiation (1 h) provided a somewhat improved 53% yield but with a drop in the stereoselectivity (Z/E = 75:25) (Table II-18, entry 4). Furthermore, an even higher 32% yield of substrate-consuming byproduct **296** was isolated.

It was obvious that forcing conditions led to higher amounts of bisgermylation. Inspired by analogous bissilylation reactions reported in the context of studies of silylzincation of alkynes,¹³⁰ we reasoned that bisgermylated alkene *E*-**296** could be formed after initial germylzincation upon reductive elimination with carbon–germanium bond formation (considering that a Ph₃Ge-group is directly bonded to the zinc atom in the vinylzinc intermediate formed (**297**)) (**Scheme II-90**). Formation of elementary zinc¹ in the reaction media argued in favor of this proposal.



SCHEME II-90. Possible explanation for the formation of bisgermylated alkene *E*-296.

We then decided to switch to THF, in order to achieve *Z* selectivity. Similar conditions to entry 2 provided a lower 30% yield (*vs* 45%), but with an improved stereoselectivity (*Z*/*E* = 94:6) and, more importantly, a negligible amount of byproduct **296** (<1% *vs* 14%) (Table II-18, entry 5). Increasing the amount of AIBN (from 10 mol% to 25 mol%) while reducing the reaction time (1 h) provided comparable results (Table II-18, entry 6). By contrast, increase of the reaction time (16 h) under the same reaction conditions furnished a better 46% yield, while still preventing the formation of byproduct **296** (Table II-18, entry 7). Increase of the amount of AIBN (to 100 mol%) provided higher yields after both 1 h (Table II-18, entry 8) and 16 h (Table II-18, entry 9), although the stereoselectivity was worse and the amount of byproduct formed was higher. Finally, switching once again to MW irradiation furnished the best results leading to a 72% yield (58% isolated) (Table II-18, entry 10) in **295**, as well as a 77% yield (62% isolated) of the deuterated-analogue with an excellent 94% of D-incorporation upon quench with ND₄Cl/D₂O (Table II-18, entry 11). Here, rise of the temperature (to 100 °C) (Table II-18, entry 12) or increase of the

ⁱ Formation of a dark gray solid was observed in the reaction vessel before quenching.

amount of triphenylgermane and the reaction time (Table II-18, entry 13), led to comparable yields in product **295**, respectively, but with lower stereoselectivities. Additional combinations of reaction conditions (not shown in Table II-18) were not successful to improve the outcomes observed in entries 10-11.

Lastly, a rationalization of the reaction mechanism for this substrate is proposed in **Scheme II-91**.



SCHEME II-91. Proposed mechanism for the *trans*-selective germylzincation of 4-octyne (detailed initiation (In•) has been omitted for the sake of simplicity).

As for our previous proposals, the germylzincation occurs through a radical chain initiated by AIBN. However, by contrast with the mechanisms proposed in this chapter up to now, the radical intermediate generated after the addition of Ph_3Ge is not a linear one, but a bent radical that exists in two diastereosiomeric forms (*Z*- and *E*-**298**) that interconvert rapidly. It seemed reasonable that the *Z* isomer *Z*-**298** would react more rapidly with the Et₂Zn in the subsequent S_H2 step than *E*-**298**, given that the dialkylzinc reagent would avoid the steric interactions with the triphenylgermyl group.

II-6.4.2. Reaction scope and limitations

Our next efforts were directed to explore the scope of this transformation and we thus considered the germylzincation of a series of (mostly) commercially available alkynes, including symmetrical (**300**) and non-symmetrical dialkylacetylenes (**301–302**), as well as (homo)propargylically-oxygenated dialkylacetylenes (**303–307**) (**Scheme II-92**).



SCHEME II-92. Dialkylacetylenes selected for the germylzincation reaction.

Symmetrical dialkylacetylenes

The reaction of symmetrical dialkylacetylene **300** under the optimized conditions did not lead to the desired product **308**, but only to the formation of allenylgermane **309** in 66% yield (**Scheme II-93**). Given the results obtained with propargylic acetate **272** (see section II-6.2.5), this was not totally surprising. Indeed, the presence of a chloride leaving group could funnel the reaction through a S_N2' mechanism by reaction with a putative Ge–Zn species (either (Ph₃Ge)₂Zn or Ph₃GeZnEt). Yet, as for acetate **272**, why no radical germylzincation was occurring to any extent remained unexplained.



SCHEME II-93. Reaction of 1,4-dichlorobut-2-yne 300 under germylzincation conditions.

Non-symmetrical dialkylacetylenes

We then moved on to non-symmetrical dialkylacetylenes (**Table II-19**), where the challenge to control the regioselectivity came into play.

$Me^{\alpha} = Pr: 301$		Et ₂ Zn (3.0 Ph ₃ GeH (2 AIBN (n 0.18 M <i>Condit</i>) equiv) .0 equiv mol%) , 1 h) → Me. Ph₃(H R ¹ +	Me H	ePh₃ ` <mark>R¹ +</mark>	GeF Me Ph ₃ Ge	^թ h ₃ <mark>Հ</mark> 1		
$R^{1} = tBu: 302$			<i>then</i> NH ₄	en NH_4CI/NH_3 β isomers α isomers 310–311					312–313		
Entry	R ¹	Solvent	AIBN (mol%)	MW	Т	Yield (%) ^a	$eta/lpha^b$	d.r. β- isomers (Z/E) ^b	d.r. α- isomers (Z/E) ^b	Yield (%) ^{a,c}	
1	<i>i</i> Pr	THF	100	Х	80 °C	310 : 59	36:64	>98:2	79:21	312 : 3	
2	<i>i</i> Pr	heptane	10	Х	100 °C	310 : 71 (56) ^{<i>d,e</i>}	44:56	90:10	62:38	312 : 8 (8) ^d	
3	<i>t</i> Bu	heptane	10	Х	100 °C	311 : 41 (20) ^{<i>d,e</i>}	56:44	74:26	56:44	313 : 2	

 TABLE II-19. Germylzincation of non-symmetrical dialkylacetylenes.

^{*a*}Yield estimated by ¹H NMR analysis of the crude reaction mixture using butadiene sulfone as internal standard. ^{*b*}Determined by ¹H NMR prior to purification. ^{*c*}E/Z > 98:2. ^{*d*}Isolated yield is shown in parenthesis. ^{*e*}Contaminated with remaining Ph₃GeH.

As shown by the reactions starting from **301** and **302**, bulky substituents on the alkyne were quite well tolerated. Unfortunately, steric bias did not allow for the control of the regioselectivity of germylzincation. A first experiment with substrate **301** having an *i*Pr substituent under the already developed reaction conditions led, almost exclusively, to the formation of vinylgermanes **310** (59% yield), but in a β/α = 36:64 ratio and with a poor stereoselectivity in the case of the α regioisomer (Table II-19, entry 1). By switching to heptane, an improved 71% yield was detected in the crude reaction mixture, still lacking regiocontrol, and with an even lower stereocontrol for both regioisomers (Table II-19, entry 2). In addition, the low polarity of the resulting vinylgermanes rendered product isolation problematic, since it was not possible to cleanly separate them from the remaining Ph₃GeH. As well, byproduct **312** was obtained in a higher 3–8% yield.

The reaction with *t*Bu-substituted alkyne **302** occurred in a lower yield, with a somewhat increased β selectivity but still with no satisfactory regiocontrol. Furthermore, a significant drop in stereoselectivity for both regioisomers was noted (Table II-19, entry 3).

Alkyl- and TMS-substituted propargylic and homopropargylic alcohols

Looking for alternatives to control the regioselectivity, while in parallel avoiding purification issues arising from the low polarity of the resultant vinylgermanes, we decided to investigate alkyl-substituted propargylic alcohols. This approach was inspired by the firm experimental evidence for O-directed radical hydrostannation of propargylically-oxygenated dialkylacetylenes conclusively gathered by Hale,^{108,136} Nativi and Taddei,¹³⁹ Curran,¹⁴⁰ Organ,^{141–144} and others (**Scheme II-94**). The origin of the O-directing effect has been the matter of much debate. Recently, Hale¹⁰⁸ strongly argued in favor of a rationale based on the coordination of Ph₃SnH to the oxygen of the propargylic alcohols that promotes the subsequent H-atom abstraction from the Sn atom to generate an O-coordinated Ph₃Sn radical. This O-coordinated tin radical might favor its own delivery proximal to the alkoxy group, thus imposing directionality onto the subsequent addition step.



SCHEME II-94. The Hale-Manaviazar proposal for the regioselectivity of O-directed free radical addition of Ph₃SnH to propargylic alcohols (initiation has been represented as •In).

Based on these grounds, we wondered if a similar directing effect could turn our germylzincation reaction regioselective and we considered the germylzincation of an array of propargylic alcohols (**Table II-20**).

	RO_{II_n} R^1	E ¹² R ² Ph ₃ G	eH (0.8 or AIBN (n m neptane, 0 100 °C, 3	2.0 equiv) 2.0 equiv) 10%) .18 M 2 h 1/NH-	$R^{1} H$ $R0 + R^{2} + R^{2}$ $Ph_{3}Ge$ $\beta \text{ isomers}$	F RO [†] α i	R ¹ Ge	₽Ph ₃ R ²	
Entr y	303–307 Substrate	Et₂Zn (equiv)	Ph3GeH (equiv)	AIBN (mol%)	314- Product	318 Yield (%) ^a	$\beta/lpha^b$	d.r. β- isomers (Z/E) ^b	d.r. α- isomers (Z/E) ^b
1	nHept	3.0	2.0	25	HO <i>n</i> Hept	97 (80) ^{c,d}	90:10	>98:2	>98:2
2	303	_	2.0	10	Ph ₃ Ge	92	76:24	38:62	38:62
3	303	_	0.8	10	β,Z -314	74^{e}	78:22	>95:5	>95:5
4	TBSO <i>n</i> Hept	3.0	2.0	25	H TBSO Ph ₃ Ge β,Z- 315	34 (21) ^{c,f}	>98:2	>98:2	-
5	HOMe Ph 305	3.0	2.0	25	Ph H HO Me Ph ₃ Ge β,Z- 316	58 (51) ^{c,g}	>98:2	>98:2	-
6	HOSiMe ₃ 306	3.0	2.0	25	HO Ph ₃ Ge β,Z- 317	76 (65) ^c	>98:2	>98:2	-
7	nHex	3.0	2.0	25	HO HO nHex	74 (57) ^{c,h}	57:43	98:2	97:3
8	HO	_	2.0	10	Ph ₃ Ge	84	55:45	34:66	33:67
9	307	_	0.8	10	β,Ζ -318	80 ^e	48:52	>98:2	>98:2

TABLE II-20. Germylzincation of alkyl- and TMS-substituted propargylic and homopropargylic alcohols.

^{*a*}Yield estimated by ¹H NMR analysis of the crude reaction mixture using butadiene sulfone or dimethyl sulfone as internal standard. ^{*b*}Determined by ¹H NMR prior to purification. ^{*c*}Isolated yield is shown in parenthesis. ^{*d*} β/α > 98:2. ^{*e*}Based on the substrate. ^{*f*}Contaminated with remaining substrate. ^{*g*}35% of **305** was recovered. ^{*h*}Isolated as mixture of regioisomers.

Beginning with dec-2-yn-1-ol **303**, germylzincation under the optimized conditions for arylsubstituted propargylic alcohols occurred in an excellent 97% yield with a good regioselectivity ($\beta/\alpha = 90:10$) and an outstanding *trans* stereoselectivity for both regioisomers (Z/E > 98:2) (Table II-20, entry 1). Vinylgermane **314** was isolated in 80% yield as a β -regiochemically pure *Z* stereoisomer. In the absence of Et₂Zn, even though direct hydrogermylation occurred in 92% yield, the regioselectivity was lower ($\beta/\alpha = 76:24$), and isomerization of the vinylgermane was observed to a large extent (Z/E = 38:62) (Table II-20, entry 2). Still without Et₂Zn, and in default Ph₃GeH, the same regiochemical outcome was obtained ($\beta/\alpha = 78:22$), but the *trans* stereoselectivity (Z/E > 95:5) was excellent (Table II-20, entry 3). These results suggest that the regioselectivity, determined in the addition step of the Ph₃Ge• radical to either the propargylic zinc alkoxide (germylzincation) or the propargylic alcohol (hydrogermylation), is markedly influenced by the nature of the O-directing group. The reaction of substrate **304** bearing a protecting propargyl OTBS group occurred with excellent regio- and stereocontrol (β/α and Z/E> 98:2) although with a poor yield (Table II-20, entry 4). The high regioselectivity observed is consistent with the powerful O-directing effect of propargyl OSiR₃ groups on Ph₃SnH alkyne hydrostannation, as has been widely evidenced.¹⁰⁸

The same O-directing effect of the zinc alkoxide was also certainly at the origin of the excellent regioselectivity observed for the germylzincation of secondary propargylic alcohol **305** (Table II-20, entry 5). β ,*Z*-**316** was isolated in 51% yield as a single *Z* isomer. Here, however, the conversion was not complete and 35% of starting material was recovered. The additional steric hindrance introduced by the Ph group probably accounts for this feature.

TMS-substituted propargylic alcohol **306** also led to excellent results taking advantage of the synergy between the O-directing effect, and the unlikelihood of addition of Ph₃Ge• in α position to a SiR₃ group. Bis-metalated compound **317** was obtained in 65% isolated yield with perfect regioand stereoselectivity (Table II-20, entry 6).

To round up, homopropargylic alcohol **307** was also investigated. The germylzincation of **307** under typical conditions furnished vinylgermane **318** in good yield but as mixture of regioisomers ($\beta/\alpha = 57:43$) (Table II-20, entry 7). The lack of regiocontrol was in line with the noted inefficiency as directing groups of homopropargyloxy functionalities on radical hydrostannation of alkynes.^{136,139} By contrast, excellent control of the stereoselectivity was achieved for both regioisomers. Direct hydrogermylation upon reaction of Ph₃GeH with this substrate provided similar regioselectivity in the presence of both excess (Table II-20, entry 8), and default Ph₃GeH (Table II-20, entry 9). Regarding the stereoselectivity, under excess-triphenylgermane regime, isomerization was observed to a large extent, but not completely toward the *E* isomer, in contrast to the above-described hydrogermylations of diarylacetylenes and (aryl, alkyl)-substituted alkynes. In turn, under default-triphenylgermane regime, excellent *trans* selectivity was obtained for both regioisomers. These results mirror the stereodivergent hydrogermylation of internal conventional alkynes developed thus far.

In general, experimental evidence for O-coordinative regiocontrol has now been gathered for the germylzincation of propargylically-oxygenated alkynes, even though other factors, e. g. steric, also play a (less) important role in the ultimate outcome.

Finally, it is worth-highlighting the excellent *trans* stereoselectivity observed under germylzincation conditions for alkyl-substituted (homo)propargylic alcohols, probably as a result of the formation of an intermediate metallacycle, resembling the one proposed in Scheme II-81, that locks the configuration of the double bond and prevents from subsequent isomerization, ensuring in this way the *Z* selectivity, even in excess Ph_3GeH .

II-6.5. C(sp²)–Zn BOND FUNCTIONALIZATION

Lastly, we explored the transformation of conventional alkynes into configurationally defined tetrasubstituted vinylgermanes in a one-pot procedure, which would provide a closing answer to the general problem that represents accessing to this overarching structure.

We first focused on allylation reactions. We therefore performed, after the initial germylzincation steps under the conditions developed for each substrate type (**Scheme II-95 A**, **B**, **C** or **D**), *in situ* transmetalation to copper, directly followed by addition of allylbromide to the reaction media.

After 16 h of reaction, tetrasubstituted vinylgermanes **319–322** bearing an allyl moiety were isolated in good-to-excellent yields (58–93%), while remarkably retaining the geometry of the corresponding vinylmetal species arising from the initial germylzincation step. X-ray crystallographic analysis of products **319** and **321** confirmed the expected (and opposite) stereoselectivities. The double bond configuration of the other functionalized vinylgermanes prepared in this section was inferred by comparison with these two compounds.



SCHEME II-95. Domino germylzincation/Cu(I)-mediated electrophilic allylation.

It is important to mention that under all the tested reaction conditions (**A–D**), the formation of allyltriphenylgermane **323** was detected in significant amounts. We reasoned that this product was arising from the allylation of Ge–Zn species and its detection was thus providing indirect evidence for the formation of the former intermediates. However, **323** was never detected to any extent when performing the allylation of vinylzinc intermediates arising from the germylzincation of neither terminal nor internal ynamides. This observation was in line with the results of our mechanistic studies (see section II-2.5.2) that showed that formation of Ge–Zn species occurred rather slowly (if at all) in the reaction conditions allowing for germylzincation of terminal ynamides. Arguably, the formation of Ge–Zn species under conditions **A–D** was ascribed to the reaction of Ph₃Ge• with Et₂Zn (homolytic substitution at Zn). Indeed, on one hand, conditions are harsher than those involving ynamides thus favoring the initiation of radical chains and, on the other hand, the lower reactivity of germyl radicals with conventional alkynes possibly renders their reaction with Et₂Zn competitive.
Beyond allylation, vinylzinc intermediates obtained by germylzincation of conventional alkynes could also be trapped by other electrophiles such as benzoyl chloride and tributyltin chloride (**Scheme II-96**).



^aYield estimated by ¹H NMR analysis of the crude reaction mixture using butadiene sulfone as internal standard. ^bIsolated yield is shown in parenthesis. ^cNon-separable mixture with **327**.

SCHEME II-96. Domino germylzincation/Cu(I)-mediated electrophilic trapping with other electrophiles.

Benzoylated vinylgermane **324** was obtained in good yield with an excellent preservation of the double bond geometry. Importantly, functionalization of the C(sp²)–Zn bond with tributyltin chloride was achieved for the first time, in sharp contrast to the failures met with ynamides. Bimetallic germyl(stannyl)ethenes **325** and **326** were obtained with excellent (and opposite) stereoselectivities in a one-pot procedure, without the need for previous preparation of the corresponding [Ge]–[Sn] reagent,^{11,13,16,18} or elaborated alkynylgermanes or alkynylstannanes as substrates.¹⁴⁵ Unluckily, germyl(stannyl)ethene **326** could not be cleanly isolated and characterized due to the difficulty in separating tin byproducts from the non-polar organic vinylgermane **326**. Notwithstanding, it was possible to identify the formation of product **327**, which confirmed, once again, the formation of Ge–Zn species during the germylzincation step. Unfortunately, domino germylzincation/Cu(I)-mediated electrophilic stannylation of aryl- or TMS-substituted propargylic alcohols was not achieved, and products **328** and **329** were not detected in the crude reaction mixtures.

To finish, domino germylzincation/Cu(I)-mediated 1,4-addition was performed (**Scheme II-97**). However, the addition of the vinylmetal intermediate on the cyclohexenone turned out to be ineffective in this case, and the functionalized product **330** was not obtained.



SCHEME II-97. Failed domino germylzincation/Cu(I)-mediated 1,4-addition.

II-6.6. TO SUM UP

In conclusion, we disclosed here the **first general methodology for the synthesis of tri**and tetrasubstituted vinylgermanes in a one-pot procedure *via* the radical germylzincation of internal alkynes (Scheme II-98).



SCHEME II-98. Summary of the germylzincation of conventional alkynes.

Even though less reactive starting materials, by careful optimization of the reaction conditions, and addition of AIBN as radical initiator, plethora of conventional internal alkynes were smoothly transformed into the corresponding vinylgermanes with high degree of stereoselectivity, despite some regioselectivity issues. Importantly, appealing aryl-, alkyl-, and TMS-substituted propargylic alcohols rendered the corresponding vinylgermanes, where the hydroxyl moiety behaved as an excellent directing group to achieve useful regiocontrol. Concerning the role of the solvent on the stereoselectivity outcome, the radical germylzincation of conventional alkynes initially delivered the *anti* addition product (kinetic product), eventually followed by a radical isomerization step to provide the *syn* addition compound (thermodynamic product). Such isomerization step was mostly favored when apolar solvents were used (*n*-hexane, heptane, benzene), in which radical chains are more efficient, while the kinetic product could be selectively formed by using THF as solvent. Finally, *in situ* functionalization of the C(sp²)–Zn bond broadens the scope of such transformation and offers a shortcut to structural diversity built upon the vinylgermane template.

Also significantly, the stereodivergent radical hydrogermylation of internal alkynes was accomplished, by means of default- or excess-triphenylgermane regimes (**Scheme II-99**).



SCHEME II-99. Stereodivergent radical hydrogermylation of internal alkynes.

II-6.7. IN PERSPECTIVE...

In the framework of this project, there are still several edges to explore. Primarily, the feasibility of performing the functionalization of the C(sp²)–Ge bond is crucial in order to demonstrate the synthetic utility of tri- and tetrasubstituted vinylgermanes for the construction of stereodefined alkenes. In this context, an initial proof of concept was performed, with a challenging carbon-substituted *triphenyl*vinylgermane (**Scheme II-100**).



SCHEME II-100. Preliminary experiment for the bromodegermylation of trisubstituted vinylgermane **260**.

Initial conditions led to full conversion with major formation of the desired vinyl bromide **331** along with minor quantities of the product arising from a second addition of Br₂ to the double bond of **332**. Further optimization studies are called for in order to obtain a clean transformation. Notwithstanding, this constitutes an important open pathway to the synthesis of stereodefined alkenes from *triphenyl*vinylgermanes.

In a broader context, multiple applications in target-oriented synthesis can be envisaged to validate the robustness and efficiency of our system, while providing new solutions to synthetic challenges. In this sense, potential application of the germylzincation reaction, combined with subsequent orthogonal functionalization of the C(sp²)–Zn and C(sp²)–Ge bonds formed are proposed below, the first approach concerning the synthesis of tamoxifen, an anticancer drug (**Scheme II-101**). Our aim would be to build on the germylzincation reaction of conventional alkynes according to the proposed retrosynthetic plan outlined in Scheme II-101.



SCHEME II-101. Possible applications of the germylzincation to the total synthesis of tamoxifen and analogues: A retrosynthetic analysis.

Either commercially available **259** or **277**, would provide alternative starting points. Capitalizing on either the *cis*-selective germylzincation of 1-phenyl-1-butyne **259** (**333**), or the *trans*-selective germylzincation of diphenylacetylene **277** (**336**), followed by *in situ* functionalization of the C(sp²)–Zn bond *via* Negishi-type cross-coupling reaction, it should be feasible to access intermediates **334** or **337**. From this point onward, two routes are proposed to reach tamoxifen: direct cross-coupling, or transformation into vinyl halides **335** or **338**, which we envision could be convertible into tamoxifen by a cross-coupling sequence. We believe that, more important than simply accessing tamoxifen itself, what is really appealing in this approach is the multiple possibilities for introducing chemical variability, thus accelerating the creation of chemical libraries.

Moreover, further applications toward the synthesis of natural products can be envisioned **(Scheme II-102)**.



precursor of (-)-(Z)-deoxypukalide



SCHEME II-102. Examples of accessible precursors of natural products.

Certainly, the simultaneous formation of a C(sp²)–Zn and a C(sp²)–Ge bonds would expedite the creation of diverse molecular architectures, that combined with the possibility of orthogonal functionalization of the elementometalated product toward stereodefined tri- and tetrasubstituted alkenes confers to this proposal high potential to make an impact in the field of organic synthesis.

In a wider perspective, the versatility of the radical germylzincation of alkynes could open new horizons to the generalization of the *radical elementometalation* concept to other reagents holding element–metal bonds.

II-7. FUTURE PERSPECTIVES: GENERALIZING THE CONCEPT

SILICON AND BORON AS POTENTIAL BRICKS FOR THE RADICAL ELEMENTOZINCATION OF CONVENTIONAL ALKYNES

A generalization of the radical elementozincation concept is contemplated toward silicon and boron. Preliminary experiments for the silyl- and borylzincation of conventional alkynes are reported.



In a growing field basically dominated by transition-metal catalysis, radical-mediated elementometalation of alkynes is conceptually appealing since such approach may offer complementary regio- or stereoselectivities to many of the classical strategies. In fact, the generality of the radical germylzincation of alkynes prompted us to extend such approach to other elementozincation processes. Silicon and boron seem to provide many opportunities in this regard, since radical hydrosilylation^{36,146} and hydroboration¹⁴⁷ of alkynes have been reported. Hence, their analogous elementozincation processes constitute an attractive testing ground for the radical approach discussed herein.

II-7.1. RADICAL SILYLZINCATION OF CONVENTIONAL ALKYNES: PRELIMINARY EXPERIMENTS

Silylmetalation of alkynes is a well-established approach for the preparation of vinylsilanes and, in a more general context, for the synthesis of stereodefined alkenes. Prevailing methods for the silylzincation of **terminal alkynes** allow controlling the sense of the regiochemistry. However, tuning of stereochemistry is rarely feasible, and products arising from *syn* addition processes are the usual outcome. But even so, **internal alkynes** still remain challenging substrates for such transformations, with scarce examples in the literature,^{127,128,130} suffering from lack of regioselectivity in most cases (**Scheme II-103**).



SCHEME II-103. General approach to the silylzincation of internal alkynes.

To the best of our knowledge, a complementary *trans*-selective approach has not been reported thus far. In the framework of the PhD work developed by Elise Romain in our group,¹¹² a new entry to the silylzincation of terminal arylacetylenes was investigated, considering two different methods: 1) a combination of (Me₃Si)₃SiH and Et₂Zn, or 2) the use of [(Me₃Si)₃Si]₂Zn as organosilyl radical source. A representative example is given in **Scheme II-104**.



SCHEME II-104. Silylzincation of terminal arylacetylene 246 with (Me₃Si)₃SiH/Et₂Zn (left) and (Me₃Si)₃Si]₂Zn/Et₂Zn (right) (*Si* = (Me₃Si)₃Si).

As can be seen, with the $(Me_3Si)_3SiH/Et_2Zn$ system, direct hydrosilylation was the main reaction outcome (Scheme II-104, left), in a similar fashion to our results with the combination Ph_3GeH/Et_2Zn , where hydrogermylation of **246** outcompeted germylzincation (see section II-6.1). However, since by switching to 1-phenyl-1-propyne as substrate we were able to avoid competitive hydrogermylation, we decided to give a try to the $(Me_3Si)_3SiH/Et_2Zn$ system with internal alkynes (**Table II-21**).

	β α Me 251	Et ₂ Zn (3.0 equiv) (Me ₃ Si) ₃ SiH (1.3 equiv) \checkmark <i>n</i> -hexane, 0.18 M 40 °C, 16 h <i>Conditions</i> <i>then</i> NH ₄ Cl/NH ₃	$(Me_3Si)_3Si + H + Me $ (Me Z-340 $\beta/\alpha > 98:2$	Ме H e ₃ Si) ₃ Si <i>E-</i> 340
Entry		Additive	Yield 340 (%) ^a	d.r. 340 (Z/E) ^b
1		-	31	85:15
2	<i>tert</i> -dode	canethiol (10 mol%)	40	84:16

TABLE II-21. Silylzincation of 1-phenyl-1-propyne with (Me₃Si)₃SiH/Et₂Zn.

*^a*Yield estimated by ¹H NMR analysis of the crude reaction mixture using butadiene sulfone as internal standard. *^b*Determined by ¹H NMR of the crude reaction mixture.

A preliminary experiment in *n*-hexane at 40 °C led to the formation of the expected product **340** with mostly *Z* stereoselectivity, albeit in a low yield (31%). Satisfyingly, only β regioisomers were detected in the crude reaction mixture. Under similar reaction conditions, this time with *tert*-dodecanethiol as additive, a slightly improved 40% yield was observed (Table II-21, entry 2).

The fundamentals behind the addition of *tert*-dodecanethiol can be found in the Polarity-Reversal Catalysis (PRC) concept (**Scheme II-105**). PRC is based on polar effects operating in the transition state of radical reactions. The idea is to replace a single-step abstraction, which is slow due to unfavorable polar effects, by a cycle of two-step transfer reactions wherein the radicals and substrates are polarity-matched.

Nuc ¹	+	H—Nuc ²	→	Nuc ¹ —H	+	Nuc ^{2*}	DISFAVORED SLOW reaction	
Nuc ¹ El	+ +	H—El H—Nuc²	►	Nuc¹—H EI—H	+ +	El [•] Nuc ^{2•}	FAVORED, FAST FAVORED, FAST	<pre>Polarity-Reversal Catalysis H−EI = PR catalyst</pre>

SCHEME II-105. The principle underlying Polarity-Reversal Catalysis (PRC).

Capitalizing on this concept, the typical H-atom transfer step of our original radical chain (**Scheme II-106**, A) should be now replaced by two more favorable H-atom transfers (Scheme II-106, B) where the *tert*-dodecanethiol (RSH) would perform as the polarity-reversal catalyst. A general mechanism, with the possible role of the RSH, is shown in Scheme II-106 (C).



SCHEME II-106. Role of RSH (tert-dodecanethiol) as polarity-reversal catalyst in the reaction mechanism.

However, under our reaction conditions, it was also possible to envisage the involvement of the RSH in other side-reactions, namely, deprotonation of the thiol functionality by Et_2Zn (1), as well as H-atom transfer to the vinyl radical intermediate **341** (2), with consequent loss of the metal functionality.

Nevertheless, despite the high performance that thiols have demonstrated as catalysts in radical hydrosilylation reactions,^{148,149} no significant improvement of the reaction outcome was observed in our working conditions (Table II-21, entry 2). We therefore did not push forward in this direction.

Turning our attention to the demonstrated more efficient $[(Me_3Si)_3Si]_2Zn/Et_2Zn$ system (Scheme II-104, right), we were pleased to find that reaction of 1-phenyl-1-propyne in *n*-hexane at 40 °C with 1.1 equiv of both $[(Me_3Si)_3Si]_2Zn$ and Et_2Zn , provided an already improved 48% yield of vinylsilane **340** with a decent *Z* stereoselectivity (Z/E = 90:10) (**Table II-22**, entry 1). Here also only β regioisomers were detected. By increasing to 2.0 equiv of $[(Me_3Si)_3Si]_2Zn/Et_2Zn$, a further improvement was obtained in both yield and stereoselectivity (62%, Z/E = 95:5) (Table II-22, entry 2). Lastly, an initial experiment with AIBN at 80 °C furnished an excellent yield (88%), but the stereocontrol vanished (Z/E = 53:47) (Table II-22, entry 3). This was not totally unexpected given our previous experience regarding the isomerization of the kinetically formed vinylzinc intermediate during the germylzincation of 1-phenyl-1-propyne and the fact that a similar radical-based isomerization process was reported for alkenes at high temperature in the presence of (Me_3Si)_3Si.¹⁵⁰

(Me ₃ Si) ₃ SiH (1.9 equiv) Fixed conditions		[(Me₃Si)₃Si]₂Zn 343 Ⅲ Si₂Zn (n equiv)	β ^α Me 251 Et ₂ Zn (n equiv) <i>n</i> -hexane, 0.18 M 16 h <i>Conditions</i> <i>then</i> NH ₄ Cl/NH ₃	$(Me_3Si)_3Si + Me + Me + H$ $Me (Me_3Si)_3Si$ $Z-340 = E-340$ $\beta/\alpha > 98:2$				
Entry	<i>Si</i> 2Zn / Et2Zn (equiv)	Additive	Т	Yield 340 (%) ^a	d.r. 340 (Z/E) ^b			
1	1.1 / 1.1	-	40 °C	48	90:10			
2	2.0 / 2.0	-	40 °C	62	95:5			
3	1.1 / 1.1	AIBN (10 mol%	%) 80 °C	88	53:47			

TABLE II-22. Silylzincation of 1-phenyl-1-propyne with [(Me₃Si)₃Si]₂Zn/Et₂Zn.

^{*a*}Yield estimated by ¹H NMR analysis of the crude reaction mixture using butadiene sulfone as internal standard. ^{*b*}Determined by ¹H NMR of the crude reaction mixture.

In conclusion, these preliminary experiments speak in favor of the feasibility of this (unprecedented) radical silylzincation of internal alkynes, with tendency toward *Z* selectivity. Further optimization studies are required, including D-labeling experiments to confirm the

formation of vinylzinc intermediates, in order to ultimately explore the scope of this transformation on the way to stereodefined tetrasubstituted vinylsilanes.

II-7.2. RADICAL BORYLZINCATION OF CONVENTIONAL ALKYNES: PRELIMINARY EXPERIMENTS

As a final point, radical borylzincation was preliminary surveyed. The major challenge involved in this transformation is the difficulty for B–H bonds to undergo radical hydrogen transfer reactions.^{147,151}

Even so, there is a class of borane reagents that behave as H-atom donors in a wide range of radical reactions: NHC-boranes (NHC–BH₃).¹⁵² Substituent effects on the radical hydrogen donor ability of NHC-boranes are remarkable, albeit the values of the rate constants for the H-atom abstraction of most NHC-boranes are around 10^4 M⁻¹ s⁻¹.³⁹ Notwithstanding, complex **344** stands out as one of the best hydrogen donors (8 × 10⁴ M⁻¹ s⁻¹) (**Scheme II-107**). Even though this rate constant is lower than those of germanium hydrides, tris(trimethylsilyl)silane, and tin hydride, it is still above the limit for propagating radical chains efficiently and not that different from the rate constant of trialkylgermanium hydrides.



SCHEME II-107. Rate constant for the H-atom abstraction of NHC-borane **344** by primary alkyl radicals in comparison with other group-14 hydrides.

In fact, the proof of concept for the feasibility of the productive addition of NHC-boryl radicals to alkynes was recently provided by Curran¹⁴⁷ (**Scheme II-108**). Radical *trans*-hydroboration of internal alkynes was achieved with complex **344** in the presence of DTBP as radical initiator. This work offered a nice access to a large variety of trisubstituted vinyl-NHC-boranes with high stereoselectivity.

Previous reports on borylzincation chemistry are scarce, with only one example involving an alkyne as starting material.¹⁵³ The borylzincation of phenylacetylene was achieved following reaction with borylzincate **346**, and vinylborane **345** was obtained (in moderate yield). Moreover,

experiments to confirm the availability for subsequent reactions of the C(sp²)–Zn bond were not performed, and no further attempts were devoted to establish the scope of this transformation. We therefore decided to explore the feasibility of achieving borylzincation of conventional alkynes through a radical approach with the aim to access tetrasubstituted vinylboranes, appealing precursors of stereodefined alkenes.



Previous work: Radical trans-hydroboration of internal alkynes with NHC-boranes

SCHEME II-108. General context of the borylzincation approach.

Capitalizing on Curran's results, we chose as starting point to consider the reaction of 1-phenyl-1-propyne with NHC-borane **344** and Et₂Zn (**Table II-23**).

Me	β ^α 251		Et ₂ Zn (3.0 equiv) HC–BH ₃ 344 (2.0 equiv) Conditions then NH ₄ Cl/NH ₃ or ND ₄ Cl/D ₂ O	Me Me N N N Z-3	ВH ₂ Ле] Ξ + β/α > 9	Me N + N N N N N N	Н ₂ В М Ие 347	e N	Me N + BH N N Me IHC-BH ₃ 3	3 44
Entry	c [M]	Solvent	Radical Initiator	Additive	MW	time	Т	E	Yield 347 (%) ^a	d.r. 347 (Z/E) ^b	[²H] (%) ^c
1	0.18	heptane	AIBN (50 mol%)	-	Х	1 h	100 °C	Η	<10	>98:2	-
2^d	0.18	benzene	DTBP (1.5 equiv)	-	-	16 h	120 °C	Н	55	60:40	-
3	0.25	benzene	DTBP (1.0 equiv)	-	-	16 h	120 °C	H	60	85:15	-
4	0.25	benzene	DTBP (1.0 equiv)	-	-	16 h	120 °C	D	56	92:8	93
5	0.25	benzene	DTBP (1.0 equiv)	-	Х	1 h	160 °C	Η	45	58:42	-
6	0.25	benzene	DTBP (1.0 equiv)	RSH (20 mol%) ^e	Х	1 h	150 °C	Н	65	60:40	-
7	0.18	fluoro- benzene	DTBP (1.0 equiv)	-	-	16 h	120 °C	Η	46	70:30	-
8	0.18	THF	DTBP (1.0 equiv)	_	-	16 h	120 °C	Н	49	67:33	-

TABLE II-23. Borylzincation of 1-phenyl-1-propyne with NHC-BH3 344/Et2Zn.

^{*a*}Yield estimated by ¹H NMR analysis of the crude reaction mixture using dimethyl sulfone as internal standard. ^{*b*}Z/E ratios estimated by ¹H and ¹¹B NMR analysis of the crude reaction mixture. ^{*c*}Percentage of deuterium incorporation estimated by ¹H NMR. ^{*d*}NHC–BH₃ (4.0 equiv). ^{*e*}RSH = *tert*-dodecanethiol.

In the first conditions tested employing AIBN as radical initiator the formation of **347** was already detected, but only in very low (<10%) yield (Table II-23, entry 1). Yet, we observed remarkable *Z* stereoselectivity, opposite to that of the reported radical *trans*-hydroboration. Following this promising result, we decided to consider the reaction conditions reported by Curran for the *trans*-hydroboration¹⁴⁷ (NHC-borane (4.0 equiv), DTBP (1.5 equiv), benzene, 120 °C), in the presence of Et₂Zn (Table II-23, entry 2). It should be noted that this implied a dilution of the reaction medium, and incorporation of Et₂Zn (used as a 1.0 M solution in *n*-hexane), brought the substrate concentration from 0.5 M (Curran's conditions) to 0.18 M (our conditions). The move was successful and a much improved 55% yield in **347** was observed. However, the stereoselectivity was rather low (*Z*/*E* = 60:40). It is important to mention that the match between our ¹H and ¹¹B NMR spectra of the crude mixtures and the spectra reported by Curran¹⁴⁷ for both stereoisomers was excellent, and allowed unambiguous identification of the products formed.

In line with the alkyne germylzincation chemistry, we speculated that *cis*-borylzincation (leading to the *Z*-configured vinylborane) was the result of the isomerization of the intermediate Z,β -boryl vinylzinc initially formed by *trans*-selective borylzincation. In such a situation, we

reasoned that the concentration of the reaction media could certainly have an influence on the stereoselectivity, since higher concentrations favor intermolecular radical additions and thus possibly the isomerization step. Accordingly, we slightly modified the reaction conditions: we increased the concentration to 0.25 M and reduce the amount of NHC-borane (2.0 equiv) and DTBP (1.0 equiv) (Table II-23, entry 3). Gratifyingly, a similar yield (60%) in **347** was achieved as well as a more decent *Z* selectivity (*Z*/*E* = 85:15). Aiming to demonstrate that formation of *Z*-**347** was result of a borylzincation process, a D-labeling experiment was carried out (Table II-23, entry 4). Pleasingly, a remarkable 93% D-incorporation at the α position was obtained, accompanied by a similar yield (56%) and even somewhat improved stereoselectivity (*Z*/*E* = 92:8).

Further variations of these reaction conditions were performed but no additional improvement was achieved. Switching to MW irradiation for 1 h at 160 °C to ensure faster decomposition of DTBP led to a somewhat lower yield in **347** with no stereocontrol (Z/E = 58:42) (Table II-23, entry 5). The same operating conditions in the presence of *tert*-dodecanethiol (20 mol%) as a polarity reversal catalyst led to an improved yield (65% *vs* 45%) but still with similar stereoselectivity (Table II-23, entry 6). Furthermore, D-labeling experiments would be necessary here to determine if this increase is caused by hydrogen-transfer from the *tert*-dodecanethiol to the vinyl radical intermediate with consequent loss of the metal functionality, or due to enhanced efficiency of the radical chain. The use of more polar solvents (fluorobenzene, THF) was also surveyed, but led to modest (46–49%) yields and low stereoselectivities (Table II-23, entries 7 and 8). Hence, thus far, the reaction conditions described in entries 3 and 4 provided the best results, and the proof of concept for the radical borylzincation approach. Obviously, there is still plenty of room for improvement here.

We also investigated briefly the borylzincation of diphenylacetylene (**Table II-24**). Under the reaction conditions giving the best results with 1-phenyl-1-propyne, the formation of vinylborane **348** was obtained from diphenylacetylene in a comparable 45% yield but with much lower stereoselectivity (Table II-24, entry 2).

Ph [~]	Ph	Et ₂ Zn (3.0 equiv) NHC–BH ₃ 344 (2.0 eq <i>Conditions</i> 120 °C, 16 h <i>then</i> NH ₄ Cl/NH ₃	$\xrightarrow{\text{uiv}} \begin{array}{c} M_{e} & P_{h} \\ & & P_{h} \\ & & & H_{2} \\ & & & N_{e} \\ & & & N_{e} \\ & & & M_{e} \\ & & & Z-348 \end{array}$	$+ \underbrace{\bigvee_{N}^{H_2} \bigvee_{N}^{H_2} \bigvee_{Ph}^{Ph}}_{E-348}$	Me N+ N Me NHC-BH ₃ 344
Entry	c [M]	Solvent	Radical Initiator	Yield 348 (%) ^a	d.r. 348 (Z/E) ^b
1	0.18	benzene	DTBP (1.0 equiv)	52%	60:40
2	0.25	benzene	DTBP (1.0 equiv)	45%	56:44
3	0.33	_	DTBP (1.0 equiv)	47%	62:38
4	0.25	heptane	DTBP (1.0 equiv)	45%	58:42
5	0.25	benzene	AIBN (1.0 equiv)	27%	68:32

 $\label{eq:TABLE II-24.} Borylzincation of diphenylacetylene with NHC-BH_3\ 344/Et_2Zn.$

^{*a*}Yield estimated by ¹H NMR analysis of the crude reaction mixture using dimethyl sulfone as internal standard. ^{*b*}Z/E ratios estimated by ¹H and ¹¹B NMR analysis of the crude reaction mixture.

Here, the concentration of the reaction media had little impact on the outcome: similar yields and stereoselectivities were obtained at 0.18 M, 0.25 M or 0.33 M (Table II-24, compare entries 1-3). Comparable results were also obtained upon switching to the less toxic solvent heptane (Table II-24, entry 4). By contrast, the use of AIBN instead of DTBP as radical initiator resulted in a significant decrease in yield (Table II-24, entry 5) as we had also observed in the case of 1-phenyl-1-propyne (Table II-23, entry 1).

The poorer performance of AIBN as radical initiator for the borylzincation reactions compared to DTBP might be the result of less favorable polarity-matching effects during the H-atom transfer reaction that initiates the process (**Scheme II-109**). AIBN and DTBP both thermally decompose to produce electrophilic radicals. However, *tert*-butoxyl radicals arising from DTBP have a more electrophilic character than cyano-substituted alkyl radicals delivered by AIBN, and therefore, subsequent H-atom transfer from nucleophilic NHC-borane **344** should be more favorable with the former.





Taking into consideration the experimental results discussed here above, we therefore propose the following reaction mechanism for the radical borylzincation of internal alkynes initiated by DTBP (**Scheme II-110**).



SCHEME II-110. Proposed mechanism for the radical borylzincation of internal alkynes initiated by DTBP.

To initiate the sequence, DTBP thermally decomposes to produce two *tert*-butoxyl radicals **349** (*t*BuO·), which in turn abstract a hydrogen atom from NHC-borane **344** to form NHC-boryl radical **350**.¹⁵¹ Subsequent addition across the triple bond of the alkyne produces vinyl radical intermediate **351** (stabilized by the phenyl ring). This addition step is regiodiscriminating and driven by the formation of the more stable vinylic radical. Next, S_H2 at the Zn atom of Et₂Zn gives stereoselectively vinylzinc intermediate *Z*-**352**, along with an ethyl radical. *Z*-**352** does not retain its stereochemical integrity in the reaction conditions and *Z*-to-*E* isomerization (possibly through a radical mechanism) accounts for the *Z*/*E* mixtures obtained. Propagation of the radical chain could occur following H-atom transfer from the NHC-borane to the ethyl radical. However, given the rather low rate constant for this step,³⁹ it cannot be excluded that the radical chain stops at this point. Hence, further conversion of the remaining starting material requires a new initiation

event to occur (formation of another *t*BuO· radical). The fact that stoichiometric amounts of the initiator are necessary to obtain decent yields argues in favor of this scenario.

II-7.3. PARTIAL CONCLUSIONS

In summary, we have demonstrated the feasibility of radical silyl- and borylzincation of internal alkynes, and the approach is highly promising in the context of the synthesis of polysubstituted vinylsilanes and vinyl-NHC-boranes.

Additional investigations are necessary to expand the scope and further optimize the reaction conditions for both the silyl- and borylzincation of conventional alkynes in order to turn these processes into useful synthetic methodology. Nevertheless, this preliminary study already constitutes an important step toward the generalization of the concept of radical elementometalation reactions, and its development as a powerful alternative to the (more) commonly used metal-catalyzed processes.

II-8. REFERENCES FOR PART II

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GENERAL CONCLUSIONS

The objective of this doctoral thesis was to develop a general radical approach for the germylzincation of alkynes as a straightforward route for the preparation of polysubstituted vinylgermanes.

In a first step, we studied the germylzincation of terminal and internal ynamides since we considered they would be highly suitable substrates and vinylgermanes decorated with a heteroatom in the β position to the germyl group had not been synthesized previously. We found that the simple combination of a hydrogermane and diethylzinc allowed for the formerly unknown germylzincation of ynamides in a radical chain process (Scheme GC-1). This methodology gave access to a wide variety of 1,2- and 1,1,2-germylenamides after protodemetalation of the vinylzinc intermediates. The key feature of this new approach was the possibility of using the C(sp²)–Zn bond created as linchpin for subsequent C–C or C–heteroatom bond formation in one pot, with complete retention of configuration through in situ Cu(I)- or Pd(0)-mediated electrophilic substitution. Importantly, exceptionally stable divinylzinc complexes were synthesized and fully characterized. These intermediates were crucial in the versatile transformations that the C(sp²)–Zn bond underwent. As a result, this approach offered modular access to valuable vinylgermanes decorated with two substituents in the β position to the germyl group, namely, 1,2,2-trisubstituted and tetrasubstituted germylenamides. Finally, the operational simplicity, ready availability of the reagents, and excellent levels of regio- and stereocontrol were also important assets of this protocol.



SCHEME GC-1. Accessible vinylgermanes through radical germylzincation of ynamides.

Notably, the synthetic potential of the accessible β -germylenamides was further assessed by means of functionalization of the C(sp²)–Ge bond, being readily converted into the corresponding

 β -haloenamides with excellent stereoselectivity. It is important to underline that this also constituted, to the best of our knowledge, the first efficient halodegermylation reaction of *triphenyl*vinylgermane derivatives. In addition, unexpected 1,2-germyl migration provided unparalleled hemiaminal-type compounds. Further work to understand the mechanism leading to the formation of the hemiaminals and evaluation of their reactivity offer interesting perspectives for future work in this area.

In a second line, the radical germylzincation approach was extended to other α -heteroatomsubstituted alkynes, and vinylgermanes decorated with arylsulfide, arylsulfoxide, O-carbamate, and phosphonates substituents β to the germanium were obtained (**Scheme GC-2**). Here, the selective functionalization of the C(sp²)–Ge bond of these original vinylgermanes remains an issue to be studied.



SCHEME GC-2. Accessible vinylgermanes through radical germylzincation of other α -heteroatom-substituted alkynes.

More importantly, we demonstrated after that the protocol for radical germylzincation was not restricted to α -heteroatom-substituted alkynes, and more challenging conventional alkynes were also converted into valuable vinylgermanes (**Scheme GC-3**), even though harsher reaction conditions and AIBN as radical initiator were necessary to achieve good yields. (Aryl, alkyl)-substituted alkynes, diarylacetylenes, dialkylacetylenes, and aryl-, alkyl-, or TMS-substituted propargylic alcohols were suitable substrates and the vinylzinc intermediates arising from the germylzincation were smoothly transformed into tetrasubstituted vinylgermanes after *in situ* Cu(I)-mediated electrophilic substitution, with excellent retention of the double bond geometry.





To sum up, an outline of the now accessible vinylgermanes starting from alkynes with C–*Ge* bond formation is presented in **Figure GC-1**, highlighting in blue the ones that have become achievable by our radical germylzincation approach. Therefore, **the radical approach for the germylzincation of alkynes has offered a direct and general route for the preparation of structurally diverse vinylgermanes**.



FIGURE GC-1. Updated outline of the accessible vinylgermanes from alkynes with C–*Ge* bond formation (*Ge* = triorganogermyl) (highlighted in blue those made in this work).

The possibility to elaborate the vinylgermanes into stereodefined alkenes confers to our protocol high potential to make an impact in organic synthesis. First, the demonstrated ability of vinylgermanes to give access to well-defined vinyl halides could lead to countless synthetic applications. Second, the lower toxicity of Ge, as opposed to Sn, should stimulate the appeal of vinylgermanes as coupling partners in Stille-type cross-coupling reactions. In this context, the flexibility in the substitution pattern of germanium offered by the germylzincation strategy should

provide a means to connect germyl radical chemistry with the known cross-coupling chemistry of organogermanes. This would introduce a further distinction with silyl- and stannylmetalation reactions where the radical and the cross-coupling chemistry have remained thus far mismatched. Toward this end, it would be important at this point to develop synthetic applications of the chemistry developed. Some possible perspectives have been discussed previously (see section II-6.7).

In summary, our findings filled-in a gap in organic synthesis by allowing the direct access to tailored vinylgermanes. This will certainly forge ahead the positioning of vinylgermanes as building blocks in organic chemistry.

As a final comment from a wider perspective, the current work is also significant because it demonstrates the generality of the radical elementozincation approach. This could certainly translate the radical elementometalation concept into a powerful alternative to the (more) commonly used metal-catalyzed processes. Notably, preliminary results prove the feasibility of radical silyl- and borylzincation of alkynes. Further experimentation remains necessary to optimize the protocols but numerous perspectives are opened, as previously discussed.

PART III. EXPERIMENTAL PART
III-1. SUMMARY OF SYNTHESIZED MOLECULES

SUBSTRATES AND REAGENTS

PRECURSORS FOR THE SYNTHESIS OF YNAMIDES AND OTHER α -HETEROATOM SUBSTITUTED ALKYNES

1,1-dibromo-1-alkenes (GP I)



219 p. 273







105 p. 274

228 p. 274

1,2-DICHLOROENAMIDE



126 p. 275

YNAMIDES (GP III-GP VI)

TIPS-Protected Ynamides



124 p. 292



122 p. 291

α -Heteroatom-Substituted Alkynes



CONVENTIONAL ALKYNES









GERMANIUM REAGENTS



RADICAL HYDROGERMYLATION OF YNAMIDE 54



Z-**59** p. 307

GERMYLZINCATION OF TERMINAL YNAMIDES (GP VII AND GP VIII)





69(E=H)p. 31170(E=H)p. 312[²H]-69(E=D)p. 312[²H]-70(E=D)p. 313

Ph₃Ge



GERMYLZINCATION OF INTERNAL YNAMIDES (GP IX AND GP X)



94 (E=H)p. 318 [²H]-94 (E=D)p. 318



129 (E=H)p. 319 [²H]-**129** (E=D) p. 319



130	(E=H)	p. 320
[² H]-130	(E=D)	p. 320

(2-furyl)₃Ge

(E=H)

(E=D)

p. 323

p. 324

135

[²H]-**135**



131 (E=H)p. 321 [²H]-131 (E=D) p. 322



132 (E=H)^{[2}H]-**132** (E=D)

MeO.







139 (E=H)p. 326 [²H]-139 (E=D) p. 326

Ph₃Ge 138 (E=H)p. 325 [²H]-138 (E=D)p. 325



136 (E=H) p. 324



ĠePh₃







142 (E=H)[²H]-**142** (E=D)

p. 328



DOMINO YNAMIDE GERMYLZINCATION/Cu(I)-MEDIATED ELECTROPHILIC TRAPPING (GP XI AND GP XII)



153 p. 339



154 p. 340



155 p. 340



156 p. 341



157 p. 342

158 p. 342

Ph₃Ge

SPh



159 p. 343



Cl GePh₃



DOMINO YNAMIDE GERMYLZINCATION/Cu(I)-MEDIATED 1,4-ADDITION



168 p. 349

DIVINYLZINC INTERMEDIATES (GP XIII)



169 p. 351









HALODEGERMYLATION OF β -TRIPHENYLGERMYLENAMIDES







188 p. 360



189 p. 360

186 p. 359

187 p. 359

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242 p. 368

REACTION WITH ACCEPTOR 86



89 p. 369

SILVLZINCATION OF YNAMIDE 54



93	(E=H)	p. 370
[² H] -93	(E=D)	p. 371







Byproducts – Germylzincation of Conventional Alkynes



DOMINO GERMYLZINCATION OF CONVENTIONAL ALKYNES/Cu(I)-MEDIATED ELECTROPHILIC TRAPPING (GP XVII)



Byproduct – Domino Germylzincation of Conventional Alkynes/Cu(I)-Mediated Electrophilic Trapping



NHC-BORANE



344 p. 396

III-2. GENERAL INFORMATION

Experiments involving organometallic compounds were carried out in dried glassware under a positive pressure of dry argon. THF, toluene, DMF, and CH₂Cl₂ were distilled to remove stabilizers and dried with a Solvent Purification System. Et₂Zn (Aldrich), triphenylgermanium hydride (Aldrich), tributylgermanium hydride (Aldrich), triethylgermanium hydride (Alfa Aesar), 1,4-dioxane (anhydrous, 99.8%, Aldrich), n-hexane (Aldrich), and all other reagents were of commercial quality and were used without purification. Flash column chromatography was performed using the indicated solvents on silica gel 60 (0.015–0.040 mm) by Merck. ¹H NMR and ¹³C NMR (or IMod) spectra were recorded with a Bruker AV 300 or 400 spectrometers. Chemical shifts are reported in parts per million (ppm) downfield from tetramethylsilane and are referenced to the residual solvent resonance as the internal standard (CHCl₃: δ = 7.26 ppm or C₆H₆: δ = 7.16 ppm for ¹H NMR and CDCl₃: δ = 77.16 ppm or C₆D₆: δ = 128.06 ppm for ¹³C NMR or JMod). Data are reported as follows: chemical shift, multiplicity (br s = broad singlet, s = singlet, d = doublet, t = triplet, q = quartet, quint = quintuplet, hept = heptaplet, m = multiplet), coupling constant (Hz) and integration. Infrared (IR) spectra were recorded with a Bruker Tensor 27 ATR diamond spectrophotometer and are reported in wavenumbers (cm⁻¹). Melting points (mp) were determined with Stuart Scientific SMP3 melting point apparatus and are not corrected. Optical rotations were measured on a JASCO P-2000 polarimeter with $[\alpha]_D$ values reported in 10⁻¹ (°·cm²·g⁻¹); concentration c is in g/100 mL. High resolution mass spectra (HRMS) were obtained on a Bruker MicrOTOF or from the HRMS core facility at Sorbonne Université. The type of ionization used is indicated in parenthesis.

All new compounds were named using the program *Chemdraw* by *Cambridgesoft*. For assigning ¹H and ¹³C NMR data, the numbering of atoms was chosen arbitrarily.

In addition, the references of this chapter have been included as footnotes for the sake of simplicity.

III-3. ¹H NMR MONITORING EXPERIMENTS

Monitoring of the Reaction between Ph₃GeH / Et₂Zn and Ynamide 54 in THF at 0 °C



Procedure:

A reference spectrum (used for t = 0) was recorded at 273 K for ynamide **54** (8 mg, 0.06 mmol) dissolved in THF- d_8 (0.5 mL).

Then, the monitored sample was prepared. In a dry Schlenk tube, ynamide **54** (35 mg, 0.25 mmol, 1.0 equiv) was dissolved in THF- d_8 (1.5 mL) and cooled to 0 °C. Et₂Zn (1.0 M in hexane, 0.75 mL, 0.75 mmol, 3.0 equiv), followed by Ph₃GeH (99 mg, 0.33 mmol, 1.3 equiv) in THF- d_8 (0.5 mL) were added (**t** = **0**) and an aliquot (~0.5 mL) was transferred to a J Young NMR tube under argon atmosphere. The tube was immediately placed in the NMR probe at 273 K. ¹H NMR spectra were recorded every 5 min during 3 h.

Monitoring of the Reaction between Ph₃GeH and Et₂Zn in THF at 0 °C

Ph₃GeH + Et₂Zn $\xrightarrow{\text{THF-}d_8}$ Ph₃Ge-[Zn] (1.3 equiv) (3.0 equiv) 273 K, 3 h

Procedure:

In a J Young NMR tube under argon atmosphere, Ph_3GeH (25 mg, 0.08 mmol) was dissolved in THF- d_8 (0.5 mL). A first spectrum (used for t = 0) was recorded at 273 K. The NMR tube was then placed in an ice-bath and Et₂Zn (1.0 M in hexane, 0.18 mL, 0.18 mmol, 3.0 equiv) was introduced. At the end of the addition (t = 0), the tube was immediately placed in the NMR probe at 273 K and ¹H NMR spectra were recorded every 5 min during 3 h.

III-4. *IN SITU* IR MONITORING OF LEWIS-PAIR FORMATION BETWEEN YNAMIDE 92 AND Et₂Zn in *n*-hexane or THF



Reaction setup:

React IR 15 with MCT Detector using HappGenzel apodization was used to collect IR reaction spectra. The instrument was fitted with a DiComp (Diamond) probe connected via AgX 6mm x 1.5m silver halide fiber. All data were collected at 8 cm⁻¹ resolution from 3000 to 650 cm⁻¹. 125 scans were collected to obtain 1 spectrum. An air background was collected prior to the experiments and Mettler Toledo iCIR version 4.3 was used for instrument control and data analysis. Baseline offset correction was applied.

Monitoring of the interaction between ynamide 92 and Et₂Zn in n-hexane at 40 °C:

Procedure:

Under argon atmosphere, *n*-hexane (2.0 mL) was introduced into a three-necked round-flask equipped with the DiComp probe and heated to 40 °C. Evolution of the system was monitored at 1–2 min intervals. Ynamide **92** (54 mg, 0.25 mmol) was introduced (t_0) and a suspension was obtained. After ~ 40 min, most of the ynamide had dissolved and the system reached a steady state. Et₂Zn (1.0 M in hexane, 0.75 mL, 0.75 mmol, 3.0 equiv) was then added (t_1) and the turbid solution became clear.

Monitoring of the interaction between ynamide 92 and Et_2Zn in THF at 0 °C:

Procedure:

Under argon atmosphere, THF (2.0 mL) was introduced into a three-necked round-flask equipped with the DiComp probe and cooled to 0 °C. Evolution of the system was monitored at 1–2 min intervals. Ynamide **92** (54 mg, 0.25 mmol) was introduced (t_0) and a colorless solution was obtained. After stabilization of the system, Et₂Zn (1.0 M in hexane, 0.75 mL, 0.75 mmol, 3.0 equiv) was added (t_1).

III-5. EXPERIMENTAL PROCEDURES AND CHARACTERIZATION DATA

III-5.1. SYNTHESIS OF SUBSTRATES AND REAGENTS

III-5.1.1. General Procedure for the synthesis of 1,1-dibromo-1-alkenes (GP I)



1,1-dibromo-1-alkenes were prepared according to a slightly modified version of Dixon's procedure.¹ A solution of PPh₃ (1.2 M in dry CH₂Cl₂, 3.0 equiv) was added through a dropping funnel to an ice-cold solution of CBr₄ (0.4 M in dry CH₂Cl₂, 1.5 equiv) under argon atmosphere. After the addition was completed, the reaction mixture was stirred for an additional 30 min at 0 °C (an orange suspension formed). Subsequently, the corresponding aldehyde (1.0 equiv) was added dropwise and the mixture was allowed to slowly warm to rt. The progress of the reaction was monitored by TLC analysis. Upon completion, the mixture was diluted with CH₂Cl₂ followed by the addition of pentane in order to precipitate the triphenylphosphine oxide formed. Triphenylphosphine oxide was then filtered off over a pad of silica gel and washed with pentane. The combined organic layers were concentrated under reduced pressure to afford the crude product. 1,1-dibromo-1-alkenes were obtained after purification of the crude product by flash chromatography on silica gel.

(2,2-dibromovinyl)benzene (97): Prepared according to GP I from CBr₄ (12.44 g, 37.5 mmol, 1.5 equiv), PPh₃ (19.67 g, 75 mmol, 3.0 equiv), and benzaldehyde (2.65 g, 2.54 mL, 25 mmol, 1.0 equiv) in CH₂Cl₂ (157 mL) with a reaction time of 30 min (after addition of the aldehyde). Purification of the crude product by flash chromatography on silica gel (eluent: pentane) afforded analytically pure **97** (4.45 g, 68%) as a pale yellow oil.



97

C₈H₆Br₂ M.W. = 261.94 g⋅mol⁻¹

¹**H NMR** (400 MHz, CDCl₃): δ 7.56–7.53 (m, 2H, H-Ar), 7.50 (s, 1H, H-2), 7.41– 7.35 (m, 3H, H-Ar).

JMod (100 MHz, CDCl₃): δ 137.0 (C-2), 135.5 (C-3), 128.7 (C-6), 128.53 (2C-Ar), 128.51 (2C-Ar), 89.7 (C-1).

ⁱ Michaelides, I. N.; Darses, B.; Dixon, D. J. Org. Lett. **2011**, *13*, 664–667.

The spectral data were in agreement with that previously reported in the literature.ⁱ

$$H_3C_0^{7}$$
 Br

C₉H₈Br₂O M.W. = 291.97 g⋅mol⁻¹



¹**H NMR** (400 MHz, CDCl₃): δ 7.56–7.52 (m, 2H, H-4), 7.43 (s, 1H, H-2), 6.94– 6.90 (m, 2H, H-5), 3.83 (s, 3H, H-7).

¹³C{¹H} NMR (100 MHz, CDCl₃): δ 159.7 (C-6), 136.3 (C-2), 129.9 (C-4), 127.7 (C-3), 113.8 (C-5), 87.2 (C-1), 55.3 (C-7).

The spectral data were in agreement with that previously reported in the literature.ⁱⁱ

1-chloro-4-(2,2-dibromovinyl)benzene (99): Prepared according to **GP I** from CBr₄ (9.95 g, 30 mmol, 1.5 equiv), PPh₃ (15.74 g, 60 mmol, 3.0 equiv), and 4-chlorobenzaldehyde (2.81 g, 20 mmol, 1.0 equiv) in CH_2Cl_2 (120 mL) with a reaction time of 3 h (after addition of the aldehyde). Purification of the crude product by flash chromatography on silica gel (eluent: pentane) afforded analytically pure **99** (5.39 g, 91%) as a pale yellow solid.

¹**H NMR** (400 MHz, CDCl₃): δ 7.48–7.45 (m, 2H, H-4), 7.43 (s, 1H, H-2), 7.36– 7.32 (m, 2H, H-5).

¹³C{¹H} NMR (100 MHz, CDCl₃): δ 135.8 (C-2), 134.5 (C-6), 133.8 (C-3), 129.8 (C-4), 128.8 (C-5), 90.6 (C-1).

The spectral data were in agreement with that previously reported in the literature. $^{\mbox{\tiny II}}$

C₈H₅Br₂Cl M.W. = 296.39 g⋅mol⁻¹

ⁱ Huh, D. H.; Jeong, J. S.; Lee, H. B.; Ryu, H.; Kim, Y. G. *Tetrahedron* **2002**, *58*, 9925–9932. ⁱⁱ Chen, X. Y.; Wang, L.; Frings, M.; Bolm, C. *Org. Lett.* **2014**, *16*, 3796–3799.

1-(2,2-dibromovinyl)-3-methoxybenzene (100): Prepared according to **GP I** from CBr₄ (9.95 g, 30 mmol, 1.5 equiv), PPh₃ (15.74 g, 60 mmol, 3.0 equiv), and 3-methoxybenzaldehyde (2.72 g, 2.43 mL, 20 mmol, 1.0 equiv) in CH₂Cl₂ (120 mL) with a reaction time of 3 h (after addition of the aldehyde). Purification of the crude product by flash chromatography on silica gel (pentane/Et₂O = 98:2) afforded analytically pure **100** (4.91 g, 84%) as a pale yellow oil.

¹**H NMR** (400 MHz, CDCl₃): δ 7.48 (s, 1H, H-2), 7.31 (t, *J* = 7.9 Hz, 1H, H-7), 7.15–7.11 (m, 2H, H-4,8), 6.94–6.91 (m, 1H, H-6), 3.83 (s, 3H, H-9).

¹³C{¹H} NMR (100 MHz, CDCl₃): δ 159.4 (C-5), 136.8 (C-2), 136.4 (C-3), 129.4 (C-7), 121.0 (C-8), 114.3 (C-4 or C-6), 113.7 (C-6 or C-4), 89.8 (C-1), 55.2 (C-9).

The spectral data were in agreement with that previously reported in the literature.ⁱ

1,3-dichloro-2-(2,2-dibromovinyl)benzene (101): Prepared according to **GP I** from CBr₄ (9.95 g, 30 mmol, 1.5 equiv), PPh₃ (15.74 g, 60 mmol, 3.0 equiv), and 2,6-dichlorobenzaldehyde (3.50 g, 20 mmol, 1.0 equiv) in CH₂Cl₂ (120 mL) with a reaction time of 3 h (after addition of the aldehyde). Purification of the crude product by flash chromatography on silica gel (eluent: pentane) afforded analytically pure **101** (6.01 g, 91%) as a white solid.

¹**H NMR** (400 MHz, CDCl₃): δ 7.39–7.35 (m, 3H, H-2,5), 7.29–7.23 (m, 1H, H-6).

¹³C{¹H} NMR (100 MHz, CDCl₃): δ 141.5 (C-3), 134.5 (C-4), 133.1 (C-2), 130.1 (C-6), 128.2 (C-5), 97.0 (C-1).

The spectral data were in agreement with that previously reported in the literature.ⁱⁱ



100

C₉H₈Br₂O M.W. = 291.97 g⋅mol⁻¹



101

C₈H₄Br₂Cl₂ M.W. = 330.83 g⋅mol⁻¹

ⁱ Chen, X. Y.; Wang, L.; Frings, M.; Bolm, C. *Org. Lett.* **2014**, *16*, 3796–3799.

ⁱⁱ Morri, A. K.; Thummala, Y.; Doddi, V. R. *Org. Lett.* **2015**, *17*, 4640–4643.





C₁₀H₈Br₂ M.W. = 287.98 g⋅mol⁻¹



¹**H NMR** (400 MHz, CDCl₃): δ 7.52–7.49 (m, 2H, H-Ar), 7.43–7.36 (m, 3H, H-Ar), 7.13 (d, *J* = 10.0 Hz, 1H, H-2), 6.86 (dd, *J* = 15.7 Hz, 10.0 Hz, 1H, H-3), 6.73 (d, *J* = 15.7 Hz, 1H, H-4).

¹³C{¹H} NMR (100 MHz, CDCl₃): δ 137.2, 136.3 (C-5), 135.8, 128.9, 128.7, 126.9, 125.2, 91.4 (C-1).

The spectral data were in agreement with that previously reported in the literature.ⁱ

(2,2-dibromovinyl)cyclohexane (103): Prepared according to GP I from CBr₄ (9.95 g, 30 mmol, 1.5 equiv), PPh₃ (15.74 g, 60 mmol, 3.0 equiv), and cyclohexanecarbaldehyde (2.24 g, 2.33 mL, 20 mmol, 1.0 equiv) in CH₂Cl₂ (120 mL) with a reaction time of 3 h (after addition of the aldehyde). Purification of the crude product by flash chromatography on silica gel (pentane) afforded analytically pure **103** (4.20 g, 78%) as a pale yellow oil.

¹**H NMR** (400 MHz, CDCl₃): δ 6.23 (s, 1H, H-2), 2.33–2.23 (m, 1H, H-3), 1.77– 1.62 (m, 5H, H-alkyl), 1.36–1.07 (m, 5H, H-alkyl).

¹³C{¹H} NMR (100 MHz, CDCl₃): δ 143.7 (C-2), 87.0 (C-1), 42.4 (C-3), 31.3, 25.7, 25.5.

The spectral data were in agreement with that previously reported in the literature.ⁱⁱ

1,1-dibromohexa-1,5-diene (104): Prepared according to **GP I** from CBr_4 (9.95 g, 30 mmol, 1.5 equiv), PPh₃ (15.74 g, 60 mmol, 3.0 equiv), and pent-4-enal (1.68 g, 2.00 mL, 20 mmol, 1.0 equiv) in CH_2Cl_2 (120 mL) with a reaction



 $C_8H_{12}Br_2$ M.W. = 267.99 g·mol⁻¹

ⁱ Michaelides, I. N.; Darses, B.; Dixon, D. J. Org. Lett. **2011**, *13*, 664–667.

ⁱⁱ Rao, M. L. N.; Jadhav, D. N.; Dasgupta, P. Org. Lett. **2010**, *12*, 2048–2051.

time of 3 h (after addition of the aldehyde). Purification of the crude product by flash chromatography on silica gel (pentane/ Et_2O = 98:2) afforded analytically pure **104** (4.13 g, 86%) as a pale yellow oil.

¹**H NMR** (400 MHz, CDCl₃): δ 6.41–6.38 (m, 1H, H-2), 5.79 (dddd, *J* = 16.6 Hz, *J* = 10.1 Hz, *J* = 7.3 Hz, *J* = 5.2 Hz, 1H, H-5), 5.09–5.00 (m, 2H, H-6), 2.24–2.16 (m, 4H, H-3,4).

¹³C{¹H} NMR (100 MHz, CDCl₃): δ 137.9 (C-5), 136.8 (C-2), 115.8 (C-6), 89.2 (C-1), 32.3 (C-3 or C-4), 31.8 (C-4 or C-3).

The spectral data were in agreement with that previously reported in the literature.ⁱ

1,1-dibromooct-1-ene (219): Prepared according to **GP I** from CBr_4 (14.92 g, 45 mmol, 1.5 equiv), PPh₃ (23.61 g, 90 mmol, 3.0 equiv), and heptanal (3.43 g, 4.19 mL, 30 mmol, 1.0 equiv) in CH_2Cl_2 (180 mL) with a reaction time of 3 h (after addition of the aldehyde). Purification of the crude product by flash chromatography on silica gel (pentane) afforded analytically pure **219** (5.41 g, 67%) as a colorless liquid.

¹**H NMR** (400 MHz, CDCl₃): δ 6.39 (t, *J* = 7.3 Hz, 1H, H-2), 2.09 (t, *J* = 7.3 Hz, 2H, H-3), 1.46–1.38 (m, 2H, H-alkyl), 1.35–1.26 (m, 6H, H-alkyl), 0.91–0.87 (m, 3H, H-8).

The spectral data were in agreement with that previously reported in the literature.ⁱⁱ



104

C₆H₈Br₂ M.W. = 239.94 g⋅mol⁻¹





C₈H₁₄Br₂ M.W. = 270.00 g⋅mol⁻¹

ⁱ Fukudome, Y.; Naito, H.; Hata, T.; Urabe, H. J. Am. Chem. Soc. **2008**, 130, 1820–1821.

ⁱⁱ Charreau, P.; Julia, M.; Verpeaux, J. N. *J. Organomet. Chem.* **1989**, *379*, 201–210.

III-5.1.2. General Procedure for the preparation of alkynylcopper reagents (GP II)



Alkynylcopper reagents were prepared according to Evano's procedure.ⁱ To a deep blue solution of copper iodide (2.0 equiv) in a mixture of ammonium hydroxide (28% NH₃ solution) and ethanol was added the corresponding alkyne (1.0 equiv) dropwise. The reaction mixture was stirred overnight at rt under argon atmosphere. The formed yellow precipitate was collected by filtration, and successively washed with ammonium hydroxide (10% NH₃ solution, x3), water (x3), ethanol (x3), and diethyl ether (x3). The yellow solid was then dried under vacuum to afford the desired polymeric alkynylcopper reagent which was used without further purification.



105

C9H7CuO M.W. = 194.70 g⋅mol⁻¹



228

C₈H₅Cu M.W. = 164.67 g·mol⁻¹ **((2-methoxyphenyl)ethynyl)copper (105):** Prepared according to **GP II** from 1-ethynyl-2-methoxybenzene (500 mg, 3.78 mmol, 1.0 equiv) and CuI (190 mg, 7.57 mmol, 2.0 equiv) in a mixture of ammonium hydroxide (28% NH₃ solution, 23 mL) and ethanol (19 mL). The alkynylcopper reagent **105** (647 mg, 88%) was obtained as a yellow solid. This compound has been previously characterized.ⁱⁱ

(Phenylethynyl)copper (228): Prepared according to GP II from phenylacetylene (1.02 g, 1.1 mL, 10.0 mmol, 1.0 equiv) and CuI (3.81 g, 20.0 mmol, 2.0 equiv) in a mixture of ammonium hydroxide (28% NH₃ solution, 50 mL) and ethanol (30 mL). The alkynylcopper reagent **228** (1.50 g, 91%) was obtained as a yellow solid. This compound has been previously characterized.ⁱ

ⁱ Jouvin, K.; Heimburger, J.; Evano, G. *Chem. Sci.* **2012**, *3*, 756–760.

ⁱⁱ Jouvin, K.; Veillard, R.; Theunissen, C.; Alayrac, C.; Gaumont, A.-C.; Evano, G. *Org. Lett.* **2013**, *15*, 4592–4595.





(E)-3-(1,2-dichlorovinyl)-4,4-dimethyloxazolidin-2-one) (126) was prepared according to a slightly modified version of Anderson's procedure. ⁱ To a stirred suspension of 4,4-dimethyloxazolidin-2-one (3.00 g, 26.1 mmol, 1.0 equiv), Cs_2CO_3 (12.74 g, 39.1 mmol, 1.5 equiv) and DMF, at 50 °C, was added trichloroethene (TCE) (3.77 g, 2.6 mL, 28.7 mmol, 1.1 equiv) dropwise over 10 min. The resulting mixture was stirred at 50 °C for 3 h. Upon cooling to rt, the mixture was partitioned between EtOAc and H₂O (2:1), the organic layer was separated and further washed with H₂O (x3). The combined organic layers were then dried over MgSO₄, filtered, and concentrated under reduced pressure to afford the crude product. Purification by flash chromatography on silica gel (pentane/Et₂O = 60:40) afforded analytically pure **126** (2.41 g, 44%) as a white solid; mp 138–141 °C.

¹**H NMR** (400 MHz, CDCl₃): δ 6.55 (s, 1H, H-6), 4.14 (s, 2H, H-2), 1.54 (s, 3H, H-4 or H-4'), 1.43 (s, 3H, H-4' or H-4).

¹³C{¹H} NMR (100 MHz, CDCl₃): δ 153.2 (C-1), 125.6 (C-5), 120.3 (C-6), 76.4 (C-2), 61.5 (C-3), 26.2 (C-4 or C-4'), 24.7 (C-4' or C-4).

IR (neat): *v* (cm⁻¹) 1760, 1408, 1386, 1376, 1082, 1024, 905, 818, 730.

HRMS (ESI): m/z calculated for $[C_7H_9Cl_2NO_2 + Na]^+$ 231.9903; found 231.9894.



126

C₇H₉Cl₂NO₂ M.W. = 210.06 g⋅mol⁻¹

ⁱ Mansfield, S. J.; Campbell, C. D.; Jones, M. W.; Anderson, E. A. *Chem. Commun.* **2015**, *51*, 3316–3319.

III-5.1.4. Synthesis of Ynamides

III-5.1.4.1. General Procedure for the synthesis of ynamides from alkynyl bromides (Hsung's methodology) (GP III)



Ynamides **49**, **51–53**, **107**, **111** and **119** were prepared according to a modified version of Hsung's procedure.¹ To a solution of the appropriate alkynyl bromide (1.00 equiv) in dry toluene were added the corresponding *N*-nucleophile (oxazolidinone or sulfonamide) (1.25 equiv), $CuSO_4 \cdot 5H_2O$ (0.10 equiv), 1,10-phenanthroline (0.20 equiv), and K_2CO_3 (2.15 equiv) under argon atmosphere. The reaction mixture was then heated at 80 °C for the given reaction time. After cooling at rt, the resulting mixture was diluted in toluene, filtered through a pad of Celite, washed with hexane/EtOAc (1:1), and the filtrate was concentrated under reduced pressure. The crude product was purified by flash chromatography on silica gel to afford the desired ynamide.

III-5.1.4.2. General Procedure for the desilylation of TIPS-protected ynamides: access to terminal ynamides (GP IV)



To a solution of the corresponding TIPS-protected ynamide (1.0 equiv, 0.2 M in THF) cooled to 0 °C was added a solution of TBAF (1.5 equiv, 1.0 M in THF) dropwise. After 1 h at 0 °C, the ice bath was removed and the mixture was allowed to warm to rt followed by quenching with saturated aq NH₄Cl. The aqueous phase was then extracted with Et₂O (x5). The combined organic layers were washed with brine (x2), dried over Na₂SO₄, filtered, and concentrated under reduced pressure to afford the crude product. Terminal ynamides were obtained after purification of the crude product by flash chromatography on silica gel.

ⁱ Zhang, Y.; Hsung, R. P.; Tracey, M. R.; Kurtz, K. C. M.; Vera, E. L. Org. Lett. 2004, 6, 1151–1154.

III-5.1.4.3. General Procedure for the synthesis of ynamides from 1,1-dibromo-1-alkenes (Evano's methodology) (GP V)



Ynamides **92**, **106**, **108–110**, **112–114**, **117–118**, **120** were prepared according to a slightly modified version of Evano's procedure. ¹ A pressure tube was charged with the corresponding *N*-nucleophile (oxazolidinone, sulfonamide or carbamate) (1.0 equiv), 1,1-dibromo-1-alkene (1.5 equiv), Cs_2CO_3 (4.0 equiv), and CuI (0.1 equiv). The tube was then fitted with a rubber septum, evacuated under vacuum and refilled with argon three times. Afterward, dry and degassed 1,4-dioxane (or DMF) was added followed by the addition of *N*,*N'*-dimethylethylenediamine (0.2 equiv). The rubber septum was then replaced by a Teflon-coated screw cap and the blue-green suspension obtained was heated at the specified temperature and for the given reaction time. Subsequently, the mixture was cooled to rt. When 1,4-dioxane was used as the solvent, the reaction mixture was filtered over a pad of silica gel, washed with EtOAc, and concentrated under reduced pressure to afford the crude product. In the case where DMF was employed as solvent, the mixture was diluted with water, extracted with cyclohexane/CH₂Cl₂ (9:1) (x3), and the combined organic layers were washed with brine, dried over Na₂SO₄, filtered, and concentrated under reduced pressure to afford the crude product. The crude was in both cases purified by flash chromatography on silica gel to obtain the desired ynamide.

III-5.1.4.4. General Procedure for the synthesis of ynamides via oxidative alkynylation of *N*-nucleophiles with alkynylcopper reagents (Evano's methodology) (GP VI)



Ynamide **116** was prepared according to a slightly modified version of Evano's procedure.ⁱⁱ A round bottom flask was charged with the corresponding alkynylcopper reagent (1.0 equiv), *N*nucleophile (oxazolidinone) (4.0 equiv), and acetonitrile. To the resulting yellow suspension was then added *N*,*N*,*N*',*N*'-tetramethylethylenediamine (1.0 equiv) and the mixture was vigorously

ⁱ Coste, A.; Karthikeyan, G.; Couty, F.; Evano, G. *Angew. Chem. Int. Ed.* **2009**, *48*, 4381–4385.

ⁱⁱ Jouvin, K.; Heimburger, J.; Evano, G. *Chem. Sci.* **2012**, *3*, 756–760.

stirred at rt under an atmosphere of O_2 (balloon). After complete transformation into a deep blue homogeneous solution (disappearance of the alkynylcopper reagent), the reaction mixture was concentrated under reduced pressure. The crude product was purified by flash chromatography on silica gel to afford the desired ynamide.



49

C₁₆H₂₉NO₂Si M.W. = 295.49 g⋅mol⁻¹

4,4-dimethyl-3-((triisopropylsilyl)ethynyl)oxazolidin-2-one (49): Prepared according to **GP III** from 4,4-dimethyloxazolidin-2-one (1.21 g, 10.50 mmol, 1.25 equiv), 1-bromo-2-triisopropylsilylacetylene (2.20 g, 8.42 mmol, 1.00 equiv), $CuSO_4 \cdot 5H_2O$ (0.21 g, 0.84 mmol, 0.10 equiv), 1,10-phenanthroline (0.30 g, 1.68 mmol, 0.20 equiv), and K_2CO_3 (2.50 g, 18.10 mmol, 2.15 equiv) in dry toluene (11 mL), with a reaction time of 6 days. Purification of the crude product by flash chromatography on silica gel (pentane/Et₂O = gradient from 85:15 to 75:25) afforded analytically pure **49** (2.40 g, 96%) as a white solid.

¹**H NMR** (400 MHz, CDCl₃): δ 4.12 (s, 2H, H-2), 1.44 (s, 6H, H-4), 1.09 (s_{app}, 21H, H-7,8).

¹³C{¹H} NMR (100 MHz, CDCl₃): δ 154.9 (C-1), 90.6 (C-5), 75.5 (C-2), 72.0 (C-6), 60.0 (C-3), 24.6 (C-4), 18.6 (C-8), 11.2 (C-7).

The spectral data were in agreement with that previously reported in the literature.ⁱ

3-((triisopropylsilyl)ethynyl)oxazolidin-2-one (51): Prepared according to **GP III** from oxazolidin-2-one (1.00 g, 11.48 mmol, 1.25 equiv), 1-bromo-2-triisopropylsilylacetylene (2.40 g, 9.19 mmol, 1.00 equiv), CuSO₄·5H₂O (0.23 g, 0.92 mmol, 0.10 equiv), 1,10-phenanthroline (0.33 g, 1.84 mmol, 0.20 equiv), and K₂CO₃ (2.73 g, 19.76 mmol, 2.15 equiv) in dry toluene (11 mL), with a reaction time of 6 days. Purification of the crude product by flash chromatography on silica gel (pentane/Et₂O = 70:30) afforded analytically pure **51** (1.56 g, 64%) as a colorless solid.

¹**H NMR** (400 MHz, CDCl₃): δ 4.44–4.40 (m, 2H, H-2), 3.95–3.91 (m, 2H, H-3), 1.08 (s_{app}, 21H, H-6,7).



51

C₁₄H₂₅NO₂Si M.W. = 267.44 g·mol⁻¹

ⁱ Romain, E.; Fopp, C.; Chemla, F.; Ferreira, F.; Jackowski, O.; Oestreich, M.; Perez-Luna, A. *Angew. Chem. Int. Ed.* **2014**, *53*, 11333–11337.

¹³C{¹H} NMR (100 MHz, CDCl₃): δ 155.8 (C-1), 93.0 (C-4), 70.0 (C-5), 62.7 (C-2), 47.0 (C-3), 18.6 (C-7), 11.2 (C-6).

The spectral data were in agreement with that previously reported in the literature.ⁱ

(S)-4-benzyl-3-((triisopropylsilyl)ethynyl)oxazolidin-2-one (52): Prepared according to GP III from (S)-4-benzyloxazolidin-2-one (2.00 g, 11.29 mmol, 1.25 equiv), 1-bromo-2-triisopropylsilylacetylene (2.36 g, 9.03 mmol, 1.00 equiv), CuSO₄·5H₂O (0.23 g, 0.90 mmol, 0.10 equiv), 1,10-phenanthroline (0.33 g, 1.81 mmol, 0.20 equiv), and K₂CO₃ (2.68 g, 19.41 mmol, 2.15 equiv) in dry toluene (11 mL), with a reaction time of 5 days. Purification of the crude product by flash chromatography on silica gel (pentane/Et₂O = 80:20) afforded analytically pure **52** (1.32 g, 47%) as a white solid.

¹**H NMR** (400 MHz, CDCl₃): δ 7.37–7.27 (m, 3H, H-Ar), 7.23–7.20 (m, 2H, H-Ar), 4.33–4.24 (m, 2H, H-2,3), 4.12–4.09 (m, 1H, H-2), 3.23 (dd, *J* = 13.8 Hz, *J* = 3.2 Hz, 1H, H-4), 2.98 (dd, *J* = 13.8 Hz, *J* = 8.1 Hz, 1H, H-4'), 1.12 (s_{app}, 21H, H-11,12).

¹³C{¹H} NMR (100 MHz, CDCl₃): δ 155.3 (C-1), 134.2 (C-5), 129.4 (C-Ar), 129.1 (C-Ar), 127.5 (C-Ar), 92.1 (C-9), 72.4 (C-10), 67.1 (C-2), 58.4 (C-3), 37.6 (C-4), 18.7 (C-12), 11.3 (C-11).

The spectral data were in agreement with that previously reported in the literature.ⁱⁱ

N-benzyl-4-methyl-N-((triisopropylsilyl)ethynyl)benzenesulfonamide

(53): Prepared according to **GP III** from *N*-benzyl-4methylbenzenesulfonamide (0.91 mg, 3.48 mmol, 1.0 equiv), 1-bromo-2triisopropylsilylacetylene (1.00 g, 3.83 mmol, 1.1 equiv), $CuSO_4 \cdot 5H_2O$ (0.10 g, 0.42 mmol, 0.1 equiv), 1,10-phenanthroline (0.13 g, 0.69 mmol, 0.2 equiv), and K₂CO₃ (1.00 g, 7.24 mmol, 2.1 equiv) in dry toluene (4 mL), with a reaction time of 4 days. Purification of the crude product by flash chromatography on



C₂₁H₃₁NO₂Si M.W. = 357.56 g⋅mol⁻¹



53

C₂₅H₃₅NO₂SSi M.W. = 441.70 g⋅mol⁻¹

ⁱ Hamada, T.; Ye, X.; Stahl, S. S. *J. Am. Chem. Soc.* **2008**, *130*, 833–835.

ⁱⁱ Frederick, M. O.; Mulder, J. A.; Tracey, M. R.; Hsung, R. P.; Huang, J.; Kurtz, K. C. M.; Shen, L.; Douglas, C. J. *J. Am. Chem. Soc.* **2003**, *125*, 2368–2369.

silica gel (pentane/Et₂O = 95:5) afforded analytically pure **53** (1.42 g, 92%) as a white solid.

¹**H NMR** (400 MHz, CDCl₃): δ 7.77 (d, *J* = 8.3 Hz, 2H, H-Ar), 7.31–7.28 (m, 7H, H-Ar), 4.52 (s, 2H, H-5), 2.46 (s, 3H, H-10), 0.97 (s_{app}, 21H, H-13,14).

¹³C{¹H} NMR (100 MHz, CDCl₃): δ 144.6 (C-9), 134.7 (C-6), 134.4 (C-4), 129.6 (C-7), 128.9 (C-2 or C-3), 128.4 (C-3 or C-2), 128.2 (C-1), 127.8 (C-8), 96.5 (C-11), 70.2 (C-12), 55.5 (C-5), 21.6 (C-10), 18.5 (C-14), 11.3 (C-13).

The spectral data were in agreement with that previously reported in the literature.ⁱ

4 3 2 N 1 6 0

54

C₇H₉NO₂ M.W. = 139.15 g⋅mol⁻¹



¹**H NMR** (400 MHz, CDCl₃): δ 4.15 (s, 2H, H-2), 2.90 (s, 1H, H-6), 1.45 (s, 6H, H-4).

¹³C{¹H} NMR (100 MHz, CDCl₃): δ 155.2 (C-1), 75.6 (C-2), 70.1 (C-5), 61.8 (C-6), 59.8 (C-3), 24.3 (C-4).

The spectral data were in agreement with that previously reported in the literature.ⁱⁱ

4 3 2 N 1 0 0 0 0

[²H]-54

C₇H₈DNO₂ M.W. = 140.16 g⋅mol⁻¹ **[²H]-54:** Prepared according to a slightly modified version of Bew's procedure.ⁱⁱⁱ 3-ethynyl-4,4-dimethyloxazolidin-2-one **54** (70 mg, 0.50 mmol, 1.0 equiv) was dissolved in CH₃CN (1.25 mL) and K₂CO₃ (104 mg, 0.75 mmol, 1.5 equiv) was added. The reaction mixture was then stirred under N₂ atmosphere for 30 min. Next, D₂O (0.50 mL, 25 mmol, 50 equiv) was added. After 1 h, the reaction was diluted with 5.0 mL of CH₂Cl₂ and transferred to a

ⁱ Yao, B.; Liang, Z.; Niu, T.; Zhang, Y. J. Org. Chem. 2009, 74, 4630–4633.

ⁱⁱ Romain, E.; Fopp, C.; Chemla, F.; Ferreira, F.; Jackowski, O.; Oestreich, M.; Perez-Luna, A. *Angew. Chem. Int. Ed.* **2014**, *53*, 11333–11337.

ⁱⁱⁱ Bew, S. P.; Hiatt-Gipson, G. D.; Lovell, J. A.; Poullain, C. Org. Lett. **2012**, *14*, 456–459.

separating funnel. The organic layer was then dried over Na_2SO_4 , filtered, and concentrated under reduced pressure to afford [²H]-**54** (65 mg, 93%) as a white solid.

¹**H NMR** (400 MHz, CDCl₃): δ 4.14 (s, 2H, H-2), 1.45 (s, 6H, H-4).

¹³C{¹H} NMR (100 MHz, CDCl₃): δ 155.2 (C-1), 75.7 (C-2), 70.1 (C-5), 59.8 (C-3), 24.4 (C-4). One C is not observed.

(*S*)-3-ethynyl-4-isopropyloxazolidin-2-one (55): Prepared according to GP IV from (*S*)-4-isopropyl-3-((triisopropylsilyl)ethynyl)oxazolidin-2-one 50ⁱ (2.35 g, 7.59 mmol, 1.0 equiv) and TBAF (1.0 M in THF, 11.39 mL, 11.39 mmol, 1.5 equiv) in THF (40 mL), with a reaction time of 1 h. Purification of the crude product by flash chromatography on silica gel (cyclohexane/EtOAc = 90:10) afforded analytically pure 55 (1.01 g, 6.53 mmol, 86%) as a brown oil.

¹**H NMR** (400 MHz, CDCl₃): δ 4.38 (t, *J* = 8.9 Hz, 1H, H-2), 4.16 (dd, *J* = 8.9 Hz, *J* = 5.7 Hz, 1H, H-2'), 3.98 (ddd, *J* = 8.9 Hz, *J* = 5.7 Hz, *J* = 4.1 Hz, 1H, H-3), 2.88 (s, 1H, H-7), 2.28–2.20 (m, 1H, H-4), 0.99 (dd, *J* = 7.0 Hz, *J* = 1.2 Hz, 6H, H-5,5').

¹³C{¹H} NMR (100 MHz, CDCl₃): δ 156.4 (C-1), 72.3 (C-6), 65.0 (C-2), 61.6 (C-3), 61.0 (C-7), 29.2 (C-4), 17.3 (C-5 or C-5'), 15.2 (C-5' or C-5).

The spectral data were in agreement with that previously reported in the literature.ⁱⁱ

3-ethynyloxazolidin-2-one (56): Prepared according to **GP IV** from 3-((triisopropylsilyl)ethynyl)oxazolidin-2-one **51** (1.55 g, 5.80 mmol, 1.0 equiv) and TBAF (1.0 M in THF, 8.75 mL, 8.75 mmol, 1.5 equiv) in THF (25 mL), with a reaction time of 1 h. Purification of the crude product by flash chromatography on silica gel (Et₂O/pentane = 80:20) afforded analytically pure **56** (0.45 g, 69%) as a white solid.



55

C₈H₁₁NO₂ M.W. = 153.18 g⋅mol⁻¹



56

C₅H₅NO₂ M.W. = 111.10 g⋅mol⁻¹

ⁱ Romain, E.; Fopp, C.; Chemla, F.; Ferreira, F.; Jackowski, O.; Oestreich, M.; Perez-Luna, A. *Angew. Chem. Int. Ed.* **2014**, *53*, 11333–11337. This product was available in the laboratory.

ⁱⁱ Naud, S.; Cintrat, J.-C. *Synthesis* **2003**, 1391–1397.

¹**H NMR** (400 MHz, CDCl₃): δ 4.44–4.38 (m, 2H, H-2), 3.93–3.87 (m, 2H, H-3), 2.83 (s, 1H, H-5).

¹³C{¹H} NMR (100 MHz, CDCl₃): δ 156.1 (C-1), 72.7 (C-4), 63.2 (C-5), 59.8 (C-2), 46.5 (C-3).

The spectral data were in agreement with that previously reported in the literature.ⁱ

(S)-4-benzyl-3-ethynyloxazolidin-2-one (57): Prepared according to GP IV from (S)-4-benzyl-3-((triisopropylsilyl)ethynyl)oxazolidin-2-one 52 (1.32 g, 4.26 mmol, 1.0 equiv) and TBAF (1.0 M in THF, 6.38 mL, 6.38 mmol, 1.5 equiv) in THF (21 mL), with a reaction time of 1 h. Purification of the crude product by flash chromatography on silica gel (pentane/Et₂O = 50:50) afforded analytically pure 57 (0.72 g, 85%) as a brown solid.

¹**H NMR** (400 MHz, CDCl₃): δ 7.39–7.28 (m, 3H, H-Ar), 7.25–7.22 (m, 2H, H-Ar), 4.37–4.27 (m, 2H, H-2,3), 4.17–4.14 (m, 1H, H-2'), 3.28–3.23 (m, 1H, H-4), 3.01 (s, 1H, H-10), 3.00–2.95 (m, 1H, H-4').

¹³C{¹H} NMR (100 MHz, CDCl₃): δ 155.8 (C-1), 134.0 (C-5), 129.4 (C-Ar), 129.1 (C-Ar), 127.6 (C-Ar), 71.8 (C-9), 67.5 (C-2), 61.9 (C-10), 58.0 (C-3), 37.6 (C-4).

The spectral data were in agreement with that previously reported in the literature.ⁱⁱ

N-benzyl-*N*-ethynyl-4-methylbenzenesulfonamide (58): Prepared according to **GP IV** from *N*-benzyl-4-methyl-*N*-((triisopropylsilyl)ethynyl) benzenesulfonamide **53** (1.40 g, 3.16 mmol, 1.0 equiv) and TBAF (1.0 M in THF, 4.75 mL, 4.75 mmol, 1.5 equiv) in THF (16 mL), with a reaction time of 1 h. Purification of the crude product by flash chromatography on silica gel (pentane/Et₂O = 85:15) afforded analytically pure **58** (0.77 g, 86%) as a white solid.

¹**H NMR** (400 MHz, CDCl₃): δ 7.77–7.75 (m, 2H, H-Ar), 7.33–7.29 (m, 7H, H-Ar), 4.50 (s, 2H, H-5), 2.68 (s, 1H, H-12), 2.46 (s, 3H, H-10).



C₁₂H₁₁NO₂ M.W. = 210.22 g⋅mol⁻¹



58

C₁₆H₁₅NO₂S M.W. = 285.36 g⋅mol⁻¹

ⁱ Chen, Y. L.; Sharma, P.; Liu, R. S. *Chem. Commun.* **2016**, *52*, 3187–3190.

ⁱⁱ Frederick, M. O.; Mulder, J. A.; Tracey, M. R.; Hsung, R. P.; Huang, J.; Kurtz, K. C. M.; Shen, L.; Douglas, C. J. *J. Am. Chem. Soc.* **2003**, *125*, 2368–2369.

¹³C{¹H} NMR (100 MHz, CDCl₃): δ 144.7 (C-9), 134.7 (C-6), 134.3 (C-4), 129.7 (C-7), 128.7 (C-2 or C-3), 128.5 (C-3 or C-2), 128.4 (C-1), 127.7 (C-8), 76.3 (C-11), 59.7 (C-12), 55.3 (C-5), 21.7 (C-10).

The spectral data were in agreement with that previously reported in the literature.ⁱ

4,4-dimethyl-3-(phenylethynyl)oxazolidin-2-one (92): Prepared according to **GP V** from 4,4-dimethyloxazolidin-2-one (0.90 g, 7.82 mmol, 1.0 equiv) and (2,2-dibromovinyl)benzene **97** (3.07 g, 11.72 mmol, 1.5 equiv), using Cs_2CO_3 (10.19 g, 31.27 mmol, 4.0 equiv), CuI (186 mg, 0.98 mmol, 0.1 equiv), and *N*,*N*'-dimethylethylenediamine (129 mg, 1.47 mmol, 0.2 equiv), in dioxane (16 mL), with a reaction time of 24 h. Purification of the crude product by flash chromatography on silica gel (pentane/Et₂O = 60:40) afforded analytically pure **92** (1.02 g, 61%) as a pale yellow solid.



92

C₁₃H₁₃NO₂ M.W. = 215.09 g⋅mol⁻¹

¹**H NMR** (400 MHz, CDCl₃): 7.47–7.43 (m, 2H, H-Ar), 7.32–7.29 (m, 3H, H-Ar), 4.19 (s, 2H, H-2), 1.50 (s, 6H, H-4).

¹³C{¹H} NMR (100 MHz, CDCl₃): δ 155.0 (C-1), 131.6 (C-Ar), 128.3 (C-Ar), 128.1 (C-Ar), 122.4 (C-7), 76.3 (C-5 or C-6), 75.7 (C-2), 73.5 (C-6 or C-5), 60.3 (C-3), 24.9 (C-4).

The spectral data were in agreement with that previously reported in the literature.ⁱⁱ

(*S*)-4-isopropyl-3-(phenylethynyl)oxazolidin-2-one (106): Prepared according to **GP V** from (*S*)-4-isopropyloxazolidin-2-one (0.25 g, 1.95 mmol, 1.0 equiv) and (2,2-dibromovinyl)benzene **97** (1.02 g, 3.89 mmol, 1.5 equiv), using Cs_2CO_3 (2.54 g, 7.78 mmol, 4.0 equiv), CuI (46 mg, 0.24 mmol, 0.1 equiv), and *N*,*N*'-dimethylethylenediamine (32 mg, 0.36 mmol, 0.2 equiv), in dioxane (4 mL), with a reaction time of 24 h. Purification of the crude product by flash chromatography on silica gel (pentane/Et₂O = 60:40) afforded analytically pure **106** (335 mg, 63%) as a white solid.

⁵ 5 5 5 5 5 5 7 0 0 0 0 0



C₁₄H₁₅NO₂ M.W. = 229.27 g⋅mol⁻¹

ⁱ Dooleweerdt, K.; Ruhland, T.; Skrydstrup, T. *Org. Lett.* **2009**, *11*, 221–224.

ⁱⁱ Kuroda, Y.; Shindoh, N.; Takemoto, Y.; Takasu, K. *Synthesis* **2013**, *45*, 2328–2329.

¹**H NMR** (400 MHz, CDCl₃): δ 7.45–7.42 (m, 2H, H-Ar), 7.31–7.29 (m, 3H, H-Ar), 4.42 (t, *J* = 8.9 Hz, 1H, H-2), 4.19 (dd, *J* = 8.9 Hz, *J* = 5.8 Hz, 1H, H-2'), 4.05 (ddd, *J* = 8.9 Hz, *J* = 5.8 Hz, *J* = 4.1 Hz, 1H, H-3), 2.33–2.25 (m, 1H, H-4), 1.04 (d, *J* = 7.0 Hz, 3H, H-5 or H-5'), 1.03 (d, *J* = 7.0 Hz, 3H, H-5' or H-5).

¹³C{¹H} NMR (100 MHz, CDCl₃): δ 156.0 (C-1), 131.5 (C-Ar), 128.3 (C-Ar), 128.1 (C-Ar), 122.4 (C-8), 78.5 (C-6), 72.3 (C-7), 64.9 (C-2), 62.1 (C-3), 29.3 (C-4), 17.3 (C-5 or C-5'), 15.3 (C-5' or C-5).

The spectral data were in agreement with that previously reported in the literature.ⁱ

(*S*)-4-benzyl-3-(phenylethynyl)oxazolidin-2-one (107): Prepared according to **GP III** from (*S*)-4-benzyloxazolidin-2-one (0.50 g, 2.82 mmol, 1.00 equiv), (bromoethynyl)benzene **95** (0.56 g, 3.10 mmol, 1.10 equiv), CuSO₄·5H₂O (70 mg, 0.28 mmol, 0.10 equiv), 1,10-phenanthroline (102 mg, 0.56 mmol, 0.20 equiv), and K₂CO₃ (0.78 g, 5.64 mmol, 2.00 equiv) in dry toluene (3 mL), with a reaction time of 3 days. Purification of the crude product by flash chromatography on silica gel (pentane/Et₂O = 65:35) afforded analytically pure **107** (297 mg, 38%) as a white solid.

¹**H NMR** (400 MHz, CDCl₃): δ 7.50–7.47 (m, 2H, H-Ar), 7.40–7.32 (m, 6H, H-Ar), 7.28–7.26 (m, 2H, H-Ar), 4.42–4.35 (m, 2H, H-2,3), 4.22–4.16 (m, 1H, H-2'), 3.34–3.30 (m, 1H, H-4), 3.07–3.02 (m, 1H, H-4').

¹³C{¹H} NMR (100 MHz, CDCl₃): δ 155.5 (C-1), 134.2 (C-5), 131.6 (C-Ar), 129.4 (C-Ar), 129.1 (C-Ar), 128.3 (C-Ar), 128.25 (C-Ar), 127.6 (C-Ar), 122.2 (C-Ar), 78.0 (C-9), 73.3 (C-10), 67.5 (C-2), 58.5 (C-3), 38.0 (C-4).

The spectral data were in agreement with that previously reported in the literature.ⁱ

3-(phenylethynyl)oxazolidin-2-one (108): Prepared according to **GP V** from oxazolidin-2-one (0.43 g, 4.96 mmol, 1.0 equiv) and (2,2-dibromovinyl)benzene **97** (1.95 g, 7.44 mmol, 1.5 equiv), using Cs_2CO_3 (6.46 g, 19.84 mmol, 4.0 equiv), CuI (118 mg, 0.62 mmol, 0.1 equiv), and *N*,*N*'-dimethylethylenediamine (82 mg, 0.93 mmol, 0.2 equiv), in dioxane (10 mL),



107

 $C_{18}H_{15}NO_2$ M.W. = 277.32 g·mol⁻¹

ⁱ Yao, B.; Liang, Z.; Niu, T.; Zhang, Y. *J. Org. Chem.* **2009**, *74*, 4630–4633.

with a reaction time of 24 h. Purification of the crude product by flash chromatography on silica gel (pentane/ Et_2O = gradient from 50:50 to 30:70) afforded analytically pure **108** (566 mg, 61%) as a pale yellow solid.

¹**H NMR** (400 MHz, CDCl₃): δ 7.44–7.42 (m, 2H, H-Ar), 7.31–7.28 (m, 3H, H-Ar), 4.47–4.43 (m, 2H, H-2), 3.99–3.95 (m, 2H, H-3).

¹³C{¹H} NMR (100 MHz, CDCl₃): δ 156.0 (C-1), 131.6 (C-Ar), 128.3 (C-Ar), 128.2 (C-Ar), 122.2 (C-6), 79.1 (C-4), 71.2 (C-5), 63.1 (C-2), 47.1 (C-3).

The spectral data were in agreement with that previously reported in the literature.ⁱ

Methyl phenyl(phenylethynyl)carbamate (109): Prepared according to **GP V** from methyl phenylcarbamate (1.00 g, 6.62 mmol, 1.0 equiv) and (2,2dibromovinyl)benzene **97** (2.60 g, 9.93 mmol, 1.5 equiv), using Cs_2CO_3 (8.63 g, 26.48 mmol, 4.0 equiv), CuI (158 mg, 0.83 mmol, 0.1 equiv), and *N*,*N'*dimethylethylenediamine (109 mg, 1.24 mmol, 0.2 equiv), in dioxane (10 mL), with a reaction time of 24 h. Purification of the crude product by flash chromatography on silica gel (pentane/Et₂O = gradient from 95:5 to 92:8) afforded analytically pure **109** (477 mg, 29%) as a pale yellow oil.

¹**H NMR** (400 MHz, CDCl₃): δ 7.57–7.55 (m, 2H, H-Ar), 7.46–7.41 (m, 4H, H-Ar), 7.33–7.28 (m, 4H, H-Ar), 3.92 (s, 3H, H-1).

¹³C{¹H} NMR (100 MHz, CDCl₃): δ 154.8 (C-1), 139.5 (C-3), 131.5 (C-Ar), 129.0 (C-Ar), 128.3 (C-Ar), 127.9 (C-Ar), 127.1 (C-Ar), 124.7 (C-Ar), 122.9 (C-9), 82.8 (C-7), 70.2 (C-8), 54.5 (C-1).

The spectral data were in agreement with that previously reported in the literature.ⁱⁱ

N-benzyl-4-methyl-*N*-(phenylethynyl)benzenesulfonamide (110):

Prepared according to **GP V** from *N*-benzyl-4-methylbenzenesulfonamide (0.42 g, 1.60 mmol, 1.0 equiv) and (2,2-dibromovinyl)benzene **97** (0.63 g, 2.40 mmol, 1.5 equiv), using Cs_2CO_3 (2.10 g, 6.40 mmol, 4.0 equiv), CuI (38 mg, 0.20 mmol, 0.1 equiv), and *N*,*N*'-dimethylethylenediamine (25 mg, 0.30 mmol,



108

C₁₁H₉NO₂ M.W. = 187.19 g⋅mol⁻¹



109

C₁₆H₁₃NO₂ M.W. = 251.28 g⋅mol⁻¹



110

C₂₂H₁₉NO₂S M.W. = 361.46 g⋅mol⁻¹

ⁱ Hamada, T.; Ye, X.; Stahl, S. S. *J. Am. Chem. Soc.* **2008**, *130*, 833–835.

ⁱⁱ Riddell, N.; Villeneuve, K.; Tam, W. *Org. Lett.* **2005**, *7*, 3681–3684.

0.2 equiv), in dioxane (3 mL), with a reaction time of 24 h. Purification of the crude product by flash chromatography on silica gel (pentane/ Et_2O = 95:5) afforded analytically pure **110** (533 mg, 92%) as a white solid.

¹**H NMR** (400 MHz, CDCl₃): δ 7.81–7.79 (m, 2H, H-Ar), 7.34–7.30 (m, 7H, H-Ar), 7.25–7.23 (m, 5H, H-Ar), 4.59 (s, 2H, H-5), 2.45 (s, 3H, H-10).

¹³C{¹H} NMR (100 MHz, CDCl₃): δ 144.6 (C-9), 134.7 (C-6), 134.5 (C-4), 131.1 (C-Ar), 129.7 (C-Ar), 128.9 (C-Ar), 128.5 (C-Ar), 128.3 (C-Ar), 128.2 (C-Ar), 127.8 (C-Ar), 127.7 (C-Ar), 122.8 (C-13), 82.7 (C-11), 71.4 (C-12), 55.7 (C-5), 21.7 (C-10).

The spectral data were in agreement with that previously reported in the literature.ⁱ

4-methyl-N-phenyl-N-(phenylethynyl)benzenesulfonamide(111):Prepared according to **GP III** from 4-methyl-N-phenylbenzenesulfonamide(0.50 g, 2.02 mmol, 1.0 equiv), (bromoethynyl)benzene **95** (0.40 g, 2.22 mmol,1.10 equiv), CuSO₄·5H₂O (50 mg, 0.20 mmol, 0.10 equiv), 1,10-phenanthroline(73 mg, 0.40 mmol, 0.20 equiv), and K₂CO₃ (0.56 g, 4.04 mmol, 2.00 equiv) indry DMF (3 mL), with a reaction time of 3 days. Purification of the crudeproduct by flash chromatography on silica gel (pentane/Et₂O = 90:10)afforded analytically pure **111** (577 mg, 82%) as a white solid.

¹**H NMR** (400 MHz, CDCl₃): δ 7.66–7.64 (m, 2H, H-Ar), 7.43–7.28 (m, 12H, H-Ar), 2.47 (s, 3H, H-9).

¹³C{¹H} NMR (100 MHz, CDCl₃): δ 145.0 (C-8), 139.0 (C-5), 133.0 (C-4), 131.4 (C-Ar), 129.5 (C-Ar), 129.1 (C-Ar), 128.3 (C-Ar), 128.28 (C-Ar), 128.2 (C-Ar), 128.0 (C-Ar), 126.3 (C-Ar), 122.7 (C-12), 83.0 (C-10), 70.5 (C-11), 21.7 (C-9).

The spectral data were in agreement with that previously reported in the literature.ⁱⁱ





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C<sub>21</sub>H<sub>17</sub>NO<sub>2</sub>S
M.W. = 347.43 g⋅mol<sup>-1</sup>
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ⁱ Coste, A.; Karthikeyan, G.; Couty, F.; Evano, G. *Angew. Chem. Int. Ed.* **2009**, *48*, 4381–4385.

ⁱⁱ Yao, B.; Liang, Z.; Niu, T.; Zhang, Y. *J. Org. Chem.* **2009**, *74*, 4630–4633.

3-((4-methoxyphenyl)ethynyl)-4,4-dimethyloxazolidin-2-one (112):

Prepared according to **GP V** from 4,4-dimethyloxazolidin-2-one (0.50 g, 4.34 mmol, 1.0 equiv) and 1-(2,2-dibromovinyl)-4-methoxybenzene **98** (1.90 g, 6.51 mmol, 1.5 equiv), using Cs₂CO₃ (5.66 g, 17.36 mmol, 4.0 equiv), CuI (103 mg, 0.54 mmol, 0.1 equiv), and *N*,*N*'-dimethylethylenediamine (72 mg, 0.81 mmol, 0.2 equiv), in dioxane (8 mL), with a reaction time of 25 h. Purification of the crude product by flash chromatography on silica gel (pentane/Et₂O = gradient from 50:50 to 30:70) afforded analytically pure **112** (0.85 g, 80%) as a white solid; mp 115–118 °C.

¹**H NMR** (400 MHz, CDCl₃): 7.42–7.39 (m, 2H, H-8), 6.86–6.82 (m, 2H, H-9), 4.18 (s, 2H, H-2), 3.81 (s, 3H, H-11), 1.48 (s, 6H, H-4).

¹³C{¹H} NMR (100 MHz, CDCl₃): δ 159.8 (C-10), 155.3 (C-1), 133.7 (C-8), 114.5 (C-7), 114.0 (C-9), 75.8 (C-2), 74.9 (C-5), 73.3 (C-6), 60.4 (C-3), 55.4 (C-11), 25.0 (C-4).

IR (neat): *v* (cm⁻¹) 2967, 2927, 1751, 1409, 1245, 1074, 828, 751.

HRMS (ESI): *m*/*z* calculated for [C₁₄H₁₅NO₃ + Na]⁺ 268.0944; found 268.0943.

3-((4-chlorophenyl)ethynyl)-4,4-dimethyloxazolidin-2-one (113):

Prepared according to **GP V** from 4,4-dimethyloxazolidin-2-one (1.00 g, 8.69 mmol, 1.0 equiv) and 1-chloro-4-(2,2-dibromovinyl)benzene **99** (3.86 g, 13.03 mmol, 1.5 equiv), using Cs₂CO₃ (11.32 g, 34.74 mmol, 4.0 equiv), CuI (207 mg, 1.09 mmol, 0.1 equiv), and *N*,*N*'-dimethylethylenediamine (144 mg, 1.63 mmol, 0.2 equiv), in dioxane (16 mL), with a reaction time of 24 h. Purification of the crude product by flash chromatography on silica gel (pentane/Et₂O = gradient from 70:30 to 50:50) afforded analytically pure **113** (1.48 g, 68%) as a pale yellow solid; mp 100–102 °C.

¹**H NMR** (400 MHz, CDCl₃): 7.39–7.36 (m, 2H, H-8), 7.30–7.26 (m, 2H, H-9), 4.19 (s, 2H, H-2), 1.49 (s, 6H, H-4).

¹³C{¹H} NMR (100 MHz, CDCl₃): δ 155.1 (C-1), 134.3 (C-7), 132.9 (C-8), 128.8 (C-9), 121.1 (C-10), 77.4 (C-5), 75.9 (C-2), 72.7 (C-6), 60.5 (C-3), 25.1 (C-4).

IR (neat): *v* (cm⁻¹) 2976, 1763, 1401, 1273, 1176, 1078, 829, 751.

HRMS (ESI): m/z calculated for $[C_{13}H_{12}CINO_2 + Na]^+ 272.0449$; found 272.0456.



112

C₁₄H₁₅NO₃ M.W. = 245.27 g⋅mol⁻¹



113

C₁₃H₁₂ClNO₂ M.W. = 249.69 g⋅mol⁻¹


114

C₁₄H₁₅NO₃ M.W. = 245.27 g⋅mol⁻¹

3-((3-methoxyphenyl)ethynyl)-4,4-dimethyloxazolidin-2-one (114): Prepared according to **GP V** from 4,4-dimethyloxazolidin-2-one (1.00 g, 8.69 mmol, 1.0 equiv) and 1-(2,2-dibromovinyl)-3-methoxybenzene **100** (3.80 g, 13.03 mmol, 1.5 equiv) using Cs₂CO₃ (11.32 g, 34.74 mmol, 4.0 equiv), CuI (207 mg, 1.09 mmol, 0.1 equiv), and *N*,*N*'-dimethylethylenediamine (144 mg, 1.63 mmol, 0.2 equiv), in dioxane (16 mL), with a reaction time of 24 h. Purification of the crude product by flash chromatography on silica gel (pentane/Et₂O = 50:50) afforded analytically pure **114** (1.61 g, 76%) as a pale yellow solid; mp 91–94 °C.

¹**H NMR** (400 MHz, CDCl₃): 7.23–7.19 (m, 1H, H-11), 7.04 (dt, *J* = 7.6 Hz, *J* = 1.2 Hz, 1H, H-10 or H-12), 6.98 (dd, *J* = 2.7 Hz, *J* = 1.2 Hz, 1H, H-8), 6.86 (ddd, *J* = 8.3 Hz, *J* = 2.7 Hz, *J* = 1.2 Hz, 1H, H-12 or H-10), 4.19 (s, 2H, H-2), 3.80 (s, 3H, H-13), 1.50 (s, 6H, H-4).

¹³C{¹H} NMR (100 MHz, CDCl₃): δ 159.5 (C-9), 155.1 (C-1), 129.5 (C-11), 124.2 (C-10 or C-12), 123.6 (C-7), 116.5 (C-8), 114.9 (C-12 or C-10), 76.3 (C-5), 75.8 (C-2), 73.7 (C-6), 60.5 (C-3), 55.5 (C-13), 25.1 (C-4).

IR (neat): *v* (cm⁻¹) 3073, 2974, 1769, 1574, 1393, 1281, 1169, 1076.

HRMS (ESI): *m*/*z* calculated for [C₁₄H₁₅NO₃ + Na]⁺ 268.0944; found 268.0948.





C₁₂H₁₁NO₃ M.W. = 217.22 g⋅mol⁻¹ **3-((2-methoxyphenyl)ethynyl)oxazolidin-2-one (116):** Prepared according to **GP VI** from oxazolidin-2-one (0.70 g, 8.00 mmol, 4.0 equiv) and ((2-methoxyphenyl)ethynyl)copper **105** (0.39 g, 2.00 mmol, 1.0 equiv), using N,N,N',N'-tetramethylethylenediamine (0.30 mL, 2.00 mmol, 1.0 equiv) in acetonitrile (4 mL), with a reaction time of 48 h. Purification of the crude product by flash chromatography on silica gel (Et₂O/pentane = 80:20) afforded analytically pure **116** (174 mg, 40%) as a colorless oil.

¹**H NMR** (400 MHz, CDCl₃): δ 7.43 (dd, *J* = 7.6 Hz, *J* = 1.7 Hz, 1H, H-11), 7.32– 7.28 (m, 1H, H-9), 6.92 (dd, *J* = 7.6 Hz, *J* = 1.0 Hz, 1H, H-10), 6.88 (dd, *J* = 8.5 Hz, *J* = 1.0 Hz, 1H, H-8), 4.50–4.46 (m, 2H, H-2), 4.05–4.01 (m, 2H, H-3), 3.89 (s, 3H, H-12).

¹³C{¹H} NMR (100 MHz, CDCl₃): δ 160.0 (C-7), 155.9 (C-1), 133.8 (C-11), 129.8 (C-9), 120.4 (C-10), 111.3 (C-6), 110.6 (C-8), 82.6 (C-4), 67.4 (C-5), 63.1 (C-2), 55.8 (C-12), 47.2 (C-3).

The spectral data were in agreement with that previously reported in the literature.ⁱ

3-((2,6-dichlorophenyl)ethynyl)-4,4-dimethyloxazolidin-2-one (117):

Prepared according to **GP V** from 4,4-dimethyloxazolidin-2-one (1.00 g, 8.69 mmol, 1.0 equiv) and 1,3-dichloro-2-(2,2-dibromovinyl)benzene **101** (4.91 g, 13.03 mmol, 1.5 equiv), using Cs₂CO₃ (11.32 g, 34.74 mmol, 4.0 equiv), CuI (207 mg, 1.09 mmol, 0.1 equiv), and *N*,*N*'-dimethylethylenediamine (144 mg, 1.63 mmol, 0.2 equiv), in dioxane (16 mL), with a reaction time of 24 h. Purification of the crude product by flash chromatography on silica gel (pentane/Et₂O = gradient from 70:30 to 50:50) afforded analytically pure **117** (665 mg, 27%) as a pale brown solid; mp 98–100 °C.





C₁₃H₁₁Cl₂NO₂ M.W. = 284.14 g⋅mol⁻¹

¹**H NMR** (400 MHz, CDCl₃): 7.31–7.29 (m, 2H, H-9), 7.12 (dd, *J* = 8.6 Hz, *J* = 7.7 Hz, 1H, H-10), 4.21 (s, 2H, H-2), 1.55 (s, 6H, H-4).

¹³C{¹H} NMR (100 MHz, CDCl₃): δ 154.4 (C-1), 136.2 (C-8), 128.5 (C-10), 127.5 (C-9), 123.0 (C-7), 87.1 (C-5), 75.9 (C-2), 68.7 (C-6), 60.9 (C-3), 25.0 (C-4).

IR (neat): *v* (cm⁻¹) 2977, 1772, 1390, 1371, 1272, 1200, 1076, 783.

HRMS (ESI): m/z calculated for $[C_{13}H_{11}Cl_2NO_2 + Na]^+$ 306.0059; found 306.0062.

(E)-4,4-dimethyl-3-(4-phenylbut-3-en-1-yn-1-yl)oxazolidin-2-one

(118): Prepared according to GP V from 4,4-dimethyloxazolidin-2-one (500 mg, 4.34 mmol, 1.0 equiv) and (*E*)-(4,4-dibromobuta-1,3-dien-1-yl)benzene **102** (1.64 g, 6.51 mmol, 1.5 equiv), using Cs₂CO₃ (5.66 g, 17.36 mmol, 4.0 (103 0.54 equiv), CuI mg, mmol, 0.1 equiv), and N.N'dimethylethylenediamine (72 mg, 0.81 mmol, 0.2 equiv), in dioxane (8 mL), with a reaction time of 25 h. Purification of the crude product by flash chromatography on silica gel (pentane/ Et_2O = gradient from 50:50 to 30:70) afforded analytically pure **118** (676 mg, 65%) as a yellow solid; mp 104–105 °C.



¹¹⁸

C₁₅H₁₅NO₂ M.W. = 241.29 g⋅mol⁻¹

ⁱ Jouvin, K.; Heimburger, J.; Evano, G. *Chem. Sci.* **2012**, *3*, 756–760.

¹**H NMR** (400 MHz, CDCl₃): 7.41–7.27 (m, 5H, H-Ar), 6.95 (d, *J*_{trans} = 16.2 Hz, 1H, H-8), 6.31 (d, *J*_{trans} = 16.2 Hz, 1H, H-7), 4.18 (s, 2H, H-2), 1.49 (s, 6H, H-4).

¹³C{¹H} NMR (100 MHz, CDCl₃): δ 155.1 (C-1), 140.3 (C-8), 136.3 (C-9), 128.8 (C-Ar), 128.5 (C-Ar), 126.2 (C-Ar), 107.2 (C-7), 78.4 (C-5), 75.8 (C-2), 73.3 (C-6), 60.4 (C-3), 25.0 (C-4).

IR (neat): *v* (cm⁻¹) 2974, 2920, 2231, 1759, 1400, 1167, 741, 686.

HRMS (ESI): *m*/*z* calculated for [C₁₅H₁₅NO₂ + Na]⁺ 264.0995; found 264.0989.

Note: The E configuration was determined on the basis of the ¹H NMR coupling constant of the vinylic protons (J = 16.2 Hz).



119

C₁₃H₂₁NO₂ M.W. = 223.31 g⋅mol⁻¹

4,4-dimethyl-3-(oct-1-yn-1-yl)oxazolidin-2-one (**119**): Prepared according to **GP III** from 4,4-dimethyloxazolidin-2-one (1.00 g, 8.69 mmol, 1.3 equiv) and 1-bromooct-1-yne **96** (1.32 g, 6.98 mmol, 1.0 equiv), using 1,10-phenanthroline (252 mg, 1.40 mmol, 0.2 equiv), $CuSO_4 \cdot 5H_2O$ (174 mg, 0.70 mmol, 0.1 equiv), and K_2CO_3 (2.07 g, 15.01 mmol, 2.2 equiv) in toluene (40 mL) with a reaction time of 6 days. Purification of the crude product by flash chromatography on silica gel (pentane/Et₂O = 70:30) afforded analytically pure **119** (333 mg, 21%) as a pale yellow oil.

¹**H NMR** (400 MHz, CDCl₃): 4.09 (s, 2H, H-2), 2.32 (td, *J* = 7.0 Hz, *J* = 0.5 Hz, 2H, H-7), 1.56–1.48 (m, 2H, H-alkyl), 1.42–1.34 (m, 8H, H-alkyl), 1.32–1.22 (m, 4H, H-alkyl), 0.88–0.85 (m, 3H, H-12).

¹³C{¹H} NMR (100 MHz, CDCl₃): δ 155.8 (C-1), 75.5 (C-2), 73.3 (C-5), 67.2 (C-6), 59.7 (C-3), 31.2, 28.8, 28.4, 24.6, 22.5, 18.5, 14.0.

IR (neat): *v* (cm⁻¹) 2967, 2926, 2858, 1766, 1401, 1168, 1072, 1021.

HRMS (ESI): *m*/*z* calculated for [C₁₃H₂₁NO₂ + Na]⁺ 246.1465; found 246.1462.

3-(cyclohexylethynyl)-4,4-dimethyloxazolidin-2-one (120): Prepared according to **GP V** from 4,4-dimethyloxazolidin-2-one (1.00 g, 8.69 mmol, 1.0 equiv) and (2,2-dibromovinyl)cyclohexane **103** (3.49 g, 13.03 mmol, 1.5 equiv), using Cs_2CO_3 (11.32 g, 34.74 mmol, 4.0 equiv), CuI (207 mg, 1.09 mmol, 0.1 equiv), and *N*,*N*'-dimethylethylenediamine (144 mg, 1.63 mmol, 0.2 equiv), in dioxane (16 mL), with a reaction time of 24 h. Purification of the

crude product by flash chromatography on silica gel (pentane/ $Et_20 = 60:40$) afforded analytically pure **120** (1.16 g, 60%) as a white solid; mp 74–75 °C.

¹**H NMR** (400 MHz, CDCl₃): 4.07 (s, 2H, H-2), 2.52 (tt, *J* = 8.7 Hz, *J* = 3.9 Hz, 1H, H-7), 1.80–1.74 (m, 2H, H-8), 1.69–1.62 (m, 2H, H-8'), 1.49–1.41 (m, 3H, H-alkyl), 1.36 (s, 6H, H-4), 1.33–1.28 (m, 3H, H-alkyl).

¹³C{¹H} NMR (100 MHz, CDCl₃): δ 155.6 (C-1), 77.3 (C-5), 75.5 (C-2), 67.5 (C-6), 59.8 (C-3), 32.9, 28.8 (C-7), 25.9, 24.7, 24.66.

IR (neat): *v* (cm⁻¹) 2929, 2854, 1765, 1404, 1171, 1074, 1022, 753.

HRMS (ESI): *m*/*z* calculated for [C₁₃H₁₉NO₂ + Na]⁺ 244.1308; found 244.1299.

4,4-dimethyl-3-(phenylbuta-1,3-diyn-1-yl)oxazolidin-2-one (122): Prepared according to literature proceduresⁱ from ynamide **54** (200 mg, 1.44 mmol, 1.2 equiv), (bromoethynyl)benzene **95** (217 mg, 1.20 mmol, 1.0 equiv), Pd(dba)₂ (28 mg, 0.05 mmol, 4mol%), PPh₃ (13 mg, 0.05 mmol, 4mol%), CuI (5 mg, 0.02 mmol, 2mol%), and Et₃N (243 mg, 2.40 mmol, 2.0 equiv) in dry DMF (2 mL). The reaction mixture was left overnight. Purification of the crude product by flash chromatography on silica gel (pentane/Et₂O = 90:10) afforded analytically pure **122** (152 mg, 53%) as a brown solid; mp 148-149 °C.

¹**H NMR** (400 MHz, CDCl₃): 7.50-7.47 (m, 2H, H-Ar), 7.37-7.29 (m, 3H, H-Ar), 4.17 (s, 2H, H-2), 1.49 (s, 6H, H-4).

¹³**C NMR** (100 MHz, CDCl₃): δ 155.1 (C-1), 132.5 (C-Ar), 129.3 (C-Ar), 128.5 (C-Ar), 121.9 (C-9), 81.4 (C-8), 76.0 (C-2), 73.3, 68.3, 60.9 (C-3), 60.8, 25.1 (C-4).

IR (neat): v (cm⁻¹) 2977, 2919, 2239, 1753, 1414, 1164, 745, 691.

HRMS (ESI): *m*/*z* calculated for [C₁₅H₁₃NO₂ + K]⁺ 278.0578; found 278.0587.

4,4-dimethyl-3-((triisopropylsilyl)buta-1,3-diyn-1-yl)oxazolidin-2-one (123): Prepared according to literature proceduresⁱ from ynamide **54** (200 mg, 1.44 mmol, 1.2 equiv) and (bromoethynyl)triisopropylsilane **48** (314 mg,



120

C₁₃H₁₉NO₂ M.W. = 221.30 g⋅mol⁻¹



122

C₁₅H₁₃NO₂ M.W. = 239.27 g⋅mol⁻¹

ⁱ Shi, W.; Luo, Y.; Luo, X.; Chao, L.; Zhang, H.; Wang, J.; Lei, A. *J. Am. Chem. Soc.* **2008**, *130*, 14713.



123

C₁₈H₂₉NO₂Si M.W. = 319.51 g⋅mol⁻¹

124

 $C_8H_8F_3NO_2$

M.W. = 207.15 g·mol⁻¹



¹**H NMR** (400 MHz, CDCl₃): 4.14 (s, 2H, H-2), 1.47 (s, 6H, H-4), 1.08 (s_{app}, 21H, H-9,10).

¹³C{¹H} NMR (100 MHz, CDCl₃): δ 155.3 (C-1), 88.8, 87.7, 76.0 (C-2), 62.4, 61.8, 60.8 (C-3), 25.1 (C-4), 18.7 (C-10), 11.4 (C-9).

IR (neat): *v* (cm⁻¹) 2950, 2862, 2231, 1764, 1402, 1376, 1169, 669.

HRMS (ESI): m/z calculated for $[C_{18}H_{29}NO_2Si + Na]^+$ 342.1860; found 342.1870.

4,4-dimethyl-3-(3,3,3-trifluoroprop-1-yn-1-yl)oxazolidin-2-one (124): Prepared by the method reported by Evano and Blanchardⁱ from ynamide **54** (300 mg, 2.16 mmol, 1.0 equiv) and TMSCF₃ (1.23 g, 8.64 mmol, 4.0 equiv), using CuI (617 mg, 3.24 mmol, 1.5 equiv), TMEDA (377 mg, 3.24 mmol, 1.5 equiv), and K₂CO₃ (896 mg, 6.48 mmol, 3.0 equiv), in dry DMF (10 mL), with a reaction time of 48 h. Purification of the crude product by flash chromatography on silica gel (pentane/Et₂O = gradient from 70:30 to 60:40) afforded analytically pure **124** (68 mg, 15%) as a white solid; mp 53–55 °C.

¹**H NMR** (400 MHz, CDCl₃): δ 4.20 (s, 2H, H-2), 1.48 (s, 6H, H-4).

¹³C{¹H} NMR (100 MHz, CDCl₃): δ 153.9 (C-1), 115.4 (q, *J*_{CF} = 256.9 Hz, C-7), 76.3 (C-2), 75.3 (q, *J*_{CF} = 5.9 Hz, C-5), 62.6 (q, *J*_{CF} = 54.5 Hz, C-6), 61.0 (C-3), 24.9 (C-4).

¹⁹**F NMR** (376 MHz, CDCl₃): δ –48.5 (s).

IR (neat): *v* (cm⁻¹) 2923, 2279, 2256, 1781, 1272, 1122, 1018, 680.

HRMS (ESI): *m*/*z* calculated for [C₈H₈F₃NO₂ + Na]⁺ 246.1465; found 246.1465.

ⁱ Tresse, C.; Guissart, C.; Schweizer, S.; Bouhoute, Y.; Chany, A.-C.; Goddard, M.-L.; Blanchard, N.; Evano, G. *Adv. Synth. Catal.* **2014**, *356*, 2051–2060.

III-5.1.5. Synthesis of other α -Heteroatom-Substituted Alkynes

Triisopropyl(phenylthioethynyl)silane (205): Prepared according to the following reported procedure.ⁱ To a stirred solution of triisopropylacetylene (0.82 mL, 3.64 mmol, 1.0 equiv) in THF (4 mL) was added *n*BuLi (2.5 M in hexane, 1.70 mL, 4.25 mmol, 1.2 equiv) at -78 °C. After 2 h at -78 °C, diphenylsulfide (0.87 g, 3.98 mmol, 1.1 equiv) was added, and the temperature was allowed to warm up to rt. After 2 h, the mixture was diluted with Et₂O (60 mL) and quenched with saturated aq Na₂CO₃ (60 mL). The layers were separated and the aqueous one was extracted with Et₂O (2 x 60 mL). The combined organic layers were dried over Na₂SO₄, filtered, and concentrated under reduce pressure to afford the crude product. Purification by flash chromatography on silica gel (pentane) afforded analytically pure **205** (0.92 g, 3.17 mmol, 87%) as a yellow oil.

¹**H NMR** (400 MHz, CDCl₃): δ 7.46–7.44 (m, 2H, H-2), 7.36–7.32 (m, 2H, H-3), 7.24–7.19 (m, 1H, H-1), 1.13 (s, 18H, H-8), 1.12 (s, 3H, H-7).

¹³C{¹H} NMR (100 MHz, CDCl₃): δ 133.0 (C-4), 129.3 (C-3), 126.5 (C-1), 126.2 (C-2), 103.4 (C-6), 91.3 (C-5), 18.8 (C-8), 11.5 (C-7).

The spectral data were in agreement with that previously reported in the literature.ⁱ

Ethynyl(phenyl)sulfane (206): Prepared according to the following reported procedure.ⁱⁱ To a stirred solution of **205** (0.92 g, 3.17 mmol, 1.0 equiv) in THF (18 mL) was added TBAF (1.0 M in THF, 4.80 mL, 4.80 mmol, 1.5 equiv) at 0 °C. Temperature was then allowed to warm up to rt. After 2 h, the mixture was diluted with Et_2O (30 mL) and quenched with saturated aq NH₄Cl (30 mL). The layers were separated and the aqueous one was extracted with Et_2O (3 x 30 mL). The combined organic layers were washed with brine (x2), dried over Na₂SO₄, filtered, and concentrated under reduce pressure to afford the crude product. Purification by flash chromatography on silica gel (pentane) afforded analytically pure **206** (0.24 g, 56%) as a brown oil.

C₁₇H₂₆SSi M.W. = 290.54 g⋅mol⁻¹



206

C₈H₆S M.W. = 134.20 g⋅mol⁻¹

 $H_{3}C \xrightarrow{7}_{8} H_{3}C$

²⁰⁵

ⁱ Frei, R.; Waser, J. *J. Am. Chem. Soc.* **2013**, *135*, 9620–9623.

ⁱⁱ Isomura, K. A. H. F. M. *Chem. Pharm. Bull.* **1981**, *29*, 1274–1279.

¹**H NMR** (400 MHz, CDCl₃): δ 7.50–7.47 (m, 2H, H-2), 7.40–7.35 (m, 2H, H-3), 7.29–7.25 (m, 1H, H-1), 3.25 (s, 1H, H-6).

¹³C{¹H} NMR (100 MHz, CDCl₃): δ 131.7 (C-4), 129.4 (C-3), 127.0 (C-1), 126.8 (C-2), 87.0 (C-6), 71.2 (C-5).

The spectral data were in agreement with that previously reported in the literature.ⁱ



207

C₁₄H₁₈S M.W. = 218.36 g⋅mol⁻¹ **Oct-1-yn-1-yl(phenyl)sulfane (207):** Prepared according to the following reported procedure.ⁱⁱ 1-Octyne (2.00 g, 2.7 mL, 18.10 mmol, 1.0 equiv) was dissolved in THF (20 mL) and the solution was cooled to -78 °C. At this temperature, *n*BuLi (1.5 M in hexane, 14.1 mL, 21.18 mmol, 1.17 equiv) was added. The reaction mixture was stirred for 30 min at -78 °C. Next, diphenyldisulfide (4.36 g, 19.96 mmol, 1.1 equiv) was added in portions and stirring was continued for further 30 min at low temperature. Afterward, the reaction mixture was allowed to warm to rt. After 90 min at rt, the reaction was quenched with H₂O (10 mL) at 0 °C and diluted with diethyl ether (20 mL). The organic layer was separated, washed with 0.1 M NaOH (3 x 10 mL) and then with brine (1 x 15 mL), dried over MgSO₄, filtered, and concentrated under reduce pressure to afford the crude product. Purification by flash chromatography on silica gel (pentane) afforded analytically pure **207** (1.46 g, 37%) as a yellow oil.

¹**H NMR** (400 MHz, CDCl₃): δ 7.45–7.42 (m, 2H, H-Ar), 7.35–7.31 (m, 2H, H-Ar), 7.23–7.18 (m, 1H, H-Ar), 2.47 (t, *J* = 7.1 Hz, 2H, H-7), 1.66–1.52 (m, 2H, H-alkyl), 1.51–1.43 (m, 2H, H-alkyl), 1.39–1.31 (m, 4H, H-alkyl), 0.95–0.91 (m, 3H, H-12).

¹³C{¹H} NMR (100 MHz, CDCl₃): δ 133.9 (C-4), 129.1 (C-Ar), 126.1 (C-Ar), 125.8 (C-Ar), 100.1 (C-6), 64.6 (C-5), 31.4, 28.7, 28.6, 22.6, 20.4, 14.1 (C-12).

ⁱ Isomura, K. A. H. F. M. *Chem. Pharm. Bull.* **1981**, *29*, 1274–1279.

ⁱⁱ Eller, C.; Kehr, G.; Daniliuc, C. G.; Fröhlich, R.; Erker, G. *Organometallics* **2013**, *32*, 384–386.

Phenyl(phenylethynyl)sulfane (210): Prepared according to the following reported procedure.ⁱ To a stirred solution of thiophenol (2.10 g, 1.96 mL, 19.09 mmol, 1.0 equiv) in DMSO (100 mL) was added (2,2-dibromovinyl)benzene **97** (6.00 g, 22.90 mmol, 1.2 equiv), and Cs₂CO₃ (24.88 g, 76.36 mmol, 4.0 equiv). The reaction was heated at 100 °C and stirred under N₂ atmosphere overnight. Temperature was then allowed to cool down to rt. The mixture was extracted with pentane (x4) and the combined pentane was extracted with H₂O (x2). The organic layer was dried over Na₂SO₄, filtered, and concentrated under reduce pressure to afford the crude product. Purification by flash chromatography on silica gel (pentane) afforded analytically pure **210** (1.01 g, 41%) as a colorless oil.

¹**H NMR** (400 MHz, CDCl₃): δ 7.61–7.56 (m, 4H, H-Ar), 7.44–7.40 (m, 5H, H-Ar), 7.32–7.28 (m, 1H, H-Ar).

¹³C{¹H} NMR (100 MHz, CDCl₃): δ 133.0 (C-4), 131.8, 129.3, 128.7, 128.5, 126.6, 126.3, 123.0 (C-7), 98.0 (C-6), 75.6 (C-5).

The spectral data were in agreement with that previously reported in the literature.ⁱ

(*R*)-1-(ethynylsulfinyl)-4-methylbenzene (214): Prepared according to the following reported procedure.¹¹ To a stirred solution of ethylmagnesium bromide (3.0 M in Et₂O, 3.00 mL, 9.00 mmol, 1.0 equiv) was added (trimethylsilyl)acetylene (1.40 mL, 9.84 mmol, 1.1 equiv) at 0 °C. The mixture was then allowed to warm up to rt. After 2 h, the solution was cooled to 0 °C and toluene (30 mL) plus (1R,2S,5R)-(–)-menthyl (S)-p-toluenesulfinate (2.8 g, 9.49 mmol, 1.1 equiv) were added. The reaction mixture was allowed to warm up to rt and the solution was stirred overnight. Afterward, the mixture was diluted with Et₂O/EtOAc/CH₂Cl₂ (2:2:1) (100 mL) and quenched with saturated aq NH₄Cl (100 mL). The layers were separated and the aqueous one was extracted with Et₂O/EtOAc/CH₂Cl₂ (2:2:1) (3x100 mL). The combined organic layers were washed with brine (x2), dried over MgSO₄, filtered, and concentrated under reduce pressure to afford the crude product. Purification



210

C₁₄H₁₀S M.W. = 210.29 g⋅mol⁻¹



214

C₉H₈OS M.W. = 164.22 g⋅mol⁻¹

ⁱ Ni, Z.; Wang, S.; Mao, H.; Pan, Y. *Tetrahedron Lett.* **2012**, *53*, 3907–3910.

ⁱⁱ Kosugi, H.; Kitaoka, M.; Tagami, K.; Takahashi, A.; Uda, H. *J. Org. Chem.* **1987**, *52*, 1078-1082.

by flash chromatography on silica gel (cyclohexane/EtOAc = gradient from 100:0 to 85:15) afforded analytically pure **214** (635 mg, 43%) as a beige solid.

¹**H NMR** (400 MHz, CDCl₃): δ 7.74–7.72 (m, 2H, H-4), 7.40–7.36 (m, 2H, H-3), 3.69 (s, 1H, H-7), 2.44 (s, 3H, H-1).

¹³C{¹H} NMR (100 MHz, CDCl₃): δ 143.1 (C-2), 140.3 (C-5), 130.5 (C-3), 125.4 (C-4), 90.2 (C-7), 82.1 (C-6), 21.7 (C-1).

The spectral data were in agreement with that previously reported in the literature.ⁱ



217

C₉H₁₆Br₃NO₂ M.W. = 409.94 g⋅mol⁻¹

2,2,2-tribromoethyl diisopropylcarbamate (217): Prepared according to the following reported procedure. ^{II} A stirred solution of 2,2,2-tribromoethanol (5.0 g, 16.7 mmol, 1.0 equiv) and diisopropylcarbamoyl chloride (3.5 g, 21.4 mmol, 1.3 equiv) in pyridine (4.3 mL, 53.3 mmol, 3.2 equiv) was heated at 70 °C for 16 h. After cooling at rt, the mixture was quenched with 1.0 M aq HCl (15 mL). The layers were then separated and the aqueous one was extracted with Et_2O (3x20 mL). The combined organic layers were washed with saturated aq NaHCO₃ (30 mL), dried over MgSO₄, filtered, and concentrated under reduced pressure to afford the crude product. Purification by flash chromatography on silica gel (pentane/ Et_2O = gradient from 95:5 to 90:10) afforded analytically pure **217** (5.33 g, 78%) as a colorless solid.

¹**H NMR** (300 MHz, CDCl₃): δ 4.97 (s, 2H, H-6), 4.08–3.94 (m, 2H, H-2,3), 1.38– 1.28 (m, 12H, H-1,4).

The spectral data were in agreement with that previously reported in the literature.ⁱⁱ



218

C₉H₁₅NO₂ M.W. = 169.22 g⋅mol⁻¹ **Ethynyl diisopropylcarbamate (218):** Prepared according to the following reported procedure.ⁱⁱ To a stirred solution of diisopropylamine (6.3 mL, 44.8 mmol, 4.6 equiv) in THF (30 mL) cooled at –78 °C was added *n*BuLi (1.6 M in hexane, 28.4 mL, 45.4 mmol, 2.9 equiv). After stirring 30 min at this

ⁱ Kosugi, H.; Kitaoka, M.; Tagami, K.; Takahashi, A.; Uda, H. *J. Org. Chem.* **1987**, *52*, 1078–1082. ⁱⁱ Gralla, G.; Wibbeling, B.; Hoppe, D. *Org. Lett.* **2002**, *4*, 2193–2195.

temperature, a solution of **217** (4.0 g, 9.8 mmol, 1.0 equiv) in THF (12 mL) was added dropwise over 5 min, and the mixture was stirred for 4 h. A solution of MeOH (1.2 mL, 29.6 mmol, 3.0 equiv) in THF (2 mL) was added and the mixture was allowed to warm up to rt while stirring overnight. The mixture was then quenched with H_2O (30 mL). The layers were separated and the aqueous one was extracted with Et_2O (3x30 mL). The combined organic layers were dried over MgSO₄, filtered, and concentrated under reduced pressure to afford the crude product. Purification by flash chromatography on silica gel (pentane/Et₂O = 90:10) afforded analytically pure **218** (1.20 g, 72%) as a yellow solid.

The presence of rotamers induced broadening signals: **¹H NMR** (300 MHz, C₆D₆): δ 3.39–3.34 (m, 2H, H-2,3), 2.11 (s, 1H, H-7), 1.00–0.58 (m, 12H, H-1,4).

The spectral data were in agreement with that previously reported in the literature.ⁱ

Diethyl ethynylphosphonate (227): Prepared according to the following reported procedure.¹¹ To a stirred solution of trimethylsilylacetylene (1.6 mL, 11.2 mmol, 1.0 equiv) in THF (38 mL), EtMgBr (3.0 M in Et₂O, 5.0 mL, 15.0 mmol, 1.3 equiv) was added dropwise at rt. After 2 h stirring at this temperature, the mixture was cooled to 0 °C and diethyl chlorophosphate (1.7 mL, 11.7 mmol, 1.0 equiv) was added. The mixture was then allowed to warm up to rt and the solution was stirred for 1 h. The mixture was then quenched with saturated aq NH₄Cl (5 mL) and the resulting precipitate was filtered and washed with Et_2O (2 x 10 mL). The combined organic layers were dried over MgSO₄, filtered, and concentrated under reduced pressure to afford the crude product which was immediately solubilized in CHCl₃ (40 mL). 10% aqueous Na₂CO₃ (40 mL) was added at rt and the reaction mixture was stirred for 30 min. The layers were then separated and the aqueous one was extracted with $CHCl_3$ (2 x 10 mL). The combined organic layers were dried over MgSO₄, filtered, and concentrated under reduced pressure to afford the crude product. Purification by flash chromatography on silica gel



 $C_6H_{11}O_3P$ M.W. = 162.12 g·mol⁻¹

ⁱ Gralla, G.; Wibbeling, B.; Hoppe, D. *Org. Lett.* **2002**, *4*, 2193–2195.

ⁱⁱ Vuilhorgne, M.; Malpart, J.; Mutti, S.; Mignani, S. *J. Heterocycl. Chem.* **2003**, *40*, 159–162.

(cyclohexane/EtOAc = 60:40) afforded analytically pure **227** (471 mg, 26%) as a colorless oil.

¹**H NMR** (400 MHz, CDCl₃): δ 4.18–4.07 (m, 4H, H-2), 2.93 (dt, J_{H-P} = 13.2 Hz, J = 1.7 Hz, 1H, H-4), 1.33 (dd, J = 7.1 Hz, J = 1.7 Hz, 6H, H-1).

¹³C{¹H} NMR (100 MHz, CDCl₃): δ 87.7 (d, $J_{C-P} = 50.6$ Hz, C-4), 74.6 (d, $J_{C-P} = 288.8$ Hz, C-3), 63.6 (d, $J_{C-P} = 5.6$ Hz, C-2), 16.2 (d, $J_{C-P} = 6.9$ Hz, C-1).

³¹**P NMR** (162 MHz, CDCl₃): δ –7.88 (dt, *J*_{P-H} = 13.2 Hz, *J*_{P-H} = 1.7 Hz).

³¹**P**{¹**H**} **NMR** (162 MHz, CDCl₃): δ –7.88 (s).

The spectral data were in agreement with that previously reported in the literature.¹



230

C₁₄H₁₉O₃P M.W. = 266.27 g⋅mol⁻¹

Diisopropyl (phenylethynyl)phosphonate (230): Prepared according to the following reported procedure.¹¹ A round bottom flask was successively charged with diisopropyl phosphonate (2.66 g, 2.7 mL, 16.0 mmol, 4.0 equiv), (phenylethynyl)copper **228** (0.66 g, 4.0 mmol, 1 equiv) and DMF (8 mL). The resulting bright yellow slurry was then treated with *N*-methylimidazole (0.64 mL, 8.0 mmol, 2.0 equiv) and the reaction mixture was vigorously stirred at rt under an atmosphere of oxygen (balloon). After disappearance of the alkynylcopper reagent (16 h), the reaction was diluted with aq NH₄Cl/NH₃ (1:1) and extracted with Et₂O. The combined organic layers were then washed with brine, dried over MgSO₄, filtered, and concentrated under reduced pressure to afford the crude product. Purification by flash chromatography on silica gel (pentane/Et₂O = 60:40) afforded analytically pure **230** (0.92 g, 86%) as a light orange oil.

¹**H NMR** (400 MHz, CDCl₃): δ 7.55–7.52 (m, 2H, H-Ar), 7.45–7.41 (m, 1H, H-Ar), 7.38–7.33 (m, 2H, H-Ar), 4.81 (dhept, *J*_{H-P} = 8.8 Hz, *J* = 6.2 Hz, 2H, H-2), 1.40 (dd, *J* = 6.2 Hz, *J* = 2.2 Hz, 12H, H-1,1').

¹³C{¹H} NMR (100 MHz, CDCl₃): δ 132.5 (d, J_{C-P} = 2.5 Hz, C-6), 130.5 (C-8), 128.5 (C-7), 119.9 (d, J_{C-P} = 5.5 Hz, C-5), 98.1 (d, J_{C-P} = 52.8 Hz, C-4), 79.9 (d, J_{C-P}

ⁱ Vuilhorgne, M.; Malpart, J.; Mutti, S.; Mignani, S. *J. Heterocycl. Chem.* **2003**, *40*, 159–162.

ⁱⁱ Jouvin, K.; Heimburger, J.; Evano, G. *Chem. Sci.* **2012**, *3*, 756–760.

 $_{P}$ = 298.6 Hz, C-3), 72.3 (d, J_{C-P} = 5.5 Hz, C-2), 23.9 (d, J_{C-P} = 4.6 Hz, C-1 or C-1'),

23.6 (d, J_{C-P} = 4.8 Hz, C-1' or C-1).

³¹**P**{¹**H**} **NMR** (162 MHz, CDCl₃): δ -8.24.

The spectral data were in agreement with that previously reported in the literature.ⁱ

III-5.1.6. Synthesis of Conventional Alkynes

(2R,4S)-1,7,7-trimethyl-2-(phenylethynyl)bicyclo[2.2.1]heptan-2-ol

(263): Prepared according to the following reported procedure.ⁱⁱ To a solution of phenylacetylene (0.82 g, 0.88 mL, 8.04 mmol, 1.2 equiv) in dry THF (10 mL) was added *n*BuLi (2.5 M in hexanes, 2.95 mL, 7.37 mmol, 1.1 equiv) over 10 min. After 15 min, (1*R*)-(+)-camphor (1.02 g, 6.7 mmol, 1.0 equiv) was added in THF (3.5 mL). The mixture was then allowed to slowly warm up to rt over 4 h. The mixture was then quenched with saturated aq NH₄Cl (5 mL) and extracted with Et₂O (2 x 10 mL). The combined organic layers were dried over MgSO₄, filtered, and concentrated under reduced pressure to afford the crude product. Purification by flash chromatography on silica gel (pentane/Et₂O = 90:10) afforded analytically pure **263** (0.92 g, 54%) as a white solid.

¹**H NMR** (400 MHz, CDCl₃): δ 7.44–7.42 (m, 2H, H-Ar), 7.32–7.29 (m, 3H, H-Ar), 2.32 (dt, *J* = 13.4 Hz, *J* = 3.8 Hz, 1H, H-13), 2.07 (br s, 1H, H-8), 2.03–1.96 (m, 2H, H-alkyl), 1.81 (t, *J* = 4.5 Hz, 1H, H-12), 1.78–1.69 (m, 1H, H-alkyl), 1.53 (ddd, *J* = 13.4 Hz, *J* = 11.7 Hz, *J* = 4.8 Hz, 1H, H-alkyl), 1.21 (ddd, *J* = 12.1 Hz, *J* = 9.3 Hz, *J* = 4.8 Hz, 1H, H-alkyl), 1.12 (s, 3H, H-15 or H-15'), 1.02 (s, 3H, H-16), 0.91 (s, 3H, H-15').

¹³C{¹H} NMR (100 MHz, CDCl₃): δ 131.6 (C-Ar), 128.2 (C-Ar), 128.1 (C-1), 123.2 (C-4), 93.5 (C-5 or C-6), 83.5 (C-6 or C-5), 78.4 (C-7), 53.9 (C-9 or C-14), 48.3 (C-alkyl), 48.0 (C-14 or C-9), 45.5 (C-12), 32.6 (C-alkyl), 27.0 (C-alkyl), 21.4 (C-15 or C-15'), 21.0 (C-15' or C-15), 10.4 (C-16).





C₁₈H₂₂O M.W. = 254.37 g⋅mol⁻¹

ⁱ Gao, Y.; Wang, G.; Chen, L.; Xu, P.; Zhao, Y.; Zhou, Y.; Han, L.-B. *J. Am. Chem. Soc.* **2009**, *131*, 7956–7957.

ⁱⁱ Dikusar, E. A.; Kozlov, N. G.; Moiseichuk, K. L. *Russ. J. Org. Chem.* **2002**, *38*, 182–187.

The spectral data were in agreement with that previously reported in the literature.ⁱ





C₁₁H₁₀O₂ M.W. = 174.20 g⋅mol⁻¹

3-Phenylprop-2-yn-1-yl acetate (272): To a solution of acetic anhydride (2.35 g, 2.17 mL, 23.0 mmol, 1.5 equiv), Et₃N (2.33 g, 3.21 mL, 23.0 mmol, 1.5 equiv), and *N*,*N*-dimethyl-4-aminopyridine (DMAP) (0.15 g, 1.2 mmol, 0.08 equiv), in CH₂Cl₂ (30 mL) was added 3-phenyl-2-propyn-1-ol (1.98 g, 1.87 mL, 15.0 mmol, 1.0 equiv). The reaction mixture was next stirred at rt for 16 h and then was quenched with 2 N aq HCl. The mixture was extracted with Et₂O (3 x 20 mL). The combined organic layers were washed with saturated aq NaHCO₃ (2 x 80 mL), dried over MgSO₄, filtered, and concentrated under reduce pressure to afford analytically pure **272** (2.57 g, 98%) as an orange oil.

¹**H NMR** (400 MHz, CDCl₃): δ 7.49–7.46 (m, 2H, H-Ar), 7.35–7.32 (m, 3H, H-Ar), 4.92 (s, 2H, H-7), 2.14 (s, 3H, H-9).

¹³C{¹H} NMR (100 MHz, CDCl₃): δ 170.3 (C-8), 131.9 (C-Ar), 128.8 (C-1), 128.3 (C-Ar), 122.2 (C-4), 86.4 (C-6), 83.0 (C-5), 52.8 (C-7), 20.8 (C-9).

The spectral data were in agreement with that previously reported in the literature.ⁱⁱ





C₁₆H₈F₆ M.W. = 314.23 g⋅mol⁻¹ **1,2-Bis(4-(trifluoromethyl)phenyl)ethyne (282):** Prepared according to the following reported procedure. ⁱⁱⁱ A solution of 1-iodo-4-(trifluoromethyl)benzene (0.54 g, 0.44 mL, 2.0 mmol, 1.0 equiv) and DBU (1.79 mL, 12.0 mmol, 6.0 equiv) in toluene (5 mL) was degassed by 2 freeze-pump-thaw cycles. Afterward, PdCl₂(PPh₃)₂ (84 mg, 6 mol%) and CuI (38 mg, 10 mol%) were added and the resulting reaction mixture was degassed by 1 freeze-pump-thaw cycles. Ice-chilled trimethylsilylacetylene (0.14 mL, 1.0 mmol, 0.50 equiv) was then added by syringe, followed by distilled water (0.14 mL, 40 mol%). The reaction flask was covered with aluminum foil and left stirring at a high rate of speed for 18 h, at the end of which the reaction

ⁱ Koval, S. S.; Kozlov, N. G.; Dikusar, E. A. Russ. J. Org. Chem. **2005**, 41, 832–837.

ⁱⁱ Imagawa, H.; Asai, Y.; Takano, H.; Hamagaki, H.; Nishizawa, M. *Org. Lett.* **2006**, *8*, 447–450.

^{III} Mio, M. J.; Kopel, L. C.; Braun, J. B.; Gadzikwa, T. L.; Hull, K. L.; Brisbois, R. G.; Markworth, C. J.; Grieco, P. A. *Org. Lett.* **2002**, *4*, 3199–3202.

mixture was partitioned in Et_2O and water (50 mL each). The organic layer was washed with 10% HCl (3 x 75 mL), saturated aq NaCl (1 x 75 mL), dried over MgSO₄, filtered, and concentrated under reduced pressure to afford the crude product. Purification by flash chromatography on silica gel (cyclohexane/EtOAc = 98:2) afforded analytically pure **282** (279 mg, 89%) as white crystals.

¹**H NMR** (300 MHz, CDCl₃): δ 7.67–7.61 (m, 8H, H-Ar).

¹³C{¹H} NMR (75 MHz, CDCl₃): δ 132.0 (C-4), 130.5 (q, *J* = 32.7 Hz, C-2), 125.4 (q, *J* = 3.8 Hz, C-3), 122.0 (C-5), 90.1 (C-6). *One C is not observed.*

The spectral data were in agreement with that previously reported in the literature.ⁱ

1-Methoxy-4-((4-(trifluoromethyl)phenyl)ethynyl)benzene (284): A solution of 1-iodo-4-(trifluoromethyl)benzene (1.63 g, 1.32 mL, 6.0 mmol, 1.0 equiv), CuI (57 mg, 5 mol%), PdCl₂(PPh₃)₂ (21 mg, 5 mol%), and Et₃N (10 mL) in Et₂O (20 mL) was stirred for 10 min at rt under N₂ atmosphere. Next, 1-ethynyl-4-methoxybenzene (0.93 g, 7.0 mmol, 1.2 equiv) was added. The mixture was stirred for 48 h, at the end of which the reaction mixture was extracted with Et₂O (3 x 10 mL). The concentrated ether-extract was passed over a pad of alumina to remove the catalyst. The organic layer was then concentrated under reduced pressure to afford the crude product. Purification by flash chromatography on silica gel (pentane/Et₂O = gradient from 100:0 to 95:5) afforded analytically pure **284** (1.20 g, 72%) as a white solid.

¹**H NMR** (400 MHz, CDCl₃): δ 7.62–7.58 (m, 4H, H-Ar), 7.53–7.47 (m, 2H, H-Ar), 6.95–6.86 (m, 2H, H-Ar), 3.84 (s, 3H, H-1).

¹³C{¹H} NMR (100 MHz, CDCl₃): δ 160.2 (C-2), 133.4, 131.7, 129.8, 129.4, 127.6, 125.9, 125.3, 114.7, 92.0 (C-6), 86.9 (C-7), 55.4 (C-1).

The spectral data were in agreement with that previously reported in the literature.ⁱⁱ



C₁₆H₁₁F₃O M.W. = 276.25 g⋅mol⁻¹

ⁱ Mio, M. J.; Kopel, L. C.; Braun, J. B.; Gadzikwa, T. L.; Hull, K. L.; Brisbois, R. G.; Markworth, C. J.; Grieco, P. A. *Org. Lett.* **2002**, *4*, 3199–3202.

ⁱⁱ Mouriès, V.; Waschbüsch, R.; Carran, J.; Savignac, P. *Synthesis* **1998**, 271–274.



285

C₁₃H₉N M.W. = 179.22 g⋅mol⁻¹ **3-(Phenylethynyl)pyridine (285):** A solution of 3-bromopyridine (0.95 g, 0.58 mL, 6.0 mmol, 1.0 equiv), CuI (57 mg, 5 mol%), PdCl₂(PPh₃)₂ (21 mg, 5 mol%), and Et₃N (10 mL) in Et₂O (20 mL) was stirred for 10 min at rt under N₂ atmosphere. Next, phenylacetylene (0.71 g, 0.77 mL, 7.0 mmol, 1.2 equiv) was added. The mixture was stirred for 48 h, at the end of which the reaction mixture was extracted with Et₂O (3 x 10 mL). The concentrated ether-extract was passed over a pad of alumina to remove the catalyst. The organic layer was then concentrated under reduced pressure to afford the crude product. Purification by flash chromatography on silica gel (pentane/Et₂O = gradient from 100:0 to 95:5) afforded analytically pure **285** (0.72 g, 67%) as a light brown solid.

¹**H NMR** (400 MHz, CDCl₃): δ 8.78 (s, 1H, H-1), 8.56–8.54 (m, 1H, H-2), 7.81 (dt, *J* = 7.9 Hz, *J* = 1.9 Hz, 1H, H-4), 7.56–7.52 (m, 2H, H-Ar), 7.39–7.34 (m, 3H, H-Ar), 7.30–7.28 (m, 1H, H-3).

¹³C{¹H} NMR (100 MHz, CDCl₃): δ 152.4 (C-1), 148.6 (C-2), 138.5 (C-4), 131.8 (C-Ar), 128.9 (C-Ar), 128.5 (C-Ar), 123.1 (C-8), 122.6 (C-3), 120.4 (C-5), 92.7 (C-7), 86.0 (C-6).

The spectral data were in agreement with that previously reported in the literature.ⁱ



286

 $C_{14}H_{11}N$ M.W. = 193.24 g·mol⁻¹ **2-(***p***-Tolylethynyl)pyridine (286):** Prepared according to the following reported procedure.ⁱⁱ The 2-bromopyiridine (474 mg, 0.29 mL, 3.0 mmol, 1.0 equiv), $PdCl_2(PPh_3)_2$ (42 mg, 2 mol%), CuI (11 mg, 2 mol%), and PPh_3 (31 mg, 4 mol%) were placed in an argon-filled Schlenk tube. After addition of *i*Pr₂NH (1.0 mL) and toluene (5.0 mL), the mixture was stirred at rt for 5 min and (trimethylsilyl)acetylene (354 mg, 3.6 mmol) was added. The reaction mixture was stirred at 80 °C for 16 h, and then a solution of KOH (337 mg, 6.0 mmol) in water (0.5 mL) and methanol (2.0 mL) was added in one portion at rt and the mixture was stirred for additional 3 h at this temperature. Then the 4-iodotoluene (654 mg, 3.0 mmol, 1.0 equiv) was added and stirring was continued for 16 h at rt. The reaction mixture was quenched with saturated NH₄Cl solution (60 mL) and extracted with CH₂Cl₂ (3 × 50 mL). The combined

ⁱ Cai, R.; Lu, M.; Aguilera, E. Y.; Xi, Y.; Akhmedov, N. G.; Petersen, J. L.; Chen, H.; Shi, X. *Angew. Chemie Int. Ed.* **2015**, *54*, 8772–8776.

organic layers were washed with HCl (2 N, 50 mL), water (50 mL), and saturated NaCl solution (50 mL) and dried over MgSO₄. After concentration under reduced pressure, purification of the crude product by flash chromatography on silica gel (cyclohexane/EtOAc = 80:20) afforded analytically pure **286** (319 mg, 55%) as a light yellow solid.

¹**H NMR** (400 MHz, CDCl₃): δ 8.61 (ddd, *J* = 4.9 Hz, *J* = 1.8 Hz, *J* = 1.0 Hz, 1H, H-1), 7.66 (td, *J* = 7.7 Hz, *J* = 1.8 Hz, 1H, H-3), 7.52–7.48 (m, 3H, H-Ar), 7.22 (ddd, *J* = 7.7 Hz, *J* = 4.9 Hz, *J* = 1.0 Hz, 1H, H-4), 7.17 (d, *J* = 7.9 Hz, 2H, H-10), 2.37 (s, 3H, H-12).

¹³C{¹H} NMR (100 MHz, CDCl₃): δ 150.0 (C-1), 143.7 (C-5), 139.2 (C-11), 136.1 (C-Ar), 131.0 (C-Ar), 129.2 (C-Ar), 127.0 (C-Ar), 122.5 (C-Ar), 119.2 (C-8), 89.5 (C-6 or C-7), 88.1 (C-7 or C-6), 21.6 (C-12).

The spectral data were in agreement with that previously reported in the literature.ⁱ

tert-Butyl(dec-2-yn-1-yloxy)dimethylsilane (304): To a solution of imidazole (0.53 g, 7.78 mmol, 1.2 equiv), and *N*,*N*-dimethyl-4-aminopyridine (DMAP) (79 mg, 0.65 mmol, 0.1 equiv), in CH₂Cl₂ (44 mL) was added decyn-2-yn-1-ol (1.00 g, 1.17 mL, 6.48 mmol, 1.0 equiv). Afterward, *tert*-butyldimethylsilyl chloride (TBS-Cl) (1.17 g, 7.78 mmol, 1.2 equiv) was added. The reaction mixture was next stirred at rt for 1.5 h and then was quenched with 10% aq K₂CO₃. The mixture was extracted with Et₂O (3 x 20 mL). The combined organic layers were dried over Na₂SO₄, filtered, and concentrated under reduce pressure to afford analytically pure **304** (1.61 g, 93%) as a colorless liquid.

¹**H NMR** (400 MHz, CDCl₃): δ 4.29 (s, 2H, H-10), 2.18 (td, *J* = 7.0 Hz, *J* = 3.1 Hz, 2H, H-7), 1.52–1.45 (m, 2H, H-alkyl), 1.39–1.26 (m, 8H, H-alkyl), 0.90–0.86 (m, 12H, H-1,13), 0.11 (s, 6H, H-11).

¹³C{¹H} NMR (100 MHz, CDCl₃): δ 85.4 (C-8), 78.6 (C-9), 52.0 (C-10), 31.7, 28.82, 28.8, 28.6 (C-13), 25.8, 22.6, 18.8 (C-7), 18.3 (C-12), 14.0 (C-1), -5.1 (C-11).

IR (neat): *v* (cm⁻¹) 2956, 2930, 2858, 1464, 1254, 1081, 837, 778.



304

C₁₆H₃₂OSi M.W. = 268.51 g⋅mol⁻¹

ⁱ Severin, R.; Reimer, J.; Doye, S. *J. Org. Chem.* **2010**, *75*, 3518–3521.

HRMS (ESI): *m*/*z* calculated for [C₁₆H₃₂OSi + H]⁺ 269.2295; found 269.2295.

III-5.1.7. Preparation of Germanium Reagents



79

C₁₆H₁₂GeO₄ M.W. = 340.90 g⋅mol⁻¹ **Tetra(furan-2-yl)germane (79):** Prepared according to the following reported procedure.¹ *n*BuLi (2.5 M in hexanes, 51.9 mL, 130.0 mmol, 4.4 equiv) was added through a dropping funnel to a solution of furan (9.73 g, 10.4 mL, 143.0 mmol, 4.9 equiv) in THF (81 mL) at 0 °C under argon. The solution immediately turned yellow-gold and the resulting mixture was stirred for 30 min at 0 °C. A solution of germanium tetrachloride (6.26 g, 3.4 mL, 29.2 mmol, 1.0 equiv) in toluene (26 mL) was then added through a dropping funnel over 30 min at 0 °C, and the solution was stirred for another 3 h at rt. The mixture was poured into water and extracted with EtOAc (3 x 50 mL). The combined organic layers were then washed with brine, dried over MgSO₄, filtered, and concentrated under reduced pressure to afford the crude product. Precipitation from EtOH afforded analytically pure **79** (5.33 g, 54%) as a white solid.

¹**H NMR** (400 MHz, CDCl₃): δ 7.77 (dd, *J* = 1.7 Hz, *J* = 0.7 Hz, 4H, H-4), 6.91 (dd, *J* = 3.3 Hz, *J* = 0.7 Hz, 4H, H-2), 6.50 (dd, *J* = 3.3 Hz, *J* = 1.7 Hz, 4H, H-3).

¹³C{¹H} NMR (100 MHz, CDCl₃): δ 150.8 (C-1), 147.9 (C-4), 122.1 (C-2), 110.0 (C-3).

The spectral data were in agreement with that previously reported in the literature.ⁱ





C₁₂H₁₀GeO₃ M.W. = 274.85 g⋅mol⁻¹

Tri(furan-2-yl)germane (71): Prepared according to the following reported procedure.ⁱ To a solution of tetra(2-furyl)germane **79** (3.07 g, 9.0 mmol, 1.0 equiv) in THF (9 mL) under argon, lithium metal (0.19 g, 27.0 mmol, 3.0 equiv) was added. The resulting mixture was stirred for 1.5 h at rt. The mixture was poured into water and extracted with EtOAc (3 x 15 mL). The combined organic layers were then washed with brine, dried over MgSO₄, filtered, and concentrated under reduced pressure to afford the crude

ⁱ Yorimitsu, H.; Oshima, K. Inorg. Chem. Commun. **2005**, *8*, 131–142.

product. Purification by flash chromatography on silica gel (pentane/EtOAc = 98:2) afforded analytically pure **71** (1.33 g, 54%) as a colorless liquid.

¹**H NMR** (400 MHz, CDCl₃): δ 7.74 (dd, *J* = 1.7 Hz, *J* = 0.7 Hz, 3H, H-4), 6.82 (dd, *J* = 3.3 Hz, *J* = 0.7 Hz, 3H, H-2), 6.48 (dd, *J* = 3.3 Hz, *J* = 1.7 Hz, 3H, H-3), 5.78 (s, 1H, H-5).

¹³C{¹H} NMR (100 MHz, CDCl₃): δ 150.5 (C-1), 147.6 (C-4), 121.8 (C-2), 110.0 (C-3).

The spectral data were in agreement with that previously reported in the literature.ⁱ

Tetrakis(trimethylsilyl)germane (80): Prepared according to the following reported procedure.ⁱⁱ A mixture of chopped lithium wire (2.59 g, 373.0 mmol, 10.0 equiv), Me₃SiCl (17.84 g, 20.8 mL, 164.2 mmol, 4.4 equiv) and THF (77 mL) was cooled to -78 °C, and GeCl₄ (8.00 g, 4.3 mL, 37.3 mmol, 1.0 equiv) in dry THF (19 mL) were slowly added over 1.5 h. The reaction was allowed to slowly warm up to rt, and was stirred overnight. Afterward, the mixture was filtered through Celite and 10% HCl (50 mL) were added. The brown precipitate formed was next removed by filtration. The mixture was extracted with Et₂O (3 x 50 mL). The combined organic layers were then dried over MgSO₄, filtered, and concentrated under reduced pressure to afford the crude product. After crystallization from acetonitrile, analytically pure **80** (4.96 g, 36%) was obtained as a white solid.

¹**H NMR** (400 MHz, C₆D₆): δ 0.31 (s, 36H, H-1).

¹³C{¹H} NMR (100 MHz, C₆D₆): δ 3.5 (C-1).

The spectral data were in agreement with that previously reported in the literature.ⁱⁱ

Tris(trimethylsilyl)germane (74): Prepared according to the following reported procedure.ⁱⁱⁱ To a solution of tetrakis(trimethylsilyl)germane **80** (1.03 g, 2.82 mmol, 1.0 equiv) in THF (2.6 mL), potassium *tert*-butoxide (0.33

 $H_{3}C \stackrel{1}{\underset{C}{\hookrightarrow}} H_{3}C + Si$ $H_{3}C - Si$ $Ge - Si(CH_{3})_{3}$ $(H_{3}C)_{3}Si \stackrel{2}{\underset{S}{\hookrightarrow}} Si(CH_{3})_{3}$

C₁₂H₃₆GeSi₄ M.W. = 365.40 g⋅mol⁻¹

ⁱ Yorimitsu, H.; Oshima, K. *Inorg. Chem. Commun.* **2005**, *8*, 131–142.

ⁱⁱ Brook, A. G.; Abdesaken, F.; Söllradl, H. J. Organomet. Chem. **1986**, 299, 9–13.

ⁱⁱⁱ Fischer, J.; Baumgartner, J.; Marschner, C. Organometallics **2005**, *24*, 1263–1268.

H₃C CH₃ H₃C-Si 2 Ge-H (H₃C)₃Si['] Si(CH₃)₃

74

C₉H₂₈GeSi₃ M.W. = 293.22 g⋅mol⁻¹ g, 2.96 mmol, 1.1 equiv) was added and the reaction was stirred at rt for 3 h. The obtained potassium compound was added to an $Et_2O/dilute$ sulfuric acid mixture. After separating the layers, the ether phase was dried over Na_2SO_4 and concentrated under reduced pressure to afford analytically pure **74** (0.56 g, 68%) as a colorless oil.

¹**H NMR** (400 MHz, C₆D₆): δ 2.18 (s, 1H, H-2), 0.29 (s, 27H, H-1).

¹³C{¹H} NMR (100 MHz, C₆D₆): δ 2.8 (C-1).

The spectral data were in agreement with that previously reported in the literature.ⁱ

ⁱ Fischer, J.; Baumgartner, J.; Marschner, C. Organometallics **2005**, 24, 1263–1268.

III-5.2. RADICAL HYDROGERMYLATION OF YNAMIDE 54



(*Z*)-4,4-dimethyl-3-[2-(triphenylgermyl)vinyl]oxazolidin-2-one (*Z*-59): In a dry Schlenk tube under argon atmosphere, ynamide 54 (35 mg, 0.25 mmol, 1.0 equiv) was dissolved in dry THF (2 mL). The solution was degassed by 3 freeze-pump-thaw cycles and Ph₃GeH (152 mg, 0.50 mmol, 2.0 equiv) was added. The reaction mixture was stirred for 16 h at rt and aq NH₄Cl/NH₃ (2:1) and CH₂Cl₂ were added. The layers were separated, the aqueous layer was extracted with CH₂Cl₂ (x3), and the combined organic layers were washed with brine (x2), dried over Na₂SO₄, filtered, and concentrated under reduce pressure to afford the crude product (*Z*/*E* = 96:4). Purification by flash chromatography on silica gel (pentane/Et₂O = 60:40) afforded analytically pure *Z*-59 (93 mg, 84%, *Z*/*E* = 96:4) as a white solid; mp 142–145 °C.



C₂₅H₂₅GeNO₂ M.W. = 444.11 g⋅mol⁻¹

¹**H NMR** (400 MHz, CDCl₃): (*Z* isomer) δ 7.66–7.62 (m, 6H, H-Ar), 7.41–7.34 (m, 9H, H-Ar), 6.65 (d, *J* = 10.6 Hz, 1H, H-5), 6.19 (d, *J* = 10.6 Hz, 1H, H-6), 3.30 (s, 2H, H-2), 1.16 (s, 6H, H-4,4').

¹³C{¹H} NMR (100 MHz, CDCl₃): (*Z* isomer) δ 154.9 (C-1), 137.2 (C-7), 135.3 (C-Ar), 133.6 (C-5), 128.9 (C-Ar), 128.0 (C-Ar), 121.8 (C-6), 74.2 (C-2), 58.7 (C-3), 24.1 (C-4,4').

IR (neat): *v* (cm⁻¹) 3057, 2928, 2860, 1755, 1607, 1027, 911, 732, 697.

HRMS (ESI): m/z calculated for $[C_{25}H_{25}GeNO_2 + Na]^+$ 468.0994; found 468.0991.

Note: The Z configuration was determined on the basis of the ¹H NMR coupling constant of the vinylic protons (J = 10.6 Hz).

III-5.3. GERMYLZINCATION OF TERMINAL YNAMIDES (GP VII AND GP VIII)



General Procedure for the Germylzincation of Terminal Ynamides (GP VII):

In a dry Schlenk tube under argon atmosphere, the appropriate ynamide (0.25 mmol, 1.0 equiv) was dissolved in dry THF (2 mL) and the solution was degassed by 3 freeze-pump-thaw cycles. At 0 °C, Et₂Zn (1.0 M in hexane, 0.75 mL, 0.75 mmol, 3.0 equiv) and the appropriate germanium hydride (0.33–0.50 mmol, 1.3–2.0 equiv) were successively added. The reaction mixture was stirred at this temperature for the given reaction time and then aq NH_4Cl/NH_3 (2:1) and CH_2Cl_2 were added. The layers were separated, the aqueous layer was extracted with CH_2Cl_2 (x3), and the combined organic layers were washed with brine (x2), dried over Na_2SO_4 , filtered, and concentrated under reduce pressure to afford the crude product.

General Procedure for the Germylzincation – D-labeling of Terminal Ynamides (GP VIII):



In a dry Schlenk tube under argon atmosphere, the appropriate ynamide (0.25 mmol, 1.0 equiv) was dissolved in dry THF (2 mL) and the solution was degassed by 3 freeze-pump-thaw cycles. At 0 °C, Et₂Zn (1.0 M in hexane, 0.75 mL, 0.75 mmol, 3.0 equiv) and the appropriate germanium hydride (0.33–0.50 mmol, 1.3–2.0 equiv) were successively added. The reaction mixture was stirred at this temperature for the given reaction time. A solution of ND₄Cl (300 mg) in D₂O (2 mL) was added and the mixture was stirred for 1 h at rt before adding aq NH₄Cl/NH₃ (2:1) and CH₂Cl₂. The layers were separated, the aqueous layer was extracted with CH₂Cl₂ (x3), and the combined organic layers were washed with brine (x2), dried over Na₂SO₄, filtered, and concentrated under reduce pressure to afford the crude product.

(*E*)-4,4-dimethyl-3-[2-(triphenylgermyl)vinyl]oxazolidin-2-one (*E*-59): Prepared according to **GP VII** from ynamide **54** (35 mg, 0.25 mmol, 1.0 equiv) with Ph₃GeH (99 mg, 0.33 mmol, 1.3 equiv) and a reaction time of 3 h. Purification of the crude product (E/Z > 98:2) by flash chromatography on silica gel (pentane/Et₂O = 60:40) afforded analytically pure *E*-**59** (97 mg, 87%, E/Z > 98:2) as a white solid; mp 139–142 °C.

¹**H NMR** (400 MHz, CDCl₃): δ 7.52–7.50 (m, 6H, H-Ar), 7.41–7.36 (m, 9H, H-Ar), 6.50 (d, *J* = 17.5 Hz, 1H, H-5), 5.97 (d, *J* = 17.5 Hz, 1H, H-6), 4.02 (s, 2H, H-2), 1.51 (s, 6H, H-4,4').

¹³C{¹H} NMR (100 MHz, CDCl₃): δ 155.1 (C-1), 136.3 (C-7), 135.1 (C-Ar), 134.6 (C-5), 129.3 (C-Ar), 128.4 (C-Ar), 102.9 (C-6), 75.2 (C-2), 58.8 (C-3), 25.1 (C-4,4').

IR (neat): v (cm⁻¹) 2920, 2853, 1746, 1611, 1325, 1062, 739, 698.

HRMS (ESI): m/z calculated for $[C_{25}H_{25}GeNO_2 + Na]^+$ 468.0994; found 468.1005.

Note: The E configuration was determined on the basis of the ¹H NMR coupling constant of the vinylic protons (J = 17.5 Hz).

E-[²H(α)]-59: Prepared according to **GP VIII** from ynamide **54** (35 mg, 0.25 mmol, 1.0 equiv) with Ph₃GeH (99 mg, 0.33 mmol, 1.3 equiv) and a reaction time of 3 h. Purification of the crude product (*E*/*Z* > 98:2) by flash chromatography on silica gel (pentane/Et₂O = 60:40) afforded analytically pure *E*-[²H(α)]-**59** (95 mg, 86%, *E*/*Z* > 98:2) as a white solid.

¹**H NMR** (400 MHz, CDCl₃): δ 7.56–7.53 (m, 6H), 7.44–7.38 (m, 9H), 6.00 (s, 1H), 4.02 (s, 2H), 1.52 (s, 6H).

¹³C{¹H} NMR (100 MHz, CDCl₃): δ 155.1, 136.3, 135.0, 134.3 (t, *J* = 26.4 Hz), 129.2, 128.4, 102.6, 75.2, 58.7, 25.1.

HRMS (ESI): *m*/*z* calculated for [C₂₅H₂₄DGeNO₂ + Na]⁺ 469.1057; found 469.1046.



E-39

C₂₅H₂₅GeNO₂ M.W. = 444.11 g⋅mol⁻¹



E-[²H(α)]-**59**

C₂₅H₂₄DGeNO₂ M.W. = 445.12 g⋅mol⁻¹



E-[²H(β)]-**59**

C₂₅H₂₄DGeNO₂ M.W. = 445.12 g⋅mol⁻¹ *E*-[²H(β)]-59: Prepared according to **GP VII** from ynamide [²H]-54 (30 mg, 0.21 mmol, 1.0 equiv) with Ph₃GeH (85 mg, 0.28 mmol, 1.3 equiv) and a reaction time of 3 h. Purification of the crude product (*E*/*Z* > 98:2) by flash chromatography on silica gel (pentane/Et₂O = 60:40) afforded analytically pure *E*-[²H(β)]-59 (94 mg, 99%, *E*/*Z* > 98:2) as a white solid.

¹**H NMR** (400 MHz, CDCl₃): δ 7.56–7.51 (m, 6H), 7.44–7.37 (m, 9H), 6.52 (s, 1H), 4.02 (s, 2H), 1.52 (s, 6H).

¹³C{¹H} NMR (100 MHz, CDCl₃): δ 155.1, 136.3, 135.1, 134.5, 129.3, 128.4, 102.6 (t, *J* = 23.4 Hz), 75.3, 58.8, 25.1.

HRMS (ESI): m/z calculated for $[C_{25}H_{24}DGeNO_2 + Na]^+$ 469.1057; found 469.1039.



E-[²H(α),²H(β)]-**59**

C₂₅H₂₃D₂GeNO₂ M.W. = 446.12 g⋅mol⁻¹ *E*-[²H(α),²H(β)]-59: Prepared according to **GP VIII** from ynamide [²H]-54 (30 mg, 0.21 mmol, 1.0 equiv) with Ph₃GeH (85 mg, 0.28 mmol, 1.3 equiv) and a reaction time of 3 h. Purification of the crude product (*E*/*Z* > 98:2) by flash chromatography on silica gel (pentane/Et₂O = 60:40) afforded analytically pure *E*-[²H(α),²H(β)]-59 in (85 mg, 89%, *E*/*Z* > 98:2) as a white solid.

¹**H NMR** (400 MHz, CDCl₃): δ 7.56–7.52 (m, 6H), 7.45–7.38 (m, 9H), 4.02 (s, 2H), 1.52 (s, 6H).

¹³C{¹H} NMR (100 MHz, CDCl₃): δ 155.1, 136.3, 135.1, 134.2 (t, *J* = 25.1 Hz), 129.3, 128.4, 102.4 (t, *J* = 21.4 Hz), 75.3, 58.8, 25.1.

HRMS (ESI): m/z calculated for $[C_{25}H_{23}D_2GeNO_2 + Na]^+ 470.1120$; found 470.1110.



68

C₂₆H₂₇GeNO₂ M.W. = 458.14 g⋅mol⁻¹ (*S,E*)-4-isopropyl-3-[2-(triphenylgermyl)vinyl]oxazolidin-2-one (68): Prepared according to **GP VII** from ynamide **55** (38 mg, 0.25 mmol, 1.0 equiv) with Ph₃GeH (99 mg, 0.33 mmol, 1.3 equiv) and a reaction time of 3 h. Purification of the crude product (E/Z > 98:2) by flash chromatography on silica gel (pentane/Et₂O = 70:30) afforded analytically pure **68** (76 mg, 66%, E/Z > 98:2) as a white solid; mp 141–143 °C.

¹**H NMR** (400 MHz, CDCl₃): δ 7.53–7.49 (m, 6H, H-Ar), 7.47–7.26 (m, 9H, H-Ar), 6.90 (d, *J* = 17.1 Hz, 1H, H-6), 5.36 (d, *J* = 17.1 Hz, 1H, H-7), 4.32–4.24 (m,

2H, H-2), 4.21 (dt, *J* = 8.6 Hz, *J* = 3.3 Hz, 1H, H-3), 2.57–2.49 (m, 1H, H-4), 0.97 (d, *J* = 7.0 Hz, 3H, H-5 or H-5'), 0.91 (d, *J* = 7.0 Hz, 3H, H-5' or H-5).

¹³C{¹H} NMR (100 MHz, CDCl₃): δ 155.3 (C-1), 136.2 (C-8), 135.6 (C-6), 135.0 (C-Ar), 129.3 (C-Ar), 128.5 (C-Ar), 100.7 (C-7), 63.2 (C-2), 58.1 (C-3), 26.5 (C-4), 18.1 (C-5 or C-5'), 14.1 (C-5' or C-5).

IR (neat): *v* (cm⁻¹) 3071, 2965, 2873, 1756, 1608, 1399, 732, 696.

HRMS (ESI): m/z calculated for $[C_{26}H_{27}GeNO_2 + Na]^+$ 482.1151; found 482.1170.

[α]_D²⁰: 12.0 (*c* 1.0, CH₂Cl₂).

Note: The E configuration was determined on the basis of the ¹H NMR coupling constant of the vinylic protons (J = 17.1 Hz).

[²H]-68: Prepared according to **GP VIII** from ynamide **55** (38 mg, 0.25 mmol, 1.0 equiv) with Ph₃GeH (99 mg, 0.33 mmol, 1.3 equiv) and a reaction time of 3 h. Purification of the crude product (E/Z > 98:2) by flash chromatography on silica gel (pentane/Et₂O = 70:30) afforded analytically pure [²H]-**68** (89 mg, 77%, E/Z > 98:2) as a white solid.

¹**H NMR** (400 MHz, CDCl₃): δ 7.57–7.52 (m, 6H), 7.47–7.39 (m, 9H), 5.37 (s, 1H), 4.33–4.25 (m, 2H), 4.22 (dt, *J* = 8.5 Hz, *J* = 3.4 Hz, 1H), 2.58–2.51 (m, 1H), 0.98 (d, *J* = 7.0 Hz, 3H), 0.92 (d, *J* = 7.0 Hz, 3H).

¹³C{¹H} NMR (100 MHz, CDCl₃): δ 155.3, 136.2, 135.0, 129.3, 128.5, 100.4,
63.2, 58.1, 26.5, 18.1, 14.1. One C is not observed.

HRMS (ESI): m/z calculated for $[C_{26}H_{26}DGeNO_2 + Na]^+$ 483.1214; found 483.1211.

(E)-3-(2-(triphenylgermyl)vinyl)oxazolidin-2-one (69): Prepared according to GP VII from ynamide 56 (28 mg, 0.25 mmol, 1.0 equiv) with Ph₃GeH (99 mg, 0.33 mmol, 1.3 equiv) and a reaction time of 3 h. The reaction quench was modified by adding CuTC (48 mg, 0.25 mmol, 1.0 equiv) and, 5 min after, NH₄Cl (300 mg) in H₂O (2 mL) and stirring the resulting mixture for 1 h at rt before workup with aq NH₄Cl/NH₃ (2:1) and CH₂Cl₂. Purification of the crude product (E/Z > 98:2) by flash chromatography on silica gel



[²H]-68

C₂₆H₂₆DGeNO₂ M.W. = 459.14 g⋅mol⁻¹





C₂₃H₂₁GeNO₂ M.W. = 416.06 g⋅mol⁻¹



[²H]-69

C₂₃H₂₀DGeNO₂ M.W. = 417.06 g⋅mol⁻¹ (pentane/Et₂O = gradient from 70:30 to 50:50) afforded analytically pure **69** (73 mg, 70%, E/Z > 98:2) as a white solid; mp 121–124 °C.

¹**H NMR** (400 MHz, CDCl₃): δ 7.56–7.50 (m, 6H, H-Ar), 7.45–7.36 (m, 9H, H-Ar), 7.00 (d, *J* = 16.8 Hz, 1H, H-4), 5.21 (d, *J* = 16.8 Hz, 1H, H-5), 4.46–4.42 (m, 2H, H-2), 3.86–3.82 (m, 2H, H-3).

¹³C{¹H} NMR (100 MHz, CDCl₃): δ 155.0 (C-1), 136.4 (C-4), 136.1 (C-6), 135.0 (C-Ar), 129.3 (C-Ar), 128.5 (C-Ar), 100.6 (C-5), 62.4 (C-2), 42.2 (C-3).

IR (neat): v (cm⁻¹) 3058, 1761, 1608, 1402, 1184, 1084, 733, 697.

HRMS (ESI): m/z calculated for $[C_{23}H_{21}GeNO_2 + Na]^+$ 440.0681; found 440.0671.

Note: The E configuration was determined on the basis of the ¹H NMR coupling constant of the vinylic protons (J = 16.8 Hz).

[²H]-69: Prepared according to **GP VIII** from ynamide **56** (28 mg, 0.25 mmol, 1.0 equiv) with Ph₃GeH (99 mg, 0.33 mmol, 1.3 equiv) and a reaction time of 3 h. The reaction quench was modified by adding CuTC (48 mg, 0.25 mmol, 1.0 equiv) 5 min before ND₄Cl/D₂O. Purification of the crude product (E/Z > 98:2) by flash chromatography on silica gel (pentane/Et₂O = gradient from 70:30 to 50:50) afforded analytically pure [²H]-**69** (69 mg, 66%, E/Z > 98:2) as a white solid.

¹**H NMR** (400 MHz, CDCl₃): δ 7.55–7.50 (m, 6H), 7.44–7.36 (m, 9H), 5.20 (s, 1H), 4.47–4.43 (m, 2H), 3.86–3.82 (m, 2H).

¹³C{¹H} NMR (100 MHz, CDCl₃): δ 155.0, 136.1, 135.0, 129.3, 128.5, 100.4, 62.4, 42.2. *One C is not observed.*

HRMS (ESI): m/z calculated for $[C_{23}H_{20}DGeNO_2 + Na]^+$ 441.0743; found 441.0743.

(S,E)-4-benzyl-3-(2-(triphenylgermyl)vinyl)oxazolidin-2-one(70):Prepared according to GP VII from ynamide 57 (50 mg, 0.25 mmol, 1.0 equiv)with Ph_3GeH (99 mg, 0.33 mmol, 1.3 equiv) and a reaction time of 16 h. Thereaction quench was modified by adding CuTC (48 mg, 0.25 mmol, 1.0 equiv)and, 5 min after, NH₄Cl (300 mg) in H₂O (2 mL) and stirring the resulting

mixture for 1 h at rt before workup with aq NH₄Cl/NH₃ (2:1) and CH₂Cl₂. Purification of the crude product (E/Z > 98:2) by flash chromatography on silica gel (toluene/Et₂O = 90:10) afforded analytically pure **70** (89 mg, 70%, E/Z > 98:2) as a white solid; mp 111–114 °C.

¹**H NMR** (400 MHz, CDCl₃): δ 7.58–7.56 (m, 6H, H-Ar [Ph₃Ge]), 7.45–7.41 (m, 9H, H-Ar [Ph₃Ge]), 7.38–7.34 (m, 2H, H-Ar [Bn]), 7.32–7.28 (m, 1H, H-Ar [Bn]), 7.23–7.21 (m, 2H, H-Ar [Bn]), 6.96 (d, *J* = 17.2 Hz, 1H, H-9), 5.50 (d, *J* = 17.2 Hz, 1H, H-10), 4.49 (tt, *J* = 8.5 Hz, *J* = 3.1 Hz, 1H, H-3), 4.28 (dd, *J* = 9.0 Hz, *J* = 7.7 Hz, 1H, H-2), 4.23 (dd, *J* = 9.0 Hz, *J* = 3.1 Hz, 1H, H-2'), 3.35 (dd, *J* = 13.9 Hz, *J* = 3.3 Hz, 1H, H-4), 2.89 (dd, *J* = 13.9 Hz, *J* = 8.8 Hz, 1H, H-4').

¹³C{¹H} NMR (100 MHz, CDCl₃): δ 154.8 (C-1), 136.1 (C-11), 135.5, (C-9) 135.3 (C-5), 135.0 (C-Ar [Ph₃Ge]), 129.393 (C-Ar [Bn]), 129.387 (C-Ar [Ph₃Ge]), 129.1 (C-Ar [Bn]), 128.5 (C-Ar [Ph₃Ge]), 127.5 (C-Ar [Bn]), 101.1 (C-10), 66.7 (C-2), 54.6 (C-3), 36.5 (C-4).

IR (neat): v (cm⁻¹) 3068, 1752, 1608, 1400, 1089, 907, 727, 696.

HRMS (ESI): m/z calculated for $[C_{30}H_{27}GeNO_2 + Na]^+$ 530.1152; found 530.1167.

[α]_D²⁰: 11.7 (*c* 1.0, CH₂Cl₂).

Note: The E configuration was determined on the basis of the ¹H NMR coupling constant of the vinylic protons (J = 17.2 Hz).

[²H]-70: Prepared according to **GP VIII** from ynamide **57** (50 mg, 0.25 mmol, 1.0 equiv) with Ph₃GeH (99 mg, 0.33 mmol, 1.3 equiv) and a reaction time of 16 h. The reaction quench was modified by adding CuTC (48 mg, 0.25 mmol, 1.0 equiv) 5 min before ND₄Cl in D₂O. Purification of the crude product (E/Z > 98:2) by flash chromatography on silica gel (toluene/Et₂O = 90:10) afforded analytically pure [²H]-**70** in (96 mg, 76%, E/Z > 98:2) as a white solid.

¹**H NMR** (400 MHz, CDCl₃): δ 7.58–7.55 (m, 6H), 7.45–7.41 (m, 9H), 7.38–7.34 (m, 2H), 7.32–7.28 (m, 1H), 7.23–7.21 (m, 2H), 5.49 (s, 1H), 4.52–4.46 (m, 1H), 4.28 (dd, *J* = 9.0 Hz, *J* = 7.7 Hz, 1H), 4.23 (dd, *J* = 9.0 Hz, *J* = 3.0 Hz, 1H), 3.35 (dd, *J* = 13.9 Hz, *J* = 3.3 Hz, 1H), 2.89 (dd, *J* = 13.9 Hz, *J* = 8.9 Hz, 1H).

¹³C{¹H} NMR (100 MHz, CDCl₃): δ 154.8, 136.1, 135.3, 135.0, 129.4, 129.38, 129.1, 128.5, 127.5, 100.9, 66.7, 54.6, 36.5. *One C is not observed.*



C₃₀H₂₇GeNO₂ M.W. = 506.18 g⋅mol⁻¹



[²H]**-70**

C₃₀H₂₆DGeNO₂ M.W. = 507.19 g⋅mol⁻¹

HRMS (ESI): m/z calculated for $[C_{30}H_{26}DGeNO_2 + Na]^+$ 531.1215; found 531.1224.

(E)-4,4-dimethyl-3-(2-(tri(furan-2-yl)germyl)vinyl)oxazolidin-2-one

(75): Prepared according to **GP VII** from ynamide **54** (35 mg, 0.25 mmol, 1.0 equiv) with (2-furyl)₃GeH (89 mg, 0.33 mmol, 1.3 equiv) and a reaction time of 3 h. The reaction quench was modified by adding CuTC (48 mg, 0.25 mmol, 1.0 equiv) and, 5 min after, NH₄Cl (300 mg) in H₂O (2 mL) and stirring the resulting mixture for 1 h at rt before workup with aq NH₄Cl/NH₃ (2:1) and CH₂Cl₂. Purification of the crude product (E/Z > 98:2) by flash chromatography on silica gel (pentane/EtOAc = 70:30) afforded analytically pure **75** (75 mg, 72%, E/Z > 98:2) as a white solid; mp 142–145 °C.

¹**H NMR** (400 MHz, CDCl₃): δ 7.74 (dd, *J* = 1.7 Hz, *J* = 0.6 Hz, 3H, H-10), 6.81 (dd, *J* = 3.2 Hz, *J* = 0.6 Hz, 3H, H-8), 6.75 (d, *J* = 17.5 Hz, 1H, H-5), 6.47 (dd, *J* = 3.2 Hz, *J* = 1.7 Hz, 3H, H-9), 5.78 (d, *J* = 17.5 Hz, 1H, H-6), 4.01 (s, 2H, H-2), 1.51 (s, 6H, H-4,4').

¹³C{¹H} NMR (100 MHz, CDCl₃): δ 155.0 (C-1), 152.5 (C-7), 147.7 (C-10), 135.4 (C-5), 121.6 (C-8), 110.0 (C-9), 99.1 (C-6), 75.3 (C-2), 58.8 (C-3), 25.1 (C-4,4').

IR (neat): v (cm⁻¹) 2978, 1754, 1612, 1326, 1066, 1001, 891, 748.

HRMS (ESI): m/z calculated for $[C_{19}H_{19}GeNO_5 + Na]^+$ 438.0371; found 438.0375.

Note: The E configuration was determined on the basis of the ¹H NMR coupling constant of the vinylic protons (J = 17.5 Hz).



75

 $C_{19}H_{19}GeNO_5$

M.W. = 414.00 g·mol⁻¹

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[<sup>2</sup>H]-75
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C₁₉H₁₈DGeNO₅ M.W. = 415.00 g·mol⁻¹ [²H]-75: Prepared according to **GP VIII** from ynamide **54** (35 mg, 0.25 mmol, 1.0 equiv) with (2-furyl)₃GeH (89 mg, 0.33 mmol, 1.3 equiv) and a reaction time of 3 h. The reaction quench was modified by adding CuTC (48 mg, 0.25 mmol, 1.0 equiv) 5 min before ND₄Cl/D₂O. Purification of the crude product (E/Z > 98:2) by flash chromatography on silica gel (pentane/EtOAc = 70:30) afforded analytically pure [²H]-**75** in (86 mg, 83%, E/Z > 98:2) as white crystals.

¹**H NMR** (400 MHz, CDCl₃): δ 7.74 (dd, *J* = 1.7 Hz, *J* = 0.6 Hz, 3H), 6.81 (dd, *J* = 3.3 Hz, *J* = 0.6 Hz, 3H), 6.47 (dd, *J* = 3.3 Hz, *J* = 1.7 Hz, 3H), 5.77 (s, 1H), 4.01 (s, 2H), 1.51 (s, 6H).

¹³C{¹H} NMR (100 MHz, CDCl₃): δ 155.0, 152.5, 147.7, 135.1 (t, *J* = 26.9 Hz), 121.6, 110.0, 98.8, 75.3, 58.7, 25.0.

HRMS (ESI): m/z calculated for $[C_{19}H_{18}DGeNO_5 + Na]^+ 439.0434$; found 439.0420.

(*E*)-4,4-dimethyl-3-(2-(tributylgermyl)vinyl)oxazolidin-2-one (76): Prepared according to **GP VII** from ynamide **54** (35 mg, 0.25 mmol, 1.0 equiv) with *n*Bu₃GeH (123 mg, 0.50 mmol, 2.0 equiv) and a reaction time of 16 h. Purification of the crude product (E/Z = 96:4) by flash chromatography on silica gel (pentane/Et₂O = 90:10) afforded analytically pure **76** (74 mg, 77%, E/Z = 96:4) as a colorless oil.

¹**H NMR** (400 MHz, CDCl₃): (*E* isomer) δ 6.39 (d, *J* = 17.9 Hz, 1H, H-5), 5.34 (d, *J* = 17.9 Hz, 1H, H-6), 3.98 (s, 2H, H-2), 1.50 (s, 6H, H-4,4'), 1.36–1.29 (m, 12H, H-8,9), 0.89–0.86 (m, 9H, H-10), 0.81–0.77 (m, 6H, H-7).

¹³C{¹H} NMR (100 MHz, CDCl₃): (*E* isomer) δ 155.5 (C-1), 130.9 (C-5), 106.8 (C-6), 75.4 (C-2), 58.7 (C-3), 27.5 (C-8 or C-9), 26.5 (C-9 or C-8), 25.0 (C-4,4'), 13.9 (C-10), 13.1 (C-7).

IR (neat): v (cm⁻¹) 2961, 2921, 1755, 1610, 1325, 1182, 1067, 789, 689.

HRMS (ESI): m/z calculated for $[C_{19}H_{37}GeNO_2 + Na]^+$ 408.1932; found 408.1945.

Note: The E configuration was determined on the basis of the ¹H NMR coupling constant of the vinylic protons (J = 17.9 Hz).

[²H]-76: Prepared according to **GP VIII** from ynamide **54** (35 mg, 0.25 mmol, 1.0 equiv) with *n*Bu₃GeH (123 mg, 0.50 mmol, 2.0 equiv) and a reaction time of 16 h. Purification of the crude product (E/Z = 96:4) by flash chromatography on silica gel (pentane/Et₂O = 90:10) afforded analytically pure [²H]-**76** (64 mg, 67%, E/Z > 98:2) as a colorless oil.





C₁₉H₃₇GeNO₂ M.W. = 384.14 g⋅mol⁻¹



[²H]-76

C₁₉H₃₆DGeNO₂ M.W. = 385.15 g⋅mol⁻¹ ¹**H NMR** (400 MHz, CDCl₃): δ 5.33 (t, *J* = 2.3 Hz, 1H), 3.98 (s, 2H), 1.50 (s, 6H), 1.37–1.28 (m, 12H), 0.90–0.86 (m, 9H), 0.81–0.77 (m, 6H).

¹³C{¹H} NMR (100 MHz, CDCl₃): δ 155.5, 130.6 (t, *J* = 26.7), 106.6, 75.4, 58.7, 27.5, 26.5, 25.0, 13.9, 13.2.

HRMS (ESI): m/z calculated for $[C_{19}H_{36}DGeNO_2 + Na]^+ 409.1994$; found 409.1994.

(*E*)-4,4-dimethyl-3-(2-(triethylgermyl)vinyl)oxazolidin-2-one (77): Prepared according to **GP VII** from ynamide **54** (35 mg, 0.25 mmol, 1.0 equiv) with Et₃GeH (80 mg, 0.50 mmol, 2.0 equiv) and a reaction time of 16 h. Purification of the crude product (E/Z = 95:5) by flash chromatography on silica gel (pentane/EtOAc = 90:10) afforded analytically pure **77** (57 mg, 76%, E/Z = 95:5) as a colorless oil.

¹**H NMR** (400 MHz, CDCl₃): (*E* isomer) δ 6.39 (d, *J* = 17.9 Hz, 1H, H-5), 5.32 (d, *J* = 17.9 Hz, 1H, H-6), 3.98 (s, 2H, H-2), 1.49 (s, 6H, H-4,4'), 1.03–0.99 (m, 9H, H-8), 0.82–0.76 (m, 6H, H-7).

¹³C{¹H} NMR (100 MHz, CDCl₃): (*E* isomer) δ 155.4 (C-1), 131.2 (C-5), 105.6 (C-6), 75.4 (C-2), 58.7 (C-3), 25.0 (C-4,4'), 9.0 (C-8), 4.6 (C-7).

IR (neat): v (cm⁻¹) 2952, 1752, 1609, 1325, 1181, 1066, 790, 703.

HRMS (ESI): m/z calculated for $[C_{13}H_{25}GeNO_2 + Na]^+$ 324.0991; found 324.1004.

Note: The E configuration was determined on the basis of the ¹H NMR coupling constant of the vinylic protons (J = 17.9 Hz).



[²H]-77

C₁₃H₂₄DGeNO₂ M.W. = 300.99 g⋅mol⁻¹ **[²H]-77:** Prepared according to **GP VIII** from ynamide **54** (35 mg, 0.25 mmol, 1.0 equiv) with Et₃GeH (80 mg, 0.50 mmol, 2.0 equiv) and a reaction time of 16 h. Purification of the crude product (E/Z = 91:9) by flash chromatography on silica gel (pentane/EtOAc = 90:10) afforded analytically pure [²H]-**77** (69 mg, 92%, E/Z = 87:13) as a colorless oil.

¹H NMR (400 MHz, CDCl₃): (*E* isomer) δ 5.31 (t, *J* = 2.5 Hz, 1H), 3.97 (s, 2H),
1.49 (s, 6H), 1.03–0.98 (m, 9H), 0.81–0.75 (m, 6H).





C₁₃H₂₅GeNO₂ M.W. = 299.98 g⋅mol⁻¹

¹³C{¹H} NMR (100 MHz, CDCl₃): (*E* isomer) δ 155.4, 130.9 (t, *J* = 26.8 Hz), 105.3, 75.4, 58.6, 24.9, 9.0, 4.6.

HRMS (ESI): m/z calculated for $[C_{13}H_{24}DGeNO_2 + Na]^+$ 325.1054; found 325.1055.

III-5.4. GERMYLZINCATION OF INTERNAL YNAMIDES (GP IX AND GP X)

General Procedure for the Germylzincation of Internal Ynamides (GP IX):



In a dry Schlenk tube under argon atmosphere, the appropriate ynamide (0.15 mmol, 1.0 equiv) was suspended in dry *n*-hexane (1.2 mL). At 0 °C, Et₂Zn (1.0 M in hexane, 0.45 mL, 0.45 mmol, 3.0 equiv) and the corresponding germanium hydride (0.20–0.30 mmol, 1.3–2.0 equiv) were successively added. The reaction mixture was then heated at 40 °C and the resulting solution stirred for the given reaction time. The reaction mixture was then cooled to rt and aq NH₄Cl/NH₃ (2:1) and CH₂Cl₂ were added. The layers were separated, the aqueous layer was extracted with CH₂Cl₂ (x3), and the combined organic layers were washed with brine (x2), dried over Na₂SO₄, filtered, and concentrated under reduce pressure to afford the crude product.

General Procedure for the Germylzincation – D-labeling of Internal Ynamides (GP X):



In a dry Schlenk tube under argon atmosphere, the appropriate ynamide (0.15 mmol, 1.0 equiv) was suspended in dry *n*-hexane (1.2 mL). At 0 °C, Et_2Zn (1.0 M in hexane, 0.45 mL, 0.45 mmol, 3.0 equiv) and the corresponding germanium hydride (0.20–0.30 mmol, 1.3–2.0 equiv)

were successively added. The reaction mixture was then heated at 40 °C and the resulting solution stirred for the given reaction time. After cooling the reaction mixture to rt, a solution of ND₄Cl (300 mg) in D₂O (2 mL) was added followed by THF (2 mL) 10 min after. The mixture was stirred for 1 h at rt and then aq NH₄Cl/NH₃ (2:1) and CH₂Cl₂ were added. The layers were separated, the aqueous layer was extracted with CH₂Cl₂ (x3), and the combined organic layers were washed with brine (x2), dried over Na₂SO₄, filtered, and concentrated under reduce pressure to afford the crude product.





C₃₁H₂₉GeNO₂ M.W. = 520.21 g⋅mol⁻¹



[²H]-94

C₃₁H₂₈DGeNO₂ M.W. = 521.21 g⋅mol⁻¹

(E)-4,4-dimethyl-3-[2-phenyl-2-(triphenylgermyl)vinyl]oxazolidin-2-

one (94): Prepared according to **GP IX** from ynamide **92** (32 mg, 0.15 mmol, 1.0 equiv) with Ph₃GeH (60 mg, 0.20 mmol, 1.3 equiv) and a reaction time of 3 h. Purification of the crude product (E/Z > 98:2) by flash chromatography on silica gel (pentane/Et₂O = 60:40) afforded analytically pure **94** (72 mg, 92%, E/Z > 98:2) as a white solid; mp 162–166 °C.

¹**H NMR** (400 MHz, CDCl₃): δ 7.46–7.44 (m, 6H, H-Ar [Ph₃Ge]), 7.40–7.33 (m, 9H, H-Ar [Ph₃Ge]), 7.15–7.13 (m, 3H, H-Ar [Ph]), 7.07–7.05 (m, 2H, H-Ar [Ph]), 6.00 (s, 1H, H-5), 3.87 (s, 2H, H-2), 1.16 (s, 6H, H-4,4').

JMod (100 MHz, CDCl₃): δ 154.9 (C-1), 141.9 (C-6), 139.5 (C-7), 135.5 (C-Ar [Ph₃Ge]), 135.3 (C-11), 129.4 (C-Ar [Ph₃Ge]), 128.4 (C-Ar [Ph₃Ge]), 128.0 (2C, C-Ar [Ph]), 127.9 (C-5), 126.6 (C-Ar [Ph]), 75.0 (C-2), 59.7 (C-3), 24.9 (C-4,4').

IR (neat): v (cm⁻¹) 3058, 2971, 1755, 1338, 735, 698.

HRMS (ESI): m/z calculated for $[C_{31}H_{29}GeNO_2 + Na]^+$ 544.1309; found 544.1296.

[²**H]-94:** Prepared according to **GP X** from ynamide **92** (32 mg, 0.15 mmol, 1.0 equiv) with Ph₃GeH (60 mg, 0.20 mmol, 1.3 equiv) and a reaction time of 3 h. Purification of the crude product (E/Z > 98:2) by flash chromatography on silica gel (pentane/Et₂O = 60:40) afforded analytically pure [²H]-**94** (69 mg, 88%, E/Z > 98:2) as a white solid.

¹**H NMR** (400 MHz, CDCl₃): δ 7.47–7.44 (m, 6H), 7.42–7.33 (m, 9H), 7.18–7.12 (m, 3H), 7.09–7.06 (m, 2H), 3.88 (s, 2H), 1.16 (s, 6H).

¹³C{¹H} NMR (100 MHz, CDCl₃): δ 154.8, 141.5, 139.4, 135.5, 135.3, 129.3, 128.4, 128.0 (2C), 126.5, 74.9, 59.6, 24.9. One C is not observed.

HRMS (ESI): m/z calculated for $[C_{31}H_{28}DGeNO_2 + Na]^+$ 545.1371; found 545.1383.

(S,E)-4-isopropyl-3-(2-phenyl-2-(triphenylgermyl)vinyl)oxazolidin-2-

one (129): Prepared according to **GP IX** from ynamide **106** (34 mg, 0.15 mmol, 1.0 equiv) with Ph₃GeH (60 mg, 0.20 mmol, 1.3 equiv) and a reaction time of 3 h. Purification of the crude product (E/Z = 92:8) by flash chromatography on silica gel (pentane/Et₂O = 80:20) afforded analytically pure **129** (69 mg, 86%, E/Z > 98:2) as a white solid; mp 147–150 °C.

¹**H NMR** (400 MHz, CDCl₃): δ 7.42–7.32 (m, 15H, H-Ar [Ph₃Ge]), 7.19–7.15 (m, 3H, H-Ar [Ph]), 6.99–6.97 (m, 2H, H-Ar [Ph]), 6.83 (s, 1H, H-6), 4.03–3.95 (m, 2H, H-2), 3.21 (dt, *J* = 8.2 Hz, *J* = 3.0 Hz, 1H, H-3), 1.97 (heptd, *J* = 7.0 Hz, *J* = 3.0 Hz, 1H, H-4), 0.76 (d, *J* = 7.0 Hz, 3H, H-5 or H-5'), 0.37 (d, *J* = 7.0 Hz, 3H, H-5' or H-5).

JMod (100 MHz, CDCl₃): δ 156.8 (C-1), 139.7, 135.5, 135.45, 129.6 (C-6), 129.3, 128.9, 128.4, 128.3, 126.6, 122.7, 62.6 (C-2), 58.5 (C-3), 26.9 (C-4), 17.4 (C-5 or C-5'), 13.4 (C-5' or C-5).

IR (neat): v (cm⁻¹) 3059, 2920, 2871, 1756, 1611, 1218, 909, 730, 698.

HRMS (ESI): m/z calculated for $[C_{32}H_{31}GeNO_2 + Na]^+$ 558.1466; found 558.1484.

[α]_D²⁰: -171.2 (*c* 1.0, CH₂Cl₂).

[²H]-129: Prepared according to **GP X** from ynamide **106** (34 mg, 0.15 mmol, 1.0 equiv) with Ph₃GeH (60 mg, 0.20 mmol, 1.3 equiv) and a reaction time of 3 h. Purification of the crude product (E/Z = 90:10) by flash chromatography on silica gel (pentane/Et₂O = 80:20) afforded [²H]-**129** (66 mg, 83%, E/Z = 86:14) as a white solid, contaminated with 6% of unidentified triphenylgermyl-containing residues.

¹**H NMR** (400 MHz, CDCl₃): (*E* isomer) δ 7.46–7.31 (m, 15H), 7.20–7.11 (m, 3H), 6.99–6.96 (m, 2H), 4.04–3.94 (m, 2H), 3.21 (dt, *J* = 8.3 Hz, *J* = 3.0 Hz, 1H), 1.97 (heptd, *J* = 7.0 Hz, *J* = 3.0 Hz, 1H), 0.75 (d, *J* = 7.0 Hz, 3H), 0.37 (d, *J* = 7.0 Hz, 3H).







C₃₂H₃₁GeNO₂ M.W. = 534.23 g⋅mol⁻¹



[²H]-129

C₃₂H₃₀DGeNO₂ M.W. = 535.24 g⋅mol⁻¹ JMod (100 MHz, CDCl₃): (*E* isomer) δ 156.8, 139.7, 135.6, 135.5, 129.3, 128.9, 128.35, 128.28, 126.6, 122.7, 62.6, 58.4, 26.9, 17.4, 13.4. *One C is not observed.* HRMS (ESI): *m/z* calculated for [C₃₂H₃₀DGeNO₂ + Na]⁺ 559.1528; found 559.1547.







C₃₆H₃₁GeNO₂ M.W. = 582.28 g⋅mol⁻¹

(*S,E*)-4-benzyl-3-(2-phenyl-2-(triphenylgermyl)vinyl)oxazolidin-2-one (130): Prepared according to **GP IX** from ynamide **107** (42 mg, 0.15 mmol, 1.0 equiv) with Ph₃GeH (60 mg, 0.20 mmol, 1.3 equiv) and a reaction time of 3 h. Purification of the crude product (E/Z > 98:2) by flash chromatography on silica gel (pentane/Et₂O = 75:25) afforded analytically pure **130** (74 mg, 85%, E/Z > 98:2) as a white solid; mp 173–176 °C.

¹**H NMR** (400 MHz, CDCl₃): δ 7.45–7.32 (m, 15H, H-Ar [Ph₃Ge]), 7.29–7.23 (m, 3H, H-Ar [Ph]), 7.19–7.07 (m, 5H, H-Ar [Bn]), 6.89 (s, 1H, H-9), 6.62–6.54 (m, 2H, H-Ar [Ph]), 3.96–3.85 (m, 2H, H-4), 3.76 (ddt, *J* = 10.5 Hz, *J* = 6.8 Hz, *J* = 3.6 Hz, 1H, H-3), 3.01 (dd, *J* = 13.3 Hz, *J* = 3.6 Hz, 1H, H-2), 2.37 (dd, *J* = 13.3 Hz, *J* = 10.5 Hz, 1H, H-2').

¹³C{¹H} NMR (100 MHz, CDCl₃): δ 156.5 (C-1), 139.9, 135.6, 135.5, 135.3, 129.6, 129.4, 129.37, 129.3, 128.8, 128.7, 128.4, 127.1, 126.9, 121.8, 65.6 (C-4), 55.2 (C-3), 37.0 (C-2).

IR (neat): v (cm⁻¹) 3060, 2920, 1761, 1395, 1085, 734, 699.

HRMS (ESI): m/z calculated for $[C_{36}H_{31}GeNO_2 + Na]^+$ 606.1467; found 606.1468.

[α]_D²⁰: -168.5 (*c* 0.25, CH₂Cl₂).



[²H]-130

C₃₆H₃₀DGeNO₂ M.W. = 583.28 g⋅mol⁻¹ **[²H]-130**: Prepared according to **GP X** from ynamide **107** (42 mg, 0.15 mmol, 1.0 equiv) with Ph₃GeH (60 mg, 0.20 mmol, 1.3 equiv) and a reaction time of 3 h. Purification of the crude product (E/Z > 98:2) by flash chromatography on silica gel (pentane/Et₂O = 75:25) afforded analytically pure [²H]-**130** (63 mg, 72%, E/Z > 98:2) as a white solid.

¹**H NMR** (400 MHz, CDCl₃): δ 7.48–7.31 (m, 15H), 7.29–7.23 (m, 3H), 7.17– 7.06 (m, 5H), 6.60–6.45 (m, 2H), 3.96–3.84 (m, 2H), 3.82–3.71 (m, 1H), 3.00 (dd, *J* = 13.3 Hz, *J* = 3.5 Hz, 1H), 2.36 (dd, *J* = 13.3 Hz, *J* = 10.5 Hz, 1H). ¹³C{¹H} NMR (100 MHz, CDCl₃): δ 156.4, 139.8, 135.6, 135.5, 135.3, 129.4, 129.37, 129.3, 128.8, 128.7, 128.4, 127.1, 126.9, 121.5, 65.6, 55.2, 37.0. *One C is not observed.*

HRMS (ESI): m/z calculated for $[C_{36}H_{30}DGeNO_2 + Na]^+$ 607.1529; found 607.1549.

The E configuration was determined by X-ray crystallographic analysis.



(*E*)-3-(2-phenyl-2-(triphenylgermyl)vinyl)oxazolidin-2-one (131): Prepared according to **GP IX** from ynamide **108** (28 mg, 0.15 mmol, 1.0 equiv) with Ph₃GeH (60 mg, 0.20 mmol, 1.3 equiv) and a reaction time of 3 h. Purification of the crude product (E/Z > 98:2) by flash chromatography on silica gel (pentane/Et₂O = 70:30) afforded analytically pure **131** (51 mg, 69%, E/Z > 98:2) as a white solid; mp 217–220 °C.

¹**H NMR** (400 MHz, CDCl₃): δ 7.40–7.30 (m, 15H, H-Ar [Ph₃Ge]), 7.14–7.11 (m, 3H, H-Ar [Ph]), 6.97–6.94 (m, 2H, H-Ar [Ph]), 6.89 (s, 1H, H-4), 4.13–4.09 (m, 2H, H-2), 3.18–3.14 (m, 2H, H-3).

¹³C{¹H} NMR (100 MHz, CDCl₃): δ 156.7 (C-1), 139.4, 135.5, 135.4, 130.5, 129.6, 129.3, 128.3, 127.8, 126.5, 119.5, 62.5 (C-2), 45.1 (C-3).

IR (neat): v (cm⁻¹) 3059, 1757, 1395, 1229, 1082, 907, 731, 695.

HRMS (ESI): m/z calculated for $[C_{29}H_{25}GeNO_2 + Na]^+$ 516.0995; found 516.1015.





C₂₉H₂₅GeNO₂ M.W. = 492.15 g⋅mol⁻¹



[²H]-131

C₂₉H₂₄DGeNO₂ M.W. = 493.16 g·mol⁻¹ **[²H]-131:** Prepared according to **GP X** from ynamide **108** (28 mg, 0.15 mmol, 1.0 equiv) with Ph₃GeH (60 mg, 0.20 mmol, 1.3 equiv) and a reaction time of 3 h. Purification of the crude product (E/Z > 98:2) by flash chromatography on silica gel (pentane/Et₂O = 70:30) afforded analytically pure [²H]-**131** (59 mg, 80%, E/Z > 98:2) as a white solid.

¹**H NMR** (400 MHz, CDCl₃): δ 7.43–7.31 (m, 15H), 7.15–7.12 (m, 3H), 6.97– 6.95 (m, 2H), 4.13–4.09 (m, 2H), 3.18–3.14 (m, 2H).

¹³C{¹H} NMR (100 MHz, CDCl₃): δ 156.7, 139.3, 135.5, 135.4, 129.6, 129.3, 128.3, 127.8, 126.5, 119.2, 62.6, 45.1. *One C is not observed.*

HRMS (ESI): m/z calculated for $[C_{29}H_{24}DGeNO_2 + Na]^+$ 517.1058; found 517.1073.





C₃₄H₂₉GeNO₂ M.W. = 556.24 g⋅mol⁻¹

(*E*)-methyl phenyl(2-phenyl-2-(triphenylgermyl)vinyl)carbamate (132): Prepared according to GP IX from ynamide 109 (38 mg, 0.15 mmol, 1.0 equiv) with Ph₃GeH (60 mg, 0.20 mmol, 1.3 equiv) and a reaction time of 16 h. Purification of the crude product (E/Z > 98:2) by flash chromatography on silica gel (pentane/Et₂O = 90:10) afforded analytically pure 132 (61 mg, 73%, E/Z > 98:2) as a white solid; mp 136–138 °C.

¹**H NMR** (400 MHz, CDCl₃): δ 7.41–7.31 (m, 15H, H-Ar [Ph₃Ge]), 7.05 (s, 1H, H-7), 7.02–6.98 (m, 2H, H-Ar), 6.96–6.89 (m, 3H, H-Ar), 6.87–6.81 (m, 3H, H-Ar), 6.60–6.58 (m, 2H, H-Ar), 3.65 (s, 3H, H-1).

¹³C{¹H} NMR (100 MHz, CDCl₃): δ 155.3 (C-2), 140.7, 139.2, 136.3 (C-7), 135.8, 135.6, 129.2, 128.5, 128.3, 128.2, 127.6, 127.4, 126.0, 125.6, 53.4 (C-1). *One C is not observed.*

IR (neat): v (cm⁻¹) 3059, 1717, 1601, 1437, 1329, 1289, 733, 696.

HRMS (ESI): m/z calculated for $[C_{34}H_{29}GeNO_2 + Na]^+$ 580.1310; found 580.1329.

The E configuration was determined by X-ray crystallographic analysis.



[²H]-132: Prepared according to **GP X** from ynamide **109** (38 mg, 0.15 mmol, 1.0 equiv) with Ph₃GeH (60 mg, 0.20 mmol, 1.3 equiv) and a reaction time of 16 h. Purification of the crude product (E/Z > 98:2) by flash chromatography on silica gel (pentane/Et₂O = 90:10) afforded analytically pure [²H]-**132** (61 mg, 73%, E/Z > 98:2) as a white solid.

¹**H NMR** (400 MHz, CDCl₃): δ 7.42–7.32 (m, 15H), 7.03–6.98 (m, 2H), 6.96–6.90 (m, 3H), 6.88–6.81 (m, 3H), 6.61–6.59 (m, 2H), 3.66 (s, 3H).

¹³C{¹H} NMR (100 MHz, CDCl₃): δ 155.3, 140.7, 139.1, 135.8, 135.5, 129.2, 128.5, 128.3, 128.2, 127.6, 127.4, 126.0, 125.5, 53.4. *Two Cs are not observed*.

HRMS (ESI): *m*/*z* calculated for [C₃₄H₂₈DGeNO₂ + Na]⁺ 581.1372; found 581.1365.

(E)-4,4-dimethyl-3-(2-phenyl-2-(tri(furan-2-

yl)germyl)vinyl)oxazolidin-2-one (135): Prepared according to **GP IX** from ynamide **92** (32 mg, 0.15 mmol, 1.0 equiv) with $(2-\text{furyl})_3$ GeH (74 mg, 0.20 mmol, 1.3 equiv) and a reaction time of 16 h. Purification of the crude product (*E*/*Z* > 98:2) by flash chromatography on silica gel (pentane/EtOAc = 70:30) afforded analytically pure **135** (65 mg, 88%, *E*/*Z* > 98:2) as a white solid; mp 133–135 °C.

¹**H NMR** (400 MHz, CDCl₃): δ 7.73 (dd, *J* = 1.7 Hz, *J* = 0.6 Hz, 3H, H-14), 7.26– 7.11 (m, 5H, H-Ar [Ph]), 6.71 (dd, *J* = 3.3 Hz, *J* = 0.6 Hz, 3H, H-12), 6.45 (dd, *J* = 3.3 Hz, *J* = 1.7 Hz, 3H, H-13), 6.18 (s, 1H, H-5), 3.90 (s, 2H, H-2), 1.21 (s, 6H, H-4,4').



[²H]-132

C₃₄H₂₈DGeNO₂ M.W. = 557.25 g⋅mol⁻¹



135

C₂₅H₂₃GeNO₅ M.W. = 490.09 g·mol⁻¹
¹³C{¹H} NMR (100 MHz, CDCl₃): δ 154.4 (C-1), 151.6 (C-11), 147.7 (C-14), 138.4 (C-6 or C-7), 136.9 (C-7 or C-6), 128.1 (C-Ar), 128.08 (C-5), 127.9 (C-Ar), 126.9 (C-Ar), 122.4 (C-12), 110.1 (C-13), 75.0 (C-2), 59.8 (C-3), 24.9 (C-4,4').

IR (neat): v (cm⁻¹) 2974, 1759, 1341, 1204, 1003, 897, 752, 698.

HRMS (ESI): m/z calculated for $[C_{25}H_{23}GeNO_5 + Na]^+$ 514.0685; found 514.0702.

Ph D (2-furyl)₃Ge

[²H]-135

C₂₅H₂₂DGeNO₅ M.W. = 491.10 g⋅mol⁻¹



136 (*β* isomer)



136 (*α* isomer)

C₁₉H₂₉GeNO₂ M.W. = 376.08 g·mol⁻¹ **[²H]-135:** Prepared according to **GP X** from ynamide **92** (32 mg, 0.15 mmol, 1.0 equiv) with (2-furyl)₃GeH (74 mg, 0.20 mmol, 1.3 equiv) and a reaction time of 16 h. Purification of the crude product (E/Z > 98:2) by flash chromatography on silica gel (pentane/EtOAc = 70:30) afforded analytically pure [²H]-**135** (65 mg, 88%, E/Z > 98:2) as a white solid.

¹H NMR (400 MHz, CDCl₃): δ 7.73 (dd, *J* = 1.7 Hz, *J* = 0.6 Hz, 3H), 7.24–7.11 (m, 5H), 6.71 (dd, *J* = 3.3 Hz, *J* = 0.6 Hz, 3H), 6.45 (dd, *J* = 3.3 Hz, *J* = 1.7 Hz, 3H), 3.90 (s, 2H), 1.22 (s, 6H).

¹³C{¹H} NMR (100 MHz, CDCl₃): δ 154.4, 151.6, 147.7, 138.4, 136.5, 128.1, 127.9, 126.9, 122.4, 110.1, 75.0, 59.7, 24.9. *One C is not observed.*

HRMS (ESI): m/z calculated for $[C_{25}H_{22}DGeNO_5 + Na]^+$ 515.0748; found 515.0746.

(*E*)-4,4-dimethyl-3-(2-phenyl-2-(triethylgermyl)vinyl)oxazolidin-2-one / 4,4-dimethyl-3-(2-phenyl-1-(triethylgermyl)vinyl)oxazolidin-2-one (136): Prepared according to GP IX from ynamide 92 (32 mg, 0.15 mmol, 1.0 equiv) with Et₃GeH (48 mg, 0.30 mmol, 2.0 equiv) and a reaction time of 16 h. A mixture of regioisomers (β/α = 55:45) was obtained in the crude and they could not be separated during purification. Flash chromatography on silica gel (pentane/EtOAc = 90:10) afforded **136** (35 mg, 63%, mixture of regioisomers β/α = 55:45) as a colorless oil.

¹**H NMR** (400 MHz, CDCl₃): δ 7.29–7.16 (m, 2H_{β -isomer} + 6H_{α -isomer}), 7.10–7.06 (m, 1H_{β -isomer}, H-Ar), 6.99–6.97 (m, 2H_{β -isomer}, H-Ar), 5.76 (s, 1H_{β -isomer}, H-5), 4.01 (s, 2H_{α -isomer}, H-2), 3.77 (s, 2H_{β -isomer}, H-2), 1.37 (s, 6H_{α -isomer}, H-4,4'), 1.07 (s,

6H_{β-isomer}, H-4,4'), 0.98–0.93 (m, 9H_{β-isomer}, H-12), 0.89–0.85 (m, 9H_{α-isomer}, H-12), 0.82–0.75 (m, 6H_{β-isomer}, H-11), 0.72–0.66 (m, 6H_{α-isomer}, H-11).

¹³C{¹H} NMR (100 MHz, CDCl₃): δ 156.2 (C-1_{*a*-isomer}), 156.0 (C-1_{*β*-isomer}), 147.2 (C-7_{*β*-isomer}), 142.9 (C-6_{*a*-isomer}), 141.1 (C_{*a*-isomer}), 140.6 (C-6_{*β*-isomer}), 137.0 (C_{*a*-isomer}), 128.7 (C_{*a*-isomer}), 128.2 (C_{*a*-isomer}), 128.0 (C_{*β*-isomer}), 127.96 (C_{*a*-isomer}), 127.3 (C_{*β*-isomer}), 126.1 (C_{*β*-isomer}), 123.9 (C-5_{*β*-isomer}), 76.2 (C-2_{*a*-isomer}), 75.0 (C-2_{*β*-isomer}), 60.9 (C-3_{*a*-isomer}), 59.8 (C-3_{*β*-isomer}), 26.5 (C-4,4'_{*a*-isomer}), 24.8 (C-4,4'_{*β*-isomer}), 9.1 (C-12_{*a*-isomer}), 8.9 (C-12_{*β*-isomer}), 6.7 (C-11_{*a*-isomer}), 4.3 (C-11_{*β*-isomer}).

HRMS (ESI): m/z calculated for $[C_{19}H_{29}GeNO_2 + Na]^+$ 400.1302; found 400.1304.

(E)-3-(2-(4-methoxyphenyl)-2-(triphenylgermyl)vinyl)-4,4-

dimethyloxazolidin-2-one (138): Prepared according to **GP IX** from ynamide **112** (37 mg, 0.15 mmol, 1.0 equiv) with Ph₃GeH (60 mg, 0.20 mmol, 1.3 equiv) and a reaction time of 3 h. Purification of the crude product (E/Z > 98:2) by flash chromatography on silica gel (pentane/Et₂O = gradient from 60:40 to 50:50) afforded analytically pure **138** (78 mg, 94%, E/Z > 98:2) as a white solid; mp 151–153 °C.

¹**H NMR** (400 MHz, CDCl₃): δ 7.49–7.46 (m, 6H, H-Ar [Ph₃Ge]), 7.42–7.34 (m, 9H, H-Ar [Ph₃Ge]), 7.04–7.00 (m, 2H, H-Ar [Ph]), 6.73–6.70 (m, 2H, H-Ar [Ph]), 5.99 (s, 1H, H-5), 3.89 (s, 2H, H-2), 3.74 (s, 3H, H-11), 1.15 (s, 6H, H-4,4').

¹³C{¹H} NMR (100 MHz, CDCl₃): δ 158.3 (C-10), 155.0 (C-1), 141.7 (C-6 or C-7), 135.5 (C-Ar [Ph₃Ge]), 135.47 (C-12), 131.6 (C-7 or C-6), 129.3 (C-Ar [Ph₃Ge]), 129.2 (C-Ar [Ph]), 128.4 (C-Ar [Ph₃Ge]), 127.8 (C-5), 113.5 (C-Ar [Ph]), 74.9 (C-2), 59.7 (C-3), 55.1 (C-11), 24.9 (C-4,4').

IR (neat): v (cm⁻¹) 3058, 2969, 1750, 1510, 1244, 1030, 735, 698.

HRMS (ESI): m/z calculated for $[C_{32}H_{31}GeNO_3 + Na]^+$ 574.1415; found 574.1431.

[²**H]-138:** Prepared according to **GP X** from ynamide **112** (37 mg, 0.15 mmol, 1.0 equiv) with Ph₃GeH (60 mg, 0.20 mmol, 1.3 equiv) and a reaction time of 3 h. Purification of the crude product (E/Z > 98:2) by flash chromatography



C₃₂H₃₁GeNO₃ M.W. = 550.23 g·mol⁻¹



[²H]-138

C₃₂H₃₀DGeNO₃ M.W. = 551.24 g·mol⁻¹



139

C₃₁H₂₈ClGeNO₂ M.W. = 554.65 g⋅mol⁻¹



[²H]-139

C₃₁H₂₇DClGeNO₂ M.W. = 555.66 g·mol⁻¹ on silica gel (pentane/Et₂O = gradient from 60:40 to 50:50) afforded analytically pure [²H]-**138** (75 mg, 90%, E/Z > 98:2) as a white solid.

¹**H NMR** (400 MHz, CDCl₃): δ 7.49–7.45 (m, 6H), 7.42–7.33 (m, 9H), 7.03–7.00 (m, 2H), 6.73–6.69 (m, 2H), 3.89 (s, 2H), 3.74 (s, 3H), 1.15 (s, 6H).

¹³C{¹H} NMR (100 MHz, CDCl₃): δ 158.3, 155.0, 141.4, 135.5, 135.48, 131.6, 129.3, 129.2, 128.4, 113.5, 75.0, 59.7, 55.2, 24.9. *One C is not observed.*

HRMS (ESI): *m*/*z* calculated for [C₃₂H₃₀DGeNO₃ + Na]⁺ 575.1478; found 575.1497.

(E)-3-(2-(4-chlorophenyl)-2-(triphenylgermyl)vinyl)-4,4-

dimethyloxazolidin-2-one (139): Prepared according to **GP IX** from ynamide **113** (38 mg, 0.15 mmol, 1.0 equiv) with Ph₃GeH (60 mg, 0.20 mmol, 1.3 equiv) and a reaction time of 3 h. Purification of the crude product (E/Z > 98:2) by flash chromatography on silica gel (pentane/Et₂O = 65:35) afforded analytically pure **139** (74 mg, 89%, E/Z > 98:2) as a white solid; mp 168–170 °C.

¹**H NMR** (400 MHz, CDCl₃): δ 7.47–7.35 (m, 15H, H-Ar [Ph₃Ge]), 7.15–7.11 (m, 2H, H-Ar [Ph]), 7.01–6.97 (m, 2H, H-Ar [Ph]), 6.00 (s, 1H, H-5), 3.90 (s, 2H, H-2), 1.19 (s, 6H, H-4,4').

¹³C{¹H} NMR (100 MHz, CDCl₃): δ 154.5 (C-1), 140.3 (C-6 or C-7), 138.1 (C-7 or C-6), 135.5 (C-Ar [Ph₃Ge]), 134.9 (C-11), 132.3 (C-10), 129.5 (C-Ar), 129.3 (C-Ar), 128.5 (C-Ar), 128.3 (C-Ar or C-5), 128.2 (C-5 or C-Ar), 74.9 (C-2), 59.5 (C-3), 24.9 (C-4,4').

IR (neat): v (cm⁻¹) 3059, 2972, 1756, 1338, 1084, 912, 734, 698.

HRMS (ESI): m/z calculated for $[C_{31}H_{28}ClGeNO_2 + Na]^+$ 578.0915; found 578.0932.

[²H]-139: Prepared according to **GP X** from ynamide **113** (38 mg, 0.15 mmol, 1.0 equiv) with Ph₃GeH (60 mg, 0.20 mmol, 1.3 equiv) and a reaction time of 3 h. Purification of the crude product (E/Z > 98:2) by flash chromatography on silica gel (pentane/Et₂O = 65:35) afforded analytically pure [²H]-**139** (72 mg, 87%, E/Z > 98:2) as a white solid.

¹**H NMR** (400 MHz, CDCl₃): δ 7.47–7.34 (m, 15H), 7.14–7.11 (m, 2H), 7.00– 6.97 (m, 2H), 3.90 (s, 2H), 1.18 (s, 6H).

¹³C{¹H} NMR (100 MHz, CDCl₃): δ 154.5, 140.0, 138.1, 135.5, 134.9, 132.3, 129.5, 129.3, 128.5, 128.3, 74.9, 59.5, 24.9. *One C is not observed.*

HRMS (ESI): m/z calculated for $[C_{31}H_{27}DClGeNO_2 + Na]^+$ 579.0977; found 579.0987.

(E)-3-(2-(3-methoxyphenyl)-2-(triphenylgermyl)vinyl)-4,4-

dimethyloxazolidin-2-one (140): Prepared according to **GP IX** from ynamide **114** (37 mg, 0.15 mmol, 1.0 equiv) with Ph₃GeH (60 mg, 0.20 mmol, 1.3 equiv) and a reaction time of 4 h. Purification of the crude product (E/Z > 98:2) by flash chromatography on silica gel (pentane/Et₂O = 60:40) afforded analytically pure **140** (69 mg, 83%, E/Z > 98:2) as a white solid; mp 130–132 °C.

¹**H NMR** (400 MHz, CDCl₃): δ 7.48–7.45 (m, 6H, H-Ar [Ph₃Ge]), 7.42–7.34 (m, 9H, H-Ar [Ph₃Ge]), 7.07 (dd, *J* = 8.3 Hz, *J* = 7.6 Hz, 1H, H-11), 6.70–6.66 (m, 2H, H-10,12), 6.61 (dd, *J* = 2.5 Hz, *J* = 1.6 Hz, 1H, H-8), 6.00 (s, 1H, H-5), 3.89 (s, 2H, H-2), 3.53 (s, 3H, H-13), 1.16 (s, 6H, H-4,4').

¹³C{¹H} NMR (100 MHz, CDCl₃): δ 159.2 (C-9), 155.0 (C-1), 142.1 (C-6 or C-7), 140.7 (C-7 or C-6), 135.5 (C-Ar [Ph₃Ge]), 135.3 (C-14), 129.4 (C-Ar [Ph₃Ge]), 129.0 (C-11), 128.4 (C-Ar [Ph₃Ge]), 127.9 (C-5), 120.4 (C-10 or C-12), 113.1 (C-12 or C-10), 113.0 (C-8), 75.0 (C-2), 59.7 (C-3), 55.0 (C-13), 24.9 (C-4,4').

IR (neat): v (cm⁻¹) 3059, 2969, 1754, 1602, 1338, 1082, 735, 698.

HRMS (ESI): m/z calculated for $[C_{32}H_{31}GeNO_3 + Na]^+$ 574.1415; found 574.1432.

[²H]-140: Prepared according to **GP X** from ynamide **114** (37 mg, 0.15 mmol, 1.0 equiv) with Ph₃GeH (60 mg, 0.20 mmol, 1.3 equiv) and a reaction time of 5 h. Purification of the crude product (E/Z > 98:2) by flash chromatography on silica gel (pentane/Et₂O = 60:40) afforded analytically pure [²H]-**140** (73 mg, 88%, E/Z > 98:2) as a white solid.





C₃₂H₃₁GeNO₃ M.W. = 550.23 g⋅mol⁻¹



[²H]-**140**

C₃₂H₃₀DGeNO₃ M.W. = 551.24 g⋅mol⁻¹ ¹**H NMR** (400 MHz, CDCl₃): δ 7.48–7.45 (m, 6H), 7.42–7.34 (m, 9H), 7.07 (dd, *J* = 8.3 Hz, *J* = 7.5 Hz, 1H), 6.70–6.67 (m, 2H), 6.61 (dd, *J* = 2.5 Hz, *J* = 1.6 Hz, 1H), 3.89 (s, 2H), 3.53 (s, 3H), 1.16 (s, 6H).

¹³C{¹H} NMR (100 MHz, CDCl₃): δ 159.1, 155.0, 141.7, 140.7, 135.5, 135.3, 129.4, 129.0, 128.4, 120.4, 113.1, 113.0, 75.0, 59.7, 55.0, 24.9. One C is not observed.

HRMS (ESI): m/z calculated for $[C_{32}H_{30}DGeNO_3 + Na]^+$ 575.1478; found 575.1489.

3-(2-(2-methoxyphenyl)-2-(triphenylgermyl)vinyl)oxazolidin-2-one

(141): Prepared according to **GP IX** from ynamide **116** (33 mg, 0.15 mmol, 1.0 equiv) with Ph₃GeH (60 mg, 0.20 mmol, 1.3 equiv) and a reaction time of 6 h. Purification of the crude product (E/Z = 60:40) by flash chromatography on silica gel (pentane/Et₂O = gradient from 70:30 to 60:40) afforded two fractions containing, respectively, analytically pure *E*-**141** (38 mg, 49%, E/Z > 98:2) and analytically pure *Z*-**141** (25 mg, 32%, Z/E > 98:2), as white solids.

E-**141**

mp 151-153 °C.

¹**H NMR** (400 MHz, CDCl₃): δ 7.37–7.26 (m, 15H, H-Ar [Ph₃Ge]), 7.10 (ddd, *J* = 8.2 Hz, *J* = 7.4 Hz, *J* = 1.8 Hz, 1H, H-9), 6.95 (dd, *J* = 7.4 Hz, *J* = 1.8 Hz, 1H, H-11), 6.89 (s, 1H, H-4), 6.77 (td, *J* = 7.4 Hz, *J* = 1.1 Hz, 1H, H-10), 6.51 (dd, *J* = 8.2 Hz, *J* = 1.1 Hz, 1H, H-8), 4.14 (t, *J* = 8.1 Hz, 2H, H-2), 3.33–3.22 (m, 2H, H-3), 3.20 (s, 3H, H-12).

¹³C{¹H} NMR (100 MHz, CDCl₃): δ 156.8 (C-1), 156.6 (C-7), 136.3 (C-13), 135.4 (C-Ar [Ph₃Ge]), 130.5 (C-11), 130.48 (C-4), 129.0 (C-Ar [Ph₃Ge]), 128.3 (C-5 or C-6), 128.1 (C-9), 128.0 (C-Ar [Ph₃Ge]), 119.9 (C-10), 116.1 (C-6 or C-5), 110.3 (C-8), 62.5 (C-2), 54.8 (C-12), 44.4 (C-3).

IR (neat): v (cm⁻¹) 3059, 1759, 1629, 1397, 1236, 1082, 740, 700.

HRMS (ESI): m/z calculated for $[C_{30}H_{27}GeNO_3 + Na]^+$ 546.1101; found 546.1122.

Z-141

mp 151–153 °C.



141

C₃₀H₂₇GeNO₃ M.W. = 522.18 g⋅mol⁻¹

¹**H NMR** (400 MHz, CDCl₃): δ 7.52–7.48 (m, 6H, H-Ar [Ph₃Ge]), 7.45 (s, 1H, H-4), 7.34–7.23 (m, 10H, H-11 + H-Ar [Ph₃Ge]), 7.00 (ddd, *J* = 8.1 Hz, *J* = 7.4 Hz, *J* = 1.7 Hz, 1H, H-9), 6.83 (td, *J* = 7.4 Hz, *J* = 1.1 Hz, 1H, H-10), 6.27 (dd, *J* = 8.1 Hz, *J* = 1.1 Hz, 1H, H-8), 3.79 (dd, *J* = 8.7 Hz, *J* = 7.0 Hz, 2H, H-2), 3.41 (dd, *J* = 8.7 Hz, *J* = 7.0 Hz, 2H, H-3), 3.20 (s, 3H, H-12).

¹³C{¹H} NMR (100 MHz, CDCl₃): δ 157.0 (C-1), 156.4 (C-7), 138.0 (C-13), 135.4 (C-4), 134.9 (C-Ar [Ph₃Ge]), 132.6 (C-5), 129.9 (C-11), 129.0 (C-Ar [Ph₃Ge]), 128.1 (C-Ar [Ph₃Ge]), 128.0 (C-9), 120.4 (C-10), 118.8 (C-6), 109.4 (C-8), 62.3 (C-2), 54.1 (C-12), 45.8 (C-3).

IR (neat): v (cm⁻¹) 3059, 1760, 1610, 1483, 1399, 911, 737, 698.

HRMS (ESI): m/z calculated for $[C_{30}H_{27}GeNO_3 + Na]^+$ 546.1101; found 546.1103.

[²**H]-141**: Prepared according to **GP X** from ynamide **116** (33 mg, 0.15 mmol, 1.0 equiv) with Ph₃GeH (60 mg, 0.20 mmol, 1.3 equiv) and a reaction time of 6 h. Purification of the crude product (E/Z = 52:48) by flash chromatography on silica gel (pentane/Et₂O = gradient from 70:30 to 60:40) afforded two fractions containing, respectively, analytically pure E-[²H]-**141** (33 mg, 42%, E/Z > 98:2) and analytically pure Z-[²H]-**141** (33 mg, 42%, Z/E > 98:2), as white solids.



[²H]-141

C₃₀H₂₆DGeNO₃ M.W. = 523.19 g⋅mol⁻¹

E-[²H]-**141**

¹**H NMR** (400 MHz, CDCl₃): δ 7.38–7.27 (m, 15H), 7.11 (ddd, *J* = 8.2 Hz, *J* = 7.4 Hz, *J* = 1.8 Hz, 1H), 6.96 (dd, *J* = 7.4 Hz, *J* = 1.8 Hz, 1H), 6.78 (td, *J* = 7.4 Hz, *J* = 1.1 Hz, 1H), 6.52 (dd, *J* = 8.2 Hz, *J* = 1.1 Hz, 1H), 4.14 (t, *J* = 8.1 Hz, 2H), 3.34–3.23 (m, 2H), 3.21 (s, 3H).

¹³C{¹H} NMR (100 MHz, CDCl₃): δ 156.8, 156.6, 136.2, 135.4, 130.5, 129.0, 128.3 128.1, 128.0, 119.9, 115.9, 110.3, 62.5, 54.8, 44.3. *One C is not observed.*HRMS (ESI): *m/z* calculated for [C₃₀H₂₆DGeNO₃ + Na]⁺ 547.1164; found 547.1144.

Z-[²H]-**141**

¹**H NMR** (400 MHz, CDCl₃): δ 7.51–7.47 (m, 6H), 7.32–7.22 (m, 10H), 6.99 (ddd, *J* = 8.2 Hz, *J* = 7.4 Hz, *J* = 1.8 Hz, 1H), 6.81 (td, *J* = 7.4 Hz, *J* = 1.1 Hz, 1H),

6.25 (dd, *J* = 8.2 Hz, *J* = 1.1 Hz, 1H), 3.77 (dd, *J* = 8.7 Hz, *J* = 7.0 Hz, 2H), 3.40 (dd, *J* = 8.7 Hz, *J* = 7.0 Hz, 2H), 3.18 (s, 3H).

¹³C{¹H} NMR (100 MHz, CDCl₃): δ 157.0, 156.4, 138.0, 134.9, 132.6, 129.9, 128.9, 128.1, 128.0, 120.4, 118.5, 109.4, 62.3, 54.1, 45.8. One C is not observed.
HRMS (ESI): m/z calculated for [C₃₀H₂₆DGeNO₃ + Na]⁺ 547.1164; found 547.1184.

(E)-3-(2-(2,6-dichlorophenyl)-2-(triphenylgermyl)vinyl)-4,4-

dimethyloxazolidin-2-one (142): Prepared according to **GP IX** from ynamide **117** (43 mg, 0.15 mmol, 1.0 equiv) with Ph₃GeH (60 mg, 0.20 mmol, 1.3 equiv) and a reaction time of 16 h. Purification of the crude product (E/Z > 98:2) by flash chromatography on silica gel (pentane/Et₂O = 60:40) afforded analytically pure **142** (61 mg, 69%, E/Z > 98:2) as a white solid; mp 159–160 °C.

¹**H NMR** (400 MHz, CDCl₃): δ 7.55–7.53 (m, 6H, H-Ar [Ph₃Ge]), 7.39–7.29 (m, 9H, H-Ar [Ph₃Ge]), 7.10–7.08 (m, 2H, H-9), 6.91 (dd, *J* = 8.5, 7.6 Hz, 1H, H-10), 6.17 (s, 1H, H-5), 3.95 (s, 2H, H-2), 1.31 (s, 6H, H-4,4').

¹³C{¹H} NMR (100 MHz, CDCl₃): δ 153.2 (C-1), 138.4 (C-7), 136.1 (C-11), 135.3 (C-Ar [Ph₃Ge]), 133.9 (C-8), 130.3 (C-5), 129.2 (C-Ar [Ph₃Ge]), 128.0 (C-Ar [Ph₃Ge]), 127.6 (C-9), 127.5 (C-10), 126.7 (C-6), 74.8 (C-2), 60.1 (C-3), 25.2 (C-4,4').

IR (neat): v (cm⁻¹) 3059, 1765, 1432, 1340, 1083, 912, 734, 697.

HRMS (ESI): m/z calculated for $[C_{31}H_{27}Cl_2GeNO_2 + Na]^+$ 612.0521; found 612.0546.



[²H]-**142**

C₃₁H₂₆DCl₂GeNO₂ M.W. = 590.10 g⋅mol⁻¹ **[²H]-142:** Prepared according to **GP X** from ynamide **117**(43 mg, 0.15 mmol, 1.0 equiv) with Ph₃GeH (60 mg, 0.20 mmol, 1.3 equiv) and a reaction time of 16 h. The reaction quench was modified by adding CuTC (48 mg, 0.25 mmol, 1.7 equiv) and stirring for 5 min before the addition of ND₄Cl/D₂O. Purification of the crude product (E/Z > 98:2) by flash chromatography on silica gel (pentane/Et₂O = 60:40) afforded analytically pure [²H]-**142** (64 mg, 72%, E/Z > 98:2) as a white solid.



142

C₃₁H₂₇Cl₂GeNO₂ M.W. = 589.10 g⋅mol⁻¹

¹**H NMR** (400 MHz, CDCl₃): δ 7.56–7.53 (m, 6H), 7.37–7.30 (m, 9H), 7.10–7.08 (m, 2H), 6.92 (dd, *J* = 8.5, 7.5 Hz, 1H), 3.95 (s, 2H), 1.31 (s, 6H).

¹³C{¹H} NMR (100 MHz, CDCl₃): δ 153.2, 138.4, 136.1, 135.3, 133.9, 129.1, 128.0, 127.6, 127.5, 126.3, 74.7, 60.0, 25.2. One C is not observed.

HRMS (ESI): m/z calculated for $[C_{31}H_{26}DCl_2GeNO_2 + Na]^+$ 613.0584; found 613.0604.

4,4-dimethyl-3-((1*E***,3***E***)-4-phenyl-2-(triphenylgermyl)buta-1,3-dien-1yl)oxazolidin-2-one (143): Prepared according to GP IX from ynamide 118 (36 mg, 0.15 mmol, 1.0 equiv) with Ph₃GeH (60 mg, 0.20 mmol, 1.3 equiv) and a reaction time of 16 h. Purification of the crude product (E/Z > 98:2) by flash chromatography on silica gel (pentane/Et₂O = 60:40) afforded analytically pure 143** (70 mg, 85%, E/Z > 98:2) as a yellow solid; mp 149–151 °C.

¹**H NMR** (400 MHz, CDCl₃): δ 7.70–7.65 (m, 6H, H-Ar [Ph₃Ge]), 7.45–7.38 (m, 9H, H-Ar [Ph₃Ge]), 7.33 (dd, *J*_{trans} = 16.2 Hz, *J* = 1.0 Hz, 1H, H-7), 7.24–7.14 (m, 5H, H-Ar [Ph]), 6.53 (d, *J*_{trans} = 16.2 Hz, 1H, H-8), 5.63 (t, *J* = 1.0 Hz, 1H, H-5), 4.10 (s, 2H, H-2), 1.22 (s, 6H, H-4,4').

¹³C{¹H} NMR (100 MHz, CDCl₃): δ 154.4 (C-1), 137.6 (C-9), 136.1 (C-13), 135.4 (C-Ar [Ph₃Ge]), 135.2 (C-7), 132.8 (C-6), 129.3 (C-Ar [Ph₃Ge]), 128.6 (C-5), 128.5 (C-Ar [Ph₃Ge]), 128.46 (C-Ar [Ph]), 127.7 (C-Ar [Ph]), 127.1 (C-8), 126.7 (C-Ar [Ph]), 74.9 (C-2), 59.7 (C-3), 24.9 (C-4,4').

IR (neat): v (cm⁻¹) 3071, 2970, 1752, 1338, 1074, 909, 734, 697.

HRMS (ESI): m/z calculated for $[C_{33}H_{31}GeNO_2 + Na]^+$ 570.1466; found 570.1470.

[²H]-143: Prepared according to **GP X** from ynamide **118** (36 mg, 0.15 mmol, 1.0 equiv) with Ph₃GeH (60 mg, 0.20 mmol, 1.3 equiv) and a reaction time of 16 h. Purification of the crude product (E/Z > 98:2) by flash chromatography on silica gel (pentane/Et₂O = 60:40) afforded analytically pure [²H]-**143** (66 mg, 80%, E/Z > 98:2) as a white solid.

¹**H NMR** (400 MHz, CDCl₃): δ 7.69–7.65 (m, 6H), 7.43–7.38 (m, 9H), 7.33 (d, J_{trans} = 16.2 Hz, 1H), 7.23–7.16 (m, 5H), 6.53 (d, J_{trans} = 16.2 Hz, 1H), 4.10 (s, 2H), 1.22 (s, 6H).





C₃₃H₃₁GeNO₂ M.W. = 546.24 g⋅mol⁻¹



[²H]-143

C₃₃H₃₀DGeNO₂ M.W. = 547.25 g⋅mol⁻¹ ¹³C{¹H} NMR (100 MHz, CDCl₃): δ 154.4, 137.6, 136.1, 135.4, 135.1, 132.5, 129.3, 128.5, 128.46, 127.7, 127.1, 126.7, 74.9, 59.7, 24.9. One C is not observed.

HRMS (ESI): m/z calculated for $[C_{33}H_{30}DGeNO_2 + Na]^+$ 571.1529; found 571.1545.





C₃₆H₄₅GeNO₂Si M.W. = 624.47 g⋅mol⁻¹

(*E*)-4,4-dimethyl-3-(4-(triisopropylsilyl)-2-(triphenylgermyl)but-1-en-3-yn-1-yl) oxazolidin-2-one (146): Prepared according to GP IX from ynamide 123 (48 mg, 0.15 mmol, 1.0 equiv) with Ph₃GeH (60 mg, 0.20 mmol, 1.3 equiv) and a reaction time of 16 h. Purification of the crude product (*E*/*Z* > 98:2) by flash chromatography on silica gel (pentane/EtOAc = 95:5) afforded analytically pure 146 (42 mg, 45%, *E*/*Z* > 98:2) as a white solid; mp 147–149 °C.

¹**H NMR** (400 MHz, CDCl₃): δ 7.68–7.63 (m, 6H, H-Ar), 7.42–7.39 (m, 9H, H-Ar), 6.24 (s, 1H, H-5), 3.84 (s, 2H, H-2), 1.11 (s, 6H, H-4,4'), 1.08 (s_{app}, 21H, H-9,10).

¹³C{¹H} NMR (100 MHz, CDCl₃): δ 154.9 (C-1), 147.5 (C-6), 135.52 (C-11), 135.47 (C-Ar), 129.5 (C-Ar), 128.9 (C-5), 128.6 (C-Ar), 102.1 (C-7 or C-8), 101.4 (C-8 or C-7), 76.1 (C-2), 61.5 (C-3), 26.2 (C-4,4'), 18.7 (C-10), 11.4 (C-9).

IR (neat): v (cm⁻¹) 2938, 2863, 1749, 1345, 1080, 738, 702, 669.

HRMS (ESI): m/z calculated for $[C_{36}H_{45}GeNO_2Si + Na]^+ 648.2331$; found 648.2357.



[²H]-146

C₃₆H₄₄DGeNO₂Si M.W. = 625.48 g·mol⁻¹ **[²H]-146:** Prepared according to **GP X** from ynamide **123** (48 mg, 0.15 mmol, 1.0 equiv) with Ph₃GeH (60 mg, 0.20 mmol, 1.3 equiv) and a reaction time of 16 h. Purification of the crude product (E/Z > 98:2) by flash chromatography on silica gel (pentane/EtOAc = 95:5) afforded analytically pure [²H]-**146** (42 mg, 45%, E/Z > 98:2) as a white solid.

¹**H NMR** (400 MHz, CDCl₃): δ 7.68–7.64 (m, 6H), 7.42–7.39 (m, 9H), 3.84 (s, 2H), 1.12 (s, 6H), 1.09 (s_{app}, 21H).

¹³C{¹H} NMR (100 MHz, CDCl₃): δ 154.9, 147.4, 135.53, 135.5, 129.5, 128.6, 102.1, 101.4, 76.1, 61.5, 26.2, 18.7, 11.4. *One C is not observed.*

HRMS (ESI): m/z calculated for $[C_{36}H_{44}DGeNO_2Si + Na]^+$ 649.2386; found 649.2385.

(E)-3-(3-((tert-butyldimethylsilyl)oxy)-2-(triphenylgermyl)prop-1-en-

1-yl)oxazolidin-2-one (147): Prepared according to **GP IX** from ynamide 3-((tert-butyldimethylsilyl)ethynyl)-4,4-dimethyloxazolidin-2-one (38 mg, 0.15 mmol, 1.0 equiv) with Ph₃GeH (60 mg, 0.20 mmol, 1.3 equiv) and a reaction time of 3 h. Purification of the crude product (E/Z > 98:2) by flash chromatography on silica gel (pentane/Et₂O = 70:30) afforded analytically pure **147** (44 mg, 52%, E/Z > 98:2) as colorless crystals; mp 116–119 °C.

¹**H NMR** (400 MHz, CDCl₃): δ 7.57–7.55 (m, 6H, H-Ar), 7.39–7.35 (m, 9H, H-Ar), 6.41 (t, *J* = 1.3 Hz, 1H, H-4), 4.45 (d, *J* = 1.3 Hz, 2H, H-6), 4.40–4.36 (m, 2H, H-2), 4.10–4.07 (m, 2H, H-3), 0.73 (s, 9H, H-9), –0.25 (s, 6H, H-7).

¹³C{¹H} NMR (100 MHz, CDCl₃): δ 156.5 (C-1), 136.4 (C-10), 135.5 (C-Ar), 132.3 (C-4), 129.1 (C-Ar), 128.3 (C-Ar), 121.4 (C-5), 62.3 (C-2), 60.4 (C-6), 45.6 (C-3), 25.9 (C-9), 18.3 (C-8), -5.7 (C-7).

IR (neat): v (cm⁻¹) 3058, 2926, 2854, 1761, 1622, 1092, 843, 736, 700.

HRMS (ESI): *m*/*z* calculated for [C₃₀H₃₇GeNO₃Si + Na]⁺ 584.1653; found 584.1664.

The E configuration was determined by X-ray crystallographic analysis.





C₃₀H₃₇GeNO₃Si M.W. = 560.35 g⋅mol⁻¹



[²H]-147

C₃₀H₃₆DGeNO₃Si M.W. = 561.35 g⋅mol⁻¹



148

C₃₁H₃₇GeNO₂ M.W. = 528.27 g·mol⁻¹



[²H]-**148**

C₃₁H₃₆DGeNO₂ M.W. = 529.28 g⋅mol⁻¹ chromatography on silica gel (pentane/ $Et_2O = 70:30$) afforded analytically pure [²H]-**147** (35 mg, 42%, *E*/*Z* > 98:2) as white crystals.

¹**H NMR** (400 MHz, CDCl₃): δ 7.57–7.55 (m, 6H), 7.39–7.35 (m, 9H), 4.45 (s, 2H), 4.40–4.36 (m, 2H), 4.11–4.07 (m, 2H), 0.73 (s, 9H), –0.26 (s, 6H).

¹³C{¹H} NMR (100 MHz, CDCl₃): δ 156.5, 136.4, 135.5, 129.1, 128.3, 120.9, 62.3, 60.3, 45.5, 25.9, 18.3, -5.8. One C is not observed.

HRMS (ESI): m/z calculated for $[C_{30}H_{36}DGeNO_3Si + Na]^+$ 585.1716; found 585.1732.

(*E*)-4,4-dimethyl-3-(2-(triphenylgermyl)oct-1-en-1-yl)oxazolidin-2-one (148): Prepared according to GP IX from ynamide 119 (34 mg, 0.15 mmol, 1.0 equiv) with Ph₃GeH (60 mg, 0.20 mmol, 1.3 equiv) and a reaction time of 16 h. Purification of the crude product (E/Z = 90:10) by flash chromatography on silica gel (toluene/Et₂O = 90:10) afforded analytically pure 148 (67 mg, 85%, E/Z = 90:10) as a colorless oil.

¹**H NMR** (400 MHz, CDCl₃): (*E* isomer) δ 7.59–7.53 (m, 6H, H-Ar), 7.43–7.36 (m, 9H, H-Ar), 5.71 (t, *J* = 1.1 Hz, 1H, H-5), 4.05 (s, 2H, H-2), 2.37–2.33 (m, 2H, H-7), 1.29–0.90 (m, 14H, H-4,4', H-8–H-11), 0.79–0.74 (m, 3H, H-12).

¹³C{¹H} NMR (100 MHz, CDCl₃): (*E* isomer) δ 154.6 (C-1), 141.6 (C-6), 136.0 (C-13), 135.4 (C-Ar), 129.3 (C-Ar), 128.4 (C-Ar), 126.5 (C-5), 75.0 (C-2), 59.2 (C-3), 31.37, 31.35, 29.7, 28.7, 24.9, 22.6, 14.1 (C-12).

IR (neat): v (cm⁻¹) 2964, 2923, 2857, 1755, 1613, 1335, 739, 701.

HRMS (ESI): m/z calculated for $[C_{31}H_{37}GeNO_2 + Na]^+$ 552.1935; found 552.1950.

[²**H]-148:** Prepared according to **GP X** from ynamide **119** (34 mg, 0.15 mmol, 1.0 equiv) with Ph₃GeH (60 mg, 0.20 mmol, 1.3 equiv) and a reaction time of 16 h. Purification of the crude product (E/Z = 92:8) by flash chromatography on silica gel (toluene/Et₂O = 90:10) afforded analytically pure [²H]-**148** (69 mg, 87%, E/Z = 92:8) as a colorless oil.

¹**H NMR** (400 MHz, CDCl₃): (*E* isomer) δ 7.59–7.53 (m, 6H), 7.43–7.36 (m, 9H), 4.05 (s, 2H), 2.37–2.33 (m, 2H), 1.28–0.90 (m, 14H), 0.79–0.74 (m, 3H).

¹³C{¹H} NMR (100 MHz, CDCl₃): (*E* isomer) δ 154.6, 141.3, 136.1, 135.4, 129.3, 128.4, 75.0, 59.2, 31.4, 31.3, 29.7, 28.7, 24.9, 22.6, 14.1. *One C is not observed.*

HRMS (ESI): m/z calculated for $[C_{31}H_{36}DGeNO_2 + Na]^+$ 553.1997; found 553.2019.

(Z)-3-(2-cyclohexyl-2-(triphenylgermyl)vinyl)-4,4-dimethyloxazolidin-

2-one (149): Prepared according to **GP IX** from ynamide **120** (33 mg, 0.15 mmol, 1.0 equiv) with Ph₃GeH (92 mg, 0.30 mmol, 2.0 equiv) and a reaction time of 16 h. Purification of the crude product (Z/E = 92:8) by flash chromatography on silica gel (toluene/Et₂O = 92:8) afforded analytically pure **149** (50 mg, 63%, Z/E = 92:8) as a white solid; mp 155–158 °C.

¹**H NMR** (400 MHz, CDCl₃): (*Z* isomer) δ 7.67–7.63 (m, 6H, H-Ar), 7.40–7.33 (m, 9H, H-Ar), 6.35 (d, *J* = 1.0 Hz, 1H, H-5), 3.13 (s, 2H, H-2), 2.16–2.09 (m, 1H, H-7), 1.82–1.78 (m, 2H, H-Cy), 1.65–1.53 (m, 3H, H-Cy), 1.28–1.18 (m, 2H, H-Cy), 1.15 (s, 6H, H-4,4'), 1.12–1.04 (m, 1H, H-Cy), 1.01–0.90 (m, 2H, H-Cy).

¹³C{¹H} NMR (100 MHz, CDCl₃): (*Z* isomer) δ 155.7 (C-1), 145.0 (C-6), 137.4 (C-11), 135.8 (C-Ar), 128.8 (C-Ar), 128.1 (C-5), 127.9 (C-Ar), 74.0 (C-2), 59.3 (C-3), 42.8 (C-7), 34.6 (C-8), 27.0 (C-9), 26.2 (C-10), 23.6 (C-4,4').

IR (neat): v (cm⁻¹) 2927, 2851, 1753, 1370, 1091, 911, 734, 698.

HRMS (ESI): m/z calculated for $[C_{31}H_{35}GeNO_2 + Na]^+$ 550.1778; found 550.1766.

The Z configuration was assigned by analogy with **150**.

[²**H]-149**: Prepared according to **GP X** from ynamide **120** (33 mg, 0.15 mmol, 1.0 equiv) with Ph₃GeH (92 mg, 0.30 mmol, 2.0 equiv) and a reaction time of 16 h. The reaction quench was modified by adding CuTC (48 mg, 0.25 mmol, 1.7 equiv) and stirring for 5 min before the addition of ND₄Cl/D₂O. Purification of the crude product (Z/E = 98:2) by flash chromatography on silica gel (toluene/Et₂O = 92:8) afforded analytically pure [²H]-**149** (50 mg, 63%, Z/E = 98:2) as a white solid.

149

 $C_{31}H_{35}GeNO_2$

M.W. = 526.26 g·mol⁻¹





C₃₁H₃₄DGeNO₂ M.W. = 527.26 g⋅mol⁻¹

¹**H NMR** (400 MHz, CDCl₃): δ 7.67–7.64 (m, 6H), 7.40–7.32 (m, 9H), 3.13 (s, 2H), 2.13 (tt, *J* = 11.7 Hz, *J* = 3.0 Hz, 1H), 1.83–1.78 (m, 2H), 1.65–1.54 (m, 3H), 1.29–1.16 (m, 2H), 1.16 (s, 6H), 1.14–1.05 (m, 1H), 1.02–0.90 (m, 2H).

¹³C{¹H} NMR (100 MHz, CDCl₃): δ 155.6, 144.7, 137.4, 135.8, 128.7, 127.9, 74.0, 59.2, 42.8, 34.6, 27.0, 26.2, 23.6. *One C is not observed.*

HRMS (ESI): m/z calculated for $[C_{31}H_{34}DGeNO_2 + Na]^+$ 551.1841; found 551.1834.



150

C₂₆H₂₄F₃GeNO₂ M.W. = 512.11 g⋅mol⁻¹ (Z)-4,4-dimethyl-3-(3,3,3-trifluoro-2-(triphenylgermyl)prop-1-en-1yl)oxazolidin-2-one (150): Prepared according to GP IX from ynamide 124 (31 mg, 0.15 mmol, 1.0 equiv) with Ph₃GeH (60 mg, 0.20 mmol, 1.3 equiv) and a reaction time of 16 h. Purification of the crude product (Z/E > 98:2) by flash chromatography on silica gel (pentane/Et₂O = 70:30) afforded analytically pure 150 (44 mg, 57%, Z/E > 98:2) as a white solid; mp 203–206 °C.

¹**H NMR** (400 MHz, CDCl₃): δ 7.64–7.62 (m, 6H, H-Ar), 7.40–7.33 (m, 9H, H-Ar), 7.07 (q, ⁴*J*_{H-F} = 1.7 Hz, 1H, H-5), 3.29 (s, 2H, H-2), 1.28 (s, 6H, H-4,4').

¹³C{¹H} NMR (100 MHz, CDCl₃): δ 153.8 (C-1), 137.0 (C-5, q, ³*J*_{C-F} = 1.7 Hz), 135.7 (C-8), 135.6 (C-Ar), 129.1 (C-Ar), 128.0 (C-Ar), 126.4 (C-7, q, ¹*J*_{C-F} = 273.7 Hz), 122.2 (C-6, q, ²*J*_{C-F} = 30.2 Hz), 74.3 (C-2), 59.6 (C-3), 24.0 (C-4,4').

¹⁹**F NMR** (376 MHz, CDCl₃): δ –53.8 (d, ⁴*J*_{F-H} = 1.7 Hz).

IR (neat): v (cm⁻¹) 2974, 1769, 1614, 1268, 1228, 1118, 739, 697.

HRMS (ESI): m/z calculated for $[C_{26}H_{24}F_{3}GeNO_{2} + Na]^{+}$ 536.0868; found 536.0869.

The Z configuration was determined by X-ray crystallographic analysis.



[²H]-150: Prepared according to **GP X** from ynamide **124** (31 mg, 0.15 mmol, 1.0 equiv) with Ph₃GeH (60 mg, 0.20 mmol, 1.3 equiv) and a reaction time of 16 h. Purification of the crude product (Z/E > 98:2) by flash chromatography on silica gel (pentane/Et₂O = 70:30) afforded analytically pure [²H]-**150** (42 mg, 55%, Z/E > 98:2) as a white solid.



[²H]-150

¹**H NMR** (400 MHz, CDCl₃): δ 7.66–7.63 (m, 6H), 7.41–7.34 (m, 9H), 3.29 (s, 2H), 1.28 (s, 6H).

¹³C{¹H} NMR (100 MHz, CDCl₃): δ 153.8, 135.7, 135.5, 129.1, 127.9, 126.5 (q, ¹J_{C-F} = 274.0 Hz), 121.8 (q, ²J_{C-F} = 30.2 Hz), 74.3, 59.6, 24.0. One C is not observed.

¹⁹**F NMR** (376 MHz, CDCl₃): δ –53.8 (s).

HRMS (ESI): m/z calculated for $[C_{26}H_{23}DF_{3}GeNO_{2} + Na]^{+}$ 537.0931; found 537.0950.

C₂₆H₂₃DF₃GeNO₂ M.W. = 513.12 g·mol⁻¹

III-5.5. DOMINO YNAMIDE GERMYLZINCATION / CU(I)-MEDIATED ELECTROPHILIC TRAPPING (GP XI AND GP XII)

Procedure for the preparation of CuCN·2LiCl (1.0 M solution in THF):

CuCN + 2 LiCI THF CuCN • 2LiCI

CuCN (896 mg, 10 mmol, 1.0 equiv) and LiCl (848 mg, 20 mmol, 2.0 equiv) were heated under vacuum with a heat gun for 1 h. After cooling to rt, previously degassed THF (10 mL) was added slowly and the mixture was stirred until complete solubility.

General Procedure for Domino Germylzincation/Cu(I)-Mediated Electrophilic Trapping of Terminal Ynamides (GP XI):



In a dry Schlenk tube under argon atmosphere, the appropriate ynamide (0.25 mmol, 1.0 equiv) was dissolved in dry THF (2 mL) and the solution was degassed by 3 freeze-pump-thaw cycles. At 0 °C, Et₂Zn (1.0 M in hexane, 0.75 mL, 0.75 mmol, 3.0 equiv) and Ph₃GeH (0.33 mmol, 1.3 equiv) were successively added. The reaction mixture was stirred at this temperature for 3 h and then cooled to -30 °C. The appropriate Cu(I)-salt (0.75 mmol, 3.0 equiv) followed by the appropriate electrophile (1.75 mmol, 7.0 equiv) were added at this temperature and the reaction mixture was allowed to warm slowly to rt overnight under stirring. Then, aq NH₄Cl/NH₃ (2:1) and CH₂Cl₂ were added and after 1 h stirring the layers were separated. The aqueous layer was extracted with CH₂Cl₂ (x3), and the combined organic layers were washed with brine (x2), dried over Na₂SO₄, filtered, and concentrated under reduce pressure to afford the crude product.

General Procedure for Domino Germylzincation/Cu(I)-Mediated Electrophilic Trapping of Internal Ynamides (GP XII):



In a dry Schlenk tube under argon atmosphere, the appropriate ynamide (0.15 mmol, 1.0 equiv) was suspended in dry *n*-hexane (1.2 mL). At 0 °C, Et₂Zn (1.0 M in hexane, 0.45 mL, 0.45 mmol, 3.0 equiv) and Ph₃GeH (0.20–0.30 mmol, 1.3–2.0 equiv) were successively added. The reaction mixture was then heated at 40 °C and the resulting solution stirred for the given reaction time. After cooling the reaction mixture to -30 °C, the appropriate Cu(I)-salt (0.45 mmol, 3.0 equiv), followed by the appropriate electrophile (1.05 mmol, 7.0 equiv) and THF (1 mL) were added and the reaction mixture was allowed to warm slowly to rt overnight under stirring. Then, aq NH₄Cl/NH₃ (2:1) and CH₂Cl₂ were added and after 1 h stirring the layers were separated. The aqueous layer was extracted with CH₂Cl₂ (x3), and the combined organic layers were washed with brine (x2), dried over Na₂SO₄, filtered, and concentrated under reduce pressure to afford the crude product.

(E)-4,4-dimethyl-3-(1-(triphenylgermyl)penta-1,4-dien-2-

yl)oxazolidin-2-one (153): Prepared according to **GP XI** from ynamide **54** (35 mg, 0.25 mmol, 1.0 equiv) using CuCN·2LiCl (1.0 M in THF, 0.75 mL, 0.75 mmol, 3.0 equiv) and allyl bromide (212 mg, 1.75 mmol, 7.0 equiv). Purification of the crude product by flash chromatography on silica gel (pentane/Et₂O = 70:30) afforded analytically pure **153** (111 mg, 92%, *E*/*Z* > 98:2) as a white solid; mp 131–133 °C.

¹**H NMR** (400 MHz, CDCl₃): δ 7.60–7.57 (m, 6H, H-Ar), 7.42–7.39 (m, 9H, H-Ar), 5.86 (s, 1H, H-6), 5.40–5.29 (m, 1H, H-12), 4.87 (ddt, J_{cis} = 10.1 Hz, J = 2.0 Hz, J = 1.1 Hz, 1H, H-13_{cis}), 4.76 (dq, J_{trans} = 17.0 Hz, J = 1.5 Hz, 1H, H-13_{trans}), 4.02 (s, 2H, H-2), 3.20 (dt, J = 7.0 Hz, J = 1.3 Hz, 2H, H-11), 1.47 (s, 6H, H-4,4').

¹³C{¹H} NMR (100 MHz, CDCl₃): δ 155.4 (C-1), 148.3 (C-5), 136.5 (C-7), 134.9 (C-Ar), 133.9 (C-12), 129.3 (C-Ar), 128.6 (C-Ar), 119.0 (C-6), 118.2 (C-13), 76.1 (C-2), 60.6 (C-3), 39.2 (C-11), 26.2 (C-4,4').

IR (neat): v (cm⁻¹) 3075, 2974, 1746, 1332, 1063, 733, 696.

HRMS (ESI): m/z calculated for $[C_{28}H_{29}GeNO_2 + Na]^+$ 508.1308; found 508.1320.

The E configuration was confirmed by NOESY enhancements.



153

C₂₈H₂₉GeNO₂ M.W. = 484.18 g⋅mol⁻¹





C₃₇H₃₅GeNO₂S M.W. = 630.38 g·mol⁻¹

(E)-N-benzyl-4-methyl-N-(1-(triphenylgermyl)penta-1,4-dien-2-

yl)benzenesulfonamide (154): Prepared according to GP XI from ynamide 58 (71 mg, 0.25 mmol, 1.0 equiv) using CuTC (143 mg, 0.75 mmol, 3.0 equiv) and allyl bromide (212 mg, 1.75 mmol, 7.0 equiv). The workup procedure was modified. The reaction mixture was filtered directly through a Celite[®] pad and the residue rinsed with THF. The filtrate was concentrated under reduced pressure to afford the crude product. Purification by flash chromatography on silica gel (pentane/Et₂O = 90:10 + 1% Et₃N) afforded analytically pure 154 (137 mg, 87%, E/Z > 98:2) as a white solid; mp 120–123 °C.

¹**H NMR** (400 MHz, C₆D₆): δ 7.84–7.80 (m, 2H, H-Ar [*p*-tolyl]), 7.46–7.43 (m, 6H, H-Ar [Ph₃Ge]), 7.22–7.19 (m, 2H, H-Ar [*p*-tolyl]), 7.16–7.11 (m, 9H, H-Ar [Ph₃Ge]), 7.07–7.05 (m, 3H, H-Ar [Bn]), 6.78–6.75 (m, 2H, H-Ar [Bn]), 5.81 (s, 1H, H-12), 5.24 (ddt, *J*_{trans} = 17.0 Hz, *J*_{cis} = 10.1 Hz, *J* = 7.0 Hz, 1H, H-18), 4.59 (ddd, *J*_{cis} = 10.1 Hz, *J* = 2.1 Hz, *J* = 1.1 Hz, 1H, H-19_{cis}), 4.52 (s, 2H, H-6), 4.52–4.47 (m, 1H, H-19_{trans}), 3.14 (dt, *J* = 7.0 Hz, *J* = 1.4 Hz, 2H, H-17), 1.91 (s, 3H, H-1).

¹³C{¹H} NMR (100 MHz, CDCl₃): δ 151.3, 143.7 (C-2), 136.2, 135.7, 135.2, 134.8, 134.5, 133.4, 129.9, 129.4, 129.2, 128.4, 128.1, 127.9, 123.7 (C-12), 117.3 (C-19), 53.5 (C-6), 41.8 (C-17), 21.7 (C-1).

IR (neat): v (cm⁻¹) 3072, 1427, 1158, 1090, 908, 728, 699, 650.

HRMS (ESI): m/z calculated for $[C_{37}H_{35}GeNO_2S + Na]^+$ 654.1499; found 654.1524.

The E configuration was assigned by analogy with **153**.

((E)-3-(1-(cyclohex-2-en-1-yl)-2-(triphenylgermyl)vinyl)-4,4-



155

C₃₁H₃₃GeNO₂ M.W. = 524.24 g·mol⁻¹ **dimethyloxazolidin-2-one (155):** Prepared according to **GP XI** from ynamide **54** (35 mg, 0.25 mmol, 1.0 equiv) using CuCN·2LiCl (1.0 M in THF, 0.75 mL, 0.75 mmol, 3.0 equiv) and 3-bromocyclohex-1-ene (282 mg, 1.75 mmol, 7.0 equiv). Purification of the crude product by flash chromatography on silica gel (pentane/Et₂O = 60:40) afforded analytically pure **155** (106 mg, 81%, E/Z > 98:2) as a white solid; mp 146–148 °C.

¹**H NMR** (400 MHz, CDCl₃): δ 7.64–7.60 (m, 6H, H-Ar), 7.41–7.38 (m, 9H, H-Ar), 6.10 (s, 1H, H-6), 5.52–5.49 (m, 1H, H-12 or H-13), 5.29–5.25 (m, 1H, H-

13 or H-12), 4.04 (s, 2H, H-2), 3.28–3.24 (m, 1H, H-11), 1.79–1.73 (m, 2H, H-14), 1.60–1.48 (m, 3H, H-alkyl), 1.38 (s, 3H, H-4 or H-4'), 1.377 (s, 3H, H-4' or H-4), 1.03–0.97 (m, 1H, H-alkyl).

¹³C{¹H} NMR (100 MHz, CDCl₃): δ 157.3 (C-1), 153.7 (C-5), 136.5 (C-7), 135.0 (C-Ar), 129.8 (C-6), 129.3 (C-Ar), 128.7 (C-12 or C-13), 128.6 (C-13 or C-12), 128.5 (C-Ar), 76.2 (C-2), 60.3 (C-3), 43.9 (C-11), 27.2 (C-15 or C-16), 27.0 (C-4 or C-4'), 26.3 (C-4' or C-4), 24.6 (C-14), 21.7 (C-16 or C-15).

IR (neat): v (cm⁻¹) 3073, 2933, 1742, 1596, 1331, 910, 732, 695.

HRMS (ESI): m/z calculated for $[C_{31}H_{33}GeNO_2 + Na]^+$ 548.1622; found 548.1612.

The E configuration was assigned by analogy with **153**.

(*E*)-4,4-dimethyl-3-(3-oxo-3-phenyl-1-(triphenylgermyl)prop-1-en-2yl)oxazolidin-2-one (156): Prepared according to GP XI from ynamide 54 (35 mg, 0.25 mmol, 1.0 equiv) using CuCN-2LiCl (1.0 M in THF, 0.75 mL, 0.75 mmol, 3.0 equiv) and benzoyl chloride (246 mg, 1.75 mmol, 7.0 equiv). Purification of the crude product by flash chromatography on silica gel (pentane/Et₂O = 60:40) afforded **156** (104 mg, 76%, *E/Z* > 98:2) contaminated with product **2** (23 mg, 17%, *E/Z* = 50:50); mp 142–144 °C.

¹**H NMR** (400 MHz, CDCl₃): δ 7.64–7.60 (m, 2H, H-Ar [Ph]), 7.53–7.47 (m, 6H, H-Ar [Ph₃Ge]), 7.42–7.35 (m, 3H, H-Ar [Ph]), 7.30–7.18 (m, 9H, H-Ar [Ph₃Ge]), 6.68 (s, 1H, H-6), 3.99 (s, 2H, H-2), 1.34 (s, 6H, H-4,4').

¹³C{¹H} NMR (100 MHz, CDCl₃): δ 193.3 (C-11), 155.5 (C-1), 145.4 (C-5), 135.9 (C-12), 135.4 (C-7), 135.1 (C-Ar [Ph₃Ge]), 133.1 (C-Ar [Ph]), 129.6 (C-Ar [Ph]), 129.2 (C-6), 129.1 (C-Ar [Ph₃Ge]), 128.2 (C-Ar [Ph]), 128.1 (C-Ar [Ph₃Ge]), 75.6 (C-2), 60.6 (C-3), 25.4 (C-4,4').

HRMS (ESI): m/z calculated for $[C_{32}H_{29}GeNO_3 + Na]^+$ 572.1258; found 572.1267.

The E configuration was confirmed by the following NOESY enhancements.





C₃₂H₂₉GeNO₃

M.W. = 548.22 g·mol⁻¹



157

C₃₃H₂₉GeNO₂ M.W. = 544.23 g⋅mol⁻¹

(E)-4,4-dimethyl-3-(4-phenyl-1-(triphenylgermyl)but-1-en-3-yn-2yl)oxazolidin-2-one (157): Prepared according to GP XI from ynamide 54 (35 mg, 0.25 mmol, 1.0 equiv) using CuCN·2LiCl (1.0 M in THF, 0.75 mL, 0.75 mmol, 3.0 equiv) and (bromoethynyl)benzene (317 mg, 1.75 mmol, 7.0 equiv). Purification of the crude product by flash chromatography on silica gel (pentane/Et₂O = 60:40) afforded analytically pure 157 (128 mg, 94%, *E/Z* > 98:2) as a yellow solid; mp 113–115 °C.

¹**H NMR** (400 MHz, CDCl₃): δ 7.62–7.58 (m, 6H, H-Ar [Ph₃Ge]), 7.36–7.31 (m, 9H, H-Ar [Ph₃Ge]), 7.24–7.19 (m, 1H, H-16]), 7.13–7.09 (m, 2H, H-15), 6.76 (s, 1H, H-6), 6.70–6.68 (m, 2H, H-14), 4.06 (s, 2H, H-2), 1.58 (s, 6H, H-4,4').

¹³C{¹H} NMR (100 MHz, CDCl₃): δ 155.5 (C-1), 136.1 (C-7), 135.1 (C-Ar [Ph₃Ge]), 132.9 (C-6), 131.4 (C-14), 129.2 (C-Ar [Ph₃Ge]), 128.9 (C-5 or C-16), 128.85 (C-16 or C-5), 128.4 (C-Ar [Ph₃Ge]), 128.1 (C-15), 121.7 (C-13), 92.7 (C-12), 87.6 (C-11), 75.6 (C-2), 60.4 (C-3), 26.0 (C-4,4').

IR (neat): v (cm⁻¹) 3058, 2971, 1750, 1351, 965, 911, 730, 694.

HRMS (ESI): m/z calculated for $[C_{33}H_{29}GeNO_2 + Na]^+$ 568.1309; found 568.1300.

The E configuration was assigned by analogy with 156.

(Z)-4,4-dimethyl-3-(1-(phenylthio)-2-

(triphenylgermyl)vinyl)oxazolidin-2-one (158): Prepared according to GP XI from ynamide 54 (35 mg, 0.25 mmol, 1.0 equiv) using CuCN·2LiCl (1.0 M in THF, 0.75 mL, 0.75 mmol, 3.0 equiv) and S-phenyl benzenethiosulfonate (438 mg, 1.75 mmol, 7.0 equiv). Purification of the crude product by flash chromatography on silica gel (pentane/Et₂O = 60:40) afforded analytically pure **158** (104 mg, 75%, *Z/E* > 98:2) as colorless crystals; mp 184–187 °C.

¹**H NMR** (400 MHz, CDCl₃): δ 7.69–7.65 (m, 6H, H-Ar [Ph₃Ge]), 7.40–7.36 (m, 9H, H-Ar [Ph₃Ge]), 7.20–7.10 (m, 5H, H-Ar [Ph]), 6.57 (s, 1H, H-6), 3.82 (s, 2H, H-2), 1.32 (s, 6H, H-4,4').

¹³C{¹H} NMR (100 MHz, CDCl₃): δ 156.4 (C-1), 142.2 (C-5), 136.5 (C-7), 135.1 (C-Ar [Ph₃Ge]), 134.8 (C-6), 133.0 (C-11), 130.5 (C-Ar [Ph]), 129.1 (C-Ar [Ph₃Ge]), 128.8 (C-Ar [Ph]), 128.3 (C-Ar [Ph₃Ge]), 127.2 (C-Ar [Ph]), 75.5 (C-2), 60.3 (C-3), 25.6 (C-4,4').



158

C₃₁H₂₉GeNO₂S M.W. = 552.27 g⋅mol⁻¹

IR (neat): v (cm⁻¹) 3058, 1749, 1558, 1322, 1078, 913, 734, 695.

HRMS (ESI): m/z calculated for $[C_{31}H_{29}GeNO_2S + Na]^+$ 576.1028; found 576.1032.

The E configuration was assigned by analogy with **156**.

(E)-4,4-dimethyl-3-(1-phenyl-1-(triphenylgermyl)penta-1,4-dien-2-

yl)oxazolidin-2-one (159): Prepared according to **GP XII** from ynamide **92** (32 mg, 0.15 mmol, 1.0 equiv) with Ph₃GeH (60 mg, 0.20 mmol, 1.3 equiv), a reaction time of 3 h, and using CuCN·2LiCl (1.0 M in THF, 0.45 mL, 0.45 mmol, 3.0 equiv) and allyl bromide (127 mg, 1.05 mmol, 7.0 equiv). Purification of the crude product by flash chromatography on silica gel (pentane/Et₂O = 70:30) afforded analytically pure **159** (80 mg, 95%, *E/Z* > 98:2) as a white solid; mp 138–139 °C.

¹**H NMR** (400 MHz, CDCl₃): δ 7.50–7.47 (m, 6H, H-Ar [Ph₃Ge]), 7.36–7.28 (m, 9H, H-Ar [Ph₃Ge]), 7.25–6.45 (m, 5H, H-Ar [Ph]), 5.65 (dddd, *J*_{trans} = 17.0 Hz, *J*_{cis} = 10.1 Hz, *J* = 8.0 Hz, *J* = 5.5 Hz, 1H, H-12), 4.89 (dq, *J*_{cis} = 10.1 Hz, *J* = 1.5 Hz, 1H, H-13_{cis}), 4.72 (dq, *J*_{trans} = 17.0 Hz, *J* = 1.6 Hz, 1H, H-13_{trans}), 3.83 (d, *J* = 7.8 Hz, 1H, H-2), 3.48 (d, *J* = 7.8 Hz, 1H, H-2'), 3.38 (ddt, *J* = 16.0 Hz, *J* = 5.5 Hz, *J* = 1.8 Hz, 1H, H-11), 2.81 (ddt, *J* = 16.0 Hz, *J* = 8.0 Hz, *J* = 1.2 Hz, 1H, H-11'), 1.34 (s, 3H, H-4 or H-4'), 0.90 (s, 3H, H-4' or H-4).

¹³C{¹H} NMR (100 MHz, CDCl₃): δ 157.1 (C-1), 143.7, 140.5, 140.0, 136.2 (C-7), 135.2, 134.0 (C-12), 129.1, 128.7 (br), 128.4, 126.0, 118.1 (C-13), 76.4 (C-2), 60.4 (C-3), 42.7 (C-11), 26.9 (C-4 or C-4'), 25.1 (C-4' or C-4). *One CH(Ar) signal is not observed.*

IR (neat): v (cm⁻¹) 3058, 2980, 2898, 1739, 1338, 912, 731, 695.

HRMS (ESI): m/z calculated for $[C_{34}H_{33}GeNO_2 + Na]^+$ 584.1623; found 584.1642.

(*E*)-3-(1-(4-methoxyphenyl)-1-(triphenylgermyl)penta-1,4-dien-2-yl)-4,4-dimethyloxazolidin-2-one (160): Prepared according to GP XII from ynamide 112 (245 mg, 1.0 mmol, 1.0 equiv), Et₂Zn (1.0 M in hexane, 3.0 mL, 3.0 mmol, 3.0 equiv), and Ph₃GeH (396 mg, 1.3 mmol, 1.3 equiv), with a reaction time of 6 h, followed by addition of CuCN·2LiCl (1.0 M in THF, 3.0 mL,



C₃₄H₃₃GeNO₂ M.W. = 560.27 g⋅mol⁻¹





C₃₅H₃₅GeNO₃ M.W. = 590.30 g·mol⁻¹

3.0 mmol, 3.0 equiv) and allyl bromide (847 mg, 7.0 mmol, 7.0 equiv). Purification of the crude product by flash chromatography on silica gel (pentane/Et₂0 = 60:40) afforded analytically pure **160** (503 mg, 85%, E/Z >98:2) as a white solid; mp 196–199 °C.

¹H NMR (400 MHz, CDCl₃): δ 7.50–7.47 (m, 6H, H-Ar [Ph₃Ge]), 7.36–7.29 (m, 9H, H-Ar [Ph₃Ge]), 7.25–6.10 (br m, 4H, H-Ar [Ph]), 5.65 (dddd, J_{trans} = 17.1 Hz, *J*_{cis} = 10.1 Hz, *J* = 8.0 Hz, *J* = 5.5 Hz, 1H, H-12), 4.89 (dd, *J*_{cis} = 10.1 Hz, *J* = 1.3 Hz, 1H, H-13_{*cis*}), 4.72 (dd, J_{trans} = 17.1Hz, J = 1.5 Hz, 1H, H-13_{*trans*}), 3.84 (d, J = 7.8 Hz, 1H, H-2), 3.67 (s, 3H, H-18), 3.53 (d, *J* = 7.8 Hz, 1H, H-2'), 3.37 (ddt, *J* = 16.0 Hz, *J* = 5.5 Hz, *J* = 1.8 Hz, 1H, H-11), 2.79 (ddt, *J* = 16.0 Hz, *J* = 8.0 Hz, *J* = 1.1 Hz, 1H, H-11'), 1.34 (s, 3H, H-4 or H-4'), 0.91 (s, 3H, H-4' or H-4).

¹³C{¹H} NMR (100 MHz, CDCl₃): δ 157.9 (C-17), 157.2 (C-1), 143.3, 140.1, 136.3 (C-7), 135.2, 134.1 (C-12), 132.9, 129.9 (br), 129.1, 128.3, 118.0 (C-13), 113.0, 76.4 (C-2), 60.4 (C-3), 55.3 (C-18), 42.8 (C-11), 26.9 (C-4 or C-4'), 25.3 (C-4' or C-4).

IR (neat): v (cm⁻¹) 3062, 1743, 1510, 1340, 1248, 1035, 735, 699.

HRMS (ESI): m/z calculated for $[C_{35}H_{35}GeNO_3 + Na]^+$ 614.1729; found 614.1719.

(E)-3-(1-(2,6-dichlorophenyl)-1-(triphenylgermyl)penta-1,4-dien-2vl)-4,4-dimethyloxazolidin-2-one (161): Prepared according to GP XII from ynamide 117 (43 mg, 0.15 mmol, 1.0 equiv) with Ph_3GeH (60 mg, 0.20 mmol, 1.3 equiv), a reaction time of 16 h, and using CuCN·2LiCl (1.0 M in THF, 0.45 mL, 0.45 mmol, 3.0 equiv) and allyl bromide (127 mg, 1.05 mmol, 7.0

equiv). Purification of the crude product by flash chromatography on silica gel (pentane/Et₂0 = 70:30) afforded analytically pure **161** (74 mg, 79%, E/Z >98:2) as a white solid; mp 221–224 °C.

¹H NMR (400 MHz, CDCl₃): δ 8.50–6.50 (br m, 15H, H-Ar [Ph₃Ge]), 7.20 (dd, *J* = 7.8 Hz, / = 1.5 Hz, 1H, H-Ar [Ph]), 6.86 (t, / = 7.8 Hz, 1H, H-Ar [Ph]), 6.82 (dd, *J* = 7.8 Hz, *J* = 1.5 Hz, 1H, H-Ar [Ph]), 5.51 (dddd, *J*_{trans} = 16.8 Hz, *J*_{cis} = 10.1 Hz, *J* = 8.4 Hz, J = 6.0 Hz, 1H, H-12), 5.01–4.93 (m, 2H, H-13), 3.90–3.83 (m, 2H, H-2), 3.78 (dd, / = 15.4 Hz, / = 8.4 Hz, 1H, H-11), 3.23 (dd, / = 15.4 Hz, / = 6.0 Hz, 1H, H-11'), 1.39 (s, 3H, H-4 or H-4'), 0.63 (s, 3H, H-4' or H-4).





C₃₄H₃₁Cl₂GeNO₂ M.W. = $629.16 \text{ g} \cdot \text{mol}^{-1}$

¹³C{¹H} NMR (100 MHz, CDCl₃): δ 156.0 (C-1), 145.1, 138.9, 136.3 (br), 135.4 (br), 135.2, 135.0, 134.5, 134.4 (C-12), 129.0 (br), 128.7, 128.4, 128.0 (br), 127.4, 119.3 (C-13), 77.7 (C-2), 61.7 (C-3), 40.7 (C-11), 26.1 (C-4 or C-4'), 23.6 (C-4' or C-4).

IR (neat): v (cm⁻¹) 3059, 1743, 1605, 1428, 1319, 910, 731, 695.

HRMS (ESI): m/z calculated for $[C_{34}H_{31}Cl_2GeNO_2 + Na]^+$ 652.0835; found 652.0840.

(E)-N-benzyl-4-methyl-N-(1-phenyl-1-(triphenylgermyl)penta-1,4-

dien-2-yl) benzenesulfonamide (162): Prepared according to **GP XII** from ynamide **110** (54 mg, 0.15 mmol, 1.0 equiv) with Ph₃GeH (92 mg, 0.30 mmol, 2.0 equiv), a reaction time of 24 h at rt, and using CuTC (86 mg, 0.45 mmol, 3.0 equiv) and allyl bromide (127 mg, 1.05 mmol, 7.0 equiv). The workup procedure was modified. The reaction mixture was filtered directly through a Celite[®] pad and the residue rinsed with CH₂Cl₂. The filtrate was concentrated under reduced pressure to afford the crude product. Purification by flash chromatography on silica gel (pentane/Et₂O = 90:10 + 1% Et₃N) afforded analytically pure **162** (93 mg, 88%, *E/Z* > 98:2) as a white solid; mp 167–169 °C.

¹**H NMR** (400 MHz, C₆D₆): δ 7.59–7.56 (m, 6H, H-Ar), 7.44–7.42 (m, 2H, H-Ar), 7.16–7.11 (m, 11H, H-Ar), 7.04–6.87 (m, 8H, H-Ar), 6.68–6.66 (m, 2H, H-Ar), 5.36 (ddt, *J*_{trans} = 17.2 Hz, *J*_{cis} = 10.3 Hz, *J* = 7.0 Hz, 1H, H-18), 4.60 (dq, *J*_{cis} = 10.3 Hz, *J* = 1.5 Hz, 1H, H-19_{cis}), 4.37–4.31 (m, 2H, H-19_{trans} + H-6), 4.14 (d, *J* = 14.3 Hz, 1H, H-6'), 3.68–3.61 (m, 1H, H-17), 3.40–3.35 (m, 1H, H-17'), 1.84 (s, 3H, H-1).

¹³C{¹H} NMR (100 MHz, C₆D₆): δ 143.4, 142.8, 141.9, 140.8, 139.1, 136.9, 136.3, 135.7, 134.0, 130.8, 129.7 (br), 129.3, 129.2, 128.6, 128.56, 128.2, 128.1, 127.9, 125.9, 117.6, 52.5 (C-6), 42.2 (C-17), 21.1 (C-1).

IR (neat): v (cm⁻¹) 3072, 1430, 1333, 1155, 1088, 912, 731, 699.

HRMS (ESI): m/z calculated for $[C_{43}H_{39}GeNO_2S + Na]^+$ 730.1814; found 730.1839.



C₄₃H₃₉GeNO₂S M.W. = 706.48 g⋅mol⁻¹



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C₄₂H₃₇GeNO₂S M.W. = 692.45 g·mol⁻¹

(E)-4-methyl-N-phenyl-N-(1-phenyl-1-(triphenylgermyl)penta-1,4-

dien-2-yl) benzenesulfonamide (163): Prepared according to **GP XII** from ynamide **111** (52 mg, 0.15 mmol, 1.0 equiv) with Ph₃GeH (92 mg, 0.30 mmol, 2.0 equiv), a reaction time of 24 h at rt, and using CuTC (86 mg, 0.45 mmol, 3.0 equiv) and allyl bromide (127 mg, 1.05 mmol, 7.0 equiv). The workup procedure was modified. The reaction mixture was filtered directly through a Celite[®] pad and the residue rinsed with CH₂Cl₂. The filtrate was concentrated under reduced pressure to afford the crude product. Purification by flash chromatography on silica gel (benzene) afforded **163** (80 mg, 77%, *E/Z* = 92:8) as a white solid; mp 181–183 °C.

¹**H NMR** (400 MHz, C₆D₆) (*E* isomer): δ 7.63–7.61 (m, 6H, H-Ar), 7.49–7.47 (m, 2H, H-Ar), 7.34–7.31 (m, 2H, H-Ar), 7.17–7.09 (m, 13H, H-Ar), 6.93–6.89 (m, 2H, H-Ar), 6.84–6.82 (m, 2H, H-Ar), 6.53–6.51 (m, 2H, H-Ar), 5.43 (ddt, *J*_{trans} = 17.2 Hz, *J*_{cis} = 10.1 Hz, *J* = 7.0 Hz, 1H, H-17), 4.64 (dd, *J*_{cis} = 10.1 Hz, *J* = 1.7 Hz, 1H, H-18_{cis}), 4.10 (dd, *J*_{trans} = 17.2 Hz, *J* = 1.7 Hz, 1H, H-18_{trans}), 4.25–3.80 (br s, 1H, H-16), 3.80–3.50 (br s, 1H, H-16'), 1.72 (s, 3H, H-1).

¹³C{¹H} NMR (100 MHz, C₆D₆) (*E* isomer): δ 147.6, 142.9, 142.1, 141.8, 140.7, 139.2, 136.8, 136.0, 135.7, 134.5, 129.4, 129.334, 129.328, 128.63, 128.6, 127.6, 127.5, 125.9, 125.8, 117.9, 41.9 (C-16), 21.0 (C-1).

IR (neat): v (cm⁻¹) 3061, 1348, 1159, 1088, 907, 733, 696, 605.

HRMS (ESI): *m*/*z* calculated for [C₄₂H₃₇GeNO₂S + Na]⁺ 716.1657; found 716.1666.

(E)-4,4-dimethyl-3-(1-phenyl-1-(triphenylgermyl)prop-1-en-2-

yl)oxazolidin-2-one (164): Prepared according to GP XII from ynamide 92 (32 mg, 0.15 mmol, 1.0 equiv) with Ph₃GeH (60 mg, 0.20 mmol, 1.3 equiv), a reaction time of 3 h, and using CuCN·2LiCl (1.0 M in THF, 0.45 mL, 0.45 mmol, 3.0 equiv) and methyl iodide (149 mg, 1.05 mmol, 7.0 equiv). Purification of the crude product by flash chromatography on silica gel (pentane/Et₂O = 70:30) afforded analytically pure **164** (36 mg, 45%, E/Z > 98:2) as a white solid; mp 207–210 °C.

¹**H NMR** (400 MHz, CDCl₃): δ 7.49–7.47 (m, 6H, H-Ar [Ph₃Ge]), 7.34–7.29 (m, 9H, H-Ar [Ph₃Ge]), 7.22–6.65 (br m, 5H, H-Ar [Ph]), 3.88 (d, *J* = 8.0 Hz, 1H, H-



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C₃₂H₃₁GeNO₂ M.W. = 534.23 g·mol⁻¹ 2), 3.56 (d, *J* = 8.0 Hz, 1H, H-2'), 1.90 (s, 3H, H-11), 1.32 (s, 3H, H-4 or H-4'), 0.81 (s, 3H, H-4' or H-4).

JMod (100 MHz, CDCl₃): δ 156.7 (C-1), 142.9 (quaternary C), 140.6 (quaternary C), 138.2 (quaternary C), 136.2 (C-7), 135.1 (C-Ar [Ph₃Ge]), 129.1 (C-Ar [Ph₃Ge]), 128.4 (C-Ar [Ph₃Ge]), 127.4 (br), 126.0 (C-Ar [Ph]), 76.1 (C-2), 60.8 (C-3), 27.1 (C-4 or C-4'), 25.5 (C-4' or C-4), 25.0 (C-11). *One CH(Ar) signal is not observed.*

IR (neat): v (cm⁻¹) 2974, 1742, 1394, 1339, 1085, 1036, 736, 699.

HRMS (ESI): m/z calculated for $[C_{32}H_{31}GeNO_2 + Na]^+$ 558.1466; found 558.1472.

(E)-3-(1,4-diphenyl-1-(triphenylgermyl)but-1-en-3-yn-2-yl)-4,4-

dimethyloxazolidin-2-one (165): Prepared according to **GP XII** from ynamide **92** (32 mg, 0.15 mmol, 1.0 equiv) with Ph₃GeH (60 mg, 0.20 mmol, 1.3 equiv), a reaction time of 3 h, and using CuCN·2LiCl (1.0 M in THF, 0.45 mL, 0.45 mmol, 3.0 equiv) and (bromoethynyl)benzene (190 mg, 1.05 mmol, 7.0 equiv). Purification of the crude product by flash chromatography on silica gel (pentane/Et₂O = 70:30) afforded analytically pure **165** (88 mg, 95%, *E/Z* > 98:2) as a pale yellow solid; mp 209–211 °C.

¹**H NMR** (400 MHz, CDCl₃): δ 7.55–7.52 (m, 6H, H-Ar [Ph₃Ge]), 7.32–7.24 (m, 9H, H-Ar [Ph₃Ge]), 7.17–7.13 (m, 1H, H-Ar), 7.06–6.98 (m, 7H, H-Ar), 6.60–6.58 (m, 2H, H-Ar), 3.92 (br s, 1H, H-2), 3.63 (br s, 1H, H-2'), 1.52 (br s, 3H, H-4 or H-4'), 1.01 (br s, 3H, H-4' or H-4).

¹³C{¹H} NMR (100 MHz, CDCl₃): δ 156.3 (C-1), 154.3, 139.2, 135.7, 135.3, 131.3, 128.9, 128.6, 128.18, 128.16, 127.8, 127.5, 126.6, 123.2, 122.0, 94.3 (C-12), 89.6 (C-11), 76.0 (C-2), 61.1 (C-3), 25.7 (C-4 or C-4', br), 25.1 (C-4' or C-4, br).

IR (neat): v (cm⁻¹) 3058, 2972, 1746, 1340, 1080, 911, 730, 693.

HRMS (ESI): m/z calculated for $[C_{39}H_{33}GeNO_2 + Na]^+$ 644.1624; found 644.1618.

The E configuration was determined by X-ray crystallographic analysis.



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C₃₉H₃₃GeNO₂ M.W. = 620.32 g⋅mol⁻¹



(*E*)-3-(1-(4-methoxyphenyl)-4-phenyl-1-(triphenylgermyl)but-1-en-3yn-2-yl)-4,4-dimethyloxazolidin-2-one (166): Prepared according to GP XII from ynamide 112 (245 mg, 1.0 mmol, 1.0 equiv), Et₂Zn (1.0 M in hexane, 3.0 mL, 3.0 mmol, 3.0 equiv), and Ph₃GeH (396 mg, 1.30 mmol, 1.3 equiv) with a reaction time of 6 h, followed by addition of CuTC (572 mg, 3.0 mmol, 3.0 equiv), dry THF (4 mL) and (bromoethynyl)benzene (1.27 g, 7.0 mmol, 7.0 equiv). Purification of the crude product by flash chromatography on silica gel (pentane/Et₂O = 60:40) afforded analytically pure 166 (350 mg, 54%, *E/Z* > 98:2) as a pale orange solid; mp 240–241 °C.

¹**H NMR** (400 MHz, CDCl₃): δ 7.45–7.43 (m, 6H, H-Ar [Ph₃Ge]), 7.22–7.15 (m, 9H, H-Ar [Ph₃Ge]), 7.07–7.03 (m, 1H, H-Ar), 6.97–6.92 (m, 2H, H-Ar), 6.83–6.81 (m, 2H, H-Ar), 6.51–6.48 (m, 4H, H-Ar), 3.84 (br s, 1H, H-2), 3.59 (s, 3H, H-21), 3.58 (br s, 1H, H-2'), 1.41 (br s, 3H, H-4 or H-4'), 0.89 (br s, 3H, H-4' or H-4).

¹³C{¹H} NMR (100 MHz, CDCl₃): δ 158.4 (C-20), 156.4 (C-1), 153.9 (quaternary C), 135.9 (C-7), 135.3 (C-Ar [Ph₃Ge]), 131.5 (quaternary C), 131.2 (C-Ar), 129.6 (C-Ar), 128.9 (C-Ar [Ph₃Ge]), 128.5 (C-Ar), 128.1 (C-Ar [Ph₃Ge]), 127.8 (C-Ar), 123.1 (quaternary C), 122.1 (quaternary C), 112.9 (C-Ar), 94.2 (C-12), 89.7 (C-11), 75.9 (C-2), 61.1 (C-3), 55.2 (C-21), 25.8 (C-4 or C-4', br), 25.1 (C-4' or C-4, br).

IR (neat): v (cm⁻¹) 3059, 1746, 1499, 1247, 1031, 911, 732, 695.

HRMS (ESI): m/z calculated for $[C_{40}H_{35}GeNO_3 + Na]^+$ 674.1730; found 674.1755.

The E configuration was assigned by analogy with 165.





C₄₀H₃₅GeNO₃ M.W. = 650.35 g⋅mol⁻¹

(E)-4,4-dimethyl-3-(1-phenyl-6-(triisopropylsilyl)-4-

(triphenylgermyl)hexa-3-en-1,5-diyn-3-yl)oxazolidin-2-one

Prepared according to **GP XII** from ynamide **123** (48 mg, 0.15 mmol, 1.0 equiv) with Ph₃GeH (60 mg, 0.20 mmol, 1.3 equiv), a reaction time of 16 h, and using CuCN·2LiCl (1.0 M in THF, 0.45 mL, 0.45 mmol, 3.0 equiv) and (bromoethynyl)benzene (190 mg, 1.05 mmol, 7.0 equiv). Purification of the crude product by flash chromatography on silica gel (pentane/Et₂O = 80:20) afforded analytically pure **167** (22 mg, 20%, E/Z > 98:2) as a yellow gum.

¹**H NMR** (400 MHz, CDCl₃): δ 7.78–7.73 (m, 6H, H-Ar [Ph₃Ge]), 7.35–7.33 (m, 9H, H-Ar [Ph₃Ge]), 7.18–7.14 (m, 1H, H-Ar [Ph]), 7.07–7.03 (m, 2H, H-Ar [Ph]), 6.57–6.55 (m, 2H, H-Ar [Ph]), 3.97 (d, *J* = 8.0 Hz, 1H, H-2), 3.60 (d, *J* = 8.0 Hz, 1H, H-2'), 1.56 (s, 3H, H-4 or H-4'), 1.54 (s, 3H, H-4' or H-4), 1.13–1.12 (m, 21H, H-19,20).

¹³C{¹H} NMR (100 MHz, CDCl₃): δ 154.8 (C-1), 151.0, 135.7 (C-7), 135.5, 131.4, 129.2, 128.8, 128.4, 127.9, 126.5, 122.0, 102.6 (C=), 99.1 (C=), 97.6 (C=), 87.4 (C=), 76.2 (C-2), 62.6 (C-3), 26.9 (C-4 or C-4'), 26.1 (C-4' or C-4), 18.8 (C-20), 11.5 (C-19).

IR (neat): v (cm⁻¹) 2935, 2862, 1743, 1433, 914, 732, 692, 663.

HRMS (ESI): *m*/*z* calculated for [C₄₄H₄₉GeNO₂Si + Na]⁺ 748.2647; found 748.2634.

(E)-4,4-dimethyl-3-(1-(3-oxocyclohexyl)-2-

(triphenylgermyl)vinyl)oxazolidin-2-one (168): In a dry Schlenk tube under argon atmosphere, ynamide 54 (35 mg, 0.25 mmol, 1.0 equiv) was dissolved in dry THF (2 mL) and the solution was degassed by 3 freeze-pumpthaw cycles. At 0 °C, Et₂Zn (1.0 M in hexane, 0.75 mL, 0.75 mmol, 3.0 equiv) and Ph₃GeH (99 mg, 0.33 mmol, 1.3 equiv) were successively added. The reaction mixture was stirred at this temperature for 3 h and then cooled to – 30 °C. CuCN·2LiCl (1.0 M in THF, 0.75 mL, 0.75 mmol, 3.0 equiv) was added and the reaction was further cooled to –78 °C. Chlorotrimethylsilane (380 mg, 3.50 mmol, 14.0 equiv) and cyclohex-2-enone (168 mg, 1.75 mmol, 7.0 equiv) were added at this temperature and the reaction mixture was allowed to warm slowly to rt overnight under stirring. Then, aq NH₄Cl/NH₃ (2:1) and CH₂Cl₂ were added and after 1 h stirring the layers were separated. The



(167):

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C₄₄H₄₉GeNO₂Si M.W. = 724.59 g⋅mol⁻¹





C₃₁H₃₃GeNO₃ M.W. = 540.24 g⋅mol⁻¹

aqueous layer was extracted with CH_2Cl_2 (x3), and the combined organic layers were washed with brine (x2), dried over Na_2SO_4 , filtered, and concentrated under reduce pressure to afford the crude product. Purification by flash chromatography on silica gel (pentane/Et₂O = 75:25) afforded analytically pure **168** (90 mg, 67%, E/Z > 98:2) as a white solid; mp 165–168 °C.

¹**H NMR** (400 MHz, CDCl₃): δ 7.58–7.53 (m, 6H, H-Ar), 7.43–7.37 (m, 9H, H-Ar), 6.11 (s, 1H, H-6), 4.11–4.06 (m, 2H, H-2), 2.75–2.69 (m, 1H, H-11), 2.42–2.35 (m, 1H), 2.26–2.21 (m, 1H), 2.08–2.04 (m, 1H), 2.00–1.95 (m, 1H), 1.69–1.60 (m, 3H), 1.46 (s, 3H, H-4 or H-4'), 1.41 (s, 3H, H-4' or H-4), 0.77–0.65 (m, 1H).

¹³C{¹H} NMR (100 MHz, CDCl₃): δ 209.9 (C-13), 157.0 (C-1), 151.8 (C-5), 136.0 (C-7), 134.8 (C-Ar), 129.6 (C-Ar), 128.7 (C-Ar), 127.4 (C-6), 76.1 (C-2), 61.5 (C-3), 46.1 (C-12), 45.9 (C-11), 40.7 (C-14), 30.8 (C-15 or C-16), 27.0 (C-4 or C-4'), 26.4 (C-4' or C-4), 24.6 (C-16 or C-15).

IR (neat): v (cm⁻¹) 2969, 2936, 1748, 1707, 1597, 1328, 734, 697.

HRMS (ESI): m/z calculated for $[C_{31}H_{33}GeNO_3 + Na]^+$ 564.1571; found 564.1591.

The E configuration was assigned by analogy with **153**.

III-5.6. DOMINO YNAMIDE GERMYLZINCATION / CU(I)-MEDIATED ELECTROPHILIC TRAPPING *VIA* DIVINYLZINC INTERMEDIATES (GP XIII AND GP XIV)

Characterization of divinylzinc intermediates (GP XIII):



In a dry Schlenk tube under argon atmosphere, the appropriate ynamide (0.25 mmol, 1.0 equiv) was dissolved in dry THF (2 mL) and the solution was degassed by 3 freeze-pump-thaw cycles. At 0 °C, Et_2Zn (1.0 M in hexane, 0.75 mL, 0.75 mmol, 3.0 equiv) and Ph_3GeH (0.33 mmol, 1.3 equiv) were successively added. The reaction mixture was stirred at this temperature for 3 h and then concentrated under vacuum (0.1 mmHg) to remove all the volatiles. After placing the residue under argon, C_6D_6 (2 mL) was added and the mixture concentrated again under vacuum (the procedure was repeated two times) to afford the crude product.

bis((Z)-1-(4,4-dimethyl-2-oxooxazolidin-3-yl)-2-

(triphenylgermyl)vinyl)zinc (169): Prepared according to GP XIII from ynamide 54 (35 mg, 0.25 mmol, 1.0 equiv). Purification of the crude product by flash chromatography on silica gel (pentane/Et₂O = gradient from 60:40 to 0:100) afforded 169 (79 mg, 33%) as a white solid contaminated with 5% of product *E*-59. White crystals suitable for X-ray crystallographic analysis were obtained by recrystallization from pentane/CH₂Cl₂.

¹**H NMR** (300 MHz, CDCl₃): δ 7.43–7.39 (m, 12H, H-Ar), 7.30–7.20 (m, 18H, H-Ar), 5.96 (s, 2H, H-6), 3.99 (d, *J* = 8.1 Hz, 2H, H-2), 3.89 (d, *J* = 8.1 Hz, 2H, H-2'), 1.63 (s, 6H, H-4 or H-4'), 1.57 (s, 6H, H-4' or H-4).

¹³C{¹H} NMR (75 MHz, CDCl₃): δ 165.7 (C-5), 161.8 (C-1), 138.0 (C-7), 135.6 (C-Ar), 128.6 (C-Ar), 128.0 (C-Ar), 109.3 (C-6), 75.3 (C-2), 60.0 (C-3), 25.6 (C-4,4').

HRMS (ESI): m/z calculated for $[C_{50}H_{48}Ge_2N_2O_4Zn + Na]^+$ 975.1223; found 975.1231.



 $C_{50}H_{48}Ge_2N_2O_4Zn$ M.W. = 951.59 g·mol⁻¹

The structure was confirmed by X-ray crystallographic analysis.



bis((Z)-1-((S)-4-isopropyl-2-oxooxazolidin-3-yl)-2-

(triphenylgermyl)vinyl)zinc (170): Prepared according to GP XIII from ynamide **55** (38 mg, 0.25 mmol, 1.0 equiv). Purification of the crude product by flash chromatography on silica gel (pentane/Et₂O = gradient from 50:50 to 0:100) afforded **170** (105 mg, 43%) as a white solid contaminated with 5% of product *E*-68. White crystals suitable for X-ray crystallographic analysis were obtained by recrystallization from pentane/CH₂Cl₂.

¹**H NMR** (400 MHz, C₆D₆): δ 7.49–7.46 (m, 12H, H-Ar), 6.96–6.89 (m, 18H, H-Ar), 5.38 (s, 2H, H-6), 3.43–3.38 (m, 4H, H-2), 3.33–3.29 (m, 2H, H-3), 2.21–2.14 (m, 2H, H-4), 0.30 (d, *J* = 7.0 Hz, 6H, H-5 or H-5'), 0.09 (d, *J* = 7.0 Hz, 6H, H-5' or H-5).

JMod (100 MHz, C₆D₆): δ 164.9 (C-6), 162.4 (C-1), 138.4 (C-8), 136.1 (C-Ar), 128.7 (C-Ar), 128.4 (C-Ar), 108.3 (C-7), 64.7 (C-2), 57.8 (C-3), 26.2 (C-4), 17.6 (C-5 or C-5'), 13.7 (C-5' or C-5).

HRMS (ESI): m/z calculated for $[C_{52}H_{52}Ge_2N_2O_4Zn + Na]^+$ 1003.1536; found 1003.1559.

The structure was confirmed by X-ray crystallographic analysis.







 $C_{52}H_{52}Ge_2N_2O_4Zn$ M.W. = 979.64 g·mol⁻¹

General procedure for domino terminal ynamide germylzincation/Cu(I)- or Pd(0)mediated electrophilic substitution *via* divinylzinc intermediate 169 (GP XIV):



Divinylzinc intermediate **169** was prepared from ynamide **54** (35 mg, 0.25 mmol, 1.0 equiv) according to **GP XIII**. The resulting solid was redissolved in dry and degassed THF (2 mL) and cooled to -30° C. The appropriate Cu(I)-salt (0.50–0.55 mmol, 2.0–2.2 equiv) followed by the appropriate electrophile (0.50–0.63 mmol, 2.0–2.5 equiv) were added at this temperature and the reaction mixture was allowed to warm slowly to rt overnight under stirring. Then, aq NH₄Cl/NH₃ (2:1) and CH₂Cl₂ were added and after 1 h stirring the layers were separated. The aqueous layer was extracted with CH₂Cl₂ (x3), and the combined organic layers were washed with brine (x2), dried over Na₂SO₄, filtered, and concentrated under reduce pressure to afford the crude product.

(Z)-3-(1-iodo-2-(triphenylgermyl)vinyl)-4,4-dimethyloxazolidin-2-one

(172): Prepared according to **GP XIV** using CuCN·2LiCl (1.0 M in THF, 0.50 mL, 0.50 mmol, 2.0 equiv) and I₂ (1.0 M in THF, 0.50 mL, 0.50 mmol, 2.0 equiv) (addition at -40 °C). The reaction was left to warm slowly to 0 °C overnight after addition of the electrophile. Purification of the crude product by flash chromatography on silica gel (pentane/Et₂O = 60:40) afforded analytically pure **172** (94 mg, 66%, Z/E > 98:2) as white crystals; mp 113–116 °C.

¹**H NMR** (400 MHz, CDCl₃): δ 7.66–7.63 (m, 6H, H-Ar), 7.44–7.40 (m, 9H, H-Ar), 7.15 (s, 1H, H-6), 4.07 (s, 2H, H-2), 1.53 (s, 6H, H-4,4').

¹³C{¹H} NMR (100 MHz, CDCl₃): δ 154.2 (C-1), 144.4 (C-6), 135.2 (C-Ar), 134.6 (C-7), 129.5 (C-Ar), 128.5 (C-Ar), 100.3 (C-5), 75.9 (C-2), 61.5 (C-3), 25.5 (C-4,4').

IR (neat): v (cm⁻¹) 2972, 1757, 1587, 1320, 1078, 911, 734, 697.

HRMS (ESI): m/z calculated for $[C_{25}H_{24}GeINO_2 + Na]^+$ 593.9961; found 593.9979.

The Z configuration was assigned by analogy with 156.





C₂₅H₂₄GeINO₂ M.W. = 570.01 g⋅mol⁻¹





C₂₅H₂₄BrGeNO₂ M.W. = 523.01 g⋅mol⁻¹

(Z)-3-(1-bromo-2-(triphenylgermyl)vinyl)-4,4-dimethyloxazolidin-2-

one (173): Prepared according to **GP XIV** using CuCN·2LiCl (1.0 M in THF, 0.50 mL, 0.50 mmol, 2.0 equiv) and *N*-bromo succinimide (89 mg, 0.50 mmol, 2.0 equiv) (addition at –40 °C). The reaction was left to warm slowly to 0 °C overnight after addition of the electrophile. Purification of the crude product by flash chromatography on silica gel (pentane/Et₂O = 60:40) afforded **173** (60 mg, 46%, *Z*/*E* > 98:2) contaminated with 6% of product **59**; mp 160–163 °C.

¹**H NMR** (400 MHz, CDCl₃): δ 7.63–7.60 (m, 6H, H-Ar), 7.43–7.39 (m, 9H, H-Ar), 6.75 (s, 1H, H-6), 4.09 (s, 2H, H-2), 1.50 (s, 6H, H-4,4').

¹³C{¹H} NMR (100 MHz, CDCl₃): δ 154.4 (C-1), 135.6 (C-6), 135.1 (C-Ar), 135.0 (C-7), 129.5 (C-Ar), 128.5 (C-Ar), 126.3 (C-5), 76.0 (C-2), 61.1 (C-3), 25.7 (C-4,4').

IR (neat): v (cm⁻¹) 2973, 1762, 1604, 1323, 1079, 911, 735, 698.

HRMS (ESI): m/z calculated for $[C_{25}H_{24}BrGeNO_2 + Na]^+$ 546.0093; found 546.0081.

The Z configuration was assigned by analogy with 156.

(Z)-3-(1-fluoro-2-(triphenylgermyl)vinyl)-4,4-dimethyloxazolidin-2-



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C₂₅H₂₄FGeNO₂ M.W. = 462.10 g·mol⁻¹ ¹**H NMR** (400 MHz, CDCl₃): δ 7.59–7.56 (m, 6H, H-Ar), 7.42–7.38 (m, 9H, H-Ar), 5.51 (d, ³*J*_{H-F} = 52.7 Hz, 1H, H-6), 4.06 (s, 2H, H-2), 1.46 (d, ⁵*J*_{H-F} = 1.3 Hz, 6H, H-4,4').

¹³C{¹H} NMR (100 MHz, CDCl₃): δ 154.3 (C-1, d, ³*J*_{C-F} = 3.1 Hz), 152.5 (C-5, d, ¹*J*_{C-F} = 255.3 Hz), 136.1 (C-7), 134.8 (C-Ar), 129.3 (C-Ar), 128.4 (C-Ar), 92.8 (C-6, d, ²*J*_{C-F} = 39.3 Hz), 75.3 (C-2), 60.3 (C-3, d, ³*J*_{C-F} = 3.4 Hz), 26.0 (C-4,4', d, ⁴*J*_{C-F} = 3.0 Hz).

¹⁹**F NMR** (376 MHz, CDCl₃): δ –71.0 (d, ³*J*_{F-H} = 52.7 Hz).

IR (neat): v (cm⁻¹) 3069, 1762, 1648, 1339, 1078, 908, 730, 696.

HRMS (ESI): m/z calculated for $[C_{25}H_{24}FGeNO_2 + Na]^+$ 486.0900; found 486.0906.

The Z configuration was assigned by analogy with 153.

(E)-4,4-dimethyl-3-(3,3,3-trifluoro-1-(triphenylgermyl)prop-1-en-2-

yl)oxazolidin-2-one (175): Prepared according to **GP XIV** using CuCN-2LiCl (1.0 M in THF, 0.55 mL, 0.55 mmol, 2.2 equiv) and 5-(trifluoromethyl)dibenzothiophenium tetrafluoroborate (Umemoto's reagent) (213 mg, 0.63 mmol, 2.5 equiv). Purification of the crude product by flash chromatography on silica gel (toluene/Et₂O = 92:8) afforded analytically pure **175** (50 mg, 39%, E/Z = 92:8) as a white solid; mp 178–180 °C.

¹**H NMR** (400 MHz, CDCl₃): (*E* isomer) δ 7.55–7.53 (m, 6H, H-Ar), 7.45–7.38 (m, 9H, H-Ar), 6.85 (q, ⁴*J*_{H-F} = 1.2 Hz, 1H, H-6), 4.14 (s, 2H, H-2), 1.40 (s, 6H, H-4,4').

¹³**C NMR** (100 MHz, CDCl₃): (*E* isomer) δ 156.1 (C-1), 143.1 (C-6, q, ³*J*_{C-F} = 2.8 Hz), 136.3 (C-5, q, ²*J*_{C-F} = 36.6 Hz), 135.0 (C-7), 134.8 (C-Ar), 129.6 (C-Ar), 128.6 (C-Ar), 120.7 (C-11, q, ¹*J*_{C-F} = 276.5 Hz), 76.1 (C-2), 60.9 (C-3), 25.9 (C-4,4').

¹⁹**F NMR** (376 MHz, CDCl₃): (*E* isomer) δ –62.5 (s).

IR (neat): v (cm⁻¹) 2992, 1759, 1325, 1173, 1123, 895, 735, 698.

HRMS (ESI): m/z calculated for $[C_{26}H_{24}F_{3}GeNO_{2} + Na]^{+}$ 536.0863; found 536.0863.

The E configuration was assigned by analogy with **153**.

(E)-4,4-dimethyl-3-(1-(4-nitrophenyl)-2-

(triphenylgermyl)vinyl)oxazolidin-2-one (176): Divinylzinc intermediate 169 was prepared from ynamide 54 (35 mg, 0.25 mmol, 1.0 equiv) according to GP XIII. The resulting solid was redissolved in dry and degassed THF (1 mL) and a THF (1 mL) solution of Pd_2dba_3 (11 mg, 0.0125 mmol, 5 mol%), tri(2-furyl)phosphine (6 mg, 0.030 mmol, 10 mol%), and 1-bromo-4-nitrobenzene (101 mg, 0.50 mmol, 2.0 equiv) was then added dropwise at rt. The reaction mixture was heated at 65 °C for 40 h under stirring. It was then cooled to rt and filtered over a pad of silica gel using CH_2Cl_2 as eluent, and



C₂₆H₂₄F₃GeNO₂ M.W. = 512.11 g⋅mol⁻¹



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C₃₁H₂₈GeN₂O₄ M.W. = 565.21 g⋅mol⁻¹

concentrated under reduce pressure to afford the crude product. Purification by flash chromatography on silica gel (pentane/Et₂O/toluene = 50:40:10) afforded analytically pure **176** (79 mg, 56%, E/Z > 98:2) as a pale yellow solid; mp 157–159 °C.

¹**H NMR** (400 MHz, CDCl₃): δ 7.57–7.54 (m, 2H, H-Ar [Ph]), 7.35–7.31 (m, 6H, H-Ar [Ph₃Ge]), 7.26–7.15 (m, 11H, H-Ar [Ph₃Ge] + [Ph]), 6.49 (s, 1H, H-6), 4.00 (s, 2H, H-2), 1.21 (s, 6H, H-4,4').

¹³C{¹H} NMR (100 MHz, CDCl₃): δ 156.1 (C-1), 147.6, 145.7, 144.8, 136.0, 134.7, 129.8, 129.3, 128.9, 128.5, 123.0, 75.7 (C-2), 60.5 (C-3), 26.3 (C-4,4').

IR (neat): v (cm⁻¹) 2973, 1747, 1517, 1338, 909, 859, 728, 696.

HRMS (ESI): m/z calculated for $[C_{31}H_{28}GeN_2O_4 + Na]^+$ 589.1153; found 589.1160.

The E configuration was confirmed by NOESY enhancements.



III-5.7. GERMYL 1,2-MIGRATION

3-(2,2-dibromo-1-(triethylgermyl)ethyl)-4,4-dimethyloxazolidin-2-one

(179): To a stirred solution of *E*-77 (47 mg, 0.16 mmol, 1.0 equiv) in CH_2Cl_2 (0.60 mL) at -78 °C, a solution of bromine (1.0 M in CH_2Cl_2 , 0.16 mL, 0.16 mmol, 1.0 equiv) was added dropwise. The reaction mixture was stirred at this temperature for 1 h and then at rt for 2 h, followed by removal of the solvent under reduced pressure. ¹*H NMR spectrum of the crude product is reported below.*

¹**H NMR** (400 MHz, CDCl₃): δ 6.61 (d, *J* = 9.7 Hz, 1H, H-6), 5.41 (d, *J* = 9.7 Hz, 1H, H-5), 4.14–4.07 (m, 2H, H-2), 1.51–1.43 (m, 6H, H-4,4'), 1.26–1.08 (m, 15H, H-7,8).



one (180): To a stirred solution of *E*-**59** (44 mg, 0.10 mmol, 1.0 equiv) in CH_2Cl_2 (0.40 mL) at -78 °C, a solution of bromine (1.0 M in CH_2Cl_2 , 0.10 mL, 0.10 mmol, 1.0 equiv) was added dropwise. The reaction mixture was stirred at this temperature for 1 h and then at rt for 2 h, followed by removal of the solvent under reduced pressure. ¹H NMR spectrum of the crude product is reported below.

¹**H NMR** (400 MHz, CDCl₃): δ 7.67–7.63 (m, 6H, H-Ar), 7.50–7.41 (m, 9H, H-Ar), 6.65 (d, *J* = 9.7 Hz, 1H, H-6), 5.42 (d, *J* = 9.7 Hz, 1H, H-5), 4.11–4.08 (m, 2H, H-2), 1.53–1.44 (m, 6H, H-4,4').

3-(2,2-dibromo-1-hydroxyethyl)-4,4-dimethyloxazolidin-2-one (181): Purification of the crude product of **179** by flash chromatography on silica gel (eluent pentane/EtOAc = gradient from 70:30 to 60:40) afforded analytically pure **181** (34 mg, 68%) as a white solid; mp 131–134 °C. Likewise, purification of the crude product of **180** by flash chromatography on silica gel (same eluent) afforded analytically pure **181** (22 mg, 69%).

¹**H NMR** (400 MHz, CDCl₃): δ 6.33 (d, *J* = 8.9 Hz, 1H, H-6), 4.81-4.76 (m, 1H, H-5), 4.20 (d, *J* = 10.6 Hz, 1H, H-7), 4.10 (d, *J* = 8.3 Hz, 1H, H-2), 4.05 (d, *J* = 8.3 Hz, 1H, H-2'), 1.44 (s, 3H, H-4 or H-4'), 1.42 (s, 3H, H-4' or H-4).



179

C₁₃H₂₅Br₂GeNO₂ M.W. = 459.79 g⋅mol⁻¹



180

C₂₅H₂₅Br₂GeNO₂ M.W. = 603.92 g⋅mol⁻¹





C₇H₁₁Br₂NO₃ M.W. = 316.98 g⋅mol⁻¹

¹³**C NMR** (100 MHz, CDCl₃): δ 156.9 (C-1), 82.0 (C-5), 75.9 (C-2), 59.7 (C-3), 44.9 (C-6), 25.7 (C-4 or C-4'), 25.3 (C-4' or C-4).

IR (neat): *v* (cm⁻¹) 3377 (br), 2975, 1725, 1420, 1329, 1033, 713, 665.

HRMS (ESI): m/z calculated for $[C_7H_{11}Br_2NO_3 + Na]^+$ 337.8998; found 337.9008.

The structure was confirmed by X-ray crystallographic analysis.



 $\begin{array}{c} 2 \\ 4 \\ 4 \\ 4 \end{array} \\ \mathbf{N} \\ \mathbf{N}$

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C₈H₁₃Br₂NO₃ M.W. = 331.00 g·mol⁻¹ **3-(2,2-dibromo-1-methoxyethyl)-4,4-dimethyloxazolidin-2-one (184):** To a stirred solution of *E*-**59** (44 mg, 0.10 mmol, 1.0 equiv) in CH_2Cl_2 (0.40 mL) at -78 °C, a solution of bromine (1.0 M in CH_2Cl_2 , 0.10 mL, 0.10 mmol, 1.0 equiv) was added dropwise. The reaction mixture was stirred at this temperature for 1 h and then at rt for 2 h, followed by removal of the solvent under reduced pressure. The crude product was redissolved in MeOH/CH₂Cl₂ (0.50 mL/0.40 mL) and stirred for 1 h at rt. Purification of the crude product by flash chromatography on silica gel (eluent pentane/EtOAc = 60:40) afforded analytically pure **184** (29 mg, 87%) as a white solid; mp 87–88 °C.

¹**H NMR** (400 MHz, CDCl₃): δ 6.18 (d, *J* = 9.3 Hz, 1H, H-6), 5.06 (d, *J* = 9.3 Hz, 1H, H-5), 4.01 (s, 2H, H-2), 3.53 (s, 3H, H-7), 1.47 (s, 3H, H-4 or H-4'), 1.46 (s, 3H, H-4' or H-4).

¹³**C NMR** (100 MHz, CDCl₃): δ 157.0 (C-1), 90.3 (C-5), 75.7 (C-2), 59.1 (C-3), 58.3 (C-7), 43.9 (C-6), 26.6 (C-4 or C-4'), 25.7 (C-4' or C-4).

IR (neat): *v* (cm⁻¹) 2974, 1743, 1378, 1319, 1083, 1036, 704, 666.

HRMS (ESI): m/z calculated for $[C_8H_{13}Br_2NO_3 + Na]^+$ 353.9134; found 353.9127.

III-5.8. HALODEGERMYLATION OF β -TRIPHENYLGERMYLENAMIDES



(*E*)-3-(2-iodovinyl)-4,4-dimethyloxazolidin-2-one (186): To a stirred solution of *E*-59 (44 mg, 0.10 mmol, 1.0 equiv) in CH₂Cl₂ (0.40 mL) at –78 °C, ICl (1.0 M in CH₂Cl₂, 0.12 mL, 0.12 mmol, 1.2 equiv) was added dropwise. The reaction mixture was stirred at –78 °C for 1 h and then at rt for 2 h. The mixture was then concentrated under vacuum to afford the crude product. Purification by flash chromatography on silica gel (pentane/Et₂O = 70:30) afforded analytically pure **186** (25 mg, 93%, *E*/*Z* > 98:2) as a white solid; mp 62–65 °C.

¹**H NMR** (400 MHz, CDCl₃): δ 6.84 (d, *J* = 14.1 Hz, 1H, H-5), 6.17 (d, *J* = 14.1 Hz, 1H, H-6), 4.03 (s, 2H, H-2), 1.45 (s, 6H, H-4,4').

¹³C{¹H} NMR (100 MHz, CDCl₃): δ 154.7 (C-1), 131.6 (C-5), 75.2 (C-2), 59.4 (C-6), 58.9 (C-3), 25.4 (C-4,4').

IR (neat): v (cm⁻¹) 2975, 1744, 1396, 1371, 1324, 1169, 1070, 762.

HRMS (ESI): *m*/*z* calculated for [C₇H₁₀INO₂ + Na]⁺ 289.9648; found 289.9644.

Note: The E configuration was determined on the basis of the ¹H NMR coupling constant of the vinylic protons (J = 14.1 Hz).

(E)-3-(2-bromo-2-(4-methoxyphenyl)vinyl)-4,4-dimethyloxazolidin-2-

one (187): To a stirred solution of *E*-**138** (55 mg, 0.10 mmol, 1.0 equiv) in CH_2Cl_2 (0.40 mL) at -78 °C, Br_2 (1.0 M in CH_2Cl_2 , 0.10 mL, 0.10 mmol, 1.0 equiv) was added dropwise. The reaction mixture was stirred at -78 °C for 1 h and then at rt for 15 min. The mixture was then concentrated under vacuum to afford the crude product. Purification by flash chromatography on silica gel (pentane/EtOAc = 60:40) afforded analytically pure **187** (24 mg, 73%, *E/Z* > 98:2) as a colorless gum.

¹**H NMR** (400 MHz, CDCl₃): δ 7.42–7.40 (m, 2H, H-Ar), 6.85–6.83 (m, 2H, H-Ar), 6.36 (s, 1H, H-5), 3.93 (s, 2H, H-2), 3.80 (s, 3H, H-11), 1.18 (s, 6H, H-4,4').



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 $C_7H_{10}INO_2$ M.W. = 267.06 g·mol⁻¹



C₁₄H₁₆BrNO₃ M.W. = 326.19 g⋅mol⁻¹
¹³C{¹H} NMR (100 MHz, CDCl₃): δ 160.3 (C-10), 155.7 (C-1), 130.3 (C-Ar), 129.2 (C-6 or C-7), 129.1 (C-7 or C-6), 120.2 (C-5), 113.7 (C-Ar), 75.3 (C-2), 60.5 (C-3), 55.4 (C-11), 24.6 (C-4,4').

IR (neat): v (cm⁻¹) 2972, 1753, 1409, 1250, 1175, 1074, 1027, 833.

HRMS (ESI): m/z calculated for $[C_{14}H_{16}BrNO_3 + Na]^+$ 348.0206; found 348.0210.

(E)-3-(1-bromopenta-1,4-dien-2-yl)-4,4-dimethyloxazolidin-2-one

(188): To a stirred solution of *E*-153 (48 mg, 0.10 mmol, 1.0 equiv) in CH₂Cl₂ (0.40 mL) at -78 °C, Br₂ (1.0 M in CH₂Cl₂, 0.10 mL, 0.10 mmol, 1.0 equiv) was added dropwise. The reaction mixture was stirred at -78 °C for 1 h and then at rt for 15 min. The mixture was then concentrated under vacuum to afford the crude product. Purification of the crude product by flash chromatography on silica gel (pentane/EtOAc = 60:40) afforded analytically pure **188** (11 mg, 43%, *E/Z* > 98:2) as a white solid; mp 66–68 °C.

¹**H NMR** (400 MHz, CDCl₃): δ 6.31 (s, 1H, H-6), 5.79 (ddt, *J* = 16.9 Hz, *J* = 10.0 Hz, *J* = 6.8 Hz, 1H, H-8), 5.21–5.13 (m, 2H, H-9), 4.04 (s, 2H, H-2), 3.29 (dtd, *J* = 6.8 Hz, *J* = 1.5 Hz, *J* = 0.6 Hz, 2H, H-7), 1.34 (s, 6H, H-4,4').

¹³C{¹H} NMR (100 MHz, CDCl₃): δ 155.8 (C-1), 137.2 (C-5), 132.5 (C-8), 118.6 (C-9), 109.2 (C-6), 75.9 (C-2), 60.3 (C-3), 36.9 (C-7), 26.5 (C-4,4').

IR (neat): v (cm⁻¹) 2976, 1745, 1406, 1386, 1343, 1186, 1071, 764.

HRMS (ESI): m/z calculated for $[C_{10}H_{14}BrNO_2 + Na]^+$ 282.0100; found 282.0090.

The E configuration was confirmed by the following NOESY enhancements.



(Z)-3-(1-bromo-3-oxo-3-phenylprop-1-en-2-yl)-4,4-

dimethyloxazolidin-2-one (189): To a stirred solution of *E*-**156** (55 mg, 0.10 mmol, 1.0 equiv) in CH_2Cl_2 (0.40 mL) at -78 °C, Br_2 (1.0 M in CH_2Cl_2 , 0.10 mL, 0.10 mmol, 1.0 equiv) was added dropwise. The reaction mixture was



188

C₁₀H₁₄BrNO₂ M.W. = 260.13 g·mol⁻¹ stirred at –78 °C for 1 h and then at rt for 15 min. The mixture was then concentrated under vacuum to afford the crude product. Purification of the crude product by flash chromatography on silica gel (eluent pentane/EtOAc = 70:30) afforded analytically pure **189** (Z/E = 95:5) in 99% yield (32 mg) as a white solid.

¹**H NMR** (400 MHz, CDCl₃): δ 7.84–7.81 (m, 2H, H-10), 7.62–7.58 (m, 1H, H-11), 7.57 (s, 1H, H-6), 7.50–7.46 (m, 2H, H-9), 4.15 (s, 2H, H-2), 1.28 (s, 6H, H-4).

¹³C{¹H} NMR (100 MHz, CDCl₃): δ 191.3 (C-7), 154.1 (C-1), 138.2 (C-5), 136.3 (C-8), 133.6 (C-11), 129.5 (C-10), 129.0 (C-9), 128.0 (C-6), 76.3 (C-2), 61.4 (C-3), 26.1 (C-4).

The spectral data were in agreement with that previously reported in the literature.ⁱ



189

C₁₄H₁₄BrNO₃ M.W. = 324.17 g⋅mol⁻¹

ⁱ Romain, E.; Fopp, C.; Chemla, F.; Ferreira, F.; Jackowski, O.; Oestreich, M.; Perez-Luna, A. *Angew. Chem. Int. Ed.* **2014**, *53*, 11333–11337.

III-5.9. GERMYLZINCATION OF α -HETEROATOM-SUBSTITUTED ALKYNES



232

C₂₆H₂₂GeS M.W. = 439.16 g⋅mol⁻¹ (*E*)-triphenyl(2-(phenylthio)vinyl)germane (232): Prepared following the same procedure as GP VII with ethynyl(phenyl)sulfane 206 (34 mg, 0.25 mmol, 1.0 equiv) as substrate, Et₂Zn (1.0 M in hexane, 0.75 mL, 0.75 mmol, 3.0 equiv), Ph₃GeH (99 mg, 0.33 mmol, 1.3 equiv) and 3 h reaction time. Purification of the crude product (E/Z > 98:2) by flash chromatography on silica gel (pentane/Et₂O = 99:1) afforded analytically pure 232 (58 mg, 53%, E/Z > 98:2) as a white solid; mp 107–110 °C.

¹**H NMR** (400 MHz, CDCl₃): δ 7.41–7.38 (m, 6H, H-Ar [Ph₃Ge]), 7.31–7.27 (m, 9H, H-Ar [Ph₃Ge]), 7.26–7.13 (m, 5H, H-Ar [Ph]), 6.65 (d, *J* = 17.7 Hz, 1H, H-5), 6.31 (d, *J* = 17.7 Hz, 1H, H-6).

JMod (100 MHz, CDCl₃): δ 141.4 (C-5), 136.2 (C-7), 135.1 (C-Ar [Ph₃Ge]), 133.6 (C-4), 131.6 (C-Ar [Ph]), 129.4 (C-Ar [Ph]), 129.3 (C-Ar [Ph₃Ge]), 128.4 (C-Ar [Ph₃Ge]), 127.7 (C-Ar [Ph]), 122.8 (C-6).

IR (neat): v (cm⁻¹) 3058, 1528, 1428, 1091, 951, 792, 736, 691.

HRMS (ESI): *m*/*z* calculated for [C₂₆H₂₂GeS + Na]⁺ 463.0550; found 463.0552.

Note: The E configuration was determined on the basis of the ¹H NMR coupling constant of the vinylic protons (J = 17.7 Hz).



[²H]-232

C₂₆H₂₁DGeS M.W. = 440.16 g⋅mol⁻¹ **[²H]-232:** Prepared following the same procedure as **GP VIII** with ethynyl(phenyl)sulfane **206** (34 mg, 0.25 mmol, 1.0 equiv) as substrate, Et₂Zn (1.0 M in hexane, 0.75 mL, 0.75 mmol, 3.0 equiv), Ph₃GeH (99 mg, 0.33 mmol, 1.3 equiv) and 3 h reaction time. Purification of the crude product (E/Z > 98:2) by flash chromatography on silica gel (pentane/Et₂O = 99:1) afforded analytically pure [²H]-**232** (66 mg, 60%, E/Z > 98:2) as a white solid.

¹**H NMR** (300 MHz, CDCl₃): δ 7.43–7.39 (m, 6H), 7.33–7.27 (m, 9H), 7.27–7.15 (m, 5H), 6.31 (t, *J* = 2.3 Hz, 1H).

¹³C{¹H} NMR (75 MHz, CDCl₃): δ 136.2, 135.1, 133.5, 131.6, 129.4, 129.3, 128.4, 127.7, 122.6. One C is not observed.

HRMS (ESI): m/z calculated for $[C_{26}H_{21}DGeS + Na]^+$ 464.0613; found 464.0603.

(*R*,*E*)-triphenyl(2-(*p*-tolylsulfinyl)vinyl)germane (238): Prepared following the same procedure as **GP VII** with ethynyl *p*-tolyl (*R*)-sulfoxide **214** (41 mg, 0.25 mmol, 1.0 equiv) as substrate, Et_2Zn (1.0 M in hexane, 0.75 mL, 0.75 mmol, 3.0 equiv), Ph₃GeH (99 mg, 0.33 mmol, 1.3 equiv) and 3 h reaction time. Purification of the crude product (*E*/*Z* > 98:2) by flash chromatography on silica gel (pentane/ Et_2O = gradient from 80:20 to 70:30) afforded analytically pure **238** (53 mg, 45%, *E*/*Z* > 98:2) as a white solid; mp 147–150 °C.

¹**H NMR** (400 MHz, CDCl₃): δ 7.58 (d, *J* = 17.4 Hz, 1H, H-6), 7.51–7.49 (m, 2H, H-3), 7.47–7.45 (m, 6H, H-Ar [Ph₃Ge]), 7.43–7.35 (m, 9H, H-Ar [Ph₃Ge]), 7.31–7.29 (m, 2H, H-4), 6.74 (d, *J* = 17.4 Hz, 1H, H-7), 2.41 (s, 3H, H-1).

¹³C{¹H} NMR (100 MHz, CDCl₃): δ 150.1 (C-7), 142.0 (C-2), 140.2 (C-5), 135.0 (C-Ar [Ph₃Ge]), 134.9 (C-8), 131.0 (C-6), 130.3 (C-4), 129.6 (C-Ar [Ph₃Ge]), 128.6 (C-Ar [Ph₃Ge]), 125.3 (C-3), 21.6 (C-1).

IR (neat): v (cm⁻¹) 3046, 2920, 1483, 1429, 1092, 1051, 737, 696.

HRMS (ESI): m/z calculated for $[C_{27}H_{24}GeOS + Na]^+$ 493.0652; found 493.0650.

Note: The E configuration was determined on the basis of the ¹H NMR coupling constant of the vinylic protons (J = 17.4 Hz).

[²H]-238: Prepared following the same procedure as **GP VIII** with ethynyl *p*tolyl (*R*)-sulfoxide **214** (41 mg, 0.25 mmol, 1.0 equiv) as substrate, Et₂Zn (1.0 M in hexane, 0.75 mL, 0.75 mmol, 3.0 equiv), Ph₃GeH (99 mg, 0.33 mmol, 1.3 equiv) and 3 h reaction time. Purification of the crude product (E/Z > 98:2) by flash chromatography on silica gel (pentane/Et₂O = gradient from 80:20 to 70:30) afforded analytically pure [²H]-**238** (51 mg, 43%, E/Z > 98:2) as a white solid.

¹**H NMR** (400 MHz, CDCl₃): δ 7.57 (s, 1H), 7.51–7.49 (m, 2H), 7.47–7.45 (m, 6H), 7.43–7.35 (m, 9H), 7.31–7.29 (m, 2H), 2.41 (s, 3H).

¹³C{¹H} NMR (100 MHz, CDCl₃): δ 149.7 (t, *J* = 26.0 Hz), 142.0, 140.2, 135.0, 134.9, 130.8, 130.3, 129.6, 128.6, 125.3, 21.6.

HRMS (ESI): m/z calculated for $[C_{27}H_{23}DGeOS + Na]^+$ 494.0715; found 494.0713.



238

C₂₇H₂₄GeOS M.W. = 469.18 g⋅mol⁻¹





C₂₇H₂₃DGeOS M.W. = 470.19 g⋅mol⁻¹





C₂₇H₃₁GeNO₂ M.W. = 474.18 g⋅mol⁻¹

(E)-2-(triphenylgermyl)vinyl diisopropylcarbamate (241): Prepared following the same procedure as **GP** VII with ethynyl *N*,*N*-diisopropylcarbamate **218** (25 mg, 0.15 mmol, 1.0 equiv) as substrate, Et₂Zn (1.0 M in hexane, 0.45 mL, 0.45 mmol, 3.0 equiv), Ph₃GeH (60 mg, 0.20 mmol, 1.3 equiv) and 3 h reaction time. Purification of the crude product (*E*/*Z* > 98:2) by flash chromatography on silica gel (pentane/Et₂O = 95:5) afforded analytically pure **241** (26 mg, 37%, *E*/*Z* > 98:2) as a white solid; mp 107–109 °C.

¹**H NMR** (400 MHz, CDCl₃): δ 7.53–7.51 (m, 6H, H-Ar), 7.40–7.36 (m, 9H, H-Ar), 7.24 (d, *J* = 14.6 Hz, 1H, H-6), 5.68 (d, *J* = 14.6 Hz, 1H, H-7), 4.10–3.80 (m, 2H, H-2,3), 1.28–1.22 (m, 12H, H-1,4).

¹³C{¹H} NMR (100 MHz, CDCl₃): δ 152.5 (C-5), 147.3 (C-6), 136.3 (C-8), 135.1 (C-Ar), 129.3 (C-Ar), 128.4 (C-Ar), 100.6 (C-7), 46.7 (C-2 or C-3, br), 46.1 (C-3 or C-2, br), 21.8 (C-1 or C-4, br), 20.5 (C-4 or C-1, br).

IR (neat): v (cm⁻¹) 2963, 2934, 1711, 1611, 1429, 1310, 962, 739.

HRMS (ESI): *m/z* calculated for [C₂₇H₃₁GeNO₂ + Na]⁺ 498.1459; found 498.1456.

Note: The E configuration was determined on the basis of the ¹H NMR coupling constant of the vinylic protons (J = 14.6 Hz).

[²H]-241

C₂₇H₃₀DGeNO₂ M.W. = 475.19 g⋅mol⁻¹ **[²H]-241:** Prepared following the same procedure as **GP VIII** with ethynyl *N*,*N*-diisopropylcarbamate **218** (25 mg, 0.15 mmol, 1.0 equiv) as substrate, Et₂Zn (1.0 M in hexane, 0.45 mL, 0.45 mmol, 3.0 equiv), Ph₃GeH (60 mg, 0.20 mmol, 1.3 equiv) and 3 h reaction time. Purification of the crude product (*E*/*Z* > 98:2) by flash chromatography on silica gel (pentane/Et₂O = 95:5) afforded analytically pure [²H]-**241** (20 mg, 28%, *E*/*Z* > 98:2) as a white solid.

¹**H NMR** (400 MHz, CDCl₃): δ 7.53–7.51 (m, 6H), 7.41–7.35 (m, 9H), 5.67 (s, 1H), 4.10–3.80 (m, 2H), 1.28–1.22 (m, 12H).

¹³C{¹H} NMR (100 MHz, CDCl₃): δ 152.5, 136.3, 135.1, 129.3, 128.4, 100.4, 46.7 (br), 46.1 (br), 21.8 (br), 20.5 (br). *One C is not observed.*

HRMS (ESI): m/z calculated for $[C_{27}H_{30}DGeNO_2 + Na]^+$ 499.1522; found 499.1519.

(*E*)-diethyl (2-(triphenylgermyl)vinyl)phosphonate (244): In a dry Schlenk tube under argon atmosphere, diethyl ethynylphosphonate 227 (41 mg, 0.25 mmol, 1.0 equiv) was dissolved in dry *n*-hexane (1.2 mL). At 0 °C, Et₂Zn (1.0 M in hexane, 0.75 mL, 0.75 mmol, 3.0 equiv) was added and the mixture stirred for 1 h. Ph₃GeH (99 mg, 0.33 mmol, 1.3 equiv) was then added at the same temperature and the reaction was stirred for 16 h at rt. Then, aq NH₄Cl/NH₃ (2:1) and CH₂Cl₂ were added and the layers were separated. The aqueous layer was extracted with CH₂Cl₂ (x3), and the combined organic layers were washed with brine (x2), dried over Na₂SO₄, filtered, and concentrated under reduce pressure to afford the crude product (*E/Z* > 98:2). Purification by flash chromatography on silica gel (pentane/EtOAc = 50:50) afforded analytically pure **244** (82 mg, 70%, *E/Z* > 98:2) as colorless crystals; mp 98–99 °C.



244

C₂₄H₂₇GeO₃P M.W. = 467.08 g⋅mol⁻¹

¹**H NMR** (400 MHz, CDCl₃): δ 7.75 (dd, J_{HP} = 31.6 Hz, J_{HH} = 20.1 Hz, 1H, H-4), 7.49–7.45 (m, 6H, H-Ar), 7.44–7.36 (m, 9H, H-Ar), 6.37 (dd, J_{HP} = 27.0 Hz, J_{HH} = 20.1 Hz, 1H, H-3), 4.10 (dqd, J_{HP} = 8.3 Hz, J_{HH} = 7.1 Hz, J_{HH} = 1.2 Hz, 4H, H-2), 1.32 (t, J_{HH} = 7.1 Hz, 6H, H-1).

¹³C{¹H} NMR (100 MHz, CDCl₃): δ 150.8 (C-4, d, ²*J*_{CP} = 3.7 Hz), 135.8 (C-3, d, ¹*J*_{CP} = 171.8 Hz), 135.2 (C-Ar), 134.6 (C-5), 129.6 (C-Ar), 128.6 (C-Ar), 62.1 (C-2, d, ²*J*_{CP} = 5.7 Hz), 16.5 (C-1, d, ³*J*_{CP} = 6.0 Hz).

³¹**P NMR** (162 MHz, CDCl₃): δ 15.5 (ddquint, *J*_{PH} = 31.6 Hz, *J*_{PH} = 27.0 Hz, *J*_{PH} = 8.3 Hz).

IR (neat): v (cm⁻¹) 2984, 2905, 2858, 1483, 1244, 959, 738, 701.

HRMS (ESI): m/z calculated for $[C_{24}H_{27}GeO_3P + Na]^+$ 491.0807; found 491.0819.

Note: The E configuration was determined on the basis of the ¹H NMR coupling constant of the vinylic protons (J = 20.1 Hz).

[²H]-244: In a dry Schlenk tube under argon atmosphere, diethyl ethynylphosphonate **227** (41 mg, 0.25 mmol, 1.0 equiv) was dissolved in dry *n*-hexane (1.2 mL). At 0 °C, Et₂Zn (1.0 M in hexane, 0.75 mL, 0.75 mmol, 3.0 equiv) was added and the mixture stirred for 1 h. Ph₃GeH (99 mg, 0.33 mmol, 1.3 equiv) was then added at the same temperature and the reaction was

$$\begin{array}{c} O_{\geq} P(OEt)_2 \\ D \\ D \\ Ph_3Ge \end{array}$$

[²H]-244

C₂₄H₂₅D₂GeO₃P M.W. = 469.10 g⋅mol⁻¹ stirred for 16 h at rt. A solution of ND₄Cl (300 mg) in D₂O (2 mL) was added followed by THF (2 mL) 10 min after. The mixture was stirred for 1 h at rt and then aq NH₄Cl/NH₃ (2:1) and CH₂Cl₂ were added. The layers were separated, the aqueous layer was extracted with CH₂Cl₂ (x3), and the combined organic layers were washed with brine (x2), dried over Na₂SO₄, filtered, and concentrated under reduce pressure to afford the crude product (*E*/*Z* > 98:2). Purification of the crude product by flash chromatography on silica gel (pentane/EtOAc = 50:50) afforded analytically pure [²H]-**244** (73 mg, 62%, *E*/*Z* > 98:2) as a white solid.

¹**H NMR** (400 MHz, CDCl₃): δ 7.50–7.47 (m, 6H), 7.45–7.37 (m, 9H), 4.11 (dqd, $J_{\text{HP}} = 8.2 \text{ Hz}, J_{\text{HH}} = 7.1 \text{ Hz}, J_{\text{HH}} = 1.1 \text{ Hz}, 4\text{H}$), 1.33 (t, $J_{\text{HH}} = 7.1 \text{ Hz}, 6\text{H}$).

¹³C{¹H} NMR (100 MHz, CDCl₃): δ 150.2 (m), 135.5 (dm, ¹*J*_{CP} = 171.8 Hz), 135.1, 134.6, 129.6, 128.6, 62.0 (d, ²*J*_{CP} = 5.8 Hz), 16.5 (d, ³*J*_{CP} = 6.1 Hz).

³¹**P NMR** (162 MHz, CDCl₃): δ 16.5 (s).

HRMS (ESI): m/z calculated for $[C_{24}H_{25}D_2GeO_3P + Na]^+$ 493.0927; found 493.0926.

(E)-diisopropyl (2-phenyl-2-(triphenylgermyl)vinyl)phosphonate

(245): Prepared following the same procedure as **GP IX** with diisopropyl (phenylethynyl)phosphonate **230** (40 mg, 0.15 mmol, 1.0 equiv) as substrate, Et₂Zn (1.0 M in hexane, 0.45 mL, 0.45 mmol, 3.0 equiv), Ph₃GeH (60 mg, 0.20 mmol, 1.3 equiv), and 16 h reaction time. Purification of the crude product (E/Z > 98:2) by flash chromatography on silica gel (pentane/EtOAc = 75:25) afforded analytically pure **245** (60 mg, 70%, E/Z > 98:2) as colorless crystals; mp 82–86 °C.

¹**H NMR** (400 MHz, CDCl₃): δ 7.43–7.29 (m, 15H, H-Ar [Ph₃Ge]), 7.19–7.13 (m, 3H, H-Ar [Ph]), 7.11–7.05 (m, 2H, H-Ar [Ph]), 6.27 (d, *J*_{HP} = 23.1 Hz, 1H, H-3), 4.47 (dhept, *J*_{HP} = 7.8 Hz, *J*_{HH} = 6.2 Hz, 2H, H-2), 1.14 (d, *J* = 6.2 Hz, 6H, H-1 or H-1'), 1.03 (d, *J* = 6.2 Hz, 6H, H-1' or H-1).

¹³C{¹H} NMR (100 MHz, CDCl₃): δ 163.5 (C-9, d, ³*J*_{CP} = 5.7 Hz), 141.2 (C-4, d, ²*J*_{CP} = 12.3 Hz), 135.6 (C-Ar [Ph₃Ge]), 134.7 (C-5), 131.4 (C-3, d, ¹*J*_{CP} = 171.7 Hz), 129.5 (C-Ar [Ph₃Ge]), 128.4 (C-Ar [Ph₃Ge]), 127.7 (C-Ar [Ph]), 127.5 (C-10, d, ⁴*J*_{CP} = 2.0 Hz), 127.0 (C-Ar [Ph]), 70.4 (C-2, d, ²*J*_{CP} = 6.4 Hz), 24.0 (C-1 or C-1', d, ³*J*_{CP} = 4.0 Hz), 23.8 (C-1' or C-1, d, ³*J*_{CP} = 5.0 Hz).





C₃₂H₃₅GeO₃P M.W. = 571.23 g⋅mol⁻¹ ³¹**P** NMR (162 MHz, CDCl₃): δ 11.8 (dt, ²*J*_{PH} = 23.1 Hz, ³*J*_{PH} = 7.8 Hz).

IR (neat): v (cm⁻¹) 3058, 2979, 1433, 1237, 979,786, 737, 699.

HRMS (ESI): m/z calculated for $[C_{32}H_{35}GeO_3P + Na]^+$ 595.1435; found 595.1451.

[²H]-245: Prepared following the same procedure as **GP X** with diisopropyl (phenylethynyl)phosphonate **230** (40 mg, 0.15 mmol, 1.0 equiv) as substrate, Et₂Zn (1.0 M in hexane, 0.45 mL, 0.45 mmol, 3.0 equiv), Ph₃GeH (60 mg, 0.20 mmol, 1.3 equiv), and 16 h reaction time. Purification of the crude product (E/Z > 98:2) by flash chromatography on silica gel (pentane/EtOAc = 75:25) afforded analytically pure [²H]-**245** (58 mg, 68%, E/Z > 98:2) as colorless crystals.

¹**H NMR** (400 MHz, CDCl₃): δ 7.41–7.31 (m, 15H), 7.18–7.14 (m, 3H), 7.10–7.06 (m, 2H), 4.47 (dhept, J_{HP} = 7.8 Hz, J_{HH} = 6.2 Hz, 2H), 1.14 (d, J = 6.2 Hz, 6H), 1.03 (d, J = 6.2 Hz, 6H).

¹³C{¹H} NMR (100 MHz, CDCl₃): δ 163.4 (d, ³*J*_{CP} = 5.7 Hz), 141.2 (d, ²*J*_{CP} = 12.2 Hz), 135.5, 134.7, 129.0, 127.9, 127.2, 127.0 (d, ⁴*J*_{CP} = 2.1 Hz), 126.5, 69.9 (d, ²*J*_{CP} = 6.4 Hz), 23.5 (d, ³*J*_{CP} = 4.0 Hz), 23.2 (d, ³*J*_{CP} = 5.0 Hz). *One C is not observed.*

³¹**P NMR** (162 MHz, CDCl₃): δ 11.8 (t, ${}^{3}J_{PH}$ = 7.8 Hz).

HRMS (ESI): m/z calculated for $[C_{32}H_{34}DGeO_3P + Na]^+$ 596.1497; found 596.1519.

The E configuration was determined by X-ray crystallographic analysis.





C₃₂H₃₄DGeO₃P M.W. = 572.24 g⋅mol⁻¹



234

C₂₆H₂₀Ge M.W. = 405.08 g⋅mol⁻¹

Triphenyl(phenylethynyl)germane (234): The product was isolated (21 mg, 34%) as byproduct of the reaction using alkynyl sulfide **210** (28 mg, 0.15 mmol, 1.0 equiv) as substrate, Et₂Zn (1.0 M in hexane, 0.45 mL, 0.45 mmol, 3.0 equiv), Ph₃GeH (91 mg, 0.30 mmol, 2.0 equiv), in *n*-hexane (1.2 mL) with a reaction time of 16 h, according to **GP X**.

White solid, mp 87–90 °C.

¹**H NMR** (400 MHz, CDCl₃): δ 7.73–7.67 (m, 6H, H-Ar [Ph₃Ge]), 7.62–7.58 (m, 2H, H-Ar [Ph]), 7.45–7.40 (m, 9H, H-Ar [Ph₃Ge]), 7.36–7.34 (m, 3H, H-Ar [Ph]).

¹³C{¹H} NMR (100 MHz, CDCl₃): δ 135.3 (C-4), 134.7 (C-Ar [Ph₃Ge]), 132.3 (C-Ar [Ph]), 129.7 (C-Ar [Ph₃Ge]), 128.8 (C-Ar [Ph]), 128.6 (C-Ar [Ph₃Ge]), 128.4 (C-Ar [Ph]), 123.2 (C-7), 108.3 (C-6), 88.8 (C-5).

IR (neat): v (cm⁻¹) 3068, 2156, 1773, 1650, 1431, 1092, 734, 694.

HRMS (ESI): m/z calculated for $[C_{26}H_{20}Ge + Na]^+$ 429.0674; found 429.0680.

Ethynyltriphenylgermane (242): The product was isolated (27 mg, 56%) as byproduct of the preparation of compound **241**; white solid.

¹**H NMR** (400 MHz, CDCl₃): δ 7.66–7.63 (m, 6H, H-Ar), 7.44–7.39 (m, 9H, H-Ar), 2.67 (s, 1H, H-6).

¹³C{¹H} NMR (100 MHz, CDCl₃): δ 135.1 (C-4), 134.5 (C-Ar), 129.7 (C-Ar), 128.5 (C-Ar), 95.9 (C-6), 84.8 (C-5).

The spectral data were in agreement with that previously reported in the literature.ⁱ



242

C₂₀H₁₆Ge M.W. = 328.98 g⋅mol⁻¹

ⁱ David-Quillot, F.; Marsacq, D.; Balland, A.; Thibonnet, J.; Abarbri, M.; Duchêne, A. *Synthesis* **2003**, 448–454.

III-5.10. REACTION WITH ACCEPTOR 86

In a dry Schlenk tube under argon atmosphere, β -(propargyloxy)enoate **86** (40 mg, 0.18 mmol) was dissolved in dry THF (4.5 mL) and the solution was degassed by 3 freeze-pump-thaw cycles. At 0 °C, Ph₃GeH (165 mg, 0.54 mmol, 3.0 equiv) and Et₂Zn (1.0 M in hexane, 0.54 mL, 0.54 mmol, 3.0 equiv) were successively added and the reaction mixture was stirred for 16 h at 0 °C. Et₂O (5 mL) and 1M aq. HCl (5 mL) were added. The aqueous layer was extracted with Et₂O (x3) and the combined organics were washed with brine, dried over MgSO₄ and concentrated under reduced pressure. The crude product contained *Z*-**89**, *E*-**89**, and *Z*-**90** in *Z*-**89**/*E*-**89**/*Z*-**90** = 35:6:59 ratio. Purification by flash chromatography on silica gel (pentane/Et₂O = 90:10) afforded two fractions containing mixtures of **89** and *Z*-**90**.

Fraction 1 (38 mg): **89** (32 mg, *Z/E* = 86:14, 34%) + *Z*-**90**ⁱ (6 mg, 13%).

Fraction 2 (24 mg): *Z*-**90** (18 mg, 39%) + **89** (6 mg, *Z/E* = 64:36, 6%).

Deuterium labeling:

The above-described procedure was followed, but D_2O (1 mL) was added and the mixture stirred for 1 h at rt prior to the acidic quench. The crude product contained *Z*-[²H]-**89** (80% D-incorporation), *E*-**89** (<10% D-incorporation), and *Z*-[²H]-**90**ⁱ (80% D-incorporation) in *Z*-[²H]-**89**/*E*-**89**/*Z*-[²H]-**90** = 34:5:61 ratio.

Methyl 4-((trimethylsilyl)methylene)-3-((triphenylgermyl)methyl)tetrahydrofuran-3-carboxylate (89):

Characterization data for both isomers of **89** could be extracted from the analysis of *Fraction 1.*

Z-**89**:

¹**H NMR** (400 MHz, CDCl₃): δ 7.53–7.51 (m, 6H, H-Ar), 7.38–7.36 (m, 9H, H-Ar), 5.72 (t, *J* = 2.4 Hz, 1H, H-5), 4.34 (t_{app}, *J* = 2.4 Hz, 2H, H-4), 4.12 (dd, *J* = 9.0 Hz, *J* = 1.0 Hz, 1H, H-1), 3.65 (d, *J* = 9.0 Hz, 1H, H-1'), 3.22 (s, 3H, H-8), 2.38 (dd, *J* = 14.0 Hz, *J* = 1.0 Hz, 1H, H-9), 1.93 (d, *J* = 14.0 Hz, 1H, H-9'), 0.07 (s, 9H, H-6).



89

C₂₉H₃₄GeO₃Si M.W. = 531.30 g⋅mol⁻¹

ⁱ Perez-Luna, A.; Botuha, C.; Ferreira, F.; Chemla, F. *Chem. Eur. J.* **2008**, *14*, 8784–8788.

¹³C{¹H} NMR (100 MHz, CDCl₃): δ 173.4 (C-7), 161.1 (C-2), 136.9 (C-10), 135.2 (C-Ar), 129.1 (C-Ar), 128.31 (C-Ar), 119.2 (C-5), 76.0 (C-1), 70.7 (C-4), 57.2 (C-3), 52.1 (C-8), 23.7 (C-9), -0.58 (C-6).

E-**89:**

¹**H NMR** (400 MHz, CDCl₃): δ 7.53–7.51 (m, 6H, H-Ar), 7.38–7.36 (m, 9H, H-Ar), 5.40 (t, *J* = 2.0 Hz, 1H, H-5), 4.32–4.30 (m, 1H, H-4), 4.23 (dd, *J* = 13.1 Hz, *J* = 2.0 Hz, 1H, H-4'), 3.97 (d, *J* = 9.0 Hz, 1H, H-1), 3.75 (d, *J* = 9.0 Hz, 1H, H-1'), 3.34 (s, 3H, H-8), 2.54 (dd, *J* = 13.9 Hz, *J* = 1.1 Hz, 1H, H-9), 2.00–1.90 (m, 1H, H-9'), 0.17 (s, 9H, H-6).

¹³C{¹H} NMR (100 MHz, CDCl₃): δ 174.0 (C-7), 161.6 (C-2), 137.3 (C-10), 135.3 (C-Ar), 129.0 (C-Ar), 128.3 (C-Ar), 119.9 (C-5), 79.3 (C-1), 75.5 (C-4), 55.5 (C-3), 52.2 (C-8), 23.5 (C-9), 0.9 (C-6).

HRMS (ESI): m/z calculated for $[C_{29}H_{34}GeO_3Si + Na]^+$ 555.1381; found 555.1388.

III-5.11. SILYLZINCATION OF YNAMIDE 54 IN THF





93

C₁₆H₃₇NO₂Si₄ M.W. = 387.81 g⋅mol⁻¹ **3-(2-(1,1,1,3,3,3-hexamethyl-2-(trimethylsilyl)trisilan-2-yl)vinyl)-4,4dimethyloxazolidin-2-one (93):** In a dry Schlenk tube under argon atmosphere, ynamide **54** (35 mg, 0.25 mmol, 1.0 equiv) was dissolved in dry THF (2 mL) and the solution was degassed by 3 freeze-pump-thaw cycles. At 0 °C, (Me₃Si)₃SiH (80 mg, 0.33 mmol, 1.3 equiv) and Et₂Zn (1.0 M in hexane, 0.75 mL, 0.75 mmol, 3.0 equiv) were successively added. The reaction mixture was stirred at this temperature for 3 h and then aq NH₄Cl/NH₃ (2:1) and CH₂Cl₂ were added. The layers were separated, the aqueous layer was extracted with CH₂Cl₂ (x3), and the combined organic layers were washed with brine (x2), dried over Na₂SO₄, filtered, and concentrated under reduce pressure to afford the crude product (*E*/*Z* = 90:10). Purification by flash chromatography on silica gel (pentane/Et₂O = gradient from 95:5 to 80:20) afforded analytically pure *Z*-**93**ⁱ (15 mg, 14%, *Z*/*E* > 98:2) and *E*-**93** (62 mg, 64%, *E*/*Z* > 98:2) as colorless liquids.

E-**93:**

¹**H NMR** (400 MHz, CDCl₃): δ 6.46 (d, *J* = 17.7 Hz, 1H, H-5), 5.22 (d, *J* = 17.7 Hz, 1H, H-6), 3.97 (s, 2H, H-2), 1.47 (s, 6H, H-4,4'), 0.18 (s, 27H, H-7).

JMod (100 MHz, CDCl₃): δ 155.1 (C-1), 132.2 (C-5), 100.4 (C-6), 75.2 (C-2), 58.7 (C-3), 25.2 (C-4,4'), 0.9 (C-7).

IR (neat): *v* (cm⁻¹) 2969, 2898, 1748, 1380, 1035, 938, 836, 693.

HRMS (ESI): m/z calculated for $[C_{16}H_{37}NO_2Si_4 + Na]^+$ 410.1794; found 410.1795.

E-**[**²**H]**-**93**: In a dry Schlenk tube under argon atmosphere, ynamide **54** (35 mg, 0.25 mmol, 1.0 equiv) was dissolved in dry THF (2 mL) and the solution was degassed by 3 freeze-pump-thaw cycles. At 0 °C, (Me₃Si)₃SiH (80 mg, 0.33 mmol, 1.3 equiv) and Et₂Zn (1.0 M in hexane, 0.75 mL, 0.75 mmol, 3.0 equiv) were successively added and the reaction mixture was stirred at this temperature for 3 h. A solution of ND₄Cl (300 mg) in D₂O (2 mL) was added and the mixture was stirred for 1 h at rt before adding aq NH₄Cl/NH₃ (2:1) and CH₂Cl₂. The layers were separated, the aqueous layer was extracted with CH₂Cl₂ (x3), and the combined organic layers were washed with brine (x2), dried over Na₂SO₄, filtered, and concentrated under reduce pressure to afford the crude product (*E*/*Z* = 95:5). Purification by flash chromatography on silica gel (pentane/Et₂O = gradient from 95:5 to 80:20) afforded analytically pure (*E*)-[²H]-**93** (68 mg, 70%, *E*/*Z* > 98:2).

¹**H NMR** (300 MHz, CDCl₃): δ 5.21 (t, *J* = 2.4 Hz, 1H), 3.98 (s, 2H), 1.47 (s, 6H), 0.18 (s, 27H).

¹³C{¹H} NMR (100 MHz, CDCl₃): δ 155.1, 131.9 (t, *J* = 27.2 Hz), 100.2, 75.2, 58.6, 25.2, 0.9.

HRMS (ESI): m/z calculated for $[C_{16}H_{36}DNO_2Si_4 + H]^+$ 389.2037; found 389.2039.





C₁₆H₃₆DNO₂Si₄ M.W. = 388.82 g·mol⁻¹

ⁱ Romain, E.; Fopp, C.; Chemla, F.; Ferreira, F.; Jackowski, O.; Oestreich, M.; Perez-Luna, A. *Angew. Chem. Int. Ed.* **2014**, *53*, 11333–11337.

III-5.12. GERMYLZINCATION OF CONVENTIONAL ALKYNES (GP XV AND XVI)



General Procedure for the Germylzincation of Conventional Alkynes (GP XV):

In a dry tube under argon atmosphere, the appropriate alkyne (0.25 mmol, 1.0 equiv), Ph_3GeH (153 mg, 0.50 mmol, 2.0 equiv), and AIBN (10–100 mol%) were dissolved in the appropriate solvent (0.64 mL). The tube was then sealed with a cap with septum, and Et₂Zn (1.0 M in hexane, 0.75 mL, 0.75 mmol, 3.0 equiv) was added at rt. The reaction mixture was either placed in an oil bath pre-heated at the suitable temperature or placed in the microwave reactor (Biotage, Model: INITIATOR ROBOT EIGHT 355380, 30310-38V), and stirred for the given reaction time. After cooling the reaction mixture to rt, aq NH₄Cl/NH₃ (2:1) and CH₂Cl₂ were added. The layers were separated, the aqueous layer was extracted with CH₂Cl₂ (x3), and the combined organic layers were washed with brine (x2), dried over Na₂SO₄, filtered, and concentrated under reduce pressure to afford the crude product.

General Procedure for the Germylzincation – D-labeling of Conventional Alkynes (GP XVI):



In a dry tube under argon atmosphere, the appropriate alkyne (0.25 mmol, 1.0 equiv), Ph_3GeH (153 mg, 0.50 mmol, 2.0 equiv), and AIBN (10–100 mol%) were dissolved in the appropriate solvent (0.64 mL). The tube was then sealed with a cap with septum, and Et₂Zn (1.0 M in hexane, 0.75 mL, 0.75 mmol, 3.0 equiv) was added at rt. The reaction mixture was either placed in an oil bath pre-heated at the suitable temperature or placed in the microwave reactor (Biotage, Model: INITIATOR ROBOT EIGHT 355380, 30310-38V), and stirred for the given reaction time. After cooling the reaction mixture to rt, a solution of ND₄Cl (300 mg) in D₂O (2 mL) was added (followed by THF (2 mL) 10 min after in the case that heptane was used as solvent), and the mixture was stirred for 1 h at rt before adding aq NH₄Cl/NH₃ (2:1) and CH₂Cl₂. The layers were separated, the aqueous layer was extracted with CH₂Cl₂ (x3), and the combined organic

layers were washed with brine (x2), dried over Na_2SO_4 , filtered, and concentrated under reduce pressure to afford the crude product.

(Z)-triphenyl(1-phenylprop-1-en-2-yl)germane (Z-252): Prepared according to GP XV using 1-phenyl-1-propyne 251 (29 mg, 0.25 mmol, 1.0 equiv) as substrate, Et₂Zn (1.0 M in hexane, 0.75 mL, 0.75 mmol, 3.0 equiv), Ph₃GeH (99 mg, 0.33 mmol, 1.3 equiv) in dry THF (2 mL) and a reaction time of 16 h at 40 °C. Purification of the crude product (Z/E = 90:10) by flash chromatography on silica gel (pentane/Et₂O = 99:1) afforded analytically pure Z-252 (42 mg, 40%, Z/E = 87:13) as a white solid. The spectral data were in good agreement with that previously reported.ⁱ

¹**H NMR** (400 MHz, CDCl₃): (*Z* isomer) δ 7.54 (s, 1H, H-5), 7.51–7.48 (m, 6H, H-Ar [Ph₃Ge]), 7.34–7.28 (m, 9H, H-Ar [Ph₃Ge]), 7.10–7.06 (m, 2H, H-Ar [Ph]), 6.91–6.81 (m, 3H, H-Ar [Ph]), 2.09 (d, *J* = 1.8 Hz, 3H, H-7).

¹³C{¹H} NMR (100 MHz, CDCl₃): (*Z* isomer) δ 143.1 (C-5), 138.1, 137.1, 135.2, 135.0, 128.7, 128.6, 128.1, 127.4, 126.8, 28.0 (C-7).

Z-**[**²**H]**-**252**: Prepared according to **GP XVI** using 1-phenyl-1-propyne **251** (29 mg, 0.25 mmol, 1.0 equiv) as substrate, Et₂Zn (1.0 M in hexane, 0.75 mL, 0.75 mmol, 3.0 equiv), Ph₃GeH (99 mg, 0.33 mmol, 1.3 equiv) in dry THF (2 mL) and a reaction time of 16 h at 40 °C. Purification of the crude product (*Z*/*E* = 90:10) by flash chromatography on silica gel (eluent pentane:Et₂O = 99:1) afforded analytically pure *Z*-[²H]-**252** (45 mg, 43%, *Z*/*E* = 91:9) as a white solid.

¹**H NMR** (400 MHz, CDCl₃): (*Z* isomer) δ 7.52–7.50 (m, 6H), 7.36–7.29 (m, 9H), 7.11–7.09 (m, 2H), 6.93–6.83 (m, 3H), 2.11 (s, 3H).

¹³C{¹H} NMR (100 MHz, CDCl₃): (Z isomer) δ 138.0, 137.1, 135.2, 134.9, 128.7, 128.6, 128.1, 127.4, 126.8, 27.9. One C is not observed.

HRMS (ESI): *m*/*z* calculated for [C₂₇H₂₃DGe + K]⁺ 462.0784; found 462.0786.





C₂₇H₂₄Ge M.W. = 421.12 g⋅mol⁻¹



C₂₇H₂₃DGe M.W. = 422.13 g⋅mol⁻¹

ⁱ Schwier, T.; Gevorgyan, V. *Org Lett.* **2005**, *7*, 5191–5194.



E-**252**

C₂₇H₂₄Ge M.W. = 421.12 g⋅mol⁻¹

(*E*)-triphenyl(1-phenylprop-1-en-2-yl)germane (*E*-252): Prepared according to **GP XV** using 1-phenyl-1-propyne **251** (29 mg, 0.25 mmol, 1.0 equiv) as substrate, Et₂Zn (1.0 M in hexane, 0.75 mL, 0.75 mmol, 3.0 equiv), Ph₃GeH (153 mg, 0.50 mmol, 2.0 equiv), AIBN (4 mg, 0.03 mmol, 10 mol%) in heptane (0.64 mL) and a reaction time of 2 h at 100 °C. Purification of the crude product (*E*/*Z* = 95:5) by flash chromatography on silica gel (pentane/toluene = 90:10) afforded analytically pure *E*-**252** (98 mg, 93%, β/α = 97:3, *E*/*Z* = 96:4) as a white solid; mp 165–168 °C.

¹**H NMR** (400 MHz, CDCl₃): (*E* isomer) δ 7.67–7.64 (m, 6H, H-Ar [Ph₃Ge]), 7.49–7.45 (m, 9H, H-Ar [Ph₃Ge]), 7.42–7.37 (m, 4H, H-Ar [Ph]), 7.31–7.28 (m, 1H, H-Ar [Ph]), 6.91 (q, *J* = 1.8 Hz, 1H, H-5), 2.26 (d, *J* = 1.8 Hz, 3H, H-7).

¹³C{¹H} NMR (100 MHz, CDCl₃): (*E* isomer) δ 141.0 (C-5), 138.0, 136.7, 136.2, 135.6, 129.18, 129.17, 128.4, 128.2, 126.9, 19.1 (C-7).

IR (neat): v (cm⁻¹) 3067, 3049, 3022, 1485, 1430, 1090, 735, 698.

HRMS: Ionization was not achieved with APCI.

The E configuration was determined by X-ray crystallographic analysis.



Me Ph₃Ge

E-[²H]-**252**

C₂₇H₂₃DGe M.W. = 422.13 g⋅mol⁻¹ *E*-**[**²**H]**-**252**: Prepared according to **GP XVI** using 1-phenyl-1-propyne **251** (29 mg, 0.25 mmol, 1.0 equiv) as substrate, Et₂Zn (1.0 M in hexane, 0.75 mL, 0.75 mmol, 3.0 equiv), Ph₃GeH (153 mg, 0.50 mmol, 2.0 equiv), AIBN (4 mg, 0.03 mmol, 10 mol%) in heptane (0.64 mL) and a reaction time of 2 h at 100 °C. Purification of the crude product (*E*/*Z* = 98:2) by flash chromatography on silica gel (pentane/toluene = 90:10) afforded analytically pure *E*-[²H]-**252** (104 mg, 99%, *E*/*Z* = 97:3) as a white solid.

¹**H NMR** (400 MHz, CDCl₃): (*E* isomer) δ 7.67–7.65 (m, 6H, H-Ar [Ph₃Ge]), 7.50–7.45 (m, 9H, H-Ar [Ph₃Ge]), 7.42–7.38 (m, 4H, H-Ar [Ph]), 7.32–7.28 (m, 1H, H-Ar [Ph]), 2.26 (s, 3H, H-7).

¹³C{¹H} NMR (100 MHz, CDCl₃): (*E* isomer) δ 137.9, 136.5, 136.2, 135.6, 129.2, 129.17, 128.4, 128.2, 126.9, 19.0 (C-7). One C is not observed.

HRMS: Ionization was not achieved with APCI.

(*E*)-triphenyl(1-phenylbut-1-en-2-yl)germane (260): Prepared according to **GP XV** using 1-phenyl-1-butyne **259** (130 mg, 1.00 mmol, 1.0 equiv) as substrate, Et₂Zn (1.0 M in hexane, 3.00 mL, 3.00 mmol, 3.0 equiv), Ph₃GeH (305 mg, 2.00 mmol, 2.0 equiv), AIBN (41 mg, 0.25 mmol, 25 mol%) in heptane (5.6 mL) and a reaction time of 5 h at 100 °C. Purification of the crude product (*E*/*Z* = 95:5) by flash chromatography on silica gel (pentane/toluene = 90:10) afforded analytically pure **260** (409 mg, 94%, β/α = 95:5, *E*/*Z* = 95:5) as a white solid; mp 112–115 °C.

¹**H NMR** (400 MHz, CDCl₃): (*β*,*E* isomer) δ 7.51–7.49 (m, 6H, H-Ar [Ph₃Ge]), 7.30–7.25 (m, 9H, H-Ar [Ph₃Ge]), 7.24–7.20 (m, 4H, H-Ar [Ph]), 7.17–7.10 (m, 1H, H-Ar [Ph]), 6.73 (t, *J* = 1.0 Hz, 1H, H-5), 2.47 (qd, *J* = 7.5 Hz, *J* = 1.0 Hz, 2H, H-7), 0.84 (t, *J* = 7.5 Hz, 3H, H-8).

¹³C{¹H} NMR (100 MHz, CDCl₃): (*β*,*E* isomer) δ 143.5, 140.9 (C-5), 138.0, 136.8, 135.6, 129.1, 128.8, 128.4, 128.3, 127.0, 25.1 (C-7), 14.8 (C-8).

IR (neat): v (cm⁻¹) 3067, 3049, 2963, 1485, 1430, 1089, 734, 697.

HRMS (ESI): *m*/*z* calculated for [C₂₈H₂₆Ge + K]⁺ 475.0878; found 475.0879.

The E configuration was assigned by analogy with E-252.

(*Z*)-3-phenyl-2-(triphenylgermyl)prop-2-en-1-ol (265): Prepared according to **GP XV** using 3-phenylprop-2-yn-1-ol **261** (33 mg, 0.25 mmol, 1.0 equiv) as substrate, Et₂Zn (1.0 M in hexane, 0.75 mL, 0.75 mmol, 3.0 equiv), Ph₃GeH (153 mg, 0.50 mmol, 2.0 equiv), AIBN (10 mg, 0.06 mmol, 25 mol%) in heptane (0.64 mL) and a reaction time of 2 h at 100 °C. Purification of the crude product (*Z*/*E* > 98:2) by flash chromatography on silica gel (toluene/Et₂O = 90:10) afforded analytically pure **265** (96 mg, 87%, β/α > 98:2, *Z*/*E* > 98:2) as a colorless liquid.





C₂₈H₂₆Ge M.W. = 435.15 g⋅mol⁻¹



265

C₂₇H₂₄GeO M.W. = 437.12 g⋅mol⁻¹

¹**H NMR** (400 MHz, CDCl₃): δ 7.75 (s, 1H, H-5), 7.58–7.56 (m, 6H, H-Ar [Ph₃Ge]), 7.40–7.30 (m, 9H, H-Ar [Ph₃Ge]), 7.20–7.18 (m, 2H, H-Ar [Ph]), 7.00–6.96 (m, 1H, H-Ar [Ph]), 6.93–6.90 (m, 2H, H-Ar [Ph]), 4.39 (s, 2H, H-7), 1.61 (br s, 1H, H-8).

¹³C{¹H} NMR (100 MHz, CDCl₃): δ 143.2 (C-5), 138.2, 137.3, 136.6, 135.2, 129.0, 128.8, 128.3, 127.5, 127.4, 69.9 (C-7).

IR (neat): v (cm⁻¹) 3302 (br), 3022, 1485, 1430, 1088, 908, 732, 695.

HRMS (ESI): *m*/*z* calculated for [C₂₇H₂₄GeO + K]⁺ 477.0671; found 477.0674.

The Z configuration was assigned on the basis of the chemical shift of H-5 (7.75 ppm). The chemical shift of H-5 for the other (E) isomer was found at 6.98 ppm.



266

C₂₈H₂₆GeO M.W. = 451.15 g⋅mol⁻¹ (*Z*)-3-phenyl-2-(triphenylgermyl)prop-2-en-1-ol (266): Prepared according to **GP XV** using 4-phenylbut-3-yn-2-ol **262** (37 mg, 0.25 mmol, 1.0 equiv) as substrate, Et₂Zn (1.0 M in hexane, 0.75 mL, 0.75 mmol, 3.0 equiv), Ph₃GeH (153 mg, 0.50 mmol, 2.0 equiv), AIBN (10 mg, 0.06 mmol, 25 mol%) in heptane (0.64 mL) and a reaction time of 2 h at 100 °C. Purification of the crude product (*Z/E* > 98:2) by flash chromatography on silica gel (pentane/Et₂O/toluene = 75:15:10) afforded analytically pure **266** (94 mg, 83%, β/α > 98:2, *Z/E* > 98:2) as a colorless liquid.

¹**H NMR** (400 MHz, CDCl₃): δ 7.84 (s, 1H, H-5), 7.56–7.55 (m, 6H, H-Ar [Ph₃Ge]), 7.37–7.30 (m, 9H, H-Ar [Ph₃Ge]), 7.17–7.15 (m, 2H, H-Ar [Ph]), 6.94–6.90 (m, 1H, H-Ar [Ph]), 6.87–6.84 (m, 2H, H-Ar [Ph]), 4.60 (q, *J* = 6.4 Hz, 1H, H-7), 1.70 (br s, 1H, H-9), 1.36 (d, *J* = 6.4 Hz, 3H, H-8).

¹³C{¹H} NMR (100 MHz, CDCl₃): δ 143.2, 140.6 (C-5), 137.3, 137.1, 135.3, 128.9, 128.85, 128.2, 127.4, 127.2, 72.4 (C-7), 24.4 (C-8).

IR (neat): v (cm⁻¹) 3322 (br), 3023, 1485, 1430, 1088, 908, 732, 696.

HRMS (ESI): *m*/*z* calculated for [C₂₈H₂₆GeO + K]⁺ 491.0827; found 491.0832.

The Z configuration was assigned by analogy with Z-265.

Triphenyl(1-phenylpropa-1,2-dien-1-yl)germane (274): Prepared according to **GP XV** using 3-phenylprop-2-yn-1-yl acetate **272** (44 mg, 0.25 mmol, 1.0 equiv) as substrate, Et₂Zn (1.0 M in hexane, 0.75 mL, 0.75 mmol, 3.0 equiv), Ph₃GeH (153 mg, 0.50 mmol, 2.0 equiv), AIBN (10 mg, 0.06 mmol, 25 mol%) in heptane (0.64 mL) and a reaction time of 2 h at 100 °C. Purification of the crude product by flash chromatography on silica gel (pentane/toluene = 92:8) afforded analytically pure **274** (59 mg, 56%) as a white solid; mp 119–121 °C.

¹**H NMR** (400 MHz, CDCl₃): δ 7.46–7.44 (m, 6H, H-Ar [Ph₃Ge]), 7.30–7.20 (m, 11H, H-Ar [Ph₃Ge] + [Ph]), 7.08–7.01 (m, 3H, H-Ar [Ph]), 4.53 (s, 2H, H-7).

¹³C{¹H} NMR (100 MHz, CDCl₃): δ 211.4 (C-6), 136.5, 136.2, 135.4, 129.3, 128.5, 128.4, 128.3, 126.6, 95.7 (C-5), 72.6 (C-7).

IR (neat): v (cm⁻¹) 3067, 3050, 1920, 1486, 1431, 1090, 735, 696.

HRMS (ESI): *m*/*z* calculated for [C₂₇H₂₂Ge + K]⁺ 459.0565; found 459.0570.

(Z)-(1,2-diphenylvinyl)triphenylgermane (Z-278): Prepared according to GP XV using diphenylacetylene 277 (45 mg, 0.25 mmol, 1.0 equiv) as substrate, Et₂Zn (1.0 M in hexane, 0.75 mL, 0.75 mmol, 3.0 equiv), Ph₃GeH (153 mg, 0.50 mmol, 2.0 equiv), AIBN (10 mg, 0.06 mmol, 25 mol%) in dry THF (0.64 mL) and a reaction time of 1 h at 80 °C. Purification of the crude product by flash chromatography on silica gel (gradient from pentane to pentane/Et₂O = 99:1) afforded analytically pure Z-278 (81 mg, 67%, *Z/E* = 92:8) as a white solid; mp 104–106 °C.

¹**H NMR** (400 MHz, CDCl₃): (*Z* isomer) δ 7.54 (s, 1H, H-5), 7.31–7.27 (m, 6H, H-Ar [Ph₃Ge]), 7.16–7.03 (m, 13H, H-Ar [Ph₃Ge] + [Ph]), 7.01–6.95 (m, 3H, H-Ar [Ph]), 6.82–6.78 (m, 1H, H-Ar [Ph]), 6.76–6.72 (m, 2H, H-Ar [Ph]).

¹³C{¹H} NMR (100 MHz, CDCl₃): (*Z* isomer) δ 146.3 (C-5), 146.1, 141.3, 137.6, 137.2, 135.3, 128.9, 128.6, 128.3, 128.0, 127.8, 127.5, 127.3, 126.1.

IR (neat): v (cm⁻¹) 3051, 1595, 1496, 1431, 1089, 763, 734, 696.

HRMS (APCI): *m*/*z* calculated for [C₃₂H₂₆Ge]⁺ 484.1241; found 484.1239.

The Z configuration was assigned by analogy with Z-252.



C₂₇H₂₂Ge M.W. = 419.10 g⋅mol⁻¹



Z-278

C₃₂H₂₆Ge M.W. = 483.19 g⋅mol⁻¹



Z-[2H]-278

C₃₂H₂₅DGe M.W. = 484.20 g⋅mol⁻¹ *Z*-[²H]-278: Prepared according to **GP XVI** using diphenylacetylene 277 (45 mg, 0.25 mmol, 1.0 equiv) as substrate, Et₂Zn (1.0 M in hexane, 0.75 mL, 0.75 mmol, 3.0 equiv), Ph₃GeH (153 mg, 0.50 mmol, 2.0 equiv), AIBN (10 mg, 0.06 mmol, 25 mol%) in dry THF (0.64 mL) and a reaction time of 1 h at 80 °C. Purification of the crude product by flash chromatography on silica gel (gradient from pentane to pentane/Et₂O = 99:1) afforded analytically pure *Z*-[²H]-**278** (86 mg, 71%, *Z*/*E* = 92:8) as a white solid.

¹**H NMR** (400 MHz, CDCl₃): (*Z* isomer) δ 7.31–7.26 (m, 6H), 7.16–7.02 (m, 13H), 7.01–6.93 (m, 3H), 6.82–6.78 (m, 1H), 6.76–6.71 (m, 2H).

¹³C{¹H} NMR (100 MHz, CDCl₃): (*Z* isomer) δ 146.1, 141.2, 137.5, 137.1, 135.3, 128.9, 128.6, 128.3, 128.0, 127.8, 127.5, 127.3, 126.0. One C is not observed.

HRMS (ESI): m/z calculated for $[C_{32}H_{25}DGe + NH_4]^+$ 503.1647; found 503.1648.

(*E*)-(1,2-diphenylvinyl)triphenylgermane (*E*-278): Prepared by hydrogermylation under excess-Ph₃GeH regime, using diphenylacetylene 277 (43 mg, 0.24 mmol, 1.0 equiv) as substrate, Ph₃GeH (150 mg, 0.42 mmol, 1.8 equiv), AIBN (4 mg, 0.03 mmol, 10 mol%) in heptane (1.4 mL) and a reaction time of 2 h at 100 °C. Purification of the crude product by flash chromatography on silica gel (gradient from pentane to pentane/Et₂O = 99:1) afforded analytically pure *E*-278 (104 mg, 90%, *E*/*Z* > 98:2) as a white solid; mp 92–95 °C.

¹**H NMR** (400 MHz, CDCl₃): δ 7.46–7.44 (m, 6H, H-Ar [Ph₃Ge]), 7.43–7.33 (m, 9H, H-Ar [Ph₃Ge]), 7.17–7.15 (m, 3H, H-Ar [Ph]), 7.12–7.11 (m, 3H, H-Ar [Ph]), 7.03–6.97 (m, 4H, H-Ar [Ph]), 6.92 (s, 1H, H-5).

¹³C{¹H} NMR (100 MHz, CDCl₃): δ 142.6, 142.2, 140.6 (C-5), 137.1, 136.1, 135.7, 129.7, 129.2, 128.7, 128.3, 128.1, 128.08, 127.4, 126.2.

The E configuration was assigned by analogy with E-252.

(Z)-(1,2-bis(4-butylphenyl)vinyl)triphenylgermane (287): Prepared according to GP XV using 1,2-bis(4-butylphenyl)ethyne 280 (73 mg, 0.25 mmol, 1.0 equiv) as substrate, Et_2Zn (1.0 M in hexane, 0.75 mL, 0.75 mmol, 3.0 equiv), Ph₃GeH (153 mg, 0.50 mmol, 2.0 equiv), AIBN (10 mg, 0.06 mmol, 25



E-278

C₃₂H₂₆Ge M.W. = 483.19 g⋅mol⁻¹ mol%) in dry THF (0.64 mL) and a reaction time of 1 h at 80 °C. Purification of the crude product by flash chromatography on silica gel (pentane/toluene = 90:10) afforded analytically pure **287** (101 mg, 68%, Z/E = 90:10) as a white solid; mp 75–78 °C.

¹**H NMR** (400 MHz, CDCl₃): (*Z* isomer) δ 7.70 (s, 1H, H-9), 7.50–7.45 (m, 6H, H-Ar [Ph₃Ge]), 7.33–7.24 (m, 9H, H-Ar [Ph₃Ge]), 7.16–7.11 (m, 4H, H-Ar [Ph]), 6.99–6.97 (m, 2H, H-Ar [Ph]), 6.74–6.72 (m, 2H, H-Ar [Ph]), 2.58 (t, *J* = 7.6 Hz, 2H, H-4 or H-15), 2.45 (t, *J* = 7.6 Hz, 2H, H-15 or H-4), 1.59 (quint, *J* = 7.6 Hz, 2H, H-3 or H-16), 1.49 (quint, *J* = 7.6 Hz, 2H, H-16 or H-3), 1.39–1.28 (m, 4H, H-2, H-17), 0.98 (td, *J* = 7.3 Hz, *J* = 2.9 Hz, 6H, H-1, H-18).

¹³C{¹H} NMR (100 MHz, CDCl₃): (*Z* isomer) δ 145.9 (C-9), 143.5, 141.9, 140.5, 140.2, 137.5, 135.7, 135.3, 128.8, 128.5, 128.2, 127.9, 127.87, 127.5, 35.32 (C-4 or C-15), 35.3 (C-15 or C-4), 33.7 (C-3 or C-16), 33.5 (C-16 or C-3), 22.3 (C-2 or C-17), 22.2 (C-17 or C-2), 14.1 (C-1, C-18).

IR (neat): v (cm⁻¹) 2955, 2927, 2856, 1430, 1088, 907, 732, 697.

HRMS (APCI): *m*/*z* calculated for [C₄₀H₄₂Ge + H]⁺ 597.2571; found 597.2557.

The Z configuration was assigned by analogy with Z-252.

(Z)-(1,2-bis(4-bromophenyl)vinyl)triphenylgermane (288): Prepared according to GP XV using 1,2-bis(4-bromophenyl)ethyne 281 (84 mg, 0.25 mmol, 1.0 equiv) as substrate, Et₂Zn (1.0 M in hexane, 0.75 mL, 0.75 mmol, 3.0 equiv), Ph₃GeH (153 mg, 0.50 mmol, 2.0 equiv), AIBN (10 mg, 0.06 mmol, 25 mol%) in dry THF (0.64 mL) and a reaction time of 1 h at 80 °C. Purification of the crude product by flash chromatography on silica gel (pentane/toluene = 90:10) afforded analytically pure **288** (105 mg, 66%, *Z/E* = 87:13) as a white solid; mp 205–208 °C.

¹**H NMR** (400 MHz, CDCl₃): (*Z* isomer) δ 7.42 (s, 1H, H-5), 7.27–7.25 (m, 6H, H-Ar [Ph₃Ge]), 7.20–7.18 (m, 2H, H-Ar [Ph]), 7.14–7.10 (m, 9H, H-Ar [Ph₃Ge]), 6.90–6.88 (m, 2H, H-Ar [Ph]), 6.87–6.81 (m, 4H, H-Ar [Ph]).

¹³C{¹H} NMR (100 MHz, CDCl₃): (*Z* isomer) δ 145.3 (C-5), 144.7, 141.8, 136.4, 135.1, 130.9, 130.6, 130.3, 129.9, 128.9, 128.2, 128.1, 121.7 (C-1 or C-10), 120.3 (C-10 or C-1).

IR (neat): v (cm⁻¹) 2997, 2956, 1484, 1431, 1089, 826, 733, 697.



C₄₀H₄₂Ge M.W. = 595.40 g⋅mol⁻¹



288

C₃₂H₂₄Br₂Ge M.W. = 640.98 g·mol⁻¹

HRMS: Ionization was not achieved with ESI.

The Z configuration was assigned by analogy with Z-252.



289



(Z)-(1,2-bis(4-(trifluoromethyl)phenyl)vinyl)triphenylgermane (289): Prepared according to GP XV using 1,2-bis(4-(trifluoromethyl)phenyl)ethyne 282 (79 mg, 0.25 mmol, 1.0 equiv) as substrate, Et₂Zn (1.0 M in hexane, 0.75 mL, 0.75 mmol, 3.0 equiv), Ph₃GeH (153 mg, 0.50 mmol, 2.0 equiv), AIBN (10 mg, 0.06 mmol, 25 mol%) in dry THF (0.64 mL) and a reaction time of 1 h at 80 °C. Purification of the crude product by flash chromatography on silica gel (cyclohexane/toluene = 90:10) afforded analytically pure **289** (128 mg, 83%, *Z/E* > 98:2) as white crystals; mp 164–166 °C.

¹**H NMR** (400 MHz, CDCl₃): δ 7.46–7.36 (m, 19H, H-Ar [Ph₃Ge] + [Ph]), 7.07 (d, *J* = 8.2 Hz, 2H, H-Ar [Ph]), 7.03 (d, *J* = 8.0 Hz, 2H, H-Ar [Ph]), 7.00 (s, 1H, H-5).

¹³C{¹H} NMR (100 MHz, CDCl₃): δ 145.7, 144.9, 140.0, 139.8 (C-5), 135.6, 135.1, 134.9, 132.1, 129.7, 129.6, 128.6, 128.3, 125.8 (C-1 or C-10, q, *J* = 3.6 Hz), 125.2 (C-10 or C-1, q, *J* = 3.8 Hz). *Two C are not observed (CF₃).*

¹⁹**F**{¹**H**} **NMR** (376 MHz, CDCl₃): δ –62.7, –62.4.

(2-(4-methoxyphenyl)-1-(4-(trifluoromethyl)phenyl)vinyl)



¹**H NMR** (400 MHz, CDCl₃): δ 7.46 (s), 7.33 (s), 7.31–7.00 (m), 6.81–6.74 (m), 6.61–6.53 (m), 6.30–6.26 (m), 3.63 (s, OMe), 3.60 (s, OMe), 3.59 (s, OMe), 3.49 (s, OMe).





C₃₄H₂₇F₃GeO M.W. = 581.21 g⋅mol⁻¹ ¹⁹**F**{¹**H**} **NMR** (376 MHz, CDCl₃): δ –62.7, –62.5, –62.24, –62.2.

(Z)-3-(2-phenyl-2-(triphenylgermyl)vinyl)pyridine / (Z)-3-(2-phenyl-1-(triphenylgermyl)vinyl)pyridine (292): Prepared according to GP XV using 3-(phenylethynyl)pyridine 285 (45 mg, 0.25 mmol, 1.0 equiv) as substrate, Et₂Zn (1.0 M in hexane, 0.75 mL, 0.75 mmol, 3.0 equiv), Ph₃GeH (153 mg, 0.50 mmol, 2.0 equiv), AIBN (10 mg, 0.06 mmol, 25 mol%) in dry THF (0.64 mL) and a reaction time of 1 h at 80 °C. Purification of the crude product by flash chromatography on silica gel (pentane/toluene/Et₂O = 50:30:20) afforded **292** (123 mg, 99%) as mixture of regioisomers in a 65:35 ratio. An analytically pure fraction of the major regioisomer was isolated in 57% yield (70 mg, *Z*/*E* > 98:2) as a white solid; mp 169–172°C.

¹H and ¹³C NMR spectra are reported for the major isomer (configuration to be determined).

¹**H NMR** (400 MHz, CDCl₃): δ 8.27 (dd, *J* = 4.8 Hz, *J* = 2.0 Hz, 1H, H-3), 8.13 (d, *J* = 2.0 Hz, 1H, H-1), 7.38–7.35 (m, 6H, H-Ar [Ph₃Ge]), 7.30–7.24 (m, 9H, H-Ar [Ph₃Ge]), 7.11 (dt, *J* = 7.8 Hz, *J* = 2.0 Hz, 1H, H-5), 7.03–7.00 (m, 3H, H-Ar [Ph]), 6.95 (s, 1H, H-7), 6.95–6.92 (m, 1H, H-4), 6.89–6.85 (m, 2H, H-Ar [Ph]).

¹³C{¹H} NMR (100 MHz, CDCl₃): δ 149.1, 147.3, 142.8 (C-7), 138.6, 138.1, 136.5, 135.7, 135.6, 135.2, 129.6, 129.4, 128.5, 128.3, 127.8, 123.3.

IR (neat): v (cm⁻¹) 3068, 3049, 1484, 1431, 1090, 1025, 734, 697.

2-(2-(*p*-tolyl)-2-(triphenylgermyl)vinyl)pyridine / 2-(2-(*p*-tolyl)-1-(triphenylgermyl)vinyl)pyridine (293): Prepared according to GP XV using 2-(*p*-tolylethynyl)pyridine 286 (49 mg, 0.25 mmol, 1.0 equiv) as substrate, Et₂Zn (1.0 M in hexane, 0.75 mL, 0.75 mmol, 3.0 equiv), Ph₃GeH (153 mg, 0.50 mmol, 2.0 equiv), AIBN (10 mg, 0.06 mmol, 25 mol%) in dry THF (0.64 mL) and a reaction time of 1 h at 80 °C. Purification of the crude product (mixture of regio- and diastereosiomers in a 54:24:11:11 ratio) by flash chromatography on silica gel (cyclohexane/EtOAc = 95:5) afforded 293 (56 mg, 45%) as a single diastereoisomer (configuration to be determined); yellow oil.





C₃₁H₂₅GeN M.W. = 484.18 g⋅mol⁻¹



293

C₃₂H₂₇GeN M.W. = 498.20 g⋅mol⁻¹

¹**H NMR** (400 MHz, CDCl₃): δ 8.47 (dt, *J* = 5.0 Hz, *J* = 1.2 Hz, 1H, H-2), 7.53–7.51 (m, 6H, H-Ar [Ph₃Ge]), 7.39–7.31 (m, 10H), 7.00–6.97 (m, 2H, H-Ar), 6.95–6.91 (m, 3H, H-Ar), 6.86–6.84 (m, 2H, H-Ar).

¹³C{¹H} NMR (100 MHz, CDCl₃): δ 137.8, 135.5, 135.0, 134.1, 133.7, 131.0, 130.5, 129.3, 129.0, 128.8, 128.7, 128.6, 128.2, 128.15, 121.0, 21.2 (C-13).

(Z)-oct-4-en-4-yltriphenylgermane (295): Prepared according to GP XV using 4-octyne 294 (28 mg, 0.25 mmol, 1.0 equiv) as substrate, Et₂Zn (1.0 M in hexane, 0.75 mL, 0.75 mmol, 3.0 equiv), Ph₃GeH (153 mg, 0.50 mmol, 2.0 equiv), AIBN (41 mg, 0.25 mmol, 100 mol%) in dry THF (0.64 mL). *The reaction mixture was then heated in the microwave at 80 °C (50 W) for 1 h (normal absorption level).* Purification of the crude product (Z/E = 91:9) by flash chromatography on silica gel (pentane/toluene = 90:10) afforded analytically pure 295 (60 mg, 58%, Z/E = 96:4) as a colorless liquid.

¹**H NMR** (400 MHz, CDCl₃): (*Z* isomer) δ 7.58–7.54 (m, 6H, H-Ar), 7.38–7.34 (m, 9H, H-Ar), 6.27 (tt, *J* = 7.4 Hz, *J* = 1.2 Hz, 1H, H-4), 2.13–2.09 (m, 2H, H-6), 1.84 (q, *J* = 7.4 Hz, 2H, H-3), 1.28–1.12 (m, 4H, H-2,7), 0.69 (t, *J* = 7.4 Hz, 3H, H-8), 0.58 (t, *J* = 7.4 Hz, 3H, H-1).

¹³C{¹H} NMR (100 MHz, CDCl₃): (*Z* isomer) δ 143.4 (C-4), 137.9 (C-9 or C-5), 136.0 (C-5 or C-9), 135.3 (C-Ar), 128.8 (C-Ar), 128.2 (C-Ar), 41.1 (C-6), 35.6 (C-3), 23.7 (C-7), 22.8 (C-2), 13.74 (C-1 or C-8), 13.7 (C-8 or C-1).

IR (neat): v (cm⁻¹) 2997, 2958, 2870, 1460, 1431, 1089, 735, 699.

HRMS (ESI): *m*/*z* calculated for [C₂₆H₃₀Ge + Na]⁺ 439.1452; found 439.1451.



[²H]-295

C₂₆H₂₉DGe M.W. = 416.16 g⋅mol⁻¹ [²H]-295: Prepared according to **GP XVI** using 4-octyne **294** (28 mg, 0.25 mmol, 1.0 equiv) as substrate, Et₂Zn (1.0 M in hexane, 0.75 mL, 0.75 mmol, 3.0 equiv), Ph₃GeH (153 mg, 0.50 mmol, 2.0 equiv), AIBN (41 mg, 0.25 mmol, 100 mol%) in dry THF (0.64 mL). *The reaction mixture was then heated in the microwave at 80 °C (50 W) for 1 h (normal absorption level).* Purification of the crude product by flash chromatography on silica gel (pentane/toluene = 90:10) afforded analytically pure [²H]-**295** (64 mg, 62%, *Z/E* = 89:11) as a colorless liquid.



295

C₂₆H₃₀Ge M.W. = 415.16 g⋅mol⁻¹ ¹**H NMR** (400 MHz, CDCl₃): (*Z* isomer) δ 7.57–7.54 (m, 6H), 7.40–7.33 (m, 9H), 2.12–2.08 (m, 2H), 1.83 (t, *J* = 7.4 Hz, 2H), 1.28–1.11 (m, 4H), 0.69 (t, *J* = 7.4 Hz, 3H), 0.58 (t, *J* = 7.4 Hz, 3H).

¹³C{¹H} NMR (100 MHz, CDCl₃): (Z isomer) δ 137.9, 135.9, 135.3, 128.8, 128.2,
41.0, 35.5, 23.7, 22.8, 13.74, 13.7. One C is not observed.

HRMS (ESI): *m*/*z* calculated for [C₂₆H₂₉DGe + Na]⁺ 440.1514; found 440.1514.

Triphenyl(1-phenylpropa-1,2-dien-1-yl)germane (309): Prepared according to **GP XV** using 1,4-dichlorobut-2-yne **300** (31 mg, 0.25 mmol, 1.0 equiv) as substrate, Et₂Zn (1.0 M in hexane, 0.75 mL, 0.75 mmol, 3.0 equiv), Ph₃GeH (153 mg, 0.50 mmol, 2.0 equiv), AIBN (41 mg, 0.25 mmol, 100 mol%) in dry THF (0.64 mL). *The reaction mixture was then heated in the microwave at 80 °C (50 W) for 1 h (normal absorption level).* Purification of the crude product by flash chromatography on silica gel (pentane/toluene = 90:10) afforded analytically pure **309** (50 mg, 51%) as a white solid; mp 94–96 °C.



309

C₂₂H₁₉ClGe M.W. = 391.48 g⋅mol⁻¹

¹**H NMR** (400 MHz, CDCl₃): δ 7.62–7.59 (m, 6H, H-Ar), 7.47–7.40 (m, 9H, H-Ar), 4.71 (t, *J* = 2.6 Hz, 2H, H-4), 4.18 (t, *J* = 2.6 Hz, 2H, H-1).

¹³C{¹H} NMR (100 MHz, CDCl₃): δ 210.6 (C-3), 135.3 (C-Ar), 135.0 (C-5), 129.6 (C-Ar), 128.4 (C-Ar), 91.6 (C-2), 73.4 (C-4), 44.9 (C-1).

IR (neat): v (cm⁻¹) 3068, 3049, 1930, 1484, 1431, 1091, 735, 698.

HRMS (ESI): *m*/*z* calculated for [C₂₂H₁₉ClGe + Na]⁺ 415.0279; found 415.0282.

(4-methylpent-2-en-2-yl)triphenylgermane / (4-methylpent-2-en-3yl)triphenylgermane (310): Prepared according to GP XV using 4methylpent-2-yne 301 (21 mg, 0.25 mmol, 1.0 equiv) as substrate, Et₂Zn (1.0 M in hexane, 0.75 mL, 0.75 mmol, 3.0 equiv), Ph₃GeH (153 mg, 0.50 mmol, 2.0 equiv), AIBN (4 mg, 0.025 mmol, 10 mol%) in heptane (0.64 mL). *The reaction mixture was then heated in the microwave at 100 °C (160 W) for 1 h (normal absorption level)*. Purification of the crude product (β ,*Z*/ β ,*E*/ α ,*Z*/ α ,*E* = 40:4:35:21) by flash chromatography on silica gel (pentane) afforded 310 (54 mg, 56%, β ,*Z*/ β ,*E*/ α ,*Z*/ α ,*E* = 44:4:35:17), contaminated with remaining Ph₃GeH. A second fraction containing compound 312 (14 mg, 8%, *E*/*Z* > 98:2) was also isolated.



 α isomer

310

C₂₄H₂₆Ge M.W. = 387.10 g⋅mol⁻¹







 α isomer

311

C₂₅H₂₈Ge M.W. = 401.13 g⋅mol⁻¹

¹**H NMR** (400 MHz, CDCl₃): δ 7.65–7.58 (m, 6H, H-Ar **310** + Ph₃GeH), 7.44– 7.39 (m, 9H, H-Ar **310** + Ph₃GeH), 6.49 (qd, *J* = 6.9 Hz, *J* = 1.2 Hz, 1H, H-4_{*α*,*Z*-isomer}), 6.10 (dq, *J* = 10.3 Hz, *J* = 1.6 Hz, 1H, H-3_{*β*,*Z*-isomer}), 5.85 (qd, *J* = 6.7 Hz, *J* = 0.8 Hz, 1H, H-4_{*α*,*E*-isomer}), 5.71 (dq, *J* = 8.9 Hz, *J* = 1.7 Hz, 1H, H-3_{*β*,*E*-isomer}), 3.17– 3.07 (m, 1H, H-2_{*α*,*E*-isomer}), 2.90 (dhept, *J* = 8.9 Hz, *J* = 6.6 Hz, 1H, H-2_{*β*,*E*-isomer}), 2.49–2.39 (m, 1H, H-2_{*α*,*Z*-isomer}), 2.21 (dhept, *J* = 10.3 Hz, *J* = 6.5 Hz, 1H, H-2_{*β*,*Z*-isomer}), 1.95 (d, *J* = 1.8 Hz, 3H, H-5_{*β*,*E*-isomer}), 1.90–1.88 (m, 3H, H-5_{*β*,*Z*-isomer + *α*,*E*-isomer}), 1.56 (dd, *J* = 6.9 Hz, *J* = 0.9 Hz, 3H, H-5_{*α*,*Z*-isomer}), 1.05–1.00 (m, 6H, H-1,1'_{*β*,*E*-isomer + *α*,*E*-isomer}), 0.75 (d, *J* = 6.5 Hz, 6H, H-1,1'_{*β*,*Z*-isomer}).}}}

¹³C{¹H} NMR (100 MHz, CDCl₃): δ 150.9, 144.7, 143.8, 138.4, 138.1, 137.6, 136.9, 135.7, 135.66, 135.5, 135.31, 135.3, 133.3, 129.3, 128.9, 128.88, 128.8, 128.7, 128.5, 128.24, 128.22, 128.2, 128.1, 128.05, 34.2, 31.9, 30.9, 26.6, 23.1, 22.63, 22.6, 19.8, 15.1.

HRMS: Ionization was not achieved with APCI.

(4,4-dimethylpent-2-en-2-yl)triphenylgermane / (4,4-dimethylpent-2en-3-yl)triphenylgermane (311): Prepared according to GP XV using 4,4dimethylpent-2-yne 302 (24 mg, 0.25 mmol, 1.0 equiv) as substrate, Et₂Zn (1.0 M in hexane, 0.75 mL, 0.75 mmol, 3.0 equiv), Ph₃GeH (153 mg, 0.50 mmol, 2.0 equiv), AIBN (4 mg, 0.025 mmol, 10 mol%) in heptane (0.64 mL). *The reaction mixture was then heated in the microwave at 100 °C (160 W) for 1 h* (*normal absorption level*). Purification of the crude product (β ,*Z*/ β ,*E*/ α ,*Z*/ α ,*E* = 41:15:25:19) by flash chromatography on silica gel (pentane) afforded 311 (20 mg, 20%, β ,*Z*/ α ,*Z*/ α ,*E* = 57:30:13), contaminated with remaining Ph₃GeH.

¹**H** NMR (400 MHz, CDCl₃): δ 7.62–7.54 (m, H-Ar **311** + Ph₃GeH), 7.44–7.36 (m, H-Ar **311** + Ph₃GeH), 6.46 (q, *J* = 7.1 Hz, 1H, H-4_{*α*,*Z*-isomer}), 5.88–5.82 (m, H-4_{*β*,*Z*-isomer} + H-4_{*α*,*E*-isomer}), 2.06 (d, *J* = 1.8 Hz, 3H, H-5_{*β*,*Z*-isomer}), 1.97 (d, *J* = 7.2 Hz, 3H, H-5_{*α*,*E*-isomer}), 1.42 (d, *J* = 7.1 Hz, 3H, H-5_{*α*,*Z*-isomer}), 1.23 (s, 9H, H-1,1',1"_{*α*,*E*-isomer}), 1.21 (s, 9H, H-1,1',1"_{*β*,*Z*-isomer}), 1.12 (s, 9H, H-1,1',1"_{*α*,*Z*-isomer}).

¹³C{¹H} NMR (100 MHz, CDCl₃): δ 152.9, 147.5, 139.8, 139.6, 136.8, 135.6, 135.5, 135.44, 135.4, 135.2, 135.0, 134.1, 131.9, 130.6, 129.2, 128.8, 128.7, 128.5, 128.4, 128.2, 128.1, 128.04, 128.0, 38.5, 35.0, 31.7, 30.9, 30.6, 19.8, 18.1.

HRMS: Ionization was not achieved with APCI.

(*Z*)-2-(triphenylgermyl)dec-2-en-1-ol (314): Prepared according to GP XV using dec-2-yn-1-ol 303 (39 mg, 0.25 mmol, 1.0 equiv) as substrate, Et₂Zn (1.0 M in hexane, 0.75 mL, 0.75 mmol, 3.0 equiv), Ph₃GeH (153 mg, 0.50 mmol, 2.0 equiv), AIBN (10 mg, 0.06 mmol, 25 mol%) in heptane (0.64 mL) and a reaction time of 2 h at 100 °C. Purification of the crude product (β/α = 90:10, *Z/E* > 98:2) by flash chromatography on silica gel (pentane/toluene/Et₂O = 80:10:10) afforded analytically pure β -314 (92 mg, 80%, β/α > 98:2, *Z/E* > 98:2) as a colorless liquid.

¹**H NMR** (400 MHz, CDCl₃): δ 7.63–7.61 (m, 6H, H-Ar), 7.41–7.39 (m, 9H, H-Ar), 6.55 (t, *J* = 7.4 Hz, 1H, H-8), 4.19 (s, 2H, H-10), 1.94 (q, *J* = 7.4 Hz, 2H, H-7), 1.34 (br s, 1H, H-11), 1.26–0.93 (m, 10H, H-2–H-6), 0.87 (t, *J* = 7.2 Hz, 3H, H-1).

¹³C{¹H} NMR (100 MHz, CDCl₃): δ 145.4 (C-8), 136.9 (C-12), 135.7 (C-9), 135.1 (C-Ar), 129.0 (C-Ar), 128.3 (C-Ar), 69.1 (C-10), 33.3 (C-7), 31.7 (C-alkyl), 29.21 (C-alkyl), 29.2 (C-alkyl), 29.0 (C-alkyl), 22.6 (C-alkyl), 14.1 (C-1).

IR (neat): v (cm⁻¹) 3328 (br), 2923, 2853, 1623, 1430, 1088, 733, 698.

HRMS (ESI): *m*/*z* calculated for [C₂₈H₃₄GeO + K]⁺ 499.1453; found 499.1454.

The Z configuration was confirmed by NOESY enhancements.

Ph₃Ge



(315): Prepared according to **GP XV** using *tert*-butyl(dec-2-yn-1yloxy)dimethylsilane **304** (67 mg, 0.25 mmol, 1.0 equiv) as substrate, Et₂Zn (1.0 M in hexane, 0.75 mL, 0.75 mmol, 3.0 equiv), Ph₃GeH (153 mg, 0.50 mmol, 2.0 equiv), AIBN (10 mg, 0.06 mmol, 25 mol%) in heptane (0.64 mL) and a reaction time of 2 h at 100 °C. Purification of the crude product ($\beta/\alpha > 98:2$, Z/E > 98:2) by flash chromatography on silica gel (pentane/toluene = 90:10) afforded **315** (30 mg, 21%, $\beta/\alpha > 98:2$, Z/E > 98:2) as a colorless liquid, contaminated with remaining substrate.





C₂₈H₃₄GeO M.W. = 459.21 g⋅mol⁻¹





C₃₄H₄₈GeOSi M.W. = 573.47 g⋅mol⁻¹

¹**H NMR** (400 MHz, CDCl₃): δ 7.58–7.55 (m, 6H, H-Ar), 7.39–7.32 (m, 9H, H-Ar), 6.53 (tt, *J* = 7.5 Hz, *J* = 1.7 Hz, 1H, H-8), 4.13 (q, *J* = 1.7 Hz, 2H, H-10), 1.88 (q, *J* = 7.5 Hz, 2H, H-7), 1.55–0.88 (m, 13H, H-1–H-6 + remaining **304**), 0.82 (s, 9H, H-13), 0.07 (s, 6H, H-11).

¹³C{¹H} NMR (100 MHz, CDCl₃): δ 142.8 (C-8), 137.3 (C-14), 135.3 (C-Ar), 134.6 (C-9), 128.9 (C-Ar), 128.2 (C-Ar), 68.6 (C-10), 33.1 (C-7), 31.9 (C-alkyl), 29.4 (C-alkyl), 29.3 (C-alkyl), 29.1 (C-alkyl), 26.0 (C-13), 22.7 (C-alkyl), 18.5 (C-12), 14.2 (C-1), -5.28 (C-11).

The Z configuration was assigned by analogy with Z-314.

(*Z*)-1-phenyl-2-(triphenylgermyl)but-2-en-1-ol (316): Prepared according to GP XV using 1-phenylbut-2-yn-1-ol 305 (37 mg, 0.25 mmol, 1.0 equiv) as substrate, Et₂Zn (1.0 M in hexane, 0.75 mL, 0.75 mmol, 3.0 equiv), Ph₃GeH (153 mg, 0.50 mmol, 2.0 equiv), AIBN (10 mg, 0.06 mmol, 25 mol%) in heptane (0.64 mL) and a reaction time of 2 h at 100 °C. Purification of the crude product ($\beta/\alpha > 98:2$, *Z/E* > 98:2) by flash chromatography on silica gel (pentane/Et₂O/toluene = 75:15:10) afforded analytically pure **316** (58 mg, 51%, $\beta/\alpha > 98:2$, *Z/E* > 98:2) as a white paste.

¹**H NMR** (400 MHz, CDCl₃): δ 7.48–7.45 (m, 6H, H-Ar [Ph₃Ge]), 7.39–7.30 (m, 9H, H-Ar [Ph₃Ge]), 7.20–7.17 (m, 3H, H-Ar [Ph]), 7.10–7.07 (m, 2H, H-Ar [Ph]), 6.66 (qd, *J* = 6.9 Hz, *J* = 1.2 Hz, 1H, H-2), 5.33 (s, 1H, H-4), 1.87 (br s, 1H, H-9), 1.65 (dd, *J* = 6.9 Hz, *J* = 0.9 Hz, 3H, H-1).

¹³C{¹H} NMR (100 MHz, CDCl₃): δ 142.6 (C-5), 140.2 (C-3), 139.0 (C-2), 137.0 (C-10), 135.2 (C-Ar [Ph₃Ge]), 128.9 (C-Ar [Ph₃Ge]), 128.2 (C-Ar [Ph₃Ge]), 128.1 (C-Ar [Ph]), 127.1 (C-Ar [Ph]), 126.9 (C-Ar [Ph]), 78.6 (C-4), 19.5 (C-1).

IR (neat): v (cm⁻¹) 3413 (br), 3066, 3049, 1485, 1449, 1089, 734, 698.

HRMS (ESI): m/z calculated for [C₂₈H₂₆GeO + Na]⁺ 475.1088; found 475.1093.

The Z configuration was assigned by analogy with Z-314.





C₂₈H₂₆GeO M.W. = 451.15 g⋅mol⁻¹

(Z)-3-(trimethylsilyl)-2-(triphenylgermyl)prop-2-en-1-ol (317):

Prepared according to **GP XV** using 3-(trimethylsilyl)prop-2-yn-1-ol **306** (32 mg, 0.25 mmol, 1.0 equiv) as substrate, Et₂Zn (1.0 M in hexane, 0.75 mL, 0.75 mmol, 3.0 equiv), Ph₃GeH (153 mg, 0.50 mmol, 2.0 equiv), AIBN (10 mg, 0.06 mmol, 25 mol%) in heptane (0.64 mL) and a reaction time of 2 h at 100 °C. Purification of the crude product ($\beta/\alpha > 98$:2, Z/E > 98:2) by flash chromatography on silica gel (pentane/toluene/Et₂O = 50:45:5) afforded analytically pure **317** (70 mg, 65%, $\beta/\alpha > 98$:2, Z/E > 98:2) as a colorless liquid.

¹**H NMR** (400 MHz, CDCl₃): δ 7.62–7.59 (m, 6H, H-Ar), 7.42–7.36 (m, 9H, H-Ar), 6.94 (t, *J* = 1.7 Hz, 1H, H-2), 4.15 (d, *J* = 1.7 Hz, 2H, H-4), 1.49 (br s, 1H, H-5), -0.22 (s, 9H, H-1).

¹³C{¹H} NMR (100 MHz, CDCl₃): δ 152.8 (C-3), 144.0 (C-2), 137.2 (C-6), 135.3 (C-Ar), 129.1 (C-Ar), 128.3 (C-Ar), 79.2 (C-4), -0.1 (C-1).

IR (neat): v (cm⁻¹) 3325 (br), 2997, 2952, 1430, 1247, 836, 732, 697.

HRMS (ESI): m/z calculated for $[C_{24}H_{28}GeOSi + Na]^+$ 457.1013; found 457.1019.

The Z configuration was confirmed by NOESY enhancements.

(Z)-3-(triphenylgermyl)dec-3-en-1-ol (318): Prepared according to GP XV using dec-3-yn-1-ol 307 (39 mg, 0.25 mmol, 1.0 equiv) as substrate, Et₂Zn (1.0 M in hexane, 0.75 mL, 0.75 mmol, 3.0 equiv), Ph₃GeH (153 mg, 0.50 mmol, 2.0 equiv), AIBN (10 mg, 0.06 mmol, 25 mol%) in heptane (0.64 mL) and a reaction time of 2 h at 100 °C. Purification of the crude product ($\beta/\alpha = 57:43$, β isomer: Z/E = 98:2, α isomer: Z/E = 97:3) by flash chromatography on silica gel (pentane/Et₂O/toluene = 75:15:10) afforded **318** (65 mg, 57%) as mixture of regioisomers. An analytically pure fraction of the major regioisomer β -**318** was isolated in 25% yield (28 mg, Z/E > 98:2) as a colorless liquid.









C₂₄H₂₈GeOSi M.W. = 433.20 g·mol⁻¹

¹**H NMR** (400 MHz, CDCl₃): δ 7.56–7.53 (m, 6H, H-Ar), 7.39–7.36 (m, 9H, H-Ar), 6.38 (tt, *J* = 7.3 Hz, *J* = 1.2 Hz, 1H, H-7), 3.40 (t, *J* = 6.5 Hz, 2H, H-10), 2.44–2.40 (m, 2H, H-9), 1.88 (q, *J* = 7.3 Hz, 2H, H-6), 1.25 (br s, 1H, H-11), 1.16–1.08 (m, 4H, H-alkyl), 1.01–0.87 (m, 4H, H-alkyl), 0.79 (t, *J* = 7.3 Hz, 3H, H-1).

¹³C{¹H} NMR (100 MHz, CDCl₃): δ 147.0 (C-7), 137.0 (C-12), 135.0 (C-Ar), 131.9 (C-8), 128.9 (C-Ar), 128.2 (C-Ar), 61.9 (C-10), 41.7 (C-9), 33.8 (C-6), 31.5 (C-alkyl), 29.4 (C-alkyl), 28.9 (C-alkyl), 22.5 (C-alkyl), 14.0 (C-1).

IR (neat): v (cm⁻¹) 3322 (br), 2925, 2854, 1431, 1089, 1043, 735, 699.

HRMS (ESI): *m*/*z* calculated for [C₂₈H₃₄GeO + Na]⁺ 483.1714; found 483.1713.

The Z configuration was assigned by analogy with Z-314.



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C₄₄H₄₄Ge₂ M.W. = 718.10 g⋅mol⁻¹

(*E*)-oct-4-ene-4,5-diylbis(triphenylgermane) (296): The product was isolated (57 mg, 32%, E/Z > 98:2) as byproduct of the reaction using 4-octyne 294 (28 mg, 0.25 mmol, 1.0 equiv) as substrate, Et₂Zn (1.0 M in hexane, 0.75 mL, 0.75 mmol, 3.0 equiv), Ph₃GeH (153 mg, 0.50 mmol, 2.0 equiv), AIBN (20 mg, 0.125 mmol, 50 mol%) in heptane (0.64 mL) according to **GP XV**. The reaction mixture was then heated in the microwave at 100 °C (160 W) for 1 h (normal absorption level).

¹**H NMR** (400 MHz, CDCl₃): δ 7.87–7.84 (m, 12H, H-Ar), 7.60–7.57 (m, 18H, H-Ar), 2.38–2.34 (m, 4H, H-3,3'), 0.91–0.82 (m, 4H, H-2,2'), 0.00 (t, *J* = 7.2 Hz, 6H, H-1,1').

¹³C{¹H} NMR (100 MHz, CDCl₃): δ 150.0 (C-4,4'), 138.3 (C-5,5'), 135.3 (C-Ar), 128.7 (C-Ar), 128.1 (C-Ar), 42.0 (C-3,3'), 23.1 (C-2,2'), 13.2 (C-1,1').

IR (neat): v (cm⁻¹) 3068, 3049, 2958, 2928, 1431, 1088, 734, 699.

HRMS: Ionization was not achieved with APCI.

The E configuration was determined by X-ray crystallographic analysis.



(*E*)-oct-4-ene-4,5-diylbis(triphenylgermane) (312): The product was isolated (14 mg, 8%, E/Z > 98:2) as byproduct of the preparation of compound **310**.

¹**H NMR** (400 MHz, CDCl₃): δ 7.65–7.60 (m, 12H, H-Ar), 7.40–7.35 (m, 18H, H-Ar), 2.87–2.80 (m, 1H, H-2), 1.64 (s, 3H, H-5), 0.59 (d, *J* = 6.7 Hz, 6H, H-1,1').

¹³C{¹H} NMR (100 MHz, CDCl₃): δ 142.7 (C-3 or C-4), 141.5 (C-4 or C-3), 139.7 (C-6 or C-10), 138.2 (C-10 or C-6), 135.4 (C-Ar), 135.2 (C-Ar), 128.7 (C-Ar), 128.5 (C-Ar), 128.2 (C-Ar), 128.0 (C-Ar), 40.5 (C-2), 28.5 (C-5), 21.4 (C-1,1').

IR (neat): v (cm⁻¹) 3067, 3049, 2958, 1430, 1088, 910, 734, 699.

HRMS: Ionization was not achieved with APCI.



C₄₂H₄₀Ge₂ M.W. = 690.05 g⋅mol⁻¹

III-5.13. DOMINO GERMYLZINCATION OF CONVENTIONAL ALKYNES / CU(I)-MEDIATED ELECTROPHILIC TRAPPING (GP XVII)

General Procedure for the Domino Germylzincation of Conventional Alkynes / Cu(I)-Mediated Electrophilic Trapping (GP XVII):



In a dry tube under argon atmosphere, the appropriate alkyne (0.25 mmol, 1.0 equiv), Ph₃GeH (153 mg, 0.50 mmol, 2.0 equiv), and AIBN (10–100 mol%) were dissolved in the appropriate solvent (0.64 mL). The tube was then sealed with a cap with septum, and Et₂Zn (1.0 M in hexane, 0.75 mL, 0.75 mmol, 3.0 equiv) was added at rt. The reaction mixture was either placed in an oil bath pre-heated at the suitable temperature or placed in the microwave reactor (Biotage, Model: INITIATOR ROBOT EIGHT 355380, 30310-38V), and stirred for the given reaction time. The reaction was then progressively cooled to -30 °C. Next, CuCN·2LiCl (1.0 M in THF, 0.75 mmol, 3.0 equiv) followed by the appropriate electrophile (1.75 mmol, 7.0 equiv) were added at this temperature and the reaction mixture was allowed to warm slowly to rt overnight under stirring. Then, aq NH₄Cl/NH₃ (2:1) and CH₂Cl₂ were added and after 1 h stirring the layers were separated. The aqueous layer was extracted with CH₂Cl₂ (x3), and the combined organic layers were washed with brine (x2), dried over Na₂SO₄, filtered, and concentrated under reduce pressure to afford the crude product.





C₃₀H₂₈Ge M.W. = 461.18 g⋅mol⁻¹ *(E)*-triphenyl(1-phenylprop-1-en-2-yl)germane (319): Prepared according to **GP XVII** using 1-phenyl-1-propyne **251** (29 mg, 0.25 mmol, 1.0 equiv) as substrate, Et₂Zn (1.0 M in hexane, 0.75 mL, 0.75 mmol, 3.0 equiv), Ph₃GeH (153 mg, 0.50 mmol, 2.0 equiv), AIBN (4 mg, 0.03 mmol, 10 mol%) in heptane (0.64 mL) and a reaction time of 2 h at 100 °C for the germylzincation step and CuCN·2LiCl (1.0 M in THF, 0.75 mL, 0.75 mmol, 3.0 equiv) and allyl bromide (212 mg, 1.75 mmol, 7.0 equiv) for the electrophilic substitution step. Purification of the crude product (*E/Z* > 98:2) by flash chromatography on silica gel (pentane/toluene = 92:8) afforded analytically pure **319** (107 mg, 93%, *E/Z* > 98:2) as a white solid; mp 116–119 °C.

¹**H NMR** (400 MHz, CDCl₃): δ 7.74–7.70 (m, 6H, H-Ar [Ph₃Ge]), 7.49–7.45 (m, 9H, H-Ar [Ph₃Ge]), 7.44–7.42 (m, 2H, H-Ar [Ph]), 7.34–7.30 (m, 1H, H-Ar [Ph]),

7.28–7.25 (m, 2H, H-Ar [Ph]), 5.29 (ddt, J = 17.0 Hz, J = 10.1 Hz, J = 6.8 Hz, 1H, H-13), 4.65 (ddt, J = 10.1 Hz, J = 2.2 Hz, J = 1.2 Hz, 1H, H-14_{cis}), 4.38 (dq_{app}, J = 17.0 Hz, J = 1.6 Hz, 1H, H-14_{trans}), 3.17 (dq_{app}, J = 6.8 Hz, J = 1.2 Hz, 2H, H-12), 1.73 (t, J = 1.2 Hz, 3H, H-7).

¹³C{¹H} NMR (100 MHz, CDCl₃): δ 151.2 (C-5), 142.5 (C-6), 137.7 (C-8), 135.3 (C-Ar), 134.9 (C-13), 128.9 (C-Ar), 128.8 (C-Ar), 128.7 (C-Ar), 128.3 (C-Ar), 128.1 (C-Ar), 126.4 (C-Ar), 116.1 (C-14), 44.6 (C-12), 22.4 (C-7).

IR (neat): v (cm⁻¹) 3068, 3018, 1484, 1430, 1069, 908, 731, 697.

HRMS (ESI): *m*/*z* calculated for [C₃₀H₂₈Ge + K]+ 501.1034; found 501.1038.

Ge

The E configuration was determined by X-ray crystallographic analysis.



¹**H NMR** (400 MHz, CDCl₃): δ 7.54–7.52 (m, 6H, H-Ar [Ph₃Ge]), 7.33–7.27 (m, 9H, H-Ar [Ph₃Ge]), 6.84 (d, *J* = 7.6 Hz, 2H, H-3), 6.77 (t, *J* = 7.6 Hz, 1H, H-1), 6.67 (t, *J* = 7.6 Hz, 2H, H-2), 5.80 (ddt, *J* = 16.7 Hz, *J* = 10.4 Hz, *J* = 6.4 Hz, 1H, H-15),



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C₃₁H₃₀GeO M.W. = 491.21 g⋅mol⁻¹ 5.14–5.05 (m, 3H, H-7,H-16), 3.40 (d, *J* = 6.4 Hz, 2H, H-14), 1.65 (br s, 1H, H-9), 1.40 (d, *J* = 6.4 Hz, 3H, H-8).

¹³C{¹H} NMR (100 MHz, CDCl₃): δ 150.9 (C-5), 142.5 (C-4), 141.4 (C-6), 139.3 (C-10), 135.3 (C-Ar), 135.0 (C-15), 128.7 (C-Ar), 128.2 (C-Ar), 127.8 (C-Ar), 127.1 (C-Ar), 126.6 (C-Ar), 116.0 (C-16), 70.5 (C-7), 41.0 (C-14), 24.5 (C-8).

IR (neat): v (cm⁻¹) 3427 (br), 3068, 3049, 1485, 1430, 909, 732, 697.

HRMS (APCI): m/z calculated for $[C_{31}H_{30}GeO + H] + 493.1581$; found 493.1583.

The Z configuration was confirmed by NOESY enhancements.





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C₃₅H₃₀Ge M.W. = 523.25 g⋅mol⁻¹

(Z)-(1,2-diphenylpenta-1,4-dien-1-

yl)triphenylgermanetriphenylgermane (321): Prepared according to GP XVII using diphenylacetylene 277 (45 mg, 0.25 mmol, 1.0 equiv) as substrate, Et₂Zn (1.0 M in hexane, 0.75 mL, 0.75 mmol, 3.0 equiv), Ph₃GeH (153 mg, 0.50 mmol, 2.0 equiv), AIBN (10 mg, 0.06 mmol, 25 mol%) in dry THF (0.64 mL) and a reaction time of 1 h at 80 °C for the germylzincation step and CuCN·2LiCl (1.0 M in THF, 0.75 mL, 0.75 mmol, 3.0 equiv) and allyl bromide (212 mg, 1.75 mmol, 7.0 equiv) for the electrophilic substitution step. Purification of the crude product by flash chromatography on silica gel (pentane/toluene = 92:8) afforded analytically pure **321** (76 mg, 58%, Z/E > 98:2) as a white solid; mp 89–92 °C.ⁱ

¹**H NMR** (400 MHz, CDCl₃): δ 7.04–7.00 (m, 9H, H-Ar), 6.97–6.87 (m, 9H, H-Ar), 6.84–6.81 (m, 4H, H-Ar), 6.63–6.54 (m, 3H, H-Ar), 5.45 (ddt, *J* = 17.0 Hz, *J* = 10.1 Hz, *J* = 6.8 Hz, 1H, H-16), 4.68 (ddd, *J* = 10.1 Hz, *J* = 2.1 Hz, *J* = 1.1 Hz, 1H, H-17_{cis}), 4.61 (dq_{app}, *J* = 17.0 Hz, *J* = 1.6 Hz, 1H, H-17_{trans}), 2.94 (dt, *J* = 6.8 Hz, *J* = 1.4 Hz, 2H, H-15).

 $[^]i$ A second fraction containing allyltriphenylgermane (323) was also isolated (96 mg, 55% - Based on Ph₃GeH).

¹³C{¹H} NMR (100 MHz, CDCl₃): δ 152.9 (C-5), 143.0, 141.7, 138.3, 137.7, 135.8 (C-16), 135.2, 129.0, 128.7, 128.1, 127.8, 127.6, 127.3, 126.8, 125.5, 115.9 (C-17), 42.2 (C-15).

IR (neat): v (cm⁻¹) 3138, 3050, 1596, 1485, 1430, 909, 731, 695.

HRMS (APCI): *m*/*z* calculated for [C₃₅H₃₀Ge + H]⁺ 525.1632; found 525.1633.

The Z configuration was determined by X-ray crystallographic analysis.



(*E*)-triphenyl(5-propylocta-4,7-dien-4-yl)germane (322): Prepared according to GP XVII using 4-octyne 294 (28 mg, 0.25 mmol, 1.0 equiv) as substrate, Et₂Zn (1.0 M in hexane, 0.75 mL, 0.75 mmol, 3.0 equiv), Ph₃GeH (153 mg, 0.50 mmol, 2.0 equiv), AIBN (41 mg, 0.25 mmol, 100 mol%) in dry THF (0.64 mL) and *microwave-heating at 80 °C (50 W) for 1 h (normal absorption level)* for the germylzincation step and CuCN·2LiCl (1.0 M in THF, 0.75 mL, 0.75 mmol, 3.0 equiv) and allyl bromide (212 mg, 1.75 mmol, 7.0 equiv) for the electrophilic substitution step. Purification of the crude product (*E/Z* = 89:11) by flash chromatography on silica gel (pentane/toluene = 92:8) afforded analytically pure **322** (68 mg, 60%, *E/Z* = 89:11) as a white solid; mp 71–74 °C.

¹**H NMR** (400 MHz, CDCl₃): (*Z* isomer) δ 7.57–7.55 (m, 6H, H-Ar), 7.38–7.34 (m, 9H, H-Ar), 5.89 (ddt, *J* = 17.1 Hz, *J* = 10.0 Hz, *J* = 6.5 Hz, 1H, H-14), 5.15 (dq_{app}, *J* = 17.1 Hz, *J* = 1.7 Hz, 1H, H-15_{trans}), 5.09 (dq_{app}, *J* = 10.0 Hz, *J* = 1.7 Hz, 1H, H-15_{trans}), 3.04 (dt, *J* = 6.5 Hz, *J* = 1.7 Hz, 2H, H-13), 2.20–2.05 (m, 2H, H-6), 1.95–1.91 (m, 2H, H-3), 1.22–1.16 (m, 2H, H-2), 1.04–0.98 (m, 2H, H-7), 0.57 (t, *J* = 7.3 Hz, 3H, H-1 or H-8), 0.23 (t, *J* = 7.3 Hz, 3H, H-8 or H-1).

¹³C{¹H} NMR (100 MHz, CDCl₃): δ (Z isomer) 149.2 (C-4 or C-5), 138.4 (C-9), 137.0 (C-14), 135.2 (C-Ar), 131.8 (C-5 or C-4), 128.5 (C-Ar), 128.0 (C-Ar),





C₂₉H₃₄Ge M.W. = 455.22 g⋅mol⁻¹

115.3 (C-15), 40.7 (C-3), 35.7 (C-13), 34.7 (C-6), 23.6 (C-7), 21.4 (C-2), 13.9 (C-1 or C-8), 13.7 (C-8 or C-1).

IR (neat): v (cm⁻¹) 2957, 2929, 2869, 1430, 1089, 911, 734, 699.

HRMS (ESI): m/z calculated for $[C_{29}H_{33}Ge]^+$ 455.1789; found 455.1790.

The E configuration was confirmed by NOESY enhancements.





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 $C_{34}H_{28}GeO$ M.W. = 525.23 g·mol⁻¹

(Z)-1,2-diphenyl-3-(triphenylgermyl)but-2-en-1-one (324): Prepared according to GP XVII using 1-phenyl-1-propyne 251 (29 mg, 0.25 mmol, 1.0 equiv) as substrate, Et₂Zn (1.0 M in hexane, 0.75 mL, 0.75 mmol, 3.0 equiv), Ph₃GeH (153 mg, 0.50 mmol, 2.0 equiv), AIBN (4 mg, 0.03 mmol, 10 mol%) in heptane (0.64 mL) and a reaction time of 2 h at 100 °C for the germylzincation step and CuCN·2LiCl (1.0 M in THF, 0.75 mL, 0.75 mmol, 3.0 equiv) and benzoyl chloride (246 mg, 1.75 mmol, 7.0 equiv) for the electrophilic substitution step. Purification of the crude product (Z/E > 98:2) by flash chromatography on silica gel (pentane/toluene/Et₂O = 80:18:2) afforded analytically pure **324** (83 mg, 63%, Z/E > 98:2) as a white solid; mp 144–146 °C.

¹**H NMR** (400 MHz, CDCl₃): δ 7.59–7.56 (m, 6H, H-Ar), 7.50–7.48 (m, 2H, H-Ar), 7.41–7.35 (m, 4H, H-Ar), 7.32–7.25 (m, 11H, H-Ar), 7.13–7.09 (m, 2H, H-Ar), 2.11 (s, 3H, H-7).

¹³C{¹H} NMR (100 MHz, CDCl₃): δ 195.9 (C-12), 152.9, 140.4, 137.5, 136.6, 136.1, 135.5, 132.1, 129.8, 129.3, 128.7, 128.5, 127.9, 127.6, 21.9 (C-7). *One C is not observed.*

IR (neat): v (cm⁻¹) 3051, 1659, 1431, 1260, 1089, 908, 768, 697.

HRMS (APCI): *m*/*z* calculated for [C₃₄H₂₈GeO + H]⁺ 527.1425; found 527.1415.

(Z)-triphenyl(1-phenyl-1-(tributylstannyl)prop-1-en-2-yl)germane

(325): Prepared according to **GP XVII** using 1-phenyl-1-propyne **251** (29 mg, 0.25 mmol, 1.0 equiv) as substrate, Et₂Zn (1.0 M in hexane, 0.75 mL, 0.75 mmol, 3.0 equiv), Ph₃GeH (153 mg, 0.50 mmol, 2.0 equiv), AIBN (4 mg, 0.03 mmol, 10 mol%) in heptane (0.64 mL) and a reaction time of 2 h at 100 °C for the germylzincation step and CuCN·2LiCl (1.0 M in THF, 0.75 mL, 0.75 mmol, 3.0 equiv) and tributyltin chloride (570 mg, 1.75 mmol, 7.0 equiv) for the electrophilic substitution step. Purification of the crude product (*Z/E* > 98:2) by flash chromatography on silica gel (pentane/toluene = 95:5) afforded analytically pure **325** (115 mg, 65%, *Z/E* > 98:2) as a white solid; mp 84–86 °C.

¹**H NMR** (400 MHz, CDCl₃): δ 7.68–7.65 (m, 6H, H-Ar [Ph₃Ge]), 7.43–7.34 (m, 11H, H-Ar [Ph₃Ge] + [Ph]), 7.19–7.14 (m, 1H, H-Ar [Ph]), 7.07–7.04 (m, 2H, H-Ar [Ph]), 1.69 (s, 3H, H-7), 1.05–1.00 (m, 12H, H-13,14), 0.75–0.72 (m, 9H, H-15), 0.39–0.22 (m, 6H, H-12).

¹³C{¹H} NMR (100 MHz, CDCl₃): δ 163.6, 148.0, 144.3, 138.1, 135.4, 128.9, 128.2, 128.15, 126.5, 124.8, 29.0 (C-13 or C-14), 27.3 (C-14 or C-13), 24.7 (C-7), 13.5 (C-15), 11.8 (C-12).

IR (neat): v (cm⁻¹) 2954, 2920, 1953, 1882, 1431, 1088, 734, 699.

HRMS: Ionization was not achieved with ESI.

The Z configuration was confirmed by NOESY enhancements.



Allyltriphenylgermane (323): The product was isolated (96 mg, 55%) as byproduct of the preparation of compound **321**; white solid, mp 87–90 °C.

¹**H NMR** (400 MHz, CDCl₃): δ 7.59–7.56 (m, 6H, H-Ar), 7.48–7.42 (m, 9H, H-Ar), 6.07–5.97 (m, 1H, H-2), 5.08 (d, *J* = 16.9 Hz, 1H, H-1_{trans}), 4.96 (d, *J* = 10.2 Hz, H-1_{cis}), 2.58 (d, *J* = 8.1 Hz, 2H, H-3).

C₂₁H₂₀Ge M.W. = 345.02 g⋅mol⁻¹

323



325

C₃₉H₅₀GeSn M.W. = 710.16 g⋅mol⁻¹
¹³C{¹H} NMR (100 MHz, CDCl₃): δ 136.7 (C-4), 135.1 (C-Ar), 134.6 (C-2), 129.1 (C-Ar), 128.3 (C-Ar), 114.6 (C-1), 21.4 (C-3).

IR (neat): v (cm⁻¹) 3062, 1629, 1483, 1428, 1090, 733, 697, 674.

HRMS: Ionization was not achieved with APCI.

III-5.14. PREPARATION OF NHC-BORANE 344



(1,3-dimethyl-1*H*-imidazol-3-ium-2-yl)trihydroborate (344) was prepared according to a slightly modified version of Curran-Fensterbank-Lacôte-Malacria's procedure.¹ A solution of sodium bis-(trimethylsilyl) amide (NaHMDS) (1.0 M in THF, 15 mL, 15 mmol) was added to a suspension of 1,3-dimethyl-1*H*-imidazol-3-ium iodide (3.36 g, 15 mmol) in THF (105 mL) at –78 °C. The yellow mixture was stirred at –78 °C for 1 h, before addition of a solution of BH₃-THF (1.0 M in THF, 15 mL, 15 mmol) at the same temperature. The resulting yellow mixture was stirred at –78 °C to rt for 18 h, and then the solvent was removed under reduced pressure to give a yellow solid. Purification of the crude product by flash chromatography on silica gel (CH₂Cl₂/MeOH = 99:1) afforded analytically pure **344** (922 mg, 56%) as a white solid.

 H_3C $\frac{1}{H}$ IH NMR (400 MHz, CDCl₃): δ 6.79 (s, 2H, H-4), 3.72 (s, 6H, H-3), 1.00 (q, $J_{H-B} =$ H_3C $\frac{1}{B}H_3$ 86.3 Hz, 3H, H-1). H_3C H_3C

 $C_5H_{11}BN_2$ M.W. = 109.97 g·mol⁻¹ The spectral data were in agreement with that previously reported in the literature.ⁱⁱ

ⁱ Makhlouf Brahmi, M.; Monot, J.; Desage-El Murr, M.; Curran, D. P.; Fensterbank, L.; Lacôte, E.; Malacria, M. *J. Org. Chem.* **2010**, *75*, 6983–6985.

ⁱⁱ Walton, J. C.; Makhlouf Brahmi, M.; Fensterbank, L.; Lacôte, E.; Malacria, M.; Chu, Q.; Ueng, S.-H.; Solovyev, A.; Curran, D. P. *J. Am. Chem. Soc.* **2010**, *132*, 2350–2358.

Resume

Les vinylgermanes (**Schéma R-1**) font depuis longtemps l'objet d'une attention particulière des chimistes organiciens. De manière surprenante, bien que ces réactifs présentent une réactivité similaire à celle des vinylsilanes et des vinylstannanes, leur application en synthèse est beaucoup moins répandue que celle des homologues plus populaires du groupe 14. Un coût plus élevé ainsi qu'une disponibilité commerciale limitée des composés organogermaniums jusqu'au début des années 2000 en sont certainement quelques-unes des causes. Pourtant, des caractéristiques spécifiques telles qu'une stabilité accrue envers la protonolyse, une halodégermylation facilement réalisable, la nature non toxique du germanium et la réactivité orthogonale avec de nombreux autres groupes fonctionnels font des vinylgermanes une alternative utile aux vinylsilanes et vinylstannanes lorsque ceux-ci présentent des défauts.



SCHEMA R-1. Nucléophiles vinyliques du groupe 14.

Notamment, ces intermédiaires ont été impliqués en tant que précurseurs dans l'étape clé de la synthèse stéréosélective de produits naturels ou pharmaceutiques (**Schéma R-2**), démontrant ainsi leur potentiel en tant qu'éléments constitutifs polyvalents. En conséquence, l'intérêt actuel pour cette chimie connait un essor considérable. Néanmoins, une condition essentielle pour étendre et généraliser ces applications est la préparation du motif vinylgermane de manière régioet stéréocontrôlée. Pour ce faire, plusieurs méthodologies ont été développées ; mais les inconvénients rencontrés jusqu'à présent ont limité la préparation générale des vinylgermanes structurellement diversifiés. Par conséquent, la synthèse régio- et stéréosélective de cette structure est un domaine de recherche intense et continue.



SCHEMA R-2. Exemples de l'utilisation des vinylgermanes comme intermédiaires clés dans la synthèse totale de produits naturels et pharmaceutiques.

De nos jours, la principale voie de synthèse directe des vinylgermanes repose sur la formation de liaisons carbone-germanium par réaction d'addition des alcynes (**Figure R-1**).



FIGURE R-1. Synthèse de vinylgermanes à partir d'alcynes par des réactions de formation de liaisons C–*Ge* (*Ge* = triorganogermyle).

Dans ce contexte, l'approche la plus efficace et la plus économique sur le plan atomique est l'hydrogermylation des alcynes, qui consiste en l'addition d'une liaison Ge–H sur une triple liaison C-C. Cette réaction d'addition des hydrogermanes sur des alcynes peut être réalisée par des processus catalysés par les métaux de transition, catalysés par les acides de Lewis du groupe principal ou par des processus radicalaires. Les réactions d'hydrogermylation ont jusqu'à présent dominé la préparation des vinylgermanes (1,1- ou 1,2-)-disubstitués et 1,1,2-trisubstitués. Toutefois, ces approches comportent encore des limitations. Par exemple, l'accès général aux alcènes ayant deux substituants distaux par rapport à la position du groupement germyle est hors de portée de l'hydrogermylation des alcynes.

D'une manière générale, la synthèse des vinylgermanes 1,2,2-trisubstitués et tétrasubstitués souffre de plusieurs limitations. En ce qui concerne les analogues 1,2,2-trisubstitués, les protocoles disponibles reposent principalement sur les réactions d'addition de liaison *Ge*–

Element (*Ge*–Sn, *Ge*–Ge, *Ge*–B, *Ge*–CN). Ces protocoles permettent une fonctionnalisation diversifiée de la position 2 uniquement dans le cas de l'introduction d'un groupement stannyle. Cependant, dans un tel cas, l'accès à la cible vinylgermane trisubstitué en position 1,2,2 nécessite deux étapes de synthèse, l'utilisation de réactifs toxiques à base d'étain et la préparation préalable du réactif Ge–Sn. En ce qui concerne les vinylgermanes tétrasubstitués plus difficilement accessibles, presque rien n'a été décrit hormis les premiers travaux de Piers concernant l'addition d'espèces stannylgermanes sur des propiolates internes.

A ce jour, **il n'existe donc pas de solution directe et générale pour la préparation régio et stéréosélective de vinylgermanes 1,2,2-trisubstitués ou tétrasubstitués**. Combler ces lacunes est l'objectif majeur du travail décrit ci-après.

L'élémentométallation des alcynes (**Schéma R-3**), c'est-à-dire l'ajout de liaisons élémentmétal sur la triple liaison carbone-carbone des alcynes, est une approche conceptuellement intéressante qui permet de créer simultanément une liaison C(sp²)–élément et une liaison C(sp²)– métal avec une réactivité orthogonale. La liaison organométallique C(sp²)–métal nouvellement formée peut alors être impliquée dans des réactions de substitutions électrophiles *in-situ*, tandis que la liaison élément C(sp²)–élément peut être fonctionnalisée ultérieurement pour accéder à des alcènes stéréodéfinis.



SCHEMA R-3. Elémentométallation d'alcynes.

Cependant, les tentatives précédentes par divers groupes du développement de la germylmétallation des alcynes ont échoué. En effet, la réaction entre le (triméthylgermyle)cuivre et un alcyne terminal a été reporté avec un faible rendement. De plus, la germylmétallation des acétylènes terminaux avec les cuprates de (triéthylgermyle)- et (triphénylgermyle)-cuprates a été réalisée : une excellente stéréosélectivité *cis* a été observée, mais le contrôle de la régiosléctivité n'a été obtenu qu'avec les réactifs triphénylgermyles. De plus, dans ce cas, l'addition s'est avérée réversible et en faveur des produits de départ ; la formation de vinylgermane ne peut se faire qu'en présence d'un donneur de protons et la liaison C(sp²)–Cu formée n'est plus disponible pour une modification ultérieure (**Schéma R-4**, a).



SCHEMA R-4. Contexte général de ce travail (Ge = triorganogermyle).

Ces dernières années, notre groupe a développé une approche radicalaire de la silylzincation des alcynes terminaux substitués par des hétéroatomes utilisant une combinaison de (Me₃Si)₃SiH et Et₂Zn (Schéma R-4, b). Compte tenu de la faisabilité d'effectuer des réactions radicalaires avec des hydrogermanes, comme l'a largement démontré l'hydrogermylation radicalaire des alcynes (Schéma R-4, c), notre idée était d'envisager une approche radicalaire similaire comme indiqué dans Schéma R-4 (**ce travail**).

Nous avons raisonné, comme le montre le **Schéma R-5**, qu'après une étape d'initiation (pas visualisable sur le schéma), les radicaux centrés sur le germanium R"₃Ge•, générés par transfert d'atomes entre l'hydrogermane et le radical éthyle **34**, devraient s'additionner sur l'alcyne **42** pour mener régiosélectivement aux radicaux **43** ($42 \rightarrow 43$). Les radicaux **43** réagiraient alors avec le diéthylzinc par substitution homolytique (S_H2) sur l'atome de zinc ($43 \rightarrow 44$) pour obtenir des vinylzinciques **44** ainsi que le radical éthyle **34** qui propagerait la chaîne radicalaire. Notons toutefois que pour qu'un tel procédé soit possible, le radical vinyle intermédiaire **43** devrait subir un transfert d'atomes de Zn ($43 \rightarrow 44$) plus rapidement que le transfert d'atomes d'hydrogène concurrent de R₃GeH ($43 \rightarrow 45$). Dans ce cas, l'hydrogermylation radicalaire serait le principal résultat de la réaction et la fonctionnalité du Zn serait perdue. Une autre source de complications pourrait être la carbozincation compétitive résultant de l'addition directe du radical éthyle **34** sur la triple liaison C-C des alcynes **42**.



SCHEMA R-5. Approche radicalaire anticipée pour la germylzincation des alcynes.

A priori, une estimation des constantes de vitesse pour chaque étape élémentaire impliquée dans cette chaîne radicalaire a permis d'étayer la faisabilité de la réaction de germylzincation radicalaire, puisqu'elles sont toutes supérieures à $10^2 \text{ M}^{-1} \text{ s}^{-1}$, qui est la valeur généralement admise pour une propagation de la chaîne radicalaire dans une solution diluée. Cependant, il n'y

a pas suffisamment de données pour prédire la vitesse de réaction entre les radicaux vinyles et le diéthylzinc. Néanmoins, les travaux antérieurs développés dans notre groupe sur la silylzincation radicalaire ont démontré que cette étape convenait à la propagation en chaîne et pouvait faire concurrence au transfert de l'atome H de l'hydrosilane. Étant donné que les cinétiques d'abstraction radicalaire d'hydrogène sont comparables pour les hydrogermanes et pour les hydrosilanes, nous nous attendons à une situation similaire ici.

L'objectif principal de cette thèse de doctorat est donc de développer une approche radicalaire générale pour la germylzincation des alcynes comme voie simple pour la préparation des vinylgermanes polysubstitués.

Pour ce faire, les ynamides terminaux et internes ont d'abord été considérés en tenant compte de leur réactivité élevée et intéressante. D'autres alcynes substitués par un hétéroatome ont ensuite été pris en considération. Enfin, des alcynes conventionnels plus difficiles ont été étudiés. Dans tous les cas, la possibilité de fonctionnalisation de la liaison C(sp²)–Zn a été examinée, comme condition clé pour accéder aux vinylgermanes avec deux substituants en position β du groupe germyle, ce qui représente un de nos principaux objectifs. La fonctionnalisation de la liaison C(sp²)–Ge a également été étudiée. Pour terminer, les perspectives de généralisation de cette approche d'élémentozincation radicalaire à la silylation et à la borylzincation des alcynes conventionnels ont été examinées de façon préliminaire.

Nous avons commencé notre travail en étudiant la germylzincation de l'ynamide modèle 54 possédant un alcyne terminal, avec Ph₃GeH, un réactif d'hydrogermylation radicalaire bien établi, disponible sur le marché et facile à utiliser (**Tableau R-1**). Les conditions initiales impliquant 1,3 équivalent d'hydrogermane et 3,0 équivalents d'Et₂Zn à 0 °C dans le *n*-hexane, ont conduit à la formation exclusive de β -germylénamide **59** sous forme d'un mélange d'isomères E/Z = 30:70, mais la réaction était incomplète et seulement environ 60% de l'ynamide de départ a été consommé (Tableau R-1, entrée 1). Dans le but d'obtenir des niveaux de conversion plus élevés, un criblage d'autres solvants a ensuite été réalisé. Bien qu'aucune amélioration n'ait été observée dans le CH₂Cl₂ et l'Et₂O, les réactions effectuées dans le benzène et le méthyl-tert-butyléther (MTBE) ont amélioré la conversion (~ 80%) (Tableau R-1, entrées 2-5). Néanmoins, la stéréosélectivité de la réaction a été modeste dans tous les cas, et souvent en faveur de l'isomère E, ce qui contraste fortement avec les expériences réalisées avec le n-hexane. De plus, une carbozincation concurrentielle a également été détectée dans le MTBE. En fin de compte, une conversion complète et un contrôle total de la stéréosélectivité, également en faveur de l'isomère E, ont été obtenus en utilisant le Me-THF et le THF (Tableau R-1, entrées 6 and 7). Cependant, la carbozincation de 54 s'est produite dans une certaine mesure avec l'éther plus encombré Me-THF (Tableau R-1, entrée 6), et un meilleur rendement en **59** a été obtenu dans le THF (87% contre 64%).

	$\beta = N + O O O O O O O O O O O O O O O O O O$	1) Ph ₃ GeH (1,3 e Et ₂ Zn (n équi 3 h <i>2)</i> NH ₄ Cl/NH	équiv.) iv.) H ₃ P	H Ph ₃ Ge <i>E-59</i>		+ N Et 66a	õ
Entrée	Solvant	Et2Zn (équiv.)	Т	Conversion [(59+66a)/54] ^{a,b}	Ratio 59 (<i>E/Z</i>) ^a	Rdt 59 (%) ^c	Rdt 66a (%) ^c
1	<i>n</i> -hexane	3,0	0 °C	60:40	30:70	nc ^e	nd ^d
2	CH_2Cl_2	3,0	0 °C	50:50	70:30	37	nd ^d
3	Et_2O	3,0	0 °C	54:46	48:52	29	nd ^d
4	Benzene	3,0	0 °C	85:15	57:43	nc ^e	nd^d
5	MTBE	3,0	0 °C	80:20	68:32	62	6
6	Me-THF	3,0	0 °C	>99:1	98:2	64	10
7	THF	3,0	0 °C	>99:1	>98:2	87 <i>f</i>	\mathbf{nd}^d
8	THF	1,8	0 °C	>99:1	90:10	nc ^e	nd ^d
9	THF	1,2	0 °C	89:11	76:24	nc ^e	\mathbf{nd}^{d}

TABLEAU R-1. Optimisation des conditions de germylzincation d'ynamide 54.

^{*a*}Déterminé par analyse RMN ¹H avant purification. ^{*b*}On n'a détecté que β -régioisomères. ^{*c*}Rendement déterminé par RMN ¹H en utilisant la butadiène sulfone comme étalon interne. ^{*d*}N'est pas détecté dans le brut réactionnel. ^{*e*}N'est pas calculé. ^{*f*}Rendement isolé de **59** sous forme d'un mélange d'isomères.

L'excellente stéréosélectivité de l'isomère *E* obtenue dans le THF n'était pas attendue, et les expériences de marquage isotopique avec du deutérium ont démontré que la germylzincation (et non l'hydrogermylation) avait lieu. En effet, en traitant le milieu réactionnel avec ND₄Cl/D₂0, *E*- $[^{2}H]$ -**59** a été récupéré avec une excellente incorporation de deutérium à hauteur de 97% en position *a*, démontrant la formation de l'intermédiaire vinylzincique **67** (**Schéma R-6**).



SCHEMA R-6. Essai de deutération.

Ensuite, la possibilité de réduire la quantité d' Et_2Zn nécessaire à la réaction a également été étudiée. Malgré une conversion élevée en utilisant 1,8 ou 1,2 équivalent d' Et_2Zn , le stéréocontrôle s'est révélé plus faible (Tableau R-1, entrées 8 and 9), probablement parce que l'hydrogermylation directe menant à l'isomère Z entrait en jeu. Plus généralement, il est également possible que la perte de stéréosélectivité dans d'autres solvants résulte du même effet, c'est-à-dire d'une compétition entre une germylzincation et une hydrogermylation directe.

En conclusion, la germylzincation *cis*-sélective des ynamides terminaux a été réalisée dans le THF en utilisant une combinaison de Ph_3GeH et $Et_2Zn \ge 0$ °C. En choisissant soigneusement les conditions de réaction (température, quantité d' Et_2Zn , solvant), il a été possible de minimiser ou d'éviter l'hydrogermylation ou la carbozincation concurrentielle.

Le champ d'application de cette nouvelle réaction de germylzincation des ynamides terminaux a ensuite été examiné (**Schéma R-7**).



SCHEMA R-7. Germylzincation des ynamides terminaux.

D'une manière générale, la modification de la substitution en α à l'atome d'azote du cycle oxazolidinone a été bien tolérée et les β -germylénamides **59**, **68–70** ont été isolés avec de bons rendements et sous la forme unique de l'isomère *E*. Fait important, d'autres hydrogermanes ont également pu être utilisés. Ainsi, le trifurylgermane a réagi doucement pour fournir *E*-**75** sous la forme d'un seul stéréosisomère et un rendement de 72%. Cependant, en présence de *n*Bu₃GeH, la conversion n'était pas complète (50%) et le produit **76** a été obtenu avec un rendement inférieur de 40% accompagnée du produit d'addition de carbozincation à hauteur de 10%. Cela n'était pas précisément inattendu puisque le coefficient de vitesse de réaction entre les trialkylgermanes et les radicaux alkyles est inférieur d'environ 1 ordre de grandeur à celui des triarylgermanes, ce qui rend l'addition des radicaux éthyles plus compétitive et la propagation de la chaîne des radicaux moins efficace. Néanmoins, avec des quantités plus élevées d'hydrogermane (2,0 équivalents) et des temps de réaction plus longs, le *n*Bu₃GeH et le Et₃GeH ont fourni respectivement **76** et **77**, avec des rendements élevés et d'excellentes stéréosélectivités, en évitant totalement la réaction compétitive d'éthylzincation.

Dans tous les cas, la formation d'intermédiaires vinylzinc par réaction avec R_3GeH/Et_2Zn a été systématiquement étudiée par des expériences de marquage au deutérium. Une excellente incorporation D (>96%) à la position α a été observée dans tous les cas. Il faut cependant noter que ces expériences ont été compliquées par la remarquable stabilité à l'égard de l'hydrolyse de la liaison C(sp²)–Zn de l'espèce du divinylzinc (**Schéma R-8**), probablement formée par l'équilibre de Schlenk des intermédiaires résultant de la germylzincation (voir ci-dessous).



SCHEMA R-8. Equilibre de Schlenk.

Dans certains cas, les espèces du divinylzinc n'ont réagi que partiellement avec ND₄Cl/D₂O ou MeOD, ce qui a conduit à des valeurs d'incorporation de D faibles et des quantités significatives du divinylzinc ont été récupérées dans le brut réactionnel même après une exposition prolongée aux solutions aqueuses ou après chromatographie sur gel de silice ! Une deutério-démétallation efficace des intermédiaires du divinylzinc a néanmoins été obtenue par l'ajout de CuTC (Copper(I)-thiophene-2-carboxylate) avant le quenchage de la réaction et des données fiables sur le marquage D ont pu être recueillies. Des conditions similaires (CuTC/NH₄Cl/H₂O) ont également été utilisées dans la préparation de **68–70** non marqués.

Par ailleurs, la réaction de germylzincation s'est également avérée bien adaptée aux ynamides internes (**Schéma R-9**).



SCHEMA R-9. Germylzincation des ynamides internes.

Pour cette classe de substrats, les meilleures conditions de réaction consistaient à utiliser du *n*-hexane comme solvant à 40 °C. Ici, l'hydrogermylation directe n'a pas perturbé le processus de germylzincation, et le β -germylénamide *E*-**94** a été obtenu à partir de l'ynamide **92** avec un rendement de 92%, une régiosélectivité β et stéréosélectivité *cis*. Les même régiosélectivité et stéréosélectivité remarquables ont été observées à basse température et/ou dans le THF, mais la conversion du produit de départ n'était pas complète. En partant d'ynamides substitués par un groupement phényle, la modification du substituant azoté a également été bien tolérée ici, et les β -énamides **129–132** correspondants ont été obtenus avec des rendements de 69–86% et une stéréosélectivité *E* remarquable. De plus, contrairement à nos observations antérieures concernant la formation mineure d'adduits de carbozincation avec des ynamides cycliques terminaux, aucune addition de radicaux éthyles concurrente n'a été observée avec des ynamides internes. Ceci est en accord avec la réaction plus difficile des radicaux alkyles avec des alcynes disubstitués qu'avec des monosubstitués. De plus, l'énamide **132** acyclique *N*-carbamate substitué a été isolé avec un rendement de 73%, même si un temps de réaction plus long était nécessaire (16 h).

Le champ d'application concernant les autres hydrogermanes a ensuite été évalué. Le trifurylgermane a bien réagi avec **92** fournissant le produit avec un excellent rendement de 88%. Par contre, la réaction avec Et₃GeH a été plus problématique : en effet, malgré un rendement décent de 63%, presque aucune régiosélectivité n'a été observée.

La substitution du noyau phényle a eu un impact mineur sur le résultat de la réaction : les substituants donneurs d'électrons et attracteurs d'électrons ont été bien tolérés quelle que soit la position du substituant dans le noyau aromatique. En conséquence, les énamides **138** et **140** portant un groupe méthoxy donneur d'électrons en positions *para* et *méta*, respectivement, ainsi que les énamides **139** et **142** portant des substituants *para*-chloro et *ortho, ortho*-dichloro, ont tous les deux été obtenus avec des rendements de bons à excellents (69–94%). Dans tous les cas, une sélectivité *E* remarquable a été observée, seule exception à cette tendance, l'énamide **141**, avec un noyau phényle substitué par un groupement methoxy en position *ortho*.

Par ailleurs, l'approche de la germylzincation n'a pas été restreintes aux ynamides substitués par un groupement aryle, puisque les énamides trisubstitués ayant des substituants alcényle (143)-, alcynyle (146)-, alkyle primaire (147 et 148)-, alkyle secondaire (149) et trifluorométhyle (150) en β de l'azote ont pour la plupart été obtenus avec des bons rendements, même si des temps de réactions plus longs ont parfois été nécessaire. D'excellentes stéréosélectivités ont été obtenues dans tous les cas sauf pour les énamides 149 et 150 substitués respectivement par un groupement cyclohexyle et trifluorométhyle, l'inversion de la stéréosélectivité en faveur d'une germylzincation *trans*-sélective a été observée. De plus, lors de la formation de l'énamide 150, une carbozincation compétitive et une germylzincation sélective ont été détectées dans une certaine mesure. Les configurations des produits 147 (*E*) et 150 (*Z*) ont été établies par analyse cristallographique aux rayons X.

Enfin, des énamides marqués au deutérium ont été obtenus dans tous les cas en traitant le milieu réactionnel avec ND₄Cl/D₂O/THF après réaction dans les conditions les mieux adaptées déterminées auparavant. L'excellente incorporation de deutérium dans les produits finis a

confirmé la formation d'intermédiaires de vinylzinc lors de la germylzincation des ynamides internes et exclu toute possibilité d'un procédé d'hydrogermylation concurrent.

Nos efforts suivants visaient à mieux comprendre le mécanisme de cette nouvelle réaction de germylzincation. L'influence possible de la métallation de l'ynamide terminal dans le milieu réactionnel pendant le processus de germylzincation a d'abord été étudié (**Schéma R-10**).



SCHEMA R-10. Influence de la métallation de l'ynamide 54.

En absence de Ph₃GeH, une déprotonation de 43% de **54** par Et₂Zn (3,0 équiv.) a été observée dans le THF après 3 h à 0 °C (Schéma R-10, dessus). Pourtant, la germylzincation dans les mêmes conditions opérationnelles sur l'ynamide [²H]-**54** marqué au deutérium a conduit exclusivement à l'isomère E-[²H(β)]-**59** sans perte de deutérium en position β (Schéma R-10, dessous). Par conséquent, la déprotonation de **54** (ni par Et₂Zn ni par des intermédiaires du vinylzinc) n'a pas lieu pendant la germylzincation. Des expériences de marquage au deutérium à partir de l'ynamide [²H]-**54** marqué ont confirmé ce point ainsi que le fait que seule une réaction de germylzincation s'est produite, car une excellente déutériation a été observée aux positions α et β .

Il fallait ensuite confirmer le caractère radicalaire de la réaction de germylzincation. La présence de TEMPO a complètement inhibé la réaction de germylzincation (**Schéma R-11**) puisqu'aucune conversion n'a été observée lorsqu'il était présent en début de réaction à hauteur de 110 mol% ou dans des quantités aussi faibles que 10 mol%. Dans ce cas, seulement 26% de *E*-**59** a été formé après 5 min de réaction.

+	Et ₂ Zn (3,0 équiv.) Ph ₃ GeH (1,3 équiv.)	ТЕМРО		t₁ (min)	TEMPO (mol%)	59/54
β Ň U	 THF 0 ℃, t ₁ (min)	THF 0 °C, 3 h		0	110	0:100
Ý 0			Ph ₃ Ge	0	10	0:100
54			59 (<i>E</i> / <i>Z</i> > 98:2)	5	10	26:74

SCHEMA R-11. Caractère radicalaire de la	germylzincation.
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Ces expériences démontrent clairement la nature radicalaire de la réaction de germylzincation. Cependant, elles ne rejettent pas un scénario radical/polaire dans lequel le Et₂Zn réagirait avec l'hydrogermane par un procédé de transfert de groupe alkylzinc radicalaire et fournirait un intermédiaire germanium-zinc qui réagirait ensuite avec le système π de la triple liaison du ynamide de manière *cis*-stéréoselective. La formation reportée de (Ph₃Ge)₂Zn à partir de Et₂Zn et de Ph₃GeH dans le THF a été requis afin d'exclure cette possibilité. A cette fin, la réaction de Ph₃GeH / Et₂Zn avec la sonde mécanistique **86** a été envisagée (**Schéma R-12**).



SCHEMA R-12. Réaction de germylzincation avec la sonde mécanistique 86.

La formation de produits cyclisés [²H]-**89** (33%) et [²H]-**90** (52%) (résultant de l'addition de radicaux éthyle concurrents) a fourni la preuve d'une addition de radicaux 1,4 (conduisant à un radical β -alkoxy intermédiaire **87** qui subit une fermeture de cycle 5-*exo-dig*) alors qu'aucun produit provenant de la fragmentation d'un anion β -alkoxy intermédiaire (non montré) qui pourrait supporter une addition polaire d'intermédiaire germanium-zinc n'a été détecté. De plus, nous avons également réalisé le suivi par RMN ¹H *in situ* de la disparition du Ph₃GeH au contact avec Et₂Zn dans le THF en l'absence d'ynamide. Après 3 h à 0 °C, 40% de la quantité initiale de Ph₃GeH avait disparu. Par conséquent, la vitesse de formation d'un hypothétique intermédiaire germanium-zinc dans ces conditions était trop lente pour contribuer aux réactions de germylzincation. Dans l'ensemble, ces résultats appuient fortement le mécanisme prévu au début de notre travail (illustré dans le Schéma R-5) qui consiste à ajouter des radicaux centrés sur le germanium sur la triple liaison C-C des ynamides.

La stéréochimie résultant des réactions de germylzincation a également été rationalisée sur la base de ce scénario : la stéréosélectivité de la réaction de germylzincation est celle du transfert de groupe alkylzinc (c'est-à-dire $151 \rightarrow 152$). Les radicaux 151 hybridés sp² ont une géométrie coudée et sont considérés comme existant sous deux formes diastéréoisomériques équilibrant avec une faible barrière énergétique de conversion. La réaction de *E*-151 avec Et₂Zn donne *Z*-152 et celle de *Z*-151 produit *E*-152. Par conséquent, le rapport *Z/E* pour la formation du vinylzinc 152 dépendrait de la stabilité relative des deux isomères du radical vinylique 151 (K_{eq}), ainsi que de la facilité relative de chaque forme diastéréomérique à subir le transfert du groupe alkylzinc ($k_Z vs k_E$) (Schéma R-13).



SCHEMA R-13. Modèle de stéréosélectivité des réactions de germylzincation.

Lorsque R³ est un "petit" substituant (H, aryle, alkyle primaire), l'équilibre est largement tirée vers de la forme *E* plus stable ($K_{eq} \gg 1$) et la formation du vinylzinc *Z*-**152** est favorisée. Cependant, dans un scénario général, on s'attendrait à ce que le radical *Z*-**151** réagisse plus rapidement que le radical *E*-**151** avec l'Et₂Zn ($k_Z > k_E$), puisque l'interaction stérique de l'Et₂Zn est moins importante avec un substituant R³ qu'avec un fragment germylique trisubstitué (R₃Ge). Ainsi, lorsque R³ est un substituant "plus grand" (alkyle secondaire ou CF₃ – de taille similaire à un groupement *i*Pr, avec un rayon de van der Waals de 2,2 Å), la forme *E* du radical vinyle **151** devient déstabilisée, abaissant ainsi le K_{eq} , et l'approche plus favorable du Et₂Zn du côté moins encombré opposé au groupe R₃Ge ($k_Z > k_E$) explique l'inversion de la stéréosélectivité observée.

Après avoir établi le champ d'application de la réaction de germylzincation, nous avons étudié le potentiel synthétique de la fonctionnalisation de la liaison C(sp²)–Zn pour donner accès

à des vinylgermanes comportant deux substituants en β de l'atome de germanium. Une substitution électrophile *in situ* en utilisant du Cu(I) après germylzincation a pu être réalisé facilement avec une rétention complète de la géométrie de double liaison (**Schéma R-14**).



SCHEMA R-14. Piégeage électrophile de l'intermédiaire vinylzincique.

La procédure typique consistait à utiliser le sel CuCN-2LiCl soluble dans le THF, mais le CuTC (disponible dans le commerce) pourrait être aussi utilisé avec des résultats comparables. Les deux protocoles se sont avérés tout aussi efficaces pour les intermédiaires vinylzinc issus de la germylzincation des ynamides terminaux ou internes, donnant ainsi accès à des vinylgermanes tri- ou tétrasubstitués avec une géométrie définie, et diversement substitués. Les électrophiles carbonés et non carbonés possibles comprennent des halogénures allyliques (**153–155** et **159–163**), des halogénures d'acyle (**156**), des bromures d'alcynyle (**157**, **165–167**), de l'iodure de méthyle (**164**) ou une phénylthio sulfone (**158**).

Dans le but d'élargir davantage les possibilités de fonctionnalisation de la liaison C(sp²)–Zn, nous avons également démontré que l'intermédiaire β -germyl vinylzinc pouvait participer à des additions conjuguées. La cyclohex-2-énone a réagi en présence de Me₃SiCl avec le produit d'addition de germylzincation de **54** dans des conditions similaires à celles décrites par Knochel, pour donner 67% du produit d'addition de Michael **168** (**Schéma R-15**).



SCHEMA R-15. Fonctionnalisation de la liaison C(sp²)–Zn par addition conjuguée.

Cependant, l'excès d'Et₂Zn nécessaire à l'étape de germylzincation, complique dans certains cas la fonctionnalisation efficace de la liaison C(sp²)–Zn, en particulier pour les réactions d'halodézincation où le contrôle de la quantité de l'électrophile s'est révélé être un problème critique pour obtenir des réactions propres. Afin de remédier à ce problème, et puisque l'Et₂Zn est volatil, nous avons envisagé l'élimination de l'excès d'Et₂Zn par évaporation du mélange réactionnel sous pression réduite avant l'étape de substitution électrophile. Lors de l'élimination de l'Et₂Zn, le déplacement des équilibres de Schlenk (Schéma R-8) a conduit à la formation exclusive de divinylzinc intermédiaires.



FIGURE R-2. Divinylzinc intermédiaires 169 et 170.

En particulier, la structure des composés **169** et **170** a été analysée par cristallographie aux rayons X et a montré des caractéristiques similaires (**Figure R-2**). Nous avons donc pu sécuriser la géométrie *cis* entre le zinc et le germanium après germylzincation. Les deux structures cristallines présentaient des caractéristiques similaires. Une disposition presque linéaire des deux liaisons carbone-zinc a été observée, comme en témoignent les angles de liaison autour de 165–170° (**169** : C1–Zn–C26 = 170,8(3)° ; **170** : C1–Zn–C27 = 165,5(3)°). En ce qui concerne les longueurs de liaison, elles se situaient toutes dans la fourchette prévue pour les composés diorganozinciques (**169** : Zn–C1 = 1,995(8) Å, Zn–C26 = 1,985(8) Å ; **170** : C1–Zn–C3 = 91,3(3)°), adoptant une géométrie peu commune tétracoordinée à bascule. La position des noyaux aromatiques du groupement Ph₃Ge est également intéressante. Même s'il n'y a pas de contact entre le zinc et la position *ipso* des phényles, deux d'entre eux protègent stériquement l'atome envers l'hydrolyse et l'oxydation.

Les intermédiaires divinylzinc issus de la séquence de germylzincation / évaporation ont également été engagé dans des réactions de substitution électrophile en présence de Cu(I) dans le THF ce qui a offert des possibilités supplémentaires de fonctionnalisation C(sp²)–Zn (**Schéma R-16**). L'utilisation d'électrophiles halogénés a été possible et des germylénamides β décorés en position β avec de l'iode (**172**), du brome (**173**) ou du fluor (**174**) ont été préparés avec des rendements acceptables. La trifluorométhylation avec le réactif d'Umemoto pour fournir **175** a été également possible. Un atout supplémentaire de ce protocole est qu'il permet l'utilisation de quantités catalytiques de sel de Cu(I), comme montré pour la formation de **153** avec 87% de rendement à partir de **54** en utilisant 10 mol% de CuTC pour promouvoir l'étape d'allylation.



SCHEMA R-16. Piégeage électrophile de les intermédiaires divinylzinc.

Pour illustrer le potentiel synthétique des germylénamides β accessibles par la nouvelle chimie de germylzincation, nous nous sommes ensuite concentrés sur la fonctionnalisation ultérieure de la liaison C(sp²)–Ge.

La réaction du *triéthyl*germylénamide **77** avec le brome a conduit à la formation inattendue du produit d'addition **179**, qui a été isolé en tant qu'hémiaminal **181** stable avec 68% de rendement après chromatographie sur gel de silice, sa structure étant confirmée par cristallographie aux rayons X (**Schéma R-17**). Étonnamment, la même réactivité chimique a été observée à partir du *triphényl*germylénamide **59**. La seule formation de l'adduit **180** a été observée cette fois-ci, délivrant à nouveau l'hémiaminal **181** lors de l'exposition au gel de silice.



SCHEMA R-17. Réaction de β-germylénamides **77** et **59** avec Br₂.

La transformation subséquente des adduits **179** et **180** en **181** hémiaminal semblait se produire par attaque nucléophile au niveau du carbone adjacent à l'atome d'azote. Ceci a été confirmé par l'exposition de l'adduit **180** au méthanol (**Schéma R-18**). Après une heure de contact, nous avons observé une conversion propre et complète en composé fonctionnalisé **184**, qui a été isolé avec un excellent rendement de 87% et s'est révélé remarquablement stable.



SCHEMA R-18. Exposition de l'adduit 180 au méthanol.

En outre, le traitement à -78 °C dans CH₂Cl₂ de *E*-**59** avec de l'ICl ou de l'iode a permis d'obtenir une halodégermylation propre fournissant de l'iodoénamide disubstitué **50** avec un excellent rendement, tandis que la réaction de **138**, **153** et **156** avec Br₂ a donné des bromoénamides trisubstitués **187–189** avec des rendements de moyen à quantitatif (44–99%), dans tous les cas avec un haut degré de stéréosélectivité (**Schéma R-19**). Cependant, bien que les germylénamides **187** et **188** trisubstitués aient réagi en conservant la géométrie du double liaison, une inversion complète de la configuration a été observée à partir du substrat **156**.



SCHEMA R-19. Halodégermylation de β-germylénamides.

Pour terminer notre étude, la possibilité d'effectuer la réaction de germylzincation avec des alcynes autres que les ynamides a été envisagée. L'addition de Ph₃GeH / Et₂Zn sur la triple des alcynes terminaux substitués par du soufre, de l'oxygène et du phosphore s'est produite à 0 °C donnant les vinylgermanes α -hétéroatome-substitués correspondants **232**, **238**, **241**, **244–245** avec le contrôle complet de la régiosélectivité β et la stéréochimie *cis* (**Schéma R-20**).



SCHEMA R-20. Germylzincation d'alcynes α-hétéroatome-substitués.

Les rendements isolés se situaient entre 37% et 70%. Dans tous les cas, le marquage au deutérium a confirmé la formation d'intermédiaires vinylzinc et la disponibilité de la liaison C(sp²)–Zn formée pour une fonctionnalisation ultérieure, puisque [²H]-**232**, [²H]-**238**, [²H]-**241**, [²H]-**244–**[²H]-**245** ont été obtenus (> 90% d'incorporation D) par hydrolyse au ND₄Cl. Dans le

cas du produit **244**, l'incorporation de D en α du germanium a également été observée, ce qui indique que la germylzincation s'est produite sur l'alcyne métallé.

La nouvelle approche de germylzincation ne s'est pas limitée aux alcynes substitués par des hétéroatomes et a pu également être étendue aux alcynes classiques. Une optimisation poussée de la préparation stéréosélective de germanes vinyliques provenant de diverses alcynes a été effectuée (et les conditions optimisées sont résumées dans le **Schéma R-21**).



SCHEMA R-21. Germylzincation d'alcynes classiques.

Les alcynes (aryle, alkyl)-substitués, les diarylacétylènes, les dialkylacétylènes et les alcools propargyliques aryl-, alkyl- ou TMS-substitués conviennent comme substrats pour la réaction de germylzincation. Même si les produits de départ sont moins réactifs, par une optimisation soigneuse des conditions de réaction et l'ajout d'AIBN comme initiateur radicalaire, une pléthore d'alcynes internes ont été transformées en germanes vinyliques correspondants avec un haut degré de stéréosélectivité, malgré quelques problèmes de régiosélectivité. Il est important de noter que les alcools propargyliques substitués par des groupes aryle, alkyle et TMS ont donné les vinylgermanes correspondants, où le groupement hydroxyle s'est comporté comme un excellent groupe dirigeant pour obtenir un excellent contrôle de la régio- et stéréosélectivité. La fonctionnalisation *in situ* de la liaison C(sp²)–Zn a élargi la portée d'une telle transformation et offre un raccourci vers la diversité structurelle construite sur le motif vinylgermane.

En conclusion, nous avons décrit dans cette thèse de doctorat la **première méthodologie générale pour la synthèse de vinylgermanes tri- et tétrasubstitués en une seule étape par germylzincation radicalaire d'alcynes (Figure R-3)**. Nos découvertes ont comblé une lacune en synthèse organique en permettant l'accès direct à des vinylgermanes sur mesure. Cela permettra certainement de faire avancer le positionnement des vinylgermanes en tant motifs importants de la chimie organique.



FIGURE R-3. Conclusion générale.

En guise de dernier commentaire et d'un point de vue plus large, les travaux actuels sont également importants parce qu'ils démontrent la généralité de l'approche de l'élémentozincation radicalaire. Cela pourrait certainement amener le concept de l'élémentométallation radicalaire en une alternative puissante aux procédés (plus) couramment utilisés catalyser par les métaux. Notamment, des résultats préliminaires ont prouvé la faisabilité de la silylation et de la borylzincation radicalaire d'alcynes.

GERMYLZINCATION RADICALAIRE D'ALCYNES

Le développement d'une approche radicalaire pour la germylzincation des alcynes en tant que voie simple et générale pour la préparation de vinylgermanes polysubstitués était l'axe central de ce travail. Dans le cadre de ce projet, nous avons démontré que l'addition régio- et stéréosélective de germanium et de zinc sur la triple liaison C–C d'ynamides terminaux et internes peut être réalisée par réaction avec un mélange d'hydrogermane et de diéthylzinc dans un processus radicalaire. La principale caractéristique de cette nouvelle approche est la possibilité de fonctionnaliser la liaison C(sp²)–Zn créée par substitution électrophile *in situ* cupro- ou palladocatalysée avec rétention de la géométrie de la double liaison. Notamment, la fonctionnalisation de la liaison C(sp²)–Ge a également été réalisée, augmentant la valeur synthétique des germylénamides. L'approche de germylzincation radicalaire a été étendue à d'autres alcynes substitués avec un hétéroatome en α , ainsi qu'aux alcynes classiques, avec d'excellents niveaux de stéréocontrôle. Ce travail représenté une avancée importante par rapport à l'état de l'art en offrant un accès modulaire à des vinylgermanes di-, tri- et tétrasubstitués élaborés, inaccessibles jusqu'à présent par d'autres méthodes. Dans une perspective plus large, la généralisation de l'approche d'élémentozincation radicalaire a été abordée de manière préliminaire.

Mots clés : germylmétallation, chimie radicalaire, zinc, germanium, vinylgermanes

RADICAL GERMYLZINCATION OF ALKYNES

The development of a general radical approach for the germylzincation of alkynes as a straightforward route for the preparation of polysubstituted vinylgermanes was the central axis of this work. Within this project, we disclosed that the regio- and stereoselective addition of germanium and zinc across the C–C triple bond of terminal and internal ynamides was achieved by reaction with a combination of a hydrogermane and diethylzinc in a radical chain process. The key feature of this new approach was the possibility of using the C(sp²)–Zn bond created as linchpin for subsequent *in situ* Cu(I)- or Pd(0)-mediated electrophilic substitution with retention of the double bond geometry. Notably, functionalization of the C(sp²)–Ge bond was also achieved, enhancing germylenamides' synthetic value. The radical germylzincation approach was further extended to other α -heteroatom-substituted alkynes, as well as more challenging conventional alkynes with excellent levels of stereocontrol. This work marked an important advance over prior art by offering modular access to elaborated di-, tri- and tetrasubstituted vinylgermanes that were not accessible by other methods thus far. From a wider perspective, the generality of the radical elementozincation approach was also preliminarily considered.

Keywords: germylmetalation, radical chemistry, zinc, germanium, vinylgermanes