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Taming highly reactive metal cations and intermediates in homogeneous catalysis using a weakly coordinating anion

Zhilong Li

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Taming highly reactive metal cations and intermediates in homogeneous catalysis using a weakly coordinating anion

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Thèse présentée et soutenue à Orsay, le 21 Juillet 2020, par

Zhilong LI

Composition du Jury

Arnaud VOITURIEZ Directeur de recherche, ICSN CNRS	Président
Samuel DAGORNE Directeur de recherche, Université de Strasbourg	Rapporteur
Julie OBLE Maître de conférences, Sorbonne Université	Rapporteur
Julien MONOT Maître de conférences, Université Paul Sabatier	Examineur
Christophe BOUR Maître de conférences, Université Paris-Saclay	Directeur de thèse
Vincent GANDON Professeur des Universités, Université Paris-Saclay	Invité

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Synthèse en Français

En synthèse organique, la construction de molécules d'intérêt, telles que des composés biologiquement actifs, des produits pharmaceutiques ou des synthons importants, a aussi mis la catalyse homogène à l'honneur. En effet, le développement de la synthèse organique fine s'est basé sur la recherche de nouvelles méthodes de synthèse et de nouveaux catalyseurs extraordinairement actifs. A cet égard, la plupart des espèces catalytiques à base de métaux du groupe 13 sont utilisés comme acides de Lewis pouvant efficacement et sélectivement promouvoir de nombreuses transformations catalytiques. Cependant, l'utilisation d'espèces de gallium (I) et d'indium (I) à bas degré d'oxydation en catalyse est encore moins développée en raison de leur instabilité et de leur tendance à se disproportionner. Néanmoins il avait déjà été prouvé que certains anions faiblement coordinants (WCA) pouvaient stabiliser ces cations métalliques hautement réactifs. Ainsi, notre objectif dans cette thèse est d'étudier le comportement catalytique de ces complexes, qui combinent des cations de gallium (I) ou d'indium (I) avec un anion faiblement coordonnant, dans diverses transformations catalysées par des acides de Lewis. Finalement des recherches récentes ont également révélé que les WCA pouvaient également stabiliser des intermédiaires de type cations vinyliques hautement réactifs. Cela nous a inspirés à consacrer nos travaux aux transformations plus complexes contenant un intermédiaire de cation vinyliques ne pouvant pas être promu par les catalyseurs acides de Lewis classiques.

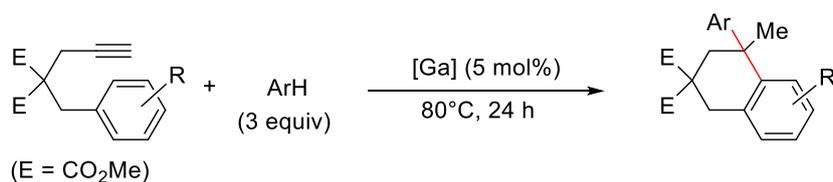
Cette thèse divisée en trois chapitres, présente le contexte de l'utilisation des complexes de gallium puis d'indium en synthèse organique. Dans une dernière partie, les intermédiaires cations vinyliques et leurs applications en synthèse a été explorées. Après chaque introduction, nous présenterons nos résultats sur les transformations catalytiques basées sur notre système catalytique, dans lequel le contre-ion est un anion faiblement coordonnant. À la fin de chaque chapitre, nous donnerons des détails expérimentaux détaillés.

CHAPITRE I: GALLIUM (I) D'ÉTAT À FAIBLE OXYDATION EN CATALYSE

L'élément gallium est un métal assez abondant, peu coûteux et peu toxique. Les espèces de gallium(III) ont été largement utilisées comme catalyseurs en tant qu'acides de Lewis dans la synthèse organique, y compris par interactions avec les électrons n, σ ou π des substrats carbonés. En revanche, seuls quelques travaux ont été publiés sur les composés de gallium(I) beaucoup moins stables. Selon le protocole de Krossing, les espèces univalentes de gallium (I) $[\text{Ga}(\text{PhF})_2][\text{Al}(\text{OC}(\text{CF}_3)_3)_4]$ peuvent être obtenues par une réaction redox entre le gallium (0) et un sel d'argent (I). Notre objectif a été d'explorer principalement ces espèces de gallium (I) dans notre laboratoire, y compris Ga_2Cl_4 et $[\text{Ga}(\text{PhF})_2][\text{Al}(\text{OC}(\text{CF}_3)_3)_4]$, dans la catalyse acide, et de comparer leur réactivité avec des sels de gallium (III) plus commun.

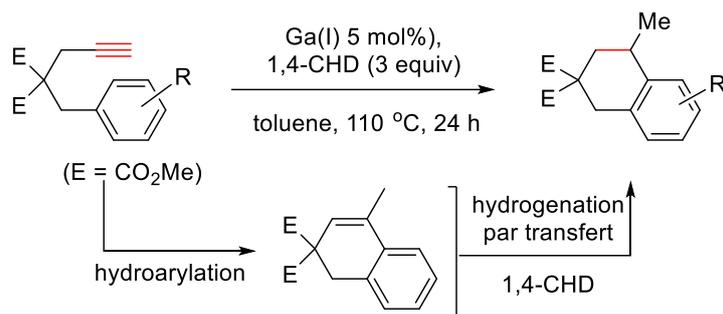
Dihydroarylation d'arenynes catalysées par du Ga(I)

Avec deux complexes de gallium (I) en main, nous avons commencé nos recherches par l'étude d'une réaction de référence que nous avons déjà utilisée précédemment pour évaluer la capacité des acides de Lewis gallium (III) à activer les alcynes et les alcènes en utilisant un seul substrat. Cette réaction implique une activation consécutive de la triple liaison C-C (étape d'hydroarylation) et d'une activation de la double liaison C=C (étape de type Friedel-Crafts)



Scheme 1. Réaction en tandem d'hydroarylation / Friedel-Crafts basée sur l'activation par le Ga(I)

cycloisomérisation d'arénynes pour favoriser la réduction de alcène cyclique généré in situ. La généralité de ce processus en tandem a été validée davantage en utilisant divers arénynes. Là encore, $[Ga][Al(OC(CF_3)_3)_4]$ et Ga_2Cl_4 se sont révélés catalytiquement actifs. Les produits de cyclisation / réduction ont été isolés avec des rendements bons à élevés.



Scheme 3. Ga (I) a catalysé la cyclisation hydrogénative des arénynes.

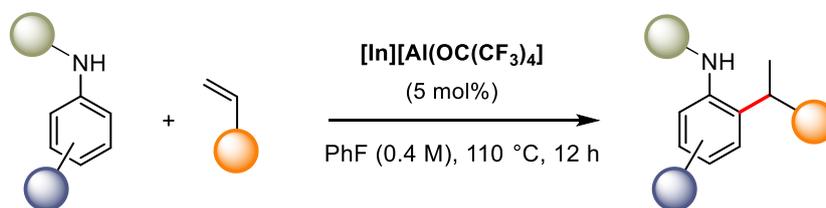
CHAPITRE II: INDIUM D'ÉTAT DE FAIBLE OXYDATION (I) EN CATALYSE

Les anilines N-alkylées jouent un rôle central dans la protection des cultures et les industries pharmaceutiques. Au cours des dernières décennies, des efforts importants ont été consacrés à la recherche de nouveaux protocoles efficaces et sélectifs pour leur synthèse. Parmi les méthodes les plus économiques en atomes et en étapes, l'hydroarylation et l'hydroamination d'alcènes à l'aide d'anilines occupent toujours une place prépondérante. Une grande variété d'acides de Lewis, de Brønsted et d'organocatalyseurs à base de métaux de transition a été développée à cet effet. Malgré des améliorations dans ce domaine, un certain nombre de défis restent à relever. Par exemple, la plupart de ces méthodes ne permettent pas la fonctionnalisation de l'azote. Dans d'autres cas, certaines hydrofonctionnalisations métallo- et proto-catalysées de styrènes avec des anilines primaires ou secondaires produisent un mélange de produits d'hydroamination (N-alkylation) et d'hydroarylation (ortho- et para-C-alkylation).

L'ortho-alkylation sélective des anilines n'a été réalisée que dans quelques cas et principalement en utilisant des anilines substituées par des groupes électroattracteurs. Les autres inconvénients de ces procédés comprennent la difficulté d'utiliser des anilines primaires car elles ont tendance à avoir une affinité de liaison trop forte avec les centres métalliques très électrophiles. Cependant, dans nos recherches précédentes, nous avons remarqué une incompatibilité majeure entre $[Ga][Al(OC(CF_3)_3)_4]$ et l'aniline dans les réactions d'hydroarylation. Nous avons émis l'hypothèse que cette inhibition due à la forte azaphilicité du métal devrait diminuer lors du déplacement vers le bas de la colonne des éléments du groupe 13, à mesure que le rayon atomique augmente et que l'oxydation à l'état bas + I devient plus stable. Par exemple, les dérivés d'In(I) sont connus pour être des acides plus doux que leurs analogues In (III) ou d'autres complexes du groupe 13 M (I) ou M (III), les rendant plus adéquats pour l'activation des N-nucléophiles.

Hydroarylation intermoléculaire des styrènes par l'aniline

Nous avons constaté que l'utilisation d'une quantité catalytique d' $[In][Al(OC(CF_3)_3)_4]$ (5 mol%) convertissait efficacement l'aniline en présence d'un équivalent de styrènes dans le fluorobenzène à 110 ° C en produits d'ortho-C-alkylation de type Markovnikov avec des rendements isolés de bons à excellents.



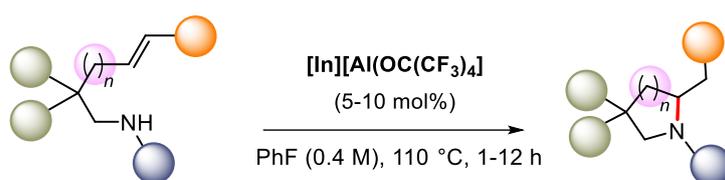
Scheme 4. Hydroarylation intermoléculaire des styrènes par l'aniline

Nous avons exploré la généralité de ce protocole avec une large gamme de dérivés de styrène, d'alcène et d'aniline, y compris les dérivés cycliques et acycliques. Les anilines présentant un groupe donneur d'électrons ou un halogénure en position para se sont

avérées compatibles dans les conditions de réaction optimisées. Les anilines portant un substituant ortho-halogénure ont également été converties avec succès en produits ortho-C-alkylés lors de la réaction avec le styrène. Remarquablement, une variété de styrènes substitués par un halogénure modérément désactivés ont été tolérés dans cette réaction. Ceci a été réalisé de manière très sélective, sans détecter la présence de produits de N-alkylation, ce qui diffère des méthodologies décrites rapportant un rapport 1/1 de produits C/N-alkylation. Les études mécanistiques ont suggérés une réaction en tandem hydroamination / réarrangement de Hoffmann-Martius et montrant que cette dernière était l'étape limitante.

Hydroamination intramoléculaire catalysée par In(I)

La réaction d'hydroamination intramoléculaire est l'une des voies les plus économiques des atomes pour accéder aux hétérocycles azotés. Comme nous l'avons montré dans la dernière sous-section, la compatibilité entre les anilines primaires et secondaires avec les cations In (I), ainsi que la présence de produits d'hydroamination intermoléculaire dans de rares cas, nous a conduit à étudier l'hydroamination intramoléculaire d'alcènes non activés par des amines primaires et secondaires non protégées.



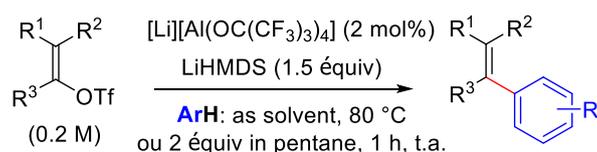
Scheme 5. hydroamination intramoléculaire des alcènes par In(I)

Après l'étude des solvants et des catalyseurs, nous avons trouvé que l'utilisation de 10% en moles d'[In][Al(OC(CF₃)₃)₄] dans le fluorobenzène à 110 °C était la meilleure condition réactionnelle. Cette l'hydroamination intramoléculaire a été appliquée à d'autres des alcènes. Une variété d'hétérocycles azotés à 5 et 6 chaînons a été facilement obtenue avec un rendement allant jusqu'à 99%. Les alcénylamines secondaires ont

également été des substrats appropriés. Les calculs théoriques de DFT ont soutenus l'activité catalytique d'un cation $\text{In}(\text{I})^+$ nu, avec un mécanisme de sphère externe pour la formation de la liaison C-N et une protodémétallation de sphère potentiellement interne. Des recherches sont en cours pour exploiter le potentiel de ces espèces ambivalentes dans d'autres réactions catalysées par d'autres acides de Lewis.

CHAPITRE III: VINYLATION BIMOLECULAIRE D'ARÈNES PAR CATIONS VINYLES

La réaction de Friedel-Crafts, découverte il y a 140 ans, reste l'une des méthodes les plus utilisées pour la fonctionnalisation des arènes. Bien que les électrophiles à base de carbone aient été largement utilisés, la vinylation directe des cycles aromatiques reste difficile à réaliser. Notre intérêt pour la réaction de Friedel-Crafts catalysée par l'acide de Lewis nous a conduit à rechercher un moyen d'utiliser les triflates de vinyle comme agents de vinylation dans des conditions douces. Nous avons donc décidé d'étudier la vinylation bimoléculaire plus difficile des arènes en utilisant des triflates de vinyle et des complexes $[\text{Li}][\text{Al}(\text{OC}(\text{CF}_3)_3)_4]$ comme catalyseurs.



Scheme 6. vinylation catalysée au lithium par l'intermédiaire de cations vinyliques

Comme indiqué ci-dessous, nos meilleures conditions sont l'utilisation de 2 mol% $[\text{Li}][\text{Al}(\text{OC}(\text{CF}_3)_3)_4]$ en présence de LiHMDS comme base. Deux conditions expérimentales différentes ont été développées pour promouvoir ces vinylations: soit en utilisant l'arène directement comme solvant (benzène, toluène et mésitylène), soit en utilisant le pentane comme solvant. Dans ce dernier cas, 2 équivalents d'arène sont uniquement nécessaires. L'utilisation de pentane permet également à la réaction d'être réduite à température ambiante au lieu de 80°C . Avec le partenaire arène utilisé comme

solvant, les substrats présentant des chaînes alkyles ont été bien tolérées, fournissant des styrènes avec de bons rendements. Les triflates composés de motifs de type cyclohexène, cycloheptène ou cyclooctène pouvaient également être couplés au benzène, au toluène ou au mésitylène. Toujours dans le pentane comme solvant, il a été possible d'utiliser des 1-phénylvinyltriflates comme substrats présentant des groupements p-F, p-Cl, p-Br et p-CF₃ électro-attracteurs, ainsi que le groupement m-CH₃ donneur d'électrons. Le mésitylène, le p-xylène, le 1,4-diméthoxy et le 1,3,5-triméthoxybenzène riches en électrons se sont avérés également parfaitement compatibles. L'étude mécanistique laisse suggérer la formation d'un cation vinylique, puis le déplacement 1,3 -d'hydrure formant carbocation tertiaire.

CONCLUSION GÉNÉRALE

En général, nous avons étudié le comportement du contre-ion aluminate faiblement coordonné [Al(OC(CF₃)₃)₄]⁻ dans les processus catalytiques basés sur les métaux cationiques. Le catalyseur [Ga][Al(OC(CF₃)₃)₄] a été appliqué dans des transformations comprenant la dihydroarylation d'arènes, l'hydrogénation par transfert d'alcènes, l'hydrogénation en tandem, la cyclisation des arènes et la cycloisomérisation enynes. Le catalyseur [In][Al(OC(CF₃)₃)₄] a été utilisé pour favoriser l'ortho-C-alkylation d'anilines non protégées en présence de styrènes et l'hydroamination d'alcénylamines primaires et secondaires non protégées. Le catalyseur [Li][Al(OC(CF₃)₃)₄] a enfin été testé dans la synthèse de dérivés styréniques à partir de triflate de vinyle et d'arènes via un cation vinylique. Nous avons prouvé que cet anion volumineux et inerte [Al(OC(CF₃)₃)₄] était capable d'appriivoiser les cations hautement réactifs, à la fois les métaux cationiques et les intermédiaires de réaction, ouvrant ainsi de nouvelles perspectives en méthodologie de synthèse.

LIST OF ABBREVIATIONS

1,4-CHD	1,4-cyclohexadiene	h	hour/hours
Ar	aryl	HRMS	high resolution mass
BINOL	1,1'-bi-2-naphthol	HR-PIB	high molecular weight polyisobutylene
Bn	benzyl	IR	infrared spectroscopy
Boc	<i>tert</i> -butyloxycarbonyl	L	ligand
bp	boiling point	LUMO	lowest unoccupied molecular orbital
cat	catalyst	<i>m</i> -	<i>meta</i> -position
Cp	cyclopentadienyl	Me	methyl
CPME	cyclopentyl methyl ether	min	minute
Cp*	pentamethylcyclopentadiene	<i>Mn</i>	molecular weight
Cy	cyclohexyl	MS	mass spectrometry
d	day	NHC	N-Heterocyclic carbene
DAC	donor-acceptor cyclopropanes	NMR	nuclear magnetic resonance
DCE	1,2-dichloroethane		spectroscopy
DFT	density functional theory	Nu	nucleophile
DMF	dimethylformamide	NTf ₂	bis(trifluoromethanesulfonyl)imide
DMSO	dimethylsulfoxide	<i>o</i> -	<i>ortho</i> -position
<i>dr</i>	diastereomeric ratio	OTf	triflate
DTBP	Di- <i>tert</i> -butyl peroxide	<i>p</i> -	<i>para</i> -position
<i>ee</i>	enantiomeric excess	pftb	perfluorotributyloxyl
EDG	electron donating group	PIB	polyisobutylene
equiv	equivalents/equivalent	pin	pinacol ester
er	enantiomeric ratio	Ph	phenyl
ESI	electrospray ionization	ppm	parts per million
Et	ethyl	PTHF	polytetrahydrofuran
EWG	electron withdrawing group	Py	pyridine
GC	gas chromatography	PyBox	2,6-bis(oxazolin-2-yl)pyridine

ref	reference
ROP	ring-opening polymerization
rt	room temperature
<i>t</i> Bu	<i>tert</i> -butyl
Tf	trifluoromethanesulfonyl
THF	tetrahydrofuran
TMS	trimethylsilyl
Ts	tosyl
UV	ultraviolet
XRD	X-RayDiffraction
)))	ultrasonication

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GENERAL INTRODUCTION

In organic synthesis, the construction of molecules of interest, such as biologically active compounds, pharmaceuticals or important synthons, brings homogeneous catalysis in the limelight. The development of advanced synthesis is based on the expansion of theory and the search of extraordinarily active catalysts. In this respect, most of the catalytic species based on group 13 metals are important Lewis acids that can efficiently and selectively promote many catalytic transformations. However, the use of low-oxidation state gallium(I) and indium(I) species in catalysis is still less developed, due to their instability and the trend of disproportionation. Since it has already been proved that the weakly coordinating anions (WCAs) can stabilize these high reactive metal cations. So, our aim in this thesis is to investigate the catalytic behavior of the complexes, which combine gallium(I) or indium(I) cations with WCA, in various transformations mostly based on Lewis acid activations. In addition, researches recently have revealed that the WCAs can also stabilize the high reactive vinyl cation intermediates. That inspired us to expand our interests into the more challenge transformations containing a vinyl cation intermediate, which cannot be promoted by classic Lewis acid catalysts.

This thesis will be divided into three chapters by introducing the background of gallium complexes, indium complexes, and vinyl cation intermediates in modern synthetic chemistry. After each introduction, we will present our results in catalytic transformations based on the catalytic system, in which the counterion is a WCA. At the end of each chapter, we will give detailed experiment procedures.

CHAPTER I: LOW OXIDATION STATE GALLIUM(I) IN CATALYSIS

1. INTRODUCTION

In the past, gallium compounds have been considered less attractive species for organic transformations than aluminum or boron analogs, mainly because its Lewis acidity is generally considered to be lower. However, recent investigations have demonstrated that gallium derivatives may also be quite effective for the catalytic construction of useful chemicals that may not be achieved by other Group 13 analogs. Although, gallium is a fairly abundant and relatively inexpensive metal displaying good functional group compatibility and low toxicity, only its stable high oxidation state +III has been well studied. In contrast, the chemistry of gallium in the less stable low oxidation state +I is largely underexplored, as it has the propensity to undergo disproportionation to form gallium(III) and gallium(0). However, the peculiar electronic properties of Ga(I) (vide infra) raised our interest in the use of such low-valent species in homogeneous catalysis. Summarized in this section are the recent developments of gallium compounds not only in the +III oxidation state but also in the low oxidation state +I in organic transformations, including some of our contributions in this area.

1.1 General Properties of Gallium Compounds

Gallium is a chemical element with the symbol **Ga** and atomic number 31, located in Group 13 of the periodic table. It has the electron configuration $[\text{Ar}] 3d^{10} 4s^2 4p^1$. Gallium is a silver-like and brittle metal in the solid state, with a low melting point of 29.8 °C. It can turn to liquid state in the hand (Figure 1). For the moment, the gallium elements and its derivatives are considered to have low toxicity, although the data on this matter is not fully conclusive. Since its discovery in 1875 by the French chemist, Paul-Émile Lecoq de Boisbaudran, gallium has been used to make alloys with low

melting points, and many pivotal materials. For example: i) gallium (and indium) alloys are found in automatic fire extinguishers, ii) gallium arsenide (GaAs) is widely used to manufacture LEDs, lasers, and transistor, iii) gallium nitride (GaN) can be used to make diodes.^[1,2]

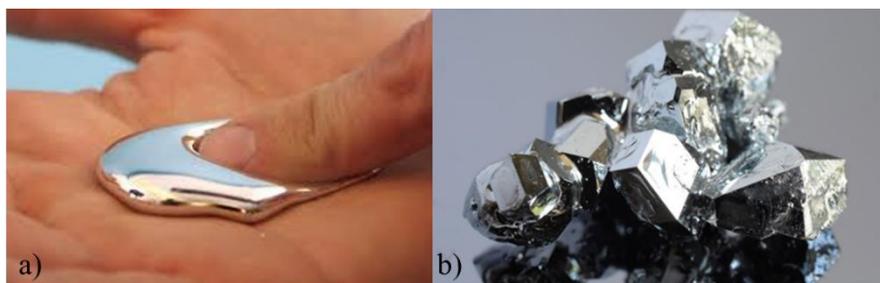


Figure 1. a) Gallium melting in the hand. b) Gallium crystals (Images from Wikipedia [1])

The abundance of gallium in the Earth's crust is approximately 16.9 ppm, which is quite abundant compared to the 0.004 ppm of gold.^[1] However, gallium does not exist free in nature. Most of it is extracted as a byproduct of aluminum and zinc production. The price of 99.99% pure gallium is 0.48 \$/g according to The Science Company quoted price in April 2020.

The most stable isotopes of gallium are ^{69}Ga and ^{71}Ga , with natural abundances of 0.60108 % and 0.39892 % respectively and a spin value of 3/2. As both of their nuclei are quadrupolar, the NMR spectrometers observe broad signals. ^{71}Ga is usually chosen as the nucleus for gallium NMR as it is more sensitive and gives narrower signals than ^{69}Ga . The reference compound is $\text{Ga}(\text{NO}_3)_3$ in D_2O .^[3]

Gallium is mainly found in the +III oxidation state. Gallium in its +I oxidation state is also attested in few compounds. However gallium(I) is much less common than its heavier congeners indium(I) and thallium(I), and it is known to easily disproportionate into gallium(0) and gallium(III) compounds. For example, “GaCl” is unstable and decomposes readily into elemental gallium(0) and gallium(III) chloride.^[4] It should be noted that the +II oxidation state of gallium is even more uncommon. In fact, the

relatively stable Ga_2Cl_4 is not a gallium(II) compound but a mixed gallium(I)/gallium(III) species of formula $[\text{Ga(I)}][\text{Ga(III)Cl}_4]$. Compounds containing Ga-Ga bonds are true gallium(II) compounds such as GaS, which can be formulated as $\text{Ga}_2^{4+}(\text{S}^{2-})_2$.^[5,6] The different oxidation states of gallium can be visualized in Figure 2.

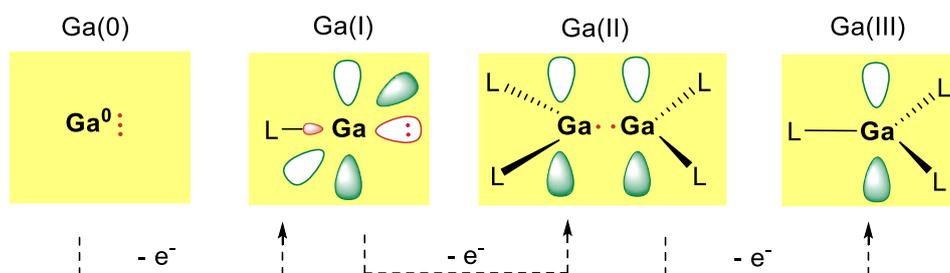


Figure 2. The different oxidation states of gallium

The highest oxidation state +III was reported to be the most stable under ambient conditions. Here, the gallium center is usually bound to three ligands and has a vacant low energy p orbital. Therefore, gallium(III) may act as a Lewis acid. Monomeric gallium(II) species were reported to be substantially less stable, but adducts may be formed fairly easily, leading to more stable ‘dimeric’ Ga(II)-Ga(II) species, which may act as relatively soft, two-center Lewis acids.^[7,8] Gallium in its low oxidation state +I may display ambiphilic properties.^[9] On one hand, due to a vacant low-energy p orbital, it may act as soft Lewis acid. On the other hand, due to an sp -type lone pair of electrons, it may act as a Lewis base. This potentially ambiphilic character represents an interesting area of research that is worth being thoroughly explored.^[10]

Gallium compounds have become very important in the electronics industry, and some gallium complexes have been examined for use as anticancer or diagnostic agents.^[11] Summarized in this chapter are their use as homogeneous catalysts, typically as Lewis acids, based on different activation modes. We will not address alkylgallium and gallium hydride reagents,^[11] gallium radical reagents,^[11] gallium-containing zeolites^[12] in organic synthesis, heterogeneous catalysis or specific coordination compounds, even though their contribution to these areas is also very impressive.

1.2 Gallium(III) Lewis Acids in Homogeneous Catalysis

In organic synthesis, gallium(III) compounds were considered as less attractive than the corresponding aluminum(III) compounds. However, recent studies have revealed that gallium(III) compounds exhibit unique properties in organic synthesis that cannot be reproduced with aluminum species.^[13,14]

In particular, trivalent gallium(III) compounds possessing a Lewis acid character have been shown to interact not only with n electrons as anyone expects, but also with π and σ electrons of organic molecules and, as a consequence, promote characteristic organic transformations. In this chapter, we will emphasize the activation of organic molecules by the Lewis acid interactions with gallium(III) compounds and their use in organic catalysis.

1.2.1 Lewis acidity and coordination properties

The Lewis acidity of Group 13 halides in the +III oxidation state, i.e. MX_3 salts, comes from the empty acceptor p orbital on M, which is the main contributor to the LUMO (Lowest Unoccupied Molecular Orbital). However, the discussion on the Lewis acidity of Group 13 halides is rather complex. One of the most useful methods for the evaluation of Lewis acidity is by using the $\text{MX}_3(\text{L})$ model, where “L” represents a solvent molecule or a ligand. Lippert suggested the use of the infrared (IR) carbonyl stretching frequency of coordinated ethyl acetate for the qualitative comparison of Lewis acidity.^[15] The order of $\text{BCl}_3 > \text{GaCl}_3 > \text{AlCl}_3$ was obtained for the perturbations in the $\nu_{\text{C=O}}$, which suggests a higher Lewis acidity for GaCl_3 compared to AlCl_3 . Barron compared the complexes of 9-fluorenone with Group 13 metal halides using IR, NMR, X-ray and UV analyses.^[16] The IR carbonyl stretching frequencies shows again the order $\text{BCl}_3 > \text{GaCl}_3 > \text{AlCl}_3$. Thus, these results reach the same conclusion as Lippert’s. However, the shift in the UV-vis spectra provides a trend of $\text{BCl}_3 > \text{AlCl}_3 > \text{GaCl}_3$. Moreover, XRD technique shows an order of $\text{AlCl}_3 > \text{BCl}_3 > \text{GaCl}_3$. Finally, Barron

concluded that no spectroscopic or structural parameters could provide a consistent prediction of Lewis acidity strength for Group 13 metal compounds.

In fact, the Lewis acidity of Group 13 metals in their +III oxidation state, depends on the nature of the base, on the dissociation equilibrium between $(MX_3)_2$ dimers and MX_3 monomers since MX_3 salts tend to strongly associate through halide bridges in non-polar solvents, and on the molecular or ion pair nature of the $L \cdot MX_3$ adduct. In that respect, it has been proven that MX_3 can be activated through dimeric association with the same or different electrophiles. As shown in Figure 3, the noncoordinating monomers **B** are more Lewis acidic than the doubly bridged saturated dimers **A**. However, the dimer compounds can also coordinate after dissociation of one bridge, as in **C**, which is more acidic than the monomer **B**. In an extreme situation, the polarization of the M-X bond may lead to its full ionization to generate ion pair **D** with the highest acidity. The relative acidity of various monomeric and dimeric species of M-X is $D > C > B > A$.^[17]

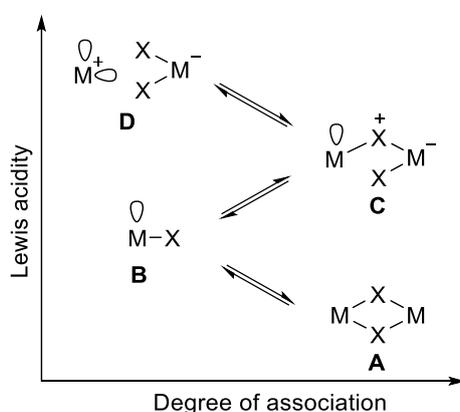
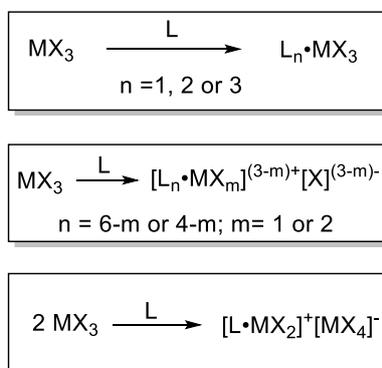


Figure 3. Relationship between Lewis acidity and state of association of M-X. (No associated X of MX_3 were omitted for clarity)

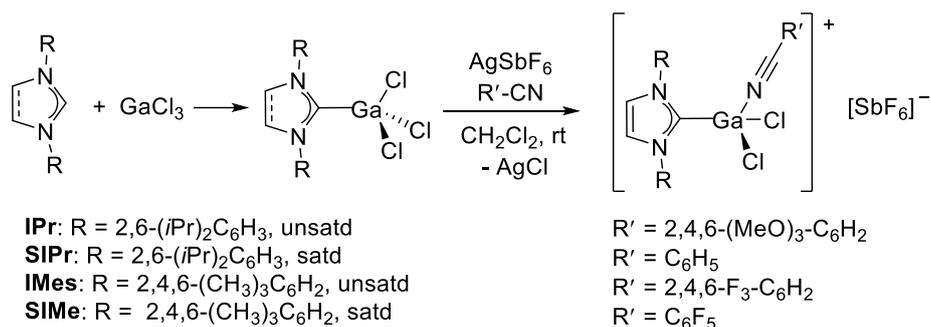
Due to the vacant p orbital, MX_3 compounds can coordinate with Lewis bases such as polar solvents. That opens an opportunity for chemists to modify their activity towards the applications in catalysis. The MX_3 compounds coordinating with solvents or other ligands might produce neutral molecular adducts of type $L_n \cdot MX_3$, or form ion pairs of

type $[L_n \cdot MX_m]^{(3-m)+}[X]^{(3-m)-}$ or $[L \cdot MX_2]^+[MX_4]^-$ as shown in Scheme 1.^[18,19] The outcome depends on the metal, on X and on the ligand. The dissolving of MX_3 will provide a solvolysis in the case of protic solvents.^[8]



Scheme 1. Coordination of MX_3 ($M = \text{Group 13 metal}$)

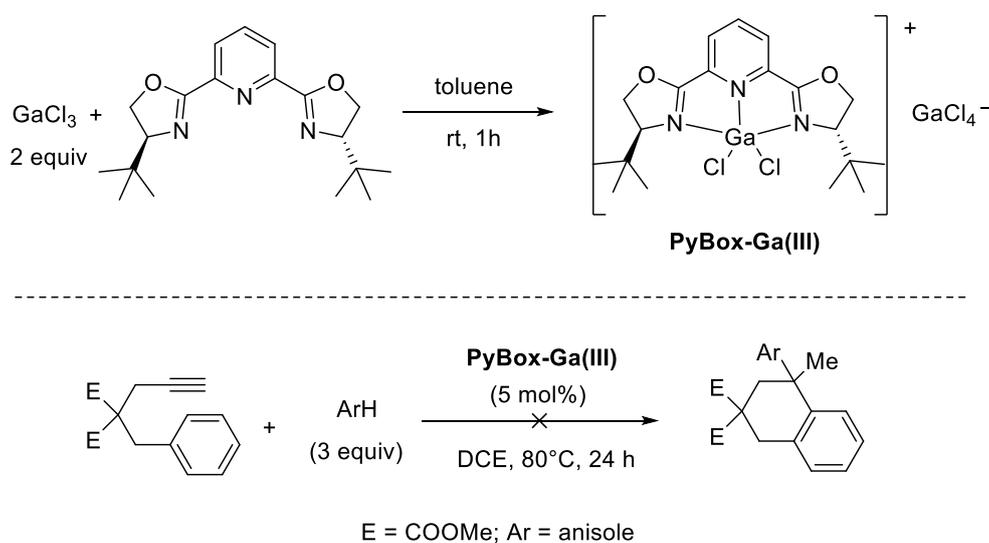
Below are some examples of molecular adducts or ion pairs that can be obtained upon coordination of $GaCl_3$ described in our group (Scheme 2).^[20] For instance, the n electrons of NHC (N-heterocyclic carbenes) interact with the metal center to form a stable NHC-Ga(III) molecular adduct. As it is an 8-electron complex, it has no Lewis acidity and is inactive in catalysis. To generate an active species, a vacant site on gallium can be obtained by halide abstraction, that is, by using a silver salt.



Scheme 2. From neutral to active cationic NHC-gallium(III) derivative

Based on this active cationic gallium(III) complex, hydroarylation of alkynes and alkenes, deoxygenation of alcohol,^[21] transfer hydrogenation of alkenes,^[22] tandem carbonyl-olefin metathesis/transfer hydrogenation and other reactions were successfully achieved.^[23]

The organometallic complexes of Al, Ga, and In primarily appear as four-coordinate metal centers, but higher valences are also common. For instance, our group synthesized the rare chiral gallium(III) complex shown in Scheme 3 by combining 2 equivalents of GaCl₃ with a chiral ligand PyBox. Its X-ray structure in Figure 4 shows this complex is an ionic pair of type [L_n·MX₂]⁺[MX₄]⁻. As much as the NHC·GaCl₃ complex discussed above, this species is saturated and therefore display no Lewis acidity. It seems to be a hypervalent 10-electron species, but because *d* orbitals of gallium are inaccessible, it is in fact an 8-electron species with formally one Ga-Cl bond ionic in nature ([N₃GaCl]⁺[Cl]⁻). As shown in Scheme 3, this complex is inactive in a cycloisomerization/Friedel-Crafts tandem reaction developed in our lab, which works very well with GaCl₃ or NHC·GaCl₂⁺ complexes.^[20] Trying to open a vacant site by chloride abstraction may in fact generate achiral GaCl₃ from GaCl₄⁻.



Scheme 3. Synthesis and study of PyBox-Ga(III) complex

Thus, there is a subtle balance between the coordination properties of Group 13 metals and their Lewis acidity. The solvent (or other ligands) can promote a solvolysis and enhance the acidity of the complex, or generate saturated inactive species (molecular adducts or ion pairs). The oxidation state is also an issue. It should be noted in this regard that the Lewis acidity of Group 13 metal compounds dramatically decreases

from +III oxidation state to +I oxidation state. The +I oxidation state induces weaker and softer Lewis acid properties.^[8]

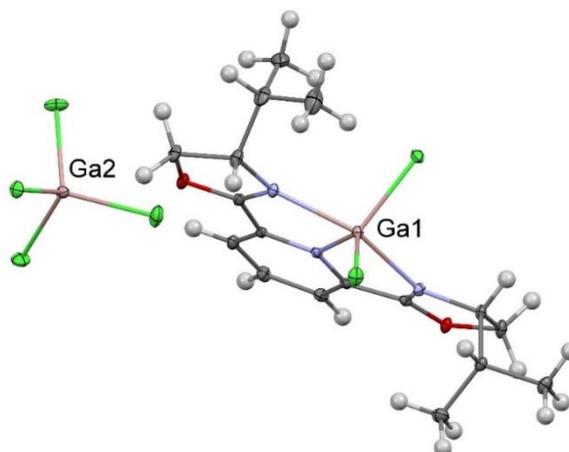


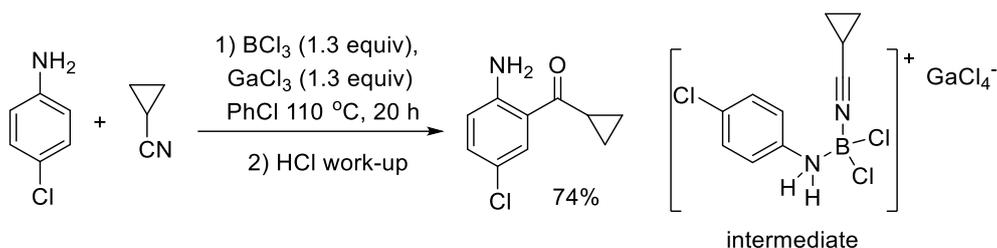
Figure 4. X-ray structure of a penta-coordinated PyBox-Ga complex

1.2.2 Lewis acid activation by interaction with n electrons

A nonbonding electron, also named n electron, is an electron in an atom that does not participate in bonding with other atoms. The term can refer to either a lone pair in which the electron is localized and associated with one atom or to a non-bonding orbital in which the electron is delocalized throughout a molecule.^[24] Gallium(III) Lewis acids catalysts can interact with the n electrons of heteroatoms such as halides, oxygen, nitrogen, sulfur, and other atoms, resulting in various organic transformations.

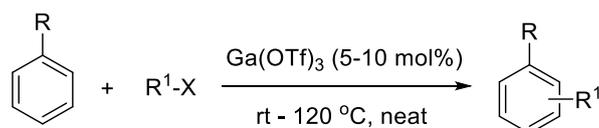
a. Halogen compounds

Houpis et al. reported a GaCl_3 assisted BCl_3 -promoted o -acylations of anilines.^[25] In this reaction, the aniline is condensed to a nitrile in the presence of $\text{BCl}_3/\text{GaCl}_3$ to give, after hydrolysis, the desired aniline derivatives regioselectively, which are useful synthons for the synthesis of reverse transcriptase inhibitor drugs. They identified the existence of a bimetallic intermediate by NMR studies. To reach this intermediate, the second Lewis acid GaCl_3 acted as a chloride ion abstractor, enhancing the activity of BCl_3 and overcoming the previously low yield issue.



Scheme 4. GaCl_3 acting as a chloride ion abstractor in catalysis

Friedel-Crafts alkylation and acylation reactions are powerful tools for C-C bond formation in organic synthesis. Gallium(III) Lewis acid catalysts can interact with alkyl or acyl halides, based on the n electron activation, resulting in the formation of an electrophilic carbocation or acylium ion which promotes the well-known $\text{S}_{\text{E}}^{\text{Ar}}$ process. For example, $\text{Ga}(\text{OTf})_3$ can be used in Friedel-Crafts alkylation,^[26] and Friedel-Crafts acylation of arenes (Scheme 5).^[27]



alkylation: $\text{R} = \text{CH}_3$, $\text{R}^1 = \text{adamantyl}$, $\text{X} = \text{Br}$, yield 100%
 $\text{R} = \text{H}$, Me, Et, di-Me(*o*, *m*, *p*), OMe, F, Cl;
 $\text{R}^1 = (\text{CH}_3)_2\text{CH}$; $\text{X} = \text{OH}$; yield 16 - 97%

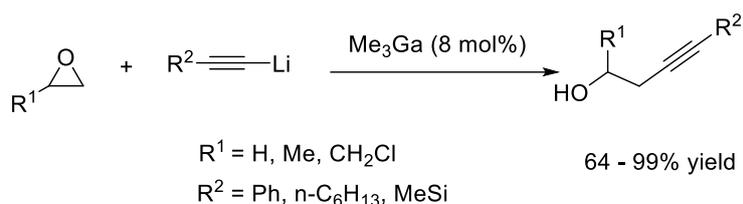
acylation: $\text{R} = \text{H}$, Me, Et, *sec*-butyl, *tert*-butyl, di-Me(*o*, *m*, *p*), tri-Me(1, 3, 5)
 $\text{R}^1 = \text{CH}_3\text{CO}$, $\text{C}_6\text{H}_5\text{CO}$; $\text{X} = \text{Cl}$; yield 10 - 97%

Scheme 5. Alkylation and acylation of aromatics using $\text{Ga}(\text{OTf})_3$ as catalyst

b. Organooxygen and organosulfur compounds

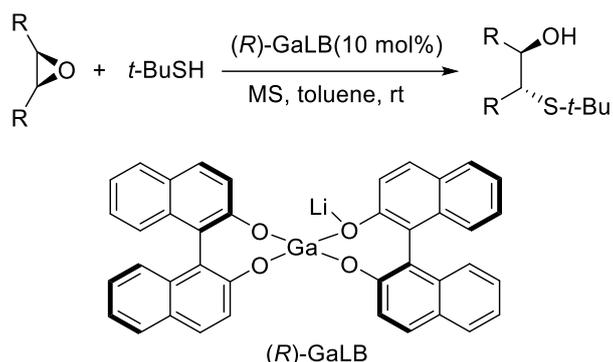
Gallium(III) Lewis acids can interact with the oxygen n electrons of strained oxiranes or alcohols, which are in turn attacked by nucleophiles.

For instance, Utimoto found that a catalytic amount (8 mol%) of Me_3Ga can promote the alkylation of oxiranes with lithium acetylides (Scheme 6).^[28] The reaction completed in 30 min at room temperature, affords the product in good yield. The alkynyl group is introduced at the less substituted carbon of the oxirane with a great regioselectivity.



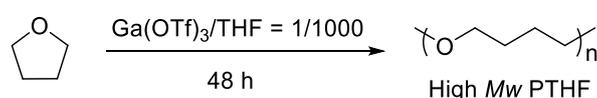
Scheme 6. Me₃Ga-catalyzed alkynylation of epoxides

The enantioselective ring-opening of epoxides with thiols catalyzed by gallium lithium bis(binaphthoxide) complex (GaLB) was achieved by the Shibasaki's group (Scheme 7).^[29] In this reaction, the lithium binaphthoxide moiety serves as a Brønsted base, activates the *tert*-butylthiol by deprotonation and subsequently controls the lithium thiolate by chelation. On the other hand, the gallium metal acts as a Lewis acid and activates the epoxide by the coordinating of the *n* electrons of oxygen. The chiral binaphthoxide induces the S_N2-like transition states enantioselectivity.



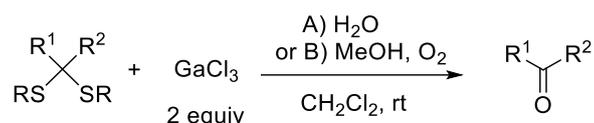
Scheme 7. Enantioselective ring opening of epoxides catalyzed by chiral GaLB complex

Ga(III) derivatives have witnessed growing attention for the applications in ring-opening polymerization (ROP) catalysis of cyclic esters, primarily lactide.^[30] In 1992, Olah et al. first reported on the use of the strong Lewis acid, Ga(OTf)₃ as an effective catalyst for the bulk polymerization of THF at ambient temperature for the production of high-molecular-weight polytetrahydrofuran (PTHF) in excellent yield (Scheme 8).^[31]



Scheme 8. Cationic polymerization of THF catalyzed by Ga(OTf)₃

The activation of organosulfur compounds by GaCl₃ was also reported. For instance, in the presence of GaCl₃ and water, thioacetals were smoothly and chemoselectively hydrolyzed to the corresponding ketones (Scheme 9).^[32] Even though the GaCl₃ loading was 2 equivalents, it still deserves to be mentioned here as the activation of sulfur is a challenge for the most common Lewis acids and the importance of the method for deprotection of thioacetals.

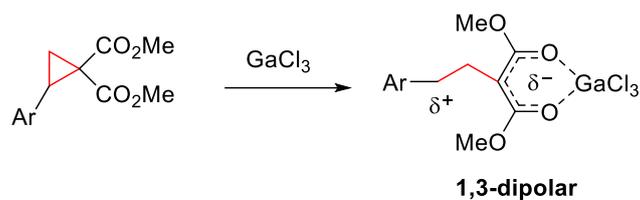


Scheme 9. Gallium chloride mediated hydrolysis to corresponding ketones

c. Carbonyl and related compounds

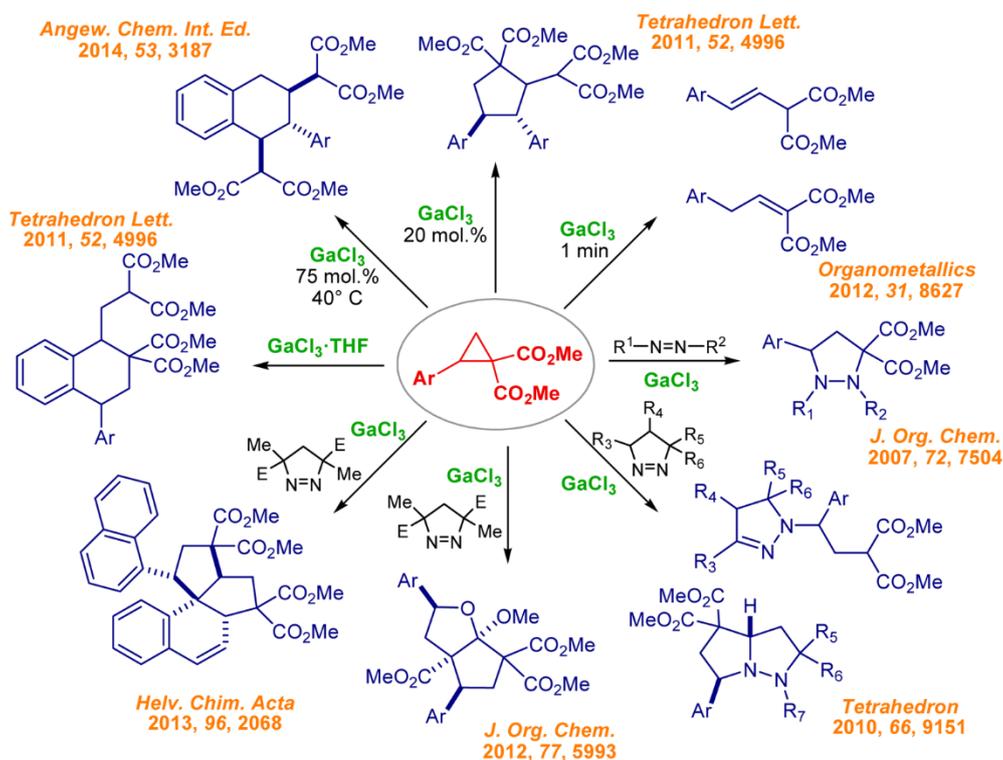
Carbonyl addition is a very important process in organic synthesis, and the Lewis acid activation of carbonyl by the interaction with n electrons is likely to be involved in the majority of the cases.

Mukaiyama aldol reaction is certainly one of the most notable C-C bonds-forming reactions. It focuses on the addition of silyl enolates to aldehydes in the presence of Lewis acids. Even though numerous catalytic Mukaiyama aldol reactions have been developed, it remains a challenge to control enantioselectivity under mild conditions. In 2005, Li's group reported an asymmetric Mukaiyama aldol reaction in aqueous media catalyzed by the combination of Ga(OTf)₃ with chiral semi-crown ligand (Scheme 10).^[33] In this reaction, ligand-acceleration effect was observed and water is essential for accessing high diastereo- and enantioselectivity. The preparation of the chiral catalyst was performed by mixing Ga(OTf)₃ with 1.2 equivalents of chiral ligand in methylene chloride at rt for 6 h. The resulting yellow solid was used directly in catalytic reactions after evaporating the solvent.



Scheme 13. GaCl_3 react with DAC to form 1,3-dipolar intermediate

Donor-Acceptor Cyclopropanes: Tomilov's group carried out considerable work based on GaCl_3 -activated donor-acceptor cyclopropanes (DAC). In general, a complex between GaCl_3 and the donor-acceptor cyclopropane is initially formed due to coordination to the electron-accepting group. As a result, a polarization of a σ bond in the cyclopropane ring occurs, resulting in its opening with generation of a 1,3-dipolar intermediate, which is involved in subsequent reactions (Scheme 13). The capability of donor-acceptor cyclopropanes to undergo [2+3], [3+3], and [3+4] dipolar cycloaddition with various substrates is now used to build five-, six-, and seven-membered carbo- and heterocycles (Scheme 14), mostly initiated by catalytic GaCl_3 .^[36]



Scheme 14. GaCl_3 mediated Donor-Acceptor Cyclopropanes (DAC) in organic synthesis (picture taken from ref [36])

1.2.3 Lewis acid activation by interaction with π electrons

An interesting feature of gallium(III) compounds among Lewis acids is their ability to interact with unsaturated bonds. GaCl_3 forms a π complex with π system, which strongly activates the triple/double bond towards nucleophilic attack (Figure 5).

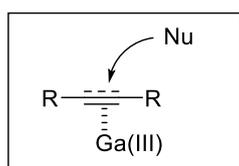
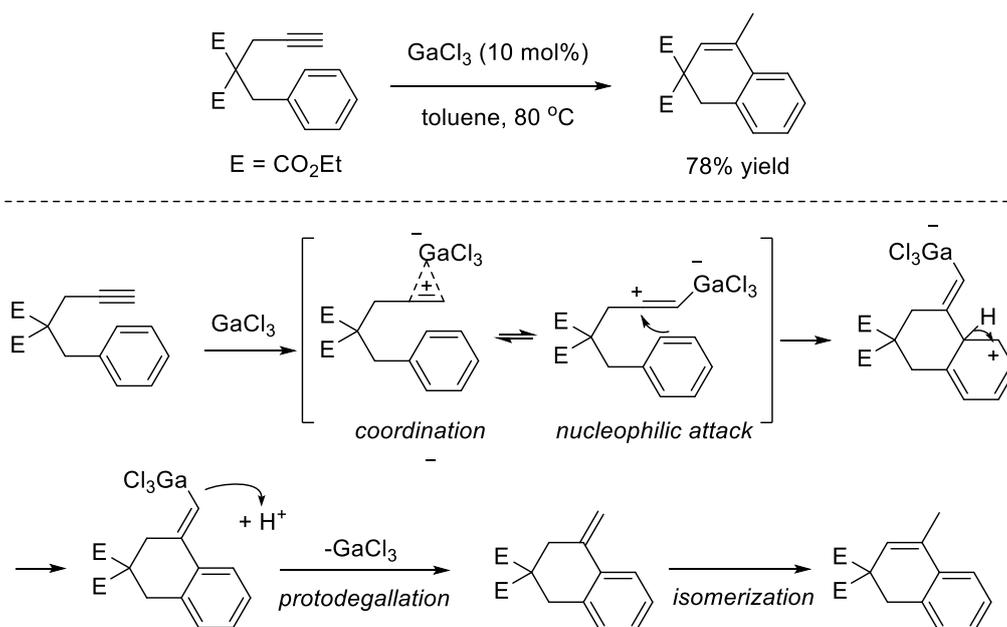


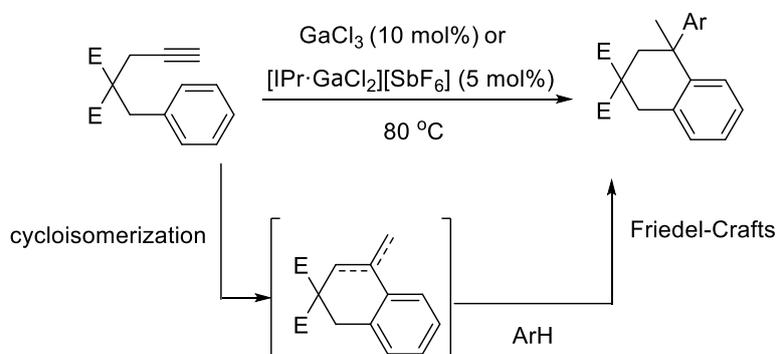
Figure 5. Gallium(III) interaction with π electrons

Chatani and Murai disclosed a cycloisomerization reaction of 1,6-arenynes catalyzed by GaCl_3 (Scheme 15).^[37] The postulated mechanism involves the coordination of GaCl_3 to the alkyne to form a π complex or a σ -vinyl gallium complex (vinyl cation). Subsequently, intramolecular nucleophilic *anti* attack of the benzene moiety produces a Wheland-type intermediate. Proton elimination and protodegallation forms an *exo* methylene product, which spontaneously isomerizes to a more substituted endocyclic alkene product.



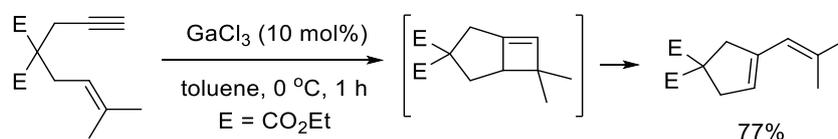
Scheme 15. Cycloisomerization of 1,6-arenyne catalyzed by GaCl_3 and its mechanism

Our group also reported related tandem reaction, involving a cycloisomerization of arenynes followed by a Friedel-Crafts reaction (Scheme 16).^[20,38] The catalysts system can be GaCl_3 or $[\text{IPr}\cdot\text{GaCl}_2][\text{SbF}_6]$.



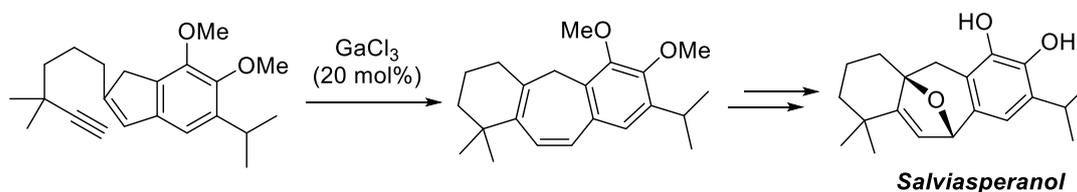
Scheme 16. Gallium-catalyzed cycloisomerization/Friedel-Crafts reaction

Moreover, Murai's group conducted the reaction of 1,6-enynes with GaCl_3 to give vinylcyclopentenes, which involves cyclobutene formation and 4π ring opening (Scheme 17).^[39]



Scheme 17. Gallium-catalyzed cycloisomerization of 1,6-enynes into vinylcyclopentenes

The method was applied into the synthesis of natural products, such as salviasperanol. In this process, a [7,6]-membered fused ring system was formed as the key step by the GaCl_3 catalyzed cycloisomerization reaction (Scheme 18).^[40]

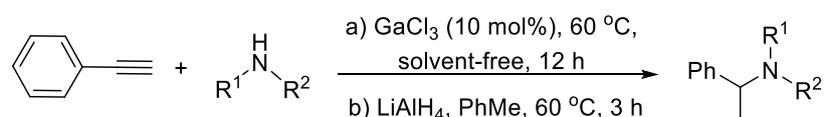


Scheme 18. GaCl_3 -catalyzed cycloisomerization strategy in total synthesis of salviasperanol

Hydroamination of olefins and alkynes is an atom economical method for the synthesis of amines. Although compounds of many elements of the periodic table have been

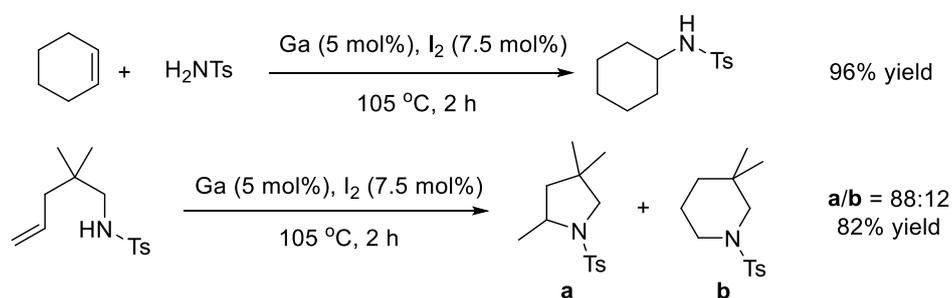
found to catalyze this reaction, the suitability of Group 13 metal compounds as hydroamination catalysts has only recently been investigated.

Yahong Li's group reported gallium trichloride catalyzed intermolecular hydroamination of alkynes. They identified GaCl₃ as an effective catalyst for the hydroamination of phenylacetylene with an aromatic amine, predominantly giving the Markovnikov products (Scheme 19).^[41]



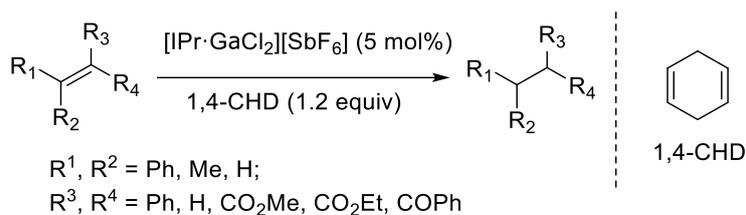
Scheme 19. GaCl₃-Catalyzed hydroamination of phenylacetylene with various amines

Doye et al. described the gallium(III) catalyzed inter- and intramolecular hydroamination addition of *p*-toluenesulfonamides to alkenes.^[42] Among the halides investigated, GaI₃, which can be conveniently formed in situ from metallic gallium and iodine, was identified as the selected catalyst. The metallic gallium can easily be recycled after each reaction. For that purpose, it is only necessary to remove the resulting crude organic reaction mixture from the metallic gallium, which usually precipitates during the course of the reaction (Scheme 20).



Scheme 20. GaI₃-catalyzed inter- and intramolecular hydroamination of alkene

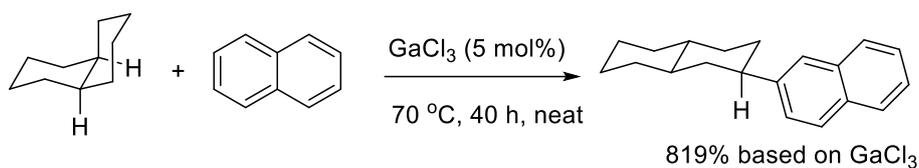
Catalytic transfer hydrogenation is a practical synthetic method that avoids the hazardous handling of gaseous molecular hydrogen. Our group first reported that gallium compounds assisted alkene transfer hydrogenation using the simple organic molecule 1,4-cyclohexadiene (1,4-CHD) as H₂ surrogate (Scheme 21).^[22]



Scheme 21. Catalytic transfer hydrogenation of alkenes

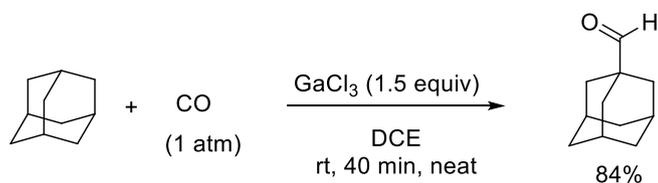
1.2.4 Lewis acid activation by interactions with σ electrons

Gallium(III) interacts even with the σ electrons of cycloalkane's C-H bonds, which could be used for catalytic aromatic alkylation (Scheme 22).^[43] The reaction of *cis*-decaline with naphthalene in the presence of a catalytic amount of gallium trichloride (5 mol%) gives corresponding 2-naphthylated *trans*-decaline. C-C bond formation occurs predominantly at the C3 position of decaline and C2 position of naphthalene. It is worth noting that *cis*-decaline reacts much more effectively than the *trans*-isomer.



Scheme 22. GaCl₃-mediated C-H activation of alkanes

Another interesting example of selective C-H activation is the reaction of adamantane with CO (1 atm) at room temperature in the presence of GaCl₃ (1.5 equivalents), which results in a formylation reaction to produce adamantane-1-carbaldehyde in 84% yield.^[44]



Scheme 23. Formylation of adamantane with CO activated by GaCl₃

In conclusion, gallium(III) compounds are widely used in convenient transformations. The coordination with various ligands allows the possibility to modify the activity of

gallium(III) for challenging chemistry. Interestingly, gallium(III) compounds are at the border between hard Lewis acids able to activate n and σ electrons just like aluminum or boron species, and soft Lewis acids able to activate π electrons just like late transition metals (gold for instance). In contrast, the applications of gallium(I) complexes in catalysis is still a research area that remains to be developed. As mentioned in Section 1.2.1, the Lewis acidity of Group 13 metal compounds decreases from +III oxidation state to +I oxidation state. The +I oxidation state induces weaker but also softer Lewis acid properties. Following on the Pearson's principle of 'hard' and 'soft' acids and bases,^[45] if gallium(I) compounds are softer acids than gallium(III) compounds, they might better interact with soft bases such as alkynes, alkenes or allenes. We will next summarize the current state-of-the-art of gallium(I) complexes and their application in organic synthesis.

1.3 Developments of Gallium(I) Catalysis

1.3.1 Low oxidation state chemistry of gallium

a. Oxidation states vs. valence states

The chemical state of the key atoms in novel compounds is a vital piece of information for understanding reactivity. Two formalisms exist for classifying the atoms of interest in a new compound: oxidation number and valence. As put forth by Parking,^[46] the oxidation number can be described as "...*the charge remaining on an atom when all ligands are removed heterolytically...*", with the electron pairs involved in bonding given to the atom with larger electronegativity. Conversely, valency indicates the "*number of electrons that an atom uses in bonding*".^[47] It should be noted that, valence doesn't have "+" or "-" charge. In contrast, the oxidation state have a charge and the oxidation number could be a fractional value.

While the oxidation and valence numbers are sometimes equal, many examples exist

for main group compounds where this is not the case. As an example, Group 13 halides in their monomeric forms are assigned oxidation and valence number of 3, illustrated using BF_3 in Figure 6. In B_2F_4 , each boron atom is assigned an oxidation number of +II, and a valence number of 3.



Figure 6. Differences in oxidation and valence numbers for BF_3 and B_2F_4

In general, when we talking about the bonding state of an element in a molecule, valency would be much suitable. when we focus on the electronic property of an element in a complex, for example a cation, the use of the oxidation state would be better.

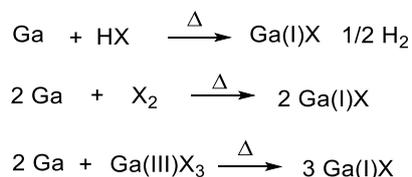
For the purposes of this dissertation, the term "mixed valent" will be used to indicate a compound that contains a Group 13 element in more than one oxidation state or valence. The oxidation state for Group 13 metals will be indicated in the form of Roman numbers instead of Arabic ones and also eliminating the "+" charge, for example, Ga(I) or gallium(I). It should also be noted that the term "sub-valent" and "univalent" has also often been used to describe such compounds.

b. Gallium(I) halides

Among the Group 13 elements, the distribution of the valence electrons as ns^2np^1 suggests the possibility of both the +III and +I oxidation states, corresponding respectively to the involvement of all the electrons and of the single p electron in bonding. The existence of the +I oxidation state would result from the presence of an "inert pair" of s electrons in the outermost electronic level of these atoms. The "inert pair" effect refers to the two electrons in the outermost atomic s -orbital prefer unionized

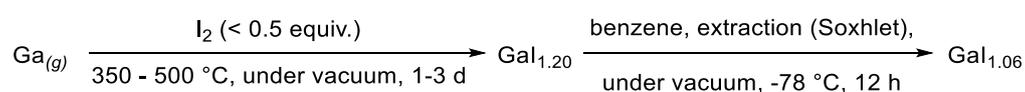
or unshared in compounds of *p*-block metals. Due to the potential hybridization of *d*- and *s*-orbitals, the stability of +I oxidation state increases with an increasing atomic weight of the elements. Therefore, the heavier thallium has greater stability in the +I oxidation state than +III.^[48]

Due to the thermodynamic instability, Ga(I) halides cannot be prepared at room temperature. Redox-disproportionation to generate gallium metal and Ga(III) trihalides in a 2:1 molar ratio can be frequently observed at low temperature, which is one major challenge for the efficient synthesis of Ga(I) compounds. In order to prepare sub-valent gallium halides, several synthetic routes have been developed.^[49] To access metastable Ga(I)X compounds, the gaseous Ga(I)X species that are thermodynamically stable at high temperature have to be made first. Three methods for their preparation are shown in Scheme 24. To largely suppress the formation of the trihalides, temperatures of 800-1000 °C are necessary. The formed gaseous Ga(I)X species have to be subsequently quenched at low temperatures in order to prevent the disproportionation which occurs on slow cooling.



Scheme 24. Synthetic routes to Ga(I)X species

For example, in 1955 Corbett and McMullan synthesized mixed-valence Ga(I) by heating gallium metal and molecular iodine under vacuum at 350-500 °C for 72 h. The mixed valence Ga(I) was isolated by washing the mixture with benzene at -78 °C (Scheme 25).^[50]

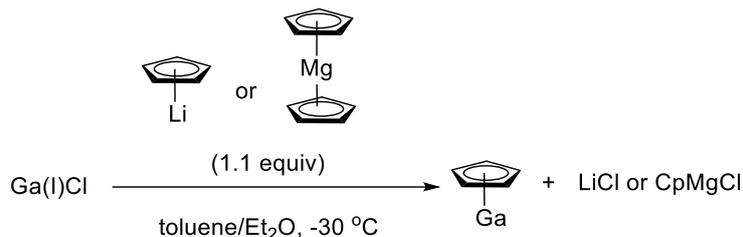


Scheme 25. Synthesis of Ga_{1.06} proposed in 1955 by Corbett and McMullan

In the following decades, this approach was optimized to overcome its harsh conditions. For instance, in 1990, an improved synthesis of mixed valence 'Ga(I)I' was reported by Green et al.^[51] The pale-green powder 'Ga(I)I' was obtained through the reaction between gallium metal and 0.5 equivalent of iodine in toluene at >300 °C under ultrasonication. Although its accurate formulation remains a puzzle, it has been confirmed by Raman spectroscopy that this type of mixed-valence 'Ga(I)I' exists as a mixed-oxidation state salt, with an average gallium oxidation state between '+I' and '+II'.^[51] This salt proved to be insoluble in non-coordinating solvents and was shown to decompose through redox-disproportionation to form Ga(II) or Ga(III) adducts alongside gallium(0). Nevertheless, due to its simple preparation and its thermal stability, it has been widely used as a precursor for 'real' gallium(I) species. Another common precursor for gallium(I) species is gallium dichloride. The structure of Ga₂Cl₄ was initially unknown, and it was uncertain as to whether Ga₂Cl₄ was a gallium(II) compound containing a gallium-gallium bond with equivalent gallium centers, or a mixed valent salt with gallium(I) cation and a tetrachlorogallate(III) anion.^[15] Following successful crystallization, it was determined that the latter description was the most accurate: [Ga]⁺[GaCl₄]⁻.

c. Gallium(I) complex containing the Cp ligand and its derivatives

As mentioned above, the univalence gallium(I) can be synthesized from the mixed-valence Ga(I)X. For example, in 1992, Schnöckel et al. reported the first organogallium(I) compound: cyclopentadienyl gallium(I): Ga(I)Cp.^[52] This colorless and air-sensitive Ga(I) species was obtained by reacting MgCp₂, or LiCp, with mixed-valence Ga(I)Cl at low temperature for 7 days (Scheme 26). It was noted that Ga(I)Cp cannot be isolated in a solvent-free state.



Scheme 26. Synthesis route for GaCp proposed by Schnöckel

In 2011, Schnepf's group synthesized the same Ga(I)Cp by suspending preliminarily generated "GaI" and a slight excess of NaCp in toluene, benzene, pentane or even dodecane at low temperature (they did not indicate the exact temperature).^[53]

This Ga(I)Cp then has been used as starting material for new Ga(I) chemistry. For example, it was converted to mixed-valent gallium triflates Ga(I)OTf.^[54] Moreover, Ga(I)Cp was shown to act as a Lewis base when reacted with the Lewis acid B(C₆F₅)₃ thereby forming a gallium(I)-boron(III) donor-acceptor complex CpGa→B(C₆F₅)₃. The X-ray structure, copied from the literature,^[55] is shown in Figure 7.

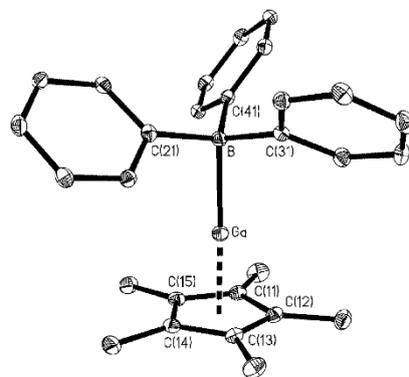
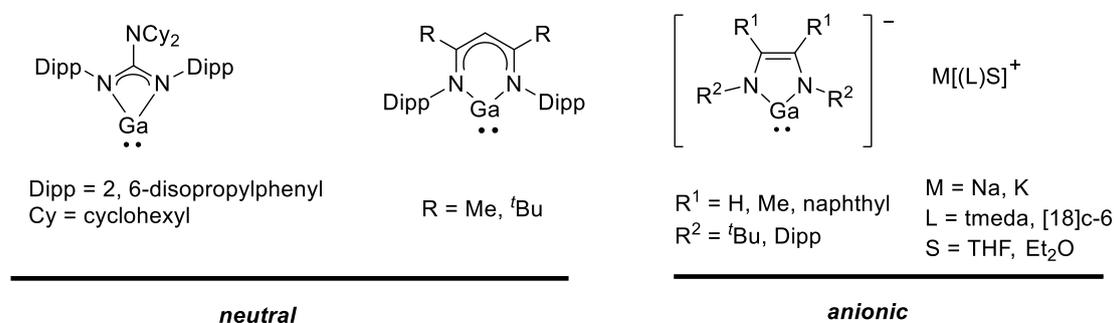


Figure 7. X-ray structure of CpGa→B(C₆F₅)₃ (hydrogen and fluorine atoms are omitted for clarity)

d. Gallium(I) species as metallic NHC analogs

Later on, several neutral and anionic Ga(I) compounds were reported and their potential as 'metallic' NHC analogs was discussed.^[56] Indeed, four-, five-, and six-membered ring systems of Ga(I) *N*-heterocycles have been well studied. Generally, they can be

classified into two categories, neutral and anionic gallium(I) analogs of NHCs (Scheme 27). All those compounds were then employed as ligands for transition metals. Many other examples were reported, but they will not be listed here.^[56]



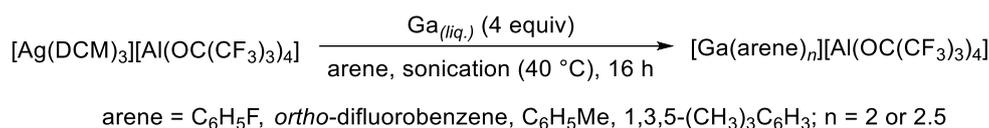
Scheme 27. Examples of neutral and anionic Ga(I) compounds as metallic NHC analogs

e. [Ga(arene)_n][Al(OC(CF₃)₃)₄]: a well-defined, cationic, gallium(I) complex

In the 2000s, improvements in the field of gallium(I) chemistry stemming from the work of the Krossing's group were considerable. Typically, gallium(I) salts have been prepared through an anion metathesis reaction using 'GaI' or Ga₂Cl₄ as starting material. However, this approach may yield product mixtures. The Krossing's group stabilized the complexes based on metals in an unstable oxidation state by synthesizing their cationic analogs, which is an already proven strategy.

Note: all the pictures in this subsection come from the related reference

In 2010, they first reported a simple and novel route for the preparation of Ga(I) salts with weakly coordinating anions. In this event, a solution of [Ag(DCM)₃][Al(OC(CF₃)₃)₄] in *o*-C₆H₄F₂/toluene was reacted with an excess of gallium metal under ultrasonication resulting in the formation of an off-white powder [Ga(toluene)₂][Al(OC(CF₃)₃)₄] in good yield. Similarly, when switching to fluorobenzene (C₆H₅F) or 1,3,5-trimethylbenzene (TMB, 1,3,5-(CH₃)₃C₆H₃) as solvent under the same conditions, several species of the type [Ga(arene)_n][Al(OC(CF₃)₃)₄] were generated in high yields (Scheme 28).^[57]



Scheme 28. Synthesis of the univalent gallium(I) salt by the Krossing's group

One crystal structure of those examples is shown in Figure 8.

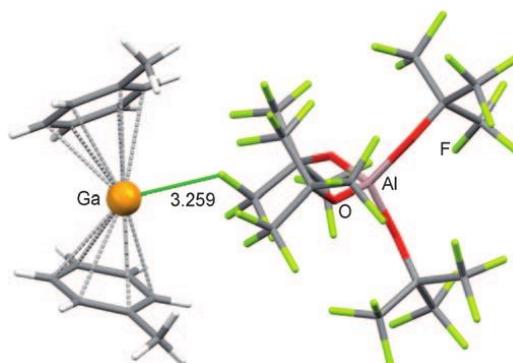


Figure 8. Molecular structure of [Ga(C₆H₅Me)₂][Al(OC(CF₃)₃)₄]

Ga(I) oxidation state was confirmed by ⁷¹Ga NMR analysis because a specific oxidation state of gallium typically displays a characteristic chemical shift. Notably, the resonance of [Ga(arene)_n][Al(OC(CF₃)₃)₄] was shown to be δ = -520 ppm in toluene; δ = -756 ppm in fluorobenzene; δ = -750 ppm in 1,2-difluorobenzene; δ = -630 ppm in CD₂Cl₂; δ = -448 ppm in THF. For gallium(III) compounds, the signal should be around +200 ppm. This evidence indicates the existence of gallium(I).

Crown ethers have been widely used in coordination chemistry, particularly with low-oxidation state metal species, such as indium(I) salts. In 2012, Krossing group examined the effect of crown ethers on gallium(I) species by mixing 18-crown-6 with [Ga(arene)_n][Al(OC(CF₃)₃)₄] in fluorobenzene.^[58] After concentrating in vacuo and storage at -30 °C, a crystal was obtained from the colorless solution (Figure 9). The structure of this gallium(I)-crown ether complex highlighted that two solvent molecules, one above and one below the coordination plane, coordinated to the Ga(I) center. The coordination of Ga(I) center by the crown ether was also confirmed by ¹H and ⁷¹Ga NMR analyses.

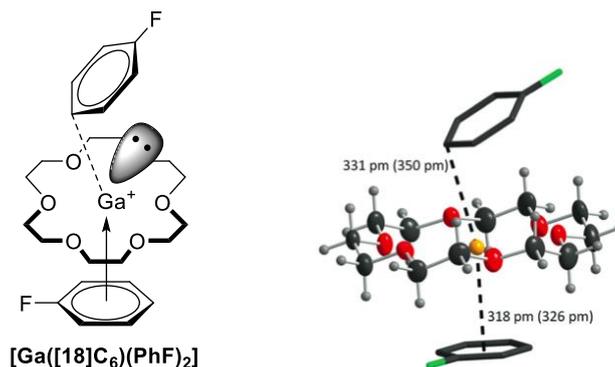


Figure 9. Molecular structure of the complex of Ga(I) and crown ether (anion is omitted)

Furthermore in 2013, Krossing's group reported the coordination chemistry of gallium(I) to NHCs. $[\text{Ga}(\text{IPr})_2][\text{Al}(\text{OC}(\text{CF}_3)_3)_4]$ was synthesized by mixing $[\text{Ga}(\text{PhF})_2][\text{Al}(\text{OC}(\text{CF}_3)_3)_4]$ with two equivalents of 1,3-bis(2,6-diisopropyl-phenyl)-imidazol-2-ylidene (IPr) in fluorobenzene. After concentrating the yellow solution, a crystal was obtained and analyzed by X-ray technique. The molecular structure is shown in Figure 10.

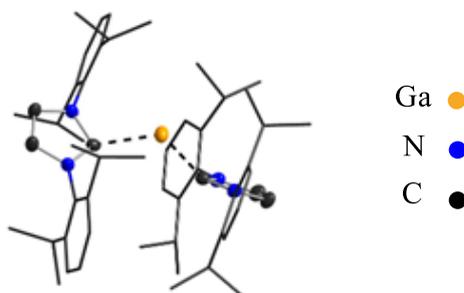


Figure 10. Molecular structure of $[\text{Ga}(\text{IPr})_2]^+$ (anion is omitted)

Analogous complexes were obtained by treating $[\text{Ga}(\text{PhF})_2][\text{Al}(\text{OC}(\text{CF}_3)_3)_4]$ with two equivalents of 1,3-bis(2,4,6-trimethylphenyl)-imidazol-2-ylidene (IMes). The reason for the unique tilted carbene coordination mode may come from the back-bonding of gallium to the p orbitals of the carbenes (Figure 11).^[59]

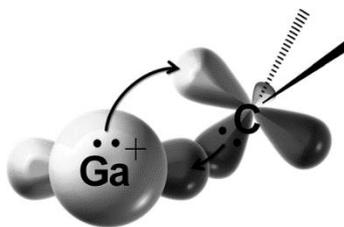


Figure 11. Postulated σ -back-bonding interaction

Univalent gallium phosphine complexes $[\text{Ga}(\text{P}^t\text{Bu}_3)_2][\text{Al}(\text{OC}(\text{CF}_3)_3)_4]$ could also be produced by condensing a solution of $[\text{Ga}][\text{Al}(\text{OC}(\text{CF}_3)_3)_4]$ and $\text{P}^t(\text{Bu})_3$ in fluorobenzene.^[60] The molecular structure is shown in Figure 12.

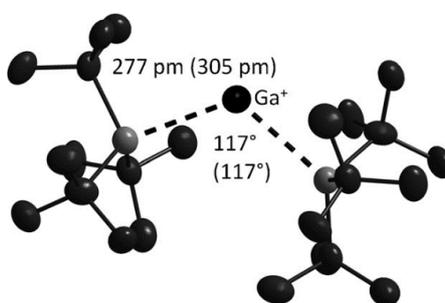


Figure 12. Section of the structure of $[\text{Ga}(\text{PtBu}_3)_2][\text{Al}(\text{OC}(\text{CF}_3)_3)_4]$. (the anion and all of the hydrogen atoms were omitted for clarity)

f. Gallium(I) cations through hydrogen elimination from gallium(III) cations

The gallium(I) species $[\text{Ga}(\text{C}_6\text{H}_5\text{F})_2][\text{CHB}_{11}\text{Cl}_{11}]$ was obtained by the Powell's group in 2019, in an attempt to synthesize $[\text{Cl}_2\text{Ga}][\text{CHB}_{11}\text{Cl}_{11}]$ according to Scheme 29.^[61]



Scheme 29. Attempt to get $[\text{Cl}_2\text{Ga}][\text{CHB}_{11}\text{Cl}_{11}]$

The failure to detect a gallium hydride signal in the ^1H NMR spectrum or an absorption around 2000 cm^{-1} ($\nu_{\text{Ga-H}}$) in the IR spectrum, and the detection of a signal in the ^{71}Ga NMR spectrum at -703 ppm , which is in the typical region for gallium(I) compounds, gave evidence that indeed a gallium(I) species was isolated. Furthermore, the structure of $[\text{Ga}(\text{C}_6\text{H}_5\text{F})_2][\text{CHB}_{11}\text{Cl}_{11}]$ was determined by single-crystal X-ray diffraction and

showed that the gallium(I) center is coordinated by two arenes in a slightly distorted fashion (Figure 13).

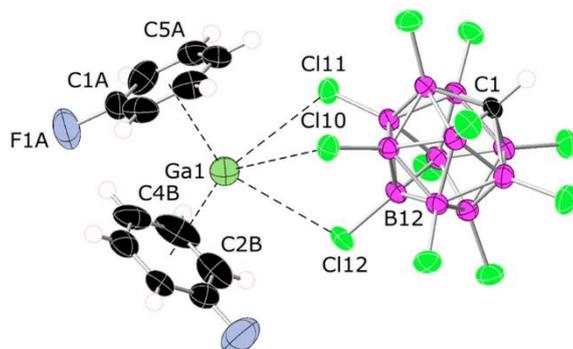


Figure 13. Crystal structure of $[Ga(C_6H_5F)_2][CHB_{11}Cl_{11}]$

It was assumed that residual Et_3SiH coming from the synthesis of the silylium ion reagent $[Et_3Si][CHB_{11}Cl_{11}]$ caused the formation of an intermediate $[H_2Ga]^+$ ion, which then eliminated H_2 to afford compound $[Ga(C_6H_5F)_2][CHB_{11}Cl_{11}]$. A proof is that they found the cationic arene-solvated species $[H_2Ga(arene)_2]^+$ can spontaneously eliminate dihydrogen at room temperature to afford the arene-solvated gallium(I) compound $[Ga(PhF)_2][CHB_{11}Cl_{11}]$. A key requirement for this gallium(I) complex appears to be the presence of a weakly coordinating anion. For example, the use of a more basic triflimide anion $[NTf_2]^-$ reverses the stability, that means the gallium(III) hydride H_2GaNTf_2 is more stable than the gallium(I) compound $GaNTf_2$.

1.3.2 Catalytic applications in organic synthesis

a. Gallium(I) initiated polymer chemistry

Over the past 80 years, high-molecular-weight polyisobutylene (HR-PIB) has been prepared by using proton-, carbocation-, and metal-based catalysts. In 2013, Krossing's group found that the polymerization of isobutylene can be performed by using 0.007 mol% of $[Ga(C_6H_5F)_2][Al(OC(CF_3)_3)_4]$ at $-10\text{ }^\circ\text{C}$ in toluene, resulting HR-PIB with an α -content of terminal olefinic double bonds up to 93 mol% and a molecular weight (M_n) of 1980 g/mol (Figure 14).^[62] Experimental results, DFT calculations, and mass

spectrometric investigations point toward a coordinative polymerization mechanism involved.

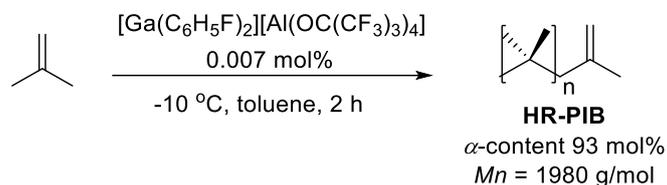
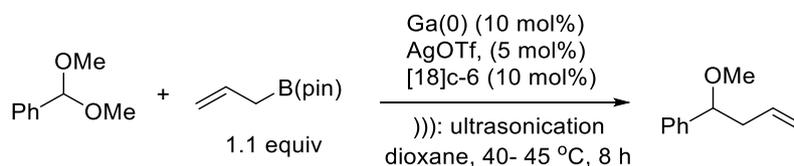


Figure 14. Polymerization of isobutylene catalyzed by $[\text{Ga}(\text{C}_6\text{H}_5\text{F})_2][\text{Al}(\text{OC}(\text{CF}_3)_3)_4]$

b. Gallium(I) for C-C bond formation reaction generated in situ from gallium(0)

As discussed in section 1.1, gallium(I) may display both Lewis acidity and basicity because of the presence of both vacant *p* orbitals and a lone electron pair.^[63] Based on this attractive feature, in 2016, Schneider reported Ga(I)-catalyzed C–C bond formation reactions between allyl or allenyl boronic esters and acetals, ketals, or aminals (Scheme 30).^[64] This method proceeds in high yields with essentially complete chemo- and regioselectivity.



Scheme 30. Gallium(I) catalyzed C-C bond formation

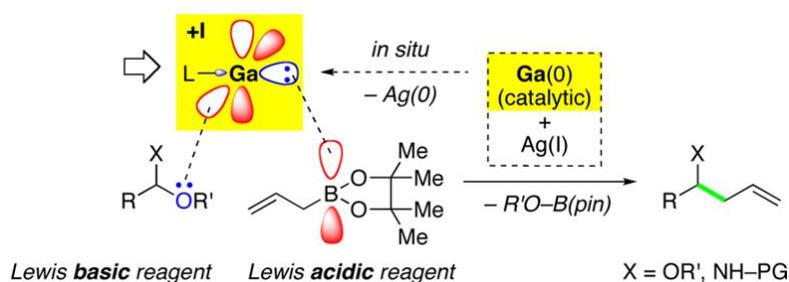
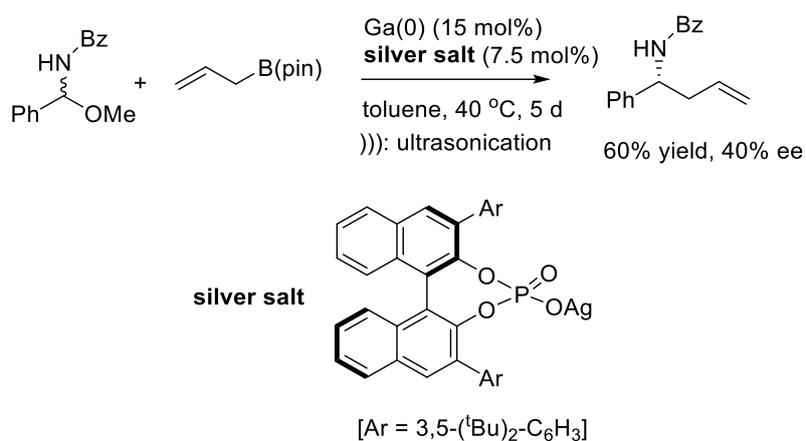


Figure 15. The concept for catalytic use of Ga(0) - in situ ambiphilic Ga(I) catalysis (picture taken from ref [64])

In this reaction, the Lewis acidic reagent allenyl boronic ester is activated by the lone electron pair of the Ga(I) ion, and Lewis basic reagent acetal is activated by the vacant

p orbitals of Ga(I) (Figure 15). The gallium(I) was formed through oxidation of element gallium(0) in situ by silver(I) salt under the ultrasonication condition. NMR spectroscopic analyses have revealed the generation of novel Ga(I) catalytic species. They have also demonstrated the possibility of asymmetric Ga(I) catalysis combined with chiral silver salt (Scheme 31). This asymmetric induction was applied to the formation of homoallyl amide in 40% *ee* from the racemic hemiaminal ether.



Scheme 31. Asymmetric induction by in situ Ga(I) catalysis

1.4 Conclusion

The continuous pursuit of chemists in the field of gallium compounds-mediated or -catalyzed synthetic transformation extended the applications of the “Lewis acids” family in organic chemistry. The vacant p orbital of gallium(III) compounds allows the activation towards n -, σ -, and π -electrons containing chemicals, qualifying them as Lewis acids, and also provide the access to coordination compounds with Lewis base ligands, which can modify the reactivity of such gallium(III) complex diversely. On the other hand, due to the existence of two empty orbitals and one occupied orbital with two electrons, gallium(I) compounds present a softer Lewis acids property, and exhibit a potential ambiphilic feature.

In this introduction, we have discussed the intrinsic reactivities of gallium(III) and gallium(I) compounds in catalysis and summarized their use in various chemical transformations such as Friedel-Craft acylation and alkylation, epoxide opening reaction, Michael addition reaction, Diels-Alder reaction, hydroamination reaction, transfer hydrogenation reaction, cycloisomerization reaction, formylation reaction and so on. It is certain that we did not include all the reported result, but the representative ones.

As it is shown in this introduction, gallium(III) compounds are used widely in catalysis, but gallium(I) compounds are less described. The purpose of our study is to fill the gap of gallium(I) compounds utilizing in catalysis to construct useful chemical skeletons. Our aim is to test the gallium (I) species (commercial available $[\text{Ga}][\text{GaCl}_4]$ and Krossing's $[\text{Ga}(\text{PhF})_2][\text{Al}(\text{OC}(\text{CF}_3)_3)_4]$) in the benchmarked transformations developed in our lab using gallium(III) (hydroarylation of arenynes, transfer hydrogenation of alkenes, hydrogenative cyclization of arenynes, and cycloisomerization of enynes) and compare the different activities of gallium in its oxidation state +I and +III.

2. RESULTS AND DISCUSSION

As outlined above, the gallium element is a quite abundant, inexpensive, and low-toxic metal. Gallium(III) species have been widely employed as Lewis acid catalysts in organic synthesis, including interactions with n , σ , or π electrons.

In contrast, only few reports have been published on the less stable gallium(I) compounds. According to Krossing's protocol, univalent gallium(I) species $[\text{Ga}(\text{PhF})_2][\text{Al}(\text{OC}(\text{CF}_3)_3)_4]$ can be obtained through a redox reaction between gallium(0) and an Ag(I) salt.

Our aim is to explore further gallium(I) species in our lab, including Ga_2Cl_4 and $[\text{Ga}(\text{PhF})_2][\text{Al}(\text{OC}(\text{CF}_3)_3)_4]$, in Lewis acid catalysis, and compare their reactivity with more common gallium(III) complexes, especially our own $[\text{IPr}\cdot\text{GaCl}_2][\text{SbF}_6]$ catalyst.

In the next part of this dissertation, the solvent ligand "PhF" have been omitted from the complex formula for convenience if necessary.

2.1 Synthesis of the Univalent Gallium(I) Catalyst

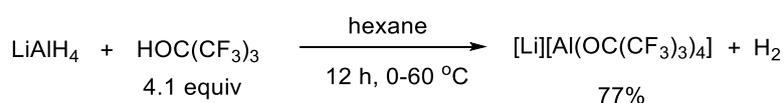
As mentioned in the introduction, gallium(I) sources are limited for the moment. For the purpose of the study on catalytic reactivity of gallium(I) in synthesis, we decided to use two gallium(I) salts in tests. One is Ga_2Cl_4 , which is now a commercially available compound and attracts chemists' interests in inorganic or coordination chemistry. The other one is $[\text{Ga}][\text{Al}(\text{OC}(\text{CF}_3)_3)_4]$. Our group has made a collaboration with Professor Ingo Krossing from the University of Freiburg (Germany). Thanks to an exchange program involving the former PhD student, Guillaume Thiery, the technic for the synthesis of $[\text{Ga}][\text{Al}(\text{OC}(\text{CF}_3)_3)_4]$ was acquired in our lab. Since it is tricky, it is necessary to discuss the synthesis of $[\text{Ga}][\text{Al}(\text{OC}(\text{CF}_3)_3)_4]$ as a subsection in detail. The synthesis route is based on three steps: 1) synthesis of $[\text{Li}][\text{Al}(\text{OC}(\text{CF}_3)_3)_4]$, which is

the main precursor to synthesize fluorinated alkoxyaluminate WCA compounds; 2) metathesis to get $[\text{Ag}][\text{Al}(\text{OC}(\text{CF}_3)_3)_4]$; 3) oxidation of gallium(0) to Ga^+ using $[\text{Ag}][\text{Al}(\text{OC}(\text{CF}_3)_3)_4]$.

2.1.1 Synthesis of $[\text{Li}][\text{Al}(\text{OC}(\text{CF}_3)_3)_4]$

The fluorinated alkoxyaluminate anion with the formula $[\text{Al}(\text{OC}(\text{CF}_3)_3)_4]^-$ was first reported by Strauss and coworkers in 1996.^[65] With the large number of peripheral C-F bonds, 36 fluoride atoms total, $[\text{Al}(\text{OC}(\text{CF}_3)_3)_4]^-$ (also abbreviated $[\text{Al}(\text{pftb})_4]^-$) is presumably the least coordinating anion known. It has been first published in 2001 by Krossing and coworkers.^[66] In contrast to the normally easily hydrolyzed alkoxyaluminates, the $[\text{Al}(\text{OC}(\text{CF}_3)_3)_4]^-$ anion is stable in 6N nitric acid. This stability towards hydrolysis was attributed to steric shielding of the oxygen atoms, provided by the bulky $\text{C}(\text{CF}_3)_3$ groups, as well as to electronic stabilization due to perfluorination. The electron-withdrawing effect of the fluorinated ligand can be demonstrated by the increased acidity of the fluorinated alcohols $\text{HOC}(\text{H})(\text{CF}_3)_2$ ($\text{pK}_a = 9.5$) and $\text{HOC}(\text{CF}_3)_3$ ($\text{pK}_a = 5.5$) in comparison to the non-fluorinated alcohol $\text{HOC}(\text{CH}_3)_3$ ($\text{pK}_a = 19.3$).^[67]

One of the major advantages of these aluminates is that they are easily accessible on a preparative scale: they can be prepared with little synthetic effort on a 200 g scale with over 95% yield within 2 days in common inorganic/organometallic laboratories.^{[75][67]} Here, we would like to describe the alterations of the preparation. The synthesis of all $[\text{Al}(\text{OC}(\text{CF}_3)_3)_4]^-$ anion based complexes begins with the preparation of the $[\text{Li}][\text{Al}(\text{OC}(\text{CF}_3)_3)_4]$ salts using LiAlH_4 and the appropriate commercially available alcohols $\text{HOC}(\text{CF}_3)_3$ (Scheme 32). Several tips should be taken into account.



Scheme 32. Synthetic route to $[\text{Li}][\text{Al}(\text{OC}(\text{CF}_3)_3)_4]$

Tip 1.

It is better to use commercially available LiAlH_4 in Et_2O solution, and remove all the solvent using inert Schlenk line under vacuum (10^{-3} mbar approx.) with heating at $80\text{ }^\circ\text{C}$ overnight (not higher! use a water bath, since LiAlH_4 may explode at about $120\text{ }^\circ\text{C}$). Care has to be taken that all traces of Et_2O are removed. The dry LiAlH_4 is a white solid in a mixture form of powder and lump, it should be put into glovebox and grinded into a fine powder before use.

Tip 2.

The alcohol was purchased and first distilled, then degassed prior to use. The alcohols have very low boiling points $\text{HOC}(\text{CH}_3)_3$ (bp = $45\text{ }^\circ\text{C}$), so it is very volatile. Thus, they tend to evaporate from the reaction through a standard reflux condenser. Instead, it is necessary to use a reflux condenser connected to a cryostat and set to a temperature of $-20\text{ }^\circ\text{C}$.

Tip 3.

It may happen that LiAlH_4 does not completely react, because of the poor solubility of the product, even during reflux, it could pack inside LiAlH_4 ; it is therefore absolutely necessary to finely grind the LiAlH_4 prior to use. Controlling the reaction scale below 20 g would be also helpful for solving the above problem. One easy way to test the exist of LiAlH_4 or any incomplete substituted products, is taking a small part of the precipitate (100 mg) from the reaction then adding it into a vial contain 2 mL of water. If residual Al-H bonds are in the mixture, the white powder reacts noisily with water, if a clear solution without hissing noise results, the product is OK.

Tip 4.

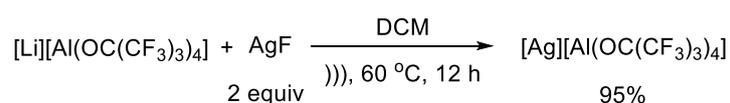
During this reaction, H_2 gas is generated. So, it should be taken into consideration to avoid explosion and also prevent to introduce water or oxygen into the reaction mixture. With these precautions, purified and finely ground LiAlH_4 , reflux overnight in aliphatic solvent, well-sealed reflux condenser set to $-20\text{ }^\circ\text{C}$, the $[\text{Li}][\text{Al}(\text{OC}(\text{CF}_3)_3)_4]$ salt is

obtained in > 75% yield within 2 days. The purity should be checked by NMR. The resulting white solid can be stored in a sealed Schlenk tube in the glovebox and be kept for years.

Notably, just after we finished the preparation of this draft, Krossing group updated an improved synthetic approach towards this [Li][Al(OC(CF₃)₃)₄] salts by changing the solvent from hexane to perfluorohexane, and using Soxhlet extractor. The typical yield is > 97%.^[68]

2.1.2 Synthesis of [Ag][Al(OC(CF₃)₃)₄]

[Ag][Al(OC(CF₃)₃)₄] was obtained by sonication of well-prepared [Li][Al(OC(CF₃)₃)₄] with AgF (Scheme 33).

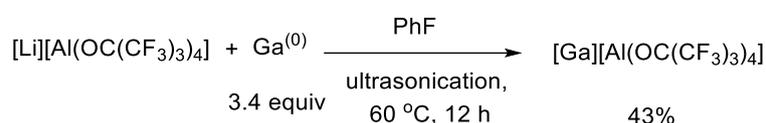


Scheme 33. Synthetic route to [Ag][Al(OC(CF₃)₃)₄]

AgF should have a light orange/beige color and be stored with the exclusion of light. If AgF has a quite dark brownish or even greenish blackish color, it should not be used for this reaction. The reaction should be better performed in small quantity (less than 0.5 g lithium salt) in a reaction tube which can bear 5 bar pressure. As sonication condition is exothermal, the temperature of water in sonicator will increase to around 60 °C. All the reaction system should avoid light as much as possible. The mixture is left in an ultrasonic bath overnight. The solution should have turned slightly brownish with only little of a dark brown (almost black) precipitate left. Afterwards, the Ag⁺ salt is dried in vacuo, finely ground in a glove box, placed in a new flask and left directly hooked to a vacuum line (10⁻³ mbar) until a constant weight is achieved. With this procedure, we obtain solvent-free [Ag][Al(OC(CF₃)₃)₄]. This silver salt should be used for the next step rapidly, because decomposition is observed within a few days, even if kept in the glovebox inside a brown fumed vial.

2.1.3 Synthesis of $[Ga][Al(OC(CF_3)_3)_4]$

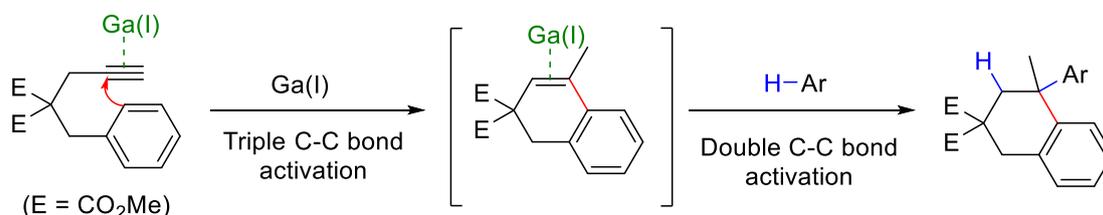
This synthesis was described by Krossing and coworkers in 2010 (Scheme 34). The oxidation of Ga(0) to Ga(I) is based on the same reaction conditions as the metathesis of Li^+ to Ag^+ . Krossing noticed that a powerful ultrasonic bath is necessary. Their group actually uses the Bandelin Sonorex RM 16U apparel, with a power of 2 x 600 W. In our group, we use less powerful ultrasonic bath 640W from SONOREX SUPER. Lower yield was obtained with 43%, comparing with Krossing group's 80%.^[57] The synthesis and purification operating of Ga(I) salt is exactly the same as corresponding Ag^+ salt. After that, the milk like white powder can store in Schlenk tube in glove box for years.



Scheme 34. Synthetic route to $[Ga][Al(OC(CF_3)_3)_4]$

2.2 Ga(I)-Catalyzed Dihydroarylation of Arenynes

With two gallium(I) complexes in hand, we started our investigations with a benchmark reaction that we have used previously to evaluate the ability of gallium(III) Lewis acids to activate alkynes and alkenes using a single substrate.^[21] This reaction involves consecutive triple C-C bond activation (cycloisomerization step) and a double C-C bond activation (Friedel-Crafts-type step) (Scheme 35).

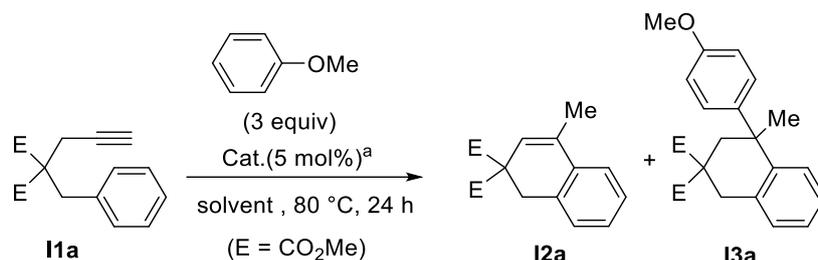


Scheme 35. Hydroarylation/Friedel-Crafts tandem reaction based on Ga(I) activation

2.2.1 Reaction optimization for the dihydroarylation of arenynes

The cycloisomerization of arenyne **I1a** can lead to the dihydronaphthalene derivative **I2a** which, in the presence of a nucleophile such as anisole, give rise to the tetrahydronaphthalene **I3a**. In a preceding study, we found that [IPr·GaCl₂][SbF₆] can catalyze the selective transformation of **I1a** into **I3a** in 1,2-dichloroethane (DCE) (entry 1) or toluene (entry 2) at 80 °C. In DCE at 80 °C, we were pleased to see that [Ga][Al(OC(CF₃)₃)₄] could also be used as catalyst to give **I2a** in 91% yield (entry 3). However, in contrast with [IPr·GaCl₂][SbF₆], the formation of **I3a** was very slow. Gratifyingly, **I3a** could be obtained selectively in toluene in 81% yield (entry 4). Since the Ga(III) and the Ga(I) complexes have different counterions, [IPr·GaCl₂][Al(OC(CF₃)₃)₄] was also tested, which could be obtained directly from IPr·GaCl₃ and [Al][Al(OC(CF₃)₃)₄]. Even though [Al(OC(CF₃)₃)₄]⁻ is an even weaker coordinating anion than [SbF₆]⁻, [IPr·GaCl₂][Al(OC(CF₃)₃)₄] actually seemed less reactive than [IPr·GaCl₂][SbF₆] as it could not promote the addition of anisole in both DCE or toluene (entries 5 and 6). This could be due to a faster hydrolysis of the former by adventitious water under such reaction conditions, as a small amount of the cationic gallium dihydroxide [$\{\text{IPr}\cdot\text{GaCl}(\mu\text{-OH})_2\}_2\cdot\text{H}_2\text{O}\}^{2+}\{\text{[Al(OC(CF}_3)_3)_4]^{-}\}_2$] could be isolated and characterized by X-ray diffraction. The crystallographic data and more information are shown in the experimental section 3.4. The corresponding silver salts AgSbF₆ and [Ag][Al(OC(CF₃)₃)₄] proved inactive (entries 7 and 8). With the Ga(I)-containing salt “GaI”, **I2a** was obtained selectively (entries 9 and 10). In toluene, Ga₂Cl₄ led to **I2a** (entry 11), but **I3a** was obtained as the major product in DCE (entry 12). This is in sharp contrast with GaCl₃, with which **I3a** was a minor product (entry 13). On the other hand, the use of GaCl₃ and [Ag(DCM)₃][Al(OC(CF₃)₃)₄] to form the putative highly electrophilic [GaCl₂][Al(OC(CF₃)₃)₄] species, provided **I3a** in both DCE and toluene (entries 14 and 15).

Table 1. Reaction optimization for Ga-catalyzed dihydroarylation



Entry	Cat.	Solvent	Yield 12a [%] ^[b]	Yield 13a [%] ^[b]
1	[IPr·GaCl ₂][SbF ₆] ^c	DCE	-	92
2	[IPr·GaCl ₂][SbF ₆] ^c	toluene	-	95
3	[Ga][Al(OC(CF ₃) ₃) ₄]	DCE	91	5
4	[Ga][Al(OC(CF ₃) ₃) ₄]	toluene	0	81
5	[IPr·GaCl ₂][Al(OC(CF ₃) ₃) ₄] ^c	DCE	90	0
6	[IPr·GaCl ₂][Al(OC(CF ₃) ₃) ₄] ^c	toluene	89	0
7	AgSbF ₆	DCE	NR	-
8	[Ag(DCM) ₃][Al(OC(CF ₃) ₃) ₄]	DCE	NR	-
9	GaI ^d	DCE	99	-
10	GaI ^d	toluene	98	-
11	Ga ₂ Cl ₄	toluene	79	11
12	Ga ₂ Cl ₄	DCE	15	77
13	GaCl ₃	DCE	77	14
14	[GaCl ₂][Al(OC(CF ₃) ₃) ₄] ^e	DCE	-	56
15	[GaCl ₂][Al(OC(CF ₃) ₃) ₄] ^e	toluene	-	80

a) Reaction conditions: 1,6-arenyne **11a** and anisole (3 equiv) in the indicated solvent (0.2 M) in the presence of catalyst at the indicated temperature for 24 h.

b) Isolated yields.

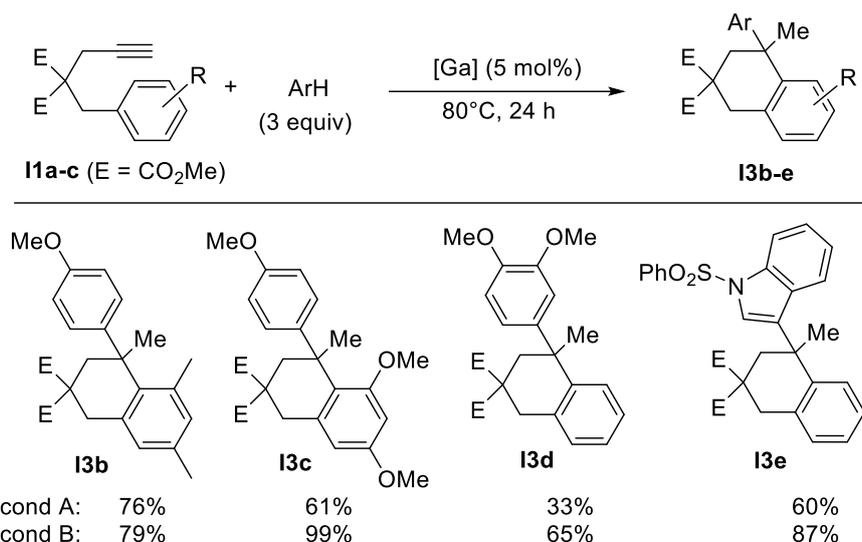
c) Generated in situ by using IPr·GaCl₃ and AgSbF₆ or [Ag(DCM)₃][Al(OC(CF₃)₃)₄].

d) 20 mol%.

e) Presumably generated in situ by using GaCl₃ and [Ag(DCM)₃][Al(OC(CF₃)₃)₄]

2.2.2 Substrate scope of the dihydroarylation of arenynes

Given the good activity of [Ga][Al(OC(CF₃)₃)₄] and Ga₂Cl₄ for the dihydroarylation of **11a**, various 1,6-arenynes and aromatic nucleophiles were then tested (Scheme 36). As shown below, we took two conditions to examine this transformation: *Conditions A*: [Ga] = Ga[Al(OC(CF₃)₃)₄] in toluene; *Conditions B*: [Ga] = Ga₂Cl₄ in DCE.



Scheme 36. Bimolecular dihydroarylation of 1,6-arenynes with aromatics.

The corresponding dihydroarylation products were isolated in moderate to excellent yields. The results obtained with Ga₂Cl₄ are markedly better for **I3c-e**. It should be noticed that previous work in our lab revealed the product **I3c** could not be obtained using [IPr·GaCl₂][SbF₆], presumably because of the two methoxy group which could exert a chelation effect with the catalyst and make it lose its activity. However, the reaction performed smoothly under conditions A and B, giving **I3c** in 61% and 99% yield respectively. Then we also tested this potential chelation inhibition effect with 1,2-dimethoxybenzene in this transformation. [Ga][Al(OC(CF₃)₃)₄] showed weak reactivity, giving 33% isolated yield, while Ga₂Cl₄ performed better, reaching 65%. Ts-protected indole was also tested as nucleophile and delivered product **I3e** in 60% yield under conditions A, and 87% yield under conditions B.

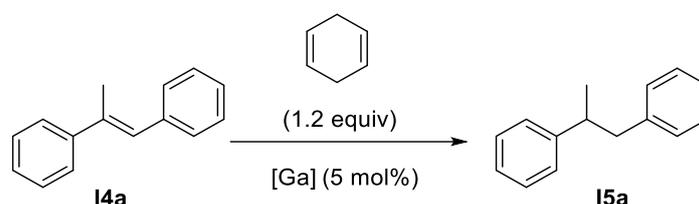
2.3 Ga(I)-Catalyzed Transfer Hydrogenation

The alkene transfer hydrogenation catalyzed by main-group NHC-gallium(III) complexes and using a simple organic molecule as hydrogen gas surrogate has been reported by our group previously.^[22] We thus decided to reinvestigate this reaction with gallium(I).

2.3.1 Reaction optimization for transfer hydrogenation

The use of $[\text{Ga}][\text{Al}(\text{OC}(\text{CF}_3)_3)_4]$ and Ga_2Cl_4 as catalysts was extended to transfer hydrogenation of alkenes, using 1,4-cyclohexadiene (1,4-CHD) as dihydrogen source. 1,4-CHD is a commercially available easy-to-handle organic liquid. The byproduct, benzene, can be easily removed by evaporation techniques. We started this study with the reduction of 1,2-diphenylpropene **I4a** (Table 2).

Table 2. Reaction optimization for Ga(I)-catalyzed transfer hydrogenation



Entry	[Ga]	Solvent	T [°C]	Yield I5a [%] ^b
1	$[\text{Ga}][\text{Al}(\text{OC}(\text{CF}_3)_3)_4]$	DCE	80	61
2	Ga_2Cl_4	DCE	80	37
3	Ga_2Cl_4	toluene	80	61
4	Ga_2Cl_4	toluene	110	94
5	$[\text{Ga}][\text{Al}(\text{OC}(\text{CF}_3)_3)_4]$	toluene	110	73

^a) Reactions conditions: **I4a** (1 equiv) and 1,4-CHD (1.2 equiv) in the indicated solvent (0.2 M) in the presence of the catalyst (5 mol%) for 24 h.

^b) Isolated yields.

We chose the well-studied solvent system DCE and toluene to test the activity. Firstly, the alkene **I4a** could be reduced into alkane **I5a** by 1,4-cyclohexadiene using both $[\text{Ga}][\text{Al}(\text{OC}(\text{CF}_3)_3)_4]$ or Ga_2Cl_4 . $[\text{Ga}][\text{Al}(\text{OC}(\text{CF}_3)_3)_4]$ gave a better yield of 61% than Ga_2Cl_4 in DCE at 80 °C (entries 1 and 2). Changing the solvent for toluene at the same temperature, the yield increased significantly from 37% to 61% when using Ga_2Cl_4 (entry 3). Subsequently, we found that a higher temperature of 110 °C in toluene could raise the yield, up to 94% with Ga_2Cl_4 and 73% with $[\text{Ga}][\text{Al}(\text{OC}(\text{CF}_3)_3)_4]$ (entries 4 and 5).

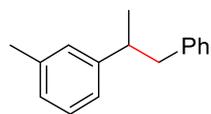
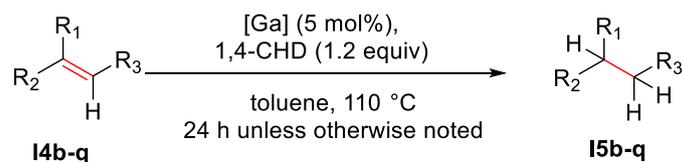
2.3.2 Substrate scope for the catalytic transfer hydrogenation

With these optimal reaction conditions in hand, we explored the scope of the Ga(I)-catalyzed transfer hydrogenation. Overall, 14 alkenes have been successfully converted into the corresponding alkane in 34-99% yield, using two possible gallium(I) species (Scheme 37). *Conditions A*: [Ga] = [Ga][Al(OC(CF₃)₃)₄] in toluene; *Conditions B*: [Ga] = Ga₂Cl₄ in toluene.

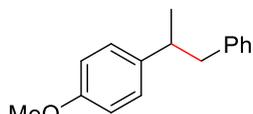
Acyclic and cyclic alkenes bearing di- or tri-substitution were tested in this transfer hydrogenation reaction. Tolerated functionalities on the alkene substrates include ester, methoxy, nitro, and bromide groups. With a few exceptions (**I5c**, **I5g**, **I5l**, **I5o**), [Ga][Al(OC(CF₃)₃)₄] proved more efficient than Ga₂Cl₄. Again, these Ga(I) species proved superior to GaCl₃. For instance, whereas the nitro derivative **I5m** was obtained in 94% and 78% yield with [Ga][Al(OC(CF₃)₃)₄] and Ga₂Cl₄ respectively, GaCl₃ furnished it in 45% yield only.

Ga₂Cl₄ proved to be a more active catalyst for this transformation, as it need less reaction time than [Ga][Al(OC(CF₃)₃)₄]. For instance, **I5b** and **I5g** can be obtained in just one hour, and for **I5c**, **I5d** in four hours. The fact that **I5d** was obtained in 34% yield using Ga₂Cl₄, but with full conversion, suggested that bromide could have an unfavorable effect. Moreover, substrate **I4i** totally decomposed (or polymerized) when using Ga₂Cl₄ as catalyst.

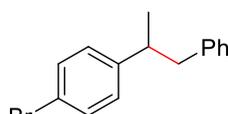
In general, for this transfer hydrogenation reaction, Ga₂Cl₄ displays high activity and lower functional group tolerance. In contrast, [Ga][Al(OC(CF₃)₃)₄] could catalyze the reaction smoothly although in prolonged reaction time and with a slight loss of yield.

**15b**

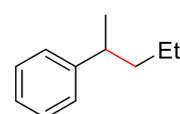
cond A: 95%
cond B: 84% (1 h)

**15c**

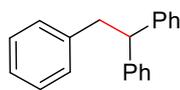
90%
92% (4 h)

**15d**

81%
34% (4 h)

**15e**

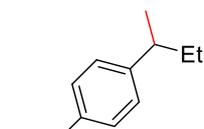
72%
58%

**15f**

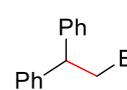
cond A: 56%
cond B: 45%

**15g**

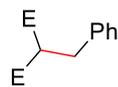
66%
98% (1 h)

**15h**

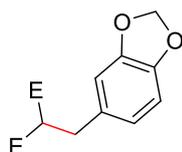
67%
34%

**15i**

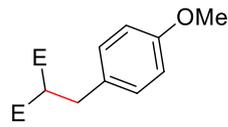
43%
0%

**15j**

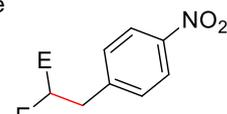
cond A: 85%
cond B: 54%

**15k**

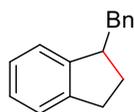
77%
41%

**15l**

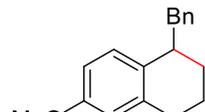
51%
52%

**15m**

94%
78%

**15o**

cond A: 82%
cond B: 85%

**15p**

99%
57%

Scheme 37. Scope of Ga(I)-catalyzed transfer hydrogenation of alkenes.

2.3.3 Mechanistic proposal

We proposed a catalytic cycle that accounts for both the hydrogen generation and transfer hydrogenation, as shown in Figure 16.

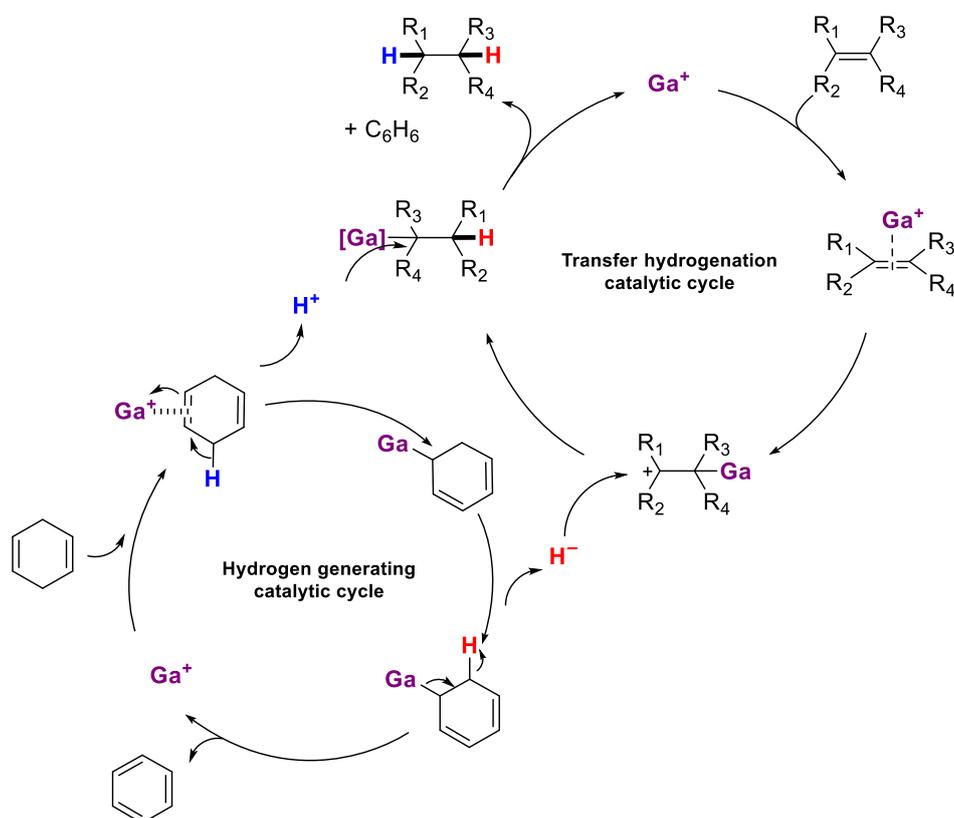
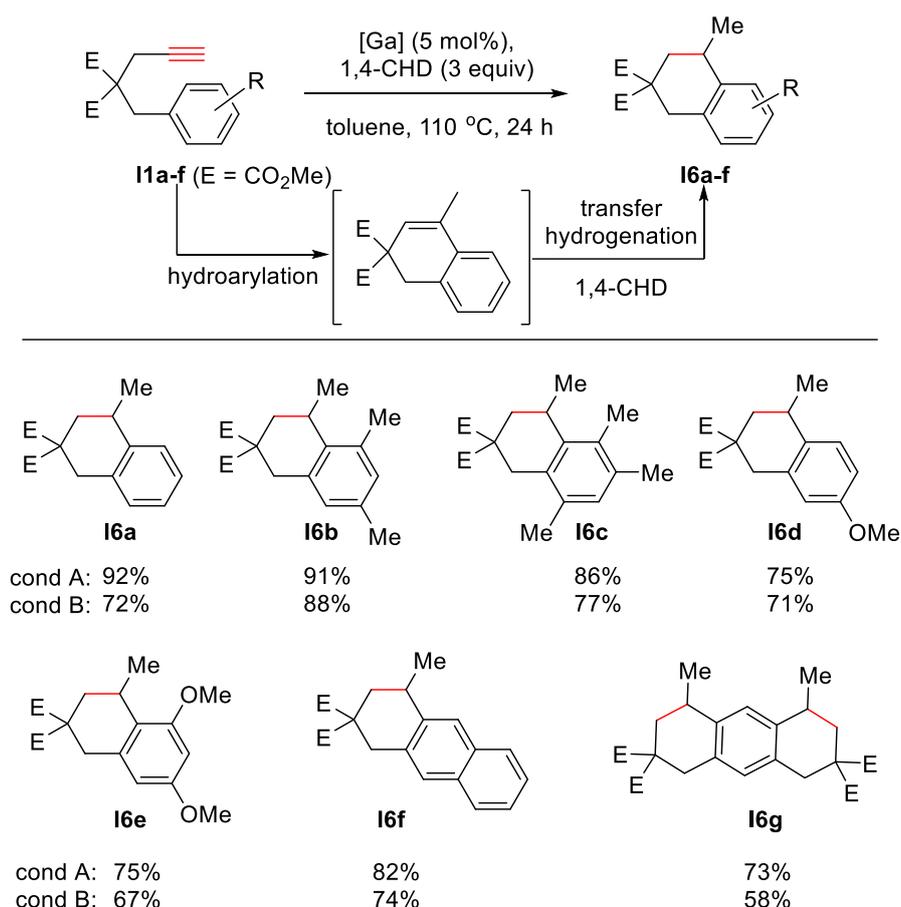


Figure 16. Mechanistic proposal for gallium(I) catalyzed transfer hydrogenation reaction

For the hydrogen generation catalytic cycle, Firstly, Ga^+ coordinates to 1,4-CHD and generates a proton (shown in blue), giving an organogallium compound. This proposed intermediate is unstable because of the powerful aromatization potential, and releases a hydride (shown in red) and regenerates Ga^+ . We do not have any direct evidence for this proposal, but the addition of a gallium(III) or gallium(I) complex directly to 1,4-cyclohexadiene can release H_2 gas and generate benzene.^[69] The transfer hydrogenation catalytic cycle is proposed as follows: coordination of Ga^+ with the alkene to form an organogallium carbocation, trapping of the later with the hydride generated from cyclohexadiene, protodegallation of the alkylgallium by the proton generated from the diene with regeneration of the catalyst.

2.4 Ga(I)-Catalyzed Hydrogenative Cyclization of Arenynes

Combining the two ideas of Subsection 2.2 and Subsection 2.3, we replaced anisole by 1,4-cyclohexadiene to promote the reduction of the intermediate cycloalkene (Scheme 38).^[22] The generality of this tandem process was validated further by using various arenynes. *Conditions A*: [Ga] = [Ga][Al(OC(CF₃)₃)₄] in toluene; *Conditions B*: [Ga] = Ga₂Cl₄ in DCE. Again, [Ga][Al(OC(CF₃)₃)₄] and Ga₂Cl₄ proved to be catalytically active. The cyclization/reduction products were isolated in good to high yields. In this tandem reaction, [Ga][Al(OC(CF₃)₃)₄] led to better yields than Ga₂Cl₄. For substrate **11g**, we used 6 equivalents of 1,4-cyclohexadiene, and we got two diastereomers *dl* : *meso* = 1:1).

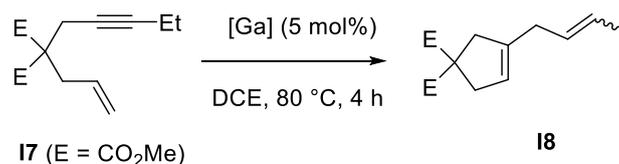


Scheme 38. Ga(I)-catalyzed hydrogenative cyclization of arenynes.

2.5 Ga(I)-Catalyzed Cycloisomerization of 1,6-Enynes

The metal-catalyzed cycloisomerization of enynes and related compounds is a well-established strategy for the rapid increase of the molecular complexity from simple substrates. While a variety of transition-metal complexes can be used as catalysts for this reaction, simple salts derived from main group elements are also efficient, notably gallium and indium halides.^[48] In this study, cycloisomerization of enyne **17** has been investigated (Table 3). With GaCl₃ and [IPr·GaCl₂][Al(OC(CF₃)₃)₄], **18** was obtained in a low 17% and 32% yield respectively (entries 1 and 2, full conversion but a high level of polymerization). With [Ga][Al(OC(CF₃)₃)₄], the yield increased to 45% (entry 3) and reached 60% with Ga₂Cl₄ (entry 4).

Table 3. Ga(I)-catalyzed cycloisomerization of enyne **17**



Entry	[Ga]	E/Z	Yield 18 [%] ^b
1	GaCl ₃	3/2	17
2	[IPr·GaCl ₂][Al(OC(CF ₃) ₃) ₄] ^b	8/1	32
3	[Ga][Al(OC(CF ₃) ₃) ₄]	3/2	45
4	Ga ₂ Cl ₄	2/1	60

^a) Isolated yields, full conversion reached in each case.

^b) Generated in situ by using IPr·GaCl₃ and [Ag(DCM)₃][Al(OC(CF₃)₃)₄].

2.6 Homogenous catalytic process investigation

It is crucial to show that all the transformation in our study based on [Ga][Al(OC(CF₃)₃)₄] complex is really catalyzed by gallium(I). As we mentioned in the introduction, gallium(I) has a strong potential to disproportionate into gallium(0) and gallium(III), which already proved to be able to catalyze those reactions. Thus, the stability of [Ga][Al(OC(CF₃)₃)₄] in DCE, which is a common solvent for our reactions, was studied by NMR. We also studied the stability of this complex in the presence of the substrate.

^{27}Al NMR

$[\text{Ga}(\text{C}_6\text{H}_5\text{F})_2]^+[\text{Al}(\text{OC}(\text{CF}_3)_3)_4]^-$: 39.5 mg
Dichloroethane: 700 μL

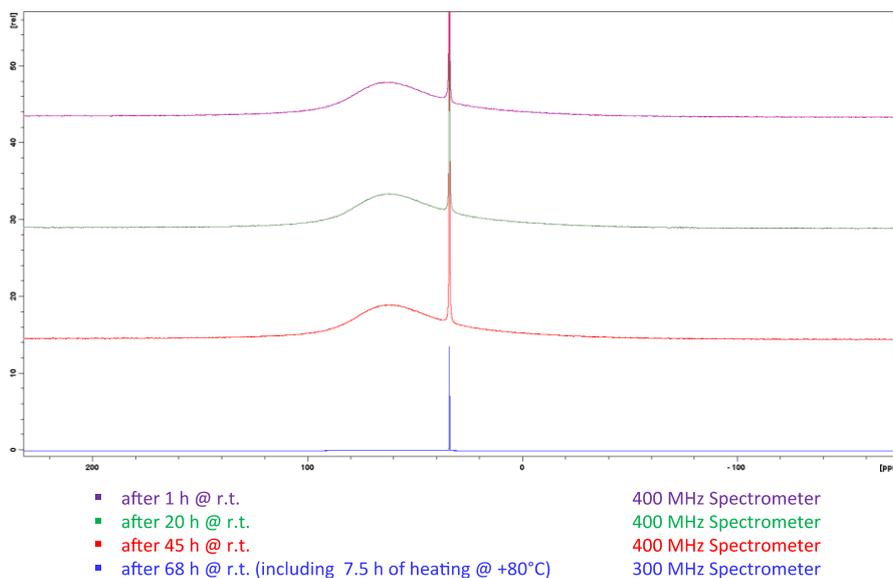


Figure 19. ^{27}Al NMR of $[\text{Ga}][\text{Al}(\text{OC}(\text{CF}_3)_3)_4]$ in DCE

^{19}F NMR

$[\text{Ga}(\text{C}_6\text{H}_5\text{F})_2]^+[\text{Al}(\text{OC}(\text{CF}_3)_3)_4]^-$: 39.5 mg
Dichloroethane: 700 μL

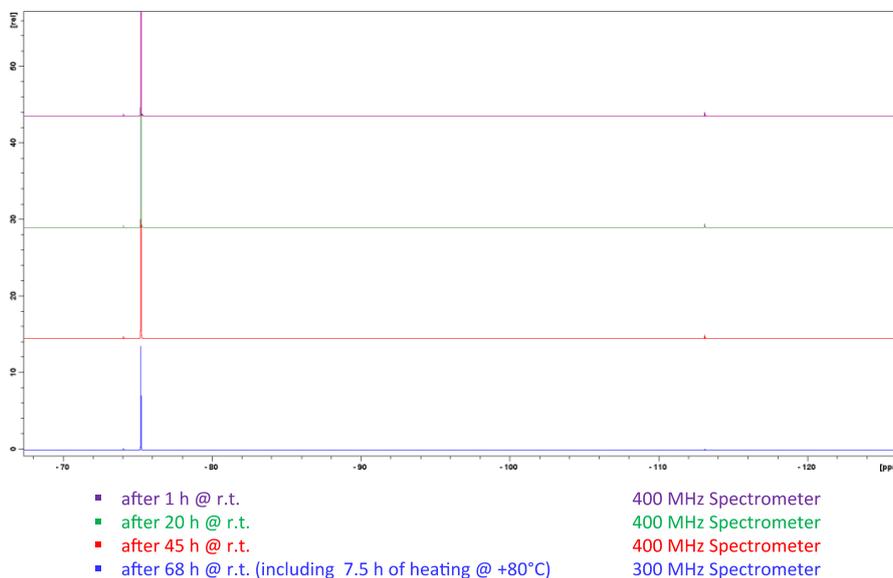


Figure 20. ^{19}F NMR of $[\text{Ga}][\text{Al}(\text{OC}(\text{CF}_3)_3)_4]$ in DCE

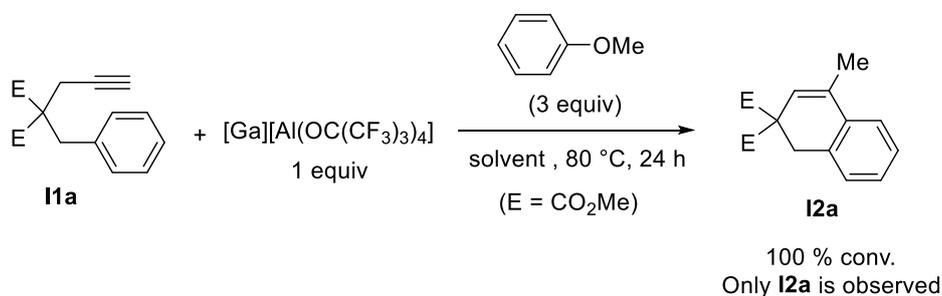
2.6.2 NMR study of [Ga][Al(OC(CF₃)₃)₄] in the reaction conditions

Next, we tested the stability of [Ga][Al(OC(CF₃)₃)₄] under our reaction conditions, since the substrates may also trigger the disproportionation of gallium(I). The results are described below. The NMR spectra are shown in Figure 22-24.

Sample A: [Ga][Al(OC(CF₃)₃)₄] (20 mg, 16 μmol) were diluted in DCE (0.7 mL) The resulting clear solution was directly analyzed by multinuclear NMR spectroscopy. ⁷¹Ga NMR (122 MHz, DCE) δ -628 ppm ([Ga][Al(OC(CF₃)₃)₄]). ²⁷Al NMR (104 MHz, DCE) δ 33.9 ppm ([Ga][Al(OC(CF₃)₃)₄]).

Sample B: [Ga][Al(OC(CF₃)₃)₄] (47mg, 38 μmol, 1.0 equiv), arenynes **IIa** (10 mg, 38 μmol, 1.0 equiv) and anisole (13 μL, 108 μmol, 3.0 equiv) in DCE (0.7 mL) at 20 °C. The resulting clear solution was directly analyzed by multinuclear NMR spectroscopy. Evidence for Ga(II) or Ga(III) species were not detected under these conditions. It suggests that the [Ga][Al(OC(CF₃)₃)₄] catalyst is stable in the presence of substrate **IIa**, even though a shift likely corresponding to the formation of a donor-acceptor adduct is observed. ⁷¹Ga NMR (122 MHz, DCE) δ -555 ppm (broad peak), which has been ascribed to unprecedented gallium(I) species involving **IIa** as ligand. ²⁷Al NMR (104 MHz, DCE) δ 33.9 ppm ([Ga][Al(OC(CF₃)₃)₄]).

Sample C:



In a glove box, the arenynes **IIa** (10 mg, 0.25 mmol, 38 μmol, 1 equiv) and anisole (13 μL, 108 μmol, 3 equiv) were introduced into a glass tube containing a magnetic stirrer. The catalyst ([Ga][Al(OC(CF₃)₃)₄] (47 mg, 38 μmol, 1 equiv)) and then dry degassed

DCE (0.25 mol.L^{-1}) were added into the reaction mixture. The tube was capped with a rubber septum and the mixture was stirred at $80 \text{ }^\circ\text{C}$ and monitored by GC using aliquots quenched by technical grade acetone (0.25 mL). After 3 h, **I2a** could be observed. The resulting yellow solution (without traces of particles, see Figure 21) was directly analyzed by multinuclear NMR spectroscopy. Both of the homogenous solution and NMR results suggested that the gallium(I) is stable and likely is the real catalyst for this transformation. ^{71}Ga NMR (122 MHz , DCE) δ -634 ppm (broad peak), which has been ascribed to a gallium(I) species involving **I2a** as ligand. Evidence for Ga(II) or Ga(III) species were not detected under these conditions. ^{27}Al NMR (104 MHz , DCE) δ 33.9 ppm ($[\text{Ga}][\text{Al}(\text{OC}(\text{CF}_3)_3)_4]$).



Figure 21. NMR Tube of Sample C after 3 h of stirring at $80 \text{ }^\circ\text{C}$.

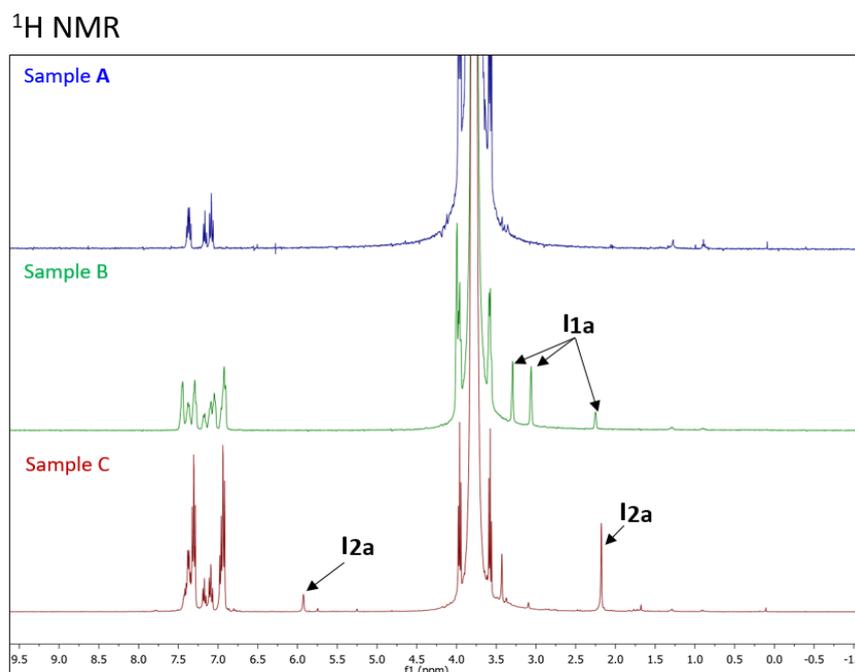


Figure 22. ^1H NMR spectrum of sample A, B and C

^{71}Ga NMR

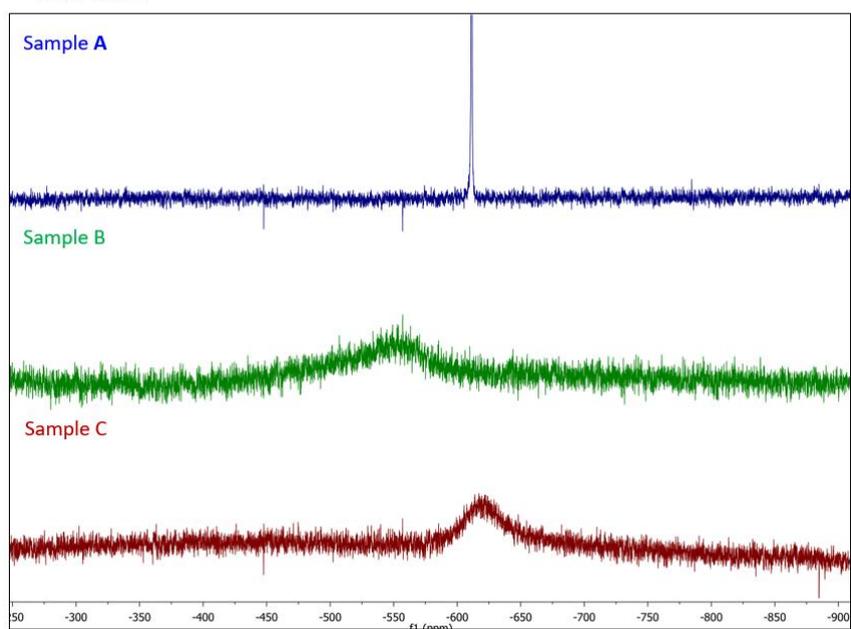


Figure 23 ^{71}Ga NMR spectrum of sample A, B and C

^{27}Al NMR

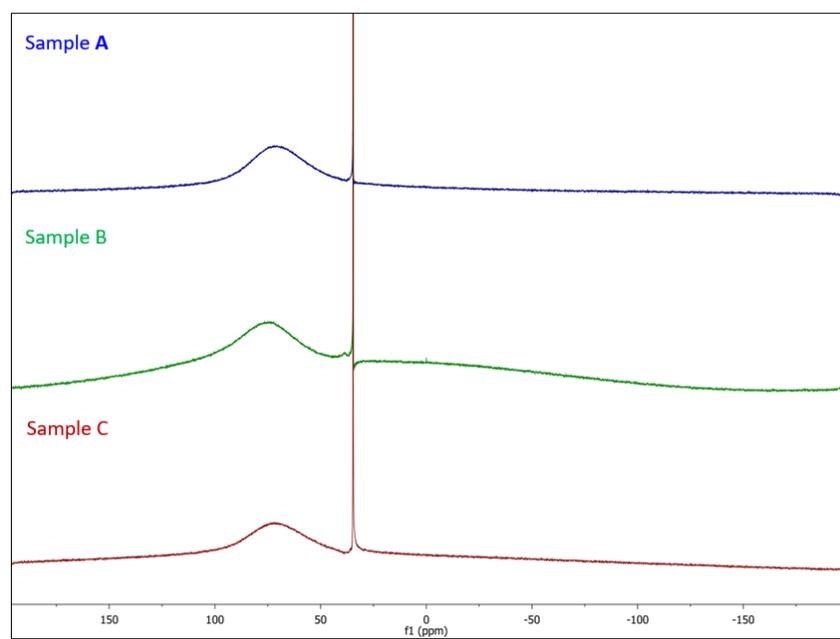


Figure 24. ^{27}Al NMR spectrum of sample A, B and C

2.7 Conclusion

In this project, we have investigated the homogeneous catalytic behavior of the gallium(I) species $[\text{Ga}][\text{Al}(\text{OC}(\text{CF}_3)_3)_4]$ and Ga_2Cl_4 , especially focusing on the π Lewis acid activation of triple and double C-C bonds. This approach was applied to four transformations, including dihydroarylation of arenynes; transfer hydrogenation of alkenes using 1,4-cyclohexadiene as hydrogen source; tandem hydrogenative cyclization of arenynes; and the cycloisomerization of enynes (Figure 25).

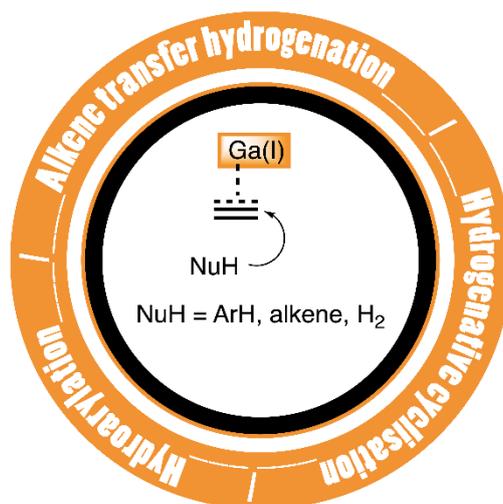


Figure 25. Catalytic Use of Low-Valent Cationic Gallium(I) Complexes as π -Acids

Meanwhile, all those transformations have been studied by multiple transition metal catalysts, even main group metal complexes such as our NHC-gallium species $[\text{IPr}\cdot\text{GaCl}_2][\text{SbF}_6]$.

This study showed that gallium(I) compounds could be attractive soft Lewis acid catalysts, giving more functional group tolerance compared to gallium(III)-based catalysts. We hope it would offer access to diverse structural skeletons and expand the accessibility to pharmaceutical and agrochemical compounds.

3. EXPERIMENTAL

3.1 General Information

All reactions were performed in oven-dried flasks under argon. Unless otherwise stated, products were purified by chromatography on silica gel. Reactions in an overheated solvent were performed in 10 mL reaction tubes sealed with a Teflon-coated rodaviss stopper and immersed in a pre-heated oil bath. Reactions were monitored using thin-layer chromatography (TLC) on silica gel plates (0.25 mm) precoated with a fluorescent indicator. The spots were visualized with ultraviolet light and/or *p*-anisaldehyde stain with heat as developing agents. GC analysis was performed on a Varian 430-GC Instrument, equipped with an autoinjector (CP8410) using a Zebron ZB-1MS or ZB-1 capillary GC column (15 m x 0.25 mm x 0.25 μ m). *dl* : *meso* ratio was determined by HPLC equipped with a Circular Dichroism detector (PU-2089 JASCO, CD-2095 JASCO) using a chiral column (chiralpak IC, 250 x 4.6 mm). NMR characterization data was collected at 296 K on a AM 250, AV 300, AV 360 or DRX 400 Bruker spectrometers operating at 250, 300, 360 or 400 MHz for ^1H NMR and ^{19}F NMR. ^1H NMR chemical shifts are reported in ppm using residual solvent peak as reference (CHCl_3 : $\delta = 7.27$ ppm). Data for ^1H NMR are presented as follows: chemical shift δ (ppm), multiplicity (s = singlet, d = doublet, t = triplet, m = multiplet, br = broad), coupling constant J (Hz) and integration; ^{13}C NMR spectra were recorded at 63, 75, 91 or 100 MHz using broadband proton decoupling and chemical shifts are reported in ppm using residual solvent peaks as reference (CHCl_3 : $\delta = 77$ ppm). ^{71}Ga (122.0 MHz) and ^{27}Al (104 MHz) NMR spectra were recorded on a Bruker DRX400 spectrometer and referenced to $\text{Ga}(\text{NO}_3)_3$ and $\text{Al}(\text{NO}_3)_3$. IR characterization data were recorded on an FT-IR spectrometer (Perkin-Elmer). MS were recorded on the DSQ Thermo Fisher instrument by the electronic impact. HRMS was performed on a MicroTOFq Bruker spectrometer.

Materials. Reagents were purchased from commercial suppliers (Alfa Aesar, Sigma Aldrich or Strem) and used as received unless stated otherwise. Anisole was distilled prior to use. 1,2-Dichloroethane and toluene were distilled from calcium hydride and degassed by the Freeze-Pump-Thaw technique. GaCl₃, Ga₂Cl₄ were obtained from Alfa Aesar and used as received. GaI was synthesized following a reported procedure.^[51]

3.2 Synthesis of [Ga][Al(OC(CF₃)₃)₄]

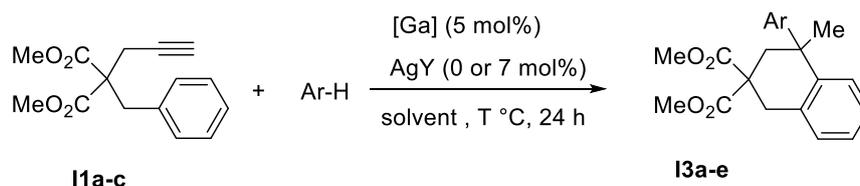
[Li][Al(OC(CF₃)₃)₄]: In the glove box, ground and dry LiAlH₄ (1 equiv, 0.643 g, 17 mmol) was transferred into a 100mL three neck-neck flask. This flask was then sealed with rubber stopper, moved out of the glove box and installed with an argon charged Schlenk system on one of the side necks. Under argon condition, the middle neck of the flask was installed with a dry reflux condenser which connected with a -20 °C cryostat. The port of this condenser sealed with rubber stopper and injected with an argon balloon. The other side neck of the flask was installed with a dropping funnel. Then perfluoro-tert-butanol (4.1 equiv, 16.4 g, 9.7 mL, 69.5 mmol) was added dropwise through this funnel at 0 °C until the end of the observed gas evolution. After that, a clear solution was formed. The reaction was heated to reflux for 16 hours, during that time white precipitate was formed. This flask containing the reaction mixture was again sealed with rubber stopper tightly and transferred in to glovebox (be careful about the exploration when making the vacuum in the entrance of glove box). The reaction mixture was filtered in the glovebox, washed with hexane, and dried under a vacuum, resulting 12.7g white [Li][Al(OC(CF₃)₃)₄] with 77% yield. This crude product was sufficient for the reparation of [Ag][Al(OC(CF₃)₃)₄]. However, it may be purified by sublimation at 150 °C and 5 × 10⁻² mbar, or Soxhlet extraction with perfluorohexane. **mp** = 145-150 °C; **⁷Li NMR** (117 MHz, CDCl₃ 25 °C): δ = 0.9; **¹³C NMR** (63 MHz, CDCl₃ 25 °C): δ = 120.9 (q, *J*(C,F) = 292.8 Hz; CF₃); **¹⁹F NMR** (235 MHz, CDCl₃ 25 °C): δ = 76.9 (s, CF₃); **²⁷Al NMR** (78 MHz, CDCl₃ 25 °C): δ = 33.8 (s, *V*_{1/2} = 130 Hz).

[Ag][Al(OC(CF₃)₃)₄]: In a Schlenk tube equipped with J. Young valves containing dried degassed (three cycles of freeze-pumping technique) DCM (5 mL) were added [Li][Al(OC(CF₃)₃)₄] (1 equiv, 1 g, 1.03 mmol) and AgF (2 equiv, 0.26 g, 2.05 mmol). The resulting suspension was sonicated at 40 °C for 12 hours, protected from light. Filtration and removal of the volatiles in vacuo (5×10^{-3} mbar) afforded 13 g (95%) of colorless, highly soluble crystals corresponding to a CH₂Cl₂ adducts. The CH₂Cl₂ could be removed under a high vacuum ($< 5 \times 10^{-3}$ mbar) with a once extra vacuum. **¹H NMR** (250 MHz, CDCl₃ 25 °C): $\delta = 5.34$ (s, CH₂Cl₂); **¹³C NMR** (63 MHz, CDCl₃ 25 °C): $\delta = 54.0$ (s, CH₂Cl₂), 121.2 (q, $J_{3 \text{ C-F}} = 292.8$ Hz; CF₃); **²⁷Al NMR** (78 MHz, CDCl₃ 25 °C): $\delta = 34.1$ (s, $V_{1/2} = 39$ Hz).

[Ga][Al(OC(CF₃)₃)₄]: A solution of [Ag][Al(OC(CF₃)₃)₄] (0.5 g, 0.38 mmol) in 10 mL fluorobenzene containing a bead of Ga (90 mg, 1.29 mmol) was allowed to react under ultrasonic activation for 13 hours. The resulting black precipitate was allowed to settle and the pale brown supernatant liquid was decanted. The solution was concentrated to a pale beige solid (0.200 g, 43% yield). **¹H NMR** (400 MHz, *o*-C₆H₄F₂, calibrated to *o*-C₆H₄F₂ 7.12 ppm, 298 K): $\delta = 6.83\text{--}7.42$ (m, Ar-H). **¹⁹F NMR** (377 MHz, *o*-C₆H₄F₂, calibrated to *o*-C₆H₄F₂ -139 ppm, 298 K): $\delta = -112, -74.9$ (s, CF₃). **²⁷Al NMR** (104 MHz, *o*-C₆H₄F₂, calibrated to [Al(OC(CF₃)₃)₄]⁻ 33.8 ppm, 298 K): $\delta = 33.8$ (s). **⁷¹Ga NMR** (122 MHz, *o*-C₆H₄F₂, 298 K): $\delta = -758$ (s).

3.3 Catalytic Reactions

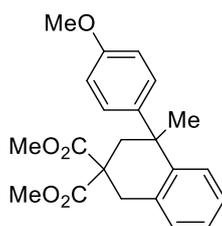
3.3.1 Procedure for the hydroarylation of 1,6-arenynes with aromatics



The gallium catalyst (5-20 mol%) and the silver salt (0 or 7 mol%) were mixed in a

screw-cap vial under argon. Dry degassed solvent (0.5 ml) was added and the mixture was stirred at rt for 5 min. Arenyne **II** (0.2 mmol, 1 equiv) and the aromatic nucleophile (0.6 mmol, 3 equiv) diluted in the solvent (0.5 mL) were added. The tube was capped with a rubber septum and the mixture was stirred at the stated temperature and monitored by GC using aliquots quenched by technical grade acetone (0.25 mL). The reaction was stirred for 24 h. The reaction mixture was filtered over a pad of celite which was rinsed with Et₂O. Volatiles were removed by rotary evaporation under vacuum. The crude was purified by flash column chromatography on silica gel (eluent: cyclohexane/ethyl acetate). *Conditions A*: [Ga] = [Ga][Al(OC(CF₃)₃)₄] in toluene; *Conditions B*: [Ga] = Ga₂Cl₄ in DCE.

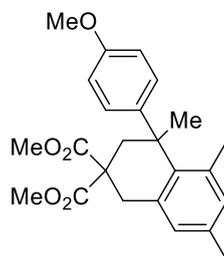
a. Analytical data of hydroalkylation products (I3a-e)



13a dimethyl 4-(4-methoxyphenyl)-4-methyl-3,4-dihydronaphthalene-2,2(1H)-dicarboxylate

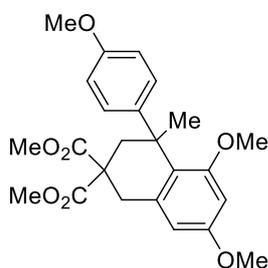
Following the general procedure, the reaction performed with **IIa** (52.0 mg, 0.2 mmol, 1.0 equiv) and anisole (65 mg, 0.6 mmol, 3 equiv) afforded, after purification by FC (SiO₂, cyclohexane/EtOAc: 5/1), **13a** (*Conditions A*: 59.6 mg, 81%, *Conditions B*: 56.4 mg, 77%) as white solid. **mp** = 99-100 °C; **¹H NMR** (250 MHz, CDCl₃) δ 7.29 – 7.19 (m, 4H), 6.99 (d, J = 8.6 Hz, 2H), 6.79 (d, J = 8.6 Hz, 2H), 3.78 (s, 3H), 3.74 (s, 3H), 3.43 (d, J = 16.2 Hz, 1H), 3.23 (s, 3H), 3.17 (d, J = 16.2 Hz, 1H), 2.96 (d, J = 14.3 Hz, 1H), 2.54 (d, J = 14.3 Hz, 1H), 1.73 (s, 3H); **¹³C NMR** (63 MHz, CDCl₃) δ 172.0, 170.7, 157.4, 141.4, 141.0, 133.7, 128.7, 128.4, 128.1, 126.3, 126.2, 112.8, 55.0, 52.4, 52.1, 52.0, 43.3, 41.4, 34.9, 32.0; **FTIR** (neat): 3469, 3031, 3008, 2951, 2930, 1738, 1608, 1579, 1508, 1437, 1277, 1246, 1176, 1129, 1093, 1057, 1037, 971, 842, 811, 768, 748, 573; **HRMS-ESI** m/z : Calcd. for C₂₂H₂₄O₅Na [M+Na]⁺ 391.1516

found: 391.1512. Spectroscopic data match those previously reported in the literature.^[70]



13b dimethyl 4-(4-methoxyphenyl)-4,5,7-trimethyl-3,4-dihydronaphthalene-2,2(1*H*)-dicarboxylate

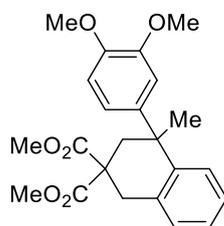
Following the general procedure, the reaction performed with **11b** (57.6 mg, 0.2 mmol, 1.0 equiv) and anisole (65 mg, 0.6 mmol, 3 equiv) afforded, after purification by FC (SiO₂, cyclohexane /EtOAc: 5/1), **13b** (*Conditions A*: 60 mg, 76%, *Conditions B*: 63 mg, 79%) as a colorless oil. ¹H NMR (300 MHz, CDCl₃) δ 7.00 (d, *J* = 8.6 Hz, 2H), 6.92 (s, 1H), 6.81 (s, 1H), 6.77 (d, *J* = 8.6 Hz, 2H), 3.78 (s, 3H), 3.72 (s, 3H), 3.40 (s, 3H), 3.28 (s, 2H), 2.61 (d, *J* = 14.1 Hz, 1H), 2.51 (d, *J* = 14.1 Hz, 1H), 2.29 (s, 3H), 1.82 (s, 3H), 1.71 (s, 3H). ¹³C NMR (90 MHz, CDCl₃) δ 172.1, 171.2, 157.3, 142.0, 137.3, 136.5, 135.7, 134.1, 132.0, 127.8, 127.7, 113.3, 55.2, 52.5, 52.3, 51.7, 47.9, 41.7, 36.6, 28.5, 22.5, 20.6. FT-IR (neat): ν 2952, 1736, 1609, 1509, 1250, 1215, 1180, 1034. HRMS-ESI *m/z*: Calcd for C₂₄H₂₈O₅Na [M+Na]⁺ 419.1829 found: 419.1813. Spectroscopic data match those previously reported in the literature.^[21]



13c dimethyl 5,7-dimethoxy-4-(4-methoxyphenyl)-4-methyl-3,4-dihydronaphthalene-2,2(1*H*)-dicarboxylate

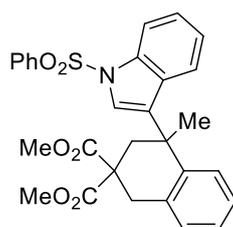
Following the general procedure, the reaction performed with **11c** (64 mg, 0.2 mmol, 1.0 equiv) and anisole (65 mg, 0.6 mmol, 3 equiv) afforded, after purification by FC

(SiO₂, cyclohexane /EtOAc: 5/1), **I3c** (Conditions A: 52 mg, 61%, Conditions B: 84 mg, 99%) as a white solid. **mp** = 165-170 °C. **¹H NMR** (250 MHz, CDCl₃) δ 6.93 (d, *J* = 8.6 Hz, 2H), 6.72 (d, *J* = 8.6 Hz, 2H), 6.38 (s, 1H), 6.32 (s, 1H), 3.81 (s, 3H), 3.75 (s, 3H), 3.70 (s, 3H), 3.43 (s, 3H), 3.32 (d, *J* = 16.0 Hz, 1H), 3.22 – 3.07 (m, 4H), 2.63 (d, *J* = 14.2 Hz, 1H), 2.45 (d, *J* = 14.2 Hz, 1H), 1.72 (s, 3H). **¹³C NMR** (63 MHz, CDCl₃) δ 172.2, 170.8, 159.5, 159.0, 157.0, 142.0, 136.2, 127.4, 122.6, 112.7, 104.5, 98.6, 55.1, 52.5, 52.2, 51.8, 46.6, 40.3, 36.4, 29.0. **FT-IR** (neat): 2997, 2953, 2837, 1735, 1606, 1509, 1462, 1248, 1158, 1089, 1036, 830, 736. **HRMS-ESI**: *m/z* calculated for C₂₄H₂₈NaO₇ [M+Na]⁺ 451.1733, found: 451.1726



I3d dimethyl 4-(3,4-dimethoxyphenyl)-4-methyl-3,4-dihydronaphthalene-2,2(1*H*)-dicarboxylate

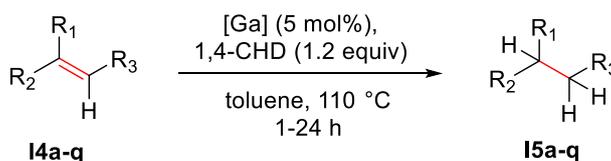
Following the general procedure, the reaction performed with **I1a** (52 mg, 0.2 mmol, 1.0 equiv) and 1,2-Dimethoxybenzene (83 mg, 0.6 mmol, 3 equiv) afforded, after purification by FC (SiO₂, cyclohexane /EtOAc: 4/1), **I-3d** (Conditions A: 26 mg, 33%, Conditions B: 52 mg, 65%) white solid. **mp** = 108-109 °C; **¹H NMR** (250 MHz, CDCl₃) δ 7.12 – 7.16 (m, 4H), 6.68 (d, *J* = 8.5 Hz, 1H), 6.62 (d, *J* = 2.3 Hz, 1H), 6.48 (dd, *J* = 8.5, 2.3 Hz, 1H), 3.81 (s, 3H), 3.75 (s, 3H), 3.69 (s, 3H), 3.34 (d, *J* = 16.1 Hz, 1H), 3.21 (s, 3H), 3.10 (d, *J* = 16.1 Hz, 1H), 2.92 (d, *J* = 14.3 Hz, 1H), 2.46 (d, *J* = 14.3 Hz, 1H), 1.69 (s, 3H); **¹³C NMR** (63 MHz, CDCl₃) δ 172.1, 171.04, 148.0, 147.0, 141.5, 141.4, 133.9, 128.7, 128.0, 126.4, 126.2, 119.7, 111.3, 110.3, 55.7, 55.6, 52.5, 52.3, 52.0, 43.3, 41.8, 34.8, 31.9; **FT-IR** (neat): 2954, 2836, 2255, 1736, 1604, 1589, 1512, 1463, 1446, 1255, 1167, 1148, 1094, 1027, 913, 808, 771, 732, 648; **HRMS-ESI**: *m/z*: Calcd. for C₂₃H₂₆O₆Na [M+Na]⁺ 421.1622 found: 421.1621. Spectroscopic data match those previously reported in the literature.^[70]



13e dimethyl 4-methyl-4-(1-(phenylsulfonyl)-1*H*-indol-3-yl)-3,4-dihydronaphthalene-2,2(1*H*)-dicarboxylate

Following the general procedure, the reaction performed with **11a** (52 mg, 0.2 mmol, 1.0 equiv) and 1-(phenylsulfonyl)-1-indole (154 mg, 0.6 mmol, 3 equiv) afforded, after purification by FC (SiO₂, cyclohexane /EtOAc: 3/1), **13e** (*Conditions A*: 62 mg, 60%, *Conditions B*: 90 mg, 87%) white solid. **mp** = 213-216 °C; **¹H NMR** (250 MHz, CDCl₃) δ 7.91 (dd, J = 12.5, 8.3 Hz, 3H), 7.60 – 7.42 (m, 3H), 7.27 – 7.05 (m, 7H), 6.97 (s, 1H), 3.71 (s, 3H), 3.40 (d, J = 16.4 Hz, 1H), 3.31 (d, J = 16.4 Hz, 1H), 3.07 (d, J = 14.2 Hz, 1H), 2.88 (s, 3H), 2.45 (d, J = 14.2 Hz, 1H), 1.73 (s, 3H); **¹³C NMR** (63 MHz, CDCl₃) δ 172.0, 170.9, 140.1, 137.8, 135.6, 133.7, 132.7, 130.3, 129.1, 128.9, 128.6, 127.6, 126.9, 126.6, 124.5, 124.2, 122.3, 121.3, 113.5, 52.6, 51.9, 51.6, 39.7, 37.9, 34.6, 29.9; **FTIR** (neat): 3409, 2973, 2360, 1737, 1448, 1368, 1179, 962, 748, 592; **HRMS** (ESI) m/z : Calcd. for C₂₉H₂₇O₆NSNa [M+Na]⁺ 540.1449 found: 540.1451. Spectroscopic data match those previously reported in the literature.^[70]

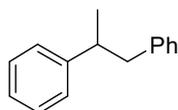
3.3.2 Procedure for Ga(I)-catalyzed transfer hydrogenation of alkenes



Under argon, the alkene (0.25 mmol, 1 equiv) was introduced into a glass tube containing a magnetic stirrer. The catalyst (5 mol%, 0.0125 mmol) and then dry degassed toluene (0.25 mol/L) were added into the reaction vessel. The tube was capped with a rubber septum. 1,4-CHD (0.3 mmol, 30 μ L, 1.2 equiv) was added through the septum with a Hamilton® syringe. The mixture was then heated at 110 °C and the reaction progress was monitored by GC. After completion, the reaction mixture was filtered over a pad of celite which was rinsed with Et₂O. Volatiles were removed by

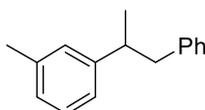
rotary evaporation under vacuum. The crude was purified by flash column chromatography on silica gel (eluent: pentane/ethyl acetate). *Conditions A*: [Ga] = [Ga][Al(OC(CF₃)₃)₄]; *Conditions B*: [Ga] = Ga₂Cl₄.

a. Analytical data of transfer hydrogenation products (I5a-p)



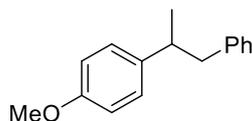
I5a propane-1,2-diyl dibenzene

Following the general procedure, the reaction performed with **I4a** (48.5 mg, 0.25 mmol, 1.0 equiv) and 1,4-CHD (0.3 mmol, 30 μ L, 1.2 equiv) afforded, after purification by FC (SiO₂, pentane), the **I5a** as a colorless oil (*Conditions A*: 30 mg, 61%, *Conditions B*: 46 mg, 94%). **¹H NMR** (400 MHz, CDCl₃, 30 °C): δ 7.31 – 7.16 (m, 8H), 7.09 – 7.07 (m, 2H), 3.06 – 2.91 (m, 2H), 2.79 – 2.73 (m, 1H), 1.24 (d, *J* = 6.9 Hz, 3H); **¹³C NMR** (100 MHz, CDCl₃, 30 °C): δ 147.2, 141.0, 129.4, 128.4, 128.2, 127.2, 126.2, 126.0, 45.2, 42.0, 21.3; **HRMS** (ESI⁺) *m/z* calcd. for C₁₅H₁₆ 196.1252 [M]⁺: found 196.1252. Spectroscopic data match those previously reported in the literature.^[22]



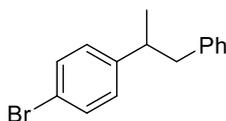
I5b 1-methyl-3-(1-phenylpropan-2-yl)benzene

Following the general procedure, the reaction performed with **I4b** (52 mg, 0.25 mmol, 1.0 equiv) and 1,4-CHD (0.3 mmol, 30 μ L, 1.2 equiv) afforded, after purification by FC (SiO₂, pentane), the **I5b** as a colorless oil (*Conditions A*: 49 mg, 95%, *Conditions B*: 44 mg, 84%). **¹H NMR** (400 MHz, CDCl₃, 30 °C): δ 7.31 – 7.07 (m, 9H), 3.01 – 2.89 (m, 2H), 2.77 – 2.69 (m, 1H), 2.32 (s, 3H), 1.21 (d, *J* = 6.7 Hz, 3H); **¹³C NMR** (100 MHz, CDCl₃, 30 °C): δ 147.3, 141.1, 137.9, 129.3, 128.4, 128.2, 128.0, 126.9, 126.0, 124.2, 45.2, 41.9, 21.7, 21.2; **HRMS** (ESI⁺) *m/z* calcd. for C₁₆H₁₈ 210.1409 [M]⁺: found 210.1411.



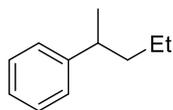
15c 1-methoxy-4-(1-phenylpropan-2-yl)benzene

Following the general procedure, the reaction performed with **14c** (56 mg, 0.25 mmol, 1.0 equiv) and 1,4-CHD (0.3 mmol, 30 μ L, 1.2 equiv) afforded, after purification by FC (SiO₂, pentane), the **15c** as a colorless oil (*Conditions A*: 51 mg, 90%, *Conditions B*: 52 mg, 92%). **¹H NMR** (400 MHz, CDCl₃, 30 °C): δ 7.25 – 7.21 (m, 3H), 7.17 – 7.06 (m, 4H), 6.83 – 6.81 (m, 2H), 3.79 (s, 3H), 3.02 – 2.86 (m, 2H), 2.77 – 2.70 (m, 1H), 1.21 (d, J = 6.9 Hz, 3H); **¹³C NMR** (100 MHz, CDCl₃, 30 °C): δ 158.0, 141.1, 139.3, 129.3, 128.2, 128.1, 125.9, 113.9, 55.4, 45.5, 41.2, 21.6; **HRMS** (ESI⁺) m/z calcd. for C₁₆H₁₈O 226.1358 [M]⁺: found 226.1360. Spectroscopic data match those previously reported in the literature.^[71]



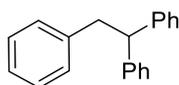
15d 1-bromo-4-(1-phenylpropan-2-yl)benzene

Following the general procedure, the reaction performed with **14d** (68 mg, 0.25 mmol, 1.0 equiv) and 1,4-CHD (0.3 mmol, 30 μ L, 1.2 equiv) afforded, after purification by FC (SiO₂, pentane), the **15d** as a colorless oil (*Conditions A*: 56 mg, 81%, *Conditions B*: 23 mg, 34%). **¹H NMR** (400MHz, CDCl₃) δ 7.44 – 7.40 (m, 2H), 7.30 – 7.16 (m, 3H), 7.11 – 7.02 (m, 4H), 3.06 – 2.93 (m, 1H), 2.90 – 2.76 (m, 2H), 1.27 (d, J = 6.8Hz, 3H). **¹³C NMR** (100 MHz, CDCl₃) δ 145.8, 140.3, 131.3, 129.1, 128.9, 128.2, 126.0, 119.6, 44.9, 41.4, 21.2. **FT-IR (neat, cm⁻¹)**: 3083, 3061, 2960, 2926, 2871, 1488, 1452, 1073, 1009, 739, 699. **MS (CI)**: m/z calculated for C₁₅H₁₅Br [M]⁺ = 274.0 found 273.9. **Elemental analysis (C, H)** calculated for C₁₅H₁₅Br: C, 65.47; H, 5.49 found C, 66.23; H, 5.52.



I5e pentan-2-ylbenzene

Following the general procedure, the reaction performed with **I4e** (38 mg, 0.25 mmol, 1.0 equiv) and 1,4-CHD (0.3 mmol, 30 μ L, 1.2 equiv) afforded, after purification by FC (SiO₂, pentane), the **I5e** as a colorless oil (*Conditions A*: 27 mg, 72%, *Conditions B*: 21 mg, 58%). ¹H NMR (400 MHz, CDCl₃) δ 7.33 – 7.28 (m, 2 H), 7.23 – 7.15 (m, 3 H), 2.71 (t, J = 7.0 Hz, 1 H), 1.65 – 1.49 (m, 3 H), 1.35 – 1.15 (m, 5 H), 0.88 (t, J = 7.0 Hz, 3 H). ¹³C NMR (100 MHz, CDCl₃) δ 147.9, 128.2, 127.0, 125.7, 40.7, 39.6, 22.3, 20.8, 14.1. HRMS (EI⁺) m/z [M]⁺ calculated for C₁₁H₁₆ 148.1252; found 148.1259. Spectroscopic data match those previously reported in the literature.^[72]



I5f ethane-1,1,2-triyltribenzene

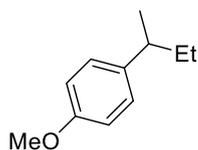
Following the general procedure, the reaction performed with **I4f** (64 mg, 0.25 mmol, 1.0 equiv) and 1,4-CHD (0.3 mmol, 30 μ L, 1.2 equiv) afforded, after purification by FC (SiO₂, pentane), the **I5f** as a colorless oil (*Conditions A*: 36 mg, 56%, *Conditions B*: 29 mg, 45%). ¹H NMR (400 MHz, CDCl₃): δ 7.32 – 7.13 (m, 13H), 7.07 – 7.03 (m, 2H), 4.28 (t, J = 7.8 Hz, 1H), 3.41 (d, J = 7.8 Hz, 2H). ¹³C NMR (101 MHz, CDCl₃): δ 144.5, 140.3, 129.1, 128.4, 128.1, 126.3, 126.0, 53.2, 42.2. Spectroscopic data match those previously reported in the literature.^[73]



I5g ethane-1,1-diylidibenzene

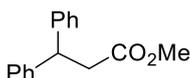
Following the general procedure, the reaction performed with **I4g** (45 mg, 0.25 mmol, 1.0 equiv) and 1,4-CHD (0.3 mmol, 30 μ L, 1.2 equiv) afforded, after purification by FC (SiO₂, pentane), the **I5g** as a colorless oil (*Conditions A*: 30 mg, 66%, *Conditions B*: 44.6 mg, 98%). ¹H NMR (400 MHz, CDCl₃): δ 1.74 (d, J = 7.2 Hz, 3H), 4.25 (q,

$J = 7.2$ Hz, 1H), 7.24 – 7.39 (m, 10H); ^{13}C NMR (101 MHz, CDCl_3): δ 22.1, 45.0, 126.2, 127.8, 128.6. Spectroscopic data match those previously reported in the literature.^[22]



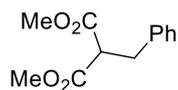
I5h 1-(sec-butyl)-4-methoxybenzene

Following the general procedure, the reaction performed with **I4h** (40.5 mg, 0.25 mmol, 1.0 equiv) and 1,4-CHD (0.3 mmol, 30 μL , 1.2 equiv) afforded, after purification by FC (SiO_2 , pentane), the **I5h** as a colorless oil (*Conditions A*: 27.5 mg, 67%, *Conditions B*: 14 mg, 34%). ^1H NMR (400 MHz, CDCl_3): δ 0.98 (t, $J = 7.33$ Hz, 3H), 1.30 (d, $J = 7.33$ Hz, 3H), 1.62 (m, 2H), 2.95 (m, 1H), 3.78 (s, 3H), 6.89 (d, $J = 7.79$ Hz, 2H), 7.09 (d, $J = 7.79$ Hz, 2H). ^{13}C NMR (100MHz, CDCl_3): δ 11.1, 21.2, 31.9, 37.2, 54.5, 112.5, 130.9, 140.5, 162.2. HRMS-ESI: calculated m/z 164.1204 found $m/z = 164.1202$. Spectroscopic data match those previously reported in the literature.^[74]



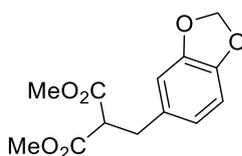
I5i methyl 3,3-diphenylpropanoate

Following the general procedure, the reaction performed with **I-4i** (59.5 mg, 0.25 mmol, 1.0 equiv) and 1,4-CHD (0.3 mmol, 30 μL , 1.2 equiv) afforded, after purification by FC (SiO_2 , pentane), the **I-5i** as a colorless oil (*Conditions A*: 26 mg, 43%, *Conditions B*: 0 mg, 0%). ^1H NMR (360 MHz, CDCl_3): δ 7.42 – 7.20 (m, 10H), 4.59 (t, $J = 7.9$ Hz, 1H), 3.60 (s, 3H), 3.09 (d, $J = 7.9$ Hz, 2H). ^{13}C NMR (90 MHz, CDCl_3): δ 172.2, 143.4, 128.5, 127.6, 126.5, 51.6, 46.9, 40.5. Spectroscopic data match those previously reported in the literature.^[22]



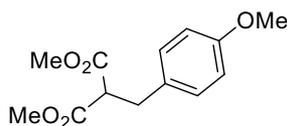
15j dimethyl 2-benzylmalonate

Following the general procedure, the reaction performed with **14j** (55 mg, 0.25 mmol, 1.0 equiv) and 1,4-CHD (0.3 mmol, 30 μ L, 1.2 equiv) afforded, after purification by FC (SiO₂, pentane), the **15j** as a colorless oil (*Conditions A*: 47 mg, 85%, *Conditions B*: 30 mg, 54%). ¹H NMR (360 MHz, CDCl₃): δ 7.30 – 7.18 (m, 5H), 3.69 (s, 6H), 3.67 (t, J = 8.0 Hz, 1H), 3.22 (d, J = 8.0 Hz, 2H), ¹³C NMR (90 MHz, CDCl₃): δ 169.2, 137.7, 128.7, 128.5, 126.8, 53.6, 52.5, 34.7. Spectroscopic data match those previously reported in the literature.^[75]



15k dimethyl 2-(benzo[d][1,3]dioxol-5-ylmethyl)malonate

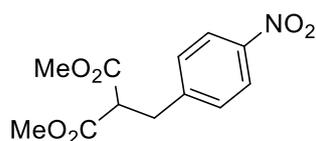
Following the general procedure, the reaction performed with **14k** (66 mg, 0.25 mmol, 1.0 equiv) and 1,4-CHD (0.3 mmol, 30 μ L, 1.2 equiv) afforded, after purification by FC (SiO₂, pentane/EtOAc:6/1), **15k** as a colorless oil (*Conditions A*: 51 mg, 77%, *Conditions B*: 27 mg, 41%). ¹H NMR (360 MHz, CDCl₃) δ 6.76 – 6.65 (m, 3H), 5.95 (s, 2H), 3.74 (s, 6H), 3.64 (t, J = 7.8 Hz, 1H), 3.17 (d, J = 7.8 Hz, 2H). ¹³C NMR (91 MHz, CDCl₃) δ 169.2, 147.7, 146.4, 131.4, 121.9, 109.2, 108.3, 101.0, 53.9, 52.6, 34.5. FT-IR (neat): 2955, 2902, 1734, 1505, 1489, 1244, 1155, 1040, 934, 814. HRMS-ESI: m/z calculated for C₁₃H₁₄NaO₆ [M+Na]⁺ 289.0688, found: 289.05686.



15l dimethyl 2-(4-methoxybenzyl)malonate

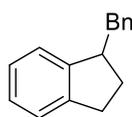
Following the general procedure, the reaction performed with **14l** (62.5 mg, 0.25 mmol, 1.0 equiv) and 1,4-CHD (0.3 mmol, 30 μ L, 1.2 equiv) afforded, after purification by

FC (SiO₂, pentane/EtOAc:6/1), **I5l** as a colorless oil (*Conditions A*: 32 mg, 51%, *Conditions B*: 33 mg, 52%). ¹H NMR (250 MHz, CDCl₃): δ 7.14 (d, *J* = 8.6 Hz, 2H), 6.82 (d, *J* = 8.6 Hz, 2H), 3.78 (s, 3H), 3.70 (s, 6H), 3.64 (t, *J* = 7.8 Hz, 1H), 3.17 (d, *J* = 7.8 Hz, 2H). ¹³C NMR (90 MHz, CDCl₃): δ 169.2, 158.4, 129.7, 129.6, 113.9, 55.2, 53.8, 52.4, 33.9. HRMS (ESI⁺) *m/z*: Calcd for C₁₃H₁₆O₅Na [M+Na]⁺ 275.0890 found: 275.0886.^[22]



I5m dimethyl 2-(4-nitrobenzyl)malonate

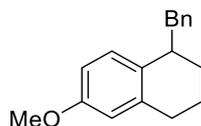
Following the general procedure, the reaction performed with **I4m** (66 mg, 0.25 mmol, 1.0 equiv) and 1,4-CHD (0.3 mmol, 30 μL, 1.2 equiv) afforded, after purification by FC (SiO₂, pentane/EtOAc:6/1), **I5m** as a colorless oil (*Conditions A*: 63 mg, 94%, *Conditions B*: 52 mg, 78%). ¹H NMR (250 MHz, CDCl₃): δ 3.20 (d, *J* = 7.9 Hz, 2H), 3.59 – 3.61 (m, 1H), 3.59 (s, 6H), 7.26 (d, *J* = 8.9 Hz, 2H), 8.02 (d, *J* = 8.9 Hz, 2H). ¹³C NMR (90 MHz, CDCl₃): δ 34.4, 52.5, 52.8, 123.7, 125.3, 129.6, 145.2, 168.4. Spectroscopic data match those previously reported in the literature.^[76]



I5o 1-benzyl-2,3-dihydro-1H-indene

Following the general procedure, the reaction performed with **I4o** (51.5 mg, 0.25 mmol, 1.0 equiv) and 1,4-CHD (0.3 mmol, 30 μL, 1.2 equiv) afforded, after purification by FC (SiO₂, pentane/EtOAc:40/1), **I5o** as a colorless oil (*Conditions A*: 43 mg, 82%, *Conditions B*: 44 mg, 85%). ¹H NMR (CDCl₃, 400 MHz) δ 7.26 – 7.21 (m, 2 H), 7.19 – 7.20 (m, 4H), 7.11 – 7.03 (m, 3H), 3.43 – 3.32 (m, 1H), 3.11 – 3.05 (m, 1H), 2.87 – 2.66 (m, 2H), 2.66 – 2.57 (m, 1H), 2.10 – 2.02 (m, 1H), 1.74 – 1.66 (m, 1H); ¹³C NMR (CDCl₃, 100 MHz) δ 147.0, 144.3, 141.0, 129.2, 128.4, 126.6, 126.1, 126.0, 124.7,

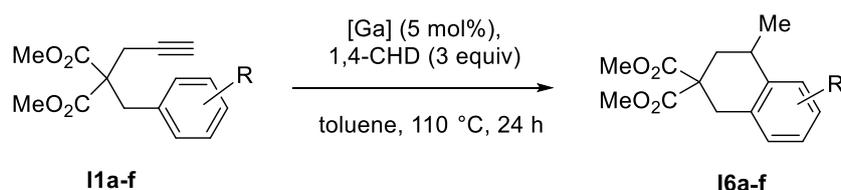
123.9, 46.6, 41.5, 32.1, 31.3. Spectroscopic data match those previously reported in the literature.^[22]



I5p 1-benzyl-6-methoxy-1,2,3,4-tetrahydronaphthalene

Following the general procedure, the reaction performed with **I4p** (62 mg, 0.25 mmol, 1.0 equiv) and 1,4-CHD (0.3 mmol, 30 μ L, 1.2 equiv) afforded, after purification by FC (SiO₂, pentane/EtOAc:40/1), **I5p** as a colorless oil (*Conditions A*: 63 mg, 99%, *Conditions B*: 36 mg, 57%). ¹H NMR (360 MHz, CDCl₃) δ 7.34 – 7.28 (m, 2H), 7.25 – 7.20 (m, 3H), 7.13 (d, J = 8.5 Hz, 1H), 6.73 (dd, J = 8.5, 2.7 Hz, 1H), 6.64 (d, J = 2.7 Hz, 1H), 3.79 (s, 3H), 3.12 – 2.99 (m, 2H), 2.79 – 2.65 (m, 3H), 1.93 – 1.81 (m, 1H), 1.72 – 1.58 (m, 3H). ¹³C NMR (75 MHz, CDCl₃) δ 157.5, 141.1, 138.3, 132.8, 129.8, 129.3, 128.3, 125.9, 113.5, 112.0, 55.2, 43.6, 38.9, 30.1, 26.9, 19.3. FT-IR (neat): 3024, 2932, 2857, 2834, 1067, 1499, 1464, 1252, 1040, 699. HRMS-ESI: m/z calculated for C₁₈H₂₀NaO [M+Na]⁺ 275.1412, found: 275.1403.

3.3.3 Procedure for Ga(I)-catalyzed hydrogenative cyclizations

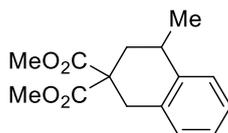


Under argon, the arenyne (0.25 mmol, 1 equiv) was introduced into a glass tube containing a magnetic stirrer. The catalyst (5 mol%, 0.0125 mmol) and then dry degassed solvent (0.25 mol/L) were added into the reaction vessel. The tube was capped with a rubber septum. 1,4-CHD (0.75 mmol, 71 μ L, 3 equiv) was added through the septum with a Hamilton® syringe. The mixture was then heated at 110 °C and the reaction progress was monitored by GC. After completion, the reaction mixture was filtered over a pad of celite which was rinsed with Et₂O. Volatiles were removed by

rotary evaporation under vacuum. The crude was purified by flash column chromatography on silica gel (eluent: cyclohexane/ethyl acetate).

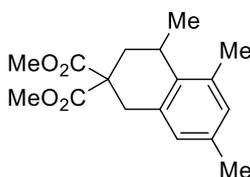
Conditions A: [Ga] = Ga[Al(OC(CF₃)₃)₄]; *Conditions B:* [Ga] = Ga₂Cl₄.

a. Analytical data of hydrogenative cyclization products I6a-g



16a dimethyl 4-methyl-3,4-dihydronaphthalene-2,2(1*H*)-dicarboxylate

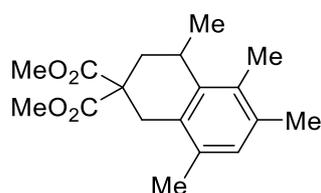
Following the general procedure, the reaction performed with **I1a** (65 mg, 0.25 mmol, 1.0 equiv) and 1,4-CHD (0.75 mmol, 71 μ L, 3 equiv) afforded, after purification by FC (SiO₂, pentane/EtOAc:10/1), **I6a** as a colorless oil (*Conditions A:* 60 mg, 92%, *Conditions B:* 47 mg, 72%). ¹H NMR (250 MHz, CDCl₃) δ 7.27-7.12 (m, 4H), 3.76 (s, 3H), 3.68 (s, 3H), 3.42 (dd, $J = 16.2$ Hz, $J = 2.2$ Hz, 1H), 3.20 (d, $J = 16.2$ Hz, 1H), 3.02-2.87 (m, 1H), 2.63 (ddd, $J = 13.5$ Hz, $J = 5.8$ Hz, $J = 2.2$ Hz, 1H), 1.87 (dd, $J = 13.5$ Hz, $J = 11.3$ Hz, 1H), 1.39 (d, $J = 6.8$ Hz, 3H). ¹³C NMR (63 MHz, CDCl₃) δ 172.3, 171.4, 139.7, 133.3, 128.7, 126.5 (2C), 126.0, 53.9, 52.7, 52.6, 37.4, 35.4, 30.0, 21.3. HRMS (ESI) m/z : Calcd for C₁₅H₁₈O₄Na [M+Na]⁺ 285.1097 found: 285.1091. Spectroscopic data match those previously reported in the literature.^[22]



16b dimethyl 4,5,7-trimethyl-3,4-dihydronaphthalene-2,2(1*H*)-dicarboxylate

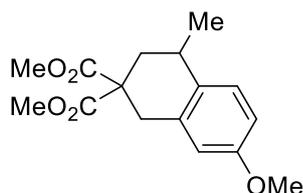
Following the general procedure, the reaction performed with **I-1b** (72 mg, 0.25 mmol, 1.0 equiv) and 1,4-CHD (0.75 mmol, 71 μ L, 3 equiv) afforded, after purification by FC (SiO₂, pentane/EtOAc:10/1), **I-6b** as a pale yellow oil (*Conditions A:* 54 mg, 91%, *Conditions B:* 52 mg, 88%). ¹H NMR (250 MHz, CDCl₃) δ 6.85 (s, 1H), 6.80 (s, 1H),

3.76 (s, 3H), 3.61 (s, 3H), 3.32 (d, $J = 15.7$ Hz, 1H), 3.32-3.25 (m, 1H), 3.12 (dd, $J = 15.7$ Hz, $J = 1.6$ Hz, 1H), 2.68 (ddd, $J = 14.0$ Hz, $J = 7.6$ Hz, $J = 1.6$ Hz, 1H), 2.28 (s, 3H), 2.26 (s, 3H), 2.07 (dd, $J = 14.0$ Hz, $J = 5.1$ Hz, 1H), 1.17 (d, $J = 7.1$ Hz, 3H). ^{13}C NMR (75 MHz, CDCl_3) δ 172.8, 171.7, 135.7, 135.4, 135.0, 133.0, 130.0, 127.3, 53.6, 52.6, 52.5, 37.1, 35.5, 28.6, 22.0, 20.7, 19.3. HRMS (ESI) m/z : Calcd for $\text{C}_{17}\text{H}_{22}\text{O}_4\text{Na}$ $[\text{M}+\text{Na}]^+$ 313.1410 found: 313.1396. Spectroscopic data match those previously reported in the literature.^[22]



16c dimethyl 4,5,6,8-tetramethyl-3,4-dihydronaphthalene-2,2(1H)-dicarboxylate

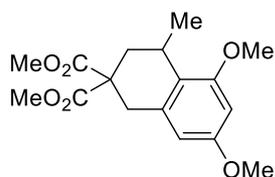
Following the general procedure, the reaction performed with **11c** (75.5 mg, 0.25 mmol, 1.0 equiv) and 1,4-CHD (0.75 mmol, 71 μL , 3 equiv) afforded, after purification by FC (SiO_2 , pentane/EtOAc:10/1), **16c** as a white solid (*Conditions A*: 65 mg, 86%, *Conditions B*: 59 mg, 77%). mp = 79 $^\circ\text{C}$. ^1H NMR (250 MHz, CDCl_3) δ 6.87 (s, 1H), 3.78 (s, 3H), 3.64 (s, 3H), 3.47-3.34 (m, 1H), 3.17 (s, 2H), 2.66 (dd, $J = 13.8$ Hz, $J = 7.5$ Hz, 1H), 2.70 (s, 3H), 2.23 (s, 3H), 2.18 (s, 3H), 2.68 (dd, $J = 13.8$ Hz, $J = 7.6$ Hz, $J = 1.6$ Hz, 1H), 2.28 (s, 3H), 2.26 (s, 3H), 2.15 (dd, $J = 13.8$ Hz, $J = 4.7$ Hz, 1H), 1.16 (d, $J = 7.2$ Hz, 3H). ^{13}C NMR (90 MHz, CDCl_3) δ 173.0, 171.9, 138.5, 134.6, 132.8, 131.3, 129.5, 129.0, 53.4, 52.6, 52.4, 36.4, 31.6, 29.2, 22.1, 20.4, 19.5, 15.1. HRMS (ESI) m/z : Calcd for $\text{C}_{18}\text{H}_{24}\text{O}_4\text{Na}$ $[\text{M}+\text{Na}]^+$ 327.1567 found: 327.1569. Spectroscopic data match those previously reported in the literature.^[22]



16d dimethyl 7-methoxy-4-methyl-3,4-dihydronaphthalene-2,2(1H)-dicarboxylate

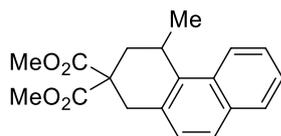
Following the general procedure, the reaction performed with **11d** (72 mg, 0.25 mmol,

1.0 equiv) and 1,4-CHD (0.75 mmol, 71 μ L, 3 equiv) afforded, after purification by FC (SiO₂, pentane/EtOAc:10/1), **I6d** as a colorless crystal (*Conditions A*: 54 mg, 75%, *Conditions B*: 52 mg, 71%). **mp** = 55-60 °C. **¹H NMR** (360 MHz, CDCl₃) δ 7.14 (d, J = 8.6 Hz, 1H), 6.73 (dd, J = 8.6, 2.6 Hz, 1H), 6.65 (d, J = 2.6 Hz, 1H), 3.77 (s, 3H), 3.75 (s, 3H), 3.67 (s, 3H), 3.36 (d, J = 16.1 Hz, 1H), 3.13 (d, J = 16.1 Hz, 1H), 2.94 – 2.75 (m, 1H), 2.57 (ddd, J = 13.4, 5.7, 2.2 Hz, 1H), 1.80 (dd, J = 13.4, 11.4 Hz, 1H), 1.32 (d, J = 6.8 Hz, 3H). **¹³C NMR** (91 MHz, CDCl₃) δ 172.4, 171.3, 157.6, 134.5, 131.9, 127.6, 113.2, 112.7, 55.2, 53.9, 52.8, 52.7, 37.5, 35.6, 29.3, 21.6. **FT-IR** (neat): 3054, 2986, 2957, 2305, 1732, 1504, 1435, 1265, 896, 736, 705. **HRMS-ESI**: m/z calculated for C₁₆H₂₀NaO₅ [M+Na]⁺ 315.1208, found: 315.1205



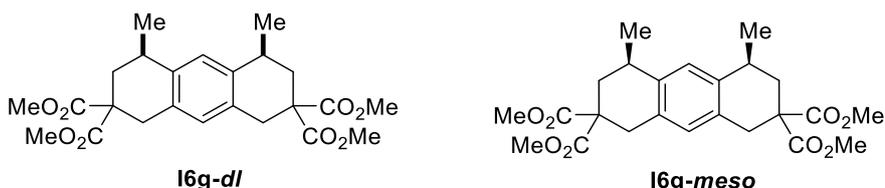
I6e dimethyl 5,7-dimethoxy-4-methyl-3,4-dihydronaphthalene-2,2(1H)-dicarboxylate

Following the general procedure, the reaction performed with **I1e** (80 mg, 0.25 mmol, 1.0 equiv) and 1,4-CHD (0.75 mmol, 71 μ L, 3 equiv) afforded, after purification by FC (SiO₂, pentane/EtOAc:10/1), **I6e** as a colorless oil (*Conditions A*: 60 mg, 75%, *Conditions B*: 54 mg, 67%). **¹H NMR** (360 MHz, CDCl₃) δ 6.30 (d, J = 2.4 Hz, 1H), 6.25 (d, J = 2.4 Hz, 1H), 3.77 (s, 3H), 3.77 (s, 3H), 3.74 (s, 3H), 3.63 (s, 3H), 3.26 (d, J = 15.9 Hz, 1H), 3.25-3.16 (m, 1H), 3.12 (dd, J = 15.9 Hz, J = 2.0 Hz, 1H), 2.64 (ddd, J = 13.8 Hz, J = 7.5 Hz, J = 2.0 Hz, 1H), 1.93 (dd, J = 13.8 Hz, J = 7.1 Hz, 1H), 1.20 (d, J = 6.9 Hz, 3H). **¹³C NMR** (90 MHz, CDCl₃) δ 172.4, 171.2, 158.5, 135.1, 121.0, 104.3, 97.0, 55.1, 55.0, 53.5, 52.5, 52.4, 37.2, 36.0, 26.4, 21.7. **HRMS** (ESI) m/z : Calcd for C₁₇H₂₃O₆ [M+H]⁺ : 323.1489 found: 323.1484. Spectroscopic data match those previously reported in the literature.^[22]



16f dimethyl 4-methyl-3,4-dihydrophenanthrene-2,2(1*H*)-dicarboxylate

Following the general procedure, the reaction performed with **11f** (77.5 mg, 0.25 mmol, 1.0 equiv) and 1,4-CHD (0.75 mmol, 71 μ L, 3 equiv) afforded, after purification by FC (SiO₂, pentane/EtOAc:10/1), **16f** as a colorless oil. (*Conditions A*: 64 mg, 82%, *Conditions B*: 58 mg, 74%). ¹H NMR (360 MHz, CDCl₃) δ 8.00 (d, *J* = 8.6 Hz, 1H), 7.82 (dd, *J* = 8.0 Hz, *J* = 1.6 Hz, 1H), 7.65 (d, *J* = 8.4 Hz, 1H), 7.51 (ddd, *J* = 8.4 Hz, *J* = 6.9 Hz, *J* = 1.6 Hz, 1H), 7.44 (ddd, *J* = 8.0 Hz, *J* = 6.7 Hz, *J* = 1.2 Hz, 1H), 7.25 (d, *J* = 8.4 Hz, 1H), 3.91 (m, 1H), 3.80 (s, 3H), 3.60 (s, 3H), 3.55 (d, *J* = 16.2 Hz, 1H), 3.33 (dd, *J* = 16.2 Hz, *J* = 2.0 Hz, 1H), 2.90 (ddd, *J* = 13.8 Hz, *J* = 7.5 Hz, *J* = 2.0 Hz, 1H), 2.21 (dd, *J* = 13.8 Hz, *J* = 5.6 Hz, 1H), 1.37 (d, *J* = 7.0 Hz, 3H). ¹³C NMR (75 MHz, CDCl₃) δ 172.6, 171.4, 135.0, 133.1, 131.2, 130.4, 128.6, 127.5, 126.6, 125.7, 124.7, 123.7, 53.3, 52.6, 52.5, 37.1, 36.0, 27.9, 23.4. HRMS (ESI) *m/z*: Calcd for C₁₉H₂₀O₄Na [M+Na]⁺ 335.1254 found: 335.1241. Spectroscopic data match those previously reported in the literature.



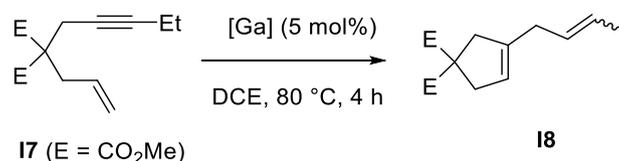
dl : *meso* = 3:1

16g tetramethyl 4,5-dimethyl-4,5,6,8-tetrahydroanthracene-2,2,7,7(1*H*,3*H*)-tetracarboxylate

Following the general procedure, the reaction performed with **11g** (111 mg, 0.25 mmol, 1.0 equiv) and 1,4-CHD (0.75 mmol, 71 μ L, 3 equiv) afforded, after purification by FC (SiO₂, pentane/EtOAc:10/1), **16g** as a brownish oil. (*Conditions A*: 81 mg, 73%, *Conditions B*: 65 mg, 58%). *dl:meso* = 3:1. The ratio was determined by HPLC-Circular Dichroism. ¹H NMR (250 MHz, CDCl₃) δ 7.09 (s, 1H, maj), 7.06 (s, 1H, min), 6.86 (s, 1H, maj), 6.84 (s, 1H, min), 3.75 (s, 6H, maj), 3.75 (s, 6H, min), 3.67 (s, 6H, maj), 3.67

(s, 6H, min), 3.38-3.28 (m, 2H maj & 2H min), 3.16-3.04 (m, 2H maj & 2H min), 2.94-2.79 (m, 2H maj & 2H min), 2.62-2.49 (m, 2H maj & 2H min), 1.87-1.73 (m, 2H maj & 2H min), 1.37-1.30 (m, 6H maj & 6H min),. ¹³C NMR (90 MHz, CDCl₃) δ 172.4 (maj & min), 171.5 (maj & min), 137.9 (maj), 137.6 (min), 131.0 (maj), 130.9 (min), 128.6 (maj), 128.5 (min), 124.5 (maj), 124.3 (min), 53.8 (maj & min), 52.7 (maj & min), 52.6 (maj & min), 37.4 (maj & min), 34.8 (maj & min), 29.8 (maj), 29.7 (min), 21.4 (maj), 21.2 (min). **HRMS** (ESI) m/z: Calcd for C₂₄H₃₁O₈ [M+H]⁺ : 447.2013 found: 447.1996. Spectroscopic data match those previously reported in the literature.^[22]

3.3.4 Procedure for Ga(I)-catalyzed cycloisomerization of enyne **18**



The gallium catalyst (5 mol%) and the silver salt (0 or 7 mol%) were mixed in a screw-cap vial under argon. Dry degassed DCE (0.5 ml) was added and the mixture was stirred at rt for 5 min. Enyne **17** (0.37 mmol, 1 equiv) diluted in DCE (0.5 mL) was added and the mixture was stirred at 80 °C and monitored by GC with an aliquot quenched by technical grade acetone (0.25 mL). The reaction was stirred for 4 h. The reaction mixture was filtered over a pad of celite which was rinsed with Et₂O. Volatiles were removed by rotary evaporation under vacuum. The crude was purified by flash column chromatography on silica gel (eluent: cyclohexane/ethyl acetate). The analytical data of **18** and E/Z ratio evaluation base on previous work in our group.^[77]

3.4 [{IPrGaCl(μ-(OH))₂·2H₂O}][Al(OC(CF₃)₃)₄]₂

To a solution of IPr·GaCl₃ (9 mg, 15 μmol) in DCE (0.8 mL) was added [Ag(DCM)₃][Al(OC(CF₃)₃)₄]₂ (26 mg, 26 μmol) in one portion at room temperature. A precipitate formed instantly. The reaction mixture was stirred for 2 h, and the

suspension was filtered off and poured into a 1,5 mL glass vessel. After 7 days the formation of colorless platelet-shaped crystals was observed. The latter was suitable for single crystal X-ray analysis.

X-ray diffraction data for $[\{\text{IPrGaCl}(\mu\text{-(OH)})_2\}_2\cdot\text{H}_2\text{O}][\text{Al}(\text{OC}(\text{CF}_3)_3)_4]_2$ was collected by using a Kappa X8 APPEX II Bruker diffractometer with graphite-monochromated $\text{MoK}\alpha$ radiation. Crystal was mounted on a CryoLoop (Hampton Research) with Paratone-N (Hampton Research) as cryoprotectant and then flashfrozen in a nitrogen-gas stream at 100 K. For compounds, the temperature of the crystal was maintained at the selected value (100K) by means of a 700 series Cryostream cooling device to within an accuracy of $\pm 1\text{K}$. The data were corrected for Lorentz polarization and absorption effects. The structures were solved by direct methods using SHELXS-97 and refined against F by full-matrix least-squares techniques using SHELXL-2016 with anisotropic displacement parameters for all non-hydrogen atoms. Hydrogen atoms were located on a difference Fourier map and introduced into the calculations as a riding model with isotropic thermal parameters. All calculations were performed by using the Crystal Structure crystallographic software package WINGX. The crystal data collection and refinement parameters are given in Figure 26. CCDC 1567727 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from the Cambridge Crystallographic Data Centre via <http://www.ccdc.cam.ac.uk/Community/Requestastructure>.

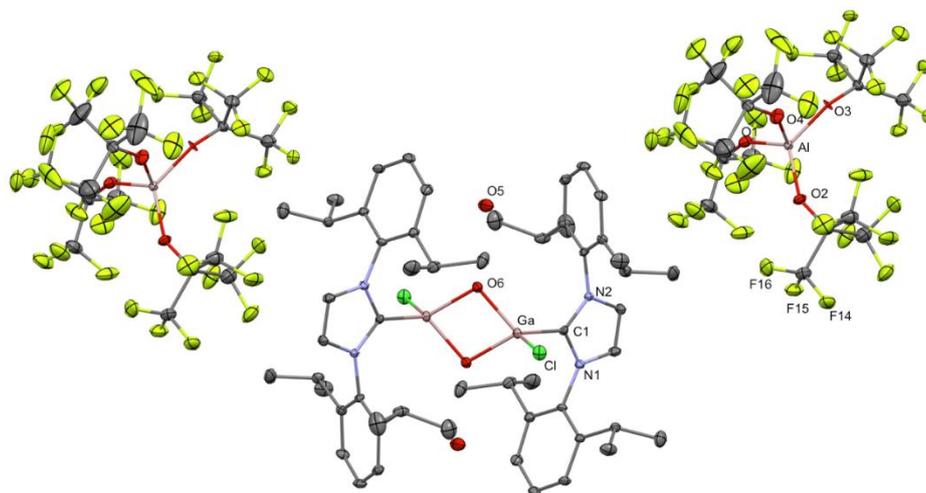


Figure 26. ORTEP drawing of $[\{IPrGaCl(\mu-(OH))_2\}_2 H_2O][Al(Al(OR^F)_4)_2]$. Thermal ellipsoids are shown at the 30% probability level.

CHAPTER II: LOW OXIDATION STATE INDIUM(I) IN CATALYSIS

1. INTRODUCTION

1.1 Properties of Indium Compounds

Indium is a chemical element with the symbol **In**, an atomic number of 49, and an electronic configuration of $[\text{Kr}]4d^{10}5s^25p^1$. Indium is a soft, silvery-white metal with a melting point of 156.6 °C. It was discovered in 1863 by spectroscopic methods and isolated the next year (Figure 27). The abundance of indium on Earth is 0.16 ppm, which is much less than gallium (16.9 ppm). Indium is mostly obtained as a by-product of zinc refining. Most of it is used to make indium tin oxide (ITO). Because ITO is electrically conductive and optically transparent, it is used to make touch screens, flatscreen TVs and solar panels, etc. Indium nitride, phosphide and antimonide are semiconductors used in transistors and microchips. Indium has no known biological role reported so far.^[78]



Figure 27. Indium metal

The most stable isotopes of indium are ^{113}In and ^{115}In , with natural abundances of 0.0429 % and 0.957 % respectively and a spin value of 9/2. As both of their nuclei are quadrupolar, the NMR spectrometers observe broad signals. ^{115}In is usually chosen as nucleus for indium NMR as it is more sensitive and give narrower signals than ^{113}In . The reference compound is $\text{In}(\text{NO}_3)_3$ in D_2O or nitric acid.^[79]

Although the first organoindium compound was prepared as early as 1928,^[80] their extensive use had to wait until the late 1980s. Araki, Butsugan, and co-workers introduced allylindium compounds for the first time in the Barbier reaction in 1988.^[81] Since then, a variety of organoindium complexes have been broadly studied in organic synthesis.

Indium salts, such as indium(III) chloride InCl_3 and indium(III) trifluoromethanesulfonate $\text{In}(\text{OTf})_3$, are another class of useful indium compounds, which play an important role in organic synthesis mostly as Lewis acid catalysts. These catalysts show good chemo- and stereoselectivities, even in aqueous media. In contrast to the lighter Group 13 elements boron, aluminum, and even gallium, low-oxidation state indium salts such as indium(I) iodide InI , indium(I) bromide InBr and indium(I) chloride InCl are stable compounds. Applications of these compounds in organic synthesis have found more attention recently. Finally, metallic indium is a good single-electron-transfer reagent owing to its low first ionization potential (5.79 eV).

Indium has two major advantages compared with other main group metal organometallic reagents or halide salts: 1) it is unaffected by air or water; 2) it exhibits a low heterophilicity. Therefore, indium compounds mediated or catalyzed reactions can normally proceed under mild conditions and with great functional group tolerance.^[82]

Numerous results have been published and reviewed in the synthetic use of indium compounds and the application of indium salts as Lewis acid catalysts. This chapter will firstly pay attention to representative examples of organoindium reagents in organic synthesis and then move to the recent developments of indium(III) and low oxidation state indium(I) (univalent indium) catalysts in synthetic chemistry.

1.2 Applications of Organoindium Reagents in Synthesis

Compared with other Group 13 metals, a unique property of indium in synthetic chemistry is its use as organoindium reagents. Although it is not a catalytic transformation, it is still worth to be mentioned in this dissertation. For about a century, organometallic reagents such as organolithium, organomagnesium, and organozinc compounds have played a significant role in synthetic organic chemistry. However, the strict avoiding of moisture and air for the preparation and handling of these organometallic species is has always been an issue. In addition, the poor compatibility of these organometallic compounds toward important functional groups such as carbonyl and hydroxyl groups also limit their extensive use in organic synthesis. In this regard, organoindium reagents have appeared as attractive organometallic species.^[83]

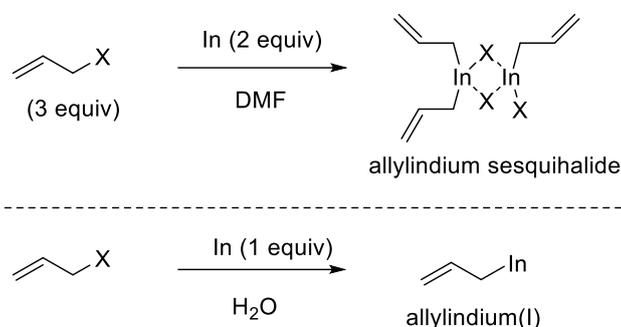
1.2.1 Allylic indium reagents

Allylic indium complexes are the most widely used organoindium compounds in organic synthesis. As mentioned above, since the first introduced allylindium reagent into allylation of carbonyl compounds in 1988 by Araki and co-workers, various works on the diastereo- and enantioselectivity of the reaction involving allylindium and carbonyl compounds/imines have been reported. After a few decades of endeavors on this topic by chemists, allylindium species have proven themselves to be powerful and versatile tools for the construction of useful organic skeletons and synthetic intermediates bearing good compatibility with important functional groups under mild reaction conditions.

a. Method for preparing allylindium compounds

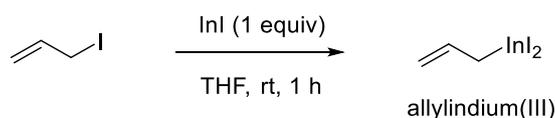
The most widely used method for preparing allylindium compounds is the oxidative addition of metallic indium to allylic substrates.^[83] Scheme 39 shows the generation of allylindium(III) sesquihalide^[81] in an organic solvent and allylindium(I)^[84] in water. Mostly, X represents iodide and bromide, as allyl chloride is unreactive under this

reaction conditions. It is worthy to be noted that in most cases allylindium reagent is prepared in situ by mixing the allyl halide with indium and directly reacted with electrophiles.



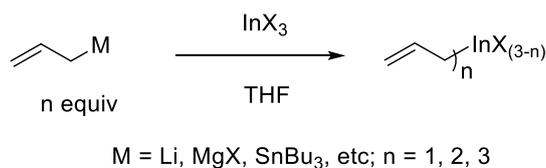
Scheme 39. Synthesis of allylindium from indium(0)

Another useful organoindium reagent is allylindium(III) diiodide, which can be formed by oxidative addition of indium(I) iodide to allyl iodide (Scheme 40).^[85] It was applied in the Reformatsky reaction and the Barbier allylation, resulting in various allylic alcohols and β -hydroxy esters. That shows that the allylindium(III) diiodide exhibits similar reactivity and selectivity than allylindium sesquihalide. This process is mediated in THF, which extends the solvent choice for the application of organoindium reagents. The higher price of InI than In metal limits the utilization of indium(III) diiodide in synthesis.



Scheme 40. Synthesis of allylindium diiodide from indium(I) iodide

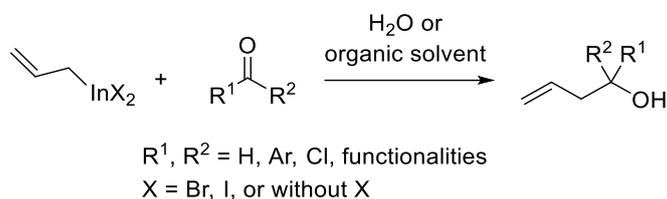
Alternatively, allylindium reagents also can be generated by transmetalation of indium(III) halides with other more reactive organometallic reagents, such as organolithium or organomagnesium (Scheme 41).^[86] The mono-, di, and triallylindium can be generated by adjusting the ratio of organometallic reagent with indium(III) halides.



Scheme 41. Synthesis of allylindium compounds by transmetalation

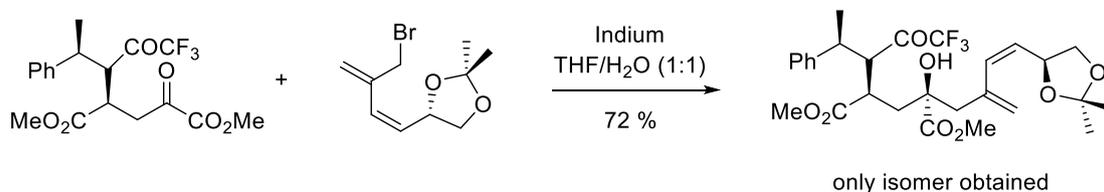
b. Allylindium addition to various compounds

Allylation of carbonyl compounds by allylindium reagents has been well investigated in organic and aqueous media (Scheme 42).



Scheme 42. Allylation of carbonyl compounds

The major advantages of the allylindium reagents, compared with other more reactive organometallic species, is the high compatibility towards various functionalities. For example, selective of 1,2-additions to aldehydes or ketones can be achieved in the presence of alkenes,^[87,88] alkynes,^[89] allenes,^[90] esters,^[91] phosphonates,^[92] diazo compounds.^[93] Allylation with a catalytic amount of indium in combination with manganese and chlorodimethylsilane has also been reported.^[94] Allylindium reagents have been applied in attempted total syntheses of natural products as a key step with excellent diastereoselectivity (Scheme 43).^[95]



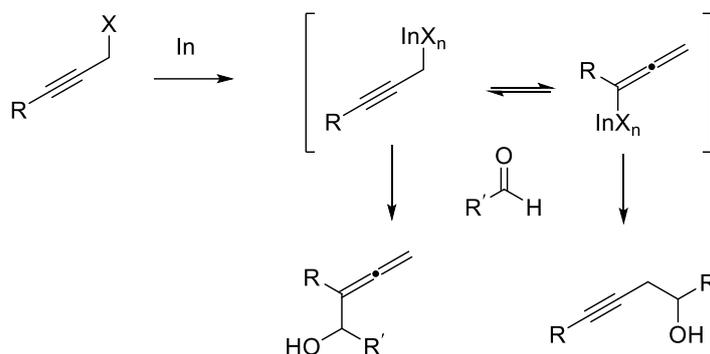
Scheme 43. Key step of attempted syntheses of natural product dysiherbaine

Allylindium compounds have also been reacted with lots of electrophiles, such as imines,^[96] epoxides,^[97] azirines,^[98] propargyl alcohols,^[99] thiocyanates,^[100] vicinal

dihalides,^[101] and quinolinium derivatives,^[102] providing luxuriant methodologies.

1.2.2 Propargylindium and allenylindium reagents

Like the preparation of the allylindium compounds, mixing indium with propargyl halides provides propargylindium species. However, they are in equilibrium with allenylindium compounds. After addition to aldehydes, allenyl or propargyl alcohols can be obtained (Scheme 44).



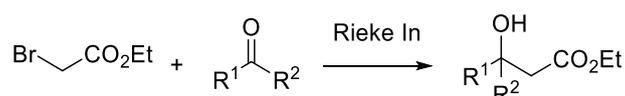
Scheme 44. Equilibrium between propargylindium and allenylindium

The position of the equilibrium is depending on the substitution of the propargyl halide used. Chan's group found that when R = H, prop-2-ynyl alcohols are preferred. When R = methyl or aryl, the corresponding allenylic alcohols are the major products.^[103]

1.2.3 Indium enolates- Reformatsky reaction

Reformatsky reaction is an organic reaction, which condenses aldehydes or ketones with α -halo esters using metallic zinc to form β -hydroxy-esters. The zinc enolates, synthesized from zinc dust with α -halo esters, are less reactive than lithium enolates and Grignard reagents and are tolerant towards esters. Taking the same consideration, the modified Reformatsky reaction using indium enolates also have the compatibility with functional groups such as esters or alcohols. The preparation of indium enolates is generally based on the reaction of indium(0) or indium(I) with α -halo ester in situ.^[104] Another method is the transmetalation of lithium enolates with InCl₃.^[105]

The first development of this Reformatsky-type reaction using indium enolates with α -bromo esters and aldehydes was reported in 1975 by Rieke and co-workers.^[106] In this work, they used Rieke indium, which is obtained by reduction of InCl_3 with potassium in xylene under reflux condition, to give activated indium. Then the active indium inserts into the α -bromo ester to give the indium enolate, which efficiently reacts with an aldehyde or a ketone in good to excellent yields.

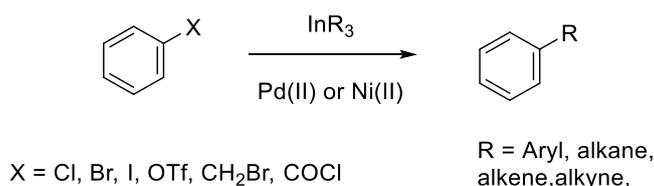


Scheme 45. Reformatsky-type reaction mediated by indium

After these seminal results, indium enolates found applications in various transformations. For more information, one can pay respect to recent reviews and books.^[107–109]

1.2.4 Organoindium reagents combined with transition metal catalysis

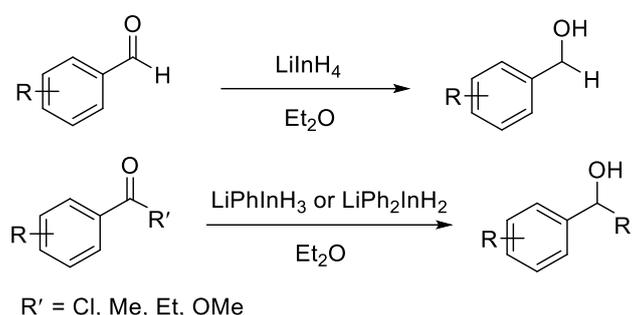
The use of organoindium reagents in combination with transition metal catalysts greatly expands the scope of indium chemistry in organic synthesis. It could be applied into various cross-coupling reactions, such as palladium-catalyzed Suzuki-type reaction,^[110] palladium-catalyzed Sonogashira-type reaction,^[111] and Tsuji–Trost-type reaction.^[112] To take one example in details, in 2001, Sarandeses and co-workers reported the cross-coupling reaction of triorganoindium compounds (R_3In) with aryl halides, vinyl triflates, benzyl bromides, and acid chlorides under palladium catalysis in excellent yields and with high chemoselectivity (Scheme 46).^[113] This reaction shows atom economy, as all the three organic groups attached to indium transfer into the final product.



Scheme 46. Cross-coupling reaction of organoindium reagents with aryl electrophiles

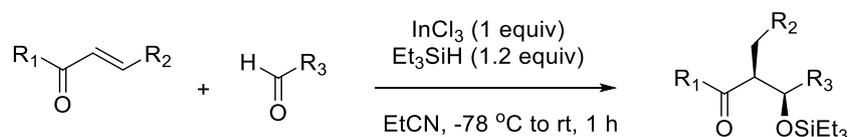
1.2.5 Organoindium hydride

Lithium indium hydride (LiInH_4), prepared in situ by mixing LiH and InCl_3 in ether, can readily reduce aldehydes.^[114] It should be noted that the reducing ability of LiInH_4 is increased by the introduction of phenyl groups. LiPhInH_3 and $\text{LiPh}_2\text{InH}_2$ can readily reduce aldehydes, ketones, acid chlorides and even esters to the corresponding alcohols (Scheme 48).^[115]



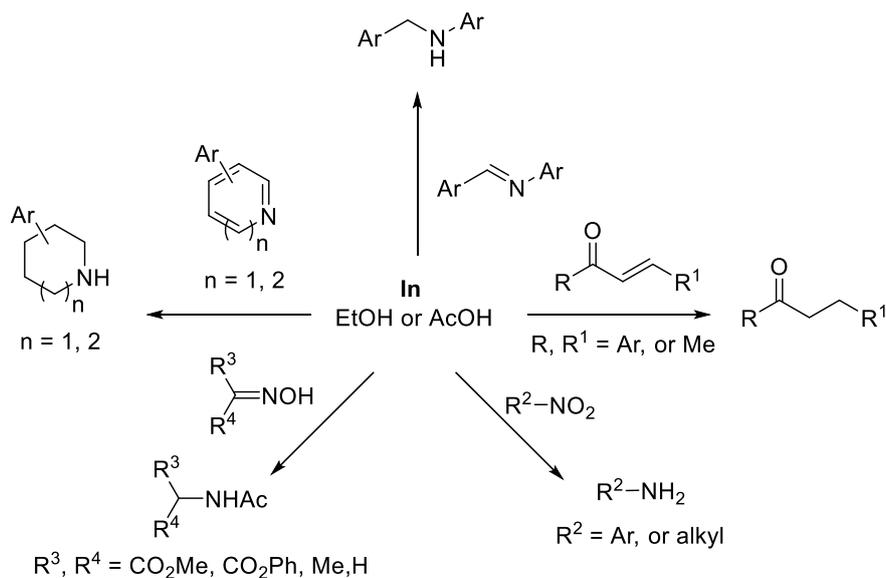
Scheme 47. Lithium indium hydride reducing aldehydes and ketones

In addition, indium hydride Cl_2InH , generated from readily available Et_3SiH or NaBH_4 and InCl_3 , is a promising alternative to Bu_3SnH . For example, Shibata and co-workers reported diastereoselective reductive aldol reaction,^[116] the *syn* selectivity obtained here being higher than that of other reductive aldol reactions, including those promoted by tin hydride (Scheme 48).



Scheme 48. Indium hydride in the reductive aldol reaction

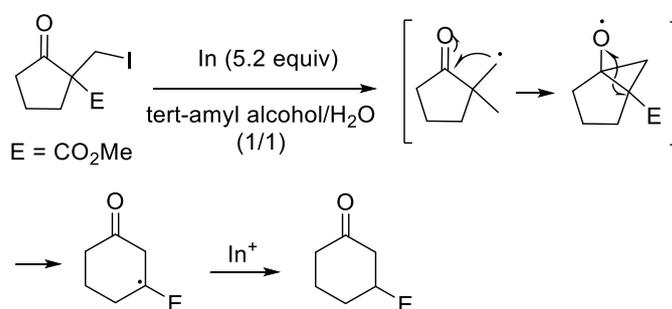
Furthermore, metallic indium can also be a useful reducing agent for organic synthesis, due to the low first ionization potential (5.8 eV) and its stability towards air and water. In 2001, Moody summarized the results of indium metal for the reduction of imines, heterocyclic rings, oximes, nitro compounds, and conjugated alkenes (Scheme 49).^[117]



Scheme 49. Indium metal as a reducing agent

1.2.6 Indium species in radical reactions

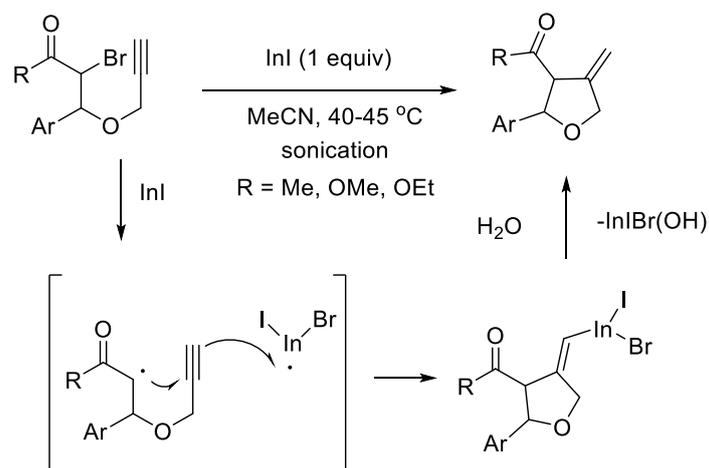
As mentioned above, indium has low first ionization potential, and that gives the possibility to promote single-electron transformation. Togo's group reported a ring-expansion reaction of α -halomethyl cyclic β -keto esters, which is mediated by indium metal, giving the corresponding one-carbon ring-expanded products in good to moderate yields (Scheme 50).^[118] The reaction proceeds through single electron transfer from indium to iodide to form methyl radicals. Then follow a 3-*exo*-trig cyclization and a radical β -cleavage.



Scheme 50. Indium-mediated ring expansion

The radical reaction could also occur using indium(I) as initiator. In 2006, Ranu's group disclosed intramolecular cyclization of δ -bromoalkynes promoted by indium(I) iodide

in a stoichiometric amount, giving substituted 4-methylenetetrahydrofurans in good yield.^[119] In this reaction, the aryl substituent and carbonyl functional group were essentially required for stabilizing the radical after the bromine abstraction. In(I) induces two reduction reactions, and turns into indium(III) (Scheme 51).



Scheme 51. Mechanism proposal for indium(I) initiated cyclization reaction

1.3 Indium(III) Lewis Acids in Homogeneous catalysis

Indium(III) species have been used as powerful Lewis acid catalysts since a long time. Due to the larger ionic radius, indium(III) shows a softer Lewis acid property than gallium(III), hence it can interact with n electrons and π electrons. The low reactivity of indium(III) makes it tolerant with air, water, and various active functionalities. The unique activity of indium(III) in catalysis also comes from the possible high coordinating number of the metal center and fast coordination-decoordination equilibria of the coordinated ligands.^[8] Together with low toxicities, indium(III) Lewis acid catalysts fit well in the current paradigm of ‘green chemistry’. The utilization of indium(III) compounds in catalysis are widely investigated, many reviews have been published since 1999 (Table 4).

Table 4. Reviews on indium(III) in catalysis

Year	Title	Ref
1999	Organic Syntheses Using Indium-Mediated and Catalyzed Reactions in Aqueous Media	[120]
2000	Advances in Indium-Catalyzed Organic Synthesis	[108]
2003	Indium Salt-Promoted Organic Reactions	[121]
2003	Indium in Organic Synthesis	[122]
2004	New Applications of Indium Catalysts in Organic Synthesis	[107]
2006	Discovery of Indium Complexes as Water-Tolerant Lewis Acids	[123]
2007	Recent Advances in Indium-Promoted Organic Reactions	[124]
2007	Advances in Indium Triflate Catalyzed Organic Syntheses	[125]
2010	Multi-Component Reactions Using Indium(III) Salts	[126]
2010	Recent Developments in Indium Metal and Its Salts in Organic Synthesis	[127]
2012	Recent Advances in InCl_3 -Catalyzed One-Pot Organic Synthesis	[128]
2017	Indium(III)-Catalyzed Transformations of Alkynes: Recent Advances in Carbo- and Heterocyclization Reactions	[129]
2018	Indium(III) as π -acid Catalyst for the Electrophilic Activation of Carbon–Carbon Unsaturated Systems	[130]
2020	InCl_3 : A Versatile Catalyst for Synthesizing a Broad Spectrum of Heterocycles	[106]

In this chapter, we cannot describe all of the applications detailed in these reviews. So, we will summarize the applications of indium(III) as Lewis acid catalyst with representative examples based on three activation models: σ -activation, π -activation and *dual-mode* activation (Figure 28).

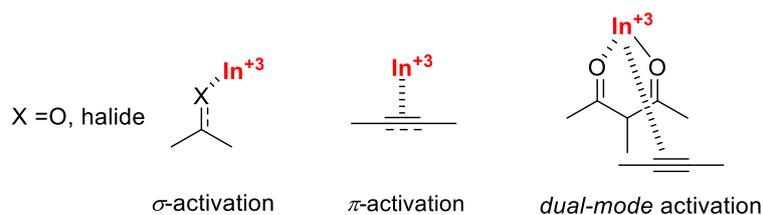


Figure 28. Indium(III) Lewis acid-type activations

1.3.1 The σ -activation of indium(III) Lewis acids

The σ -activation could be achieved by the interaction between indium(III) Lewis acids and n -electrons containing compounds such as alcohols, halides, and carbonyls, therefore promoting a rich diversity of transformations.

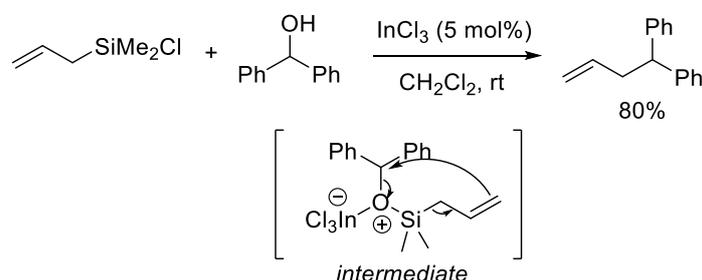
a. Interaction with chlorides

Reported by Baba's group in 2007, the coupling reaction of alkyl chlorides with silyl enolates can be catalyzed by InBr_3 in excellent yield (Scheme 52). They proposed the reaction is triggered by an interaction between In and Cl, followed by the production of a carbocation.^[131]



Scheme 52. InBr_3 -catalyzed reaction of alkyl halide with silyl enolate

b. Interaction with alcohols



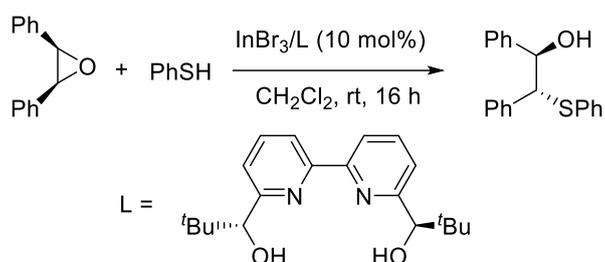
Scheme 53. InCl_3 -catalyzed allylation reaction of benzhydrol

Direct substitution of alcohols in a catalytic manner is a fascinating and ideal procedure for synthetic organic chemistry. Baba et al. reported an allylation reaction of alcohols by using an allylchlorodimethylsilane/ InCl_3 system (Scheme 53).^[132] After that, they expanded the nucleophiles to propargyl- and alkynylsilanes, resulting in the substitution of alcohol products in good yields. The possible mechanism goes through an intermediate with a Si-O bond formation and In-O activation.

c. Interaction with epoxides

Indium(III) salts may also mediate the ring opening of epoxides by interaction with the

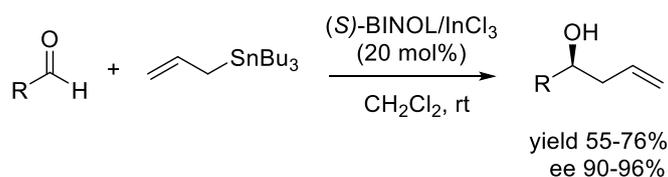
σ -electrons of oxygen. The thiolysis of *meso*-epoxides furnishing 1,2-mercapto alcohols has been performed using InBr_3 and a chiral bipyridine ligand, in good yield and excellent enantioselectivity (Scheme 54).^[133] Notably, there is no inhibition of the Lewis acid by the thiol.



Scheme 54. Indium-bipyridine-catalyzed ring opening of an epoxide

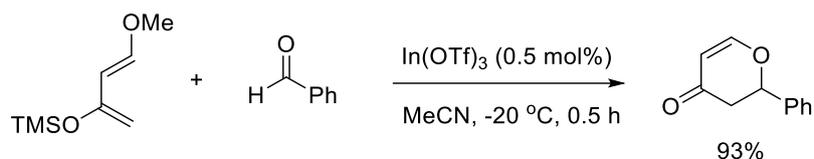
d. Interaction with carbonyls

Indium(III) species can activate carbonyl compounds through the interaction with the n -electrons of oxygen. For example, a catalytic amount (20 mol%) of a chiral complex prepared from (*S*)-BINOL and indium(III) chloride was used in an efficient enantioselective allylation of aldehydes with allyltributylstannane by Loh's group (Scheme 55).^[134] The asymmetric allylation of ketones has also been reported.^[135]



Scheme 55. Enantioselective allylation of aldehydes catalyzed by the chiral (*S*)-BINOL-In(III) complex

Indium triflate also can efficiently catalyze the hetero Diels-Alder reaction between benzaldehyde and Danishefsky's diene. Remarkably, the catalyst loading could be lowered to 0.5 mol% and the reaction was still complete in 30 minutes to afford the product with 93% isolated yield (Scheme 56).^[136]

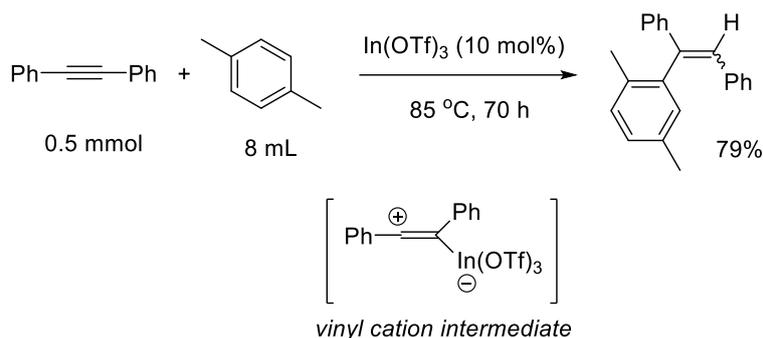


Scheme 56. $\text{In}(\text{OTf})_3$ -catalyzed hetero Diels-Alder reaction

1.3.2 The π -activation of indium(III) Lewis acids

An important application of indium(III) compounds in catalysis is their use as π -Lewis acids, especially towards the activation of alkynes. In comparison, the activation of alkenes is less reported. This section will describe the interaction of indium(III) with alkynes or alkenes by different reaction type.

a. Hydroarylation reactions

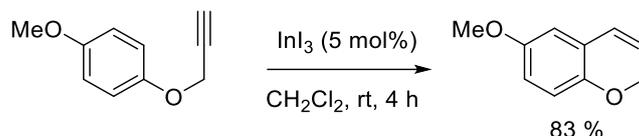


Scheme 57. $\text{In}(\text{OTf})_3$ -catalyzed hydroarylation of alkynes

The intermolecular hydroarylation of alkyne catalyzed by $\text{In}(\text{OTf})_3$ was reported by Shirakawa et al. in 2000 (Scheme 57).^[137] The existence of alkene isomers of the final compounds strongly suggests that the mechanism pathway goes through a vinyl cation intermediate. Subsequently, other heterocyclic arenes, such as pyrroles, furans, thiophenes, and indoles were also applied in this transformation.^[138–140]

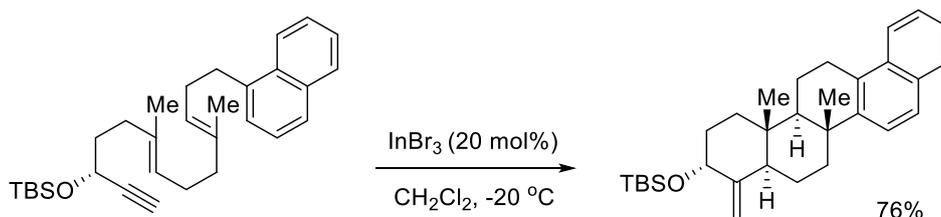
In 2014, Sestelo et al. reported the intramolecular hydroarylation reaction catalyzed by InI_3 (Scheme 58). The reaction proceeds regioselectively to produce only the 6-*endo* product by the anti-markovnikov addition. Furthermore, they expended the reaction scope to terminal and internal alkynes bearing electron-rich and electron-deficient

substituents in the benzene and alkyne moieties.



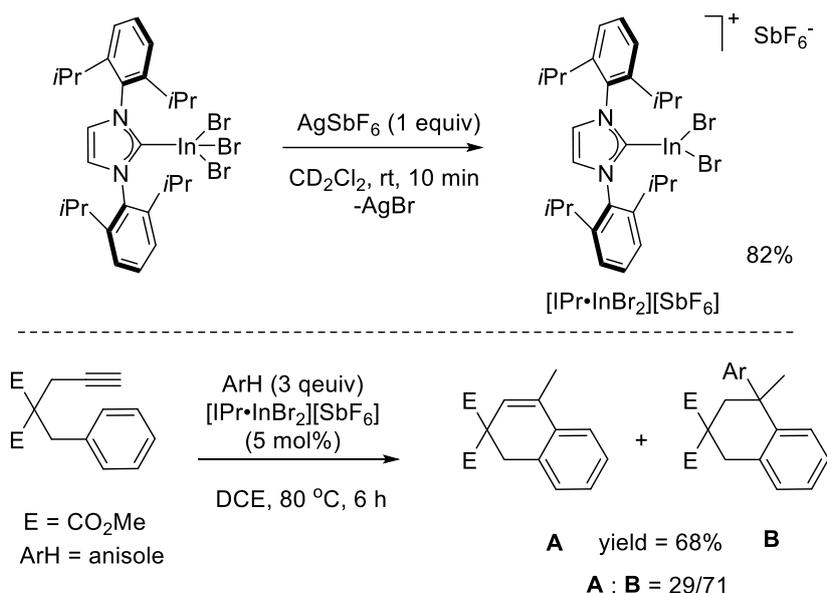
Scheme 58. InI_3 -catalyzed intramolecular hydroarylation of aryl propargyl ether

In 2011, Corey's group found that InBr_3 can be an efficient catalyst for the π -activation of $\text{C}\equiv\text{C}$ bonds to initiate the conversion of chiral propargylic alcohols to polycyclic products in excellent yields and with high stereoselectivity (Scheme 59).^[141] Furthermore, this method was extended into a variety of examples, including propargylic silyl ethers. They also found InI_3 can promote this method as well.



Scheme 59. InBr_3 -catalyzed the synthesis of chiral pentacyclic compound

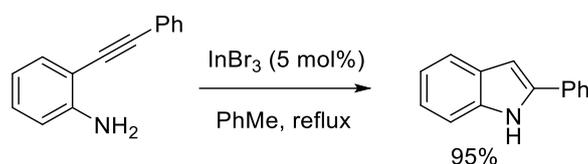
In 2015, our group developed a cationic indium(III) complex $[\text{IPr}\cdot\text{InBr}_2][\text{SbF}_6]$ by mixing stable NHC- InBr_3 adduct with the halide abstractor AgSbF_6 . We used this active catalyst for the dihydroarylation of arenynes (Scheme 60).^[70] This reaction involves the activation of an alkyne to give the intramolecular hydroarylation product **A** and then the activation of the alkene moiety of **A** to give the intermolecular hydroarylation product **B**. It should be noticed that using the $\text{InBr}_3/\text{AgSbF}_6$ catalytic system provided almost the same result.



Scheme 60. $[IPr\cdot InBr_2][SbF_6]$ catalyzed dihydroarylation of arenyne

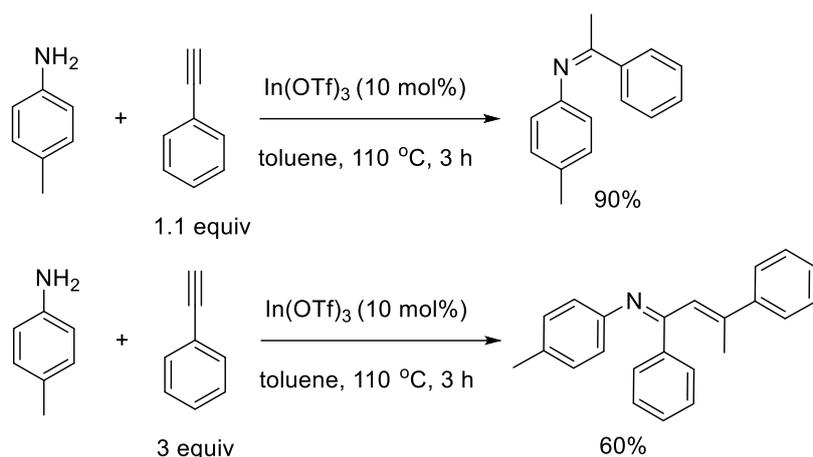
b. Hydroamination reactions

In 2006, Sakai et al. reported the synthesis of indoles through an $InBr_3$ -catalyzed hydroamination reaction of *o*-alkynylanilines (Scheme 61).^[142] This simple catalytic system is remarkably tolerant with a variety of functional groups.



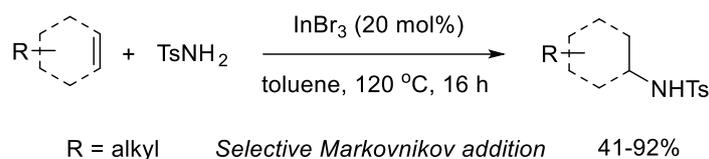
Scheme 61. $InBr_3$ catalyzed intramolecular hydroamination of 2-alkynylaniline

The intermolecular hydroamination between terminal alkynes and anilines was reported by Prajapati et al. in 2011.^[143] In this transformation, the formation of the desired imine by Markovnikov addition was obtained in excellent yield when *p*-toluidine was refluxed in toluene with 1.1 equivalents of phenylacetylene for 3 h in the presence of 10 mol% $In(OTf)_3$. Interestingly, when they carried out a reaction between *p*-toluidine and 3 equivalents of phenylacetylene under same conditions, they obtained a conjugated imine. The formation of this product can be rationalized by an initial hydroamination of the alkyne followed by a second hydroalkylation step.



Scheme 62. *In(OTf)₃-catalyzed hydroamination to imine and conjugated imine*

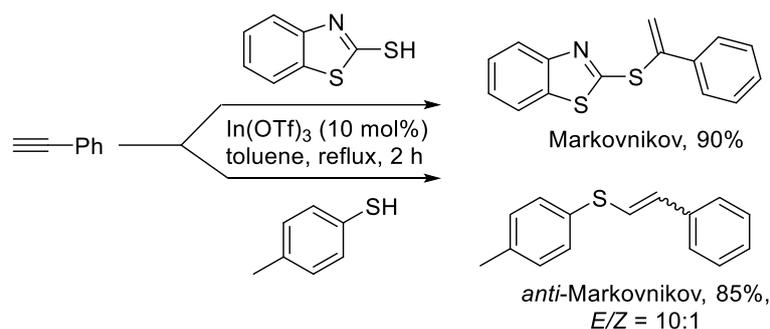
The hydroamination of unactivated alkenes with *p*-toluenesulfonamide was reported by Loh's group in 2007 (Scheme 63).^[144] In this reaction, InBr_3 had been found to be a good catalyst, affording a selective Markovnikov addition products in good yields.



Scheme 63. *InBr₃-catalyzed hydroamination of olefins with TsNH₂*

c. Hydrothiolation reactions

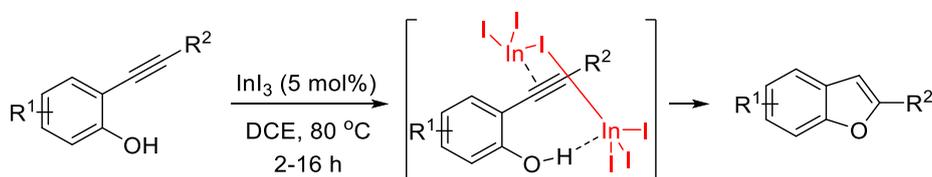
In 2012, Prajapati et al. reported a result about indium(III) triflate as catalyst for the selective Markovnikov and anti-Markovnikov hydrothiolation of terminal alkynes (Scheme 64).^[145] The nature of the substrate is found to be the key factor in determining the selectivity of the transformation. Electron-rich heteroaromatic thiols have been found to undergo selective Markovnikov hydrothiolation, whereas aromatic and aliphatic thiols show anti-Markovnikov selectivity under identical reaction conditions.



Scheme 64. $\text{In}(\text{OTf})_3$ -catalyzed selective hydrothiolation of terminal alkynes

d. Hydroalkoxylation reactions

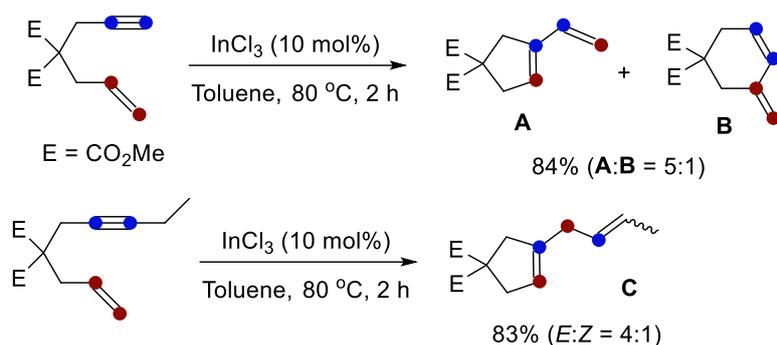
Recently, Sestelo's group reported InI_3 -catalyzed intramolecular hydroalkoxylation reaction using *ortho*-alkynylphenols as substrates (Scheme 65).^[146] The cycloisomerization takes place with *o*-alkynylphenols and internal alkynes to provide a variety of 2-substituted benzo[*b*]furans. DFT calculations suggested that the In_2I_6 dimer was the catalytically active species through double coordination with the alkyne and phenolic hydroxyl group.



Scheme 65. InI_3 -catalyzed hydroalkoxylation of *ortho*-alkynylphenols

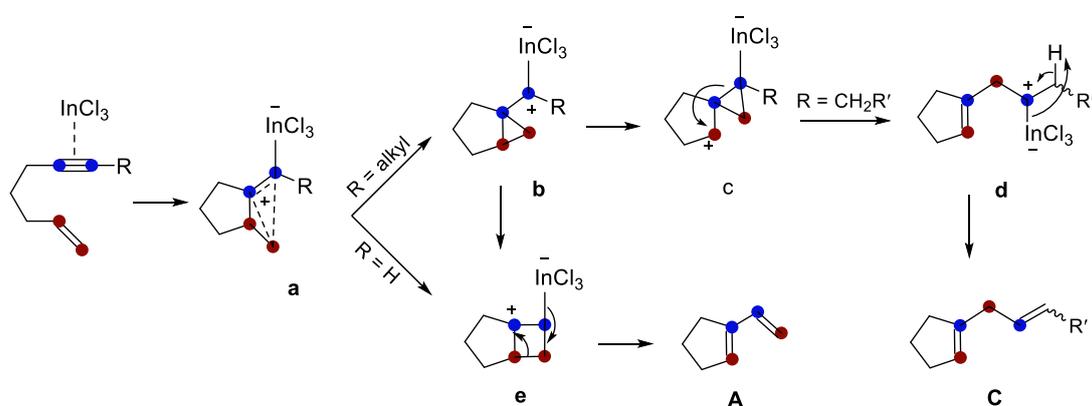
e. Cycloisomerization of enynes

The catalytic cycloisomerization of enynes has attracted chemists' interest for a long time, because of the diverse products that can be obtained based on the different substitution of the substrates and the catalysts used. In 2006, Chatani et al. reported InCl_3 catalyzed skeletal reorganization of enynes.^[147] The reaction of 1,6-enynes with terminal alkyne results in a 1-vinylcyclopentene with a six-membered cycloisomerization product. The reaction of 1,6-enynes with an alkyl group at the acetylenic carbon results in a 1-allyl-1-cyclopentene (Scheme 66).



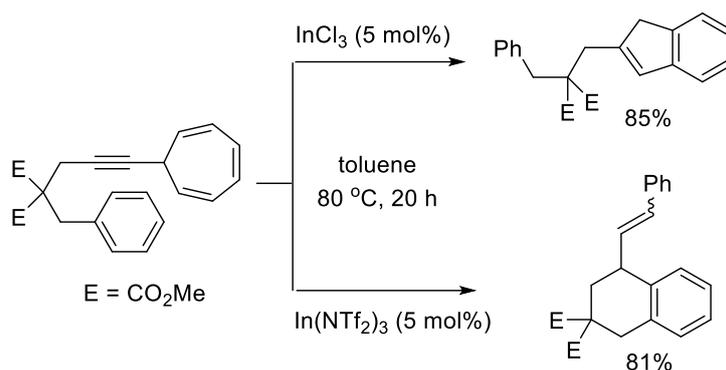
Scheme 66. Skeletal reorganization of enynes catalyzed by InCl_3

Mechanism study shows that the anti-Markovnikov addition can give product **B**. The cycloisomerization pathway is shown in Scheme 67 with simplified structures. The electrophilic interaction of the alkyne by InCl_3 gives intermediate **a**. If $\text{R} = \text{alkyl}$, **b** is generated since the cation is stabilized by the R group. Following is the ring-opening process to give final product **C** through **c** and **d**. If $\text{R} = \text{H}$, cyclobutene complex **e** is formed, and then follows its electrocyclic ring-opening process to give product **A**.



Scheme 67. Proposed mechanism

Recently, our group also performed a comparative study using different Lewis acid catalysts in the isomerization of 7-alkynylcycloheptatrienes.^[148] In this study, the selective formation of different products is achieved depending on the Lewis acidity of the catalyst. InCl_3 , as a softer Lewis acid, gives an indene product and $\text{In}(\text{NTf}_2)_3$, as a harder Lewis acid, produces an alkene product.

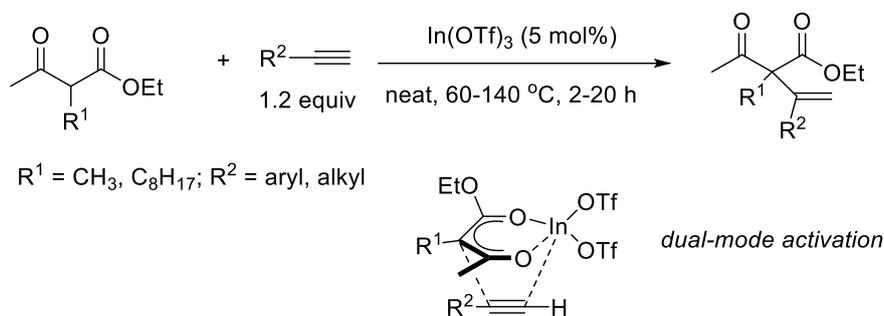


Scheme 68. *In(III)*-catalyzed isomerization of a 7-alkynylcycloheptatriene

1.3.3 The *dual-mode* activation of indium(III) Lewis acids

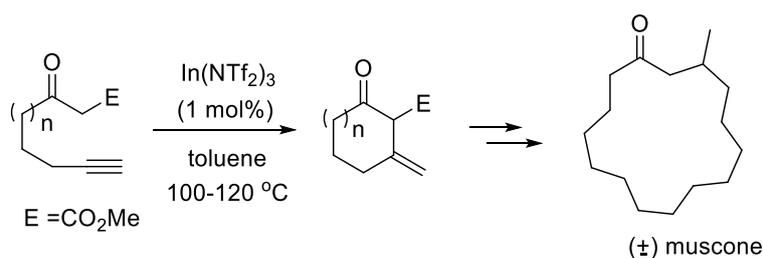
The dual-mode activation, combining σ -activation and π -activation in a single transformation, is one of the most interesting and useful applications of indium(III) in catalysis. The multiple coordinating mode may come from the hybridization of the vacant $5p$ orbital and the resulting p - d hybrids could coordinate in a bidentate mode with the two orthogonal π -bonds.^[141]

In 2007, Nakamura et al. reported $\text{In}(\text{OTf})_3$ -catalyzed Conia-ene addition reaction of 1,3-dicarbonyl compounds to alkynes.^[149] In this reaction, indium(III) played as both σ -Lewis acid towards carbonyl groups and π -Lewis acid towards alkynyl groups (Scheme 69). The resulting 2-alkenyl 1,3-dicarbonyl compounds are useful synthetic intermediates that can be used for further synthetic transformations and for the synthesis of pharmaceutically important compounds.



Scheme 69. *In(OTf)*₃-catalyzed conia-ene reaction by dual-mode activation

This methodology was extended to construct five- to fifteen-membered rings by Nakamura et al. in 2008.^[150] $\text{In}(\text{NTf}_2)_3$ proved to be the best catalyst with 1 mol%, as low as 0.01 mol % in the best case. The high reactivity of indium salts is due to the double activation of the β -ketoester substrate containing an acetylene function. This method can be applied in the synthesis of racemic muscone after decarboxylation and alkene-reduction.

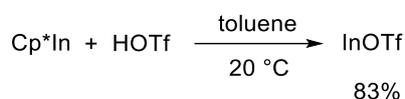


Scheme 70. Large ring construction catalyzed by $\text{In}(\text{NTf}_2)_3$

1.4 Univalent Indium(I) Compounds and their Use in Catalysis

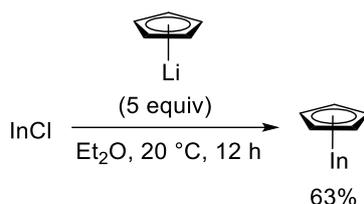
1.4.1 Univalent indium(I) compounds

The low-oxidation univalent indium(I) state is much more common than gallium(I). $\text{In}(\text{I})\text{Cl}$, $\text{In}(\text{I})\text{Br}$, and $\text{In}(\text{I})\text{I}$ are commercially available. We already showed the application of $\text{In}(\text{I})\text{I}$ in promoting allylation and radical reaction in the previous section. One of the major disadvantages of indium(I) halides is their low solubility in organic solvents. On the other hand, indium(I) triflate InOTf , is considered to be more soluble in variety organic solvents and thus allows for the reactions to be conducted under homogenous conditions. InOTf was first synthesized by mixing InCp^* (vide infra) with triflic acid in toluene by Macdonald group in 2004 (Scheme 71).^[151] It proved more stable than indium(I) halides at ambient temperature, but still remains highly sensitive to air and moisture.



Scheme 71. Synthesis of InOTf

As an indium(I) precursor, InCp* was first described by Fisher's group as early as 1957,^[152] but a more simple synthetic route was reported in 1981.^[153] In this route, InCp* is obtained through stirring of InCl and 5 equivalents of LiCp* in diethyl ether at room temperature (Scheme 72). The yield decreases when starting from InBr instead of InCl, and is almost null when starting from InI.



*Scheme 72. Synthesis of InCp**

In 2005, Macdonald group took InOTf as precursor to react with [18]crown-6 in toluene, forming a new stable indium(I) compound (Figure 29).^[154] They proposed this complex could be a useful precursor for the formation of intermetallic materials containing Group 13 elements.

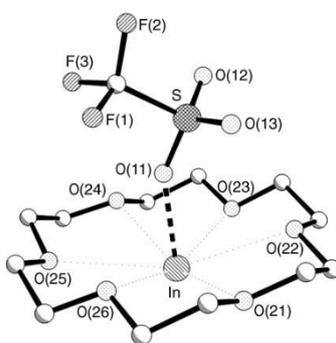
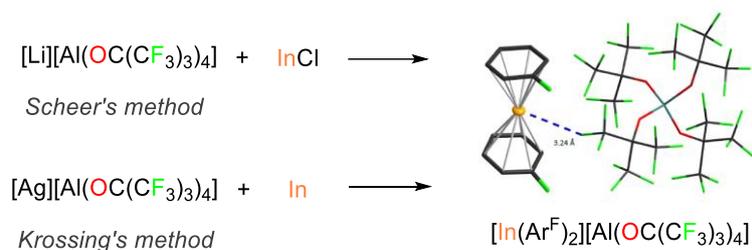


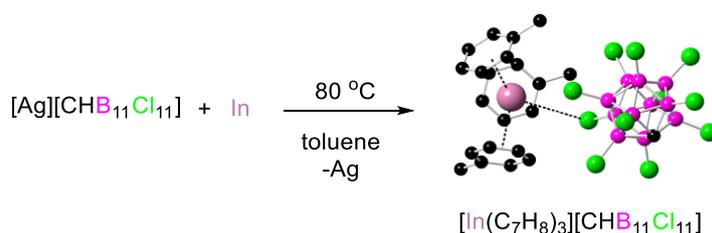
Figure 29. molecular structure of InOTf (hydrogen atoms are omitted for clarity, figure comes from [154]).

Moreover, in 2010, [In][Al(OC(CF₃)₃)₄] was synthesized by the metathesis reaction of [Li][Al(OC(CF₃)₃)₄] with a twofold excess of InCl in dichloromethane in 87% yield by Scheer and co-workers.^[155] The same indium salt could be obtained by an alternative approach reported by the Krossing group.^[60] They directly oxidized elemental indium with [Ag][Al(OC(CF₃)₃)₄] (Scheme 73).



Scheme 73. Synthetic methods to obtain $\text{In}[\text{Al}(\text{OC}(\text{CF}_3)_3)_4]$

Indium(I) was not only stabilized by an aluminate WCA, but also by carborane WCA. In 2015, the Wehmschulte's group reported a synthesis similar to the strategy of the Krossing group through the oxidation of indium(0) to indium(I) by Ag^+ salt. In this case, the carborane WCA was employed (Scheme 74).^[156] Coordination attempts with electron-rich phosphine and carbene ligands led to the reduction of the In cation to indium metal and concomitant oxidation of the ligand to phosphonium and imidazolium ions.



Scheme 74. Synthesis of $[\text{In}(\text{C}_7\text{H}_8)_3][\text{CHB}_{11}\text{Cl}_{11}]$

As shown above, indium(I) compounds are broadly studied by chemists. That makes the use of them in catalysis very attractive.

1.4.2 Ambiphilicity of indium(I) in catalysis

The electron configuration of indium(I) species is shown below (Figure 30). Because of the presence of both two vacant p orbitals and one electron lone pair in a sp orbital, the potential ambiphilicity may offer unique reactivity and unusual selectivity in synthesis compared to indium(III) and may have significant implications in catalysis, especially for dual catalytic processes.

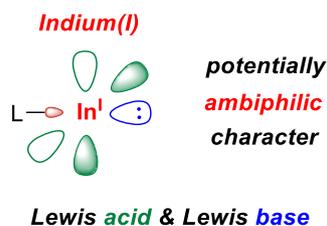
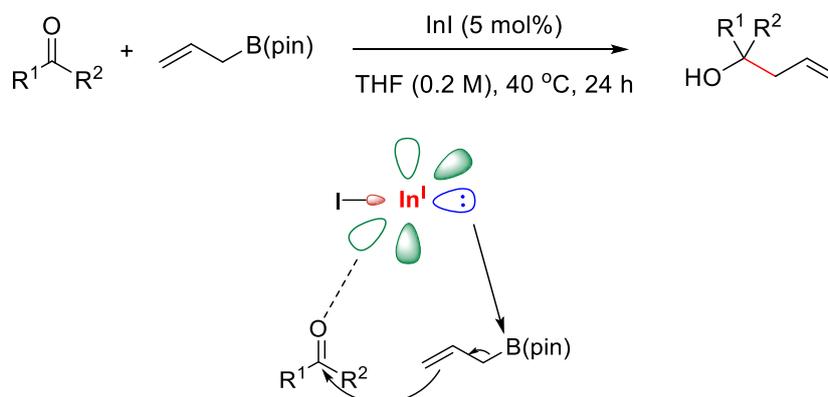


Figure 30. Ambiphilic potential of indium(I)

For the moment, to the best of our knowledge, only one group reported impressive work base on this topic, that is Shu Kobayashi's group of the University of Tokyo, including the contribution of his student Uwe Schneider who is now working in the University of Edinburgh. This sub-section will mostly be based on the recent review of their group published in 2012 to give a brief introduction about the ambiphilic behavior of indium(I) species in catalysis, even in enantioselective reactions.^[157]

Their first catalytic synthetic method involving the use of a catalytic amount of indium(I) was published in 2007 (Scheme 75).^[158] In this method, In(I) as Lewis base catalyst activates a Lewis acidic allylboronate through the formation of an In-B bond and the bimetallic allylboron reagent so generated an enhanced nucleophilicity towards ketones. On the other hand, the free *p* orbitals give the possibility of Lewis acid activation of the ketone.



Scheme 75. Allylboration of ketones activated by InI

In the mechanism investigation, they tested indium(0) and indium(III) derivatives as

catalysts but they proved to be ineffective. It means that the Lewis acid activation of the carbonyl part is not enough. Interestingly, the combined use of these two indiums in a molar ratio of 2:1 gave the product in quantitative yield, suggesting the redox synproportionation in situ to give In(I). The σ -activation of carbonyls by indium(I) is conceivable, but the catalytic activation of a Group 13 element (boron) with another member of Group 13 (indium) in its low oxidation state had never been reported. A recent report actually give credit to this hypothesis, revealing that indium(I) as a σ donor can form donor-acceptor complexes with electron acceptors such as boron derivatives.^[159] So, Lewis base activation is relevant.

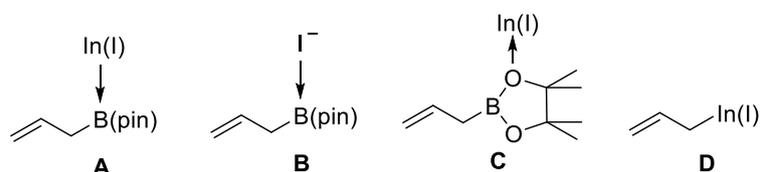


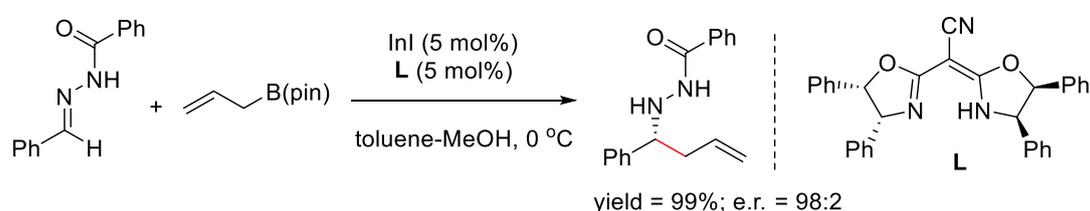
Figure 31. Possible intermediates in the indium(I) iodide mediated allylation

They hypothesized the reaction pathway involves the formation of a bimetallic allylborate **A** with enhanced nucleophilicity (Figure 31). Alternatively, the iodide-induced formation of an allylborate of type **B** might be imagined. In this context, they took tetrabutylammonium difluorotriphenylsilicate and tetrabutylammonium fluoride as fluoride anion sources in allylation. However, these metal-free Lewis base reagents proved to be only moderately effective, indicating that simple Lewis base activation is not enough. On the other hand, simple activation as in **C** is also not efficient. As mentioned above, stronger indium(III) species do not catalyze the reaction efficiently. Finally, another mechanism may involve transmetalation to generate the allylindium(I) **D**. They synthesized an allylindium reagent and use it in this reaction, but only moderate yields were obtained.

After this, they expended the method of allylation and crotylation to hydrazines.^[160] This transformation displays both a broad substrate scope and high functional group

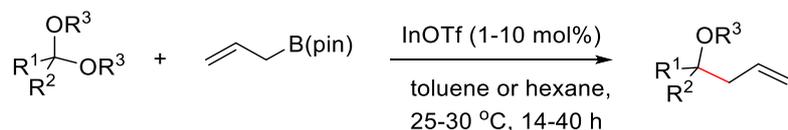
tolerance. Interestingly, they found the present toluene-methanol system to be significantly more efficient for hydrazine allylation than for ketones.

The first asymmetric low-oxidation state indium catalysis was then reported by the same group.^[161] They screened chiral ligands and found chiral bis(oxazoline) to give the best enantioselectivity (Scheme 76). Various aromatic or heteroaromatic substrates bearing reactive functionalities, such as hydroxy, methoxy, tertiary amino, and nitro groups, were alkylated in high yields with excellent enantioselectivity, mostly *er* > 90:10.



Scheme 76. Asymmetric allylation of a hydrazine using a chiral indium(I) catalyst

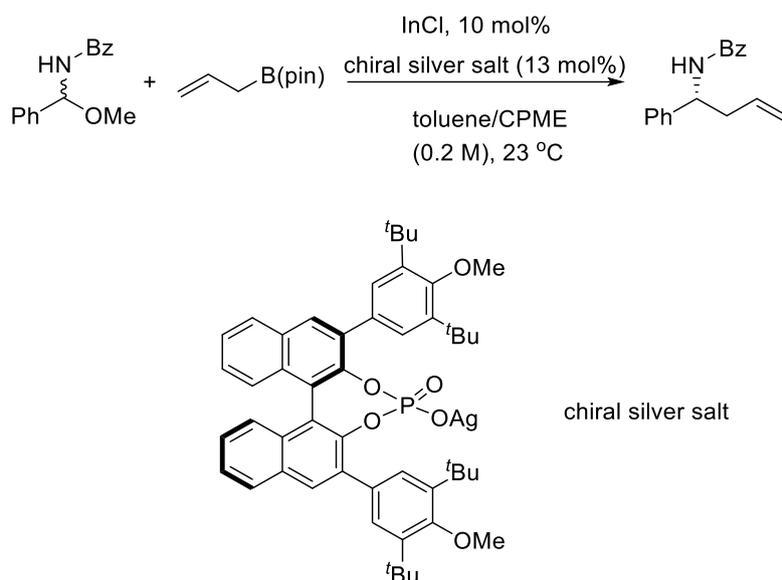
As acetals, amins, ethers, and carbohydrates are abundant in nature and play a key role in organic synthesis, allylation of these C(sp³) electrophiles providing the corresponding unsaturated products was also reported by Kobayashi's group.^[162] They found that the highly soluble indium(I) triflate promoted the reaction of acetals with allylboronates smoothly in excellent yields (Scheme 77). Afterward, propargylation was achieved with the same strategy and with excellent chemoselectivity compared to the corresponding allenylation.



Scheme 77. Acetal allylation initialized by InOTf

Based on this work, they imagined the possibility of asymmetric allylation of C(sp³) bonds.^[163] This time racemic *N,O*-aminals were chosen as substrates. After

optimization, they combined indium(I) chloride and chiral silver BINOL-phosphate in a catalytic system (Scheme 78). Under optimized conditions, the reactions between substituted aromatic, heteroaromatic, and aliphatic aminals proceeded smoothly to provide the desired products with excellent asymmetric induction, mostly *er* > 90:10.



Scheme 78. Asymmetric *N,O*-aminal allylation

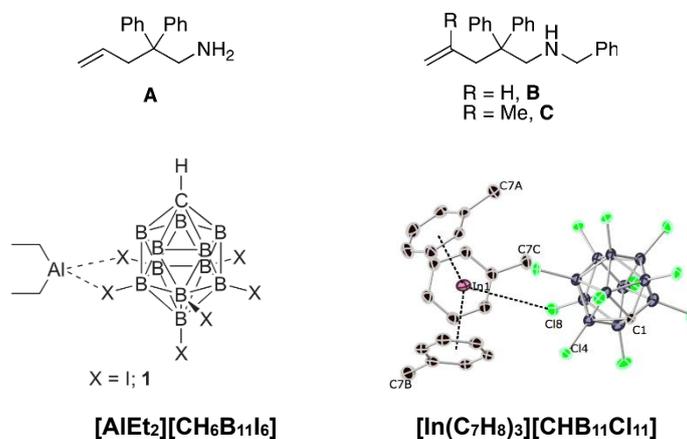
In conclusion, Kobayashi's group investigated a series of C-C bond formation reactions, some in enantioselective version, between boron allyl reagents and various electrophiles catalyzed by the univalent indium(I) species.

1.4.3 Reactivity of indium(I) carba-*closo*-undecachlorododecaborate

As mentioned in subsection 1.4.1, Wehmschulte's group reported the synthesis of $[\text{In}(\text{C}_7\text{H}_8)_3][\text{CHB}_{11}\text{Cl}_{11}]$. The activity of this indium(I) complex as catalyst for the intramolecular hydroamination of primary and secondary amines with terminal alkenes was briefly examined.^[156] With 10 mol% of catalyst, all the aminoalkenes **A**, **B**, **C**, converted into corresponding pyrrolidine derivatives in excellent yields. This result was compared with the outcome of $[\text{AlEt}_2][\text{CH}_6\text{B}_{11}\text{I}_6]$ as the catalyst, which contains a similar carborane WCA (Table 5). For primary amine compound **A**, indium(I) shows better reactivity with less reaction time and higher conversion. However,

$[\text{AlEt}_2][\text{CH}_6\text{B}_{11}\text{I}_6]$ promoted hydroamination, refer to secondary amine compound **B** and **C**, performed significantly faster than indium(I).

Table 5. Hydroamination catalyzed by $[\text{AlEt}_2][\text{CH}_6\text{B}_{11}\text{I}_6]$ and $[\text{In}(\text{C}_7\text{H}_8)_3][\text{CHB}_{11}\text{Cl}_{11}]$

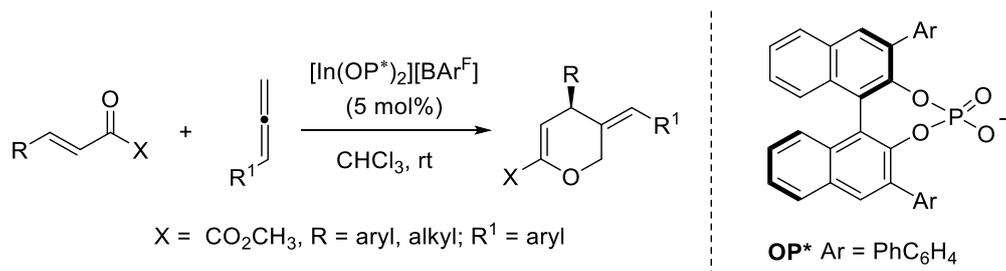


compound	R	Catalysts (10 mol%)	Time (h)	Conversion (%)
A		$[\text{AlEt}_2][\text{CH}_6\text{B}_{11}\text{I}_6]$	28	88
		$[\text{In}(\text{C}_7\text{H}_8)_3][\text{CHB}_{11}\text{Cl}_{11}]$	25	95
B	H	$[\text{AlEt}_2][\text{CH}_6\text{B}_{11}\text{I}_6]$	0.5	99
		$[\text{In}(\text{C}_7\text{H}_8)_3][\text{CHB}_{11}\text{Cl}_{11}]$	11	98
C	CH_3	$[\text{AlEt}_2][\text{CH}_6\text{B}_{11}\text{I}_6]$	11	64
		$[\text{In}(\text{C}_7\text{H}_8)_3][\text{CHB}_{11}\text{Cl}_{11}]$	94	97

It should be noticed that this seminal work on indium(I) catalyzed hydroamination reaction attracted us to think about the activity of $[\text{In}][\text{Al}(\text{OC}(\text{CF}_3)_3)_4]$. What is the limit of this indium(I) catalyst and the functional group tolerance?

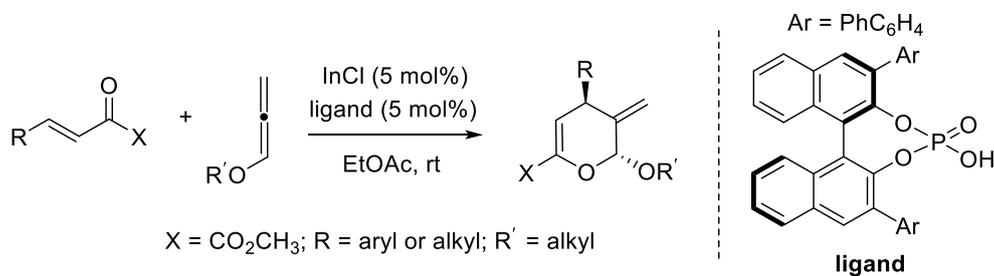
1.4.4 Enantioselective indium(I) catalyzed [4+2] annulation

In 2018, Luo's group reported another asymmetric In(I) catalysis.^[164] In the previous work of their group, they developed a chiral indium(III)-phosphoric acid catalysis for enantioselective [4+2] annulation between β,γ -unsaturated α -keto esters with unactivated terminal allenes (Scheme 79).^[165]



Scheme 79. Asymmetric In(III) catalyzed [4+2] annulation

When they explored the reaction with more electron-rich alkoxyallenes, the cationic indium(III) catalyst led to a rather poor yield with low enantioselectivity due to the instability of alkoxyallenes towards the strong Lewis acid behavior of indium(III). In contrast, In(I)-chiral phosphoric acid complex promoted the reaction in good yield, with reversed regioselectivity and high stereoselectivity (Scheme 80).^[164] According to softer Lewis acidity tendency from Ga(III) to Ga(I) concluded in this thesis, it is reasonable to believe that In(I) also displays the same behavior and is less aggressive towards sensitive substrates.



Scheme 80. Asymmetric In(I)-catalyzed [4+2] annulation

They proposed a mechanism in which In(I)Cl reacts with the chiral phosphoric acid first, then the α -keto ester binds with this complex, as shown in Figure 32, transition state **TS-I**. Besides, H-bonding between the acid and the alkoxyallene oxygen is invoked to selectively direct the attack of alkoxyallene onto the activated α -keto ester. The stability of oxonium ions is the key factor contributing to an internal, instead of terminal, addition via **TS-II**, as shown in Figure 32.

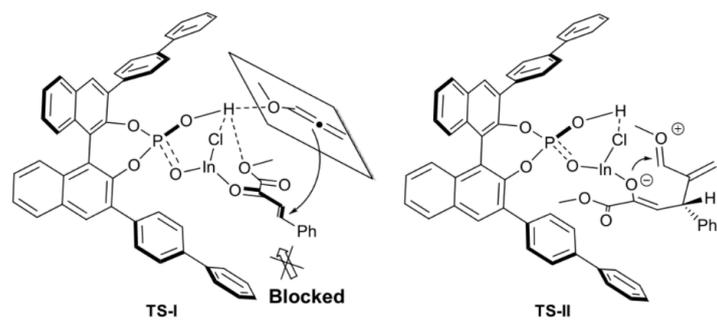


Figure 32. Proposed transition states (**TS**) (Figure comes from ref [164])

1.5 Conclusion

Over the past few decades, the applications of indium complexes in organic synthesis have mainly focused on two aspects. 1) *Organoindium reagents*, which include allylic-, propargyl-, and allenylindium reagents, and even indium hydrides. They are not only employed in allylation, propargylation or allenylation, but also in cross-coupling reactions combined with transition metals. Their compatibility with air and water gives them extra opportunities towards substrates contain useful and sensitive functional groups compared with classic organolithium, organomagnesium, and organozinc compounds. In addition, it allows an easy handling without the need of inert atmosphere. 2) *Lewis acid catalysts*, which mostly involve In(III) complex of type InX_3 , $\text{X} = \text{Cl}, \text{Br}, \text{I}, \text{OTf}$. The In(III) Lewis acid catalysts have the same advantage of tolerance toward moisture and air, perform both σ -, π -, and *due-mode* Lewis acid activation, even in enantioselective version.

Combining the continued interests for hydroarylation catalyzed by gallium(I) in our group with the softer Lewis acid property of indium(I), hydroarylation and hydroamination reactions using “free” unprotected nitrogen on substrates was envisioned (Figure 33).

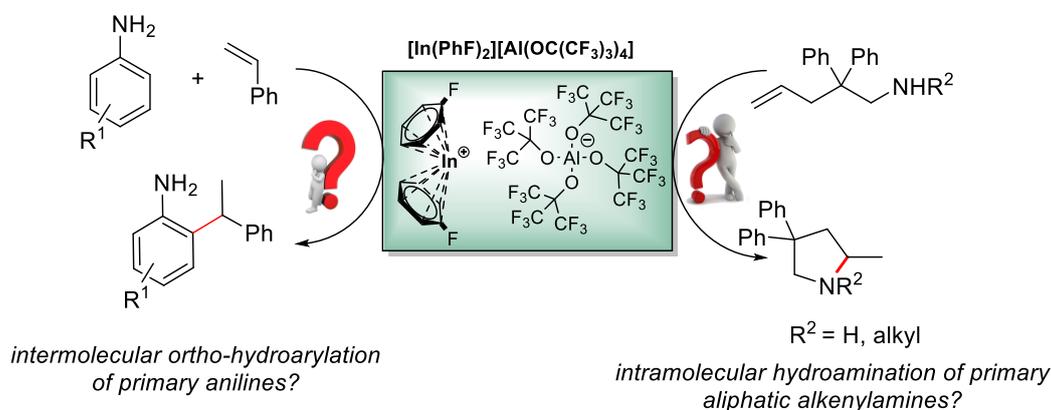


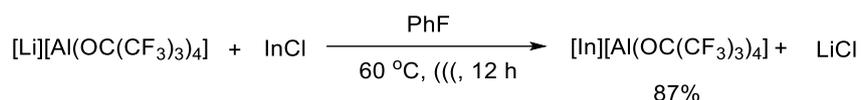
Figure 33. Use of In(I) in hydroarylation (left) and hydroamination (right)

2. RESULTS AND DISCUSSION

2.1 Synthesis of [In][Al(OC(CF₃)₃)₄]

Note: the two PhF ligands on the indium(I) complex are omitted for conciseness

[In][Al(OC(CF₃)₃)₄] was synthesized easily by the metathesis reaction of [Li][Al(OC(CF₃)₃)₄] with a twofold excess of InCl in fluorobenzene under sonication. These conditions delivered [In][Al(OC(CF₃)₃)₄] in 87% yield after 12 h (Scheme 81). This complex is a creamy white powder, however, we also found that some batches give a slight yellow powder without losing the activity. [In][Al(OC(CF₃)₃)₄] can be kept in a Schlenk tube in the glovebox for years without decomposition.



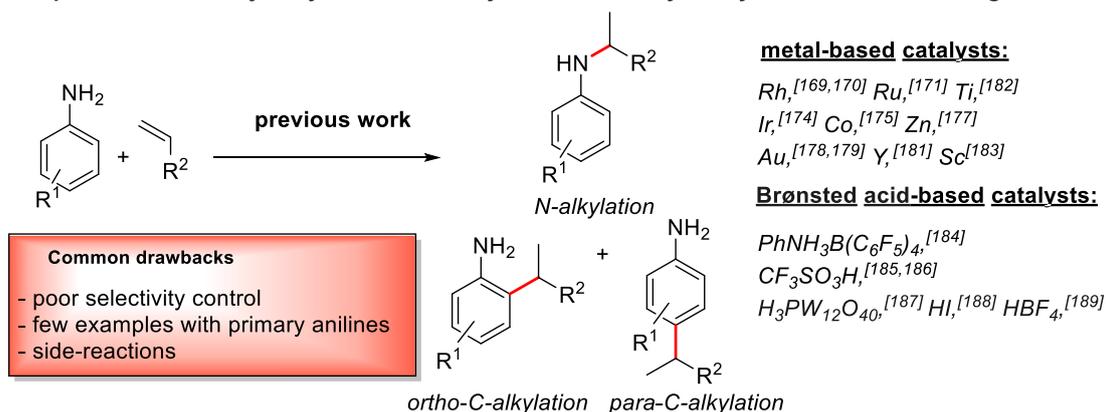
Scheme 81. Synthesis of the In(I) catalyst

2.2 In(I)-Catalyzed *ortho*-C-Alkylation Reaction

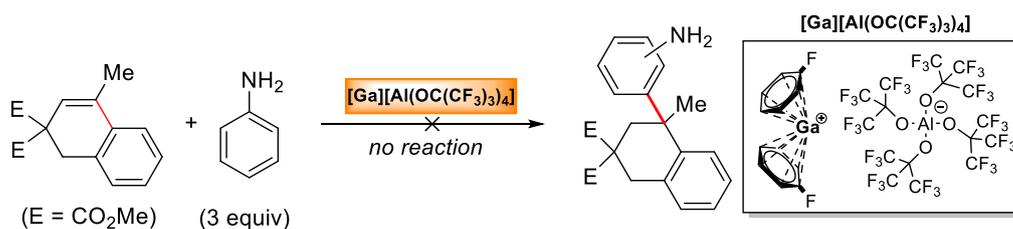
Alkyl-substituted anilines play a pivotal role in crop protection and pharmaceutical industries.^[166,167] In recent decades, major efforts have been devoted to find new, efficient and selective protocols for their synthesis. Among the most atom- and step-economical methods, the hydroarylation and hydroamination of alkenes using anilines occupy a prominent place.^[168] A wide variety of transition metal-based,^[169–176] Lewis,^[177–183] Brønsted acids,^[184–189] and organocatalysts^[190,191] have been developed for this purpose (Scheme 82A). Despite improvements in this field, a number of challenges remains to be tackled. For instance, most of these methods do not allow the same functional group tolerance on nitrogen. Some metallo- and proto-catalyzed hydrofunctionalization of styrenes (R² = Ar) with primary or secondary anilines eventually produce a mixture of hydroamination (*N*-alkylation) and hydroarylation products (*ortho*- and *para*-C-alkylation). Selective *ortho*-alkylation of anilines was

only accomplished in a few cases and mainly using anilines substituted by EWG groups.^[181,185,189,191] Other disadvantages of these processes include the difficulty of using primary anilines as they tend to have a too strong binding affinity with electrophilic metal centers.

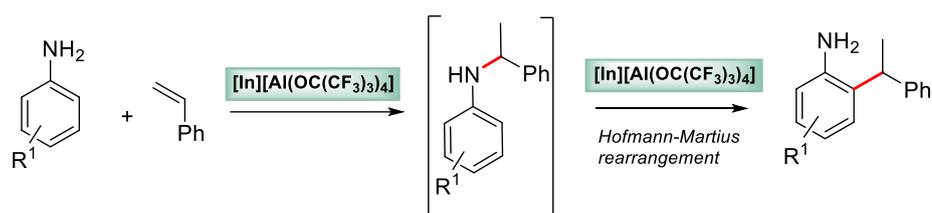
A. Representative catalytic systems for the hydroamination/hydroarylation of alkenes using anilines



B. Incompatible aniline substrates in Ga(I)-catalyzed Friedel-Crafts reaction



C. This work



Scheme 82. Hydroamination or hydroarylation of alkenes using anilines

One way to overcome this challenge would be to modulate this Lewis acidity by playing on the oxidation state of the metal. Following up on our interest to develop gallium(III)-catalyzed reactions,^[20–23,38,148,192] we recently disclosed that the use of a Ga(I) univalent cationic species as homogeneous π -Lewis acid catalyst could be more advantageous in some cases than the corresponding Ga(III) complexes.^[193] While Group 13 metal-based

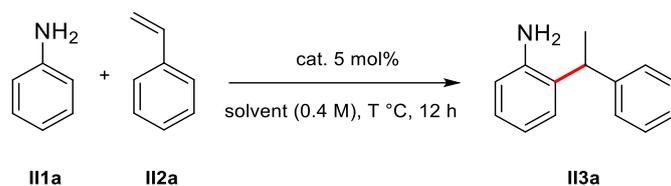
Lewis acids in their +III oxidation state are commonly employed in catalysis, their +I oxidation state has been clearly underexplored.^[14] The main reasons are their insolubility in non-polar solvents and/or their ability to readily disproportionate.^[194] Yet, we revealed the potential of the Ga(I) complex $[\text{Ga}][\text{Al}(\text{OC}(\text{CF}_3)_3)_4]$ ^[62,195] to catalyze transfer hydrogenation of alkenes, hydrogenative cyclization of enynes and hydroarylation of alkynes. However, in our precedent investigations, we noticed a major incompatibility between $[\text{Ga}][\text{Al}(\text{OC}(\text{CF}_3)_3)_4]$ and aniline in hydroarylation reactions (Scheme 82B), which limited the range of applications of such catalysts. The strong binding affinity between the $\text{Ga}(\text{I})^+$ ions and primary anilines or unprotected amines is a likely explanation for this lack of reactivity.^[196] In fact, despite some precedents in the literature featuring alkyl-aluminum catalysts,^[197,198] the use of amine nucleophiles bearing electron-withdrawing groups such as sulfonyl was often required in Group 13 metal-catalyzed alkene functionalization (Scheme 82).^[42,144] We hypothesized that this inhibition due to the high azaphilicity of the metal should decrease when moving down the Group 13 column, as the atomic radius increases and the low +I state oxidation becomes more stable.^[199] For instance, In(I) derivatives are softer acids compared to their In(III) analogs and other Group 13 M(I) or M(III) complexes, making them more adequate for the activation of *N*-nucleophiles.^[156,157] They are Lewis acidic by their three vacant *p* orbitals, but also Lewis basic by their lone electron pair. This dual property makes such catalysts truly appealing as they could enable both the alkylation of anilines with styrenes (typical for Lewis acids) and the hydroamination of unactivated alkenes with alkylamines (typical for basic complexes). Apart from these possible applications, In(I)X complexes have been scarcely used in homogeneous catalysis, including allylboration of ketones,^[157] asymmetric C-C bond formation,^[157] and C-N bond formation.^[156] Recent progresses in the coordination chemistry of cationic In(I) complexes bearing weakly coordinating anions (WCAs) such as $[\text{CHB}_{11}\text{Cl}_{11}]^{-}$ ^[156] or $[\text{Al}(\text{OC}(\text{CF}_3)_3)_4]^{-}$ ^[60,155] has made these relatively stable and soluble species more appealing for catalytic applications. We report herein that the

Lewis acidity of a univalent cationic In(I) salt bearing a WCA might be harnessed in the *hydroarylation of primary anilines by styrenes* (Scheme 82C) Mechanistic studies involving a series of control experiments and reaction monitoring revealed that the reaction likely occurs *via* a tandem hydroamination/Hofmann-Martius rearrangement to give an *ortho*-C-alkylation product.

2.2.1 Optimization of reaction conditions

Initial experiments showed that the use of a catalytic amount of [In][Al(OC(CF₃)₃)₄] (5 mol%) converted efficiently aniline **II1a** in the presence of one equivalent of styrene **II2a** in fluorobenzene at 110 °C into the Markovnikov-type *ortho*-C-alkylation product **II3a** in 61% isolated yield (Table 2, entry 1). It is worth mentioning that no *N*-alkylation or *para*-C-alkylation products could be detected. In comparison, the corresponding univalent gallium salt was far less efficient under the same reaction conditions (entry 2), which might be explained, by a stronger interaction between aniline and the metal center, hampering the catalyst turn-over.^[157] A change in the relative stoichiometry between **II1a**/**II2a** led to **II3a**, albeit in lower yields (entry 3). An excess of aniline afforded a mixture of mono- and dialkylated products with *ortho*-selectivity (entry 4). Lowering the temperature to 80 °C or performing the reaction in toluene resulted in slower rates and lower yields (entries 5-6). In addition, polar solvents were not compatible with the reaction (entries 7-10). As we^[193] and other groups^[175,184] have already noticed in related reactions, the WCA has an important effect on the efficiency of the hydroarylation. Indeed, no reaction was observed in the presence of In(I)X halides (X = Cl, I) (entries 11-12). The same observation was made with the soluble In(III) salt InBr₃ (entry 13) or the *in situ* generated In(III) complex [InBr₂][SbF₆] (entry 14). In contrast, switching SbF₆⁻ counterion by [Al(OC(CF₃)₃)₄]⁻ one provided **II3a** in 53% yield (entry 15). Even though the counterion effect is not as pronounced as with the In(I) complex (entry 2), the use of this WCA clearly has also a positive effect on the reaction outcome.

Table 6. Catalyst screening of the intermolecular hydroarylation of styrenes by anilines^a



Entry	Catalyst	Ratio	Solvent	T (°C)	Yield
		II1a:II2a			II3a ^{b,c}
1	[In][Al(OC(CF ₃) ₃) ₄]	1:1	PhF	110	61
2	[Ga][Al(OC(CF ₃) ₃) ₄]	1:1	PhF	110	34
3	[In][Al(OC(CF ₃) ₃) ₄]	3:1	PhF	110	56
4	[In][Al(OC(CF ₃) ₃) ₄]	1:3	PhF	110	22 ^d
5	[In][Al(OC(CF ₃) ₃) ₄]	1:1	PhF	80	15
6	[In][Al(OC(CF ₃) ₃) ₄]	1:1	Toluene	110	59
7	[In][Al(OC(CF ₃) ₃) ₄]	1:1	DCE	80	27
8	[In][Al(OC(CF ₃) ₃) ₄]	1:1	THF	70	NR
9	[In][Al(OC(CF ₃) ₃) ₄]	1:1	MeOH	70	NR
10	[In][Al(OC(CF ₃) ₃) ₄]	1:1	DMF	150	31
11	InCl	1:1	PhF	110	NR
12	InI	1:1	PhF	110	NR
13	InBr ₃	1:1	PhF	110	NR
14	[InBr ₂][SbF ₆] ^d	1:1	PhF	110	7
15	[InBr ₂][Al(OC(CF ₃) ₃) ₄] ^d	1:1	PhF	110	53

^a Reaction conditions: aniline (0.2 mmol) and styrene (0.2 mmol) in solvent (1 mL), 12 h.

^b Hydroamination product detected in less than 10% yield. ^c Isolated yields, NR = no reaction.

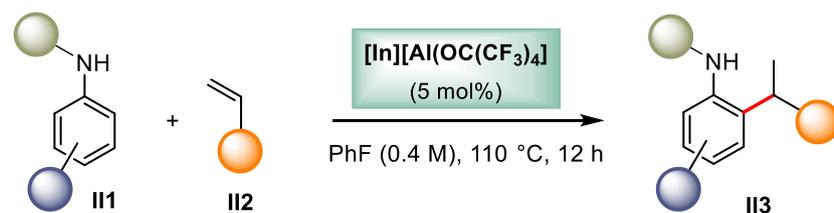
^d Mixture of mono- and dialkylated product was observed. ^e Generated *in situ* by using InBr₃ and [Ag][Al(OC(CF₃)₃)] or AgSbF₆.

2.2.2 Scope and limitations

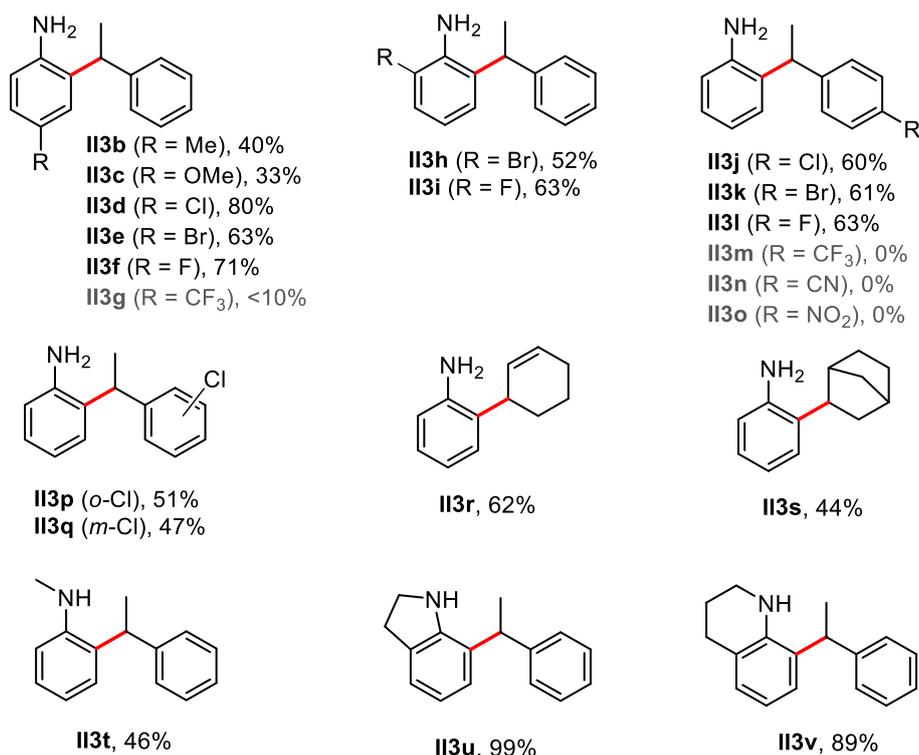
Encouraged by these results, we explored the generality of this protocol with a wide range of styrene, alkene, and aniline derivatives, including both cyclic and acyclic ones (Scheme 83). While anilines displaying an electron-donating group or a halide at the *para*-position were found compatible under the optimized reaction conditions (II3b-f), an important decrease of catalytic activity was observed with the CF₃ electron-withdrawing groups (II3g). Anilines bearing an *ortho*-halide substituent were also successfully converted into the *ortho*-C-alkylated products when reacted with styrene (II3h-i, 52-63% yields). Remarkably, a variety of moderately deactivated halide-

substituted styrenes were tolerated in this reaction (**II3j-l**, **II3p-q**). This was achieved in a very selective manner, without detecting the presence of *N*-alkylation products, which differs from methodologies described above reporting a 1/1 ratio of *C/N*-alkylation products.^[180,187]

Scheme 83. Scope and limitations of the In(I)-catalyzed *ortho*-*C*-alkylation of anilines^a



Product obtained (isolated yield)^b



^a Reaction conditions: aniline (0.2 mmol), alkene (0.2 mmol), catalyst (5 mol%), PhF (0.5 mL) at 110 °C for 12 h in an argon atmosphere. ^b Isolated yields after column chromatography on Al₂O₃ (MeOH/CH₂Cl₂ = 95/5).

However, *para*-cyano, -nitro and -trifluoromethyl styrene derivatives were found to be unreactive substrates. With such electron-poor styrenes, the hydroamination reaction prevails in most previously reported cases.^[200–202] In addition, the cyclic alkenes 1,3-

cyclohexadiene and norbornene were successfully used, affording products **II3r** and **II3s** in 62% and 44% yield respectively. We noted complete selectivity for the *C*-alkylation product, a trend that was not found in previous studies.^[203] Substrates exhibiting more basic secondary *N*-alkyl anilines were also well-tolerated (**II3t-v**). Notably, hydroarylation of 1,2,3,4-tetrahydroquinoline and indoline gave rise to addition products **II3u** and **II3v** in 89 and 99% yield respectively.

a. Limitation towards alkenes

To find the limitations of this In(I) catalyzed hydroarylation reaction, additional styrenes and alkenes were tested with aniline. Unfortunately, using 4-methylstyrene, 4-methoxystyrene and 2-vinylnaphthalene in this reaction delivered the ortho-alkylation products with poor yields (<10% NMR yield). In addition, some other styrenes derivatives or alkenes proved unreactive, including 2-vinylpyridine, 2-vinylnaphthalene, ethene-1,1-diyldibenzene, 1,2,3,4,5-pentafluoro-6-vinylbenzene, (E)-prop-1-en-1-ylbenzene, allylbenzene, cyclohexene, cyclohexa-1,4-diene, and 1,2-dihydronaphthalene (Figure 34). The reason of these unfavorable results is still under investigation.

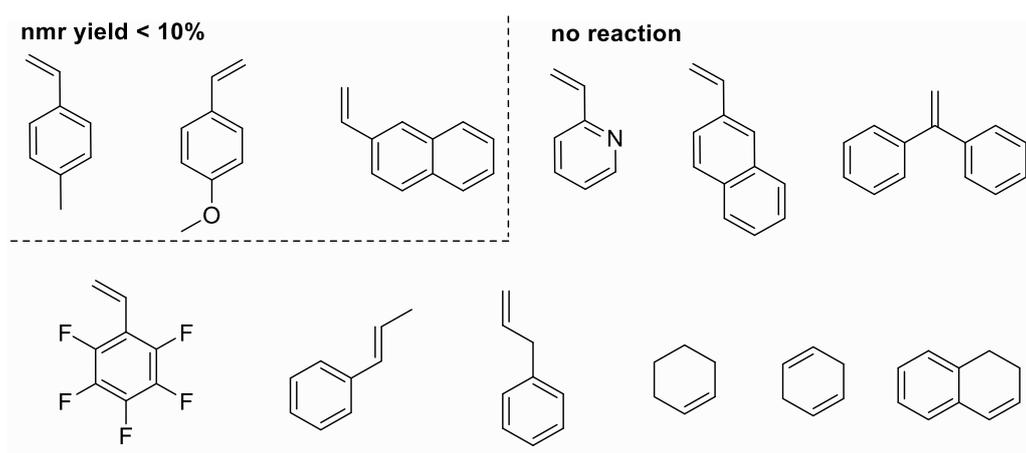


Figure 34. Ineffective styrenes and alkenes

b. Limitation towards anilines and amines

Of note, *meta*-substituted anilines and 2,4,6-trimethylaniline gave a mixture of products, which is difficult to isolate. Furthermore, 4-(trifluoromethyl)aniline, secondary and tertiary amines are totally unreactive in this methodology (Figure 35).

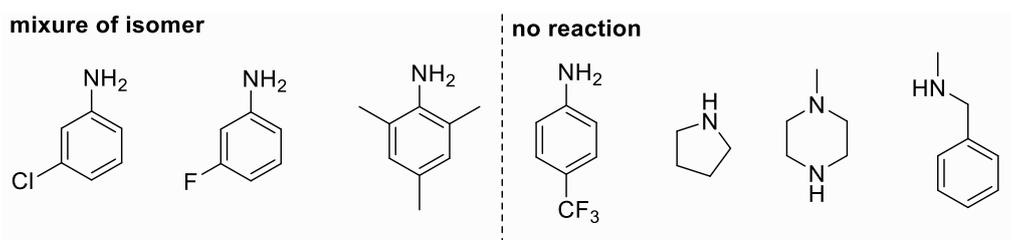
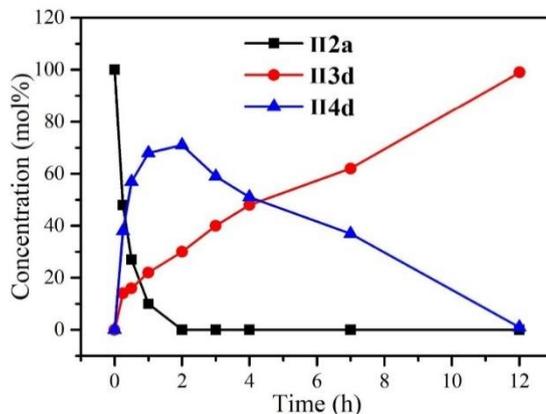
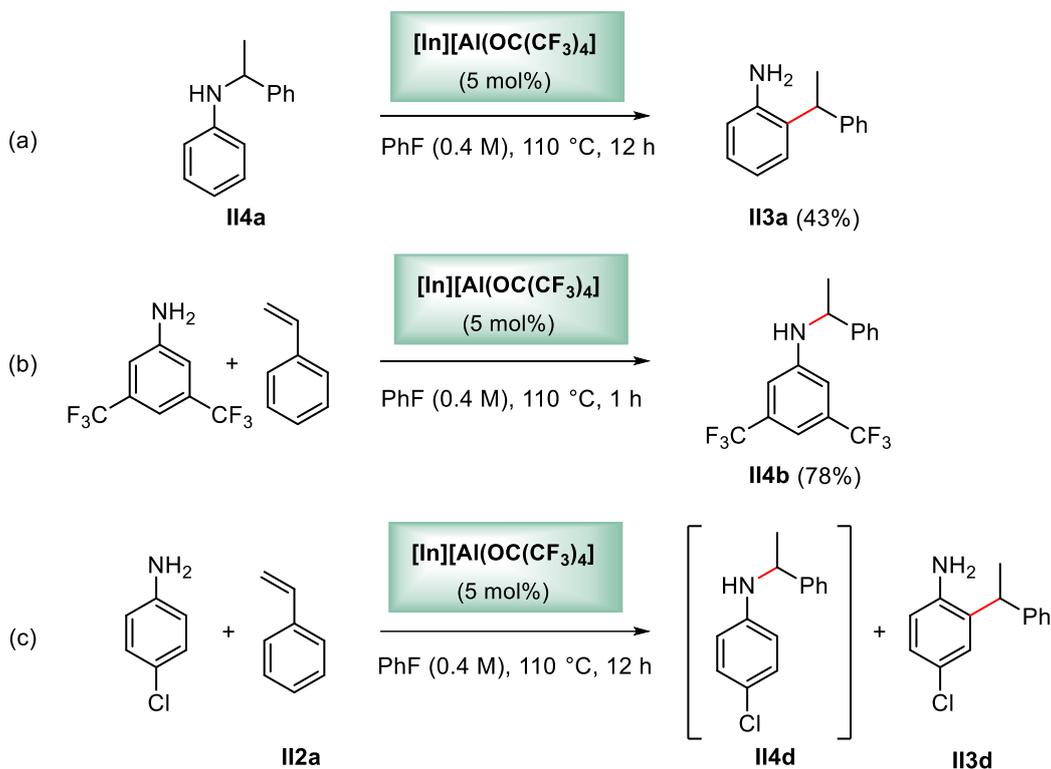


Figure 35. Ineffective anilines and amines in *ortho*-C-alkylation

2.2.3 Mechanistic investigation

After having established the catalytic activity of univalent In(I) cations for *ortho*-C-alkylation of anilines, a few control experiments were carried out to delineate its mechanism. One option could be a Friedel-Crafts type reaction. It is well known that S_E^{Ar} processes can be mediated by Group 13 salts;^[204] however, regarding the hydroarylation of styrenes with primary anilines, no examples were described. A second option could be that the C-alkylation products results from a hydroamination process followed by a Hofmann-Martius rearrangement.^[183,205,206] To test this assumption, we synthesized the secondary amine **II4a** as a putative hydroamination intermediate^[207] and subjected it to the optimized reaction conditions (Scheme 84a). This compound was indeed converted into **II3a** in 43% isolated yield. On the other hand, secondary amine **II4b**, arising from the *N*-alkylation of 3,5-bis(trifluoromethyl)aniline, was isolated as the sole product under the same reaction conditions (Scheme 84b). These results clearly suggest that the Hofmann-Martius rearrangement takes place after a first step of In(I)-catalyzed hydroamination of styrene. This second step is hampered by the presence of strongly electron-withdrawing groups at the aniline moiety.

Scheme 84. Mechanistic investigations related to the In(I)-catalyzed *ortho*-C-alkylation of anilines^{a,b,c}



^a Reaction conditions: aniline (0.2 mmol), alkene (0.2 mmol), catalyst (5 mol%), PhF (0.5 mL) at 110 °C for 12 h in an argon atmosphere. ^b Isolated yields after column chromatography on Al₂O₃ (MeOH/CH₂Cl₂ = 95/5). ^c GC reaction profiles of *para*-chloroaniline in PhF (0.4 M) at 110 °C in the presence of catalyst (5 mol%).

Moreover, with a moderately deactivating group such as Cl, the hydroamination intermediate could be detected. We thus performed a GC monitoring using *para*-chloroaniline (Scheme 84c). As it can be seen in the graphic, styrene is fully consumed within 2 h, the *N*-alkylated compound **II4d** (ca. 70% GC yield) and the final *C*-alkylated

compound **II3d** (ca. 30% GC yield) being the only detected products. This suggests a tandem hydroamination/ Hoffmann-Martius rearrangement reaction and shows that the latter is the rate-limiting step. The low proportion of **II3d** after 2 h rules out a classical Friedel-Crafts mechanism, and may also reveal a concerted mechanism.

2.3 In(I)-catalyzed intramolecular hydroamination

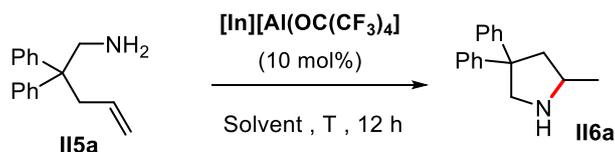
The intramolecular hydroamination reaction is one of the most atom economic pathways to access the nitrogen containing heterocycles.^[197,201,208–224] As we have shown in the last subsection, the compatibility between primary and secondary anilines with In(I) cations, as well as the presence of intermolecular hydroamination products in few cases,^[200–202] led us to investigate the *intramolecular hydroamination of unactivated alkenes by primary and secondary unprotected amines*. The proposed mechanism is supported by DFT computations, carried out by my colleague Shengwen Yang.

2.3.1 Optimization of reaction conditions

a. Solvents investigation

We took the most classic compound **II5a** as substrate for the optimization of reaction condition in the In(I) catalyzed intramolecular hydroamination (Table 7). In the presence of 10 mol% of [In][Al(OC(CF₃)₃)₄], several organic solvent were tested in this reaction under their boiling point (entry 1-4), and fluorobenzene shown to be the best choice. Afterwards, increasing the temperature and concentration improved the formation of **II6a** with 89% isolated and 99% NMR yield, with almost the same result of Wehmschulte's work described in section 1.4.3.

Table 7 Solvents screening for the intramolecular hydroamination of alkenes



Entry	Solvent	Temp.	Yield ^a
1	Toluene (0.2 M)	110 °C	56
2	PhF (0.2 M)	85 °C	71
3	DCE (0.2 M)	80 °C	24
4	THF (0.2 M)	60 °C	47
5	PhF (0.2 M)	110°C	78
6	PhF (0.4 M)	110°C	89 (99 ^b)

^a Isolated yield by chromatography column on Al₂O₃ (Cyclohexane/EtOAc = 95/5).

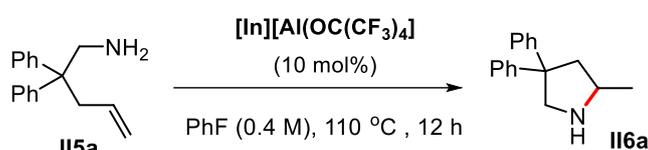
^b Determined by ¹H NMR spectroscopy using ferrocene (0.5 equiv) as the internal standard.

b. Catalysts investigation

With the best reaction condition in hands, we started to investigate the necessity of [In][Al(OC(CF₃)₃)₄] in this transformation (Table 8). It is important to stress out that this reactivity is unique for Lewis acids as they usually require the presence of an electron-withdrawing group on the nitrogen functionality to promote the reaction. Indeed, their strong coordination to more basic alkylamines generally precludes the transformation. The univalent indium(I) catalyst [In][Al(OC(CF₃)₃)₄], simplified as **A**, (10 mol%) was essential for the reaction (entries 1-10). While no reaction took place with InCl, the reaction proceeded moderately with additional WCA silver or lithium salt (entries 1-3). The use of AgSbF₆ as additive with the insoluble InCl salt did not trigger the reaction (entry 4). The utilization In(III) complexes instead of **A** as catalyst resulted in a much lower efficiency when compared to the standard reaction conditions (entries 5-9). As anticipated, InBr₃, which was previously used to promote alkene hydroamination using *N*-tosylamine,^[144] was not efficient with an unprotected amine (entry 5). The crucial role of the [Al(OC(CF₃)₃)₄]⁻ counterion was once again emphasized, as low conversions were found with other anions (e.g. OTf⁻, SbF₆⁻, entries 6-8), even in the case of a cationic In(III) complex known to be very active in other

reactions (entry 9).^[70] While the influence of the $[\text{Al}(\text{OC}(\text{CF}_3)_3)_4]^-$ counterion is pivotal in this process, the use of an univalent In(I) derivative should not be overlooked. Indeed, the univalent Ga(I) catalyst was not as efficient as **A** under the same reaction conditions (40%, entry 10), confirming that the cornerstone of this reaction is the association of a univalent In(I) cation and a WCA such as $[\text{Al}(\text{OC}(\text{CF}_3)_3)_4]^-$. In other words, a naked In(I)^+ ion is the most effective.

Table 8. Catalyst screening for the intramolecular hydroamination of alkene **II5a**^a



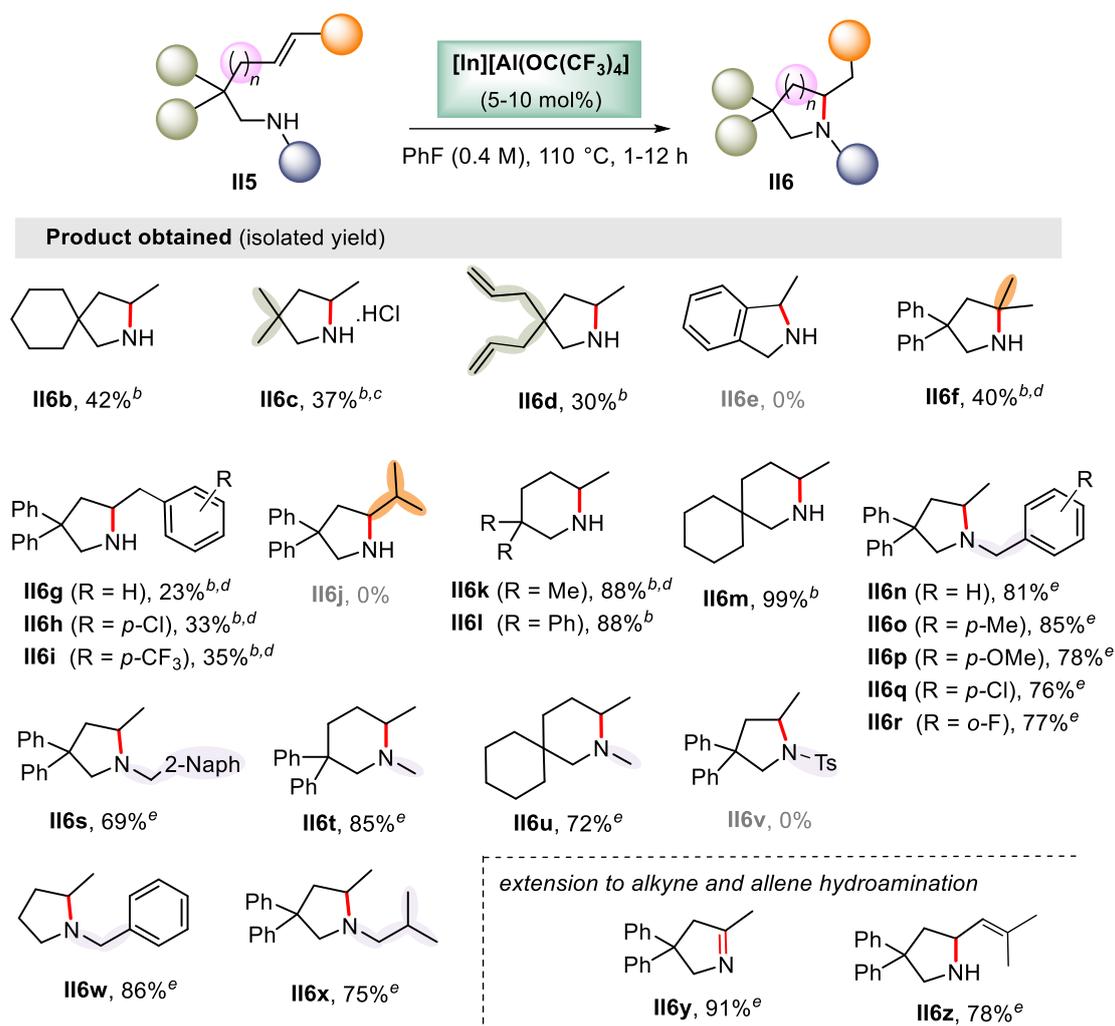
Entry	Variation from standard conditions ^a	Yield (%) ^b
1	InCl instead of A	NR
2	InCl + [Ag][Al(OC(CF ₃) ₃) ₄] instead of A	55
3	InCl + [Li][Al(OC(CF ₃) ₃) ₄] instead of A	48
4	InCl + AgSbF ₆ instead of A	NR
5	InBr ₃ instead of A	NR
6	In(OTf) ₃ instead of A	42
7	IPr·InBr ₃ + AgSbF ₆ instead of A	NR
8	InBr ₃ + [Ag][Al(OC(CF ₃) ₃) ₄] instead of A	47
9	IPr·InBr ₃ + [Ag][Al(OC(CF ₃) ₃) ₄] instead of A	44
10	[Ga][Al(OC(CF ₃) ₃) ₄] instead of A	40

^aReaction conditions: alkenylamine **II5a** (0.2 mmol), catalyst (5 mol%), PhF (0.5 mL) at 110 °C for 12 h under an argon atmosphere. ^b Isolated yields after column chromatography on Al₂O₃ (Cyclohexane/EtOAc = 95/5), NR = no reaction.

2.3.2 Scope and limitations

The optimized reaction conditions for the intramolecular hydroamination of alkenes were applicable to a broad scope of substrates (Scheme 85). A variety of 5-membered (**II6b-j**) and 6-membered nitrogen heterocycles (**II6k-m**) were readily obtained in up to 99% yield. Secondary alkenylamine were also suitable substrates (**II6n-u**, **II6w**, **II6x**).

Scheme 85. Scope and limitations of the In(I)-catalyzed intramolecular hydroamination of alkenes^{a,b}



^a Isolated yields after column chromatography on Al₂O₃ or silica gel. ^b Reaction conditions: alkenylamine **II5b-m** (0.2 mmol), **A** (10 mol%), PhF (0.5 mL) at 110 °C for 12 h under an argon atmosphere. ^d Determined by ¹H NMR spectroscopy using ferrocene (0.5 equiv) as internal standard. C₆D₆ as solvent. ^e Reaction conditions: alkenylamine **II5n-z** (0.2 mmol), **A** (5 mol%), PhF (0.5 mL) at 110 °C for 1 h under an argon atmosphere.

Both five- and six-membered nitrogen-heterocycles bearing benzyl or alkyl groups on the nitrogen have been isolated in high yields while requiring a shorter reaction time and a lower catalyst loading (1 h, with 5 mol% of **A** at 110 °C). It is worth mentioning that, unlike many examples catalyzed by metal-alkyl or -amido complexes, the absence of *gem*-dialkyl/aryl substituents does not affect the rate of the reaction (**II6w**).^[225] The Markovnikov cyclization has also been achieved efficiently from primary amines with

more reactive functionalities such as an alkyne (**II6y**) and an allene (**II6z**). Interestingly, and in contrast with In(III)-catalyzed hydroamination,^[144] the reaction does not proceed with a tosylamine (**II6j**), which raises questions about the activation mode of the alkenylamine by our cationic univalent indium(I) catalyst.

2.3.3 Mechanism investigation by DFT calculation

To elucidate how this univalent indium(I) complex is so efficient for this Lewis acid-catalyzed hydroamination, we decided to investigate the transformation of **II5a** by DFT calculations (Figure 1). *I would like to thank my colleague Shengwen YANG for this work.* For geometry optimizations, the M06-2X functional, the LANL2DZ basis set for In and the 6-31G(d,p) basis set for the other elements were used. The discussed values are ΔG_{383} in kcal/mol obtained after single point calculations at the M06-2X/def2-TZVP(In)-6-311+G(2d,p) (other elements) and solvent correction (SMD model for fluorobenzene). Since conformational sampling of the ion-pairs is particularly challenging, the $[\text{Al}(\text{OC}(\text{CF}_3)_3)_4]^-$ WCA was not taken into consideration. We have compared pathways starting from different naked In^+ /aminoalkene **II5a** complexes after releasing the two PhF ligands. The ammonium complex **2^{zero}** is the most stable starting compound, located at -15.1 kcal/mol on the PES (zero stands for no PhF). Forming the N-C bond from this complex requires the coordination of the alkene moiety to give **3^{zero}**, which is slightly less stable than **2^{zero}**, and then insertion of the alkene into the In-N bond through transition state **4^{zero}-ts**. The latter was located 15.0 kcal/mol above the reference system $[\text{II5a} + \text{In}(\text{PhF})_2^+]$ and leads to pyrrolidinium **5^{zero}** in an endergonic fashion (8.1 kcal/mol above the reference system). If intramolecular, the protodemetalation can be modeled via **12^{zero}-ts**, lying at 25.2 kcal/mol, a barrier that can be spanned at 383 K. The resulting compound is the amino indium complex **10^{zero}**, located at -29.3 kcal/mol. The final product **6a** is obtained after catalyst regeneration at the expense of 16.7 kcal/mol (-12.6 kcal/mol). The main issue with this hypothesis (Path A) is the large energy difference between **2^{zero}** and **12^{zero}-ts** of 40.3 kcal/mol, which

suggests that 2^{zero} is a resting state rather than an intermediate. We then studied Path C in which In^+ is first associated with the alkene moiety of **5a** and one of its Ph group to provide the η^6 -Ph chelate 6^{zero} with a release of 3.8 kcal/mol. Connection to the previously described intermediate 5^{zero} could be achieved after anti attack of the nitrogen to the alkene ligand ($7^{\text{zero-ts}}$) and rotation of the CH_2In fragment ($11^{\text{zero-ts}}$). These two transition states lie lower in energy than $12^{\text{zero-ts}}$ (1.9 and 11.8 kcal/mol respectively, vs 25.2 kcal/mol), which still corresponds to the RDS. However, from the lower point 6^{zero} to $12^{\text{zero-ts}}$, the barrier becomes 29.0 kcal/mol, which can be overcome at 383 K. Of note, cleavage of the C-In bond from 8^{zero} is much more energetically demanding than from 5^{zero} (Path B, $9^{\text{zero-ts}}$ lying at 34.4 kcal/mol on the PES).

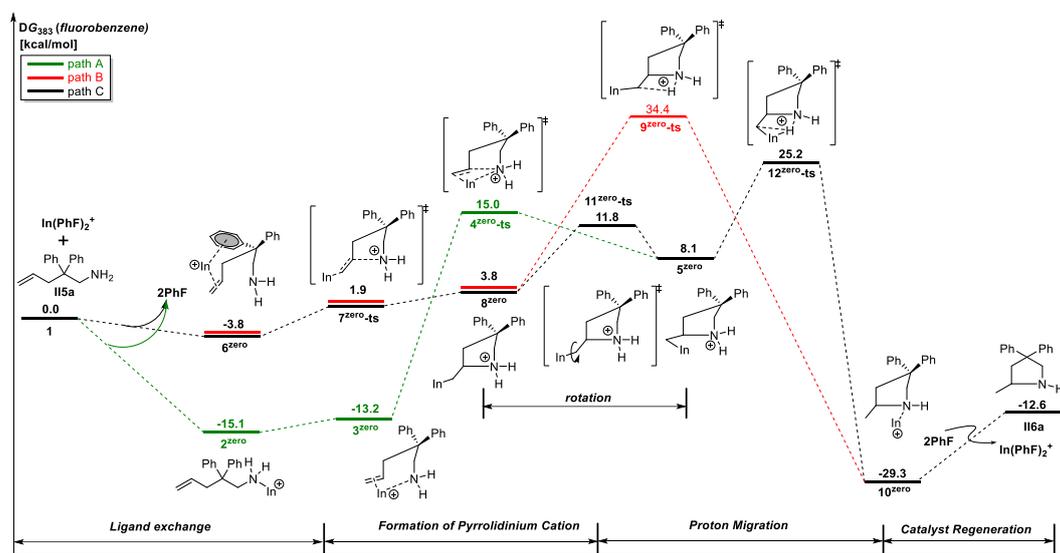


Figure 36. Calculated Gibbs Free Energy Profile

Thus, in agreement with previous reports,^[226–228] the computed catalytic cycle contains four main steps: (i) ligand exchange between the pre-catalysts and the substrate; (ii) nucleophilic attack of the amine on the bound alkene forming a free rotating alkyl-In(I) intermediate for facilitating the transfer of proton;^[228] (iii) migration of a proton from the nitrogen atom to the β -carbon to provide the secondary amine product; (iv) displacement of the secondary amine to complete the catalytic cycle. These computations support the catalytic role of naked In(I)^+ ions which reversibly bind to primary amines.

2.4 Conclusion

In summary, a selective *ortho*-C-alkylation of unprotected anilines with styrenes has been achieved using a univalent cationic In(I) catalyst. Mechanistic studies regarding the formation of *ortho*-C-alkylated anilines leads towards an intermolecular hydroamination reaction followed by Hofmann-Martius rearrangement. Remarkably, this protocol proved to be both chemo- and regioselective with respect to the widely investigated acid-catalyzed Friedel-Crafts alkylation (direct hydroarylation of styrenes). The unique properties of the In(I) catalysts led us to develop an efficient alkene hydroamination protocol using unprotected primary and secondary alkenylamines under mild conditions. Computations support the catalytic activity of naked In(I)⁺ ions, with an outer sphere mechanism for the C-N bond formation and a potentially inner sphere protodemetalation. Investigations are underway to exploit the potential of such ambivalent species in other Lewis acid-catalyzed reactions.

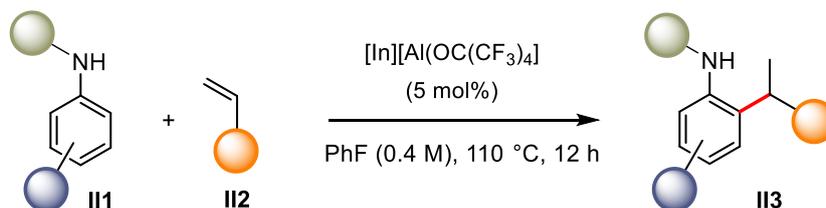
3. EXPERIMENTAL

3.1 General Information

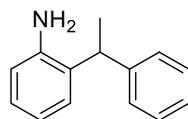
Unless otherwise noted, all reactions and manipulations were performed in an inert atmosphere (argon) in glovebox, or using standard Schlenk and high vacuum-line techniques. Glassware was dried overnight at 120 °C before use. Reactions in overheated solvent were performed in 10 mL reaction tubes sealed with Teflon-coated Rodaviss stand immersed in a pre-heated oil bath. Reactions were monitored using thin-layer chromatography (TLC) on silica gel plates precoated with a fluorescent indicator. The spots were visualized with ultraviolet light and/or *p*-anisaldehyde stain with heat as developing agents. NMR characterization data was collected at 296 K on a AM 250, AV 300, AV 360 or DRX 400 Bruker spectrometers operating at 250, 300, 360 or 400 MHz for ¹H NMR. ¹H NMR chemical shifts are reported in ppm using residual solvent peak as reference (CHCl₃: δ = 7.26 ppm). Data for ¹H NMR are presented as follows: chemical shift δ (ppm), multiplicity (s = singlet, d = doublet, t = triplet, m = multiplet, br = broad), coupling constant *J* (Hz) and integration; ¹³C NMR spectra were recorded at 63, 75, 91 or 100 MHz using broadband proton decoupling and chemical shifts are reported in ppm using residual solvent peaks as reference (CHCl₃: δ = 77.16 ppm). MS were recorded on DSQ Thermo Fisher instrument by electronic impact. HRMS was performed on a MicrOTOF Bruker spectrometer.

Materials. All materials purchased from commercial suppliers were used without further purification. All solvents for catalytic reactions were distilled under argon and degassed via three freeze-pump-thaw cycles before use. The catalysts and non-commercial substrates were synthesized by the reported procedures: [In][Al(OC(CF₃)₃)₄],^[59] [Ga][Al(OC(CF₃)₃)₄],^[57] primary aminoalkenes **II5a-h**,^[213,229] secondary aminoalkenes **II7a-j**,^[230] aminoalkyne **II10**,^[231] and aminoallene **II12**.^[232]

3.2 Procedure for In(I) Catalyzed Hydroarylation

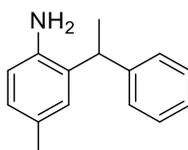


In glove box, a drying reaction tube was charged with $[\text{In}][\text{Al}(\text{OC}(\text{CF}_3)_3)_4]$ (13 mg, 0.01 mmol) and anhydrous degassed PhF (0.5 mL). Anilines **II1** (0.2 mmol), and alkenes **II2** (0.2 mmol) were then added in this solution in portions. The reaction tube was sealed with a screw cap and stirred outside of the glove box at 110 °C for 12 h. The reaction mixture was diluted with Et_2O , filtered through a pad of celite (thoroughly rinsed with Et_2O) and concentrated under reduced pressure by rotary evaporation. Purification by FC over neutral Al_2O_3 ($\text{MeOH}/\text{CH}_2\text{Cl}_2 = 95/5$) afforded desired product **II3a-v**.



II3a 2-(1-phenylethyl)aniline

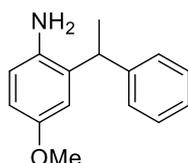
Following the general procedure, product **II3a** was obtained as a colorless oil in 61% yield after purification. ^1H NMR (250 MHz, CDCl_3) δ 7.39 – 7.19 (m, 6H), 7.14 (td, $J = 7.5, 1.6$ Hz, 1H), 6.90 (td, $J = 7.5, 1.3$ Hz, 1H), 6.68 (dd, $J = 7.8, 1.3$ Hz, 1H), 4.12 (q, $J = 7.2$ Hz, 1H), 3.25 (s, 2H), 1.67 (d, $J = 7.2$ Hz, 3H). ^{13}C NMR (63 MHz, CDCl_3) δ 145.8, 144.4, 129.9, 128.9, 127.6, 127.4, 126.5, 118.9, 116.4, 40.4, 21.9. Spectroscopic data for **II3a** match those previously reported in literature.^[175]



II3b 4-methyl-2-(1-phenylethyl)aniline

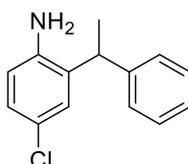
Following the general procedure, product **II3b** was obtained as a colorless oil in 40% yield after purification. ^1H NMR (360 MHz, CDCl_3) δ 7.34 – 7.27 (m, 2H), 7.23 (dt,

$J = 7.7, 1.4$ Hz, 3H), 7.13 (d, $J = 2.0$ Hz, 1H), 6.93 (dd, $J = 8.0, 2.0$ Hz, 1H), 6.58 (d, $J = 7.9$ Hz, 1H), 4.10 (q, $J = 7.2$ Hz, 1H), 3.17 (s, 2H), 2.34 (s, 3H), 1.64 (d, $J = 7.2$ Hz, 3H). ^{13}C NMR (91 MHz, CDCl_3) δ 145.9, 141.8, 130.1, 128.8, 128.0, 127.8, 127.6, 126.4, 116.5, 40.3, 21.9, 21.0. Spectroscopic data for **II3b** match those previously reported in literature for.^[175]



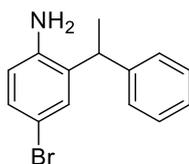
II3c 4-methoxy-2-(1-phenylethyl)aniline

Following the general procedure, product **II3c** was obtained as a colorless oil in 33% yield after purification. ^1H NMR (360 MHz, CDCl_3) δ 7.33 – 7.25 (m, 2H), 7.24 – 7.17 (m, 3H), 6.93 (d, $J = 2.8$ Hz, 1H), 6.69 (dd, $J = 8.5, 2.8$ Hz, 1H), 6.60 (d, $J = 8.5$ Hz, 1H), 4.10 (q, $J = 7.1$ Hz, 1H), 3.80 (s, 3H), 3.11 (s, 2H), 1.62 (d, $J = 7.2$ Hz, 3H). ^{13}C NMR (91 MHz, CDCl_3) δ 153.1, 145.5, 138.0, 131.9, 128.9, 127.6, 126.5, 117.2, 114.2, 111.7, 55.8, 40.4, 21.9. Spectroscopic data for **II3c** match those previously reported in literature for.^[175]



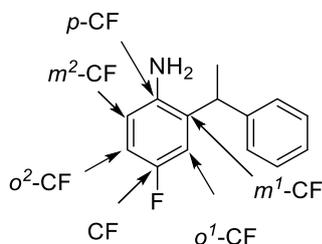
II3d 4-chloro-2-(1-phenylethyl)aniline

Following the general procedure, product **II3d** was obtained as a colorless oil in 80% yield after purification. ^1H NMR (360 MHz, CDCl_3) δ 7.35 – 7.15 (m, 6H), 7.05 (dd, $J = 8.4, 2.5$ Hz, 1H), 6.56 (d, $J = 8.4$ Hz, 1H), 4.03 (q, $J = 7.1$ Hz, 1H), 3.42 (s, 2H), 1.61 (d, $J = 7.2$ Hz, 3H). ^{13}C NMR (91 MHz, CDCl_3) δ 144.8, 143.0, 131.4, 129.0, 127.4, 127.2, 127.1, 126.7, 123.5, 117.3, 40.3, 21.9. Spectroscopic data for **II3d** match those previously reported in literature for.^[172]



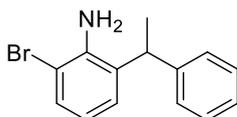
II3e 4-bromo-2-(1-phenylethyl)aniline

Following the general procedure, product **II3e** was obtained as a colorless oil in 63% yield after purification. ^1H NMR (300 MHz, CDCl_3) δ 7.39 (dd, $J = 2.4, 0.7$ Hz, 1H), 7.36 – 7.13 (m, 6H), 4.02 (q, $J = 7.2$ Hz, 1H), 3.43 (s, 2H), 1.61 (d, $J = 7.2$ Hz, 3H). ^{13}C NMR (63 MHz, CDCl_3) δ 144.9, 143.6, 132.0, 130.1, 129.0, 127.5, 126.8, 117.8, 110.8, 40.4, 21.9. HRMS (ESI, m/z) calcd for $\text{C}_{14}\text{H}_{14}\text{BrNNa}$ $[\text{M}+\text{Na}]^+$ 298.0207, found 298.0221



II3f 4-fluoro-2-(1-phenylethyl)aniline

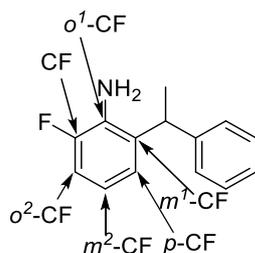
Following the general procedure, product **II3f** was obtained as a colorless oil in 71% yield after purification. ^1H NMR (300 MHz, CDCl_3) δ 7.34 – 7.16 (m, 5H), 7.03 (ddd, $J = 10.1, 2.9, 0.7$ Hz, 1H), 6.80 (td, $J = 8.5, 2.9$ Hz, 1H), 6.57 (dd, $J = 8.5, 5.0$ Hz, 1H), 4.06 (q, $J = 7.1$ Hz, 1H), 3.29 (s, 2H), 1.61 (d, $J = 7.1$ Hz, 3H). ^{13}C NMR (91 MHz, CDCl_3) δ 156.9 (d, CF, $J = 235.3$ Hz), 145.0, 140.4 ($m^1\text{-CF}$), 131.7 (d, $p\text{-CF}$, $J = 6.5$ Hz), 129.0, 127.5, 126.7, 117.0 (d, $m^2\text{-CF}$, $J = 7.8$ Hz), 114.1 (d, $o^1\text{-CF}$, $J = 23.1$ Hz), 113.55 (d, $o^2\text{-CF}$, $J = 20.7$ Hz), 40.4, 22.0. ^{19}F NMR (235 MHz, CDCl_3) δ -127.7. Spectroscopic data for **II3f** match those previously reported in literature for.^[172]



II3h 2-bromo-6-(1-phenylethyl)aniline

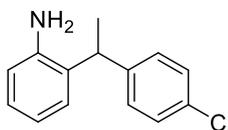
Following the general procedure, product **II3h** was obtained as a colorless oil in 52%

yield after purification. ^1H NMR (360 MHz, CDCl_3) δ 7.34 – 7.23 (m, 3H), 7.25 – 7.14 (m, 3H), 6.96 (dd, $J = 8.2, 2.1$ Hz, 1H), 6.69 (d, $J = 8.2$ Hz, 1H), 4.11 – 3.87 (m, 3H), 1.59 (d, $J = 7.2$ Hz, 3H). ^{13}C NMR (63 MHz, CDCl_3) δ 146.5, 142.2, 138.0, 131.5, 128.5, 127.8, 127.6, 126.2, 115.9, 109.5, 43.8, 22.1. HRMS (ESI, m/z) calcd for $\text{C}_{14}\text{H}_{15}\text{BrN}$ $[\text{M}+\text{H}]^+$: 276.0388, found 276.0367.



II3i 2-fluoro-6-(1-phenylethyl)aniline

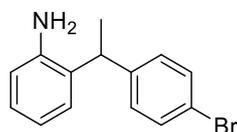
Following the general procedure, product **II3i** was obtained as a colorless oil in 61% yield after purification. ^1H NMR (250 MHz, CDCl_3) δ 7.36 – 7.09 (m, 5H), 6.91 – 6.65 (m, 3H), 4.06 (q, $J = 7.2$ Hz, 1H), 3.62 (s, 2H), 1.60 (d, $J = 7.2$ Hz, 3H). ^{13}C NMR (63 MHz, CDCl_3) δ 151.79 (d, **CF**, $J = 238.6$ Hz), 146.6, 137.6 (d, **m¹-CF**, $J = 5.5$ Hz), 132.40 (d, **o¹-CF**, $J = 13.2$ Hz), 128.5, 127.6, 126.2, 123.5 (d, **p-CF**, $J = 2.6$ Hz), 116.9 (d, **m²-CF**, $J = 4.1$ Hz), 114.56 (d, **o²-CF**, $J = 18.7$ Hz), 44.0, 22.1. ^{19}F NMR (235 MHz, CDCl_3) δ -135.0. Spectroscopic data for **II3i** match those previously reported in literature for.^[172]



II3j 2-(1-(4-chlorophenyl)ethyl)aniline

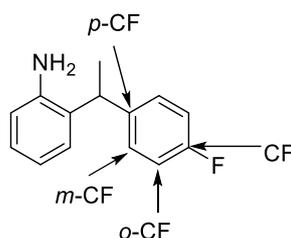
Following the general procedure, product **II3j** was obtained as a colorless oil in 60% yield after purification. ^1H NMR (360 MHz, CDCl_3) δ 7.32 – 7.24 (m, 3H), 7.21 – 7.10 (m, 3H), 6.89 (td, $J = 7.5, 1.3$ Hz, 1H), 6.70 (dd, $J = 7.8, 1.3$ Hz, 1H), 4.09 (q, $J = 7.2$ Hz, 1H), 3.43 (s, 2H), 1.64 (d, $J = 7.2$ Hz, 3H). ^{13}C NMR (63 MHz, CDCl_3) δ 144.3, 132.2,

129.4, 129.0, 127.6, 127.3, 119.0, 116.5, 39.7, 21.8. HRMS (ESI, m/z) calcd for $C_{14}H_{15}N$ $[M+H]^+$: 232.0893, found 232.0877.



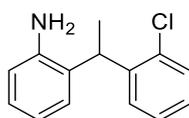
II3k 2-(1-(4-bromophenyl)ethyl)aniline

Following the general procedure, product **II3k** was obtained as a colorless oil in 61% yield after purification. 1H NMR (300 MHz, $CDCl_3$) δ 7.47 – 7.38 (m, 2H), 7.32 – 7.24 (m, 1H), 7.17 – 7.04 (m, 3H), 6.88 (td, $J = 7.5, 1.3$ Hz, 1H), 6.68 (dd, $J = 7.9, 1.3$ Hz, 1H), 4.07 (q, $J = 7.2$ Hz, 1H), 3.40 (s, 3H), 1.63 (d, $J = 7.2$ Hz, 3H). ^{13}C NMR (63 MHz, $CDCl_3$) δ 144.8, 144.2, 131.9, 129.4, 127.6, 127.3, 120.3, 119.0, 116.5, 39.8, 21.8. HRMS (ESI, m/z) calcd for $C_{14}H_{15}BrN$ $[M+H]^+$: 276.0388, found 276.0373.



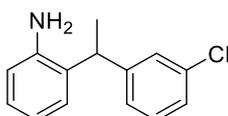
II3l 2-(1-(4-fluorophenyl)ethyl)aniline

Following the general procedure, product **II3l** was obtained as a colorless oil in 63% yield after purification. 1H NMR (300 MHz, $CDCl_3$) δ 7.34 – 7.25 (m, 1H), 7.16 (ddd, $J = 17.4, 11.6, 6.4$ Hz, 3H), 6.99 (t, $J = 8.6$ Hz, 2H), 6.88 (t, $J = 7.7$ Hz, 1H), 6.68 (d, $J = 7.9$ Hz, 1H), 4.09 (q, $J = 7.1$ Hz, 1H), 3.35 (s, 2H), 1.63 (d, $J = 7.1$ Hz, 3H). ^{13}C NMR (63 MHz, $CDCl_3$) δ 161.45 (d, CF, $J = 244.7$ Hz), 144.3 (*p*-CF), 141.4, 129.7, 129.0 (d, *m*-CF, $J = 8.0$ Hz), 127.40 (d, *o*-CF, $J = 15.9$ Hz) 119.0, 116.5, 115.8, 115.5, 39.6, 22.0. Spectroscopic data for **II3l** match those previously reported in literature for.^[188]



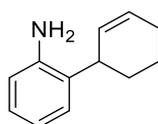
II3p 2-(1-(2-chlorophenyl)ethyl)aniline

Following the general procedure, product **II3p** was obtained as a colorless oil in 51% yield after purification. ^1H NMR (300 MHz, CDCl_3) δ 7.31 – 7.18 (m, 4H), 7.17 – 7.08 (m, 2H), 6.88 (td, $J = 7.5, 1.3$ Hz, 1H), 6.69 (dd, $J = 7.8, 1.3$ Hz, 1H), 4.09 (q, $J = 7.2$ Hz, 1H), 3.43 (s, 2H), 1.64 (d, $J = 7.2$ Hz, 3H). ^{13}C NMR (63 MHz, CDCl_3) δ 148.0, 144.2, 134.7, 130.1, 129.1, 127.7 (2CH), 127.4, 126.8, 125.8, 119.0, 116.5, 40.1, 21.8. HRMS (ESI, m/z) calcd for $\text{C}_{14}\text{H}_{15}\text{ClN}$ $[\text{M}+\text{H}]^+$: 232.0893, found 232.0905.



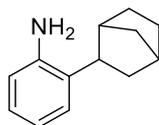
II3q 2-(1-(3-chlorophenyl)ethyl)aniline

Following the general procedure, product **II3q** was obtained as a colorless oil in 47% yield after purification. ^1H NMR (360 MHz, CDCl_3) δ 7.38 (dd, $J = 5.8, 3.5$ Hz, 1H), 7.33 – 7.28 (m, 1H), 7.18 – 7.07 (m, 3H), 7.03 (dd, $J = 5.8, 3.7$ Hz, 1H), 6.86 (td, $J = 7.5, 1.3$ Hz, 1H), 6.66 (dd, $J = 7.8, 1.3$ Hz, 1H), 4.53 (q, $J = 7.0$ Hz, 1H), 1.59 (d, $J = 7.0$ Hz, 3H). ^{13}C NMR (63 MHz, CDCl_3) δ 144.2, 143.1, 133.6, 129.6, 128.9, 128.6, 127.8, 127.5, 127.2, 118.7, 116.1, 36.3, 20.3. HRMS (ESI, m/z) calcd for $\text{C}_{14}\text{H}_{15}\text{ClN}$ $[\text{M}+\text{H}]^+$: 232.0893, found 232.0902.



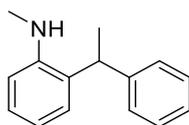
II3r 1',2',3',4'-tetrahydro-[1,1'-biphenyl]-2-amine

Following the general procedure, product **II3r** was obtained as a colorless oil in 62% yield after purification. ^1H NMR (360 MHz, CDCl_3) δ 7.12 – 7.02 (m, 2H), 6.75 (td, $J = 7.4, 1.3$ Hz, 1H), 6.68 (dd, $J = 7.8, 1.3$ Hz, 1H), 6.01 – 5.91 (m, 1H), 5.79 – 5.68 (m, 1H), 3.69 (s, 2H), 3.48 – 3.37 (m, 1H), 2.16 – 2.07 (m, 2H), 2.03 – 1.91 (m, 1H), 1.83 – 1.57 (m, 4H). ^{13}C NMR (91 MHz, CDCl_3) δ 144.1, 130.0, 129.9, 129.2, 127.2, 118.7, 116.2, 38.1, 28.5, 25.1, 21.3. Spectroscopic data for **II3r** match those previously reported in literature for.^[184]



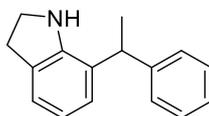
II3s 2-(bicyclo[2.2.1]heptan-2-yl)aniline

Following the general procedure, product **II3s** was obtained as a red-brown oil in 44% yield after purification. ^1H NMR (360 MHz, CDCl_3) δ 7.15 (dd, $J = 7.7, 1.4$ Hz, 1H), 7.02 (td, $J = 7.6, 1.4$ Hz, 1H), 6.76 (td, $J = 7.6, 1.3$ Hz, 1H), 6.69 (dd, $J = 7.7, 1.3$ Hz, 1H), 3.63 (s, 2H), 2.59 (dd, $J = 9.0, 5.3$ Hz, 1H), 2.50 – 2.45 (m, 1H), 2.41 – 2.35 (m, 1H), 1.84 – 1.76 (m, 1H), 1.68 – 1.53 (m, 4H), 1.37 – 1.27 (m, 3H). ^{13}C NMR (91 MHz, CDCl_3) δ 131.6, 126.4, 125.5, 118.5, 42.1, 40.5, 38.0, 37.0, 36.4, 30.4, 29.4. Spectroscopic data for **II3s** match those previously reported in literature for.^[175]



II3t *N*-methyl-2-(1-phenylethyl)aniline

Following the general procedure, product **II3t** was obtained as a colorless oil in 46% yield after purification. ^1H NMR (360 MHz, CDCl_3) δ 7.31 – 7.24 (m, 4H), 7.23 – 7.16 (m, 4H), 6.82 (td, $J = 7.4, 1.3$ Hz, 1H), 6.63 (dd, $J = 8.0, 1.3$ Hz, 1H), 4.03 (q, $J = 7.2$ Hz, 1H), 3.48 (s, 1H), 2.71 (s, 3H), 1.62 (d, $J = 7.1$ Hz, 3H). ^{13}C NMR (91 MHz, CDCl_3) δ 146.9, 145.8, 129.4, 128.9, 127.5, 126.9, 126.5, 117.1, 110.4, 40.0, 31.0, 22.4. Spectroscopic data for **II3t** match those previously reported in literature for.^[175]

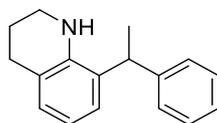


II3u 7-(1-phenylethyl)indoline

Following the general procedure, product **II3u** was obtained as a colorless oil in 99% yield after purification. ^1H NMR (360 MHz, CDCl_3) δ 7.32 – 7.25 (m, 2H), 7.25 – 7.17 (m, 3H), 7.11 – 7.03 (m, 2H), 6.78 (t, $J = 7.5$ Hz, 1H), 4.01 (q, $J = 7.2$ Hz, 1H), 3.51 – 3.30 (m, 2H), 3.06 – 2.96 (m, 2H), 1.62 (d, $J = 7.2$ Hz, 3H). ^{13}C NMR (91 MHz, CDCl_3)

δ 149.8, 145.7, 129.5, 128.8, 127.6, 127.1, 125.1, 122.8, 47.2, 40.9, 30.0, 21.2.

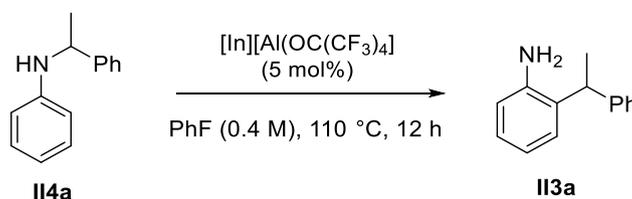
Spectroscopic data for **II3u** match those previously reported in literature for.^[191]



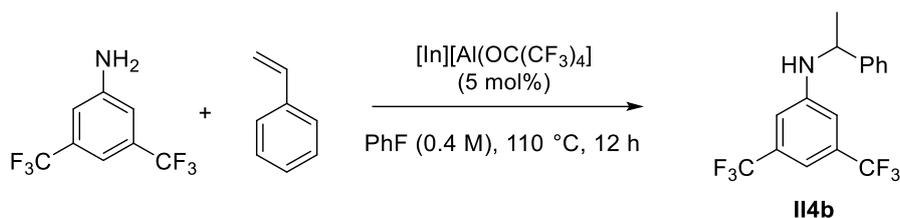
II3v 8-(1-phenylethyl)-1,2,3,4-tetrahydroquinoline

Following the general procedure, product **II3v** was obtained as a colorless oil in 89% yield after purification. ¹H NMR (360 MHz, CDCl₃) δ 7.34 – 7.27 (m, 2H), 7.26 – 7.20 (m, 3H), 7.17 – 7.11 (m, 1H), 6.95 (dd, J = 7.5, 1.4 Hz, 1H), 6.74 (t, J = 7.5 Hz, 1H), 4.00 (q, J = 7.1 Hz, 1H), 3.29 – 3.19 (m, 1H), 3.18 – 3.09 (m, 1H), 2.80 (t, J = 6.6 Hz, 2H), 1.96 – 1.80 (m, 2H), 1.63 (d, J = 7.1 Hz, 3H). ¹³C NMR (91 MHz, CDCl₃) δ 146.0, 142.3, 128.8, 128.0, 127.6, 126.4, 124.9, 122.1, 116.7, 42.4, 39.8, 27.7, 22.5, 22.0. Spectroscopic data for **II3v** match those previously reported in literature for.^[191]

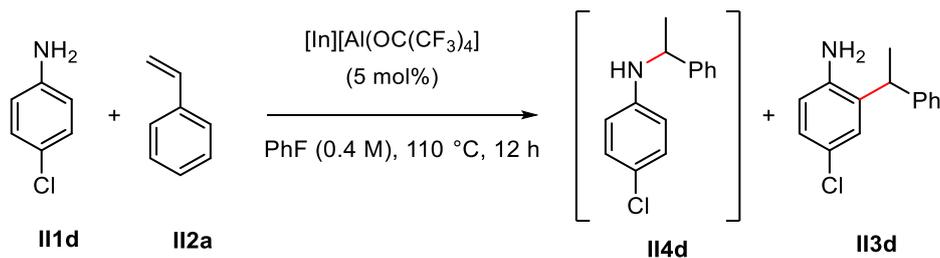
3.3 Mechanistic Investigations of Intermolecular Hydroarylation



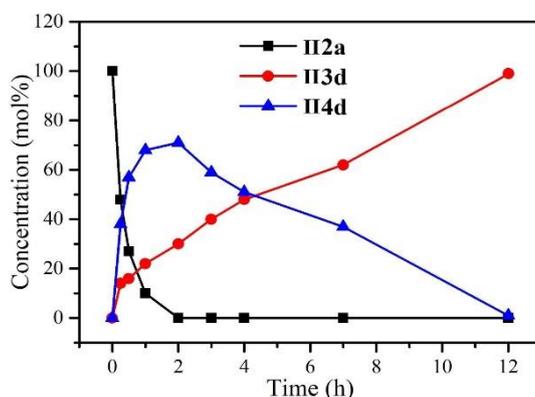
The investigation of Hoffmann-Martius rearrangement is followed by the general procedure. The substrate **II4a** was synthesized by the reported method.^[207] In glove box, a drying reaction tube was charged with [In(PhF)₂][Al(OC(CF₃)₃)₄] (0.05 equiv, 13 mg, 0.01 mmol) and anhydrous degassed PhF (0.5 mL, 0.4 M). The compounds **II4a** (1 equiv, 39.5 mg, 0.2 mmol) was added in this solution. The reaction tube was sealed with a screw cap and stirred outside of the glove box at 110 °C for 12 h. The reaction mixture was diluted with Et₂O, filtered through a pad of celite (thoroughly rinsed with Et₂O) and concentrated under reduced pressure by rotary evaporation. Purification by FC over neutral Al₂O₃ (MeOH/CH₂Cl₂ = 95/5) afforded desired product **II3a** in 43% yield.



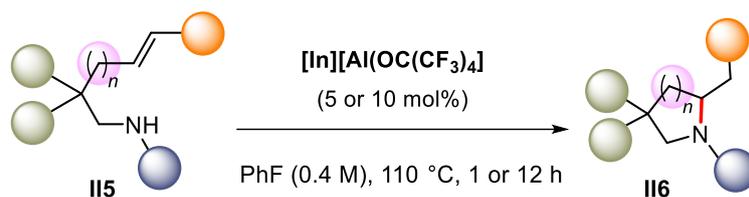
The hydroamination product **II4b** was obtained in 78% yield followed the general catalytic procedure using 3,5-bis(trifluoromethyl)aniline (1 equiv, 45.8 mg, 0.2 mmol) and styrene (1equiv, 20.8mg, 0.2 mmol). ^1H NMR (360 MHz, CDCl_3) δ 7.35 (s, 4H), 7.30 – 7.25 (m, 1H), 7.09 (s, 1H), 6.86 (s, 2H), 4.59 – 4.46 (m, 2H), 1.57 (d, $J = 6.5$ Hz, 3H). ^{13}C NMR (91 MHz, CDCl_3) δ 147.8, 132.5, 132.2, 129.1, 127.7, 125.8, 125.1, 122.1, 112.6, 112.5, 110.4, 110.3, 53.6, 24.7. ^{19}F NMR (235 MHz, CDCl_3) δ -63.2. Spectroscopic data for **II4b** match those previously reported in literature for.^[172]



The GC monitoring experiment of the generation of **II3d** was following the general experiment by taking sample at 15 min, 30 min, 1 h, 2 h, 3 h, 4 h, 7h, and 12 h. All calibrations were performed using 4-*ter*-butylcyclohexanone as an internal standard with four-point.

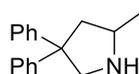


3.4 Procedures for the Intramolecular Hydroamination



For substrates II5a-m: In a glove box, $[\text{In}][\text{Al}(\text{OC}(\text{CF}_3)_3)_4]$ (26mg, 0.02 mmol, 0.1 equiv) was added into anhydrous degassed fluorobenzene (0.5 mL) in a reaction tube. Then alkenylamine **II5a-m** (0.2 mmol) was added in this solution. The reaction tube was sealed with a screw cap and stirred outside of the glove box at 110 °C for 12 h. The reaction mixture was diluted with Et_2O , filtered through a pad of aluminum oxide (thoroughly rinsed with Et_2O) and concentrated under reduced pressure by rotary evaporation. Purification by FC over neutral Al_2O_3 (cyclohexane/ EtOAc = 95/5) afforded desired product **II6a-m**.

For substrates II5n-z: In a glove box, $[\text{In}][\text{Al}(\text{OC}(\text{CF}_3)_3)_4]$ (13 mg, 0.01 mmol, 0.05 equiv) was added into anhydrous degassed fluorobenzene (0.5 mL) in a reaction tube. Then alkenylamine **II5n-z** (0.2 mmol) was added in this solution. The reaction tube was sealed with a screw cap and stirred outside of the glove box at 110 °C for 1 h. The reaction mixture was diluted with Et_2O , filtered through a pad of aluminum oxide (thoroughly rinsed with Et_2O) and concentrated under reduced pressure by rotary evaporation. Purification by FC over silica gel (cyclohexane/ EtOAc = 95/5) afforded desired product **II6n-z**.



II6a 2-methyl-4,4-diphenylpyrrolidine

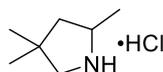
Following the general procedure, product **II6a** was obtained as a colorless oil in 89% yield after purification. ^1H NMR (250 MHz, CDCl_3) δ 7.24 – 7.06 (m, 10H), 3.60 (dd, J = 11.4, 1.1 Hz, 1H), 3.39 (d, J = 11.4 Hz, 1H), 3.34 – 3.23 (m, 1H), 2.67 (dd, J = 12.7,

6.6 Hz, 1H), 2.00 (s, 1H, *NH*), 1.98 – 1.91 (m, 1H), 1.13 (d, *J* = 6.4 Hz, 3H). ¹³C NMR (75 MHz, CDCl₃) δ 147.7, 146.9, 128.4, 127.1, 127.0, 126.1, 57.6, 57.2, 53.1, 47.0, 22.1. Spectroscopic data for **II6a** match those previously reported in the literature.^[213]



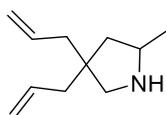
II6b 3-methyl-2-azaspiro[4.5]decane

Following the general procedure, product **II 6b** was obtained as a colorless oil in 42% yield after purification. ¹H NMR (360 MHz, CDCl₃) δ 3.21 – 3.09 (m, 1H), 2.79 (d, *J* = 11.0 Hz, 1H), 2.61 (d, *J* = 11.0 Hz, 1H), 1.95 (brs, 2H, *NH*₂), 1.75 (dd, *J* = 12.5, 6.6 Hz, 1H), 1.47 – 1.31 (m, 10H), 1.14 (d, *J* = 6.3 Hz, 3H), 1.00 (dd, *J* = 12.5, 9.2 Hz, 1H). ¹³C NMR (91 MHz, CDCl₃) δ 59.3, 54.2, 47.7, 44.1, 38.8, 37.4, 26.2, 24.0, 23.8, 21.6. Spectroscopic data for **II6b** match those previously reported in the literature.^[213]



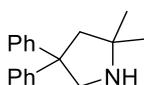
II6c 2,4,4-trimethylpyrrolidine hydrochloride

The product **II6c** was obtained as colorless crystals in 37% yield following with a modified purification procedure.³ Once the reaction was over, the reaction mixture was concentrated, and the residue was dissolved in Et₂O (15 mL). The solution was acidified with aqueous HCl (2 M, 15 mL), and extracted with aqueous HCl (2 M, 5 mL × 3). The combined aqueous layers were evaporated under reduced pressure to give the pure desired product. ¹H NMR (360 MHz, CDCl₃) δ 9.90 (s, 1H), 9.47 (s, 1H), 3.92 – 3.75 (m, 1H), 3.17 – 3.05 (m, 1H), 3.05 – 2.93 (m, 1H), 1.91 (dd, *J* = 12.9, 6.4 Hz, 1H), 1.62 – 1.55 (m, 1H), 1.52 (d, *J* = 6.4 Hz, 3H), 1.20 (s, 3H), 1.16 (s, 3H). ¹³C NMR (91 MHz, CDCl₃) δ 56.6, 55.6, 47.1, 39.0, 27.4, 18.3 (2C). Spectroscopic data for **II6c** match those previously reported in the literature.^[208]



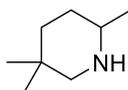
II6d 4,4-diallyl-2-methylpyrrolidine

Following the general procedure, product **II6d** was obtained as a colorless oil in 30% yield after purification. ^1H NMR (300 MHz, CDCl_3) δ 5.75 (ddt, $J = 17.5, 10.2, 7.3$ Hz, 2H), 5.23 – 5.11 (m, 4H), 3.80 – 3.66 (m, 1H), 3.16 (d, $J = 11.9$ Hz, 1H), 3.05 (d, $J = 11.9$ Hz, 1H), 2.30 (d, $J = 7.3$ Hz, 2H), 2.22 (d, $J = 7.4$ Hz, 2H), 2.02 (dd, $J = 13.4, 6.6$ Hz, 1H), 1.62 – 1.55 (m, 1H), 1.53 (d, $J = 6.6$ Hz, 3H). ^{13}C NMR (91 MHz, CDCl_3) δ 133.2, 132.9, 119.9, 119.5, 55.3, 53.1, 45.2, 43.0, 42.1, 40.9, 18.1. Spectroscopic data for **II6d** match those previously reported in the literature.^[233]



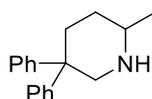
II6f 2,2-dimethyl-4,4-diphenylpyrrolidine

Following the general procedure, product **II6f** was obtained as a colorless oil in 40% yield after purification. ^1H NMR (360 MHz, CDCl_3) δ 7.25 – 7.16 (m, 8H), 7.12 – 7.05 (m, 2H), 3.60 (s, 2H), 2.49 (s, 2H), 1.10 (s, 6H). ^{13}C NMR (91 MHz, CDCl_3) δ 147.5, 128.6, 128.6, 127.1, 126.1, 59.8, 58.3, 57.1, 52.1, 30.7. Spectroscopic data for **II6f** match those previously reported in the literature.^[213]



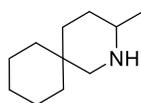
II6k 2,5,5-trimethylpiperidine

Following the general procedure, product **II6k** was obtained as a colorless oil in 88% yield after purification. ^1H NMR (300 MHz, CDCl_3) δ 2.59 (dd, $J = 12.3, 2.4$ Hz, 1H), 2.54 – 2.39 (m, 2H), 1.48 – 1.38 (m, 2H), 1.27 – 1.21 (m, 2H), 1.07 (d, $J = 6.3$ Hz, 3H), 0.96 (s, 3H), 0.83 (s, 3H). ^{13}C NMR (75 MHz, CDCl_3) δ 58.7, 52.4, 38.0, 31.2, 29.8, 29.4, 23.8, 22.7. Spectroscopic data for **II6k** match those previously reported in the literature.^[213]



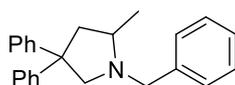
II6l 2-methyl-5,5-diphenylpiperidine

Following the general procedure, product **II6l** was obtained as a colorless oil in 88% yield after purification. ^1H NMR (360 MHz, CDCl_3) δ 6.92 – 6.89 (m, 2H), 6.87 – 6.81 (m, 2H), 6.75 – 6.59 (m, 6H), 3.40 (dd, $J = 13.7, 3.1$ Hz, 1H), 2.60 (d, $J = 13.7$ Hz, 1H), 2.34 – 2.22 (m, 1H), 2.21 (ddd, $J = 13.8, 6.6, 3.5$ Hz, 1H), 1.71 (dt, $J = 13.3, 3.5$ Hz, 1H), 1.13 (ddd, $J = 13.3, 6.6, 3.5$ Hz, 1H), 0.72 – 0.58 (m, 1H), 0.50 (d, $J = 6.3$ Hz, 3H). ^{13}C NMR (91 MHz, CDCl_3) δ 148.9, 144.8, 128.7, 128.3, 126.6, 126.5, 125.8, 125.8, 55.8, 52.3, 45.3, 35.4, 31.4, 22.5. Spectroscopic data for **II6l** match those previously reported in the literature.^[213]



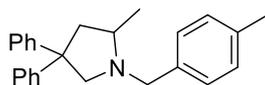
II6m 3-methyl-2-azaspiro[5.5]undecane

Following the general procedure, product **II6m** was obtained as a colorless oil in 99% yield after purification. ^1H NMR (300 MHz, CDCl_3) δ 3.17 (dd, $J = 13.1, 1.4$ Hz, 2H), 3.07 – 2.94 (m, 1H), 2.53 (d, $J = 13.1$ Hz, 1H), 1.85 – 1.72 (m, 1H), 1.73 – 1.56 (m, 4H), 1.50 (d, $J = 6.5$ Hz, 3H), 1.45 – 1.32 (m, 6H), 1.31 – 1.11 (m, 3H). ^{13}C NMR (75 MHz, CDCl_3) δ 53.3, 52.3, 37.8, 32.9, 31.6, 31.5, 26.5, 26.2, 21.2, 21.2, 18.9. Spectroscopic data for **II6m** match those previously reported in the literature.^[229]



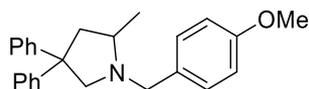
II6n 1-benzyl-2-methyl-4,4-diphenylpyrrolidine

Following the general procedure, product **II6n** was obtained as a colorless oil in 81% yield after purification. ^1H NMR (250 MHz, CDCl_3) δ 7.44 – 7.10 (m, 15H), 4.13 (d, $J = 13.3$ Hz, 1H), 3.68 (d, $J = 9.9$ Hz, 1H), 3.28 (d, $J = 13.2$ Hz, 1H), 3.02 – 2.73 (m, 3H), 2.24 (dd, $J = 12.1, 7.3$ Hz, 1H), 1.21 (d, $J = 5.7$ Hz, 3H). ^{13}C NMR (91 MHz, CDCl_3) δ 150.7, 148.8, 140.2, 128.7, 128.3, 128.3, 127.9, 127.6, 126.9, 125.9, 125.5, 66.5, 59.8, 58.1, 52.6, 48.1, 19.6. Spectroscopic data for **II6n** match those previously reported in the literature.^[209]



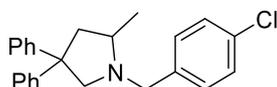
II6o 2-methyl-1-(4-methylbenzyl)-4,4-diphenylpyrrolidine

Following the general procedure, product **II6o** was obtained as a colorless oil in 81% yield after purification. ^1H NMR (250 MHz, CDCl_3) δ 7.38 – 7.08 (m, 14H), 4.13 (d, $J = 13.3$ Hz, 1H), 3.70 (d, $J = 9.8$ Hz, 1H), 3.26 (d, $J = 13.3$ Hz, 1H), 3.04 – 2.78 (m, 3H), 2.41 (s, 3H), 2.28 (dd, $J = 12.1, 7.2$ Hz, 1H), 1.24 (d, $J = 5.8$ Hz, 3H). ^{13}C NMR (63 MHz, CDCl_3) δ 150.7, 148.9, 140.2, 137.9, 129.4, 128.2, 127.9, 127.6, 127.4, 125.9, 125.7, 125.5, 66.4, 59.7, 58.0, 52.7, 48.1, 21.6, 19.6. Spectroscopic data for **II6o** match those previously reported in the literature.^[217]



II6p 1-(4-methoxybenzyl)-2-methyl-4,4-diphenylpyrrolidine

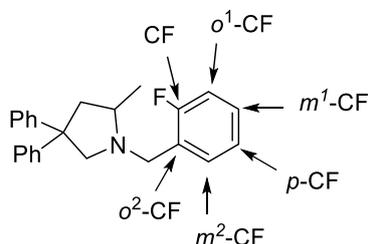
Following the general procedure, product **II6p** was obtained as a colorless oil in 78% yield after purification. ^1H NMR (250 MHz, CDCl_3) δ 7.41 – 7.08 (m, 12H), 6.98 – 6.83 (m, 2H), 4.07 (d, $J = 12.9$ Hz, 1H), 3.85 (s, 3H), 3.67 (d, $J = 9.8$ Hz, 1H), 3.22 (d, $J = 13.0$ Hz, 1H), 3.04 – 2.72 (m, 4H), 2.23 (dd, $J = 12.4, 7.5$ Hz, 1H), 1.20 (d, $J = 5.8$ Hz, 3H). ^{13}C NMR (63 MHz, CDCl_3) δ 158.6, 150.8, 148.9, 132.2, 129.8, 128.2, 127.9, 127.6, 127.4, 125.9, 125.5, 113.7, 66.4, 59.7, 57.4, 55.4, 52.6, 48.2, 19.6. Spectroscopic data for **II6p** match those previously reported in the literature.^[209]



II6q 1-(4-chlorobenzyl)-2-methyl-4,4-diphenylpyrrolidine

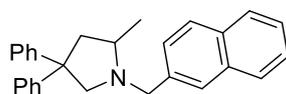
Following the general procedure, product **II6q** was obtained as a colorless oil in 76% yield after purification. ^1H NMR (360 MHz, CDCl_3) δ 7.36 – 7.13 (m, 14H), 4.06 (d, $J = 13.5$ Hz, 1H), 3.65 (d, $J = 9.9$ Hz, 1H), 3.27 (d, $J = 13.5$ Hz, 1H), 2.96 (dd, $J = 12.6, 7.7$ Hz, 1H), 2.92 – 2.75 (m, 2H), 2.26 (dd, $J = 12.5, 7.5$ Hz, 1H), 1.20 (d, $J = 5.9$ Hz, 3H). ^{13}C NMR (91 MHz, CDCl_3) δ 150.5, 148.7, 138.7, 132.5, 130.0, 128.5, 128.3,

128.0, 127.5, 127.3, 126.0, 125.6, 66.5, 59.8, 57.4, 52.7, 48.0, 19.6. Spectroscopic data for **II6q** match those previously reported in the literature.^[209]



II6r 1-(2-fluorobenzyl)-2-methyl-4,4-diphenylpyrrolidine

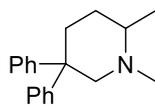
Following the general procedure, product **II6r** was obtained as a colorless oil in 77% yield after purification. ¹H NMR (300 MHz, CDCl₃) δ 7.25 (td, *J* = 7.4, 1.9 Hz, 1H), 7.12 – 6.80 (m, 13H), 3.80 (t, *J* = 13.8 Hz, 1H), 3.49 (d, *J* = 9.8 Hz, 1H), 3.36 (d, *J* = 13.8 Hz, 1H), 2.78 – 2.62 (m, 3H), 2.12 – 1.97 (m, 1H), 1.00 (d, *J* = 5.6 Hz, 3H). ¹³C NMR (63 MHz, Chloroform-*d*) δ 161.26 (d, CF, *J* = 245.9 Hz), 150.63, 148.70, 131.25 (d, *m*¹-CF, *J* = 3.8 Hz), 128.47 (d, *p*-CF, *J* = 8.5 Hz), 128.29, 127.89, 127.57, 127.35, 126.58 (d, *o*²-CF, *J* = 14.2 Hz), 125.97, 125.59, 123.99 (d, *m*²-CF, *J* = 2.8 Hz), 115.28 (d, *o*¹-CF, *J* = 22.1 Hz), 66.31, 59.40, 52.69, 50.06, 48.01, 19.57. ¹⁹F NMR (300 MHz, CDCl₃) δ -118.5. HRMS (ESI, *m/z*) calcd for C₂₄H₂₅FN [M+H]⁺: 346.1971, found 346.1967.



II6s 2-methyl-1-(naphthalen-2-ylmethyl)-4,4-diphenylpyrrolidine

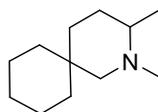
Following the general procedure, product **II6s** was obtained as a colorless oil in 85% yield after purification. ¹H NMR (360 MHz, CDCl₃) δ 7.92 – 7.80 (m, 4H), 7.62 (dd, *J* = 8.4, 1.4 Hz, 1H), 7.56 – 7.48 (m, 2H), 7.34 – 7.14 (m, 10H), 4.30 (d, *J* = 13.3 Hz, 1H), 3.72 (d, *J* = 9.8 Hz, 1H), 3.46 (d, *J* = 13.3 Hz, 1H), 3.05 – 2.83 (m, 3H), 2.32 (dd, *J* = 11.7, 6.7 Hz, 1H), 1.28 (d, *J* = 5.8 Hz, 3H). ¹³C NMR (63 MHz, CDCl₃) δ 150.6, 148.8, 137.9, 133.6, 132.9, 128.3, 128.0, 127.8, 127.5, 127.4, 127.3, 126.9, 126.0, 125.9, 125.6, 66.5, 59.9, 58.2, 52.7, 48.0, 19.7. HRMS (ESI, *m/z*) calcd for C₂₈H₂₈N [M+H]⁺:

378.2222, found 378.2215.



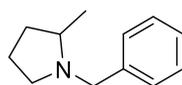
II6t 1,2-dimethyl-5,5-diphenylpiperidine

Following the general procedure, product **II6t** was obtained as a colorless oil in 85% yield after purification. ^1H NMR (300 MHz, CDCl_3) δ 7.53 – 7.46 (m, 2H), 7.35 – 7.15 (m, 8H), 3.56 (dd, $J = 12.2, 1.8$ Hz, 1H), 2.48 (dq, $J = 12.2, 3.2$ Hz, 1H), 2.42 – 2.36 (m, 1H), 2.34 (s, 3H), 2.22 (td, $J = 12.9, 3.6$ Hz, 1H), 2.15 – 2.01 (m, 1H), 1.60 (ddd, $J = 13.1, 6.8, 3.6$ Hz, 1H), 1.32 (qd, $J = 13.1, 3.0$ Hz, 1H), 1.10 (d, $J = 6.2$ Hz, 3H). ^{13}C NMR (63 MHz, CDCl_3) δ 149.0, 146.9, 128.8, 128.1, 127.8, 126.8, 125.8, 125.3, 66.0, 59.0, 46.7, 43.2, 35.2, 31.0, 19.7. Spectroscopic data for **II6t** match those previously reported in the literature.^[229]



II6u 2,3-dimethyl-2-azaspiro[5.5]undecane

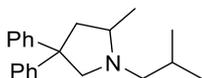
Following the general procedure, product **II6u** was obtained as a colorless oil in 72% yield after purification. ^1H NMR (300 MHz, CDCl_3) δ 2.63 (dd, $J = 11.5, 2.4$ Hz, 1H), 2.17 (s, 3H), 1.77 – 1.45 (m, 5H), 1.46 – 1.30 (m, 8H), 1.19 – 1.10 (m, 2H), 1.04 (d, $J = 6.1$ Hz, 3H), 1.02 – 0.92 (m, 1H). ^{13}C NMR (75 MHz, CDCl_3) δ 67.4, 60.4, 44.0, 38.9, 35.0, 33.2, 32.7, 30.6, 27.0, 21.7, 21.7, 20.1. Spectroscopic data for **II6u** match those previously reported in the literature.^[229]



II6w 1-benzyl-2-methylpyrrolidine

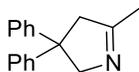
Following the general procedure, product **II6w** was obtained as a colorless oil in 86% yield after purification. ^1H NMR (360 MHz, CDCl_3) δ 7.42 – 7.20 (m, 5H), 4.03 (d, $J = 12.8$ Hz, 1H), 3.15 (d, $J = 12.8$ Hz, 1H), 3.01 – 2.86 (m, 1H), 2.49 – 2.33 (m, 1H),

2.18 – 2.06 (m, 1H), 2.00 – 1.92 (m, 1H), 1.76 – 1.58 (m, 2H), 1.51 – 1.41 (m, 1H), 1.18 (d, $J = 6.0$ Hz, 3H). ^{13}C NMR (91 MHz, CDCl_3) δ 139.6, 129.2, 128.3, 126.9, 59.7, 58.5, 54.2, 32.9, 21.6, 19.3. Spectroscopic data for **II6w** match those previously reported in the literature.^[209]



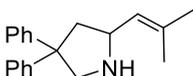
II6x 1-isobutyl-2-methyl-4,4-diphenylpyrrolidine

Following the general procedure, product **II6x** was obtained as a colorless oil in 75% yield after purification. ^1H NMR (250 MHz, CDCl_3) δ 7.39 – 7.11 (m, 10H), 3.86 (d, $J = 9.6$ Hz, 1H), 2.94 – 2.75 (m, 2H), 2.74 – 2.58 (m, 1H), 2.50 – 2.37 (m, 1H), 2.23 – 2.05 (m, 2H), 1.92 – 1.72 (m, 1H), 1.11 (d, $J = 6.0$ Hz, 3H), 1.02 (d, $J = 6.5$ Hz, 3H), 0.94 (d, $J = 6.6$ Hz, 3H). ^{13}C NMR (63 MHz, CDCl_3) δ 151.4, 149.0, 128.3, 127.9, 127.7, 127.4, 125.9, 125.5, 67.6, 62.8, 60.4, 52.9, 48.2, 27.9, 21.5, 21.0, 19.7. Spectroscopic data for **II6x** match those previously reported in the literature.^[229]



II6y 5-methyl-3,3-diphenyl-3,4-dihydro-2H-pyrrole

Following the general procedure, product **II6y** was obtained as a colorless oil in 91% yield after purification. ^1H NMR (250 MHz, CDCl_3) δ 7.43 – 6.99 (m, 10H), 4.46 (q, $J = 1.7$ Hz, 2H), 3.21 (s, 2H), 2.09 (t, $J = 1.8$ Hz, 3H). ^{13}C NMR (63 MHz, CDCl_3) δ 174.6, 148.0, 128.5, 127.1, 126.3, 73.1, 56.4, 52.8, 20.3. Spectroscopic data for **II6y** match those previously reported in the literature.^[234]



II6z 2-(2-methylprop-1-en-1-yl)-4,4-diphenylpyrrolidine

Following the general procedure, product **II6z** was obtained as a colorless oil in 78% yield after purification. ^1H NMR (360 MHz, CDCl_3) δ 7.39 – 7.24 (m, 8H), 7.23 – 7.16 (m, 2H), 5.25 – 5.20 (m, 1H), 4.02 (td, $J = 8.9, 7.0$ Hz, 1H), 3.74 (dd, $J = 11.1, 1.4$ Hz, 1H), 3.52 (d, $J = 11.1$ Hz, 1H), 2.80 – 2.72 (m, 1H), 2.21 (dd, $J = 12.7, 8.9$ Hz, 1H),

1.72 (d, $J = 1.4$ Hz, 3H), 1.66 (d, $J = 1.4$ Hz, 3H). ^{13}C NMR (63 MHz, CDCl_3) δ 146.9, 146.1, 135.9, 128.7, 128.5, 127.6, 127.4, 127.0, 126.5, 125.7, 77.2, 56.7, 56.3, 55.7, 45.7, 25.9, 18.5. Spectroscopic data for **II6z** match those previously reported in the literature.^[234]

CHAPTER III: BIMOLECULAR VINYLATION OF ARENES BY VINYL CATIONS

1. INTRODUCTION

1.1 Vinyl Cations

A vinyl cation is a carbocation with the positive charge on an alkene carbon. More generally, it is a disubstituted trivalent carbenium ion (Figure 37).^[235]

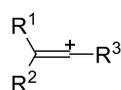


Figure 37. Vinyl cation structure

The chemistry of vinyl cations has been studied as early as the 1960s.^[236] It was first postulated by Grob and co-workers in 1964, in the solvolysis of α -aryl vinyl halides.^[237] Afterwards, numerous solvolysis reactions were established to involve vinyl cation as intermediates.^[236,238,239] However, it was not before 2004 that the first X-ray structure of a vinyl cation was reported by Reed et al.^[240] They found the molecule is linear around the dicoordinated carbon atom C_{α} (bond angle $\alpha = C_{\beta}-C_{\alpha}-C = 178.88$), which indicates a sp hybridization as previously predicted by calculations. ^{13}C NMR study showed a chemical shift with $\delta^{13}\text{C}_{\alpha} = 202.7$ ppm and $\delta^{13}\text{C}_{\beta} = 75.5$ ppm. Furthermore, the IR spectra shows that the $\text{C}=\text{C}^{+}$ stretching vibration is at $\nu = 1986$ cm^{-1} .

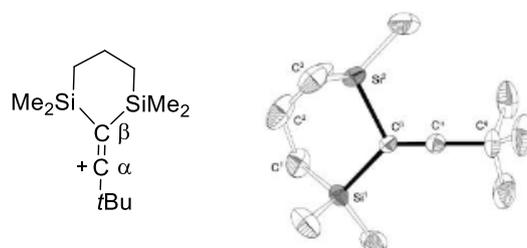


Figure 38. X-ray structure of β -silyl substituted vinyl cation (anion $[\text{CB}_{11}\text{H}_6\text{Br}_5]^-$ and hydrogen atoms omitted for clarity. Figure comes from ref [240])

More recently in 2020, Thomas et al. also reported the crystal structure of a vinyl cationic zwitterionic intermediate (Figure 39).^[241] The Fe(1)-C(2) bond suggest the stabilization of the carbocationic center is through an interaction with iron.

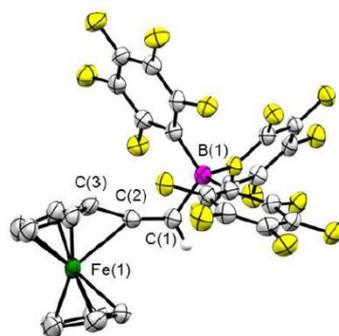
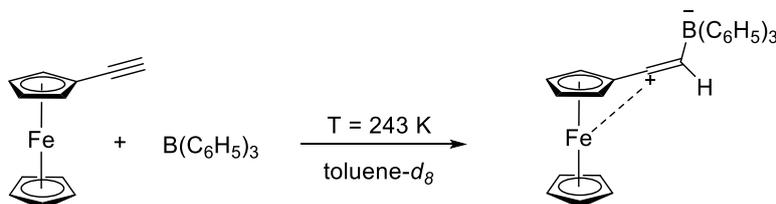


Figure 39. Crystal structure of the alkenyl ferrocene zwitterion (Figure comes from ref [241])

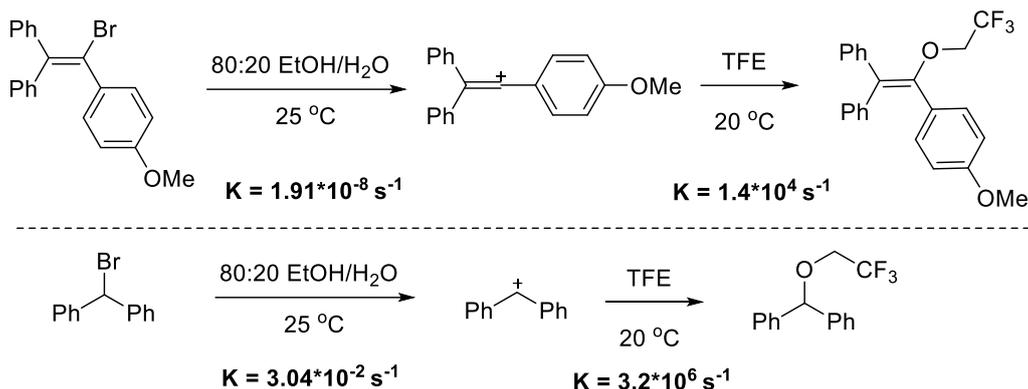
This crystal was synthesized by reaction of ethynylferrocene with $B(C_6F_5)_3$ at 243 K (Scheme 86), and also characterized by spectroscopy and computational studies. The results revealed the true nature of previously reported 1,1-carbaboration reaction.^[242]



Scheme 86. Reaction of $B(C_6F_5)_3$ and ethynylferrocene

1.1.1 Reactivity of vinyl cations

There has been a temporary flourishing of vinyl cations in synthetic chemistry in the 70s, laid mainly with solvolysis reactions. Then, for a long time, vinyl cations were considered as highly reactive and uncontrollable intermediates. The interest for vinyl cation chemistry faded away.^[236] It was from 2017 that the Mayr's group revealed the true nature of vinyl cation reactivity by comparing the solvolysis reaction rates of the vinyl and benzhydryl bromides (Scheme 87).^[243] The diarylcarbenium ion generated 10^6 times faster than the vinyl cation. Despite its much faster rate of formation, the parent benzhydrylium ion reacts only 10^2 times faster with trifluoroethanol.



Scheme 87. Solvolysis reaction rates of vinyl cation and diarylcarbenium ion

This phenomenon was investigated by high-level MO calculations, clearly illustrating that the major reason for the different solvolysis rates is the difference in the intrinsic barriers (Figure 40). The high intrinsic barriers for the $sp^2 \leftrightarrow p$ rehybridization accounts for the slow solvolysis of vinyl cations. They confirmed that the vinyl cation intermediate is as stable as the benzhydryl cation, and controllable enough to work with.

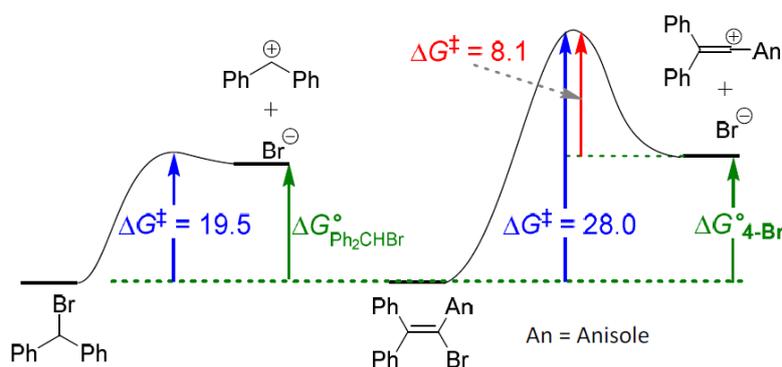


Figure 40. Schematic Gibbs energy profiles (kcal mol^{-1}) for the ionization of benzhydryl bromide and a vinyl bromide. (Figure is copied from ref [243])

The unique feature of vinyl cations is their carbene-like reactivity. In 1972, Smith et al. first postulated the insertion reaction of vinyl cations into the hydrogen molecule by MO calculation.^[244] As shown in Figure 41b, the C_α of vinyl cation has an empty p orbital perpendicular to the π bond orbital between C_α and C_β . Because of the existence of the empty p orbital, this π -orbital is highly polarized and makes the C_α to have a similar electronic structure as a methylene, as shown in Figure 41a. This means that the vinyl cation **B** can be described as a methylene with an adjacent cation, shown as **B'**.

As carbenes are well-known intermediates for insertion reaction, vinyl cations were predicted to have a similar reactivity, while forming a cation product after insertion. With this reactivity, few impressive works have been revealed by chemists (see Section 1.2). That makes us thinking “Are vinyl cations finally coming of age?” as said by Niggemann.^[245]

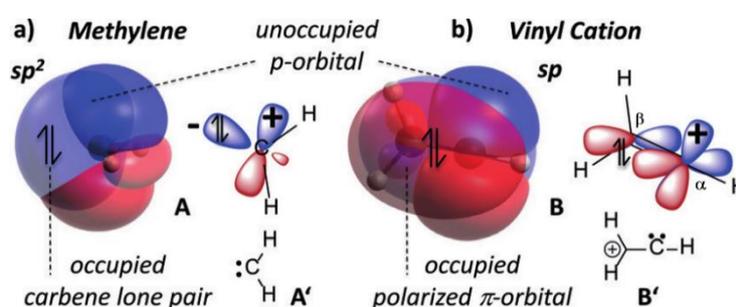


Figure 41. Electronic structure of carbenes (a) and vinyl cations (b). (Figure is copied from ref [245])

1.1.2 Formation of vinyl cations

The major methods used for the generation of vinyl cations consist of 1) electrophilic addition to alkynes, 2) heterolysis of vinyl derivatives, 3) decomposition of β -hydroxy- α -diazo compounds (Figure 42). We will describe the recent developments of vinyl cations in synthetic chemistry classified by these three formations (Figure 42).

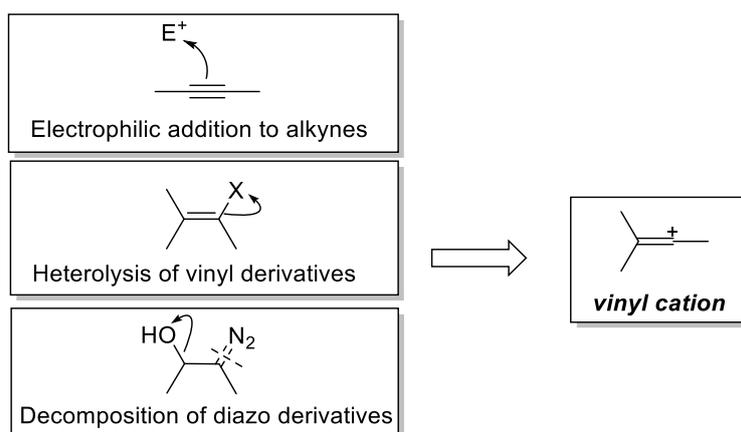
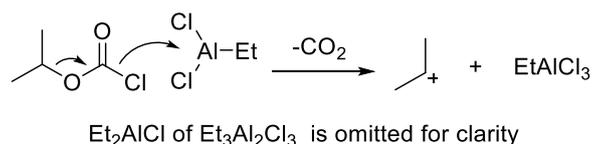


Figure 42. Main pathways of formation of vinyl cations

1.2 Recent Advances of the Use of Vinyl Cations in Synthesis

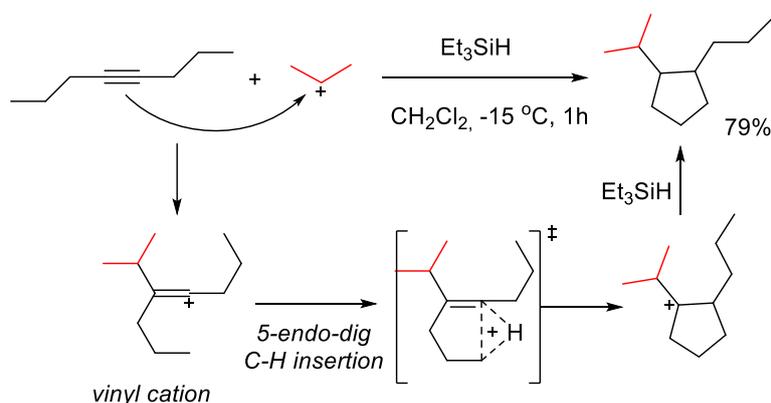
1.2.1 Electrophilic addition to alkynes

It is known that isopropyl cation can be generated from alkyl chloroformates, induced by ethylaluminum sesquichloride ($\text{Et}_3\text{Al}_2\text{Cl}_3$), shown in Scheme 88.^[246]



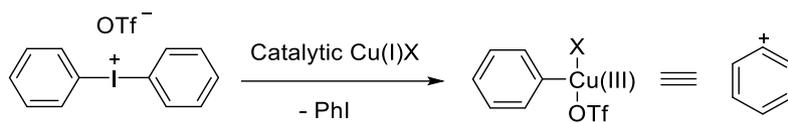
Scheme 88. Generation of isopropyl cation

In 2006, Metzger et al. exploited this isopropyl cation in a reaction with 4-octyne and they isolated the unexpected product 1-isopropyl-2-propylcyclopentane in 79% yield as a mixture of two diastereomers in a ratio of 4.6:1 (Scheme 89). This reaction proceeds through a nucleophilic addition of the alkyne to the isopropyl cation to form a vinyl cation, followed by 5-endo-dig insertion of a sp^3 C-H bond to generate a cyclic alkyl cation, which is reduced by triethylsilane to get the final product.



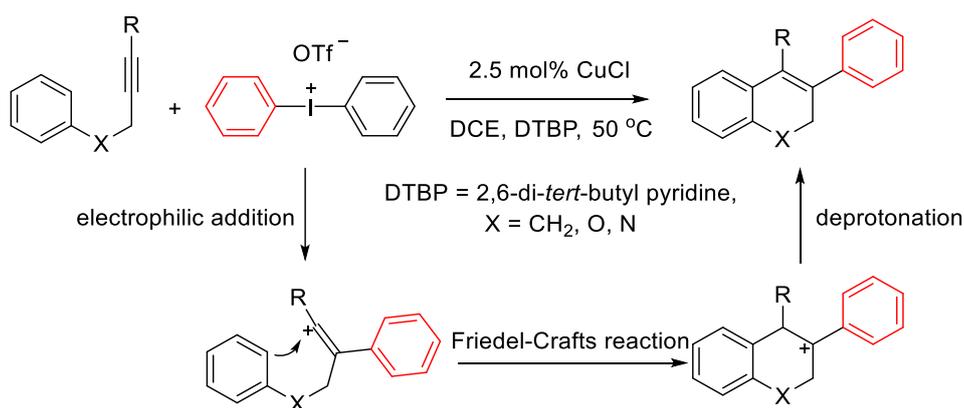
Scheme 89. Hydroalkylating cyclization of 4-octyne

After this seminal work, a few other cationic species were used in the generation of vinyl cations by electrophilic addition to alkynes, delivering various chemical skeletons. In that respect, diaryliodonium salts can be considered as precursors of arenium carbocation, after activation by a Cu(I) complex.^[247]



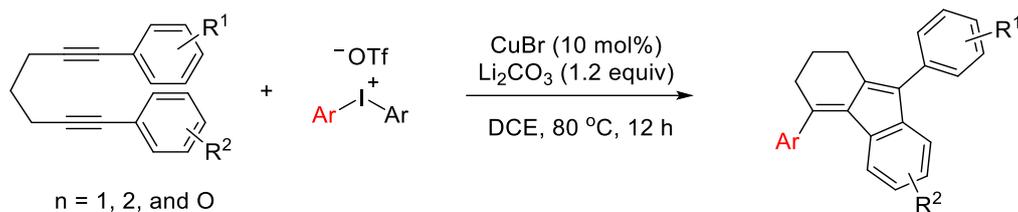
Scheme 90. *Cu(I)X* catalyzed formation of the phenylium cation

Taking this in account, Gaunt's group reported a copper-catalyzed intramolecular carboarylation process that forms cyclic tetrasubstituted alkenes in 2013 (Scheme 91).^[248] In this reaction, vinyl cations are formed by the electrophilic addition of aromatic carbocations to an alkyne, and then undergo an intramolecular Friedel-Crafts reaction to form a carbocation. After deprotonation, a tetrasubstituted cyclic alkenes is obtained. DTBP is used but its role was not commented. One can infer that it is involved in the deprotonation step. Without DTBP, complete consumption of the substrates was observed but no formation of final product occurred.



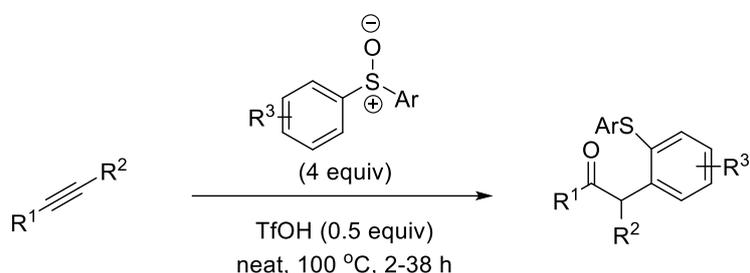
Scheme 91. *Cu(I)*-catalyzed carboarylation of alkynes via vinyl cations

In 2016, Chen et al expended this strategy to the synthesis of polycyclic compounds from linear diynes (Scheme 92).^[249] In this method, vinyl cation intermediates are generated twice, one from the electrophilic addition of Cu(III)Ar^+ (Scheme 90), and the second one from the electrophilic addition of the first vinyl cation to the alkyne. Subsequently a Friedel-Crafts reaction produced the final polycyclic products.



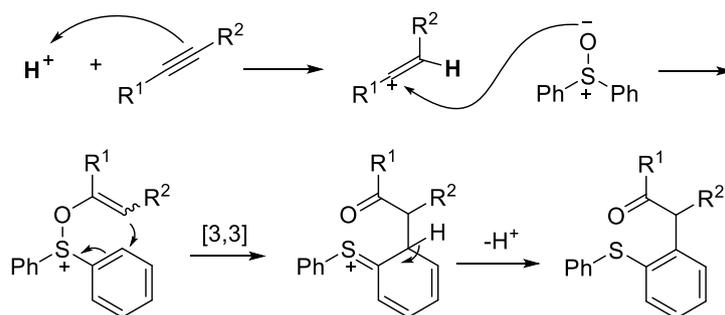
Scheme 92. CuBr-catalyzed electrophilic cyclization of diynes with diaryliodonium salts.

The generation of vinyl cations can be achieved by simple addition of H^+ to alkynes. For example, in 2016 Maulide et al. reported a carbon-carbon bond formation reaction via the interception of highly reactive vinyl cations with sulfoxides (Scheme 93).^[250]



Scheme 93. Proton catalyzed hydrative arylation of alkynes by sulfoxides

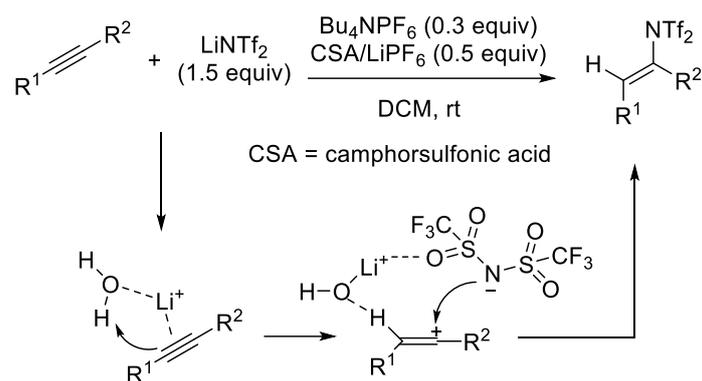
The proton of TfOH accounts for the generation of the vinyl cation, followed by the O-nucleophilic attack of the sulfoxide to the *sp*-hybridized carbocation. The final steps involve [3,3]-sigmatropic rearrangement and rearomatization (Scheme 94).



Scheme 94. Schematic profile for the reaction in Scheme 93

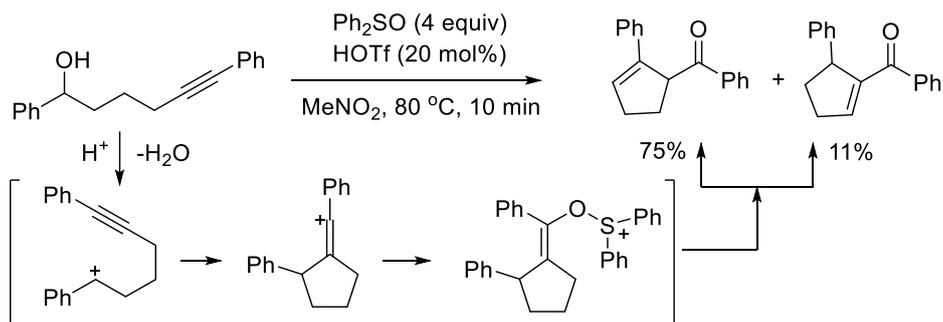
In 2019, Niggemann's group reported a method for synthesizing vinyl triflimides via vinyl cation intermediates (Scheme 95).^[251] The stoichiometric use of the superacid HNTf_2 undeniably causes poor functional group tolerance. In contrast, by using LiNTf_2

as the NTf₂⁻ source, various previously inaccessible vinyl triflimides were obtained. In this transformation, the Li⁺ ion plays a key role as it strives for a coordination number of 4–6 in non-aqueous solution. DFT calculations showed that the Li⁺ ion triggers the formation of a vinyl cation by coordinating with H₂O (traces in solvent), and guides the bistriflimide nitrogen lone pairs into the right position.



Scheme 95. Regioselective hydroaminosulfonation mediated by Li⁺ via a vinyl cation.

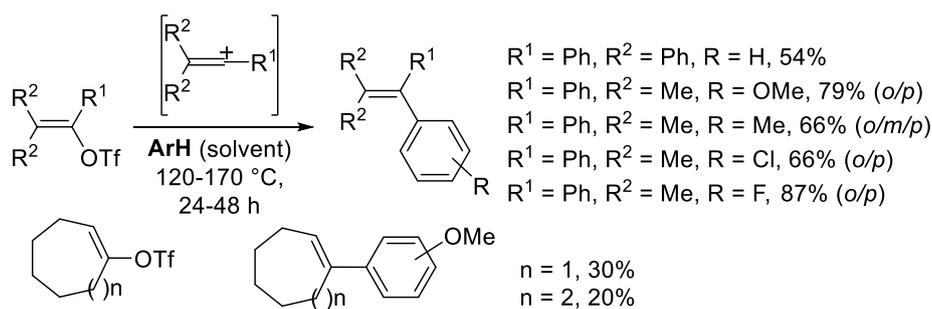
The direct dehydroxylation of alcohols is also an efficient method to generate carbocations, which can undergo an electrophilic addition to alkynes to form vinyl cations. In 2017, Maulide et Niggemann published oxidative cyclization reactions driven by sulfoxide interception of a vinyl cation (Scheme 96).^[252] The vinyl cation was formed by intramolecular addition of a carbocation, which is generated by dehydroxylation. Then follows the reduction of the sulfoxide, releasing a α -carbonyl cation, and deprotonation. Thus, complex compounds with highly congested tertiary and all-carbon-substituted quaternary carbon centers were obtained in a single step from simple precursors.



Scheme 96. Oxidative rearrangements via a vinyl cation.

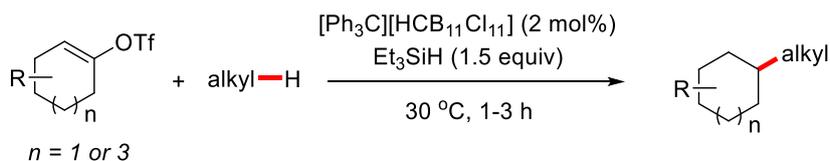
1.2.2 Heterolysis of vinyl derivatives

Heterolysis of vinyl triflates is one of the most efficient methods to generate vinyl cations. Even vinyl bromide can be used in this transformation, as shown in Section 1.1.1. As for the leaving groups in heterolysis of vinyl derivatives, OTf^- leaves 10^8 - 10^9 times faster than Br^- .^[253] In addition, the synthesis of vinyl triflates can be simply derived from ketones or alkynes, and that was well-studied by chemists a long time ago.^[253–255] Taking those advantages in all, Stang et al. reported the electrophilic aromatic alkenylation reaction in 1976 and 1977 (Scheme 97).^[254,256] In this reaction, high temperature and long reaction time are necessary, and the scope was limited to a few examples.



Scheme 97. Alkylation of aromatic substrates via vinyl cations

In 2018, a breakthrough was made by Nelson and co-workers. By using a silylium-weakly coordinating anion catalyst, vinyl cations were generated and reacted with unactivated sp^3 C-H bonds (Scheme 98).^[257] The usually unreactive solvents cycloheptane and n-pentane can react efficiently with the cyclohexenyl cation (with α selectivity), revealing the high reactivity of vinyl cations.



Scheme 98. Reductive alkylation of cyclic vinyl triflates.

To understand this unusual activity, a mechanistic cycle was proposed (Figure 43). It is known that vinyl cations can abstract a fluoride from the strong B-F bonds of the counterion.^[258] Thus, the non-nucleophilic and non-basic properties of weakly coordinating anions $[\text{HCB}_{11}\text{Cl}_{11}]^-$, meets the needs of stabilization of such cations. In the other hand, the WCA enhances the Lewis acidity of the cationic silicon center, which accounts for the heterolysis of vinyl triflates, generated by metathesis between the catalyst and the silylium reagent. Afterwards comes the most important step, insertion of this reactive vinyl cation–WCA ion pair into an alkane C–H bond, leading to the formation of a carbocation. A 1,2-hydride shift would lead to a more stable tertiary cation that, upon reduction by the silane, generates the functionalized hydrocarbon product and regenerates the silylium-carborane initiator. DFT calculation study and deuterium-labeling experiments support this proposal.

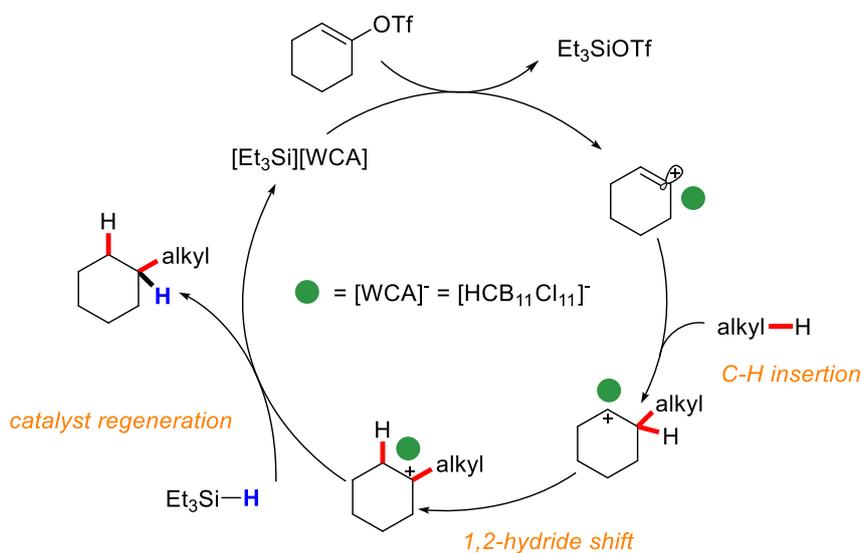
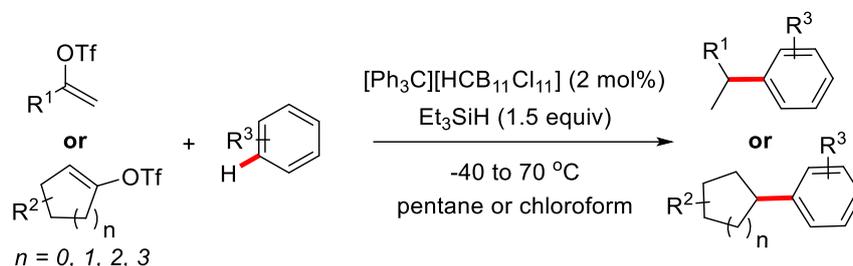


Figure 43. Proposed catalytic cycle.

Next, they employed the same catalytic system in the reductive Friedel-Crafts reactions with arenes (Scheme 99). Both cyclic and acyclic vinyl triflates were competent

electrophiles for arylation by both electron-poor and electron-rich arenes, requiring in most cases 10 equivalents of arene in pentane or chloroform.



Scheme 99. Reductive arylation of vinyl triflates.

Continuing with their finding, a synthetic method of intramolecular C-H insertion of benzosuberonyl triflates was reported in 2019 (Scheme 100).^[259] This approach relies on the combination of the lithium hexamethyldisilazide base, LiHMDS, and the commercially available catalyst $[\text{Ph}_3\text{C}][\text{B}(\text{C}_6\text{F}_5)_4]$, resulting in vast improvement in functional group compatibility with heteroatom-containing substrates.



Scheme 100. Intramolecular C-H insertion of benzosuberonyl triflates.

In this case, Li^+ was used as abstractor of OTf^- to generate the vinyl cation. After the 1,2-hydride shift, deprotonation by a lithium base is responsible for the regeneration of the active $[\text{Li}][\text{WCA}]$ catalyst (Figure 44).

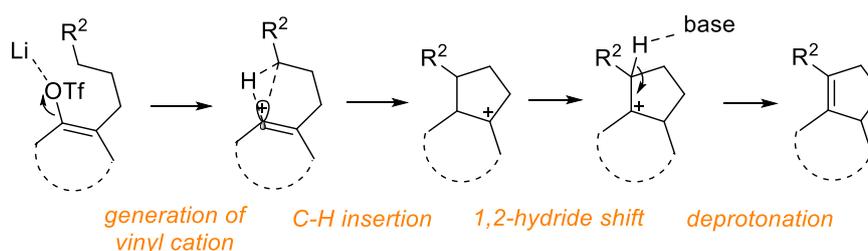
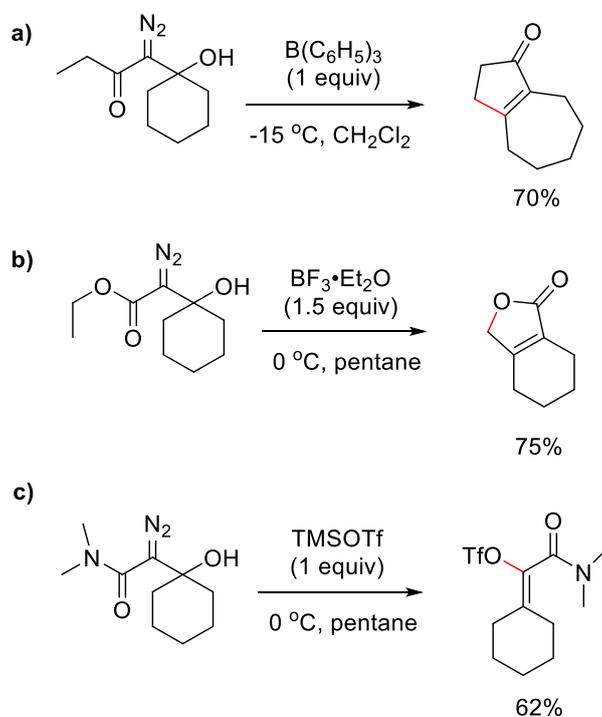


Figure 44. Proposed catalytic cycle.

1.2.3 β -hydroxy- α -diazo compounds

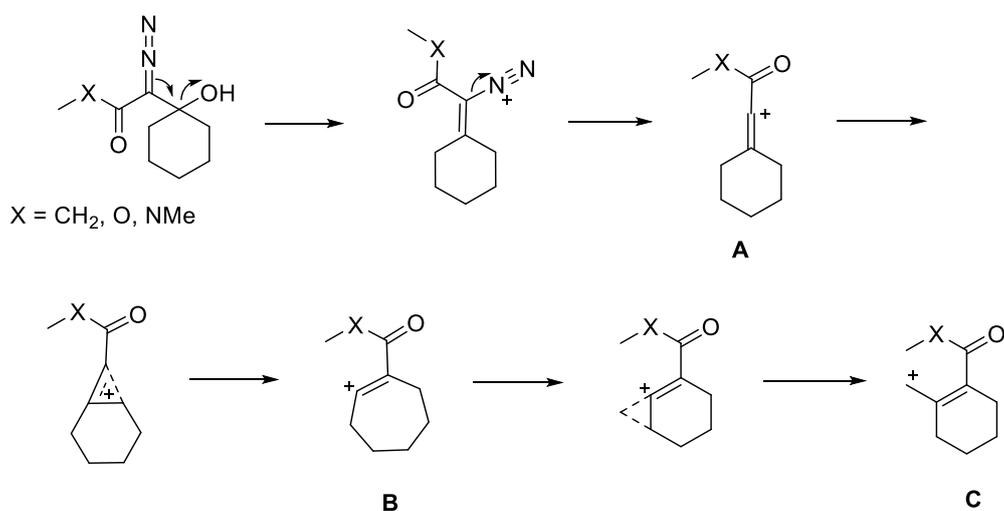
Recently, in 2019, Brewer's group investigated the reactivity of β -hydroxy- α -diazo ketones, esters, and amides in Lewis acid initiated transformations via vinyl cation intermediates.^[258] This study is based on the previously reported work, C-H insertion reaction of β -hydroxy- α -diazo ketones by their own group in 2017 (Scheme 101a),^[260] and rearrangement reaction of β -hydroxy- α -diazo esters by Pellicciari's group in 1996 (Scheme 101b).^[261] These interesting experimental results showed that three classes of β -hydroxy- α -diazo react in distinct ways when treated with Lewis acids.



Scheme 101. Lewis acid-mediated reaction of β -hydroxy- α -diazo ketones, esters, and amides.

The mechanism was proposed as shown in Scheme 102 and supported by DFT calculations. The initial steps of the reaction sequence, which lead to the formation of vinyl cation **A**, appear to be operational for each of the substrates tested. This linear vinyl cation **A** can rearrange via a 1,2-shift across the alkene to give a second (cyclic) vinyl cation **B**. This rearrangement is facile for the diazo ketone and ester but slow for the diazo amide, thus resulting in an anion-substituted product (Scheme 101c).

Computational results indicated that the relatively weaker electron-withdrawing ability of the amide limited the migration step. After the formation of **B**, the ketone substrates prefer undergoing a C-H insertion delivering a given type of product (Scheme 101a). However, for ester substrates, an allyl cation **C** occurs in a ring contraction way. It was explained by computation study that the ring contraction energy (3.7 kcal/mol) is lower than the C-H insertion energy (7.6 kcal/mol). Subsequently, a nucleophilic addition of ether gives the final product (Scheme 101b).



Scheme 102. Postulated mechanism study of transformations via vinyl cation intermediate

1.3 Conclusion

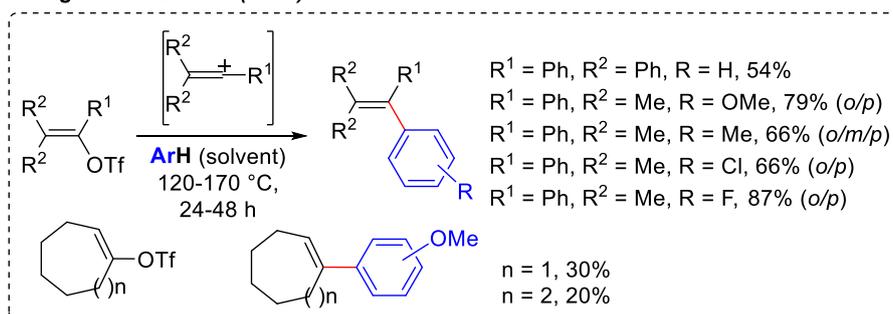
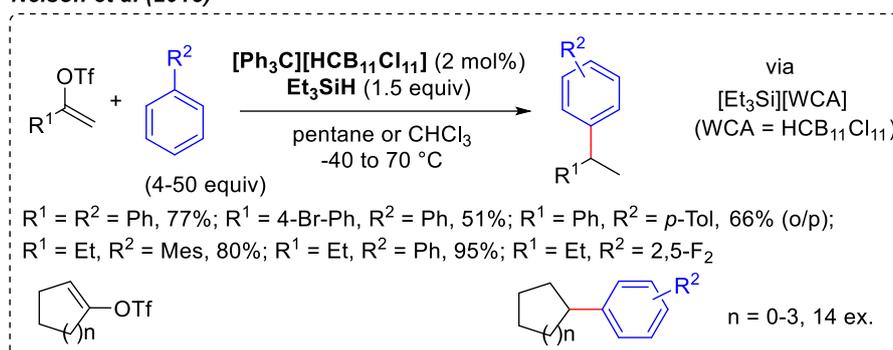
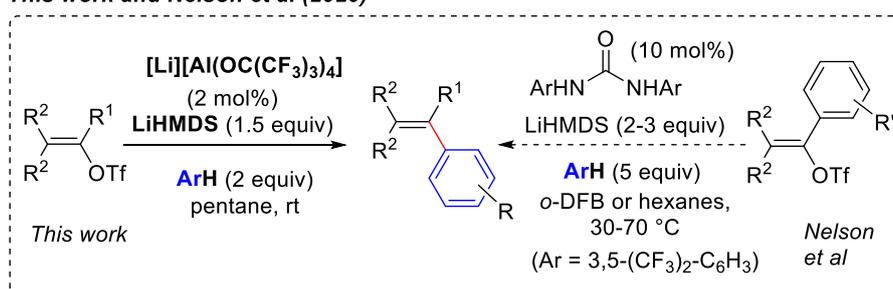
Recent developments of vinyl cation as a key intermediate moved this old chemistry into a new stage, from solvolysis to carbene like reactivity towards unreactive C-H bond. The resulting carbocations after C-H insertion allow the possibility of various transformations, such as reduction to alkyl by hydride, deprotonation of the adjacent carbon to form alkenes, or further reaction with other nucleophiles (alkynes), thus opening new opportunities to build molecules for academic as well as industrial pursuits.

Despite this renaissance, the potential of utilizing vinyl cation in synthetic chemistry is still overlooked. For example, the study about the functional group adjacent to the vinyl cation is less known. Even if Maulide's group has already shown the powerful ability of keteniminium ions in diverse transformations, which can be considered as a nitrogen conjugated with vinyl cation. But the effects of other elements, such as Si, S, O, P, adjacent to a vinyl cation is still needs to be developed.

In addition, the counterion of the vinyl cation, which has to be weakly coordinating enough to enhance the reactivity of the cation and stable enough to avoid decomposition, still needs to be expended. Following the previous work in this thesis of using $[\text{Al}(\text{OC}(\text{CF}_3)_3)_4]^-$ to stabilize low-oxidation state gallium(I) and indium(I) and catalyze distinct reactions, it appeared reasonable to imagine the application of this aluminate WCA in vinyl cation chemistry. The next chapter will introduce the results of our lab based on this vision.

2. RESULTS AND DISCUSSION

The more than 140 years old Friedel-Crafts reaction remains one the most frequently used method for the functionalization of arenes.^[262,263] Although carbon based electrophiles have been widely used, the direct vinylation of aromatic rings remains difficult to achieve. In 2018, Fang and Brewer attributed the lack of examples of vinylation of arenes to the difficulty to prepare vinyl cations compared to classical tricoordinated carbonium ions.^[264] Mayr et al stated that vinyl cations are sluggish electrophiles due to the high intrinsic barrier for $sp^2 \leftrightarrow sp$ rehybridization, hence a slow solvolysis of the precursor and a high energy level of such intermediates.^[243] However, the carbene-like reactivity of vinyl cations, revealed by concerted CH-insertion processes,^[257,265,266] has been highlighted.^[245] One way to generate vinyl cations is by adding electrophiles to alkynes^[251] but their trapping by arenes suffers from regioselectivity issues and the styrene products can be prone to polymerization under the strongly acidic conditions used (TFA, HNTf₂, TfOH, hard Lewis acids, etc).^[137,267–273] Milder reaction conditions have been developed using soft transition metal complexes as catalysts, but apart from intramolecular reactions or reactions in which the two alkyne carbons are functionalized, regioselectivity and oligomerization processes remain an issue.^[248,266,274,275] Another way to generate vinyl carbocations is by decomposing β -hydroxy- α -diazo ketones with Lewis acids. This approach allows the formation of tricyclic 1-indenones after intramolecular vinylation of the aryl rings by the vinyl cation.^[264] As for intermolecular reactions, the heterolytic solvolysis of vinyl sulfonates^[276] route has been investigated. Stang and Anderson reported that tetrasubstituted vinyl triflates or trisubstituted cyclic vinyl triflates are arylated when heated at high temperature in an aromatic solvent (Scheme 103).^[254]

Stang and Anderson (1977)**Nelson et al (2018)****This work and Nelson et al (2020)***Scheme 103. Vinylation of arenes using vinyl triflates*

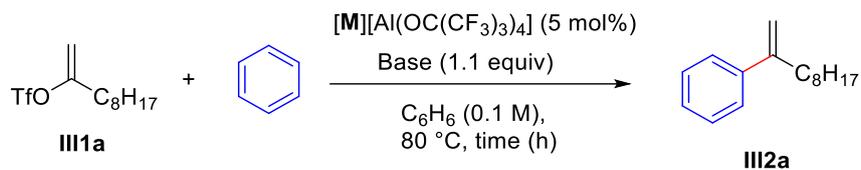
Nelson et al showed that a similar reaction could be realized under milder conditions using a silylium ion associated with a weakly coordinating anion (WCA) to activate the vinyl triflate and promote the formation of a vinyl carbocation.^[257] However, the double bond is reduced by the silane to provide an alkyl-arene. Our interest for Lewis acid catalyzed Friedel-Crafts reaction^[21,77,204] led us to investigate a way to use vinyl triflates as vinylation agents under mild conditions. Recently, we reported that univalent gallium and indium salts of the WCA $[\text{Al}(\text{OC}(\text{CF}_3)_3)_4]^-$ are excellent catalysts for the intramolecular vinylation of arenes using alkynes or allenes.^[148,193] $[\text{Al}(\text{OC}(\text{CF}_3)_3)_4]^-$ presents several important advantages compared to other WCAs, such as solubility, chemical stability and inertness.^[277,278] We thus decided to study the more challenging

bimolecular vinylation of arenes using vinyl triflates and $[M][Al(OC(CF_3)_3)_4]$ complexes as catalysts. As shown in Scheme 103, our best conditions are with $[M] = Li$ (2 mol%), in the presence of LiHMDS as base (1.5 equiv). During the preparation of this manuscript appeared a pre-print from Nelson et al. describing the same transformation, using urea derivatives as catalysts (10 mol%) and also LiHMDS as base (2-3 equiv).^[279] We report herein our own findings.

2.1 Optimization of Reaction Conditions

As mentioned above, our investigation began with the use of $[Ga][Al(OC(CF_3)_3)_4]$ and $[In][Al(OC(CF_3)_3)_4]$ (Table 9). Both proved to be unable to promote the coupling of dec-1-en-2-yl trifluoromethanesulfonate **III1a** at 80 °C with benzene, used as solvent (entries 1 and 2). LiHMDS was used as a base to possibly encourage the deprotonation step of the Friedel-Crafts reaction.^[259] The joint use of $[Ga][Al(OC(CF_3)_3)_4]$ (5 mol%) and LiHMDS (1.1 equiv) delivered the desired product **III2a** in 58% yield based on ¹H NMR (entry 3). In the absence of catalyst, no reaction took place (entry 4). Changing the Ga(I) catalyst for GaCl₃ shut down the reactivity (entry 5). With $[In][Al(OC(CF_3)_3)_4]$, **III2a** was formed in 60% yield (entry 6). We also tested the lithium salt $[Li][Al(OC(CF_3)_3)_4]$ which proved ineffective alone (entry 7), but efficient when use together with LiHMDS (entry 8). This stable complex can be readily prepared on a large scale from LiAlH₄ and HO(C(CF₃)₃)₄.^[66,67,280] Lowering the temperature to 30 °C resulted in a much longer reaction time of 24 h instead of 1 h (entry 9). Other bases were tested but none, including KHMDS, furnished product **III2a** (entries 10-14). Going back to LiHMDS, the simple salt LiBF₄ did not promote the reaction (entry 15). The best conditions are shown in entry 16: by using $[Li][Al(OC(CF_3)_3)_4]$ at the low loading of 2 mol% and LiHMDS (1.5 equiv), an NMR yield of 68% was obtained at 80 °C in 2 h.

Table 9. Optimization of the vinylation of benzene using **III1a**

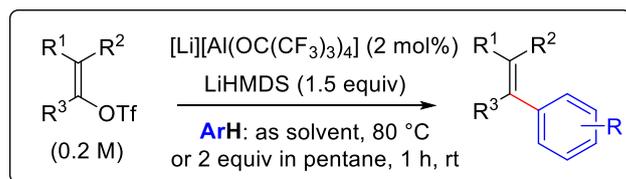


Entry	[M] or other cat.	Base	Temp	Time	Yield (%) ^a
1	[Ga]	-	80	1	-
2	[In]	-	80	1	-
3	[Ga]	LiHMDS	80	1	58
4	-	LiHMDS	80	24	-
5	GaCl ₃	LiHMDS	80	24	-
6	[In]	LiHMDS	80	1	60
7	[Li]	-	80	24	-
8	[Li]	LiHMDS	80	1	64
9	[Li]	LiHMDS	30	24	60
10	[Li]	KHMDS	80	1	-
11	[Li]	K ₂ CO ₃	80	1	-
12	[Li]	DTBP ^b	80	1	-
13	[Li]	Et ₃ N	80	1	-
14	[Li]	DMAP	80	1	-
15	LiBF ₄	LiHMDS	80	24	-
16^c	[Li] (2 mol%)	LiHMDS	80	2	68

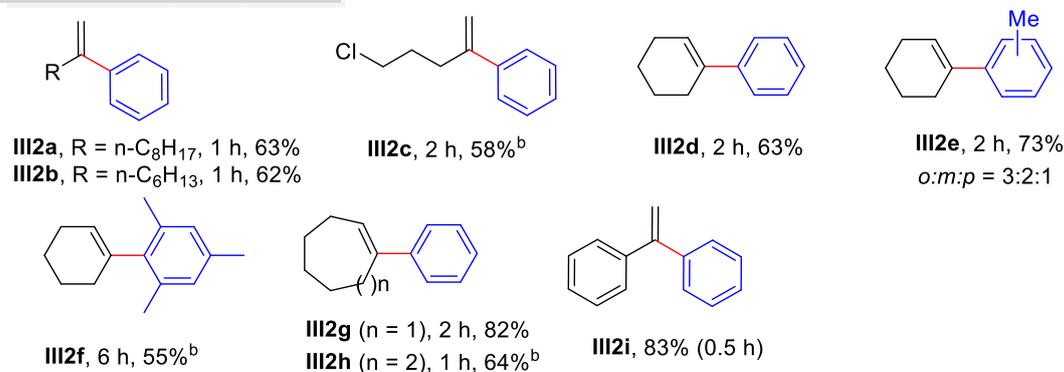
^aNMR yield using 1,3,5-trimethoxybenzene as internal standard (added after workup). A dash means no reaction. ^b 2,6-di-tert-butylpyridine. ^c 0.2 M; LiHMDS (1.5 equiv).

2.2 Scope and Limitations

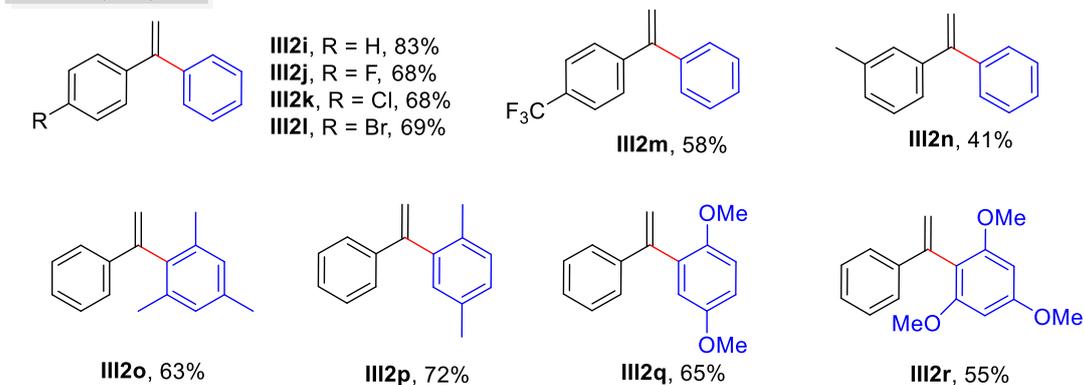
The scope of this lithium-catalyzed vinylation was then explored (Scheme 104). Two different experimental conditions were developed: either using the arene directly as solvent (benzene, toluene and mesitylene), or using pentane as solvent. In the latter case, 2 equivalents of arene were employed. The use of pentane allows the reaction to take place at rt instead of 80 °C. With the arene partner used as solvent, substrates displaying alkyl chains were well-tolerated, providing styrenes **III2a-c** in good yields. Triflates exhibiting cyclohexene, cycloheptene and cyclooctene could also be coupled to benzene (**III2d**, **III2g**, **III2h**), toluene (**III2e**) or mesitylene (**III2f**). The reaction did not proceed with a smaller 5-membered ring (see Unreactive Substrates). The use of 1-phenylvinyltriflate **III1i** furnished 1,1-diphenylethylene **III2i** in 83% yield. This product was obtained with the same isolated yield of 83% in pentane. Still in pentane as solvent, it was possible to use 1-phenylvinyltriflates displaying electron-withdrawing *p*-F (**III1j**), *p*-Cl (**III1k**), *p*-Br (**III1l**) and *p*-CF₃ (**III1m**) groups, as well as the electron-donating *m*-CH₃ (**III1n**) group. On the other hand, the *p*-NO₂ group deactivated the substrate. Arene partners such as 1,4-dichloro- or 1,4-dibromobenzene, and 1-(phenylsulfonyl)-1*H*-indole could not be used, but electron-rich mesitylene, *p*-xylene, 1,4-dimethoxy- and 1,3,5-trimethoxybenzene proved perfectly compatible (**III2o-r**). Of note, 2,2-diphenylvinyltriflate **III1s** transformed into diphenylacetylene under our reaction conditions. This is likely the result of a base promoted Fritsch-Buttenberg-Wiechell rearrangement involving a vinyl carbene. Triflate elimination was also observed using the peculiar conjugated substrate **III1t**.



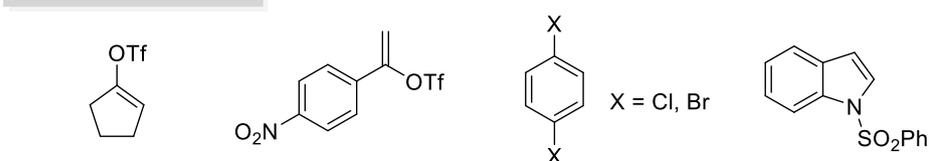
ArH as solvent, 1-2 h, 80 °C:^a



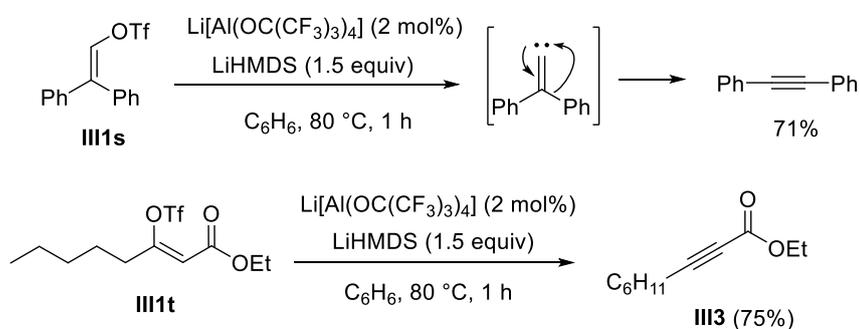
Pentane, 1 h, rt:^a



Unreactive Substrates:



Side Reactions:

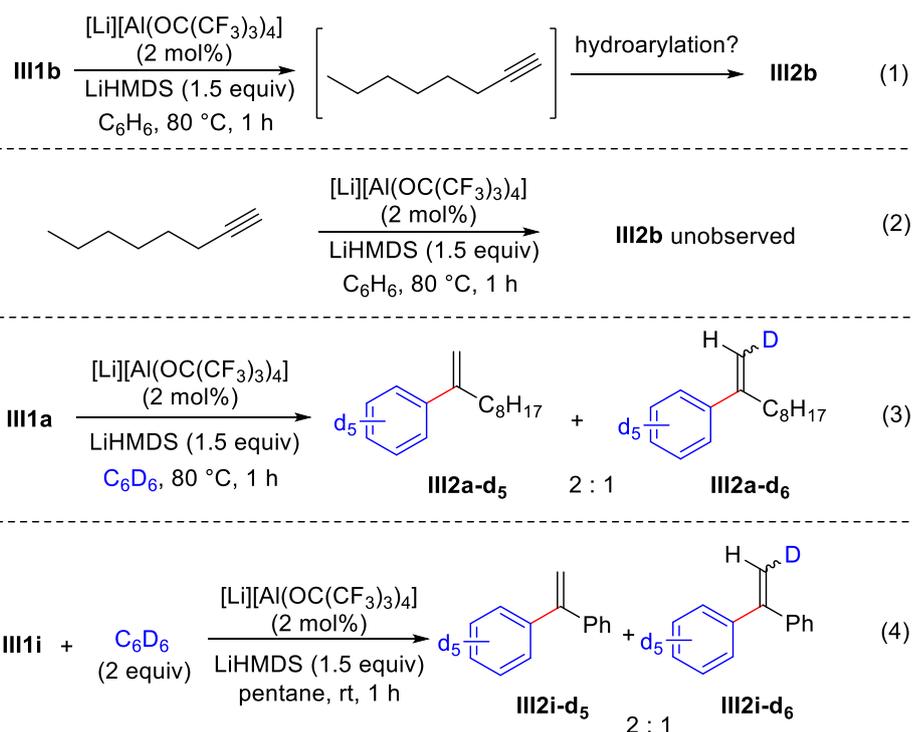


Scheme 104. Scope and limitations. ^aIsolated yield.

^bNMR yield using 1,3,5-trimethoxybenzene as internal standard (added after workup).

2.3 Mechanism Investigation

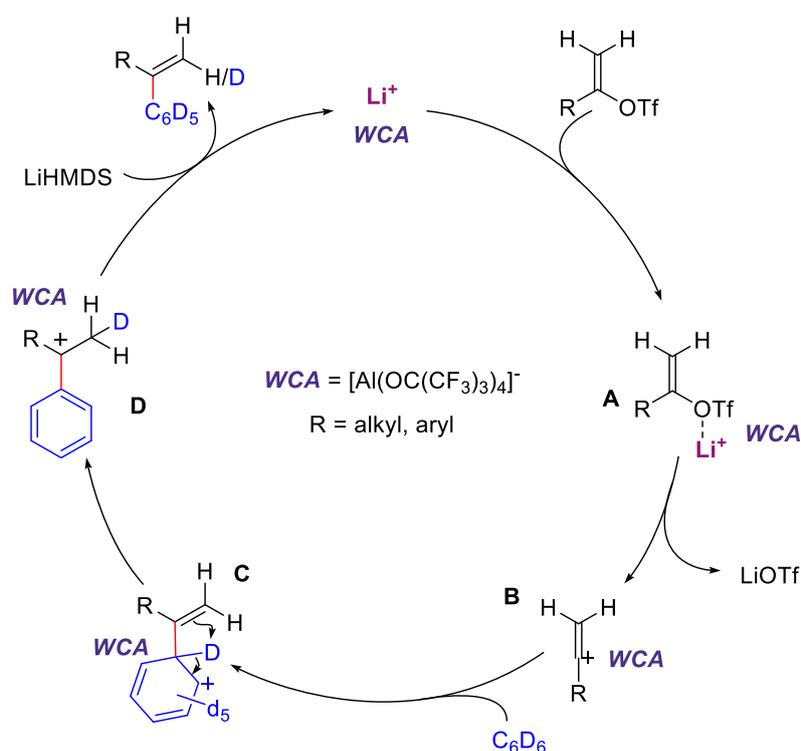
Although this alkyne formation is not surprising in this case, it raised the question of a hydroarylation pathway to explain the reaction products. One could indeed imagine that a coupling product such as **III2b** could be obtained after base-promoted triflate elimination to give 1-octyne, followed by Li⁺-catalyzed hydroarylation (Scheme 3, eq (1)). However, 1-octyne could not be converted into **III2b** with or without LiHMDS (eq (2)). The use of C₆D₆ under the two experimental conditions (eqs (3) and (4)) led to the expected styrenes **III2a-d₅** and **III2i-d₅**, yet accompanied by substantial amounts of products incorporating one deuterium at the terminal vinylic position (**III2a-d₆** and **III2i-d₆**). These structures cannot be explained by a standard Friedel-Crafts mechanism.



Scheme 105. Control experiments

A proposed catalytic cycle is summarized in Scheme 106. It could coexist with the standard Friedel-Crafts mechanism, or be the only effective one as it explains the two types of products (d₅ and d₆ series). First, lithium coordinates to the OTf moiety to give **A**. This promotes the cleavage of the C-O bond and leads to the vinyl cation **B**. Addition

of C_6D_6 gives the Wheland-type intermediate **C**. A [1,3]-D shift then gives the tertiary carbocation **D**. This step would seem symmetry-forbidden but it should be largely encouraged by the rearomatization of the C_6D_5 ring. Finally, base-promoted elimination of H^+ or D^+ provides the vinyliated benzene products of the d_5 and d_6 series.



Scheme 106. Proposed mechanism

A KIE experiment was conducted using C_6H_6 and C_6D_6 but the k_H/k_D was 1.0. DFT calculations were performed at the $\omega B97XD/6-311+G(d,p)$ -SMD(pentane) to support the above proposal (Figure 45). *I would like to thank Pro. Vincent GANDON for this work.* Since conformational sampling of the ion-pairs is particularly challenging,^[257] the $[Al(OC(CF_3)_3)_4]^-$ anion was not taken into consideration on the first place. We can yet ascertain that the ligand exchange between $[Al(OC(CF_3)_3)_4]^-$ and **III-i** to give **III-Int-a**/ $[Al(OC(CF_3)_3)_4]^-$ is an exergonic process (dashed box, -2.2 kcal/mol). In a naked form, the coordination of Li^+ to **III-i** led to **III-Int-a**, located at -17.9 kcal/mol on the energy surface. Cleavage of the C-O bond requires 21.2 kcal/mol of free energy of activation to give **III-Int-b**, lying at -8.4 kcal/mol. Exchange of LiOTf by benzene

gives **III-Int-c**, found at -4.8 kcal/mol. C-C bond formation is achieved through **TS_{cd}** at the expense of 8.5 kcal/mol. This step is exergonic by 5.4 kcal/mol. Finally, the [1,3]-H shift corresponds to the highest-lying transition state **TS_{de}**, located at 7.5 kcal/mol. As such, the RDS is this final highly exergonic process (25.4 kcal/mol from **III-Int-a** to **TS_{de}**). Since it involves H or D, it does not match the KIE experiment. Thus, the RDS could correspond to an early slow step. In fact, $[\text{Li}][\text{Al}(\text{OC}(\text{CF}_3)_3)_4]$ is a polymer in the solid state in which each unit are bound by $\text{Li}\cdots\text{F}$ interaction.^[68,281] Unlike LiHMDS, which is soluble in benzene or pentane, $[\text{Li}][\text{Al}(\text{OC}(\text{CF}_3)_3)_4]$ is not. It is possible that the reaction takes place at the surface of the salt or in the interface layer between the solid catalyst and the solution. Solid-to-solution phase transfer of Li^+ could be promoted by arene... Li^+ π interaction (from benzene or the arene reagent used in excess). Such interaction could represent a competing equilibrium to the binding step of Li^+ to **IIIi** and explain why the reaction requires heating in benzene, in which arene... Li^+ π interaction is maximized, and not in pentane. The true RDS could actually correspond to the depolymerization of $([\text{Li}][\text{Al}(\text{OC}(\text{CF}_3)_3)_4])_n$ or to the arene/triflate ligand exchange, which we cannot compute. In both cases, very little isotope effect on the reaction rate is expected. To close, it is worthy of note that a C-H insertion mechanism from **III-Int-c** could not be computed.

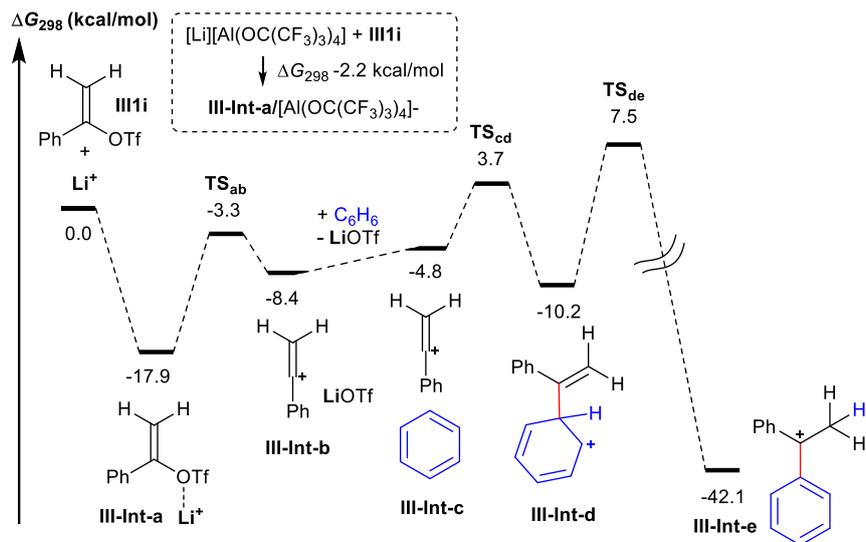


Figure 45. Computed free energy profile.

2.4 Conclusion

In conclusion, we have developed a mild and efficient method for the bimolecular vinylation of arenes. Divers vinyl triflates were applied to react with aromatics, neat at 80 °C, or in pentane at rt, resulting di- or trisubstituted alkenes in good yield. This transition metal-free protocol employs the readily available $[\text{Li}][\text{Al}(\text{OC}(\text{CF}_3)_3)_4]$ complex as catalyst. The vinyl cation intermediates, generated from Li^+ promoted heterolysis of vinyl triflates, is responsible for this uncommon transformation. The use of this robust and inert aluminate as weakly coordinating anion proved to be a decisive factor. The formation of final product from vinyl cations and arenes has been investigated carefully. Deuterium experiments and DFT calculation revealed this formation could be coexist of a Friedel-Crafts mechanism and C-H insertion pathway.

3. EXPERIMENTAL

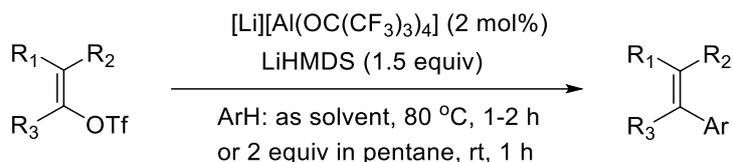
3.1 General Information

All reactions were performed in a glovebox under argon atmosphere with O_2 and H_2O < 0.5 ppm. All the glassware and stir bars were dried in a 120 °C oven for at least 24 h before use. Reactions were monitored using thin-layer chromatography (TLC) on silica gel plates (0.25 mm). The spots were visualized with ultraviolet light and/or *p*-anisaldehyde stain with heat as developing agent. Products were purified by flash chromatography on silica gel.

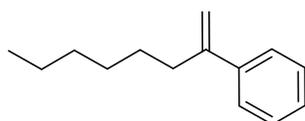
NMR characterization data was collected at 296 K on AM 250, AV 300, AV 360 or DRX 400 Bruker spectrometers operating at 250, 300, 360 or 400 MHz for 1H NMR, ^{13}C NMR and ^{19}F NMR. 1H NMR chemical shifts are reported in ppm using residual solvent peak as reference ($CHCl_3$: $\delta = 7.26$ ppm). Data for 1H NMR are presented as follows: chemical shift δ (ppm), multiplicity (s = singlet, d = doublet, t = triplet, m = multiplet, br = broad), coupling constant J (Hz) and integration; ^{13}C NMR spectra were recorded at 63, 75, 91 or 100 MHz using broadband proton decoupling and chemical shifts are reported in ppm using residual solvent peaks as reference ($CHCl_3$: $\delta = 77.16$ ppm). MS were recorded on DSQ Thermo Fisher instrument by electronic impact. HRMS was performed on a MicroTOFq Bruker spectrometer.

Materials. Reagents were purchased from commercial suppliers (Alfa Aesar, Sigma Aldrich or Strem). All the solvents were distilled, degassed (freeze-pump-thaw technique) and then stored inside the glove box over 4 Å molecular sieves. The liquid substrates were passed through a glass pipette filled with aluminum oxide before use to remove traces of water. The catalyst $[Li][Al(OC(CF_3)_3)_4]$ was synthesized according to a reported protocol.^[282] The starting vinyl triflates were synthesized according to described methods.^[257,283]

3.2 General Procedures for the Alkenylation of Aromatics

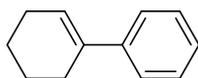


In a glovebox, a dram vial was charged with a magnetic stir bar, $[\text{Li}][\text{Al}(\text{OC}(\text{CF}_3)_3)_4]$ (0.02 equiv, 1.95 mg, 0.002 mmol) and LiHMDS (1.5 equiv, 25.10 mg, 0.15 mmol). These salts were suspended in the indicated aromatic compound (0.5 mL) or in 0.5 mL of pentane in which 2 equivalents of aromatic compound were added. The heterogeneous mixture was stirred for 5 min to improve dispersion of the lithium salts. The vinyl triflate (1 equiv, 0.1 mmol) was added to the reaction mixture, which was stirred at 80 °C for 1-2 h (arene as solvent) or at rt for 1 h (pentane as solvent). After completion (TLC monitoring), the reaction mixture was cooled to room temperature and brought outside of the glovebox. It was quenched by addition of technical diethyl ether, passed through a short plug of silica and concentrated. The crude was purified by flash chromatography on silica gel.



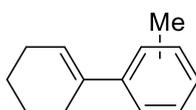
III2b oct-1-en-2-ylbenzene

Following the general procedure, using benzene as solvent at 80 °C for 1 h, product **III2b** was obtained as a colorless oil in 62% yield after purification. $^1\text{H NMR}$ (360 MHz, CDCl_3) δ 7.48 – 7.20 (m, 5H), 5.29 (d, $J = 1.6$ Hz, 1H), 5.08 (d, $J = 1.6$ Hz, 1H), 2.53 (td, $J = 7.4, 1.3$ Hz, 2H), 1.53 – 1.41 (m, 2H), 1.41 – 1.25 (m, 7H), 0.90 (t, $J = 6.7$ Hz, 3H). $^{13}\text{C NMR}$ (91 MHz, CDCl_3) δ 148.81, 141.50, 128.23, 127.23, 126.13, 112.00, 35.38, 31.69, 29.05, 28.25, 22.65, 14.10. Spectroscopic data match those previously reported in the literature.^[284]



III2c 2,3,4,5-tetrahydro-1,1'-biphenyl

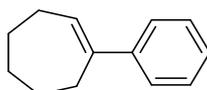
Following the general procedure, using benzene as solvent at 80 °C for 2 h, product **III2d** was obtained as a colorless oil in 63% yield after purification. $^1\text{H NMR}$ (300 MHz, CDCl_3) δ 7.45 – 7.21 (m, 5H), 6.16 (dt, $J = 4.0, 2.2$ Hz, 1H), 2.49 – 2.41 (m, 2H), 2.29 – 2.20 (m, 2H), 1.87 – 1.77 (m, 2H), 1.76 – 1.65 (m, 2H). $^{13}\text{C NMR}$ (75 MHz, CDCl_3) δ 142.69, 136.57, 128.19, 126.51, 124.93, 124.79, 27.40, 25.90, 23.08, 22.18. Spectroscopic data match those previously reported in the literature.^[285]



$o:m:p = 3:2:1$

III2e 2,3,4,5-tetrahydro-1,1'-biphenyl

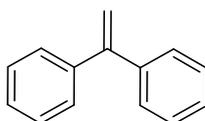
Following the general procedure, using toluene as solvent at 80 °C for 2 h, the mixture of o,m,p -product **III2e** (ratio = 3:2:1) was obtained as a colorless oil in 73% yield after purification. $^1\text{H NMR}$ (360 MHz, CDCl_3) δ 7.33 – 7.08 (m, 8H), 6.17 – 6.09 (m, 1H), 5.61 – 5.56 (m, 1H), 2.46 – 2.40 (m, 2H), 2.39 (s, 1H, o -methyl product), 2.37 (s, 2H, m -methyl product), 2.32 (s, 3H, p -methyl product), 2.26 – 2.17 (m, 6H), 1.85 – 1.66 (m, 8H). $^{13}\text{C NMR}$ (91 MHz, CDCl_3) δ 144.68, 142.77, 139.87, 138.86, 137.64, 136.71, 136.39, 136.11, 135.02, 129.96, 128.89, 128.30, 128.10, 127.28, 126.39, 125.81, 125.65, 125.48, 124.82, 124.63, 123.94, 122.10, 30.12, 27.51, 27.44, 25.88, 25.42, 23.14, 23.11, 22.23, 21.57, 21.06, 19.79. Spectroscopic data match those previously reported in the literature.^[286]



III2g 1-phenylcyclohept-1-ene

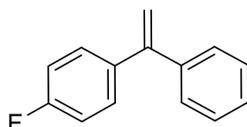
Following the general procedure, using benzene as solvent at 80 °C for 2 h, product

III2g was obtained as a colorless oil in 82% yield after purification. $^1\text{H NMR}$ (300 MHz, CDCl_3) δ 7.41 – 7.20 (m, 5H), 6.15 (t, $J = 6.8$ Hz, 1H), 2.73 – 2.61 (m, 2H), 2.38 – 2.29 (m, 2H), 1.93 – 1.85 (m, 2H), 1.74 – 1.66 (m, 2H), 1.65 – 1.56 (m, 2H). $^{13}\text{C NMR}$ (75 MHz, CDCl_3) δ 145.01, 145.00, 130.47, 128.14, 126.27, 125.68, 32.86, 32.82, 28.92, 26.97, 26.84. Spectroscopic data match those previously reported in the literature.^[285]



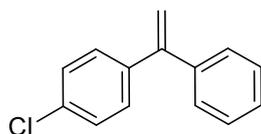
III2i ethene-1,1-diyl dibenzene

Following the general procedure, using benzene as solvent at 80 °C for 0.5 h or pentane as solvent with 2 equivalents of benzene at rt for 1 h, product **III2i** was obtained as a colorless oil in 83% yield after purification. $^1\text{H NMR}$ (360 MHz, CDCl_3) δ 7.43 – 7.34 (m, 10H), 5.52 (s, 2H). $^{13}\text{C NMR}$ (91 MHz, CDCl_3) δ 150.20, 141.62, 128.40, 128.29, 127.83, 114.42. Spectroscopic data match those previously reported in the literature.^[287]



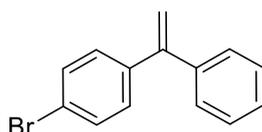
III2j 1-fluoro-4-(1-phenylvinyl)benzene

Following the general procedure, using pentane as solvent with 2 equivalents of benzene at rt for 1 h, product **III2j** was obtained as a colorless oil in 68% yield after purification. $^1\text{H NMR}$ (360 MHz, CDCl_3) δ 7.39 – 7.29 (m, 4H), 7.09 – 7.02 (m, 2H), 5.47 (d, $J = 1.2$ Hz, 1H), 5.45 (d, $J = 1.2$ Hz, 1H). $^{13}\text{C NMR}$ (91 MHz, Chloroform-*d*) δ 162.53 (d, $J = 246.7$ Hz), 149.07, 141.33, 137.56 (d, $J = 3.3$ Hz), 129.90 (d, $J = 8.0$ Hz), 128.26, 128.21, 127.89, 115.05 (d, $J = 21.3$ Hz), 114.24. $^{19}\text{F NMR}$ (235 MHz, CDCl_3) δ -114.69. Spectroscopic data match those previously reported in the literature.^[288]



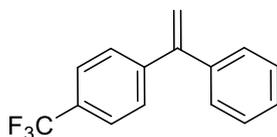
III2k 1-chloro-4-(1-phenylvinyl)benzene

Following the general procedure, using pentane as solvent with 2 equivalents of benzene at rt for 1 h, product **III2k** was obtained as a colorless oil in 68% yield after purification. $^1\text{H NMR}$ (300 MHz, CDCl_3) δ 7.41 – 7.28 (m, 9H), 5.50 (d, $J = 1.1$ Hz, 1H), 5.48 (d, $J = 1.1$ Hz, 1H). $^{13}\text{C NMR}$ (91 MHz, CDCl_3) δ 149.00, 141.04, 139.97, 133.62, 129.59, 128.37, 128.30, 128.22, 127.95, 114.72. Spectroscopic data match those previously reported in the literature.^[287]



III2l 1-bromo-4-(1-phenylvinyl)benzene

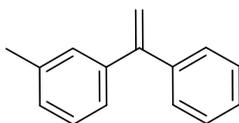
Following the general procedure, using pentane as solvent with 2 equivalents of benzene at rt for 1 h, product **III2l** was obtained as a white solid in 69% yield after purification. $^1\text{H NMR}$ (300 MHz, CDCl_3) δ 7.53 – 7.46 (m, 2H), 7.41 – 7.32 (m, 5H), 7.29 – 7.22 (m, 2H), 5.51 (d, $J = 1.1$ Hz, 1H), 5.49 (d, $J = 1.1$ Hz, 1H). $^{13}\text{C NMR}$ (91 MHz, CDCl_3) δ 149.05, 140.95, 140.44, 131.34, 129.93, 128.31, 128.22, 127.98, 121.81, 114.78. Spectroscopic data match those previously reported in the literature.^[288]



III2m 1-(1-phenylvinyl)-4-(trifluoromethyl)benzene

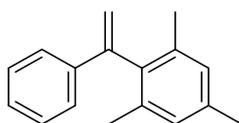
Following the general procedure, using pentane as solvent with 2 equivalents of benzene at rt for 1 h, product **III2m** was obtained as a white solid in 58% yield after purification. $^1\text{H NMR}$ (300 MHz, CDCl_3) δ 7.62 (d, $J = 8.2$ Hz, 2H), 7.48 (d, $J = 8.1$ Hz, 2H), 7.41 – 7.31 (m, 5H), 5.59 (d, $J = 1.0$ Hz, 1H), 5.54 (d, $J = 1.0$ Hz, 1H). $^{13}\text{C NMR}$ (91 MHz, CDCl_3) δ 149.10, 145.23, 140.77, 129.69 (q, $J = 32.4$ Hz), 128.69,

128.50, 128.29, 128.22, 125.30 (q, $J = 3.8$ Hz), 124.34 (d, $J = 271.8$ Hz), 116.04. ^{19}F NMR (235 MHz, CDCl_3) δ -62.43. Spectroscopic data match those previously reported in the literature.^[287]



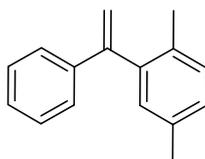
III2n 1-methyl-3-(1-phenylvinyl)benzene

Following the general procedure, using pentane as solvent with 2 equivalents of benzene for 1 h, product **III2n** was obtained as a colorless oil in 41% yield after purification. ^1H NMR (300 MHz, CDCl_3) δ 7.37 (d, $J = 1.2$ Hz, 5H), 7.29 – 7.23 (m, 1H), 7.22 – 7.14 (m, 3H), 5.48 (s, 2H), 2.38 (s, 3H). ^{13}C NMR (91 MHz, CDCl_3) δ 150.16, 141.62, 141.49, 137.74, 128.96, 128.48, 128.28, 128.14, 128.06, 127.66, 125.46, 114.17, 21.45. Spectroscopic data match those previously reported in the literature.^[288]



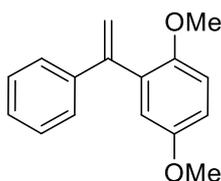
III2o 1,3,5-trimethyl-2-(1-phenylvinyl)benzene

Following the general procedure, using pentane as solvent with 2 equivalents of mesitylene for 1 h, product **III2o** was obtained as a colorless oil in 63% yield after purification. ^1H NMR (360 MHz, CDCl_3) δ 7.26 – 7.13 (m, 5H), 6.90 – 6.80 (m, 2H), 5.88 (d, $J = 1.4$ Hz, 1H), 5.02 (d, $J = 1.4$ Hz, 1H), 2.25 (s, 3H), 2.04 (s, 6H). ^{13}C NMR (91 MHz, CDCl_3) δ 146.84, 139.56, 138.17, 136.45, 136.15, 128.42, 128.10, 127.54, 125.83, 114.56, 21.06, 20.10. Spectroscopic data match those previously reported in the literature.^[289]



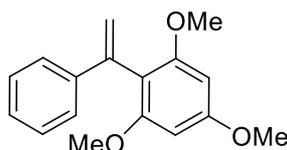
III2p 1,4-dimethyl-2-(1-phenylvinyl)benzene

Following the general procedure, using pentane as solvent with 2 equivalents of *p*-xylene for 1 h, product **III2p** was obtained as a colorless oil in 62% yield after purification. $^1\text{H NMR}$ (360 MHz, CDCl_3) δ 7.35 – 7.26 (m, 5H), 7.14 – 7.05 (m, 3H), 5.78 (d, $J = 2.0$ Hz, 1H), 5.22 (d, $J = 2.0$ Hz, 1H), 2.37 (s, 3H), 2.04 (s, 3H). $^{13}\text{C NMR}$ (91 MHz, CDCl_3) δ 149.57, 141.48, 140.68, 135.07, 132.96, 130.69, 129.98, 128.32, 128.20, 127.53, 126.52, 114.69, 20.94, 19.63. Spectroscopic data match those previously reported in the literature.^[287]



III2q 1,4-dimethoxy-2-(1-phenylvinyl)benzene

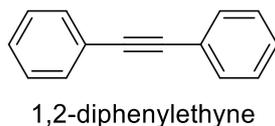
Following the general procedure, using pentane as solvent with 2 equivalents of 1,4-dimethoxybenzene for 1 h, product **III2q** was obtained as a colorless oil in 65% yield after purification. $^1\text{H NMR}$ (300 MHz, CDCl_3) δ 7.38 – 7.23 (m, 5H), 6.91 – 6.77 (m, 3H), 5.76 (d, $J = 1.4$ Hz, 1H), 5.35 (d, $J = 1.4$ Hz, 1H), 3.81 (s, 3H), 3.60 (s, 3H). $^{13}\text{C NMR}$ (91 MHz, CDCl_3) δ 153.59, 151.37, 146.86, 140.81, 132.22, 128.09, 128.05, 127.98, 127.37, 126.38, 126.34, 117.10, 115.47, 113.39, 112.78, 56.48, 55.75. Spectroscopic data match those previously reported in the literature.^[290]



III2r 1,3,5-trimethoxy-2-(1-phenylvinyl)benzene

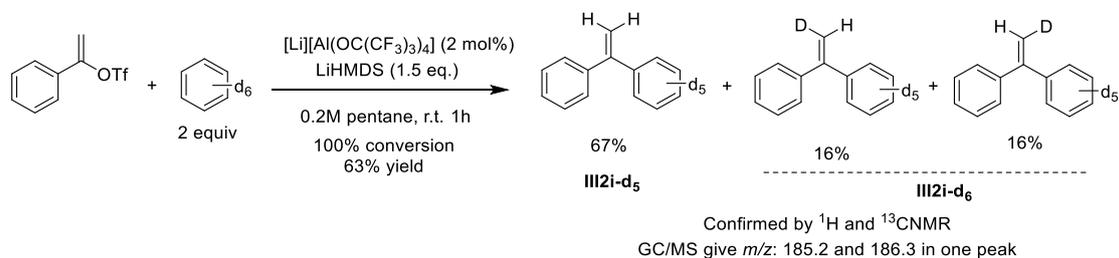
Following the general procedure, using pentane as solvent with 2 equivalents of 1,3,5-trimethoxybenzene for 1 h, product **III2r** was obtained as a white solid in 55% yield

after purification. $^1\text{H NMR}$ (360 MHz, CDCl_3) δ 7.37 – 7.32 (m, 2H), 7.28 – 7.20 (m, 3H), 6.22 (s, 2H), 5.96 (d, $J = 1.5$ Hz, 1H), 5.22 (d, $J = 1.5$ Hz, 1H), 3.88 (s, 3H), 3.71 (s, 6H). $^{13}\text{C NMR}$ (91 MHz, CDCl_3) δ 160.62, 158.72, 141.12, 140.77, 128.02, 127.98, 127.09, 125.82, 116.26, 112.37, 90.92, 56.03, 55.36. Spectroscopic data match those previously reported in the literature.^[291]



Following the general procedure, the product was obtained as a white solid in 71% yield. $^1\text{H NMR}$ (300 MHz, CDCl_3) δ 7.64 – 7.50 (m, 4H), 7.45 – 7.31 (m, 6H). $^{13}\text{C NMR}$ (75 MHz, CDCl_3) δ 131.64, 128.36, 128.27, 123.32, 89.40. Spectroscopic data match those previously reported in the literature.^[292]

3.3 Deuterium Labeling Experiment



Following the general procedure, using 2 equivalents of d^6 -benzene as the nucleophile in 0.2 M pentane, compounds **III2i-d₅**^[293] and **III2i-d₆**^[294] (1:1 mixture of *Z/E* isomer) were obtained in total 63% isolated yield. The percentage of **III2i-d₅** is 67%, *E*-**III2i-d₆** is 16%, *Z*-**III2i-d₆** is 16%, which has been determined by $^1\text{H NMR}$ and $^{13}\text{C NMR}$.

$^1\text{H NMR}$ (360 MHz, chloroform-*d*) δ 7.33 – 7.20 (m, 5H), 5.39 (s, 1.33H, **III2i-d₅**), 5.38 (s, 0.16H, **III2i-d₆**), 5.37 (s, 0.16H, **III2i-d₆**). $^{13}\text{C NMR}$ (91 MHz, CDCl_3) δ 150.03, 149.95, 141.52, 141.32, 128.30, 128.19, 127.73, 114.30 (**III2i-d₅**), 114.01 (**III2i-d₆**), 113.74(**III2i-d₆**). GC-MS: **III2i-d₅** m/z : 185.2 and **III2i-d₆** m/z : 186.3.

GENERAL CONCLUSION

In this thesis, we studied the behavior of the weakly coordinating aluminate counterion $[\text{Al}(\text{OC}(\text{CF}_3)_3)_4]^-$ in catalytic processes based on cationic metals. The catalyst $[\text{Ga}][\text{Al}(\text{OC}(\text{CF}_3)_3)_4]$ was applied into transformations including dihydroarylation of arenes, transfer hydrogenation of alkenes, tandem hydrogenation cyclization of arenes and enynes cycloisomerization. The catalyst $[\text{In}][\text{Al}(\text{OC}(\text{CF}_3)_3)_4]$ was used to promote *ortho*-C-alkylation of unprotected anilines in the presence of styrenes and hydroamination of unprotected primary and secondary alkenylamines. The catalyst $[\text{Li}][\text{Al}(\text{OC}(\text{CF}_3)_3)_4]$ has been tested in the synthesis of styrene derivatives from vinyl triflate and arenes via a vinyl cation. We proved that this bulky and inert anion $[\text{Al}(\text{OC}(\text{CF}_3)_3)_4]$ was capable of taming highly reactive cations, both cationic metals and reaction intermediates, thus opening new perspectives in synthetic methodology (Figure 46).

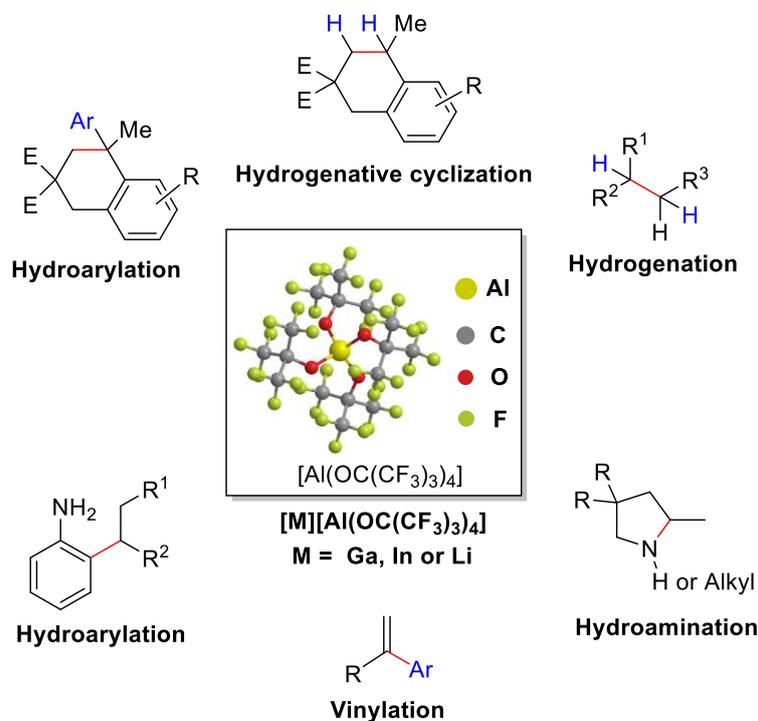


Figure 46. Panoramic view of all the transformations in the thesis

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Titre : Contrôle d'ions métalliques et d'intermédiaires hautement réactifs en catalyse homogène par l'utilisation d'un contre-ion faiblement coordonnant

Mots clés : gallium(I), indium(I), cation vinylique, anion faiblement coordonné, catalyse

Dans cette thèse, nous avons étudié le comportement du contreion aluminate faiblement coordonnant, $[\text{Al}(\text{OC}(\text{CF}_3)_3)_4]$ dans des processus catalytiques à base de métaux des cationiques comme les sels de gallium(I), d'indium à faible degré d'oxydation ainsi que des sels de lithium. Tout d'abord, nous avons étudié les transformations catalysées par $[\text{Ga}][\text{Al}(\text{OC}(\text{CF}_3)_3)_4]$, notamment pour la dihydroarylation des arènes, l'hydrogénation par transfert des alcènes en utilisant le 1,4-cyclohexadiène comme source d'hydrogène, la cyclisation hydrogénante en tandem des arènes et la cycloisomérisation des énynes. Par la suite, nous avons démontré que le catalyseur $[\text{In}][\text{Al}(\text{OC}(\text{CF}_3)_3)_4]$ était très sélectif pour favoriser l'ortho-alkylations d'anilines non protégées en présence des styrènes.

Par extension nous avons appliqué ce dernier à l'hydroamination d'alcénylamines primaires et secondaires non protégées dans des conditions douces. Enfin, le complexe $[\text{Li}][\text{Al}(\text{OC}(\text{CF}_3)_3)_4]$ s'est révélé être un catalyseur efficace pour la synthèse de dérivés du styrène à partir de vinyl triflate et d'arènes par l'intermédiaire d'un cation vinylique. Nous avons prouvé que cet anion volumineux et inerte $[\text{Al}(\text{OC}(\text{CF}_3)_3)_4]$ était capable d'appivoiser des cations hautement réactifs que ce soit des métaux cationiques ou des intermédiaires réactionnels, ouvrant ainsi de nouvelles perspectives en méthodologie de synthèse.

Title : Taming highly reactive metal cations and intermediates in homogeneous catalysis using a weakly coordinating anion

Keywords : gallium(I), indium(I), vinyl cation, weakly coordinating anion, catalysis

In this thesis, we studied the behavior of the weakly coordinating aluminate counterion, $[\text{Al}(\text{OC}(\text{CF}_3)_3)_4]$, in catalytic processes based on cationic metals such as gallium(I) and indium(I) salts with low oxidation state indium and lithium salts. Initially, we have studied $[\text{Ga}][\text{Al}(\text{OC}(\text{CF}_3)_3)_4]$ -catalyzed transformations more especially for the dihydroarylation of arenes, the transfer hydrogenation of alkenes using 1,4-cyclohexadiene as hydrogen source, the tandem hydrogenation cyclization of arenes and enynes cycloisomerization. Subsequently, we showed that the $[\text{In}][\text{Al}(\text{OC}(\text{CF}_3)_3)_4]$ catalyst was highly selective in promoting *ortho*-alkylation of unprotected anilines in the presence of styrenes.

By extension we applied the latter to the hydroamination of unprotected primary and secondary alkenylamines under mild conditions. Finally, the $[\text{Li}][\text{Al}(\text{OC}(\text{CF}_3)_3)_4]$ complex has proven to be an effective catalyst for the synthesis of styrene derivatives from vinyl triflate and arenes via a vinyl cation. We proved that this bulky and inert anion $[\text{Al}(\text{OC}(\text{CF}_3)_3)_4]$ was capable of taming highly reactive cations, both cationic metals and reaction intermediates, thus opening new perspectives in synthesis methodology.