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New olefin metathesis catalysts with fluorinated NHC ligands: synthesis and catalytic activity

Salekh Masoud

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pour le grade de

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UFR SPM Sciences et Propriétés de la Matière
et à

l'Institut Nesmeyanov des Organoéléments de Moscou (INEOS)

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**New olefin metathesis
catalysts with
fluorinated NHC ligands:
Synthesis and catalytic
activity**

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List of abbreviations

G-I, G-II, G-III	Grubbs' catalysts 1st, 2nd or 3rd generation
HG-I, HG-II	Hoveyda-Grubbs' catalysts 1st or 2nd generation
ADMET	acyclic diene metathesis polymerization
CM	cross-metathesis
RCEYM	ring-closing enyne metathesis
RCM	ring-closing metathesis
ROCM	ring-opening cross-metathesis
ROM	ring-opening metathesis
ROMP	ring-opening metathesis polymerization
RRM	ring-rearrangement metathesis
SM	self-metathesis
DCE	dichloroethane
DMA	dimethylacetamide
DMC	dimethylcarbonate
DME	dimethoxyethane
DMF	dimethylformamide
DMSO	dimethylsulfoxide
NMP	<i>N</i> -methylpyrrolidone
PFMC	perfluoro(methylcyclohexane)
THF	tetrahydrofuran
Ac	acetyl
Ac ^F	trifluoroacetyl
Ad	1-adamantyl
All	allyl
Am	amyl
ⁱ Am	isoamyl
^t Am	<i>tert</i> -amyl
Ar	aryl
Bn	benzyl
Boc	<i>tert</i> -butyloxycarbonyl
Bu	butyl
ⁱ Bu	<i>iso</i> -butyl
^t Bu	<i>tert</i> -butyl
Cp	cyclopentyl
Cp*	pentamethylcyclopentyl
Cy	cyclohexyl
DIPP	2,6-diisopropylphenyl
Et	ethyl
IMes	1,3-bis(2,4,6-trimethylphenyl)imidazolylidene

SIMes	1,3-bis(2,4,6-trimethylphenyl)-1H-imidazol-3-ylidene
Me	methyl
Mes	2,4,6-trimethylphenyl (mesityl)
Methall	methallyl
Nf	nonaflyl
Ph	phenyl
Pr	propyl
ⁱ Pr	isopropyl
Pyr	pyren-1-yl
Tf	trifluoromethylsulfonyl (triflyl)
Ts	<i>p</i> -toluenesulfonyl (tosyl)
AIBN	azobisisobutyronitrile
APCN	amphiphilic polymer conetwork
BMIM	1-butyl-3-methylimidazolium
COD	1,5-cyclooctadiene
COE	<i>cis</i> -cyclooctene
CPE	cyclopentene
CTABr	cetyltriethylammonium bromide
dba	dibenzylideneacetone
DCPD	dicyclopentadiene
DEAMM	diethyl allylmethallylmalonate
DEDAM	diethyl diallylmalonate
DEDMM	diethyl dimethallylmalonate
DEDPM	diethyl dipropargylmalonate
DPPA	diphenylphosphoryl azide
DVB	divinylbenzene
HBcat	catecholborane
HFGA	hexafluoroglutaric anhydride
HMDS	hexamethyldisilazane
KHMDS, NaHMDS	potassium or sodium bis(trimethylsilyl)amide (hexamethyldisilazide)
MCF	mesocellular foam
mCPBA	meta-chloroperoxybenzoic acid
MTBE	methyl <i>tert</i> -butyl ether
NBE	norbornene
NHC	<i>N</i> -heterocyclic carbene
PS	polystyrene
<i>p</i> TSA	<i>para</i> -toluenesulfonic acid
rGO	reduced graphene oxide
SPhos	2-dicyclohexylphosphino-2',6'-dimethoxybiphenyl
TBAB	tetrabutylammonium bromide
TEA	triethylamine
TEG	triethylene glycol
TFA	trifluoroacetic acid

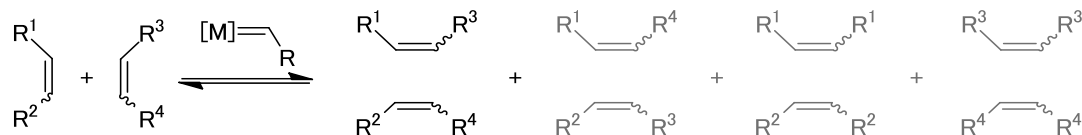
VAZO	1,1'-azobis(cyclohexanecarbonitrile)
FBS	fluorous biphasic system
GC	gas chromatography
HOESY	heteronuclear Overhauser effect spectroscopy
NMR	nuclear magnetic resonance
nOe	nuclear Overhauser effect
NOESY	nuclear Overhauser effect spectroscopy
SPE	solid-phase extraction
F-SPE	fluorous solid-phase extraction
UV	ultraviolet
sm	starting material
TON	turnover number

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GENERAL INTRODUCTION

Olefin metathesis (from the Greek word “μετάθεση”, meaning change of position¹) is a reaction that entails the redistribution of substituents of alkenes by the scission and regeneration of new double bonds (Scheme 1).



Scheme 1. General scheme of olefin metathesis.

During the last decades, olefin metathesis has become one of the most powerful and attractive tools for the formation of carbon-carbon double bonds in synthesis of wide range of different molecules from simple alkenes² to complex biologically active compounds³⁻⁵ and polymers⁶. The importance of the development of metathesis method in organic synthesis has been recognized by the award of the Nobel Prize in Chemistry for 2005 jointly to Yves Chauvin, Robert H. Grubbs, and Richard R. Schrock.

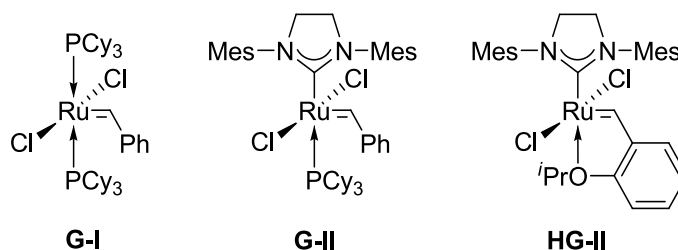
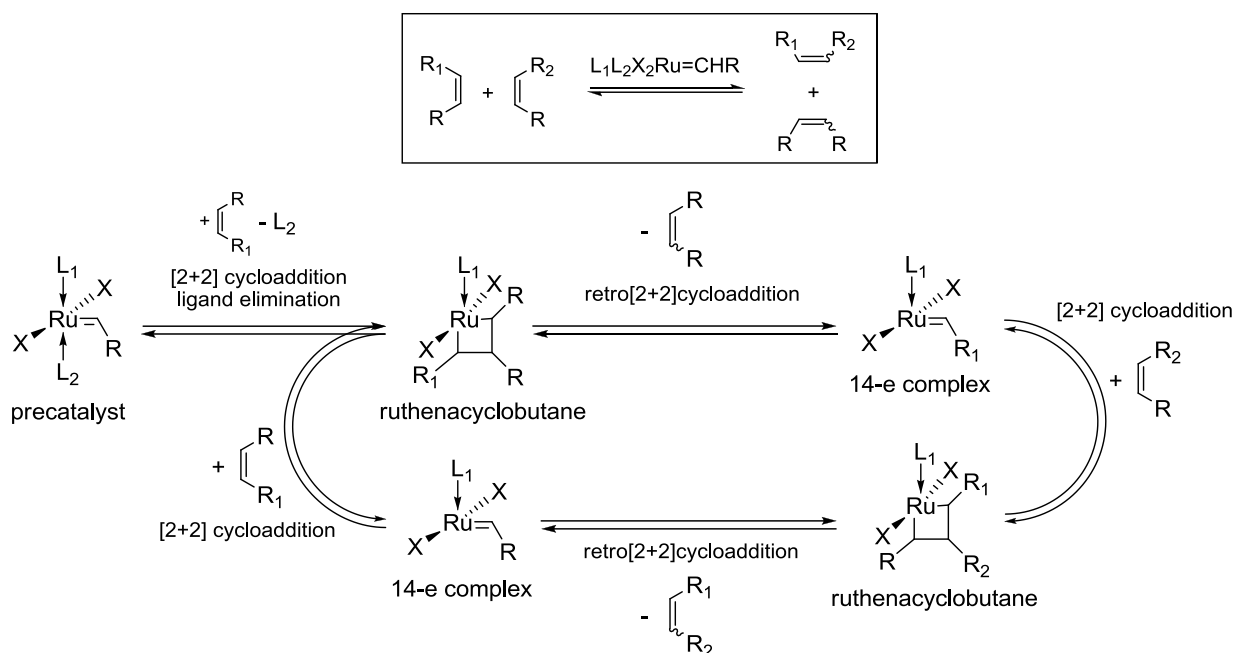


Figure 1. The most common ruthenium metathesis catalysts: First-generation Grubbs catalyst (**G-I**), second-generation Grubbs catalyst (**G-II**), second-generation Hoveyda–Grubbs catalyst (**HG-II**).

The most efficient catalysts for the olefin metathesis reaction in homogeneous conditions have been developed with well-defined ruthenium⁷, molybdenum and tungsten⁸ complexes featuring a reactive metal-carbene ligand. Among the variety of metathesis catalysts obtained up to now, ruthenium-based Grubbs-type catalysts (Figure 1) are very popular due to successful combination of remarkable air and moisture stability, relative tolerance to a wide range of functional groups (such as carboxylic acids, alcohols, ketones etc.) while maintaining good reactivity of ruthenium metal center to C=C double bond⁹. Since 1992, when the first well-defined ruthenium catalysts has been reported¹⁰, a large number of different modifications was performed¹¹. Despite the great progress that has been made during recent decades, synthesis of novel, more efficient and selective metathesis catalysts is still of great interest.

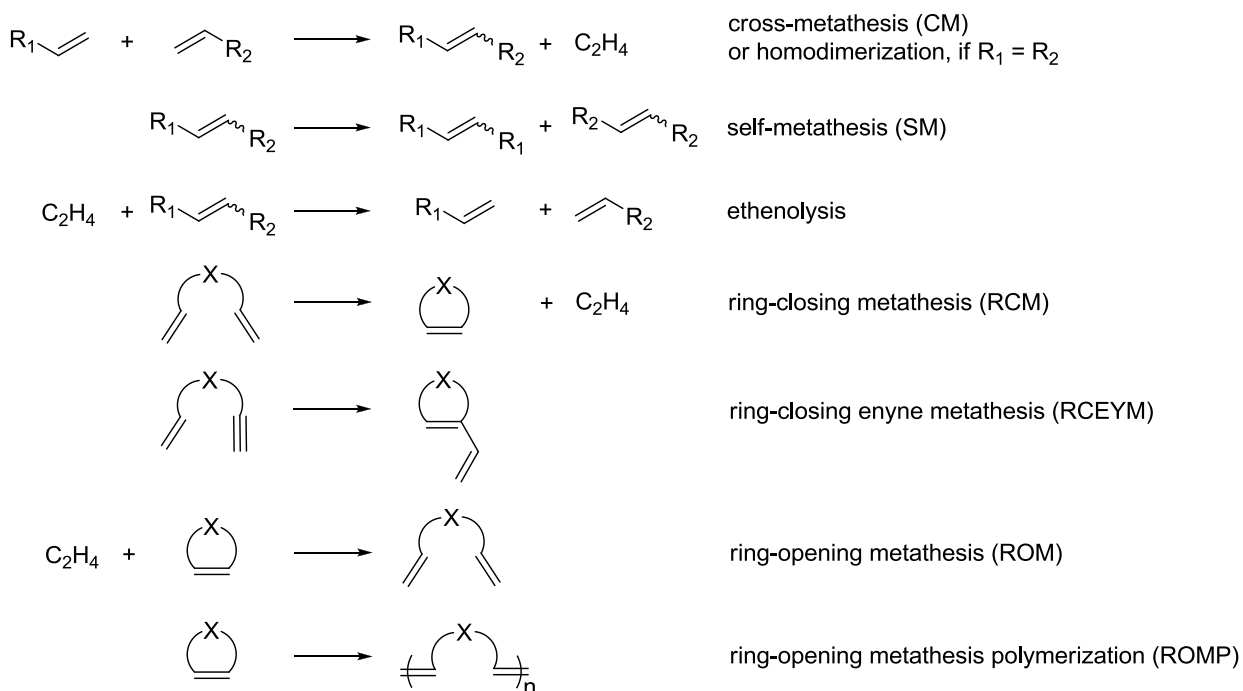
The mechanism for metal-catalyzed olefin metathesis was suggested by Y. Chauvin and J.-L. Hérisson¹². Accordingly (Scheme 2), the key steps of metathesis includes the [2+2]-cycloaddition

of olefin to a carbene complex with formation of a metallacyclobutane intermediate followed by retro[2+2]cycloaddition. It is important to note that each step of the catalytic cycle is reversible.

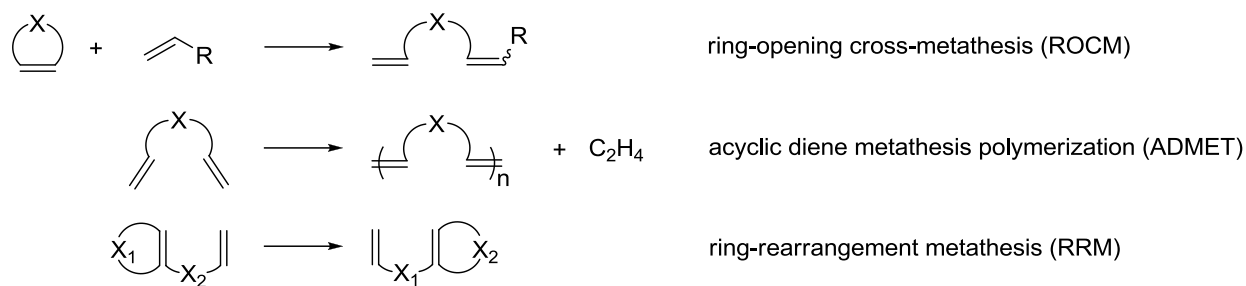


Scheme 2. The general mechanism of olefin metathesis.

It entails that the result of metathesis in the most general case is an equilibrium mixture of all possible products. Thus, olefin metathesis as preparative method could be used only in the case of shifting equilibrium in one direction. This is illustrated by the formation of 5- or 6-membered unstrained (hetero)cycles or, the opposite, ring-strain release. Depending on olefin substrates, several common types of metathesis have been described (Scheme 3).



Scheme 3. Common types of olefin metathesis.



Scheme 3 (continuation). Common types of olefin metathesis.

Among them, ring-closing metathesis (RCM) and ring-opening metathesis polymerization (ROMP) are the most widely used types of olefin metathesis in organic synthesis and polymer science, respectively. On the other hand, cross-metathesis (CM) is one of the most challenging types due to the absence of strong thermodynamic reasons for irreversibility of reaction and *E/Z*-selectivity of products. While the problem of irreversibility could be solved by formation of volatile olefins as by-products (such as ethylene or propylene), mixture of *E*- and *Z*-olefins with thermodynamically favorable major *E*-product is hard to separate. On the other hand, many natural and biologically active compounds contain *Z*-alkene moieties. Therefore, synthesis of efficient catalysts that could provide formation of only *E*- or *Z*-olefins is one of the most topical tasks of metathesis catalysts modification. These aspects have recently found elegant solution by fine tuning of steric bulk of the ligands around the metal center^{13–15}.

At the same time, the chemistry of fluorinated compounds is undergoing rapid growth. Organofluorine compounds often show unusual properties and behavior in comparison with corresponding non-fluorinated parent compounds, due to unique properties of the fluorine atom, such as high electronegativity, small size and polarizability, ability to form *H*-bonding and coordinate to transition metals¹⁶, strength of the C-F bond, which is the strongest one in organic chemistry. Moreover, high abundance in Earth's crust and possibility of easy detection by ¹⁹F NMR because of monoisotopicity and high sensitivity¹⁷ are also attractive properties for chemists. Due to this features organofluorine compounds have found a large variety of industrial applications in medicinal chemistry, crop, and material sciences. 5-Fluorouracil, Prozac, and Efavirenz are well-known examples of fluorine-containing drugs. Finally, perfluoroorganic derivatives can create a fluorous phase that is immiscible with most of organic solvents and can provide simple recovery of catalysts or reaction products¹⁸.

Up to date, only a few fluorine-containing ruthenium metathesis catalysts have been reported. In addition to the mentioned above fluorophilicity, which could be achieved due to perfluorosubstituents (*i.e.* “fluorous ponytails”), introduction of fluorine to the ligands of ruthenium metathesis catalysts might increase their electron withdrawing properties, steric bulk or

create Ru-F interactions. These properties may significantly alter the catalyst activity and selectivity.

The main target of the present work is the development of efficient methods for the synthesis of series of new unsymmetrical imidazolium salts, precursors of NHC-ligands that contain bulky hexafluoroisopropoxy group and the synthesis of corresponding Grubbs- and Hoveyda-type catalysts (Figure 2), as well as the investigation of their catalytic activity in model RCM and CM reactions.

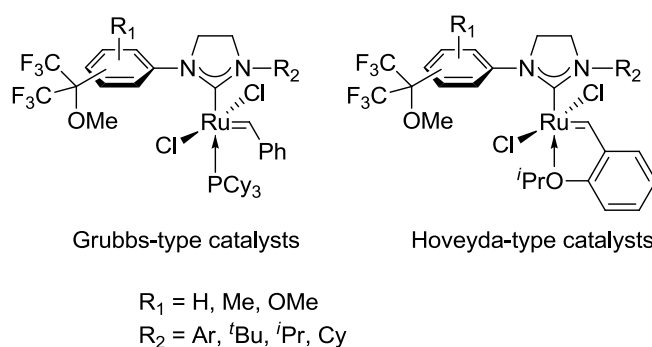


Figure 2. General structures of synthesized and tested catalysts in this work.

In **chapter 1**, the recent publications about fluoro-containing ruthenium metathesis catalysts, their synthesis and activity will be reviewed. In **chapter 2** we will describe the results of our own investigations in this field. The experimental details and conclusions will be presented in **chapter 3** and **chapter 4**, respectively.

CHAPTER I (Literature survey)

FLUORINE-CONTAINING RUTHENIUM CATALYSTS OF OLEFIN METATHESIS

1.1. Introduction

In the general case, Grubbs catalysts contain several different types of ligands (Figure 3). The first one is the reactive metal carbene ligand. In first-generation Grubbs catalyst (**G-I**) it is usually an arylidene (benzylidene) that directly participates in the [2+2] cycloaddition during metathesis. In the case of second- (**G-II** and **HG-II**) and third-generation (**G-III**) catalysts, a second type of carbene, a *N*-heterocyclic carbene is also present. Due to its electronic and steric properties, this ligand provides stability and efficiency to the catalyst. The third type is L-type ligands are phosphine (in **G-I** and **G-II**) or pyridine (in **G-III**). In the case of Hoveyda-type catalysts (**HG-II**) the L-type ligand is a part of the bidentate arylidene ligand and consists in a chelating alkoxy group. Finally, chlorides are the most common X-type ligands in Grubbs or Hoveyda-type catalysts.

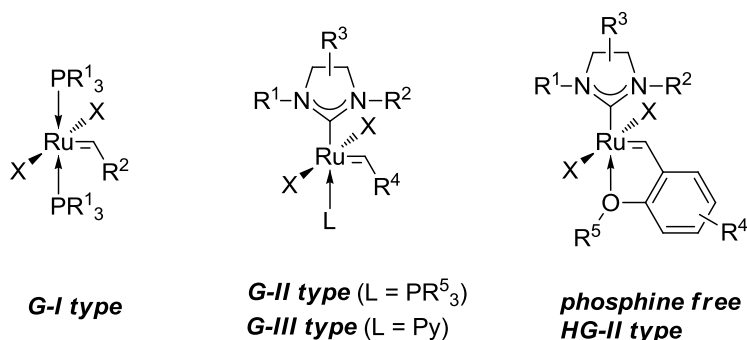
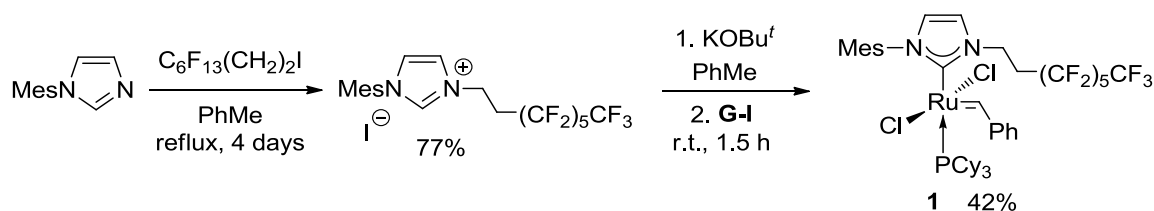


Figure 3. General structural modifications of Grubbs-types catalysts.

All these ligands can be modified in various ways depending on the particular task. During the last decades, a large number of Grubbs catalysts modifications have been described^{11,17} and until now modifications for improvement of selectivity, stability, recyclability or simplification of products isolation have been an important driving task. Some of them could be solved due to modification by fluorine-containing groups. In this literature survey, we review all known fluorine-containing olefin metathesis ruthenium catalysts and the synthesis of the corresponding fluorinated ligands. This survey is divided into parts according to the type of fluorine-containing ligand. In each part, except 1.7, the chronological order has been chosen.

1.2. Fluorine in NHC-ligands

The first example of second-generation Grubbs-type catalyst with polyfluoroalkyl $\text{C}_6\text{F}_{13}(\text{CH}_2)_2$ -group on nitrogen of NHC-ligand was published by A. Fürstner and co-workers in 2001¹⁹. This modification was performed to increase the catalyst solubility in supercritical CO_2 . The fluorinated group was introduced by alkylation of readily available *N*-mesityl imidazole with $\text{C}_6\text{F}_{13}(\text{CH}_2)_2\text{I}$ under refluxing in toluene for 4 days to afford the corresponding NHC precursor in good yield (Scheme 4)²⁰. The target catalyst **1** was obtained in moderate yield by conventional route included the phosphine ligand exchange reaction of commercially available Grubbs complex of first-generation with the NHC generated *in situ* from fluorinated imidazolium salt under the treatment of the latter with potassium *tert*-butylate (Scheme 4). The complex **1** has demonstrated an excellent solubility in supercritical carbon dioxide and good catalytic activity in RCM of *N,N*-dimethyltolosylamine.



Scheme 4. Synthesis of complex **1**.

In 2002 A. Hoveyda *et al.* described the synthesis of the catalyst **2a** (Figure 4)²⁰, containing bidentate chiral binaphthyl NHC-ligand. This catalyst was air-stable and active in series of asymmetric metathesis reactions (up to >98% ee). In 2003 synthesis and catalytic activity of fluorine-containing (**2b** and **2c**, Figure 4) modifications of **2a** were described²¹.

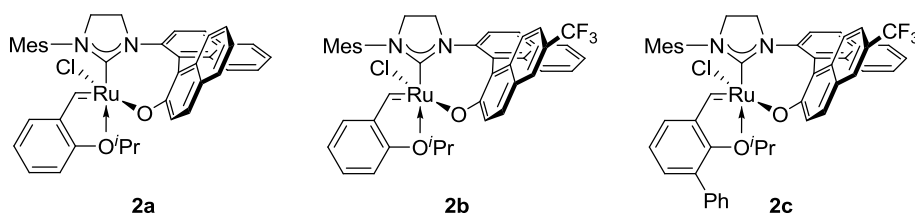
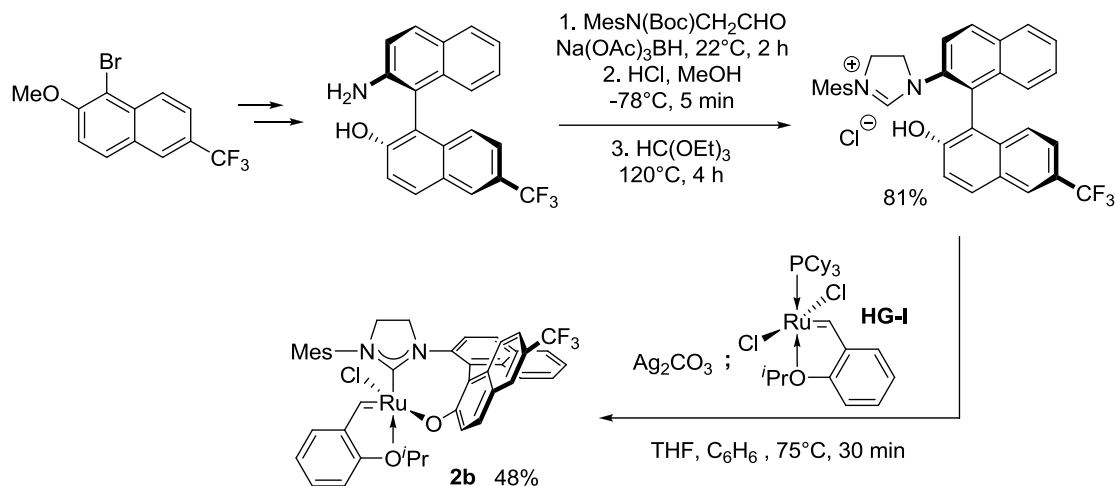


Figure 4. Complexes **2**.

The corresponding binaphthyl ligand was synthesized by multistep method using transmetalation of silver complex for synthesis of target complex **2b** (Scheme 5).



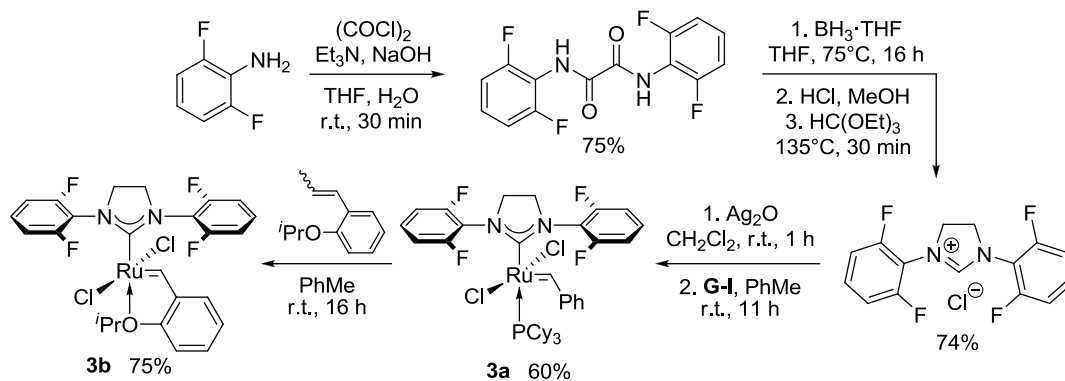
Scheme 5. Synthesis of complex **2b**.

The introduction of CF₃-groups allowed to significantly increase the activity of catalysts. For instance, in asymmetric ring-opening cross-metathesis (AROCM) of norbornenedicarboxylic anhydride and styrene the reaction rate increased in 3 times for catalyst **2b** and in 160 times for **2c** (Table 1).

Table 1. AROCM of norbornenedicarboxylic anhydride and styrene.

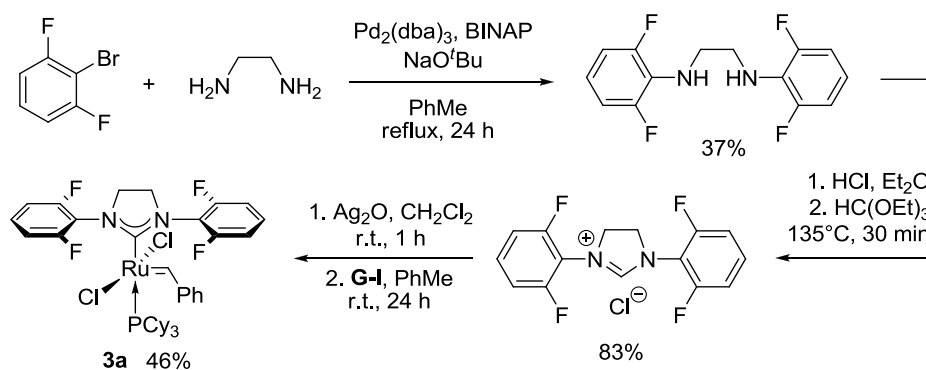
Catalyst	Time	Conversion	Yield
2a	66 h	>99%	35%
2b	22 h	>99%	55%
2c	25 min	>99%	85%

In 2006 R. Grubbs *et al.* described two catalysts that contain fluorine in *ortho*-positions in NHC ligand (**3a** and **3b**, Scheme 6)²². The catalyst **3a** demonstrated much higher activity than parental **G-II** in RCM DEDAM, while **3b** was less active than **HG-II**. Such difference was explained by possible Ru-F interaction, which stabilizes 14-e complex on the initiation step of catalyst **3a** and hinders the access of olefin to ruthenium in catalyst **3b**. Despite the relatively low activity of **3b**, it showed good results in RCM to form tetrasubstituted olefins²³. The corresponding fluorinated precursor of NHC-ligand was synthesized from commercially available 2,6-difluoroaniline.



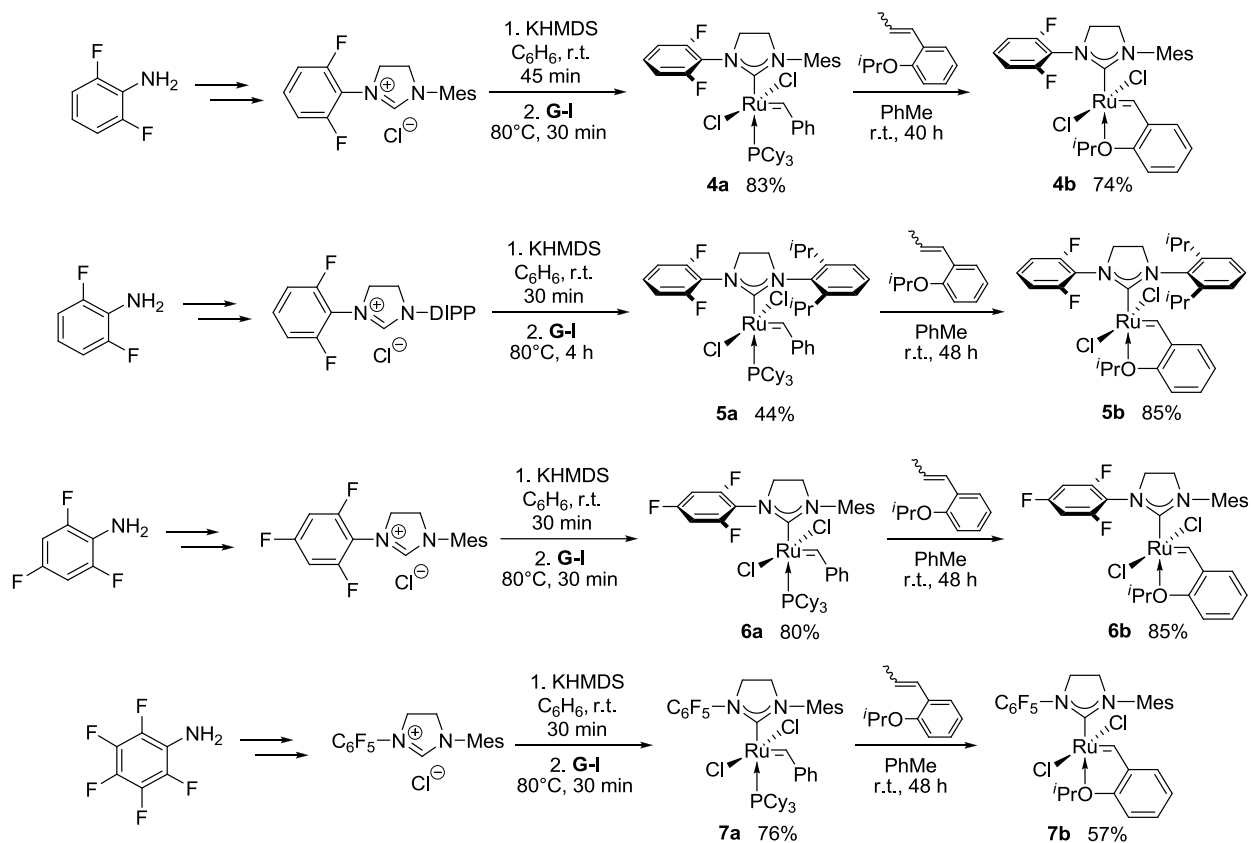
Scheme 6. Synthesis of complexes **3**.

Another approach for synthesis of **3a** using 1-bromo-2,6-difluorobenzene (Scheme 7) was proposed by C. Costabile *et al.*²⁴. In that publication catalyst **3a** was studied in the scope of RCM, ROMP and CM. Low stability of **3a** under reaction conditions in dichloromethane was marked.



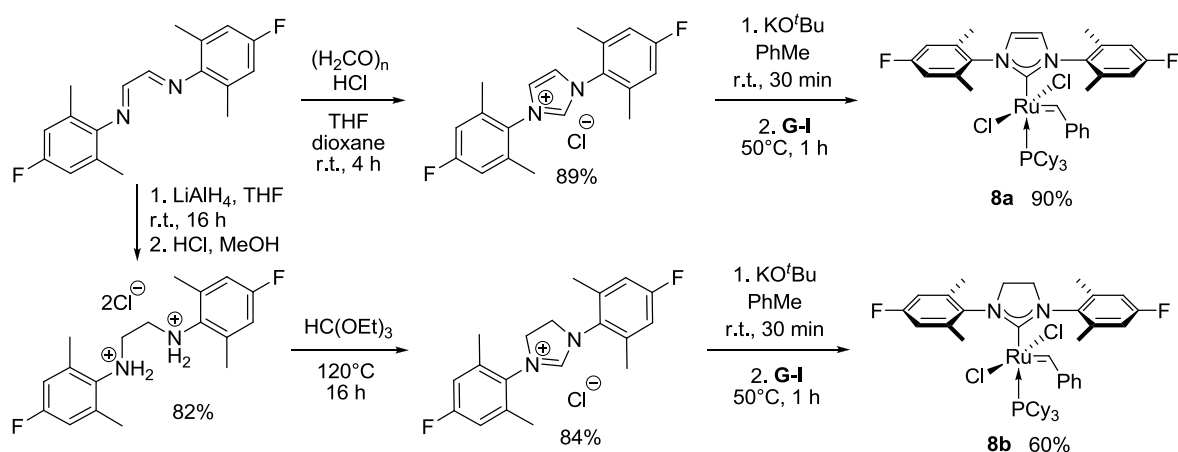
Scheme 7. Synthesis of complex **3a**.

Unsymmetrical analogues of **3a** and **3b** (catalysts **4-7**, Scheme 8) demonstrated similar tendencies in RCM, CM and ROMP^{25,26}: in all cases Grubbs-type catalysts were more active than Hoveyda-type. Synthesis of NHC-ligand precursors for was done by the adapted method for unsymmetrical imidazolium salts starting from corresponding fluoroanilines.



Scheme 8. Synthesis of complexes 4-7.

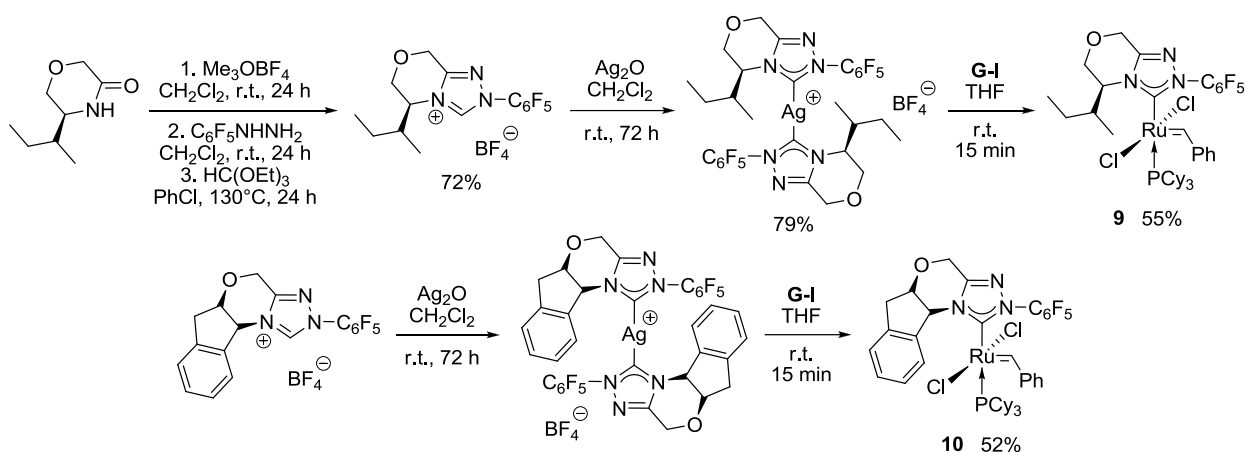
In 2008 H. Plenio *et al.* described the synthesis of second-generation Grubbs-type catalysts bearing saturated and unsaturated NHC-ligands with fluorine in *para*-positions (**8a** and **8b**, Scheme 9)²⁷. Some electrochemical properties of these complexes were described without the catalytic activity. Fluorine atom was introduced into aromatic substrate by Schiemann reaction.



Scheme 9. Synthesis of complexes 8.

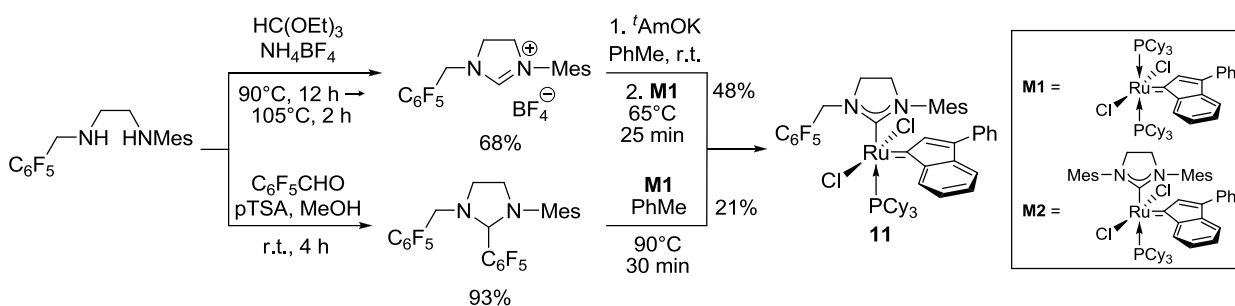
Synthesis of catalysts **9** and **10** (Scheme 10) bearing 1,2,4-triazol-5-ylidene ligands with pentafluorophenyl moiety and their test in asymmetrical metathesis reactions (ARCM and AROCM) were described by K. Grela *et al.*²⁸. The complexes demonstrated good enantioselectivity in AROCM of norbornenedicarboxylic anhydride with styrene, but

demonstrated low conversions and stability compared to their non-fluorinated analogues. Also because of their low stability for all catalytic tests **9** and **10** have been prepared *in situ*.



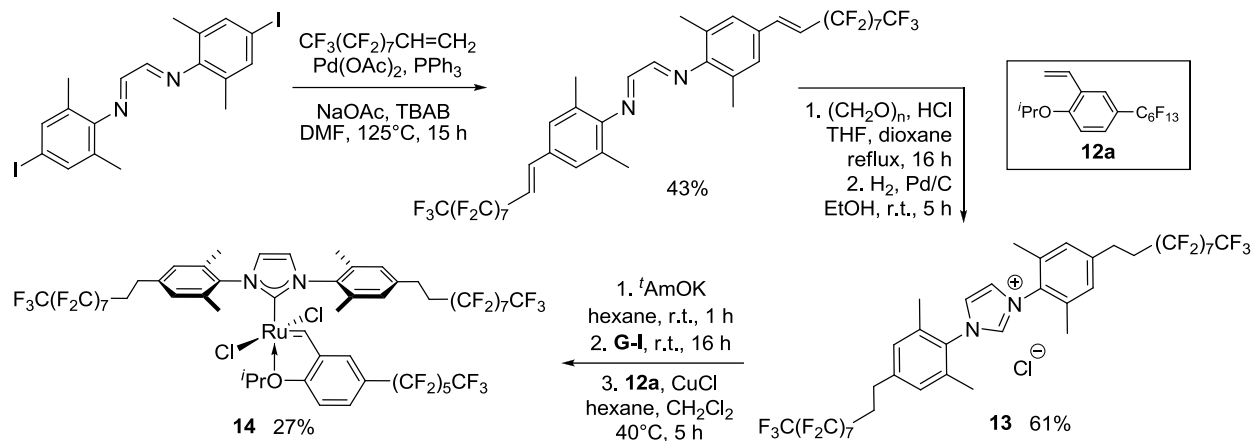
Scheme 10. Synthesis of complexes **9** and **10**.

The same group described indenylidene ruthenium catalyst bearing unsymmetrical NHC-ligand with pentafluorobenzyl group (complex **11**, Scheme 11)²⁹. In RCM DEDAM in air atmosphere³⁰ catalyst **11** demonstrated higher activity and lower stability than commercially available catalyst **M2**. Synthesis of fluorine-containing ligand was started from pentafluorobenzaldehyde. For synthesis of complex **11** two approaches were used: 1) deprotonation of corresponding imidazolium tetrafluoroborate; and 2) decomposition of pentafluorophenyl adduct. However, the latter proved to be less efficient.



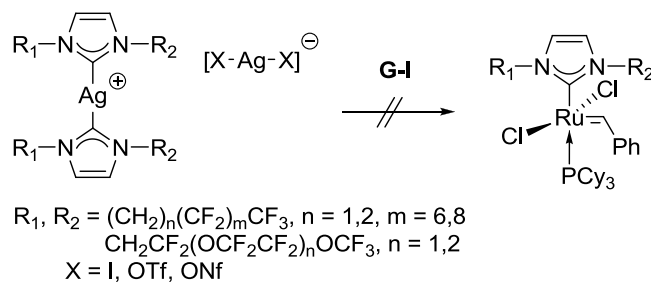
Scheme 11. Synthesis of complex **11**.

The modification of second-generation Hoveyda-Grubbs catalyst with perfluoroalkyl groups for increasing of their fluorophilicity was described by J. Kvičala *et al.*³¹. In this work, perfluoroalkyl substituents were introduced into both mesityl moieties of NHC-ligands and benzylidene ligands. Synthesis of latter will be mentioned in the next part of this survey. For synthesis of fluorous NHC-ligands perfluoroalkyl groups were added by Heck cross-coupling of iodo-containing diamine with perfluorooctylethylene followed by ring-closing of imidazolium cycle and catalytic reduction of double bonds (Scheme 12).



Scheme 12. Synthesis of complex **14**.

Despite the presence of three fluoruous ponytails in complex **14**, its partition coefficient (P_i (FBS) –the ratio of concentrations in each phase of *Fluorous Biphasic System*) between perfluoro(methylcyclohexane) (PFMC) and toluene is just P_i (FBS) = 0.16 that is too low for recovery of catalyst. The catalytic activity of complex **14** in RCM of DEDAM was moderate, not higher than **HG-II**. Earlier attempts to coordinate *N,N'*-dipolyfluoroalkyl-containing NHC-ligands without mesityl moieties to ruthenium (Scheme 13) were unsuccessful probably due to low stability of unhindered NHC complexes³².



Scheme 13. Attempt of synthesis of ruthenium fluoruous complex.

Attempts for synthesis of fluorophilic metathesis catalyst were made by K. Grela *et al.* as well. However, perfluoroalkyl-containing complexes **15a,b** (Figure 5) also demonstrated low fluorophilicity: complex **15a** was insoluble in PFMC, **15b** in PFMC formed stable emulsion³³. Due to these results **15a** and **15b** were not tested in metathesis.

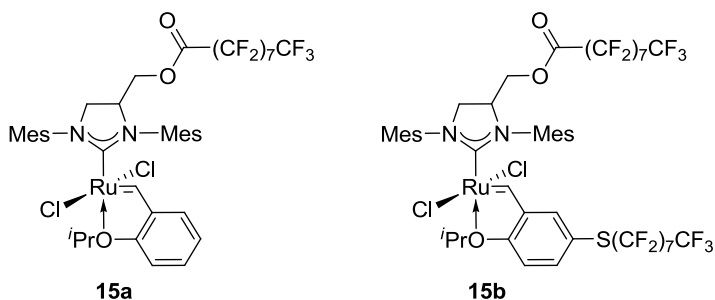


Figure 5. Complexes **15a** and **15b**.

demonstrated high selectivity to formation of alternating copolymer in ROMP of mixture of COE and norbornene (NBE) in ratio 50:1. Moreover, catalysts **21b**, **21d** and **21e** demonstrated good selectivity to formation of terminal olefins in ethenolysis of methyloleate.

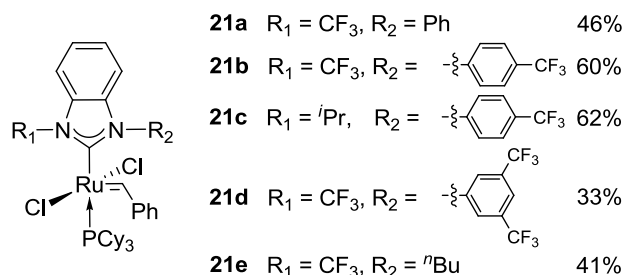
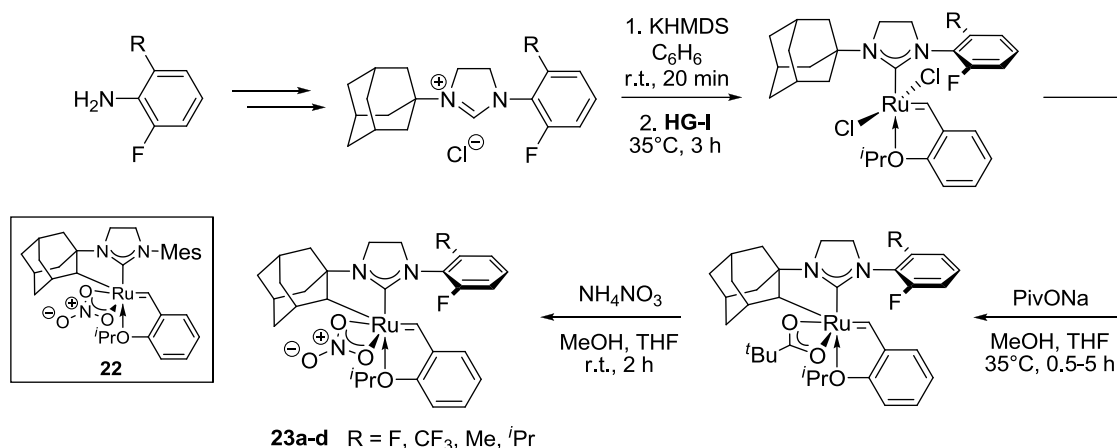


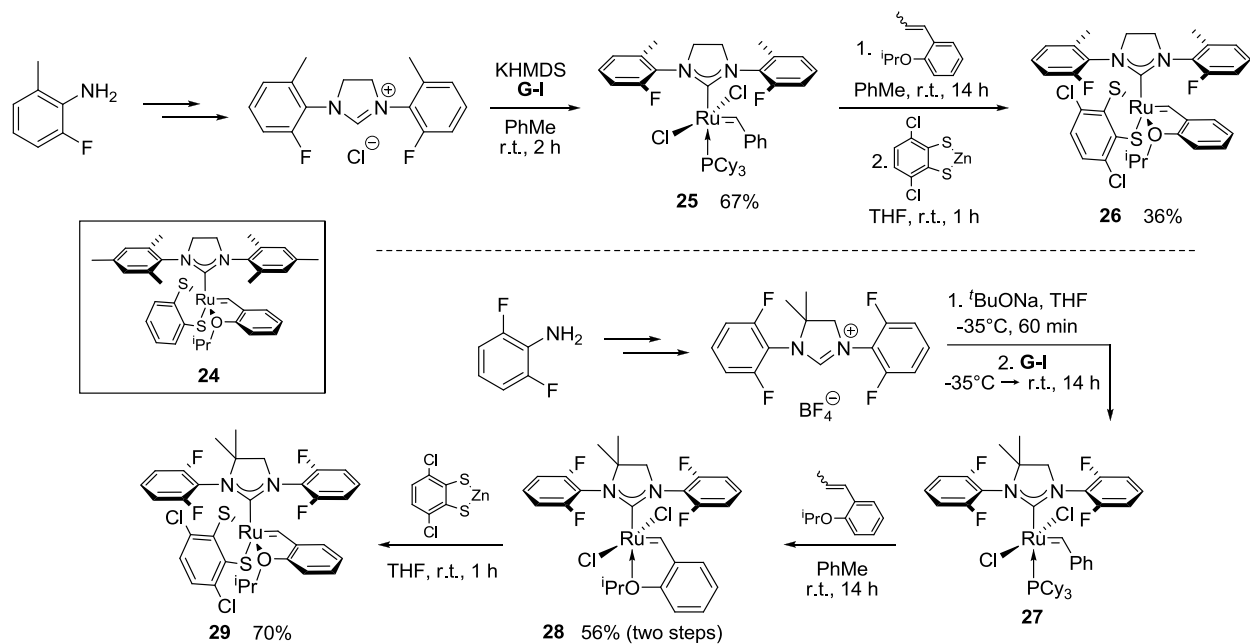
Figure 6. Synthesis of complexes **21**.

In 2016 R. Grubbs and coworkers described the synthesis of fluorine-containing derivatives of known *Z*-selective catalysts **22**³⁶ (Scheme 16) with chelating adamantyl-containing NHC-ligand and **24**^{37,38} with dithiolate ligand (Scheme 17). All the catalysts were synthesized starting from commercially available fluorinated anilines. Adamantyl-containing complexes **23a-d** showed good activity and *Z*-selectivity in series of cross-metathesis and homodimerization reactions, but they were not higher than for complex **22**³⁹.



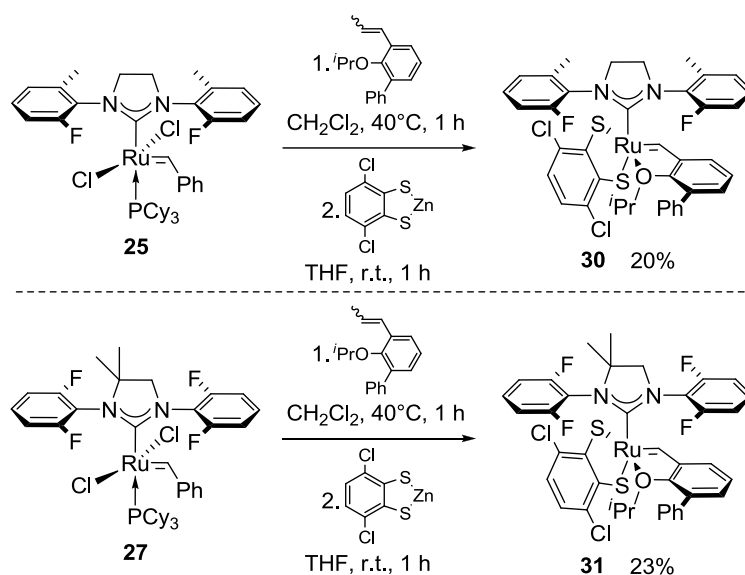
Scheme 16. Synthesis of complexes **23**.

Introduction of fluorine in *ortho*-positions of complex **24** (catalysts **26** and **29**, Scheme 23) allowed to increase yields of *trans*-olefin substrates⁴⁰. Corresponding dithiolate ligands were introduced *via* transmetalation of zinc thiolate.



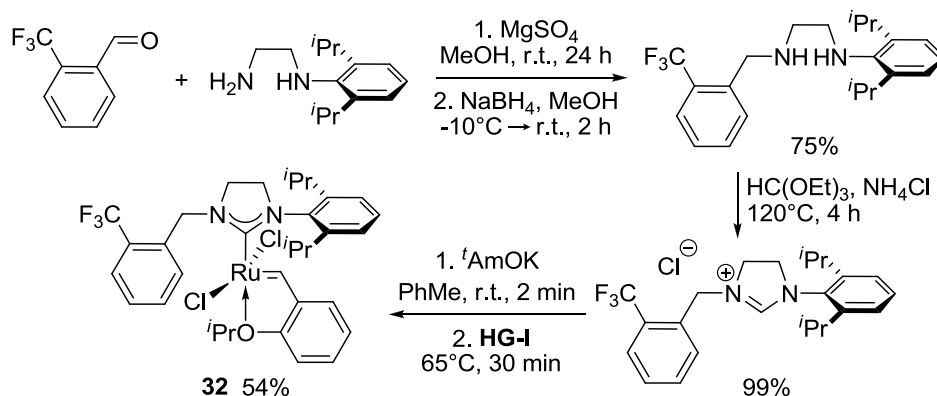
Scheme 17. Synthesis of complexes **26** and **29**.

Introduction of phenyl group into benzylidene moiety of catalysts **26** and **29** allowed to increase the rate of formation of *Z*-isomer (**30** and **31**, Scheme 18)⁴¹.



Scheme 18. Synthesis of complexes **30** and **31**.

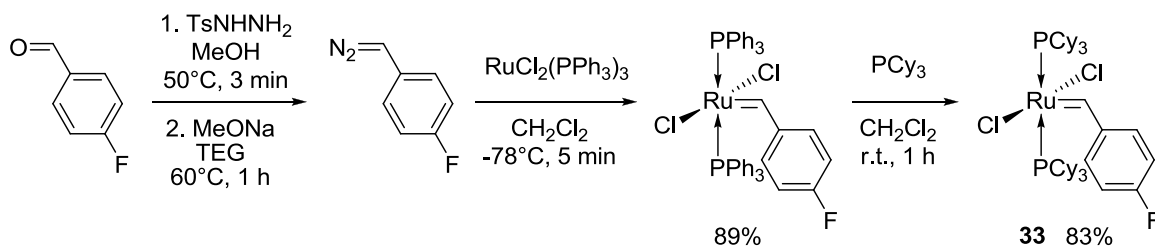
Recently K. Grela *et al.* described series of Hoveyda-type catalyst bearing trifluoromethyl-containing in NHC-ligands **32** (Scheme 19)⁴². This complex was synthesized in three steps starting from commercially available *o*-(trifluoromethyl)benzaldehyde and *N*-(2,6-diisopropylphenyl)ethan-1,2-diamine and showed high stability even at 50°C in toluene. However, in benchmark RCM reactions catalyst **32** have demonstrated less activity in compare with their non-fluorinated analogues.



Scheme 19. Synthesis of complex **32**.

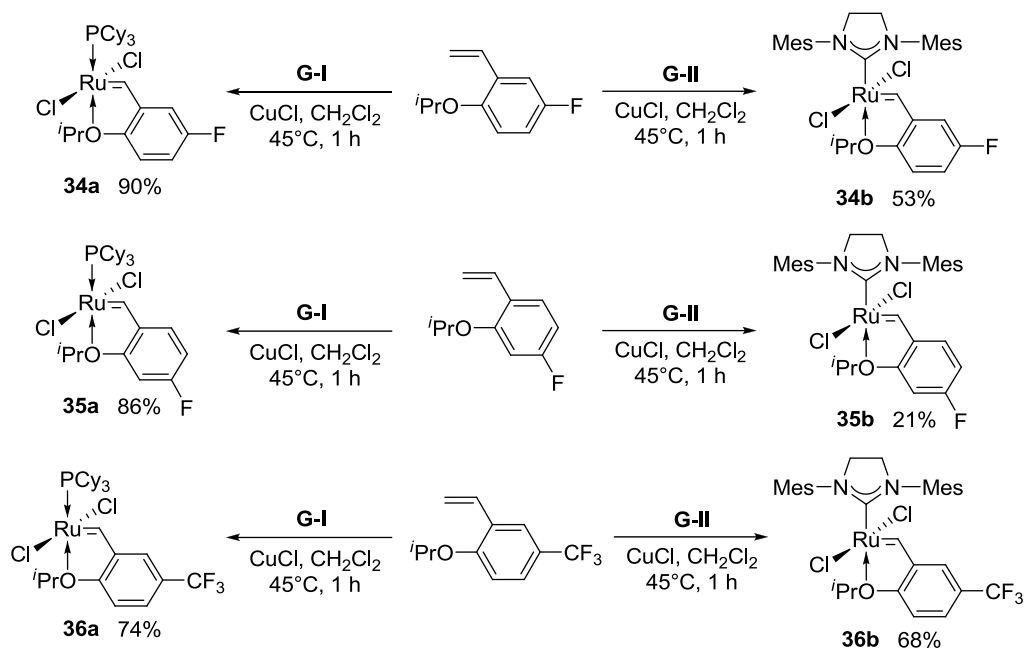
1.3. Fluorine in benzylidene ligands

The first Grubbs catalyst (**33**) bearing fluorinated benzylidene ligand was obtained by R.H. Grubbs *et al.* in 1996⁴³. Synthesis of fluorinated complex **33** implemented starting from commercially available *p*-fluorobenzaldehyde through its diazoderivative as carbene source (Scheme 20). In that contribution only weak influence of fluorine in *para*-position on initiation rate has been revealed.



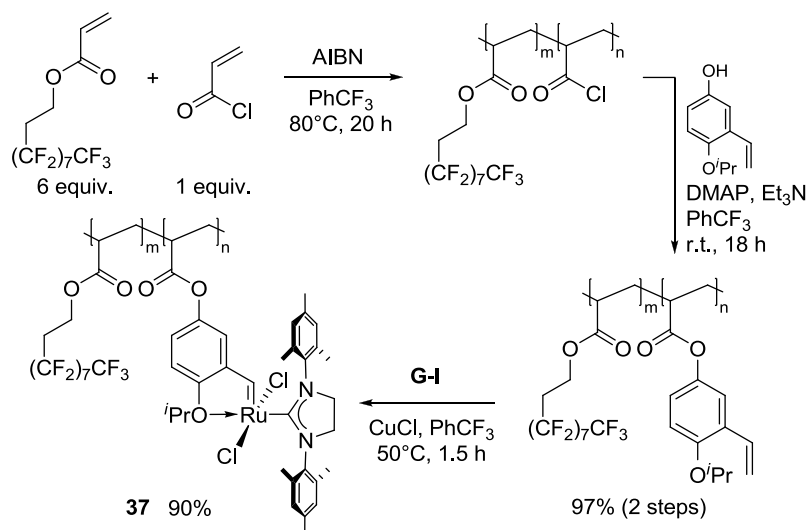
Scheme 20. Synthesis of complex **33**.

Hoveyda-type catalysts with fluorine- and trifluoromethyl-containing arylidenes were described by S. Blechert⁴⁴. Catalysts **34-36** were synthesized from fluorinated styrenes *via* ligand exchange reaction with commercially available **G-I** and **G-II** complexes (Scheme 21). Fluorinated first-generation catalysts showed higher activity than **HG-I**, whereas activity of second-generation catalysts was almost similar to **HG-II**.



Scheme 21. Synthesis of complexes **34-36**.

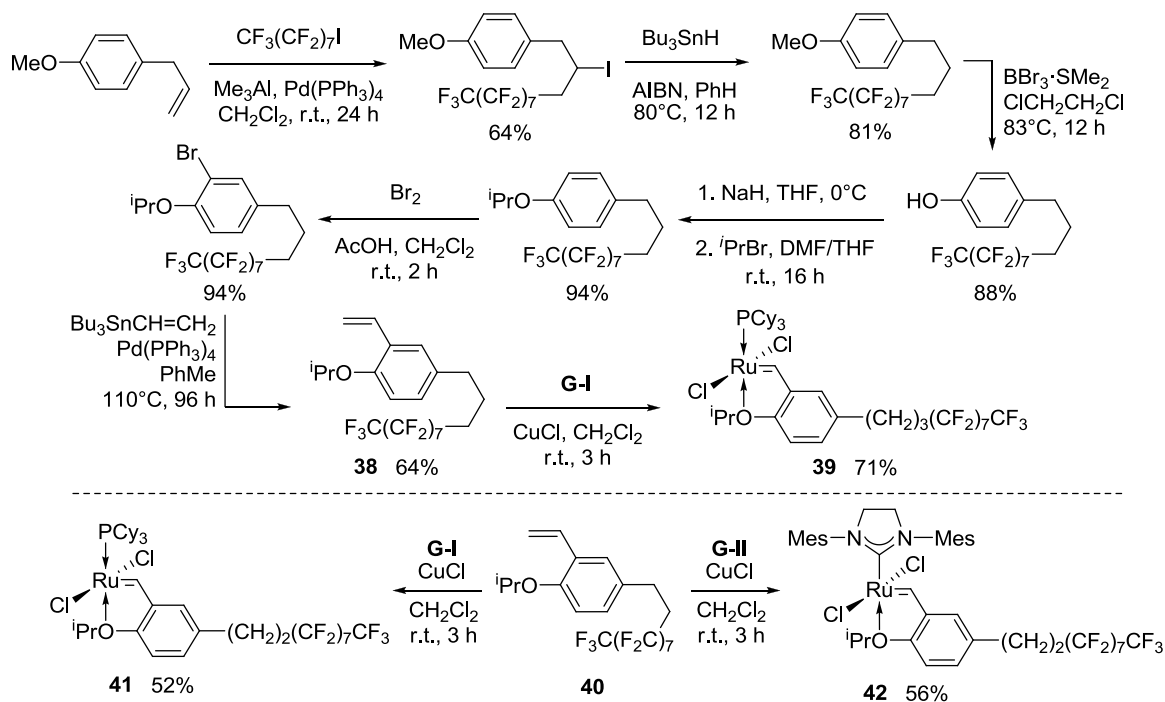
The first example of immobilized on fluororous polymer Hoveyda-Grubbs catalyst was described by Q. Yao and Y. Zhang⁴⁵. The corresponding polymer ligand was synthesized from the commercially available heptafluorodecyl acrylate (Scheme 22). The resulting catalyst **37** demonstrated good solubility in fluororous solvents, high activity in RCM of series of substrates, as well as significant ability to recyclization. Thus, in case of RCM of *N,N*-diallyltosylamide the catalyst **37** kept high activity even after 20-th cycle.



Scheme 22. Synthesis of catalyst **37**.

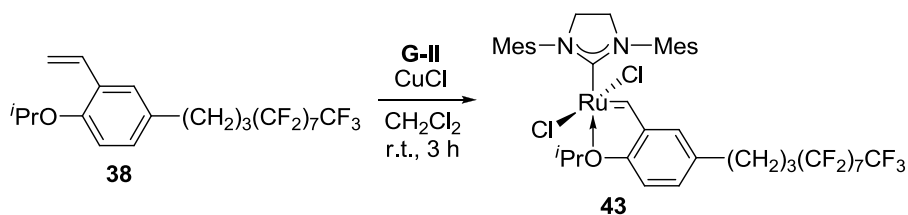
Light fluororous versions of first and second-generation Hoveyda-type catalysts were described by D. Curran and M. Matsugi in 2005⁴⁶. Introduction of fluororous ponytail for synthesis of styrene **38** was carried out by addition of perfluoro-*n*-octyl iodide to the double bond in presence of trimethylaluminum as an initiator (Scheme 23)⁴⁷ followed by the reduction of iodide with

tributyltin hydride. Styrene **40** used for synthesis of catalysts **41** and **42** was commercially available. In a series of RCM reactions fluorosubstituted catalysts **39**, **41** and **42** demonstrated similar activity with their parental analogues (**HG-I** and **HG-II**) with ability to recyclization with good yields.

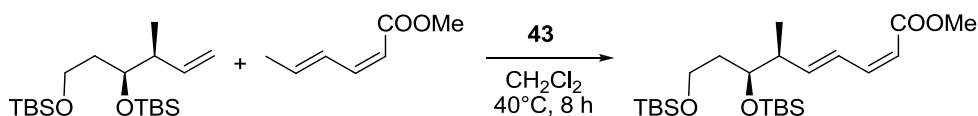


Scheme 23. Synthesis of complexes **39**, **41** and **42**.

Synthesis of second-generation analogue of **39** (catalyst **43**, Scheme 24) and its catalytic activity in ene-diene cross-metathesis (Scheme 25) was described by D. Curran and G. Moura-Letts⁴⁸. This catalyst showed similar activity with **HG-II** and ability to recyclization 3 times. The recovery was performed by fluorosubstituted solid-phase extraction (F-SPE). The catalyst **43** was found an application for synthesis of library of small, medium and macrocyclic heterocyclic compounds using RCM followed by F-SPE^{49,50}.

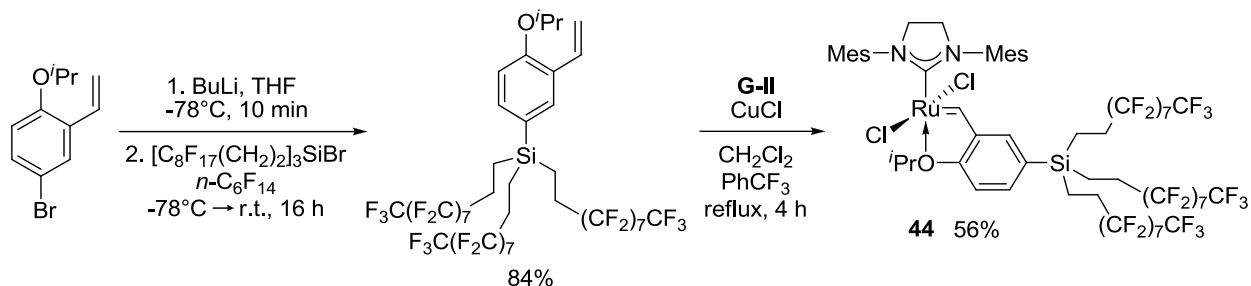


Scheme 24. Synthesis of complex **43**.



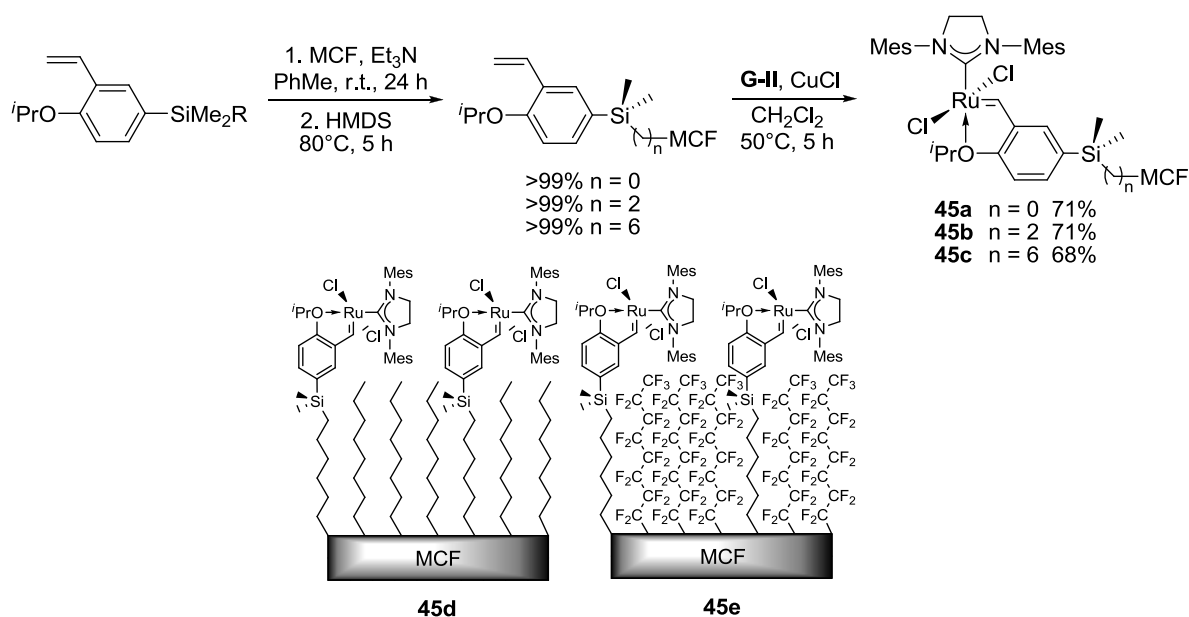
Scheme 25. Ene-diene cross-metathesis.

W. Bannwarth and F. Michalek described the synthesis of another Hoveyda-type catalyst **44** containing perfluorooctyl group for non-covalent immobilization on fluorosilica gel (Scheme 26)⁵¹. Catalytic activity of the resulting complex **44** was tested in several examples of RCM. Immobilization of **44** on amphiphilic polymer conetwork (APCN) allowed to use it in RCM reactions in aqueous media⁵². Synthesis of the corresponding perfluoroalkyl-containing styrene was performed using corresponding trialkylbromosilane⁵³.



Scheme 26. Synthesis of complexes **44**.

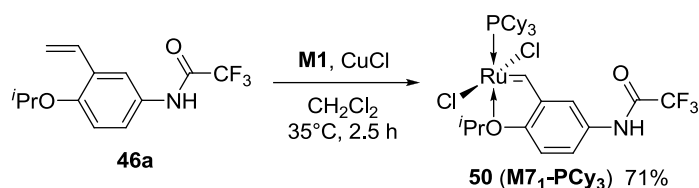
Covalent immobilization on the fluorosilica solid support through the benzylidene ligand of Hoveyda-type catalyst was performed using siliceous mesocellular foam (MCF) (**45e**, Scheme 27) was described by J. Ying. A series of immobilized catalysts **45a-e** were tested in RCM of diolefins⁵⁴. Good results on recyclability were obtained.



Scheme 27. Synthesis of catalysts **45**.

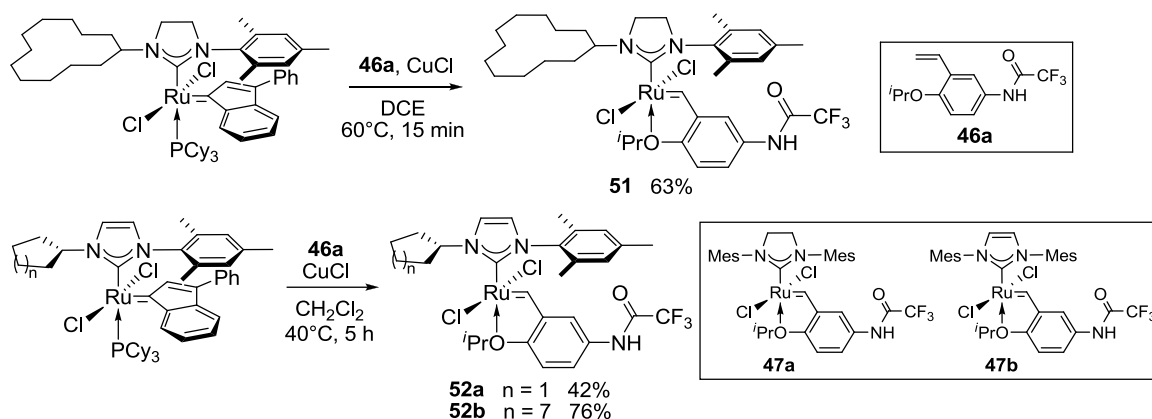
Series of trifluoroacetamide-containing Hoveyda-type catalysts (Scheme 36) was described by S. Nolan, M. Mauduit *et al.* The corresponding styrene **46a** was synthesized by acylation of 4-isopropoxy-3-vinylaniline with trifluoroacetic anhydride. The catalysts **47** and **48** (Scheme 28) demonstrated good activities in scope of RCM, RCEYM and CM reactions, including large scale^{55,56}. Pentafluoromethyl-containing complex **49a** was found less active than **47a** in RCM of

However, the best results were obtained with the first-generation catalyst **50**, synthesis of that was described in the same paper (Scheme 29)⁶³.



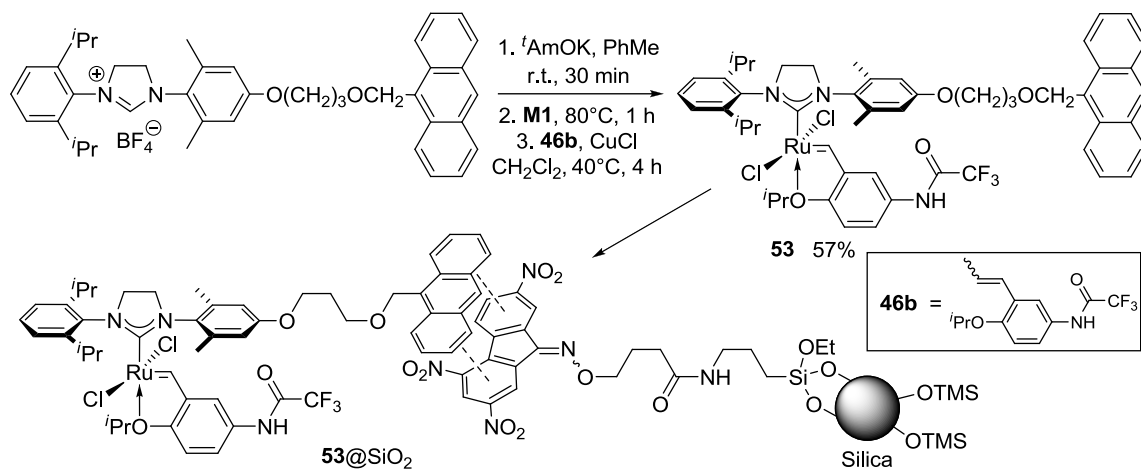
Scheme 29. Synthesis of complex **50**.

In 2014 M. Mauduit *et al.* described catalysts with trifluoroacetamide group in benzylidene ligand and unsymmetrical cycloalkyl-containing NHC ligands **51** and **52a,b** (Scheme 30). However such catalysts showed both lower stability and activity in RCM of DEDMM than their symmetrical parents **47a** or **47b**⁶⁴.



Scheme 30. Synthesis of complexes **51** and **52**.

Several attempts for synthesis of analogues of catalyst **47a** for heterogeneous catalysis were described. For example, modification of **47a** bearing an anthracenyl tag **53** (Scheme 31) was used for immobilization on TNF-grafted silica *via* the formation of charge-transfer complex, in which anthracene group is a donor and electron-deficient 2,4,7-trinitrofluoren-9-one (TNF) moiety is an acceptor⁶⁵. The resulting immobilized catalyst **53@SiO₂** kept high activity in RCM of DEDAM after four cycles and showed good yields and recyclization ability in another metathesis reaction such as RCM, RCEYM and CM.



Scheme 31. Synthesis of catalyst **53@SiO₂**.

The possibility of formation of strong hydrogen bond between trifluoroacetamide-containing complexes and silica was used for immobilization as well. Catalysts **47a** and **48a** (Figure 7) were immobilized on the silica without any surface treatment^{66,67}. The resulting catalytic systems demonstrated good activities in RCM, CM and RCEYM reactions in flow conditions. Significant decrease of catalytic activity of **47a@SiO₂** and **48a@SiO₂** was observed after fifth to seventh cycle.

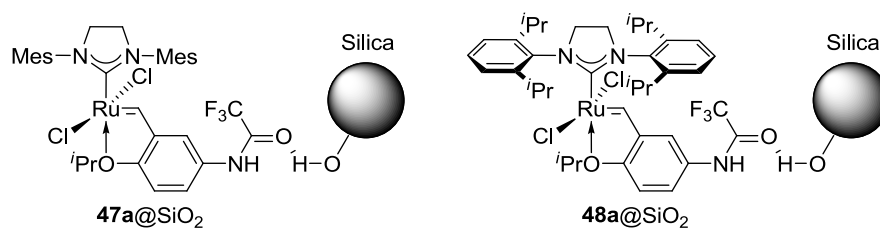
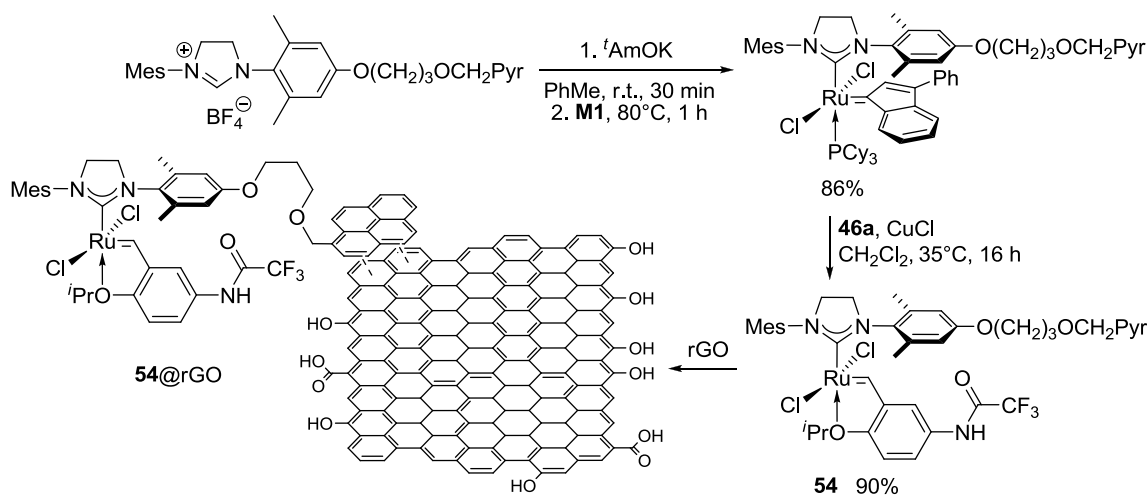


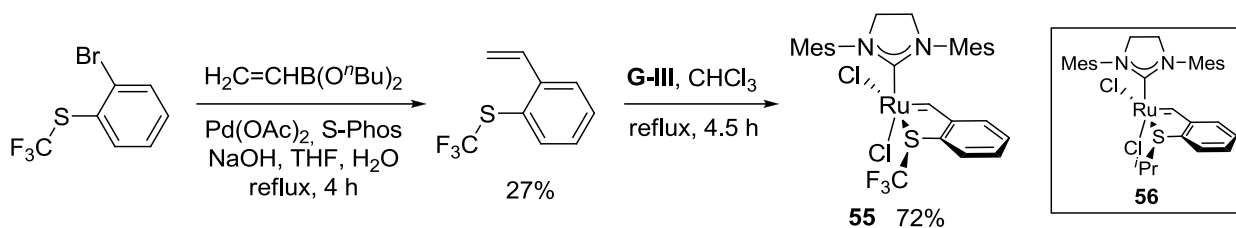
Figure 7. Catalysts **47a@SiO₂** and **48a@SiO₂**.

Immobilization of Hoveyda-type catalyst on reduced graphene oxide (rGO) was described last year (Scheme 32)⁶⁸. The catalyst **54@rGO** was tested in RCM of DEDAM, but its activity was significantly reduced after the second cycle.



Scheme 32. Synthesis of catalyst **54@rGO**.

Some fluorinated latent catalysts are known as well. N.G. Lemcoff *et al.* described catalyst **55**, that contains benzylidene ligands with chelating trifluoromethylthio-group (Scheme 33)⁶⁹. Catalyst was synthesized in two steps from the commercially available (2-bromophenyl)(trifluoromethyl)sulfane.



Scheme 33. Synthesis of complex **55**.

The catalyst **55** showed latent properties, like its non-fluorinated parent **56**⁷⁰. For instance, in RCM of DEDAM at room temperature **55** was almost inactive, while at 80°C it was even more active than **56**, however, in some cases polymerization and isomerization products were observed. Moreover, complex **55** can be activated by UV irradiation in RCM of DEDAM and ROMP of COE. Latency of such sulfur-containing catalysts as **55** or **56** could be explained by preferred inactive in metathesis *cis*-form (Figure 8). Under UV irradiation or heating active *trans*-isomer is formed.

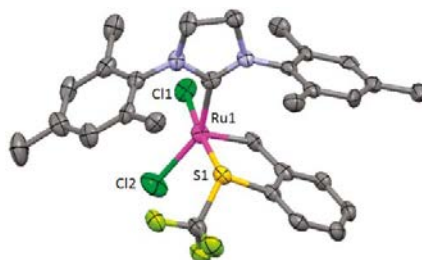
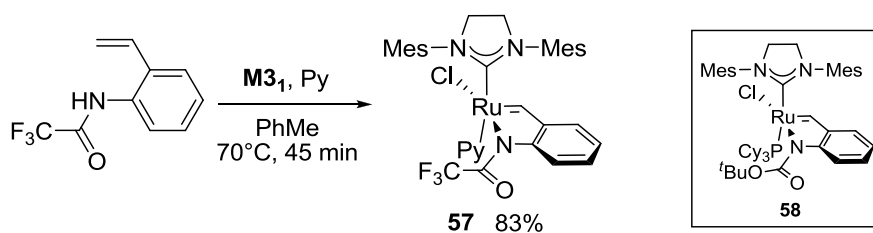


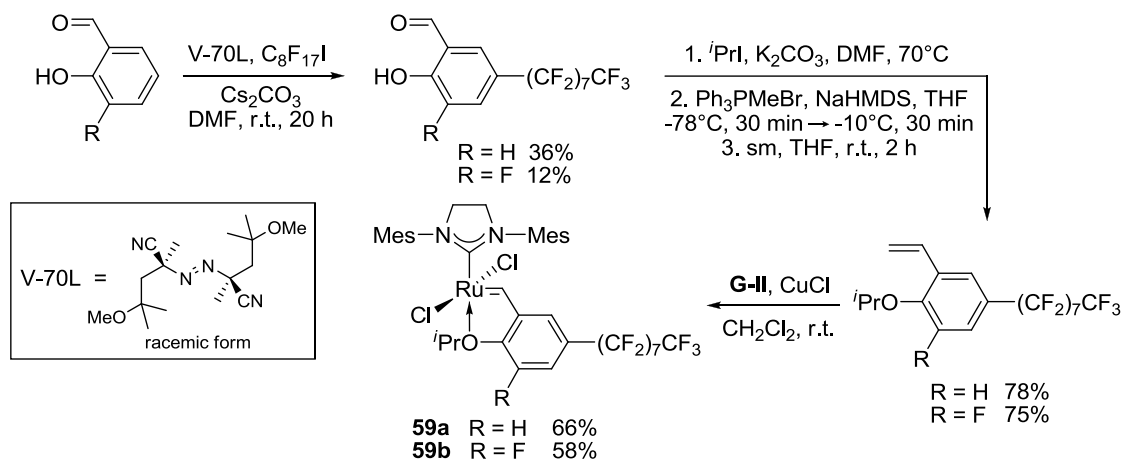
Figure 8. X-ray structure of complex **55**.

The catalyst **57** with covalent chelating amide ligand (Scheme 34) was synthesized by K. Grela *et al.* using ligand exchange in presence of excess of pyridine⁷¹. This catalyst was tested in RCM of DEDAM and DEAMM. In neutral medium activity of this catalyst was low, but in presence of HCl it was very active. Fluorine-containing catalyst **57** was more active, than its non-fluorinated analogue **58** only in RCM of DEDAM.



Scheme 34. Synthesis of complex **57**.

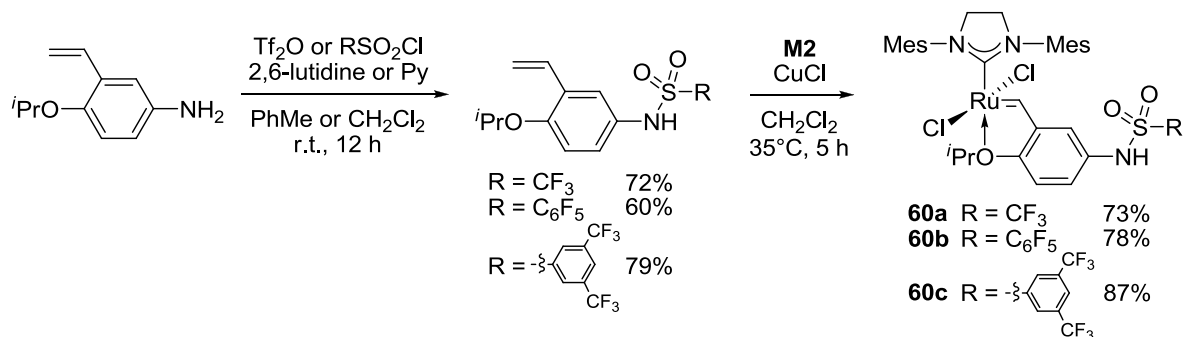
M. Matsugi *et al.* described synthesis of catalysts **59**, containing directly bonded fluororous tag with aromatic core of benzylidene ligand (Scheme 35)^{72,73}. Direct perfluoralkylation of salicylaldehyde was carried out in presence of cesium carbonate as soft base and radical initiator V-70L (light fraction of commercially available initiator V-70 with m.p. 58°C⁷⁴, (±)-2,2'-azobis(2,4-dimethyl-4-methoxyvaleronitrile)⁷⁵) that provided soft conditions of the reaction.



Scheme 35. Synthesis of complexes **59**.

These catalysts have demonstrated higher activity than **HG-II** or **42** (see Scheme 23) in RCM of *N,N*-diallyltosylamide, DEAMM and DEDAM. Catalyst **59a** has demonstrated ability for recyclization using F-SPE. During five cycles, this catalyst provided excellent yields both for metathesis and for amount of regenerated catalyst, while **59b** proved to be not able to regeneration by F-SPE.

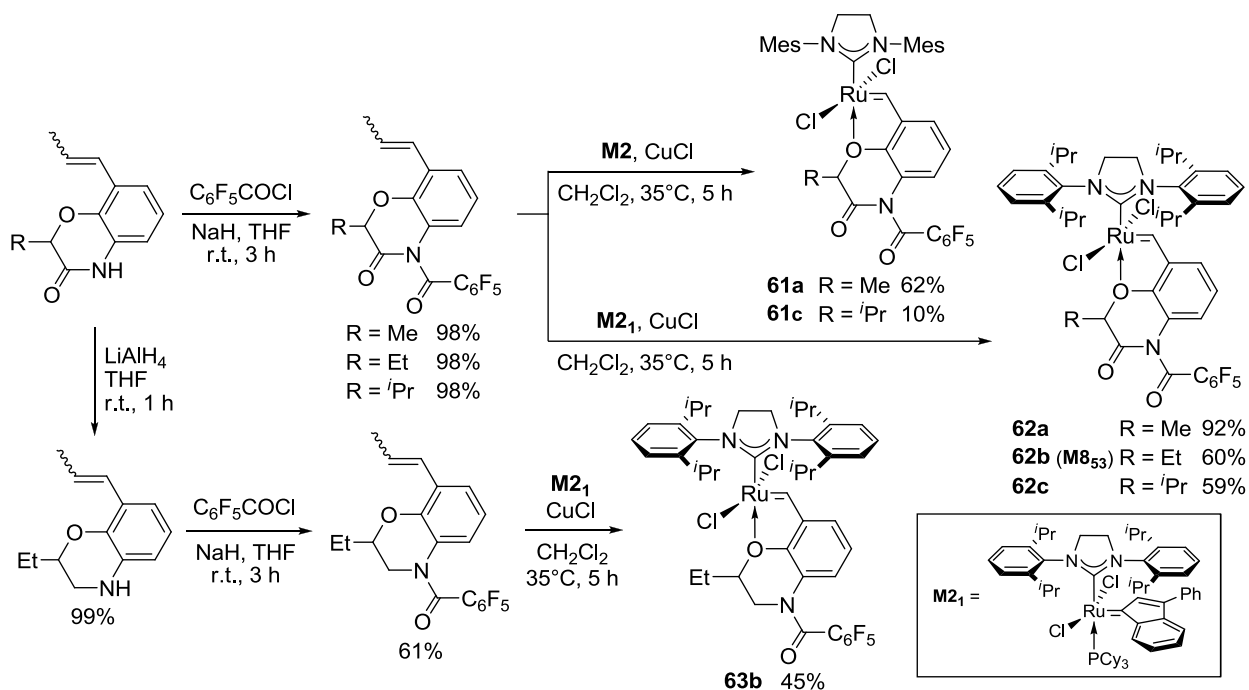
M. Mauduit *et al.* have described the synthesis of fluoro-containing Hoveyda-type catalysts containing sulfonamide groups⁷⁶. Corresponding styrenes for synthesis of **60a-c** were obtained *via* sulfonation of 4-isopropoxy-3-vinylaniline by triflic anhydride or arenesulfonyl chloride (Scheme 36). All synthesized catalysts were investigated in RCM of DEAMM and CM of several substrates. However, fluoro-containing catalysts **60a-c** have not demonstrated good results.



Scheme 36. Synthesis of complexes **60**.

M. Mauduit *et al.* described synthesis of catalysts **61a**, **62a-c**, **63b** (Scheme 37) containing 1,4-oxazine moiety in benzylidene ligand⁷⁷. This modification of Hoveyda-type complexes opened the

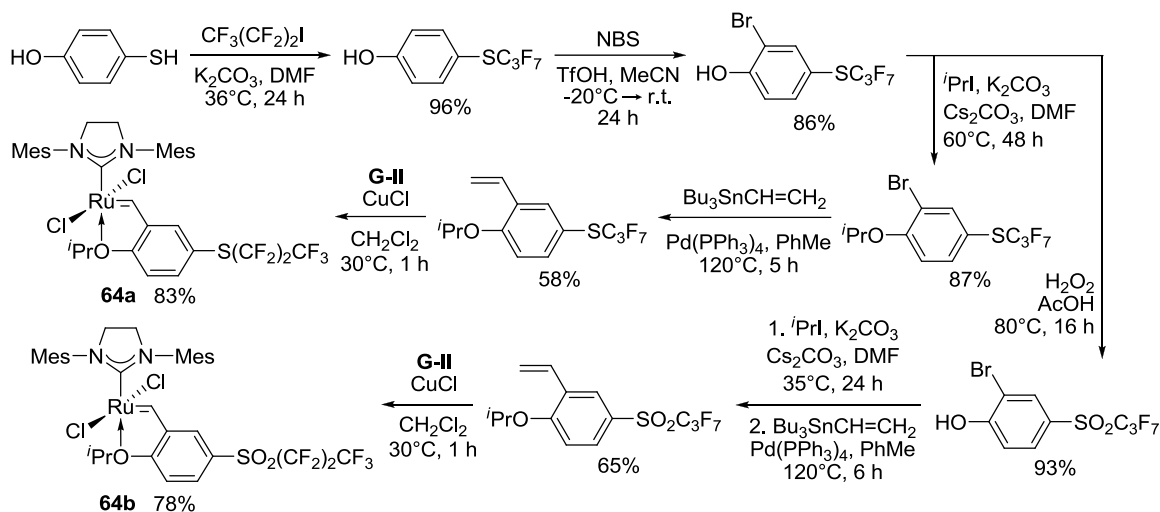
way for further synthetically facile fine-tuning. Introduction of fluorinated group was implemented *via* acylation of corresponding amide (or amine) by pentafluorobenzoyl chloride. Indenylidene complexes **M2** and **M2₁** were used and ruthenium source.



Scheme 37. Synthesis of complexes **61**, **62**, and **63**.

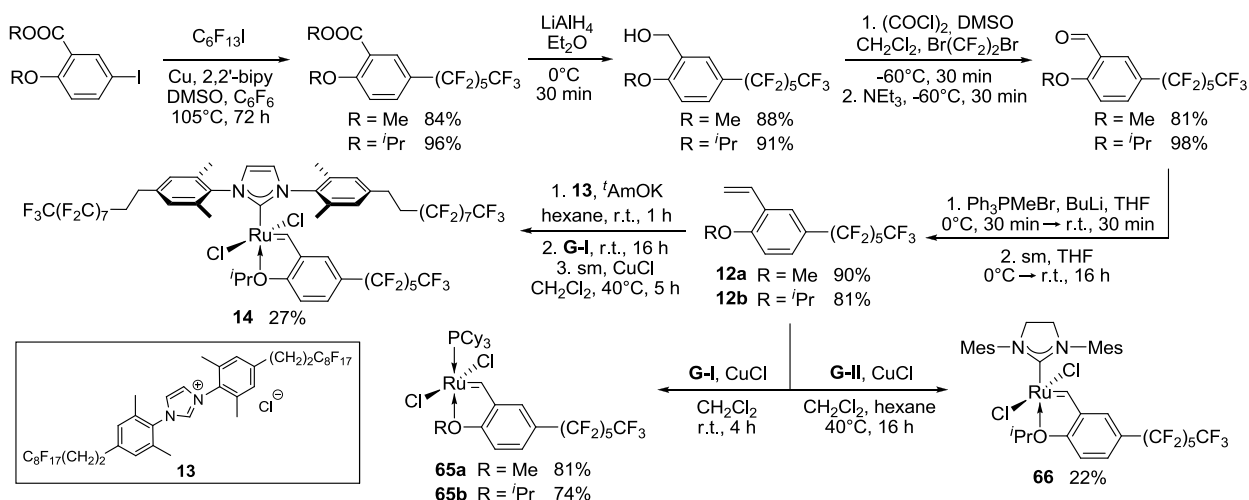
Catalysts **62b**⁷⁸ and **63b**⁷⁹ have demonstrated high activity and initiation rate in RCM of DEAMM. It was found, that replacement of SIMes to SIPr for complexes **61c** and **62c** may significantly decrease initiation rate with increase of stability of catalyst in the same time⁸⁰. Anyway, high activity of catalyst **61c** was due to the structure of benzylidene ligand.

In 2013 K. Grela *et al.* described synthesis and catalytic activity of series of Hoveyda-type catalysts with different electron-withdrawing groups⁸¹. For fine-tuning of catalysts perfluorosulfane (weak EWG, **64a**) and perfluorosulfone (strong EWG, **64b**) groups were used (Scheme 38). Perfluoroalkyl group was introduced *via* nucleophilic substitution of perfluoropropyl iodide in presence of potassium carbonate. The initiation rate of catalyst **64b** was very high, as it was expected, but this catalyst was found to be very unstable even in solid state in the freezer.



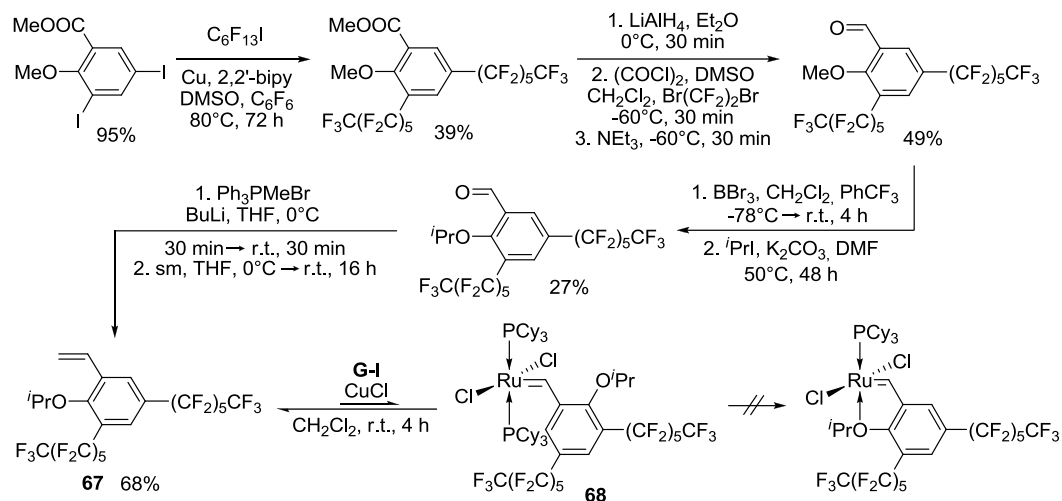
Scheme 38. Synthesis of complexes **64**.

In the paper by J. Kvičala *et al.*³¹ mentioned above the synthesis of perfluoroalkyl-containing styrenes **12a,b** (Scheme 39) and **67** (Scheme 40) and the corresponding light-fluorous catalysts **14**, **65a,b**, **66** and **68** were described. Introduction of perfluoroalkyl group was performed by mean of Ullmann reaction. Catalysts **14**, **65a,b** and **66** demonstrated high activity in RCM reactions.



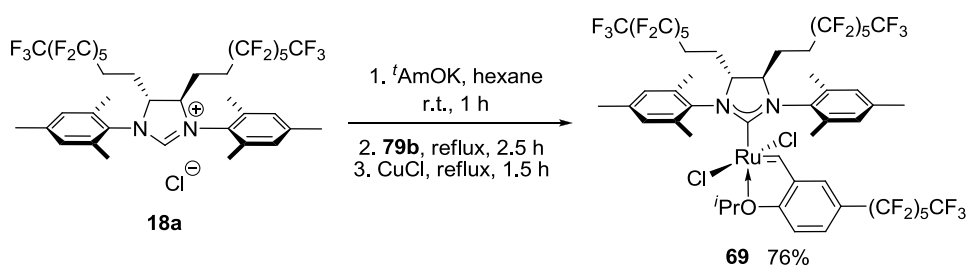
Scheme 39. Synthesis of styrenes **12a,b** and complexes **14**, **65a,b**, and **66**.

Bis-perfluoroalkyl-containing styrene **67** was almost inactive in the reaction with **G-I**, moreover, benzylidene ligand in the resulting complex **68** was not able at all for chelation (Scheme 40). Inability for chelation of electronically pure benzylidene ligands in ruthenium complexes was for the first time described by K. Grela *et al.*⁸².



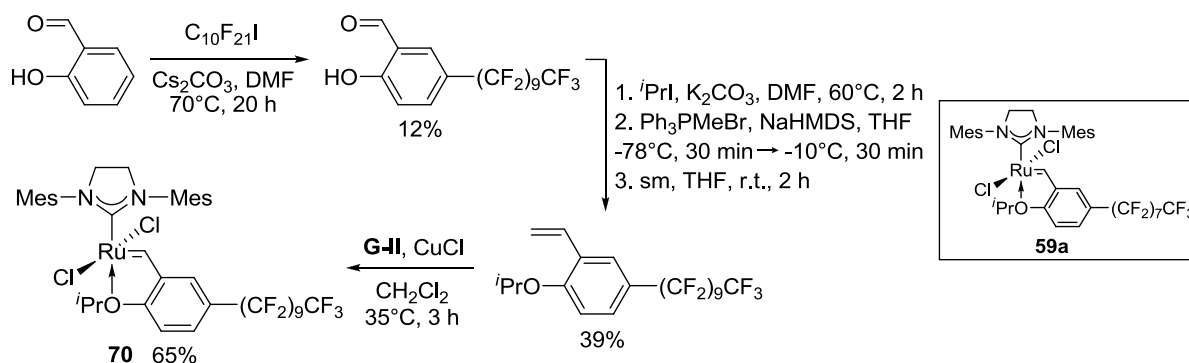
Scheme 40. Synthesis of styrene **67** and complex **68**.

More recently, J. Kvičala *et al.* synthesized complex **69** (Scheme 41)³⁴. As in previous cases this complex has proved to be not a heavy fluorinated one (its $P_f(\text{FBS}) < 1$). In RCM reactions catalyst **69** was slightly less active than **HG-II**.



Scheme 41. Synthesis of complex **69**.

Immobilization possibility of perfluoroalkyl-containing Hoveyda-type catalyst was described by M. Matsugi *et al.*⁸³. They synthesized perfluorodecyl-containing catalyst **70** (Scheme 42) that was immobilized *via* hydrophobic interaction on Teflon. This catalytic system was the first example of Hoveyda-type complex that could transfer between solid and liquid phases in RCM conditions. Such transfer was not possible of perfluorooctyl-containing complex **59a**. Catalyst **70** demonstrated excellent results in RCM reactions and good ability for recyclization.



Scheme 42. Synthesis of complex **70**.

In the recent research of M. Matsugi *et al.* eight new fluororous catalysts **71a-f** and **72a,b** (Figure 9) and their catalytic activity in RCM have been described⁸⁴. Introduction of fluororous tags was carried out using above mentioned methods (see Scheme 23). The highest activity was observed in case of 1-naphtyl-containing catalyst **71d**.

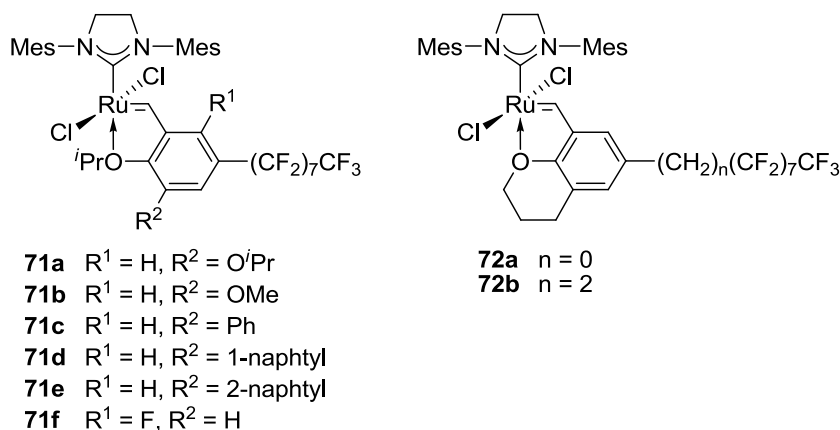
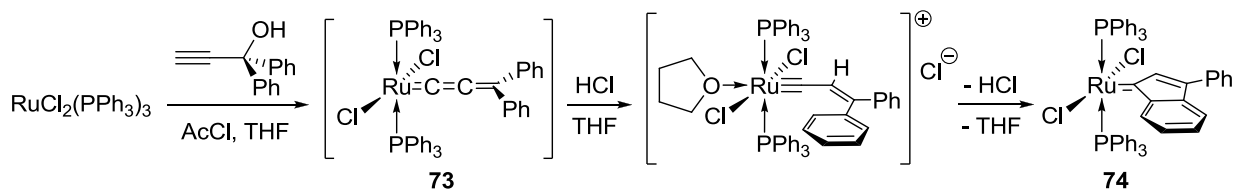


Figure 9. Complexes **71** and **72**.

1.4. Fluorine in indenylidene and allenylidene ligands

Along with the most common benzyliidene ruthenium complexes, indenylidene ones are also efficient metathesis catalysts stable for harsh conditions. One of the most important of their advantages is facile accessibility: indenylidene complex could be obtained by treatment of tris(triphenylphosphine)ruthenium(II) dichloride with 1-phenylpropargyl alcohol in acidic conditions. An intermediate allenylidene complex (**73**, Scheme 43) in most of cases could be isolated from the reaction mixture. Such method is general pathway for synthesis of not only ruthenium indenylidene complexes, but other transition metals too⁸⁵. Further transformations of complex **74** usually includes exchange of L-ligand from PPh_3 to PCy_3 using the excess of the latter.

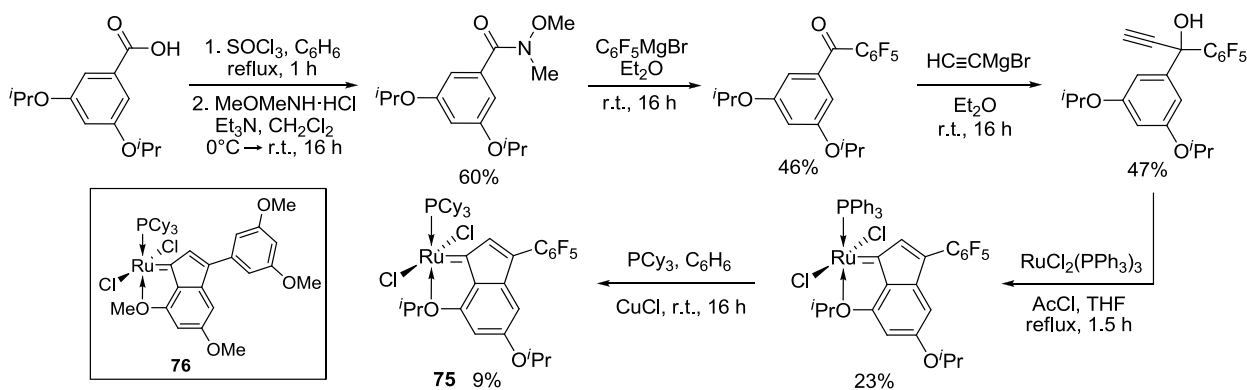


Scheme 43. Mechanism of indenylidene complex **74** formation.

Due to this synthetically important bond between allenylidene and indenylidene complexes, fluorinated derivatives of both of them will be reviewed in the same part.

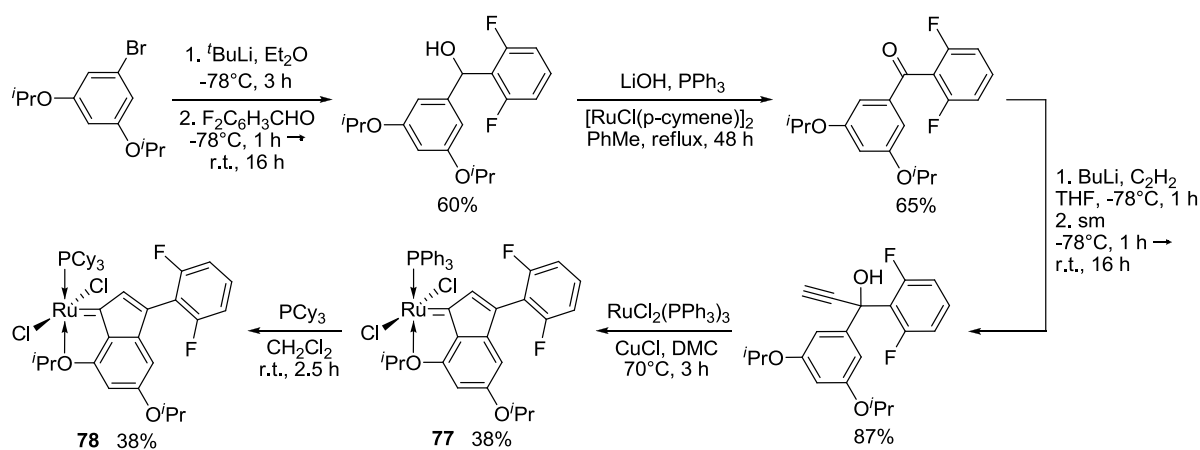
The first pentafluorophenyl-containing indenylidene catalyst **75** (Scheme 44) was described by M. Holtcamp *et al.*⁸⁶. Introduction of fluorinated group was carried out by treatment of pentafluorophenylmagnesium bromide with 3,5-diisopropoxy-N-methoxy-N-methylbenzamide.

The resulting catalyst has shown good turnover number in methyl oleate ethenolysis (TON = 4300), while, for example, analogous methoxy-containing catalyst **76** showed only TON = 1800. Such big difference could be explained by high electron-withdrawing properties of pentafluorophenyl group, that decreases Ru-O bond strength and accelerates initiation step of metathesis reaction⁸⁷.



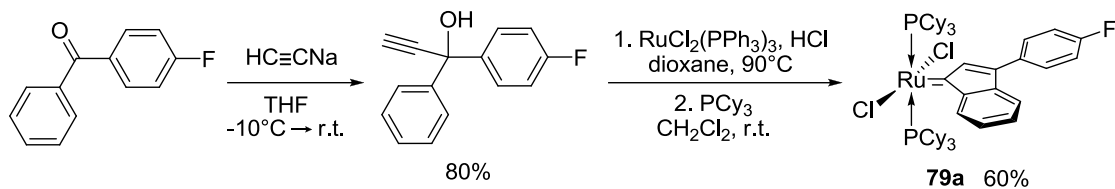
Scheme 44. Synthesis of complex **75**.

Another modification of chelating indenylidene ligand was described by C. Bruneau *et al.*⁸⁸. The fluorinated moiety was introduced into substrate by condensation of 3,5-diisopropoxyphenyllithium with 2,6-difluorobenzaldehyde (Scheme 45). Synthesis of carbene complex **77** was carried out in the green solvent dimethylcarbonate (DMC). The resulting complex **78** demonstrated good thermal stability and activity in RCM of DEDAM and DEAMM.



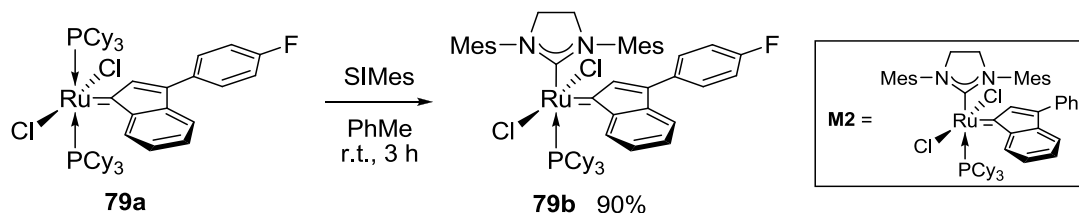
Scheme 45. Synthesis of complex **78**.

Indenylidene complexes **79a** and **79b** containing one fluorine atom in *para*-position has been described in publications of F. Verpoort *et al.* Synthesis and catalytic properties in RCM of DEDAM and DEAMM and ROMP of COD of the first-generation catalyst **79a** (Scheme 46) have been described in 2015⁸⁹. The corresponding propargyl alcohol was synthesized from the commercially available *p*-fluorobenzophenone *via* the condensation with sodium acetylide⁹⁰.



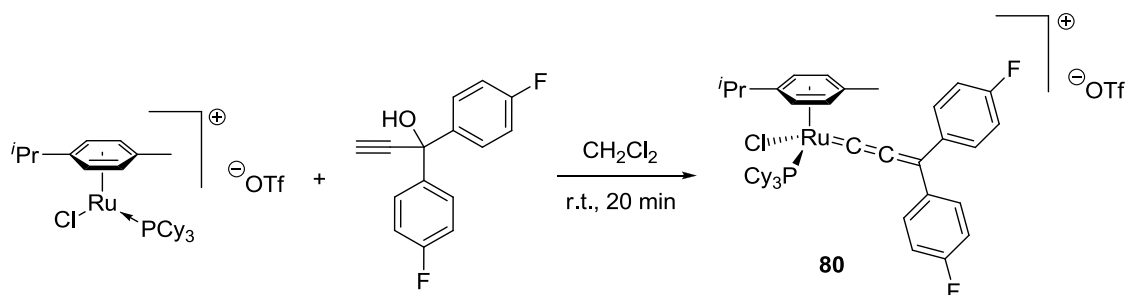
Scheme 46. Synthesis of complex **79a**.

Second-generation catalyst **79b** (Scheme 47), its activity in selected examples of RCM, RCEYM, and ROMP reactions with stability test have been described last year⁹¹. This catalyst demonstrated almost the same behavior with parental complex **M2** in every case.



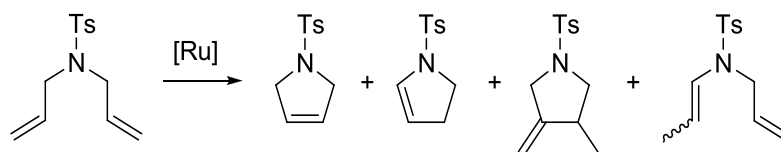
Scheme 47. Synthesis of complex **79b**.

In 2003 P. Dixneuf, C. Bruneau *et al.* published the first example of cationic allenylidene Ru-complex **80** containing fluorine atom in *para*-position of phenyl group (Scheme 48)⁹².



Scheme 48. Synthesis of complexes **80**.

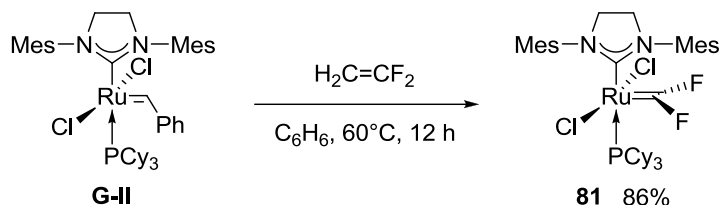
The catalyst **80** showed higher activity in RCM of *N,N*-diallyl tosylamide than its non-fluorinated analogue. However, it has proved to be less selective to give the RCM product along with a number of isomeric products depicted on Scheme 49.



Scheme 49. RCM of *N,N*-diallyltosylamide with the catalyst **80**.

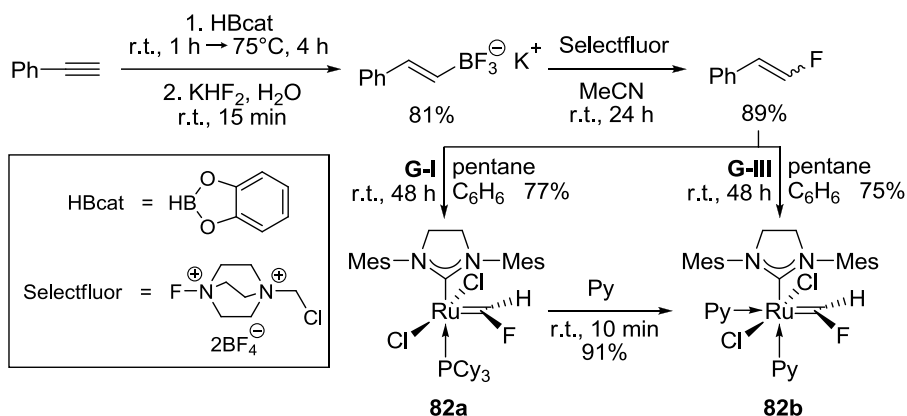
1.5. Fluorine in methyldene ligands

In 2001 R. Grubbs and co-workers obtained the first difluorocarbene ruthenium complex **81** during the investigation of challenging metathesis of 1,1-difluoroethylene using **G-II** (Scheme 50)⁹³. The resulting complex showed very low activity in ROMP of COD. Moreover, the products of a second turnover of metathesis of 1,1-difluoroethylene, namely ethylene and tetrafluoroethylene, were not observed in the product mixture, indicating that the reaction was not catalytic.



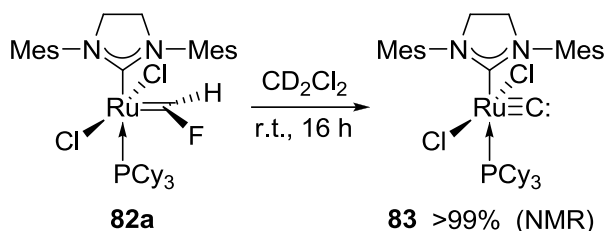
Scheme 50. Synthesis of complex **81**.

Six years later M. Johnson *et al.* described synthesis of second and third-generation monofluoromethylidene complexes (**82a** and **82b**, Scheme 51)⁹⁴. The method for synthesis of the ligand precursor β -fluorostyrene included the electrophilic fluorination of alkenyl trifluoroborate by Selectfluor in mild conditions⁹⁵. The activity of catalysts **82a** and **82b** was not high, but it was higher than that of difluoromethylidene complex **81**. Third generation catalyst **82b** demonstrated higher initiation rate and lower stability in a solution than **82a**.



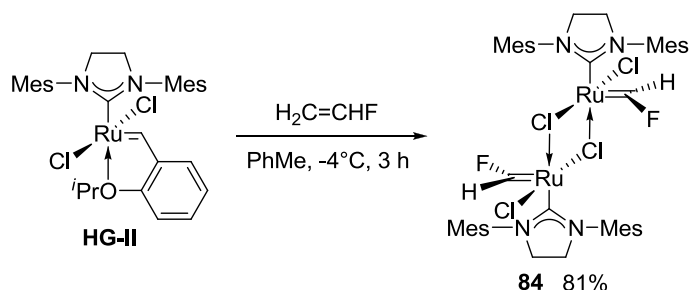
Scheme 51. Synthesis of complexes **82**.

Despite quite good stability of catalyst **82a** in solid state, there was found a tendency to formation of carbide complex **83** in a solution in dichloromethane (Scheme 52).



Scheme 52. Formation of carbide complex **83**.

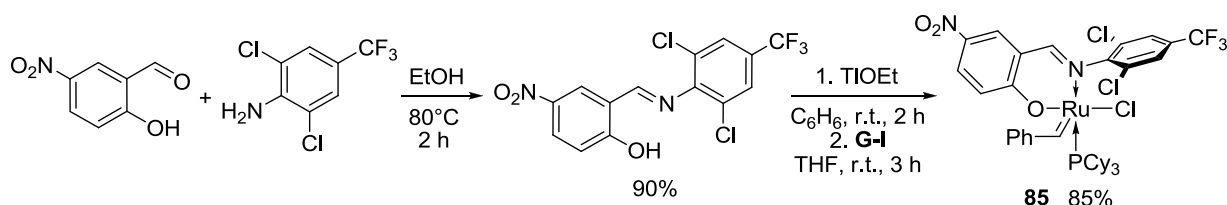
The last known up to date monofluoromethylidene ruthenium complex **84** (Scheme 53) has been described in 2009⁹⁶. Initially this complex was observed as intermediate in CM reactions of vinyl fluoride and disubstituted alkenes with the catalyst **HG-II**. Afterwards complex **84** have been directly synthesized by treatment of **HG-II** with an excess of vinyl fluoride. Dimeric structure of **84** has been confirmed by X-ray analysis. In CM of 5-decene and vinylfluoride the catalyst **84** demonstrated TON = 1.2.



Scheme 53. Synthesis of complex **84**.

1.6. Fluorine in L-type ligands

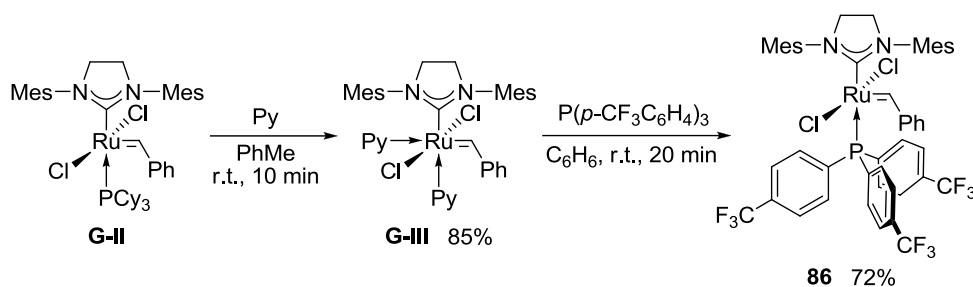
Ruthenium catalysts bearing fluorinated monodentate L-type ligands (phosphine and pyridine) will be reviewed in this section together with chelating ligands containing fluorine in L-coordinating moiety. Thus, the first ruthenium metathesis catalyst bearing chelating ligand with fluorinated L-type moiety **85** has been described in 1998 by R. Grubbs *et al.* (Scheme 54)⁹⁷. Catalyst **85** and series of its analogues with salicylaldimine ligands have found to be less active at room temperature with dramatically increase of reactivity at higher temperatures.



Scheme 54. Synthesis of complexes **85**.

Non-chelating L-type ligands in Grubbs-type catalysts are normally labile, so change of L-type ligand to another one could be carried out quite fast. In 2001 R. Grubbs *et al.* described for the

first time third-generation catalyst (**G-III**), that has been synthesized by treatment of **G-II** with an excess of pyridine (Scheme 55)⁹⁸. In this part complex **G-III** will be considered as starting material for other ruthenium complexes, including modifications with phosphine ligands, for instance, commercially available electronically pure tris[*p*-(trifluoromethyl)phenyl]phosphine (complex **86**). Notably, that less donating tris(perfluorophenyl)phosphine was inactive in the reaction with **G-III**. The resulting catalyst **86** showed higher activity than **G-II** in CM of acrylonitrile and allylbenzene and in ROMP of COD⁹⁹.



Scheme 55. Synthesis of complex **86**.

Another fluorinated phosphine complex has been described in 2003¹⁰⁰. The catalyst **87** (Figure 10) was synthesized in the same procedure as **86**. However, **87** showed lower activity than **86** in ROMP of COD.

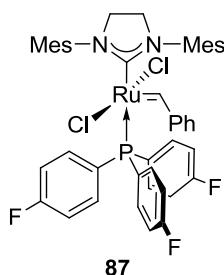


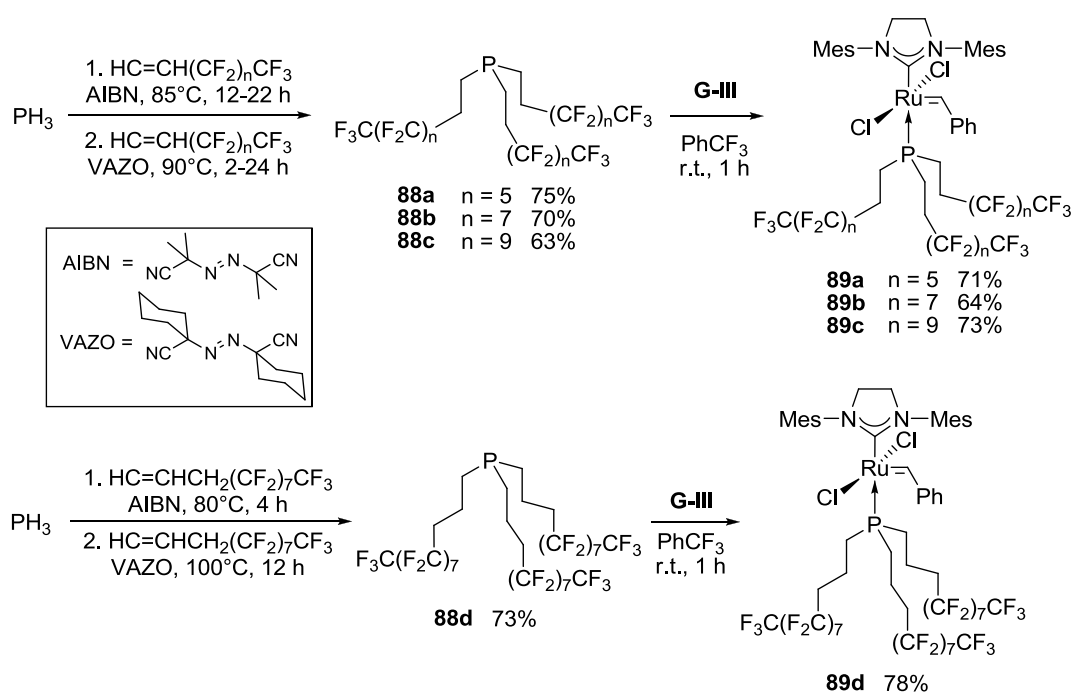
Figure 10. Complex **87**.

In 2006–2012 J. Gladysz and co-workers published a series of publications that described second generation Grubbs-type catalysts **108** (Scheme 56), containing fluororous phosphine ligands¹⁰¹. Synthesis of fluororous phosphines for these catalysts has been described by their group in earlier contribution¹⁰². The introduction of fluororous tag was carried out in two steps: on the first step PH_3 was added to corresponding perfluoroalkylethylene in presence of radical initiator azobisisobutyronitrile (AIBN). This step yields the mixture of target compound (~90%) with primary and secondary phosphines $\text{PH}_x(\text{CH}_2\text{CH}_2(\text{CF}_2)_n\text{CF}_3)_{3-x}$ ($x = 1,2; n = 5,7,9$). On the second step addition was carried out in presence of less active initiator 1,1'-azobis(cyclohexanecarbonitrile) (VAZO) to prevent polymerization. All the resulting phosphines **88** demonstrated very high fluorophilicity with partition coefficients between PFMC and toluene $P_i(\text{FBS}) > 80$ (Table 3). Catalysts **89** were synthesized by ligand exchange of **G-III** in

trifluoromethylbenzene¹⁰¹. Partition coefficients for catalysts **89** are also shown in Table 3. The complex **89c** was almost insoluble in dichloromethane due to its high fluorophilicity. During the catalytic test of **89a,b** in benchmark RCM reactions notable initiation rate acceleration has been found using biphasic systems CH₂Cl₂/fluorous solvent compare to pure CH₂Cl₂. Such acceleration explains by biphasic transfer of fluorophilic phosphine into fluorous solvent. Similar “phase transfer activation” was observed for **89b** in ROMP of NBE as well¹⁰³. Moreover, complex **89b** was recycled by fluorous/organic liquid/ liquid biphasic technique three times after RCM of DEDAM¹⁰⁴.

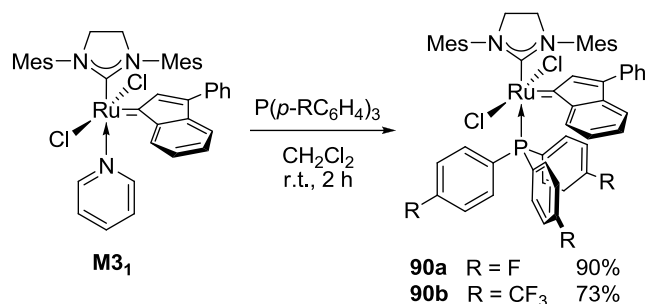
Table 3. Partition coefficients (PFMC/toluene) of fluorous phosphines **88** and metathesis catalysts **89**.

Fluorous Phosphine	P _i (FBS)	Fluorous Catalyst	P _i (FBS)
88a	82.3	89a	0.15
88b	>300	89b	0.66
88c	>300	89c	3.46
88d	82.3	89d	0.13



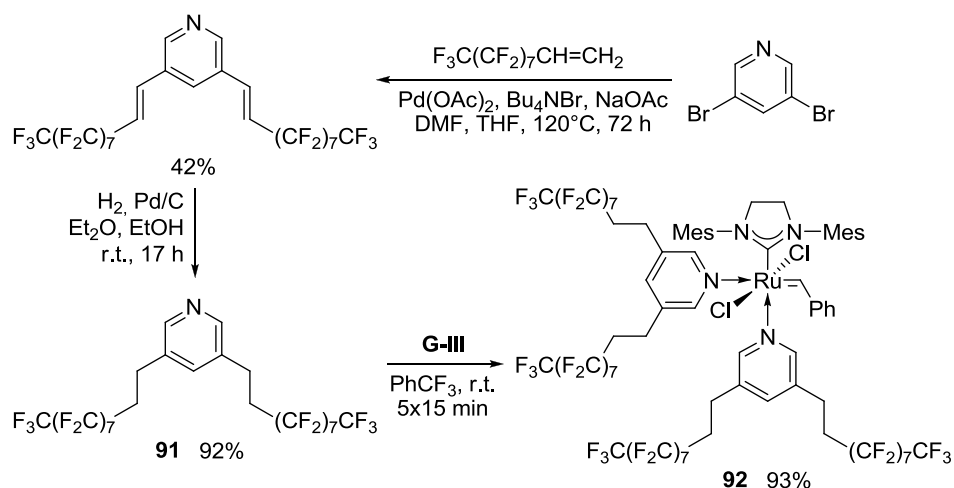
Scheme 56. Synthesis of complexes **89**.

Tris(*p*-fluorophenyl)phosphine- (**90a**) and tris[*p*-(trifluoromethyl)phenyl]phosphine-containing (**90b**) indenylidene catalysts were obtained by S. Nolan with co-workers¹⁰⁵. These complexes were synthesized from the pyridine containing indenylidene precursor **M3₁** (Scheme 57). Activity of catalysts **90a** and **90b** were tested in a scope of substrates for RCM, RCEYM, RRM and CM. In most of cases the catalyst **90b** demonstrated better activity, then corresponding non-fluorinated one (**M2₀**).



Scheme 57. Synthesis of complexes **90**.

Another approach for synthesis of ruthenium catalysts with fluoruous L-type ligands was described in the recent publication of J. Gladysz *et al.*¹⁰⁶ Pyridine **91** was synthesized *via* Heck cross-coupling of 3,5-dibromopyridine and perfluorooctylethylene followed by hydrogenation (Scheme 58). Synthesis of third-generation complex **92** was carried out via alternation of ligand exchange of **G-III** with 2.1 equivalents of **91** at room temperature degassing at low temperature for complete removal of pyridine¹⁰⁷.

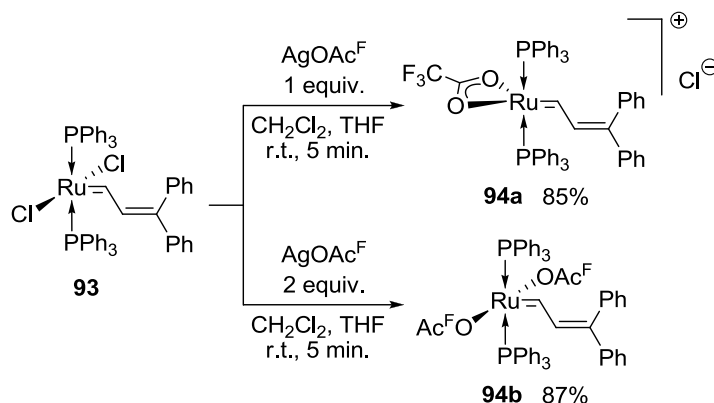


Scheme 58. Synthesis of pyridine **91** and complex **92**.

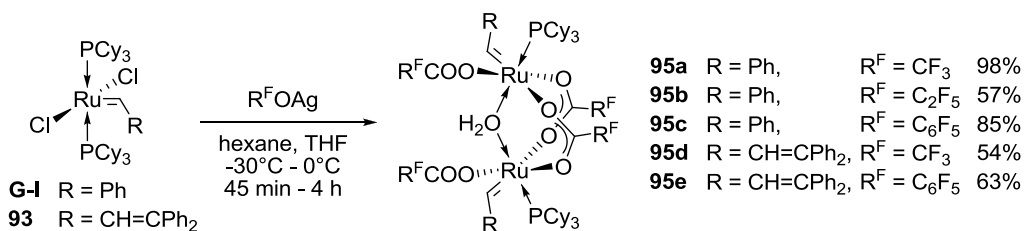
The catalyst **92** was tested in RCM reactions. Notable acceleration has been also observed using biphasic systems CH₂Cl₂/fluorous solvent like for phosphine-containing catalysts **89**.

1.7. Fluorine in X-type ligands

The first ruthenium metathesis catalyst with fluorinated X-type ligand was described by R. Grubbs *et al.* in 1994¹⁰⁸: The synthetic procedure included the exchange of chlorine in vinyliden complex **93** on trifluoroacetate group using the corresponding silver salt (Scheme 59).

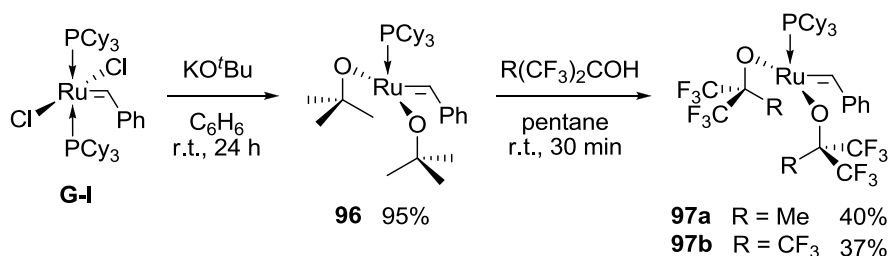


The catalyst **94a** was much more active in ROMP NBE than its non-fluorinated analogue with acetate as ligand^{109,110}. Notably, that when methylene chloride was changed for hexane the reaction led to formation of binuclear complex **95** with two trifluoroacetate groups and one water molecule as bridging ligands. The similar products were obtained when **G-I** has been used as starting material (Scheme 60)^{111,112}.



Complex **95a** demonstrated moderate activity in self-metathesis (SM) of internal olefins such as *trans*-4-decene and methyloleate. The performance of catalysts **95b** and **95d** was comparable with **95a**. In contrast, pentfluorobenzoate-containing catalysts **95c** and **95e** were inactive in this reaction.

Later a series of four-coordinate complexes **97** containing bulky fluorinated X-type ligands¹¹³ was described by the same research group. Synthesis of catalysts **97a** and **97b** was performed by the treatment of **96** with excess of the corresponding CF₃-containing alcohol (Scheme 61).



The complexes obtained (**97a,b**) have demonstrated moderate catalytic activity at 60°C and high activity at room temperature under acidic catalysis (in presence of HCl) in RCM of DEDAM.

This ligand exchange strategy was later utilized by M. Buchmeiser *et al.* in 2004-2011¹¹⁴⁻¹²² for the preparation of a number of second-generation Hoveyda-type and third-generation Grubbs-type catalysts bearing different fluoro-containing X-ligands (Figure 11). In all cases ligand exchange was performed by treatment with corresponding silver salts.

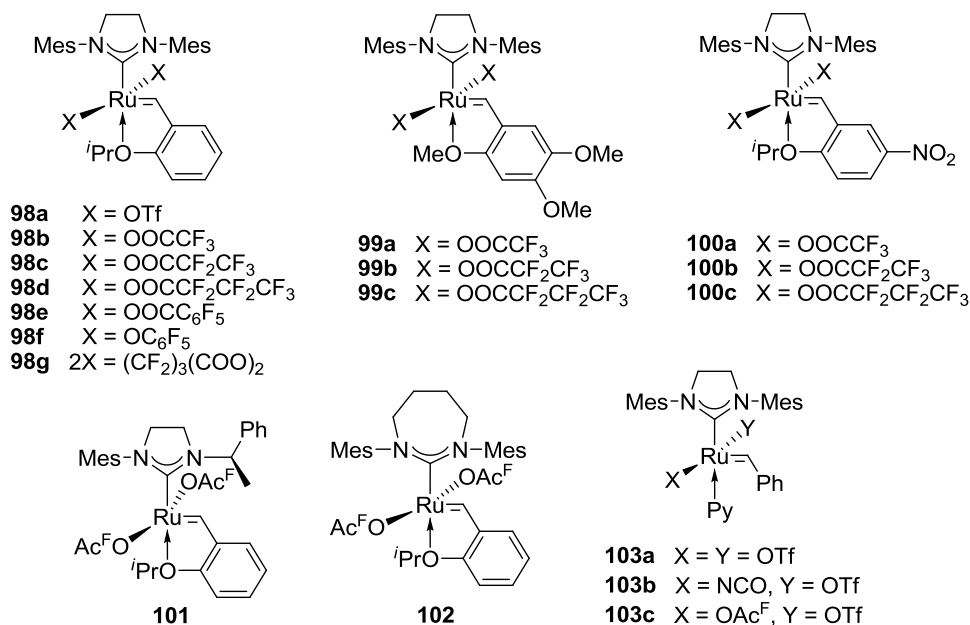
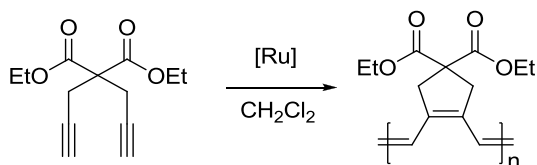


Figure 11. Catalysts **98-103**.

In the big variety of metathetic reactions trifluoroacetate-containing complex **98b** demonstrated higher activity than triflate-containing **98a**¹¹⁴. Moreover, **98b**, as its homologues **98c,d**¹¹⁷, catalyzed cyclopolymerization of diethyldipropargylmalonate (DEDPM, Scheme 62), but not in living manner¹¹⁵.

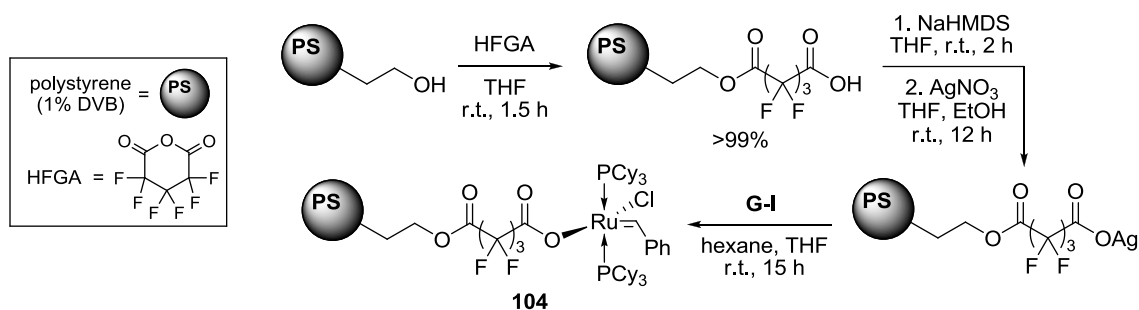


Scheme 62. Cyclopolymerization of DEDPM.

The complexes **99a-c** and **100a-c**^{115,116} were active in living polymerization of 1,6-heptadienes. The elongation of perfluoroalkyl chain led to improving of polydispersity index of the resulting polyene¹¹⁷. The catalyst **99a** was also successfully tested in cyclopolymerization of hydroxyl-containing heptadienes that was impossible under molybdenum catalysis with Schrock catalysts¹¹⁸. Moreover, catalysts **98b**, **99a**, **100a** showed activity in cyclopolymerization of *N,N*-dipropargylamines¹¹⁹. Complexes **98e** and **101** were synthesized for evaluation of influence of bulky ligands on regioselectivity of cyclopolymerization of dipropargylic substrates¹²⁰. Catalyst **102** have demonstrated high activity of cyclopolymerization of DEDPM, but was inactive in RCM of

DEDMM¹²¹. Catalysts **103a-c** and **98g** demonstrated good activity in copolymerization of NBE with CPE¹²².

In addition, the usage of fluorinated X-type ligands as a linkage unit for immobilization of metathesis catalysts on fest phase or different polymeric supports was also investigated. Thus, J. Mol *et al.* described the first example of immobilization of Grubbs catalyst on polystyrene *via* the fluorine-containing X-ligand¹²³. The initial copolymer with divinylbenzene (PS-DVB) functionalized with hydroxyethyl groups was treated with hexafluoroglutaric anhydride (HFGA) to afford the corresponding carboxylic acid. The latter was transformed into the silver salt and then reacted with **G-I** to give the final PS-supported product **104** (Scheme 63). The catalyst **104** exhibited very high activity in SM of *trans*-4-decene and methyl oleate as well as in RCM of DEDAM keeping activity even after the fifth cycle.



Scheme 63. Synthesis of catalyst **104**.

The hexafluoroglutaric moiety has proved to be a useful linkage for heterogenic catalysis. Thus, M. Buchmeiser *et al.*^{114,124,125} and D. Braddock *et al.*¹²⁶ successfully immobilized Grubbs catalysts on the polymer supports using this approach. For example, the catalysts **105a** and **105b** grafted on the amphiphilic oligomeric poly(2-oxazoline) (Figure 12) were able to polymerize of DEDPM in water media¹¹⁵.

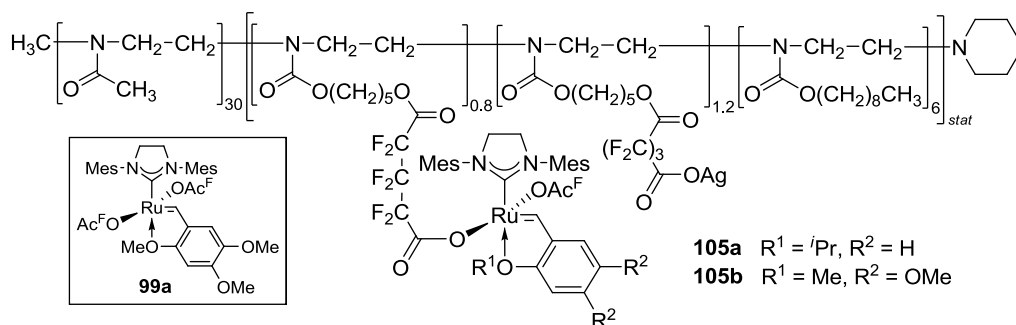


Figure 12. Catalysts **105**.

Moreover, the same hexafluoroglutaric linkage was utilized for grafting of Hoveyda-type catalysts on monolith polyetherketone column^{124,125,127} and on silica gel¹²⁸⁻¹³⁰ for flow reactors. Furthermore, hexafluoroglutaric moiety was useful for synthesis of Ru-catalysts with amphiphilic (**106**) and ionic (**107**) ligands (Figure 13)^{131,132}.

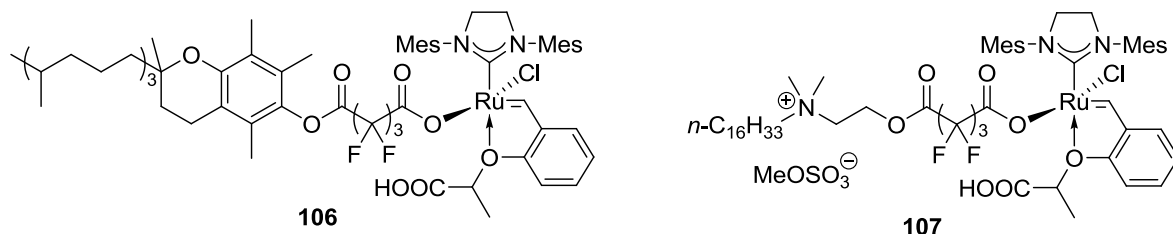
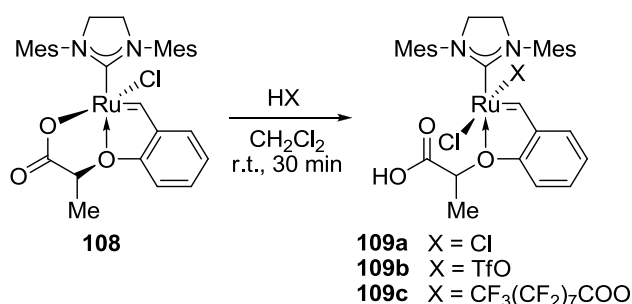


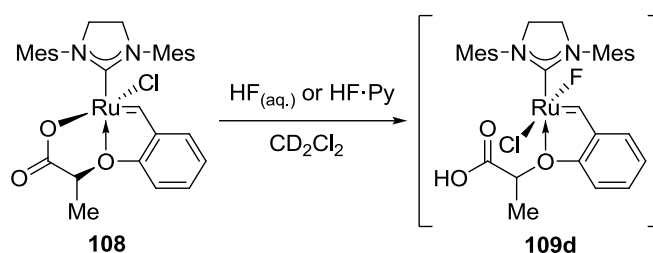
Figure 13. Complexes **106** and **107**.

In 2007 K. Grela, M. Mauduit *et al.* described the catalyst with chelating carboxylate group **108** (Scheme 64) that demonstrated a latent properties. Thus, it was inactive in RCM at room temperature and showed significant activity at heating or in presence of acids¹³³. Catalysts **109a-c** were prepared *in situ*, however fluorinated ones **109b** and **109c** demonstrated lower activity than **109a**.



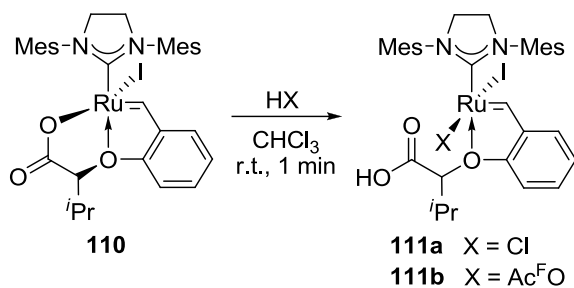
Scheme 64. Synthesis of complexes **109**.

The attempt to add aqueous hydrofluoric acid or its pyridine complex to **108** resulted in decomposition of the desired Ru-F complex **109d** in several seconds (Scheme 65)¹³⁴.



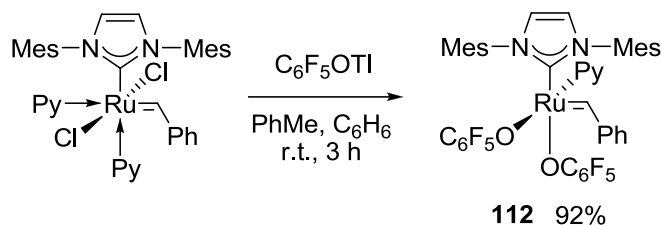
Scheme 65. Formation of unstable complex **109d**.

The stable isopropyl-containing latent complexes **110-111** were described by K. Grela *et al.* (Scheme 66)¹³⁴. The trifluoroacetate-containing catalyst **111b** was less active than non-fluorinated **111a** in RCM of DEDAM. In the same time, due to very high stability fluorinated catalyst **111b** demonstrated excellent conversion of DEDAM at elevated temperature.



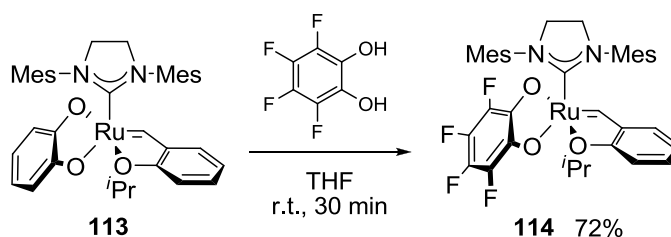
Scheme 66. Synthesis of complexes **111**.

D. Fogg *et al.* used the third generation Grubbs complex for the preparation of new catalysts with fluorinated X-type ligands. The method involved the treatment of **G-III** with thallium perfluorophenoxide (Scheme 67)¹³⁵. The resulting complex **112** exhibited high activity in RCM of DEDAM even at low catalyst loading (0.05 mol. %). In addition **112** showed good activity in RCM to form medium-size cycles¹³⁶.



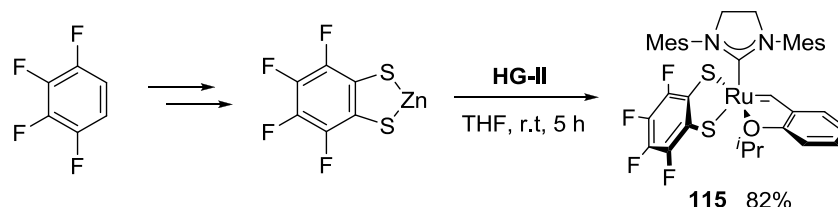
Scheme 67. Synthesis of complex **112**.

In 2014 A. Hoveyda *et al.* described an efficient synthesis of complex **113** *via* fast exchange of catecholate ligand to tetrafluorocatecholate for in presence of excess of tetrafluorocatechol (Scheme 68)¹³⁷. Catalytic activity of the resulting complex **114** was not described, but it was mentioned its high stability in methylene chloride and chloroform.



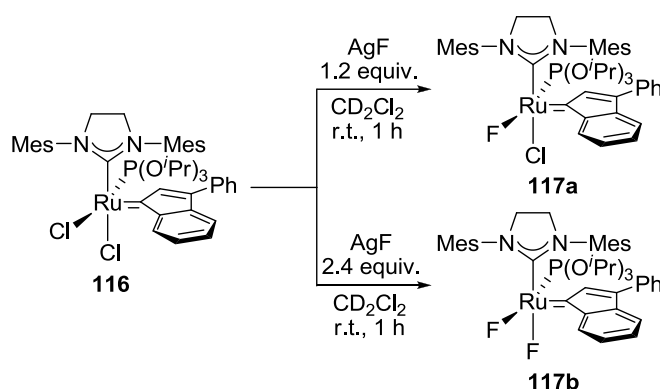
Scheme 68. Synthesis of complex **114**.

The thio-analogue of complex **114**, obtained by the same research group³⁸, has demonstrated high *Z*-selectivity (96%) in CM of *Z*-2-butene-1,4-diol with allylbenzene. The synthesis of **115** was performed starting from 1,2,3,4-tetrafluorobenzene *via* transmetalation of zinc tetrafluorocatecholthiolate (Scheme 69).



Scheme 69. Synthesis of complex **115**.

Two years ago, C. Casin *et al.* published the first olefin metathesis catalysts with Ru-F bond **117a** and **117b** (Scheme 70)¹³⁸. Complexes **117a** and **117b** were synthesized by treatment phosphorylated indenylidene complex **116** with silver fluoride. Monofluorosubstituted catalyst **117a** exhibited good activity in RCM, CM, and RCEYM and was more active than **117b**.



Scheme 70. Synthesis of complexes **117**.

A series of ruthenium catalysts containing perfluoro(polyoxa)alkanoate ligands **118-120** (Figure 14) was described by J. Kvičala *et al.* in 2014¹³⁹. Fluorophilicities $P_i(\text{FBS})$ measured for all these complexes were in interval from 0.03 for **118a** to 2.9 for **119d**. Among them only **119a-d** and **120b-d** were heavy fluororous. The highest activity was detected in RCM reactions under catalysis with **118** and **120**. Catalyst **120d** have demonstrated recycling ability in RCM of DEAMM and DEDMM using PFMC.

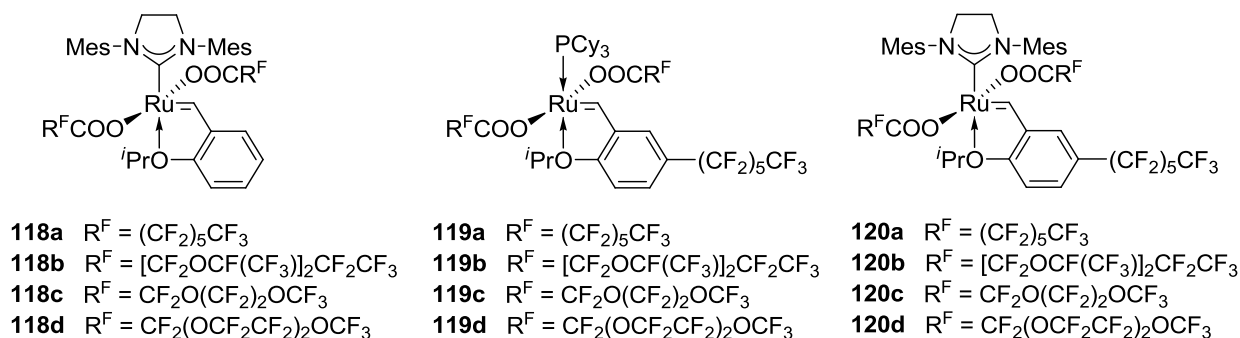


Figure 14. Complexes **118-120**.

In 2015 the same group described complex **121** (Figure 15) with very high fluorophilicity ($P_i(\text{FBS}) = 27$), however, its catalytic activity was not reported³⁴.

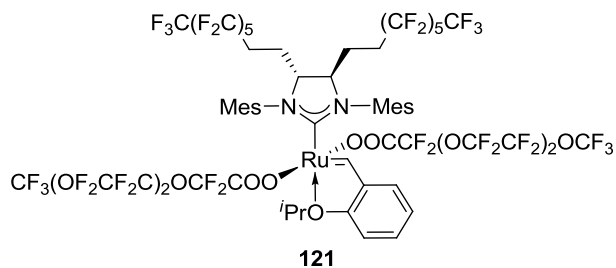


Figure 15. Synthesis of complex **121**.

A series of other fluorophilic catalysts **122a-c** and **123a,b**, containing chiral racemic perfluorooxaalkanoate ligands (Figure 16), has been described last year¹⁴⁰. These complexes were tested in benchmark RCM reactions. Catalysts **123b** and **123b** showed the highest activity due to electrophilicity along with low steric hindered of 2-fluoro-2-(perfluoropropoxy)acetate ligands.

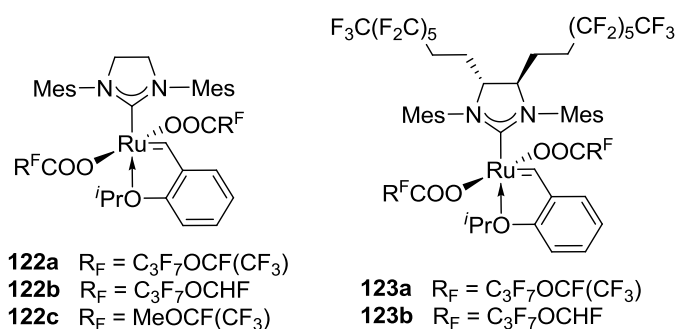


Figure 16. Complexes **122** and **123**.

As result, frequently fluorine-containing X-type ligands in ruthenium metathesis catalysts are used both for activation of catalyst and for immobilization of catalysts on the solid or polymeric support. Immobilized catalysts that were presented in this part were mentioned in several earlier reviews¹⁴¹⁻¹⁴⁴.

1.8. Conclusions

This review summarizes the data about synthetic approaches to fluorinated ruthenium metathesis catalysts and their use in metathetic transformations. In most of cases, choice of fluorinated ligands connects with attempt to reduce electronic density at carbene center in order to promote the formation of key ruthenacyclobutene intermediate at the first step of catalytic cycle. It can be achieved by the substitution of L- or X-type ligands for strong electron-withdrawing fluorine or fluoroalkyl groups. Moreover, the introduction of fluorine-containing groups could provide for better solubility, particularly in metatheses of polymerization, as well as to solve catalyst separation or recovery problems *via* fluorous biphasic systems. In some cases, an additional Ru-F interaction was shown to be crucial for enhanced catalytic activity. However, to the best of our knowledge there are only few examples of ruthenium carbene complexes with unsymmetrical fluorinated NHC ligands up to date. The construction of such catalytic system could promote the

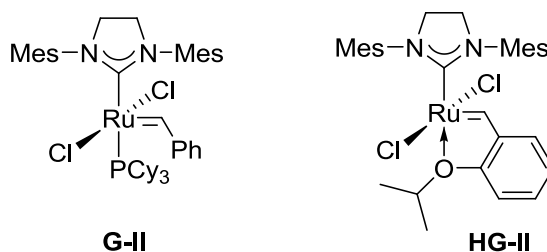
creation of more selective metathesis processes. Therefore, the development of efficient synthetic approaches to ruthenium catalysts containing bulky fluorinated groups in asymmetric NHCs is of great current interest.

CHAPTER II

RESULTS AND DISCUSSIONS

2.1. Introduction

Recent progress in development of new ruthenium-based metathesis catalysts connects mainly with the modification of *N*-heterocyclic carbene (NHC) ligand of commercially available Grubbs (**G-II**) and Hoveyda-Grubbs (**HG-II**) complexes to directly affect catalyst efficacy. For instance, the variation of electronic and steric properties of the substituents at nitrogen atoms, placed in vicinity to carbene center, can significantly alter the catalytic activity, stability and selectivity in many metathetic transformations.



On the other hand, the chemistry of fluorinated compounds is an area of tremendous expansion. The field of applications is impressively wide in scope and has the potential to concern all fields of life and material sciences. It is universally acknowledged that the presence of fluoroalkyl groups in a molecule profoundly modifies its physicochemical properties through concomitant alteration of its steric, electronic and lipophilic characteristics. This concerns in particular trifluoromethylated compounds, as CF₃-group is one of the most lipophilic groups in organic chemistry, and has one of the highest electronegativity and steric hindrance.

In the field of ruthenium-alkylidene complexes, the steric and electronic impact of fluorine and fluoroalkyl groups on their catalytic properties has been mainly studied by usage of properly modified phosphine, styrene ligands, as well as by the replacement of one or two chlorine atoms at ruthenium, *e.g.* with perfluoroalkoxylates. However, the number of publications on metathesis catalysts decorated with fluorinated NHC ligands is extremely limited¹⁷. Therefore, the development of new efficient metathesis catalysts bearing NHC ligands modified with trifluoromethyl-containing functional groups is of great interest in modern organic and organometallic chemistry.

The main goal of the present thesis is to develop efficient methods for the preparation of new ruthenium carbene complexes with unsymmetrical trifluoromethyl substituted NHC ligands and to investigate their catalytic activity in intra- and intermolecular olefin metathesis.

2.2. Synthesis of ruthenium carbene complexes with unsymmetrical fluorine-containing *N,N'*-diarylimidazoline-2-ylidene ligands

N-Heterocyclic carbenes (NHCs) have found widespread applications as important auxiliary ligands in modern organometallic and coordination chemistry. Their unique steric and electronic properties, such as high σ -basicity and low π -acidity, have made possible the development of effective metal catalysts for various applications with the most outstanding examples in the field of ruthenium-catalyzed olefin metathesis.

Due to the fact that the catalytic activity of ruthenium carbene complexes strongly depends on steric volume and electronic nature of substituents on nitrogen atoms of NHC ligand, a great attention of the researchers has been recently focused on unsymmetrical NHCs (uNHCs) as desymmetrization allows for rapid implementation of further fine-tuning. The introduction of chelation, bifunctionality, shielding effects, and chirality-transfer can influence the catalyst stability, reactivity, and selectivity, thus stimulating the search for new tailor-made systems including mono- and multidentate uNHC ligands.

Among known olefin metathesis catalysts the ruthenium carbene complexes bearing 4,5-dihydroimidazole-based NHC ligands with *ortho*-substituted *N*-aryl groups possess the highest activity. Therefore, we choose the synthetic strategy based on the initial preparation of unsymmetrical bisarylethylene diamine **A** followed by heterocyclization to imidazolium salt **B** as the precursor of the corresponding carbene **C** (Figure 1).

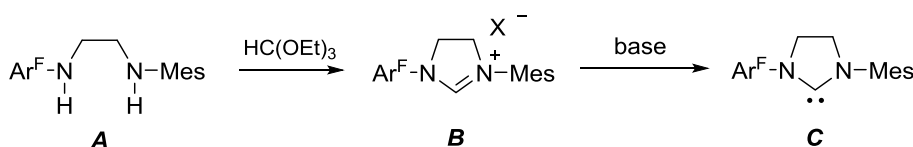
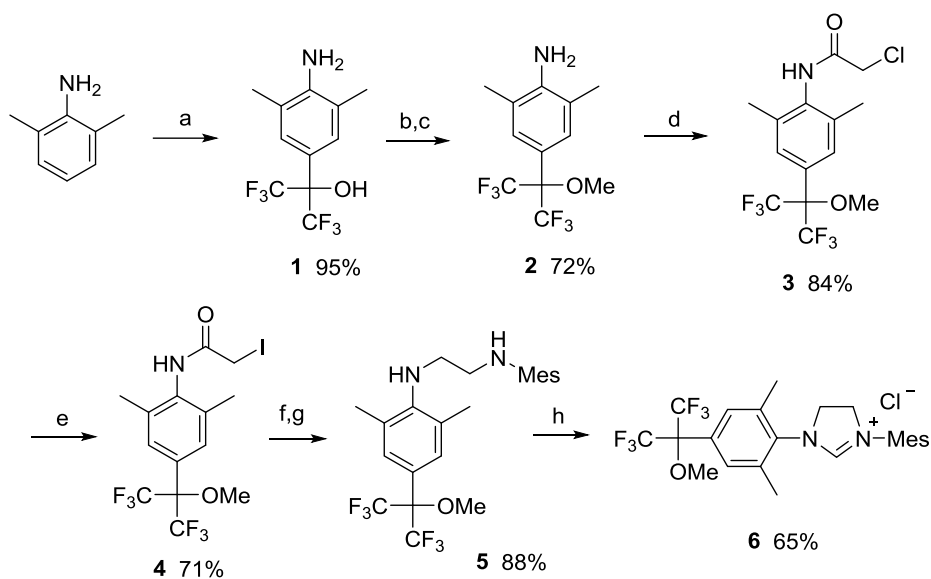


Figure 1

First, we directed our efforts towards the synthesis of the unsymmetrical 1,3-bis(aryl)-4,5-dihydroimidazolium salt **6** (Scheme 1) as a precursor of the corresponding NHC ligand bearing the hexafluoroisopropylmethoxy group in the *para*-position of *N*-aryl moiety. For this purpose the fluorinated aniline **1** was synthesized *via* simple procedure including the alkylation of 2,6-dimethylaniline with commercially available hexafluoroacetone hydrate (step *a*). Then, the

synthetic sequence included: *b*) protection of the amino function with benzaldehyde to form the corresponding Schiff base; *c*) selective *O*-methylation/*N*-deprotection to afford **2** in good yield. To construct the imidazoline ring the fluorinated aniline **2** was further acetylated by chloroacetyl chloride with subsequent halogen exchange with NaI to give the iodide **4** (steps *d,e*) After condensation **4** with mesitylamine and subsequent reduction of amide ketogroup (steps *f,g*) unsymmetrical ethylene diamine **5** was obtained that was further cyclized by treatment of the dihydrochloride of **5** with excess of triethyl *ortho*-formate to afford the desired salt **6**.

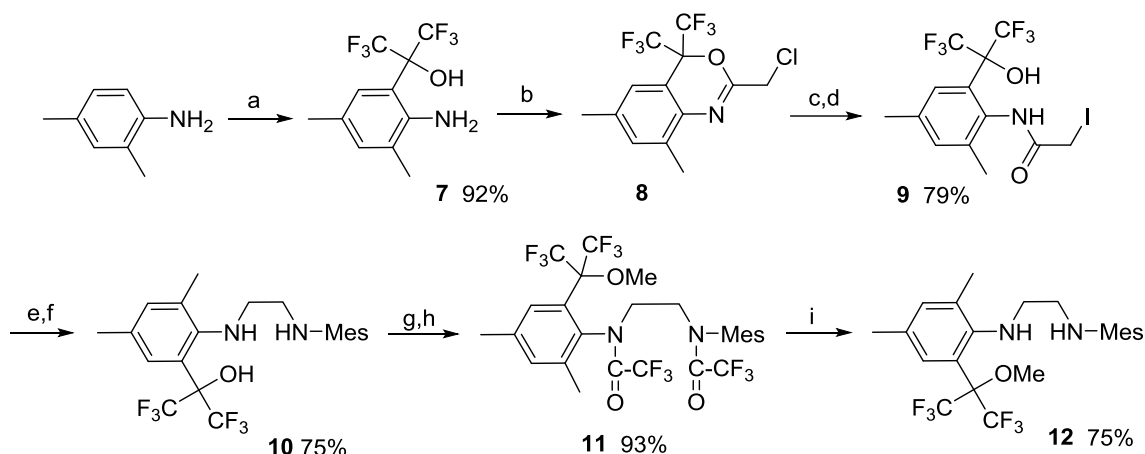


(a) HFA·1.5 H₂O, *p*-TSA (1 mol%), 100 °C, 95%; (b) PhCHO, toluene, 110 °C; (c) MeI, K₂CO₃, MeCN; 70 °C then HCl/H₂O, rt; 72% for 2 steps; (d) ClCH₂C(O)Cl, DMAP, CH₂Cl₂, rt; (e) NaI, acetone, rt; (f) MesNH₂ (15-fold excess), rt; (g) BH₃·SMe₂, THF, 88% for 2 steps; (h) MeOH/HCl, rt, then HC(OEt)₃, 100 °C, 60%. HFA = hexafluoroacetone; *p*-TSA = *p*-tolylsulphonic acid, DMAP = dimethylaminopyridine.

Scheme 1

Since it was known from the literature that the increase of steric hindrance of the substituents at NHC nitrogen atoms could bring an enhanced stability to the corresponding ruthenium complex, improving often its performance, we were interested in preparation of unsymmetrical salts with bulky hexafluoroisopropylmethoxy group in *ortho*-position of *N*-aryl moiety. For this purpose analogous *ortho*-substituted aniline **7** (Scheme 2), formed *via* alkylation 2,4-dimethylaniline by hexafluoroacetone hydrate, was quantitatively transformed into benzoxazine **8** under treatment with chloroacetic acid chloride. After mild ring opening of **8** the same procedure as for **5** (Scheme 1) was used for the preparation of hydroxyl-containing diamine **10**. To alkylate OH-function selectively, the diamine **10** was initially protected with two trifluoroacetic groups, which were

removed after successful *O*-methylation by treatment of the trifluoroacetylated derivative **11** with potassium hydroxide to yield the unsymmetrical diamine **12**.

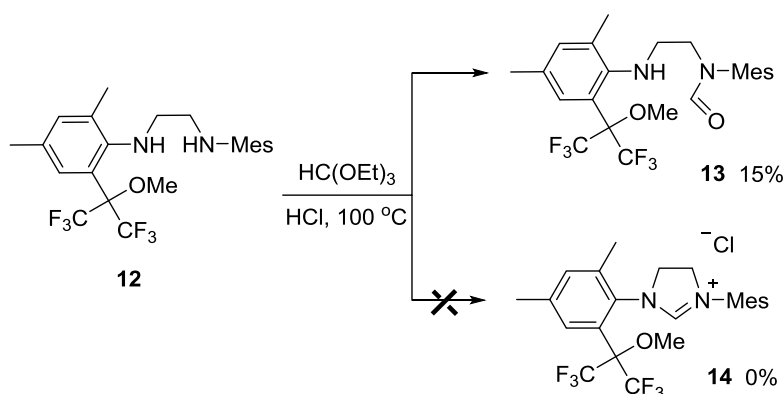


(a) HFA·1.5 H₂O, *p*-TSA (1 mol. %), 100 °C, 92%; (b) ClCH₂C(O)Cl, DMAP, CH₂Cl₂, rt; (c) HCl/MeOH, rt; (d) NaI, acetone, rt; 79% for 3 stages; (e) MesNH₂ (15-fold excess), rt; (f) BH₃·SMe₂, THF, 75% for 2 stages; (g) TFAA/Py, CH₂Cl₂, rt; (h) MeI, K₂CO₃, DMF; 93% for 2 stages; (i) KOH, 18-crown-6, DMSO/H₂O, 130 °C, 75%.

Scheme 2

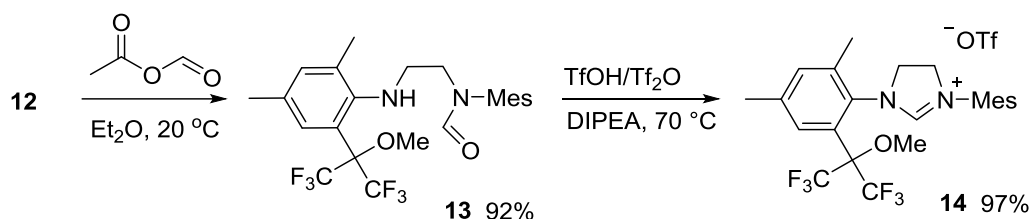
However, all our attempts to accomplish heterocyclization of **12** into the corresponding salt applying conventional methods have proved to be unsuccessful. Thus, the treatment of **12** with triethyl *ortho*-formate led to the formation of complicated mixture of products, from which the only formylated derivative **13** was isolated in poor yield (Scheme 3).

Taking into account the fact, that formamides are known decomposition products of NHCs, and precedents exists even for their inter-conversion in the case of less bulky mono-formamides¹⁴⁵, an alternative approach to imidazolium salt **14** has been developed based on intermolecular heterocyclization of mono-formamide **13**.



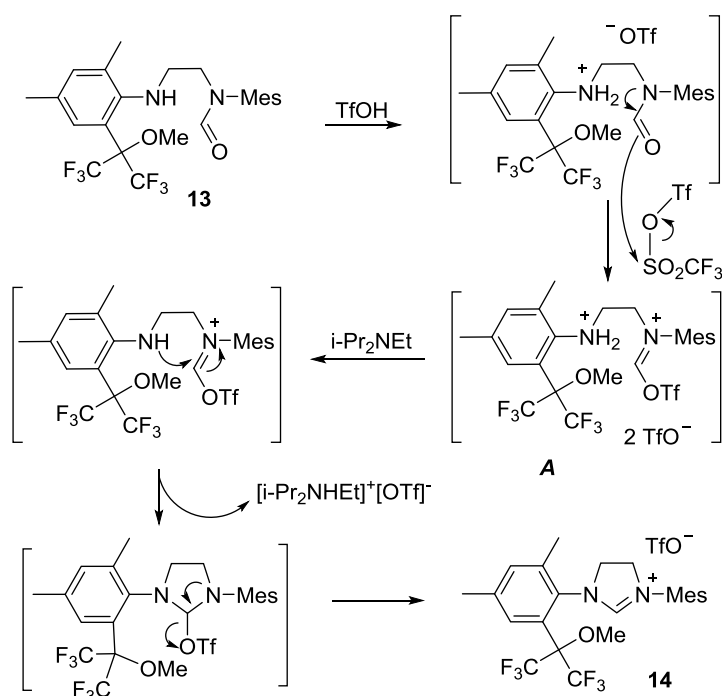
Scheme 3

For this aim, the synthesis of compound **13** was optimized *via* formylation of diamine **12** by usage of acetic-formic mixed anhydride. The reaction selectively occurs at the more sterically accessible nitrogen atom and goes to completion for 15 min at room temperature in ether to afford mono-formylated derivative **13** (Scheme 4).



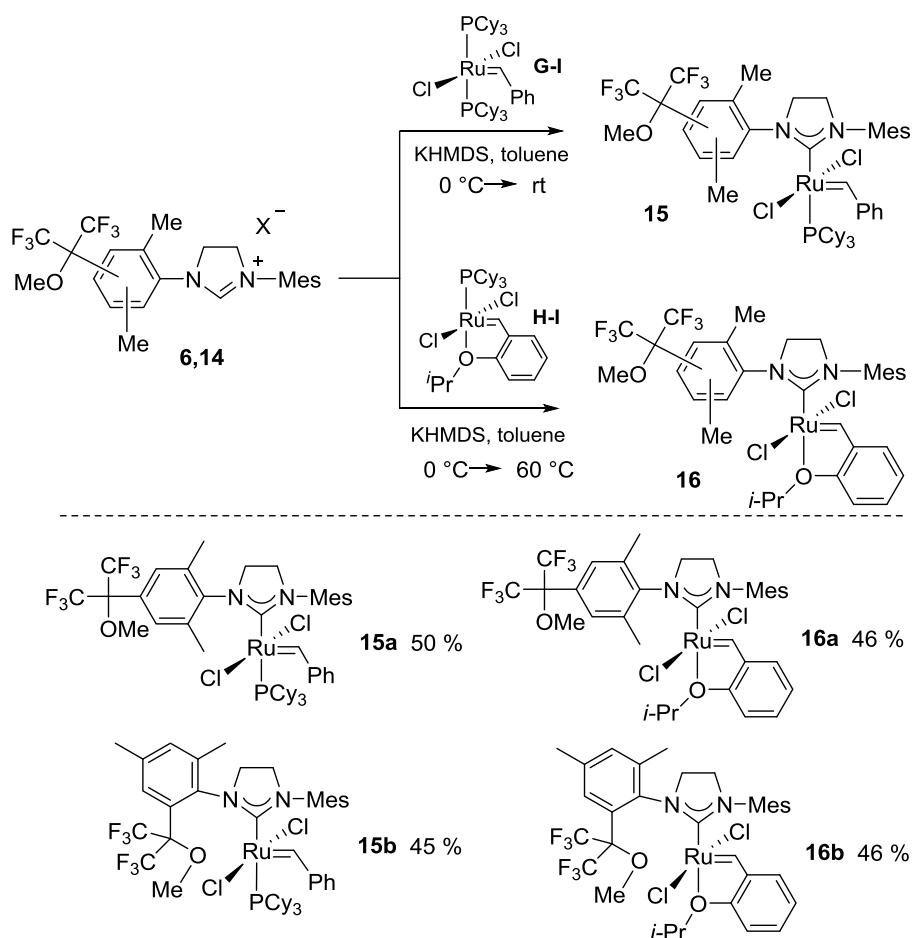
Scheme 4

Then we found, that the successive addition of stoichiometric amounts of triflic acid (TfOH) and triflic anhydride (Tf_2O) to the formylated compound **13** provided conditions for Vilsmeier-Haack reaction *via* covalent activation of amide group. The use of Hünig's base (DIPEA) has proved to be optimal for the final cyclization step to produce the desired imidazolium triflate salt **14** in excellent yield (Scheme 5). Fortunately, the final fluorinated imidazolium triflate **14** can be easily purified by single recrystallization from hexanes.



Scheme 5

With these new fluorinated uNHC salts in hand, we prepared the ruthenium complexes **15** and **16**. The corresponding carbene were generated *in situ* by the treatment of starting salts **6** and **14** with potassium hexamethyldisilazide (KHMDs) in anhydrous toluene at 0 °C under argon atmosphere with subsequent addition of first generation commercially available RuCl₂(PCy₃)₂(=CHPh) **G-I** and RuCl₂(PCy₃)₂(=CH(*o*-*i*-PrO-C₆H₄)) **H-I**. As a rule, the ligand exchange required an additional stirring of the reaction mixture at room temperature for two hours or heating at 60 °C for 30 min. Purification by silica gel chromatography and further recrystallization from a DCM/*n*-pentane mixture afforded dark-brown (**4**) and dark-green (**5**), air stable solids in moderate yields (Scheme 6).



Scheme 6

Complexes **15a,b** and **16a,b** were completely characterized by NMR spectroscopy and elemental analysis. The NHC ligands of complexes **16a,b** rotate fast on the NMR timescale and, therefore, only one signal is observed in the benzyldiene region of the ¹H NMR spectra (around 16.5 ppm) for these phosphine-free complexes. In the case of phosphine-containing complex **15a** a mixture of two rotational isomers (~2:1) is formed. It can be rationalized by different location of

mesityl and fluorinated aryl rings above the benzylidene group due to possible π - π stacking interaction. In contrast, the sole carbene proton signal of **15b** (20.2 ppm) is observed as the result of hindered rotation of NHC ligand due to anchoring effect of bulky *ortho*-substituent. 2D NMR (HMBC) experiment unambiguously evidences the location of the fluorinated aryl moiety above the benzylidene ring (cross peak between styrene *ortho*-H (7.33 ppm) and quaternary carbon (84.35 ppm) of (CF₃)₂C-OMe group (Figure 2).

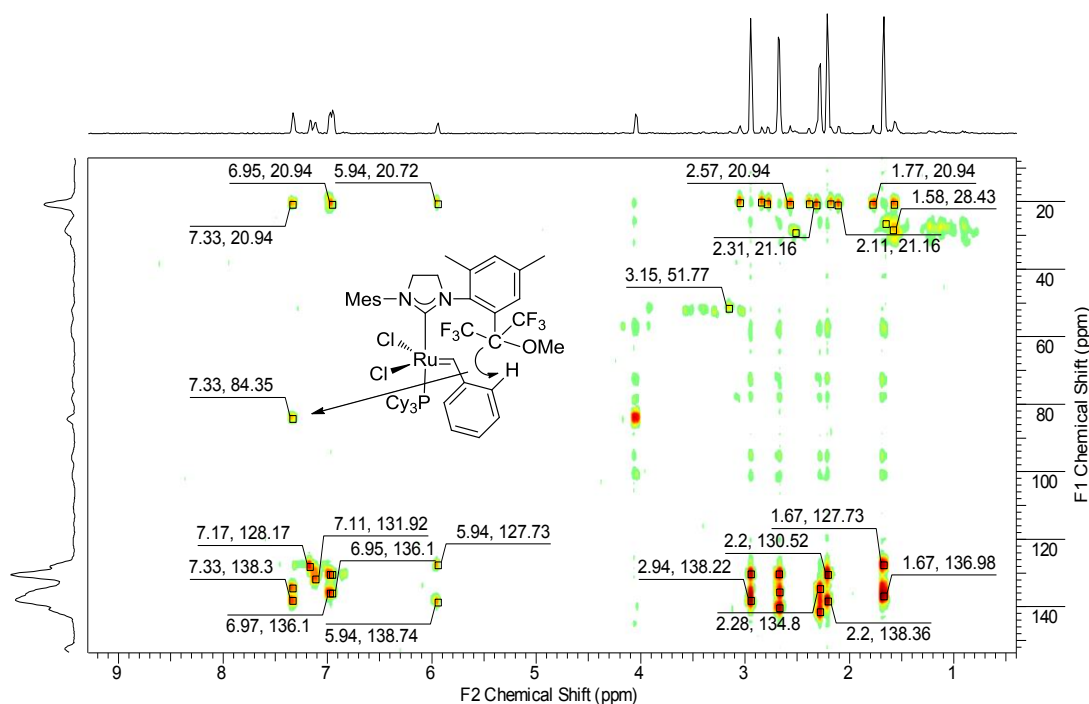


Figure 2. 2D NMR spectra (HMBC) of **15b**.

The presence of CF₃ groups in the molecule gives a unique possibility both to control the progress of reactions and to get an additional information about the structural peculiarities of the compounds obtained by usage of ¹⁹F NMR spectroscopy. For instance, in ¹⁹F NMR spectra of *para*-substituted complex **15a** one singlet at -70.24 ppm corresponds to two equivalent CF₃ groups, whereas for the complex **15b** bearing hexafluoroisopropylmethoxy group in *ortho*-position these groups become not equivalent due to hindered rotation of fluorinated aryl moiety around C-N bond that leads to the appearance of two individual singlets in the field of -63.57 and -68.96 ppm respectively (Figure 3). This situation is typical for other similar complexes also.

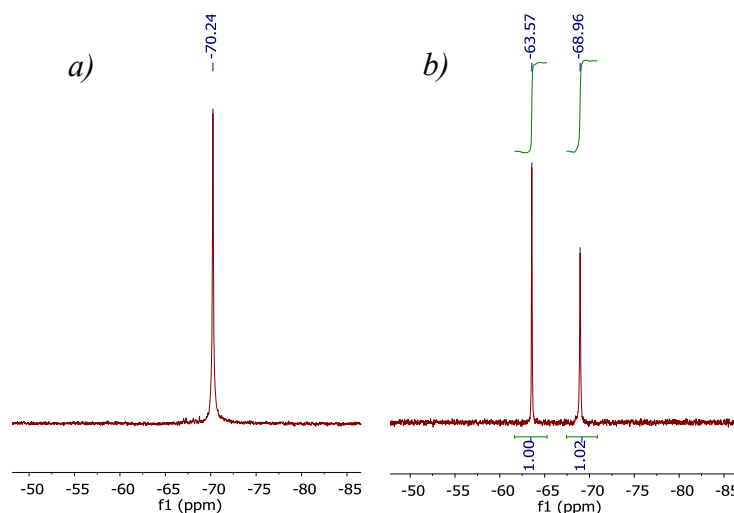


Figure 3. ^{19}F NMR spectra of **15a** (a) and **15b** (b).

In addition single crystals of good quality for X-ray analysis from complexes **16a,b** were obtained (Figure 4).

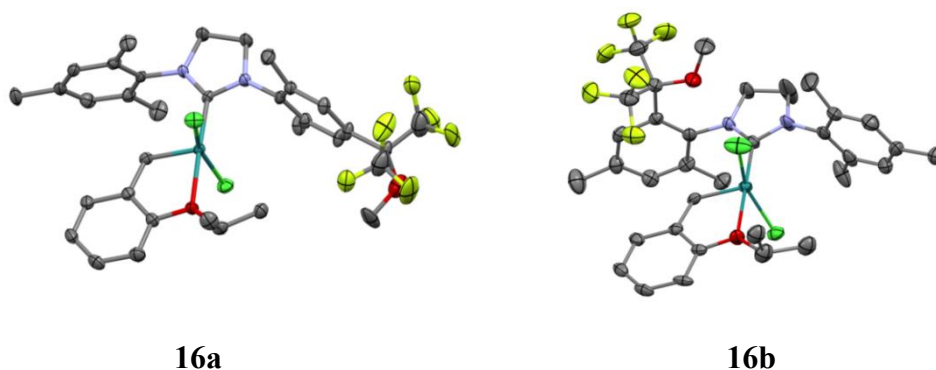


Figure 4

The structures of complexes **16a** and **16b** were compared to that of the olefin metathesis catalyst $\text{RuCl}_2(\text{bis}(\text{mesityl})\text{imidazolinyldene})(\text{ortho}\text{-isopropoxybenzylidene})$ **HG-II** (Table 1). These three complexes crystallize in a monoclinic system. All bond lengths and angles are quite similar, which shows that the substitution has not a strong effect on the structures of the different complexes, especially around the metal center. The chelate (Ru-C(1)-C(3)-O) is almost planar and parallel to the plane of the five-membered NHC ring. The two chloride atoms are in *trans*-position with a $\text{Cl}^1\text{-Ru-Cl}^2$ angle of $156\text{-}159^\circ$, in a plane, which is perpendicular to the bidentate isopropoxybenzylidene and NHC ligands. It can be noted that in the solid state, the fluorinated group in the Hoveyda type complex **16a** is located at the opposite side of the benzylidene ligand, whereas for complex **16b**, this group sits above the benzylidene ligand bringing more steric hindrance on the carbene side.

Table 1. Selected structural data for **16a** and **16b**

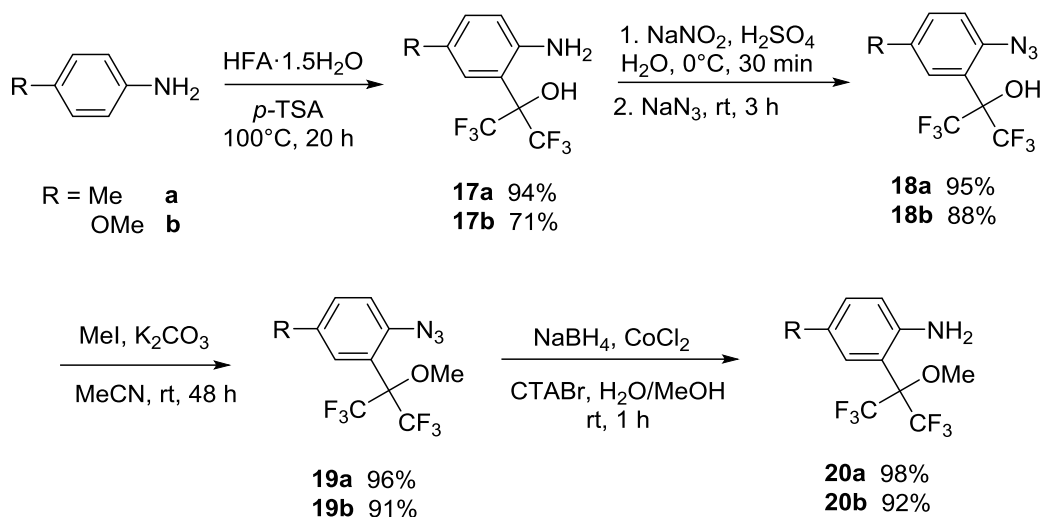
Complex	HG-II³⁰	16a	16b
<i>Bond length (Å)</i>			
Ru-C(1) (benzylidene)	1.828(5)	1.832 (4)	1.825(5)
Ru-C(2) (NHC)	1.981(5)	1.987(4)	1.975(5)
Ru-O	2.261(3)	2.257(3)	2.272(3)
Ru-Cl ¹	2.3279(12)	2.3492(11)	2.3116(14)
Ru-Cl ²	2.3393(12)	2.3505(11)	2.3393(13)
<i>Angle (°)</i>			
C(1)-Ru-C(2)	101.59(19)	102.64(17)	101.2(2)
C(1)-Ru-O	79.28(17)	79.59(15)	78.91(17)
C(2)-Ru-O	176.22(14)	177.69(14)	177.96(16)
Cl ¹ -Ru-Cl ²	156.47(5)	159.88(5)	156.80(6)
C(1)-Ru-Cl ¹	100.18(15)	98.37 (14)	98.92(15)
C(1)-Ru-Cl ²	100.12(15)	98.54(14)	100.30(15)
C(2)-Ru-Cl ¹	96.59(12)	93.46(11)	97.02(13)
C(2)-Ru-Cl ²	90.89(12)	93.40(11)	91.86(14)
<i>Torsion angle (°)</i>			
C(2)-Ru-C(1)-C(3)	171.0(3)	176.2(3)	176.6(4)
Cl ¹ -Ru-C(1)-C(3)	78.0(3)	80.8(3)	84.1(4)
Cl ² -Ru-C(1)-C(3)	90.1(3)	88.3(3)	82.9(4)
O-Ru-C(1)-C(3)	5.3(3)	3.2(3)	1.4(3)

The investigation of catalytic activity of complexes obtained will be discussed in chapter 2.6.

2.3. Synthesis of ruthenium carbene complexes with fluorine-containing mono-*ortho*-aryl substituents in NHC ligands

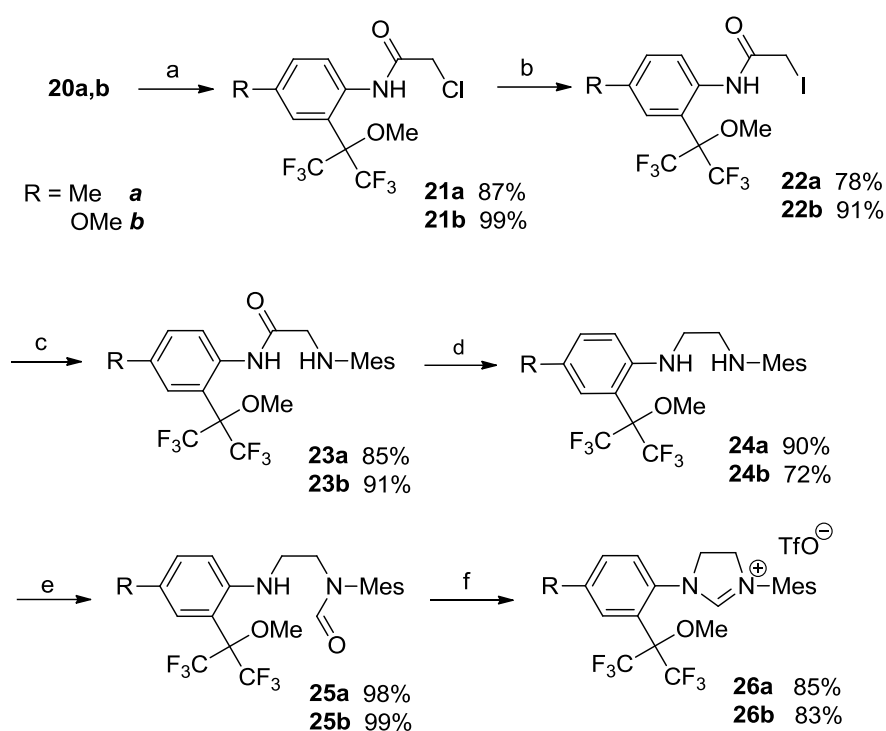
As known from the literature, the variation of the substitution pattern in *N*-aryl moieties of the NHC ligand led to extremely active catalysts for challenging transformations involving metathesis of hindered substrates. However, it is not always easy to predict how structural and electronic changes at the NHC can affect the catalyst activity. For example, the presence of bulky substituents on nitrogen has been shown to improve catalyst stability limiting decomposition pathways due to C-H bond activation of *N*-aryl rings, whereas mono-*ortho*-substituted *N*-aryl groups of the NHC ligand have been recognized as an important feature for successful ring-closing metathesis (RCM) reactions. On the other hand, *N*-*para*-methoxyaryl NHCs have been found to be excellent ligands for palladium catalysts for Buchwald-Hartwig coupling, compared to the corresponding parent NHCs. At the same time, it has been recently established that Ru metathesis catalysts bearing imidazoline-based NHCs with *N*-*para*-methoxyaryl moieties were able to increase the initiation rate in RCM reactions at very low catalyst loadings¹⁴⁶. Therefore, with the aim of evaluating the effects of mono-*ortho*-arylsubstitution and the replacement of *para*-methyl *N*-aryl group with more electron-donating methoxy group in unsymmetrical fluorinated NHC ligand on the activity of the resulting precatalysts, we have elaborated an efficient method for the preparation of the corresponding ruthenium carbene complexes.

Thus, we first directed our efforts towards the synthesis of the mono-substituted anilines **17a,b** containing hexafluoroisopropylmethoxy group in the *ortho*-position. For this purpose the commercially available *para*-toluidine and *para*-anisidine were heated with excess of hexafluoroacetone (HFA) hydrate under acid catalysis according to previously elaborated for 2,4-dimethyl derivative protocol to give the corresponding aniline **17a,b** in good to excellent yields. To perform the selective *O*-methylation the latter were preliminary transformed into azides **18a,b** *via* successive treatments with sodium nitrite and azide, and then, **18a,b** were methylated with methyl iodide under basic conditions to afford *O*-protected azides **19a,b**. Finally, the reduction of azido group of **19** was performed with sodium borohydride under cobalt dichloride-catalysis in the presence of cetyltrimethylammonium bromide to stabilize catalytic Co-species leading to excellent yields of anilines **20a,b** (Scheme 7).



Scheme 7

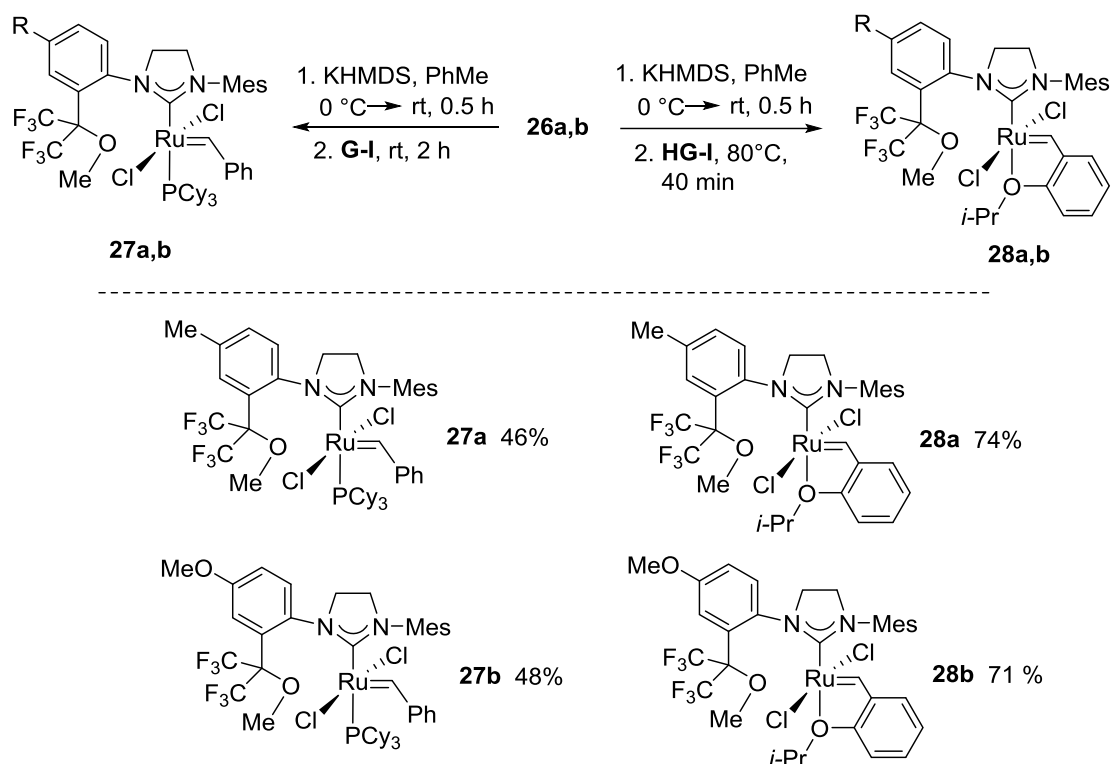
The anilines **20a,b** obtained were further used as the starting materials to construct the desired imidazolium salts **26a,b**. The synthetic sequence included: (a,b) selective *N*-acylation with chloroacetyl chloride with subsequent halogen exchange with NaI to give the iodides **22a,b** in very good yields for both steps; (c,d) condensation with mesitylamine followed by the reduction of the resulting aminoamides **23a,b** with $\text{BH}_3\cdot\text{SMe}_2$ to afford the corresponding diamines **24a,b**; and finally (e,f) selective formylation at the more sterically accessible amino group using acetic-formic mixed anhydride followed by heterocyclization *via* the treatment with stoichiometric amounts of triflic acid (TfOH) and triflic anhydride (Tf_2O) to give the target NHC precursors **26a** and **26b** in 85% and 83% yields, respectively (Scheme 8). The last two steps (e,f) were performed using a slightly modified procedure previously developed by us for sterically demanding fluorinated imidazolium salts (see chapter I). It is noteworthy that all intermediates of this synthetic sequence were isolated in high yields by simple crystallization from common organic solvents without additional purification via column chromatography.



(a) ClCOCH₂Cl, AcOH, AcONa, H₂O, rt, 10 min, (b) NaI, acetone, rt, 24 h,
 (c) MesNH₂, rt, 4 days, (d) BH₃·SMe₂, toluene, 90 °C, 4 h. (e) AcOCHO,
 CH₂Cl₂, rt, 5 min, (f) 1. TfOH, rt, 0.5 h, 2. Tf₂O, 65 °C, 1.5 h, 3. DIPEA,
 80 °C, toluene, 1.5 h.

Scheme 8

The synthesis of new ruthenium complexes was accomplished by traditional ligand exchange method using the reaction of in situ generated carbene with commercially available complexes **G-I** and **HG-I**. The reaction were performed in toluene under inert atmosphere, controlled by TLC method leading to the formation of the corresponding products **27** and **28** as air-stable solids of typical dark-brown (**27a,b**) and dark-green (**28a,b**) colors in moderate and good yields after column chromatography on silica gel (Scheme 9).



Scheme 9

The complexes obtained were fully characterized by NMR spectroscopy and elemental analysis. In ^1H NMR spectra of phosphine-containing **27a,b** as well as phosphine-free **28a,b** complexes measured at room temperature the absorptions of intrinsic benzyliidene protons are observed around 19.6 ppm and 16.9 ppm, respectively, as two broad singlets in each case. The doubling of the signals for CF_3 -groups takes place in ^{19}F NMR spectra also. This phenomenon could be attributed to the existence of two rotamers due to hindered rotation of bulky fluorinated aryl group around C-N bond. These doublets come together at 60-80 °C under NMR experiment measured in d_8 -toluene, which supports the existence of rotamers. The ^{13}C NMR spectrum of the NHC at 60 °C displays a resonance at 290 and 216 ppm for the carbene (N-C-N) and benzyliidene (Ru=C-H) carbons respectively, which are in the expected range for aryl-substituted imidazolylidenes.

A typical picture of ^1H NMR experiment measured at elevated temperature for the range of benzyliidene proton is depicted on Figure 5.

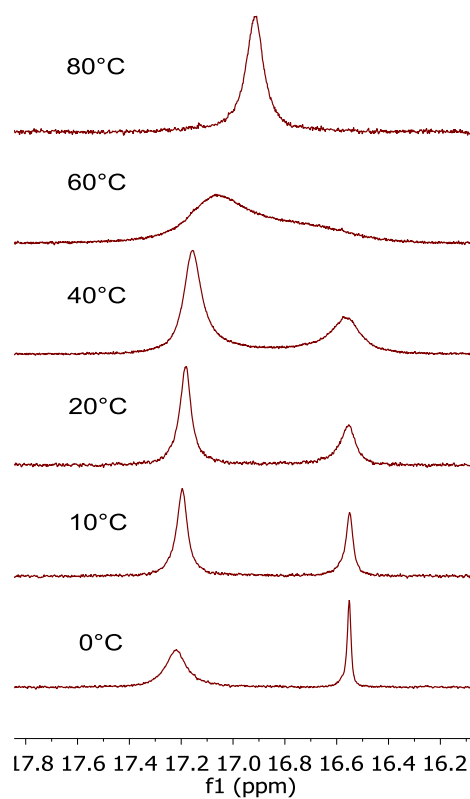


Figure 5. ^1H NMR-spectra of **28a** (range for benzylidene proton) measured at different temperature.

In addition, single crystals of good quality for X-ray analysis from complexes **28a,b** (Figure 6) were obtained by slow diffusion of pentane into a concentrated dichloromethane solution.

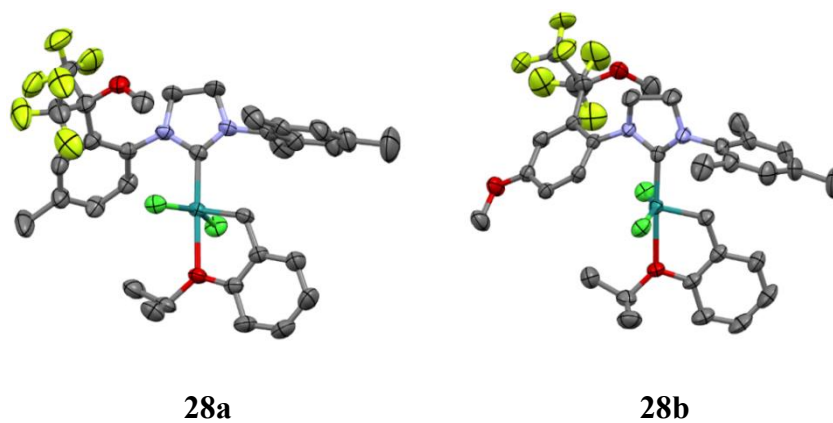
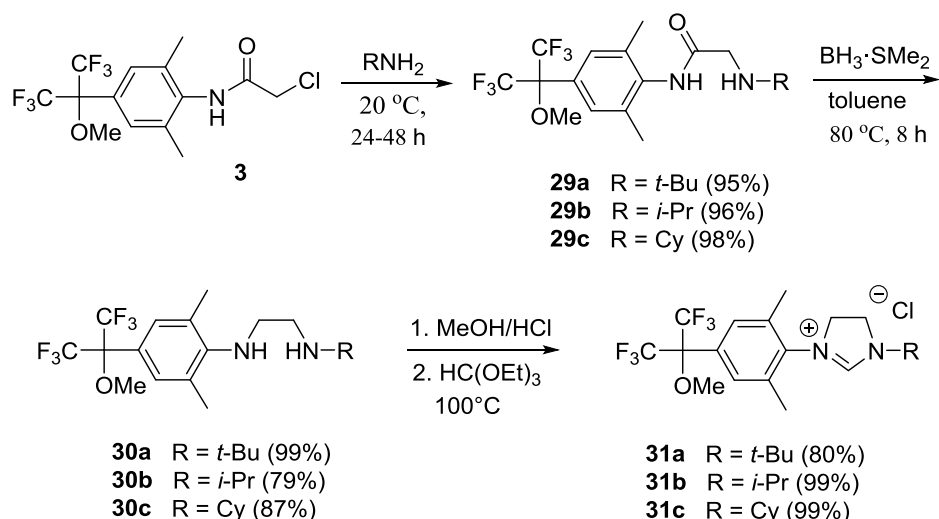


Figure 6

2.4. Synthesis of ruthenium carbene complexes with fluorinated *N*-alkyl-*N'*-arylimidazoline-2-ylidene ligands

As it is well known, the increase of NHC ligand donating properties usually leads to enhanced stability of the resulting metal complexes that in turn can favorably affect the catalyst efficiency. Taking into account this fact we have decided to synthesize unsymmetrical ruthenium carbene complexes with more donating alkyl substituent at one of the nitrogen atoms in the imidazoline-2-ylidene ligand.

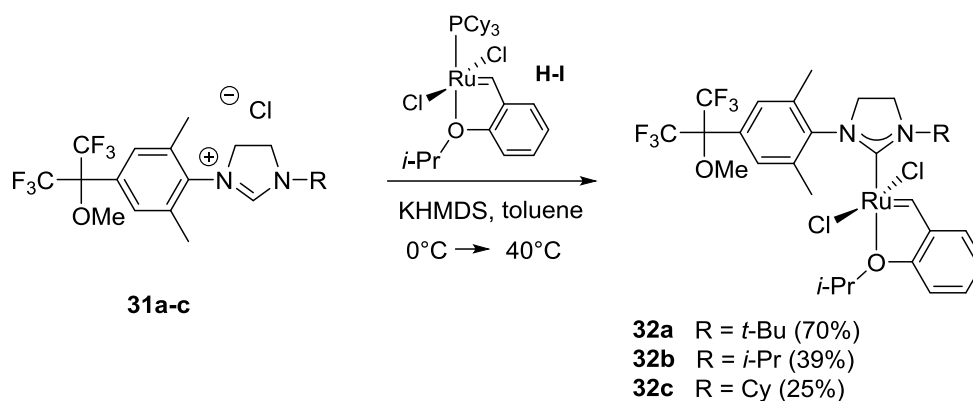
For this purpose fluorinated anilide **3**, which is easily available from commercial 2,6-dimethylaniline, hexafluoroacetone hydrate and chloroacetyl chloride (see Scheme 1), was used as starting material. Thus, it was found that its reaction with primary amines, such as *tert*-butylamine, *iso*-propylamine and cyclohexylamine, readily occurs at room temperature in excess of amine without any solvent and leads to completion after 1-3 days (TLC control) affording the corresponding aminoamides **29a-c** in almost quantitative yields (Scheme 10). The subsequent reduction of the keto group in amides **29** can be effectively performed by usage of complex $\text{BH}_3 \cdot \text{SMe}_2$ in toluene at 80 °C to give good yields of diamines **30a-c**. The latter undergo intramolecular cyclization under standard treatment with triethyl *ortho*-formate leading to the formation of the desired imidazolium salts **31a-c**.



Scheme 10

The salts obtained by this way were further utilized as precursors of the corresponding *N*-heterocyclic carbenes for the synthesis of the target ruthenium complexes **32a-c** (Scheme 11). As in the previous cases the carbenes were generated *in situ* by treatment of the starting salts **31a-c**

with potassium hexamethyldisilazide (KHMDs) in anhydrous toluene under argon atmosphere at 0 °C and with subsequent addition of Hoveyda first generation complex **HG-I** to the reaction mixture. Usually, the reaction required slight heating for 30-40 min to complete the ligand exchange process (PCy₃ for NHC). The resulting complexes **32a-c** were isolated by means of column chromatography on silica gel as dark-green solids and fully characterized using NMR spectroscopy (¹H, ¹³C, ¹⁹F) and elemental analysis.



Scheme 11

As in other cases of phosphine free complexes, in ¹H NMR spectra of all compounds the signals of intrinsic benzylidene protons (Ru=C-H) are observed in the range 16.5–17.1 ppm and correspond to the signals of carbon atoms (Ru=C-H) around 208-209 ppm in ¹³C NMR spectra. Besides that, the characteristic absorptions of carbenic atoms (N-C-N) are observed in ¹³C NMR spectra around 306, 285 and 286 ppm for **32a**, **32b** and **32c**, respectively.

As example, ¹H, ¹⁹F and ¹³C NMR-spectra of *tert*-butyl-containing complex **32a** are depicted at Figures 7 and 8, on which all intrinsic signals could be well identified.

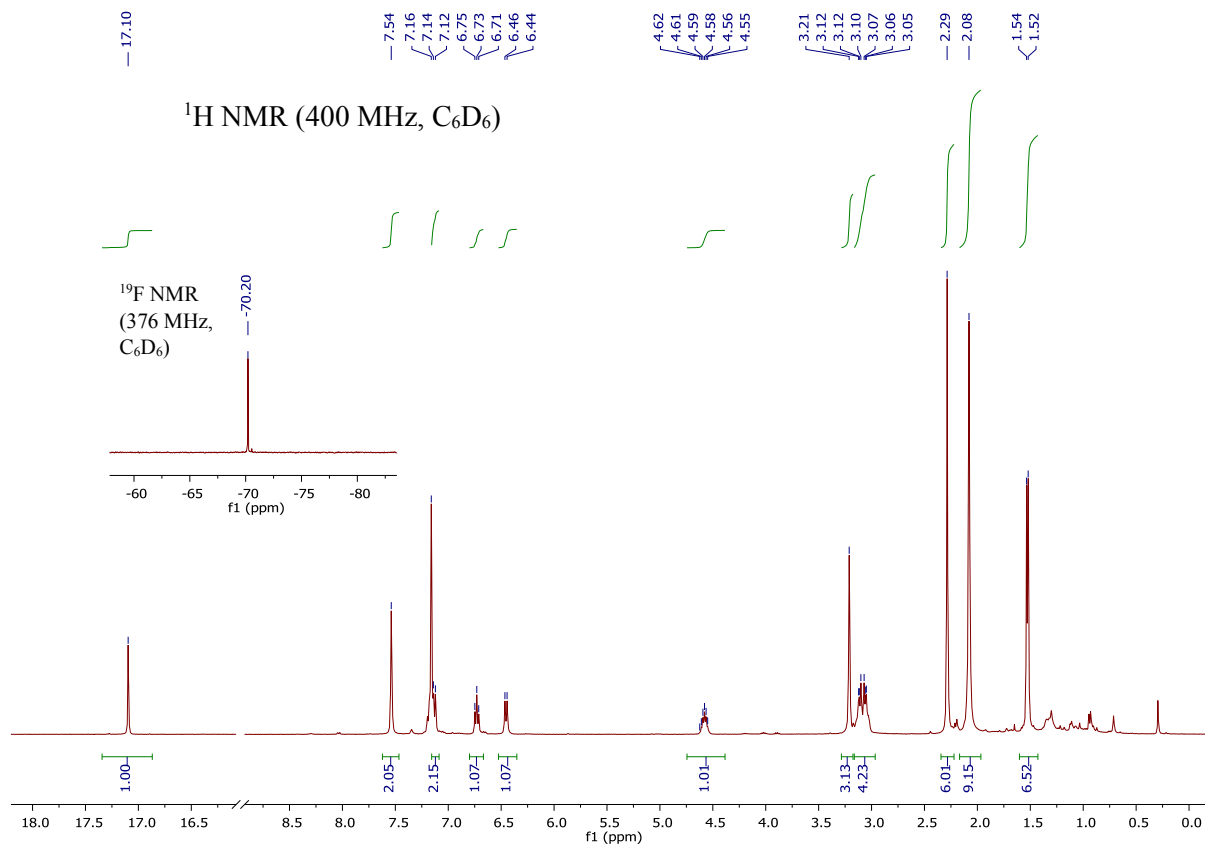


Figure 7. ^1H and ^{19}F NMR-spectra of **32a** in d_6 -benzene.

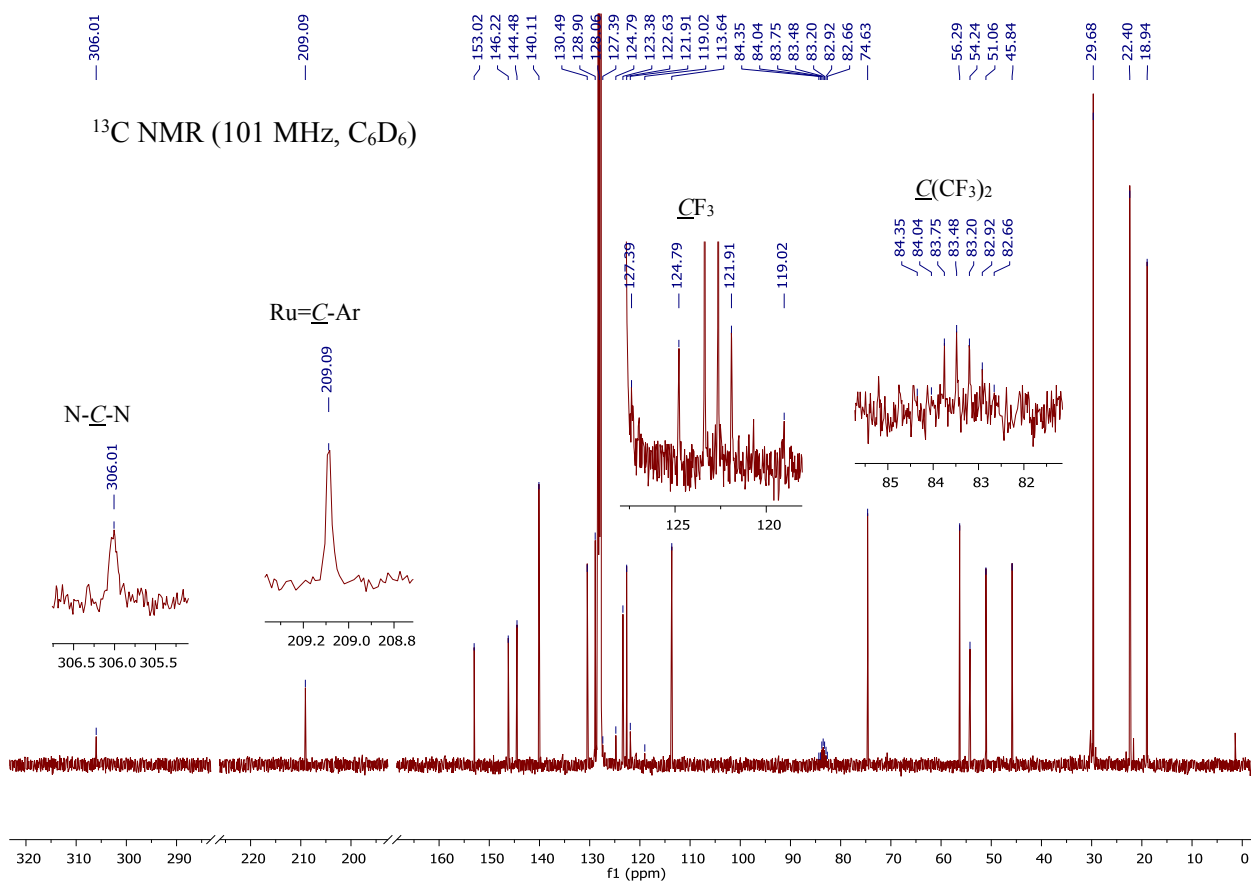
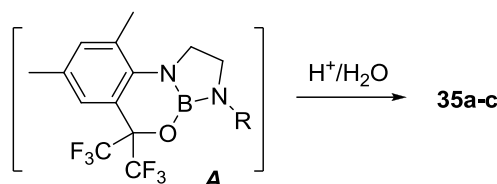
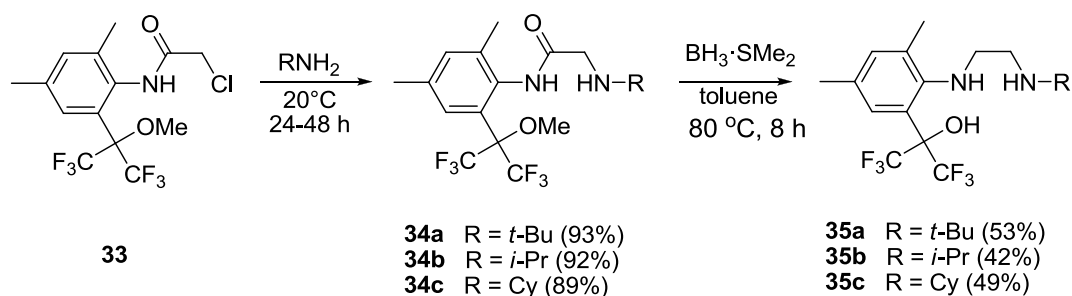


Figure 8. ^{13}C NMR-spectra of **32a** in d_6 -benzene.

Then we did several attempts to synthesize similar complexes comprising hexafluoroisopropylmethoxy group in *ortho*-position of *N*-aryl substituent in NHC ligand but failed. The synthetic sequence was interrupted at the stage of the keto group reduction of amide **34** (Scheme 12). In all cases the reaction unexpectedly led to the formation of *O*-demethylation products **35a-c** in moderate yields.



Scheme 12

Probably, it could be rationalized by the possible formation of more favorable intermediate **A** under reaction conditions due to enhanced nucleophilicity of nitrogen atom substituted with more donating alkyl group to compare with the cases of *N*-aryl group, in which the demethylation process did not occur (*e.g.* see Scheme 8, step *d*). Therefore, our further synthetic attempts to prepare the corresponding imidazolinium salts were stopped.

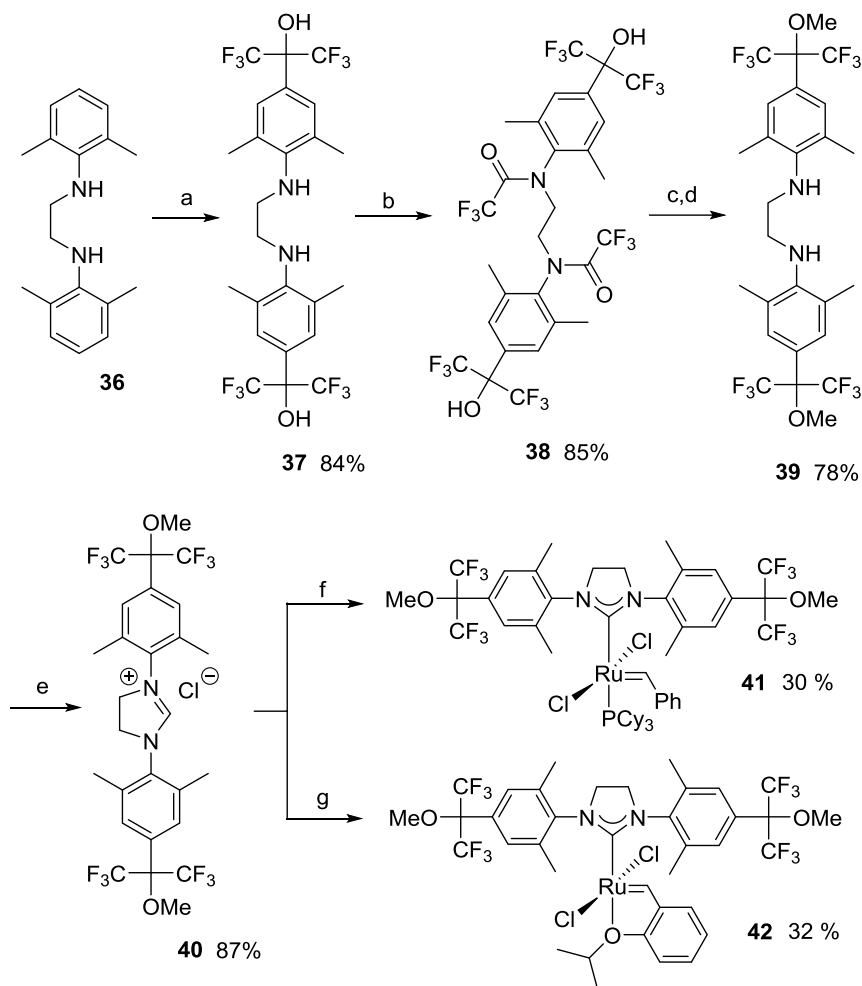
2.5. Investigation of catalytic activity of complexes obtained

The influence of structural and electronic peculiarities of fluorinated unsymmetrical NHC ligand on catalytic activity of new ruthenium carbene complexes was investigated on classical model reactions of intra- and intermolecular olefin metathesis. The commonly used commercially available Grubbs (**G-II**) and Hoveyda (**HG-II**) second generation catalysts were selected as the standards of comparison.

Because of the latter have in their structure the symmetrical *N,N*-(bis)mesitylimidazoline-2-ylidene ligands we were interested in additional determination how the desymmetrization factor

can influence on the new catalysts reactivity. For these purposes the symmetrical ruthenium complexes bearing two hexafluoroisopropylmethoxy groups in *para*-position of *N*-aryl substituents were specially synthesized.

So, a readily available diamine **36** was used as the starting compound (Scheme 13). It was found that its treatment with the excess of hexafluoroacetone hydrate led to the formation of product **37** in good yield as a result of double alkylation upon two free *para*-positions of aromatic core. Further synthetic sequence included: (b) the trifluoroacetylation of two secondary amino groups with trifluoroacetic anhydride; (c,d) selective *O*-methylation/deprotection to give symmetrical diamine **39**; (e) intramolecular heterocyclization of the latter into the corresponding NHC precursor **40** under heating in excess of triethyl *ortho*-formate. The target complexes **41** and **42** were prepared by the same manner as in previous cases using the ligand exchange reaction with phosphine-containing complexes **G-I** and **HG-I** (steps *f* and *g*, respectively).



(a) HFA·1.5H₂O, *p*-TSA (1 мол.%), 100°C, 84%; (b) TFAA/Py, Et₂O, 1 h, rt; (c) MeI, K₂CO₃, DMFA, 1.5 h, 80°C; (d) KOH, 18-crown-6, DMSO/H₂O, 1.5h, 130°C; (e) MeOH/HCl, rt, then HC(OEt)₃, 100°C; (f) KHMDS, toluene, **G-I**, rt, 2 h; (g) KHMDS, toluene, **HG-I**, 60°C, 1 h.

Scheme 14

The obtained complexes **41** and **42** were fully characterized by the modern physicochemical methods including X-ray analysis for compound **42** (Figure 9).

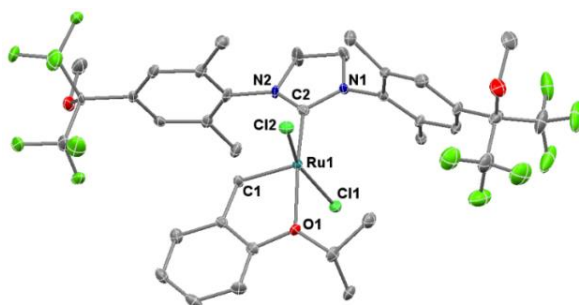


Figure 9

As a result, the catalytic activity of all synthesized new ruthenium complexes, depicted at Figure 10, was investigated and compared with activity of commercially available NHC-containing **G-II** and **HG-II** complexes (see p. 3).

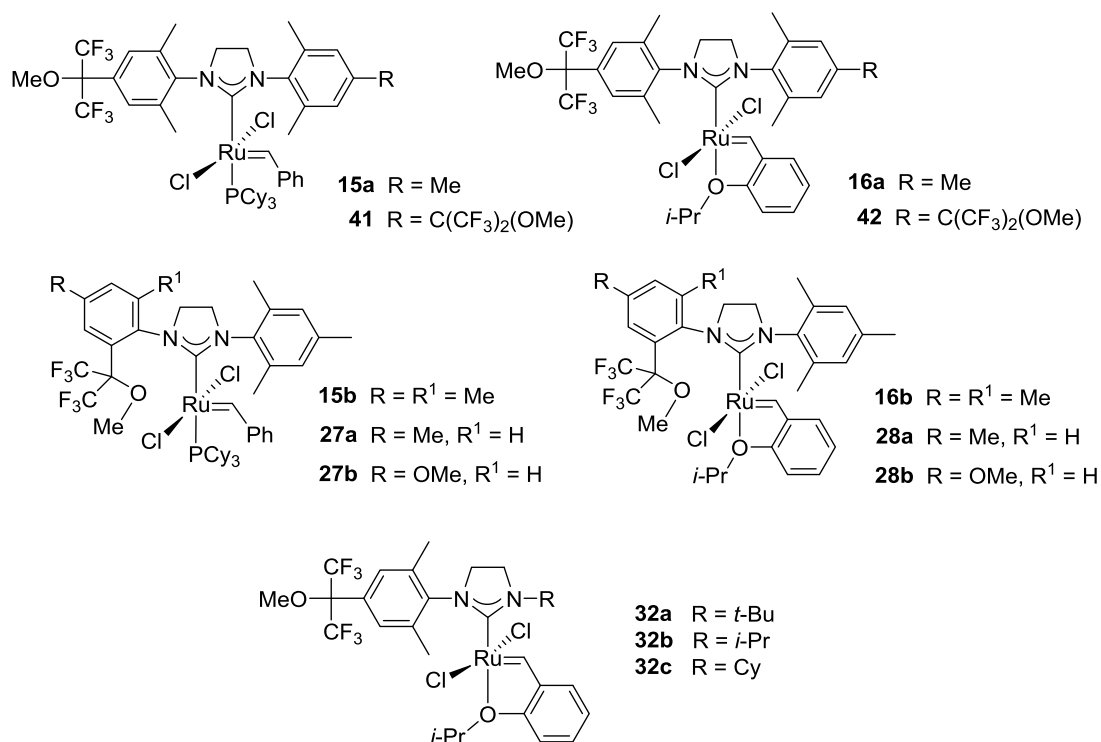
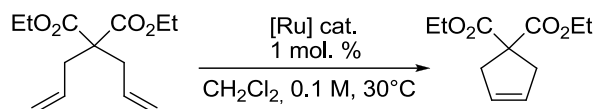


Figure 10

The kinetic experiments for all compounds were performed by taking the samples from the reaction mixture after a certain period of time suppressing the activity of the catalyst by addition to the mixture an excess of ethyl vinyl ether¹⁴⁷.

The ring closing metathesis (RCM) of diethyl diallylmalonate (DEDAM) was selected as the first model reaction, which has been performed in standard for known carbene complexes conditions (Scheme 14).



Scheme 14

For a better perception the results obtained were divided for two parts depending on the catalyst type. The data of catalytic activity of phosphine-containing complexes **15**, **27** and **41** are presented in Table 2 in comparison with the corresponding benchmark (**G-II**). The catalytic activities of phosphine-free complexes **16**, **28**, **32** and **42** along with benchmark **HG-II** are shown in Table 3.

Table 2. Catalytic activity of **G-II** type complexes in RCM

Time, min	Conversion of DEDAM, %					
	G-II	15a	15b	27a	27b	41
5	36	38	32	78	83	27
10	69	66	59	88	91	50
30	96	98	98	93	95	78

As can be seen from the table, almost all new complexes have exhibited high activity reaching the standard **G-II** level. The only exception is the complex **41** bearing symmetrical NHC ligand that demonstrates the positive impact of desymmetrization in the series of fluoroalkyl-containing ruthenium complexes.

In the case of phosphine-free complexes only **16a** has reached a level of benchmark **HG-II**. Meanwhile, both **16a** and its *ortho*-fluoroalkyl analogue **16b** have demonstrated a long initiation period before the catalytic systems operate efficiently (Table 3). Less sterically demanding complexes **28a,b** comprising fluoroalkyl-containing mono-*ortho*-aryl substituents do not possess a latent period and exhibit seamless rate's acceleration reaching a maximum conversion of 92%

within 4 hours. The symmetrical complex **42** as its phosphine-containing analogue **41** catalyzes this RCM reaction with lower rate.

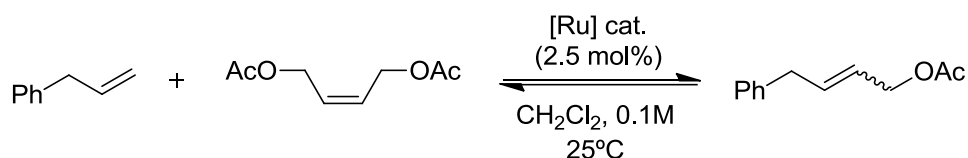
N-Alkyl substituted complexes **32b,c** have proved to be much less active. Notably, compound **32a** bearing the more bulky *tert*-butyl group at nitrogen atom does not catalyze this process at all.

Table 3. Catalytic activity of phosphine-free **HG-II** type complexes in RCM

Time, min	Conversion of DEDAM, %							
	HG-II	16a	16b	28a	28b	32b	32c	42
10	80	3	1	5	3	1	1	0
30	98	3	6	37	41	3	3	3
60	99	58	29	65	67	6	4	15
120	99	98	75	84	84	13	7	59
240	-	99	95	92	92	22 ^a	15 ^b	90

^a 68% after 20 h; ^b 35% after 20 h

Then, the catalytic activity of the synthesized complexes was investigated in cross metathesis (CM) reaction of allyl benzene with an excess of 1,3-diacetoxybut-2-ene. The reactions were performed at room temperature in methylene chloride with catalyst loading of 2.5 mol.% (Scheme 15). The data obtained were also separated in two different tables (3 and 4) according to the catalyst type.



Scheme 15

As result it was found that the complexes with PCy_3 ligand **15**, **27**, and **41** exhibit reactivity similar to the commercially available catalyst **G-II**. In all cases equilibrium around 79-82% conversion can be reached within 30 min with closely related kinetic profiles (Table 4).

Table 4. Catalytic activity of ruthenium complexes of **G-II** type in CM

Time, min	Conversion of allyl benzene, %					
	G-II	15a	15b	27a	27b	41
5	62	86	41	79	78	48
10	78	83	62	80	80	64
20	79	82	68	80	82	77
30	79	82	70	80	82	79

The activity of phosphine-free complexes in cross metathesis reaction exceeded in some cases the activity of catalyst **HG-II** (Table 5). Thus, complexes **28a** and **28b** bearing mono-*ortho*-aryl substituent in NHC ligand have demonstrated unusual high initiation rate already in two minutes after start of the reaction, reaching 10% more conversion (83%) in comparison with the same value for the benchmark catalyst **HG-II**.

Table 5. Catalytic activity of phosphine-free complexes of **HG-II** type in CM

Time, min	Conversion of allyl benzene, %							
	HG-II	16a	16b	28a	28b	32b	32c	42
2	40	45	41	72	69	0	0	10
5	75	63	45	80	78	0	0	28
10	73	66	66	81	80	0	0	45
20	72	73	73	82	84	10	4	61
30	72	76	76	83	83	15	8	65

The complexes **16a,b** with more bulky NHC ligands have similar to **HG-II** kinetic profiles.

Only *N*-alkyl-containing complexes **32b,c** as in the case of RCM reaction have demonstrated very low reactivity in CM; at that *N*-*tert*-butyl substituted complex **32a** has proved to be absolutely inert in this reaction.

On the whole, as result of the study of new fluoroalkyl-containing carbene complexes, it was found that most of complexes obtained have exhibited high catalytic activity in tested reactions of intra- and intermolecular olefin metathesis. Their reactivity was comparable with commonly used in these processes second generation Grubbs and Hoveyda catalysts. In the case of new Hoveyda type catalysts with mono-*ortho*-aryl substituted NHC ligands their performance has seemed to be even higher in comparison to benchmark catalyst **HG-II**. Moreover, it was established the influence of structural and electronic peculiarities of fluorinated unsymmetrical NHCs on the

initiation rate of the corresponding Ru-complexes, conversion of the starting olefins as well as the yield of the final metathesis products.

Below we selected the most representative examples of kinetic profiles clearly reflecting the result of structural modifications made in the frame of the present work. The unsymmetrical complexes of **G-II** type have proved to be the most active among the synthesized ones in RCM of DEDAM. As shown on the diagrams 1 the kinetic profile of **15b** is very close to commercial **G-II** catalyst. The initiation rate of complex **27b** is higher than for **G-II**. The maximum conversion for both **15b** and **27b** is reached within 30 min. The symmetrical complex **41** is less active in this reaction.

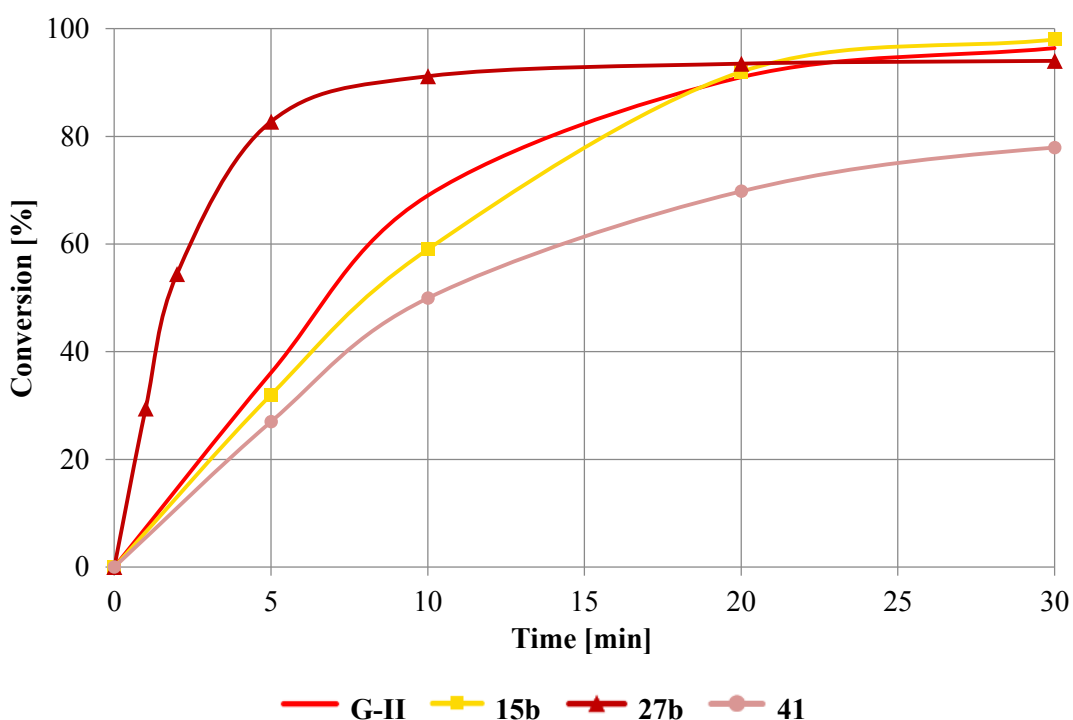


Diagram 1. Activity of **G-II** type complexes in RCM.

The unsymmetrical phosphine-free complexes of **HG-II** type have demonstrated better catalytic activity in CM reaction of allyl benzene with excess of 1,3-diacetoxybut-2-ene. Thus, complexes **28a** and **28b** have unusual high initiation rate reaching 10% more conversion in comparison with the benchmark catalyst **HG-II**. The *N*-isopropyl-containing complexes **32b** have displayed very low reactivity in this metathetic transformation (Diagram 2).

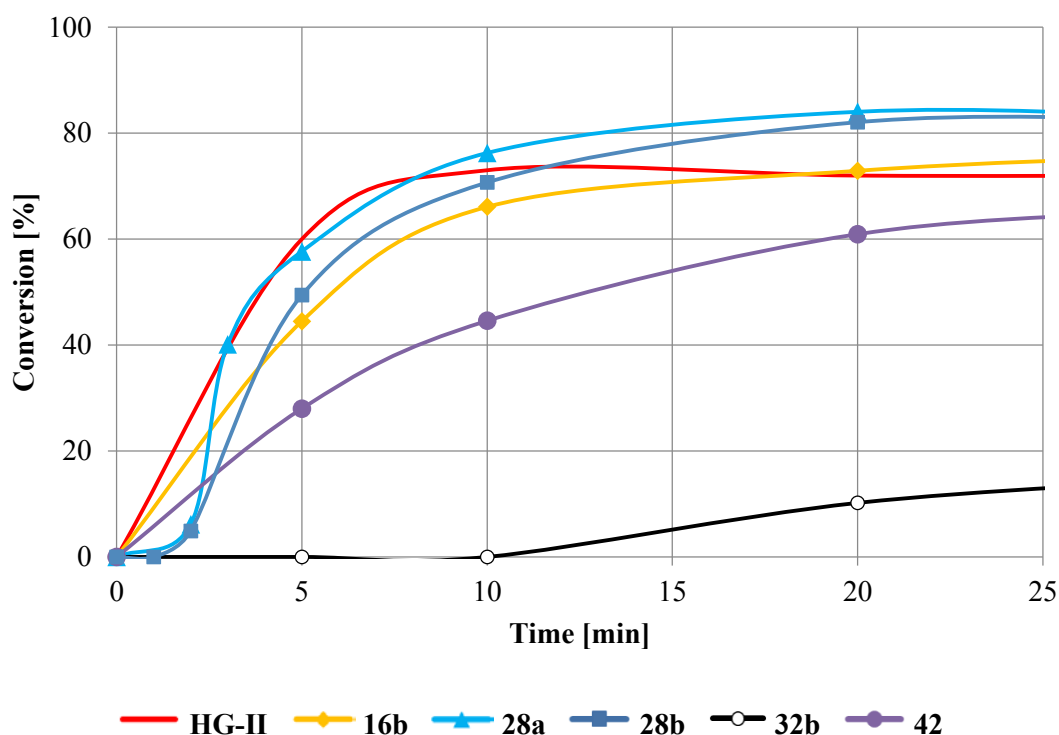


Diagram 2. Activity of **HG-II** type complexes in CM.

The results obtained give more insight in performance of unsymmetrical ruthenium carbene complexes and can open the door in the design of more selective catalysts for challenging metathesis transformation, *e.g.* such as CM and ROMP.

2.6. General conclusions

1. An efficient approach to a new family of unsymmetrical 1,3-bis(aryl)-4,5-dihydroimidazolium salts comprising bulky hexafluoroisopropylmethoxy group in *para*- or *ortho*-position in one of the *N*-aryl substituents has been developed. The introduction of fluoroalkyl substituent in aromatic core has been accomplished by means of alkylation reaction of the corresponding 2,6- or 2,4-dimethylanilines with commercially available hexafluoroacetone hydrate under PTSA-catalysis. The further construction of imidazoline ring included as a key step the heterocyclization of the corresponding unsymmetrical ethylene diamine by the treatment with triethyl *ortho*-formate or by modified Vilsmeier-Haack reaction.

2. New imidazolium salts with fluoroalkyl-containing mono-*ortho*-aryl substituent at one of the nitrogen atom have been synthesized based on alkylation of *para*-toluidine and *para*-anisidine by hexafluoroacetone hydrate.
3. A convenient method for the preparation of new *N*-alkyl-*N'*-arylimidazolium salts has been developed based on condensation of *para*-fluoroalkyl-containing chloroacetic anilide with *iso*-propyl-, cyclohexyl- and *tert*-butyl amines as a key step of the reaction sequence.
4. It was found that imidazolium salts obtained could be effectively acted as the corresponding NHC precursors. Consequently, an efficient access to a series of new ruthenium carbene complexes with unsymmetrical NHC ligands has been developed. The method involves *in situ* generation of the carbene *via* treatment of the starting salts with potassium hexamethyldisilazide and subsequent ligand exchange reaction with PCy₃-containing first generation Grubbs and Hoveyda complexes.
5. The catalytic activity of the complexes obtained has been investigated on classical model reactions of intra- and intermolecular olefin metathesis. As a result, it was found that most of the synthesized complexes have exhibited high activity in cyclization of diethyl diallylmalonate and in cross metathesis of allyl benzene with 1,3-diacetoxybut-2-ene. Their performance has proved to be comparable with commonly used second generation Grubbs and Hoveyda catalysts.
6. Structural and electronic impact of fluorinated unsymmetrical NHC on reactivity of new ruthenium complexes has been studied. In particular, it was revealed that Hoveyda type catalysts with mono-*ortho*-aryl substituted NHC ligands have demonstrated very high initiation rate in CM reaction to reach 10% more conversion in comparison with benchmark catalysts. At the same time, catalysts with more donating *N*-alkyl NHCs have displayed low activity; for instance, the *N-tert*-butyl substituted complex has proved to be absolutely inert both in RCM and CM reactions.
7. To establish the influence of desymmetrization factor on catalytic activity of fluorine-containing complexes the symmetrical ruthenium carbene complexes bearing NHC ligands with two hexafluoroisopropylmethoxy group in *para*-positions of *N*-aryl moieties have been specially synthesized. It has been established that they are significantly inferior in reactivity to their asymmetric counterparts.

Publications

1. **S.M. Masoud**, A.K. Mailyan, V. Dorcet, T. Roisnel, P.H. Dixneuf, C. Bruneau, S.N. Osipov, Metathesis Catalysts with Fluorinated Unsymmetrical NHC Ligands, *Organometallics*, **2015**, *34*, 2305–2313.
2. **S.M. Masoud**, A.K. Mailyan, A.S. Peregudov, C. Bruneau, S.N. Osipov, New fluorinated catalysts for olefin metathesis, *Mendeleev Communications*, **2016**, *26*, 474–476.
3. **S.M. Masoud**, M.A. Topchiy, A.S. Peregudov, T. Roisnel, P.H. Dixneuf, C. Bruneau, S.N. Osipov, Synthesis of metathesis catalysts with fluorinated unsymmetrical *N,N'*-diaryl imidazoline-based NHC ligands, *Journal of Fluorine Chemistry*, **2017**, *200*, 66–76.
4. **S.M. Masoud**, T.R. Akmalov, O.I. Artyushin, C. Bruneau, S.N. Osipov, New olefin metathesis catalysts with fluorinated *N*-alkyl-*N'*-arylimidazoline-2-ylidene ligands, *Russ. Chem. Bull.*, **2017**, *9*, 1601–1606 (Russ).
5. **S.M. Masoud**, A.K. Mailyan, S.N. Osipov, P.H. Dixneuf, C. Bruneau, New ruthenium metathesis catalysts featuring a fluorinated NHC ligand, Second International Green Catalysis Symposium, Rennes, France, April 2–4, 2014.
6. **S.M. Masoud**, A.K. Mailyan, S.N. Osipov, P.H. Dixneuf, C. Bruneau, New fluorine-containing olefin metathesis catalysts, International conference «Chemistry of organoelement compounds and polymers 2014», Moscow, Russia, September, 8–10, 2014.
7. **S.M. Masoud**, M.A. Topchiy, P.H. Dixneuf, C. Bruneau, S.N. Osipov, New ruthenium metathesis catalysts with CF₃-containing NHC ligands, International conference “Organometallic and Coordination Chemistry: Achievements and Challenges”, Nizhny Novgorod, Russia, September, 18–23, 2015.
8. **S.M. Masoud**, T.R. Akmalov, P.H. Dixneuf, C. Bruneau, S.N. Osipov, New Metathesis Catalysts with Fluorinated Unsymmetrical Imidazole-Based NHC-Ligands // Third International Green Catalysis Symposium, Rennes, France, March, 23–24, 2017.
9. **S.M. Masoud**, T.R. Akmalov, K.A. Palagin, P.H. Dixneuf, C. Bruneau, S.N. Osipov, Synthesis of New Ru-carbene Complexes with Unsymmetrical Fluorinated NHC Ligands // International Symposium on Olefin Metathesis and Related Chemistry ISOM-XXII, Zürich, Switzerland, July, 9–12, 2017, OC17.
10. T.R. Akmalov, **S.M. Masoud**, S.N. Osipov, Olefin Metathesis Catalysts with Fluorinated Tricyclic NHC-Ligands // 27th International Chugaev Conference on Coordination Chemistry, Nizhny Novgorod, Russia, October, 2–6, 2017, P6.

CHAPTER III

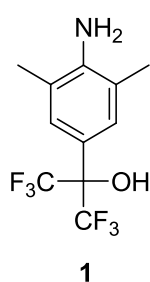
EXPERIMENTAL PART

3.1. General remarks

All solvents were freshly distilled from appropriate drying agents before use. All other reagents were recrystallized or distilled as necessary. Syntheses of ruthenium complexes were performed under an argon atmosphere using standard Schlenk techniques. Analytical TLC was performed with Merck silica gel 60 F254 plates. Visualization was accomplished by UV light (254 and 366 nm), spraying by $\text{Ce}(\text{SO}_4)_2$ solution in 5% H_2SO_4 or KMnO_4 solution in water. Column chromatography was carried out using Merck silica gel 60 (230-400 mesh ASTM) and ethyl acetate/petroleum ether. NMR spectra were recorded, unless otherwise stated, at room temperature on Bruker AV-300, AV-400, AV-500, AV-600 spectrometers operating at 300, 400, 500, and 600 MHz for ^1H ; 75, 101, 126, and 151 MHz for ^{13}C ; 282, 376, 471, and 564 MHz for ^{19}F (CFCl_3 as reference), and 121, 162, 202, and 243 MHz for ^{31}P (85% H_3PO_4 as reference). The chemical shifts are frequency referenced relative to the residual undeuterated solvent peaks. Elemental analysis was performed in the Laboratory of microanalysis of A.N. Nesmeyanov Institute of Organoelement Compounds RAS and in the Centre Régional de Mesures Physiques de l'Ouest (CRMPO) at the University of Rennes 1. Gas chromatography data were obtained using Shimadzu GC-2014 gas chromatograph equipped with Equity-5 capillary column. Compound **36** was synthesized by method that was described by L. Delaude *et al.*¹⁴⁸

3.2. Synthesis

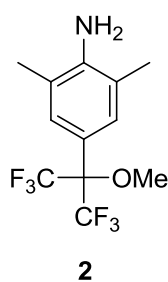
Synthesis of 2-(4-amino-3,5-dimethylphenyl)-1,1,1,3,3,3-hexafluoropropan-2-ol (1).



A mixture of 2,6-dimethylaniline (10.0 g, 82.6 mmol), hexafluoroacetone sesquihydrate (30 g, 153.8 mmol), and PTSA (200 mg, 1.1 mmol) was heated at 100 °C for 20 h. After cooling to r.t., water (50 mL) was added and a resulting mixture was extracted with EtOAc (3 × 30 mL). The combined organic layers were washed with H_2O and brine and then dried over MgSO_4 . The solvent was removed under reduced pressure, and the resulting solid was recrystallized from

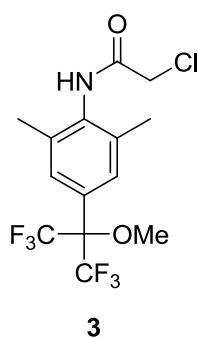
petroleum ether to give 22.7 g of the corresponding hexafluoroisopropoxyl aniline **1**. Yield: 95%. ^1H NMR (400 MHz, $\text{DMSO}-d_6$): δ 8.17 (s, 1H, OH), 7.10 (s, 2H, H_{Ar}), 4.90 (s, 2H, NH_2), 2.11 (s, 6H, Me); $^{13}\text{C}\{^1\text{H}\}$ NMR (101 MHz, $\text{DMSO}-d_6$): δ 145.9, 126.2, 123.4 (q, $^1J_{\text{C,F}} = 288$ Hz), 120.2, 116.8, 76.8 (hept, $^2J_{\text{C,F}} = 29$ Hz), 18.2; $^{19}\text{F}\{^1\text{H}\}$ NMR (376 MHz, $\text{DMSO}-d_6$): δ -74.20 (s). Elemental analysis calcd (%) for $\text{C}_{11}\text{H}_{11}\text{F}_6\text{NO}$: C, 46.00; H, 3.86; N, 4.88; found: C, 45.93; H, 3.95; N, 4.92.

Synthesis of 4-(1,1,1,3,3,3-hexafluoro-2-methoxypropan-2-yl)-2,6-dimethylaniline (2).



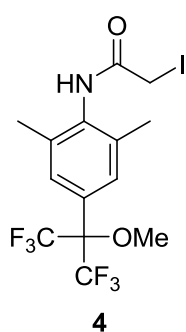
Aniline **1** (22.7 g, 79.2 mmol) was further treated with benzaldehyde (12.0 g, 113 mmol) in toluene (150 mL) in the presence of PTSA (0.7 g, 4 mmol) under refluxing in a Dean-Stark apparatus for 3 h. After cooling to r.t. and toluene removal, the residue was redissolved in acetonitrile (150 mL). Iodomethane (2.7 g, 98 mmol) and potassium carbonate (20.8 g, 151 mmol) were added to the solution, and the mixture was stirred at 70 °C for 5 h. Then, the cooled (r.t.) reaction mixture was treated with H₂O (100 mL) and extracted with EtOAc (3 × 100 mL). Organic layers were concentrated to the dryness under reduced pressure. 6 M HCl (300 mL) was added to the residue, and the mixture was stirred at r.t. for 3 h. The formed precipitate was separated by filtration, washed with petroleum ether, and treated with saturated solution of NaHCO₃ (200 mL) under stirring at r.t. for 1 h. The resulting solid was filtered off and dried to the constant weight to yield 17.2 g of **2** as a white solid. Yield: 72%. mp 84-85 °C. ¹H NMR (400 MHz, CDCl₃): δ 7.12 (s, 2H, *H*_{Ar}), 3.79 (s, 2H, NH₂), 3.47 (s, 3H, OMe), 2.22 (s, 6H, Me); ¹³C{¹H} NMR (101 MHz, CDCl₃): δ 144.6, 128.2, 122.9 (q, ¹J_{C,F} = 288 Hz), 121.5, 115.8, 83.1 (quint, ²J_{C,F} = 28 Hz), 54.0, 18.0; ¹⁹F{¹H} NMR (376 MHz, CDCl₃): δ -71.08 (s). Elemental analysis calcd (%) for C₁₂H₁₃F₆NO: C, 47.85; H, 4.35; N, 4.65; found: C, 47.79; H, 4.43; N, 4.58.

Synthesis of 2-chloro-N-[4-(1,1,1,3,3,3-hexafluoro-2-methoxypropan-2-yl)-2,6-dimethylphenyl]-acetamide (3).



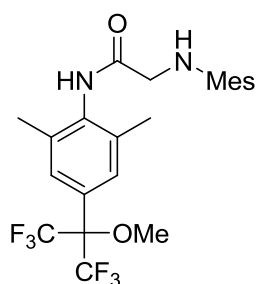
Chloroacetyl chloride (3.5 g, 31.0 mmol) was added dropwise to the solution of **2** (8.5 g, 28.2 mmol) and DMAP (4.48 g, 36.7 mmol) in 120 mL of anhydrous CH₂Cl₂ at 0 °C. The reaction mixture was stirred overnight at r.t. Then, the mixture was concentrated to 30 mL under reduced pressure, treated with 5% HCl (100 mL), and extracted with CH₂Cl₂ (3 × 50 mL). Combined organic layers were washed with saturated solution of NaHCO₃ (50 mL) and of water (50 mL) and dried over MgSO₄. After solvent removal under vacuum, the crude acetylated intermediate was purified by column chromatography in a gradient manner using EtOAc/petroleum ether (1:4-1:2-1:1-1:0) as the eluent to yield 8.9 g of the corresponding chloroacetamide **3** as a white solid. Yield: 84%. ¹H NMR (400 MHz, CDCl₃): δ 7.91 (s, 1H, NH), 7.30 (s, 1H, *H*_{Ar}), 4.26 (s, 2H, CH₂), 3.49 (s, 3H, OMe), 2.30 (s, 6H, Me); ¹⁹F{¹H} NMR (376 MHz, CDCl₃): δ -70.75 (s). Elemental analysis calcd (%) for C₁₄H₁₄ClF₆NO₂: C, 44.52; H, 3.74; N, 3.71; found C, 44.34; H, 3.89; N, 3.63.

Synthesis of N-[4-(1,1,1,3,3,3-hexafluoro-2-methoxypropan-2-yl)-2,6-dimethylphenyl]-2-iodoacetamide (4).



Compound **3** (11.1 g, 29.4 mmol) was further dissolved in acetone (190 mL), and then sodium iodide (11.0 g, 73.4 mmol) was added. The reaction mixture was stirred at r.t. for 24 h. After filtration, the mother liquor was concentrated, and the residue was dissolved in EtOAc (50 mL) and washed with a 5% solution of Na₂S₂O₃ (50 mL). The organic layer was separated, and the aqueous layer was extracted with EtOAc (3 × 30 mL). Combined organic layers were dried using CaCl₂, filtered, and concentrated. The crude product was recrystallized from petroleum ether to give 9.8 g of iodoacetamide **4** as a white solid. Yield: 71%. ¹H NMR (400 MHz, Acetone-*d*₆): δ 9.08 (s, 1H, NH), 7.33 (s, 2H, *H*_{Ar}), 3.98 (s, 2H, CH₂), 3.51 (s, 3H, OMe), 2.34 (s, 6H, Me); ¹³C{¹H} NMR (101 MHz, Acetone-*d*₆): δ 167.1, 137.6, 128.4, 126.4, 123.5 (q, ¹J_{C,F} = 290 Hz), 83.6 (q, ²J_{C,F} = 28 Hz), 54.9, 18.7, -0.8; ¹⁹F{¹H} NMR (376 MHz, Acetone-*d*₆): δ -71.40 (s). Elemental analysis calcd (%) for C₁₄H₁₄F₆INO₂: C, 35.84; H, 3.01; N, 2.99; found: C, 35.76; H, 3.13; N, 2.89.

Synthesis of N¹-[4-(1,1,1,3,3,3-hexafluoro-2-methoxypropan-2-yl)-2,6-dimethylphenyl]-N²-mesitylethane-1,2-diamine (5).

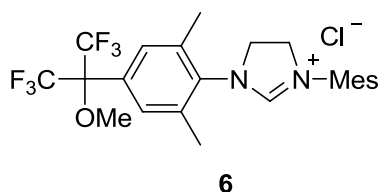


A mixture of **4** (9.8 g, 20.9 mmol) and mesitylamine (42.3 g, 313.3 mmol) was stirred at r.t. for 4 days. After reaction completion, the mixture was treated with a 10% solution of NaHCO₃ (100 mL) and extracted with EtOAc (3 × 60 mL). Combined organic layers were washed with brine and water and then dried over MgSO₄ and concentrated under reduced pressure. The excess of MesNH₂ was removed at 70 °C/0.05 mm Hg. The residual solid was recrystallized from petroleum ether to give 9.4 g of the corresponding adduct as a white solid. Yield: 94%. ¹H NMR (300 MHz, CD₃CN): δ 8.77 (s, 1H, NH), 7.34 (s, 2H, *H*_{Ar}), 6.85 (s, 2H, *H*_{Ar}), 3.80 (s, 1H, CH₂), 3.74 (br.s, 1H, NH), 3.49 (s, 3H, OMe), 2.32 (s, 6H, CH₃), 2.28 (s, 6H, CH₃), 2.21 (s, 3H, CH₃); ¹⁹F{¹H} NMR (282 MHz, CD₃CN): δ -70.86 (s).

This compound was further dissolved in anhydrous toluene (100 mL), and BH₃·SMe₂ (44.1 mL of 2 M solution in THF, 88.2 mmol) was added dropwise under an argon atmosphere at r.t. The resulting mixture was stirred at 90 °C for 3 h. After cooling to r.t., MeOH was slowly added until ceasing of gas evolution. Then, a 5% solution (300 mL) of HCl was added and resulting mixture was extracted with EtOAc (2 × 120 mL). The aqueous layer was separated, treated with NaHCO₃, and extracted with EtOAc (2 × 120 mL). Combined organic layers were washed with a saturated solution of NaHCO₃, dried over MgSO₄, and concentrated under reduced pressure. The crude product was purified by column chromatography using EtOAc/petroleum (1:6) ether as eluent to yield 8.5 g of **5** as a colorless oil.

Yield: 93% (88% for 2 steps) ^1H NMR (400 MHz, Acetone- d_6): δ 7.18 (s, 2H, H_{Ar}), 6.77 (s, 2H, H_{Ar}), 4.30 (br.s, 1H, NH), 3.52 (br.s, 1H, NH), 3.47 (s, 3H, OMe), 3.37 (t, $^3J_{\text{H,H}} = 5.9$ Hz, 2H, CH_2), 3.12 (t, $^3J_{\text{H,H}} = 6.0$ Hz, 2H, CH_2), 2.36 (s, 6H, $o\text{-CH}_3$), 2.21 (s, 6H, $o\text{-CH}_3$), 2.17 (s, 3H, $p\text{-CH}_3$); $^{13}\text{C}\{^1\text{H}\}$ NMR (101 MHz, Acetone- d_6): δ 149.6, 144.47, 131.8, 131.0, 130.1, 129.3, 129.2, 123.8 (q, $^1J_{\text{C,F}} = 290$ Hz), 119.0, 83.7 (q, $^2J_{\text{C,F}} = 28$ Hz), 54.5, 49.4, 48.8, 20.7, 19.5, 18.5; $^{19}\text{F}\{^1\text{H}\}$ NMR (376 MHz, Acetone- d_6): δ -71.55 (s). Elemental analysis calcd (%) for $\text{C}_{23}\text{H}_{28}\text{F}_6\text{N}_2\text{O}$: C, 59.73; H, 6.10; N, 6.06; found: C, 59.71; H, 6.12; N, 5.99.

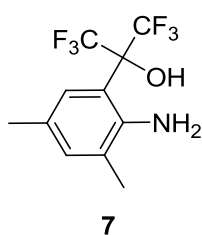
Synthesis of 1-[4-(1,1,1,3,3,3-hexafluoro-2-methoxypropan-2-yl)-2,6-dimethylphenyl]-3-mesityl-4,5-dihydro-1H-imidazol-3-ium chloride (6).



Concentrated HCl (10 mL, 120 mmol) was added to the solution of **5** (6 g, 13.0 mmol) in MeOH (100 mL) and stirred for 10 min. The solution was evaporated under reduced pressure. To the residual solid triethyl orthoformate (26.7 g, 180 mmol) was added, and the mixture was heated at 100 °C for 4 h. Then, the

excess of triethyl orthoformate was removed under vacuum and the resulting solid was washed with 100 mL of Et₂O. The recrystallization from EtOAc gave 4.31 g of pure **6** as a white solid. Yield: 65%. mp 190-194 °C. ^1H NMR (400 MHz, Acetone- d_6): δ 10.41 (s, 1H, NCHN), 7.48 (s, 2H, H_{Ar}), 7.00 (s, 2H, H_{Ar}), 4.86-4.69 (m, 4H, 2 CH_2), 3.53 (s, 3H, OMe), 2.64 (s, 6H, $o\text{-CH}_3$), 2.47 (s, 6H, $o\text{-CH}_3$), 2.28 (s, 3H, Mes $p\text{-CH}_3$); $^{13}\text{C}\{^1\text{H}\}$ NMR (101 MHz, Acetone- d_6): δ 162.0, 140.6, 138.6, 137.0, 136.7, 132.2, 130.4, 129.6, 129.4, 123.3 (q, $^1J_{\text{C,F}} = 290$ Hz), 83.6 (t, $^2J_{\text{C,F}} = 28$ Hz), 55.2, 52.6, 52.3, 21.0, 18.8, 18.2; $^{19}\text{F}\{^1\text{H}\}$ NMR (376 MHz, Acetone- d_6): δ -71.22 (s). Elemental analysis calcd (%) for $\text{C}_{24}\text{H}_{27}\text{ClF}_6\text{N}_2\text{O}$: C, 56.64; H, 5.35; N, 5.50; found: C, 56.54; H, 5.42; N, 5.48.

Synthesis of 2-(2-amino-3,5-dimethylphenyl)-1,1,1,3,3,3-hexafluoropropan-2-ol (7).

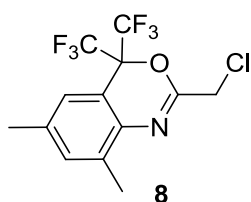


A mixture of 2,4-dimethylaniline (10.0 g, 82.6 mmol), hexafluoroacetone sesquihydrate (30 g, 153.8 mmol), and PTSA (200 mg, 1.1 mmol) was heated at 100 °C for 20 h. After cooling to r.t., water (50 mL) was added and the resulting mixture was extracted with EtOAc (3 × 30 mL). The combined organic layers were washed with H₂O and brine and then dried over MgSO₄.

The solvent was removed under reduced pressure, and the crude product was recrystallized from petroleum ether to give 21.9 g of **7** as a brown solid. Yield: 92%. mp 110-112 °C. ^1H NMR (400 MHz, CDCl₃): δ 7.26 (s, 1H, H_{Ar}), 7.12 (s, 1H, H_{Ar}), 5.58 (br.s, 3H, NH₂, OH), 2.32 (s, 3H, Me), 2.29 (s, 3H, Me); $^{13}\text{C}\{^1\text{H}\}$ NMR (101 MHz, CDCl₃): δ 137.2, 135.0, 134.3, 132.8, 127.1-127.0 (m), 123.6, 123.6 (q, $^1J_{\text{C,F}} = 289$ Hz), 80.3 (quint, $^2J_{\text{C,F}} = 30$ Hz), 21.2, 18.2; $^{19}\text{F}\{^1\text{H}\}$ NMR (376

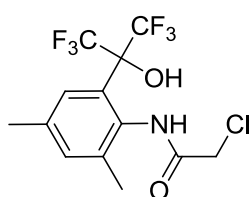
MHz, CDCl₃): δ -75.07 (s). Elemental analysis calcd (%) for C₁₁H₁₁F₆NO: C, 46.00; H, 3.86; N, 4.88; found: C, 46.05; H, 3.91; N, 4.76.

Synthesis of 2-(chloromethyl)-6,8-dimethyl-4,4-bis-(trifluoromethyl)-4H-benzo[d][1,3]oxazine (8). (isolated as intermediate in synthesis of 9).

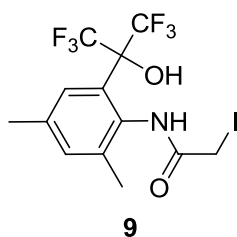


Chloroacetyl chloride (0.21 g, 1.9 mmol) was added dropwise to the solution of **7** (0.5 g, 1.7 mmol) and DMAP (0.21 g, 1.7 mmol) in 20 mL of anhydrous CH₂Cl₂ at 0 °C and stirred overnight at r.t. The reaction mixture was treated with 5% HCl (30 mL) and extracted with CH₂Cl₂ (2 \times 20 mL). Combined organic layers were washed with a solution of NaHCO₃ and water and dried over MgSO₄. The solvent was removed under reduced pressure, and the crude product was purified by column chromatography using EtOAc/petroleum ether (1:6) as the eluent to yield 250 mg of **8** as a colorless oil. Yield: 43%. ¹H NMR (300 MHz, CDCl₃): δ 7.18 (s, 1H, H_{Ar}), 7.10 (s, 1H, H_{Ar}), 4.23 (s, 2H, CH₂), 2.39 (s, 3H, Me), 2.35 (s, 3H, Me); ¹⁹F {¹H} NMR (282 MHz, CDCl₃): δ -75.86 (s). Elemental analysis calcd (%) for C₁₃H₁₀ClF₆NO: C, 45.17; H, 2.92; N, 4.05; found: C, 45.09; H, 2.99; N, 4.01.

Synthesis of N-[2-(1,1,1,3,3,3-hexafluoro-2-hydroxypropan-2-yl)-4,6-dimethylphenyl]-2-iodoacetamide (9).

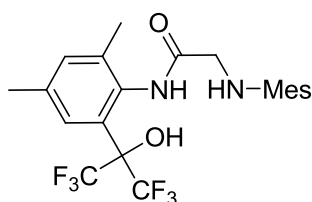


Chloroacetyl chloride (7.0 g, 62.6 mmol) was added dropwise to the solution of **7** (15 g, 52.2 mmol) and DMAP (6.4 g, 52.2 mmol) in 200 mL of anhydrous CH₂Cl₂ at 0 °C and stirred overnight at r.t. The reaction mixture was treated with 5% HCl (150 mL) and extracted with CH₂Cl₂ (3 \times 60 mL). Combined organic layers were washed with 60 mL of water and dried over MgSO₄. Then, solvents were evaporated under reduced pressure, the residue was dissolved in MeOH (300 mL), and concentrated HCl (15 mL) was added to the solution. The mixture was stirred overnight. Then, solvents were removed under reduced pressure and the residue was treated with a saturated solution of NaHCO₃ (500 mL) and extracted with EtOAc (2 \times 200 mL). Combined organic layers were washed with 200 mL of water, dried using MgSO₄, filtered, and concentrated under low pressure. The residual dark brown solid was recrystallized from petroleum ether to afford 17.7 g of the corresponding chloroacetamide as a light brown solid. Yield: 93%. ¹H NMR (300 MHz, CDCl₃): δ 8.80 (s, 1H, NH), 7.28 (s, 1H, H_{Ar}), 7.22 (s, 1H, H_{Ar}), 5.28 (br.s, 1H, OH), 4.06 (s, 2H, CH₂), 2.35 (s, 3H, CH₃), 2.21 (s, 3H, CH₃); ¹⁹F {¹H} NMR (282 MHz, CDCl₃): δ -73.82 (s).

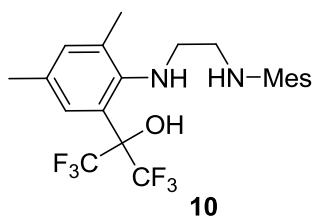


This compound was further dissolved in acetone (300 mL), and then sodium iodide (12.1 g, 80.7 mmol) was added. The reaction mixture was stirred at r.t. for 24 h. After filtration, the mother liquor was concentrated, and the residue was dissolved in EtOAc (50 mL) and washed with a 5% solution of Na₂S₂O₃ (50 mL). The organic layer was separated, and the aqueous layer was extracted with EtOAc (3 × 30 mL). Combined organic layers were dried over MgSO₄, filtered, and concentrated. The crude product was recrystallized from petroleum ether to give 12.5 g of **9** as a brown solid. Yield: 85% (79% for 3 steps). mp 143-145 °C. ¹H NMR (300 MHz, CDCl₃): δ 8.13 (s, 1H, NH), 7.26 (s, 1H, H_{Ar}), 7.20 (s, 1H, H_{Ar}), 5.04 (s, 1H, OH), 3.74 (s, 2H, CH₂), 2.35 (s, 3H, Me), 2.23 (s, 3H, Me); ¹³C{¹H} NMR (101 MHz, CDCl₃): δ 166.5, 138.7, 137.3, 134.6, 134.2, 131.9, 127.0-126.8 (m), 124.6, 121.5, 80.7-79.2 (m), 21.3, 18.8, -1.5; ¹⁹F{¹H} NMR (282 MHz, CDCl₃): δ -73.80 (s). Elemental analysis calcd (%) for C₁₃H₁₂F₆INO₂: C, 34.31; H, 2.66; N, 3.08; found: C, 34.26; H, 2.73; N, 2.98.

Synthesis of 1,1,1,3,3,3-hexafluoro-2-(2-([2-(mesitylamino)-ethyl]amino)-3,5-dimethylphenyl)propan-2-ol (10).



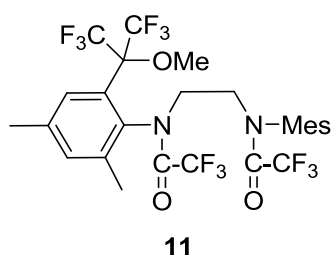
A mixture of **9** (12.5 g, 27.5 mmol) and mesitylamine (55.7 g, 412.0 mmol) was stirred at r.t. for 4 days. After reaction completion (TLC control), the mixture was treated with a 10% solution of NaHCO₃ (100 mL) and extracted with EtOAc (3 × 60 mL). Combined organic layers were washed with brine and water and then dried over MgSO₄ and concentrated under reduced pressure. The excess of MesNH₂ was removed at 70 °C/0.05 mmHg. The residual solid was recrystallized from petroleum ether to give 12.0 g of the corresponding adduct as a white solid. Yield: 94%. ¹H NMR (300 MHz, CDCl₃): δ 9.47 (br.s, 1H, NHCO), 7.77 (br.s, 1H, OH), 7.34 (s, 1H, H_{Ar}), 7.27 (s, 1H, H_{Ar}), 6.80 (s, 2H, H_{Ar}), 4.07 (br.s, 1H, NH), 3.75 (s, 2H, CH₂), 2.35 (s, 3H, CH₃), 2.28 (s, 6H, CH₃), 2.22 (s, 3H, CH₃), 2.18 (s, 3H, CH₃); ¹⁹F{¹H} NMR (282 MHz, CDCl₃): δ -73.31 (s).



This compound was further dissolved in anhydrous toluene (150 mL), and BH₃·SMe₂ (58.3 mL of 2 M solution in THF, 116.6 mmol) was added dropwise under an argon atmosphere at r.t. The resulting mixture was stirred at 90 °C for 3 h. After cooling to r.t., MeOH was slowly added until ceasing of gas evolution. Then, a 5% solution (300 mL) of HCl was added and resulting mixture was extracted with EtOAc (2 × 120 mL). The aqueous layer was separated, treated with NaHCO₃, and extracted with EtOAc (2 × 120 mL). Combined organic layers were washed with a saturated solution of NaHCO₃, dried over MgSO₄, and concentrated under reduced pressure. The crude product was recrystallized from petroleum ether

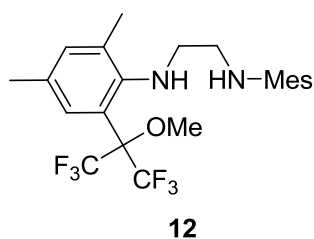
to give 9.3 g of **10** as a beige solid. Yield: 80% (75% for 2 steps). mp 148-150 °C. ¹H NMR (600 MHz, CDCl₃): δ 13.78 (s, 1H, NH), 7.34 (s, 1H, H_{Ar}), 7.16 (s, 1H, H_{Ar}), 6.87 (s, 2H, Mes H_{Ar}), 4.01 (s, 1H, NH), 3.26-3.22 (m, 2H, CH₂), 3.08-3.03 (m, 2H, CH₂), 2.35 (s, 3H, Me), 2.35 (s, 3H, Me), 2.31 (s, 6H, Mes *o*-CH₃), 2.25 (s, 3H, Me); ¹³C{¹H} NMR (151 MHz, CDCl₃): δ 142.3, 141.6, 136.4, 135.6, 133.7, 132.7, 130.6, 129.8, 127.5, 124.2, 123.5 (q, ¹J_{C,F} = 288 Hz), 80.5 (quint, ²J_{C,F} = 29 Hz), 51.0, 47.8, 21.3, 20.7, 18.5, 17.2; ¹⁹F{¹H} NMR (282 MHz, CDCl₃): δ -75.55 (s). Elemental analysis calcd (%) for C₂₂H₂₆F₆N₂O: C, 58.92; H, 5.84; N, 6.25; found: C, 58.85; H, 5.93; N, 6.20.

*Synthesis of 2,2,2-trifluoro-N-[2-(1,1,1,3,3,3-hexafluoro-2-methoxypropan-2-yl)-4,6-dimethylphenyl]-N-[2-(2,2,2-trifluoro-N-mesitylacamido)ethyl]acetamide (**11**).*



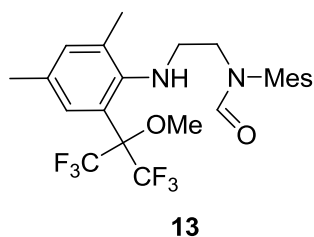
TFA (1.5 g, 13.4 mmol) and pyridine (1.1 g, 13.4 mmol) were added sequentially to the solution of **10** (3 g, 6.7 mmol) in CH₂Cl₂ (30 mL) at 0 °C. The reaction mixture was stirred at r.t. for 1 h, and then water (30 mL) was added to the mixture. The organic layer was separated; the aqueous layer was extracted with CH₂Cl₂ (2 × 20 mL). Combined organic layers were dried over MgSO₄, filtered, and concentrated under reduced pressure. The crude product was recrystallized from petroleum ether to yield 4.0 g (6.3 mmol, 94%) of the corresponding protected diamine as a white solid. This compound (2.0 g, 3.2 mmol) was dissolved in dry DMF (25 mL). MeI (1.3 g, 9.5 mmol) and anhydrous K₂CO₃ (1.74 g, 12.6 mmol) were added, and the resulting solution was heated overnight at 80 °C. Then, after cooling to r.t., 20 mL of water was added to the mixture. The crude product was extracted with EtOAc (3 × 15 mL). Combined organic layers were dried over MgSO₄, filtered, and concentrated under reduced pressure to afford 1.97 g of **11** as a white solid. Yield: 93%. mp 118-120 °C. ¹H NMR (400 MHz, CDCl₃): δ 7.30 (s, 1H, H_{Ar}), 7.27 (s, 1H, H_{Ar}), 6.93 (s, 2H, Mes H_{Ar}), 4.23 (td, *J*_{H,H} = 11.6, 3.7 Hz, 1H, CH₂), 4.13 (td, *J*_{H,H} = 11.8, 4.8 Hz, 1H, CH₂), 3.91 (td, *J*_{H,H} = 11.6, 4.8 Hz, 1H, CH₂), 3.75 (s, 3H, OMe), 3.32 (td, *J*_{H,H} = 11.9, 3.5 Hz, 1H, CH₂), 2.42 (s, 3H, Me), 2.36 (s, 3H, Me), 2.30 (s, 3H, Me), 2.17 (s, 6H, Mes *o*-CH₃); ¹³C{¹H} NMR (101 MHz, CDCl₃): δ 158.7 (q, ²J_{C,F} = 36 Hz), 158.3 (q, ²J_{C,F} = 36 Hz), 139.3, 139.0, 138.7, 136.6, 136.2, 135.8, 134.8, 134.5, 130.0, 129.7, 128.6, 126.4, 123.3 (q, ¹J_{C,F} = 293 Hz), 116.1 (q, ¹J_{C,F} = 288 Hz), 84.6-83.0 (m), 57.7, 51.1, 49.0, 21.4, 21.1, 19.6, 18.3, 18.1; ¹⁹F{¹H} NMR (376 MHz, CDCl₃): δ -67.42 – -67.57 (m, 3F), -68.04 (br.s, 3F), -69.72 – -69.88 (m, 3F), -70.75 (s, 3F). Elemental analysis calcd (%) for C₂₇H₂₆F₁₂N₂O₃: C, 49.55; H, 4.00; N, 4.28; found: C, 49.49; H, 4.13; N, 4.19.

Synthesis of N¹-[2-(1,1,1,3,3,3-hexafluoro-2-methoxypropan-2-yl)-4,6-dimethylphenyl]-N²-mesitylethane-1,2-diamine (12).



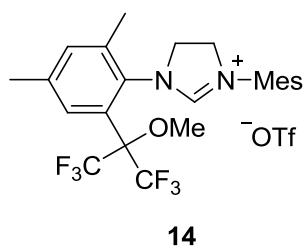
A mixture of **11** (1.97 g, 3.0 mmol), 18-crown-6 (5 mg, 0.02 mmol), and a solution of KOH (13 g, 230 mmol) in water (8 mL) was heated in DMSO (15 mL) at 130 °C for 1.5 h; then the reaction mixture was allowed to stir overnight at r.t. Water (30 mL) was added, and the crude product was extracted with EtOAc (3 × 20 mL). Combined organic layers were washed with 20 mL of water, dried over MgSO₄, and concentrated. The product was purified by column chromatography using EtOAc/petroleum ether (1:20) as eluent to yield 1.05 g of **12** as a yellowish oil. Yield: 75%. ¹H NMR (300 MHz, CDCl₃): δ 7.07 (s, 1H, H_{Ar}), 7.00 (s, 1H, H_{Ar}), 6.84 (s, 2H, Mes H_{Ar}), 5.21 (br.s, 1H, NH), 3.51 (s, 3H, OMe), 3.17 (s, 4H, 2CH₂), 2.32 (s, 3H, Me), 2.31 (s, 6H, Mes *o*-CH₃), 2.26 (s, 3H, Me), 2.24 (s, 3H, Me); ¹⁹F{¹H} NMR (282 MHz, CDCl₃): δ -69.35 (s). Elemental analysis calcd (%) for C₂₃H₂₈F₆N₂O: C, 59.73; H, 6.10; N, 6.06; found: C, 59.71; H, 6.19; N, 6.01.

Synthesis of N-(2-{[2-(1,1,1,3,3,3-hexafluoro-2-methoxypropan-2-yl)-4,6-dimethylphenyl]-amino}ethyl)-N-mesitylformamide (13).



Acetic formic anhydride (0.4 g, 4.54 mmol) was added dropwise to the solution of **12** (1.05 g, 2.27 mmol) in CH₂Cl₂ (20 mL). After homogenization, the reaction mixture was allowed to stir for 15 min at r.t. Then, 40 mL of water was added and the mixture was extracted with CH₂Cl₂ (2 × 30 mL). Combined organic layers were washed with a saturated solution of NaHCO₃ and water, dried over MgSO₄, filtered, and concentrated under reduced pressure. The crude product was purified by column chromatography using EtOAc/petroleum ether (1:4) as eluent to yield 1.03 g of **13** as a colorless oil. Yield: 92%. ¹H NMR (300 MHz, CDCl₃): δ 8.02 (s, 1H, CHO), 7.03 (s, 1H, H_{Ar}), 6.95 (s, 3H, H_{Ar}), 5.06 (s, 1H, NH), 3.80 (t, ³J_{H,H} = 7.4 Hz, 2H, CH₂), 3.43 (s, 3H, OMe), 3.13 (q, ³J_{H,H} = 7.2 Hz, 2H, CH₂), 2.30 (s, 3H, Me), 2.24 (s, 3H, Me), 2.22 (s, 9H, Me); ¹³C{¹H} NMR (101 MHz, CDCl₃): δ 163.9, 147.0, 138.3, 136.4, 135.8, 135.3, 135.2, 130.9, 129.7, 127.7, 123.9, 121.0, 85.6, 54.5, 46.7, 45.6, 29.7, 20.9, 20.6, 20.5, 18.3; ¹⁹F{¹H} NMR (282 MHz, CDCl₃): δ -69.40 (s). Elemental analysis calcd (%) for C₂₄H₂₈F₆N₂O₂: C, 58.77; H, 5.75; N, 5.71; found: C, 58.72; H, 5.81; N, 5.67.

Synthesis of 1-[2-(1,1,1,3,3,3-hexafluoro-2-methoxypropan-2-yl)-4,6-dimethylphenyl]-3-mesityl-4,5-dihydro-1H-imidazol-3-ium triflate (14).

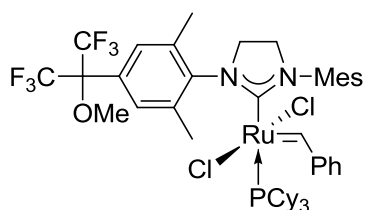


Triflic acid (0.2 g, 1.37 mmol) was added to the solution of **13** (0.67 g, 1.37 mmol) in toluene (30 mL), and the mixture was stirred at r.t. for 15 min. Then, triflic anhydride (0.29 g, 1.37 mmol) was added, and the reaction mixture was heated at 65 °C for 1.5 h. DIPEA (0.53 g, 4.11 mmol) was added, and the reaction mixture was heated at 80 °C for another 1.5 h. After cooling to r.t., solvents were removed under reduced pressure, water (30 mL) was added and the mixture was extracted with CH₂Cl₂ (3 × 20 mL). The combined organic layers were dried using MgSO₄, filtered, and concentrated under reduced pressure. The crude product was recrystallized from petroleum ether to give 0.84 g of **14** as a beige solid. Yield: 97%. ¹H NMR (400 MHz, CDCl₃): δ 8.43 (s, 1H, NCHN), 7.42 (s, 1H, H_{Ar}), 7.31 (s, 1H, H_{Ar}), 6.94 (s, 2H, Mes H_{Ar}), 4.54-4.24 (m, 4H, 2CH₂), 3.57 (s, 3H, OMe), 2.43 (s, 3H, Me), 2.40 (s, 3H, Me), 2.34 (s, 3H, Me), 2.28 (s, 3H, Me), 2.26 (s, 3H, Me); ¹³C{¹H} NMR (101 MHz, CDCl₃): δ 161.3, 141.4, 140.9, 139.0, 135.8, 135.2, 134.7, 130.5, 130.4-130.0 (m), 129.9, 124.2, 123.5, 122.1, 121.3, 120.6, 119.0, 83.5 (t, ²J_{C,F} = 30 Hz), 55.7, 53.0, 51.7, 21.5, 21.1, 18.7, 17.9, 17.4; ¹⁹F{¹H} NMR (376 MHz, CDCl₃): δ -67.22 (s, 3F), -70.97 (br.s, 3F), -78.87 (s, 3F). Elemental analysis calcd (%) for C₂₅H₂₇F₉N₂O₄S: C, 46.00; H, 3.86; N, 4.88; found: C, 45.97; H, 3.88; N, 4.86.

General procedure for synthesis of Grubbs-type catalysts 15a and 15b.

In a flame-dried Schlenk flask, imidazolium salt **6** or **14** (1.00 mmol) was mixed with 20 mL of anhydrous toluene. The resulting mixture was cooled to 0 °C and degassed three times, and then KHMDS (1.04 mL of 1 M solution in THF, 1.04 mmol) was added to the mixture under an argon atmosphere. The reaction mixture was stirred for 30 min at r.t.; then Grubbs' catalyst **G-I** (0.63 g, 0.82 mmol) was added and mixture was stirred for 2 h. During this time, the reaction mixture changed color from violet to red-brown. Once complete (TLC control), solvents were removed from the reaction mixture under reduced pressure, and the resulting substance was purified by column chromatography in a gradient manner using EtOAc/petroleum ether (1:8-1:3) as eluent under an argon atmosphere. The resulting solid was recrystallized from MeOH to yield **15** as a brown solid.

Benzylidene(dichloro){1-[4-(1,1,1,3,3,3-hexafluoro-2-methoxypropan-2-yl)-2,6-dimethylphenyl]-3-mesityl-4,5-dihydroimidazol-2-ylidene}(tricyclohexylphosphine)ruthenium(II) (15a).

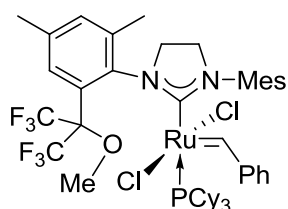


15a

Yield: 50%. Brown powder. ^1H NMR (400 MHz, C_6D_6): δ 19.79, 19.53 (s, 1H, *CHPh*), 8.35 (s, 1H, H_{Ar}), 7.61 (s, 1H, H_{Ar}), 7.05-6.71 (m, 6H, H_{Ar}), 6.23 (s, 1H), 3.33-1.04 (m, 54H); $^{13}\text{C}\{^1\text{H}\}$ NMR (101 MHz, C_6D_6): δ 296.7 (d, $^2J_{\text{C,P}} = 122$ Hz), 295.8 (d, $^2J_{\text{C,P}} = 134$ Hz) 221.5 (d, $^2J_{\text{C,P}} = 76$ Hz), 220.3 (d, $^2J_{\text{C,P}} = 79$ Hz),

153.2, 152.0, 142.5, 141.2, 140.2, 139.2, 138.9, 138.5, 137.7, 137.5, 137.1, 135.6, 130.4, 129.5, 128.8, 128.7, 128.6, 128.4, 127.5, 123.4 (q, $^1J_{\text{C,F}} = 290$ Hz), 123.0 (q, $^1J_{\text{C,F}} = 290$ Hz), 84.0-82.8 (m), 54.5, 54.3, 52.1, 51.6, 51.3, 33.0, 32.9, 32.1, 31.9, 29.6, 29.3, 28.3, 28.2, 27.9, 27.8, 26.7, 26.5, 21.2, 21.0, 20.8, 20.5, 19.4, 19.0; $^{19}\text{F}\{^1\text{H}\}$ NMR (376 MHz, C_6D_6): δ -70.24 (s); $^{31}\text{P}\{^1\text{H}\}$ NMR (162 MHz, C_6D_6): δ 28.00 (s), 23.07 (s). Elemental analysis calcd (%) for $\text{C}_{49}\text{H}_{65}\text{Cl}_2\text{F}_6\text{N}_2\text{OPRu}$: C, 57.98; H, 6.45; N, 2.76; found: C, 57.93; H, 6.49; N, 2.74.

Benzylidene(dichloro){1-(2-(1,1,1,3,3,3-hexafluoro-2-methoxypropan-2-yl)-4,6-dimethylphenyl)-3-mesityl-4,5-dihydroimidazol-2-ylidene}(tricyclohexylphosphine)ruthenium(II) (15b).



15b

Yield: 45%. Brown powder. ^1H NMR (600 MHz, C_6D_6): δ 20.19 (s, 1H, *CHPh*), 9.36 (s, 1H, H_{Ar}), 7.32 (s, 1H, H_{Ar}), 7.25 (s, 1H, H_{Ar}), 7.11 (t, $J_{\text{H,H}} = 7.2$ Hz, 1H, H_{Ar}), 7.06 (s, 1H, H_{Ar}), 6.97 (s, 1H, H_{Ar}), 6.94 (s, 1H, H_{Ar}), 6.82 (s, 1H, H_{Ar}), 5.94 (s, 1H, H_{Ar}), 4.04 (s, 3H, OMe), 3.91 (m, 1H, CH_2), 3.55 (dd, $J_{\text{H,H}} = 22.0, 10.3$ Hz, 1H, CH_2), 3.28 (m, 1H,

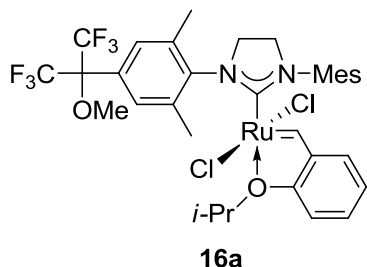
CH_2), 3.15 (dd, $J_{\text{H,H}} = 22.0, 10.3$ Hz, 1H, CH_2), 2.95 (s, 3H, Me), 2.68 (s, 3H, Me), 2.52 (q, $J_{\text{H,P}} = 11.7$ Hz, 3H, PCy_3), 2.28 (s, 3H, Me), 2.21 (s, 3H, Me), 1.67 (s, 3H, Me), 1.59 (m, 16H, PCy_3), 1.15 (m, 13H, PCy_3), 0.90 (q, $J_{\text{H,P}} = 12.4$ Hz, 3H, PCy_3); $^{13}\text{C}\{^1\text{H}\}$ NMR (151 MHz, C_6D_6): δ 294.4 (d, $^2J_{\text{C,P}} = 117$ Hz), 220.3 (d, $^2J_{\text{C,P}} = 79$ Hz), 152.5, 152.5, 141.8, 140.5, 138.6, 138.5, 138.4, 137.1, 135.9, 134.5, 132.2, 130.5, 130.4, 129.5, 128.8, 128.4, 128.1, 127.3, 125.2, 125.0, 123.2, 123.1, 84.4 (quint, $^2J_{\text{C,F}} = 26$ Hz), 57.3, 53.0, 52.05, 50.02, 31.8, 31.7, 29.8, 29.4, 28.3, 28.22, 28.15, 26.6, 21.2, 21.0, 20.9, 20.7, 20.4; $^{19}\text{F}\{^1\text{H}\}$ NMR (376 MHz, C_6D_6): δ -63.56 (s, 3F), -68.96 (s, 3F); $^{31}\text{P}\{^1\text{H}\}$ NMR (162 MHz, C_6D_6) δ 27.2 (s). Elemental analysis calcd (%) for $\text{C}_{49}\text{H}_{65}\text{Cl}_2\text{F}_6\text{N}_2\text{OPRu}$: C, 57.98; H, 6.45; N, 2.76; found: C, 58.04; H, 6.51; N, 2.67.

General procedure for synthesis of Hoveyda-type catalysts 16a and 16b.

In a flame-dried Schlenk flask, imidazolium salt **6** or **14** (0.98 mmol) was mixed with 35 mL of anhydrous toluene. The resulting mixture was cooled to 0 °C and degassed three times; then KHMDS (1.25 mL of 1 M solution in THF, 1.25 mmol) was added to the mixture under an argon atmosphere. The reaction mixture was stirred for 30 min at r.t.; then Hoveyda catalyst **HG-I** (0.49 g, 0.82 mmol) was added and mixture was stirred for 40 min at 80 °C. During this time, the reaction mixture changed color from brown to green. Once complete, solvents were removed from the reaction mixture under reduced pressure, and the resulting substance was purified by column

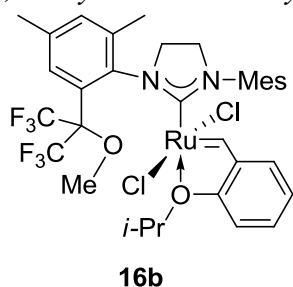
chromatography using EtOAc/petroleum ether (1:3) as eluent to yield Hoveyda-type catalyst as a green solid. Suitable for X-ray crystals of **16a** and **16b** were grown by slow diffusion of hexane vapors in CH₂Cl₂ solution.

Dichloro{1-[4-(1,1,1,3,3,3-hexafluoro-2-methoxypropan-2-yl)-2,6-dimethylphenyl]-3-mesityl-4,5-dihydroimidazol-2-ylidene}(2-isopropoxybenzylidene)ruthenium(II) (16a).



Yield: 46%. Dark-brown powder. ¹H NMR (600 MHz, C₆D₆): δ 16.61 (s, 1H, CH_{Ar}), 7.64 (s, 2H, H_{Ar}), 7.11 (d, *J*_{H,H} = 7.4 Hz, 1H, H_{Ar}), 7.08 (m, 1H, H_{Ar}), 6.87 (s, 2H, ArH), 6.64 (t, *J*_{H,H} = 7.4 Hz, 1H, H_{Ar}), 6.30 (d, *J*_{H,H} = 8.3 Hz, 1H, H_{Ar}), 4.46 (hept, ³*J*_{H,H} = 6.0 Hz, 1H, CHMe₂), 3.35 (m, 2H, 2CH₂), 3.28 (m, 5H, 2CH₂, OMe), 2.60 (s, 6H, Me), 2.43 (s, 6H, Me), 2.22 (s, 3H, *p*-CH₃), 1.28 (d, ³*J*_{H,H} = 6.1 Hz, 6H, CH(*sH*)₂); ¹³C{¹H} NMR (151 MHz, C₆D₆): δ 291.4, 213.2, 152.7, 145.7, 141.4, 138.8, 129.8, 129.3, 128.7, 128.4, 123.4 (q, ¹*J*_{C,F} = 290 Hz), 122.34, 122.27, 113.3, 83.5 (quint, ²*J*_{C,F} = 28 Hz), 75.2, 54.2, 21.4, 21.1; ¹⁹F{¹H} NMR (282 MHz, C₆D₆): δ -70.09 (s). Elemental analysis calcd (%) for C₃₄H₃₈Cl₂F₆N₂O₂Ru: C, 51.52; H, 4.83; N, 3.53; found: C, 51.49; H, 4.86; N, 3.53. CCDC 1030291 contains the supplementary crystallographic data for this compound.

Dichloro{1-[2-(1,1,1,3,3,3-hexafluoro-2-methoxypropan-2-yl)-4,6-dimethylphenyl]-3-mesityl-4,5-dihydroimidazol-2-ylidene}(2-isopropoxybenzylidene)ruthenium(II) (16b).



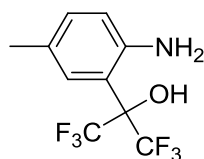
Yield: 46%. Dark-brown powder. ¹H NMR (400 MHz, C₆D₆): δ 16.68 (s, 1H, CH_{Ar}), 7.72 (s, 1H, H_{Ar}), 7.09 (m, 2H, H_{Ar}), 6.98 (d, *J*_{H,H} = 7.6 Hz, 2H, H_{Ar}), 6.74 (s, 1H, H_{Ar}), 6.66 (t, *J*_{H,H} = 7.3 Hz, 1H, H_{Ar}), 6.32 (d, *J*_{H,H} = 8.1 Hz, 1H, H_{Ar}), 4.46 (hept, ³*J*_{H,H} = 5.7 Hz, 1H, CHMe₂), 4.17 (m, 1H, 2CH₂), 3.78 (s, 3H, OMe), 3.46 (m, 3H, 2CH₂), 2.72 (s, 3H, Me), 2.64 (s, 3H, Me), 2.49 (s, 3H, Me), 2.26 (s, 3H, Me), 2.04 (s, 3H, Me), 1.29 (dd, *J*_{H,H} = 12.8, 5.9 Hz, 6H, CH(CH₃)₂); ¹³C{¹H} NMR (151 MHz, C₆D₆): δ 289.4, 215.3, 153.2, 145.4, 142.9, 140.8, 140.4, 139.7, 138.8, 138.4, 135.7, 134.8, 129.7, 129.6, 129.3, 123.8 (q, ¹*J*_{C,F} = 294 Hz), 123.5 (q, ¹*J*_{C,F} = 290 Hz), 122.2, 122.1, 113.5, 85.0 (quint, ²*J*_{C,F} = 28 Hz), 75.3, 58.2, 53.5, 51.1, 21.4, 21.31, 21.29, 21.25, 21.1, 21.0, 20.8; ¹⁹F{¹H} NMR (376 MHz, C₆D₆): δ -65.37 (s), -70.96 (s). Elemental analysis calcd (%) for C₃₄H₃₈Cl₂F₆N₂O₂Ru: C, 51.52; H, 4.83; N, 3.53; found: C, 51.48; H, 4.85; N, 3.49. CCDC 1030379 contains the supplementary crystallographic data for this compound.

General procedure for synthesis of 17.

A mixture of 6-methylaniline or 6-methoxyaniline (46.7 mmol), hexafluoroacetone sesquihydrate (18.6 g, 112.1 mmol), and PTSA (100 mg, 0.5 mmol) was heated at 100 °C for 20 h. After cooling to r.t., water (50 mL) was added and a resulting mixture was extracted with EtOAc (3 × 30 mL).

The combined organic layers were washed with H₂O and brine and then dried over MgSO₄. The solvent was removed under reduced pressure, and the resulting solid was recrystallized from petroleum ether to yield a dark solid.

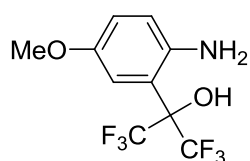
2-(2-Amino-5-methylphenyl)-1,1,1,3,3,3-hexafluoropropan-2-ol (17a).



17a

Yield: 94%. Brown solid. mp 110-113 °C; ¹H NMR (300 MHz, CDCl₃) δ 7.37 (s, 1H, H_{Ar}), 7.16 (d, ³J_{H,H} = 8.0 Hz, 1H, H_{Ar}), 6.97 (d, ³J_{H,H} = 8.0 Hz, 1H, H_{Ar}), 5.57 (br.s, 3H, NH₂, OH), 2.35 (s, 3H, Me); ¹³C{¹H} NMR (75 MHz, CDCl₃) δ 138.8, 135.3, 131.3, 129.1, 127.4, 123.5 (q, ¹J_{C,F} = 288 Hz), 123.0, 80.0 (p, ²J_{C,F} = 30 Hz), 21.2; ¹⁹F{¹H} NMR (282 MHz, CDCl₃) δ -75.14 (s). Elemental analysis calcd (%) for C₁₀H₉F₆NO: C, 43.97; H, 3.32; N, 5.13; found: C, 43.92; H, 3.38; N, 4.90.

1-(2-Amino-5-methoxyphenyl)-1,1,1,3,3,3-hexafluoropropan-2-ol (17b).



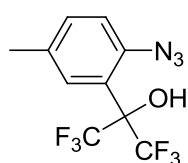
17b

Yield: 71%. Black solid. mp 104-107 °C; ¹H NMR (400 MHz, CDCl₃) δ 7.13 (s, 1H, H_{Ar}), 7.04 (d, ³J_{H,H} = 8.7 Hz, 1H, H_{Ar}), 6.90 (dd, J_{H,H} = 8.7, 2.7 Hz, 1H, H_{Ar}), 6.08 (br.s, 3H, NH₂, OH), 3.79 (s, 3H, OMe); ¹³C{¹H} NMR (101 MHz, CDCl₃) δ 157.3, 133.6, 129.4, 125.0, 123.4 (q, ¹J_{C,F} = 289 Hz), 115.8, 114.5-114.3 (m), 81.0-79.0 (m), 55.7; ¹⁹F{¹H} NMR (376 MHz, CDCl₃) δ -75.33 (s). Elemental analysis calcd (%) for C₁₀H₉F₆NO₂: C, 41.53; H, 3.14; N, 4.84; found: C, 41.57; H, 3.37; N, 4.65.

General procedure for synthesis of 18.

To a mixture of aniline **17** (20 mmol) in 60 mL of water concentrated sulfuric acid (10.7 mL, 200 mmol) was slowly added. The resulting mixture was cooled to 0 °C and solution of NaNO₂ (1.59 g, 23.0 mmol) in 6 mL of water was added dropwise and reaction mixture was stirred in an ice bath for 30 min. Then solution of NaN₃ (1.56 g, 24 mmol) in 6 mL of water was added dropwise. After full addition, the reaction mixture was allowed to stir at r.t. for 3 h. Then the reaction mixture was extracted with EtOAc (3 × 20 mL). Combined organic layer was washed with brine (20 mL), dried over MgSO₄ and concentrated under reduced pressure. The crude product was purified by flash chromatography using EtOAc/petroleum ether (1:3) as eluent to yield yellowish crystals.

2-(2-Azido-5-methylphenyl)-1,1,1,3,3,3-hexafluoropropan-2-ol (18a).

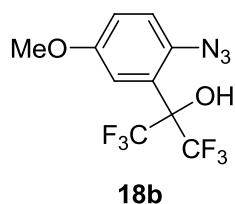


18a

Yield: 95%. mp 64-65 °C; ¹H NMR (400 MHz, CDCl₃) δ 7.44 (s, 1H, H_{Ar}), 7.33 (d, ³J_{H,H} = 8.2 Hz, 1H, H_{Ar}), 7.16 (d, ³J_{H,H} = 8.3 Hz, 1H, H_{Ar}), 7.04 (br.s, 1H, OH), 2.38 (s, 3H, Me); ¹³C{¹H} NMR (101 MHz, CDCl₃) δ 135.9, 135.4, 132.3, 130.3 (m), 122.7 (q, ¹J_{C,F} = 289 Hz), 119.8, 119.7, 79.9 (p, ²J_{C,F} = 30 Hz),

21.2; $^{19}\text{F}\{^1\text{H}\}$ NMR (376 MHz, CDCl_3) δ -74.88 (s). Elemental analysis calcd (%) for $\text{C}_{10}\text{H}_7\text{F}_6\text{N}_3\text{O}$: C, 40.15; H, 2.36; N, 14.05; found: C, 39.91; H, 2.39; N, 14.19.

2-(2-Azido-5-methoxyphenyl)-1,1,1,3,3,3-hexafluoropropan-2-ol (18b).

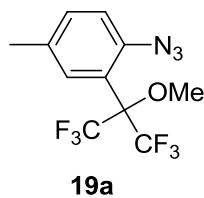


Yield: 88%. mp 67-68 °C; ^1H NMR (400 MHz, CDCl_3) δ 7.19 (d, $J = 8.8$ Hz, 1H, H_{Ar}), 7.19 (s, 1H, H_{Ar}), 7.07 (dd, $J = 8.9, 2.7$ Hz, 1H, H_{Ar}), 7.07 (br.s, 1H, OH), 3.82 (s, 3H, OMe); $^{13}\text{C}\{^1\text{H}\}$ NMR (101 MHz, CDCl_3) δ 157.1, 130.3, 122.7 (d, $^1J_{\text{C,F}} = 289$ Hz), 121.0, 120.8, 116.9, 115.8 (p, $^3J_{\text{C,F}} = 3$ Hz), 79.8 (p, $^2J_{\text{C,F}} = 30$ Hz), 55.8; $^{19}\text{F}\{^1\text{H}\}$ NMR (376 MHz, CDCl_3) δ -74.94 (s). Elemental analysis calcd (%) for $\text{C}_{10}\text{H}_7\text{F}_6\text{N}_3\text{O}_2$: C, 38.11; H, 2.24; N, 13.33; found: C, 37.79; H, 2.32; N, 13.45.

General procedure for synthesis of 19.

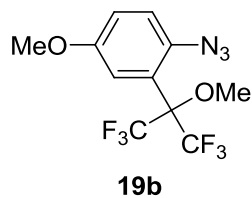
A mixture of azide **18** (17.6 mmol), iodomethane (2.2 mL, 35.3 mmol) and anhydrous K_2CO_3 (4.88 g, 35.3 mmol) in 80 mL of acetonitrile was stirred at r.t. for 2 days. After reaction completion, the solvent was evaporated under reduced pressure, residual solid was dispersed in EtOAc and filtered. The resulting filtrate was evaporated again and purified by flash chromatography using EtOAc/petroleum ether (1:8) as eluent to yield yellow oil that was crystallized after complete removal of solvent under high vacuum.

1-Azido-2-(1,1,1,3,3,3-hexafluoro-2-methoxypropan-2-yl)-4-methylbenzene (19a).



Yield: 96%. mp 51-52 °C; ^1H NMR (400 MHz, CDCl_3) δ 7.36 (s, 1H, H_{Ar}), 7.33 (d, $^3J_{\text{H,H}} = 8.3$ Hz, 1H, H_{Ar}), 7.21 (d, $^3J_{\text{H,H}} = 8.2$ Hz, 1H, H_{Ar}), 3.46 (s, 3H, OMe), 2.38 (s, 3H, Me); $^{13}\text{C}\{^1\text{H}\}$ NMR (101 MHz, CDCl_3) δ 137.2, 135.0, 132.6, 131.8, 122.6 (q, $^1J_{\text{C,F}} = 292$ Hz), 120.7, 118.2, 84.3 (p, $^2J_{\text{C,F}} = 29$ Hz), 54.6, 21.1; $^{19}\text{F}\{^1\text{H}\}$ NMR (376 MHz, CDCl_3) δ -69.86 (s). Elemental analysis calcd (%) for $\text{C}_{11}\text{H}_9\text{F}_6\text{N}_3\text{O}$: C, 42.18; H, 2.90; N, 13.42; found: C, 42.35; H, 3.11; N, 13.72.

1-Azido-2-(1,1,1,3,3,3-hexafluoro-2-methoxypropan-2-yl)-4-methoxybenzene (19b).



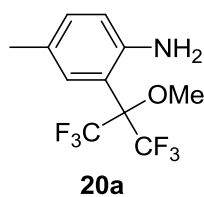
Yield: 91%. mp 52-53 °C; ^1H NMR (400 MHz, CDCl_3) δ 7.25 (d, $^3J_{\text{H,H}} = 8.8$ Hz, 1H, H_{Ar}), 7.13 (s, 1H, H_{Ar}), 7.07 (dd, $J = 8.8, 2.8$ Hz, 1H, H_{Ar}), 3.83 (s, 3H, OMe), 3.48 (s, 3H, OMe); $^{13}\text{C}\{^1\text{H}\}$ NMR (101 MHz, CDCl_3) δ 156.8, 132.2, 122.5 (q, $^1J_{\text{C,F}} = 291$ Hz), 122.0, 119.6, 117.5-117.3 (m), 117.1, 84.9-83.4 (m), 55.8, 54.7; $^{19}\text{F}\{^1\text{H}\}$ NMR (376 MHz, CDCl_3) δ -69.87 (s). Elemental analysis calcd (%) for $\text{C}_{11}\text{H}_9\text{F}_6\text{N}_3\text{O}_2$: C, 40.13; H, 2.76; N, 12.76; found: C, 40.41; H, 2.83; N, 12.97.

General procedure for synthesis of 20.

The azide **19** (13.8 mmol) was dissolved in 4.3 mL of methanol, then $\text{CoCl}_2 \cdot 6\text{H}_2\text{O}$ (290 mg, 1.4 mmol) and cetyltrimethylammonium bromide (CTABr) (426 mg, 1.4 mmol) were added with stirring at r.t. Then a solution of NaBH_4 (1.04 g, 27.6 mmol) in 26 mL of water was added

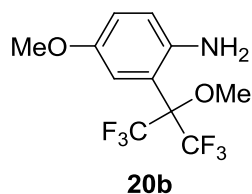
dropwise. After full addition, the reaction mixture was stirred another 30 min and extracted with Et₂O (3 × 15 mL). Combined organic layer was washed with 10 mL of water, filtered through cotton wool and evaporated under reduced pressure to yield yellow crystals.

2-(1,1,1,3,3,3-Hexafluoro-2-methoxypropan-2-yl)-4-methylaniline (20a)



Yield: 98%. mp 61-63 °C; ¹H NMR (400 MHz, CDCl₃) δ 7.09 (s, 1H, *H*_{Ar}), 7.06 (d, ³*J*_{H,H} = 8.3 Hz, 1H, *H*_{Ar}), 6.65 (d, ³*J*_{H,H} = 8.2 Hz, 1H, *H*_{Ar}), 4.56 (br.s, 2H, *NH*₂), 3.56 (s, 3H, OMe), 2.26 (s, 3H, Me); ¹³C{¹H} NMR (101 MHz, CDCl₃) δ 144.1, 132.1, 130.1 (p, ³*J*_{C,F} = 2.1 Hz), 127.5, 123.0 (q, ¹*J*_{C,F} = 292 Hz), 118.9, 109.4, 85.3 (p, ²*J*_{C,F} = 28 Hz), 54.8, 20.7; ¹⁹F{¹H} NMR (376 MHz, CDCl₃) δ -69.84 (s). Elemental analysis calcd (%) for C₁₁H₁₁F₆NO: C, 46.00; H, 3.86; N, 4.88; found: C, 45.92; H, 3.97; N, 5.03.

2-(1,1,1,3,3,3-Hexafluoro-2-methoxypropan-2-yl)-4-methoxyaniline (20b)

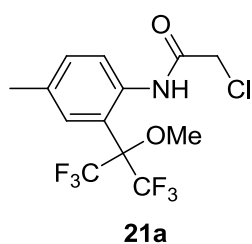


Yield: 92%. mp 51-53 °C; ¹H NMR (400 MHz, CDCl₃) δ 6.88 (s, 1H, *H*_{Ar}), 6.88 (d, ³*J*_{H,H} = 9.4 Hz, 1H, *H*_{Ar}), 6.69 (d, ³*J*_{H,H} = 9.4 Hz, 1H, *H*_{Ar}), 4.42 (br.s, 2H, *NH*₂), 3.75 (s, 3H, OMe), 3.57 (s, 3H, OMe); ¹³C{¹H} NMR (101 MHz, CDCl₃) δ 152.1, 140.4, 123.0 (q, ¹*J*_{C,F} = 292 Hz), 120.0, 118.0, 115.3-115.1 (m), 110.3, 85.9-84.3 (m), 55.9, 54.9; ¹⁹F{¹H} NMR (376 MHz, CDCl₃) δ -69.87 (s). Elemental analysis calcd (%) for C₁₁H₁₁F₆NO₂: C, 43.57; H, 3.66; N, 4.62; found: C, 43.89; H, 4.01; N, 4.64.

General procedure for synthesis of 21.

Aniline **20** (10.6 mmol) was added to 6 mL of glacial acetic acid in a round-bottomed flask followed by chloroacetyl chloride (870 μL, 10.9 mmol) and 10.4 mL of half-saturated aqueous sodium acetate. Precipitation of the amide was observed in 10 min. The product is stirred thoroughly with 10 mL of cold water and isolated by filtration. Solid product was dissolved in EtOAc and washed with saturated aqueous NaHCO₃ and brine, dried above MgSO₄. Then solvent was removed under reduced pressure, resulting solid residue was recrystallized in petroleum ether to yield a white solid.

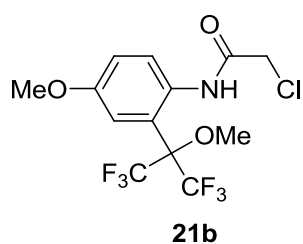
2-Chloro-N-[2-(1,1,1,3,3,3-hexafluoro-2-methoxypropan-2-yl)-4-methylphenyl]acetamide (21a)



Yield: 87%. mp 70-71 °C; ¹H NMR (400 MHz, CDCl₃) δ 9.78 (s, 1H, *NH*), 8.43 (d, *J*_{H,H} = 8.5 Hz, 1H, *H*_{Ar}), 7.32 (d, *J*_{H,H} = 8.6 Hz, 1H, *H*_{Ar}), 7.29 (s, 1H, *H*_{Ar}), 4.19 (s, 2H, *CH*₂), 3.54 (s, 3H, OMe), 2.37 (s, 3H, Me); ¹³C{¹H} NMR (101 MHz, CDCl₃) δ 164.0, 134.9, 134.8, 132.2, 130.2 (m), 123.21 (s), 122.5 (q, ¹*J*_{C,F} = 290 Hz), 114.8, 85.1 (p, ²*J*_{C,F} = 29 Hz), 54.7,

43.2, 21.2; $^{19}\text{F}\{^1\text{H}\}$ NMR (376 MHz, CDCl_3) δ -69.57 (s). Elemental analysis calcd (%) for $\text{C}_{13}\text{H}_{12}\text{ClF}_6\text{NO}_2$: C, 42.93; H, 3.33; N, 3.85; found: C, 43.11; H, 3.67; N, 4.12.

2-Chloro-N-[2-(1,1,1,3,3,3-hexafluoro-2-methoxypropan-2-yl)-4-methoxyphenyl]acetamide (21b).

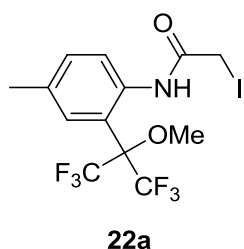


Yield: 99%. mp 101-102 °C; ^1H NMR (400 MHz, CDCl_3) δ 9.62 (s, 1H, NH), 8.41 (d, $J_{\text{H,H}} = 9.9$ Hz, 1H, H_{Ar}), 7.05 (d, $J_{\text{H,H}} = 9.9$ Hz, 1H, H_{Ar}), 7.06 (s, 1H, H_{Ar}), 4.19 (s, 2H, CH_2), 3.82 (s, 3H, OMe), 3.54 (s, 3H, OMe); $^{13}\text{C}\{^1\text{H}\}$ NMR (101 MHz, CDCl_3) δ 163.9, 156.4, 130.1, 125.0, 122.5 (q, $^1J_{\text{C,F}} = 289$ Hz), 116.7, 116.4-116.1 (m), 115.9, 84.9 (p, $^2J_{\text{C,F}} = 29$ Hz), 55.7, 54.8, 43.1; $^{19}\text{F}\{^1\text{H}\}$ NMR (376 MHz, CDCl_3) δ -69.63 (s). Elemental analysis calcd (%) for $\text{C}_{13}\text{H}_{12}\text{ClF}_6\text{NO}_3$: C, 41.12; H, 3.19; N, 3.69; found: C, 41.10; H, 3.22; N, 3.43.

General procedure for synthesis of 22.

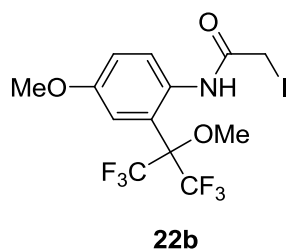
Chloroacetamide **21** (9.18 mmol) was dissolved in acetone (90 mL), and then sodium iodide (3.44 g, 23.0 mmol) was added. The reaction mixture was stirred at r.t. for 24 h. After filtration, the mother liquor was concentrated, and the residue was dissolved in EtOAc (20 mL) and washed with a 5% solution of $\text{Na}_2\text{S}_2\text{O}_3$ (10 mL). The organic layer was separated, and the aqueous layer was extracted with EtOAc (3 \times 10 mL). Combined organic layers were dried over MgSO_4 , filtered, and concentrated. The crude product was recrystallized from petroleum ether to yield a brown solid.

N-[2-(1,1,1,3,3,3-Hexafluoro-2-methoxypropan-2-yl)-4-methylphenyl]-2-iodoacetamide (22a).



Yield: 78%. mp 98-99 °C; ^1H NMR (400 MHz, CDCl_3) δ 9.04 (s, 1H, NH), 8.33 (d, $^3J_{\text{H,H}} = 8.5$ Hz, 1H, H_{Ar}), 7.31 (d, $^3J_{\text{H,H}} = 8.6$ Hz, 1H, H_{Ar}), 3.84 (s, 2H, CH_2), 3.58 (s, 3H, OMe), 2.36 (s, 3H, Me); $^{13}\text{C}\{^1\text{H}\}$ NMR (101 MHz, CDCl_3) δ 164.8, 135.2, 134.7, 132.2, 130.1, 123.4, 122.6 (q, $^1J_{\text{C,F}} = 292$ Hz), 114.6, 85.1 (p, $^2J_{\text{C,F}} = 29$ Hz), 54.9, 21.2, 0.1; $^{19}\text{F}\{^1\text{H}\}$ NMR (376 MHz, CDCl_3) δ -69.40 (s). Elemental analysis calcd (%) for $\text{C}_{13}\text{H}_{12}\text{F}_6\text{INO}_2$: C, 34.31; H, 2.66; N, 3.08; found: C, 34.03; H, 2.69; N, 2.78.

N-[2-(1,1,1,3,3,3-Hexafluoro-2-methoxypropan-2-yl)-4-methoxyphenyl]-2-iodoacetamide (22b).



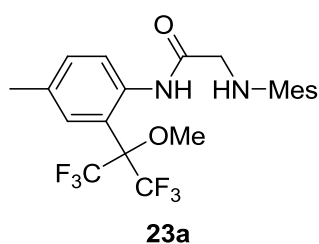
Yield: 91%. mp 87-88 °C; ^1H NMR (400 MHz, CDCl_3) δ 8.87 (s, 1H, NH), 8.31 (d, $^3J_{\text{H,H}} = 8.9$ Hz, 1H, H_{Ar}), 7.04 (d, $J = 9.1$ Hz, 1H, H_{Ar}), 7.03 (s, 1H, H_{Ar}), 3.84 (s, 2H, CH_2), 3.81 (s, 3H, OMe), 3.57 (s, 3H, OMe); $^{13}\text{C}\{^1\text{H}\}$ NMR (101 MHz, CDCl_3) δ 164.7, 156.3, 130.5, 125.3, 122.5 (q, $^1J_{\text{C,F}} = 290$ Hz), 116.6, 116.2, 115.9, 84.9 (p, $^2J_{\text{C,F}} = 29$ Hz),

55.7, 54.9, 0.1; $^{19}\text{F}\{^1\text{H}\}$ NMR (376 MHz, CDCl_3) δ -69.46 (s). Elemental analysis calcd (%) for $\text{C}_{13}\text{H}_{12}\text{F}_6\text{INO}_3$: C, 33.14; H, 2.57; N, 2.97; found: C, 33.10; H, 2.72; N, 3.18.

General procedure for synthesis of 23.

A mixture of **22** (4.4 mmol) and mesitylamine (9.3 mL, 65.9 mmol) was stirred at r.t. for 4 days. After reaction completion, the mixture was treated with a 10% solution of NaHCO_3 (60 mL) and extracted with EtOAc (3×30 mL). Combined organic layers were washed with brine and water and then dried over MgSO_4 and concentrated under reduced pressure. The excess of MesNH_2 was removed at $70^\circ\text{C}/0.05$ mmHg. The residual solid was recrystallized from petroleum ether to yield the corresponding aminoacetamide **7** as a white solid.

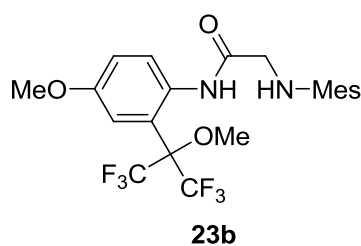
N-[2-(1,1,1,3,3,3-Hexafluoro-2-methoxypropan-2-yl)-4-methylphenyl]-2-(mesitylamino)-acetamide (**23a**).



Yield: 85%. mp $160\text{--}161^\circ\text{C}$; ^1H NMR (400 MHz, Acetone- d_6) δ 10.12 (s, 1H, NHCO), 8.58 (d, $J_{\text{H,H}} = 8.6$ Hz, 1H, H_{Ar}), 7.40 (d, $J_{\text{H,H}} = 8.6$ Hz, 1H, H_{Ar}), 7.33 (s, 1H, H_{Ar}), 6.82 (s, 2H, H_{Ar}), 4.25 (t, $^3J_{\text{H,H}} = 8.0$ Hz, 1H, NHCH_2), 3.74 (d, $^3J_{\text{H,H}} = 8.1$ Hz, 2H, CH_2), 3.59 (s, 3H, OMe), 2.38 (s, 3H, Me), 2.30 (s, 6H, Me), 2.19 (s, 3H, Me); $^{13}\text{C}\{^1\text{H}\}$

NMR (101 MHz, Acetone- d_6) δ 170.3, 143.6, 137.0, 134.5, 132.8, 132.5, 130.5, 130.4, 124.3, 123.6 (d, $^1J_{\text{C,F}} = 291$ Hz), 114.9, 85.9 (p, $^2J_{\text{C,F}} = 28$ Hz), 55.4, 53.8, 20.9, 20.6, 18.4; $^{19}\text{F}\{^1\text{H}\}$ NMR (376 MHz, Acetone- d_6) δ -69.99 (s). Elemental analysis calcd (%) for $\text{C}_{22}\text{H}_{24}\text{F}_6\text{N}_2\text{O}_2$: C, 57.14; H, 5.23; N, 6.06; found: C, 57.17; H, 5.23; N, 5.71.

N-[2-(1,1,1,3,3,3-Hexafluoro-2-methoxypropan-2-yl)-4-methoxyphenyl]-2-(mesitylamino)-acetamide (**23b**).



Yield: 91%. mp $137\text{--}138^\circ\text{C}$; ^1H NMR (400 MHz, Acetone- d_6) δ 9.93 (s, 1H, NHCO), 8.53 (d, $^3J_{\text{H,H}} = 9.2$ Hz, 1H, H_{Ar}), 7.21 (dd, $J = 9.2, 2.8$ Hz, 1H, H_{Ar}), 7.02 (s, 1H, H_{Ar}), 6.82 (s, 2H, H_{Ar}), 4.24 (t, $^3J_{\text{H,H}} = 7.8$ Hz, 1H, NHCH_2), 3.85 (s, 3H, OMe), 3.73 (d, $^3J_{\text{H,H}} = 7.9$ Hz, 2H, CH_2), 3.59 (s, 3H, OMe), 2.30 (s, 6H, Me), 2.19 (s,

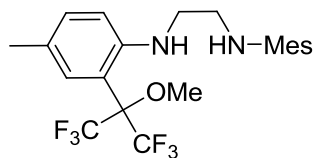
3H, Me); $^{13}\text{C}\{^1\text{H}\}$ NMR (101 MHz, Acetone- d_6) δ 170.1, 156.7, 143.7, 132.5, 132.2, 130.5, 130.4, 126.5, 123.5 (q, $^1J_{\text{C,F}} = 292$ Hz), 116.8, 116.7, 116.3, 86.5-85.0 (m), 56.0, 55.5, 53.7, 20.6, 18.4; $^{19}\text{F}\{^1\text{H}\}$ NMR (376 MHz, Acetone- d_6) δ -70.06 (s). Elemental analysis calcd (%) for $\text{C}_{22}\text{H}_{24}\text{F}_6\text{N}_2\text{O}_3$: C, 55.23; H, 5.06; N, 5.86; found: C, 55.42; H, 5.03; N, 5.96.

General procedure for synthesis of 24.

Aminoacetamide **23** (3.46 mmol) was dissolved in anhydrous toluene (30 mL), and $\text{BH}_3\cdot\text{SMe}_2$ (15.6 mL of 1 M solution in THF, 15.6 mmol) was added dropwise under an argon atmosphere at r.t. The resulting mixture was stirred at 90°C for 3 h. After cooling to r.t., MeOH was slowly

added until ceasing of gas evolution. Then, a 10% solution (60 mL) of HCl was added and resulting mixture was extracted with EtOAc (2 × 20 mL). The aqueous layer was separated, treated with NaHCO₃, and extracted with EtOAc (2 × 20 mL). Combined organic layers were washed with a saturated solution of NaHCO₃, dried over MgSO₄, and concentrated under reduced pressure. The crude product was recrystallized from petroleum ether to yield a beige solid.

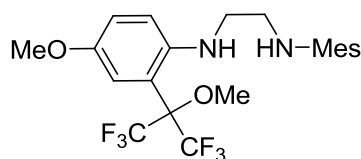
*N*¹-[2-(1,1,1,3,3,3-Hexafluoro-2-methoxypropan-2-yl)-4-methylphenyl]-*N*²-mesitylethane-1,2-diamine (**24a**).



24a

Yield: 90%; mp 53-54 °C; ¹H NMR (400 MHz, CDCl₃) δ 7.13 (d, ³J_{H,H} = 8.9 Hz, 1H, H_{Ar}), 7.11 (s, 1H, H_{Ar}), 6.86 (s, 2H, H_{Ar}), 6.72 (d, ³J_{H,H} = 8.4 Hz, 1H, H_{Ar}), 5.70 (br.s, 1H, NH), 3.54 (s, 3H, OMe), 3.46-3.39 (m, 2H, CH₂), 3.20 (t, ³J_{H,H} = 5.9 Hz, 2H, CH₂), 2.30 (s, 6H, Me), 2.27 (s, 3H, Me), 2.25 (s, 3H, Me); ¹³C {¹H} NMR (101 MHz, CDCl₃) δ 146.2, 132.2, 130.8, 130.7, 129.7, 125.6, 123.0 (q, ¹J_{C,F} = 293 Hz), 112.8, 108.7, 85.7 (p, ¹J_{C,F} = 28 Hz), 54.6, 48.1, 44.7, 20.7, 20.6, 18.2; ¹⁹F {¹H} NMR (376 MHz, CDCl₃) δ -69.46 (s). Elemental analysis calcd (%) for C₂₂H₂₆F₆N₂O: C, 58.92; H, 5.84; N, 6.25; found: C, 58.81; H, 5.87; N, 5.96.

*N*¹-[2-(1,1,1,3,3,3-Hexafluoro-2-methoxypropan-2-yl)-4-methoxyphenyl]-*N*²-mesitylethane-1,2-diamine (**24b**).



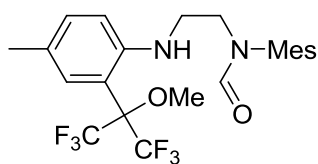
24b

Yield: 72%; mp 56-57 °C; ¹H NMR (400 MHz, CDCl₃) δ 6.97 (d, ³J_{H,H} = 8.9 Hz, 1H, H_{Ar}), 6.95 (s, 1H, H_{Ar}), 6.86 (s, 2H, H_{Ar}), 6.76 (d, ³J_{H,H} = 8.8 Hz, 1H, H_{Ar}), 5.54 (s, 1H, NH), 3.77 (s, 3H, OMe), 3.56 (s, 3H, OMe), 3.37 (dd, ³J_{H,H} = 10.9, 5.3 Hz, 2H, CH₂), 3.19 (t, ³J_{H,H} = 5.8 Hz, 2H, CH₂), 2.93 (br.s, 1H, NH), 2.29 (s, 6H, Me), 2.26 (s, 3H, Me); ¹³C {¹H} NMR (101 MHz, CDCl₃) δ 150.8, 143.1, 142.9, 132.3, 130.7, 129.7, 122.9 (q, ¹J_{C,F} = 292 Hz), 117.5, 116.5, 113.9, 109.6, 85.6 (p, ²J_{C,F} = 28 Hz), 56.0, 54.8, 48.1, 45.5, 20.7, 18.2; ¹⁹F {¹H} NMR (376 MHz, CDCl₃) δ -69.50 (s). Elemental analysis calcd (%) for C₂₂H₂₆F₆N₂O₂: C, 56.89; H, 5.64; N, 6.03; found: C, 57.08; H, 5.65; N, 6.15.

General procedure for synthesis of **25**.

Acetic formic anhydride (360 μL, 4.13 mmol) was added dropwise to the solution of **24** (2.06 mmol) in CH₂Cl₂ (13 mL). After homogenization, the reaction mixture was allowed to stir for 15 min at r.t. Then, 40 mL of water was added and the mixture was extracted with CH₂Cl₂ (2 × 30 mL). Combined organic layers were washed with a saturated solution of NaHCO₃ and water, dried over MgSO₄, filtered, and concentrated under reduced pressure. The crude product was purified by column chromatography using EtOAc/petroleum ether (1:4) as eluent to yield white solid.

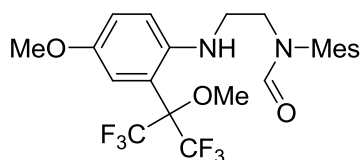
N-(2-([2-(1,1,1,3,3,3-Hexafluoro-2-methoxypropan-2-yl)-4-methylphenyl]amino)ethyl)-*N*-mesitylformamide (**25a**).



25a

Yield: 98%. mp 101-102 °C; mixture of two rotamers 85:15, signals of major product are given: ¹H NMR (400 MHz, CDCl₃) δ 8.06 (s, 1H, CHO), 7.13 (d, *J*_{H,H} = 8.5 Hz, 1H, *H*_{Ar}), 7.10 (s, 1H, *H*_{Ar}), 6.97 (s, 2H, *H*_{Ar}), 6.75 (d, *J*_{H,H} = 8.5 Hz, 1H, *H*_{Ar}), 5.80 (br.s, 1H, NH), 3.81 (t, ³*J*_{H,H} = 7.0 Hz, 2H, CH₂), 3.52 (s, 3H, OMe), 3.37 (t, ³*J*_{H,H} = 7.0 Hz, 2H, CH₂), 2.32 (s, 3H, Me), 2.25 (s, 3H, Me), 2.21 (s, 6H, Me); ¹³C{¹H} NMR (75 MHz, CDCl₃) δ 164.2, 145.3, 138.7, 136.6, 136.0, 132.4, 130.6, 129.9, 126.2, 123.0 (q, ¹*J*_{C,F} = 292 Hz), 113.1, 109.3, 86.5-84.7 (m), 54.7, 45.7, 42.6, 21.0, 20.6, 18.3; ¹⁹F{¹H} NMR (376 MHz, CDCl₃) δ -69.55 (s). Elemental analysis calcd (%) for C₂₃H₂₆F₆N₂O₂: C, 57.98; H, 5.50; N, 5.88; found: C, 57.69; H, 5.63; N, 6.04.

N-(2-([2-(1,1,1,3,3,3-Hexafluoro-2-methoxypropan-2-yl)-4-methoxyphenyl]amino)ethyl)-*N*-mesitylformamide (**25b**).



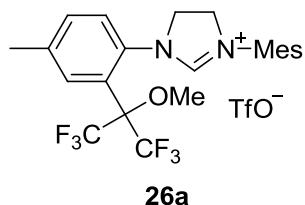
25b

Yield: 99%. mp 115-116 °C; mixture of two rotamers 90:10, signals of major product are given: ¹H NMR (400 MHz, CDCl₃) δ 8.06 (s, 1H, CHO), 6.97 (s, 2H, *H*_{Ar}), 6.95 (d, *J*_{H,H} = 9.2 Hz, 1H, *H*_{Ar}), 6.91 (s, 1H, *H*_{Ar}), 6.81 (d, *J*_{H,H} = 9.0 Hz, 1H, *H*_{Ar}), 5.84 (br.s, 1H, NH), 3.80 (t, ³*J*_{H,H} = 7.0 Hz, 2H, CH₂), 3.74 (s, 3H, OMe), 3.52 (s, 3H, OMe), 3.36 (t, ³*J*_{H,H} = 7.0 Hz, 2H, CH₂), 2.31 (s, 3H, Me), 2.21 (s, 6H, Me); ¹³C{¹H} NMR (75 MHz, CDCl₃) δ 164.2, 151.2, 141.8, 138.7, 136.6, 136.0, 129.9, 122.9 (q, ¹*J*_{C,F} = 293 Hz), 117.6, 116.6, 114.3, 110.2, 85.5 (p, ²*J*_{C,F} = 28 Hz), 56.0, 54.8, 45.8, 43.0, 21.0, 18.3; ¹⁹F{¹H} NMR (376 MHz, CDCl₃) δ -69.61 (s). Elemental analysis calcd (%) for C₂₃H₂₆F₆N₂O₃: C, 56.10; H, 5.32; N, 5.69; found: C, 56.11; H, 5.55; N, 5.91.

General procedure for synthesis of 26.

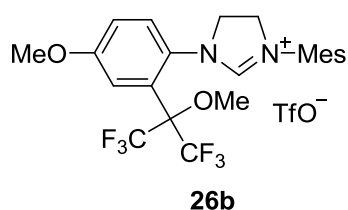
Triflic acid (180 μL, 2.0 mmol) was added to the solution of **25** (2.0 mmol) in toluene (50 mL), and the mixture was stirred at r.t. for 15 min. Then, triflic anhydride (340 μL, 2.0 mmol) was added, and the reaction mixture was heated at 65 °C for 1.5 h. DIPEA (1.04 mL, 6.0 mmol) was added, and the reaction mixture was heated at 80 °C for another 1.5 h. After cooling to r.t., 50 mL of water was added and the mixture was extracted with CH₂Cl₂ (3 × 30 mL). The combined organic layers were dried using MgSO₄, filtered, and concentrated under reduced pressure. The crude product was recrystallized from petroleum ether to yield a beige solid.

1-[2-(1,1,1,3,3,3-Hexafluoro-2-methoxypropan-2-yl)-4-methylphenyl]-3-mesityl-4,5-dihydro-1*H*-imidazol-3-ium triflate (**26a**).



Yield: 85%. mp 167-169 °C; ^1H NMR (400 MHz, CDCl_3) δ 8.08 (s, 1H, NCHN), 7.74 (d, $J_{\text{H,H}}=8.1$ Hz, 1H, H_{Ar}), 7.53 (s, 1H, H_{Ar}), 7.46 (d, $J_{\text{H,H}}=8.0$ Hz, 1H, H_{Ar}), 6.95 (s, 2H, H_{Ar}), 4.64 (t, $^3J_{\text{H,H}}=10.6$ Hz, 2H, CH_2), 4.40 (t, $^3J_{\text{H,H}}=10.6$ Hz, 2H, CH_2), 3.61 (s, 3H, Me), 2.44 (s, 3H, Me), 2.34 (s, 6H, Me), 2.29 (s, 3H, Me); $^{13}\text{C}\{^1\text{H}\}$ NMR (101 MHz, CDCl_3) δ 159.7, 141.9, 141.0, 135.1, 133.9, 132.3, 132.0, 131.6, 130.2, 130.1, 125.0, 122.3 (q, $^1J_{\text{C,F}}=290$ Hz), 120.7 (q, $^1J_{\text{C,F}}=320$ Hz), 84.2-82.8 (m), 55.7, 55.1, 51.8, 21.6, 21.1, 17.7; $^{19}\text{F}\{^1\text{H}\}$ NMR (376 MHz, CDCl_3) δ -69.24 (s, 6F), -78.59 (s, 3F). Elemental analysis calcd (%) for $\text{C}_{24}\text{H}_{25}\text{F}_9\text{N}_2\text{O}_4\text{S}$: C, 47.37; H, 4.14; N, 4.60; found: C, 47.61; H, 4.14; N, 4.58.

1-[2-(1,1,1,3,3,3-Hexafluoro-2-methoxypropan-2-yl)-4-methoxyphenyl]-3-mesityl-4,5-dihydro-1H-imidazol-3-ium triflate (26b).

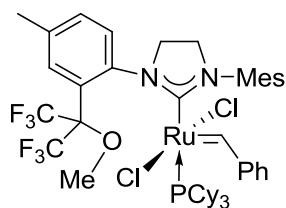


Yield: 83%. mp 171-173 °C; ^1H NMR (400 MHz, CDCl_3) δ 8.04 (s, 1H, NCHN), 7.85 (d, $J_{\text{H,H}}=8.7$ Hz, 1H, H_{Ar}), 7.25 (s, 1H, H_{Ar}), 7.15 (dd, $J_{\text{H,H}}=8.7, 2.6$ Hz, 1H, H_{Ar}), 6.95 (s, 2H, H_{Ar}), 4.61 (t, $^3J_{\text{H,H}}=10.5$ Hz, 2H, CH_2), 4.39 (t, $^3J_{\text{H,H}}=10.4$ Hz, 2H, CH_2), 3.84 (s, 3H, OMe), 3.61 (s, 3H, OMe), 2.34 (s, 6H, Me), 2.29 (s, 3H, Me); $^{13}\text{C}\{^1\text{H}\}$ NMR (101 MHz, CDCl_3) δ 161.0, 159.9, 141.0, 135.1, 133.9, 130.2, 130.1, 126.9, 126.7, 122.3 (q, $^1J_{\text{C,F}}=291$ Hz), 120.7 (q, $^1J_{\text{C,F}}=320$ Hz), 118.3, 116.8, 84.2-82.6 (m), 56.0, 55.8, 55.1, 51.8, 21.1, 17.7; $^{19}\text{F}\{^1\text{H}\}$ NMR (376 MHz, CDCl_3) δ -69.27 (s, 6F), -78.55 (s, 3F). Elemental analysis calcd (%) for $\text{C}_{24}\text{H}_{25}\text{F}_9\text{N}_2\text{O}_5\text{S}$: C, 46.16; H, 4.03; N, 4.49; found: C, 46.21; H, 4.06; N, 4.51.

General procedure for synthesis of Grubbs-type catalysts 27.

In a flame-dried Schlenk flask, imidazolium salt **26** (0.49 mmol) was mixed with 20 mL of anhydrous toluene. The resulting mixture was cooled to 0 °C and degassed three times, and then KHMDS (1 mL of 0.5 M solution in toluene, 0.50 mmol) was added to the mixture under an argon atmosphere. The reaction mixture was stirred for 30 min at r.t.; then Grubbs catalyst **G-I** (0.33 g, 0.40 mmol) was added and mixture was stirred for 2 h. During this time, the reaction mixture changed color from violet to red-brown. Once complete (TLC control), solvents were removed from the reaction mixture under reduced pressure, and the resulting substance was purified by column chromatography in a gradient manner using EtOAc/petroleum ether (1:8-1:3) as eluent under an argon atmosphere. The resulting solid was recrystallized from MeOH to yield **27** as a brown solid.

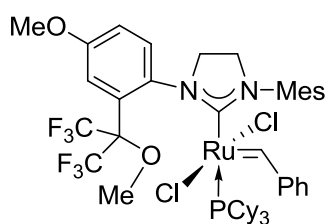
Benzylidene(dichloro){1-[2-(1,1,1,3,3,3-hexafluoro-2-methoxypropan-2-yl)-4-methylphenyl]-3-mesityl-4,5-dihydroimidazol-2-ylidene}(tricyclohexylphosphine)ruthenium(II) (27a).



27a

Yield: 46%. Mixture of two rotamers 4:1 at 60 °C, signals of major product are given: ^1H NMR (400 MHz, Toluene- d_8 , 60 °C) δ 19.62 (s, 1H, CHAr), 9.47 (d, $J_{\text{H,H}} = 7.9$ Hz, 1H, H_{Ar}), 8.25 (s, 1H, H_{Ar}), 7.74 (s, 1H, H_{Ar}), 7.35 (d, $J_{\text{H,H}} = 7.5$ Hz, 1H, H_{Ar}), 7.20-7.10 (m, 2H, H_{Ar}), 6.94-6.72 (m, 2H, H_{Ar}), 6.34 (br.s, 1H, H_{Ar}), 6.01 (m, 1H, H_{Ar}), 4.43 (s, 1H, CH_2), 4.12 (s, 3H, OMe), 3.78 (s, 1H, CH_2), 3.39 (s, 1H, CH_2), 3.24 (s, 1H, CH_2), 2.48 (s, Me), 2.74-0.92 (m, 42H, PCy_3 , Me); $^{13}\text{C}\{^1\text{H}\}$ NMR (126 MHz, Toluene- d_8 , 60 °C) δ 298.2, 223.4, 152.4, 139.6, 142.2, 138.9, 138.7, 137.0, 136.7, 135.4, 131.9 (br.s), 130.6, 130.4, 129.7, 129.5, 128.3, 123.6 (q, $^1J_{\text{C,F}} = 289$ Hz), 123.4 (q, $^1J_{\text{C,F}} = 290$ Hz), 117.6, 117.3, 85.6-84.1 (m), 58.5, 54.9, 52.2, 29.8, 29.5, 29.4, 28.1-28.0 (m), 26.8, 21.0, 19.3, 19.0; $^{19}\text{F}\{^1\text{H}\}$ NMR (376 MHz, Toluene- d_8 , 60 °C) δ -65.29 (br.s, 3F), -71.15 (br.s, 3F); $^{31}\text{P}\{^1\text{H}\}$ NMR (202 MHz, Toluene- d_8 , 60 °C) δ 24.2 (s). Elemental analysis calcd (%) for $\text{C}_{48}\text{H}_{63}\text{Cl}_2\text{F}_6\text{N}_2\text{OPRu}$: C, 57.60; H, 6.34; N, 2.80; found: C, 57.39; H, 6.47; N, 2.84.

Benzylidene(dichloro){1-[2-(1,1,1,3,3,3-hexafluoro-2-methoxypropan-2-yl)-4-methoxyphenyl]-3-mesityl-4,5-dihydroimidazol-2-ylidene}(tricyclohexylphosphine)ruthenium(II) (27b).



27b

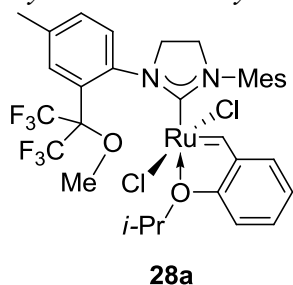
Yield: 48%. Mixture of two rotamers 4:1 at 50 °C, signals of major product are given: ^1H NMR (400 MHz, Toluene- d_8 , 50 °C) δ 19.59 (s, 1H, CHAr), 9.62 (br.s, 1H, H_{Ar}), 9.47 (br.s, 1H, H_{Ar}), 7.61 (s, 1H, H_{Ar}), 7.21 (t, $J_{\text{H,H}} = 7.3$ Hz, 1H, H_{Ar}), 7.12 (dd, $J_{\text{H,H}} = 8.8, 2.6$ Hz, 1H, H_{Ar}), 7.08-6.86 (m, 4H, H_{Ar}), 6.54 (br.s, 1H, H_{Ar}), 4.39 (br.s, 1H, CH_2), 4.10 (s, 3H, OMe), 3.76 (br.s, 1H, CH_2), 3.43 (s, 3H, OMe), 3.38 (br.s, 1H, CH_2), 3.25 (s, 1H, CH_2), 2.77-0.81 (m, 42H, PCy_3 , Me); $^{13}\text{C}\{^1\text{H}\}$ NMR (126 MHz, Toluene- d_8 , 50 °C) δ 298.2, 223.3, 159.3, 152.4, 139.8, 138.9, 138.7, 137.0, 136.7, 135.4, 132.0 (br.s), 130.6, 130.4, 129.7, 129.5, 128.3, 123.63 (q, $^1J_{\text{C,F}} = 284$ Hz), 123.58 (q, $^1J_{\text{C,F}} = 288$ Hz), 117.6, 117.3, 85.4-84.1 (m), 58.5, 56.3, 54.9, 52.2, 29.8, 29.4, 28.2-28.1 (m), 26.8, 21.0, 19.3, 18.9; $^{19}\text{F}\{^1\text{H}\}$ NMR (471 MHz, Toluene- d_8 , 50 °C) δ -65.50 (br.s, 3F), -71.13 (br.s, 3F); $^{31}\text{P}\{^1\text{H}\}$ NMR (202 MHz, Toluene- d_8 , 50 °C) δ 24.6 (s). Elemental analysis calcd (%) for $\text{C}_{48}\text{H}_{63}\text{Cl}_2\text{F}_6\text{N}_2\text{O}_2\text{PRu}$: C, 56.69; H, 6.24; N, 2.75; found: C, 56.68; H, 6.42; N, 2.77.

General procedure for synthesis of Hoveyda-type catalysts 28.

In a flame-dried Schlenk flask, imidazolium salt **26** (0.40 mmol) was mixed with 9 mL of anhydrous toluene. The resulting mixture was cooled to 0 °C and degassed three times; then KHMDS (840 μL of 0.5 M solution in toluene, 0.42 mmol) was added to the mixture under an argon atmosphere. The reaction mixture was stirred for 30 min at r.t.; then Hoveyda-Grubbs

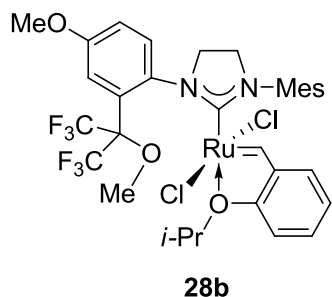
catalyst first generation **HG-I** (0.20 g, 0.30 mmol) was added and mixture was stirred for 40 min at 80 °C. During this time, the reaction mixture changed color from brown to dark green. Once complete, solvents were removed from the reaction mixture under reduced pressure, and the resulting substance was purified by column chromatography using EtOAc/petroleum ether (1:3) as eluent to yield Hoveyda-type catalyst as a green solid. Suitable for X-ray crystals of **28** were grown by slow diffusion of hexane vapors in CH₂Cl₂ solution.

*Dichloro{1-[2-(1,1,1,3,3,3-hexafluoro-2-methoxypropan-2-yl)-4-methylphenyl]-3-mesityl-4,5-dihydroimidazol-2-ylidene}(2-isopropoxybenzylidene)ruthenium(II) (**28a**).*



Yield: 74%. ¹H NMR (500 MHz, Toluene-*d*₈, 80 °C) δ 16.91 (s, 1H, CHAr), 9.14 (br.s, 1H, H_{Ar}), 7.78 (s, 1H, H_{Ar}), 7.21 (br.s, 1H, H_{Ar}), 7.10 (m, 1H, H_{Ar}), 6.94 (dd, *J*_{H,H} = 7.5, 1.1 Hz, 1H, H_{Ar}), 6.89 (s, 1H, H_{Ar}), 6.82 (s, 1H, H_{Ar}), 6.59 (t, ³*J*_{H,H} = 7.4 Hz, 1H, H_{Ar}), 6.43 (d, ³*J*_{H,H} = 8.3 Hz, 1H, H_{Ar}), 4.56 (hept, ³*J*_{H,H} = 6.3 Hz, 1H, CHMe₂), 4.51 (m, 1H, CH₂), 3.86 (s, 3H, OMe), 3.69 (q, *J*_{H,H} = 9.9 Hz, 1H, CH₂), 3.48 (q, *J*_{H,H} = 9.9 Hz, 1H, CH₂), 3.42 (q, *J*_{H,H} = 9.3 Hz, 1H, CH₂), 2.51 (s, 3H, Me), 2.37 (s, 3H, Me), 2.21 (s, 3H, Me), 2.16 (s, 3H, Me), 1.39 (s, 3H, CH(CH₃)₂), 1.31 (d, ³*J*_{H,H} = 6.1 Hz, 3H, CH(CH₃)₂); ¹³C {¹H} NMR (126 MHz, Toluene-*d*₈, 80 °C) δ 294.0, 216.8, 153.3, 145.6, 142.4, 138.8, 138.7, 137.8, 134.1 (br.s), 130.4, 130.1, 130.0, 129.5, 123.8 (q, ²*J*_{C,F} = 289 Hz), 123.4 (q, ²*J*_{C,F} = 289 Hz), 122.4, 122.3, 113.4, 85.4 (hept, ¹*J*_{C,F} = 27 Hz), 75.1, 58.0, 54.6 (br.s), 53.1 (br.s), 22.4, 22.2, 22.1, 21.9; ¹⁹F {¹H} NMR (471 MHz, Toluene-*d*₈, 60 °C) δ -65.6 (br.s, 3F), -71.7 (br.s, 3F). Elemental analysis calcd (%) for C₃₃H₃₆Cl₂F₆N₂O₂Ru: C, 50.90; H, 4.66; N, 3.60; found: C, 50.78; H, 4.89; N, 3.42. CCDC 1543696 contains the supplementary crystallographic data for this compound.

*Dichloro{1-[2-(1,1,1,3,3,3-hexafluoro-2-methoxypropan-2-yl)-4-methoxyphenyl]-3-mesityl-4,5-dihydroimidazol-2-ylidene}(2-isopropoxybenzylidene)ruthenium(II) (**28b**).*

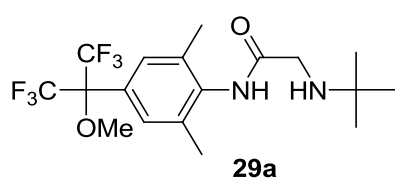


Yield: 71%. ^1H NMR (500 MHz, Toluene- d_8 , 80 °C) δ 16.92 (br.s, 1H, CHAr), 9.13 (br.s, 1H, H_{Ar}), 7.61 (s, 1H, H_{Ar}), 7.10 (m, 1H, H_{Ar}), 6.98 (dd, $J_{\text{H,H}} = 1.5, 7.4$ Hz, 1H, H_{Ar}), 6.92 (br.s, 1H, H_{Ar}), 6.89 (s, 1H, H_{Ar}), 6.83 (s, 1H, H_{Ar}), 6.58 (t, $^3J_{\text{H,H}} = 7.4$ Hz, 1H, H_{Ar}), 6.42 (d, $^3J_{\text{H,H}} = 8.3$ Hz, 1H, H_{Ar}), 4.56 (hept, $^3J_{\text{H,H}} = 6.1$ Hz, 1H, CHMe_2), 4.48 (td, $J_{\text{H,H}} = 9.6, 3.2$ Hz, 1H, CH_2), 3.85 (s, 3H, OMe), 3.70 (m, 1H, CH_2), 3.48 (m, 1H, CH_2), 3.40 (m, 1H, CH_2), 3.38 (s, 3H, OMe), 2.52 (s, 3H, Me), 2.39 (s, 3H, Me), 2.22 (s, 3H, Me), 1.32 (d, $^3J_{\text{H,H}} = 6.1$ Hz, 6H, $\text{CH}(\text{CH}_3)_2$); $^{13}\text{C}\{^1\text{H}\}$ NMR (126 MHz, Toluene- d_8 , 80 °C) δ 294.0, 216.8, 159.7, 153.3, 145.7, 138.8, 138.7, 137.8, 134.7 (br.s), 130.4, 130.1, 129.5, 129.1, 123.8 (q, $^1J_{\text{C,F}} = 293$ Hz), 123.4 (q, $^1J_{\text{C,F}} = 289$ Hz), 122.4, 122.3, 113.4, 85.3 (hept, $^1J_{\text{C,F}} = 27$ Hz), 75.1, 58.0, 55.4, 54.8 (br.s), 53.0 (br.s), 22.3, 22.2, 22.1, 21.9; $^{19}\text{F}\{^1\text{H}\}$ NMR (282 MHz, Toluene- d_8 , 60 °C) δ -65.89, -70.73. Elemental analysis calcd (%) for $\text{C}_{33}\text{H}_{36}\text{Cl}_2\text{F}_6\text{N}_2\text{O}_3\text{Ru}$: C, 49.88; H, 4.57; N, 3.53; found: C, 49.91; H, 4.52; N, 3.27. CCDC 1543695 contains the supplementary crystallographic data for this compound.

General procedure for synthesis of aminoacetamides 29.

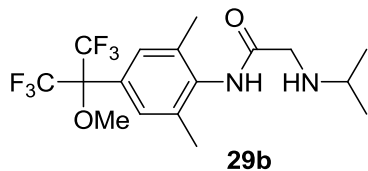
Chloroacetamide **3** (1.5 g, 4.0 mmol) was dissolved in 20-fold excess of a corresponding alkylamine (80 mmol). The reaction mixture was allowed to stir at room temperature until full disappearance of starting material **3** (TLC control). Afterwards the mixture was treated with 10% solution of NaHCO_3 (20 mL) and extracted with ethylacetate (3×20 mL). Combined organic layers were washed with brine and water, dried over MgSO_4 , filtered and concentrated under reduced pressure. The excess of starting amine was removed under high vacuum. The resulting solid residue was recrystallized from petroleum ether.

2-(tert-Butylamino)-N-[4-(1,1,1,3,3,3-hexafluoro-2-methoxypropan-2-yl)-2,6-dimethylphenyl]-acetamide (29a).



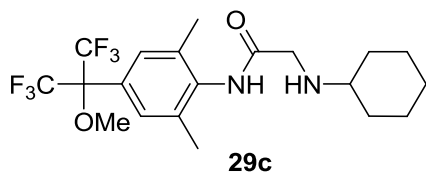
The reaction was finished in 3 days. Yield: 95%. mp 126-128 °C. ^1H NMR (400 MHz, CDCl_3) δ 9.19 (s, 1H, NHCO), 7.27 (s, 2H, H_{Ar}), 3.48 (s, 3H, OMe), 3.43 (s, 2H, CH_2), 2.28 (s, 6H, Me), 1.70 (br.s, 1H, NHCH_2), 1.17 (s, 9H, $\text{C}(\text{CH}_3)_3$); $^{13}\text{C}\{^1\text{H}\}$ NMR (101 MHz, CDCl_3) δ 171.2, 136.3, 135.7, 128.1, 126.1, 122.5 (q, CF_3 , $^1J_{\text{C,F}} = 290$ Hz), 83.7-82.1 (m, $\text{C}(\text{CF}_3)_2$), 54.4, 51.4, 46.3, 29.2, 19.2; $^{19}\text{F}\{^1\text{H}\}$ NMR (376 MHz, CDCl_3) δ -70.79 (s). Elemental analysis calcd (%) for $\text{C}_{18}\text{H}_{24}\text{F}_6\text{N}_2\text{O}_2$: C, 51.94; H, 5.89; N, 6.72; found: C, 52.17; H, 5.84; N, 6.76.

N-[4-(1,1,1,3,3,3-Hexafluoro-2-methoxypropan-2-yl)-2,6-dimethylphenyl]-2-(isopropylamino)-acetamide (29b).



The reaction was finished in 1 day. Yield: 96%. mp 74-76 °C. ^1H NMR (400 MHz, CDCl_3) δ 9.13 (s, 1H, NHCO), 7.26 (s, 2H, H_{Ar}), 3.47 (s, 5H, CH_2 , OMe), 2.92 (hept, $^3J = 6.1$ Hz, 1H, CHMe_2), 2.27 (s, 6H, Me), 2.21 (br.s, 1H, NHCH_2), 1.14 (d, $^3J = 6.2$ Hz, 6H, $\text{CH}(\text{CH}_3)_2$); $^{13}\text{C}\{^1\text{H}\}$ NMR (101 MHz, CDCl_3) δ 170.5, 136.5, 135.7, 128.0, 126.2, 122.5 (q, $^1J_{\text{C,F}} = 289$ Hz), 83.7-82.1 (m), 54.4, 50.3, 50.0, 23.0, 19.1; $^{19}\text{F}\{^1\text{H}\}$ NMR (376 MHz, CDCl_3) δ -70.80 (s). Elemental analysis calcd (%) for $\text{C}_{17}\text{H}_{22}\text{F}_6\text{N}_2\text{O}_2$: C, 50.87; H, 5.59; N, 6.94; found: C, 51.00; H, 5.54; N, 7.00.

2-(Cyclohexylamino)-N-[4-(1,1,1,3,3,3-hexafluoro-2-methoxypropan-2-yl)-2,6-dimethylphenyl]-acetamide (29c).

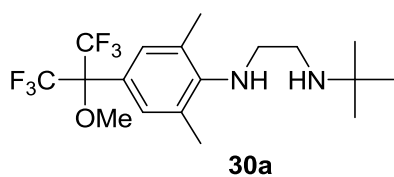


The reaction was finished in 1 day. Yield: 98%. mp 96-98 °C. ^1H NMR (400 MHz, CDCl_3) δ 9.11 (br.s, 2H, NHCO), 7.26 (s, 2H, H_{Ar}), 3.47 (s, 5H, CH_2 , OMe), 2.52-2.47 (m, 1H, H_{Cy}), 2.27 (s, 6H, Me), 1.96-1.06 (m, 10H, H_{Cy}); $^{13}\text{C}\{^1\text{H}\}$ NMR (101 MHz, CDCl_3) δ 170.8, 136.2, 135.7, 128.0, 126.1, 122.5 (q, $^1J_{\text{C,F}} = 290$ Hz), 83.7-82.1 (m), 57.8, 54.4, 50.1, 34.0, 26.0, 25.1, 19.1; $^{19}\text{F}\{^1\text{H}\}$ NMR (376 MHz, CDCl_3) δ -70.79 (s). Elemental analysis calcd (%) for $\text{C}_{20}\text{H}_{26}\text{F}_6\text{N}_2\text{O}_2$: C, 54.51; H, 5.85; N, 6.32; found: C, 54.54; H, 5.95; N, 6.36.

General procedure for synthesis of diamines 30.

Aminoacetamide **29** (2.9 mmol) was dissolved in anhydrous toluene (18 mL), then $\text{BH}_3 \cdot \text{SMe}_2$ (6.5 mL of 2 M solution THF, 13.0 mmol) was dissolved dropwise at room temperature under argon atmosphere. The resulting mixture was heated at 80 °C for 8 hours. After cooling to r.t., MeOH was slowly added until ceasing of gas evolution. Then, a 10% solution (20 mL) of HCl was added and resulting mixture was extracted with EtOAc (2×30 mL). The aqueous layer was separated, treated with NaHCO_3 , and also extracted with EtOAc (2×30 mL). Combined organic layers were washed with a saturated solution of NaHCO_3 , dried over MgSO_4 , and concentrated under reduced pressure.

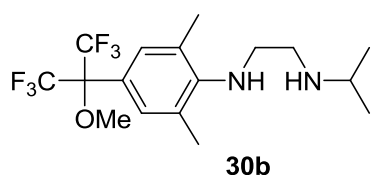
N^1 -tert-Butyl- N^2 -[4-(1,1,1,3,3,3-hexafluoro-2-methoxypropan-2-yl)-2,6-dimethylphenyl]ethane-1,2-diamine (30a).



Yield: 99%. mp 58-60 °C. ^1H NMR (400 MHz, CDCl_3) δ 7.11 (s, 2H, H_{Ar}), 4.09 (br.s, 2H, NH), 3.45 (s, 3H, OMe), 3.17 (t, $J_{\text{H,H}} = 5.6$ Hz, 2H, CH_2), 2.79 (t, $J_{\text{H,H}} = 5.6$ Hz, 2H, CH_2), 2.32 (s, 6H, Me), 1.12 (s, 9H, $\text{C}(\text{CH}_3)_3$); $^{13}\text{C}\{^1\text{H}\}$ NMR (101 MHz, CDCl_3) δ 148.6, 128.7, 127.8, 122.8 (q, $^1J_{\text{C,F}} = 291$ Hz), 118.7, 83.9-82.2 (m), 54.1, 50.4, 48.7,

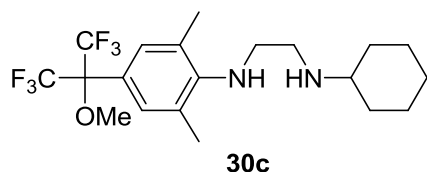
42.7, 29.3, 19.5; $^{19}\text{F}\{^1\text{H}\}$ NMR (376 MHz, CDCl_3) δ -70.99 (s). Elemental analysis calcd (%) for $\text{C}_{18}\text{H}_{26}\text{F}_6\text{N}_2\text{O}$: C, 54.17; H, 6.85; N, 7.18; found: C, 53.99; H, 6.55; N, 7.00.

*N*¹-[4-(1,1,1,3,3,3-Hexafluoro-2-methoxypropan-2-yl)-2,6-dimethylphenyl]-*N*²-isopropylethane-1,2-diamine (**30b**).



Yield: 79%. Yellow oil. ^1H NMR (400 MHz, CDCl_3) δ 7.12 (s, 2H, H_{Ar}), 3.97 (br.s, 2H, NH), 3.45 (s, 3H, OMe), 3.21 (t, $J_{\text{H,H}} = 5.6$ Hz, 2H, CH_2), 2.93-2.84 (m, 3H, CH_2 , CHMe_2), 2.32 (s, 6H, Me), 1.12 (d, $^3J_{\text{H,H}} = 6.3$ Hz, 6H, $\text{CH}(\text{CH}_3)_2$); $^{13}\text{C}\{^1\text{H}\}$ NMR (101

MHz, CDCl_3) δ 148.4, 128.7, 128.3, 122.8 (q, $^1J_{\text{C,F}} = 291$ Hz), 119.1, 83.0 (hept, $^2J_{\text{C,F}} = 28$ Hz), 54.1, 49.0, 47.5, 47.2, 22.7, 19.4; $^{19}\text{F}\{^1\text{H}\}$ NMR (376 MHz, CDCl_3) δ -70.98 (s). Elemental analysis calcd (%) for $\text{C}_{17}\text{H}_{24}\text{F}_6\text{N}_2\text{O}$: C, 52.85; H, 6.26; N, 7.25; found: C, 52.68; H, 6.26; N, 7.40. *N*¹-Cyclohexyl-*N*²-[4-(1,1,1,3,3,3-hexafluoro-2-methoxypropan-2-yl)-2,6-dimethylphenyl]ethane-1,2-diamine (**30c**).



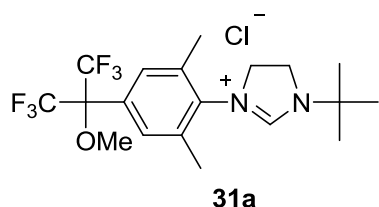
Yield: 87%. mp 171-173 °C. ^1H NMR (400 MHz, CDCl_3) δ 7.11 (s, 2H, H_{Ar}), 4.07 (br.s, 2H, NH), 3.45 (s, 3H, OMe), 3.25 (t, $J_{\text{H,H}} = 5.6$ Hz, 2H, CH_2), 2.92 (t, $J_{\text{H,H}} = 5.7$ Hz, 2H, CH_2), 2.61-2.52 (m, 1H, H_{Cy}), 2.33 (s, 6H, Me), 2.04-1.10

(m, 10H, H_{Cy}); $^{13}\text{C}\{^1\text{H}\}$ NMR (101 MHz, CDCl_3) δ 148.3, 128.7, 128.3, 122.8 (q, $^1J_{\text{C,F}} = 291$ Hz); 119.2, 83.0 (hept, $^2J_{\text{C,F}} = 28$ Hz), 57.0, 54.1, 47.1, 46.7, 32.9, 25.9, 25.0, 19.5; $^{19}\text{F}\{^1\text{H}\}$ NMR (376 MHz, CDCl_3) δ -70.97 (s). Elemental analysis calcd (%) for $\text{C}_{20}\text{H}_{28}\text{F}_6\text{N}_2\text{O}$: C, 56.33; H, 6.62; N, 6.57; found: C, 56.62; H, 6.75; N, 6.69.

General procedure for synthesis of imidazolium chlorides 31.

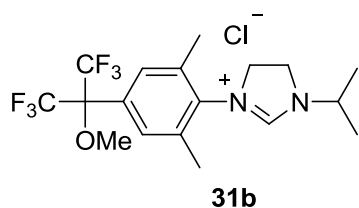
Concentrated HCl (1 mL, 12 mmol) was added to the solution of **30** (1.1 mmol) in MeOH (10 mL) and stirred for 10 min. Then, solvents were removed under reduced pressure. The residual solid was mixed with anhydrous *ortho*-xylene (60 mL) and boiled under argon atmosphere for 10 minutes to remove traces of water. Then, mixture was cooled to room temperature and triethyl orthoformate (200 μL , .1.1 mmol) was added. The resulting mixture was stirred at 90 °C for 8 h. After reaction complete (TLC control) all volatiles were removed under reduced pressure and the resulting solid was washed with THF and petroleum ether.

1-tert-Butyl-3-[4-(1,1,1,3,3,3-hexafluoro-2-methoxypropan-2-yl)-2,6-dimethylphenyl]-4,5-dihydro-1H-imidazol-3-ium chloride (31a).



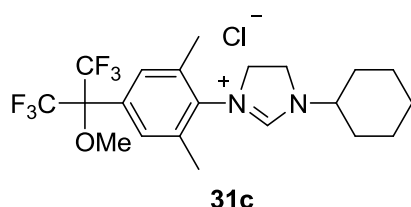
Yield: 80%. mp 220-222 °C (decomp.). ^1H NMR (400 MHz, CDCl_3) δ 9.32 (s, 1H, NCHN), 7.29 (s, 2H, H_{Ar}), 4.34 (s, 4H, CH_2), 3.46 (s, 3H, OMe), 2.44 (s, 6H, Me), 1.59 (s, 9H, $\text{C}(\text{CH}_3)_3$); $^{13}\text{C}\{^1\text{H}\}$ NMR (75 MHz, CDCl_3) δ 157.5, 136.8, 135.4, 129.5, 128.8, 122.07 (q, $^1J_{\text{C,F}} = 289$ Hz), 83.5-81.3 (m), 58.0, 54.6, 51.2, 46.7, 28.3, 18.8; $^{19}\text{F}\{^1\text{H}\}$ NMR (376 MHz, CDCl_3) δ -70.57 (s). Elemental analysis calcd (%) for $\text{C}_{19}\text{H}_{25}\text{ClF}_6\text{N}_2\text{O}$: C, 51.07; H, 5.64; N, 6.27; found: C, 51.22; H, 5.79; N, 6.22.

3-[4-(1,1,1,3,3,3-hexafluoro-2-methoxypropan-2-yl)-2,6-dimethylphenyl]-1-isopropyl-4,5-dihydro-1H-imidazol-3-ium chloride (31b).



Yield: 99%. mp 210-215 °C (decomp.). ^1H NMR (400 MHz, $\text{DMSO}-d_6$) δ 9.00 (s, 1H, NCHN), 7.43 (s, 2H, H_{Ar}), 4.28-4.15 (m, 4H, CH_2), 4.01 (hept, $^3J_{\text{H,H}} = 6.5$ Hz, 1H, CHMe_2), 3.47 (s, 3H, OMe), 2.41 (s, 6H, Me), 1.34 (d, $^3J_{\text{H,H}} = 6.6$ Hz, 6H, $\text{CH}(\text{CH}_3)_2$); $^{13}\text{C}\{^1\text{H}\}$ NMR (101 MHz, $\text{DMSO}-d_6$) δ 157.4, 137.6, 136.3, 128.1, 127.8, 122.1 (q, $^1J_{\text{C,F}} = 292$ Hz), 82.2 (hept, $^2J_{\text{C,F}} = 28$ Hz), 54.6, 50.3, 49.9, 46.5, 20.4, 17.8; $^{19}\text{F}\{^1\text{H}\}$ NMR (376 MHz, $\text{DMSO}-d_6$) δ -70.07 (s). Elemental analysis calcd (%) for $\text{C}_{18}\text{H}_{23}\text{ClF}_6\text{N}_2\text{O}$: C, 49.95; H, 5.36; N, 6.47; found: C, 50.13; H, 5.45; N, 6.45.

1-Cyclohexyl-3-[4-(1,1,1,3,3,3-hexafluoro-2-methoxypropan-2-yl)-2,6-dimethylphenyl]-4,5-dihydro-1H-imidazol-3-ium chloride (31c).



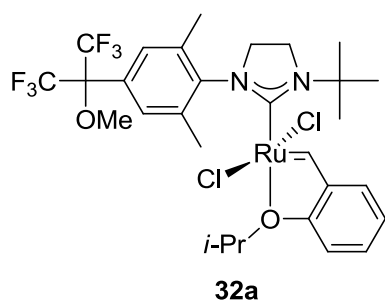
Yield: 99%. mp 224-226 °C (decomp.). ^1H NMR (400 MHz, $\text{DMSO}-d_6$) δ 9.09 (s, 1H, NCHN), 7.42 (s, 2H, H_{Ar}), 4.24 (s, 4H, CH_2), 3.71-3.61 (m, 1H, H_{Cy}), 3.47 (s, 3H, OMe), 2.41 (s, 6H, Me), 1.57 (m, 10H, H_{Cy}); $^{13}\text{C}\{^1\text{H}\}$ NMR (101 MHz, $\text{DMSO}-d_6$) δ 157.4, 137.6, 136.3, 128.1, 127.7, 122.1, (q, $^1J_{\text{C,F}} = 290$ Hz), 82.2 (hept, $^2J_{\text{C,F}} = 28$ Hz), 57.0, 54.6, 49.8, 47.0, 30.4, 24.6, 24.3, 17.8; $^{19}\text{F}\{^1\text{H}\}$ NMR (376 MHz, $\text{DMSO}-d_6$) δ -70.10 (s). Elemental analysis calcd (%) for $\text{C}_{21}\text{H}_{27}\text{ClF}_6\text{N}_2\text{O}$: C, 53.34; H, 5.75; N, 5.92; found: C, 53.13; H, 5.84; N, 5.65.

General procedure for synthesis of Hoveyda-type catalysts 32.

In a flame-dried Schlenk flask, imidazolium salt **31** (0.40 mmol) was mixed with 9 mL of anhydrous toluene. The resulting mixture was cooled to 0 °C and degassed three times; then KHMDS (420 μL of 1 M solution in THF, 0.42 mmol) was added to the mixture under an argon atmosphere. The reaction mixture was stirred for 10 min at r.t.; then Hoveyda catalyst **HG-I** (0.20 g, 0.33 mmol) was added and mixture was stirred for 40 min at 40 °C. During this time, the reaction mixture changed color from brown to dark-green. Once complete, solvents were removed under

reduced pressure, and the resulting substance was purified by column chromatography using EtOAc/petroleum ether (1:3) as eluent to yield Hoveyda-type catalyst as a green solid.

{1-tert-Butyl-3-[4-(1,1,1,3,3,3-hexafluoro-2-methoxypropan-2-yl)-2,6-dimethylphenyl]-4,5-dihydro-1H-imidazol-2-ylidene}dichloro(2-isopropoxybenzylidene)ruthenium(II) (32a).

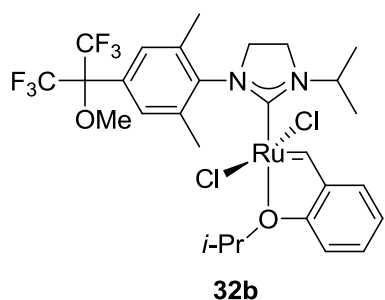


Yield: 70%. $^1\text{H NMR}$ (400 MHz, C_6D_6) δ 17.10 (s, 1H, CHAr), 7.54 (s, 2H, H_{Ar}), 7.18 (t, $J_{\text{H,H}} = 8.0$ Hz, 1H, H_{Ar}), 7.13 (d, $J_{\text{H,H}} = 7.7$ Hz, 1H, H_{Ar}), 6.73 (t, $J_{\text{H,H}} = 7.3$ Hz, 1H, H_{Ar}), 6.45 (d, $J_{\text{H,H}} = 8.1$ Hz, 1H, H_{Ar}), 4.58 (hept, $^3J_{\text{H,H}} = 5.9$ Hz, 1H, CHMe_2), 3.21 (s, 3H, OMe), 3.15-3.01 (m, 4H, CH_2), 2.29 (s, 6H, Me), 2.08 (s, 9H, $\text{C}(\text{CH}_3)_3$), 1.53 (d, $^3J_{\text{H,H}} = 6.0$ Hz, 6H, $\text{CH}(\text{CH}_3)_2$);

$^{13}\text{C}\{^1\text{H}\}$ NMR (101 MHz, C_6D_6) δ 306.0, 209.1, 153.0, 146.2, 144.5, 140.1, 130.5, 128.9, 123.4 (q, $^1J_{\text{C,F}} = 291$), 123.4, 122.6, 113.7, 84.0-82.9 (m), 74.6, 56.3, 54.2, 51.1, 45.8, 29.7, 22.4, 18.9;

$^{19}\text{F}\{^1\text{H}\}$ NMR (376 MHz, C_6D_6) δ -70.20 (s). Elemental analysis calcd (%) for $\text{C}_{29}\text{H}_{36}\text{Cl}_2\text{F}_6\text{N}_2\text{O}_2\text{Ru}$: C, 47.68; H, 4.97; N, 3.83; found: C, 47.87; H, 5.11; N, 3.86.

Dichloro{3-(4-(1,1,1,3,3,3-hexafluoro-2-methoxypropan-2-yl)-2,6-dimethylphenyl)-1-isopropyl-4,5-dihydro-1H-imidazol-2-ylidene}(2-isopropoxybenzylidene)ruthenium(II) (32b).

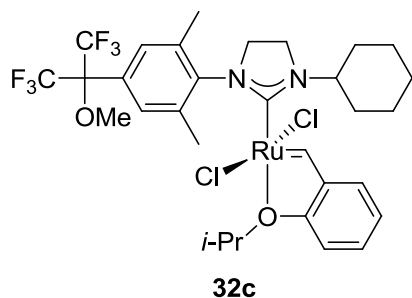


Yield: 39%. $^1\text{H NMR}$ (400 MHz, C_6D_6) δ 16.46 (s, 1H, CHAr), 7.59 (s, 2H, H_{Ar}), 7.23-7.15 (m, 2H, H_{Ar}), 6.79 (t, $J_{\text{H,H}} = 7.4$ Hz, 1H, H_{Ar}), 6.49 (d, $J_{\text{H,H}} = 8.2$ Hz, 1H, H_{Ar}), 5.84 (hept, $^3J_{\text{H,H}} = 5.8$ Hz, 1H, NCHMe_2), 4.72 (hept, $^3J_{\text{H,H}} = 5.8$ Hz, 1H, OCHMe_2), 3.29 (s, 3H, OMe), 3.16-3.04 (m, 4H, CH_2), 2.25 (s, 6H, Me), 1.78 (d, $^3J_{\text{H,H}} = 5.9$ Hz, $\text{NCH}(\text{sH}_3)_2$), 6H, 1.56 (d, $^3J_{\text{H,H}} = 6.3$ Hz, 6H, $\text{OCH}(\text{sH}_3)_2$);

$^{13}\text{C}\{^1\text{H}\}$ NMR (101 MHz, C_6D_6) δ 285.8, 208.1, 152.9, 144.8, 143.1, 140.3, 129.2, 128.8, 128.5, 123.3 (q, $^1J_{\text{C,F}} = 290$ Hz), 122.6, 122.2, 113.3, 83.5 (hept, $^2J_{\text{C,F}} = 29$ Hz), 75.1, 54.2, 52.9, 50.8, 41.8, 22.0, 20.7, 18.7; $^{19}\text{F}\{^1\text{H}\}$ NMR (376 MHz, C_6D_6) δ -70.22 (s).

Elemental analysis calcd (%) for $\text{C}_{28}\text{H}_{34}\text{Cl}_2\text{F}_6\text{N}_2\text{O}_2\text{Ru}$: C, 46.93; H, 4.78; N, 3.91; found: C, 46.87; H, 4.89; N, 3.99.

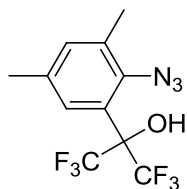
Dichloro{1-cyclohexyl-3-[4-(1,1,1,3,3,3-hexafluoro-2-methoxypropan-2-yl)-2,6-dimethylphenyl]-4,5-dihydro-1H-imidazol-2-ylidene}(2-isopropoxybenzylidene)ruthenium(II) (32c).



Yield: 25%. ^1H NMR (400 MHz, C_6D_6) δ 16.41 (s, 1H, CHAr), 7.52 (s, 2H, H_{Ar}), 7.20-7.07 (m, 2H, H_{Ar}), 6.72 (t, $J_{\text{H,H}} = 7.2$ Hz, 1H, H_{Ar}), 6.43 (d, $J_{\text{H,H}} = 8.1$ Hz, 1H, H_{Ar}), 5.35-5.23 (m, 1H, H_{Cy}), 4.65 (hept, $^3J_{\text{H,H}} = 5.6$ Hz, 1H, CHMe_2), 3.21 (s, 3H, OMe), 3.12 (s, 4H, CH_2), 2.78-2.67 (m, 2H, H_{Cy}), 2.19 (s, 6H, Me), 1.93-1.64 (m, 5H, H_{Cy}), 1.74 (d, 6H, $^3J_{\text{H,H}}$

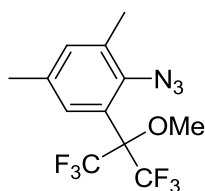
= 5.5 Hz, $\text{CH}(\text{CH}_3)_2$), 1.42-1.00 (m, 3H, H_{Cy}); $^{13}\text{C}\{^1\text{H}\}$ NMR (101 MHz, C_6D_6) δ 286.0, 208.4, 152.9, 144.9, 143.0, 140.4, 129.1, 128.8, 128.5, 123.4 (q, $^1J_{\text{C,F}} = 291$ Hz), 122.6, 122.2, 113.3, 83.20 (hept, $^2J_{\text{C,F}} = 28$ Hz), 74.9, 61.2, 54.2, 50.9, 43.3, 31.2, 26.3, 25.9, 22.1, 18.7; $^{19}\text{F}\{^1\text{H}\}$ NMR (376 MHz, C_6D_6) δ -70.18 (s). Elemental analysis calcd (%) for $\text{C}_{31}\text{H}_{38}\text{Cl}_2\text{F}_6\text{N}_2\text{O}_2\text{Ru}$: C, 49.21; H, 5.06; N, 3.70; found: C, 48.95; H, 4.98; N, 3.83.

Synthesis of 2-(1,1,1,3,3,3-hexafluoro-2-methoxypropan-2-yl)-4,6-dimethylaniline.



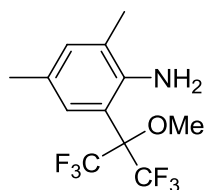
To a mixture of aniline **7** (10 g, 34.8 mmol) in 80 mL of water concentrated sulfuric acid (18.6 mL, 348 mmol) was slowly added. The resulting mixture was cooled to 0 °C and solution of NaNO_2 (2.76 g, 40.0 mmol) in 10 mL of water was added dropwise and reaction mixture was stirred in an ice bath for

30 min. Then solution of NaN_3 (2.72 g, 41.8 mmol) in 10 mL of water was added dropwise. After full addition, the reaction mixture was allowed to stir at r.t. for 3 h. Then the reaction mixture was extracted with EtOAc (3 \times 30 mL). Combined organic layer was washed with brine (30 mL), dried over MgSO_4 and concentrated under reduced pressure. The crude product was purified by flash chromatography using EtOAc/petroleum ether (1:3) as eluent to yield 9.84 g of yellowish crystals. Yield: 90%. ^1H NMR (400 MHz, CDCl_3) δ 7.35 (br.s, 1H, OH), 7.31 (s, 1H, H_{Ar}), 7.17 (s, 1H, H_{Ar}), 2.44 (s, 3H, Me), 2.35 (s, 3H, Me); $^{13}\text{C}\{^1\text{H}\}$ NMR (101 MHz, CDCl_3) δ 137.1, 134.6, 134.4, 134.1, 127.8-127.6 (m), 122.8, 122.8 (q, $^1J_{\text{C,F}} = 288$ Hz), 79.8 (hept, $^2J_{\text{C,F}} = 30$ Hz), 21.2, 18.1; $^{19}\text{F}\{^1\text{H}\}$ NMR (376 MHz, CDCl_3) δ -74.68 (s). Elemental analysis calcd (%) for $\text{C}_{11}\text{H}_9\text{F}_6\text{N}_3\text{O}$: C, 42.18; H, 2.90; N, 13.42; found: C, 41.93; H, 3.12; N, 13.53.



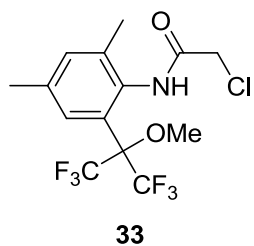
A mixture of the resulting azide (9.84 g, 31.4 mmol), iodomethane (3.9 mL, 62.8 mmol) and anhydrous K_2CO_3 (8.7 g, 62.8 mmol) in 150 mL of acetonitrile was stirred at r.t. for 2 days. After reaction completion (TLC control), the solvent was evaporated under reduced pressure, residual solid was dispersed in EtOAc and filtered. The resulting filtrate was evaporated again and purified by flash chromatography using EtOAc/petroleum ether (1:8) as eluent to yield 9.99 g of yellow oil that was crystallized after complete removal of solvent under high vacuum. Yield: 97%. ^1H NMR (400 MHz, CDCl_3) δ 7.25 (s, 1H, H_{Ar}), 7.18 (s, 1H, H_{Ar}), 3.46 (s, 3H, OMe), 2.44 (s, 3H, Me), 2.35 (s, 3H, Me); $^{13}\text{C}\{^1\text{H}\}$ NMR (101 MHz, CDCl_3) δ 136.4, 135.6, 135.3, 134.4, 129.1, 121.6,

122.6 (q, $^1J_{C,F} = 292$ Hz), 121.6, 84.5 (hept, $^2J_{C,F} = 29$ Hz), 54.7, 21.2, 18.5; $^{19}\text{F}\{^1\text{H}\}$ NMR (376 MHz, CDCl_3) δ -70.04 (s). Elemental analysis calcd (%) for $\text{C}_{12}\text{H}_{11}\text{F}_6\text{N}_3\text{O}$: C, 44.05; H, 3.39; N, 12.84; found: C, 43.86; H, 3.41; N, 12.64.



The methylated azide (9.99 g, 30.5 mmol) was dissolved in 10 mL of methanol, then $\text{CoCl}_2 \cdot 6\text{H}_2\text{O}$ (730 mg, 3.1 mmol) and cetyltrimethylammonium bromide (CTABr) (1.11 g, 3.1 mmol) were added with stirring at r.t. Then a solution of NaBH_4 (2.30 g, 61.1 mmol) in 60 mL of water was added dropwise. After full addition, the reaction mixture was stirred another 30 min and extracted with Et_2O (3×30 mL). Combined organic layer was washed with 10 mL of water, filtered through cotton wool and evaporated under reduced pressure to yield 8.95 g of yellow crystals. Yield: 97%. ^1H NMR (400 MHz, CDCl_3) δ 7.01 (s, 2H, H_{Ar}), 4.60 (br.s, 2H, NH), 3.56 (s, 3H, OMe), 2.25 (s, 3H, Me), 2.18 (s, 3H, Me); $^{13}\text{C}\{^1\text{H}\}$ NMR (101 MHz, CDCl_3) δ 142.6, 133.4, 128.1, 126.5, 124.7, 123.1 (q, $^1J_{C,F} = 293$ Hz), 108.7, 85.5 (hept, $^2J_{C,F} = 29$ Hz), 54.8, 20.7, 18.3; $^{19}\text{F}\{^1\text{H}\}$ NMR (376 MHz, CDCl_3) δ -69.61 (s). Elemental analysis calcd (%) for $\text{C}_{12}\text{H}_{13}\text{F}_6\text{NO}$: C, 47.85; H, 4.35; N, 4.65; found: C, 48.01; H, 4.39; N, 4.63.

Synthesis of 2-chloro-N-[2-(1,1,1,3,3,3-hexafluoro-2-methoxypropan-2-yl)-4,6-dimethylphenyl]-acetamide (33).



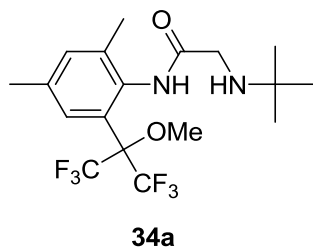
Chloroacetyl chloride (3.75 g, 33.2 mmol) was added dropwise to the solution of methylated aniline (5 g, 16.6 mmol) and DMAP (2.4 g, 19.9 mmol) in 70 mL of anhydrous CH_2Cl_2 at 0 °C. The reaction mixture was stirred overnight at r.t. Then, the mixture was concentrated to 30 mL under reduced pressure, treated with 5% HCl (100 mL), and extracted with CH_2Cl_2 (3×50 mL). Combined organic layers were washed with water (30 mL) and dried over MgSO_4 . After solvent removal under vacuum, the crude acetylated intermediate was purified by flash chromatography using EtOAc /petroleum ether 1:3 as the eluent to yield 3.15 g of the corresponding chloroacetamide **33** as a white solid. Yield: 50%. ^1H NMR (400 MHz, CDCl_3) δ 8.55 (s, 1H, NH), 7.25 (s, 1H, H_{Ar}), 7.23 (s, 1H, H_{Ar}), 4.20 (s, 2H, CH_2), 3.46 (s, 3H, OMe), 2.36 (s, 3H, Me), 2.24 (s, 3H, Me); $^{13}\text{C}\{^1\text{H}\}$ NMR (101 MHz, CDCl_3) δ 163.8, 138.3, 137.4, 134.6, 131.2, 128.6, 122.7 (q, $^1J_{C,F} = 290$ Hz), 122.8, 84.9 (hept, $^2J_{C,F} = 28$ Hz), 54.9, 42.8, 21.3, 19.4; $^{19}\text{F}\{^1\text{H}\}$ NMR (376 MHz, CDCl_3) δ -69.57 (br.s). Elemental analysis calcd (%) for $\text{C}_{14}\text{H}_{14}\text{ClF}_6\text{NO}_2$: C, 44.52; H, 3.74; N, 3.71; found: C, 44.63; H, 3.91; N, 3.49.

General procedure for synthesis of aminoacetamides 34.

Compound **33** (1 g, 2.6 mmol) was dissolved in 20-fold excess of corresponding amine (52 mmol). The reaction mixture was allowed to stir at room temperature until full disappearance of starting

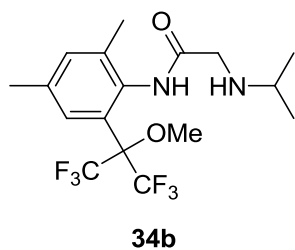
material (TLC control). Afterwards the mixture was treated with 10% solution of NaHCO₃ (10 mL) and extracted with ethylacetate (3 × 15 mL). Combined organic layers were washed with brine and water, dried over MgSO₄, filtered and concentrated under reduced pressure. The excess of starting amine was removed under high vacuum. The resulting solid residue was recrystallized from petroleum ether.

2-(tert-Butylamino)-N-[2-(1,1,1,3,3,3-hexafluoro-2-methoxypropan-2-yl)-4,6-dimethylphenyl]-acetamide (34a).



The reaction was finished in 3 days. Yield: 93%. ¹H NMR (400 MHz, CDCl₃) δ 9.62 (s, 1H, NHCO), 7.22 (s, 1H, H_{Ar}), 7.19 (s, 1H, H_{Ar}), 3.41 (s, 5H, CH₂, OMe), 2.34 (s, 3H, Me), 2.23 (s, 3H, Me), 1.52 (s, 1H, NH), 1.17 (s, 9H, CMe₃); ¹⁹F{¹H} NMR (376 MHz, CDCl₃) δ -68.57 (br.s), -70.35 (br.s). Elemental analysis calcd (%) for C₁₈H₂₄F₆N₂O₂: C, 52.17; H, 5.84; N, 6.76; found: C, 52.28; H, 5.88; N, 6.89.

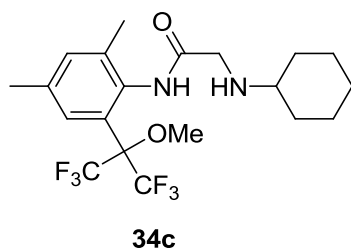
N-[2-(1,1,1,3,3,3-Hexafluoro-2-methoxypropan-2-yl)-4,6-dimethylphenyl]-2-(isopropylamino)-acetamide (34b).



The reaction was finished in 1 day. Yield: 92%. ¹H NMR (400 MHz, CDCl₃) δ 9.43 (s, 1H, NHCO), 7.22 (s, 1H, H_{Ar}), 7.20 (s, 1H, H_{Ar}), 3.53 (s, 2H, CH₂), 3.42 (s, 3H, OMe), 2.98 (hept, ³J_{H,H} = 6.0 Hz, 1H, CHMe₂), 2.34 (s, 3H, Me), 2.23 (s, 3H, Me), 1.17 (d, ³J_{H,H} = 6.2 Hz, 6H, CH(CH₃)₂); ¹⁹F{¹H} NMR (376 MHz, CDCl₃) δ -69.47 (br.s).

Elemental analysis calcd (%) for C₁₇H₂₂F₆N₂O₂: C, 51.00; H, 5.54; N, 7.00; found: C, 50.79; H, 5.63; N, 6.95.

2-(Cyclohexylamino)-N-[2-(1,1,1,3,3,3-hexafluoro-2-methoxypropan-2-yl)-4,6-dimethylphenyl]-acetamide (34c).



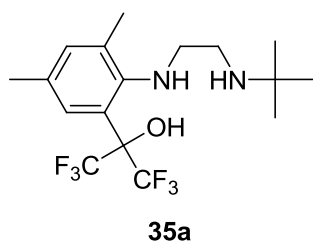
The reaction was finished in 1 day. Yield: 89%. ¹H NMR (400 MHz, CDCl₃) δ 9.46 (s, 2H, NHCO), 7.22 (s, 1H, H_{Ar}), 7.19 (s, 1H, H_{Ar}), 3.54 (s, 2H, CH₂), 3.42 (s, 3H, OMe), 2.62-2.50 (m, 1H, H_{Cy}), 2.34 (s, 3H, Me), 2.23 (s, 3H, Me), 2.01-1.09 (m, 10H, H_{Cy}); ¹⁹F{¹H} NMR (376 MHz, CDCl₃) δ -69.50 (s). Elemental analysis calcd (%) for C₂₀H₂₆F₆N₂O₂: C, 54.54; H, 5.95; N, 6.36; found: C, 54.32; H, 6.10; N, 6.32.

General procedure for synthesis of diamines 35.

Aminoacetamide **34** (2.3 mmol) was dissolved in anhydrous toluene (20 mL), then BH₃·SMe₂ (5.1 mL of 2 M solution THF, 10.2 mmol) was dissolved dropwise at room temperature under argon

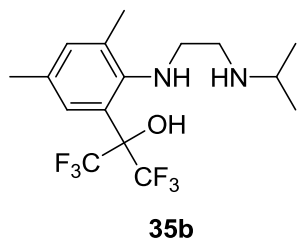
atmosphere. The resulting mixture was heated at 80 °C for 8 hours. After cooling to r.t., MeOH was slowly added until ceasing of gas evolution. Then, a 10% solution (20 mL) of HCl was added and resulting mixture was extracted with EtOAc (2 × 30 mL). The aqueous layer was separated, treated with NaHCO₃, and also extracted with EtOAc (2 × 20 mL). Combined organic layers were washed with a saturated solution of NaHCO₃, dried over MgSO₄, and concentrated under reduced pressure.

2-{2-[2-(tert-Butylamino)ethylamino]-3,5-dimethylphenyl}-1,1,1,3,3,3-hexafluoropropan-2-ol (35a).



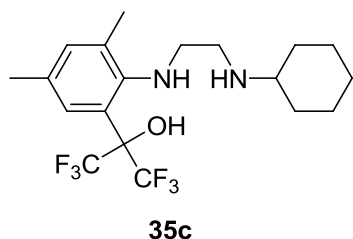
Yield: 53%. ¹H NMR (400 MHz, CDCl₃) δ 7.26 (s, 1H, *H*_{Ar}), 7.12 (s, 1H, *H*_{Ar}), 4.38 (br.s, 2H, NH), 2.86 (s, 4H, CH₂), 2.32 (s, 6H, Me), 1.12 (s, 9H, CMe₃); ¹³C{¹H} NMR (101 MHz, CDCl₃) δ 142.3, 135.6, 135.4, 133.6, 127.3 (hept, ³*J*_{C,F} = 3 Hz), 124.1, 123.6 (q, ¹*J*_{C,F} = 289 Hz), 80.5 (hept, ²*J*_{C,F} = 29 Hz), 50.7, 50.6, 41.5, 29.2, 21.3, 17.5; ¹⁹F{¹H} NMR (376 MHz, CDCl₃) δ -75.53 (s). Elemental analysis calcd (%) for C₁₇H₂₄F₆N₂O: C, 52.85; H, 6.26; N, 7.25; found: C, 52.84; H, 6.36; N, 6.98.

1,1,1,3,3,3-Hexafluoro-2-{2-[2-(isopropylamino)ethylamino]-3,5-dimethylphenyl}propan-2-ol (35b).



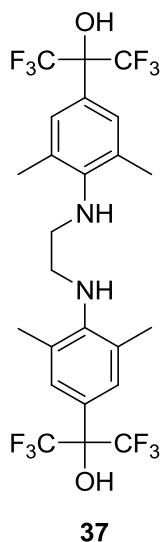
Yield: 42%. ¹H NMR (400 MHz, CDCl₃) δ 7.26 (s, 1H, *H*_{Ar}), 7.09 (s, 1H, *H*_{Ar}), 3.19 (br.s, 5H, CH₂, CHMe₂), 2.39 (s, 3H, Me), 2.31 (s, 3H, Me), 1.34 (d, ³*J*_{H,H} = 6.2 Hz, 6H, CH(CH₃)₂); ¹⁹F{¹H} NMR (376 MHz, CDCl₃) δ -75.48 (s). Elemental analysis calcd (%) for C₁₆H₂₂F₆N₂O: C, 51.61; H, 5.96; N, 7.52; found: C, 51.55; H, 6.24; N, 7.77.

2-{2-[2-(Cyclohexylamino)ethylamino]-3,5-dimethylphenyl}-1,1,1,3,3,3-hexafluoropropan-2-ol (35c).



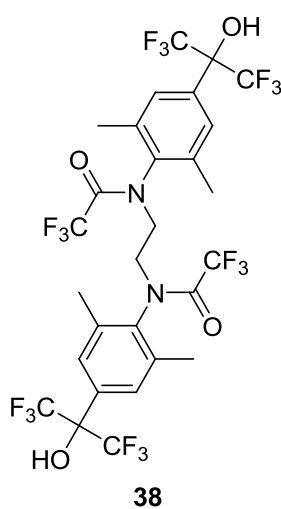
Yield: 49%. ¹H NMR (400 MHz, CDCl₃) δ 7.26 (s, 1H, *H*_{Ar}), 7.10 (s, 1H, *H*_{Ar}), 3.09 (s, 4H, CH₂), 2.73-2.63 (m, 1H, *H*_{Cy}), 2.36 (s, 3H, Me), 2.31 (s, 3H, Me), 2.09-1.08 (m, 10H, *H*_{Cy}); ¹³C{¹H} NMR (101 MHz, MeOH-*d*₄) δ 143.3, 138.0, 137.2, 134.8, 127.9, 124.9 (q, ¹*J*_{C,F} = 289 Hz), 124.9, 81.9 (hept, ²*J*_{C,F} = 28 Hz), 58.2, 48.3, 45.2, 31.8, 26.6, 25.8, 21.1, 17.7; ¹⁹F{¹H} NMR (376 MHz, CDCl₃) δ -75.46 (s). Elemental analysis calcd (%) for C₁₉H₂₆F₆N₂O: C, 55.33; H, 6.35; N, 6.79; found: C, 55.14; H, 6.51; N, 7.04.

Synthesis of 2,2'-{4,4'-[ethane-1,2-diylbis(azanediyl)]bis(3,5-dimethyl-4,1-phenylene)}bis(1,1,1,3,3,3-hexafluoropropan-2-ol) (37).



A mixture of diamine **36** (1.3 g, 4.8 mmol), hexafluoroacetone sesquihydrate (3.7 g, 19.2 mmol), and PTSA (5 mg, 0.03 mmol) was heated at 100 °C for 20 h. After cooling to r.t., water (50 mL) was added and the resulting mixture was extracted with EtOAc (3 × 30 mL). The combined organic layers were washed with water and brine and then dried over MgSO₄. The solvent was removed under reduced pressure, and the resulting solid was recrystallized from light petroleum and dried to give 2.5 g of **37** as white powder. Yield: 84%. ¹H NMR (300 MHz, CDCl₃): δ 7.29 (s, 4H, *H*_{Ar}), 3.49 (s, 2H, NH), 3.27 (s, 4H, CH₂), 2.29 (s, 12H, Me); ¹⁹F{¹H} NMR (282 MHz, CDCl₃): δ -75.58 (s). Elemental analysis calcd (%) for C₂₄H₂₄F₁₂N₂O₂: C 48.01, H 4.03, N 4.67; found: C 47.99, H 4.16, N 4.93.

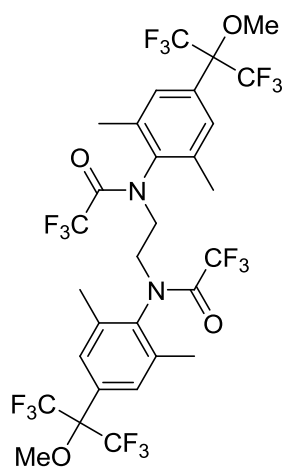
Synthesis of N,N'-(ethane-1,2-diyl)bis(2,2,2-trifluoro-N-(4-(1,1,1,3,3,3-hexafluoro-2-hydroxypropan-2-yl)-2,6-dimethylphenyl)acetamide) (38).



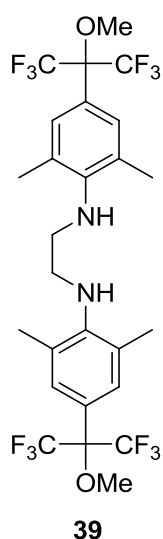
TFAA (0.86 g, 8.2 mmol) and pyridine (0.32 g, 8.2 mmol) were added sequentially to the solution of diamine **37** (2.45 g, 4.1 mmol) in diethyl ether (40 mL) at 0 °C. The reaction mixture was stirred at r.t. for 1 h, and then 5% aqueous solution of hydrochloric acid (20 mL) was added to the mixture. The organic layer was separated; the aqueous layer was extracted with diethyl ether (2 × 20 mL). Combined organic layers were washed with water, dried over MgSO₄, filtered, and concentrated under reduced pressure. The crude product was recrystallized from petroleum ether to yield 2.76 g of the corresponding bis-amide as a white solid.

Yield: 85%. ¹H NMR (300 MHz, Acetone-*d*₆): δ 7.63 (d, *J* = 6.3 Hz, 4H, *H*_{Ar}), 4.14 (s, 4H, CH₂), 2.41 (s, 12H, Me); ¹⁹F{¹H} NMR (282 MHz, Acetone-*d*₆): δ -70.81 (s), -74.77 (s). Elemental analysis calcd (%) for C₂₈H₂₂F₁₈N₂O₄: C 42.44, H 2.80, N 3.54; found: C 42.54, H 3.13, N 3.65.

Synthesis of N¹,N²-bis[4-(1,1,1,3,3,3-hexafluoro-2-methoxypropan-2-yl)-2,6-dimethylphenyl]ethane-1,2-diamine (39).

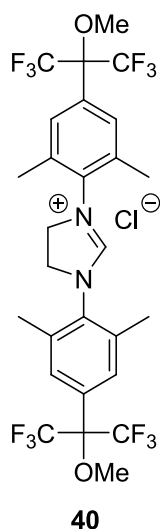


Bis-amide **38** (2.76 g, 3.5 mmol) was dissolved in dry DMF (40 mL). MeI (1.3 g, 9.1 mmol) and anhydrous K₂CO₃ (1.93 g, 14 mmol) were added, and the resulting mixture was heated for 1.5 h at 80 °C. Then, after cooling to r.t., 20 mL of brine was added. The resulting mixture was extracted with EtOAc (3 × 15 mL). Combined organic layers were dried over MgSO₄, filtered, and concentrated under reduced pressure to afford 2.17 g of corresponding methylated product as a white solid. Yield: 76%. ¹H NMR (300 MHz, CDCl₃): δ 7.36 (s, 4H, H_{Ar}), 4.03 (s, 4H, CH₂), 3.51 (s, 6H, OMe), 2.33 (s, 12H, Me); ¹³C{¹H} NMR (75 MHz, CDCl₃): δ 158.2 (q, ²J_{C,F} = 37 Hz), 139.4, 137.2, 129.4, 128.9, 122.3 (q, ¹J_{C,F} = 291 Hz), 115.8 (q, ¹J_{C,F} = 288 Hz), 83.5-81.9 (m), 54.7, 49.3, 18.8; ¹⁹F{¹H} NMR (282 MHz, CDCl₃): δ -70.61 (s). Elemental analysis calcd (%) for C₃₀H₂₆F₁₈N₂O₄: C 43.91, H 3.19, N 3.41; found: C 43.58, H 3.20, N 3.46.



Then a mixture of this product (2.17 g, 2.6 mmol), 18-crown-6 (5 mg, 0.02 mmol), and a solution of KOH (14.6 g, 260 mmol) in water (20 mL) was stirred vigorously and heated in DMSO (40 mL) at 130 °C for 1.5 h. After that water (50 mL) was added, and the crude product was extracted with EtOAc (3 × 30 mL). Combined organic layers were washed with 20 mL of water, dried over MgSO₄, and concentrated. The product was purified by column chromatography using EtOAc/petroleum ether (1:5) as eluent to yield 1.32 g of diamine **39** as a white powder. Yield: 80%. ¹H NMR (300 MHz, CDCl₃): δ 7.16 (s, 4H, H_{Ar}), 3.53 (br.s, 2H, NH), 3.47 (s, 6H, OMe), 3.30 (s, 4H, CH₂), 2.30 (s, 12H, Me); ¹⁹F{¹H} NMR (282 MHz, CDCl₃): δ -70.96 (s); ¹³C{¹H} NMR (126 MHz, CDCl₃): δ 147.6, 128.9, 128.8, 122.7 (q, ²J_{C,F} = 289 Hz), 120.1, 83.0 (quint, ¹J_{C,F} = 28 Hz), 54.2, 48.3, 19.2. Elemental analysis calcd (%) for C₂₆H₂₈F₁₂N₂O₂: C 49.69, H 4.49, N 4.46; found: C 49.84, H 4.74, N 4.37.

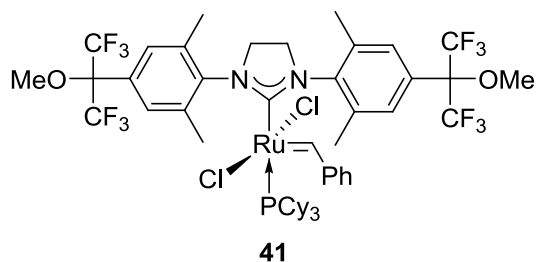
Synthesis of 1,3-bis[4-(1,1,1,3,3,3-hexafluoro-2-methoxypropan-2-yl)-2,6-dimethylphenyl]-4,5-dihydro-1H-imidazol-3-ium chloride (40).



Concentrated HCl (5 mL, 60 mmol) was added to the solution of diamine **39** (1.32 g, 2.1 mmol) in MeOH (60 mL) and stirred for 10 min. The solution was evaporated under reduced pressure. This operation was repeated two more times. To the resulting solid, CH(OEt)₃ (15 g, 100 mmol) was added, and the mixture was heated at 100 °C for 4 h. Then, the excess of CH(OEt)₃ was removed under vacuum and the resulting solid was washed with 20 mL of Et₂O. The recrystallization from EtOAc gave pure 1 g of imidazolium chloride **40** as a white solid. Yield: 71%. ¹H NMR (400 MHz, CDCl₃): δ 9.97 (s, 1H, NCHN), 7.30 (s, 4H, H_{Ar}), 4.54 (s, 4H, CH₂), 3.44 (s, 6H, OMe), 2.43 (s, 12H, Me); ¹⁹F{¹H} NMR (282 MHz, CDCl₃): δ -71.36 (s); ¹³C{¹H} NMR (101 MHz,

CDCl₃): δ 160.4, 136.4, 134.6, 130.4, 129.1, 122.2 (q, ¹J_{C,F} = 289 Hz), 82.5 (quint, ²J_{C,F} = 28 Hz), 54.7, 51.8, 18.5. Elemental analysis calcd (%) for C₂₇H₂₇ClF₁₂N₂O₂: C 48.05, H 4.03, N 4.15; found: C 47.74, H 4.10, N 4.07.

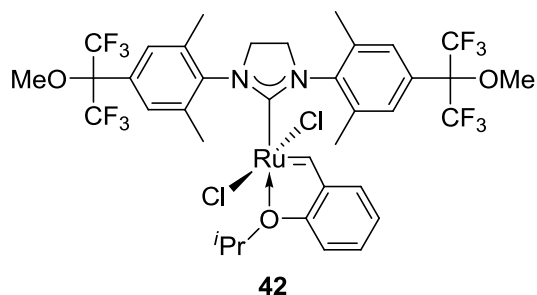
*Synthesis of benzylidene(dichloro){1,3-bis[4-(1,1,1,3,3,3-hexafluoro-2-methoxypropan-2-yl)-2,6-dimethylphenyl]-4,5-dihydroimidazol-2-ylidene}(tricyclohexylphosphine)ruthenium(II) (**41**).*



In a flame-dried Schlenk flask compound **40** (300 mg, 0.44 mmol) was mixed with 20 mL of anhydrous toluene. The mixture was cooled to 0 °C, degassed three times, and then KHMDS (460 μL of 1 M solution in THF, 0.46 mmol) was added to the

mixture under an argon atmosphere. The reaction mixture was stirred for 30 min; then **G-I** (305 mg, 0.37 mmol) was added and the mixture was stirred for 2 h at room temperature. After removal of volatiles, the residue was purified by column chromatography on silica gel in a gradient manner using EtOAc/petroleum ether (1:8-1:3) as eluent under an argon atmosphere to yield 130 mg of complex **41** as a brown solid. Yield: 30%. ¹H NMR (600 MHz, C₆D₆): δ 19.55 (s, 1H, CHPh), 8.33 (br.s, 2H, H_{Ar}), 7.59 (s, 2H, H_{Ar}), 7.15-6.92 (m, 5H, H_{Ar}), 3.30 (s, 3H, OMe), 3.10 (t, ³J_{H,H} = 10.2 Hz, 2H, CH₂), 3.01 (s, 3H, OMe), 2.93 (t, ³J_{H,H} = 10.2 Hz, 2H, CH₂), 2.76 (s, 6H, Me), 2.43 (s, 6H, Me), 2.04 (q, J_{H,P} = 11.7 Hz, 3H, PCy₃), 1.68-1.50 (m, 16H, PCy₃), 1.37-1.26 (m, 6H, PCy₃), 1.11-1.00 (m, 8H, PCy₃); ¹⁹F{¹H} NMR (376 MHz, C₆D₆): δ -70.17 (s); ³¹P{¹H} NMR (162 MHz, C₆D₆): δ 20.93 (s); ¹³C{¹H} NMR (151 MHz, C₆D₆): δ 299.7 (br.s), 220.2 (d, ²J_{C,P} = 79 Hz), 152.8, 152.7, 142.2, 141.0, 139.9, 138.8, 123.3 (d, ¹J_{C,F} = 290 Hz), 123.1 (d, ¹J_{C,F} = 289 Hz), 83.4 (m), 54.5, 54.3, 51.3, 35.9, 35.5, 33.0 (d, ¹J_{C,P} = 16 Hz), 29.1, 27.9 (d, ³J_{C,P} = 10 Hz), 27.2 (d, ²J_{C,P} = 12 Hz), 20.8, 19.4. Elemental analysis calcd (%) for C₅₂H₆₅Cl₂F₁₂N₂O₂PRu: C 52.88, H 5.55, N 2.37; found: C 53.04, H 5.56, N 2.44.

Synthesis of dichloro{1,3-bis[4-(1,1,1,3,3,3-hexafluoro-2-methoxypropan-2-yl)-2,6-dimethylphenyl]-4,5-dihydroimidazol-2-ylidene}(2-isopropoxybenzylidene)ruthenium(II) (**42**).



In a flame-dried Schlenk flask compound **40** (360 mg, 0.54 mmol) was mixed with 20 mL of anhydrous toluene. The mixture was cooled to 0 °C and degassed three times; then KHMDS (560 μ L of 1 M solution in THF, 0.56 mmol) was added to the mixture under an argon atmosphere. The reaction mixture was stirred for 30 min at r.t.; then **HG-I** (270 mg, 0.45 mmol) was added and mixture was stirred for 1 h at 60 °C. After removal of volatiles, the residue was purified by column chromatography on silica gel using EtOAc/petroleum ether (1:3) as eluent to yield 140 mg of complex **42** as a green solid. Suitable for X-ray crystals were grown by slow diffusion of hexane vapors in CH_2Cl_2 solution. Yield: 32%. ^1H NMR (600 MHz, C_6D_6): δ 16.53 (s, 1H, CHAr), 7.61 (s, 4H, H_{Ar}), 7.12 (d, $J_{\text{H,H}} = 7.6$ Hz, 1H, H_{Ar}), 7.07 (t, $J_{\text{H,H}} = 7.8$ Hz, 1H, H_{Ar}), 6.65 (t, $J_{\text{H,H}} = 7.5$ Hz, 1H, H_{Ar}), 6.29 (d, $J_{\text{H,H}} = 8.2$ Hz, 1H, H_{Ar}), 4.45 (hept, $^3J_{\text{H,H}} = 6.1$ Hz, 1H, CHMe_2), 3.26 (s, 6H, OMe), 3.22 (s, 4H, CH_2), 2.49 (s, 12H, Me), 1.27 (d, $^3J_{\text{H,H}} = 6.2$ Hz, 6H, $\text{CH}(\text{CH}_3)_2$); $^{19}\text{F}\{^1\text{H}\}$ NMR (282 MHz, C_6D_6): δ -70.14 (s); $^{13}\text{C}\{^1\text{H}\}$ NMR (151 MHz, C_6D_6): δ 301.3, 213.2, 152.8, 145.6, 140.9, 129.7, 128.9, 128.8, 128.4, 123.3 (q, $^2J_{\text{C,F}} = 290$ Hz), 122.4, 122.3, 113.3, 83.5 (quint, $^1J_{\text{C,F}} = 29$ Hz), 75.3, 54.3, 51.0, 21.4. Elemental analysis calcd (%) for $\text{C}_{37}\text{H}_{38}\text{Cl}_2\text{F}_{12}\text{N}_2\text{O}_3\text{Ru}$: C 46.36, H 4.00, N 2.92; found: C 46.65, H 4.21, N 2.94. CCDC 1030290 contains the supplementary crystallographic data for this compound.

3.3. Catalysis

RCM of diethyl diallylmalonate or diethyl allylmethylmalonate.

A flame-dried Schlenk flask was charged with solution of catalyst (4.0 μ mol, 1.0 mol.%) and dodecane (10 μ L) in anhydrous degassed CH_2Cl_2 (4 mL) under argon atmosphere. The reaction mixture was stirred at 30 °C before starting material (0.4 mmol, 0.1 M) was added via syringe. Data points were collected over an appropriate period of time by taking the probes (\sim 0.4 mL) from the reaction mixture. The reaction was quenched using excess of ethyl vinyl ether (0.5 mL). The conversion to RCM product was determined by GC.

CM of allylbenzene with cis-1,4-diacetoxy-2-butene.

A flame-dried Schlenk flask was charged with allylbenzene (94.6 mg, 0.8 mmol, 0.2 M), *cis*-1,4-diacetoxy-2-butene (275.5 mg, 1.6 mmol, 0.4 M) and tetradecane (10 μ L) in anhydrous degassed CH_2Cl_2 (4 mL) under argon atmosphere. The mixture was stirred at 25 °C before the catalyst (0.02 mmol, 2.5 mol.%) was added. Data points were collected over an appropriate period of time by

taking the probes (~0.4 mL) from the reaction mixture. The reaction was quenched using excess of ethyl vinyl ether (0.5 mL). The conversion to CM product was determined by GC.

REFERENCES

- (1) Calderon, N.; Chen, H. Y.; Scott, K. W. Olefin Metathesis - A Novel Reaction for Skeletal Transformations of Unsaturated Hydrocarbons. *Tetrahedron Lett.* **1967**, 8 (34), 3327–3329.
- (2) Mol, J. C. Industrial Applications of Olefin Metathesis. *J. Mol. Catal. A Chem.* **2004**, 213 (1), 39–45.
- (3) Morzycki, J. W. Application of Olefin Metathesis in the Synthesis of Steroids. *Steroids* **2011**, 76 (10), 949–966.
- (4) Herbert, M. B.; Marx, V. M.; Pederson, R. L.; Grubbs, R. H. Concise Syntheses of Insect Pheromones Using Z-Selective Cross Metathesis. *Angew. Chem. Int. Ed.* **2013**, 52 (1), 310–314.
- (5) Mol, J. C. Application of Olefin Metathesis in Oleochemistry: An Example of Green Chemistry. *Green Chem.* **2002**, 4 (1), 5–13.
- (6) Slugovc, C. Industrial Applications of Olefin Metathesis Polymerization. In *Olefin Metathesis*; John Wiley & Sons, Inc., 2014; pp 329–333.
- (7) Vougioukalakis, G. C. Ruthenium-Benzylidene Olefin Metathesis Catalysts. In *Olefin Metathesis*; John Wiley & Sons, Inc., 2014; pp 397–416.
- (8) Schrock, R. R. High-Oxidation State Molybdenum and Tungsten Complexes Relevant to Olefin Metathesis. In *Handbook of Metathesis*; Wiley-VCH Verlag GmbH & Co. KGaA, 2015; pp 1–32.
- (9) Trnka, T. M.; Grubbs, R. H. The Development of L₂X₂RuCHR Olefin Metathesis Catalysts: An Organometallic Success Story. *Acc. Chem. Res.* **2001**, 34 (1), 18–29.
- (10) Nguyen, S. T.; Johnson, L. K.; Grubbs, R. H.; Ziller, J. W. Ring-Opening Metathesis Polymerization (ROMP) of Norbornene by a Group VIII Carbene Complex in Protic Media. *J. Am. Chem. Soc.* **1992**, 114 (10), 3974–3975.
- (11) Vougioukalakis, G. C.; Grubbs, R. H. Ruthenium-Based Heterocyclic Carbene-Coordinated Olefin Metathesis Catalysts. *Chem. Rev.* **2010**, 110 (3), 1746–1787.
- (12) Jean-Louis Hérisson, P.; Chauvin, Y. Catalyse de Transformation Des Oléfines Par Les Complexes Du Tungstène. II. Télomérisation Des Oléfines Cycliques En Présence D'oléfines Acycliques. *Makromol. Chem.* **1971**, 141 (1), 161–176.
- (13) Lam, J. K.; Zhu, C.; Bukhryakov, K. V; Müller, P.; Hoveyda, A.; Schrock, R. R. Synthesis and Evaluation of Molybdenum and Tungsten Monoaryloxide Halide Alkylidene Complexes for Z-Selective Cross-Metathesis of Cyclooctene and Z-1,2-Dichloroethylene. *J. Am. Chem. Soc.* **2016**, 138 (48), 15774–15783.
- (14) Koh, M. J.; Nguyen, T. T.; Lam, J. K.; Torker, S.; Hyvl, J.; Schrock, R. R.; Hoveyda, A. H.

- Molybdenum Chloride Catalysts for Z-Selective Olefin Metathesis Reactions. *Nature* **2017**, *542* (7639), 80–85.
- (15) Marx, V. M.; Rosebrugh, L. E.; Herbert, M. B.; Grubbs, R. H. Cyclometalated Ruthenium Alkylidene Complexes: A Powerful Family of Z-Selective Olefin Metathesis Catalysts BT - Ruthenium in Catalysis; Dixneuf, P. H., Bruneau, C., Eds.; Springer International Publishing: Cham, 2014; pp 1–17.
- (16) Plenio, H. The Coordination Chemistry of the CF Unit in Fluorocarbons. *Chem. Rev.* **1997**, *97* (8), 3363–3384.
- (17) Fustero, S.; Simón-Fuentes, A.; Barrio, P.; Haufe, G. Olefin Metathesis Reactions with Fluorinated Substrates, Catalysts, and Solvents. *Chem. Rev.* **2015**, *115* (2), 871–930.
- (18) Horváth, I. T.; Curran, D. P.; Gladysz, J. A. Fluorous Chemistry: Scope and Definition. In *Handbook of Fluorous Chemistry*; Wiley-VCH Verlag GmbH & Co. KGaA, 2005; pp 1–4.
- (19) Füstner, A.; Ackermann, L.; Gabor, B.; Goddard, R.; Lehmann, C. W.; Mynott, R.; Stelzer, F.; Thiel, O. R. Comparative Investigation of Ruthenium-Based Metathesis Catalysts Bearing *N*-Heterocyclic Carbene (NHC) Ligands. *Chem. – A Eur. J.* **2001**, *7* (15), 3236–3253.
- (20) Gardiner, M. G.; Herrmann, W. A.; Reisinger, C.-P.; Schwarz, J.; Spiegler, M. Dicationic Chelating *N*-Heterocyclic Carbene Complexes of Palladium: New Catalysts for the Copolymerisation of C₂H₄ and CO. *J. Organomet. Chem.* **1999**, *572* (2), 239–247.
- (21) Van Veldhuizen, J. J.; Gillingham, D. G.; Garber, S. B.; Kataoka, O.; Hoveyda, A. H. Chiral Ru-Based Complexes for Asymmetric Olefin Metathesis: Enhancement of Catalyst Activity through Steric and Electronic Modifications. *J. Am. Chem. Soc.* **2003**, *125* (41), 12502–12508.
- (22) Ritter, T.; Day, M. W.; Grubbs, R. H. Rate Acceleration in Olefin Metathesis through a Fluorine–Ruthenium Interaction. *J. Am. Chem. Soc.* **2006**, *128* (36), 11768–11769.
- (23) Berlin, J. M.; Campbell, K.; Ritter, T.; Funk, T. W.; Chlenov, A.; Grubbs, R. H. Ruthenium-Catalyzed Ring-Closing Metathesis to Form Tetrasubstituted Olefins. *Org. Lett.* **2007**, *9* (7), 1339–1342.
- (24) Siano, V.; D’Auria, I.; Grisi, F.; Costabile, C.; Longo, P. Activity and Stereoselectivity of Ru-Based Catalyst Bearing a Fluorinated Imidazolium Ligand. *Cent. Eur. J. Chem.* **2011**, *9*, 605–609.
- (25) Vougioukalakis, G. C.; Grubbs, R. H. Ruthenium Olefin Metathesis Catalysts Bearing an *N*-Fluorophenyl-*N*-Mesityl-Substituted Unsymmetrical *N*-Heterocyclic Carbene. *Organometallics* **2007**, *26* (9), 2469–2472.
- (26) Vougioukalakis, G. C.; Grubbs, R. H. Ruthenium-Based Olefin Metathesis Catalysts

- Coordinated with Unsymmetrical *N*-Heterocyclic Carbene Ligands: Synthesis, Structure, and Catalytic Activity. *Chem. – A Eur. J.* **2008**, *14* (25), 7545–7556.
- (27) Leuthäuser, S.; Schmidts, V.; Thiele, C. M.; Plenio, H. π -Face Donor Properties of *N*-Heterocyclic Carbenes in Grubbs II Complexes. *Chem. – A Eur. J.* **2008**, *14* (18), 5465–5481.
- (28) Gawin, R.; Pieczykolan, M.; Malińska, M.; Woźniak, K.; Grela, K. Testing New Ruthenium Complexes Bearing Chiral 1,2,4-Triazol-5-ylidene-Ligands as Catalysts for Asymmetric Olefin Metathesis. *Synlett* **2013**, *24* (10), 1250–1254.
- (29) Ablialimov, O.; Kędziorek, M.; Malińska, M.; Woźniak, K.; Grela, K. Synthesis, Structure, and Catalytic Activity of New Ruthenium(II) Indenylidene Complexes Bearing Unsymmetrical *N*-Heterocyclic Carbenes. *Organometallics* **2014**, *33* (9), 2160–2171.
- (30) Piola, L.; Nahra, F.; Nolan, S. P. Olefin Metathesis in Air. *Beilstein J. Org. Chem.* **2015**, *11*, 2038–2056.
- (31) Kvíčala, J.; Schindler, M.; Kelbichová, V.; Babuněk, M.; Rybáčková, M.; Kvíčalová, M.; Cvačka, J.; Březinová, A. Experimental and Theoretical Study of Hoveyda–Grubbs Catalysts Modified by Perfluorohexyl Ponytail in the Alkoxybenzylidene Ligand. *J. Fluor. Chem.* **2013**, *153*, 12–25.
- (32) Skalický, M.; Skalická, V.; Paterová, J.; Rybáčková, M.; Kvíčalová, M.; Cvačka, J.; Březinová, A.; Kvíčala, J. Ag Complexes of NHC Ligands Bearing Polyfluoroalkyl And/or Polyfluoropolyalkoxy Ponytails. Why Are Polyethers More Fluorous Than Alkyls? *Organometallics* **2012**, *31* (4), 1524–1532.
- (33) Szczepaniak, G.; Kosinski, K.; Grela, K. Towards “cleaner” olefin Metathesis: Tailoring the NHC Ligand of Second Generation Ruthenium Catalysts to Afford Auxiliary Traits. *Green Chem.* **2014**, *16* (10), 4474–4492.
- (34) Hošek, J.; Rybáčková, M.; Čejka, J.; Cvačka, J.; Kvíčala, J. Synthesis of Heavy Fluorous Ruthenium Metathesis Catalysts Using the Stereoselective Addition of Polyfluoroalkyllithium to Sterically Hindered Diimines. *Organometallics* **2015**, *34* (13), 3327–3334.
- (35) Engl, P. S.; Fedorov, A.; Copéret, C.; Togni, A. *N*-Trifluoromethyl NHC Ligands Provide Selective Ruthenium Metathesis Catalysts. *Organometallics* **2016**, *35* (6), 887–893.
- (36) Endo, K.; Grubbs, R. H. Chelated Ruthenium Catalysts for *Z*-Selective Olefin Metathesis. *J. Am. Chem. Soc.* **2011**, *133* (22), 8525–8527.
- (37) Khan, R. K. M.; Torker, S.; Hoveyda, A. H. Readily Accessible and Easily Modifiable Ru-Based Catalysts for Efficient and *Z*-Selective Ring-Opening Metathesis Polymerization and Ring-Opening/Cross-Metathesis. *J. Am. Chem. Soc.* **2013**, *135* (28), 10258–10261.

- (38) Koh, M. J.; Khan, R. K. M.; Torker, S.; Yu, M.; Mikus, M. S.; Hoveyda, A. H. High-Value Alcohols and Higher-Oxidation-State Compounds by Catalytic Z-Selective Cross-Metathesis. *Nature* **2015**, *517* (7533), 181–186.
- (39) Hartung Jr., J.; Quigley, B. L.; Dornan, P. K.; Grubbs, R. H. Selective Olefin Metathesis with Cyclometalated Ruthenium Complexes. US patent 2016/0185684 A1.
- (40) Johns, A. M.; Ahmed, T. S.; Jackson, B. W.; Grubbs, R. H.; Pederson, R. L. High Trans Kinetic Selectivity in Ruthenium-Based Olefin Cross-Metathesis through Stereoretention. *Org. Lett.* **2016**, *18* (4), 772–775.
- (41) Ahmed, T. S.; Grubbs, R. H. Fast-Initiating, Ruthenium-Based Catalysts for Improved Activity in Highly E-Selective Cross Metathesis. *J. Am. Chem. Soc.* **2017**, *139* (4), 1532–1537.
- (42) Małecki, P.; Gajda, K.; Ablialimov, O.; Malińska, M.; Gajda, R.; Woźniak, K.; Kajetanowicz, A.; Grela, K. Hoveyda–Grubbs-Type Precatalysts with Unsymmetrical N-Heterocyclic Carbenes as Effective Catalysts in Olefin Metathesis. *Organometallics* **2017**, *36* (11), 2153–2166.
- (43) Schwab, P.; Grubbs, R. H.; Ziller, J. W. Synthesis and Applications of RuCl₂(CHR^c)(PR₃)₂: The Influence of the Alkylidene Moiety on Metathesis Activity. *J. Am. Chem. Soc.* **1996**, *118* (1), 100–110.
- (44) Zaja, M.; Connon, S. J.; Dunne, A. M.; Rivard, M.; Buschmann, N.; Jiricek, J.; Blechert, S. Ruthenium Olefin Metathesis Catalysts with Modified Styrene Ethers: Influence of Steric and Electronic Effects. *Tetrahedron* **2003**, *59* (34), 6545–6558.
- (45) Yao, Q.; Zhang, Y. Poly(fluoroalkyl acrylate)-Bound Ruthenium Carbene Complex: A Fluorous and Recyclable Catalyst for Ring-Closing Olefin Metathesis. *J. Am. Chem. Soc.* **2004**, *126* (1), 74–75.
- (46) Matsugi, M.; Curran, D. P. Synthesis, Reaction, and Recycle of Light Fluorous Grubbs–Hoveyda Catalysts for Alkene Metathesis. *J. Org. Chem.* **2005**, *70* (5), 1636–1642.
- (47) Maruoka, K.; Sano, H.; Fukutani, Y.; Yamamoto, H. Organoaluminium-Induced Addition of Polyhalomethane to Olefins. *Chem. Lett.* **1985**, *14* (11), 1689–1692.
- (48) Moura-Letts, G.; Curran, D. P. Selective Synthesis of (2Z,4E)-Dienyl Esters by Ene–Diene Cross Metathesis. *Org. Lett.* **2007**, *9* (1), 5–8.
- (49) Leach, S. G.; Cordier, C. J.; Morton, D.; McKiernan, G. J.; Warriner, S.; Nelson, A. A Fluorous-Tagged Linker from Which Small Molecules Are Released by Ring-Closing Metathesis. *J. Org. Chem.* **2008**, *73* (7), 2753–2759.
- (50) Morton, D.; Leach, S.; Cordier, C.; Warriner, S.; Nelson, A. Synthesis of Natural-Product-Like Molecules with Over Eighty Distinct Scaffolds. *Angew. Chem. Int. Ed.* **2009**, *48* (1),

104–109.

- (51) Michalek, F.; Bannwarth, W. Application of a Grubbs–Hoveyda Metathesis Catalyst Noncovalently Immobilized by Fluorous–Fluorous Interactions. *Helv. Chim. Acta* **2006**, *89* (5), 1030–1037.
- (52) Hensle, E. M.; Tobis, J.; Tiller, J. C.; Bannwarth, W. Ring-Closing Olefin Metathesis in the Aqueous Phase of Amphiphilic Conetworks Consisting of Fluorophilic and Hydrophilic Compartments. *J. Fluor. Chem.* **2008**, *129* (10), 968–973.
- (53) Andrushko, V.; Schwinn, D.; Tzschucke, C. C.; Michalek, F.; Horn, J.; Mössner, C.; Bannwarth, W. Tris(perfluoroalkyl)silyl Entities as Unexpectedly Potent Tags for the Noncovalent Immobilization of Catalysts by Fluorous–Fluorous Interactions: Application to the Synthesis of Several Perfluoro-Tagged Ligands. *Helv. Chim. Acta* **2005**, *88* (5), 936–949.
- (54) Lim, J.; Lee, S. S.; Ying, J. Y. Silica-Supported Catalysts for Ring-Closing Metathesis: Effects of Linker Group and Microenvironment on Recyclability. *Chem. Commun.* **2008**, No. 36, 4312–4314.
- (55) Rix, D.; Caijo, F.; Laurent, I.; Boeda, F.; Clavier, H.; Nolan, S. P.; Mauduit, M. Aminocarbonyl Group Containing Hoveyda–Grubbs-Type Complexes: Synthesis and Activity in Olefin Metathesis Transformations. *J. Org. Chem.* **2008**, *73* (11), 4225–4228.
- (56) Clavier, H.; Caijo, F.; Borré, E.; Rix, D.; Boeda, F.; Nolan, S. P.; Mauduit, M. Towards Long-Living Metathesis Catalysts by Tuning the *N*-Heterocyclic Carbene (NHC) Ligand on Trifluoroacetamide-Activated Boomerang Ru Complexes. *Eur. J. Org. Chem.* **2009**, *2009* (25), 4254–4265.
- (57) Mauduit, M.; Laurent, I.; Clavier, H. Complexes Catalytiques a Base de Ruthenium et Utilisation de Tels Complexes Pour La Metathese D’olefines. WO patent 2008/065187 A1.
- (58) Mohapatra, D. K.; Somaiah, R.; Rao, M. M.; Caijo, F.; Mauduit, M.; Yadav, J. S. Catalytic Activity Studies of Aminocarbonyl Group Containing Hoveyda-Grubbs-Type Complexes for the Syntheses of Herbarumin I and Stagonolide A. *Synlett* **2010**, *2010* (8), 1223–1226.
- (59) Borré, E.; Dinh, T. H.; Caijo, F.; Crévisy, C.; Mauduit, M. Terpenic Compounds as Renewable Sources of Raw Materials for Cross-Metathesis. *Synthesis* **2011**, *2011* (13), 2125–2130.
- (60) Hemelaere, R.; Caijo, F.; Mauduit, M.; Carreaux, F.; Carboni, B. Ruthenium-Catalyzed One-Pot Synthesis of (*E*)-(2-Arylvinyl)boronates through an Isomerization/Cross-Metathesis Sequence from Allyl-Substituted Aromatics. *Eur. J. Org. Chem.* **2014**, *2014* (16), 3328–3333.
- (61) Bonin, H.; Keraani, A.; Dubois, J.-L.; Brandhorst, M.; Fischmeister, C.; Bruneau, C. Cross-

- Metathesis of Fatty Acid Methyl Esters with Acrolein: An Entry to a Variety of Bifunctional Compounds. *Eur. J. Lipid Sci. Technol.* **2015**, *117* (2), 209–216.
- (62) Bidange, J.; Dubois, J.-L.; Couturier, J.-L.; Fischmeister, C.; Bruneau, C. Ruthenium Catalyzed Ethenolysis of Renewable Oleonitrile. *Eur. J. Lipid Sci. Technol.* **2014**, *116* (11), 1583–1589.
- (63) Chevalley, A.; Prunet, J.; Mauduit, M.; Férézou, J.-P. Model Studies for a Ring-Closing Metathesis Approach to the Bafilomycin Macrolactone Core from a 2,2-Dimethoxy Tetraenic Ester Precursor. *Eur. J. Org. Chem.* **2013**, *2013* (36), 8265–8278.
- (64) Rouen, M.; Borre, E.; Falivene, L.; Toupet, L.; Berthod, M.; Cavallo, L.; Olivier-Bourbigou, H.; Mauduit, M. Cycloalkyl-Based Unsymmetrical Unsaturated (*U2*)-NHC Ligands: Flexibility and Dissymmetry in Ruthenium-Catalysed Olefin Metathesis. *Dalton Trans.* **2014**, *43* (19), 7044–7049.
- (65) Nasrallah, H.; Pagnoux, A.; Didier, D.; Magnier, C.; Toupet, L.; Guillot, R.; Crévisy, C.; Mauduit, M.; Schulz, E. Immobilization of an Anthracene-Tagged Ruthenium Complex on a 2,4,7-Trinitrofluoren-9-one-Grafted Silica: Efficiency and Recyclability in Olefin Metathesis Reactions. *Eur. J. Org. Chem.* **2014**, *2014* (35), 7781–7787.
- (66) Solodenko, W.; Doppiu, A.; Frankfurter, R.; Vogt, C.; Kirschning, A. Silica Immobilized Hoveyda Type Pre-Catalysts: Convenient and Reusable Heterogeneous Catalysts for Batch and Flow Olefin Metathesis. *Aust. J. Chem.* **2013**, *66* (2), 183–191.
- (67) Nasrallah, H.; Dragoe, D.; Magnier, C.; Crévisy, C.; Mauduit, M.; Schulz, E. Direct Immobilization of Ru-Based Catalysts on Silica: Hydrogen Bonds as Non-Covalent Interactions for Recycling in Metathesis Reactions. *ChemCatChem* **2015**, *7* (16), 2493–2500.
- (68) Nasrallah, H.; Germain, S.; Queval, P.; Bouvier, C.; Mauduit, M.; Crévisy, C.; Schulz, E. Non Covalent Immobilization of Pyrene-Tagged Ruthenium Complexes onto Graphene Surfaces for Recycling in Olefin Metathesis Reactions. *J. Mol. Catal. A Chem.* **2016**, *425*, 136–146.
- (69) Ginzburg, Y.; Anaby, A.; Vidavsky, Y.; Diesendruck, C. E.; Ben-Asuly, A.; Goldberg, I.; Lemcoff, N. G. Widening the Latency Gap in Chelated Ruthenium Olefin Metathesis Catalysts. *Organometallics* **2011**, *30* (12), 3430–3437.
- (70) Ben-Asuly, A.; Tzur, E.; Diesendruck, C. E.; Sigalov, M.; Goldberg, I.; Lemcoff, N. G. A Thermally Switchable Latent Ruthenium Olefin Metathesis Catalyst. *Organometallics* **2008**, *27* (5), 811–813.
- (71) Pietraszuk, C.; Rogalski, S.; Powała, B.; Miętkiewski, M.; Kubicki, M.; Spólnik, G.; Danikiewicz, W.; Woźniak, K.; Pazio, A.; Szadkowska, A.; Kozłowska, A.; Grela, K.

- Ruthenium–Amido Complexes: Synthesis, Structure, and Catalytic Activity in Olefin Metathesis. *Chem. – A Eur. J.* **2012**, *18* (21), 6465–6469.
- (72) Matsugi, M. Simplification of an Organic Synthetic Process Based on a Light Fluorous Strategy. *J. Synth. Org. Chem. Japan* **2008**, *66* (7), 694–704.
- (73) Matsugi, M.; Kobayashi, Y.; Suzumura, N.; Tsuchiya, Y.; Shioiri, T. Synthesis and RCM Reactions Using a Recyclable Grubbs–Hoveyda Metathesis Catalyst Activated by a Light Fluorous Tag. *J. Org. Chem.* **2010**, *75* (22), 7905–7908.
- (74) Matsugi, M.; Hasegawa, M.; Hasebe, S.; Takai, S.; Suyama, R.; Wakita, Y.; Kudo, K.; Imamura, H.; Hayashi, T.; Haga, S. Direct Perfluoroalkylation of Non-Activated Aromatic C–H Bonds of Phenols. *Tetrahedron Lett.* **2008**, *49* (26), 4189–4191.
- (75) Kita, Y.; Gotanda, K.; Murata, K.; Suemura, M.; Sano, A.; Yamaguchi, T.; Oka, M.; Matsugi, M. Practical Radical Additions under Mild Conditions Using 2,2′-Azobis(2,4-dimethyl-4-methoxyvaleronitrile) [V-70] as an Initiator. *Org. Process Res. Dev.* **1998**, *2* (4), 250–254.
- (76) Borré, E.; Caijo, F.; Crévisy, C.; Mauduit, M. New Library of Aminosulfonyl-Tagged Hoveyda–Grubbs Type Complexes: Synthesis, Kinetic Studies and Activity in Olefin Metathesis Transformations. *Beilstein J. Org. Chem.* **2010**, *6*, 1159–1166.
- (77) Caijo, F.; Mauduit, M. Novel Stable and Highly Tunable Metathesis Catalysts. WO patent 2012/013208 A1.
- (78) Caijo, F.; Tripoteau, F.; Bellec, A.; Crévisy, C.; Basle, O.; Mauduit, M.; Briel, O. Screening of a Selection of Commercially Available Homogeneous Ru-Catalysts in Valuable Olefin Metathesis Transformations. *Catal. Sci. Technol.* **2013**, *3* (2), 429–435.
- (79) Borré, E.; Rouen, M.; Laurent, I.; Magrez, M.; Caijo, F.; Crévisy, C.; Solodenko, W.; Toupet, L.; Frankfurter, R.; Vogt, C.; Kirschning, A.; Mauduit, M. A Fast-Initiating Ionically Tagged Ruthenium Complex: A Robust Supported Pre-Catalyst for Batch-Process and Continuous-Flow Olefin Metathesis. *Chem. – A Eur. J.* **2012**, *18* (51), 16369–16382.
- (80) Nelson, D. J.; Queval, P.; Rouen, M.; Magrez, M.; Toupet, L.; Caijo, F.; Borré, E.; Laurent, I.; Crévisy, C.; Baslé, O.; Mauduit, M.; Percy, J. M. Synergic Effects Between *N*-Heterocyclic Carbene and Chelating Benzylidene–Ether Ligands Toward the Initiation Step of Hoveyda–Grubbs Type Ru Complexes. *ACS Catal.* **2013**, *3* (2), 259–264.
- (81) Olszewski, T. K.; Bieniek, M.; Skowerski, K.; Grela, K. A New Tool in the Toolbox: Electron-Withdrawing Group Activated Ruthenium Catalysts for Olefin Metathesis. *Synlett* **2013**, *24* (8), 903–919.
- (82) Michrowska, A.; Bujok, R.; Harutyunyan, S.; Sashuk, V.; Dolgonos, G.; Grela, K. Nitro-Substituted Hoveyda–Grubbs Ruthenium Carbenes: Enhancement of Catalyst Activity

- through Electronic Activation. *J. Am. Chem. Soc.* **2004**, *126* (30), 9318–9325.
- (83) Kobayashi, Y.; Inukai, S.; Kondo, N.; Watanabe, T.; Sugiyama, Y.; Hamamoto, H.; Shioiri, T.; Matsugi, M. A Medium Fluorous Grubbs–Hoveyda 2nd Generation Catalyst for Phase Transfer Catalysis of Ring Closing Metathesis Reactions. *Tetrahedron Lett.* **2015**, *56* (11), 1363–1366.
- (84) Kobayashi, Y.; Suzumura, N.; Tsuchiya, Y.; Goto, M.; Sugiyama, Y.; Shioiri, T.; Matsugi, M. Grubbs–Hoveyda Second-Generation Catalysts Activated by the Introduction of a Light Fluorous Tag onto the Bidentate Ligands. *Synthesis* **2017**, *49* (8), 1796–1807.
- (85) Bruce, M. I. Transition Metal Complexes Containing Allenylidene, Cumulenylidene, and Related Ligands. *Chem. Rev.* **1998**, *98* (8), 2797–2858.
- (86) Holtcamp, M. W.; Faler, C. A.; Huff, C. P.; Bedoya, M. S.; Hagadorn, J. R. Metathesis Catalyst and Process for Use Thereof. WO patent 2012/013208 A1.
- (87) Xie, Y.; Yuan, Y.; Mousavi, B.; Cai, Y.; Kai, C.; Lu, Y.; Yusubov, M.; Verpoort, F. Oxygen-Chelated Indenylidene Ruthenium Catalysts for Olefin Metathesis. *Appl. Organomet. Chem.* **2015**, *29* (9), 573–579.
- (88) Kabro, A.; Ghattas, G.; Roisnel, T.; Fischmeister, C.; Bruneau, C. New Ruthenium Metathesis Catalysts with Chelating Indenylidene Ligands: Synthesis, Characterization and Reactivity. *Dalton Trans.* **2012**, *41* (13), 3695–3700.
- (89) Yu, B.; Xie, Y.; Hamad, F. B.; Leus, K.; Lyapkov, A. A.; Van Hecke, K.; Verpoort, F. Synthesis and Characterization of Non-Chelating Ruthenium-Indenylidene Olefin Metathesis Catalysts Derived from Substituted 1,1-Diphenyl-2-propyn-1-ols. *New J. Chem.* **2015**, *39* (3), 1858–1867.
- (90) Alberti, A.; Teral, Y.; Roubaud, G.; Faure, R.; Campredon, M. On the Photochromic Activity of Some Diphenyl-3H-naphtho[2,1-B]pyran Derivatives: Synthesis, NMR Characterisation and Spectrokinetic Studies. *Dye. Pigment.* **2009**, *81* (2), 85–90.
- (91) Yu, B.; Luo, Z.; Hamad, F. B.; Leus, K.; van Hecke, K.; Verpoort, F. Effect of the Bulkiness of Indenylidene Moieties on the Catalytic Initiation and Efficiency of Second-Generation Ruthenium-Based Olefin Metathesis Catalysts. *Catal. Sci. Technol.* **2016**, *6* (7), 2092–2100.
- (92) Bassetti, M.; Centola, F.; Sémeril, D.; Bruneau, C.; Dixneuf, P. H. Rate Studies and Mechanism of Ring-Closing Olefin Metathesis Catalyzed by Cationic Ruthenium Allenylidene Arene Complexes. *Organometallics* **2003**, *22* (22), 4459–4466.
- (93) Trnka, T. M.; Day, M. W.; Grubbs, R. H. Olefin Metathesis with 1,1-Difluoroethylene. *Angew. Chem. Int. Ed.* **2001**, *40* (18), 3441–3444.
- (94) Macnaughtan, M. L.; Johnson, M. J. A.; Kampf, J. W. Synthesis, Structure, and Olefin Metathesis Activity of Two Ruthenium Monofluoromethylidene Complexes.

- Organometallics* **2007**, *26* (4), 780–782.
- (95) Petasis, N. A.; Yudin, A. K.; Zavialov, I. A.; Prakash, G. K. S.; Olah, G. A. Facile Preparation of Fluorine-Containing Alkenes, Amides and Alcohols via the Electrophilic Fluorination of Alkenyl Boronic Acids and Trifluoroborates. *Synlett* **1997**, *1997* (5), 606–608.
- (96) Macnaughtan, M. L.; Gary, J. B.; Gerlach, D. L.; Johnson, M. J. A.; Kampf, J. W. Cross-Metathesis of Vinyl Halides. Scope and Limitations of Ruthenium-Based Catalysts. *Organometallics* **2009**, *28* (9), 2880–2887.
- (97) Chang, S.; Jones, L.; Wang, C.; Henling, L. M.; Grubbs, R. H. Synthesis and Characterization of New Ruthenium-Based Olefin Metathesis Catalysts Coordinated with Bidentate Schiff-Base Ligands. *Organometallics* **1998**, *17* (16), 3460–3465.
- (98) Sanford, M. S.; Love, J. A.; Grubbs, R. H. A Versatile Precursor for the Synthesis of New Ruthenium Olefin Metathesis Catalysts. *Organometallics* **2001**, *20* (25), 5314–5318.
- (99) Love, J. A.; Morgan, J. P.; Trnka, T. M.; Grubbs, R. H. A Practical and Highly Active Ruthenium-Based Catalyst That Effects the Cross Metathesis of Acrylonitrile. *Angew. Chem. Int. Ed.* **2002**, *41* (21), 4035–4037.
- (100) Love, J. A.; Sanford, M. S.; Day, M. W.; Grubbs, R. H. Synthesis, Structure, and Activity of Enhanced Initiators for Olefin Metathesis. *J. Am. Chem. Soc.* **2003**, *125* (33), 10103–10109.
- (101) da Costa, R.; Gladysz, J. A. Fluorous Phase-Transfer Activation of Catalysts: Application of a New Rate-Enhancement Strategy to Alkene Metathesis. *Chem. Commun.* **2006**, No. 24, 2619–2621.
- (102) Alvey, L. J.; Rutherford, D.; Juliette, J. J. J.; Gladysz, J. A. Additions of PH_3 to Monosubstituted Alkenes of the Formula $\text{H}_2\text{CCH}(\text{CH}_2)_x(\text{CF}_2)_y\text{CF}_3$: Convenient, Multigram Syntheses of a Family of Partially Fluorinated Trialkylphosphines with Modulated Electronic Properties and Fluorous Phase Affinities. *J. Org. Chem.* **1998**, *63* (18), 6302–6308.
- (103) Tuba, R.; Corrêa da Costa, R.; Bazzi, H. S.; Gladysz, J. A. Phase Transfer Activation of Fluorous Analogs of Grubbs' Second-Generation Catalyst: Ring-Opening Metathesis Polymerization. *ACS Catal.* **2012**, *2* (1), 155–162.
- (104) da Costa, R. C.; Gladysz, J. A. Syntheses and Reactivity of Analogues of Grubbs' Second Generation Metathesis Catalyst with Fluorous Phosphines: A New Phase-Transfer Strategy for Catalyst Activation. *Adv. Synth. Catal.* **2007**, *349* (1–2), 243–254.
- (105) Broggi, J.; Urbina-Blanco, C. A.; Clavier, H.; Leitgeb, A.; Slugovc, C.; Slawin, A. M. Z.; Nolan, S. P. The Influence of Phosphane Ligands on the Versatility of Ruthenium–

- Indenylidene Complexes in Metathesis. *Chem. – A Eur. J.* **2010**, *16* (30), 9215–9225.
- (106) Balogh, J.; Hlil, A. R.; Su, H.-L.; Xi, Z.; Bazzi, H. S.; Gladysz, J. A. An Analogue of Grubbs Third-Generation Catalyst with Fluorophilic Pyridine Ligands: Fluorous/Organic Phase-Transfer Activation of Ring-Closing Alkene Metathesis. *ChemCatChem* **2016**, *8* (1), 125–128.
- (107) Samanta, D.; Kratz, K.; Zhang, X.; Emrick, T. A Synthesis of PEG- and Phosphorylcholine-Substituted Pyridines To Afford Water-Soluble Ruthenium Benzylidene Metathesis Catalysts. *Macromolecules* **2008**, *41* (3), 530–532.
- (108) Grubbs, R. H.; Johnson, L. K.; Nguyen, S. T. Ruthenium and Osmium Metal Carbene Complexes for Olefin Metathesis Polymerization. WO patent 1993/020111 A2.
- (109) Dias, E. L.; Nguyen, S. T.; Grubbs, R. H. Well-Defined Ruthenium Olefin Metathesis Catalysts: Mechanism and Activity. *J. Am. Chem. Soc.* **1997**, *119* (17), 3887–3897.
- (110) Wu, Z.; Nguyen, S. T.; Grubbs, R. H.; Ziller, J. W. Reactions of Ruthenium Carbenes of the Type $(PPh_3)_2(X)_2Ru=CH-CH=CPh_2$ ($X = Cl$ and CF_3COO) with Strained Acyclic Olefins and Functionalized Olefins. *J. Am. Chem. Soc.* **1995**, *117* (20), 5503–5511.
- (111) Buchowicz, W.; Mol, J. C.; Lutz, M.; Spek, A. L. A Novel Ruthenium Carbene Dimer That Is Active in the Metathesis of Internal Alkenes; the Crystal Structure of $Ru_2(=CHPh)_2(CF_3CO_2)_2(\mu-CF_3CO_2)_2(PCy_3)_2(\mu-H_2O)$. *J. Organomet. Chem.* **1999**, *588* (2), 205–210.
- (112) Buchowicz, W.; Ingold, F.; Mol, J. C.; Lutz, M.; Spek, A. L. Novel Ruthenium(II)₂ Carboxylates as Catalysts for Alkene Metathesis. *Chem. – A Eur. J.* **2001**, *7* (13), 2842–2847.
- (113) Sanford, M. S.; Henling, L. M.; Day, M. W.; Grubbs, R. H. Ruthenium-Based Four-Coordinate Olefin Metathesis Catalysts. *Angew. Chem. Int. Ed.* **2000**, *39* (19), 3451–3453.
- (114) Krause, J. O.; Nuyken, O.; Wurst, K.; Buchmeiser, M. R. Synthesis and Reactivity of Homogeneous and Heterogeneous Ruthenium-Based Metathesis Catalysts Containing Electron-Withdrawing Ligands. *Chem. – A Eur. J.* **2004**, *10* (3), 777–784.
- (115) Krause, J. O.; Zarka, M. T.; Anders, U.; Weberskirch, R.; Nuyken, O.; Buchmeiser, M. R. Simple Synthesis of Poly(acetylene) Latex Particles in Aqueous Media. *Angew. Chem. Int. Ed.* **2003**, *42* (48), 5965–5969.
- (116) Buchmeiser, M. R. Recent Advances in the Regio- and Stereospecific Cyclopolymerization of α,ω -Diyne by Tailored Ruthenium Alkylidenes and Molybdenum Imido Alkylidene N-Heterocyclic Carbene Complexes. *Polym. Rev.* **2017**, *57* (1), 15–30.
- (117) Krause, J. O.; Nuyken, O.; Buchmeiser, M. R. Factors Relevant for the Ruthenium-Benzylidene-Catalyzed Cyclopolymerization of 1,6-Heptadiynes. *Chem. – A Eur. J.* **2004**,

10 (8), 2029–2035.

- (118) Halbach, T. S.; Krause, J. O.; Nuyken, O.; Buchmeiser, M. R. Stereoselective Cyclopolymerization of Polar 1,6-Heptadiynes by Novel, Tailor-Made Ruthenium-Based Metathesis Catalysts. *Macromol. Rapid Commun.* **2005**, *26* (10), 784–790.
- (119) Vygodskii, Y. S.; Shaplov, A. S.; Lozinskaya, E. I.; Vlasov, P. S.; Malyshkina, I. A.; Gavrilova, N. D.; Santhosh Kumar, P.; Buchmeiser, M. R. Cyclopolymerization of *N,N*-Dipropargylamines and *N,N*-Dipropargyl Ammonium Salts. *Macromolecules* **2008**, *41* (6), 1919–1928.
- (120) Kumar, P. S.; Wurst, K.; Buchmeiser, M. R. Factors Relevant for the Regioselective Cyclopolymerization of 1,6-Heptadiynes, *N,N*-Dipropargylamines, *N,N*-Dipropargylammonium Salts, and Dipropargyl Ethers by Ru^{IV}-Alkylidene-Based Metathesis Initiators. *J. Am. Chem. Soc.* **2009**, *131* (1), 387–395.
- (121) Kumar, P. S.; Wurst, K.; Buchmeiser, M. R. Ru-Alkylidene Metathesis Catalysts Based on 1,3-Dimesityl-4,5,6,7-tetrahydro-1,3-diazepin-2-ylidenes: Synthesis, Structure, and Activity. *Organometallics* **2009**, *28* (6), 1785–1790.
- (122) Buchmeiser, M. R.; Ahmad, I.; Gurram, V.; Kumar, P. S. Pseudo-Halide and Nitrate Derivatives of Grubbs and Grubbs–Hoveyda Initiators: Some Structural Features Related to the Alternating Ring-Opening Metathesis Copolymerization of Norborn-2-Ene with Cyclic Olefins. *Macromolecules* **2011**, *44* (11), 4098–4106.
- (123) Niecypor, P.; Buchowicz, W.; Meester, W. J. N.; Rutjes, F. P. J. T.; Mol, J. C. Synthesis and Application of a New Polystyrene-Supported Ruthenium Carbene Catalyst for Alkene Metathesis. *Tetrahedron Lett.* **2001**, *42* (40), 7103–7105.
- (124) Buchmeiser, M. R.; Schmidt, C.; Wang, D. Cyclopolymerization of *N,N*-Dipropargyl-3,4-Dialkoxyanilines Using Schrock and Grubbs–Hoveyda Initiators: Influence of Initiator Structure on the Mode of Insertion. *Macromol. Chem. Phys.* **2011**, *212* (18), 1999–2008.
- (125) Halbach, T. S.; Mix, S.; Fischer, D.; Maechling, S.; Krause, J. O.; Sievers, C.; Blechert, S.; Nuyken, O.; Buchmeiser, M. R. Novel Ruthenium-Based Metathesis Catalysts Containing Electron-Withdrawing Ligands: Synthesis, Immobilization, and Reactivity. *J. Org. Chem.* **2005**, *70* (12), 4687–4694.
- (126) Braddock, D. C.; Tanaka, K.; Chadwick, D.; Böhm, V. P. W.; Roeper, M. Vacuum-Driven Anionic Ligand Exchange in Buchmeiser–Hoveyda–Grubbs Ruthenium(II) Benzylidenes. *Tetrahedron Lett.* **2007**, *48* (30), 5301–5303.
- (127) Krause, J. O.; Lubbad, S. H.; Nuyken, O.; Buchmeiser, M. R. Heterogenization of a Modified Grubbs–Hoveyda Catalyst on a ROMP-Derived Monolithic Support. *Macromol. Rapid Commun.* **2003**, *24* (15), 875–878.

- (128) Vehlow, K.; Maechling, S.; Köhler, K.; Blechert, S. Versatile Ru-Based Metathesis Catalysts Designed for Both Homogeneous and Heterogeneous Processes. *J. Organomet. Chem.* **2006**, *691* (24–25), 5267–5277.
- (129) Vehlow, K.; Maechling, S.; Köhler, K.; Blechert, S. A New Stable Hoveyda–Grubbs Catalyst with Mixed Anionic Ligands. *Tetrahedron Lett.* **2006**, *47* (48), 8617–8620.
- (130) Bruneau, C.; Fischmeister, C.; Miao, X.; Malacea, R.; Dixneuf, P. H. Cross-Metathesis with Acrylonitrile and Applications to Fatty Acid Derivatives. *Eur. J. Lipid Sci. Technol.* **2010**, *112* (1), 3–9.
- (131) Gawin, R.; Czarnecka, P.; Grela, K. Ruthenium Catalysts Bearing Chelating Carboxylate Ligands: Application to Metathesis Reactions in Water. *Tetrahedron* **2010**, *66* (5), 1051–1056.
- (132) Levin, E.; Ivry, E.; Diesendruck, C. E.; Lemcoff, N. G. Water in *N*-Heterocyclic Carbene-Assisted Catalysis. *Chem. Rev.* **2015**, *115* (11), 4607–4692.
- (133) Gawin, R.; Makal, A.; Woźniak, K.; Mauduit, M.; Grela, K. A Dormant Ruthenium Catalyst Bearing a Chelating Carboxylate Ligand: In Situ Activation and Application in Metathesis Reactions. *Angew. Chem. Int. Ed.* **2007**, *46* (38), 7206–7209.
- (134) Gawin, R.; Grela, K. Synthesis of Stable Ruthenium Olefin Metathesis Catalysts with Mixed Anionic Ligands. *Eur. J. Inorg. Chem.* **2012**, *2012* (9), 1477–1484.
- (135) Conrad, J. C.; Amoroso, D.; Czechura, P.; Yap, G. P. A.; Fogg, D. E. The First Highly Active, Halide-Free Ruthenium Catalyst for Olefin Metathesis. *Organometallics* **2003**, *22* (18), 3634–3636.
- (136) Conrad, J. C.; Parnas, H. H.; Snelgrove, J. L.; Fogg, D. E. Highly Efficient Ru–Pseudohalide Catalysts for Olefin Metathesis. *J. Am. Chem. Soc.* **2005**, *127* (34), 11882–11883.
- (137) Khan, R. K. M.; Torker, S.; Hoveyda, A. H. Reactivity and Selectivity Differences between Catecholate and Catechthiolate Ru Complexes. Implications Regarding Design of Stereoselective Olefin Metathesis Catalysts. *J. Am. Chem. Soc.* **2014**, *136* (41), 14337–14340.
- (138) Guidone, S.; Songis, O.; Falivene, L.; Nagra, F.; Slawin, A. M. Z.; Jacobsen, H.; Cavallo, L.; Cazin, C. S. J. Ruthenium Olefin Metathesis Catalysts Containing Fluoride. *ACS Catal.* **2015**, *5* (7), 3932–3939.
- (139) Babuněk, M.; Šimůnek, O.; Hošek, J.; Rybáčková, M.; Cvačka, J.; Březinová, A.; Kvičala, J. Heavy Fluorous Phosphine-Free Ruthenium Catalysts for Alkene Metathesis. *J. Fluor. Chem.* **2014**, *161*, 66–75.
- (140) Lipovská, P.; Rathouská, L.; Šimůnek, O.; Hošek, J.; Kolaříková, V.; Rybáčková, M.;

- Cvačka, J.; Svoboda, M.; Kvičala, J. Synthesis and Catalytic Activity of Ruthenium Complexes Modified with Chiral Racemic Per- and Polyfluorooxaalkanoates. *J. Fluor. Chem.* **2016**, *191*, 14–22.
- (141) Anderson, E. B.; Buchmeiser, M. R. “Pseudo-Halide” Derivatives of Grubbs- and Schrock-Type Catalysts for Olefin Metathesis. *Synlett* **2012**, *2012* (2), 185–207.
- (142) Buchmeiser, M. R. Polymer-Supported Well-Defined Metathesis Catalysts. *Chem. Rev.* **2009**, *109* (2), 303–321.
- (143) Copéret, C.; Basset, J.-M. Strategies to Immobilize Well-Defined Olefin Metathesis Catalysts: Supported Homogeneous Catalysis vs. Surface Organometallic Chemistry. *Adv. Synth. Catal.* **2007**, *349* (1–2), 78–92.
- (144) Sommer, W. J.; Weck, M. Supported *N*-Heterocyclic Carbene Complexes in Catalysis. *Coord. Chem. Rev.* **2007**, *251* (5–6), 860–873.
- (145) Emin G., M.; Özdemir, N.; Ulusoy, M.; Uçak, M.; Dinçer, M.; Çetinkaya, B. The Influence of Moisture on Deprotonation Mode of Imidazolium Chlorides with Palladacycle Acetate Dimer. *J. Organomet. Chem.* **2009**, *694* (14), 2179–2184.
- (146) Manzini, S.; Urbina Blanco, C. A.; Nelson, D. J.; Poater, A.; Lebl, T.; Meiries, S.; Slawin, A. M. Z.; Falivene, L.; Cavallo, L.; Nolan, S. P. Evaluation of an Olefin Metathesis Pre-Catalyst with a Bulky and Electron-Rich *N*-Heterocyclic Carbene. *J. Organomet. Chem.* **2015**, *780*, 43–48.
- (147) Maynard, H. D.; Grubbs, R. H. Synthesis of Functionalized Polyethers by Ring-Opening Metathesis Polymerization of Unsaturated Crown Ethers. *Macromolecules* **1999**, *32* (21), 6917–6924.
- (148) Delaude, L.; Hans, M.; Chowdhury, S. Microwave-Assisted Synthesis Of 1,3-Dimesitylimidazolium Chloride. *Org. Synth.* **2010**, *87*, 77–87.

New olefin metathesis catalysts with fluorinated NHC ligands: Synthesis and catalytic activity

Summary

An efficient approach to a new family of unsymmetrical 1,3-bis(aryl)-4,5-dihydroimidazolium salts comprising bulky hexafluoroisopropylmethoxy group in *para*- or *ortho*-position in one of the *N*-aryl substituents has been developed. New imidazolium salts with fluoroalkyl-containing mono-*ortho*-aryl substituent at one of the nitrogen atom have also been synthesized. It was found that these imidazolium salts are effective NHC precursors and provided an efficient access to a series of new ruthenium carbene complexes with unsymmetrical fluorinated NHC ligands. The method involves *in situ* generation of the carbene *via* treatment of the starting salts with potassium hexamethyldisilazide and subsequent ligand exchange reaction with PCy₃-containing first generation Grubbs and Hoveyda complexes.

The catalytic activity of the new complexes has been investigated on model reactions of intra- and intermolecular olefin metathesis. It was found that most of the synthesized complexes exhibited high activity in cyclization of diethyl diallylmalonate and in cross metathesis of allyl benzene with 1,3-diacetoxybut-2-ene. Their performance has proved to be comparable with commonly used second generation Grubbs and Hoveyda catalysts, with sometimes some differences in the initiation step.

Structural and electronic impact of fluorinated unsymmetrical NHC on reactivity of new ruthenium complexes has been studied. In particular, it was revealed that Hoveyda type catalysts with mono-*ortho*-aryl substituted NHC ligands have demonstrated very high initiation rate in CM reactions. On the contrary, catalysts with more donating *N*-alkyl NHCs have displayed low activity; for instance, the *N*-*tert*-butyl substituted complex has proved to be absolutely inert both in RCM and CM reactions.

Symmetrical ruthenium carbene complexes bearing NHC ligands with two hexafluoroisopropylmethoxy group in *para*-positions of *N*-aryl moieties are significantly inferior in reactivity with respect to their asymmetric counterparts showing the strong influence of the desymmetrization factor on catalytic activity.

Keywords

N-heterocyclic carbenes
Fluorinated carbenes
Olefin metathesis catalysts

Ring closing metathesis
Cross metathesis

Nouveaux catalyseurs de métathèse des oléfines à ligands carbènes *N*-hétérocycliques fluorés: Synthèse et activité catalytique

Résumé

La préparation efficace d'une nouvelle famille de sels de 1,3-bis(aryl)-4,5-dihydroimidazolium non symétriques comprenant un groupement encombrant hexafluoroisopropylmethoxy en position *para*- ou *ortho*- sur l'un des substituants *N*-aryle a été développée. De nouveaux sels d'imidazolium contenant un substituant fluoroalkyle en position *ortho* d'un des substituant aryle ont aussi été synthétisés. Ces sels sont d'excellents précurseurs de carbènes *N*-hétérocycliques qui ont permis l'accès efficace à une série de nouveaux complexes carbéniques du ruthénium à ligands NHC non symétriques. La méthode repose sur la génération *in situ* du carbène par traitement des sels d'imidazolium avec le potassium hexamethyldisilazide suivie d'un échange du ligand tricyclohexylphosphine à partir des complexes de Grubbs et Hoveyda de première génération.

L'activité de ces nouveaux complexes a été étudiée sur des réactions modèles intra- et intermoléculaires de métathèse des oléfines. Il a été montré que la plupart des complexes synthétisés ont de bonnes activités catalytiques en fermeture de cycle à partir du diallylmalonate d'éthyle et en métathèse croisée de l'allylbenzène avec le 1,3-diacetoxybut-2-ene. Leurs performances sont comparables à celles des catalyseurs de Grubbs et Hoveyda de seconde génération, avec toutefois quelques différences dans les étapes d'initiation. Les effets structuraux et électroniques des ligands NHC non symétriques sur la réactivité des nouveaux complexes du ruthénium ont été étudiés. En particulier, il a été montré que les catalyseurs de type Hoveyda porteurs de ligands monosubstitués par un groupement fluoroalkyle en position *ortho* d'un des substituant *N*-aryle présentent une initiation très rapide dans les réactions de métathèse croisée. Au contraire, les complexes porteurs d'un groupement donneur alkyle ont montré une activité catalytique très faible, comme par exemple le complexe porteur d'un ligand (*tert*-butyl)NHC qui s'est révélé inerte à la fois en fermeture de cycle et métathèse croisée.

Les complexes porteurs d'un ligand NHC symétrique avec deux groupes hexafluoroisopropylmethoxy ont des activités catalytiques nettement inférieures à leurs homologues non symétriques, révélant ainsi la forte influence de l'absence de symétrie du ligand carbène NHC dans l'activité catalytique des complexes.

Mots-clés

Carbènes *N*-hétérocycliques

Carbènes fluorés

Catalyseurs de métathèse des oléfines

Fermeture de cycle par métathèse

Métathèse croisée



Résumé

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et à

l'Institut Nesmeyanov des Organoéléments de Moscou (INEOS)

New olefin metathesis catalysts with fluorinated NHC ligands: Synthesis and catalytic activity

Nouveaux catalyseurs de métathèse des oléfines à ligands carbènes N-hétérocycliques fluorés: Synthèse et activité catalytique

Thèse soutenue à Moscou le 14/12/2017

devant le jury composé de :

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Introduction générale

La métathèse des oléfines est une réaction de redistribution des substitutents des oléfines par scission et génération d'une nouvelle oléfine (Schéma 1).

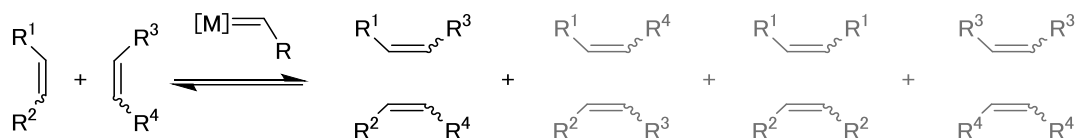


Schéma 1. Schéma général de la métathèse des oléfines

Durant les dernières décennies, la métathèse des oléfines est devenue un des outils les plus puissants et attractifs pour la formation de doubles liaisons carbone-carbone pour la préparation d'une large gamme de produits allant des alcènes simples aux molécules complexes d'intérêt biologique et aux polymères. L'importance du développement de cette réaction catalytique en synthèse organique a été reconnue par l'attribution du prix Nobel de Chimie en 2005 conjointement à Yves Chauvin, Robert H. Grubbs et Richard R. Schrock.

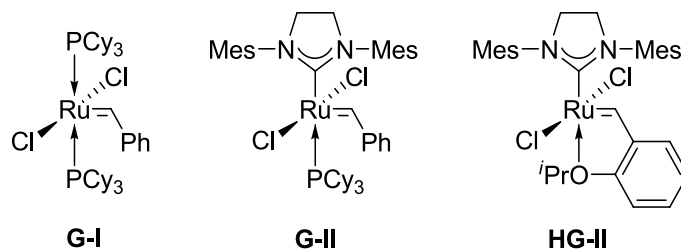


Figure 1. Les catalyseurs de métathèse à base de ruthénium les plus communs: catalyseur de Grubbs de première génération (G-I), catalyseur de Grubbs de deuxième génération (G-II), catalyseur de Hoveyda-Grubbs de seconde génération (HG-II).

En catalyse homogène, les catalyseurs de métathèse des oléfines les plus performants ont été développés à partir de complexes bien définis du ruthénium, du molybdène et du tungstène portant un site métal-carbène réactif. Parmi la variété de catalyseurs de métathèse obtenus à ce jour, les catalyseurs à base de ruthénium de type Grubbs (Figure 1) sont très populaires en raison de leur grande stabilité à l'air et à l'humidité, leur tolérance aux groupements fonctionnels (acides carboxyliques, alcools, cétones,...) qui leur permet de garder une bonne réactivité vis-à-vis des doubles liaisons dans ces conditions. Depuis 1992, quand les premiers catalyseurs bien définis du ruthénium ont été décrits, de nombreuses modifications ont été apportées aux structures de base. Malgré les énormes progrès réalisés durant les dernières décennies, la synthèse de nouveaux catalyseurs plus efficaces et sélectifs présente toujours un intérêt majeur.

Parallèlement à la métathèse des alcènes, la chimie des composés fluorés connaît une croissance rapide. En raison des propriétés spécifiques de l'atome de fluor telles que sa grande électronégativité, sa faible taille et polarisabilité, son aptitude à former des liaisons hydrogène et à coordonner des métaux de transition et de la forte énergie de la liaison C-F, les dérivés fluorés présentent des propriétés inhabituelles par rapport à leurs analogues non fluorés. Jusqu'à maintenant, seulement quelques catalyseurs de métathèse des oléfines porteurs de ligands fluorés ont été décrits. Les propriétés de ligands fluorés préalablement énumérées pourraient avoir une influence notable sur les propriétés catalytiques de complexes du ruthénium.

L'objectif principal du travail est le développement de méthodes efficaces pour la synthèse d'une série de nouveaux sels d'imidazolium non symétriques, précurseurs de ligands carbéniques contenant le groupement encombrant hexafluoroisopropoxy, ainsi que la préparation des catalyseurs de type Grubbs et Hoveyda correspondants et l'évaluation de leurs propriétés catalytiques dans des réactions de fermeture de cycle par métathèse et de métathèse croisée (Figure 2).

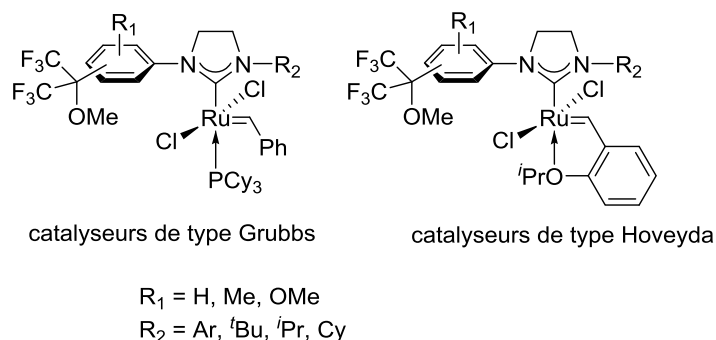


Figure 2. Structures des catalyseurs préparés et testés

Le chapitre **1** rassemble la bibliographie sur les catalyseurs à base de ruthénium contenant des ligands fluorés. Les résultats et les discussions du travail de cette thèse sont exprimés dans le chapitre **2**. Les parties expérimentales et les conclusions sont présentées dans les chapitres **3** et **4**.

Chapitre 1 (revue bibliographique)

Catalyseurs de métathèse des oléfines à base de ruthénium contenant des ligands fluorés

1.1. Introduction

De façon générale, les catalyseurs de Grubbs contiennent des ligands de différents types suivant la terminologie de M. Green (Figure 3). Le site réactif est un ligand carbénique lié directement au métal. Dans le cas des complexes de Grubbs (**G-I**, **G-II**), il s'agit d'un ligand aryldène (benzylidène le plus souvent) qui participe à la cycloaddition [2+2] pendant la métathèse. Dans le cas des complexes de deuxième (**G-II** and **HG-II**) et de troisième génération (**G-III**), un second type de carbène cette fois *N*-hétérocyclique est aussi présent. Par ces propriétés électroniques et stériques, ce ligand confère au complexe sa stabilité et sa réactivité. Le troisième type de ligand est représenté par des ligands de type donneur L comme des phosphines (**G-I**, **G-II**) ou la pyridine (**G-III**). Dans le cas des catalyseurs de Hoveyda, ce ligand L est intégré dans un ligand bidentant aryldène porteur d'un groupement chélatant alkoxy (**HG-II**). Finalement les chlorures sont les deux ligands X les plus communément associés aux structures de ces catalyseurs.

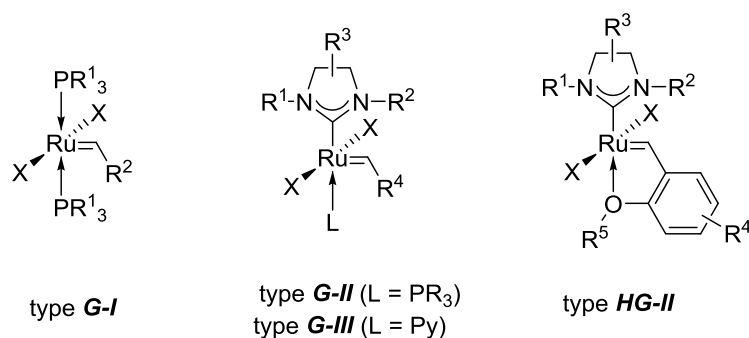


Figure 3. Structures générales des catalyseurs de ruthénium.

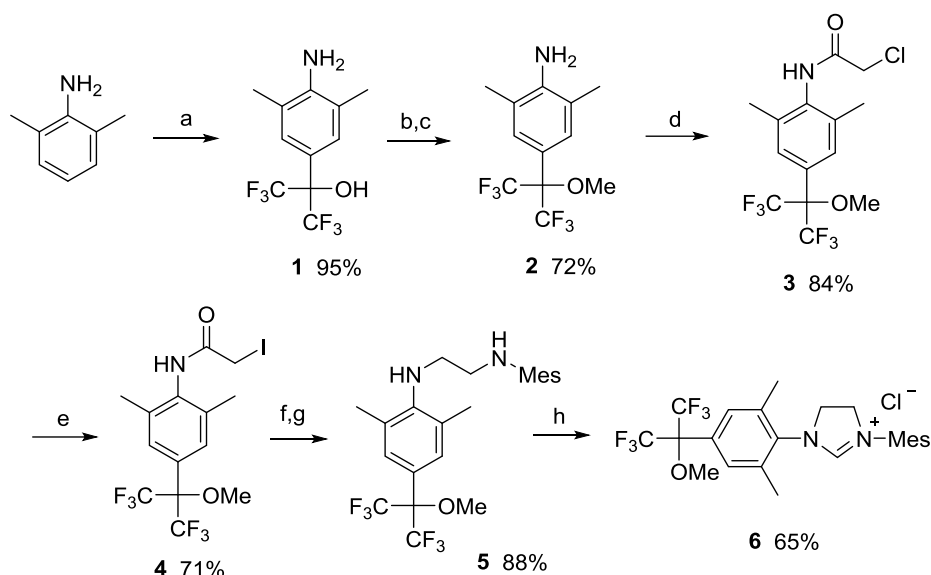
Des modifications des propriétés électroniques et stériques de tous ces ligands peuvent être apportées pour construire des catalyseurs de métathèse plus performants. En particulier l'introduction de ligands fluorés a déjà été tentée avec cet objectif. Ce chapitre rassemble les données relatives à ces travaux présentées dans un ordre chronologique. Pour chaque section, les synthèses de ligands, de complexes du ruthénium et la description des performances en catalyse de métathèse d'oléfinés dans des réactions modèles sont décrites.

1.2. Ligands *N*-hétérocycliques (NHC) fluorés

1.3. Ligands benzylidène fluorés

1.4. Ligands carbéniques indénylidène et allénylidène fluorés

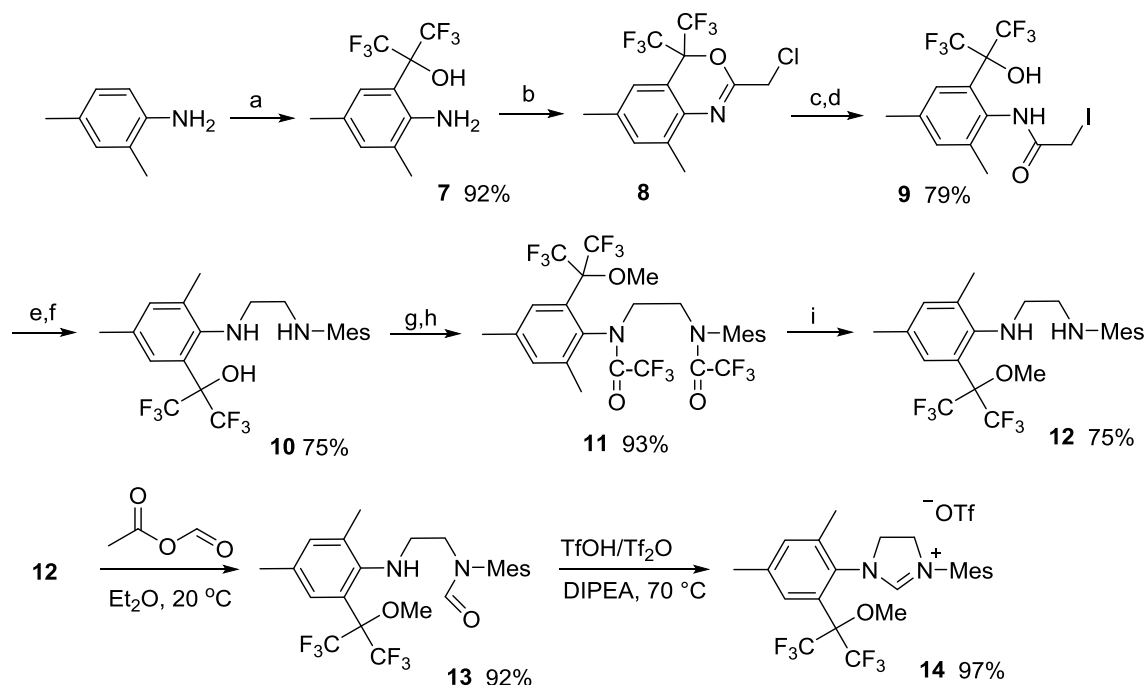
1.5. Ligands méthylidène fluorés



(a) HFA·1.5 H₂O, *p*-TSA (1 mol%), 100 °C, 95%; (b) PhCHO, toluène, 110 °C; (c) MeI, K₂CO₃, MeCN; 70 °C puis HCl/H₂O, t.a.; 72% pour les 2 étapes; (d) ClCH₂C(O)Cl, DMAP, CH₂Cl₂, t.a.; (e) NaI, acétone, t.a.; (f) MesNH₂ (en excès (x15)), t.a.; (g) BH₃·SMe₂, THF, 88% pour les 2 étapes; (h) MeOH/HCl, t.a., puis HC(OEt)₃, 100 °C, 60%. HFA = hexafluoroacétone; *p*-TSA = acid *p*-tolylsulfonique, DMAP = diméthylaminopyridine; t.a. = température ambiante.

Schéma 2

Comme il est connu dans la littérature que l'augmentation de l'encombrement stérique des substituants portés par les atomes d'azote des carbènes *N*-hétérocycliques a un effet positif sur les performances des catalyseurs, le sel d'imidazolidium **14** plus encombré portant le groupement hexafluoroisopropylmethoxy en position *ortho* d'un substituent *N*-aryle a été préparé selon le schéma 3.



(a) HFA·1.5 H₂O, *p*-TSA (1 mol. %), 100 °C, 92%; (b) ClCH₂C(O)Cl, DMAP, CH₂Cl₂, t.a.; (c) HCl/MeOH, t.a.; (d) NaI, acétone, t.a.; 79% pour 3 étapes; (e) MesNH₂ (excès (x15)), t.a.; (f) BH₃·SMe₂, THF, 75% pour 2 étapes; (g) TFAA/Py, CH₂Cl₂, t.a.; (h) MeI, K₂CO₃, DMF; 93% pour 2 étapes; (i) KOH, 18-crown-6, DMSO/H₂O, 130 °C, 75%.

Schéma 3

A partir de ces nouveaux précurseurs de carbènes N-hétérocycliques non symétriques, les complexes du ruthenium **15** et **16** ont été préparés.

Les carbènes ont été générés *in situ* par traitement des sels **6** et **14** avec KHMDS dans du toluène anhydre à 0 °C sous atmosphère d'argon, puis les complexes de première génération RuCl₂(PCy₃)₂(=CHPh) **G-I** et RuCl₂(PCy₃)(=CH(*o*-*i*PrO-C₆H₄)) **H-I** ont été additionnés. L'échange de ligand nécessite une agitation à température ambiante pendant deux heures ou un chauffage à 60 °C pendant 30 minutes. Les purifications sur gel de silice et recristallisation dans un mélange dichlorométhane/n-pentane conduisent aux complexes brun foncé (**15**) et vert foncé (**16**) (Schéma 4).

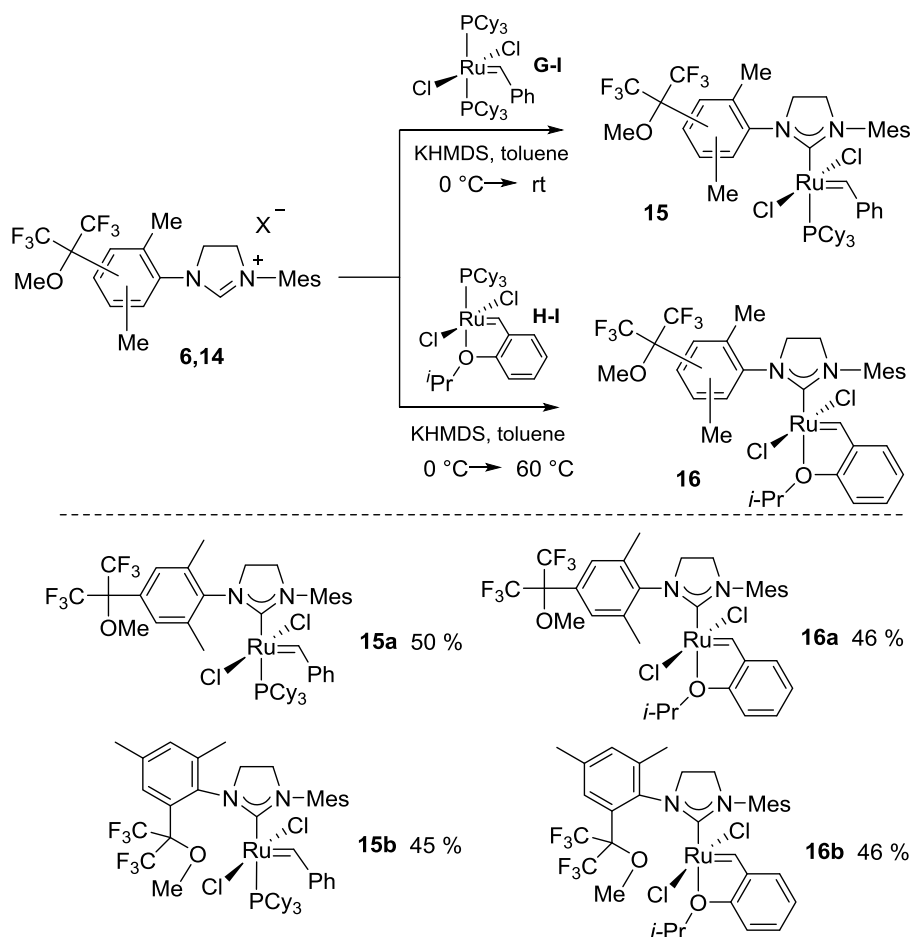


Schéma 4

Les complexes **15** et **16** ont été caractérisés par spectroscopie RMN du proton, du carbone et du fluor, et par analyse élémentaire. Des structures ont été obtenues par diffraction des rayons X à partir des complexes **16** (Figure 5).

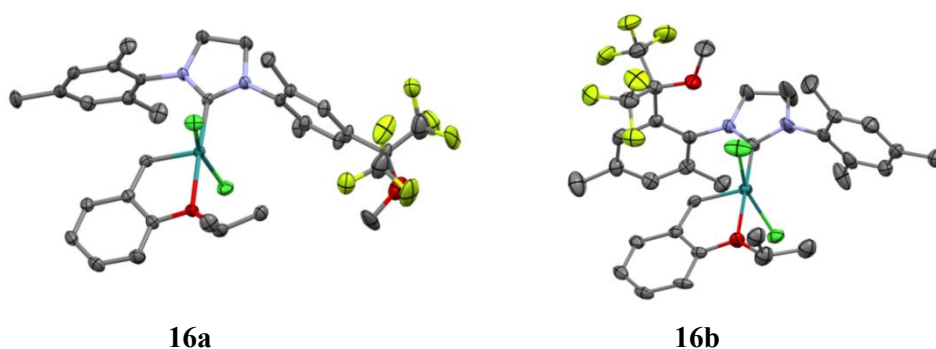


Figure 5

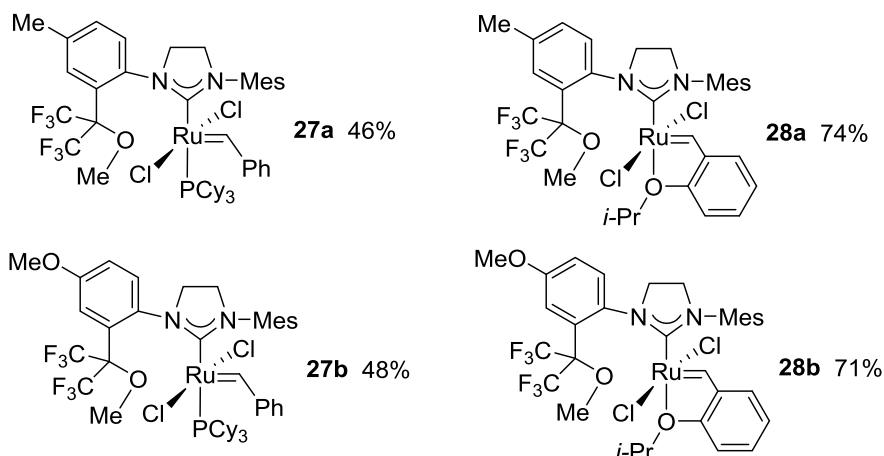
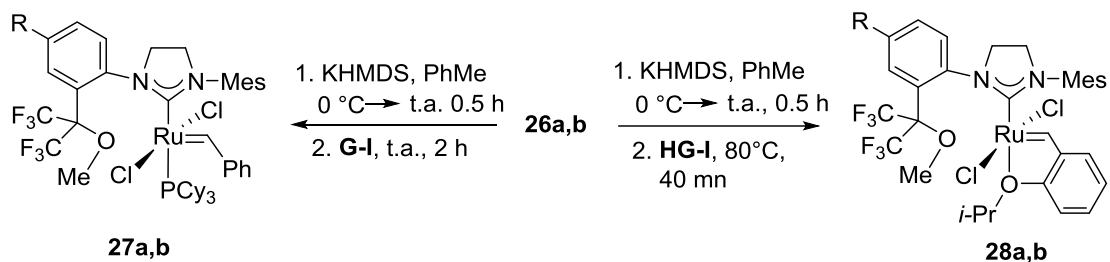


Schéma 7

Ces complexes **27** et **28** ont été caractérisés par les mêmes méthodes analytiques que les complexes précédents **15** et **16**.

De la même façon que pour les complexes **16**, les cristaux obtenus à partir des complexes **28** ont permis d'obtenir les structures de ces composés (Figure 6).

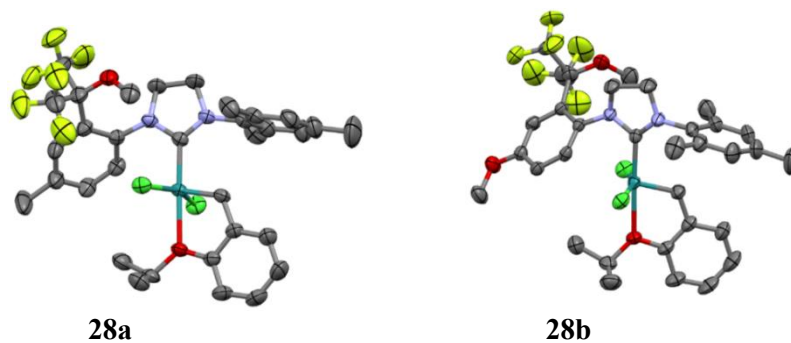


Figure 6

2.4. Synthèse de complexes du ruthénium à ligand *N*-alkyl-*N*'-arylimidazolin-2-ylidène fluorés

Des complexes du ruthénium porteurs d'un ligand NHC plus donneur équipé d'un groupe alkyle lié à un atome d'azote et d'un aryle fluoré sur l'autre atome d'azote ont été préparés.

Les sels d'imidazolium **31a-c** comportant un atome d'azote substitué par un *t*-butyle, *i*-propyle et cyclohexyle ont été préparés selon le schéma 8.

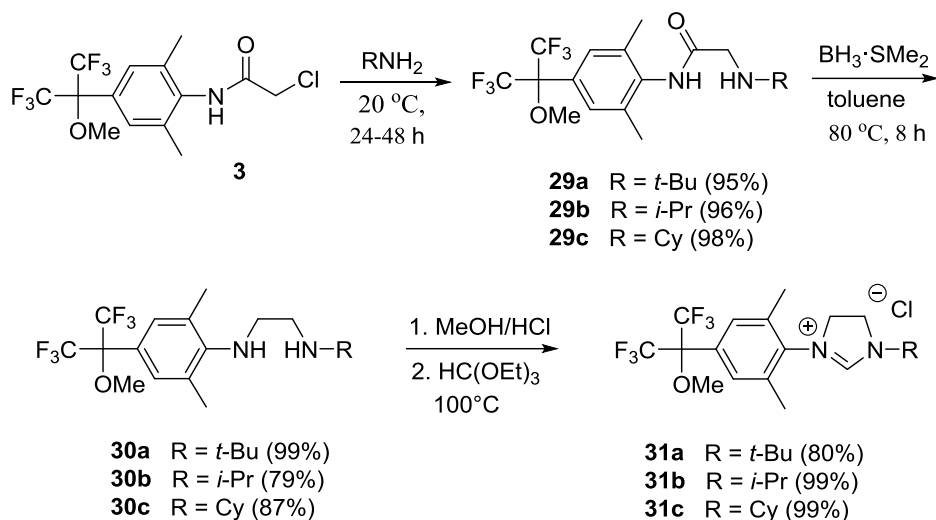


Schéma 8

Les complexes carbéniques du ruthénium ont été synthétisés suivant le même mode opératoire que précédemment et des analyses satisfaisantes ont été obtenus (Schéma 9).

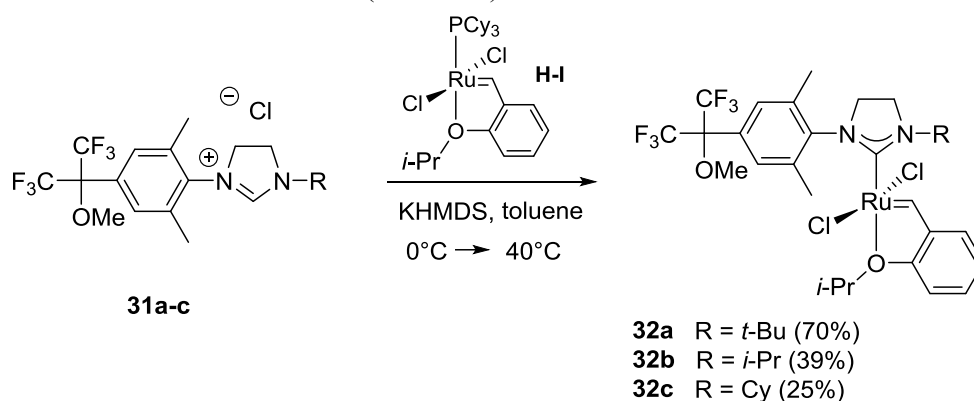
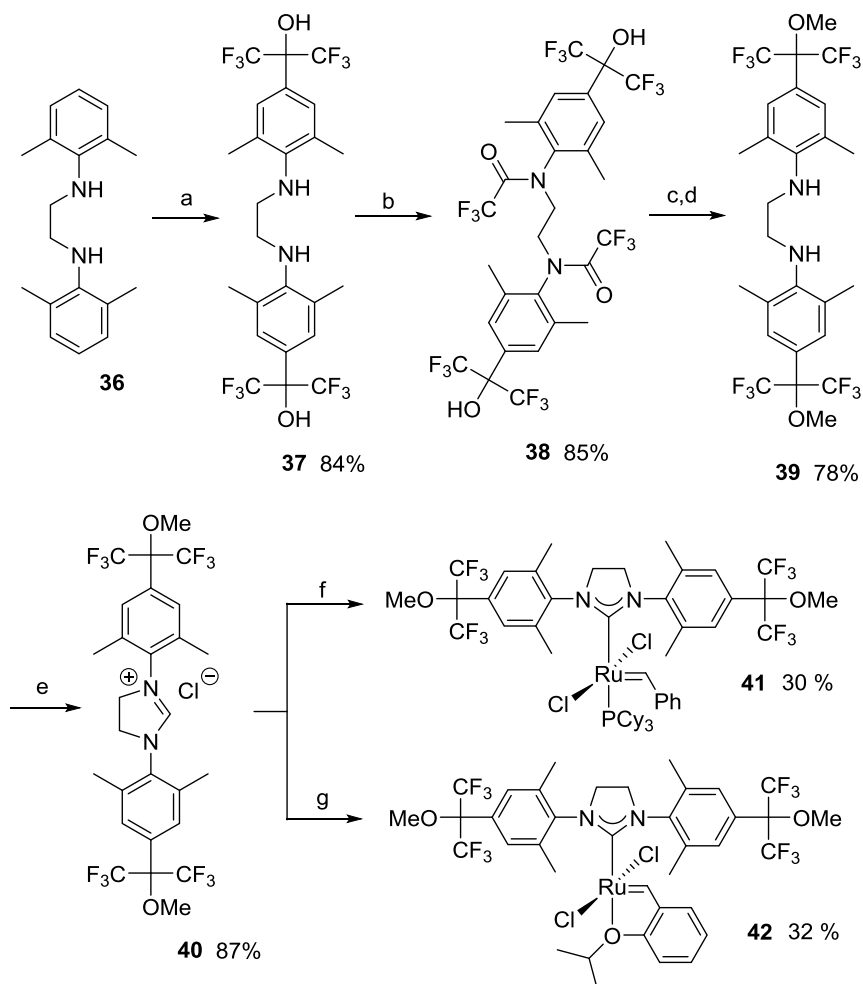


Schéma 9

2.5 Synthèse de complexes duruthénium à ligand N-hétérocyclique fluoré symétrique

Dans un objectif de comparaison des propriétés catalytiques entre les catalyseurs à ligand NHC symétrique et dissymétrique, les complexes de Grubbs **41** et Hoveyda-Grubbs **42** à ligand NHC symétrique ont été préparés selon le schéma 10.



(a) HFA·1.5H₂O, *p*-TSA (1 mol%), 100 °C, 84%; (b) TFAA/Py, Et₂O, 1 h, t.a.; (c) MeI, K₂CO₃, DMFA, 1.5 h, 80 °C; (d) KOH, 18-crown-6, DMSO/H₂O, 1.5 h, 130 °C; (e) MeOH/HCl, t.a., puis HC(OEt)₃, 100 °C; (f) KHMDS, toluène, **G-I**, t.a., 2 h; (g) KHMDS, toluène, **HG-I**, 60 °C, 1 h.

Schéma 10

2.5. Etude de l'activité catalytique des nouveaux complexes

L'influence des propriétés structurales et électroniques des différents complexes préparés (Figure 7) a été étudiée sur deux réactions modèles de métathèse des oléfines, la fermeture de cycle et la métathèse croisée, par comparaison à l'activité des complexes **G-II** et **HG-II**.

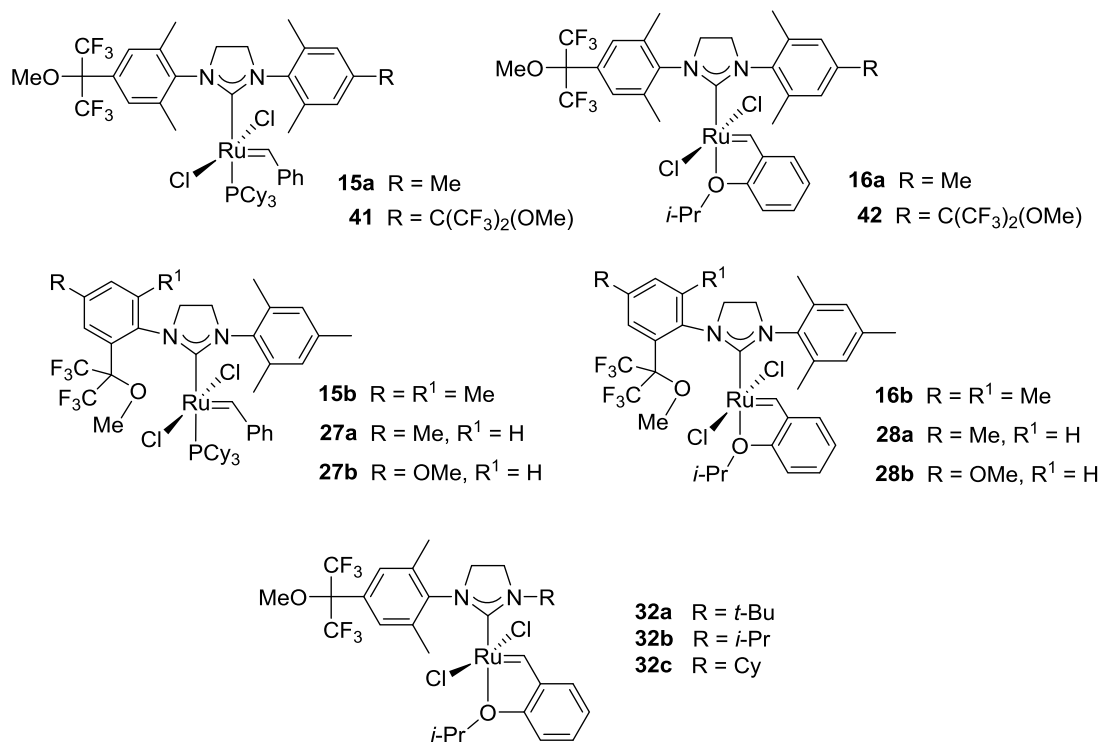


Figure 7

La fermeture du diallylmalonate de diéthyle par métathèse a été choisie comme réaction modèle (Schéma 11).

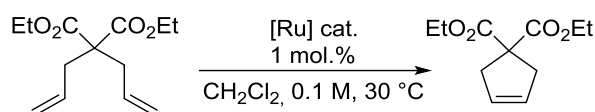


Schéma 11

La réaction de métathèse croisée qui a été sélectionnée met en jeu l'allylbenzène et le 1,3-diacétoxybut-2-ène (Schéma 12).

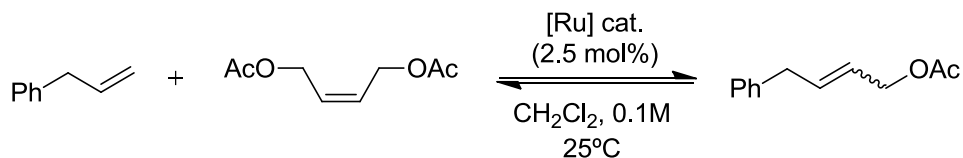


Schéma 12

Les comparaisons des activités ont été réalisées à partir des courbes cinétiques obtenues dans les expériences avec chacun des catalyseurs testés.

La plupart des complexes synthétisés ont de bonnes activités catalytiques en fermeture de cycle à partir du diallylmalonate d'éthyle et en métathèse croisée de l'allylbenzène avec le 1,3-diacétoxybut-2-ène. Leurs performances sont comparables à celles des catalyseurs de Grubbs et Hoveyda de seconde génération, avec toutefois quelques différences dans les étapes d'initiation. En particulier, il a été montré que les catalyseurs de type Hoveyda porteurs de ligands monosubstitués par un groupement fluoroalkyle en position *ortho* d'un des substituant *N*-aryle présentent une initiation très rapide dans les réactions de métathèse croisée. Au contraire, les complexes porteurs d'un groupement donneur alkyle ont montré une activité catalytique très faible, comme par exemple le complexe porteur d'un ligand (*tert*-butyl)NHC qui s'est révélé inerte à la fois en fermeture de cycle et métathèse croisée.

Les complexes porteurs d'un ligand NHC symétrique avec deux groupes hexafluoroisopropylmethoxy ont des activités catalytiques nettement inférieures à leurs homologues non symétriques, révélant ainsi la forte influence de l'absence de symétrie du ligand carbène NHC dans l'activité catalytique des complexes.

Conclusion générale

1. De nouvelles familles de sels d'imidazolium non symétriques porteurs du groupement hexafluoroisopropylmethoxy en position *para*- ou *ortho* d'un substituant *N*-aryle ont été préparées par de nouvelles méthodologies efficaces.
2. Ces sels d'imidazolium sont de bons précurseurs de carbènes *N*-hétérocycliques. En conséquence, une voie d'accès à des complexes du ruthénium porteurs d'un ligand *N*-hétérocyclique non symétrique a été développée. La méthode utilisée implique la déprotonation du sel d'imidazolium par KHMDS suivie de l'échange du ligand phosphine des complexes de première génération de type Grubbs et Hoveyda-Grubbs.
3. L'activité des nouveaux catalyseurs à ligands non symétriques a été évaluée dans des réactions modèles classiques de métathèse d'oléfines intra- et inter-moléculaire. La plupart de ces complexes du ruthénium présentant deux substituants purement aromatiques sont actifs en cyclisation du diallylmalonate de diéthyle et en métathèse croisée de l'allylbenzène avec le 1,3-diacétoxybut-2-ène, avec des performances comparables à celles des catalyseurs de deuxième génération de Grubbs et de Hoveyda-Grubbs.
4. Au contraire, les complexes porteurs d'un groupement donneur *N*-alkyle ont montré une activité catalytique très faible. De même, les complexes porteurs d'un ligand NHC symétrique avec deux groupes hexafluoroisopropylmethoxy ont des activités catalytiques nettement inférieures à leurs homologues non symétriques, révélant ainsi la forte influence de l'absence de symétrie du ligand carbène NHC dans l'activité catalytique des complexes.