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New fluorinated catalysts for olefin metathesis

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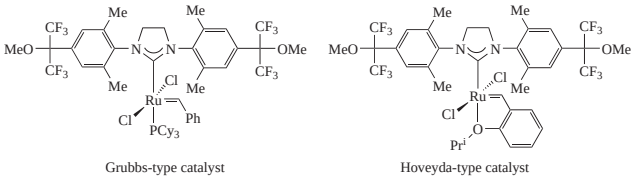
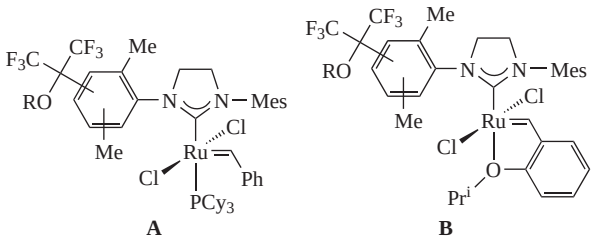
New olefin metathesis catalysts, analogues of Grubbs II ones, bearing hexafluoroisopropylmethoxy groups in NHC ligand, provide high conversions in model ring closing metathesis of diallylmalonate and cross metathesis of allylbenzene with 1,3-diacetoxybut-2-ene.



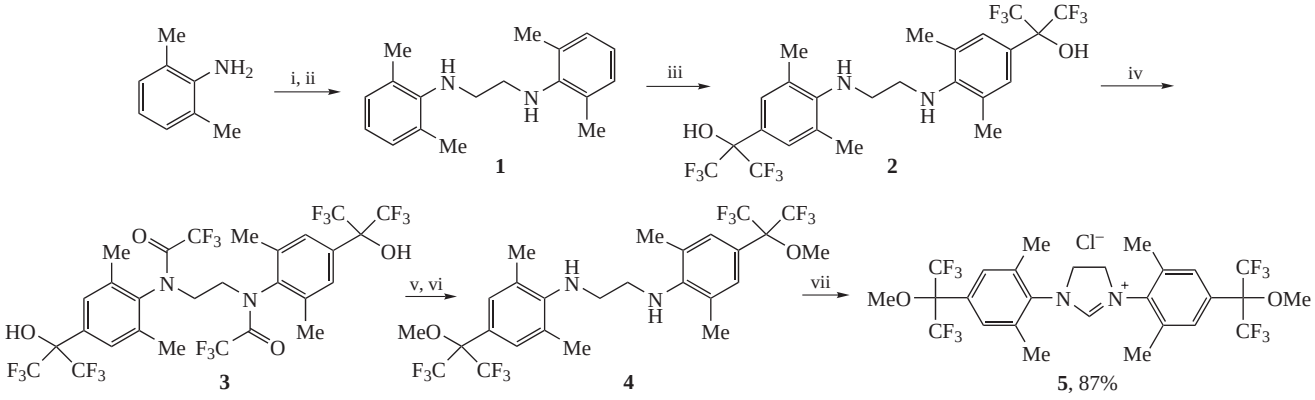
Over the past decade, olefin metathesis, with the advent of efficient ruthenium carbene complexes, has experienced dramatic development.[1,2] A significant progress in catalyst design was achieved when N-heterocyclic carbenes (NHCs) were introduced as ancillary ligands. The formal replacement of phosphine ligand in first generation of Grubbs catalyst (**G-I**) for sterically demanding NHCs, *e.g.* such as *N*,*N'*-dimesitylimidazolin-2-ylidene generally provides the metal center with considerable steric protection. Due to typical σ-donor properties the non-labile and bulky NHCs can also stabilize both the catalyst and catalytically relevant intermediates formed in metathesis pathways.[3] Therefore, the fine-turning of these ligands by the introduction of different functionalities into *N*-aryl substituents to afford enhanced thermal stability, improved reactivity and selectivity remains highly desirable.

At the same time, the chemistry of fluorinated compounds is an area of tremendous expansion.[4] In particular, CF_3 group is one of the most lipophilic groups in organic chemistry, has one of the highest electronegativity and steric hindrance[5] (Van-der-Waals volume of CF_3 group is close to that of isopropyl group[5(*c*)]). Therefore, fluorinated metal catalysts are attracting interest.

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,[6] styrene[7] ligands, as well as by the replacement of one or two chlorine atoms at ruthenium, for example, with perfluoroalkoxylates and fluorocatecholates.[8] Therefore, it is somewhat surprising that the number of publications on metathesis catalysts decorated with fluorinated NHC ligands is extremely limited,[9–11] with the first report appearing in early 2000.



Recently we have prepared unsymmetrical 1,3-bis(aryl)-4,5-dihydroimidazolium salts bearing the hexafluoroisopropylalkoxy group on one of *N*-aryl moieties and have demonstrated their potential as precursors for the corresponding NHC ligands of new family of metathesis catalysts **A** and **B**.[12] Herein, we report



Scheme 1 *Reagents and conditions*: i, glyoxal, H_2O, Pr^iOH, 24 h, room temperature, 85%; ii, $NaBH_4$, HCl, THF, H_2O, 2.5 h, 0 °C, 70%; iii, HFA·1.5 H_2O, *p*-TSA (1 mol%), 100 °C, 84%; iv, $(CF_3CO)_2O$/Py, Et_2O, 1 h, room temperature, 85%; v, MeI, K_2CO_3, DMF, 1.5 h, 80 °C, 76%; vi, KOH, 18-crown-6, DMSO/H_2O, 1.5 h, 130 °C, 80%; vii, HCl / MeOH, then $CH(OEt)_3$, 100 °C.

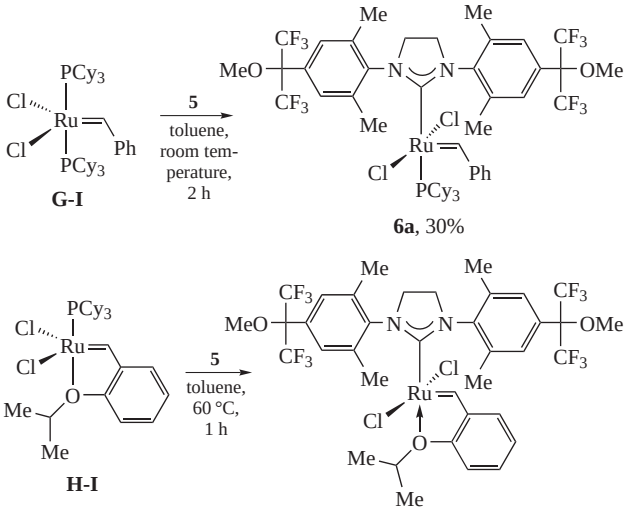
on their symmetrical representatives and their use in ring-closing metathesis (RCM) of diallylmalonate and in cross-metathesis (CM) of allylbenzene with 1,3-diacetoxybut-2-ene.

First, we synthesized symmetrical *N*,*N*′-bis(aryl)ethylenediamine **2** (Scheme 1) with two hexafluoroisopropoxy groups in the *para*-position of *N*-aryl moieties. For this purpose, diamine **1** was prepared *via* slightly modified literature protocol including (i) the condensation of 2,6-dimethylaniline with glyoxal followed by (ii) the reduction of the resulting diimine with $NaBH_4$ to afford **1** in good yield. Then diamine **1** was (iii) directly alkylated with commercially available hexafluoroacetone (HFA) hydrate.[13] The reaction smoothly proceeded at 100 °C in excess of HFA hydrate under acid catalysis to give the desired dialkylation product **2** in high yield. Further the synthetic sequence included (iv) protection of the two secondary amino functions by treatment of **2** with trifluoroacetic anhydride in pyridine to yield **3**, and (v, vi) selective O-methylation / N-deprotection to afford **4** in 80% yield. The final heterocyclization of fluorinated diamine **4** to construct the desired imidazolinium salt **5** was successfully achieved using conventional treatment of **4** with HCl and triethyl orthoformate.

With this new fluorinated NHC salt in hand, we prepared the ruthenium complexes **6a**,**b**. Following the standard literature conditions by the reaction of *in situ* generated carbene with commercially available Grubbs I catalyst $RuCl_2(PCy_3)_2$(=CHPh) **G-I**[14] and Hoveyda one $RuCl_2(PCy_3)$(=CH(*o*-Pr^{i}OC_6H_4)) **H-I**,[15] complexes **6a**,**b** were obtained in moderate yields. Purification by silica gel chromatography and further crystallization from a DCM/*n*-pentane mixture afforded dark-brown (**6a**) and dark-green (**6b**) air stable solids (Scheme 2).†

Complexes **6a**,**b** were completely characterized by NMR spectroscopy and elemental analysis. In addition, single crystal of **6b** was studied by X-ray analysis (Figure 1).‡

Catalytic activities of the prepared catalysts **6a**,**b** were investigated in RCM reactions with diethyl diallylmalonate and in CM reaction of allylbenzene with 1,4-diacetoxybut-2-ene following standard protocols for evaluation of olefin metathesis catalysts.[16] The commercially available **G-II**[17] and **H-II**[18] catalysts were used as reference ones.



Scheme 2

The **G-II** and **H-II** catalysts are efficient for the RCM of diethyl diallylmalonate at 30 °C and full conversion obtained within 30 min.[16] The Grubbs type catalyst **6a** behaves similarly with very close kinetic profiles (Figure 2). On the other hand, the Hoveyda type catalyst **6b** presented a very different reactivity from the **H-II** catalyst. Pronounced initiation period (about 30 min)

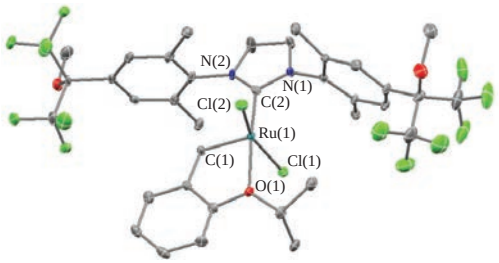


Figure 1 Molecular structure of complex **6b**. Thermal ellipsoids are drawn at 30% probability. Hydrogen atoms are omitted for clarity.

† *Synthesis of complex* **6a**. In a flame-dried Schlenk flask compound **5** (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 argon. The 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–light petroleum (1 : 8 → 1 : 3) as eluent under an argon atmosphere to yield 130 mg (30%) of complex **6a** as a brown solid. ^{1}H NMR (600 MHz, C_6D_6) δ: 19.55 (s, 1H, C*H*Ph), 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, 2H, CH_2, $^3J_{H,H}$ 10.2 Hz), 3.01 (s, 3H, OMe), 2.93 (t, 2H, CH_2, $^3J_{H,H}$ 10.2 Hz), 2.76 (s, 6H, Me), 2.43 (s, 6H, Me), 2.04 (q, 3H, PCy_3, $J_{H,P}$ 11.7 Hz), 1.68–1.50 (m, 16H, PCy_3), 1.37–1.26 (m, 6H, PCy_3), 1.11–1.00 (m, 8H, PCy_3). ^{19}F{^{1}H} NMR (376 MHz, C_6D_6) δ: 7.49 (s). ^{31}P NMR (162 MHz, C_6D_6) δ: 20.93 (s). ^{13}C NMR (151 MHz, C_6D_6) δ: 299.7 (br. s), 220.2 (d, $^2J_{C,P}$ 79.3 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. Found (%): C, 53.04; H, 5.56; N, 2.44. Calc. for $C_{52}H_{65}Cl_2F_{12}N_2O_2PRu$ (%): C, 52.88; H, 5.55; N, 2.37.

Synthesis of complex **6b**. In a flame-dried Schlenk flask compound **5** (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 μl 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 room temperature; then Hoveyda catalyst **H-I** (270 g, 0.45 mmol) was added and the 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–light petroleum (1 : 3) as eluent to yield 140 mg (32%) of complex **6b** as a green solid. Suitable for X-ray crystals were grown by slow diffusion of hexane vapors in CH_2Cl_2 solution. ^{1}H NMR (600 MHz, C_6D_6) δ: 16.53 (s, 1H, C*H*Ar), 7.61 (s, 4H, H_{Ar}), 7.12 (d, 1H, H_{Ar}, $J_{H,H}$ 7.6 Hz), 7.07 (t, 1H, H_{Ar}, $J_{H,H}$ 7.8 Hz), 6.65 (t, 1H, H_{Ar}, $J_{H,H}$ 7.5 Hz), 6.29 (d, 1H, H_{Ar}, $J_{H,H}$ 8.2 Hz), 4.45 [hept., 1H, OC*H*(Me)$_2$, $^3J_{H,H}$ 6.1 Hz], 3.26 (s, 6H, OMe), 3.22 [s, 4H, $(CH_2)_2$], 2.49 (s, 12H, Me), 1.27 [d, 6H, OCH(*Me*)$_2$, $^3J_{H,H}$ 6.2 Hz]. ^{19}F{^{1}H} NMR (282 MHz, C_6D_6) δ: 7.52 (s). ^{13}C 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, $^2J_{C,F}$ 290 Hz), 122.4, 122.3, 113.3, 83.5 (quint., $^1J_{C,F}$ 29 Hz), 75.3, 54.3, 51.0, 21.4. Found (%): C, 46.65; H, 4.21; N, 2.94. Calc. for $C_{37}H_{38}Cl_2F_{12}N_2O_3Ru$ (%): C, 46.36; H, 4.00; N, 2.92.

‡ *Crystal data for* **6b**: $C_{37}H_{38}Cl_2F_{12}N_2O_3Ru$, M = 958.67. APEXII, Bruker-AXS diffractometer, MoKα radiation (λ = 0.71073 Å), T = 150(2) K, orthorhombic, space group $Pc2_1b$ (#29), a = 11.7016(12), b = 13.0525(14) and c = 26.190(3) Å, V = 4000.1(7) Å^3, Z = 4, d = 1.588 g cm^{-3}, μ = = 0.620 mm^{-1}. The structure was solved by direct methods using the SIR97 program, and then refined with full-matrix least-square methods based on F^2 (SHELXL-97) with the aid of the WINGX program. All non-hydrogen atoms were refined with anisotropic atomic displacement parameters. H atoms were finally included in their calculated positions. A final refinement on F^2 with 7338 unique intensities and 516 parameters converged at $\omega R(F^2)$ = 0.1105 [$R(F)$ = 0.0516] for 5541 observed reflections with $I > 2\sigma(I)$.

CCDC 1030290 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre *via* http://www.ccdc.cam.ac.uk.

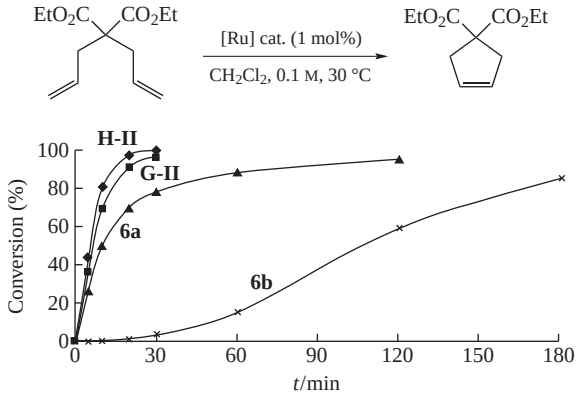


Figure 2 RCM of diethyl diallylmalonate with catalysts **6a** and **6b** as compared to **G-II** and **H-II**.

was necessary before it could achieve full conversion with lower reaction rates and thus in longer reaction times (4 h).

In CM of allylbenzene with an excess of 1,3-diacetoxybut-2-ene, these differences in reactivity did not exist and all complexes allowed an equilibrium to be reached at 70–80% conversion within 30 min with closely related kinetic profiles (Figure 3).

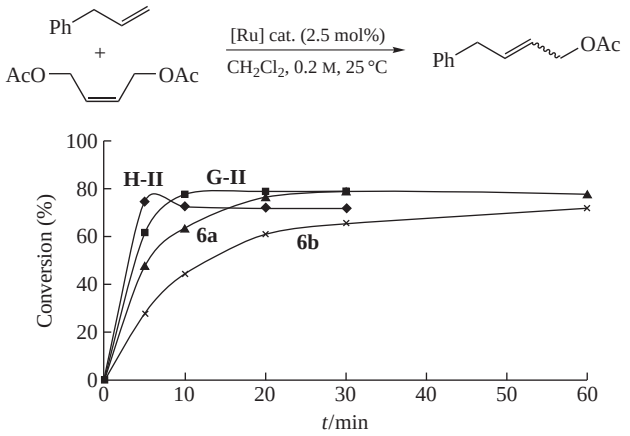


Figure 3 CM of allylbenzene with 1,3-diacetoxybut-2-ene with catalysts **6a** and **6b** as compared to **G-II** and **H-II**.

In conclusion, we prepared new symmetrical fluorinated *N*,*N'*-diarylimidazolidinium salt containing two hexafluoroisopropylmethoxy groups in *para*-positions of *N*-aryl substituents serving as precursors for the corresponding N-heterocyclic carbene ligands. Two ruthenium carbene complexes with these ligands belonging to the families of second generation Grubbs and Hoveyda olefin metathesis catalysts were obtained. The performance of the new Grubbs type catalyst in olefin metathesis has proved to be similar to that of the classical Grubbs second generation catalyst. Meantime, the new Hoveyda type catalyst behaves differently from the symmetrical Hoveyda-II catalyst equipped with the H_2IMes carbene ligand in ring closing metathesis of malonate derivatives and shows a latent character testified by an induction period followed by a lower reaction rate.

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Online Supplementary Materials

Supplementary data associated with this article can be found in the online version at doi:10.1016/j.mencom.2016.11.004.

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