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Synthesis and Activity of a New Generation of Ruthenium-Based Olefin Metathesis Catalysts Coordinated with 1,3-Dimesityl-4,5-dihydroimidazol-2-ylidene Ligands[§]

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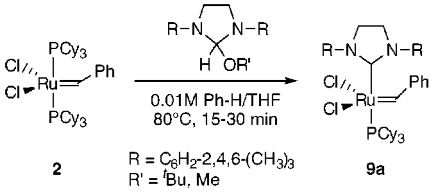
ABSTRACT



A new family of 1,3-dimesityl-4,5-dihydroimidazol-2-ylidene-substituted ruthenium-based complexes 9a–c has been prepared starting from $RuCl_2({=}CHPh)(PCy_3)_2$ 2. These air- and water-tolerant complexes were shown to exhibit an increased ring-closing metathesis activity at elevated temperature when compared to that of the parent complex 2 and the previously developed complex 3. In many instances the activity of these complexes also rivaled or exceeded that of the alkoxy–imido molybdenum complex 1. Catalyst loadings of as low as 0.05 mol % could be used.

With the advent of efficient catalysts, the olefin metathesis reaction has emerged as a powerful tool for the formation of C−C bonds.[1] Well-defined alkylidene−metal complexes which are widely used for this transformation include the alkoxy−imido molybdenum complex **1**[2] and the benzylidene ruthenium complex **2**.[3] The molybdenum complex **1** exhibits the higher reactivity of the two toward a broad range of substrates with many steric or electronic variations;[4] however, it also suffers from extreme sensitivity to air and moisture as well as decomposition upon storage. To increase the utility

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[§] Dedicated to Prof. Gregory C. Fu on the occasion of his 36th birthday.

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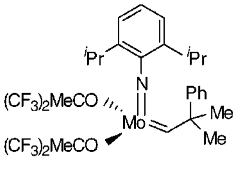
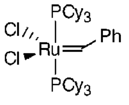
of the ruthenium family of complexes by increasing their activity, we recently prepared ruthenium-based complexes coordinated with 1,3-dimesitylimidazol-2-ylidene ligands **3**.[5] These complexes exhibited a high ring-closing metathesis activity similar to that of the molybdenum complex **1**, yet have also retained the remarkable air and water stability characteristic of the parent benzylidene ruthenium complex **2**.



1



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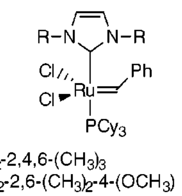
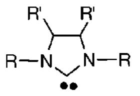


3

In search for even more efficient ligands for our ruthenium olefin metathesis catalysts, we have focused on the related 4,5-dihydroimidazol-2-ylidenes **4**.[6−8] We reasoned that due to the lack of carbene stabilization provided by the absence of π-interactions, these saturated imidazole ligands might be more basic then their unsaturated analogues.[9] The higher basicity of these ligands should in turn translate into an increased activity of the desired catalysts.[10]



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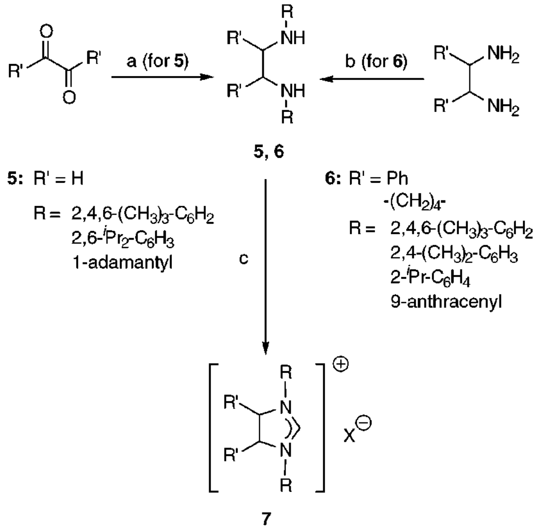
We began the synthesis of ligands **4** with the preparation of ethane-1,2-diamines **5** (R′ = H) and 1,2-disubstituted ethane-1,2-diamines **6** (R′ = Ph, alkyl). The diamines **5** were easily made via the condensation of a variety of aromatic and aliphatic amines with glyoxal, followed by a reduction of the resulting Schiff bases with either $NaCNBH_3$ or with H_2 and Pd/C (Scheme 1).[11] The diamines **6** were obtained in one step via the palladium-catalyzed amination reaction of various aryl bromides with 1,2-disubstituted ethane-1,2-diamines.[12]

Scheme 1. Precursor Synthesis



(a): (i) $R\text{-}NH_2$, acetone/water, (ii) H_2, Pd/C, EtOH or $NaCNBH_3$, HCl, MeOH; (b): R-Br, Pd_2dba_3, (±)-BINAP, NaO^{t}Bu, Ph-CH_3, 100°C; (c) $HC(OEt)_3$, NH_4BF_4, 120°C.

The diamines **5** and **6** were subsequently converted to the corresponding imidazolium salts through treatment with triethyl orthoformate in the presence of 1 equiv of ammonium tetrafluoroborate at 120 °C (Scheme 1).[13] The resultant imidazolium tetrafluoroborate salts **7** were obtained quantitatively and could be purified further by recrystallization from ethanol/hexanes.

We had hoped that these precursors could be readily deprotonated with metal hydrides to yield the desired ligands **4** directly,[7] especially since similar procedures have worked well for many unsaturated imidazolium salts.[14] Unfortunately, we were unsuccessful at extending the published procedures[7,14] to our saturated systems.

Parallel work in our group, however, revealed the possibility of using protected carbenes as precursors to generate the free carbene ligands in situ. Specifically, it was found that 5-methoxytriazoles could be reacted directly with metal complexes at elevated temperatures via the in situ conversion to the free triazol-5-ylidenes.[15] Correspondingly, we prepared the similar 2-alkoxy-4,5-dihydroimidazoles **8** by treatment of tetrafluoroborate salts **7** with sodium methoxide in methanol or potassium *tert*-butoxide in THF at ambient temperature (Scheme 2).

The alkoxy-protected species **8** did not react with benzylidene ruthenium complex **2** in benzene at ambient temperature. However, they readily reacted with complex **2**

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(7) For the first report of isolation of 1,3-dimesityl-4,5-dihydroimidazol-2-ylidenes, see: Arduengo, A. J.; Goerlich, J. R.; Marshall, W. J. *J. Am. Chem. Soc.* **1995**, *117*, 11027−11028.

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(9) Ding, S.; Feldmann, M. T.; Grubbs, R. H.; Goddard, W. A. *J. Am. Chem. Soc.* **1999**, submitted.

(10) Dias, E. L.; Nguyen, S. T.; Grubbs, R. H. *J. Am. Chem. Soc.* **1997**, *119*, 3887−3897.

(11) For examples, see: (a) Hutchins, R. O.; Su, W.-Y.; Sivakumar, R.; Cistone, F.; Stercho, Y. P. *J. Org. Chem.* **1983**, *48*, 3412−3422. (b) Dieck, H. t.; Verfürth, U.; Diblitz, K.; Ehlers, J.; Fendesak, G. *Chem. Ber.* **1989**, *122*, 129−131.

(12) For example, see: Wolfe, J. P.; Wagaw, S.; Buchwald, S. L. *J. Am. Chem. Soc.* **1996**, *118*, 7215−7216. For a recent review of palladium-catalyzed amination of aryl halides, see: Yang, B. H.; Buchwald, S. L. *J. Organomet. Chem.* **1999**, *576*, 125−146.

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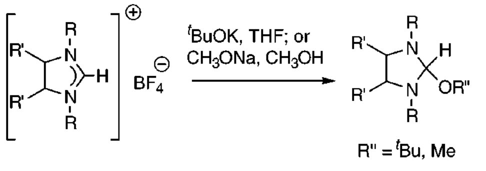
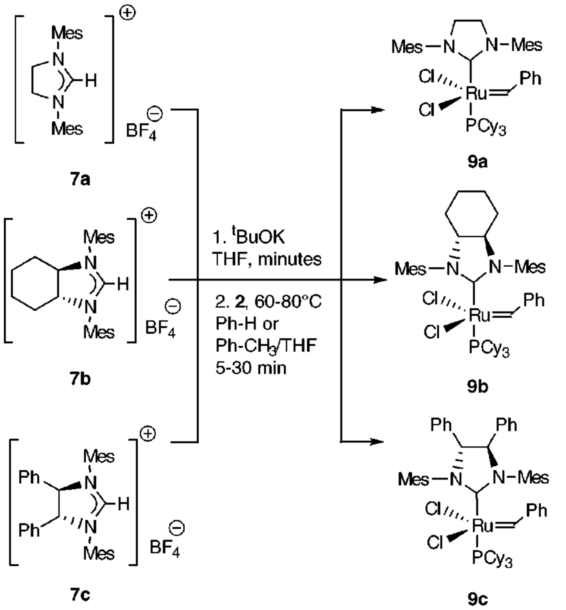
Scheme 2. Formation of 2-Alkoxy-4,5-dihydroimidazoles **8**



7 **8**

when deprotected in situ by heating to 60−80 °C. Specifically, when alkoxy-protected ligands **8** were heated in the presence of complex **2** at 60−80 °C, the desired ruthenium complexes **9a**−**c** coordinated with 1,3-dimesityl-4,5-dihydroimidazol-2-ylidenes were readily obtained as pinkish-brown microcrystalline solids in good yields (Scheme 3).[16]

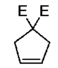
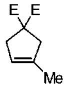
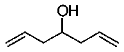
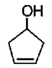
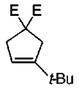
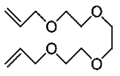
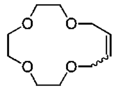
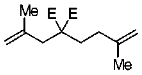
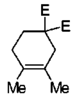
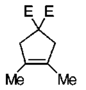
Scheme 3. Formation of Ruthenium Complexes **9a**−**c**



These complexes could be purified further by washing with methanol (**9a**) or pentane (**9b**,**c**).

The RCM activity of complexes **9a**,**b** was briefly explored and compared to that of complexes **1** and **2** as illustrated in Table 1. All complexes catalyzed the ring closure of diethyl diallylmalonate to form the corresponding disubstituted cycloolefin within minutes at 45 °C (entry 1). In the case of 2-substituted α,*ω*-dienes, however, the increased ring-closing metathesis activity of the complexes **9a**,**b** was readily evident.[17] For example, compound **10** was converted within minutes to the corresponding trisubstituted cycloolefin using complexes **9a**,**b** and complex **1**. In the same time duration the previously developed complex **3** facilitated a conversion of 85% and parent ruthenium complex **2** a conversion of only 20% (entry 2). For comparison, the same reaction at room temperature was completed within 1 h with complex **9a**, while little (<5%) or no conversion was achieved with complexes **2** and **3**.

Table 1. Results of Ring-Closing Metathesis at 45 °C Utilizing 5 mol % of Catalysts **1**, **2**, and **9a**,**b**

Entry	Substrate	Product	Time	Yield of product (%) using: 1	2	7a	7b
1.			10 min	quant.	quant.	quant.	quant.
2.	 **10**		10 min	quant.	20	quant.	quant.
3.			10 min	N.P.	N.P.	quant.	quant.
4.	 **11**		60 min	37	N.P.	quant.	quant.
5.			60 min	(15)^a	(39)^a	(35)^b	(45)^b
6.			90 min	52	N.P.	90	87
7.			24 hrs	93	N.P.	31	55

E = CO_2Et; quant. = quantitative conversion; N.P. = no product observed by ^{1}H NMR; yields in parentesis are isolated, all other yields are determined by ^{1}H NMR; ^{a} E:Z = 1.6:1; ^{b} E:Z = 2.0:1

A more dramatic illustration of the ring-closing metathesis activity of complexes **9a**,**b** was observed during cyclization of compound **11** at 45 °C (entry 3). This compound was readily converted to the corresponding trisubstituted cycloolefin with catalytic amounts of complexes **9a**,**b**. However, in the same time duration molybdenum complex **1** resulted in a conversion of only 37%, and the parent ruthenium complex **2** completely failed to promote the cyclization.

Similarly, while the parent ruthenium complex **2** was not active for the formation of tetrasubstituted olefins, these

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(16) **Representative Procedure for the Preparation of 9a**−**c.** A 500-mL flame-dried Schlenk flask equipped with a magnetic stirbar was charged with 1,3-dimesityl-4,5-dihydroimidazolium tetrafluoroborate (4.02 g, 10.2 mmol, 1.4 equiv) and dry THF (100 mL) under a nitrogen atmosphere. To this suspension was added a solution of potassium *tert*-butoxide (1.25 g, 10.2 mmol, 1.4 equiv) in dry THF (200 mL) slowly at room temperature. The tetrafluoroborate salt dissolved immediately to give a cloudy yellow solution. The reaction mixture was allowed to stir at room temperature for 1 h, followed by cannula transfer of the reaction mixture to another 1000-mL flame-dried Schlenk flask under argon. To this solution were added dry benzene (400 mL) and $RuCl_2(=CHPh)(PCy_3)_2$ (6.00 g, 7.29 mmol, 1.0 equiv). The reaction mixture was heated at 80 °C for 30 min, at which point the reaction was complete as indicated by ^{1}H NMR. The volatiles were removed under high vacuum, and the residue was washed with anhydrous methanol (4 × 100 mL) to give **9a** as a pinkish-brown microcrystalline solid (4.64 g) in 75% yield: ^{1}H NMR (CD_2Cl_2, 400 MHz) δ 19.16 (s, 1H), 7.37−7.05 (m, 9H), 3.88 (s, 4H), 2.56−0.15 (m, 51H); ^{31}P NMR (CD_2Cl_2, 161.9 MHz) δ 31.41; HRMS (FAB) $C_{45}H_{65}Cl_2N_2PRu$ [M^+] 848.3306, found 848.3286.

(17) For a study of the effects of olefin substitution on the ring-closing metathesis of dienes with complexes **1** and **2**, see ref 4.

compounds could be prepared in moderate to excellent yields using both complexes **9a**,**b** as well as complex **1** (entries 6 and 7). For example, in the formation of the six-membered tetrasubstituted cycloolefin, a higher conversion was achieved with catalysts **9a**,**b** than with catalyst **1** (entry 6). This trend was reversed in the formation of the tetrasubstituted five-membered cycloolefin (entry 7).

Furthermore, the advantage of ruthenium carbene complexes **9a**,**b** over complexes **1** and **2** could be demonstrated in cases where the molybdenum complex **1** was inactive due to its incompatibility with functional groups,[2] while parent ruthenium complex **2** also failed, presumably due to a formation of unreactive chelates. Specifically, the ring-closing metathesis of unprotected 1,6-heptadien-4-ol was quantitative with both **9a**,**b** while no reaction was observed with either complexes **1** or **2** (entry 3).

Since the complexes **9a**,**b** showed enhanced ring-closing metathesis activities and the propagating species of these complexes in RCM reactions were long-lived,[18] the use of lower catalysts loadings for RCM reactions was investigated. The ring closure of diethyl diallylmalonate in refluxing methylene chloride was conducted using 0.1, 0.05, and 0.01 mol % of catalysts **9a**,**b** with respect to the substrate. In the first case (0.1 mol % catalyst), quantitative conversions within 1 h were observed with both catalysts; in the second case (0.05 mol % catalyst), the conversions were quantitative with **9a** (1 h) and nearly quantitative (94%) with **9b** (3 h). In the third case (0.01 mol % catalyst), the yields were nearly zero with both catalysts. These results indicated a lower limit for the catalyst loading of approximately 0.05 mol %, which is about 2 orders of magnitude lower than that for parent complex **2** in this reaction. This feature might be especially useful, since ruthenium-based compounds are generally expensive, highly colored, and moderately toxic.[19]

In conclusion, the novel 4,5-dihydroimidazol-2-ylidene-substituted ruthenium-based complexes exhibit high olefin metathesis activity in RCM reactions and extend the potential of the ruthenium family of complexes. Di-, tri-, and tetra-substituted cycloolefins can be prepared in moderate to excellent yields through RCM. With certain substrates, similar yields may be obtained when catalyst loadings are reduced to as low as 0.05 mol %. Further detailed studies regarding the mechanistic description, the scope, including applications of complexes **9b**,**c** to asymmetric reactions, and the steric/electronic tuning of these complexes are under investigation.

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[18] The decomposition half-life at 55 °C in benzene of the (tricyclohexylphosphine)(1,3-dimesityl-4,5-dihydoimidazol-2-ylidene)methylidene ruthenium dichloride is approximately 6 h: Ulman, M. 1999, unpublished results. This is significantly longer than the corresponding half-life for the decomposition of bis(tricyclohexylphosphine)methylideneruthenium dichloride, which is only approximately 40 min: Ulman, M.; Grubbs, R. H. *J. Org. Chem.* **1999**, accepted.

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