Communications

Ruthenium Metathesis Catalysts with Saturated Unsymmetrical N-Heterocyclic Carbene Ligands

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*Summary: The facile synthesis of two new unsymmetrical N-heterocyclic carbene (NHC) ligands from commercially available monosubstituted diamines is presented. The resultant unsymmetrical NHC ligands have been complexed to ruthenium to give novel olefin metathesis initiators. Of particular interest, the new complexes (**7a** and **8a**) gave significantly different E:Z ratios in cross-metathesis reactions and gave an improved selectivity in diastereoselective ring-closing metathesis, in comparison to the corresponding Grubbs 2 (**2**) and Hoveyda−Grubbs (**3**) complexes.*

Since the discovery that well-defined ruthenium alkylidene complexes catalyze the ring-opening metathesis polymerization reaction,[1] there has been considerable effort devoted to synthesizing related derivatives with improved properties.[2] The introduction of N-heterocyclic carbenes (NHCs) in the early 1990s[3] has led to significant developments in olefin metathesis and palladium-catalyzed cross-coupling reactions.[4−6] The disclosure that substitution of a PCy_3 ligand with an NHC in the Grubbs 1 catalyst (**1**)[7,8] gives complexes exhibiting improved activity[9] and stability led to the introduction of the Grubbs 2 (**2**),[10−12] Hoveyda−Grubbs (**3**),[13] and Hoveyda−Blechert[14] classes of metathesis initiators (Figure 1).

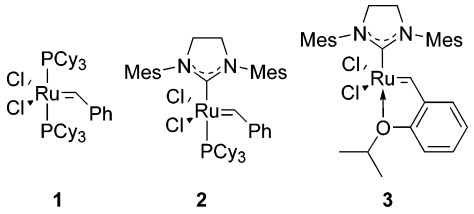

Figure 1.

An advantage of using NHCs is the possibility to fine-tune catalyst activity by modifying the ligand both at nitrogen and on the carbon backbone. This allows the steric and electronic

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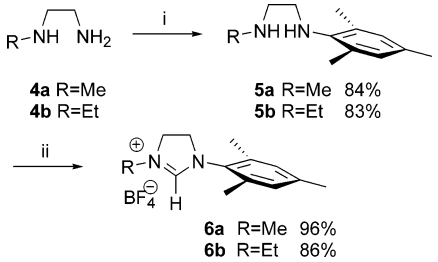
properties of the ligand to be tailored for a particular reaction.[15] It is interesting to note, therefore, that there are very few reports concerning modifications within the NHC framework for ruthenium-based olefin metathesis initiators,[16,17] and to the best of our knowledge metathesis complexes bearing saturated unsymmetrical NHCs are limited to disclosures by Mol,[18] who introduced a large sterically encumbered mixed adamantyl/mesityl based NHC, and the bidentate asymmetric ligand developed by Hoveyda.[19]

We were interested in investigating unsymmetrical saturated NHC ligands. We anticipated that replacement of one mesityl ring with a more electron donating alkyl group could lead to enhanced σ-donor properties. Increased σ-donation has been suggested as one reason to explain the higher activity of second-generation complexes in comparison to their first-generation counterparts.[5a] We also postulated that unsymmetrical ligands could alter the steric environment of key metathesis intermediates to effect *E*:*Z* selectivity in cross-metathesis (CM) reactions and selectivity in diastereoselective ring-closing metathesis (RCM) reactions.[20] We confined our studies to the saturated class of 4,5-dihydroimidazol-2-ylidene ligands,[21] due to the higher metathesis activity associated with complexes bearing these ligands,[22] when compared to their unsaturated counterparts.

Synthesis of the ligand precursors commenced with Buchwald−Hartwig coupling of commercially available diamines **4a** and **4b** with 2-bromomesitylene,[23] followed by cyclization, affording **6a** and **6b** as their tetrafluoroborate salts[24] in high yields (Scheme 1).

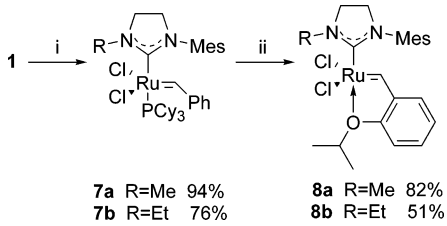
Complexes **7a** and **7b** could be isolated in excellent yields by generation of the free carbene from **6a** or **6b** in situ with potassium *tert*-amylate and reaction with **1** in hexane.[25,26] Treatment of **7a** and **7b** with 2-isopropoxystyrene in the presence of CuCl afforded the complexes **8a** and **8b** in good isolated yields as green, air-stable solids that were readily purifiable by silica gel chromatography (Scheme 2).

Scheme 1 [a]



[a] Legend: (i) $Pd_2(dba)_3$, (+/−)-BINAP, 2-bromomesitylene, NaO^{t}Bu, toluene; (ii) NH_4BF_4, $CH(OEt)_3$, 130 °C.

Scheme 2 [a]



[a] Legend: (i) **6a** or **6b**, potassium *tert*-amylate, hexane, 50 °C, 12 h; (ii) CuCl, 2-isopropoxystyrene, DCM, 1 h.

Table 1. ^{1}H, ^{13}C, and ^{31}P NMR Data[a]

entry	cat.	^{1}H	^{13}C	^{31}P
1	**2**	19.16	220.3	31.41
2	**7a**	18.85	219.8	34.33
3	**7b**	18.91	218.3	34.87
4	**3**	16.52	211.1	n/a
5	**8a**	16.18	209.0	n/a
6	**8b**	16.13	208.4	n/a

[a] Chemical shifts are given in ppm and measured in CD_2Cl_2.

The ruthenium complexes exhibited characteristic signals in ^{1}H NMR, displaying high-field-shifted singlets for the benzylidene proton compared to the signals for **2** and **3**. The ^{13}C NMR data followed a similar trend with the bound carbene, suggesting an increase in electron density at the metal center due to the effect of the electron-donating alkyl group (Table 1).

Unfortunately, it was not possible to obtain crystals of **7a** and **7b** of sufficient quality, but the NMR results strongly suggest that only one isomer is isolated from the reaction. Indication that the NHC ligand is orientated with the benzylidene proton directly under the mesityl ring was shown in NOE studies. Irradiation of the benzylidene proton in both **7a** and **7b** led to a positive enhancement to the methyl groups of the mesityl ring, as did irradiation of the aromatic proton of the styrene at 7.10 ppm (**7a** and **7b**). Upon irradiation of both **7a** and **7b** no NOE could be detected between the N-alkyl group of the NHC ligand and the benzylidene proton. Again the ^{1}H NMR data of **8a** and **8b** indicated the formation of a single isomer, which was confirmed by obtaining the single-crystal X-ray structures of **8a** (Figure 2) and **8b** (Figure 3).[27] Selected bond lengths and angles are provided (Table 2).

Complexes **8a** and **8b** both display slightly decreased Ru−C(11) and Ru−C(1) bond lengths in comparison to those of **3** (Table 2, entries 1 and 2). These observations are consistent with our expectations of stronger σ-donation of the NHC ligand. However, the Ru−O bond remains within the same range. The reduced N−C(11) bond lengths (Table 2, entries 4 and 5) suggests slightly increased p_π overlap between the NHC carbon

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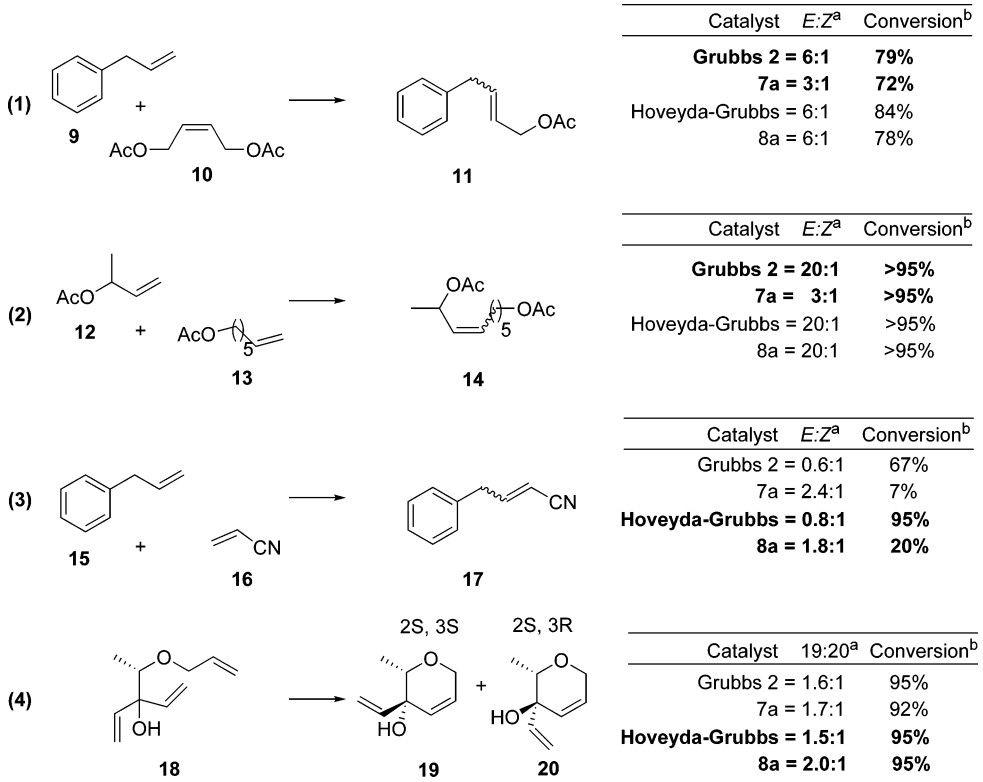
Scheme 3



Catalyst	*E*:*Z*[a]	Conversion[b]
Grubbs 2	**6:1**	**79%**
7a	**3:1**	**72%**
Hoveyda-Grubbs	6:1	84%
8a	6:1	78%

Catalyst	*E*:*Z*[a]	Conversion[b]
Grubbs 2	**20:1**	**>95%**
7a	**3:1**	**>95%**
Hoveyda-Grubbs	20:1	>95%
8a	20:1	>95%

Catalyst	*E*:*Z*[a]	Conversion[b]
Grubbs 2	0.6:1	67%
7a	2.4:1	7%
Hoveyda-Grubbs	**0.8:1**	**95%**
8a	**1.8:1**	**20%**

Catalyst	19:20[a]	Conversion[b]
Grubbs 2	1.6:1	95%
7a	1.7:1	92%
Hoveyda-Grubbs	**1.5:1**	**95%**
8a	**2.0:1**	**95%**

[a] Ratios measured by NMR. [b]Reactions performed in refluxing DCM with 3 mol % catalyst loading and conversions determined by NMR.

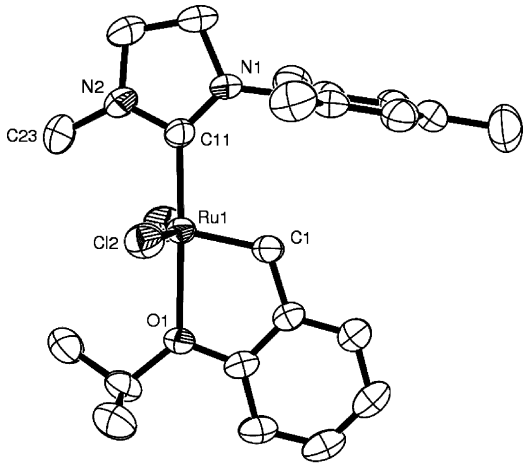


Figure 2. X-ray structure of **8a** with 50% probability ellipsoids. Hydrogen atoms have been omitted for clarity.

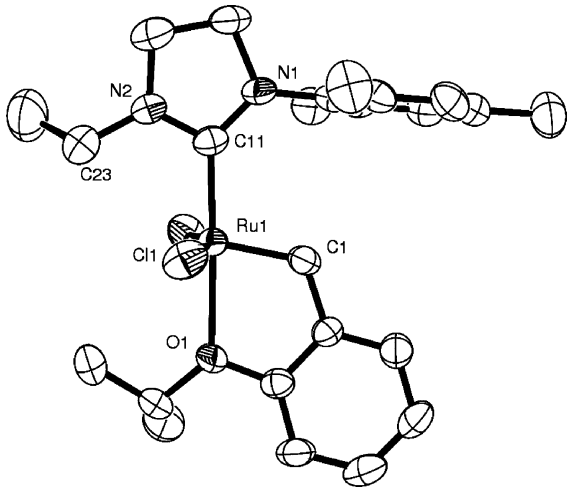


Figure 3. X-ray structure of **8b** with 50% probability ellipsoids. Hydrogen atoms have been omitted for clarity.

and the adjacent nitrogen atom. In both **8a** and **8b** the N-alkyl group bends toward the chloride−benzylidene plane, displaying nonsymmetric coordination (Table 2, entries 6 and 7), with the benzylidene proton being located directly under the mesityl aromatic ring.

Initially, the complexes **7a** and **8a** were tested in the model RCM reaction of *N*,*N*-diallyl-*p*-toluenesulfonamide, to gain an impression of their catalytic activity. The reaction was carried out in DCM at reflux with a catalyst loading of 0.02 mol %. After 14 h **7a** gave 56% conversion, compared to 50% conversion with **2**. Interestingly, **8a** also delivered 56% conversion, compared to 66% with **3**, demonstrating activity comparable to that of the Grubbs 2 catalyst (**2**).[28]

We next investigated the activity of **7a** and **8a** in representative CM reactions (Scheme 3, eqs 1−3) and a diastereoselective RCM (Scheme 3, eq 4).[29]

(27) The data for **8a** and **8b** were collected on a SMART CCD (graphite-monochromated Mo Kα radiation, ω-scan technique, $\lambda = 0.710\ 73$ Å). The structures were solved by direct methods using SHELXS-97 and were refined on F^2 using all reflections with SHELXL-97. SADABS was used to perform area-detector scaling and absorption corrections. (a) Sheldrick, G. M. SHELXS-97: Program for the Solution of Crystal Structures; University of Göttingen, Göttingen, Germany, 1990. (b) Sheldrick, G. M. SHELXL-97: Program for the Refinement of Crystal Structures; University of Göttingen, Göttingen, Germany, 1997. (c) Sheldrick, G. M. SADABS: Program for Empirical Absorption Correction of Area Detector Data; University of Göttingen, Göttingen, Germany, 1996.

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Table 2. Selected Bond Lengths and Angles for 3, 8a, and 8b

entry		3	8a	8b
	Bond Lengths (Å)			
1	Ru−C(11)	1.981	1.978	1.966
2	Ru−C(1)	1.828	1.821	1.817
3	Ru−O	2.261	2.269	2.269
4	N(1)−C(11)	1.350	1.345	1.344
5	N(2)−C(11)	1.351	1.341	1.341
	Bond Angles (deg)			
6	N(1)−C(11)−Ru	131.6	134.26	134.4
7	N(2)−C(11)−Ru	120.8	118.2	118.4
8	C(11)−Ru−C(1)	101.5	102.68	102.46
9	C(11)−Ru−O	176.2	178.16	177.46
10	Cl(1)−Ru−Cl(2)	156.5	153.53	151.11

Complexes **7a** and **8a** displayed conversions similar to those for **2** and **3** under identical reaction conditions (Scheme 3, eqs 1 and 2). Interestingly, greater amounts of the *Z* isomer were obtained with **7a**, whereas **8a** gave a comparable *E*:*Z* ratio, in comparison to the results for **2** and **3**. A greatly changed *E*:*Z* ratio (3:1), compared to the almost exclusive *Z* geometry obtained with complexes **2**, **3**, and **8a**, was observed with **7a** in eq 2 (Scheme 3). CM with acrylonitrile (Scheme 3, eq 3) proceeded with low conversion when **7a** and **8a** were utilized; however, a *complete* reversal of selectivity was observed. In a representative diastereoselective RCM reaction,[30] **7a** and **8a** gave improved selectivities of 1.7:1 and 2.0:1 compared to 1.6:1 and 1.5:1 with **2** and **3**, respectively, with excellent conversions (Scheme 3, eq 4).

In summary, two new unsymmetrical NHC ligands have been synthesized and have been complexed to ruthenium to give novel olefin metathesis initiators. In the RCM reaction of *N*,*N*-diallyl-*p*-toluenesulfonamide, the novel metathesis initiators displayed activities similar to those of their symmetrical counterparts. Of particular interest, complex **7a** gave significantly different *E*:*Z* ratios in cross-metathesis reactions, and both **7a** and **8a** gave improved selectivity in diastereoselective ring-closing metathesis. To further understand these selectivity effects, the synthesis of other unsymmetrical NHCs is being investigated and will be reported in due course.

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Supporting Information Available: Text giving details of the synthesis and spectroscopic characterization of all new compounds and text, figures, and tables giving details of the X-ray crystallographic information for complexes **8a** and **8b**; crystal data are also available as CIF files. This material is available free of charge via the Internet at http://pubs.acs.org.

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