

Synthesis and Reactivity of Olefin Metathesis Catalysts Bearing Cyclic (Alkyl)(Amino)Carbenes**

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The evolution of olefin metathesis into a reaction routinely used to form new carbon–carbon double bonds has been enabled by the development of well-defined transition-metal catalysts.^[1,2] Many metathesis catalysts based on the $[L_2X_2Ru=CHR]$ scaffold have been synthesized in an effort to increase catalyst stability, activity, and substrate scope.^[3–10] A significant gain in these areas was achieved after exchanging a single PCy_3 ligand of **1** with H_2IMes (H_2IMes = 1,3-dimesityl-4,5-dihydroimidazol-2-ylidene), an N-heterocyclic carbene (NHC), to produce catalyst **2** (Figure 1).^[5] These

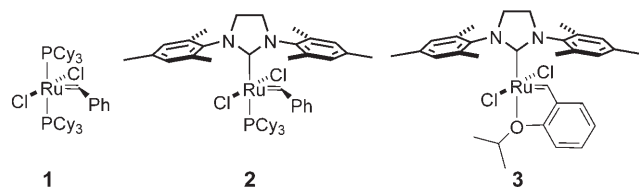


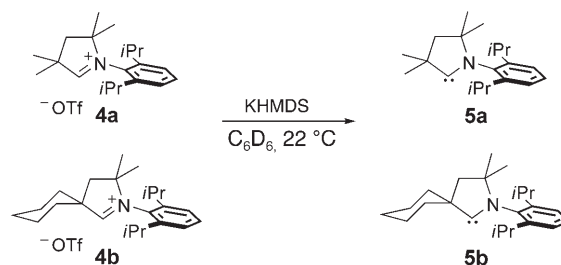
Figure 1. Commonly utilized ruthenium olefin metathesis catalysts. Cy = cyclohexyl.

results are attributed to the increased σ -donor ability of H_2IMes over PCy_3 , which increases the affinity for π -acidic olefins relative to σ -donating phosphines.^[11] Additionally,

exchange of the remaining PCy_3 ligand with a chelating ether moiety provides a more stable complex, catalyst **3**.^[6]

Recently, the synthesis of cyclic (alkyl)(amino)carbenes (CAACs), in which one amino group from an NHC has been replaced by an alkyl group, was reported.^[12] The greater σ -donor ability of carbon versus nitrogen results in more electron-donating ligands, as indicated by the ν_{CO} absorption of cis - $[Rh(Cl)(CO)_2L]$ complexes ($L = H_2IMes$, $\tilde{\nu}_{CO} = 1996$, 2081 cm^{-1} ; $L = \mathbf{5b}$, $\tilde{\nu}_{CO} = 1994$, 2077 cm^{-1}).^[13] The exchange of an sp^2 -hybridized nitrogen atom for an sp^3 -hybridized carbon atom also changes the steric environment relative to NHCs. Although most NHCs are C_{2v} -symmetric, the CAACs reported to date are C_s - or C_1 -symmetric, which may have implications for the microscopic reversibility of the olefin-binding and cycloreversion steps in the metathesis catalytic cycle.^[14,15] The unique properties of CAACs led us to explore the utility of this new class of stable carbenes as ligands in olefin metathesis catalysts.

We first chose to investigate carbenes **5a,b**, which can be prepared from their respective salts **4a,b** (Scheme 1).^[12,16] These ligands each contain an *N*-DIPP (DIPP = 2,6-diisopropyl



Scheme 1. Synthesis of carbenes **5a,b**.

pylphenyl) group and vary the steric bulk at the quaternary carbon adjacent to the carbene center, with either two Me groups (**5a**) or a spiro-fused cyclohexyl group (**5b**). Upon addition of potassium hexamethyldisilazide (KHMDS) to salts **4a,b** at 22°C in benzene, the corresponding carbenes **5a,b** are obtained in good conversion as observed by ^1H NMR spectroscopy.

Ruthenium olefin metathesis catalysts bearing a pyridine ligand typically undergo facile ligand exchange with stronger donors such as phosphines or NHCs.^[17] Thus, upon addition of pyridine complex **6**^[18] to an NHC, the resulting ruthenium complex is typically coordinated by a carbene ligand and a phosphine ligand (e.g. **2**), rather than a pyridine ligand. However, upon treatment of pyridine complex **6** with carbenes **5a,b** (generated in situ), no evidence for the

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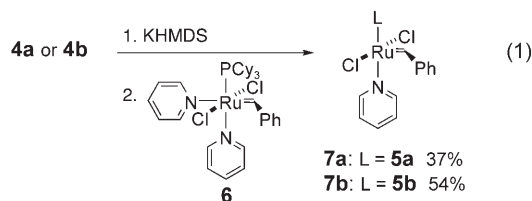
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expected phosphine complexes was obtained by ^1H or ^{31}P NMR spectroscopy [Eq. (1)]. Instead, air-sensitive pyridine adducts **7a,b** were isolated in modest yields.



X-ray crystallographic analysis of compounds **7a,b** was conducted. These complexes exhibit a distorted square-pyramidal geometry with the benzylidene ligand in the apical position (Figure 2). The bond lengths and angles of

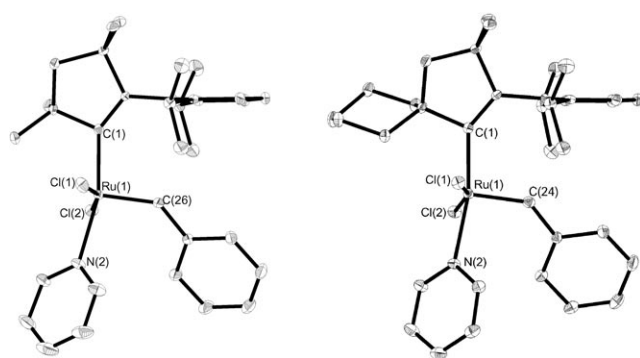
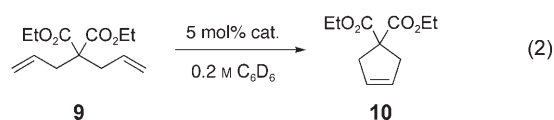


Figure 2. X-ray crystal structures of **7a** (left) and **7b** (right). Thermal ellipsoids are drawn at 50% probability and hydrogen atoms are omitted for clarity.

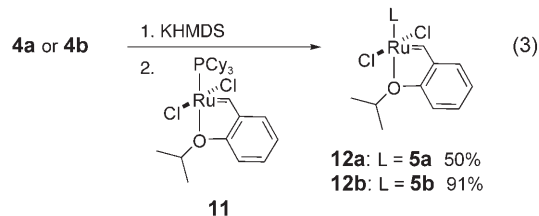
the pyridine catalysts **7a,b** are similar to those of $[(\text{H}_2\text{IMes})(\text{py})_2(\text{Cl})_2\text{Ru}=\text{CHPh}]$ (**8**) (see the Supporting Information).^[17] The $\text{Ru}-\text{C}_{\text{carbene}}$ distance is $\approx 0.05 \text{ \AA}$ shorter than in **8** which is consistent with the increased σ -donating ability of CAACs relative to H_2IMes . In addition, the $\text{Ru}-\text{C}_{\text{benzylidene}}$ bond length is $\approx 0.03 \text{ \AA}$ shorter in **7a,b** than in **8**, possibly a result of the trans influence of the additional pyridine ligand in **8**.

The efficiency of catalysts **7a,b** was examined in the ring-closing metathesis of diethyl diallylmalonate (**9**) [Eq. (2)].



Maximum conversions to cyclopentene **10** observed by ^1H NMR spectroscopy were less than 50% after 24 h at 22°C or 60°C , which is attributed to catalyst decomposition. These results are consistent with those obtained previously with pyridine-containing catalysts.^[19] For comparison, complexes **2** and **3** can achieve 95% conversion to **10** in 30 and 20 min, respectively, at 30°C and 1 mol% catalyst loading.^[19]

To obtain more stable complexes, we targeted complexes **12a,b**. After addition of **5a,b** (prepared in situ) to ruthenium precursor **11**,^[8] catalysts **12a,b** were isolated and purified in good yields by column chromatography [Eq. (3)]. Chelating ether complexes **12a,b** are air- and moisture-stable compounds.



Similar to complexes **7a,b**, the solid-state structures of **12a,b** show a distorted square-pyramidal structure with the benzylidene moiety at the apical position (Figure 3). Comparing complexes **12a,b** with the H_2IMes -containing analogue **3**, the $\text{Ru}-\text{C}_{\text{carbene}}$ distances are $\approx 0.04\text{--}0.05 \text{ \AA}$ shorter and the $\text{Ru}-\text{O}$ distances are $0.04\text{--}0.09 \text{ \AA}$ longer than in complex **3** (see the Supporting Information).^[6] These observations are consistent with the increased σ -donating properties of ligands **5a,b** over their NHC counterparts.

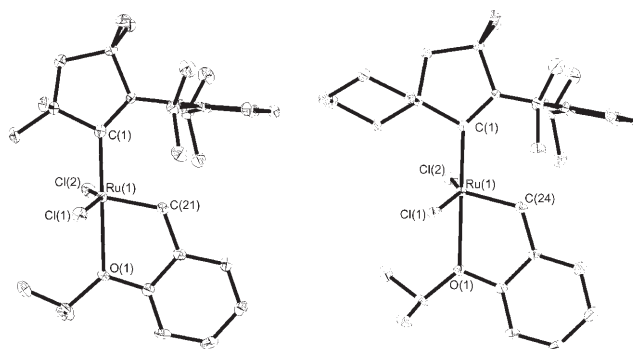


Figure 3. X-ray crystal structures of **12a** (left) and **12b** (right). Thermal ellipsoids are drawn at 50% probability and hydrogen atoms are omitted for clarity.

In all solid-state structures obtained, the CAAC exhibits the same orientation relative to the benzylidene group (Figure 4). The N-aryl ring is located above the benzylidene moiety, while the quaternary carbon adjacent to the carbene center is positioned over an empty coordination site. In the case of pyridine complexes **7a,b**, this observed preference may be due to π - π stacking between the N-aryl ring and the benzylidene ring. For chelating ether complexes **12a,b** this structural preference may be a result of negative steric interactions between the Me groups on the quaternary carbon adjacent to the carbene carbon and the benzylidene proton (Figure 4). From this side view, it is apparent that the benzylidene proton would be in close contact with one Me group on the quaternary carbon center if the ligand were rotated 180° relative to the remainder of the molecule.

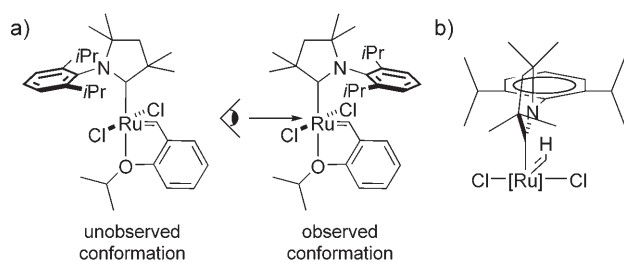


Figure 4. View of complex **12a** looking down the Ru=CHR bond. It can be observed that rotating the carbene 180° would place the protons on the benzylidene and Me group on the quaternary carbon center in close proximity.

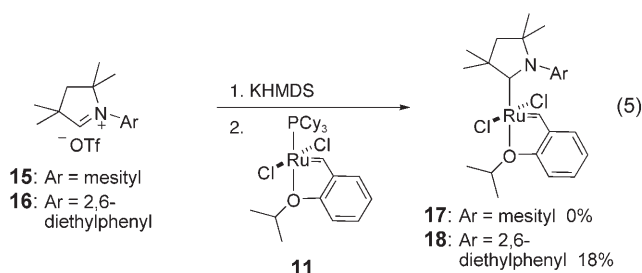
¹H NMR spectroscopy data suggest that the solid-state conformation of **12a,b** is maintained in solution. 2D-ROESY experiments performed on complexes **12a,b** in C₆D₆ at 22 °C demonstrate Overhauser effects between the benzylidene resonance and the aryl protons on the *N*-DIPP moiety, the equivalent methine resonances of the aryl isopropyl groups, and the enantiotopic Me groups facing the benzylidene proton (Figure 4b). Overhauser effects are not observed between the benzylidene proton and the gem-dimethyl(ene) groups adjacent to the carbene center. This interaction might be expected if there is fast exchange between two orientations of the carbene ligand relative to the ruthenium benzylidene.

The efficiency of catalysts **12a,b** was examined in the ring-closing metathesis of **9**, **13a**, and **13b** [Eq. (4)]. At a catalyst



loading of 1 mol% catalyst loading, chelating ether catalysts **12a,b** achieved 97% and 95% conversion of diethyl diallylmalonate (**9**) after heating at 60 °C for 3.3 h and 10 h, respectively. Uninitiated catalyst is observed for both catalysts even at high conversions, indicating that only a fraction of added catalyst is engaged in the reaction. Catalyst **12a** converts **13a** to 95% of trisubstituted olefin **14a** in 20 h at 60 °C, whereas catalyst **12b** achieves 96% conversion after 48 h at 60 °C. However, catalysts **12a,b** showed no reactivity in the conversion of **13b** to tetrasubstituted olefin **14b**.

We hypothesized that sterics could be responsible for the lower activity of catalysts **12a,b** relative to **2** and **3**. CAACs without the quaternary carbon center adjacent to the carbene carbon are not synthetically accessible; thus, decreasing the steric bulk of the *N*-aryl ring was targeted. Both the *N*-mesityl- and *N*-DEP (DEP = 2,6-diethylphenyl)-substituted salts, **15** and **16**, respectively, were synthesized; deprotonation of **15** and **16** under a variety of conditions did not afford the desired free carbenes [Eq. (5)]. In situ deprotonations of **15** and **16** with KHMDS at –78 °C in THF in the presence of ruthenium precursor **11** were also attempted. Although **17** was not observed by NMR spectroscopy, complex **18** could be



observed and isolated. Similar to **12a,b**, complex **18** is an air- and moisture-stable solid. X-ray diffraction studies of catalyst **18** show similar bond lengths and angles to those in **12a,b** (Figure 5).

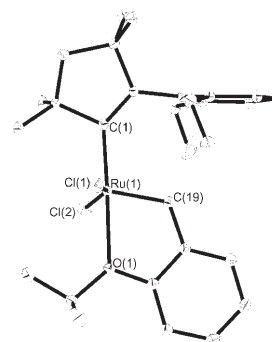


Figure 5. X-ray crystal structure of **18**. Thermal ellipsoids are drawn at 50% probability and hydrogen atoms are omitted for clarity.

Catalyst **18**, which differs from **12a** only by replacement of *N*-DIPP with *N*-DEP, demonstrates significantly increased activity in the formation of di- and trisubstituted olefins. In the presence of 1 mol% **18**, 95% conversion of **9** to substituted cyclopentene **10** is observed in 15 min at 30 °C, as compared to 3 h at 60 °C required for catalyst **12a** (Table 1). Catalyst **18** achieves 95% conversion of **13a** to trisubstituted cyclopentene **14a** at 30 °C in 1 h, which is comparable to the performance of catalysts **2** and **3**. However, catalyst **18** showed no reactivity in the conversion of **13b** to **14b**.

The dramatic increase in activity observed after slightly decreasing the steric bulk of the *N*-aryl group is attributed to catalyst initiation. We postulate that catalyst initiation requires dissociation of the ether moiety and rotation of the benzylidene ring into a plane parallel to the *N*-aryl group to open a coordination site for incoming olefin.^[20] For complexes **12a,b** this process may be sterically unfavorable, thus result-

Table 1: Comparison of the activities of catalysts **12a**, **12b**, **18**, **2**, and **3**.

Catalyst	Conversion (9 → 10)	Conversion (9 → 14b)
12a	97% (3.3 h at 60 °C)	95% (20 h at 60 °C)
12b	95% (10 h at 60 °C)	96% (48 h at 60 °C)
18	95% (15 min at 30 °C)	95% (1 h at 30 °C)
2	95% (30 min at 30 °C)	95% (45 min at 30 °C)
3	95% (20 min at 30 °C)	95% (45 min at 30 °C)

ing in poor initiation (Figure 6). The steric bulk of the *ortho*-aryl substituents may have a significant effect on initiation for two reasons. First, the Ru–C_{carbene} bond length is slightly shorter than in NHC analogues, thus bringing the aryl ring in closer proximity to the ruthenium center. Second, the quaternary carbon adjacent to the N-aryl group restricts rotation around the N-aryl bond and the C_{aryl}–C_{iPr} bond, as indicated by NMR spectroscopy experiments discussed earlier.

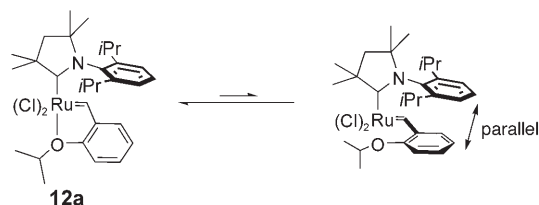


Figure 6. Proposed rotation required for catalyst initiation.

Interestingly, replacement of the *N*-mesityl groups in complex **3** with *N*-DIPP groups,^[21] results in a catalyst with increased activity for the ring-closing metathesis of **9** (97% conversion in 13 min vs. 20 min).^[20] However, this bulkier catalyst differs from the CAAC complexes owing to the absence of substitution at the carbon adjacent to the nitrogen atom.

Our investigation of the use of CAACs as ligands for olefin metathesis catalysts has shown promising results. By tuning the steric bulk of the N-aryl group, the results of ring-closing metathesis for the formation of di- and trisubstituted olefins are comparable to those achieved with standard catalysts **2** and **3**.

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