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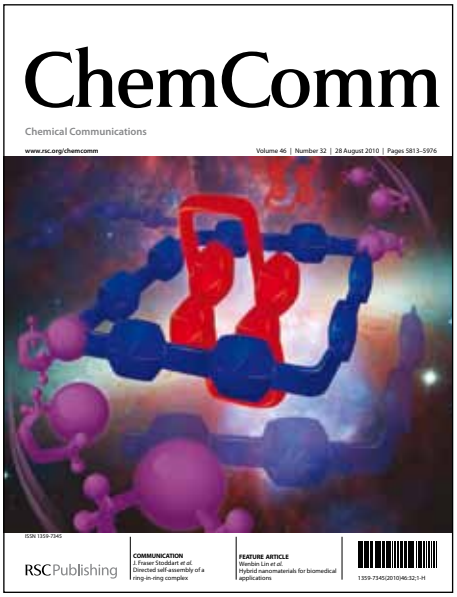

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COMMUNICATION

Ruthenium-catalyzed Olefin Metathesis Accelerated by Steric Effect of Backbone Substituent in Cyclic (Alkyl)(Amino)Carbenes

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Three ruthenium complexes bearing backbone-monosubstituted CAACs were prepared and displayed considerable improvement on catalytic efficiency not only in RCM reaction but also in the ethenolysis of methyl oleate, compared to those bearing backbone-disubstituted CAACs.

Over the last decade, N-heterocyclic carbenes (NHCs) have received much attention mainly due to their widespread and spectacular applications as organocatalysts and as ligands for organometallic catalysis.[1] The number, electronic nature, steric effect and position of the substituents on both the nitrogen atoms and the backbone of NHCs have played important roles in NHC-promoted reactions.[2] In 2005, Bertrand etc. synthesized cyclic(alkyl)(amino) carbenes (CAACs), in which one amino group derived from an NHC imidazolidin-2-ylidene has been replaced by a quaternary alkyl group (Figure 1).[3] Due to the presence of a quaternary carbon atom in a position α to the carbene center, CAACs featured peculiar electronic and steric properties that are dramatically different from NHCs. Grubbs and Bertrand etc. found that the CAAC-ligated Hoveyda-Grubbs catalysts **1** (**1a**: $R^1 = {}^i$Pr; R^2-$R^2 = (CH_2)_5$; **1b**: $R^1 = {}^i$Pr; R^2 = Me; **1c**: R^1 = Et; R^2 = Me) were very reactive in ring-closing metathesis, and a dramatic increase in catalytic activity was observed after slightly decreasing the steric bulkiness of the N-aryl group from 2,6-diisopropylphenyl group (**1a**, **1b**) to 2,6-diethylphenyl group (**1c**).[4] Another study showed **1a**~**1c** also exhibited high efficiency for the formation of terminal olefins in the ethenolysis of methyl oleate.[5] At 100ppm catalyst loading, **1b** displayed higher selectivity (92%) and TON (5600) than **1c** (73% of selectivity and 5300 of TON) did. At a low catalyst loading of 10ppm, only complex **1c** is reactive, though lower selectivity of 83% obtained, and achieves TONs of 35000, the highest TON recorded so far for this reaction.[5]

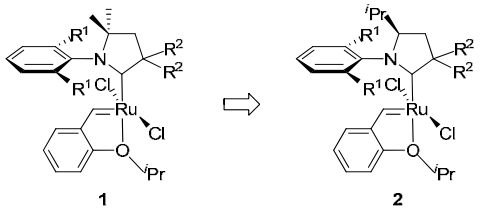
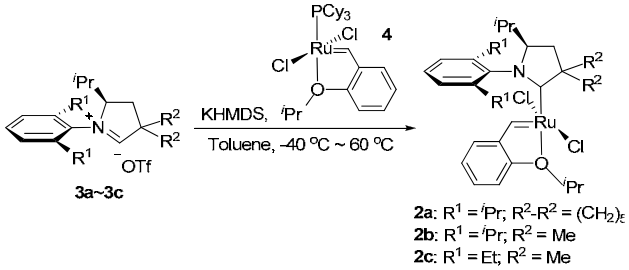


Figure 1. Known Ru complexes **1** ligated by backbone-disubstituted CAACs and targeted ruthenium complexes **2** ligated by backbone-monosubstituted CAACs



Scheme 1. Synthesis of ruthenium complexes **2a**~**2c**

Most modifications in CAAC ligands are made on their N-substituents and/or C-substituents adjacent to the carbene center, and almost CAACs employed are those bearing two methyl groups in their backbone.[3~5] To the best of our knowledge, the effect of backbone substitution of CAAC in catalytic performance is not yet investigated. As part of our studies on the design and synthesis of backbone-substituted carbenes and their application in catalysis,[6] we herein report a series of Ru complexes **2** ligated by CAACs bearing a bulky isopropyl group in their backbone. We also demonstrate that, compared to **1**, ruthenium complexes **2** displayed considerable improvement on catalytic efficiency not only in RCM reaction but also in the ethenolysis of methyl oleate. With 10 ppm catalyst loading, complex **2b** ($R^1 = {}^i$Pr; R^2 = Me) displayed high selectivity (97%) in the ethenolysis of methyl oleate and achieved 26000 TONs.

We first synthesized three new pyrrolidinium salts **3a**~**3c** according to a published procedure reported by Bertrand

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† Electronic Supplementary Information (ESI) available: Experimental and spectroscopic data for all compounds. CCDC 887373 (**2a**). For ESI and crystallographic data in CIF or other electronic format See DOI: 10.1039/b000000x/

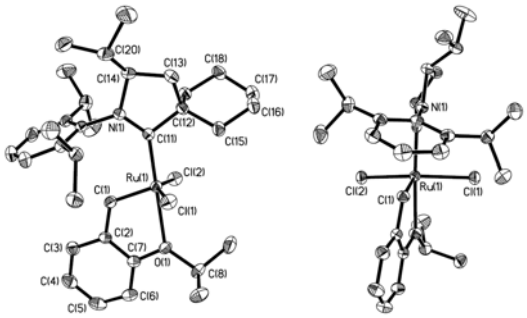


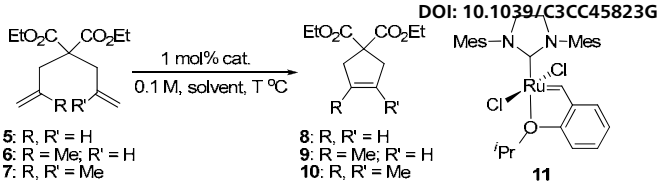
Figure 2. Left: Molecular structure of **2a**. Right: side-view of **2a** (cyclohexyl group omitted for clarity).

etc.[3,4] The corresponding CAACs were generated in situ by treatment of **3a**~**3c** with potassium hexamethyldisilazide (KHMDS) and then reacted with $RuCl_2(PCy_3)(=CH–o\text{-}O^iPrC_6H_4)$ (**4**) to afford the desired Ru complexes **2a**~**2c** (Scheme 1). These complexes were isolated as air- and moisture-stable solids by column chromatography. Both mass and NMR spectra, and in particular the X-ray diffraction analyses of **2a** confirmed the formation of these CAAC-Ru complexes (Figure 2). Similar to **1a**~**1c**,[4] the solid-state structure of **2a** adopts a square-pyramidal geometry. The benzylidene moiety is located at the apical position, and the N-aryl ring is situated above the benzylidene moiety.

RCM is the first widely used olefin metathesis reaction in organic synthesis and has been used as the standard reaction to evaluate the catalytic efficiency of most ruthenium-based complexes.[1] We initially investigated the catalytic activity of **2a**~**2c** in the RCM of diethyl diallylmalonate **5**, diethyl allylmethallyl malonate **6**, and diethyl dimethallylmalonate **7**, and the catalytic performances are summarized in Table 1. A study reported by Grubbs etc. showed Ru complexes **1a**, **1b** are highly active in RCM of **5** at 60 °C, but a longer reaction time is required for **1a** (Table 1, runs 2 and 3).[4] The RCM of **6** is more sterically demanding than the corresponding RCM of **5**. At 60 °C, **1b** converted **6** to 95% of trisubstituted olefin **9** in 20 h at 60 °C, while **1a** achieved 96% conversion after 48 h (Table 1, runs 11 and 12). We found that, at lower reaction temperature of 30 °C, complex **1b** afforded moderate conversion of 60% after 20 h for the RCM of **5** (Table 1, run 1), and very low conversion of 3% after 23 h for the RCM of **6** (Table 1, run 9). **2a** and **2b** bearing a backbone-monosubstituted CAAC were identified to be much more efficient in these RCM reactions than their congeners **1a** and **1b** bearing a backbone-disubstituted CAAC. **2a** and **2b** achieved 77% and 85% conversion of **5** at 30 °C in 20 h (Table 1, runs 4 and 5), and 52% and 90% conversion of **6** at 30 °C in 23 h (Table 1, runs 13 and 15), respectively. At higher reaction temperature of 60 °C, **2a** and **2b** achieved 65% and 90% conversion of **6** in 5 h (Table 1, runs 14 and 16), while **1b** achieved 11% conversion in 5 h (Table 1, run 10).

The reasonable explanation for the improvement on catalytic activities of **2a** and **2b** can be given by invoking steric factors. Grubbs etc. postulated that, in catalyst **1**, 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.[4]

Table 1. Comparison of Ruthenium Catalysts in the RCM Reaction of **5**~**7**[a]



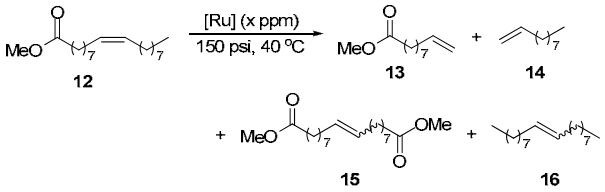
Cat.	Run	Conversion (**5** to **8**)[b]	Run	Conversion (**6** to **9**)[b]
1b	1	60% (20 h at 30 °C)	9	3 % (23 h at 30 °C)
			10	11 % (5 h at 60 °C)
	2[c]	97 % (3.3 h at 60 °C)	11[c]	95 % (20 h at 60 °C)
1a	3[c]	95 % (10 h at 60 °C)	12[c]	96 % (48 h at 60 °C)
2a	4	77 % (20 h at 30 °C)	13	52 % (23 h at 30 °C)
			14	65 % (5 h at 60 °C)
2b	5	85 % (20 h at 30 °C)	15	90 % (23 h at 30 °C)
			16	90 % (5 h at 60 °C)
2c	6	98 % (15 min at 30 °C)	17	95 % (50 min at 30 °C)
1c	7[c]	95 % (15 min at 30 °C)	18[c]	95 % (60 min at 30 °C)
11	8	78 % (15 min at 30 °C)	19	98 % (50 min at 30 °C)

[a] General conditions: Diolefin (0.1 M), catalyst (1.0 mol%), 30 °C in CD_2Cl_2 or 60 °C in C_6D_6. [b] Determined by NMR. [c] Taken from Ref. 4

For **1a** and **1b** bearing bulky N-aryl group, this process may be sterically unfavorable, thus resulting in poor initiation. A dramatic increase in catalytic activity was observed using **1c** bearing less bulky N-aryl group (Table 1, runs 7 and 18).[4] In the case of **2a** and **2b**, due to the repulsion between the backbone isopropyl group and one *ortho*-isopropyl substituent of N-aryl group in right side, another *ortho*-isopropyl substituent in left side is rotated away from the metal reactive centre (Figure 2), which could release more space in the left side of CAAC for the dissociation of the ether moiety and subsequent rotation of the benzylidene ring, thus resulting in accelerated catalyst initiation. Complex **2c**, which differs from **2b** only by replacement of *ortho*-isopropyl substituent of N-aryl group with *ortho*-ethyl substituent, exhibited dramatically increased catalytic activity in the RCM reaction of **5** and **6**. **2c** achieved 98% conversion of **5** to cyclopentene **8** in 15 min at 30 °C, and 95% conversion of **6** to trisubstituted olefin **9** at 30 °C in 50 min (Table 1, entries 6 and 17), which is comparable to the catalytic performance of **1c** (Table 1, entries 7 and 18) and NHC-Ru catalyst **11** (Table 1, entries 8 and 19). Unfortunately, like **1c**, **2c** showed no catalytic activity in the RCM of sterically bulky **7** to tetrasubstituted olefin **10**.

We next examined the ethenolysis of methyl oleate (**12**), a process that produces terminal olefin from internal olefins derived from renewable seed oils. Most of catalysts for ethenolysis reactions generally suffered from poor to moderate selectivity, turnover numbers and/or conversion, due to lower stability of catalysts and competing processes taking place.[7] Self-metathesis of ethenolysis products of terminal

Table 2. Comparison of Ruthenium Catalysts in the Ethenolysis of **12**[a]



Run	Cat. (ppm)	Time (h)	Conv. (%)[b]	Selectivity (%)[c]	Yield (%)[d]	TON (%)[e]
1	**2a** (100)	4	50	97	48	4800
2	**2a** (15)	4	16	96	15	10000
3	**2b** (100)	4	60	96	58	5800
4	**2b** (15)	4	30	96	29	19300
5	**2c** (50)	1	53	80	42	8000
6	**1a** (100)	6	36	95	35	3500
7	**1a** (15)	6	-	-	-	-
8[f]	**2b** (10)	4	27	97	26	26000
9[f,g]	**1a** (100)	6	46	94	43	4200
10[f,g]	**1b** (100)	22	61	93	56	5600
11[f,g]	**1c** (100)	< 0.5	73	73	53	5300
12[f,g]	**1c** (10)	< 0.5	42	83	35	35000

[a] General conditions: neat **12** (96%, 3 g), 150 psi ethylene, 40 °C. [b] Conversion = 100 – [(final moles of **12**) × 100/(initial moles of **12**)]. [c] Selectivity = (moles of ethenolysis products **13** + **14**) × 100/(moles of total products **13** + **14** + **15** + **16**). [d] Yield = (moles of ethenolysis products **13** + **14**) × 100/(initial moles of **12**) = conversion × selectivity/100. [e] TON = yield × [(moles of **12**)/(moles of cat.)]. [f] neat **12** (99%, 3 g). [g] Taken from Ref. 5

olefins 9-methyldecenoate (**13**) and 1-decene (**14**) is the primary competing process, which leads to the formation of undesired internal olefins, 1,18-dimethyl 9-octadecenoate (**15**) and 9-octadecene (**16**). Several pioneer studies pointed out high reagent purity is essential to ensure good conversions with a low catalyst loading, and in most cases, >99% purity of methyl oleate was used.[5] Considering that purifications are cost-consuming and time-consuming, which is not desired for industrial application, we focused our study on the development of the efficient catalyst under a low catalyst loading using commercially available methyl oleate with 96% purity, which is much cheaper than 99% purity methyl oleate.

Grubbs etc. reported, among **1a**~**1c**, **1b** achieved the highest TON of 5600 with high selectivity of 93% at 100 ppm catalyst loading, but extended reaction time of 22 h was necessary for **1b** to reach the maximum conversion of 61% (Table 2, runs 9, 10, and 11).[5] Complexes **2a** and **2b** bearing backbone-monosubstituted CAAC were also found to be more efficient in the ethenolysis reaction than their congeners **1a**,**1b**. At 100 ppm catalyst loading and using methyl oleate with 96% purity, **2a** and **2b** achieved TONs of 4800 and 5800 with high selectivity (97% of selectivity for **2a** and 96% of selectivity for **2b**) in 4 h, respectively, and moderate conversions were obtained (50% conversion achieved by **2a** and 60% conversion by **2b**) (Table 2, runs 1 and 3). At 15 ppm catalyst loading, complex **2b** exhibits high selectivity (96%) and obtains higher conversion (30%) than **2a** does (16%) (Table 2, runs 2 and 4). Complex **1a** showed no active toward the ethenolysis reaction at 15 ppm catalyst loading (Table 2, run 7). Complex **2c** with a less sterically bulky N-aryl substituent exhibited much lower selectivity of 80% compared with that of **2a** and **2b** (Table 2, runs 5, 1, and 3). The same trend on selectivity is also observed in **1a**~**1c** (Table 2, runs 9, 10, and 11). Using methyl oleate with 99% purity and at 10 ppm catalyst loading, **2b** displayed highest selectivity of 97% and achieved high TONs of 26000 (Table 2, Run 8).

In conclusion, compared to their congeners **1a**, **1b** bearing backbone-disubstituted CAACs, **2a**, **2b** ligated by CAACs bearing a sterically bulky isopropyl group on the backbone are featured with fast catalyst activation, and displayed considerable improvement on catalytic efficiency not only in ring-closing metathesis but also in the ethenolysis of methyl oleate. With 10 ppm catalyst loading, complex **2b** displayed high selectivity (97%) in the ethenolysis of methyl oleate for the formation of terminal olefins with highest TONs (26000).

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