Synthesis of Imidazolium-Tagged Ruthenium Carbene Complex: Remarkable Activity and Reusability in Regard to Olefin Metathesis in Ionic Liquids

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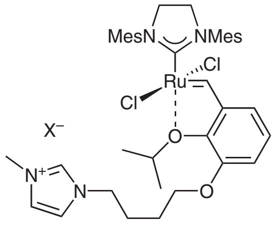
Received 11 March 2008

Abstract: We have demonstrated the synthesis of a new ionic liquid supported ruthenium carbene complex **1a**,**b** and its applications to olefin metathesis. These catalysts can be used for ring-closing metathesis in the construction of five-to-eight-membered rings with high activity and good recyclability.

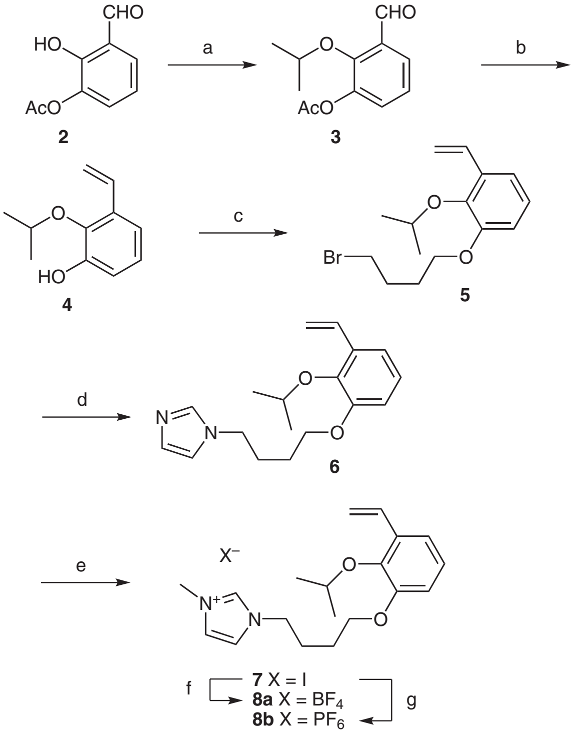
Keywords: ruthenium, catalysis, metathesis, ionic liquids, carbene complexes

Olefin metathesis[1] has become a powerful method for the synthesis of carbon–carbon double bonds, and a large number of applications for natural product synthesis have already been reported using ruthenium- or molybdenum-catalyzed ring-closing metathesis (RCM). Since cross metathesis (CM)[2] and enyne metathesis[3] are also useful for the synthesis of acyclic unsaturated compounds and 1,3-diene derivatives, the metathesis reaction is one of the most important methods in the field of synthetic organic chemistry. On the other hand, ionic liquids have attracted attention as a reaction field in organic chemistry, due to alternative organic solvents and their interesting properties which provide a wide range of good solubility for organic and inorganic compounds.[4] Since the first examples of ionic liquids for metal-catalyzed propene dimerization by Chauvin et al.[5] and ethylene polymerization by Wilkes et al.,[6] extensive transition-metal-catalyzed reactions in ionic liquids have been reported. Initial attempts at alkene metathesis in ionic liquids have already succeeded.[7] Also, several interesting results in regard to the ionic ruthenium initiator, which has excellent reusability combined with high activity, have recently been described.[8]



1a X = BF_4
1b X = PF_6

Figure 1 Ionic liquid supported highly active ruthenium catalysts

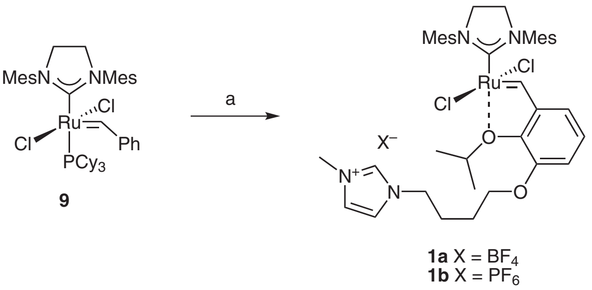


Scheme 1 Synthesis of new ligands **8**. *Reagents and conditions*: a) *i*-PrBr, K_2CO_3, 4 Å MS, DMF, 50 °C, 12 h, 97%; b) KO*t*-Bu, Ph_3PCH_3Br, Et_2O, 0 °C, 50 min, then K_2CO_3, MeOH, r.t., 3 h, 95%; c) NaH, DMF, r.t., 1 h, then $Br(CH_2)_4Br$, r.t., 30 min, 70%; d) $C_3H_3N_2Na$, r.t., 1.5 h, 91%; e) MeI, r.t., 2 h; f) $AgBF_4$, CH_2Cl_2, r.t., 18 h, 56%; g) $AgPF_6$, CH_2Cl_2, r.t., 18 h, 73%.

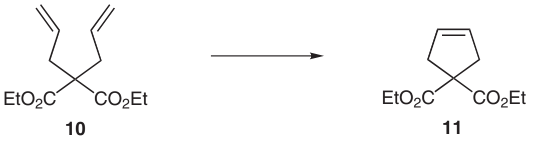
Herein we report the synthesis of a highly active ruthenium carbene complex with very good recyclability for RCM in ionic liquid media. We planned to prepare complex **1** (Figure 1). We thought that *ortho* substitution of the benzylidene ligand should have high reactivity due to fast initiation by steric repulsion,[9] and that the imidazolium ion structure should provide good immobilization for ionic liquids as a solvent and reusability for the ruthenium carbene complex after isolation of the product.

3-Acetoxy-2-isopropoxy-benzaldehyde (**3**) was synthesized from **2**[10] by alkylation with isopropyl bromide in the presence of K_2CO_3 in DMF (Scheme 1). The Wittig reaction of methylene ylide with **3**, followed by deacetylation, yielded **4**, which was transformed into **5** by alkylation with 1,4-dibromobutane. The introduction of an imidazole ring was achieved by the coupling of imidazole sodium salt with **5** to give **6** in 91% yield. Methylation of **6**

SYNLETT 2008, No. 12, pp 1805–1808
Advanced online publication: 19.06.2008
DOI: 10.1055/s-2008-1077888; Art ID: U01908ST



Scheme 2 Preparation of ionic liquid supported ruthenium catalysts. *Reagents and conditions*: a) **8a** or **8b**, CuCl, CH_2Cl_2, reflux, 9 h.



Scheme 3 Ring-closing metathesis of diethyl diallylmalonate **10**

with methyl iodide, followed by anion exchange with silver tetrafluoroborate or silver hexafluorophosphate, provided **8a** (56%) and **8b** (73%), respectively.

When a 1.0 equivalent of ligand **8** was exposed to **9**[11] in the presence of CuCl in CH_2Cl_2 under reflux for 9 hours, the anticipated ruthenium complex **1** was obtained (Scheme 2).[12] In the ^{1}H NMR study of complex **1**, it was revealed that the isopropoxy group coordinated to the ruthenium metal, because of the chemical shift of the carbine proton at $\delta = 16.6$ ppm.[13]

Table 1 Ring-closing metathesis of **10** Using Ionic Liquid Supported Ruthenium Catalyst **1a**[a]

Entry	Solvent[b]	Cycle 1	 2	 3
		Time/yield of **11** (%)[c]		
1	CH_2Cl_2/[Bmim]BF_4	0.5 h/94	2.5 h/44[d]	–
2	CH_2Cl_2/[Bmim]PF_6	10 min/85	30 min/89	2.5 h/71[e]

[a] Reaction conditions: **1a** (5 mol%), CH_2Cl_2–ionic liquid (9:1), r.t.
[b] [Bmim]: 1-butyl-3-methylimidazolium.
[c] Isolated yield.
[d] Starting material **10** was recovered in 51% yield.
[e] Starting material **10** was recovered in 25% yield.

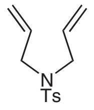
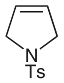
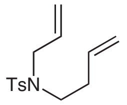
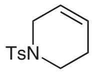
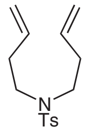
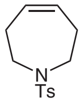
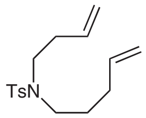
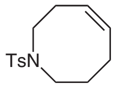
Table 2 Ring-closing metathesis of **10** Using Ionic Liquid Supported Ruthenium Catalyst **1b**[a]

Cycle	1	2	3	4	5	6
Time	10 min	15 min	20 min	30 min	2.5 h	48 h
Yield of **11** (%)[b]	90	93	95	91	77	32[c]

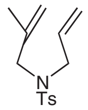
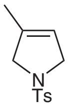
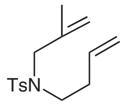
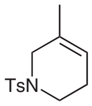
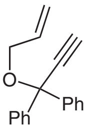
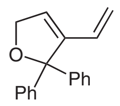
[a] Reaction conditions: **1b** (5 mol%), CH_2Cl_2–[Bmim]PF_6 (9:1), r.t.
[b] Isolated yield.
[c] Starting material **10** was recovered in 58% yield.

Table 3 RCM of Miscellaneous Substrates Using **1b**[a]

Entry 1

Cycle	Substrates	Products	Time (min)	Yield (%)[b]
1	 **12**	 **13**	<5	99
2	 **14**	 **15**	<5	99
3	 **16**	 **17**	10	99
4	 **18**	 **19**	90	98
5	**12**	**13**	180	93
6	**12**	**13**	48 h	8[c]

Entry 2

Cycle	Substrates	Products	Time (min)	Yield (%)[b]
1	 **20**	 **21**	10	99
2	 **22**	 **23**	10	92
3	 **24**	 **25**	5	89
4	**12**	**13**	15	97
5	**12**	**13**	20	97
6	**12**	**13**	30	98
7	**12**	**13**	120	95
8	**12**	**13**	48 h	44[d]

[a] Reaction conditions: **1b** (5 mol%), CH_2Cl_2–[Bmim]PF_6 (9:1), r.t.
[b] Isolated yield.
[c] Starting material **12** was recovered in 90% yield.
[d] Starting material **12** was recovered in 52% yield.

At first, RCM of diethyl diallylmalonate **10** (Scheme 3) using new catalyst **1a** was attempted (Table 1). When the reaction was carried out under an argon atmosphere in the presence of 5 mol% **1a** in CH_2Cl_2/[Bmim]BF_4 (9:1) at room temperature, the starting material was consumed after 0.5 hours to provide **11** in 94% yield (entry 1, cycle 1). After extraction of the product from an ionic liquid with Et_2O,[14] a second loading of **10** was added to an ionic liquid containing ruthenium carbene complex **1a**. The reuse of **1a** was achieved, and cyclization product **11** was obtained in 44% yield (entry 1, cycle 2). The effect of a counteranion on ionic liquid as a solvent was examined by changing from BF_4^- to PF_6^- (entry 2).

When the first run of **10** with **1a** in CH_2Cl_2/[Bmim]PF_6 (9:1) was done, a quick conversion of **10** to **11** was observed and **11** was isolated in 85% yield (cycle 1). A gratifying result was obtained in the second run, and the third cycle led to a 71% yield of **11** and a longer reaction time.

Catalyst **1b** was also examined in regard to RCM of **10** (Table 2). Ring-closing metathesis was carried out in the presence of 5 mol% **1b** at room temperature. Continuous fast conversion was observed, and reliable reusability was realized until the fifth cycle.

Next, tolerance for miscellaneous substrates with recyclability was tested (Table 3). The construction of five-to-eight-membered rings smoothly proceeded by the same catalyst in an ionic liquid solution to provide products in quantitative yield (entry 1, cycle 1–4), and additional ring closure of a five-membered ring also succeeded (cycle 5). Trisubstituted olefin was obtained in high yield (entry 2, cycles 1 and 2), and ene-yne metathesis proceeded to provide diene derivative **25** (cycle 3) with good reusability of the catalyst (cycles 4–7).

We have studied the synthesis of a new ionic liquid supported ruthenium carbene complex **1a**,**b** and its applications to olefin metathesis. These catalysts can be used for ring-closing metathesis of miscellaneous substrates with excellent activity and very good recyclability. Further studies of ionic liquid supported catalysts and the field of metathesis in ionic liquids are in progress in our laboratory.

Acknowledgment

This work was supported by Tohoku Pharmaceutical University.

References and Notes

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(12) **Procedure for the Synthesis of Catalyst 1b**
To a solution of **9** (184.9 mg, 0.22 mmol) and CuCl (21.6 mg, 0.22 mmol) in CH_2Cl_2 (20 mL) was added **8b** (120.3 mg, 0.26 mmol). The reaction mixture was stirred at reflux for 9 h under argon atmosphere. The volatiles were removed under reduce pressure. The residue was purified by column chromatography on SiO_2 (CH_2Cl_2–acetone, 3:1) to afford **1b** (137.2 mg, 68%). ^1H NMR (400 MHz, CD_2Cl_2): $\delta = 1.14$ (d, $J = 6.3$ Hz, 6 H), 1.66–1.74 (m, 2 H), 1.89–1.94 (m, 2 H), 2.20–2.65 (br, 18 H), 3.72 (s, 3 H), 4.06 (t, $J = 5.7$ Hz, 2 H), 4.08 (t, $J = 6.9$ Hz, 2 H), 4.16 (s, 4 H), 5.64 (sept, $J = 6.3$ Hz, 1 H), 6.56 (dd, $J = 1.3$, 7.5 Hz, 1 H), 6.87 (dd, $J = 7.5$, 8.2 Hz, 1 H), 7.06 (br, 4 H), 7.11 (dd, $J = 1.3$, 8.2 Hz, 1 H), 7.13 (dd, $J = 1.9$, 1.9 Hz, 1 H), 7.25 (dd, $J = 1.3$, 1.9 Hz, 1 H), 8.48 (br, 1 H), 16.57 (s, 1 H). ^{13}C NMR (100 MHz, CD_2Cl_2):

δ = 19.6, 21.2, 21.7, 25.4, 26.9, 36.6, 49.9, 51.8, 68.8, 81.0, 115.9, 122.7, 123.9, 124.3, 129.6, 136.0, 136.1, 138.5, 139.3, 140.3, 148.3, 148.6, 210.0, 298.3. IR (KBr): ν = 1574 (w), 1470 (m), 1269 (m) cm^{-1}. HRMS–FAB: *m*/*z* calcd for $C_{39}H_{51}{}^{35}Cl_2N_4O_2{}^{102}Ru$: 779.2433; found: 779.2454. Anal. Calcd for $C_{39}H_{51}Cl_2F_6N_4O_2PRu$: C, 50.65; H, 5.56; N, 6.06. Found: C, 50.62; H, 5.58; N, 5.82.

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(14) **Typical Procedure for Metathesis Reaction Promoted by Ionic Liquid Supported Ruthenium Catalyst**
To a catalyst solution of **1b** (38.1 mg, 0.04 mmol) in $[Bmim]PF_6$ (1 mL) was added **10** (0.20 mL, 0.82 mmol) in CH_2Cl_2 (9 mL). The reaction mixture was stirred at r.t. until starting material was consumed. After the volatiles were removed under reduce pressure, ionic liquid phase was extracted with Et_2O (several times). The ethereal phase was evaporated to provide **11**, and the ionic liquid phase was dried under reduce pressure to use a catalyst solution for the next cycle.