

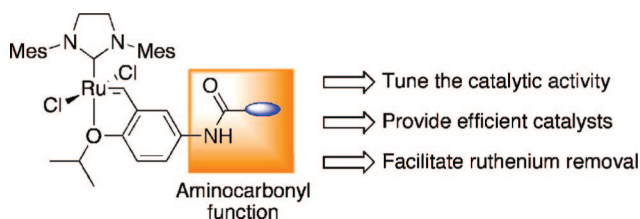
Aminocarbonyl Group Containing Hoveyda–Grubbs-Type Complexes: Synthesis and Activity in Olefin Metathesis Transformations

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Three novel “boomerang” precatalysts bearing different aminocarbonyl functions are reported. Comparative kinetic studies show that this functional group allows for a control of the catalytic activity in metathesis transformations. The scope of the more active catalyst is investigated and shows a good tolerance to various substrates in ring-closing metathesis, enyne metathesis, and cross metathesis. ICP-MS analyses illustrate the good affinity of this catalyst for silica gel, as levels of Ru contamination lower than 6 ppm are detected in the final products.

Since the discovery of the well-defined ruthenium-based catalyst $\text{Cl}_2(\text{PCy}_3)_2\text{Ru}=\text{CHPh}^1$ that possesses a fairly broad reaction scope, high tolerance to functional groups, olefin metathesis has become a mainstream synthetic tool.² Despite developments focusing on new precatalysts, such as **1**,³ olefin metathesis still suffers from the required use of high catalytic

charges.⁴ Remarkable progress was achieved when Hoveyda reported the “boomerang” precatalyst **2a**⁵ based on a release/return concept of the benzylidene ether fragment. Further developments by Blechert (**2b**),⁶ Grela (**2c**),⁷ and Zhan (**2d**)⁸ have led to more easily activated catalysts enabling a decrease in the “boomerang” precatalyst loading (down to 1 mol %). In the course of developing more environmentally friendly metathesis catalysts,⁹ we recently reported a pyridinium-containing precatalyst **2e**.¹⁰ Unfortunately, the remarkable activity enhancement observed with **2e** was counter-balanced by its poor recyclability combined with an important Ru-contamination of the products. We concluded that a faster acting precatalyst is not always desired but improved control of the catalyst activity should be targeted.

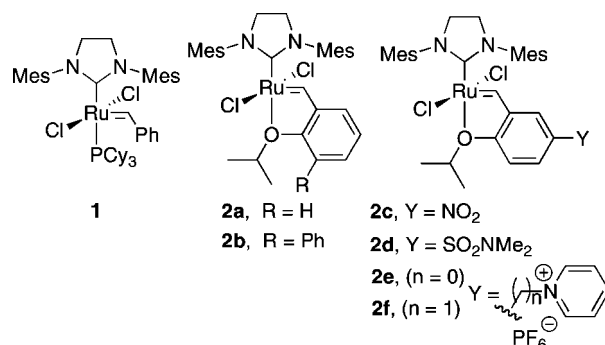


FIGURE 1. Ruthenium-based olefin metathesis precatalysts.

Aiming our synthetic efforts in this direction, we designed an improved version of complex **2f** (Figure 1) bearing a methylene spacer and reached the forementioned goal where excellent activity and recyclability can be combined with generation of low levels of ruthenium-waste.¹¹ We decided to

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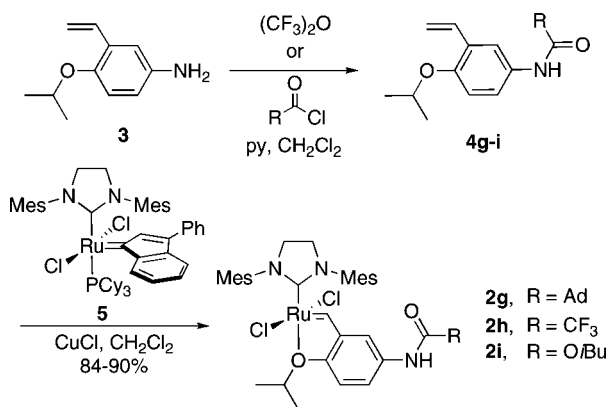
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SCHEME 1. Synthesis of Amide-Grafted Precatalysts **2g–i**

investigate more tunable chemical functions dedicated not only to improve the activity of a “boomerang”-type complex, but also to facilitate the anchoring of such catalysts onto various supports. In view of its high structural modularity and its tunable electronics via various substituents, the aminocarbonyl function caught our attention and is the focus of this report.

We initially introduced different aminocarbonyl functions such as amides (**2g** and **2h**) and carbamates (**2i**) onto the Hoveyda-type “boomerang” styrenyl ether fragment. The required aminocarbonyl-containing ligands **4g–i** were synthesized in one step from the previously reported functionalized aniline **3**¹⁰ (Scheme 1). Reaction of ligands **4** with the second generation Ru–indenylidene complex **5**¹² in the presence of CuCl⁵ led to a family of air- and moisture-stable green microcrystalline solids **2g–i**.

The structures and atom connectivities of precatalysts were unambiguously confirmed by single-crystal diffraction studies. The molecular structures show oxygen coordination to the ruthenium center (Figure 2). The bond lengths and angles were found in the same range as those reported for similar complexes,¹³ except for the Ru(1)–O(1) bond, which is significantly shorter than in **2b**, in particular for complex **2g**. Of note, the C(1)–Ru(1)–C(22) angle was found significantly more acute than in **2b**, indicating a tilt of the *N*-heterocyclic carbene.

We then investigated reactivity profiles of these aminocarbonyl-grafted precatalysts and examined if these different functions would be reflected on reaction reactivity. A model ring-closing metathesis (RCM) reaction involving 2-allyl-2-methylmalonate **6** was chosen for the present comparative investigation, using 1 mol % catalyst at 30 °C in CD₂Cl₂ (Figure 3). Remarkably, significant differences between initiation rates were observed and three different classes of complexes can be identified: the weakly enhanced precatalyst **2g**, the moderately activated carbamate **2i**, and the highly improved precatalyst **2h** bearing the trifluoroacetamide function. These differences in reactivity can be linked to the switchable electronic properties of the aminocarbonyl group itself (EDG or EWG).¹⁴ Consequently, by a judicious choice of the group directly anchored

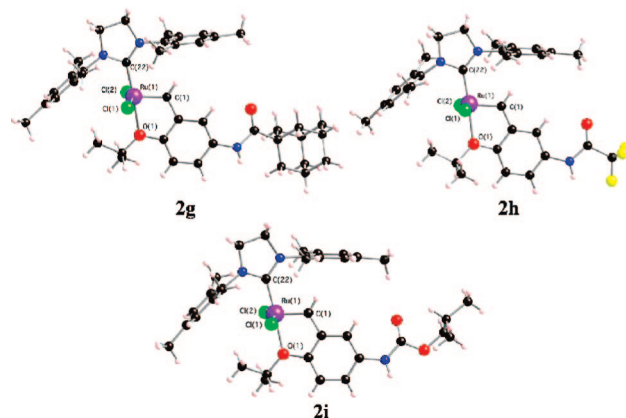


FIGURE 2. Ball-and-stick representation of precatalysts **2g–i**. Selected bond lengths (Å) and angles (deg): **2g**, Ru(1)–C(1) 1.8408(9), Ru(1)–C(22) 1.9779(8), Ru(1)–O(1) 2.2221(6), C(1)–Ru(1)–C(22) 103.38(3), C(1)–Ru(1)–O(1) 80.13(3); **2h**, Ru(1)–C(1) 1.8338(9), Ru(1)–C(22) 1.9852(8), Ru(1)–O(1) 2.2383(7), C(1)–Ru(1)–C(22) 103.42(4), C(1)–Ru(1)–O(1) 79.98(3); **2i**, Ru(1)–C(1) 1.823(3), Ru(1)–C(22) 1.975(3), Ru(1)–O(1) 2.257(2), C(1)–Ru(1)–C(22) 102.32(11), C(1)–Ru(1)–O(1) 79.19(10).

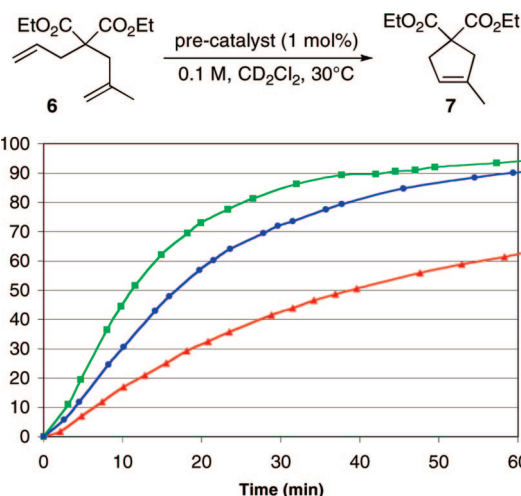


FIGURE 3. Kinetic studies of RCM of trisubstituted olefin **6** (0.1 M) with precatalysts **2g–i** (1 mol %) in CD₂Cl₂ at 30 °C; (**2g**, ▲), (**2h**, ■), (**2i**, ●). Conversions are given by NMR measurement.

to the aminocarbonyl-function, a tuning of the precatalyst activity can be achieved.

To further examine this aminocarbonyl effect, the reaction profile of a more activated complex, e.g., trifluoroacetamide precatalyst **2h**, was compared to the RCM reaction involving diallyltosylamine **8** at 0 °C (Figure 4). As evidence of the beneficial role of the trifluoroacetamide group, its activity was found significantly improved compared to commercially available precatalysts **1** and more particularly **2a**, but slightly lower than the highly efficient **2c**⁷ and **2d**.⁸

These promising results led us to investigate the scope of the activity of **2h** by using selected benchmark substrates for RCM and enyne metathesis (EM) (Table 1). RCM of various amide-, ester-, and ether-containing substrates were carried out at rt in less than 1 h with 1 mol % of **2h**. The formation of 5- and 6-membered rings was also achieved easily; RCM leading

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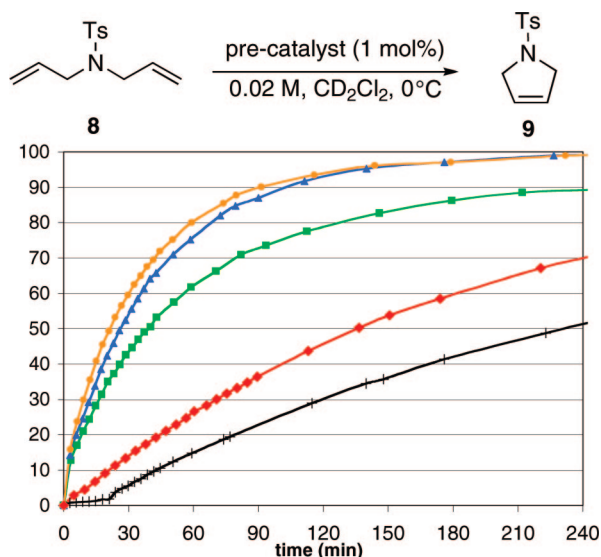


FIGURE 4. Kinetic studies of RCM of disubstituted olefin **8** (0.02 M) with commercially available precatalysts and **2h** (1 mol %) in CD_2Cl_2 at 0 °C: (**1**, +), (**2a**, ♦), (**2c**, ●), (**2d**, ▲), (**2h**, ■). Conversion determined by NMR spectroscopy.

to 7-membered-ring translated into a substantial increase in the required reaction time (entries 5 and 8). Various degrees of diene substitution are well tolerated, even tetrasubstituted tosylamide **18** required only 2 mol % of **2h** and 24 h of heating at 40 °C to produce 80% of **19** (entry 6). For several dienes, the enhanced activity of **2h** allowed us to decrease the catalyst loading to 0.3 mol %, without any detrimental effect on reaction times (entries 1–3, and 7). We extended the reaction scope of **2h** to two enynes (entries 9 and 10). Although cyclization of enyne **24** required a slight thermal activation, **25** was isolated in good yields after 6 h. On the other hand, **27** was isolated quantitatively after 30 min when 0.3 mol % of **2h** was used (entry 10). More interestingly, the contamination in ruthenium waste of **7** and **13** was determined by ICP-MS analyses. With use of 1 mol % of catalyst loading, respectively only 1.8 and 5.5 ppm of Ru were observed in the products after silica gel chromatography. We believe these results are a consequence of a beneficial affinity of the ruthenium catalyst or/and its derivatives (degradation species) for silica.¹⁵

We also examined the CM reactions of terminal alkenes and α,β -unsaturated olefins (Table 2). Excellent yields were obtained in short reaction times with use of only 1 mol % of **2h**. However, in the case of more problematic substrates such as acrylonitrile or allyltosylamine (entries 3 and 4), the cross metathesis reactions performed with the ester **28** were incomplete, yielding only 40% and 60% of the desired products **32** and **33**, respectively, even when 2 mol % of **2h** was used at 40 °C over 24 h.

In summary, we have synthesized in a straightforward manner three novel Ru-based olefin precatalysts. The use of the aminocarbonyl function led to a simple and efficient control (enhancement) of the catalytic activity of these “boomerang” catalysts. The scope of the best precatalyst **2h** was evaluated for several metathesis transformations with use of as low as

TABLE 1. Scope of **2h** for RCM Transformations^a

Entry	Substrate	Product	Time (h)	Yield (%) ^b
1			0.75 1.5	> 98 > 98 ^c
2			0.75 1.5	> 98 > 98 ^c
3			0.75 2.5	> 98 > 98 ^c
4			0.25	> 98
5			3.5	> 98
6			24	80 ^d
7			0.25 0.75	> 98 > 98 ^c
8			1.5	> 98
9			6	> 98 ^e
10			0.3 0.5	> 98 > 98 ^c

^a Reaction condition: 1 mol % of **2h**, CH_2Cl_2 , 0.1 M, rt. ^b Isolated yield. ^c 0.3 mol % of **2h** was used. ^d Reaction performed at 40 °C with 2 mol % of **2h**. ^e Reaction performed at 40 °C.

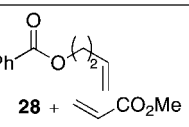
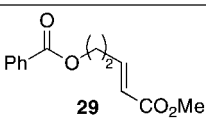
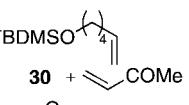
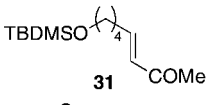
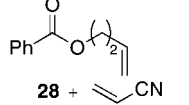
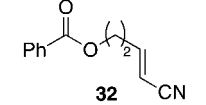
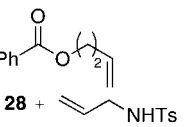
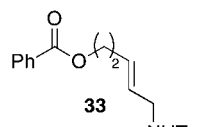
0.3 mol % of catalyst without the need for long reaction times. Moreover, extremely low levels of residual ruthenium contamination were detected in the final products (below 6 ppm). In view of the modular aspect of the aminocarbonyl function, further advances through elaboration of the function appear promising for the purpose of immobilization onto supports. Such investigations are currently underway in our laboratories and will be disclosed shortly.

Experimental Section

General Procedure for Catalyst Formation. To a solution of catalyst **5** and copper chloride (1.1 equiv) in dry DCM (1 mL for 0.02 mmol of Ru-indenylidene complex) was added **4g–i** (1 equiv) in DCM solution (1 mL for 0.05 mmol of ligand). The resulting

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TABLE 2. Scope of **2h** in Cross Metathesis^a

Entry	Substrate	Product	Time (h)	Yield (%) ^b
1	 28 + $\text{CH}_2=\text{CH}-\text{CO}_2\text{Me}$	 29	0.5	76 (E/Z > 20/1)
2	 30 + $\text{CH}_2=\text{CH}-\text{COMe}$	 31	0.5	86 (E/Z > 20/1)
3	 28 + $\text{CH}_2=\text{CH}-\text{CN}$	 32	24	40 ^c (E/Z = 1/4)
4	 28 + $\text{CH}_2=\text{CH}-\text{NHTs}$	 33	24	60 ^c (E/Z > 20/1)

^a Reactions conditions: 1 mol % of **2h**, CH_2Cl_2 , 0.1 M, rt. ^b Isolated yield. ^c Reaction performed at 40 °C with 2 mol % of **2h**.

mixture was stirred at 35 °C for 5 h. Volatiles were removed under reduced pressure, acetone was added to the residue, and the solution was filtered through a pad of Celite. The filtrate was concentrated and purified by chromatography on silica gel (pentane/acetone, 75/25) to yield to catalysts **2g–i** as green microcrystalline solids.

(1,3-Bis(2,4,6-trimethylphenyl)imidazolidin-2-ylidene)(2-isopropoxy-5-(adamantanamido)benzylidene)ruthenium(II) Dichloride (2g). Following the general procedure with ligand **4g** afforded the title product (28 mg, 86% yield). ¹H NMR (400 MHz, acetone-*d*₆, 25 °C, TMS): δ (ppm) 16.39 (s, 1H), 8.42 (s, 1H), 7.64 (dd, ³*J*(H,H) = 8.7 Hz, ⁴*J*(H,H) = 2.5 Hz, 1H), 7.61 (d, ⁴*J*(H,H) = 2.5 Hz, 1H), 7.07 (s, 4H), 6.92 (d, ³*J*(H,H) = 8.7 Hz, 1H), 4.90 (sept, ³*J*(H,H) = 6.1 Hz, 1H), 4.28 (s, 4H), 2.78 (s, 3H), 2.47 (s, 12H), 2.44 (s, 6H), 2.00 (s, 6H), 1.78 (s, 6H), 1.24 (d, ³*J*(H,H) = 6.1 Hz, 6H). ¹³C NMR (100 MHz, acetone-*d*₆, 25 °C, TMS): δ (ppm) 293.3 (d, *J*(C,Ru) = 11.9 Hz, CH), 210.9, 175.5, 148.1, 144.9, 138.6, 134.3, 129.4, 129.1, 120.7, 114.4, 112.5, 74.6, 51.3, 41.1, 38.8, 36.3, 28.3, 20.6, 20.3. HRMS (ESI): *m/z* calcd for $\text{C}_{42}\text{H}_{53}\text{Cl}_2\text{F}_3\text{N}_3\text{O}_2\text{Ru} - \text{Cl} + \text{CH}_3\text{CN}$ 908.3135 [*M*⁺ - Cl + CH₃CN], found 809.3161. Elemental analysis calcd (%) for $\text{C}_{42}\text{H}_{53}\text{Cl}_2\text{F}_3\text{N}_3\text{O}_2\text{Ru}$: C 62.75, H 6.65, N 5.23. Found: C 62.32, H 6.71, N 5.15.

(1,3-Bis(2,4,6-trimethylphenyl)imidazolidin-2-ylidene)(2-isopropoxy-5-(2,2,2-trifluoroacetamido)benzylidene)ruthenium(II) Dichloride (2h). Following the general procedure with ligand **4h** afforded

the title product (243 mg, 90% yield). ¹H NMR (400 MHz, acetone-*d*₆, 25 °C, TMS): δ (ppm) 16.44 (s, 1H), 7.79 (dd, ³*J*(H,H) = 8.8 Hz, ⁴*J*(H,H) = 2.5 Hz, 1H), 7.61 (d, ⁴*J*(H,H) = 2.6 Hz, 1H), 7.08–7.06 (m, 5H), 4.97 (sept, ³*J*(H,H) = 6.1 Hz, 1H), 4.28 (s, 4H), 2.47 (s, 12H), 2.43 (s, 6H), 1.26 (d, ³*J*(H,H) = 6.1 Hz, 6H). ¹³C NMR (100 MHz, acetone-*d*₆, 25 °C, TMS): δ (ppm) 291.3 (d, *J*(C,Ru) = 12.3 Hz), 209.9, 149.5, 145.0, 138.7, 131.3, 129.1, 121.1, 121.0, 116.0 (q, *J*(C,F) = 286.7 Hz), 114.2, 114.1, 113.2, 75.3, 51.4, 20.6, 20.3. ¹⁹F NMR (376 MHz, acetone-*d*₆, 25 °C, TMS): δ (ppm) -76.2 (s). HRMS (ESI): *m/z* calcd for $\text{C}_{33}\text{H}_{38}\text{Cl}_2\text{F}_3\text{N}_3\text{O}_2\text{Ru} - \text{Cl} + \text{CH}_3\text{CN}$ 743.1914 [*M*⁺ - Cl + CH₃CN], found 743.1926.

(1,3-Bis(2,4,6-trimethylphenyl)imidazolidin-2-ylidene)(2-isopropoxy-5-(isobutylcarbamido)benzylidene)ruthenium(II) Dichloride (2i). Following the general procedure with ligand **4i** afforded the title product (45 mg, 84% yield). ¹H NMR (400 MHz, CD₂Cl₂, 25 °C, TMS): δ (ppm) 16.45 (s, 1H), 7.65 (d, *J* = 8.7 Hz, 1H), 7.09 (s, 4H), 6.99 (s broad, 1H), 6.78 (d, *J* = 8.7 Hz, 1H), 6.62 (s broad, 1H), 4.85 (sept, *J* = 6.0 Hz, 1H), 4.18 (s, 4H), 3.95 (d, *J* = 6.6 Hz, 1H), 2.45 (s, 18H), 2.02–1.95 (m, 1H), 1.23 (d, *J* = 6.0 Hz, 6H), 0.99 (d, *J* = 6.7 Hz, 6H). ¹³C NMR (125 MHz, CD₂Cl₂, 25 °C, TMS): δ (ppm) 294.3, 210.4, 153.8, 148.0, 145.0, 139.0, 133.2, 129.2, 119.5, 112.9, 112.5, 75.2, 71.2, 51.1, 29.7, 28.0, 20.8, 18.8. HRMS (ESI): *m/z* calcd for $\text{C}_{36}\text{H}_{47}\text{Cl}_2\text{N}_3\text{O}_3\text{Ru} + \text{Na}$ 764.1936 [*M*⁺ + Na], found 764.1939. Elemental analysis calcd (%) for $\text{C}_{36}\text{H}_{47}\text{Cl}_2\text{N}_3\text{O}_3\text{Ru}$: C 58.29, H 6.39, N 5.66. Found: C 58.28, H 6.46, N 5.24.

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Supporting Information Available: Synthetic procedure and characterization of new compounds, data of kinetic studies and crystallographic informations files (CIF) of complexes **2g–i**. This material is available free of charge via the Internet at <http://pubs.acs.org>. The CIF files have also been deposited with the CCDC, Nos. CCDC-634625, 666288, and 675653; copies of the data can be obtained free of charge on applications to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK, fax +44 1223 336 033, <http://www.ccdc.cam.ac.uk>, e-mail deposit@ccdc.cam.ac.uk.

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