ORGANIC LETTERS

2011
Vol. 13, No. 18
4758–4761

Intramolecular Hydroamination of Aminoalkenes Catalyzed by a Cationic Zirconium Complex

Xinke Wang,[†] Zhou Chen,[†] Xiu-Li Sun,[†] Yong Tang,*[,†] and Zuowei Xie*[,‡]

State Key Laboratory of Organometallic Chemistry, Shanghai Institute of Organic Chemistry, Chinese Academy of Sciences, 345 Lingling Road, Shanghai 200032, China, and Shanghai-Hong Kong Joint Laboratory in Chemical Synthesis, Shanghai Institute of Organic Chemistry and Department of Chemistry, The Chinese University of Hong Kong, Shatin, New Territories, Hong Kong, China

tangy@mail.sioc.ac.cn; zxie@cuhk.edu.hk

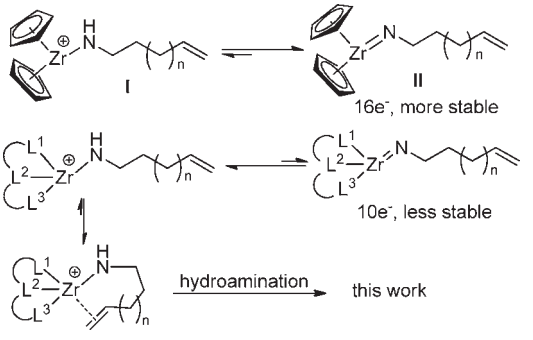
Received March 24, 2011

ABSTRACT

A new cationic [N⁻O⁻S]zirconium complex (*cat.*) was developed to be an excellent catalyst for the intramolecular hydroamination of aminoalkenes with a large substrate scope from terminal alkenes to internal alkenes, and primary amines to secondary amines. The catalyst system can also tolerate various functional groups and perform sequential hydroamination of primary aminodienes.

N-containing compounds play a significant role in pharmaceuticals and materials, and the synthesis of these compounds is of considerable interest in both academic and industrial research. Hydroamination,[1−4] a formal addition of an N−H bond to carbon−carbon unsaturated bonds, provides an easy access to N-containing compounds. Recently, cationic zirconocenes proved to be good catalysts for such transformations but the reaction was restricted to intramolecular cyclization of secondary aminoalkenes.[4a,b] When the substrates were extended to primary aminoalkenes, such a hydroamination of alkenes did not work, probably due to the formation of the zirconium imido species **II** that was reported to be less active in hydroamination (Scheme 1).[4a,b,5] If the two cyclopentadienyl π ligands in **II** were replaced by a dianionic tridentate σ ligand, the resultant 10e⁻ zirconium imide would be destabilized, which favors the formation of zirconium amide leading to the hydroamination reaction (Scheme 1). In this regard, it is possible to control the catalytic behaviors of a cationic zirconium complex on the hydroamination of alkenes by the change of ligands. We report here a cationic [O⁻N⁻S]zirconium complex (Scheme 2) catalyzed the intramolecular hydroamination of both primary and secondary aminoalkenes, disubstituted unactivated alkenes, and alkenes with functional

Scheme 1. Design of Zirconium Cation Catalyst for Hydroamination of Primary Aminoalkene[a]



[a] Counteranion was omitted for clarity.

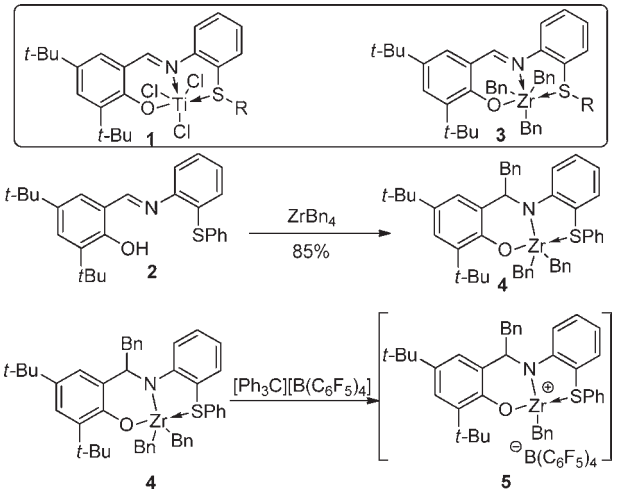
[†] Chinese Academy of Sciences.
[‡] The Chinese University of Hong Kong.

(1) For review on the hydroamination of alkenes and alkynes, see: Müller, T. E.; Hultzsch, K. C.; Yus, M.; Foubelo, F.; Tada, M. *Chem. Rev.* **2008**, *108*, 3795–3892.

10.1021/ol201731m
Published on Web 08/12/2011

groups such as ester and nitro groups. Moreover, the aminodienes can afford bicyclic amines via tandem hydroamination of primary and secondary aminoalkenes, thus broadening the substrate scope of zirconium-catalyzed hydroamination.

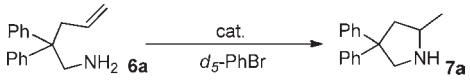
Scheme 2. Synthesis of Zirconium Complexes



We have previously developed a tridentate [O⁻NS] ligand system for an olefin polymerization catalyst such as [O⁻NS]titanium complexes **1**.[6] Treatment of the ligand **2** with $ZrBn_4$ (Bn = $C_6H_5CH_2$) did not afford the desired product **3**, but rather gave [N⁻O⁻S]zirconium dibenzyl **4** in 85% isolated yield. Single-crystal X-ray analyses of the obtained complex displayed a dianionic tridentate ligating system.[7] The corresponding cationic complex **5** was then generated in situ by treating **4** with $[Ph_3C][B(C_6F_5)_4]$ (Scheme 2).[8]

Hydroamination of 2,2-diphenylpent-4-enyl-amine **6a** was initially examined. It was found that this amine was completely converted into pyrroline **7a** at 100 °C within 1.5 h (Table 1, entry 1), which supported our initial idea. A similar result was obtained when **4** was activated with $[PhMe_2NH][B(C_6F_5)_4]$, showing that the released $NPhMe_2$ has no influence on this reaction (entry 2). A longer reaction time was required if the catalyst loading was reduced to 5 mol % (entry 3). Meanwhile, the neutral complex **4** also catalyzed the reaction under the same conditions but with a longer reaction time, indicating that the cationic one is more active than its neutral counterpart (entry 1 vs 4).[9,10] In sharp contrast, Cp_2ZrMe_2 **8** was almost inactive under the same conditions (entries 5–7), even if it was activated with $[PhMe_2NH][B(C_6F_5)_4]$ or $[Ph_3C]$-$[B(C_6F_5)_4]$. Only a trace amount of desired product was observed when the reaction was prolonged to 120 h (entries 6 and 7). Thus, it represents the first example of a group 4 metal cationic catalyst for hydroamination of the primary aminoalkenes.

Table 1. Catalytic Trial on Hydroamination of 2,2-Diphenyl-pent-4-enyl-amine **6a**[a]



entry	cat.	time (h)	yield (%)[b]
1	**4**/TB	1.5	>95
2	**4**/AB	1.5	>95
3[c]	**4**/TB	4	>95
4	**4**	3	>95
5	Cp_2ZrMe_2 (**8**)	6	--[d]
6	Cp_2ZrMe_2 (**8**)/TB	6	--[d]
7	Cp_2ZrMe_2 (**8**)/AB	6	--[d]

[a] Conditions: **6a** (23.7 mg, 0.1 mmol), cat. (0.01 mmol), TB or AB (0.01 mmol) if necessary, d_5-PhBr (0.5 mL), 100 °C. TB = $[Ph_3C][B(C_6F_5)_4]$, AB = $[PhMe_2NH][B(C_6F_5)_4]$. [b] Yield determined by ^1H NMR; ferrocene (2.0 mg) as internal standard. [c] 5 mol % catalyst loading (0.2 mmol **6a**). [d] A trace amount of product was detected when the reaction time was prolonged to 120 h.

Under the optimal conditions, a variety of aminoalkenes with different structures were examined. The results were summarized in Table 2. Primary aminoalkenes worked well, affording the desired cyclic secondary amines in high

(2) For selected papers on intramolecular hydroaminations of alkenes catalyzed by lanthanide and actinide complexes, see: (a) Hong, S.; Marks, T. J. *Acc. Chem. Res.* **2004**, *37*, 673–686. (b) Kim, Y. K.; Livinghouse, T.; Horino, Y. *J. Am. Chem. Soc.* **2003**, *125*, 9560–9561. (c) Stubbert, B. D.; Marks, T. J. *J. Am. Chem. Soc.* **2007**, *129*, 4253–4271. (d) Rastatter, M.; Zulys, A.; Roesky, P. W. *Chem.—Eur. J.* **2007**, *13*, 3606–3616. (e) Stubbert, B. D.; Marks, T. J. *J. Am. Chem. Soc.* **2007**, *129*, 6149–6167. (f) Stanlake, L.; Schafer, L. L. *Organometallics* **2009**, *28*, 3990–3998. (g) Reznichenko, A. L.; Hampel, F.; Hultzsch, K. C. *Chem.—Eur. J.* **2009**, *15*, 12819–12827. (h) Xu, X.; Chen, Y.; Feng, J.; Zou, G.; Sun, J. *Organometallics* **2010**, *29*, 549–553.

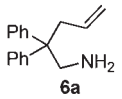
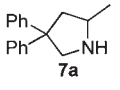
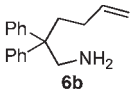
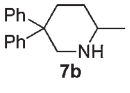
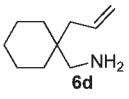
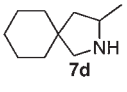
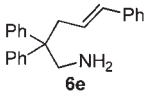
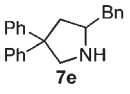
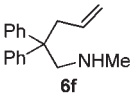
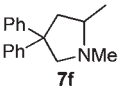
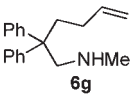
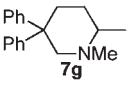
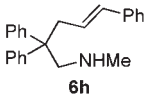
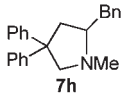
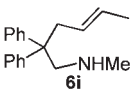
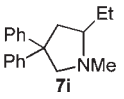
(3) For late transition metal catalyzed intramolecular hydroamination of alkenes, see: (a) Bender, C. F.; Widenhoefer, R. A. *J. Am. Chem. Soc.* **2005**, *127*, 1070–1071. (b) Liu, Z.; Hartwig, J. F. *J. Am. Chem. Soc.* **2008**, *130*, 1570–1571. (c) Bender, C. F.; Hudson, W. B.; Widenhoefer, R. A. *Organometallics* **2008**, *27*, 2356–2358. (d) Ohmiya, M.; Moriya, T.; Sawamura, M. *Org. Lett.* **2009**, *11*, 2145–2147. (e) Hesp, K. D.; Tobisch, S.; Stradiotto, M. *J. Am. Chem. Soc.* **2010**, *132*, 413–426. (f) Shen, X.; Buchwald, S. L. *Angew. Chem., Int. Ed.* **2010**, *49*, 564–567. (g) Liu, Z.; Yamamichi, H.; Madrahimov, S.; Hartwig, J. F. *J. Am. Chem. Soc.* **2011**, *133*, 2772–2782.

(4) For selected papers on intramolecular hydroaminations of alkenes catalyzed by group 4 metals, see: (a) Knight, P. D.; Munslow, I.; O'Shaughnessy, P. N.; Scott, P. *Chem. Commun.* **2004**, 894–895. (b) Gribkov, D. V.; Hultzsch, K. C. *Angew. Chem., Int. Ed.* **2004**, *43*, 5542–5546. (c) Wood, M. C.; Leitch, D. C.; Yeung, C. S.; Kozak, J. A.; Schafer, L. L. *Angew. Chem., Int. Ed.* **2007**, *46*, 354–358. (d) Majumder, S.; Odom, A. L. *Organometallics* **2008**, *27*, 1174–1177. (e) Müller, C.; Saak, W.; Doye, S. *Eur. J. Org. Chem.* **2008**, 2731–2739. (f) Cho, J.; Hollis, T. K.; Helgert, T. R.; Valente, E. J. *Chem. Commun.* **2008**, 5001–5003. (g) Leitch, D. C.; Payne, P. R.; Dunbar, C. R.; Schafer, L. L. *J. Am. Chem. Soc.* **2009**, *131*, 18246–18247. (h) Reznichenko, A. L.; Hultzsch, K. C. *Organometallics* **2010**, *29*, 24–27. (i) Manna, K.; Ellern, A.; Sadow, A. D. *Chem. Commun.* **2010**, *46*, 339–341. (j) Bexrud, J. A.; Schafer, L. L. *Dalton Trans.* **2010**, *39*, 361–363. See also refs 1, 2b.

(5) (a) Kissounko, D. A.; Epshteyn, A.; Fettinger, J. C.; Sita, L. R. *Organometallics* **2006**, *25*, 1076–1078. (b) Gott, A. L.; Clarke, A. J.; Clarkson, G. J.; Scott, P. *Chem. Commun.* **2008**, 1422–1424.

(6) (a) Wang, C.; Sun, X. -L.; Guo, Y. -H.; Gao, Y.; Liu, B.; Ma, Z.; Xia, W.; Shi, L. -P.; Tang, Y. *Macromol. Rapid Commun.* **2005**, *26*, 1609–1614. (b) Wang, C.; Ma, Z.; Sun, X.-L.; Gao, Y.; Guo, Y.-H.; Tang, Y.; Shi, L.-P. *Organometallics* **2006**, *25*, 3259–3266. (c) Gao, M.; Wang, C.; Sun, X.; Qian, C.; Ma, Z.; Bu, S.; Tang, Y.; Xie, Z. *Macromol. Rapid Commun.* **2007**, *28*, 1511–1516. (d) Yang, X.-H.; Liu, C.-R.; Wang, C.; Sun, X.-L.; Guo, Y.-H.; Wang, X.; Wang, Z.; Xie, Z.; Tang, Y. *Angew. Chem., Int. Ed.* **2009**, *48*, 8099–8102.

Table 2. Intramolecular Hydroamination of Primary and Secondary Aminoalkenes Catalyzed by Cationic Zirconium[a]

entry	aminoalkene	conditions	product	yield (%[b])
1	 **6a**	100 °C 6 h	 **7a**	92
2	 **6b**	100 °C 17 h	 **7b**	97
3	 **6c**	140 °C 36 h	 **7c**	72 [c]
4	 **6d**	100 °C 24 h	 **7d**	85
5	 **6e**	130 °C 48 h	 **7e**	97
6	 **6f**	25 °C 3 h	 **7f**	94
7	 **6g**	80 °C 36 h	 **7g**	96
8	 **6h**	80 °C 36 h	 **7h**	96
9	 **6i**	120 °C 36 h	 **7i**	98

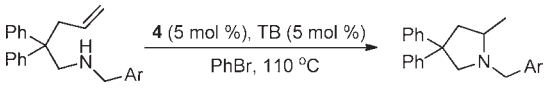
[a] Conditions: **6** (1.0 mmol), **4** (39 mg, 5 mol %), $[Ph_3C][B(C_6F_5)_4]$ (46 mg, 0.05 mmol, 5 mol %), PhBr (2.5 mL). [b] Isolated yield; average of two runs. [c] 10 mol % catalyst was used; isolated as its tosylate product.

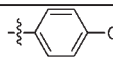
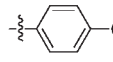
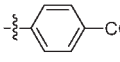
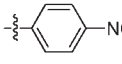
to excellent yields. For example, in the presence of 5 mol % precatalyst, aminoalkene **6a** gave the corresponding pyrrolidine in 92% yield (entry 1). The Thorpe–Ingold effect was also investigated, and substrate **6c** worked well (entry 3). The reactions of secondary amines proceeded nicely, providing tertiary amines in excellent yields (entries 6–9). For instance, the reaction of **6f** proceeded smoothly at room temperature. In contrast, only a 35% yield of product **7f** was obtained when complex **4** was used as the catalyst under the same conditions, showing again that cationic zirconium complex **5** is much more active than the corresponding neutral one. Only a few group 4 metal complexes could catalyze the hydroamination of aminoalkenes with nonterminal olefins.[4d,e,g,j] Fortunately, the cationic zirconium **5** proved to be suitable for the internal aminoalkenes (entries 5, 8, and 9).

When 1,2-disubstituted alkenyl methylamines **6h** and **6i** were employed, the desired products **7h** and **7i** were obtained in excellent yields, respectively.

The tolerability toward various functional groups is one of the major challenges for early transition metal catalysts.[11] Very recently, a bis(amido) zirconium complex was reported to be an efficient catalyst for the hydroamination of both primary and secondary amine substrates bearing a protected catechol, a pyrrole, or a tertiary aniline.[4g] In our study, the catalyst was examined (Table 3), and it was found that the cationic catalyst **5** was compatible with secondary aminoalkenes bearing polar groups such as methoxy (entry 1), halide (entry 2), ester (entry 3), furanyl (entry 5), and nitro groups (entry 4). In all of these cases, high yields were obtained as shown in Table 3.

Table 3. Hydroamination of Functional Aminoalkenes Catalyzed by Cationic Zirconium[a]



entry	Ar	time (h)	7 (yield %) [b]
1	 **6j**	72	**7j** (86)
2	 **6k**	10	**7k** (82)
3	 **6l**	8	**7l** (84)
4	 **6m**	48	**7m** (97)
5	 **6n**	8	**7n** (96)

[a] Conditions: **6** (1.0 mmol), **4** (39 mg, 5 mol %), $[Ph_3C][B(C_6F_5)_4]$ (TB) (46 mg, 0.05 mmol, 5 mol %), PhBr (2.5 mL), 110 °C. [b] Isolated yield.

As catalyst **5** is active for both primary and secondary aminoalkenes, it might also be effective for the subsequent hydroamination of intramolecular aminodienes. As shown in Table 4, **6o** and **6p** worked well giving the corresponding bicyclic tertiary amines **7o** and **7p** in 96% and 85% yield, respectively (entries 1–2). Symmetrical aminodiene **6q** smoothly underwent cyclization to quantitatively afford hexahydro-1*H*-pyrrolizine **7q**. Thus, this method provides an easy access to bicyclic amines.

The cationic species derived from Cp_2ZrMe_2 did not promote the hydroamination of primary amines. However, as described above, cationic zirconium complex **5** worked well for both primary and secondary amines.

(7) See Supporting Information.

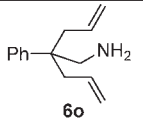
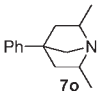
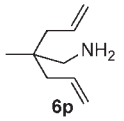
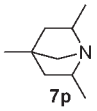
(8) (a) Chien, J. C.; Tsai, W. W.-M.; Rausch, M. D. *J. Am. Chem. Soc.* **1991**, *113*, 8570–8571. (b) Chen, E. Y.; Marks, T. J. *Chem. Rev.* **2000**, *100*, 1391–1434.

(9) (a) Lauterwasser, F.; Hayes, P. G.; Brase, S.; Piers, W. E.; Schafer, L. L. *Organometallics* **2004**, *23*, 2234–2237. (b) Bambirra, S.; Tsurugi, H.; van Leusen, D.; Hessen, B. *Dalton Trans.* **2006**, 1157–1161.

(10) Bergman and co-workers reported that a cationic zirconium complex generated by treating Cp_2ZrMe_2 with $B(C_6F_5)_3$ was active for the intramolecular hydroamination of aminoallene. See: Ackermann, L.; Bergman, R. G.; Loy, R. N. *J. Am. Chem. Soc.* **2003**, *125*, 11956–11963.

(11) No desired imido complex was obtained even if 3 equiv of pyridine was added and the mixture was heated at 110 °C for 3 days.

Table 4. Hydroamination of Aminodienes Catalyzed by Cationic Zirconium[a]

entry	aminodiene	conditions	product	yield (%)
1	 **6o**	130 °C 48 h	 **7o**	96[b]
2	 **6p**	130 °C 144 h	 **7p**	85[c]
3	 **6q**	130 °C 24 h then 150 °C 36 h	 **7q**	100[d]

[a] Conditions: **6** (1.0 mmol), **4** (39 mg, 5 mol %), $[Ph_3C][B(C_6F_5)_4]$ (46 mg, 0.05 mmol, 5 mol %), PhBr (2.5 mL). [b] Isolated yield; 1.2:1 mixture of diastereomers. [c] Yield of NMR reaction in d_5-PhBr; ferrocene as internal standard; 10 mol % cat was used; 1:1 mixture of diastereomers. [d] A single diastereoisomer was obtained; isolated as HCl salt.

In order to gain some insight into the mechanism, treatment of **4** with *tert*-butylamine did not give the imido-Zr complex,[7,11] but rather afforded the bisamide complex $[O^-N^-S]Zr(NHBu^t)_2$ **9** that was confirmed by X-ray analyses.[7] This result suggests that the imido-Zr complex may not be involved in the reaction. It is likely that this reaction proceeds via a Zr-amide intermediate shown in Scheme 1.[2c,4d,5]

In summary, the cationic zirconium complex bearing a planar [NOS] ligand has been demonstrated to be an efficient catalyst for the intramolecular hydroamination of both terminal and internal alkenes with a primary and/or secondary amino moiety. Such a catalyst is tolerant to many functional groups. In the presence of a catalytic amount of such a complex, tandem intramolecular hydroamination of primary aminodienes proceeds very well, providing an easy access to bicyclic amines. The results greatly broaden the scope of the cationic zirconium-catalyzed hydroamination and provide clues for catalyst design for hydroamination of olefins.

Acknowledgment. Financial support was provided by the National Natural Science Foundation of China (Nos. 20821002 and 20932008), the Major State Basic Research Development Program (Grant No. 2009CB825300), NSFC/RGC Joint Research Scheme (N_CUHK470/10 to Z.X. and No. 21061160493 to T.Y.), and the CAS-Croucher Funding Scheme (Project No. GJHZ200816). Prof. Guangyu Li and Prof. Huaping Mo are thanked for their help on NMR analyses. This work is dedicated to Prof. Christian Bruneau on the occasion of his 60th birthday.

Supporting Information Available. General experimental procedures, complete characterization data, and X-ray data for **4** and **9** in CIF format. This material is available free of charge via the Internet at http://pubs.acs.org.