

## BiCl<sub>3</sub>-Catalyzed Hydroamination of Norbornene with Aromatic Amines

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A BiCl<sub>3</sub>-catalyzed hydroamination reaction of norbornene, in which a variety of electron-withdrawing groups were tolerated on amines, was presented. The current transformation possesses the advantages of being highly selective, cheap, and eco-friendly, and this process also represents a rare sys-

tem for main-group Lewis acid catalyzed intermolecular hydroamination of unactivated alkenes.

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### Introduction

The hydroamination of alkenes represents an atom economic process for the synthesis of amine and amine derivatives that are prevalent in natural products and compounds of pharmaceutical significance.<sup>[1]</sup> Efforts to develop such processes have been intensified in recent years. To achieve efficient transformation, the late transition metals are widely used as catalysts. Both intramolecular and intermolecular hydroamination of alkenes have been successfully developed by using Au,<sup>[2]</sup> Pt,<sup>[3]</sup> Rh,<sup>[4]</sup> and other noble-transition-metal complexes.<sup>[5]</sup> Recently, through the elegant work of the Bergman and Ackermann groups, great advances have been made to use early transition metals, as evidenced by the hydroamination of norbornene and styrene.<sup>[6]</sup> Along with the transition-metal catalysts, there also have been examples using lanthanide complexes,<sup>[7]</sup> Bronsted acids,<sup>[8]</sup> and other catalysts,<sup>[9]</sup> which provide alternative procedures for olefin hydroamination.

Whereas transition-metal catalyzed hydroamination reactions are widely pursued, it should be noted that these catalysts have the drawbacks of high cost, toxicity, and demanding reaction conditions, as most of the transition metals are sensitive to moisture and air. Recent work on olefin hydroamination with commonly used transition-metal Lewis acids are outstanding,<sup>[6b,6c,10]</sup> although the mechanisms of these reactions are still unrevealed. As an ongoing

project with an aim to discover novel catalysts for olefin hydroamination, we found that only limited attention has been paid to main-group metals in hydroamination reactions.<sup>[11]</sup> Among the few publications in this field, the recent work of Shibasaki and co-workers has achieved remarkable progress,<sup>[12]</sup> in which Bi(OTf)<sub>3</sub> was found to be an efficient catalyst for diene and vinylarene hydroaminations. We wondered whether commonly used main-group Lewis acids could also serve as competent catalysts; therefore, we studied the intermolecular hydroamination of norbornene with aromatic amines by using several main-group metal salts. Herein our preliminary results are reported with the focus on the performance of BiCl<sub>3</sub>. The bismuth salt is highly selective and air and moisture tolerable, and it is also recoverable with additional procedures; its activity is superior to that of early transition metals. A plausible mechanism for the reaction is proposed and discussed.

### Results and Discussion

Initial experiments were performed with norbornene (**1**) and 2,5-dichloroaniline (**2a**), and several readily available Lewis acids were screened as the catalyst for the reactions. Under ambient conditions, the catalyst, **1**, **2a**, and toluene were sealed in a pressure tube and heated in an oil bath at 169 °C. Subsequently, the resulting mixture was analyzed by GC-MS, and the products were isolated by flash chromatography. The results are summarized in Table 1.

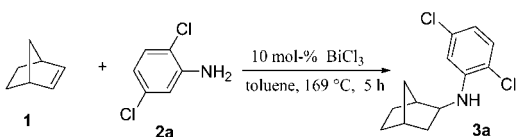
As shown in Table 1, when the strong Lewis acid B(C<sub>6</sub>F<sub>5</sub>)<sub>3</sub> was used (Table 1, Entry 1), no product was detected during a period of 5 h, and 80% of norbornene starting material was recovered. This may be attributed to the fact that the coordination of the amine to B(C<sub>6</sub>F<sub>5</sub>)<sub>3</sub> somewhat hindered the hydroamination and hydroalkylations.<sup>[13]</sup> All the chloride salts, AlCl<sub>3</sub> (Table 1, Entry 2), FeCl<sub>3</sub> (Table 1, Entry 3),<sup>[10]</sup> BiCl<sub>3</sub> (Table 1, Entry 4), and SnCl<sub>4</sub> (Table 1, Entry 8), were competent catalysts and afforded

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Table 1. Hydroamination reaction between norbornene (**1**) and 2,5-dichloroaniline (**2a**) catalyzed by various Lewis acids.


| Entry | Catalyst                                       | Isolated yield of <b>3a</b> [%] |
|-------|------------------------------------------------|---------------------------------|
| 1     | B(C <sub>6</sub> F <sub>5</sub> ) <sub>3</sub> | 0                               |
| 2     | AlCl <sub>3</sub>                              | 86                              |
| 3     | FeCl <sub>3</sub>                              | 88                              |
| 4     | BiCl <sub>3</sub>                              | 92                              |
| 5     | ZnF <sub>2</sub>                               | 0                               |
| 6     | ZnCl <sub>2</sub>                              | trace                           |
| 7     | I <sub>2</sub>                                 | 6                               |
| 8     | SnCl <sub>4</sub>                              | 84                              |

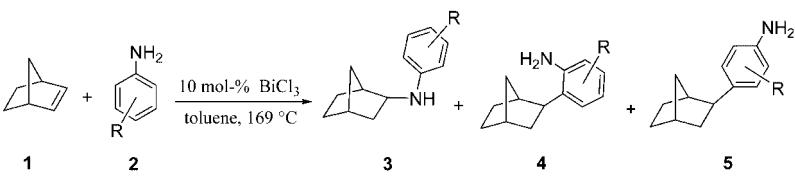
quite good yields of **3a**. To our disappointment, no reaction occurred when ZnF<sub>2</sub> was used (Table 1, Entry 5), and only a trace amount of product was detected in the case of ZnCl<sub>2</sub> (Table 1, Entry 6). It is noteworthy that molecular iodine (Table 1, Entry 7), which can be defined as a weak Lewis acid,<sup>[14]</sup> could also promote the hydroamination reaction, yet the yield was only 6% under the nonoptimized conditions.

These initial results indicated that several main-group Lewis acids could serve as catalysts in the intermolecular hydroamination of norbornene with aromatic amines, and BiCl<sub>3</sub> was found to give the best yield. Given that BiCl<sub>3</sub> can be easily recovered from the heterogeneous reaction system,<sup>[15]</sup> it is believed that BiCl<sub>3</sub>-catalyzed reactions also have the advantage of being environmentally benign. To further test the performance of this useful catalyst, the

BiCl<sub>3</sub>-catalyzed intermolecular hydroamination of norbornene with various aniline derivatives was studied.

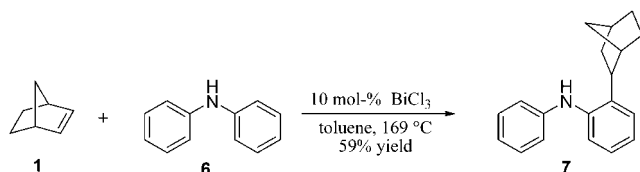
As shown in Table 2, BiCl<sub>3</sub> catalyzed the reactions between norbornene (**1**) and a number of aniline derivatives, and the hydroamination products were obtained as the major products.<sup>[16]</sup> The reaction of aniline itself gave a moderate yield of **3b**, whereas a comparable amount of byproduct **4** was isolated (Table 2, Entry 1). The electron-withdrawing groups enhance the chemoselectivity with the yields of the hydroamination products from moderate-to-excellent (Table 1, Entry 4; Table 2, Entries 2–12). Notably, when the aniline was monosubstituted with NO<sub>2</sub> (Table 2, Entry 2), Cl (Table 2, Entry 7), or Br (Table 2, Entry 9) groups in the *para* position, type **3** products were obtained as the sole product, and 80% yield of **3m** was obtained with 2,4-dichloroaniline (Table 2, Entry 12). However, in some cases, hydroarylation occurred during the hydroamination process as a minor side reaction (Table 2, Entries 4–6, 8, 10, and 11). Two hydroarylation byproducts were detected occasionally (Table 2, Entries 5, 6, 8, and 10), yet the yields of these byproducts were significantly lower relative to those of the side reaction of unsubstituted aniline (Table 2, Entry 1). These results are different from TiCl<sub>4</sub>-catalyzed hydroamination of norbornene, in which an *ortho* hydroarylation product was the only side product.<sup>[6b]</sup> It is interesting to find that electron-donating groups in the *para* position of the aniline inhibit the reaction, as no products were observed with 4-methoxyaniline or 4-methylaniline as the nitrogen sources (Table 2, Entries 13 and 14).

The hydroamination of secondary amine **6** with norbornene was also investigated (Scheme 1). No hydroamination reaction was detected, and *ortho*-substituted hydroarylation product **7** was obtained in moderate yield.<sup>[17]</sup>

Table 2. Scope of the BiCl<sub>3</sub>-catalyzed hydroamination reaction of norbornene (**1**).<sup>[a]</sup>


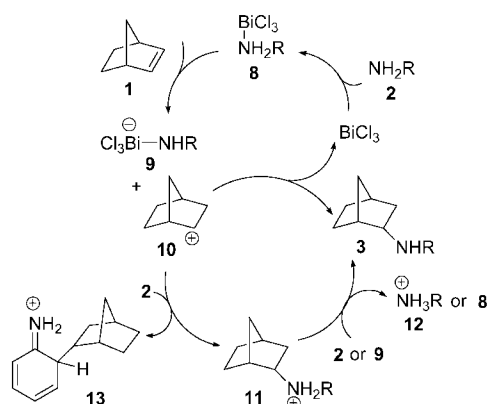
| Entry | Amine               | Time [h] | Ratio of <b>3/4/5</b> <sup>[b]</sup> | <b>3</b>  | Isolated yield of <b>3</b> [%] |
|-------|---------------------|----------|--------------------------------------|-----------|--------------------------------|
| 1     | aniline             | 5        | 58:42:0                              | <b>3b</b> | 43                             |
| 2     | 4-nitroaniline      | 6        | 100:0:0                              | <b>3c</b> | 67                             |
| 3     | 2-nitroaniline      | 6        | 100:0:0                              | <b>3d</b> | 69                             |
| 4     | 3-nitroaniline      | 6        | 98:2:0                               | <b>3e</b> | 80                             |
| 5     | 2-chloroaniline     | 4        | 83:13:4                              | <b>3f</b> | 84                             |
| 6     | 3-chloroaniline     | 4        | 82:8:10                              | <b>3g</b> | 65                             |
| 7     | 4-chloroaniline     | 3        | 100:0:0                              | <b>3h</b> | 54                             |
| 8     | 3,4-dichloroaniline | 4        | 96:3:1                               | <b>3i</b> | 61                             |
| 9     | 4-bromoaniline      | 5        | 100:0:0                              | <b>3j</b> | 63                             |
| 10    | 2-fluoroaniline     | 4        | 87:10:3                              | <b>3k</b> | 73                             |
| 11    | 4-fluoroaniline     | 6        | 78:22:0                              | <b>3l</b> | 59                             |
| 12    | 2,4-dichloroaniline | 4        | 100:0:0                              | <b>3m</b> | 80                             |
| 13    | 4-methoxyaniline    | 6        | 0:0:0                                | none      | 0                              |
| 14    | 4-methylaniline     | 6        | 0:0:0                                | none      | 0                              |

[a] Reaction conditions: **1** (2 mmol), **2** (8 mmol), BiCl<sub>3</sub> (10 mol-%), toluene (4 mL). [b] By GC–MS analysis.



Scheme 1. BiCl<sub>3</sub>-catalyzed reaction of norbornene with a secondary amine.

A mechanistic hypothesis, which accounts for the catalytic cycle for the formation of the hydroamination products as well as hydroarylation products, is provided in Scheme 2.



Scheme 2. Proposed mechanism for the hydroamination and hydroarylation reactions (R = aryl).

In the process, complex **8** can be firstly formed from the Lewis acid/base interaction between BiCl<sub>3</sub> and aniline **2**, in which the acidity of the amido H is increased as the result of the electron donation from N to the metal. Protonation of norbornene **1** by complex **8** will give rise to carbocationic intermediate **10** and an anionic bismuth complex **9** as well. The formation of hydroamination product **3** and regeneration of the BiCl<sub>3</sub> catalyst can be accomplished from nucleophilic attack of **9** to **10**. Alternatively, the cationic intermediate **10** can be trapped more likely by the abundant amine **2** in the system. Either the heteroatom or the aromatic ring can act as the nucleophile to generate intermediate **11** or **13**, which can be further transformed to the hydroamination or hydroarylation products, respectively, through deprotonation reactions with possible bases in the system.

It should be clarified that this reaction may also be promoted by acid, particularly HCl, which could be involved in the reaction system from the hydrolysis of the metal chloride under the current conditions. However, only a trace amount of the hydroamination product was detected with 10 mol-% HCl as the catalyst.<sup>[18]</sup> An in-depth mechanistic study is needed to achieve comprehensive understanding of the reaction.

## Conclusions

We presented here efficient Lewis acidic BiCl<sub>3</sub>-catalyzed hydroamination reactions of norbornene (**1**), in which a variety of electron-withdrawing groups were tolerated in amines. This reaction is not only an atom-economic process with high chemoselectivity, simple operation, and further reusable catalyst, but also represents a rare system for main-group metal-catalyzed intermolecular hydroamination of unactivated alkenes. A general mechanism for the reaction, in which the carbocation was proposed as the key intermediate, was provided. Further studies on the development of the catalyst, the scope of the substrate, and the mechanism in the field of hydroamination are undergoing in our group.

**Supporting Information** (see footnote on the first page of this article): Detailed experimental procedures for the hydroamination reaction and spectroscopic data.

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- a) K. C. Hultzs, *Org. Biomol. Chem.* **2005**, 3, 1819–1824; b) K. C. Hultzs, *Adv. Synth. Catal.* **2005**, 347, 367–391; c) P. W. Roesky, T. E. Mueller, *Angew. Chem. Int. Ed.* **2003**, 42, 2708–2710; d) T. E. Muller, M. Beller, *Chem. Rev.* **1998**, 98, 675–704.
- a) R. A. Widenhoefer, X. Han, *Eur. J. Org. Chem.* **2006**, 4555–4563; b) C. F. Bender, R. A. Widenhoefer, *Chem. Commun.* **2006**, 4143–4144; c) J. E. Kang, H. B. Kim, J. W. Lee, S. Shin, *Org. Lett.* **2006**, 8, 3537–3540; d) X. Y. Liu, C. H. Li, C. M. Che, *Org. Lett.* **2006**, 8, 2707–2710; e) J. L. Zhang, C. G. Yang, C. He, *J. Am. Chem. Soc.* **2006**, 128, 1798–1799.
- a) D. Karstedt, A. T. Bell, T. D. Tilley, *J. Am. Chem. Soc.* **2005**, 127, 12640–12646; b) C. F. Bender, R. A. Widenhoefer, *J. Am. Chem. Soc.* **2005**, 127, 1070–1071; c) X. Wang, R. A. Widenhoefer, *Organometallics* **2004**, 23, 1649–1651.
- a) J. R. Briggs, J. Klosin, G. T. Whiteker, *Org. Lett.* **2005**, 7, 4795–4798; b) M. Ahmed, A. M. Seayad, R. Jackstell, M. Beller, *Angew. Chem. Int. Ed.* **2003**, 42, 5615–5619; c) M. Beller, H. Trauthwein, M. Eichberger, C. Breindl, J. Herwig, T. E. Muller, O. R. Thiel, *Chem. Eur. J.* **1999**, 5, 1306–1319.
- a) F. E. Michael, B. M. Cochran, *J. Am. Chem. Soc.* **2006**, 128, 4246–4247; b) M. Tada, M. Shimamoto, T. Sasaki, Y. Iwasawa, *Chem. Commun.* **2004**, 2562–2563; c) M. Utsunomiya, J. F. Hartwig, *J. Am. Chem. Soc.* **2004**, 126, 2702–2703; d) Y. Uchimar, *Chem. Commun.* **1999**, 1133–1134.
- a) L. L. Anderson, J. Arnold, R. G. Bergman, *Org. Lett.* **2004**, 6, 2519–2522; b) L. Ackermann, L. T. Kaspar, C. J. Gschrei, *Org. Lett.* **2004**, 6, 2515–2518; c) L. T. Kaspar, F. Benjamin, L. Ackermann, *Angew. Chem. Int. Ed.* **2005**, 44, 5972–5974.
- a) J. S. Ryu, Y. Li, T. J. Marks, *J. Am. Chem. Soc.* **2003**, 125, 12584–12605; b) Y. Li, T. J. Marks, *J. Am. Chem. Soc.* **1998**, 120, 1757–1771; c) Y. Li, T. J. Marks, *Organometallics* **1996**, 15, 3770–3772; d) E. Barnea, M. S. Eisen, *Coord. Chem. Rev.* **2006**, 250, 855–859; e) S. Hong, T. J. Marks, *Acc. Chem. Res.* **2004**, 37, 673–686.
- a) L. L. Anderson, J. Arnold, R. G. Bergman, *J. Am. Chem. Soc.* **2005**, 127, 14542–14543; b) D. C. Rosenfeld, S. Shekhar, A. Takemiya, M. Utsunomiya, J. F. Hartwig, *Org. Lett.* **2006**, 8, 4179–4182; c) B. Schlummer, J. F. Hartwig, *Org. Lett.* **2002**,

- 4, 1471–1474; d) K. Marcsekova, S. Doye, *Synthesis* **2007**, 145–154.
- [9] a) V. Khedkar, A. Tillack, C. Benisch, J. P. Melder, M. Beller, *J. Mol. Catal. A* **2005**, *241*, 175–183; b) M. Beller, C. Breindl, *Tetrahedron* **1998**, *54*, 6359–6368; c) J. Seayad, A. Tillack, C. G. Hartung, M. Beller, *Adv. Synth. Catal.* **2002**, *344*, 795–813; d) Q. Ruo, E. M. Thomas, *Tetrahedron* **2001**, *57*, 6027–6033; e) J. J. Brunet, N. C. Chu, O. Diallo, E. Mothes, *J. Mol. Catal. A* **2003**, *198*, 107–110; f) A. A. M. Lapis, B. A. DaSilveira, J. D. Scholten, F. M. Nachtigall, M. N. Eberlin, J. Dupont, *Tetrahedron Lett.* **2006**, *47*, 6775–6779.
- [10] Recently, FeCl<sub>3</sub>-catalyzed intramolecular and intermolecular olefin hydroaminations were developed, see: a) K. Komeyama, T. Morimoto, K. Takaki, *Angew. Chem. Int. Ed.* **2006**, *45*, 2938–2941; b) J. Michaux, V. Terrason, S. Marque, J. Wehbe, D. Prim, J.-M. Campagne, *Eur. J. Org. Chem.* **2007**, 2601–2603.
- [11] H. Lehmkuhl, D. Reinehr, *J. Organomet. Chem.* **1973**, *55*, 215–220.
- [12] a) H. Qin, N. Yamagiwa, S. Matsunaga, M. Shibasaki, *Chem. Asian J.* **2007**, *2*, 150–154; b) H. Qin, N. Yamagiwa, S. Matsunaga, M. Shibasaki, *J. Am. Chem. Soc.* **2006**, *128*, 1611–1614.
- [13] a) S. Kobayashi, I. Komoto, J. I. Matsuo, *Adv. Synth. Catal.* **2001**, *343*, 71–74; b) M. Beller, O. R. Thiel, H. Trauthwein, *Synlett* **1999**, 243–245.
- [14] M. T. Kelly, A. B. Bocarsly, *Chem. Mater.* **1997**, *9*, 1659–1664 and references cited therein.
- [15] 90% of BiCl<sub>3</sub> could be recovered by filtration after the first cycle of the reaction. The recovered BiCl<sub>3</sub> catalyzed the reaction of norbornene with 2,5-dichloroaniline to afford the hydroamination product in 78% yield. Similar results can be achieved by using a literature method, see: S. Repichet, C. L. Roux, N. Roques, J. Dubac, *Tetrahedron Lett.* **2003**, *44*, 2037–2040.
- [16] We found that no hydroamination products could be detected by using *tert*butylamine and phenylmethanamine under the current reaction conditions. By using 4methylbenzenesulfonamide, a 32% isolated yield was obtained; further optimization is needed to obtain desirable results.
- [17] A similar result was previously reported, see ref.<sup>[6b]</sup>
- [18] Previous studies found no reaction with the use of catalytic amounts of HCl, see refs.<sup>[6b,12a]</sup> For a recent hydroamination catalyzed by HI, see ref.<sup>[8d]</sup>

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