J|A|C|S
ARTICLES
Published on Web 01/17/2006

Bismuth-Catalyzed Intermolecular Hydroamination of 1,3-Dienes with Carbamates, Sulfonamides, and Carboxamides

Hongbo Qin, Noriyuki Yamagiwa, Shigeki Matsunaga,* and Masakatsu Shibasaki*

Contribution from the Graduate School of Pharmaceutical Sciences, The University of Tokyo, Hongo, Bunkyo-ku, Tokyo 113-0033, Japan

Received September 6, 2005; E-mail: smatsuna@mol.f.u-tokyo.ac.jp; mshibasa@mol.f.u-tokyo.ac.jp

Abstract: A $Bi(OTf)_3/Cu(CH_3CN)_4PF_6$ system efficiently promoted intermolecular 1:1 hydroamination of 1,3-dienes with various carbamates, sulfonamides, and carboxamides to afford allylic amines in good yield (up to 96%). Reaction proceeded with 0.5−10 mol % catalyst loading at 25−100 °C (generally at 50 °C) in 1,4-dioxane within 24 h. The $Bi(OTf)_3/Cu(CH_3CN)_4PF_6$ system constitutes a new entry into series of intermolecular hydroamination catalysis. Mechanistic studies and the postulated reaction mechanism are also discussed.

Introduction

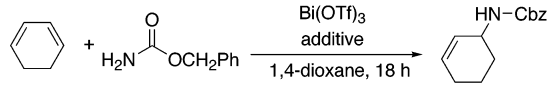
The importance of amine derivatives for the synthesis of pharmaceuticals and fine chemicals has attracted considerable interest in catalytic olefin-amination.[1] Intermolecular hydroamination of olefins is one of the most important topics in this area. Despite recent progress in intermolecular olefin-hydroamination,[2−11] mild and selective 1:1 reactions of amines with 1,3-dienes without telomerizations are still limited.[12] Most notably, Hartwig reported effective hydroamination of 1,3-dienes with arylamines[12a] and alkylamines[12d] catalyzed by either a palladium[12a] or a nickel[12d] complex; however, intermolecular selective 1:1 hydroamination of 1,3-dienes with weaker nucleophiles, such as carbamates, sulfonamides, and carboxamides, has not yet been achieved. Herein, we report a new bismuth-catalyzed intermolecular hydroamination with various amides to produce allylic amines in good yield (up to 96%).[13] The catalyst system is different from the series of catalysts that are effective for intermolecular hydroaminations of olefins, such as late-transition metal complexes,[2−6] Cp-lanthanides,[1,7] and group IV metals.[1,8a]

Results and Discussion

A. Development of a Bismuth-Catalyzed Intermolecular Hydroamination of Dienes. To find a suitable catalyst for hydroaminations, various metals were screened for the reaction of diene **1a** (4 equiv) with carbamate **2a**, and 10 mol % of $Bi(OTf)_3$ afforded a 1:1 adduct **3aa** in 17% yield, albeit with polymerized byproducts (Table 1, entry 1). The addition of 10 mol % $Cu(CH_3CN)_4PF_6$ **4** suppressed the polymerization and cleanly promoted the reaction at 25 °C in 1,4-dioxane to afford

(1) For recent reviews, see: (a) Müller, T. E.; Beller, M. *Chem. Rev.* **1998**, *98*, 675. (b) Hong, S.; Marks, T. J. *Acc. Chem. Res.* **2004**, *37*, 673. (c) Bystschkov, I.; Doye, S. *Eur. J. Org. Chem.* **2003**, 935. (d) Roesky, P. W.; Müller, T. E. *Angew. Chem., Int. Ed.* **2003**, *42*, 2708. (e) Nobis, M.; Drieβen-Hölscher, B. *Angew. Chem., Int. Ed.* **2001**, *40*, 3983.
(2) Ir catalysts: (a) Casalnuovo, A. L.; Calabrese, J. C.; Milstein, D. *J. Am. Chem. Soc.* **1988**, *110*, 6738. (b) Dorta, R.; Egli, P.; Zürcher, F.; Togni, A. *J. Am. Chem. Soc.* **1997**, *119*, 10857.
(3) Pd catalysts: (a) Kawatsura, M.; Hartwig, J. F. *J. Am. Chem. Soc.* **2000**, *122*, 9546. (b) Nettekoven, U.; Hartwig, J. F. *J. Am. Chem. Soc.* **2002**, *124*, 1166. (c) Utsunomiya, M.; Hartwig, J. F. *J. Am. Chem. Soc.* **2003**, *125*, 14286. See also refs 12a and 12b.
(4) Rh catalysts: (a) Beller, B.; Breindl, C.; Eichberger, M.; Hartung, C. J.; Seayad, J.; Thiel, O. R.; Tillack, A.; Trauthwein, H. *Synlett* **2002**, 1579 and references therein. (b) Utsunomiya, M.; Kuwano, R.; Kawatsura, M.; Hartwig, J. F. *J. Am. Chem. Soc.* **2003**, *125*, 5608.
(5) Pt catalysts: (a) Brunet, J. J.; Cadena, M.; Chu, N. C.; Diallo, O.; Jacob, K.; Mothes, E. *Organometallics* **2004**, *23*, 1264. (b) Qian, H.; Pei, T.; Widenhoefer, R. A. *Organometallics* **2004**, *23*, 1649. (c) Qian, H.; Widenhoefer, R. A. *Org. Lett.* **2005**, *7*, 1635 and references therein. (d) Karshtedt, D.; Bell, A. T.; Tilley, T. D. *J. Am. Chem. Soc.* **2005**, *127*, 12640 and references therein.
(6) Ru catalyst: (a) Utsunomiya, M.; Hartwig, J. F. *J. Am. Chem. Soc.* **2004**, *126*, 2702. (b) Takaya, J.; Hartwig, J. F. *J. Am. Chem. Soc.* **2005**, *127*, 5756. See also ref 12c.
(7) Cp-lanthanides catalysts: Ryu, J. S.; Li, G. Y.; Marks, T. J. *J. Am. Chem. Soc.* **2003**, *125*, 12584. For applications to intramolecular hydroaminations, see ref 1b and references therein.
(8) Early transition metal catalysts: (a) Ackermann, L.; Kaspar, L. T.; Gschrei, C. J. *Org. Lett.* **2004**, *6*, 2515. (b) Anderson, L. L.; Arnold, J.; Bergman, R. G. *Org. Lett.* **2004**, *6*, 2519. (c) Kaspar, L. T.; Fingerhut, B.; Ackermann, L. *Angew. Chem., Int. Ed.* **2005**, *44*, 5972 and references therein.
(9) (a) Anderson, L. L.; Arnold, J.; Bergman, R. G. *J. Am. Chem. Soc.* **2005**, *127*, 14542. (b) Talluri, S. K.; Sudalai, A. *Org. Lett.* **2005**, *7*, 855. For other examples, see reviews in ref 1.
(10) For related hydrohydrazination, see: (a) Waser, J.; Carreira, E. M. *J. Am. Chem. Soc.* **2004**, *126*, 5676. (b) Waser, J.; Carreira, E. M. *Angew. Chem., Int. Ed.* **2004**, *43*, 4099. See also ref 12e.
(11) For related intermolecular oxidative amination with carboxamides, carbamates, and sulfonamides, see: (a) Timokhin, V. I.; Anastasi, N. R.; Stahl, S. S. *J. Am. Chem. Soc.* **2003**, *125*, 12996. (b) Brice, J. L.; Harang, J. E.; Timokhin, V. I.; Anastasi, N. R.; Stahl, S. S. *J. Am. Chem. Soc.* **2005**, *127*, 2868 and references therein. For other works of catalytic 1,3-diene manipulations using transition metals, see: (c) Bäckvall, J. E. In *The Chemistry of Functional Groups: Polyenes and Dienes*; Patai, S., Rappoport, Z., Eds.; Wiley: New York, 1997; pp 653−681 and references therein. For early works on amination of 1,3-dienes with a selenium reagent, see: (d) Sharpless, K. B.; Singer, S. P. *J. Org. Chem.* **1976**, *41*, 2504.
(12) Arylamine as donor: (a) Löber, O.; Kawatsura, M.; Hartwig, J. F. *J. Am. Chem. Soc.* **2001**, *123*, 4366. (b) Minami, T.; Okamoto, H.; Ikeda, S.; Tanaka, R.; Ozawa, F.; Yoshifuji, M. *Angew. Chem., Int. Ed.* **2001**, *40*, 4051. (c) Yi, C. S.; Yun, S. Y. *Org. Lett.* **2005**, *7*, 2181 and references therein for other less satisfactory examples. Alkylamine as donor: (d) Pawlas, J.; Nakao, Y.; Kawatsura, M.; Hartwig, J. F. *J. Am. Chem. Soc.* **2002**, *124*, 3669. Hydrohydrazination: (e) Waser, J.; González-Gómez, J. C.; Nambu, H.; Huber, P.; Carreira, E. M. *Org. Lett.* **2005**, *7*, 4249.
(13) Review for allylic amine synthesis: Johannsen, M.; Jørgensen, K. A. *Chem. Rev.* **1998**, *98*, 1689 and references therein.

Table 1. Optimization of Reaction Conditions



1a **2a** **3aa**

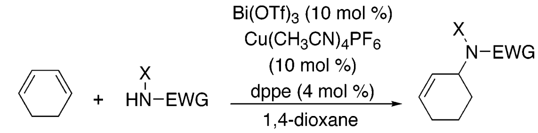
entry	$Bi(OTf)_3$ (*x* mol %)	additive (*y* mol %)	**1a** (equiv)	temp (°C)	yield (%)
1	10	0	4	25	17
2	10	$Cu(CH_3CN)_4PF_6$ **4** (10)	4	25	79
3	10	$Cu(OTf)(C_6H_6)_{1/2}$ **5** (10)	4	25	24
4	10	KPF_6 **6** (10)	4	25	79
5	10	NH_4PF_6 **7** (10)	4	25	74
6	0	**4** (10)	4	25	0
7	10	**4** (10)	2	25	71
8	10	**4** (10)	2	50	66
9	10	**4** (10) + dppe (4)	2	50	80
10	10	**6** (10)	2	50	73
11	10	**6** (10) + dppe (4)	2	50	42

3aa in 79% yield (entry 2). Another Cu source such as $Cu(OTf)(C_6H_6)_{1/2}$ **5** was not effective (entry 3); instead, KPF_6 **6** and NH_4PF_6 **7** gave comparable results with **4** (entries 4 and 5). Control experiments with **4** alone did not promote the reaction (entry 6). With 2 equiv of diene **1a**, the yield of **3aa** decreased to 71% at 25 °C (entry 7). By performing the reaction at 50 °C with dppe, we obtained **3aa** in 80% yield after 18 h with 2 equiv of **1a** (entry 9). We assume that dppe might coordinate to Cu in entry 9 to suppress the undesired reaction at higher temperature. KPF_6 **6** additive also worked well using 2 equiv of diene **1a** (entry 10, 73%), although the yield of **3aa** was slightly lower than $Cu(CH_3CN)_4PF_6$ **4**. In case of KPF_6 **6** additive, dppe had negative effects (entry 11, 42% yield). In entry 11, dppe would coordinate to Bi rather than to K to decrease the Lewis acidity of Bi, resulting in low reactivity.

The optimized reaction conditions were applicable to various carbamates, sulfonamides, and carboxamides (Tables 2 and 3), and the reactions completed within 3−24 h. Results using the $Bi(OTf)_3/Cu(CH_3CN)_4PF_6$/dppe system are summarized in Table 2. Both acyclic and cyclic carbamates **2a**−**2d** gave 1:1 adducts in good yield (80−96%) at 50 °C (entries 1−4). Sulfonamides **2e**−**2i** also gave products in good yield, regardless of the presence of an electron-donating group (entries 6 and 7) or electron-withdrawing group (entry 8). *o*-$NsNH_2$ **2i** required a lower reaction temperature (25 °C) to avoid side reactions and 4 equiv of **1a** to afford **3ai** in 67% yield. Carboxamides **2j** and **2k** were less reactive and required a higher reaction temperature (90−100 °C) to obtain 1:1 adducts in 75% and 77% yield, respectively (entries 10 and 11). Results using the $Bi(OTf)_3/KPF_6$ system are summarized in Table 3. With carbamates and carboxamides as nucleophiles (Table 3, entries 1−4, 10, and 11), the isolated yields of products were slightly lower than those obtained with $Cu(CH_3CN)_4PF_6$ **4** in Table 2. With sulfonamides, the $Bi(OTf)_3/KPF_6$ system promoted the reaction at 25−50 °C using 5−10 mol % of catalyst (entries 5−9). It is noteworthy that, with sulfonamides **2e**, **2f**, and **2g**, the desired 1:1 adducts were obtained in good yield using only 1.2 equiv of diene **1a**, indicating the high chemoselectivity of the present system (entries 5−7).

The attempts to reduce catalyst loading using sulfonamide **2f** are summarized in Table 4. The reaction proceeded without any problems using as little as 0.5 mol % of $Bi(OTf)_3$, affording **3af** in 80% yield after 24 h (entry 5). Table 5 shows the

Table 2. $Bi(OTf)_3/Cu(CH_3CN)_4PF_6$/dppe-Catalyzed Hydroamination of **1a** with Various Carbamates, Sulfonamides, and Carboxamides

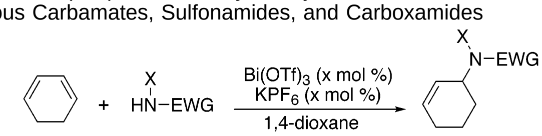


1a (2 equiv) **2** X = H, alkyl **3**

entry	nucleophile			temp (°C)	time (h)	yield[a] (%)	product
1	H_2NC(O)OR	R = CH_2Ph	**2a**	50	18	80	**3aa**
2		R = CH_3	**2b**	50	18	96	**3ab**
3		R = *n*-Bu	**2c**	50	18	85	**3ac**
4	oxazolidin-2-one (HN, O)		**2d**	50	18	92	**3ad**
5	H_2N−S(O)(O)−R	R = Ph	**2e**	50	3	80	**3ae**
6		R = *p*-tol	**2f**	50	3	84	**3af**
7		R = *p*-MeO-C_6H_4	**2g**	50	5	84	**3ag**
8		R = *p*-CF_3-C_6H_4	**2h**	50	5	75	**3ah**
9[b]		R = *o*-NO_2-C_6H_4	**2i**	25	24	67	**3ai**
10[b]	H_2NC(O)R	R = Ph	**2j**	100	12	75	**3aj**
11[b]		R = *p*-CF_3-C_6H_4	**2k**	90	17	77	**3ak**

[a] Yields are for pure, isolated compounds. [b] 4 equiv of **1a** was used.

Table 3. $Bi(OTf)_3/KPF_6$-Catalyzed Hydroamination of **1a** with Various Carbamates, Sulfonamides, and Carboxamides



1a[a] **2** X = H, alkyl **3aa-3ak**

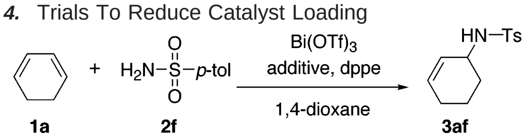
entry	nucleophile			cat. (*x* mol %)	temp (°C)	time (h)	yield[b] (%)
1	H_2NC(O)OR	R = CH_2Ph	**2a**	10	50	18	72
2		R = CH_3	**2b**	10	50	18	94
3		R = *n*-Bu	**2c**	10	50	18	72
4	oxazolidin-2-one (HN, O)		**2d**	10	50	18	88
5	H_2N−S(O)(O)−R	R = Ph	**2e**	5	25	5	73
6		R = *p*-tol	**2f**	5	25	3	83
7		R = *p*-MeO-C_6H_4	**2g**	5	25	5	84
8		R = *p*-CF_3-C_6H_4	**2h**	5	50	5	79
9		R = *o*-NO_2-C_6H_4	**2i**	10	25	24	62
10	H_2NC(O)R	R = Ph	**2j**	10	100	12	69
11		R = *p*-CF_3-C_6H_4	**2k**	10	90	17	60

[a] Entries 1−4 and 8, 2 equiv of **1a** was used; entries 5−7: 1.2 equiv of **1a** was used; entries 9−11: 4 equiv of **1a** was used. [b] Yields are for pure, isolated compounds.

hydroaminations of several acyclic 1,3-dienes **1b**−**1g** with carbamate **2d**. Acyclic 1,3-dienes were also applicable to give products in 60−94% yield; however, the isomer ratio (1,2-adduct vs 1,4-adduct) depended on the dienes. Diene **1c** exclusively gave 1,4-hydroamination adduct **3cd** (entry 2), while diene **1d** exclusively gave 1,2-hydroamination adduct **3dd** (entry 3). Dienes **1e**−**1g** gave mixtures of isomers (entries 4−6).

B. Mechanistic Studies. The present hydroamination gave unsatisfactory results with either $Bi(OTf)_3$ or $Cu(CH_3CN)_4PF_6$ **4** alone (Table 1, entries 1 and 6). The results of entries 2−5 in Table 1 suggest that PF_6^- is important rather than Cu metal.

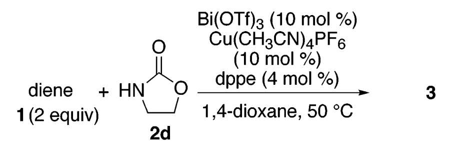
Table 4. Trials To Reduce Catalyst Loading

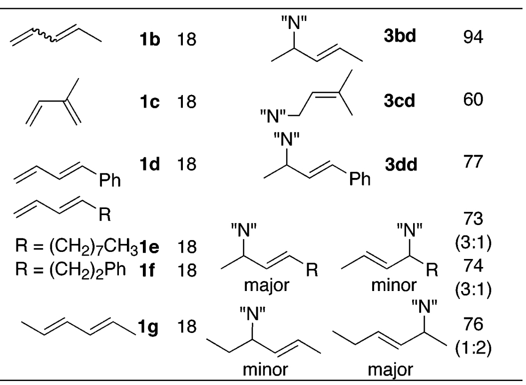


entry	$Bi(OTf)_3$ (x mol %)	additive (y mol %)	dppe (z mol %)	**1a** (equiv)	temp (°C)	time (h)	yield (%)
1	10	**4** (10)	4	2	50	3	84
2	5	**4** (5)	2	2	50	8	86
3	3	**4** (3)	1.2	2	50	8	87
4	1	**4** (1)	0.4	2	50	21	83
5	0.5	**4** (0.5)	0.2	2	50	24	80

[a] Yields are for pure, isolated compounds.

Table 5. Hydroamination of Various 1,3-Dienes with Carbamate **2d**





entry	diene	time (h)	product	yield[a] (%)
1	**1b**	18	**3bd**	94
2	**1c**	18	**3cd**	60
3	**1d**	18	**3dd**	77
4[b]	R = $(CH_2)_7CH_3$ **1e**	18	major : minor	73 (3:1)
5[b]	R = $(CH_2)_2Ph$ **1f**	18	major : minor	74 (3:1)
6[b]	**1g**	18	minor : major	76 (1:2)

[a] Yields are for pure, isolated compounds. [b] Isomer ratio was determined by NMR analysis.

The results obtained by 1,3-dienes **1c** (1,4-adduct alone), **1d** (1,2-adduct alone), and **1e**−**1g** (mixture of isomers) indicated that both 1,2-attack and 1,4-attack are possible depending on the substrate. To gain insight into the reaction mechanism, the reaction profiles were monitored with (A) **1a** and $Bi(OTf)_3$; (B) **1a** and $Cu(CH_3CN)_4PF_6$ **4**; (C) **1a**, $Bi(OTf)_3$, and **4**; (D) **1a**, $Bi(OTf)_3$, and amide **2f**; (E) **1a**, $Bi(OTf)_3$, **4**, and amide **2f**; and (F) **1a**, $Bi(OTf)_3$, KPF_6 **6**, and amide **2f**. Reaction conditions and profiles are summarized in Figures 1 and 2.[14] In Figure 1 without amide **2f**, the polymerization rate of **1a** was monitored. GC analysis of **1a** indicated that $Bi(OTf)_3$ alone (Figure 1, conditions A) promoted polymerization of the diene, while $Cu(CH_3CN)_4PF_6$ **4** alone did not cause any polymerization (Figure 1, conditions B). These results suggest that Bi activates diene **1a** to generate allyl cationic species. The polymerization rate in the absence of amide **2f** increased with $Bi(OTf)_3$ and $Cu(CH_3CN)_4PF_6$ **4** (conditions A vs C), indicating the formation of more active bismuth species. Figure 2 shows the reaction profile in the presence of amide **2f**. Concentration of **1a** was monitored by GC, and the desired product **3af** was isolated after 3 h to determine the ratio of polymerization:desired 1:1 addition.

(14) For detailed reaction conditions and results, see the Supporting Information.

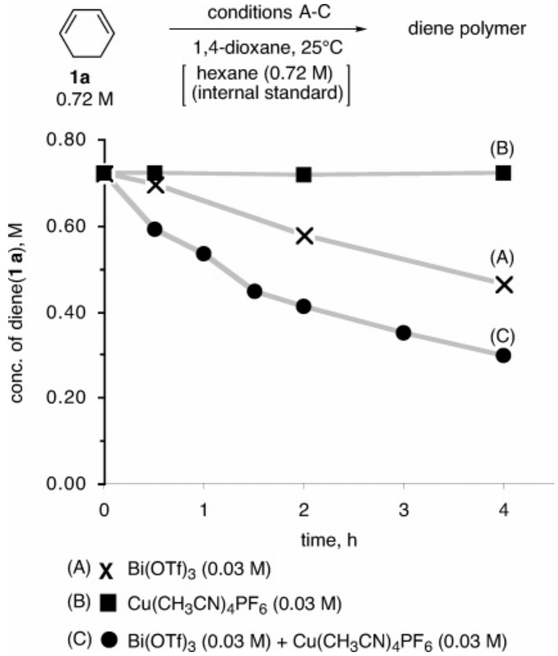


Figure 1. Reaction profile in the absence of amide **2f** using (A) $Bi(OTf)_3$, (B) $Cu(CH_3CN)_4PF_6$ **4**, and (C) $Bi(OTf)_3$ and $Cu(CH_3CN)_4PF_6$ **4**.

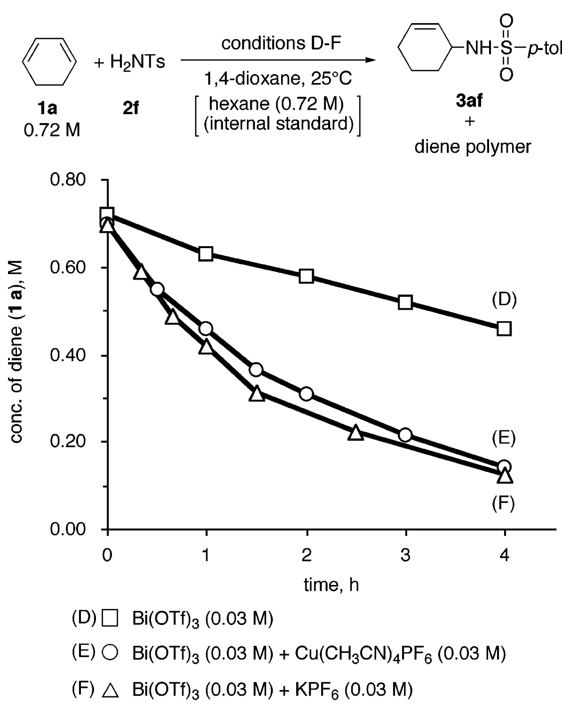
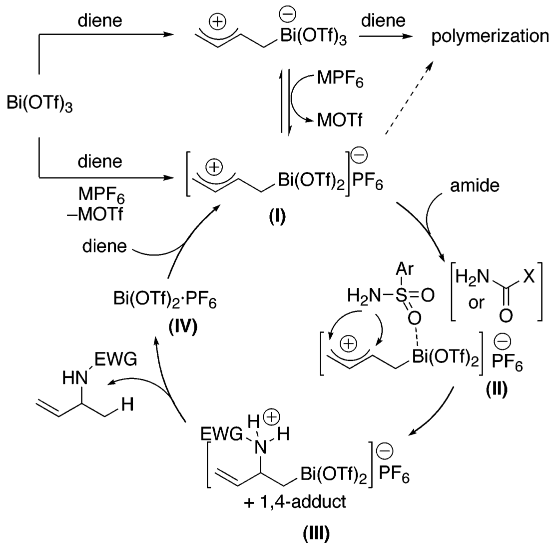


Figure 2. Reaction profile in the presence of amide **2f** using (D) $Bi(OTf)_3$, (E) $Bi(OTf)_3$ and $Cu(CH_3CN)_4PF_6$ **4**, and (F) $Bi(OTf)_3$ and KPF_6 **6**.

Under conditions D, the profile of [diene **1a**] was similar to that observed under conditions B. Under conditions D, 0.20 mmol of **1a** was consumed after 3 h, while only 0.108 mmol of the desired 1:1 adduct **3af** was isolated at 3 h. Thus, the desired 1:1 addition and undesired polymerization competed under conditions D. Under conditions E and F, the best reaction rate was observed among conditions A−F. Similar reaction rates in conditions E and F would suggest the generation of similar active species. Under conditions E, 0.50 mmol of **1a** was consumed after 3 h. 0.438 mmol (conditions E) and 0.498 mmol (conditions F) of the desired 1:1 adduct **3af** were isolated after

Scheme 1. Postulated Catalytic Cycle



3 h, suggesting that the desired reaction was the major pathway in conditions E and F. Thus, PF_6^- clearly accelerated the desired 1:1 addition over undesired polymerization. In conditions D, polymerization and the desired 1:1 addition competed with each other, while the desired reaction was the major pathway in conditions E and F.

The hypothetical mechanism is shown in Scheme 1. We assume that $Bi(OTf)_3$ activates diene to generate an allyl cationic species, which is trapped with amides (desired) or with diene (polymerization). Counteranion exchange with PF_6^- would then generate intermediate I. With PF_6^- as the counteranion, the coordination site of Bi would be available. Therefore, the amide can interact with the Bi center and be positioned close to the reaction site II, accelerating the desired 1:1 addition. Protonation of III regenerates catalyst IV. The ability of Bi metal to interact with the carbonyl group of benzamide **2j** was confirmed by IR and NMR analysis.[15] In IR analysis, the peak corresponding to the carbonyl of **2j** (1733 cm^{-1}) shifted to 1653 cm^{-1} in the presence of $Bi(OTf)_3$ (without adding diene), supporting the interaction of Bi with the carbonyl group of **2j**. ^{13}C NMR analysis also supported the interaction of Bi with **2j**. Low field shift of the carbonyl peak of **2j** in the presence of $Bi(OTf)_3$ was observed in ^{13}C NMR (with $Bi(OTf)_3$, 173.5 ppm vs without $Bi(OTf)_3$, 167.9 ppm).

In summary, we developed bismuth-catalyzed (0.5−10 mol %) intermolecular 1:1 hydroamination of 1,3-dienes with carbamates, sulfonamides, and carboxamides. The present system using a main group metal constitutes a new entry into the series of hydroamination catalyses. Further applications of the present catalysis including asymmetric variants are ongoing.

Acknowledgment. We are thankful for financial support through a Grant-in-Aid for Specially Promoted Research and a Grant-in-Aid for Encouragements for Young Scientists (B) (for S.M.) from JSPS and MEXT.

Supporting Information Available: Experimental procedures, characterization of the products, and detailed data for mechanistic studies. This material is available free of charge via the Internet at http://pubs.acs.org.

JA056112D

(15) For more detailed data of React IR analysis and ^{13}C NMR analysis of amide **2j** in the presence and absence of $Bi(OTf)_3$, see the Supporting Information.