

Brønsted Acid Catalyzed Asymmetric Hydroamination of Alkenes: Synthesis of Pyrrolidines Bearing a Tetrasubstituted Carbon Stereocenter**

Jin-Shun Lin, Peng Yu, Lin Huang, Pan Zhang, Bin Tan,* and Xin-Yuan Liu*

In memory of Carlos F. Barbas III

Abstract: The first highly enantioselective Brønsted acid catalyzed intramolecular hydroamination of alkenes enables the efficient construction of a series of chiral (spirocyclic) pyrrolidines with an α -tetrasubstituted carbon stereocenter with excellent functional group tolerance. A unique feature of this strategy is the use of a thiourea group acting as both the activating and the directing group through cooperative multiple hydrogen bonding with a Brønsted acid and the double bond. The utility of this method is highlighted by the facile construction of chiral synthetic intermediates and important structural motifs that are widely found in organic synthesis.

Chiral amines bearing an α -tetrasubstituted carbon stereocenter are important structural motifs in numerous biologically active compounds and potent pharmaceutical agents.^[1] Consequently, methods that enable their asymmetric construction are in great demand,^[1,2] as this process still remains a formidable synthetic challenge because of the difficulties associated with overcoming the steric hindrance and controlling the correct orientation of the four attached substituents. Recent years have witnessed a significant increase in the utilization of asymmetric intramolecular hydroamination reactions of alkenes as a highly valuable synthetic approach for the construction of chiral azaheterocycles with applications as biologically active compounds and powerful organocatalysts or ligands.^[3] Numerous elegant metal-catalyzed asymmetric intramolecular olefin hydroaminations have been developed that either proceed by olefin activation through coordination to increase the electrophilicity of the olefin or by N–H bond activation to increase the nucleophilicity of the amine.^[3,4] Despite these studies, a method with which the more challenging hydroamination products that

bear a chiral quaternary center can be obtained with high enantioselectivity has not been reported to date.^[5]

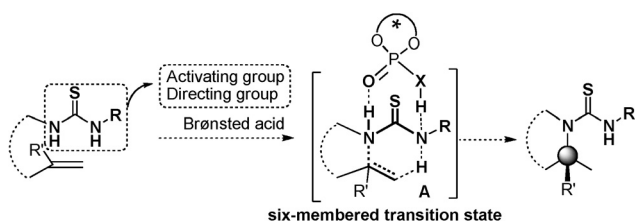
On the other hand, unlike the well-established metal-catalyzed counterparts, the organocatalytic hydroamination of alkenes still represents a formidable challenge.^[3d,6] The first enantioselective variant of this transformation, which involved the use of a chiral phosphoric acid as the catalyst, resulted in poor stereocontrol with up to 17 % *ee*.^[6a] However, only recently Toste et al. achieved a significant breakthrough by using a dithiophosphoric acid to enable the hydroamination of dienes and allenes. Their approach involved the transient covalent attachment of a chiral leaving group to the allylic system to obtain high enantioselectivities,^[3d,6b] which was supported by the finding that the presence of the sulfur atom in the catalyst was necessary because the oxygenated analogues of the dithiophosphoric acid were less efficient. Alternatively, Jacobsen and co-workers have developed asymmetric thiourea-catalyzed Cope-type alkene hydroamination reactions that proceed through dipolar transition states with multiple hydrogen bonding interactions.^[6c] Although these pioneering reports provide strong evidence that asymmetric hydroamination reactions can be performed with an organocatalyst by using rationally designed substrates or catalysts, they have also focused only on the construction of tertiary chiral centers. Therefore, the development of new strategies to achieve enantioselective organocatalytic alkene hydroaminations that yield products with chiral quaternary centers is still in high demand.^[3e]

To address these challenges and as part of our continuous efforts in hydroamination^[7] and Brønsted acid catalyzed transformations,^[8] we became interested in developing an asymmetric Brønsted acid catalyzed hydroamination of alkenes to obtain products with more challenging quaternary carbon stereocenters. Owing to the propensity of thioureas to simultaneously act as a nucleophile and a hydrogen-bond donor through their acidic N–H bonds,^[9] we envisioned that an intramolecular hydroamination of *N*-alkenyl thioureas could proceed via a six-membered transition state **A**,^[4] to achieve C–N and C–H bond formation in a concerted fashion (Scheme 1). We further anticipated that the key transition state **A**, which features Brønsted acidic (N–H) and Brønsted basic (N) sites, might in turn offer new opportunities for an asymmetric variant by activation with Brønsted acids^[10] through cooperative multiple hydrogen bonding to achieve stereoinduction. Such transformations should thus yield the desired enantioenriched pyrrolidines with an α -tetrasubsti-

[*] Dr. J.-S. Lin, P. Yu, L. Huang, P. Zhang, Prof. Dr. B. Tan, Prof. Dr. X.-Y. Liu
Department of Chemistry
South University of Science and Technology of China
Shenzhen, 518055 (P. R. China)
E-mail: tanb@sustc.edu.cn
liuxy3@sustc.edu.cn

[**] Financial support from the National Natural Science Foundation of China (21302088, 21302087) is greatly appreciated. We are grateful to the reviewers for their insightful comments on the mechanistic discussion.

Supporting information for this article is available on the WWW under <http://dx.doi.org/10.1002/anie.201501762>.



Scheme 1. Strategy for the first Brønsted acid catalyzed hydroamination of alkenes to construct a quaternary chiral center.

tuted carbon stereocenter, which are intensively investigated structures that are in high demand in the pharmaceutical and agricultural industries.^[1,2] To the best of our knowledge, such an activation mode has never been described for catalytic asymmetric intramolecular alkene hydroamination reactions. Herein, we disclose the first asymmetric alkene hydroamination that involves a thiourea group as both the activating and directing group and is catalyzed by Brønsted acids under mild reaction conditions (Scheme 1).

To validate the feasibility of our proposed transformation, we initially investigated the reaction of *N*-alkenyl thiourea **1a** with 9-anthryl-SPINOL-derived chiral phosphoric acid (CPA)^[11] **A1**. To our delight, the reaction proceeded slowly to provide pyrrolidine **2a** in 21% yield with 52% *ee* after stirring at room temperature for four days (Table 1, entry 1). To improve the reactivity and stereoselectivity, we turned our attention to the more acidic *N*-triflyl phosphoramides **B1** and **B2** (entries 2 and 3), which were first reported by Yamamoto and Nakashima.^[12] As expected, in the presence of either of these catalysts, the reaction was remarkably accelerated to provide **2a** in nearly quantitative yield with up to 87% *ee*. We next resorted to Brønsted acids **A2–A4**, which feature a spirocyclic backbone^[13] (entries 4–6). Among the catalysts screened, (*R*)-SPINOL-derived **A2** gave both a good yield of 95% and an excellent enantioselectivity of 94% *ee* (entry 4). Further solvent screening indicated that the solvent had a significant influence on the enantioselectivity (entries 4 and 7–10), and dichloromethane was identified as the best choice (entry 4). Lowering the catalyst loading to 10 mol% affected the chemical yield, but did not lead to a decrease in enantioselectivity (entry 11). Further investigations revealed that the reaction reached completion within 36 hours to give the desired product in 96% yield and 94% *ee* (entry 12).

We next set out to explore the substrate scope of this hydroamination reaction (Table 2). The positions and electronic properties of substituents on the aromatic rings have a very limited effect on the stereoselectivity of the process. For example, substrates **1** bearing electron-withdrawing ($R' = \text{CF}_3$, F, Cl, Br, CN) or electron-donating groups ($R' = \text{OMe}$) at different positions (*para* or *meta*) of the aryl ring reacted efficiently to afford the corresponding products **2a–2i** in 63–95% yield with 85–96% *ee* (entries 1–9). Furthermore, replacing the dimethyl tethers (**1a**) with other groups, such as the cyclohexanyl (**1j**) or cyclopentanyl variants (**1k**), had no significant influence on the reaction, and the spirocyclic pyrrolidines **2j** and **2k** were efficiently obtained (entries 10 and 11).

Table 1: Optimization of the reaction conditions.^[a]

Entry	Catalyst	Solvent	Yield ^[b] [%]	<i>ee</i> ^[c] [%]
1 ^[d]	A1	CH_2Cl_2	21	52
2	B1	CH_2Cl_2	98	–87
3	B2	CH_2Cl_2	97	–80
4	A2	CH_2Cl_2	95	94
5	A3	CH_2Cl_2	60	92
6	A4	CH_2Cl_2	87	80
7	A2	toluene	33	80
8	A2	DCE	70	95
9	A2	CHCl_3	86	91
10	A2	CH_3CN	44	85
11 ^[e]	A2	CH_2Cl_2	68	94
12 ^[f]	A2	CH_2Cl_2	96	94

[a] Reactions were run on a 0.05 mmol scale at 0 °C for four days.

[b] Determined by ^1H NMR spectroscopy of the crude reaction mixture.

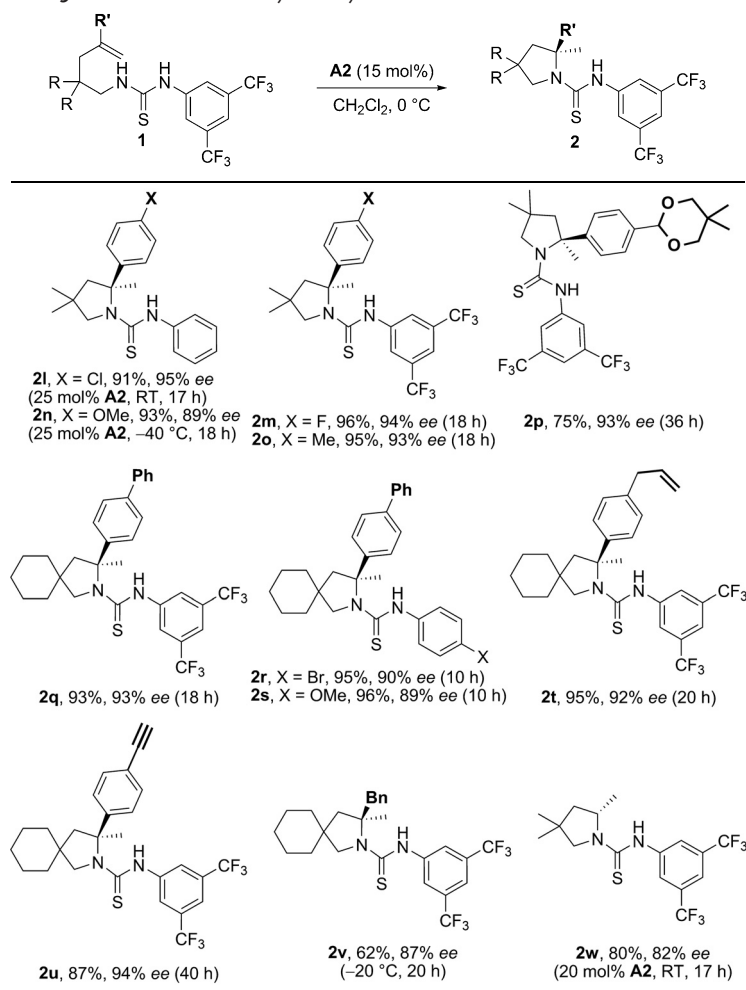
[c] Determined by HPLC analysis on a chiral stationary phase. [d] At room temperature. [e] The catalyst loading was 10 mol%. [f] The reaction was run at 0 °C for 36 hours. DCE = 1,2-dichloroethane.

Table 2: Variation of the thiourea group and tether.^[a]

Entry	R'	R	2	<i>t</i> [h]	Yield ^[b] [%]	<i>ee</i> ^[c] [%]
1	3,5-(CF_3) $_2\text{C}_6\text{H}_3$	Me	2a	36	95	94
2	4- $\text{CF}_3\text{C}_6\text{H}_4$	Me	2b	48	84	88
3	3- $\text{CF}_3\text{C}_6\text{H}_4$	Me	2c	40	82	96
4	4- ClC_6H_4	Me	2d	48	75	92
5	4- BrC_6H_4	Me	2e	40	84	89
6	4- FC_6H_4	Me	2f	48	86	89
7	3- FC_6H_4	Me	2g	48	73	89
8	4- CNC_6H_4	Me	2h	36	63	85
9	4- MeOC_6H_4	Me	2i	48	64	91
10	3,5-(CF_3) $_2\text{C}_6\text{H}_3$	-(CH_2) $_5$ -	2j	36	98	93
11	3,5-(CF_3) $_2\text{C}_6\text{H}_3$	-(CH_2) $_4$ -	2k	18	94	94

[a] All of the reactions were conducted on 0.1 mmol scale. [b] Yield of isolated product based on **1**. [c] Determined by HPLC analysis on a chiral stationary phase.

Next, we expanded the substrate scope with a variety of *gem*-disubstituted alkenes (Table 3). Aryl rings with different electronic properties were well tolerated, giving the corresponding products **2l–2s** in high yields (75–96%) and enantioselectivities (89–95% *ee*). To our surprise, the acetal

Table 3: Variation of the alkenyl moiety.^[a]


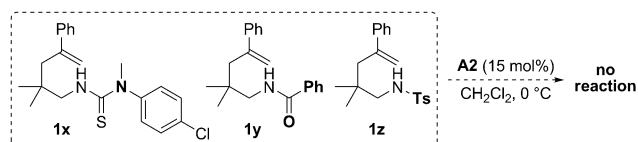
[a] All of the reactions were conducted on 0.1 mmol scale. Yield of isolated product based on **1**. The ee values were determined by HPLC analysis on a chiral stationary phase.

group, which is very sensitive to acids, did not affect the catalytic activity, and **2p** was still obtained in good yield and enantioselectivity. Notably, substrates containing another reactive terminal double or triple bond also afforded the desired products in excellent yield and stereocontrol with the additional double or triple bond remaining intact (**2t** and **2u**). Most importantly, substrates with benzyl-substituted or terminal alkenes, as exemplified by **1v** and **1w**, were also suitable for this reaction, and the corresponding products were isolated in 62 and 80 % yield and 87 and 82 % ee (**2v** and **2w**), respectively.

Our findings, together with the generally proposed dual activation model for phosphoric acid catalysts,^[10] suggest that the thiourea group might play an important role in activating the double bond in a six-membered transition state while simultaneously interacting with the Brønsted acid via multiple hydrogen bonding (Scheme 1). The cooperative binding of the thiourea group to the catalyst and the double bond is believed to create a steric environment that determines the relative orientation of the approaching substrate for C–N bond formation, thus inducing stereoselectivity (see the

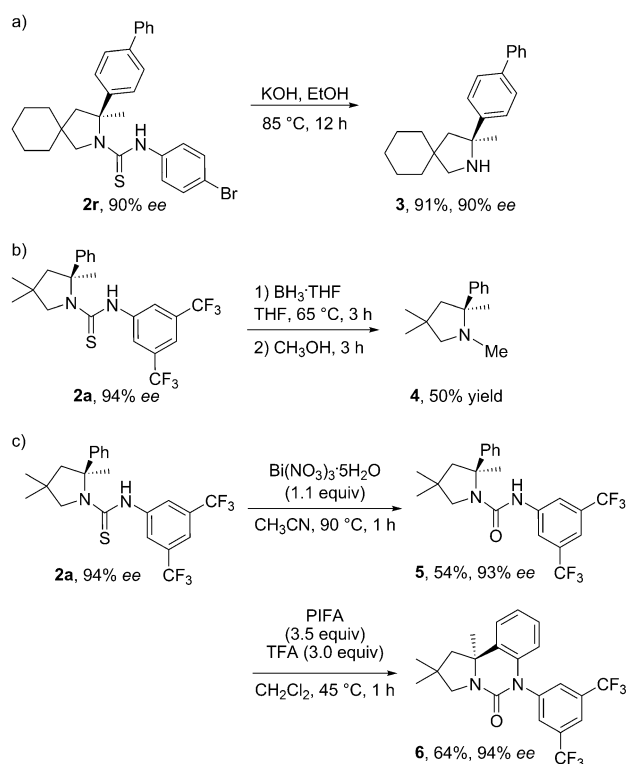
Supporting Information, Scheme S1a,b for the proposed transition states).^[4j,13,14] The absolute configuration of **2q** was determined to be *S* by X-ray crystallographic analysis (Figure S1),^[15] which is in accordance with the configuration predicted based on Simon and Goodman's model.^[14] Furthermore, the lack of reactivity observed with methyl-protected thiourea derivative **1x**, benzoyl amide **1y**, and tosyl amide **1z** (Scheme 2 and Scheme S2) clearly indicates that the thiourea plays a crucial role in determining the asymmetric induction: Both acidic N–H bonds are thus involved in cooperative hydrogen bonding interactions with the catalyst and the double bond.^[16]

To demonstrate the synthetic utility of our method, the thiourea group of the resulting chiral pyrrolidine product **2r** was readily removed to provide secondary amine **3** in 91 % yield without affecting the enantiopurity (Scheme 3a). Furthermore, the selective reduction of **2a** with $\text{BH}_3\cdot\text{THF}$ successfully afforded the desired tertiary amine **4** in 50 % yield (Scheme 3b). The obtained chiral compounds have been suggested to have potential applications as effective chiral organocatalysts^[17] and could be further converted into other alkaloid analogues of potential medicinal importance.^[2] Notably, our procedure is also applicable to the synthesis of a novel type of nitrogen-containing tricyclic molecular structure bearing an α -tetrasubstituted carbon stereocenter, which is an important structural motif in many biologically active natural alkaloids, such as hinckdentine A.^[18] Therefore, treatment of **2a** with excess $\text{Bi}(\text{NO}_3)_3\cdot(5\text{H}_2\text{O})$ yielded the desired urea **5**,^[19] which was smoothly oxidized with [bis(trifluoroacetoxy)iodo]benzene


Scheme 2. Mechanistic studies.

(PIFA) into tricyclic amine **6** in 64 % yield without a decrease in the ee value (Scheme 3c).^[20]

In conclusion, we have developed the first highly enantioselective Brønsted acid catalyzed hydroamination of alkenes that provides access to a variety of pyrrolidine derivatives with an α -tetrasubstituted carbon stereocenter with good to excellent yields and enantioselectivities under mild reaction conditions. A thiourea group that acts as both the activating and directing group is crucial for the hydroamination to proceed with high levels of stereoinduction by cooperative multiple hydrogen bonding with the Brønsted acid and the double bond. Notably, this strategy tolerates a variety of reactive alkenyl and alkynyl moieties and sensitive acetal groups and enables the construction of



Scheme 3. Transformations of compounds **2a** and **2r**.

quaternary stereogenic centers; it thus constitutes a complementary approach to conventional metal- or organocatalyzed asymmetric hydroamination methods.^[3–6] Furthermore, this transformation enables the efficient construction of spirocyclic pyrrolidines and tricyclic amines. Further studies to expand the scope of this process and to develop more challenging intermolecular alkene hydroamination reactions^[21] are ongoing in our laboratory.

Keywords: alkenes · asymmetric catalysis · Brønsted acid catalysis · hydroamination · pyrrolidines

How to cite: *Angew. Chem. Int. Ed.* **2015**, *54*, 7847–7851
Angew. Chem. **2015**, *127*, 7958–7962

[1] M. Shibasaki, M. Kanai, *Chem. Rev.* **2008**, *108*, 2853.

[2] For selected recent examples, see: a) N. S. Sheikh, D. Leonori, G. Barker, J. D. Firth, K. R. Campos, A. J. H. M. Meijer, P. O'Brien, I. Coldham, *J. Am. Chem. Soc.* **2012**, *134*, 5300; b) G. Yang, C. Shen, W. Zhang, *Angew. Chem. Int. Ed.* **2012**, *51*, 9141; *Angew. Chem.* **2012**, *124*, 9275; c) H. Wang, T. Jiang, M.-H. Xu, *J. Am. Chem. Soc.* **2013**, *135*, 971.

[3] For leading reviews on asymmetric hydroamination, see: a) P. W. Roesky, T. E. Müller, *Angew. Chem. Int. Ed.* **2003**, *42*, 2708; *Angew. Chem.* **2003**, *115*, 2812; b) T. E. Müller, K. C. Hultsch, M. Yus, F. Foubelo, M. Tada, *Chem. Rev.* **2008**, *108*, 3795; c) S. R. Chemler, *Org. Biomol. Chem.* **2009**, *7*, 3009; d) I. Dion, A. M. Beauchemin, *Angew. Chem. Int. Ed.* **2011**, *50*, 8233; *Angew. Chem.* **2011**, *123*, 8383; e) J. Hannedouche, E. Schulz, *Chem. Eur. J.* **2013**, *19*, 4972; for selected reviews on gold-catalyzed asymmetric hydroamination, see: f) R. A. Widenhoefer, *Chem.*

Eur. J. **2008**, *14*, 5382; g) Y.-M. Wang, A. D. Lackner, F. D. Toste, *Acc. Chem. Res.* **2014**, *47*, 889.

[4] For selected examples, see: a) M. A. Giardello, V. P. Conticello, L. Brard, M. R. Gagne, T. J. Marks, *J. Am. Chem. Soc.* **1994**, *116*, 10241; b) S. Hong, S. Tian, M. V. Metz, T. J. Marks, *J. Am. Chem. Soc.* **2003**, *125*, 14768; c) D. V. Gribkov, K. C. Hultsch, F. Hampel, *J. Am. Chem. Soc.* **2006**, *128*, 3748; d) M. C. Wood, D. C. Leitch, C. S. Yeung, J. A. Kozak, L. L. Schafer, *Angew. Chem. Int. Ed.* **2007**, *46*, 354; *Angew. Chem.* **2007**, *119*, 358; e) Z. Zhang, C. F. Bender, R. A. Widenhoefer, *J. Am. Chem. Soc.* **2007**, *129*, 14148; f) R. L. LaLonde, B. D. Sherry, E. J. Kang, F. D. Toste, *J. Am. Chem. Soc.* **2007**, *129*, 2452; g) G. L. Hamilton, E. J. Kang, M. Mba, F. D. Toste, *Science* **2007**, *317*, 496; h) X. Shen, S. L. Buchwald, *Angew. Chem. Int. Ed.* **2010**, *49*, 564; *Angew. Chem.* **2010**, *122*, 574; i) O. Kanno, W. Kuriyama, Z. J. Wang, F. D. Toste, *Angew. Chem. Int. Ed.* **2011**, *50*, 9919; *Angew. Chem.* **2011**, *123*, 10093; j) K. Manna, S. Xu, A. D. Sadow, *Angew. Chem. Int. Ed.* **2011**, *50*, 1865; *Angew. Chem.* **2011**, *123*, 1905; k) X. Zhang, T. J. Emge, K. C. Hultsch, *Angew. Chem. Int. Ed.* **2012**, *51*, 394; *Angew. Chem.* **2012**, *124*, 406; l) S. Zhu, N. Niljianskul, S. L. Buchwald, *J. Am. Chem. Soc.* **2013**, *135*, 15746; m) N. Matsuda, K. Hirano, T. Satoh, M. Miura, *J. Am. Chem. Soc.* **2013**, *135*, 4934; n) K. Manna, N. Eedugurala, A. D. Sadow, *J. Am. Chem. Soc.* **2015**, *137*, 425; o) S.-L. Shi, S. L. Buchwald, *Nat. Chem.* **2015**, *7*, 28.

[5] For the first report of an enantioselective formation of a quaternary center (55% ee) in a metal-catalyzed hydroamination reaction, see: Y. Chapurina, H. Ibrahim, R. Guillot, E. Kolodziej, J. Collin, A. Trifonov, E. J. Schulz, J. Hannedouche, *J. Org. Chem.* **2011**, *76*, 10163.

[6] a) L. Ackermann, A. Althammer, *Synlett* **2008**, 995; b) N. D. Shapiro, V. Rauniyar, G. L. Hamilton, J. Wu, F. D. Toste, *Nature* **2011**, *470*, 245; c) A. R. Brown, C. Uyeda, C. A. Brotherton, E. N. Jacobsen, *J. Am. Chem. Soc.* **2013**, *135*, 6747; for an elegant organocatalytic tether-based approach to achieve formal asymmetric intramolecular hydroamination, see: d) M. J. MacDonald, D. J. Schipper, P. J. Ng, J. Moran, A. M. Beauchemin, *J. Am. Chem. Soc.* **2011**, *133*, 20100; e) N. Guimond, M. J. MacDonald, V. Lemieux, A. M. Beauchemin, *J. Am. Chem. Soc.* **2012**, *134*, 16571; f) M. J. MacDonald, C. R. Hesp, D. J. Schipper, M. Pesant, A. M. Beauchemin, *Chem. Eur. J.* **2013**, *19*, 2597.

[7] a) X.-Y. Liu, C.-H. Li, C.-M. Che, *Org. Lett.* **2006**, *8*, 2707; b) X.-Y. Liu, P. Ding, J.-S. Huang, C.-M. Che, *Org. Lett.* **2007**, *9*, 2645; c) X.-Y. Liu, C.-M. Che, *Angew. Chem. Int. Ed.* **2008**, *47*, 3805; *Angew. Chem.* **2008**, *120*, 3865; d) X.-Y. Liu, C.-M. Che, *Angew. Chem. Int. Ed.* **2009**, *48*, 2367; *Angew. Chem.* **2009**, *121*, 2403; e) J.-S. Lin, Y.-P. Xiong, C.-L. Ma, L.-J. Zhao, B. Tan, X.-Y. Liu, *Chem. Eur. J.* **2014**, *20*, 1332; f) J.-S. Lin, X.-G. Liu, X.-L. Zhu, B. Tan, X.-Y. Liu, *J. Org. Chem.* **2014**, *79*, 7084.

[8] a) D.-J. Cheng, L. Yan, S.-K. Tian, M.-Y. Wu, L.-X. Wang, Z.-L. Fan, S.-C. Zheng, X.-Y. Liu, B. Tan, *Angew. Chem. Int. Ed.* **2014**, *53*, 3684; *Angew. Chem.* **2014**, *126*, 3758; b) P. Yu, J.-S. Lin, L. Li, S.-C. Zheng, Y.-P. Xiong, L.-J. Zhao, B. Tan, X.-Y. Liu, *Angew. Chem. Int. Ed.* **2014**, *53*, 11890; *Angew. Chem.* **2014**, *126*, 12084.

[9] For selected reviews, see: a) E. N. Jacobsen, A. G. Doyle, *Chem. Rev.* **2007**, *107*, 5713; b) Z. Zhang, P. R. Schreiner, *Chem. Soc. Rev.* **2009**, *38*, 1187.

[10] For comprehensive reviews on asymmetric Brønsted acid catalysis, see: a) T. Akiyama, *Chem. Rev.* **2007**, *107*, 5744; b) S.-L. You, Q. Cai, M. Zeng, *Chem. Soc. Rev.* **2009**, *38*, 2190; c) D. Kampen, C. M. Reisinger, B. List, *Top. Curr. Chem.* **2010**, *291*, 395; d) M. Terada, *Synthesis* **2010**, 1929; e) J. Wu, F. Shi, L.-Z. Gong, *Acc. Chem. Res.* **2011**, *44*, 1156; f) M. Terada, *Curr. Org. Chem.* **2011**, *15*, 2227; g) M. Rueping, A. Kuenkel, I. Atodiresei, *Chem. Soc. Rev.* **2011**, *40*, 4539; h) M. Mahlau, B. List, *Angew. Chem. Int. Ed.* **2013**, *52*, 518; *Angew. Chem.* **2013**, *125*, 540; i) R. J. Phipps, G. L. Hamilton, F. D. Toste, *Nat. Chem.*

- 2012**, *4*, 603; j) D. Parmar, E. Sugiono, S. Raja, M. Rueping, *Chem. Rev.* **2014**, *114*, 9047.
- [11] For pioneering work on the use of chiral phosphoric acids as Brønsted acid catalysts, see: a) T. Akiyama, J. Itoh, K. Yokota, K. Fuchibe, *Angew. Chem. Int. Ed.* **2004**, *43*, 1566; *Angew. Chem.* **2004**, *116*, 1592; b) D. Uraguchi, M. Terada, *J. Am. Chem. Soc.* **2004**, *126*, 5356; for selected recent examples, see: c) K. Saito, Y. Shibata, M. Yamanaka, T. Akiyama, *J. Am. Chem. Soc.* **2013**, *135*, 11740; d) K. Kaupmees, N. Tolstoluzhsky, S. Raja, M. Rueping, I. Leito, *Angew. Chem. Int. Ed.* **2013**, *52*, 11569; *Angew. Chem.* **2013**, *125*, 11783; e) M. R. Monaco, B. Poladura, M. Diaz de Los Bernardos, M. Leutzsch, R. Goddard, B. List, *Angew. Chem. Int. Ed.* **2014**, *53*, 7063; *Angew. Chem.* **2014**, *126*, 7183; f) M. R. Monaco, S. Prevost, B. List, *J. Am. Chem. Soc.* **2014**, *136*, 16982; g) W. Zi, Y.-M. Wang, F. D. Toste, *J. Am. Chem. Soc.* **2014**, *136*, 12864; h) T. Yamanaka, A. Kondoh, M. Terada, *J. Am. Chem. Soc.* **2015**, *137*, 1048; i) S.-G. Wang, Q. Yin, C.-X. Zhuo, S.-L. You, *Angew. Chem. Int. Ed.* **2015**, *54*, 647; *Angew. Chem.* **2015**, *127*, 657; j) H. Qian, W. Zhao, Z. Wang, J. Sun, *J. Am. Chem. Soc.* **2015**, *137*, 560.
- [12] For the first report of chiral BINOL-based *N*-triflyl phosphoramidate catalysts, see: D. Nakashima, H. Yamamoto, *J. Am. Chem. Soc.* **2006**, *128*, 9626.
- [13] For the first report of this kind of SPINOL-based *N*-triflyl phosphoramidate catalyst, see: X. Hong, H. B. Küçük, M. S. Maji, Y.-F. Yang, M. Rueping, K. N. Houk, *J. Am. Chem. Soc.* **2014**, *136*, 13769.
- [14] L. Simon, J. M. Goodman, *J. Org. Chem.* **2011**, *76*, 1775.
- [15] CCDC 1050965 (**2q**) contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.
- [16] However, an alternative mechanism, which proceeds by protonation of the alkene by the Brønsted acid and subsequent nucleophilic attack of the thiourea to the protonated alkene, cannot be ruled out at the present stage. Therefore, rigorous investigations will be necessary to unambiguously elucidate the exact mechanism; see: K. Motokura, N. Nakagiri, K. Mori, T. Mizugaki, K. Ebitani, K. Jitsukawa, K. Kaneda, *Org. Lett.* **2006**, *8*, 4617.
- [17] For selected reviews on chiral secondary amine catalysts, see: a) S. Mukherjee, J. W. Yang, S. Hoffmann, B. List, *Chem. Rev.* **2007**, *107*, 5471; b) K. L. Jensen, G. Dickmeiss, H. Jiang, L. Albrecht, K. A. Jørgensen, *Acc. Chem. Res.* **2012**, *45*, 248.
- [18] K. Higuchi, Y. Sato, M. Tsuchimochi, K. Sugiura, M. Hatori, T. Kawasaki, *Org. Lett.* **2009**, *11*, 197.
- [19] I. Mohammadpoor-Baltork, M. M. Khodaei, K. Nikoofar, *Tetrahedron Lett.* **2003**, *44*, 591.
- [20] K. Inoue, Y. Ishikawa, S. Nishiyama, *Org. Lett.* **2010**, *12*, 436.
- [21] For a recent highlight on asymmetric intermolecular hydroamination, see: K. D. Hesp, *Angew. Chem. Int. Ed.* **2014**, *53*, 2034; *Angew. Chem.* **2014**, *126*, 2064.

Received: February 24, 2015

Published online: May 26, 2015