ChemPubSoc Europe

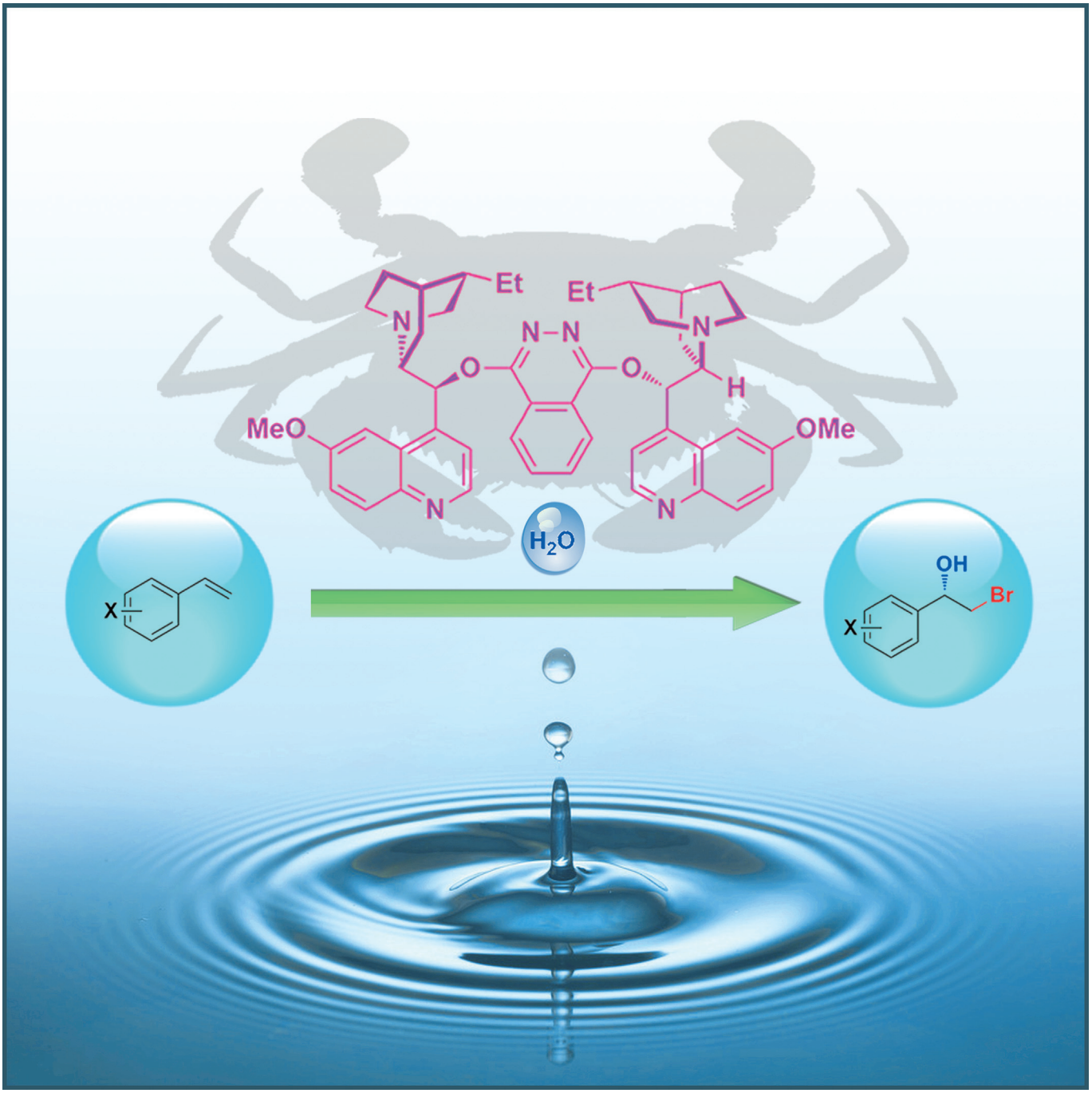
DOI: 10.1002/chem.201502133

CHEMISTRY
A European Journal
Communication

Synthetic Methods

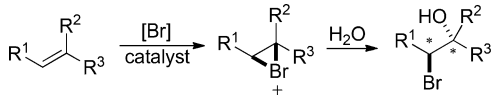
Catalytic Asymmetric Bromination of Unfunctionalized Olefins with H_2O as a Nucleophile

Xun Zhang,[a] Jing Li,[a] Hua Tian,[a] and Yian Shi*[a, b, c]



Abstract: The dimeric cinchona alkaloid $(DHQD)_2PHAL$ is used to catalyze an effective asymmetric bromohydroxylation of unfunctionalized olefins with H_2O as nucleophile an *N*-bromobenzamide as a bromine source. A variety of optically active bromohydrins are formed with up to 88% *ee*.

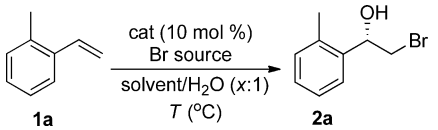
Electrophilic halogenation of olefins is among the most important transformations in organic chemistry and allows simultaneous installation of two C–X bonds by stereoselective ring-opening of a halonium ion intermediate with a nucleophile. Although asymmetric halogenation had proven to be highly challenging, significant progress has been made in recent years.[1–3] For the intermolecular process,[4] great success has been achieved with olefin substrates containing various functional groups.[5–11] However, for unfunctionalized olefins, asymmetric halogenation presents new challenges, owing to the lack of directing groups, and only limited examples have been reported, primarily with carboxylic acids as nucleophiles.[9,12,13] The formation of halohydrins via halonium ion intermediates with H_2O is a classic reaction for halogenation of olefins (Scheme 1) and has great synthetic value. An asymmetric version of this process would thus be highly desirable and has yet to be reported.[8] Herein, we report our preliminary efforts on this subject.



Scheme 1. Asymmetric intermolecular bromohydroxylation.

Several acid and base catalysts were initially investigated for bromohydroxylation with 2-methylstyrene (**1a**) as a test substrate and *N*-bromobenzamide as bromine source in an acetone/H_2O solvent mixture at −30 °C to give bromohydrin **2a** (Figure 1). In the absence of catalyst, a trace amount of bromination product **2a** was formed (Table 1, entry 1). When chiral phosphoric acid **3a** (Table 1, entry 2) or chiral phosphine–$Sc(OTf)_3$ complex **3b** (Table 1, entry 3) were used as catalysts, bromohydrin **2a** was obtained as a racemate in 39% and 82% yield, respectively, indicating that these catalysts were able to promote the reaction but not enantioselectively. Although good yields of **2a** were obtained in all cases with chiral bases examined, the enantioselectivities varied dramatically with the catalyst structures (Table 1, entries 4–8). To our delight, with dimeric cinchona alkaloid $(DHQD)_2PHAL$ (**3d**) as catalyst **2a** was obtained with 78% *ee* (Table 1, entry 5). Other reaction conditions, including bromine sources, solvents, and reaction temperatures, were thus investigated with **3d** as the catalyst. Among the different bromine sources examined (Table 1, entries 5, 9–13), *N*-bromobenzamide gave the highest enantioselectivity for the reaction (Table 1, entry 5). Several solvent systems were also investigated (Table 1, entries 5, 14–18). A combination of acetone and H_2O worked the best. Increasing the ratio of acetone to H_2O led to slightly higher *ee* values but lower yields (Table 1, entries 5, 19–21). The *ee* was slightly increased by lowering the reaction temperature (Table 1, entries 5, 22, and 23). The reaction with $(DHQD)_2PHAL$ (**3d**) as catalyst and *N*-bromobenzamide as bromine source in 5:1 acetone/H_2O at −40 °C appeared to be optimal in terms of the overall results of the yield and enantioselectivity (Table 1,

Table 1. Studies on the reaction conditions.[a]



1a 2a

Entry	Cat.	Br source	Solvent system (ratio)	Yield [%][b]	*ee* [%][c]
1	–	PhCONHBr	acetone/H_2O (5:1)	trace	–
2	**3a**	PhCONHBr	acetone/H_2O (5:1)	39	0
3	**3b**	PhCONHBr	acetone/H_2O (5:1)	82	0
4	**3c**	PhCONHBr	acetone/H_2O (5:1)	73	0
5	**3d**	PhCONHBr	acetone/H_2O (5:1)	87	78
6	**3e**	PhCONHBr	acetone/H_2O (5:1)	83	7
7	**3f**	PhCONHBr	acetone/H_2O (5:1)	65	−9
8	**3g**	PhCONHBr	acetone/H_2O (5:1)	73	−46
9	**3d**	NBS	acetone/H_2O (5:1)	93	58
10	**3d**	NBP	acetone/H_2O (5:1)	93	36
11	**3d**	TBCO	acetone/H_2O (5:1)	69	0
12	**3d**	DBDMH	acetone/H_2O (5:1)	91	16
13	**3d**	MeCONHBr	acetone/H_2O (5:1)	72	63
14	**3d**	PhCONHBr	MeCN/H_2O (5:1)	87	65
15	**3d**	PhCONHBr	THF/H_2O (5:1)	15	25
16	**3d**	PhCONHBr	DME/H_2O (5:1)	59	0
17	**3d**	PhCONHBr	DCM/H_2O (5:1)	29	76
18	**3d**	PhCONHBr	EtOAc/H_2O (5:1)	19	60
19	**3d**	PhCONHBr	acetone/H_2O (2:1)	99	74
20	**3d**	PhCONHBr	acetone/H_2O (10:1)	85	78
21	**3d**	PhCONHBr	acetone/H_2O (20:1)	56	80
22[d]	**3d**	PhCONHBr	acetone/H_2O (5:1)	76	83
23[e]	**3d**	PhCONHBr	acetone/H_2O (5:1)	57	84

[a] Reactions were carried out with substrate **1a** (0.30 mmol), catalyst (0.030 mmol), and Br source (0.36 mmol) in solvent/H_2O *x*:1 solvent mixture (3.0 mL + $\frac{3.0}{x}$ mL) at −30 °C for 48 h, unless otherwise noted. [b] Yield of isolated product. [c] Determined by chiral HPLC analysis. [d] At −40 °C for 72 h. [e] At −50 °C for 144 h.

[a] *Dr. X. Zhang, Dr. J. Li, H. Tian, Prof. Dr. Y. Shi*
Beijing National Laboratory for Molecular Sciences
CAS Key Laboratory of Molecular Recognition and Function
Institute of Chemistry, Chinese Academy of Sciences
Beijing, 10090 (P. R. China)

[b] *Prof. Dr. Y. Shi*
State Key Laboratory of Coordination Chemistry
Center for Multimolecular Organic Chemistry
School of Chemistry and Chemical Engineering
Nanjing University, Nanjing, 210093 (P. R. China)

[c] *Prof. Dr. Y. Shi*
Department of Chemistry, Colorado State University
Fort Collins, Colorado, 80523 (USA)
E-mail: Yian.Shi@colostate.edu

Supporting information for this article is available on the WWW under http://dx.doi.org/10.1002/chem.201502133.

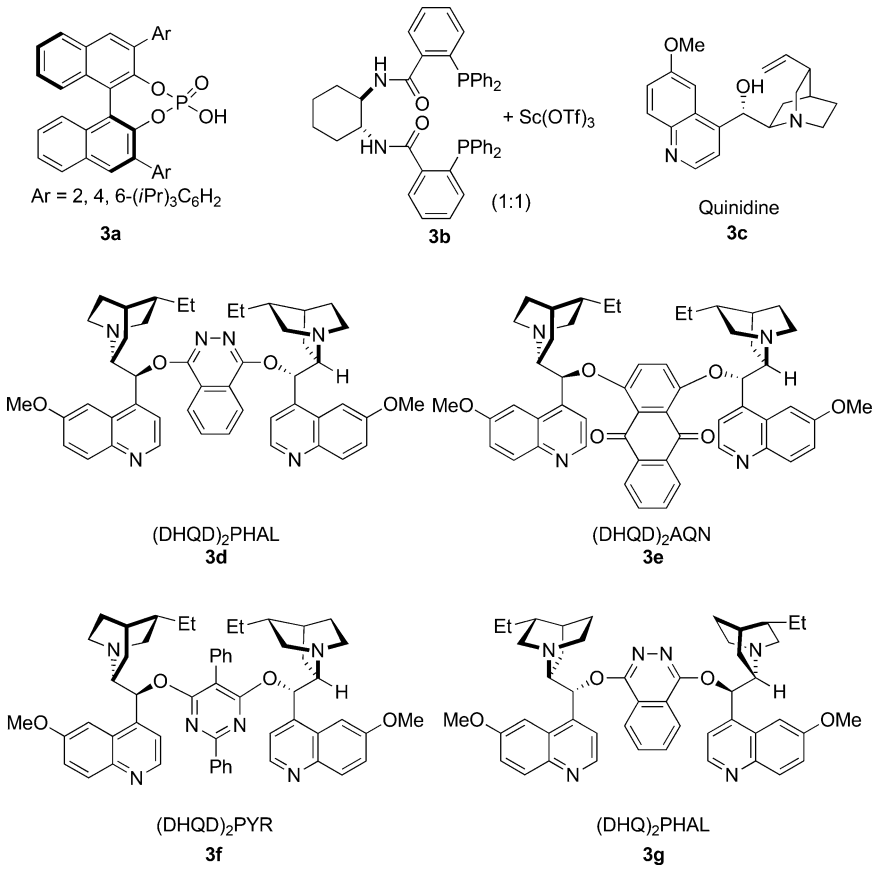


Figure 1. Structures of catalysts examined.

entry 22). Under these reaction conditions, the *ee* did not vary over time.

With the optimized reaction conditions in hand, the substrate scope was subsequently investigated for the bromohydroxylation. The reaction can be extended to a variety of substituted styrenes, giving the corresponding bromohydrins in 52–94% yield with 60–83% *ee* (Table 2, entries 1–10; the X-ray structure of **2j** is shown in Figure 2). In comparison to styrene (Table 2, entry 2), substituents were found to be generally beneficial to the enantioselectivity. The extent of the increase in *ee* depended on the nature of the substituents and their positions relative to the reacting double bond. When vinylnaphthalenes were subjected to the reaction conditions, the resulting bromohydrins were obtained in 75–82% yield with 70–72% *ee* (Table 2, entries 11 and 12). α-Substituted styrenes were also found to be suitable substrates for the reaction. This class of compounds displayed higher reactivity than styrenes, which allowed the reaction to be carried out at lower temperature. The corresponding bromohydrins were obtained in 66–77% yield and 55–82% *ee* at −50 °C (Table 2, entries 13–15). The *ee* was increased to 88% for 4-chloro-α-methylstyrene when the reaction temperature was lowered to −60 °C, although the yield of product **2o** was decreased to 40% (Table 2, entry 16). The reaction was also extended to 1,2-dihydronaphthalenes, giving the bromohydrins in 73–83% yield and 68–75% *ee* (Table 2, entries 17 and 18). *trans*-β-Methylstyrene and 1-phenylcyclohexene were found to be less effective substrates. The corresponding bromohydrins were formed in 39% *ee* and 36% *ee*, respectively (Table 2, entries 19 and 20). No enantioselectivity was obtained for bromohydroxylation of cyclohexene (Table 2, entry 21). However, for all other substrates (Table 2, entries 1–20), the reaction proceeded regioselectively and the other regioisomer was not isolated. The absolute configurations of bromohydrins **2b**, **2f**, **2k**, **2m**, and **2p** were determined by comparing the optical rotations with reported values.[14] In all cases, the major enantiomer was found to have the (*S*)-configuration.

Based on the absolute configuration determined, a plausible transition state model is proposed in Figure 3.[3h,at,bc,6a,9,13] The substrate is situated in the chiral pocket, owing to via π,π-

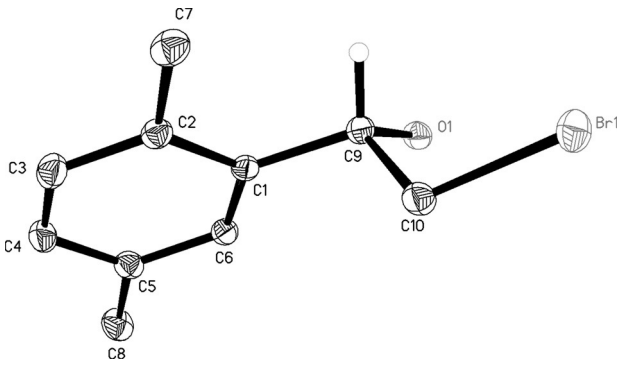


Figure 2. X-ray structure of bromohydrin **2j**. Thermal ellipsoids are shown at the 30% level of probability. Hydrogen atoms are not fully shown for clarity.

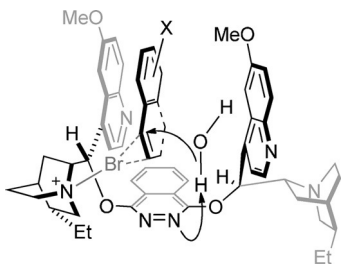
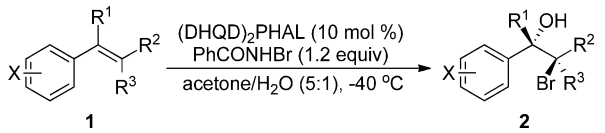


Figure 3. Proposed transition-state model for bromohydroxylation.

stacking with the quinoline of the catalyst. The tertiary amine of the catalyst activates *N*-bromobenzamide[15] and directs the bromine toward the double bond of the substrate. The phthalazine nitrogen likely increases the nucleophilicity of the H_2O and steers it to the reacting site by formation of hydrogen bonds. Apparently, the substituent on the substrate could influence the interaction between the substrate and the catalyst, consequently affecting the enantioselectivity of the reaction. A precise understanding of the reaction mode and the origin of the enantioselectivity awaits further study.

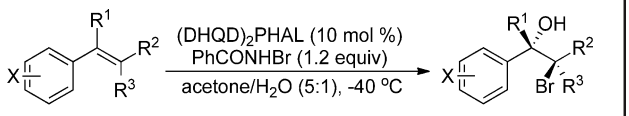
Table 2. Asymmetric bromohydroxylation of olefins.[a]



1 2

Entry	Substrate	Product[b]	Yield [%][c]	*ee* [%][d]
1	X = *o*-Me, **1a**	**2a**	78	83
2	X = H, **1b**	**2b**	64	60
3	X = *o*-Et, **1c**	**2c**	68	71
4	X = *o*-*i*Pr, **1d**	**2d**	56	76
5	X = *m*-Me, **1e**	**2e**	52	73
6	X = *p*-Me, **1f**	**2f**	94	78
7	X = *p*-Ph, **1g**	**2g**	91	80
8	X = *p*-F, **1h**	**2h**	71	82
9[e]	X = *p*-Cl, **1i**	**2i**	64	82
10	**1j**	**2j**	79	83
11	**1k**	**2k**	82	70
12	**1l**	**2l**	75	72
13[f]	X = H, **1m**	**2m**	77	55
14[f]	X = Br, **1n**	**2n**	66	82
15[f]	X = Cl, **1o**	**2o**	74	82
16[g]	X = Cl, **1o**	**2o**	40	88
17	X = H, **1p**	**2p**	83	68
18	X = Ph, **1q**	**2q**	73	75
19	**1r**	**2r**	29	39
20	**1s**	**2s**	79	36

Table 2. (Continued)



1 2

Entry	Substrate	Product[b]	Yield [%][c]	*ee* [%][d]
21	**1t**	**2t**	58	0

[a] Reactions were carried out with substrate **1** (0.50 mmol), $(DHQD)_2PHAL$ (0.050 mmol), and PhCONHBr (0.60 mmol) in acetone (5.0 mL) and water (1.0 mL) at −40 °C for 72 h, unless otherwise noted. [b] For entries 2, 6, 11, 13, and 17, the absolute configurations were determined by comparing the optical rotations of the corresponding bromohydrins with reported values. For entries 1, 3–5, 7–10, 12, 14–16, and 18, the absolute configurations were tentatively assigned by analogy. For entries 19–21, the stereochemistry indicated is relative stereochemistry. [c] Yield of isolated product. [d] Determined by chiral HPLC analysis. [e] At −40 °C for 120 h. [f] At −50 °C for 72 h. [g] At −60 °C for 120 h.

In summary, we have developed an effective enantioselective intermolecular bromohydroxylation of unfunctionalized olefins using dimeric cinchona alkaloid $(DHQD)_2PHAL$ as catalyst, *N*-bromobenzamide as bromine source, and H_2O as nucleophile, giving a variety of optically active bromohydrins in up to 88% *ee*. Although the bromohydroxylation of olefins with H_2O via a bromonium ion intermediate to form bromohydrins is a classic reaction in organic chemistry, to our knowledge, no asymmetric version has to date been reported. Although the enantioselectivity needs to be improved, the results obtained herein represent a significant advance in asymmetric intermolecular halogenation of unfunctionalized olefins, which is still extremely challenging. Further efforts will be devoted to understanding the reaction mechanism and expanding the scope of substrate and nucleophile, as well as developing more effective catalytic systems.

Experimental Section

Representative procedure for asymmetric bromohydroxylation (Table 2, entry 1): A mixture of $(DHQD)_2PHAL$ (0.0389 g, 0.050 mmol) and *N*-bromobenzamide (0.120 g, 0.60 mmol) in acetone (5.0 mL) and water (1.0 mL) was stirred at −40 °C for 15 min. 2-methylstyrene (**1a**) (0.0591 g, 0.50 mmol) was then added. The reaction mixture was stirred at −40 °C for 72 h, quenched with saturated aqueous $Na_2S_2O_3$ (10 mL) at −40 °C, extracted with dichloromethane (3×10 mL), dried over $MgSO_4$, filtered, concentrated under reduced pressure, and purified by flash chromatography on silica gel (eluent = 15:1 petroleum ether/ethyl acetate) to afford bromohydrin **2a** as a pale yellow oil (0.0843 g, 78% yield, 83% *ee*).

Acknowledgements

We gratefully acknowledge the National Basic Research Program of China (973 program, 2011CB808600), the National Natural Science Foundation of China (21172221), and the Chinese Academy of Sciences for financial support.

Keywords: bromination · cinchona alkaloids · enantioselectivity · olefins · water

[1] For leading reviews on halogenation of olefins, see: a) M. D. Dowle, D. I. Davies, *Chem. Soc. Rev.* **1979**, *8*, 171; b) G. Li, S. R. S. S. Kotti, C. Timmons, *Eur. J. Org. Chem.* **2007**, 2745.

[2] For leading reviews on asymmetric halogenation of olefins, see: a) G. Chen, S. Ma, *Angew. Chem. Int. Ed.* **2010**, *49*, 8306; *Angew. Chem.* **2010**, *122*, 8484; b) A. Castellanos, S. P. Fletcher, *Chem. Eur. J.* **2011**, *17*, 5766; c) C. K. Tan, L. Zhou, Y.-Y. Yeung, *Synlett* **2011**, 1335; d) U. Hennecke, *Chem. Asian J.* **2012**, *7*, 456; e) S. E. Denmark, W. E. Kuester, M. T. Burk, *Angew. Chem. Int. Ed.* **2012**, *51*, 10938; *Angew. Chem.* **2012**, *124*, 11098; f) K. Murai, H. Fujioka, *Heterocycles* **2013**, *87*, 763; g) S. R. Chemler, M. T. Bovino, *ACS Catal.* **2013**, *3*, 1076; h) C. K. Tan, Y.-Y. Yeung, *Chem. Commun.* **2013**, *49*, 7985; i) C. B. Tripathi, S. Mukherjee, *Synlett* **2014**, *25*, 163; j) Y. A. Cheng, W. Z. Yu, Y.-Y. Yeung, *Org. Biomol. Chem.* **2014**, *12*, 2333; k) S. Zheng, C. M. Schienebeck, W. Zhang, H.-Y. Wang, W. Tang, *Asian J. Org. Chem.* **2014**, *3*, 366.

[3] For leading references on intramolecular enantioselective halogenation of olefins, see: a) T. Inoue, O. Kitagawa, O. Ochiai, M. Shiro, T. Taguchi, *Tetrahedron Lett.* **1995**, *36*, 9333; b) T. Inoue, O. Kitagawa, A. Saito, T. Taguchi, *J. Org. Chem.* **1997**, *62*, 7384; c) S. H. Kang, S. B. Lee, C. M. Park, *J. Am. Chem. Soc.* **2003**, *125*, 15748; d) M. Wang, L. X. Gao, W. P. Mai, A. X. Xia, F. Wang, S. B. Zhang, *J. Org. Chem.* **2004**, *69*, 2874; e) A. Sakakura, A. Ukai, K. Ishihara, *Nature* **2007**, *445*, 900; f) H. Y. Kwon, C. M. Park, S. B. Lee, J.-H. Youn, S. H. Kang, *Chem. Eur. J.* **2008**, *14*, 1023; g) Z. Ning, R. Jin, J. Ding, L. Gao, *Synlett* **2009**, 2291; h) D. C. Whitehead, R. Yousefi, A. Jaganathan, B. Borhan, *J. Am. Chem. Soc.* **2010**, *132*, 3298; i) W. Zhang, S. Zheng, N. Liu, J. B. Werness, I. A. Guzei, W. Tang, *J. Am. Chem. Soc.* **2010**, *132*, 3664; j) L. Zhou, C. K. Tan, X. Jiang, F. Chen, Y.-Y. Yeung, *J. Am. Chem. Soc.* **2010**, *132*, 15474; k) G. E. Veitch, E. N. Jacobsen, *Angew. Chem. Int. Ed.* **2010**, *49*, 7332; *Angew. Chem.* **2010**, *122*, 7490; l) K. Murai, T. Matsushita, A. Nakamura, S. Fukushima, M. Shimura, H. Fujioka, *Angew. Chem. Int. Ed.* **2010**, *49*, 9174; *Angew. Chem.* **2010**, *122*, 9360; m) A. Jaganathan, A. Garzan, D. C. Whitehead, R. J. Staples, B. Borhan, *Angew. Chem. Int. Ed.* **2011**, *50*, 2593; *Angew. Chem.* **2011**, *123*, 2641; n) R. Yousefi, D. C. Whitehead, J. M. Mueller, R. J. Staples, B. Borhan, *Org. Lett.* **2011**, *13*, 608; o) U. Hennecke, C. H. Müller, R. Fröhlich, *Org. Lett.* **2011**, *13*, 860; p) L. Zhou, J. Chen, C. K. Tan, Y.-Y. Yeung, *J. Am. Chem. Soc.* **2011**, *133*, 9164; q) Z.-M. Chen, Q.-W. Zhang, Z.-H. Chen, H. Li, Y.-Q. Tu, F.-M. Zhang, J.-M. Tian, *J. Am. Chem. Soc.* **2011**, *133*, 8818; r) C. K. Tan, L. Zhou, Y.-Y. Yeung, *Org. Lett.* **2011**, *13*, 2738; s) O. Lozano, G. Blessley, T. M. Campo, A. L. Thompson, G. T. Giuffredi, M. Bettati, M. Walker, R. Borman, V. Gouverneur, *Angew. Chem. Int. Ed.* **2011**, *50*, 8105; *Angew. Chem.* **2011**, *123*, 8255; t) H. Li, F.-M. Zhang, Y.-Q. Tu, Q.-W. Zhang, Z.-M. Chen, Z.-H. Chen, J. Li, *Chem. Sci.* **2011**, *2*, 1839; u) C. K. Tan, F. Chen, Y.-Y. Yeung, *Tetrahedron Lett.* **2011**, *52*, 4892; v) C. H. Müller, M. Wilking, A. Rühlmann, B. Wibbeling, U. Hennecke, *Synlett* **2011**, 2043; w) V. Rauniyar, A. D. Lackner, G. L. Hamilton, F. D. Toste, *Science* **2011**, *334*, 1681; x) D. Huang, H. Wang, F. Xue, H. Guan, L. Li, X. Peng, Y. Shi, *Org. Lett.* **2011**, *13*, 6350; y) J. Chen, L. Zhou, C. K. Tan, Y.-Y. Yueng, *J. Org. Chem.* **2012**, *77*, 999; z) S. E. Denmark, M. T. Burk, *Org. Lett.* **2012**, *14*, 256; aa) W. Zhang, N. Liu, C. M. Schienebeck, K. Decloux, S. Zheng, J. B.Werness, W. Tang, *Chem. Eur. J.* **2012**, *18*, 7296; ab) M. C. Dobish, J. N. Johnston, *J. Am. Chem. Soc.* **2012**, *134*, 6068; ac) M. T. Bovino, S. R. Chemler, *Angew. Chem. Int. Ed.* **2012**, *51*, 3923; *Angew. Chem.* **2012**, *124*, 3989; ad) J. Chen, L. Zhou, Y.-Y. Yeung, *Org. Biomol. Chem.* **2012**, *10*, 3808; ae) C. K. Tan, C. Li, Y.-Y. Yeung, *Chem. Commun.* **2012**, *48*, 5793; af) K. Murai, A. Nakamura, T. Matsushita, M. Shimura, H. Fujioka, *Chem. Eur. J.* **2012**, *18*, 8448; ag) X. Jiang, C. K. Tan, L. Zhou, Y.-Y. Yeung, *Angew. Chem. Int. Ed.* **2012**, *51*, 7771; *Angew. Chem.* **2012**, *124*, 7891; ah) D. H. Paull, C. Fang, J. R. Donald, A. D. Pansick, S. F. Martin, *J. Am. Chem. Soc.* **2012**, *134*, 11128; ai) Y.-M. Wang, J. Wu, C. Hoong, V. Rauniyar, F. D. Toste, *J. Am. Chem. Soc.* **2012**, *134*, 12928; aj) H. J. Lee, D. Y. Kim, *Tetrahedron Lett.* **2012**, *53*, 6984; ak) J. E. Tungen, J. M. J. Nolsøe, T. V. Hansen, *Org. Lett.* **2012**, *14*, 5884; al) K. Ikeuchi, S. Ido, S. Yoshimura, T. Asakawa, M. Inai, Y. Hamashima, T. Kan, *Org. Lett.* **2012**, *14*, 6016; am) C. Fang, D. H. Paull, J. C. Hethcox, C. R. Shugrue, S. F. Martin, *Org. Lett.* **2012**, *14*, 6290; an) L. Zhou, D. W. Tay, J. Chen, G. Y. C. Leung, Y.-Y. Yeung, *Chem. Commun.* **2013**, *49*, 4412; ao) F. Chen, C. K. Tan, Y.-Y. Yeung, *J. Am. Chem. Soc.* **2013**, *135*, 1232; ap) X. Zeng, C. Miao, S. Wang, C. Xia, W. Sun, *Chem. Commun.* **2013**, *49*, 2418; aq) A. Garzan, A. Jaganathan, N. S. Marzijarani, R. Yousefi, D. C. Whitehead, J. E. Jackson, B. Borhan, *Chem. Eur. J.* **2013**, *19*, 9015; ar) D. Huang, X. Liu, L. Li, Y. Cai, W. Liu, Y. Shi, *J. Am. Chem. Soc.* **2013**, *135*, 8101; as) C. S. Brindle, C. S. Yeung, E. N. Jacobsen, *Chem. Sci.* **2013**, *4*, 2100; at) M. Wilking, C. Mück-Lichtenfeld, C. G. Daniliuc, U. Hennecke, *J. Am. Chem. Soc.* **2013**, *135*, 8133; au) D. H. Miles, M. Veguillas, F. D. Toste, *Chem. Sci.* **2013**, *4*, 3427; av) K. Murai, T. Matsushita, A. Nakamura, N. Hyogo, J. Nakajima, H. Fujioka, *Org. Lett.* **2013**, *15*, 2526; aw) F. Romanov-Michailidis, L. Guénée, A. Alexakis, *Angew. Chem. Int. Ed.* **2013**, *52*, 9266; *Angew. Chem.* **2013**, *125*, 9436; ax) Y. Zhao, X. Jiang, Y.-Y. Yeung, *Angew. Chem. Int. Ed.* **2013**, *52*, 8597; *Angew. Chem.* **2013**, *125*, 8759; ay) C. B. Tripathi, S. Mukherjee, *Angew. Chem. Int. Ed.* **2013**, *52*, 8450; *Angew. Chem.* **2013**, *125*, 8608; az) Y. Sawamura, H. Nakatsuji, A. Sakakura, K. Ishihara, *Chem. Sci.* **2013**, *4*, 4181; ba) R. Yousefi, K. D. Ashtekar, D. C. Whitehead, J. E. Jackson, B. Borhan, *J. Am. Chem. Soc.* **2013**, *135*, 14524; bb) A. Jaganathan, R. J. Staples, B. Borhan, *J. Am. Chem. Soc.* **2013**, *135*, 14806; bc) Q. Yin, S.-L. You, *Org. Lett.* **2013**, *15*, 4266; bd) A. Armstrong, D. C. Braddock, A. X. Jones, S. Clark, *Tetrahedron Lett.* **2013**, *54*, 7004; be) W. Xie, G. Jiang, H. Liu, J. Hu, X. Pan, H. Zhang, X. Wan, Y. Lai, D. Ma, *Angew. Chem. Int. Ed.* **2013**, *52*, 12924; *Angew. Chem.* **2013**, *125*, 13162; bf) L. Filippova, Y. Stenstrøm, T. V. Hansen, *Tetrahedron Lett.* **2014**, *55*, 419; bg) X. Han, C. Dong, H. Zhou, *Adv. Synth. Catal.* **2014**, *356*, 1275; bh) C. K. Tan, J. C. Er, Y.-Y. Yeung, *Tetrahedron Lett.* **2014**, *55*, 1243; bi) D. W. Tay, G. Y. C. Leung, Y.-Y. Yeung, *Angew. Chem. Int. Ed.* **2014**, *53*, 5161; *Angew. Chem.* **2014**, *126*, 5261; bj) H. Nakatsuji, Y. Sawamura, A. Sakakura, K. Ishihara, *Angew. Chem. Int. Ed.* **2014**, *53*, 6974; *Angew. Chem.* **2014**, *126*, 7094; bk) H. Liu, G. Jiang, X. Pan, X. Wan, Y. Lai, D. Ma, W. Xie, *Org. Lett.* **2014**, *16*, 1908; bl) Q. Yin, S.-L. You, *Org. Lett.* **2014**, *16*, 1810; bm) C. H. Müller, C. Rösner, U. Hennecke, *Chem. Asian J.* **2014**, *9*, 2162; bn) Q. Yin, S.-L. You, *Org. Lett.* **2014**, *16*, 2426; bo) A. Jaganathan, B. Borhan, *Org. Lett.* **2014**, *16*, 3616; bp) Z. Ke, C. K. Tan, F. Chen, Y.-Y. Yeung, *J. Am. Chem. Soc.* **2014**, *136*, 5627; bq) T. Arai, N. Sugiyama, H. Masu, S. Kado, S. Yabe, M. Yamanaka, *Chem. Commun.* **2014**, *50*, 8287; br) M. Wilking, C. G. Daniliuc, U. Hennecke, *Synlett* **2014**, *25*, 1701; bs) C. B. Tripathi, S. Mukherjee, *Org. Lett.* **2014**, *16*, 3368; bt) K. Murai, N. Shimizu, H. Fujioka, *Chem. Commun.* **2014**, *50*, 12530; bu) Y. Toda, M. Pink, J. N. Johnston, *J. Am. Chem. Soc.* **2014**, *136*, 14734; bv) H. Huang, H. Pan, Y. Cai, M. Liu, H. Tian, Y. Shi, *Org. Biomol. Chem.* **2015**, *13*, 3566; bw) Y. Kawato, A. Kubota, H. Ono, H. Egami, Y. Hamasjima, *Org. Lett.* **2015**, *17*, 1244.

[4] For a leading review on the asymmetric intermolecular halogenation of olefins, see: J. Chen, L. Zhou, *Synthesis* **2014**, *46*, 586.

[5] For leading references on the asymmetric aminohalogenation of α,β-unsaturated carbonyl compounds, see: a) Y. Cai, X. Liu, Y. Hui, J. Jiang, W. Wang, W. Chen, L. Lin, X. Feng, *Angew. Chem. Int. Ed.* **2010**, *49*, 6160; *Angew. Chem.* **2010**, *122*, 6296; b) Y. Cai, X. Liu, J. Jiang, W. Chen, L. Lin, X. Feng, *J. Am. Chem. Soc.* **2011**, *133*, 5636; c) Y. Cai, X. Liu, J. Li, W. Chen, W. Wang, L. Lin, X. Feng, *Chem. Eur. J.* **2011**, *17*, 14916; d) Y. Cai, X. Liu, P. Zhou, Y. Kuang, L. Lin, X. Feng, *Chem. Commun.* **2013**, *49*, 8054.

[6] For leading references on the asymmetric dihalogenation of allylic alcohols, see: a) K. C. Nicolaou, N. L. Simmons, Y. Ying, P. M. Heretsch, J. S. Chen, *J. Am. Chem. Soc.* **2011**, *133*, 8134; b) D. X. Hu, G. M. Shibuya, N. Z. Burns, *J. Am. Chem. Soc.* **2013**, *135*, 12960; c) D. X. Hu, F. J. Seidl, C. Bucher, N. Z. Burns, *J. Am. Chem. Soc.* **2015**, *137*, 3795 – 3798.

[7] For a leading reference on asymmetric bromoamination of enecarbamates, see: A. Alix, C. Lalli, P. Retailleau, G. Masson, *J. Am. Chem. Soc.* **2012**, *134*, 10389.

[8] For a leading reference on asymmetric oxyfluorination of enamides, see: T. Honjo, R. J. Phipps, V. Rauniyar, F. D. Toste, *Angew. Chem. Int. Ed.* **2012**, *51*, 9684; *Angew. Chem.* **2012**, *124*, 9822.

[9] For a leading reference on asymmetric bromoesterification of allylic sulfonamides, see: W. Zhang, N. Liu, C. M. Schienebeck, X. Zhou, I. I. Izhar, I. A. Guzei, W. Tang, *Chem. Sci.* **2013**, *4*, 2652.
[10] For a leading reference on asymmetric bromohydroxylation of allylic alcohols, see: Y. Zhang, H. Xing, W. Xie, X. Wan, Y. Lai, D. Ma, *Adv. Synth. Catal.* **2013**, *355*, 68.
[11] For a leading reference on asymmetric bromoamination of allylic alcohols, see: J. Qi, G.-T. Fan, J. Chen, M.-H. Sun, Y.-T. Dong, L. Zhou, *Chem. Commun.* **2014**, *50*, 13841.
[12] G.-X. Li, Q.-Q. Fu, X.-M. Zhang, J. Jiang, Z. Tang, *Tetrahedron: Asymmetry* **2012**, *23*, 245.
[13] L. Li, C. Su, X. Liu, H. Tian, Y. Shi, *Org. Lett.* **2014**, *16*, 3728.
[14] a) M. Kasai, K.-i. Kawai, M. Imuta, H. Ziffer, *J. Org. Chem.* **1984**, *49*, 675; b) V. J. Forrat, D. J. Ramon, M. Yus, *Tetrahedron: Asymmetry* **2007**, *18*, 400; c) S. Wei, R. Messerer, S. B. Tsogoeva, *Chem. Eur. J.* **2011**, *17*, 14380; d) X. Wu, C. Min, E. Nyamzundui, H. Zhou, C. Dong, *Tetrahedron: Asymmetry* **2011**, *22*, 1640.
[15] A MS signal corresponding to the brominated $(DHQD)_2PHAL$ (m/z = 859.3357) was detected when $(DHQD)_2PHAL$ was treated with *N*-bromobenzamide.

Received: June 1, 2015
Published online on July 2, 2015