JACS
JOURNAL OF THE AMERICAN CHEMICAL SOCIETY

Communication

pubs.acs.org/JACS

Axially Chiral Dicarboxylic Acid Catalyzed Activation of Quinone Imine Ketals: Enantioselective Arylation of Enecarbamates

Takuya Hashimoto, Hiroki Nakatsu, Yuka Takiguchi, and Keiji Maruoka*

Department of Chemistry, Graduate School of Science, Kyoto University, Sakyo, Kyoto 606-8502, Japan

Supporting Information

ABSTRACT: The synthetic utility of quinone imine ketals in the context of asymmetric catalysis was disclosed for the first time. By expanding the utility of chiral Brønsted acid catalysis to the electrophilic activation of quinone imine ketals, we succeeded in the development of highly enantioselective arylation of encarbamates to give α-amino-β-aryl ethers wherein quinone imine ketals act as functionalized aromatic ring surrogate. Further transformations of the products were also examined to establish procedures to provide chiral β-aryl amines and α-aryl esters.

Quinones and quinone ketals, as well as cyclohexadienones, have long served as useful synthetic intermediates to construct densely functionalized aromatic rings and cyclohexanes.[1] Accordingly, their application in asymmetric catalysis, especially organocatalysis, has been on the rise as an expedient means to deliver a range of optically enriched molecules.[2,3] On the other hand, their nitrogen analogs, quinone imines and quinone imine ketals have rarely been utilized in asymmetric catalysis, despite their ready accessibility from the corresponding aniline derivatives[4] and wide use in natural product synthesis.[5−7] To the best of our knowledge, use of N-sulfonyl quinone imines in enamine catalysis as a way to perform α-arylation of aldehydes is the only example reported to date,[8] and quinone imine ketals have never been applied in asymmetric catalysis. Moreover, regardless of the general fact that these imines can be electrophilically activated by a catalytic amount of an acid,[6,7] chiral acid catalyzed asymmetric transformations have yet to be developed. Given our interest in the development of axially chiral dicarboxylic acid as chiral Brønsted acid catalyst and its capability to effectively activate imino functionalities,[9,10] we became interested in its use to tap into this unexplored research area.

We report herein axially chiral dicarboxylic acid catalyzed highly enantioselective arylation of encarbamates[11,12] using quinone imine ketals as electrophilic aryl group surrogate.[2a,b,8] As shown in Figure 1, we postulated the stereodefining C−C bond formation would first occur by the nucleophilic addition of an enecarbamate to the chiral Brønsted acid-activated quinone imine ketal. From this initial product, one alkoxy group of the ketal would be expelled to generate an aromatic ring, and the liberated alcohol sequentially would add to the transient imine to form an α-amino-β-aryl ether.[13,14] Here, we also carried out transformations of functionality-rich products into a variety of chiral building blocks as well as a mechanistic

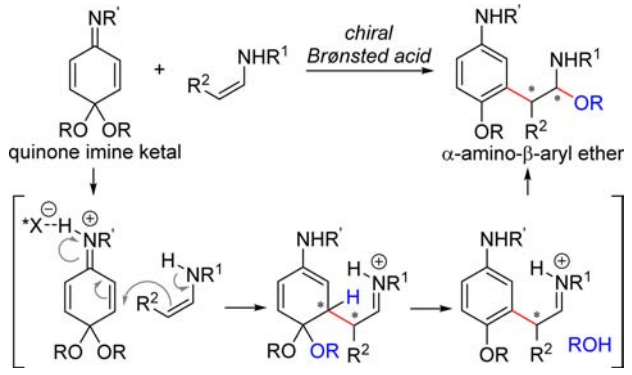


Figure 1. Chiral Brønsted acid catalyzed reaction of quinone imine ketals and enecarbamates.

investigation to provide more accurate understanding of the reaction.

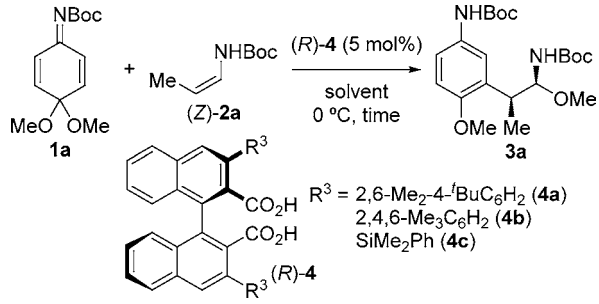
Initially, we selected N-Boc quinone imine ketal **1a** and propanal-derived N-Boc enecarbamate (*Z*)-**2a**[15] as model substrates and performed the reaction in the presence of 5 mol % of axially chiral dicarboxylic acid (*R*)-**4a** (Table 1, entry 1).[9a] The desired α-amino-β-aryl ether **3a** was obtained in good yield with high diastereo- and enantioselectivity. Prolongation of the reaction time to increase the product yield was found to be detrimental to the diastereoselectivity, as the epimerization of the hemiaminal ether moiety proceeded gradually by the reversible addition of methanol to the imine under the acidic reaction condition (entry 2).[16] Further screening of solvents revealed the effectiveness of toluene to suppress this epimerization (entries 3 and 4). Although other representative catalysts **4b** and **4c** also exhibited fairly good catalytic activity,[9b,c] none of them outperformed (*R*)-**4a** (entries 5 and 6). While this optimization was carried out in a test tube without any precaution against air and oxygen, we opted for the use of molecular sieves in the further study to prevent a variable degree of hydrolysis of the substrate by the adventitious water. In addition, the amount of (*Z*)-**2a** was reduced to 1.2 equiv without affecting the yield. Under the optimized reaction conditions, **3a** was obtained diastereoselectively in 83% yield with 97% ee (entry 7). At this stage, we confirmed the scalability of this reaction by carrying out the reaction on 1.0 mmol scale with a reduced 2 mol % catalyst loading (entry 8).

With the optimized reaction conditions in hand, enecarbamate substrate scope was examined (Table 2). Use of

Received: July 26, 2013
Published: October 15, 2013

dx.doi.org/10.1021/ja407501h | J. Am. Chem. Soc. 2013, 135, 16010−16013

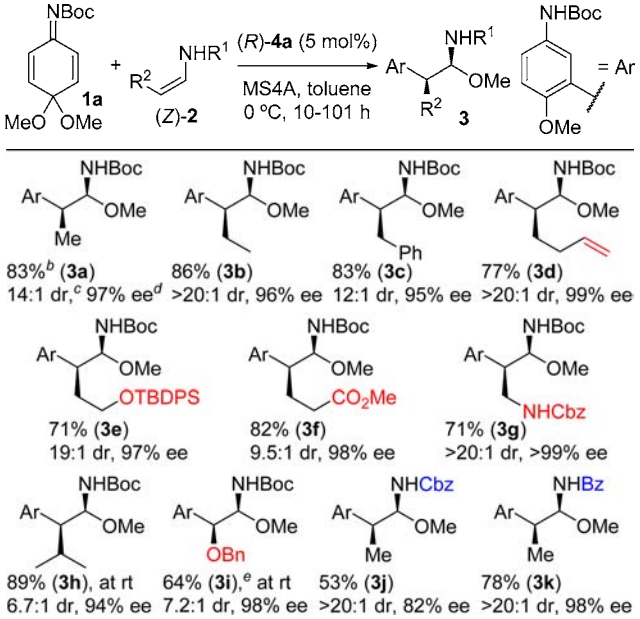
Table 1. Optimization of the Reaction Conditions[a]



entry	cat.	time (h)	solvent	% yield[b]	dr[c]	% ee[d]
1	**4a**	5	CH_2Cl_2	73	10:1	94/83
2	**4a**	10	CH_2Cl_2	83	5.5:1	93/91
3	**4a**	6	$CHCl_3$	77	7.1:1	91/92
4	**4a**	10	toluene	81	11:1	95/91
5	**4b**	11	toluene	71	12:1	89/76
6	**4c**	11	toluene	68	5.9:1	93/85
7[e]	**4a**	10	toluene	83	14:1	97/–
8[f]	**4a**	31	toluene	86	14:1	97/–

[a]Performed with **1a** (0.10 mmol), (*Z*)-**2a** (0.15 mmol) and (*R*)-**4** (0.005 mmol). [b]Combined yield of diastereomers. [c]Determined by ^{1}H NMR analysis of the crude material. [d]Determined by chiral HPLC analysis. [e](*Z*)-**2a** (0.12 mmol) and MS4A. [f]Performed on 1.0 mmol scale with 2 mol % catalyst loading.

Table 2. Enecarbamate Scope[a]

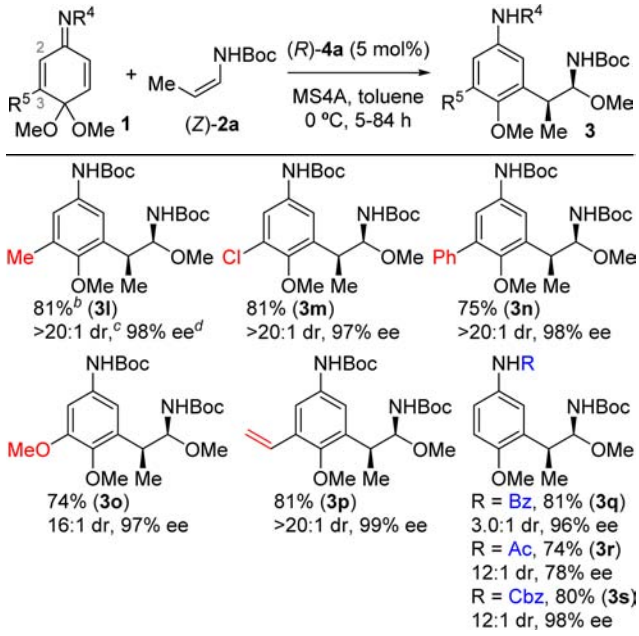


[a]Performed with **1a** (0.10 mmol), (*Z*)-**2** (0.12 mmol) and (*R*)-**4a** (0.005 mmol). [b]Combined yield of diastereomers. [c]Determined by ^{1}H NMR analysis of the crude material. [d]Determined by chiral HPLC analysis. [e](*Z*)-**2** (0.50 mmol).

enecarbamates (*Z*)-**2** derived from butyraldehyde and hydrocinnamaldehyde gave **3b** and **3c** in high yields with high stereoselectivities. Enecarbamates having an alkenyl, a silyloxy, an ester, or a protected amino group could be used to give **3d**–**g**, underlining the functional group tolerance. Due to the low reactivity of the sterically hindered enecarbamate derived from isovaleraldehyde, the reaction was carried out at rt to give **3h** in 89% yield without severely compromising the selectivities. Use of the enecarbamate with a benzyloxy group gave **3i** having a vicinal amino alcohol structure, although the reaction must be carried out at rt with 5.0 equiv of the enecarbamate to compensate for its low reactivity. The reaction could also be extended to the use of N-Cbz enecarbamate and N-Bz enamide to give **3j** and **3k** respectively, offering a way to give α-amino-β-aryl ethers having orthogonal protecting groups on two nitrogen atoms.

We then investigated the quinone imine ketal substrate scope (Table 3). A variety of 3-substituted N-Boc quinone imine

Table 3. Quinone Imine Ketal Scope[a]



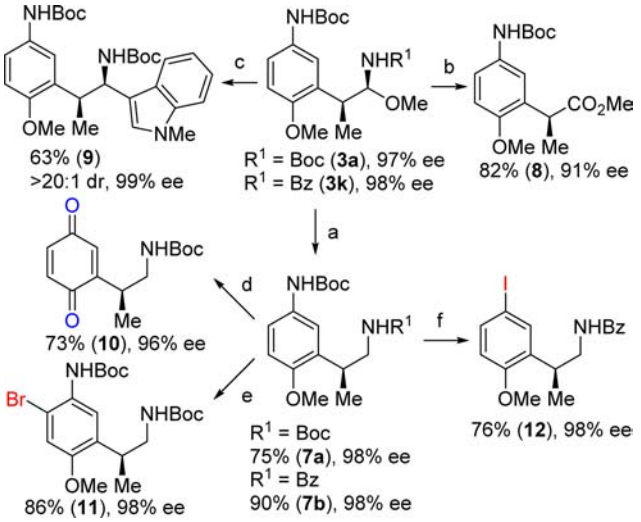
[a]Performed with **1** (0.10 mmol), (*Z*)-**2a** (0.12 mmol) and (*R*)-**4a** (0.005 mmol). [b]Combined yield of diastereomers. [c]Determined by ^{1}H NMR analysis of the crude material. [d]Determined by chiral HPLC analysis.

ketals gave the corresponding products **3l**–**o** in good yields with high stereoselectivities. The quinone imine ketal having a vinyl group could be applied to give **3p** despite the susceptibility of the terminal alkene to the nucleophilic attack. By use of other N-protected quinone imine ketals, the orthogonally protected product **3q**–**3s** were obtained with high enantioselectivities albeit with slightly lower diastereoselectivities. The stereochemistry of **3m** was unambiguously determined by X-ray crystallographic analysis (see Supporting Information, SI). In this study, it became obvious that 2-substituted quinone imine ketals have a completely different reactivity from 3-substituted ones, giving indolines as a major product.[17−19]

Next, transformations of the products into a variety of chiral building blocks were examined (Scheme 1). Hydride reduction of **3a** and **3k** led to the formation of N-Boc β-aryl amine **7a** and N-Bz β-aryl amine **7b** in good yields with no loss of the enantioselectivities, respectively. To convert the hemiaminal ether moiety into an ester, **3a** was hydrolyzed into the aldehyde and subsequently subjected to Pinnick oxidation to give the carboxylic acid. It was necessary to carry out these two steps in one pot to minimize the deterioration of the enantioselectivity. The carboxylic acid was then transformed into methyl ester **8** in 82% overall yield. The hemiaminal ether moiety could also be

dx.doi.org/10.1021/ja407501h | J. Am. Chem. Soc. 2013, 135, 16010−16013

Scheme 1. Transformations of α-Amino-β-aryl Ethers

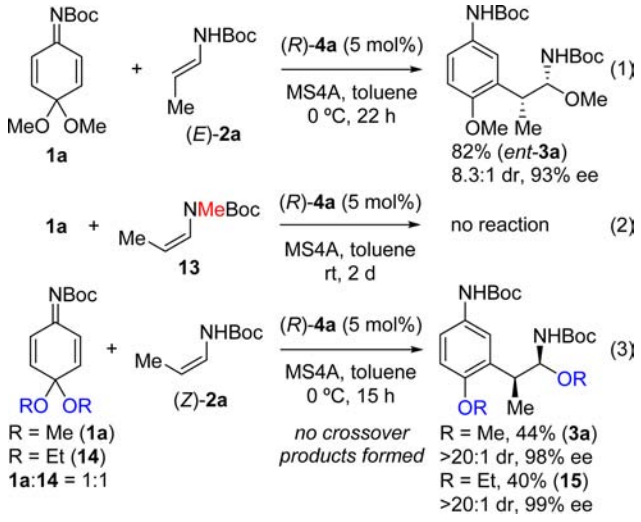


Conditions: (a) **3**, $LiAlH_4$ (1.5 equiv), THF, −20 °C. (b) (i) **3a**, 3N HCl, THF, 0 °C, then $NaClO_2$ (3 equiv), $(CH_3)_2C{=}CHCH_3$ (10 equiv), ^{t}BuOH, rt. (ii) $TMSCHN_2$ (2 equiv), benzene, MeOH, rt. (c) **3a**, 1-Me-indole (2 equiv), (*R*)-**4a** (5 mol %), toluene, rt, MS4A. (d) **7a**, $PhI(OAc)_2$ (1.2 equiv), ^{t}BuOH, H_2O, 0 °C. (e) **7a**, Br_2 (1.6 equiv), THF, −40 °C. (f) (i) **7b**, conc. HCl, dioxane, rt. (ii) I_2 (1.1 equiv), isoamyl nitrite (2.0 equiv), benzene, 85 °C.

exploited as a masked imine.[12d] In the presence of a catalytic amount of (*R*)-**4a**, the addition of 1-methylindole to **3a** proceeded to give **9** with high diastereoselectivity,[20,21] thus paving a way for one-pot sequential transformation of quinone imine ketal to **9** (see SI). We then focused on the derivatization of the aromatic rings of β-aryl amines **7a** and **7b**. Oxidation of **7a** by $PhI(OAc)_2$ in aqueous solution led to the direct conversion to quinone **10**. Bromination of **7a** proceeded at the ortho-position of the NHBoc group to give **11**, thereby making up for the inability to use 2-substituted quinone imine ketals.[17] By taking advantage of the orthogonally protected amino groups of **7b**, the NHBoc moiety was selectively deprotected to give an aniline, which was then converted to iodoarene **12** by the diazotization and iodination.

To get insight on the reaction mechanism, we performed three additional experiments (Scheme 2). One was the use of (*E*)-**2a** in place of (*Z*)-isomer to investigate the effect of the *E*/*Z* geometry on the reactivity and selectivity. Interestingly, this study resulted in the selective formation of the same diastereomer **3a** with high enantioselectivity, while the sense of asymmetric induction was opposite (eq 1).[22] Therefore, this method provides a unique example in which both enantiomers can be accessed by switching the geometry of a substrate while using a single enantiomer catalyst. In terms of the reactivity, an apparent deceleration of the reaction was observed with (*E*)-**2a**. Next, we conducted a reaction by using N-methyl encarbamate **13** (eq 2). It turned out to be completely unreactive, implying the importance of the hydrogen bonding between the N−H hydrogen of the enecarbamate and the catalyst to facilitate the reaction. Finally, the mechanism of the transfer of the methoxy group was examined since not only the intermolecular pathway as we initially proposed in Figure 1 but also the intramolecular pathway are also conceivable. A crossover experiment using a 1:1 mixture of the dimethyl ketal **1a** and diethyl ketal **14** revealed no formation of the crossover products (eq 3), thereby confirming the unique intramolecularity of the process.

Scheme 2. Exploration of the Reaction Mechanism



From these observations, we postulated the reaction mechanism using (*Z*)- and (*E*)-enecarbamates as follows (Figure 2). In both reactions, the first step is the highly

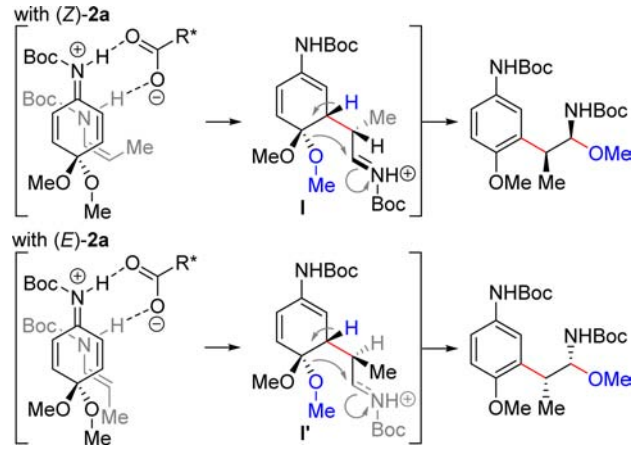


Figure 2. Plausible reaction mechanism.

diastereo- and enantioselective C−C bond formation between two substrates hydrogen bonded by the carboxylic acid.[9d,10] It is assumed that the catalyst recognizes the identical prochiral face of the quinone imine ketal,[23] and the diastereomeric intermediates **I** and **I′** are generated depending on the geometry of the enecarbamate.[24] The steric repulsion between the methyl group of the (*E*)-enecarbamate and the methoxy group of the quinone imine ketal may explain its lower reactivity. From each intermediate, the intramolecular methoxy group transfer occurs in the opposite sense of diastereoselectivity while minimizing the 1,3-allylic strain. As a consequence of two diastereodivergent processes, the same diastereomers with the opposite sense of enantioselectivity are finally obtained.[25]

In summary, we have developed the first asymmetric transformation using quinone imine ketals with enecarbamates to give chiral α-amino-β-aryl ethers, by shedding light on the reactivity of quinone imine ketals in chiral acid catalysis. Transformations of these products were examined to secure their use as a synthetic handle to deliver a variety of enantiomerically enriched molecules. Further research to use

dx.doi.org/10.1021/ja407501h | J. Am. Chem. Soc. 2013, 135, 16010−16013

quinone imine ketals in other asymmetric transformations is currently underway in this laboratory.

■ ASSOCIATED CONTENT

Supporting Information

Experimental details and characterization data. This material is available free of charge via the Internet at http://pubs.acs.org.

■ AUTHOR INFORMATION

Corresponding Author

maruoka@kuchem.kyoto-u.ac.jp

Notes

The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

This work was partially supported by a Grant-in-Aid for Scientific Research from the MEXT (Japan). H.N. thank a Grant-in-Aid for the Research Fellowship of JSPS for Young Scientists.

■ REFERENCES

(1) General reviews: (a) Nicolaou, K. C.; Snyder, S. A.; Montagnon, T.; Vassilikogiannakis, G. *Angew., Chem. Int. Ed.* **2002**, *41*, 1668. (b) Magdziak, D.; Meek, S. J.; Pettus, T. R. R. *Chem. Rev.* **2004**, *104*, 1383. (c) Roche, S. P.; Porco, J. A., Jr. *Angew., Chem. Int. Ed.* **2011**, *50*, 4068. (d) Zhuo, C. X.; Zhang, W.; You, S. L. *Angew., Chem. Int. Ed.* **2012**, *51*, 12662.

(2) Use of quinones and quinone ketals: (a) Alemán, J.; Richter, B.; Jørgensen, K. A. *Angew. Chem., Int. Ed.* **2007**, *46*, 5515. (b) *Angew. Chem., Int. Ed.* **2007**, *46*, 5520. (c) Aleman, J.; Jacobsen, C. B.; Frisch, K.; Overgaard, J.; Jørgensen, K. A. *Chem. Commun.* **2008**, 632. (d) Mikami, K.; Motoyama, Y.; Terada, M. *J. Am. Chem. Soc.* **1994**, *116*, 2812. (e) Evans, D. A.; Wu, J. *J. Am. Chem. Soc.* **2003**, *125*, 10162. (f) Ryu, D. H.; Zhou, G.; Corey, E. J. *J. Am. Chem. Soc.* **2004**, *126*, 4800. (g) Jarvo, E. R.; Lawrence, B. M.; Jacobsen, E. N. *Angew. Chem., Int. Ed.* **2005**, *44*, 6043. (h) Wang, C.; Chen, X.-H.; Zhou, S.-M.; Gong, L.-Z. *Chem. Commun.* **2010**, *46*, 1275. (i) Han, Z.-Y.; Chen, D.-F.; Wang, Y.-Y.; Guo, R.; Wang, P.-S.; Wang, C.; Gong, L.-Z. *J. Am. Chem. Soc.* **2012**, *134*, 6532.

(3) Use of cyclohexadienones: (a) Liu, Q.; Rovis, T. *J. Am. Chem. Soc.* **2006**, *128*, 2552. (b) Rubush, D. M.; Morges, M. A.; Rose, B. J.; Thamm, D. H.; Rovis, T. *J. Am. Chem. Soc.* **2012**, *134*, 13554. (c) Vo, N. T.; Pace, R. D. M.; O'Hara, F.; Gaunt, M. J. *J. Am. Chem. Soc.* **2008**, *130*, 404. (d) Gu, Q.; You, S. L. *Chem. Sci* **2011**, *2*, 1519. (e) Gu, Q.; You, S. L. *Org. Lett.* **2011**, *13*, 5192. Gu, Q.; Rong, Z.-Q.; Zheng, C.; You, S.-L. *J. Am. Chem. Soc.* **2010**, *132*, 4056. (f) Takizawa, S.; Nguyen, T. M.-N.; Grossmann, A.; Enders, D.; Sasai, H. *Angew. Chem., Int. Ed.* **2012**, *51*, 5423. (g) Wu, W.; Li, X.; Huang, H.; Yuan, X.; Lu, J.; Zhu, K.; Ye, J. *Angew. Chem., Int. Ed.* **2013**, *52*, 1743. (h) Corbett, M. T.; Johnson, J. S. *Chem. Sci.* **2013**, *4*, 2828.

(4) (a) Carreño, M. C.; Ribagorda, M. *J. Org. Chem.* **2000**, *65*, 1231. (b) Bodipati, N.; Peddinti, R. K. *Org. Biomol. Chem.* **2012**, *10*, 4549.

(5) Applications in total synthesis: (a) Chou, C. T.; Swenton, J. S. *J. Am. Chem. Soc.* **1987**, *109*, 6898. (b) Shair, M. D.; Yoon, T. Y.; Mosny, K. K.; Chou, T. C.; Danishefsky, S. J. *J. Am. Chem. Soc.* **1996**, *118*, 9509. (c) Myers, A. G.; Tom, N. J.; Fraley, M. E.; Cohen, S. B.; Madar, D. J. *J. Am. Chem. Soc.* **1997**, *119*, 6072. (d) Tohma, H.; Harayama, Y.; Hashizume, M.; Iwata, M.; Kiyono, Y.; Egi, M.; Kita, Y. *J. Am. Chem. Soc.* **2003**, *125*, 11235. (e) Jackson, S. K.; Banfield, S. C.; Kerr, M. A. *Org. Lett.* **2005**, *7*, 1215. (f) Ganton, M. D.; Kerr, M. A. *J. Org. Chem.* **2007**, *72*, 574. (g) Lebold, T. P.; Kerr, M. A. *Org. Lett.* **2007**, *9*, 1883. (h) Leduc, A. B.; Kerr, M. A. *Eur. J. Org. Chem.* **2007**, 237. (i) Lebold, T. P.; Kerr, M. A. *Org. Lett.* **2008**, *10*, 997. (j) T. Chuang, K. V.; Navarro, R.; Reisman, S. E. *Angew. Chem., Int. Ed.* **2011**, *50*, 9447. (j) T. Chuang, K. V.; Navarro, R.; Reisman, S. E. *Chem. Sci* **2011**, *2*, 1086. (k) Navarro, R.; Reisman, S. E. *Org. Lett.* **2012**, *14*, 4354.

(6) Nair, V.; Dhanya, R.; Rajesh, C.; Devipriya, S. *Synlett* **2005**, 2407.

(7) Other representative developments: (a) Chen, C.-P.; Chou, C.-T.; Swenton, J. S. *J. Am. Chem. Soc.* **1987**, *109*, 946. (b) Swenton, J. S.; Bonke, B. R.; Chen, C.-P.; Chou, C.-T. *J. Org. Chem.* **1989**, *54*, 51. (c) Swenton, J. S.; Bonke, B. R.; Clark, W. M.; Chen, C.-P.; Martin, K. V. *J. Org. Chem.* **1990**, *55*, 2027. (d) Banfield, S. C.; England, D. B.; Kerr, M. A. *Org. Lett.* **2001**, *3*, 3325. (e) Banfield, S. C.; Kerr, M. A. *Can. J. Chem.* **2004**, *82*, 131.

(8) Jensen, K. L.; Franke, P. T.; Nielsen, L. T.; Daasbjerg, K.; Jørgensen, K. A. *Angew., Chem. Int. Ed.* **2010**, *49*, 129.

(9) (a) Hashimoto, T.; Maruoka, K. *J. Am. Chem. Soc.* **2007**, *129*, 10054. (b) Hashimoto, T.; Uchiyama, N.; Maruoka, K. *J. Am. Chem. Soc.* **2008**, *130*, 14380. (c) Hashimoto, T.; Kimura, H.; Kawamata, Y.; Maruoka, K. *Nat. Chem.* **2011**, *3*, 642. (d) Hashimoto, T.; Kimura, H.; Nakatsu, H.; Maruoka, K. *J. Org. Chem.* **2011**, *76*, 6030.

(10) General reviews: (a) Akiyama, T. *Chem. Rev.* **2007**, *107*, 5744. (b) Terada, M. *Synthesis* **2010**, 1929.

(11) Matsubara, R.; Kobayashi, S. *Acc. Chem. Res.* **2008**, *41*, 292.

(12) Enecarbamates and enamides as nucleophile in chiral Brønsted acid catalysis: (a) Terada, M.; Machioka, K.; Sorimachi, K. *Angew., Chem. Int. Ed.* **2006**, *45*, 2254. (b) Terada, M.; Machioka, K.; Sorimachi, K. *J. Am. Chem. Soc.* **2007**, *129*, 10336. (c) Terada, M.; Soga, N.; Momiyama, N. *Angew. Chem., Int. Ed.* **2008**, *47*, 4122. (d) Terada, M.; Machioka, K.; Sorimachi, K. *Angew. Chem., Int. Ed.* **2009**, *48*, 2553. (e) Liu, H.; Dagousset, G.; Masson, G.; Retailleau, P.; Zhu, J. *J. Am. Chem. Soc.* **2009**, *131*, 4598. (f) Dagousset, G.; Drouet, F.; Masson, G.; Zhu, J. *Org. Lett.* **2009**, *11*, 5546. (g) Dagousset, G.; Zhu, J.; Masson, G. *J. Am. Chem. Soc.* **2011**, *133*, 14804. (h) Alix, A.; Claudia, L.; Retailleau, P.; Masson, G. *J. Am. Chem. Soc.* **2012**, *134*, 10389. (i) Lu, M.; Lu, Y.; Zhu, D.; Zeng, X.; Li, X.; Zhong, G. *Angew. Chem., Int. Ed.* **2010**, *49*, 8588.

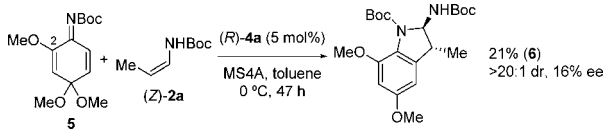
(13) Chiral Brønsted acid catalyzed enantioselective synthesis of hemiaminal ethers: (a) Li, G.; Fronczek, F. R.; Antilla, J. C. *J. Am. Chem. Soc.* **2008**, *130*, 12216. (b) Vellalath, S.; Čorić, I.; List, B. *Angew. Chem., Int. Ed.* **2010**, *49*, 9749.

(14) Honjo, T.; Phipps, R. J.; Rauniyar, V.; Toste, F. D. *Angew. Chem., Int. Ed.* **2012**, *51*, 9684.

(15) (a) Pansare, S. V.; Vederas, J. C. *J. Org. Chem.* **1989**, *54*, 2311. (b) Mecozzi, T.; Petrini, M. *Synlett* **2000**, 73.

(16) Use of stronger chiral Brønsted acids, see SI.

(17) E.g., use of 2-methoxy quinone imine ketal **5** gave rise to 2-amino-3-methylindoline **6** as the only isolable compound with low enantioselectivity.



(18) Avdeenko, A. P.; Konovalova, S. A.; Mikhailichenko, O. N.; Yusia, A. L.; Santalova, A. A.; Palamarchyk, G. V.; Zubatyuk, R. I.; Shishkin, O. V.; Burmistrov, K. S. *Russ. J. Org. Chem.* **2011**, *47*, 1169.

(19) (a) Dalidowicz, P.; Swenton, J. S. *J. Org. Chem.* **1993**, *58*, 4802. (b) Engler, T. A.; Scheibe, C. M. *J. Org. Chem.* **1998**, *63*, 6247. (c) Hu, Y.; Kamitanaka, T.; Mishima, Y.; Dohi, T.; Kita, Y. *J. Org. Chem.* **2013**, *78*, 5530.

(20) Terada, M.; Sorimachi, K. *J. Am. Chem. Soc.* **2007**, *129*, 292.

(21) Diastereoselectivity was essentially governed by the substrate, and the use of a weaker acid resulted in a cleaner conversion.

(22) Chang, L.; Kuang, Y.; Qin, B.; Zhou, X.; Liu, X.; Lin, L.; Feng, X. *Org. Lett.* **2010**, *12*, 2214.

(23) VT NMR experiments revealed facile interconversion of the C═N double bond of the quinone imine ketal.

(24) (a) Matsubara, R.; Nakamura, Y.; Kobayashi, S. *Angew., Chem. Int. Ed.* **2004**, *43*, 3258. (b) Matsubara, R.; Kawai, N.; Kobayashi, S. *Angew., Chem. Int. Ed.* **2006**, *45*, 3814.

(25) Transition-state model discussion, see SI.