Communication

Pyridinium 1,1#-Binaphthyl-2,2#-disulfonates as Highly Effective Chiral Brønsted Acid#Base Combined Salt Catalysts for Enantioselective Mannich-Type Reaction

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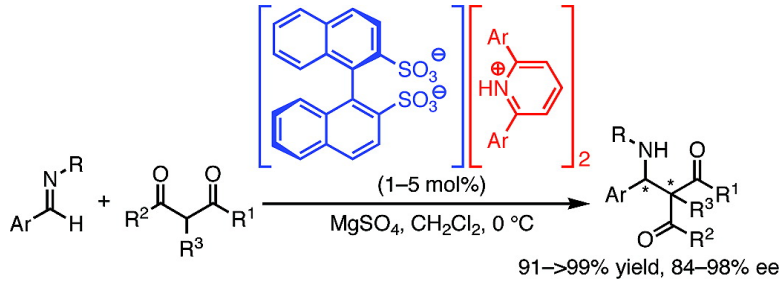

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Pyridinium 1,1′-Binaphthyl-2,2′-disulfonates as Highly Effective Chiral Brønsted Acid−Base Combined Salt Catalysts for Enantioselective Mannich-Type Reaction

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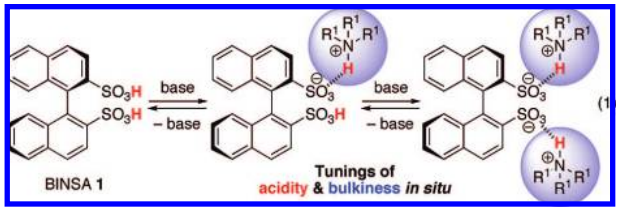
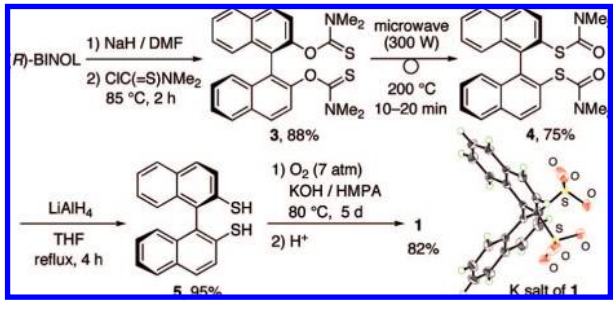
A chiral organic salt which consists of a Brønsted acid and a Brønsted base is one of the most promising catalysts in modern asymmetric syntheses.[1−3] In general, acid−base combined salts have several advantages over single-molecule catalysts, with regard to the flexibility in the design of their dynamic complexes. Chiral ammonium sulfonates[4] and ammonium phosphates[5] are typical examples of these organocatalysts with enantioselective properties. In particular, 2,2′-disubstituted 1,1′-binaphthyl compounds are some of the most useful chiral organocatalysts.[6,7] However, these compounds often require bulky substituents at the 3,3′-positions to achieve high enantioselectivity in asymmetric catalyses. In sharp contrast, chiral 1,1′-binaphthyl-2,2′-disulfonic acid (BINSA, **1**)[8] should be a promising chiral Brønsted acid catalyst, since both the Brønsted acidity and bulkiness can be easily controlled by complexation with achiral amines without substitutions at the 3,3′-position in a binaphthyl skeleton (eq 1).[9,10] However, despite this potential, there have been no reports on the applications of chiral **1** to asymmetric catalyses since the first synthesis of rac-**1** in 1928 by Barber and Smiles.[8] We report here a practical synthesis of chiral **1** from inexpensive 1,1′-bi(2-naphthol) (BINOL) and efficient enantioselective catalysis in direct Mannich-type reactions using **1**−2,6-diarylpyridine (**2**) combined salts as tailor-made chiral Brønsted acid−base organocatalysts in situ.



At the beginning of our research, we examined the preparation of **1** from (*R*)-BINOL via the oxidation of dithiol **5**[11,12] (Scheme 1). First, thermolysis in the Newman−Kwart rearrangement of **3**

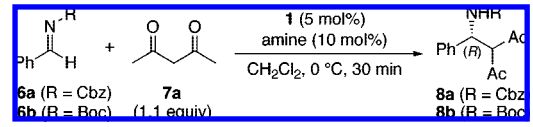
Scheme 1. Synthesis of BINSA (**1**)



to **4** was dramatically improved by using a microwave technique at milder temperature (200 °C).[11,13] Next, according to the reported procedures, the oxidation of thiols (RSH) to sulfonic acids (RSO_3H) is usually accompanied by the generation of disulfides (RS−SR) via intermolecular reactions.[14] In particular, dithiol **5** bearing two SH groups at the 2,2′-positions in a binaphthyl skeleton would be suitable for the formation of an oxidative S−S bond, intramolecularly.[11] Surprisingly, however, after optimization of the reaction conditions, the unprecedented oxidation of **3** proceeded smoothly in 82% yield without epimerization under 7 atm of O_2/KOH in HMPA. Before protonation by ion-exchange, a single crystal of potassium salt of **1** was obtained, which was suitable for X-ray analysis. Eventually, compound **1** could be prepared in 51% yield over five steps from (*R*)-BINOL or in 82% yield in one step from commercially available **5**.[15]

Encouraged by the successful preparation of **1**, we examined the enantioselective direct Mannich-type reaction[7,16] using **1** as a chiral Brønsted acid catalyst (Table 1). Since the reaction between

Table 1. Ammonium Salts of **1** as Tailor-Made Catalysts[a]



entry	6	amine	yield [%]	ee [%]
1	**6a**		81	17
2	**6a**	C_5H_5N	8	5
3	**6a**	2-Ph-C_5H_4N	11	10
4	**6a**	2,6-Me_2-C_5H_3N	19	0
5	**6a**	2,6-*t*-Bu_2-C_5H_3N	32	76
6	**6a**	2,6-Ph_2-C_5H_3N (**2a**)	74	92
7	**6b**	**2a**	83	85

[a] Acetylacetone **7a** was added at 0 °C over 1 h, and the resultant mixture was stirred for 30 min.

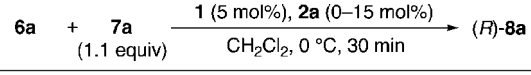
N-Cbz-phenylaldimine (**6a**) and acetylacetone (**7a**) proceeded without catalysts in dichloromethane at 0 °C, the slow addition of **7a** was the key to preventing the achiral pathway. However, despite such care, the enantioselectivity of **8a** was low (17% ee) when 5 mol % of **1** was used (entry 1). Next, we examined chiral **1**−achiral amine combined salts as chiral Brønsted acid−base catalysts prepared in situ (eq. 1). Some preliminary results using **1** (5 mol %)−amines (10 mol %), suggested that pyridines with weak Brønsted basicity would be better Brønsted bases, while trialkylamines with strong Brønsted basicity were much less active, and anilines caused side reactions such as the Friedel−Crafts reaction. Even then, pyridine, 2-phenylpyridine, and 2,6-lutidine also gave **8a** in low yield owing to the insolubility of the corresponding salts (entries 2−4). In sharp contrast, 2,6-di-*tert*-butylpyridine improved the enantioselectivity up to 76% ee (entry 5). Moreover, **1** with 2,6-diphenylpyridine (**2a**), which led to a homogeneous catalyst in situ, was found to be highly effective, and **8a** was obtained in 74%

10.1021/ja806875c CCC: $40.75

yield with 92% ee (entry 6). To our delight, *N*-Boc-phenylaldimine (**6b**), which has been reported as a sole protecting group by Terada and co-workers using pioneering chiral phosphoric acids,[7] was compatible with our reaction conditions using **1**·**2a**$_2$, and the corresponding adduct **8b** was obtained in 83% yield with 85% ee (entry 7).[17]

Next, the molar ratio of **2a** (0−15 mol %) to **1** (5 mol %) was optimized for the above direct Mannich-type reaction of **7a** with **6a** (Table 2). Interestingly, the enantioselectivities of **8a** were

Table 2. Effect of the Ratio of **1**:**2a**

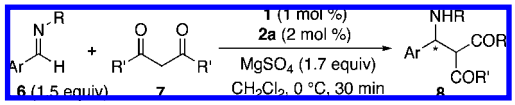


entry	**1**·**2a**$_n$	yield [%]	ee [%]	entry	**1**·**2a**$_n$	yield [%]	ee [%]
1	**1**	81	17	6	**1**·**2a**$_{1.5}$	84	90
2	**1**·**2a**$_{0.25}$	82	17	7	**1**·**2a**$_2$	74	92
3	**1**·**2a**$_{0.5}$	83	34	8	**1**·**2a**$_{2.5}$	76	95
4	**1**·**2a**$_{0.75}$	81	79	9	**1**·**2a**$_3$	68	86
5	**1**·**2a**	82	84				

dramatically improved when a more than 1:0.75 ratio of **1**:**2a** (i.e., **1**·**2a**$_{0.75}$) was examined (entries 4−9 vs entries 1−3). We found that a 1:1.5 to 1:2.5 ratio of **1**:**2a** was effective for achieving both a high yield and a high enantioselectivity (entries 6−8). Probably, the wide range of suitable ratio of **1**:**2a** was due to the dynamic structure of the catalysts (eq 1).[18]

Fortunately, **8a** was obtained in 91% yield with 90% ee with the use of 1 mol % of **1**·**2a**$_2$ in the presence of 1.7 equiv of $MgSO_4$, which would prevent the decomposition of **6a** (1.5 equiv) due to adventitious moisture (Table 3, entry 1). Under these optimized

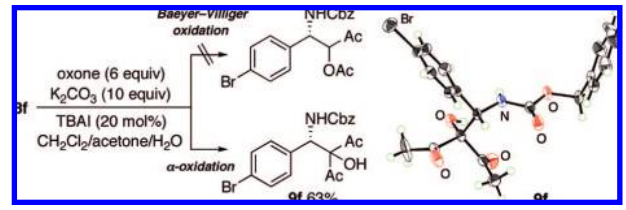
Table 3. Catalytic Enantioselective Direct Mannich-Type Reaction



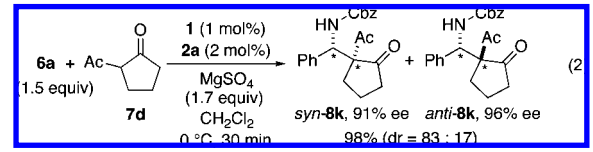
entry	**6** (R, Ar)	**7** (R′)	**8**	yield [%]	ee [%]
1	**6a** (Cbz, Ph)	**7a** (Me)	**8a**	91	90 (*R*)
2	**6b** (Boc, Ph)	**7a** (Me)	**8b**	99	84 (*R*)
3	**6c** (Cbz, *o*-MeC$_6$H$_4$)	**7a** (Me)	**8c**	99	96
4	**6d** (Cbz, *m*-MeC$_6$H$_4$)	**7a** (Me)	**8d**	99	89
5	**6e** (Cbz, *p*-MeOC$_6$H$_4$)	**7a** (Me)	**8e**	95	96
6	**6f** (Cbz, *p*-BrC$_6$H$_4$)	**7a** (Me)	**8f**	92	98 (*R*)
7	**6g** (Cbz, 1-Naph)	**7a** (Me)	**8g**	99	96
8	**6h** (Cbz, 3-Thionyl)	**7a** (Me)	**8h**	98	98
9	**6a** (Cbz, Ph)	**7b** (Et)	**8i**	95	95
10	**6a** (Cbz, Ph)	**7c** (Ph)	**8j**	>99	84

conditions, *N*-Boc-Mannich product **8b** was obtained in 99% yield with 84% ee (entry 2). From **7a** and a variety of *N*-Cbz-arylaldimines bearing electron-donating or electron-withdrawing groups in the aryl or heteroaryl moiety, the corresponding adducts (**8c**−**j**) were obtained in excellent yields (92 to >99%) and with high enantioselectivities (89−98% ee) (entries 3−8). When other diketones such as 3,5-heptanedione (**7b**) and 1,3-diphenylpropane-1,3-dione (**7c**) were reacted with **6a**, **8i** and **8j** were obtained with 95% ee and 84% ee, respectively (entries 9 and 10). The absolute stereochemistry of the products **8a** and **8b** was determined by following Terada's procedure which includes the Baeyer−Villiger oxidation (see the Supporting Information).[7a] However, unexpected tertiary alcohols **9**[19] were obtained exclusively instead of the Baeyer−Villiger products when Mannich adducts **8** were oxidized under the same reaction conditions as Terada reported. In particular, compound **9f** was determined by X-ray analysis (Scheme 2).

Scheme 2. Unexpected Oxidation of **8f** and X-ray Analysis of **9f**

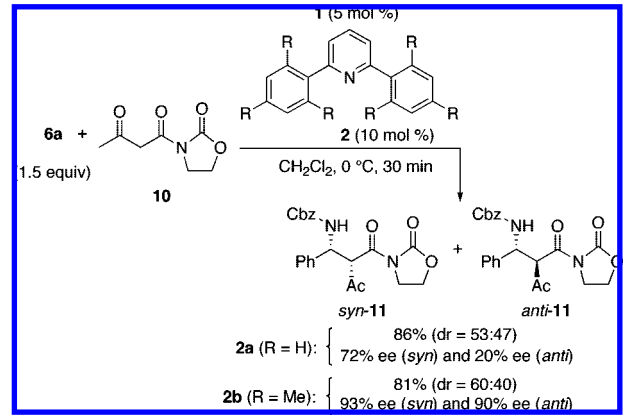


Moreover, cyclic 1,3-diketone **7d** could also be used, and the corresponding adduct **8k** with a quaternary carbon center was obtained in 98% yield with a syn/anti diastereomer ratio of 83/17 and high enantioselectivity (91% ee and 96% ee, respectively) (eq 2).[17]

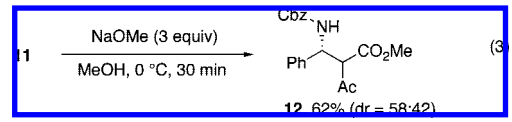


A suitable chiral ammonium salt was easily tailor-made for a ketoester equivalent such as 3-acetoacetyl-2-oxazolidinone (**10**) (Scheme 3). The chiral ammonium salt **1**·**2a**$_2$, which was optimized

Scheme 3. Enantio- and Diastereoselective Direct Mannich-Type Reaction between **6a** and 1,3-Ketoamide (**10**)



for the reaction of diketones **7** with **6**, was not effective, and the desired product **11** was obtained in 86% yield with low diastereo- and enantioselectivities. In contrast, the enantioselectivity of **11** increased to 93% ee when 2,6-dimesitylpyridine (**2b**) was used in place of **2a**.[17] In this way, tailor-made salts **1**·**2**$_2$ made it possible to avoid preparing single-molecule catalysts in advance and offered a quick solution to this type of optimization problem. Compound **11** was easily transformed to β-amino carbonyl compound **12** via deprotection of the oxazolidinone moiety without a loss of enantioselectivity (eq 3).



In summary, we have developed a practical asymmetric synthesis of optically pure **1** from BINOL for the first time. BINSA **1** was found to be a highly effective chiral Brønsted acid that could be

combined with an achiral Brønsted base.[17,20] The combination of the achiral bulky 2,6-biarylpyridine (**2**) with the simple disulfonic acid (**1**) circumvented the trouble of having to build bulky substituents at the 3,3′-position as is normally required in the analogous binaphthyl phosphoric acid catalysts. In the presence of 1 mol % of **1** and 2 mol % of **2**, highly enantioselective direct Mannich-type reactions of a variety of 1,3-diketones and a 1,3-ketoester equivalent with arylaldimines proceeded smoothly with high enantioselectivities. We believe that BINSA should be a powerful chiral auxiliary like BINOL, BINAP (2,2′-bis(diphenylphosphino)-1,1′-binaphthalene), BINAM (2,2′-diamino-1,1′-binaphthalene), etc., and could trigger a new frontier in acid−base chemistry in asymmetric catalyses.

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Supporting Information Available: Experimental procedures and the comparisons with a chiral phosphoric acid catalyst. This material is available free of charge via the Internet at http://pubs.acs.org.

References

(1) For excellent reviews in acid−base chemistry: (a) Shibasaki, M.; Yoshikawa, N. *Chem. Rev.* **2002**, *102*, 2187. (b) List, B. *Tetrahedron* **2002**, *58*, 5573. (c) Maruoka, K.; Ooi, T. *Chem. Rev.* **2003**, *103*, 3013. (d) Notz, W.; Tanaka, F.; Barbas, C. F., III. *Acc. Chem. Res.* **2004**, *37*, 580. (e) Tian, S.-K.; Chen, Y.; Hang, J.; Tang, L.; Mcdaid, P.; Deng, L. *Acc. Chem. Res.* **2004**, *37*, 621. (f) Lelais, G.; MacMillan, D. W. C. *Aldrichimica Acta* **2006**, *39*, 79.

(2) For our account: Ishihara, K.; Sakakura, A.; Hatano, M. *Synlett* **2007**, 686.

(3) For an excellent textbook: Berkessel, H., Gröger, H., Eds. *Asymmetric Organocatalysis*; Wiley-VCH: Weinheim, 2005.

(4) Achiral diarylammonium arenesulfonates for ester condensation reactions: (a) Wakasugi, K.; Misaki, T.; Yamada, K.; Tanabe, Y. *Tetrahedron Lett.* **2000**, *41*, 5249. (b) Ishihara, K.; Nakagawa, S.; Sakakura, A. *J. Am. Chem. Soc.* **2005**, *127*, 4168. (c) Sakakura, A.; Nakagawa, S.; Ishihara, K. *Tetrahedron* **2006**, *62*, 422. (d) Sakakura, A.; Watanabe, H.; Nakagawa, S.; Ishihara, K. *Chem. Asian J.* **2007**, *2*, 477.

(5) Aza-Henry reactions: (a) Nugent, B. M.; Yoder, R. A.; Johnston, J. N. *J. Am. Chem. Soc.* **2004**, *126*, 3418. Diels−Alder reactions: (b) Ishihara, K.; Nakano, K. *J. Am. Chem. Soc.* **2005**, *127*, 10504. (c) Sakakura, A.; Suzuki, K.; Nakano, K.; Ishihara, K. *Org. Lett.* **2006**, *8*, 2229. (d) Kano, T.; Tanaka, Y.; Maruoka, K. *Org. Lett.* **2006**, *8*, 2687. Aza-Diels−Alder reactions: (e) Itoh, J.; Fuchibe, K.; Akiyama, T. *Angew. Chem., Int. Ed.* **2006**, *45*, 4796. (f) Rueping, M.; Azap, C. *Angew. Chem., Int. Ed.* **2006**, *45*, 7832. Hydrogenations: (g) Hoffmann, S.; Seayad, A. M.; List, B. *Angew. Chem., Int. Ed.* **2005**, *44*, 7424. (h) Mayer, S.; List, B. *Angew. Chem., Int. Ed.* **2006**, *45*, 4193. (i) Martin, N. J. A.; List, B. *J. Am. Chem. Soc.* **2006**, *128*, 13368. [2 + 2] Cycloadditions: (j) Ishihara, K.; Nakano, K. *J. Am. Chem. Soc.* **2007**, *129*, 8930.

(6) Organocatalyses with chiral 3,3′-disubstituted binaphthyl compounds: (a) McDougal, N. T.; Schaus, S. E. *J. Am. Chem. Soc.* **2003**, *125*, 12094. (b) Akiyama, T.; Itoh, J.; Yokota, K.; Fuchibe, K. *Angew. Chem., Int. Ed.* **2004**, *43*, 1566. (c) Matsui, K.; Takizawa, S.; Sasai, H. *J. Am. Chem. Soc.* **2005**, *127*, 3680. (d) Rueping, M.; Sugiono, E.; Azap, C.; Theissmann, T.; Bolte, M. *Org. Lett.* **2005**, *7*, 3781. (e) Rowland, G. B.; Zhang, H.; Rowland, E. B.; Chennamadhavuni, S.; Wang, Y.; Antilla, J. C. *J. Am. Chem. Soc.* **2005**, *127*, 15696. (f) Liu, H.; Cun, L.-F.; Mi, A.-Q.; Jiang, Y.-Z.; Gong, L.-Z. *Org. Lett.* **2006**, *8*, 6023. (g) Storer, R. I.; Carrera, D. E.; Ni, Y.; MacMillan, D. W. C. *J. Am. Chem. Soc.* **2006**, *128*, 84. (h) Nakashima, D.; Yamamoto, H. *J. Am. Chem. Soc.* **2006**, *128*, 9626. (i) Kang, Q.; Zhao, Z.-A.; You, S.-L. *J. Am. Chem. Soc.* **2007**, *129*, 1484. (j) Hashimoto, T.; Maruoka, K. *J. Am. Chem. Soc.* **2007**, *129*, 10054. (k) Guo, Q.-S.; Du, D.-M.; Xu, J. *Angew. Chem., Int. Ed.* **2008**, *47*, 759.

(7) Terada and co-workers reported the pioneering catalytic enantioselective direct Mannich-type reaction by using chiral BINOL-derived phosphoric acids. In their catalytic enantioselective reactions, acetylacetone (**7a**) was the sole nucleophile. Moreover, *N*-Boc protection in aldimines is essential for achieving high enantioselectivities. (a) Uraguchi, D.; Terada, M. *J. Am. Chem. Soc.* **2004**, *126*, 5356. (b) Terada, M.; Sorimachi, K.; Uraguchi, D. *Synlett* **2006**, 133. (c) Gridnev, I. D.; Kouchi, M.; Sorimachi, K.; Terada, M. *Tetrahedron Lett.* **2007**, *48*, 497.

(8) (a) Barber, H. J.; Smiles, S. *J. Chem. Soc.* **1928**, 1141. (b) Armarego, W. L. F.; Turner, E. E. *J. Chem. Soc.* **1957**, 13. (c) Takahashi, K.; Fukishi, K. Jpn. Patent 2005132815, 2005.

(9) Reviews for chiral Brønsted acid catalysts: (a) Pihko, P. M. *Angew. Chem., Int. Ed.* **2004**, *43*, 2062. (b) Pihko, P. M. *Lett. Org. Chem.* **2005**, *2*, 398. (c) Akiyama, T.; Itoh, J.; Fuchibe, K. *Adv. Synth. Catal.* **2006**, *348*, 999. (d) Taylor, M. S.; Jacobsen, E. N. *Angew. Chem., Int. Ed.* **2006**, *45*, 1520. (e) Connon, S. J. *Angew. Chem., Int. Ed.* **2006**, *45*, 3909. (f) Akiyama, T. *Chem. Rev.* **2007**, *107*, 5744.

(10) Other recent chiral acid catalysts and acid−base catalysts: (a) Sigman, M. S.; Jacobsen, E. N. *J. Am. Chem. Soc.* **1998**, *120*, 4901. (b) Corey, E. J.; Grogan, M. J. *Org. Lett.* **1999**, *1*, 157. (c) List, B.; Lerner, R. A.; Barbas, C. F., III. *J. Am. Chem. Soc.* **2000**, *122*, 2395. (d) Hodous, B. L.; Fu, G. C. *J. Am. Chem. Soc.* **2002**, *124*, 10006. (e) Huang, Y.; Unni, A. K.; Thadani, A. N.; Rawal, V. H. *Nature* **2003**, *424*, 146. (f) Okino, T.; Hoashi, Y.; Takemoto, Y. *J. Am. Chem. Soc.* **2003**, *125*, 12672. (g) Huang, J.; Corey, E. J. *Org. Lett.* **2004**, *6*, 5027. (h) Ouellet, S. G.; Tuttle, J. B.; MacMillan, D. W. C. *J. Am. Chem. Soc.* **2005**, *127*, 32. (i) Wiskur, S. L.; Fu, G. C. *J. Am. Chem. Soc.* **2005**, *127*, 6176.

(11) (a) Fabbri, D.; Delogu, G.; De Lucchi, O. *J. Org. Chem.* **1993**, *58*, 1748. (b) Bandarage, U. K.; Simpson, J.; Smith, R. A. J.; Weavers, R. T. *Tetrahedron* **1994**, *50*, 3463.

(12) Compound **5** is commercially available from International Laboratory, Interchim, and WaterstoneTech.

(13) In the original literature in ref 11, the Newman−Kwart rearrangement of **3** to **4** was examined at 285−400 °C. Moreover, during the preparation of this manuscript, a 1−400 kg-scale synthesis of aryl *S*-thiocarbamates from aryl *O*-thiocarbamates in microwave reactors was reported by Moseley and co-workers. The industrial synthesis of **1** should be a great advantage. (a) Moseley, J. D.; Lenden, P.; Lockwood, M.; Ruda, K.; Sherlock, J.-P.; Thomson, A. D.; Gilday, J. P. *Org. Process Res. Dev.* **2008**, *12*, 30. (b) Gilday, J. P.; Lenden, P.; Moseley, J. D.; Cox, B. G. *J. Org. Chem.* **2008**, *73*, 3130.

(14) (a) Wallace, T. J.; Schriesheim, A. *Tetrahedron* **1965**, *21*, 2271. (b) Agami, C.; Prince, B.; Puchot, C. *Synth. Commun.* **1990**, *20*, 3289.

(15) 3,3′-Bis[4-(β-naphthyl)phenyl]-substituted chiral binaphthol phosphoric acid catalyst, which was proved to be the most effective in direct Mannich-type reaction by Terada and co-workers, was prepared from (*R*)-BINOL in 31% over seven steps. See ref 7. Also see: Wipf, P.; Jung, J.-K. *J. Org. Chem.* **2000**, *65*, 6319.

(16) (a) Poulsen, T. B.; Alemparte, C.; Saaby, S.; Bella, M.; Jørgensen, K. A. *Angew. Chem., Int. Ed.* **2005**, *44*, 2896. (b) Lou, S.; Taoka, B.; Ting, A.; Schaus, S. E. *J. Am. Chem. Soc.* **2005**, *127*, 11256. (c) Tillman, A. L.; Ye, J.; Dixon, D. J. *Chem. Commun.* **2006**, 1191. (d) Rueping, M.; Sugiono, F.; Schoepke, F. R. *Synlett* **2007**, 1441. (e) Ting, A.; Schaus, S. E. *Eur. J. Org. Chem.* **2007**, 5797.

(17) To understand the character of our catalysts, we also examined some reactions by using the Terada's chiral phosphoric acid catalyst. See the Supporting Information in detail.

(18) Probably, **1**·**2** rather than **1**·$\mathbf{2}_2$ may be the active species in situ, since there should be a dynamic equilibrium among **1**, **1**·**2**, and **1**·$\mathbf{2}_2$ even if there is a large amount of **2** relative to **1** (see eq 1 and Table 2).

(19) House, H. O.; Gannon, W. F. *J. Org. Chem.* **1958**, *23*, 879.

(20) 1,1′-Binaphthyl-2,2′-dicarboxylic acid−$\mathbf{2}_2$ (5 mol %) showed low catalytic activity and low enantioselectivity (<10% ee) in the reactions in Table 3, Scheme 3, and eq 2. Also see ref 6j.

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