

Enantioselective Synthesis of Tertiary α -Hydroxy Phosphonates Catalyzed by Carbohydrate/Cinchona Alkaloid Thiourea Organocatalysts**

Shasha Kong, Weidong Fan, Guiping Wu, and Zhiwei Miao*

In memory of Ruyu Chen

Functionalization of C_{α} -H bonds in phosphonic acid compounds have attracted extensive attention because of their use in pharmaceutical applications^[1] and excellent inhibitory bioactivities towards several important groups of enzymes, including rennin,^[2] HIV protease,^[1b] and various classes of protein tyrosine kinases and phosphatases.^[1c] It has been established that the biological activity of phosphonic acids is largely determined by the absolute configuration of the stereogenic α -carbon atom.^[3] The development of methodologies for their preparation,^[4] particularly in enantiomerically enriched forms has received deserved attention. Although some asymmetric methods for preparing α -hydroxy phosphonates have been described, including both enzymatic^[5] and chemical methods,^[6] these methods are primarily concentrated on the synthesis of secondary α -hydroxy phosphonates. To the best of our knowledge, there are only a few examples of organocatalyst-promoted aldol reactions with acyl phosphonates to produce tertiary α -hydroxy phosphonates.^[7]

For the past decade, hydrogen-bond catalysis has received a great deal of attention because of their high asymmetry-inducing ability and ready availability.^[8] Chiral thiourea-based organic molecules have proven to be extraordinarily useful as catalysts for the enantioselective activation of imine and carbonyl derivatives toward nucleophilic addition.^[9] Bifunctional cinchona alkaloid derivatives possessing hydrogen-bonding moieties, such as thiourea, have been widely used in a diverse range of asymmetric organic reactions in recent years.^[10] In the meantime, a large number of carbohydrates have been used as ligands for numerous enantioselective reactions.^[11] Additionally, organocatalysts derived from

the combination of carbohydrates and tertiary amine thioureas have been reported in recent years.^[12] However, there is no precedent for the combination of both cinchona alkaloid and carbohydrate moieties in a single chiral organic molecule for asymmetric reactions. The objective of this work is to explore the viability of integrating cinchona alkaloid and carbohydrate fragments into a unique thiourea derivative for enantioselective addition of trimethylsilyl cyanide (TMSCN) to acylphosphonates to produce tertiary α -hydroxy phosphonates.

The catalytic asymmetric cyanation of carbonyl compounds is a well-studied reaction in asymmetric catalysis.^[13] We initially investigated the use of catalysts **1–6** (Figure 1) for

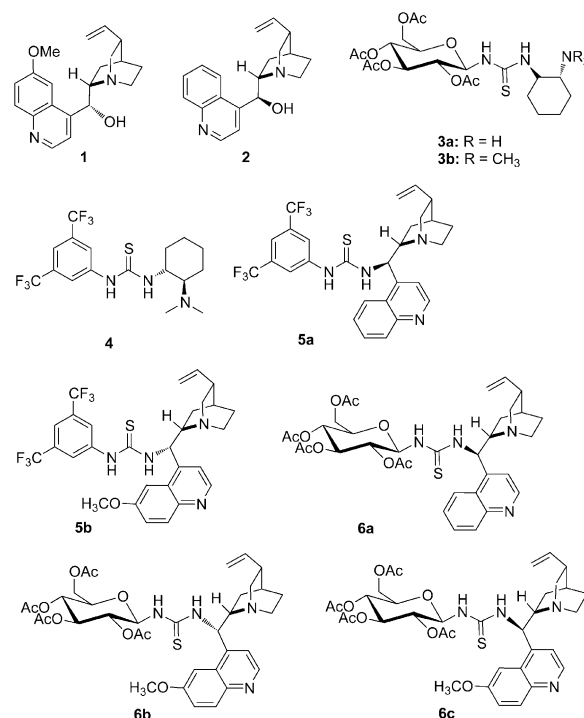


Figure 1. Catalyst structures.

the catalytic asymmetric addition reaction of TMSCN (**8**) to diethyl benzoyl phosphonate (**7a**) as a model reaction. Catalyst screening was performed in toluene in the presence of 10 mol % of the catalyst at -78°C for 24 hours. Cinchona alkaloid derivatives (**1** and **2**) and bifunctional thioureas (**3–6**) bearing different chiral diamine skeletons were chosen as the

[*] S. S. Kong, W. D. Fan, G. P. Wu, Prof. Dr. Z. W. Miao
State Key Laboratory and Institute of Elemento-Organic Chemistry,
Nankai University
Weijin Road 94, Tianjin 300071 (P.R. China)
E-mail: miaozhiwei@nankai.edu.cn

Prof. Dr. Z. W. Miao

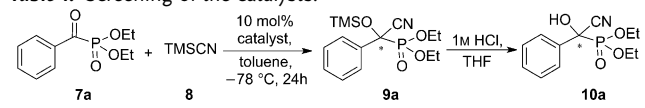
Key Laboratory of Bioorganic Phosphorus Chemistry & Chemical
Biology (Ministry of Education), Tsinghua University
Qinghuayuan, Beijing 100084 (P.R. China)

[**] We thank the National Natural Science Foundation of China
(21072102), the Committee of Science and Technology of Tianjin
(11JCYBJC04200), and the State Key Laboratory of Elemento-
Organic Chemistry in Nankai University for financial support.

Supporting information for this article is available on the WWW
under <http://dx.doi.org/10.1002/ange.201204287>.

catalyst candidates (Table 1).^[14] The reaction of the phosphonate **7a** with **8** in the presence of the catalyst **1** in toluene as solvent at -78°C afforded the desired addition product **9a** with 29% *ee* and in 89% yield (Table 1, entry 1). The

Table 1: Screening of the catalysts.^[a]



Entry	Catalyst	Solvent	Yield [%] ^[b]	<i>ee</i> [%] ^[c]
1	1	PhCH ₃	89	29
2	2	PhCH ₃	85	-17
3	3a	PhCH ₃	81	-14
4	3b	PhCH ₃	89	-57
5	4	PhCH ₃	85	-47
6	5a	PhCH ₃	87	-43
7	5b	PhCH ₃	81	45
8	6a	PhCH ₃	80	-69
9	6b	PhCH ₃	90	81
10 ^[d]	6b	PhCH ₃	88	72
11	6b	CH ₂ Cl ₂	88	49
12	6b	THF	84	68
13	6b	MTBE	85	71
14	6b	MTBE/PhCH ₃ ^[e]	94	79
15	6b	MTBE/PhCH ₃ ^[f]	90	77
16 ^[g]	6b	PhCH ₃	89	70
17 ^[h]	6b	PhCH ₃	90	83
18	6b	PhCH ₃	90	81 ^[i]

[a] Unless otherwise specified, all reactions were carried out using diethyl benzoylphosphonate (**7a**; 0.5 mmol, 1 equiv) and TMSCN (**8**; 0.6 mmol, 1.2 equiv) in 2 mL solvent with 10 mol% of the catalyst at -78°C for 24 h. [b] Yield of the isolated product **9a** after column chromatography. [c] Determined by HPLC (Chiralcel AS-H) analysis of **9a**. [d] The reaction was performed at -40°C for 10 h. [e] $\nu/\nu = 1:1$. [f] $\nu/\nu = 2:1$. [g] 5 mol% of catalyst **6b** was used. [h] 15 mol% of catalyst **6b** was used. [i] Determined by HPLC (Chiralcel AD-H) analysis of **10a**. THF = tetrahydrofuran. MTBE = methyl tertbutyl ether.

replacement of **1** with cinchonine **2** as the catalyst resulted asymmetric induction in the opposite sense with up to 17% *ee* and in a similar yield (entry 2). The catalyst **3a** could also catalyze this reaction to provide the desired α -hydroxy phosphonate **9a** in 81% yield, but the enantioselectivity was rather poor (entry 3). Moreover, the *N,N*-dimethyl-protected thiourea catalyst **3b** was employed and effectively provided the silylcyanation product in 89% and 57% *ee* (entry 4). This result suggested that a tertiary amine thiourea structure is essential to effect this reaction. Next, we explored the 3,5-bis(trifluoromethyl)phenylthiourea **4** and cinchona-based thioureas **5a** and **5b** as catalysts, and found that the desired products were obtained in yields of 81–87% with moderate *ee* values of 43–47% (entries 5–7). Consequently, the carbohydrate/cinchona alkaloid thiourea derivatives **6a** and **6b** were tested, and a better result (90% yield, 81% *ee*) was obtained with **6b** (entries 8 and 9). This result indicated that compared with **5a** and **5b**, the carbohydrate/cinchona alkaloid thioureas **6a** and **6b** had an advantage in the catalytic asymmetric reaction as a result of the chiral auxiliary. When the reaction was carried out at -40°C using **6b** as the catalyst, a lower enantiomeric excess value of 72% was obtained

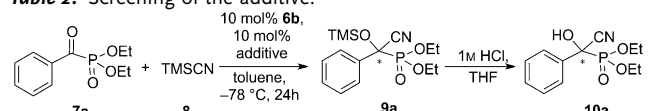
(entry 10), therefore **6b** was selected as the best catalyst for additional optimization.

To optimize the reaction conditions further, the solvent effects were investigated with **6b**, and the best result was obtained in toluene. When the reaction was performed in CH₂Cl₂ or THF, a lower *ee* value was obtained (Table 1, entries 11 and 12). A similar result was obtained when the reaction was performed in methyl *tert*-butyl ether (MTBE; entry 13). Further screening indicated that the reaction conducted in a mixture of MTBE/PhCH₃ (ν/ν , 1:1) or MTBE/PhCH₃ (ν/ν , 2:1) offered a better reaction yield with a moderate enantioselectivity (entries 14 and 15). Adjusting the catalyst loading demonstrated only a small influence on the outcome of the enantioselectivity of the reaction. The use of 5 mol% of **6b** led to a slight decrease on enantioselectivity and yield (entry 16). Increasing the amount of the catalyst from 10 to 15 mol% did not affect the yield, but resulted in a higher *ee* value (entry 17). Acid hydrolysis of the trimethylsilyl oxycyanophosphonate **9a** can deliver the α -hydroxy- α -cyanophosphonate **10a** in quantitative yield without any purification (entry 18).

To further improve the reactivity and enantioselectivity, the effect of additives was investigated. Alcohol additives were reported to improve the reactivity and enantioselectivity on cyanosilylation of carbonyl groups.^[15] In our investigation, the beneficial effects of CF₃CH₂OH, CH₃OH, *i*PrOH, and *t*BuOH were observed (Table 2, entries 1–4). After screening different kinds of aromatic phenolic compounds (entries 5–10), it was found that *p*-nitrophenol gave superior results in terms of reactivity and enantioselectivity (entry 7). When using 3 mL toluene as the solvent and a prolonged reaction time of 36 hours, the optimal result was gained (entry 11). Thus, the optimal reaction conditions for this transformation were determined to be 0.5 mmol acylphosphonate, 1.2 equivalents of TMSCN, 10 mol% of **6b** combined with 10 mol% of *p*-nitrophenol in 3 mL toluene at -78°C for 36 hours.

Based on the above optimization efforts, the substrate scope of this reaction was investigated. As shown in Table 3,

Table 2: Screening of the additive.^[a]



Entry	Additive	Yield [%] ^[b]	<i>ee</i> [%] ^[c]
1	CF ₃ CH ₂ OH	97	81
2	CH ₃ OH	95	82
3	<i>i</i> PrOH	97	84
4	<i>t</i> BuOH	98	85
5	2,4-di- <i>tert</i> -butylphenol	94	79
6	2,4-dichlorophenol	95	77
7	4-nitrophenol	94	85
8	3,5-dinitrophenol	98	82
9	1,4-dihydroxybenzene	95	83
10	4-nitrobenzoic acid	95	81
11 ^[d]	4-nitrophenol	90	91

[a] Reactions were carried out on a 0.5 mmol scale with 1.2 equiv of TMSCN in 2 mL of toluene. [b] Yield of isolated **9a** after column chromatography. [c] Determined by HPLC (Chiralcel AD-H) analysis of **10a**. [d] The reaction time is 36 h in 3 mL of toluene.

Table 3: Scope of the reaction.^[a]

$ \begin{array}{c} \text{O} \\ \parallel \\ \text{R}^1-\text{C}-\text{P}(\text{OR}^2)_3 \\ \text{7a-h} \end{array} + \text{TMSCN} \xrightarrow[\text{toluene, } -78^\circ\text{C, 36 h}]{\text{10 mol\% 6b, 10 mol\% } p\text{-nitrophenol}} \begin{array}{c} \text{O} \quad \text{CN} \\ \parallel \quad \diagup \\ \text{R}^1-\text{C}-\text{P}(\text{OR}^2)_3 \\ \text{9a-h} \end{array} \xrightarrow[\text{THF}]{\text{1M HCl}} \begin{array}{c} \text{HO} \quad \text{CN} \\ \parallel \quad \diagup \\ \text{R}^1-\text{C}-\text{P}(\text{OR}^2)_3 \\ \text{10a-h} \end{array} $						
Entry	Product	R ¹	R ²	t [h]	Yield [%] ^[b]	ee [%] ^[c]
1	10b	C ₆ H ₅	Me	48	85	99
2	10c	<i>p</i> -ClC ₆ H ₄	Me	48	82	86
3	10d	<i>p</i> -CH ₃ C ₆ H ₄	Me	36	89	94
4	10e	<i>p</i> -BrC ₆ H ₄	Me	48	89	93
5	10f	<i>p</i> -FC ₆ H ₄	Me	36	88	93
6	10g	<i>p</i> -CH ₃ OC ₆ H ₄	Me	36	80	89
7	10h	<i>m</i> -CH ₃ C ₆ H ₄	Me	48	89	92
8	10a	C ₆ H ₅	Et	36	90	91
9	10i	<i>p</i> -ClC ₆ H ₄	Et	36	85	84
10	10j	<i>p</i> -CH ₃ C ₆ H ₄	Et	36	85	83
11	10k	<i>p</i> -BrC ₆ H ₄	Et	36	90	87
12	10l	<i>p</i> -FC ₆ H ₄	Et	36	87	86
13	10m	<i>p</i> -CH ₃ OC ₆ H ₄	Et	36	85	86
14	10n	<i>m</i> -CH ₃ C ₆ H ₄	Et	36	83	85
15	10o	<i>o</i> -CH ₃ OC ₆ H ₄	Et	36	85	58
16	10p	<i>o</i> -CH ₃ OC ₆ H ₄	Me	36	86	56
17	10q	C ₂ H ₅	Et	36	80	27
18	10r	C ₂ H ₅	Me	36	82	58
19	10s	<i>trans</i> -PhCH=CH	Et	36	85	93
20	10t ^[d]	C ₆ H ₅	Et	36	85	−94

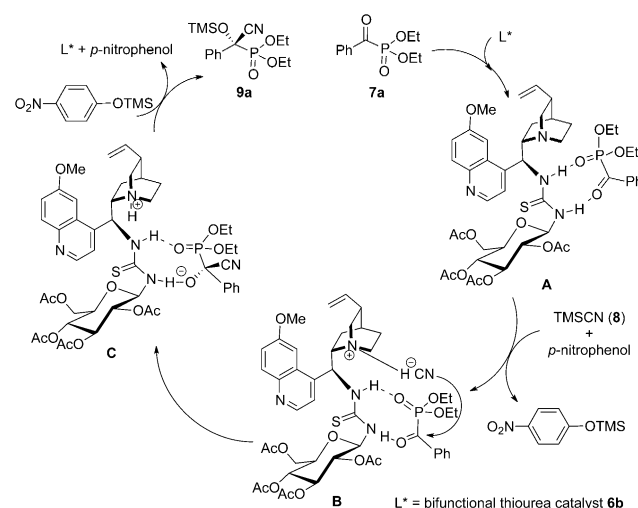
[a] Reaction conditions: α -ketophosphonates **7** (0.5 mmol), TMSCN (**8**; 0.6 mmol), in 3 mL of toluene at -78°C in the presence of 10 mol % of the catalyst **6b** and 10 mol % *p*-nitrophenol as additive for 36 h. [b] Yield of isolated product after silica gel chromatography of **9**. [c] Determined by HPLC analysis of **10** using a chiral stationary phase. [d] 10 mol % of catalyst **6c** was employed.

a broad range of α -ketophosphonates were subjected to the addition reaction, and converted into the corresponding tertiary α -hydroxy phosphonates in high yields with moderate to good enantioselectivities. A variety of α -ketophosphonates (**7**) bearing aromatic rings with electron-donating and electron-withdrawing groups at either the *para* or *meta* position underwent the reaction to afford high enantioselectivities ranging from 83 to 99% *ee* (Table 3, entries 1–14). The enantioselectivity was dependent upon the size of the R² group. When the bulk of R² group was increased from methyl to ethyl, a lower enantioselectivity resulted (entries 8–14). Remarkably, when *ortho*-methoxybenzoyl phosphonate was employed in this reaction with the same catalyst loading, the reaction proceeded in high yield and with low enantioselectivity (entries 15 and 16). When aliphatic α -ketophosphonates were employed as substrates, the reaction gave the corresponding products with poor enantiomeric excesses and moderate yields (entries 17 and 18). α -Hydroxy phosphonates having unsaturated side chains are very useful, as the side chain can be elaborated to introduce other functional groups.^[16] Thus, we briefly studied the addition reaction of diethyl cinnamoyl phosphonate. The reaction proceeded smoothly at -78°C , and the desired product was obtained in 85% yield and 93% *ee* (entry 19). Although for this specific substrate Michael addition is possible, no such product was observed in the crude reaction mixture. Notably, the chiral catalyst **6c** exhibited a similar level of stereoselec-

tivity with an opposite sense of asymmetric induction and up to 94% *ee* (entry 20).

To determine the absolute configuration of the main isomer of TMSCN addition to the α -ketophosphonates **7**, a single-crystal X-ray diffraction study of **10b** was performed.^[17] The molecular structure of **10b** shows that the absolute configuration of the α -hydroxy phosphonate product is *S*.

A possible mechanism for the reaction is shown in Scheme 1. In complex **A** α -ketophosphonate coordinates to the thiourea moiety of bifunctional catalyst **6b** through



Scheme 1. Plausible reaction mechanism.

a hydrogen-bonding interaction. The role of the *p*-nitrophenol additive is presumably to generate HCN as the active nucleophile in the addition reaction. The nucleophilic attack of cyanide (CN[−]) from the Si face of the α -ketophosphonate leads to the formation of the *S*-configured enantiomer as the major product. The attack of cyanide to the *Re* face of the α -ketophosphonate is restricted by the cinchona alkaloid scaffold of the catalyst, and the carbohydrate moiety serves as the chiral auxiliary. The mechanism indicates that the thiourea and carbohydrate moieties as well as cinchona alkaloid scaffold of the bifunctional catalyst play a significant role in controlling the enantioselectivity of the addition reaction.

To further investigate the mechanism, the formation of **9a** was monitored by ³¹P NMR spectroscopy as shown in Figure 2. The starting **7a** in toluene showed signal in the ³¹P NMR spectrum at $\delta = -1.27$ ppm. After catalyst **6b** (0.0356 g, 10 mol %) was added to the solution of **7a**, the peak shifted from $\delta = -1.27$ to -1.12 ppm as complex **A** is formed; a new single peak at $\delta = 7.26$ ppm also appeared. The new single peak was assigned as the decomposition product, diethyl phosphite, of **7a**. When TMSCN and *p*-nitrophenol were added to the mixture, the expected nucleophilic addition product was produced (single peak at $\delta = 12.00$ ppm) in 30 minutes. In the meantime, there are two intermediates that appeared during the synthesis of **9a**. The signals at $\delta_p = -2.14$ and $\delta_p = 12.95$ ppm may belong to intermediates **B** and **C**,

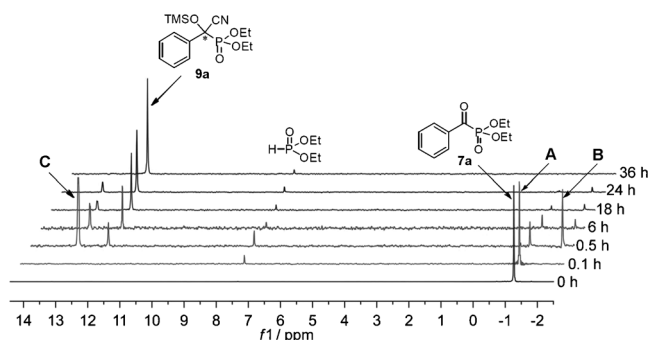


Figure 2. Time-elapsed ^{31}P NMR spectra for the synthesis of **9a**.

respectively. As time progressed, the ^{31}P NMR signals of the starting material disappeared gradually and the signals of **9a** (single peak at $\delta = 12.00$ ppm) increased. The reaction was almost complete after 36 hours according to the ^{31}P NMR spectra (Figure 2).

In conclusion, we have developed a novel carbohydrate/cinchonine-based thiourea as an organocatalyst for the catalytic asymmetric addition reaction of α -ketophosphonates and TMSCN with good to excellent enantiomeric excess and high yields. The initial product, the TMS ether cyanophosphonate, can readily be transformed into cyanohydrin phosphonate by mild acidic hydrolysis. A plausible reaction mechanism has been proposed to explain the origin of the asymmetric induction. Additional applications of these catalysts to other asymmetric reactions are currently underway in our laboratory.

Received: June 2, 2012

Published online: July 29, 2012

Keywords: asymmetric synthesis · carbohydrate · organocatalysis · tertiary α -hydroxy phosphonates · thiourea

- [1] a) R. L. Hilderbrand, T. O. Henderson, *The Role of Phosphonates in Living Systems*, CRC, Boca Raton, **1983**; b) B. Stowasser, K. H. Budt, J. Q. Li, A. Peyman, D. Ruppert, *Tetrahedron Lett.* **1992**, 33, 6625–6628; c) M. L. Moore, G. B. Dreyer, *Perspect. Drug Discovery Des.* **1993**, 1, 85–108; d) B. Z. Leder, H. M. Kronenberg, *Gastroenterology* **2000**, 119, 866–869; e) M. L. Peters, M. Leonard, A. A. Licata, *Clev. Clin. J. Med.* **2001**, 68, 945–951.
- [2] a) J. F. Dellaria Jr., R. G. Maki, H. H. Stein, J. Cohen, D. Whittern, K. Marsh, D. J. Hoffman, J. J. Plattner, T. J. Perun, *J. Med. Chem.* **1990**, 33, 534–542; b) M. Tao, R. Bihovsky, G. J. Wells, J. P. Mallamo, *J. Med. Chem.* **1998**, 41, 3912–3926.
- [3] a) A. B. Smith, K. M. Yager, C. M. Taylor, *J. Am. Chem. Soc.* **1995**, 117, 10879–10888; b) O. I. Kolodiazny, *Tetrahedron: Asymmetry* **2005**, 16, 3295–3340.
- [4] A. S. Demir, O. Reis, M. Kayalar, S. Eymur, B. Reis, *Synlett* **2006**, 3329–3333.
- [5] a) P. Kafarski, B. Lecjak, *J. Mol. Catal. B* **2004**, 29, 99–104; b) F. Wuggenig, F. Hammerschmidt, *Monatsh. Chem.* **1998**, 129, 423–436; c) A. Maly, B. Lejczak, P. Kafarski, *Tetrahedron: Asymmetry* **2003**, 14, 1019–1024.
- [6] For selected examples on chemical methods: a) D. F. Wiemer, *Tetrahedron* **1997**, 53, 16609–16644; b) H. Gröger, B. Hammer, *Chem. Eur. J.* **2000**, 6, 943–948; c) D. M. Cermak, Y. M. Du, D. F. Wiemer, *J. Org. Chem.* **1999**, 64, 388–393; d) T. Mandal, S. Samanta, C. G. Zhao, *Org. Lett.* **2007**, 9, 943–945; e) X. Zhou, X. H. Liu, X. Yang, D. J. Shang, J. G. Xin, X. M. Feng, *Angew. Chem.* **2008**, 120, 398–400; *Angew. Chem. Int. Ed.* **2008**, 47, 392–394; f) F. Yang, D. B. Zhao, J. B. Lan, P. H. Xi, L. Yang, S. H. Xiang, J. S. You, *Angew. Chem.* **2008**, 120, 5728–5731; *Angew. Chem. Int. Ed.* **2008**, 47, 5646–5649.
- [7] a) S. Samanta, C. G. Zhao, *J. Am. Chem. Soc.* **2006**, 128, 7442–7443; b) V. B. Gondí, K. Hagihara, V. H. Rawal, *Angew. Chem.* **2009**, 121, 790–793; *Angew. Chem. Int. Ed.* **2009**, 48, 776–779.
- [8] Recent reviews on enantioselective reactions catalyzed by hydrogen-bond donors: a) J. D. McGilvra, V. B. Gondí, V. H. Rawal, *Enantioselective organocatalysis* (Ed.: P. I. Dalko), Wiley-VCH, Weinheim, **2007**, pp. 189–254; b) A. G. Doyle, E. N. Jacobsen, *Chem. Rev.* **2007**, 107, 5713–5743; c) X. Yu, W. Wang, *Chem. Asian J.* **2008**, 3, 516–532; d) Y. Takemoto, *Org. Biomol. Chem.* **2005**, 3, 4299–4306.
- [9] For examples of hydrogen-bond-catalyzed asymmetric reactions of imines and carbonyl electrophiles, see: a) M. S. Sigman, P. Vachal, E. N. Jacobsen, *Angew. Chem.* **2000**, 112, 1336–1338; *Angew. Chem. Int. Ed.* **2000**, 39, 1279–1281; b) B. M. Nugent, R. A. Yoder, J. N. Johnston, *J. Am. Chem. Soc.* **2004**, 126, 3418–3419; c) J. C. Wilt, M. Pink, J. N. Johnston, *Chem. Commun.* **2008**, 4177–4179; d) D. Nakashima, H. Yamamoto, *J. Am. Chem. Soc.* **2006**, 128, 9626–9627; e) M. Terada, K. Soga, N. Momiyama, *Angew. Chem.* **2008**, 120, 4190–4193; *Angew. Chem. Int. Ed.* **2008**, 47, 4122–4125.
- [10] For selected examples of the bifunctional Cinchona alkaloid derivatives, see: a) B. Vakulya, S. Varga, A. Csámpai, T. Soós, *Org. Lett.* **2005**, 7, 1967–1969; b) A. Pesciulli, Y. Gun'ko, S. J. Connon, *J. Org. Chem.* **2008**, 73, 2454–2457; c) S. H. McCooley, S. J. Connon, *Angew. Chem.* **2005**, 117, 6525–6528; *Angew. Chem. Int. Ed.* **2005**, 44, 6367–6370; d) P. Dinér, M. Nielsen, S. Bertelsen, B. Niess, K. A. Jorgensen, *Chem. Commun.* **2007**, 3646–3648; e) S. H. McCooley, T. McCabe, S. J. Connon, *J. Org. Chem.* **2006**, 71, 7494–7497; f) S. H. Oh, H. S. Rho, J. W. Lee, J. E. Lee, S. H. Youk, J. Chin, C. E. Song, *Angew. Chem.* **2008**, 120, 7990–7993; *Angew. Chem. Int. Ed.* **2008**, 47, 7872–7875.
- [11] M. Diéguez, O. Pàmies, C. Claver, *Chem. Rev.* **2004**, 104, 3189–3215.
- [12] a) X. W. Pu, F. Z. Peng, H. B. Zhang, Z. H. Shao, *Tetrahedron* **2010**, 66, 3655–3661; b) A. Puglisi, M. Benaglia, L. Raimondi, L. Lay, L. Poletti, *Org. Biomol. Chem.* **2011**, 9, 3295–3302; c) P. Gao, C. G. Wang, Y. Wu, Z. H. Zhou, C. C. Tang, *Eur. J. Org. Chem.* **2008**, 4563–4566.
- [13] For a review on the synthetic utility of cyanohydrins see: R. J. H. Gregory, *Chem. Rev.* **1999**, 99, 3649–3682.
- [14] For synthesis of the catalysts see the Supporting Information.
- [15] a) M. Hayashi, N. Matsuda, N. Oguni, *J. Chem. Soc. Perkin Trans. 1* **1992**, 3135–3140; b) J. M. Brunel, O. Legrand, G. Buono, *Tetrahedron: Asymmetry* **1999**, 10, 1979–1984; c) H. Deng, M. P. Isler, M. L. Snapper, A. M. Hoveyda, *Angew. Chem.* **2002**, 114, 1051–1054; *Angew. Chem. Int. Ed.* **2002**, 41, 1009–1012.
- [16] For an example of the synthesis of racemic tertiary *R*-configured hydroxy phosphonates by allylation, see: D. F. Wiemer, D. Y. Kim, *Tetrahedron Lett.* **2003**, 44, 2803–2805.
- [17] See the Supporting Information for details on the crystal structure of **10b**. The crystallographic data for the structural analysis of compound **10b** have been deposited at the Cambridge Crystallographic Data Centre as No. CCDC 874973 it 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.