Chiral Phosphoric Acid Catalyzed Enantioselective Allylation of Aldehydes with Allyltrichlorosilane

Cheng, Ke[a,b](程柯) Fan, Tiantian[a](范甜甜) Sun, Jian*[,a](孙健)

[a] *Natural Products Research Center, Chengdu Institute of Biology, Chinese Academy of Sciences, Chengdu, Sichuan 610041, China*

[b] *Chengdu Institute of Organic Chemistry, Chinese Academy of Sciences, Chengdu, Sichuan 610041, China*

Easily accessible chiral phosphoric acid **1b** has been applied as efficient organocatalyst for the asymmetric allylation of aldehydes with allyltrichlorosilane. In the presence of 20 mol% of **1b**, the allylation of a broad range of aldehydes proceeded smoothly to give the corresponding homoallylic alcohol with up to 87% *ee* and 97% yield.

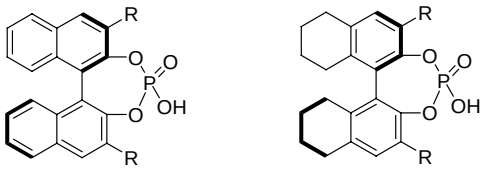
Keywords phosphoric acid, allylation, aldehydes, allyltrichlorosilane

Introduction

The asymmetric allylation of aldehydes is one of the most straightforward methods for the preparation of stereogenic homoallylic alcohols.[1] Activation of allyl trichlorosilane by a catalytic amount of chiral Lewis base has been shown to be an efficient asymmetric allylation method. In 1994, the first example of this transformation was reported by Denmark using chiral phosphoramide derivatives as the Lewis base catalyst.[2] Since then, several different types of chiral Lewis base catalysts have been developed, including phosphoramides,[3-5] formamides,[6-8] *N*-oxides,[9-12] and sulfoxides.[13] Herein, we report that chiral BINOL-derived phosphoric acids, a new type of organocatalysts that have recently emerged as excellent promoters for a number of enantioselective transformations,[14] could also effectively catalyze the asymmetric allylation of aldehydes.

Results and discussion

Initial attempts to evaluate easily available chiral phosphoric acid **1a** as catalyst for the enantioselective allylation of benzaldehyde **2a** with allyltrichorosilane in toluene at −20 ℃ gave moderate results (76% yield and 45% *ee*). We then prepared a series of chiral (*R*)-BINOL-phosphoric acid derivatives (Figure 1) and tested their efficacies in the allylation of **2a** with allyltrichlorosilane. As shown in Table 1, catalyst **1b** bearing 3,3'-dimethyl substitutents exhibited the best reactivity and enantioselectivity, affording 93% yield and 87% *ee*, whereas **1d** with 3,3'-diphenyl substituents had almost no detectable reactivity (Entry 4). Catalysts **1f**—**1h** with a partial hydrogenated binaphthyl backbone exhibited substantially lower reactivity and enantioselectivity than their counterparts **1a**—**1c** (Entries 6—8). Catalyst **1b**

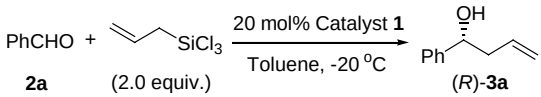


(*R*)-**1a**, R = H
(*R*)-**1b**, R = CH_3
(*R*)-**1c**, R = Br
(*R*)-**1d**, R = Ph
(*R*)-**1e**, R = I

(*R*)-**1f**, R = H
(*R*)-**1g**, R = CH_3
(*R*)-**1h**, R = Br

Figure 1 Structure of the catalysts.

Table 1 Enantioselective allylation of benzaldehyde **2a** with allyltrichlorosilane catalyzed by **1**[a]



2a (2.0 equiv.) (*R*)-**3a**

Entry	Cat.	Yield[b]/%	*ee*[c,d]/%
1	**1a**	76	45
2	**1b**	93	87
3	**1c**	65	77
4	**1d**	N.R.	
5	**1e**	36	67
6	**1f**	66	32
7	**1g**	44	69
8	**1h**	25	35

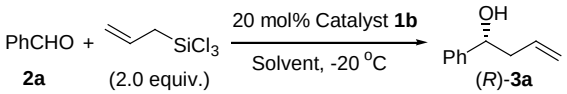
[a] Unless specified otherwise, reactions were carried out with 2.0 equiv. of allyltrichlorosilane on a 0.1 mmol scale for 48 h. [b] Isolated yield based on benzaldehyde. [c] Determined by HPLC. [d] Product **3a** was *R* configured in all cases, as revealed by comparison of the optical rotation with literature data.[2]

* E-mail: sunjian@cib.ac.cn; Tel.: 0086-028-85211220; Fax: 0086-028-85222753
Received March 12, 2011; revised and accepted April 15, 2011.
Project supported by the National Natural Science Foundation of China (Nos. 20732006 and 20972152).

exhibiting the best overall efficacy was then selected for further studies.

To optimize the reaction conditions, different solvents were examined for the **1b**-catalyzed allylation of **2a**. When toluene was replaced with either dichloromethane, chloroform or dichloroethane, a dramatic decrease was observed in both reactivity and enantioselectivity (Table 2, Entries 2—4). Although tetrachlorocarbon (CCl_4) as solvent can also afford good enantioselectivity, only 30% yield was obtained in 48 h (Entry 5). Lowering the reaction temperature from −20 to −40 ℃ had slightly beneficial effects on enantioselectivity, but caused unacceptable loss of reactivity (Entry 6).

Table 2 Enantioselective allylation of benzaldehyde **2a** with allyltrichlorosilane catalyzed by **1b** under different conditions



Entry	*T*/℃	Solvent	Yield[b]/%	*ee*[c]/%
1	−20	Toluene	93	87
2	−20	CH_2Cl_2	76	49
3	−20	$CHCl_3$	52	48
4	−20	$ClCH_2CH_2Cl$	78	23
5	−20	CCl_4	30	83
6	−40	Toluene	34	88

[a] Unless specified otherwise, reactions were carried out with 2.0 equiv. of allyltrichlorosilane on a 0.1 mmol scale for 48 h. [b] Isolated yield based on benzaldehyde. [c] Determined by HPLC.

After having established the optimal reaction conditions, we set out to examine the substrate spectrum of the present catalyst system. In the presence of 20 mol% **1b**, various aldehydes were checked (Table 3).[15] Generally, the aromatic aldehydes with different electronic natures all underwent smooth asymmetic allylations to furnish the desired homoallylic alcohol products in good to excellent yields with moderate to good enantioselectivities. Benzaldehyde **2a** gave the highest enantioselectivity (87% *ee*, Entry 1). The aliphatic aldehyde **2n** could also be allylated to afford the desired product **3n** in good yield, albeit with moderate enantioselectivity (Entry 14).

To gain some insights into the possible mechanism

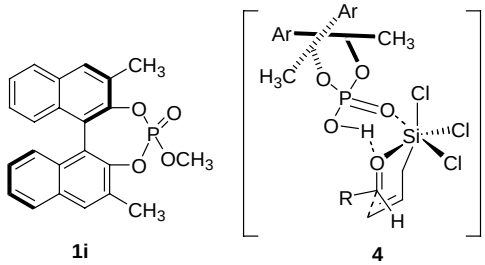
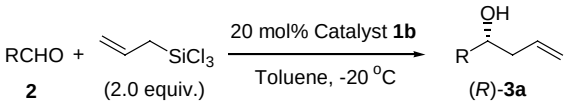


Figure 2 A possible transition structure.

Table 3 Enantioselective allylation of various benzaldehydes **2** with allyltrichlorosilane catalyzed by **1b**[a]



Entry		R	Yield[b]/%	*ee*[c]/%
1	**2a**	C_6H_5	93	87
2	**2b**	4-FC_6H_4	96	82
3	**2c**	4-BrC_6H_4	96	78
4	**2d**	4-$CH_3C_6H_4$	98	83
5	**2e**	4-$CH_3OC_6H_4$	72	62
6	**2f**	4-$NO_3C_6H_4$	84	72
7	**2g**	4-CNC_6H_4	95	68
8	**2h**	3-$CH_3C_6H_4$	84	65
9	**2i**	3-ClC_6H_4	74	59
10	**2j**	3-$CF_3C_6H_4$	68	63
11	**2k**	2-ClC_6H_4	95	79
12	**2l**	2-BrC_6H_4	98	84
13	**2m**	2-Naphthyl	75	62
14	**2n**	$Ph(CH_2)_2$	88	43

[a] Unless specified otherwise, reactions were carried out with 2.0 equiv. of allyltrichlorosilane on a 0.1 mmol scale for 48 h. [b] Isolated yield based on aldehyde. [c] Determined by HPLC.

for the present reaction system, the chiral methylphosphate **1i** was also tested as catalyst and was found to have no activity towards the model allylation of benzaldehyde **2a**, suggesting that the acidic functionality is crucial for the catalysis. Thus, we proposed a plausible bicyclic transition structure **4** featuring a hexavalent silicon species and a hydrogen bond between the phosphoric acid and the aldehyde.

Conclusion

In summary, chiral phosphoric acid **1b** has been applied as an efficient organocatalyst for the enantioselective allylation of aldehydes. This easily prepared catalyst promoted the allylation of a broad range of aldehydes in high yield (up to 98%) and good enantioselectivities (up to 87%). The detailed mechanism and the further application of the present system are under active investigation.

References and note

1 For leading reviews, see:
(a) Denmark, S. E.; Almstead, N. G. In *Modern Carbonyl Chemistry*, Ed.: Otera, J., Wiley-VCH, Weinheim, **2000**, Chapter h10, pp. 299—402.
(b) Chemler, S. R.; Roush, W. R. In *Modern Carbonyl Chemistry*, Ed.: Otera, J., Wiley-VCH, Weinheim, **2000**, Chapter 11, pp. 403—490.
(c) Yamamoto, Y.; Asao, N. *Chem. Rev.* **1993**, *93*, 2207.
(d) Helmchen, G.; Hoffmann, R.; Mulzer, J.; Schaumann, E.

In *Stereoselective Synthesis Methods of Organic Chemistry* (*Houben-Weyl*), Vol. 3, 21st ed., Thieme Stuttgart, New York, **1996**, pp. 1357—1602.
(e) Denmark, S. E.; Fu, J. *Chem. Rev*. **2003**, *103*, 2763.
2 Denmark, S. E.; Coe, D. M.; Pratt, N. E.; Griedel, B. D. *J. Org. Chem*. **1994**, *59*, 6161.
3 (a) Iseki, K.; Kuroki, Y.; Takahashi, M.; Kishimoto, S.; Kobayashi, Y. *Tetrahedron* **1997**, *53*, 3513.
(b) Wadamoto, M.; Ozasa, N.; Yanagisawa, A.; Yamamoto, H. *J. Org. Chem*. **2003**, *63*, 5593.
4 (a) Denmark, S. E.; Fu, J. *J. Am. Chem. Soc*. **2000**, *122*, 12021.
(b) Denmark, S. E.; Fu, J. *J. Am. Chem. Soc*. **2001**, *123*, 9488.
(c) Denmark, S. E.; Fu, J. *Org. Lett*. **2002**, *4*, 1951.
(d) Denmark, S. E.; Fu, J.; Coe, D. M.; Su, X.; Pratt, N. E.; Griedel, B. D. *J. Org. Chem*. **2006**, *71*, 1513.
(e) Denmark, S. E.; Pham, S. M.; Stavenger, R. A.; Su, X.; Wong, K.-T.; Nishigaichi, Y. *J. Org. Chem*. **2006**, *71*, 3904.
5 Hellwig, J.; Belser, T.; Müller, J. F. K. *Tetrahedron Lett*. **2001**, *42*, 5417.
6 (a) Kobayashi, S.; Nishio, K. *Tetrahedron Lett*. **1993**, *34*, 3453.
(b) Kobayashi, S.; Nishio, K. *J. Org. Chem*. **1994**, *59*, 6620.
(c) Kobayashi, S.; Nishio, K. *Synthesis* **1994**, 457.
7 (a) Iseki, K.; Mizuno, S.; Kurki, Y.; Kobayashi, Y. *Tetrahedron Lett*. **1998**, *39*, 2767.
(b) Iseki, K.; Mizuno, S.; Kurki, Y.; Kobayashi, Y. *Tetrahedron* **1999**, *55*, 977.
(c) Malkov, A. V.; Mariani, A.; MacDougall, K. N.; Koèovský, P. *Org. Lett*. **2004**, *6*, 2253.
8 Kobayashi, S.; Nishio, K. *Chem. Lett*. **1994**, 1773.
9 (a) Nakajima, M.; Saito, M.; Shiro, M.; Hashimoto, S. *J. Am. Chem. Soc*. **1998**, *120*, 6419.
(b) Nakajima, M.; Saito, M.; Shiro, M.; Hashimoto, S. *Chem. Pharm. Bull*. **2000**, *48*, 306.
10 (a) Shimada, T.; Kina, A.; Ikeda, S.; Hayashi, T. *Org. Lett*. **2002**, *4*, 2799.
(b) Shimada, T.; Kina, A.; Hayashi, T. *J. Org. Chem*. **2003**, *68*, 6329.
(c) Kina, A.; Shimada, T.; Hayashi, T. *Adv. Synth. Catal*. **2004**, *346*, 1169.
(d) Traverse, J. F.; Zhao, Y.; Hoveyda, A. H.; Snapper, M. L. *Org. Lett*. **2005**, *7*, 3151.
(e) Hrdina, R.; Valterová, I.; Hodaèová, J.; Císaøová, I.; Kotora, M. *Adv. Synth. Catal*. **2007**, *349*, 822.
11 (a) Malkov, A. V.; Orsini, M.; Pernazza, D.; Muir, K. W.; Langer, V.; Meghani, P.; Koèovský, P. *Org. Lett*. **2002**, *4*, 1047.
(b) Malkov, A. V.; Bell, M.; Orsini, M.; Pernazza, D.; Massa, A.; Herrmann, P.; Meghani, P.; Koèovský, P. *J. Org. Chem*. **2003**, *68*, 9659.
(c) Malkov, A. V.; Bell, M.; Vassieu, M.; Bugatti, V.; Koèovský, P. *J. Mol. Catal. A* **2003**, *196*, 179.
(d) Malkov, A. V.; Bell, M.; Castelluzzo, F.; Koèovský, P. *Org. Lett*. **2005**, *7*, 3219.
(e) Malkov, A. V.; Dufková, L.; Farrugia, L.; Koèovský, P. *Angew. Chem., Int. Ed*. **2003**, *42*, 3674.
(f) Malkov, A. V.; Ramírez-López, P.; Biedermannová (nèe Bendová), L.; Rulíšek, L.; Dufková, L.; Kotora, M.; Zhu, F.; Koèovský, P. *J. Am. Chem. Soc*. **2008**, *130*, 5341.
12 For recent reviews, see:
(a) Taylor, M. S.; Jacobsen, E. N. *Angew. Chem., Int. Ed*. **2006**, *45*, 1520.
(b) Connon, S. J. *Angew. Chem., Int. Ed*. **2006**, *45*, 3909.
(c) Akiyama, T.; Itoh, J.; Fuchibe, K. *Adv. Synth. Catal*. **2006**, *348*, 999.
13 (a) Rowlands, G. J.; Barnes, W. K. *Chem. Commun*. **2003**, 2712.
(b) Massa, A.; Capozzolo, L.; Scettri, A. *Cent. Eur. J. Chem.* **2010**, *8*, 1210.
(c) Massa, A.; Malkov, A. V.; Koèovský, P.; Scettri, A. *Tetrahedron Lett.* **2003**, *44*, 7179.
(d) Kobayashi, S.; Ogana, C.; Konishi, H.; Sugiura, M. *J. Am. Chem. Soc*. **2003**, *125*, 6610.
14 For reviews, see:
(a) Akiyama, T. *Chem. Rev*. **2007**, *107*, 5744.
(b) Terada, M. *Chem. Commun*. **2008**, 4097.
(c) Terada, M. *Synthesis* **2010**, 1929.
15 General procedure for allylation of aromatic aldehydes with allyltrichlorosilanes: To a stirred solution of catalyst (20 mol%) and aldehyde (0. 1 mmol) in toluene (1. 0 mL) was added allyltrichlorosilane (2.0 equiv.) under argon at −20 ℃. After being stirred at the same temperature for 48 h, the reaction was quenched with saturated aqueous $NaHCO_3$ solution (1. 0 mL). The mixture was extracted with ethyl acetate. The combined organic phases were washed with brine, dried over $MgSO_4$, and concentrated under vacuum. The crude product was purified by column chromatography (silica gel, hexane/ethyl acetate) to give the desired product. The *ee* value was determined by HPLC analyses (for **3c**—**3g**, **3i**, **3k**, **3l**, HPLC condition: AD-H, 1.0 mL/min, *V*(*i*-PrOH)∶*V*(Hexane)=5∶95; for **3b**, HPLC condition: AD-H, 1.0 mL/min, *V*(*i*-PrOH)∶*V*(Hexane)=2∶98; for **3a**, HPLC condition: OD-H, 1.0 mL/min, *V*(*i*-PrOH)∶*V*(Hexane)=10∶90; for **3m** and **3n**, HPLC condition: OD-H, 1.0 mL/min, *V*(*i*-PrOH)∶*V*(Hexane)=5∶95).

(E1103121 Pan, B.)