Tetrahedron 65 (2009) 4950–4956

Contents lists available at ScienceDirect

Tetrahedron

journal homepage: www.elsevier.com/locate/tet

Chiral Brønsted acid-catalyzed hydrophosphonylation of imines—DFT study on the effect of substituents of phosphoric acid

Takahiko Akiyama [a,*], Hisashi Morita [a], Prabhakar Bachu [a], Keiji Mori [a], Masahiro Yamanaka [b,*], Takashi Hirata [b]

[a] Department of Chemistry, Faculty of Science, Gakushuin University, 1-5-1 Mejiro, Toshima-ku, Tokyo 171-8588, Japan
[b] Department of Chemistry, Faculty of Science, Rikkyo University, 3-34-1 Nishi-Ikebukuro, Toshima-ku, Tokyo 171-8501, Japan

ARTICLE INFO

Article history:
Received 29 January 2009
Received in revised form 9 March 2009
Accepted 9 March 2009
Available online 14 March 2009

This paper is dedicated to Professor Michael J. Krische for the Tetrahedron Young Investigator Award

Keywords:
Chiral Brønsted acid
Phosphoric acid
Hydrophosphonylation
α-Amino phosphonate
DFT calculation

ABSTRACT

The enantioselective hydrophosphonylation reaction of diisopropyl phosphite with aldimine furnished α-amino phosphonates with high enantioselectivities by means of a chiral phosphoric acid. DFT calculation of the effect of 3,3′-substituents of the phosphoric acid revealed the reason for the high enantioselectivities.

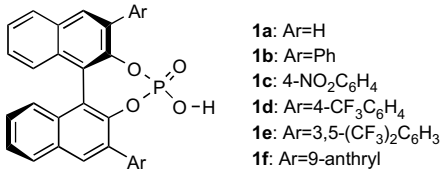
1. Introduction

α-Amino phosphonic acid and phosphonates are biologically attractive peptide mimics of α-amino acids.[1] Because they have intriguing biological activities such as anti-HIV,[2] protease inhibitory,[3] and antibacterial activities,[4] the development of an efficient method for the preparation of α-amino phosphonates is highly desired. The acid-catalyzed addition of dialkyl phosphite to imines provides useful method for the preparation of α-amino phosphonates. The diastereoselective addition of phosphite derivatives to chiral imines was successfully achieved.[5] Recently, the enantioselective synthesis of α-amino phosphonates catalyzed by chiral acid catalysts has attracted much attention.[6] Both metal complexes such as lanthanide[7] and aluminum,[8] and organocatalysts such as chiral thiourea,[9] cinchona alkaloid,[10] and chiral phosphoric acids[11,12] have been successfully employed.

Chiral Brønsted acids are rapidly gaining popularity as green catalysts (metal-free catalysts). We have designed and synthesized chiral phosphoric acids, derived from (*R*)-BINOL (Fig. 1),[13] and have demonstrated their catalytic activity as chiral Brønsted acid catalysts. As part of our unrelenting effort to develop chiral Brønsted acid-catalyzed reactions,[14,15] we wish to report herein the chiral Brønsted acid-catalyzed enantioselective hydrophosphonylation of imines and the DFT study of the effect of the 3,3′-substituents of the phosphoric acid on the enantioselectivity.[16]

2. Results and discussion

At the outset, we studied the hydrophosphonylation reaction of diethyl phosphite with *N*-benzylidene *p*-anisidine (**2a**: Ar=Ph) in the presence of chiral phosphoric acid **1e** (10 mol %) in toluene at room temperature. α-Amino phosphonate **4a** was obtained in 99%



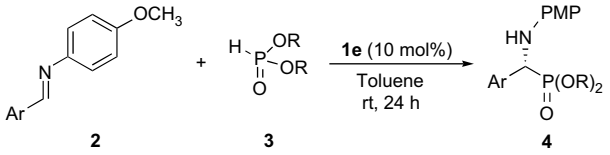
1a: Ar=H
1b: Ar=Ph
1c: 4-$NO_2C_6H_4$
1d: Ar=4-$CF_3C_6H_4$
1e: Ar=3,5-$(CF_3)_2C_6H_3$
1f: Ar=9-anthryl

Figure 1. Chiral phosphoric acids.

* Corresponding authors. Tel.: +81 3 3986 0221; fax: +81 3 5992 1029 (T.A.); tel./fax: +81 3 3985 2395 (M.Y.).
E-mail addresses: takahiko.akiyama@gakushuin.ac.jp (T. Akiyama), myamanak@rikkyo.ac.jp (M. Yamanaka).

0040-4020/$ – see front matter © 2009 Elsevier Ltd. All rights reserved.
doi:10.1016/j.tet.2009.03.023

Table 1
Hydrophosphonylation reaction catalyzed by **1e**



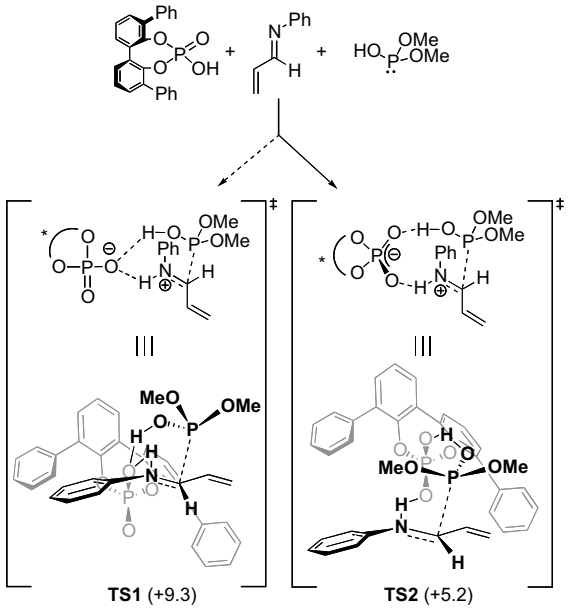
Entry	Ar	R	Yield/%	ee/%
1	Ph	Et	99	43
2	Ph	*i*-Pr	84	52
3	PhCH=CH	*i*-Pr	92	84

yield with 43% ee (Table 1, entry 1). Use of diisopropyl phosphite improved the enantioselectivity to 52% ee (entry 2). Interestingly, an aldimine derived from cinnamaldehyde **2b** furnished the corresponding adduct in 84% ee (entry 3).

The absolute stereochemistry of α-amino diethyl phosphonate **4a** (Ar=Ph, R=Et) was determined to be *R* by deprotection of the *p*-$MeOC_6H_4$ moiety of **4a** by means of CAN and comparison of its optical rotation with literature data.[17] The absolute stereochemistries of the other phosphonates were speculated to be *R* by analogy.

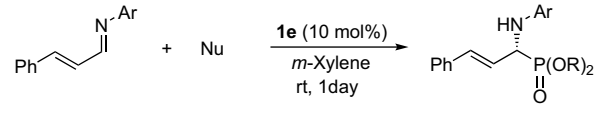
To elucidate the reason for the high enantioselectivity of **1e**, we studied the effect of phosphorus nucleophile and *N*-substituents of aldimines (Table 2). Among the dialkyl phosphites examined, diisopropyl phosphite gave the highest enantioselectivity. We noted that the use of trialkyl phosphite as a nucleophile deteriorated both reactivity and enantioselectivity (entry 3). Based on the results, we suggest that the OH moiety of the dialkyl phosphite plays an important role in achieving the high enantioselectivity. DFT calculation suggested that the hydrophosphonylation reaction proceeds via the nine-membered zwitterionic transition state (TS) with the chiral phosphoric acid as reported by Yamanaka and Hirata.[18] In the nine-membered zwitterionic **TS2**, aldimine and phosphite could be activated by the Brønsted acidic site and the Lewis basic site, respectively. Therefore, the dicoordinated pathway via **TS2**, namely, the dual activation pathway, is overwhelmingly favored over the monocoordinated pathway via **TS1** (Scheme 1). In **TS1**, both iminium and phosphite are located at the empty upper right-hand quadrant due to their coordination with one phosphoryl oxygen atom. As a result, both substrates are directed away from the bulky 3,3′-Ph groups, which are responsible for asymmetric induction. In sharp contrast, the energetically favored **TS2** results from placing the bulky substituents of iminium and phosphite in the empty site of the phosphoric acid catalyst. These transition structures indicate that the facial selectivity of nucleophilic addition to iminium could not be controlled in **TS1** but in **TS2**.

An examination of the *N*-substituent of imine showed that the presence of an *o*-hydroxy moiety decreased the enantioselectivity



Scheme 1. Dual activation mechanism of the phosphoric acid-catalyzed hydrophosphonylation (BHandHLYP/6-31G*). Free energies based on the sum of phosphoric acid, aldimine, and phosphite are shown in parentheses (kcal/mol).

Table 2
Effect of nucleophiles and *N*-substituents



Entry	Ar	Nu	Yield/%	ee/%
1	4-$MeOC_6H_5$	$HPO(Oi\text{-}Pr)_2$	92	84
2	4-$MeOC_6H_5$	$HPO(OEt)_2$	70	73
3	4-$MeOC_6H_5$	$P(Oi\text{-}Pr)_3$	23	3
4	4-$MeOC_6H_5$	$HPO(Oi\text{-}Pr)_2$	58	87
5	C_6H_5	$HPO(Oi\text{-}Pr)_2$	74	88
6	2-HOC_6H_5	$HPO(Oi\text{-}Pr)_2$	33	39

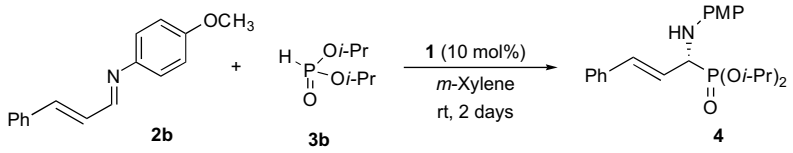
(entry 6). This result quite contrasts the results of the Mannich-type reaction we investigated, in which the presence of an *o*-hydroxy moiety is essential to attain high chiral induction. The *o*-hydroxy moiety would promote the formation of a two-point binding complex of the chiral phosphoric acid with the imine, and consequently decreasing Lewis basicity on phosphoryl oxygen.

The effect of the substituents on the 3,3′-position of the phosphoric acid was investigated in the addition reaction of diisopropyl phosphite with aldimine **2b** in *m*-xylene at room temperature and the results are shown in Table 3. Phosphoric acid **1c** (Ar=4-$NO_2C_6H_4$), which exhibited the highest enantioselectivity in the Mannich-type reaction, turned out to be less effective (entry 3). Among the Brønsted acids examined, **1e** (Ar=3,5-$(CF_3)_2C_6H_3$) exhibited the highest enantioselectivity and reactivity (entry 5).

To clarify the origin of the effect of the 3,3′-substituents of the chiral phosphoric acid derived from (*R*)-BINOL, DFT calculation (BHandHLYP/6-31G*) was carried out based on the nine-membered zwitterionic TS reported previously. The energy differences (Δ*E*) between the *re*-facial attacking TS (**TSr**) and the *si*-facial attacking TS (**TSs**) were explored for a wide variety of 3,3′-substituents (Table 4). We have already fully optimized **TSr3b** and **TSs3b** at the BHandHLYP/6-31G* level.[19–21] To reduce computational cost and to focus on the 3,3′-substituent effect, only the 3,3′-substituents (e.g., Ar) were only optimized in other TS geometries (**TS3a** and **TS3c**–**e**) at the same level as the geometry optimization of **TS3b**. In all cases, **TSr** was more stable than **TSs** and consequently, the *re*-facial attack is predicted to be more favored than the *si*-facial attack. **TS3c**, **TS3d**, and **TS3e** bearing structurally similar Ar groups on the 3,3′-position showed larger Δ*E*, similar to **TS3b** (entries 2–5). In agreement with the experimental results, **TSr3e** leading to the highest enantioselectivity exhibited the maximum Δ*E* (4.3 kcal/mol). On the other hand, **TS3a** and **TS3f** showed comparatively small Δ*E* in spite of the remarkably different steric environment on the 3,3′-position (entries 1 and 6).

Structural analysis was carried out to investigate the origin of the tendency of Δ*E* (Fig. 2). In **TS3c** and **TS3e**, both of which showed comparatively large Δ*E*, the *si*-facial attacking phosphite in **TSs3** was located at the sterically demanding upper left-hand quadrant, leading to steric repulsion between phosphite and 3,3′-Ar group. In

Table 3
Effect of the 3,3′-substituents of the phosphoric acid



Entry	Catalyst	Yield/%	ee/%
1	**1a**	71	11
2	**1b**	75	30
3	**1c**	71	30
4	**1d**	66	33
5	**1e**	82	84
6	**1f**	31	26

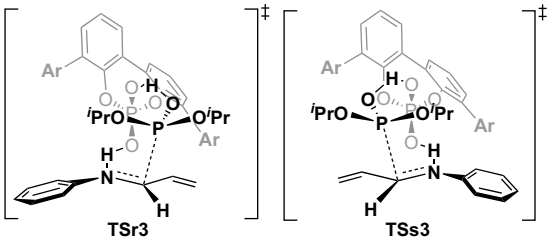
contrast, the *re*-facial attacking phosphite in **TSr3** was located in the vacant upper right-hand quadrant. Therefore, the bulky 3,5-$(CF_3)_3C_6H_3$ group enhanced the steric repulsion between phosphite and the 3,3′-Ar group in **TSs3** to increase Δ*E* (**TS3c**: 3.4 kcal/mol, **TS3e**: 4.3 kcal/mol). On the other hand, no steric influence was noted on the 3,3′-position of **TS3a**. There was no steric environmental difference between upper left- and upper right-hand quadrants, and hence, Δ*E* was decreased to 1.0 kcal/mol. In **TS3f**, the sterically demanding 9-anthryl group on the 3,3′-position expanded to the upper right-hand quadrant from the left-hand one to reduce the steric environment difference. The steric repulsion between phosphite and 9-anthryl group would be overestimated by the slightly deformed aromatic ring structure of the 9-anthryl group because the carbon atoms on the 3,3′-position were fixed. Despite this overestimation of the instability of the TS structures, the 9-anthryl group obviously decreased Δ*E* between **TSr3f** and **TSs3f**.

The results of the hydrophosphonylation of diisopropyl phosphite are shown in Table 5. A range of imines **2** were treated with 10 mol % of a phosphoric acid **1e** in *m*-xylene at room temperature. α-Amino phosphonates **4** were obtained in high yields with good to high enantioselectivities. In particular, aldimines derived from cinnamaldehyde exhibited high enantioselectivities.

3. Conclusion

In summary, the hydrophosphonylation of aldimines with diisopropyl phosphite was found to be catalyzed by a chiral Brønsted acid derived from (*R*)-BINOL. The process afforded α-amino phosphonates in good to high enantioselectivities. Aldimines, in particular, those derived from cinnamaldehyde derivatives, exhibited high enantioselectivities. DFT calculation elucidated the effects of the 3,3′-substituents of the chiral Brønsted acid. The sterically demanding 3,5-$(CF_3)_3C_6H_3$ group enhanced the steric repulsion with phosphite to destabilize the *si*-facial attacking TS. The absence of the 3,3-Ar group minimized the *C*2 symmetric chiral environment to decrease Δ*E* between diastereomeric transition states as well as the 9-anthryl group.

Table 4
Energy differences between **TSs** and **TSr** at the BHandHLYP/6-31G* level. Δ*E*=*E*(**TSs**)−*E*(**TSr**)



Ar = H (**a**), Ph (**b**), 4-$NO_2C_6H_4$ (**c**), 4-$CF_3C_6H_4$ (**d**), 3,5-$(CF_3)_2C_6H_3$ (**e**), 9-anthryl (**f**)

Entry	Ar	Δ*E* (kcal/mol)	Exp (ee/%)
1	H (**TS3a**)	1.0	11
2	Ph (**TS3b**)	3.2	30
3	4-$NO_2C_6H_4$ (**TS3c**)	3.4	30
4	4-$CF_3C_6H_4$ (**TS3d**)	3.9	33
5	3,5-$(CF_3)_2C_6H_3$ (**TS3e**)	4.3	84
6	9-Anthryl (**TS3f**)	0.1	26

3.1. Computational details

To reduce computational cost and to focus on the 3,3′-substituent effect, the 3,3′-substituents were only optimized based on **TS3b** (Ar=Ph) fully optimized at the BHandHLYP/6-31G* level. In **TS3a**, geometry optimization was employed for hydrogen atoms located on the 3,3′-position instead of Ph groups. In **TS3c–f**, substituents were added to Ph groups on the 3,3′-position and subsequently partially optimized (shown in gray color) other than the carbon atoms (shown by black dots) connecting the 3,3′-position of the BINOL framework (Fig. 3).

4. Experimental

4.1. General

NMR spectra were recorded on Unity Inova-400 instrument (Varian Japan Ltd., 400 MHz for ^{1}H, 100 MHz for ^{13}C) and JNM-Al300 instrument (JEOL, 300 MHz for ^{1}H, 75 MHz for ^{13}C) using $CDCl_3$ as a solvent. Chemical shifts (δ) for ^{1}H were referenced to tetramethylsilane (δ=0.00 ppm) as an internal standard. Chemical shifts (δ) for ^{13}C were referenced to a solvent signal ($CDCl_3$, δ=77.00 ppm). IR spectra were recorded on FTIR-8600PC instrument (Shimadzu Co.) using $CHCl_3$ as a solvent. Elemental analysis (EA) was carried out on EA1110 instrument (Amco Inc.). Mass spectra (MS) were recorded on JMS-AX505HA instrument (JEOL). Specific rotation was recorded on SEPA-300 instrument (HORIBA, Ltd.).

Chiral catalysts are prepared based on the procedure reported by Wipf and Jung.[22]

4.2. (*R*)-3,3′-[3,5-Bis(trifluoromethyl)phenyl]$_2$-1,1′-binaphthol

To a solution of $Pd(PPh_3)_4$ (167.9 mg, 0.15 mM, 0.06 equiv) and 3,5-bis(trifluoromethyl)bromobenzene (1.3 mL, 7.54 mM, 3.0 equiv) in dimethoxyethane (15 mL) were added a solution of (*R*)-3,3′-bis(dihydroxyborane)-2,2′-dimethoxy-1,1′-binaphthyl[1]

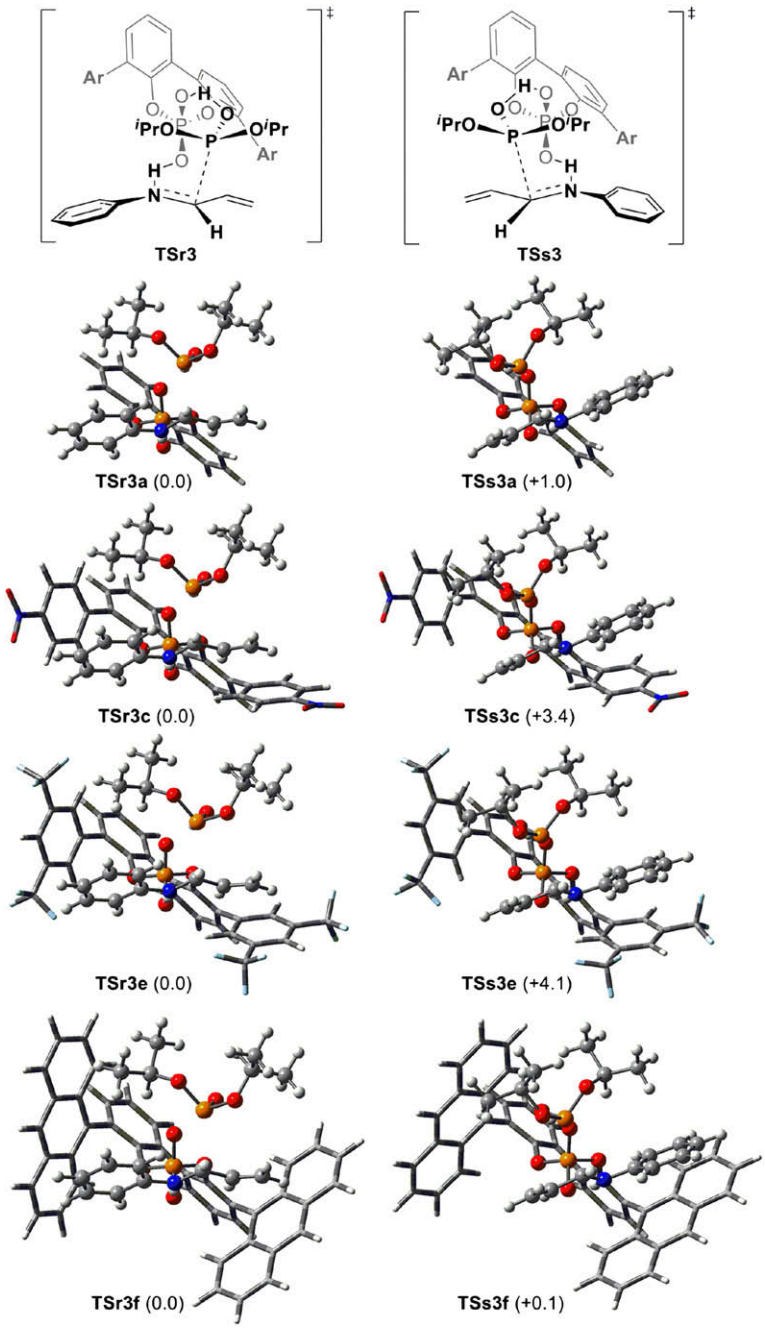


Figure 2. 3D structures and schematic representation models of **TSr3** and **TSs3** (**a**: H, **c**: 4-$NO_2C_6H_4$, **e**: 3,5-$(CF_3)_2C_6H_3$, **f**: 9-anthryl) at the BHandHLYP/6-31G* level. Relative energies (kcal/mol) are shown in parentheses.

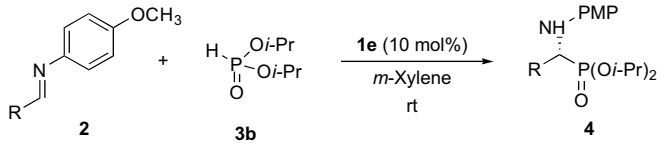
(1.0 g, 2.56 mM) in ethanol (10 mL) and 2 N NaOH solution (3.8 mL, 7.6 mM). After being refluxed for 18.5 h, the solution was cooled to room temperature. The solvent was removed in vacuo and the residue was extracted with CH_2Cl_2 (3×10 mL) and the combined organic layers were successively washed with 10% aq HCl and brine, dried over anhydrous Na_2SO_4, and concentrated to dryness. The resulting oil was dissolved in CH_2Cl_2 (100 mL) and a solution of BBr_3 (2.88 g, 11.5 mM) in CH_2Cl_2 (12 mL) was added dropwise at 0 °C for 12 min. After stirring at room temperature for 5 h, water was added to stop the reaction. The mixture was extracted with CH_2Cl_2 (3×10 mL) and the combined organic layers were washed with brine, dried over anhydrous Na_2SO_4, and concentrated to dryness. The residue was purified by column chromatography (SiO_2, hexane/CH_2Cl_2=4:1/v:v) to give the title compound (1.4 g, 2.01 mM) in 79% yield.

$[\alpha]_D^{26}$ 45.3 (*c* 1.1, $CHCl_3$). IR ($CHCl_3$) 3522, 1622, 1597, 1502, 1474, 1462, 1427, 1377, 1358, 1335, 1281, 1236, 1182, 1140, 1036, 989, 897, 845 cm^{-1}. R_f 0.3 (hexane/CH_2Cl_2=4:1). ^1H NMR (400 MHz, $CDCl_3$) δ=8.24 (s, 4H), 8.12 (s, 2H), 8.00 (d, 2H, *J*=7.9 Hz), 7.91 (s, 2H), 7.50–7.40 (m, 4H), 7.24–7.22 (m, 2H), 5.38 (s, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ=149.9, 139.5, 133.2, 132.4, 131.6 (q, *J*=33.4 Hz), 129.9, 129.5, 128.9, 128.7, 127.7, 125.2, 124.0, 123.4 (q, *J*=272.9 Hz), 121.3, 111.8. ^{19}F NMR (376 MHz, $CDCl_3$) δ=99.0. Found: C, 61.03; H, 2.25%. Calcd for $C_{36}H_{18}F_{12}O_2$: C, 60.86; H, 2.55%.

4.3. (*R*)-3,3′-[3,5-Bis(trifluoromethyl)phenyl]$_2$-1,1′-binaphthyl phosphate (1e)

To a solution of (*R*)-3,3′-[3,5-bis(trifluoromethyl)phenyl]$_2$-1,1′-binaphthol (1.11 g, 1.56 mmol) in pyridine (6.4 mL) was added

Table 5
Results of hydrophosphonylation by means of **1e**



Entry	R	Time/h	Yield/%	ee/%
1	C_6H_5	24	84	52
2	*o*-$CH_3C_6H_4$	46	76	69
3	*o*-$NO_2C_6H_4$	24	72	77
4	$C_6H_5CH{=}CH$	101	92	84
5	*p*-$CH_3C_6H_4CH{=}CH$	170	88	86
6	*p*-$ClC_6H_4CH{=}CH$	145	97	83
7	*o*-$CH_3C_6H_4CH{=}CH$	171	80	82
8	*o*-$ClC_6H_4CH{=}CH$	70	82	87
9	*o*-$NO_2C_6H_4CH{=}CH$	49	92	88
10	*o*-$CF_3C_6H_4CH{=}CH$	46	86	90
11	1-NaphthylCH=CH	168	76	81

phosphoryl chloride (210 μL, 2.25 mmol) at room temperature for 3 min and the mixture was stirred for 2 h at room temperature. After the reaction mixture was cooled to room temperature, pyridine was removed in vacuo and 6 N HCl (17 mL) was added and the resulting mixture was heated to reflux for 2 h and cooled to 0 °C. The precipitate thus formed was collected by filtration and washed with water. The crude material was dissolved in ethanol and reprecipitated by addition of 6 N HCl. The solids were collected by filtration and dissolved in CH_2Cl_2 and reprecipitated by addition of hexane. The resulting crystals were collected by filtration and washed with water to give the title compound (0.877 g, 1.14 mM) in 73% yield.

$[\alpha]_D^{26}$ −197.5 (*c* 0.97, $CHCl_3$) dec 163.5–180.0 °C. IR ($CHCl_3$) 1620, 1501, 1474, 1379, 1325, 1281, 1246, 1178, 1140, 1109, 1084, 1024, 988, 964, 891, 870, 867 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ=8.01 (s, 8H), 7.61–7.58 (m, 4H), 7.42–7.39 (m, 4H). ^{31}P NMR (189 MHz, $CDCl_3$) δ=4.61. ^{13}C NMR (100 MHz, $CDCl_3$) δ=143.5 (d, J_{P-C}=9.3 Hz), 138.6, 132.3, 132.0, 131.4, 131.4 (q, J_{C-F}=33.4 Hz), 131.1 (d, J_{P-C}=3.1 Hz), 129.9, 128.7, 127.6, 127.1, 126.8, 123.1 (q, J_{C-F}=272.9 Hz), 122.5 (d, J_{P-C}=1.9 Hz), 121.5. ^{19}F NMR (376 MHz, $CDCl_3$) δ=96.6. Found: C, 55.96; H, 2.13%. Calcd for $C_{36}H_{17}F_{12}O_4P$: C, 55.97; H, 2.22%.

A typical procedure for the hydrophosphonylation: entry 10 of Table 5 is shown.

To a solution of an aldimine derived from *o*-CF_3-substituted cinnamaldehyde (41.4 mg, 0.135 mmol) and a Brønsted acid **1e** (10.5 mg, 0.0135 mmol) in *m*-xylene (2 mL) was added diisopropyl phosphite (46 μL, 0.271 mM). After being stirred at room temperature for 46 h, satd $NaHCO_3$ solution was added to the mixture to stop the reaction. The mixture was extracted with EtOAc (3×10 mL) and the combined organic layers were washed with brine, dried over anhydrous Na_2SO_4, and concentrated to dryness. The residue was purified by *p*-TLC (SiO_2, CH_2Cl_2/hexane/EtOAc=6:5:1/v:v:v) to give α-amino phosphonate **4** (54.8 mg, 0.116 mmol) in 90% ee.

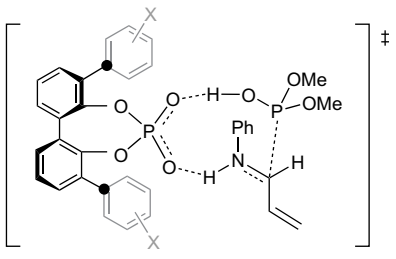


Figure 3.

4.4. Diethyl [*N*-(4-methoxyphenyl)amino]-phenylmethylphosphonate

Oil. IR ($CHCl_3$) 3001, 1512, 1240,1221,1028, and 974 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ=7.46–7.25 (m, 5H), 6.68 (d, 2H, *J*=7.7 Hz), 6.54 (d, 2H, *J*=7.9 Hz), 6.69 (dd, 1H *J*=7.5, 23.6 Hz), 4.58–4.54 (m, 1H), 4.14–3.67 (m, 7H), 1.28 (t, 3H, *J*=7.0 Hz), 1.11 (t, 3H, *J*=7.0 Hz). ^{13}C NMR (75 MHz, $CDCl_3$) δ=152.6, 140.2 (d, *J*=15.9 Hz), 136.0 (d, *J*=2.8 Hz), 128.5 (d, *J*=2.8 Hz), 127.8 (d, *J*=2.1 Hz), 127.8, 115.2, 114.7, 63.2 (d, *J*=4.2 Hz), 63.1 (d, *J*=4.2 Hz), 56.9 (d, *J*=150.1 Hz), 55.6, 16.4 (d, *J*=5.5 Hz), 16.1 (d, *J*=5.5 Hz). ^{31}P NMR(121 MHz, $CDCl_3$) δ=23.5. Found: C, 61.90; H, 6.81; N, 3.92%. Calcd for $C_{18}H_{24}NO_4P$: C, 61.88; H, 6.92; N, 4.01%. $[\alpha]_D^{24}$ +20.5 (*c* 0.5, $CHCl_3$) (45% ee). HPLC: Daicel Chiralpak AS-H (hexane/*i*-PrOH=30:1/v:v), flow rate=0.5 mL/min, UV=254 nm, t_R (minor)=23.4 min (*S*), t_R (major)=25.2 min (*R*).

4.5. Diisopropyl [*N*-(4-methoxyphenyl)amino]-phenylmethylphosphonate

Yellow oil. IR ($CHCl_3$) 2993, 1512, 1238, and 997 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ=7.46–7.22 (m, 5H), 6.69–6.52 (m, 4H), 4.71–4.44 (m, 4H), 3.68 (s, 3H), 1.32–0.92 (m, 12H). ^{13}C NMR (75 MHz, $CDCl_3$) δ=152.6, 140.3 (d, *J*=15.9 Hz), 136.6, 128.5, 127.8 (d, *J*=4.2 Hz), 115.2, 114.7, 63.2, 56.9 (d, *J*=150.8 Hz), 55.6, 16.4 (d, *J*=6.2 Hz), 16.2 (d, *J*=6.2 Hz). ^{31}P NMR (121 MHz, $CDCl_3$) δ=23.5. Found: C, 63.44; H, 7.59; N, 3.91%. Calcd for $C_{20}H_{28}NO_4P$: C, 63.65; H, 7.48; N, 3.71%. $[\alpha]_D^{24}$ +16.7 (*c* 1.0, $CHCl_3$) (59% ee). HPLC: Daicel Chiralcel OD-H (hexane/*i*-PrOH=40/1), flow rate=0.5 mL/min, UV=254 nm, t_R (major)=16.7 min (*R*), t_R (minor)=19.3 min (*S*).

4.6. Diisopropyl [*N*-(4-methoxyphenyl)amino]-2-methylphenylmethylphosphonate

IR ($CHCl_3$) 2984, 1512, 1238, 1103, and 995 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ=7.48–7.13 (m, 4H), 6.66 (d, 2H, *J*=8.8 Hz), 6.47 (d, 2H, *J*=8.8 Hz), 4.85 (dd, 1H, *J*=7.7, 24.0 Hz), 4.77–4.69 (m, 1H), 4.60 (dd, 1H, *J*=7.7, 17.4 Hz), 4.43–4.35 (m, 1H), 3.67 (s, 3H), 2.49 (s, 3H), 1.92–1.23 (m, 9H), 0.97 (d, 3H, *J*=6.2 Hz). ^{13}C NMR (75 MHz, $CDCl_3$) δ=152.4, 140.6 (d, *J*=15.2 Hz), 136.5 (d, *J*=6.2 Hz), 134.8 (d, *J*=2.0 Hz), 130.3 (d, *J*=2.8 Hz), 127.4 (d, *J*=3.4 Hz), 127.0 (d, *J*=4.1 Hz), 126.3 (d, *J*=3.5 Hz), 114.8, 114.7, 72.0 (d, *J*=7.6 Hz), 71.7 (d, *J*=6.9 Hz), 55.6, 53.2 (d, *J*=153.5 Hz), 24.3 (d, *J*=3.5 Hz), 24.2 (d, *J*=3.5 Hz), 23.8 (d, *J*=5.5 Hz), 22.8 (d, *J*=5.5 Hz), 19.8. ^{31}P NMR (121 MHz, $CDCl_3$) δ=22.7. Found: C, 64.51; H, 7.86; N, 3.48%. Calcd for $C_{21}H_{30}NO_4P$: C, 64.43; H, 7.72; N, 3.58%. $[\alpha]_D^{24}$ +23.4 (*c* 1.1, $CHCl_3$) (69% ee). HPLC: Daicel Chiralcel OD-H (hexane/*i*-PrOH=40:1), flow rate=0.5 mL/min, UV=254 nm, t_R (major)=14.4 min (*R*), t_R (minor)=15.9 min (*S*).

4.7. Diisopropyl *N*-(4-methoxyphenyl)-2-nitrophenylmethylphosphonate

IR ($CHCl_3$) 3034, 2341, 1528, 1514, 1225, and 1001 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ=7.99–7.38 (m, 4H), 6.72 (d, 2H, *J*=9.0 Hz), 6.63 (d, 2H, *J*=9.0 Hz), 6.05 (dd, 1H, *J*=9.0, 26.2 Hz), 4.76–4.53 (m, 3H), 3.70 (s, 3H), 1.32–1.21 (m, 9H), 0.90 (d, 3H, *J*=6.2 Hz). ^{13}C NMR (75 MHz, $CDCl_3$) δ=152.7, 149.7, 139.5 (d, *J*=14.5 Hz), 133.3 (d, *J*=2.8 Hz), 132.6, 128.7 (d, *J*=4.2 Hz), 128.2 (d, *J*=3.5 Hz), 125.1 (d, *J*=2.1 Hz), 114.94, 114.7, 72.5 (d, *J*=6.9 Hz), 72.1 (d, *J*=7.6 Hz), 55.6, 51.0 (d, *J*=152.2 Hz), 24.1 (d, *J*=4.2 Hz), 23.7 (d, *J*=4.8 Hz), 23.7 (d, *J*=4.2 Hz), 23.1 (d, *J*=4.8 Hz). ^{31}P NMR (121 MHz, $CDCl_3$) δ=19.7. Found: C, 56.63; H, 6.63; N, 6.47%. Calcd for $C_{20}H_{27}N_2O_6P$: C, 56.87; H, 6.44; N, 6.33%. $[\alpha]_D^{24}$ +111.8 (*c* 0.8, $CHCl_3$) (60% ee). HPLC: Daicel

Chiralpak AD-H (hexane/*i*-PrOH=1:1/v:v), flow rate=0.5 mL/min, UV=254 nm, t_R (major)=14.4 min (*R*), t_R (minor)=28.9 min (*S*).

4.8. Diisopropyl 1-[*N*-(4-methoxyphenyl)amino]-3-phenyl-2-propenylphosphonate

Yellow oil. IR ($CHCl_3$) 2986, 1512, 1240, 1209, and 995 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ=7.36–7.20 (m, 5H), 6.75 (d, *J*=8.9 Hz), 6.70–6.64 (m, 3H), 6.29–6.22 (m, 1H), 4.80–4.70 (m, 2H), 4.30 (br s, 1H), 4.03 (br s, 1H), 3.77 (s, 3H), 1.34 (d, 6H, *J*=6.2 Hz), 1.28–1.25 (m, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ=152.7, 140.8 (d, *J*=13.1 Hz), 136.5 (d, *J*=3.4 Hz), 132.7 (d, *J*=12.5 Hz), 128.5, 127.6, 126.5, 126.5, 124.3 (d, *J*=4.9 Hz), 115.2, 114.8, 71.9 (d, *J*=6.9 Hz), 71.6 (d, *J*=7.6 Hz), 55.7, 55.5 (d, *J*=153.5 Hz), 24.2 (d, *J*=2.7 Hz), 24.1 (d, *J*=3.5 Hz), 23.9 (d, *J*=5.2 Hz), 23.8 (dd, *J*=5.2 Hz). ^{31}P NMR (121 MHz, $CDCl_3$) δ 21.3. Found: C, 65.31; H, 7.37; N, 3.58%. Calcd for $C_{22}H_{30}NO_4P$: C, 65.49; H, 7.49; N, 3.47%. $[\alpha]_D^{26}$ +72.3 (*c* 0.75, $CHCl_3$) (84% ee). HPLC: Daicel Chiralpak AD-H (hexane/*i*-PrOH=1:1/v:v), flow rate=0.5 mL/min, UV=254 nm, t_R (major)=15.1 min (*R*), t_R (minor)=23.0 min (*S*).

4.9. Diisopropyl 1-[*N*-(4-methoxyphenyl)amino]-3-(4-methylphenyl)-2-propenylphosphonate

Yellow oil. IR ($CHCl_3$) 2986, 1512, 1240, and 995 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ=7.25–6.60 (m, 9H), 6.22–6.16 (m, 1H), 4.80–4.69 (m, 2H), 4.33–4.00 (m, 2H), 3.72 (s, 3H), 2.31 (s, 3H), 1.37–1.22 (m, 12H). ^{13}C NMR (75 MHz, $CDCl_3$) δ=152.5, 140.7 (d, *J*=13.8 Hz), 137.4, 133.6 (d, *J*=2.8 Hz), 132.5 (d, *J*=12.5 Hz), 129.1, 126.3 (d, *J*=1.4 Hz), 123.0 (d, *J*=4.8 Hz), 115.1, 114.7, 71.9 (d, *J*=6.9 Hz), 71.5 (d, *J*=7.6 Hz), 55.7, 55.6 (d, *J*=153.6 Hz), 24.4 (d, *J*=3.5 Hz), 24.3 (d, *J*=3.5 Hz), 24.0 (d, *J*=4.8 Hz), 23.9 (d, *J*=4.8 Hz), 21.3. ^{31}P NMR (121 MHz, $CDCl_3$) δ=21.5. Found: C, 66.35; H, 7.68; N, 3.27%. Calcd for $C_{23}H_{32}NO_4P$: C, 66.17; H, 7.73; N, 3.36%. $[\alpha]_D^{26}$ +72.7 (*c* 1.0, $CHCl_3$) (86% ee). HPLC: Daicel Chiralpak AD-H (hexane/*i*-PrOH=1:1/v:v), flow rate=0.5 mL/min, UV=254 nm, t_R (major)=22.9 min (*R*), t_R (minor)=25.6 min (*S*).

4.10. Diisopropyl 3-(4-chlorophenyl)-1-[*N*-(4-methoxyphenyl)amino]-2-propenylphosphonate

Yellow oil. IR ($CHCl_3$) 2986, 1512, 1240, and 995 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ=7.28–6.60 (m, 9H), 6.28–6.21 (m, 1H), 4.79–4.72 (m, 2H), 4.35–4.01 (m, 2H), 3.73 (s, 3H), 1.34 (d, 6H, *J*=6.2 Hz), 1.28–1.25 (m, 6H). ^{13}C NMR (75 MHz, $CDCl_3$) δ=152.7, 140.6 (d, *J*=13.1 Hz), 135.0, 133.3, 131.3 (d, *J*=12.4 Hz), 128.7, 127.7, 125.1 (d, *J*=5.0 Hz), 115.1, 114.8, 72.0 (d, *J*=7.6 Hz), 71.6 (d, *J*=7.6 Hz), 55.7, 55.4 (d, *J*=153.5 Hz), 24.3 (d, *J*=5.5 Hz), 24.2 (d, *J*=5.5 Hz), 23.9 (d, *J*=5.5 Hz), 23.8 (d, *J*=6.2 Hz). ^{31}P NMR (121 MHz, $CDCl_3$) δ=21.0. Found: C, 60.48; H, 6.64; N, 3.05%. Calcd for $C_{22}H_{29}ClNO_4P$: C, 60.34; H, 6.68; N, 3.20%. $[\alpha]_D^{27}$ +59.4 (*c* 0.9, $CHCl_3$) (83% ee). HPLC: Daicel Chiralcel AD-H (hexane/*i*-PrOH=1:1/v:v), flow rate=0.5 mL/min, UV=254 nm, t_R (major)=35.0 min (*R*), t_R (minor)=39.2 min (*S*).

4.11. Diisopropyl 1-[*N*-(4-methoxyphenyl)amino]-3-(2-methylphenyl)-2-propenylphosphonate

Yellow oil. IR ($CHCl_3$) 2986, 1510, 1238, 1217, and 997 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ=7.40–6.85 (m, 9H), 6.13–6.06 (m, 1H), 4.81–4.74 (m, 1H), 4.36–4.05 (m, 2H), 3.73 (s, 3H), 2.49 (s, 3H), 1.36–0.79 (m, 12H). ^{13}C NMR (75 MHz, $CDCl_3$) δ=152.5, 140.7 (d, *J*=14.5 Hz), 135.6, 135.3, 130.8 (d, *J*=11.8 Hz), 130.0, 127.4, 125.8 (d, *J*=19.4 Hz), 125.4, 125.3, 115.3, 114.6, 71.8 (d, *J*=6.9 Hz), 71.4 (d, *J*=7.6 Hz), 55.8 (d, *J*=154.3 Hz), 55.7, 24.1 (d, *J*=5.5 Hz), 24.0 (d, *J*=5.5 Hz), 24.3 (d, *J*=5.5 Hz), 24.2 (d, *J*=5.5 Hz), 19.8. ^{31}P NMR (121 MHz, $CDCl_3$) δ=21.4. Found: C, 66.29; H, 7.98; N, 3.30%. Calcd for $C_{23}H_{32}NO_4P$: C, 66.17; H, 7.73; N, 3.36%. $[\alpha]_D^{27}$ +69.5 (*c* 1.0, $CHCl_3$) (82% ee). HPLC: Daicel Chiralpak AD-H (hexane/*i*-PrOH=1:1/v:v), flow rate=0.5 mL/min, UV=254 nm, t_R (major)=16.9 min (*R*), t_R (minor)=20.1 min (*S*).

4.12. Diisopropyl 3-(2-chlorophenyl)-1-[*N*-(4-methoxyphenyl)amino]-2-propenylphosphonate

Yellow oil. IR ($CHCl_3$) 2984, 1512, 1240, and 997 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ=7.50–6.65 (m, 9H), 6.26–6.19 (m, 1H), 4.82–4.70 (m, 2H), 4.40–4.02 (m, 2H), 3.73 (s, 3H), 1.37–1.32 (m, 6H), 1.29 (d, 6H, *J*=6.2 Hz). ^{13}C NMR (75 MHz, $CDCl_3$) δ=152.6, 140.6 (d, *J*=13.8 Hz), 134.5 (d, *J*=2.8 Hz), 132.9, 129.5, 129.1 (d, *J*=12.5 Hz), 128.5, 127.4 (d, *J*=4.2 Hz), 126.8 (d, *J*=1.4 Hz), 126.7, 115.3, 114.7, 72.1 (d, *J*=6.9 Hz), 71.6 (d, *J*=6.9 Hz), 55.9 (d, *J*=153.6 Hz), 55.7 (s), 24.3 (d, *J*=3.5 Hz), 24.2 (d, *J*=3.5 Hz), 24.0 (d, *J*=4.8 Hz), 23.9 (d, *J*=4.8 Hz). ^{31}P NMR (121 MHz, $CDCl_3$) δ=20.9. Found: C, 60.30; H, 6.64; N, 2.94%. Calcd for $C_{22}H_{29}ClNO_4P$: C, 60.34; H, 6.68; N, 3.20%. $[\alpha]_D^{27}$ +55.2 (*c* 0.9, $CHCl_3$) (87% ee). HPLC: Daicel Chiralpak AD-H (hexane/*i*-PrOH=1:1/v:v), flow rate=0.5 mL/min, UV=254 nm, t_R (major)=21.8 min (*R*), t_R (minor)=25.0 min (*S*).

4.13. Diisopropyl 1-[*N*-(4-methoxyphenyl)amino]-3-(2-nitrolphenyl)-2-propenylphosphonate

Yellow oil. IR ($CHCl_3$) 2995, 1512, 1348, 1240, and 997 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ=8.16–6.62 (m, 9H), 6.54–6.45 (m, 1H), 4.83–4.68 (m, 2H), 4.42–4.05 (m, 2H), 3.73 (s, 3H), 1.35 (d, 6H, *J*=6.2 Hz), 1.27–1.23 (m, 6H). ^{13}C NMR (75 MHz, $CDCl_3$) δ=152.9, 140.5 (d, *J*=13.8 Hz), 133.1, 132.3 (d, *J*=2.8 Hz), 130.6 (d, *J*=4.2 Hz), 128.8 (d, *J*=2.8 Hz), 128.41, 128.2, 128.2, 124.5, 115.3, 114.8, 72.2 (d, *J*=6.9 Hz), 71.7 (d, *J*=6.9 Hz), 55.8 (d, *J*=152.8 Hz), 55.6, 24.2 (d, *J*=3.5 Hz), 24.0 (d, *J*=3.5 Hz), 23.9 (d, *J*=4.8 Hz), 23.8 (d, *J*=5.6 Hz). ^{31}P NMR (121 MHz, $CDCl_3$) δ=20.4. Found: C, 58.87; H, 6.59; N, 6.49%. Calcd for $C_{22}H_{29}NO_6P$: C, 58.92; H, 6.52; N, 6.25%. $[\alpha]_D^{27}$ +60.8 (*c* 1.0, $CHCl_3$) (88% ee). HPLC: Daicel Chiralpak AD-H (hexane/*i*-PrOH=1:1/v:v), flow rate=0.5 mL/min, UV=254 nm, t_R (major)=20.0 min (*R*), t_R (minor)=24.2 min (*S*).

4.14. Diisopropyl 1-[*N*-(4-methoxyphenyl)amino]-3-(2-trifluoromethylphenyl)-2-propenylphosphonate

Yellow oil. IR ($CHCl_3$) 2986, 1512, 1315, 1240, 1128, and 997 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ=7.60–7.04 (m, 5H), 6.76 (d, 2H, *J*=8.8 Hz), 6.66 (d, 2H, *J*=8.8 Hz), 6.26–6.19 (m, 1H), 4.82–4.72 (m, 1H), 4.39–4.29 (m, 1H), 4.06–4.02 (m, 1H), 3.73 (s, 3H), 1.89–1.21 (m, 12H). ^{13}C NMR (75 MHz, $CDCl_3$) δ=152.8, 140.6 (d, *J*=14.5 Hz), 135.6, 131.8, 129.4 (d, *J*=4.2 Hz), 129.0 (d, *J*=10.4 Hz), 127.5 (d, *J*=34.7 Hz), 127.4, 126.0, 125.7 (d, *J*=5.5 Hz), 122.4, 115.4, 114.7, 72.1 (d, *J*=6.9 Hz), 71.6 (d, *J*=6.9 Hz), 55.9 (d, *J*=153.5 Hz), 55.7, 24.2 (d, *J*=3.5 Hz), 24.1 (d, *J*=4.1 Hz), 23.8 (d, *J*=5.5 Hz), 23.7 (d, *J*=5.5 Hz). ^{31}P NMR (121 MHz, $CDCl_3$) δ=20.7. ^{19}F NMR (282 MHz, $CDCl_3$) δ=1.7. Found: C, 58.84; H, 6.13; N, 2.90%. Calcd for $C_{23}H_{29}F_3NO_4P$: C, 58.60; H, 6.20; N, 2.97%. $[\alpha]_D^{21}$ +58.1 (*c* 0.9, $CDCl_3$) (90% ee). HPLC: Daicel Chiralpak AD-H (hexane/*i*-PrOH=3:1/v:v), flow rate=0.5 mL/min, UV=254 nm, t_R (major)=16.7 min (*R*), t_R (minor)=19.6 min (*S*).

4.15. Diisopropyl 1-[*N*-(4-methoxyphenyl)amino]-3-(1-naphthyl)-2-propenylphosphonate

Yellow oil. IR ($CHCl_3$) 2988, 2361, 2341, 1510, 1240, and 995 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ=7.91–6.75 (m, 12H), 6.31–6.24 (m, 1H), 4.85–4.77 (m, 2H), 4.47–4.11 (m, 2H), 3.74 (s, 3H), 1.37 (d, 6H, *J*=6.2 Hz), 1.34–1.10 (m, 6H). ^{13}C NMR (75 MHz, $CDCl_3$) δ=152.6, 140.7 (d, *J*=13.8 Hz), 134.3, 133.4, 130.3, 130.1, 128.3, 127.9, 127.3, 127.2, 125.9, 125.5 (d, *J*=14.5 Hz), 123.8, 123.8, 115.4, 114.7, 72.0 (d, *J*=6.9 Hz), 71.5 (d, *J*=6.9 Hz), 55.9 (d, *J*=153.6 Hz), 55.8, 24.4 (d, *J*=3.5 Hz), 24.3 (d, *J*=3.5 Hz), 24.1 (d, *J*=5.4 Hz), 24.0 (d,

J=5.4 Hz). ^{31}P NMR (121 MHz, $CDCl_3$) δ=21.3. Found: C, 68.19; H, 6.98; N, 3.13%. Calcd for $C_{26}H_{32}NO_4P$: C, 68.86; H, 7.11; N, 3.09%. $[\alpha]_D^{26}$ +58.9 (c 0.5, $CHCl_3$) (81% ee). HPLC: Daicel Chiralpak AD-H (hexane/*i*-PrOH=1:1/v:v), flow rate=0.5 mL/min, UV=254 nm, t_R (major)=15.0 min (R), t_R (minor)=19.0 min (S).

Acknowledgements

This work was supported by a Grant-in-Aid for Scientific Research from the Ministry of Education, Science, Sports, Culture, and Technology, Japan. Computational time from the Research Center for Computational Science, Okazaki, Japan is deeply acknowledged.

Supplementary data

Supplementary data associated with this article can be found in the online version, at doi:10.1016/j.tet.2009.03.023.

References and notes

1. Smith, A. B.; Yager, K. M.; Taylor, C. M. *J. Am. Chem. Soc.* **1995**, *117*, 10879.
2. Alonso, E.; Alonso, E.; Solís, A.; Pozo, C. d. *Synlett* **2000**, 698.
3. Hirschmann, R.; Smith, A. B., III; Taylor, C. M.; Benkovic, P. A.; Taylor, S. D.; Yager, K. M.; Sprengeler, P. A.; Benkovic, S. J. *Science* **1994**, *265*, 234.
4. (a) Allen, J. G.; Atherton, F. R.; Hall, M. J.; Hassal, C. H.; Holmes, S. W.; Lambert, R. W.; Nisbet, L. J.; Ringrose, P. S. *Nature* **1978**, *272*, 56; (b) Atherton, F. R.; Hassall, C. H.; Lambert, R. W. *J. Med. Chem.* **1986**, *29*, 29.
5. (a) Yager, K. M.; Taylor, C. M.; Smith, A. B., III. *J. Am. Chem. Soc.* **1994**, *116*, 9377; (b) Lefebvre, I. M.; Evans, S. A., Jr. *J. Org. Chem.* **1997**, *62*, 7532; (c) Davis, F. A.; Lee, S.; Yan, H.; Titus, D. D. *Org. Lett.* **2001**, *3*, 1757.
6. For reviews, see: Gröger, H.; Hammer, B. *Chem.—Eur. J.* **2000**, *6*, 943; Merino, P.; Marqués-López, E.; Herrera, R. P. *Adv. Synth. Catal.* **2008**, *350*, 1195.
7. (a) Sasai, H.; Arai, S.; Tahara, Y.; Shibasaki, M. *J. Org. Chem.* **1995**, *60*, 6656; (b) Groeger, H.; Saida, Y.; Arai, S.; Martens, J.; Sasai, H.; Shibasaki, M. *Tetrahedron Lett.* **1996**, *37*, 9291; (c) Groger, H.; Saida, Y.; Sasai, H.; Yamaguchi, K.; Martens, J.; Shibasaki, M. *J. Am. Chem. Soc.* **1998**, *120*, 3089; (d) Saida, Y.; Gröger, H.; Maison, W.; Durot, N.; Sasai, H.; Shibasaki, M.; Martens, J. *J. Org. Chem.* **2000**, *65*, 4818.
8. Saito, B.; Egami, H.; Katsuki, T. *J. Am. Chem. Soc.* **2007**, *129*, 1978; Abell, J. P.; Yamamoto, H. *J. Am. Chem. Soc.* **2008**, *130*, 10521.
9. Joly, G. D.; Jacobsen, E. N. *J. Am. Chem. Soc.* **2004**, *126*, 4102.
10. Pettersen, D.; Marcolini, M.; Bernardi, L.; Fini, F.; Herrera, R. P.; Sgarzani, V.; Ricci, A. *J. Org. Chem.* **2006**, *71*, 6269.
11. For a preliminary communucation, see: Akiyama, T.; Morita, H.; Itoh, J.; Fuchibe, K. *Org. Lett.* **2005**, *7*, 2583.
12. Cheng, X.; Goddard, R.; Buth, G.; List, B. *Angew. Chem., Int. Ed.* **2008**, *47*, 5079.
13. For reviews, see: Connon, S. J. *Angew. Chem., Int. Ed.* **2006**, *45*, 3909; Akiyama, T.; Itoh, J.; Fuchibe, K. *Adv. Synth. Catal.* **2006**, *348*, 999; Akiyama, T. *Chem. Rev.* **2007**, *107*, 5744.
14. (a) Akiyama, T.; Itoh, J.; Yokota, K.; Fuchibe, K. *Angew. Chem., Int. Ed.* **2004**, *43*, 1566; (b) Akiyama, T.; Saitoh, Y.; Morita, H.; Fuchibe, K. *Adv. Synth. Catal.* **2005**, *347*, 1523; (c) Akiyama, T.; Tamura, Y.; Itoh, J.; Morita, H.; Fuchibe, K. *Synlett* **2006**, 141; (d) Akiyama, T.; Morita, H.; Fuchibe, K. *J. Am. Chem. Soc.* **2006**, *128*, 13070; (e) Itoh, J.; Fuchibe, K.; Akiyama, T. *Angew. Chem., Int. Ed.* **2006**, *45*, 4796; (f) Yamanaka, M.; Itoh, J.; Fuchibe, K.; Akiyama, T. *J. Am. Chem. Soc.* **2007**, *129*, 6756; (g) Itoh, J.; Fuchibe, K.; Akiyama, T. *Angew. Chem., Int. Ed.* **2008**, *47*, 4016; (h) Itoh, J.; Fuchibe, K.; Akiyama, T. *Synthesis* **2008**, 1319; (i) Akiyama, T.; Honma, Y.; Itoh, J.; Fuchibe, K. *Adv. Synth. Catal.* **2008**, *350*, 399.
15. For selected examples, see: (a) Uraguchi, D.; Terada, M. *J. Am. Chem. Soc.* **2004**, *126*, 5356; (b) Uraguchi, D.; Sorimachi, K.; Terada, M. *J. Am. Chem. Soc.* **2004**, *126*, 11804; (c) Uraguchi, D.; Sorimachi, K.; Terada, M. *J. Am. Chem. Soc.* **2005**, *127*, 9360; (d) Rowland, G. B.; Zhang, H.; Rowland, E. B.; Chennamadhavuni, S.; Wang, Y.; Antilla, J. C. *J. Am. Chem. Soc.* **2005**, *127*, 15696; (e) Hoffmann, S.; Seayad, A. M.; List, B. *Angew. Chem., Int. Ed.* **2005**, *44*, 7424; (f) Terada, M.; Machioka, K.; Sorimachi, K. *Angew. Chem., Int. Ed.* **2006**, *45*, 2254; (g) Terada, M.; Sorimachi, K.; Uraguchi, D. *Synlett* **2006**, 133; (h) Storer, R. I.; Carrera, D. E.; Ni, Y.; MacMillan, D. W. C. *J. Am. Chem. Soc.* **2006**, *128*, 84; (i) Seayad, J.; Seayad, A. M.; List, B. *J. Am. Chem. Soc.* **2006**, *128*, 1086; (j) Chen, X.-H.; Xu, X.-Y.; Liu, H.; Cun, L.-F.; Gong, L.-Z. *J. Am. Chem. Soc.* **2006**, *128*, 14802; (k) Terada, M.; Sorimachi, K. *J. Am. Chem. Soc.* **2007**, *129*, 292; (l) Kang, Q.; Zhao, Z.-A.; You, S.-L. *J. Am. Chem. Soc.* **2007**, *129*, 1484; (m) Guo, Q.-X.; Liu, H.; Guo, C.; Luo, S.-W.; Gu, Y.; Gong, L.-Z. *J. Am. Chem. Soc.* **2007**, *129*, 3790; (n) Jia, Y.-X.; Zhong, J.; Zhu, S.-F.; Zhang, C.-M.; Zhou, Q.-L. *Angew. Chem., Int. Ed.* **2007**, *46*, 5565; (o) Rueping, M.; Sugiono, E.; Schoepke, F. R. *Synlett* **2007**, 1441; (p) Rueping, M.; Sugiono, E.; Theissmann, T.; Kuenkel, A.; Koeckritz, A.; Pews-Davtyan, A.; Nemati, N.; Beller, M. *Org. Lett.* **2007**, *9*, 1065; (q) Rueping, M.; Theissmann, T.; Kuenkel, A.; Koenigs, R. M. *Angew. Chem., Int. Ed.* **2008**, *47*, 6798; (r) Terada, M.; Tanaka, H.; Sorimachi, K. *Synlett* **2008**, 1661.
16. For theoretical studies on the chiral phosphoric acid catalysis, see lit. 14f, and Simón, L.; Goodman, J. M. *J. Am. Chem. Soc.* **2008**, *130*, 8741; Marcelli, T.; Hammar, P.; Himo, F. *Chem.—Eur. J.* **2008**, *14*, 8562.
17. Deprotection of *N*-*p*-methoxyphenyl group of **3** by means of CAN gave free amine in 57% yield. $[\alpha]_D^{25}$ +11.5 (c 1.9, $CHCl_3$), lit., (*R*)-form: $[\alpha]_D^{20}$ +17.2 (c 1.0, $CHCl_3$).
18. Yamanaka, M.; Hirata, T., *J. Org. Chem.*, in press. doi:10.1021/jo900404b
19. The details of chemical models of the DFT calculations were shown in the computational section. All calculations were performed with the Gaussian 98 package, see: Frisch, M. J.; Trucks, G. W.; Schlegel, H. B.; Scuseria, G. E.; Robb, M. A.; Cheeseman, J. R.; Zakrzewski, V. G.; Montgomery, J. A., Jr.; Stratmann, R. E.; Burant, J. C.; Dapprich, S.; Millam, J. M.; Daniels, A. D.; Kudin, K. N.; Strain, M. C.; Farkas, O.; Tomasi, J.; Barone, V.; Cossi, M.; Cammi, R.; Mennucci, B.; Pomelli, C.; Adamo, C.; Clifford, S.; Ochterski, J.; Petersson, G. A.; Ayala, P. Y.; Cui, Q.; Morokuma, K.; Salvador, P.; Dannenberg, J. J.; Malick, D. K.; Rabuck, A. D.; Raghavachari, K.; Foresman, J. B.; Cioslowski, J.; Ortiz, J. V.; Baboul, A. G.; Stefanov, B. B.; Liu, G.; Liashenko, A.; Piskorz, P.; Komaromi, I.; Gomperts, R.; Martin, R. L.; Fox, D. J.; Keith, T.; Al-Laham, M. A.; Peng, C. Y.; Nanayakkara, A.; Challacombe, M.; Gill, P. M. W.; Johnson, B.; Chen, W.; Wong, M. W.; Andres, J. L.; Gonzalez, C.; Head-Gordon, M.; Replogle, E. S.; Pople, J. A. *Gaussian 98, Revision A.11.4*; Gaussian: Pittsburgh, PA, 2002.
20. The default Gaussian 98 implementation of the BHandHLYP method does not correspond to the original definition by Becke. The original version, see: Becke, A. D. *J. Chem. Phys.* **1993**, *98*, 1372.
21. Hehre, W. J.; Radom, L.; Schleyer, P. v. R.; Pople, J. A. *Ab Initio Molecular Orbital Theory*; John Wiley: New York, NY, 1986 and references cited therein.
22. Wipf, P.; Jung, J.-K. *J. Org. Chem.* **2000**, *65*, 6319.