Tetrahedron 69 (2013) 9373–9380

Contents lists available at ScienceDirect

Tetrahedron

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

Systematic study for the stereochemistry of the Atherton–Todd reaction

Biquan Xiong [a], Yongbo Zhou [a], Changqiu Zhao [b], Midori Goto [c], Shuang-Feng Yin [a,*], Li-Biao Han [a,c,*]

[a] State Key Laboratory of Chemo/Biosensing and Chemometrics, College of Chemistry and Chemical Engineering, Hunan University, Changsha 410082, PR China
[b] Department of Chemistry, College of Chemistry and Chemical Engineering, Liaocheng University, Liaocheng 252000, PR China
[c] National Institute of Advanced Industrial Science and Technology (AIST), Tsukuba, Ibaraki 305-8565, Japan

ARTICLE INFO

Article history:
Received 27 June 2013
Received in revised form 24 August 2013
Accepted 2 September 2013
Available online 11 September 2013

Keywords:
Atherton–Todd reaction
Stereochemistry
H-Phosphinates
Nucleophiles

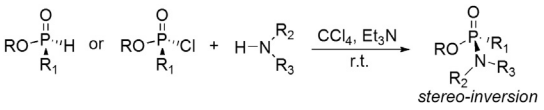
ABSTRACT

Under the Atherton–Todd reaction conditions, the stereochemistry on the reaction of *H*-phosphinates with different nucleophiles (e.g., amines, alcohols, phenols) was investigated. All reactions took place stereospecifically with inversion of configurations at the phosphorus centers. The reaction might proceed via a phosphoryl chloride intermediate with retention of configuration at phosphorus, followed by the attack of nucleophiles from the backside of Cl to give the substitution products with inversion of configuration at the phosphorus center. A plausible mechanism was proposed for these reactions.

1. Introduction

Optically active phosphonates and organophosphorus acid derivatives are valuable compounds,[1,2] which not only show biological activities related to antitumor,[3] HIV transcriptase inhibition, and immunomodulation,[4] but also are important chiral auxiliaries for asymmetric catalysis and asymmetric synthesis.[5] It is well known that *P*-chirogenic organophosphorus compounds can hardly be found in the natural product and the synthesis of such compounds in enantiomeric pure forms is usually a hard job.[1a,b,6]

Atherton–Todd reaction is a powerful classical synthetic method, which is widely used for the preparation of phosphates and related phosphorus compounds.[7] However, despite extensive studies, the mechanism of the Atherton–Todd reaction is not fully understood.[7c–h] Atherton and Todd discovered this reaction in 1945 and proposed a possible mechanism involving a trichloromethyl phosphonate intermediate.[7a] Later, Steinberg investigated the Atherton–Todd reaction's mechanism in 1950, and confirmed the formation of $(RO)_2P(O)Cl$ intermediates in the reaction.[7e] In 1985, Engel also proposed a plausible mechanism via a pentacoordinated phosphoryl chloride intermediate.[7f] Moreover, little is known on the stereochemistry of the Atherton–Todd reaction at phosphorus. In 1972, Mikolajczyk studied the stereochemistry of the reaction of optically active phosphoryl halides with alcohols and amines, and found the reaction proceeded with inversion of configuration at the phosphorus center.[7g] In 1980, Inch investigated the stereochemistry and mechanism of bond forming and breaking at phosphorus in some five-/six-membered cyclic phosphorus esters.[7h] In 2010, we studied the reaction of *H*-phosphinate with amines under the Atherton–Todd reaction conditions. On the basis of the X-ray structure of the product of optically active *H*-phosphinate with ammonia, we deduced that this reaction might proceed with inversion of configuration at the phosphorus center (Scheme 1).[8]



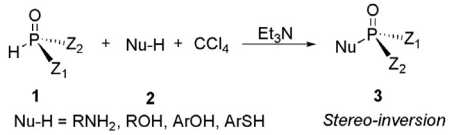
Scheme 1. Previous work: stereospecific coupling of optically active *H*-phosphinates or phosphoryl chlorides with amines.[8]

To ensure the generality of the conclusion that Atherton–Todd reaction proceeds stereospecifically with inversion of configuration at the phosphorus center, the stereochemistry on the reactions of optically active *H*-phospinates (**1**) with other nucleophiles (**2**)

* Corresponding authors. Tel./fax: +86 731 88821171; e-mail addresses: sf_yin@hnu.edu.cn, yinsf73@163.com (S.-F. Yin), libiao-han@aist.go.jp (L.-B. Han).

0040-4020/$ – see front matter © 2013 Elsevier Ltd. All rights reserved.
http://dx.doi.org/10.1016/j.tet.2013.09.001

(RNH_2, ROH, ArOH, ArSH) was studied. Based on the X-ray diffraction analysis, we confirmed that all the reactions took place efficiently with inversion of configurations at the phosphorus centers (Scheme 2).

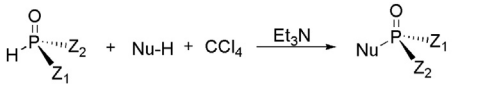


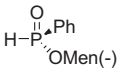
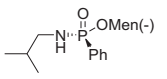
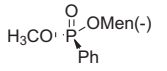
Scheme 2. Outline of the present work.

2. Results and discussion

In the present study, we first conducted the reaction of *Rp*-(−)-menthyl phenyl *H*-phosphinate (*Rp*-**1a**, *Rp*/*Sp*>99:1) with *iso*-butyl amine (**2a**) under the Atherton–Todd reaction conditions, the corresponding P–N coupling product *Rp*-**3a** (*Rp*/*Sp*>99:1) was generated stereospecifically in 94% yields (Table 1, entry 1). The stereochemistry of compound *Rp*-**3a** was confirmed by X-ray diffraction analysis (Fig. 1). It was shown that this reaction proceeded with inversion of configuration at the phosphorus center in *Rp*-**1a**, which is in consistent with our previous report.[8a] We further used *H*-phosphinate (*Rp*-**1a**, *Rp*/*Sp*>99:1) to react with methanol (**2b**) under the same reaction conditions, the expected product of *Sp*-**3b** (*Sp*/*Rp*>99:1) was obtained in 86% isolated yield. By the comparison of configuration of compound *Sp*-**3b** with *Rp*-**2a**, the reaction of *H*-phosphinates with methanol also took place stereospecifically with inversion of configuration at the phosphorus center (Table 1, entry 2, and Fig. 2).

Table 1
Stereospecific coupling of optically active *H*-phosphinates with *iso*-butyl amine/methanol under the Atherton–Todd reaction conditions[a]



Entry	P*(O)H (**1**)	Nu-H (**2**)	Product (**3**)	Yield[b] (%)
1	 ***Rp*-1a**	*iso*-Butyl amine **2a**	 ***Rp*-3a**	94
2	*Rp*-**1a**	CH_3OH **2b**	 ***Sp*-3b**	86

[a] Reaction conditions: nucleophiles (1 mmol) and optically active *H*-phosphinates (1 mmol) were dissolved in CCl_4 (5 mL), Et_3N (2 mmol) was added under N_2 atmosphere, stirred at room temperature overnight.
[b] Isolated yield.

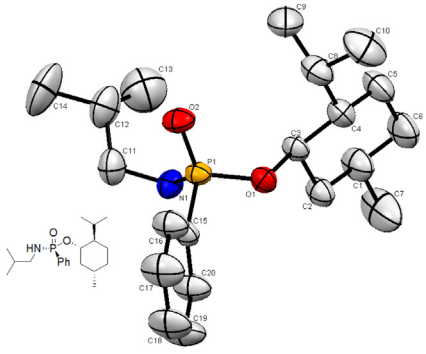


Fig. 1. ORTEP drawing of *Rp*-(−)-menthyl phenyl *N*-isobutyl phosphoramidate (*Rp*-**3a**). Hydrogen atoms are omitted for clarity; ellipsoids are drawn at 50% probability. Selected bond lengths [Å] and angles [°]: P1–O1 1.572(2), P1–O2 1.4722(19), P1–N1 1.626(2), P1–C15 1.802(3), C3–O1 1.472(3), C11–N1 1.463(4), P1–O1–C3 124.06(18), P1–N1–C11 121.4(2), N1–P1–C15 110.92(13), O1–P1–C15 99.64(12), O1–P1–N1 105.33(11), O2–P1–C15 111.60(13), O2–P1–O1 116.63(12), O2–P1–N1 111.96(12).

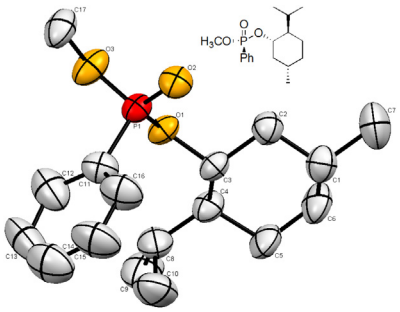
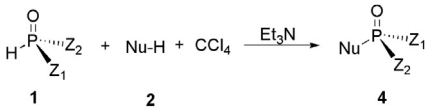


Fig. 2. ORTEP drawing of *Sp*-(−)-menthyl *O*-methyl phenylphosphate (*Sp*-**3b**). Hydrogen atoms are omitted for clarity; ellipsoids are drawn at 50% probability. Selected bond lengths [Å] and angles [°]: P1–O1 1.571(2), P1–O2 1.458(3), P1–O3 1.575(3), P1–C11 1.789(4), O1–C3 1.468(5), O3–C17 1.438(5), P1–O1–C3 120.1(2), P1–O3–C17 119.0(3), O2–P1–C11 111.0(2), O2–P1–O3 116.0(2), O2–P1–O1 116.7(2), O3–P1–C11 107.7(2), O1–P1–C11 106.6(2).

With these results in hand, we further conducted the reaction of optically active *H*-phosphinates with phenols under the same reaction conditions. We first operated the reaction using phenol (**2c**, 1 mmol) as a model substrate, treated with *Rp*-(−)-menthyl phenyl *H*-phosphinate (*Rp*-**1a**, *Rp*/*Sp*>99:1, 1 mmol) in CCl_4 (5 mL), and Et_3N (2 mmol) was added. The resulting mixture was stirred at room temperature overnight, then a considerable amount of *Rp*-(−)-menthyl *O*-phenyl phenylphosphonate (*Rp*-**4a**, *Rp*/*Sp*>99:1) was generated in quantitative yield. As shown in Table 2, the substrates bearing different functional groups, such as alkyl, alkoxyl, nitro-, and trifluoromethyl could be all efficiently coupled under this reaction conditions to afford the corresponding optically active phosphonates with good to excellent isolated yields (Table 2, entries 2–10). For most cases, electron-donating groups (Table 2, entries 5, 9, and 16) or electron-withdrawing groups (Table 2, entries 6, 7, 10, 13, and 18) on the phenols did not change the yields of the coupling products significantly. Similarly, the reaction of α-/β-naphthol (**2m**, **2n**) or hydroquinone (**2p**) with *Rp*-**1a** also gave the expected P–O coupling products in 95–97% yields. Substituted optically active *H*-phosphinates, such as (−)-menthyl phenyl phosphinate (*Rp*-**1a**, *Rp*/*Sp*>99:1), (−)-menthyl 2,4,6-trimethyl-phenyl phosphinate (*Rp*-**1b**, *Rp*/*Sp*=97:3), and (−)-menthyl benzyl phosphinate (*Rp*-**1c**, *Rp*/*Sp*>99:1) could react efficiently with phenol (**2c**) to provide the corresponding products of *Rp*-**4a** (*Rp*/*Sp*>99:1), *Rp*-**4o** (*Rp*/*Sp*=97:3), and *Rp*-**4q** (*Rp*/*Sp*>99:1) in 99%, 94%, and 96% yields (Table 1, entries 1, 15, 17), respectively.[9]

It is worth noting that the other diastereomer (*Sp*) was not detected from the crude products by employing ^1H NMR and ^{31}P NMR techniques during the reaction. Moreover, when a diastereomeric mixture of **1a** (*Rp*/*Sp*=52:48) was employed as the substrate in the above reaction, **4s** was obtained as a mixture of diastereomers with the same ratio of *Rp*/*Sp*=52:48 (Table 2, entry 19). Therefore, it is deduced that this reaction proceeds stereospecifically. In addition, the stereochemistry at phosphorus in *Rp*-**4l** (*Rp*/*Sp*>99:1) and *Rp*-**4r** (*Rp*/*Sp*>99:1) was unambiguously determined by X-ray analysis, showing that this reaction proceeded

Table 2
Stereospecific coupling of optically active *H*-phosphinates with phenols under the Atherton–Todd reaction conditions[a]



1 **2** **4**

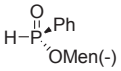
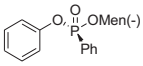
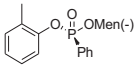
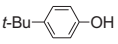
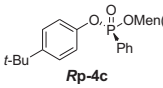
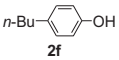
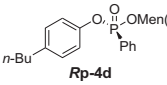
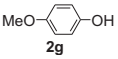
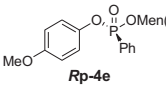
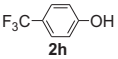
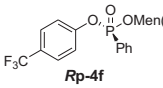
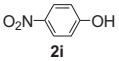
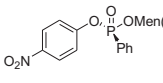
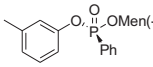
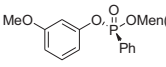
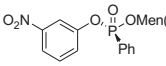
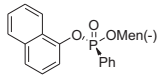
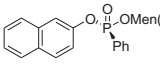
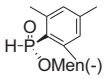
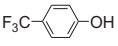
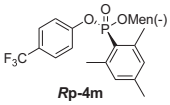
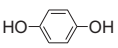
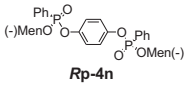
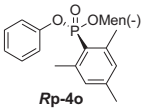
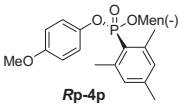
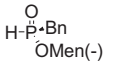
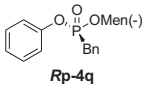
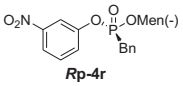
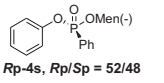
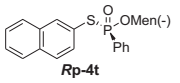
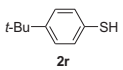
Entry	P*(O)–H (**1**)	Nu–H (**2**)	Product (**4**)	Yield[b] (%)
1	 ***Rp*-1a**	 **2c**	 ***Rp*-4a**	99
2	*Rp*-**1a**	 **2d**	 ***Rp*-4b**	98
3	*Rp*-**1a**	 **2e**	 ***Rp*-4c**	98
4	*Rp*-**1a**	 **2f**	 ***Rp*-4d**	96
5	*Rp*-**1a**	 **2g**	 ***Rp*-4e**	98
6	*Rp*-**1a**	 **2h**	 ***Rp*-4f**	97
7	*Rp*-**1a**	 **2i**		99
8	*Rp*-**1a**	 **2j**	 ***Rp*-4h**	93
9	*Rp*-**1a**	 **2k**	 ***Rp*-4i**	96
10	*Rp*-**1a**	 **2l**	 ***Rp*-4j**	96
11	*Rp*-**1a**	 **2m**	 ***Rp*-4k**	97
12	*Rp*-**1a**	 **2n**	 ***Rp*-4l**	95
13	 ***Rp*-1b**	 **2o**	 ***Rp*-4m**	96
14	*Rp*-**1a**	 **2p**	 ***Rp*-4n**	95
15	*Rp*-**1b**	**2c**	 ***Rp*-4o**	94

Table 2 (*continued*)

Entry	P*(O)–H (**1**)	Nu–H (**2**)	Product (**4**)	Yield[b] (%)
16	*Rp*-**1b**	**2g**	 ***Rp*-4p**	96
17	 ***Rp*-1c**	**2c**	 ***Rp*-4q**	96
18	*Rp*-**1c**	**2l**	 ***Rp*-4r**	92
19	*Rp*-**1a**, *Rp*/*Sp*=52:48	**2c**	 ***Rp*-4s**, ***Rp*/*Sp* = 52/48**	92
20	*Rp*-**1a**	 **2q**	 ***Rp*-4t**	88
21	*Rp*-**1c**	 **2r**	***Rp*-4u**	91

[a] Reaction conditions: phenol (1 mmol) and optically active *H*-phosphinate (1 mmol) were dissolved in CCl_4 (5 mL), Et_3N (2 mmol) was added under N_2 atmosphere, stirred at room temperature overnight.
[b] Isolated yield.

highly stereospecifically with inversion of configuration at the phosphorus center through the comparison of configuration with compound *Rp*-**2a** (*Rp*/*Sp*>99:1) (Figs. 3 and 4). It is noted that this conclusion is in consistent with our previous speculation.[8]

Fig. 3. ORTEP drawing of *Rp*-(−)-menthyl *O*-naphthalen-6-yl phenylphosphonate (*Rp*-**4l**). Hydrogen atoms are omitted for clarity; ellipsoids are drawn at 50% probability. Selected bond lengths [Å] and angles [°]: P1–O1 1.540(3), P1–O2 1.441(4), P1–O3 1.576(4), P1–C11 1.768(6), C2–O3 1.383(6), C21–O1 1.487(5), O1–P1–O2 112.2(2), P1–O1–C21 128.7(3), C2–O3–P1 129.1(3), O3–P1–C11 105.3(3), O2–P1–O3 116.6(2), O1–P1–O3 101.67(19), O2–P1–C11 112.6(3), O1–P1–C11 107.5(2).

Moreover, we conducted the reaction using thiophenols (e.g., 2-naphthalene-thiol (**2q**) and 4-*tert*-butyl thiophenol (**2r**)) as the substrates to react with *H*-phosphinates under the Atherton–Todd reaction conditions, and the corresponding P–S coupling products were obtained in 88% (*Rp*-**4t**, *Rp*/*Sp*>99:1) and 91% (*Rp*-**4u**, *Rp*/*Sp*>99:1) isolated yields, respectively (Table 2, entries 20 and 21). The stereochemistry of compound *Rp*-**4u** was unambiguously determined by X-ray diffraction analysis, showing that this reaction also proceeds with inversion of configuration at the phosphorus center in *Rp*-**1c** (Fig. 5).

On the basis of the above results, we also operated the reaction of optically active phosphoryl chloride *Sp*-**5a** (*Rp*/*Sp*>99:1) with

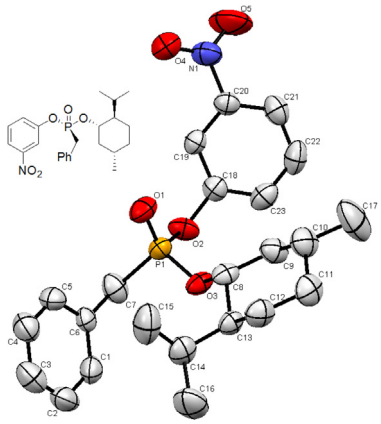


Fig. 4. ORTEP drawing of *R*p-benzyl (−)-menthyl *O*-3-nitrophenylphosphonate (*R*p-**4r**). Hydrogen atoms are omitted for clarity; ellipsoids are drawn at 50% probability. Selected bond lengths [Å] and angles [°]: P1–O1 1.461(3), P1–O2 1.597(3), P1–O3 1.561(3), P1–C7 1.790(4), C6–C7 1.506(6), C8–O3 1.477(4), C18–O2 1.398(5), N1–O4 1.220(5), N1–O5 1.210(5), N1–C20 1.472(6), O1–P1–O2 113.94(17), O1–P1–O3 114.78(17), O1–P1–C7 118.0(2), O2–P1–O3 105.21(19), O2–P1–C7 97.55(18), P1–O3–C8 124.5(3), C6–C7–P1 116.3(3), C7–P1–O3 105.31(18), C18–O2–P1 125.1(3), O4–N1–O5 123.2(5), O4–N1–C20 118.5(5), O5–N1–C20 118.3(5).

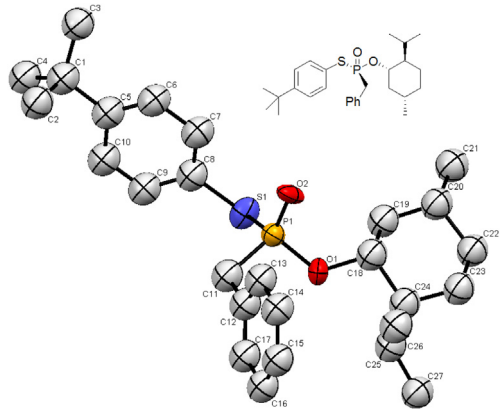
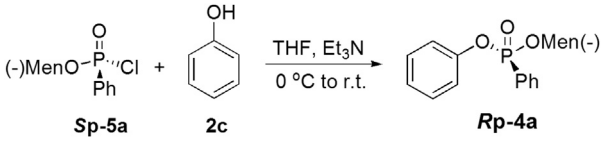


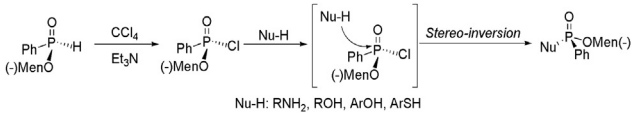
Fig. 5. ORTEP drawing of *R*p-(−)-menthyl *S*-4-*tert*-butylphenyl benzyl phosphonothioate (*R*p-**4u**). Hydrogen atoms are omitted for clarity; ellipsoids are drawn at 50% probability. Selected bond lengths [Å] and angles [°]: P1–O1 1.608(9), P1–O2 1.409(9), P1–S1 2.103(5), P1–C11 1.766(19), C8–S1 1.778(18), C18–O1 1.488(18), C11–C12 1.50(3), P1–O1–C18 119.0(9), P1–S1–C8 99.9(7), P1–C11–C12 114.6(14), O1–P1–S1 98.1(4), O1–P1–C11 105.4(7), S1–P1–C11 106.5(7), O1–P1–P2 113.5(5), S1–P1–O2 114.6(4), O2–P1–C11 116.8(8).

phenol under the nucleophilic substitution reaction conditions,[8b] and the expected product was obtained stereospecifically in 91% isolated yield (*R*p/*S*p>99:1, Scheme 3). By comparison of the ^{1}H and ^{31}P NMR data of this product with those of *R*p-**4a** (*R*p/*S*p>99:1), it was confirmed that the stereochemistry of the nucleophilic substitution reaction of phosphoryl chloride with phenol proceeds stereospecifically with inversion of configuration at the phosphorus center.



Scheme 3. Stereospecific substitution reaction of the optically active phosphoryl chloride with phenol.

The stereochemistry and mechanism of nucleophilic substitution reactions at phosphorus were well studied by Debruin, Holmes, and Mislow et al.[10] Although not fully understood for the current substitutions, a plausible mechanism is proposed in Scheme 4. Under the Atherton–Todd reaction condition, the optically active *H*-phosphinate is converted to an optical active phosphoryl chloride with retention of configuration at phosphorus.[8b,10] Nucleophiles can attack phosphorus from the backside of Cl to give the substitution products stereospecifically with inversion of configurations at the phosphorus centers.



Scheme 4. A plausible mechanism for the Atherton–Todd reaction.

3. Conclusion

In conclusion, we have investigated the stereochemistry of *H*-phosphinates with different nucleophiles (e.g., amines, alcohols, phenols) under the Atherton–Todd reaction conditions. Through the X-ray diffraction analysis for the corresponding products, it is confirmed that all the reactions proceed stereospecifically with inversion of configurations at the phosphorus centers. By using this method, we have successfully prepared a series of optically active phosphonates or phosphorus acid derivatives via reactions of the easily available optically active *H*-phosphinates with nucleophiles under the mild conditions, which are highly useful materials for the construction of biologically active molecules, asymmetric catalytic ligands, and *P*-chirogenic organophosphorus compounds.

4. Experimental section

4.1. General information and materials

All solvents used in reactions were freshly distilled. All other reagents were recrystallized or distilled as necessary. All reactions were performed under an atmosphere of dry nitrogen. ^{1}H (400 MHz), ^{13}C (100 MHz), and ^{31}P (162 MHz) spectra were recorded on a 400 MHz spectrometer in $CDCl_3$. ^{1}H NMR chemical shifts are reported using TMS as internal standard; ^{13}C NMR chemical shifts are reported relative to $CDCl_3$ as internal standard. The electron ionization method was used as the ionization method for the HRMS measurement, and the mass analyzer type is double-focusing.

4.2. Crystallographic information

CCDC-921548 (*R*p-**4r**), 921549 (*R*p-**4l**), 921550 (*R*p-**3a**), 921551 (*R*p-**4u**), and 799888 (*S*p-**3b**) contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Center via www.ccdc.cam.ac.uk/data_request/cif.

4.3. General procedure

A nucleophile (1 mmol) and an optically active *H*-phosphinates (1 mmol) were dissolved in CCl_4 (5 mL), Et_3N (2 mmol) was added under N_2 atmosphere, the resulting mixture was stirred at room temperature for 16–24 h. Then the reaction mixture was concentrated in vacuo, and the crude was purified by flash column chromatography (EtOAc/Hexane=1:10 to 1:5) to afford the product.

A typical procedure for the preparation of optically pure H-phosphinates (R_P)-**1a**.[9] The mixture of (L)-(−)-menthol (100 g, 641 mmol) and pyridine (51.3 mL, 641 mmol) in Et_2O (200 mL) was added dropwise with stirring to a $PhPCl_2$ (87.2 mL, 641 mmol) solution in Et_2O (400 mL) at 0 °C and then stirred at room temperature overnight. Water (12 mL, 667 mmol) was added, and the reaction mixture was washed with water and extracted with hexane. The hexane layer was dried over magnesium sulfate, filtered, and concentrated. Recrystallization of the mixture in hexane (twice) at −30 °C gave pure (R_P)-**1a** as a white crystal (R_P)-**1a** (R_P/S_P>99:1).

Preparation of H-phosphinates (R_P)-**1b** *and* (R_P)-**1c**.[9] $PhCH_2$−MgCl (1.0 M in Et_2O, 800 mL, 800 mmol) was added dropwise to the Et_2O (800 mL) solution of (−)-$MenOPCl_2$ (206.4 g, 800 mmol) at 0 °C and then stirred at room temperature overnight. Recrystallization of the mixture at −30 °C gave pure (R_P)-**1c** as white needles (R_P/S_P>99:1). (R_P)-**1b** was prepared similarly starting from (−)-$MenOPCl_2$ and mesitylmagnesium bromide.

*4.3.1. (−)-Menthyl phenyl N-iso-butyl phosphoramidate (Rp-**3a**).* Yield: 329.7 mg, *Rp*/*Sp*>99:1, (94%). White solid. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.71–7.76 (m, 2H), 7.40–7.44 (m, 1H), 7.34–7.38 (m, 2H), 4.10–4.19 (m, 1H), 2.60–2.63 (m, 3H), 2.26–2.29 (m, 1H), 1.91–1.98 (m, 1H), 1.01–1.39 (m, 4H), 0.86 (d, *J*=6.4 Hz, 3H), 0.78–0.81 (m, 7H), 0.76 (d, *J*=7.2 Hz, 3H), 0.47 (d, *J*=6.8 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 130.7 (d, J_{P-C}=171.4 Hz), 130.6 (d, J_{P-C}=9.5 Hz), 130.5 (d, J_{P-C}=2.9 Hz), 127.2 (d, J_{P-C}=14.0 Hz), 75.2 (d, J_{P-C}=6.4 Hz), 47.7 (d, J_{P-C}=6.6 Hz), 47.4, 42.5, 33.1, 30.5, 28.9 (d, J_{P-C}=6.7 Hz), 24.5, 21.7, 21.1, 20.0, 18.9 (d, J_{P-C}=1.9 Hz), 14.3; ^{31}P NMR ($CDCl_3$, 160 MHz): δ 21.49. HRMS calcd for $C_{20}H_{34}NO_2P$: 351.2327, found: 351.2305.

*4.3.2. (−)-Menthyl O-methyl phenylphosphate (Sp-**3b**).*[8a] Yield: 266.5 mg, *Sp*/*Rp*>99:1, (86%). White solid. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.71–7.76 (m, 2H), 7.45–7.47 (m, 1H), 7.38–7.41 (m, 2H), 4.13–4.21 (m, 1H), 3.64 (d, *J*=11.2 Hz, 3H), 2.23–2.28 (m, 1H), 1.77–1.84 (m, 1H), 1.52–1.60 (m, 2H), 1.11–1.41 (m, 3H), 0.86 (d, *J*=6.4 Hz, 3H), 0.75–0.89 (m, 2H), 0.72 (d, *J*=7.2 Hz, 3H), 0.43 (d, *J*=7.2 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 131.2 (d, J_{P-C}=3.0 Hz), 130.7 (d, J_{P-C}=9.7 Hz), 127.3 (d, J_{P-C}=14.9 Hz), 127.1 (d, J_{P-C}=188.3 Hz), 76.8 (d, J_{P-C}=6.6 Hz), 51.3 (d, J_{P-C}=5.3 Hz), 47.4 (d, J_{P-C}=7.0 Hz), 42.3, 33.0, 30.5, 24.5, 21.7, 21.0, 19.9, 14.2; ^{31}P NMR ($CDCl_3$, 160 MHz): δ 19.55.

*4.3.3. (−)-Menthyl O-phenyl phenylphosphonate (Rp-**4a**).*[8a] Yield: 368.2 mg, *Rp*/*Sp*>99:1, (99%). Colorless oil. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.83–7.89 (m, 2H), 7.51–7.55 (m, 1H), 7.41–7.46 (m, 2H), 7.23–7.27 (m, 2H), 7.15–7.17 (dd, J_{H-H}=1.2 Hz, J_{P-H}=6.4 Hz, 2H), 7.07–7.11 (m, 1H), 4.37–4.40 (m, 1H), 2.16–2.25 (m, 1H), 1.91–1.95 (m, 1H), 1.45–1.65 (m, 2H), 1.34–1.44 (m, 2H), 1.16–1.24 (m, 1H), 0.95–0.99 (m, 2H), 0.89 (d, *J*=6.4 Hz, 3H), 0.82 (d, *J*=6.8 Hz, 3H), 0.58 (d, *J*=6.8 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 150.7 (d, J_{P-C}=7.6 Hz), 132.5 (d, J_{P-C}=2.8 Hz), 131.9 (d, J_{P-C}=10.5 Hz), 129.5, 128.4 (d, J_{P-C}=15.3 Hz), 128.3 (d, J_{P-C}=191.6 Hz), 124.6, 120.7 (d, J_{P-C}=4.7 Hz), 78.8 (d, J_{P-C}=7.6 Hz), 48.5 (d, J_{P-C}=7.6 Hz), 43.2, 34.1, 31.6, 25.7, 22.9, 22.0, 20.9, 15.4; ^{31}P NMR ($CDCl_3$, 160 MHz): δ 14.69.

*4.3.4. (−)-Menthyl O-o-tolyl phenylphosphonate (Rp-**4b**).* Yield: 378.3 mg, *Rp*/*Sp*>99:1, (98%). Colorless oil. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.86–7.92 (m, 2H), 7.52–7.56 (m, 1H), 7.43–7.47 (m, 2H), 7.26–7.29 (m, 1H), 7.10–7.15 (m, 1H), 7.03–7.09 (m, 1H), 7.01 (t, *J*=7.2 Hz), 4.35–4.38 (m, 1H), 2.26 (s, 3H), 2.13–2.17 (m, 1H), 1.89–1.93 (m, 1H), 1.60–1.64 (m, 2H), 1.32–1.39 (m, 2H), 1.08–1.17 (m, 1H), 0.95–0.98 (m, 2H), 0.86 (d, *J*=6.4 Hz, 3H), 0.81 (d, *J*=6.8 Hz, 3H), 0.58 (d, *J*=7.2 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 149.3 (d, J_{P-C}=7.6 Hz), 132.4 (d, J_{P-C}=2.9 Hz), 131.8 (d, J_{P-C}=10.5 Hz), 131.2, 129.6 (d, J_{P-C}=11.4 Hz), 128.6 (d, J_{P-C}=175.4 Hz), 128.4 (d, J_{P-C}=15.2 Hz), 126.8, 124.6, 120.5 (d, J_{P-C}=2.9 Hz), 78.7 (d, J_{P-C}=7.7 Hz), 48.6 (d, J_{P-C}=6.7 Hz), 43.1, 34.1, 31.6, 25.7, 22.8, 22.0, 21.0, 16.7, 15.4; ^{31}P NMR ($CDCl_3$, 160 MHz): δ 14.55. HRMS calcd for $C_{23}H_{31}O_3P$: 386.2011, found: 386.2002.

*4.3.5. (−)-Menthyl O-4-tert-butylphenyl phenylphosphonate (Rp-**4c**).* Yield: 419.2 mg, *Rp*/*Sp*>99:1, (98%). Colorless oil. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.85–7.90 (m, 2H), 7.52–7.56 (m, 1H), 7.42–7.48 (m, 2H), 7.26–7.28 (m, 2H), 7.07–7.09 (m, 2H), 4.33–4.41 (m, 1H), 2.16–2.21 (m, 1H), 1.89–1.95 (m, 1H), 1.61–1.65 (m, 2H), 1.33–1.45 (m, 2H), 1.27 (s, 9H), 1.02–1.18 (m, 1H), 0.95–0.99 (m, 2H), 0.88 (d, *J*=6.8 Hz, 3H), 0.82 (d, *J*=7.2 Hz, 3H), 0.59 (d, *J*=6.8 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 148.3 (d, J_{P-C}=7.6 Hz), 147.4, 132.4 (d, J_{P-C}=2.8 Hz), 131.9 (d, J_{P-C}=9.5 Hz), 128.5 (d, J_{P-C}=191.5 Hz), 128.3 (d, J_{P-C}=15.3 Hz), 126.3, 120.1 (d, J_{P-C}=3.8 Hz), 78.7 (d, J_{P-C}=6.7 Hz), 60.4, 48.5 (d, J_{P-C}=6.7 Hz), 43.1, 34.4, 34.1, 31.6, 31.4, 25.7, 22.9, 22.0, 20.9, 15.4, 14.2; ^{31}P NMR ($CDCl_3$, 160 MHz): δ 15.31. HRMS calcd for $C_{26}H_{37}O_3P$: 428.2480, found: 428.2470.

*4.3.6. (−)-Menthyl O-4-butylphenyl phenylphosphonate (Rp-**4d**).* Yield: 402.5 mg, *Rp*/*Sp*>99:1, (96%). Colorless oil. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.83–7.89 (m, 2H), 7.51–7.55 (m, 1H), 7.41–7.46 (m, 2H), 7.03–7.08 (m, 4H), 4.36–4.39 (m, 1H), 2.51–2.55 (m, 2H), 2.20–2.23 (m, 1H), 1.90–1.95 (m, 1H), 1.64–1.65 (m, 2H), 1.20–1.63 (m, 7H), 0.95–0.99 (m, 2H), 0.91 (s, 6H), 0.88 (d, *J*=7.2 Hz, 3H), 0.81 (d, *J*=6.8 Hz, 3H), 0.58 (d, *J*=6.8 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 148.6 (d, J_{P-C}=6.6 Hz), 139.2, 132.4 (d, J_{P-C}=2.8 Hz), 131.9 (d, J_{P-C}=9.5 Hz), 129.4, 128.4 (d, J_{P-C}=183 Hz), 128.3 (d, J_{P-C}=15.2 Hz), 120.4 (d, J_{P-C}=3.8 Hz), 78.7 (d, J_{P-C}=6.7 Hz), 48.5 (d, J_{P-C}=6.7 Hz), 43.2, 34.9, 34.1, 33.7, 31.6, 25.7, 22.9, 22.3, 22.0, 21.0, 15.4, 14.0; ^{31}P NMR ($CDCl_3$, 160 MHz): δ 14.74. HRMS calcd for $C_{26}H_{37}O_3P$: 428.2480, found: 428.2467.

*4.3.7. (−)-Menthyl O-4-methoxy-phenyl phenylphosphonate (Rp-**4e**).* Yield: 393.9 mg, *Rp*/*Sp*>99:1, (98%). Colorless oil. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.82–7.87 (m, 2H), 7.51–7.53 (m, 1H), 7.41–7.46 (m, 2H), 7.06–7.08 (m, 2H), 6.74–6.79 (m, 2H), 4.35–4.38 (m, 1H), 3.73 (s, 3H), 2.22–2.25 (m, 1H), 1.91–1.94 (m, 1H), 1.61–1.66 (m, 2H), 1.34–1.40 (m, 2H), 1.18–1.24 (m, 1H), 0.95–0.99 (m, 2H), 0.89 (d, *J*=6.4 Hz, 3H), 0.81 (d, *J*=6.8 Hz, 3H), 0.57 (d, *J*=6.8 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 156.4, 144.2 (d, J_{P-C}=7.6 Hz), 132.4 (d, J_{P-C}=2.9 Hz), 132.0 (d, J_{P-C}=9.6 Hz), 128.3 (d, J_{P-C}=190.6 Hz), 128.3 (d, J_{P-C}=15.2 Hz), 121.6 (d, J_{P-C}=3.8 Hz), 114.5, 78.8 (d, J_{P-C}=7.6 Hz), 55.6, 48.5 (d, J_{P-C}=6.7 Hz), 43.2, 34.1, 31.6, 25.7, 22.9, 22.0, 21.0, 15.4; ^{31}P NMR ($CDCl_3$, 160 MHz): δ 15.04. HRMS calcd for $C_{23}H_{31}O_4P$: 402.1960, found: 402.1956.

*4.3.8. (−)-Menthyl O-4-trifluoromethyl-phenyl phenylphosphonate (Rp-**4f**).* Yield: 426.6 mg, *Rp*/*Sp*>99:1, (97%). Yellow oil. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.83–7.89 (m, 2H), 7.44–7.58 (m, 5H), 7.28–7.30 (m, 2H), 4.37–4.45 (m, 1H), 2.21–2.24 (m, 1H), 1.89–1.95 (m, 1H), 1.63–1.67 (m, 2H), 1.35–1.47 (m, 2H), 1.18–1.26 (m, 1H), 0.97–1.03 (m, 2H), 0.89 (d, *J*=6.4 Hz, 3H), 0.82 (d, *J*=6.8 Hz, 3H), 0.59 (d, *J*=6.8 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 153.3 (d, J_{P-C}=6.7 Hz), 132.8 (d, J_{P-C}=2.9 Hz), 131.9 (d, J_{P-C}=10.5 Hz), 128.5 (d, J_{P-C}=12.4 Hz), 127.0 (d, J_{P-C}=5.7 Hz), 126.9 (d, J_{P-C}=2.9 Hz), 126.7 (d, J_{P-C}=6.7 Hz), 123.9 (d, J_{P-C}=269.7 Hz), 120.9 (d, J_{P-C}=4.7 Hz), 79.3 (d, J_{P-C}=6.6 Hz), 48.5 (d, J_{P-C}=6.7 Hz), 43.2, 34.0, 31.6, 25.7, 22.8, 22.0, 20.9, 15.4; ^{31}P NMR ($CDCl_3$, 160 MHz): δ 15.04. HRMS calcd for $C_{23}H_{28}F_3O_3P$: 440.1728, found: 440.1726.

*4.3.9. (−)-Menthyl O-4-nitrophenyl phenylphosphonate (Rp-**4g**).* Yield: 412.7 mg, *Rp*/*Sp*>99:1, (99%). Yellow oil. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.15–8.19 (m, 2H), 7.83–7.88 (m, 2H), 7.56–7.60

(m, 1H), 7.45–7.50 (m, 2H), 7.32–7.35 (m, 2H), 4.40–4.46 (m, 1H), 2.25–2.29 (m, 1H), 1.90–1.94 (m, 1H), 1.64–1.68 (m, 2H), 1.43–1.59 (m, 2H), 1.22–1.31 (m, 1H), 0.95–1.01 (m, 2H), 0.92 (d, J=6.4 Hz, 3H), 0.83 (d, J=7.6 Hz, 3H), 0.59 (d, J=6.8 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 155.7 (d, J_{P-C}=6.7 Hz), 144.4, 133.1 (d, J_{P-C}=2.9 Hz), 131.9 (d, J_{P-C}=10.5 Hz), 128.7 (d, J_{P-C}=15.3 Hz), 127.2 (d, J_{P-C}=191.6 Hz), 125.5, 121.1 (d, J_{P-C}=4.7 Hz), 79.6 (d, J_{P-C}=7.7 Hz), 48.5 (d, J_{P-C}=6.7 Hz), 43.2, 34.0, 31.7, 25.8, 22.9, 22.0, 20.9, 15.4; ^{31}P NMR ($CDCl_3$, 160 MHz): δ 15.22. HRMS calcd for $C_{22}H_{28}NO_5P$: 417.1705, found: 417.1698.

*4.3.10. (−)-Menthyl O-m-tolyl phenylphosphonate (Rp-**4h**).* Yield: 358.9 mg, *R*p/*S*p>99:1, (93%). Colorless oil. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.85–7.90 (m, 2H), 7.51–7.55 (m, 1H), 7.41–7.46 (m, 2H), 7.12 (t, J=7.6 Hz, 1H), 7.02 (s, 1H), 6.95 (d, J=8.4 Hz, 1H), 6.90 (d, J=7.2 Hz, 1H), 4.35–4.42 (m, 1H), 2.28 (s, 3H), 2.23–2.27 (m, 1H), 1.89–1.95 (m, 1H), 1.61–1.67 (m, 2H), 1.34–1.47 (m, 2H), 1.16–1.26 (m, 1H), 0.92–0.99 (m, 2H), 0.89 (d, J=6.4 Hz, 3H), 0.81 (d, J=7.2 Hz, 3H), 0.59 (d, J=7.2 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 150.5 (d, J_{P-C}=6.9 Hz), 139.6, 132.3 (d, J_{P-C}=3 Hz), 131.8 (d, J_{P-C}=9.9 Hz), 129.1, 128.3 (d, J_{P-C}=190.7 Hz), 128.2 (d, J_{P-C}=15.2 Hz), 125.3, 121.2 (d, J_{P-C}=3.1 Hz), 117.4 (d, J_{P-C}=4.6 Hz), 78.6 (d, J_{P-C}=6.9 Hz), 48.4 (d, J_{P-C}=6.8 Hz), 43.1, 34.0, 31.5, 25.6, 22.7, 21.9, 21.2, 20.8, 15.3; ^{31}P NMR ($CDCl_3$, 160 MHz): δ 15.68. HRMS calcd for $C_{23}H_{31}O_3P$: 386.2011, found: 386.2005.

*4.3.11. (−)-Menthyl O-3-methoxyphenyl phenylphosphonate (Rp-**4i**).* Yield: 385.7 mg, *R*p/*S*p>99:1, (96%). Yellow oil. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.85–7.90 (m, 2H), 7.51–7.53 (m, 1H), 7.41–7.46 (m, 2H), 7.13 (t, J=8 Hz, 1H), 6.75–6.78 (m, 2H), 6.63–6.66 (m, 1H), 4.37–4.43 (m, 1H), 3.72 (s, 3H), 2.25–2.31 (m, 1H), 1.91–1.95 (m, 1H), 1.61–1.66 (m, 2H), 1.34–1.47 (m, 2H), 1.18–1.27 (m, 1H), 0.93–1.00 (m, 2H), 0.89 (d, J=6.8 Hz, 3H), 0.81 (d, J=6.8 Hz, 3H), 0.58 (d, J=7.2 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 160.4, 151.5 (d, J_{P-C}=6.9 Hz), 132.4 (d, J_{P-C}=3 Hz), 131.8 (d, J_{P-C}=10.0 Hz), 129.7, 128.2 (d, J_{P-C}=15.3 Hz), 128.1 (d, J_{P-C}=190.7 Hz), 112.7 (d, J_{P-C}=3.8 Hz), 110.6, 106.5, 78.7 (d, J_{P-C}=6.9 Hz), 55.2 (d, J_{P-C}=2.3 Hz), 48.4 (d, J_{P-C}=6.8 Hz), 43.1, 33.9, 31.5, 25.6, 22.7, 21.9, 20.8, 15.3; ^{31}P NMR ($CDCl_3$, 160 MHz): δ 15.65. HRMS calcd for $C_{23}H_{31}O_4P$: 402.1960, found: 402.1949.

*4.3.12. (−)-Menthyl O-3-nitrophenyl phenylphosphonate (Rp-**4j**).* Yield: 400.1 mg, *R*p/*S*p>99:1, (96%). Yellow solid. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.98–8.03 (m, 2H), 7.85–7.91 (m, 2H), 7.57–7.61 (m, 2H), 7.44–7.51 (m, 3H), 4.40–4.46 (m, 1H), 2.24–2.28 (m, 1H), 1.90–1.94 (m, 1H), 1.64–1.70 (m, 2H), 1.38–1.49 (m, 2H), 1.21–1.30 (m, 1H), 0.94–1.01 (m, 2H), 0.91 (d, J=6.0 Hz, 3H), 0.83 (d, J=6.8 Hz, 3H), 0.59 (d, J=6.8 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 151.1 (d, J_{P-C}=6.9 Hz), 148.8, 133.0, 131.8 (d, J_{P-C}=10.7 Hz), 130.1, 128.6 (d, J_{P-C}=16.0 Hz), 127.2 (d, J_{P-C}=191.5 Hz), 127.0 (d, J_{P-C}=3.8 Hz), 119.6, 116.2 (d, J_{P-C}=5.4 Hz), 79.5 (d, J_{P-C}=6.8 Hz), 48.4 (d, J_{P-C}=6.9 Hz), 43.2, 33.9, 31.6, 25.7, 22.8, 21.9, 20.8, 15.3; ^{31}P NMR ($CDCl_3$, 160 MHz): δ 16.57. HRMS calcd for $C_{22}H_{28}NO_5P$: 417.1705, found: 417.1681.

*4.3.13. (−)-Menthyl O-naphthalen-5-yl phenylphosphonate (Rp-**4k**).* Yield: 408.9 mg, *R*p/*S*p>99:1, (97%). Colorless oil. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.16–8.18 (m, 1H), 7.92–7.98 (m, 2H), 7.76–7.78 (m, 1H), 7.48–7.58 (m, 2H), 7.44–7.46 (m, 3H), 7.38–7.43 (m, 2H), 7.30–7.34 (m, 1H), 4.41–4.50 (m, 1H), 2.18–2.24 (m, 1H), 1.92–2.01 (m, 1H), 1.58–1.64 (m, 2H), 1.33–1.43 (m, 2H), 1.10–1.18 (m, 1H), 0.86–1.01 (m, 2H), 0.82 (s, 3H), 0.81 (s, 3H), 0.61 (d, J=7.2 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 146.5 (d, J_{P-C}=7.7 Hz), 134.6, 132.4 (d, J_{P-C}=3.1 Hz), 131.7 (d, J_{P-C}=9.9 Hz), 128.3 (d, J_{P-C}=15.3 Hz), 128.1 (d, J_{P-C}=191.5 Hz), 127.5, 126.5 (d, J_{P-C}=6.1 Hz), 126.3, 125.9, 125.4, 124.3, 121.8, 115.3 (d, J_{P-C}=3.8 Hz), 78.8 (d, J_{P-C}=6.9 Hz), 48.3 (d, J_{P-C}=6.9 Hz), 43.0, 33.8, 31.4, 25.6, 22.7, 21.8, 20.8, 15.2; ^{31}P NMR ($CDCl_3$, 160 MHz): δ 16.08. HRMS calcd for $C_{26}H_{31}O_3P$: 422.2011, found: 422.2003.

*4.3.14. (−)-Menthyl O-naphthalen-6-yl phenylphosphonate (Rp-**4l**).* Yield: 400.6 mg, *R*p/*S*p>99:1, (94%). White solid. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.88–7.93 (m, 2H), 7.72–7.74 (m, 3H), 7.66 (s, 1H), 7.46–7.54 (m, 1H), 7.37–7.46 (m, 4H), 7.31–7.34 (m, 1H), 4.41–4.46 (m, 1H), 2.20–2.31 (m, 1H), 1.94–1.98 (m, 1H), 1.61–1.66 (m, 2H), 1.36–1.46 (m, 2H), 1.19–1.28 (m, 1H), 0.88–1.01 (m, 2H), 0.86 (d, J=7.6 Hz, 3H), 0.83 (d, J=7.2 Hz, 3H), 0.61 (d, J=7.2 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 148.3 (d, J_{P-C}=6.8 Hz), 133.8, 132.5, 131.9 (d, J_{P-C}=9.9 Hz), 130.7, 129.5, 128.3 (d, J_{P-C}=15.3 Hz), 128.1 (d, J_{P-C}=190.7 Hz), 127.6, 127.4, 126.4, 125.2, 120.7 (d, J_{P-C}=4.6 Hz), 117.0 (d, J_{P-C}=4.6 Hz), 78.9 (d, J_{P-C}=6.9 Hz), 48.4 (d, J_{P-C}=6.8 Hz), 43.1, 34.0, 31.5, 25.6, 22.8, 21.9, 20.89, 15.3; ^{31}P NMR ($CDCl_3$, 160 MHz): δ 15.95. HRMS calcd for $C_{26}H_{31}O_3P$: 422.2011, found: 422.2002.

*4.3.15. (−)-Menthyl O-4-(trifluoromethyl)phenyl 2,4,6-trimethylphenylphosphonate (Rp-**4m**).* Yield: 462.5 mg, *R*p/*S*p=97:3, (96%). Yellow oil. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.51 (d, J=8.4 Hz, 2H), 7.25 (s, 2H), 7.23 (s, 2H), 4.49–4.58 (m, 1H), 2.65 (d, J=1.2 Hz, 1H), 2.29 (s, 3H), 2.19–2.23 (m, 1H), 1.81–1.89 (m, 1H), 1.63–1.68 (m, 2H), 1.44–1.49 (m, 2H), 1.19–1.38 (m, 1H), 0.91–1.01 (m, 2H), 0.91 (d, J=6.8 Hz, 3H), 0.81 (d, J=6.8 Hz, 3H), 0.68 (d, J=6.8 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 153.5 (d, J_{P-C}=6.7 Hz), 143.6 (d, J_{P-C}=12.4 Hz), 142.4 (d, J_{P-C}=2.9 Hz), 130.5 (d, J_{P-C}=16.2 Hz), 126.9 (d, J_{P-C}=3.8 Hz), 126.5 (d, J_{P-C}=32.4 Hz), 121.6 (d, J_{P-C}=195.4 Hz), 120.6 (d, J_{P-C}=5.7 Hz), 78.5 (d, J_{P-C}=7.6 Hz), 48.6 (d, J_{P-C}=6.6 Hz), 43.2, 34.1, 31.7, 25.9, 23.4, 23.3, 23.0, 22.1, 21.2, 20.9, 15.5; ^{31}P NMR ($CDCl_3$, 160 MHz): δ 16.96. HRMS calcd for $C_{26}H_{34}F_3O_3P$: 482.2198, found: 482.2207.

*4.3.16. Di-(−)-menthyl O-diphenyl 1,4-phenylene diphosphonate (Rp-**4n**).* Yield: 632.6 mg, *R*p/*S*p>99:1, (95%). Colorless oil. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.77–7.83 (m, 4H), 7.49–7.54 (m, 2H), 7.39–7.44 (m, 4H), 7.05 (s, 4H), 4.31–4.39 (m, 2H), 2.21–2.24 (m, 2H), 1.87–1.93 (m, 2H), 1.62–1.64 (m, 4H), 1.32–1.44 (m, 4H), 1.14–1.23 (m, 2H), 0.94–1.01 (m, 4H), 0.88 (d, J=6.4 Hz, 1H), 0.80 (d, J=7.2 Hz, 2H), 0.56 (d, J=6.8 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 147.2 (d, J_{P-C}=6.6 Hz), 132.5 (d, J_{P-C}=3.8 Hz), 131.9, 131.8, 128.4 (d, J_{P-C}=15.2 Hz), 128.0 (d, J_{P-C}=190.7 Hz), 121.5 (d, J_{P-C}=4.8 Hz), 78.9 (d, J_{P-C}=6.7 Hz), 48.5 (d, J_{P-C}=7.7 Hz), 43.2, 34.0, 31.6, 25.7, 22.8, 22.0, 20.9, 15.4; ^{31}P NMR ($CDCl_3$, 160 MHz): δ 14.85. HRMS calcd for $C_{38}H_{52}O_6P_2$: 666.3239, found: 666.3236.

*4.3.17. (−)-Menthyl O-phenyl 2,4,6-trimethylphenylphosphonate (Rp-**4o**).* Yield: 389.1 mg, *R*p/*S*p=97:3, (94%). Colorless oil. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.22–7.24 (m, 2H), 7.05–7.14 (m, 3H), 6.89 (d, J=4.8 Hz, 2H), 4.48–4.52 (m, 1H), 2.65 (d, J=1.6 Hz, 1H), 2.28 (s, 3H), 2.19–2.25 (m, 1H), 1.77–1.88 (m, 1H), 1.61–1.67 (m, 2H), 1.40–1.51 (m, 2H), 1.16–1.36 (m, 1H), 0.97–1.05 (m, 2H), 1.04 (d, J=10.0 Hz, 3H), 0.80 (d, J=7.2 Hz, 3H), 0.67 (d, J=6.8 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 150.9 (d, J_{P-C}=6.6 Hz), 143.6 (d, J_{P-C}=12.4 Hz), 142.0 (d, J_{P-C}=2.9 Hz), 130.4 (d, J_{P-C}=16.2 Hz), 129.4, 124.3, 122.3 (d, J_{P-C}=184.9 Hz), 120.4 (d, J_{P-C}=4.7 Hz), 78.0 (d, J_{P-C}=7.6 Hz), 48.6 (d, J_{P-C}=6.7 Hz), 43.2, 34.1, 31.7, 25.8, 23.4 (d, J_{P-C}=1.9 Hz), 23.0, 22.1, 21.2, 21.0, 15.5; ^{31}P NMR ($CDCl_3$, 160 MHz): δ 16.56. HRMS calcd for $C_{25}H_{35}O_3P$: 414.2324, found: 414.2312.

*4.3.18. (−)-Menthyl O-4-methoxy-phenyl 2,4,6-trimethylphenylphosphonate (Rp-**4p**).* Yield: 426.2 mg, *R*p/*S*p=97:3, (96%). Colorless oil. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.03–7.05 (m, 2H), 6.77 (d, J=3.6 Hz, 2H), 6.73–6.76 (m, 2H), 4.48–4.51 (m, 1H), 3.73 (s, 3H), 2.64 (d, J=1.2 Hz, 6H), 2.28 (s, 3H),

2.18–2.21 (m, 1H), 1.82–1.86 (m, 1H), 1.61–1.67 (m, 2H), 1.35–1.47 (m, 2H), 1.15–1.32 (m, 1H), 0.99–1.02 (m, 2H), 0.90 (d, J=6.4 Hz, 3H), 0.81 (d, J=6 Hz, 3H), 0.66 (d, J=6.8 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 156.2, 144.4 (d, J_{P-C}=7.6 Hz), 143.6 (d, J_{P-C}=12.3 Hz), 141.9 (d, J_{P-C}=2.8 Hz), 130.3 (d, J_{P-C}=16.2 Hz), 122.3 (d, J_{P-C}=184.9 Hz), 121.3 (d, J_{P-C}=4.8 Hz), 114.4, 78.0 (d, J_{P-C}=7.6 Hz), 55.6, 48.6 (d, J_{P-C}=6.7 Hz), 43.2, 34.2, 31.7, 25.8, 23.4 (d, J_{P-C}=2.9 Hz), 23.0, 22.1, 21.2, 21.0, 15.5; ^{31}P NMR ($CDCl_3$, 160 MHz): δ 16.98. HRMS calcd for $C_{26}H_{37}O_4P$: 444.2429, found: 444.2424.

*4.3.19. (−)-Menthyl O-phenyl benzylphosphonate (Rp-**4q**).* Yield: 370.3 mg, *Rp*/*Sp*>99:1, (96%). Colorless oil. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.23–7.33 (m, 7H), 7.10–7.14 (m, 3H), 4.30–4.35 (m, 1H), 3.21–3.36 (m, 2H), 1.92–1.96 (m, 1H), 1.78–1.83 (m, 1H), 1.58–1.62 (m, 2H), 1.26–1.37 (m, 2H), 1.01–1.06 (m, 1H), 0.98–1.01 (m, 2H), 0.83 (d, J=7.2 Hz, 3H), 0.81 (d, J=6.4 Hz, 3H), 0.63 (d, J=7.2 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 150.8 (d, J_{P-C}=8.5 Hz), 131.2 (d, J_{P-C}=8.6 Hz), 130.0 (d, J_{P-C}=6.7 Hz), 129.6, 128.5 (d, J_{P-C}=2.9 Hz), 126.9 (d, J_{P-C}=3.8 Hz), 124.7, 120.6 (d, J_{P-C}=4.7 Hz), 78.5 (d, J_{P-C}=8.6 Hz), 48.5 (d, J_{P-C}=7.7 Hz), 43.1, 34.0, 33.9 (d, J_{P-C}=139.2 Hz), 31.5, 25.4, 22.7, 21.9, 21.0, 15.4; ^{31}P NMR ($CDCl_3$, 160 MHz): δ 22.41. HRMS calcd for $C_{23}H_{31}O_3P$: 386.2011, found: 386.2005.

*4.3.20. (−)-Menthyl O-3-nitro-phenyl benzylphosphonate (Rp-**4r**).* Yield: 418.1 mg, *Rp*/*Sp*>99:1, (97%). White solid. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.95–7.98 (m, 1H), 7.86 (s, 1H), 7.42 (d, J=5.6 Hz, 2H), 7.25–7.33 (m, 3H), 4.33–4.41 (m, 1H), 3.34 (d, J_{P-H}=21.6 Hz, 2H), 1.95–1.98 (m, 1H), 1.83–1.89 (m, 1H), 1.62–1.66 (m, 2H), 1.30–1.42 (m, 2H), 0.93–1.26 (m, 3H), 0.86 (d, J=7.2 Hz, 3H), 0.83 (d, J=6.8 Hz, 3H), 0.69 (d, J=6.8 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 151.4 (d, J_{P-C}=8.0 Hz), 148.8, 130.4 (d, J_{P-C}=9.6 Hz), 130.0 (d, J_{P-C}=4.8 Hz), 129.9, 128.7 (d, J_{P-C}=2.9 Hz), 127.3 (d, J_{P-C}=4.0 Hz), 126.8 (d, J_{P-C}=3.8 Hz), 119.4, 116.0 (d, J_{P-C}=4.7 Hz), 79.1 (d, J_{P-C}=8.2 Hz), 48.5 (d, J_{P-C}=6.4 Hz), 34.2 (d, J_{P-C}=138.0 Hz), 33.9, 31.5, 25.6, 22.8, 21.9, 20.9, 15.5; ^{31}P NMR ($CDCl_3$, 160 MHz): δ 23.16. HRMS calcd for $C_{23}H_{30}NO_5P$: 431.1862, found: 431.1844.

*4.3.21. (−)-Menthyl O-phenyl phenylphosphonate (Rp-**4s**).*[8] Yield: 342.1 mg, *Rp*/*Sp*=52:48, (92%). Colorless oil. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.85–7.90 (m, 2H), 7.50–7.54 (m, 1H), 7.42–7.45 (m, 2H), 7.22–7.27 (m, 2H), 7.15–7.18 (m, 2H), 7.06–7.10 (m, 1H), 4.37–4.53 (m, 1H), 2.16–2.26 (m, 1H), 1.92–1.96 (m, 1H), 1.41–1.65 (m, 2H), 1.22–1.39 (m, 2H), 1.14–1.19 (m, 1H), 0.95–0.99 (m, 2H), 0.84–0.90 (m, 3H), 0.78–0.83 (m, 4.5H), 0.59 (d, J=6.8 Hz, 1.5H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 149.9 (d, J_{P-C}=7.0 Hz), 149.7 (d, J_{P-C}=7.0 Hz), 131.5 (d, J_{P-C}=2.9 Hz), 131.4 (d, J_{P-C}=1.9 Hz), 130.9 (d, J_{P-C}=4.6 Hz), 130.8 (d, J_{P-C}=4.7 Hz), 128.5, 128.1 (d, J_{P-C}=190.9 Hz), 127.4 (d, J_{P-C}=4.8 Hz), 127.3 (d, J_{P-C}=191.1 Hz), 127.2 (d, J_{P-C}=4.9 Hz), 123.6, 123.5, 119.7 (d, J_{P-C}=4.5 Hz), 119.5 (d, J_{P-C}=4.5 Hz), 78.1 (d, J_{P-C}=7.2 Hz), 77.8 (d, J_{P-C}=7.0 Hz), 47.6 (d, J_{P-C}=6.4 Hz), 47.5 (d, J_{P-C}=7.0 Hz), 42.1, 42.0, 33.0, 30.6, 30.5, 24.7, 24.5, 21.9, 20.9, 20.8, 22.0, 19.9, 14.6, 14.4; ^{31}P NMR ($CDCl_3$, 160 MHz): δ 14.56, δ 13.91.

*4.3.22. (−)-Menthyl S-naphthalen-6-yl phenylphosphonothioate (Rp-**4t**).* Yield: 385.5 mg, *Rp*/*Sp*>99:1, (88%). Yellow oil. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.79 (s, 1H), 7.57–7.68 (m, 5H), 7.23–7.9 (m, 6H), 4.39–4.48 (m, 1H), 2.24–2.27 (m, 1H), 1.82–1.90 (m, 1H), 1.57 (d, J=12.0 Hz, 2H), 1.28–1.40 (m, 2H), 1.12–1.21 (m, 1H), 0.82–0.93 (m, 1H), 0.81 (d, J=6.8 Hz, 3H), 0.75–0.80 (m, 1H), 0.73 (d, J=7.2 Hz, 3H), 0.56 (d, J=6.8 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 134.2 (d, J_{P-C}=5.6 Hz), 132.4 (d, J_{P-C}=2.2 Hz), 131.8 (d, J_{P-C}=1.7 Hz), 131.2 (d, J_{P-C}=3.1 Hz), 131.2 (d, J_{P-C}=148.9 Hz), 130.6 (d, J_{P-C}=3.3 Hz), 130.5 (d, J_{P-C}=10.6 Hz), 127.5 (d, J_{P-C}=1.4 Hz), 127.1 (d, J_{P-C}=14.8 Hz), 126.7, 126.5, 125.8, 125.4, 123.1 (d, J_{P-C}=5.4 Hz), 78.0 (d, J_{P-C}=8.2 Hz), 47.5 (d, J_{P-C}=5.9 Hz), 42.2, 32.9, 30.6, 24.5, 21.7, 20.9, 19.9, 14.3; ^{31}P NMR ($CDCl_3$, 160 MHz): δ 40.05. HRMS calcd for $C_{26}H_{31}O_2PS$: 438.1782, found: 438.1770.

*4.3.23. (−)-Menthyl S-4-tert-butylphenyl benzyl phosphonothioate (Rp-**4u**).* Yield: 416.8 mg, *Rp*/*Sp*>99:1, (91%). White solid. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.39–7.42 (m, 2H), 7.27 (d, J=8.4 Hz, 2H), 7.16–7.18 (m, 5H), 4.27–4.36 (m, 1H), 3.16–3.30 (m, 2H), 2.20–2.24 (m, 1H), 1.13–1.57 (m, 3H), 1.24 (s, 9H), 1.02–1.20 (m, 3H), 0.70–0.93 (m, 2H), 0.83 (d, J=6.8 Hz, 3H), 0.63 (d, J=7.2 Hz, 3H), 0.48 (d, J=6.8 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 150.9 (d, J_{P-C}=2.4 Hz), 133.5 (d, J_{P-C}=4.2 Hz), 129.9 (d, J_{P-C}=9.9 Hz), 129.2 (d, J_{P-C}=6.8 Hz), 127.2 (d, J_{P-C}=3.2 Hz), 125.9 (d, J_{P-C}=2.9 Hz), 125.4 (d, J_{P-C}=1.6 Hz), 122.9 (d, J_{P-C}=5.1 Hz), 76.9 (d, J_{P-C}=8.6 Hz), 47.6 (d, J_{P-C}=5.6 Hz), 41.9, 39.2 (d, J_{P-C}=100.7 Hz), 33.6, 32.9, 30.5, 30.2, 23.9, 21.5, 21.1, 20.0, 14.1; ^{31}P NMR ($CDCl_3$, 160 MHz): δ 46.86. HRMS calcd for $C_{27}H_{39}O_2PS$: 458.2408, found: 458.2397.

Acknowledgements

This work was supported by the program for New Century Excellent Talents in Universities (NCET-10−0371), the NSF of Hunan Province (10JJ1003), the NSFC (21273066, 21273067), Program for Changjiang Scholars and Innovative Research Team in University (IRT1238), the Fundamental Research Funds for the Central Universities, and the Canon Foundation. B.X. and Dr. Y.Z. contributed equally to this work.

Supplementary data

Supplementary data associated with this article can be found in the online version, at http://dx.doi.org/10.1016/j.tet.2013.09.001. These data include MOL files and InChiKeys of the most important compounds described in this article.

References and notes

1. (a) Imamoto, T. In *Handbook of Organophosphorus Chemistry*; Engel, R., Ed.; Marcel Dekker: New York, NY, 1992; Chapter 1, pp 5–8; (b) Quin, L. D. *A Guide to Organophosphorus Chemistry*; Wiley-Interscience: New York, NY, 2000; Chapter 9272; (c) Sasaki, M. In *Chirality in Agrochemicals*; Kurihara, N., Miyamoto, J., Eds.; Wiley & Sons: Chichester, UK, 1998; p 85.
2. (a) Baumgartner, T.; Réau, R. *Chem. Rev.* **2006**, *106*, 4681; (b) Engel, R. *Chem. Rev.* **1977**, *77*, 349; (c) Witt, M.; Roesky, H. W. *Chem. Rev.* **1994**, *94*, 1163; (d) Arduengo, A. J.; Stewart, C. A. *Chem. Rev.* **1994**, *94*, 1215; (e) Cristau, H. J. *Chem. Rev.* **1994**, *94*, 1299; (f) Gorenstein, D. G. *Chem. Rev.* **1994**, *94*, 1315; (g) Pietrusiewicz, K. M.; Zablocka, M. *Chem. Rev.* **1994**, *94*, 1375.
3. (a) Kim, Y. C.; Brown, S. G.; Harden, T. K.; Boyer, J. L.; Dubyak, G.; King, B. F.; Burnstock, G.; Jacobson, K. A. *J. Med. Chem.* **2001**, *44*, 340; (b) Kumar, T. S.; Zhou, S. Y.; Joshi, B. V.; Balasubramanian, R.; Yang, T. H.; Liang, B. T.; Jacobson, K. A. *J. Med. Chem.* **2010**, *53*, 2562; (c) Shie, J. J.; Fang, J. M.; Wang, S. Y.; Tsai, K. C.; Cheng, Y. S.; Yang, A. S.; Hsiao, S. C.; Su, C. Y.; Wong, C. H. *J. Am. Chem. Soc.* **2007**, *129*, 11892.
4. (a) Kukhar, V. P.; Hudson, H. R. *Aminophosphonic and Aminophosphinic Acids: Chemistry and Biological Activity*; Wiley & Sons: Chichester, UK, 2000; (b) Sawa, M.; Tsukamoto, T.; Kiyoi, T.; Kurokawa, K.; Nakajima, F.; Nakada, Y.; Yokota, K.; Inoue, Y.; Kondo, H.; Yoshino, K. *J. Med. Chem.* **2002**, *45*, 930; (c) Camp, N. P.; Perry, D. A.; Kinchington, D.; Hawkins, P. C. D.; Hitchcock, P. B.; Gani, D. *Bioorg. Med. Chem.* **1995**, *3*, 297; (d) Zhou, Y.; Yin, S.; Gao, Y.; Zhao, Y.; Goto, M.; Han, L.-B. *Angew. Chem., Int. Ed.* **2010**, *49*, 6852.
5. (a) *Asymmetric Synthesis*; Morrison, J. D., Ed.; Academic: Orlando, FL, 1985; Vols. I–V; (b) Kagan, H. B. In *Comprehensive Organometallic Chemistry*; Wilkinson, G., Gordon, F., Stone, S., Eds.; Pergamon: New York, NY, 1982; Vol. 8; (c) Knowles, W. S. *Acc. Chem. Res.* **1983**, *16*, 106; (d) Hamashima, Y.; Kanai, M.; Shibasaki, M. *J. Am. Chem. Soc.* **2000**, *122*, 7412; (e) Sawada, D.; Kanai, M.; Shibasaki, M. *J. Am. Chem. Soc.* **2000**, *122*, 10521; (f) Yabu, K.; Masumoto, S.; Yamasaki, S.; Hamashima, Y.; Kanai, M.; Du, W.; Curran, D. P.; Shibasaki, M. *J. Am. Chem. Soc.* **2001**, *123*, 9908.
6. (a) Koizumi, T.; Yanada, R.; Takagi, H.; Hirai, H.; Yoshii, E. *Tetrahedron Lett.* **1981**, *22*, 477; (b) Koizumi, T.; Yanada, R.; Takagi, H.; Hirai, H.; Yoshii, E. *Tetrahedron Lett.* **1981**, *22*, 571; (c) Cooper, D. B.; Hall, C. R.; Harrison, J. M.; Inch, T. D. *J. Chem. Soc., Perkin Trans. 1* **1977**, 1969; (d) Hall, C. R.; Inch, T. D.; Peacock, G.; Pottage, C.; Williams, N. E. *J. Chem. Soc., Perkin Trans. 1* **1984**, 669.
7. (a) Atherton, F. R.; Openshaw, H. T.; Todd, A. R. *J. Chem. Soc.* **1945**, 660; (b) Atherton, F. R.; Todd, A. R. *J. Chem. Soc.* **1947**, 674; (c) Jones, S.; Selitsianos, D. *Org.*

Lett. **2002**, *4*, 3671; (d) Jones, S.; Selitsianos, D.; Thompson, K. J.; Toms, S. M. *J. Org. Chem.* **2003**, *68*, 5211; (e) Steinberg, G. M. *J. Org. Chem.* **1950**, 637; (f) Kong, A.; Engel, R. *Bull. Chem. Soc. Jpn.* **1985**, *58*, 3671; (g) Stec, W.; Mikolajczyk, M. *Tetrahedron* **1973**, *29*, 539; (h) Hall, C. R.; Inch, T. D. *Tetrahedron* **1980**, *36*, 2059; (i) Cao, S.; Guo, Y.; Wang, J.; Qi, L.; Gao, P.; Zhao, H.; Zhao, Y.-F. *Tetrahedron Lett.* **2012**, *53*, 6302; (j) Tang, C. C.; Wu, G. P. *Chem. J. Chin. Univ.* **1983**, *4*, 87.

8. (a) Wang, G.; Shen, R. W.; Xu, Q.; Goto, M.; Zhao, Y. F.; Han, L.-B. *J. Org. Chem.* **2010**, *75*, 3890; (b) Zhou, Y. B.; Wang, G.; Yuta, S.; Shen, R. W.; Goto, M.; Zhao, Y. F.; Han, L.-B. *J. Org. Chem.* **2010**, *75*, 7924.
9. Optically pure H–P(O) compounds can be purchased from Katayama Chemical Industries Ltd. (http://www.katayamaka-gaku.co.jp). For their preparation, see: (a) Farnham, W. B.; Murray, R. K.; Mislow, K. *J. Am. Chem. Soc.* **1970**, *92*, 5808; (b) Reiff, L. P.; Aaron, H. S. *J. Am. Chem. Soc.* **1970**, *92*, 5275; (c) Xu, Q.; Zhao, C.-Q.; Han, L.-B. *J. Am. Chem. Soc.* **2008**, *130*, 12648; (d) Bodalski, R.; Koszuk, J. *Phosphorus, Sulfur Silicon Relat. Elem.* **1989**, *44*, 99.
10. (a) Korpiun, O.; Lewis, R. A.; Chickos, A.; Mislow, K. *J. Am. Chem. Soc.* **1968**, *90*, 4842; (b) DeBruin, K. E.; Petersen, J. R. *J. Org. Chem.* **1972**, *37*, 2272; (c) DeBruin, K. E.; Perrin, D. E. *J. Org. Chem.* **1975**, *40*, 1523; (d) Gordillo, B.; Garduno, C.; Guadarrama, G.; Hernandez, J. *J. Org. Chem.* **1995**, *60*, 5180; (e) kolodiazhnyi, O. I. *Tetrahedron: Asymmetry* **1998**, *9*, 1279; (f) Baechler, R. D.; Mislow, K. *J. Am. Chem. Soc.* **1971**, *93*, 773; (g) DeBruin, E.; Padilla, A. G.; Campbell, M. T. *J. Am. Chem. Soc.* **1973**, *95*, 4681; (h) Kolodiazhnyi, O. I.; Grishkun, E. V. *Tetrahedron: Asymmetry* **1996**, *7*, 967; (i) Chodkiewicz, W. *J. Organomet. Chem.* **1984**, *273*, C55; (j) DeBruin, K. E.; Johnson, D. M. *J. Am. Chem. Soc.* **1973**, *95*, 4675; (k) Holmes, R. R. *Pentacoordinated Phosphorus*; American Chemical Society: Washington, DC, 1980, Vols. 1–2; (l) Hartley, F. R. *The Chemistry of Organophosphorus Compounds*; John Wiley & Sons: New York, NY, 1992.