A New and Convenient Asymmetric Synthesis of α-Amino- and α-Alkyl-α-aminophosphonic Acids Using *N-tert*-Butylsulfinyl Imines as Chiral Auxiliaries

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Received 16 August 2007; revised 11 September 2007

Abstract: Nucleophilic addition of dialkyl phosphites to *N-tert*-butylsulfinyl aldimines or ketimines occurs successfully at room temperature with potassium carbonate as base to afford α-amino- and α-alkyl-α-amino-*N*-(*tert*-butylsulfinyl)phosphonates in good to excellent chemical yield and diastereoselectivity. The major diastereomers were separated and smoothly converted into enantiopure α-amino- and α-alkyl-α-aminophosphonic acids.

Key words: α-aminophosphonic acids, α-alkyl-α-aminophosphonic acids, *N-tert*-butylsulfinyl imines, asymmetric synthesis, nucleophilic addition

Optically active α-aminophosphonic acids are compounds with significant biological activities which have found widespread use as surrogates for α-amino acids and enzyme inhibitors. They also show antibacterial and antifungal activities. It is well known that the biological activities of α-aminophosphonic acids depend strongly on the absolute configuration of the stereogenic carbon atom bearing the amino group.[1] Therefore, investigations aimed at convenient and effective routes leading to enantiopure α-aminophosphonic acids and their derivatives have received considerable attention. The methods so far available for the preparation of such molecules include direct resolutions, both chemical and enzymatic,[2–4] and asymmetric synthesis using either a chiral auxiliary or an organocatalyst.[5] In fact, the asymmetric addition of dialkyl or trialkyl phosphites to chiral aldimines or ketimines has proved to be one of the facile approaches. Gilmore and McBride reported the first synthesis of optically active α-aminophosphonic acids in 1972 using a diastereoselective addition of diethyl phosphite to chiral imines.[6] As reported by our group, such an asymmetric nucleophilic addition is remarkably influenced by the electronic and steric effects of the substrates.[7] Recently, asymmetric synthesis using *N*-tolylsulfinyl imines as chiral auxiliary has aroused the interest of organic chemists.[8] These enantiopure sulfinimines, pioneered by Davis, are versatile chiral imine building blocks which have been employed in the asymmetric synthesis of amines,[9] α- and β-amino acids,[10] α- and β-aminophosphonates,[11,12] and heterocycles.[13] These experimental data demonstrate that enantiopure *N*-tolylsulfinyl imines have found wide application in the asymmetric synthesis of chiral molecules.

More recently, Ellman introduced *N-tert*-butylsulfinyl imines as nucleophilic addition acceptors. The *N-tert*-butylsulfinyl group activates the imines for the nucleophilic addition, serves as a powerful chiral directing group, and after the addition reaction is readily cleaved upon treatment of the product with acid. Most importantly, competitive nucleophilic attack at sulfur should be minimized for addition to *N-tert*-butylsulfinyl versus *N-p*-tolylsulfinyl imines due to the greater steric hindrance and reduced electronegativity of the *tert*-butyl group relative to the *p*-tolyl moiety.[14]

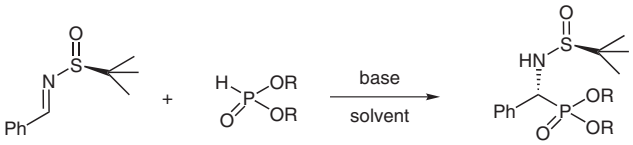
Nevertheless, asymmetric synthesis of α- and β-aminophosphonic acids has been reported based on the nucleophilic addition of dialkyl phosphites to *N*-tolylsulfinyl aldimines or ketimines;[11b] herein we describe our results using *N-tert*-butylsulfinyl aldimines and ketimines as chiral auxiliaries in order to compare the chemical behavior of these two sulfinimine types during the nucleophilic addition reactions of dialkyl phosphites.

The required (*S*)-*N-tert*-butylsulfinyl imine **1** or **3** was readily prepared by adding aldehyde or ketone to (*S*)-(–)-*tert*-butanesulfinamide in the presence of 2 equivalents of titanium(IV) ethoxide at room temperature to 60 °C in tetrahydrofuran.[15] Optically active α-aminophosphonates were obtained by the reaction of imines **1** with dialkyl phosphites **2** under various reaction conditions. For optimization of the reaction, the structural effect of the corresponding aldimine or ketimine and dialkyl phosphite, as well as the influence of various bases on the diastereoselectivity of this nucleophilic addition was briefly examined (Table 1).

As indicated in Table 1, the base used in the addition has a crucial impact on the diastereoselectivity of the reaction. When dimethyl or diethyl phosphite was employed, the α-(*tert*-butylsulfinylamino)phosphonates **4a** were obtained in excellent chemical yield but the diastereoselectivity was poor (Table 1, entries 1–3). Since the reaction proceeded very rapidly even at –78 °C (<1 h) in the presence of LiHMDS, it is obvious that LiHMDS is not a suitable base for use in this reaction. To our delight, the reaction was successful when potassium carbonate was employed; the diastereoselectivity improved dramatically with the de of the reaction increasing from 38.9% to 81.8% (Table 1,

SYNTHESIS 2007, No. 24, pp 3779–3786
Advanced online publication: 31.10.2007
DOI: 10.1055/s-2007-990872; Art ID: F14907SS

Table 1 Screening Dialkyl Phosphites and Optimization of the Reaction Conditions



(S_s)-**1a** **2** (S_s,*R*)-**4a**

Entry	R	Base	Temp (°C)	Solvent	Time (h)	Yield[a] (%)	de[b] (%)
1	Et	LiHMDS	–78 °C	THF	1	85	37.6
2	Me	LiHMDS	–78 °C	THF	1	83	38.9
3	Me	CaH_2	0 °C	THF	3	80	40.4
4	Me	Et_3N	0 °C	Et_2O	10	0	–
5	Me	KF	r.t.	Et_2O	30	<10% conversion	–
6	Me	CsF	r.t.	Et_2O	30	<30% conversion	–
7	Me	Li_2CO_3	r.t.	Et_2O	30	<10% conversion	–
8	Me	Na_2CO_3	r.t.	Et_2O	30	<30% conversion	–
9	Me	K_2CO_3	r.t.	Et_2O	15	85	69.4
10	Me	K_2CO_3	r.t.	benzene	20	85	70.9
11	Me	K_2CO_3	r.t.	CH_2Cl_2	30	81	81.8

[a] Isolated total yield of two isomers.
[b] From the ^{31}P NMR spectrum of the crude reaction mixture.

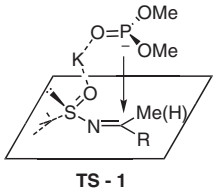
entry 2 vs 11). The solvent also has an influence on the reaction rate and the diastereoselectivity (Table 1, entries 9–11). The best result was obtained when potassium carbonate was used and the reaction was carried out at room temperature using dichloromethane as solvent.

The optimized protocol was then expanded to a variety of sulfinimines derived from aldimines and ketimines. The results are summarized in Table 2.

The data in Table 2 indicate that the reaction of *N*-*tert*-butylsulfinyl ketimines generally results in a much higher diastereoselectivity than reaction of the corresponding aldimines (Table 2, entries 8–16 vs 1–7). The electronic effect of the R group in either aldimine or ketimine has no significant effect on either the chemical yield or diastereoselectivity.

Thus, the optimized protocol was applied to the asymmetric synthesis of quaternary α-aminophosphonates using *N*-sulfinyl ketimines. The phosphorus analogues of quaternary α-amino acids are of considerable value because it has been found that incorporation of such molecules into peptides results in increased rigidity and resistance to protease enzymes and therefore enhanced bioactivity.[15] Fairly good diastereoselectivities were obtained not only for aromatic but also for aliphatic *N*-sulfinyl ketimines in the presence of potassium carbonate at room temperature (Table 2, entries 8–16). The electronic effect of the R group has no significant influence on the selectivity as only one isomer was detected in the ^{31}P NMR spectra of the reaction mixtures, except for entry 14 (72.4% de) probably because of a 6.5:1 ratio of *E*/*Z*-isomers in the starting (–)-**3g** (R^1 = Et) where phosphite addition to both isomers results in the lower diastereoselectivity.[13]

During the course of the reaction, the potassium cation is probably chelated to the sulfinyl and phosphonate oxygens. Nucleophilic attack of the phosphite anion takes place from the least hindered *n*-face (*anti* to the *tert*-butyl group at sulfur, **TS-1**) (Figure 1).[12]



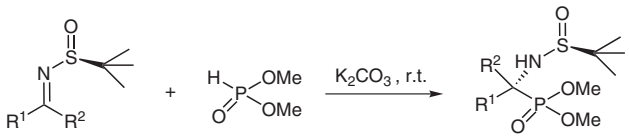
TS - 1

Figure 1

The major diastereomers of the (*tert*-butylsulfinylamino)methylphosphonates **4a**–**g** were isolated by flash column chromatography on silica gel. Then, the *N*-*tert*-butylsulfinyl group in **4a**, **4d**, **4g**, and **5a** was selectively removed in excellent yield to give the corresponding enantiopure benzyloxycarbonyl-protected aminomethylphosphonates (*R*)-**6a**–**d**.

Free aminomethylphosphonic acids (*R*)-**7** were obtained upon refluxing enantiopure phosphonates **4** and **5** in 10 N

Table 2 Addition of Dimethyl Phosphite to *N-tert*-Butylsulfinyl Imines (*S*)-**1**,(*S*)-**3**



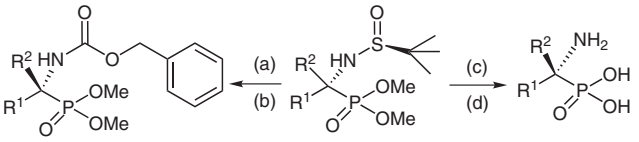
S_S-**1** (R^2 = H)
S_S-**3** (R^2 = Me)

(S_S,*R*)-**4** (R^2 = H)
(S_S,*R*)-**5** (R^2 = Me)

Entry		R^1	R^2	Solvent	Time (h)	Yield[a] (%)	de[b] (%)
1	**4a**	Ph	H	CH_2Cl_2	30	81	81.8
2	**4b**	4-$MeOC_6H_4$	H	CH_2Cl_2	30	78	85.2
3	**4c**	4-MeC_6H_4	H	CH_2Cl_2	20	81	80.2
4	**4d**	4-ClC_6H_4	H	CH_2Cl_2	20	82	72.4
5	**4e**	Et	H	CH_2Cl_2	20	80	77.0
6	**4f**	*i*-Pr	H	CH_2Cl_2	30	79	85.1
7	**4g**	*t*-Bu	H	CH_2Cl_2	30	77	86.9
8	**5a**	Ph	Me	Et_2O	24	85	>95
9	**5b**	4-MeC_6H_4	Me	Et_2O	24	82	>95
10	**5c**	4-ClC_6H_4	Me	Et_2O	20	85	>95
11	**5d**	4-$NO_2C_6H_4$	Me	Et_2O	20	81	>95
12	**5e**	1-$C_{10}H_7$	Me	Et_2O	24	83	>95
13	**5f**	4-PhC_6H_4	Me	Et_2O	24	80	>95
14	**5g**	Et	Me	CH_2Cl_2	30	73	72.4
15	**5h**	*n*-Bu	Me	CH_2Cl_2	30	75	>95
16	**5i**	*t*-Bu	Me	CH_2Cl_2	40	73	>95

[a] Isolated yield of the mixture of diastereomers.
[b] From the ^{31}P NMR spectrum of the crude reaction mixture.

Table 3 Removal of the *N-tert*-Butylsulfinyl Group[a]



(*R*)-**6** (S_S,*R*)-**4**,**5** (*R*)-**7**

R^2 = H, Me >99% ee

Entry		R^1	R^2	Yield[b] (%)	^{31}P (δ)	$[\alpha]_D^{20}$	Config[c]
1	**6a**	Ph	H	84	24.41	10.6[d]	*R*
2	**6b**	4-ClC_6H_4	H	85	23.86	14.0[d]	*R*
3	**6c**	*t*-Bu	H	81	27.87	20.3[d]	*R*
4	**6d**	Ph	Me	83	27.14	20.1[d]	*R*
5	**7a**	Ph	H	81	18.06	20.9[e]	*R*
6	**7b**	Ph	Me	83	21.60	51.1[e]	*R*
7	**7c**	4-ClC_6H_4	Me	88	21.25	53.9[e]	*R*
8	**7d**	4-$NO_2C_6H_4$	Me	84	20.57	82.6[e]	*R*
9	**7e**	1-$C_{10}H_7$	Me	85	18.59	50.7[e]	*R*
10	**7f**	4-PhC_6H_4	Me	83	21.38	75.9[e]	*R*
11	**7g**	Et	Me	84	16.71	0.1[e]	*R*

[a] Reaction conditions: (a) 4 N HCl, MeOH, r.t., 6 h; (b) 5% $NaHCO_3$, CH_2Cl_2, CbzCl, 0 °C, 4 h; (c) 10 N HCl, reflux, 18 h; (d) propylene oxide, EtOH.
[b] Isolated yield.
[c] Established based on a comparison of the sign of the optical rotation with that reported in the literature.
[d] Determined in $CHCl_3$.
[e] Determined in 1 N NaOH.

hydrochloric acid and isolation in the usual manner by the addition of propylene oxide (Table 3).

The absolute configuration of the aminomethylphosphonic acids **7** thus obtained was established based on a comparison of the sign of the optical rotation with that reported in the literature.[14]

In summary, we have shown that nucleophilic addition of dialkyl phosphites to *N-tert*-butylsulfinyl aldimines or ketimines, followed by subsequent deprotection and hydrolysis, constitutes a new synthetic route leading to chiral α-amino- and α-alkyl-α-aminophosphonic acids in good to excellent chemical yield and enantioselectivity. As found by us, *N-tert*-butylsulfinyl imines behave much better as chiral Michael addition acceptors than *N*-tolylsulfinyl imines. Furthermore, nucleophilic addition takes place under milder conditions, i.e. at room temperature with potassium carbonate as base, than for Davis' sulfinimines where such additions have to be carried out under rather complicated reaction conditions, i.e. at –78 °C in the presence of LiHMDS as base. Studies on the fields of application of such a reaction system are now ongoing in our laboratory.

All solvents used throughout these experiments were dried using standard procedures. IR spectra were measured on a Shimadzu IR 440 spectrometer, ^1H NMR spectra were recorded at 300 MHz with $CDCl_3$ as solvent (unless otherwise indicated) on a Bruker Avance 300 or a Varian Mercury 300 spectrometer, and ^{31}P NMR spectra were recorded at 120 MHz with $CDCl_3$ as solvent on a Varian EM 390 or a Bruker AM 300 spectrometer (external 85% H_3PO_4). EI-MS measurements were performed at 2010 eV on a Hewlett–Packard HP 5989A apparatus. HRMS data were recorded on a Finnigan MAT 8430 spectrometer. Elemental analyses were conducted on a Heraeus Rapid–CHNO apparatus. Optical rotation values were measured on a Perkin–Elmer 241MC polarimeter.

(*S*)-*N-tert*-Butylsulfinyl Ketimines (*S*)-3; General Procedure

In a 20-mL, single-necked, round-bottom flask equipped with a magnetic stirrer bar was placed (*S*)-(–)-*tert*-butanesulfinamide (1.212 g, 10.0 mmol) in THF (5 mL), and then a mixture of the corresponding ketone (12 mmol) and $Ti(OEt)_4$ (4.565 g, 20 mmol) was

added into the solution. The reaction mixture was then stirred at 60 °C for 6 h and finally was quenched with H_2O (5 mL). At this time EtOAc (10 mL) was added to the mixture. The H_2O phase was extracted with EtOAc (2 × 5 mL). The combined organic layers were washed with brine (20 mL) and dried (Na_2SO_4). The solvent was removed and the residue was subjected to column chromatography on silica gel (PE–CH_2Cl_2, 2:1).

(*S*)-(–)-*N*-(1-Phenylethylidene)-*tert*-butanesulfinamide (3a, R^1 = Ph)
Yield: 85%.

^{1}H NMR ($CDCl_3$): δ = 1.32 (s, 9 H), 2.77 (s, 3 H), 7.45 (m, 3 H), 7.89 (d, *J* = 7.5 Hz, 2 H).

(*S*)-(–)-*N*-[1-(4-Methylphenyl)ethylidene]-*tert*-butanesulfinamide (3b, R^1 = 4-MeC_6H_4)
Yield: 87%; yellow solid; mp 51–54 °C.

$[\alpha]_D^{20}$ –11.1 (*c* 1.0, $CHCl_3$).

IR (KBr): 2962, 1596, 1567, 1277, 1186, 1068, 823 cm^{-1}.

^{1}H NMR ($CDCl_3$): δ = 1.30 (s, 9 H), 2.38 (s, 3 H), 2.73 (s, 3 H), 7.20 (d, *J* = 8.4 Hz, 2 H), 7.78 (d, *J* = 8.1 Hz, 2 H).

ESI-MS: *m*/*z* = 238.1 [M + H^+].

Anal. Calcd for $C_{13}H_{19}NOS$: C, 65.78; H, 8.07; N, 5.90. Found: C, 65.40; H, 8.24; N, 5.70.

(*S*)-(–)-*N*-[1-(4-Chlorophenyl)ethylidene]-*tert*-butanesulfinamide (3c, R^1 = 4-ClC_6H_4)
Yield: 86%; yellow solid; mp 84–86 °C.

$[\alpha]_D^{20}$ –67.5 (*c* 0.5, $CHCl_3$).

IR (KBr): 2964, 1687, 1589, 1262, 1095, 1013, 832 cm^{-1}.

^{1}H NMR ($CDCl_3$): δ = 1.26 (s, 9 H), 2.75 (s, 3 H), 7.96 (d, *J* = 8.4 Hz, 2 H), 8.19 (d, *J* = 8.7 Hz, 2 H).

ESI-MS: *m*/*z* = 258.2 [M + H^+].

Anal. Calcd for $C_{12}H_{16}ClNOS$: C, 55.91; H, 6.26; N, 5.43. Found: C, 55.92; H, 6.22; N, 5.23.

(*S*)-(–)-*N*-[1-(4-Nitrophenyl)ethylidene]-*tert*-butanesulfinamide (3d, R^1 = 4-$NO_2C_6H_4$)
Yield: 83%; colorless oil.

$[\alpha]_D^{20}$ –136.3 (*c* 1.4, $CHCl_3$).

IR (KBr): 2958, 1672, 1582, 1256, 1085, 1015, 829 cm^{-1}.

^{1}H NMR ($CDCl_3$): δ = 1.23 (s, 9 H), 2.66 (s, 3 H), 7.30 (d, *J* = 8.4 Hz, 2 H), 7.72 (d, *J* = 8.7 Hz, 2 H).

ESI-MS: *m*/*z* = 269.3 [M + H^+].

Anal. Calcd for $C_{12}H_{16}N_2O_3S$: C, 53.71; H, 6.01; N, 10.44. Found: C, 53.65; H, 6.18; N, 10.33.

(*S*)-(–)-*N*-[1-(1-Naphthyl)ethylidene]-*tert*-butanesulfinamide (3e, R^1 = 1-$C_{10}H_7$)
Yield: 88%; yellow solid; mp 120–122 °C.

$[\alpha]_D^{20}$ –16.7 (*c* 1.0, $CHCl_3$).

IR (KBr): 2956, 1689, 1592, 1258, 1091, 1019, 827 cm^{-1}.

^{1}H NMR ($CDCl_3$): δ = 1.36 (s, 9 H), 2.89 (s, 3 H), 7.56 (m, 2 H), 7.84–8.06 (m, 5 H).

ESI-MS: *m*/*z* = 274.2 [M + H^+].

Anal. Calcd for $C_{16}H_{19}NOS$: C, 70.29; H, 7.00; N, 5.12. Found: C, 70.18; H, 6.99; N, 4.79.

(*S*)-(–)-*N*-[1-(1,1′-Biphenyl-4-yl)ethylidene]-*tert*-butanesulfinamide (3f, R^1 = 4-PhC_6H_4)
Yield: 83%; yellow solid; mp 138–149 °C.

$[\alpha]_D^{20}$ –89.05 (*c* 1.0, $CHCl_3$).

IR (KBr): 2978, 1591, 1364, 1087, 767 cm^{-1}.

^{1}H NMR ($CDCl_3$): δ = 1.34 (s, 9 H), 2.80 (s, 3 H), 7.26 (m, 3 H), 7.61 (m, 4 H), 7.96 (m, 2 H).

ESI-MS: *m*/*z* = 300.2 [M + Na^+].

Anal. Calcd for $C_{18}H_{21}NOS$: C, 72.20; H, 4.68; N, 7.07. Found: C, 72.21; H, 4.43; N, 6.99.

(*S*)-*N*-(*sec*-Butylidene)-*tert*-butanesulfinamide (3g, R^1 = Et)
Yield: 74%.

^{1}H NMR ($CDCl_3$): δ = 0.63 (t, *J* = 7.8 Hz, 3 H), 0.76 (s, 9 H), 1.84 (s, 3 H), 1.96 (m, 2 H).

(*S*)-*N*-(Hex-2-ylidene)-*tert*-butanesulfinamide (3h, R^1 = *n*-Bu)
Yield: 75%.

^{1}H NMR ($CDCl_3$): δ = 0.47 (m, 3 H), 0.78 (s, 9 H), 0.90 (m, 2 H), 1.13 (m, 2 H), 1.86 (s, 3 H), 1.95 (m, 2 H).

(*S*)-*N*-(3,3-Dimethylbut-2-ylidene)-*tert*-butanesulfinamide (3i, R^1 = *t*-Bu)
Yield: 71%.

^{1}H NMR ($CDCl_3$): δ = 1.32 (s, 9 H), 2.77 (s, 3 H), 2.81 (m, 3 H).

Dimethyl (S_S,*R*)-(+)-(*tert*-Butylsulfinylamino)methylphosphonates 4,5; General Procedure
In a 15-mL round-bottom flask fitted with a magnetic stirrer bar was placed a soln of dimethyl phosphite (0.44 g, 4 mmol) in CH_2Cl_2 (10 mL), and K_2CO_3 (0.690 g, 5 mmol) was added. The reaction mixture was stirred for 0.25 h at r.t., then *N*-*tert*-butylsulfinyl imine (*S*)-**1** or (*S*)-**3** (1.0 mmol) was added. After being stirred for 15–40 h at r.t., the reaction mixture was quenched with sat. aq NH_4Cl (5 mL), which was followed by extraction with CH_2Cl_2 (2 × 5 mL). The organic layer was successively washed with H_2O (5 mL) and brine (5 mL), then dried (Na_2SO_4). The solvent was removed and the residue was subjected to column chromatography on silica gel (acetone–EtOAc, 1:2).

Dimethyl (S_S,*R*)-(+)-(*tert*-Butylsulfinylamino)(phenyl)methylphosphonate (4a)
Yield: 81%; 81.8% de; colorless oil.

$[\alpha]_D^{20}$ +99.5 (*c* 1.0, $CHCl_3$).

IR (KBr): 3219, 2958, 1456, 1250, 1032, 834, 556 cm^{-1}.

^{1}H NMR ($CDCl_3$): δ = 1.17 (s, 9 H), 3.45 (d, J_{HP} = 10.5 Hz, 3 H), 3.77 (d, J_{HP} = 10.8 Hz, 3 H), 4.08 (m, 1 H), 4.65 (m, 1 H), 7.30–7.49 (m, 5 H).

^{31}P NMR ($CDCl_3$): δ = 24.05.

ESI-MS: *m*/*z* = 342.1 [M + Na^+].

Anal. Calcd for $C_{13}H_{22}NO_4PS$: C, 48.89; H, 6.94; N, 4.39. Found: C, 48.71; H, 7.00; N, 4.07.

Dimethyl (S_S,*R*)-(+)-(*tert*-Butylsulfinylamino)(4-methoxyphenyl)methylphosphonate (4b)
Yield: 78%; 85.2% de; colorless oil.

$[\alpha]_D^{20}$ +124.6 (*c* 0.8, $CHCl_3$).

IR (KBr): 3186, 2958, 1447, 1243, 1018, 837, 578 cm^{-1}.

^{1}H NMR ($CDCl_3$): δ = 1.14 (s, 9 H), 3.40 (d, J_{HP} = 10.5 Hz, 3 H), 3.53 (d, J_{HP} = 10.5 Hz, 3 H), 3.73 (s, 3 H), 4.00 (m, 1 H), 4.68 (d, *J* = 18.0 Hz, 1 H), 6.83 (m, 2 H), 7.28 (m, 2 H).

^{31}P NMR ($CDCl_3$): δ = 23.79.

ESI-MS: *m/z* = 372.1 [M + Na^+].

HRMS: *m/z* calcd for $C_{14}H_{24}NO_5PSNa$ [M + Na^+]: 372.1015; found: 372.1005.

Dimethyl (*S*$_S$,*R*)-(+)-(*tert*-Butylsulfinylamino)(4-methylphenyl)methylphosphonate (4c)
Yield: 81%; 80.2% de; colorless oil.

$[\alpha]_D^{20}$ +117.3 (*c* 1.0, $CHCl_3$).

IR (KBr): 3186, 2958, 1447, 1243, 1018, 837, 578 cm^{-1}.

^{1}H NMR ($CDCl_3$): δ = 1.15 (s, 9 H), 2.26 (s, 3 H), 3.51 (d, J_{HP} = 10.5 Hz, 3 H), 3.77 (d, J_{HP} = 10.2 Hz, 3 H), 4.06 (m, 1 H), 4.68 (d, *J* = 18.3 Hz, 1 H), 7.11 (m, 2 H), 7.25 (m, 2 H).

^{31}P NMR ($CDCl_3$): δ = 23.37.

ESI-MS: *m/z* = 356.1 [M + Na^+].

Anal. Calcd for $C_{14}H_{24}NO_4PS$: C, 50.44; H, 7.26; N, 4.20. Found: C, 50.96; H, 7.58; N, 3.91.

Dimethyl (*S*$_S$,*R*)-(+)-(*tert*-Butylsulfinylamino)(4-chlorophenyl)methylphosphonate (4d)
Yield: 82%; 72.4% de; colorless oil.

$[\alpha]_D^{20}$ +119.1 (*c* 1.0, $CHCl_3$).

IR (KBr): 3219, 2958, 1456, 1250, 1032, 834, 556 cm^{-1}.

^{1}H NMR ($CDCl_3$): δ = 1.22 (s, 9 H), 3.57 (d, J_{HP} = 10.5 Hz, 3 H), 3.74 (d, J_{HP} = 11.7 Hz, 3 H), 4.05 (m, 1 H), 4.75 (m, 1 H), 7.25–7.47 (m, 4 H).

^{31}P NMR ($CDCl_3$): δ = 23.32.

ESI-MS: *m/z* = 376.2 [M + Na^+].

Anal. Calcd for $C_{13}H_{21}ClNO_4PS$: C, 44.13; H, 5.98; N, 3.96. Found: C, 45.08; H, 6.19; N, 3.58.

Dimethyl (*S*$_S$,*R*)-(+)-1-(*tert*-Butylsulfinylamino)propylphosphonate (4e)
Yield: 80%; 77.0% de; colorless oil.

$[\alpha]_D^{20}$ +65.9 (*c* 1.0, $CHCl_3$).

IR (KBr): 3443, 2959, 1461, 1241, 1055, 830, 565 cm^{-1}.

^{1}H NMR ($CDCl_3$): δ = 0.98 (m, 3 H), 1.18 (s, 9 H), 1.58–1.94 (m, 2 H), 3.40 (m, 1 H), 3.73 (d, J_{HP} = 10.8 Hz, 3 H), 3.78 (d, J_{HP} = 10.2 Hz, 3 H).

^{31}P NMR ($CDCl_3$): δ = 28.51.

ESI-MS: *m/z* = 294.1 [M + Na^+].

Anal. Calcd for $C_9H_{22}NO_4PS$: C, 39.84; H, 8.17; N, 5.16. Found: C, 39.63; H, 8.06; N, 4.29.

Dimethyl (*S*$_S$,*R*)-(+)-1-(*tert*-Butylsulfinylamino)-2-methylpropylphosphonate (4f)
Yield: 79%; 85.1% de; colorless oil.

$[\alpha]_D^{20}$ +66.0 (*c* 1.0, $CHCl_3$).

IR (KBr): 3450, 2964, 1468, 1241, 1041, 831, 563 cm^{-1}.

^{1}H NMR ($CDCl_3$): δ = 0.92 (m, 6 H), 1.21 (s, 9 H), 2.18 (m, 1 H), 3.40 (m, 1 H), 3.72 (d, J_{HP} = 10.8 Hz, 3 H), 3.80 (d, J_{HP} = 10.8 Hz, 3 H).

^{31}P NMR ($CDCl_3$): δ = 28.06.

ESI-MS: *m/z* = 308.2 [M + Na^+].

HRMS: *m/z* calcd for $C_{10}H_{24}NO_4PSNa$ [M + Na^+]: 308.1059; found: 308.1056.

Dimethyl (*S*$_S$,*R*)-(+)-1-(*tert*-Butylsulfinylamino)-2,2-dimethylpropylphosphonate (4g)
Yield: 77%; 86.9% de; colorless oil.

$[\alpha]_D^{20}$ +63.19 (*c* 1.0, $CHCl_3$).

IR (KBr): 3486, 2958, 1473, 1237, 1081, 830, 577 cm^{-1}.

^{1}H NMR ($CDCl_3$): δ = 0.77 (s, 9 H), 0.98 (s, 9 H), 3.00 (m, 1 H), 3.49 (d, J_{HP} = 8.7 Hz, 3 H), 3.53 (d, J_{HP} = 8.4 Hz, 3 H), 3.65 (m, 1 H).

^{31}P NMR ($CDCl_3$): δ = 28.01.

ESI-MS: *m/z* = 322.1 [M + Na^+].

HRMS: *m/z* calcd for $C_{11}H_{26}NO_4PSNa$ [M + Na^+]: 322.1216; found: 322.1212.

Dimethyl (*S*s,*R*)-(+)-1-(*tert*-Butylsulfinylamino)-1-phenylethylphosphonate (5a)
Yield: 85%; >95% de; colorless oil.

$[\alpha]_D^{20}$ +67.8 (*c* 1.0, $CHCl_3$).

IR (KBr): 3480, 2958, 1458, 1244, 1032, 830, 570 cm^{-1}.

^{1}H NMR ($CDCl_3$): δ = 1.26 (s, 9 H), 2.10 (d, *J* = 16.2 Hz, 3 H), 3.60 (d, J_{HP} = 1.5 Hz, 3 H), 3.64 (d, J_{HP} = 1.8 Hz, 3 H), 4.08 (m, 1 H), 7.38 (m, 3 H), 7.61 (m, 2 H).

^{31}P NMR ($CDCl_3$): δ = 26.28.

ESI-MS: *m/z* = 356.1 [M + Na^+].

Anal. Calcd for $C_{14}H_{24}NO_4PS$: C, 50.44; H, 7.26; N, 4.20. Found: C, 50.81; H, 7.32; N, 3.93.

Dimethyl (*S*$_S$,*R*)-(+)-1-(*tert*-Butylsulfinylamino)-1-(4-methylphenyl)ethylphosphonate (5b)
Yield: 82%; >95% de; colorless oil.

$[\alpha]_D^{20}$ +85.2 (*c* 1.0, $CHCl_3$).

IR (KBr): 3477, 2984, 1458, 1245, 1031, 833, 751, 564 cm^{-1}.

^{1}H NMR ($CDCl_3$): δ = 1.25 (s, 9 H), 2.06 (d, *J* = 16.2 Hz, 3 H), 2.35 (d, *J* = 2.1 Hz, 3 H), 3.61 (s, 3 H), 3.65 (s, 3 H), 4.01 (m, 1 H), 7.18 (m, 2 H), 7.46 (m, 2 H).

^{31}P NMR ($CDCl_3$): δ = 26.21.

MS (EI): *m/z* = 348 [M + H^+].

HRMS: *m/z* calcd for $C_{15}H_{26}NO_4PSNa$ [M + Na^+]: 370.1210; found: 370.1212.

Dimethyl (*S*$_S$,*R*)-(+)-1-(*tert*-Butylsulfinylamino)-1-(4-chlorophenyl)ethylphosphonate (5c)
Yield: 85%; >95% de; colorless oil.

$[\alpha]_D^{20}$ +85.1 (*c* 1.0, $CHCl_3$).

IR (KBr): 3478, 2959, 1466, 1245, 1060, 840, 562 cm^{-1}.

^{1}H NMR ($CDCl_3$): δ = 1.16 (s, 9 H), 2.00 (d, *J* = 16.2 Hz, 3 H), 3.55 (d, J_{HP} = 3.9 Hz, 3 H), 3.59 (d, J_{HP} = 3.6 Hz, 3 H), 4.00 (m, 1 H), 7.28 (m, 2 H), 7.45 (m, 2 H).

^{31}P NMR ($CDCl_3$): δ = 25.42.

MS (EI): *m/z* = 368 [M + H^+].

Anal. Calcd for $C_{14}H_{23}ClNO_4PS$: C, 45.72; H, 6.30; N, 3.81. Found: C, 45.69; H, 6.43; N, 3.37.

Dimethyl (*S*$_S$,*R*)-(+)-1-(*tert*-Butylsulfinylamino)-1-(4-nitrophenyl)ethylphosphonate (5d)
Yield: 81%; >95% de; colorless oil.

$[\alpha]_D^{20}$ +65.3 (*c* 1.0, $CHCl_3$).

IR (KBr): 3478, 2959, 1521, 1245, 1028, 857, 560 cm^{-1}.

^{1}H NMR ($CDCl_3$): δ = 1.20 (s, 9 H), 2.06 (d, J = 15.9 Hz, 3 H), 3.62 (d, J_{HP} = 8.4 Hz, 3 H), 3.66 (d, J_{HP} = 8.7 Hz, 3 H), 4.07 (m, 1 H), 7.75 (m, 2 H), 8.18 (m, 2 H).

^{31}P NMR ($CDCl_3$): δ = 24.95.

MS (EI): m/z = 379 [M + H$^+$].

HRMS: m/z calcd for $C_{14}H_{23}N_2O_6PSNa$ [M + Na$^+$]: 401.0905; found: 401.0906.

Dimethyl (*S*$_S$,*R*)-(+)-1-(*tert*-Butylsulfinylamino)-1-(1-naphthyl)ethylphosphonate (5e)
Yield: 83%; >95% de; colorless oil.

$[\alpha]_D^{20}$ +76.8 (*c* 1.3, $CHCl_3$).

IR (KBr): 3450, 2958, 1702, 1459, 1365, 1242, 1056, 827, 561 cm^{-1}.

^{1}H NMR ($CDCl_3$): δ = 1.19 (s, 9 H), 2.13 (d, J = 15.9 Hz, 3 H), 3.56 (d, J_{HP} = 10.5 Hz, 6 H), 4.02 (s, 1 H), 7.41 (m, 2 H), 7.65–7.80 (m, 4 H), 7.94 (s, 1 H).

^{31}P NMR ($CDCl_3$): δ = 25.71.

ESI-MS: m/z = 406.2 [M + Na$^+$].

HRMS: m/z calcd for $C_{18}H_{26}NO_4PSNa$ [M + Na$^+$]: 406.1226; found: 406.1226.

Anal. Calcd for $C_{18}H_{26}NO_4PS$: C, 56.38; H, 6.83; N, 3.65. Found: C, 56.45; H, 7.43; N, 2.94.

Dimethyl (*S*$_S$,*R*)-(+)-1-(1,1′-Biphenyl-4-yl)-1-(*tert*-butylsulfinylamino)ethylphosphonate (5f)
Yield: 80%; >95% de; colorless oil.

$[\alpha]_D^{20}$ +97.2 (*c* 1.0, $CHCl_3$).

IR (KBr): 3480, 2958, 1489, 1365, 1243, 1031, 847, 577 cm^{-1}.

^{1}H NMR ($CDCl_3$): δ = 1.19 (s, 9 H), 2.06 (d, J = 15.6 Hz, 3 H), 3.58 (d, J_{HP} = 10.5 Hz, 6 H), 4.01 (s, 1 H), 7.30 (m, 3 H), 7.53 (m, 6 H).

^{31}P NMR ($CDCl_3$): δ = 24.74.

ESI-MS: m/z = 432.3 [M + Na$^+$].

HRMS: m/z calcd for $C_{20}H_{28}NO_4PSNa$ [M + Na$^+$]: 432.1371; found: 432.1369.

Anal. Calcd for $C_{20}H_{28}NO_4PS$: C, 58.66; H, 6.89; N, 3.42. Found: C, 58.89; H, 6.18; N, 3.51.

Dimethyl (*S*$_S$,*R*)-(+)-1-(*tert*-Butylsulfinylamino)-1-methylpropylphosphonate (5g)
Yield: 73%; 72.4% de; colorless oil.

$[\alpha]_D^{20}$ +22.6 (*c* 1.0, $CHCl_3$).

IR (KBr): 3467, 2957, 1461, 1238, 1035, 827, 560 cm^{-1}.

^{1}H NMR ($CDCl_3$): δ = 0.95 (t, J = 7.5 Hz, 3 H), 1.16 (s, 9 H), 1.42 (d, J = 15.6 Hz, 3 H), 1.80 (m, 2 H), 3.58 (m, 1 H), 3.73 (d, J_{HP} = 13.5 Hz, 3 H), 3.78 (d, J_{HP} = 10.5 Hz, 3 H).

^{31}P NMR ($CDCl_3$): δ = 30.25.

MS (EI): m/z = 286 [M + H$^+$].

Anal. Calcd for $C_{10}H_{24}NO_4PS$: C, 42.09; H, 8.48; N, 4.91. Found: C, 42.26; H, 8.28; N, 4.51.

Dimethyl (*S*$_S$,*R*)-(+)-1-(*tert*-Butylsulfinylamino)-1-methylpentylphosphonate (5h)
Yield: 75%; >95% de; colorless oil.

$[\alpha]_D^{20}$ +45.9 (*c* 1.0, $CHCl_3$).

IR (KBr): 3467, 2957, 1461, 1238, 1035, 827, 560 cm^{-1}.

^{1}H NMR ($CDCl_3$): δ = 0.83 (m, 3 H), 1.15 (s, 9 H), 1.24–1.43 (m, 7 H), 1.70 (m, 2 H), 3.52 (m, 1 H), 3.75 (m, 6 H).

^{31}P NMR ($CDCl_3$): δ = 29.80.

ESI-MS: m/z = 336.2 [M + Na$^+$].

HRMS: m/z calcd for $C_{12}H_{29}NO_4PS$ [M + H$^+$]: 314.1558; found: 314.1549.

Anal. Calcd for $C_{12}H_{28}NO_4PS$: C, 45.99; H, 9.01; N, 4.47. Found: C, 46.79; H, 9.22; N, 3.84.

Dimethyl (*Ss*,*R*)-(+)-1-(*tert*-Butylsulfinylamino)-1,2,2-trimethylpropylphosphonate (5i)
Yield: 73%; >95% de; colorless oil.

$[\alpha]_D^{20}$ +39.7 (*c* 1.0, $CHCl_3$).

IR (KBr): 3484, 2958, 1470, 1236, 1071, 813, 759, 567 cm^{-1}.

^{1}H NMR ($CDCl_3$): δ = 1.01 (s, 9 H), 1.18 (s, 9 H), 1.49 (d, J = 16.8 Hz, 3 H), 3.73 (d, J_{HP} = 10.5 Hz, 3 H), 3.79 (d, J_{HP} = 10.2 Hz, 3 H).

^{31}P NMR ($CDCl_3$): δ = 30.23.

MS (EI): m/z = 314 [M + H$^+$].

HRMS: m/z calcd for $C_{12}H_{28}NO_4PSNa$ [M + Na$^+$]: 336.1370; found: 336.1369.

Dimethyl (*R*)-(+)-(Benzyloxycarbonylamino)methylphosphonates 6; General Procedure
In a 20-mL, single-necked, round-bottom flask equipped with a magnetic stirrer bar was placed phosphonate **4** or **5** (1.0 mmol) in MeOH (5 mL), then 4 N HCl (5 mL) was added into the solution. The reaction mixture was then stirred at r.t. for 6 h. After that, the resulting mixture was concentrated under reduced pressure for 0.5 h. At this time, CH_2Cl_2 (10 mL) was added to the flask and the solution was cooled to 0 °C in an ice bath. This was followed by the addition of Et_3N until pH 7. Then, 5% aq $NaHCO_3$ (5 mL) and CbzCl (0.20 g, 1.2 mmol) were added in sequence. The reaction mixture was stirred at 0 °C for 4 h, which was followed by the addition of H_2O (5 mL). The aqueous phase was extracted successively with Et_2O (5 mL) and EtOAc (2 × 5 mL). The combined organic layers were washed with brine (20 mL) and dried (Na_2SO_4). The solvent was removed and the residue was subjected to column chromatography on silica gel (PE–EtOAc, 1:1).

Dimethyl (*R*)-(+)-(Benzyloxycarbonylamino)(phenyl)methylphosphonate (6a)
Yield: 84%; >99% ee; white powder; mp 129–130 °C.

$[\alpha]_D^{20}$ +10.6 (*c* 1.0, $CHCl_3$).

IR (KBr): 3222, 3033, 2955, 1714, 1552, 1254, 1041, 698 cm^{-1}.

^{1}H NMR ($CDCl_3$): δ = 3.49 (d, J_{HP} = 10.5 Hz, 3 H), 3.73 (d, J_{HP} = 11.1 Hz, 3 H), 5.08–5.17 (m, 3 H), 5.72 (m, 1 H), 7.26–7.41 (m, 10 H).

^{31}P NMR ($CDCl_3$): δ = 24.41.

ESI-MS: m/z = 372.1 [M + Na$^+$].

Anal. Calcd for $C_{17}H_{20}NO_5P$: C, 58.45; H, 5.77; N, 4.01. Found: C, 58.72; H, 5.93; N, 3.61.

Dimethyl (*R*)-(+)-(Benzyloxycarbonylamino)(4-chlorophenyl)methylphosphonate (6b)
Yield: 85%; >99% ee; white powder; mp 119–120 °C.

$[\alpha]_D^{20}$ +14.0 (*c* 1.0, $CHCl_3$).

IR (KBr): 3242, 3038, 2957, 1720, 1547, 1250, 1031, 564 cm^{-1}.

^{1}H NMR ($CDCl_3$): δ = 3.55 (d, J_{HP} = 10.5 Hz, 3 H), 3.73 (d, J_{HP} = 10.8 Hz, 3 H), 5.00–5.21 (m, 3 H), 5.68 (m, 1 H), 7.20–7.40 (m, 9 H).

^{31}P NMR ($CDCl_3$): δ = 23.86.

ESI-MS: *m*/*z* = 406.0 [M + Na^+].

Anal. Calcd for $C_{17}H_{19}ClNO_5P$: C, 53.21; H, 4.99; N, 3.65. Found: C, 53.55; H, 5.14; N, 3.31.

Dimethyl (*R*)-(+)-1-(Benzyloxycarbonylamino)-2,2-dimethylpropylphosphonate (6c)
Yield: 81%; >99% ee; colorless oil.

$[\alpha]_D^{20}$ +20.3 (*c* 1.0, $CHCl_3$).

IR (KBr): 3285, 2960, 1714, 1534, 1239, 1035, 821, 700, 560 cm^{-1}.

^{1}H NMR ($CDCl_3$): δ = 1.06 (s, 9 H), 3.65 (d, J_{HP} = 10.2 Hz, 3 H), 3.71 (d, J_{HP} = 11.1 Hz, 3 H), 5.03–5.21 (m, 3 H), 5.32 (m, 1 H), 7.35 (m, 5 H).

^{31}P NMR ($CDCl_3$): δ = 27.87.

ESI-MS: *m*/*z* = 352.1 [M + Na^+].

Anal. Calcd for $C_{15}H_{24}NO_5P$: C, 54.71; H, 7.35; N, 4.25. Found: C, 54.46; H, 7.31; N, 4.13.

Dimethyl (*R*)-(+)-1-(Benzyloxycarbonylamino)-1-phenylethylphosphonate (6d)
Yield: 83%; >99% ee; colorless oil.

$[\alpha]_D^{20}$ +20.1 (*c* 1.0, $CHCl_3$).

IR (KBr): 3240, 3036, 2957, 1715, 1548, 1251, 1029, 849, 564 cm^{-1}.

^{1}H NMR ($CDCl_3$): δ = 2.19 (d, *J* = 16.8 Hz, 3 H), 3.48 (d, J_{HP} = 10.8 Hz, 3 H), 3.57 (d, J_{HP} = 11.1 Hz, 3 H), 5.02 (s, 2 H), 5.17 (s, 1 H), 5.98 (m, 1 H), 7.31 (m, 7 H), 7.50 (m, 2 H).

^{31}P NMR ($CDCl_3$): δ = 27.14.

ESI-MS: *m*/*z* = 386.1 [M + Na^+].

Anal. Calcd for $C_{18}H_{22}NO_5P$: C, 59.50; H, 6.10; N, 3.85. Found: C, 59.20; H, 5.94; N, 3.60.

(*R*)-(+)-Aminomethylphosphonic Acids 7; General Procedure
In a 25-mL, single-necked, round-bottom flask equipped with a magnetic stirrer bar and a reflux condenser was placed phosphonate (+)-**4** or (+)-**5** (0.3 mmol) in 10 N HCl (5 mL). The solution was refluxed for 18 h, which was followed by removal of the low-boiling fraction under high vacuum for 3 h. The residue was dissolved in a minimum amount of hot EtOH (2 mL). The solution was cooled to r.t., excess propylene oxide (1 mL) was then introduced, and the mixture was stirred for 3 h. The white solid was collected by filtration to afford (+)-**7**.

(*R*)-(+)-Amino(phenyl)methylphosphonic Acid (7a)
Yield: 81%; white solid; mp 274–275 °C.

$[\alpha]_D^{20}$ +20.9 (*c* 1.0, 1 N NaOH).

IR (KBr): 3141, 2924, 2612, 2307, 1622, 1540, 1269, 1188, 1066, 917 cm^{-1}.

^{1}H NMR (D_2O, 0.5 N NaOH): δ = 3.69 (d, *J* = 16.5 Hz, 1 H), 7.25 (m, 5 H).

^{31}P NMR (D_2O, 0.5 N NaOH): δ = 18.06.

ESI-MS: *m*/*z* = 186.1 [M – 1].

HRMS: *m*/*z* calcd for $C_7H_{10}NO_3PNa$ [M + Na^+]: 210.0297; found: 210.0290.

Anal. Calcd for $C_7H_{10}NO_3P$: C, 44.93; H, 5.39; N, 7.48. Found: C, 44.33; H, 5.41; N, 7.13.

(*R*)-(+)-1-Amino-1-phenylethylphosphonic Acid (7b)
Yield: 83%; white solid; mp 250–255 °C.

$[\alpha]_D^{20}$ +51.1 (*c* 1.0, 1 N NaOH).

IR (KBr): 3263, 2872, 1618, 1543, 1188, 1062, 927 cm^{-1}.

^{1}H NMR (D_2O, 0.5 N NaOH): δ = 1.43 (d, *J* = 12.9 Hz, 3 H), 7.12–7.39 (m, 5 H).

^{31}P NMR (D_2O, 0.5 N NaOH): δ = 21.60.

ESI-MS: *m*/*z* = 200.2 [M – 1].

HRMS: *m*/*z* calcd for $C_8H_{12}NO_3PNa$ [M + Na^+]: 224.0455; found: 224.0447.

(*R*)-(+)-1-Amino-1-(4-chlorophenyl)ethylphosphonic Acid (7c)
Yield: 88%; white solid; mp 225–230 °C.

$[\alpha]_D^{20}$ +53.9 (*c* 0.6, 1 N NaOH).

IR (KBr): 3273, 2868, 1615, 1541, 1189, 1060, 922 cm^{-1}.

^{1}H NMR (D_2O, 0.5 N NaOH): δ = 1.35 (d, *J* = 12.6 Hz, 3 H), 7.16 (s, 2 H), 7.25 (s, 2 H).

^{31}P NMR (D_2O, 0.5 N NaOH): δ = 21.25.

ESI-MS: *m*/*z* = 234.6 [M – 1].

HRMS: *m*/*z* calcd for $C_8H_{11}ClNO_3PNa$ [M + Na^+]: 258.0058; found: 258.0057.

(*R*)-(+)-1-Amino-1-(4-nitrophenyl)ethylphosphonic Acid (7d)
Yield: 84%; white solid; mp 230–235 °C.

$[\alpha]_D^{20}$ +82.6 (*c* 0.45, 1 N NaOH).

IR (KBr): 3282, 2834, 1606, 1516, 1191, 1064, 926 cm^{-1}.

^{1}H NMR (D_2O, 0.5 N NaOH): δ = 1.42 (d, *J* = 12.3 Hz, 3 H), 7.21 (s, 2 H), 7.33 (s, 2 H).

^{31}P NMR (D_2O, 0.5 N NaOH): δ = 20.57.

ESI-MS: *m*/*z* = 245.2 [M – 1].

(*R*)-(+)-1-Amino-1-(1-naphthyl)ethylphosphonic Acid (7e)
Yield: 85%; white solid; mp 244–247 °C.

$[\alpha]_D^{20}$ +50.7 (*c* 0.75, 1 N NaOH).

IR (KBr): 3114, 2907, 1614, 1538, 1184, 1063, 928 cm^{-1}.

^{1}H NMR (D_2O, 0.5 N NaOH): δ = 1.49 (d, *J* = 12.6 Hz, 3 H), 7.35 (m, 2 H), 7.62–7.76 (m, 5 H).

^{31}P NMR (D_2O, 0.5 N NaOH): δ = 18.59.

ESI-MS: *m*/*z* = 250.1 [M – 1].

HRMS: *m*/*z* calcd for $C_{12}H_{14}NO_3PNa$ [M + Na^+]: 274.0616; found: 274.0603.

(*R*)-(+)-1-Amino-1-(1,1′-biphenyl-4-yl)ethylphosphonic Acid (7f)
Yield: 83%; white solid; mp 260–262 °C.

$[\alpha]_D^{20}$ +75.9 (*c* 0.75, 1 N NaOH).

IR (KBr): 2972, 1614, 1488, 1147, 1091, 765 cm^{-1}.

^{1}H NMR (D_2O, 0.5 N NaOH): δ = 1.48 (d, *J* = 12.9 Hz, 3 H), 7.30–7.64 (m, 9 H).

^{31}P NMR (D_2O, 0.5 N NaOH): δ = 21.38.

ESI-MS: *m*/*z* = 276.2 [M – 1].

(*R*)-(+)-1-Amino-1-methylpropylphosphonic Acid (7g)
Yield: 84%; white solid; mp 249–253 °C.

$[\alpha]_D^{20}$ +0.1 (*c* 0.5, 1 N NaOH).

IR (KBr): 3238, 2837, 1544, 1185, 1064, 925 cm^{-1}.

^{1}H NMR (D_2O, 0.5 N NaOH): δ = 0.85 (t, *J* = 7.5 Hz, 3 H), 1.25 (d, *J* = 13.2 Hz, 3 H), 1.69 (m, 2 H).

^{31}P NMR (D_2O, 0.5 N NaOH): δ = 16.71.

ESI-MS: *m*/*z* = 152.2 [M – 1].

HRMS: *m*/*z* calcd for $C_4H_{12}NO_3PNa$ [M + Na^+]: 176.0453; found: 176.0447.

Acknowledgment

This project was supported by the National Natural Science Foundation of China (Grant No. 20372706, 20672132).

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