CHAPTER II

EXPERIMENTAL

2.1 General and materials

Air-sensitive materials were transferred by syringe or cannula under a nitrogen atmosphere. Solvents for the reaction were used as received unless otherwise noted. Tetrahydrofuran was dried over sodium/benzophenone. Commercial grade solvents for column chromatography were distilled before use. All chemicals were purchased from Fluka, Merck or Aldrich Chemical Co., Ltd. and were used as received without further purification. HPLC grade hexanes and 2-propanol for HPLC experiments on a chiral column, obtained from J.T. Baker and Merck, respectively.

Melting points were recorded on an Electrothermal 9100. Evaporation of solvents was carried on a Büchi Rotavapor R-114 and Büchi water bath B-480. The progress of the reactions was followed by Thin Layer Chromatography (TLC) performed on Merck D. C. silica gel 60 F_{254} 0.2 mm precoated aluminium plates and visualized using either UV light (254 nm), iodine, potassium permanganate, or $Co(SCN)_2$. Isolation of compounds was performed on the 230-400 mesh silica gel for flash column chromatography or the 70-230 mesh for chromatography.

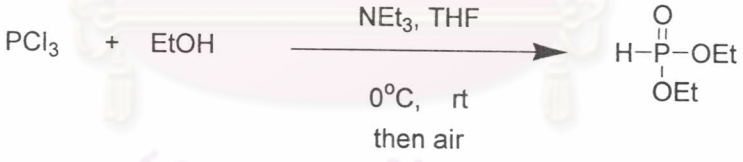
Elemental analyses were conducted on a Perkin Elmer PE 2400 Series II. Low resolution mass spectrometry was performed on GC-MS GCQ Mas Finnigan Mat operated in the electron impact (EI) mode (70 eV). Masses are reported in units of mass over charge (*m/z*). Intensities are reported as a percent of the base peak intensity. The molecular ion is indicated by $[MH]^+$ or $[M]^+$.

Proton (^1H), carbon (^{13}C) nuclear magnetic resonance (NMR) spectra were obtained in $CDCl_3$, DMSO or D_2O on a Bruker ACF200 spectrometer operating at 200 MHz (^1H) and 50 MHz (^{13}C), a Mercury Varian 400 spectrometer operating at 400 MHz (^1H) at the chemistry department, Faculty of Science, Chulalongkorn University, or a Varian Gemini 2000 YH200 spectrometer operating at 200 MHz (^1H) at Chulabhorn Research Institute (CRI). Phosphorus (^{31}P) nuclear magnetic resonance spectra were recorded in $CDCl_3$ on a Jeol JNM A-500 spectrometer operating at 202.35 MHz at the Scientific and Technology Research Equipment

Center, Chulalongkorn University. Chemical shifts (δ) are reported in parts per million (ppm) relative to tetramethylsilane (TMS) (0.00) or with the solvent as an internal reference for ^{1}H and ^{13}C NMR. A phosphoric acid (H_3PO_4) capillary in an appropriate solvent was used as an external reference (0.00) for the ^{31}P spectra. Multipicities are abbreviated as followed: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet. Coupling constants (J) are reported as proton-proton (J_{HH}) and proton-phosphorus (J_{HP}) coupling and are reported in Hertz (Hz).

High performance liquid chromatography (HPLC) separation of products were performed on a Gilson HPLC system equipped with a 112 UV/Vis detector. A Daicel Chiralcel OD® column (cellulose tris(3,5-dimethylphenyl carbamate) on a 10 μm silica gel substrate, 250 mm × 4.6 mm) and a Daicel Chiralpak AD® column (amylase tris-(3,5-dimethylphenylcarbamate) on 10 μm silica gel substrate, 250 mm × 4.6 mm) were used in attempts for separation of enantiomers. HPLC solvents were filtered through a membrane filter (0.5 μm Millipore®-FH) before use. Each sample was filtered through a 0.45 μm Millex®-HV syringe filter unit prior to injection onto the liquid chromatograph.

2.2 Synthesis of diethyl phosphite

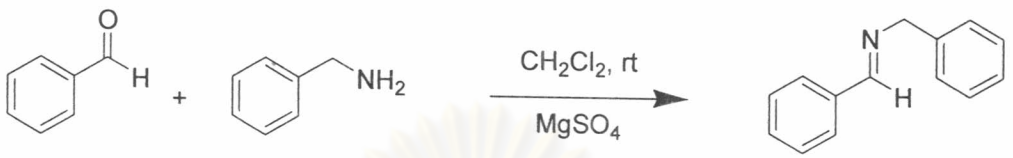


A solution of ethanol (29 mL, 0.495 mol) in dry THF (500 mL) was placed in a three-neck round bottom flask cooled in an ice bath. A solution of phosphorus trichloride (13 mL, 0.15 mol) in dry THF (50 mL) was added dropwise with vigorous stirring under a nitrogen atmosphere. The reaction mixture was allowed to warm up to room temperature and stirred for additional for 2-3 h. Air was passed through the mixture. After 0.5 h, triethylamine (46 mL, 0.33 mol) in THF (100 mL) was added to the flask at 0°C (ice bath). The mixture was let stand at room temperature for 2 h. The precipitates were then removed by filtration. The THF was removed to afford a colorless liquid (60-65%). ^{1}H NMR ($CDCl_3$, 200 MHz) δ 1.27 (s, $^{3}J_{HH}$ = 7.1 Hz, 3H, OCH_2CH_3), 4.05 (dq, $^{3}J_{HH}$ = 7.1 Hz, $^{2}J_{HP}$ = 9.0 Hz, 2H, OCH_2CH_3), 4.11 (dq, $^{3}J_{HH}$ = 7.1 Hz, $^{2}J_{PH}$ = 9.0 Hz, 2H, OCH_2CH_3), 6.75 (d, $^{1}J_{HP}$ = 692.4 Hz, 1H, C*H*P).

2.3 Catalytic asymmetric synthesis of α-aminophosphonates

2.3.1 Synthesis of imines

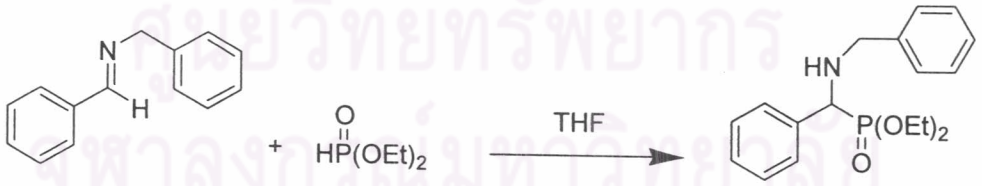
Synthesis of *N*-benzylidene benzylamine (I-1)



I-1

Imine **I-1** was prepared according to the method by Jacobsen *et al.*.[45] To a 25 mL round bottom flask was added magnesium sulfate ($MgSO_4$) and 5 mL of dichloromethane. To this solution, benzylamine (0.55 mL, 5 mmol) was added followed by a slow syringe addition of benzaldehyde (0.51 mL, 5 mmol). When the starting materials disappeared, magnesium sulfate was removed by filtration. The filtrate was collected and the solvent removed *in vacuo* to obtain the desired product **I-1** as a yellow oil (0.86 g, 4.4 mmol, 88%). ^{1}H NMR ($CDCl_3$, 200 MHz) δ 4.89 (s, 2H, C*H*$_2$Ph), 7.33-7.51 (m, 8H, Ar), 7.84-7.89 (m, 2H, Ar), 8.43 (s, 1H, C*H*=N); ^{13}C NMR ($CDCl_3$, 50 MHz, {^{1}H}) δ 62.12 (*C*H$_2$Ph), 127.12, 128.11, 128.42, 128.63, 128.72, 130.90, 136.23, 139.40, 162.13 (H*C*=N).

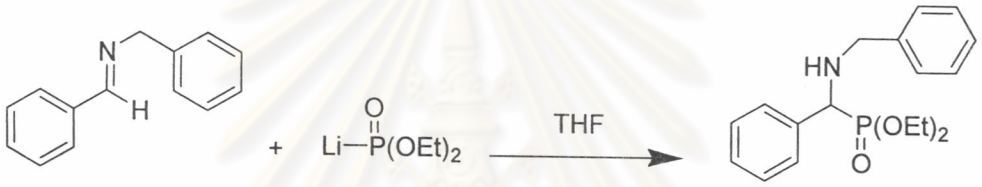
2.3.2 Procedures for the preparation of racemic α-aminophosphonates



I-1 **II-1**

Method A: To an oven-dried 10 mL round bottom flask equipped with a stirrer bar was added a solution of imine **I-1** (0.0975 g, 0.5 mmol) in 4 mL of dry THF, and a solution of 10 mol% of Ti(O^{i}Pr)$_4$ in 1 mL of dry THF. A reaction was stirred for 10 min then diethyl phosphite (225 μL, 1.75 mmol) was added *via* syringe. The solution was allowed to stir for 3d at 70°C under a nitrogen atmosphere. The mixture was quenched with H_2O (2 mL). Most of the THF was removed *in vacuo* and

the product was extracted with EtOAc. The organic layer was dried with anhydrous sodium sulfate and then concentrated. Analytically pure **II-1** was then obtained by column chromatography (gradient elution, 10%-25% EtOAc/hexanes) as a yellow oil (0.1184 g, 0.36 mmol, 71%). ^{1}H NMR ($CDCl_3$, 200 MHz) δ 1.10 (t, $^{3}J_{HH}$ = 7.0 Hz, 3H, OCH_2CH_3), 1.25 (t, $^{3}J_{HH}$ = 7.1 Hz, 3H, OCH_2CH_3), 3.55-4.05 (m, 7H, OCH_2CH_3, CH_2Ph, CHP), 7.21-7.39 (m, 10H, Ar); ^{13}C NMR ($CDCl_3$, 50 MHz, {^{1}H}) δ 16.28 (d, $^{3}J_{CP}$ = 9.5 Hz, OCH_2CH_3), 16.44 (d, $^{3}J_{CP}$ = 5.9 Hz, OCH_2CH_3), 51.15 (d, $^{3}J_{CP}$ = 17.3 Hz, CH_2Ph), 59.51 (d, $^{1}J_{CP}$ = 152.8 Hz, CHP), 62.86 (d, $^{2}J_{CP}$ = 8.0 Hz, OCH_2CH_3), 63.01 (d, $^{2}J_{CP}$ = 7.7 Hz, OCH_2CH_3), 127.14, 127.98, 128.37, 128.47, 128.62, 128.75, 135.65, 139.25.



I-1 **II-1**

Method B: *n*-Butyl lithium (1.64 M in hexanes, 0.30 mL, 0.5 mmol) was added *via* syringe to a solution of diethyl phosphite (1 mmol, 0.128 mL) in dry THF (1 mL) at -78°C under a nitrogen atmosphere. The reaction was stirred for 0.5 h then warmed to room temperature. This mixture was then added to a solution of imine **I-1** (0.0975 g, 0.5 mmol) in dry THF (1 mL). After 1d, the mixture was quenched with water (1 mL). Solvent was removed and the aqueous layer was extracted with EtOAc (4 × 2 mL). The combined extracts were dried ($NaSO_4$), filtered, and concentrated. Purification of crude material by column chromatography (gradient elution, 10% to 25% EtOAc/Hexane) resulted in the desired α-aminophosphonates **II-1** (0.063 g, 0.19 mmol, 38%).

2.3.3 General methods for optical purity determination of α-aminophosphonates

2.3.3.1 Analysis of α-aminophosphonates II-1 using a chiral HPLC column

α-Aminophosphonates were dissolved in an appropriate solvent composition (9:1 hexanes/2-propanol) and filtered through a membrane filter. An aliquot of the solution was injected into the Daicel Chiralcel OD® column. Elution

with the mobile phase 95:5 to 90:10 (hexanes/2-propanol) resulted in no separation. An alternative Daicel Chiralpak AD® column was employed. Elution of an α-aminophosphonate mixture by the mobile phase 90:10 to 98:2 (hexanes/2-propanol) gave a satisfactory separation of enantiomeric peaks of α-aminophosphonate **II-1**.

2.3.3.2 Analysis of α-aminophosphonates II-1 using ^{1}H NMR spectroscopy

The enantiomeric purities of the optically active α-aminophosphonates were determined by ^{1}H NMR spectroscopy at 200 MHz from a solution in $CDCl_3$ upon an addition of chiral solvating agents such as *R*-(-)-α-methoxy-α-trifluoromethylphenylacetic acid (Mosher's acid), (*1S*)-(+)-camphor-10-sulfonic acid (CSA), *R*-(-)-α-acetoxyphenylacetic acid (APA), *R*-(+)-1,1'-binaphthalene-2,2'-diyl hydrogenphosphate (BNP), and *R*-(+)-1,1'-bi(2-naphthol). The ^{1}H NMR spectra were recorded at intervals of each 1 eq of chiral solvating agent added.

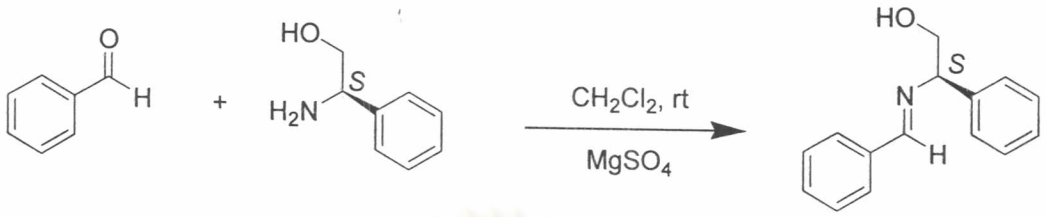
2.3.4 General procedure for asymmetric synthesis of α-aminophosphonate (II-1)

Method A : A chiral ligand (0.025 mmol) and $Ti(O^iPr)_4$ (0.025 mmol) were placed in an oven-dried 10 mL round bottom flask. The mixture was dissolved in dry THF (1 mL) and stirred for 15 min at room temperature. Subsequently, a solution of imine **I-1** (0.25 mmol) in 1 mL of dry THF was added by syringe. Diethyl phosphite (0.064 mL, 2 eq) was added to the mixture and was stirred for 3 d at 70°C. The solvent was then removed by distillation at reduced pressure to give a crude product. Purification of the crude material by column chromatography (gradient elution, 10% to 25% EtOAc/hexanes) yielded the desired α-aminophosphonate **II-1**.

Method B : In an oven-dried round bottom flask, a solution of diethyl phosphite (0.128 mL, 1 mmol) in dry THF (1 mL) was cooled to -78°C and treated dropwise with *n*-butyl lithium (1.64 M in hexanes, 0.30 mL, 0.5 mmol). After 0.5 h, the mixture was warmed to room temperature and added *via* syringe to a solution of a chiral ligand such as (-)-sparteine (0.5 mmol) in dry THF (1 mL) at room temperature. The reaction mixture was stirred for 0.5 h and then treated with a solution of imine **I-1** (0.0975 g, 0.5 mmol) in dry THF (1 mL). The reaction was let stand for 1 d at room temperature, quenched with water (2 mL) and extracted with Et_2O (4 × 2 mL). The organic layer was dried over Na_2SO_4. Evaporation of the solvent followed by purification with column chromatography gave **II-1**.

2.4 Synthesis of α-aminophosphonates by using chiral auxiliary imine

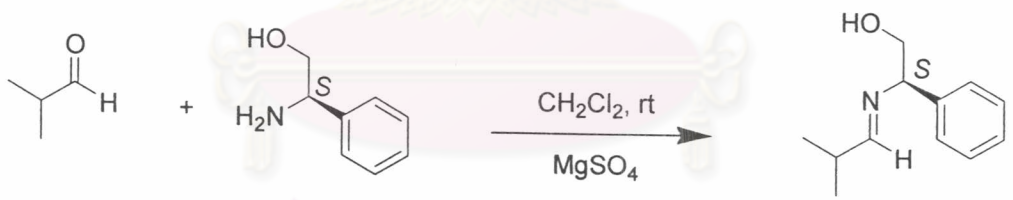
2.4.1 synthesis of imine III-1



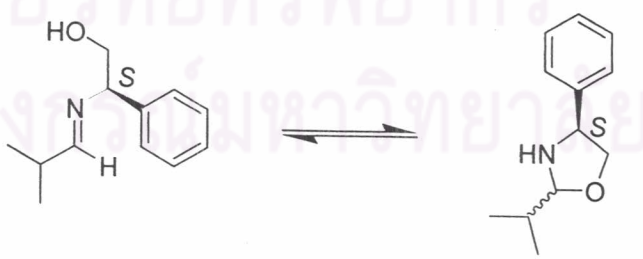
III-1

Imine **III-1** was obtained from a reaction of L-(+)-α-phenylglycinol (0.0664 g, 0.5 mmol) and benzaldehyde (0.049 mL, 0.5 mmol) in the presence of anhydrous magnesium sulfate in CH_2Cl_2 (2 mL). The mixture was stirred at room temperature overnight. Magnesium sulfate was removed by filtration and the filtrate was concentrated under reduced pressure to obtain the desired product **III-1** as a yellow oil (0.078 g, 0.35 mmol, 70%). ^{1}H NMR ($CDCl_3$, 200 MHz) δ 3.93 (m, 2H, C*H*$_2$OH), 4.50 (m, 1H, PhC*H*CH$_2$OH), 7.24-7.89 (m, 10H, Ar), 8.36 (s, 1H, *H*C=N).

2.4.2 synthesis of imine III-2



III-2

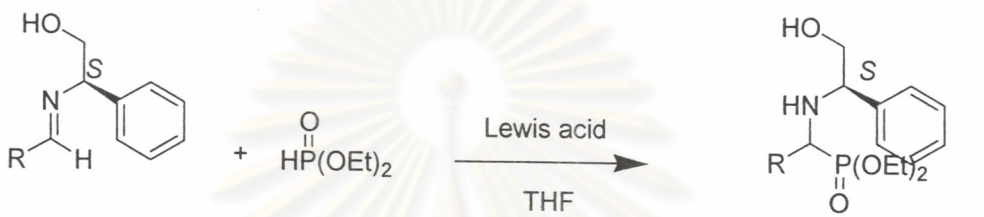


III-2a **III-2b**

To a 25 mL round bottom flask was added L-(+)-α-phenylglycinol (0.5 mmol, 0.0664 g) in CH_2Cl_2 in the presence of anhydrous magnesium sulfate. The solution of isobutyraldehyde (0.036 mL, 0.5 mmol) in CH_2Cl_2 was added by slow syringe and stirred for overnight. Filtration of magnesium sulfate, collection of the filtrate,

followed by a removal of solvent *in vacuo* resulted in the imine **III-2** as a colourless oil (0.062 g, 0.33 mmol, 65%). ^{1}H NMR ($CDCl_3$, 200 MHz) δ 0.99 (s, 3H, C*H*$_3$), 1.06 (s, 3H, C*H*$_3$), 1.80-1.91 (m, 1H, C*H*$(CH_3)_2$), 3.57-3.67 (m, 1H, PhC*H*CH_2OH), 4.07-4.46 (m, 3H, C*H*$_2$OH, C*H*), 7.21-7.66 (m, 5H, Ar).

2.4.3 General procedure for the preparation of diastereomeric α-aminophosphonate (IV-1, IV-2)



III-1 : R = Ph
III-2 : R = ^{i}Pr

Lewis acid = LiCl, LiBr, Li(OTf), $Ti(O^iPr)_4$, $Al(O^iPr)_3$, $InCl_3$, $SnCl_4$, $ZnCl_2$, $MgCl_2$, $ZrCl_4$, $Sc(OTf)_3$, $Yb(OTf)_3$

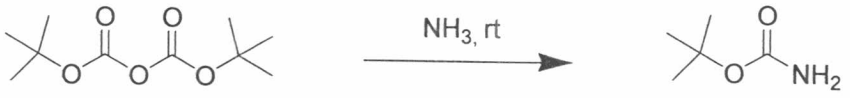
IV-1 : R = Ph
IV-2 : R = ^{i}Pr

A reaction of imine **III-1** (0.25 mmol) and a Lewis acid (10 mol%) in dry THF (2 mL) was placed in oven-dried test tube. To the solution was added diethyl phosphite (0.035 mL, 0.275 mmol) and the mixture was refluxed for 1 d. The reaction mixture was shaked with a solution of 10% $NaHCO_3$, extracted with EtOAc. The organic layer was combined and the solvent was evaporated by reduced pressure. The crude product was purified by column chromatography to afford the desired product **IV-1** as a yellow oil. (Major + Minor isomer): ^{1}H NMR ($CDCl_3$, 200 MHz) δ 1.08 (t, $^3J_{HH}$ = 7.1 Hz, 3H, OCH_2CH_3), 1.29 (t, $^3J_{HH}$ = 7.1 Hz, 3H, OCH_2CH_3), 2.91 (br, 1H, O*H*), 3.57-4.14 (m, 9H, C*H*P, OCH_2CH_3, C*H*Ph, CH_2OH, N*H*), 7.14-7.31 (m, 10H, Ar); ^{13}C NMR ($CDCl_3$, 50 MHz, {^{1}H}) δ 16.30 (OCH_2CH_3), 16.42 (OCH_2CH_3), 58.45 (d, $^1J_{CP}$ = 151.0 Hz, *C*HP, major), 57.46 (d, $^1J_{CP}$ = 155.0 Hz, *C*HP, minor), 62.64 (d, $^2J_{CP}$ = 7.5 Hz, OCH_2CH_3), 62.96 (d, $^2J_{CP}$ = 10.0 Hz, OCH_2CH_3), 63.23 (CH_2OH), 66.14 (*C*HPh, major), 67.19 (*C*HPh, minor), 127.40, 127.59, 127.80, 128.28, 128.46, 128.83, 135.24 (minor), 136.50 (major), 139.29 (minor), 140.48 (major).

The product **IV-2** was prepared from a reaction of imine **III-2** according to the general procedure for the preparation of **IV-1** described above. **IV-2** was obtained as a yellow oil. (Major + Minor isomer): ^{1}H NMR ($CDCl_3$, 200 MHz) δ 0.84-1.05 (m, 6H, C*H*$_3$), 1.17-1.35 (m, 6H, OCH_2CH_3), 1.95-2.15 (m, 1H C*H*$(CH_3)_2$), 2.37 (br, 1H, O*H*), 2.70 (dd, $^{2}J_{HP}$ = 12.7 Hz, $^{3}J_{HH}$ = 3.5 Hz, 1H, C*H*P), 3.47-3.71 (m, 1H, C*H*Ph), 3.94-4.20 (m, 4H, OCH_2CH_3), 7.21-7.33 (m, 5H, Ar); ^{13}C NMR ($CDCl_3$, 50 MHz, {^{1}H}) δ 16.46 (OCH_2CH_3, major), 16.55 (OCH_2CH_3, major), 17.64 (OCH_2CH_3, minor), 17.81 (OCH_2CH_3, minor), 18.45 (CH_3, minor), 19.76 (CH_3, minor), 20.47 (CH_3, major), 20.67 (CH_3, major), 28.65 ($CH(CH_3)_2$, minor), 29.40 ($CH(CH_3)_2$, major), 57.16 (d, $^{1}J_{CP}$ = 146.5 Hz, *C*HP, minor), 58.60 (d, $^{1}J_{CP}$ = 141.7 Hz, *C*HP, major), 61.53 (d, $^{2}J_{CP}$ = 8.0 Hz, *C*HP, major), 61.91 (d, $^{2}J_{CP}$ = 11.0 Hz, *C*HP, minor), 62.42 (d, $^{2}J_{CP}$ = 7.3 Hz, *C*HP, major), 63.03 (d, $^{2}J_{CP}$ = 10.0 Hz, *C*HP, minor), 64.54 (*C*HPh), 66.61 (CH_2OH, minor), 67.68 (CH_2OH, major), 127.69, 127.87, 128.40, 140.29 (minor), 140.56 (major).

2.5 Synthesis of α-aminophosphonates by using an activated imines

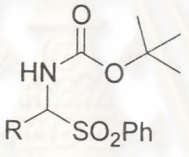
2.5.1 The preparation of *tert*-butyl carbamate (V)



V

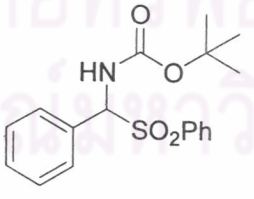
Di-*tert*-butyl dicarbonate (10 mmol) was added slowly to concentrated aqeous ammonia solution (excess). The mixture was stirred at room temperature for overnight. *Tert*-butyl carbamate (**V**) precipitate was filtered off as white crystals in quantitative yield. The filtrate was then washed with water, and dried under vacuum.

2.5.2 General procedure for the preparation of *tert*-Butyl *N*-((benzenesulfonyl)alkyl)carbamate (VI)



VI

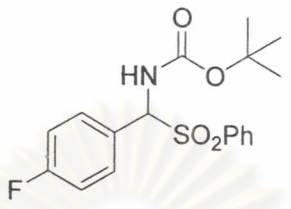
A mixture of the aldehyde (10 mmol), *tert*-butylcarbamate (**V**) (10 mmol), sodium benzenesulfinate (10 mmol), water (10 mL), methanol (5 mL), and formic acid (2.75 mL) was stirred at room temperature overnight. Crystals were collected by filtration and washed sequentially with water and diethyl ether to give the pure product.



VI-1

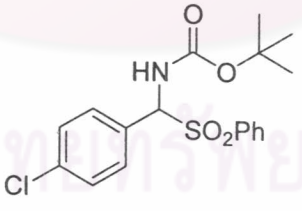
***tert*-Butyl *N*-((benzenesulfonyl)benzyl)carbamate (VI-1)** was prepared from a reaction of benzaldehyde (1.06 g, 10 mmol), *tert*-butyl carbamate (**V**) (1.17 g, 10 mmol), and sodium benzenesulfinate (1.64 g, 10 mmol) according to the general procedure for the preparation of *tert*-butyl *N*-((benzenesulfonyl)benzyl)carbamate as described earlier to give 2.51 g of **VI-1** (7.27 mmol, 73%) as a white solid. ^{1}H NMR

($CDCl_3$, 200 MHz) δ 1.23 (s, 9H, $C(CH_3)_3$), 5.77 (d, $^3J_{HH}$ = 9.8 Hz, 1H, $CHSO_2Ph$), 5.91 (d, $^3J_{HH}$ = 10.7 Hz, 1H, N*H*), 7.36-7.91 (m, 10H, Ar); ^{13}C NMR ($CDCl_3$, 50 MHz, {^1H}) δ 27.98 ($C(CH_3)_3$), 73.95 ($CHSO_2Ph$), 81.20 ($C(CH_3)_3$), 124.93, 128.76, 128.96, 129.05, 129.50, 129.85, 133.96, 136.89, 153.52 (*C*=O).



VI-2

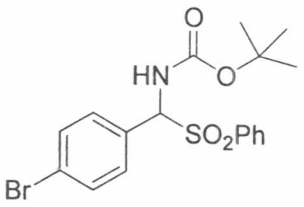
***tert*-Butyl *N*-((benzenesulfonyl)-4-fluorobenzyl)carbamate (VI-2)** was prepared from a reaction of 4-fluorobenzaldehyde (1.24 g, 10 mmol), *tert*-butyl carbamate (**V**) (1.16 g, 10 mmol), and sodium benzenesulfinate (1.64 g, 10 mmol) according to the general procedure to give **VI-2** (1.86 g, 5.09 mmol, 51%) as a white solid. ^1H NMR ($CDCl_3$, 200 MHz) δ 1.23 (s, 9H, $C(CH_3)_3$), 5.80 (d, $^3J_{HH}$ = 10.2 Hz, 1H, $CHSO_2Ph$), 5.92 (d, $^3J_{HH}$ = 10.6 Hz, 1H, N*H*), 7.05-7.92 (m, 9H, Ar); ^{13}C NMR ($CDCl_3$, 125.65 MHz, {^1H}) δ 27.94 ($C(CH_3)_3$), 73.12 ($CHSO_2Ph$), 81.33 ($C(CH_3)_3$), 115.74, 115.91, 124.89, 125.76, 129.08, 129.40, 130.80, 130.86, 131.78, 134.04, 136.42, 153.43 (*C*=O).



VI-3

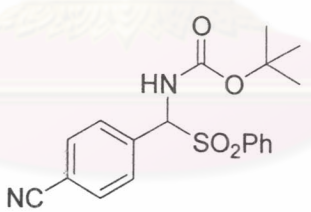
***tert*-Butyl *N*-((benzenesulfonyl)-4-chlorobenzyl)carbamate (VI-3)** was prepared from a reaction of 4-chlorobenzaldehyde (1.40 g, 10 mmol), *tert*-butyl carbamate (**V**) (1.17 g, 10 mmol), and sodium benzenesulfinate (1.64 g, 10 mmol) according to the general procedure to give **VI-3** (0.98 g, 2.57 mmol, 26%) as a white solid. ^1H NMR ($CDCl_3$, 200 MHz) δ 1.23 (s, 9H, $C(CH_3)_3$), 5.78 (d, $^3J_{HH}$ = 9.4 Hz, 1H, $CHSO_2Ph$), 5.90 (d, $^3J_{HH}$ = 10.8 Hz, 1H, N*H*), 7.32-7.91 (m, 9H, Ar); ^{13}C NMR ($CDCl_3$, 50 MHz, {^1H}) δ 27.97 ($C(CH_3)_3$), 73.28 ($CHSO_2Ph$), 81.43 ($C(CH_3)_3$),

124.92, 128.41, 128.98, 129.14, 129.47, 130.26, 130.92, 134.13, 136.08, 136.62, 153.48 (*C*=O).



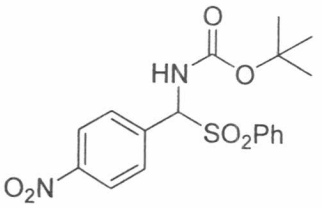
VI-4

***tert*-Butyl *N*-((benzenesulfonyl)-4-bromobenzyl)carbamate (VI-4)** was prepared from a reaction of 4-bromobenzaldehyde (1.85 g, 10 mmol), *tert*-butyl carbamate (**V**) (1.17 g, 10 mmol), and sodium benzenesulfinate (1.64 g, 10 mmol) according to the general procedure outlined earlier to give 0.85 g of **VI-4** (1.99 mmol, 20%) as a white solid. ^{1}H NMR ($CDCl_3$, 200 MHz) δ 1.23 (s, 9H, C(CH_3)$_3$), 5.72 (d, $^{3}J_{HH}$ = 10.2 Hz, 1H, C*H*SO_2Ph), 5.87 (d, $^{3}J_{HH}$ = 10.5 Hz, 1H, N*H*), 7.28-7.96 (m, 9H, Ar); ^{13}C NMR ($CDCl_3$, 125.65 MHz, {^{1}H}) δ 27.93 (C(CH_3)$_3$), 73.27 (*C*HSO_2Ph), 81.34 (*C*(CH_3)$_3$), 124.28, 128.82, 129.08, 129.40, 130.48, 130.94, 131.87, 132.38, 134.09, 136.52, 153.43 (*C*=O).



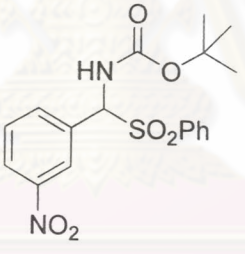
VI-5

***tert*-Butyl *N*-((benzenesulfonyl)-4-cyanobenzyl)carbamate (VI-5)** was prepared from a reaction of 4-cyanobenzaldehyde (1.31 g, 10 mmol), *tert*-butyl carbamate (**V**) (1.17 g, 10 mmol), and sodium benzenesulfinate (1.64 g, 10 mmol) according to the general procedure described earlier to give 2.21 g of **VI-5** (5.36 mmol, 54%) as a white solid. ^{1}H NMR ($CDCl_3$, 200 MHz) δ 1.22 (s, 9H, C(CH_3)$_3$), 5.86 (d, $^{3}J_{HH}$ = 9.8 Hz, 1H, C*H*SO_2Ph), 5.99 (d, $^{3}J_{HH}$ = 10.8 Hz, 1H, N*H*), 7.51-7.92 (m, 9H, Ar); ^{13}C NMR ($CDCl_3$, 50 MHz, {^{1}H}) δ 27.95 (C(CH_3)$_3$), 73.26 (*C*HSO_2Ph), 81.80 (*C*(CH_3)$_3$), 113.73, 118.07, 129.30, 129.44, 129.70, 132.35, 134.44, 135.06, 136.33, 153.33 (*C*=O).



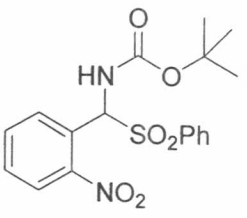
VI-6

***tert*-Butyl *N*-((benzenesulfonyl)-4-nitrobenzyl)carbamate (VI-6)** was prepared from a reaction of 4-nitrobenzaldehyde (1.51 g, 10 mmol), *tert*-butyl carbamate (**V**) (1.17 g, 10 mmol), and sodium benzenesulfinate (1.64 g, 10 mmol) following the general procedure outlined earlier to give **VI-6** (2.97 g, 7.57 mmol, 76%) as a pale yellow solid. ^{1}H NMR ($CDCl_3$, 200 MHz) δ 1.23 (s, 9H, C(CH_3)$_3$), 5.94 (d, $^{3}J_{HH}$ = 10.1 Hz, 1H, C*H*SO_2Ph), 6.05 (d, $^{3}J_{HH}$ = 10.6 Hz, 1H, N*H*), 7.52-8.31 (m, 9H, Ar); ^{13}C NMR ($CDCl_3$, 125.65 MHz, {^{1}H}) δ 27.91 (C(CH_3)$_3$), 73.00 ($CHSO_2Ph$), 81.79 ($C(CH_3)_3$), 123.69, 129.30, 129.41, 130.01, 134.48, 136.19, 136.82, 148.60, 136.08, 153.35 (*C*=O).



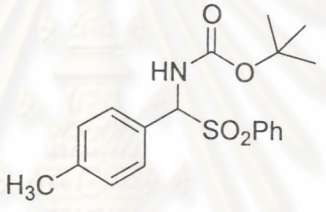
VI-7

***tert*-Butyl *N*-((benzenesulfonyl)-3-nitrobenzyl)carbamate (VI-7)** was prepared from a reaction of 3-nitrobenzaldehyde (1.51 g, 10 mmol), *tert*-butyl carbamate (**V**) (1.17 g, 10 mmol), and sodium benzenesulfinate (1.64 g, 10 mmol) according to the general procedure outlined earlier to give **VI-7** (3.29 g, 8.39 mmol, 84%) as a white solid. ^{1}H NMR ($CDCl_3$, 200 MHz) δ 1.25 (s, 9H, C(CH_3)$_3$) , 5.94 (d, $^{3}J_{HH}$ = 11.0 Hz, 1H, C*H*SO_2Ph), 6.08 (d, $^{3}J_{HH}$ = 11.0 Hz, 1H, N*H*), 7.55-8.33 (m, 9H, Ar).



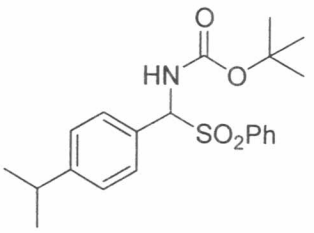
VI-8

***tert*-Butyl *N*-((benzenesulfonyl)-2-nitrobenzyl)carbamate (VI-8)** was prepared from a reaction of 2-nitrobenzaldehyde (1.51 g, 10 mmol), *tert*-butyl carbamate (**V**) (1.17 g, 10 mmol), and sodium benzenesulfinate (1.64 g, 10 mmol) using the general procedure to give 3.23 g of **VI-8** (8.24 mmol, 82%) as a pale yellow solid. ^{1}H NMR ($CDCl_3$, 200 MHz) δ 1.27 (s, 9H, C(CH_3)$_3$), 6.01 (d, $^3J_{HH}$ = 11.0 Hz, 1H, C*H*SO_2Ph), 7.47 (d, $^3J_{HH}$ = 11.0 Hz, 1H, N*H*), 7.56-8.18 (m, 9H, Ar).



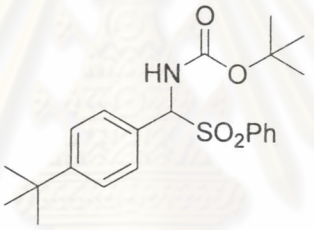
VI-9

***tert*-Butyl *N*-((benzenesulfonyl)-4-methylbenzyl)carbamate (VI-9)** was prepared from a reaction of 4-tolualdehyde (1.20 g, 10 mmol), *tert*-butyl carbamate (**V**) (1.17 g, 10 mmol), and sodium benzenesulfinate (1.64 g, 10 mmol) following the general procedure to give 2.45 g of **VI-9** (6.78 mmol, 68%) as a white solid. ^{1}H NMR ($CDCl_3$, 200 MHz) δ 1.22 (s, 9H, C(CH_3)$_3$), 2.35 (s, 3H, CH_3), 5.78 (d, $^3J_{HH}$ = 10.3 Hz, 1H, C*H*SO_2Ph), 5.88 (d, $^3J_{HH}$ = 10.9 Hz, 1H, N*H*), 7.18-7.92 (m, 9H, Ar); ^{13}C NMR ($CDCl_3$, 50 MHz, {^{1}H}) δ 21.30 (CH_3), 27.99 (C(CH_3)$_3$), 73.76 (*C*HSO_2Ph), 81.14 (*C*(CH_3)$_3$), 124.94, 126.72, 128.79, 129.02, 129.49, 129.88, 133.89, 136.99, 140.02, 153.46 (*C*=O).



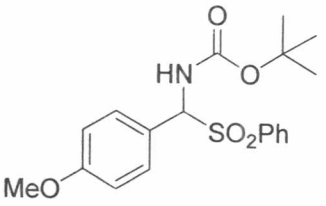
VI-10

***tert*-Butyl *N*-((benzenesulfonyl)-4-*iso*-propylbenzyl)carbamate (VI-10)** was prepared from a reaction of cuminaldehyde (1.48 g, 10 mmol), *tert*-butyl carbamate (**V**) (1.17 g, 10 mmol), and sodium benzenesulfinate (1.64 g, 10 mmol) according to the general procedure described earlier to give 0.23 g of **VI-10** (0.59 mmol, 60%) as a white solid. ^{1}H NMR ($CDCl_3$, 200 MHz) δ 1.17-1.30 (m, 15H, C(C*H*$_3$)$_3$, CH(C*H*$_3$)$_2$), 2.84-2.98 (m, 1H, C*H*), 5.73 (d, $^3J_{HH}$ = 10.9 Hz, 1H, C*H*SO_2Ph), 5.88 (d, $^3J_{HH}$ = 10.5 Hz, 1H, N*H*), 7.20-7.93 (m, 9H, Ar).



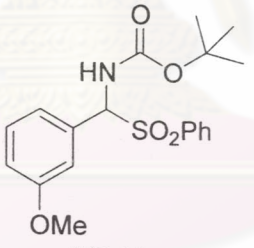
VI-11

***tert*-Butyl *N*-((benzenesulfonyl)-4-*tert*-butylbenzyl)carbamate (VI-11)** was prepared from a reaction of 4-*tert*-butylbenzaldehyde (1.62 g, 10 mmol), *tert*-butyl carbamate (**V**) (1.17 g, 10 mmol), and sodium benzenesulfinate (1.64 g, 10 mmol) according to the general procedure described earlier to give 2.28 g of **VI-11** (5.65 mmol, 57%) as a white solid. ^{1}H NMR ($CDCl_3$, 200 MHz) δ 1.22 (s, 9H, C(C*H*$_3$)$_3$), 1.30 (s, 9H, C(C*H*$_3$)$_3$), 5.73 (d, $^3J_{HH}$ = 10.9 Hz, 1H, C*H*SO_2Ph), 5.88 (d, $^3J_{HH}$ = 10.9 Hz, 1H, N*H*), 6.78-7.93 (m, 9H, Ar); ^{13}C NMR ($CDCl_3$, 125.65 MHz, {^{1}H}) δ 27.98 (C(*C*H$_3$)$_3$), 31.18 (C(*C*H$_3$)$_3$), 73.60 (*C*HSO_2Ph), 81.06 (*C*(CH$_3$)$_3$), 124.92, 125.81, 125.98, 126.63, 128.62, 128.97, 129.45, 129.70, 133.84, 137.01, 153.05, 153.35 (*C*=O).



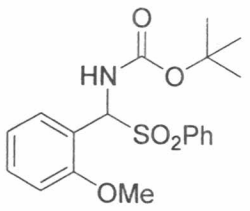
VI-12

***tert*-Butyl *N*-((benzenesulfonyl)-4-methoxybenzyl)carbamate (VI-12)** was prepared from a reaction of 4-methoxybenzaldehyde (1.36 g, 10 mmol), *tert*-butyl carbamate (**V**) (1.17g, 10 mmol), and sodium benzenesulfinate (1.64 g, 10 mmol) according to the general procedure described earlier to give 2.11 g of **VI-12** (5.59 mmol, 56%) as a white solid. ^{1}H NMR ($CDCl_3$, 200 MHz) δ 1.24 (s, 9H, C(CH_3)$_3$), 3.81 (s, 3H, OCH_3), 5.70 (d, $^{3}J_{HH}$ = 10.1 Hz, 1H, CHSO$_2$Ph), 5.86 (d, $^{3}J_{HH}$ = 10.1Hz, 1H, N*H*), 6.90-8.00 (m, 9H, Ar); ^{13}C NMR ($CDCl_3$, 125.65 MHz, {^{1}H}) δ 27.94 (C(CH_3)$_3$), 55.33 (OCH_3), 73.46 (CHSO$_2$Ph), 81.10 (C(CH$_3$)$_3$), 113.64, 114.20, 121.58, 124.89, 128.99, 129.40, 130.20, 131.80, 132.23, 133.82, 136.93, 160.75, 153.45 (C=O).



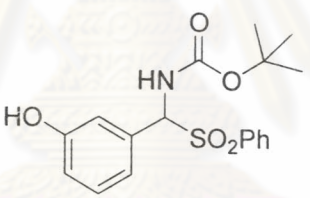
VI-13

***tert*-Butyl *N*-((benzenesulfonyl)-3-methoxybenzyl)carbamate (VI-13)** was prepared from a reaction of 3-methoxybenzaldehyde (1.36 g, 10 mmol), *tert*-butyl carbamate (**V**) (1.17 g, 10 mmol), and sodium benzenesulfinate (1.64 g, 10 mmol) according to the general procedure described earlier to give 2.11 g of **VI-13** (5.59 mmol, 56%) as a white solid. ^{1}H NMR ($CDCl_3$, 200 MHz) δ 1.24 (s, 9H, C(CH_3)$_3$), 3.78 (s, 3H, OCH_3), 5.74 (d, $^{3}J_{HH}$ = 9.6 Hz, 1H, CHSO$_2$Ph), 5.87 (d, $^{3}J_{HH}$ = 10.5 Hz, 1H, N*H*), 6.93-7.92 (m, 9H, Ar); ^{13}C NMR ($CDCl_3$, 125.65 MHz, {^{1}H}) δ 27.94 (C(CH_3)$_3$), 55.28 (OCH_3), 73.87 (CHSO$_2$Ph), 81.11 (C(CH$_3$)$_3$), 114.38, 115.61, 121.19, 128.99, 129.41, 129.71, 131.19, 133.89, 136.87, 159.63, 153.48 (C=O).



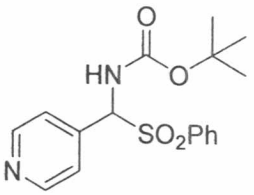
VI-14

***tert*-Butyl *N*-((benzenesulfonyl)-2-methoxybenzyl)carbamate (VI-14)** was prepared from a reaction of 2-methoxybenzaldehyde (1.36 g, 10 mmol), *tert*-butyl carbamate (**V**) (1.17 g, 10 mmol), and sodium benzenesulfinate (1.64 g, 10 mmol) using to the general procedure described earlier to give **VI-14** (0.49 g, 1.30 mmol, 13%) as a white solid. ^{1}H NMR ($CDCl_3$, 200 MHz) δ 1.30 (s, 9H, C(CH_3)$_3$), 3.71 (s, 3H, OCH_3), 6.24 (d, $^{3}J_{HH}$ = 10.8 Hz, 1H, CHSO$_2$Ph), 6.33 (d, $^{3}J_{HH}$ = 10.7 Hz, 1H, NH), 6.82-7.84 (m, 9H, Ar); ^{13}C NMR ($CDCl_3$, 50 MHz, {^{1}H}) δ 28.11 (C(CH_3)$_3$), 55.80 (OCH_3), 71.10 (CHSO$_2$Ph), 80.95 (C(CH$_3$)$_3$), 111.43, 118.67, 120.94, 124.89, 128.71, 129.46, 130.27, 131.13, 133.59, 135.99, 137.52, 157.84, 153.86 (C=O).



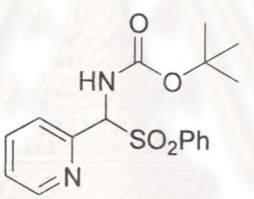
VI-15

***tert*-Butyl *N*-((benzenesulfonyl)-3-hydroxybenzyl)carbamate (VI-15)** was prepared from a reaction of 3-hydroxybenzaldehyde (1.22 g, 10 mmol), *tert*-butyl carbamate (**V**) (1.17 g, 10 mmol), and sodium benzenesulfinate (1.64 g, 10 mmol) according to the general procedure outlined earlier to give 1.45 g of **VI-15** (4.0 mmol, 40%) as a pale yellow solid. ^{1}H NMR ($CDCl_3$, 200 MHz) δ 1.23 (s, 9H, C(CH_3)$_3$), 5.86 (d, $^{3}J_{HH}$ = 9.7 Hz, 1H, CHSO$_2$Ph), 5.97 (d, $^{3}J_{HH}$ = 10.0 Hz, 1H, NH), 6.85-7.91 (m, 9H, Ar); ^{13}C NMR ($CDCl_3$, 125.65 MHz, {^{1}H}) δ 27.99 (C(CH_3)$_3$), 74.07 (CHSO$_2$Ph), 81.39 (C(CH$_3$)$_3$), 115.87, 117.32, 121.02, 129.07, 129.45, 129.97, 134.07, 136.49, 156.34, 153.71 (C=O).



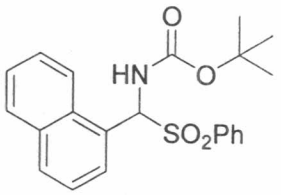
VI-16

***tert*-Butyl *N*-((benzenesulfonyl)-4-pyridyl)carbamate (VI-16)** was prepared from a reaction of 4-pyridinecarboxaldehyde (1.07 g, 10 mmol), *tert*-butyl carbamate (**V**) (1.17 g, 10 mmol), and sodium benzenesulfinate (1.64 g, 10 mmol) according to the general procedure to give 0.49.g of **VI-16** (1.41 mmol, 14%) as a white solid. ^{1}H NMR ($CDCl_3$, 200 MHz) δ 1.23 (s, 9H, C(CH_3)$_3$), 6.0 (d, $^{3}J_{HH}$ = 8.6 Hz, 1H, C*H*SO_2Ph), 6.90 (d, $^{3}J_{HH}$ = 9.1 Hz, 1H, N*H*), 7.25-8.69 (m, 9H, Ar); ^{13}C NMR ($CDCl_3$, 50 MHz, {^{1}H}) δ 27.97 (C(CH_3)$_3$), 72.95 (*C*HSO_2Ph), 81.62 (*C*(CH_3)$_3$), 123.61, 129.26,129.52, 134.41, 136.30, 138.98, 150.01, 153.57 (*C*=O).



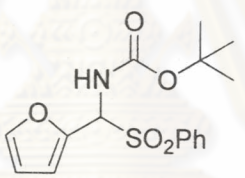
VI-17

***tert*-Butyl *N*-((benzenesulfonyl)-2-pyridyl)carbamate (VI-17)** was prepared from a reaction of 2-pyridinecarboxaldehyde (1.07 g, 10 mmol), *tert*-butyl carbamate (**V**) (1.17 g, 10 mmol), and sodium benzenesulfinate (1.64 g, 10 mmol) according to the general procedure outlined earlier to give **VI-17** (2.05 g, 5.88 mmol, 59%) as a white solid. ^{1}H NMR ($CDCl_3$, 200 MHz) δ 1.24 (s, 9H, C(CH_3)$_3$), 6.00 (d, $^{3}J_{HH}$ = 10.8 Hz, 1H, C*H*SO_2Ph), 6.30 (d, $^{3}J_{HH}$ = 10.8 Hz, 1H, N*H*), 7.25-8.69 (m, 9H, Ar); ^{13}C NMR ($CDCl_3$, 50 MHz, {^{1}H}) δ 28.02 (C(*C*H_3)$_3$), 74.51 (*C*HSO_2Ph), 80.78 (*C*(CH_3)$_3$), 124.45, 125.59, 128.91, 129.81, 133.95, 136.68, 147.85, 149.48, 153.66 (*C*=O).



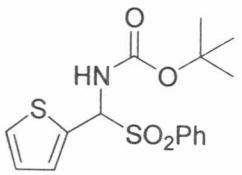
VI-18

***tert*-Butyl *N*-((benzenesulfonyl)-1-naphthyl)carbamate (VI-18)** was prepared from a reaction of 1-naphthaldehyde (1.56 g, 10 mmol), *tert*-butyl carbamate (**V**) (1.17 g, 10 mmol), and sodium benzenesulfinate (1.64 g, 10 mmol) according to the general procedure to give **VI-18** (0.38 g, 0.96 mmol, 10%) as a white solid. ^{1}H NMR ($CDCl_3$, 200 MHz) δ 1.25 (s, 9H, C(CH_3)$_3$), 5.90 (d, $^{3}J_{HH}$ = 10.7 Hz, 1H, C*H*SO_2Ph), 6.84 (d, $^{3}J_{HH}$ = 11.5 Hz, 1H, N*H*), 6.81-8.13 (m, 12H, Ar); ^{13}C NMR ($CDCl_3$, 50 MHz, {^{1}H}) δ 28.02 (C(CH_3)$_3$), 69.10 (*C*HSO_2Ph), 81.31 (*C*(CH_3)$_3$), 122.88, 124.90, 125.13, 126.15, 126.61, 127.01, 127.20, 129.09, 129.42, 130.54, 131.77, 133.70, 133.95, 137.37, 153.63 (*C*=O).



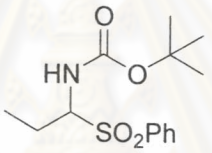
VI-19

***tert*-Butyl *N*-((benzenesulfonyl)-2-furyl)carbamate (VI-19)** was prepared from a reaction of 2-furfuraldehyde (1.20 g, 10 mmol), *tert*-butyl carbamate (**V**) (1.17 g, 10 mmol), and sodium benzenesulfinate (1.64 g, 10 mmol) following to the general procedure to give **VI-19** (2.52 g, 6.97 mmol, 70%) as a brown solid. ^{1}H NMR ($CDCl_3$, 200 MHz) δ 1.28 (s, 9H, C(CH_3)$_3$), 5.85 (d, $^{3}J_{HH}$ = 10.2 Hz, 1H, C*H*SO_2Ph), 6.03 (d, $^{3}J_{HH}$ = 11.0 Hz, 1H, N*H*), 6.44 (dd, $^{3}J_{HH}$ = 3.0, 3.6 Hz, 1H, furyl C_4*H*),6.58 (d, $^{3}J_{HH}$ = 3.6 Hz, 1H, furyl C_3*H*), 7.90 (d, $^{3}J_{HH}$ = 7.4 Hz, 1H, furyl C_5*H*), 7.49-7.69 (m, 5H, Ar).



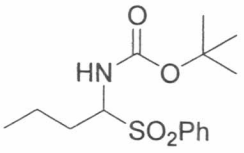
VI-20

***tert*-Butyl *N*-((benzenesulfonyl)-2-thienyl)carbamate (VI-20)** was prepared from a reaction of 2-thiophenecarboxaldehyde (1.12 g, 10 mmol), *tert*-butyl carbamate (**V**) (1.17 g, 10 mmol), and sodium benzenesulfinate (1.64 g, 10 mmol) according to the general procedure described earlier to give 0.66 g of **VI-20** (1.87 mmol, 19%) as a white solid. ^{1}H NMR ($CDCl_3$, 200 MHz) δ 1.26 (s, 9H, C(CH_3)$_3$), 5.68 (d, $^3J_{HH}$ = 10.4 Hz, 1H, C*H*SO_2Ph), 6.18 (d, $^3J_{HH}$ = 11.0 Hz, 1H, N*H*), 7.00-7.10 (m, 2H, thienyl C_3H, C_4H), 7.41-7.44 (m, 1H, thienyl C_5H), 7.05-7.95 (m, 5H, Ar).



VI-21

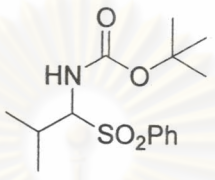
***tert*-Butyl *N*-((benzenesulfonyl)propyl)carbamate (VI-21)** was prepared from a reaction of propionaldehyde (0.58 g, 10 mmol), *tert*-butyl carbamate (**V**) (1.17 g, 10 mmol), and sodium benzenesulfinate (1.64 g, 10 mmol) as described earlier with a slight modification. The mixture was heated at 70 °C for 1 h. After cooling, white crystals were filtered and washed sequentially with water and diethyl ether to give 0.30 g of **VI-21** (1.00 mmol, 10%) as a white solid. ^{1}H NMR ($CDCl_3$, 200 MHz) δ 1.06 (t, $^3J_{HH}$ = 7.3 Hz, 3H, CH_3), 1.71-1.79 (m, 1H, CH_2), 2.23-2.32 (m, 1H, CH_2), 4.76 (dt, $^3J_{HH}$ = 10.5 Hz, 1H, C*H*SO_2Ph), 5.00 (d, $^3J_{HH}$ = 10.8 Hz, 1H, *NH*), 7.47-7.91 (m, 5H, Ar).



VI-22

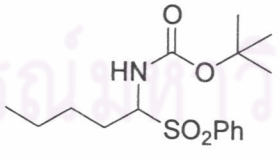
***tert*-Butyl *N*-((benzenesulfonyl)butyl)carbamate (VI-22)** was prepared from a reaction of butyraldehyde (0.58 g, 10 mmol), *tert*-butyl carbamate (**V**) (1.17 g, 10 mmol), and sodium benzenesulfinate (1.64 g, 10 mmol) as described earlier with a

slight modification. The mixture was heated at 70 °C for 1 h. After cooling, white crystals were filtered and washed sequentially with water and diethyl ether to give 0.60 g of **VI-22** (1.90 mmol, 19%) as a white solid. ^{1}H NMR ($CDCl_3$, 200 MHz) δ 0.93 (t, 3H, CH_3), 1.23 (s, 9H, (CH_3)$_3$), 1.30-1.50 (m, 2H, CH_2), 1.63-1.74 (m, 2H, CH_2), 2.17-2.28 (m, 2H, CH_2), 4.81 (dt, $^3J_{HH}$ = 10.7 Hz, 1H, C*H*SO_2Ph), 4.97 (d, $^3J_{HH}$ = 10.8 Hz, 1H, *NH*), 7.47-7.91 (m, 5H, Ar).



VI-23

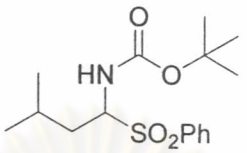
***tert*-Butyl *N*-((benzenesulfonyl)*iso*-butyl)carbamate (VI-23)** was *iso*-butyraldehyde (0.72 g, 10 mmol), *tert*-butyl carbamate (**V**) (1.17 g, 10 mmol), and sodium benzenesulfinate (1.64 g, 10 mmol) as described earlier with a slight modification. The mixture was heated at 70 °C for 1 h. After cooling, white crystals were filtered and washed sequentially with water and diethyl ether to give 1.36 g of **VI-23** (7.95 mmol, 80%) as a white solid. ^{1}H NMR ($CDCl_3$, 200 MHz) δ 1.06 (d, $^3J_{HH}$ = 6.7 Hz, 3H, CH(CH_3)$_2$), 1.12 (d, $^3J_{HH}$ = 6.8 Hz, 3H, CH(CH_3)$_2$), 1.20 (s, 9H, C(CH_3)$_3$), 2.72-2.81 (m, 1H, C*H*(CH$_3$)$_2$), 4.72 (dd, $^3J_{HH}$ = 11.3 Hz, 3.4 Hz, 1H, C*H*SO_2Ph), 5.13 (d, $^3J_{HH}$ = 11.0 Hz, 1H, N*H*), 7.46-7.89 (m, 5H, Ar); ^{13}C NMR ($CDCl_3$, 50 MHz, {^{1}H}) δ 16.90, 20.67 (CH(*C*H$_3$)$_2$), 26.72 (*C*H(CH$_3$)$_2$), 27.97 (C(*C*H$_3$)$_3$), 74.27 (*C*HSO_2Ph), 80.75 (*C*(CH$_3$)$_3$), 129.08, 133.71, 138.03, 154.08 (*C*=O).



VI-24

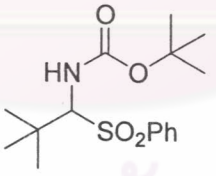
***tert*-Butyl *N*-((benzenesulfonyl)pentyl)carbamate (VI-24)** was pentaldehyde (0.86 g, 10 mmol), *tert*-butyl carbamate (**V**) (1.17 g, 10 mmol), and sodium benzenesulfinate (1.64 g, 10 mmol) as described earlier with a slight modification. The mixture was heated at 70 °C for 1 h. After cooling, white crystals were filtered and washed sequentially with water and diethyl ether to give **VI-24** (1.31

g, 4.00 mmol, 40%) as a white solid. ^{1}H NMR ($CDCl_3$, 200 MHz) δ 0.90 (t, $^3J_{HH}$ = 6.8 Hz, 3H, CH_3), 1.26 (s, 9H, (CH_3)$_3$), 1.04-1.69 (m, 4H, (CH_2)$_2$), 2.18-2.28 (m, 2H, CH_2), 4.84 (dt, $^3J_{HH}$ = 10.6 Hz, 3.2 Hz, 1H, C*H*SO_2Ph), 4.99 (d, $^3J_{HH}$ = 10.3 Hz, 1H, N*H*), 7.47-7.91 (m, 5H, Ar).



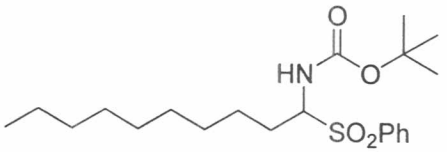
VI-25

***tert*-Butyl *N*-((benzenesulfonyl)iso-pentyl)carbamate (VI-25)** was isovaleraldehyde (0.86 g, 10 mmol), *tert*-butyl carbamate (**V**) (1.17 g, 10 mmol), and sodium benzenesulfinate (1.64 g, 10 mmol) as outlined earlier with a slight modification. The mixture was heated at 70 °C for 1 h. After cooling, white crystals were filtered and washed sequentially with water and diethyl ether to give 1.60 g of **VI-25** (4.89 mmol, 49%) as a white solid. ^{1}H NMR ($CDCl_3$, 200 MHz) δ 0.91 (t, $^3J_{HH}$ = 6.5 Hz, 3H, CH_3), 0.98 (t, $^3J_{HH}$ = 6.4 Hz, 3H, CH_3), 1.20 (s, 9H, (CH_3)$_3$), 1.63-1.80 (m, 1H, C*H*(CH_3)$_2$), 1.95-2.00 (m, 2H, CH_2), 4.60 (d, $^3J_{HH}$ = 10.3 Hz, 1H, N*H*), 4.70 (dt, $^3J_{HH}$ = 10.6 Hz, 3.2 Hz, 1H, C*H*SO_2Ph), 7.47-7.92 (m, 5H, Ar).



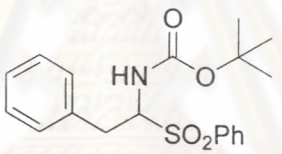
VI-26

***tert*-Butyl *N*-((benzenesulfonyl)*tert*-butyl)carbamate (VI-26)** was pivalaldehyde (0.86 g, 10 mmol), *tert*-butyl carbamate (**V**) (1.17 g, 10 mmol), and sodium benzenesulfinate (1.64 g, 10 mmol) as described earlier with a slight modification. The mixture was heated at 70 °C for 1 h. After cooling, white crystals were filtered and washed sequentially with water and diethyl ether to give 0.81 g of **VI-26** (2.47 mmol, 25%) as a white solid. ^{1}H NMR ($CDCl_3$, 200 MHz) δ 1.18, (s, 9H, (CH_3)$_3$), 1.25 (s, 9H, (CH_3)$_3$), 4.64 (d, $^3J_{HH}$ = 11.6 Hz, 1H, C*H*SO_2Ph), 5.25 (d, $^3J_{HH}$ = 11.0 Hz, 1H, N*H*), 7.46-7.93 (m, 5H, Ar).



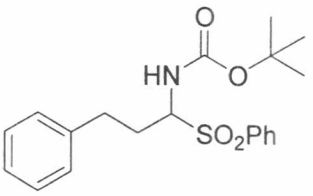
VI-27

***tert*-Butyl *N*-((benzenesulfonyl)decyl)carbamate (VI-27)** was prepared from a reaction of decanaldehyde (1.56 g, 10 mmol), *tert*-butyl carbamate (**V**) (1.17 g, 10 mmol), and sodium benzenesulfinate (1.64 g, 10 mmol) as outlined earlier with a slight modification. The mixture was heated at 70 °C for 1 h. After cooling, white crystals were filtered and washed sequentially with water and diethyl ether to give **VI-27** (0.59 g, 1.48 mmol, 15%) as a white solid. ^{1}H NMR ($CDCl_3$, 200 MHz) δ 0.86 (t, 3H, C*H*$_3$), 1.19 (s, 9H, (C*H*$_3$)$_3$), 1.09-1.78 (m, 14H, (C*H*$_2$)$_7$), 2.15-2.27 (m, 2H, C*H*$_2$), 4.81 (dt, $^3J_{HH}$ = 10.6 Hz, 1H, C*H*SO$_2$Ph), 4.95 (d, $^3J_{HH}$ = 10.9 Hz, 1H, *NH*), 7.47-7.91 (m, 5H, Ar).



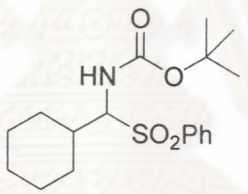
VI-28

***tert*-Butyl *N*-((benzenesulfonyl)-2-phenylethyl)carbamate (VI-28)** was prepared from a reaction of phenylacetaldehyde (1.20 g, 10 mmol), *tert*-butyl carbamate (**V**) (1.17 g, 10 mmol), and sodium benzenesulfinate (1.64 g, 10 mmol) as described earlier with a slight modification. The mixture was heated at 70 °C for 1 h. After cooling, white crystals were filtered and washed sequentially with water and diethyl ether to give 2.35 g of **VI-28** (6.50 mmol, 65%) as a white solid. ^{1}H NMR ($CDCl_3$, 200 MHz) δ 1.05 (s, 9H, (C*H*$_3$)$_3$), 2.97 (d, 1H, C*H*$_2$), 3.05 (d, 2H, C*H*$_2$), 5.01 (d, $^3J_{HH}$ = 10.4 Hz, 1H, *NH*), 5.14 (dt, $^3J_{HH}$ = 10.4 Hz, 3.4 Hz, 1H, C*H*SO$_2$Ph), 7.18-7.95 (m, 10H, Ar).



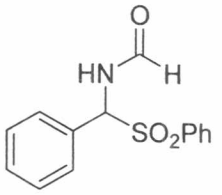
VI-29

***tert*-Butyl *N*-((benzenesulfonyl)3-phenylpropyl)carbamate (VI-29)** was prepared from a reaction of 3-phenylpropionaldehyde (1.34 g, 10 mmol), *tert*-butyl carbamate (**V**) (1.17 g, 10 mmol), and sodium benzenesulfinate (1.64 g, 10 mmol) as described earlier with a slight modification. The mixture was heated at 70 °C for 1 h. After cooling, white crystals were filtered and washed sequentially with water and diethyl ether to give **VI-29** (1.61 g,4.31 mmol, 43%) as a white solid. ^{1}H NMR ($CDCl_3$, 200 MHz) δ 1.20 (s, 9H, $(CH_3)_3$), 2.03-2.12 (m, 2H, CH_2), 2.50-2.89 (m, 2H, CH_2), 4.84 (t, $^3J_{HH}$ = 10.4 Hz, 1H, $CHSO_2Ph$), 5.03 (d, $^3J_{HH}$ = 11.3 Hz, 1H, *NH*), 7.11-7.89 (m, 10H, Ar).



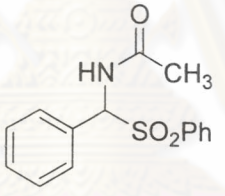
VI-30

***tert*-Butyl *N*-((benzenesulfonyl)cyclohexyl)carbamate (VI-30)** was prepared from a reaction of cyclohexanecarboxaldehyde (1.12 g, 10 mmol), *tert*-butyl carbamate (**V**) (1.17 g, 10 mmol), and sodium benzenesulfinate (1.64 g, 10 mmol) as outlined earlier with a slight modification. The mixture was heated at 70 °C for 1 h. After cooling, white crystals were filtered and washed sequentially with water and diethyl ether to give 2.54 g of **VI-30** (7.19 mmol, 72%) as a white solid. ^{1}H NMR ($CDCl_3$, 200 MHz) δ 1.21 (s, 9H, $(CH_3)_3$), 1.05-2.17 (m, 10H, $(CH_2)_5$), 2.40-2.53 (m, 1H, *CH*), 4.71 (dd, $^3J_{HH}$ = 11.8 Hz, 3.2 Hz, 1H, $CHSO_2Ph$), 5.17 (d, $^3J_{HH}$ = 11.8 Hz, 1H, *NH*), 7.47-7.90 (m, 5H, Ar).



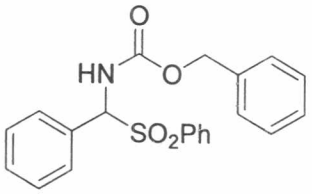
VII-1

***N*-(benzylsulfonyl)formamide (VII-1)** The procedure of Leusen et al.was followed.[46] A stirred mixture of sodium benzene sulfinate (0.98 g, 6.0 mmol), benzaldehyde (0.96 g, 9.0 mmol), formamide (2.70 g, 60.0 mmol), water (3 mL), and formic acid (0.8 mL) was heated at 60°C for 6 h. The mixture was cooled to room temperature with continuous stirring, and the precipitate was collected and washed thoroughly with water and diethyl ether (6×5 mL), providing 0.048 g of **VII-1** (0.17 mmol, 10%) as a yellow solid. ^{1}H NMR ($CDCl_3$, 400 MHz), 6.33 (d, $^3J_{HH}$ = 10.8 Hz, 1H, C*H*SO_2Ph), 6.84 (d, $^3J_{HH}$ = 10.0 Hz, 1H, N*H*), 7.23-8.06 (m, 10H, Ar), 8.14 (s, 1H, C*H*O).



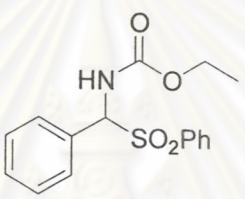
VII-2

***N*-(benzylsulfonyl)acetamide (VII-2)** The procedure of Leusen et al.was followed.[46] A stirred mixture of sodium benzene sulfinate (0.98 g, 6.0 mmol), benzaldehyde (0.96 g, 9.0 mmol), acetamide (3.54 g, 60.0 mmol), water (3 mL), and formic acid (0.8 mL) was heated at 60°C for 6 h. The mixture was cooled to room temperature with continuous stirring, and the precipitate was collected and washed thoroughly with water and diethyl ether (6×5 mL), providing 0.026 g of **VII-2** (0.90 mmol, 15%) as a white solid. ^{1}H NMR ($CDCl_3$, 400 MHz), 1.97 (s, 3H, CH_3), 6.36 (d, $^3J_{HH}$ = 10.5 Hz, 1H, C*H*SO_2Ph), 7.00 (d, $^3J_{HH}$ = 10.5 Hz, 1H, N*H*), 7.30-7.91 (m, 10H, Ar).



VII-3

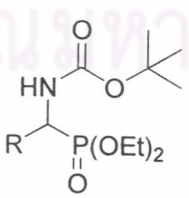
Benzyl *N*-((benzenesulfonyl)benzyl)carbamate (VII-3) was prepared from a reaction of benzaldehyde (1.05 g, 10 mmol), benzylcarbamate (1.52g, 10 mmol), and sodium benzenesulfinate (1.64 g, 10 mmol) according to the general procedure to give 1.05.g of **VII-3** (2.75 mmol, 27%) as a white solid. ^{1}H NMR ($CDCl_3$, 200 MHz) δ 4.94 (s, 2H, C*H*$_2$Ph), 5.96 (m, 2H, C*H*SO$_2$Ph, N*H*), 7.33-7.86 (m, 10H, Ar).



VII-4

Ethyl *N*-((benzenesulfonyl)benzyl)carbamate (VII-4) was prepared from a reaction of benzaldehyde (1.05 g, 10 mmol), ethylcarbamate (1.76g, 10 mmol), and sodium benzenesulfinate (1.64 g, 10 mmol) according to the general procedure outlined earlier to give **VII-4** (1.96 g, 6.14 mmol, 62%) as a white solid. ^{1}H NMR ($CDCl_3$, 200 MHz) δ 1.13 (t, 3H, CH_2CH_3), 3.96 (q, 2H, CH_2CH_3), 5.95 (s, 1H, C*H*SO$_2$Ph), 7.27-7.89 (m, 10H, Ar).

2.5.3 General procedure for the preparation of α-aminophosphonates (VIII)

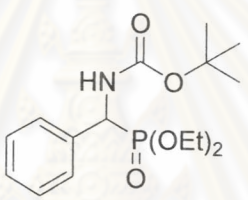


VIII

Method A (for VI derived from aromatic aldehyde) : To a solution of *tert*-butyl *N*-((benzenesulfonyl)alkyl)carbamate (**VI**) (0.25 mmol) in THF (2 mL) was added diethyl phosphite (0.035 mL, 0.275 mmol) and DBU (0.075 mL, 0.5 mmol). The mixture was stirred at room temperature for 1 h then solvent was evaporated to

give the crude product. Purification of crude material by column chromatography (gradient elution, 10% to 20% EtOAc/Hexane) resulted in the desired α-aminophosphonates (**VIII**).

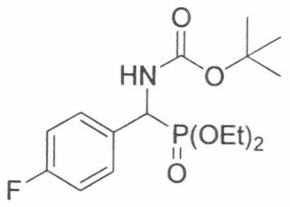
Method B (for VI derived from aliphatic aldehyde) : A reaction of *tert*-butyl *N*-((benzenesulfonyl)alkyl)carbamate (**VI**) (0.25 mmol), diethyl phosphite (0.035 mL, 0.275 mmol), and K_2CO_3 (0.069 mg, 0.5 mmol) in CH_3CN (2 mL). The mixture was stirred at room temperature for 2 d. Water (2 mL) were added to a reaction and the mixture was extracted with CH_2Cl_2 (4×3 mL). Solvent was evaporated to give the crude product. Purification of crude material by column chromatography (gradient elution, 2% to 15% EtOAc/Hexane) yielded the desired α-aminophosphonates (**VIII**).



VIII-1

Diethyl [1-(*N*-*tert*-butoxycarbonylamino)benzyl]phosphonate (VIII-1)

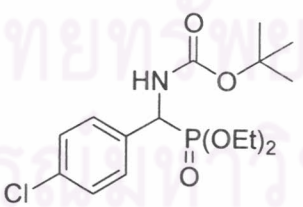
A reaction of *tert*-butyl *N*-((benzenesulfonyl)benzyl)carbamate (**VI-1**) (86.8 mg, 0.25 mmol), diethyl phosphite (0.035 mL, 0.275 mmol), and DBU (0.075 mL, 0.5 mmol) via method A afforded α-aminophosphonate **VIII-1** as a white solid (0.071 g, 0.21 mmol, 83%), mp: 118-119°C (lit.[47] : 118-120°C). ^{1}H NMR ($CDCl_3$, 200 MHz) δ 1.09 (t, $^3J_{HH}$ = 7.0 Hz, 3H, OCH_2CH_3), 1.28 (t, $^3J_{HH}$ = 7.1 Hz, 3H, OCH_2CH_3), 1.40 (s, 9H, $C(CH_3)_3$), 3.74-4.13 (m, 4H, OCH_2CH_3), 5.09 (dd, $^2J_{HP}$ = 20.4 Hz, $^3J_{HH}$ = 10.3 Hz, 1H, CHP), 7.26-7.37 (m, 5H, Ar); ^{31}P NMR ($CDCl_3$, 202.35 MHz, {^{1}H}) δ 21.89; ^{13}C NMR ($CDCl_3$, 125.65 MHz, {^{1}H}) δ 16.09 (d, $^3J_{CP}$ = 6.2 Hz, OCH_2CH_3), 16.34 (d, $^3J_{CP}$ = 4.2 Hz, OCH_2CH_3), 28.21 ($C(CH_3)_3$), 51.73 (d, $^1J_{CP}$ = 153.0 Hz, CHP), 62.99 (d, $^2J_{CP}$ = 6.2 Hz, OCH_2CH_3), 63.18 (d, $^2J_{CP}$ = 8.3 Hz, OCH_2CH_3), 80.24 ($C(CH_3)_3$), 127.75, 127.79, 127.97, 128.51, 135.42, 154.84 (d, $^3J_{CP}$ = 10.3 Hz, C=O); EIMS (70 eV) *m/z* (relative intensity) 344 $[MH]^+$ (100), 288 (20), 206 (10), 150 (44), 106 (36), 79 (14); Anal. Calcd for $C_{16}H_{26}NO_5P$: C, 55.97; H, 7.63; N, 4.08. Found: C, 55.90; H, 7.96; N, 4.09.



VIII-2

Diethyl [1-(*N-tert*-butoxycarbonylamino)(4′-fluorobenzyl)]phosphonate (VIII-2)

Via the general procedure of method A described above, a reaction of *tert*-butyl *N*-((benzenesulfonyl)-4-fluorobenzyl)carbamate (**VI-2**) (91.2 mg, 0.25 mmol), diethyl phosphite (0.035 mL, 0.275 mmol), and DBU (0.075 mL, 0.5 mmol) yielded α-aminophosphonate **VIII-2** as a white solid (0.073 g, 0.20 mmol, 80%), mp: 101-102 °C. ^{1}H NMR ($CDCl_3$, 200 MHz) δ 1.11 (t, $^{3}J_{HH}$ = 7.1 Hz, 3H, OCH_2CH_3), 1.27 (t, $^{3}J_{HH}$ = 7.1 Hz, 3H, OCH_2CH_3), 1.39 (s, 9H, $C(CH_3)_3$), 3.69-4.16 (m, 4H, OCH_2CH_3), 5.05 (dd, $^{2}J_{HP}$ = 21.7 Hz, $^{3}J_{HH}$ = 9.5 Hz, 1H, CHP), 5.53 (br, 1H, NH), 6.96-7.40 (m, 4H, Ar); ^{31}P NMR ($CDCl_3$, 202.35 MHz, {^{1}H}) δ 22.01; ^{13}C NMR ($CDCl_3$, 50 MHz, {^{1}H}) δ 16.16 (d, $^{3}J_{CP}$ = 5.7 Hz, OCH_2CH_3), 16.37 (d, $^{3}J_{CP}$ = 5.7 Hz, OCH_2CH_3), 28.22 ($C(CH_3)_3$), 51.17 (d, $^{1}J_{CP}$ = 153.5 Hz, CHP), 63.25 (d, $^{2}J_{CP}$ = 5.9 Hz, OCH_2CH_3), 80.47 ($C(CH_3)_3$), 115.25, 115.68, 129.36, 129.48, 131.48, 154.96 (C=O); EIMS (70 eV) *m/z* (relative intensity) 362 $[MH]^+$ (100), 344 (16), 306 (22), 168 (52), 124 (37), 97 (10); Anal. Calcd for $C_{16}H_{25}FNO_5P$: C, 53.18; H, 6.97; N, 3.88. Found: C, 53.39; H, 6.96; N, 3.75.

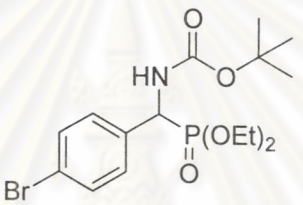


VIII-3

Diethyl [1-(*N-tert*-butoxycarbonylamino)(4′-chlorobenzyl)]phosphonate (VIII-3)

Via the general procedure of method A described above, a reaction of *tert*-butyl *N*-((benzenesulfonyl)-4-chlorobenzyl)carbamate (**VI-3**) (95.4 mg, 0.25 mmol), diethyl phosphite (0.035 mL, 0.275 mmol), and DBU (0.075 mL, 0.5 mmol) resulted in 0.071 g of α-aminophosphonate **VIII-3** as a white solid (0.19 mmol, 75%), mp:

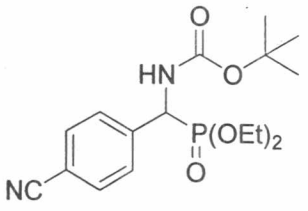
131-132°C. ^{1}H NMR ($CDCl_3$, 200 MHz) δ 1.13 (t, $^{3}J_{HH}$ = 7.1 Hz, 3H, OCH_2CH_3), 1.27 (t, $^{3}J_{HH}$ = 7.1 Hz, 3H, OCH_2CH_3), 1.39 (s, 9H, $C(CH_3)_3$), 3.72-4.16 (m, 4H, OCH_2CH_3), 5.04 (dd, $^{2}J_{HP}$ = 22.2 Hz, $^{3}J_{HH}$ = 9.6 Hz, 1H, CHP), 5.48 (br, 1H, NH), 7.26-7.51 (m, 4H, Ar); ^{31}P NMR ($CDCl_3$, 202.35 MHz, {^{1}H}) δ 21.89; ^{13}C NMR ($CDCl_3$, 50 MHz, {^{1}H}) δ 16.31 (OCH_2CH_3), 16.42 (OCH_2CH_3), 28.21 ($C(CH_3)_3$), 51.29 (d, $^{1}J_{CP}$ = 155.1 Hz, CHP), 63.25 (OCH_2CH_3), 80.51 ($C(CH_3)_3$), 128.69, 129.08, 129.19, 133.89, 134.24, 154.78 (C=O); EIMS (70 eV) *m/z* (relative intensity) 380 $[M+2]^+$ (12), 378 $[M]^+$ (43), 377 (16), 322 (18), 240 (17), 233 (13), 186 (34), 185 (10), 184 (100), 142 (15), 140 (50), 138 (12), 109 (11); Anal. Calcd for $C_{16}H_{25}ClNO_5P$: C, 50.87; H, 6.67; N, 3.71. Found: C, 50.72; H, 6.60; N, 3.59.



VIII-4

Diethyl [1-(*N-tert*-butoxycarbonylamino)(4′-bromobenzyl)]phosphonate (VIII-4)

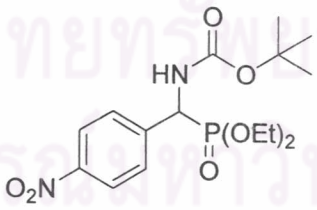
Via the general procedure of method A described above, a reaction of *tert*-butyl *N*-((benzenesulfonyl)-4-bromobenzyl)carbamate (**VI-4**) (106.5 mg, 0.25 mmol), diethyl phosphite (0.035 mL, 0.275 mmol), and DBU (0.075 mL, 0.5 mmol) gave α-aminophosphonate **VIII-4** (0.081 g, 0.19 mmol, 77%) as a white solid, mp: 112-114°C. ^{1}H NMR ($CDCl_3$, 200 MHz) δ 1.15 (t, $^{3}J_{HH}$ = 7.1 Hz, 3H, OCH_2CH_3), 1.29 (t, $^{3}J_{HH}$ = 7.1 Hz, 3H, OCH_2CH_3), 1.40 (s, 9H, $C(CH_3)_3$), 3.73-4.18 (m, 4H, OCH_2CH_3), 5.05(dd, $^{2}J_{HP}$ = 24.3 Hz, $^{3}J_{HH}$ = 9.8 Hz, 1H, CHP), 5.57 (br, 1H, NH), 7.29-7.90 (m, 4H, Ar); ^{31}P NMR ($CDCl_3$, 202.35 MHz, {^{1}H}) δ 21.78; ^{13}C NMR ($CDCl_3$, 50 MHz, {^{1}H}) δ 16.32 (OCH_2CH_3), 16.44 (OCH_2CH_3), 28.23 ($C(CH_3)_3$), 51.38 (d, $^{1}J_{CP}$ = 140.3 Hz, CHP), 63.29 (OCH_2CH_3), 80.58 ($C(CH_3)_3$), 122.04, 129.48, 131.65, 134.70, 154.78 (C=O); EIMS (70 eV) *m/z* (relative intensity) 424 $[M+2]^+$ (82), 422 $[M]^+$ (85), 421 (30), 368 (30), 367 (15), 366 (38), 350 (11), 316 (14), 289 (21), 284 (24), 230 (97), 229 (12), 228 (100), 186 (55), 185 (13), 184 (57), 83 (12); Anal. Calcd for $C_{16}H_{25}BrNO_5P$: C, 45.51; H, 5.97; N, 3.32. Found: C, 45.30; H, 5.93; N, 3.01.



VIII-5

Diethyl [1-(*N-tert*-butoxycarbonylamino)(4′-cyanobenzyl)]phosphonate (VIII-5)

A reaction of *tert*-butyl *N*-((benzenesulfonyl)-4-cyanobenzyl)carbamate (**VI-5**) (10.3 mg, 0.25 mmol), diethyl phosphite (0.035 mL, 0.275 mmol), and DBU (0.075 mL, 0.5 mmol) via method A provided α-aminophosphonate **VIII-5** as a white solid (0.082 g, 0.20 mmol, 80%), mp: 148-149°C. ^{1}H NMR ($CDCl_3$, 200 MHz) δ 1.16 (t, $^{3}J_{HH}$ = 7.1 Hz, 3H, OCH_2CH_3), 1.29 (t, $^{3}J_{HH}$ = 7.1 Hz, 3H, OCH_2CH_3), 1.41 (s, 9H, $C(CH_3)_3$), 3.76-4.17 (m, 4H, OCH_2CH_3), 5.12 (dd, $^{2}J_{HP}$ = 22.7 Hz, $^{3}J_{HH}$ = 9.3 Hz, 1H, CHP), 5.52 (br, 1H, NH), 7.20-7.70 (m, 4H, Ar); ^{31}P NMR ($CDCl_3$, 202.35 MHz, {^{1}H}) δ 20.96; ^{13}C NMR ($CDCl_3$, 125.65 MHz, {^{1}H}) δ 16.16 (d, $^{3}J_{CP}$ = 4.1 Hz, OCH_2CH_3), 16.35 (d, $^{3}J_{CP}$ = 4.1 Hz, OCH_2CH_3), 28.17 ($C(CH_3)_3$), 51.88 (d, $^{1}J_{CP}$ = 153.0 Hz, CHP), 63.42 (d, $^{2}J_{CP}$ = 6.2 Hz, OCH_2CH_3), 80.90 ($C(CH_3)_3$), 111.81, 118.54, 128.36, 128.39, 132.24, 141.21, 154.84 (d, $^{3}J_{CP}$ = 10.3 Hz, C=O); EIMS (70 eV) *m/z* (relative intensity) 369 $[MH]^+$ (100), 368 (19), 363 (10), 313 (16), 133 (11), 131 (27); Anal. Calcd for $C_{17}H_{25}N_2O_5P$: C, 55.43; H, 6.84; N, 7.60. Found: C, 55.52; H, 6.75; N, 7.52.

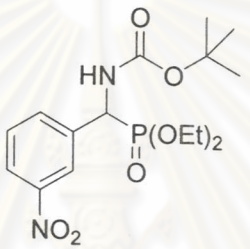


VIII-6

Diethyl [1-(*N-tert*-butoxycarbonylamino)(4′-nitrobenzyl)]phosphonate (VIII-6)

A reaction of *tert*-butyl *N*-((benzenesulfonyl) 4-nitrobenzyl)carbamate (**VI-6**) (98.0 mg, 0.25 mmol), diethyl phosphite (0.035 mL, 0.275 mmol), and DBU (0.075 mL, 0.5 mmol) via method A afforded 0.055 g of α-aminophosphonate **VIII-6** as a yellow solid (0.14 mmol, 57%), mp: 138-139°C. ^{1}H NMR ($CDCl_3$, 200 MHz) δ 1.17

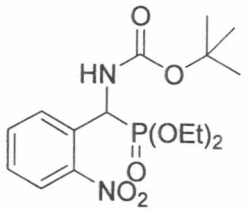
(t, $^3J_{HH}$ = 7.0 Hz, 3H, OCH_2CH_3), 1.28 (t, $^3J_{HH}$ = 7.1 Hz, 3H, OCH_2CH_3), 1.40 (s, 9H, $C(CH_3)_3$), 3.84-4.18 (m, 4H, OCH_2CH_3), 5.17 (dd, $^2J_{HP}$ = 23.6, $^3J_{HH}$ = 8.7 Hz, 1H, CHP), 5.59 (br, 1H, NH), 7.74-7.22 (m, 4H, Ar); ^{31}P NMR ($CDCl_3$, 202.35 MHz, {^{1}H}) δ 20.73; ^{13}C NMR ($CDCl_3$, 50 MHz, {^{1}H}) δ 16.30 (OCH_2CH_3), 16.42 (OCH_2CH_3), 28.19 ($C(CH_3)_3$), 51.66 (d, $^1J_{CP}$ = 166.4 Hz, CHP), 63.56 (OCH_2CH_3), 80.97 ($C(CH_3)_3$), 123.65, 128.64, 143.27, 147.52, 155.50 (C=O); EIMS (70 eV) *m/z* (relative intensity) 388 $[M]^+$ (100), 362 (18), 344 (21), 333 (57), 315 (10), 288 (16), 195 (48), 151 (40), 83 (13); Anal. Calcd for $C_{16}H_{25}N_2O_7P$: C, 49.48; H, 6.49; N, 7.21. Found: C, 49.45; H, 6.54; N, 7.21.



VIII-7

Diethyl [1-(*N-tert*-butoxycarbonylamino)(3′-nitrobenzyl)]phosphonate (VIII-7)

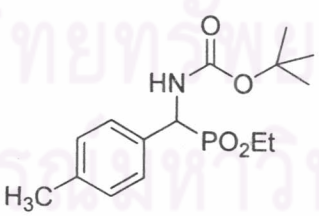
Via the general procedure of method A described above, a reaction of *tert*-butyl *N*-((benzenesulfonyl) 3-nitrobenzyl)carbamate (**VI-7**) (98.0 mg, 0.25 mmol), diethyl phosphite (0.035 mL, 0.275 mmol), and DBU (0.075 mL, 0.5 mmol) afforded α-aminophosphonate **VIII-7** as a pale yellow solid (0.055 g, 0.14 mmol, 57%), mp: 115-116°C. ^{1}H NMR ($CDCl_3$, 200 MHz) δ 1.18 (t, $^3J_{HH}$ = 6.9 Hz, 3H, OCH_2CH_3), 1.29 (t, $^3J_{HH}$ = 7.0 Hz, 3H, OCH_2CH_3), 1.41 (s, 9H, $C(CH_3)_3$), 3.81-4.18 (m, 4H, OCH_2CH_3), 5.19 (dd, $^2J_{HP}$ = 20.8 Hz, $^3J_{HH}$ = 8.4 Hz, 1H, CHP), 5.57 (br, 1H, NH), 7.48-8.24 (m, 4H, Ar); ^{13}C NMR ($CDCl_3$, 50 MHz, {^{1}H}) δ 16.32 (OCH_2CH_3), 16.43 (OCH_2CH_3), 28.21 ($C(CH_3)_3$), 51.47 (d, $^1J_{CP}$ =148.2 Hz, CHP), 63.51 (OCH_2CH_3), 81.03 ($C(CH_3)_3$), 122.42, 122.99, 129.44, 133.88, 138.15, 148.30 (C=O); EIMS (70 eV) *m/z* (relative intensity) 388 $[M]^+$ (33), 333 (44), 315 (30), 286 (17), 271 (11), 244 (13), 195 (61), 178 (25), 152 (13), 151 (100), 134 (12), 111 (15), 105 (22), 104 (22), 83 (30); Anal. Calcd for $C_{16}H_{25}N_2O_7P$: C, 49.48; H, 6.49; N, 7.21. Found: C, 49.49; H, 6.41; N, 7.18.



VIII-8

Diethyl [1-(*N-tert*-butoxycarbonylamino)(2′-nitrobenzyl)]phosphonate (VIII-8)

Via the general procedure of method A described above, a reaction of *tert*-butyl *N*-((benzenesulfonyl) 2-nitrobenzyl)carbamate **VI-8** (98.0 mg, 0.25 mmol), diethyl phosphite (0.035 mL, 0.275 mmol), and DBU (0.075 mL, 0.5 mmol) afforded α-aminophosphonate **VIII-8** (0.067 g, 0.17 mmol, 70%) as a yellow solid, mp: 105-107°C. ^{1}H NMR ($CDCl_3$, 200 MHz) δ 1.07 (t, $^{3}J_{HH}$ = 6.9 Hz, 3H, OCH_2CH_3), 1.30 (t, $^{3}J_{HH}$ = 7.3 Hz, 3H, OCH_2CH_3), 1.40 (s, 9H, $C(CH_3)_3$), 3.75-4.21 (m, 4H, OCH_2CH_3), 6.41 (dd, $^{2}J_{HP}$ = 23.8 Hz, $^{3}J_{HH}$ = 9.2 Hz, 1H, CHP), 5.77 (br, 1H, NH), 7.41-8.15 (m, 4H, Ar); ^{13}C NMR ($CDCl_3$, 50 MHz, {^{1}H}) δ 16.14 (d, $^{3}J_{CP}$ = 12.0 Hz, OCH_2CH_3), 16.32 (d, $^{3}J_{CP}$ = 5.7 Hz, OCH_2CH_3), 28.22 ($C(CH_3)_3$), 47.20 (d, $^{1}J_{CP}$ = 151.4 Hz, CHP), 63.51 (d, $^{2}J_{CP}$ = 7.3 Hz, OCH_2CH_3), 63.87 (d, $^{2}J_{CP}$ = 7.4 Hz, OCH_2CH_3), 80.85 ($C(CH_3)_3$), 125.34, 128.60, 131.76, 133.43, 154.66, 148.35 (C=O); EIMS (70 eV) *m/z* (relative intensity) 389 $[MH]^+$ (28), 388 (14), 333 (36), 315 (35), 289 (11), 287 (20), 259 (15), 214 (12), 195 (22), 151 (100), 134 (19), 105 (23), 104 (22), 83 (30); Anal. Calcd for $C_{16}H_{25}N_2O_7P$: C, 49.48; H, 6.49; N, 7.21. Found: C, 49.48; H, 6.46; N, 7.14.

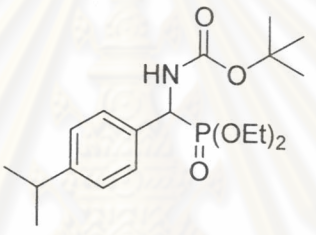


VIII-9

Diethyl [1-(*N-tert*-butoxycarbonylamino)(4′-methylbenzyl)]phosphonate (VIII-9)

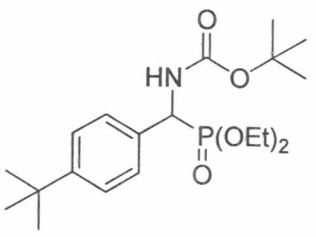
Via the general procedure of method A described above, a reaction of *tert*-butyl *N*-((benzenesulfonyl)-4-methylbenzyl)carbamate (**VI-9**) (90.3 mg, 0.25 mmol), diethyl phosphite (0.035 mL, 0.275 mmol), and DBU (0.075 mL, 0.5 mmol) obtained α-aminophosphonate **VIII-9** as a white solid (0.078 g, 0.22 mmol, 88%), mp: 85-

86°C. ^{1}H NMR ($CDCl_3$, 200 MHz) δ 1.09 (t, $^{3}J_{HH}$ = 7.1 Hz, 3H, OCH_2CH_3), 1.27 (t, $^{3}J_{HH}$ = 7.1 Hz, 3H, OCH_2CH_3), 1.38 (s, 9H, $C(CH_3)_3$), 2.29 (s, 3H, CH_3Ph), 3.65-4.16 (m, 4H, OCH_2CH_3), 5.04 (dd, $^{2}J_{HP}$ = 21.8 Hz, $^{3}J_{HH}$ = 9.3 Hz, 1H, CHP), 5.51 (br, 1H, NH), 7.09-7.28 (m, 4H, Ar); ^{31}P NMR ($CDCl_3$, 202.35 MHz, {^{1}H}) δ 22.66; ^{13}C NMR ($CDCl_3$, 50 MHz, {^{1}H}) δ 16.15 (d, $^{3}J_{CP}$ = 5.8 Hz, OCH_2CH_3), 16.37 (d, $^{3}J_{CP}$ = 5.8 Hz, OCH_2CH_3), 21.10 ($C(CH_3)_3$), 51.47 (d, $^{1}J_{CP}$ = 154.5 Hz, CHP), 63.02 (d, $^{2}J_{CP}$ = 7.8 Hz, OCH_2CH_3), 63.17 (d, $^{2}J_{CP}$ = 7.3 Hz, OCH_2CH_3), 80.19 ($C(CH_3)_3$), 127.65, 127.77, 129.22, 132.40, 137.70, 154.87 (d, $^{3}J_{CP}$ = 9.9 Hz, C=O); EIMS (70 eV) *m/z* (relative intensity) 358 $[MH]^+$ (100), 302 (22), 220 (13), 164 (58), 120 (52), 93 (16), 91 (16); Anal. Calcd for $C_{17}H_{28}NO_5P$: C, 57.13; H, 7.90; N, 3.92. Found: C, 57.42; H, 8.06; N, 4.10.



VIII-10

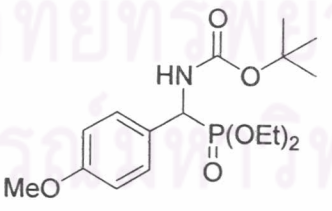
Diethyl [1-(*N*-*tert*-butoxycarbonylamino)(4′-iso-propylbenzyl)] phosphornate (VIII-10) was synthesized via the general procedure of method A described above from a reaction of *tert*-butyl *N*-((benzenesulfonyl)-4-isopropylbenzyl)carbamate (**VI-10**) (97.3 mg, 0.25 mmol), diethyl phosphite (0.035 mL, 0.275 mmol), and DBU (0.075 mL, 0.5 mmol) gave α-aminophosphonate **VIII-10** as colorless crystal (0.080 g, 0.21mmol, 84%), mp: 92-94°C. ^{1}H NMR ($CDCl_3$, 200 MHz) δ 1.07 (t, $^{3}J_{HH}$ = 6.9 Hz, 3H, OCH_2CH_3), 1.27 (t, $^{3}J_{HH}$ = 7.3 Hz, 3H, OCH_2CH_3), 1.19 (d, $^{3}J_{HH}$ = 7.2 Hz, 9H, $CH(CH_3)_2$), 2.85 (m, 1H, $CH(CH_3)_2$), 3.66-3.85 (m, 4H, OCH_2CH_3), 5.06 (dd, $^{2}J_{HP}$ = 21.2 Hz, $^{3}J_{HH}$ = 10.2 Hz, 1H, CHP), 5.51 (br, 1H, NH), 7.14-7.30 (m, 4H, Ar); ^{13}C NMR ($CDCl_3$, 50 MHz, {^{1}H}) δ 16.25 (d, $^{3}J_{CP}$ = 8.2 Hz, OCH_2CH_3), 16.38 (d, $^{3}J_{CP}$ = 5.5 Hz, OCH_2CH_3), 23.91 ($CH(CH_3)_2$), 28.25 ($C(CH_3)_3$), 33.80 ($CH(CH_3)_2$), 51.45 (d, $^{1}J_{CP}$ = 158.2 Hz, CHP), 63.09 (OCH_2CH_3), 63.23 (OCH_2CH_3), 80.22 ($C(CH_3)_3$), 126.64, 127.73, 132.64, 148.70, 154.85 (d, $^{3}J_{CP}$ = 9.6 Hz, C=O); EIMS (70 eV) *m/z* (relative intensity) 385 $[M]^+$ (57), 330 (17), 248 (13), 193 (13), 192 (100), 148 (65), 132 (11); Anal. Calcd for $C_{19}H_{32}NO_5P$: C, 59.21; H, 8.37; N, 3.63. Found: C, 59.29; H, 8.33; N, 3.61.



VIII-11

Diethyl [1-(*N-tert*-butoxycarbonylamino)(4′-*tert*-butylbenzyl)] phosphonate (VIII-11)

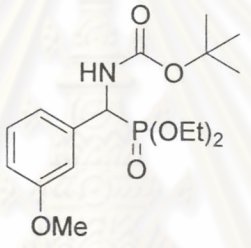
Via the general procedure of method A described above, a reaction of *tert*-butyl *N*-((benzenesulfonyl)-4-*tert*-butylbenzyl)carbamate (**VI-11**) (100.8 mg, 0.25 mmol), diethyl phosphite (0.035 mL, 0.275 mmol), and DBU (0.075 mL, 0.5 mmol) yielded 0.094 g of α-aminophosphonate **VIII-11** as a white solid (0.24 mmol, 94%), mp: 121-123°C. ^{1}H NMR ($CDCl_3$, 200 MHz) δ 1.03-1.39 (m, 24H, OCH_2CH_3, $(CH_3)_3$, $C(CH_3)_3Ar$), 3.66-4.44 (m, 4H, OCH_2CH_3,), 5.08 (dd, $^{2}J_{HP}$ = 21.3 Hz, $^{3}J_{HH}$ = 9.5 Hz, 1H, CHP), 5.53 (br, 1H, NH), 7.27-8.24 (m, 4H, Ar); ^{31}P NMR ($CDCl_3$, 202.35 MHz, {^{1}H}) δ 22.76; ^{13}C NMR ($CDCl_3$, 50 MHz, {^{1}H}) δ 16.14 (OCH_2CH_3), 16.44 (OCH_2CH_3), 28.26 ($C(CH_3)_3$), 31.28 ($C(CH_3)_3Ar$), 51.36 (d, $^{1}J_{CP}$ = 154.8 Hz, CHP), 62.97 (OCH_2CH_3), 63.12 (OCH_2CH_3), 80.19 ($C(CH_3)_3$), 125.50, 127.43, 127.54, 130.25, 151.00, 156.50 (C=O); EIMS (70 eV) *m/z* (relative intensity) 400 $[MH]^+$ (58), 344 (20), 262 (16), 207 (15), 206 (100), 162 (73), 147 (16); Anal. Calcd for $C_{20}H_{34}NO_5P$: C, 60.13; H, 8.58; N, 3.51. Found: C, 60.06; H, 8.54; N, 3.39.



VIII-12

Diethyl [1-(*N-tert*-butoxycarbonylamino)(4′-methoxybenzyl)]phosphonate (VIII-12) was synthesized via the general procedure of method A described above from a reaction of *tert*-butyl *N*-((benzenesulfonyl)-4-methoxybenzyl)carbamate (**VI-12**) (94.3 mg, 0.25 mmol), diethyl phosphite (0.035 mL, 0.275 mmol), and DBU (0.075 mL, 0.5 mmol) obtained α-aminophosphonate **VIII-12** (0.073 g, 0.20 mmol, 78%) as clear colorless crystals, mp: 85-87°C (lit.[48] : 78-80°C). ^{1}H NMR ($CDCl_3$,

200 MHz) δ 1.07 (t, $^3J_{HH}$ = 7.1 Hz, 3H, OCH_2CH_3), 1.25 (t, $^3J_{HH}$ = 7.1 Hz, 3H, OCH_2CH_3), 1.36 (s, 9H, $C(CH_3)_3$), 3.63-4.14 (m, 4H, OCH_2CH_3,), 3.77 (s, 3H, OCH_3), 5.00 (dd, $^2J_{HP}$ = 21.2 Hz, $^3J_{HH}$ = 9.7 Hz, 1H, CHP), 5.52 (br, 1H, NH), 6.75-7.34 (m, 4H, Ar); ^{31}P NMR ($CDCl_3$, 202.35 MHz, {^{1}H}) δ 22.74; ^{13}C NMR ($CDCl_3$, 50 MHz, {^{1}H}) δ 16.17 (d, $^3J_{CP}$ = 5.7 Hz, OCH_2CH_3), 16.38 (d, $^3J_{CP}$ = 5.7 Hz, OCH_2CH_3), 28.22 ($C(CH_3)_3$), 51.10 (d, $^1J_{CP}$ = 154.9 Hz, CHP), 55.20 (OCH_3), 62.96 (d, $^2J_{CP}$ = 8.7 Hz, OCH_2CH_3), 63.12 (d, $^2J_{CP}$ = 7.7 Hz, OCH_2CH_3), 80.15 ($C(CH_3)_3$), 113.94, 127.55, 128.98, 129.10, 159.33, 154.97 (C=O); EIMS (70 eV) *m/z* (relative intensity) 374 $[MH]^+$ (37), 318 (18), 317 (17), 357 (10), 181 (11), 180 (100), 162 (11), 136 (54), 134 (20), 109 (23); Anal. Calcd for $C_{17}H_{28}NO_6P$: C, 54.68; H, 7.56; N, 3.75. Found: C, 54.95; H, 7.43; N, 3.80.

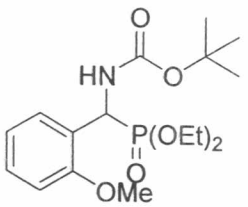


VIII-13

Diethyl [1-(*N-tert*-butoxycarbonylamino)(3′-methoxybenzyl)]phosphonate (VIII-13)

A reaction of *tert*-butyl *N*-((benzenesulfonyl)-3-methoxybenzyl)carbamate (**VI-13**) (94.3 mg, 0.25 mmol), diethyl phosphite (0.035 mL, 0.275 mmol), and DBU (0.075 mL, 0.5 mmol) via method A yielded 0.087 g of α-aminophosphonate **VIII-13** as a white solid (0.23 mmol, 93%), mp: 130-132°C. ^{1}H NMR ($CDCl_3$, 200 MHz) δ 1.12 (t, $^3J_{HH}$ = 7.1 Hz, 3H, OCH_2CH_3), 1.29 (t, $^3J_{HH}$ = 7.1 Hz, 3H, OCH_2CH_3), 1.38 (s, 9H, $C(CH_3)_3$), 3.68-4.13 (m, 4H, OCH_2CH_3), 3.79 (s, 3H, OCH_3), 5.06 (dd, $^2J_{HP}$ = 21.9 Hz, $^3J_{HH}$ = 9.5 Hz, 1H, CHP), 5.48 (br, 1H, NH), 6.79-7.28 (m, 4H, Ar); ^{31}P NMR ($CDCl_3$, 202.35 MHz, {^{1}H}) δ 22.39; ^{13}C NMR ($CDCl_3$, 50 MHz, {^{1}H}) δ 16.17 (OCH_2CH_3), 16.45 (OCH_2CH_3), 28.25 ($C(CH_3)_3$), 51.81 (d, $^1J_{CP}$ = 155.0 Hz, CHP), 55.22 (OCH_3), 63.22 (OCH_2CH_3), 80.37 ($C(CH_3)_3$), 113.35, 113.76, 120.17, 129.55, 136.92, 159.65, 155.00 (C=O); EIMS (70 eV) *m/z* (relative intensity) 373 $[M]^+$ (16), 317 (35), 316 (13), 273 (48), 272 (49), 244 (14), 180 (99), 162 (13), 136

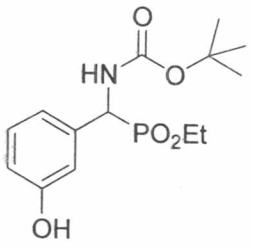
(100), 109 (41), 94 (19); Anal. Calcd for $C_{17}H_{28}NO_6P$: C, 54.48; H, 7.56; N, 3.75. Found: C, 54.49; H, 7.63; N, 3.72.



VIII-14

Diethyl [1-(*N-tert*-butoxycarbonylamino)(2′-methoxybenzyl)]phosphonate (VIII-14)

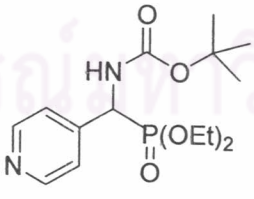
A reaction of *tert*-butyl *N*-((benzenesulfonyl)-2-methoxybenzyl)carbamate (**VI-14**) (94.3 mg, 0.25 mmol), diethyl phosphite (0.035 mL, 0.275 mmol), and DBU (0.075 mL, 0.5 mmol) affored α-aminophosphonate **VIII-14** 0.069 g as a white solid (0.19 mmol, 74%), mp: 143-145°C. ^{1}H NMR ($CDCl_3$, 200 MHz) δ 1.05 (t, $^3J_{HH}$ = 7.0 Hz, 3H, OCH_2CH_3), 1.27 (t, $^3J_{HH}$ = 7.0 Hz, 3H, OCH_2CH_3), 1.40 (s, 9H, $C(CH_3)_3$), 3.63-4.20 (m, 4H, OCH_2CH_3), 3.90 (s, 3H, OCH_3), 5.54 (d, $^3J_{HH}$ = 9.1 Hz, 1H, CHP), 5.67 (br, 1H, NH), 6.84-7.33 (m, 4H, Ar); ^{31}P NMR ($CDCl_3$, 202.35 MHz, {^{1}H}) δ 22.96; ^{13}C NMR ($CDCl_3$, 50 MHz, {^{1}H}) δ 16.11 (d, $^3J_{CP}$ = 5.9 Hz, OCH_2CH_3), 16.42 (d, $^3J_{CP}$ = 5.7 Hz, OCH_2CH_3), 28.28 ($C(CH_3)_3$), 46.44 (d, $^1J_{CP}$ = 154.8 Hz, CHP), 55.74 (OCH_3), 62.85 (d, $^2J_{CP}$ = 7.2 Hz, OCH_2CH_3), 63.00 (d, $^2J_{CP}$ = 7.0 Hz, OCH_2CH_3), 80.02 ($C(CH_3)_3$), 110.95, 120.75, 123.99, 128.82, 129.18, 157.00, 154.82 (d, $^3J_{CP}$ = 8.8 Hz, C=O); EIMS (70 eV) *m/z* (relative intensity) 373 $[M]^+$ (15), 236 (17), 180 (50), 137 (11), 136 (100), 107 (15); Anal. Calcd for $C_{17}H_{28}NO_6P$: C, 54.48; H, 7.56; N, 3.75. Found: C, 54.64; H, 7.56; N, 3.74.



VIII-15

Diethyl [1-(*N-tert*-butoxycarbonylamino)(3′-hydroxybenzyl)]phosphonate (VIII-15)

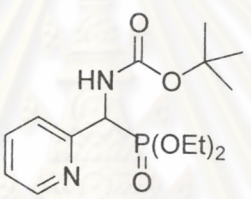
Via the general procedure of method A described above, a reaction of *tert*-butyl *N*-((benzenesulfonyl)3-hydroxybenzyl)carbamate (**VI-15**) (90.8 mg, 0.25 mmol), diethyl phosphite (0.035 mL, 0.275 mmol), and DBU (0.075 mL, 0.5 mmol) resulted in α-aminophosphonate **VIII-15** as a white solid (0.07 g, 0.19 mmol, 77%), mp: 131-132°C. ^{1}H NMR ($CDCl_3$, 200 MHz) δ 1.11 (t, $^{3}J_{HH}$ = 7.0 Hz, 3H, OCH_2CH_3), 1.29 (t, $^{3}J_{HH}$ = 7.1 Hz, 3H, OCH_2CH_3), 1.40 (s, 9H, $C(CH_3)_3$), 3.69-4.19 (m, 4H, OCH_2CH_3), 5.07 (dd, $^{2}J_{HP}$ = 21.1 Hz, $^{3}J_{HH}$ = 9.72 Hz, 1H, CHP), 5.56 (d, $^{3}J_{HH}$ = 6.4 Hz, 1H, NH), 6.74-7.24 (m, 4H, Ar), 8.20 (s, 1H, OH); ^{31}P NMR ($CDCl_3$, 202.35 MHz, {^{1}H}) δ 22.66; ^{13}C NMR ($CDCl_3$, 50 MHz) δ 16.16 (OCH_2CH_3), 16.30 (OCH_2CH_3), 28.26 ($C(CH_3)_3$), 53.12 (CHP), 63.42 (OCH_2CH_3), 63.69 (OCH_2CH_3), 80.51 ($C(CH_3)_3$), 114.71, 115.77, 119.57, 129.73, 136.14, 157.17, 155.07, (C=O); EIMS (70 eV) *m/z* (relative intensity) 359 $[M]^+$ (96), 304 (61), 303 (34), 302 (11), 286 (12), 260 (15), 259 (73), 258 (68), 230 (16), 215 (14), 202 (11), 166 (94), 148 (16), 139 (14), 122 (100), 121 (13), 120 (15), 95 (30), 83 (15), 77 (20); Anal. Calcd for $C_{16}H_{26}NO_6P$: C, 53.48; H, 7.29; N, 3.90. Found: C, 53.31; H, 7.15; N, 3.67.



VIII-16

Diethyl [1-(*N-tert*-butoxycarbonylamino)(4-pyridylbenzyl)]phosphonate (VIII-16) was synthesized via the general procedure of method A described above from a reaction of *tert*-butyl *N*-((benzenesulfonyl)-4-pyridylbenzyl)carbamate (**VI-16**) (87.1 mg, 0.25 mmol), diethyl phosphite (0.035 mL, 0.275 mmol), and DBU (0.075 mL, 0.5 mmol) provided α-aminophosphonate **VIII-16** as a white yellow solid (0.068

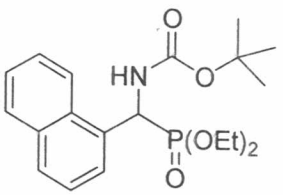
g, 0.20 mmol, 79%), mp: 107-108°C. ^{1}H NMR ($CDCl_3$, 200 MHz) δ 1.17 (t, $^3J_{HH}$ = 7.1 Hz, 3H, OCH_2CH_3), 1.26 (t, $^3J_{HH}$ = 7.1 Hz, 3H, OCH_2CH_3), 1.40 (s, 9H, $C(CH_3)_3$), 3.77-4.16 (m, 4H, OCH_2CH_3), 5.08 (dd, $^2J_{HP}$ = 22.9 Hz, $^3J_{HH}$ = 9.0 Hz, 1H, CHP), 5.64 (br, 1H, NH), 7.20-8.57 (m, 4H, Ar); ^{31}P NMR ($CDCl_3$, 202.35 MHz, {^{1}H}) δ 19.94; ^{13}C NMR ($CDCl_3$, 50 MHz, {^{1}H}) δ 16.20 (d, $^3J_{CP}$ = 8.7 Hz, OCH_2CH_3), 16.34 (d, $^3J_{CP}$ = 6.0 Hz, OCH_2CH_3), 28.20 ($C(CH_3)_3$), 51.31 (d, $^1J_{CP}$ = 149.2 Hz, CHP), 63.40 (OCH_2CH_3), 63.54 (OCH_2CH_3), 80.89 ($C(CH_3)_3$), 122.49, 144.90, 149.77, 156.0 (C=O); EIMS (70 eV) *m/z* (relative intensity) 345 $[MH]^+$ (100), 344 (18), 289 (18), 288 (29), 271 (26), 244 (60), 243 (15), 215 (16), 151 (46), 107 (68), 83 (24), 80 (21); Anal. Calcd for $C_{15}H_{25}N_2O_5P$: C, 52.32; H, 7.32; N, 8.14. Found: C, 52.31; H, 7.33; N, 8.24.



VIII-17

Diethyl [1-(*N-tert*-butoxycarbonylamino)(2-pyridylbenzyl)]phosphonate (VIII-17) was synthesized via the general procedure of method A described above, a reaction of *tert*-butyl *N*-((benzenesulfonyl)-2-pyridylbenzyl)carbamate (**VI-17**) (87.1 mg, 0.25 mmol), diethyl phosphite (0.035 mL, 0.275 mmol), and DBU (0.075 mL, 0.5 mmol) affored α-aminophosphonate **VIII-17** as a pale yellow solid (0.074 g, 0.22 mmol, 86%), mp: 103-104°C. ^{1}H NMR ($CDCl_3$, 200 MHz) δ 1.18 (t, $^3J_{HH}$ = 7.0 Hz, 3H, OCH_2CH_3), 1.19 (t, $^3J_{HH}$ = 7.0 Hz, 3H, OCH_2CH_3), 1.39 (s, 9H, $C(CH_3)_3$), 3.87-4.11 (m, 4H, OCH_2CH_3), 5.27 (dd, $^2J_{HP}$ = 19.9 Hz, $^3J_{HH}$ = 9.2 Hz, 1H, CHP), 6.17 (d, $^3J_{HH}$ = 9.2 Hz, 1H, NH), 7.14-8.53 (m, 4H, Ar); ^{31}P NMR ($CDCl_3$, 202.35 MHz, {^{1}H}) δ 20.86; ^{13}C NMR ($CDCl_3$, 50 MHz, {^{1}H}) δ 16.20 (d, $^3J_{CP}$ = 6.2 Hz, OCH_2CH_3), 16.31 (d, $^3J_{CP}$ = 5.4 Hz, OCH_2CH_3), 28.23 ($C(CH_3)_3$), 53.00 (d, $^1J_{CP}$ = 151.2 Hz, CHP), 63.01 (d, $^2J_{CP}$ = 6.5 Hz, OCH_2CH_3), 63.35 (d, $^2J_{CP}$ = 7.0 Hz, OCH_2CH_3), 80.10 ($C(CH_3)_3$), 122.81, 123.39, 136.50, 149.07, 153.63, 155.15 (C=O); EIMS (70 eV) *m/z* (relative intensity) 345 $[MH]^+$ (60), 289 (17), 271 (32), 245 (13), 244 (61), 243 (22), 215 (18), 151 (85), 133 (70), 108 (14), 107 (100), 106 (11), 105

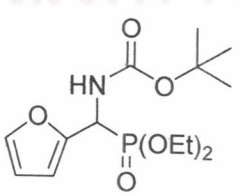
(27), 80 (20), 79 (18), 78 (14); Anal. Calcd for $C_{15}H_{25}N_2O_5P$: C, 52.32; H, 7.32; N, 8.14. Found: C, 52.32; H, 7.38; N, 8.17.



VIII-18

Diethyl [1-(*N-tert*-butoxycarbonylamino)(1-naphthylbenzyl)] phosphonate (VIII-18)

Via the general procedure of method A described above, a reaction of *tert*-butyl *N*-((benzenesulfonyl)-1-naphthylbenzyl)carbamate (**VI-18**) (99.3 mg, 0.25 mmol), diethyl phosphite (0.035 mL, 0.275 mmol), and DBU (0.075 mL, 0.5 mmol) resulted in α-aminophosphonate **VIII-18** 0.086 g as a white solid (0.22 mmol, 87%), mp: 126-127°C. ^{1}H NMR ($CDCl_3$, 200 MHz) δ 0.79 (t, $^3J_{HH}$ = 7.1 Hz, 3H, OCH_2CH_3), 1.27-1.35 (m, 12H, $C(CH_3)_3$, OCH_2CH_3), 3.36-4.27 (m, 4H, OCH_2CH_3), 5.71 (br, 1H, N*H*), 6.00 (dd, $^2J_{HP}$ = 21.8 Hz, $^3J_{HH}$ = 9.7 Hz, 1H, C*H*P), 7.42-8.22 (m, 7H, Ar); ^{31}P NMR ($CDCl_3$, 202.35 MHz, {^{1}H}) δ 22.85; ^{13}C NMR ($CDCl_3$, 50 MHz, {^{1}H}) δ 15.88 (d, $^3J_{CP}$ = 5.6Hz, OCH_2CH_3), 16.24 (OCH_2CH_3), 28.26 ($C(CH_3)_3$), 47.30 (d, $^1J_{CP}$ = 155.4 Hz, *C*HP), 63.21 (OCH_2CH_3), 80.36 ($C(CH_3)_3$), 123.40, 125.27, 125.86, 126.57, 128.74, 131.31, 131.99, 133.76, 154.95 (*C*=O); EIMS (70 eV) *m/z* (relative intensity) 394 $[MH]^+$ (40), 393 (26), 338 (19), 337 (12), 293 (25), 256 (11), 201 (14), 200 (100), 182 (12), 157 (14), 156 (73), 155 (12), 154 (42), 129 (40), 128 (16), 127 (17); Anal. Calcd for $C_{20}H_{28}NO_5P$: C, 61.06; H, 7.17; N, 3.56. Found: C, 61.11; H, 7.16; N, 3.53.

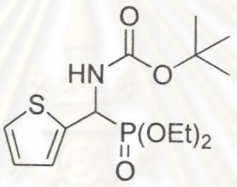


VIII-19

Diethyl [1-(*N-tert*-butoxycarbonylamino)(2-furyl)]phosphonate (VIII-19)

A reaction of *tert*-butyl *N*-((benzenesulfonyl)-2-furyl)carbamate (**VI-19**) (90.0 mg, 0.25 mmol), diethyl phosphite (0.035 mL, 0.275 mmol), and DBU (0.075 mL, 0.5

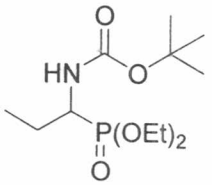
mmol) resulted in α-aminophosphonate **VIII-19** 0.069 g as a pale yellow solid (0.205 mmol, 82%), mp: 94-95°C. ^{1}H NMR ($CDCl_3$, 200 MHz) δ 1.19 (t, $^3J_{HH}$ = 7.0 Hz, 3H, OCH_2CH_3), 1.30 (t, $^3J_{HH}$ = 7.0 Hz, 3H, OCH_2CH_3), 1.41 (s, 9H, $C(CH_3)_3$), 3.82-4.20 (m, 5H, OCH_2CH_3, CHP), 5.30 (br, 1H, NH), 6.31-6.39 (m, 2H, furyl C_3H, C_4H), 7.37 (d, 1H, furyl C_5H); ^{13}C NMR ($CDCl_3$, 50 MHz, {^{1}H}) δ 16.36 (OCH_2CH_3), 28.24 ($C(CH_3)_3$), 46.02 (d, $^1J_{CP}$ = 156.1 Hz, CHP), 63.23 (OCH_2CH_3), 63.36 (OCH_2CH_3), 80.54 ($C(CH_3)_3$), 108.67, 110.70, 142.66, 148.30 (furyl CH), 155.50, (C=O); EIMS (70 eV) *m/z* (relative intensity) 334 $[MH]^+$ (37), 278 (26), 277 (80), 233 (77), 217 (15), 204 (63), 176 (29), 140 (65), 107 (11), 96 (100), 94 (14), 83 (15), 69 (28); Anal. Calcd for $C_{14}H_{24}NO_6P$: C, 50.45; H, 7.26; N, 4.20. Found: C, 50.45; H, 7.05; N, 4.16.



VIII-20

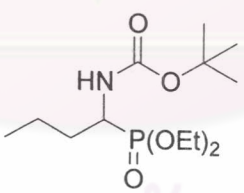
Diethyl [1-(*N*-*tert*-butoxycarbonylamino)(2-thienyl)]phosphonate (VIII-20)

A reaction of *tert*-butyl *N*-((benzenesulfonyl)-2-thienyl)carbamate (**VI-20**) (88.0 mg, 0.25 mmol), diethyl phosphite (0.035 mL, 0.275 mmol), and DBU (0.075 mL, 0.5 mmol) via method A yielded α-aminophosphonate **VIII-14** as a colorless solid (0.051 g, 0.15 mmol, 59%), mp: 104-106°C. ^{1}H NMR ($CDCl_3$, 200 MHz) δ 1.14 (t, $^3J_{HH}$ = 7.4 Hz, 3H, OCH_2CH_3), 1.24 (t, $^3J_{HH}$ = 7.3 Hz, 3H, OCH_2CH_3), 1.37 (s, 9H, $C(CH_3)_3$), 3.76-4.17 (m, 5H, OCH_2CH_3, CHP), 5.28 (br, 1H, NH), 6.89-6.93 (m, 2H, thienyl C_3H, C_4H), 7.16-7.20 (m, 1H, thienyl C_5H); ^{13}C NMR ($CDCl_3$, 50 MHz, {^{1}H}) δ 16.34 (OCH_2CH_3), 16.46 (OCH_2CH_3), 28.24 ($C(CH_3)_3$), 47.42 (d, $^1J_{CP}$ = 164.3 Hz, CHP), 63.35 (OCH_2CH_3), 63.48 (OCH_2CH_3), 80.58 ($C(CH_3)_3$), 125.37, 126.61, 127.08, 138.02 (thienyl CH), 154.59 (C=O); EIMS (70 eV) *m/z* (relative intensity) 350 $[MH]^+$ (80), 349 (44), 294 (63), 293 (82), 249 (64), 248 (11), 233 (22), 220 (67), 205 (10), 192 (18), 156 (100), 139 (12), 138 (23), 123 (22), 112 (76), 111 (11), 110 (30), 85 (35), 83 (17); Anal. Calcd for $C_{14}H_{24}NO_5SP$: C, 48.13; H, 6.92; N, 4.01. Found: C, 48.26; H, 7.32; N, 3.97.



VIII-21

Diethyl [1-(*N-tert*-butoxycarbonylamino)(propyl)]phosphonate (VIII-21) was synthesized via the general procedure of method B described earlier from a reaction of *tert*-butyl *N*-((benzenesulfonyl)propyl)carbamate (**VI-21**) (74.8 mg, 0.25 mmol), diethyl phosphite (0.035 mL, 0.275 mmol), and K_2CO_3 (0.069 mg, 0.5 mmol) in CH_3CN (2 mL) resulted in α-aminophosphonate **VIII-21** as colorless oil (0.0417 g, 0.135 mmol, 54%). ^{1}H NMR ($CDCl_3$, 200 MHz) δ 0.96 (t, $^3J_{HH}$ = 7.4 Hz, 3H, C*H*$_3$), 1.27 (t, $^3J_{HH}$ = 7.1 Hz, 6H, OCH$_2$C*H*$_3$), 1.44 (s, 9H, (C*H*$_3$)$_3$), 4.00-4.15 (m, 5H, OC*H*$_2$CH$_3$, C*H*P), 4.75 (d, $^3J_{HH}$ = 10.5 Hz, 1H, N*H*); ^{13}C NMR ($CDCl_3$, 50 MHz, {^{1}H}) δ 10.31 (*C*H$_3$), 16.39 (OCH$_2$*C*H$_3$), 23.33 (*C*H$_2$), 28.25 (C(*C*H$_3$)$_3$), 48.20 (d, $^1J_{CP}$ = 154.3 Hz, *C*HP), 62.44 (O*C*H$_2$CH$_3$), 62.58 (O*C*H$_2$CH$_3$), 79.84 (*C*(CH$_3$)$_3$), 155.43 (*C*=O); EIMS (70 eV) *m/z* (relative intensity) 296 [MH]$^+$ (100), 295 (11), 240 (21), 222 (12), 197 (10), 102 (13), 83 (23), 58 (15); Anal. Calcd for $C_{12}H_{26}NO_5P$: C, 48.81; H, 8.87; N, 4.74. Found: C, 49.29; H, 8.88; N, 4.78.

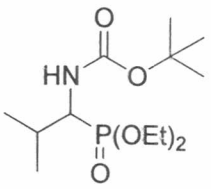


VIII-22

Diethyl [1-(*N-tert*-butoxycarbonylamino)(butyl)]phosphonate (VIII-22)

Via the general procedure of method B described earlier, a reaction of *tert*-butyl *N*-((benzenesulfonyl)butyl)carbamate (**VI-22**) (78.4 mg, 0.25 mmol), diethyl phosphite (0.035 mL, 0.275 mmol), and K_2CO_3 (0.069 mg, 0.5 mmol) in CH_3CN (2 mL) provided α-aminophosphonate **VIII-22** as colorless oil (0.050 g, 0.16 mmol, 65%). ^{1}H NMR ($CDCl_3$, 200 MHz) δ 0.91 (t, $^3J_{HH}$ = 7.2 Hz, 3H, C*H*$_3$), 1.30 (t, $^3J_{HH}$ = 7.1 Hz, 6H, OCH$_2$C*H*$_3$), 1.37-1.74 (m, 13H, (C*H*$_3$)$_3$, (C*H*$_2$)$_2$), 3.96-4.18 (m, 5H, OC*H*$_2$CH$_3$, C*H*P), 4.63 (d, $^3J_{HH}$ = 10.5 Hz, 1H, N*H*); ^{13}C NMR ($CDCl_3$, 50 MHz, {^{1}H}) δ 13.57 (*C*H$_3$), 16.37 (*C*H$_2$), 19.02 (d, $^3J_{CP}$ = 12.9 Hz, OCH$_2$*C*H$_3$), 28.23 (C(*C*H$_3$)$_3$), 31.91 (*C*H$_2$), 46.54 (d, $^1J_{CP}$ = 154.6 Hz, *C*HP), 62.32 (O*C*H$_2$CH$_3$), 62.59

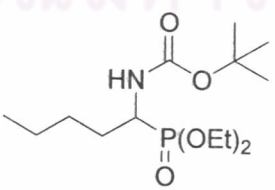
(OCH_2CH_3), 79.79 ($C(CH_3)_3$), 155.31 (C=O); EIMS (70 eV) *m/z* (relative intensity) 310 $[MH]^+$ (100), 254 (22), 236 (17), 208 (11), 116 (21), 111 (11), 83 (26).



VIII-23

Diethyl [1-(*N-tert*-butoxycarbonylamino)(*iso*-butyl)]phosphonate (VIII-23)

A reaction of *tert*-butyl *N*-((benzenesulfonyl)iso-butyl)carbamate (**VI-23**) (78.4 mg, 0.25 mmol), diethyl phosphite (0.035 mL, 0.275 mmol), and K_2CO_3 (0.069 mg, 0.5 mmol) in CH_3CN (2 mL) via method B resulted in 0.069g of α-aminophosphonate **VIII-23** (0.20 mmol, 80%) as colorless crystals, mp: 52-54°C (lit.[48] : 52-55°C). ^{1}H NMR ($CDCl_3$, 200 MHz) δ 0.94 (d, $^3J_{HH}$ = 7.4 Hz, 3H, $CH(CH_3)_2$), 0.95 (d, $^3J_{HH}$ = 7.4 Hz, 3H, $CH(CH_3)_2$), 1.26 (t, $^3J_{HH}$ = 7.0 Hz, 6H, $(OCH_2CH_3)_2$), 1.39 (s, 9H, $C(CH_3)_3$), 2.05-2.19 (m, 1H, $CH(CH_3)_2$), 3.82-4.14 (m, 5H, CHP, $(OCH_2CH_3)_2$), 4.80 (d, $^3J_{HH}$ = 9.6 Hz, 1H, NH); ^{31}P NMR ($CDCl_3$, 202.23 MHz, {^{1}H}) δ 25.40; ^{13}C NMR ($CDCl_3$, 50 MHz, {^{1}H}) δ 16.38 (d, $^3J_{CP}$ = 5.4 Hz, OCH_2CH_3), 16.43 (d, $^3J_{CP}$ = 5.3 Hz, OCH_2CH_3), 20.53 ($CH(CH_3)_2$), 28.25 ($C(CH_3)_3$), 28.92 (d, $^2J_{CP}$ = 4.8 Hz, $CH(CH_3)_2$), 51.69 (d, $^1J_{CP}$ = 151.6 Hz, CHP), 62.18 (d, $^2J_{CP}$ = 7.0 Hz, OCH_2CH_3), 62.32 (d, $^2J_{CP}$ = 7.7 Hz, OCH_2CH_3), 79.88 ($C(CH_3)_3$), 155.66 (d, $^3J_{CP}$ = 6.6 Hz, C=O); EIMS (70 eV) *m/z* (relative intensity) 310 $[MH]^+$ (100), 254 (18), 116 (16), 83 (12); Anal. Calcd for $C_{13}H_{28}NO_5P$: C, 50.48; H, 9.12; N, 4.53. Found: C, 50.89; H, 9.18; N, 4.52.

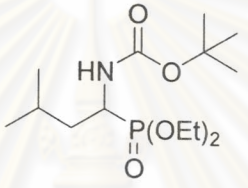


VIII-24

Diethyl [1-(*N-tert*-butoxycarbonylamino)(butyl)]phosphonate (VIII-24)

A reaction of *tert*-butyl *N*-((benzenesulfonyl)butyl)carbamate (**VI-24**) (81.9 mg, 0.25 mmol), diethyl phosphite (0.035 mL, 0.275 mmol), and K_2CO_3 (0.069 mg,

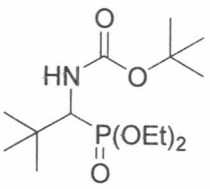
0.5 mmol) in CH_3CN (2 mL) via method B gave α-aminophosphonate **VIII-24** (0.0475 g, 0.147 mmol, 59%) as colorless oil. ^1H NMR ($CDCl_3$, 200 MHz) δ 0.80-1.39 (m, 13H, OCH_2CH_3, CH_2, CH_3), 1.42 (s, 9H, $C(CH_3)_3$), 1.76-1.98 (m, 1H CH_2), 3.90-4.15 (m, 5H, CHP, OCH_2CH_3), 4.71 (d, $^3J_{HH}$ = 10.4 Hz, NH); ^{13}C NMR ($CDCl_3$, 50 MHz, {^1H}) δ 13.85 (CH_3), 16.37 (OCH_2CH_3), 22.20 (CH_2), 27.73 (CH_2), 28.24 ($C(CH_3)_3$), 29.59 (CH_2), 46.76 (d, $^1J_{CP}$ = 154.6 Hz, CHP), 79.80 ($C(CH_3)_3$), 155.33 (C=O); EIMS (70 eV) *m/z* (relative intensity) 324 $[M]^+$ (100), 323 (12), 268 (25), 267 (36), 250 (43), 224 (14), 222 (21), 194 (13), 130 (44), 111 (22), 86 (11), 83 (35), 74 (14).



VIII-25

Diethyl [1-(*N*-*tert*-butoxycarbonylamino)(*tert*-pentyl)]phosphonate (VIII-25)

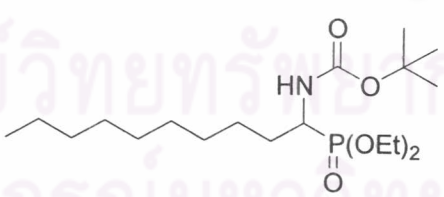
Via the general procedure of method B described earlier, a reaction of *tert*-butyl *N*-((benzenesulfonyl)*tert*-pentyl)carbamate (**VI-25**) (81.9 mg, 0.25 mmol), diethyl phosphite (0.035 mL, 0.275 mmol), and K_2CO_3 (0.069 mg, 0.5 mmol) in CH_3CN (2 mL) yielded α-aminophosphonate **VIII-25** (0.0544 g, 0.17 mmol, 68%) as colorless crystals, mp: 64-65°C. ^1H NMR ($CDCl_3$, 200 MHz) δ 0.89 (d, $^3J_{HH}$ = 6.4 Hz, 3H, CH_3), 0.90 (d, $^3J_{HH}$ = 6.6 Hz, 3H, CH_3), 1.20- 1.89 (m, 7H, OCH_2CH_3, $CH(CH_3)_2$), 1.40 (s, 9H, $C(CH_3)_3$), 3.96-4.21 (m, 5H, CHP, OCH_2CH_3), 4.56 (d, $^3J_{HH}$ = 10.4 Hz, NH); ^{13}C NMR ($CDCl_3$, 50 MHz, {^1H}) δ 16.40 (OCH_2CH_3), 21.13, (CH_3), 23.33 (CH_3), 24.58 ($CH(CH_3)_2$), 28.25 ($C(CH_3)_3$), 38.60 (CH_2), 45.10 (d, $^1J_{CP}$ = 154.7 Hz, CHP), 79.79 ($C(CH_3)_3$), 155.14 (C=O); EIMS (70 eV) *m/z* (relative intensity) 324 $[MH]^+$ (100), 268 (20), 267 (18), 250 (37), 224 (12), 222 (19), 130 (35), 112 (14), 111 (13), 83 (34), 74 (13).



VIII-26

Diethyl [1-(*N-tert*-butoxycarbonylamino)(*tert*-butyl)]phosphonate (VIII-26)

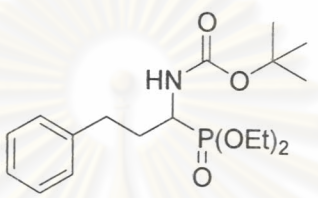
Via the general procedure of method B described earlier, a reaction of *tert*-butyl *N*-((benzenesulfonyl)*tert*-butyl)carbamate (**VI-26**) (82.0 mg, 0.25 mmol), diethyl phosphite (0.035 mL, 0.275 mmol), and K_2CO_3 (0.069 mg, 0.5 mmol) in CH_3CN (2 mL) resulted in 0.063 g of α-aminophosphonate **VIII-26** (0.19 mmol, 70%) as colorless crystals, mp: 69-70°C. ^{1}H NMR ($CDCl_3$, 200 MHz) δ 1.05 (s, 9H, $(CH_3)_3$), 1.29 (t, $^3J_{HH}$ = 7.1 Hz, 3H, OCH_2CH_3), 1.47 (s, 9H, $(CH_3)_3$), 3.81 (dd, $^2J_{HP}$ = 19.1 Hz, $^3J_{HH}$ = 10.9 Hz, 1H, C*H*P), 4.01-4.17 (m, 4H, OCH_2CH_3), 4.87 (d, $^3J_{HH}$ = 9.5 Hz, N*H*); ^{13}C NMR ($CDCl_3$, 50 MHz, {^{1}H}) δ 16.26 (d, $^3J_{CP}$ = 6.5 Hz, OCH_2CH_3), 16.39 (d, $^3J_{CP}$ = 6.0 Hz, OCH_2CH_3), 27.24, 28.25 ($C(CH_3)_3$), 34.50 (d, $^2J_{CP}$ = 5.8 Hz, $C(CH_3)_3$), 55.51 (d, $^1J_{CP}$ = 147.8 Hz, *C*HP), 62.00 (d, $^2J_{CP}$ = 6.5 Hz, OCH_2CH_3), 62.14 (d, $^2J_{CP}$ = 7.1 Hz, OCH_2CH_3), 79.78 ($C(CH_3)_3$), 155.53 (d, $^3J_{CP}$ = 6.0 Hz, *C*=O); EIMS (70 eV) *m/z* (relative intensity) 324 $[MH]^+$ (8), 268 (12), 250 (13), 211 (45), 130 (34), 112 (16), 111 (11), 83 (12); Anal. Calcd for $C_{14}H_{30}NO_5P$: C, 52.00; H, 9.35; N, 4.33. Found: C, 52.09; H, 9.34; N, 4.31.



VIII-27

Diethyl [1-(*N-tert*-butoxycarbonylamino)(decyl)]phosphonate (VIII-27) was synthesized via the general procedure of method B described earlier from a reaction of *tert*-butyl *N*-((benzenesulfonyl)decyl)carbamate (**VI-27**) (99.4 mg, 0.25 mmol), diethyl phosphite (0.035 mL, 0.275 mmol), and K_2CO_3 (0.069 mg, 0.5 mmol) in CH_3CN (2 mL) afforded 0.060 g of α-aminophosphonate **VIII-27** (0.15 mmol, 62%) as colorless oil. ^{1}H NMR ($CDCl_3$, 200 MHz) δ 0.80-1.75 (m, 34H, OCH_2CH_3, $(CH_3)_3$, CH_3, $(CH_2)_8$), 3.87-4.16 (m, 5H, C*H*P, OCH_2CH_3), 4.65 (d, $^3J_{HH}$ = 10.2 Hz,

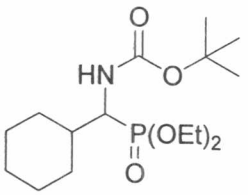
1H, N*H*); ^{13}C NMR ($CDCl_3$, 50 MHz, {^{1}H}) δ 14.09 (*C*H_3), 16.39 (OCH$_2$*C*H$_3$), 22.63, 25.60, 25.85, 29.09, 29.25, 29.44, 29.89, 31.84 (*C*H$_2$), 28.25 (C(*C*H$_3$)$_3$), 46.77 (d, $^1J_{CP}$ = 154.1 Hz, *C*HP), 62.44 (O*C*H$_2$CH$_3$), 62.58 (O*C*H$_2$CH$_3$), 79.81 (*C*(CH$_3$)$_3$), 155.32 (*C*=O); EIMS (70 eV) *m/z* (relative intensity) 394 [MH]$^+$ (60), 393 (60), 338 (45), 337 (62), 320 (46), 292 (34), 264 (28), 224 (11), 211 (20), 201 (16), 200 (100), 156 (95), 139 (15), 138 (13), 111 (19), 83 (75), 81 (13), 65 (16), 55 (16); Anal. Calcd for $C_{18}H_{30}NO_5P$: C, 57.99; H, 10.25; N, 3.56. Found: C, 58.35; H, 10.99; N, 3.46.



VIII-29

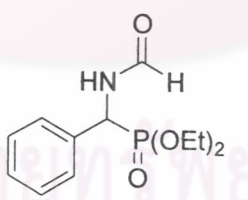
Diethyl [1-(*N-tert*-butoxycarbonylamino)(3-phenylpropyl)]phosphonate (VIII-29)

Via the general procedure of method B described earlier, a reaction of *tert*-butyl *N*-((benzenesulfonyl)3-phenylpropyl)carbamate (**VI-29**) (93.8 mg, 0.25 mmol), diethyl phosphite (0.035 mL, 0.275 mmol), and K_2CO_3 (0.069 mg, 0.5 mmol) in CH_3CN (2 mL) resulted in α-aminophosphonate **VIII-29** (0.0464 g, 0.125 mmol, 50%) as colorless oil. ^{1}H NMR ($CDCl_3$, 200 MHz) δ 1.26 (t, $^3J_{HH}$ = 7.1 Hz, OCH$_2$C*H*$_3$), 1.27 (t, $^3J_{HH}$ = 7.1 Hz, OCH$_2$C*H*$_3$), 1.43 (s, 9H, C(C*H*$_3$)$_3$), 1.80-2.13 (m, 2H, C*H*$_2$Ph), 2.59-2.79 (m, 2H, C*H*$_2$CH$_2$Ph), 3.95-4.16 (m, 5H, C*H*P, OC*H*$_2$CH$_3$), 4.81 (d, $^3J_{HH}$ = 10.3 Hz, 1H, N*H*), 7.11-7.28 (m, 5H, Ar); ^{13}C NMR ($CDCl_3$, 50 MHz, {^{1}H}) δ 16.40 (OCH$_2$*C*H$_3$), 28.28 (C(*C*H$_3$)$_3$), 31.90 (*C*H$_2$), 46.57 (d, $^1J_{CP}$ = 154.7 Hz, *C*HP), 62.48 (O*C*H$_2$CH$_3$), 62.45 (O*C*H$_2$CH$_3$), 79.98 (*C*(CH$_3$)$_3$), 126.05, 128.44, 140.99, 155.28 (*C*=O); EIMS (70 eV) *m/z* (relative intensity) 372 [MH]$^+$ (49), 371 (12), 316 (19), 315 (35), 298 (11), 211 (100), 160 (14), 134 (15), 132 (10), 117 (61), 115 (19), 91 (22), 83 (11).



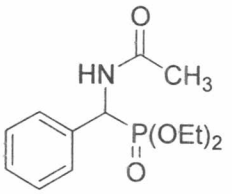
VIII-30

Diethyl [1-(*N*-*tert*-butoxycarbonylamino)(cyclohexyl)]phosphonate (VIII-30) was synthesized via the general procedure of method B described earlier from a reaction of *tert*-butyl *N*-((benzenesulfonyl)cyclohexyl)carbamate (**VI-30**) (88.3 mg, 0.25 mmol), diethyl phosphite (0.035 mL, 0.275 mmol), and K_2CO_3 (0.069 mg, 0.5 mmol) in CH_3CN (2 mL) gave α-aminophosphonate **VIII-30** (0.0759 g, 0.22 mmol, 87%) as colorless crystals, mp: 73-74°C. ^{1}H NMR ($CDCl_3$, 200 MHz) δ 1.00-1.90 (m, 26H, C*H*$_2$, C*H*, OCH$_2$C*H*$_3$, C(C*H*$_3$)$_3$), 3.90 (dt, $^2J_{HP}$ = 8.1 Hz, $^3J_{HH}$ = 4.0 Hz, 1H, C*H*P), 3.99-4.17 (m, 4H, OC*H*$_2$CH$_3$), 4.78 (d, $^3J_{HH}$ = 12.0 Hz, N*H*); ^{13}C NMR ($CDCl_3$, 50 MHz, {^{1}H}) δ 16.36 (OCH$_2$*C*H$_3$), 25.88, 26.00, 27.98, 30.40, 30.63 (*C*H$_2$), 28.25 (C(*C*H$_3$)$_3$), 38.61 (*C*H), 51.59 (d, $^1J_{CP}$ = 151.1 Hz, *C*HP), 79.79 (*C*(CH$_3$)$_3$), 155.48 (*C*=O); EIMS (70 eV) *m/z* (relative intensity) 350 [MH]$^+$ (63), 294 (18), 276 (24), 248 (12), 212 (12), 211 (13), 156 (100), 138 (17), 112 (21), 111 (11), 95 (78), 93 (11), 83 (25), 67 (28), 65 (13); Anal. Calcd for $C_{16}H_{32}NO_5P$: C, 55.00; H, 9.23; N, 4.01. Found: C, 55.26; H, 9.31; N, 4.04.



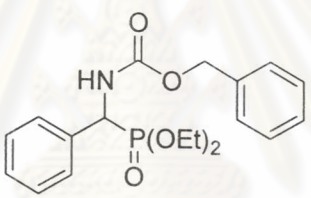
IX-1

Diethyl [1-*N*-formylaminobenzyl]phosphonate (IX-1) was synthesized via the general procedure of method A described above from a reaction of *N*-(benzenesulfonyl)formamide (**VII-1**) (46.0 mg, 0.167 mmol), diethyl phosphite (0.024 mL, 0.184 mmol), and DBU (0.05 mL, 0.334 mmol) gave 0.027 g of α-aminophosphonate **IX-1** as colorless oil (0.099 mmol, 60%). ^{1}H NMR ($CDCl_3$, 200 MHz) δ 1.05 (t, $^3J_{HH}$ = 7.1 Hz, 3H, OCH$_2$C*H*$_3$), 1.32 (t, $^3J_{HH}$ = 7.1 Hz, 3H, OCH$_2$C*H*$_3$), 3.58-4.18 (m, 4H, OC*H*$_2$CH$_3$), 5.57 (dd, $^2J_{HP}$ = 20.7 Hz, $^3J_{HH}$ = 9.7 Hz, 1H, C*H*P), 7.28-7.49 (m, 5H, Ar), 7.62 (br, 1H, N*H*), 8.22 (s, 1H C*H*O).



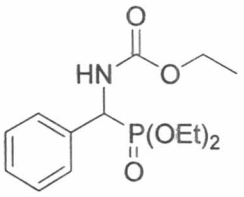
IX-2

Diethyl [1-*N*-acetylaminobenzyl]phosphonate (IX-2) was synthesized via the general procedure of method A described above from a reaction of *N*-(benzenesulfonyl)acetamide (**VII-2**) (72.0 mg, 0.25 mmol), diethyl phosphite (0.035 mL, 0.275 mmol), and DBU (0.075 mL, 0.5 mmol) gave 0.035 g of α-aminophosphonate **IX-2** as a white solid (0.125 mmol, 50%). ^{1}H NMR ($CDCl_3$, 200 MHz) δ 1.04 (t, $^{3}J_{HH}$ = 7.0 Hz, 3H, OCH_2CH_3), 1.32 (t, $^{3}J_{HH}$ = 7.1 Hz, 3H, OCH_2CH_3), 1.99 (s, 3H, CH_3), 3.65-4.18 (m, 4H, OCH_2CH_3), 5.52 (dd, $^{2}J_{HP}$ = 21.0 Hz, $^{3}J_{HH}$ = 9.9 Hz, 1H, CHP), 7.28-7.48 (m, 5H, Ar).



IX-3

Diethyl {1-*N*-benzyloxycarbonylaminobenzyl]phosphonate (IX-3) was synthesized via the general procedure of method A described above from a reaction of benzyl *N*-((benzenesulfonyl)benzyl)carbamate (**VII-3**) (95.0 mg, 0.25 mmol), diethyl phosphite (0.035 mL, 0.275 mmol), and DBU (0.075 mL, 0.5 mmol) gave 0.070 g of α-aminophosphonate **IX-3** as a white solid (0.18 mmol, 74%), mp: 114-116°C (lit.[49] : 113-114°C). ^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.09 (t, $^{3}J_{HH}$ = 7.0 Hz, 3H, OCH_2CH_3), 1.26 (t, $^{3}J_{HH}$ = 7.0 Hz, 3H, OCH_2CH_3), 3.68-4.13 (m, 4H, OCH_2CH_3), 5.04-5.18 (m, 3H, CHP, CH_2Ph), 5.82 (br, 1H, NH), 7.25-7.42 (m, 10H, Ar); ^{13}C NMR ($CDCl_3$, 50 MHz, {^{1}H}) δ 16.30 (OCH_2CH_3), 52.54 (d, $^{1}J_{CP}$ = 156.2 Hz, CHP), 63.27 (d, $^{2}J_{CP}$ = 7.2 Hz, OCH_2CH_3), 63.41 (d, $^{2}J_{CP}$ = 6.9 Hz, OCH_2CH_3), 67.31 (CH_2Ph), 128.22, 128.63, 135.19, 136.07, 155.56 (C=O); EIMS (70 eV) *m/z* (relative intensity) 377 $[M]^+$ (8), 242 (33), 240 (68), 196 (53), 91 (100), 65 (14); Anal. Calcd for $C_{19}H_{24}NO_5P$: C, 60.47; H, 6.41; N, 3.71. Found: C, 60.10; H, 6.62; N, 3.62.



IX-4

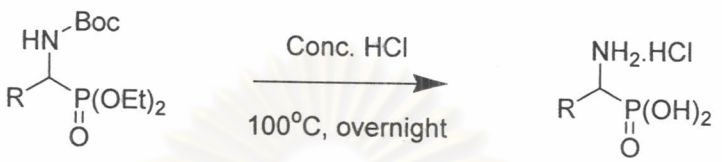
Diethyl [1-*N*-ethoxycarbonylaminobenzyl]phosphonate (IX-4)

Via the general procedure of method A described above, a reaction of benzyl *N*-((benzenesulfonyl)benzyl)carbamate (**VII-4**) (80.0 mg, 0.25 mmol), diethyl phosphite (0.035 mL, 0.275 mmol), and DBU (0.075 mL, 0.5 mmol) resulted in α-aminophosphonate **IX-4** as a colorless solid (0.062 g, 0.20 mmol, 79%), mp: 75-77°C. ^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.08 (t, $^3J_{HH}$ = 7.0 Hz, 3H, OCH_2CH_3), 1.19 (t, $^3J_{HH}$ = 6.8 Hz, 3H, OCH_2CH_3), 1.28 (t, $^4J_{HH}$ = 7.0 Hz, 3H, OCH_2CH_3), 3.66-4.12 (m, 5H, $CHSO_2Ph$, OCH_2CH_3), 5.12 (dd, $^2J_{HP}$ = 22.0 Hz, $^3J_{HH}$ = 9.6 Hz, 1H, CHP), 5.96 (br, 1H, NH), 7.25-7.41 (m, 5H, Ar); ^{13}C NMR ($CDCl_3$, 50 MHz, {^{1}H}) δ 14.48 (OCH_2CH_3), 16.20 (d, $^3J_{CP}$ = 6.9 Hz, OCH_2CH_3), 16.36 (d, $^3J_{CP}$ = 5.6 Hz, OCH_2CH_3), 52.28 (d, $^1J_{CP}$ = 157.9 Hz, CHP), 61.46 (OCH_2CH_3), 63.08 (d, $^2J_{CP}$ = 7.1 Hz, OCH_2CH_3), 63.35 (d, $^2J_{CP}$ = 6.7 Hz, OCH_2CH_3), 127.90, 135.34, 155.82 (C=O); EIMS (70 eV) *m/z* (relative intensity) 316 $[MH]^+$ (66), 179 (11), 178 (100), 150 (13), 134 (18), 106 (42), 104 (11), 79 (35), 77 (24); Anal. Calcd for $C_{14}H_{22}NO_5P$: C, 53.33; H, 7.03; N, 4.44. Found: C, 53.34; H, 7.10; N, 4.45.

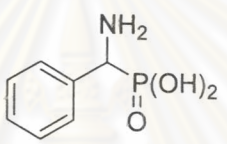
2.6 Hydrolysis of α-aminophosphonates

2.6.1 General procedure for the preparation of α-aminophosphonic acids

A mixture of diethyl phosphonates and concentrated aqueous HCl (2 mL) was refluxed overnight. The mixture was then concentrated *in vacuo* to afford the desired α-aminophosphonic acids (**X**) as a hydrochloride salt in high yield.

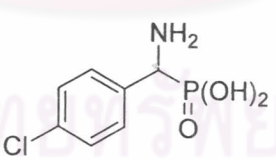


X



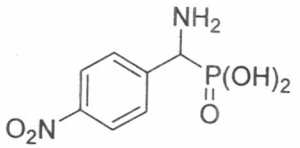
X-1

1-Aminobenzyl phosphonic acid (X-1) was prepared from a mixture of diethyl [1-(*N-tert*-butoxycarbonylamino)benzyl]phosphonate (**VIII-1**) (30.0 mg, 0.087 mmol) and concentrated HCl (2 mL) according to the general procedure described earlier to give 19.0 mg of **X-1** (0.019 mmol, 98%) as a white solid. ^{1}H NMR (D_2O, 200 MHz) δ 4.25 (d, $^2J_{HP}$ = 16.3 Hz, 1H, C*H*P), 7.18-7.27 (m, 5H, Ar).



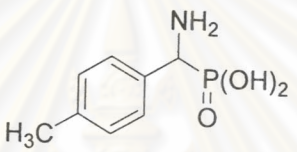
X-2

1-Amino(4-chlorobenzyl) phosphonic acid (X-2) was prepared from a mixture of diethyl [1-(*N-tert*-butoxycarbonylamino)(4′-chlorobenzyl)]phosphonate (**VIII-3**) (29.6 mg, 0.078 mmol) and concentrated HCl (2 mL) according to the general procedure described earlier to give 18.1 mg of **X-2** (0.07 mmol, 90%) as a white solid. ^{1}H NMR (D_2O, 200 MHz) δ 4.25 (d, $^2J_{HP}$ = 16.2 Hz, 1H, C*H*P), 7.20-7.29 (m, 4H, Ar).



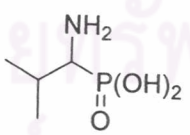
X-3

1-Amino(4-nitrobenzyl) phosphonic acid (X-3) was prepared from a mixture of diethyl [1-(*N-tert*-butoxycarbonylamino)(4′-nitrobenzyl)]phosphonate (**VIII-6**) (18.5 mg, 0.048 mmol) and concentrated HCl (2 mL) according to the general procedure described earlier to give 12.6 mg of **X-3** (0.047 mmol, 99%) as a white solid. ^{1}H NMR (D_2O, 400 MHz) δ 4.44 (d, $^2J_{HP}$ = 16.4 Hz, 1H, C*H*P), 7.49-8.14 (m, 4H, Ar).



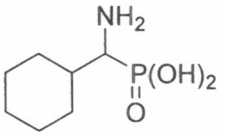
X-4

1-Amino(4-methylbenzyl) phosphonic acid (X-4) was prepared from a mixture of diethyl [1-(*N-tert*-butoxycarbonylamino)(4′-methylbenzyl)] phosphonate (**VIII-9**) (30.8 mg, 0.086 mmol) and concentrated HCl (2 mL) according to the general procedure described earlier to give 17.8 mg of **X-4** (0.075 mmol, 87%) as a white solid. ^{1}H NMR (D_2O, 400 MHz) δ 2.15 (s, 3H, CH_3), 4.21 (d, $^2J_{HP}$ = 16.4 Hz, 1H, C*H*P), 7.09-7.15 (m, 4H, Ar).



X-5

1-Amino(*iso*-butyl) phosphonic acid (X-5) was prepared from a mixture of diethyl [1-(*N-tert*-butoxycarbonylamino)(*iso*-butyl)]phosphonate (**VIII-23**) (154.0 mg, 0.50 mmol) and concentrated HCl (2 mL) according to the general procedure described earlier to give 76.3 mg of **X-5** (0.40 mmol, 82%) as a white solid. ^{1}H NMR (D_2O, 400 MHz) δ 0.89 (d, $^3J_{HH}$ =7.0 Hz, 3H, CH_3), 0.93 (d, $^3J_{HH}$ =7.0 Hz, 3H, CH_3), 2.03-2.06 (m, 1H, CH(CH_3)$_2$), 2.92 (dd, $^2J_{HP}$ = 14.8 Hz, $^3J_{HH}$ = 6.2 Hz, 1H, C*H*P).



X-6

1-Amino(cyclohexyl) phosphonic acid (X-6) was prepared from a mixture of diethyl [1-(*N-tert*-butoxycarbonylamino)(cyclohexyl)]phosphonate (**VIII-30**) (253.0 mg, 0.72 mmol) and concentrated HCl (2 mL) according to the general procedure described earlier to give 156.2 mg of **X-6** (0.68 mmol, 95%) as a white solid. ^{1}H NMR (D_2O, 400 MHz) δ 3.48-4.27 (m, 11H, C*H*$_2$, C*H*), 5.49 (dd, $^{2}J_{HP}$ = 14.0 Hz, $^{3}J_{HH}$ = 6.2 Hz, 1H, C*H*P).