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A method for the synthesis of usymmetric bisphosphoric analogs of α-amino acids

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Supporting Information

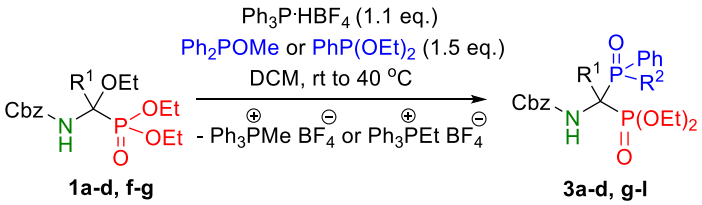
1. General Information

All reagents and solvents were purchased from commercial suppliers and used without further purification. Diethyl 1-(*N*-benzyloxycarbonylamino)-1-ethoxyalkylphosphonates **1a-g** (see **Scheme S1**) were prepared according to our previously described procedure.[1] TLC was performed using commercially available Merck TLC silica gel 60 F_{254} plates. TLC plates were visualized by exposing UV light (254 nm) and/or dipped in a solution of cerium sulfate and tetrahydrate of ammonium heptamolybdate in H_2SO_{4aq} and heated. Purification of crude compounds was carried out by column chromatography using silica gel (Merck, 0.040–0.063 mm). Recycling preparative HPLC (prep-HPLC) was performed on JAI LaboACE 560 (Japan Analytic Industry, Tokyo, Japan). Analytical HPLC was performed on Dionex Ultimate 3000.

Melting points were determined in capillaries in a Stuart Scientific SMP3 melting point apparatus and were uncorrected. IR-spectra were measured on a Nicolet 6700 FT-IR spectrophotometer, Thermo Scientific (attenuated total reflectance method; ATR). ^{1}H NMR and ^{13}C NMR spectra were recorded on Varian 400 spectrometer at frequencies of 400 MHz and 100 MHz. ^{1}H NMR chemical shifts are reported relative to tetramethylsilane (TMS) as the internal standard. ^{13}C NMR chemical shifts are reported from the solvent resonance employed as the internal standard ($CDCl_3$ at 77.16 ppm). ^{31}P NMR spectra were recorded at an operating frequency of 162 MHz without the chemical shift standard, with respect to H_3PO_4 set as 0 ppm. All chemical shifts (δ) are reported in ppm and coupling constants (*J*) in Hz. HRMS were recorded on a Waters Corporation Xevo G2 QTOF instrument using ESI (electrospray ionization).

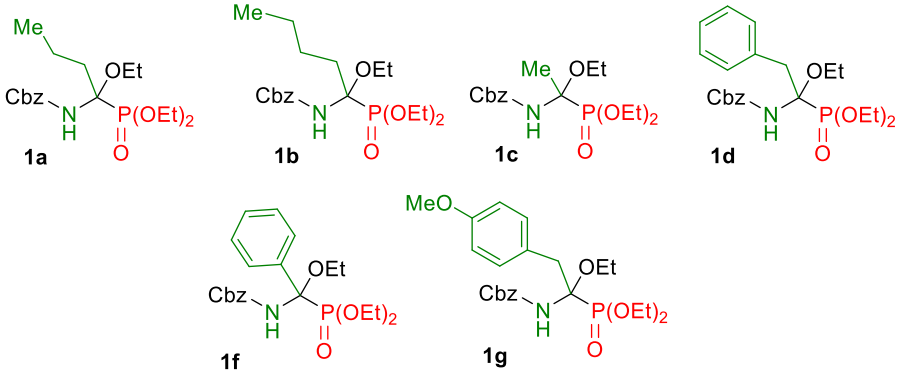
2. Experimental procedure for the synthesis of 3a-d, g-l

(One-pot transformation)



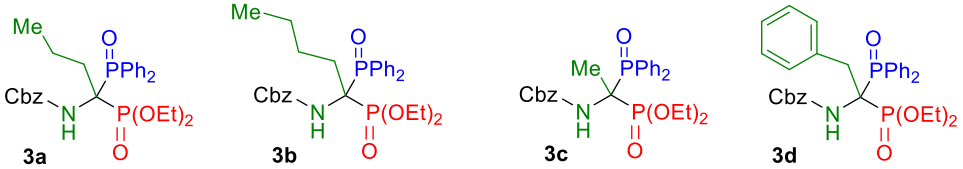
R^1 = Alk, Ar; R^2 = OEt, Ph

Substrates **1**



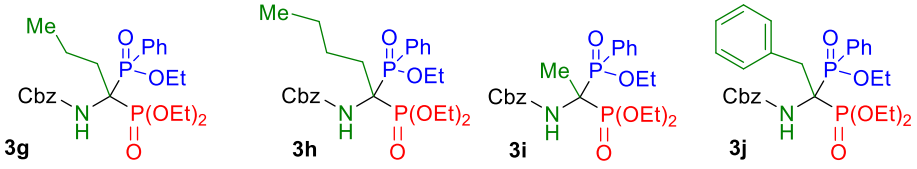
Products **3**

A: *phosphonyl-phosphinoyl analogs*

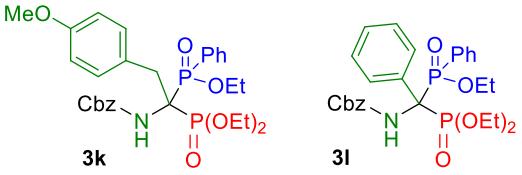


rt, 6h, 76% | rt, 3h, 53% or 40 °C, 3h, 76% | 40 °C, 6h, 57% | rt, 2h, 77%

B: *phosphonyl-phosphinyl analogs*



40 °C, 1h, 80%, dr 1:1.6 | 40 °C, 1h, 82% dr 1:1.5 | 40 °C, 1h, 80% dr 1:1.4 | 40 °C, 1h, 91% dr 1:1.7



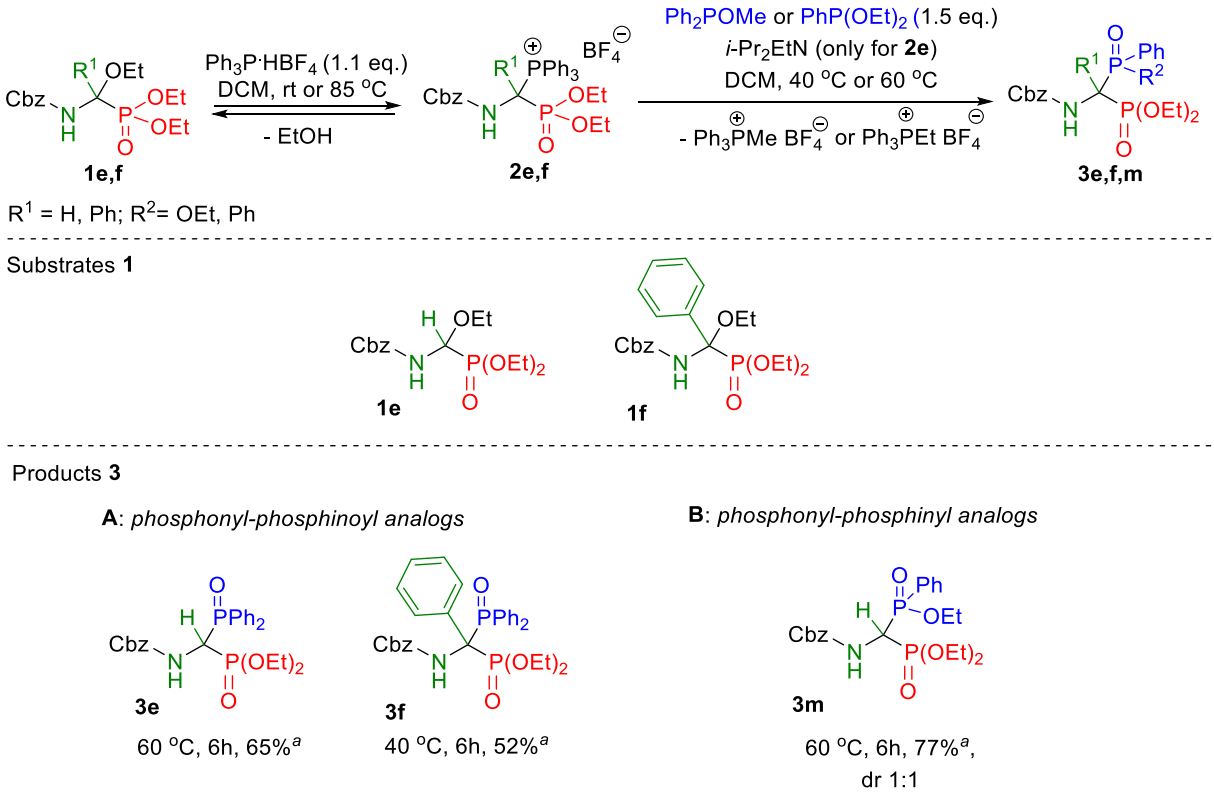
40 °C, 1h, 73% dr 1:1.7 | rt, 24h, 62% dr 1:4

Scheme S1

To a round-bottomed flask the appropriate diethyl 1-(*N*-benzyloxycarbonylamino)-1-ethoxyalkylphosphonate **1a-d**, **f-g** (1.0 mmol), triphenylphosphonium tetrafluoroborate (1.1 mmol, 385 mg) and CH_2Cl_2 (5 mL) were added. Reagents were stirred at room temperature until dissolved, then methyl diphenylphosphinite (1.5 mmol, 324 mg, 300 μL) or diethyl phenylphosphonite (1.5 mmol, 297 mg, 270 μL) was added dropwise. The reaction was carried out at room or elevated temperature for appropriate time (see **Scheme S1**). After the reaction completed, solvent was evaporated under reduced pressure. The residue was extracted with toluene (3x5 mL) to separate the methyl or ethyl triphenylphosphonium tetrafluoroborate. The extracts were combined, then toluene was removed under reduced pressure and obtained residue was further purified by twice column chromatography (CH_2Cl_2/MeOH 20:1, then CH_2Cl_2/MeOH 40:1 for **3a-d, g-k** or AcOEt/Hex/MeOH 14:4:1, then CH_2Cl_2/MeOH 40:1 for **3l**) to obtain the desired product.

3. Experimental procedure for the synthesis of compounds 3e,f,m

(Step-by-step transformation)



[a] from phosphonium salt **2e,f** used in situ; yield calculated according to starting α-ethoxyphosphonate **1e,f**.

Scheme S2

Synthesis of diethyl 1-(*N*-benzyloxycarbonylamino)-1-(diphenylphosphinoyl)methyl-phosphonate (3e) and diethyl 1-(*N*-benzyloxycarbonylamino)-1-[ethoxy(phenyl-phosphinyl)]methylphosphonate (3m) via phosphonium salt (2e).

Step 1. Phosphosphonium salt **2e** was prepared as previously described by Kuźnik et al.[2] In brief, α-ethoxyphosphonate **1e** (1.0 mmol, 345 mg), and triphenylphosphonium tetrafluoroborate (1.1 mmol, 385 mg) were dissolved in CH_2Cl_2 for homogenization. Then, the solvent was evaporated under reduced pressure and the obtained residue was heated in an oil bath at 85 °C for 8h under vacuum. Obtained phosphonium salt **2e** was used in the next step without further purification.

Step 2. Phosphonium salt **2e** was dissolved in CH_2Cl_2, then methyl diphenylphosphinite (1.5 mmol, 324 mg, 300 μL, for **3e**) or diethyl phenylphosphonite (1.5 mmol, 297 mg, 270 μL, for **3m**) and Hünig's base (0.4 mmol, 52 mg, 70μL) were added dropwise. The reaction was carried out in a glass vial sealed with a screw-cap at 60 °C for 6h. Next, solvent was evaporated under reduced pressure. The residue was extracted with toluene (3x5 mL) to separate the methyl or ethyl triphenylphosphonium tetrafluoroborate. The extracts were combined, then toluene was removed under reduced pressure, and provided residue was further purified by twice column chromatography (CH_2Cl_2/MeOH 20:1, then CH_2Cl_2/MeOH 40:1) to obtain the desired products **3e,m**.

Synthesis of diethyl 1-(*N*-benzyloxycarbonylamino)-1-(diphenylphosphinoyl)phenyl-methylphosphonate (3f) via phosphonium salt (2f).

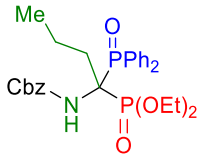
Step 1. α-Ethoxyphosphonate **1f** (1.0 mmol, 421 mg), and triphenylphosphonium tetrafluoroborate (1.1 mmol, 385 mg) were dissolved in CH_2Cl_2 and stirred at room temperature for 40 min. Then, the solvent was evaporated and the obtained phosphonium salt **2f** was dried under reduced pressure for 40 min. It was used in the next step without further purification.

Step 2. Phosphonium salt **2f** was dissolved in CH_2Cl_2 and then methyl diphenylphosphinite (1.5 mmol, 324 mg, 300 μL) was added dropwise. The reaction was carried out at 40 °C for 6h. Product **3f** was isolated and purified as products **3e,m**. Product **3f** was obtained with 52% yield (289 mg).

4. Attempts of separation of diastereomers 3g-m

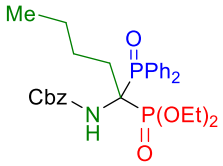
The phosphonyl-phosphinyl analogs of 1-aminobisphosphonates **3g-m** were obtained as mixtures of diastereomers (dr 1:1 – 1:4). Only, product **3l** (dr 1:4) was separated and isolated as single isomers by twice column chromatography (AcOEt/Hex/MeOH 14:4:1, then CH_2Cl_2/MeOH 40:1). Unfortunately, other diastereomeric mixtures **3g-k**,**m** could not be separated. Attempts to select an appropriate system for their separation by gravity column chromatography have failed. Separation of diastereomers on TLC plates wasn't observed in any of the tested eluents (Hex/AcOEt 5:3, Hex/AcOEt/Me_2CO 5:3:2, Hex/AcOEt/MeOH 5:3:2, AcOEt/Hex/MeOH 14:4:1, CH_2Cl_2/MeOH 20:1). However, during the initial purification of the products by gravity column chromatography (CH_2Cl_2/MeOH 20:1), the ^{1}H NMR spectra of particular fractions showed differences in the ratio of diastereomers in each of them, which suggested that their separation could be possible. In the case of compound **3i**, after repeated chromatographic separations of selected fractions (CH_2Cl_2/MeOH 40:1 or 60:1), only 7 mg of the major diastereomer (92% purity) was isolated. The separation of the minor diastereomer failed. In the case of compound **3j**, any of the diastereomer could not be isolated. Attempts to separate diastereomers by recycled prep-HPLC (silica-based RP JAIGEL-ODS-AP-L SP-120-10 column (20 x 500 mm, 10 μm), 100% MeOH or tandem set of GPC JAIGEL-2HR+2.5 HR columns, 100% CH_2Cl_2) and analytic HPLC (TSKgel ODS-100V column (4.6 mm x 15 cm, 5 μm), H_20/MeCN 70:30) have also failed.

5. Characterization data of compounds 3a-m

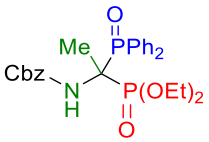


Diethyl 1-(*N*-benzyloxycarbonylamino)-1-(diphenylphosphinoyl)butylphosphonate (3a). Colorless crystals; 76% yield (413 mg); mp 135.5-137.0°C. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.32-8.27 (m, 2H), 7.97-7.92 (m, 2H), 7.59-7.46 (m, 4H), 7.42-7.31 (m, 7H), 6.19 (dd, *J* = 13.0, 6.6 Hz, 1H), 5.03 (ABq, *J* = 12.4 Hz, 2H), 4.20-4.10 (m, 1H), 4.05-3.97 (m, 1H), 3.93-3.84 (m, 1H), 3.75-3.65 (m, 1H), 2.56-2.41 (m, 1H), 2.13-1.98 (m, 1H), 1.51-1.33 (m, 2H), 1.23 (t, *J* = 7.2 Hz, 3H), 1.07 (t, *J* = 7.2 Hz, 3H), 0.62 (t, *J* = 7.2 Hz, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 154.7 (br s), 136.6, 133.4 (d, *J* = 8.7 Hz), 133.0 (d, *J* = 9.1 Hz), 132.3 (d, *J* = 2.7 Hz), 132.0 (d, *J* = 3.1 Hz), 131.7 (d, *J* = 97.5 Hz), 129.0 (d, *J* = 98.6 Hz), 128.6, 128.4 (d, *J* = 12.0 Hz), 128.26, 128.24, 128.0 (d, *J* = 12.1 Hz), 66.9, 63.8 (d, *J* = 7.5 Hz), 62.5 (dd, *J* = 147.9, 60.7 Hz), 62.9 (d, *J* = 7.6 Hz), 32.7, 17.4

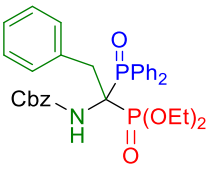
(dd, *J* = 7.8, 5.9 Hz), 16.6 (d, *J* = 5.3 Hz), 16.2 (d, *J* = 6.1 Hz), 14.3. **^{31}P NMR** (162 MHz, $CDCl_3$) δ 34.7 (d, *J* = 16.8 Hz), 20.9 (d, *J* = 16.7 Hz). **IR** (ATR) 3182, 1727, 1541, 1442, 1257, 1057, 961, 692 cm^{-1}. **HRMS** (ESI) *m/z*: calcd for $C_{28}H_{36}NO_6P_2$ $[M+H]^+$ 544.2018, found 544.2014.



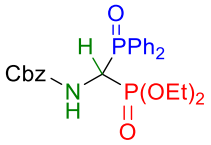
Diethyl 1-(*N*-benzyloxycarbonylamino)-1-(diphenylphosphinoyl)pentylphosphonate (3b). Colorless crystals; 76% yield (423 mg); mp 131.5-134°C. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.34-8.29 (m, 2H), 7.96-7.91 (m, 2H), 7.58-7.29 (m, 11H), 6.25 (dd, *J* = 13.4, 7.0 Hz, 1H), 5.04 (ABq, *J* = 12.4 Hz, 2H), 4.20-4.10 (m, 1H), 4.05-3.95 (m, 1H), 3.92-3.82 (m, 1H), 3.73-3.63 (m, 1H), 2.59-2.43 (m, 1H), 2.13-1.99 (m, 1H), 1.46-1.36 (m, 1H), 1.35-1.27 (m, 1H), 1.23 (t, *J* = 7.2 Hz, 3H), 1.06 (t, *J* = 7.2 Hz, 3H), 1.10-1.02 (m, 1H), 0.96-0.87 (m, 1H), 0.62 (t, *J* = 7.4 Hz, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 154.7 (br s), 136.6, 133.4 (d, *J* = 8.8 Hz), 133.1 (d, *J* = 9.5 Hz), 132.4 (d, *J* = 3.1 Hz), 130.0 (d, *J* = 3.1 Hz), 131.8 (d, *J* = 98.6 Hz), 128.8 (d, *J* = 99.2 Hz), 128.6, 128.4 (d, *J* = 12.1 Hz), 128.23, 128.22, 127.9 (d, *J* = 12.2 Hz), 66.9, 63.7 (d, *J* = 7.3 Hz), 62.9 (d, *J* = 7.6 Hz), 62.3 (dd, *J* = 148.3, 60.6 Hz), 30.3, 25.6 (dd, *J* = 7.6, 5.3 Hz), 22.8, 16.6 (d, *J* = 5.4 Hz), 16.2 (d, *J* = 6.1 Hz), 13.6. **^{31}P NMR** (162 MHz, $CDCl_3$) δ 34.9 (d, *J* = 16.0 Hz), 20.9 (d, *J* = 16.4 Hz). **IR** (ATR) 3184, 1727, 1542, 1442, 1261, 1026, 1026, 960, 692 cm^{-1}. **HRMS** (ESI) *m/z*: calcd for $C_{29}H_{38}NO_6P_2$ $[M+H]^+$ 558.2174, found 558.2173.



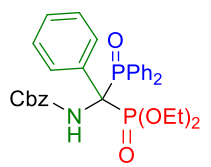
Diethyl 1-(*N*-benzyloxycarbonylamino)-1-(diphenylphosphinoyl)ethylphosphonate (3c). Oil; 57% yield (292 mg). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.08-7.98 (m, 4H), 7.58-7.42 (m, 6H), 7.39-7.31 (m, 5H), 5.77 (br s, 1H), 4.99 (s, 2H), 4.17-3.88 (m, 4H), 1.98 (t, *J* = 16.6 Hz, 3H), 1.20 (t, *J* = 7.0 Hz, 3H), 1.16 (t, *J* = 7.0 Hz, 3H).**^{13}C NMR** (100 MHz, $CDCl_3$) δ 154.5 (br s), 136.5, 132.94 (d, *J* = 8.7 Hz), 132.88 (d, *J* = 8.3 Hz), 132.4 (d, *J* = 3.1 Hz), 129.6 (dd, *J* = 97.3, 2.5 Hz), 129.4 (dd, *J* = 96.8, 1.9 Hz), 128.6, 128.5 (d, *J* = 11.8 Hz), 128.4 (d, *J* = 11.8 Hz), 128.29, 128.25, 66.9, 63.8 (d, *J* = 7.6 Hz), 63.6 (d, *J* = 7.2 Hz), 58.5 (dd, *J* = 146.5, 65.7 Hz), 17.2 (d, *J* = 3.8 Hz), 16.47 (d, *J* = 5.3 Hz), 16.44 (d, *J* = 5.3 Hz). **^{31}P NMR** (162 MHz, $CDCl_3$) δ 32.1 (s, *J* = 23.3 Hz), 20.2 (s, *J* = 23.5 Hz). **IR** (ATR) 3383, 1735, 1229, 1019, 965, 743 cm^{-1}. **HRMS** (ESI) *m/z*: calcd for $C_{26}H_{32}NO_6P_2$ $[M+H]^+$ 516.1705, found 516.1697.



Diethyl 1-(*N*-benzyloxycarbonylamino)-1-(diphenylphosphinoyl)phenylethylphosphonate (3d). Colorless crystals; 77% yield (459 mg); mp 132.5-134.5°C. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.15-8.09 (m, 4H), 7.55-7.26 (m, 11H), 7.15-6.99 (m, 5H), 5.94 (dd, *J* = 14.4, 8.0 Hz, 1H), 5.01 (ABq, *J* = 12.0 Hz, 2H), 3.98-3.53 (m, 6H), 1.07 (t, *J* = 8.0 Hz, 3H), 0.97 (t, *J* = 8.0 Hz, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 154.9 (dd, *J* = 11.5, 4.3 Hz), 136.3, 135.2 (dd, *J* = 9.6, 6.2 Hz), 133.6 (d, *J* = 9.1 Hz), 133.2 (d, *J* = 9.1 Hz), 131.99 (d, *J* = 3.0 Hz), 131.93 (d, 2.9 Hz), 131.1, 131.07 (dd, *J* = 9.6Hz, 1.8 Hz), 130.7 (d, *J* = 90.3 Hz), 128.6, 128.5, 128.3, 128.1 (d, *J* = 12.1 Hz), 127.9 (d, *J* = 12.2 Hz), 127.7, 126.7, 67.1, 63.9 (dd, *J* = 145.7, 60.0 Hz), 63.2 (d, *J* = 7.2 Hz), 63.0 (d, *J* = 7.6 Hz), 35.8, 16.2 (d, *J* = 5.7 Hz), 16.0 (d, *J* = 6.5 Hz). **^{31}P NMR** (162 MHz, $CDCl_3$) δ 36.3 (br s), 19.6 (d, *J* = 8.6 Hz). **IR** (ATR) 3193, 1732, 1542, 1239, 1022, 975 ,694 cm^{-1}. **HRMS** (ESI) *m/z*: calcd for $C_{32}H_{36}NO_6P_2$ $[M+H]^+$ 592.2018, found 592.2005.

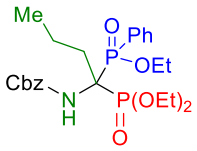


Diethyl 1-(*N*-benzyloxycarbonylamino)-1-(diphenylphosphinoyl)methylphosphonate (3e). Colorless crystals; 65% yield (325 mg); mp 206-207.5°C. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.93-7.80 (m, 4H), 7.56-7.15 (m, 11H), 5.54 (d, *J* = 10.6 Hz, 1H), 5.17 (ddd, *J* = 21.2, 10.6, 10.0 Hz, 1H), 4.98 (ABq, *J* = 12.4 Hz, 2H), 4.13-3.95 (m, 4H), 1.20 (t, *J* = 7.2 Hz, 3H), 1.15 (t, *J* = 7.2 Hz, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 155.8 (br s), 136.0, 132.5 (d, *J* = 2.9 Hz), 132.4 (d, *J* = 2.9 Hz), 131.6 (d, *J* = 9.8 Hz), 131.4 (d, *J* = 9.5 Hz), 130.7 (d, *J* = 100.7 Hz), 128.7 (d, *J* = 12.2 Hz), 128.6 (d, *J* = 12.4 Hz), 128.6, 128.3, 128.1, 67.6, 63.8 (d, *J* = 7.1 Hz), 63.3 (d, *J* = 6.8 Hz), 48.9 (dd, *J* = 146.0, 66.7 Hz), 16.4 (d, *J* = 6.0 Hz), 16.2 (d, *J* = 5.7 Hz). **^{31}P NMR** (162 MHz, $CDCl_3$) δ 29.4 (d, *J* = 19.3 Hz), 16.6 (d, *J* = 19.1 Hz). **IR** (ATR) 3193, 1705, 1540, 1254, 1019, 978, 750 cm^{-1}. **HRMS** (ESI) *m/z*: calcd for $C_{25}H_{30}NO_6P_2$ $[M+H]^+$ 502.1548, found 502.1542.

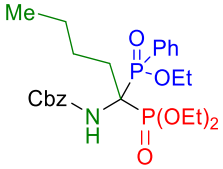


Diethyl 1-(*N*-benzyloxycarbonylamino)-1-(diphenylphosphinoyl)phenylmethylphosphonate (3f). Oil; 52% yield (289 mg). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.99-7.95 (m, 2H), 7.79-7.75 (m,

2H), 7.51-7.10 (m, 16H), 6.54 (dd, *J* = 9.8, 7.0 Hz, 1H), 4.97 (ABq, *J* = 12.4 Hz, 2H), 4.13-3.86 (m, 4H), 1.11 (t, *J* = 7.2 Hz, 6H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 154.6 (br s), 136.3, 133.6 (d, *J* = 9.0 Hz), 133.4 (d, *J* = 8.8 Hz), 132.2 (d, *J* = 2.9 Hz), 132.1 (d, *J* = 3.0 Hz), 131.9 (d, *J* = 10.2 Hz), 130.2 (d, *J* = 97.2 Hz), 128.7 (t, *J* = 5.0 Hz), 128.5, 128.2, 127.9 (d, *J* = 12.1 Hz), 127.8 (d, *J* = 12.1 Hz), 127.7 (t, *J* = 2.7 Hz), 127.2 (t, *J* = 2.3 Hz), 67.5 (dd, *J* = 146.7, 56.4 Hz), 67.2, 64.4 (d, *J* = 5.0 Hz), 63.6 (d, *J* = 7.6 Hz), 16.4 (d, *J* = 5.7 Hz), 16.3 (d, *J* = 6.1 Hz). **^{31}P NMR** (162 MHz, $CDCl_3$) δ 38.3 (s), 17.3 (d, *J* = 9.2 Hz). **IR** (ATR) 2927, 1741, 1438, 1236, 1026, 969, 697 cm^{-1}. **HRMS** (ESI) *m/z*: calcd for $C_{31}H_{34}NO_6P_2$ $[M+H]^+$ 578.1861, found 578.1847.

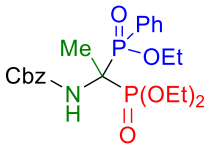


Diethyl 1-(*N*-benzyloxycarbonylamino)-1-[ethoxy(phenylphosphinyl)]butylphosphonate (3g). Oil; 80% yield (409 mg), dr 1:1.6. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.87–7.81 (m, 2H)[a], 7.56-7.52 (m, 1H)[a], 7.43–7.32 (m, 7H)[a], 5.54-5.48 (m, 2H)[a], 5.00 (ABq, *J* = 13.4 Hz, 2H)[b], 4.97 (s, 2H)[b], 4.26-4.00 (m, 6H)[a], 2.39-2.12 (m, 2H)[a], 1.68-1.59 (m, 1H)[a], 1.57-1.45 (m, 1H)[a], 1.34-1.28 (m, 6H)[a], 1.26 (t, *J* = 7.2 Hz, 3H)[b], 1.24 (t, *J* = 7.0 Hz, 3H)[b], 0.85 (t, *J* = 7.2 Hz, 3H)[b], 0.84 (t, *J* = 7.2 Hz, 3H)[b]. **^{13}C NMR** (100 MHz, $CDCl_3$) δ 154.3 (br s)[a], 136.5[a], 133.8 (d, *J* = 9.6 Hz)[b], 133.7 (d, *J* = 9.5 Hz)[b], 132.74 (d, *J* = 3.5 Hz)[b], 132.71 (d, *J* = 3.3 Hz)[b], 129.2 (dd, *J* = 128.2, 2.6 Hz)[a], 129.0 (d, *J* = 131.1 Hz)[b], 128.6[a], 128.32[b], 128.31[b], 128.27[a], 128.2 (d, *J* = 12.4 Hz)[b], 128.1 (d, *J* = 12.8 Hz)[b], 66.9[a], 63.63 (d, *J* = 7.2 Hz)[b], 63.59 (d, *J* = 7.3 Hz)[b], 63.42 (d, *J* = 6.8 Hz)[b], 63.35 (d, *J* = 6.4 Hz)[b], 62.4 (d, *J* = 7.0 Hz)[a], 62.0 (dd, *J* = 144.1, 94.4 Hz)[b], 61.9 (dd, *J* = 143.6, 94.1 Hz)[b], 32.4 (d, *J* = 4.0 Hz)[b], 32.0 (d, *J* = 3.5 Hz)[b], 18.0 (dd, *J* = 7.1, 4.3 Hz)[b], 17.8 (dd, *J* = 6.5, 5.1 Hz)[b], 16.7-16.4 (m)[c], 14.7[b], 14.6[b]. **^{31}P NMR** (162 MHz, $CDCl_3$) δ 38.81 (d, *J* = 18.7 Hz), 38.08 (d, *J* = 20.3 Hz), 19.99 (d, *J* = 20.4 Hz), 19.72 (d, *J* = 18.5 Hz). **IR** (ATR) 2976, 1737, 1488, 1247, 1234, 1021, 957, 748, 695 cm^{-1}. **HRMS** (ESI) *m/z*: calcd for $C_{24}H_{36}NO_7P_2$ $[M+H]^+$ 512.1967, found 512.1964. [a] Overlapping signals of diastereomers. [b] Separate diastereomer signal. [c] Overlapping signals of $P(O)(OCH_2\underline{C}H_3)_2$ and $P(O)Ph(OCH_2\underline{C}H_3)$ groups.

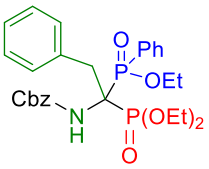


Diethyl 1-(*N*-benzyloxycarbonylamino)-1-[ethoxy(phenylphosphinyl)]pentylphosphonate (3h). Colorless crystals; 82% yield (430 mg), dr 1:1.5. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.88–7.81 (m, 2H)[a], 7.56-7.52 (m, 1H)[a], 7.43–7.32 (m, 7H)[a], 5.55-5.47 (m, 2H)[a], 5.00 (ABq, *J* = 12.2 Hz,

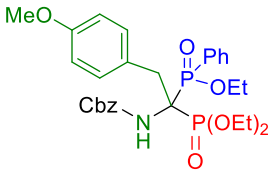
2H)[b], 4.98 (s, 2H)[b], 4.25-4.00 (m, 6H)[a], 2.43-2.12 (m, 2H)[a], 1.64-1.53 (m, 1H)[a], 1.51-1.42 (m, 1H)[a], 1.34-1.22 (m, 11H)[a], 0.84 (t, *J* = 7.2 Hz, 3H)[b], 0.83 (t, *J* = 7.2 Hz, 3H)[b]. **^{13}C NMR** (100 MHz, $CDCl_3$) δ 154.3 (br s)[a], 136.6[a], 133.8 (d, *J* = 9.9 Hz)[b], 133.7 (d, *J* = 10.3 Hz)[b], 132.74 (d, *J* = 3.4 Hz)[b], 132.71 (d, *J* = 3.1 Hz)[b], 129.1 (dd, *J* = 127.1, 2.6 Hz)[a], 129.0 (d, *J* = 130.2 Hz)[a], 128.6[a], 128.32[a], 128.27[a], 128.2 (d, *J* = 13.6 Hz)[b], 128.1 (d, *J* = 12.8 Hz)[b], 66.9[a], 63.6 (d, *J* = 7.2 Hz)[a], 63.43 (d, *J* = 7.6 Hz)[b], 63.35 (d, *J* = 7.3 Hz)[b], 62.39 (d, *J* = 7.0 Hz)[b], 62.36 (d, *J* = 7.0 Hz)[b], 61.9 (dd, *J* = 144.2, 94.5 Hz)[b], 61.8 (dd, *J* = 143.8, 94.1 Hz)[b], 30.2 (d, *J* = 4.2 Hz)[b], 29.8 (d, *J* = 3.4 Hz)[b], 26.5 (dd, *J* = 6.9, 4.2 Hz)[b], 26.4 (t, *J* = 5.5 Hz)[b], 23.4[b], 23.3[b], 16.7-16.4 (m)[c], 14.0[a]. **^{31}P NMR** (162 MHz, $CDCl_3$) δ 38.9 (d, *J* = 18.4 Hz), 38.1 (d, *J* = 19.9 Hz), 20.0 (d, *J* = 19.8 Hz), 19.9 (d, *J* = 18.6 Hz). **IR** (ATR) 2960, 1737, 1498, 1232, 1021, 955, 747, 696 cm^{-1}. **HRMS** (ESI) *m/z*: calcd for $C_{25}H_{38}NO_6P_2$ $[M+H]^+$ 526.2124, found 526.2126. [a] Overlapping signals of diastereomers. [b] Separate diastereomer signal. [c] Overlapping signals of $P(O)(OCH_2\underline{C}H_3)_2$ and $P(O)Ph(OCH_2\underline{C}H_3)$ groups.



Diethyl 1-(*N*-benzyloxycarbonylamino)-1-[ethoxy(phenylphosphinyl)]ethylphosphonate (3i). Oil; 80% yield (384 mg), dr 1:1.4. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.85–7.80 (m, 2H)[a], 7.78–7.29 (m, 8H)[a], 5.58 (br s, 1H)[b], 5.46 (br s, 1H)[b], 4.98 (s, 2H)[b], 4.92 (ABq, *J* = 12.2 Hz, 2H)[b], 4.31-4.05 (m, 6H)[a], 1.90 (t, *J* = 17.2 Hz, 3H)[b], 1.85 (t, *J* = 17.2 Hz, 3H)[b], 1.36 (t, *J* = 7.0 Hz, 3H)[b], 1.33 (t, *J* = 7.0 Hz, 3H)[b], 1.32 (t, *J* = 7.2 Hz, 3H)[b], 1.30 (t, *J* = 7.0 Hz, 3H)[b], 1.27 (t, *J* = 7.2 Hz, 3H)[b], 1.26 (t, *J* = 7.1 Hz, 3H)[b]. **^{13}C NMR** (100 MHz, $CDCl_3$) δ 154.2 (br s)[a], 136.3[a], 133.40 (d, *J* = 9.1 Hz)[b], 133.37 (d, *J* = 9.1 Hz)[b], 132.8 (d, *J* = 2.9 Hz)[b], 132.7 (d, *J* = 2.9 Hz)[b], 128.45[b], 128.42[b], 128.23 (d, *J* = 12.4 Hz)[b], 128.20 (d, *J* = 13.2 Hz)[b], 128.15[a], 128.08[b], 128.05[b], 128.0 (dd, *J* = 130.1, 3.1 Hz)[b], 127.8 (dd, *J* = 132.5, 3.1 Hz)[b], 66.6[b], 66,5[b], 63.9 (d, *J* = 7.0 Hz)[b], 63.6 (d, *J* = 7.4 Hz)[b], 63.5 (d, *J* = 7.2 Hz)[b], 63.4 (d, *J* = 7.4 Hz)[b], 62.7 (d, *J* = 7.0 Hz)[b], 62.5 (d, *J* = 6.7 Hz)[b], 57.33 (dd, *J* = 146.8, 97.3 Hz)[b], 57.36 (dd, *J* = 145.1, 98.3 Hz)[b], 16.5-16.3 (m)[c], 16.1 (br s)[b], 16.0 (br s)[b]. **^{31}P NMR** (162 MHz, $CDCl_3$) δ 37.8 (d, *J* = 21.5 Hz), 37.4 (d, *J* = 23.4 Hz), 19.9 (d, *J* = 22.2 Hz), 19.7 (d, *J* = 23.3 Hz). **IR** (ATR) 2983, 1738, 1501, 1228, 1017, 954, 821, 749, 695 cm^{-1}. **HRMS** (ESI) *m/z*: calcd for $C_{22}H_{32}NO_7P_2$ $[M+H]^+$ 484.1654, found 484.1643. [a] Overlapping diastereomers signals. [b] Separate diastereomer signal. [c] Overlapping signals of $P(O)(OCH_2\underline{C}H_3)_2$ and $P(O)Ph(OCH_2\underline{C}H_3)$ groups.

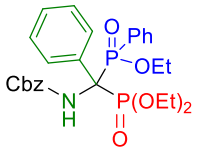


Diethyl 1-(*N*-benzyloxycarbonylamino)-1-[ethoxy(phenylphosphinyl)]phenylethylphosphonate (**3j**). Colorless crystals; 91% yield (509 mg), dr 1:1.7. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.97–7.84 (m, 2H)[a], 7.54–7.11 (m, 13H)[a], 5.54 (dd, *J* = 16.4, 8.6 Hz, 1H)[b], 5.39 (dd, *J* = 11.6, 8.1 Hz, 1H)[b], 5.16 (ABq, *J* = 12.0 Hz, 2H)[b], 5.05 (s, 2H)[b], 4.25-3.57 and 3.45-3.40 (m, 8H)[a], 1.32 (t, *J* = 7.0 Hz, 3H)[b], 1.18 (td, *J* = 7.1, 0.7 Hz, 3H)[b], 1.14 (td, *J* = 7.2, 0.8 Hz, 3H)[b], 1.11 (t, *J* = 7.2 Hz, 3H)[b], 1.08 (td, *J* = 7.2, 0.8 Hz, 3H)[b], 1.05 (t, *J* = 7.2 Hz, 3H)[b]. **^{13}C NMR** (100 MHz, $CDCl_3$) δ 154.9 (dd, *J* = 8.0 Hz, 7.9 Hz)[b], 154.71 (dd, *J* = 14.5, 2.7 Hz)[b], 136.3[a], 135.6 (dd, *J* = 11.7, 4.3 Hz)[b], 135.4 (dd, *J* = 8.7, 7.5 Hz)[b], 133.8 (d, *J* = 10.0 Hz)[b], 133.7 (d, *J* = 9.9 Hz)[b], 132.4 (d, *J* = 2.9 Hz)[b], 132.3 (d, *J* = 2.9 Hz)[b], 131.3[b], 131.1[b], 129.6 (d, *J* = 131.0 Hz)[b], 129.5 (d, *J* = 130.8 Hz)[b], 128.5[a], 128.4[b], 128.30[b], 128.28[b], 128.1[b], 127.69 (d, *J* = 13.3 Hz)[b], 127.67 (d, *J* = 15.2 Hz)[b], 127.61[a], 126.6[b], 126.5[b], 67.0[b], 66.9[b], 63.4 (d, *J* = 7.3 Hz)[b], 63.2 (d, *J* = 7.0 Hz)[b], 63.10 (d, *J* = 7.7 Hz)[b], 62.91 (dd, *J* = 143.7, 93.6 Hz)[b], 62.93 (dd, *J* = 143.2, 94.1 Hz)[b], 62.8 (d, *J* = 7.5 Hz)[b], 62.3 (d, *J* = 7.0 Hz)[b], 61.6 (d, *J* = 6.8 Hz)[b], 35.15 (t, *J* = 3.4 Hz), 34.79, 16.37 (d, *J* = 6.1 Hz), 16.12 (d, *J* = 6.2 Hz). 35.2 (t, *J* = 3.4 Hz)[b], 34.8[b], 16.4 (d, *J* = 6.1 Hz)[b], 16.1 (d, *J* = 6.2 Hz)[b], 16.01 (d, *J* = 6.2 Hz)[b], 15.99 (d, *J* = 6.4 Hz)[b], 15.95 (d, *J* = 6.1 Hz)[b]. **^{31}P NMR** (162 MHz, $CDCl_3$) δ 39.3 (d, *J* = 6.8 Hz), 36.7 (d, *J* = 6.0 Hz), 19.1 (d, *J* = 7.1 Hz), 18.4 (d, *J* = 8.4 Hz). **IR** (ATR) 2928, 1737, 1498, 1244, 1019, 954, 751, 698 cm^{-1}. **HRMS** (ESI) *m/z*: calcd for $C_{28}H_{36}NO_7P_2$ $[M+H]^+$ 590.1967, found 590.1965. [a] Overlapping signals of diastereomers. [b] Separate diastereomer signal.



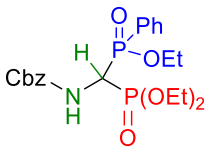
Diethyl 1-(*N*-benzyloxycarbonylamino)-1-[ethoxy(phenylphosphinyl)]-2-(4-methoxyphenyl)ethylphosphonate (**3k**). Oil; 73% yield (418 mg), dr 1:1.7. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.95–7.83 (m, 2H)[a], 7.54–7.10 (m, 10H)[a], 6.71–6.66 (m, 2H)[a], 5.54 (dd, *J* = 16.3, 8.7 Hz, 1H)[b], 5.38 (dd, *J* = 11.7, 8.1 Hz, 1H)[b],5.15 (ABq, *J* = 12.2 Hz, 2H)[b], 5.04 (s, 2H)[b], 4.25-3.38 (m, 8H)[a], 3.75 (s, 3H)[b], 3.74 (s, 3H)[b], 1.32 (t, *J* = 7.1 Hz, 3H)[b], 1.20 (t, *J* = 7.0 Hz, 3H)[b], 1.17 (t, *J* = 6.8 Hz, 3H)[b], 1.12 (t, *J* = 7.2 Hz, 3H)[b], 1.11 (t, *J* = 7.2 Hz, 3H)[b], 1.08 (t, *J* = 7.0 Hz, 3H)[b]. **^{13}C NMR** (100 MHz, $CDCl_3$) δ 158.4[a], 154.9 (t, *J* = 8.0 Hz)[b], 154.7 (dd, *J* = 13.8, 2.7 Hz)[b], 136.3[a], 133.8 (d, *J* = 10.6 Hz)[b], 133.7 (d, *J* = 10.0 Hz)[b], 132.4 (d, *J* = 2.9 Hz)[b], 132.3 (d, *J* = 3.0 Hz)[b], 132.3[b], 132.1[b], 129.7 (d, *J* = 130.9 Hz)[b], 129.6 (d, *J* = 130.5 Hz)[b], 128.54[b], 128.50[b], 128.4[b], 128.33[b], 128.27[b],

128.1[b], 127.70 (d, *J* = 13.3 Hz)[b], 127.68 (d, *J* = 13.3 Hz)[b], 127.4 (dd, *J* = 9.2, 4.4 Hz)[b], 127.33 (t, *J* = 8.2 Hz)[b], 113.0[a], 67.0[b], 66.9[b], 63.38 (d, *J* = 7.2 Hz), 63.22 (d, *J* = 7.0 Hz), 63.09 (d, *J* = 7.5 Hz), 62.93 (dd, *J* = 143.4, 93.7 Hz)[b], 62.87 (dd, *J* = 143.0, 94.0 Hz)[b], 62.85 (d, *J* = 7.6 Hz), 62.26 (d, *J* = 6.9 Hz), 61.67 (d, *J* = 6.8 Hz), 55.2[b], 55.1[b], 34.4 (br s)[b], 34.0[b], 16.4 (d, *J* = 6.0 Hz)[b], 16.18 (d, *J* = 6.1 Hz)[b], 16.17 (d, *J* = 6.0 Hz)[b], 16.07 (d, *J* = 6.1 Hz)[b], 16.05 (d, *J* = 6.1 Hz)[b], 16.03 (d, *J* = 6.1 Hz)[b]. **^{31}P NMR** (162 MHz, $CDCl_3$) δ 39.1 (d, *J* = 7.5 Hz), 36.8 (d, *J* = 8.5 Hz), 19.3 (d, *J* = 7.6 Hz), 18.6 (d, *J* = 8.6 Hz). **IR** (ATR) 2928, 1732, 1511, 1247, 1019, 950, 822, 747, 696 cm^{-1}. **HRMS** (ESI) *m/z*: calcd for $C_{29}H_{37}NO_8NaP_2$ $[M+Na]^+$ 612.1892, found 612.1887. [a] Overlapping signals of diastereomers. [b] Separate diastereomer signal.



Major diastereomer of diethyl 1-(*N*-benzyloxycarbonylamino)-1-[ethoxy(phenyl-phosphinyl)]phenylmethyllphosphonate (**3l**). Oil; 50% yield (270 mg). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.52-7.17 (m, 15H), 6.04 (br s, 1H), 5.09-4.99 (m, 2H), 4.14-3.98 (m, 6H), 1.27 (t, *J* = 7.0 Hz, 3H), 1.20 (t, *J* = 7.0 Hz, 3H), 1.16 (br s, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 154.5 (br s), 136.5 (br s), 134.06 (d, *J* = 9.2 Hz), 132.71 (d, *J* = 3.1 Hz), 131.5, 128.8 (t, *J* = 5.0 Hz), 128.5, 128.3 (br s), 127.7, 127.6, 127.3 (t, *J* = 2.3 Hz), 67.2, 66.6 (dd, *J* = 144.3, 86.0 Hz), 64.0 (d, *J* = 7.5 Hz), 63.7 (d, *J* = 7.2 Hz), 63.0 (d, *J* = 7.1 Hz), 16.5 (d, *J* = 6.1 Hz), 16.43 (d, *J* = 6.4 Hz), 16.40 (d, *J* = 5.7 Hz). **^{31}P NMR** (162 MHz, $CDCl_3$) δ 36.5 (d, *J* = 11.8 Hz), 17.1 (d, *J* = 11.7 Hz). **IR** (ATR) 2981, 1747, 1495, 1247, 1236, 1018, 953, 727, 694 cm^{-1}. **HRMS** (ESI) *m/z*: calcd for $C_{27}H_{34}NO_7P_2$ $[M+H]^+$ 546.1811, found 546.1808.

Minor diastereomer of diethyl 1-(*N*-benzyloxycarbonylamino)-1-[ethoxy(phenyl-phosphinyl)]phenylmethyllphosphonate (**3l**). Oil; 12% yield (67 mg). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.49-7.12 (m, 15H), 6.14 (br s), 5.11-5.07 (m, 2H), 4.32-3.82 (m, 6H), 1.32 (t, *J* = 6.9 Hz, 3H), 1.26 (t, *J* = 7.1 Hz, 3H), 1.17 (br s, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 154.4 (br s), 136.5 (br s), 133.7 (d, *J* = 9.2 Hz), 132.6 (d, *J* = 3.1 Hz), 128.8-128.2 (m), 127.7, 127.6, 127.4 (t, *J* = 2.5 Hz), 67.1, 64.1 (d, *J* = 7.2 Hz), 63.9 (d, *J* = 7.2 Hz), 63.6 (d, *J* = 7.2 Hz), 16.6 (d, *J* = 5.7 Hz), 16.5 (d, *J* = 5.3 Hz), 16.4 (d, *J* = 5.7 Hz). **^{31}P NMR** (162 MHz, $CDCl_3$) δ 38.6 (d, *J* = 6.8 Hz), 17.3 (d, *J* = 6.9 Hz). **IR** (ATR) 2923, 1744, 1590, 1239, 1023, 971, 877, 744, 696 cm^{-1}. **HRMS** (ESI) *m/z*: calcd for $C_{27}H_{34}NO_7P_2$ $[M+H]^+$ 546.1810, found 546.1805.



Diethyl 1-(*N*-benzyloxycarbonylamino)-1-[ethoxy(phenylphosphinyl)]methylphosphonate (**3m**). Oil; 77% yield (363 mg), dr 1:1. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.86-7.80 (m, 2H)[a], 7.58-7.52 (m, 1H)[a], 7.47-7.41 (m, 2H)[a], 7.37-7.28 (m, 4H)[a], 7.19-7.17 (m, 1H)[a], 5.43 (d, *J* = 11.1 Hz, 1H)[b], 5.25 (d, *J* = 11.2 Hz, 1H)[b], 5.06 (ABq, *J* = 12.2 Hz, 2H)[b] 4.95 (s, 2H)[b], 4.71 (ddd, *J* = 23.2, 21.6, 10.8 Hz, 1H)[b], 4.67 (td, *J* = 21.6, 10.8 Hz, 1H)[b], 4.29-4.01 (m, 6H)[a], 1.34 (t, *J* = 7.0 Hz, 3H)[b], 1.303 (t, *J* = 7.0 Hz, 3H)[b], 1.297 (t, *J* = 7.2 Hz, 3H)[b], 1.29 (t, *J* = 7.2 Hz, 3H)[b], 1.25 (t, *J* = 7.2 Hz, 3H)[b], 1.21 (t, *J* = 7.2 Hz, 3H)[b]. **^{13}C NMR** (100 MHz, $CDCl_3$) δ 155.6 (dd, *J* = 5.0, 4.0 Hz)[b], 155.4 (t, *J* = 4.6 Hz)[b], 136.11[b], 136.05[b], 133.1 (d, *J* = 3.0 Hz)[b], 133.0 (d, *J* = 2.9 Hz)[b], 132.34 (d, *J* = 10.1 Hz)[b], 132.27 (d, *J* = 9.9 Hz)[b], 129.0 (dd, *J* = 133.6, 3.1 Hz)[b], 128.9 (dd, *J* = 134.7, 4.6 Hz)[b], 128.64[b], 128.58[b], 128.55 (d, *J* = 12.9 Hz)[b], 128.53 (d, *J* = 13.3 Hz)[b], 128.4[b], 128.3[b], 128.0[a], 67.7[b], 67.5[b], 63.61 (d, *J* = 6.6 Hz)[b], 63.50 (d, *J* = 6.9 Hz)[b], 63.48 (d, *J* = 6.3 Hz)[b], 63.42 (d, *J* = 5.9 Hz)[b], 62.61 (d, *J* = 6.6 Hz)[b], 62.29 (d, *J* = 6.5 Hz)[b], 49.3 (dd, *J* = 146.6, 96.8 Hz)[b], 48.5 (dd, *J* = 143.7, 100.3 Hz)[b], 16.59 (d, *J* = 5.9 Hz)[b], 16.57 (d, *J* = 6.0 Hz)[b], 16.49 (d, *J* = 5.9 Hz)[b], 16.43 (d, *J* = 5.9 Hz)[b], 16.40 (d, *J* = 6.2 Hz)[b], 16.37 (d, *J* = 6.1 Hz)[b]. **^{31}P NMR** (162 MHz, $CDCl_3$) δ 33.63 (d, *J* = 21.3 Hz), 32.57 (d, *J* = 27.2 Hz), 16.55 (d, *J* = 21.3 Hz), 16.30 (d, *J* = 27.6 Hz)[b]. **IR** (ATR) 2926, 1705, 1585, 1266, 1024, 972, 877, 744, 696 cm^{-1}. **HRMS** (ESI) *m/z*: calcd for $C_{21}H_{30}NO_7P_2$ $[M+H]^+$ 470.1498, found 470.1494. [a] Overlapping signals of diastereomers. [b] Separate diastereomer signal.

6. References

1. Kuźnik, A.; Kozicka, D.; Hawranek, W.; Socha, K.; Erfurt, K. One-Pot and Catalyst-Free Transformation of *N*-Protected 1-Amino-1-Ethoxyalkylphosphonates into Bisphosphonic Analogs of Protein and Non-Protein α-Amino Acids. *Molecules*, **2022**, *27* (11), 3571.

2. Kuźnik, A.; Mazurkiewicz, R.; Zięba, M.; Erfurt, K. 1-(*N*-Acylamino)-1-Triphenylphosphoniumalkylphosphonates: General Synthesis and Prospects for Further Synthetic Applications. *Tetrahedron Lett*. **2018**, *59*, 3307–3310.

7. NMR spectra of compounds 3a-m

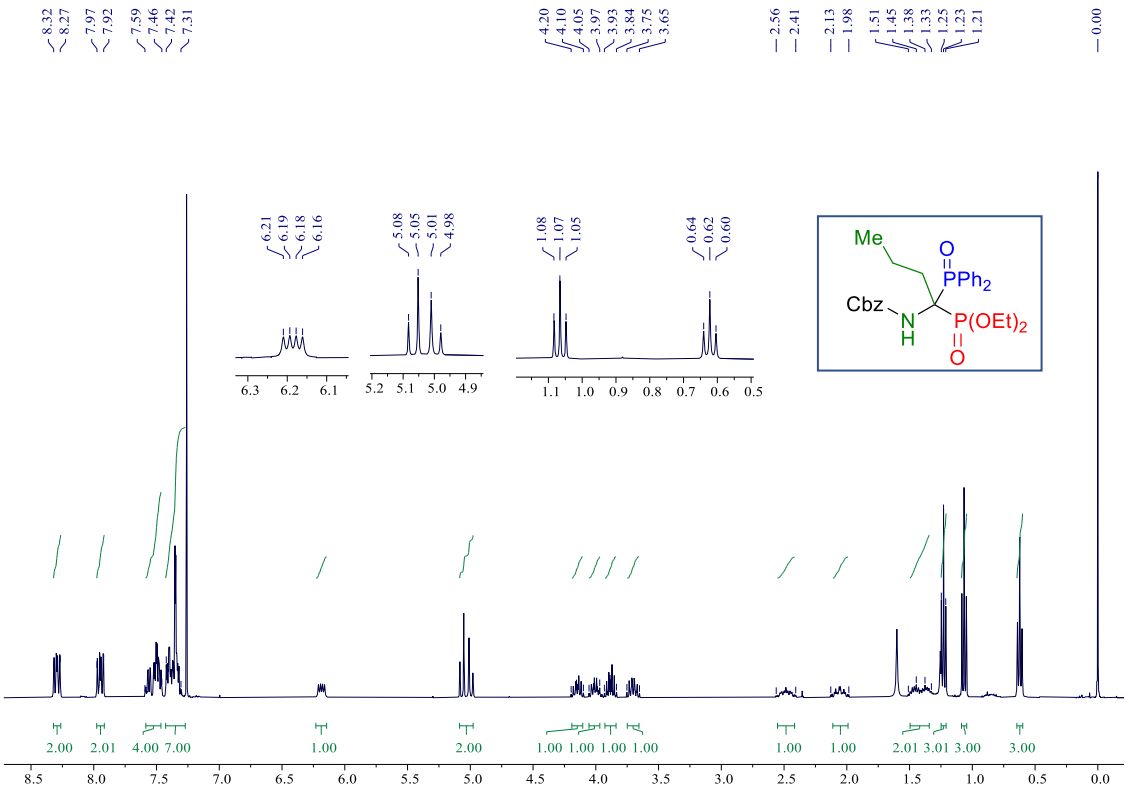


Fig. S1 ^{1}H NMR spectrum of **3a** in $CDCl_3$ (400 MHz)

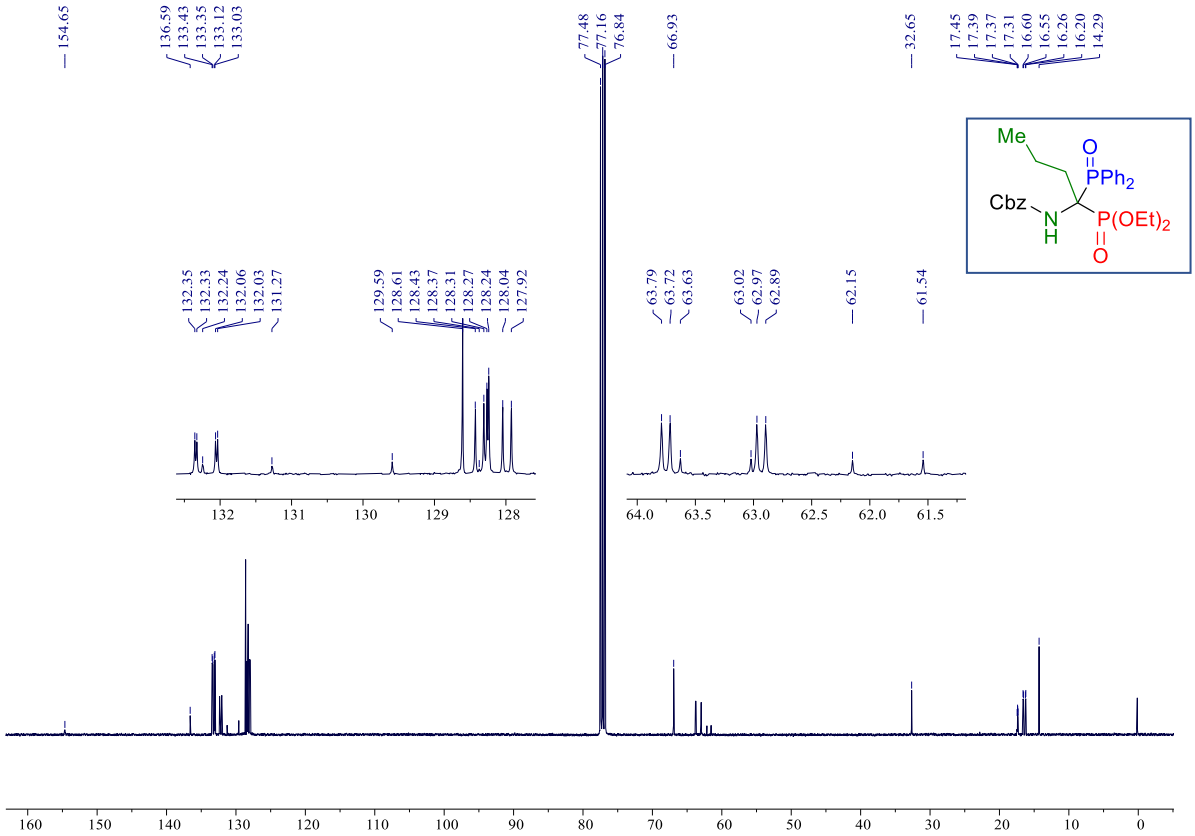


Fig. S2 ^{13}C NMR spectrum of **3a** in $CDCl_3$ (100 MHz)

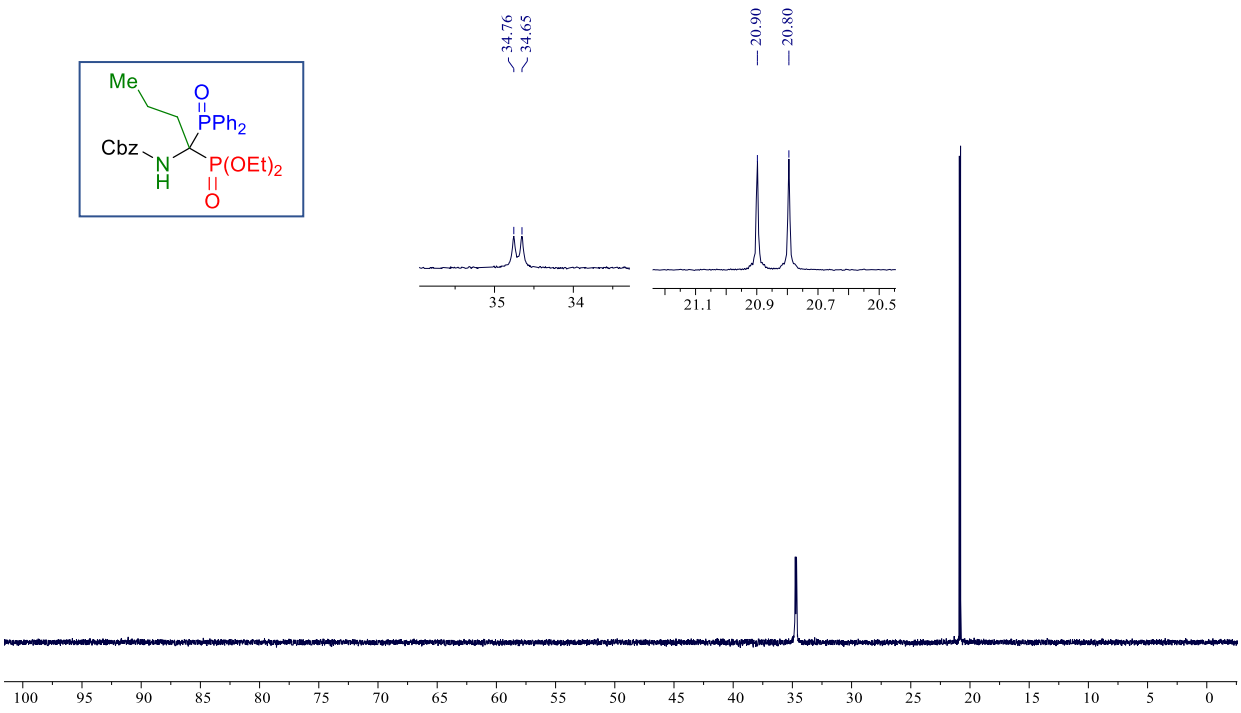


Fig. S3 ^{31}P NMR spectrum of **3a** in $CDCl_3$ (162 MHz)

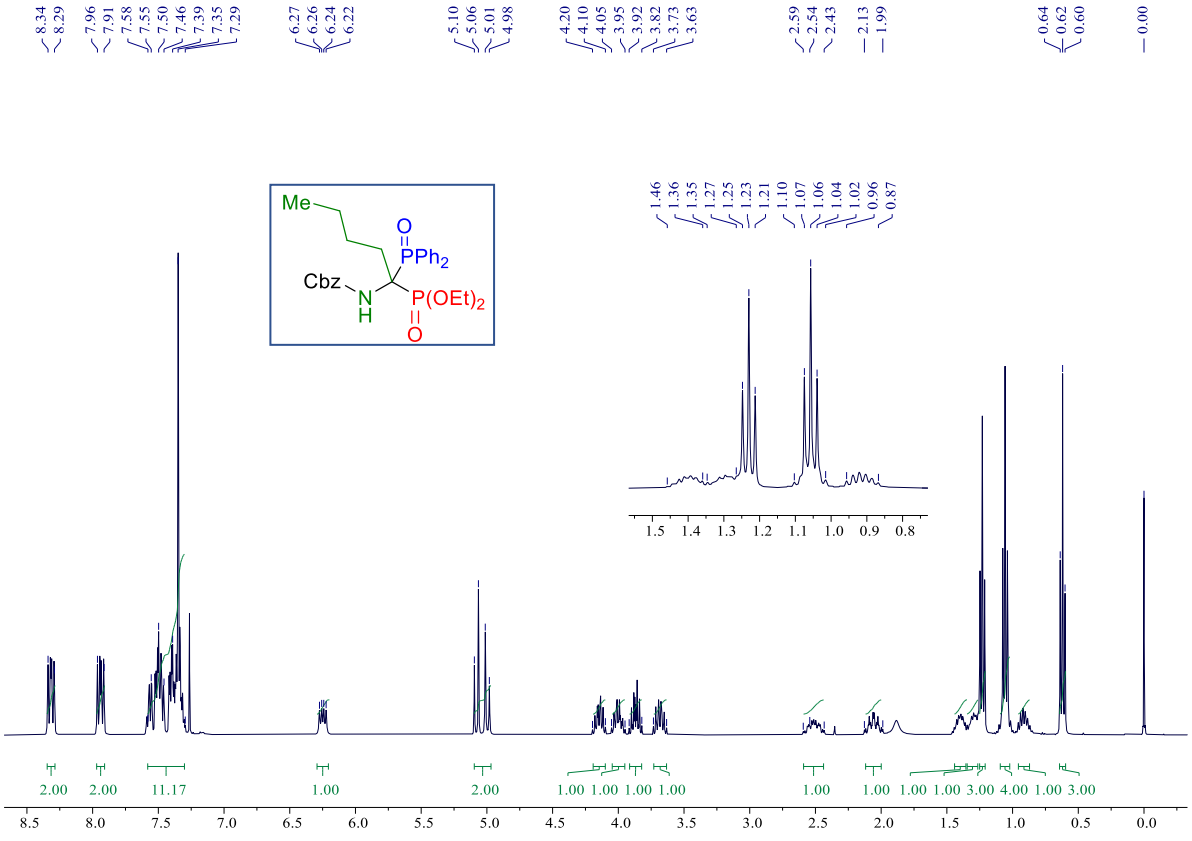


Fig. S4 ^{1}H NMR spectrum of **3b** in $CDCl_3$ (400 MHz)

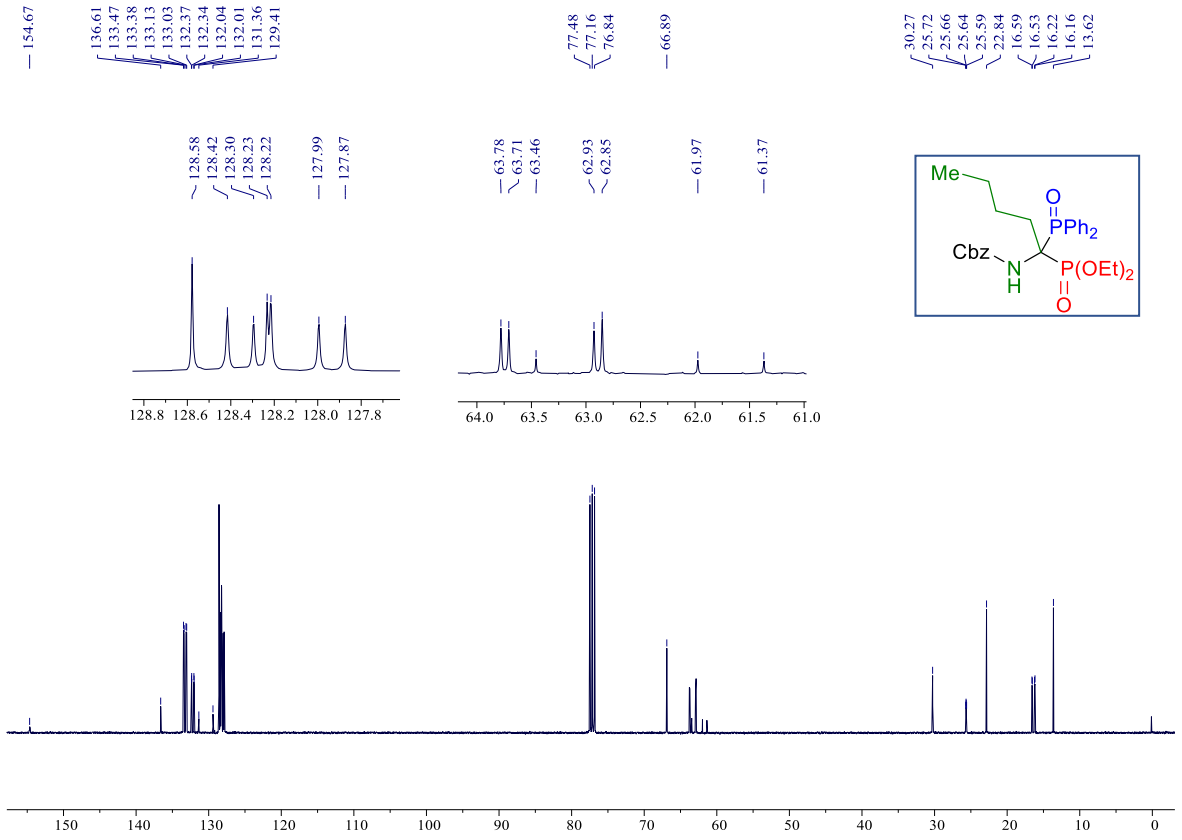


Fig. S5 ^{13}C NMR spectrum of **3b** in $CDCl_3$ (100 MHz)

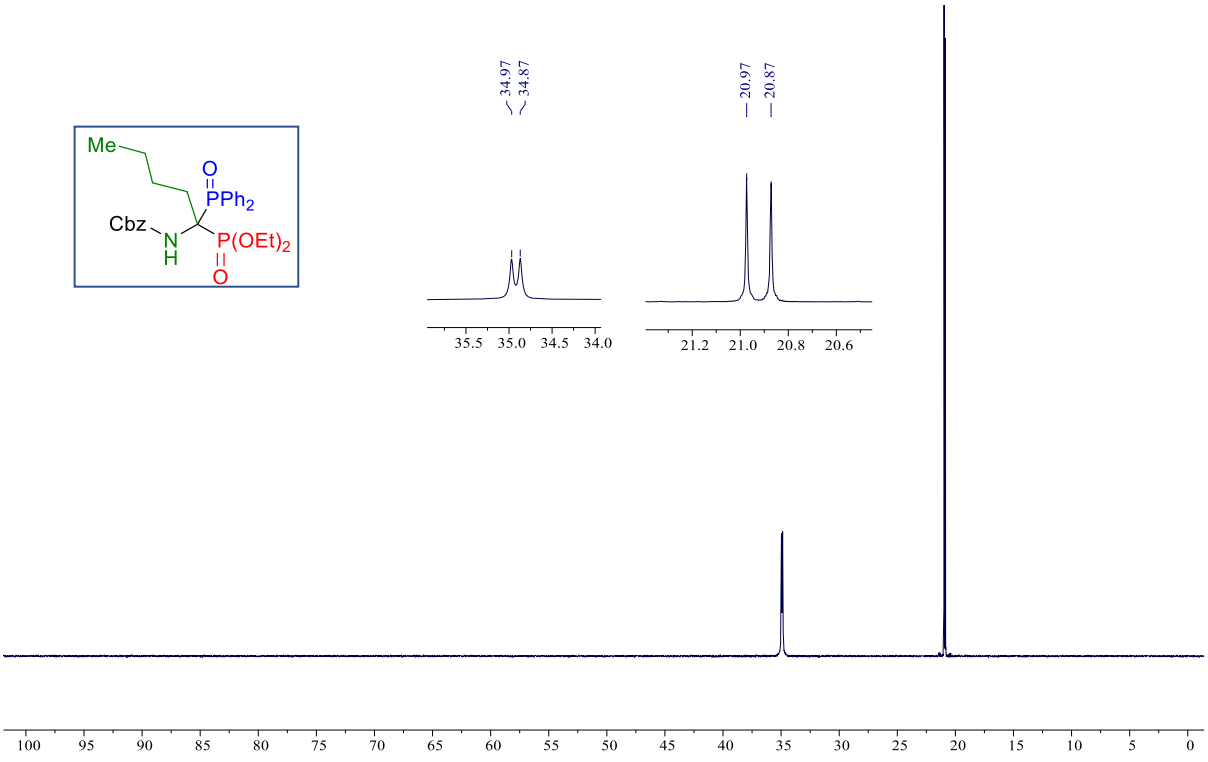


Fig. S6 ^{31}P NMR spectrum of **3b** in $CDCl_3$ (162 MHz)

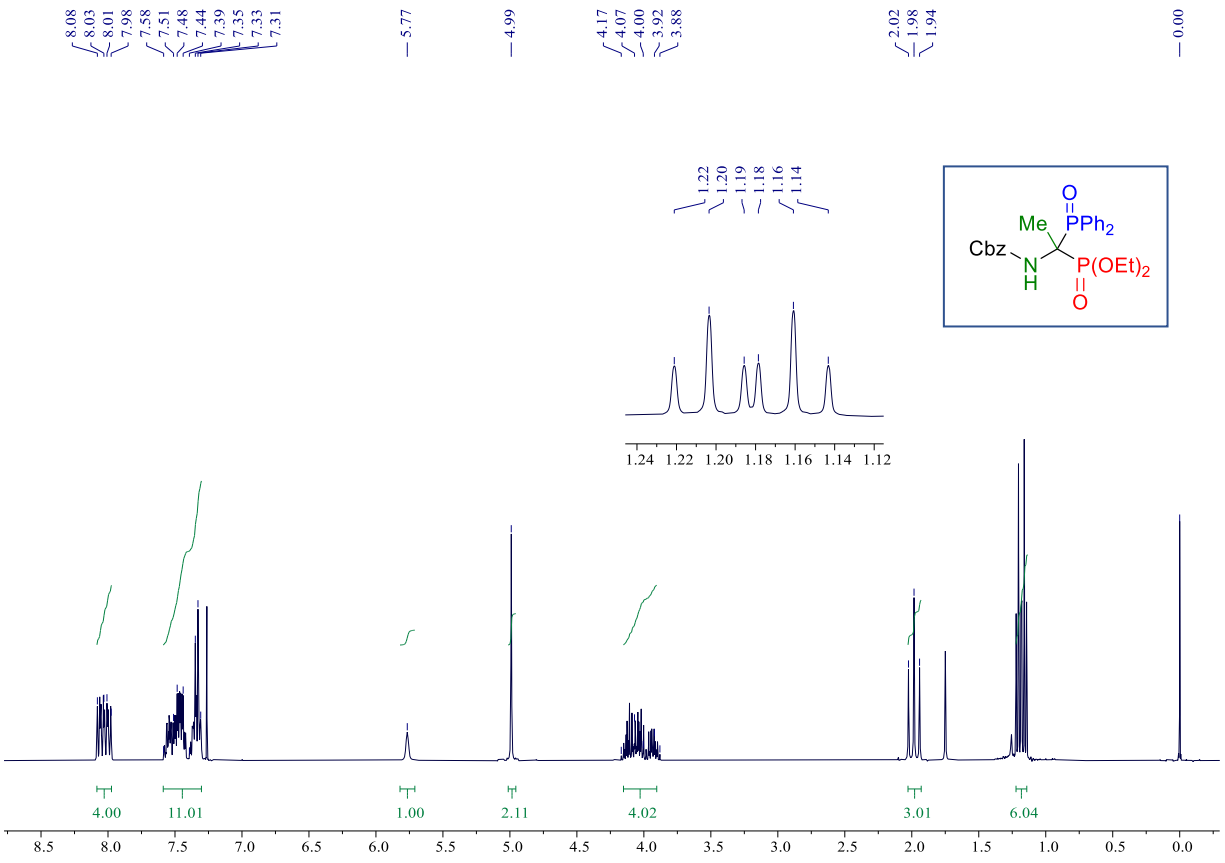


Fig. S7 ^{1}H NMR spectrum of **3c** in $CDCl_3$ (400 MHz)

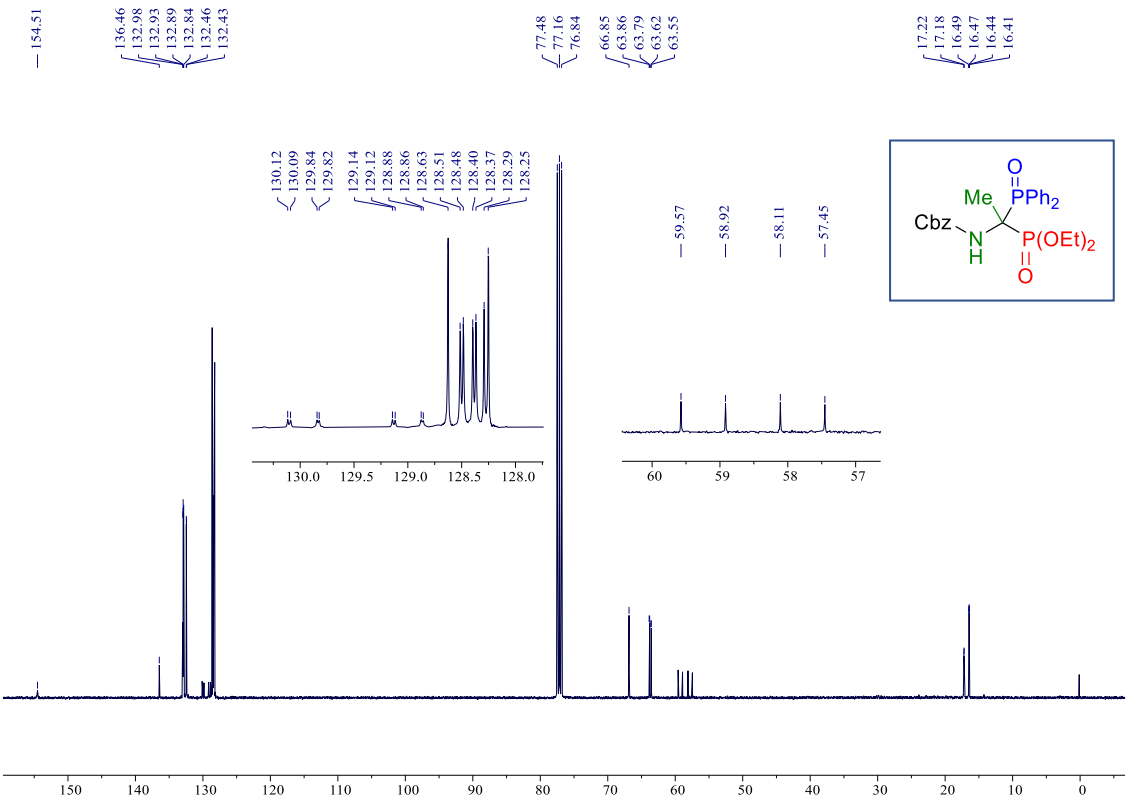


Fig. S8 ^{13}C NMR spectrum of **3c** in $CDCl_3$ (100 MHz)

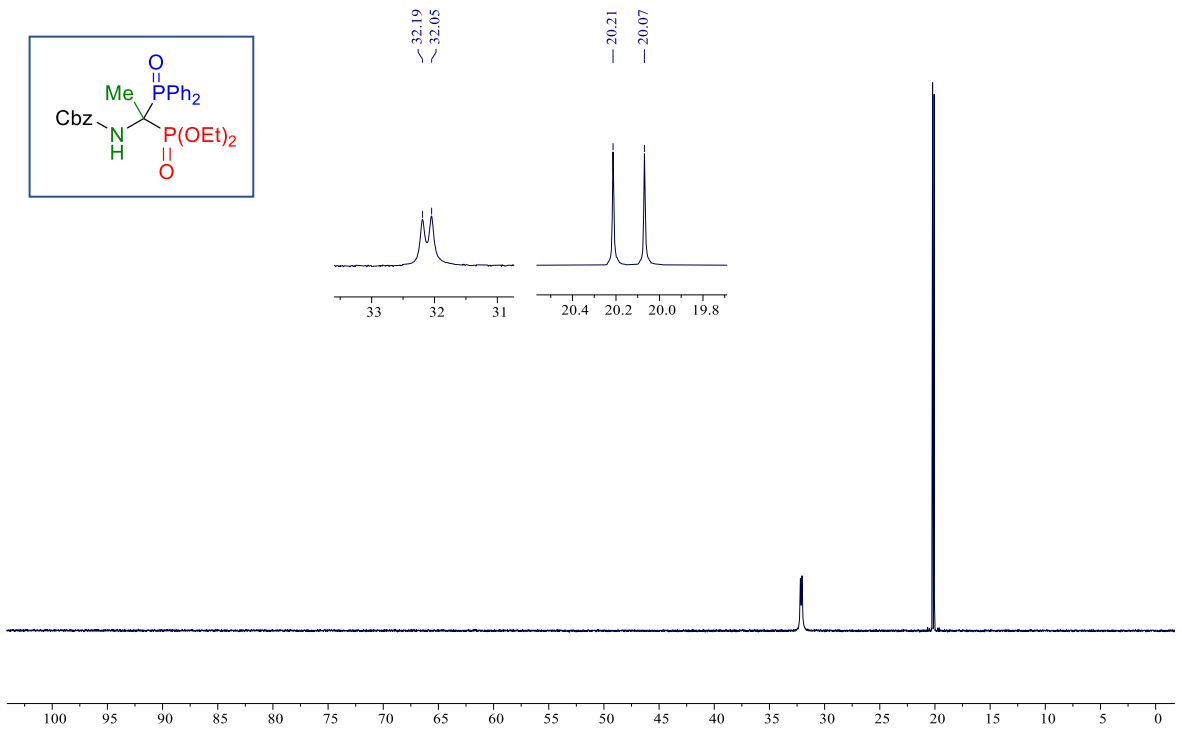


Fig. S9 ^{31}P NMR spectrum of **3c** in $CDCl_3$ (162 MHz)

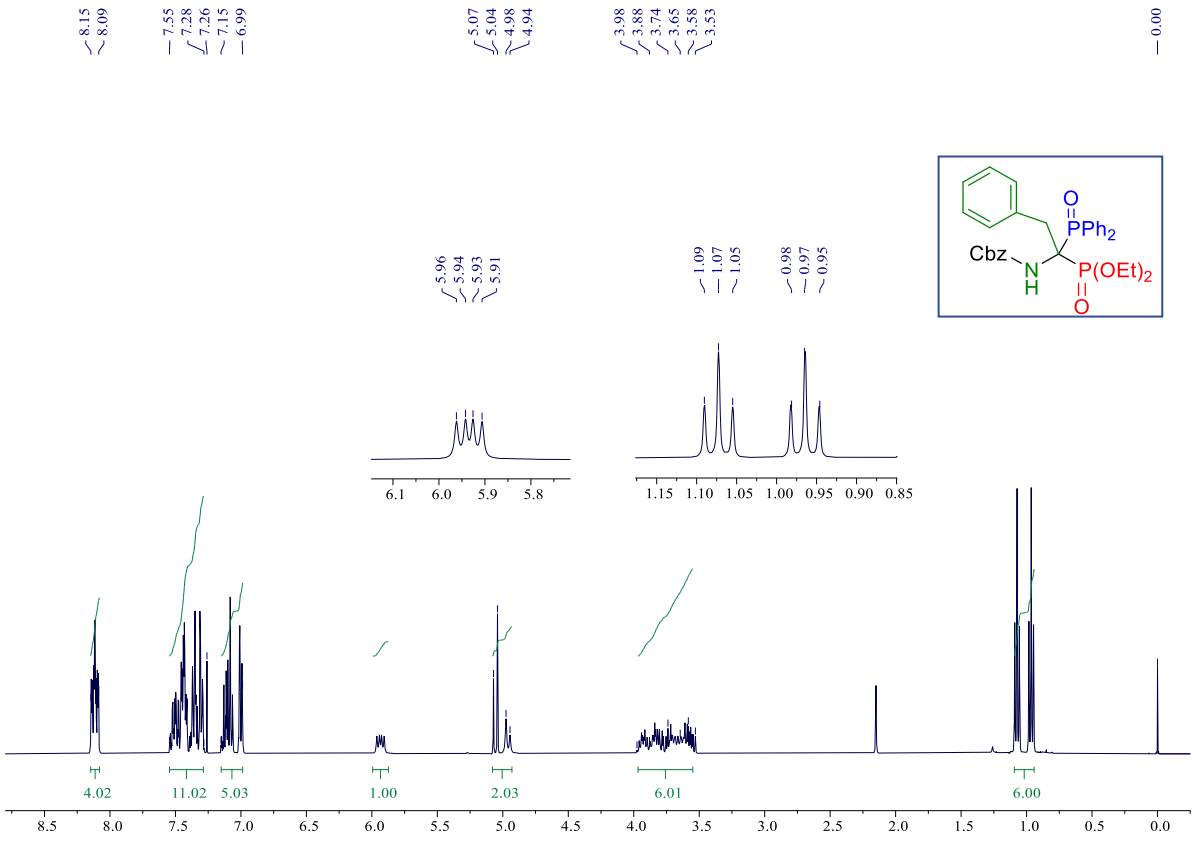


Fig. S10 ^{1}H NMR spectrum of **3d** in $CDCl_3$ (400 MHz)

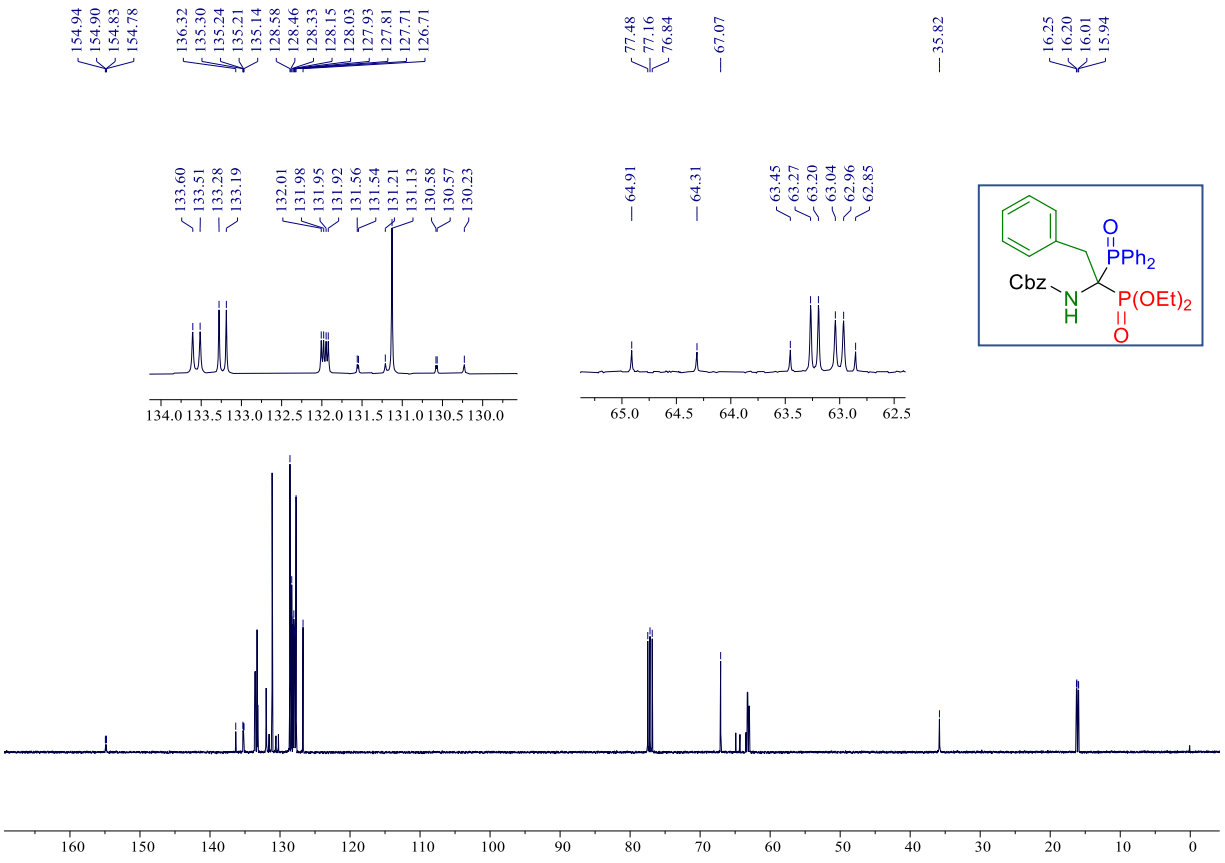


Fig. S11 ^{13}C NMR spectrum of **3d** in $CDCl_3$ (100 MHz)

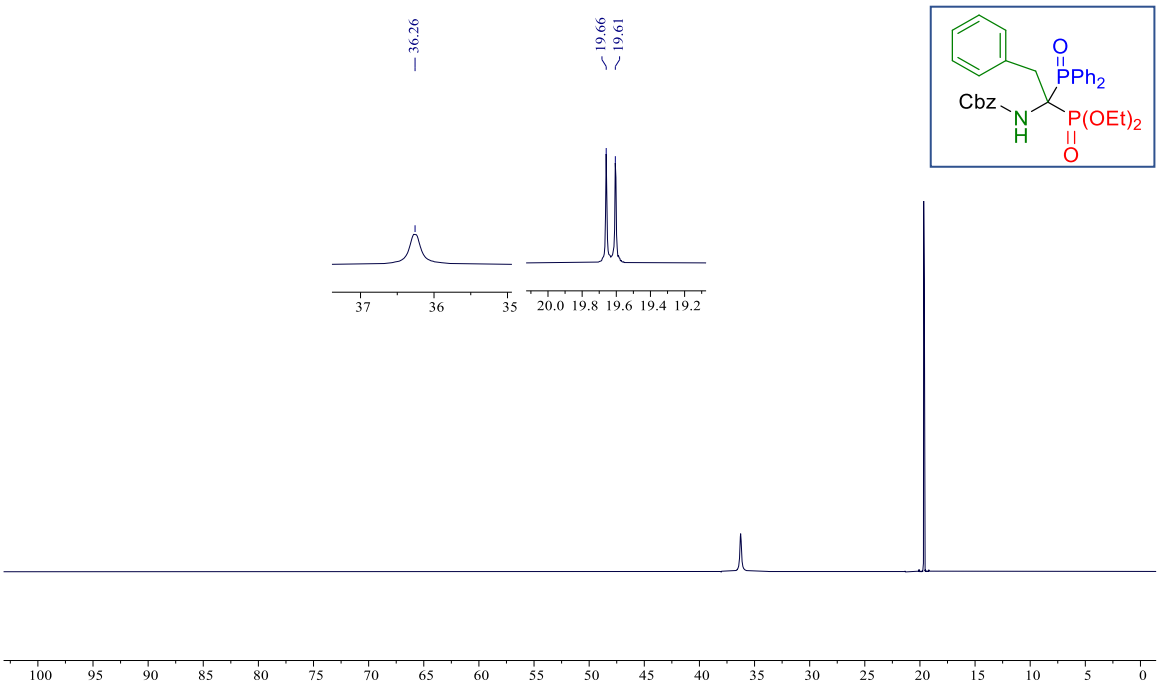


Fig. S12 ^{31}P NMR spectrum of **3d** in $CDCl_3$ (162 MHz)

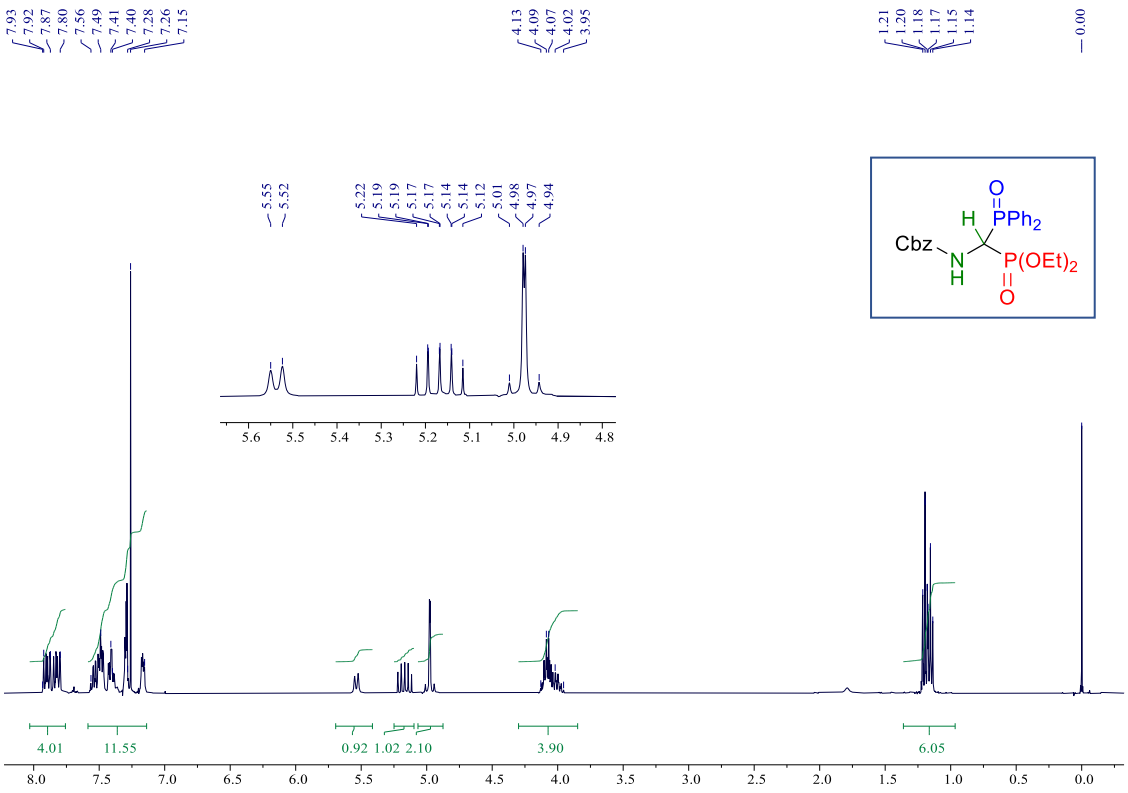


Fig. S13 ^{1}H NMR spectrum of **3e** in $CDCl_3$ (400 MHz)

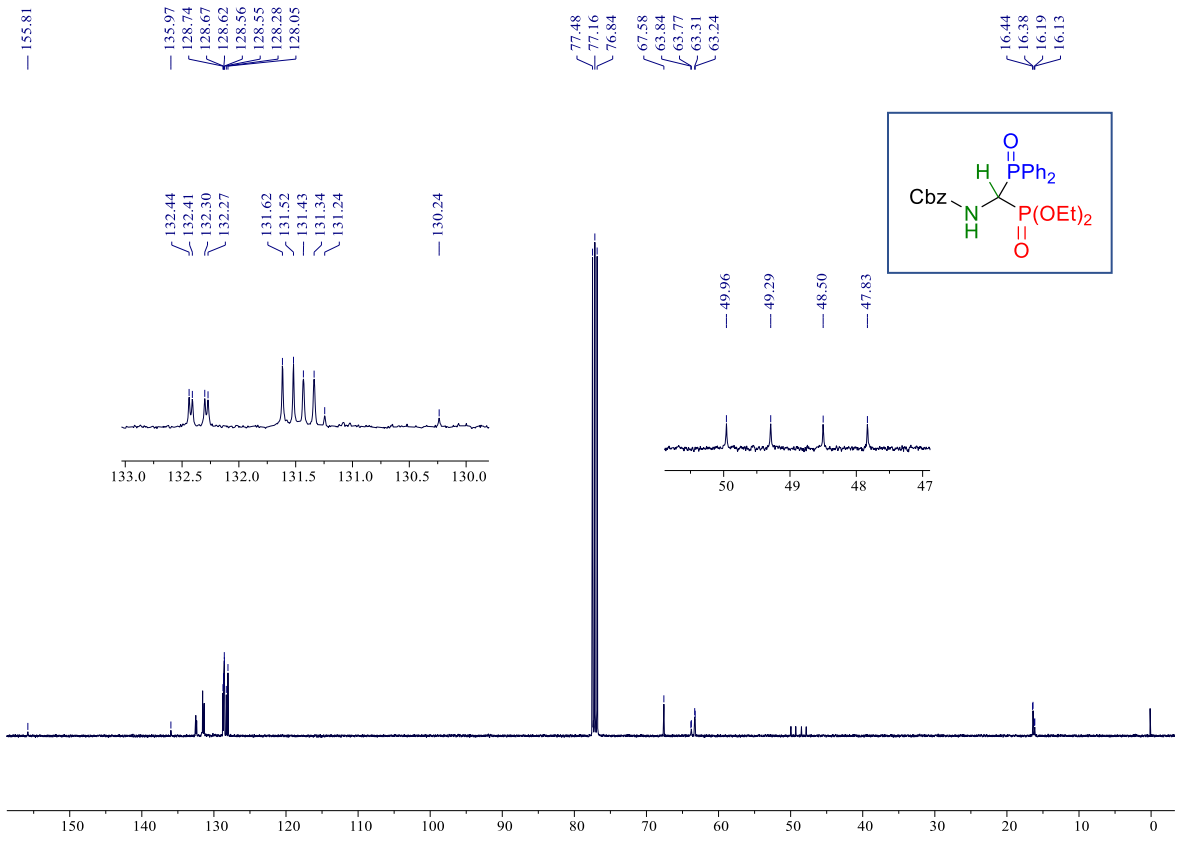


Fig. S14 ^{13}C-NMR spectrum of **3e** in $CDCl_3$ (100 MHz)

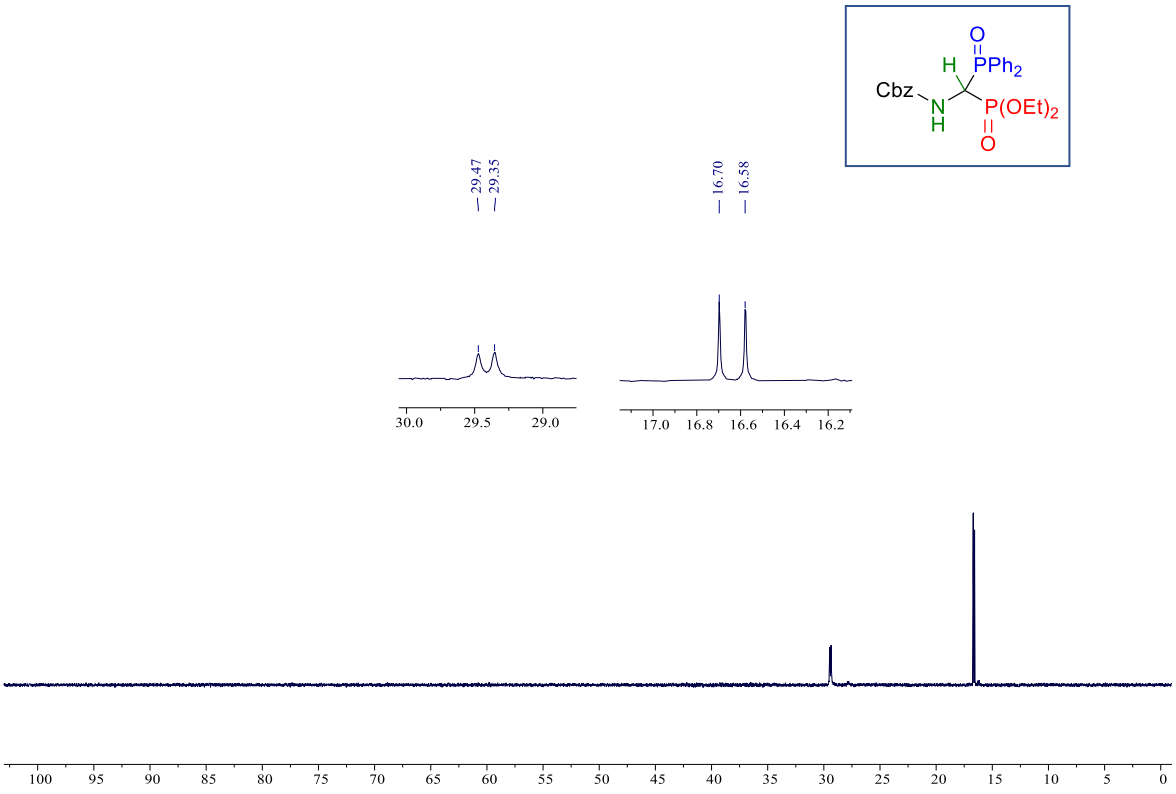


Fig. S15 ^{31}P-NMR spectrum of **3e** in $CDCl_3$ (162 MHz)

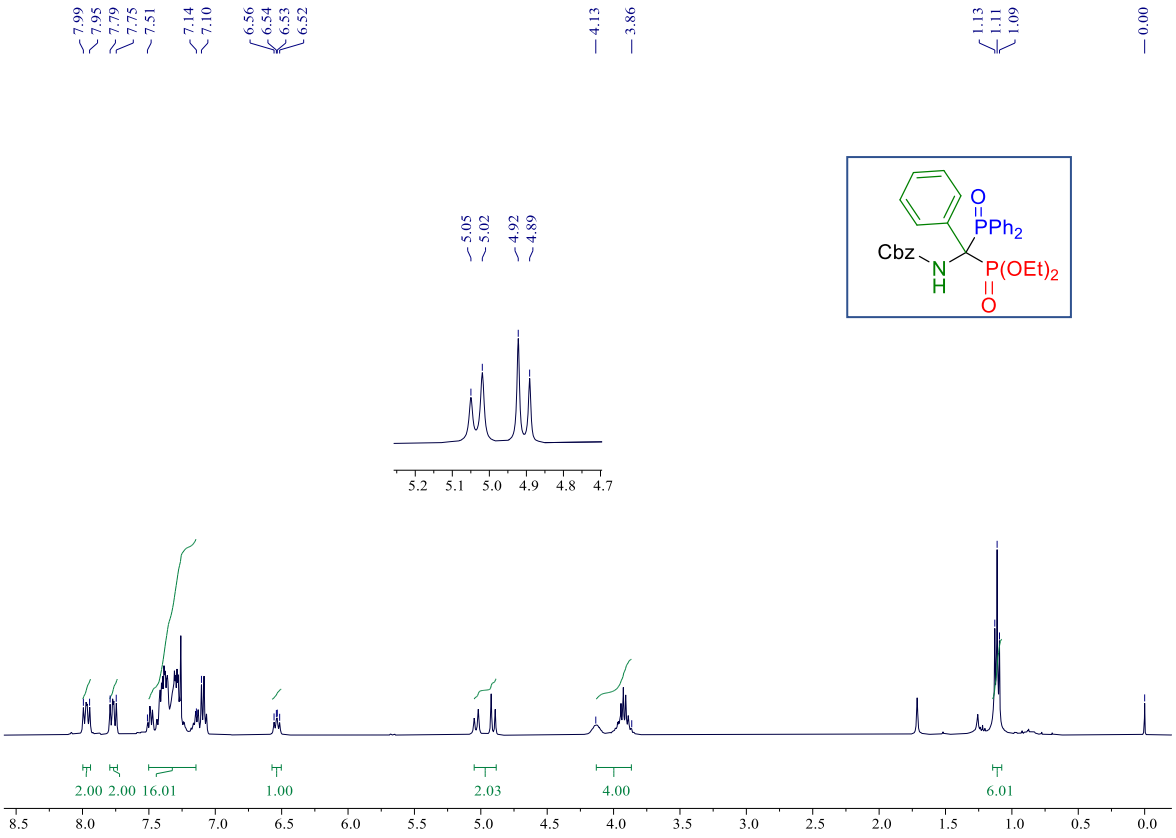


Fig. S16 ^{1}H NMR spectrum of **3f** in $CDCl_3$ (400 MHz)

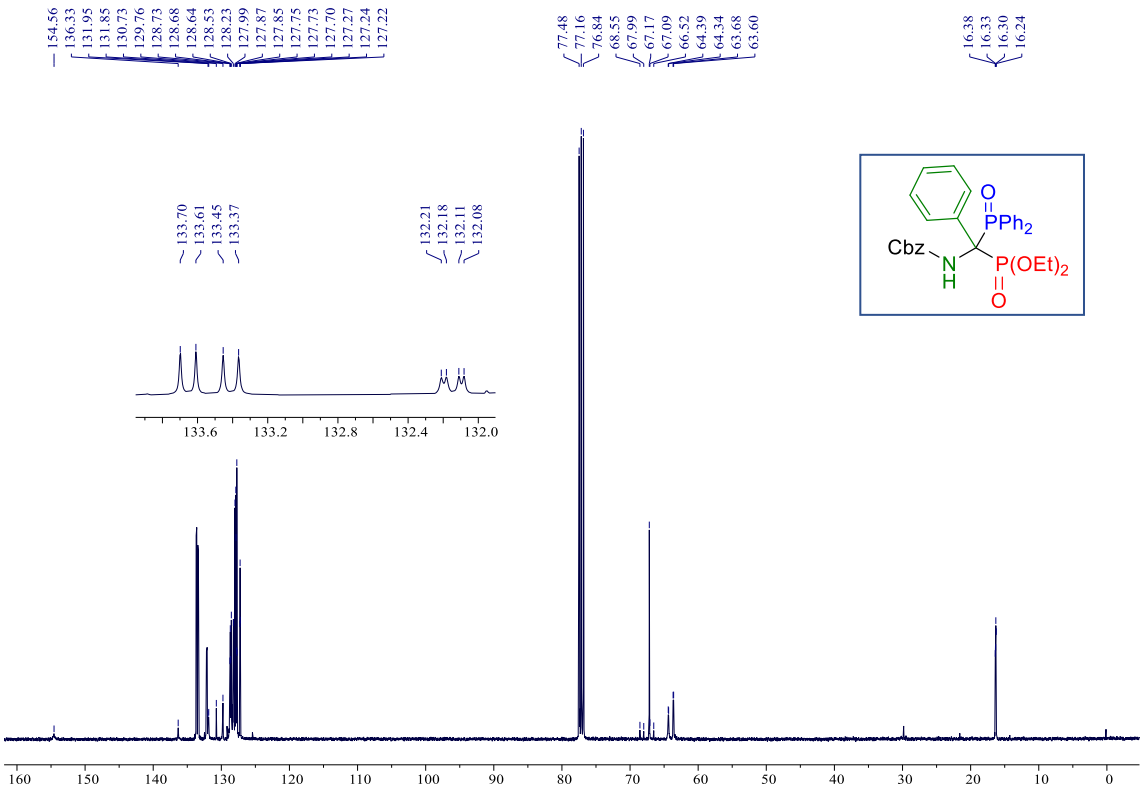


Fig. S17 ^{13}C NMR spectrum of **3f** in $CDCl_3$ (100 MHz)

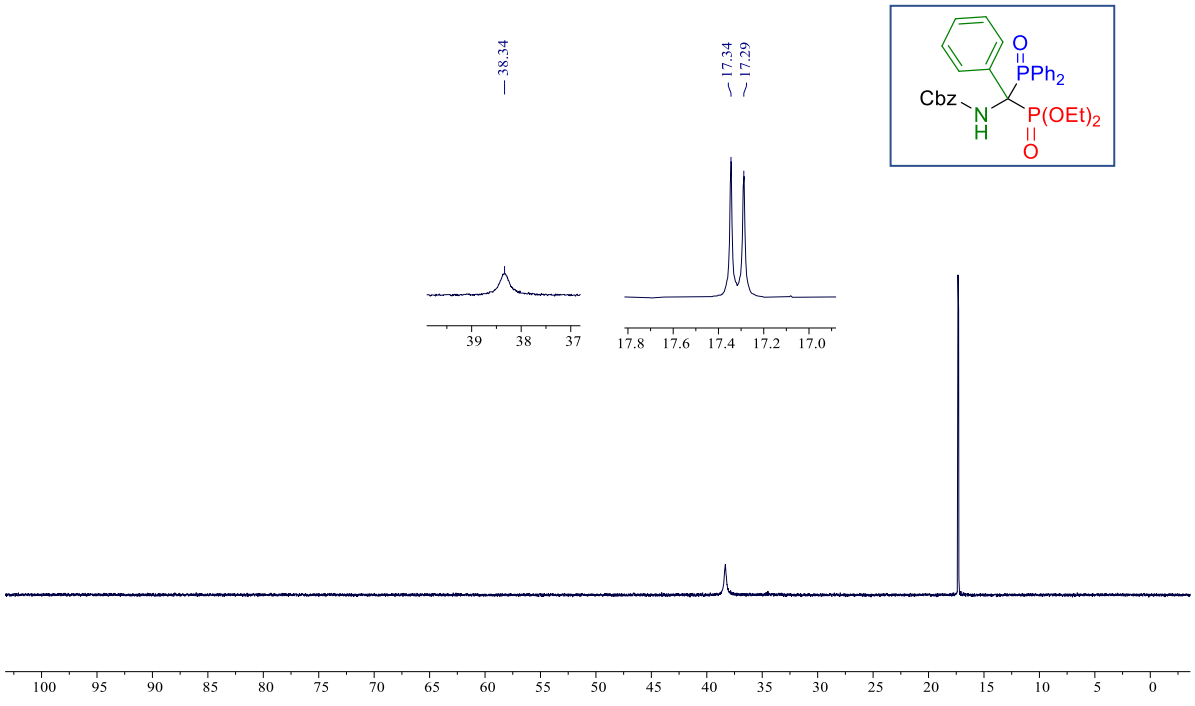


Fig. S18 ^{31}P NMR spectrum of **3f** in $CDCl_3$ (162 MHz)

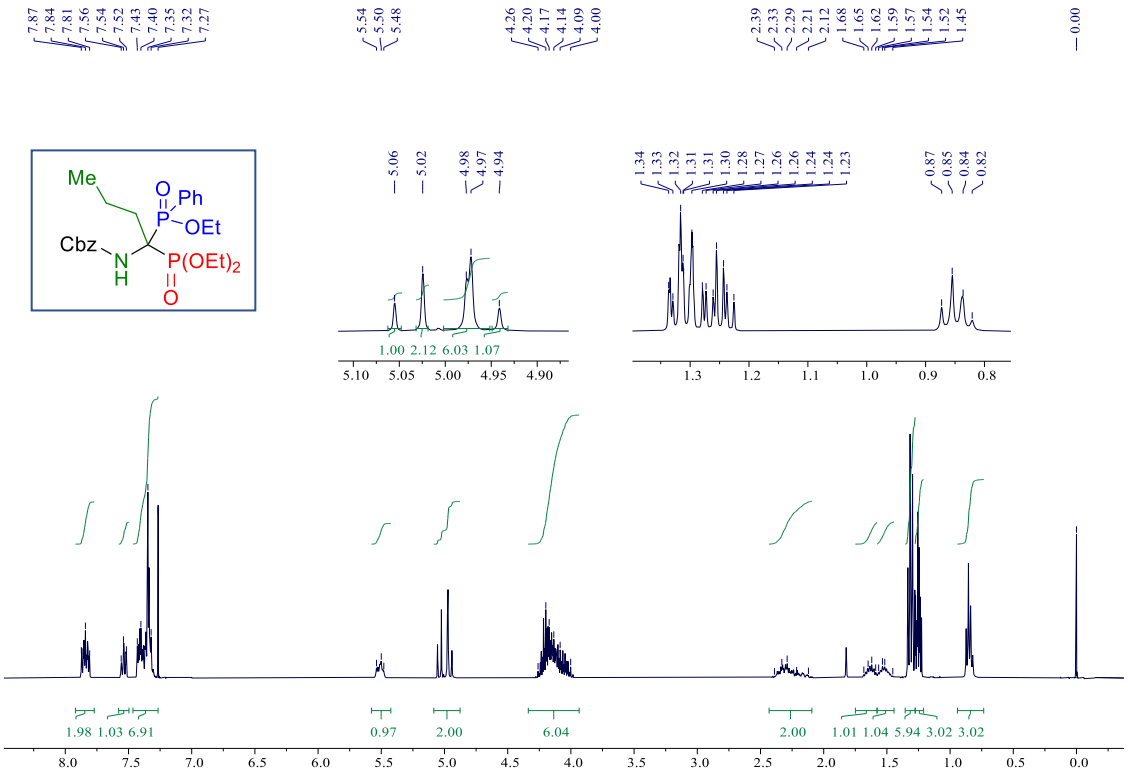


Fig. S19 ^{1}H NMR spectrum of **3g** in $CDCl_3$ (400 MHz)

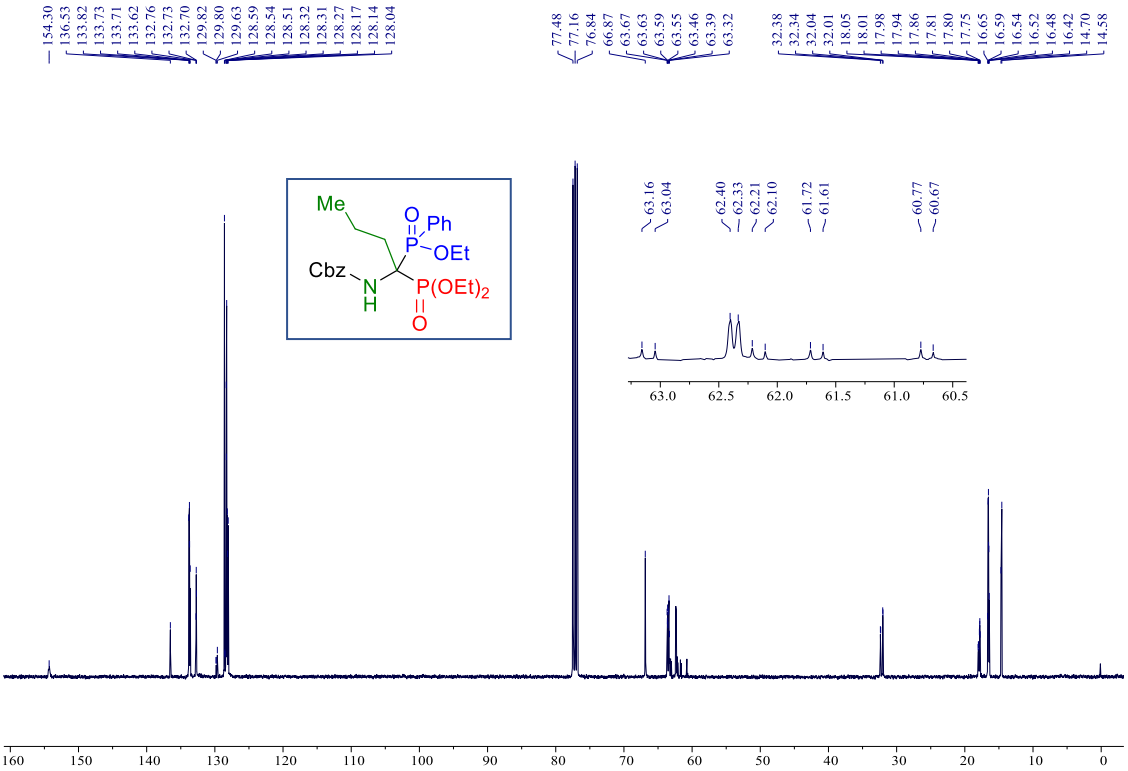


Fig. S20 ^{13}C NMR spectrum of **3g** in $CDCl_3$ (100 MHz)

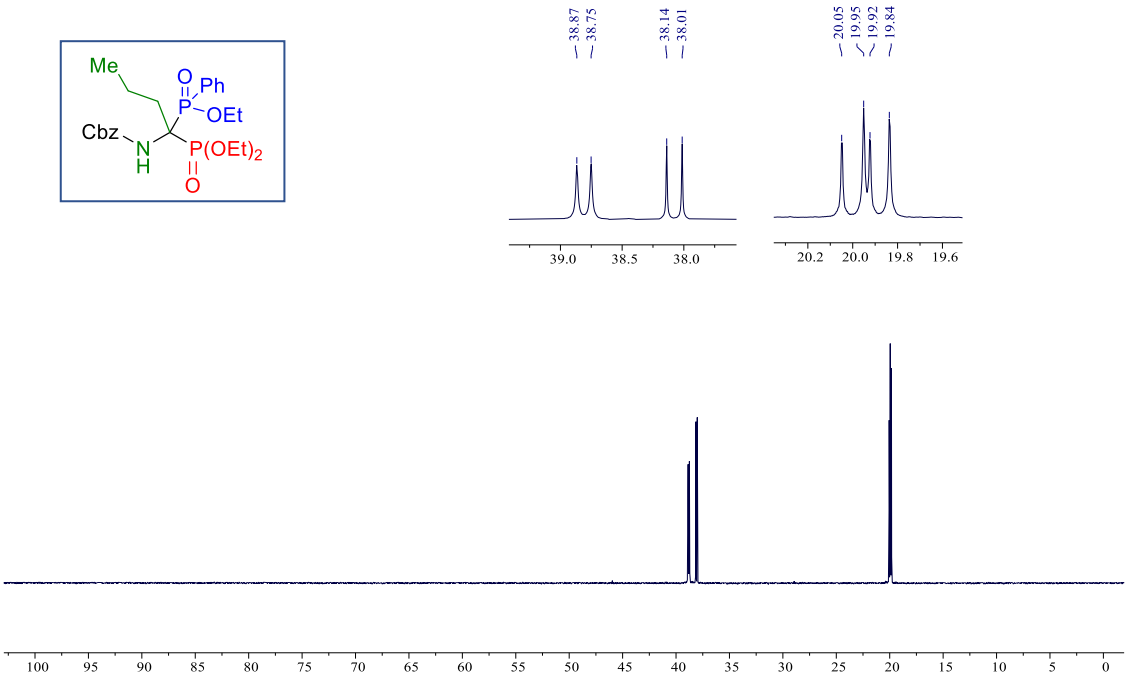


Fig. S21 ^{31}P NMR spectrum of **3g** in $CDCl_3$ (162 MHz)

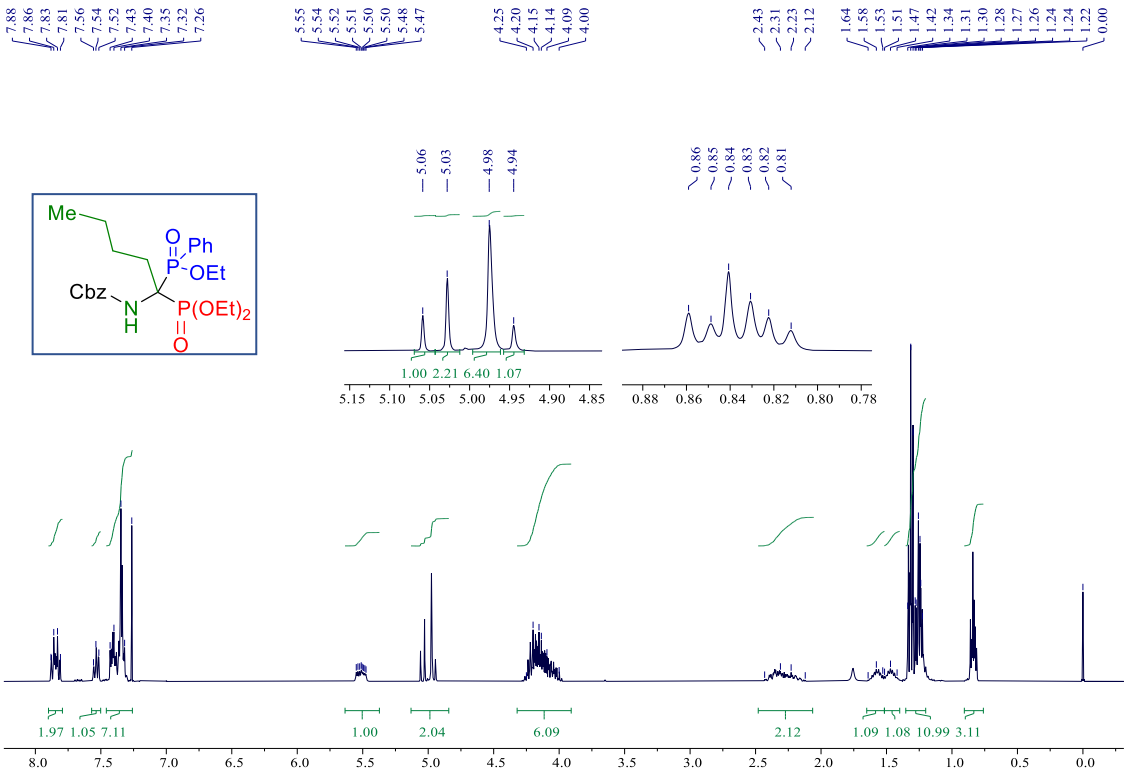


Fig. S22 ^{1}H NMR spectrum of **3h** in $CDCl_3$ (400 MHz)

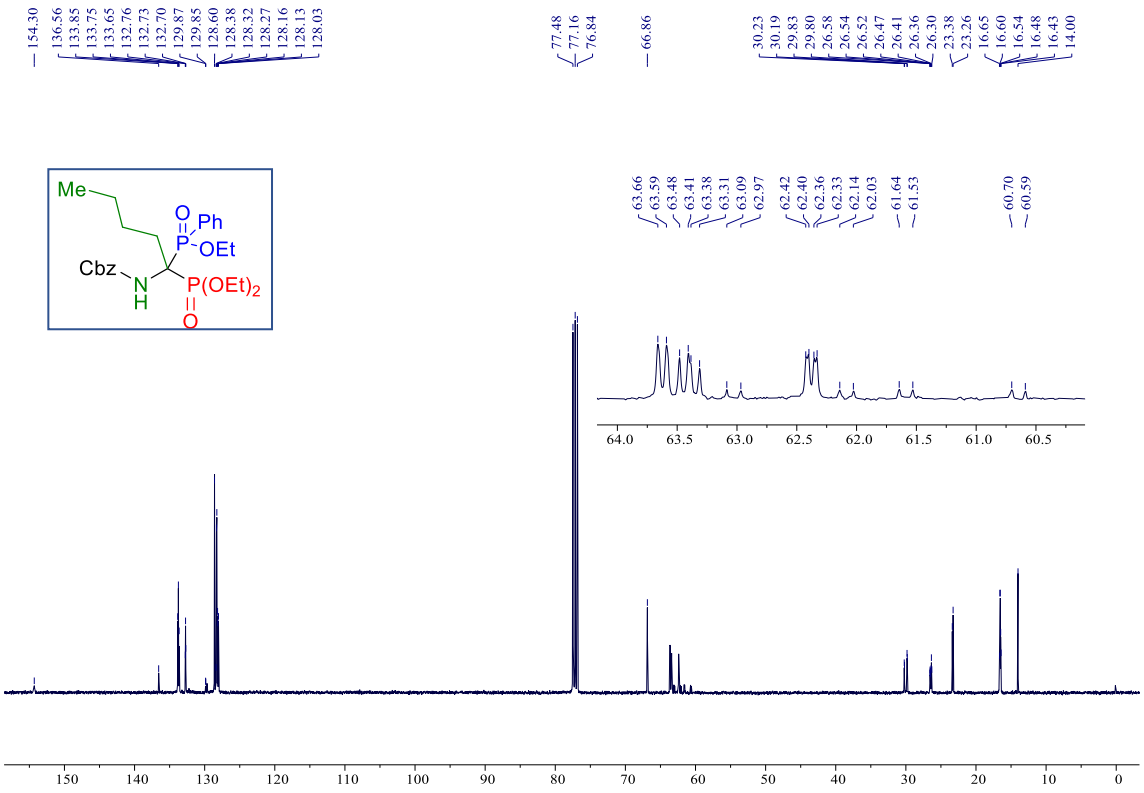


Fig. S23 ^{13}C NMR spectrum of **3h** in $CDCl_3$ (100 MHz)

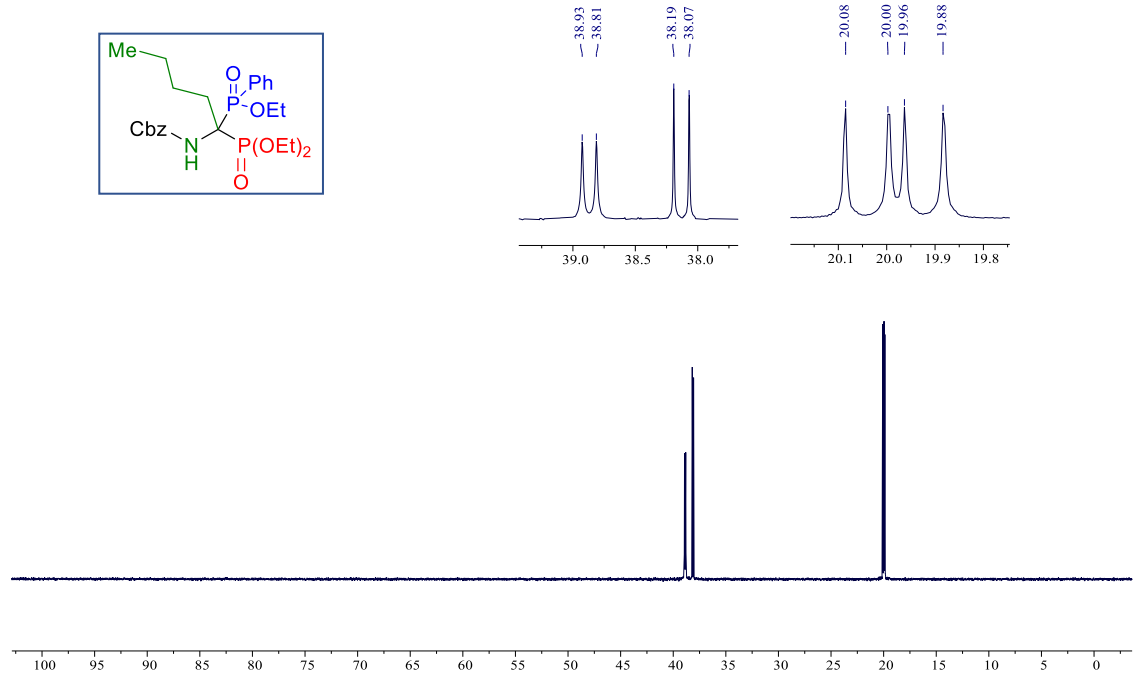


Fig. S24 ^{31}P NMR spectrum of **3h** in $CDCl_3$ (162 MHz)

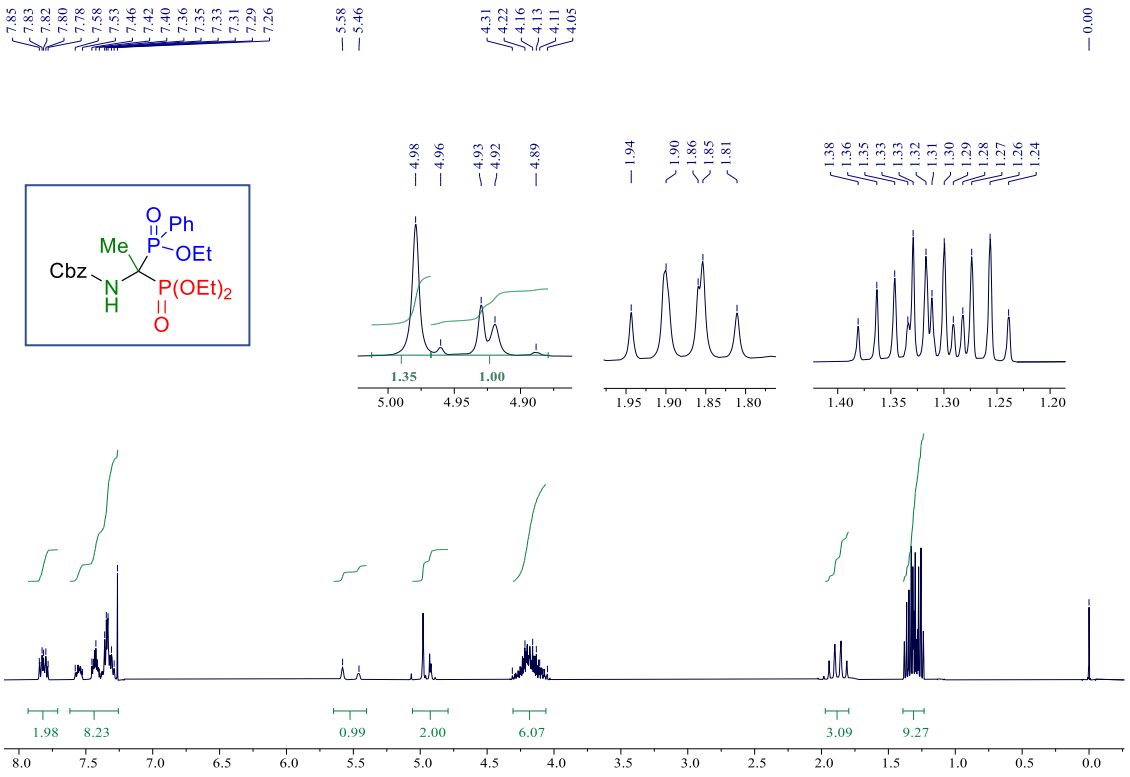


Fig. S25 ^{1}H NMR spectrum of **3i** in $CDCl_3$ (400 MHz)

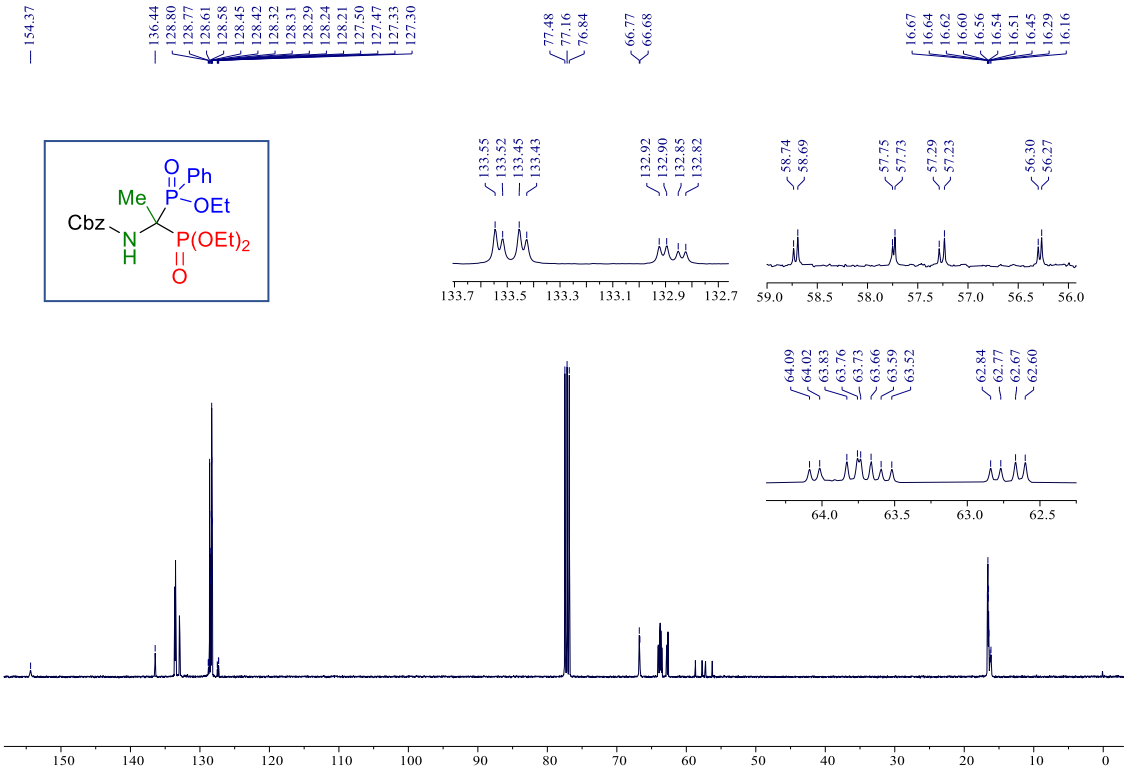


Fig. S26 ^{13}C NMR spectrum of **3i** in $CDCl_3$ (100 MHz)

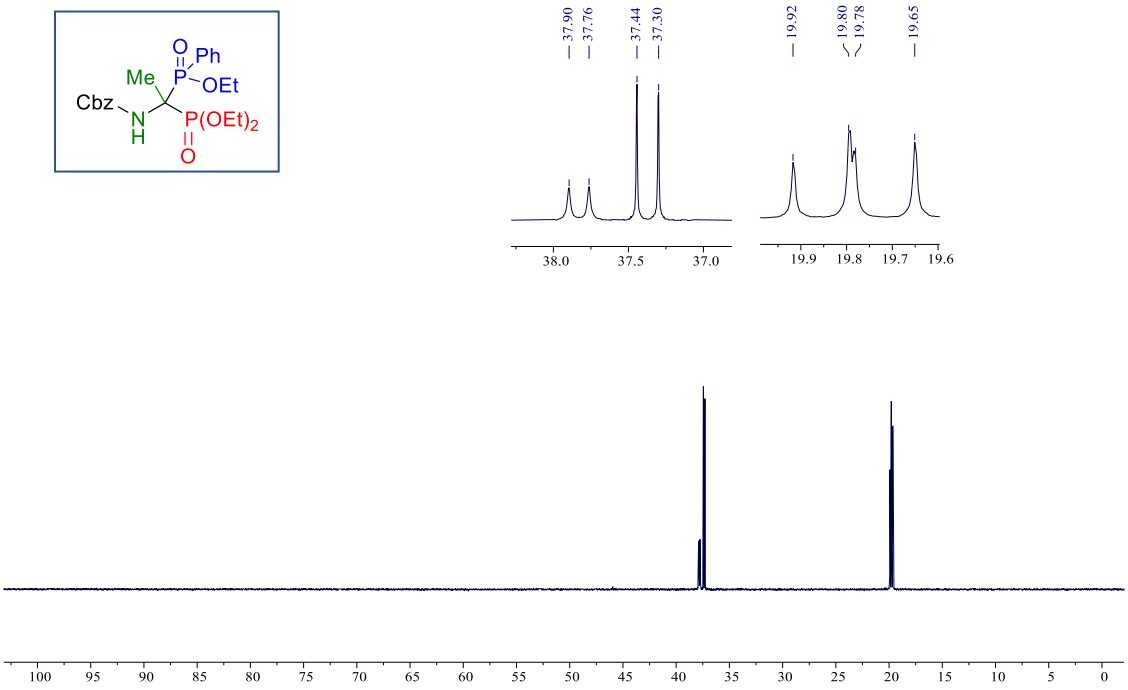


Fig. S27 ^{31}P NMR spectrum of **3i** in $CDCl_3$ (162 MHz)

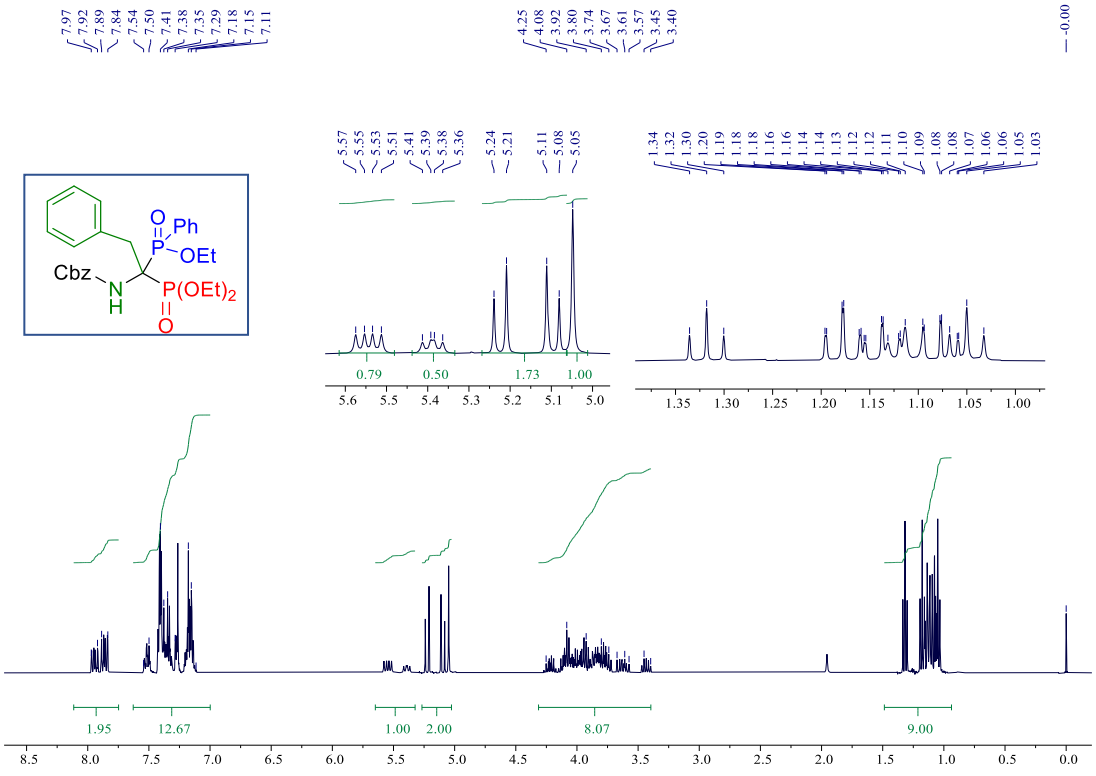


Fig. S28 ^{1}H NMR spectrum of **3j** in $CDCl_3$ (400 MHz)

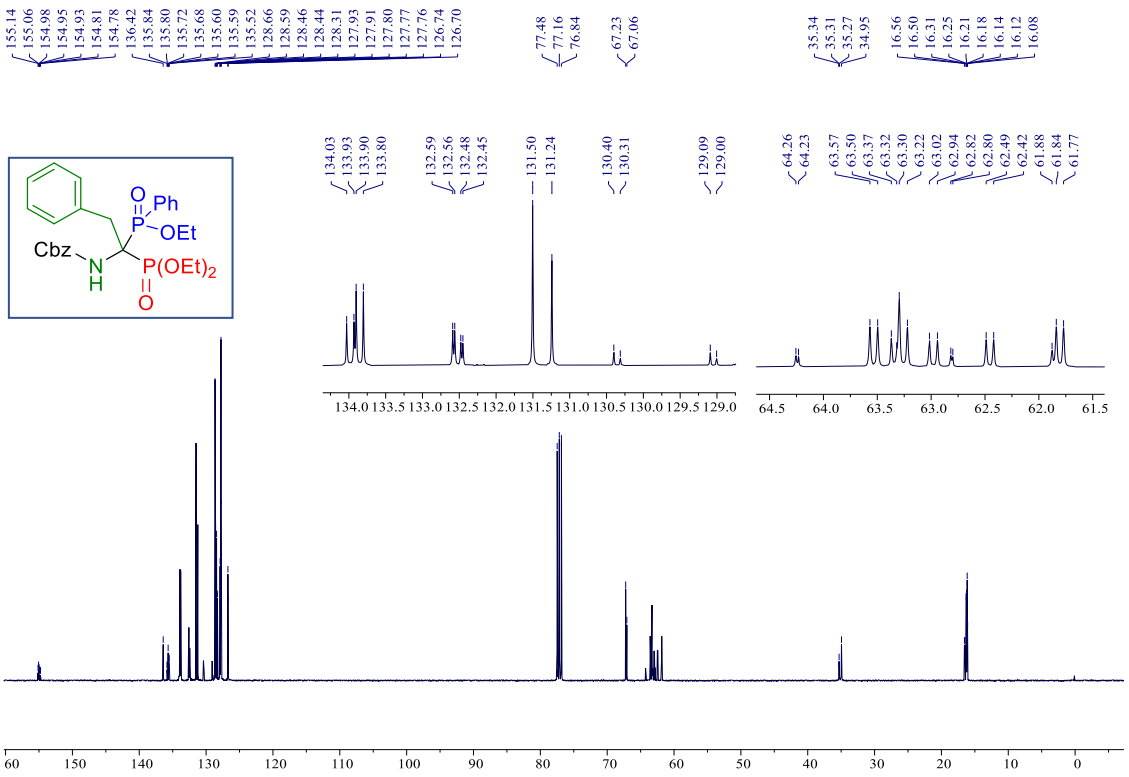


Fig. S29 ^{13}C NMR spectrum of **3j** in $CDCl_3$ (100 MHz)

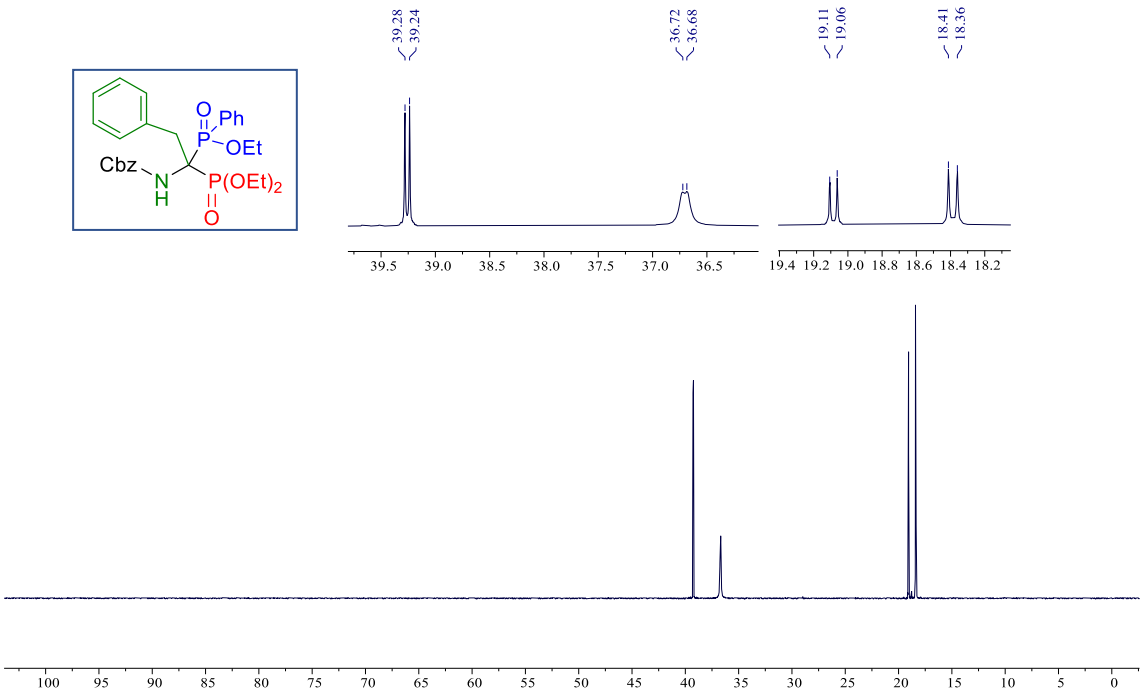


Fig. S30 ^{31}P NMR spectrum of **3j** in $CDCl_3$ (162 MHz)

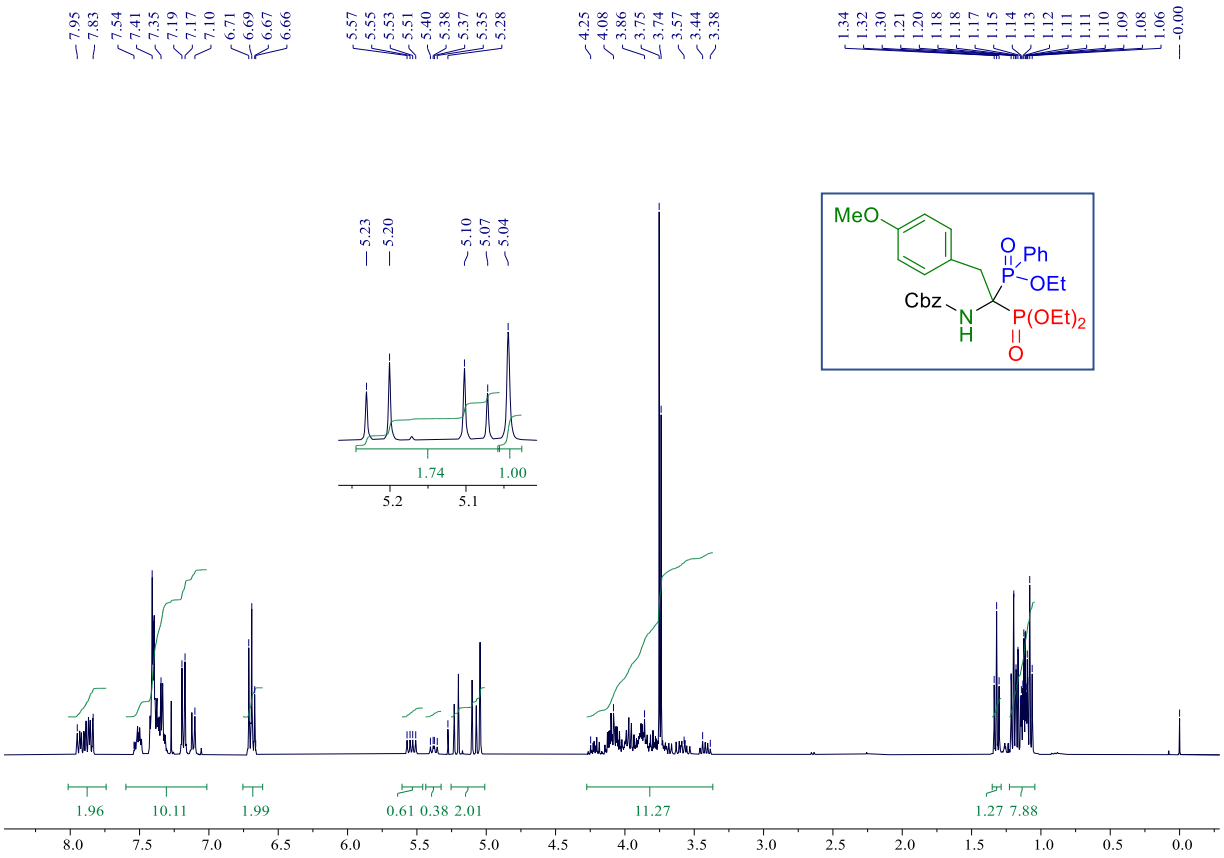


Fig. S31 ^{1}H NMR spectrum of **3k** in $CDCl_3$ (400 MHz)

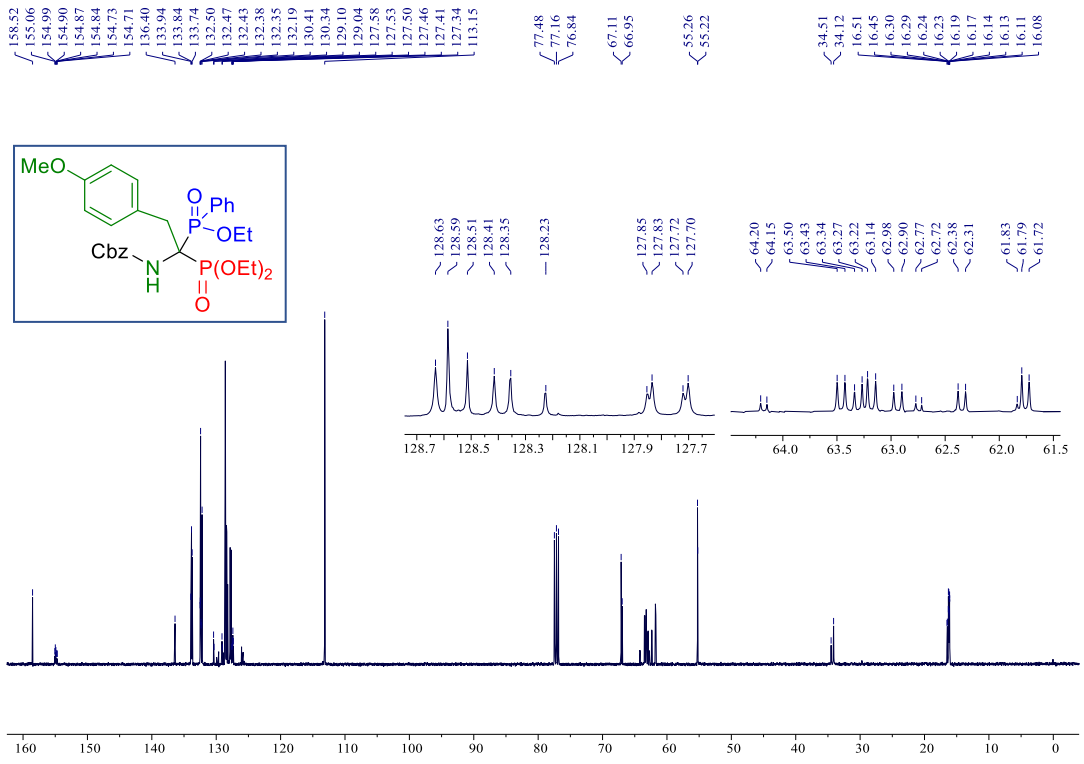


Fig. S32 ^{13}C NMR spectrum of **3k** in $CDCl_3$ (100 MHz)

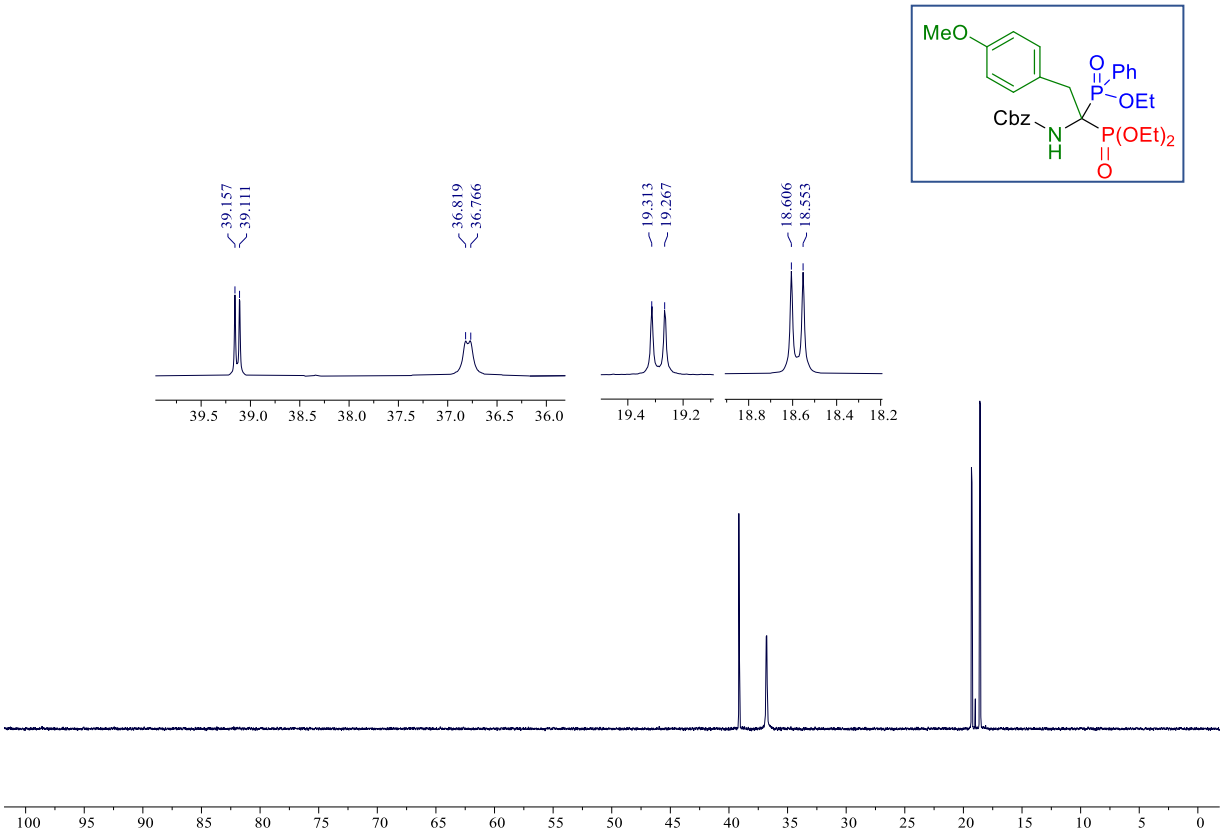


Fig. S33 ^{31}P NMR spectrum of **3k** in $CDCl_3$ (162 MHz)

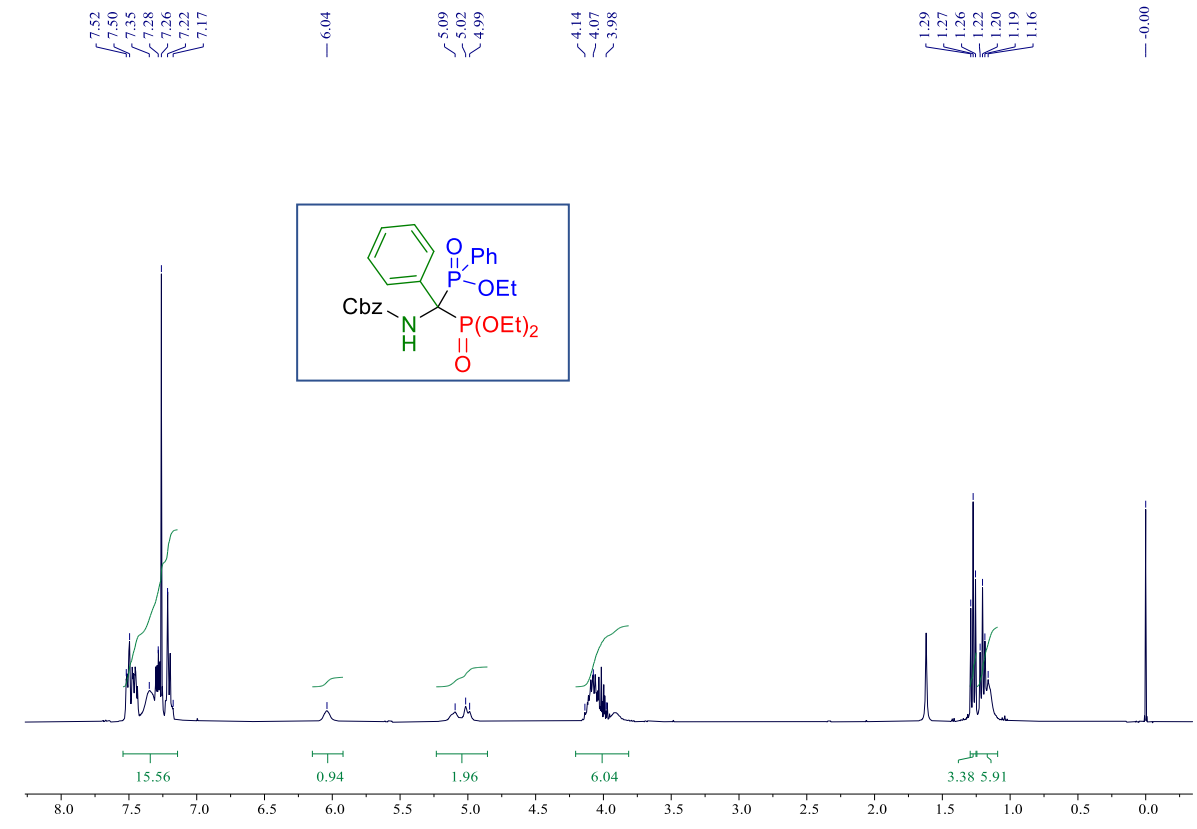


Fig. S34 ^{1}H NMR spectrum of major diastereomer of **3l** in $CDCl_3$ (400 MHz)

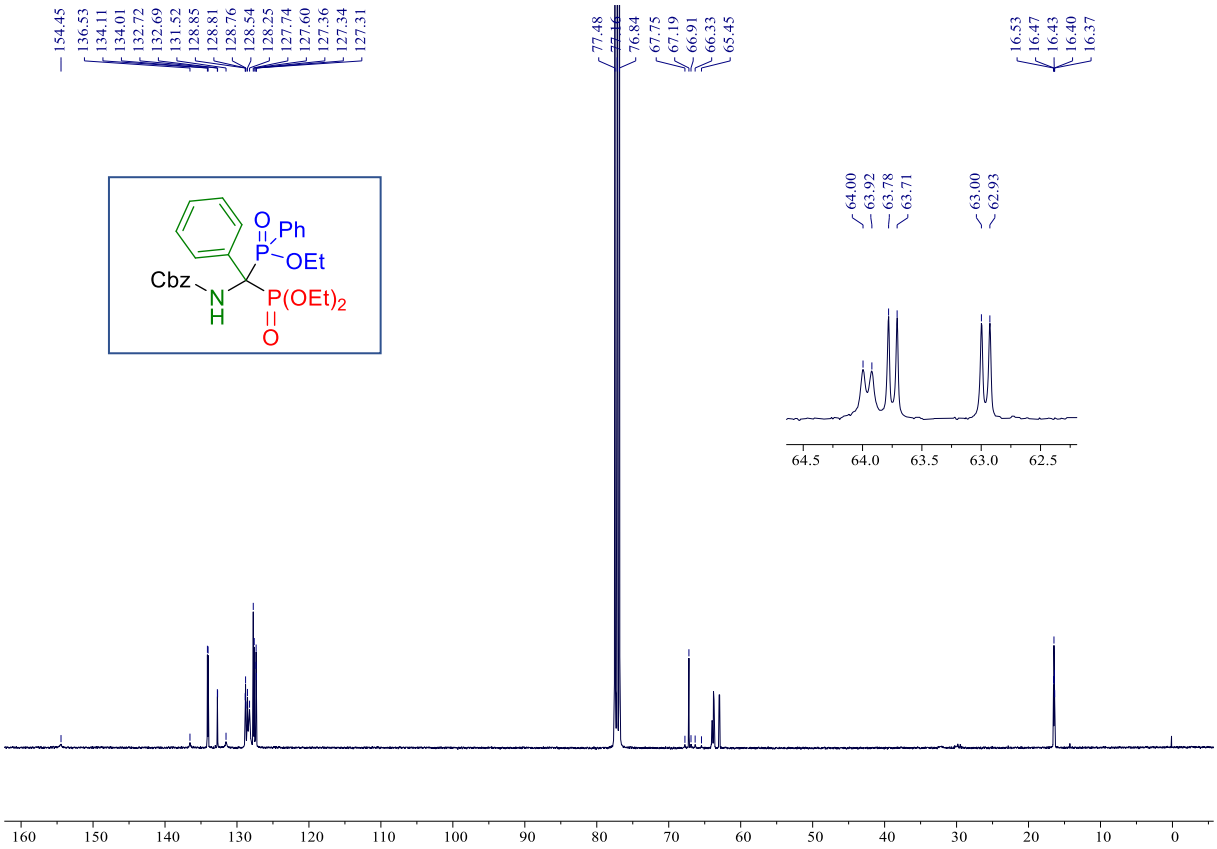


Fig. S35 ^{13}C NMR spectrum of major diastereomer of **3l** in $CDCl_3$ (100 MHz)

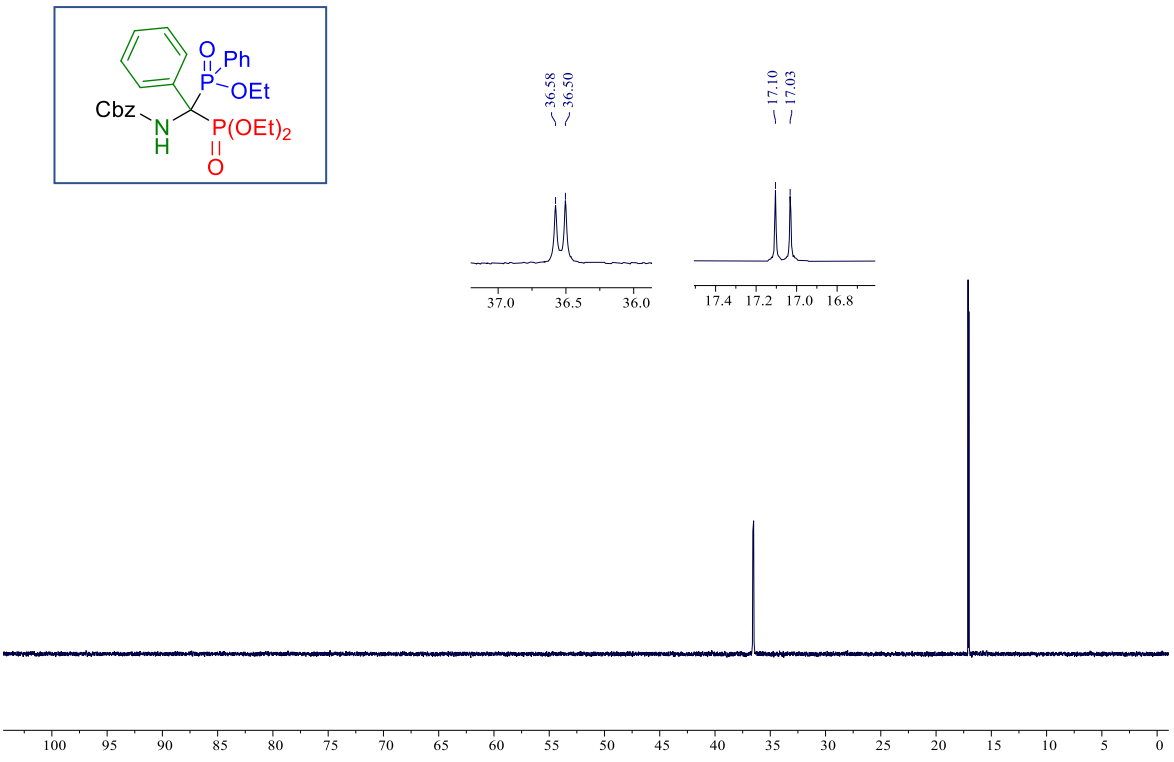


Fig. S36 ^{31}P NMR spectrum of major diastereomer of **3l** in $CDCl_3$ (162 MHz)

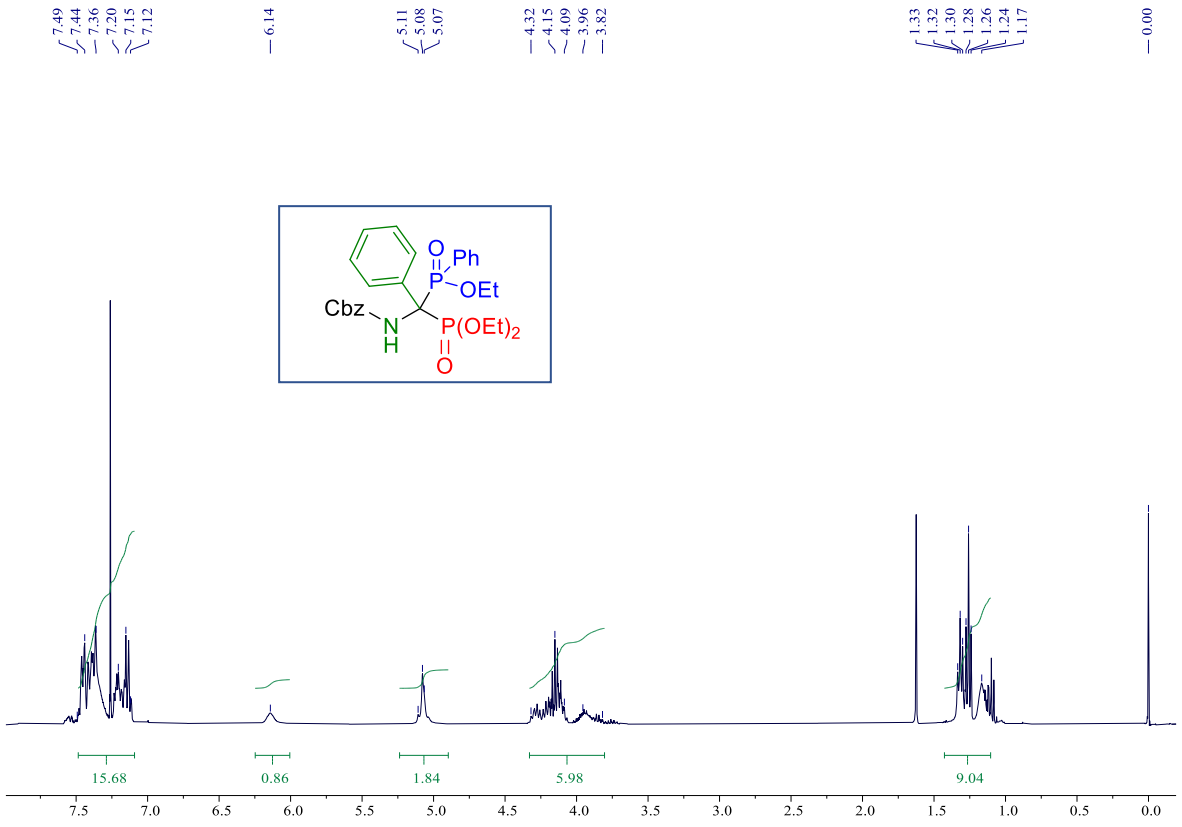


Fig. S37 ^{1}H NMR spectrum of minor diastereomer of **3l** in $CDCl_3$ (400 MHz)

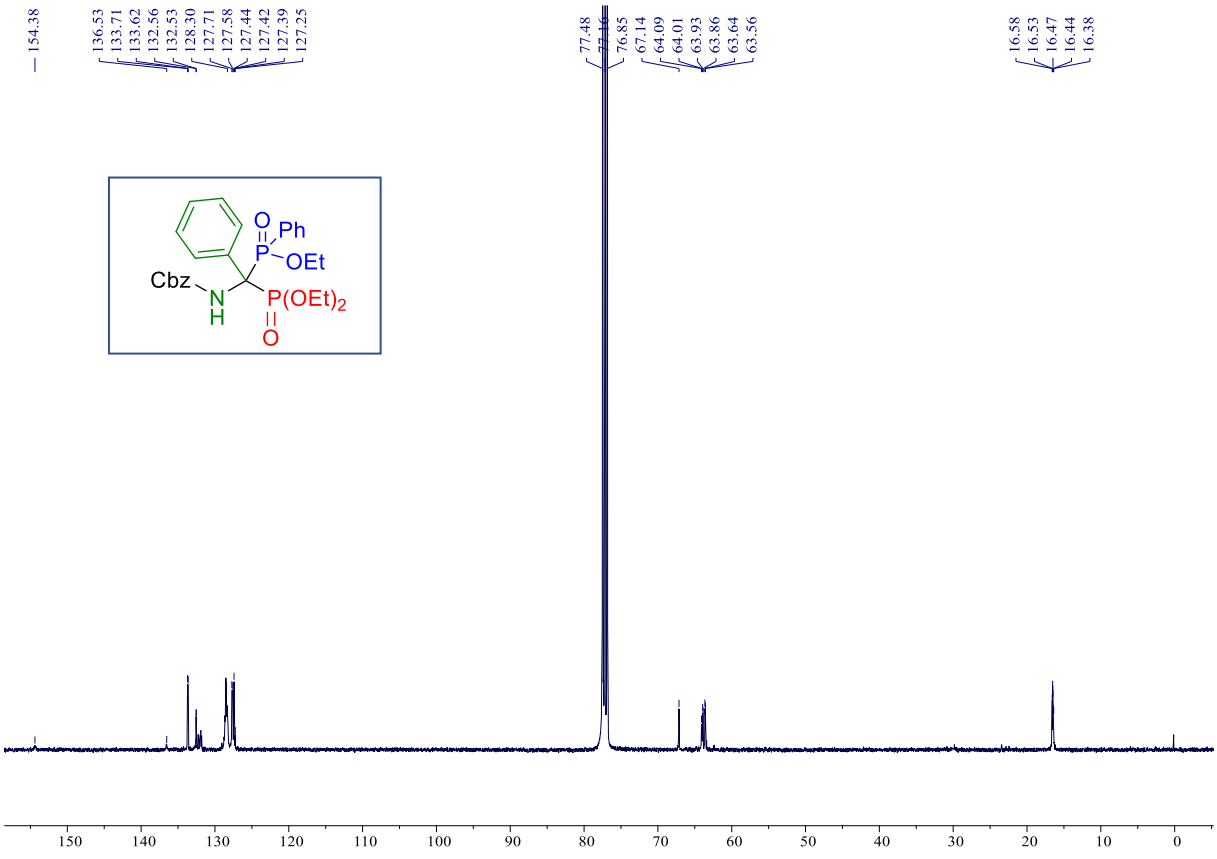


Fig. S38 ^{13}C NMR spectrum of minor diastereomer of **3l** in $CDCl_3$ (100 MHz)

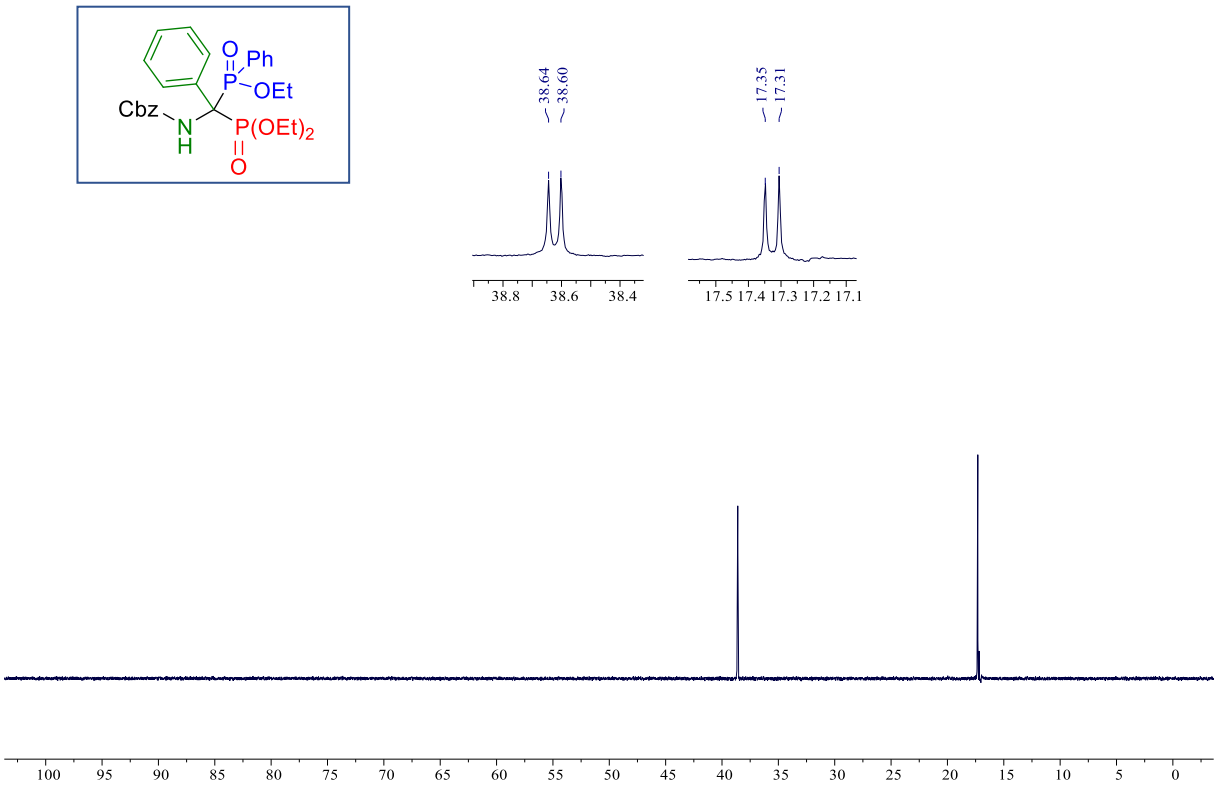


Fig. S39 ^{31}P NMR spectrum of minor diastereomer of **3l** in $CDCl_3$ (162 MHz)

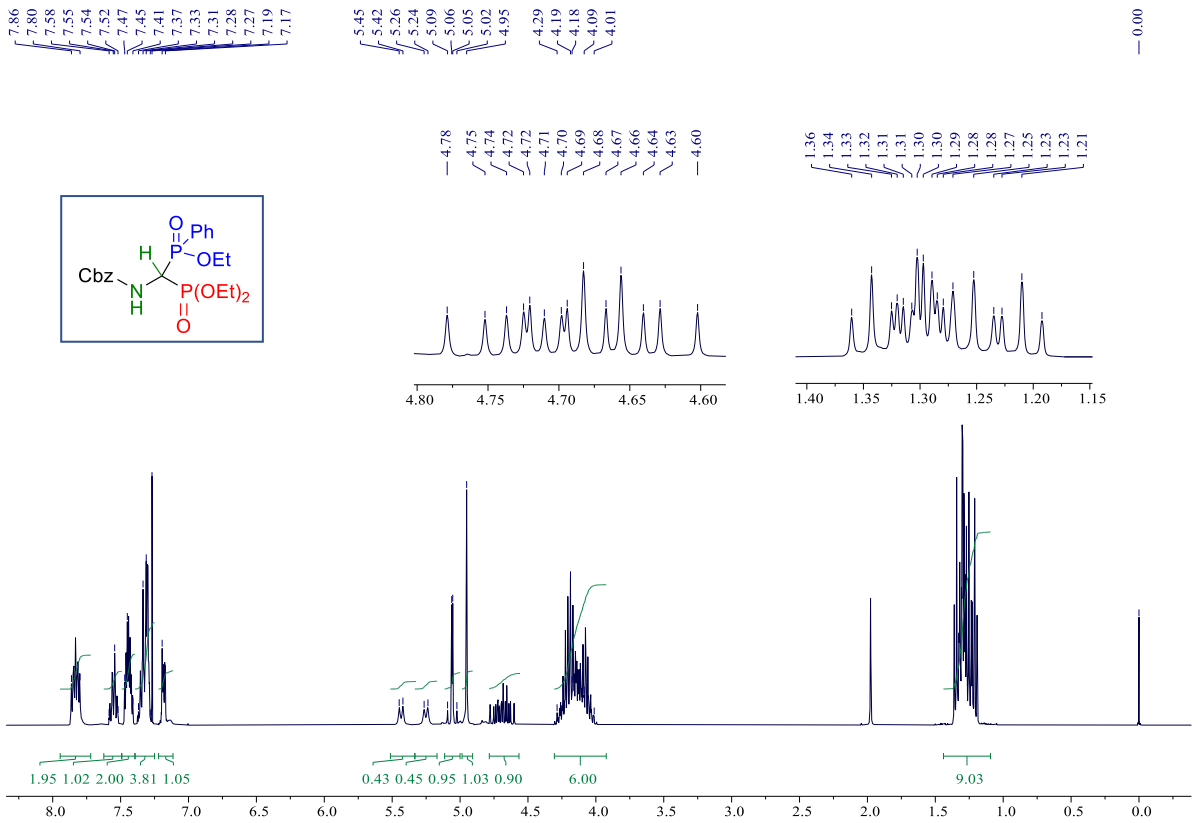


Fig. S40 ^{1}H NMR spectrum of **3m** in $CDCl_3$ (400 MHz)

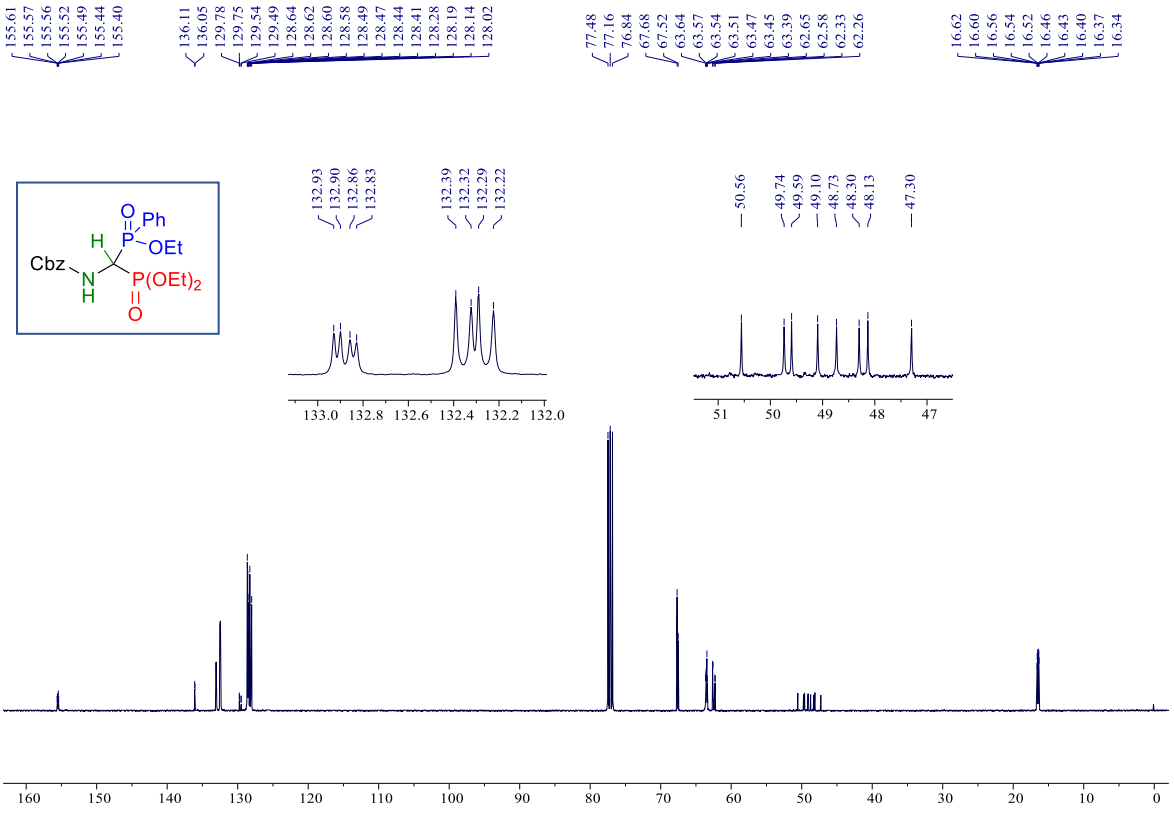


Fig. S41 ^{13}C NMR spectrum of **3m** in $CDCl_3$ (100 MHz)

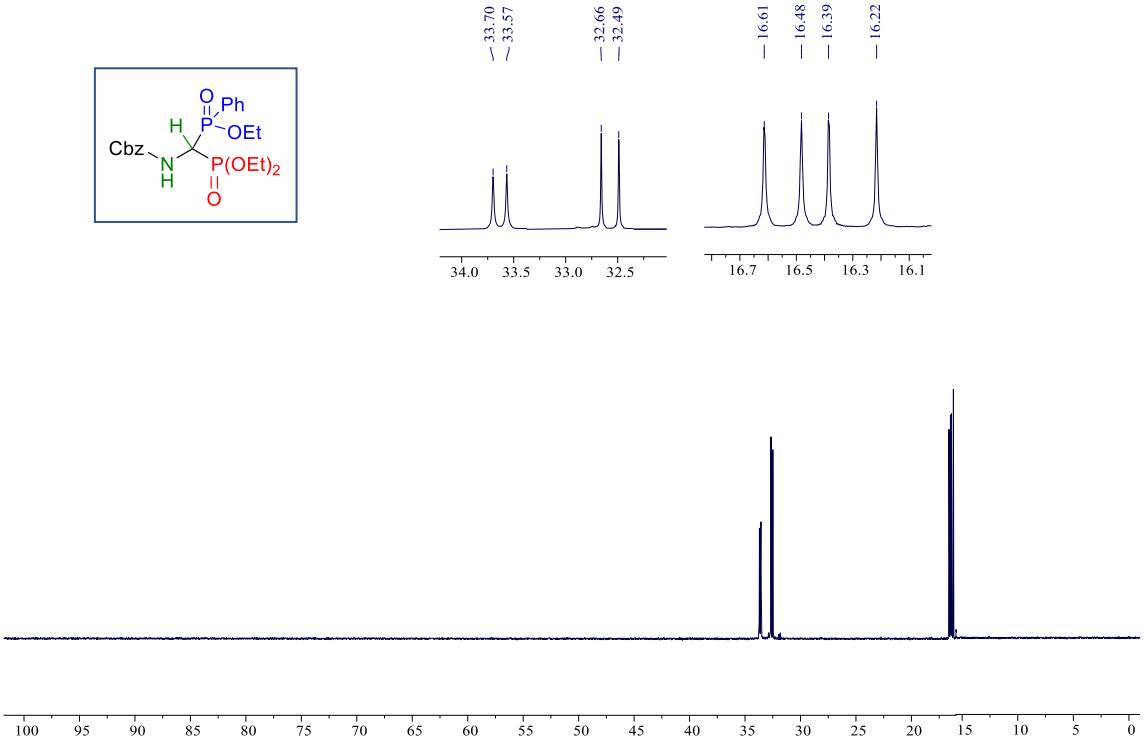


Fig. S42 ^{31}P NMR spectrum of **3m** in $CDCl_3$ (162 MHz)