Electronic Supplementary Material (ESI) for Organic & Biomolecular Chemistry

Combined C-H Functionalization/O-H Insertion Reaction to Form Tertiary β-Alkoxy Substituted β-Aminophosphonates Catalyzed by $[Cu(MeCN)_4]PF_6$

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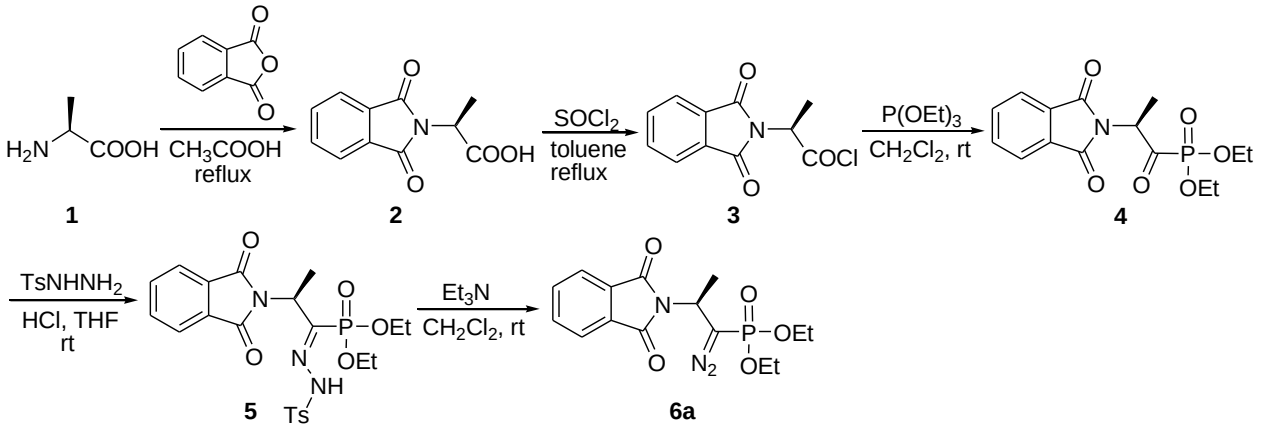
Supporting Information

List of contents (pages)

General Comments.

All reactions and manipulations were performed using standard Schlenk techniques. All solvents were purified and dried according to standard procedures before use. Unless otherwise indicated, all materials were obtained from commercial sources, and used as purchased without dehydration. Flash column chromatography was performed on silica gel (particle size 10-40 μm, Ocean Chemical Factory of Qingdao, China). Nitrogen gas (99.999%) was purchased from Boc Gas Inc. Preparative high performance liquid chromatography (HPLC) for separations were performed using Agilent 1260 Infinity machines. ^{1}H NMR, ^{13}C NMR and ^{31}P NMR spectra were recorded on Brucker-400 (400 MHz for ^{1}H, 101MHz for ^{13}C) spectrometers. Chemical shifts were reported in ppm downfield from internal $Si(CH_3)_4$. H_3PO_4 served as internal standard (δ = 0 ppm) for ^{31}P NMR. The crystal structure was determined on a Bruker SMART 1000 CCD diffractometer. Mass spectra were recorded on a LCQ advantage spectrometer with ESI resource. HR-MS were recorded on APEXII and ZAB-HS spectrometer. Melting points were determined on a T-4 melting point apparatus (uncorrected). Optical rotations were recorded on a Perkin Elemer 241 Polarimeter.

General procedure for the synthesis of α-diazophosphonate 6a



A solution of L-α-alanine **1** (5 g, 0.056 mol) and phthalicacidanhydride (7.4 g, 0.05 mol) in 10 mL acetic acid was stirred at room temperature for several minutes, then the solution was heated to reflux for 2h. The mixture was cooled to room temperature, after evaporation acetic acid with rotate evaporator, (*S*)-2-(1,3-dioxoisoindolin-2-yl)propanoic acid **2** was obtained as a white solid. The product **2** was directly used for next reactions without further purification.

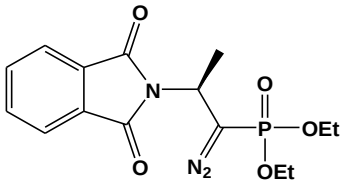
A solution of **2** (8.4 g, 0.038 mol) in 50 mL toluene was stirred at room temperature for several minutes, then thionyl chloride (4.2 mL, 0.057 mol) was added dropwise. The solution was heated to reflux for 2h and then the mixture was cooled to room temperature. The solvent and excess thionyl chloride were removed with rotate evaporator, a brownish yellow oil which contained (*S*)-2-(1,3-dioxoisoindolin-2-yl)propanoyl chloride **3** was obtained.

After dissolved the brownish oil in 10 mL of CH_2Cl_2, triethyl phosphate (6.6 mL, 0.038 mol) was introduced, and the mixture was stirred at room temperature for 4h. After evaporated the solvent under reduced pressure, a light brownish yellow oil which contained (*S*)-diethyl (2-(1,3-dioxoisoindolin-2-yl)propanoyl)phosphonate **4** was obtained.

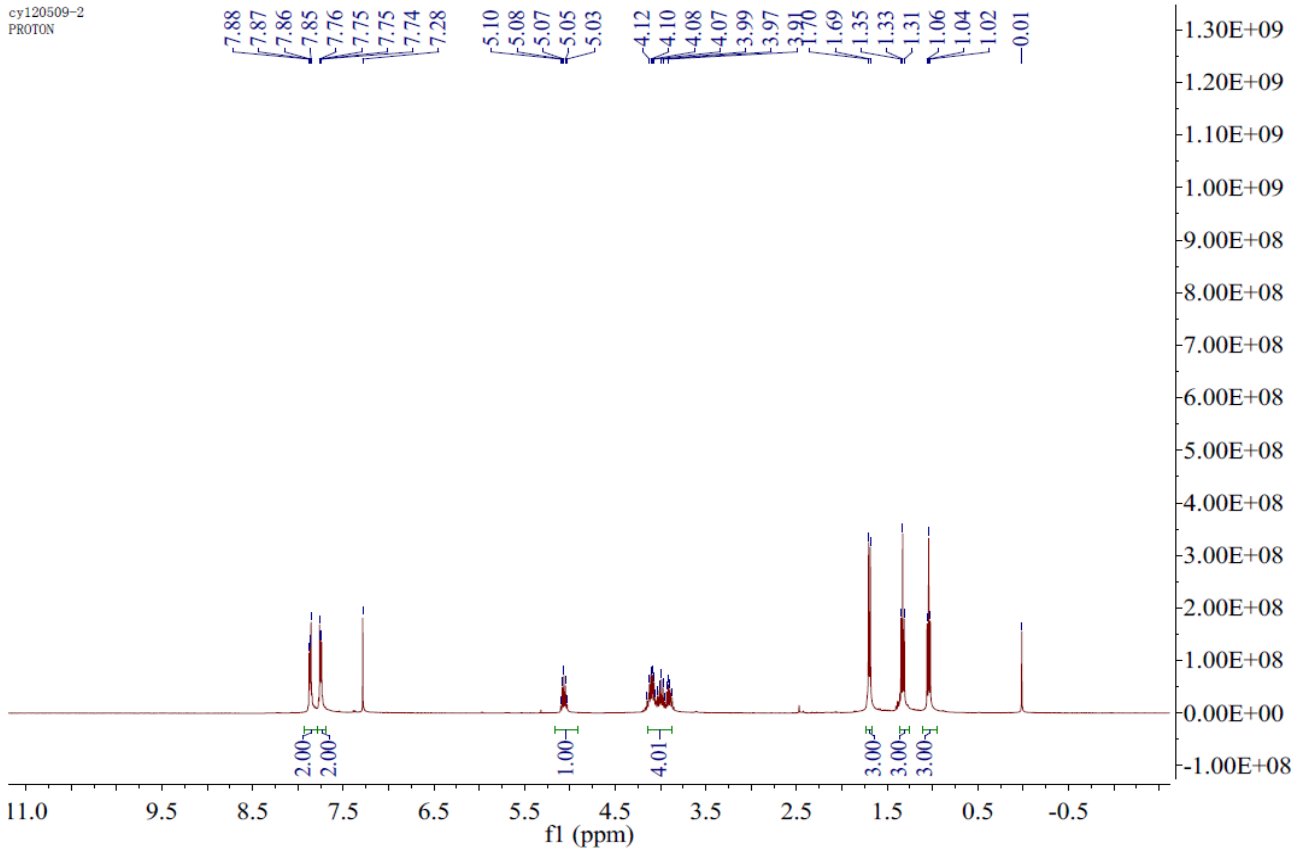
The light brownish yellow oil was dissolved in 50 mL of THF, followed by addition of 4-methylbenzenesulfonhydrazide (7 g, 0.038 mol) and 50 μL concentrated HCl aq. The mixture was stirred at room temperature for 10h. After remove the solvent under reduced pressure, a light yellow oil which contained (*S*)-diethyl (2-(1,3-dioxoisoindolin-2-yl)-1-(2-tosyl-hydrazono)propyl)phosphonate **5** was obtained. Then added 20 mL CH_2Cl_2 to dissolve the light yellow oil, triethylamine (12 mL, 0.086

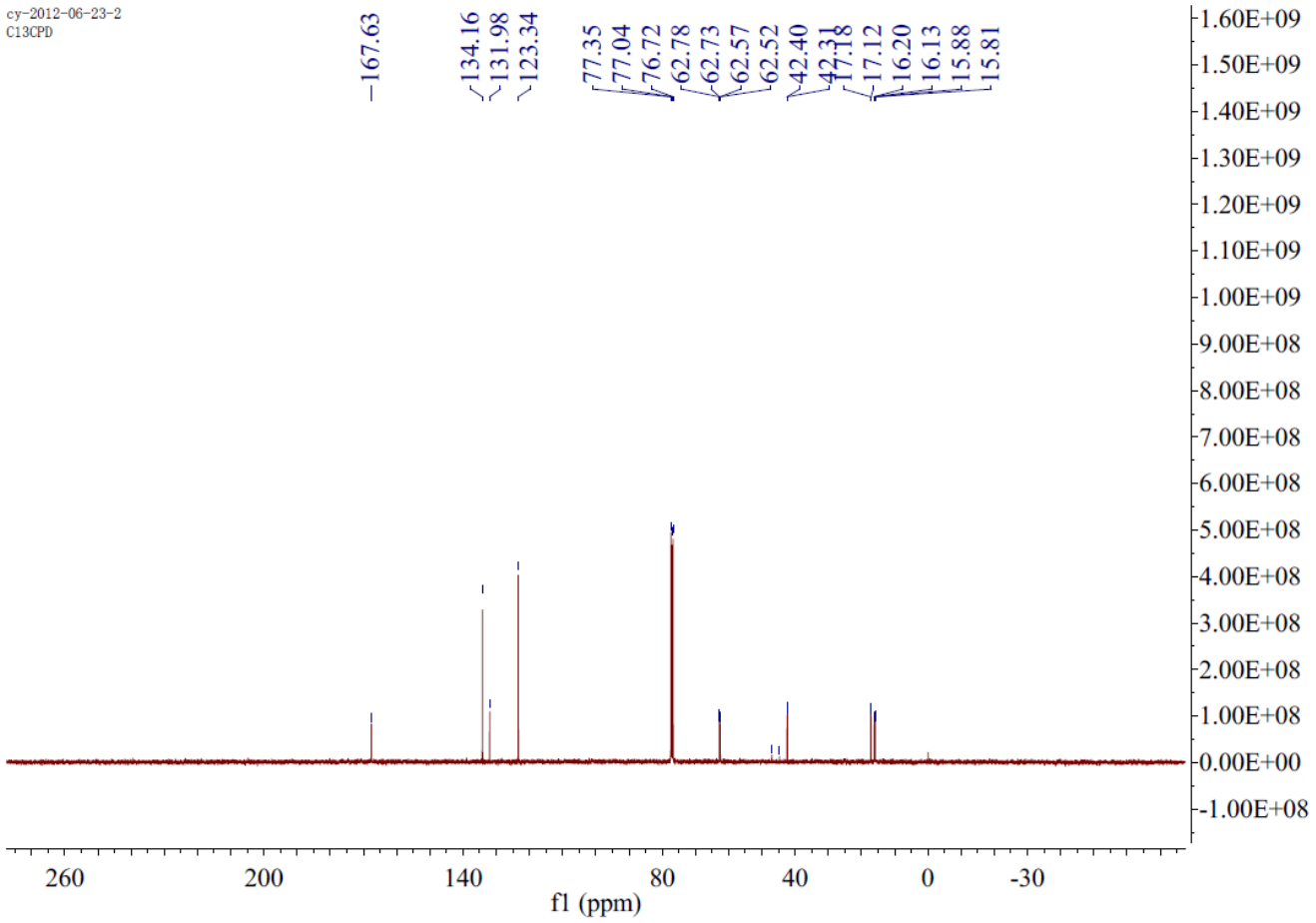
mol) was added to the solution. The mixture was stirred at room temperature for 16h. After the solvent and excess triethylamine were removed under reduced pressure, the residue was purified by column chromatograph on silica gel with the eluent (CH_2Cl_2/AcOEt: 10/1) to give the yellow solid (*S*)-diethyl(1-diazo-2-(1,3-dioxoisoindolin- 2-yl)pro-pyl)phosphonate **6a**. The overall yield upon to 42% for this five-step sequence reaction.

(*S*)-Diethyl (1-diazo-2-(1,3-dioxoisoindolin-2-yl)propyl)phosphonate (6a):

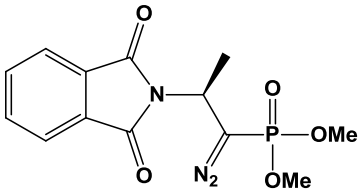


Yellow solid; 42% overall yield; mp 59-61°C; $[\alpha]_D^{25}$ -204 (c 0.02, CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.85-7.88 (m, 2H, Ph), 7.74-7.76 (m, 2H, Ph), 5.03-5.10 (m, 1H, CH), 3.87-4.15 (m, 4H, $2OCH_2$), 1.69 (d, *J* = 7.2 Hz, 3H, CH_3), 1.33 (t, *J* = 7.1 Hz, 3H, CH_3), 1.04 (t, *J* = 7.1 Hz, 3H, CH_3); ^{13}C NMR (101 MHz, $CDCl_3$): δ 167.63 (C=O), 134.16, 131.98, 123.34 (Ph), 62.76 (d, *J* = 5.6 Hz, OCH_2), 62.55 (d, *J* = 5.6 Hz, OCH_2), 45.83 (d, *J* = 235.3 Hz, C-P), 42.35 (CH), 17.15 (CH_3), 16.16 (d, *J* = 6.9 Hz, CH_3), 15.85 (d, *J* = 6.9 Hz, CH_3); ^{31}P NMR (162 MHz, $CDCl_3$): δ 18.53 (s). ESI-HRMS calcd for $C_{15}H_{18}N_3O_5P$: 352.1057 $(M+1)^+$; Found: 352.1055.

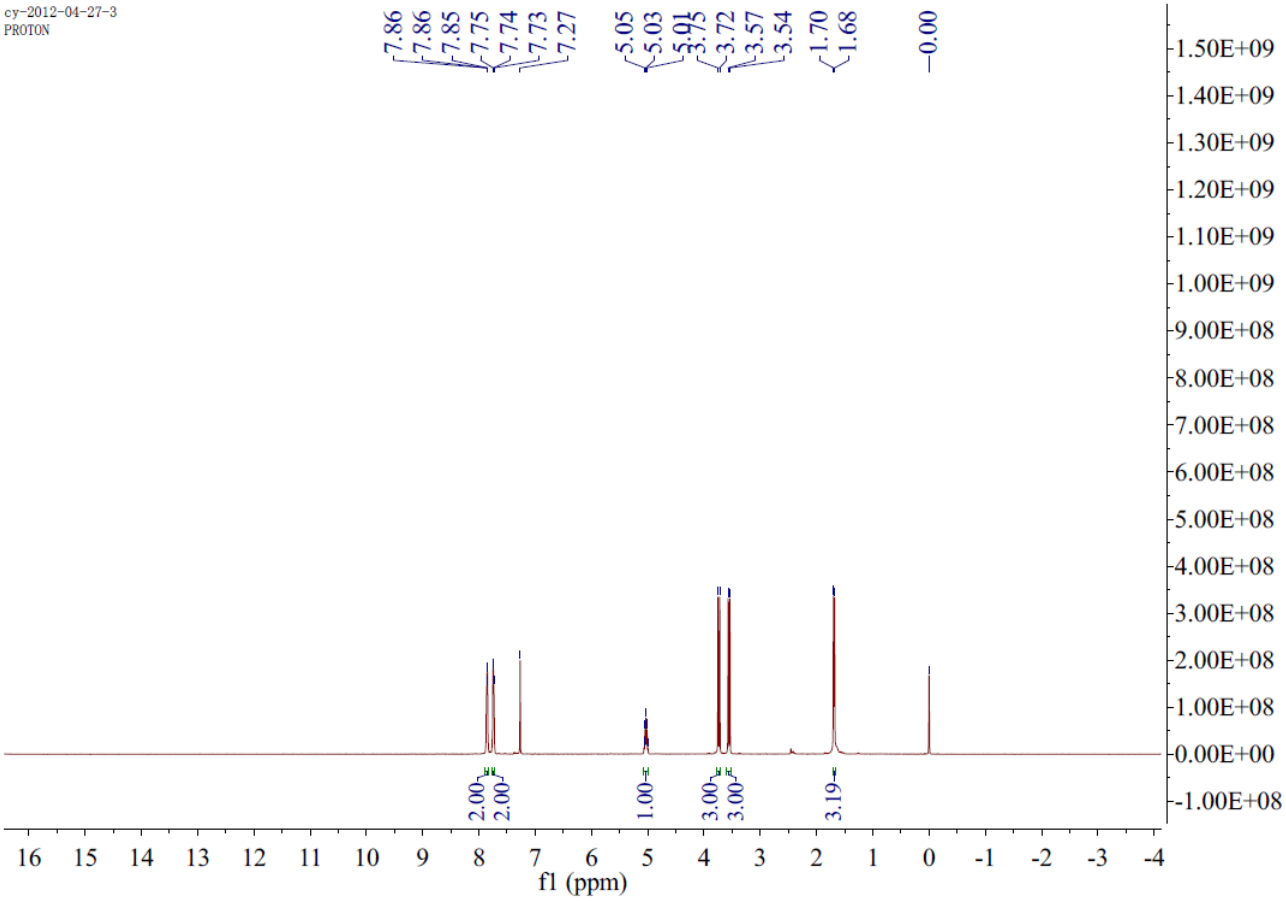


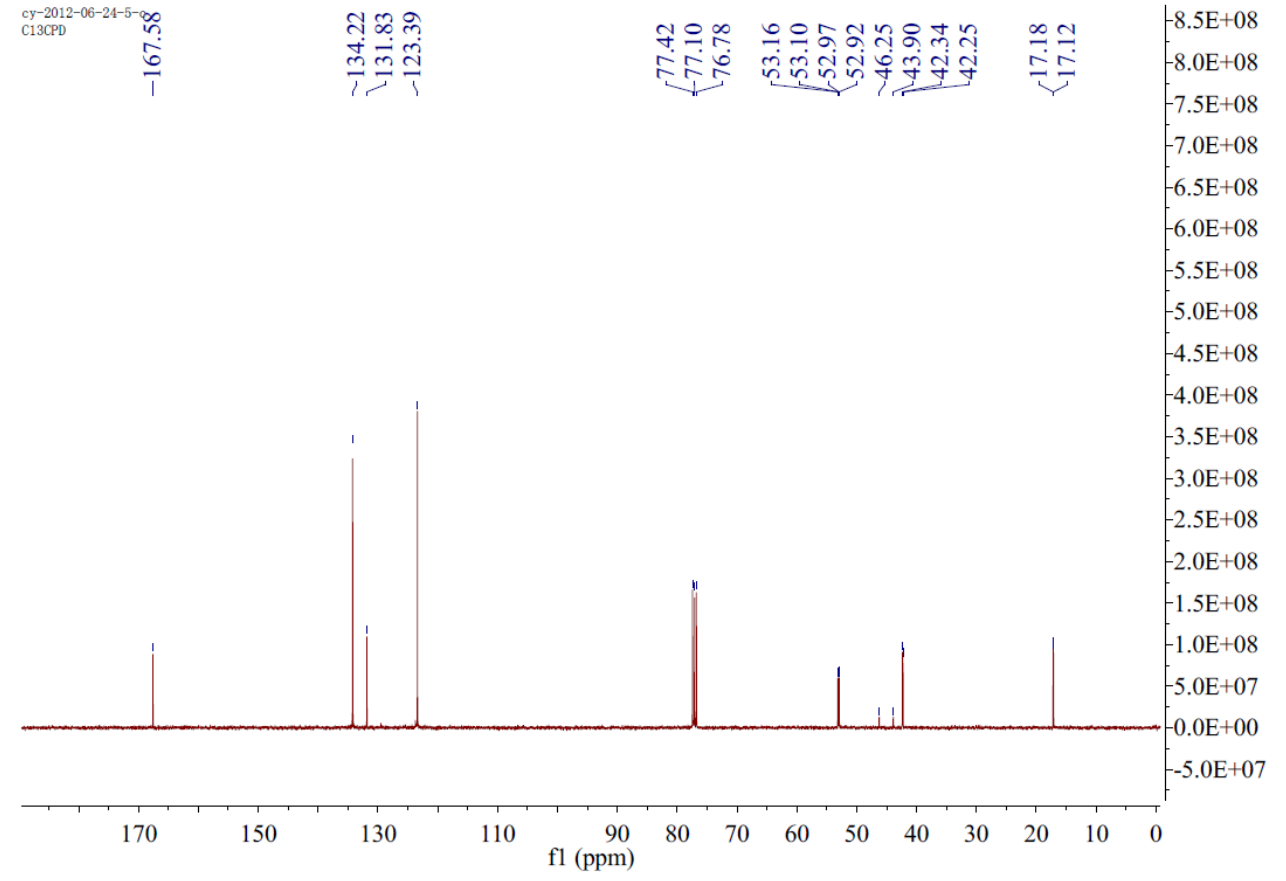


(*S*)-Dimethyl (1-diazo-2-(1,3-dioxoisoindolin-2-yl)propyl)phosphonate (6b):

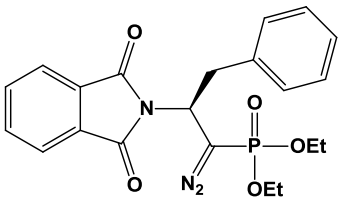


Yellow solid; 15% overall yield; mp 98-101°C; $[\alpha]_D^{25}$ -213.3 (c 0.02, CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.83-7.88 (m, 2H, Ph), 7.71-7.78 (m, 2H, Ph), 5.00-5.07 (m, 1H, CH), 3.74 (d, *J* = 11.6 Hz, 3H, OCH_3), 3.56 (d, *J* = 11.6 Hz, 3H, OCH_3), 1.69 (d, *J* = 7.1 Hz, 3H, CH_3); ^{13}C NMR (101 MHz, $CDCl_3$): δ 167.58 (C=O), 134.22, 131.83, 123.39 (Ph), 53.13 (d, *J* = 5.6 Hz, OCH_3), 52.95 (d, *J* = 5.6 Hz, OCH_3), 45.07 (d, *J* = 236.5 Hz, C-P), 42.30 (d, *J* = 9.1 Hz, CH), 17.15 (d, *J* = 6.2 Hz, CH_3); ^{31}P NMR (162 MHz, $CDCl_3$): δ 21.64 (s). ESI-HRMS calcd for $C_{13}H_{14}N_3O_5P$: 341.1009 $(M+NH_4)^+$; Found: 341.1004.

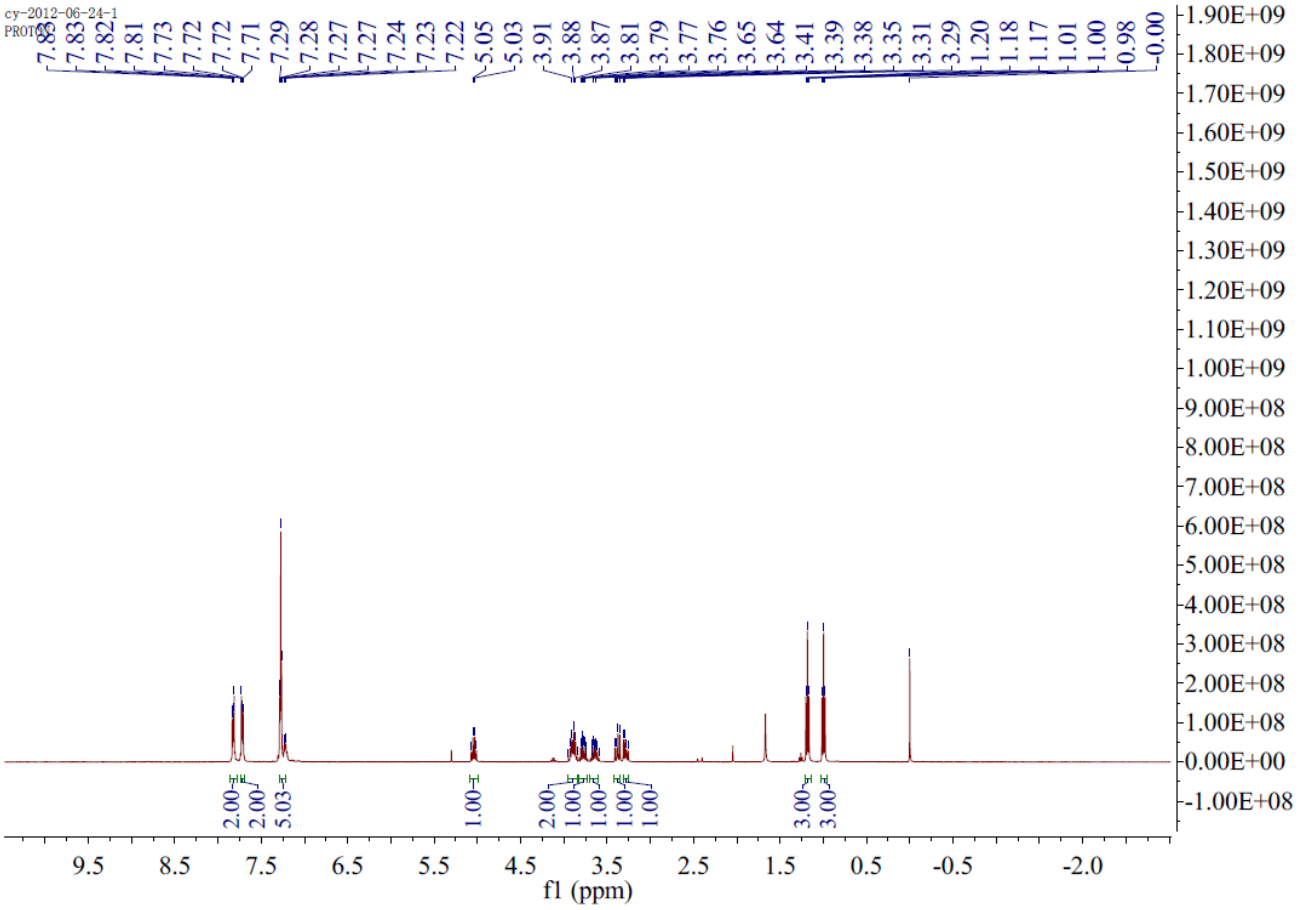


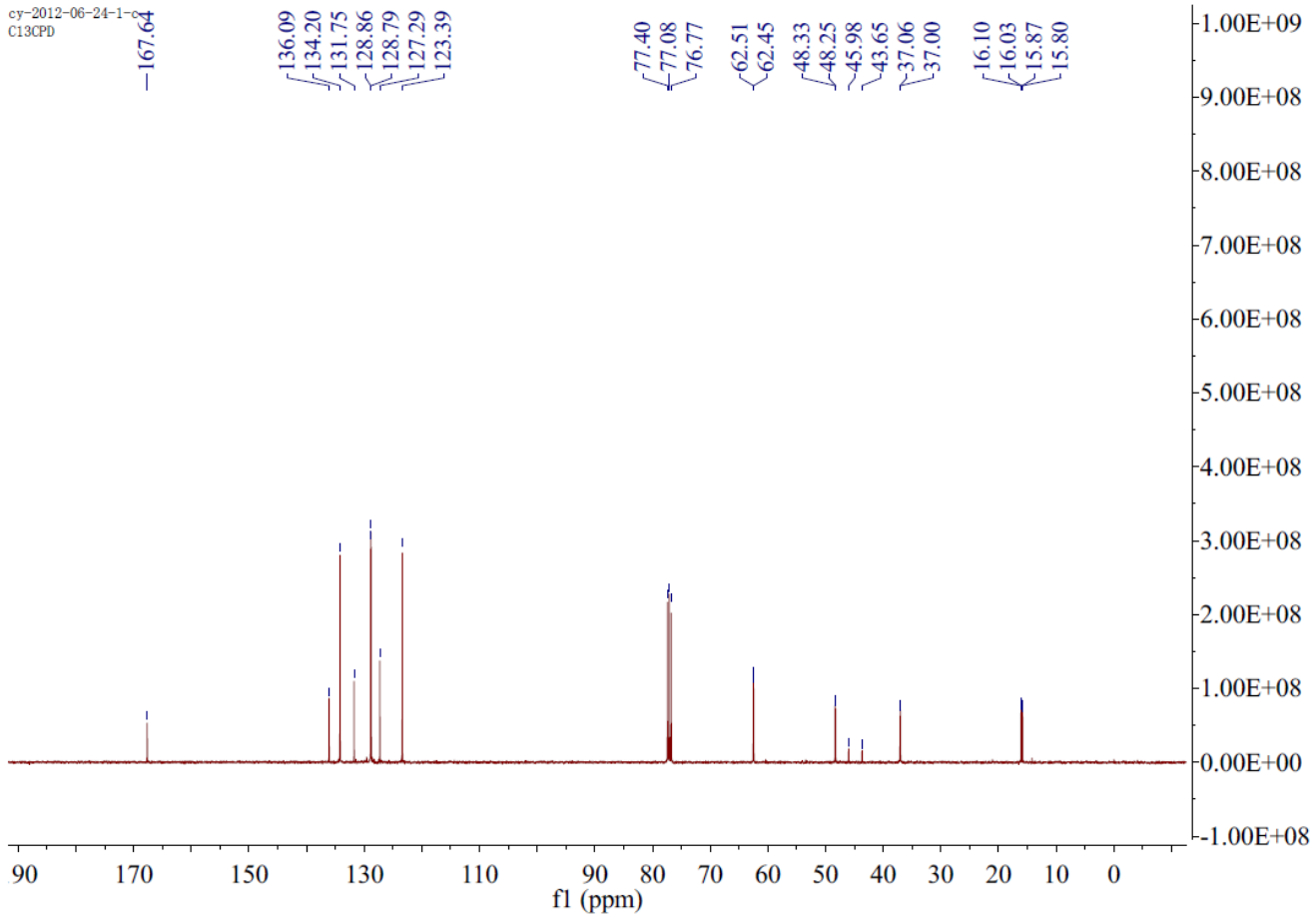


(*S*)-Diethyl (1-diazo-2-(1,3-dioxoisoindolin-2-yl)-3-phenylpropyl)phosphonate (6c):

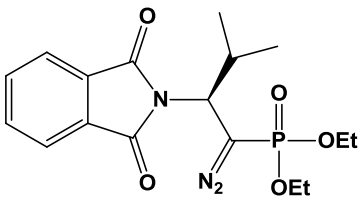


Yellow oil; 47% overall yield; $[\alpha]_D^{25}$ -182.5 (c 0.22, CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.81-7.84 (m, 2H, Ph), 7.70-7.74 (m, 2H, Ph), 7.22-7.30 (m, 5H, Ph), 5.04 (dd, *J* = 16.2, 7.8 Hz, 1H, CH), 3.84-3.96 (m, 2H, OCH_2), 3.64-3.81 (m, 2H, OCH_2), 3.38 (dd, *J* = 13.7, 8.4 Hz, 1H, CH_2), 3.28 (dd, *J* = 13.7, 8.4 Hz, 1H, CH_2), 1.18 (t, *J* = 7.1 Hz, 3H, CH_3), 1.00 (t, *J* = 7.1 Hz, 3H, CH_3); ^{13}C NMR (101 MHz, $CDCl_3$): δ 167.64 (C=O), 136.09, 134.20, 131.75, 128.86, 128.79, 127.29, 123.39 (Ph), 62.48 (d, *J* = 5.4 Hz, OCH_2), 48.29 (d, *J* = 8.9 Hz, CH), 44.81 (d, *J* = 234.5 Hz, C-P), 37.03 (d, *J* = 5.9 Hz, CH_2), 16.06 (d, *J* = 7.1 Hz, CH_3), 15.83 (d, *J* = 7.1 Hz, CH_3); ^{31}P NMR (162 MHz, $CDCl_3$): δ 18.36 (s). ESI-HRMS calcd for $C_{21}H_{22}N_3O_5P$: 450.1189 $(M+Na)^+$; Found: 450.1182.

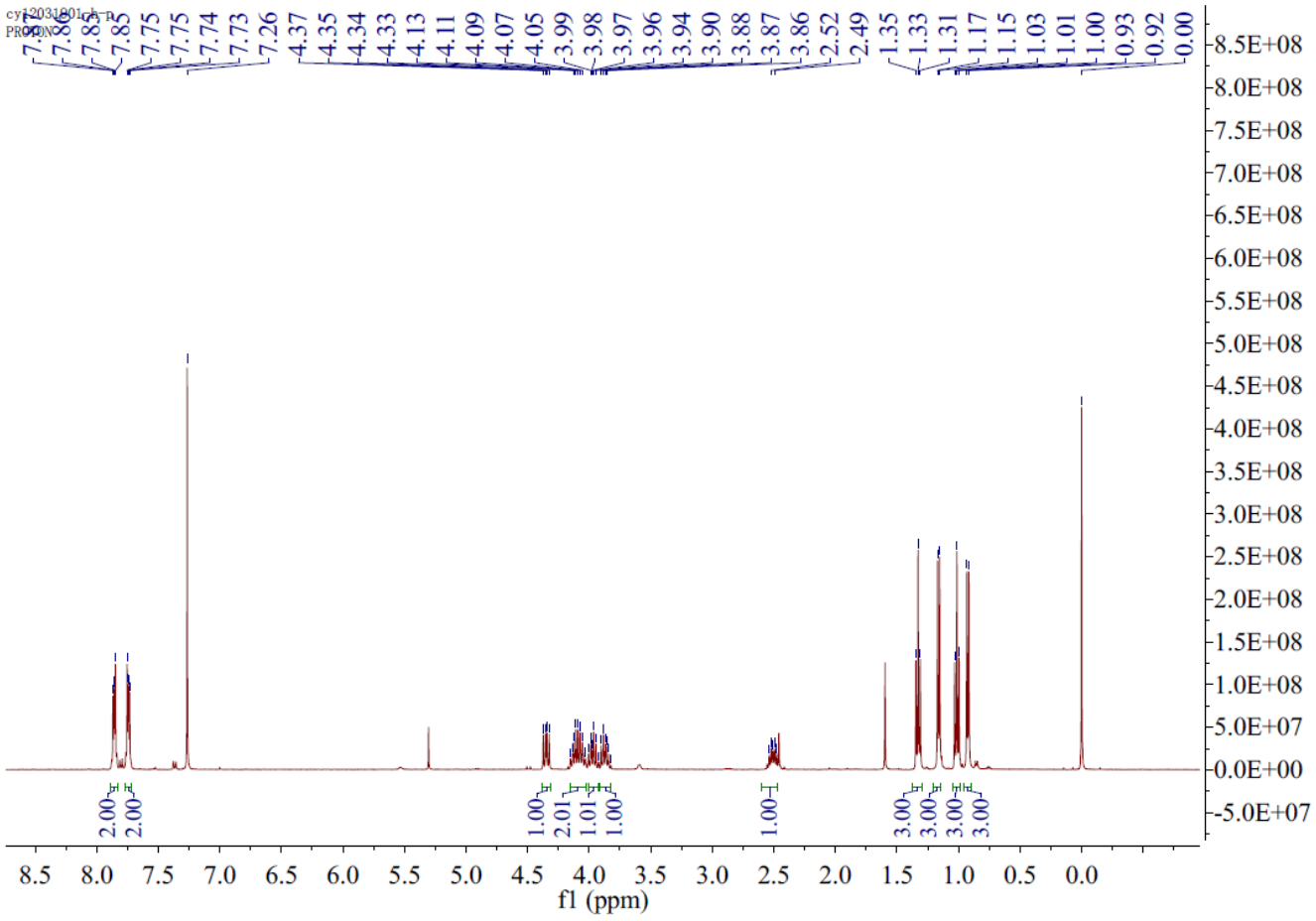


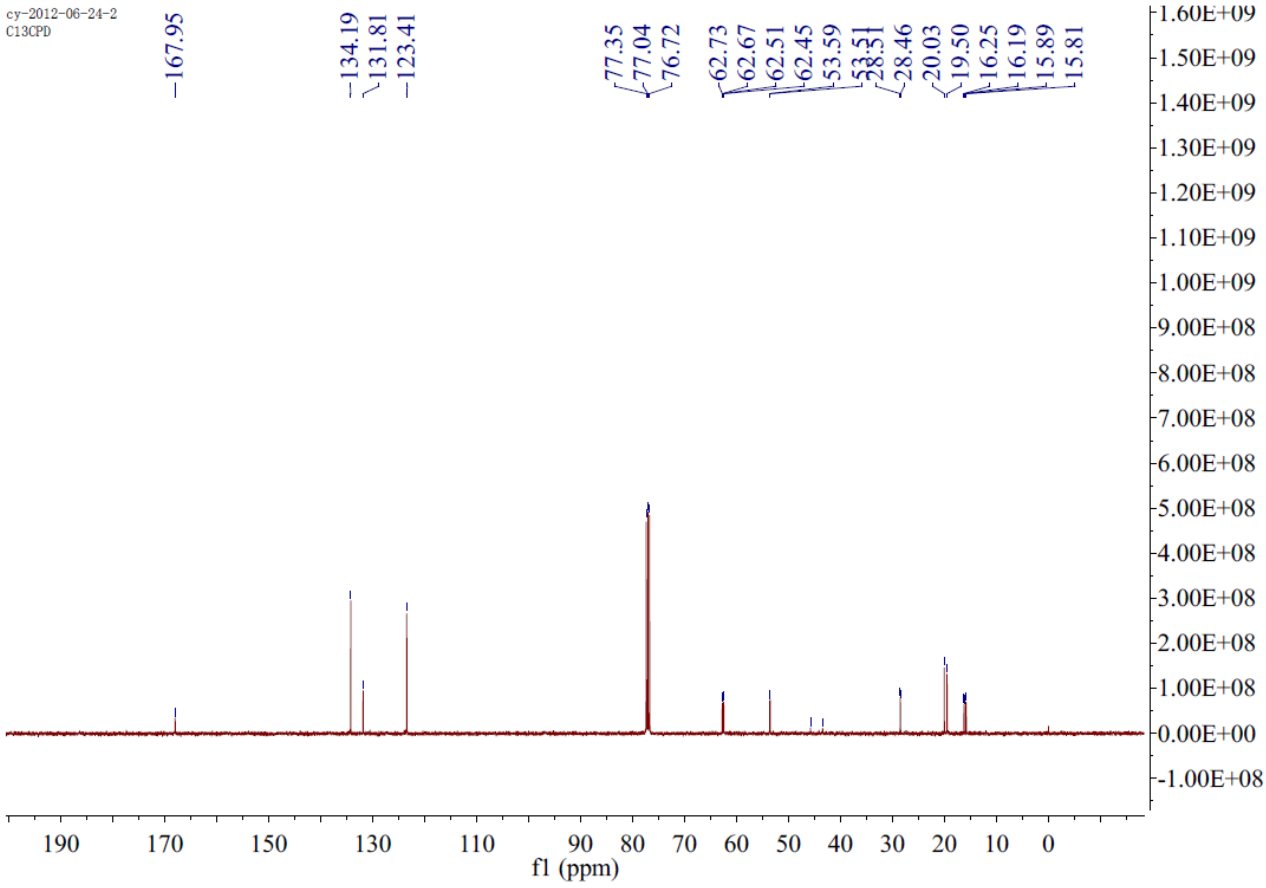


(*S*)-Diethyl (1-diazo-2-(1,3-dioxoisoindolin-2-yl)-3-methylbutyl)phosphonate (6d):

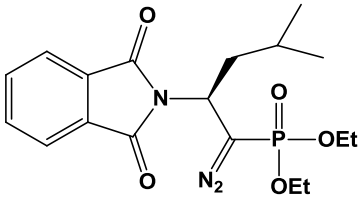


Yellow solid; 52% overall yield; mp 67-69 °C; $[\alpha]_D^{25}$ -142 (c 0.22, CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.84-7.87 (m, 2H, Ph), 7.72-7.76 (m, 2H, Ph), 4.35 (dd, *J* = 11.4, 7.4 Hz, 1H, CH), 4.03-4.16 (m, 2H, OCH_2), 3.82-4.01 (m, 2H, OCH_2), 2.46-2.56 (m, 1H, CH), 1.33 (t, *J* = 7.1 Hz, 3H, CH_3), 1.16 (d, *J* = 6.6 Hz, 3H, CH_3), 1.01 (t, *J* = 7.1 Hz, 3H, CH_3), 0.92 (d, *J* = 6.6 Hz, 3H, CH_3); ^{13}C NMR (101 MHz, $CDCl_3$): δ 167.95 (C=O), 134.19, 131.81, 123.41 (Ph), 62.70 (d, *J* = 5.8 Hz, OCH_2), 62.48 (d, *J* = 5.8 Hz, OCH_2), 53.55 (d, *J* = 8.0 Hz, CH), 44.59 (d, *J* = 235.9 Hz, C-P), 28.49 (d, *J* = 5.8 Hz, CH), 20.03 (CH_3), 19.50 (CH_3), 16.22 (d, *J* = 7.0 Hz, CH_3), 15.85 (d, *J* = 7.0 Hz, CH_3); ^{31}P NMR (162 MHz, $CDCl_3$): δ 19.4 (s). ESI-HRMS calcd for $C_{17}H_{22}N_3O_5P$: 402.1189 $(M+Na)^+$; Found: 402.1182.

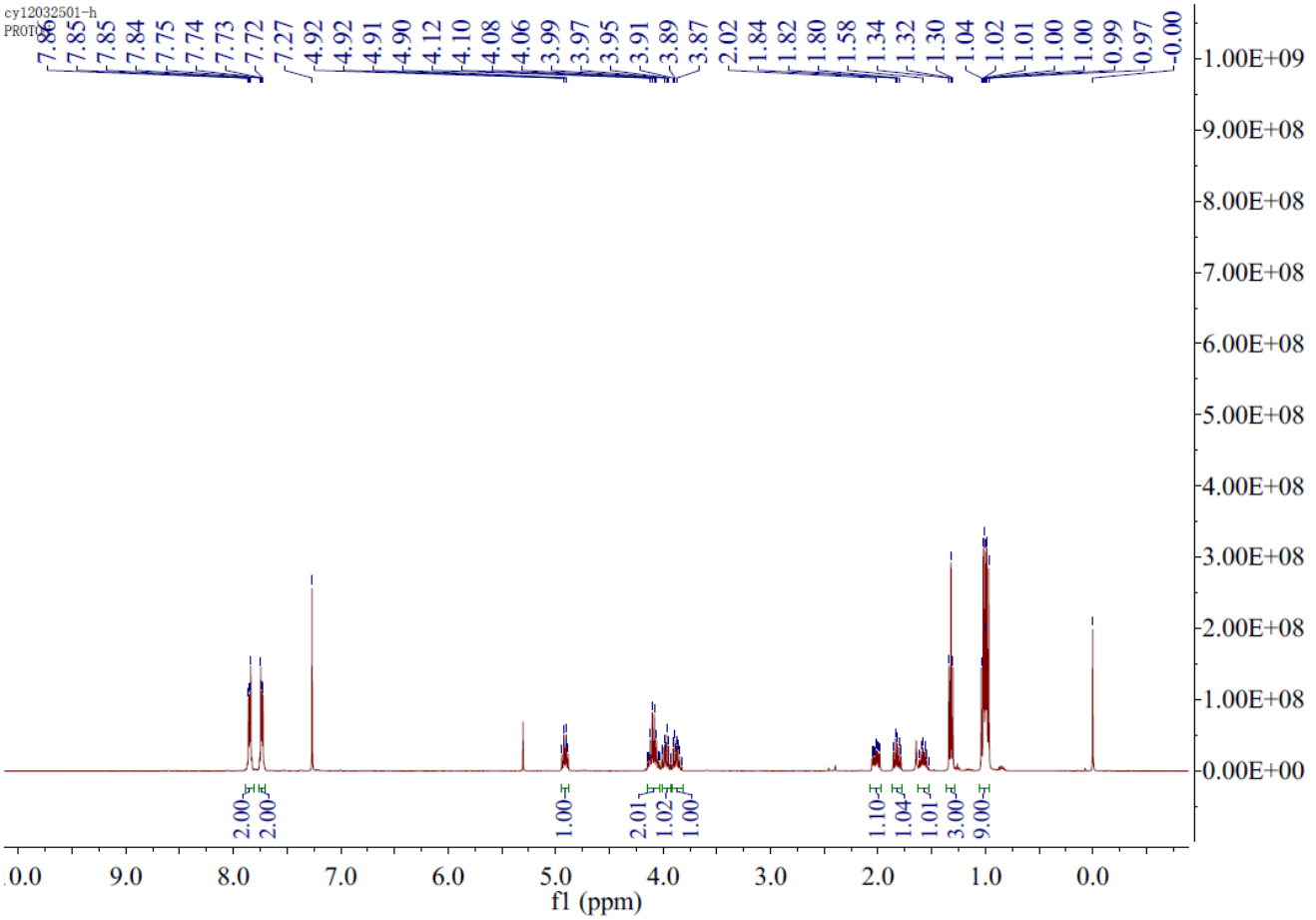


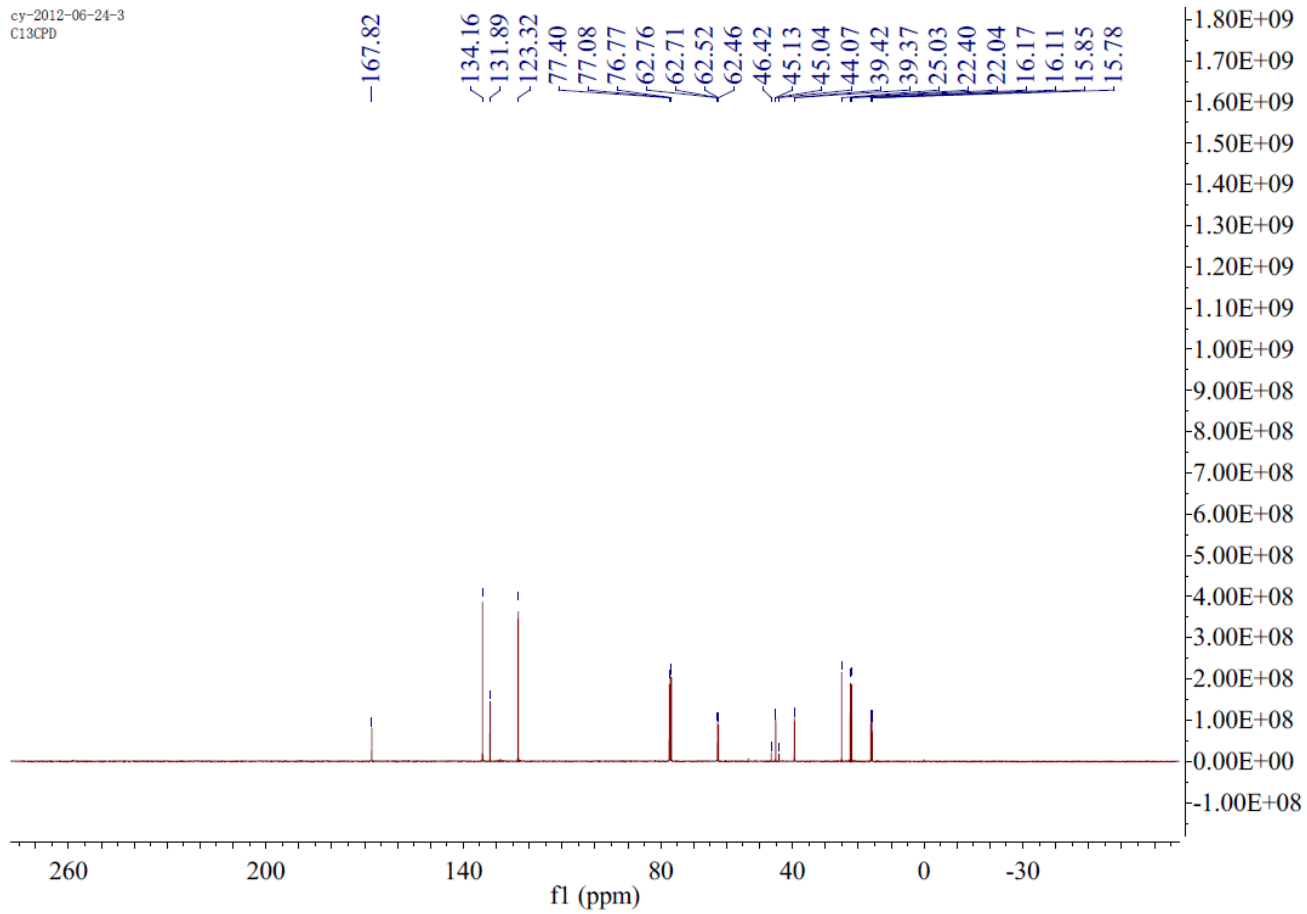


(*S*)-Diethyl (1-diazo-2-(1,3-dioxoisoindolin-2-yl)-4-methylpentyl)phosphonate (6e):

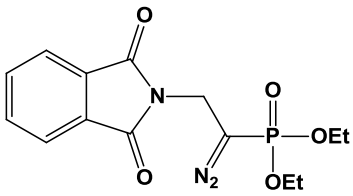


Yellow sticky oil; 46% overall yield; $[\alpha]_D^{25}$ -184 (0.22, CH_2Cl_2); ^1H NMR (400 MHz, $CDCl_3$): δ 7.83-7.86 (m, 2H, Ph), 7.72-7.75 (m, 2H, Ph), 4.91 (dt, *J* = 8.9, 7.0 Hz, 1H, CH), 4.03-4.15 (m, 2H, OCH_2), 3.82-4.02 (m, 2H, OCH_2), 1.97-2.06 (m, 1H, CH), 1.77-1.87 (m, 1H, CH_2), 1.52-1.62 (m, 1H, CH_2), 1.32 (t, *J* = 7.1 Hz, 3H, CH_3), 0.96-1.05 (m, 9H, $3CH_3$); ^{13}C NMR (101 MHz, $CDCl_3$): δ 167.82 (C=O), 134.16, 131.89, 123.32 (Ph), 62.73 (d, *J* = 5.8 Hz, OCH_2), 62.49 (d, *J* = 5.8 Hz, OCH_2), 45.24 (d, *J* = 235.99 Hz, C-P), 45.09 (d, *J* = 8.5 Hz, CH), 39.39 (d, *J* = 5.6 Hz, CH_2), 25.03 (CH), 22.40 (CH_3), 22.04 (CH_3), 16.14 (d, *J* = 6.9 Hz, CH_3), 15.81 (d, *J* = 6.9 Hz, CH_3); ^{31}P NMR (162 MHz, $CDCl_3$): δ 18.94 (s). ESI-HRMS calcd for $C_{18}H_{24}N_3O_5P$: 394.1526 $(M+H)^+$; Found: 394.1521.

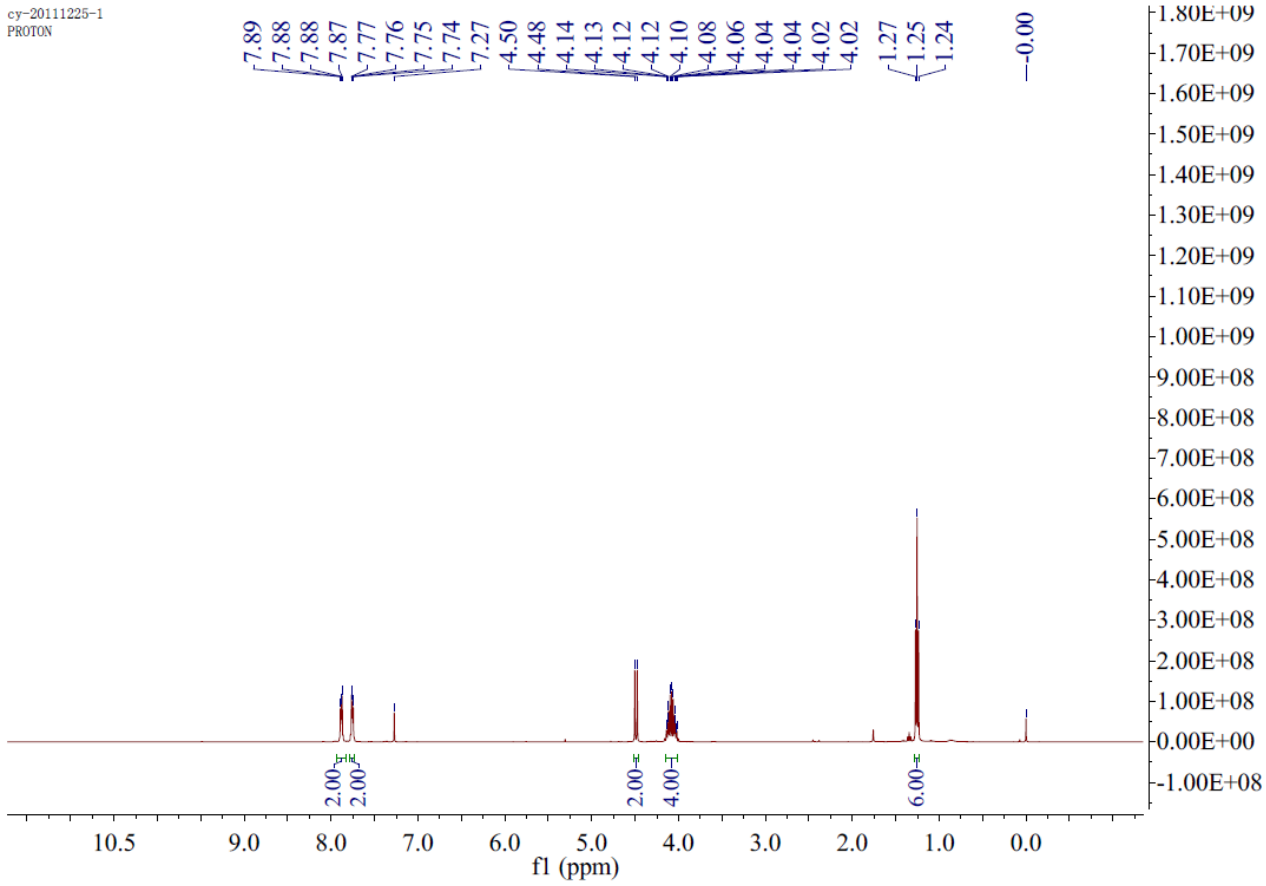


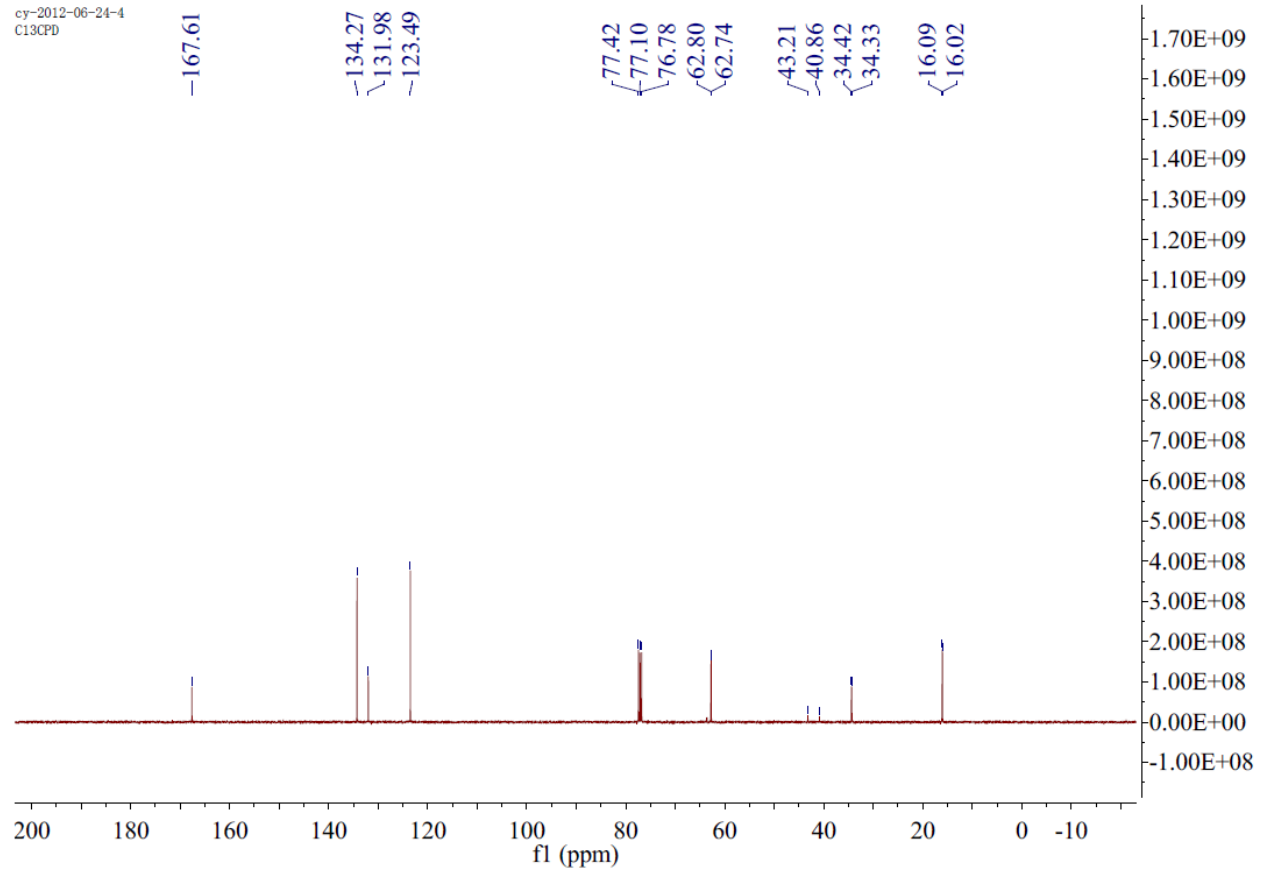


Diethyl (1-diazo-2-(1,3-dioxoisoindolin-2-yl)ethyl)phosphonate (6f):



Yellow solid; 11% overall yield; mp 67-71 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.87-7.90 (m, Ph), 7.73-7.78 (m, 2H, Ph), 4.49 (d, *J* = 11.3 Hz, 2H, CH_2), 4.01-4.15 (m, 4H, $2OCH_2$), 1.25 (t, *J* = 7.1 Hz, 6H, $2CH_3$); ^{13}C NMR (101 MHz, $CDCl_3$): δ 167.61 (C=O), 134.27, 131.98, 123.49 (Ph), 62.77 (d, *J* = 5.6 Hz, OCH_2), 42.04 (d, *J* = 235.9 Hz, C-P), 34.38 (d, *J* = 9.4 Hz, CH_2), 16.05 (d, *J* = 6.7 Hz, CH_3); ^{31}P NMR (162 MHz, $CDCl_3$): δ 18.36 (s). ESI-HRMS calcd for $C_{14}H_{16}N_3O_5P$: 338.0900 $(M+H)^+$; Found: 338.0903.

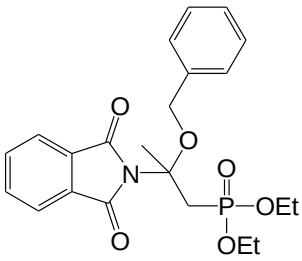




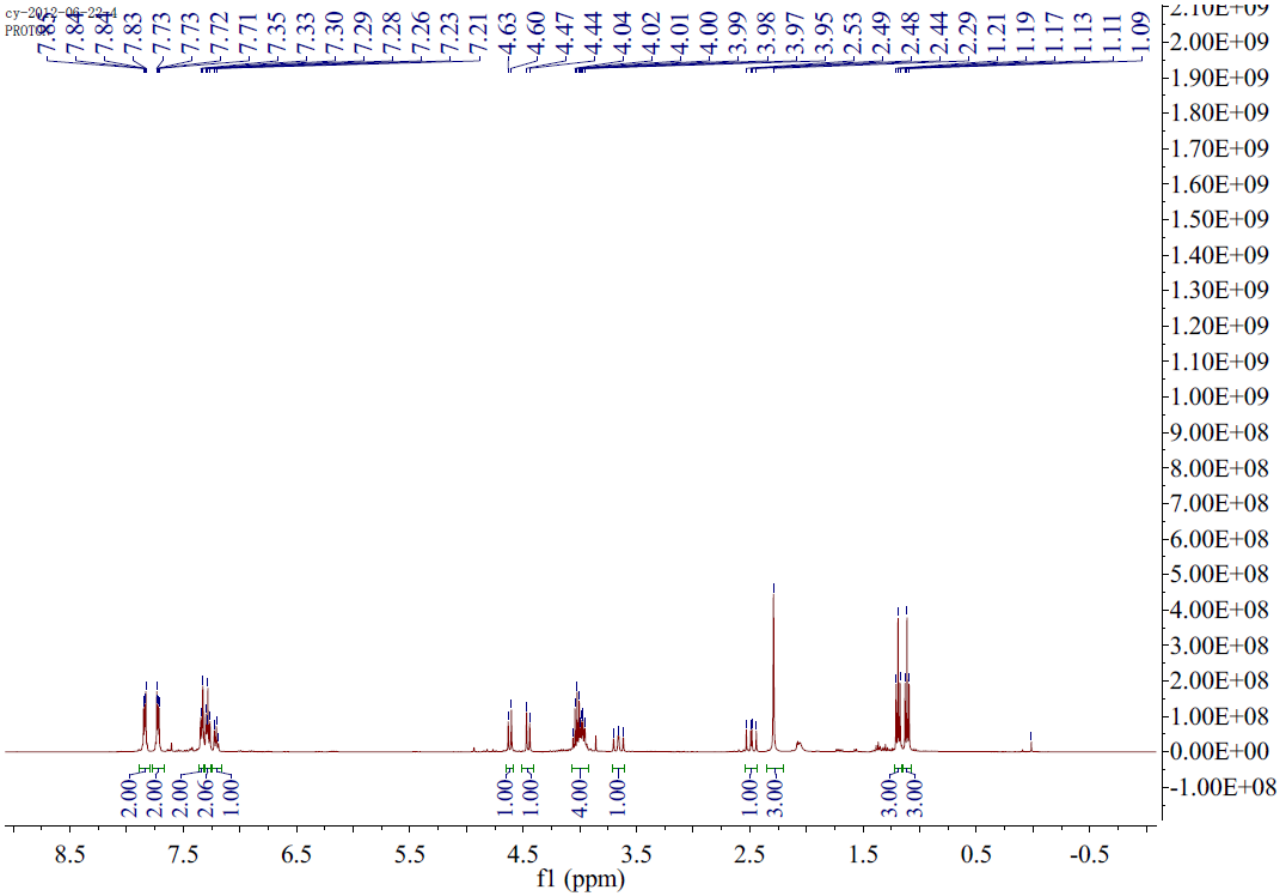
General procedure for the preparation of 8:

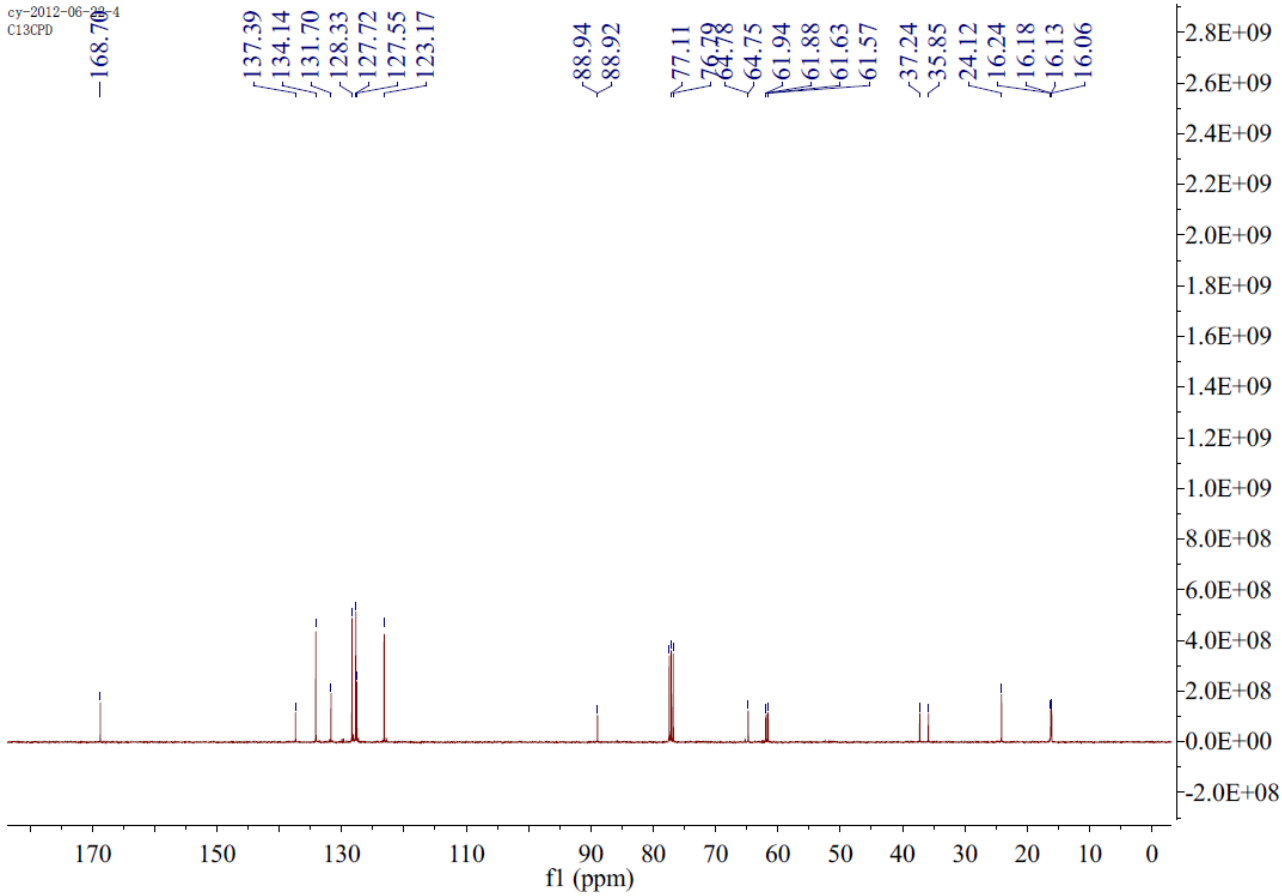
The $[Cu(MeCN)_4]PF_6$ (0.014 mmol) and I_2 (0.056 mmol) in an oven-dried Schlenk tube was dissolved in 4 mL of freshly distilled CH_2Cl_2 under nitrogen, alcohol **7** (1.4 mmol) was added and the solution was stirred for 30 min at 25 °C. α-Diazophosphonates **6** (0.28 mmol) was diluted with 2 mL of CH_2Cl_2 and was drawn into a gastight syringe. It was then added to the reaction mixture dropwise over a period of 1.5h with the help of a syringe pump. After the addition was complete, the reaction mixture was stirred for another 3 hour at 25 °C. The solvent was then removed under reduced pressure and the crude residue was purified by silica gel chromatography with the eluent (CH_2Cl_2/EtOAc = 15:1) or purified by preparative HPLC [HPLC condition: YMC-Pack ODS-A column, MeOH/H_2O (v/v) with the gradient from 20% to 100% in 20min, flow rate = 2 mL/min, wavelength = 254 nm] to give the corresponding products **8** and by-products **9**.

Diethyl (2-(benzyloxy)-2-(1,3-dioxoisoindolin-2-yl)propyl)phosphonate (8a):

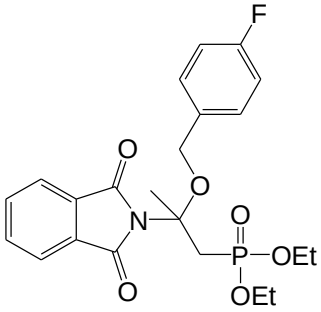


Colourless oil; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.81-7.86 (m, 2H, Ph), 7.70-7.75 (m, 2H, Ph), 7.34 (d, *J* = 7.2 Hz, 2H, Ph), 7.16-7.31 (m, 3H, Ph), 4.62 (d, *J* = 11.2 Hz, 1H, OCH_2Ph), 4.46 (d, *J* = 11.2 Hz, 1H, OCH_2Ph), 3.92-4.08 (m, 4H, $2OCH_2$), 3.66 (dd, *J* = 18.9, 15.7 Hz, 1H, CH_2-P), 2.49 (dd, *J* = 18.9, 15.7 Hz, 1H, CH_2-P), 2.29 (s, 1H, CH_3), 1.19 (t, *J* = 7.1 Hz, 3H, CH_3), 1.11 (t, *J* = 7.1 Hz, 3H, CH_3); ^{13}C NMR (101 MHz, $CDCl_3$): δ 168.70 (C=O), 137.39, 134.14, 131.70, 128.33, 127.72, 127.55, 123.17 (Ph), 88.93 (d, *J* = 1.4 Hz, O-C-N), 64.76 (d, *J* = 1.4 Hz, OCH_2Ph), 61.91 (d, *J* = 6.5 Hz, OCH_2), 61.60 (d, *J* = 6.5 Hz, OCH_2), 36.55 (d, *J* = 140.0 Hz, C-P), 24.12 (CH_3), 16.21 (d, *J* = 6.4 Hz,CH_3), 16.09 (d, *J* = 6.4 Hz, CH_3); ^{31}P NMR (162 MHz, $CDCl_3$): δ 24.34 (s). ESI-HRMS calcd for $[C_{22}H_{26}NO_6P$, $M+Na]^+$: 454.1390; Found: 454.1393.

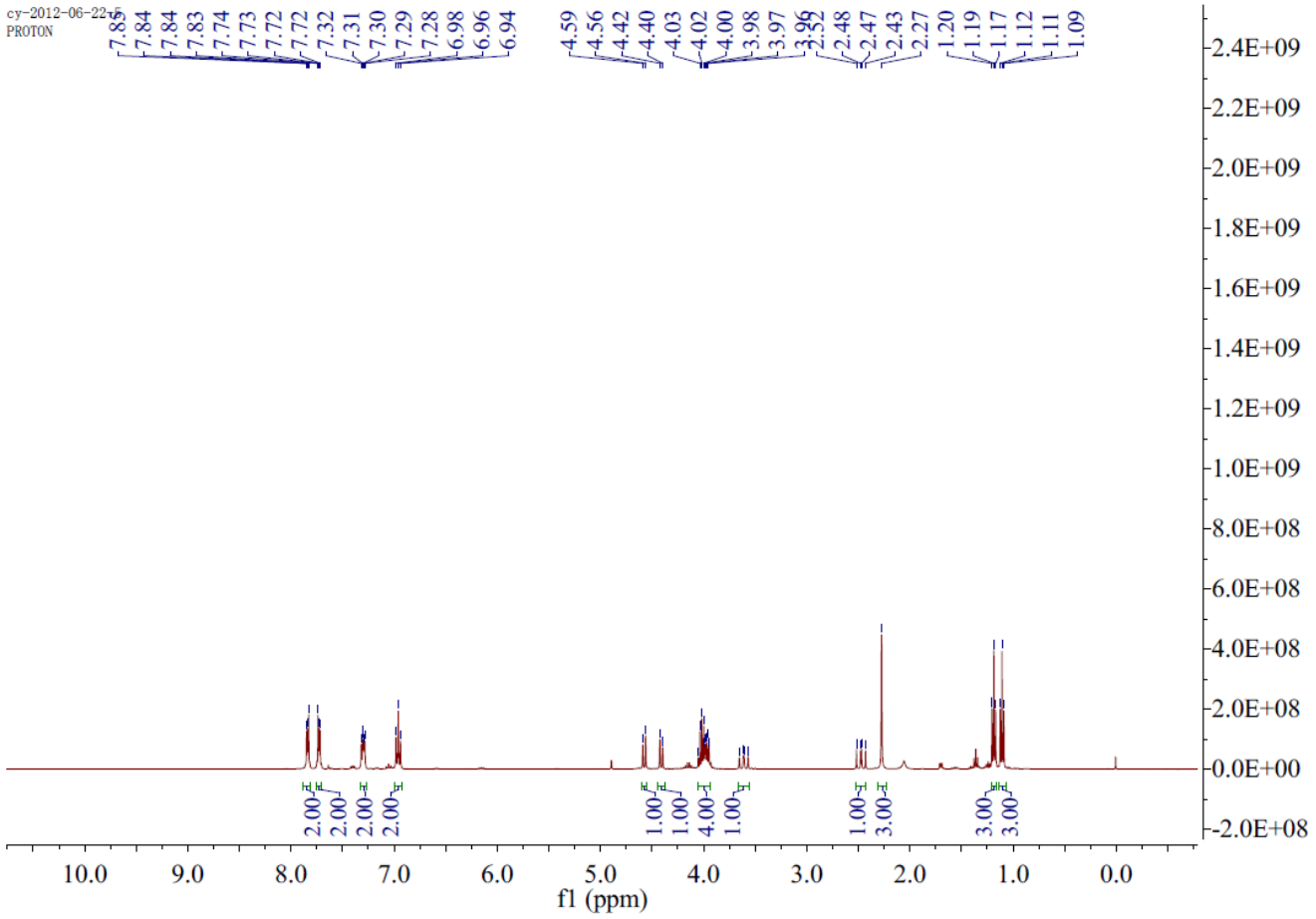


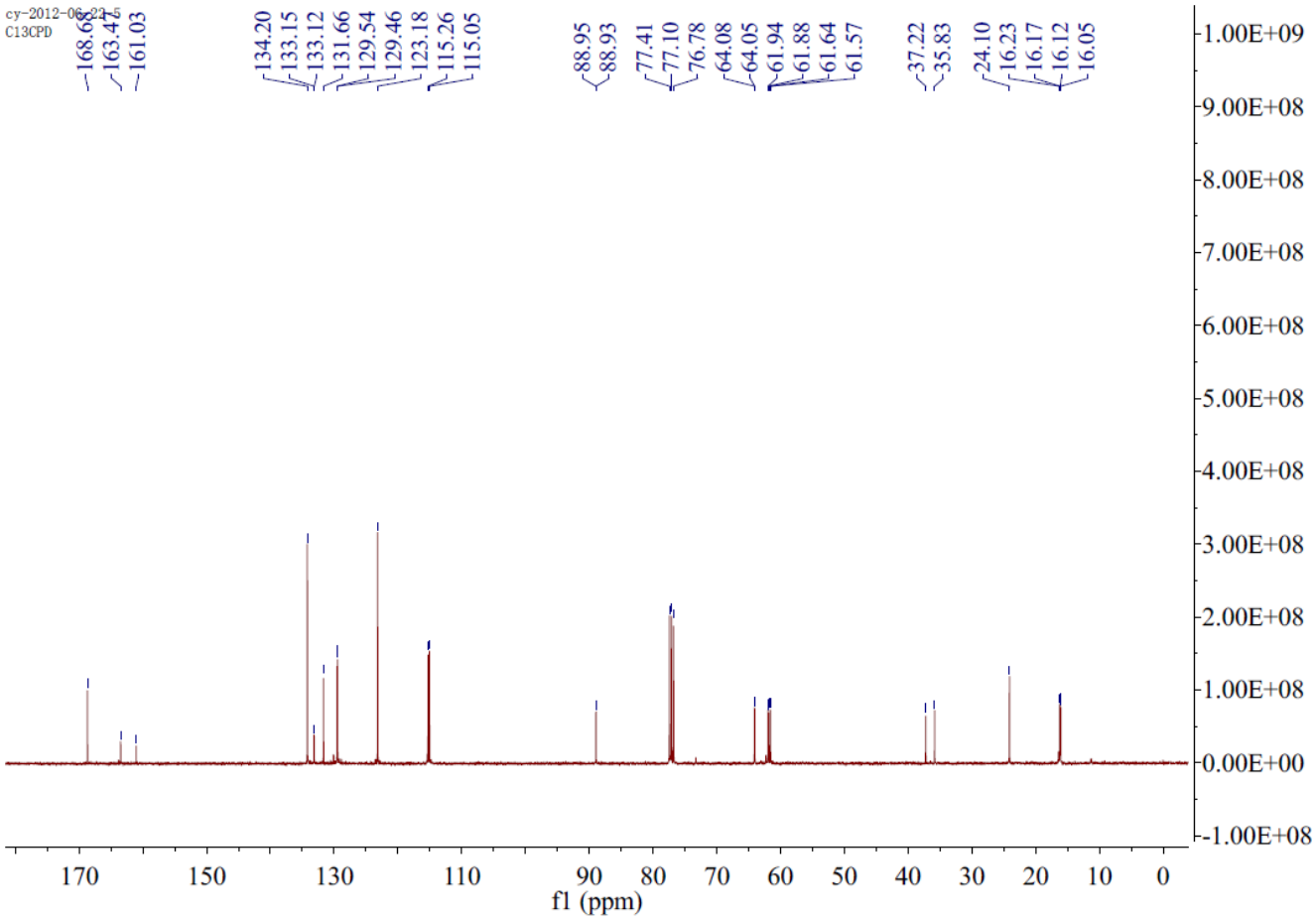


Diethyl(2-(1,3-dioxoisoindolin-2-yl)-2-((4-fluorobenzyl)oxy)propyl)phosphonate (8b):

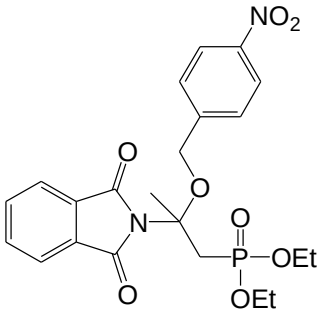


Light yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.80-7.87 (m, 2H, Ph), 7.69-7.78 (m, 2H, Ph), 7.26-7.38 (m, 2H, Ph), 6.96 (t, *J* = 8.7 Hz, 2H, Ph), 4.58 (d, *J* = 11.0 Hz, 1H, OCH_2Ar), 4.41 (d, *J* = 11.0 Hz, 1H, OCH_2Ar), 3.91-4.09 (m, 4H, $2OCH_2$), 3.61 (dd, *J* = 18.9, 15.7 Hz, 1H, CH_2-P), 2.47 (dd, *J* = 18.9, 15.7 Hz, 1H, CH_2-P), 2.27 (s, 1H, CH_3), 1.19 (t, *J* = 7.1 Hz, 3H, CH_3), 1.11 (t, *J* = 7.1 Hz, 3H, CH_3); ^{13}C NMR (101 MHz, $CDCl_3$): δ 168.68 (C=O), 162.25 (d, *J* = 245.5 Hz, C-F), 134.20 (Ph), 133.14 (d, *J* = 3.0 Hz, Ar), 131.66 (Ph), 129.50 (d, *J* = 8.1 Hz, Ar), 123.18 (Ph), 115.16 (d, *J* = 3.0 Hz, Ar), 88.94 (d, *J* = 1.5 Hz, O-C-N), 64.06 (d, *J* = 2.6 Hz, OCH_2Ph), 61.91 (d, *J* = 6.5 Hz, OCH_2), 61.61 (d, *J* = 6.5 Hz, OCH_2), 36.52 (d, *J* = 140.1 Hz, C-P), 24.10 (CH_3), 16.20 (d, *J* = 6.4 Hz, CH_3), 16.08 (d, *J* = 6.4 Hz, CH_3); ^{31}P NMR (162 MHz, $CDCl_3$): δ 24.20 (s); ESI-HRMS calcd for $[C_{22}H_{25}FNO_6P, M+Na]^+$: 472.1296; Found: 472.1298.

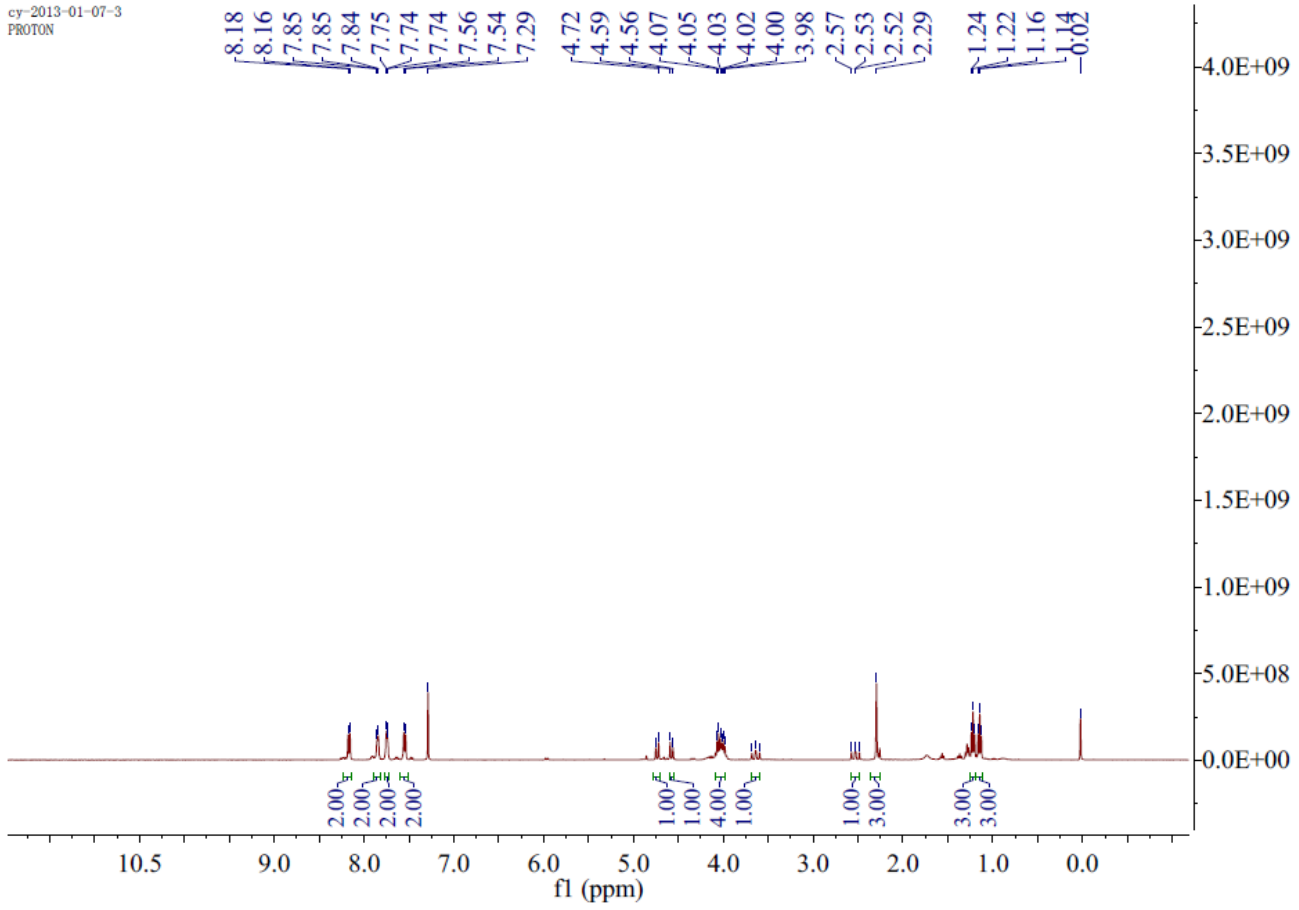


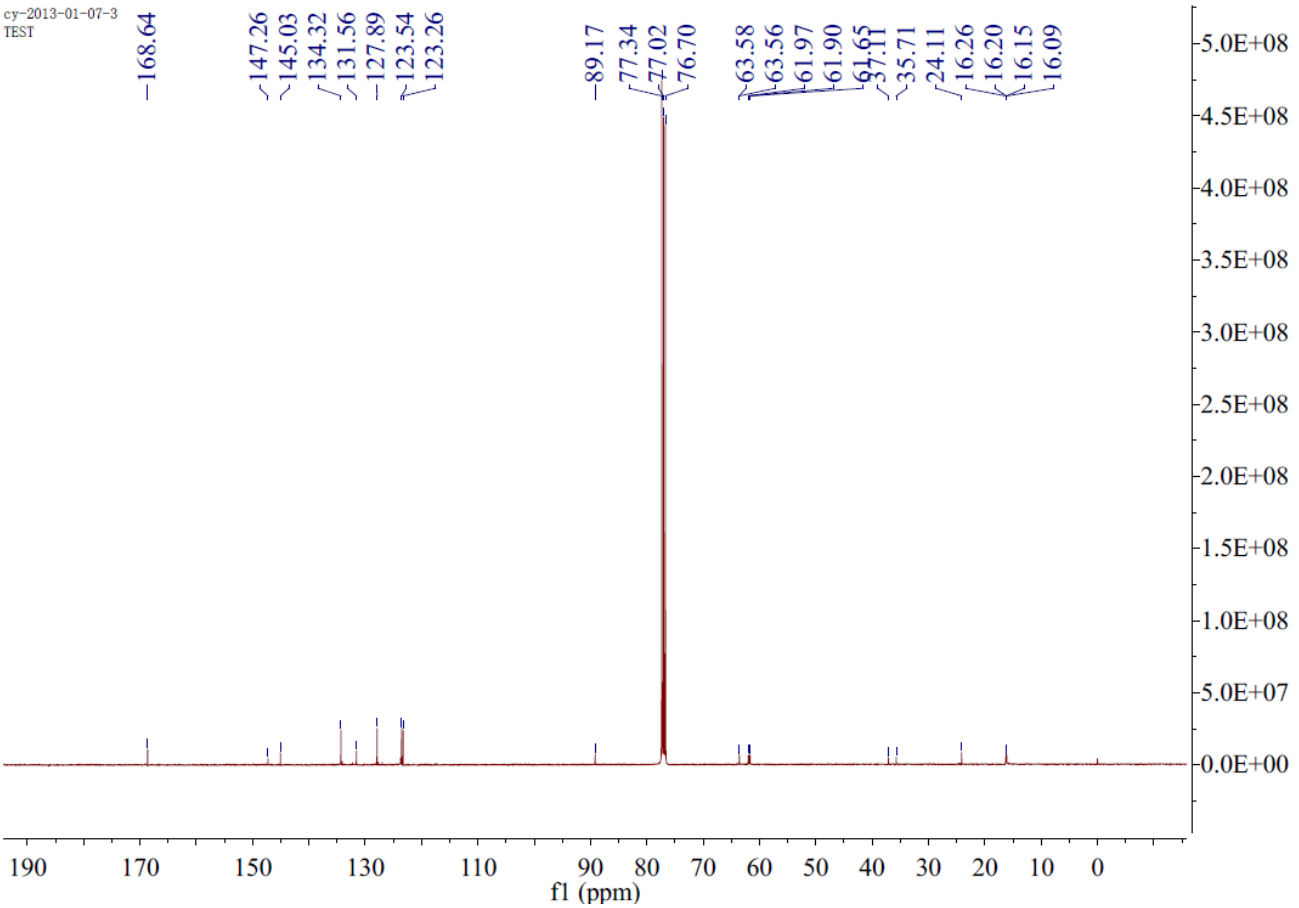


Diethyl (2-(1,3-dioxoisoindolin-2-yl)-2-((4-nitrobenzyl)oxy)propyl)phosphonate (8c):

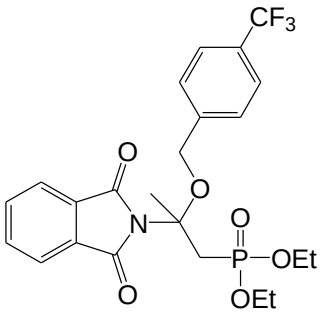


Colourless oil; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.17 (d, *J* = 7.7 Hz, 2H, Ph), 7.83-7.87 (m, 2H, Ph), 7.71-7.78 (m, 2H, Ph), 7.55 (d, *J* = 7.7 Hz , 2H, Ph), 4.74 (d, *J* = 12.7 Hz, 1H, OCH_2Ar), 4.58 (d, *J* = 12.7 Hz, 1H, OCH_2Ar), 3.97-4.08 (m, 4H, $2OCH_2$), 3.64 (dd, *J* = 19.8 , 15.8 Hz, 1H, CH_2-P), 2.53 (dd, *J* = 19.8, 15.8, 1H, CH_2-P), 2.29 (s, 3H, CH_3), 1.22 (t, *J* = 7.1 Hz, 3H, CH_3), 1.14 (t, *J* = 7.1 Hz, 3H, CH3); ^{13}C NMR (101 MHz, $CDCl_3$) δ: 168.64 (C=O), 147.26, 145.03, 134.32, 131.56, 127.89, 123.54, 123.26 (Ph), 89.17 (s, O-C-N), 63.57 (d, *J* = 2.3 Hz, OCH_2Ar), 61.93 (d, *J* = 6.6 Hz, OCH_2), 61.68 (d, *J* = 6.6 Hz, OCH_2), 36.41 (d, *J* = 140.5 Hz, C-P), 24.11 (CH_3), 16.23 (d, *J* = 6.3 Hz, CH_3), 16.12 (d, *J* = 6.3 Hz, CH_3); ^{31}P NMR (162 MHz, $CDCl_3$): δ 23.87 (s); ESI-HRMS calcd for $[C_{22}H_{25}N_2O_8P, M+Na]^+$: 499.1241; Found: 499.1242.

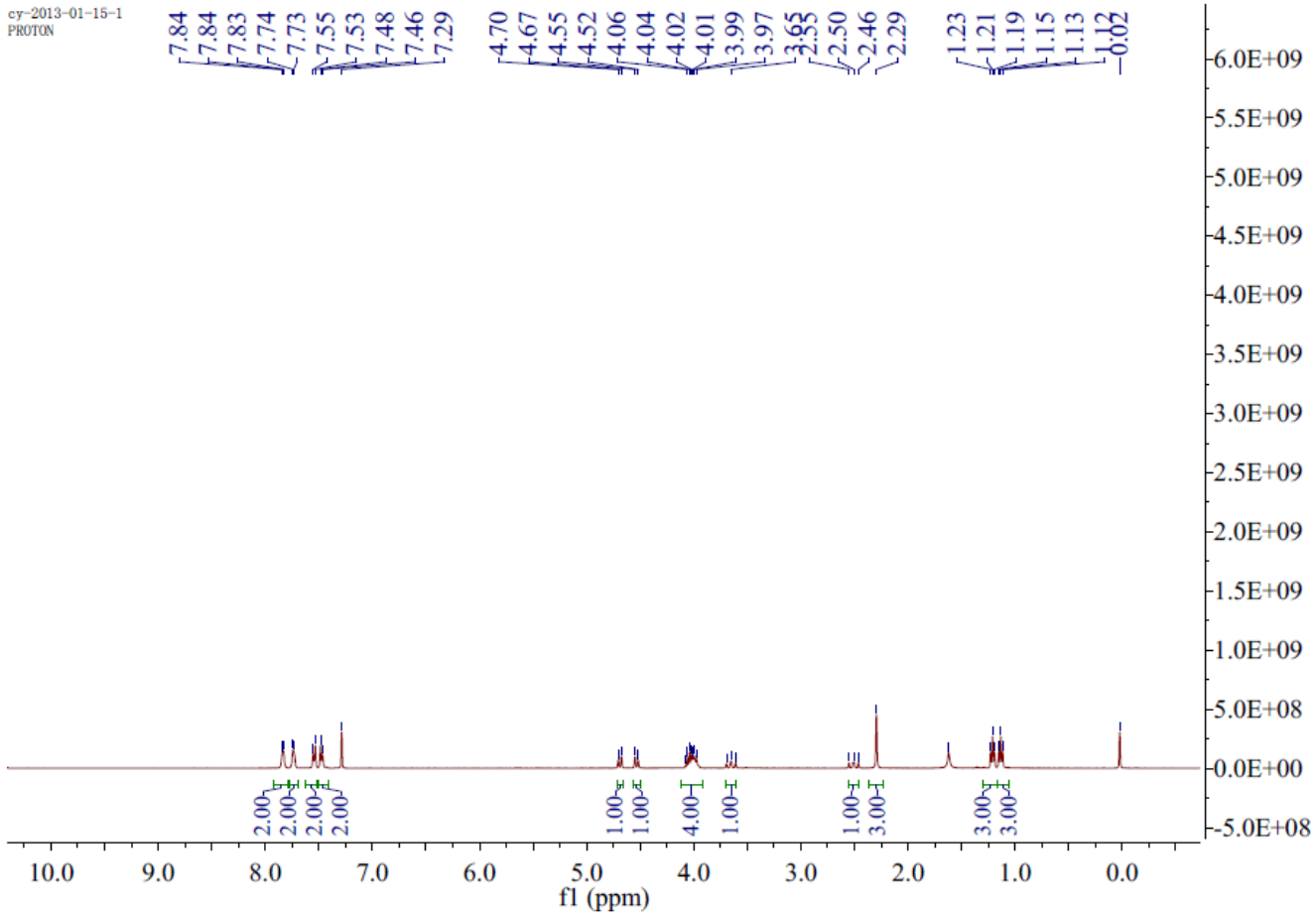


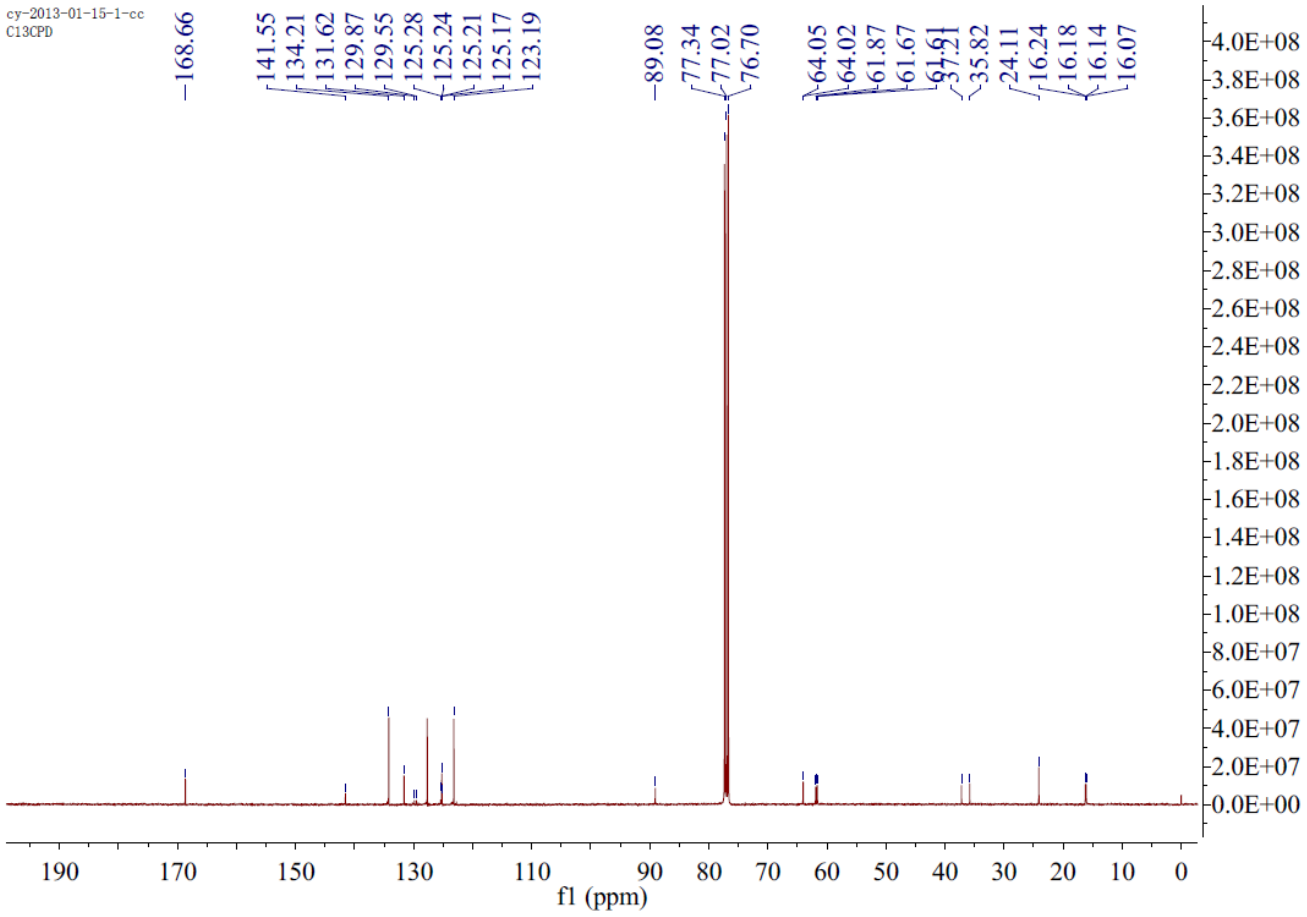


Diethyl(2-(1,3-dioxoisoindolin-2-yl)-2-((4-(trifluoromethyl)benzyl)oxy)propyl)phosphonate (8d):

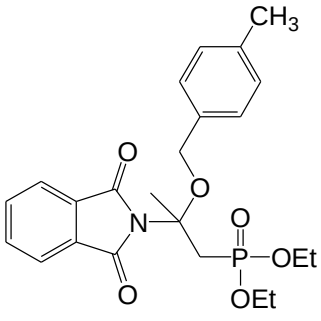


Colourless oil; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.80-7.88 (m, 2H, Ph), 7.70-7.77 (m, 2H, Ph), 7.54 (d, *J* = 7.9 Hz, 2H, Ph), 7.47 (d, *J* = 7.9 Hz, 2H, Ph), 4.69 (d, *J* = 11.9 Hz, 1H, OCH_2Ar), 4.53 (d, *J* = 11.9 Hz, 1H, OCH_2Ar), 3.93-4.11 (m, 4H, $2OCH_2$), 3.59-3.73 (m, 1H, CH_2-P), 2.45-2.58 (m, 1H, CH_2-P), 2.29 (s, 3H, CH_3), 1.21 (t, *J* = 7.0 Hz, 3H, CH_3), 1.13 (t, *J* = 7.0 Hz, 3H, CH_3); ^{13}C NMR (101 MHz, $CDCl_3$) δ: 168.66 (C=O), 141.55, 134.21, 131.62 (Ph), 129.71 (d, *J* = 32.6 Hz, Ph), 127.69 (Ph), 125.23 (q, *J* = 3.7 Hz, CF_3), 123.19 (Ph), 89.08 (O-C-N), 64.03 (d, *J* = 2.7 Hz, OCH_2Ar), 61.90 (d, *J* = 6.4 Hz, OCH_2), 61.64 (d, *J* = 6.4 Hz, OCH_2), 36.51 (d, *J* = 140.3 Hz, C-P), 24.11 (CH_3), 16.21 (d, *J* = 6.2 Hz, CH_3), 16.10 (d, *J* = 6.2 Hz, CH_3); ^{31}P NMR (162 MHz, $CDCl_3$): δ 24.06 (s); ESI-HRMS calcd for $[C_{23}H_{25}F_3NO_6P, M+Na]^+$: 522.1264; Found: 522.1266.

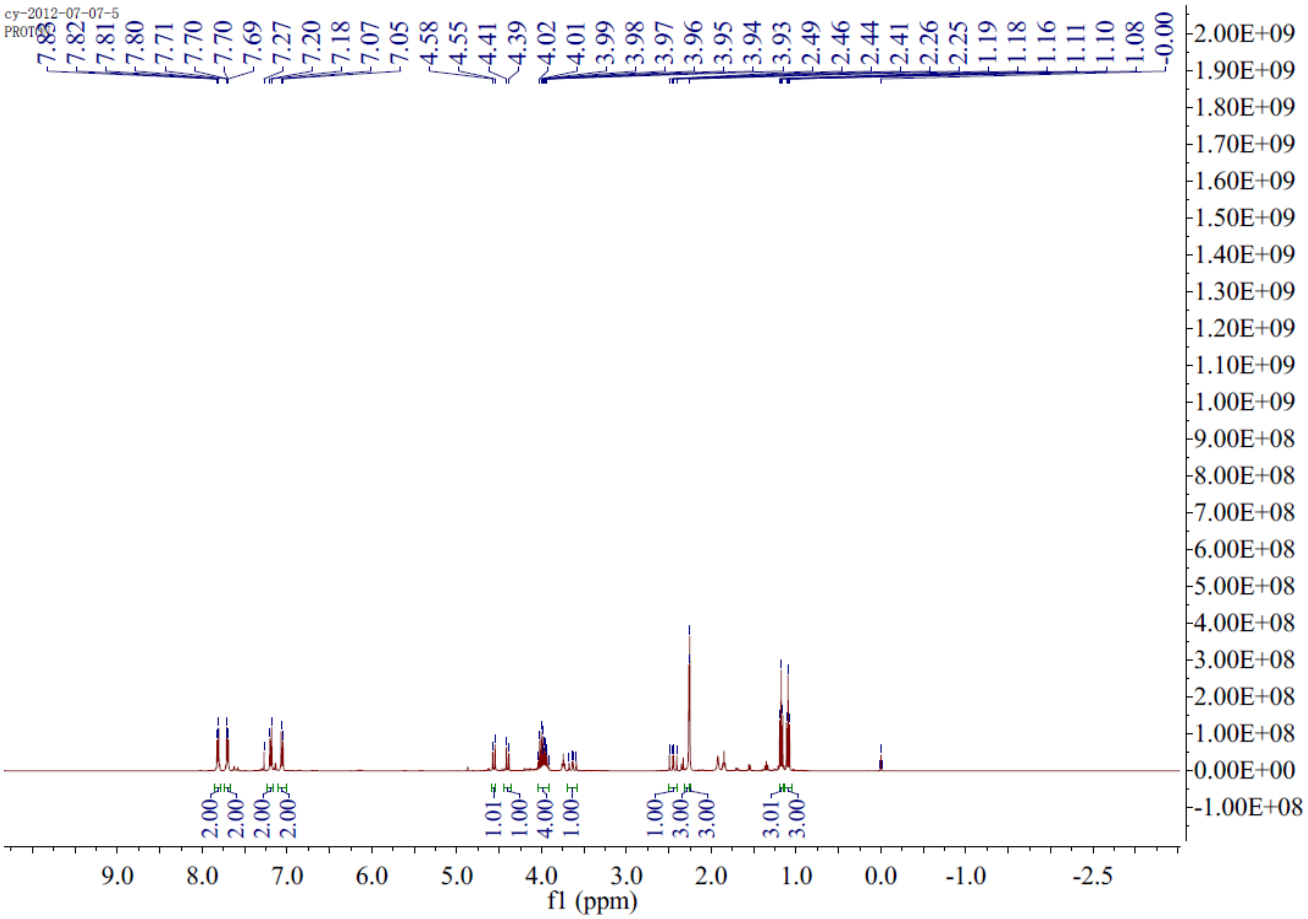


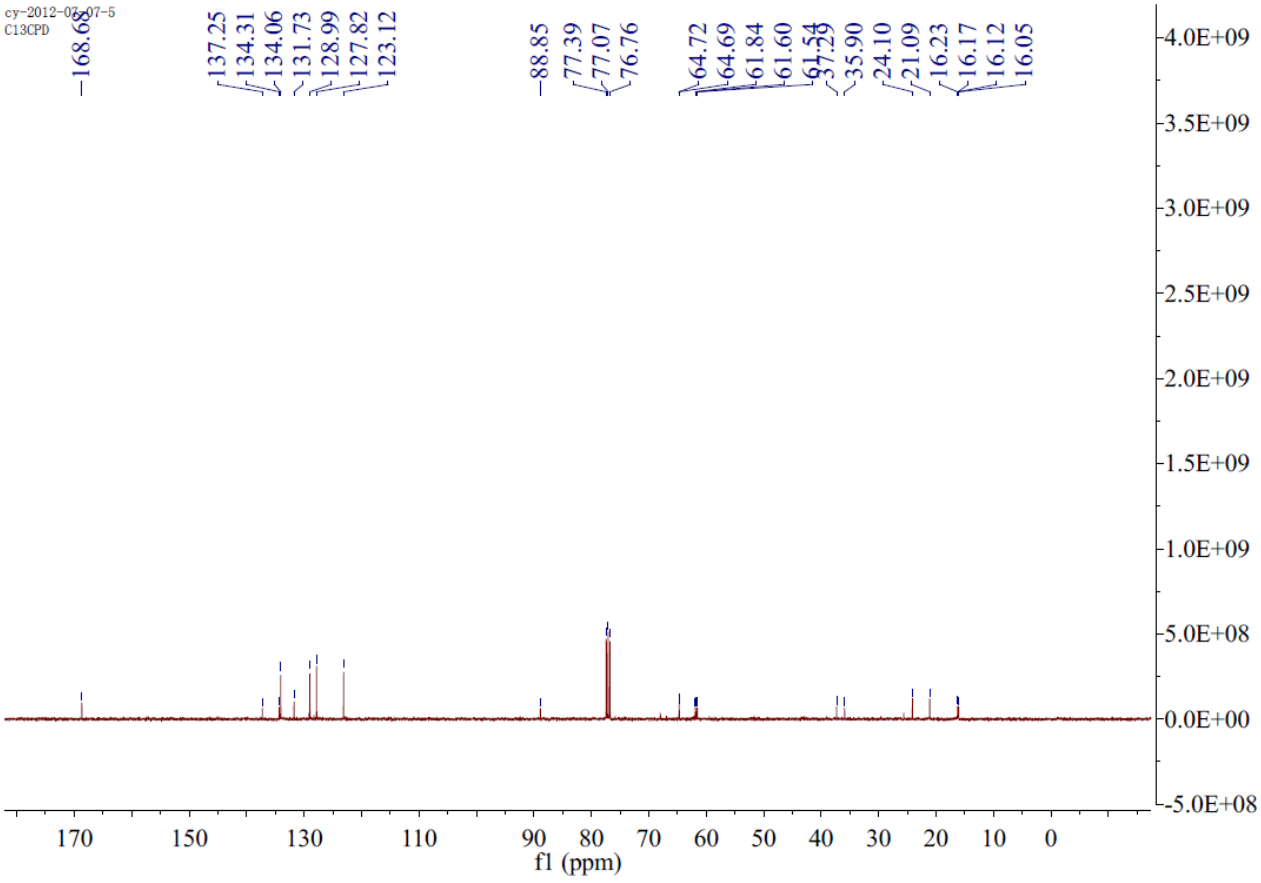


Diethyl (2-(1,3-dioxoisoindolin-2-yl)-2-((4-methylbenzyl)oxy)propyl)phosphonate (8e):

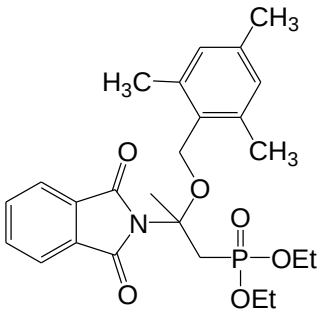


Colourless oil; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.78-7.83 (m, 2H, Ph), 7.68-7.73 (m, 2H, Ph), 7.19 (d, *J* = 8.0 Hz, 2H, Ph), 7.06 (d, *J* = 8.0 Hz, 2H, Ph), 4.56 (d, *J* = 11.0 Hz, 1H, OCH_2Ph), 4.40 (d, *J* = 11.0 Hz, 1H, OCH_2Ph), 3.90-4.06 (m, 4H, $2OCH_2$), 3.63 (dd, *J* = 18.9, 15.7 Hz, 1H, CH_2-P), 2.45 (dd, *J* = 18.9, 15.7 Hz, 1H, CH_2-P), 2.26 (s, 3H, CH_3), 2.25 (s, 3H, CH_3), 1.18 (t, *J* = 7.1 Hz, 3H, CH_3), 1.10 (t, *J* = 7.1 Hz, 3H, CH_3); ^{13}C NMR (101 MHz, $CDCl_3$): δ 168.68 (s, C=O), 137.25, 134.31, 134.06, 131.73, 128.99, 127.82, 123.12 (Ph), 88.85 (O-C-N), 64.70 (d, *J* = 2.6 Hz, OCH_2Ar), 61.88 (d, *J* = 6.3 Hz, OCH_2), 61.57 (d, *J* = 6.3 Hz, OCH_2), 36.60 (d, *J* = 140.0 Hz, C-P), 24.10 (CH_3), 21.09 (CH_3), 16.20 (d, *J* = 6.5 Hz, CH_3), 16.08 (d, *J* = 6.5 Hz, CH_3); ^{31}P NMR (162 MHz, $CDCl_3$): δ 24.40 (s); ESI-HRMS calcd for $[C_{23}H_{28}NO_6P, M+Na]^+$: 468.1546; Found: 468.1545.

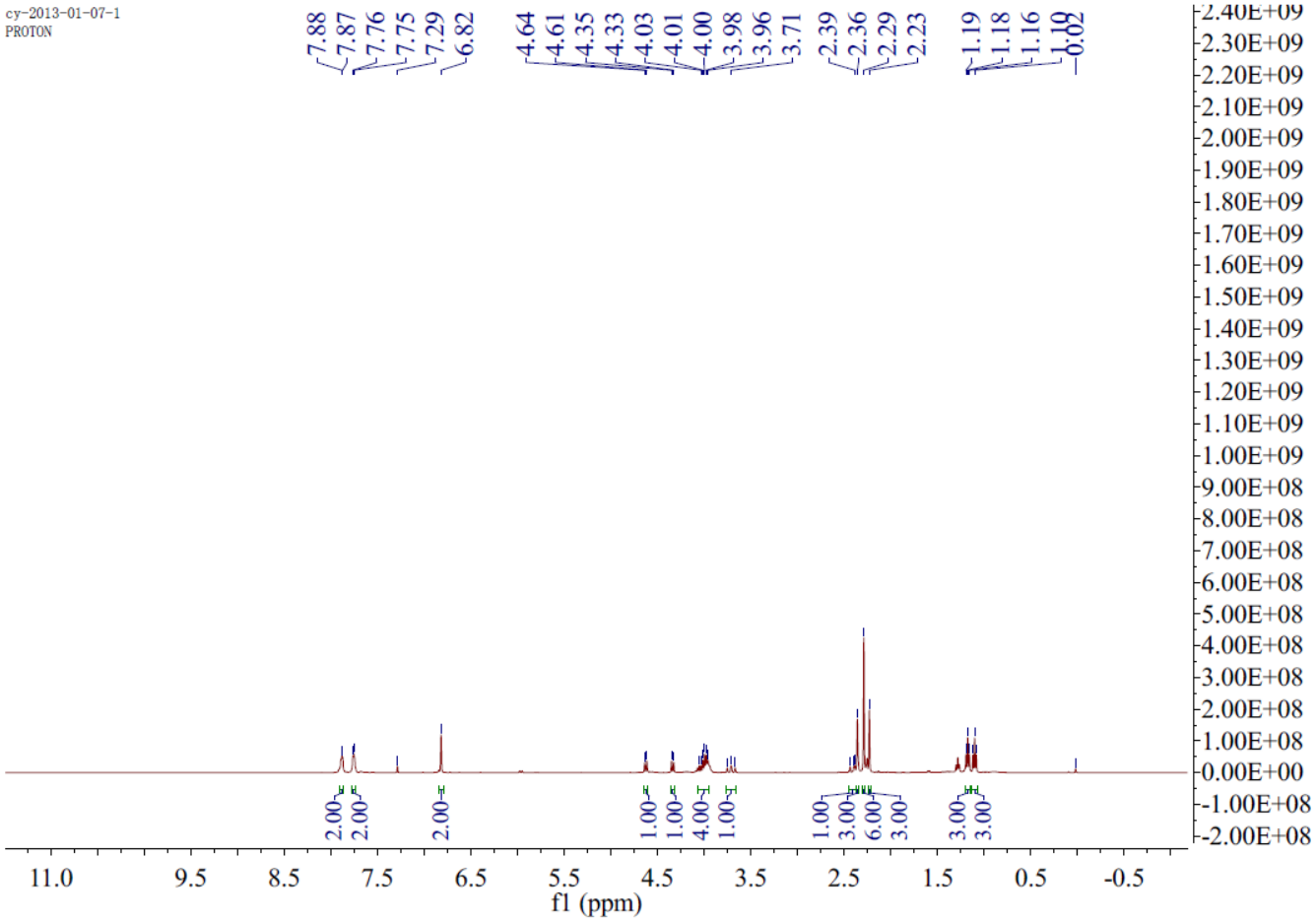


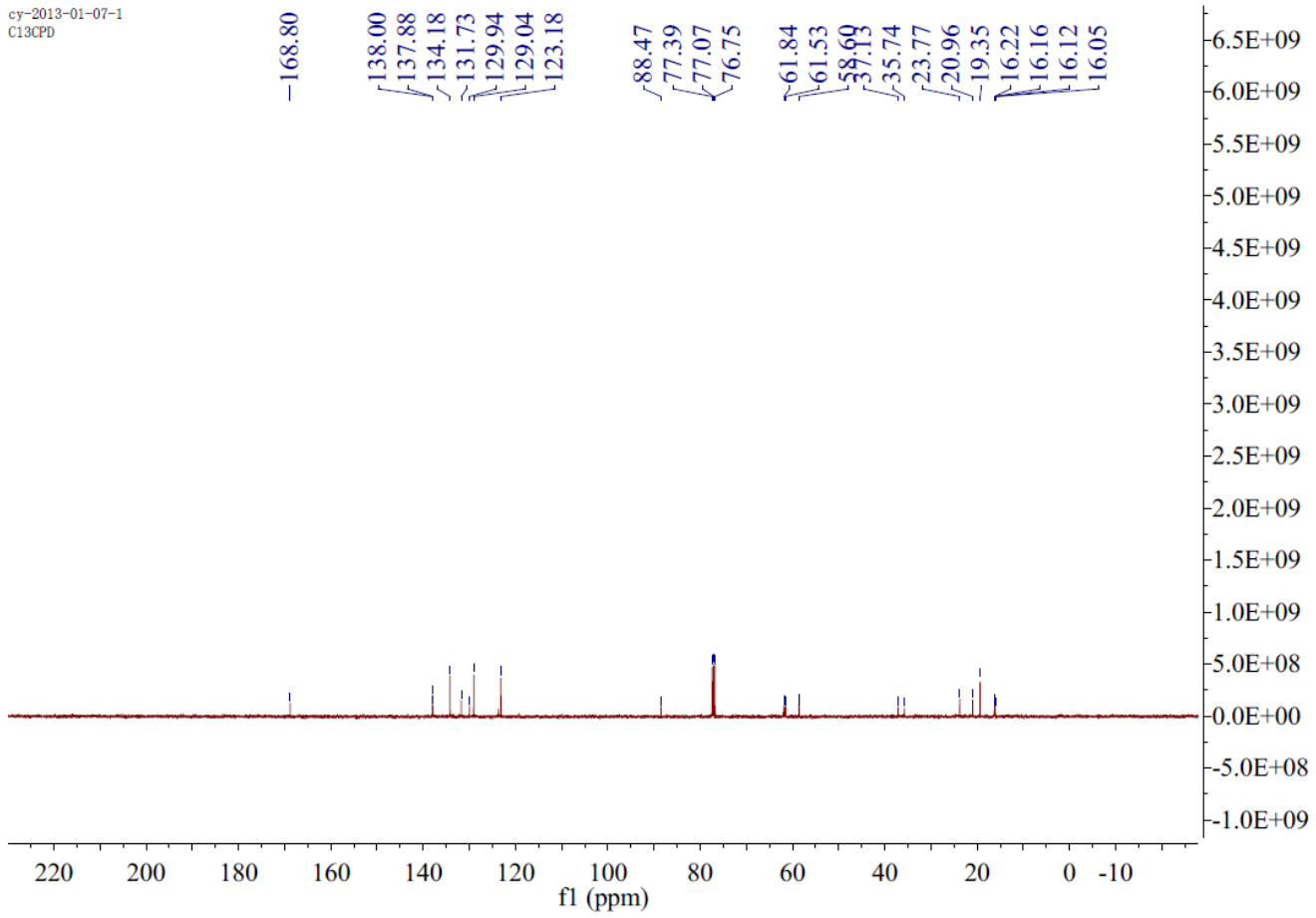


Diethyl(2-(1,3-dioxoisoindolin-2-yl)-2-((2,4,6-trimethylbenzyl)oxy)propyl)phosphonate (8f):

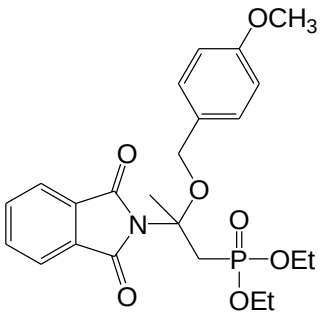


Colourless oil; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.86-7.91 (m, 2H, Ph), 7.73-7.79 (m, 2H, Ph), 6.82 (s, 2H, Ph), 4.63 (d, *J* = 9.4 Hz, 1H, OCH_2Ar), 4.34 (d, *J* = 9.4 Hz, 1H, OCH_2Ar), 3.93-4.10 (m, 4H, $2OCH_2$), 3.65-3.78 (m, 1H, CH_2-P), 2.38-2.45 (m, 1H, CH_2-P), 2.36 (s, 3H, CH_3), 2.29 (s, 6H, $2CH_3$), 2.23 (s, 1H, CH_3), 1.18 (t, *J* = 7.0 Hz, 3H, CH_3), 1.10 (t, *J* = 7.0 Hz, 1H, CH_3). ^{13}C NMR (101 MHz, $CDCl_3$): δ 168.80 (C=O), 138.00, 137.88, 134.18, 131.73, 129.94, 129.04, 123.18 (Ph), 88.47 (O-C-N), 61.81 (d, *J* = 6.5 Hz, OCH_2), 61.50 (d, *J* = 6.5 Hz, OCH_2), 58.58 (d, *J* = 2.8 Hz, CH_2Ar), 36.43 (d, *J* = 139.0 Hz, C-P), 23.77 (CH_3), 20.96 (CH_3), 19.35 (CH_3), 16.19 (d, *J* = 6.5 Hz, CH_3), 16.09 (d, *J* = 6.5 Hz, CH_3). ^{31}P NMR (162 MHz, $CDCl_3$): δ 24.58 (s); ESI-HRMS calcd for $[C_{25}H_{32}NO_6P, M+Na]^+$: 496.1859; Found: 496.1862.

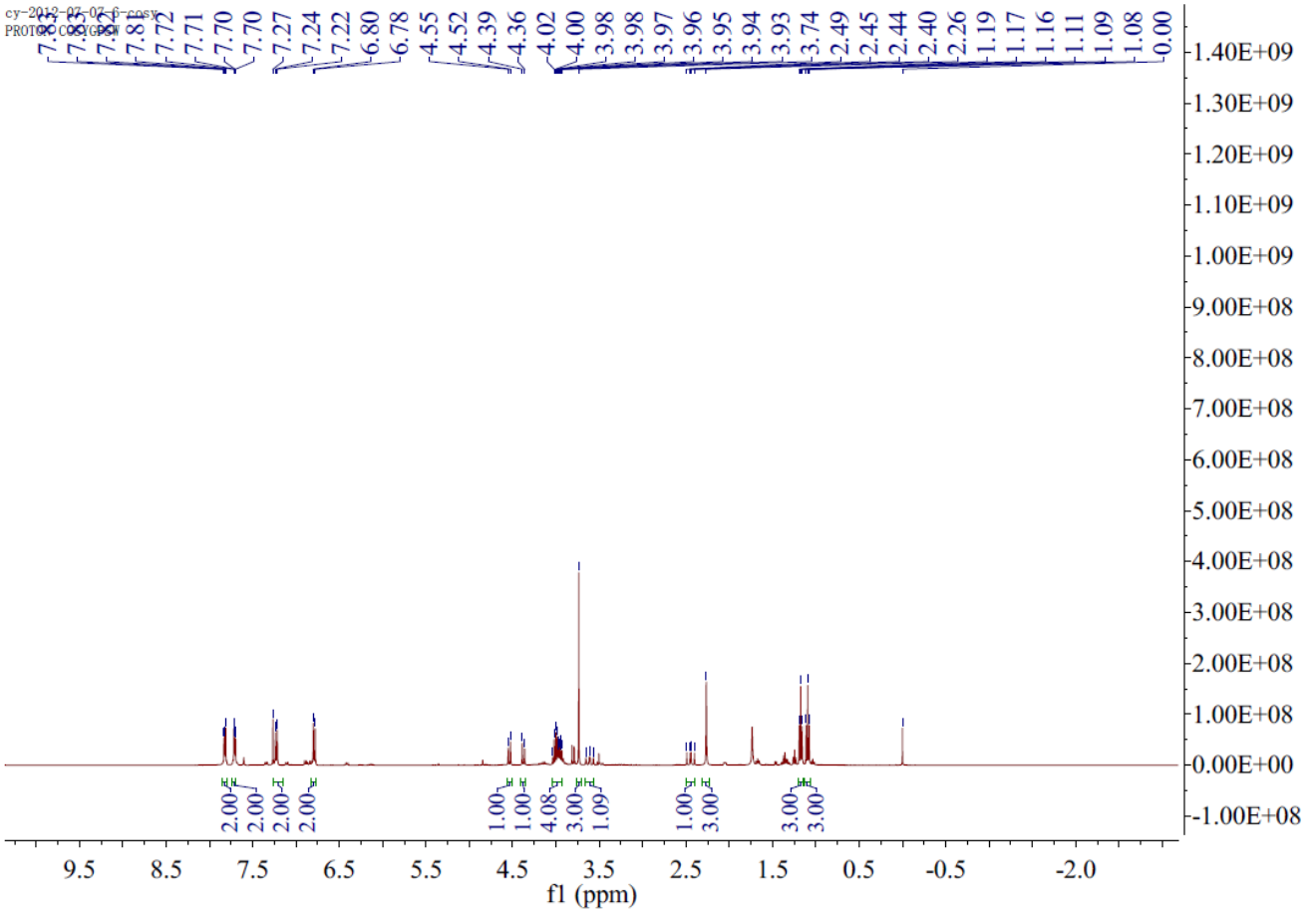


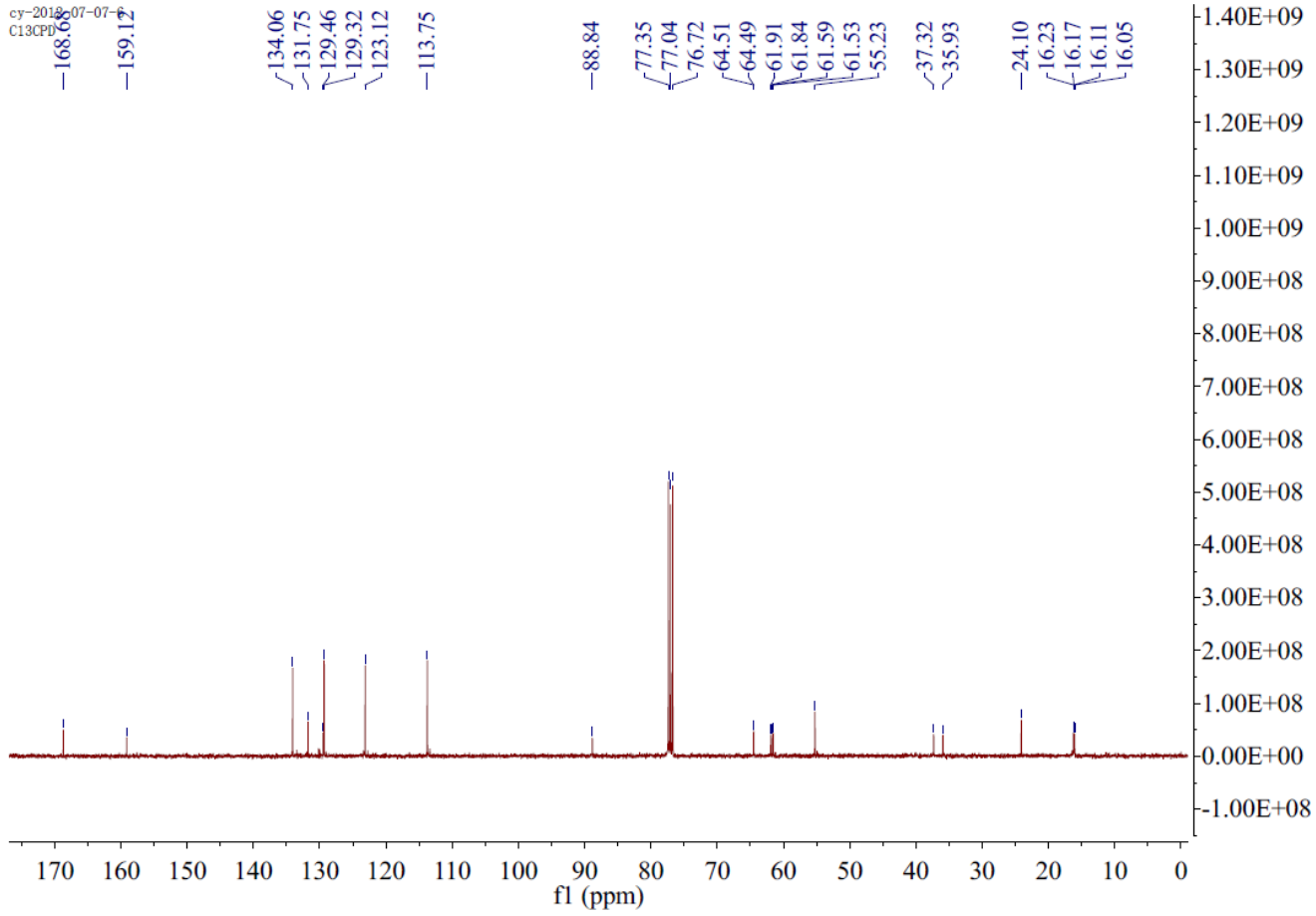


Diethyl(2-(1,3-dioxoisoindolin-2-yl)-2-((4-methoxybenzyl)oxy)propyl)phosphonate (8g):

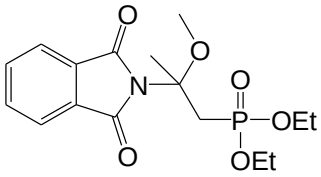


Colourless oil; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.80-7.85 (m, 2H, Ph), 7.68-7.74 (m, 2H, Ph), 7.23 (d, *J* = 8.7 Hz, 2H, Ph), 6.79 (d, *J* = 8.7 Hz, 2H, Ph), 4.54 (d, *J* = 10.8 Hz, 1H, OCH_2Ph), 4.37 (d, *J* = 10.8 Hz, 1H, OCH_2Ph), 3.93-4.05 (m, 4H, $2OCH_2$), 3.74 (s, 3H, OMe), 3.61 (dd, *J* = 18.9, 15.7 Hz, 1H, CH_2-P), 2.45 (dd, *J* = 18.9, 15.7 Hz, 1H, CH_2-P), 2.26 (s, 3H, CH_3), 1.17 (t, *J* = 7.1 Hz, 3H, CH_3), 1.09 (t, *J* = 7.1 Hz, 3H, CH_3); ^{13}C NMR (101 MHz, $CDCl_3$): δ 168.68 (C=O), 159.12, 134.06, 131.75, 129.46, 129.32, 123.12, 113.75 (Ph), 88.84 (O-C-N), 64.50 (d, *J* = 2.4 Hz, OCH_2Ar), 61.88 (d, *J* = 6.4 Hz, OCH_2), 61.56 (d, *J* = 6.4 Hz, OCH_2), 55.23 (OCH_3), 36.62 (d, *J* = 139.8 Hz, C-P), 24.10 (CH_3), 16.20 (d, *J* = 6.4 Hz, CH_3), 16.08 (d, *J* = 6.4 Hz, CH_3); ^{31}P NMR (162 MHz, $CDCl_3$): δ 24.37 (s); ESI-HRMS calcd for $[C_{23}H_{28}NO_7P, M+Na]^+$: 484.1501; Found: 484.1504.

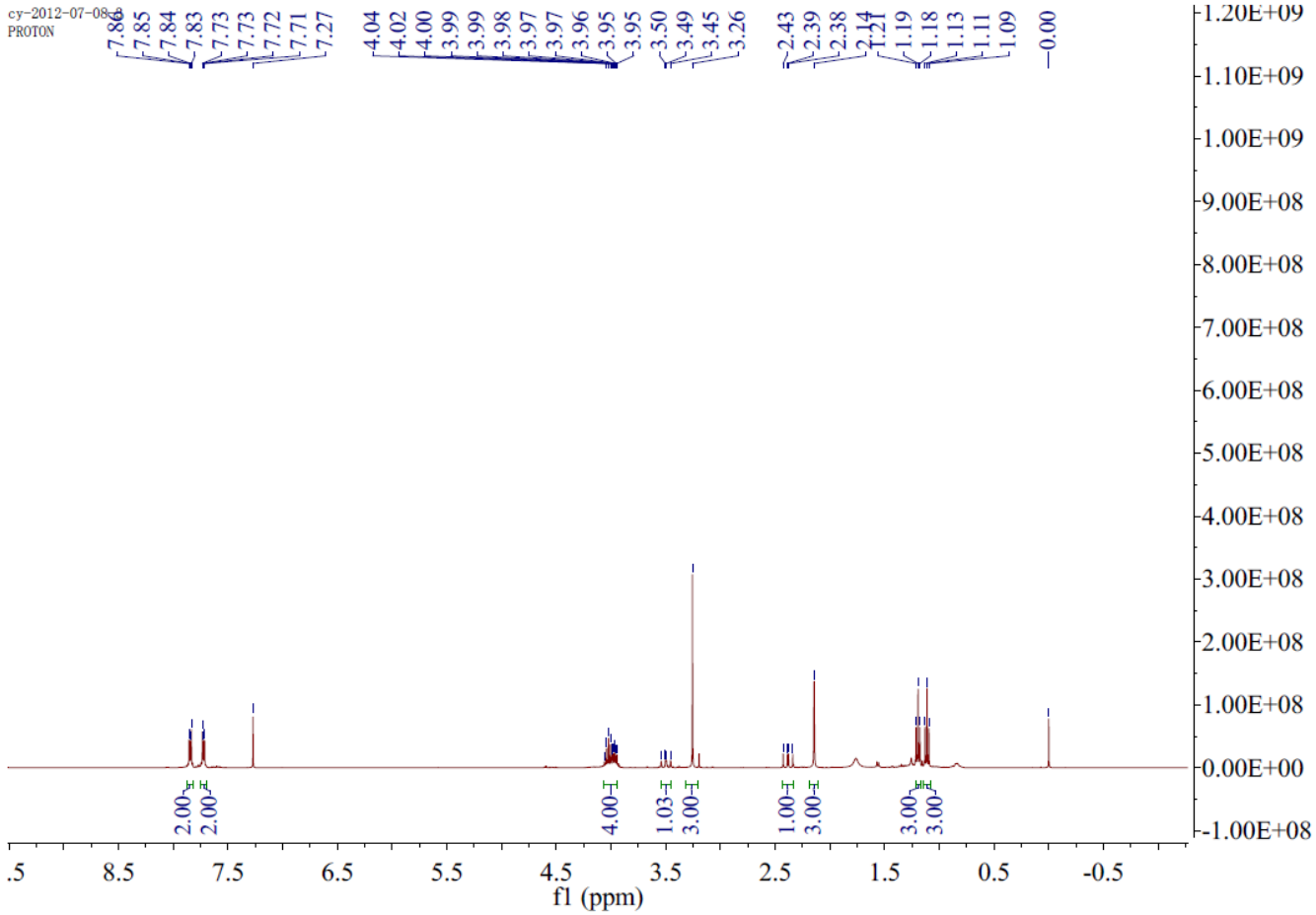


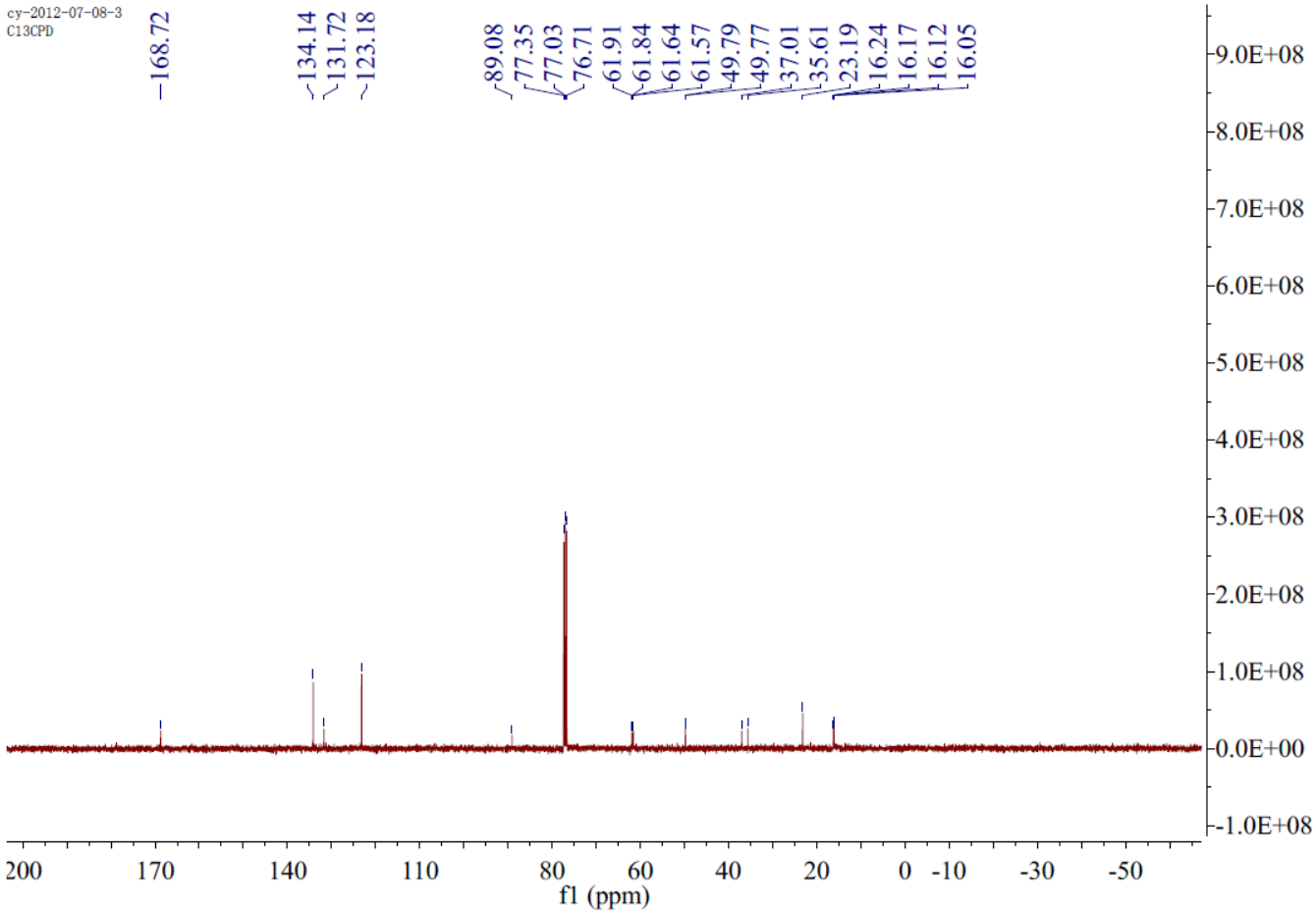


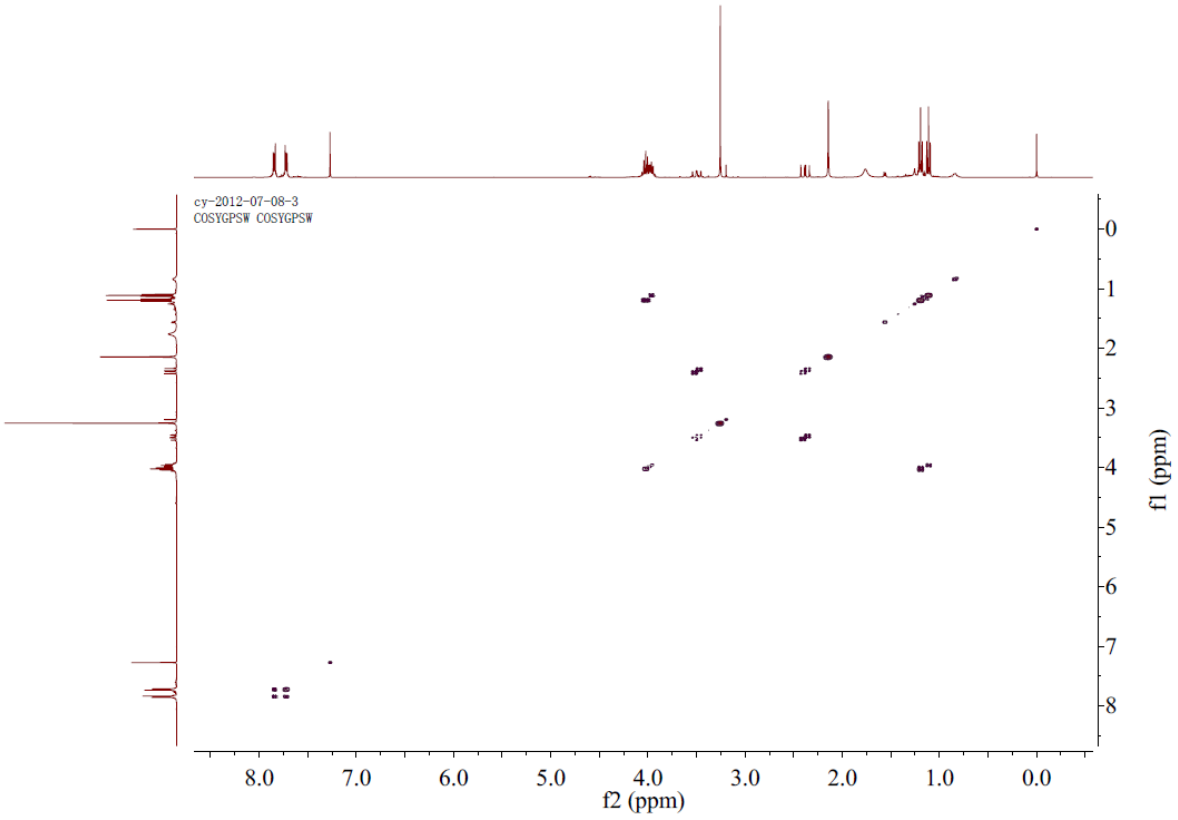
Diethyl (2-(1,3-dioxoisoindolin-2-yl)-2-methoxypropyl)phosphonate (8h):



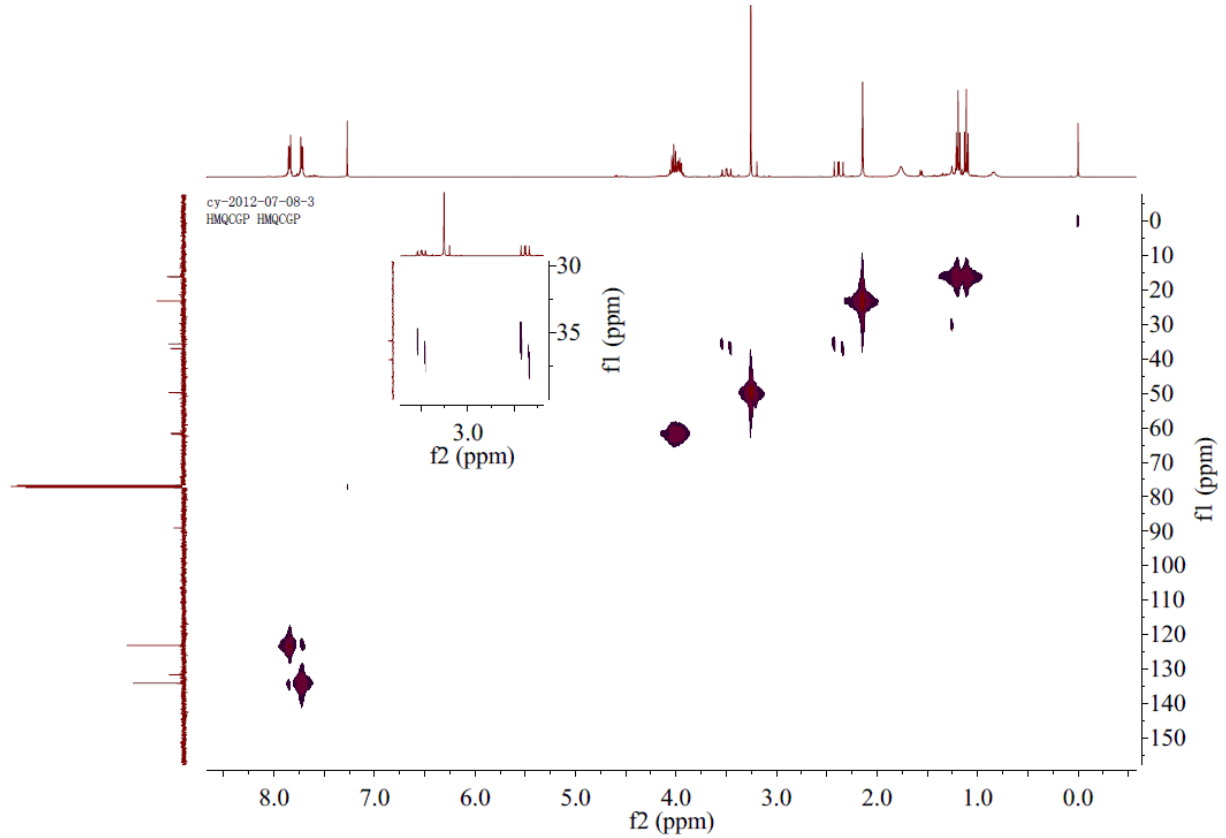
Colourless oil; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.83-7.86 (m, 2H, Ph), 7.70-7.74 (m, 2H, Ph), 3.94-4.07 (m, 4H, $2OCH_2$), 3.50 (dd, *J* = 19.6, 15.5 Hz, 1H, CH_2-P), 3.26 (s, 3H, OCH_3), 2.38 (dd, *J* = 19.6, 15.5 Hz, 1H, CH_2-P), 2.14 (s, 3H, CH_3), 1.19 (t, *J* = 7.1 Hz, 3H, CH_3), 1.11 (t, *J* = 7.1 Hz, 3H, CH_3); ^{13}C NMR (101 MHz, $CDCl_3$): δ 168.72 (C=O), 134.14, 131.72, 123.18 (Ph), 89.08 (O-C-N), 61.88 (d, *J* = 6.6Hz, OCH_2), 61.60 (d, *J* = 6.6Hz, OCH_2), 49.78 (d, *J* = 2.8 Hz, OCH_3), 36.31 (d, *J* = 140.7 Hz, C-P), 23.19 (CH_3), 16.20 (d, *J* = 6.4 Hz,CH_3), 16.09 (d, *J* = 6.4 Hz, CH_3); ^{31}P NMR (162 MHz, $CDCl_3$): δ 24.36 (s); ESI-HRMS calcd for $[C_{16}H_{22}NO_6P, M+Na]^+$: 378.1077; Found: 378.1073.



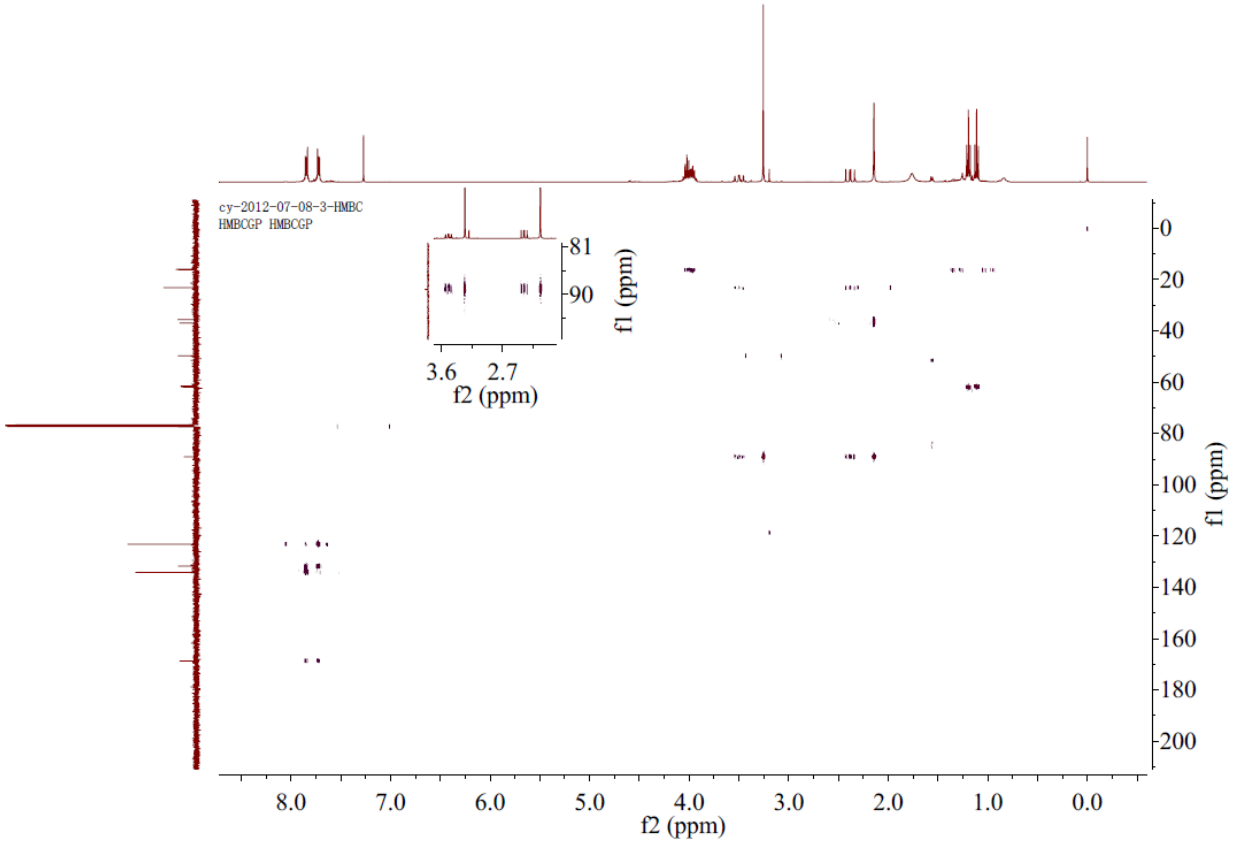




^{1}H-^{1}H COSY spectrum of **8h**

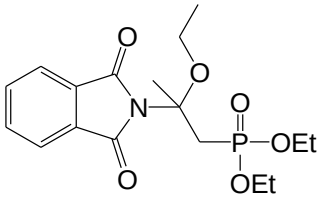


HMQC spectrum of **8h**

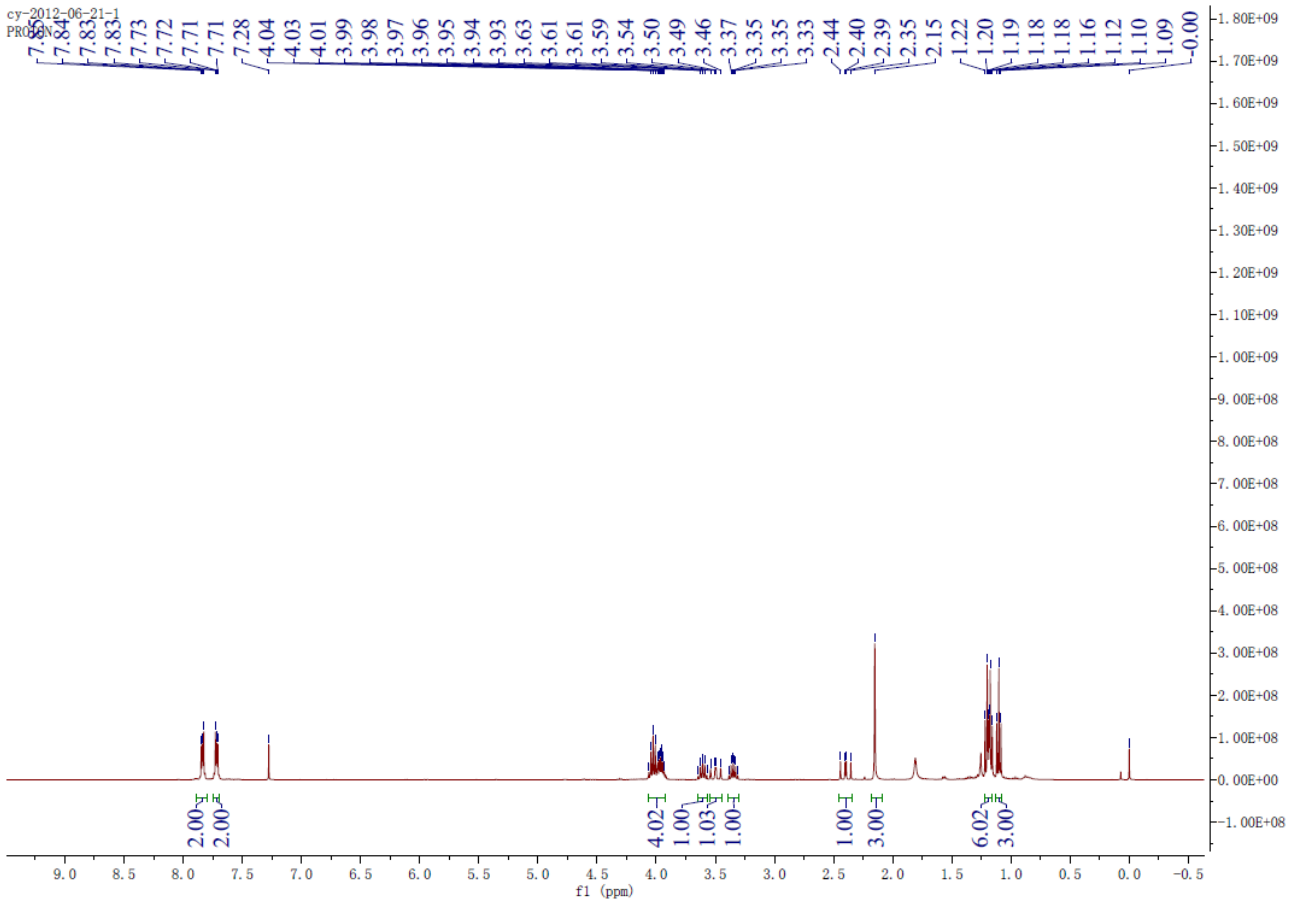


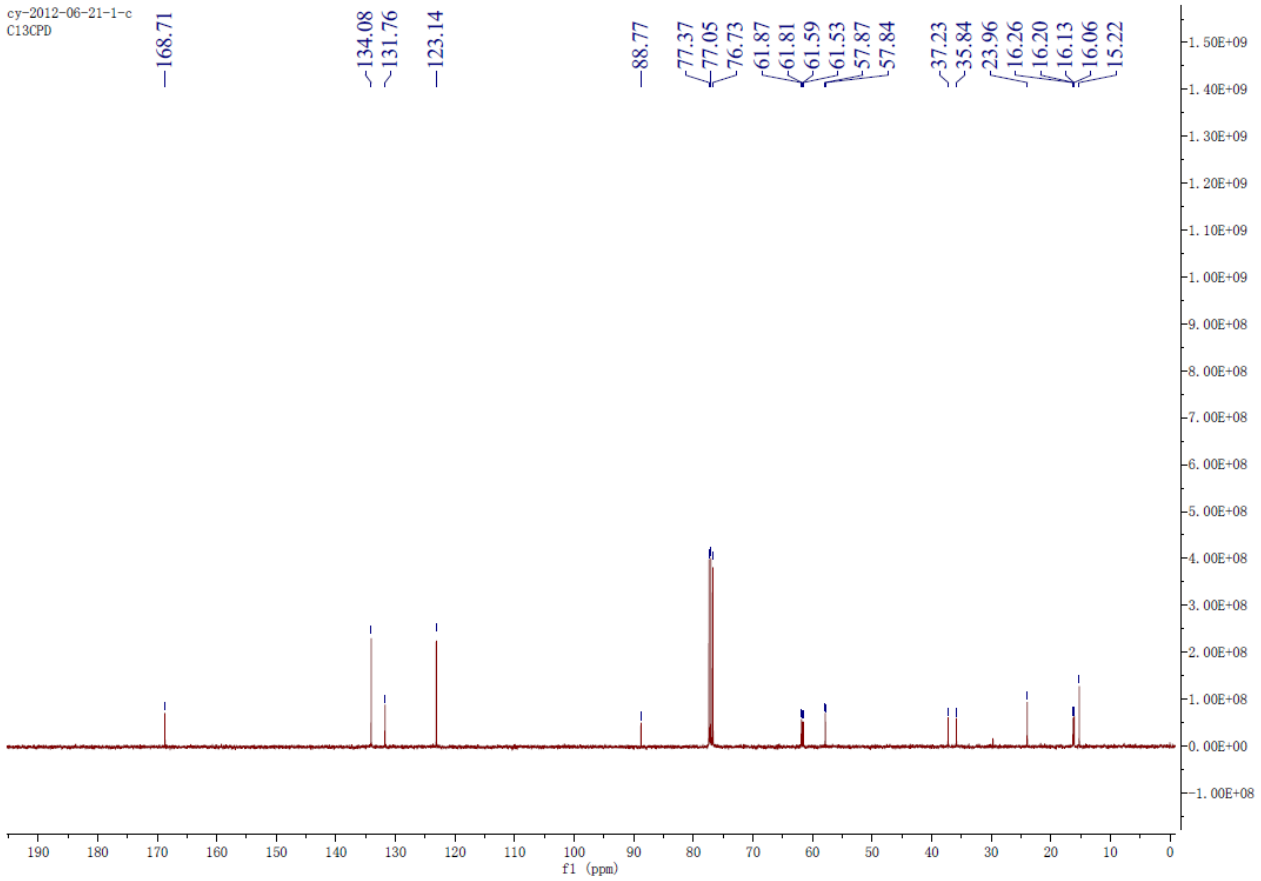
HMBC spectrum of **8h**

Diethyl (2-(1,3-dioxoisoindolin-2-yl)-2-ethoxypropyl)phosphonate (8i):

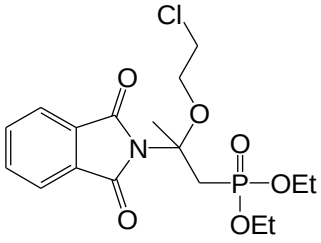


Colourless oil; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.82-7.85 (m, 2H, Ph), 7.70-7.73 (m, 2H, Ph), 3.90-4.09 (m, 4H, $2OCH_2$), 3.61 (dq, *J* = 14.1, 7.0 Hz, 1H, OCH_2), 3.50 (dd, *J* = 19.0, 15.6 Hz, 1H, CH_2-P), 3.35 (dq, *J* = 14.1, 7.0 Hz, 1H, OCH_2), 2.40 (dd, *J* = 19.0, 15.6 Hz, 1H, CH_2-P), 2.15 (s, 3H, CH_3), 1.19 (dt, *J* = 10.1, 7.0 Hz, 6H, $2CH_3$), 1.10 (t, *J* = 7.1 Hz, 3H, CH_3); ^{13}C NMR (101 MHz, $CDCl_3$): δ 168.71 (C=O), 134.08, 131.76, 123.14 (Ph), 88.77 (O-C-N), 61.84 (d, *J* = 6.4 Hz, OCH_2), 61.56 (d, *J* = 6.4 Hz, OCH_2), 57.85 (d, *J* = 2.5 Hz, OCH_2), 36.54 (d, *J* = 139.9 Hz, C-P), 23.96 (CH_3), 16.23 (d, *J* = 6.4 Hz, CH_3), 16.10 (d, *J* = 6.4 Hz, CH_3), 15.22 (CH_3); ^{31}P NMR (162 MHz, $CDCl_3$): δ 24.48 (s); ESI-HRMS calcd for $[C_{17}H_{24}NO_6P, M+Na]^+$: 392.1233; Found: 392.1231.

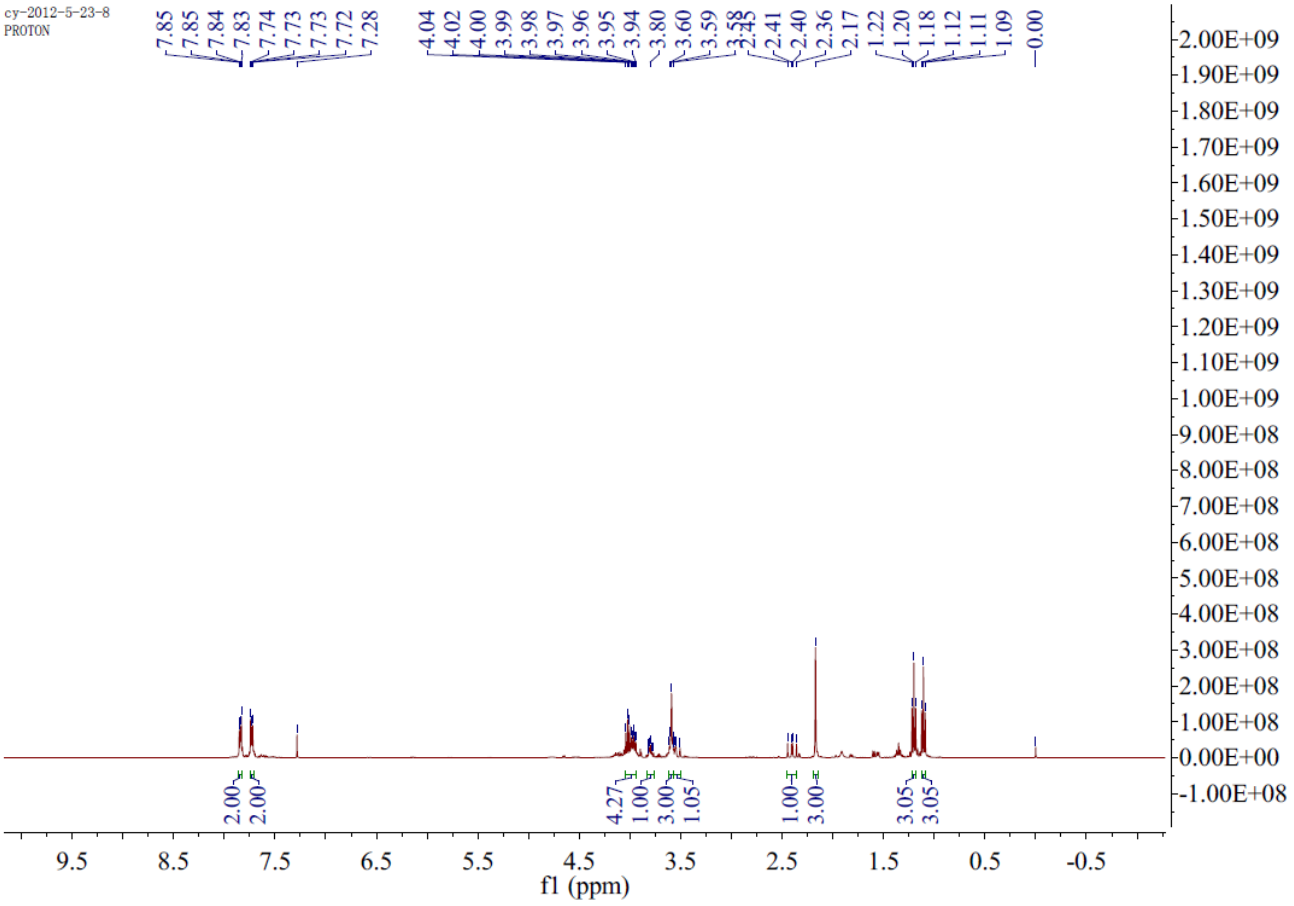


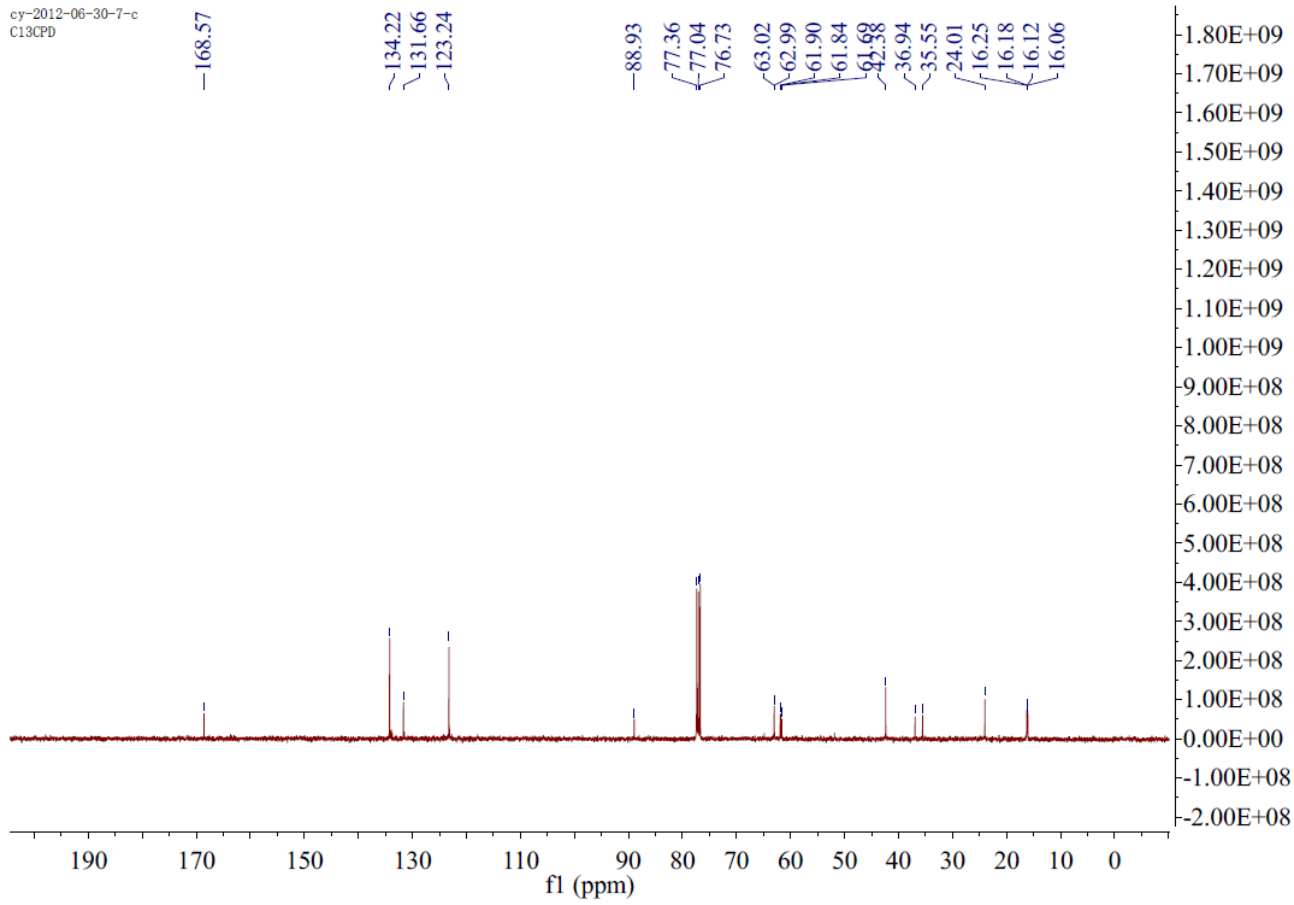


Diethyl (2-(2-chloroethoxy)-2-(1,3-dioxoisoindolin-2-yl)propyl)phosphonate (8j):

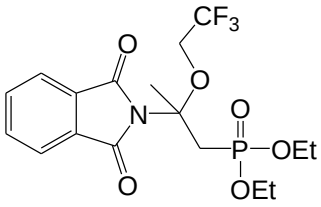


Colourless oil; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.83-7.86 (m, 2H, Ph), 7.72-7.75 (m, 2H, Ph), 3.93-4.05 (m, 4H, $2OCH_2$), 3.76-3.83 (m, 1H, OCH_2), 3.57-3.63 (m, 3H, OCH_2, CH_2Cl), 3.54 (dd, *J* = 13.8, 10.9 Hz, 1H, CH_2-P), 2.40 (dd, *J* = 19.6, 15.5 Hz, 1H, CH_2-P), 2.17 (s, 3H, CH_3), 1.20 (t, *J* = 7.1 Hz, 3H, CH_3), 1.11 (t, *J* = 7.1 Hz, 3H, CH_3); ^{13}C NMR (101 MHz, $CDCl_3$): δ 168.57 (C=O), 134.22, 131.66, 123.24 (Ph), 88.93 (O-C-N), 63.01 (d, *J* = 2.7 Hz, OCH_2), 61.87 (d, *J* = 6.3 Hz, OCH_2), 61.66 (d, *J* = 6.3 Hz, OCH_2), 42.38 (CH_2Cl), 36.25 (d, *J* = 140.4 Hz, C-P), 24.01 (CH_3), 16.22 (d, *J* = 6.5 Hz, CH_3), 16.09 (d, *J* = 6.5 Hz, CH_3); ^{31}P NMR (162 MHz, $CDCl_3$): δ 24.03 (s); ESI-HRMS calcd for $[C_{17}H_{23}ClNO_6P, M+Na]^+$: 426.0844; Found: 426.0839.

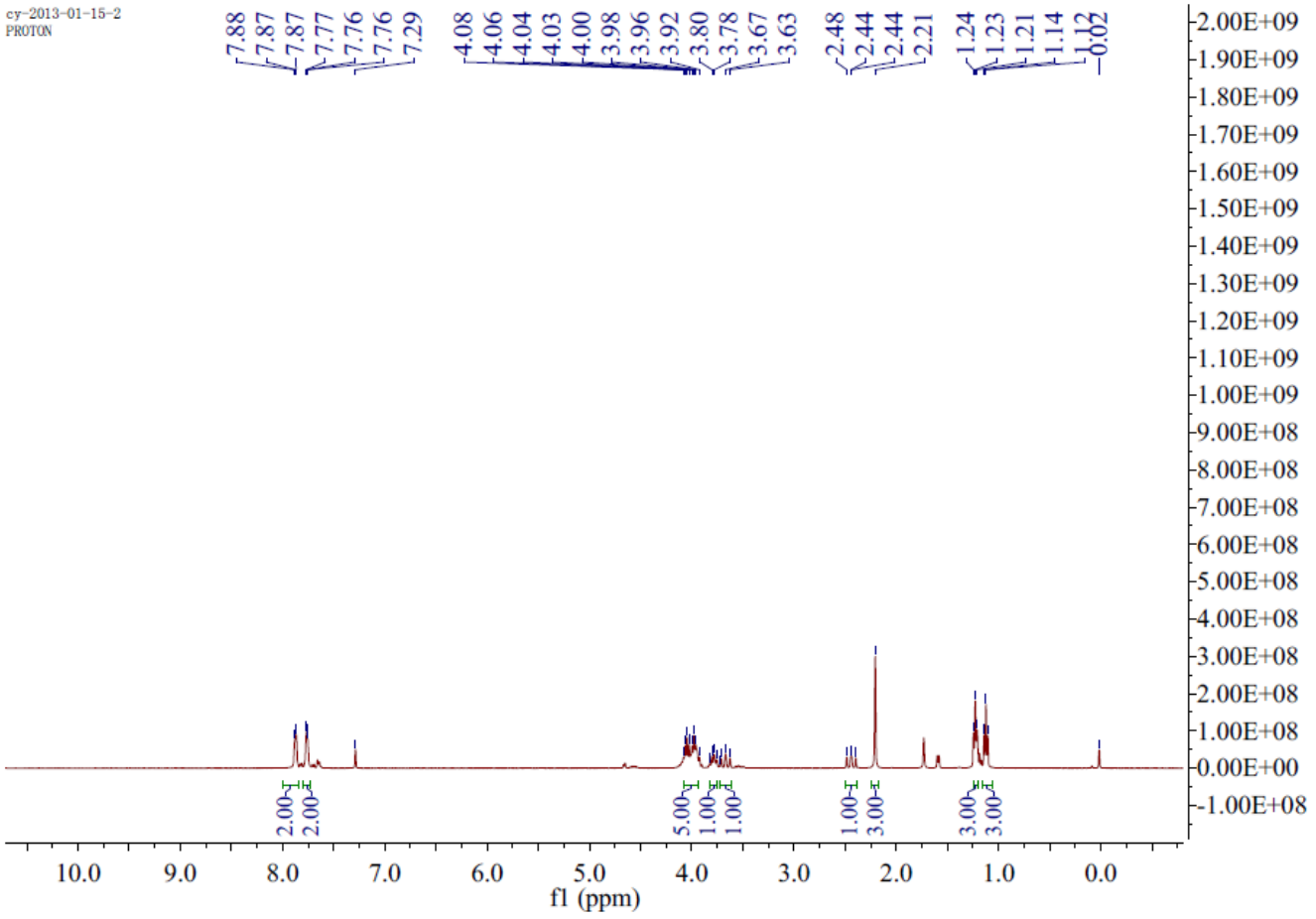


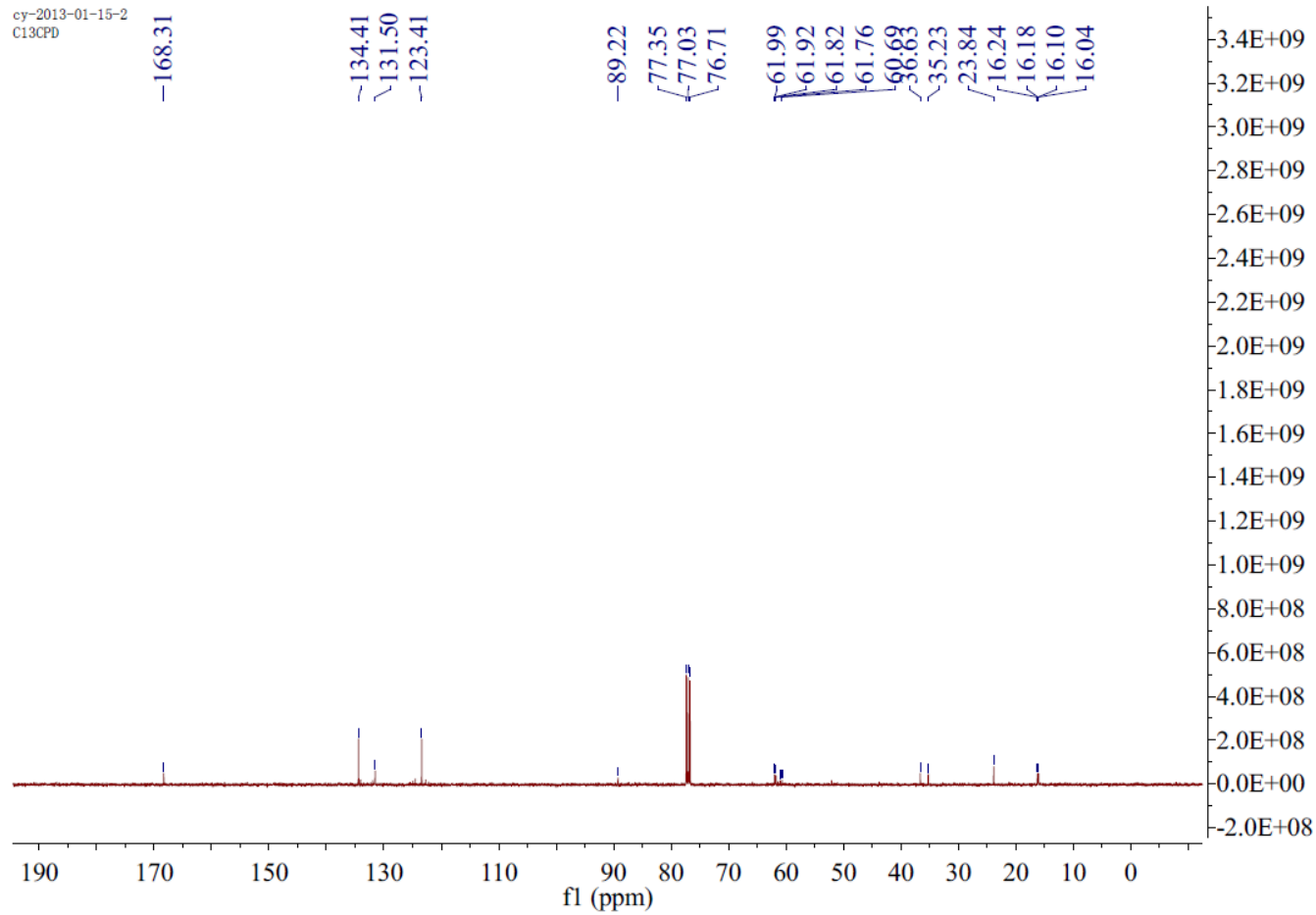


Diethyl (2-(1,3-dioxoisoindolin-2-yl)-2-(2,2,2-trifluoroethoxy)propyl)phosphonate (8k):

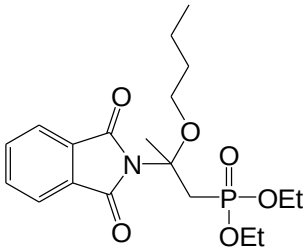


Colourless oil; ^{1}H NMR (400 MHz, $CDCl_3$): δ7.84-7.90 (m, 2H, Ph), 7.73-7.80 (m, 2H, Ph), 3.90-4.13 (m, 5H, $2OCH_2$, OCH_2CF_3), 3.75-3.84 (m, 1H, OCH_2CF_3), 3.61-3.72 (m, 1H, CH_2-P), 2.37-2.50 (m, 1H, CH_2-P), 2.21 (s, 1H, CH_3), 1.23 (t, J = 7.1 Hz, 3H, CH_3), 1.12 (t, J = 7.1 Hz, 3H, CH_3); ^{13}C NMR (101 MHz, $CDCl_3$): δ 168.31 (C=O), 134.41, 131.50, 123.41 (Ph), 89.22 (N-C-O),61.96 (d, J = 6.5 Hz, OCH_2), 61.79 (d, J = 6.5 Hz, OCH_2), 61.03 (d, J = 3.2 Hz, OCH_2), 60.67 (d, J = 2.9 Hz, CF_3), 35.93 (d, J = 140.8 Hz, C-P), 23.84 (CH_3), 16.21 (d, J = 6.3 Hz, CH_3), 16.07 (d, J = 6.3 Hz, CH_3); ^{31}P NMR (162 MHz, $CDCl_3$): δ 23.38 (s); ESI-HRMS calcd for $[C_{17}H_{21}F_3NO_6P, M+Na]^+$: 446.0951; Found: 446.0954.

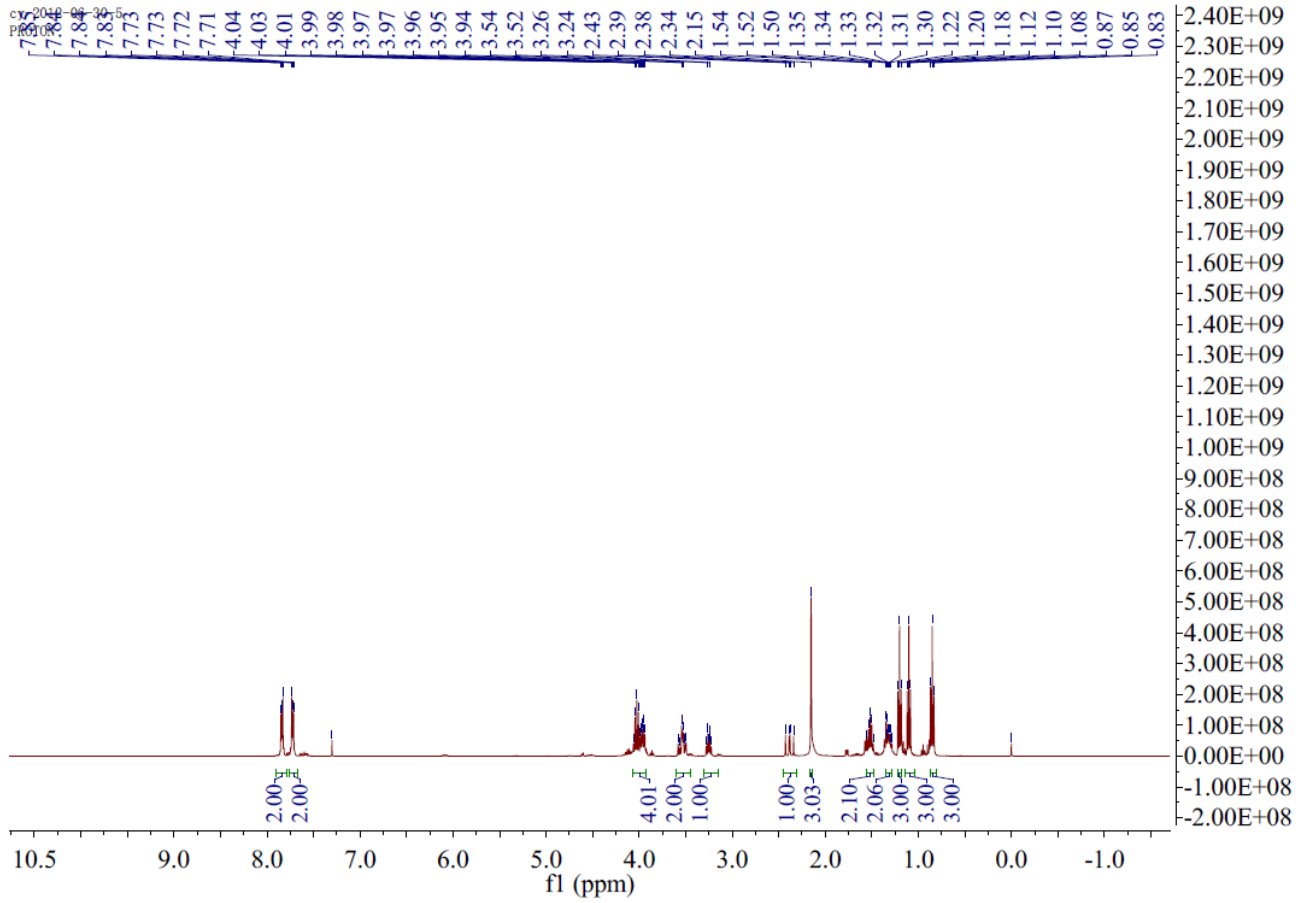


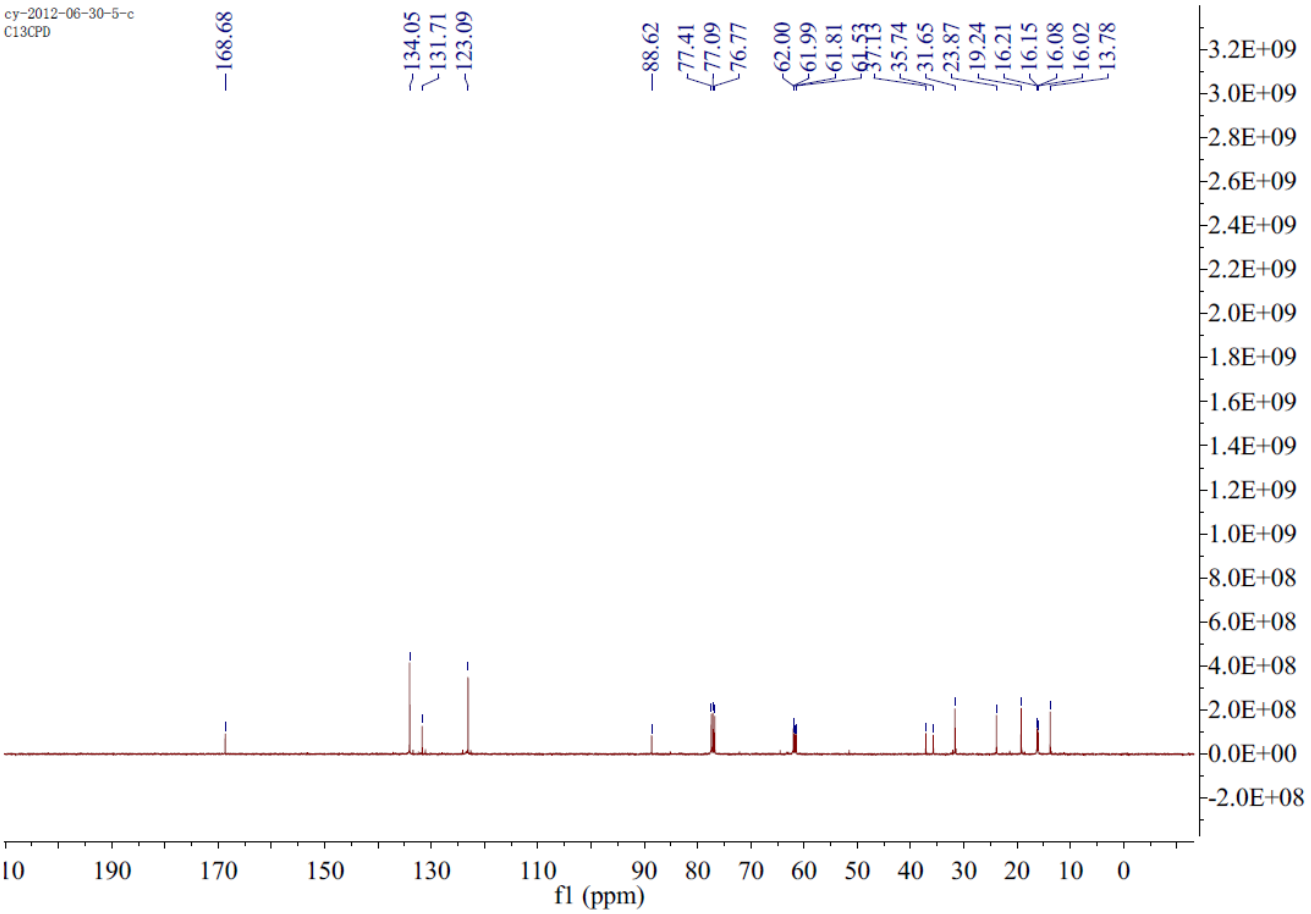


Diethyl (2-butoxy-2-(1,3-dioxoisoindolin-2-yl)propyl)phosphonate (8l):

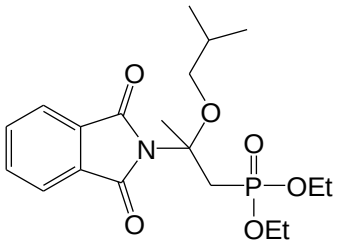


Colourless oil; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.82-7.86 (m, 2H, Ph), 7.70-7.74 (m, 2H, Ph), 3.93-4.07 (m, 4H, $2OCH_2$), 3.49-3.59 (m, 2H, OCH_2, CH_2-P), 3.25 (dt, *J* = 8.6, 6.6 Hz, 1H, OCH_2), 2.38 (dd, *J* = 19.6, 15.5 Hz, 1H, CH_2-P), 2.15 (s, 3H, CH_3), 1.48-1.55 (m, 2H, CH_2), 1.28-1.34 (m, 2H, CH_2), 1.20 (t, *J* = 7.1 Hz, 3H, CH_3), 1.10 (t, *J* = 7.1 Hz, 3H, CH_3), 0.85 (t, *J* = 7.4 Hz, 3H, CH_3); ^{13}C NMR (101 MHz, $CDCl_3$): δ 168.68 (C=O), 134.05, 131.71, 123.09 (Ph), 88.62 (O-C-N), 61.99 (OCH_2), 61.78 (d, *J* = 6.5 Hz, OCH_2), 61.50 (d, *J* = 6.5 Hz, OCH_2), 36.44 (d, *J* = 140.0 Hz, C-P), 31.65 (CH_2), 23.87 (CH_3), 19.24 (CH_2), 16.18 (d, *J* = 6.4 Hz, CH_3), 16.05 (d, *J* = 6.4 Hz, CH_3), 13.78 (CH_3); ^{31}P NMR (162 MHz, $CDCl_3$): δ 24.56 (s); ESI-HRMS calcd for $[C_{19}H_{28}NO_6P, M+Na]^+$: 420.1546; Found: 420.1543.

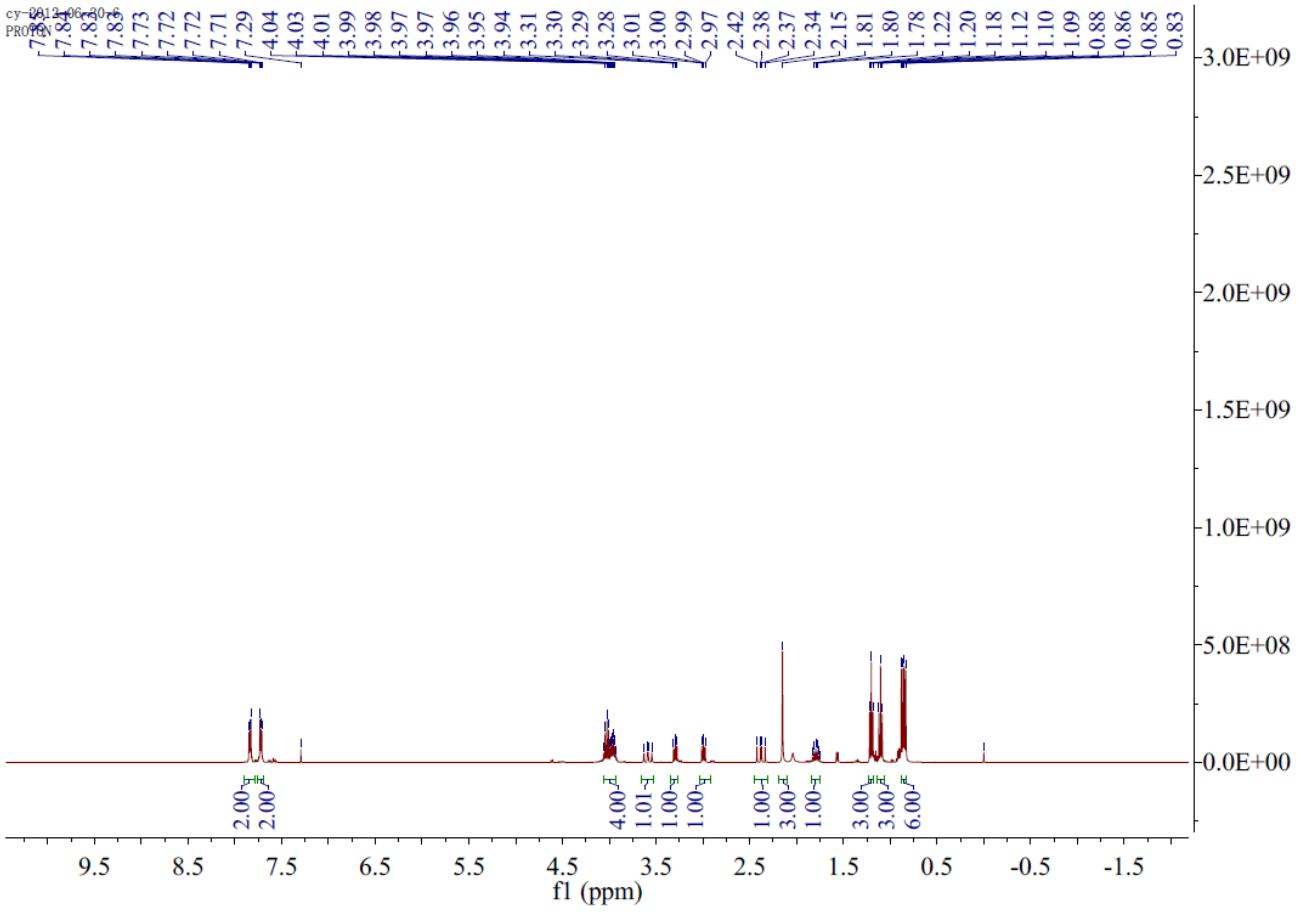


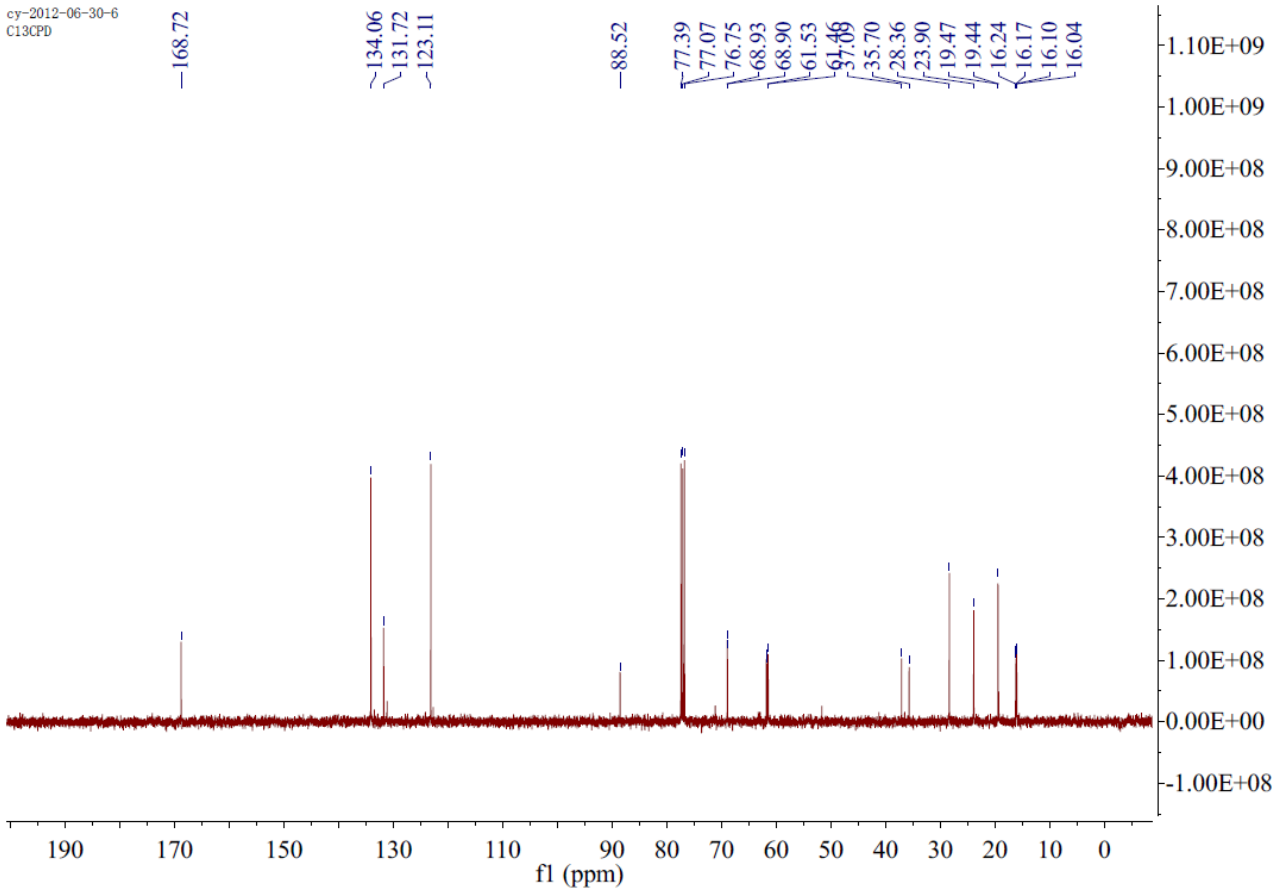


Diethyl (2-(1,3-dioxoisoindolin-2-yl)-2-isobutoxypropyl)phosphonate (8m):

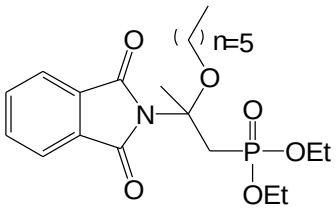


Colourless oil; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.82-7.85 (m, 2H, Ph), 7.70-7.74 (m, 2H, Ph), 3.92-4.07 (m, 4H, $2OCH_2$), 3.59 (dd, *J* = 18.9, 15.7 Hz, 1H, CH_2-P), 3.30 (dd, *J* = 8.4, 6.7 Hz, 1H, OCH_2), 2.99 (dd, *J* = 8.4, 6.7 Hz, 1H, OCH_2), 2.38 (dd, *J* = 18.9, 15.7 Hz, 1H, CH_2-P), 2.15 (s, 3H, CH_3), 1.73-1.84 (m, 1H, CH), 1.20 (t, *J* = 7.1 Hz, 3H, CH_3), 1.10 (t, *J* = 7.1 Hz, 3H, CH_3), 0.86 (dd, *J* = 12.6, 6.7 Hz, 6H, $2CH_3$); ^{13}C NMR (101 MHz, $CDCl_3$): δ 168.72 (C=O), 134.06, 131.72, 123.11 (Ph), 88.52 (O-C-N), 68.92 (d, *J* = 2.3 Hz, OCH_2), 61.77 (d, *J* = 6.4 Hz, OCH_2), 61.50 (d, *J* = 6.4 Hz, OCH_2), 36.39 (d, *J* = 139.7 Hz, C-P), 28.36 (CH), 23.90 (CH_3), 19.47 (CH_3), 19.44(CH_3), 16.20 (d, *J* = 6.5 Hz, CH_3), 16.07 (d, *J* = 6.5 Hz, CH_3); ^{31}P NMR (162 MHz, $CDCl_3$): δ 24.64 (s); ESI-HRMS calcd for $[C_{19}H_{28}NO_6P, M+Na]^+$: 420.1552; Found: 420.1554.

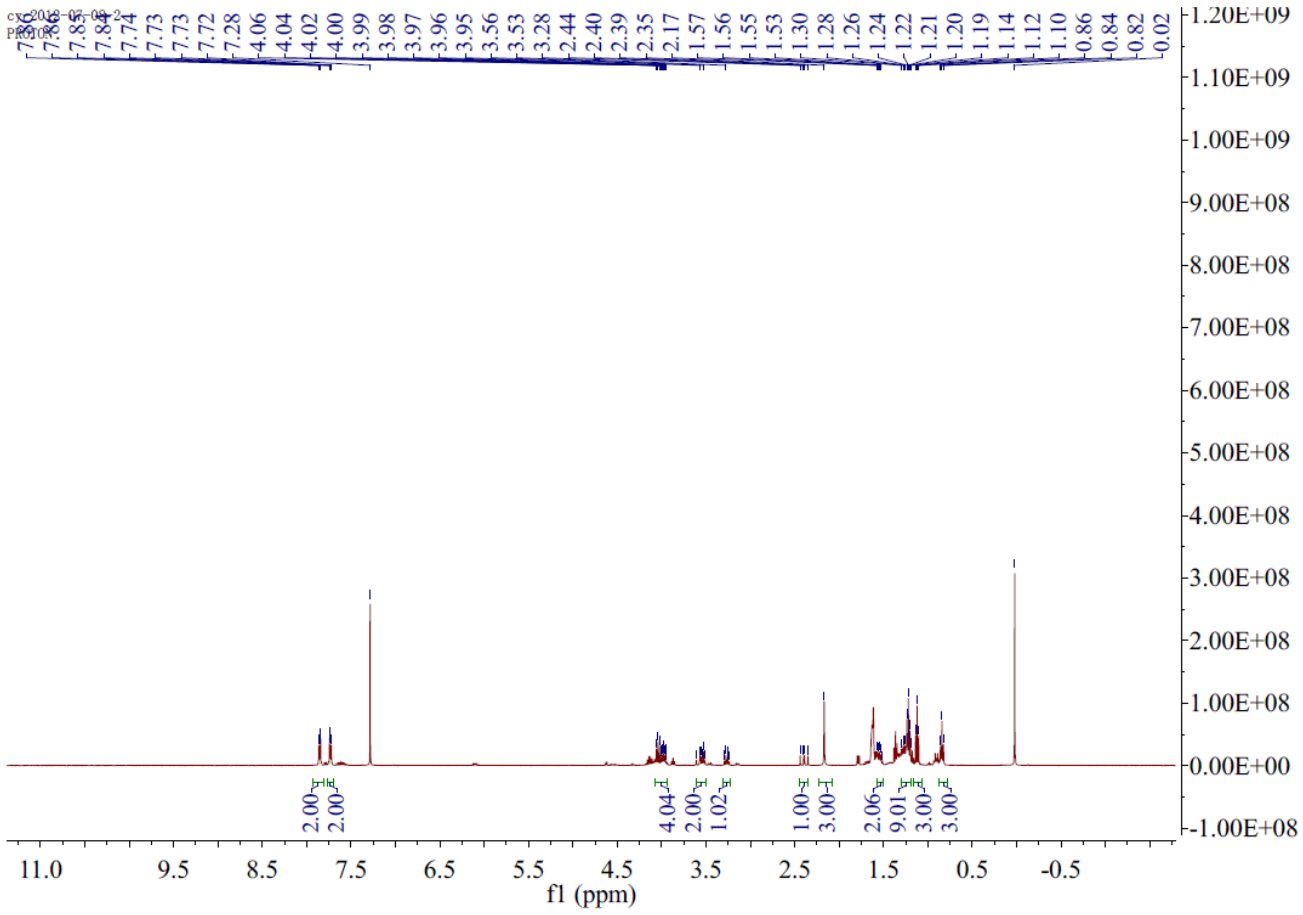


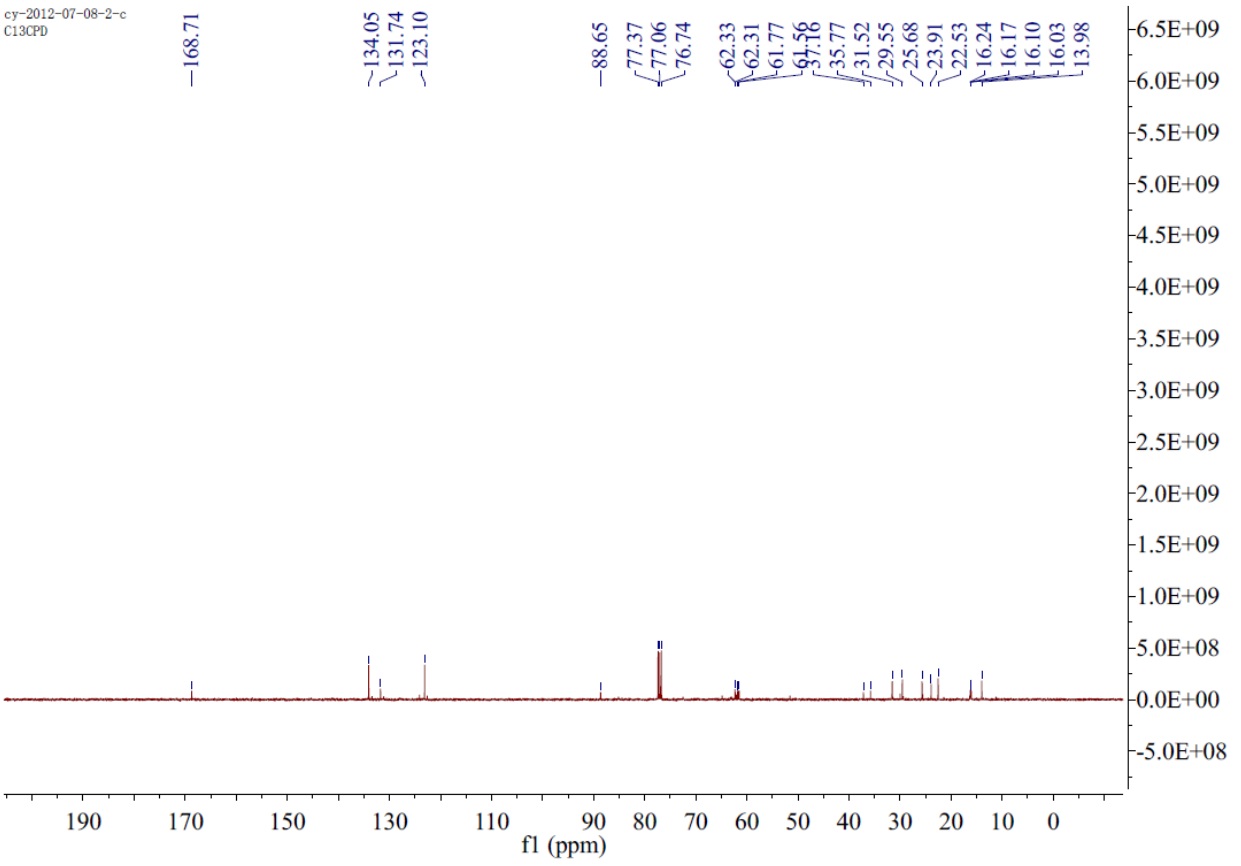


Diethyl (2-(1,3-dioxoisoindolin-2-yl)-2-(hexyloxy)propyl)phosphonate (8n):

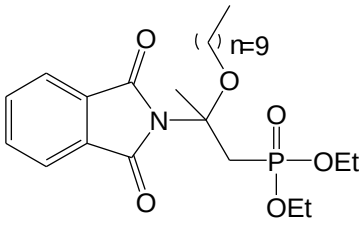


Colourless oil; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.83-7.88 (m, 2H, Ph), 7.71-7.75 (m, 2H, Ph), 3.94-4.07 (m, 4H, $2OCH_2$), 3.50-3.62 (m, 2H, OCH_2, CH_2-P), 3.23-3.30 (m, 1H, OCH_2), 2.39 (dd, *J* = 19.6, 15.4 Hz, 1H, CH_2-P), 2.17 (s, 3H, CH_3), 1.50-1.60 (m, 2H, CH_2), 1.19-1.30 (m, 9H, $3CH_2$, CH_3), 1.12 (t, *J* = 7.1 Hz, 3H, CH_3), 0.84 (t, *J* = 6.9 Hz, 3H, CH_3); ^{13}C NMR (101 MHz, $CDCl_3$): δ 168.71 (C=O), 134.05, 131.74, 123.10 (Ph), 88.65 (O-C-N), 62.32 (d, *J* = 2.2 Hz, OCH_2), 61.80 (d, *J* = 6.4 Hz, OCH_2), 61.53 (d, *J* = 6.4 Hz, OCH_2), 36.46 (d, *J* = 139.8 Hz, C-P), 31.52 (CH_2), 29.55 (CH_2), 25.68 (CH_2), 23.91 (CH_3), 22.53 (CH_2), 16.21 (d, *J* = 6.5 Hz, CH_3), 16.07 (d, *J* = 6.5 Hz, CH_3), 13.98 (CH_3); ^{31}P NMR (162 MHz, $CDCl_3$): δ 24.57 (s); ESI-HRMS calcd for $[C_{21}H_{32}NO_6P, M+Na]^+$: 448.1859; Found: 448.1851.

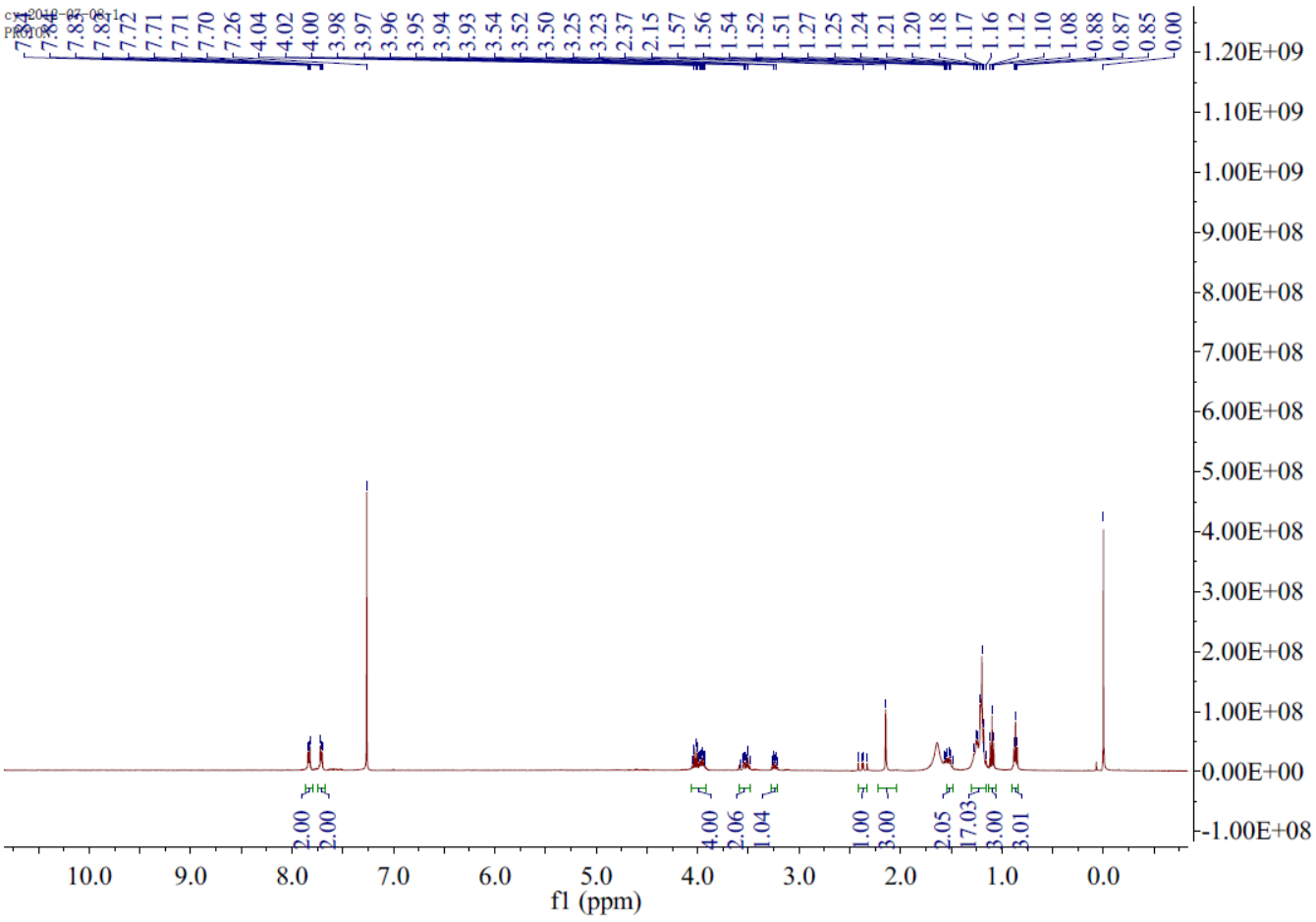


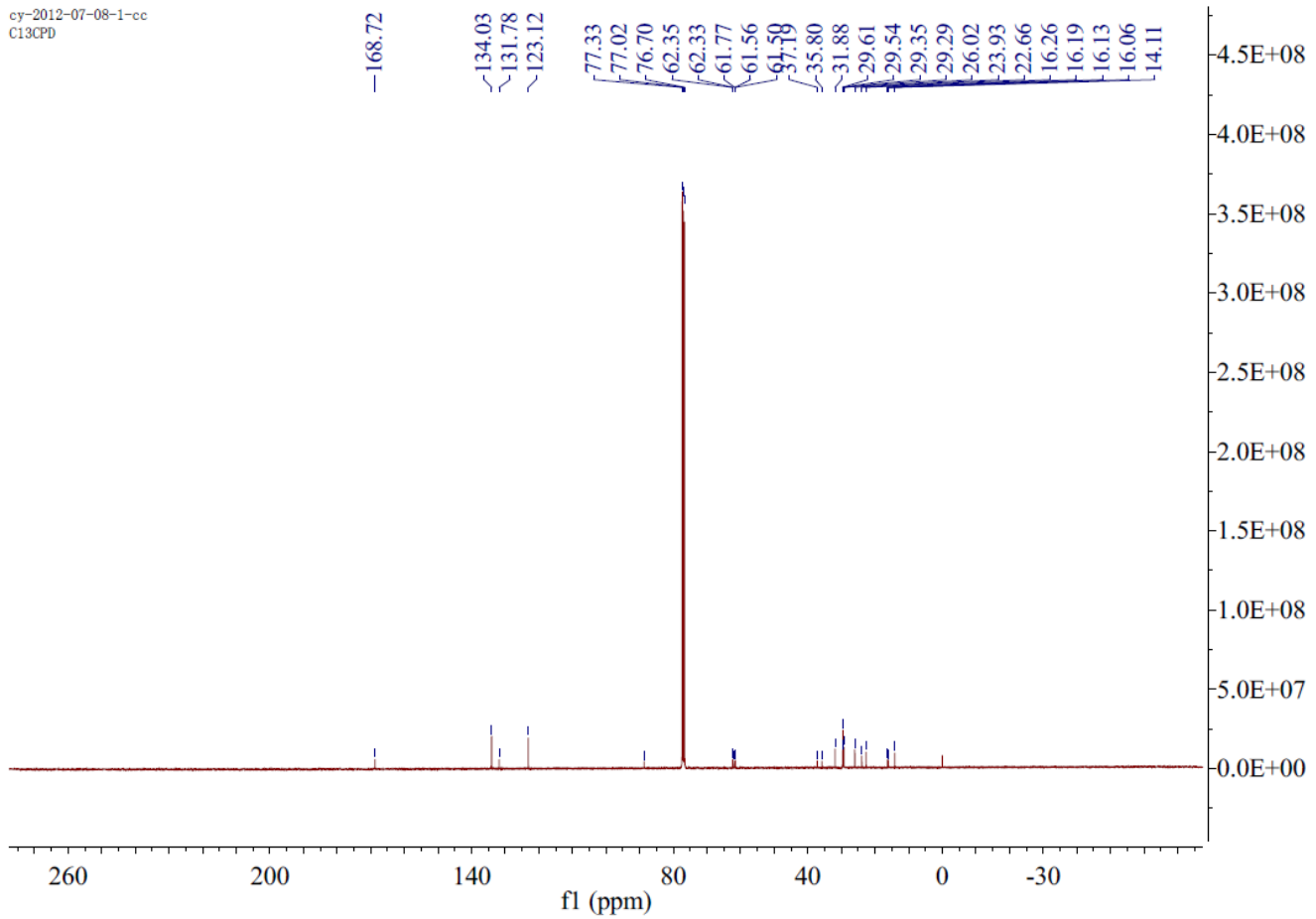


Diethyl (2-(decyloxy)-2-(1,3-dioxoisoindolin-2-yl)propyl)phosphonate (8o):

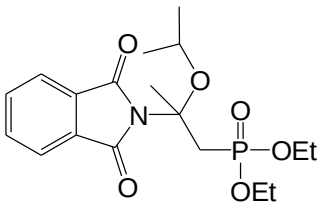


Colourless oil; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.81-7.85 (m, 2H, Ph), 7.69-7.73 (m, 2H, Ph), 3.92-4.06 (m, 4H, $2OCH_2$), 3.48-3.60 (m, 2H, OCH_2, CH_2-P), 3.21-3.28 (m, 1H, OCH_2), 2.37 (dd, *J* = 19.7, 15.5 Hz, 1H, CH_2-P), 2.15 (s, 3H, CH_3), 1.48-1.58 (m, 2H, CH_2), 1.15-1.31 (m, 17H, $7CH_2$, CH_3), 1.10 (t, *J* = 7.1 Hz, 3H, CH_3), 0.87 (t, *J* = 6.9 Hz, 3H, CH_3); ^{13}C NMR (101 MHz, $CDCl_3$): δ 168.72 (C=O), 134.03, 131.78, 123.12 (Ph), 88.68 (O-C-N), 62.34 (d, *J* = 2.0 Hz, OCH_2), 61.80 (d, *J* = 6.5 Hz, OCH_2), 61.53 (d, *J* = 6.5 Hz, OCH_2), 36.50 (d, *J* = 140.0 Hz, C-P), 31.88 (CH_2), 29.61 (CH_2), 29.54 (CH_2), 29.35 (CH_2), 29.29 (CH_2), 26.02 (CH_2), 23.93 (CH_3), 22.66 (CH_2), 16.23 (d, *J* = 6.5 Hz, CH_3), 16.09 (d, *J* = 6.5 Hz, CH_3), 14.11 (CH_3); ^{31}P NMR (162 MHz, $CDCl_3$): δ 24.59 (s); ESI-HRMS calcd for $[C_{25}H_{40}NO_6P, M+Na]^+$: 504.2485; Found: 504.2487.

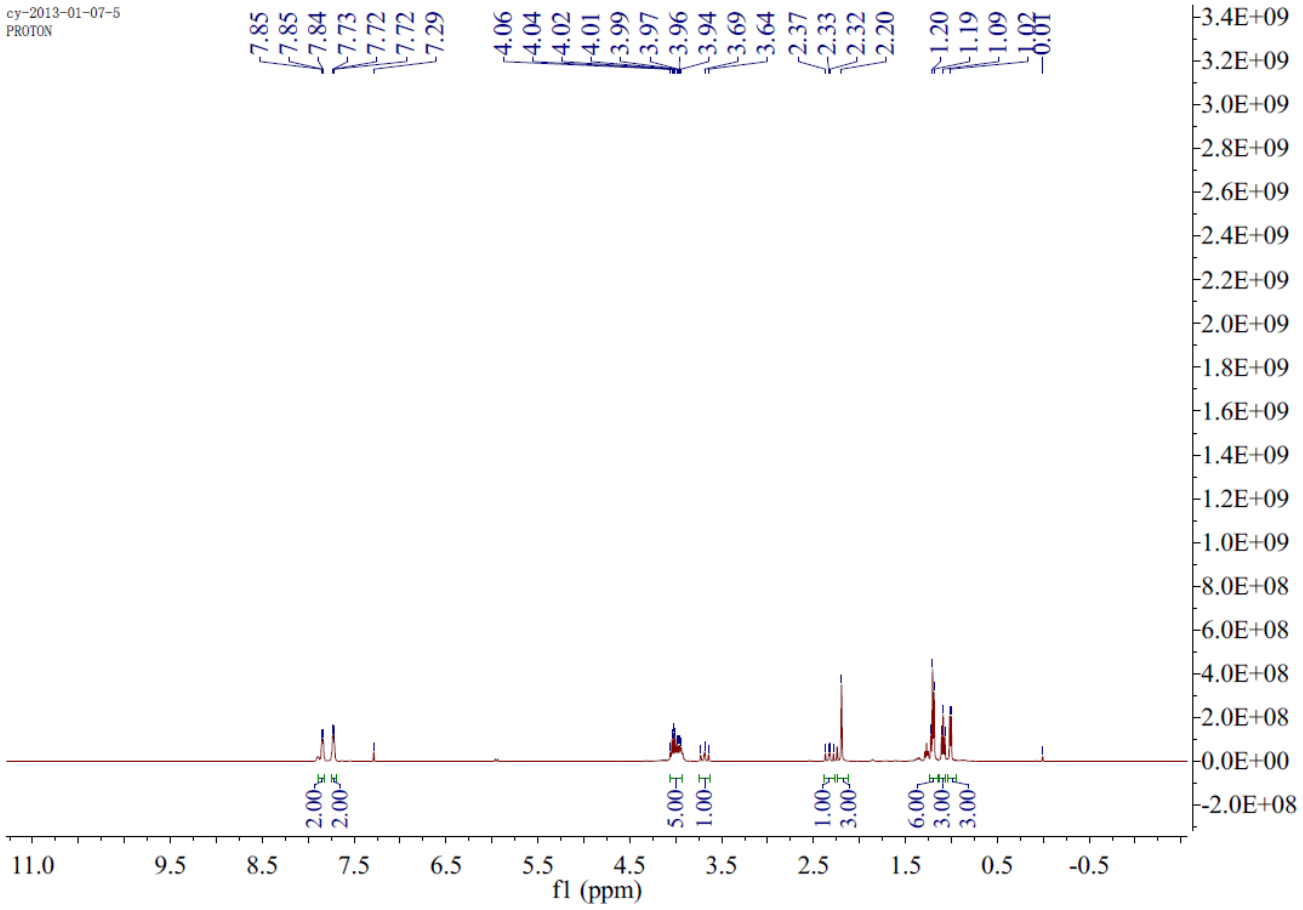


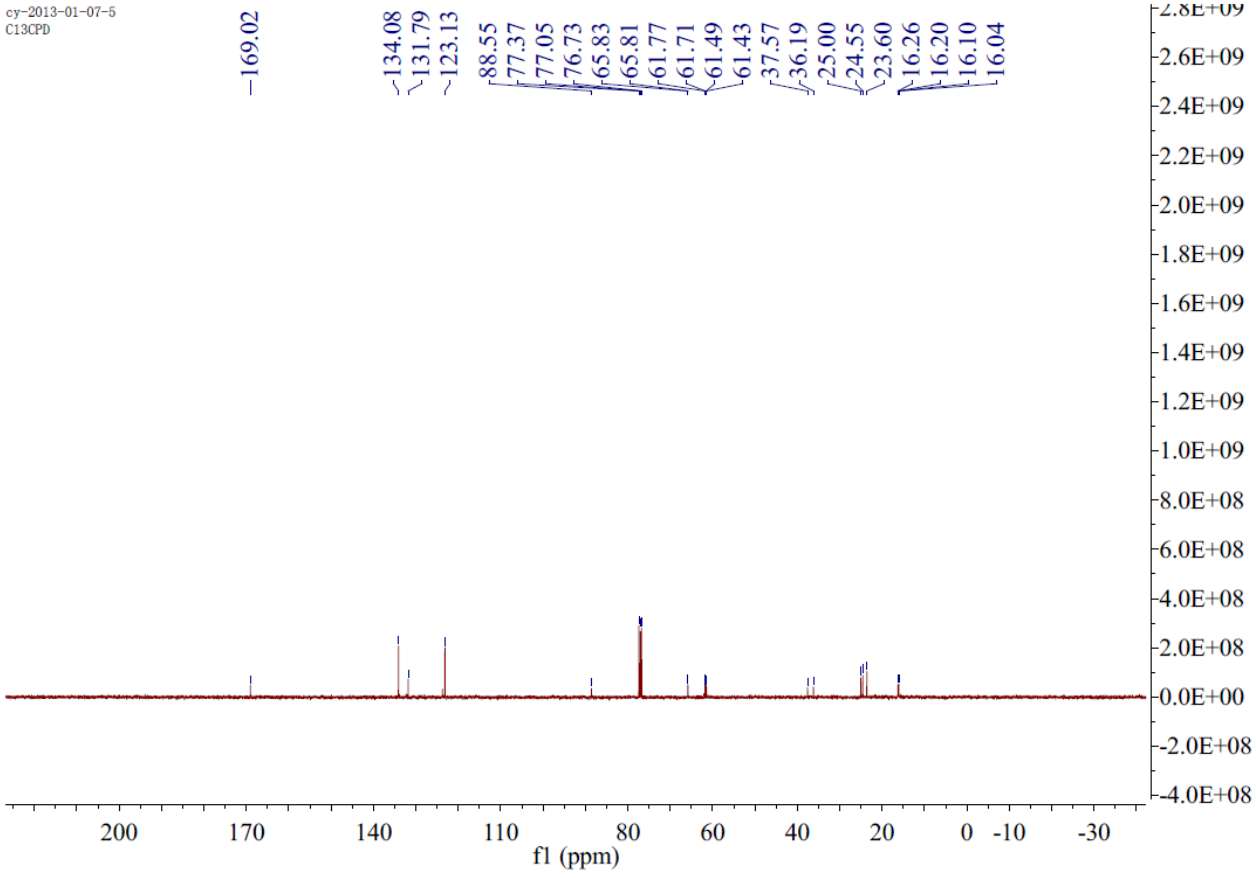


Diethyl (2-(1,3-dioxoisoindolin-2-yl)-2-isopropoxypropyl)phosphonate (8p):

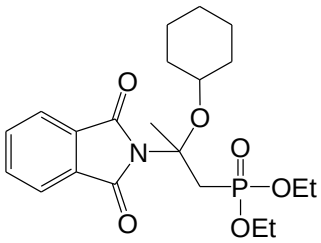


Colourless oil; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.82-7.87 (m, 2H), 7.69-7.75 (m, 2H), 3.92-4.08 (m, 5H, $2OCH_2$, CH), 3.61-3.75 (dd, *J* = 19.7, 15.5 Hz, 1H, CH_2-P), 2.33 (dd, *J* = 19.7, 15.5 Hz, 1H, CH_2-P), 2.20 (s, 3H, CH_3), 1.21 (t, *J* = 6.8 Hz, 6H, $2CH_3$), 1.09 (t, *J* = 7.0 Hz, 3H, CH_3), 1.01 (d, *J* = 6.1 Hz, 3H, CH_3); ^{13}C NMR (101 MHz, $CDCl_3$): δ 169.02 (C=O), 134.08, 131.79, 123.13 (Ph), 88.55 (O-C-N), 65.82 (d, *J* = 2.6 Hz, OCH), 61.74 (d, *J* = 6.5 Hz, OCH_2), 61.46 (d, *J* = 6.5 Hz, OCH_2), 36.88 (d, *J* = 139.2 Hz, C-P), 25.00 (CH_3), 24.55 (CH_3), 23.60 (CH_3), 16.23 (d, *J* = 6.4 Hz, CH_3), 16.07 (d, *J* = 6.4 Hz, CH_3). ^{31}P NMR (162 MHz, $CDCl_3$): δ 24.55 (s); ESI-HRMS calcd for $[C_{18}H_{26}NO_6P, M+Na]^+$: 406.1390; Found: 406.1394.

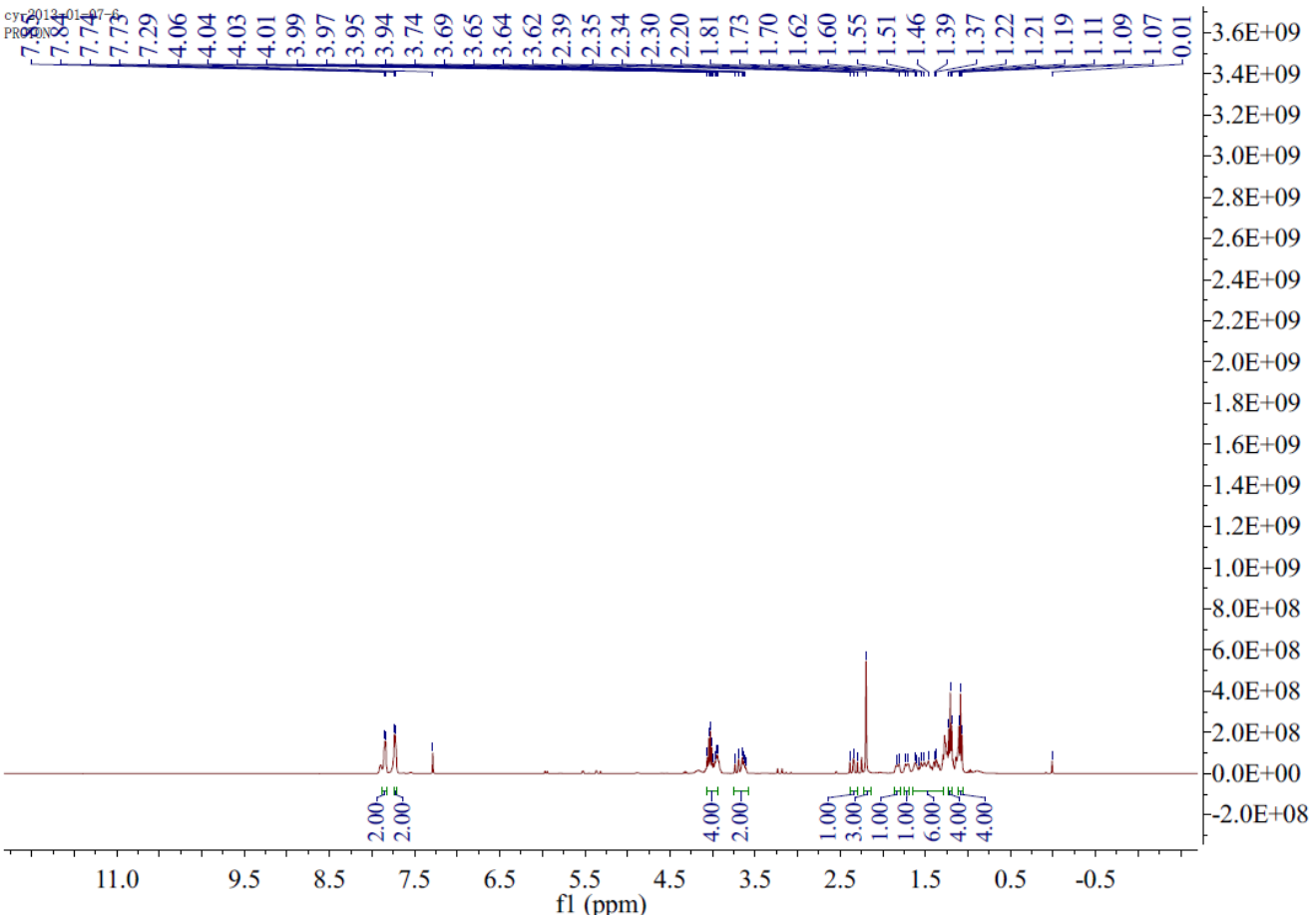


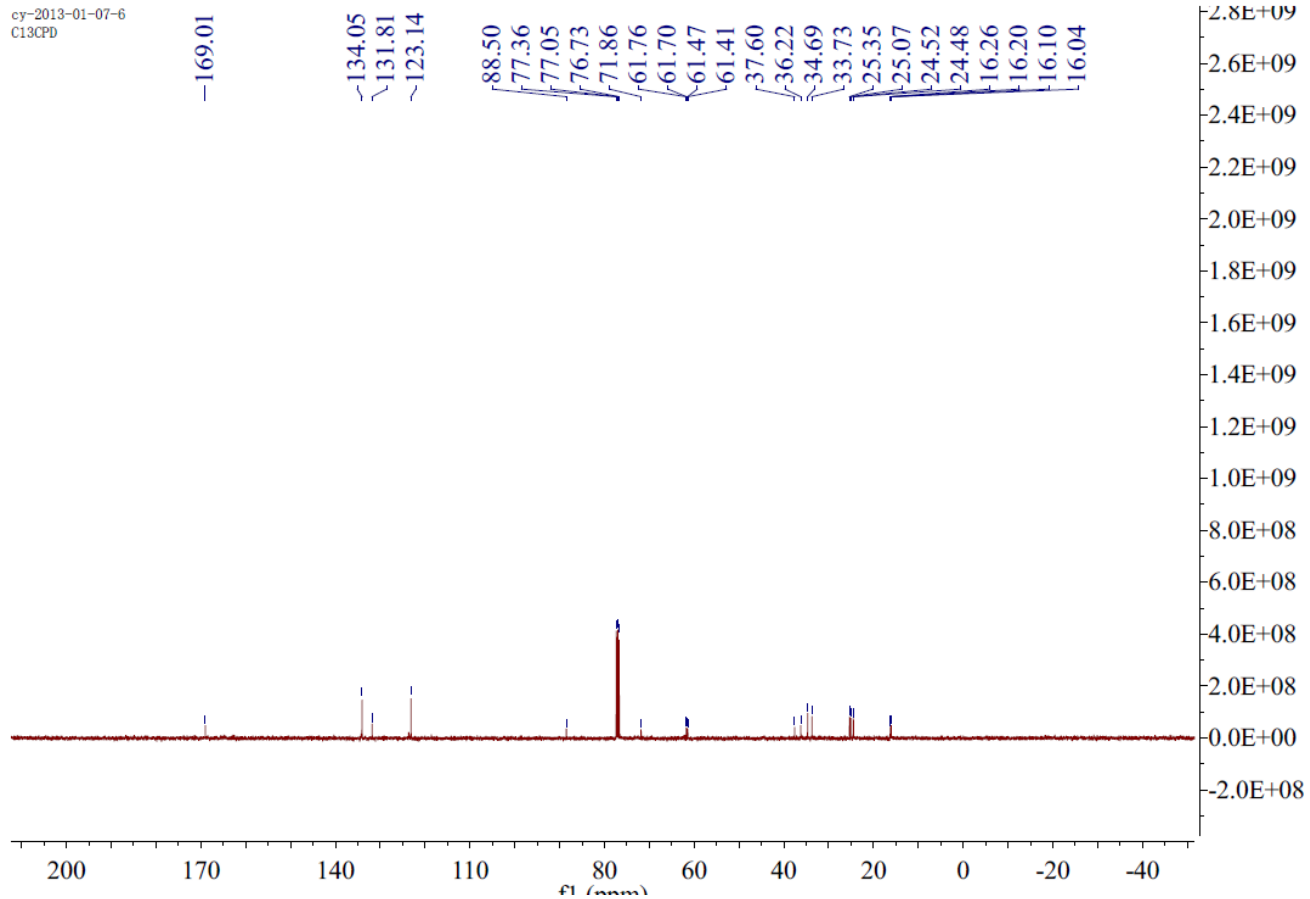


Diethyl (2-(cyclohexyloxy)-2-(1,3-dioxoisoindolin-2-yl)propyl)phosphonate (8q):

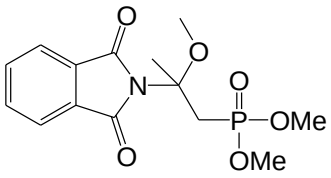


Colourless oil; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.84-7.87 (m, 2H, Ph), 7.70-7.73 (m, 2H, Ph), 3.92-4.08 (m, 4H, $2OCH_2$), 3.58-3.76 (m, 2H, CH, CH_2P), 2.34 (dd, *J* = 19.2, 16.0, Hz, 1H, CH_2P), 2.20 (s, 3H, CH_3), 1.29-1.88 (m, 8H, $4CH_2$). 1.07-1.22 (m, 8H, CH_2, $2CH_3$); ^{13}C NMR (101 MHz, $CDCl_3$): δ 169.01 (C=O), 134.05, 131.81, 123.14 (Ph), 88.50 (O-C-N), 71.86 (CH), 61.73 (d, *J* = 6.3 Hz, OCH_2), 61.44 (d, *J* = 6.3 Hz, OCH_2), 36.91 (d, *J* = 138.7 Hz, C-P), 34.69 (CH_2), 33.73 (CH_2), 25.35 (CH_2), 25.07 (CH_2), 24.52 (CH_2), 24.48 (CH_3), 16.23 (d, *J* = 6.4 Hz, CH_3), 16.07 (d, *J* = 6.4 Hz, CH_3); ^{31}P NMR (162 MHz, $CDCl_3$): δ 24.63 (s); ESI-HRMS calcd for $[C_{21}H_{30}NO_6P, M+Na]^+$: 446.1703; Found: 446.1702.

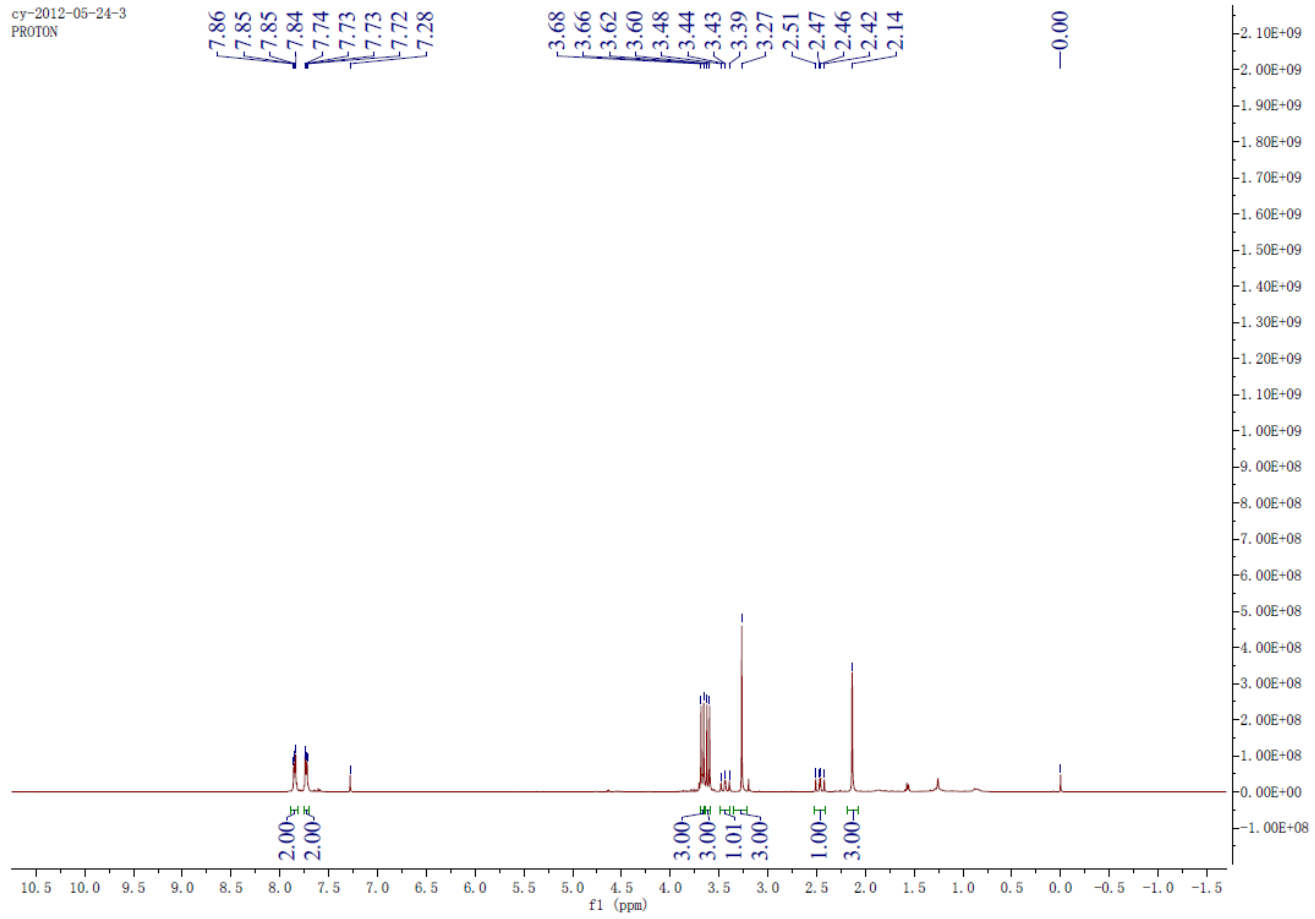


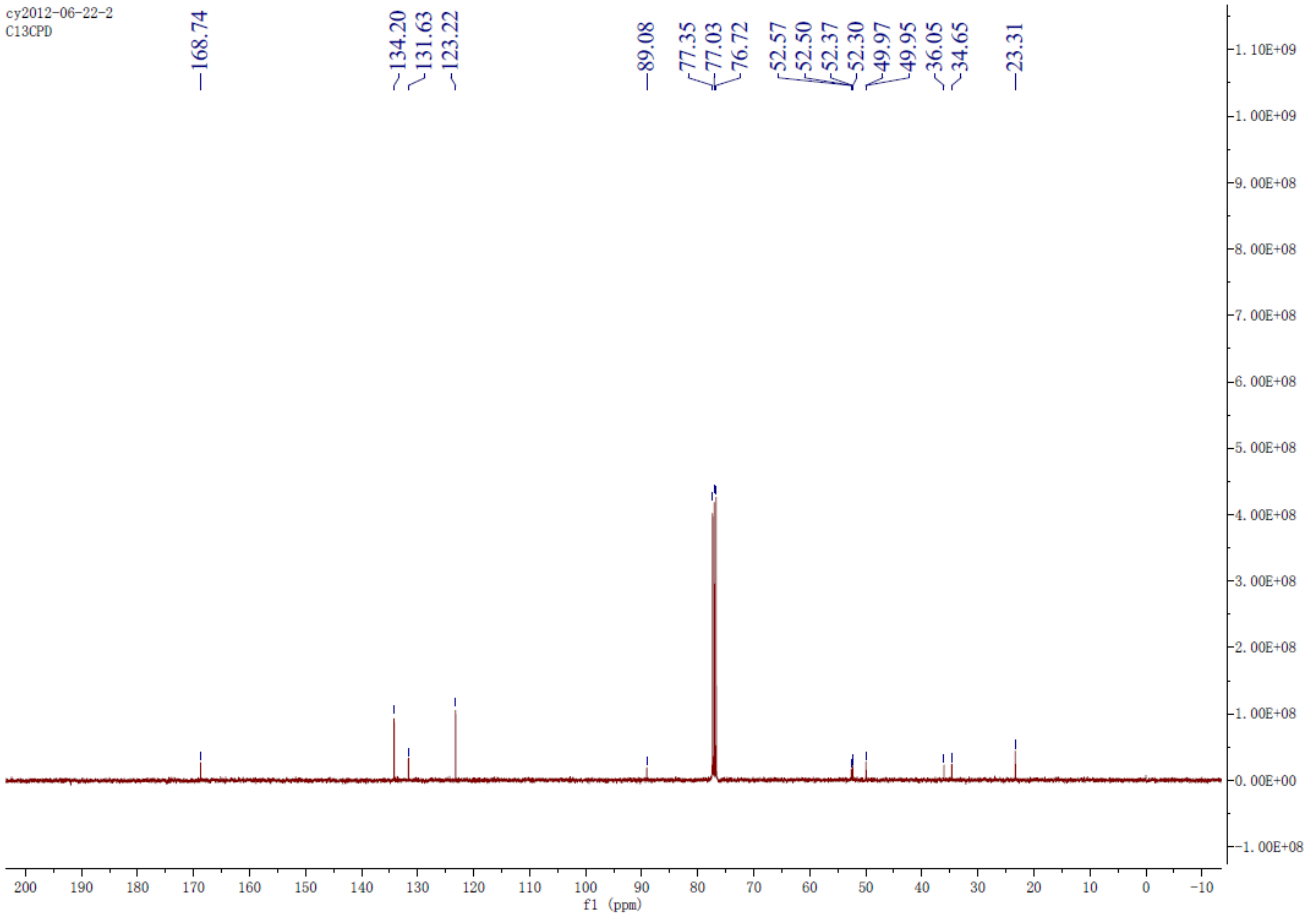


Dimethyl (2-(1,3-dioxoisoindolin-2-yl)-2-methoxypropyl)phosphonate (8s):

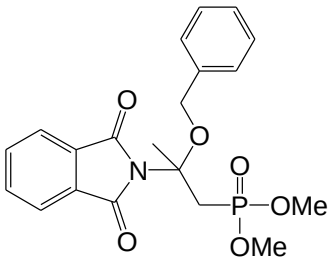


Colourless oil; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.82-7.87 (m, 2H, Ph), 7.71-7.75 (m, 2H, Ph), 3.67 (d, *J* = 11.0 Hz, 3H, OCH_3), 3.61 (d, *J* = 11.0 Hz, 3H, OCH_3), 3.44 (dd, *J* = 19.1, 15.6 Hz, 1H, CH_2-P), 3.27 (s, 3H, OCH_3), 2.47 (dd, *J* = 19.1, 15.6 Hz, 1H, CH_2-P), 2.14 (s, 3H, CH_3); ^{13}C NMR (101 MHz, $CDCl_3$): δ 168.74 (C=O), 134.20, 131.63, 123.22 (Ph), 89.08 (O-C-N), 52.54 (d, *J* = 6.5 Hz, OCH_3), 52.34 (d, *J* = 6.5 Hz, OCH_3), 49.96 (d, *J* = 2.6 Hz, OCH_3), 35.35 (d, *J* = 141.0 Hz, C-P), 23.31 (CH_3); ^{31}P NMR (162 MHz, $CDCl_3$): δ 27.08 (s); ESI-HRMS calcd for $[C_{14}H_{18}NO_6P, M+Na]^+$: 350.0764; Found: 350.0763.

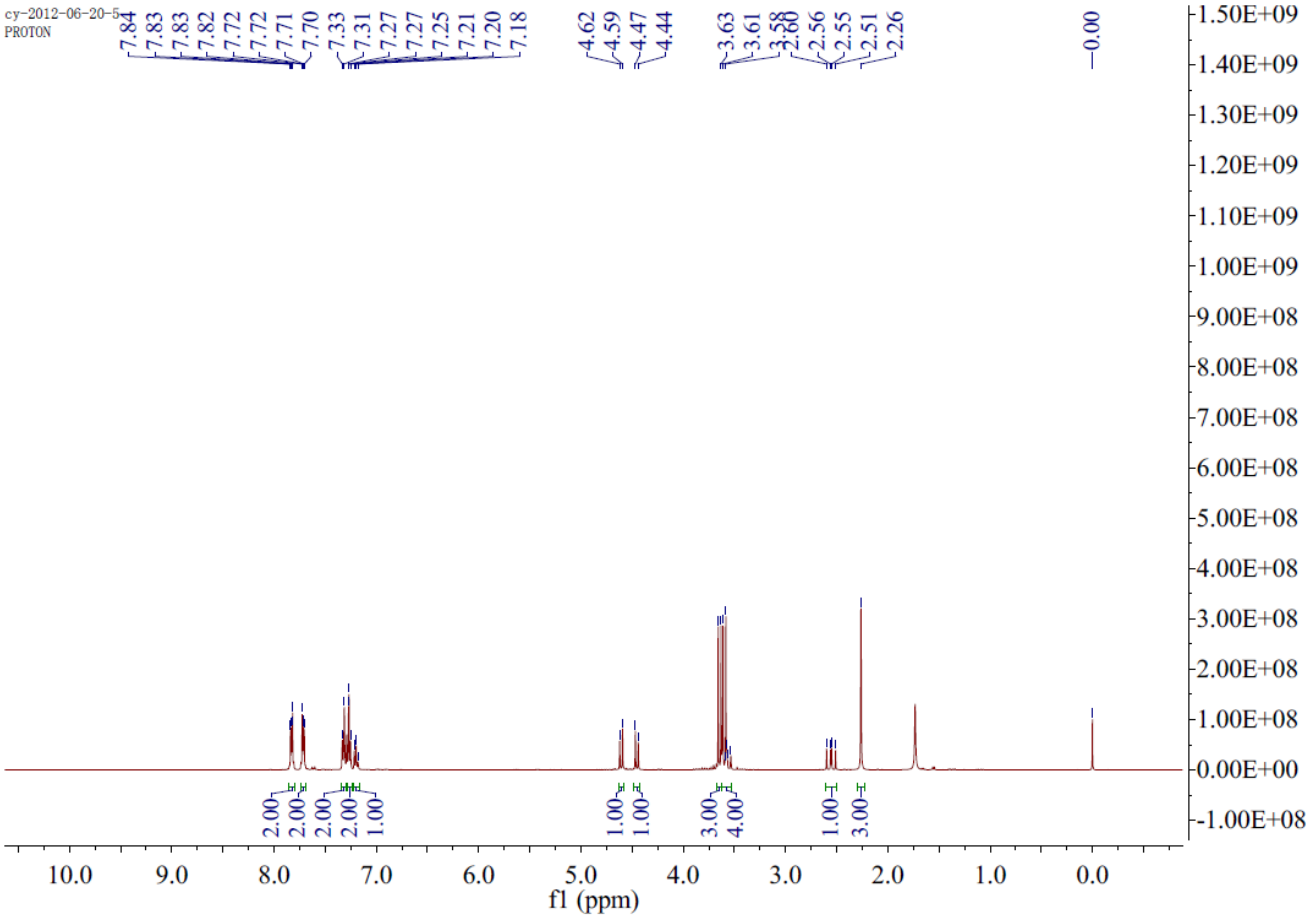


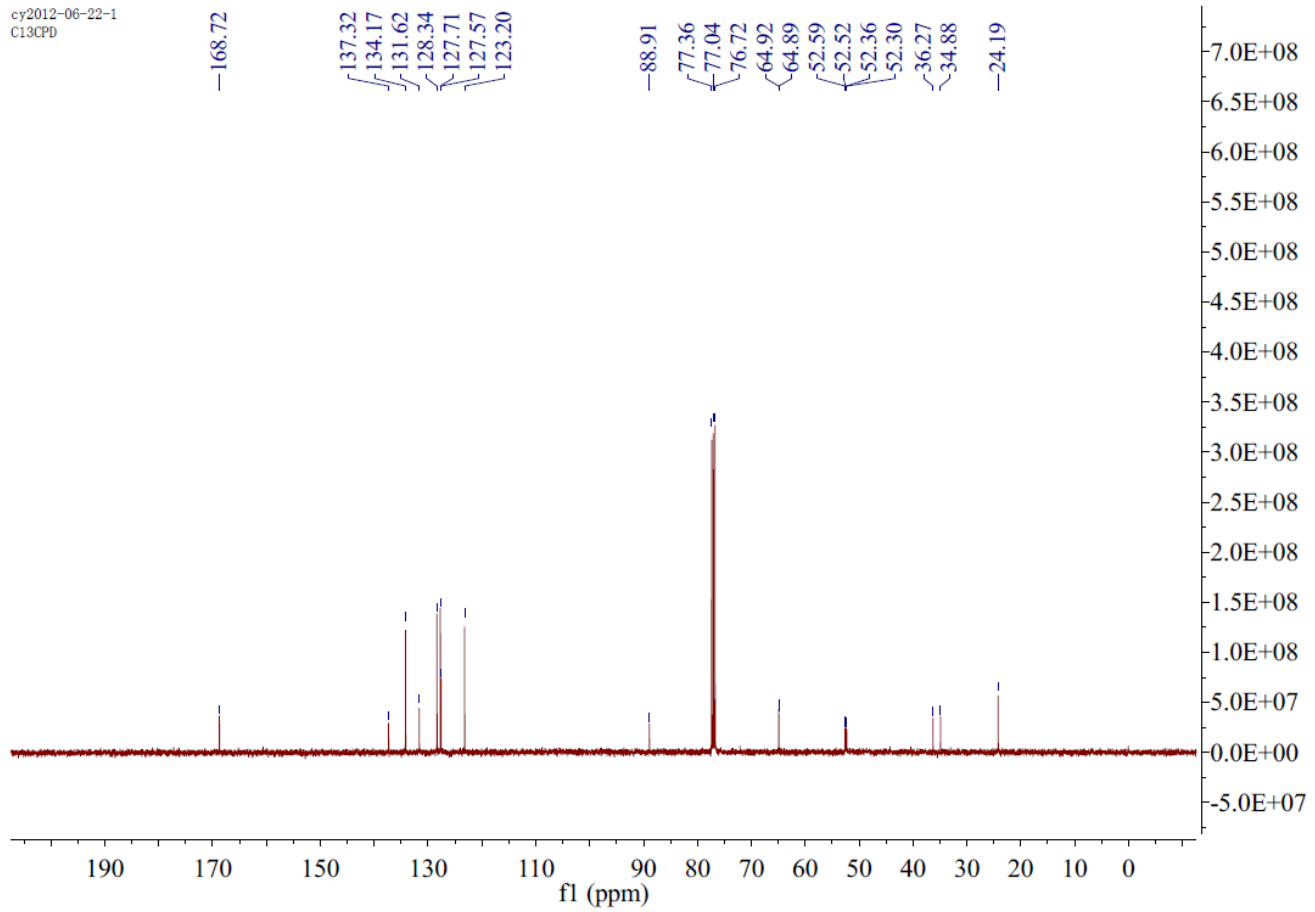


Dimethyl (2-(benzyloxy)-2-(1,3-dioxoisoindolin-2-yl)propyl)phosphonate (8t):

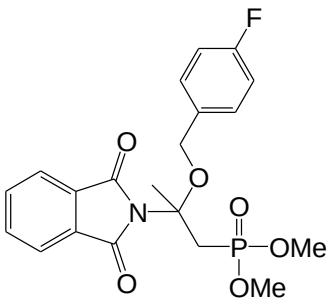


Colourless oil; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.81-7.85 (m, 2H, Ph), 7.68-7.74 (m, 2H, Ph), 7.32 (d, *J* = 7.2 Hz, 2H, Ph), 7.24-7.28 (m, 2H, Ph), 7.20 (t, *J* = 7.1 Hz, 1H, Ph), 4.61 (d, *J* = 11.2 Hz, 1H, OCH_2Ph), 4.45 (d, *J* = 11.2 Hz, 1H, OCH_2Ph), 3.64 (d, *J* = 11.0 Hz, 3H, OCH_3), 3.53-3.62 (m, 4H, OCH_3, CH_2-P), 2.55 (dd, *J* = 19.7, 15.5 Hz, 1H, CH_2-P), 2.26 (s, 3H, CH_3); ^{13}C NMR (101 MHz, $CDCl_3$): δ 168.72 (C=O), 137.32, 134.17, 131.62, 128.34, 127.71, 127.57, 123.20 (Ph), 88.91 (O-C-N), 64.90 (d, *J* = 2.5 Hz, OCH_2Ph), 52.55 (d, *J* = 6.5 Hz, OCH_3), 52.33 (d, *J* = 6.5 Hz, OCH_3), 35.58 (d, *J* = 140.2 Hz, C-P), 24.19 (CH_3); ^{31}P NMR (162 MHz, $CDCl_3$): δ 27.09 (s); ESI-HRMS calcd for $[C_{20}H_{22}NO_6P, M+Na]^+$: 426.1077; Found: 426.1076.

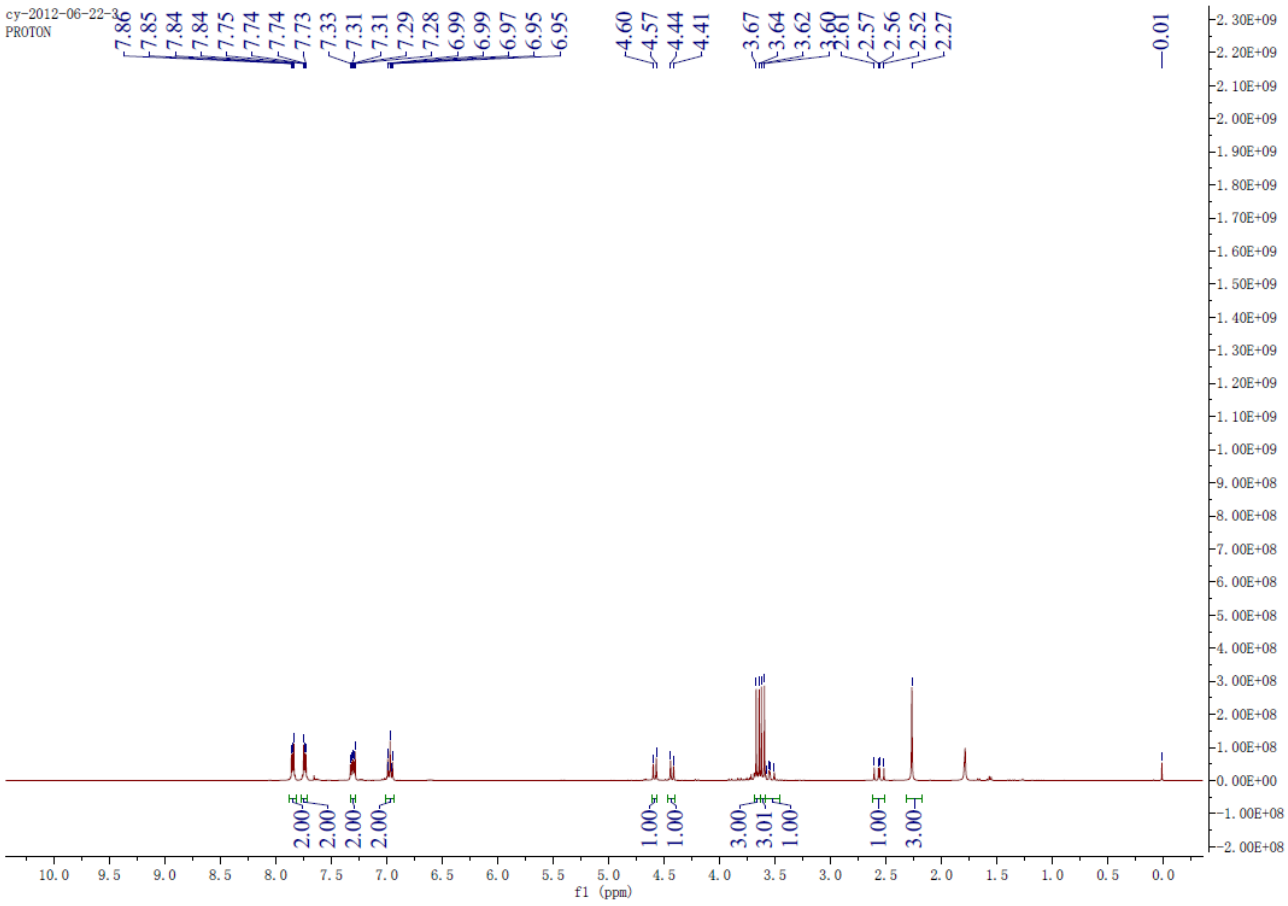


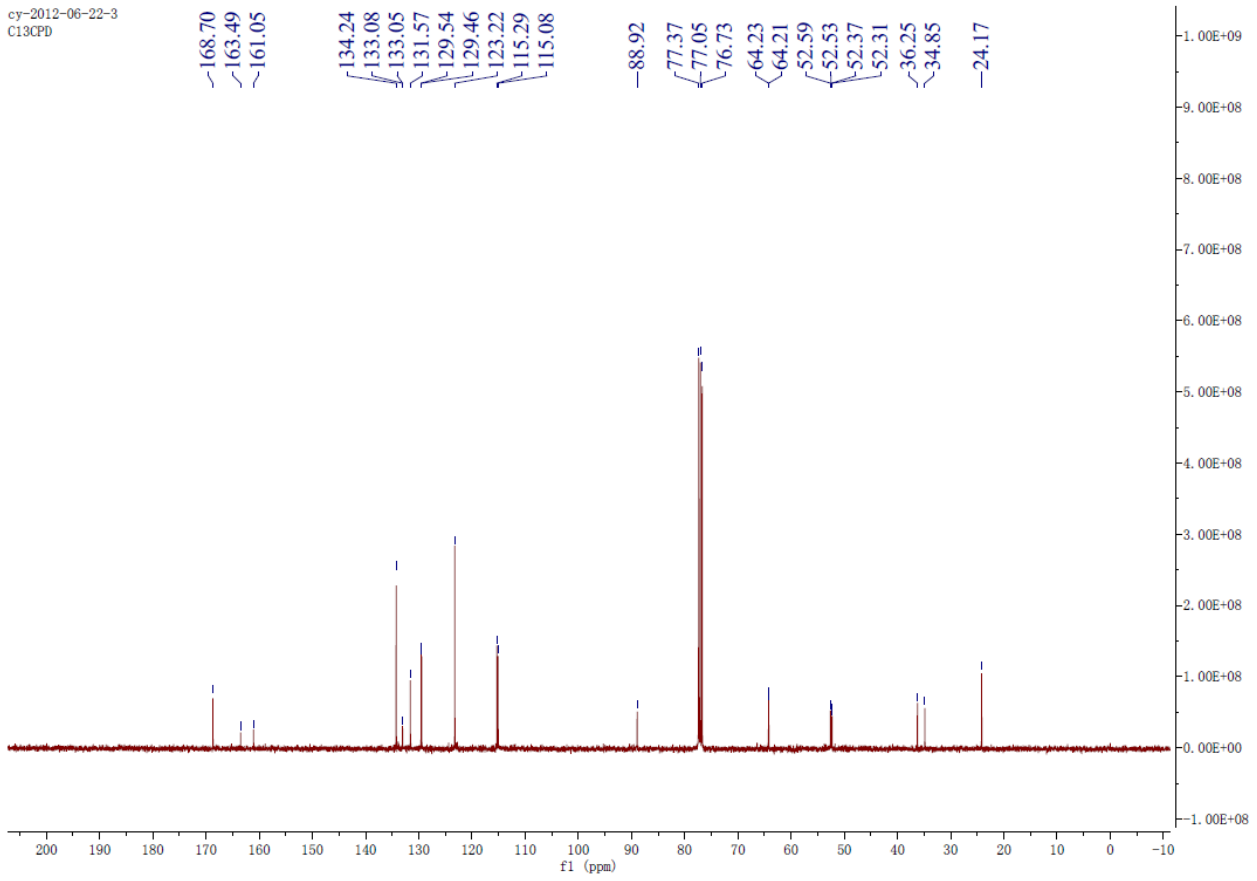


Dimethyl (2-(1,3-dioxoisoindolin-2-yl)-2-((4-fluorobenzyl)oxy)propyl)phosphonate (8u):

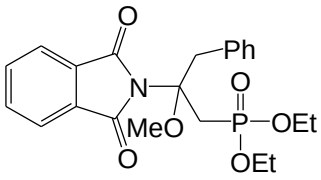


Colourless oil; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.82-7.87 (m, 2H, Ph), 7.71-7.77 (m, 2H, Ph), 7.25-7.35 (m, 2H, Ph), 6.93-7.01 (m, 2H, Ph), 4.58 (d, *J* = 11.0 Hz, 1H, OCH_2Ar), 4.43 (d, *J* = 11.0 Hz, 1H, OCH_2Ar), 3.66 (d, *J* = 11.0 Hz, 3H, OCH_3), 3.61 (d, *J* = 11.0 Hz, 3H, OCH_3), 3.55 (dd, *J* = 16.6, 13.5 Hz, 1H, CH_2-P), 2.56 (dd, *J* = 19.7, 15.5 Hz, 1H, CH_2-P), 2.27 (s, 3H, CH_3); ^{13}C NMR (101 MHz, $CDCl_3$): δ 168.70 (C=O), 162.27 (d, *J* = 245.6 Hz, Ph), 134.24 (Ph), 133.06 (d, *J* = 3.1 Hz, Ar), 131.57 (s, Ph), 129.50 (d, *J* = 7.9 Hz, Ar), 123.22 (Ph), 115.18 (d, *J* = 21.5 Hz, Ar), 88.92 (O-C-N), 64.22 (d, *J* = 2.2 Hz, OCH_2Ar), 52.56 (d, *J* = 6.6 Hz, OCH_3), 52.34 (d, *J* = 6.6 Hz, OCH_3), 35.55 (d, *J* = 140.3 Hz, C-P), 24.17 (CH_3); ^{31}P NMR (162 MHz, $CDCl_3$): δ 26.95 (s); ESI-HRMS calcd for $[C_{20}H_{21}FNO_6P, M+Na]^+$: 444.0983; Found: 444.0982.

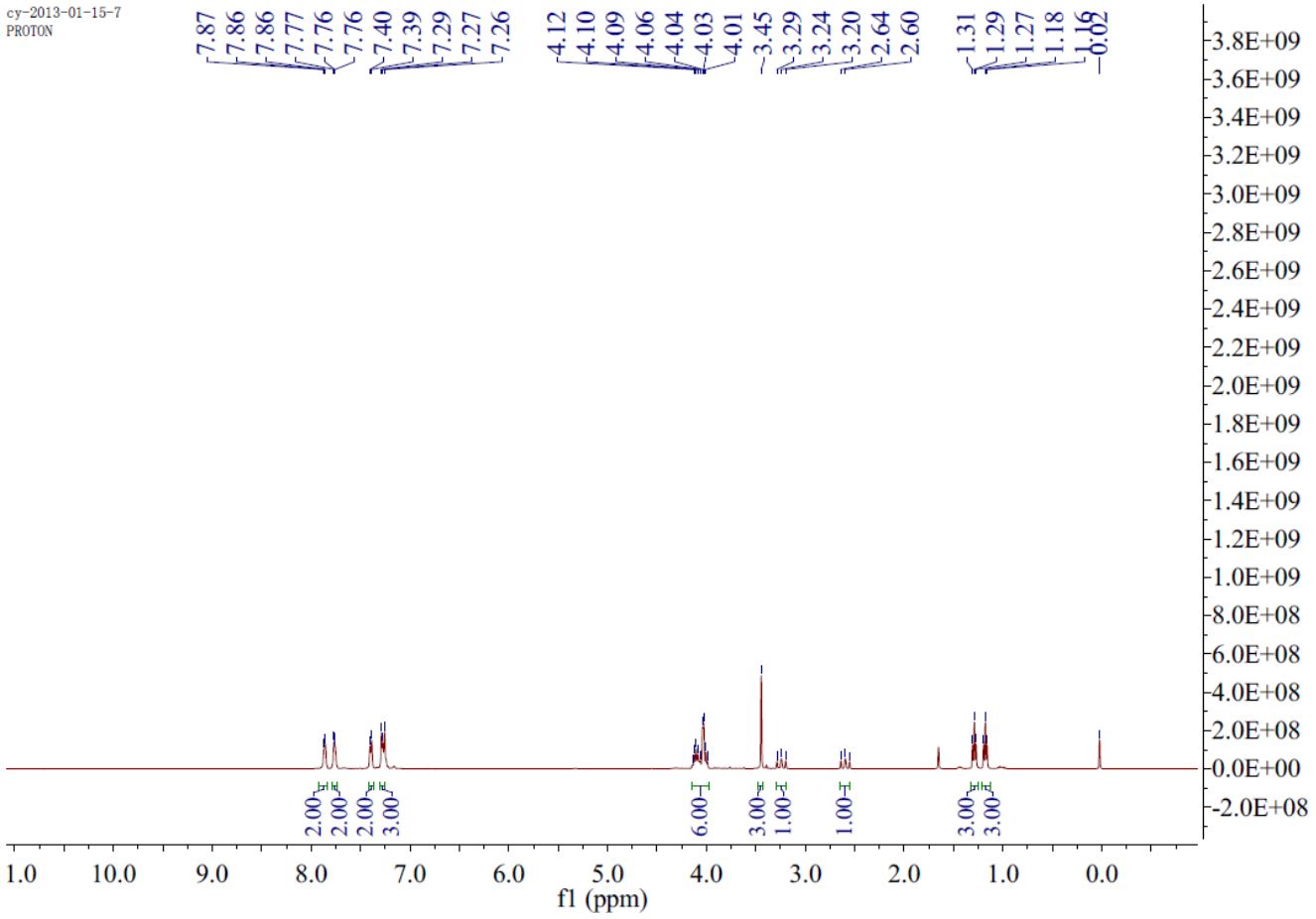


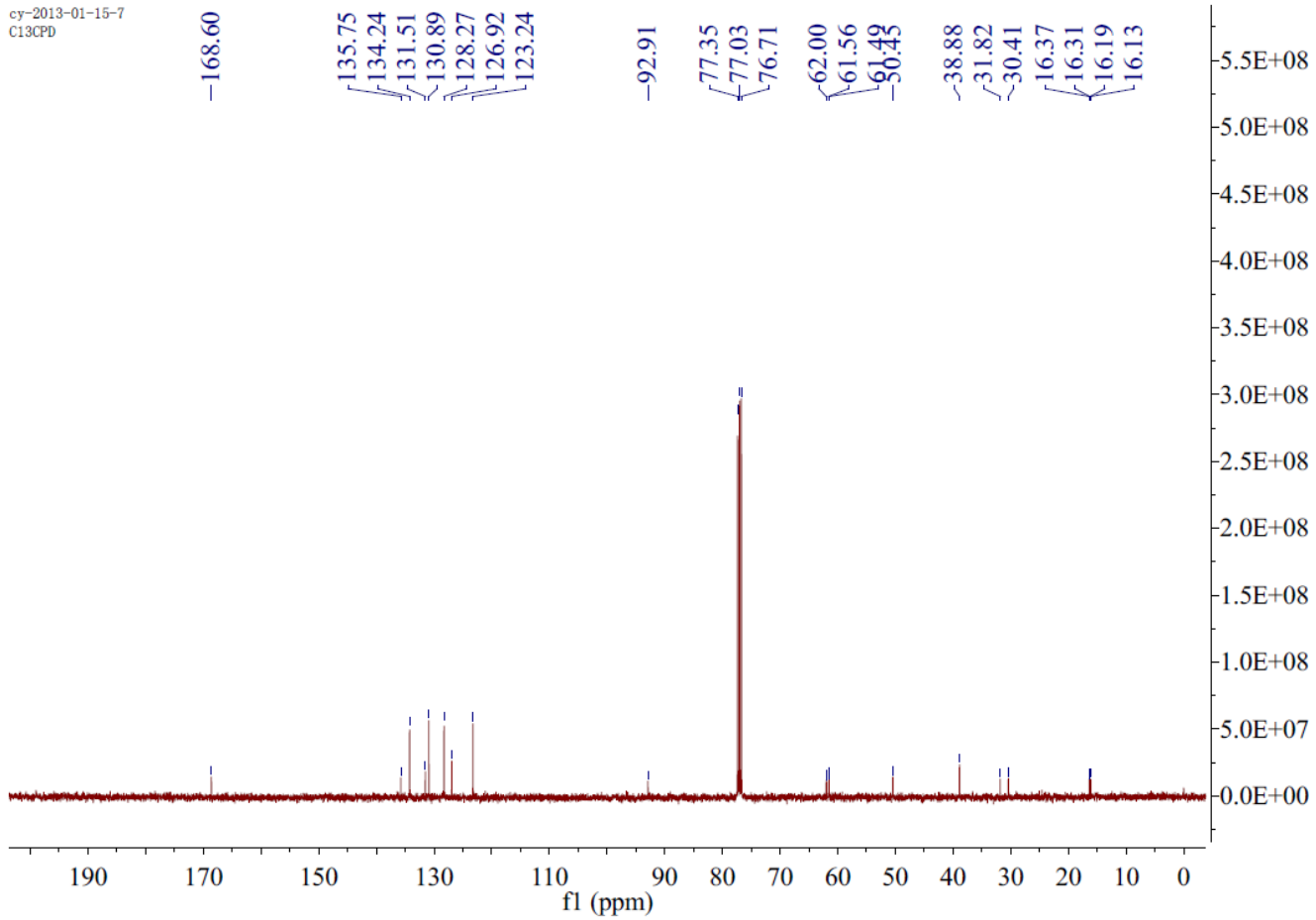


Diethyl (2-(1,3-dioxoisoindolin-2-yl)-2-methoxy-3-phenylpropyl)phosphonate (8v):

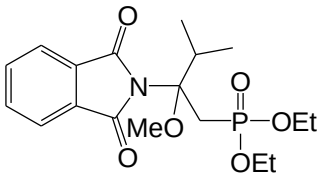


Colourless oil; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.82-7.90 (m, 2H, Ph), 7.73-7.80 (m, 2H, Ph), 7.40 (d, *J* = 6.9 Hz, 1H, Ph), 7.25-7.30 (m, 3H, Ph), 3.97-4.17 (m, 6H, $2OCH_2$, CH_2Ph), 3.45 (s, 3H, OCH_3), 3.18-3.31 (m, 1H, CH_2-P), 2.52-2.68 (m, 1H, CH_2-P), 1.29 (t, *J* = 7.0 Hz, 3H, CH_3), 1.18 (t, *J* = 7.0 Hz, 3H, CH_3); ^{13}C NMR (101 MHz, $CDCl_3$): δ 168.60 (C=O), 135.75, 134.24, 131.51, 130.89, 128.27, 126.92, 123.24 (Ph), 92.91 (N-C-O), 61.97 (d, *J* = 6.5 Hz, OCH_2), 61.53 (d, *J* = 6.5 Hz, OCH_2), 50.45 (s, OCH_3), 38.88 (CH_2Ph), 31.12 (d, *J* = 141.4 Hz, C-P), 16.34 (d, *J* = 6.3 Hz, CH_3), 16.16 (d, *J* = 6.3 Hz, CH_3); ^{31}P NMR (162 MHz, $CDCl_3$): δ 24.40 (s); ESI-HRMS calcd for $[C_{22}H_{26}NO_6P, M+Na]^+$: 454.1390; Found: 454.1394.

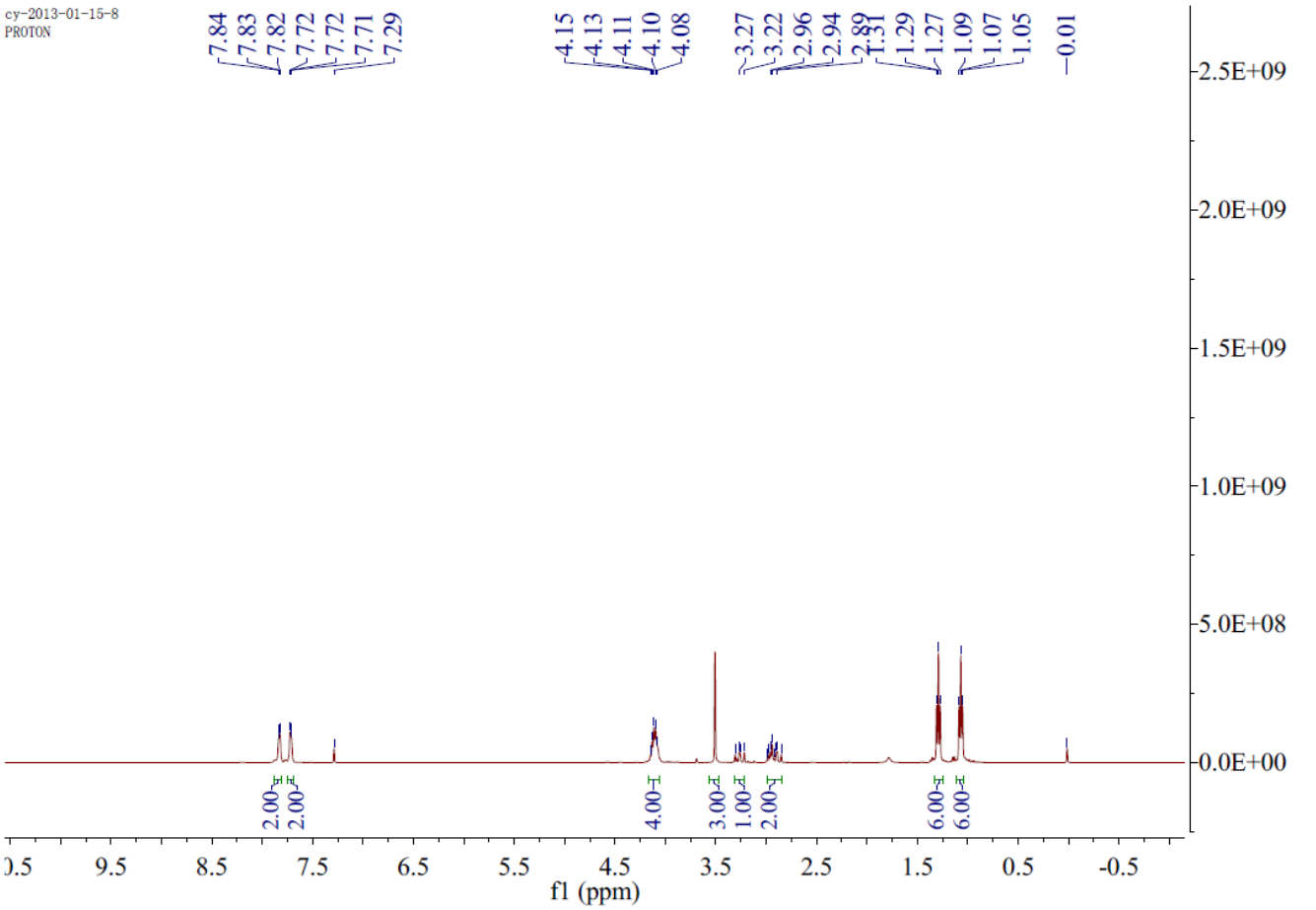




Diethyl (2-(1,3-dioxoisoindolin-2-yl)-2-methoxy-3-methylbutyl)phosphonate (8w):



Colourless oil; ^{1}H NMR (400 MHz, $CDCl_3$): δ7.81-7.86 (m, 2H, Ph), 7.70-7.74 (m, 2H, Ph), 4.05-4.19 (m, 4H, $2OCH_2$), 3.51 (s, 3H, OCH_3), 3.26 (dd, J = 20.3, 16.1 Hz, 1H, CH_2-P), 2.83-3.00 (m, 2H, CH_2-P, CH), 1.29 (t, J = 7.0 Hz, 6H, $2CH_3$), 1.07 (t, J = 7.0 Hz, 6H, $2CH_3$); ^{13}C NMR (101 MHz, $CDCl_3$): δ 169.18 (C=O), 133.97, 131.78, 123.00 (Ph), 96.61 (O-C-N), 61.87 (d, J = 6.4 Hz, OCH_2), 61.53 (d, J = 6.4 Hz, OCH_2), 53.04 (OCH_3), 37.25 (d, J = 5.7 Hz, CH), 30.99 (d, J = 142.1 Hz, C-P), 18.05 (CH_3), 17.40 (CH_3), 16.33 (d, J = 5.5 Hz, CH_3), 16.28 (d, J = 5.5 Hz, CH_3); ^{31}P NMR (162 MHz, $CDCl_3$): δ 25.56 (s); ESI-HRMS calcd for $[C_{18}H_{26}NO_6P, M+Na]^+$: 406.1390; Found: 406.1392.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7.72
7.72
7.71
7.29
4.15
4.13
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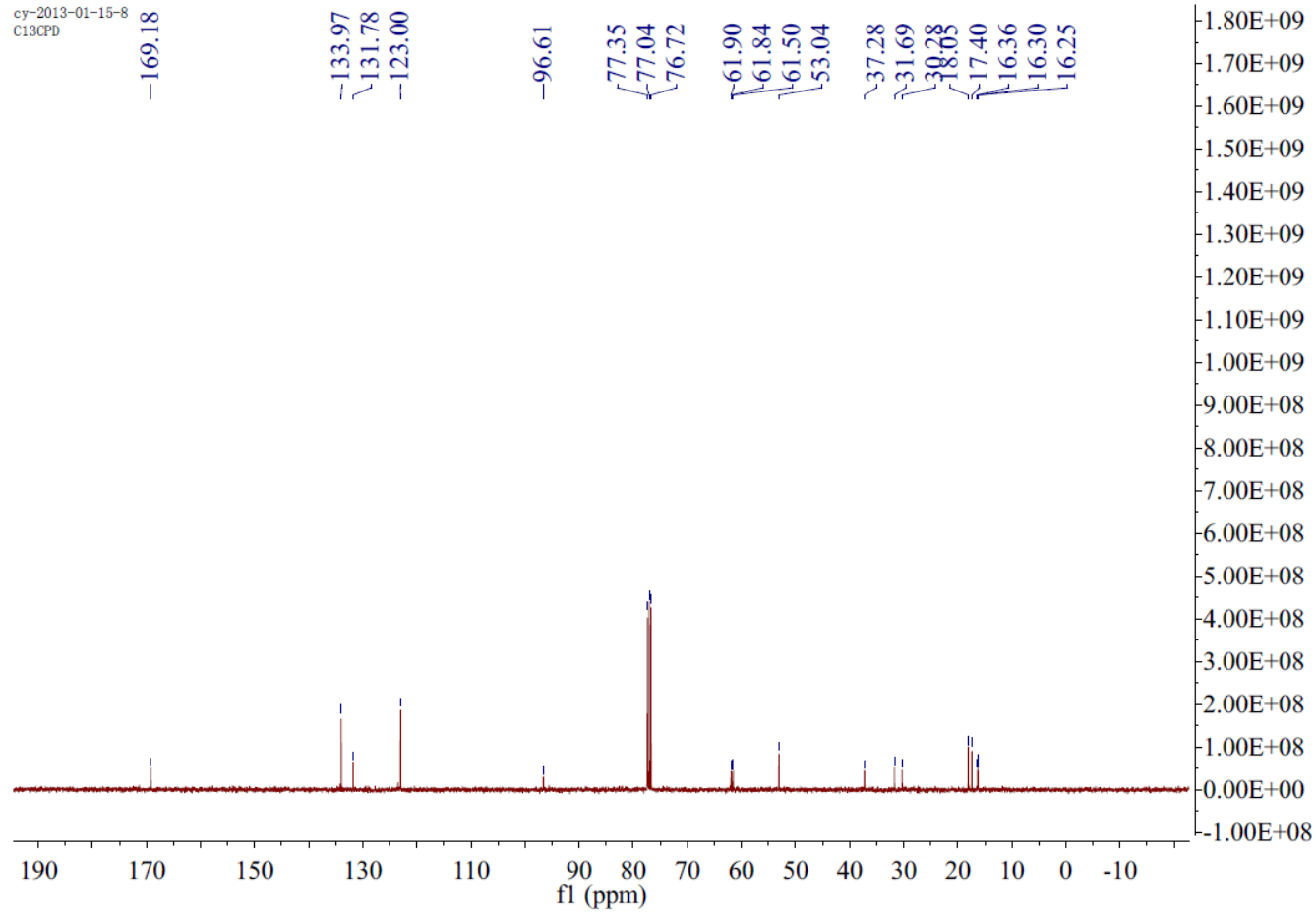
4.10
4.08
3.27
3.22
2.96
2.94
2.89
1.31
1.29
1.27
1.09
1.07
1.05
0.01
2.00
2.00
4.00
3.00
1.00
2.00
6.00
6.00
f1 (ppm)


cy-2013-01-15-8
C13CPD
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96.61
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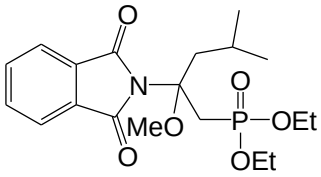
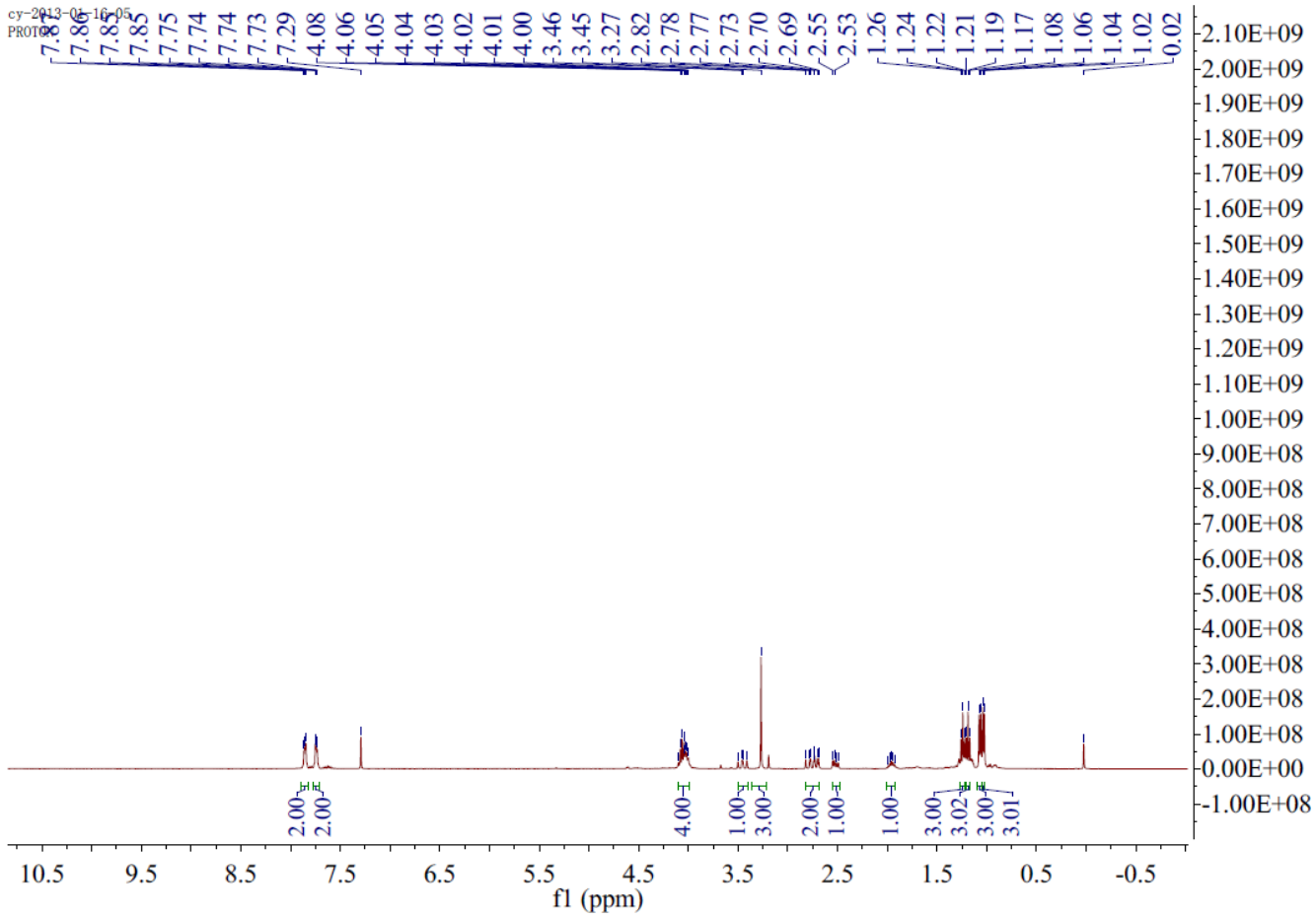
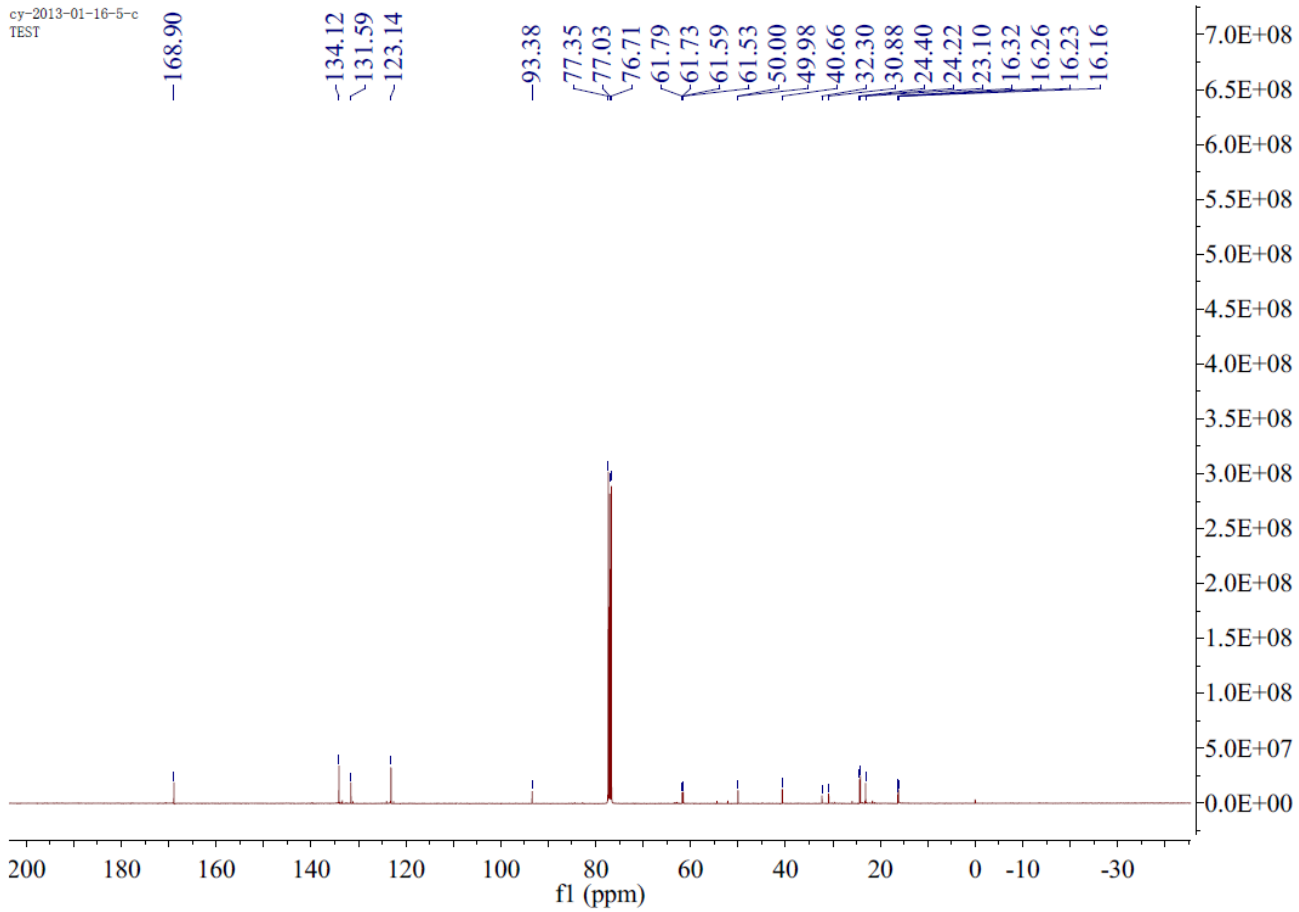
77.04
76.72
61.90
61.84
61.50
53.04
37.28
31.69
30.28
18.05
17.40
16.36
16.30
16.25
f1 (ppm)

Diethyl (2-(1,3-dioxoisoindolin-2-yl)-2-methoxy-4-methylpentyl)phosphonate (8x):

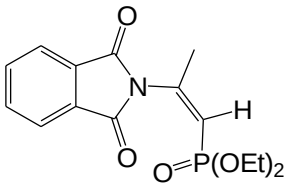


Colourless oil; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.83-7.87 (m, 2H, Ph), 7.73-7.76 (m, 2H, Ph), 3.99-4.11 (m, 4H, $2OCH_2$), 3.46 (dd, *J* = 19.1, 16.5 Hz, 1H, CH_2-P), 3.27 (s, 3H, OCH_3), 2.67-2.84 (m, 2H, CH_2-P, CH_2), 2.52 (dd, *J* = 15.1, 7.2, Hz, 1H, CH_2), 1.92-2.01 (m, 1H, CH), 1.24 (t, *J* = 7.1 Hz, 3H, CH_3), 1.20 (t, *J* = 7.1 Hz, 3H, CH_3), 1.07 (d, *J* = 6.6 Hz, 3H, CH_3), 1.03 (d, *J* = 6.6 Hz, 3H, CH_3); ^{13}C NMR (101 MHz, $CDCl_3$): δ 168.90 (C=O), 134.12, 131.59, 123.14 (Ph), 93.38 (O-C-N), 61.76 (d, *J* = 6.5 Hz, OCH_2), 61.56 (d, *J* = 6.5 Hz, OCH_2), 49.99 (d, *J* = 2.0 Hz, OCH_3), 40.66 (CH_2), 31.59 (d, *J* = 142.3 Hz, C-P), 24.40 (CH_3), 24.22 (CH_3), 23.10 (CH), 16.29 (d, *J* = 6.5 Hz, CH_3), 16.20 (d, *J* = 6.5 Hz, CH_3); ^{31}P NMR (162 MHz, $CDCl_3$): δ 24.52 (s); ESI-HRMS calcd for $[C_{19}H_{28}NO_6P, M+Na]^+$: 420.1546; Found: 420.1550.

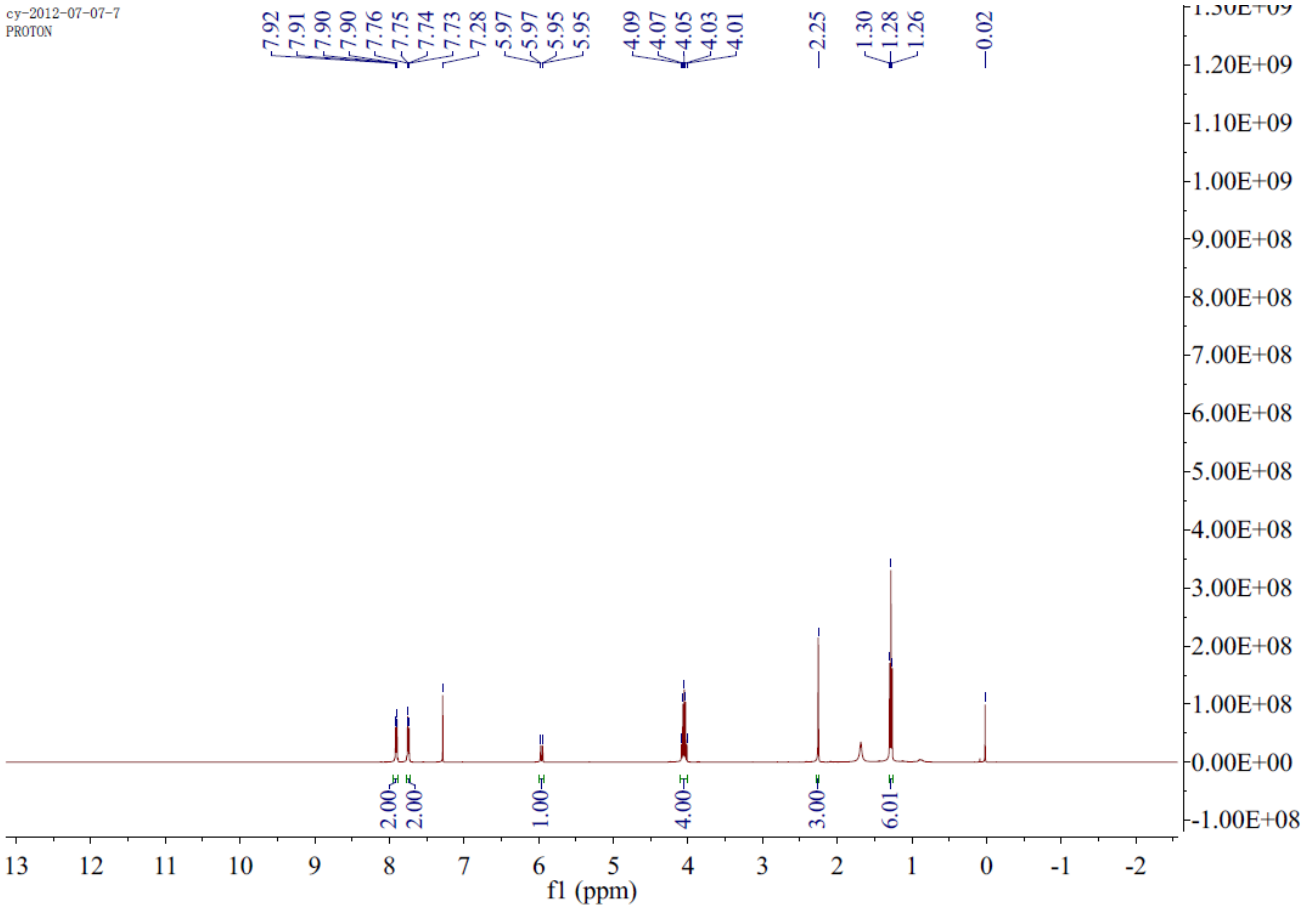


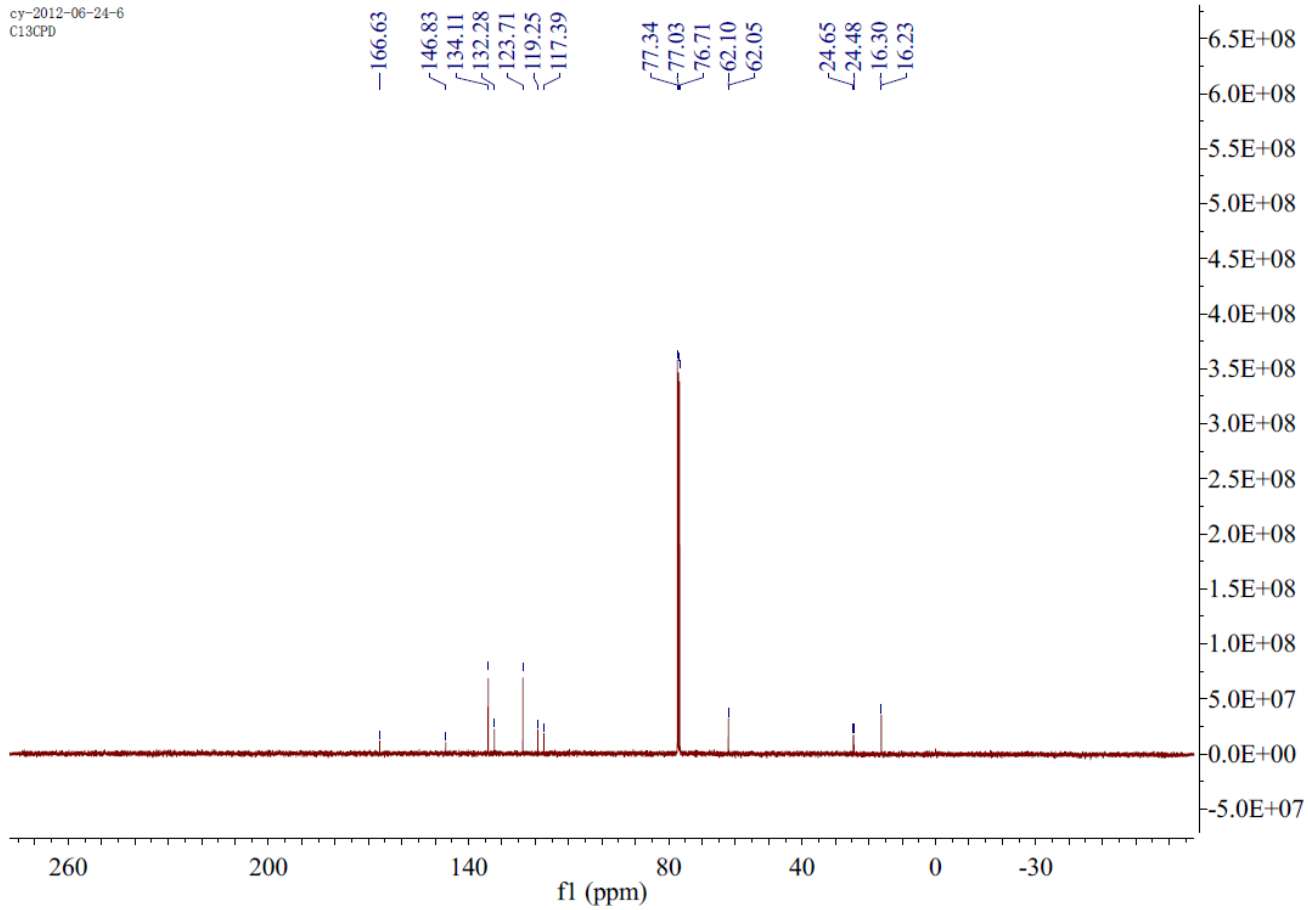


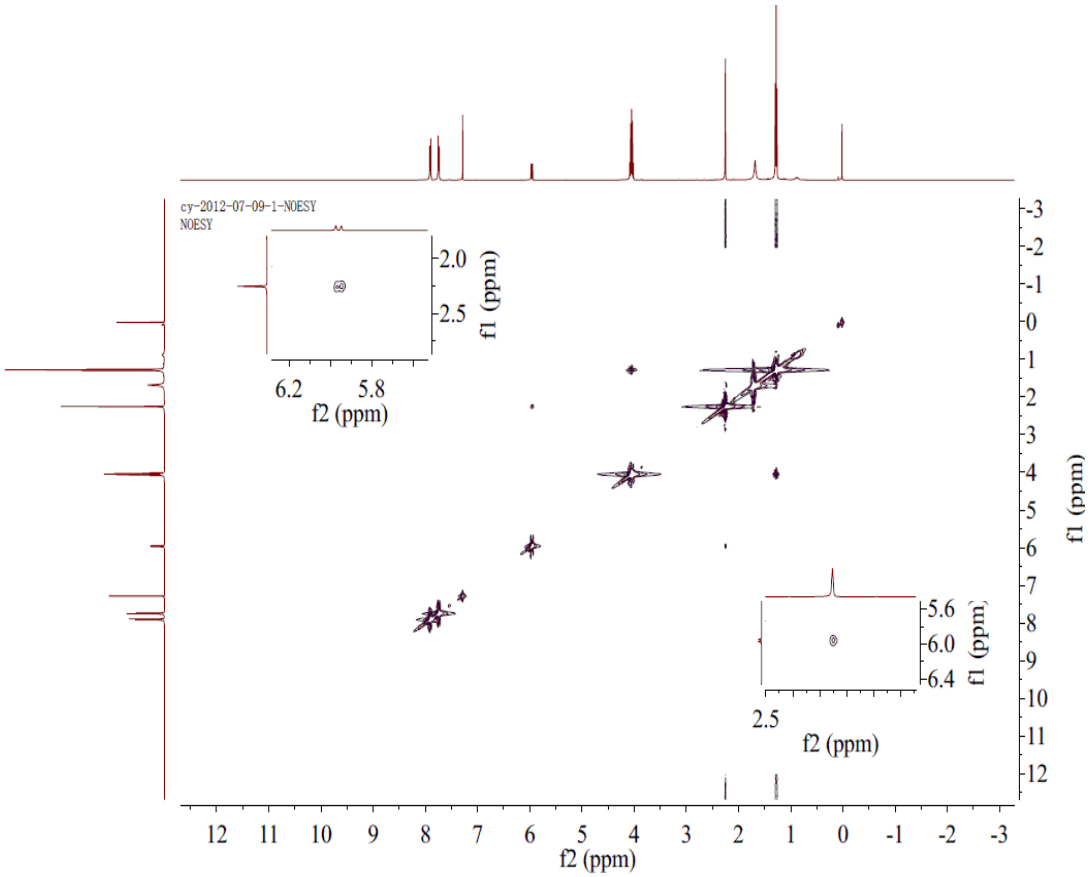
(*Z*)-Diethyl (2-(1,3-dioxoisoindolin-2-yl)prop-1-en-1-yl)phosphonate (9a):



White solid; mp 140-143°C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.87-7.94 (m, 2H, Ph), 7.69-7.80 (m, 2H, Ph), 5.96 (dd, *J* = 10.4, 1.2 Hz, 1H, =CH), 3.98-4.13 (m, 4H, $2OCH_2$), 2.25 (s, 3H, CH_3), 1.28 (t, *J* = 7.1 Hz, 6H, $2CH_3$); ^{13}C NMR (101 MHz, $CDCl_3$): δ 166.63 (C=O), 146.83 (=CN), 134.11, 132.28, 123.71 (Ph), 118.32 (d, *J* = 186.2 Hz, C-P), 62.08 (d, *J* = 5.3 Hz, OCH_2), 24.56 (d, *J* = 17 Hz, CH_3), 16.27 (d, *J* = 6.6 Hz, CH_3); ^{31}P NMR (162 MHz, $CDCl_3$): δ 11.34 (s). ESI-HRMS calcd for $[C_{15}H_{18}NO_5P, M+Na]^+$: 346.0815; Found: 346.0815.







^{1}H-^{1}H NOESY spectrum of **9a**

Single Crystal X-Ray Analysis **9a** (CCDC 893994 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge by contacting The Cambridge Crystallographic Data Centre, 12, Union Road, Cambridge CB2 1EZ, UK; fax: +44 1223 336033; E-mail: deposit@ccdc.cam.ac.uk.)

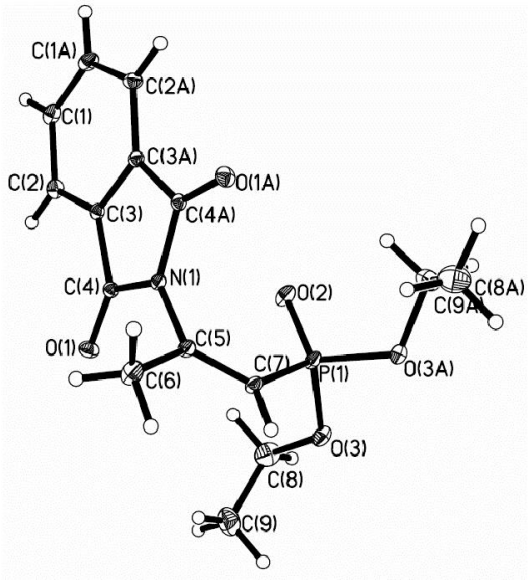


Table 1. Crystal data and structure refinement for shelx.

Identification code	shelx
Empirical formula	C15 H18 N O5 P
Formula weight	323.27
Temperature	293(2) K
Wavelength	0.71073 A
Crystal system, space group	Orthorhombic, Pnma
Unit cell dimensions	a = 14.554(3) A α = 90°
	b = 12.849(3) A β = 90°
	c = 8.6466(17) A γ = 90°
Volume	1617.0(6) A^3
Z, Calculated density	4, 1.328 Mg/m^3
Absorption coefficient	0.192 mm^-1
F(000)	680.0
Crystal size	0.20 x 0.18 x 0.10 mm
Theta range for data collection	2.80 to 27.86°
Limiting indices	-19 <= h <= 19, -16 <= k <= 16, -11<= l <= 11
Reflections collected / unique	15501/2001 [R(int) = 0.0374]
Completeness to theta = 27.87	99.3%
Absorption correction	Semi-empirical from equivalents

Max. and min. transmission	0.9811 and 0.9626
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	2001/13/112
Goodness-of-fit on F^2	1.054
Final R indices [I>2sigma(I)]	R1 = 0.0501, wR2 = 0.1450
R indices (all data)	R1 = 0.0616, wR2 = 0.1570
Absolute structure parameter	0.072(12)
Largest diff. peak and hole	0.229 and -0.265 e.A^-3