

Supporting information

Synthesis, biological evaluation and molecular docking of novel nereistoxin derivatives related phosphonates as insecticidal/AChE inhibitory agents

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1 Chemistry

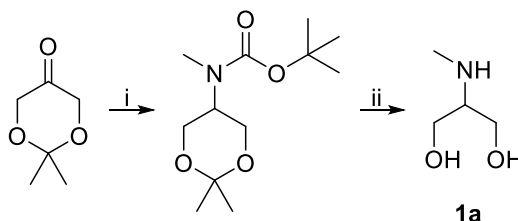
1.1. General Procedures

All solvents and reagents were purchased from commercial sources and used without further purification. High-resolution mass spectra (HRMS) were obtained with Agilent 1290/6545 UHPLC-QTOF/MS. With tetramethylsilane as the internal standard, a Bruker 300 spectrometer was used to record ^1H , ^{13}C and ^{31}P nuclear magnetic resonance (NMR) spectra in chloroform (CDCl_3) and deuterioxide (D_2O). Melting points were determined using METTLER TOLEDO MP90 Melting Point System.

1.2. General Procedure for the Preparation of **1a–1e**

Preparation of **1a**:

Compound **1a** was synthesized according to literature information [1].



Date for **1a**: ^1H NMR (300 MHz, CDCl_3) δ 3.88 (ddd, $J = 18.0, 13.6, 8.0$ Hz, 5H), 2.97 (s, 3H), 1.41 (s, 9H), 1.38 (d, $J = 5.0$ Hz, 6H). ^{13}C NMR (75 MHz, CDCl_3) δ 155.53 (s), 98.24 (s), 79.78 (s), 61.49 (s), 28.39 (s).

Preparation of **1b** and **1c**:

To a 250 mL round-bottomed flask, 50 mL of toluene, 2-amino-1,3-propanediol (1 mmol), 1-bromoethane, and K_2CO_3 (2.2 mmol) were added. The reactions were refluxed for 5 h. After the reactions were complete, the reaction liquids were filtered. The precipitations were washed 3 times with chloroform, and the filtrates were combined and concentrated under reduced pressure to produce light yellow oil.

Preparation of **1d** and **1e**:

To a 250 mL round-bottomed flask, 50 mL of toluene, 2-amino-1,3-propanediol (1 mmol), 1-bromopropane, and K_2CO_3 were added. The reactions were refluxed for 5 h. After the reactions were complete, the reaction liquids were filtered. The precipitations were washed 3 times with chloroform, and the filtrates were combined and concentrated under reduced pressure to produce light yellow oil.

1.3. General Procedure for the Preparation of **2a–2e**

To a 25 mL round bottom flask, crude **1a–1e** (0.1 mol) was added, SOCl₂ (36.6 mL, 0.6 mol) was dropped slowly in an ice bath and then stirred in reflux for 0.5 h. Excess SOCl₂ was removed and 2-(methylamino)-1,3-dichloropropane **2a**, 2-(ethylamino)-1,3-dichloropropane **2c**, 2-(propylamino)-1,3-dichloropropane **2e** were obtained by recrystallization from chloroform. The reaction mixtures of **2c** and **2e** were concentrated in vacuo and then alkalized with ammonia and purified by column to yield **2b** and **2e**.

Date for **2a**: White solid, m.p.: 99.6°C, yield 20%. ¹H NMR (300 MHz, D₂O) δ 4.07 – 4.01 (m, 4H), 4.00 – 3.89 (m, 1H), 2.86 (s, 3H). ¹³C NMR (75 MHz, D₂O) δ 59.46 (s), 40.33 (s), 30.66 (s). MS (HRMS-ESI): Calcd for C₄H₉Cl₂N, [M+H]⁺: 142.0185, found: 142.0168.

Date for **2b**: Yellow-brown liquid, yield 35%. ¹H NMR (300 MHz, CDCl₃) δ 4.06 (ddd, *J* = 10.2, 8.1, 5.4 Hz, 1H), 3.94 – 3.79 (m, 2H), 2.86 (dd, *J* = 13.9, 8.1 Hz, 1H), 2.70 (dd, *J* = 13.9, 5.7 Hz, 1H), 2.64 – 2.50 (m, 4H), 1.02 (t, *J* = 7.1 Hz, 6H). ¹³C NMR (75 MHz, CDCl₃) δ 59.46 (s), 57.39 (s), 47.97 (s), 47.43 (s), 12.04 (s). MS (HRMS-ESI): Calcd for C₇H₁₅Cl₂N, [M+H]⁺: 184.0654, found: 184.0644.

Date for **2c**: White solid, m.p.: 145.1°C, yield 42%. ¹H NMR (300 MHz, D₂O) δ 4.06 – 3.86 (m, 5H), 3.25 (q, *J* = 7.2 Hz, 2H), 1.31 (t, *J* = 7.2 Hz, 3H). ¹³C NMR (75 MHz, D₂O) δ 57.94 (s), 41.28 (s), 40.32 (s), 10.38 (s). MS (HRMS-ESI): Calcd for C₅H₁₁Cl₂N, [M+H]⁺: 156.0341, found: 156.0328.

Date for **2d**: Orange liquid, yield 43%. ¹H NMR (300 MHz, CDCl₃) δ = 4.16 – 3.97 (m, 1H), 3.87 (qd, *J* = 11.5, 4.8, 2H), 2.86 (dd, *J* = 13.8, 8.5, 1H), 2.76 – 2.61 (m, 1H), 2.52 – 2.30 (m, 4H), 1.54 – 1.32 (m, 4H), 0.87 (t, *J* = 7.3, 6H). ¹³C NMR (75 MHz, CDCl₃) δ 59.43 (s), 58.80 (s), 57.01 (s), 47.50 (s), 20.47 (s), 11.79 (s). MS (HRMS-ESI): Calcd for C₉H₁₉Cl₂N, [M+H]⁺: 212.0967, found: 212.0957.

Date for **2e**: White solid, m.p.: 135.2°C, yield 45%. ¹H NMR (300 MHz, D₂O) δ 4.06 – 3.85 (m, 5H), 3.21 – 3.06 (m, 2H), 1.80 – 1.60 (m, 2H), 0.95 (t, *J* = 7.4 Hz, 3H). ¹³C NMR (75 MHz, D₂O) δ 58.25 (s), 47.33 (s), 40.22 (s), 19.04 (s), 10.07 (s). (HRMS-ESI): Calcd for C₆H₁₃Cl₂N, [M+H]⁺: 170.0498, found: 170.0482.

1.4. General Procedure for the Preparation of **3a–3h**

Some phosphite diesters were obtained from commercial sources and others were synthesized according to previously reported procedures [2]. To a solution of the corresponding alcohol (0.3 mol) and pyridine (15.82 g, 0.2 mol) in Et₂O (50 mL) at 0°C was added PCl₃ (13.74 g, 0.1 mol) over the course of 1 h. After complete addition, the reaction mixture was allowed to slowly warm to ambient temperature and it was stirred for 16 h. The white suspension was then filtered under suction, and the residual pyridinium chloride was washed twice with Et₂O (50 mL). The filtrates were concentrated under reduced pressure and dried under reduced pressure to yield the desired phosphonates which were colorless liquids.

1.5. General Procedure for the Preparation of **4a–4h**

Compounds **4a–4h** were synthesized based on literature information [2]. To a suspension of the appropriate phosphonate (20 mmol) and S₈ (0.704 g, 22 mmol) in Et₂O in a round-bottom flask was slowly added NEt₃ (2.23 g, 22 mmol) in an ice bath. After the full conversion of the phosphonate, as

monitored by ^{31}P NMR spectroscopy, the suspension was diluted with Et_2O to 100 mL and then washed with aqueous HCl (100 mL, 1 M), dried over MgSO_4 and concentrated under reduced pressure. The resulting suspension was filtered to yield the S-hydrogen phosphorothioates **4a–4h**.

1.6. General Procedure for the Preparation of **5–9**

A mixture of S-hydrogen phosphorothioates **4a–4h** (3 mmol), NaH (60% in mineral oil, 0.12 g, 3 mmol) in dry acetonitrile (10 mL) was stirred at room temperature. A quantity of **2a–2e** (1 mmol) was added after 10 min and the reaction was stirred at 50°C , as monitored by TLC. After completion, the reaction mixture was filtered and the organic phase concentrated *in vacuo*. The products were purified by silica gel column chromatography.

2 Data for **5–9**

Data for **5b**: Yellow oil, yield 36%. ^{31}P NMR (121 MHz, CDCl_3) δ 27.43 (s). ^1H NMR (300 MHz, CDCl_3) δ 4.25 – 4.04 (m, 8H), 3.10 – 2.91 (m, 5H), 2.42 (s, 3H), 1.33 (t, $J = 7.1$ Hz, 12H). ^{13}C NMR (75 MHz, CDCl_3) δ 63.79 (d, $J = 6.3$ Hz), 59.23 (t, $J = 4.7$ Hz), 33.52 (s), 33.49 (s), 16.06 (d, $J = 7.2$ Hz). MS (HRMS-ESI): Calcd for $\text{C}_{12}\text{H}_{29}\text{NO}_6\text{P}_2\text{S}_2$, $[\text{M}+\text{H}]^+$: 410.0984, found: 410.0983.

Data for **5c**: Yellow oil, yield 48%. ^{31}P NMR (121 MHz, CDCl_3) δ 27.61 (s). ^1H NMR (300 MHz, CDCl_3) δ 4.15 – 3.90 (m, 8H), 3.12 – 2.94 (m, 5H), 2.43 (s, 3H), 1.80 – 1.60 (m, 8H), 1.02 – 0.87 (m, 12H). ^{13}C NMR (75 MHz, CDCl_3) δ 69.27 (d, $J = 6.7$ Hz), 59.28 (t, $J = 4.7$ Hz), 34.56 – 32.36 (m), 23.56 (d, $J = 7.3$ Hz), 10.06 (s). MS (HRMS-ESI): Calcd for $\text{C}_{16}\text{H}_{37}\text{NO}_6\text{P}_2\text{S}_2$, $[\text{M}+\text{H}]^+$: 466.1610, found: 466.1611.

Data for **5d**: Yellow oil, yield 87%. ^{31}P NMR (121 MHz, CDCl_3) δ 25.02 (s). ^1H NMR (300 MHz, CDCl_3) δ 4.83 – 4.64 (m, 4H), 3.15 – 2.91 (m, 5H), 2.43 (s, 3H), 1.41 – 1.27 (m, 24H). ^{13}C NMR (75 MHz, CDCl_3) δ 72.98 (dd, $J = 6.7, 1.5$ Hz), 59.21 (t, $J = 5.0$ Hz), 33.65 (d, $J = 2.8$ Hz), 33.49 (s), 23.87 (d, $J = 4.1$ Hz), 23.68 (dd, $J = 5.4, 1.4$ Hz). MS (HRMS-ESI): Calcd for $\text{C}_{16}\text{H}_{37}\text{NO}_6\text{P}_2\text{S}_2$, $[\text{M}+\text{H}]^+$: 466.1610, found: 466.1619.

Data for **5e**: Yellow oil, yield 45%. ^{31}P NMR (121 MHz, CDCl_3) δ 27.61 (s). ^1H NMR (300 MHz, CDCl_3) δ 4.17 – 3.97 (m, 8H), 3.08 – 2.94 (m, 5H), 2.43 (s, 3H), 1.75 – 1.56 (m, 8H), 1.48 – 1.29 (m, 8H), 1.01 – 0.83 (m, 12H). ^{13}C NMR (75 MHz, CDCl_3) δ 67.54 (d, $J = 6.7$ Hz), 59.30 (t, $J = 4.7$ Hz), 33.51 (s), 33.40 (d, $J = 3.6$ Hz), 32.17 (d, $J = 7.2$ Hz), 18.73 (s), 13.57 (s). MS (HRMS-ESI): Calcd for $\text{C}_{20}\text{H}_{45}\text{NO}_6\text{P}_2\text{S}_2$, $[\text{M}+\text{H}]^+$: 522.2136, found: 522.2238.

Data for **5g**: Yellow oil, yield 10%. ^{31}P NMR (121 MHz, CDCl_3) δ 21.21 (s). ^1H NMR (300 MHz, CDCl_3) δ 7.53 – 6.96 (m, 20H), 2.97 (dd, $J = 15.7, 5.3$ Hz, 4H), 2.73 (d, $J = 5.5$ Hz, 1H), 2.19 (s, 3H). ^{13}C NMR (75 MHz, CDCl_3) δ 149.99 (s), 129.92 (s), 125.82 (s), 120.75 (dd, $J = 4.9, 2.3$ Hz), 59.02 (s), 33.26 (s). MS (HRMS-ESI): Calcd for $\text{C}_{28}\text{H}_{29}\text{NO}_6\text{P}_2\text{S}_2$, $[\text{M}+\text{H}]^+$: 602.0984, found: 602.0942.

Data for **6a**: Yellow oil, yield 20%. ^{31}P NMR (121 MHz, CDCl_3) δ 31.73 (s). ^1H NMR (300 MHz, CDCl_3) δ 3.80 (d, $J = 12.6$ Hz, 12H), 2.99 (tt, $J = 26.6, 9.8$ Hz, 5H), 2.53 (d, $J = 6.8$ Hz, 4H), 1.05 (t, $J = 6.8$ Hz, 6H). MS (HRMS-ESI): Calcd for $\text{C}_{11}\text{H}_{27}\text{NO}_6\text{P}_2\text{S}_2$, $[\text{M}+\text{H}]^+$: 396.0828, found: 396.0833.

Data for **6b**: Yellow oil, yield 46%. ^{31}P NMR (121 MHz, CDCl_3) δ 28.34 (s). ^1H NMR (300 MHz, CDCl_3) δ 4.30 – 3.98 (m, 8H), 3.20 – 2.78 (m, 5H), 2.52 (q, $J = 7.1$ Hz, 4H), 1.35 (t, $J = 7.1$ Hz, 12H), 1.03 (t, $J = 7.1$ Hz, 6H). ^{13}C NMR (75 MHz, CDCl_3) δ 63.61 (d, $J = 5.1$ Hz), 60.78 (t, $J = 5.9$ Hz), 43.00 (s), 31.26 (d, $J =$

3.2 Hz), 16.10 (d, $J = 7.1$ Hz), 14.46 (s). MS (HRMS-ESI): Calcd for $C_{15}H_{35}NO_6P_2S_2$, $[M+H]^+$: 452.1454, found: 452.1477.

Data for **6c**: Yellow oil, yield 64%. ^{31}P NMR (121 MHz, $CDCl_3$) δ 28.47 (s). 1H NMR (300 MHz, $CDCl_3$) δ 4.14 – 3.91 (m, 8H), 3.17 – 2.81 (m, 5H), 2.52 (q, $J = 7.1$ Hz, 4H), 1.80 – 1.61 (m, 8H), 1.11 – 0.99 (m, 6H), 0.96 (t, $J = 7.4$ Hz, 12H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 69.06 (dd, $J = 6.5, 1.1$ Hz), 60.71 (t, $J = 6.2$ Hz), 43.01 (s), 31.24 (d, $J = 3.1$ Hz), 23.58 (d, $J = 7.3$ Hz), 14.46 (s), 10.08 (d, $J = 0.7$ Hz). MS (HRMS-ESI): Calcd for $C_{19}H_{43}NO_6P_2S_2$, $[M+H]^+$: 508.2080, found: 508.2099.

Data for **6d**: Yellow oil, yield 68%. ^{31}P NMR (121 MHz, $CDCl_3$) δ 25.85 (s). 1H NMR (300 MHz, $CDCl_3$) δ 4.82 – 4.60 (m, 4H), 3.20 – 2.81 (m, 5H), 2.52 (q, $J = 7.1$ Hz, 4H), 1.45 – 1.29 (m, 24H), 1.03 (t, $J = 7.1$ Hz, 6H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 72.58 (d, $J = 6.5$ Hz), 60.47 (t, $J = 6.6$ Hz), 42.97 (s), 31.49 (d, $J = 3.2$ Hz), 25.05 – 22.54 (m), 14.47 (s). MS (HRMS-ESI): Calcd for $C_{19}H_{43}NO_6P_2S_2$, $[M+H]^+$: 508.2080, found: 508.2100.

Data for **6e**: Yellow oil, yield 34%. ^{31}P NMR (121 MHz, $CDCl_3$) δ 28.46 (s). 1H NMR (300 MHz, $CDCl_3$) δ 4.18 – 3.94 (m, 8H), 2.98 (qdd, $J = 19.5, 13.3, 7.1$ Hz, 5H), 2.52 (q, $J = 7.1$ Hz, 4H), 1.68 (dt, $J = 14.7, 6.7$ Hz, 8H), 1.50 – 1.32 (m, 8H), 1.04 (t, $J = 7.1$ Hz, 6H), 0.93 (t, $J = 7.4$ Hz, 12H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 67.32 (dd, $J = 6.5, 1.2$ Hz), 60.69 (t, $J = 6.2$ Hz), 43.02 (s), 32.20 (d, $J = 7.1$ Hz), 31.27 (d, $J = 3.2$ Hz), 18.76 (s), 14.46 (s), 13.59 (s). MS (HRMS-ESI): Calcd for $C_{23}H_{51}NO_6P_2S_2$, $[M+H]^+$: 564.2706, found: 564.2720.

Data for **6g**: Yellow oil, yield 20%. ^{31}P NMR (121 MHz, $CDCl_3$) δ 21.82 (s). 1H NMR (300 MHz, $CDCl_3$) δ 7.46 – 7.09 (m, 20H), 3.13 – 2.75 (m, 5H), 2.36 (q, $J = 7.1$ Hz, 4H), 0.87 (t, $J = 7.1$ Hz, 6H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 150.17 (dd, $J = 8.1, 7.0$ Hz), 129.88 (d, $J = 1.0$ Hz), 125.70 (d, $J = 1.5$ Hz), 120.72 (dd, $J = 7.0, 4.9$ Hz), 60.28 (t, $J = 6.2$ Hz), 42.83 (s), 32.12 (d, $J = 3.3$ Hz), 14.27 (s). MS (HRMS-ESI): Calcd for $C_{31}H_{35}NO_6P_2S_2$, $[M+H]^+$: 644.1454, found: 644.1431.

Data for **6h**: Yellow oil, yield 31%. ^{31}P NMR (121 MHz, $CDCl_3$) δ 29.42 (s). 1H NMR (300 MHz, $CDCl_3$) δ 7.39 – 7.27 (m, 20H), 5.18 – 4.99 (m, 8H), 3.01 – 2.89 (m, 1H), 2.89 – 2.70 (m, 4H), 2.36 (q, $J = 7.1$ Hz, 4H), 0.95 (t, $J = 7.1$ Hz, 6H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 135.52 (dd, $J = 7.4, 1.9$ Hz), 128.63 (s), 128.15 (s), 68.97 (d, $J = 6.0$ Hz), 60.24 (t, $J = 6.5$ Hz), 42.86 (s), 31.32 (d, $J = 3.0$ Hz), 14.43 (s). MS (HRMS-ESI): Calcd for $C_{35}H_{43}NO_6P_2S_2$, $[M+H]^+$: 700.2080, found: 700.2053.

Data for **7a**: Yellow oil, yield 24%. ^{31}P NMR (121 MHz, $CDCl_3$) δ 30.97 (s). 1H NMR (300 MHz, $CDCl_3$) δ 3.94 – 3.67 (m, 12H), 3.14 – 2.92 (m, 5H), 2.66 (q, $J = 7.1$ Hz, 2H), 1.15 – 1.03 (m, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 57.57 (t, $J = 4.4$ Hz), 54.04 (d, $J = 6.2$ Hz), 41.26 (s), 33.88 (d, $J = 3.6$ Hz), 15.31 (s). MS (HRMS-ESI): Calcd for $C_9H_{23}NO_6P_2S_2$, $[M+H]^+$: 368.0515, found: 368.0493.

Data for **7b**: Yellow oil, yield 51%. ^{31}P NMR (121 MHz, $CDCl_3$) δ 27.57 (s). 1H NMR (300 MHz, $CDCl_3$) δ 4.32 – 4.02 (m, 8H), 3.22 – 2.86 (m, 5H), 2.67 (q, $J = 7.1$ Hz, 2H), 1.35 (t, $J = 7.1$ Hz, 12H), 1.10 (t, $J = 7.1$ Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 63.80 (d, $J = 6.2$ Hz), 57.57 (t, $J = 4.6$ Hz), 41.32 (s), 33.97 (d, $J = 3.6$ Hz), 16.11 (d, $J = 7.3$ Hz), 15.35 (s). MS (HRMS-ESI): Calcd for $C_{13}H_{31}NO_6P_2S_2$, $[M+H]^+$: 424.1141, found: 424.1152.

Data for **7c**: Yellow oil, yield 58%. ^{31}P NMR (121 MHz, $CDCl_3$) δ 27.74 (s). 1H NMR (300 MHz, $CDCl_3$)

δ 4.20 – 3.90 (m, 8H), 3.19 – 2.90 (m, 5H), 2.67 (q, J = 7.1 Hz, 2H), 1.82 – 1.61 (m, 8H), 1.10 (t, J = 7.1 Hz, 3H), 0.96 (t, J = 7.4 Hz, 12H). ^{13}C NMR (75 MHz, CDCl_3) δ 69.24 (d, J = 6.7 Hz), 57.56 (t, J = 4.7 Hz), 41.32 (s), 33.92 (d, J = 3.6 Hz), 23.58 (d, J = 7.3 Hz), 15.35 (s), 10.09 (s). MS (HRMS-ESI): Calcd for $\text{C}_{17}\text{H}_{39}\text{NO}_6\text{P}_2\text{S}_2$, $[\text{M}+\text{H}]^+$: 480.1767, found: 480.1784.

Data for **7d**: Yellow oil, yield 58%. ^{31}P NMR (121 MHz, CDCl_3) δ 25.14 (s). ^1H NMR (300 MHz, CDCl_3) δ 4.88 – 4.65 (m, 4H), 3.21 – 2.90 (m, 5H), 2.70 (dd, J = 13.7, 6.7 Hz, 2H), 1.44 – 1.32 (m, 24H), 1.13 (t, J = 7.1 Hz, 3H). ^{13}C NMR (75 MHz, CDCl_3) δ 73.36 – 72.30 (m), 57.56 (s), 41.34 (s), 34.08 (s), 24.30 – 23.26 (m), 15.24 (s). MS (HRMS-ESI): Calcd for $\text{C}_{17}\text{H}_{39}\text{NO}_6\text{P}_2\text{S}_2$, $[\text{M}+\text{H}]^+$: 480.1767, found: 480.1784..

Data for **7e**: Yellow oil, yield 52%. ^{31}P NMR (121 MHz, CDCl_3) δ 27.87 (d, J = 31.2 Hz). ^1H NMR (300 MHz, CDCl_3) δ 4.23 – 3.96 (m, 8H), 3.17 – 2.92 (m, 5H), 2.67 (q, J = 7.1 Hz, 2H), 1.68 (dt, J = 14.6, 6.6 Hz, 8H), 1.40 (dq, J = 14.5, 7.3 Hz, 8H), 1.11 (t, J = 7.1 Hz, 3H), 0.93 (t, J = 7.4 Hz, 12H). ^{13}C NMR (75 MHz, CDCl_3) δ 67.50 (d, J = 6.7 Hz), 57.57 (s), 41.33 (s), 33.92 (d, J = 3.5 Hz), 32.19 (d, J = 7.2 Hz), 18.75 (s), 15.35 (s), 13.61 (s). MS (HRMS-ESI): Calcd for $\text{C}_{21}\text{H}_{47}\text{NO}_6\text{P}_2\text{S}_2$, $[\text{M}+\text{H}]^+$: 536.2393, found: 536.2372.

Data for **7g**: Yellow oil, yield 72%. ^{31}P NMR (121 MHz, CDCl_3) δ 21.24 (s). ^1H NMR (300 MHz, CDCl_3) δ 7.50 – 7.10 (m, 20H), 2.98 (dd, J = 15.7, 5.6 Hz, 4H), 2.84 (dd, J = 11.1, 5.5 Hz, 1H), 2.43 (q, J = 7.1 Hz, 2H), 0.92 (t, J = 7.1 Hz, 3H). ^{13}C NMR (75 MHz, CDCl_3) δ 150.05 (dd, J = 8.2, 3.8 Hz), 129.86 (s), 125.74 (s), 120.68 (dd, J = 4.8, 3.7 Hz), 57.31 (t, J = 4.5 Hz), 41.04 (s), 34.64 (d, J = 3.7 Hz), 15.09 (s). MS (HRMS-ESI): Calcd for $\text{C}_{29}\text{H}_{31}\text{NO}_6\text{P}_2\text{S}_2$, $[\text{M}+\text{H}]^+$: 616.1141, found: 616.1101.

Data for **8a**: Yellow oil, yield 30%. ^{31}P NMR (121 MHz, CDCl_3) δ 31.75 (s). ^1H NMR (300 MHz, CDCl_3) δ 3.78 (d, J = 12.6 Hz, 12H), 3.13 – 2.76 (m, 5H), 2.38 (t, J = 7.0 Hz, 4H), 1.42 (dd, J = 14.3, 7.2 Hz, 4H), 0.87 (t, J = 7.3 Hz, 6H). ^{13}C NMR (75 MHz, CDCl_3) δ 61.71 (s), 53.88 (d, J = 6.1 Hz), 51.57 (s), 30.96 (s), 22.12 (s), 11.79 (s). MS (HRMS-ESI): Calcd for $\text{C}_{13}\text{H}_{31}\text{NO}_6\text{P}_2\text{S}_2$, $[\text{M}+\text{H}]^+$: 424.1141, found: 424.1142.

Data for **8b**: Yellow oil, yield 37%. ^{31}P NMR (121 MHz, CDCl_3) δ 28.35 (s). ^1H NMR (300 MHz, CDCl_3) δ 4.29 – 4.02 (m, 8H), 3.19 – 2.80 (m, 5H), 2.48 – 2.29 (m, 4H), 1.45 (dt, J = 14.4, 7.3 Hz, 4H), 1.37 (t, J = 7.1 Hz, 12H), 0.94 – 0.81 (m, 6H). ^{13}C NMR (75 MHz, CDCl_3) δ 63.61 (dd, J = 6.1, 1.0 Hz), 61.59 (t, J = 6.0 Hz), 51.61 (s), 31.15 (s), 22.17 (s), 16.12 (d, J = 7.2 Hz), 11.80 (s). MS (HRMS-ESI): Calcd for $\text{C}_{17}\text{H}_{39}\text{NO}_6\text{P}_2\text{S}_2$, $[\text{M}+\text{H}]^+$: 480.1767, found: 480.1760.

Data for **8c**: Yellow oil, yield 48%. ^{31}P NMR (121 MHz, CDCl_3) δ 28.49 (s). ^1H NMR (300 MHz, CDCl_3) δ 4.16 – 3.93 (m, 8H), 3.11 – 2.82 (m, 5H), 2.44 – 2.32 (m, 4H), 1.83 – 1.62 (m, 8H), 1.52 – 1.34 (m, 4H), 0.97 (t, J = 7.4 Hz, 12H), 0.88 (t, J = 7.3 Hz, 6H). ^{13}C NMR (75 MHz, CDCl_3) δ 69.05 (d, J = 5.4 Hz), 61.49 (t, J = 6.2 Hz), 51.63 (s), 31.10 (d, J = 3.3 Hz), 23.59 (d, J = 7.3 Hz), 22.17 (s), 11.79 (s), 10.09 (s). MS (HRMS-ESI): Calcd for $\text{C}_{21}\text{H}_{47}\text{NO}_6\text{P}_2\text{S}_2$, $[\text{M}+\text{H}]^+$: 536.2393, found: 536.2409.

Data for **8d**: Yellow oil, yield 48%. ^{31}P NMR (121 MHz, CDCl_3) δ 25.85 (s). ^1H NMR (300 MHz, CDCl_3) δ 4.80 – 4.61 (m, 4H), 3.22 – 2.73 (m, 5H), 2.42 – 2.30 (m, 4H), 1.43 (dd, J = 14.5, 7.3 Hz, 28H), 1.35 (t, J = 5.6 Hz, 6H), 0.87 (t, J = 7.3 Hz, 2H). ^{13}C NMR (75 MHz, CDCl_3) δ 72.56 (d, J = 6.4 Hz), 61.24 (t, J = 6.7 Hz), 51.58 (s), 31.36 (d, J = 3.3 Hz), 24.58 – 22.95 (m), 22.17 (s), 11.78 (s). MS (HRMS-ESI): Calcd for $\text{C}_{21}\text{H}_{47}\text{NO}_6\text{P}_2\text{S}_2$, $[\text{M}+\text{H}]^+$: 536.2393, found: 536.2416.

Data for **8e**: Yellow oil, yield 40%. ^{31}P NMR (121 MHz, CDCl_3) δ 28.46 (s). ^1H NMR (300 MHz, CDCl_3) δ 4.18 – 3.94 (m, 8H), 3.12 – 2.80 (m, 5H), 2.48 – 2.30 (m, 4H), 1.68 (dt, J = 14.6, 6.7 Hz, 8H), 1.51 – 1.32 (m, 12H), 0.90 (dt, J = 17.7, 7.4 Hz, 18H). ^{13}C NMR (75 MHz, CDCl_3) δ 67.30 (dd, J = 6.5, 1.2 Hz), 61.48 (t, J = 6.4 Hz), 51.64 (s), 32.21 (d, J = 7.2 Hz), 31.12 (d, J = 3.2 Hz), 22.18 (s), 18.76 (s), 13.59 (s), 11.79 (s). MS (HRMS-ESI): Calcd for $\text{C}_{25}\text{H}_{55}\text{NO}_6\text{P}_2\text{S}_2$, $[\text{M}+\text{H}]^+$: 592.3019, found: 592.3032.

Data for **8g**: Yellow oil, yield 38%. ^{31}P NMR (121 MHz, CDCl_3) δ 21.75 (s). ^1H NMR (300 MHz, CDCl_3) δ 7.48 – 6.92 (m, 20H), 3.05 – 2.83 (m, 4H), 2.73 (dd, J = 14.5, 7.0 Hz, 1H), 2.27 – 2.03 (m, 4H), 1.27 – 1.04 (m, 4H), 0.67 (t, J = 7.3 Hz, 6H). ^{13}C NMR (75 MHz, CDCl_3) δ 150.18 (dd, J = 8.1, 6.6 Hz), 129.89 (d, J = 1.1 Hz), 125.69 (s), 120.71 (dd, J = 7.5, 4.9 Hz), 61.08 (t, J = 6.2 Hz), 51.42 (s), 31.97 (d, J = 3.4 Hz), 21.98 (s), 11.71 (s). MS (HRMS-ESI): Calcd for $\text{C}_{33}\text{H}_{39}\text{NO}_6\text{P}_2\text{S}_2$, $[\text{M}+\text{H}]^+$: 672.1767, found: 672.1761.

Data for **8h**: Yellow oil, yield 13%. ^{31}P NMR (121 MHz, CDCl_3) δ 29.38 (s). ^1H NMR (300 MHz, CDCl_3) δ 7.33 (d, J = 5.1 Hz, 20H), 5.19 – 4.96 (m, 8H), 2.99 – 2.67 (m, 5H), 2.33 – 2.15 (m, 4H), 1.33 (dd, J = 14.5, 7.3 Hz, 4H), 0.89 – 0.71 (m, 6H). ^{13}C NMR (75 MHz, CDCl_3) δ 135.52 (dd, J = 7.4, 2.1 Hz), 128.63 (s), 128.14 (d, J = 1.9 Hz), 68.95 (d, J = 5.9 Hz), 61.05 (t, J = 6.4 Hz), 51.48 (s), 31.15 (d, J = 3.0 Hz), 22.09 (s), 11.79 (s). MS (HRMS-ESI): Calcd for $\text{C}_{37}\text{H}_{47}\text{NO}_6\text{P}_2\text{S}_2$, $[\text{M}+\text{H}]^+$: 728.2393, found: 728.2360.

Data for **9a**: Yellow oil, yield 28%. ^{31}P NMR (121 MHz, CDCl_3) δ 31.02 (s). ^1H NMR (300 MHz, CDCl_3) δ 3.82 (d, J = 12.6 Hz, 12H), 3.16 – 2.95 (m, 5H), 2.62 (dd, J = 9.1, 5.2 Hz, 2H), 1.59 – 1.44 (m, 2H), 1.02 – 0.88 (m, 3H). ^{13}C NMR (75 MHz, CDCl_3) δ 57.71 (t, J = 4.4 Hz), 54.07 (d, J = 6.2 Hz), 48.74 (s), 33.86 (d, J = 3.6 Hz), 23.22 (s), 11.73 (s). MS (HRMS-ESI): Calcd for $\text{C}_{10}\text{H}_{25}\text{NO}_6\text{P}_2\text{S}_2$, $[\text{M}+\text{H}]^+$: 382.0671, found: 382.0649.

Data for **9b**: Yellow oil, yield 65%. ^{31}P NMR (121 MHz, CDCl_3) δ 27.60 (s). ^1H NMR (300 MHz, CDCl_3) δ 4.31 – 4.05 (m, 8H), 3.16 – 2.94 (m, 5H), 2.60 (t, J = 7.1 Hz, 2H), 1.63 – 1.44 (m, 2H), 1.37 (t, J = 7.1 Hz, 12H), 0.94 (t, J = 7.4 Hz, 3H). ^{13}C NMR (75 MHz, CDCl_3) δ 63.76 (d, J = 6.2 Hz), 57.60 (t, J = 4.7 Hz), 48.80 (s), 34.02 (d, J = 3.6 Hz), 23.30 (s), 16.10 (d, J = 7.2 Hz), 11.74 (s). MS (HRMS-ESI): Calcd for $\text{C}_{14}\text{H}_{33}\text{NO}_6\text{P}_2\text{S}_2$, $[\text{M}+\text{H}]^+$: 438.1297, found: 438.1299.

Data for **9c**: Yellow oil, yield 78%. ^{31}P NMR (121 MHz, CDCl_3) δ 27.76 (s). ^1H NMR (300 MHz, CDCl_3) δ 4.17 – 3.94 (m, 8H), 3.06 (td, J = 14.6, 5.7 Hz, 5H), 2.60 (t, J = 7.1 Hz, 2H), 1.90 – 1.63 (m, 5H), 1.58 – 1.41 (m, 2H), 1.09 – 0.85 (m, 15H). ^{13}C NMR (75 MHz, CDCl_3) δ 69.21 (d, J = 6.6 Hz), 57.60 (t, J = 4.7 Hz), 48.81 (s), 33.95 (d, J = 3.5 Hz), 23.56 (d, J = 7.3 Hz), 23.29 (s), 11.73 (s), 10.07 (s). MS (HRMS-ESI): Calcd for $\text{C}_{18}\text{H}_{41}\text{NO}_6\text{P}_2\text{S}_2$, $[\text{M}+\text{H}]^+$: 494.1923, found: 494.1918.

Data for **9d**: Yellow oil, yield 78%. ^{31}P NMR (121 MHz, CDCl_3) δ 25.19 (s). ^1H NMR (300 MHz, CDCl_3) δ 4.79 – 4.61 (m, 4H), 3.13 – 2.91 (m, 5H), 2.56 (t, J = 7.1 Hz, 2H), 1.46 (dd, J = 14.5, 7.3 Hz, 2H), 1.32 (dd, J = 5.9, 5.2 Hz, 24H), 0.88 (t, J = 7.4 Hz, 3H). ^{13}C NMR (75 MHz, CDCl_3) δ 72.82 (dd, J = 6.6, 2.0 Hz), 57.54 (t, J = 5.1 Hz), 48.82 (s), 34.23 (d, J = 3.6 Hz), 24.06 – 23.45 (m), 23.27 (s), 11.73 (s). MS (HRMS-ESI): Calcd for $\text{C}_{18}\text{H}_{41}\text{NO}_6\text{P}_2\text{S}_2$, $[\text{M}+\text{H}]^+$: 494.1923, found: 494.1952.

Data for **9e**: Yellow oil, yield 28%. ^{31}P NMR (121 MHz, CDCl_3) δ 27.70 (s). ^1H NMR (300 MHz, CDCl_3) δ 4.11 – 3.86 (m, 8H), 3.05 – 2.83 (m, 5H), 2.49 (t, J = 7.1 Hz, 2H), 1.68 – 1.50 (m, 8H), 1.45 – 1.20 (m,

10H), 0.83 (td, $J = 7.4, 3.4$ Hz, 15H). ^{13}C NMR (75 MHz, CDCl_3) δ 67.36 (d, $J = 6.6$ Hz), 57.54 (t, $J = 4.7$ Hz), 48.75 (s), 33.90 (d, $J = 3.5$ Hz), 32.09 (d, $J = 7.2$ Hz), 23.24 (s), 18.66 (s), 13.51 (s), 11.66 (s). MS (HRMS-ESI): Calcd for $\text{C}_{22}\text{H}_{49}\text{NO}_6\text{P}_2\text{S}_2$, $[\text{M}+\text{H}]^+$: 550.2549, found: 550.2542.

Data for **9g**: Yellow oil, yield 37%. ^{31}P NMR (121 MHz, CDCl_3) δ 21.26 (s). ^1H NMR (300 MHz, CDCl_3) δ 7.45 – 7.08 (m, 20H), 2.98 (dd, $J = 15.5, 5.6$ Hz, 4H), 2.88 – 2.76 (m, 1H), 2.34 (t, $J = 7.1$ Hz, 2H), 1.28 (dt, $J = 14.5, 7.2$ Hz, 2H), 0.80 (t, $J = 7.4$ Hz, 3H). ^{13}C NMR (75 MHz, CDCl_3) δ 150.07 (dd, $J = 8.2, 3.6$ Hz), 129.87 (s), 125.74 (s), 120.69 (dd, $J = 4.9, 3.4$ Hz), 57.38 (t, $J = 4.5$ Hz), 48.49 (s), 34.70 (d, $J = 3.7$ Hz), 23.05 (s), 11.60 (s). MS (HRMS-ESI): Calcd for $\text{C}_{30}\text{H}_{33}\text{NO}_6\text{P}_2\text{S}_2$, $[\text{M}+\text{H}]^+$: 630.1297, found: 630.1258.

Compounds **5a**, **5h**, **7h**, and **9h** were unstable during purification. **5f**, **6f**, **7f**, **8f**, **9f** are easily hydrolyzed during storage.

3 NMR and HRMS for 5-9

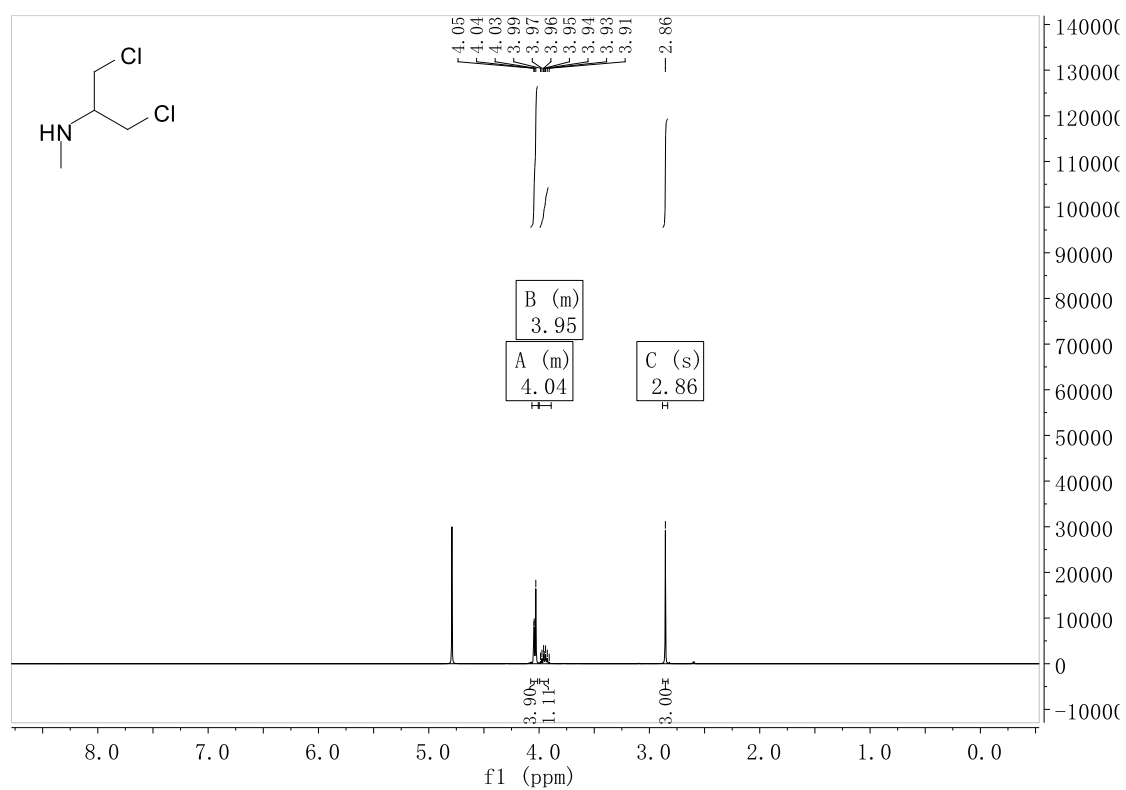


Figure S1. ¹H NMR of compound 2a.

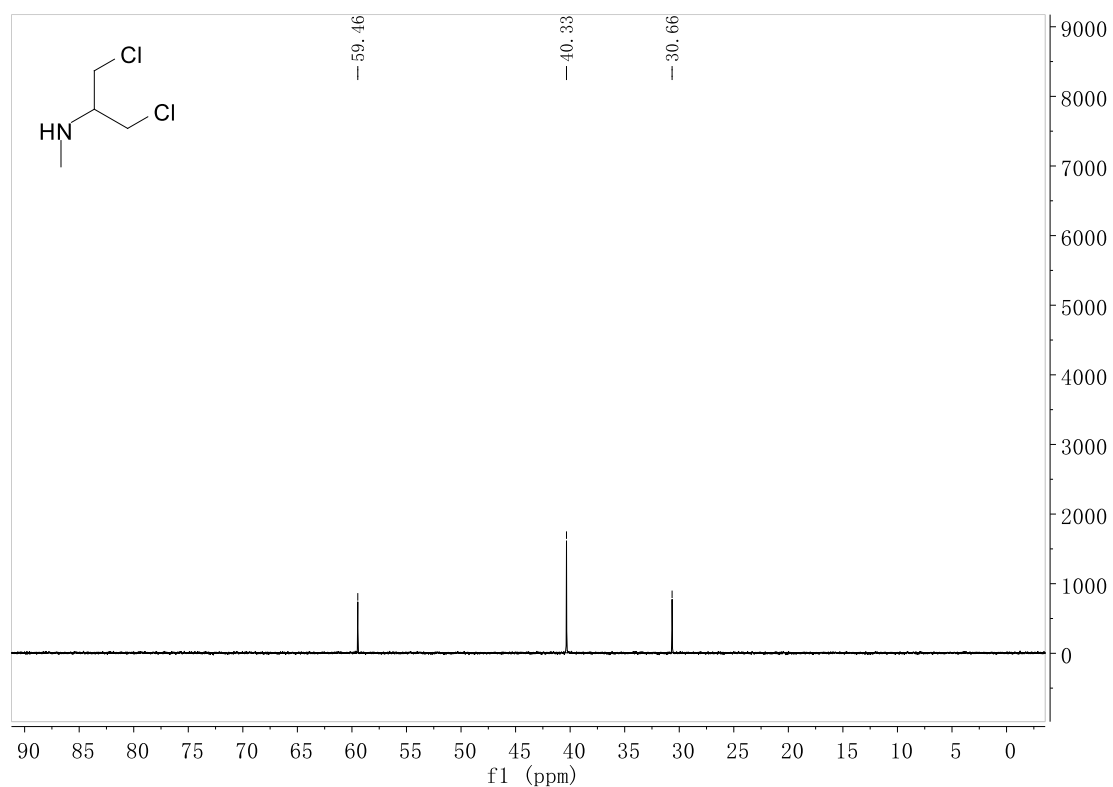


Figure S2. ¹³C NMR of compound 2a.

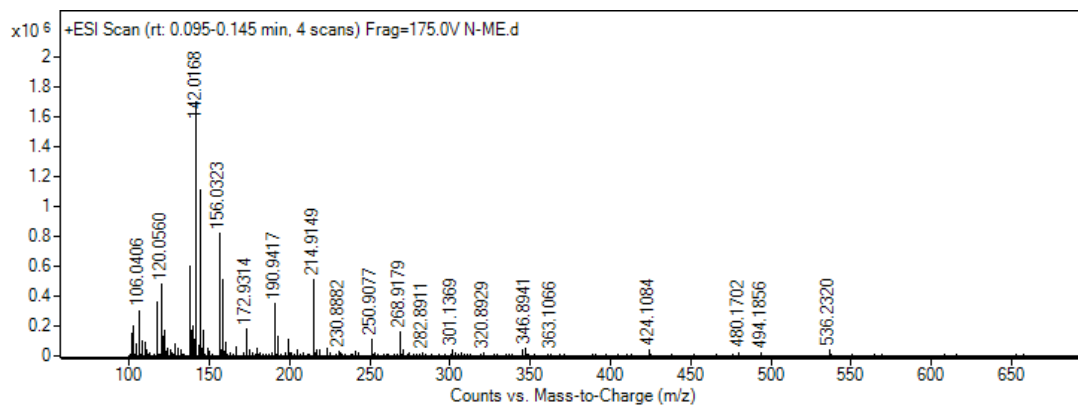


Figure S3. HRMS of compound **2a**.

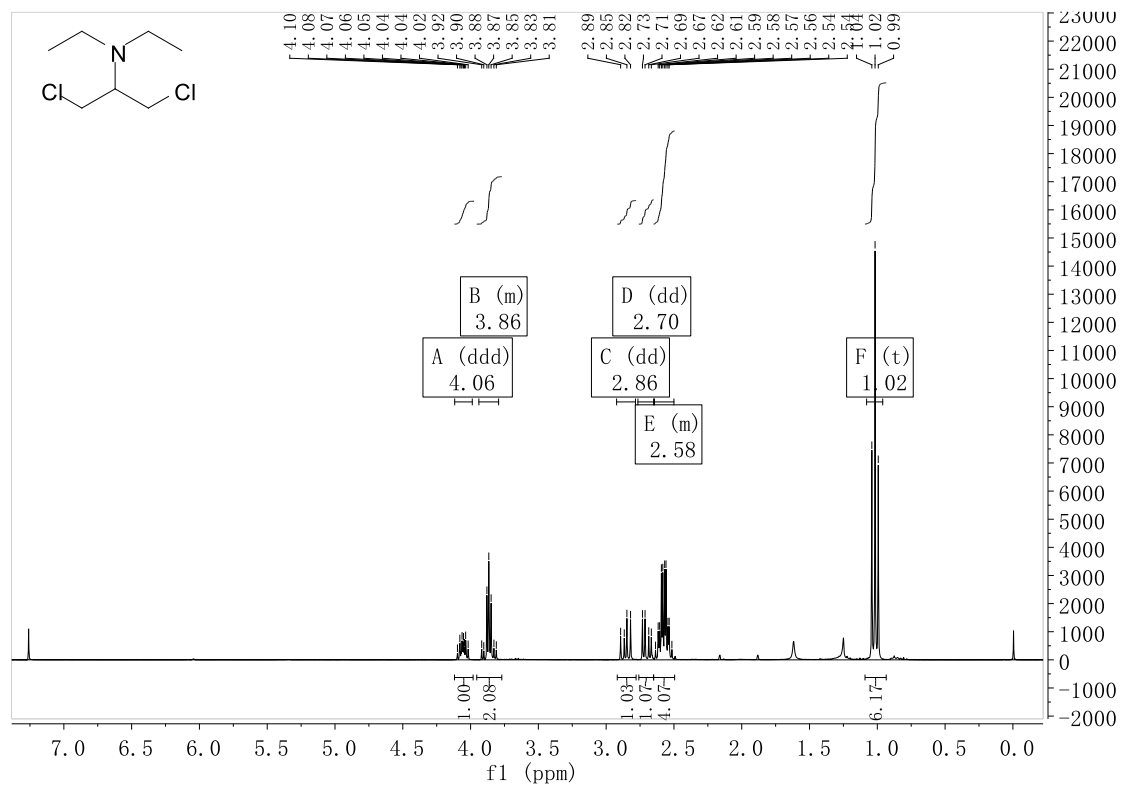


Figure S4. ¹H NMR of compound 2b.

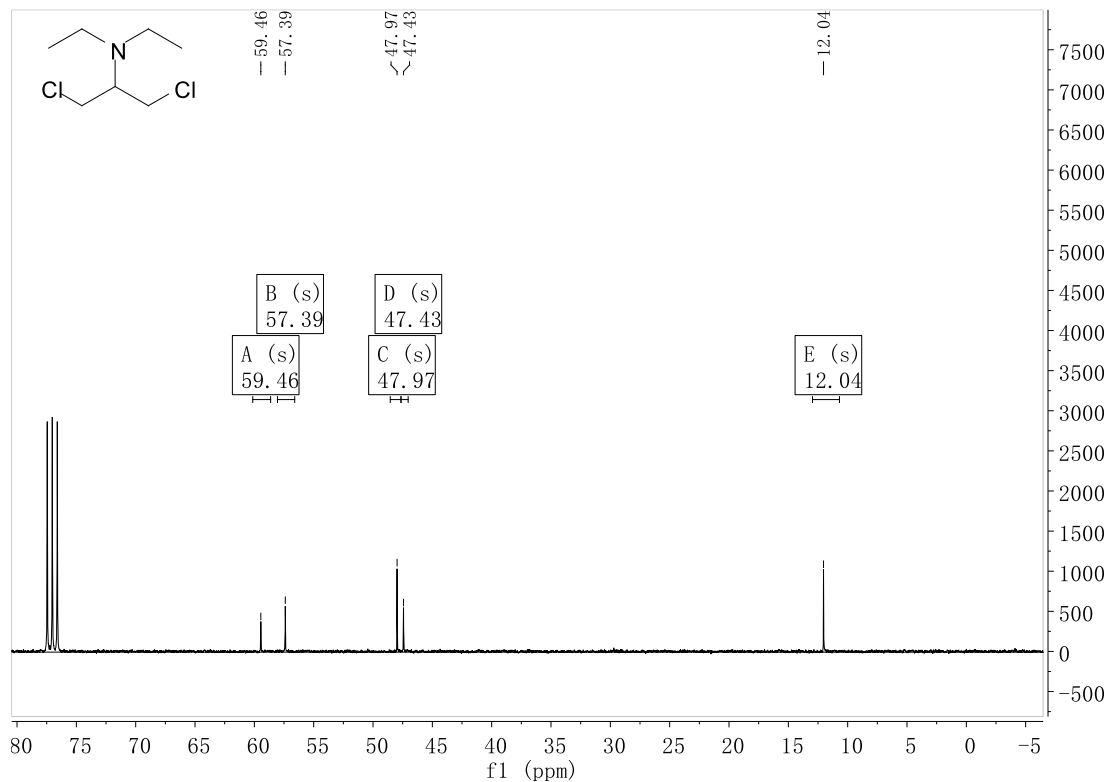


Figure S5. ¹³C NMR of compound 2b.

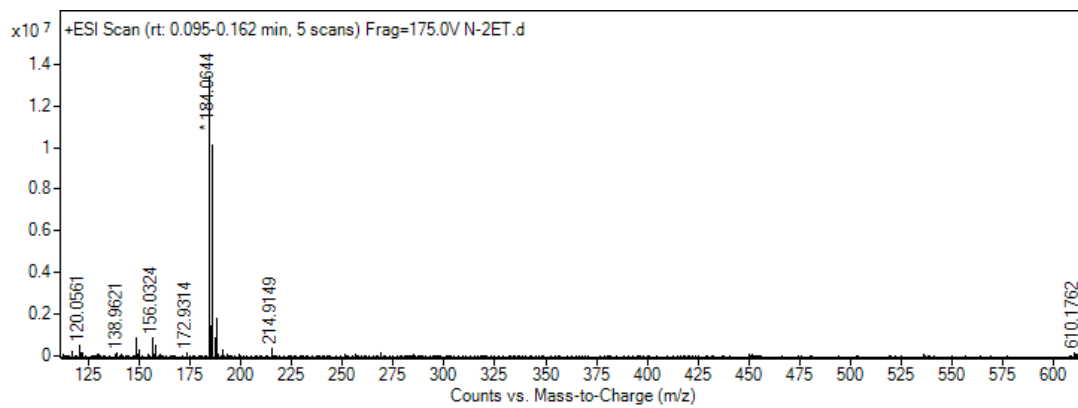


Figure S6. HRMS of compound **2b**.

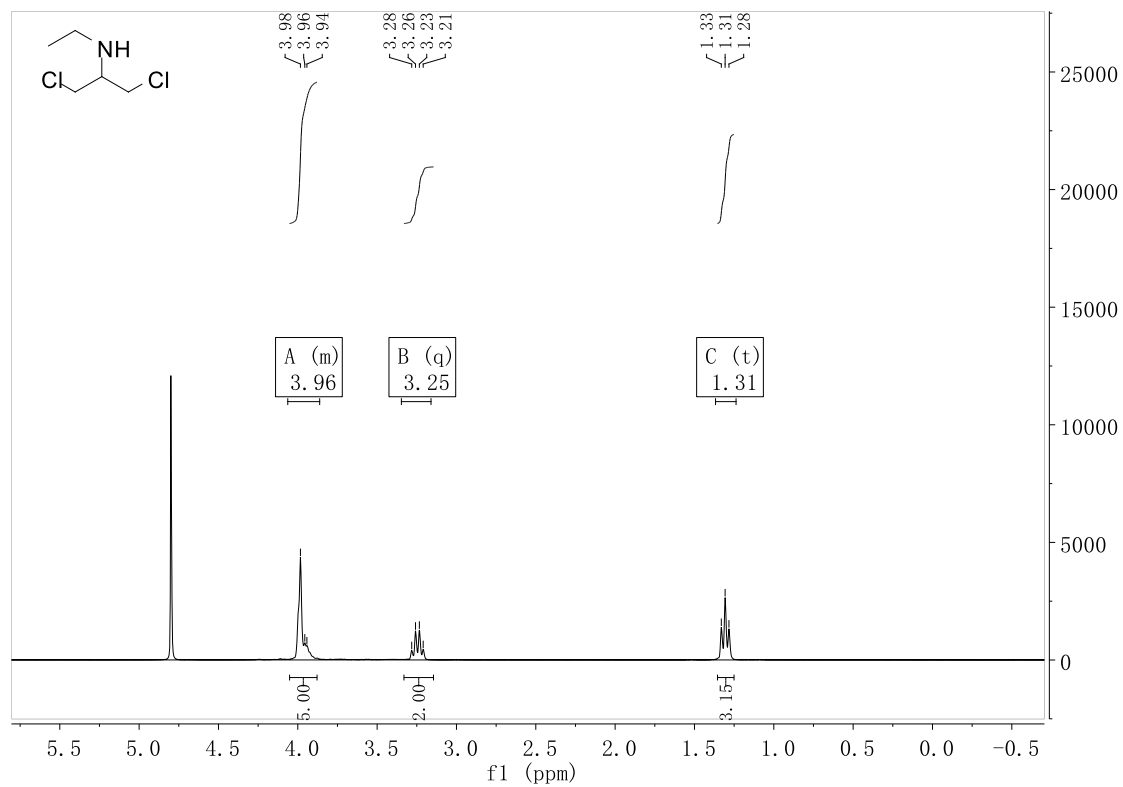


Figure S7. ^1H NMR of compound 2c.

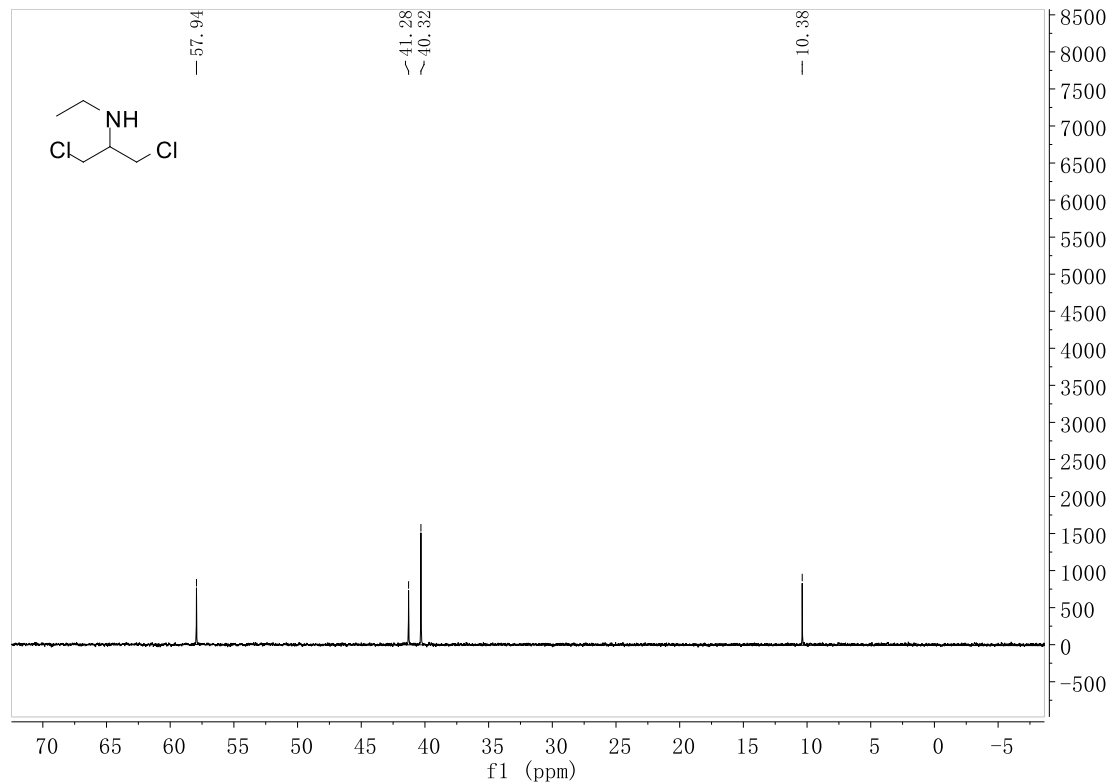


Figure S8. ^{13}C NMR of compound 2c.

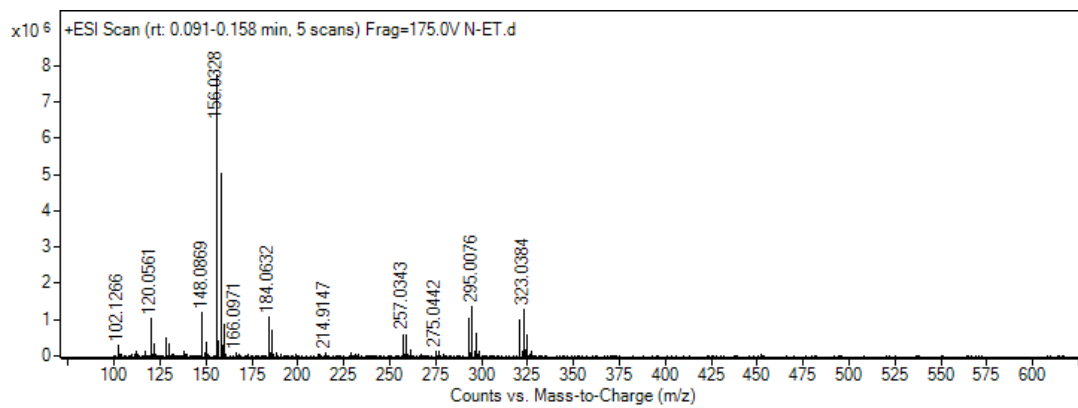


Figure S9. HRMS of compound **2c**.

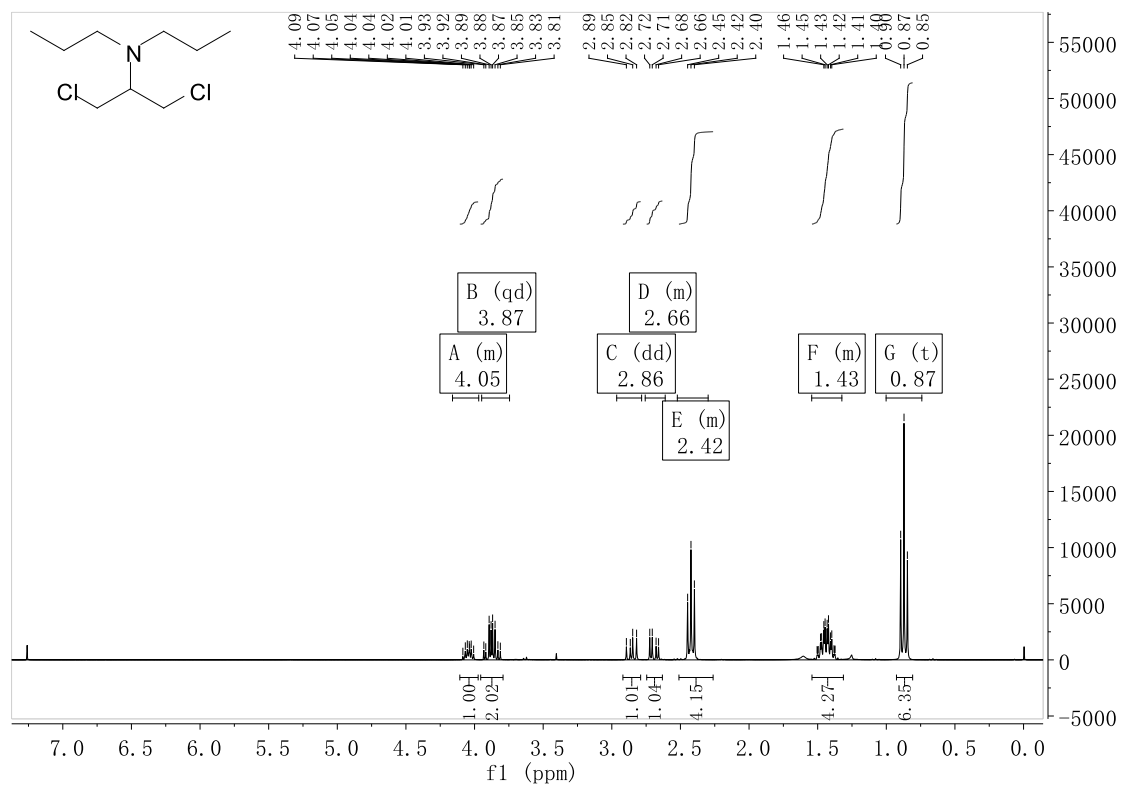


Figure S10. ¹H NMR of compound 2d.

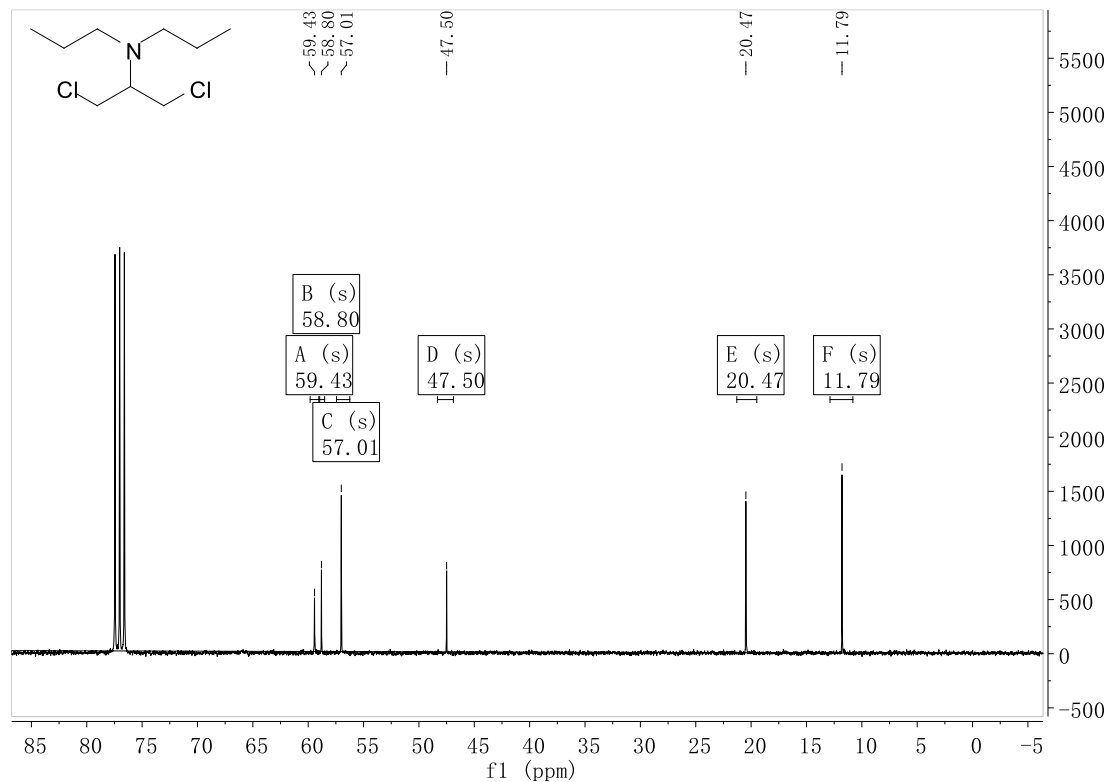


Figure S11. ¹³C NMR of compound 2d.

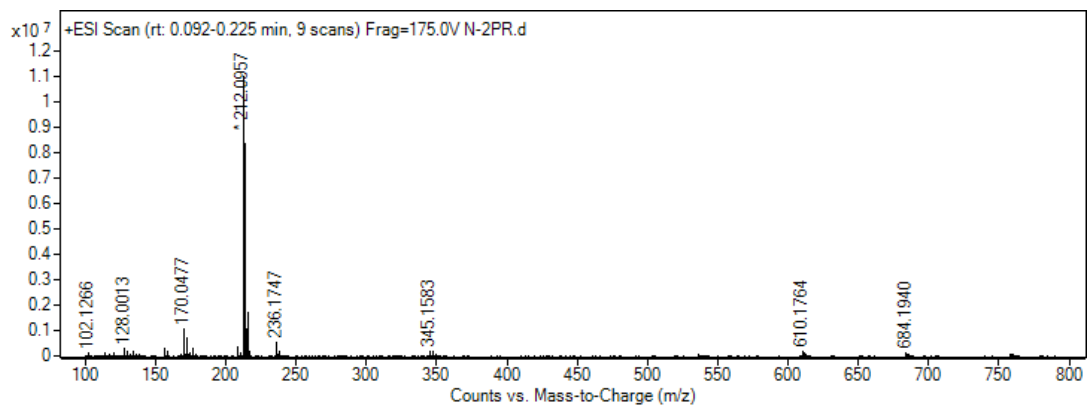


Figure S12. HRMS of compound **2d**.

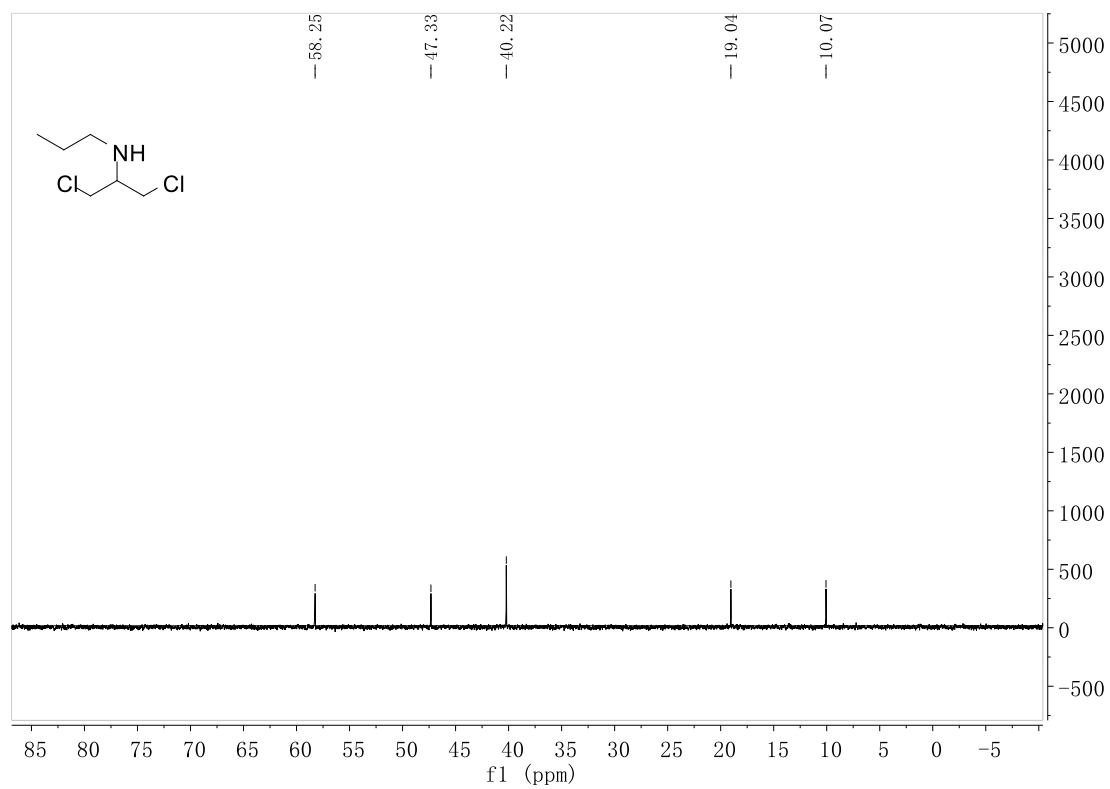
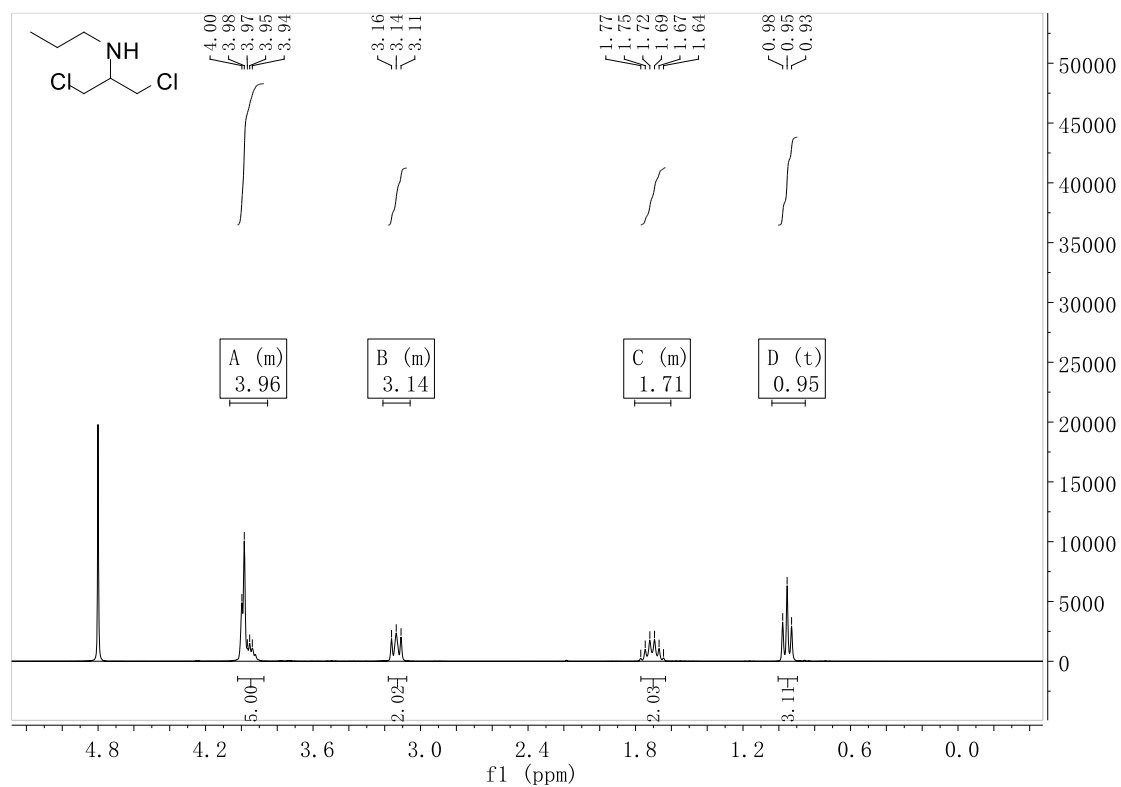


Figure S14. ^{13}C NMR of compound 2e.

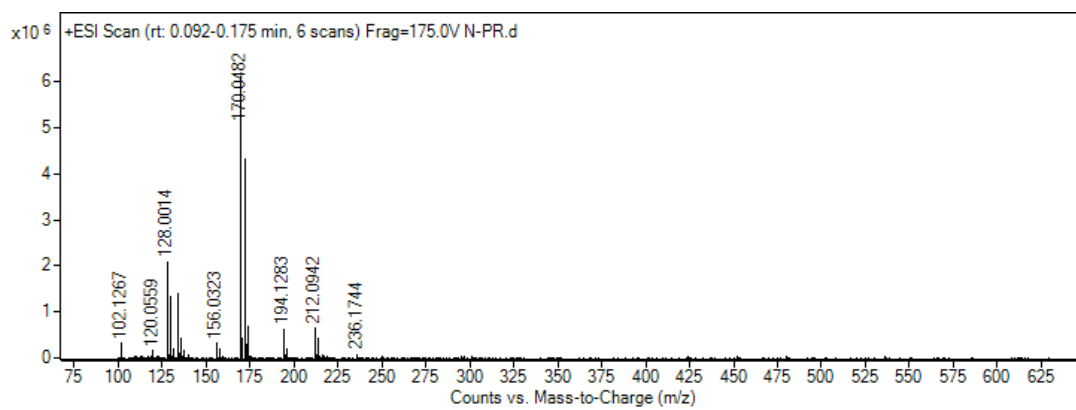


Figure S15. HRMS of compound **2e**.

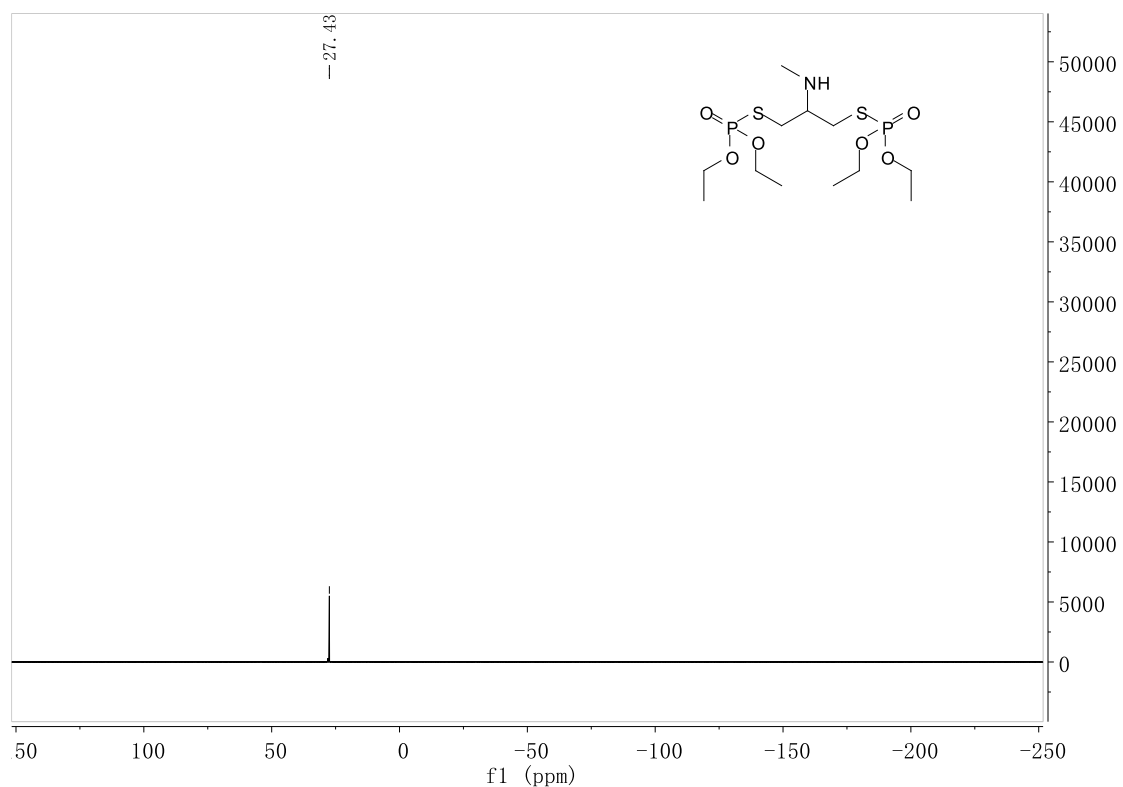


Figure S16. ^{31}P NMR of compound 5b.

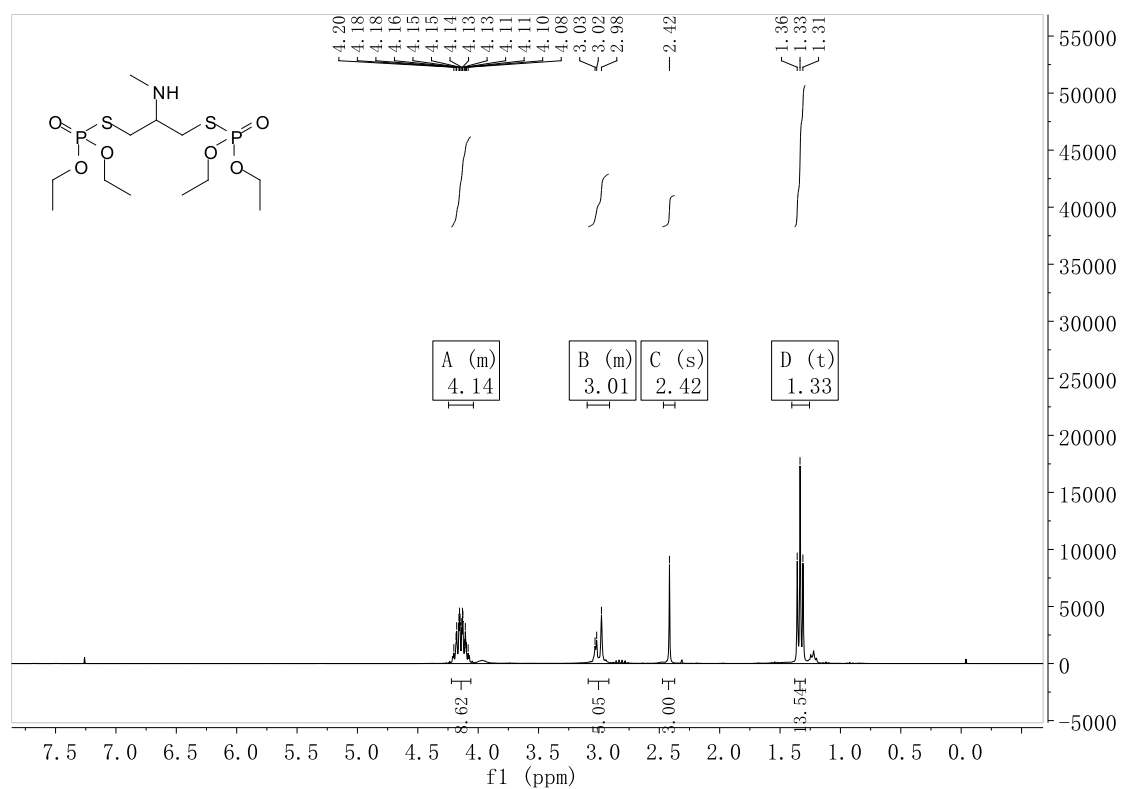


Figure S17. ^1H NMR of compound 5b.

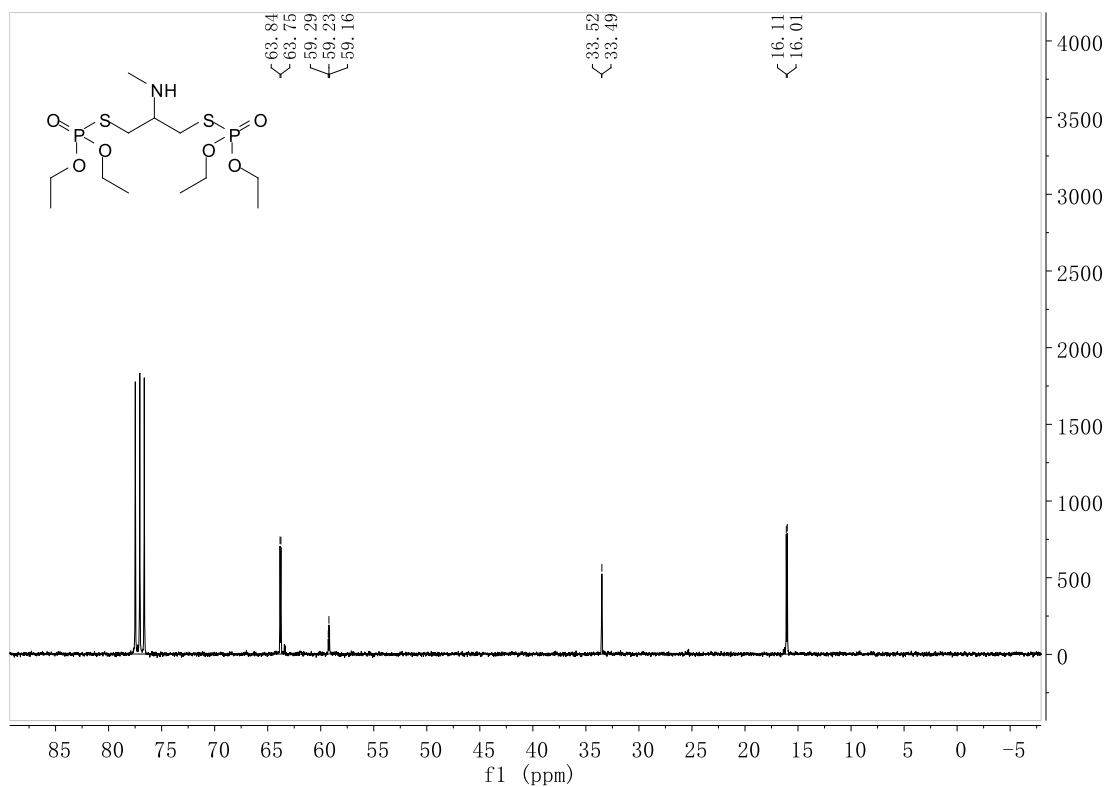


Figure S18. ^{13}C NMR of compound 5b.

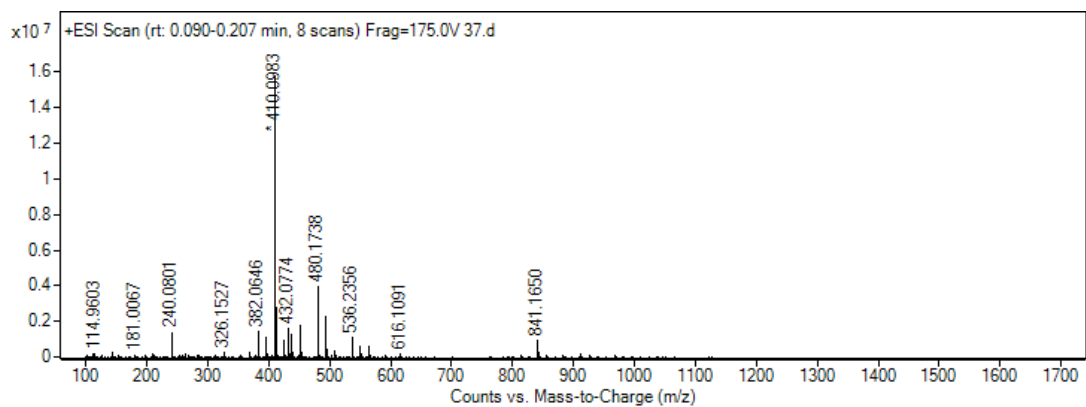


Figure S19. HRMS of compound 5b.

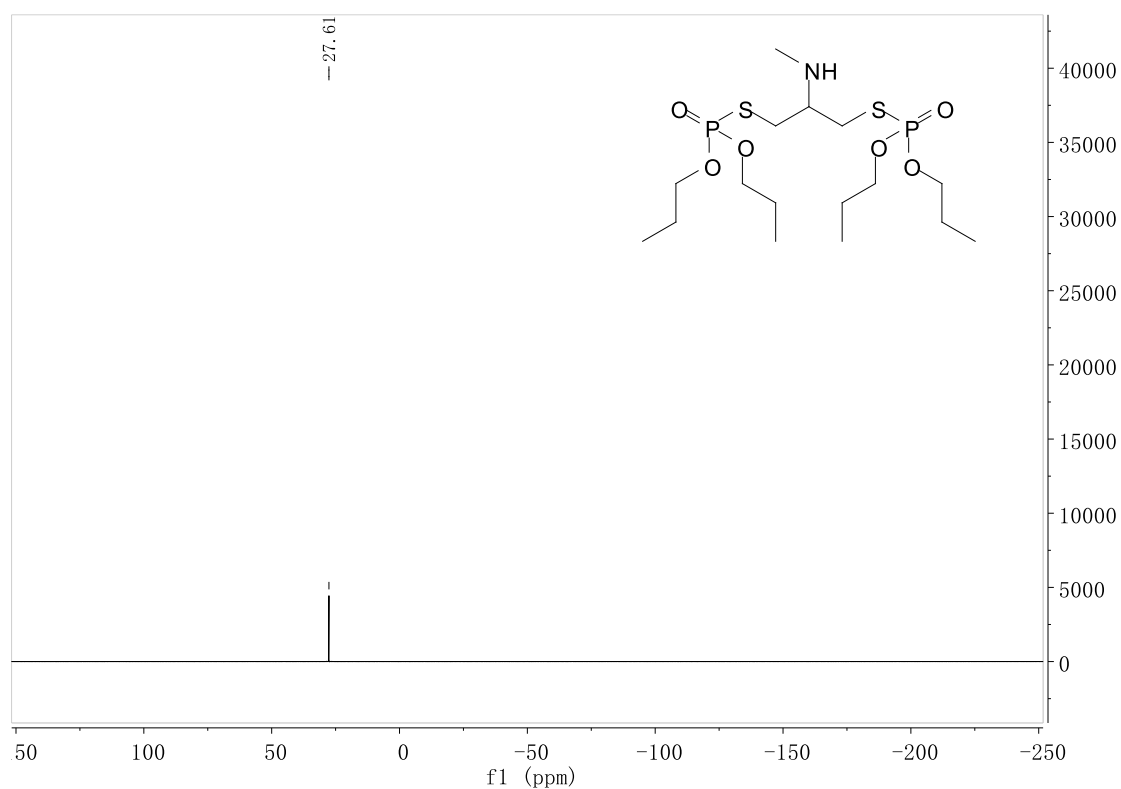


Figure S20. ^{31}P NMR of compound 5c.

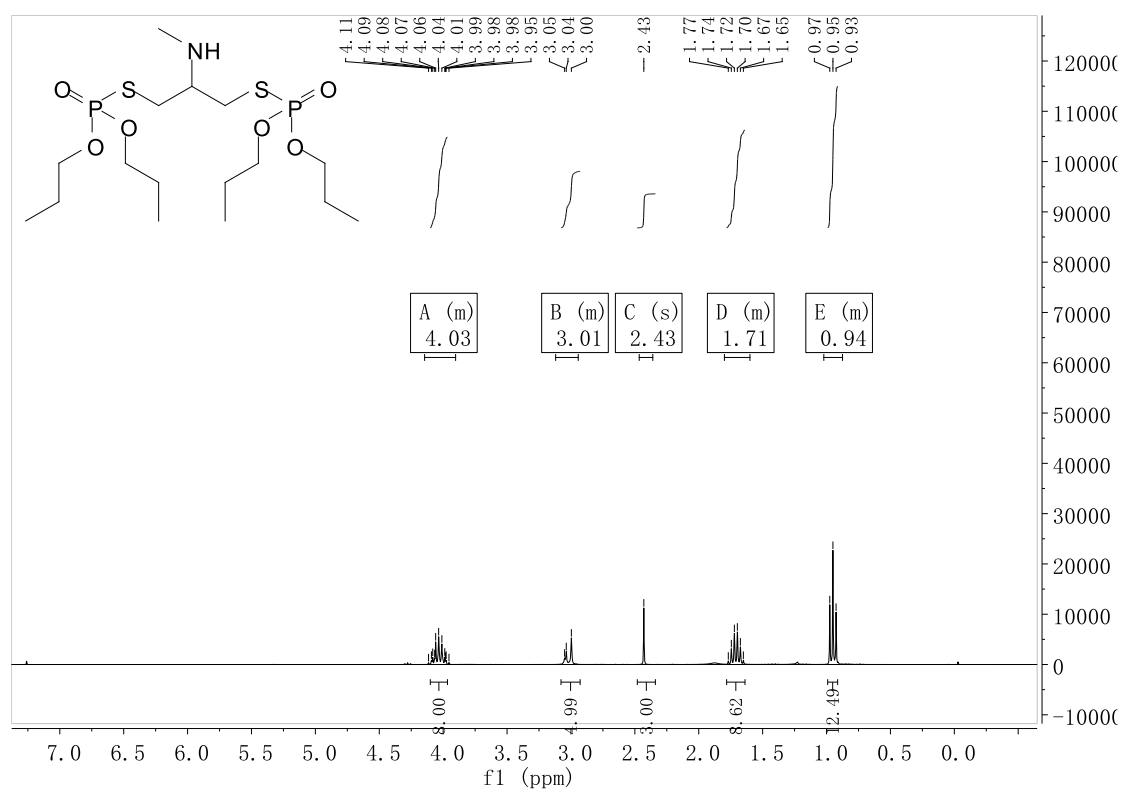


Figure S21. ^1H NMR of compound 5c.

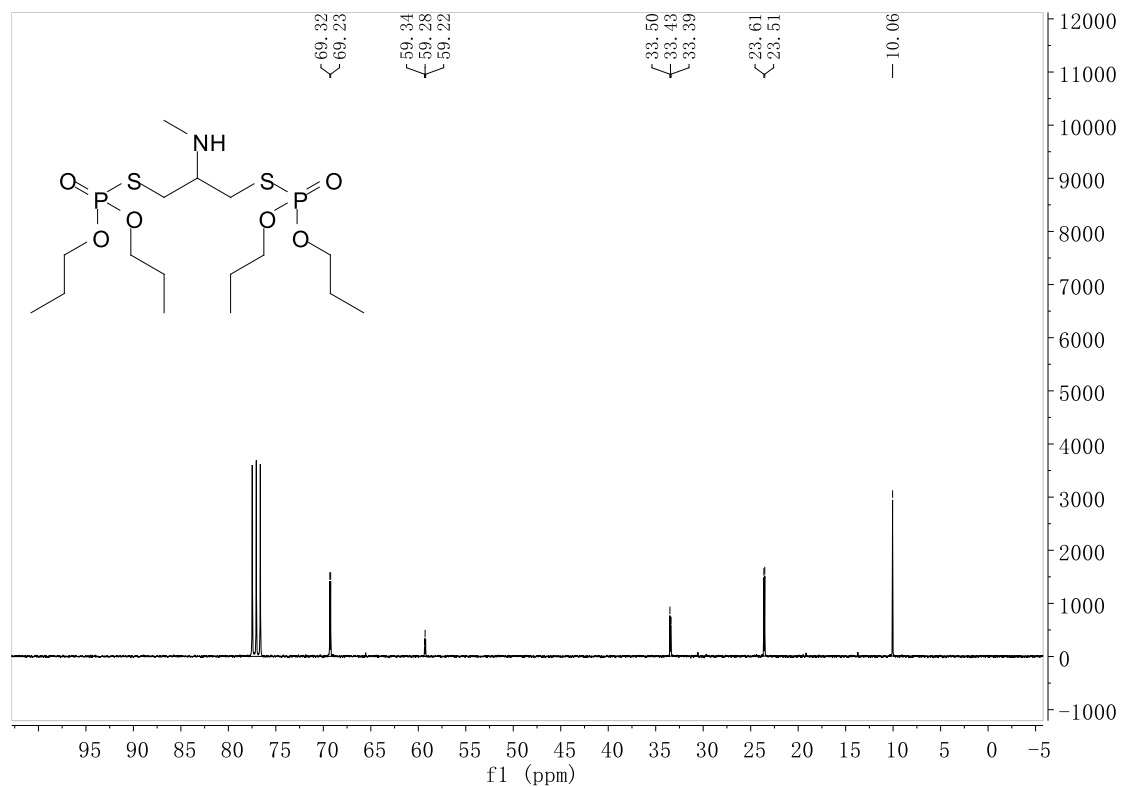


Figure S22. ¹³C NMR of compound 5c.

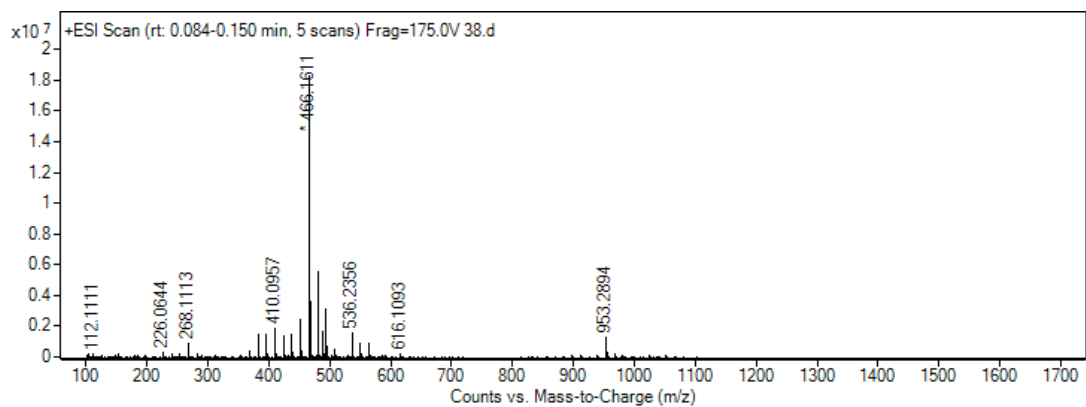


Figure S23. HRMS of compound 5c.

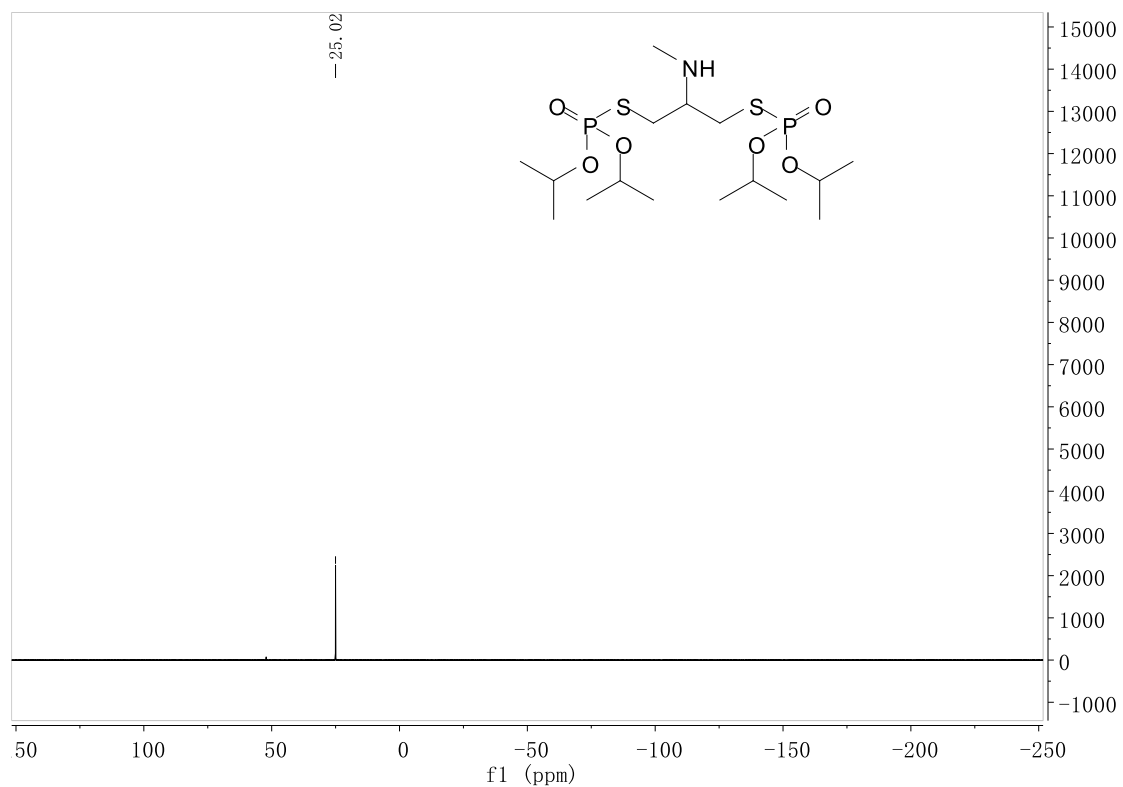


Figure S24. ^{31}P NMR of compound 5d.

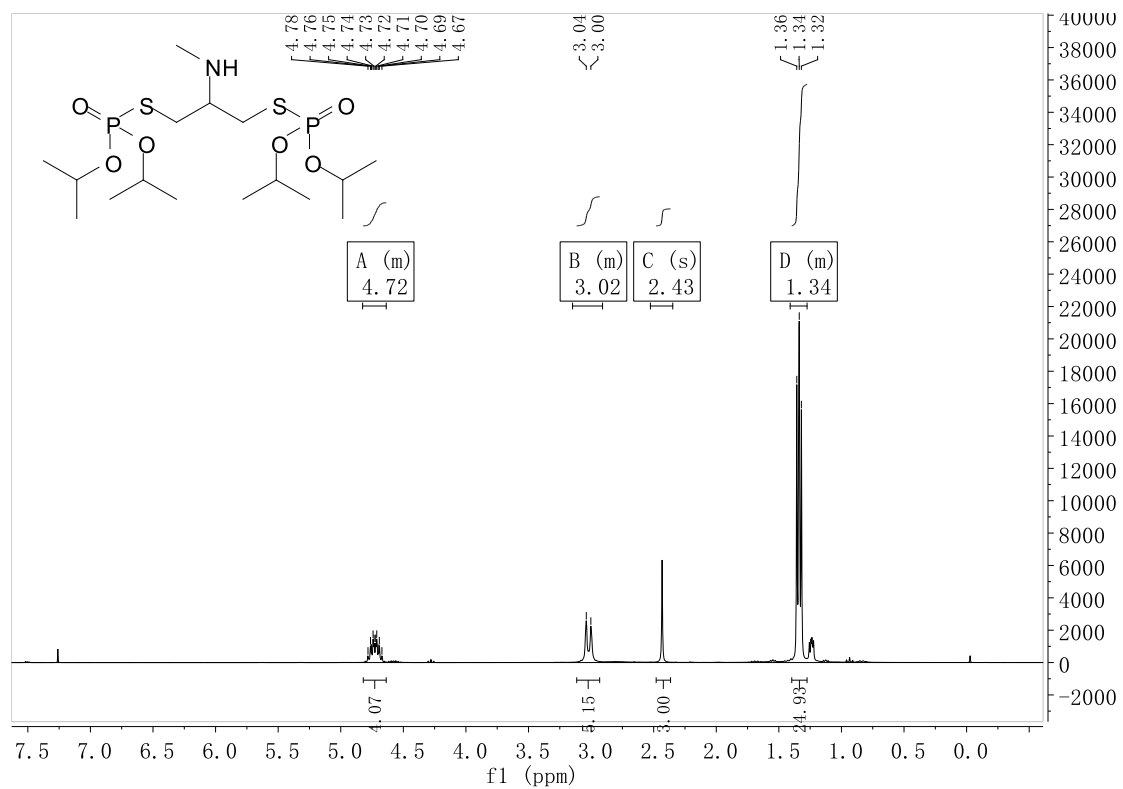


Figure S25. ^1H NMR of compound 5d.

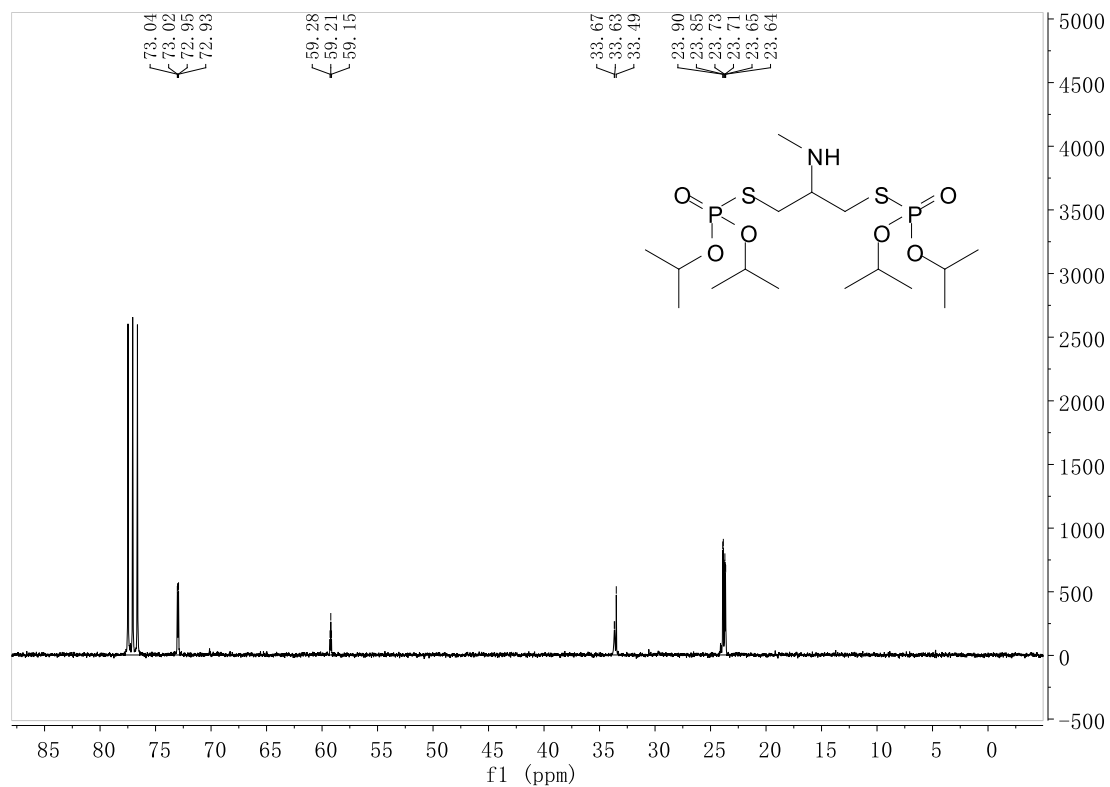


Figure S26. ¹³C NMR of compound 5d.

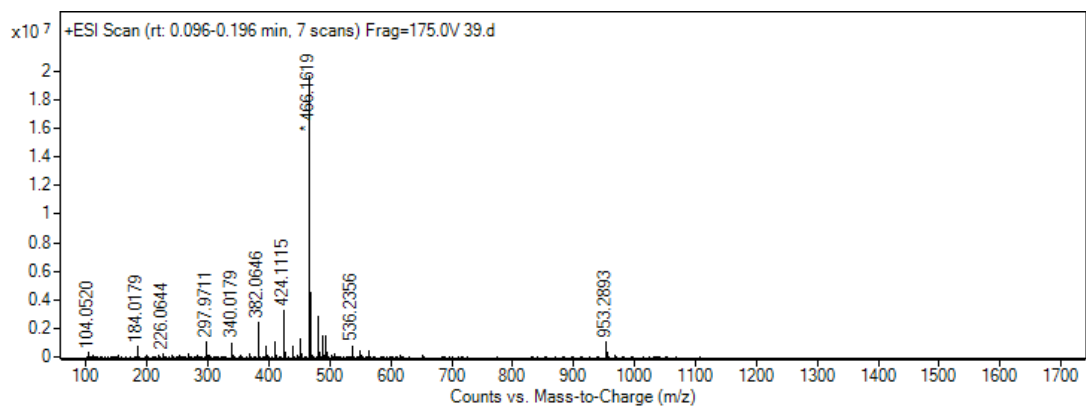


Figure S27. HRMS of compound 5d.

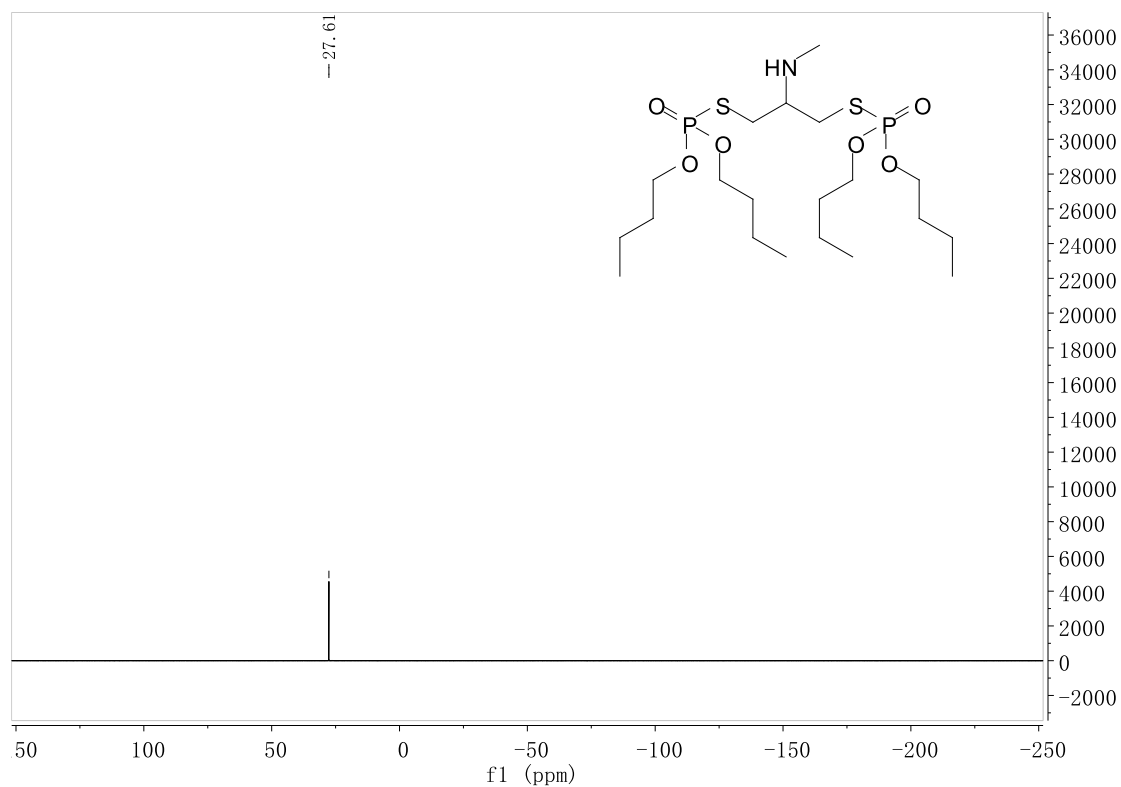


Figure S28. ^{31}P NMR of compound 5e.

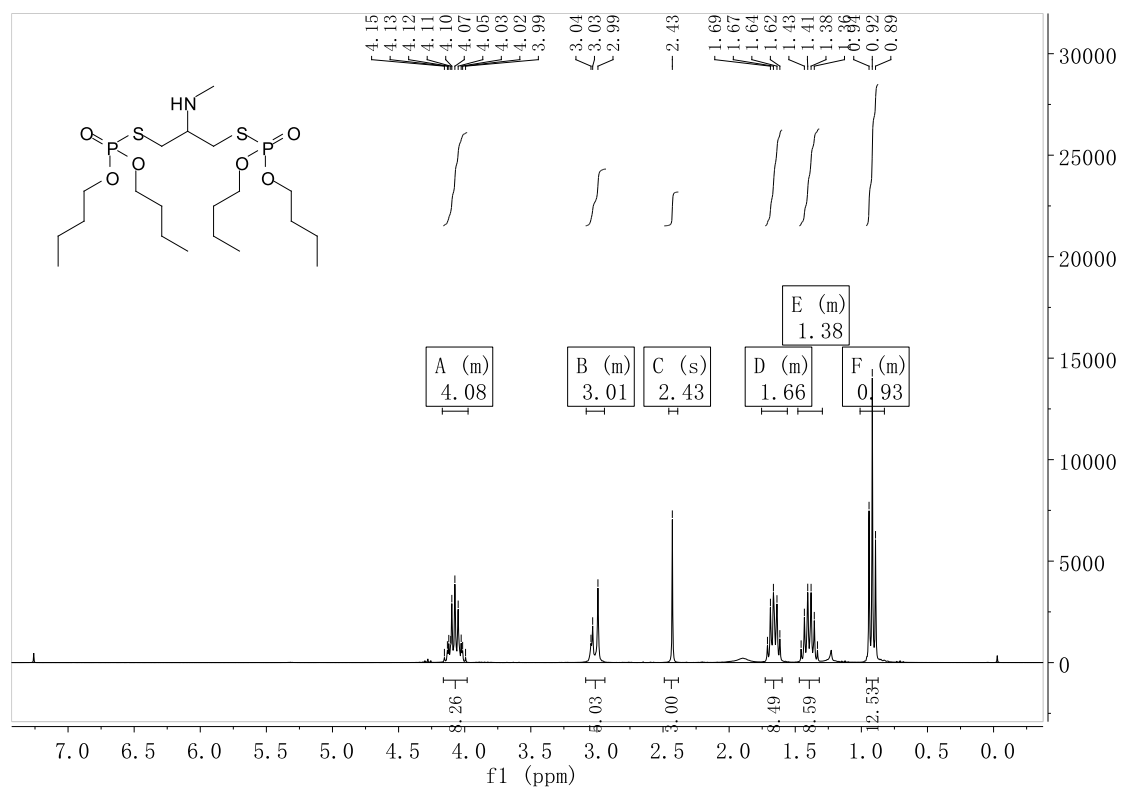


Figure S29. ^1H NMR of compound 5e.

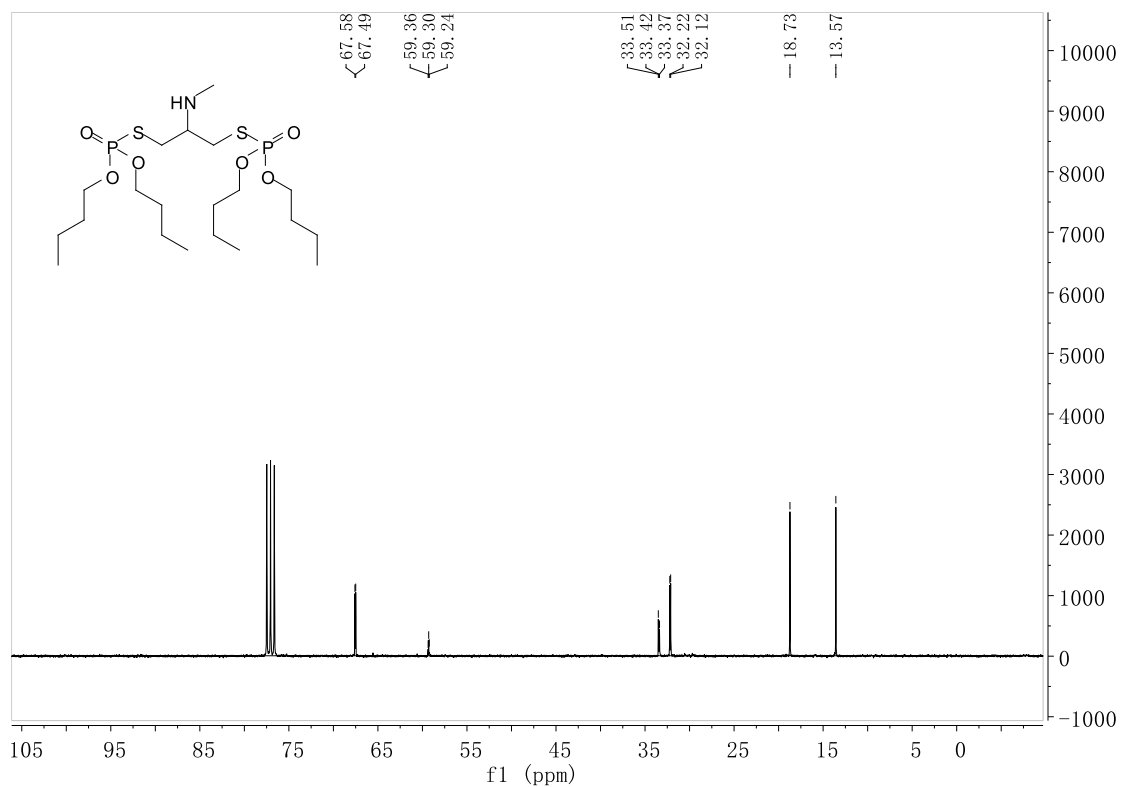


Figure S30. ^{13}C NMR of compound 5e.

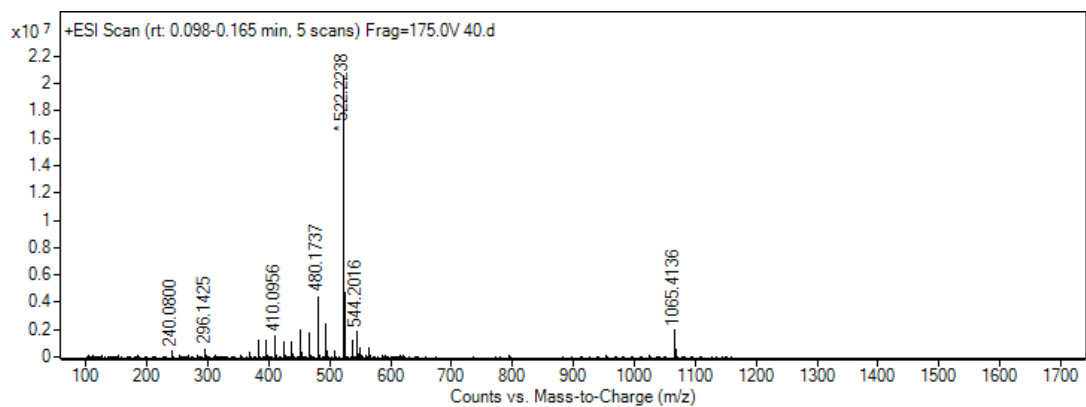


Figure S31. HRMS of compound 5e.

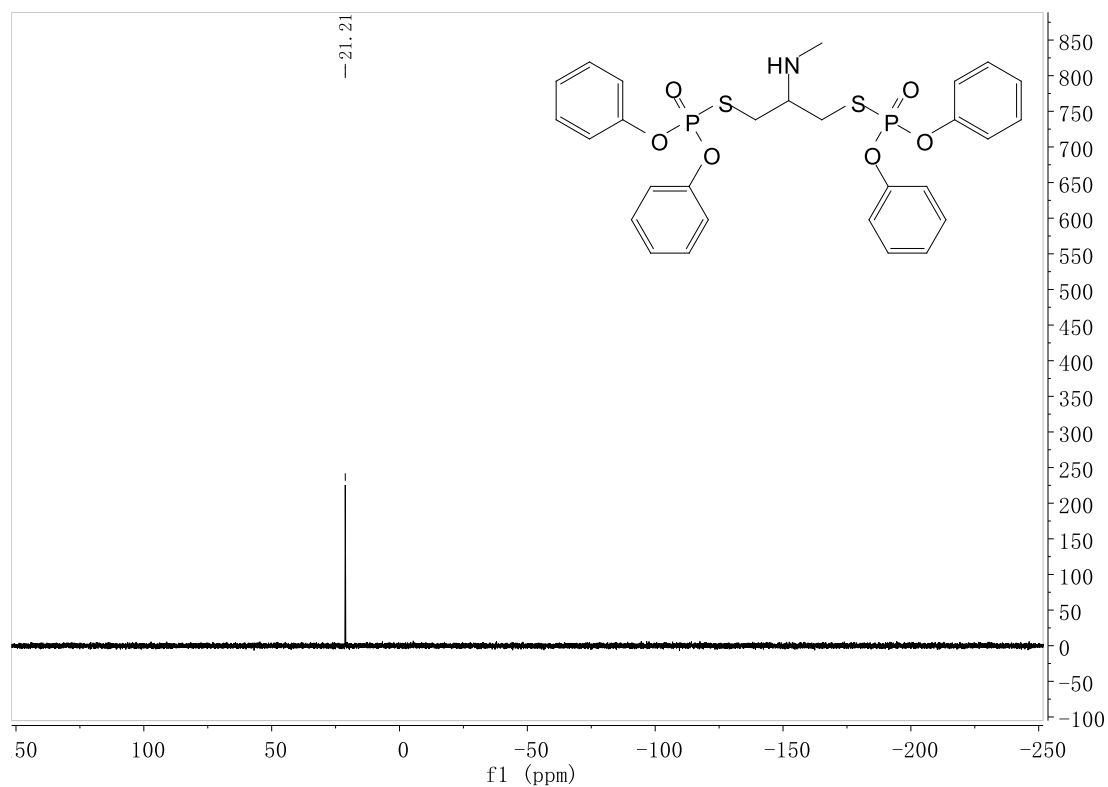


Figure S32. ^{31}P NMR of compound 5g.

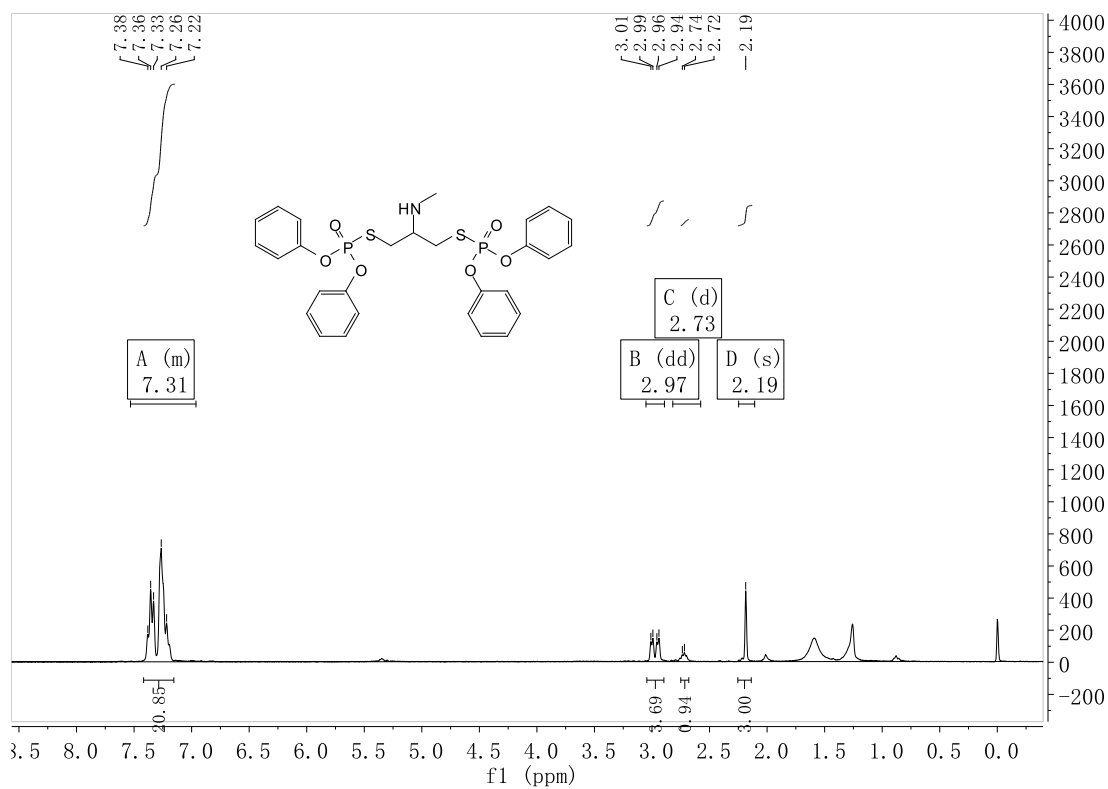


Figure S33. ^1H NMR of compound 5g.

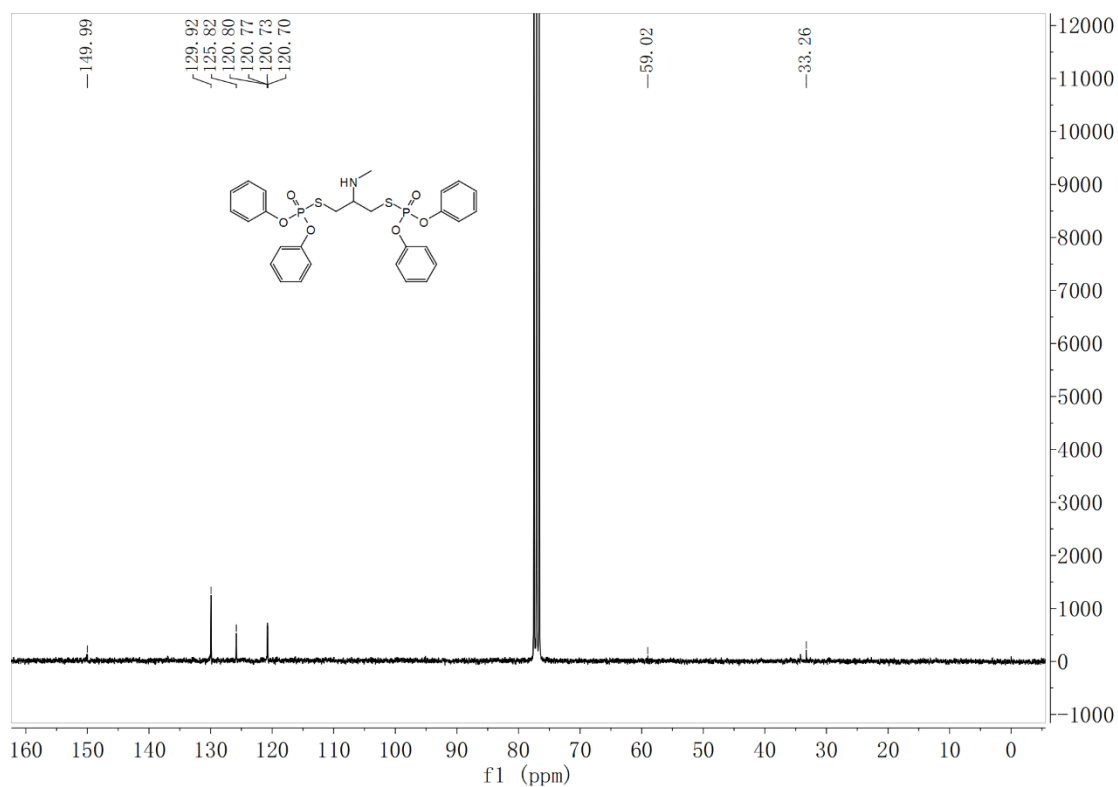


Figure S34. ¹³C NMR of compound 5g.

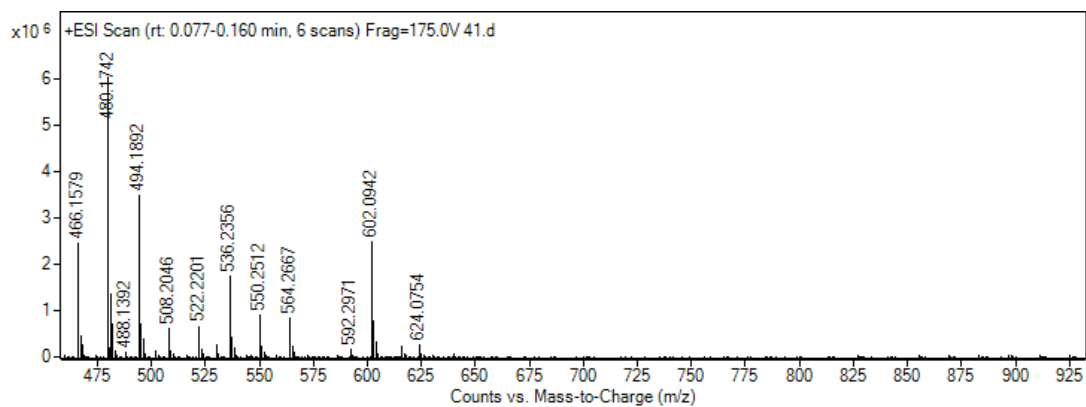


Figure S35. HRMS of compound 5g.

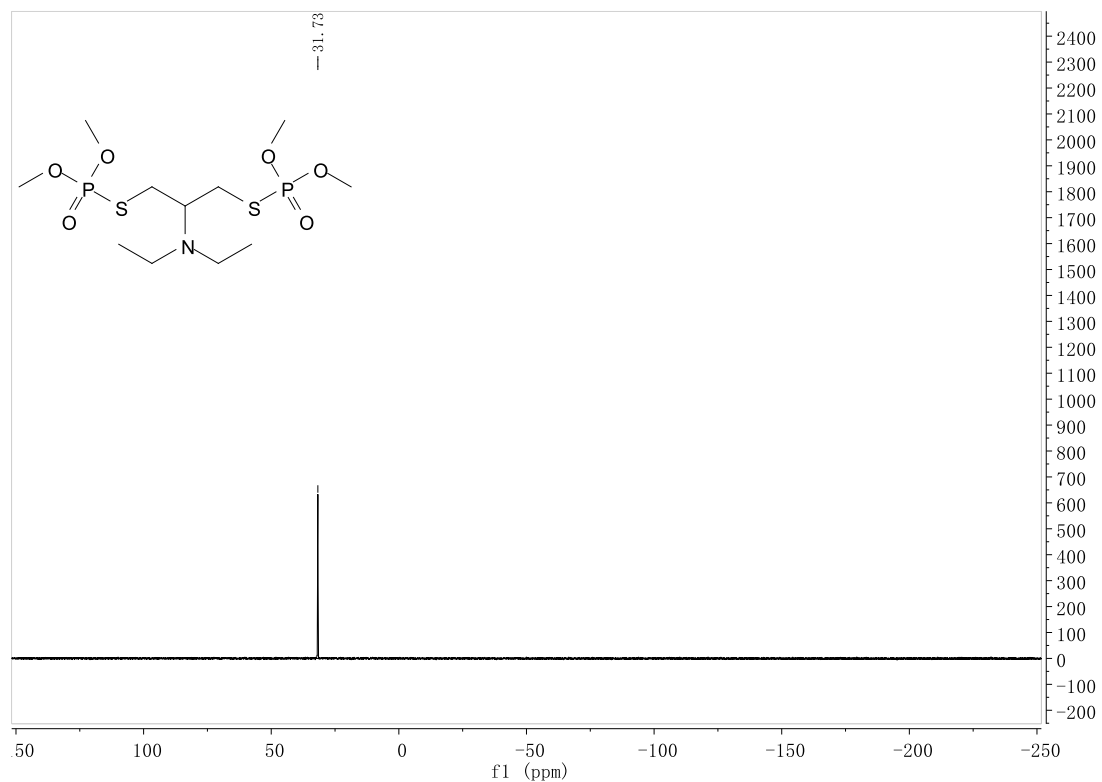


Figure S36. ^{31}P NMR of compound 6a.

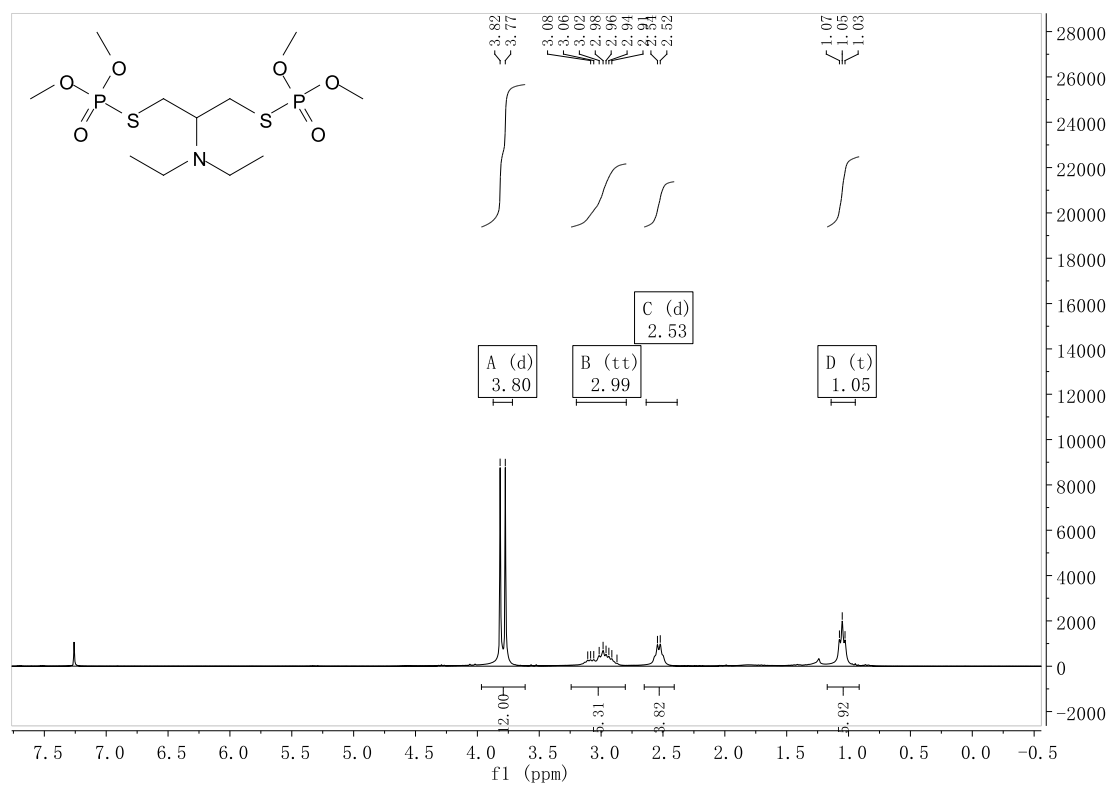


Figure S37. ^1H NMR of compound 6a.

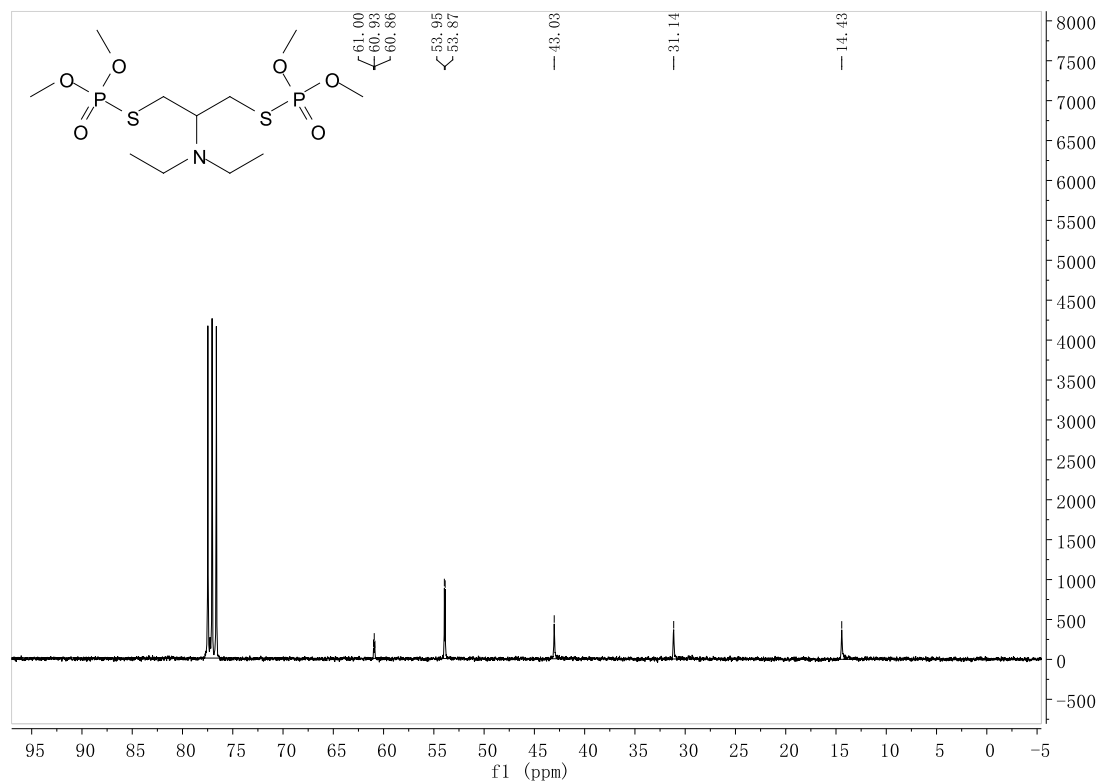


Figure S38. ^{13}C NMR of compound 6a.

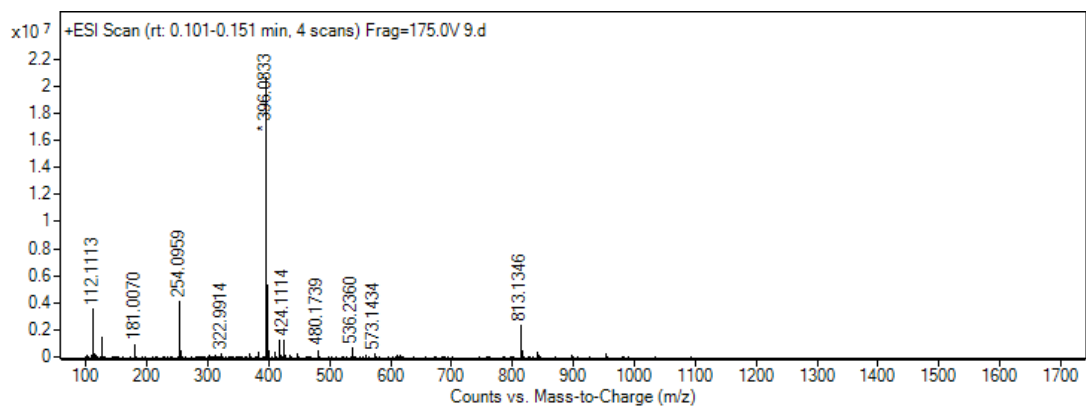


Figure S39. HRMS of compound 6a.

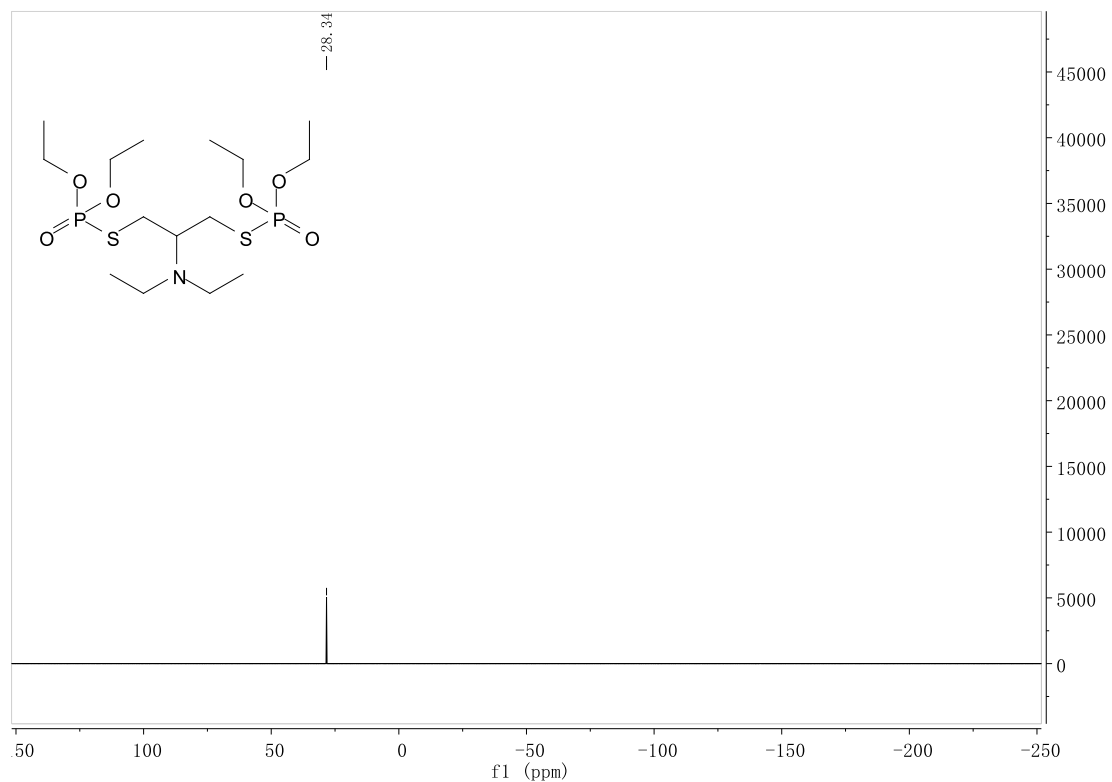


Figure S40. ^{31}P NMR of compound 6b.

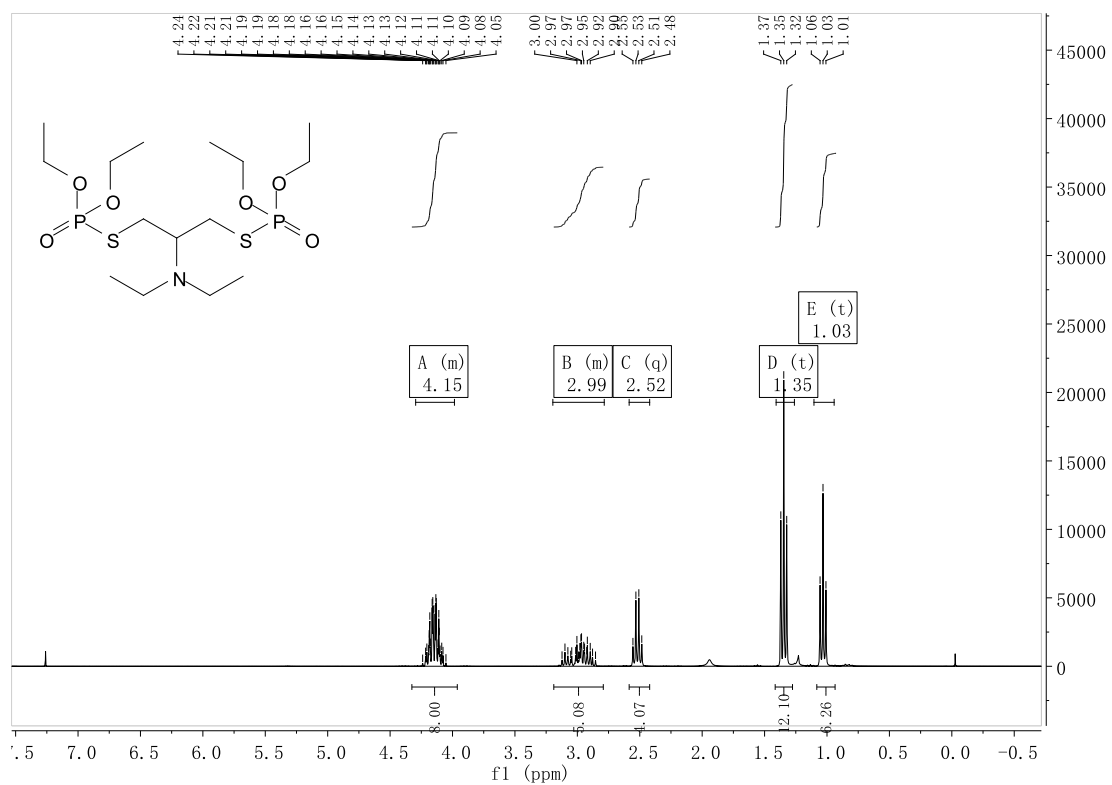


Figure S41. ^1H NMR of compound 6b.

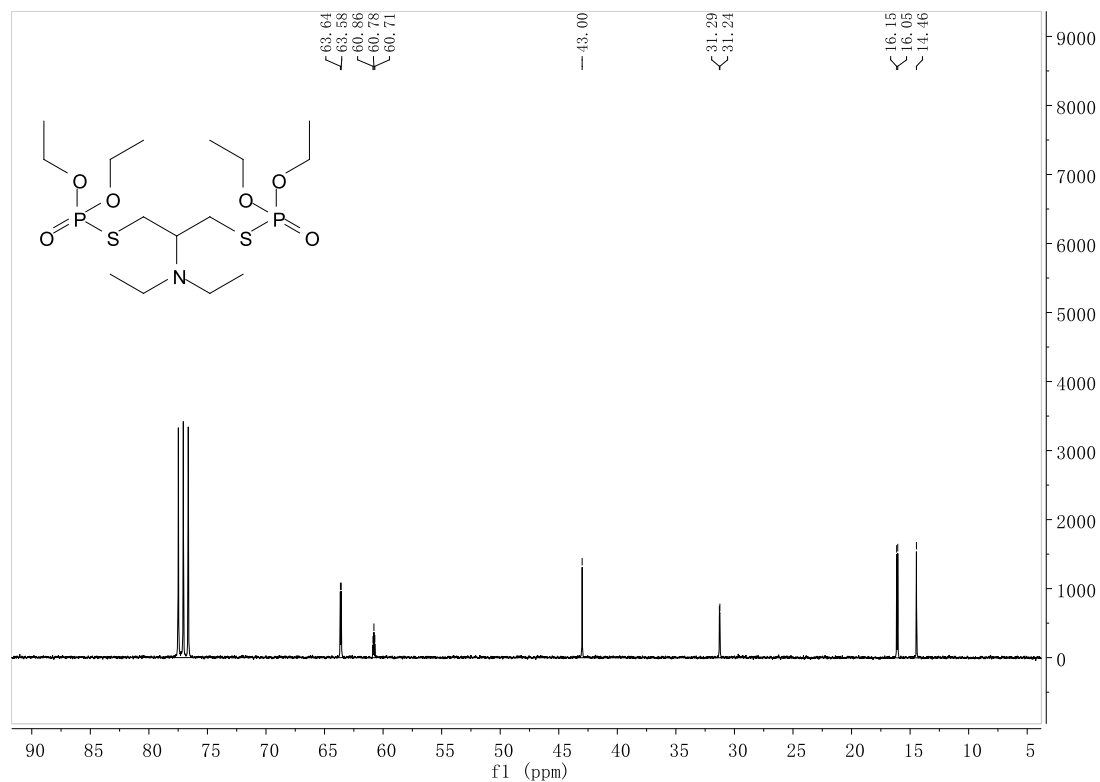


Figure S42. ¹³C NMR of compound 6b.

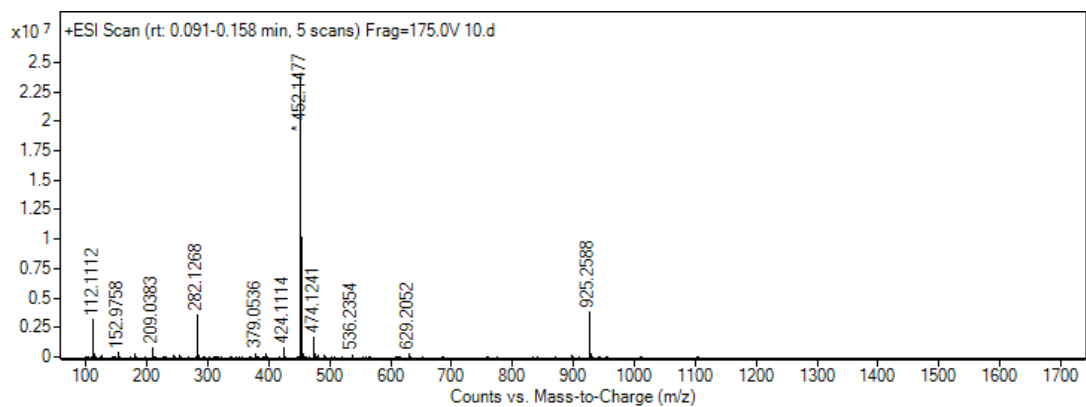


Figure S43. HRMS of compound 6b.

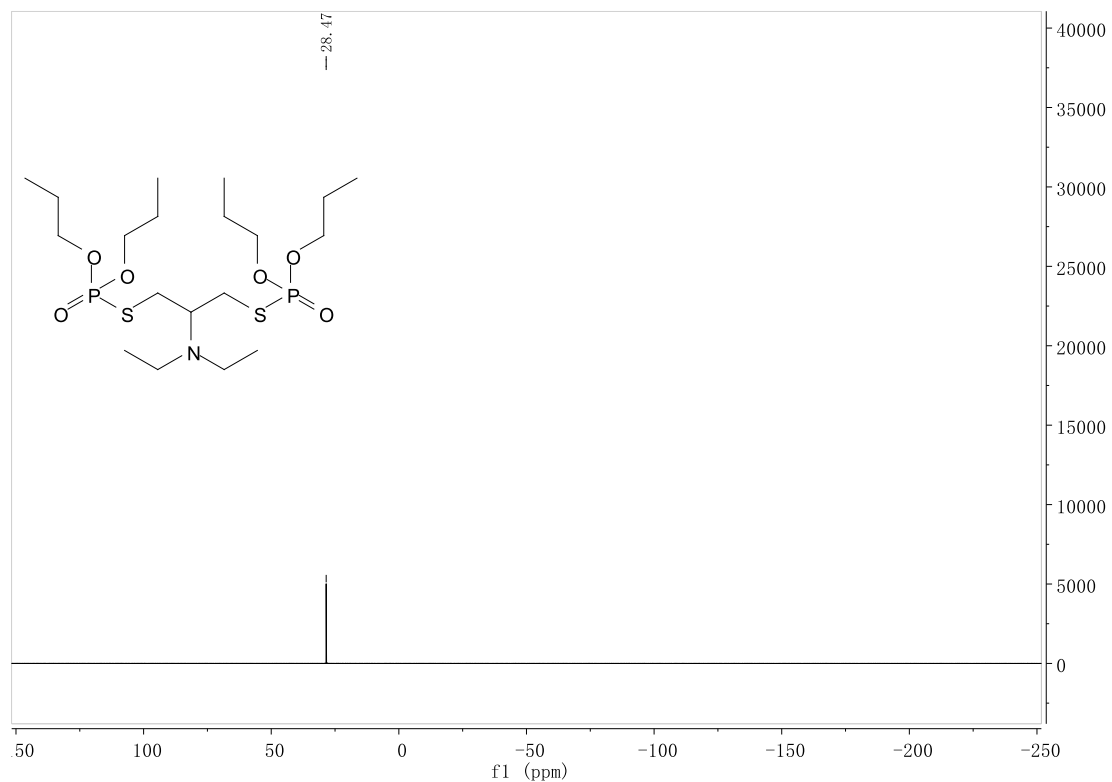


Figure S44. ^{31}P NMR of compound 6c.

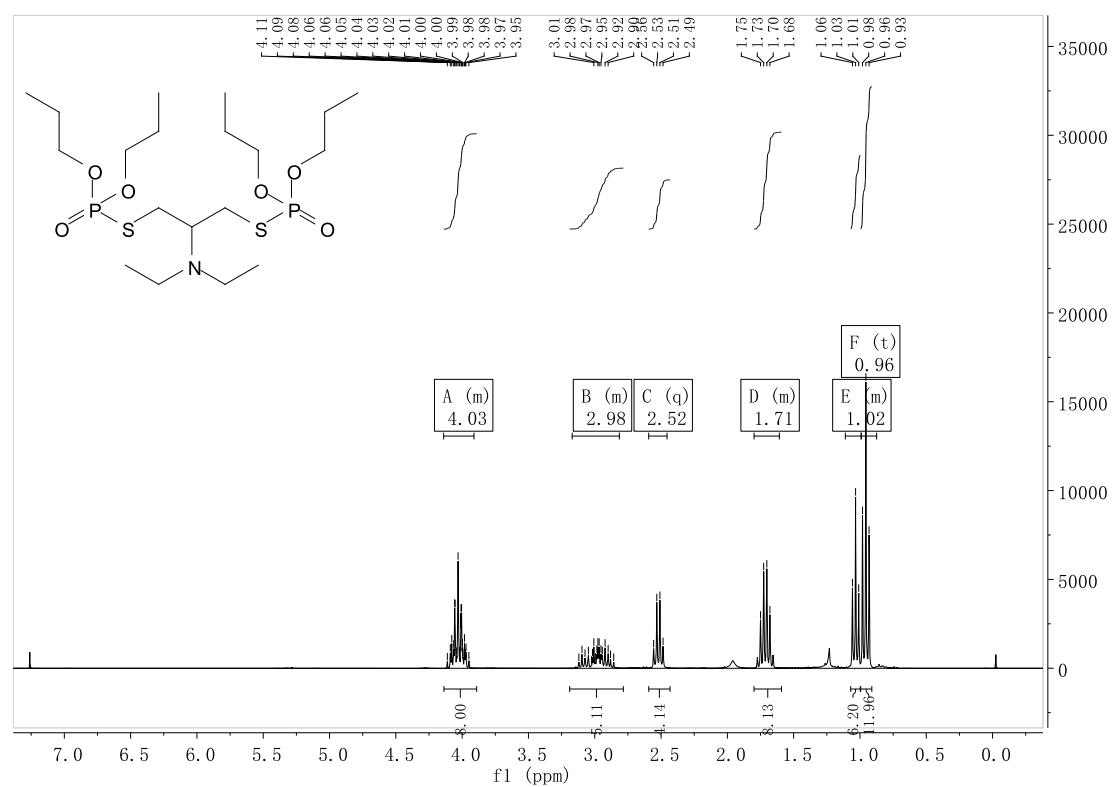


Figure S45. ^1H NMR of compound 6c.

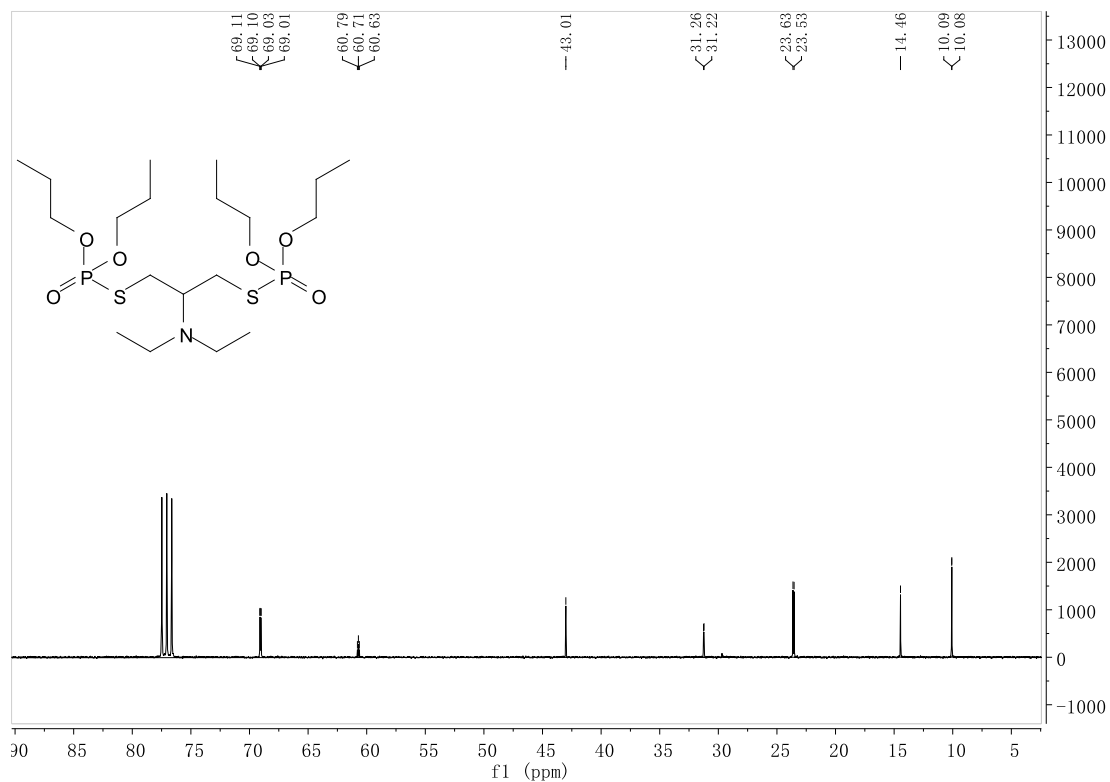


Figure S46. ^{13}C NMR of compound 6c.

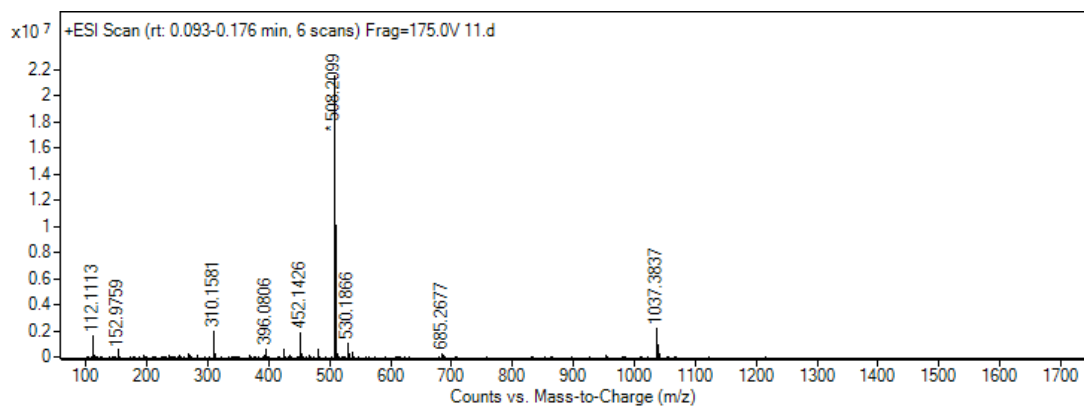


Figure S47. HRMS of compound 6c.

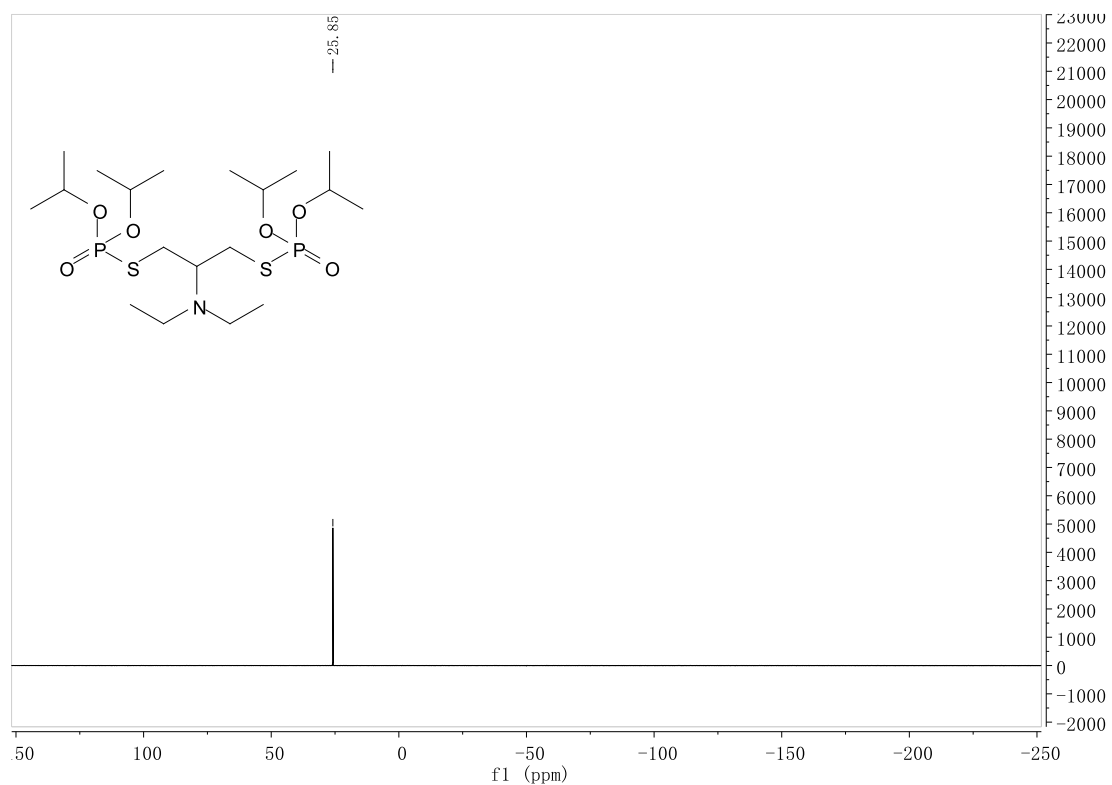


Figure S48. ^{31}P NMR of compound 6d.

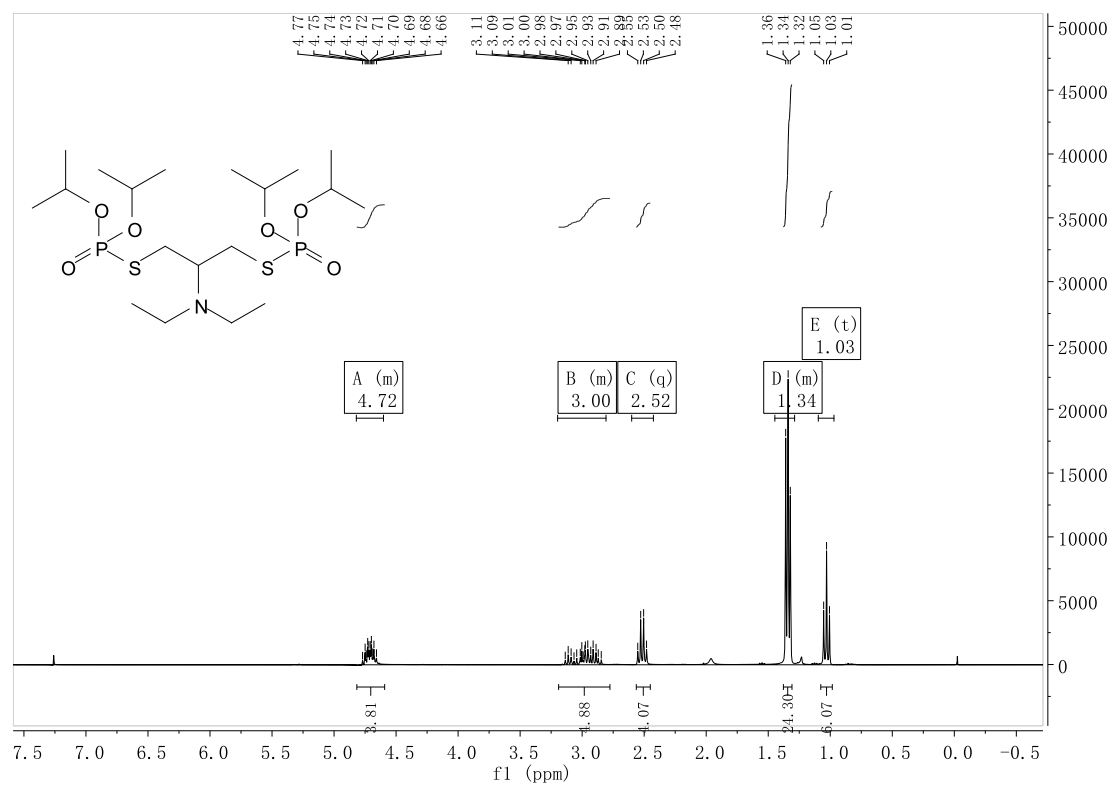


Figure S49. ^1H NMR of compound 6d.

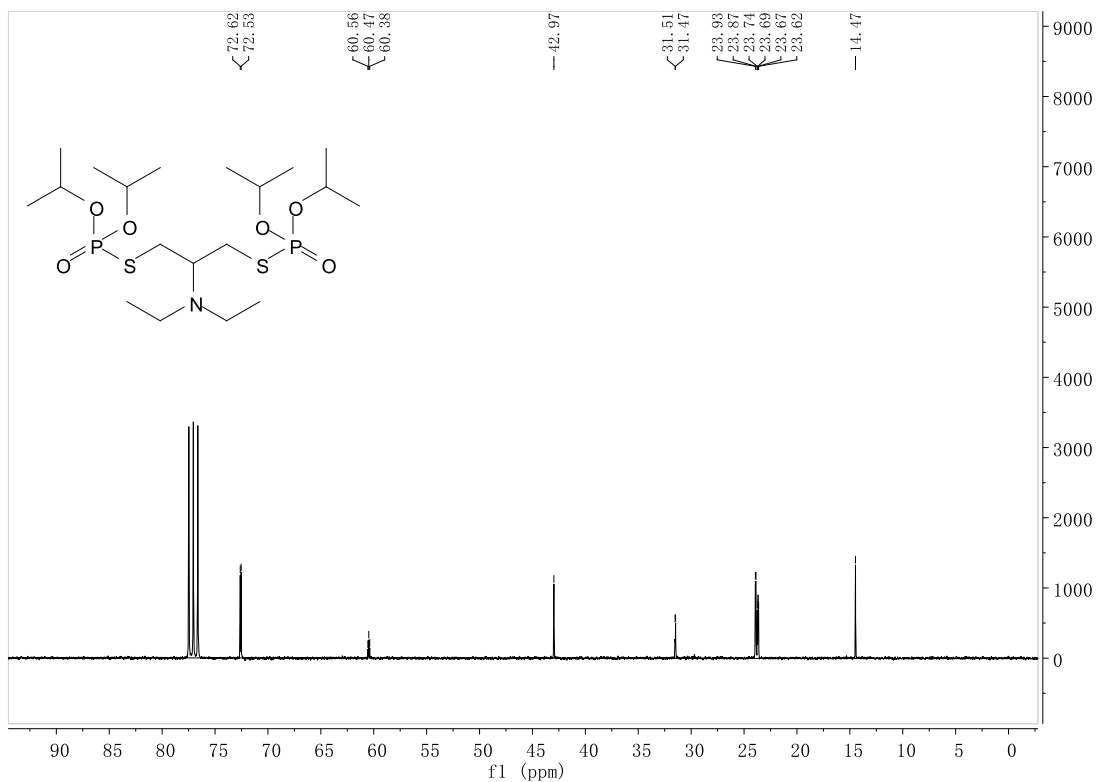


Figure S50. ^{13}C NMR of compound 6d.

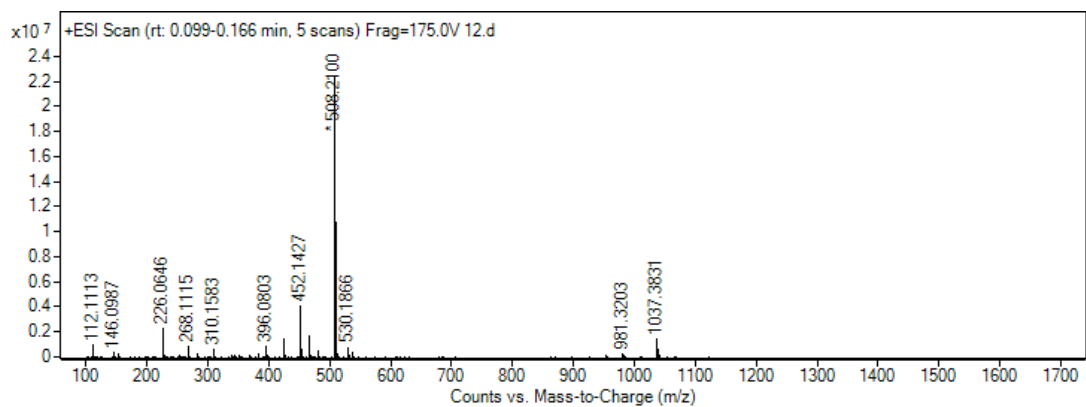


Figure S51. HRMS of compound 6d.

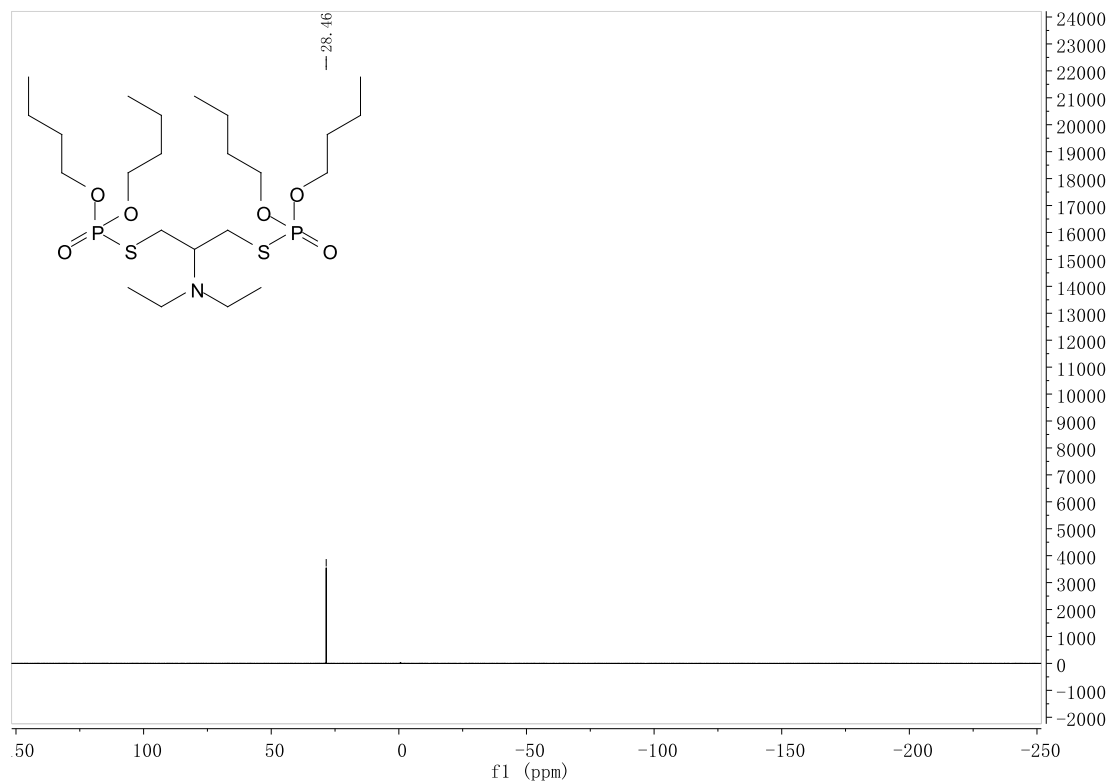


Figure S52. ^{31}P NMR of compound 6e.

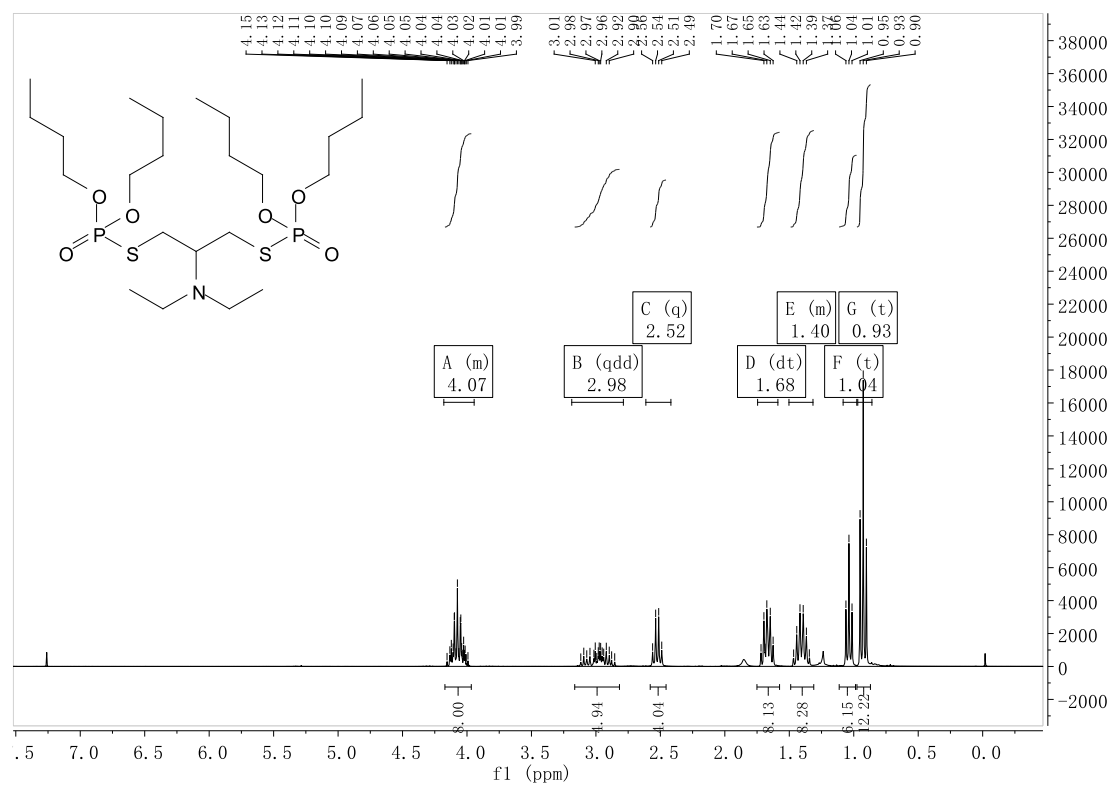


Figure S53. ^1H NMR of compound 6e.

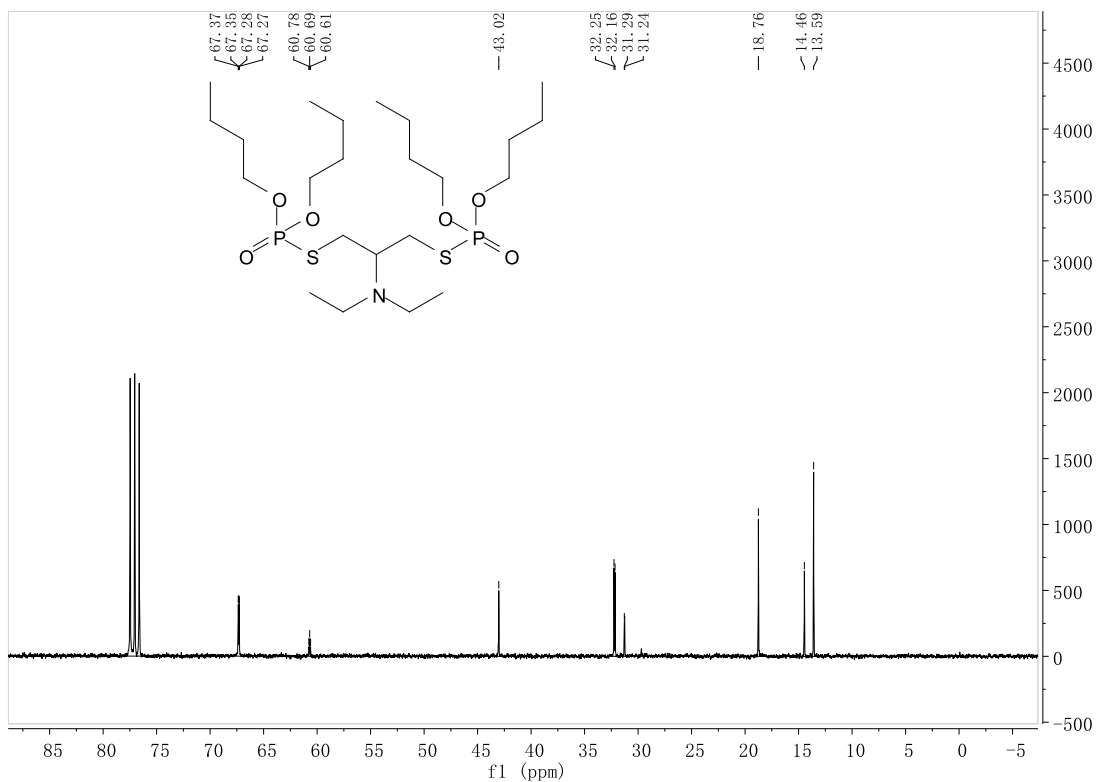


Figure S54. ^{13}C NMR of compound 6e.

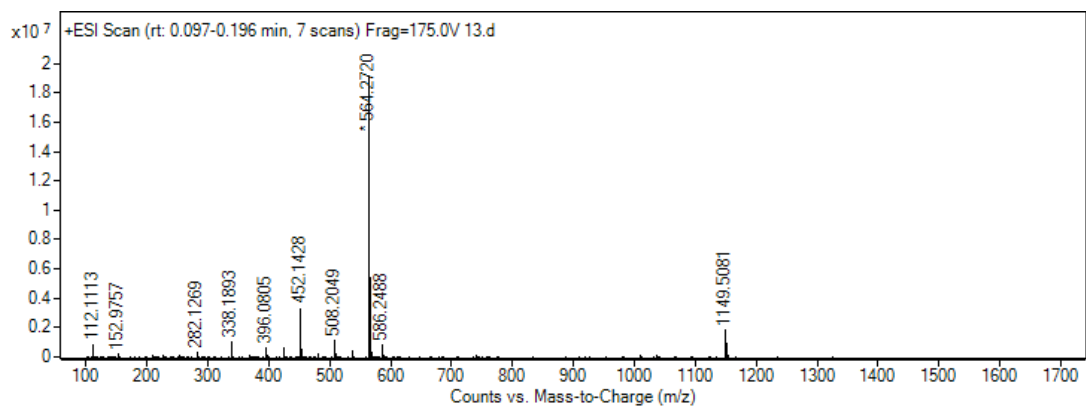
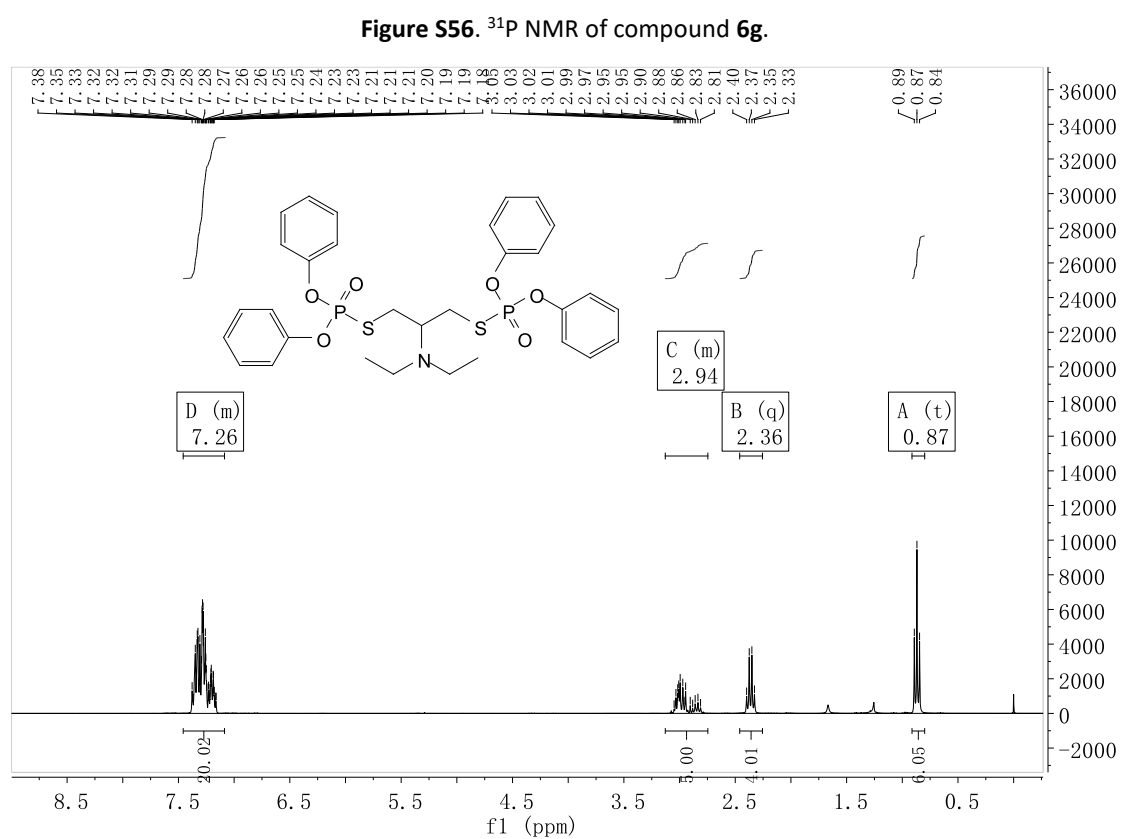
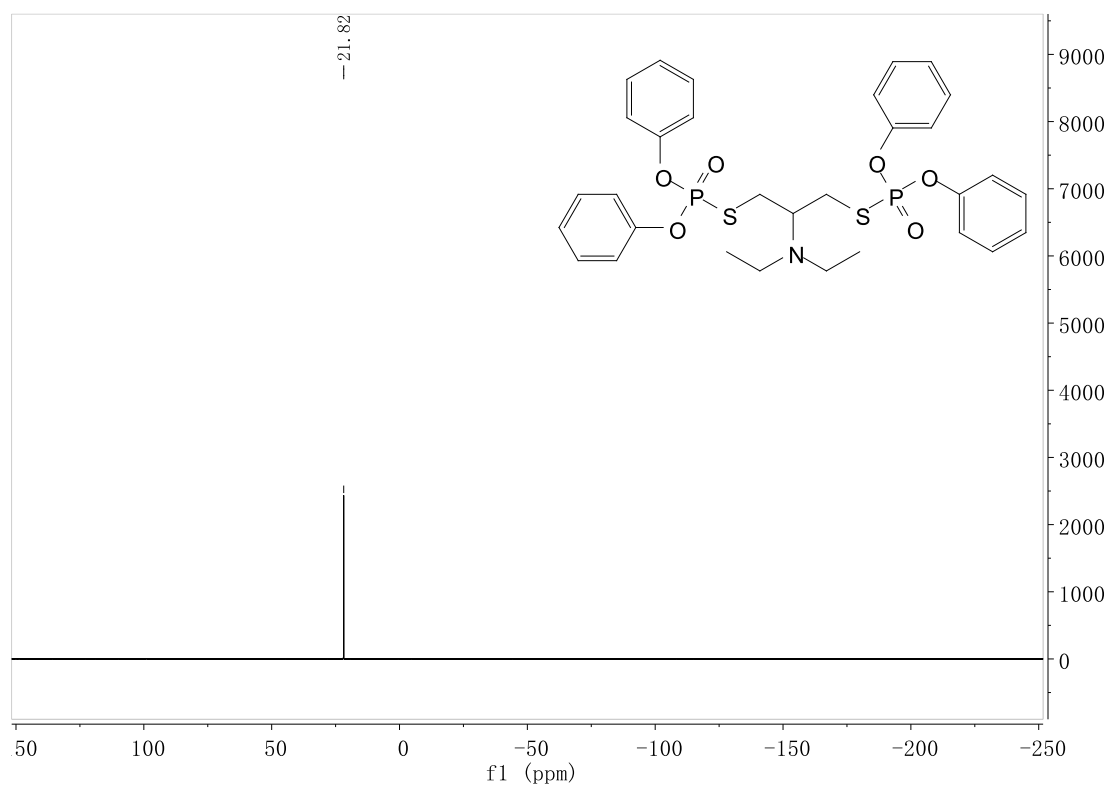


Figure S55. HRMS of compound 6e.



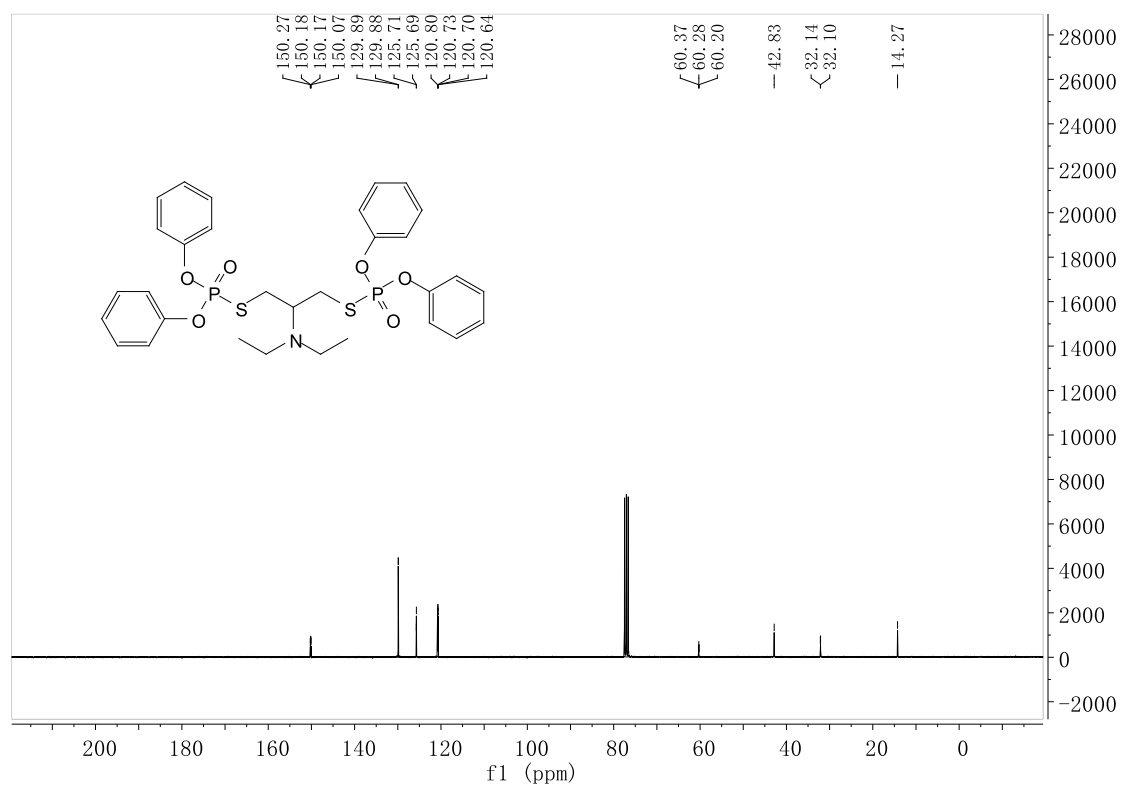


Figure S58. ¹³C NMR of compound 6g.

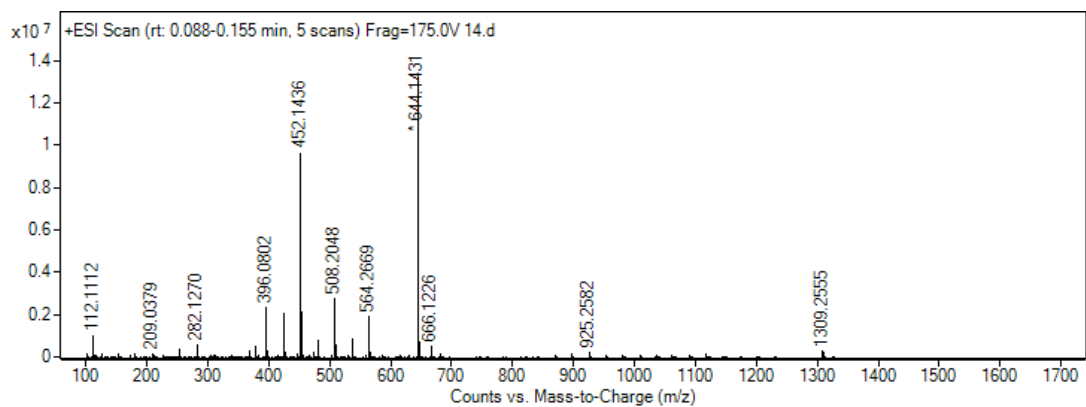
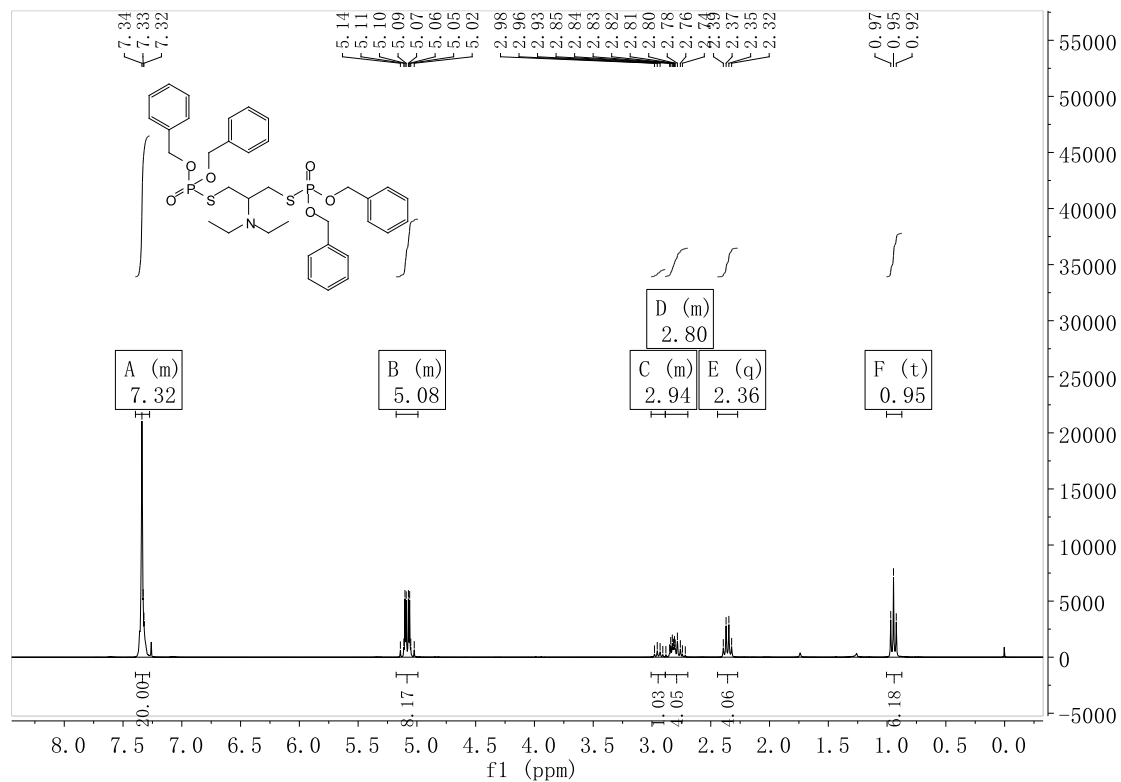
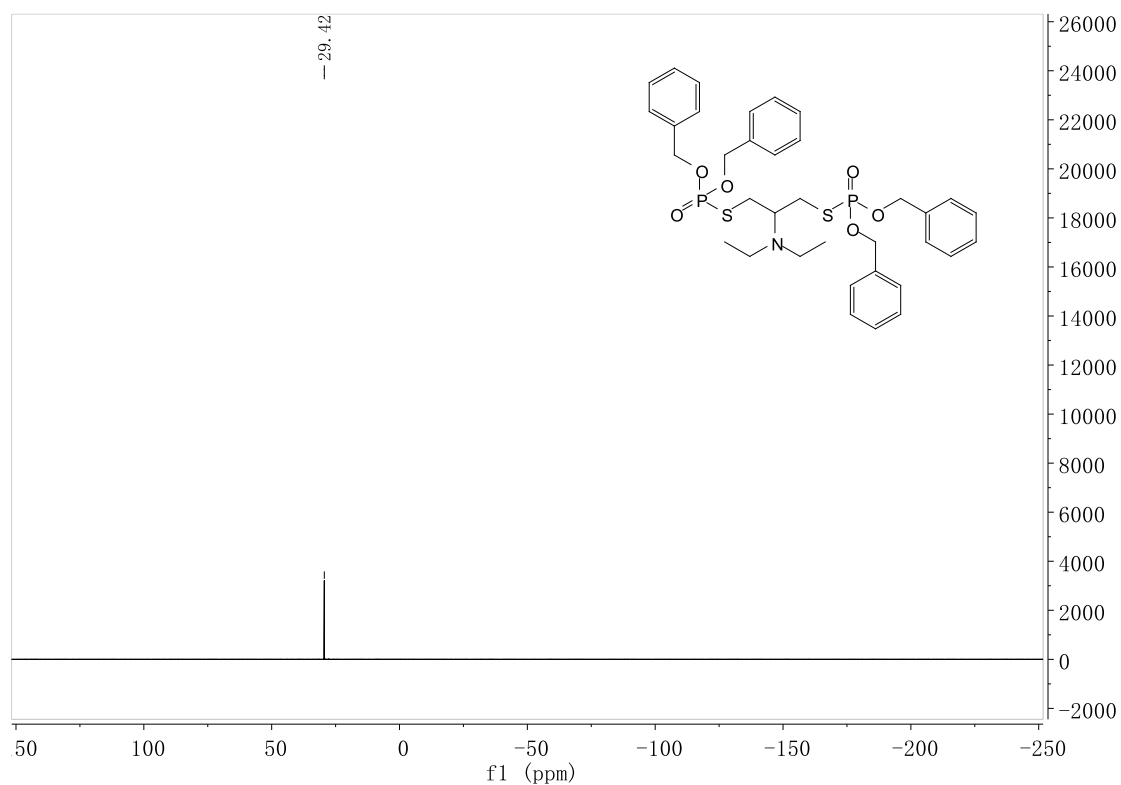


Figure S59. HRMS of compound 6g.



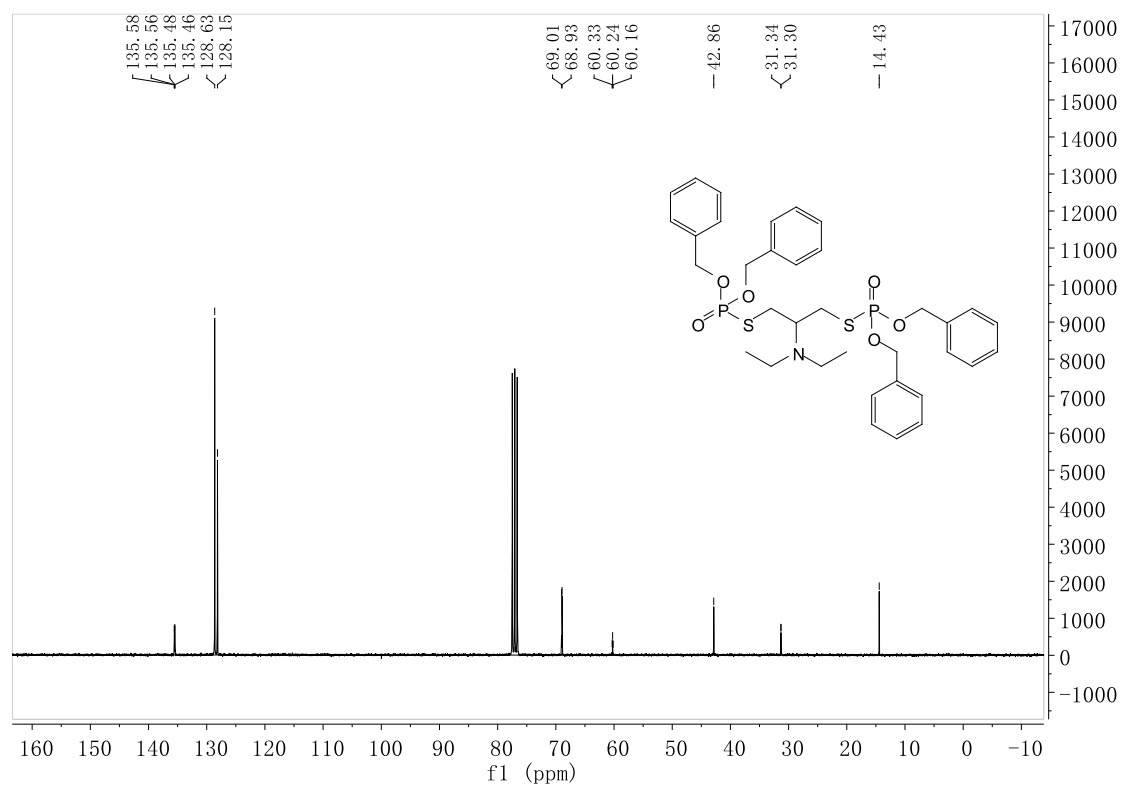


Figure S62. ^{13}C NMR of compound 6h.

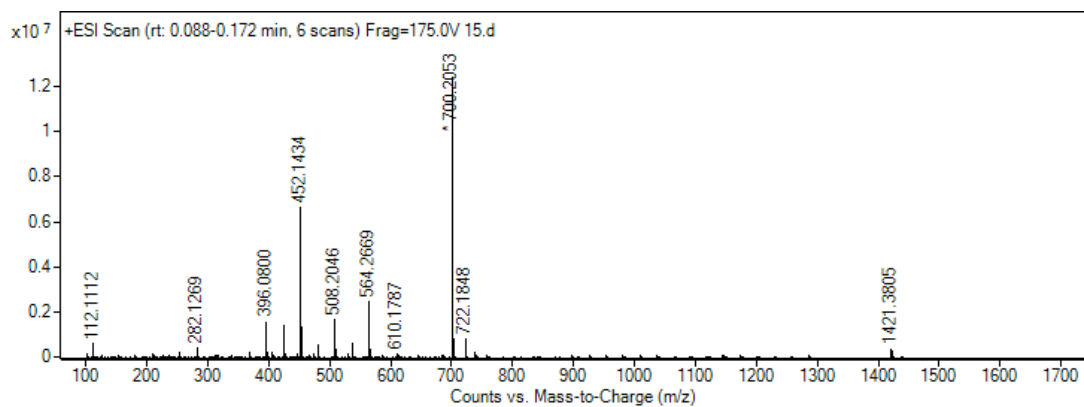


Figure S63. HRMS of compound 6h.

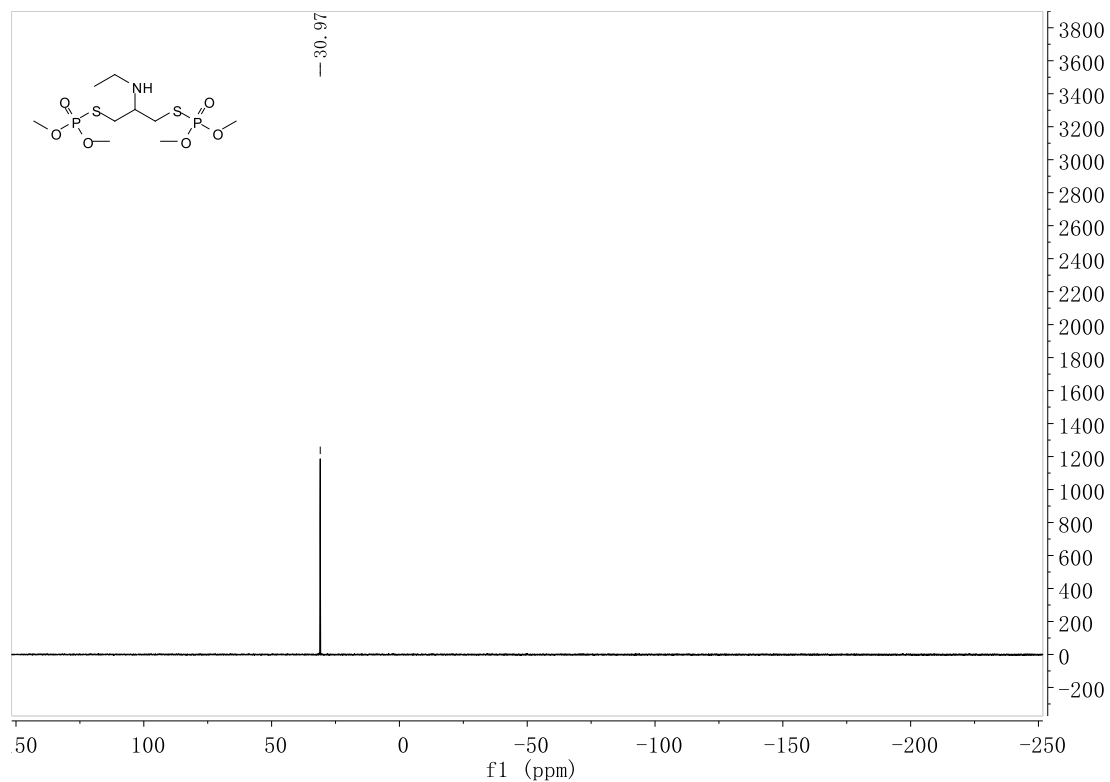


Figure S64. ^{31}P NMR of compound 7a.

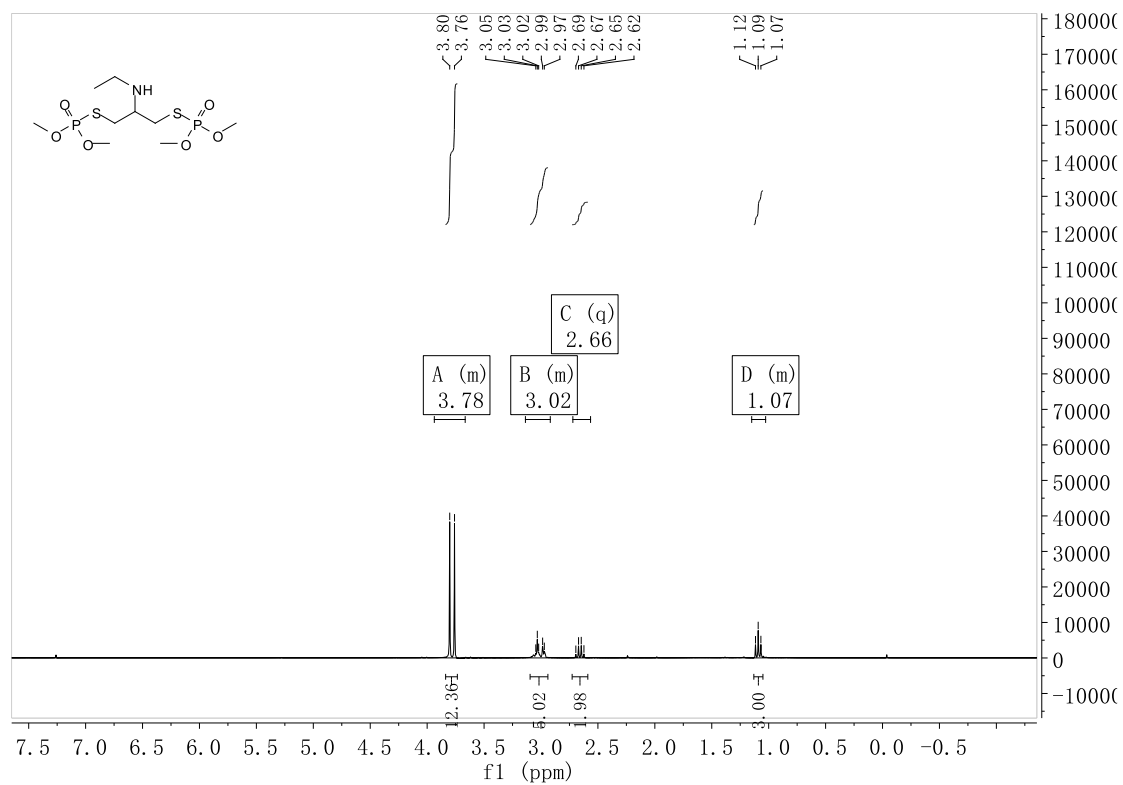


Figure S65. ^1H NMR of compound 7a.

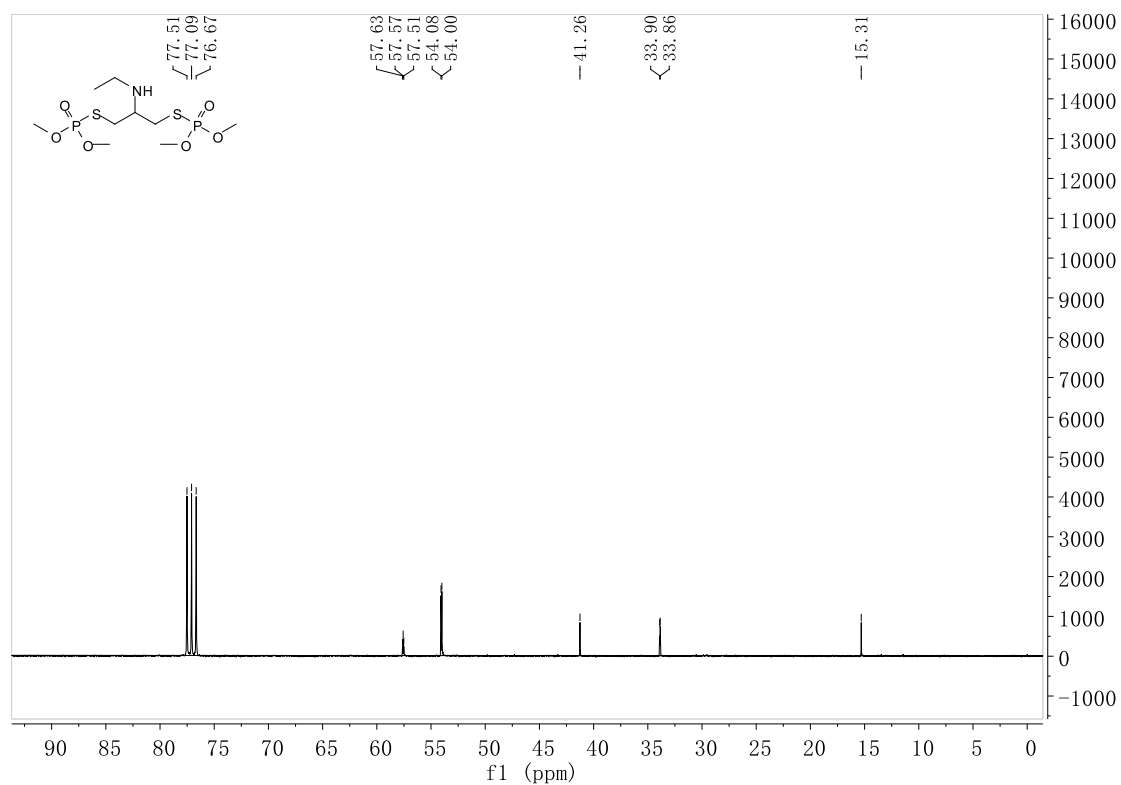


Figure S66. ^{13}C NMR of compound 7a.

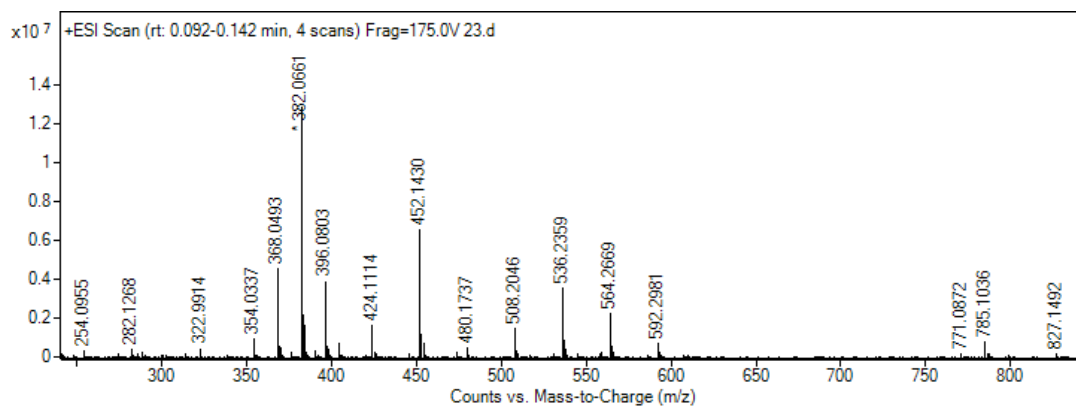


Figure S67. HRMS of compound 7a.

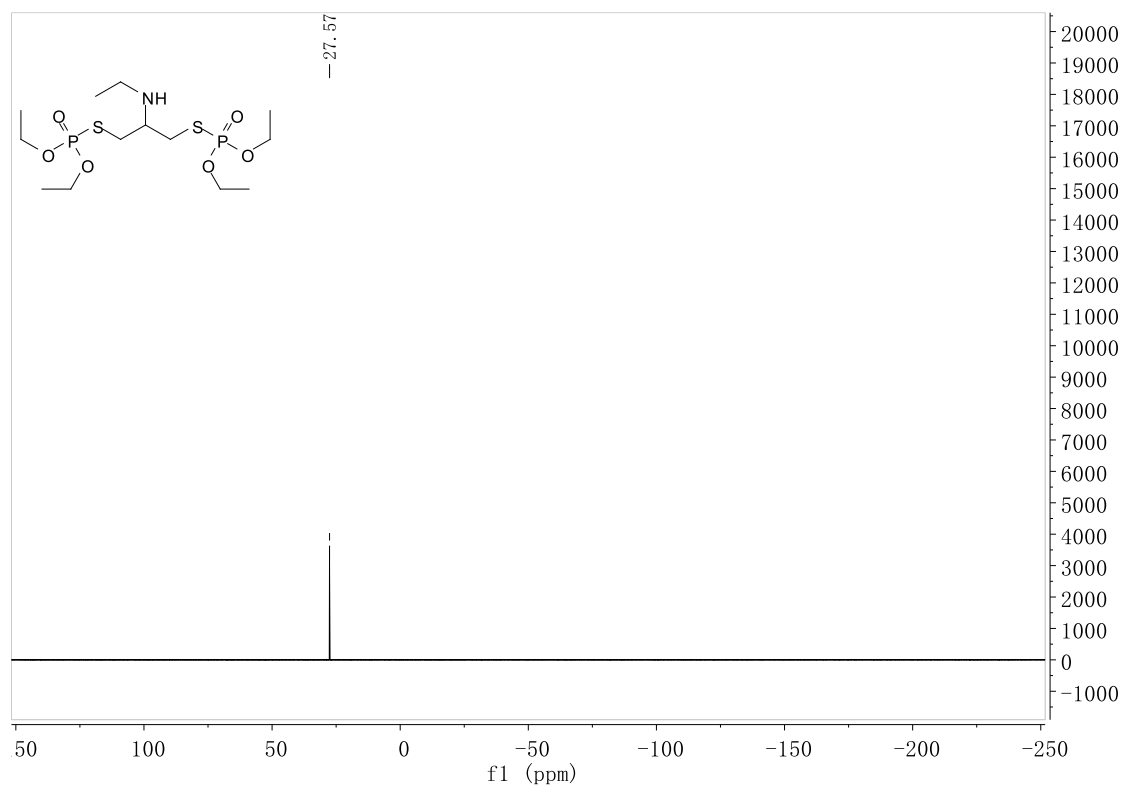


Figure S68. ^{31}P NMR of compound 7b.

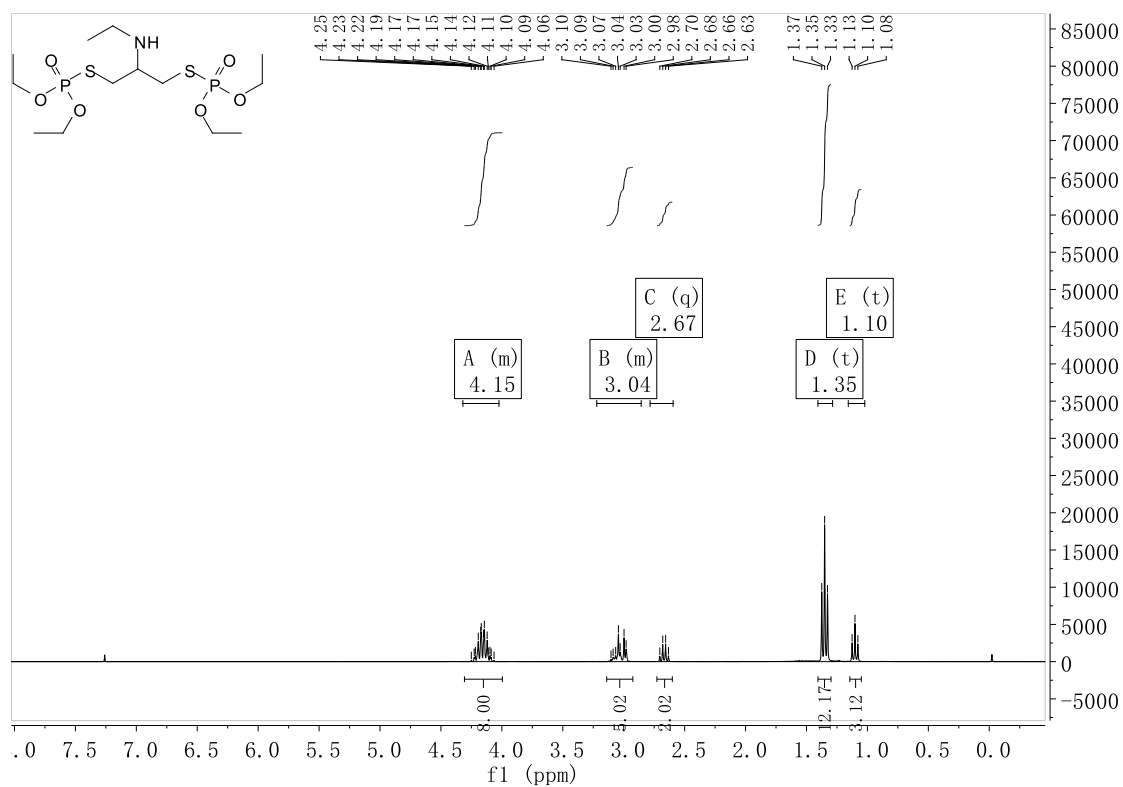


Figure S69. ^1H NMR of compound 7b.

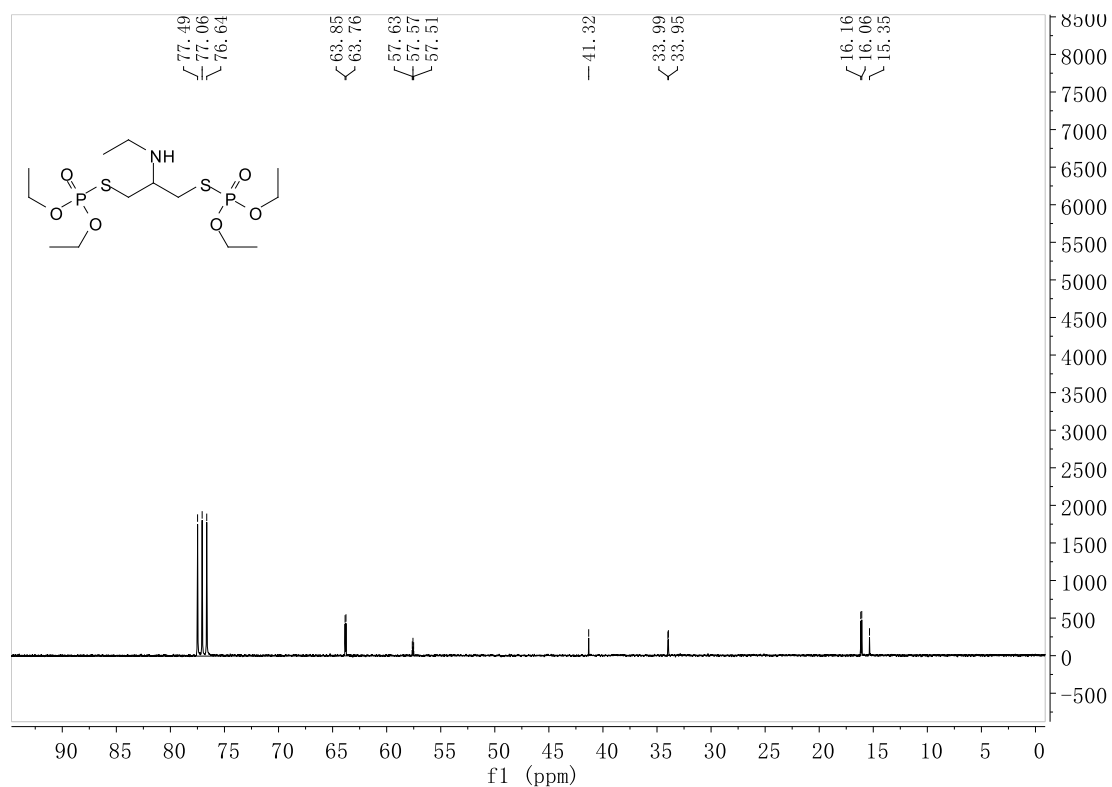


Figure S70. ^{13}C NMR of compound **7b**.

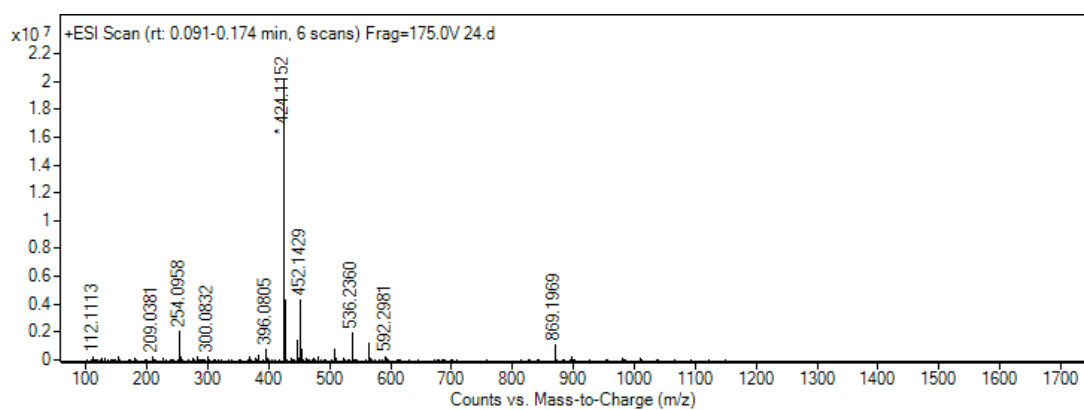


Figure S71. HRMS of compound **7b**.

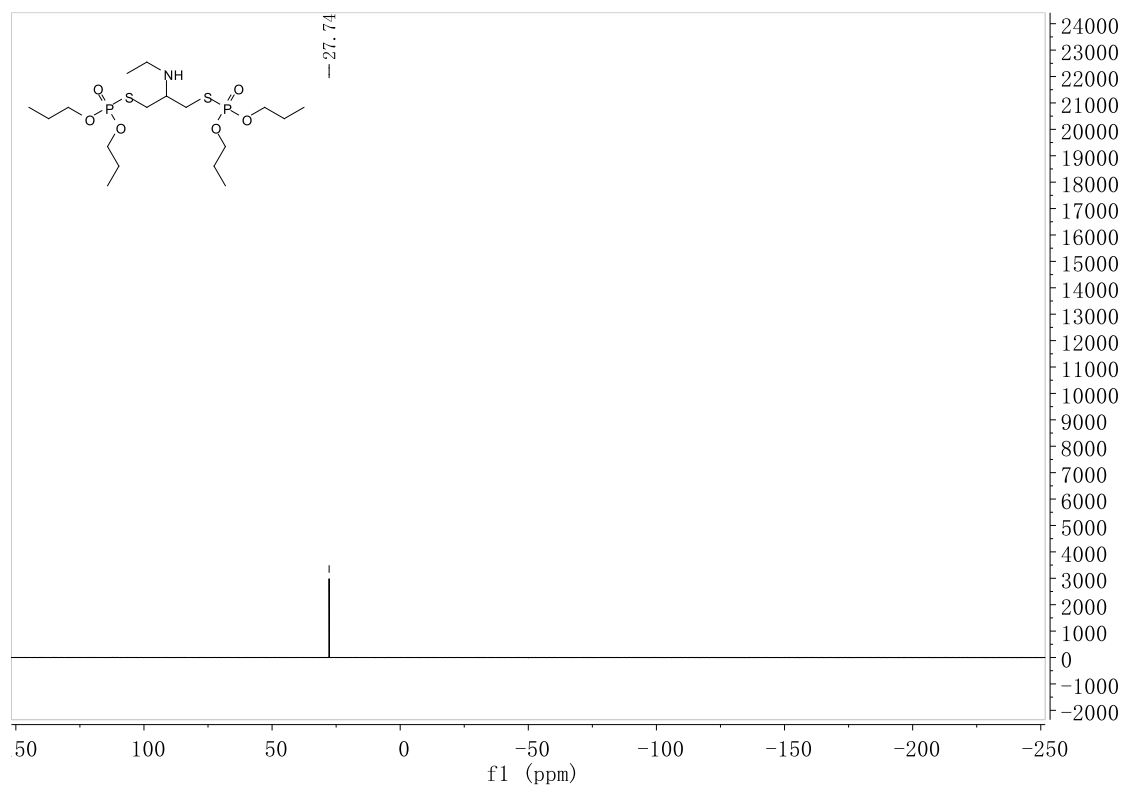


Figure S72. ^{31}P NMR of compound 7c.

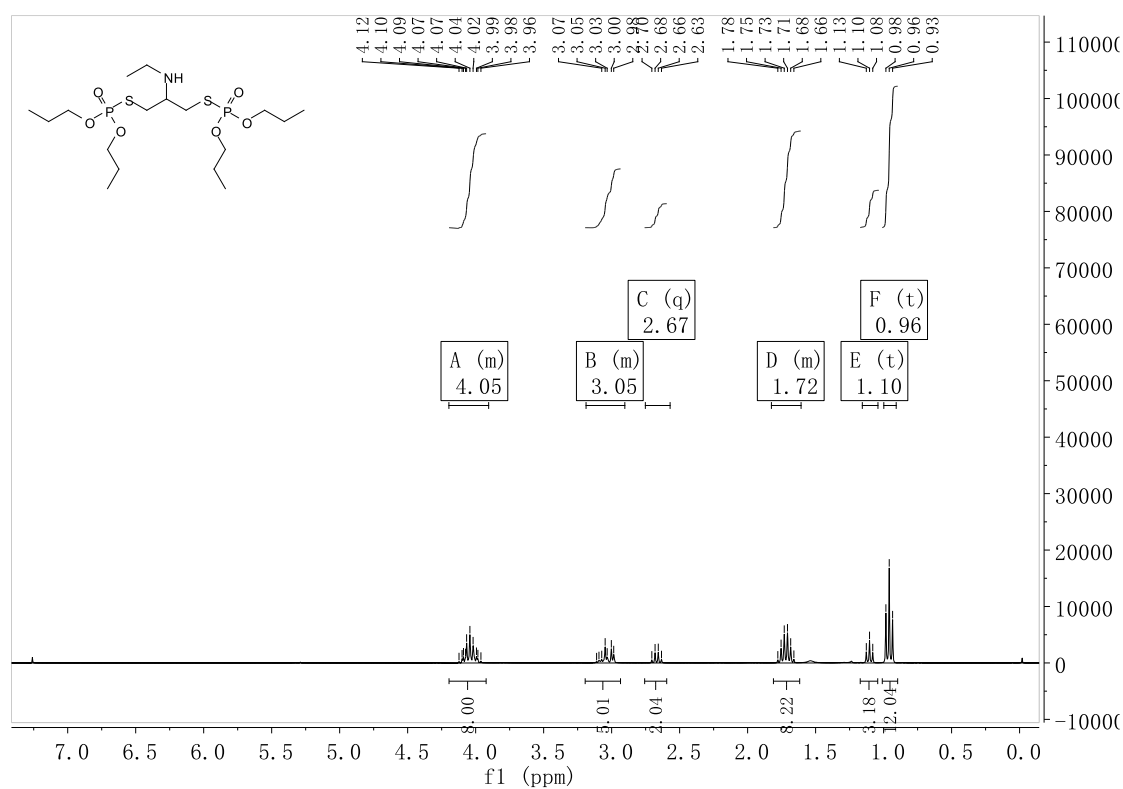


Figure S73. ^1H NMR of compound 7c.

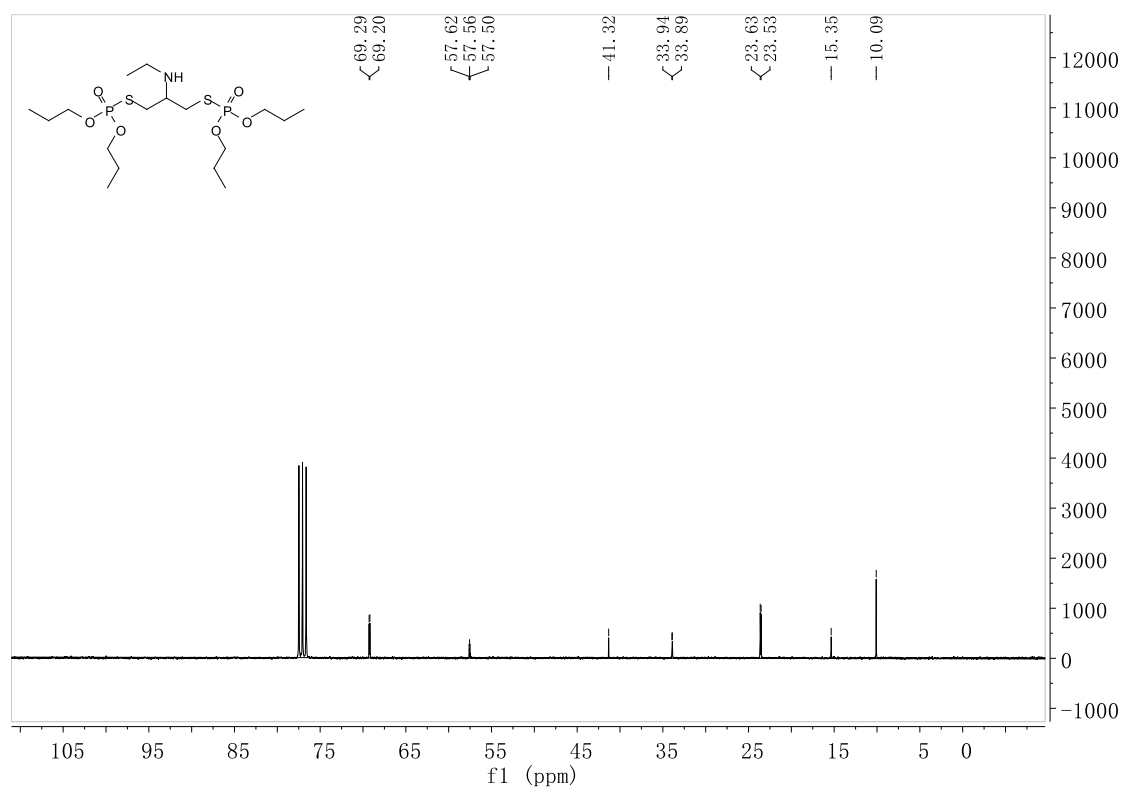


Figure S74. ^{13}C NMR of compound **7c**.

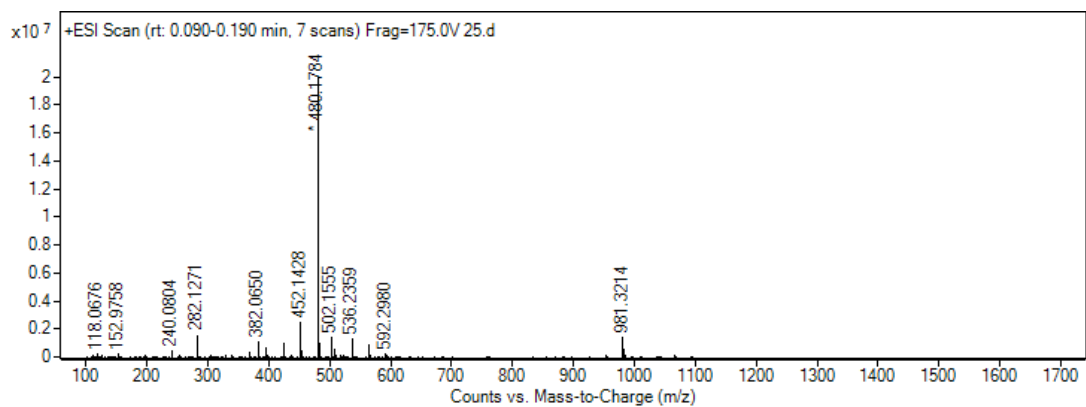


Figure S75. HRMS of compound **7c**.

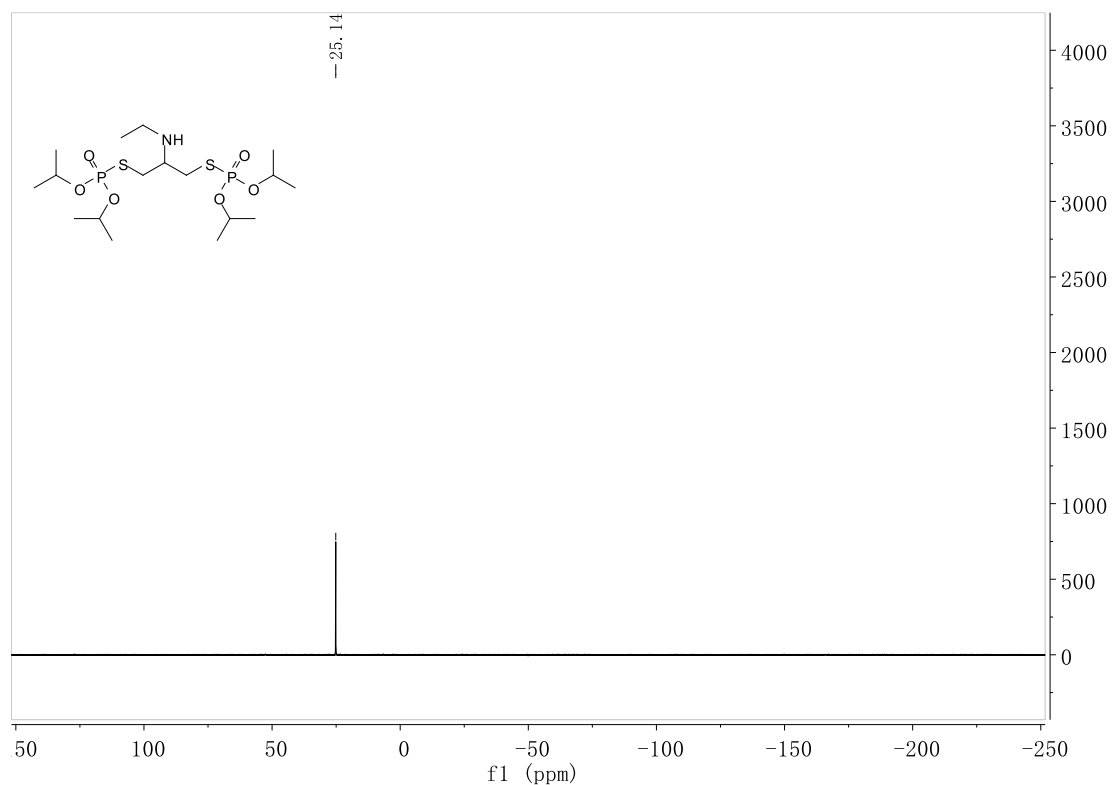


Figure S76. ³¹P NMR of compound 7d.

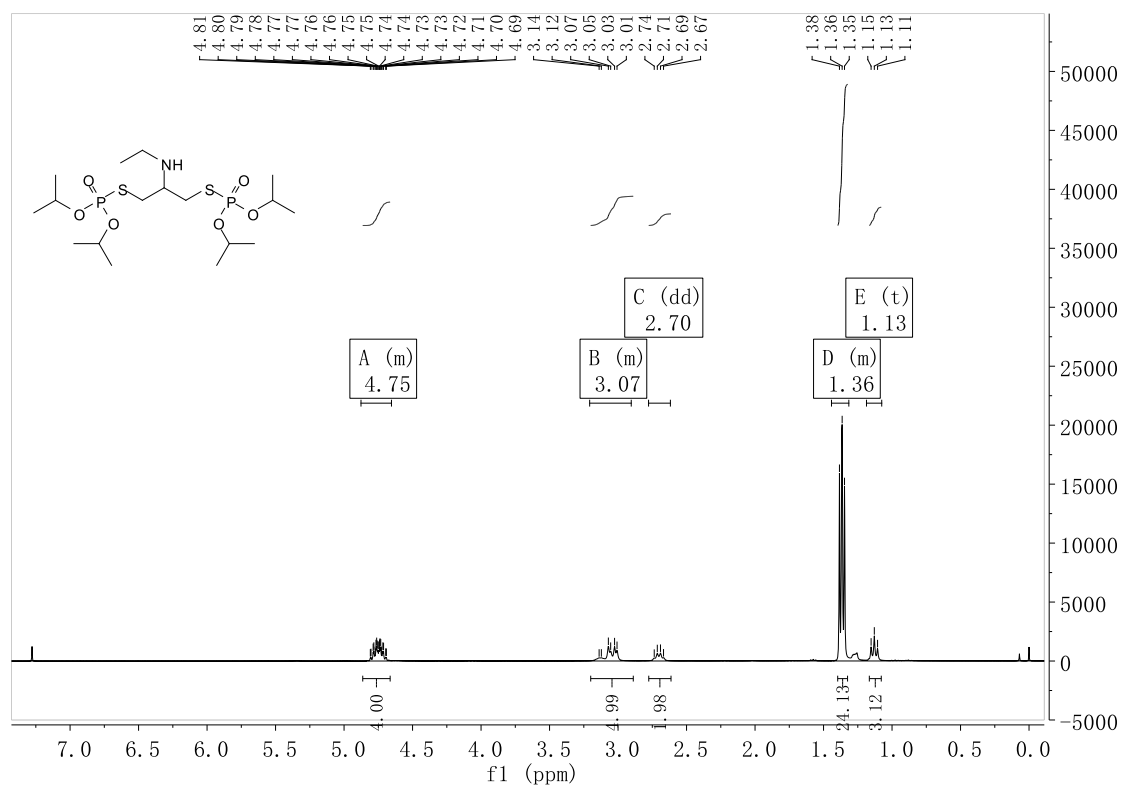


Figure S77. ¹H NMR of compound 7d.

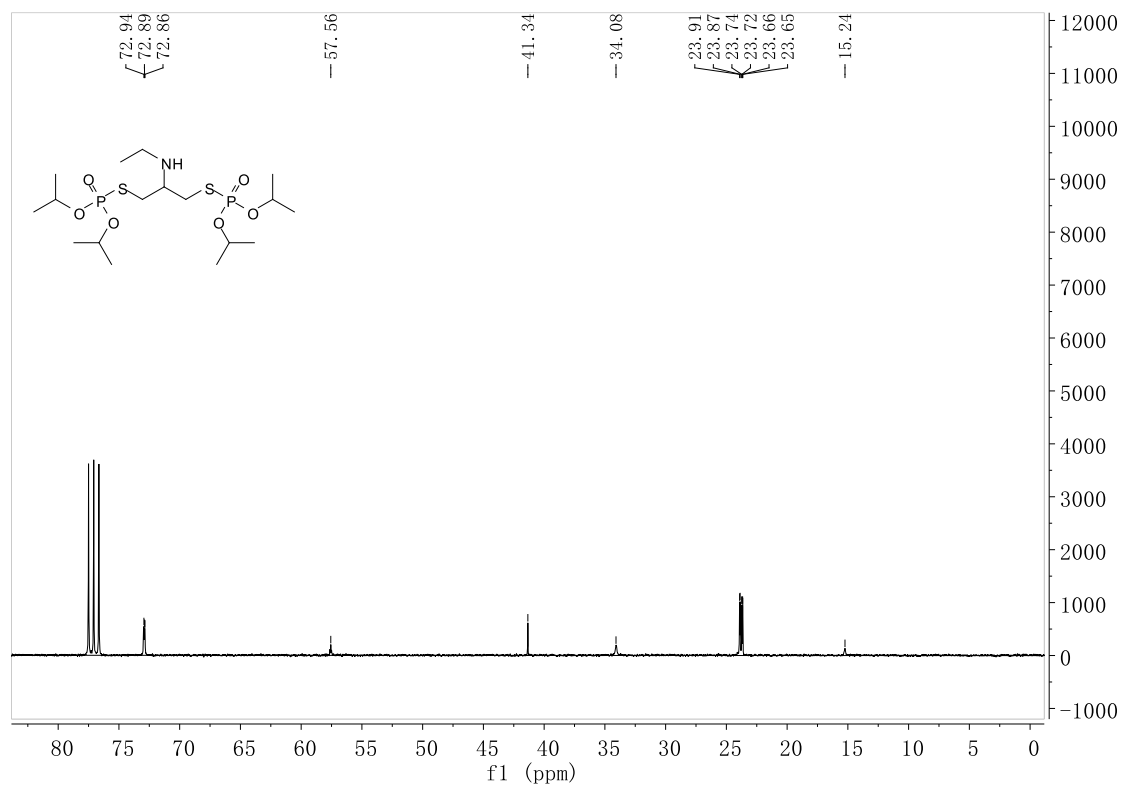


Figure S78. ¹³C NMR of compound 7d.

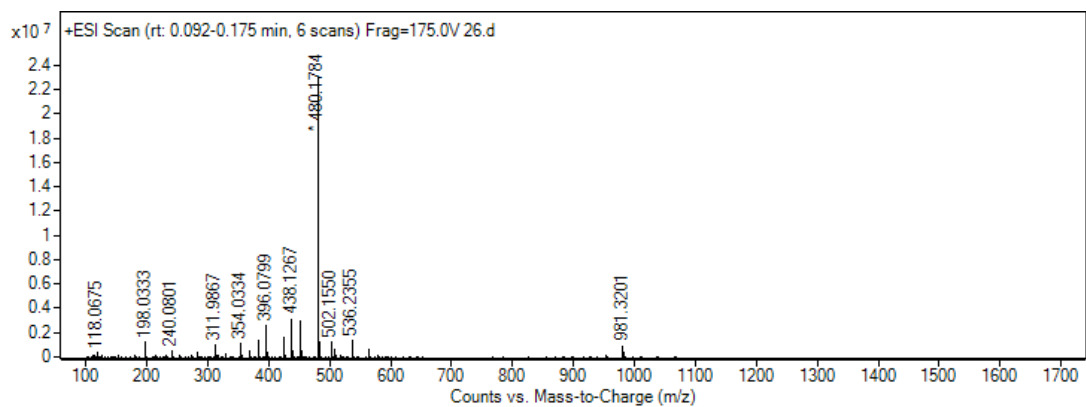


Figure S79. HRMS of compound 7d.

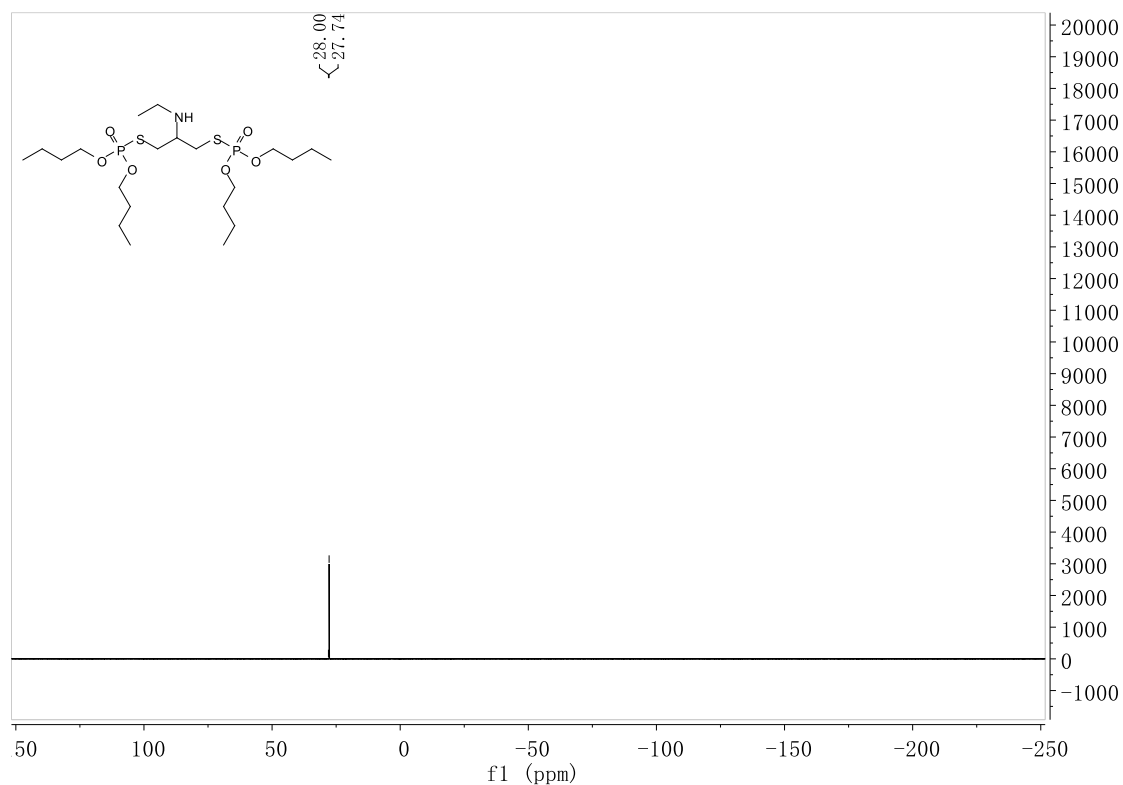


Figure S80. ^{31}P NMR of compound 7e.

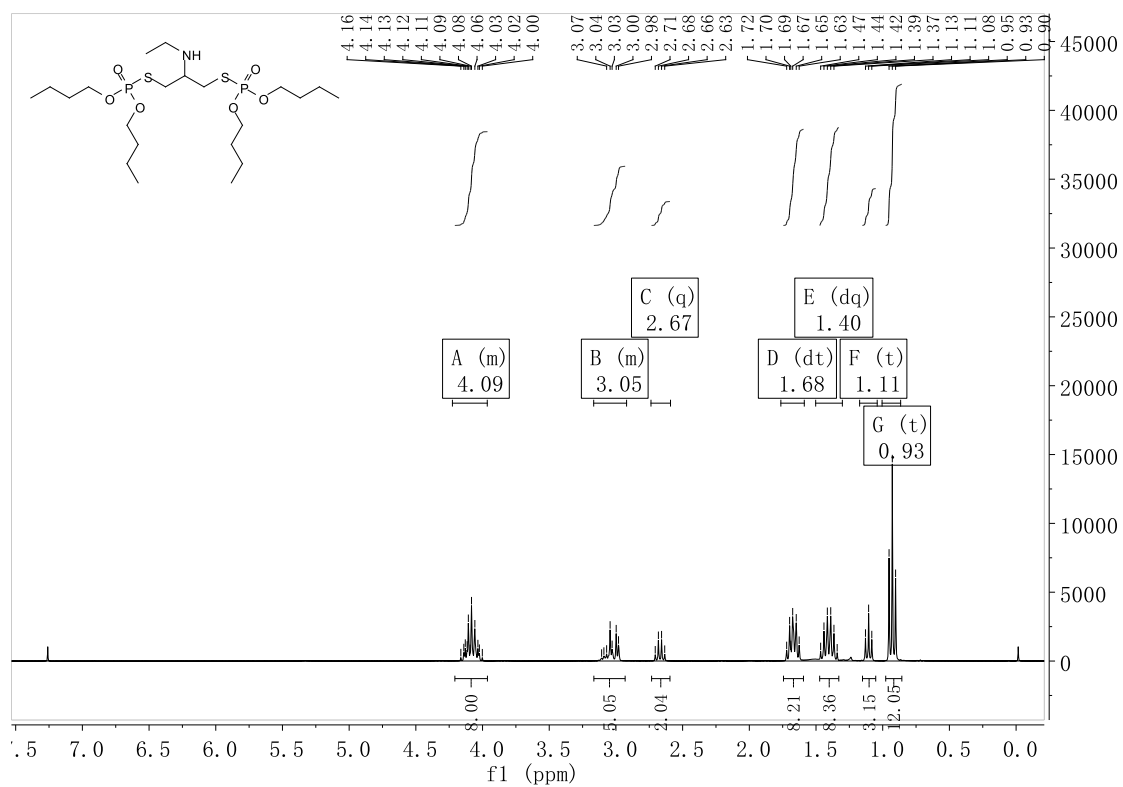


Figure S81. ^1H NMR of compound 7e.

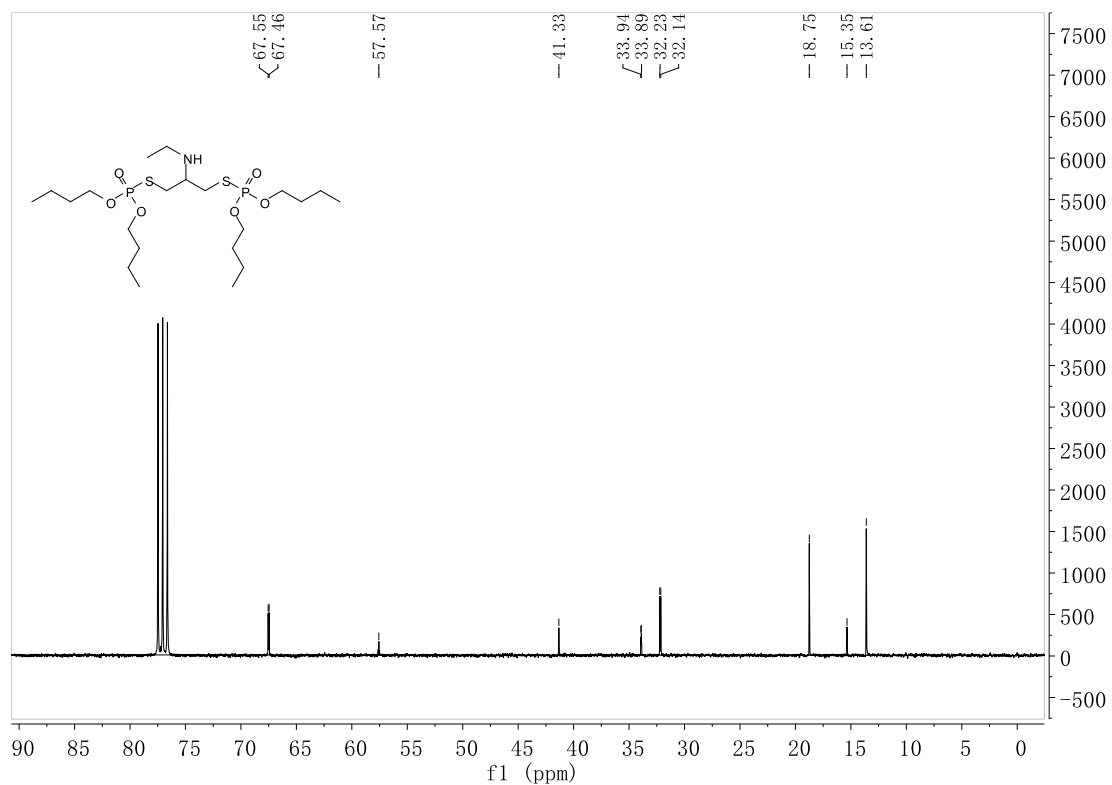


Figure S82. ¹³C NMR of compound 7e.

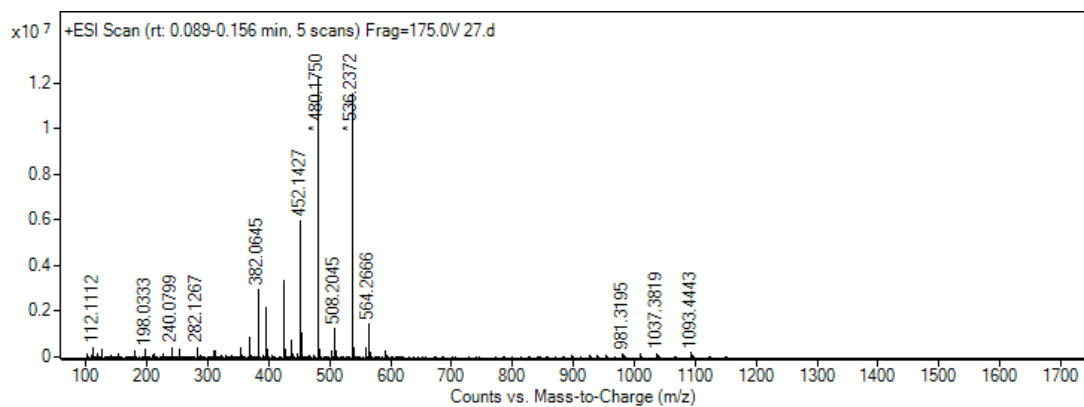


Figure S83. HRMS of compound 7e.

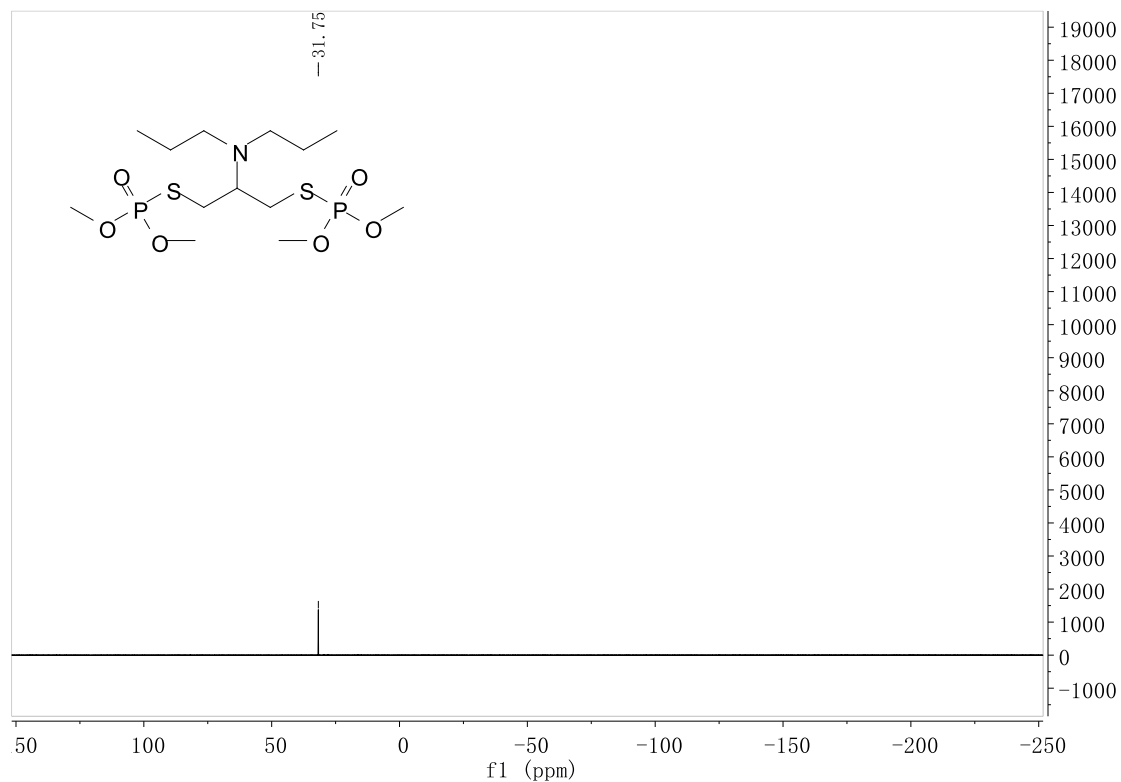


Figure S88. ^{31}P NMR of compound 8a.

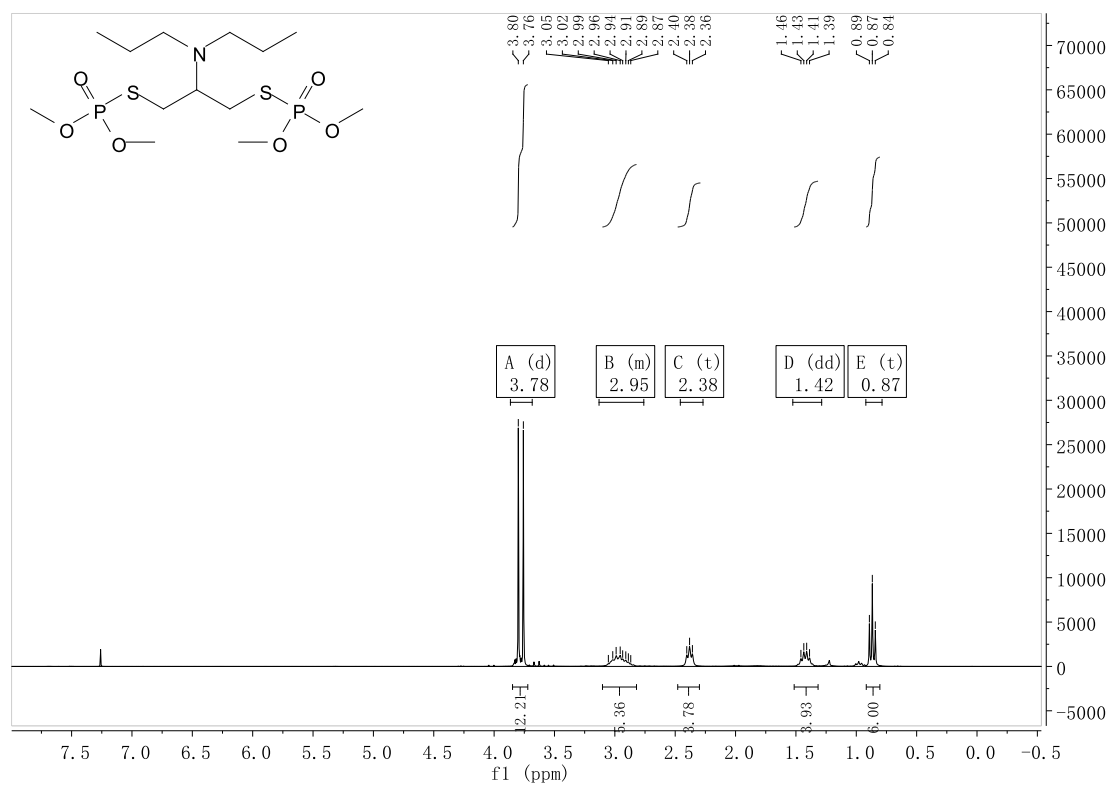


Figure S89. ^1H NMR of compound 8a.

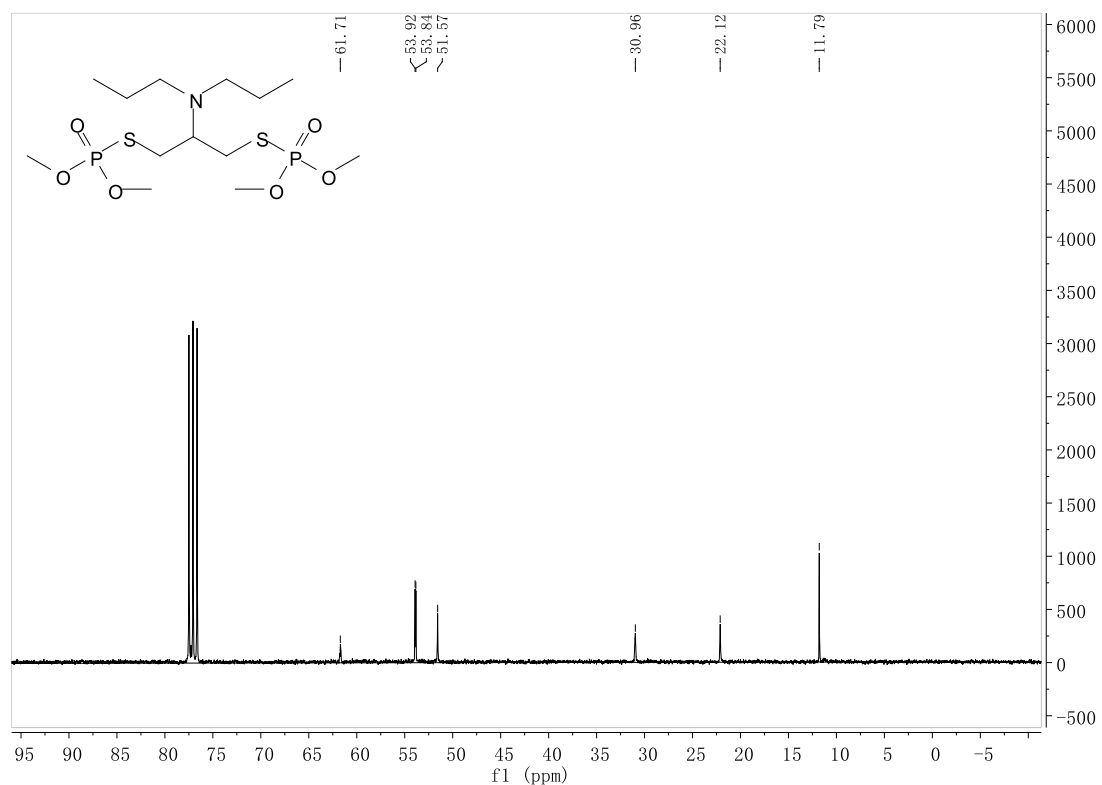


Figure S90. ^{13}C NMR of compound 8a.

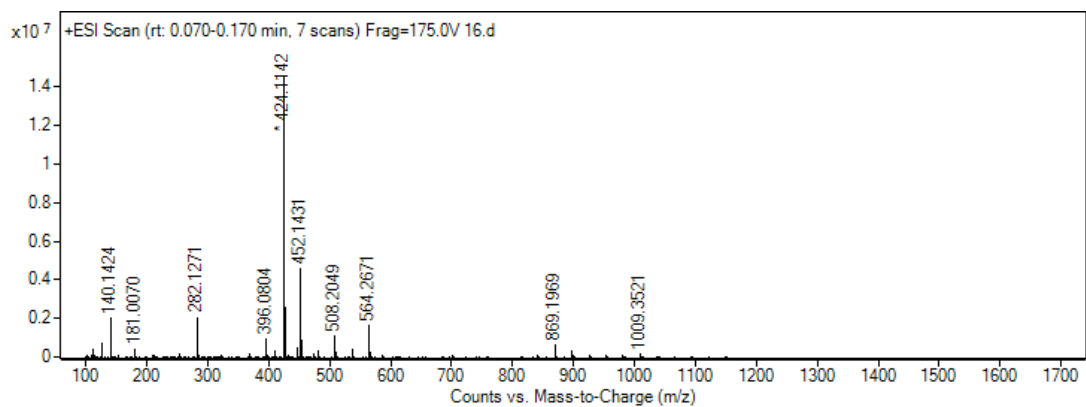


Figure S91. HRMS of compound 8a.

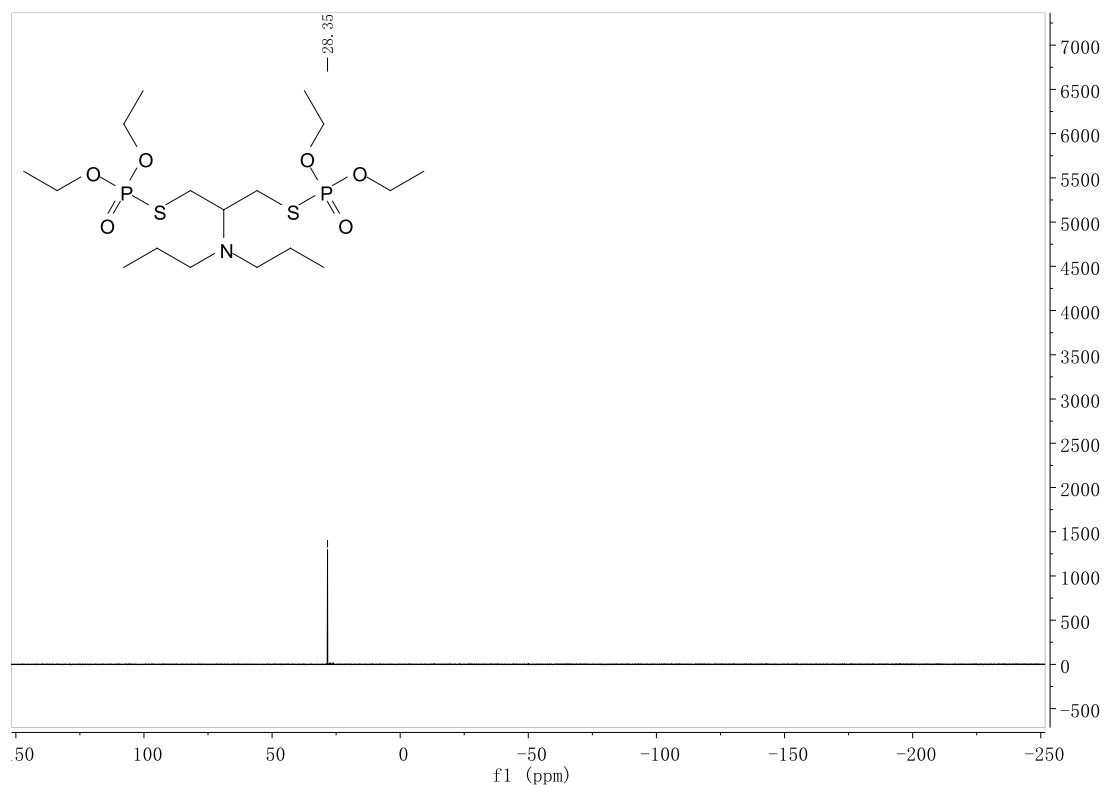


Figure S92. ^{31}P NMR of compound **8b**.

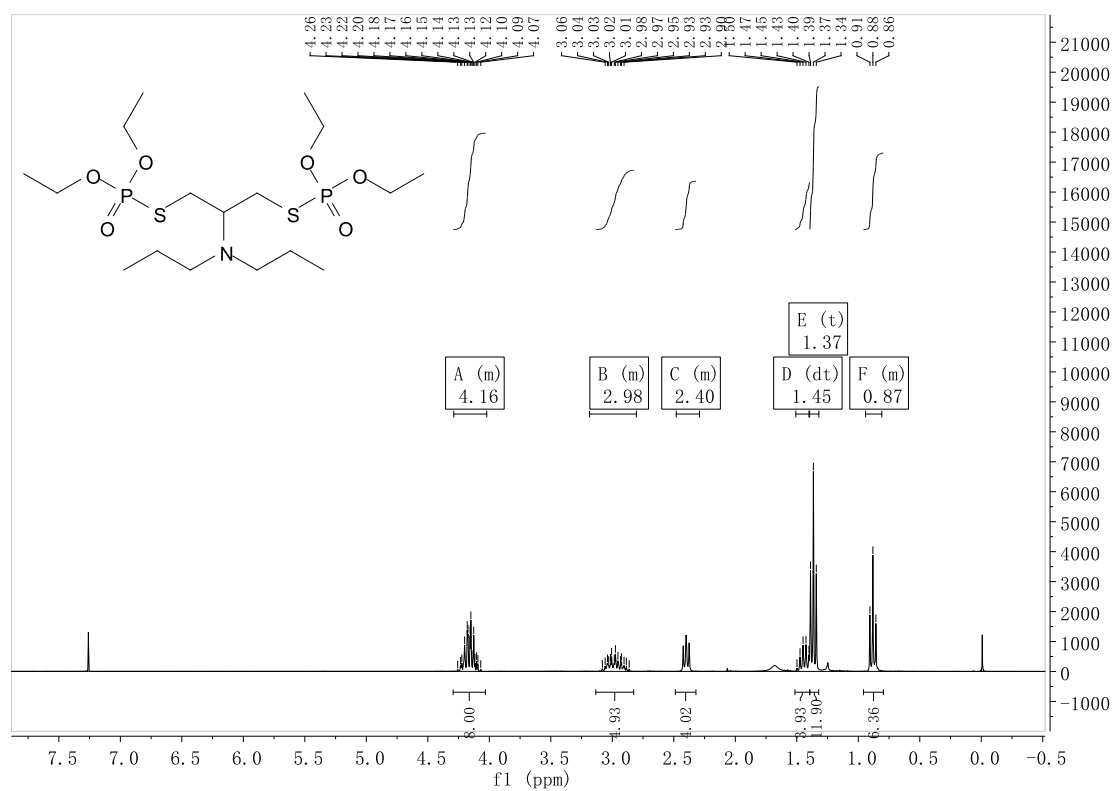


Figure S93. ^1H NMR of compound **8b**.

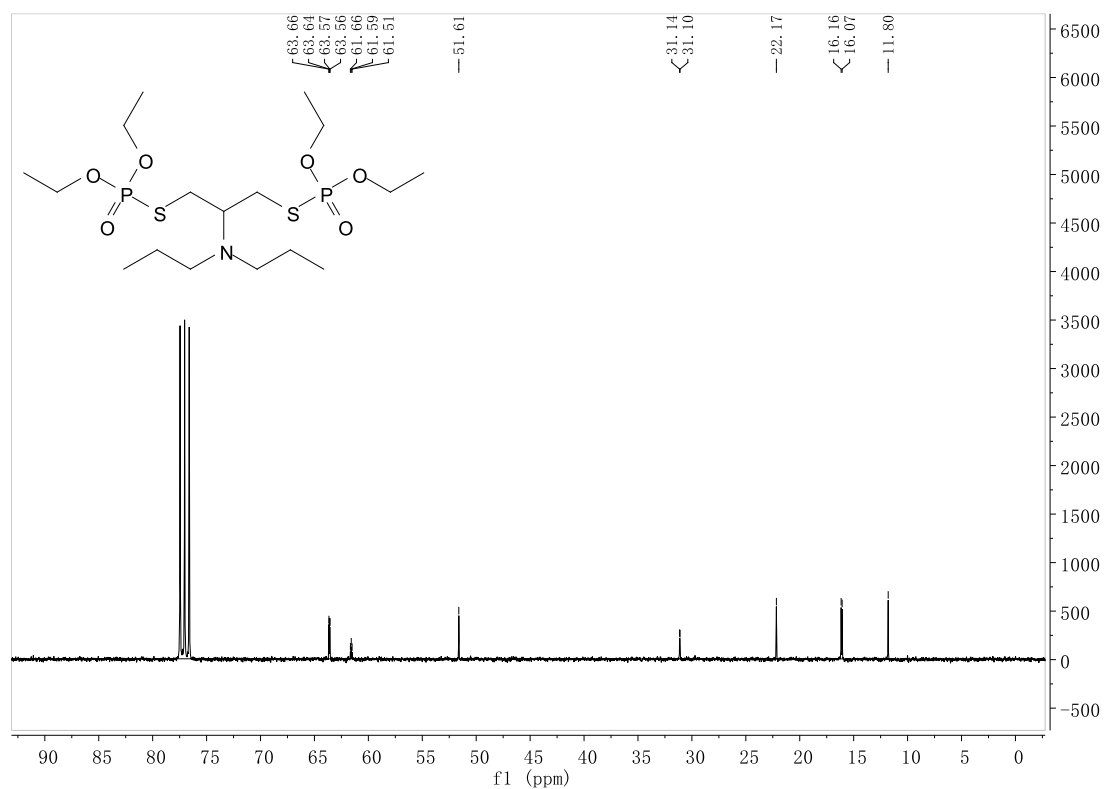


Figure S94. ¹³C NMR of compound 8b.

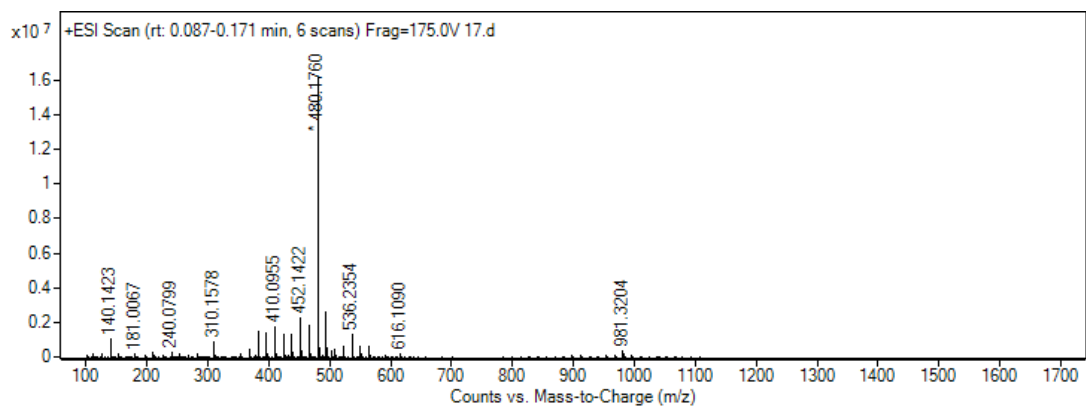


Figure S95. HRMS of compound 8b.

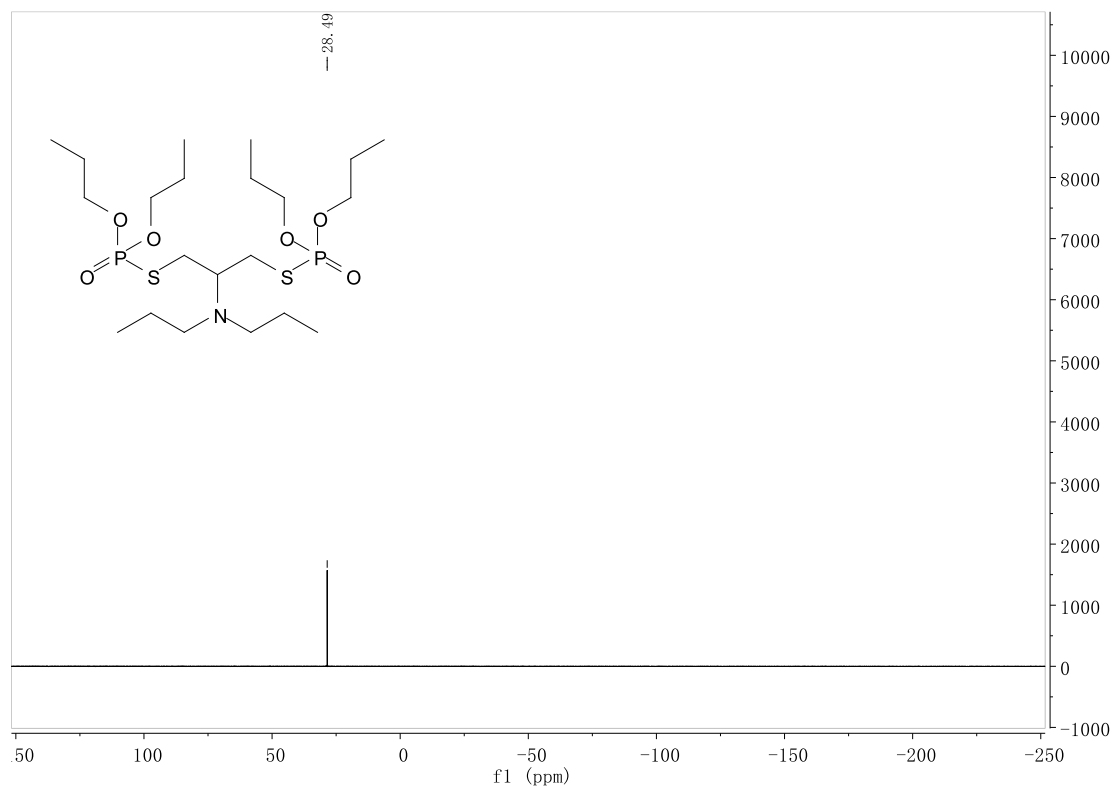


Figure S96. ^{31}P NMR of compound 8c.

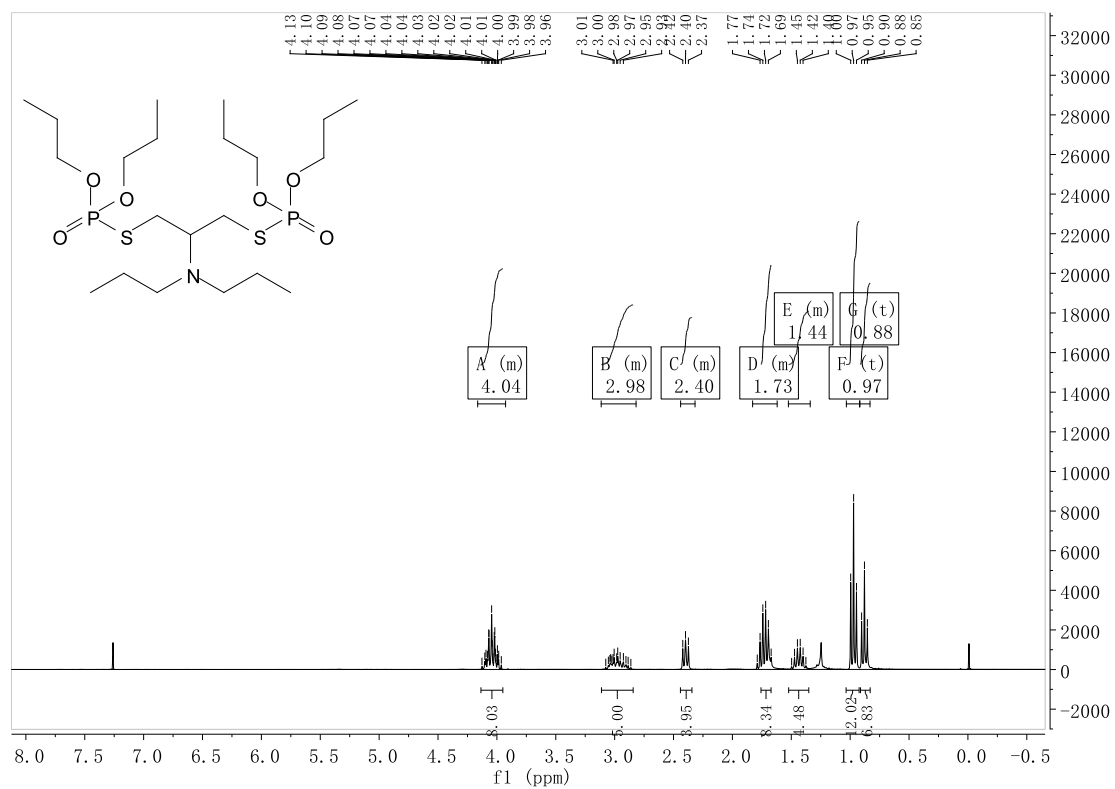


Figure S97. ^1H NMR of compound 8c.

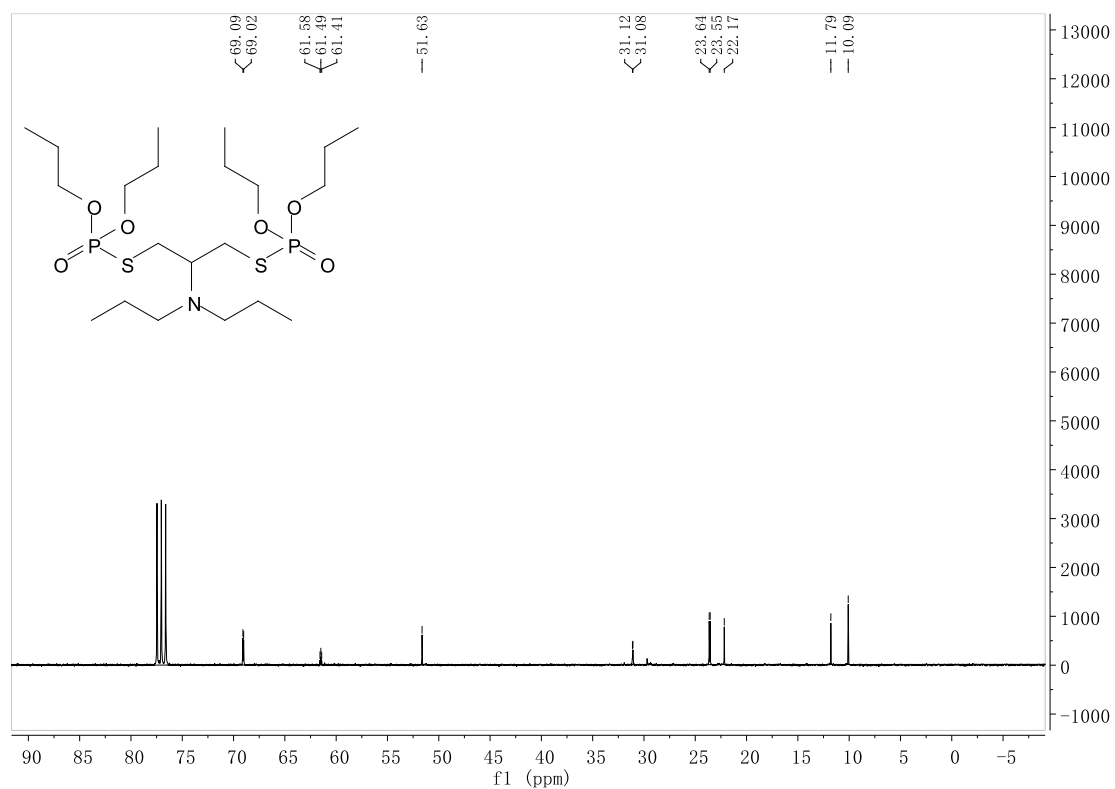


Figure S98. ^{13}C NMR of compound 8c.

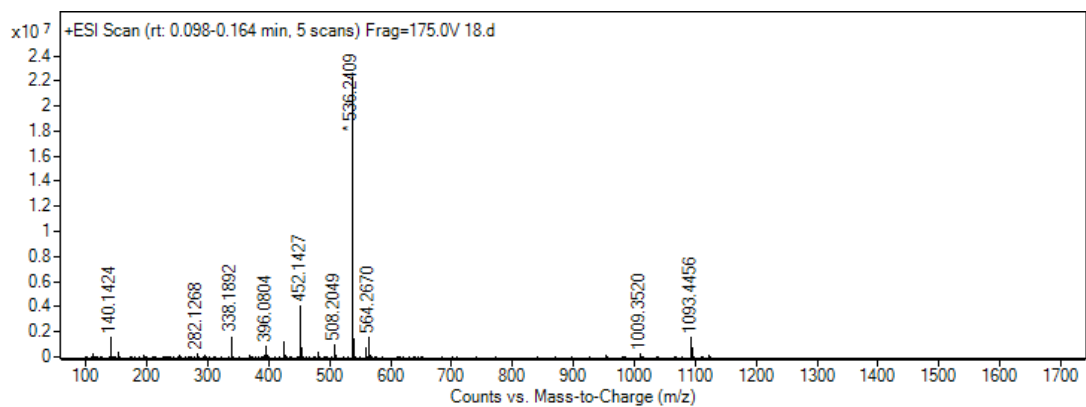


Figure S99. HRMS of compound 8c.

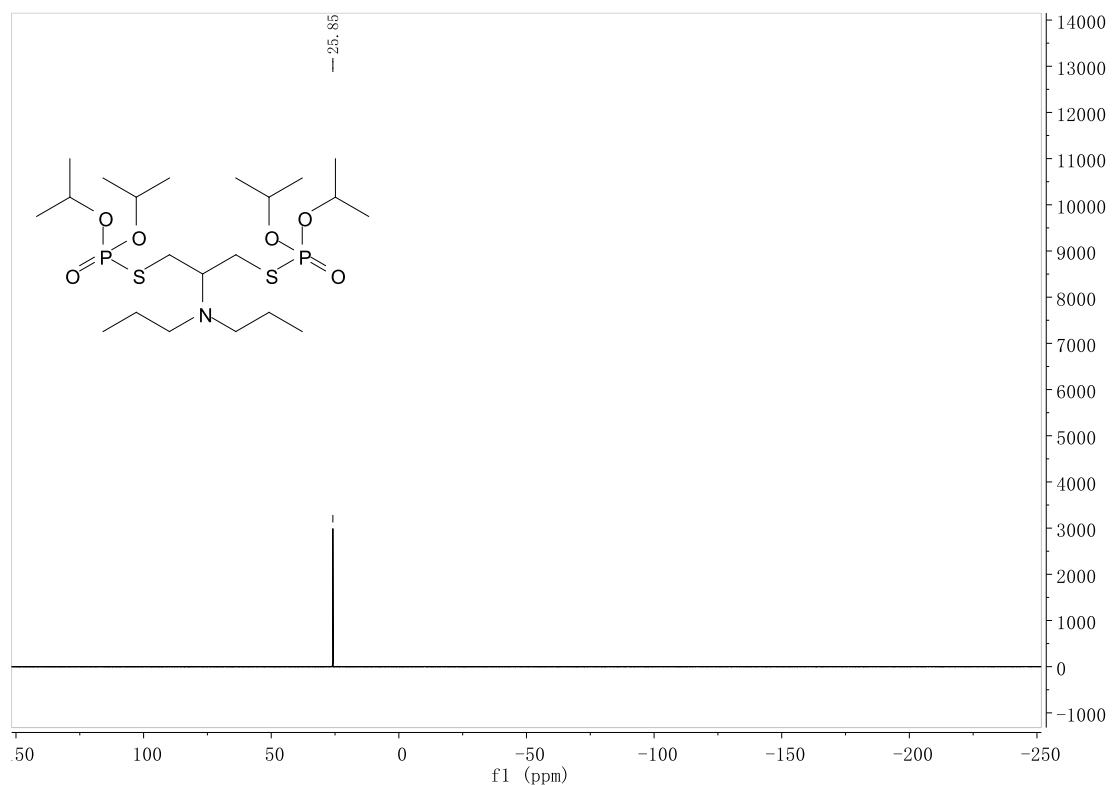


Figure S100. ^{31}P NMR of compound 8d.

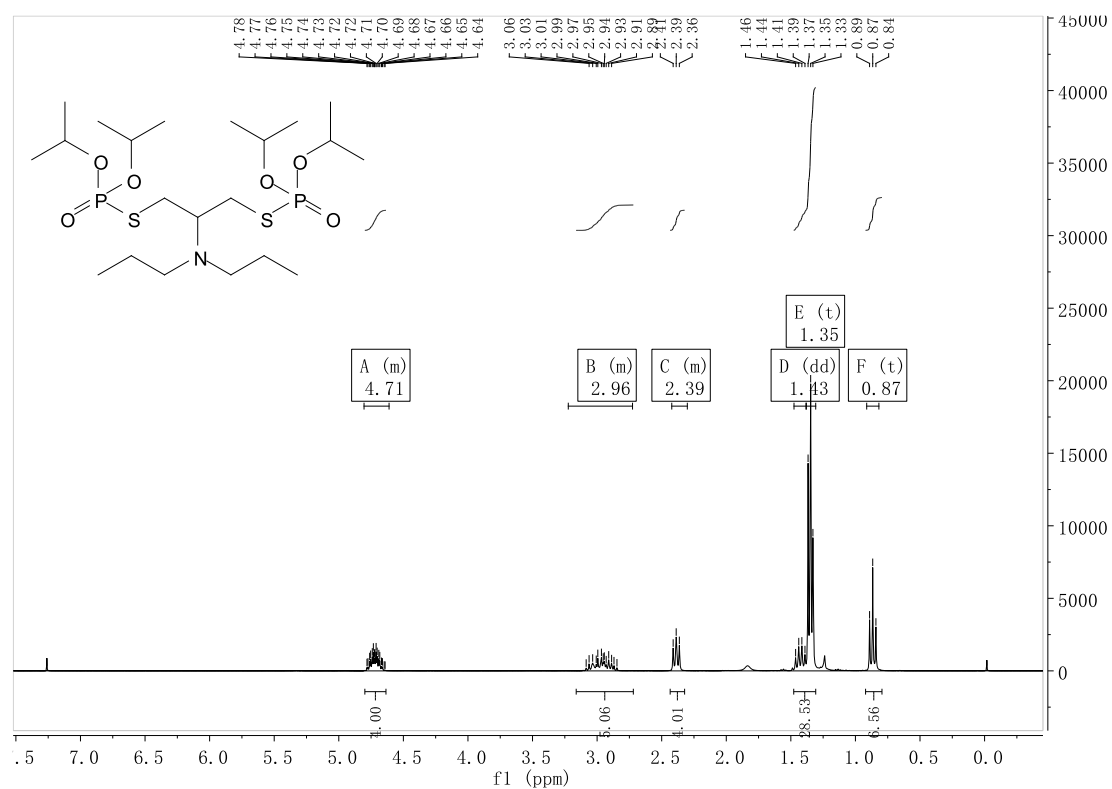


Figure S101. ^1H NMR of compound 8d.

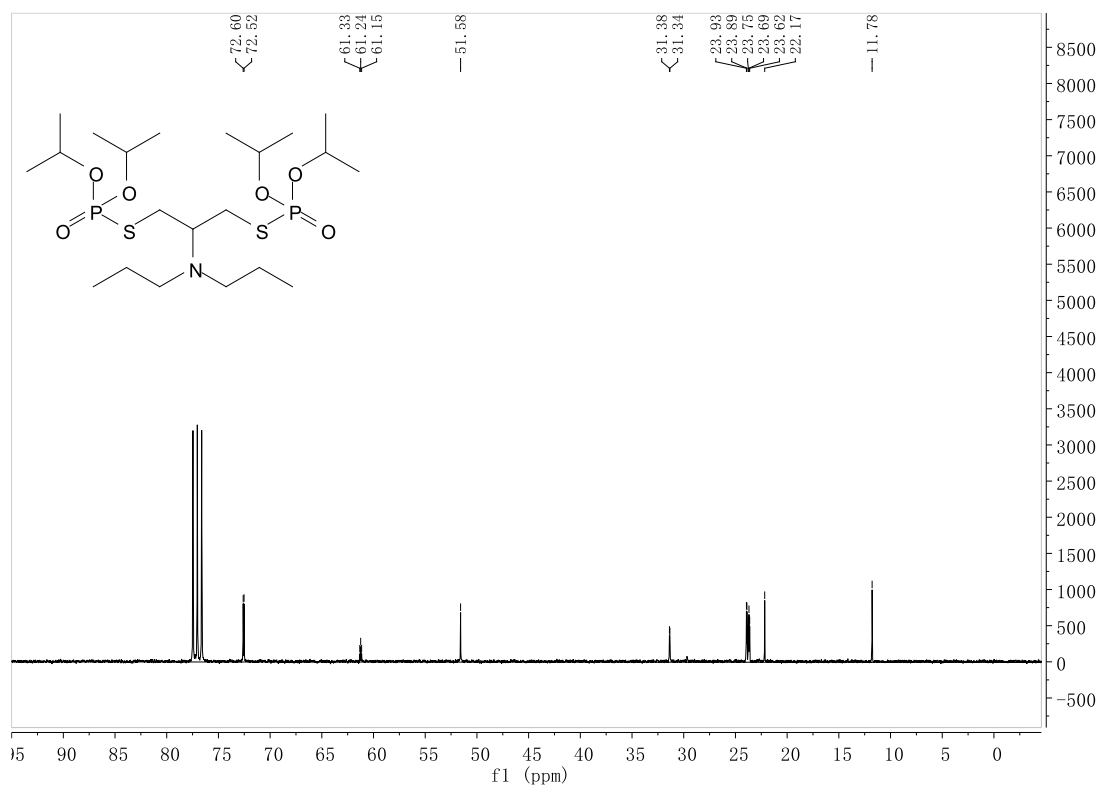


Figure S102. ¹³C NMR of compound 8d.

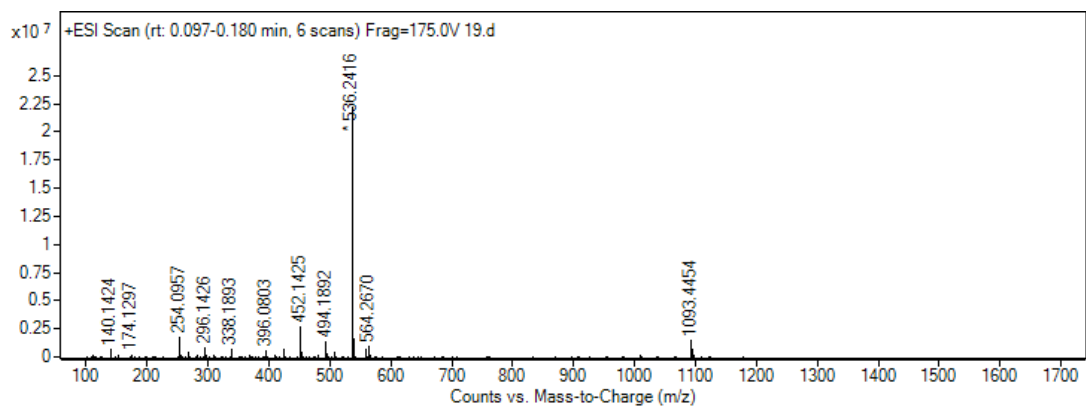


Figure S103. HRMS of compound 8d.

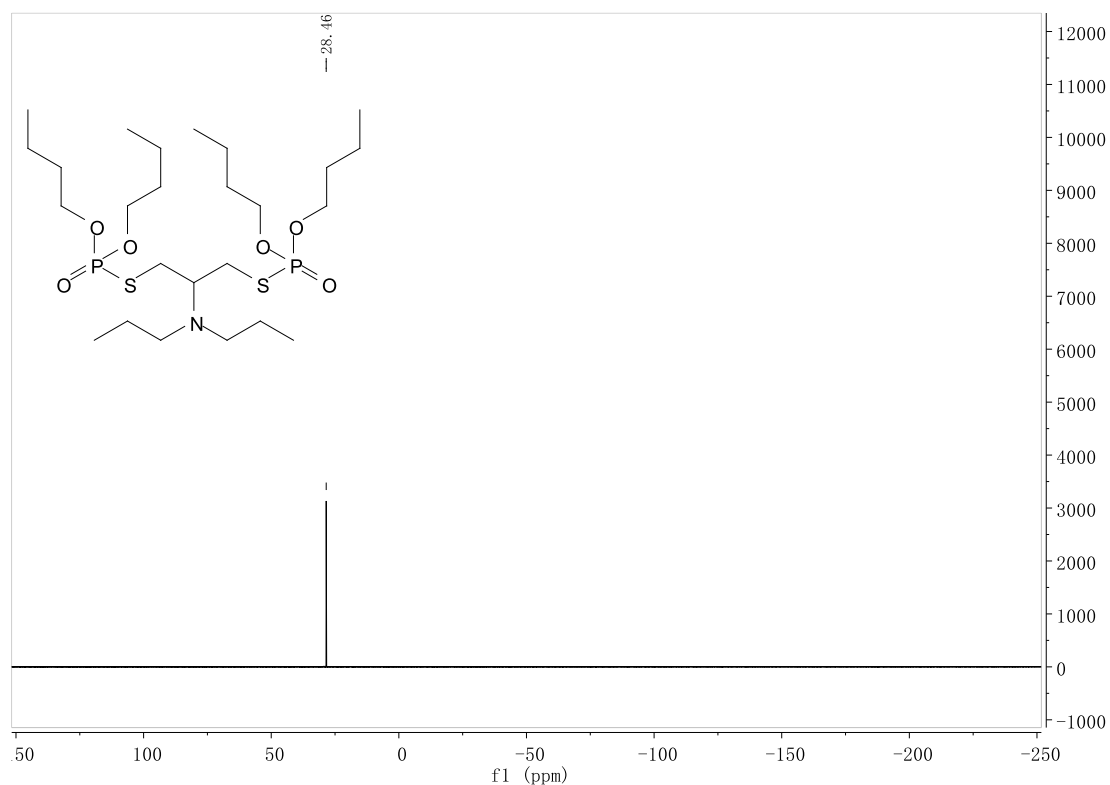


Figure S104. ^{31}P NMR of compound 8e.

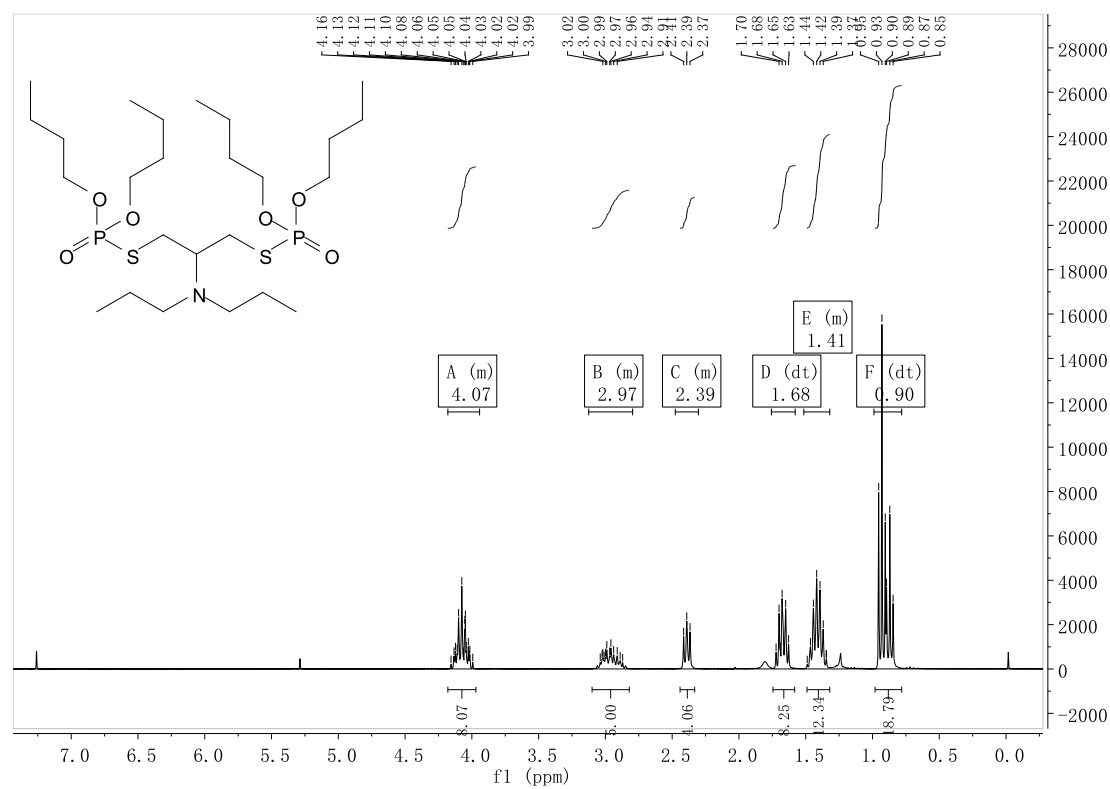


Figure S105. ^1H NMR of compound 8e.

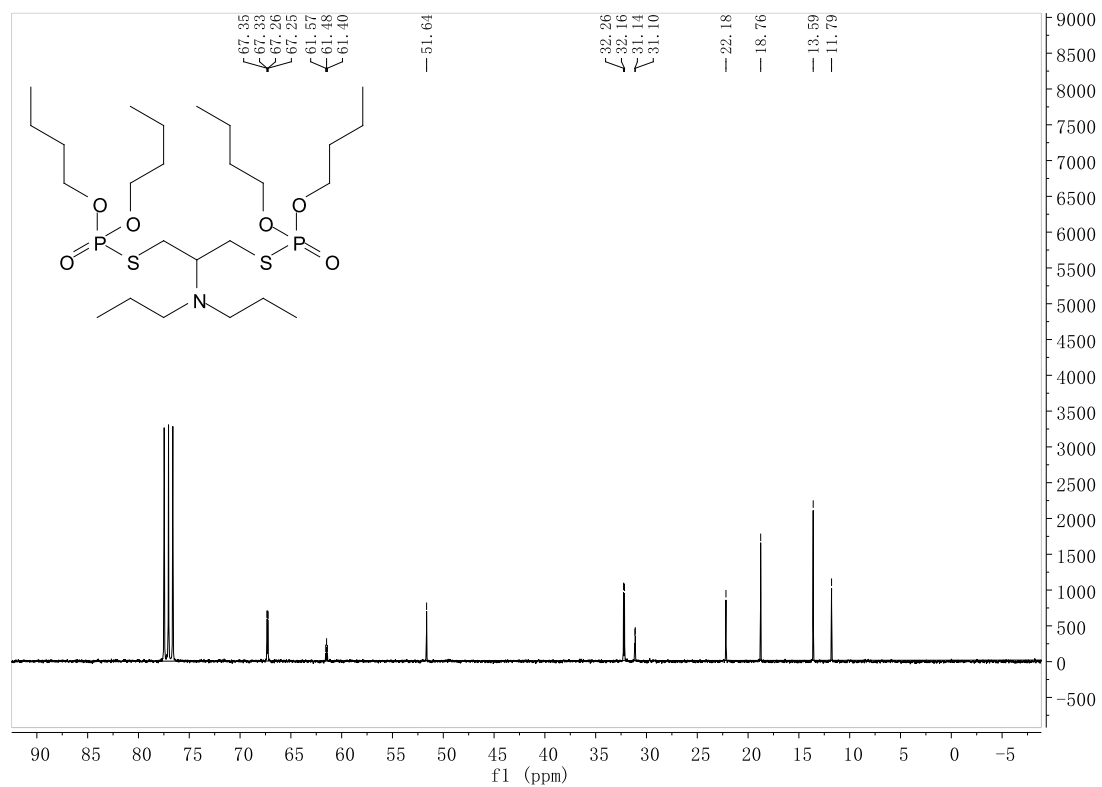


Figure S106. ^{13}C NMR of compound 8e.

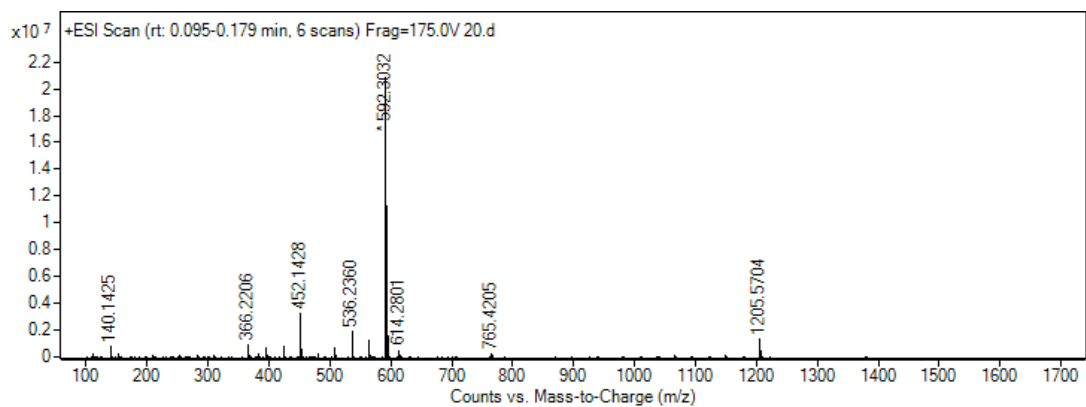


Figure S107. HRMS of compound 8e.

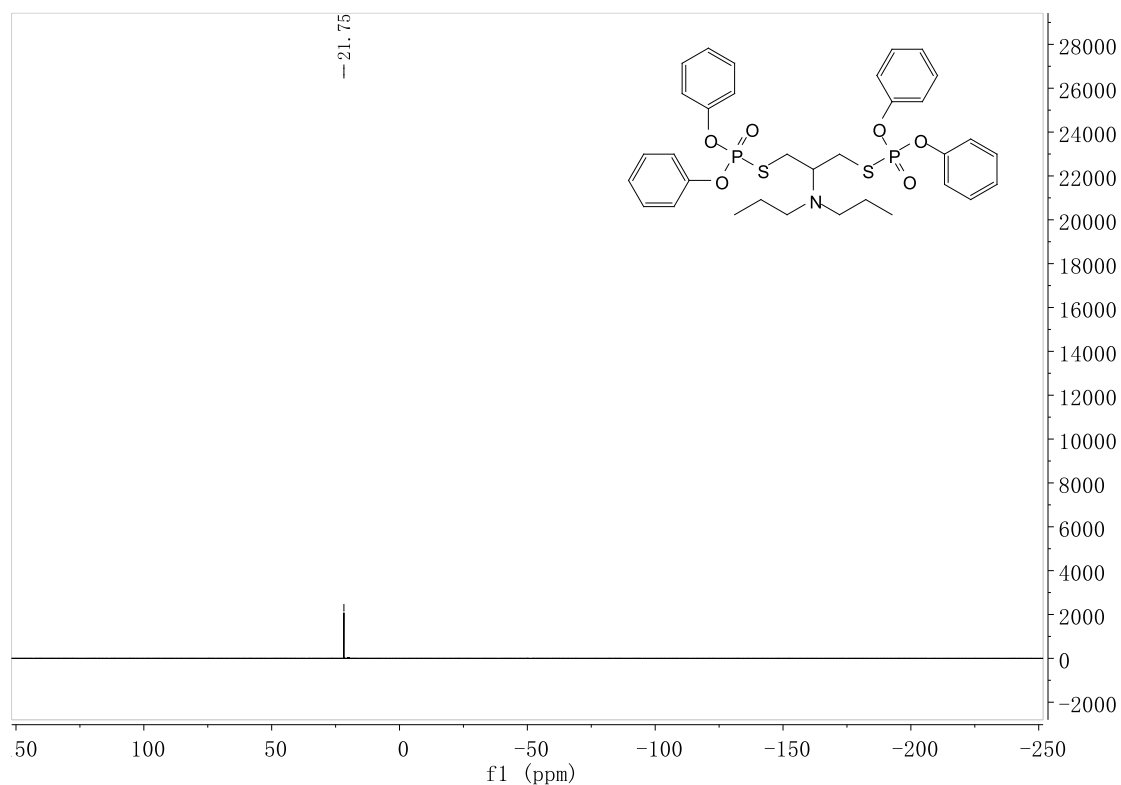


Figure S108. ^{31}P NMR of compound 8g.

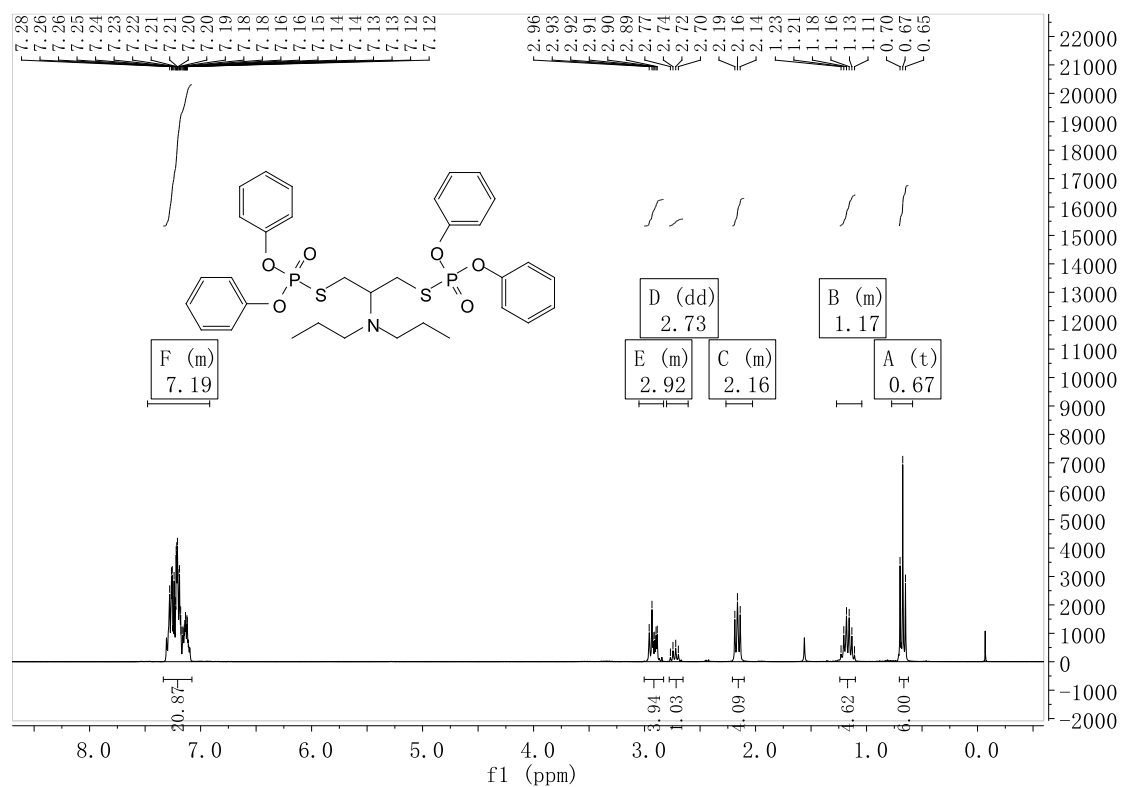


Figure S109. ^1H NMR of compound 8g.

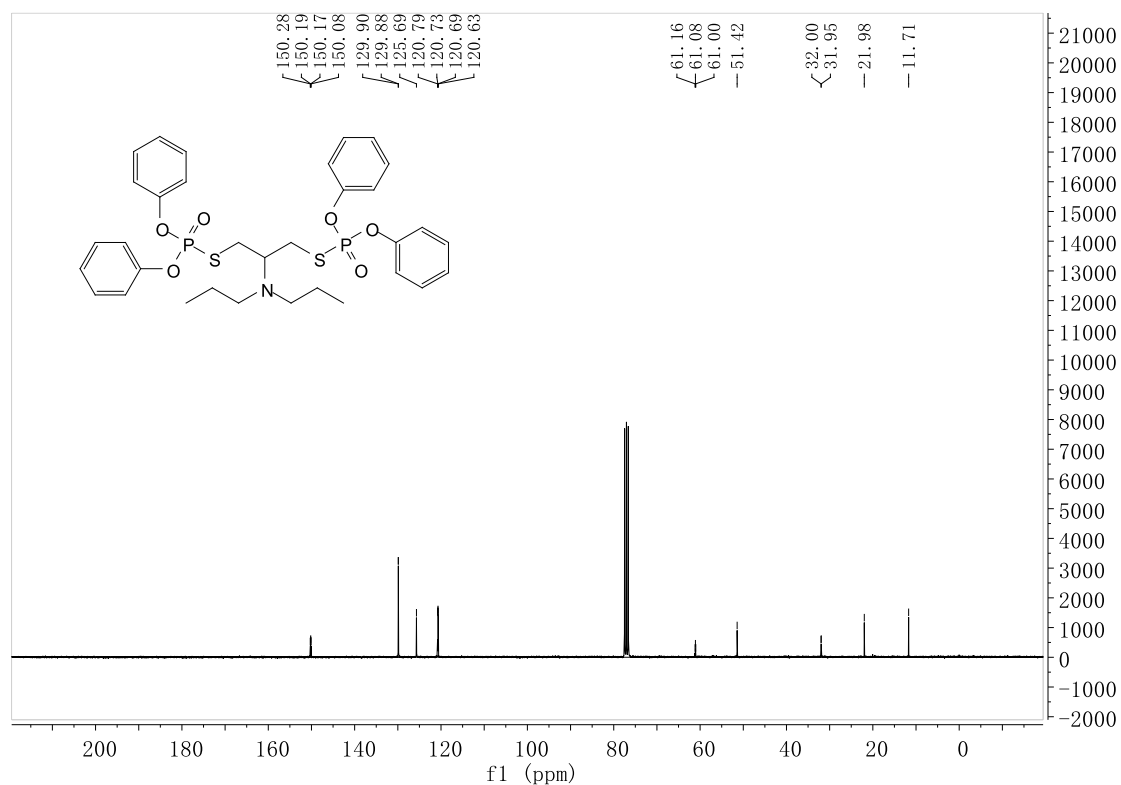


Figure S110. ^{13}C NMR of compound 8g.

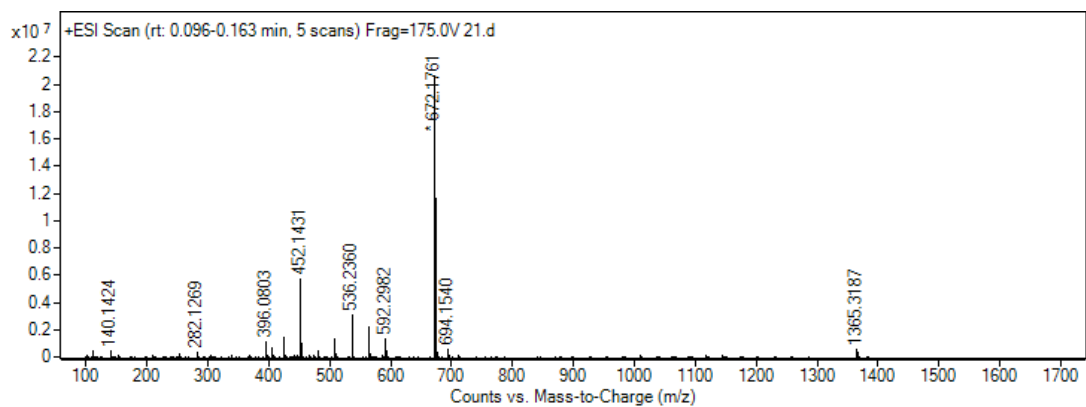


Figure S111. HRMS of compound 8g.

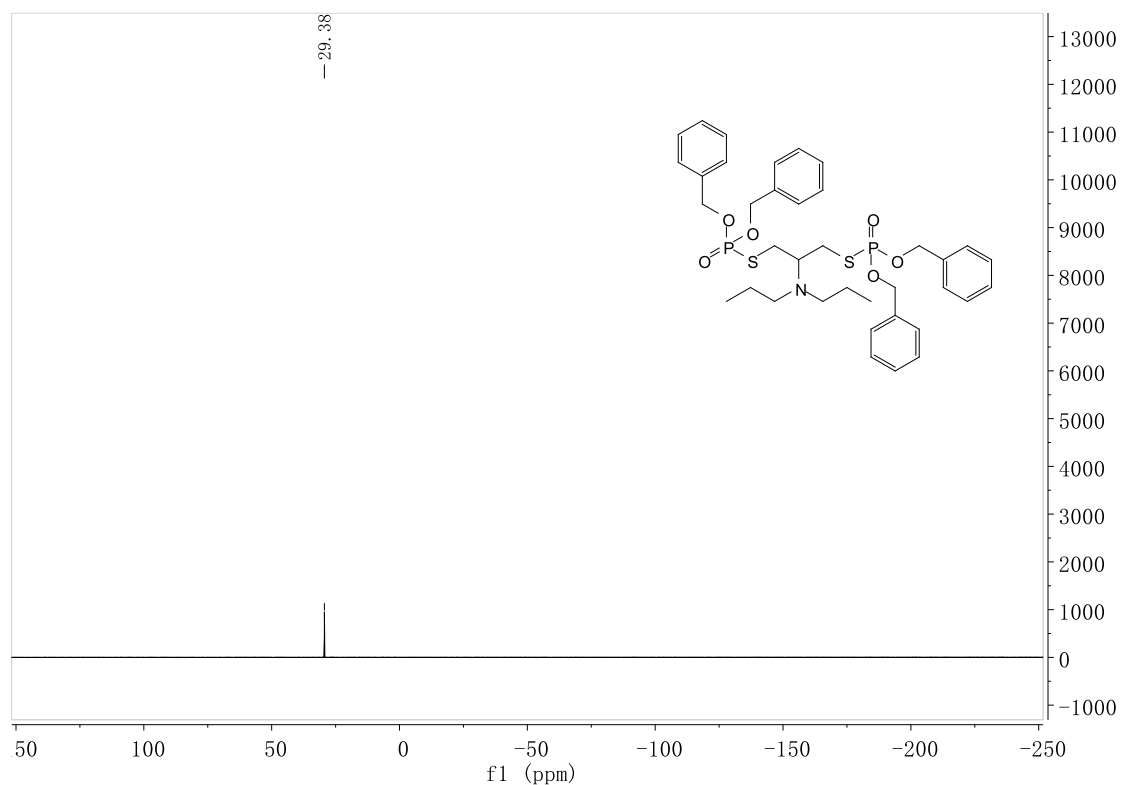


Figure S112. ^{31}P NMR of compound **8h**.

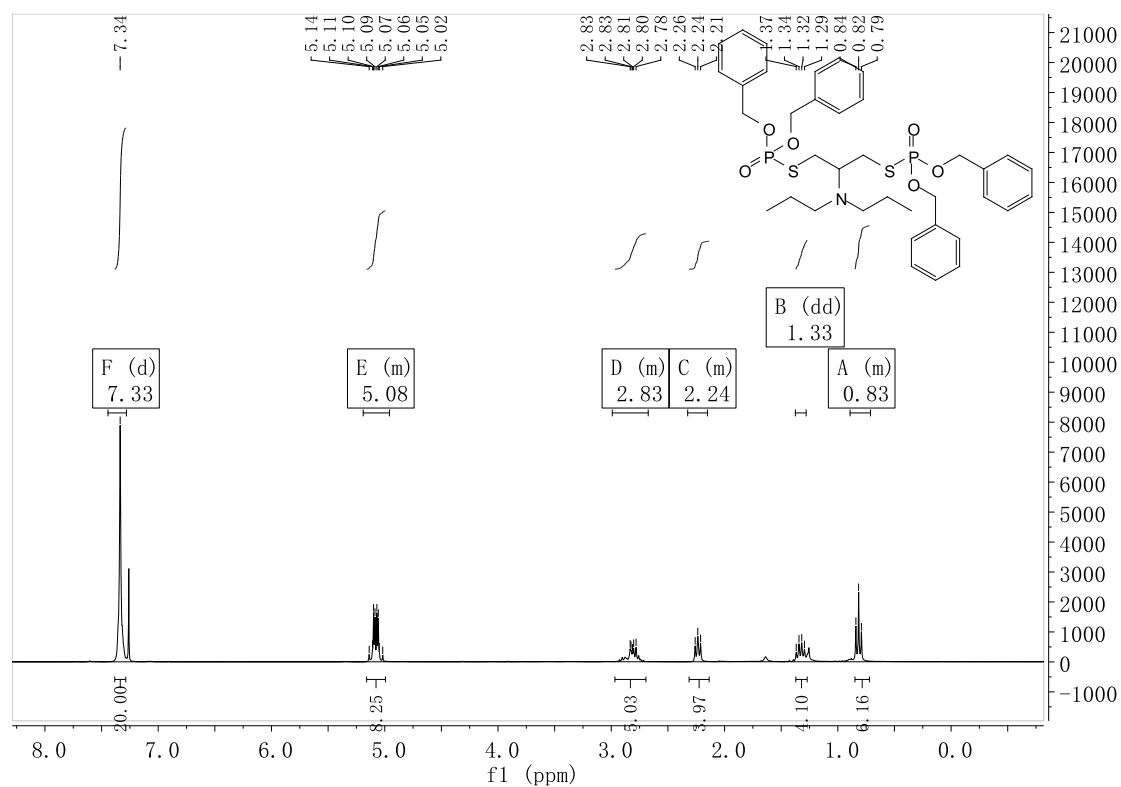


Figure S113. ^1H NMR of compound **8h**.

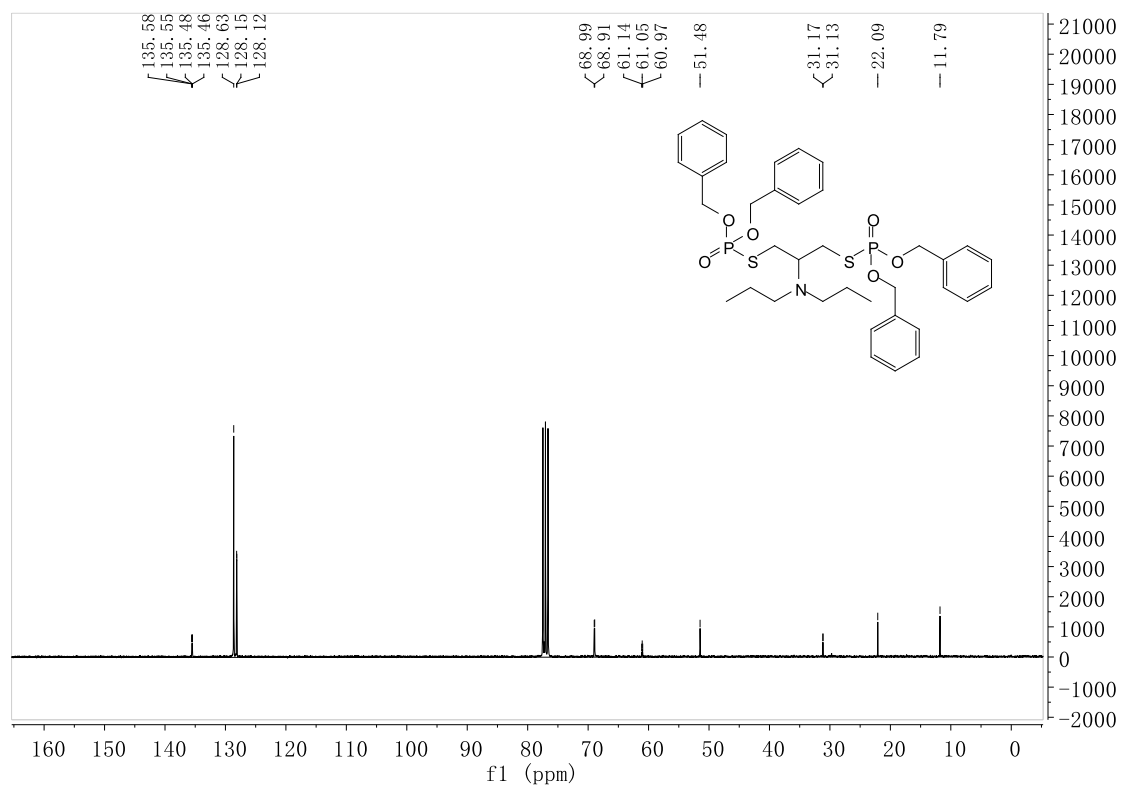


Figure S114. ^{13}C NMR of compound 8h.

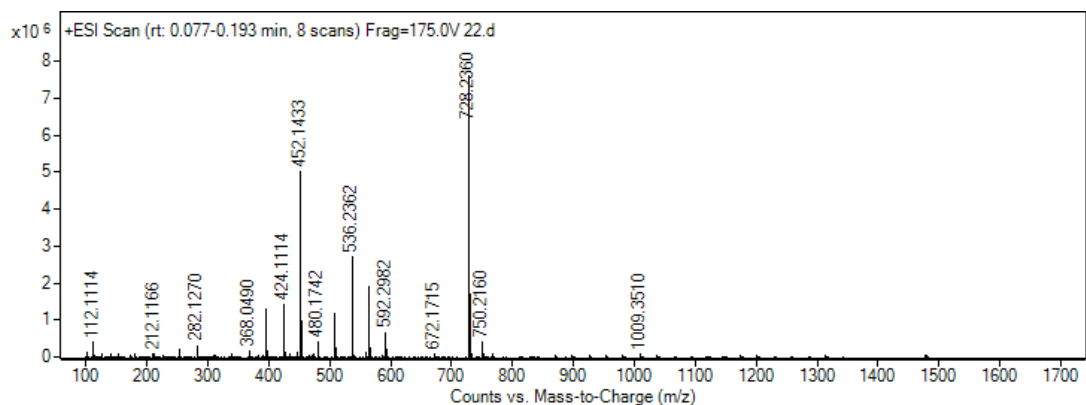


Figure S115. HRMS of compound 8h.

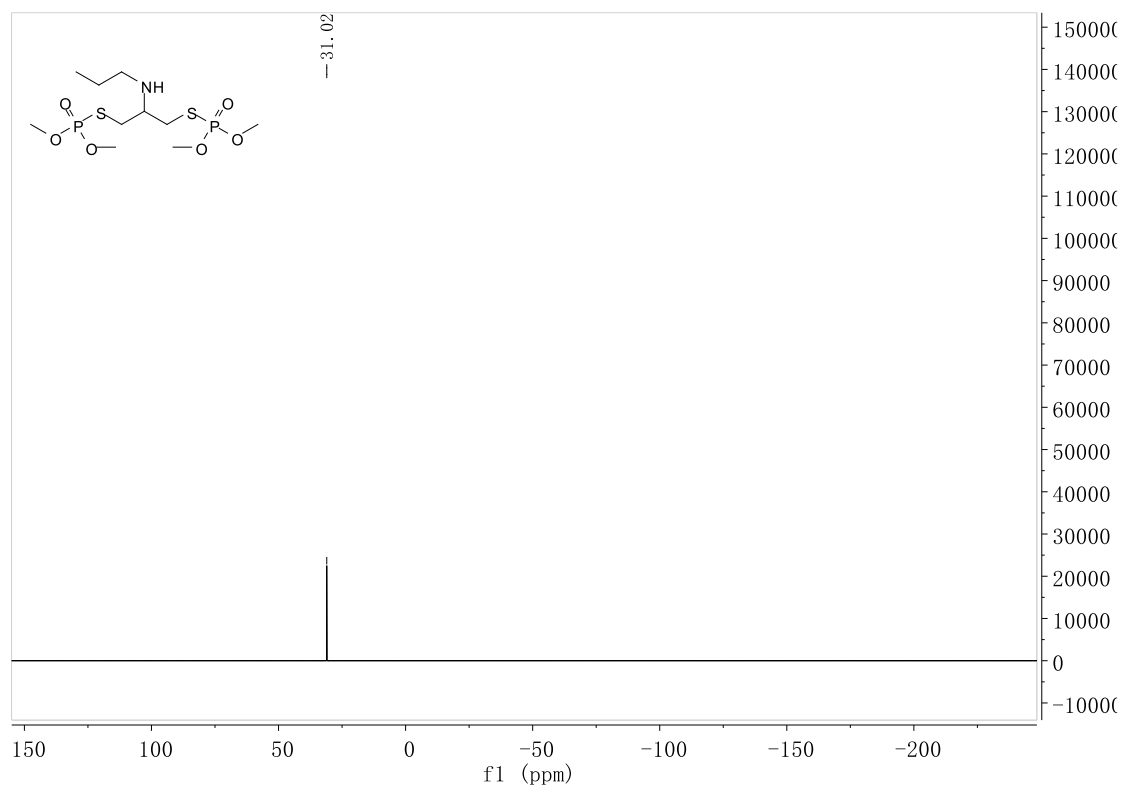


Figure S116. ^{31}P NMR of compound 9a.

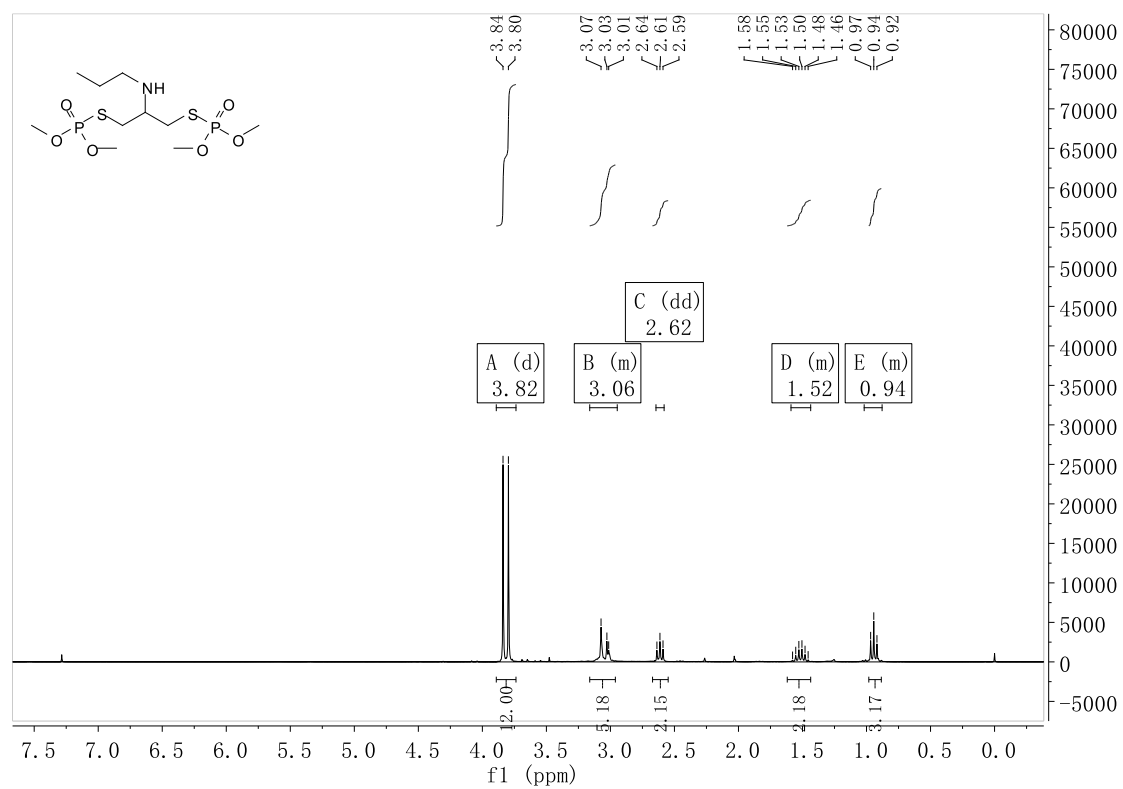


Figure S117. ^1H NMR of compound 9a.

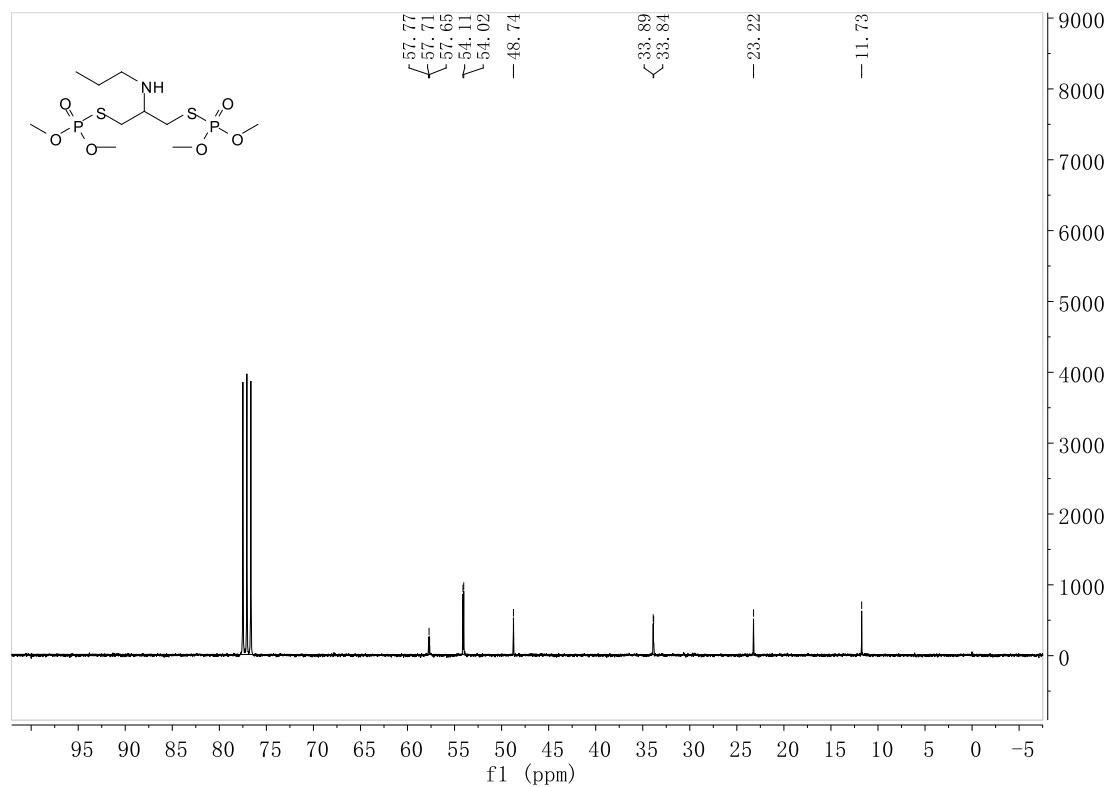


Figure S118. ¹³C NMR of compound 9a.

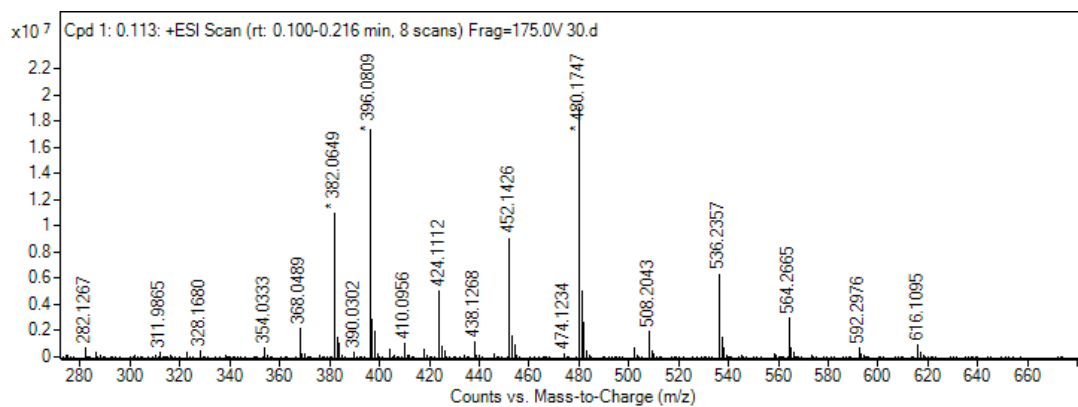


Figure S119. HRMS of compound 9a.

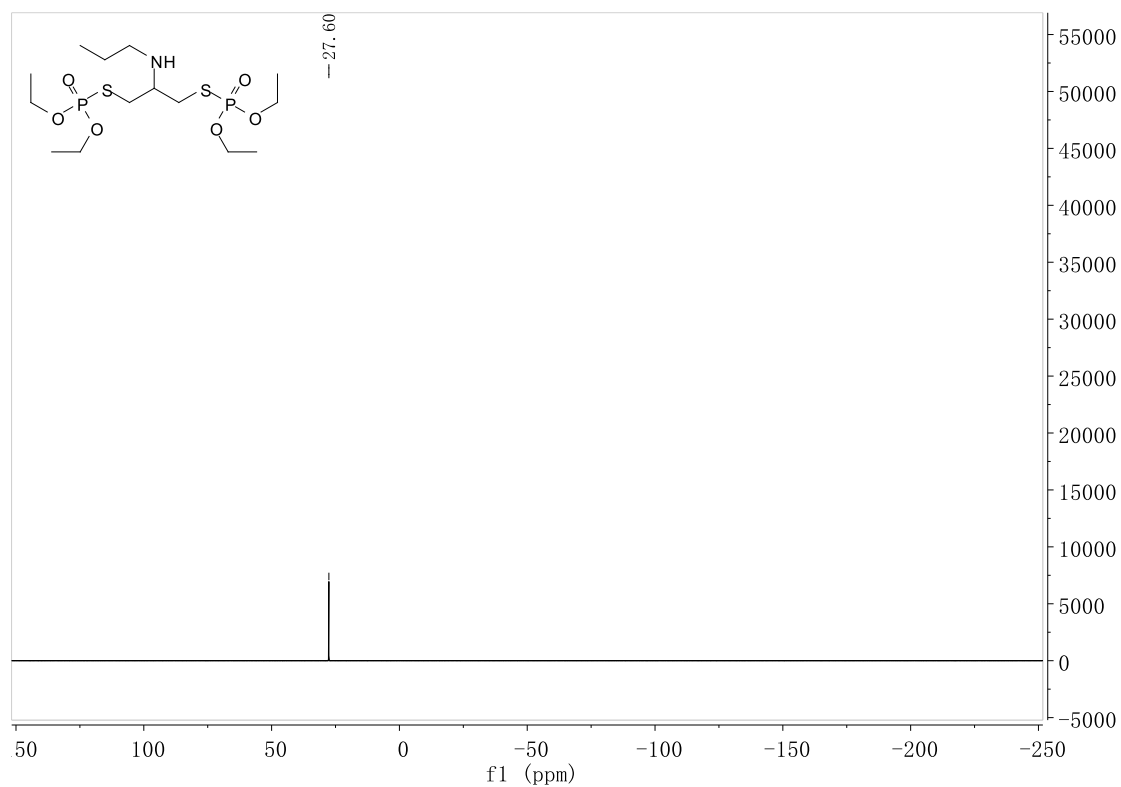


Figure S120. ^{31}P NMR of compound 9b.

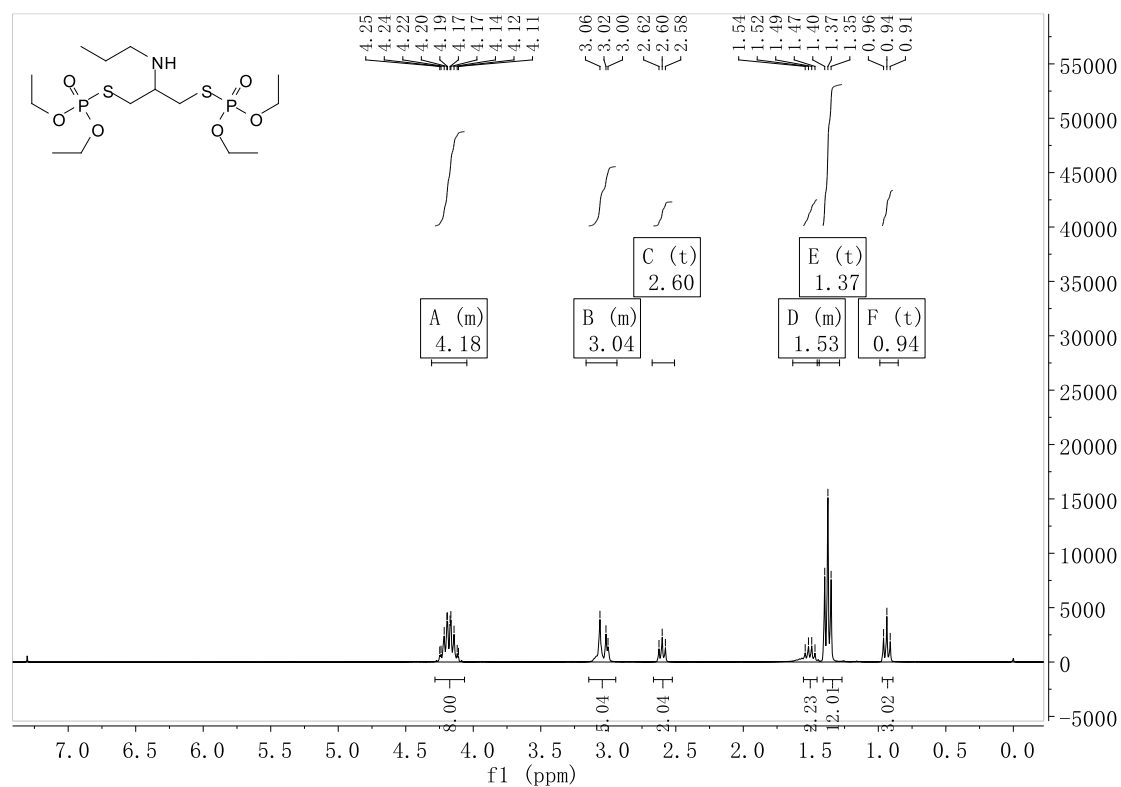


Figure S121. ^1H NMR of compound 9b.

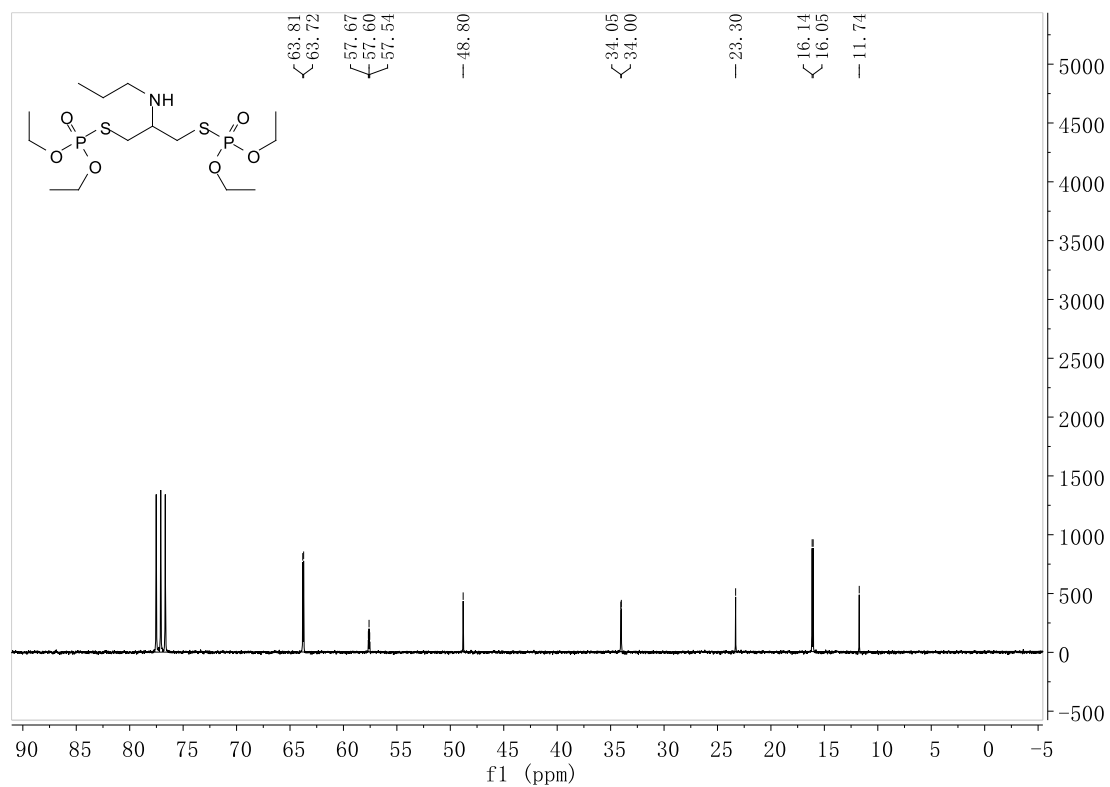


Figure S122. ¹³C NMR of compound 9b.

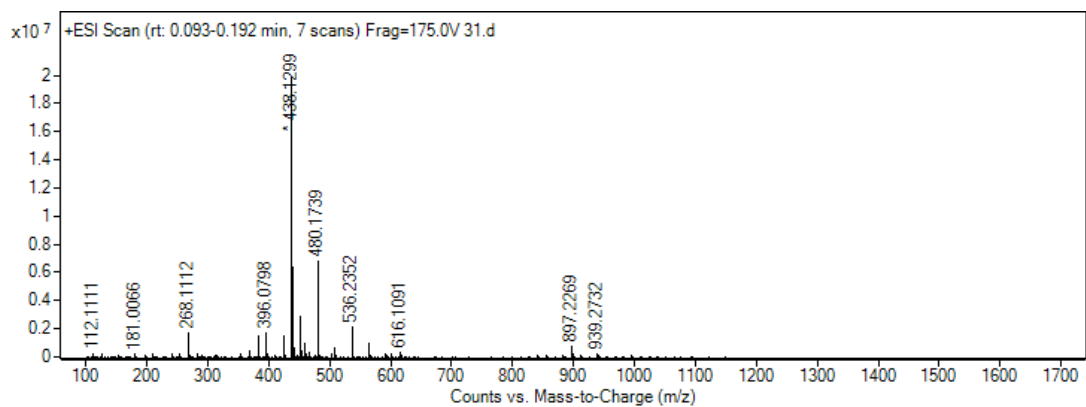


Figure S123. HRMS of compound 9b.

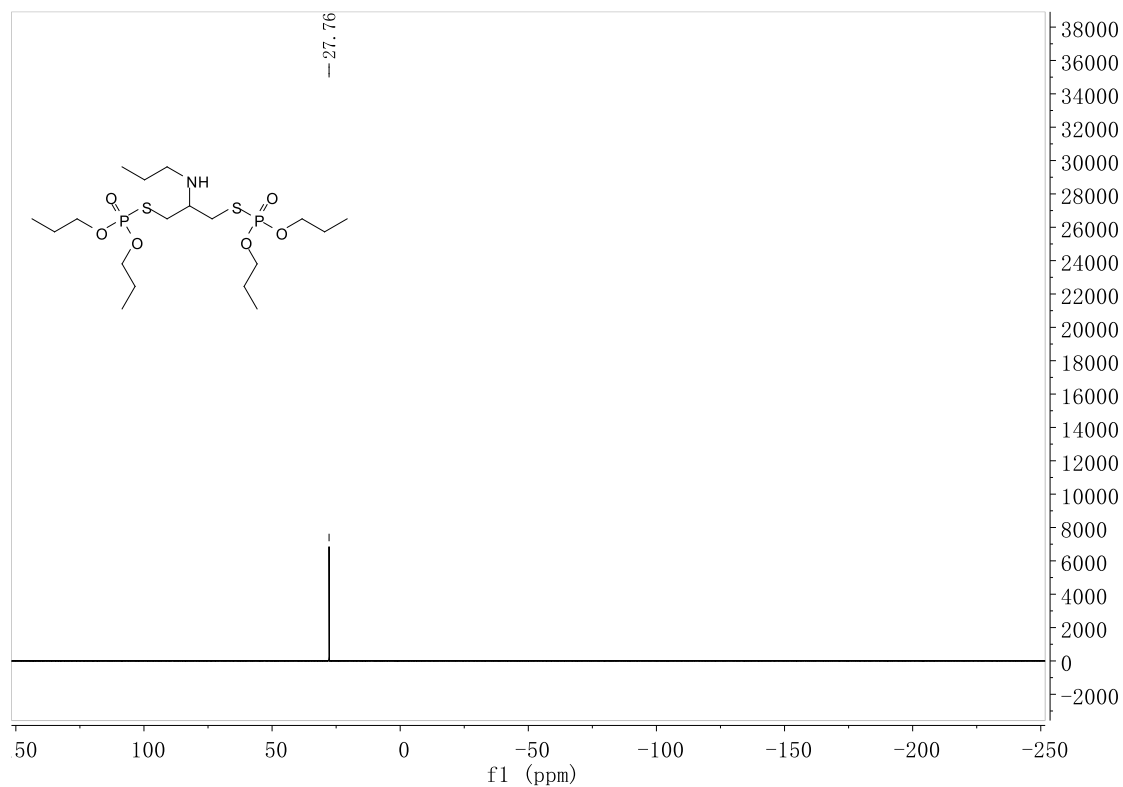


Figure S124. ³¹P NMR of compound 9c.

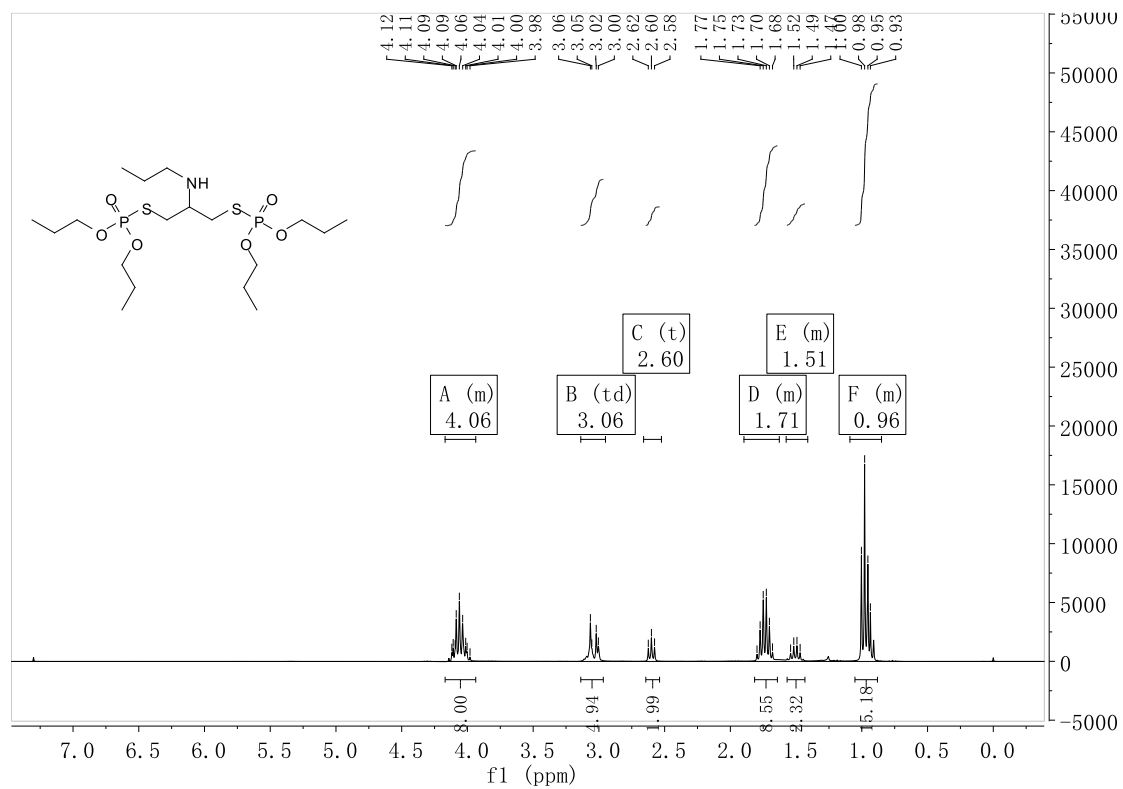


Figure S125. ¹H NMR of compound 9c.

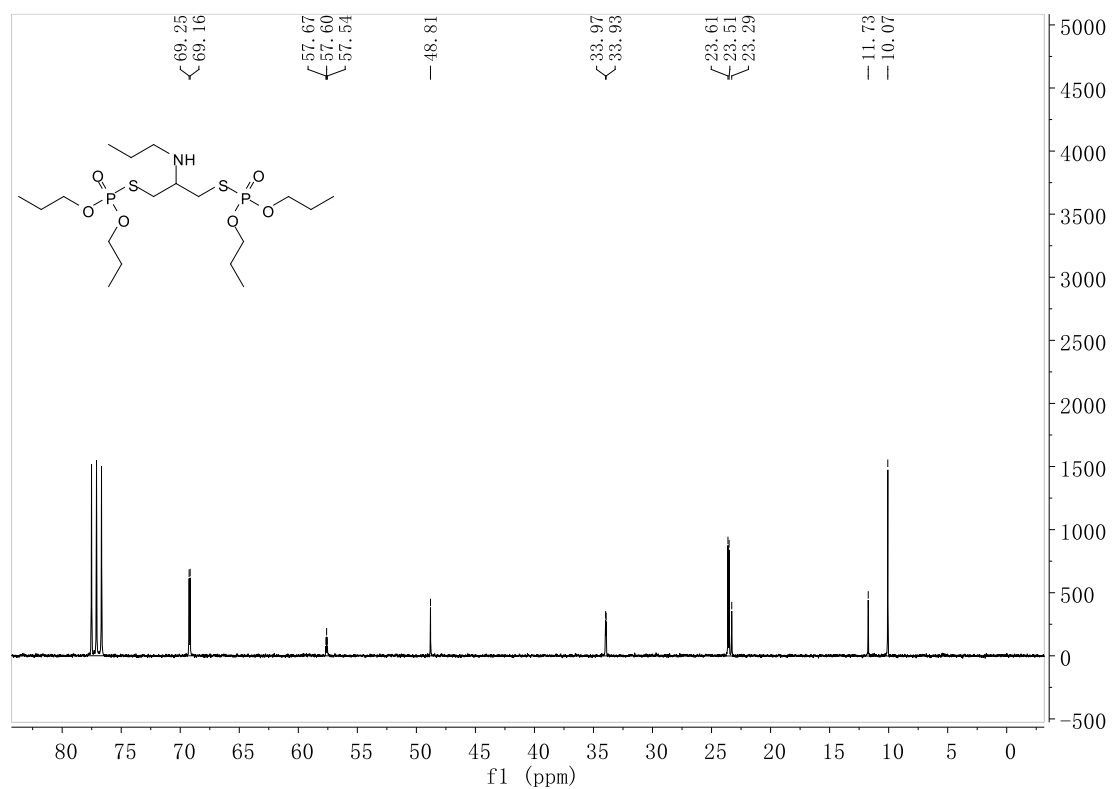


Figure S126. ^{13}C NMR of compound **9c**.

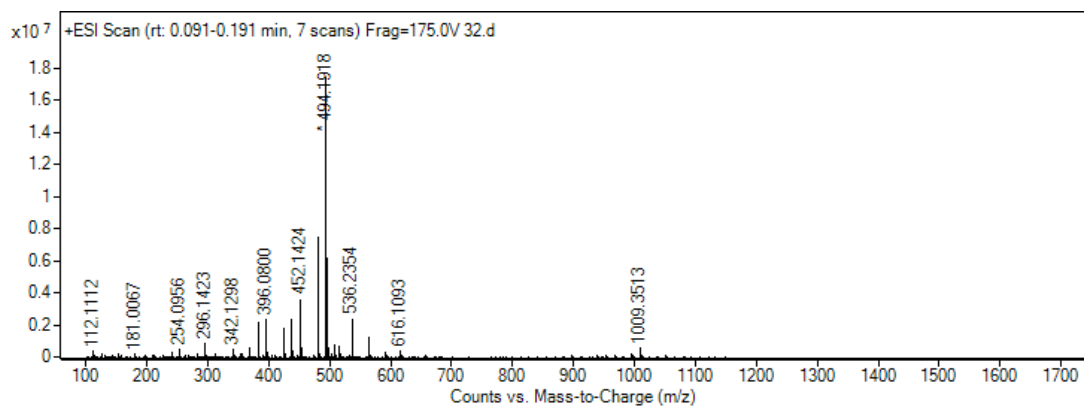


Figure S127. HRMS of compound **9c**.

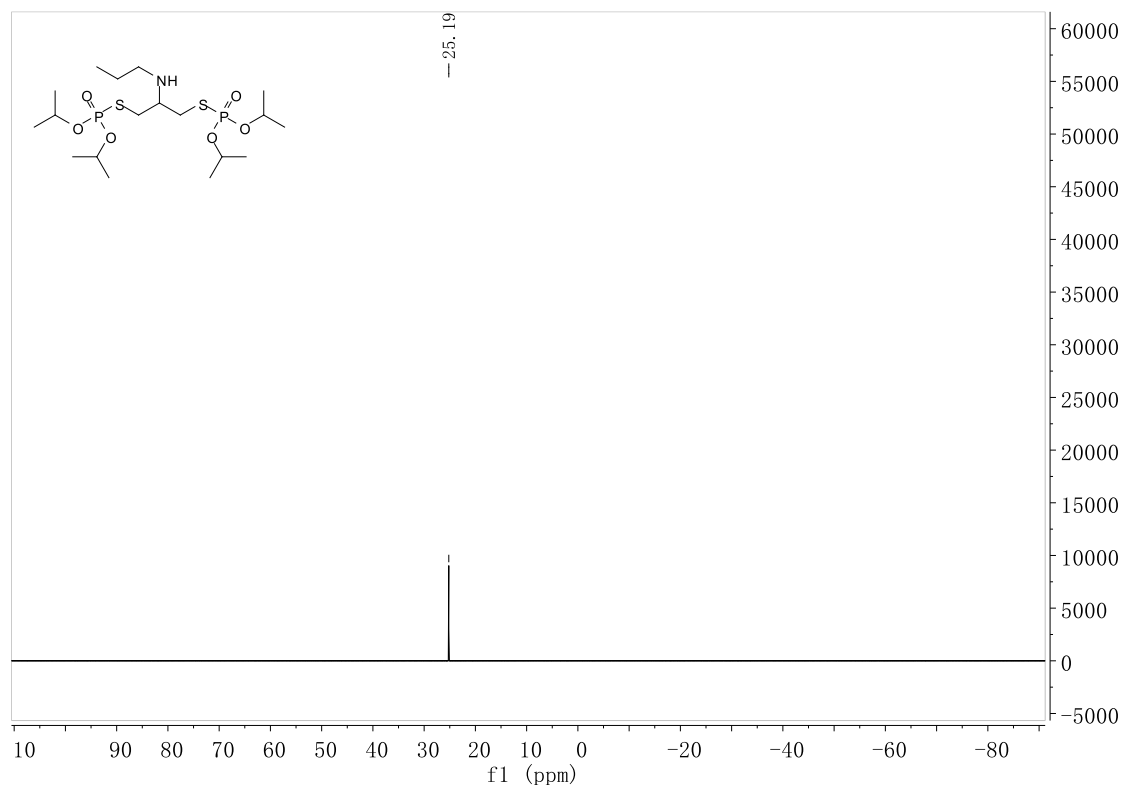


Figure S128. ^{31}P NMR of compound 9d.

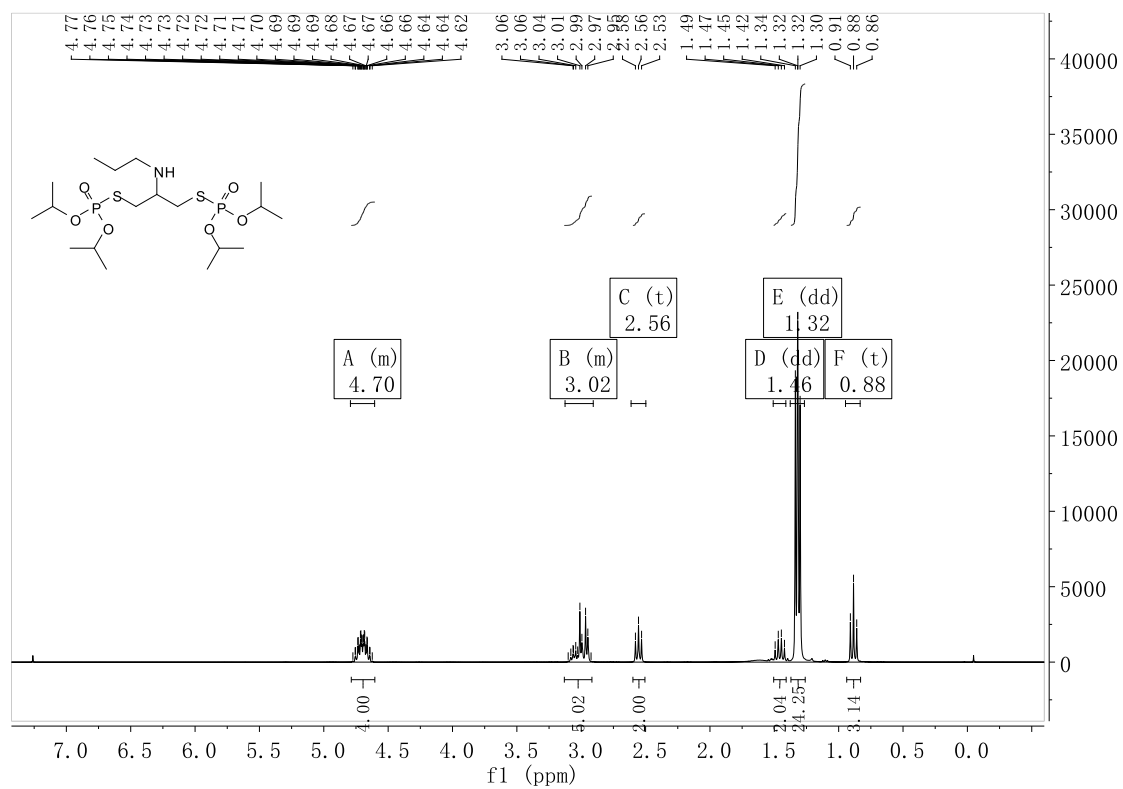


Figure S129. ^1H NMR of compound 9d.

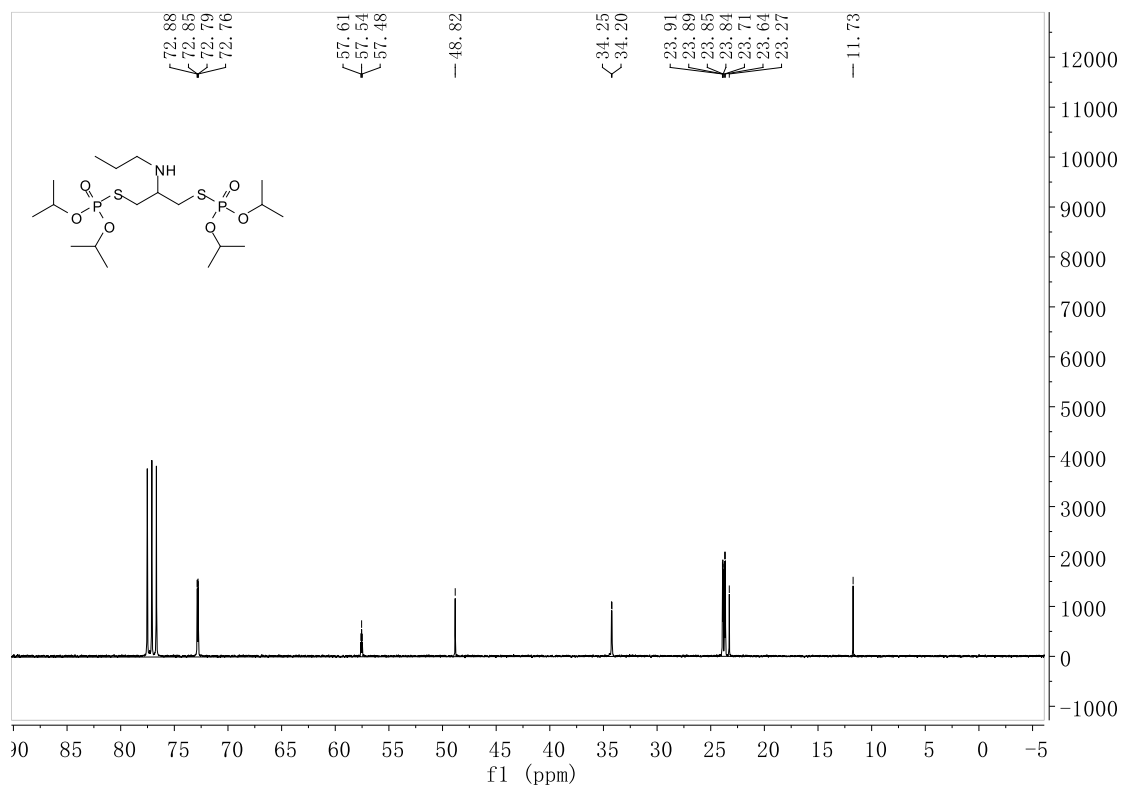


Figure S130. ¹³C NMR of compound 9d.

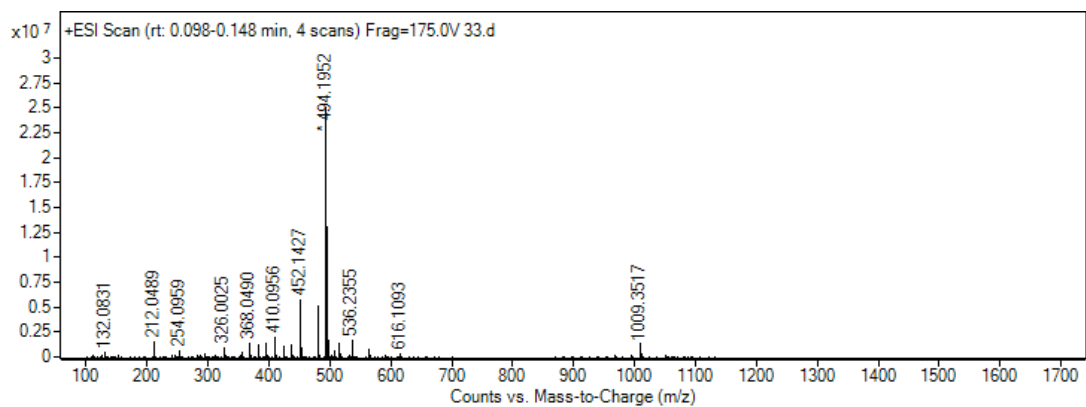


Figure S131. HRMS of compound 9d.

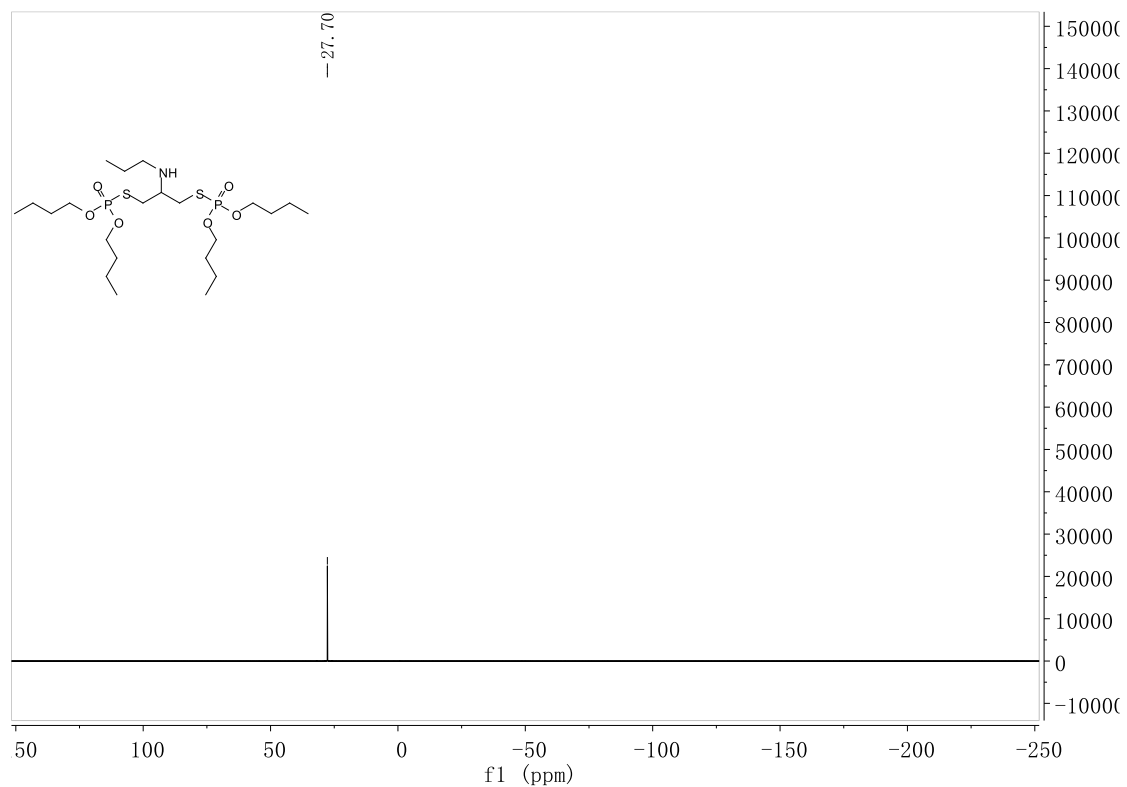


Figure S132. ^{31}P NMR of compound 9e.

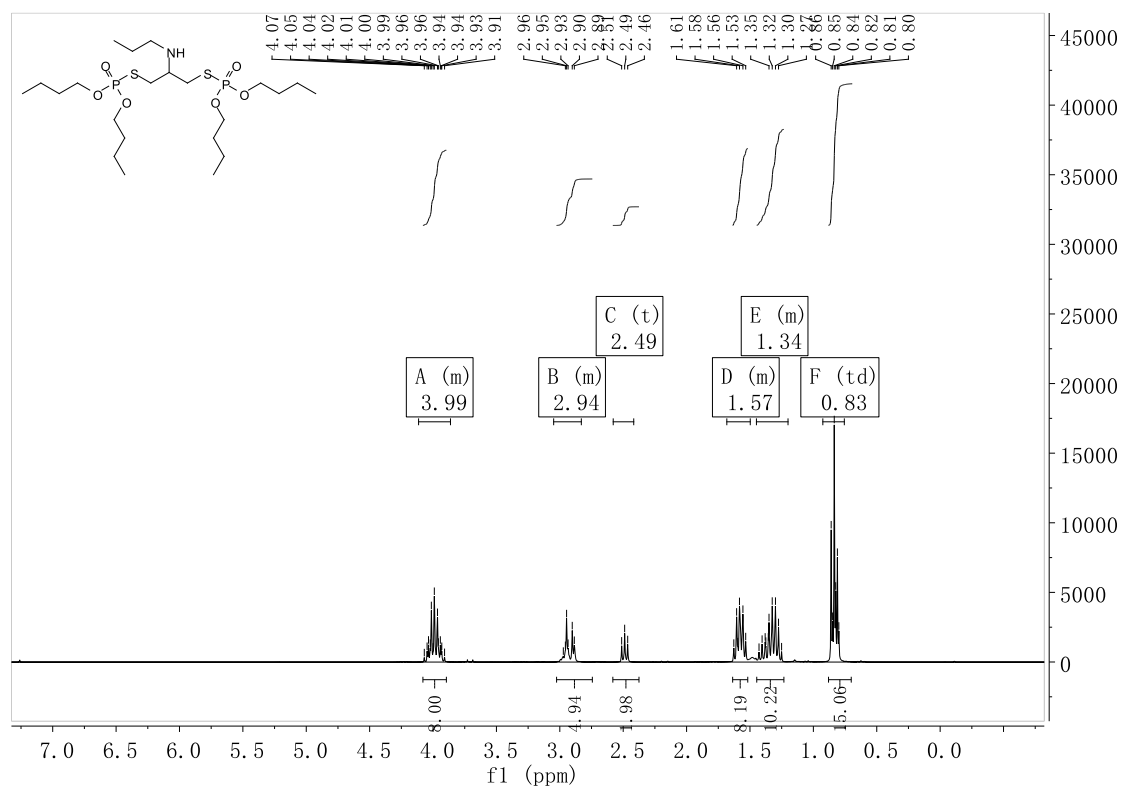


Figure S133. ^1H NMR of compound 9e.

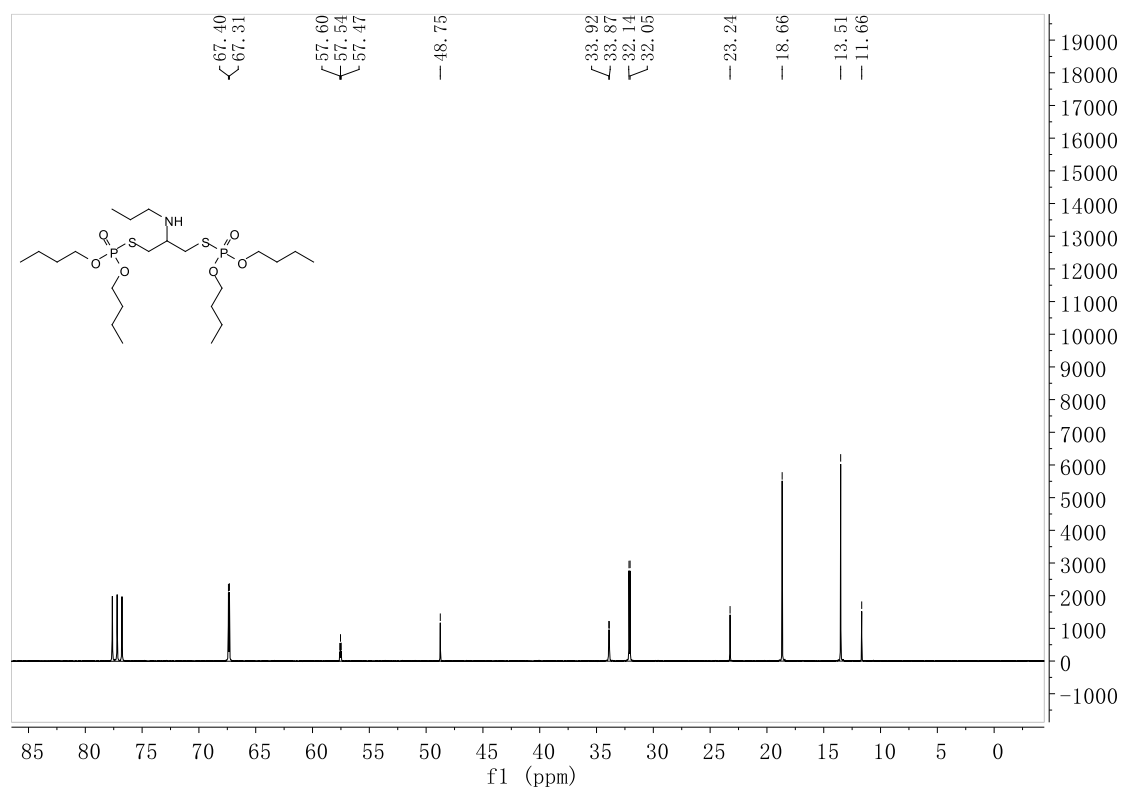


Figure S134. ^{13}C NMR of compound 9e.

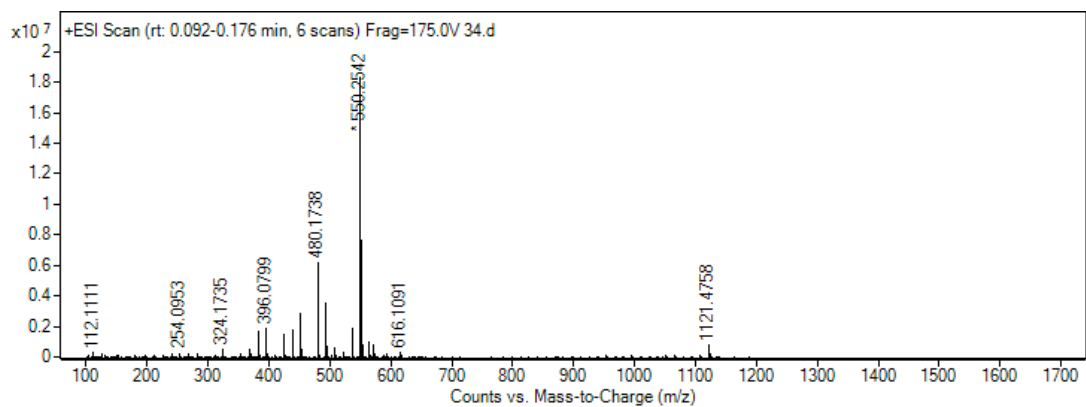


Figure S135. HRMS of compound 9e.

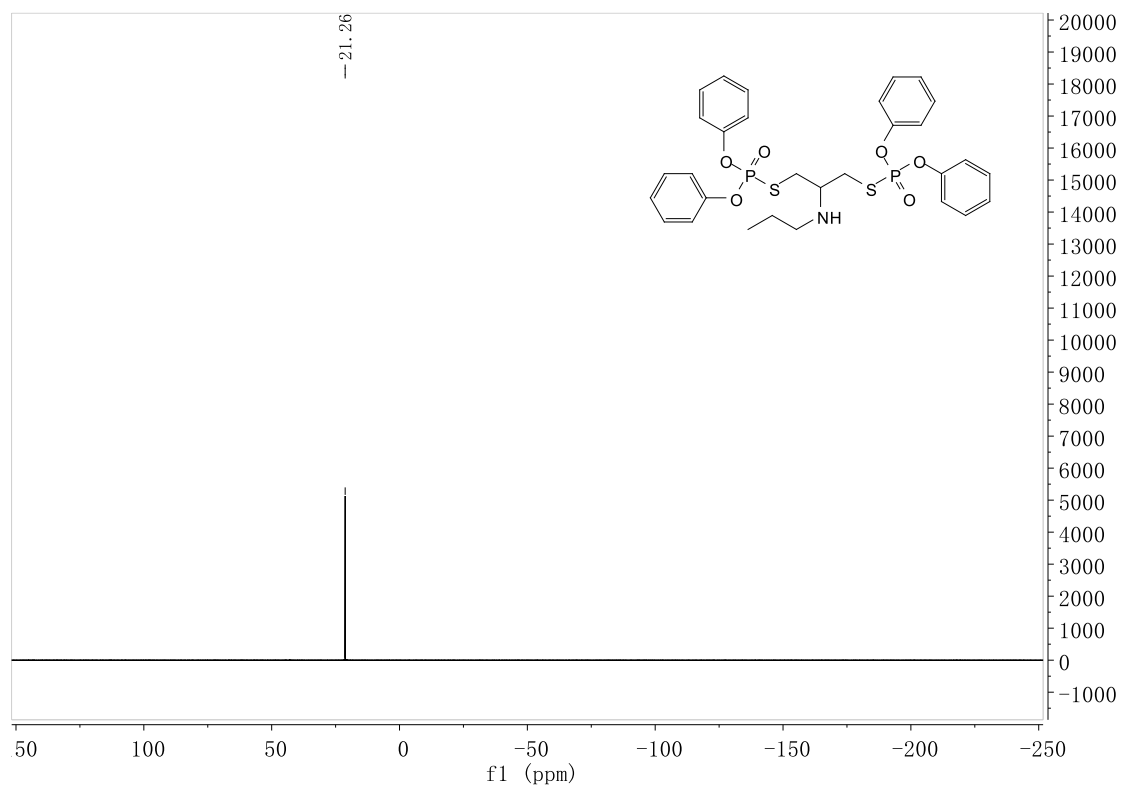


Figure S136. ^{31}P NMR of compound 9g.

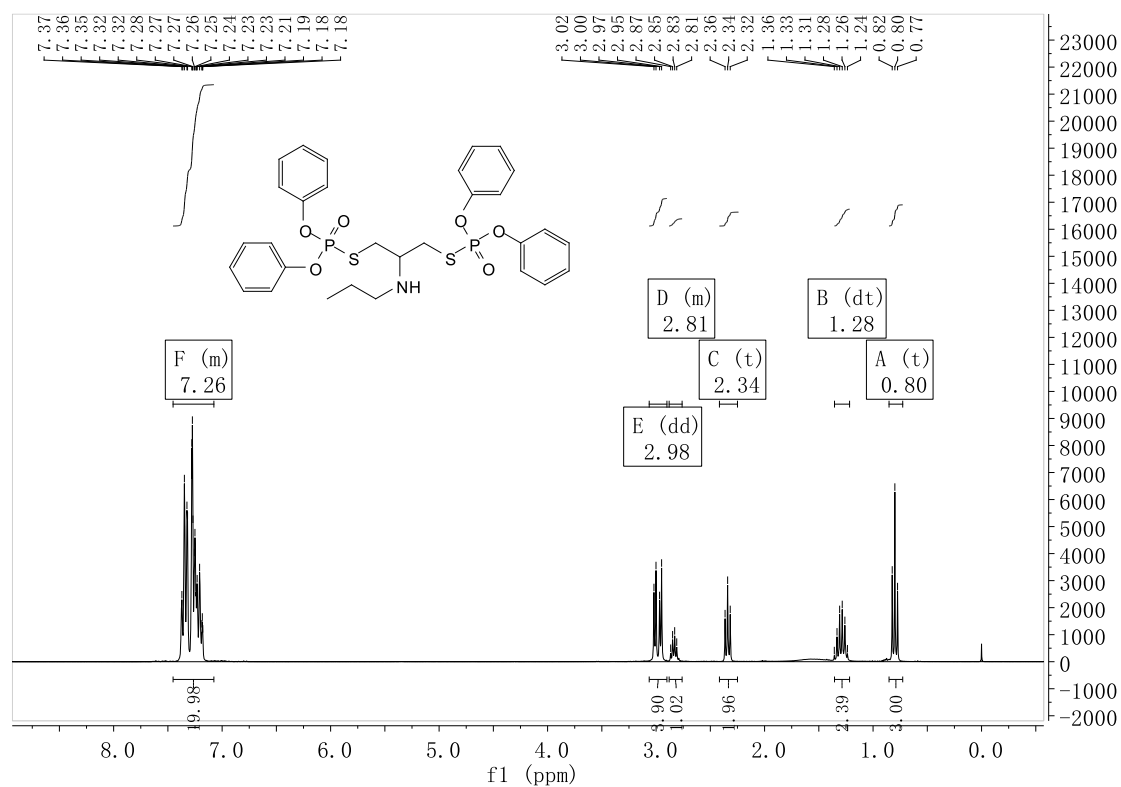


Figure S137. ^1H NMR of compound 9g.

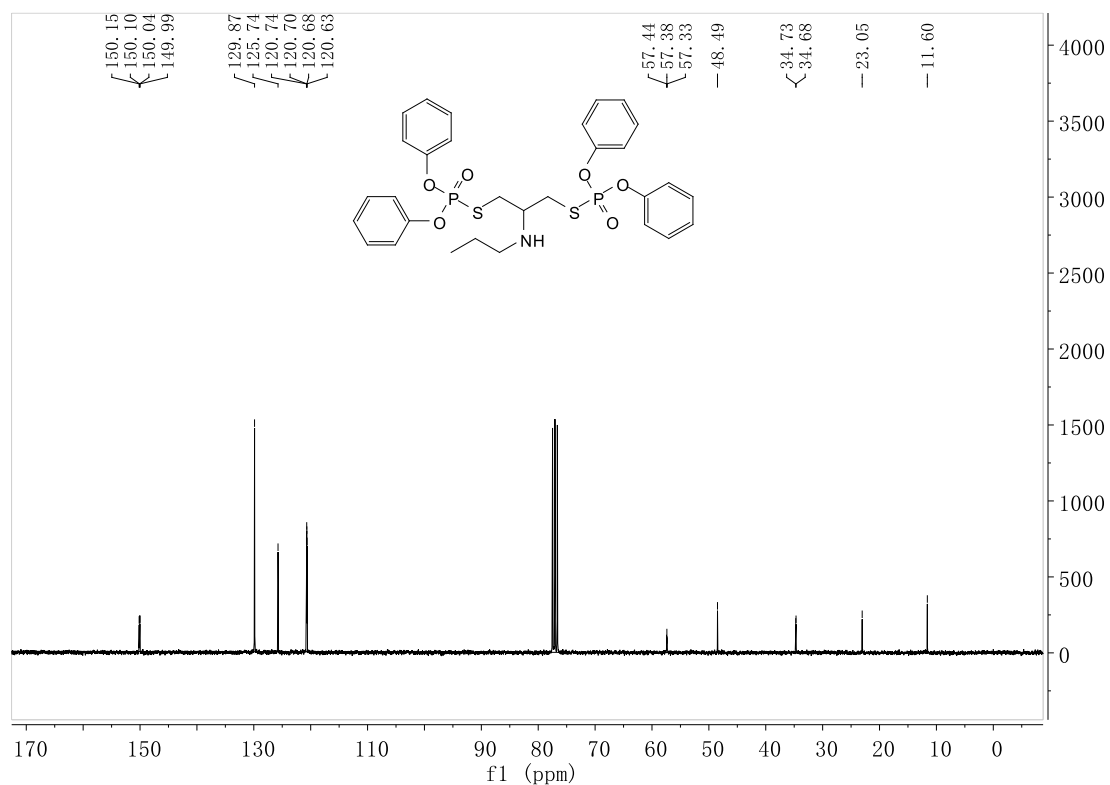


Figure S138. ¹³C NMR of compound 9g.

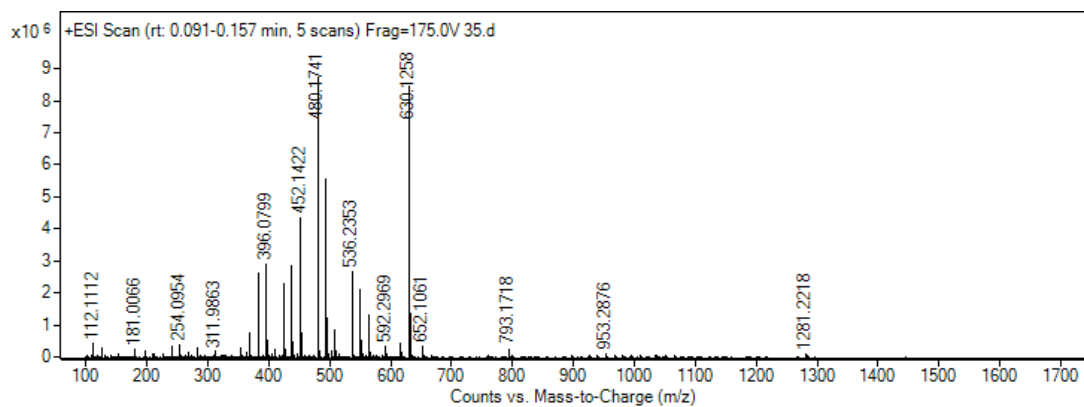


Figure S139. HRMS of compound 9g.

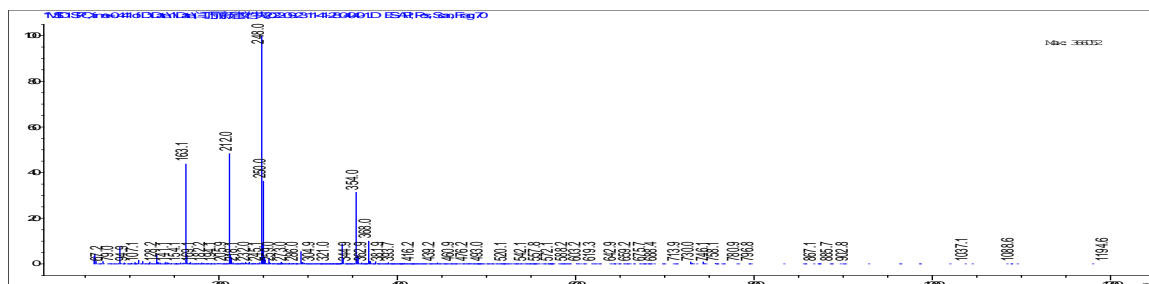


Figure S140. The mass spectrum of 5a reaction solution.

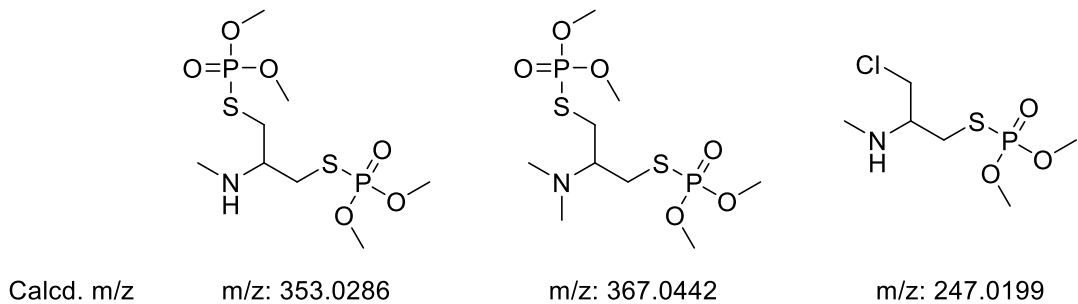


Figure S141. The calculated m/z of **5a** and by-products.

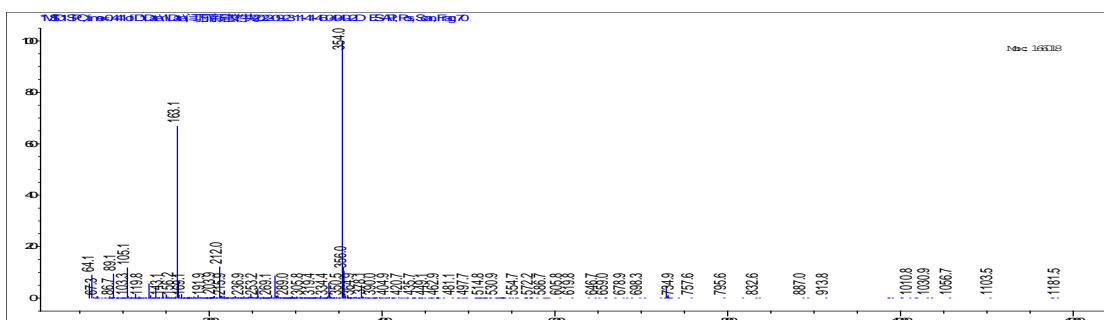


Figure S142. Mass spectrometry after purification of **5a**.

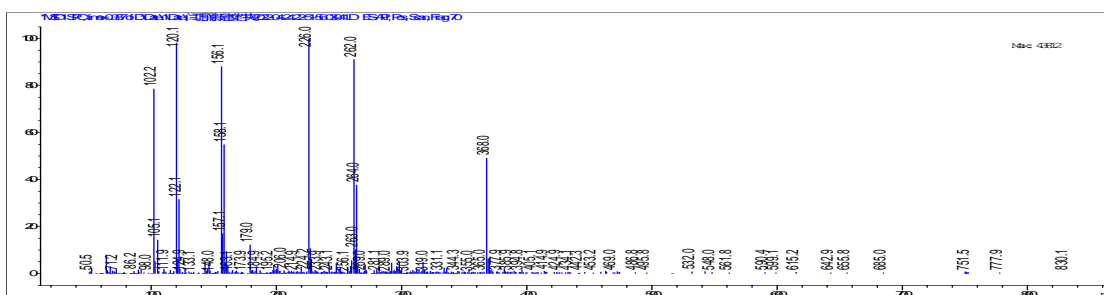


Figure S143. The mass spectrum of **7a** reaction solution.

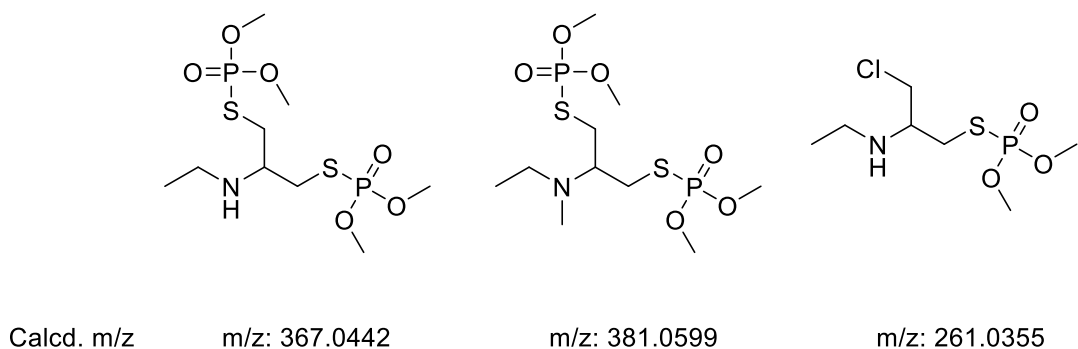


Figure S144. The calculated m/z of **7a** and by-products.

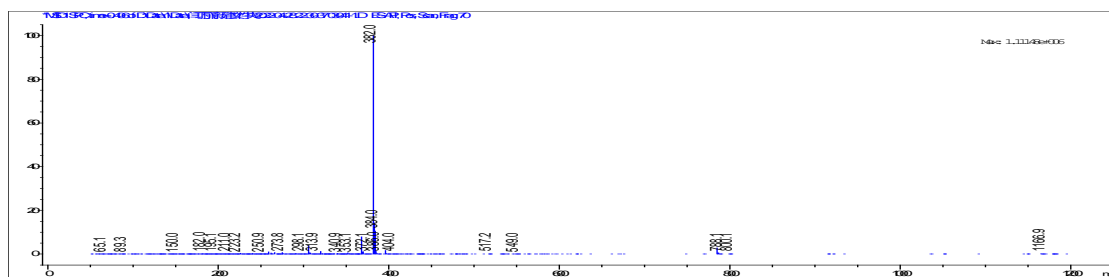


Figure S145. Mass spectrometry of converted product of **7a** during purification.

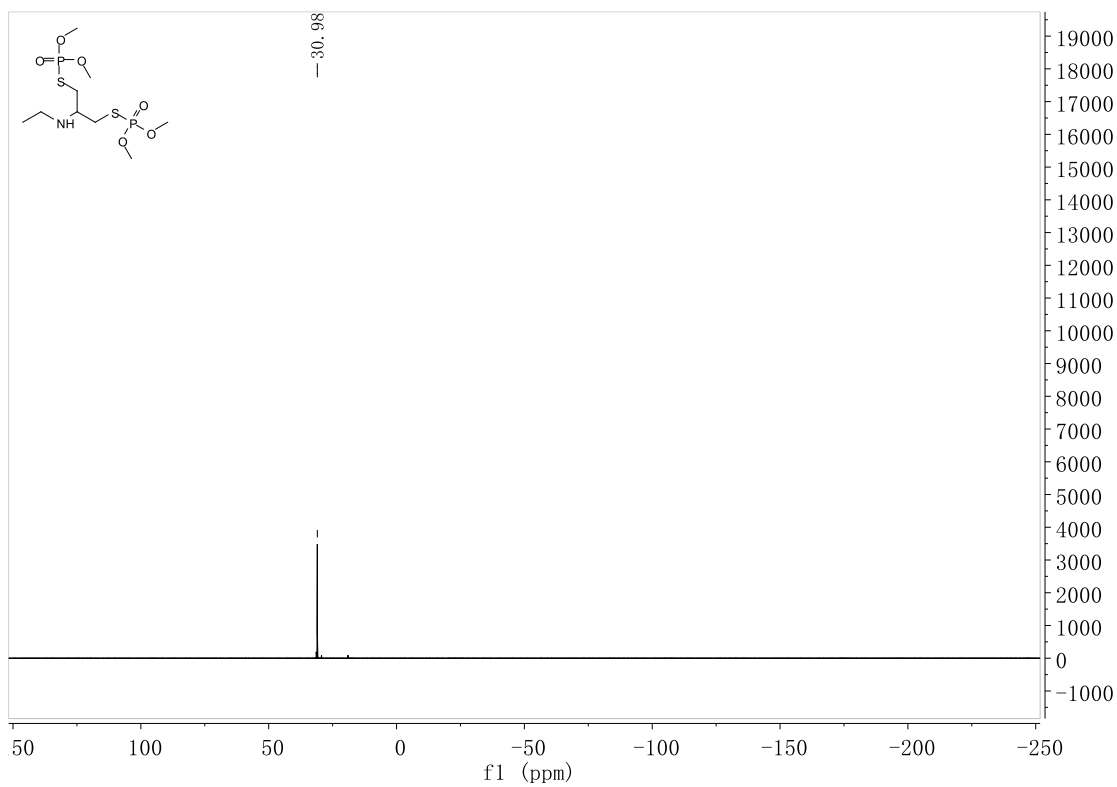


Figure S146. ^{31}P NMR of compound **7a**.

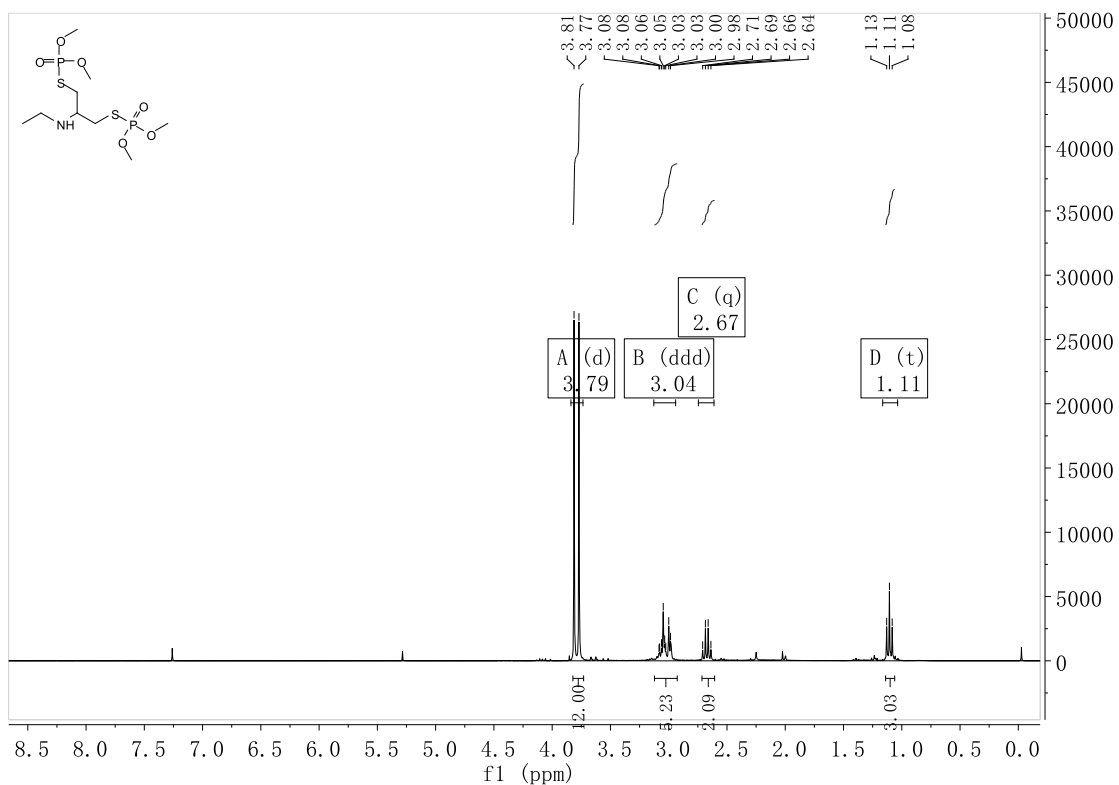


Figure S147. ^1H NMR of compound **7a** (with dichloromethane in compound).

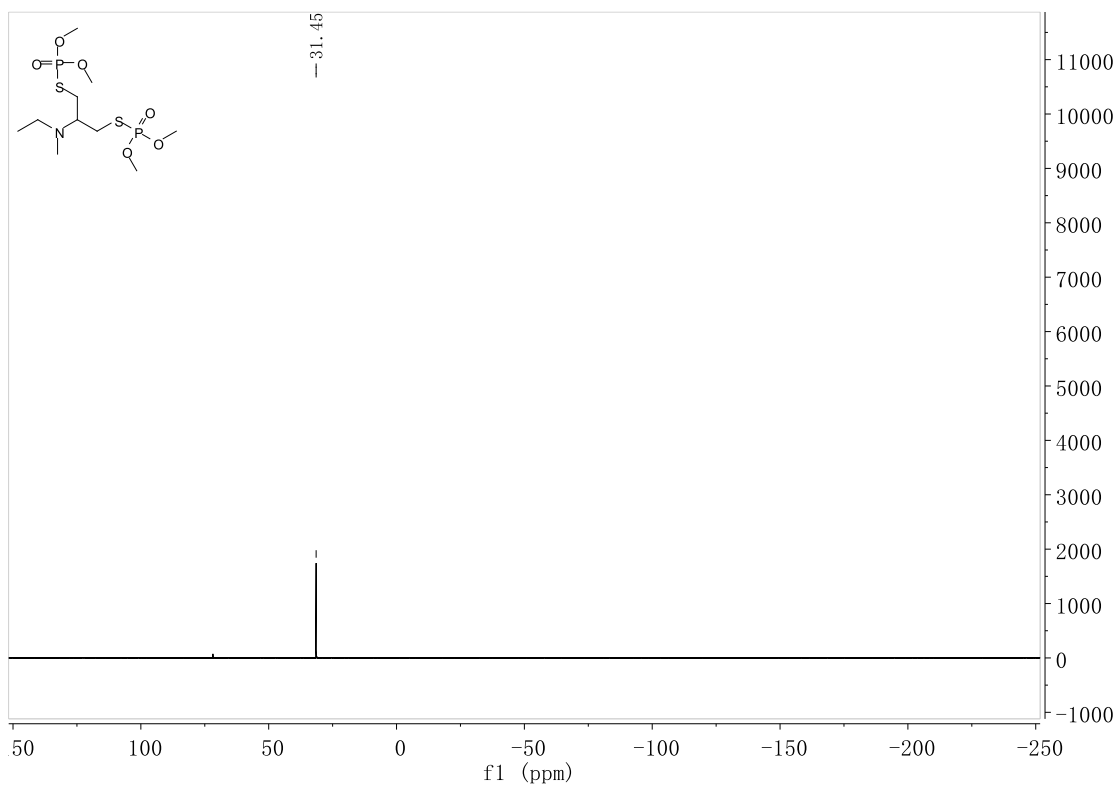


Figure S148. ^{31}P NMR of converted product of **7a**.

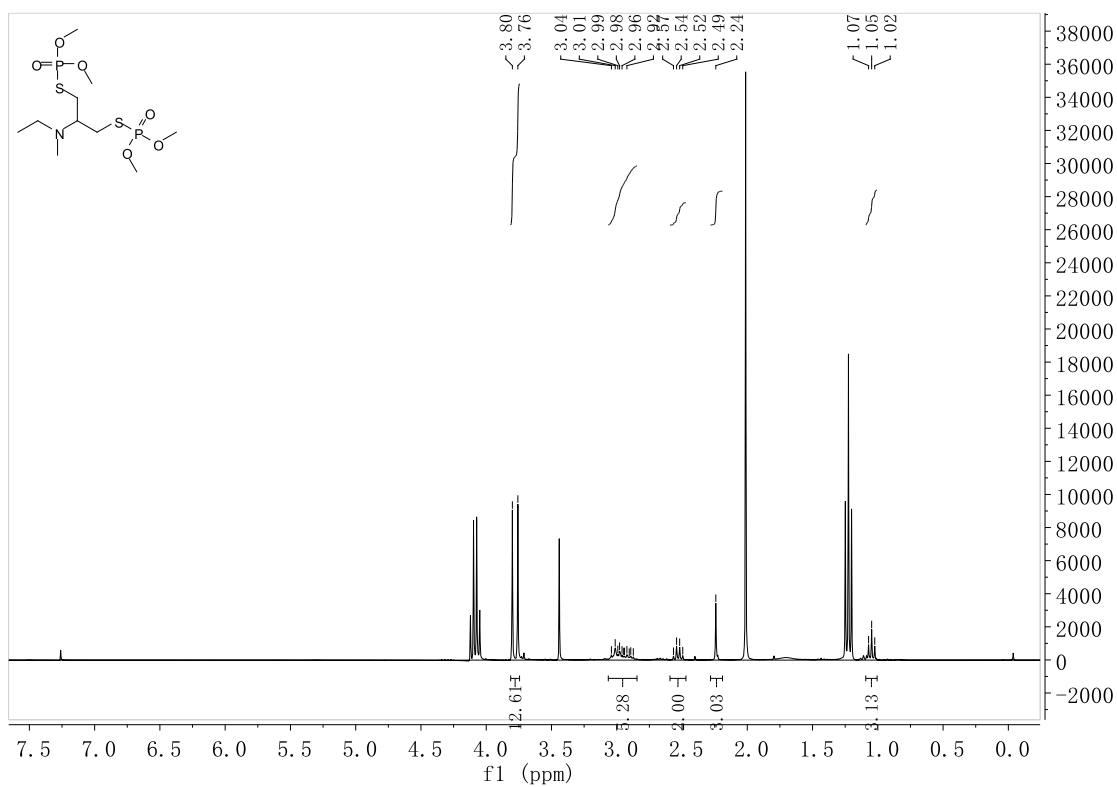


Figure S149. ^1H NMR of converted product of **7a** (with methanol and ethyl acetate in compound).

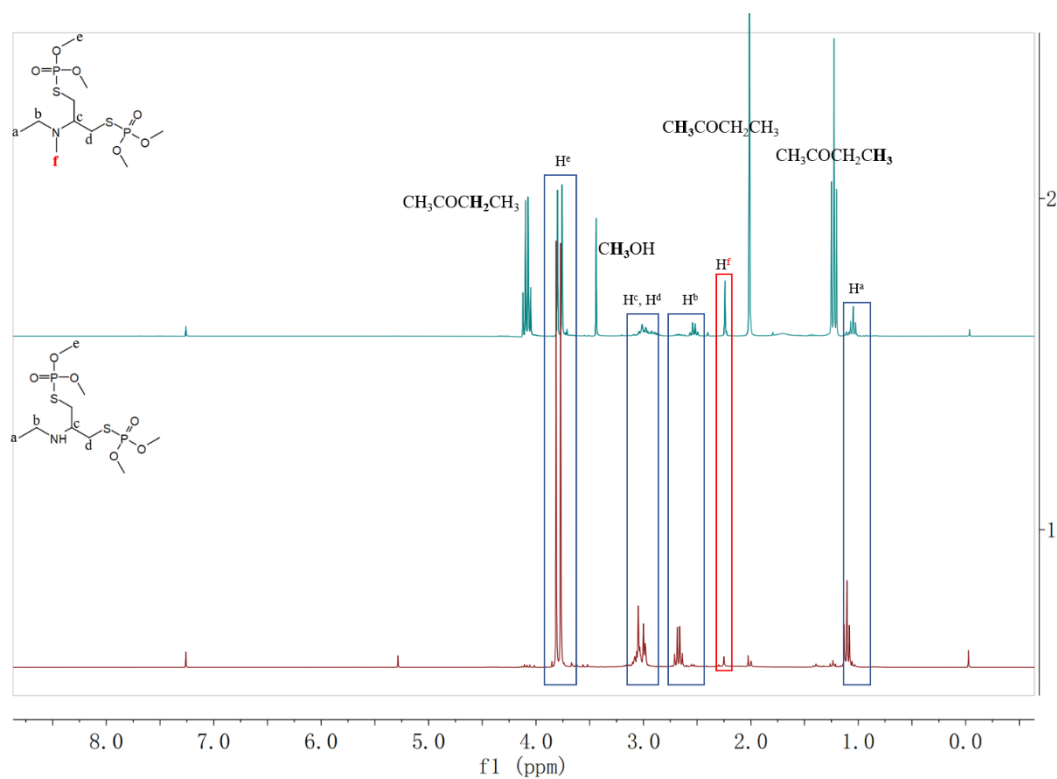


Figure S150. Comparison of ^1H NMR of **7a** and its converted product.

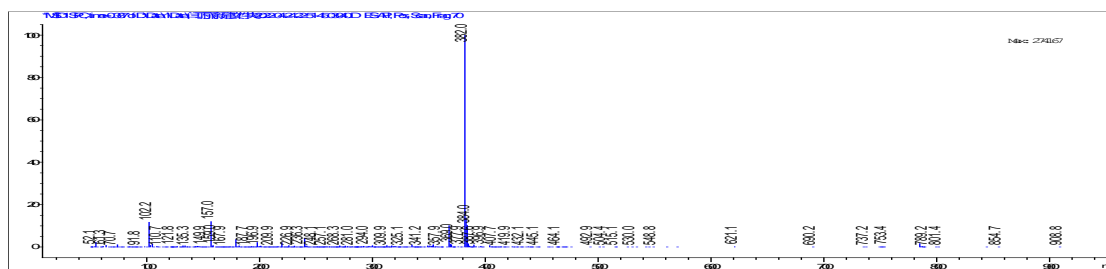


Figure S151. The mass spectrum of 9a reaction solution.

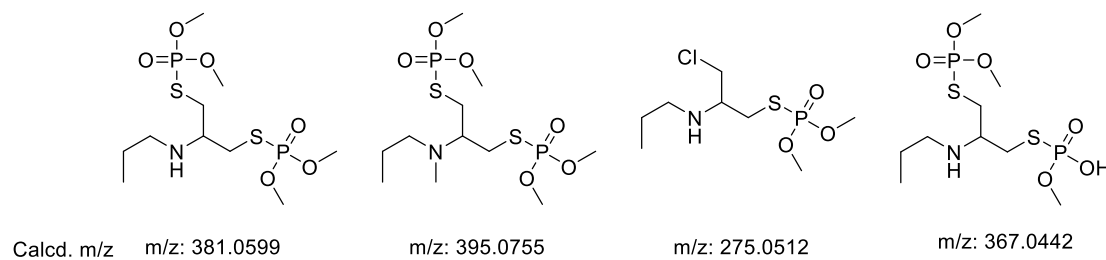


Figure S152. The calculated m/z of 9a and by-products.

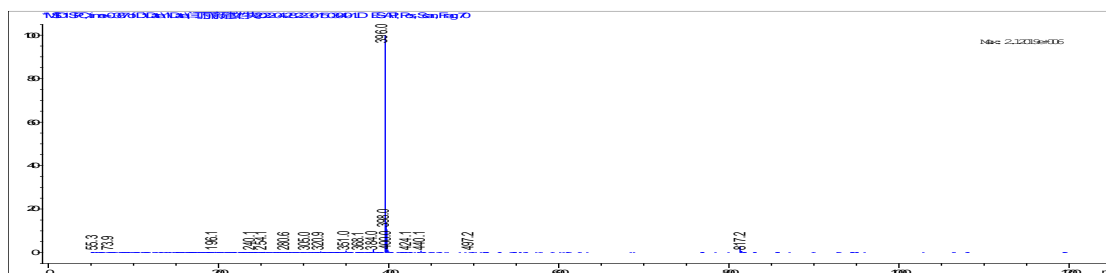


Figure S153. Mass spectrometry of converted product of 9a during purification on April 28, 2022.

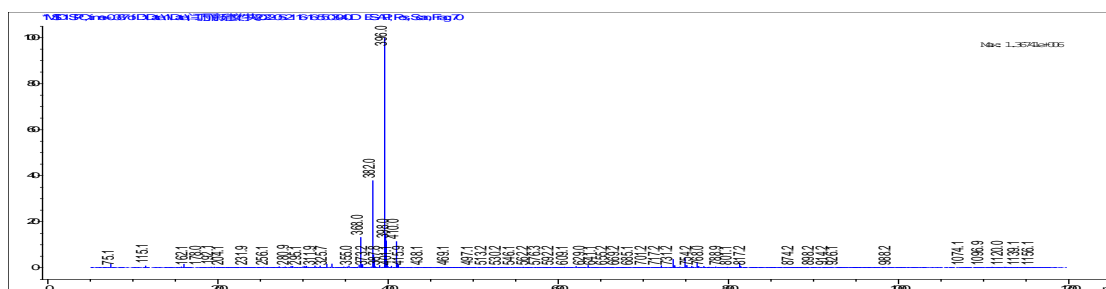


Figure S154. Mass spectrometry of 9a on May 21, 2022.

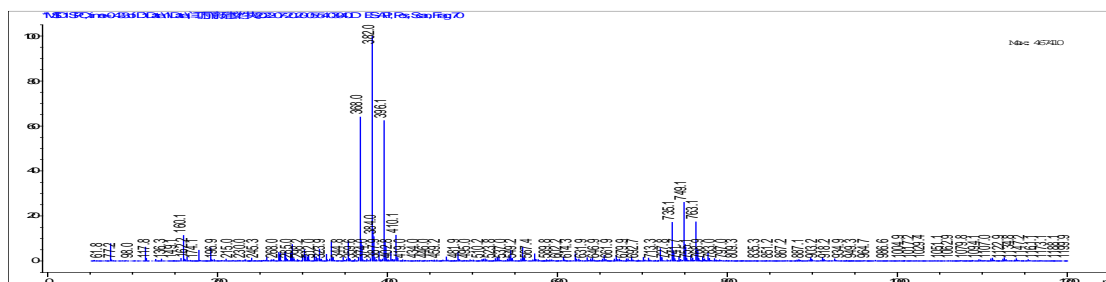
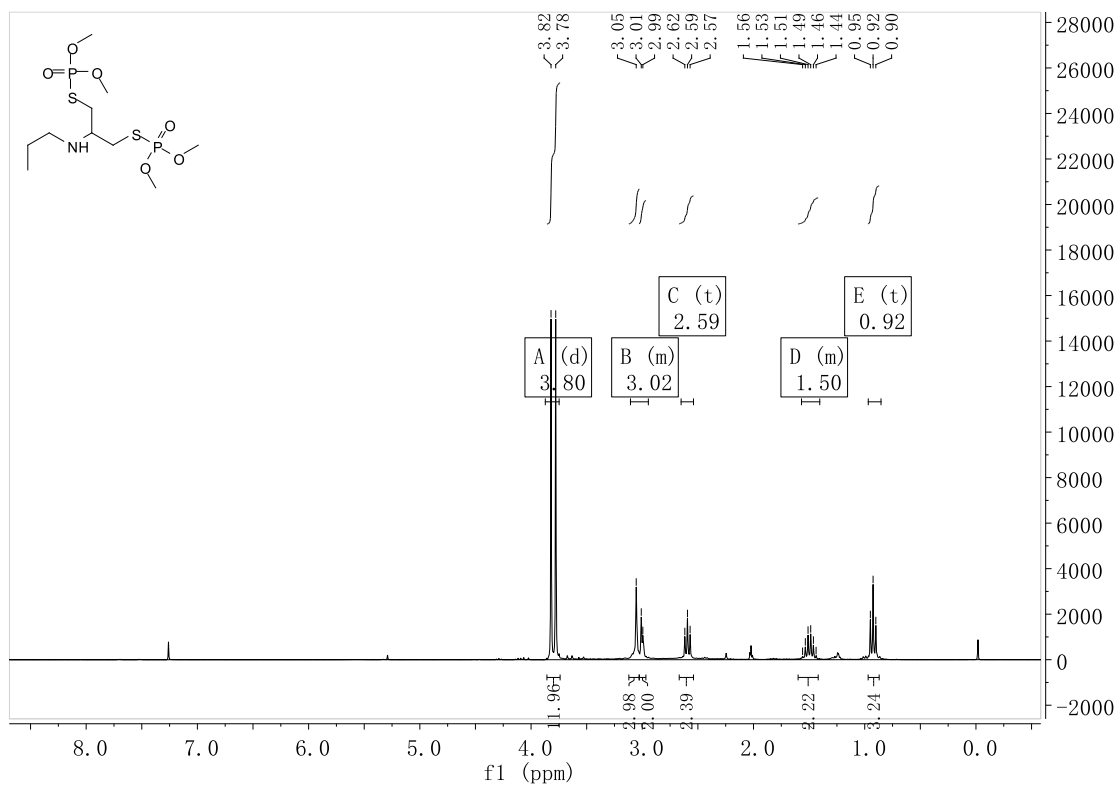
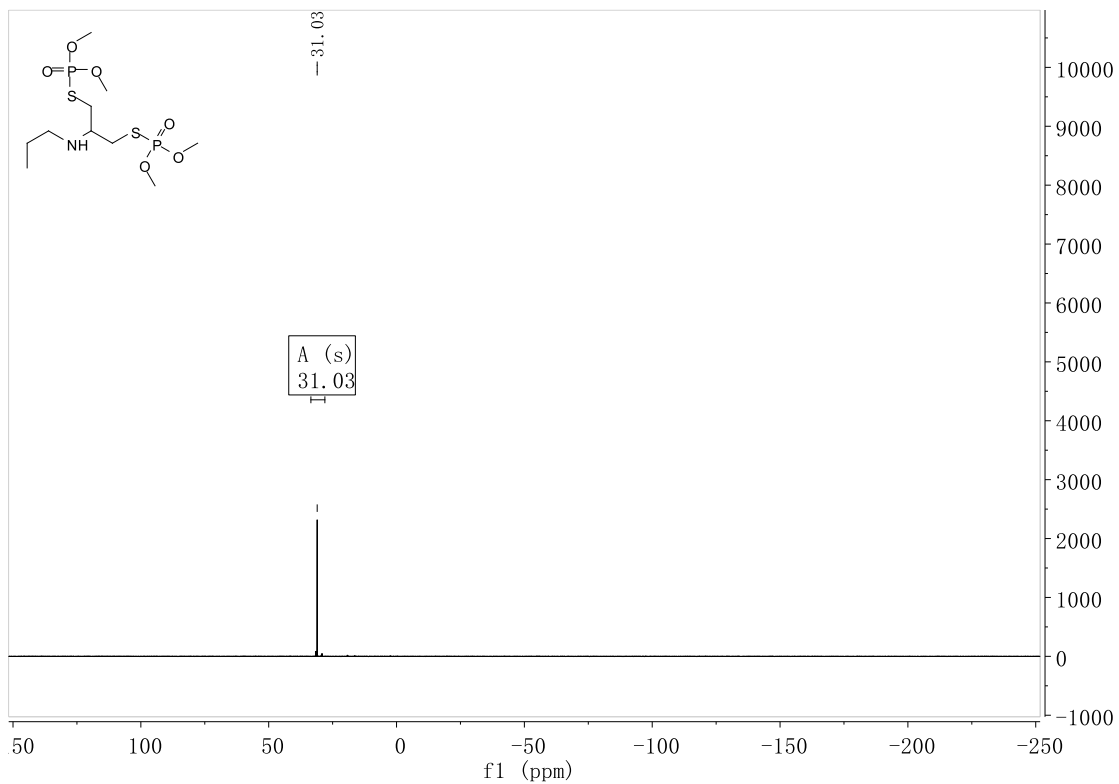


Figure S155. Mass spectrometry of 9a on July 20, 2022.



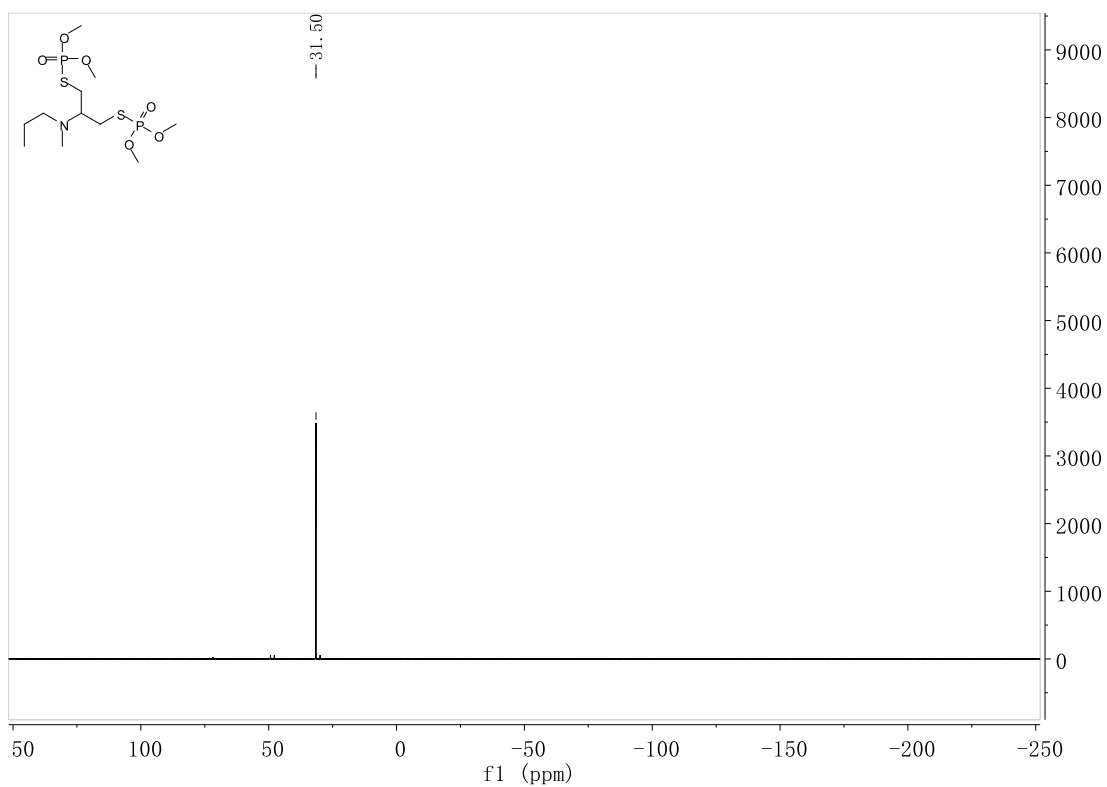


Figure S158. ^{31}P NMR of converted product of **9a**.

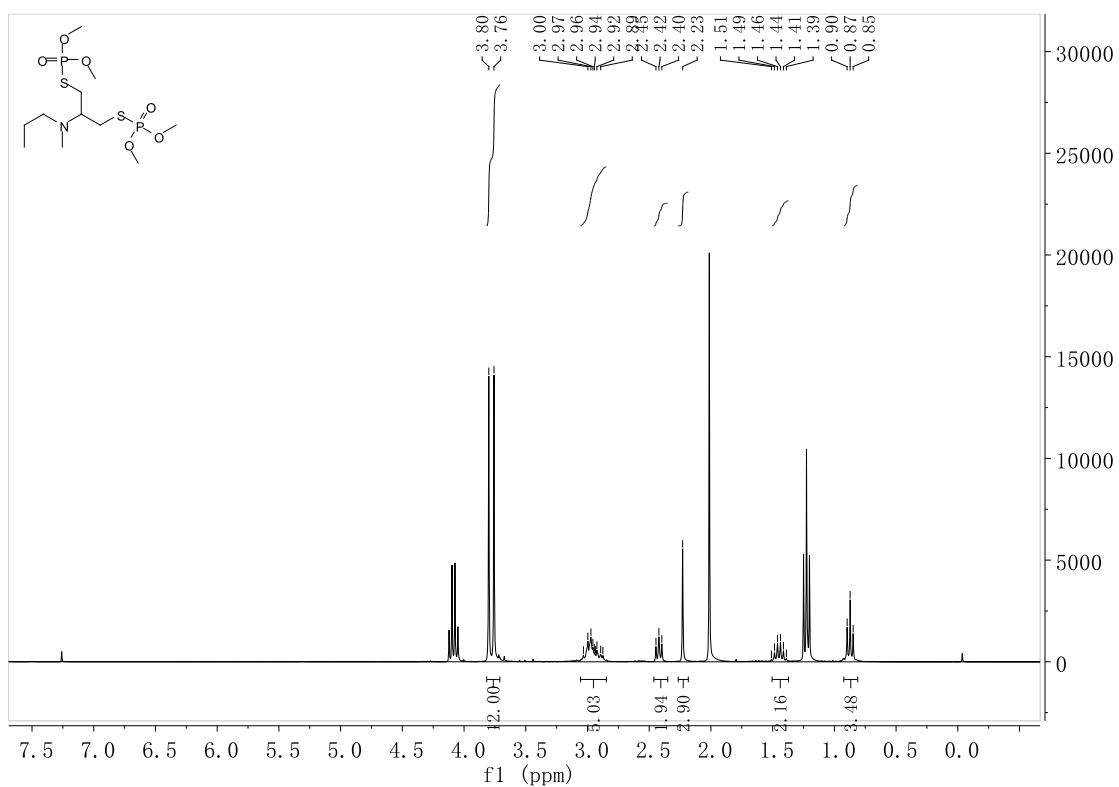


Figure S159. ^1H NMR of converted product of **9a** (with ethyl acetate in compound).

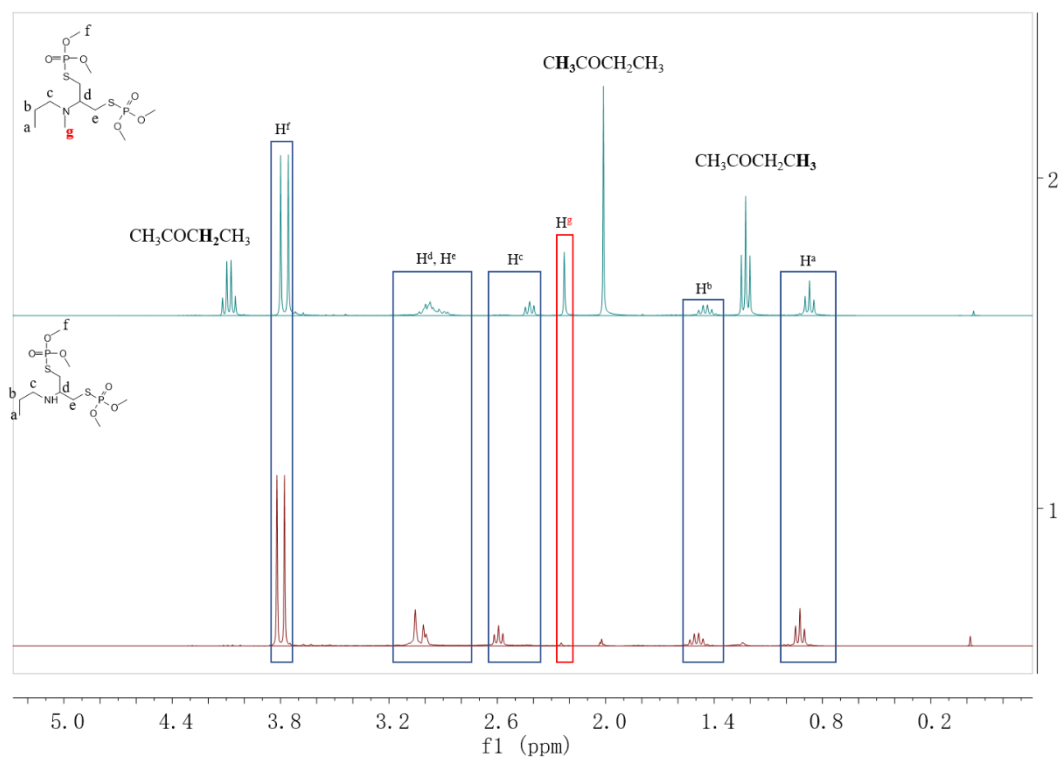


Figure S160. Comparison of ^1H NMR of **9a** and its converted product.

Reference

- [1] P. Brown-Sean, A. Lanman-Brian, L. Ke and L. Yun, B. Reed-Anthony. **2019**, WO 2019/036575 Al.
- [2] N. Santschi and A. Togni, *J. Org. Chem.* **2011**, *76*, 4189.