Electronic Supplementary Material (ESI) for Organic & Biomolecular Chemistry.

Supporting Information

TsCl Promoted Deoxygenative Phosphorothiolation of Quinoline *N*-oxides towards S-quinolyl Phosphorothioates

Li-Yao Wu [#], Tian Huang [#], Zhong-Ying Tian, Xiang-Qin Xu, Sha Peng *, and Long-Yong Xie *

College of Chemistry and Bioengineering, Hunan University of Science and Engineering, Hunan, 425100, China

longyongxie@yeah.net

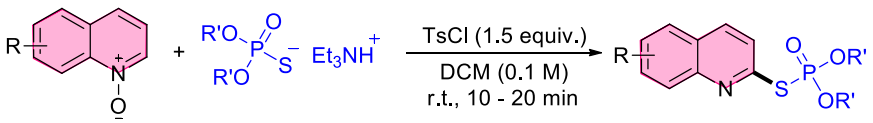
Table of Content

1. General information

Unless otherwise noted, all solvents and reagents in this study were commercial and used without further purification. ^{1}H, ^{13}C and ^{31}P NMR spectra were recorded at 400, 100 and 162 MHz, respectively. Chemical shifts were quoted in ppm relative to $CDCl_3$ (δ_H = 7.26, δ_C = 77.0 ppm). Datas are reported as follows: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, dd = doublet of doublet, etc. The reactions were monitored by thin-layer chromatography (TLC) using GF254 silica gel-coated TLC plates. Mass spectra were performed on a spectrometer operating on ESI-TOF.

2. Experimental Section

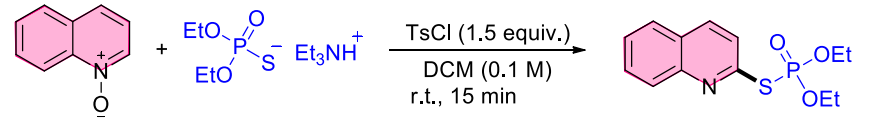
General procedure for the synthesis of *S*-quinolyl phosphorothioates 3



1 **2** **3**

To a round bottom flask was consecutively added quinoline *N*-oxide **1** (0.3 mmol, 1 eq.), *O*,*O*-dialkylphosphorothioate **2** (0.45 mmol, 1.5 eq.) and TsCl (0.45 mmol, 1.5 eq.) in CH_2Cl_2 (3 mL). The reaction mixture was stirred at room temperature for about 10-20 min. Upon completion, CH_2Cl_2 (10 mL) and water (10 mL) were added to the mixture, the organic layer was separated and the aqueous layer was further extracted with CH_2Cl_2 (2 × 10 mL). The combined organic layers were dried with anhydrous Na_2SO_4, filtered and concentrated under reduced pressure. The residue was purified by flash chromatography column over silica gel to afford the desired products **3**.

Procedure for gram-scale Synthesis of 3aa

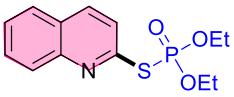


1a, 6 mmol, 0.8703 g

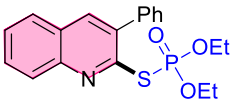
3aa, 1.3189 g, yielding 75%

To a round bottom flask was consecutively added quinoline *N*-oxide **1a** (6 mmol, 0.8703 g), *O*,*O*-diethylphosphorothioate **2a** (9 mmol, 2.4392 g) and TsCl (9 mmol, 1.7099 g) in CH_2Cl_2 (60 mL). The reaction mixture was stirred at room temperature for about 15 min. Upon completion, water (30 mL) was added to the mixture, the organic layer was separated and the aqueous layer was further extracted with CH_2Cl_2 (2 × 20 mL). The combined organic layers were dried with anhydrous Na_2SO_4, filtered and concentrated under reduced pressure. The residue was purified by flash chromatography column over silica gel to afford 1.3189 g of **3aa**, yield: 75%.

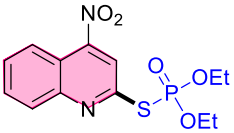
3. Characterization data of products



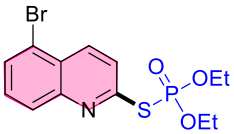
***O*,*O*-diethyl *S*-quinolin-2-yl phosphorothioate (3aa):** Yellow oil (69.5 mg, 78%), ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.93 (s, 1H), 8.42 (s, 1H), 8.09 (d, *J* = 8.5 Hz, 1H), 7.79 (d, *J* = 8.2 Hz, 1H), 7.75 (t, *J* = 7.7 Hz, 1H), 7.57 (t, *J* = 7.5 Hz, 1H), 4.22 (dq, *J* = 14.1, 6.8 Hz, 4H), 1.31 (t, *J* = 7.1 Hz, 6H); ^{13}C NMR (100 MHz, Chloroform-*d*) δ 153.7 (d, $J_{C\text{-}P}$ = 4.2 Hz), 147.4 (d, $J_{C\text{-}P}$ = 1.9 Hz), 142.2 (d, $J_{C\text{-}P}$ = 5.8 Hz), 130.6 (d, $J_{C\text{-}P}$ = 0.7 Hz), 129.3 (d, $J_{C\text{-}P}$ = 0.6 Hz), 128.0 (d, $J_{C\text{-}P}$ = 2.2 Hz), 127.6, 127.5, 120.8 (d, $J_{C\text{-}P}$ = 7.2 Hz), 64.4 (d, $J_{C\text{-}P}$ = 6.4 Hz), 16.0 (d, $J_{C\text{-}P}$ = 7.0 Hz); ^{31}P NMR (162 MHz, Chloroform-*d*) δ 21.68; HRMS (ESI) m/z calcd. for $C_{13}H_{17}NO_3PS$ $[M+H]^+$: 298.0661, found 298.0667.



***O,O*-diethyl *S*-(3-phenylquinolin-2-yl) phosphorothioate (3ba):** Yellow oil (79.4 mg, 71%), ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.94 (s, 1H), 8.69 (d, *J* = 8.3 Hz, 1H), 8.18 (d, *J* = 8.2 Hz, 1H), 7.78 (t, *J* = 7.2 Hz, 1H), 7.71 (t, *J* = 7.4 Hz, 1H), 7.58 (d, *J* = 7.2 Hz, 2H), 7.51 (t, *J* = 7.3 Hz, 2H), 7.47 – 7.42 (m, 1H), 3.80 (dq, *J* = 15.0, 7.3 Hz, 2H), 3.65 (dq, *J* = 16.5, 7.2 Hz, 2H), 1.06 (t, *J* = 7.0 Hz, 6H); ^{13}C NMR (100 MHz, Chloroform-*d*) δ 151.4, 147.6, 141.1 (d, $J_{C\text{-}P}$ = 5.7 Hz), 138.1, 132.9 (d, $J_{C\text{-}P}$ = 9.0 Hz), 130.6, 130.2, 129.8, 129.7, 128.1, 128.0, 127.8, 127.1, 64.1 (d, $J_{C\text{-}P}$ = 6.7 Hz), 15.8 (d, $J_{C\text{-}P}$ = 7.2 Hz); ^{31}P NMR (162 MHz, Chloroform-*d*) δ 19.61; HRMS (ESI) m/z calcd. for $C_{19}H_{21}NO_3PS$ $[M+H]^+$: 374.0974, found 374.0976.

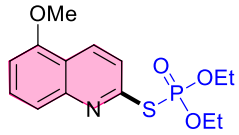


***O,O*-diethyl *S*-(4-nitroquinolin-2-yl) phosphorothioate (3ca):** Yellow oil (62.6 mg, 61%), ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.37 (d, *J* = 8.6 Hz, 1H), 8.25 (s, 1H), 8.16 (d, *J* = 8.5 Hz, 1H), 7.87 (t, *J* = 7.7 Hz, 1H), 7.76 (t, *J* = 7.7 Hz, 1H), 4.46 – 4.29 (m, 4H), 1.38 (t, *J* = 7.0 Hz, 6H); ^{13}C NMR (100 MHz, Chloroform-*d*) δ 152.7, 152.5 (d, $J_{C\text{-}P}$ = 5.2 Hz), 150.2, 131.7, 130.1, 129.6, 122.8, 118.7 (d, $J_{C\text{-}P}$ = 3.2 Hz), 117.5, 65.0 (d, $J_{C\text{-}P}$ = 5.9 Hz), 16.0 (d, $J_{C\text{-}P}$ = 7.2 Hz); ^{31}P NMR (162 MHz, Chloroform-*d*) δ 18.73; HRMS (ESI) m/z calcd. for $C_{13}H_{16}N_2O_5PS$ $[M+H]^+$: 343.0512, found 343.0516.

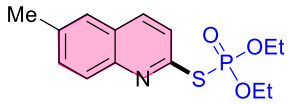


***S*-(5-bromoquinolin-2-yl) *O,O*-diethyl phosphorothioate (3da):** Yellow oil (72.0 mg, 64%), ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.96 (s, 1H), 8.78 (s, 1H), 8.08 (d, *J* = 8.5 Hz, 1H), 7.87 (d, *J* = 7.5 Hz, 1H), 7.61 (t, *J* = 8.0 Hz, 1H), 4.35 – 4.21 (m, 4H), 1.35 (t, *J* = 7.0 Hz, 6H); ^{13}C NMR (100 MHz,

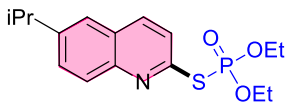
Chloroform-*d*) δ 154.4 (d, $J_{C\text{-}P}$ = 4.2 Hz), 148.2, (d, $J_{C\text{-}P}$ = 1.9 Hz), 141.4 (d, $J_{C\text{-}P}$ = 5.8 Hz), 131.2, 130.8, 129.3, 127.6 (d, $J_{C\text{-}P}$ = 2.1 Hz), 123.0 (d, $J_{C\text{-}P}$ = 7.3 Hz), 121.5 (d, $J_{C\text{-}P}$ = 1.3 Hz), 64.5 (d, $J_{C\text{-}P}$ = 6.3 Hz), 16.0 (d, $J_{C\text{-}P}$ = 7.2 Hz); ^{31}P NMR (162 MHz, Chloroform-*d*) δ 21.06; HRMS (ESI) m/z calcd. for $C_{13}H_{16}BrNO_3PS$ $[M+H]^+$: 375.9766, found 375.9763.



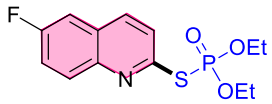
***O,O*-diethyl *S*-(5-methoxyquinolin-2-yl) phosphorothioate (3ea):** Yellow oil (81.4 mg, 83%), ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.91 (s, 1H), 8.87 – 8.70 (m, 1H), 7.69 – 7.60 (m, 2H), 6.91 – 6.84 (m, 1H), 4.40 – 4.10 (m, 4H), 3.99 (s, 3H), 1.32 (t, *J* = 5.8 Hz, 6H); ^{13}C NMR (100 MHz, Chloroform-*d*) δ 154.8, 154.2 (d, $J_{C\text{-}P}$ = 4.0 Hz), 148.2 (d, $J_{C\text{-}P}$ = 2.0 Hz), 137.4 (d, $J_{C\text{-}P}$ = 5.5 Hz), 130.8, 121.2, 120.6 (d, $J_{C\text{-}P}$ = 2.2 Hz), 119.8 (d, $J_{C\text{-}P}$ = 7.4 Hz), 105.0, 64.3 (d, $J_{C\text{-}P}$ =6.2 Hz), 55.8, 16.0 (d, $J_{C\text{-}P}$ =7.2 Hz); ^{31}P NMR (162 MHz, Chloroform-*d*) δ 21.90; HRMS (ESI) m/z calcd. for $C_{14}H_{19}NO_4PS$ $[M+H]^+$: 328.0767, found 328.0769.



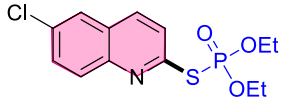
***O,O*-diethyl *S*-(6-methylquinolin-2-yl) phosphorothioate (3fa):** Yellow oil (75.6 mg, 81%), ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.86 (s, 1H), 8.33 (s, 1H), 7.99 (d, *J* = 8.2 Hz, 1H), 7.58 (d, *J* = 15.6 Hz, 2H), 4.31 – 4.18 (m, 4H), 2.54 (s, 3H), 1.32 (t, *J* = 6.8 Hz, 6H)；^{13}C NMR (100 MHz, Chloroform-*d*) δ 152.8 (d, $J_{C\text{-}P}$ = 4.3 Hz), 146.0, 141.6 (d, $J_{C\text{-}P}$ = 5.7 Hz), 137.6, 133.0, 128.9, 128.1 (d, $J_{C\text{-}P}$ = 1.7 Hz), 126.4, 120.8 (d, $J_{C\text{-}P}$ = 7.5 Hz), 64.4 (d, $J_{C\text{-}P}$ = 6.5 Hz), 21.6, 16.0 (d, $J_{C\text{-}P}$ = 7.0 Hz); ^{31}P NMR (162 MHz, Chloroform-*d*) δ 21.77; HRMS (ESI) m/z calcd. for $C_{14}H_{19}NO_3PS$ $[M+H]^+$: 312.0818, found 312.0819.



***O,O*-diethyl *S*-(6-isopropylquinolin-2-yl) phosphorothioate (3ga):** Yellow oil (75.3 mg, 74%), ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.86 (s, 1H), 8.37 (s, 1H), 8.02 (d, *J* = 8.7 Hz, 1H), 7.66 (d, *J* = 8.7 Hz, 1H), 7.58 (s, 1H), 4.23 (dq, *J* = 14.5, 7.1 Hz, 4H), 3.13 – 3.06 (m, 1H), 1.37 – 1.29 (m, 12H); ^{13}C NMR (100 MHz, Chloroform-*d*) δ 152.9 (d, $J_{C\text{-}P}$ = 4.3 Hz), 148.2, 146.4 (d, $J_{C\text{-}P}$ = 1.8 Hz), 141.9 (d, $J_{C\text{-}P}$ = 5.7 Hz), 130.7, 129.1, 128.2 (d, $J_{C\text{-}P}$ = 2.2 Hz), 123.7, 120.6 (d, $J_{C\text{-}P}$ = 7.2 Hz), 64.4 (d, $J_{C\text{-}P}$ =6.4 Hz), 34.1, 23.7, 16.0 (d, $J_{C\text{-}P}$ =7.0 Hz); ^{31}P NMR (162 MHz, Chloroform-*d*) δ 21.85; HRMS (ESI) m/z calcd. for $C_{16}H_{22}NNaO_3PS$ $[M+Na]^+$: 362.0950, found 362.0956.

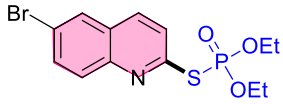


***O,O*-diethyl *S*-(6-fluoroquinolin-2-yl) phosphorothioate (3ha):** Yellow oil (71.8 mg, 76%), ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.89 (s, 1H), 8.37 (s, 1H), 8.09 (dd, *J* = 9.1, 5.3 Hz, 1H), 7.56 – 7.48 (m, 1H), 7.41 (dd, *J* = 8.5, 2.4 Hz, 1H), 4.24 (dp, *J* = 14.7, 7.3 Hz, 4H), 1.32 (t, *J* = 7.0 Hz, 6H); ^{13}C NMR (100 MHz, Chloroform-*d*) δ 160.8 (d, $J_{C\text{-}F}$ = 248.4 Hz), 152.9 (dd, *J* = 4.2 Hz, 3.2 Hz), 144.5, 141.2 (dd, *J* = 5.6 Hz, 4.2 Hz), 131.9 (d, $J_{C\text{-}F}$ = 9.1 Hz), 128.8 (dd, *J* = 10.2 Hz, 2.1 Hz), 122.2 (d, $J_{C\text{-}P}$ = 7.2 Hz), 120.9 (d, $J_{C\text{-}F}$= 25.8 Hz), 110.6 (d, $J_{C\text{-}F}$= 21.9 Hz), 64.6 (d, $J_{C\text{-}P}$ =6.4 Hz), 16.0 (d, $J_{C\text{-}P}$ =7.0Hz); ^{19}F NMR (376 MHz, Chloroform-*d*) δ -111.47; ^{31}P NMR (162 MHz, Chloroform-*d*) δ 21.30; HRMS (ESI) m/z calcd. for $C_{13}H_{16}FNO_3PS$ $[M+H]^+$: 316.0567, found 316.0569.

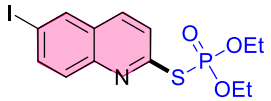


***S*-(6-chloroquinolin-2-yl) *O,O*-diethyl phosphorothioate (3ia):** Yellow oil (77.4 mg, 78%), ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.92 (s, 1H), 8.34 (s, 1H), 8.03 (d, *J* = 9.0 Hz, 1H), 7.78 (s, 1H), 7.68 (d, *J* = 9.0 Hz, 1H), 4.28 – 4.18 (m, 4H), 1.33 (t, *J* = 7.1 Hz, 6H); ^{13}C NMR (100 MHz,

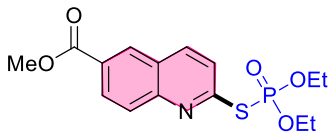
Chloroform-*d*) δ 153.8 (d, $J_{C\text{-}P}$ = 4.4 Hz), 145.7 (d, $J_{C\text{-}P}$ = 2.0 Hz), 140.8 (d, $J_{C\text{-}P}$ = 5.8 Hz), 133.3, 131.5, 130.9, 128.6 (d, $J_{C\text{-}P}$ = 2.2 Hz), 126.2, 122.4 (d, $J_{C\text{-}P}$ = 7.1 Hz), 64.6 (d, $J_{C\text{-}P}$ = 6.5 Hz), 16.0 (d, $J_{C\text{-}P}$ = 7.0 Hz); ^{31}P NMR (162 MHz, Chloroform-*d*) δ 21.20; HRMS (ESI) m/z calcd. for $C_{13}H_{16}ClNO_3PS$ $[M+H]^+$: 332.0272, found 332.0269.



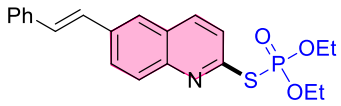
S-(6-bromoquinolin-2-yl) O,O-diethyl phosphorothioate (3ja): Yellow oil (88.9 mg, 79%), ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.93 (s, 1H), 8.33 (s, 1H), 7.96 (d, *J* = 4.1 Hz, 2H), 7.81 (d, *J* = 8.9 Hz, 1H), 4.31 – 4.17 (m, 4H), 1.33 (t, *J* = 7.0 Hz, 6H); ^{13}C NMR (100 MHz, Chloroform-*d*) δ 154.0 (d, $J_{C\text{-}P}$ = 4.5 Hz), 145.9 (d, $J_{C\text{-}P}$ = 1.8 Hz), 140.7 (d, $J_{C\text{-}P}$ = 5.8 Hz), 134.1, 131.0, 129.6, 129.0 (d, $J_{C\text{-}P}$ = 2.1 Hz), 122.4 (d, $J_{C\text{-}P}$ = 7.1 Hz), 121.5, 64.6 (d, $J_{C\text{-}P}$ =6.5 Hz), 16.0 (d, $J_{C\text{-}P}$ =7.0Hz); ^{31}P NMR (162 MHz, Chloroform-*d*) δ 21.23; HRMS (ESI) m/z calcd. for $C_{13}H_{16}BrNO_3PS$ $[M+H]^+$: 375.9766, found 375.9771.



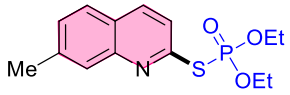
***O,O*-diethyl *S*-(6-iodoquinolin-2-yl) phosphorothioate (3ka):** Yellow oil (93.9 mg, 74%), ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.93 (s, 1H), 8.30 (s, 1H), 8.19 (s, 1H), 7.97 (d, *J* = 8.9 Hz, 1H), 7.81 (d, *J* = 8.9 Hz, 1H), 4.28 – 4.17 (m, 4H), 1.33 (t, *J* = 7.0 Hz, 6H); ^{13}C NMR (100 MHz, Chloroform-*d*) δ 154.2 (d, $J_{C\text{-}P}$ = 4.4 Hz), 146.3 (d, $J_{C\text{-}P}$ = 1.8 Hz), 140.5 (d, $J_{C\text{-}P}$ = 5.9 Hz), 139.3, 136.3, 130.9, 129.5 (d, $J_{C\text{-}P}$ = 2.1 Hz), 122.1 (d, $J_{C\text{-}P}$ = 7.1 Hz), 93.2, 64.6 (d, $J_{C\text{-}P}$ =6.5 Hz), 16.0 (d, $J_{C\text{-}P}$ =7.0 Hz); ^{31}P NMR (162 MHz, Chloroform-*d*) δ 21.22; HRMS (ESI) m/z calcd. for $C_{13}H_{16}INO_3PS$ $[M+H]^+$: 423.9628, found 423.9622.



methyl 2-((diethoxyphosphoryl)thio)quinoline-6-carboxylate (3la): Yellow oil (76.7 mg, 72%), ^{1}H NMR (400 MHz, Chloroform-*d*) δ 9.02 (s, 1H), 8.56 (s, 1H), 8.51 (s, 1H), 8.33 (d, *J* = 8.6 Hz, 1H), 8.14 (d, *J* = 8.5 Hz, 1H), 4.30 – 4.16 (m, 4H), 3.99 (s, 3H), 1.33 (t, *J* = 7.2 Hz, 6H); ^{13}C NMR (100 MHz, Chloroform-*d*) δ 166.2, 155.7 (d, $J_{C\text{-}P}$ = 4.3 Hz), 149.0, 143.1 (d, $J_{C\text{-}P}$ = 5.7 Hz), 130.7, 130.1, 129.7, 129.0, 127.2 (d, $J_{C\text{-}P}$ = 1.4 Hz), 122.4 (d, $J_{C\text{-}P}$ = 7.0 Hz), 64.6 (d, $J_{C\text{-}P}$ = 6.5 Hz), 52.6, 16.1 (d, $J_{C\text{-}P}$ = 6.9 Hz); ^{31}P NMR (162 MHz, Chloroform-*d*) δ 21.15; HRMS (ESI) m/z calcd. for $C_{15}H_{19}NO_5PS$ $[M+H]^+$: 356.0716, found 356.0721.

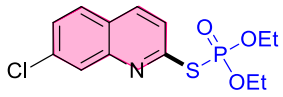


***O,O*-diethyl *S*-(6-styrylquinolin-2-yl) phosphorothioate (3ma):** Yellow oil (77.8 mg, 65%), ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.90 (s, 1H), 8.42 (s, 1H), 8.09 (d, *J* = 8.9 Hz, 1H), 8.03 (d, *J* = 9.1 Hz, 1H), 7.82 (s, 1H), 7.59 (d, *J* = 7.6 Hz, 2H), 7.42 (t, *J* = 7.4 Hz, 2H), 7.28 (d, *J* = 3.3 Hz, 3H), 4.33 – 4.21 (m, 4H), 1.36 (t, *J* = 7.0 Hz, 6H); ^{13}C NMR (100 MHz, Chloroform-*d*) δ 153.3 (d, $J_{C\text{-}P}$ = 4.4 Hz), 147.2 (d, $J_{C\text{-}P}$ = 1.5 Hz), 141.9 (d, $J_{C\text{-}P}$ = 5.6 Hz), 136.7, 136.6, 130.9, 129.6, 128.8, 128.4, 128.2, 127.3, 126.7, 126.6, 125.5, 121.4 (d, $J_{C\text{-}P}$ = 7.0 Hz), 64.5 (d, $J_{C\text{-}P}$ = 6.4 Hz), 16.1 (d, $J_{C\text{-}P}$ = 7.1 Hz); ^{31}P NMR (162 MHz, Chloroform-*d*) δ 21.65; HRMS (ESI) m/z calcd. for $C_{21}H_{22}NNaO_3PS$ $[M+Na]^+$: 422.0950, found 422.0955.

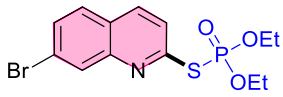


***O,O*-diethyl *S*-(7-methylquinolin-2-yl) phosphorothioate (3na):** Yellow oil (70.9 mg, 76%), ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.89 (s, 1H), 8.37 (s, 1H), 7.87 (s, 1H), 7.69 (d, *J* = 8.2 Hz, 1H),

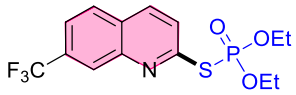
7.41 (d, *J* = 8.2 Hz, 1H), 4.28 – 4.17 (m, 4H), 2.56 (s, 3H), 1.31 (t, *J* = 6.9 Hz, 6H); ^{13}C NMR (100 MHz, Chloroform-*d*) δ 153.7 (d, $J_{C\text{-}P}$ = 4.0 Hz), 147.5, 142.1 (d, $J_{C\text{-}P}$ = 5.6 Hz), 141.4, 129.8, 128.1, 127.3, 126.1, 119.7 (d, $J_{C\text{-}P}$ = 7.2 Hz), 64.4 (d, $J_{C\text{-}P}$ = 6.4 Hz), 21.9, 16.0 (d, $J_{C\text{-}P}$ = 7.0 Hz); ^{31}P NMR (162 MHz, Chloroform-*d*) δ 21.83; HRMS (ESI) m/z calcd. for $C_{14}H_{19}NO_3PS$ $[M+H]^+$: 312.0818, found 312.0820.



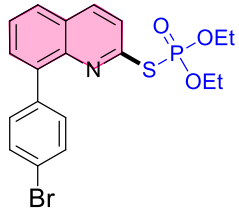
***S*-(7-chloroquinolin-2-yl) *O,O*-diethyl phosphorothioate (3oa):** Yellow oil (72.5 mg, 73%), ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.92 (s, 1H), 8.39 (s, 1H), 8.07 (s, 1H), 7.73 (d, *J* = 8.7 Hz, 1H), 7.52 (d, *J* = 8.7 Hz, 1H), 4.31 – 4.13 (m, 4H), 1.31 (t, *J* = 7.0 Hz, 6H); ^{13}C NMR (100 MHz, Chloroform-*d*) δ 154.6 (d, $J_{C\text{-}P}$ = 4.3 Hz), 147.6 (d, $J_{C\text{-}P}$ = 1.9 Hz), 141.9 (d, $J_{C\text{-}P}$ = 5.7 Hz), 136.5, 128.8, 128.6, 128.3, 126.3 (d, $J_{C\text{-}P}$ = 2.1 Hz), 121.3 (d, $J_{C\text{-}P}$ = 7.1 Hz), 64.6 (d, $J_{C\text{-}P}$ =6.5 Hz), 16.0 (d, $J_{C\text{-}P}$ =7.0 Hz); ^{31}P NMR (162 MHz, Chloroform-*d*) δ 21.32; HRMS (ESI) m/z calcd. for $C_{13}H_{16}ClNO_3PS$ $[M+H]^+$: 332.0272, found 332.0268.



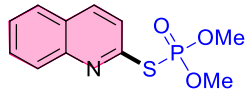
***S*-(7-bromoquinolin-2-yl) *O,O*-diethyl phosphorothioate (3pa):** Yellow oil (92.2 mg, 82%), ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.95 (s, 1H), 8.44 (s, 1H), 8.32 (s, 1H), 7.72 – 7.63 (m, 2H), 4.30 – 4.15 (m, 4H), 1.33 (t, *J* = 7.1 Hz, 6H); ^{13}C NMR (100 MHz, Chloroform-*d*) δ 154.5 (d, $J_{C\text{-}P}$ = 4.5 Hz), 147.6 (d, $J_{C\text{-}P}$ = 2.2 Hz), 142.2 (d, $J_{C\text{-}P}$ = 5.7 Hz), 131.5, 131.2, 128.8, 128.1 (d, $J_{C\text{-}P}$ = 5.0 Hz), 126.6 (d, $J_{C\text{-}P}$ = 2.2 Hz), 121.6 (d, $J_{C\text{-}P}$ = 7.4 Hz), 64.7 (d, $J_{C\text{-}P}$ = 6.6 Hz), 16.0 (d, $J_{C\text{-}P}$ = 7.2 Hz); ^{31}P NMR (162 MHz, Chloroform-*d*) δ 21.12; HRMS (ESI) m/z calcd. for $C_{13}H_{16}BrNO_3PS$ $[M+H]^+$: 375.9766, found 375.9768.



***O,O*-diethyl *S*-(7-(trifluoromethyl)quinolin-2-yl) phosphorothioate (3qa):** Yellow oil (73.4 mg, 67%), ^{1}H NMR (400 MHz, Chloroform-*d*) δ 9.04 (s, 1H), 8.51 (s, 1H), 8.41 (s, 1H), 7.94 (d, *J* = 8.4 Hz, 1H), 7.77 (d, *J* = 8.5 Hz, 1H), 4.32 – 4.17 (m, 4H), 1.34 (t, *J* = 6.9 Hz, 6H); ^{13}C NMR (100 MHz, Chloroform-*d*) δ 154.9 (d, $J_{C\text{-}P}$ = 4.4 Hz), 146.2, 141.6 (d, $J_{C\text{-}P}$ = 6.0 Hz), 132.4, 129.4, 128.9, 127.2 (q, $J_{C\text{-}F}$= 4.1 Hz), 123.9 (d, $J_{C\text{-}P}$ = 6.9 Hz), 123.6 (q, $J_{C\text{-}F}$= 270.9 Hz), 123.3 (q, $J_{C\text{-}F}$= 2.8 Hz), 64.7 (d, $J_{C\text{-}P}$ = 6.6 Hz), 16.0 (d, $J_{C\text{-}P}$ = 6.9 Hz); ^{31}P NMR (162 MHz, Chloroform-*d*) δ 20.84; ^{19}F NMR (376 MHz, Chloroform-*d*) δ -62.81; HRMS (ESI) m/z calcd. for $C_{14}H_{16}F_3NO_3PS$ $[M+H]^+$: 366.0535, found 366.0541.

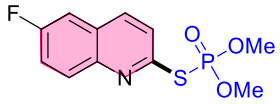


***S*-(8-(4-bromophenyl)quinolin-2-yl) *O,O*-diethyl phosphorothioate (3ra):** Yellow oil (105.5 mg, 78%), ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.18 – 8.05 (m, 1H), 7.80 (d, *J* = 7.4 Hz, 1H), 7.72 (d, *J* = 6.2 Hz, 1H), 7.66 – 7.51 (m, 6H), 4.26 – 4.03 (m, 4H), 1.24 – 1.15 (m, 6H); ^{13}C NMR (100 MHz, Chloroform-*d*) δ 151.8 (d, $J_{C\text{-}P}$ = 5.5 Hz), 145.7, 138.9, 137.6, 137.4, 132.6, 130.8, 130.7, 127.6, 127.3, 126.8, 124.6, 124.5, 64.2 (d, $J_{C\text{-}P}$ = 5.8 Hz), 15.8 (d, $J_{C\text{-}P}$ = 7.5 Hz); ^{31}P NMR (162 MHz, Chloroform-*d*) δ 20.04; HRMS (ESI) m/z calcd. for $C_{19}H_{20}BrNO_3PS$ $[M+H]^+$: 452.0079, found 452.0086.

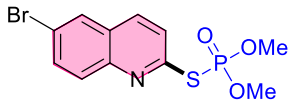


***O,O*-dimethyl *S*-quinolin-2-yl phosphorothioate (3ab):** Yellow oil (54.9 mg, 68%), ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.94 (s, 1H), 8.44 (s, 1H), 8.12 (d, *J* = 8.3 Hz, 1H), 7.86 – 7.75 (m, 2H),

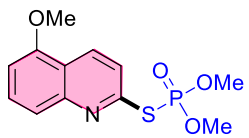
7.61 (t, J = 6.7 Hz, 1H), 3.91 – 3.83 (m, 6H); ^{13}C NMR (100 MHz, Chloroform-*d*) δ 153.5 (d, $J_{C\text{-}P}$ = 4.2 Hz), 147.3 (d, $J_{C\text{-}P}$ = 1.8 Hz), 142.4 (d, $J_{C\text{-}P}$ = 5.8 Hz), 130.9, 129.2, 128.1 (d, $J_{C\text{-}P}$ = 2.2 Hz), 127.7, 127.6, 120.4 (d, $J_{C\text{-}P}$ = 7.2 Hz), 54.5 (d, $J_{C\text{-}P}$ = 6.3 Hz); ^{31}P NMR (162 MHz, Chloroform-*d*) δ 24.92; HRMS (ESI) m/z calcd. for $C_{11}H_{13}NO_3PS$ $[M+H]^+$: 270.0348, found 270.0350.



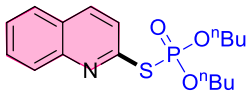
***S*-(6-fluoroquinolin-2-yl) *O,O*-dimethyl phosphorothioate (3hb):** Yellow oil (54.2 mg, 63%), ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.90 (s, 1H), 8.37 (s, 1H), 8.15 – 8.07 (m, 1H), 7.53 (t, J = 8.6 Hz, 1H), 7.43 (d, J = 8.5 Hz, 1H), 3.93 – 3.80 (m, 6H); ^{13}C NMR (100 MHz, Chloroform-*d*) δ 160.9 (d, $J_{C\text{-}F}$ = 248.8 Hz), 152.8 (d, $J_{C\text{-}P}$ = 3.6 Hz), 144.6, 141.3 (d, $J_{C\text{-}P}$ = 5.7 Hz), 132.0 (d, $J_{C\text{-}F}$ = 9.3 Hz), 128.8 (d, $J_{C\text{-}F}$ = 11.4 Hz), 121.8 (d, $J_{C\text{-}P}$ = 7.4 Hz), 121.0 (d, $J_{C\text{-}F}$ = 25.7 Hz), 110.7 (d, $J_{C\text{-}F}$ = 22.0 Hz), 54.6 (d, $J_{C\text{-}P}$ = 6.3 Hz); ^{31}P NMR (162 MHz, Chloroform-*d*) δ 24.59; ^{19}F NMR (376 MHz, Chloroform-*d*) δ -111.31; HRMS (ESI) m/z calcd. for $C_{11}H_{12}FNO_3PS$ $[M+H]^+$: 288.0254, found 288.0249.



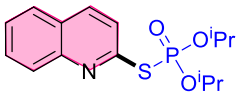
***S*-(6-bromoquinolin-2-yl) *O,O*-dimethyl phosphorothioate (3jb):** Yellow oil (63.5 mg, 61%), ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.93 (s, 1H), 8.33 (s, 1H), 7.97 (d, J = 6.6 Hz, 2H), 7.82 (d, J = 8.9 Hz, 1H), 3.92 – 3.79 (m, 6H); ^{13}C NMR (100 MHz, Chloroform-*d*) δ 153.9 (d, $J_{C\text{-}P}$ = 4.6 Hz), 146.0, 140.9 (d, $J_{C\text{-}P}$ = 5.8 Hz), 134.2, 131.1, 129.6, 129.1, 121.9 (d, $J_{C\text{-}P}$ = 6.8 Hz), 121.6, 54.6 (d, $J_{C\text{-}P}$ = 6.3 Hz); ^{31}P NMR (162 MHz, Chloroform-*d*) δ 24.52; HRMS (ESI) m/z calcd. for $C_{11}H_{12}BrNO_3PS$ $[M+H]^+$: 347.9453, found 347.9456.



***S*-(5-methoxyquinolin-2-yl) *O,O*-dimethyl phosphorothioate (3eb):** Yellow oil (65.5 mg, 73%), ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.91 (s, 1H), 8.79 (s, 1H), 7.70 – 7.63 (m, 2H), 6.89 (s, 1H), 4.00 (s, 3H), 3.88 (s, 3H), 3.84 (s, 3H); ^{13}C NMR (100 MHz, Chloroform-*d*) δ 154.8, 154.1 (d, $J_{C\text{-}P}$ = 3.9 Hz), 148.2 (d, $J_{C\text{-}P}$ = 2.1 Hz), 137.5 (d, $J_{C\text{-}P}$ = 5.8 Hz), 130.9, 121.2, 120.6 (d, $J_{C\text{-}P}$ = 2.2 Hz), 119.3 (d, $J_{C\text{-}P}$ = 7.4 Hz), 105.1, 55.9, 54.4 (d, $J_{C\text{-}P}$ = 6.1 Hz); ^{31}P NMR (162 MHz, Chloroform-*d*) δ 25.23; HRMS (ESI) m/z calcd. for $C_{12}H_{15}NO_4PS$ $[M+H]^+$: 300.0454, found 300.0452.

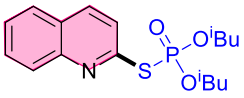


***O,O*-dibutyl *S*-quinolin-2-yl phosphorothioate (3ac):** Yellow oil (78.4 mg, 74%), ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.93 (s, 1H), 8.42 (s, 1H), 8.09 (d, *J* = 8.3 Hz, 1H), 7.83 – 7.70 (m, 2H), 7.58 (t, *J* = 7.0 Hz, 1H), 4.21 – 4.09 (m, 4H), 1.71 – 1.56 (m, 4H), 1.41 – 1.28 (m, 4H), 0.87 (t, *J* = 7.3 Hz, 6H); ^{13}C NMR (100 MHz, Chloroform-*d*) δ 153.7 (d, $J_{C\text{-}P}$ = 4.3 Hz), 147.4 (d, $J_{C\text{-}P}$ = 1.7 Hz), 142.1 (d, $J_{C\text{-}P}$ = 5.8 Hz), 130.6, 129.3, 128.0 (d, $J_{C\text{-}P}$ = 2.0 Hz), 127.5, 127.4, 120.9 (d, $J_{C\text{-}P}$ = 7.2 Hz), 68.2 (d, $J_{C\text{-}P}$ = 6.9 Hz), 32.1 (d, $J_{C\text{-}P}$ = 7.0 Hz), 18.6, 13.5; ^{31}P NMR (162 MHz, Chloroform-*d*) δ 21.79; HRMS (ESI) m/z calcd. for $C_{17}H_{25}NO_3PS$ $[M+H]^+$: 354.1287, found 354.1292.

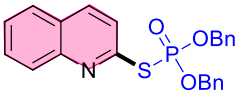


***O,O*-diisopropyl *S*-quinolin-2-yl phosphorothioate (3ad):** Yellow oil (80.9 mg, 83%), ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.96 (s, 1H), 8.46 (s, 1H), 8.09 (d, *J* = 8.4 Hz, 1H), 7.80 (d, *J* = 8.1 Hz, 1H), 7.74 (t, *J* = 7.7 Hz, 1H), 7.57 (t, *J* = 7.5 Hz, 1H), 4.85 – 4.74 (m, 2H), 1.31 (dd, *J* = 13.3, 6.1 Hz, 12H); ^{13}C NMR (100 MHz, Chloroform-*d*) δ 153.7 (d, $J_{C\text{-}P}$ = 4.6 Hz), 147.3 (d, $J_{C\text{-}P}$ = 1.8 Hz), 141.9 (d, $J_{C\text{-}P}$ = 5.9 Hz), 130.5, 129.3, 128.0 (d, $J_{C\text{-}P}$ = 2.0 Hz), 127.6, 127.4, 121.6 (d, $J_{C\text{-}P}$ = 7.1 Hz), 73.9 (d, $J_{C\text{-}P}$ = 7.0 Hz), 23.8, 23.8, 23.6, 23.5; ^{31}P NMR (162 MHz, Chloroform-*d*) δ 19.21; HRMS (ESI) m/z calcd.

for $C_{15}H_{21}NO_3PS$ $[M+H]^+$: 326.0974, found 326.0977.

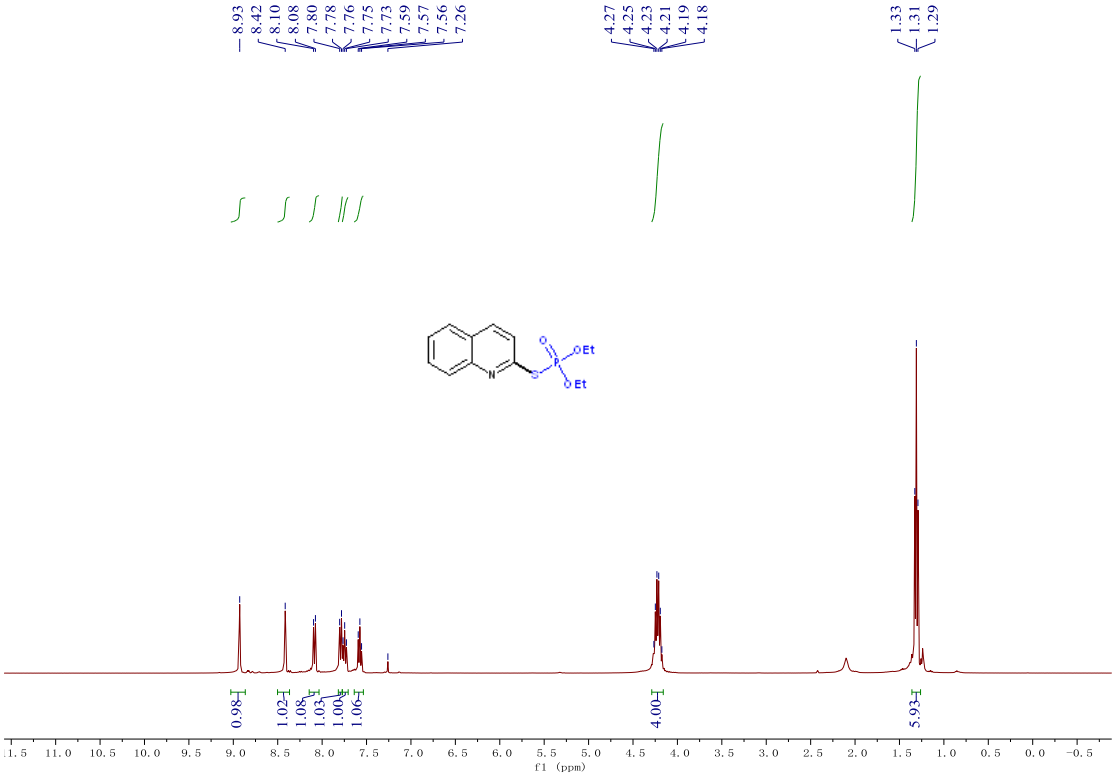


***O,O*-diisobutyl *S*-quinolin-2-yl phosphorothioate (3ae):** Yellow oil (77.3 mg, 73%), ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.94 (s, 1H), 8.44 (s, 1H), 8.10 (d, *J* = 8.3 Hz, 1H), 7.83 – 7.72 (m, 2H), 7.59 (t, *J* = 7.1 Hz, 1H), 4.00 – 3.85 (m, 4H), 2.02 – 1.86 (m, 2H), 1.01 – 0.81 (m, 12H); ^{13}C NMR (100 MHz, Chloroform-*d*) δ 153.7 (d, $J_{C\text{-}P}$ = 4.4 Hz), 147.4 (d, $J_{C\text{-}P}$ = 4.4 Hz), 142.1 (d, $J_{C\text{-}P}$ = 5.7 Hz), 130.6, 129.3, 128.0, 127.6, 127.5, 120.9 (d, $J_{C\text{-}P}$ = 7.0 Hz), 74.2 (d, $J_{C\text{-}P}$ = 7.3 Hz), 29.0 (d, $J_{C\text{-}P}$ = 7.3 Hz), 18.6; ^{31}P NMR (162 MHz, Chloroform-*d*) δ 21.62; HRMS (ESI) m/z calcd. for $C_{17}H_{25}NO_3PS$ $[M+H]^+$: 354.1287, found 354.1291.

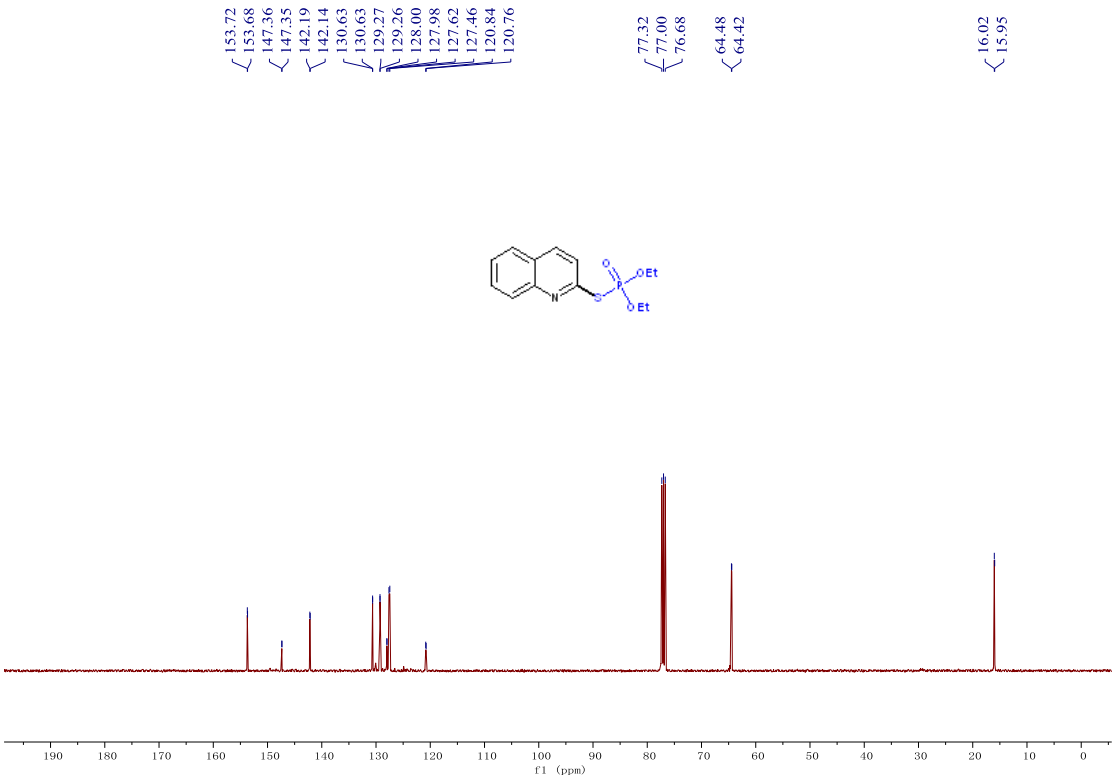


***O,O*-dibenzyl *S*-quinolin-2-yl phosphorothioate (3af):** Yellow oil (78.3 mg, 62%), ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.85 (s, 1H), 8.17 (s, 1H), 8.12 (d, *J* = 8.5 Hz, 1H), 7.78 (t, *J* = 7.5 Hz, 1H), 7.67 – 7.57 (m, 2H), 7.37 – 7.28 (m, 10H), 5.24 – 5.15 (m, 4H); ^{13}C NMR (100 MHz, Chloroform-*d*) δ 153.7 (d, $J_{C\text{-}P}$ = 4.2 Hz), 147.3 (d, $J_{C\text{-}P}$ = 2.0 Hz), 142.6 (d, $J_{C\text{-}P}$ = 5.8 Hz), 135.0 (d, $J_{C\text{-}P}$ = 6.9 Hz), 130.7, 129.2, 128.8, 128.6, 128.2, 127.9 (d, $J_{C\text{-}P}$ = 2.3 Hz), 127.7, 127.3, 120.1 (d, $J_{C\text{-}P}$ = 7.4 Hz), 69.8 (d, $J_{C\text{-}P}$ = 6.5 Hz); ^{31}P NMR (162 MHz, Chloroform-*d*) δ 22.76; HRMS (ESI) m/z calcd. for $C_{23}H_{21}NO_3PS$ $[M+H]^+$: 422.0974, found 422.0977.

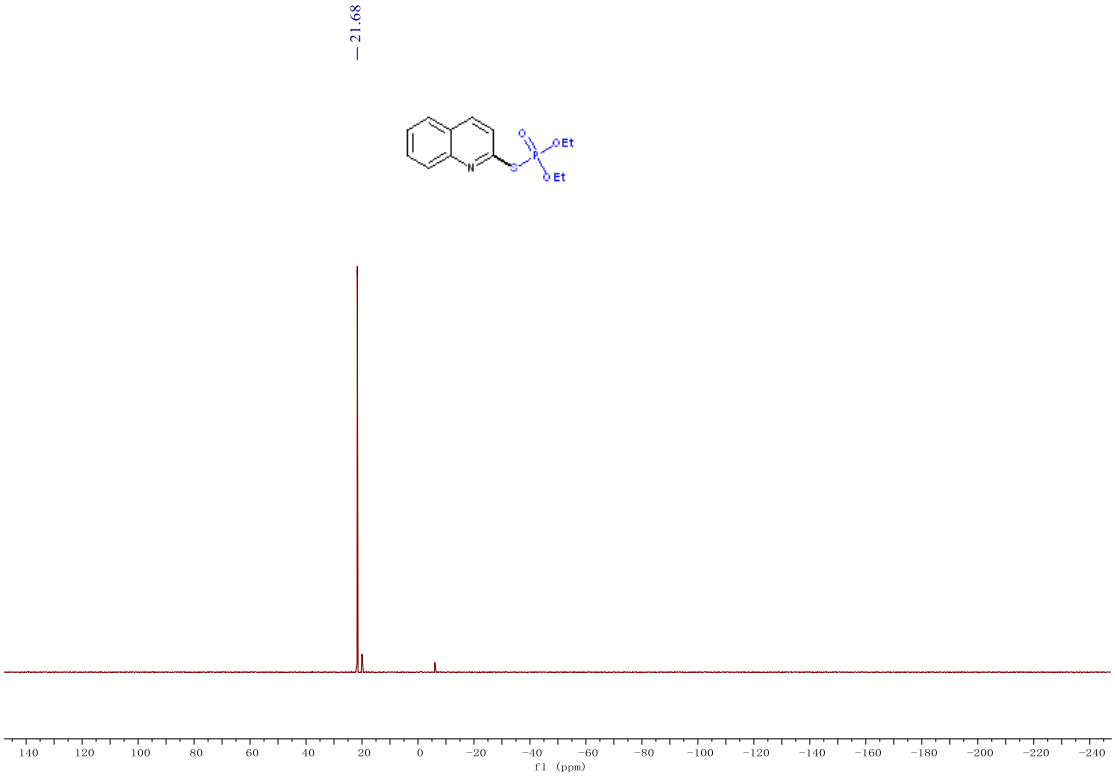
4. NMR spectrum of products



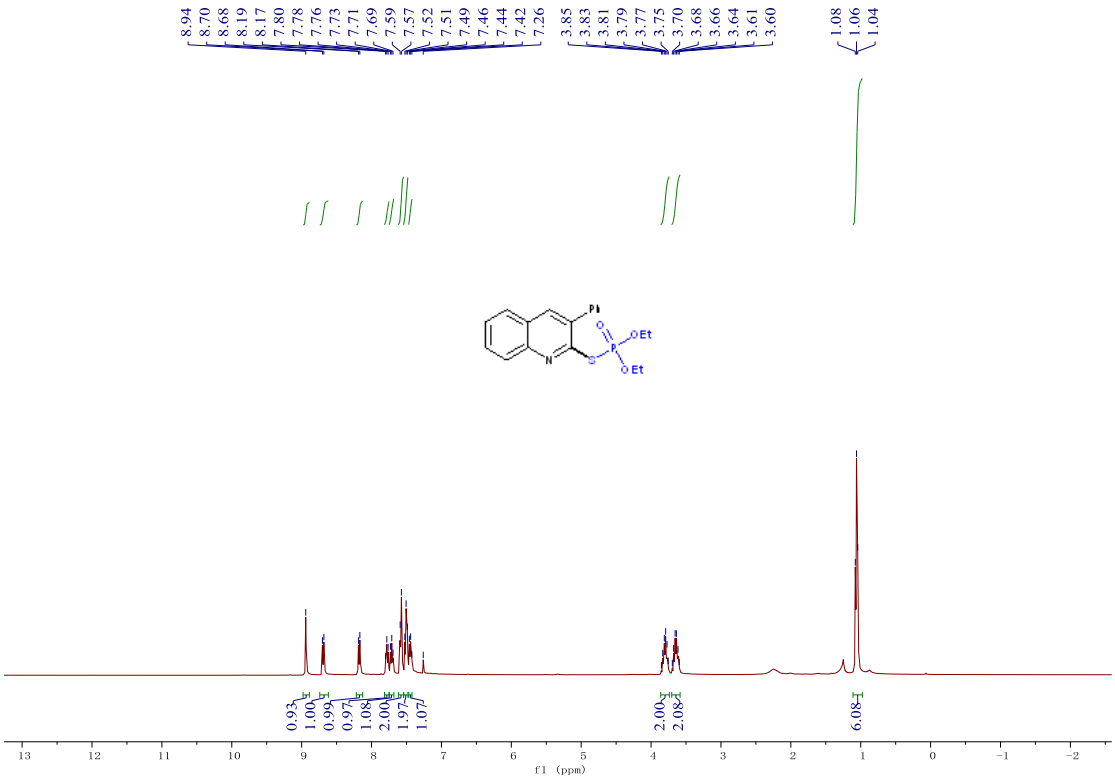
^{1}H spectrum of compound **3aa**



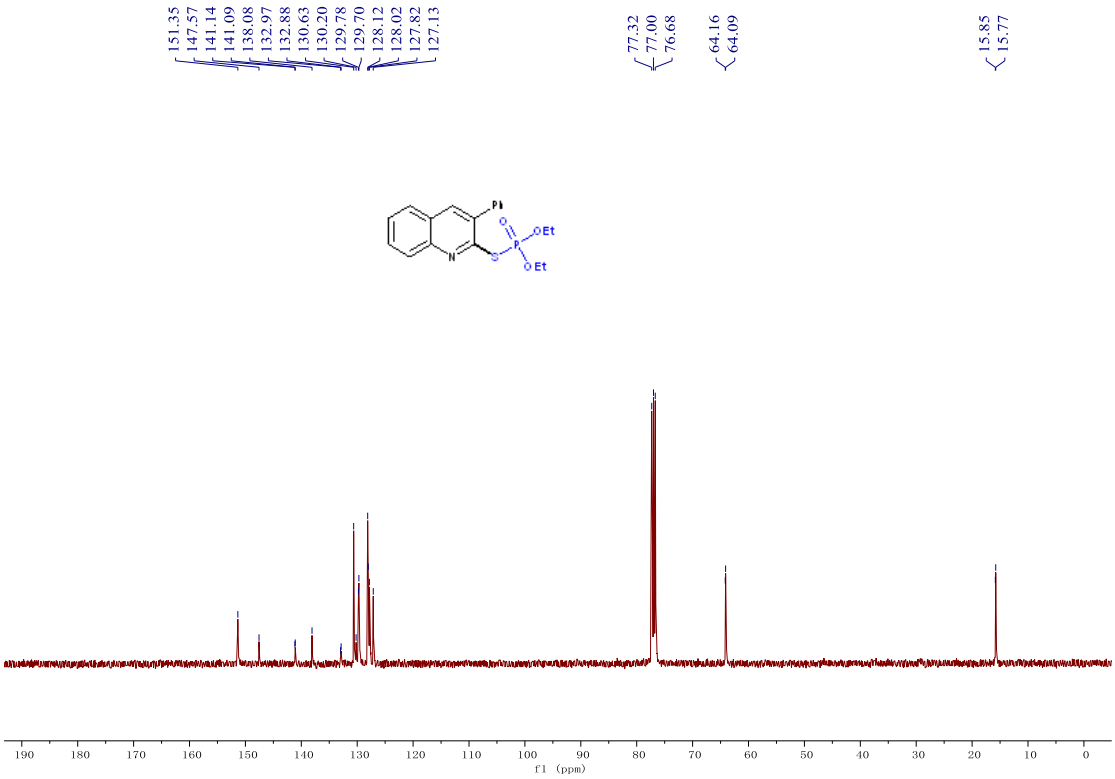
^{13}C spectrum of compound **3aa**



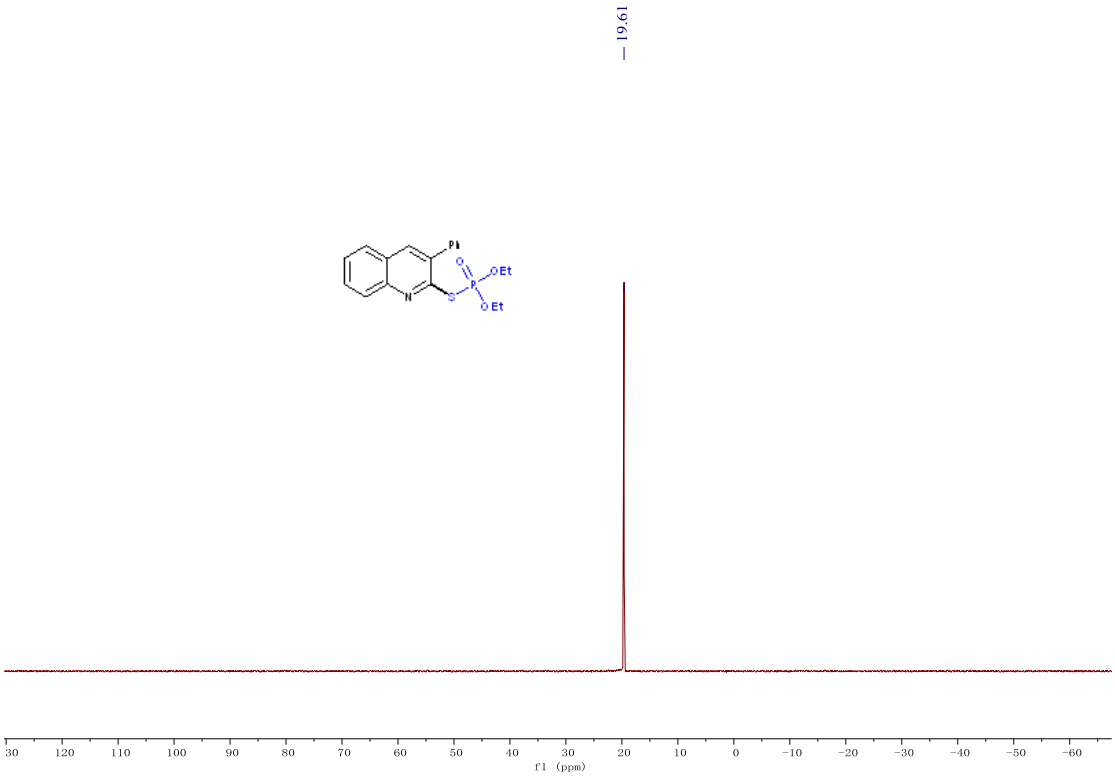
^{31}P spectrum of compound **3aa**



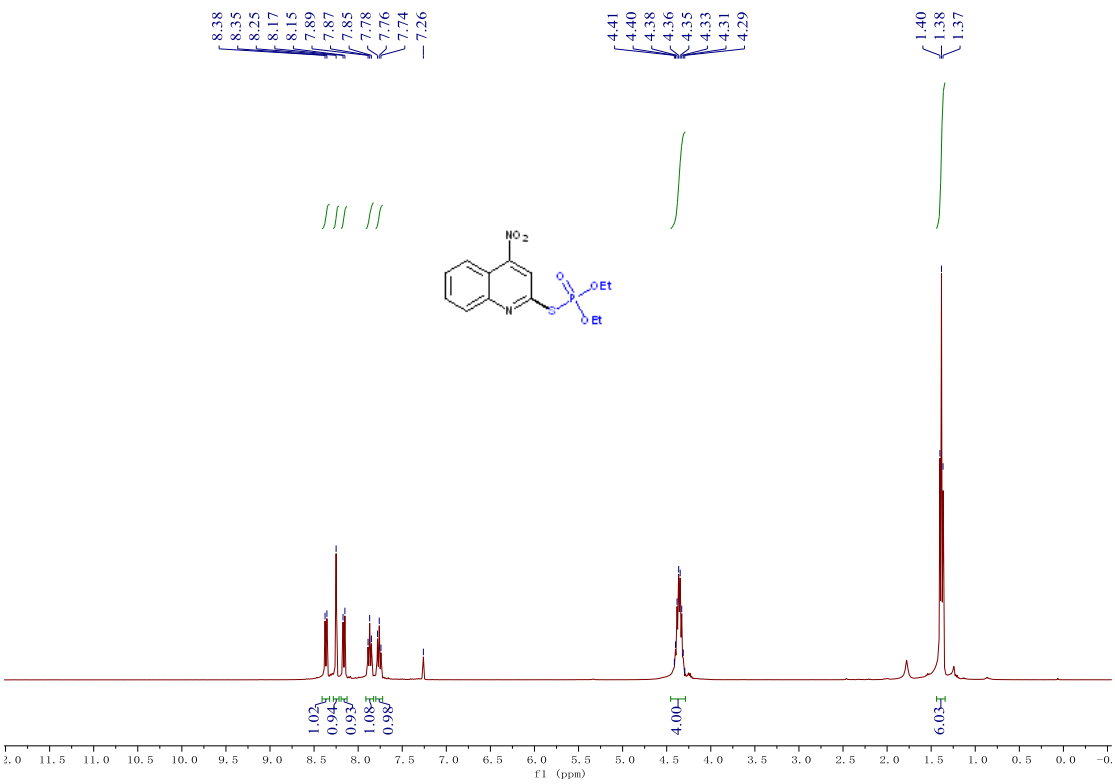
^{1}H spectrum of compound **3ba**



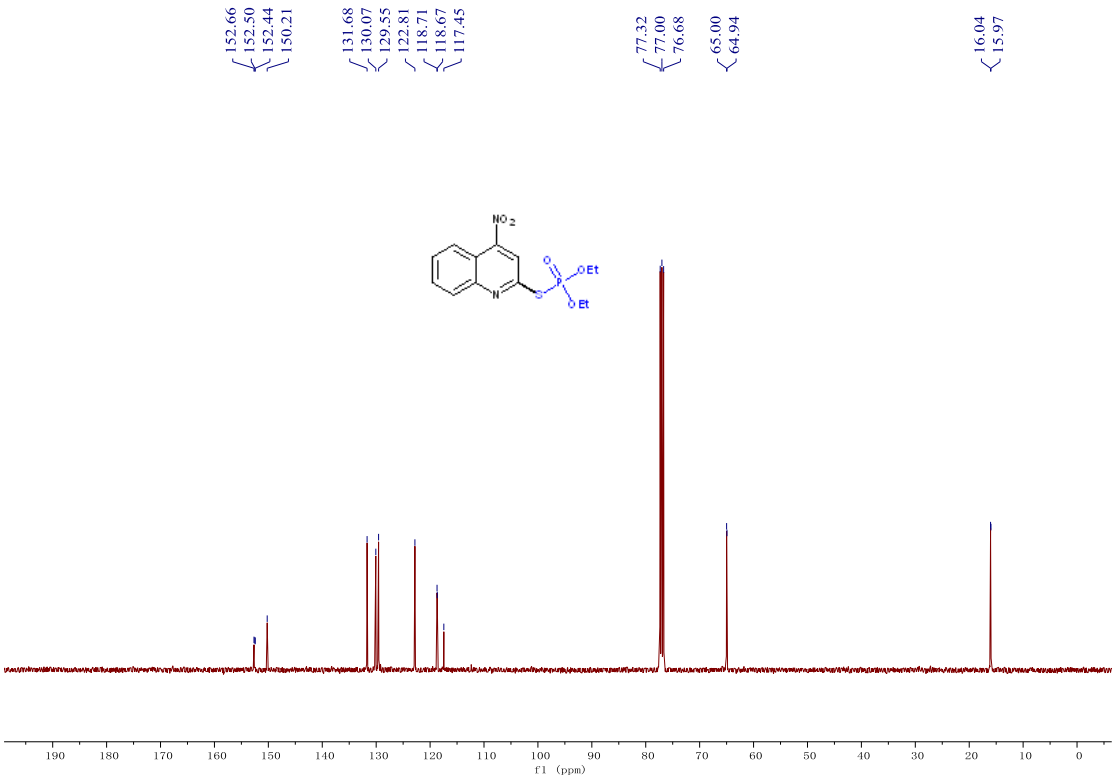
^{13}C spectrum of compound **3ba**



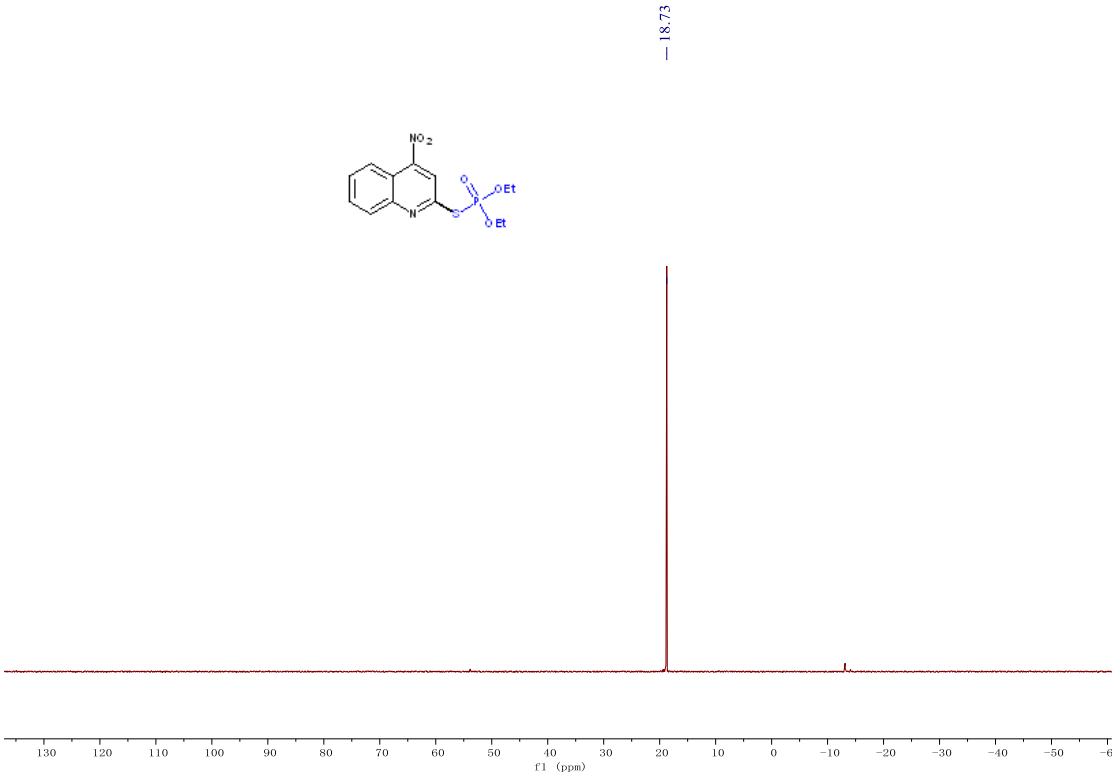
^{31}P spectrum of compound **3ba**



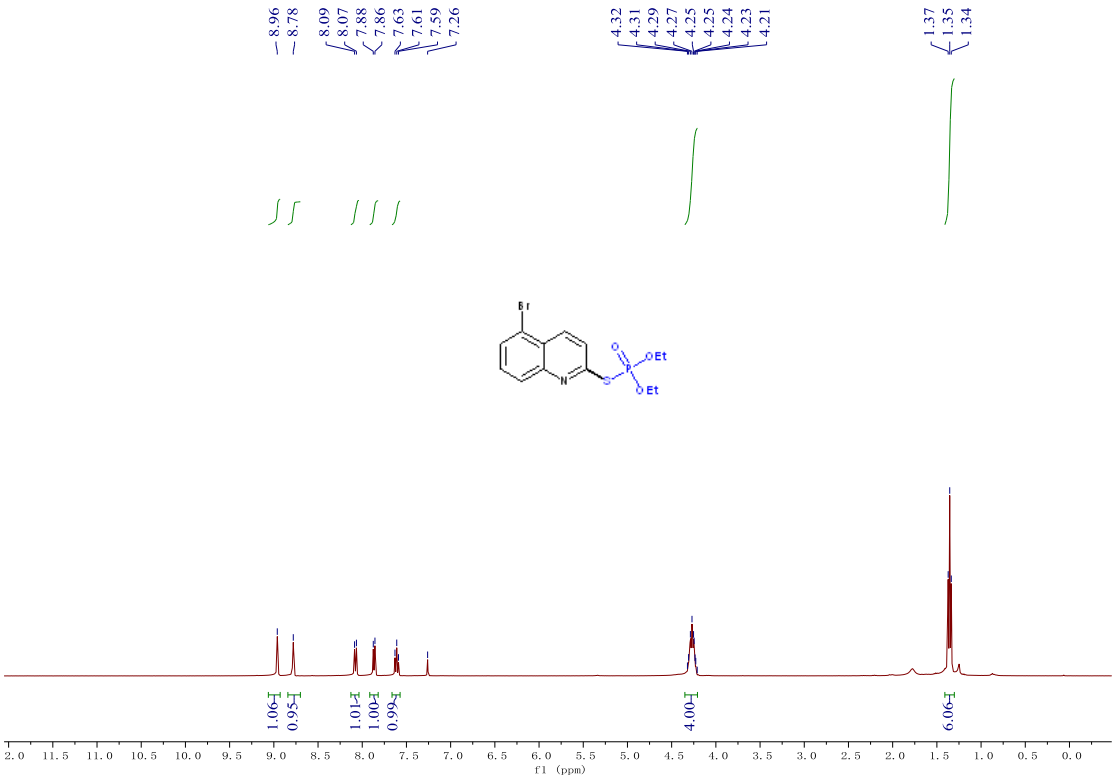
^{1}H spectrum of compound **3ca**



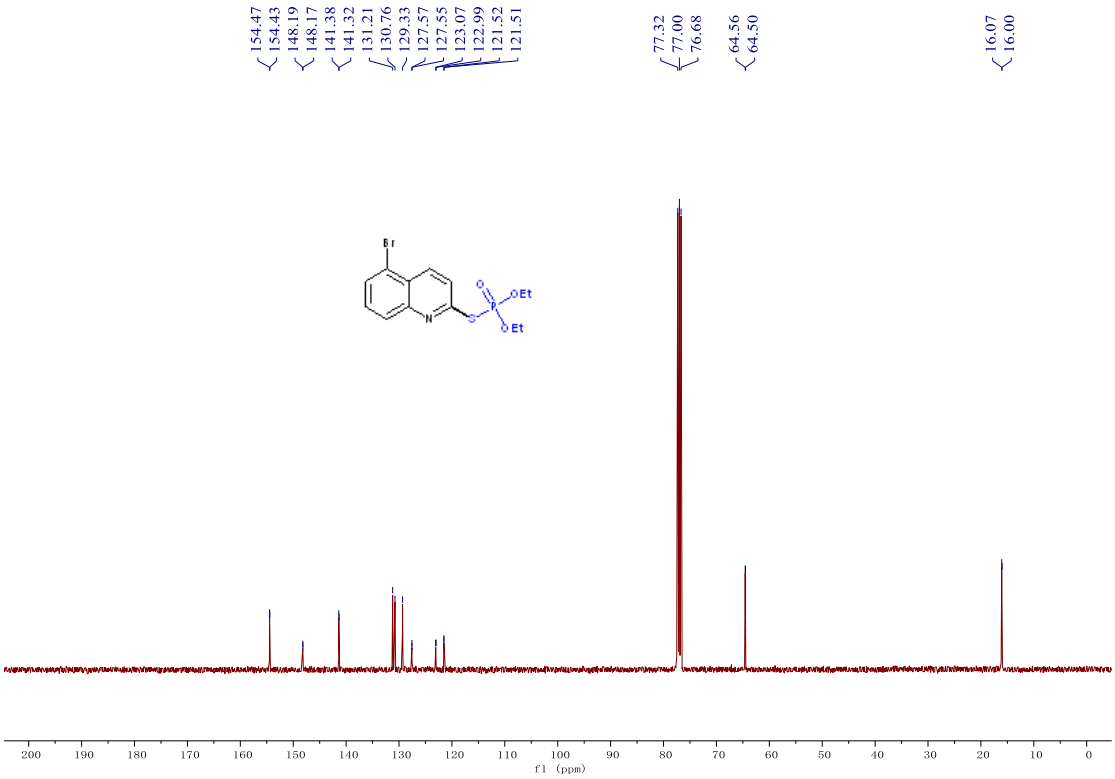
^{13}C spectrum of compound **3ca**



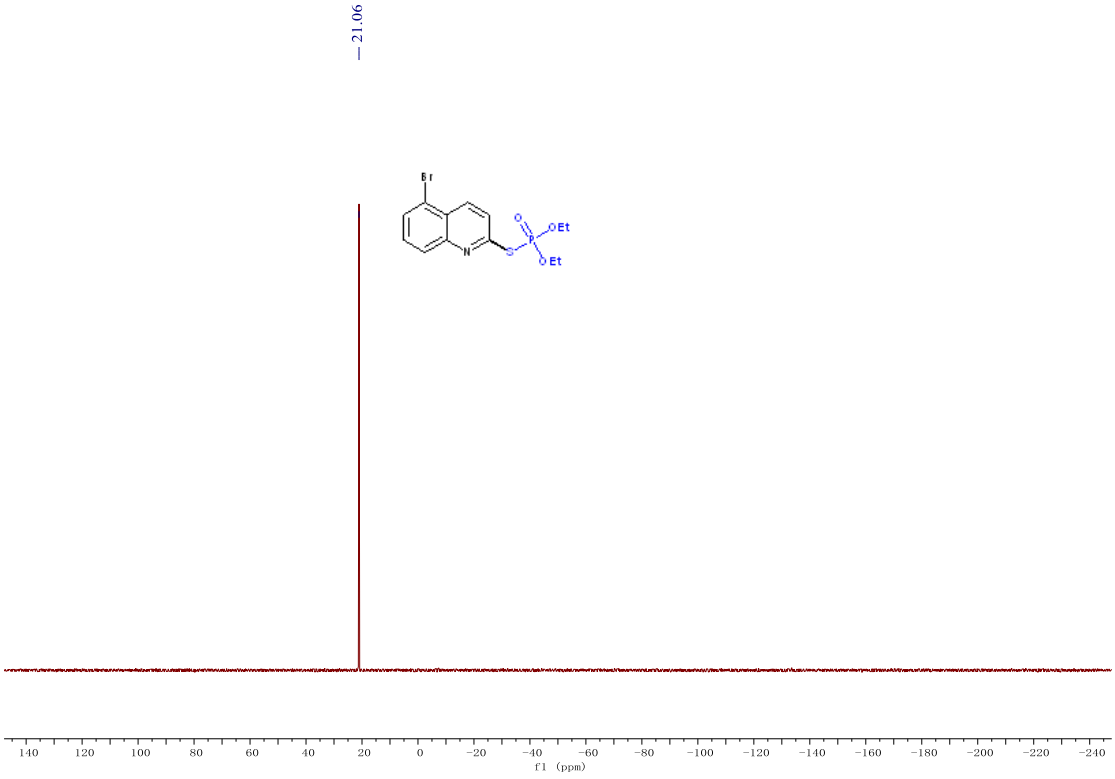
^{31}P spectrum of compound **3ca**



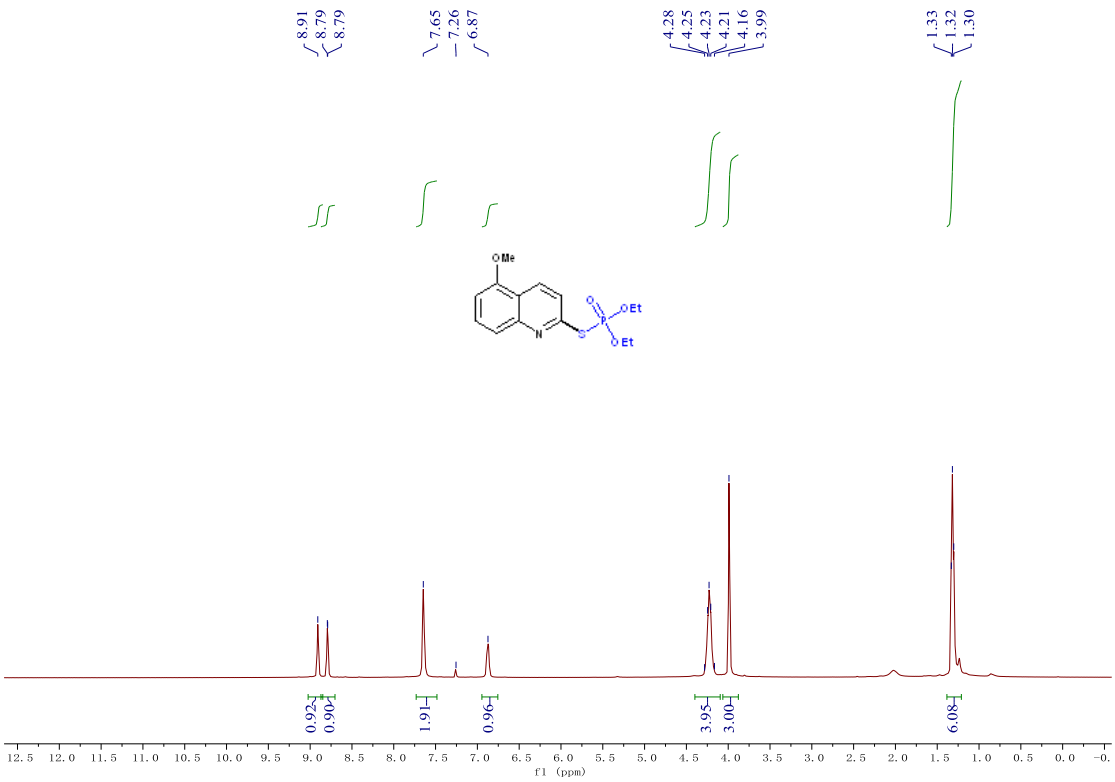
^{1}H spectrum of compound **3da**



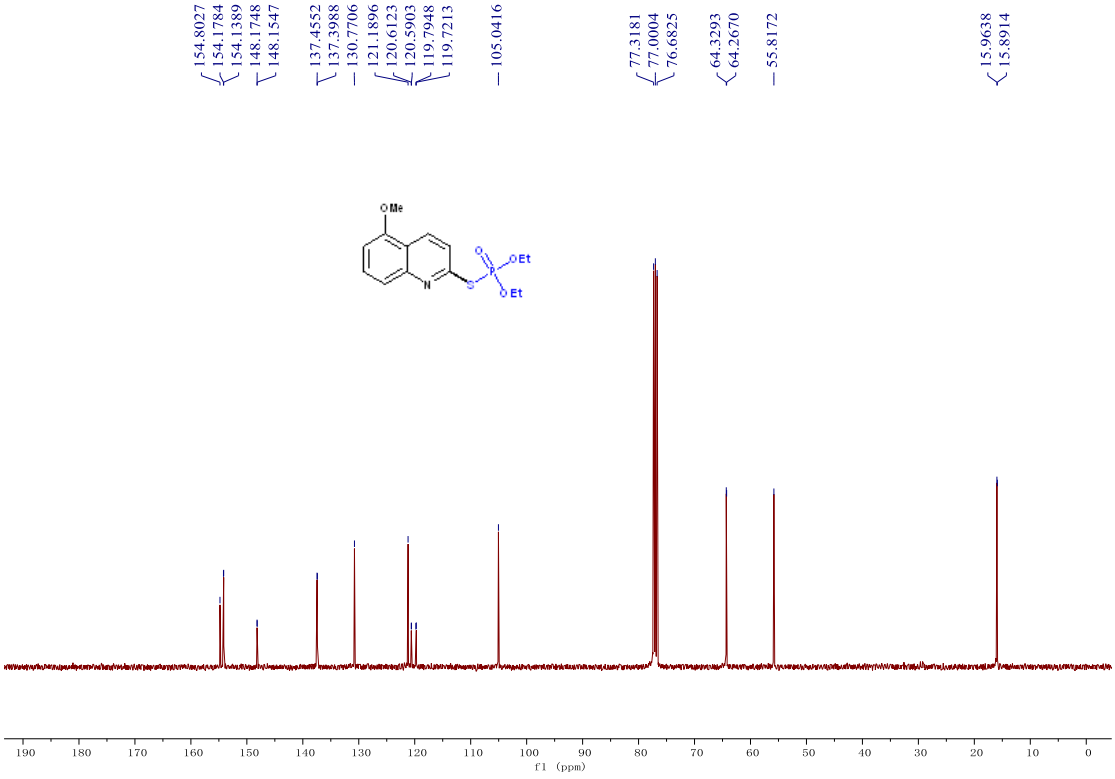
^{13}C spectrum of compound **3da**



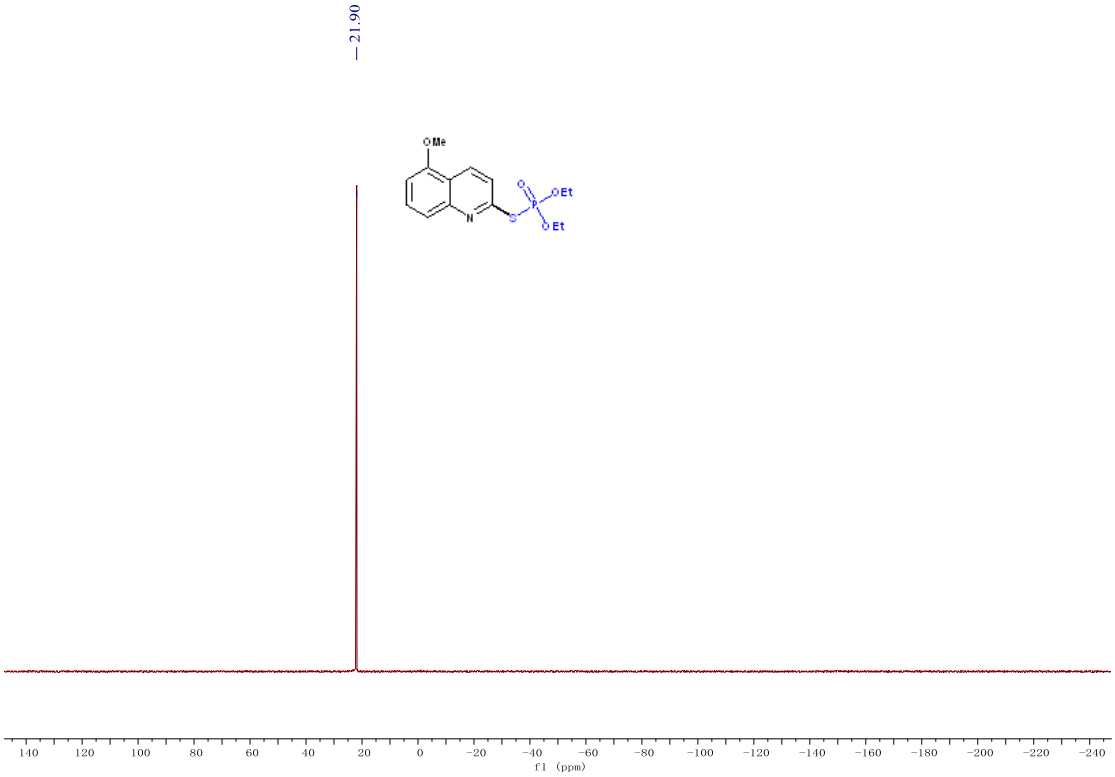
^{31}P spectrum of compound **3da**



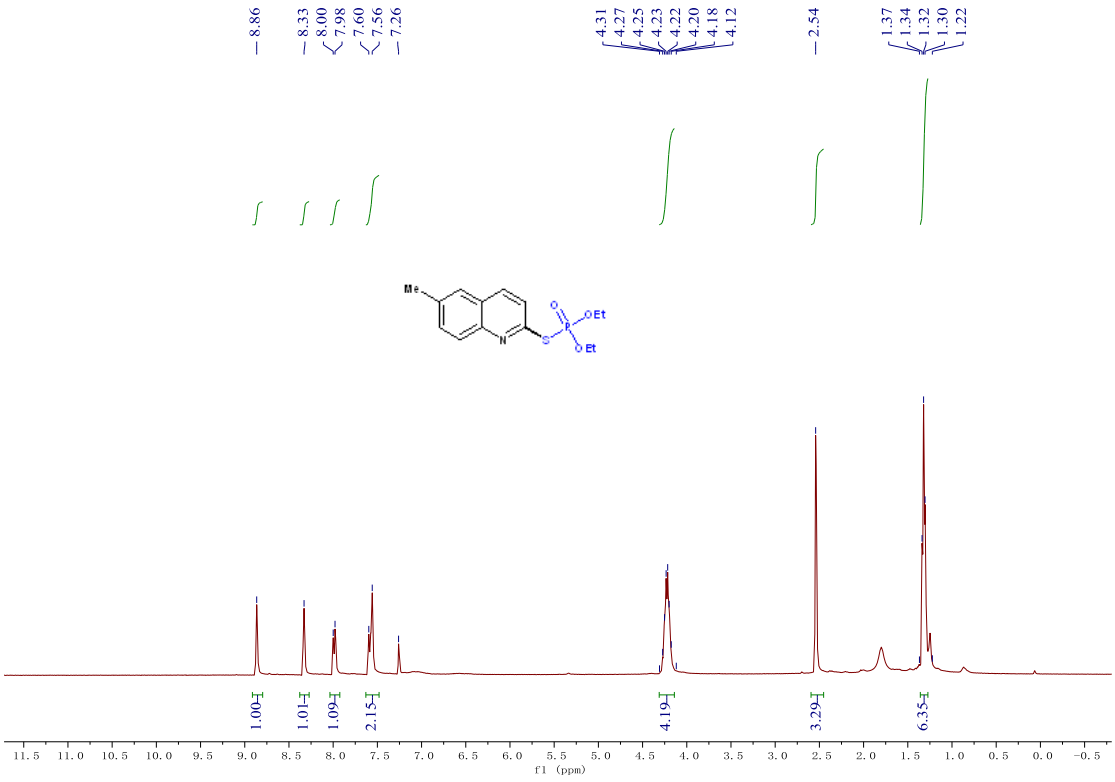
^{1}H spectrum of compound **3ea**



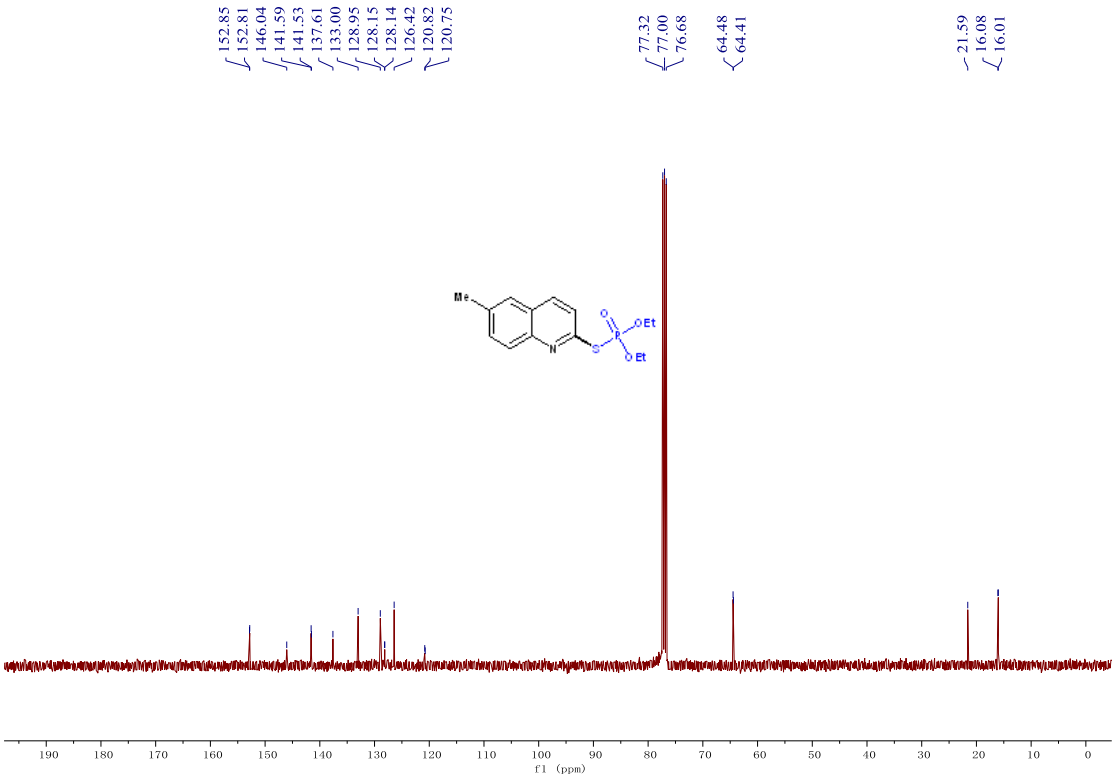
^{13}C spectrum of compound **3ea**



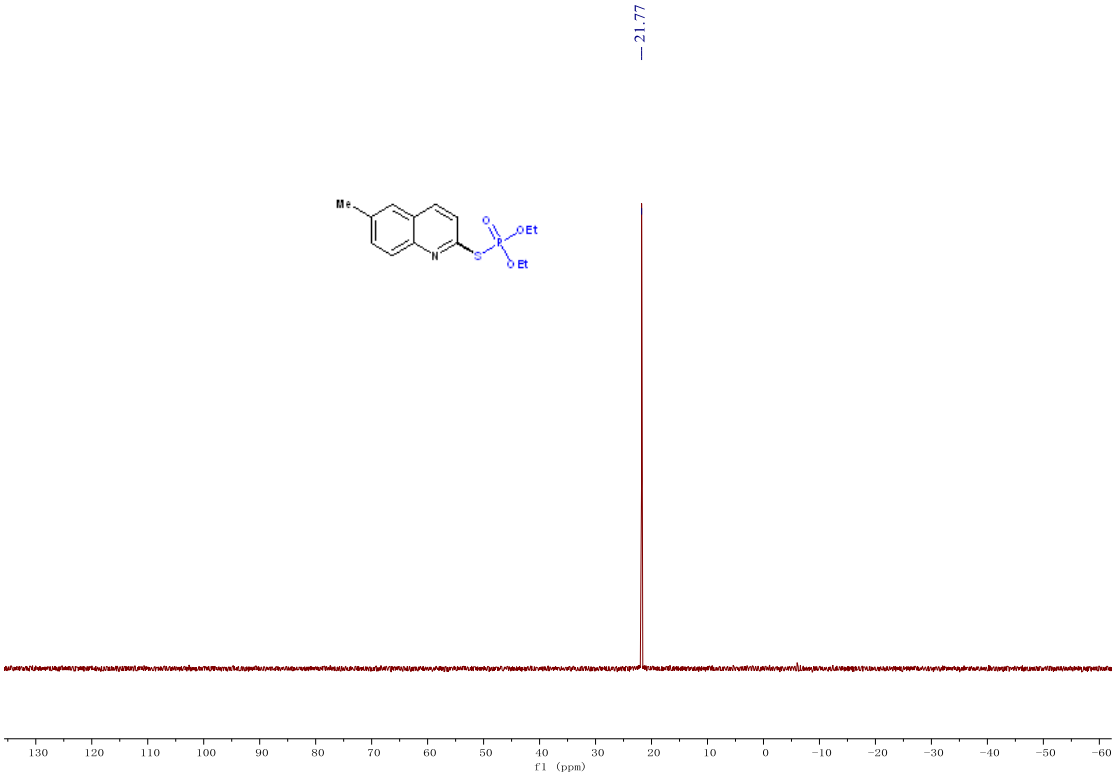
^{31}P spectrum of compound **3ea**



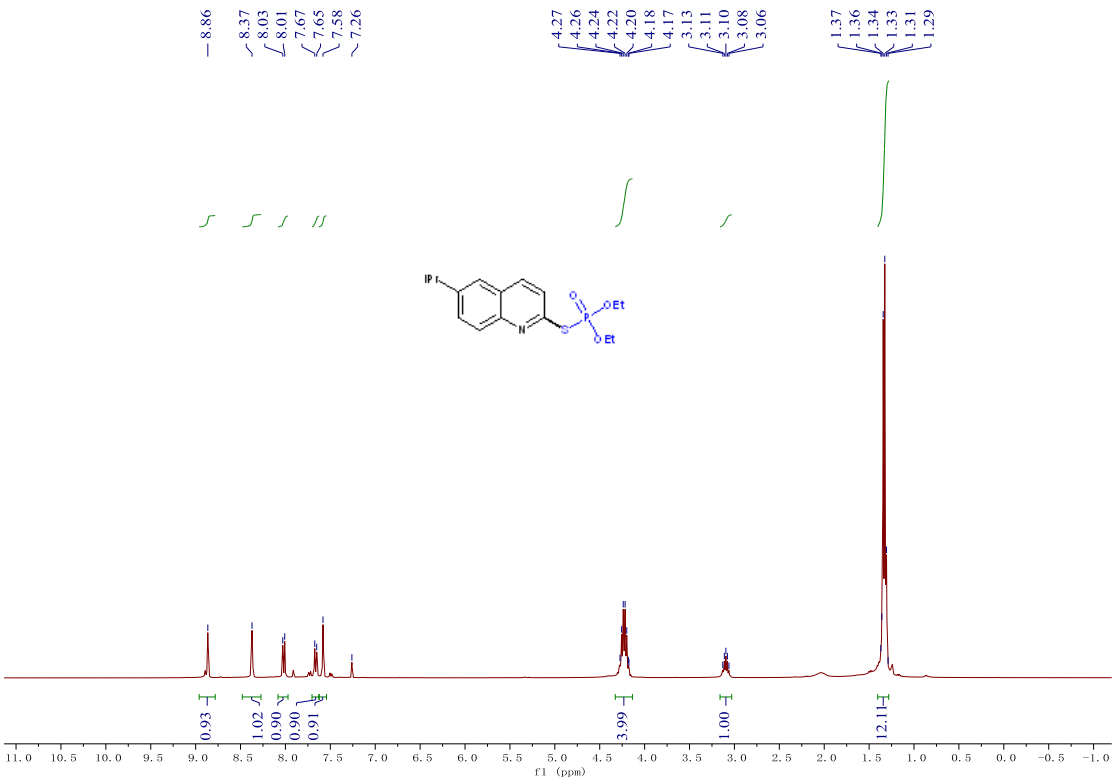
^{1}H spectrum of compound **3fa**



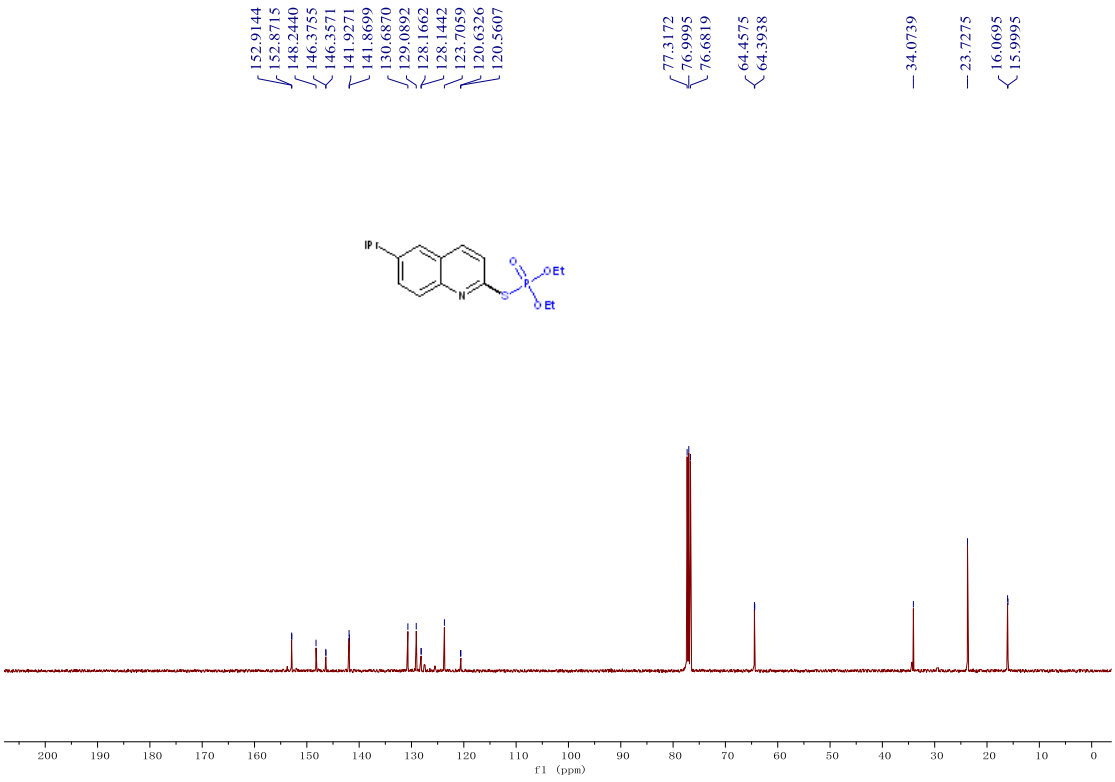
^{13}C spectrum of compound **3fa**



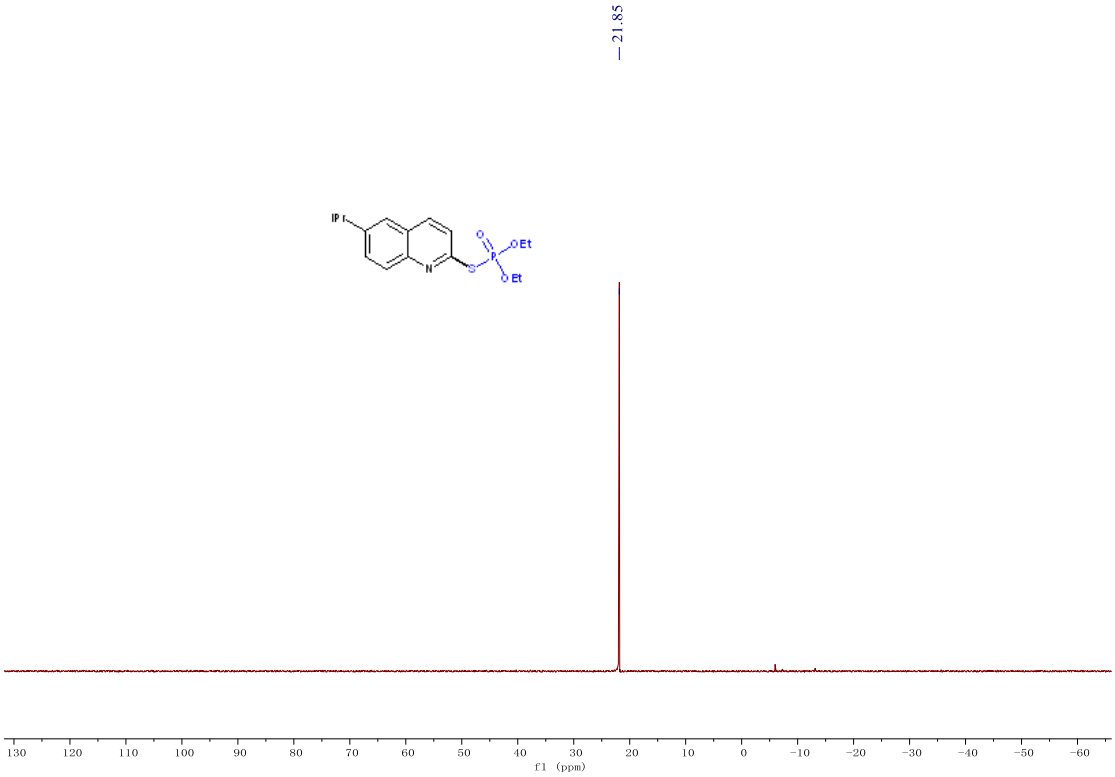
^{31}P spectrum of compound **3fa**



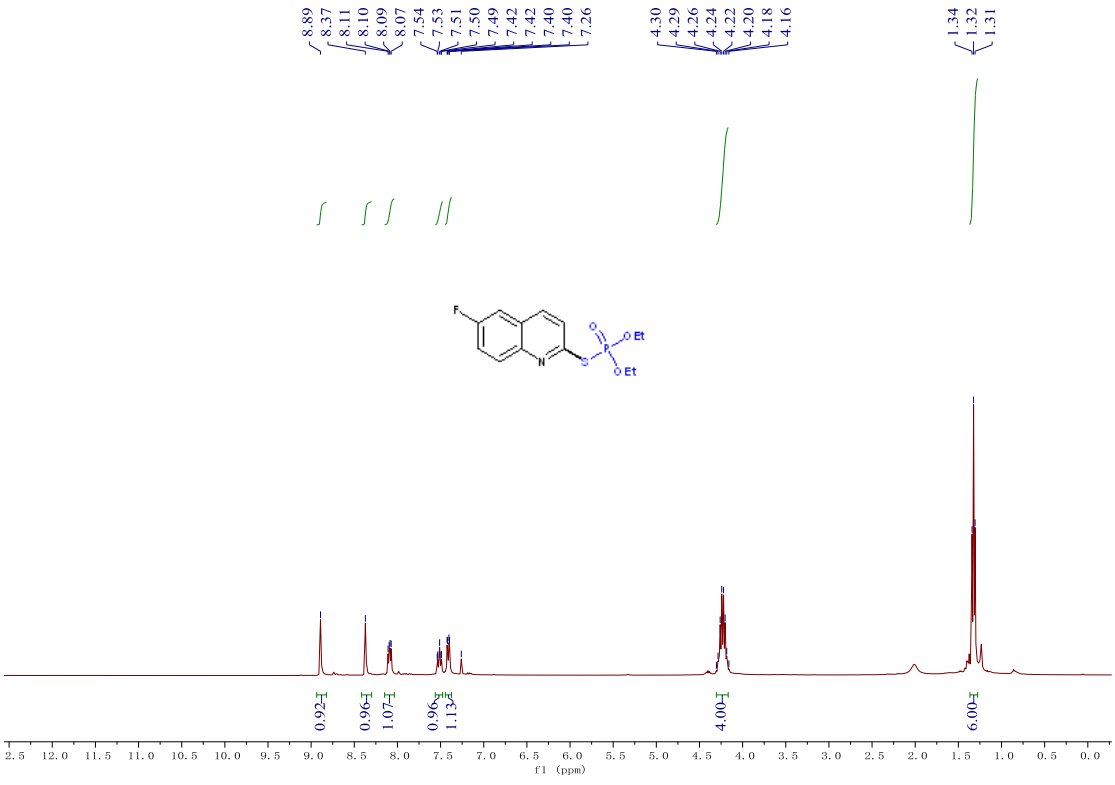
^{1}H spectrum of compound **3ga**



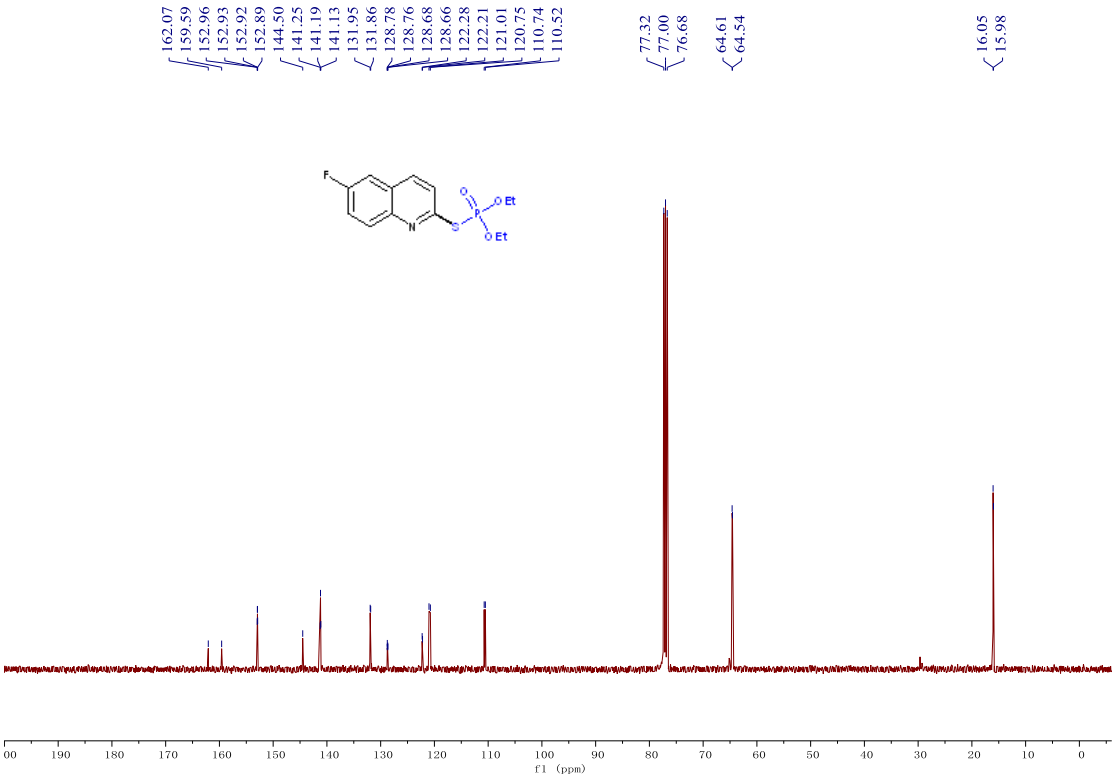
^{13}C spectrum of compound **3ga**



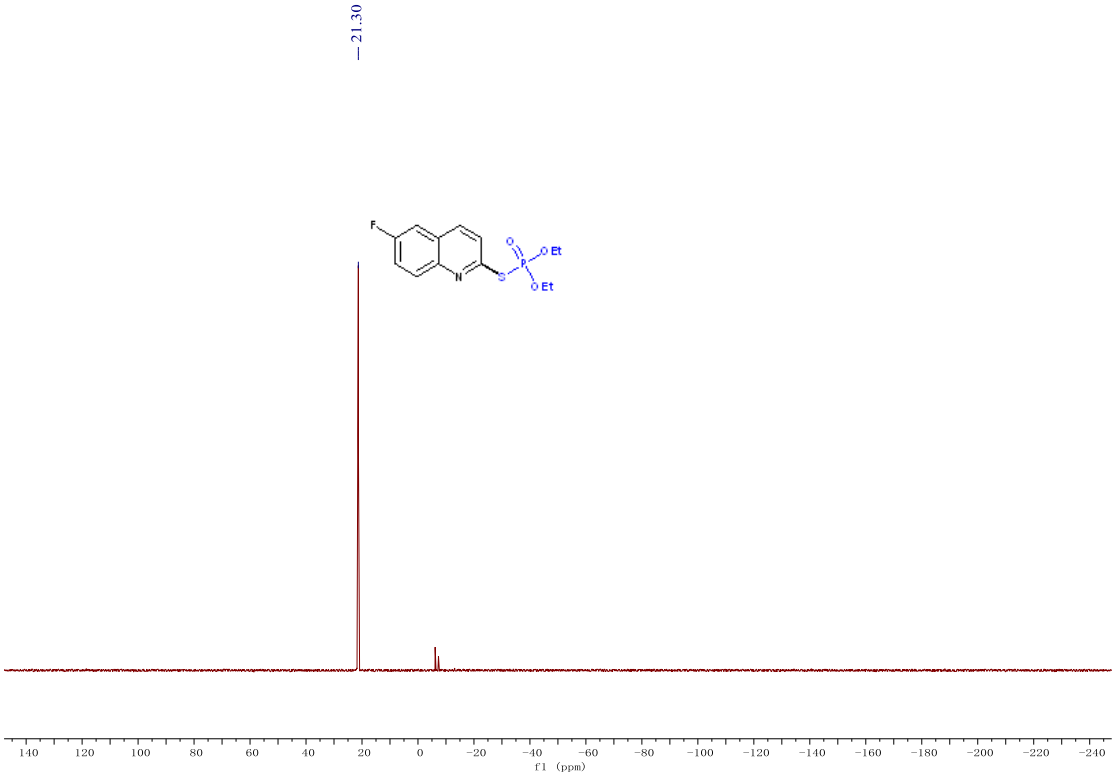
^{31}P spectrum of compound **3ga**



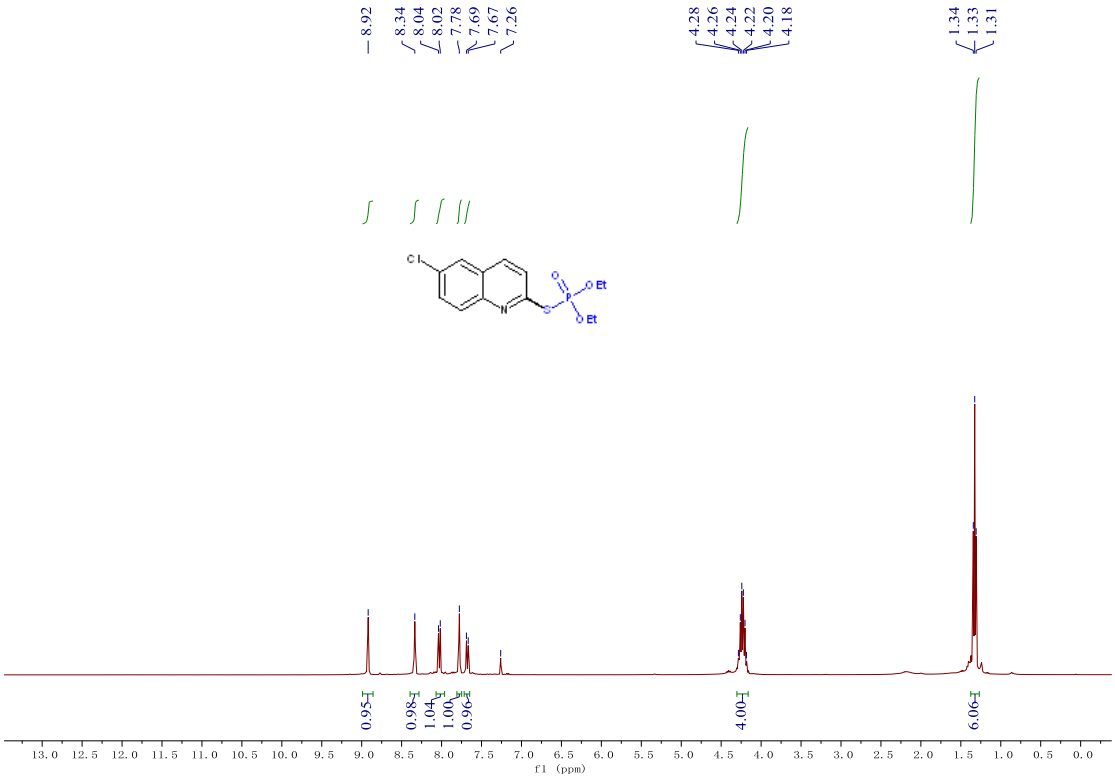
^{1}H spectrum of compound **3ha**



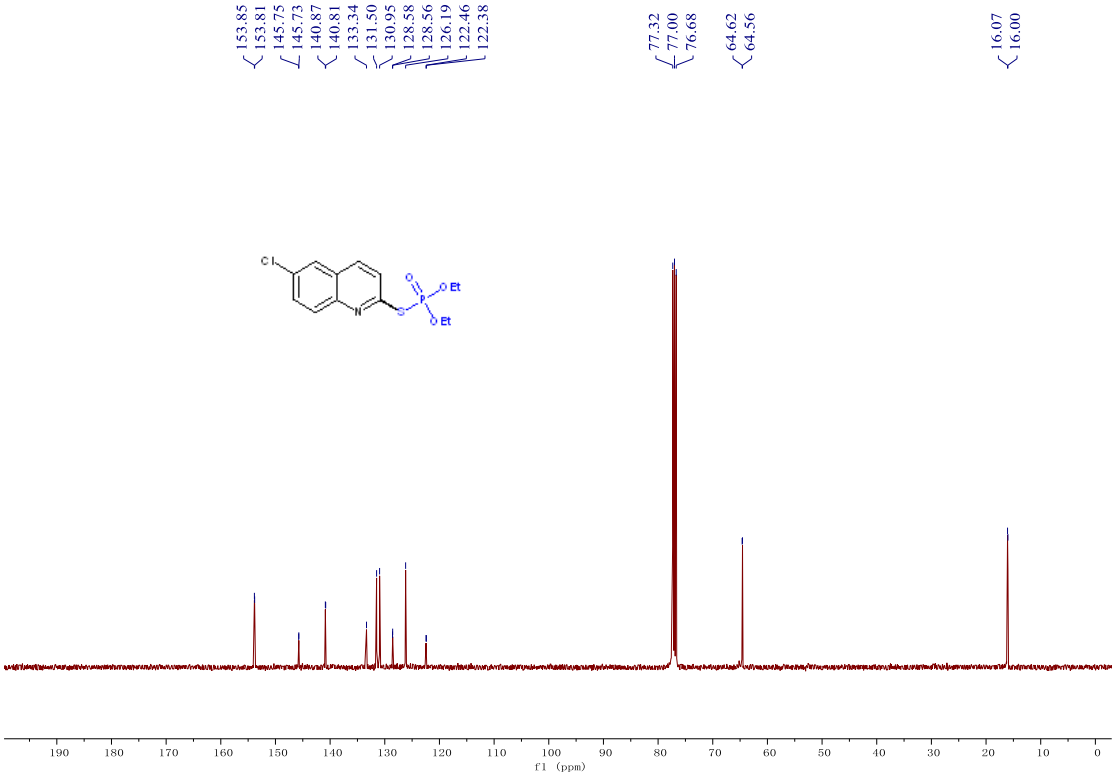
^{13}C spectrum of compound **3ha**



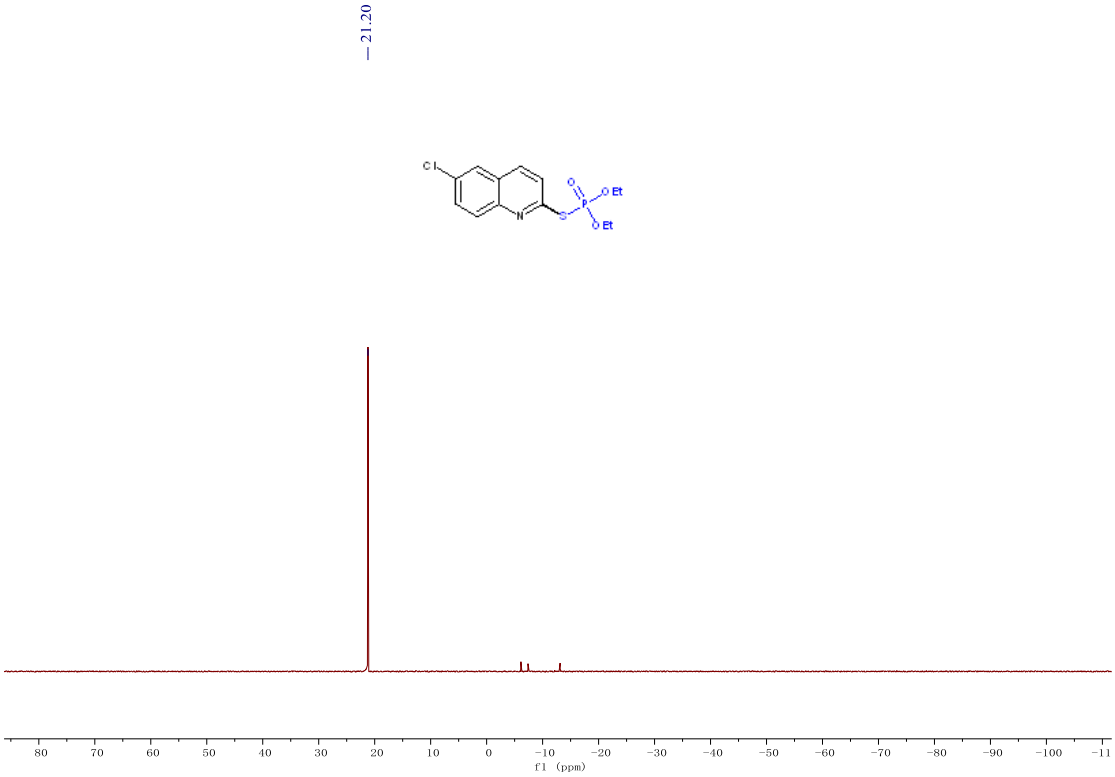
^{31}P spectrum of compound **3ha**



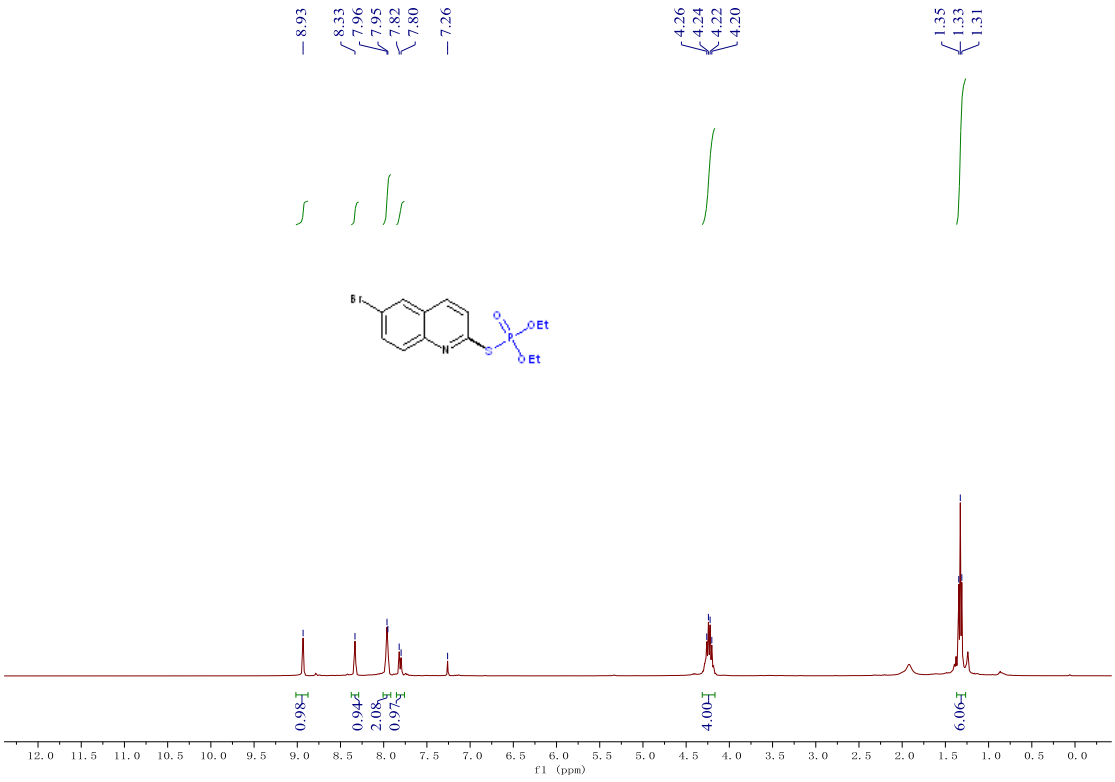
^{1}H spectrum of compound **3ia**



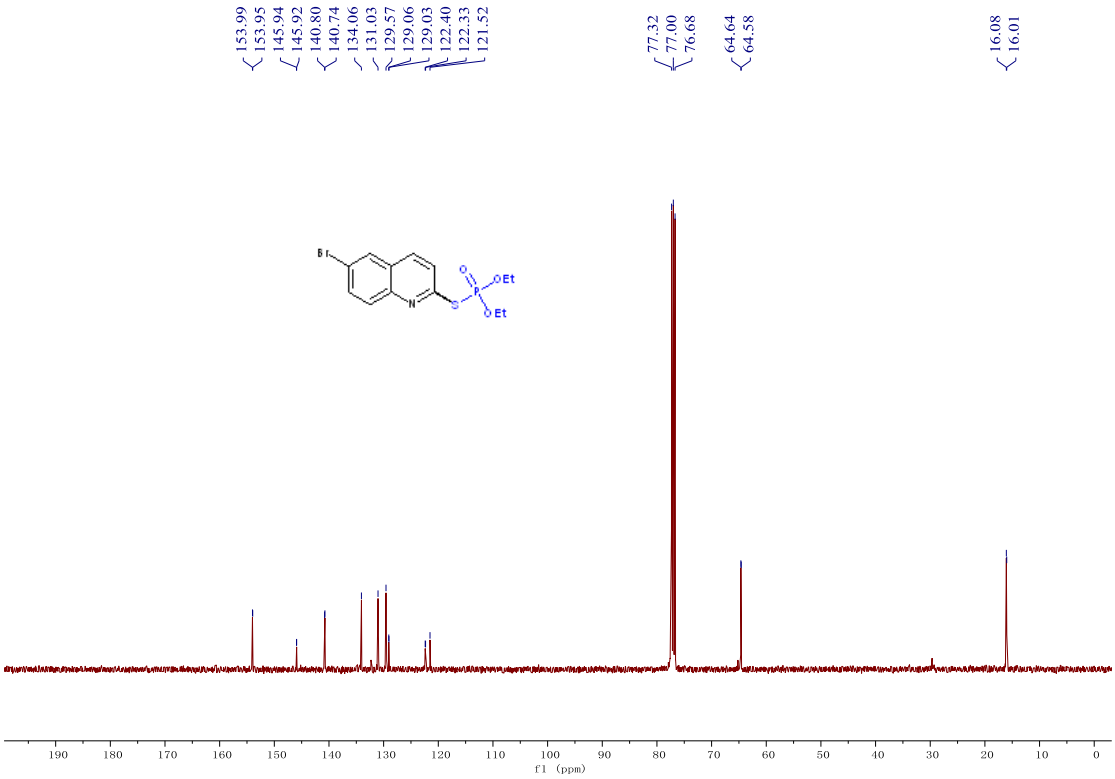
^{13}C spectrum of compound **3ia**



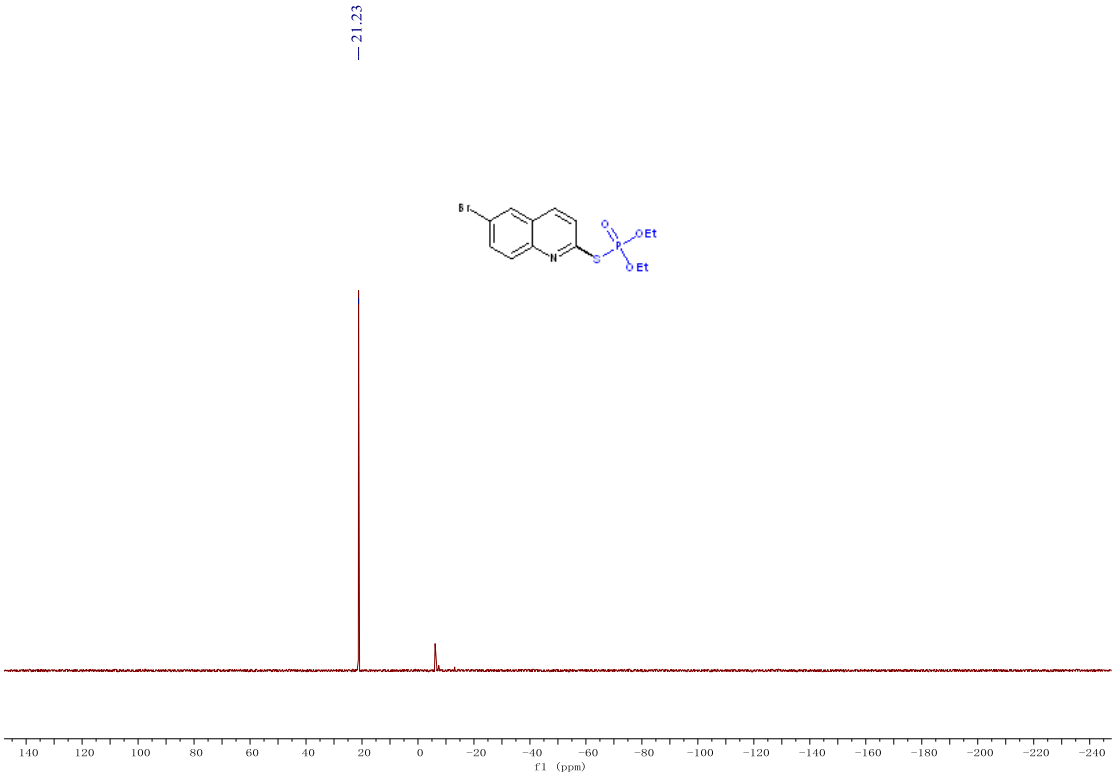
^{31}P spectrum of compound **3ia**



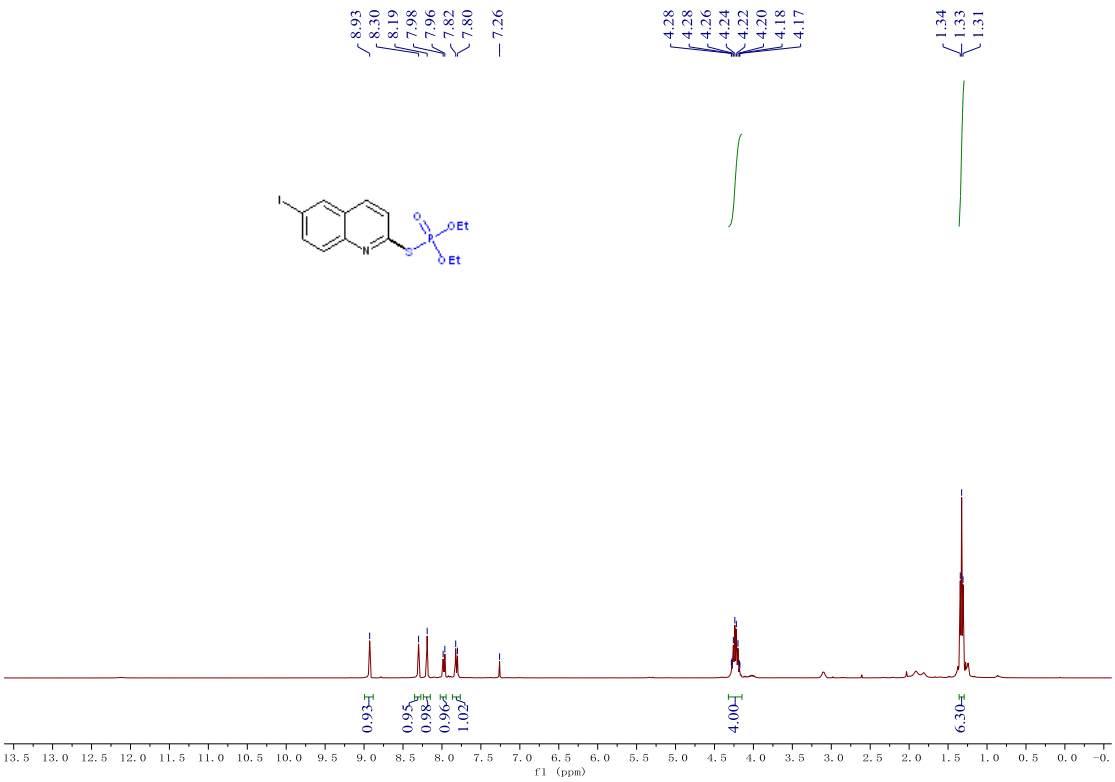
^{1}H spectrum of compound **3ja**



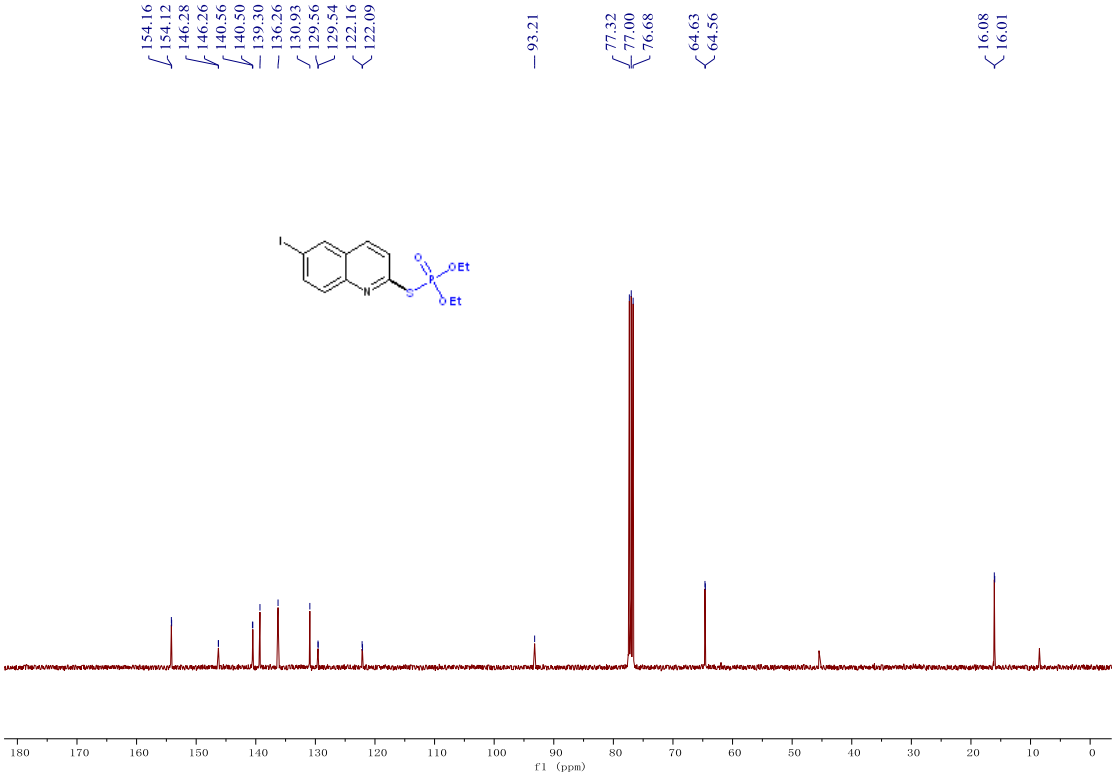
^{13}C spectrum of compound **3ja**



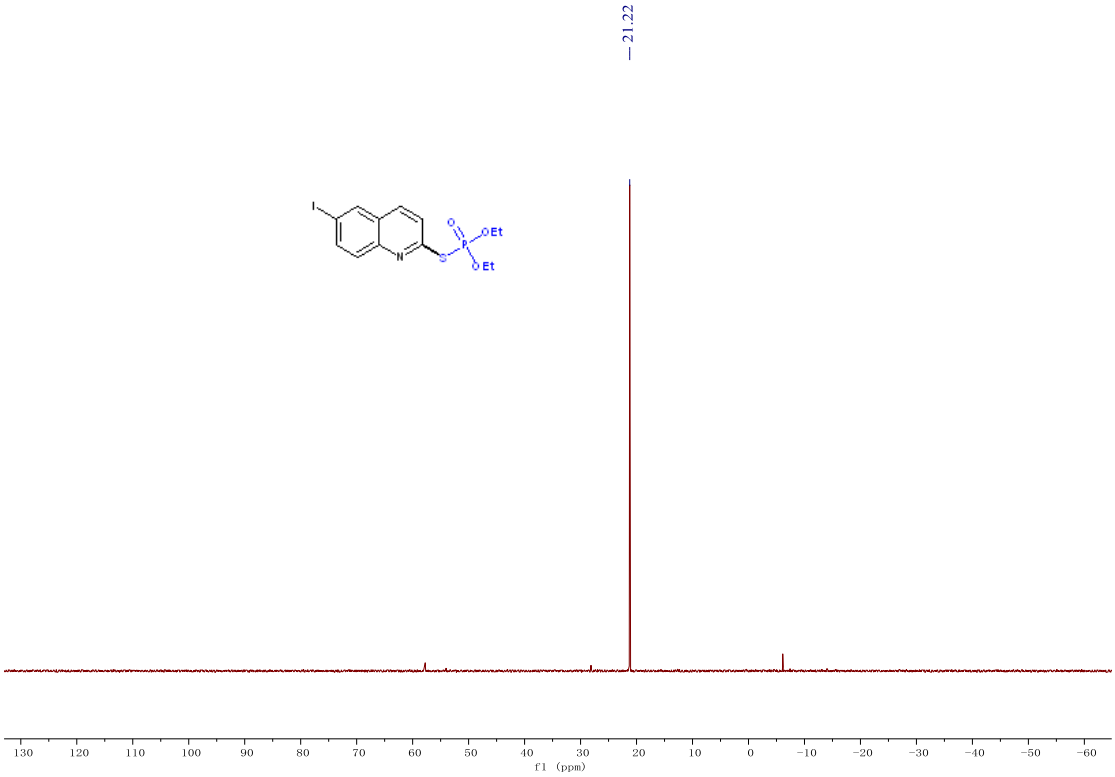
^{31}P spectrum of compound **3ja**



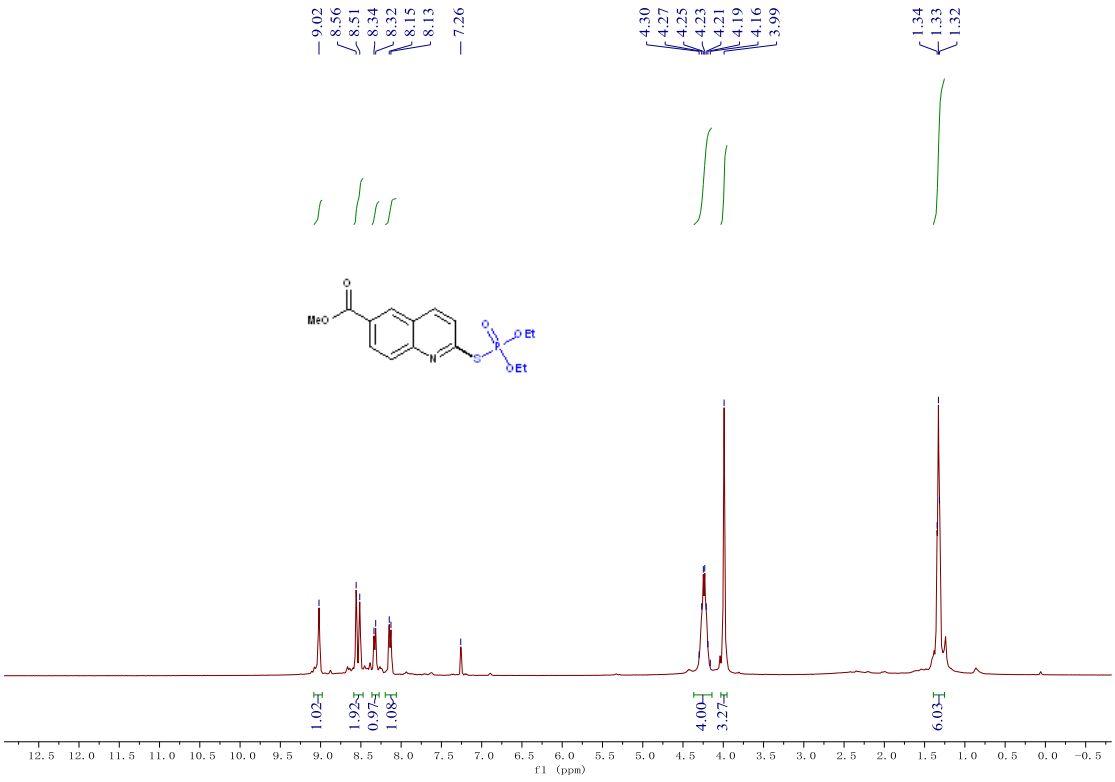
^{1}H spectrum of compound **3ka**



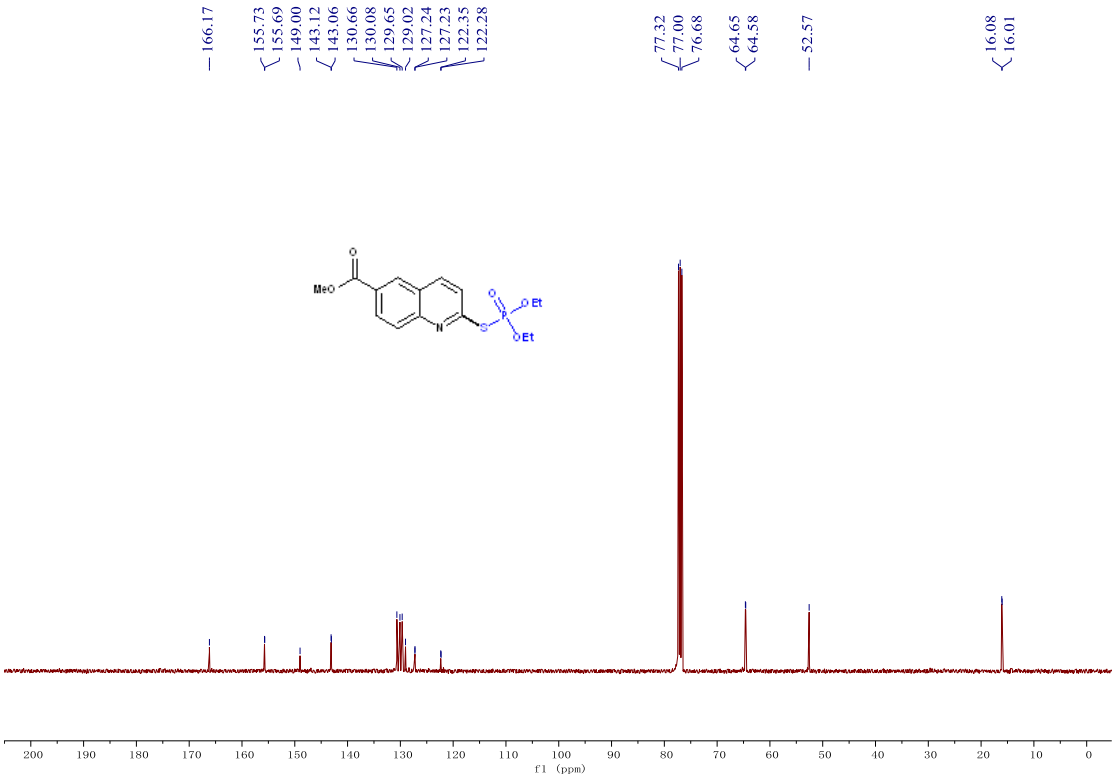
^{13}C spectrum of compound **3ka**



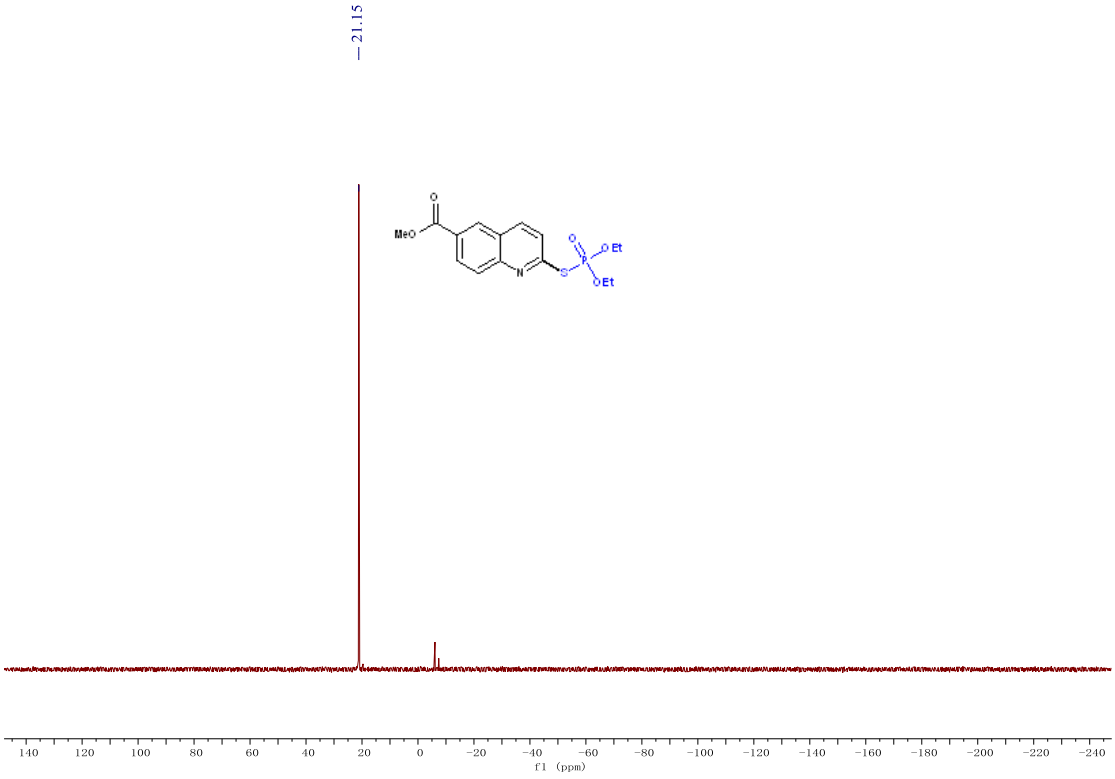
^{31}P spectrum of compound **3ka**



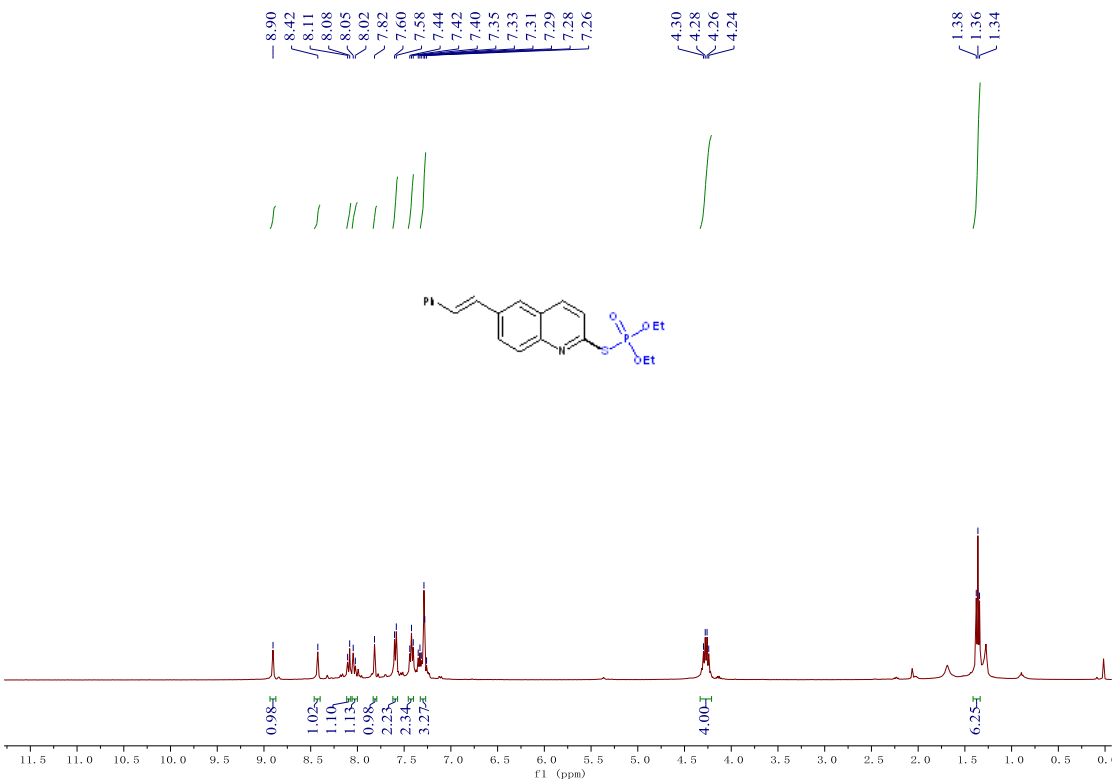
^{1}H spectrum of compound **3la**



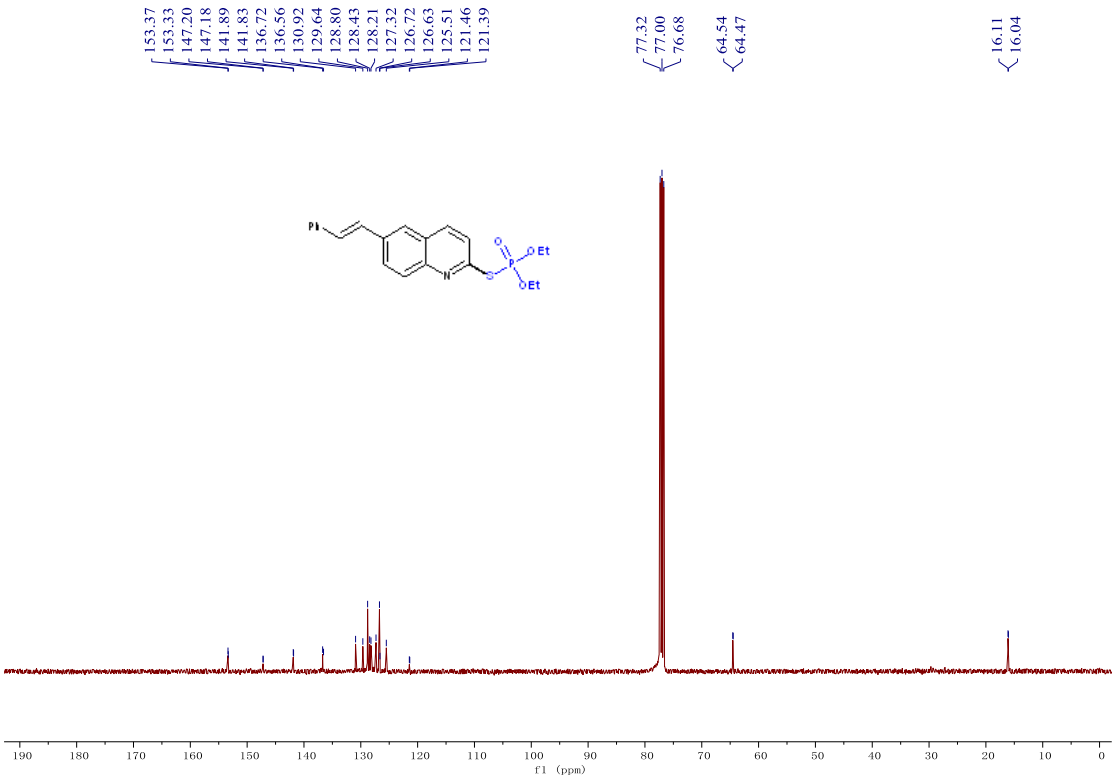
^{13}C spectrum of compound **3la**



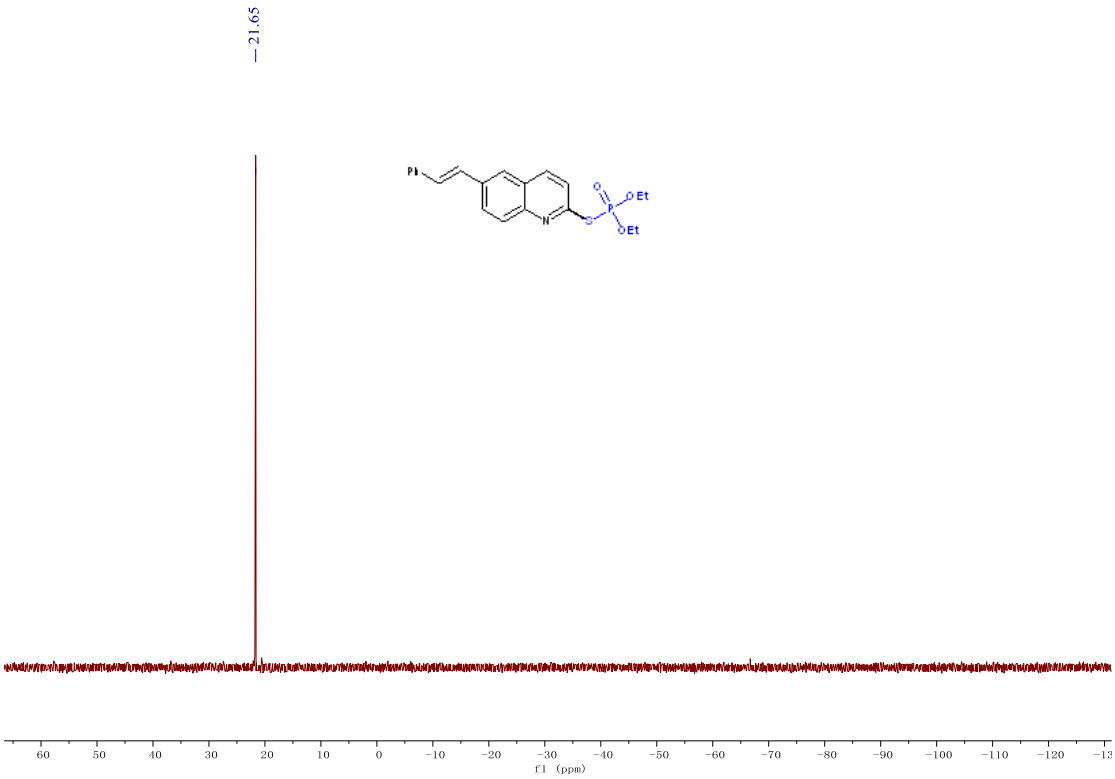
^{31}P spectrum of compound **3la**



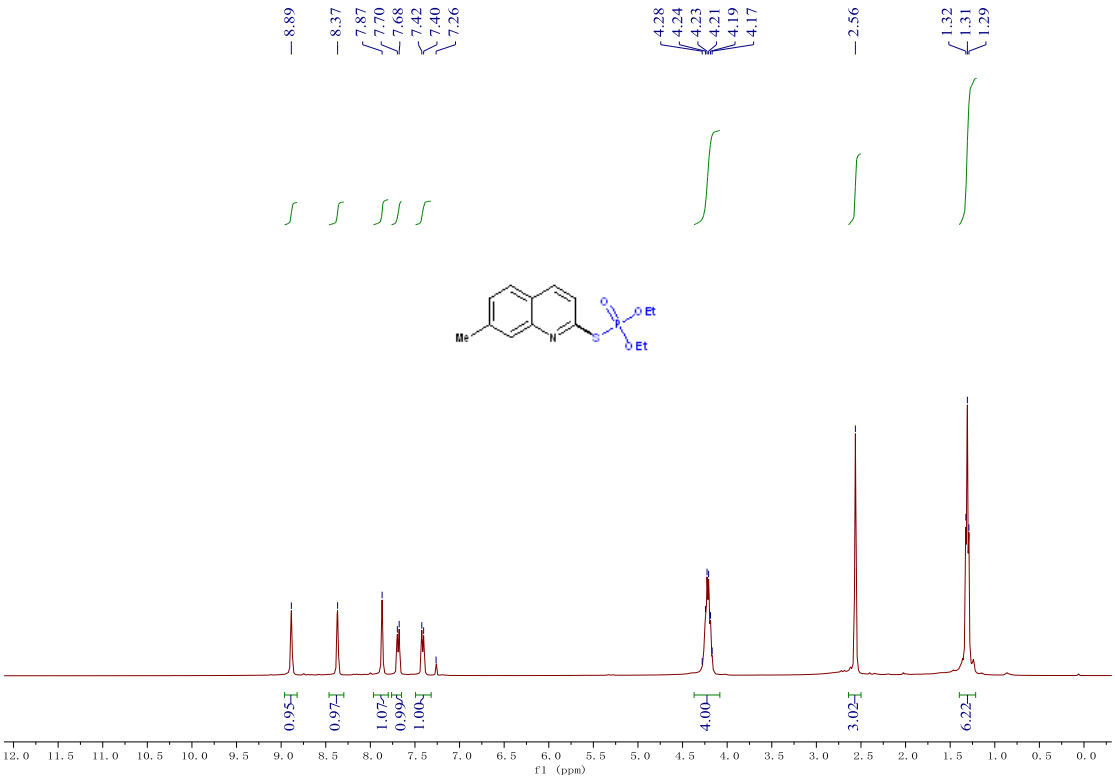
^{1}H spectrum of compound **3ma**



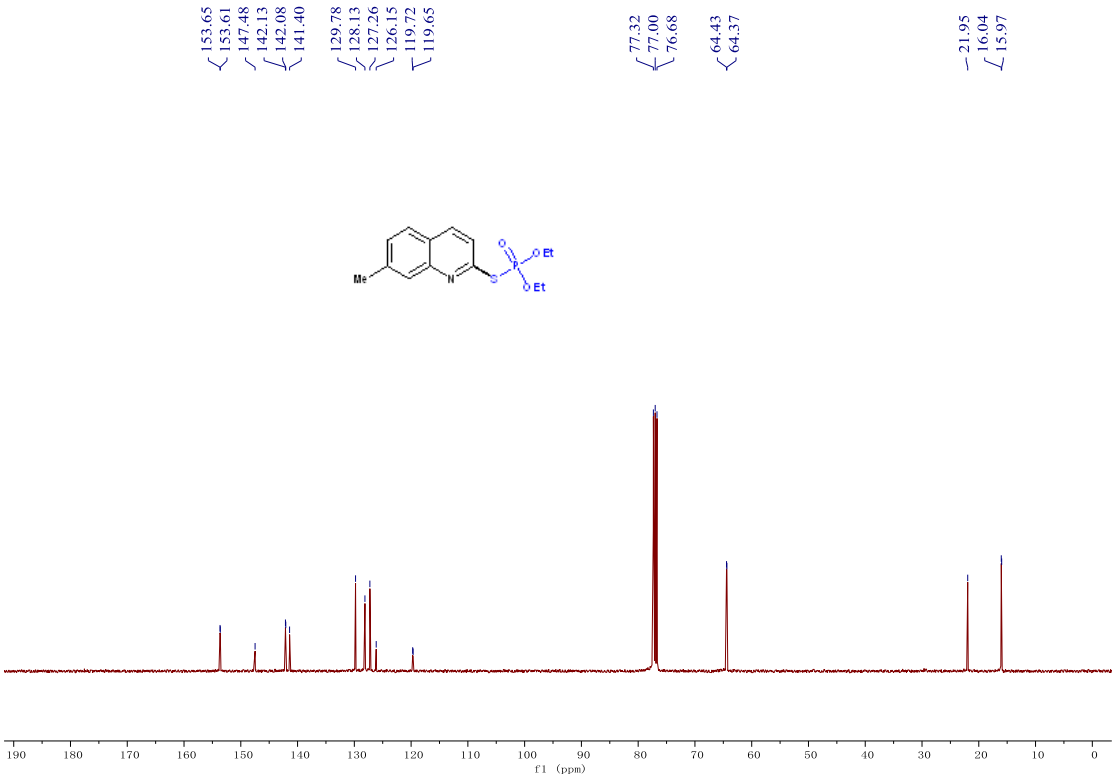
^{13}C spectrum of compound **3ma**



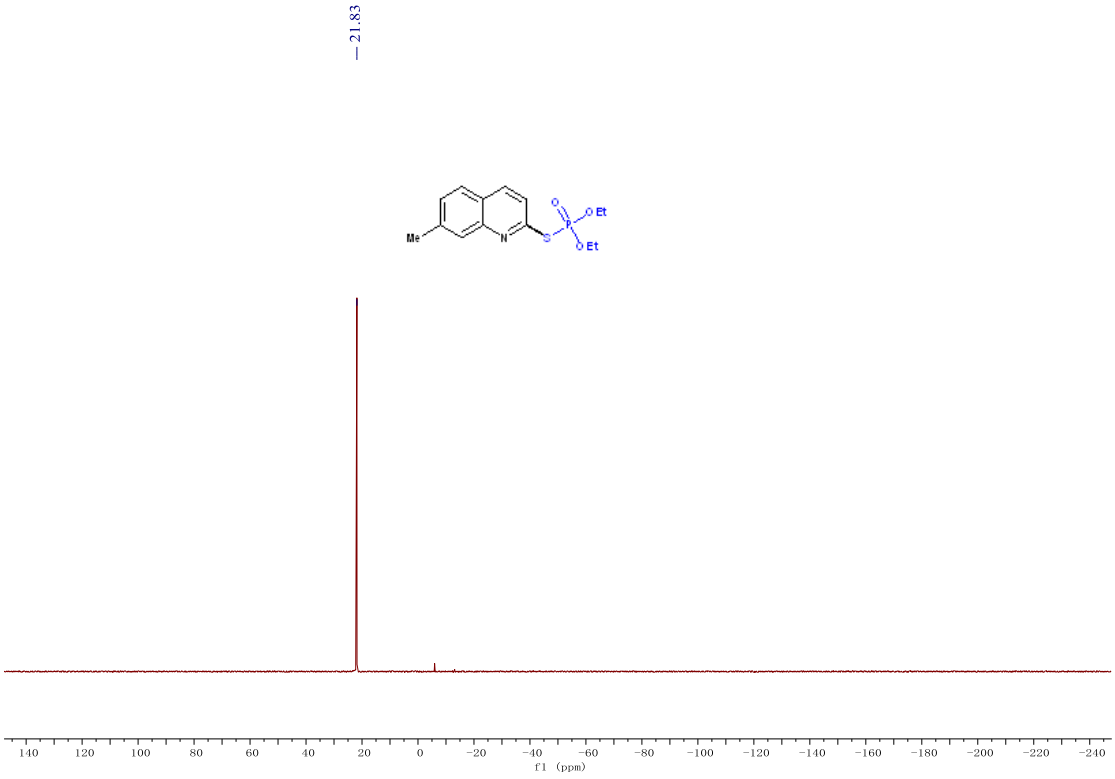
^{31}P spectrum of compound **3ma**



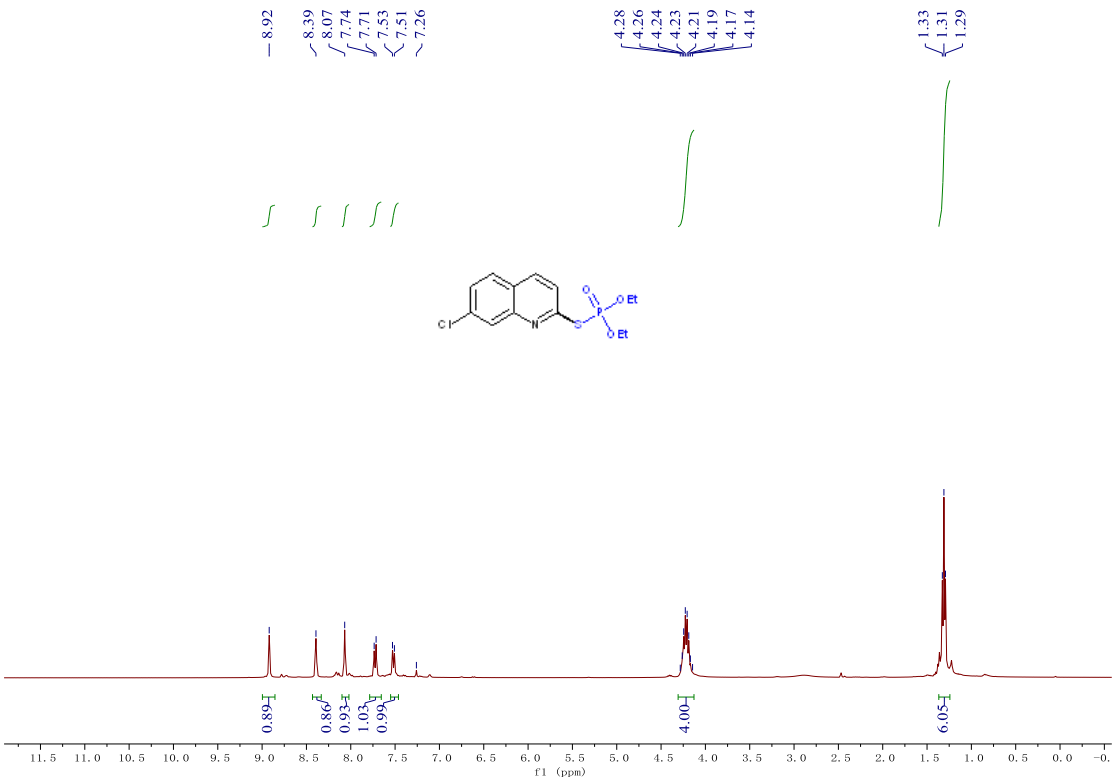
^{1}H spectrum of compound **3na**



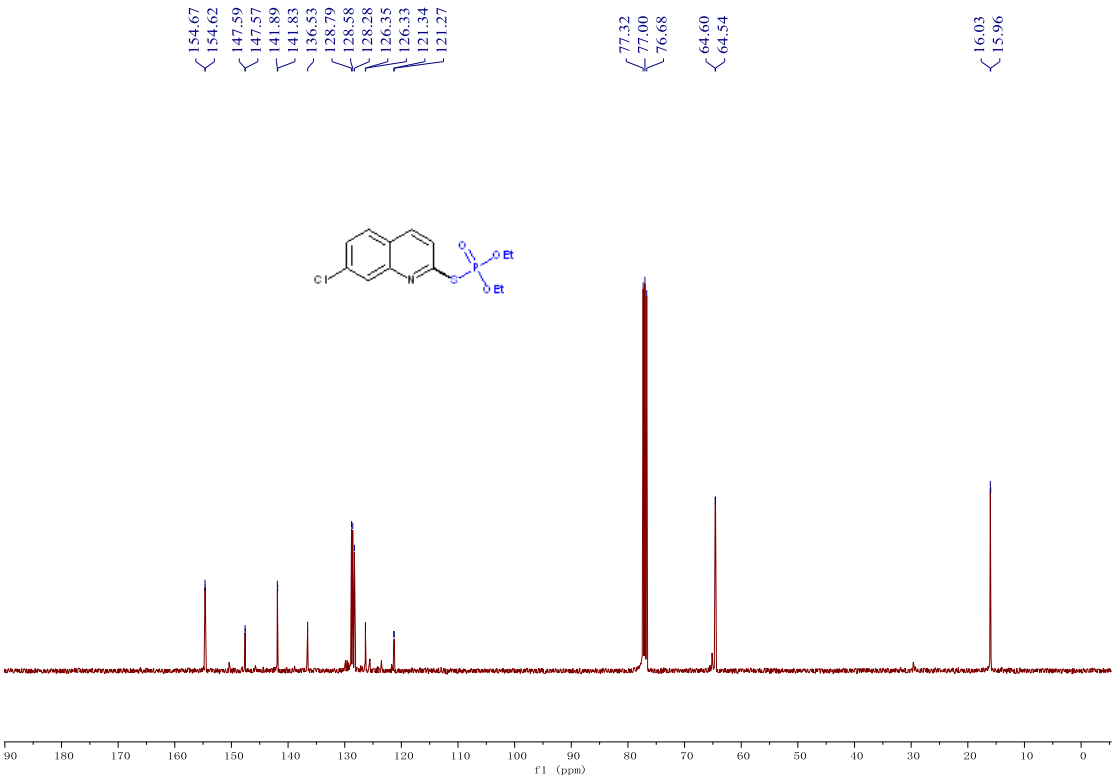
^{13}C spectrum of compound **3na**



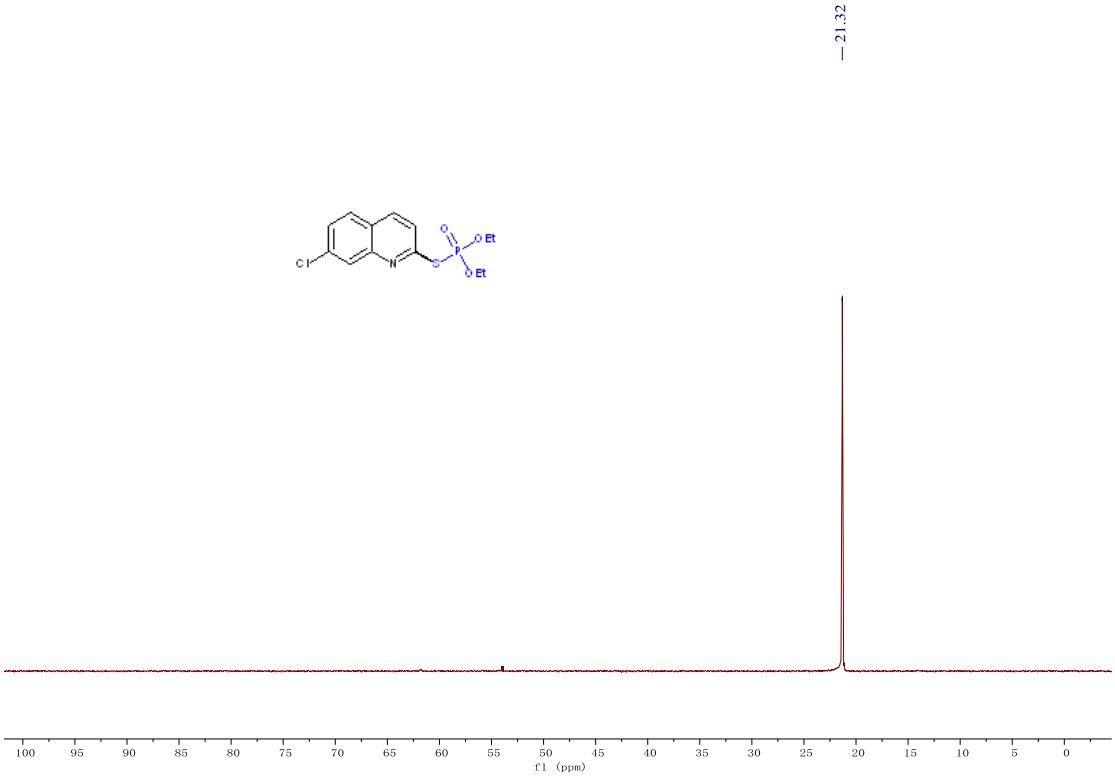
^{31}P spectrum of compound **3na**



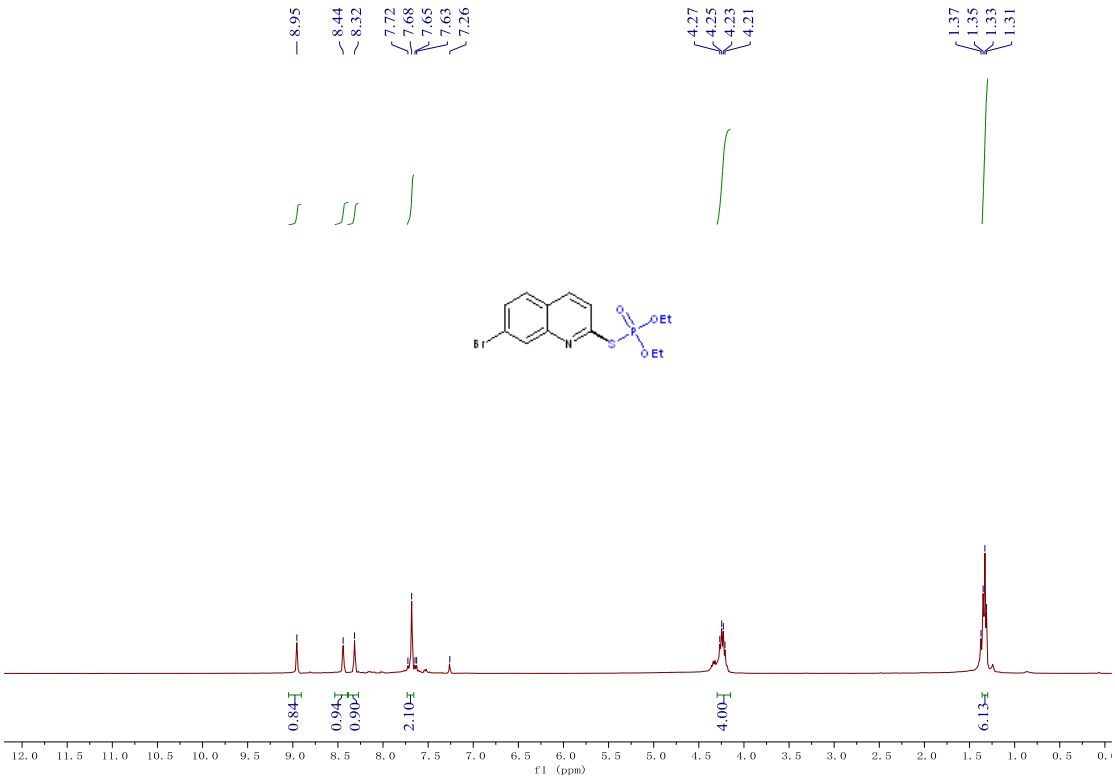
^{1}H spectrum of compound **3oa**



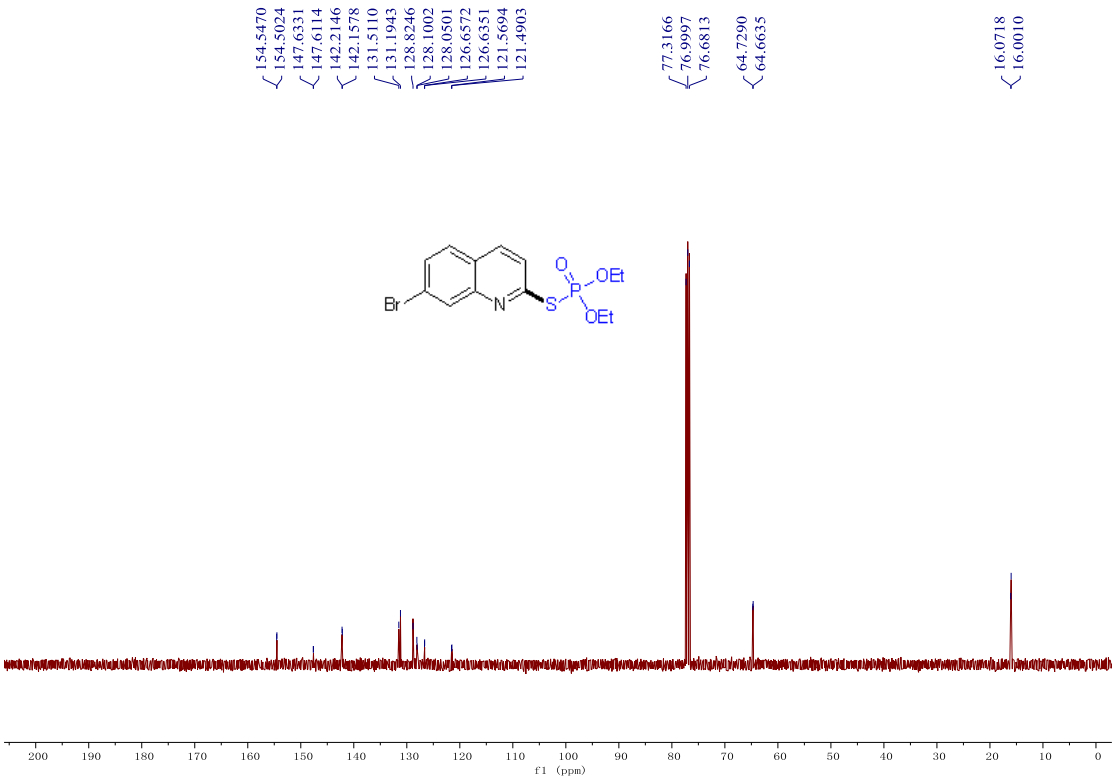
^{13}C spectrum of compound **3oa**



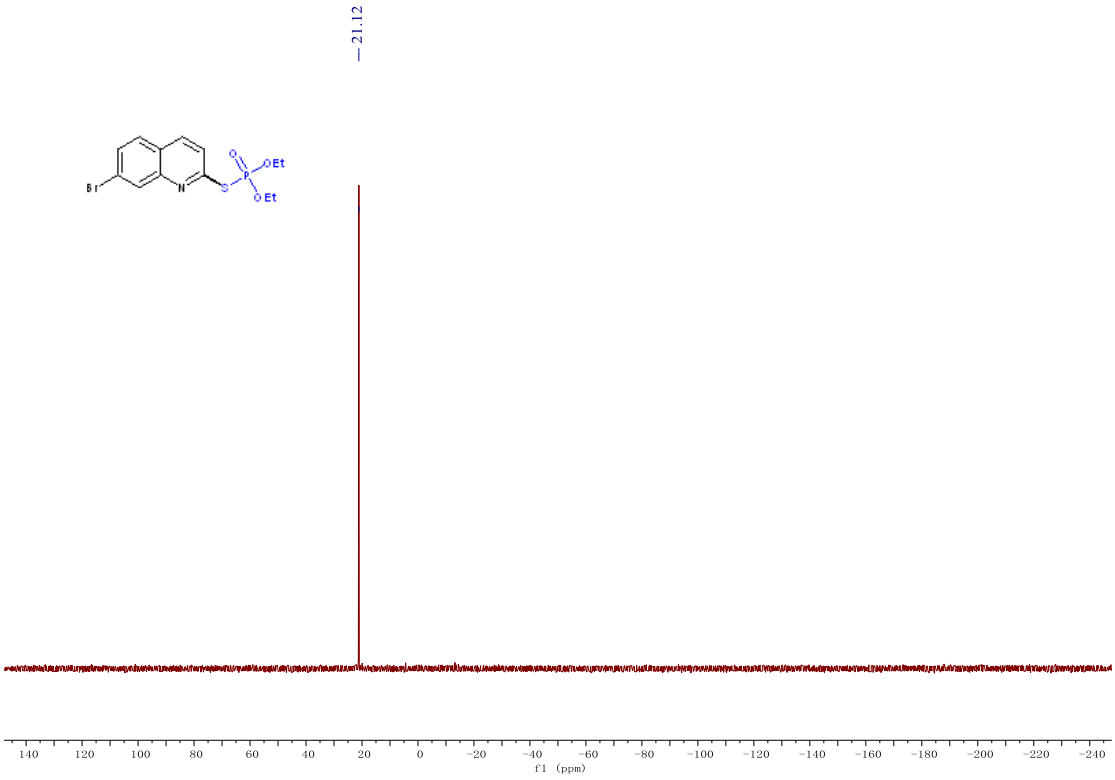
^{31}P spectrum of compound **3oa**



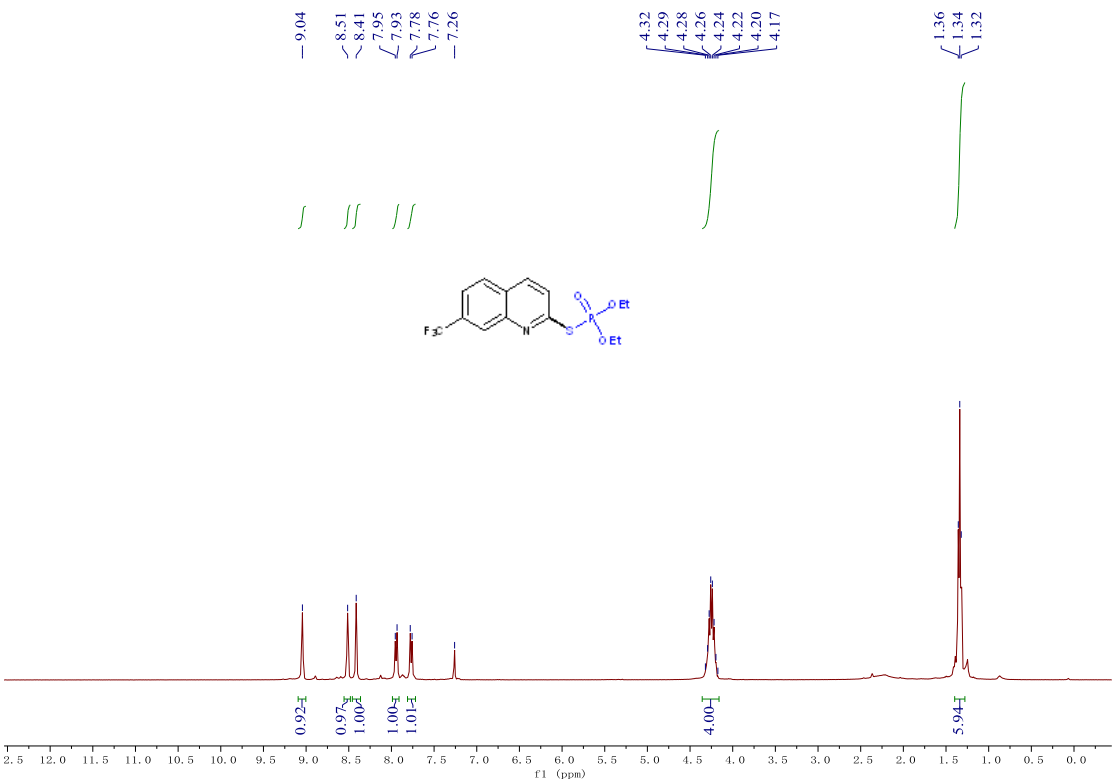
^{1}H spectrum of compound **3pa**



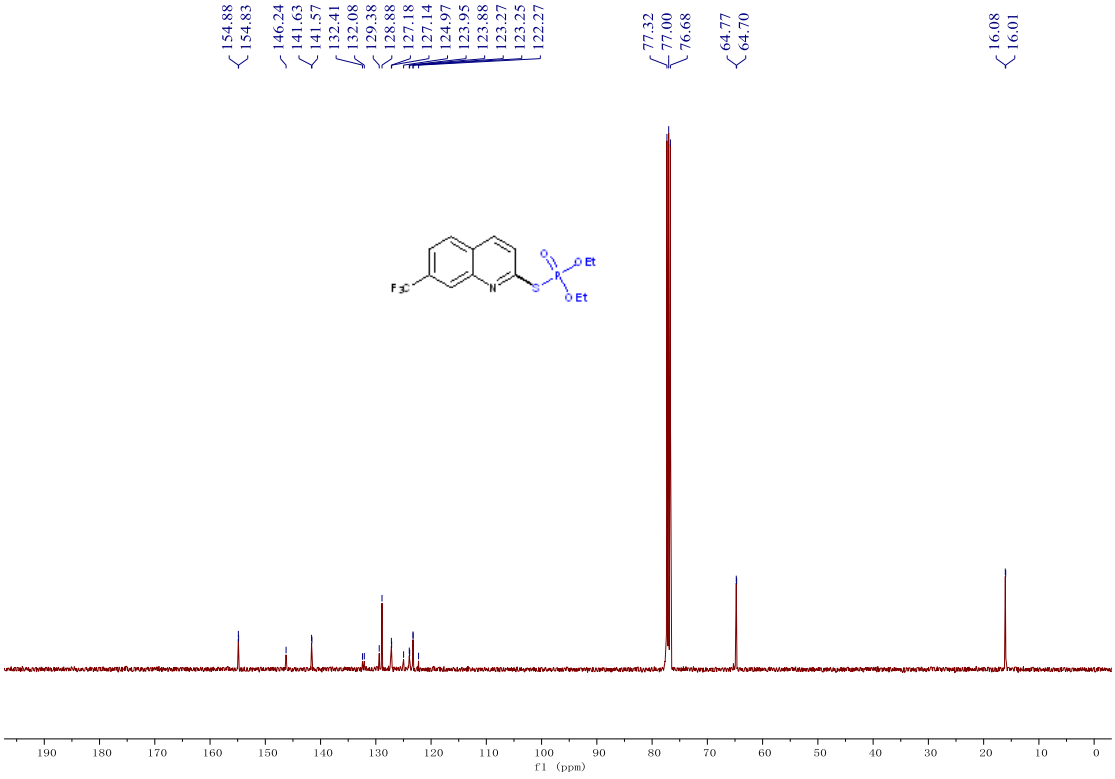
^{13}C spectrum of compound **3pa**



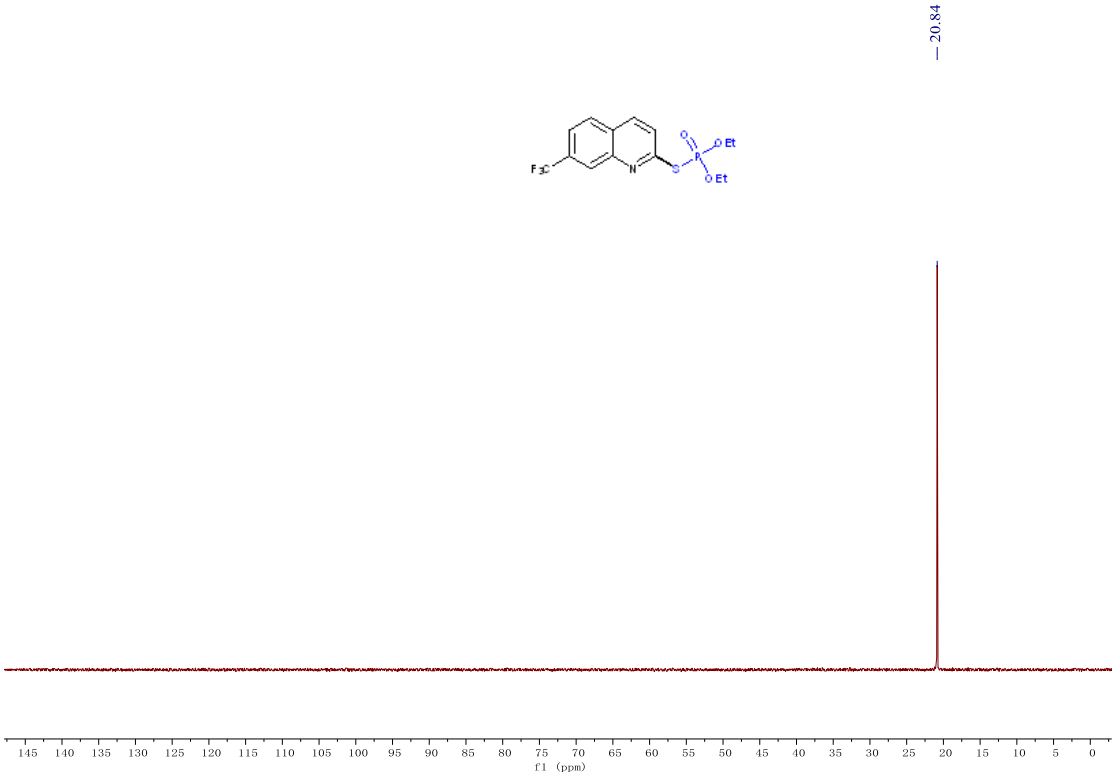
^{31}P spectrum of compound **3pa**



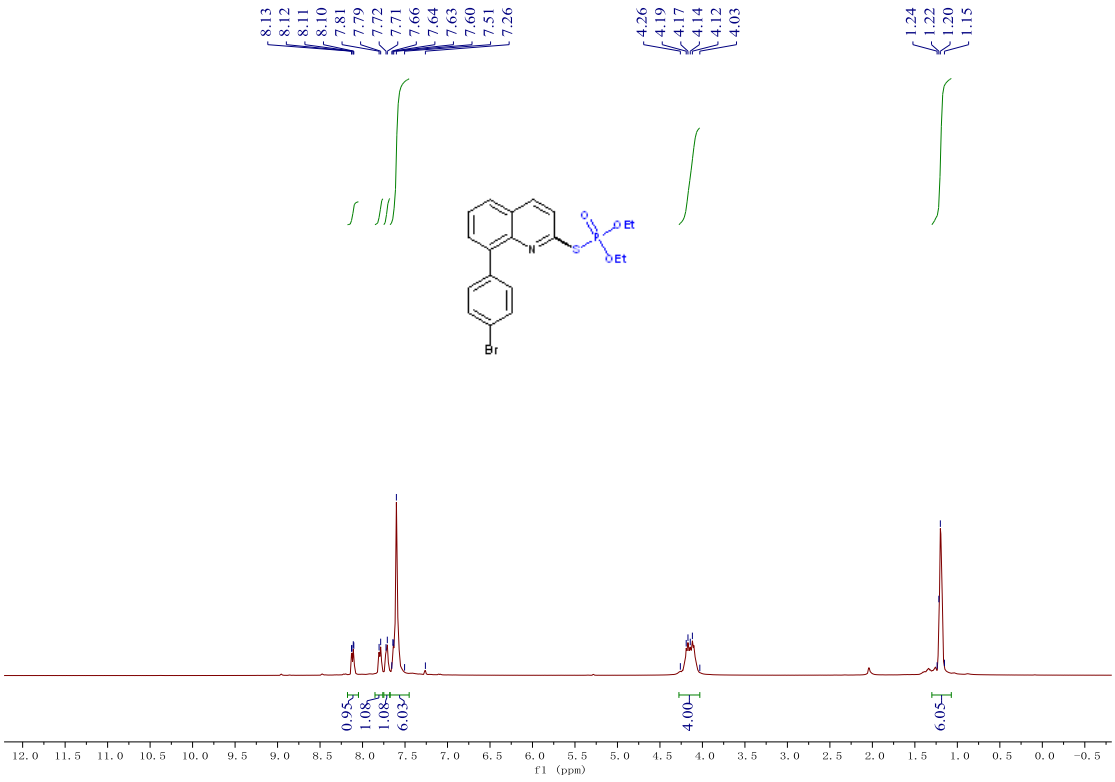
^{1}H spectrum of compound **3qa**



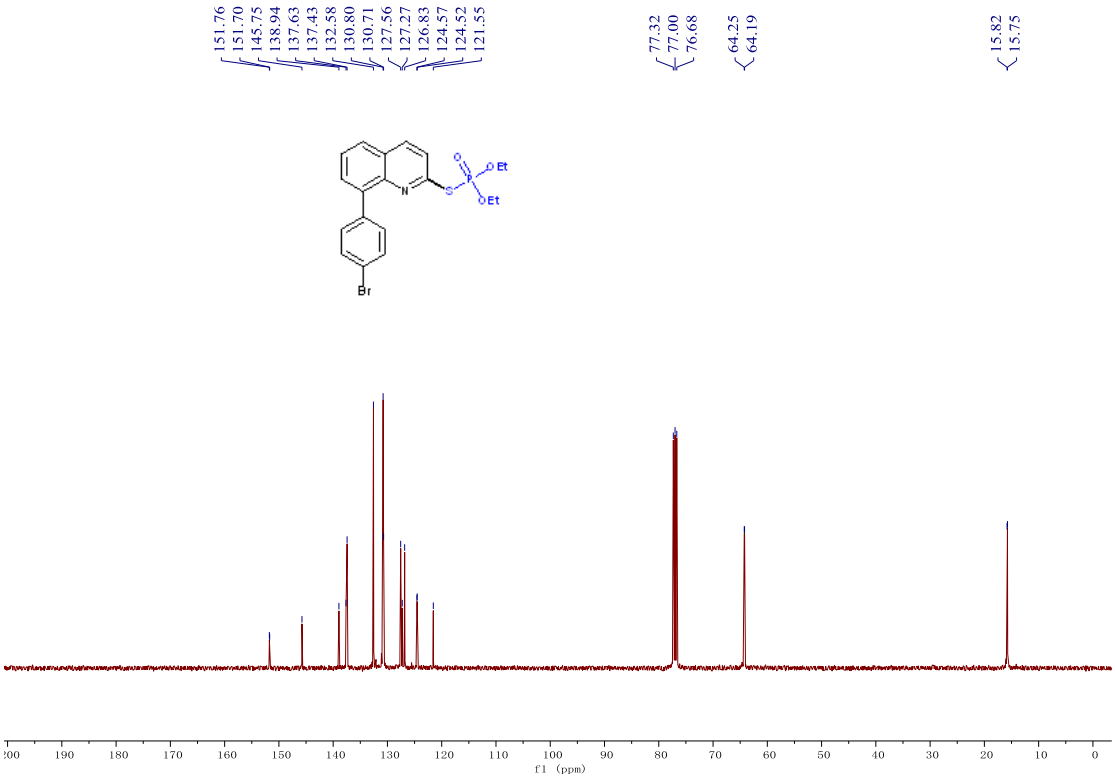
^{13}C spectrum of compound **3qa**



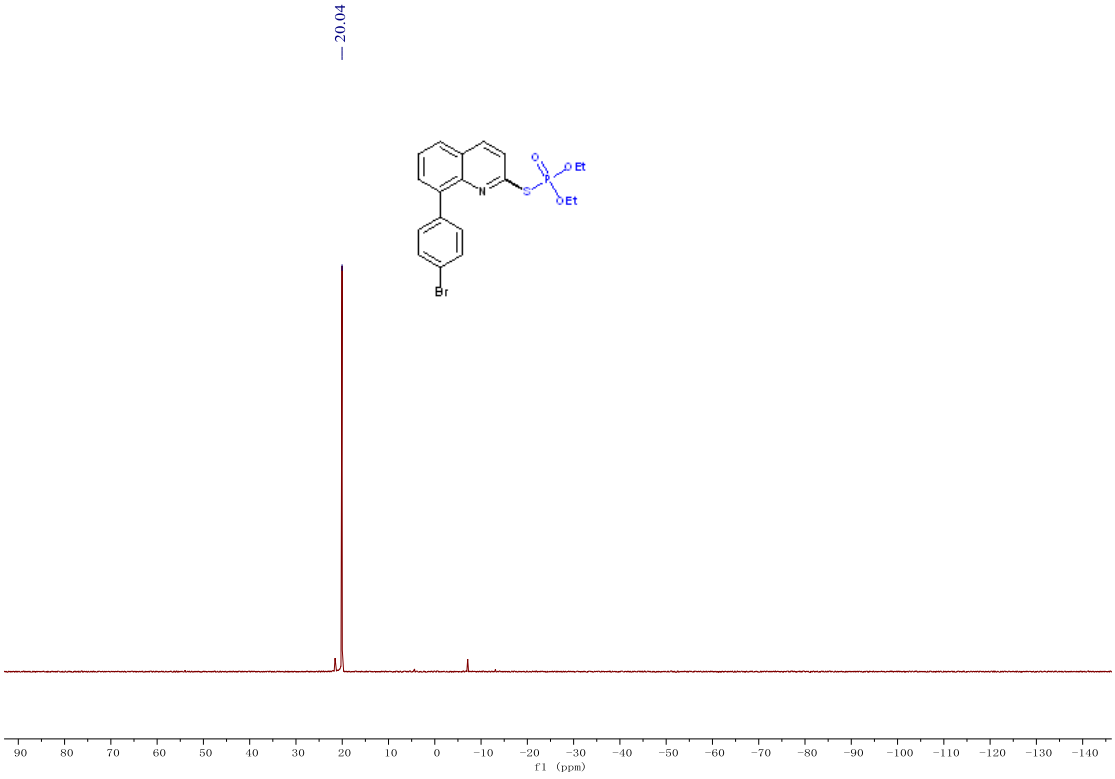
^{31}P spectrum of compound **3qa**



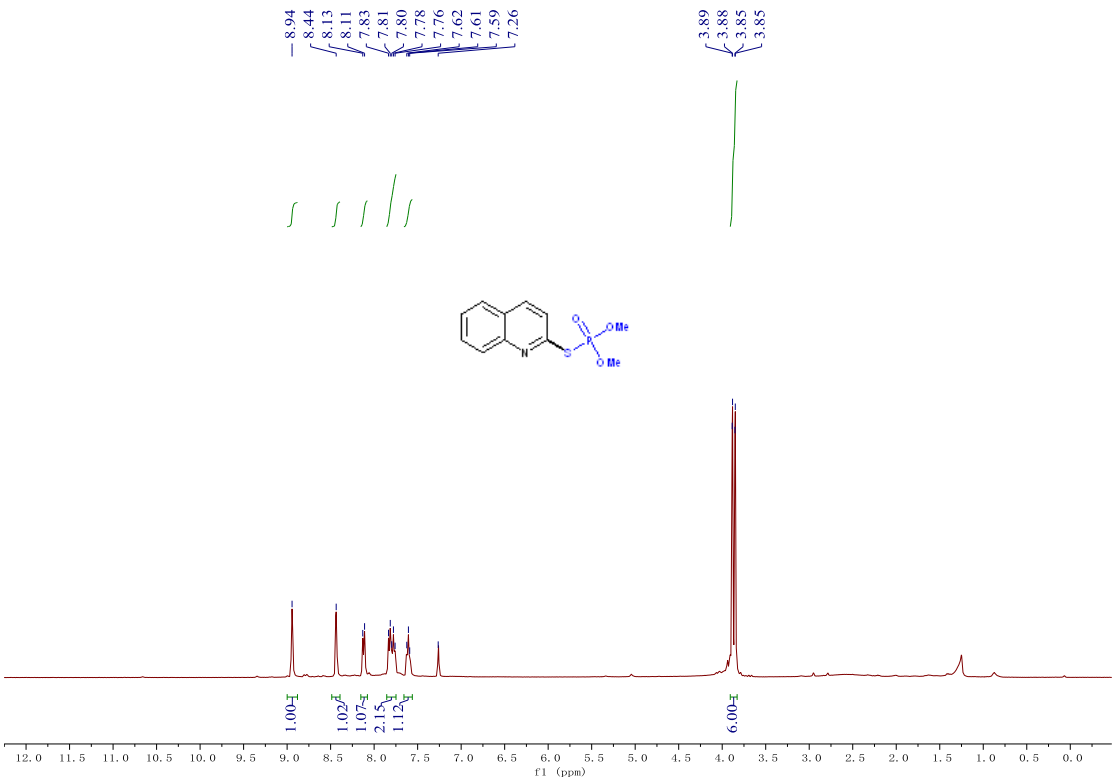
^{1}H spectrum of compound **3ra**



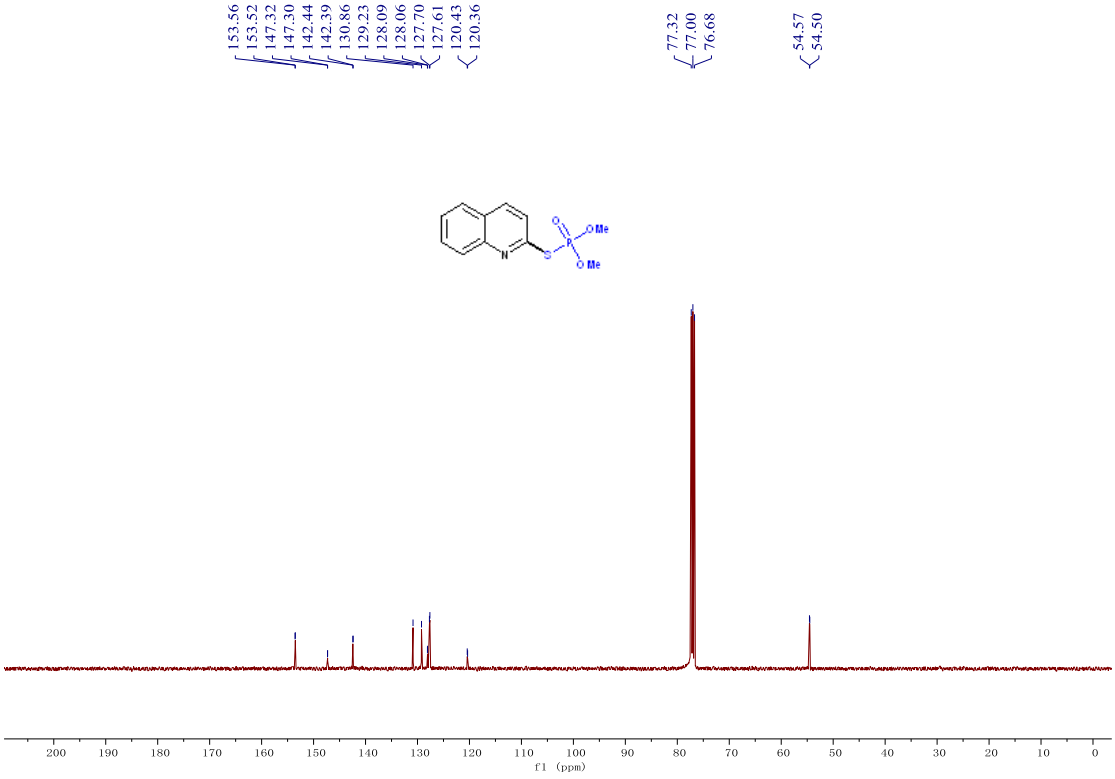
^{13}C spectrum of compound **3ra**



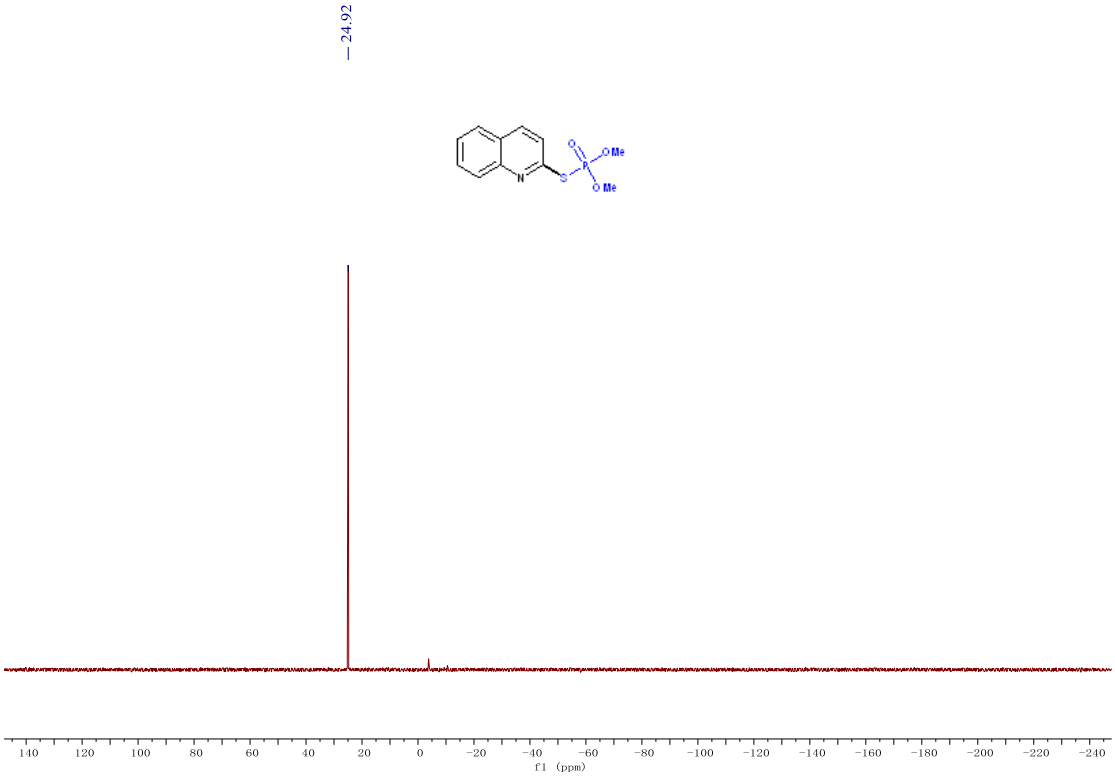
^{31}P spectrum of compound **3ra**



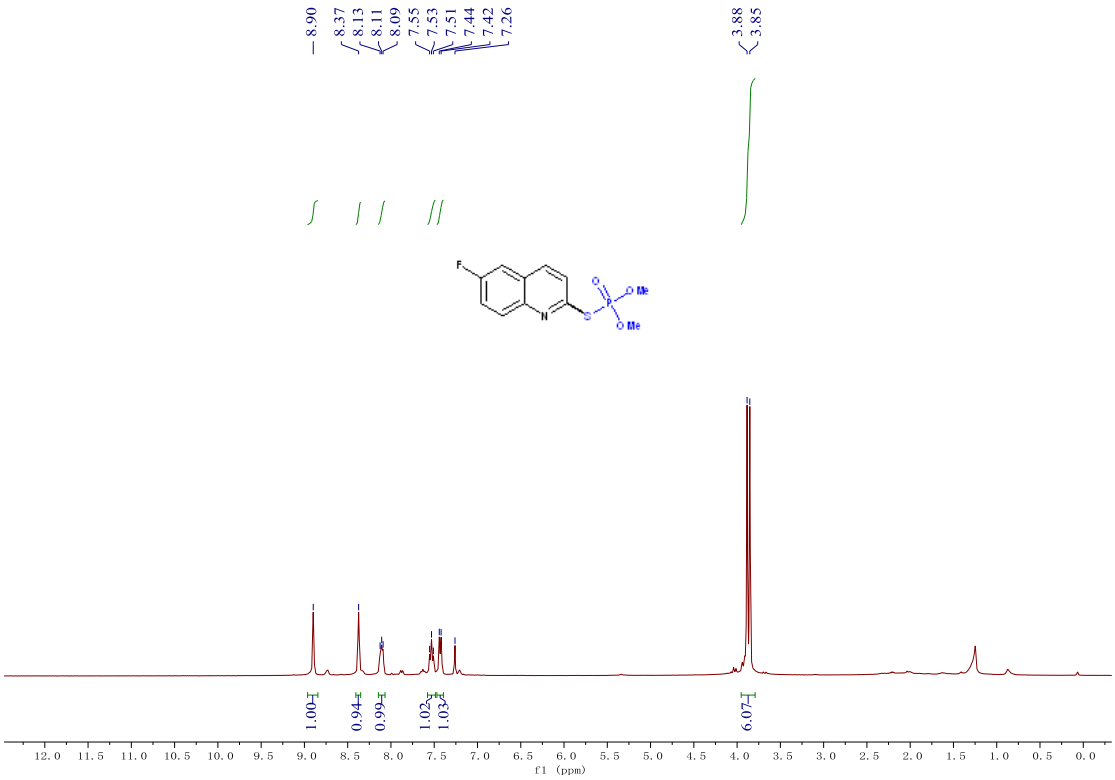
^{1}H spectrum of compound **3ab**



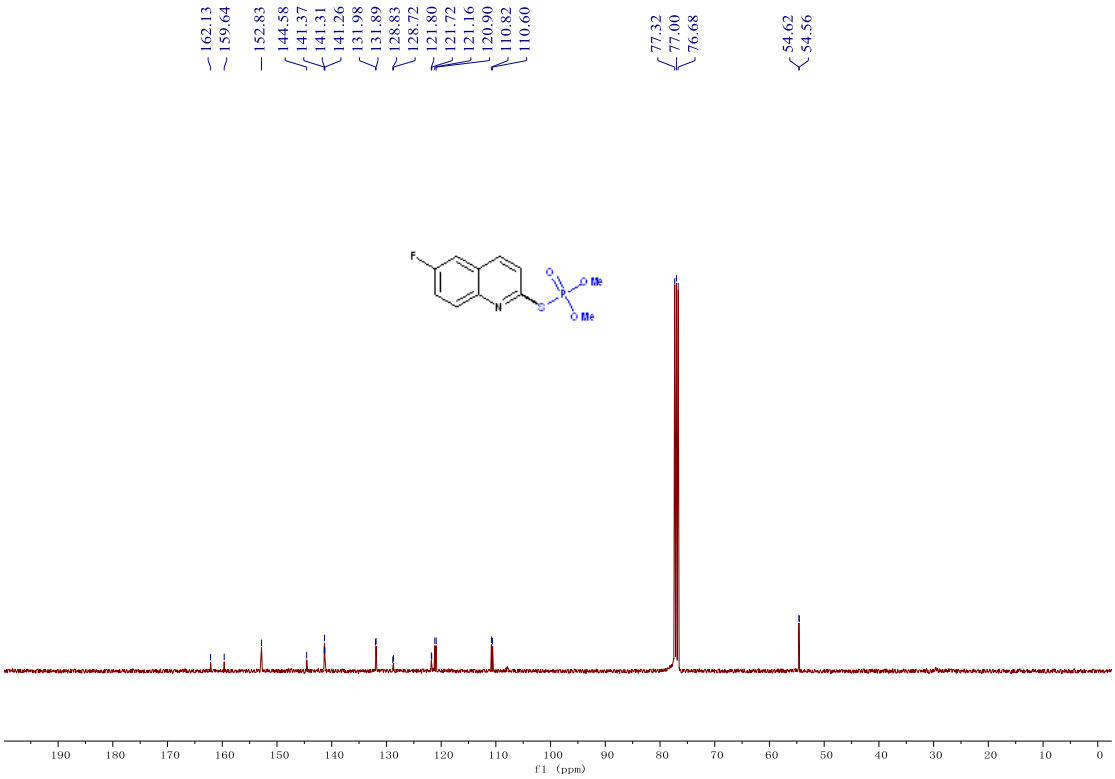
^{13}C spectrum of compound **3ab**



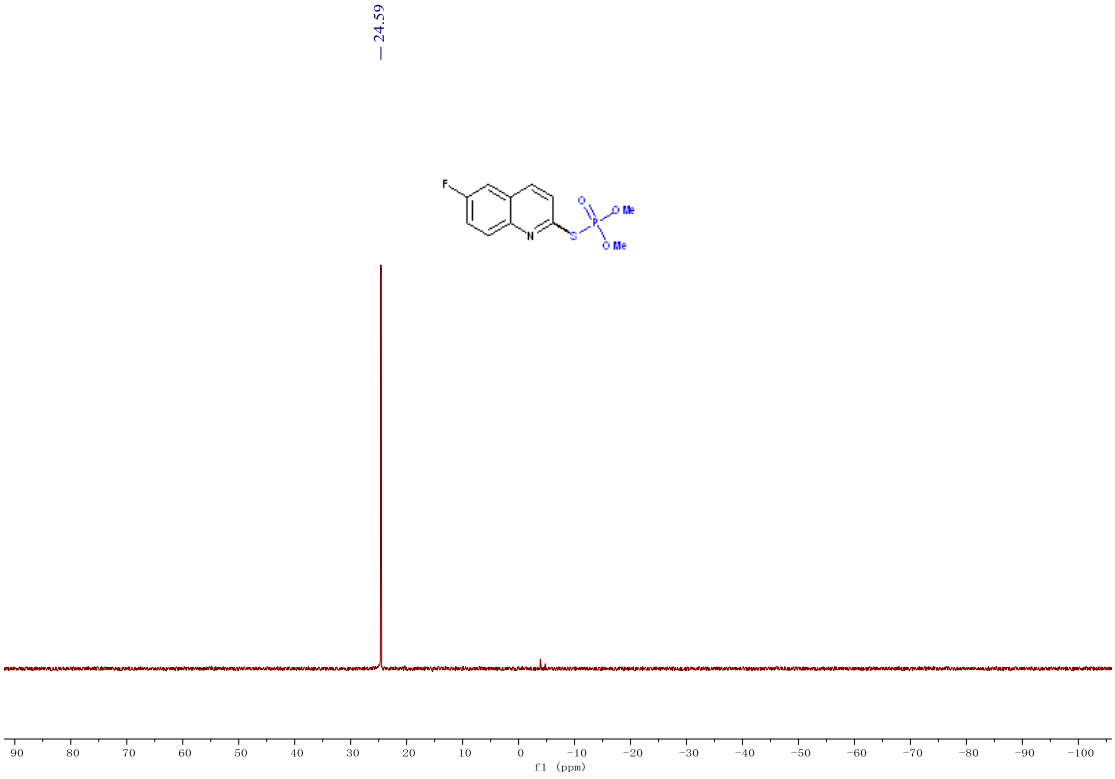
^{31}P spectrum of compound **3ab**



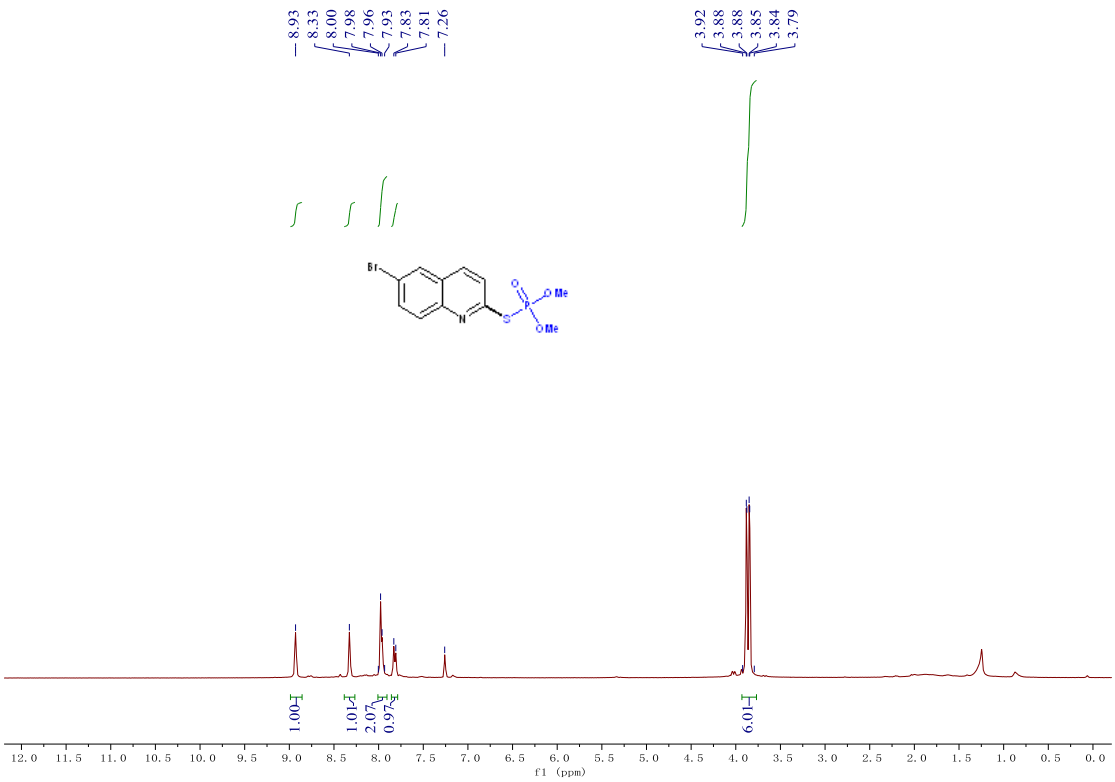
^{1}H spectrum of compound **3hb**



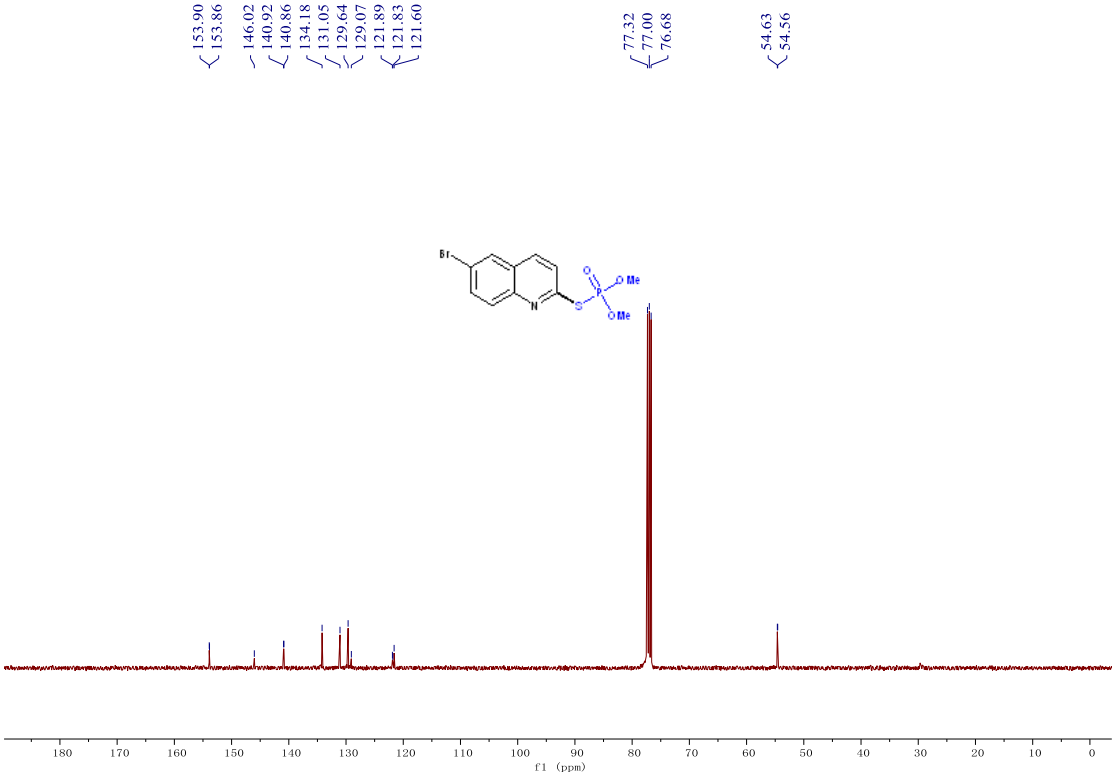
^{13}C spectrum of compound **3hb**



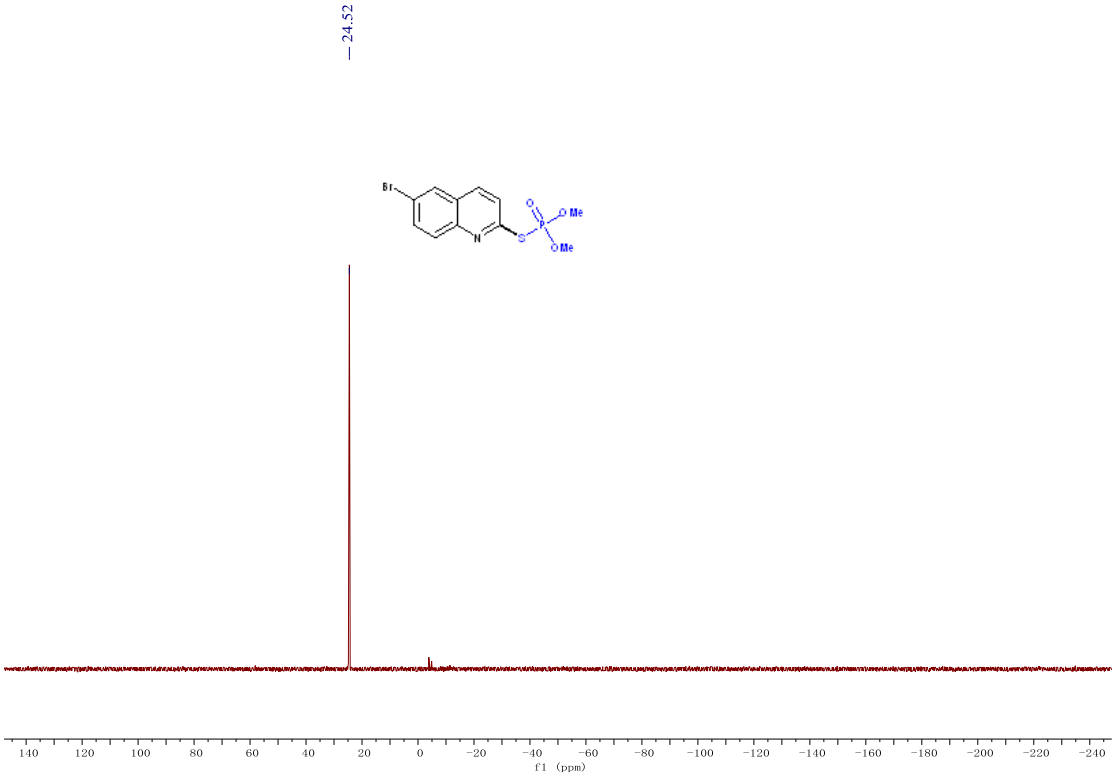
^{31}P spectrum of compound **3hb**



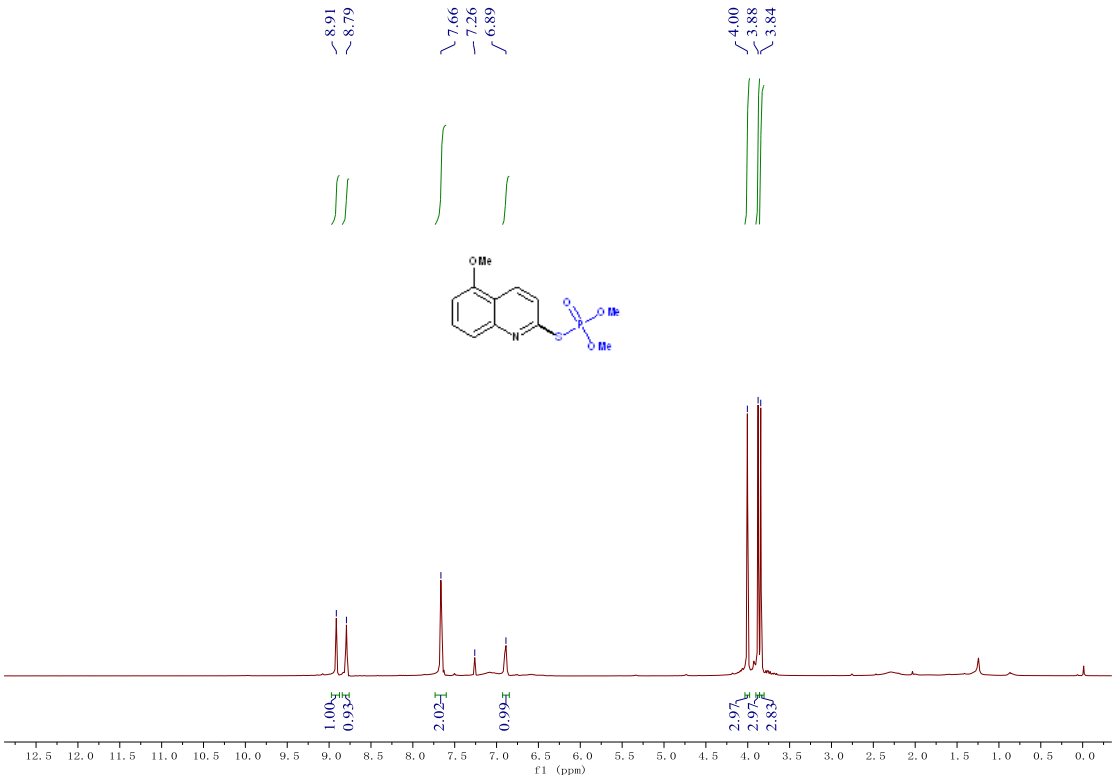
^{1}H spectrum of compound **3jb**



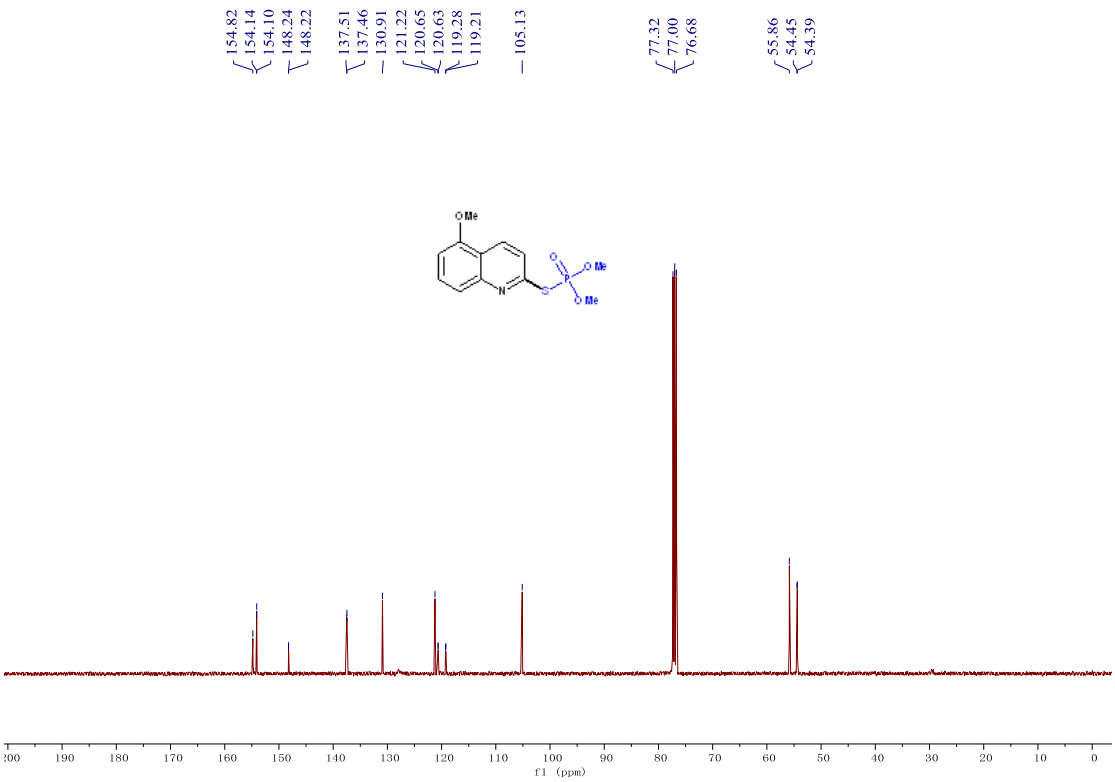
^{13}C spectrum of compound **3jb**



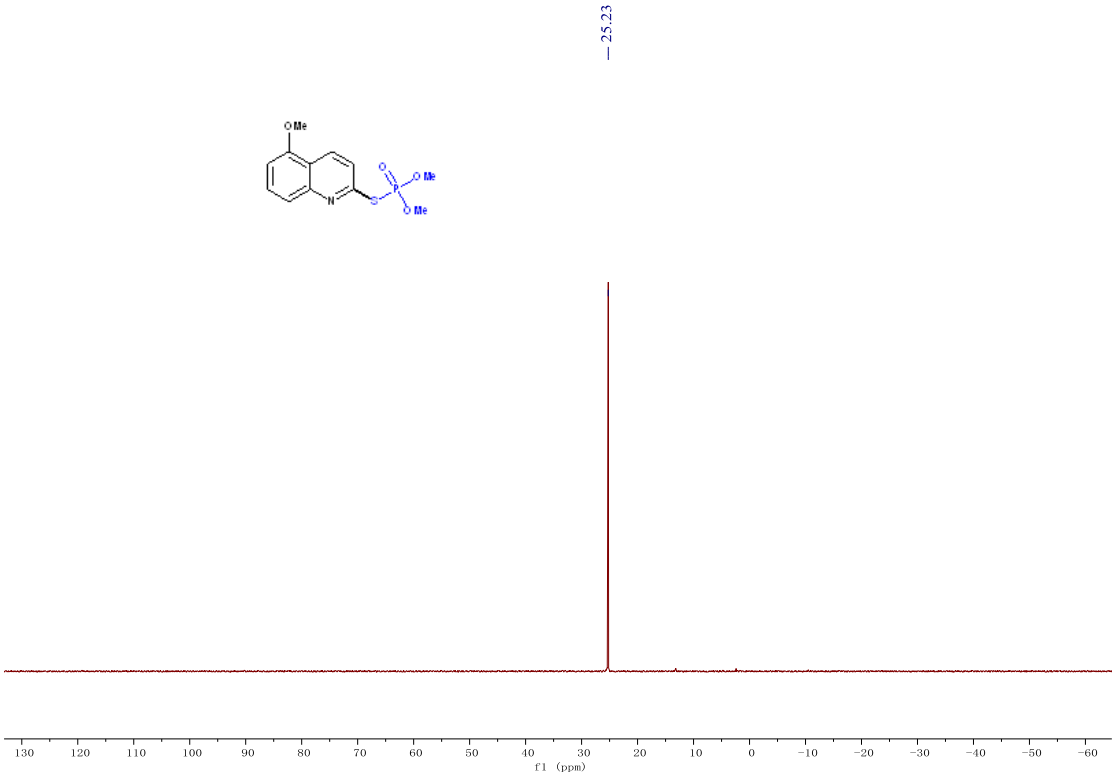
^{31}P spectrum of compound **3jb**



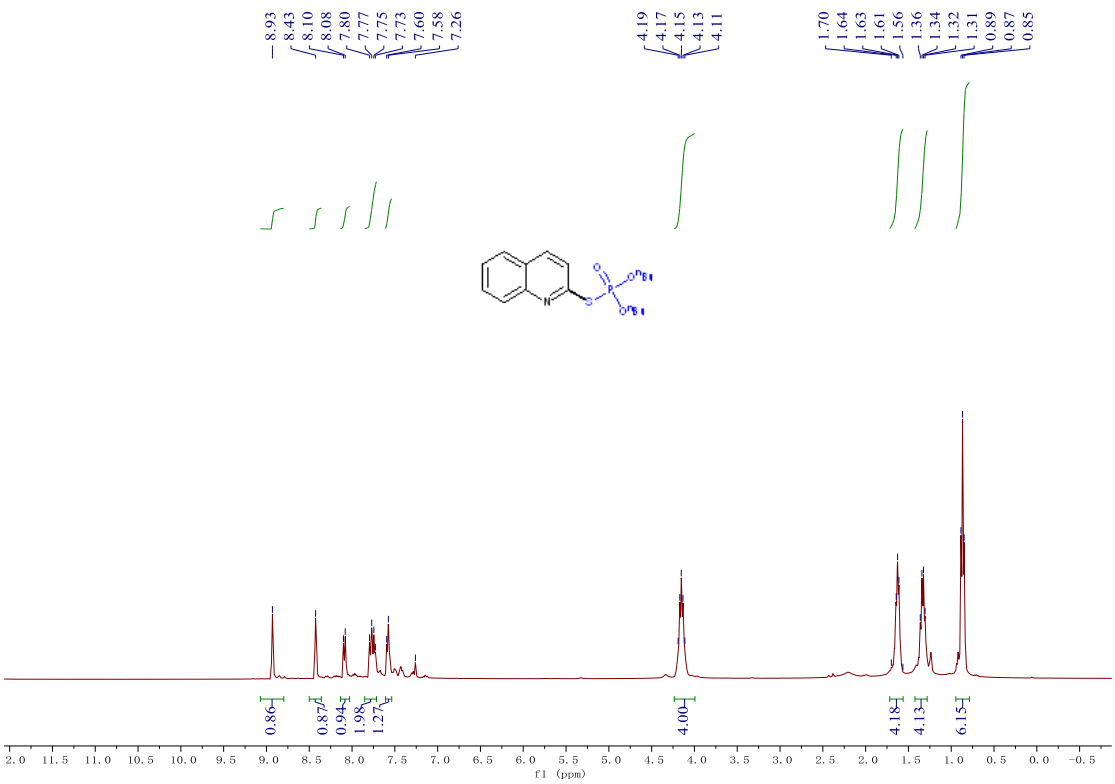
^{1}H spectrum of compound **3eb**



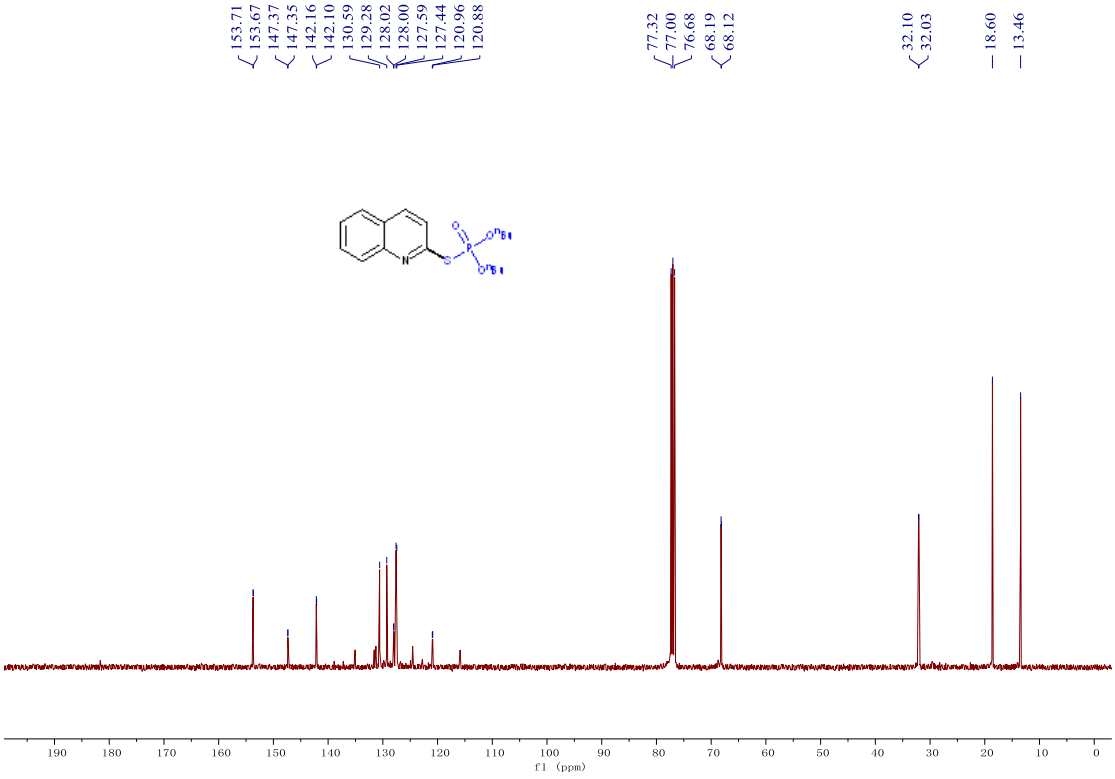
^{13}C spectrum of compound **3eb**



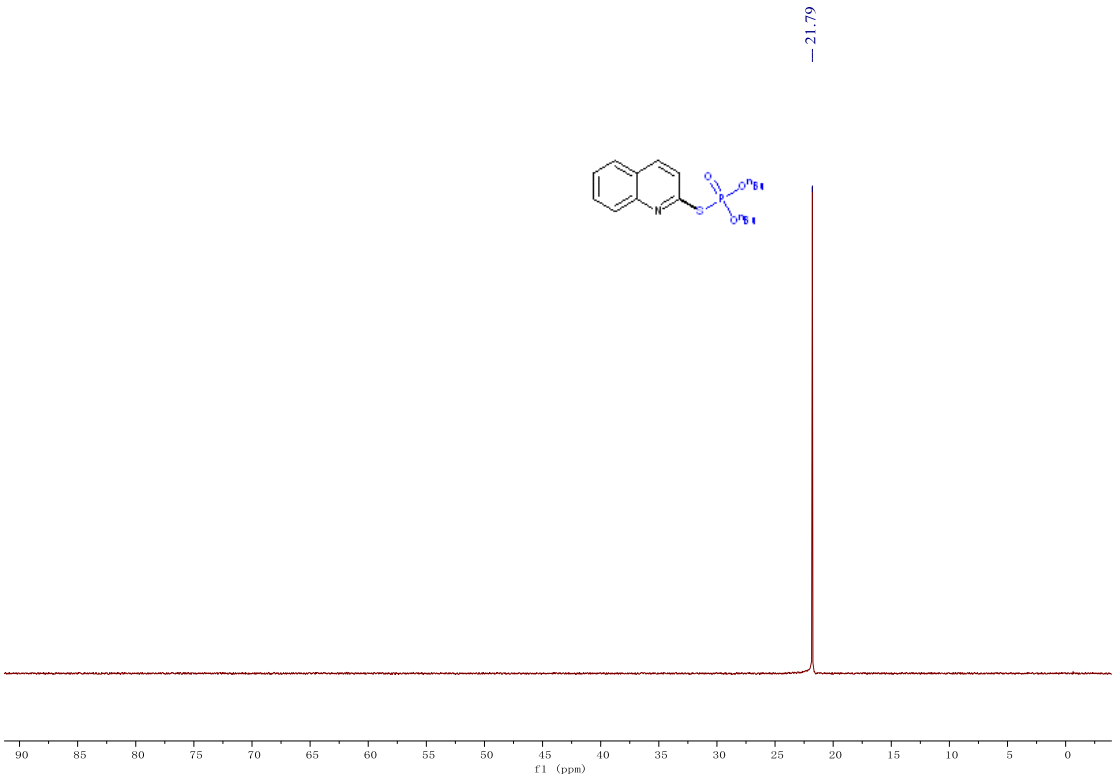
^{31}P spectrum of compound **3eb**



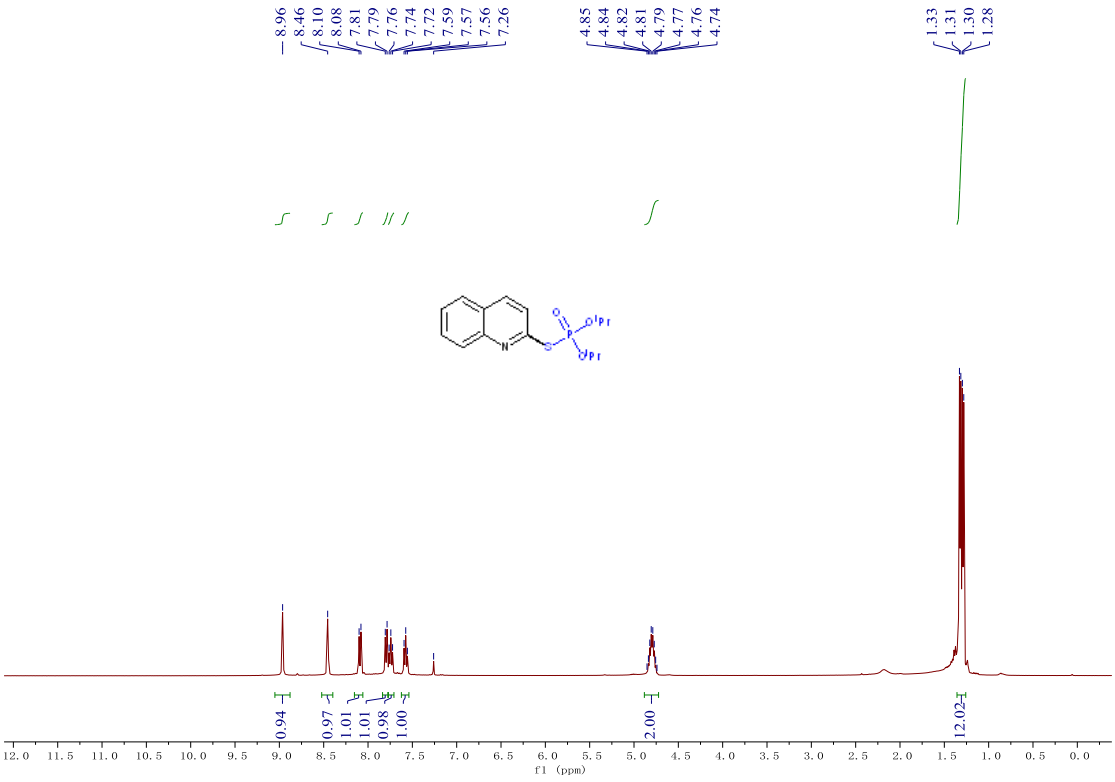
^{1}H spectrum of compound **3ac**



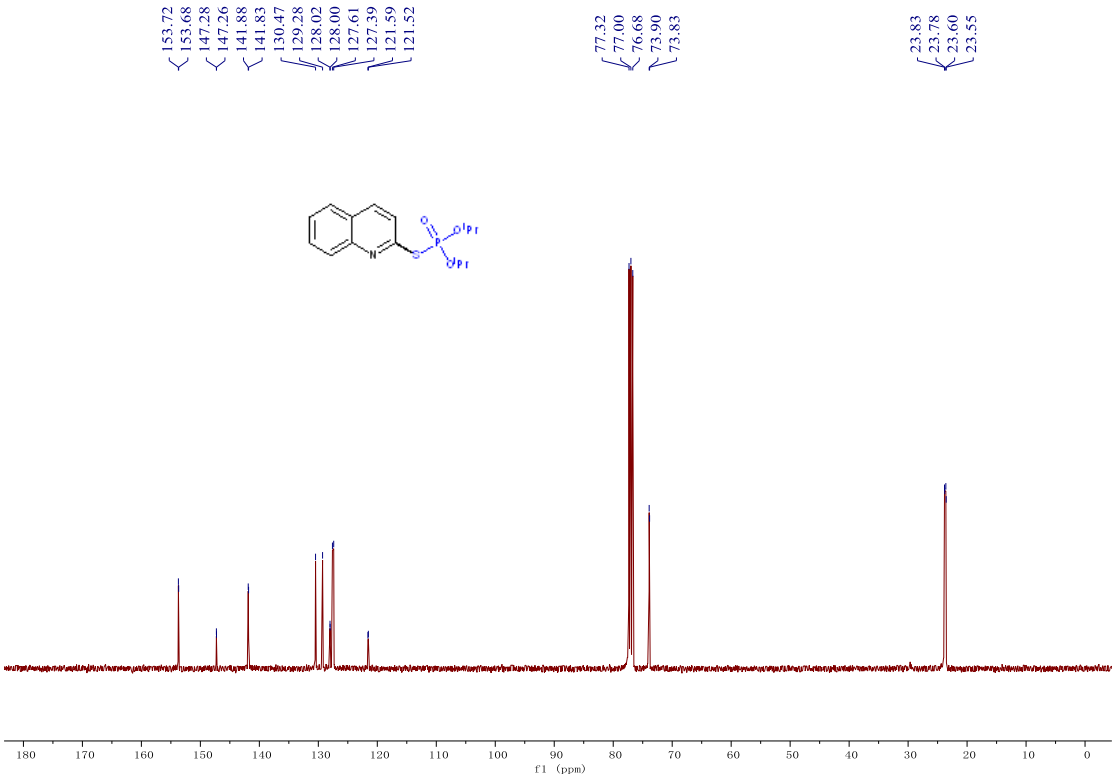
^{13}C spectrum of compound **3ac**



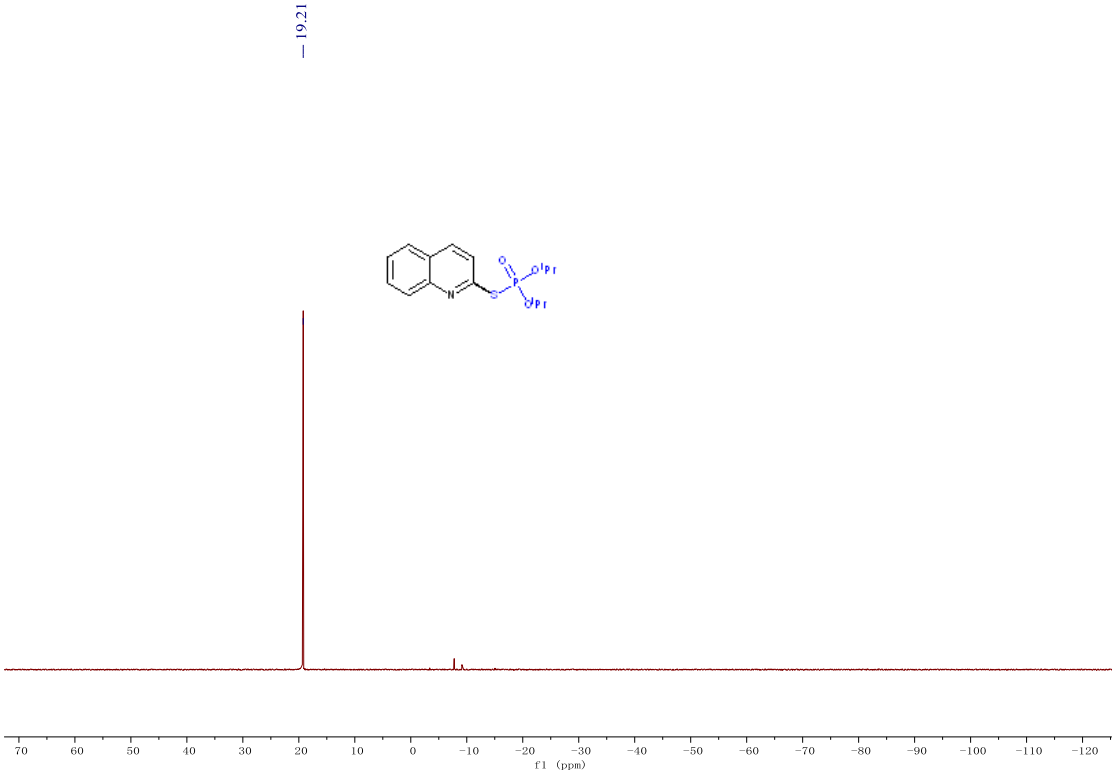
^{31}P spectrum of compound **3ac**



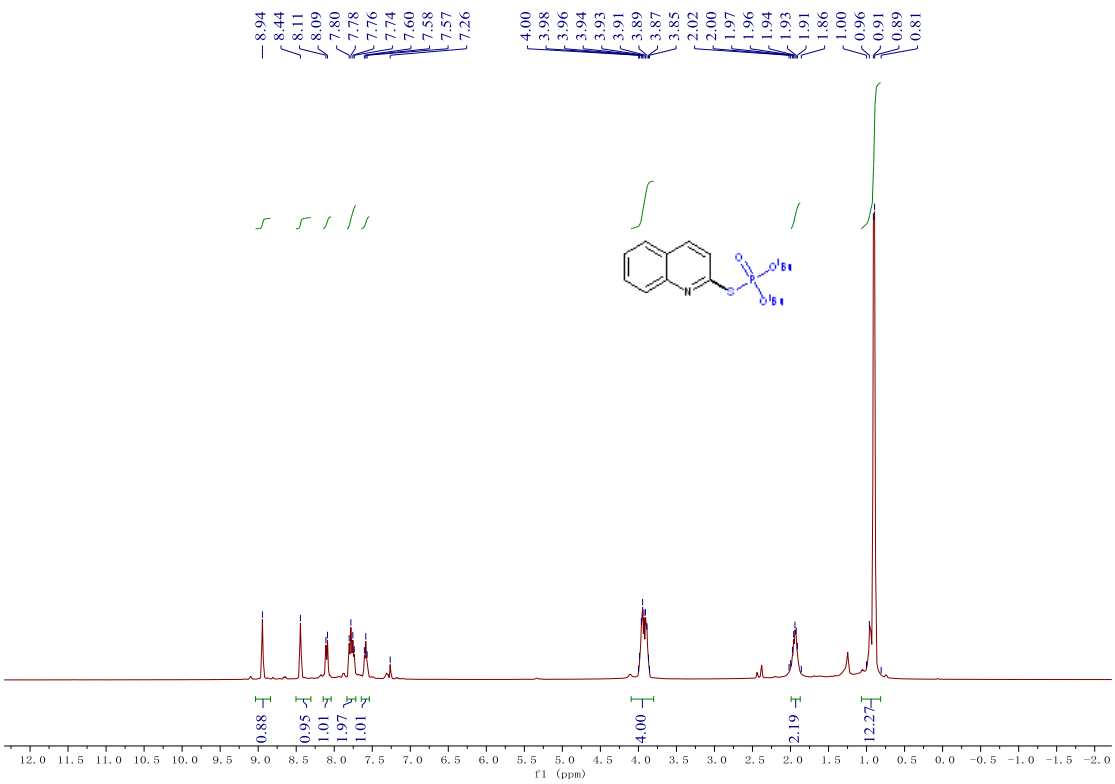
^{1}H spectrum of compound **3ad**



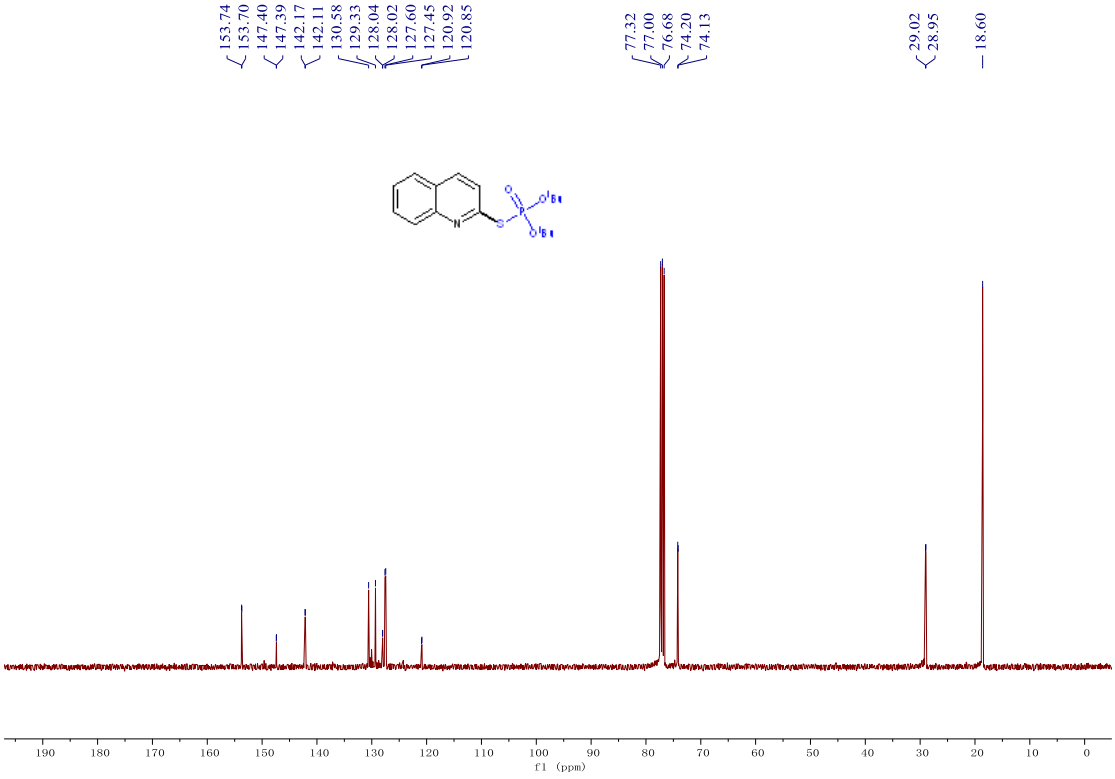
^{13}C spectrum of compound **3ad**



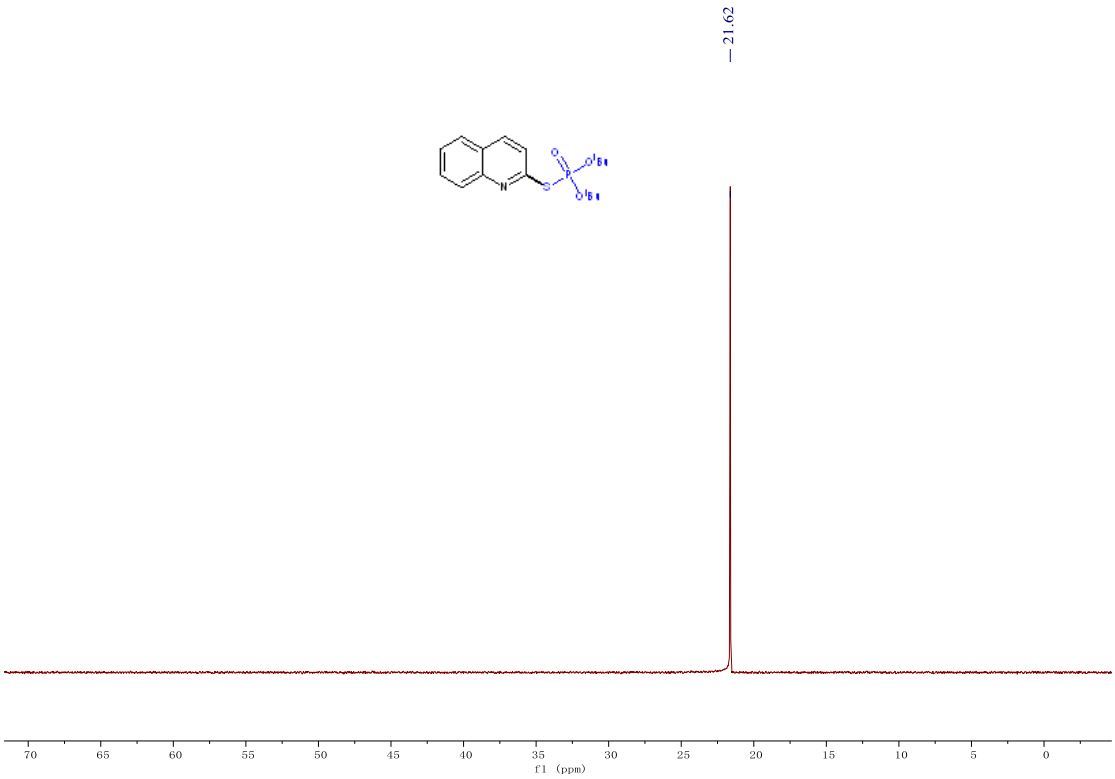
^{31}P spectrum of compound **3ad**



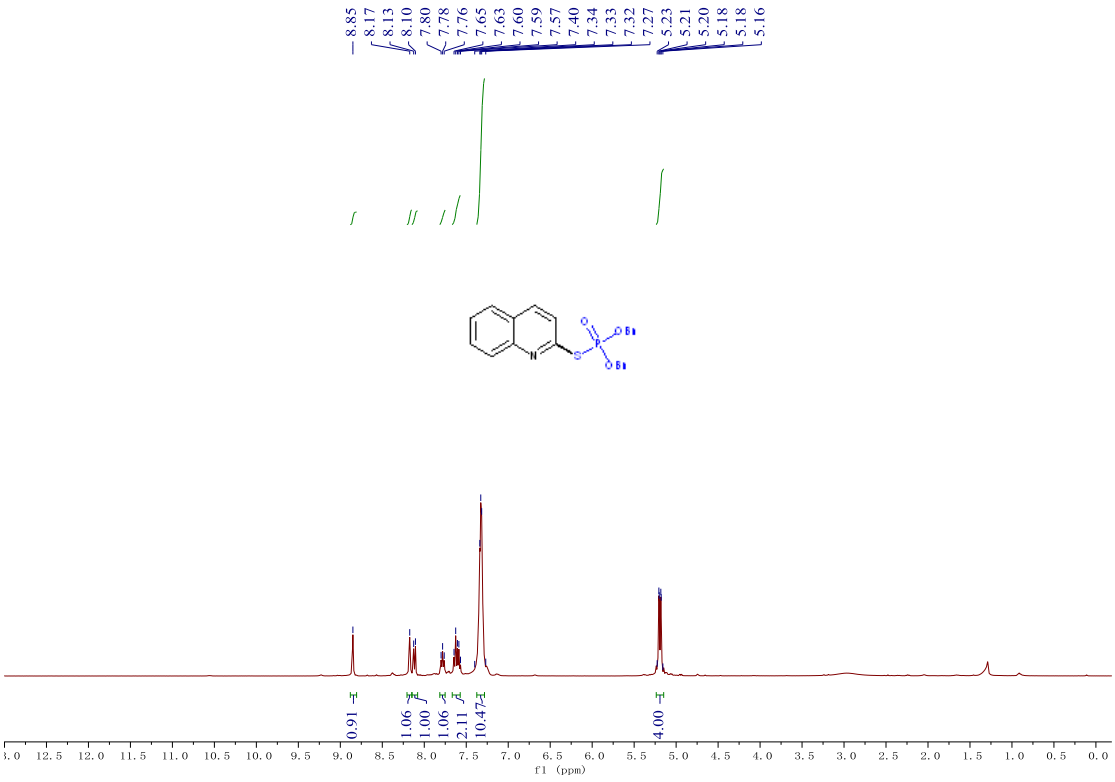
^{1}H spectrum of compound **3ae**



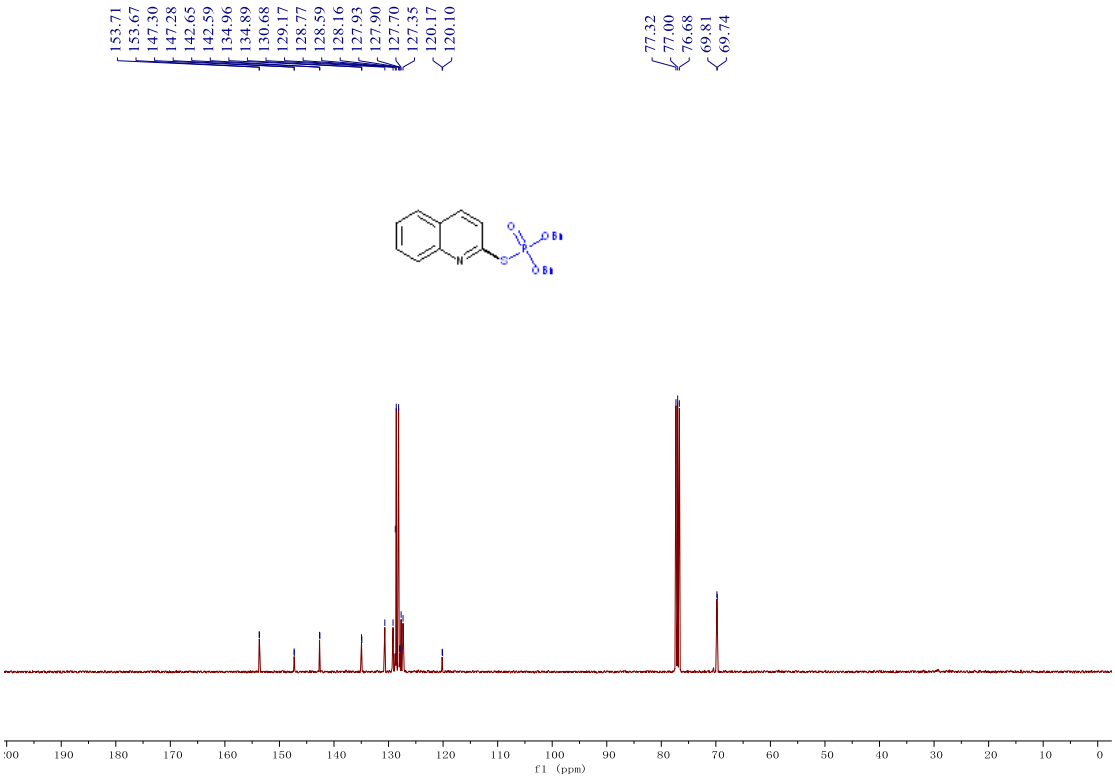
^{13}C spectrum of compound **3ae**



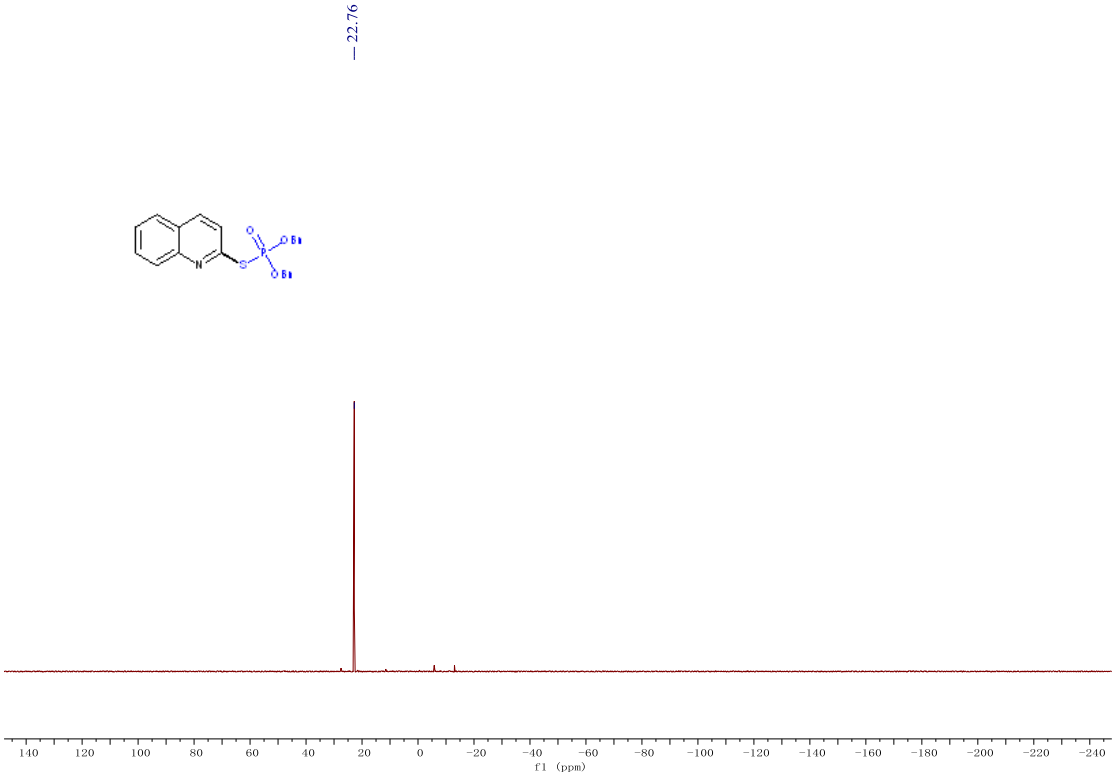
^{31}P spectrum of compound **3ae**



^{1}H spectrum of compound **3af**



^{13}C spectrum of compound **3af**



^{31}P spectrum of compound **3af**