Electronic Supplementary Material (ESI) for Organic Chemistry Frontiers.

Supporting information

Highly Selective C-H Bond Activation of *N*-Arylbenzimidamide and Divergent Couplings with Diazophosphonate Compounds: A Catalyst-controlled Selective Synthetic Strategy for 3-Phosphorylindoles and 4-Phosphorylisoquinolines

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Contents

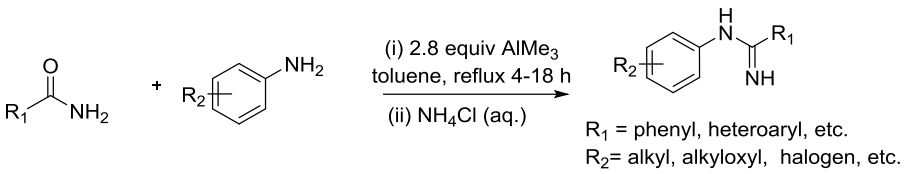
I. General Information

The reagents were purchased from commercial suppliers and used without further purification. Analytical thin-layer chromatography (TLC) was performed on HSGF 254 (0.15-0.2 mm thickness), visualized by irradiation with UV light (254 nm). Column chromatography was performed using silica gel FCP 300–400. Nuclear magnetic resonance spectra were recorded on a Brucker AMX-400MHz instrument (TMS as IS). Chemical shifts were reported in parts per million (ppm, δ) downfield from tetramethylsilane. Proton coupling patterns were described as singlet (s), doublet (d), triplet (t), quartet (q), multiplet (m), and broad (br). Low and high resolution mass were measured by the ESI method with a Tsou-ESI mass spectrometer.

II. Synthesis of Substrates

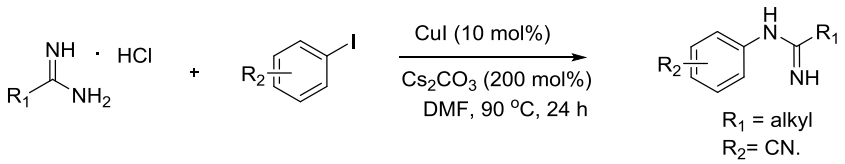
Procedure for the preparation of compound **1**: Starting materials were prepared according to literature procedures.[1a,1b]

Method A:



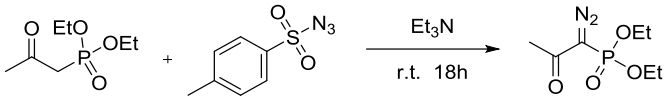
A solution of $AlMe_3$ (2 M in toluene, 2.8 mmol) was added dropwise to a mixture of aromatic amine (1.1 mmol) and primary carboxamide (1 mmol) in anhydrous toluene (3 mL) at 0 °C in a flame-dried two-necked flask, under an argon atmosphere. The resulting mixture was stirred for 30 min at room temperature and heated to 110 °C (oil bath temperature) for 4-18 hours. The mixture was cooled to 0 °C and diluted with CH_2Cl_2 (20 vol) and then slowly poured into ice-cold saturated NH_4Cl solution (4 mL). THF (15 vol) was added and the mixture was stirred for 30 min at room temperature then filtered through a Celite bed, dried with $MgSO_4$, and concentrated to give the crude product. The crude product was then recrystallized with EtOAc/PE (1:5) to give pure solid product.

Method B:



To a screw-cap reaction tube was added benzamidine hydrochloride (1 mmol), Aryl iodide (1 mmol), CuI (0.1 mmol), and Cs_2CO_3 (2 mmol). The reaction tube was placed under high vacuum, backfilled with argon and repeated several times. Dimethylformamide (2 mL) was added using a syringe and the mixture was heated to 90 °C under oil bath. After the resulting solution was stirred for 24 hours, the product was extracted using ethyl acetate, washed with water times. The organic layer was dried over anhydrous Na_2SO_4 and filtered. Following concentration under reduced pressure, the residue was purified by silica gel chromatography (PE/EA = 1:4) to afford the desired product.

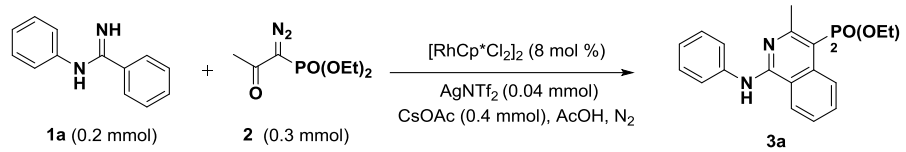
procedure for the preparation of compound 2[2]

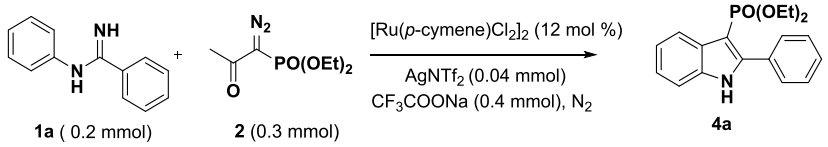


A mixture of crude diethyl (2-oxopropyl)phosphonate, toluenesulfonyl azide (4.93g, 25 mmol) and triethylamine (25 mL) was stirred at room temperature for 15 h. After evaporation of triethylamine under reduced pressure the residue was dissolved in diethylether. The precipitate was filtered off, the filtrate was evaporated and the residue was purified by flash chromatography on silica gel to give the desired product as yellow liquid. **^{1}H NMR** (400 MHz, DMSO-d_6) δ 4.18 – 4.09 (m, 4H), 2.23 (s, 3H), 1.28 (t, J = 7.1 Hz, 6H).

III. General Synthetic Procedures and Characterization Data

(a) General procedure for the synthesis of products 3a and 4a





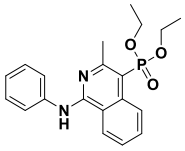
A pressure tube was charged with **1a** (0.2 mmol), **2** (0.3 mmol), [RhCp*Cl_2]$_2$ (8 mol %), $AgNTf_2$ (0.04 mmol), CsOAc (0.4 mmol), AcOH (0.4 mmol), DCE (2 mL). The reaction mixture was stirred at 100 ℃ for 14 h under an argon atmosphere. After that, the solvent was removed under reduced pressure and the residue was purified by silica gel chromatography using PE/EA (2:1) to afford the desired product **3a**.

A pressure tube was charged with **1a** (0.2 mmol), **2** (0.3 mmol), [Ru(*p*-cymene)Cl_2]$_2$ (12 mol %), $AgNTf_2$ (0.04 mmol), CF_3COONa (0.4 mmol), MeOH (2 mL). The reaction mixture was stirred at

80 ℃ for 14h under an argon atmosphere. After that, the solvent was removed under reduced pressure and the residue was purified by silica gel chromatography using PE/EA (2:1) to afford the desired product **4a**.

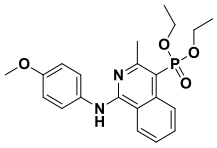
(b) Characterization data of products

Diethyl (3-methyl-1-(phenylamino) isoquinolin-4-yl) phosphonate (3a)



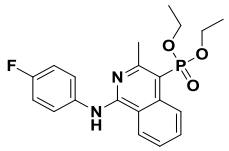
Product **3a** was obtained as white solid (81% yield); **^{1}H NMR** (400 MHz, DMSO-d_6) δ 9.54 (s, 1H), 8.72 (d, J = 8.6 Hz, 1H), 8.55 (d, J = 8.3 Hz, 1H), 7.93 (d, J = 7.8 Hz, 2H), 7.74 (t, J = 7.6 Hz, 1H), 7.59 (t, J = 7.4 Hz, 1H), 7.36 (t, J = 7.9 Hz, 2H), 7.07 (t, J = 7.3 Hz, 1H), 4.12 – 4.01 (m, 2H), 4.00 – 3.91 (m, 2H), 2.75 (d, J = 1.5 Hz, 3H), 1.20 (t, J = 7.0 Hz, 6H); **^{13}C NMR** (100 MHz, DMSO-d_6) δ 158.7 (d, $J_{C\text{-}P}$= 14.7 Hz), 154.5 (d, $J_{C\text{-}P}$ = 2.0 Hz), 140.7, 138.5 (d, $J_{C\text{-}P}$ = 12.8 Hz), 131.1, 128.8, 126.4 (d, $J_{C\text{-}P}$ = 2.5 Hz), 126.0, 123.8, 123.3, 122.0, 116.7 (d, $J_{C\text{-}P}$ = 10.2 Hz), 105.2 (d, $J_{C\text{-}P}$ = 188.0 Hz), 61.5, 61.4, 26.4, 16.7, 16.6; **^{31}P NMR** (162MHz, DMSO-d_6) δ 20.43; **ESI-MS**(*m/z*) calculated for $C_{20}H_{24}N_2O_3P$ $(M+H)^+$ 371.1519, found: 371.1517.

Diethyl (1-((4-methoxyphenyl)amino)-3-methylisoquinolin-4-yl)phosphonate (3b)



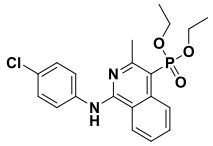
Product **3b** was obtained as white solid (77% yield); **^{1}H NMR** (400 MHz, DMSO-d_6) δ 9.46 (s, 1H), 8.69 (d, J = 8.4 Hz, 1H), 8.51 (d, J = 8.5 Hz, 1H), 7.78 (d, J = 9.1 Hz, 2H), 7.71 (t, J = 7.3 Hz, 1H), 7.56 (t, J = 8.0 Hz, 1H), 6.95 (d, J = 9.1 Hz, 2H), 4.10 – 3.87 (m, 4H), 3.76 (s, 3H), 2.71 (d, J = 1.7 Hz, 3H), 1.20 (t, J = 7.1 Hz, 6H); **^{13}C NMR** (100 MHz, DMSO-d_6) δ 158.9 (d, $J_{C\text{-}P}$= 14.6 Hz), 155.7, 154.7 (d, $J_{C\text{-}P}$ = 1.8 Hz), 138.4 (d, $J_{C\text{-}P}$ = 12.9 Hz), 133.5, 130.9, 126.3 (d, $J_{C\text{-}P}$ = 2.3 Hz), 125.8, 124.0, , 123.7, 116.5 (d, $J_{C\text{-}P}$ = 10.1 Hz), 114.0, 104. 2 (d, $J_{C\text{-}P}$ = 188.6 Hz), 61.4, 61.3, 55.6, 26.4, 16.7, 16.6 ; **^{31}P NMR** (162MHz, DMSO-d_6) δ 20.76; **ESI-MS** (*m/z*) calculated for $C_{21}H_{26}N_2O_4P$ $(M+H)^+$ 401.1625, found: 401.1622**.**

Diethyl (1-((4-fluorophenyl)amino)-3-methylisoquinolin-4-yl)phosphonate (3c)



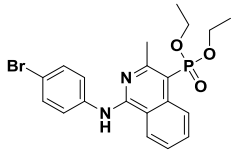
Product **3c** was obtained as white solid (51% yield); **^{1}H NMR** (400 MHz, DMSO-d_6) δ 9.58 (s, 1H), 8.72 (d, J = 8.6 Hz, 1H), 8.52 (d, J = 8.2 Hz, 1H), 7.93 (dd, J = 8.9, 5.1 Hz, 2H), 7.74 (t, J = 7.7 Hz, 1H), 7.59 (t, J = 7.5 Hz, 1H), 7.20 (t, J = 8.8 Hz, 2H), 4.15 – 3.84 (m, 4H), 2.74 (s, 3H), 1.20 (t, J = 7.0 Hz, 6H); **^{13}C NMR** (100 MHz, DMSO-d_6) δ 159.2 (d, J = 88.7 Hz), 157.9 (d, J_{C-F} = 136.2 Hz), 154.5(d, J = 1.7 Hz), 138.5 (d, J = 12.8 Hz), 137.0 (d, J = 2.4 Hz), 131.1, 126.4 (d, J = 2.1 Hz), 126.0, 123.9, 123.9, 123.8, 116.6 (d, J = 10.1 Hz), 115.4, 115.2, 105.2 (d, J_{C-P}= 188.1 Hz), 61.5, 61.4, 26.4, 16.7, 16.6; **^{31}P NMR** (162MHz, DMSO-d_6) δ 20.41; **ESI-MS** (*m/z*) calculated for $C_{20}H_{23}FN_2O_3P$ $(M+H)^+$ 389.1425, found: 389.1425

Diethyl (1-((4-chlorophenyl)amino)-3-methylisoquinolin-4-yl)phosphonate (3d)



Product **3d** was obtained as white solid (46% yield); **^{1}H NMR** (400 MHz, DMSO-d_6) δ 9.63 (s, 1H), 8.73 (d, J = 8.2 Hz, 1H), 8.53 (d, J = 7.2 Hz, 1H), 7.99 (d, J = 8.0 Hz, 2H), 7.75 (t, 7.5 Hz, 1H), 7.60 (t, 7.2 Hz, 1H), 7.41 (d, J = 8.0 Hz, 2H), 4.13 –3.86 (m, 4H), 2.76 (s, 3H), 1.20 (t, J = 6.6 Hz, 6H); **^{13}C NMR**(101 MHz, DMSO-d_6) δ 158.5 (d, J_{C-P} = 14.8 Hz), 154.2 (d, J_{C-P} = 2.1 Hz), 139.7, 138.5 (d, J_{C-P} = 12.8 Hz), 131.2, 128.7, 126.7, 126.4 (d, J_{C-P} = 2.2 Hz), 126.1, 123.8, 123.4, 116.7 (d, J_{C-P} = 10.1 Hz), 105.7 (d, J_{C-P}= 187.8 Hz), 61.5, 61.5, 26.3, 16.7, 16.6; **^{31}P NMR** (162 MHz, DMSO-d_6) δ 20.17; **ESI-MS** (*m/z*) calculated for $C_{20}H_{23}ClN_2O_3P$ $(M+H)^+$ 405.1129, found: 405.1128.

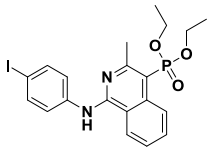
Diethyl (1-((4-bromophenyl)amino)-3-methylisoquinolin-4-yl)phosphonate (3e)



Product **3e** was obtained as white solid (42% yield); **^{1}H NMR** (400 MHz, DMSO-d_6) δ 9.64 (s, 1H), 8.73 (d, J = 8.6 Hz, 1H), 8.54 (d, J = 8.0 Hz, 1H), 7.94 (d, J = 8.8 Hz, 2H), 7.76 (t,7.2Hz , 1H), 7.61 (t,

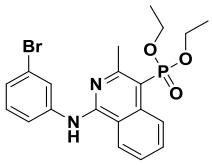
J = 7.5 Hz, 1H), 7.54 (d, *J* = 8.7 Hz, 2H), 4.13 – 3.88 (m, 4H), 2.77 (s, 3H), 1.21 (t, *J* = 7.0 Hz, 6H); **^{13}C NMR** (100 MHz, DMSO-d_6) δ158.4 (d, J_{C-P} = 14.6 Hz), 154.2 (d, J_{C-P} = 1.8 Hz), 140.1, 138.5 (d, J_{C-P} = 12.7 Hz), 131.6, 131.2, 126.4, 126.1, 123.8, 123.8, 116.7 (d, J_{C-P} = 10.3 Hz), 114.7, 105. 8 (d, J_{C-P} = 187.8 Hz), 61.5, 61.5, 26.3, 16.7, 16.6; **^{31}P NMR** (162MHz, DMSO-d_6) δ 20.15; **ESI-MS** (*m/z*) calculated for $C_{20}H_{23}BrN_2O_3P$ $(M+H)^+$ 449.0624, found: 449.0629.

Diethyl (1-((4-iodophenyl)amino)-3-methylisoquinolin-4-yl)phosphonate (3f)



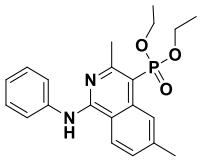
Product **3f** was obtained as white solid (41% yield); **^{1}H NMR** (400 MHz, DMSO-d_6) δ 9.61 (s, 1H), 8.73 (d, *J* = 8.4 Hz, 1H), 8.53 (d, *J* = 8.6 Hz, 1H), 7.81 (d, *J* = 8.9 Hz, 2H), 7.75(t, *J* =8.2 Hz , 1H), 7.69 (d, *J* = 8.9 Hz, 2H), 7.60 (t, *J* = 8.1 Hz, 1H), 4.13 – 3.86 (m, 4H), 2.76 (d, *J* = 1.8 Hz, 3H), 1.20 (t, *J* = 7.1 Hz, 6H); **^{13}C NMR** (100 MHz, DMSO-d_6) δ158.41 (d, J_{C-P} = 14.6 Hz), 154.2 (d, J_{C-P} = 1.9 Hz), 140.6, 138.5, 137.4, 131.2, 126.4, 126.1, 124.1, 123.8, 116.8 (d, J_{C-P} = 10.1 Hz), 105.8 (d, J_{C-P} = 187.7 Hz), 100.0, 61.5, 61.5, 26.3, 16.7, 16.6; **^{31}P NMR** (162MHz, DMSO-d_6) δ 20.15; **ESI-MS** (*m/z*) calculated for $C_{20}H_{23}IN_2O_3P$ $(M+H)^+$ 497.0485, found: 497.0497.

Diethyl (1-((3-bromophenyl)amino)-3-methylisoquinolin-4-yl)phosphonate (3g)



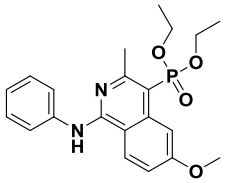
Product **3g** was obtained as white solid (52% yield); **^{1}H NMR** (400 MHz, DMSO-d_6) δ 9.45 (s, 1H), 8.73 (d, *J* = 8.6 Hz, 1H), 8.46 (d, *J* = 8.3 Hz, 1H), 7.73 (d, *J* = 7.9 Hz, 2H), 7.65 (d, *J* = 9.2 Hz, 1H), 7.59 (t, *J* = 7.4 Hz, 1H), 7.45 (t, *J* = 8.3 Hz, 1H), 7.21 (t, *J* = 7.0 Hz, 1H), 4.11–3.88 (m, 4H), 2.59 (s, 3H), 1.20 (t, *J* = 7.0 Hz, 6H); **^{13}C NMR** (100 MHz, DMSO-d_6) δ 158.9 (d, J_{C-P} = 14.8 Hz), 155.3 (d, J_{C-P} = 1.5 Hz), 138.7, 138.6 (d, J_{C-P} = 13.1 Hz), 133.2, 131.1, 129.7, 128.5, 127.7, 126.4, 126.1, 123.8, 121.8, 116.3 (d, J_{C-P} = 10.5 Hz), 104.8 (d, J_{C-P} = 188.4 Hz), 61.4, 61.4, 26.5, 16.7, 16.6 ; **^{31}P NMR** (162MHz, DMSO-d_6) δ 20.59; **ESI-MS** (*m/z*) calculated for $C_{20}H_{23}BrN_2O_3P$ $(M+H)^+$ 449.0624, found: 449.0632.

Diethyl (3,6-dimethyl-1-(phenylamino)isoquinolin-4-yl)phosphonate (3h)



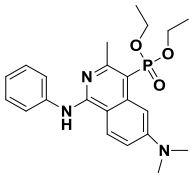
Product **3h** was obtained as white solid (72% yield); **^{1}H NMR** (400 MHz, DMSO-d_6) δ 9.42 (s, 1H), 8.47 (dd, J = 9.3, 2.4 Hz, 1H), 8.24 (d, J = 2.5 Hz, 1H), 7.90 (d, J = 7.6 Hz, 2H), 7.34 (t, 2H), 7.22 (dd, J = 9.2, 2.6 Hz, 1H), 7.08 – 7.00 (m, 1H), 4.10 – 3.90 (m, 4H), 3.87 (s, 3H), 2.71 (d, J = 1.7 Hz, 3H), 1.21 (t, J = 7.0 Hz, 6H); **^{13}C NMR** (100 MHz, DMSO-d_6) δ 160.2 (d, J_{C-P} = 13.6 Hz), 154.5 (d, J_{C-P} = 1.8 Hz), 140.4, 140.0 (d, J_{C-P} = 13.2 Hz), 136.4, 128.8, 126.7, 126.1, 125.1, 123.6, 122.3, 115.2 (d, J_{C-P} = 10.1 Hz), 104.1 (d, J_{C-P} = 188.7 Hz), 61.7, 61.6, 26.4, 26.4, 16.6, 16.6; **^{31}P NMR** (162 MHz, DMSO-d_6) δ 19.80; **ESI-MS** (*m/z*) calculated for $C_{21}H_{26}N_2O_3P$ $(M+H)^+$ 385.1676, found: 385.1672.

Diethyl (6-methoxy-3-methyl-1-(phenylamino)isoquinolin-4-yl)phosphonate (3i)



Product **3i** was obtained as white solid (66% yield); **^{1}H NMR** (400 MHz, DMSO-d_6) δ 9.42 (s, 1H), 8.47 (dd, J = 9.3, 2.4 Hz, 1H), 8.24 (d, J = 2.5 Hz, 1H), 7.90 (d, J = 7.6 Hz, 2H), 7.34 (t, J = 7.5Hz, 2H), 7.22 (dd, J = 9.2, 2.6 Hz, 1H), 7.08 – 7.00 (m, 1H), 4.10 – 3.90 (m, 4H), 3.87 (s, 3H), 2.71 (d, J = 1.7 Hz, 3H), 1.21 (t, J = 7.0 Hz, 6H); **^{13}C NMR** (100 MHz, DMSO-d_6) δ 161.0, 159.4 (d, J_{C-P} = 15.2 Hz), 154.3 (d, J_{C-P} = 1.8 Hz), 141.0, 140.8 (d, J_{C-P} = 1.7 Hz), 128.8, 125.8, 123.1, 121.9, 116.6, 111.4 (d, J_{C-P} = 10.1 Hz), 106.7, 104.5 (d, J_{C-P} = 188.1 Hz), 61.4, 61.4, 55.7, 26.4, 16.7, 16.6; **^{31}P NMR** (162 MHz, DMSO-d_6) δ 20.87; **ESI-MS** (*m/z*) calculated for $C_{21}H_{26}F_3N_2O_4P$ $(M+H)^+$ 401.1625, found: 401.1623.

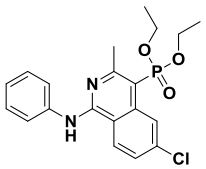
Diethyl (6-(dimethylamino)-3-methyl-1-(phenylamino)isoquinolin-4-yl)phosphonate (3j)



Product **3j** was obtained as white solid (71% yield); **^{1}H NMR** (400 MHz, DMSO-d_6) δ 9.23 (s, 1H),

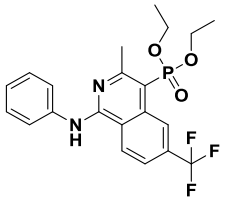
8.33 (dd, *J* = 9.4, 2.5 Hz, 1H), 7.91 (d, *J* = 7.6 Hz, 2H), 7.76 (d, *J* = 2.5 Hz, 1H), 7.44 – 7.27 (m, 2H), 7.14 (dd, *J* = 9.3, 2.5 Hz, 1H), 7.01 (t, *J* = 7.3 Hz, 1H), 4.13 – 4.01 (m, 2H), 3.94 – 3.81 (m, 2H),3.06 (s, 6H), 2.69 (d, *J* = 1.7 Hz, 3H), 1.21 (t, *J* = 7.1 Hz, 6H); **^{13}C NMR** (100 MHz, DMSO-d_6) δ159.1 (d, J_{C-P} = 15.3 Hz), 154.2, 151.5, 141.2, 140.3 (d, J_{C-P} = 12.2 Hz), 128.7, 124.9, 122.6, 121.6, 113.8, 108.2 (d, J_{C-P} = 10.0 Hz), 105.0, 103.6 (d, J_{C-P} = 187.4 Hz), 61.1, 61.1,40.16, 40.16, 26.5, 16.7, 16.7; **^{31}P NMR** (162 MHz, DMSO-d_6) δ 20.86; **ESI-MS** (*m/z*) calculated for $C_{22}H_{29}N_3O_3P$ $(M+H)^+$ 414.1941, found: 414.1945.

Diethyl (6-chloro-3-methyl-1-(phenylamino)isoquinolin-4-yl)phosphonate (3k)



Product **3k** was obtained as white solid (81% yield); **^{1}H NMR** (400 MHz, DMSO-d_6) δ 9.67 (s, 1H), 8.97 (d, *J* = 2.1 Hz, 1H), 8.60 (dd, *J* = 9.0, 2.4 Hz, 1H), 7.90 (d, *J* = 7.6 Hz, 2H), 7.66 (dd, *J* = 9.0, 2.1 Hz, 1H), 7.37 (t, *J* = 7.9 Hz, 2H), 7.09 (t, *J* = 7.4 Hz, 1H), 4.27 – 3.78 (m, 4H), 2.72 (d, *J* = 1.6 Hz, 3H), 1.22 (t, *J* = 7.0 Hz, 6H); **^{13}C NMR** (100 MHz, DMSO-d_6) δ160.2 (d, J_{C-P} = 13.6 Hz), 154.4 (d, J_{C-P} = 1.9 Hz), 140.3, 140.0 (d, J_{C-P} = 13.2 Hz), 136.4, 128.8, 126.3, 126.2, 125.2 (d, J_{C-P} = 2.0 Hz), 123.6, 122.2, 115.1 (d, J_{C-P} = 10.2 Hz), 104.2 (d, J_{C-P} = 188.8 Hz), 61.7, 61.7, 26.4, 16.6, 16.6; **^{31}P NMR** (162 MHz, DMSO-d_6) δ 19.73; **ESI-MS** (*m/z*) calculated for $C_{20}H_{23}ClN_2O_3P$ $(M+H)^+$ 405.1129, found: 405.1126.

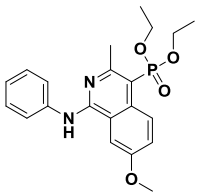
Diethyl (3-methyl-1-(phenylamino)-6-(trifluoromethyl)isoquinolin-4-yl)phosphonate (3l)



Product **3l** was obtained as white solid (80% yield); **^{1}H NMR** (400 MHz, DMSO-d_6) δ 9.82 (s, 1H), 9.31 (s, 1H), 8.80 (d, *J* = 10.0 Hz, 1H), 7.91 (t, *J* = 10.2 Hz, 3H), 7.40 (t, *J* = 8.3Hz, 2H), 7.12 (t, *J* = 7.4 Hz, 1H), 4.20 – 3.90 (m, 4H), 2.76 (d, *J* = 1.6 Hz, 3H), 1.22 (t, *J* = 7.0 Hz, 6H); **^{13}C NMR** (100 MHz, DMSO-d_6) δ 160.4 (d, *J* = 13.8 Hz), 154.4 (d, *J* = 1.7 Hz), 140.2, 138.3 (d, *J* = 13.0 Hz), 130.9 (d,

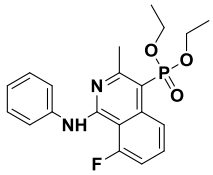
J = 31.3 Hz), 128.9, 125.8, 124.6 (d, J_{C-F} = 272.7 Hz), 123.8, 123.7, 122.3, 121.4 (d, *J* = 3.1 Hz), 118.3 (d, *J* = 9.6 Hz), 105.2 (d, J_{C-P} = 188.9 Hz), 61.8, 61.7, 26.3, 16.5, 16.5; **^{31}P NMR** (162 MHz, DMSO-d_6) δ 19.34; **ESI-MS**(*m/z*) calculated for $C_{21}H_{23}F_3N_2O_3P$ $(M+H)^+$439.1393, found:439.1397.

Diethyl (7-methoxy-3-methyl-1-(phenylamino)isoquinolin-4-yl)phosphonate (3m)



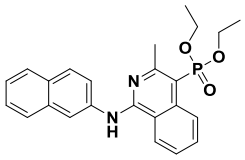
Product **3m** was obtained as white solid (65% yield); **^{1}H NMR** (400 MHz, DMSO-d_6) δ9.38 (s, 1H), 8.69 (d, *J* = 9.5 Hz, 1H), 7.88 (d, *J* = 8.0 Hz, 3H), 7.54 – 7.23 (m, 3H), 7.08 (t, *J* = 7.3 Hz, 1H), 4.08-3.91 (m, 7H), 2.72 (d, *J* = 1.4 Hz, 3H), 1.20 (t, *J* = 7.0 Hz, 6H); **^{13}C NMR** (100 MHz, DMSO-d_6) δ 157.5, 156.0 (d, J_{C-P}= 14.4 Hz), 153.7 (d, J_{C-P} = 1.0 Hz), 140.8, 133.3 (d, J_{C-P} = 13.1 Hz), 128.8, 128.2 (d, J_{C-P} = 1.6 Hz), 123.3, 122.2, 122.0, 117.9 (d, J_{C-P} = 10.3 Hz), 105.2 (d, J_{C-P} = 187.4 Hz), 103.7, 61.4, 61.4, 56.3, 26.0, 16.6, 16.6 ; **^{31}P NMR** (162 MHz, DMSO-d_6) δ 20.43; **ESI-MS** (*m/z*) calculated for $C_{21}H_{26}F_3N_2O_4P$ $(M+H)^+$ 401.1625, found: 401.1629

Diethyl (8-fluoro-3-methyl-1-(phenylamino)isoquinolin-4-yl)phosphonate (3n)



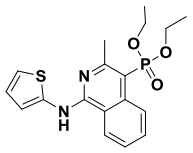
Product **3n** was obtained as white solid (85% yield); **^{1}H NMR** (400 MHz, DMSO-d_6) δ 9.05 (d, *J* = 15.3 Hz, 1H), 8.58 (d, *J* = 8.7 Hz, 1H), 7.86 (d, *J* = 7.6 Hz, 2H), 7.76 – 7.64 (m, 1H), 7.42 – 7.27(m, 3H), 7.08 (t, *J* = 7.4 Hz, 1H), 4.18 – 3.82 (m, 4H), 2.74 (d, *J* = 1.7 Hz, 3H), 1.20 (t, *J* = 7.1 Hz, 6H); **^{13}C NMR** (100 MHz, DMSO-d_6) δ 160.3, 159.0 (dd, J_{C-F} = 178.1, 7.8 Hz), 152.2 (d, *J* = 4.3 Hz), 141.8 (dd, *J* = 92.0, 25.9 Hz), 139.9, 131.7 (d, *J* = 10.3 Hz), 129.7, 128.9, 126.1, 123.8, 122.6, 122.2, 111.7 (d, *J* = 23.6 Hz), 106.7 (t, *J* = 10.6 Hz), 104.9 (d, J_{C-P}= 190.0 Hz), 61.6, 61.6, 26.3, 16.6, 16.5; **^{31}P NMR** (162 MHz, DMSO-d_6) δ 20.17; **ESI-MS** (*m/z*) calculated for $C_{20}H_{23}FN_2O_3P$ $(M+H)^+$ 389.1425, found: 389.1436.

Diethyl(3-methyl-1-(naphthalen-2-ylamino)isoquinolin-4-yl)phosphonate (3o)



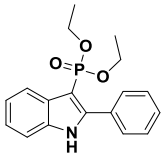
Product **3o** was obtained as white solid (85% yield); **^{1}H NMR** (400 MHz, DMSO-d_6) δ 9.83 (s, 1H), 8.76 (d, J = 8.6 Hz, 1H), 8.67 (d, J = 8.3 Hz, 1H), 7.96 (dd, J = 15.3, 8.1 Hz, 2H), 7.86 (d, J = 8.1 Hz, 1H), 7.76 (t, J = 8.2 Hz, 1H), 7.68 – 7.57 (m, 3H), 7.57 – 7.43 (m, 2H), 4.10 – 3.89 (m, 4H), 2.46 (d, J = 1.7 Hz, 3H), 1.20 (t, J = 7.1 Hz, 6H) ; **^{13}C NMR** (100 MHz, DMSO-d_6) δ159.19 (d, J_{C-P} = 14.7 Hz), 156.7 (d, J_{C-P} = 1.9 Hz), 138.7 (d, J_{C-P} = 13.1 Hz), 136.2, 134.4, 131.0, 130.5, 128.6, 126.4, 126.4, 126.4, 126.2, 126.1, 126.0, 125.0, 124.1, 124.0, 116.3 (d, J_{C-P} = 10.4 Hz), 104.2 (d, J_{C-P} = 189.0 Hz), 61.4, 61.3, 26.5, 16.7, 16.6; **^{31}P NMR** (162 MHz, DMSO-d_6) δ 21.83; **ESI-MS** (*m/z*) calculated for $C_{24}H_{26}N_2O_3P$ $(M+H)^+$ 421.1676, found: 421.1665.

Diethyl(3-methyl-1-(thiophen-2-ylamino)isoquinolin-4-yl)phosphonate (3p)



Product **3p** was obtained as white solid (70% yield); **^{1}H NMR** (400 MHz, DMSO-d_6) δ 10.95 (s, 1H), 8.72 (d, J = 8.4 Hz, 1H), 8.57 (d, J = 8.5 Hz, 1H), 7.76 (m, 1H), 7.63 (m, 1H), 7.06 (dd, J = 3.7, 1.6 Hz, 1H), 6.99 (dd, J = 5.5, 1.4 Hz, 1H), 6.95 (m, 1H), 4.17 – 3.84 (m, 4H), 2.88 (d, J = 1.9 Hz, 3H), 1.21 (t, J = 7.0 Hz, 6H); **^{13}C NMR** (100 MHz, DMSO-d_6) δ 158.3 (d, J_{C-P} = 15.1 Hz), 151.0, 141.7, 138.3 (d, J_{C-P} = 12.8 Hz), 131.2, 126.5 (d, J_{C-P} = 2.5 Hz), 126.2, 124.2, 123.4, 117.9, 116.0 (d, J_{C-P} = 10.3 Hz), 112.0, 104.9(d, J_{C-P} = 187.7 Hz), 61.5, 61.5, 25.5, 16.7, 16.6; **^{31}P NMR** (162 MHz, DMSO-d_6) δ 20.18; **ESI-MS** (*m/z*) calculated for $C_{18}H_{22}N_2O_3PS$ $(M+H)^+$ 377.1083, found: 377.1083.

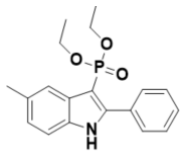
Diethyl (2-phenyl-1H-indol-3-yl)phosphonate (4a)



Product **4a** was obtained as white solid (65% yield); **^{1}H NMR** (400 MHz, DMSO-d_6) δ 12.16 (s, 1H), 7.91 (d, J = 7.9 Hz, 1H), 7.76 (d, J = 7.7 Hz, 2H), 7.56 – 7.42 (m, 4H), 7.22 (t, J = 7.4 Hz, 1H), 7.15 (t, J = 7.5 Hz, 1H), 3.95 – 3.79 (m, 4H), 1.07 (t, J = 7.0 Hz, 6H); **^{13}C NMR** (100 MHz, DMSO-d_6) δ 145.7

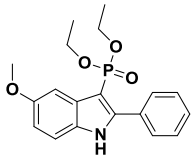
(d, J_{C-P} = 23.3 Hz), 136.7 (d, J_{C-P} = 15.0 Hz), 132.2, 130.4 (d, J_{C-P} = 13.1 Hz), 130.0, 129.4, 128.5, 122.9, 121.4, 121.2, 112.2, 96.9 (d, J_{C-P} = 214.5 Hz), 61.2, 61.2, 16.5, 16.4; **^{31}P NMR** (162MHz, DMSO-d_6) δ 16.87; **ESI-MS** (*m/z*) calculated for $C_{18}H_{21}NO_3P$ $(M+H)^+$ 330.1254, found: 330.1253.

Diethyl (5-methyl-2-phenyl-1H-indol-3-yl)phosphonate (4b)



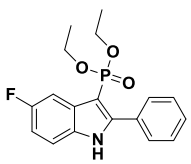
Product **4b** was obtained as white solid (60% yield); **^{1}H NMR** (400 MHz, DMSO-d_6) δ 12.04 (d, J = 3.9 Hz, 1H), 7.76 -7.73 (m, 3H), 7.53 – 7.45 (m, 3H), 7.36 (dd, J = 8.2, 2.1 Hz, 1H), 7.04 (dd, J = 8.3, 1.3 Hz, 1H), 3.99 – 3.71 (m, 4H), 2.41 (s, 3H), 1.07 (t, J = 7.1 Hz, 6H); **^{13}C NMR** (100 MHz, DMSO-d_6) δ 145.6 (d, J_{C-P} = 23.3 Hz), 135.1 (d, J_{C-P} = 15.1 Hz), 132.3, 130.8 (d, J_{C-P} = 13.2 Hz), 129.9, 129.8, 129.3, 128.4, 124.4, 121.0, 111.9, 96.3 (d, J_{C-P} = 214.2 Hz), 61.2, 61.1, 21.9, 16.4, 16.4; **^{31}P NMR** (162 MHz, DMSO-d_6) δ 17.15; **ESI-MS** (*m/z*) calculated for $C_{19}H_{23}NO_3P$ $(M+H)^+$ 344.1410, found: 344.1407.

Diethyl (5-methoxy-2-phenyl-1H-indol-3-yl)phosphonate (4c)



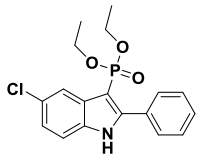
Product **4c** was obtained as white solid (41% yield); **^{1}H NMR** (400 MHz, DMSO-d_6) δ 12.03 (d, J = 3.8 Hz, 1H), 7.75 (dd, J = 8.0, 1.5 Hz, 2H), 7.54 – 7.45 (m, 3H), 7.42 -7.35 (m, 2H), 6.86 (dd, J = 8.8, 2.5 Hz, 1H), 3.95 – 3.80 (m, 4H), 3.78 (s, 3H), 1.08 (t, J = 7.0 Hz, 6H); **^{13}C NMR** (100 MHz, DMSO-d_6) δ154.9, 145.8 (d, J_{C-P} = 23.2 Hz), 132.2, 131.7 (d, J_{C-P} = 15.0 Hz), 131.2 (d, J_{C-P} = 12.8 Hz), 129.8, 129.3, 128.5, 113.0, 112.9, 103.0, 96.5 (d, J_{C-P} = 214.5 Hz), 61.2, 61.2, 55.7, 16.5, 16.4; **^{31}P NMR** (162 MHz, DMSO-d_6) δ 17.22; **ESI-MS** (m/z) calculated for $C_{19}H_{23}NO_4P$ $(M+H)^+$ 360.1359, found: 360.1369.

Diethyl (5-fluoro-2-phenyl-1H-indol-3-yl)phosphonate (4d)



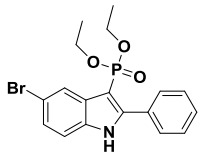
Product **4d** was obtained as white solid (67% yield); **^{1}H NMR** (400 MHz, DMSO-d_6) δ 12.30 (d, J = 3.7 Hz, 1H), 7.77 (m, 2H), 7.63 (dd, J = 10.4, 2.6 Hz, 1H), 7.56 – 7.44 (m, 4H), 7.08 (m, 1H), 4.04 – 3.76 (m, 4H), 1.07 (t, J = 7.0 Hz, 6H); **^{13}C NMR** (100 MHz, DMSO-d_6) δ 158.2 (d, J_{C-F} = 232.9 Hz), 147.2 (d, J = 22.7 Hz), 133.4 (d, J = 14.8 Hz), 131.8, 131.2 (dd, J = 12.7, 11.1 Hz), 129.9, 129.6, 128.6, 113.4 (d, J = 9.8 Hz), 111.2 (d, J = 26.1 Hz), 106.1 (d, J = 24.9 Hz), 97.2 (dd, J_{C-P} = 215.1, 4.6 Hz), 61.4, 61.3, 16.4, 16.4; **^{31}P NMR** (162 MHz, DMSO-d_6) δ 16.29; **ESI-MS** (m/z) calculated for $C_{18}H_{20}FNO_3P$ $(M+H)^+$ 348.1159, found: 348.1159.

Diethyl (5-chloro-2-phenyl-1H-indol-3-yl)phosphonate (4e)



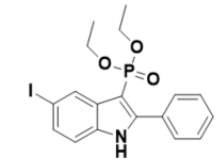
Product **4e** was obtained as white solid (66% yield); **^{1}H NMR** (400 MHz, DMSO-d_6) δ 12.39 (d, J = 3.7 Hz, 1H), 7.95 (d, J = 2.1 Hz, 1H), 7.77 (dd, J = 7.8, 1.7 Hz, 2H), 7.55-7.48 (m, 4H), 7.24 (dd, J = 8.6, 2.1 Hz, 1H), 4.13 – 3.70 (m, 4H), 1.06 (t, J = 7.0 Hz, 6H); **^{13}C NMR** (100 MHz, DMSO-d_6) δ 147.0 (d, J_{C-P} = 22.5 Hz), 135.2 (d, J_{C-P} = 14.7 Hz), 131.8 (d, J_{C-P} = 13.1 Hz), 131.6, 129.9, 129.7, 128.6, 125.9, 123.0, 120.5, 113.8, 96.9 (d, J_{C-P} = 214.7 Hz), 61. 4, 61.4, 16.4, 16.3; **^{31}P NMR** (162 MHz, DMSO-d_6) δ 15.93; **ESI-MS** (m/z) calculated for $C_{18}H_{20}ClNO_3P$ $(M+H)^+$ 364.0864, found: 364.0857.

Diethyl (5-bromo-2-phenyl-1H-indol-3-yl)phosphonate (4f)



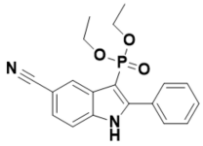
Product **4f** was obtained as white solid (64% yield); **^{1}H NMR** (400 MHz, DMSO-d_6) δ 12.36 (d, J = 3.5 Hz, 1H), 8.31 (s, 1H), 7.76 (dd, J = 7.5, 1.6 Hz, 2H), 7.50 (m, 3H), 7.44 (t, J = 7.4 Hz, 1H), 7.32 (dd, J = 8.5, 1.9 Hz, 1H), 3.96 – 3.75 (m, 4H), 1.06 (t, J = 7.0 Hz, 6H); **^{13}C NMR** (100 MHz, DMSO-d_6) δ 146.8 (d, J_{C-P} = 22.4 Hz), 135.5 (d, J_{C-P} = 14.7 Hz), 132.4 (d, J_{C-P} = 13.0 Hz), 131.6, 129.9, 129.7, 128.6, 125.5, 123.5, 114.3, 113.9, 96.8 (d, J_{C-P} = 214.7 Hz), 61.5, 61.4, 16.4, 16.3; **^{31}P NMR** (162 MHz, DMSO-d_6) δ 15.90; **ESI-MS** (*m/z*) calculated for $C_{18}H_{20}BrNO_3P$ $(M+H)^+$ 408.0359, found: 408.0369.

Diethyl (5-iodo-2-phenyl-1H-indol-3-yl)phosphonate (4g)



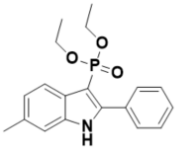
Product **4g** was obtained as white solid (41% yield); **^{1}H NMR** (400 MHz, DMSO-d_6) δ 12.36 (d, J = 3.5 Hz, 1H), 8.31 (s, 1H), 7.76 (dd, J = 7.5, 1.6 Hz, 2H), 7.50 (t, J = 7.6 Hz, 3H), 7.44 (t, J = 7.4 Hz, 1H), 7.32 (dd, J = 8.5, 1.9 Hz, 1H), 3.96 – 3.75 (m, 4H), 1.06 (t, J = 7.0 Hz, 6H); **^{13}C NMR** (100 MHz, DMSO-d_6) δ146.3 (d, J_{C-P} = 22.5 Hz), 135.8 (d, J_{C-P} = 14.8 Hz), 134.7, 133.2 (d, J_{C-P} = 13.4 Hz), 131.6 (d, J_{C-P} = 10.7 Hz), 130.9, 129.9, 129.7, 129.7, 128.7, 128.6, 127.9, 114.6, 96.4 (d, J_{C-P} = 214.7 Hz), 61.4, 61.4, 16.4, 16.3; **^{31}P NMR** (162 MHz, DMSO-d_6) δ 15.97; **ESI-MS** (m/z) calculated for $C_{18}H_{20}INO_3P$ $(M+H)^+$ 456.0220, found: 456.0233.

Diethyl (5-cyano-2-phenyl-1H-indol-3-yl)phosphonate (4h)



Product **4h** was obtained as white solid (61% yield); **^{1}H NMR** (400 MHz, DMSO-d_6) δ 12.75 (d, J = 1.8 Hz, 1H), 8.34 (d, J = 0.7 Hz, 1H), 7.79 (dd, J = 7.4, 2.2 Hz, 2H), 7.62 (m, 2H), 7.54 (m, 3H), 4.02 – 3.79 (m, 4H), 1.07 (t, J = 7.0 Hz, 6H); **^{13}C NMR** (100 MHz, DMSO-d_6) δ 147.9 (d, J_{C-P} = 22.0 Hz), 138.7 (d, J_{C-P} = 14.4 Hz), 131.2, 130.4(d, J = 13.2 Hz), 130.0, 130.0, 128.7, 126.6, 125.7, 120.7, 113.7, 103.5, 98.1 (d, J_{C-P} = 214.4 Hz), 61.7, 61.6, 16.4, 16.3; **^{31}P NMR** (162 MHz, DMSO-d_6) δ 15.02; **ESI-MS** (m/z) calculated for $C_{19}H_{20}N_2O_3P$ $(M+H)^+$ 355.1206, found: 355.1211.

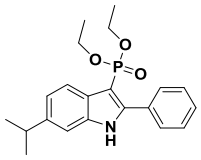
Diethyl (6-methyl-2-phenyl-1H-indol-3-yl)phosphonate (4i)



Product **4i** was obtained as white solid (61% yield); **^{1}H NMR** (400 MHz, DMSO-d_6) δ 12.00 (d, J = 3.8 Hz, 1H), 7.86 – 7.68 (m, 3H), 7.67 – 7.36 (m, 3H), 7.26 (s, 1H), 6.99 (d, J = 9.1 Hz, 1H), 4.06 – 3.66 (m, 4H), 2.42 (s, 3H), 1.07 (t, J = 7.0 Hz, 6H); **^{13}C NMR** (100 MHz, DMSO-d_6) δ 145.1 (d, J_{C-P} = 23.4

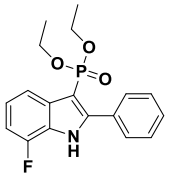
Hz), 137.1 (d, J_{C-P} = 15.0 Hz), 132.3, 132.1, 129.9, 129.2, 128.4, 128.3 (dd, J_{C-P} = 43.6, 30.4 Hz), 123.0, 121.1, 111.9, 96.7 (d, J_{C-P} = 214.5 Hz), 61.2, 61.2, 21.8, 16.5, 16.4; **^{31}P NMR** (162 MHz, DMSO-d_6) δ 17.14; **ESI-MS** (*m/z*) calculated for $C_{19}H_{23}NO_3P$ $(M+H)^+$ 344.1410, found: 344.1419.

Diethyl (6-isopropyl-2-phenyl-1H-indol-3-yl)phosphonate (4j)



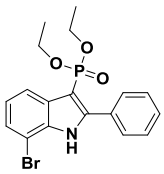
Product **4j** was obtained as white solid (64% yield); **^{1}H NMR** (400 MHz, DMSO-d_6) δ 12.00 (d, J = 3.8 Hz, 1H), 7.81 (d, J = 8.3 Hz, 1H), 7.74 (dd, J = 7.9, 1.3 Hz, 2H), 7.49 (m, 3H), 7.28 (s, 1H), 7.07 (dd, J = 8.4, 1.2 Hz, 1H), 3.98 – 3.78 (m, 4H), 3.04 – 2.95 (m, 1H), 1.26 (d, J = 6.9 Hz, 6H), 1.07 (t, J = 7.0 Hz, 6H); **^{13}C NMR** (100 MHz, DMSO-d_6) δ 145.3 (d, J_{C-P} = 23.4 Hz), 143.6, 137.0 (d, J_{C-P} = 15.0 Hz), 132.3, 129.9, 129.2, 128.6 (d, J_{C-P} = 13.2 Hz), 128.4, 121.2, 120.5, 109.0, 96.6 (d, J_{C-P} = 214.3 Hz), 61.2, 61.1, 34.0, 24.8, 24.8, 16.5, 16.4; **^{31}P NMR** (162 MHz, DMSO-d_6) δ 17.12; **ESI-MS** (*m/z*) calculated for $C_{21}H_{27}NO_3P$ $(M+H)^+$ 372.1723, found: 372.1730.

Diethyl (7-fluoro-2-phenyl-1H-indol-3-yl)phosphonate (4k)



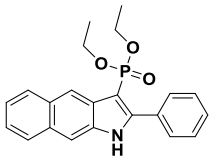
Product **4k** was obtained as white solid (66% yield); **^{1}H NMR** (400 MHz, DMSO-d_6) δ 12.58 (d, J = 3.7 Hz, 1H), 7.89 – 7.59 (m, 3H), 7.51 (m, 3H), 7.23 – 6.85 (m, 2H), 3.87 (m, 4H), 1.06 (t, J = 7.0 Hz, 6H); **^{13}C NMR** (100 MHz, DMSO-d_6) δ149.4 (dd, J_{C-F} = 244.7, 2.3 Hz), 147.0 (d, J = 23.0 Hz), 134.0 (dd, J = 13.7, 5.1 Hz), 131.6, 130.4, 129.6, 128.3, 124.8 (dd, J = 15.1, 13.5 Hz), 121.7 (d, J = 6.2 Hz), 117. 5 (d, J = 3.3 Hz), 107.8 (d, J = 15.8 Hz), 98.5 (d, J_{C-P} = 214.4 Hz), 61.4, 61.4, 16.4, 16.3; **^{31}P NMR** (162 MHz, DMSO-d_6) δ 15.84; **ESI-MS** (*m/z*) calculated for $C_{18}H_{20}FNO_3P$ $(M+H)^+$ 348.1159, found: 348.1163.

Diethyl (7-bromo-2-phenyl-1H-indol-3-yl)phosphonate (4l)



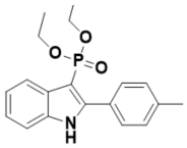
Product **4l** was obtained as white solid (60% yield); **^{1}H NMR** (400 MHz, DMSO-d_6) δ 12.27 (d, J = 3.5 Hz, 1H), 7.94 (d, J = 8.0 Hz, 1H), 7.71 (m, 2H), 7.53 – 7.48 (m, 3H), 7.45 (dd, J = 7.6, 0.8 Hz, 1H), 7.12 (t, J = 7.9 Hz, 1H), 4.01 – 3.72 (m, 4H), 1.05 (t, J = 7.0 Hz, 6H); **^{13}C NMR** (100 MHz, DMSO-d_6) δ 147.4 (d, J_{C-P} = 22.5 Hz), 135.3 (d, J_{C-P} = 14.7 Hz), 131.8 (d, J_{C-P} = 13.6 Hz), 131.5 (d, J_{C-P} = 0.4 Hz), 130.7, 129.6, 128.1, 125.8, 122.7, 120.7, 104.6 (d, J_{C-P} = 1.9 Hz), 99.1 (d, J_{C-P}= 214.0 Hz), 61.4, 61.3, 16.4, 16.3; **^{31}P NMR** (162 MHz, DMSO-d_6) δ 15.53; **ESI-MS** (*m/z*) calculated for $C_{18}H_{20}BrNO_3P$ $(M+H)^+$ 408.0359, found: 408.0369

Diethyl (2-phenyl-1H-benzo[f]indol-3-yl)phosphonate (4m)



Product **4m** was obtained as white solid (60% yield); **^{1}H NMR** (400 MHz, DMSO-d_6) δ 12.78 (d, J = 3.8 Hz, 1H), 8.58 (d, J = 8.2 Hz, 1H), 8.06 (d, J = 8.8 Hz, 1H), 7.97 (d, J = 8.0 Hz, 1H), 7.82 – 7.76 (m, 2H), 7.66 – 7.45 (m, 6H), 4.07 – 3.78 (m,4H), 1.08 (t, J = 7.1 Hz, 6H); **^{13}C NMR** (100 MHz, DMSO-d_6) δ 144.0 (d, J_{C-P} = 22.9 Hz), 132.3, 131.6 (d, J_{C-P} = 15.0 Hz), 130.5, 130.4, 129.2, 128.8, 128.4, 126.7 (d, J_{C-P} = 13.3 Hz), 126.3, 124.9, 122.10 (d, J_{C-P} = 1.0 Hz), 122.0, 121.7, 121.0, 99.3 (d, J_{C-P} = 213.2 Hz), 61.3, 61.3, 16.5, 16.4; **^{31}P NMR** (162 MHz, DMSO-d_6) δ 16.58; **ESI-MS** (*m/z*) calculated for $C_{22}H_{23}NO_3P$ $(M+H)^+$ 380.1410, found: 380.1419.

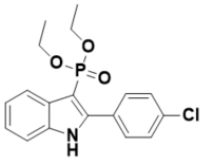
Diethyl (2-(p-tolyl)-1H-indol-3-yl)phosphonate (4n)



Product **4n** was obtained as white solid (57% yield); **^{1}H NMR** (400 MHz, DMSO-d_6) δ 12.09 (d, J = 3.9 Hz, 1H), 7.92 (d, J = 7.9 Hz, 1H), 7.67 (d, J = 8.1 Hz, 2H), 7.46 (d, J = 9.0 Hz, 1H), 7.31 (d, J = 8.0 Hz, 2H), 7.20- 7.14(m, 2H), 3.97 – 3.79 (m, 4H), 2.38 (s, 3H), 1.08 (t, J = 7.0 Hz, 6H); **^{13}C NMR** (100 MHz, DMSO-d_6) δ 145.9 (d, J_{C-P} = 23.4 Hz), 138.9, 136. 7 (d, J_{C-P} = 15.0 Hz), 130.5 (d, J_{C-P} = 13.2

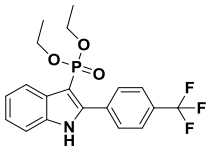
Hz), 129.8, 129.3, 129.0, 122.7, 121.3, 121.2, 112.1, 96.5 (d, J_{C-P} = 214.7 Hz), 61.2, 61.2, 21.4, 16.5, 16.4; **^{31}P NMR** (162 MHz, DMSO-d_6) δ 17.16; **ESI-MS** (*m/z*) calculated for $C_{19}H_{23}NO_3P$ $(M+H)^+$ 344.1410, found: 344.1404

Diethyl (2-(4-chlorophenyl)-1H-indol-3-yl)phosphonate (4o)



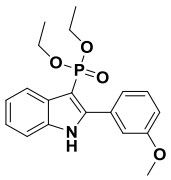
Product **4o** was obtained as white solid (52% yield); **^{1}H NMR** (400 MHz, DMSO-d_6) δ 12.50 – 12.06 (m, 1H), 7.91 (d, *J* = 7.5 Hz, 1H), 7.78 (dd, 2H), 7.59 (d, *J* = 8.6 Hz, 2H), 7.48 (d, *J* = 8.1 Hz, 1H), 7.25 – 7.15 (m, 2H) , 4.09 – 3.72 (m, 4H), 1.10 (t, *J* = 7.1 Hz, 6H); **^{13}C NMR** (100 MHz, DMSO-d_6) δ 144.3 (d, J_{C-P} = 23.2 Hz), 136.8 (d, J_{C-P} = 15.0 Hz), 134.2, 131.8, 131.0, 130.3 (d, J_{C-P} = 12.9 Hz), 129.32 (d, J_{C-P} = 111.5 Hz), 128.5, 123.1, 121.4, 112.3, 97.4 (d, J_{C-P} = 214.1 Hz), 61.3, 61.3, 16.5, 16.4 ; **^{31}P NMR** (162 MHz, DMSO-d_6) δ 16.57; **ESI-MS** (m/z) calculated for $C_{18}H_{20}ClNO_3P$ $(M+H)^+$ 364.0864, found: 364.0871.

Diethyl (2-(4-(trifluoromethyl)phenyl)-1H-indol-3-yl)phosphonate (4p)



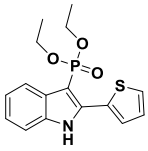
Product **4p** was obtained as white solid (53% yield); **^{1}H NMR** (400 MHz, DMSO-d_6) δ 12.35 (d, *J* = 2.5 Hz, 1H), 7.93 (m, 5H), 7.51 (d, *J* = 8.1 Hz, 1H), 7.26-7.19 (m, 2H), 4.09 – 3.66 (m, 4H), 1.09 (t, *J* = 7.0 Hz, 6H); **^{13}C NMR** (100 MHz, DMSO-d_6) δ 143.9 (d, *J* = 23.1 Hz), 136.9 (d, *J* = 14.9 Hz), 136.2, 130.9, 130.2 (d, *J* = 12.7 Hz), 129.5 (d, *J* = 31.9 Hz), 125.3 (d, *J* = 3.5 Hz), 125.3 (d, *J* = 3.8 Hz), 124.7 (d, J_{C-F} = 272.1 Hz), 123.4 121.5, 112.4, 98.2 (d, J_{C-P}= 213.7 Hz), 61.4, 61.4, 16.4, 16.4; **^{31}P NMR** (162 MHz, DMSO-d_6) δ 16.16; **ESI-MS** (*m/z*) calculated for $C_{19}H_{20}F_3NO_3P$ $(M+H)^+$ 398.1127, found: 398.1125.

Diethyl (2-(3-methoxyphenyl)-1H-indol-3-yl)phosphonate (4q)



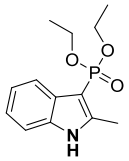
Product **4q** was obtained as white solid (43% yield); **^{1}H NMR** (400 MHz, DMSO-d_6) δ 12.15 (d, J = 3.9 Hz, 1H), 7.93 (d, J = 7.9 Hz, 1H), 7.48-7.33 (m, 4H), 7.24 – 7.18 (m, 1H), 7.18 – 7.12 (m, 1H), 7.04 (ddd, J = 8.2, 2.5, 0.8 Hz, 1H), 3.96 – 3.85 (m, 4H), 3.83 (s, 3H), 1.08 (t, J = 7.0 Hz, 6H); **^{13}C NMR** (100 MHz, DMSO-d_6) δ 159.2, 145.4 (d, $J_{C\text{-}P}$ = 23.2 Hz), 136.6 (d, $J_{C\text{-}P}$ = 15.0 Hz), 133.3, 130.5 (d, $J_{C\text{-}P}$ = 13.2 Hz), 129.6, 122.9, 122.1, 121.4, 121.3, 115.5, 115.2, 112.2, 97.0 (d, $J_{C\text{-}P}$= 214.3 Hz), 61.3, 61.2, 55.6, 16.5, 16.4; **^{31}P NMR** (162 MHz, DMSO-d_6) δ 16.97; **ESI-MS** (*m/z*) calculated for $C_{19}H_{23}NO_4P$ $(M+H)^+$ 360.1359, found: 360.1366.

Diethyl (2-(thiophen-2-yl)-1 H-indol-3-yl)phosphonate (4r)



Product **4r** was obtained as white solid (58% yield); **^{1}H NMR** (400 MHz, DMSO-d_6) δ 12.16 (d, J = 3.6 Hz, 1H), 7.94 (d, J = 8.0 Hz, 1H), 7.77-7.72 (m, 2H), 7.45 (d, J = 8.0 Hz, 1H), 7.25 – 7.18 (m, 2H), 7.17 – 7.11 (m, 1H), 4.02 – 3.84 (m, 4H), 1.13 (t, J = 7.1 Hz, 6H); **^{13}C NMR** (100 MHz, DMSO-d_6) δ 138.5 (d, $J_{C\text{-}P}$ = 22.4 Hz), 136.6 (d, $J_{C\text{-}P}$ = 15.0 Hz), 132.7, 130.66 (dd, J = 73.3, 60.3 Hz), 129.9, 128.8, 128.7 (d, $J_{C\text{-}P}$ = 76.7 Hz), 128.0, 123.2, 121.4, 112.1, 97.1 (d, $J_{C\text{-}P}$ =213.7 Hz), 61.4, 61.3, 16.5, 16.5; **^{31}P NMR** (162 MHz, DMSO-d_6) δ 16.40; **ESI-MS** (*m/z*) calculated for $C_{16}H_{19}NO_3PS$ $(M+H)^+$ 336.0818, found: 336.0818.

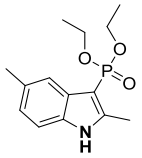
Diethyl(2-methyl-1 H-indol-3-yl)phosphite (4s)



Product **4s** was obtained as white solid (86% yield); **^{1}H NMR** (400 MHz, DMSO-d_6) δ 11.76 (d, J = 2.8 Hz, 1H), 7.64 (d, J = 7.6 Hz, 1H), 7.36 (m, 1H), 7.08 (m, 2H), 3.92 (m, 4H), 2.59 (d, J = 1.7 Hz, 3H), 1.19 (t, J = 7.1 Hz, 6H); **^{13}C NMR** (100 MHz, DMSO-d_6) δ 145.6 (d, $J_{C\text{-}P}$ = 25.2 Hz), 136.1 (d, $J_{C\text{-}P}$ = 14.6 Hz), 129.5 (d, $J_{C\text{-}P}$ = 13.1 Hz), 121.9, 120.8, 120.0, 111.5, 96.1 (d, $J_{C\text{-}P}$ = 215.8 Hz), 61.0,

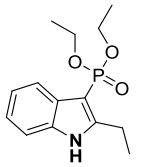
60.9, 16.7, 16.6, 13.4; **^{31}P NMR** (162 MHz, DMSO-d_6) δ 18.20; **ESI-MS** (*m/z*) calculated for $C_{13}H_{19}NO_3P$ $(M+H)^+$ 268.1097, found: 268.1099

2,5-Dimethyl-1H-indol-3-yl diethyl phosphite (4t)



Product **4t** was obtained as white solid (86% yield); **^{1}H NMR** (400 MHz, DMSO-d_6) δ11.64 (d, J = 3.4 Hz, 1H), 7.44 (s, 1H), 7.24 (dd, J = 8.2, 2.2 Hz, 1H), 6.92 (dd, J = 8.2, 1.3 Hz, 1H), 4.04 – 3.76 (m, 4H), 2.56 (d, J = 1.7 Hz, 3H), 2.36 (s, 3H), 1.20 (t, J = 7.1 Hz, 6H); **^{13}C NMR** (100 MHz, DMSO-d_6) δ 145.5 (d, J_{C-P} = 25.3 Hz), 134.4 (d, J_{C-P} = 14.7 Hz), 129.8 (d, J_{C-P} = 13.1 Hz), 129.3, 123.4 , 119.8, 111.2, 95.5 (d, J_{C-P} = 215.6 Hz), 60.9, 60.9, 21.8, 16.7, 16.7, 13.5; **^{31}P NMR** (162 MHz, DMSO-d_6) δ 18.51; **ESI-MS** (*m/z*) calculated for $C_{14}H_{21}NO_3P$ $(M+H)^+$ 282.1254, found: 282.1262.

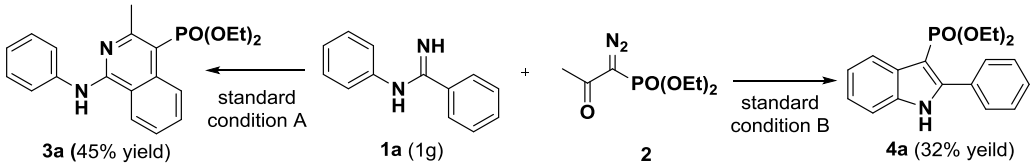
Diethyl (2-ethyl-1H-indol-3-yl) phosphite (4u)



Product **4u** was obtained as white solid (84% yield); **^{1}H NMR** (400 MHz, DMSO-d_6) δ 11.74 (d, J = 3.2 Hz, 1H), 7.64 (d, J = 7.7 Hz, 1H), 7.37 (m, 1H), 7.09 (m, 2H), 4.03 – 3.85 (m, 4H), 3.01 (dd, J = 7.5, 1.1 Hz, 2H), 1.26 (t, J = 7.6 Hz, 3H), 1.19 (t, J = 7.1 Hz, 6H); **^{13}C NMR** (100 MHz, DMSO-d_6) δ 151.4 (d, J_{C-P} = 26.0 Hz), 136.2 (d, J_{C-P} = 14.6 Hz), 129.3 (d, J_{C-P} = 13.1 Hz), 122.0, 120.8, 120.2, 111.7 , 95.2 (d, J_{C-P} = 215.5 Hz), 61.0, 60.9 , 20.6, 16.7, 16.7, 15.0; **^{31}P NMR** (162 MHz, DMSO-d_6) δ 18.13; **ESI-MS** (*m/z*) calculated for $C_{14}H_{21}NO_3P$ $(M+H)^+$ 282.1254, found: 282.1256.

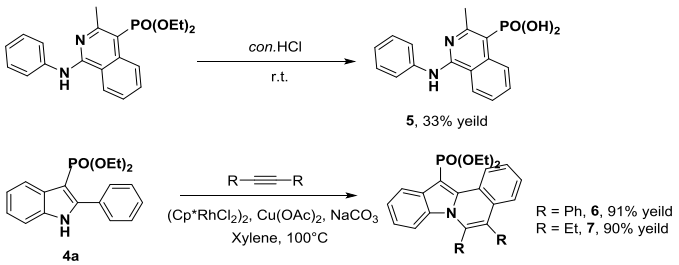
IV. Gram-scale Synthesis, Synthetic Utility and mechanism Studies[3-4]

(1) Gram-scale synthesis of 3a and 4a



N-phenylbenzenecarboximidamide (**1a**, 1g), **2a**(7.7 mmol) $[Cp^*RhCl_2]_2$ (0.41 mmol), $AgNTf_2$ (0.82 mmol), CsOAc (2.5 mol), AcOH (2 mL), were dissolved in DCE (40 mL) in a pressure tube. The mixture was stirred under N_2 atmosphere at 100°C for 14h. After that, the solvent was removed under vacuum and the residue was purified by silica gel chromatography afford product **3a** as white solid (45%). *N*-phenylbenzenecarboximidamide (**1a**, 1 g), **2a** (7.7 mmol) $[Ru(p\text{-cymene})Cl_2]_2$ (0.61 mmol), $AgNTf_2$ (0.82 mmol), CF_3COONa (2.5 mol), were dissolved in MeOH (40 mL) in a pressure tube. The mixture was stirred under N_2 atmosphere at 80°C for 14h. After that, the solvent was removed under vacuum and the residue was purified by silica gel chromatography afford product **4a** as white solid (32%).

(2) Synthetic utility



Diethyl (3-methyl-1-(phenylamino)isoquinolin-4-yl) phosphonate (**3a)** were dissolved in condense HCl solution in a pressure tube. The mixture was stirred at r.t. for 24h. After that, the solvent was removed under vacuum and the residue was purified by silica gel chromatography afford product **5** as yellow solid. (33% yield); **^{1}H NMR** (400 MHz, DMSO-d_6) δ 9.51 (s, 1H), 8.72 (d, J = 8.6 Hz, 1H), 8.55 (d, J = 8.3 Hz, 1H), 7.93 (d, J = 7.8 Hz, 2H), 7.74 (t, J = 7.6 Hz, 1H), 7.59 (t, J = 7.4 Hz, 1H), 7.36 (t, J = 7.9 Hz, 2H), 7.07 (t, J = 7.3 Hz, 1H), 4.12 –3.89 (m, 4H); **^{13}C NMR** (100 MHz, DMSO-d_6) δ 158.7 (d, $J_{C\text{-}P}$ = 14.7 Hz), 154.5 (d, $J_{C\text{-}P}$ = 2.0 Hz), 140.7, 138.5 (d, $J_{C\text{-}P}$ = 12.8 Hz), 131.1, 128.8, 126.4 (d, $J_{C\text{-}P}$ = 2.5 Hz), 126.0, 123.8, 123.3, 122.0, 116.7 (d, $J_{C\text{-}P}$ = 10.2 Hz), 105.1 (d, $J_{C\text{-}P}$ = 188.1 Hz), 26.4; **^{31}P NMR** (162MHz, DMSO-d_6) δ 20.41; **ESI-MS** (*m/z*) calculated for $C_{16}H_{15}N_2O_3P$ $(M+H)^+$ 314.0820, found: 314.0818.

Diethyl (2-phenyl-1H-indol-3-yl)phosphonate (**4a**) (0.5 mmol) was treated with diphenylacetylene (0.5 mmol) in the presence of $[Cp^*RhCl_2]_2$ (0.01 mmol), $Cu(OAc)_2 \cdot H_2O$ (0.05 mmol), and AgOAc (0.5 mmol) Na_2CO_3 (1 mmol) in o-xylene(3 mL) at 100°C under N_2 for 6h. After that, the solvent was removed under reduced pressure and the residue was purified by silica gel chromatography afford **6** as

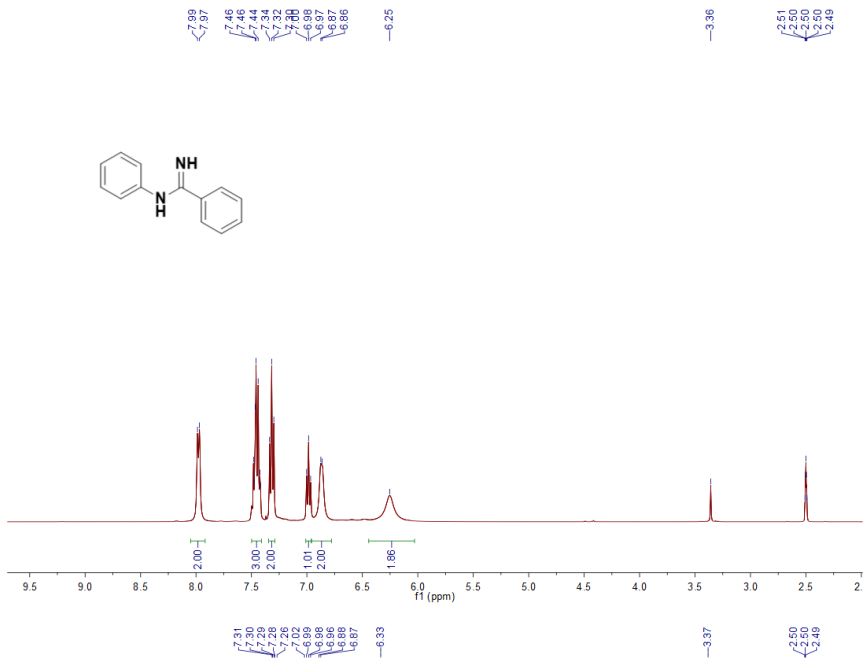
white solid. **^{1}H NMR** (400 MHz, DMSO-d_6) δ 9.44 (d, J = 8.2 Hz, 1H), 8.52 (d, J = 8.2 Hz, 1H), 7.68 (t, J = 7.6 Hz, 1H), 7.59 (t, J = 7.4 Hz, 1H), 7.42 (dd, J = 11.2, 5.9 Hz, 5H), 7.33 – 7.21 (m, 6H), 7.12 (d, J = 7.9 Hz, 1H), 6.84 (t, J = 7.8 Hz, 1H), 5.91 (d, J = 8.7 Hz, 1H), 4.25 – 3.93 (m, 4H), 1.25 (t, J = 7.0 Hz, 6H); **^{13}C NMR** (100 MHz, DMSO-d_6) δ 140.2, 139.9, 136.4, 136.1, 135.2, 132.9 (d, $J_{C\text{-}P}$ = 13.6 Hz), 132.1 (d, $J_{C\text{-}P}$ = 11.9 Hz), 131.9, 131.8 , 131.2, 129.8, 129.7, 129.2, 128.5, 127.7, 127.4, 126.1, 124.4, 123.9, 123.4, 122.1, 121.7, 115.0, 95.2 (d, $J_{C\text{-}P}$ = 238.6 Hz), 61.9, 61.8, 16.7, 16.6; **^{31}P NMR** (162 MHz, DMSO-d_6) δ 18.51; **ESI-MS** (*m/z*) calculated for $C_{32}H_{28}NO_3P$ $(M+H)^+$ 505.5538, found: 505.5537.

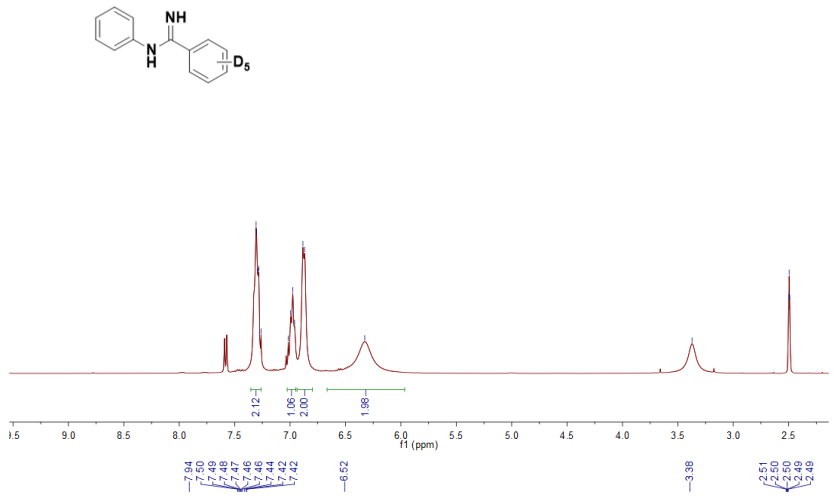
Diethyl (2-phenyl-1H-indol-3-yl)phosphonate (**4a**) (0.5 mmol) was treated with hex-3-yne (0.5 mmol) in the presence of $[Cp^*RhCl_2]_2$ (0.01 mmol), $Cu(OAc)_2 \cdot H_2O$ (0.05 mmol), and AgOAc (0.5 mmol) Na_2CO_3 (1 mmol) in o-xylene(3 mL) at 100 ℃ under N_2 for 6h. After that, the solvent was removed under reduced pressure and the residue was purified by silica gel chromatography afford **7** as white solid. **^{1}H NMR** (400 MHz, DMSO-d_6) δ 9.23 (dd, J = 8.3, 0.9 Hz, 1H), 8.58 (d, J = 7.7 Hz, 1H), 8.23 (d, J = 8.2 Hz, 1H), 7.97 (d, J = 7.9 Hz, 1H), 7.76 – 7.69 (m, 1H), 7.64 – 7.57 (m, 1H), 7.47 – 7.34 (m, 2H), 4.15 – 3.92 (m, 4H), 3.51 (q, J = 7.3 Hz, 2H), 3.04 (q, J = 7.4 Hz, 2H), 1.48 (t, J = 7.4 Hz, 3H), 1.26 (dd, J = 12.2, 4.8 Hz, 3H), 1.18 (t, J = 7.1 Hz, 6H); **^{13}C NMR** (101 MHz, DMSO-d_6) δ 140.52 (d, $J_{C\text{-}P}$ = 23.9 Hz), 137.85, 132.93, 132.21 (dd, $J_{C\text{-}P}$ = 12.9, 4.6 Hz), 130.19 (d, $J_{C\text{-}P}$ = 3.7 Hz), 129.96, 129.75, 129.00, 126.19 (d, $J_{C\text{-}P}$ = 17.5 Hz), 123.69, 123.46 (d, $J_{C\text{-}P}$ = 16.5 Hz), 122.57, 122.17, 120.77, 115.99, 92.46 (d, $J_{C\text{-}P}$ = 214.4 Hz), 61.73, 61.68, 22.90, 20.46, 16.55, 16.49, 15.11, 13.76 ; **^{31}P NMR** (162 MHz, DMSO-d_6) δ 17.82 (s); **ESI-MS** (*m/z*) calcd for $C_{24}H_{29}NO_3P$ (M+H)+ 410.1880, found: 410.1876.

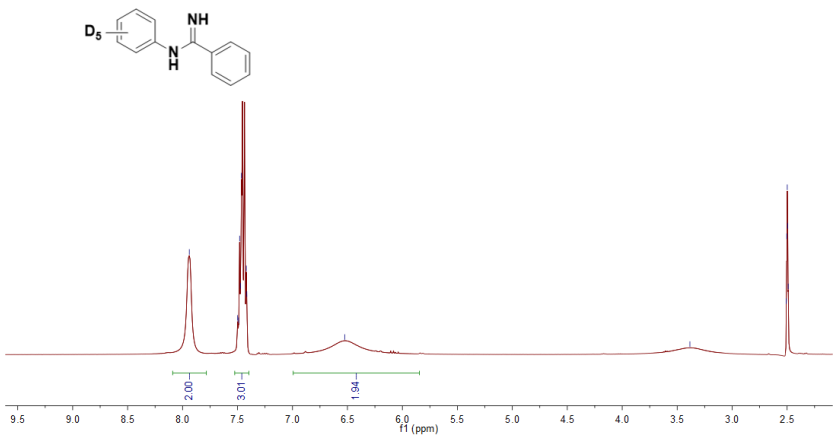
(3) Mechanism studies

a) Synthesis of deuterated substrates:

N-phenylbenzimidamide (**1a**), *N*-phenylbenzimidamide-2,3,4,5,6-d_5 (D_5-**1a**) and *N*-(phenyl-d_5)benzimidamide (D_5-**1a'**) and was synthesized according to the reported procedure. [1b] The structure of **1a**, **D_5-1a** and **D_5-1a'** was characterized by ^{1}H NMR analysis (see below).


7.99
7.97
7.46
7.46
7.44
7.34
7.32
7.00
6.98
6.97
6.87
6.86
6.25
3.36
2.51
2.50
2.50
2.50
2.49
NH
N
H
2.00
3.00
2.00
1.01
2.00
1.86
f1 (ppm)
7.31
7.30
7.29
7.28
7.26
7.02
6.98
6.98
6.96
6.88
6.87
6.33
3.37
2.50
2.50
2.49


NH
N
H
D5
2.12
1.06
2.00
1.98
f1 (ppm)
7.94
7.50
7.49
7.48
7.47
7.46
7.46
7.44
7.42
7.42
6.52
3.38
2.51
2.50
2.50
2.49
2.49

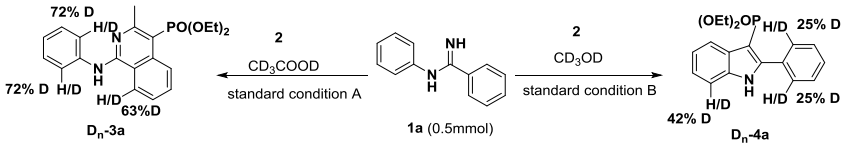

D5
NH
N
H
2.00
3.01
1.94
f1 (ppm)

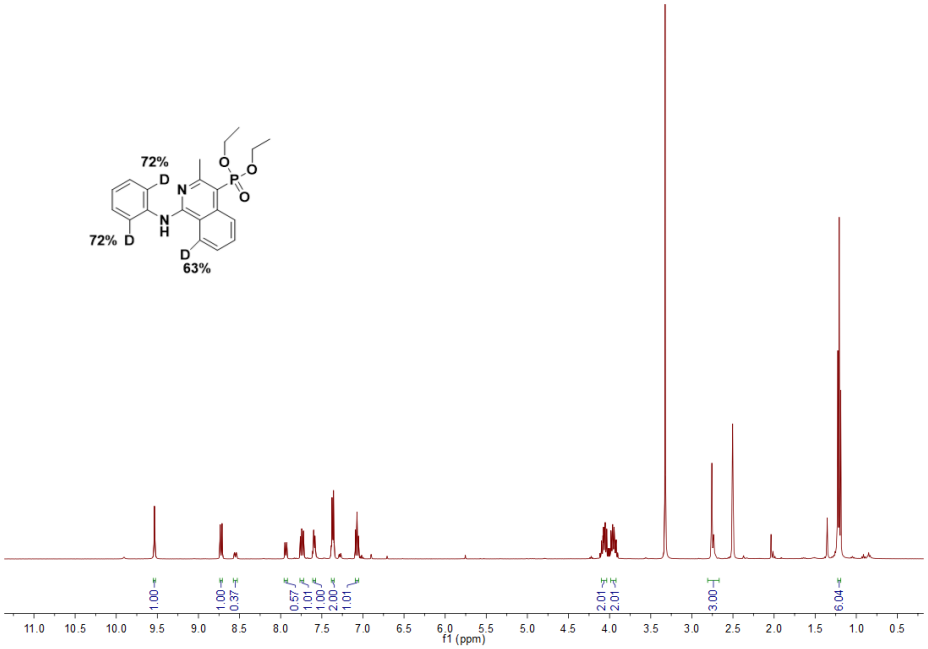
N-phenylbenzimidamide (**1a**) **^{1}H NMR** (400 MHz, DMSO-d_6) δ 7.98 (d, *J* = 6.9 Hz, 2H), 7.53 – 7.38 (m, 3H), 7.32 (t, *J* = 7.7 Hz, 2H), 6.98 (t, *J* = 7.3 Hz, 1H), 6.87 (d, *J* = 4.9 Hz, 2H), 6.25 (s, 2H).

N-phenylbenzimidamide-2,3,4,5,6-d_5 (D_5-**1a**) **^{1}H NMR** (400 MHz, DMSO-d_6) δ 7.41 – 7.14 (m, 2H), 6.99 (m, 1H), 6.88 (d, *J* = 6.2 Hz, 2H), 6.33 (s, 2H).

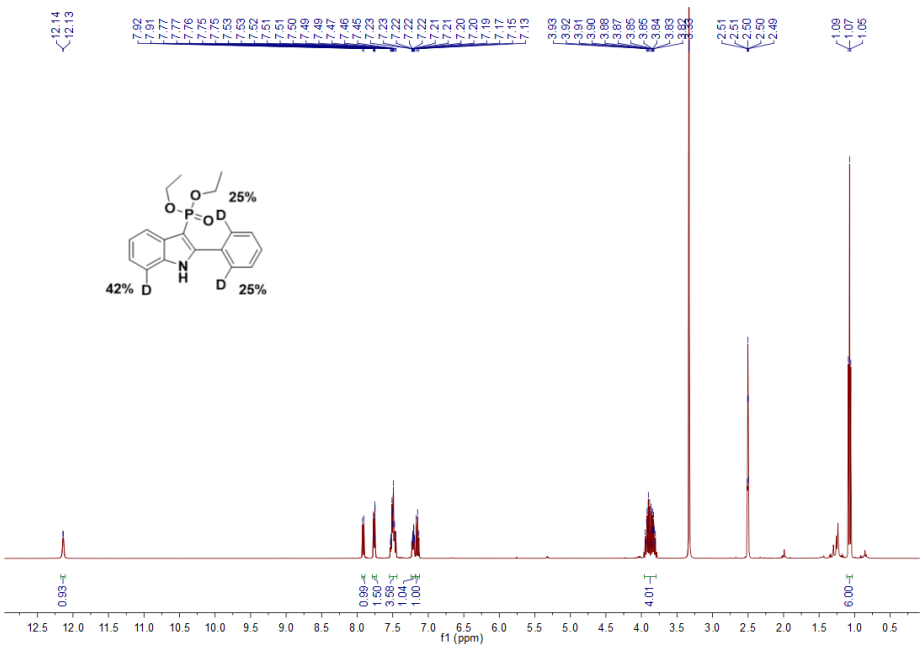
N-(phenyl-d_5)benzimidamide (D_5-**1a'**) **^{1}H NMR** (400 MHz, DMSO-d_6) δ 7.94 (s, 2H), 7.62 – 7.03 (m, 3H), 6.52 (s, 2H).

b) H/D exchange experiments (with substrate 2)



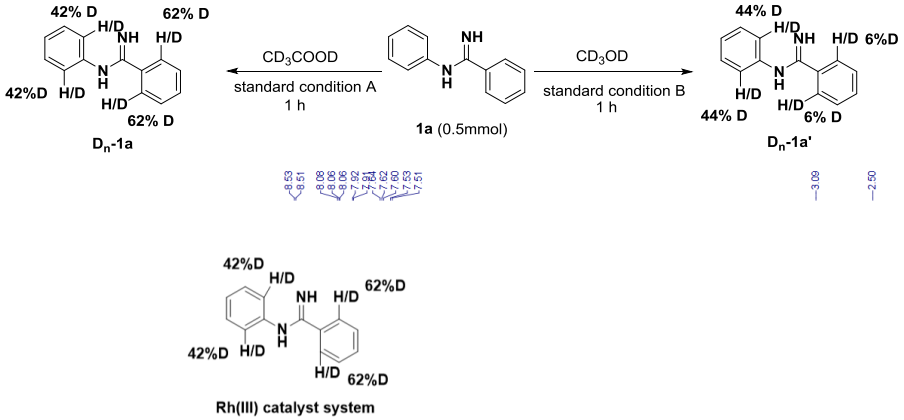


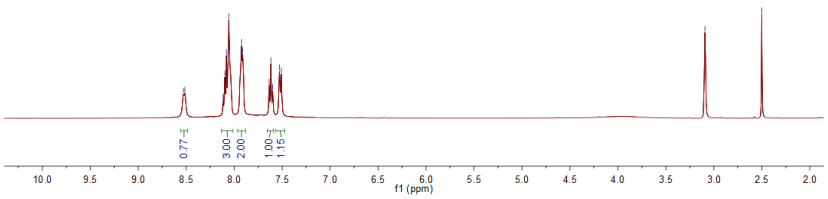
A mixture of **1a** (0.5 mmol), **2** (0.75 mmol), and CD_3OOD (6 mL) were treated under standard conditions A for 14h. After that, the solvent was removed under reduced pressure and the residue was purified by silica gel chromatography afford white solid, which was characterized by ^{1}HNMR spectroscopy. ^{1}HNMR analysis of the coupled product **3a** revealed 63% deuteration at the ortho' position (8-position of the isoquinoline).



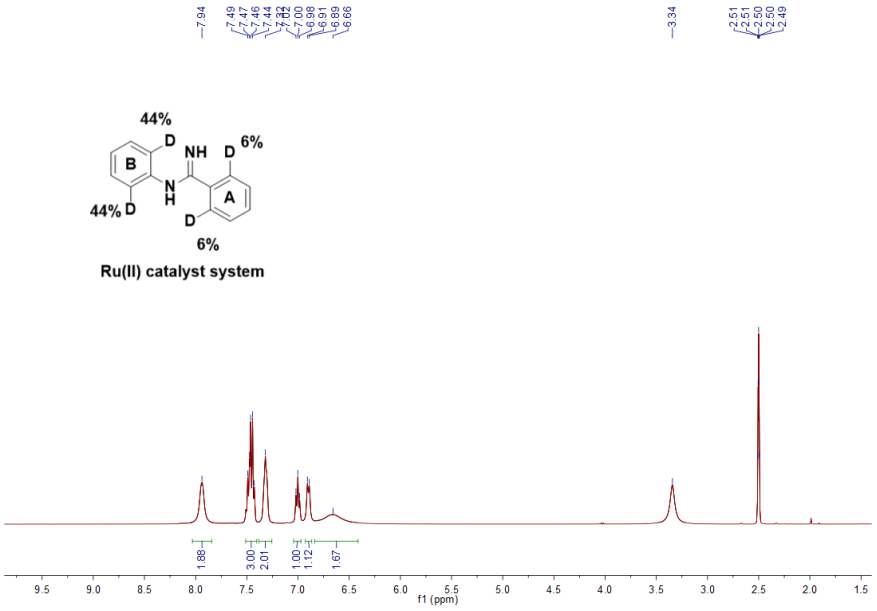
A mixture of **1a** (0.5 mmol), **2** (0.75 mmol), and MeOD (6 ml) were treated under standard conditions B for 14 h. After that, the solvent was removed under reduced pressure and the residue was purified by silica gel chromatography afford white solid, which was characterized by ^{1}HNMR spectroscopy. ^{1}HNMR analysis of the coupled product **4a** revealed 42% deuteration at the ortho' position (7-position of the indole).

c) H/D exchange experiments (without substrate 2)



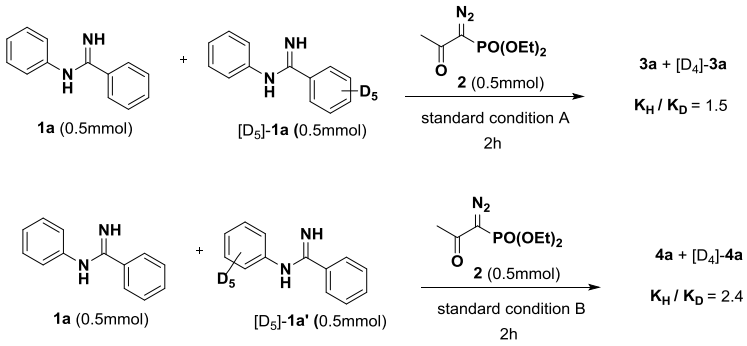


A mixture of **1a** (0.5 mmol), and CD_3OOD (2 mL) under standard conditions A for 1h. After that, the solvent was removed under reduced pressure and the residue was purified by silica gel chromatography afford white solid, which was characterized by ^{1}HNMR spectroscopy. ^{1}HNMR analysis revealed that of the coupled product **1a** revealed 62% deuteration at the ortho' position of C-phenyl ring.



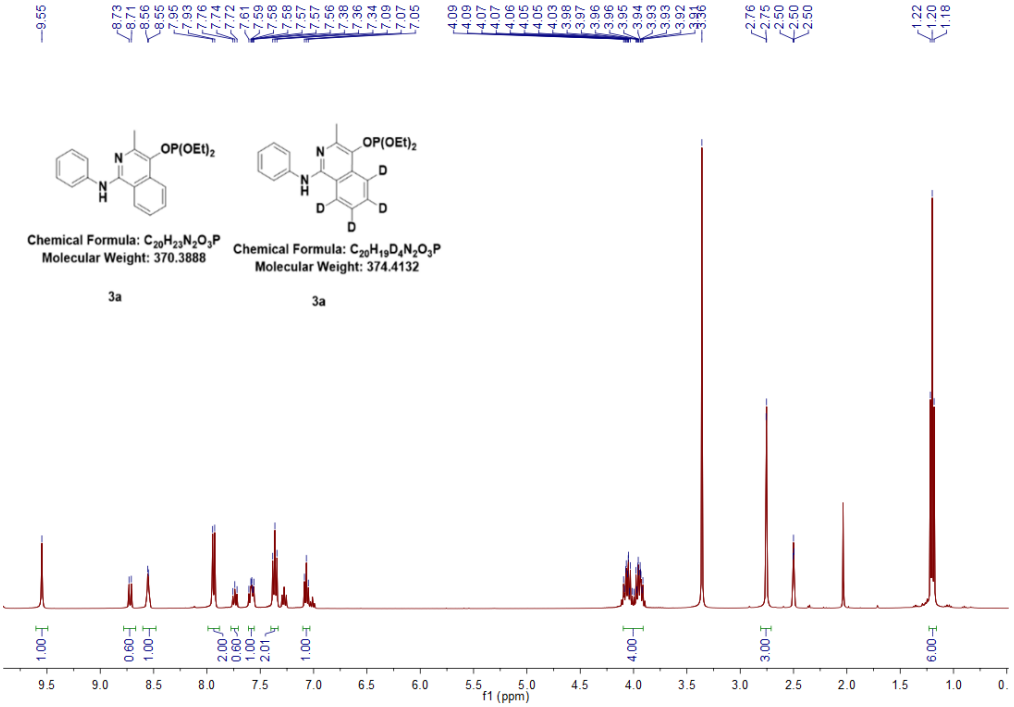
A mixture of **1a** (0.5 mmol), and MeOD (6 mL) under standard conditions B for 1h. After that, the solvent was removed under reduced pressure and the residue was purified by silica gel chromatography afford white solid, which was characterized by 1HNMR spectroscopy. ^{1}HNMR analysis revealed that of the coupled product **1a** revealed 44% deuteration at the ortho' position of *N*-phenyl ring.

d) KIE experiment

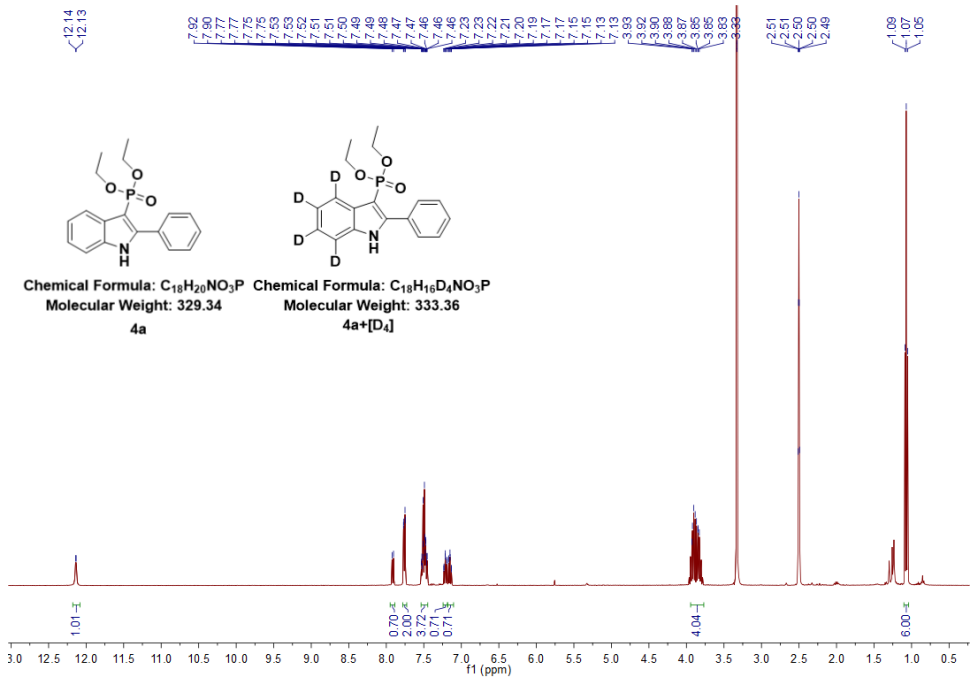


A pressure tube was charged with $[Cp^*RhCl_2]_2$ (8 mol %), $AgNTf_2$ (16 mol%), CsOAc (0.4 mmol), AcOH (0.4 mmol), **1a** (0.5 mmol), $[D_5]$-**1a** (0.5 mmol), **2a** (0.5 mmol) and DCE (6 mL). The reaction mixture was under N_2 atmosphere stirred at 100℃ for 2h. After that, the solvent was removed under

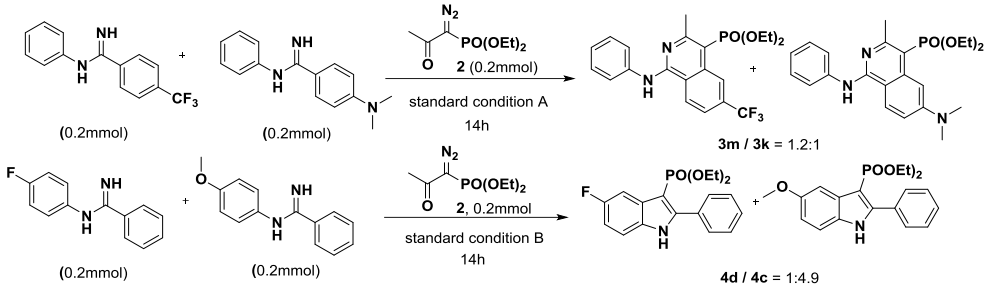
reduced pressure and the residue was purified by silica gel chromatography to afford the product **3a** and [D_4]-**3a**. The KIE value was determined to be K_H/K_D = 1.5 on the basis of ^{1}HNMR analysis.



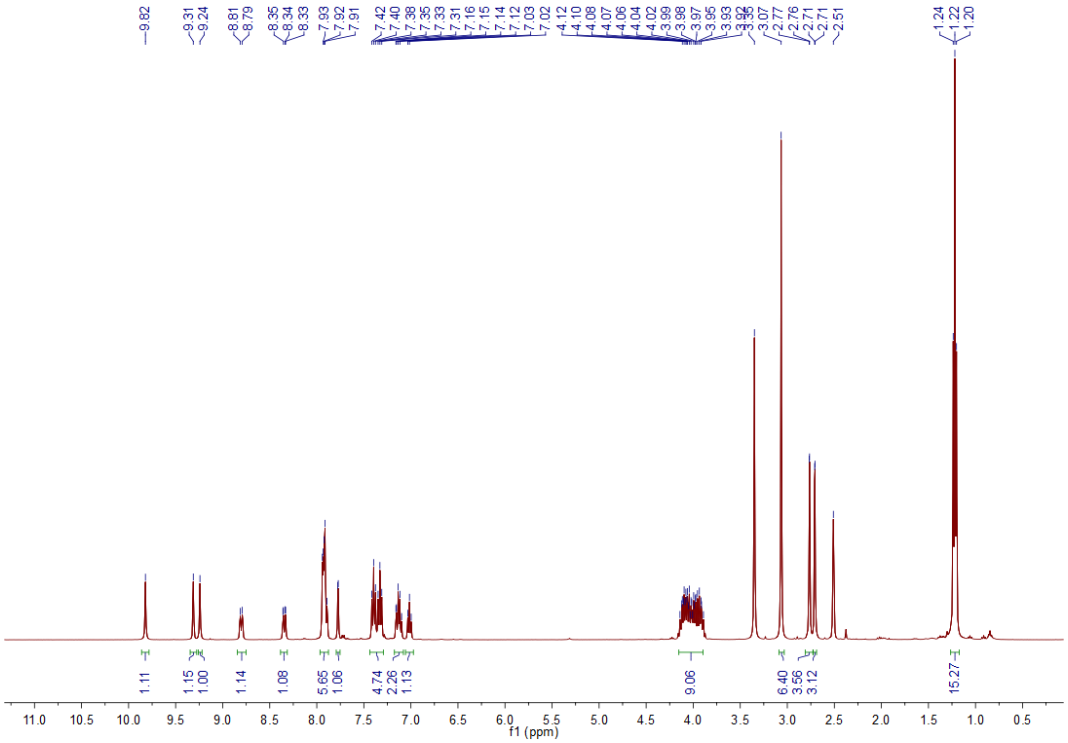
A pressure tube was charged with [Ru(*p*-cymene)Cl_2]$_2$ (12 mol %), $AgNTf_2$ (16 mol%), CF_3COONa (0.4 mmol), **1** (0.5 mmol), [D_5]-**1a'** (0.5 mmol), **2a** (0.5 mmol) and MeOH (6mL). The reaction mixture was under N_2 atmosphere stirred at 80℃ for 2h. After that, the solvent was removed under reduced pressure and the residue was purified by silica gel chromatography to afford the product **4a** and [D_4]-**4a**. The KIE value was determined to be K_H/K_D = 2.4 on the basis of ^{1}HNMR analysis.



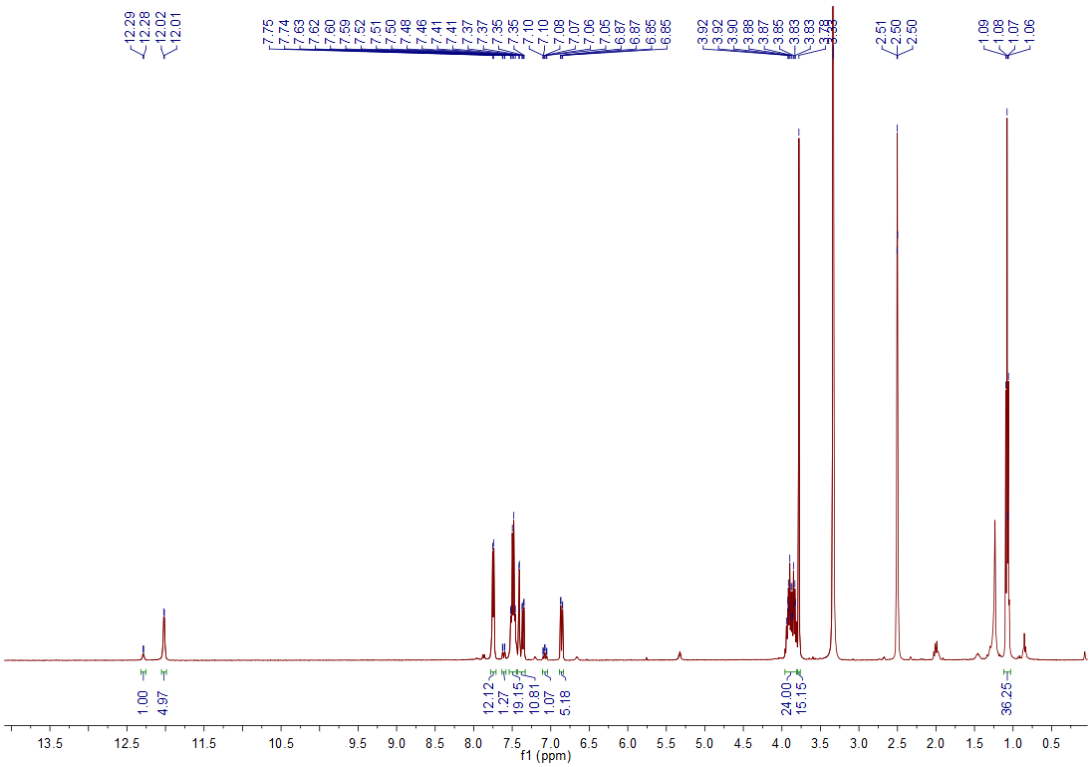
(e) Competition experiment



A pressure tube was charged with **1a** (each 0.2 mmol), **2** (0.3 mmol), $[RhCp^*Cl_2]_2$ (8 mol %), $AgNTf_2$ (20 mol %), CsOAc (0.4 mmol), AcOH (0.4 mmol), DCE (2 mL), 100 °C, 14 h. The reaction mixture was under N_2 atmosphere stirred at 80□ for 14h. After that, the solvent was removed under vacuum and the residue was purified by silica gel chromatography to afford product **3m** and **3k** as white solid. The ratio of **3m**: **3k** = 1.2:1 was determined on the basis of ^1H NMR analysis.



A pressure tube was charged with **1a** (each 0.2 mmol), **2a** (0.2 mmol), $[Ru(p\text{-cymene})Cl_2]_2$ (12 mol %), $AgNTf_2$ (20 mmol%), CF_3COONa (0.4 mmol) and MeOH (6 mL). The reaction mixture was under N_2 atmosphere stirred at 80□ for 14h. After that, the solvent was removed under vacuum and the residue was purified by silica gel chromatography to afford product **4d** and **4c** as white solid. The ratio of **4d**: **4c**= 1:4.9 was determined on the basis of ^1H NMR analysis



V. X-ray Crystallographic Data

(a) The Single Crystal Stucture of 3a

X-ray Single Crystal Stucture Analysis of **3a**:

X-ray crystallographic data of **3a** were solutions at Temperature=173K, formula $C_{20}H_{23}N_2O_3P$, Formula weight=370.37, Crystal system: triclinic, Space group: P-1, a=9.115(3)Å, b=9.448(2)Å, c=11.944(3)Å, α=101.46(2)°, β=91.031(6)°, γ=106.620(7)°, Volume= 962.9(5)Å^3, Z=2.

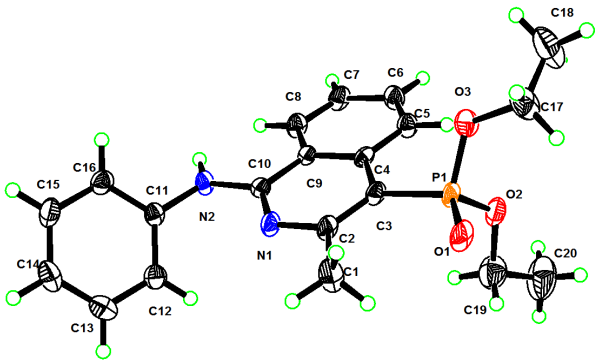


Figure 1: The crystal structure of **3a** by X-ray analysis.

These data can be obtained free of charge from the Cambridge Crystallographic Data Centre *via www.ccdc.cam.ac.uk/data_request/cif*, the CCDC number is 1873308.

(b) The Single Crystal Stucture of 4a

X-ray Single Crystal Stucture Analysis of **4a**:

X-ray crystallographic data of **4a** were solutions at Temperature=173K, formula $C_{18}H_{20}NO_3P$, Formula weight=329.32, Crystal system: monoclinic, Space group: Pc, a=7.6453(19)Å, b=11.642(3)Å, c=9.808(3) Å, α=90°, β=102.969(8)°, γ=90°, Volume= 850.7(4)Å^3, Z=2.

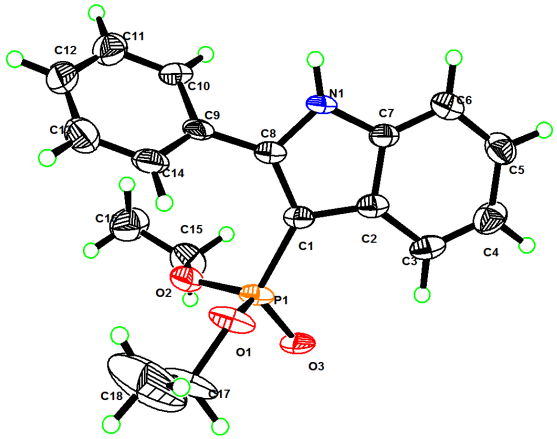


Figure 2: The crystal structure of **4a** by X-ray analysis.

These data can be obtained free of charge from the Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif, the CCDC number is 1873345.

REFERENCE

1. (a) Cortes-Salva, M.; Garvin, C.; Antilla, J. C. *J. Org. Chem.* **2011**, 76, 1456; (b) Velavan, A.; Sumathi, S.; Balasubramanian, K. K. *Eur. J. Org Chem.* **2014**, 2014, 5806.
2. Meffre, P.; Hermann, S.; Durand, P.; Reginato, G.; Riu, A., Practical one-step synthesis of ethynylglycine synthon from Garner's aldehyde. *Tetrahedron* **2002,** *58* (25), 5159-5162.
3. Morimoto, K.; Hirano, K.; Satoh, T.; Miura, M., Rhodium-catalyzed oxidative coupling/cyclization of 2-phenylindoles with alkynes via C-H and N-H bond cleavages with air as the oxidant. *Org. Lett.* **2010,** *12* (9), 2068-71.
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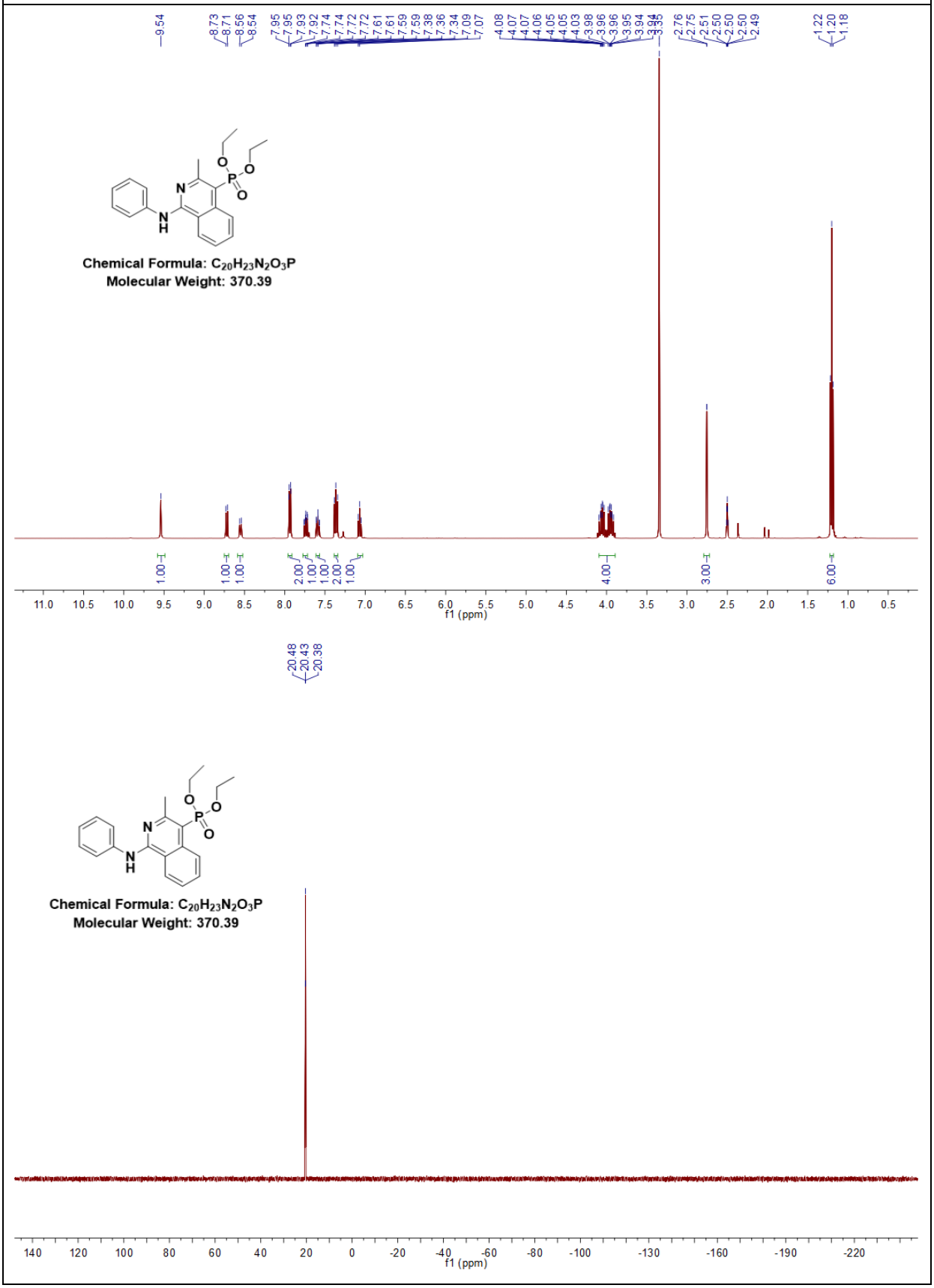
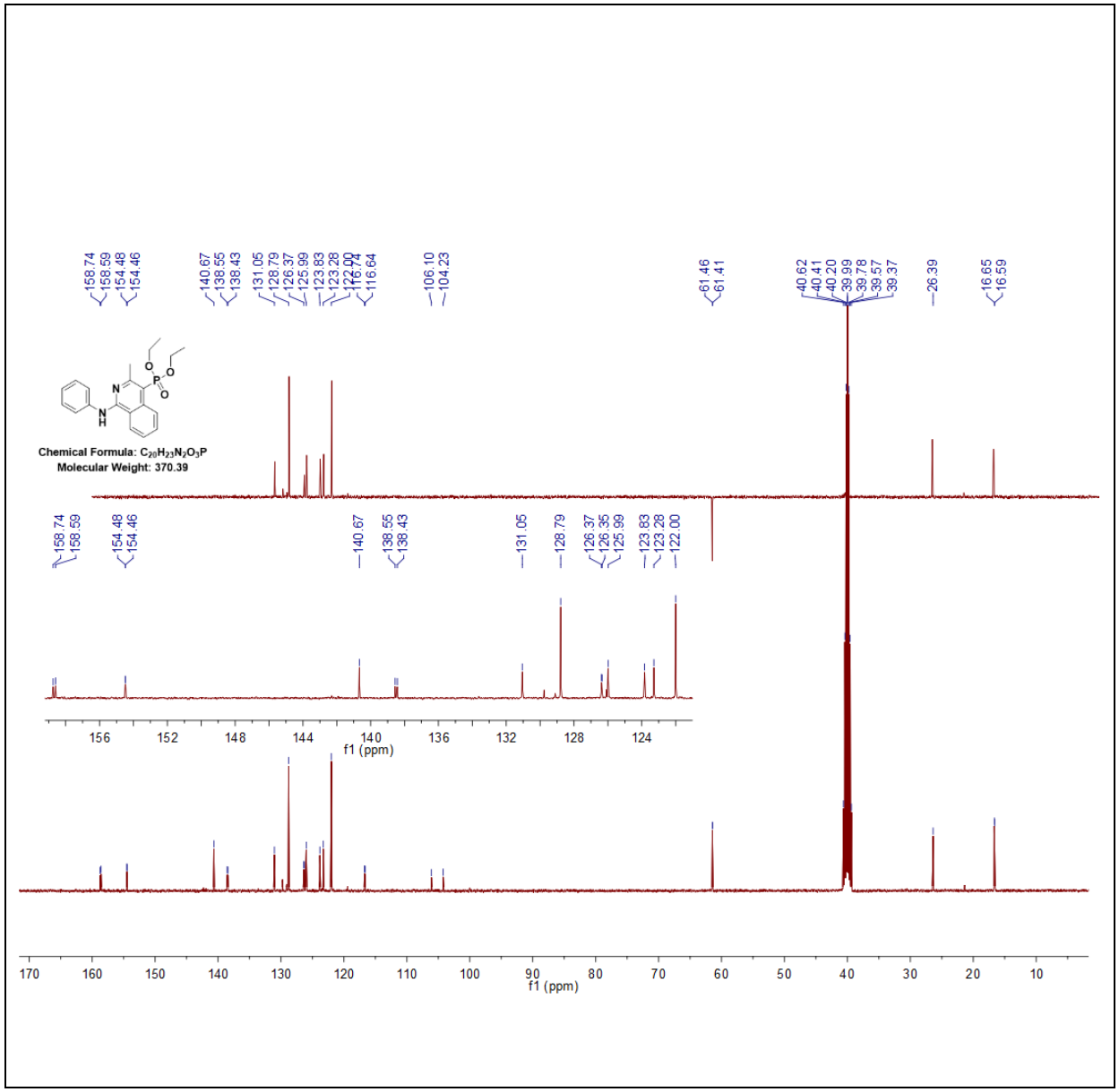
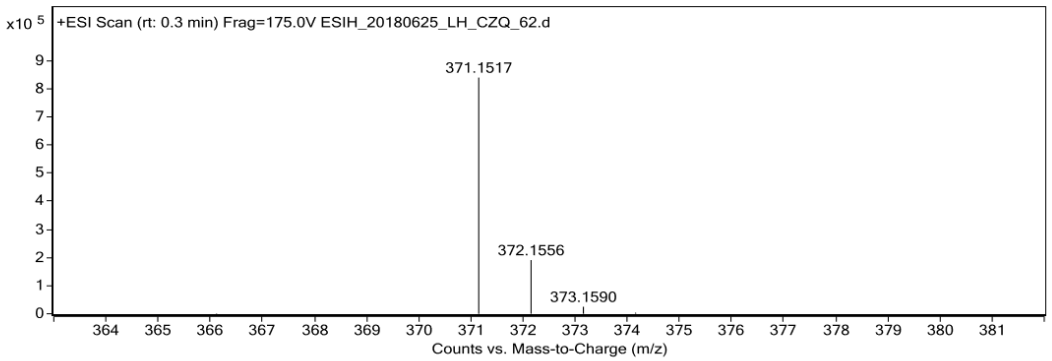
VI.·^{1}H, ^{31}P and ^{13}C NMR Spectra

Diethyl (3-methyl-1-(phenylamino) isoquinolin-4-yl) phosphonate (3a)





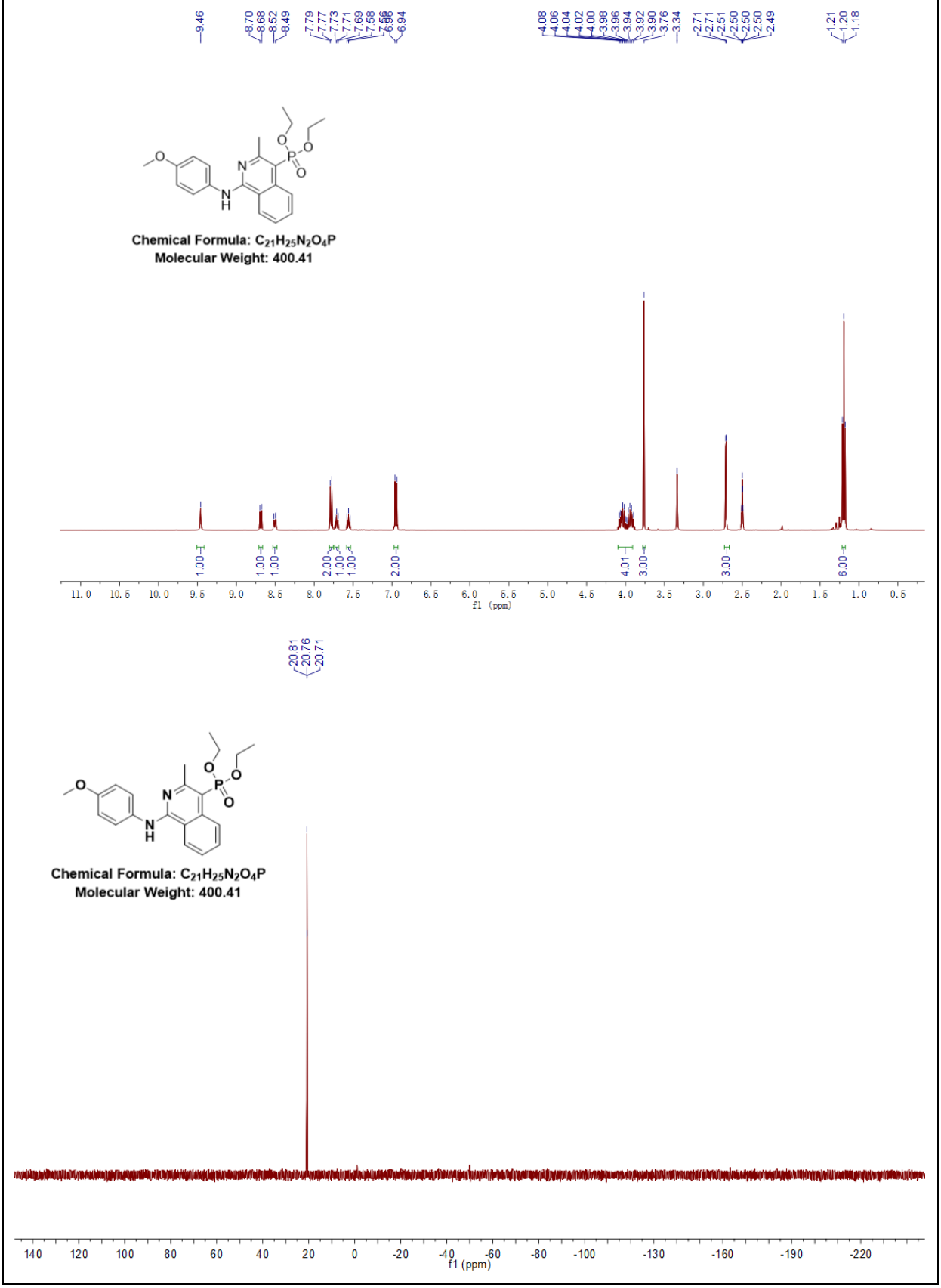
Fragmentor Voltage	Collision Energy	Ionization Mode
175	0	ESI

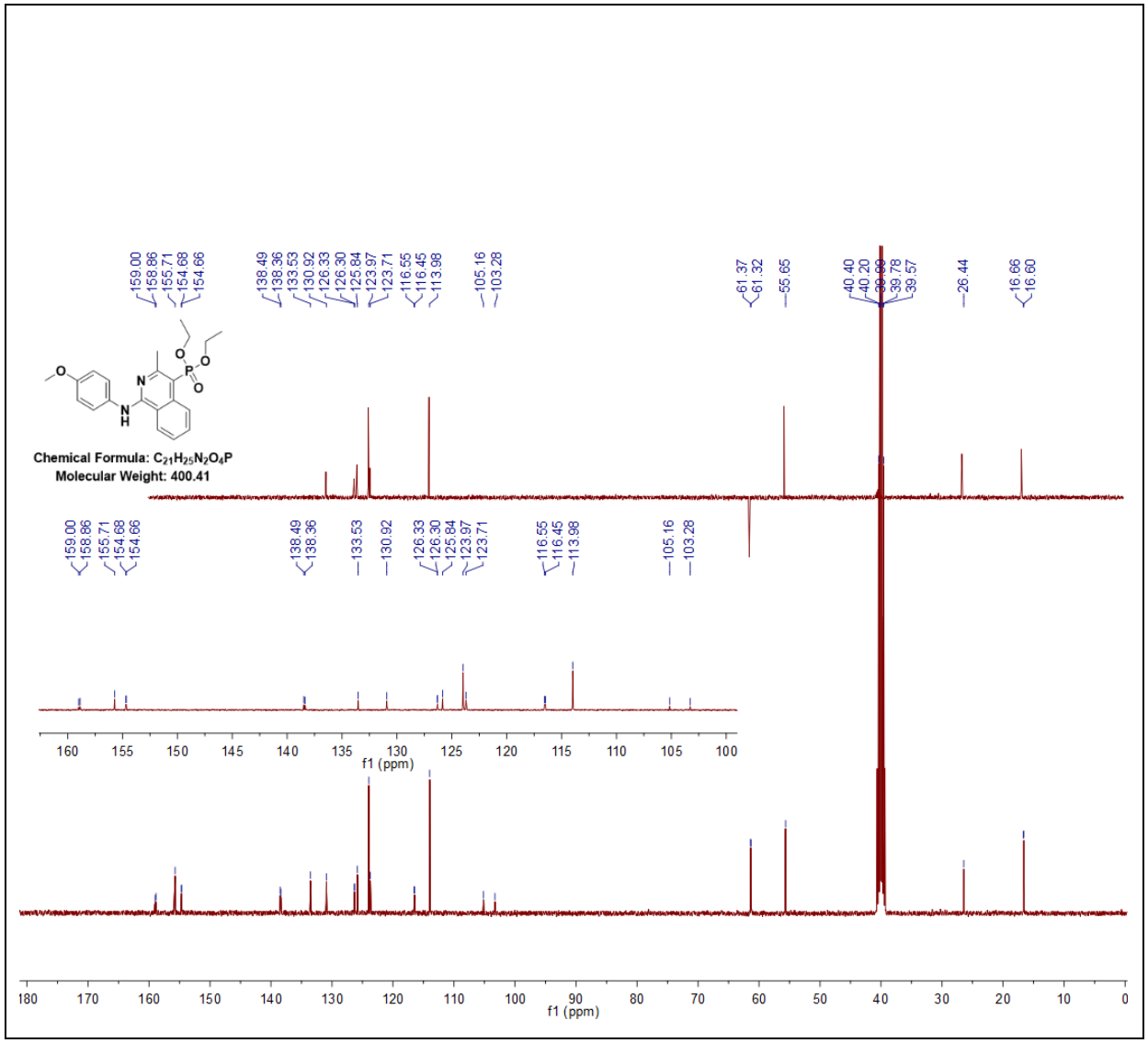


Formula Calculator Results

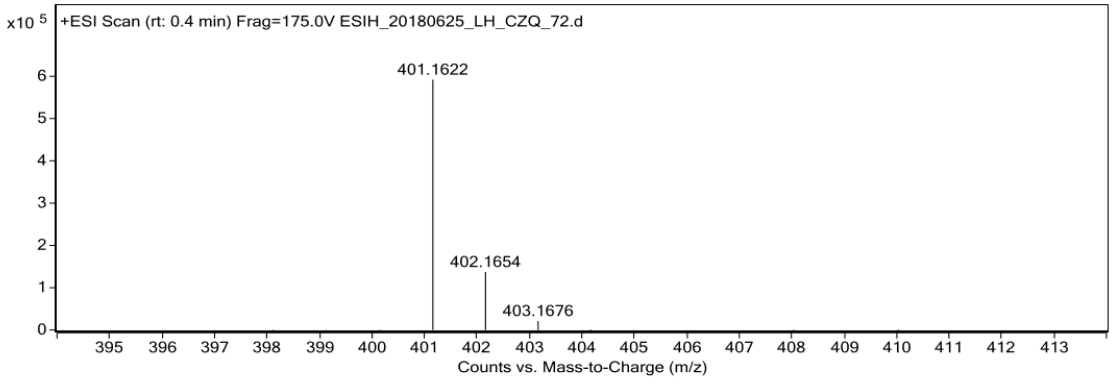
m/z	Calc m/z	Diff (mDa)	Diff (ppm)	Ion Formula	Ion
371.1517	371.1519	0.19	0.51	C20 H24 N2 O3 P	(M+H)+

Diethyl (1-((4-methoxyphenyl)amino)-3-methylisoquinolin-4-yl)phosphonate (3b)





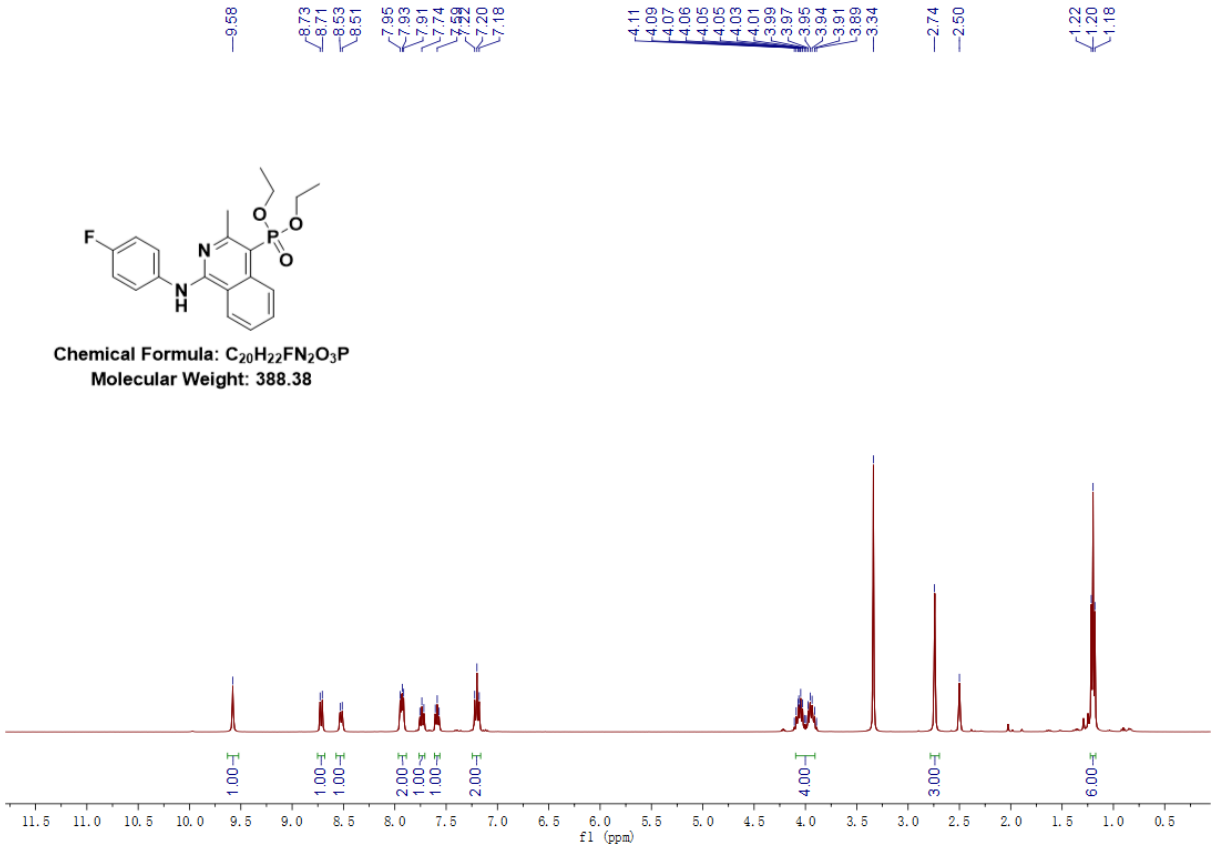
Fragmentor Voltage	Collision Energy	Ionization Mode
175	0	ESI

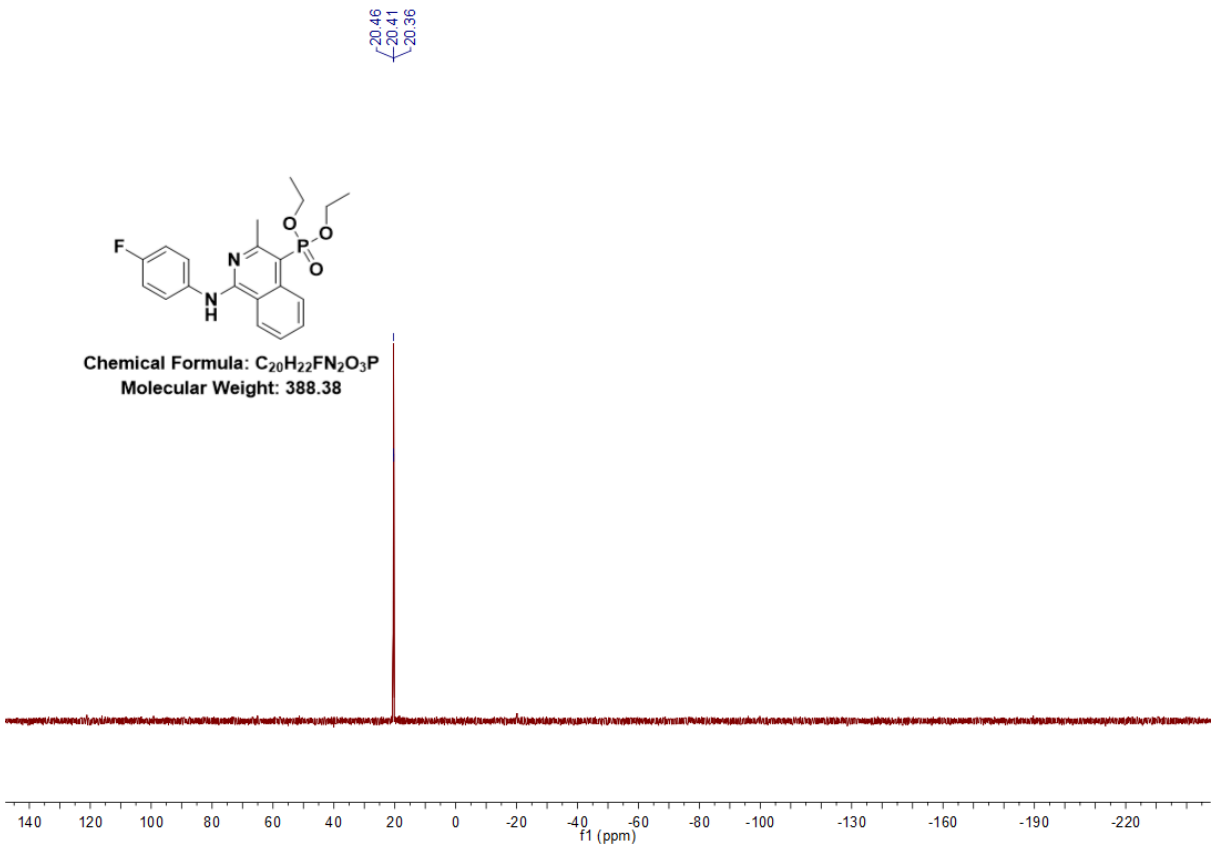


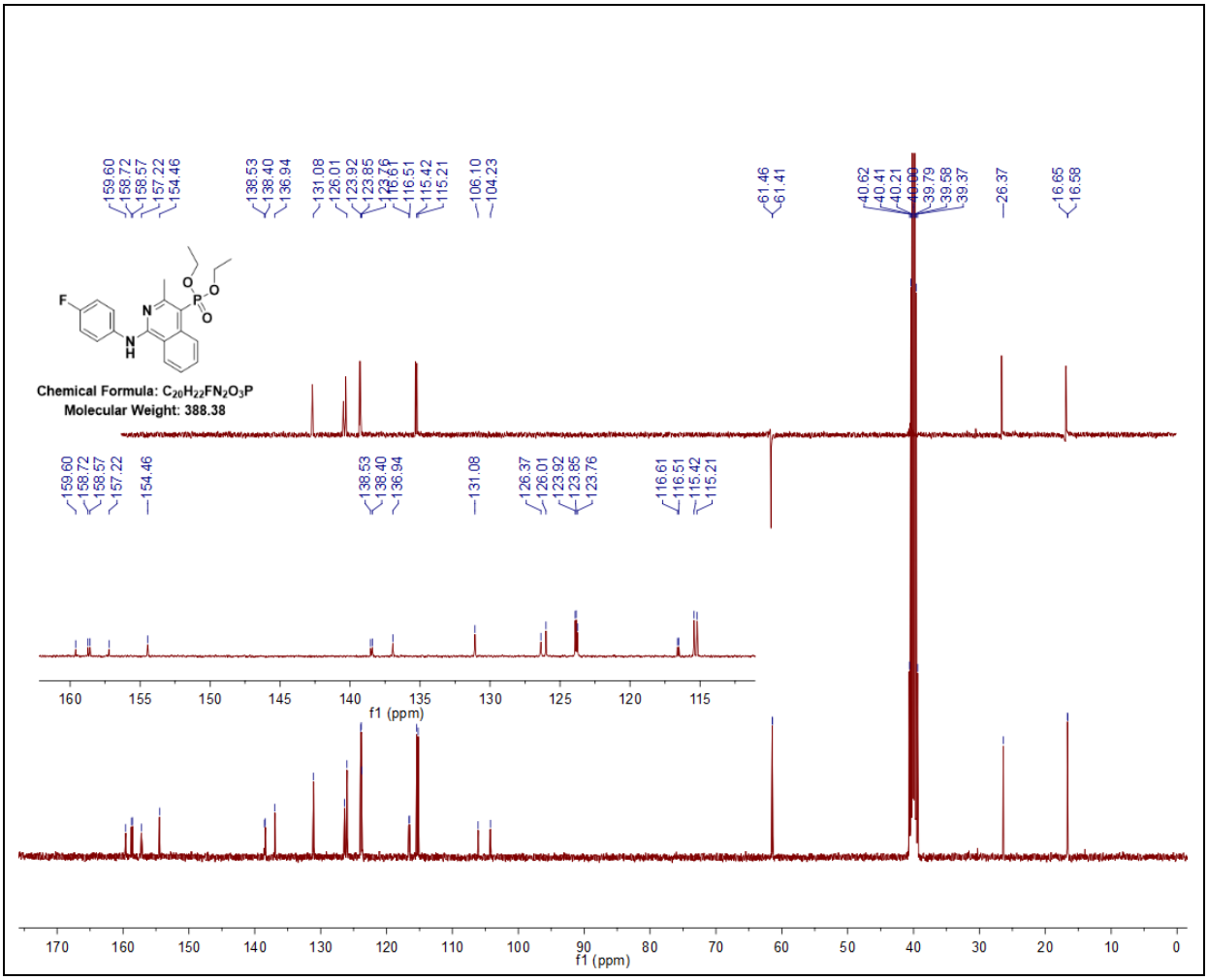
Formula Calculator Results

m/z	Calc m/z	Diff (mDa)	Diff (ppm)	Ion Formula	Ion
401.1622	401.1625	0.25	0.61	C21 H26 N2 O4 P	(M+H)+

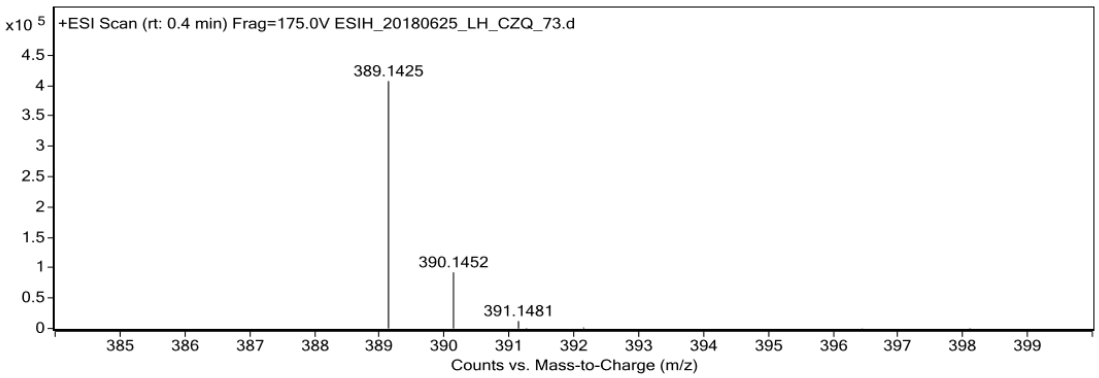
Diethyl (1-((4-fluorophenyl)amino)-3-methylisoquinolin-4-yl)phosphonate (3c)







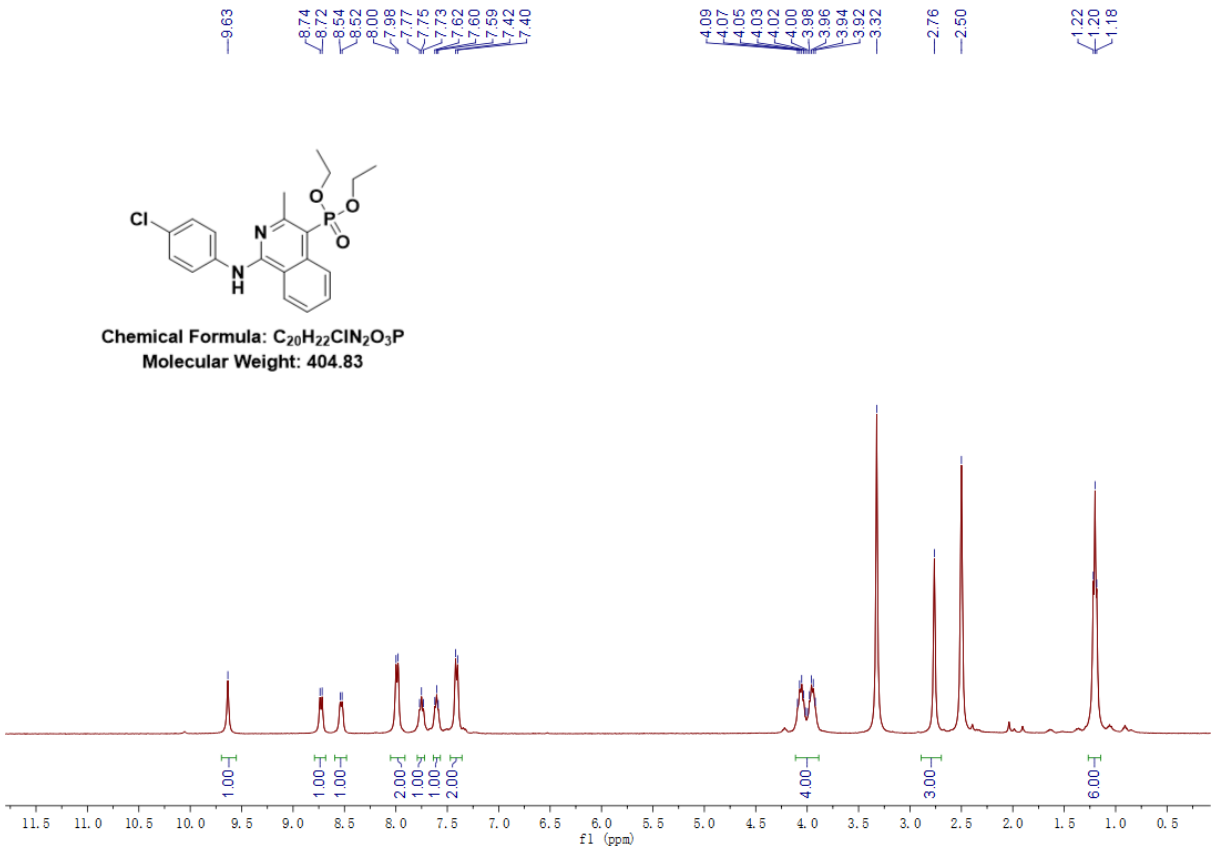
Fragmentor Voltage	Collision Energy	Ionization Mode
175	0	ESI



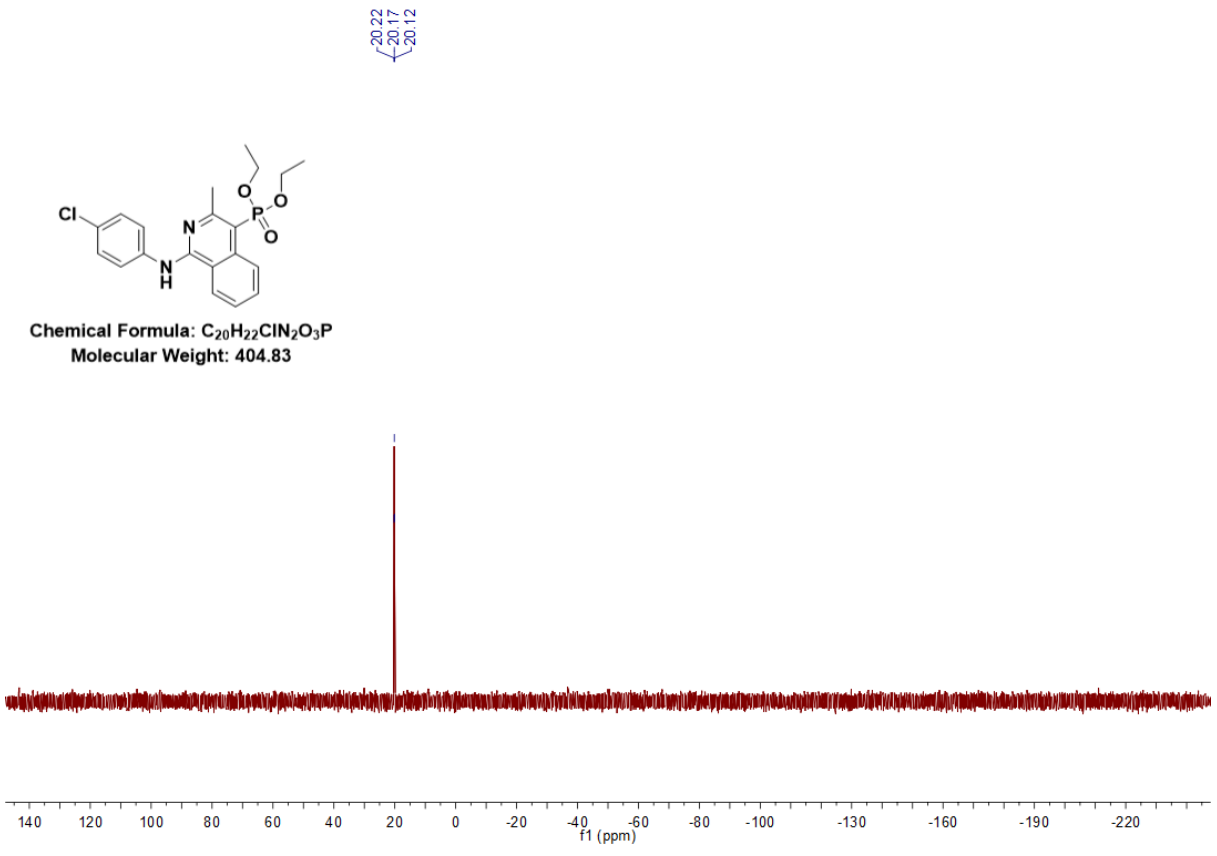
Formula Calculator Results

m/z	Calc m/z	Diff (mDa)	Diff (ppm)	Ion Formula	Ion
389.1425	389.1425	0.01	0.03	C20 H23 F N2 O3 P	(M+H)+

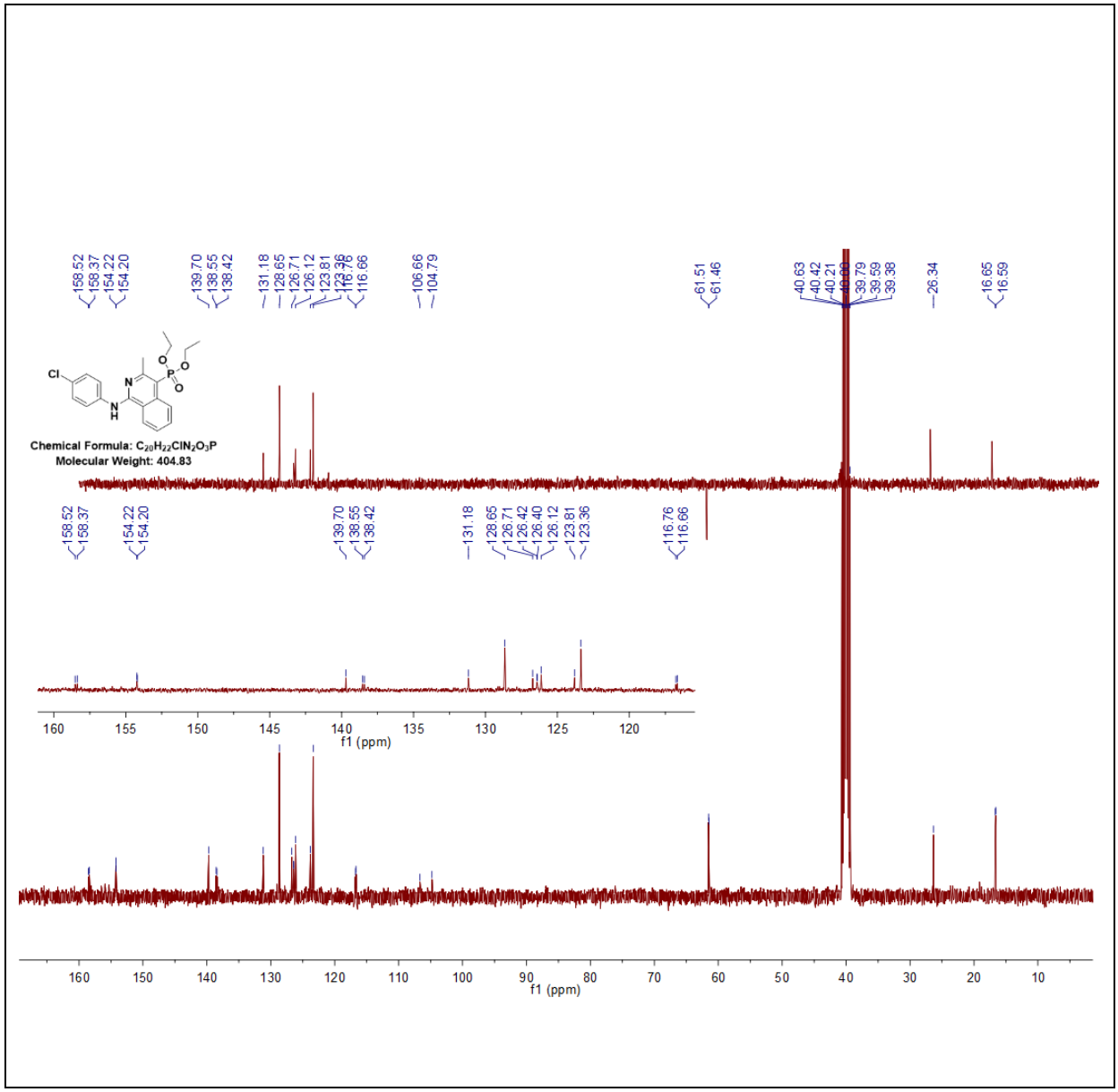
Diethyl (1-((4-chlorophenyl)amino)-3-methylisoquinolin-4-yl)phosphonate (3d)

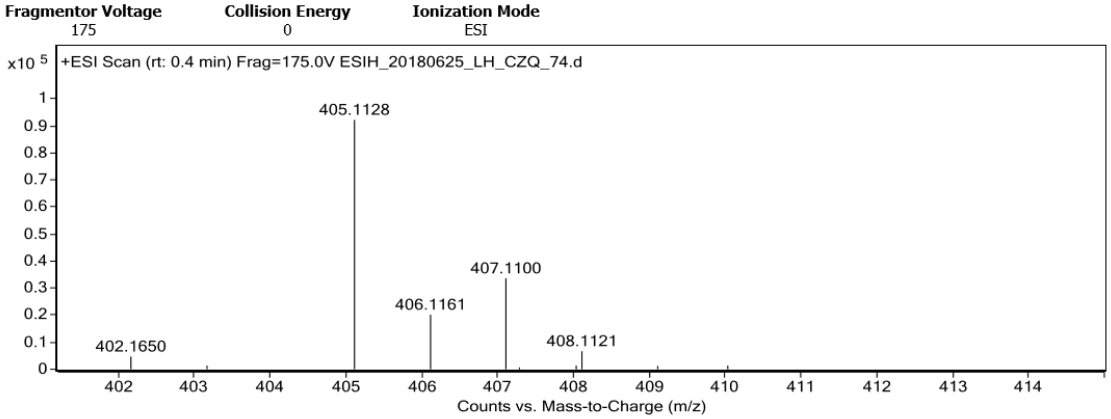


Chemical Formula: $C_{20}H_{22}ClN_2O_3P$
Molecular Weight: 404.83



Chemical Formula: $C_{20}H_{22}ClN_2O_3P$
Molecular Weight: 404.83

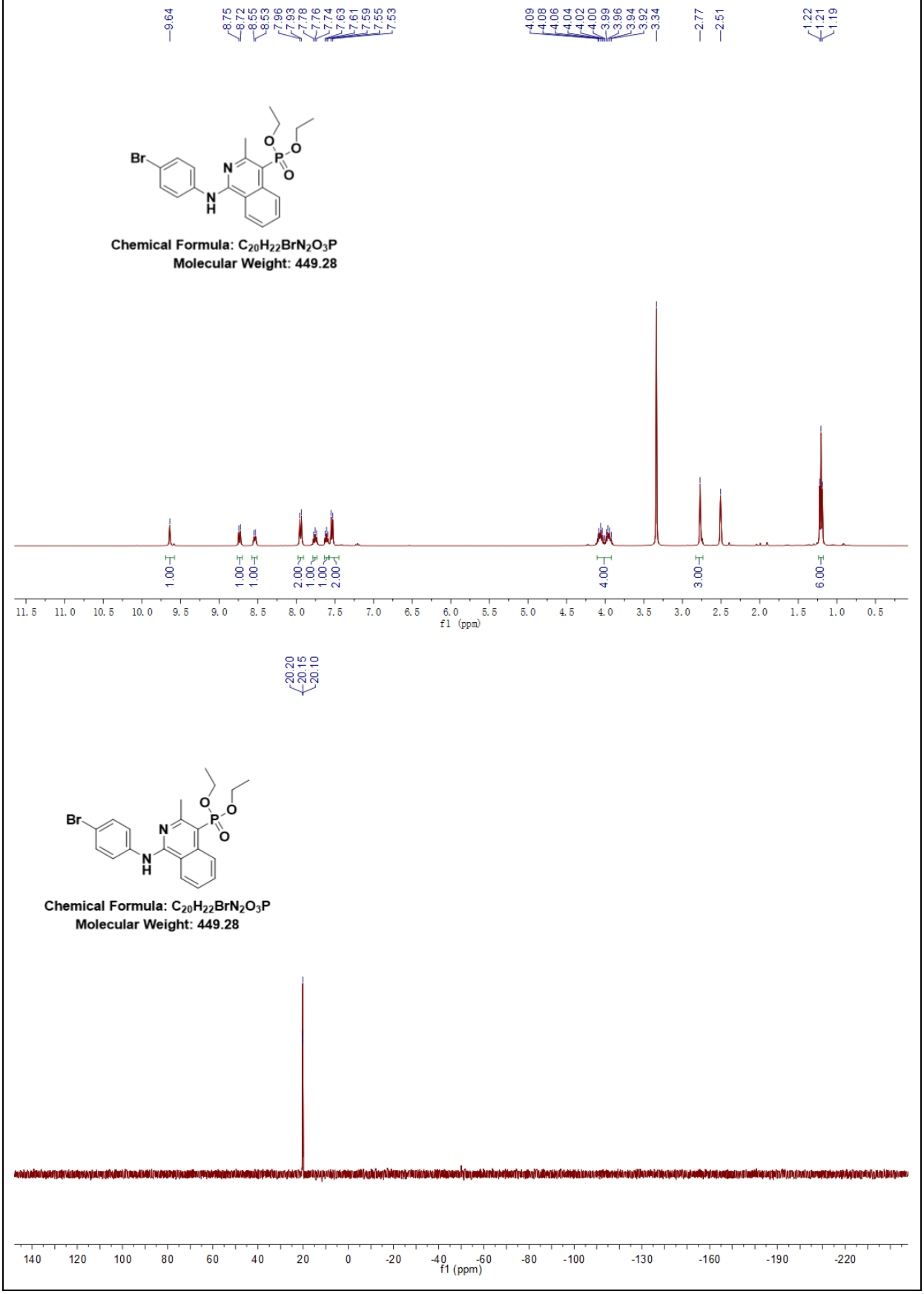


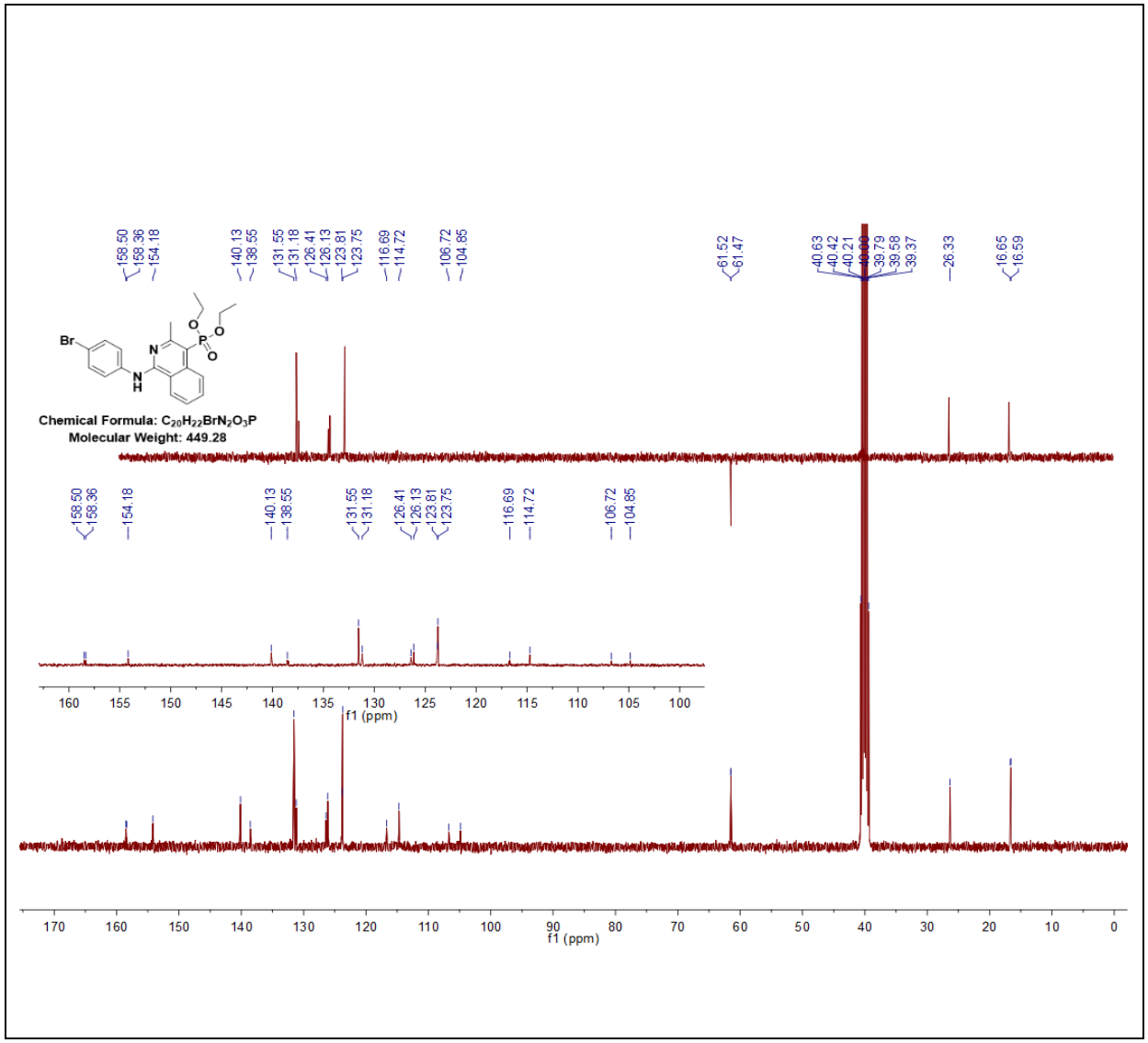


Formula Calculator Results

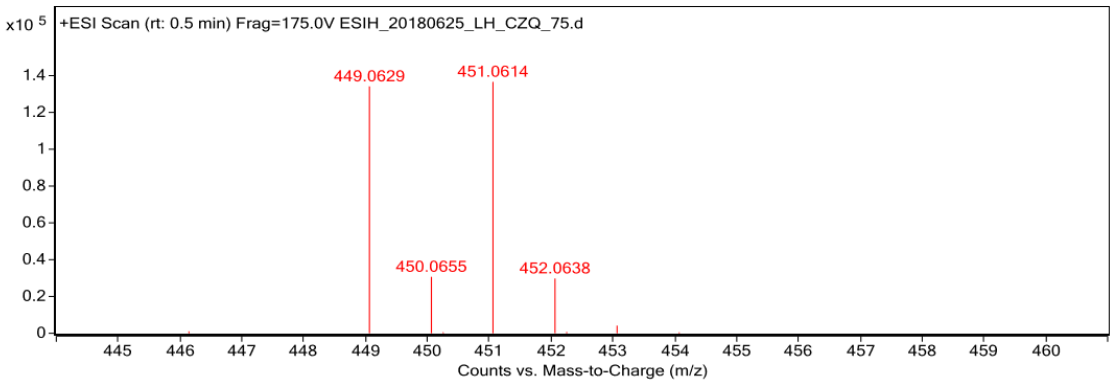
m/z	Calc m/z	Diff (mDa)	Diff (ppm)	Ion Formula	Ion
405.1128	405.1129	0.17	0.43	C20 H23 Cl N2 O3 P	(M+H)+

Diethyl (1-((4-bromophenyl)amino)-3-methylisoquinolin-4-yl)phosphonate (3e)





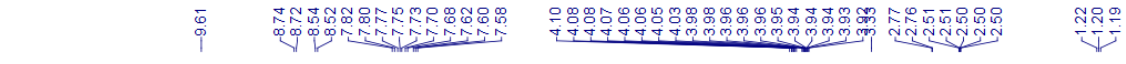
Fragmentor Voltage	Collision Energy	Ionization Mode
175	0	ESI

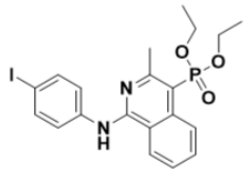


Formula Calculator Results

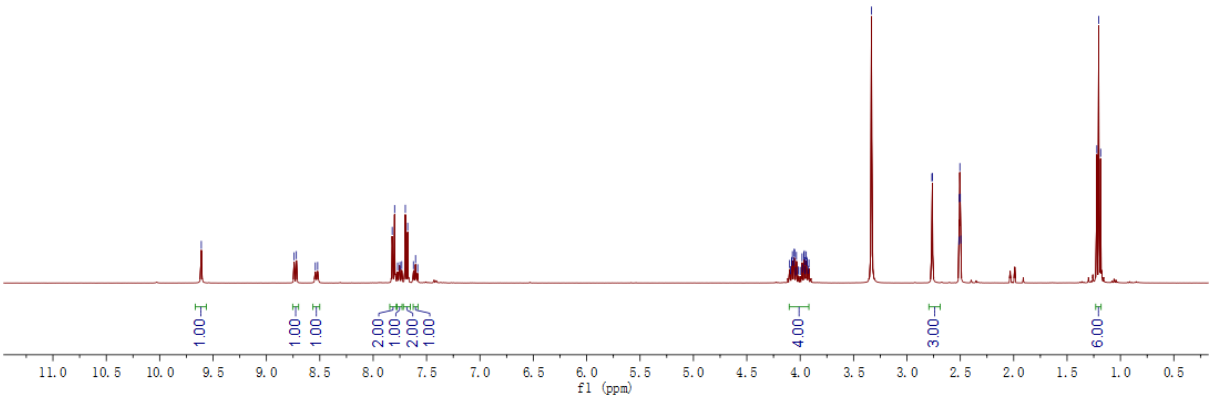
m/z	Calc m/z	Diff (mDa)	Diff (ppm)	Ion Formula	Ion
449.0629	449.0624	-0.48	-1.07	C20 H23 Br N2 O3 P	(M+H)+

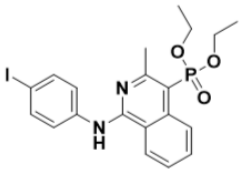
Diethyl (1-((4-iodophenyl)amino)-3-methylisoquinolin-4-yl)phosphonate (3f)



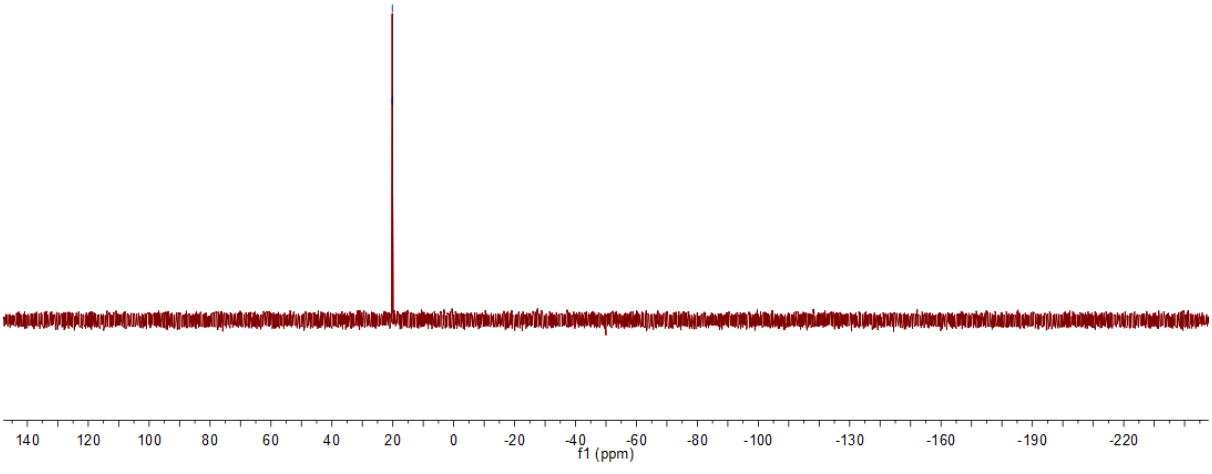


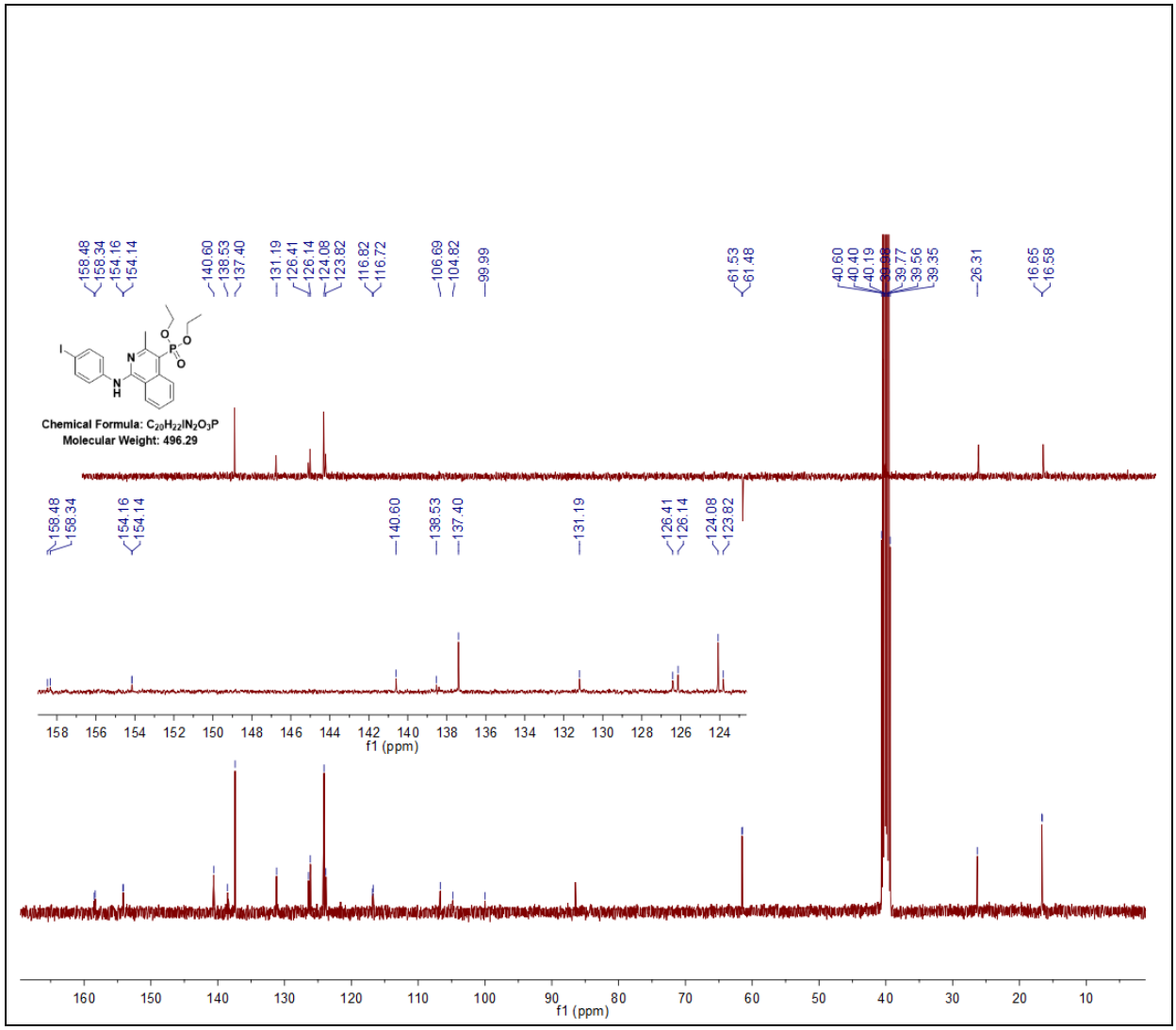
Chemical Formula: $C_{20}H_{22}IN_2O_3P$
Molecular Weight: 496.29



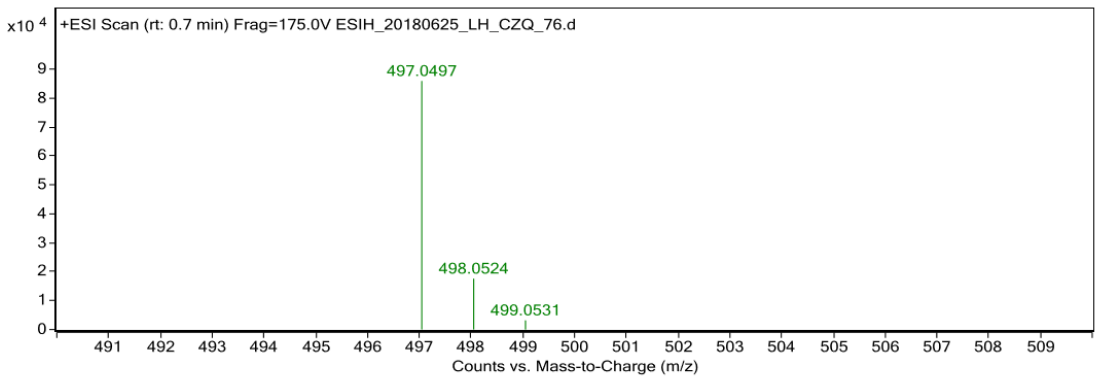


Chemical Formula: $C_{20}H_{22}IN_2O_3P$
Molecular Weight: 496.29





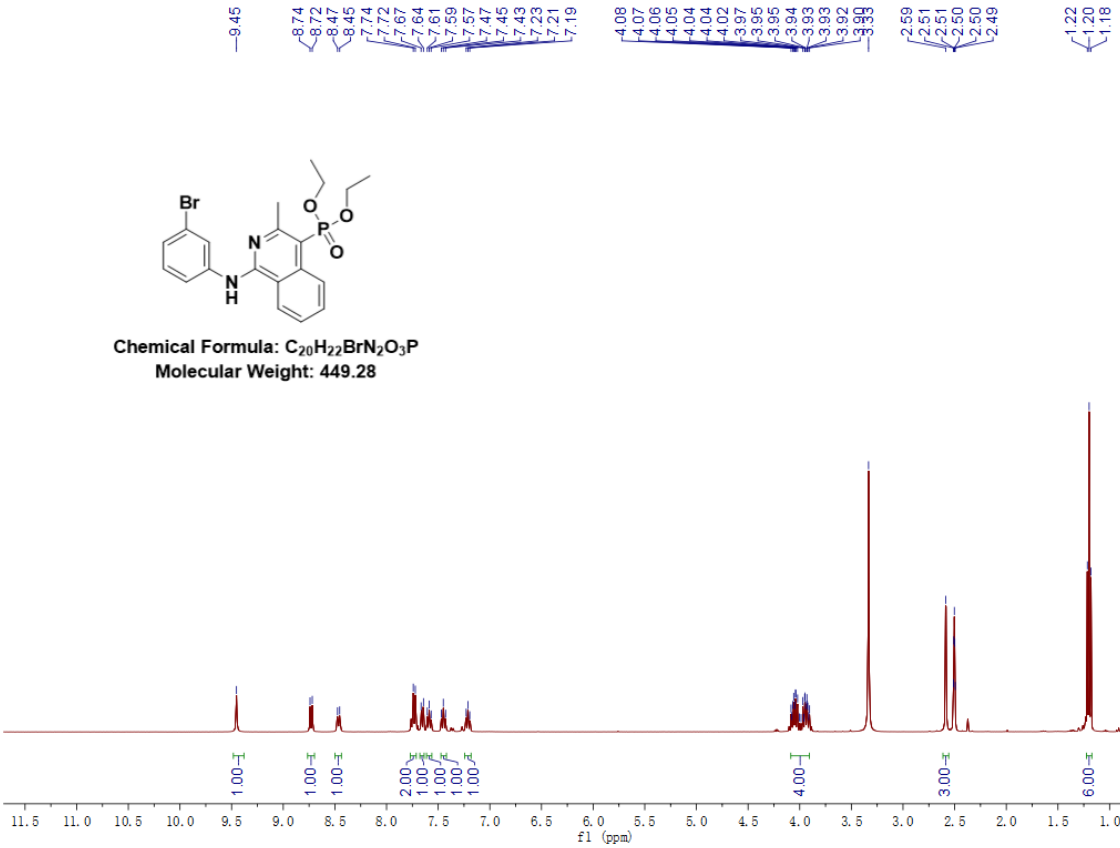
Fragmentor Voltage	Collision Energy	Ionization Mode
175	0	ESI

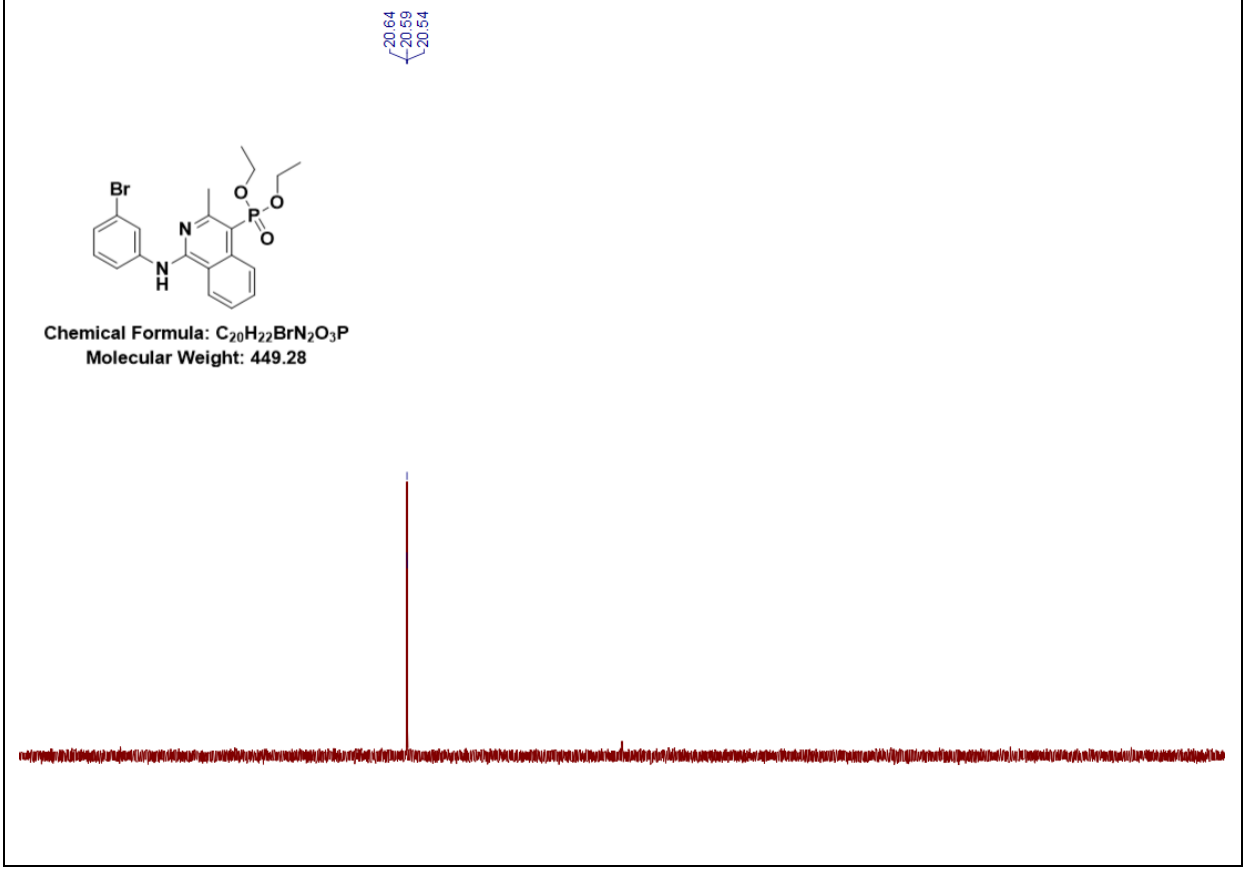


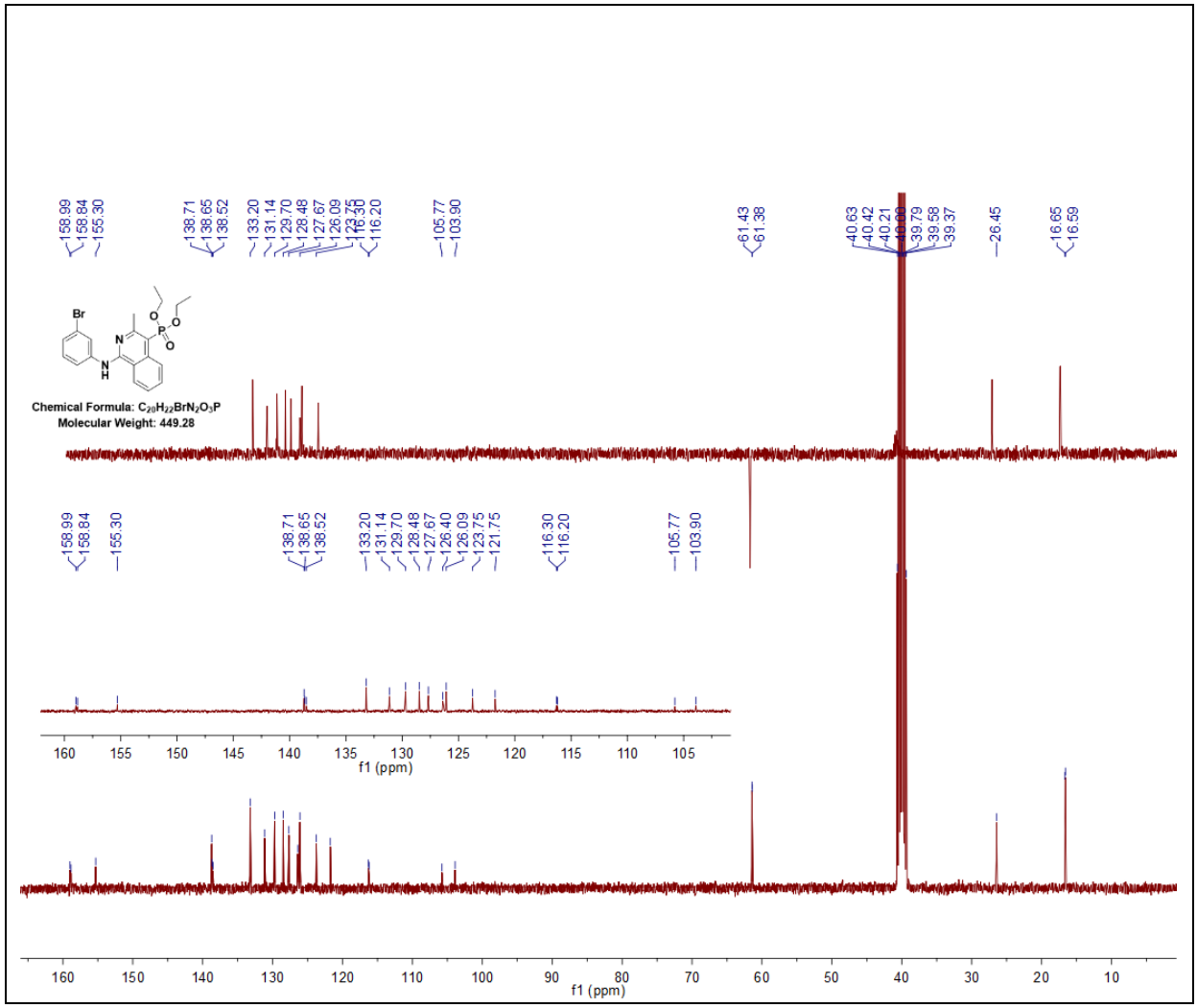
Formula Calculator Results

m/z	Calc m/z	Diff (mDa)	Diff (ppm)	Ion Formula	Ion
497.0497	497.0485	-1.11	-2.24	C20 H23 I N2 O3 P	(M+H)+

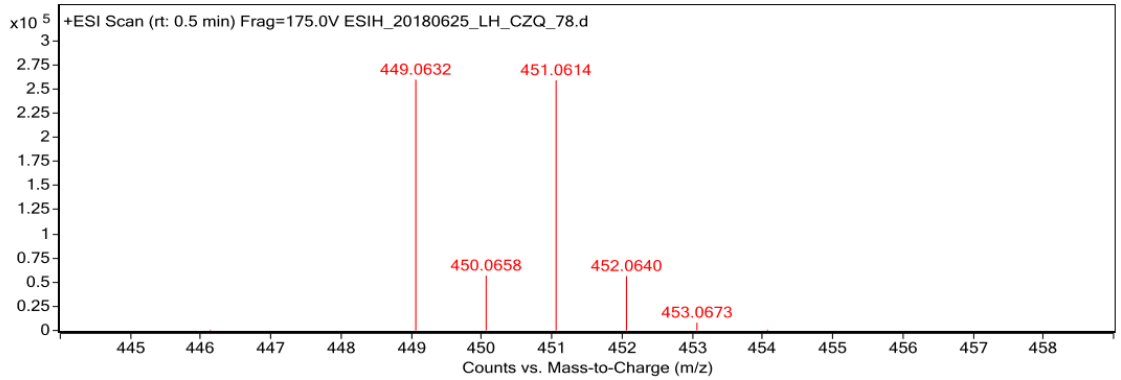
Diethyl (1-((3-bromophenyl)amino)-3-methylisoquinolin-4-yl)phosphonate (3g)







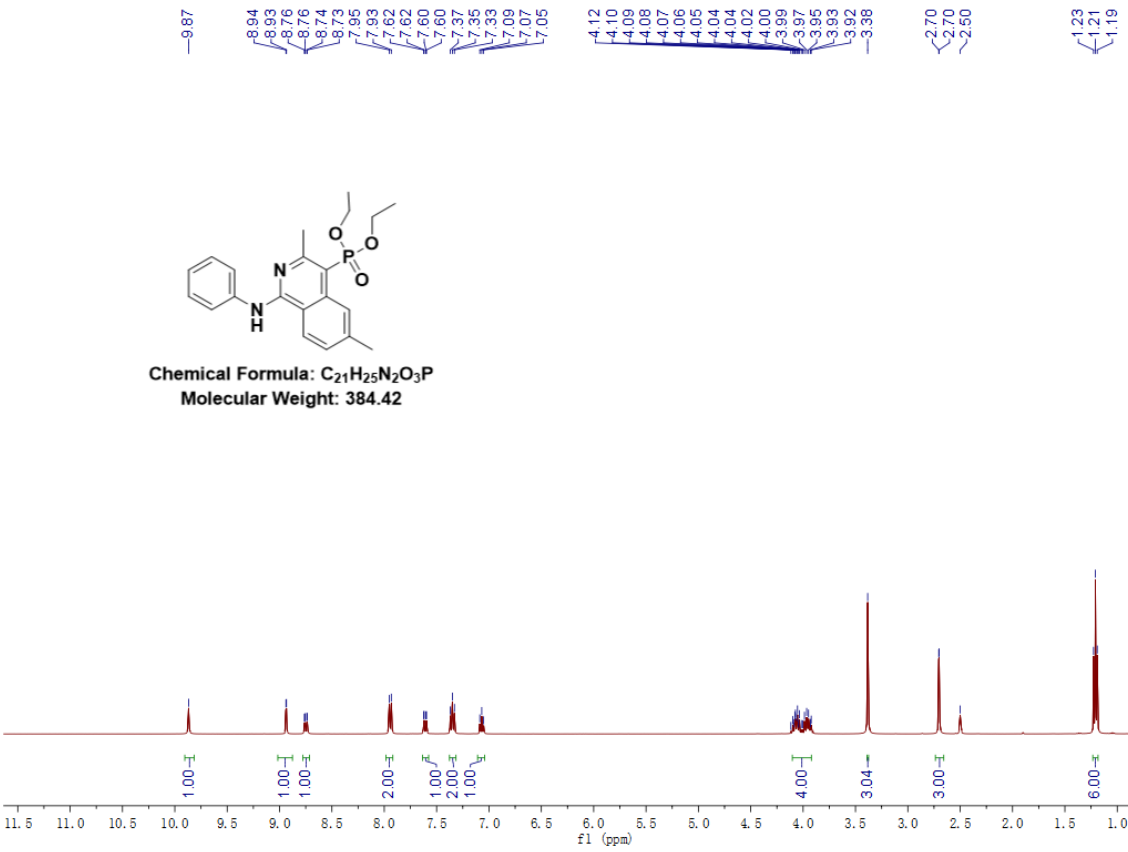
Fragmentor Voltage 175 **Collision Energy** 0 **Ionization Mode** ESI

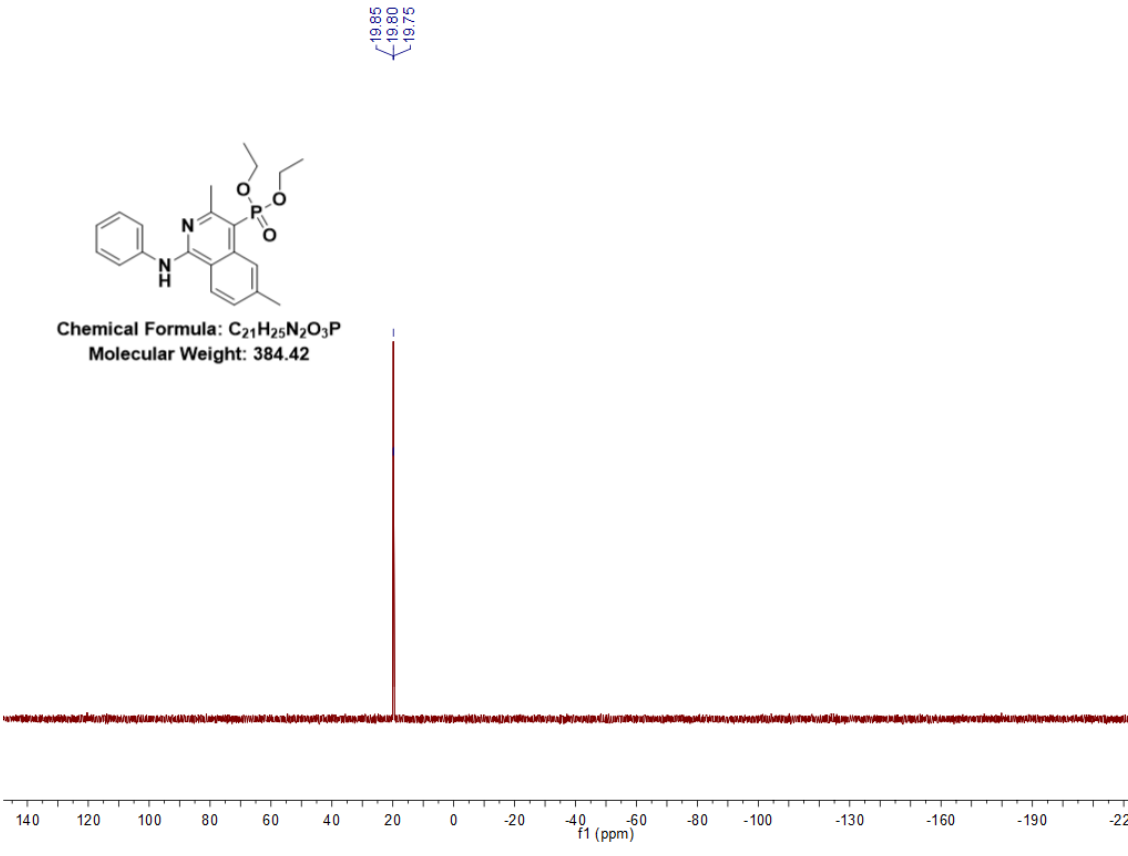


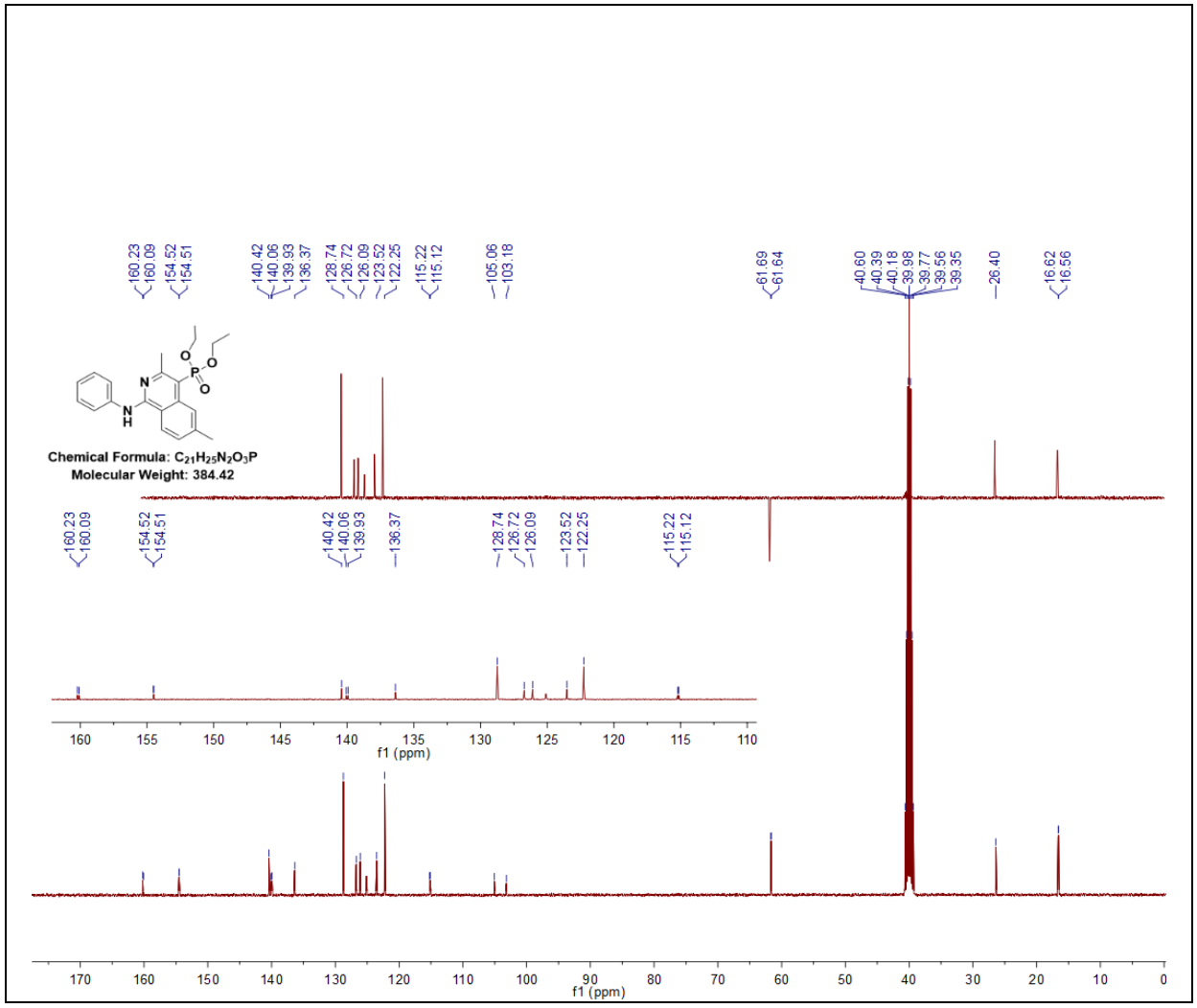
Formula Calculator Results

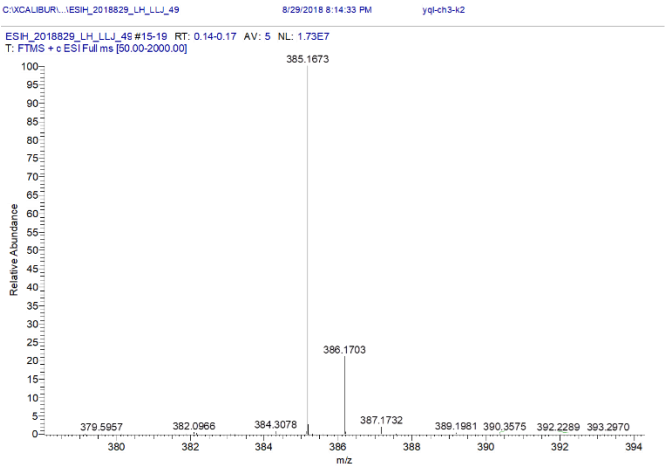
m/z	Calc m/z	Diff (mDa)	Diff (ppm)	Ion Formula	Ion
449.0632	449.0624	-0.74	-1.66	C20 H23 Br N2 O3 P	(M+H)+

Diethyl (3,6-dimethyl-1-(phenylamino)isoquinolin-4-yl)phosphonate (3h)







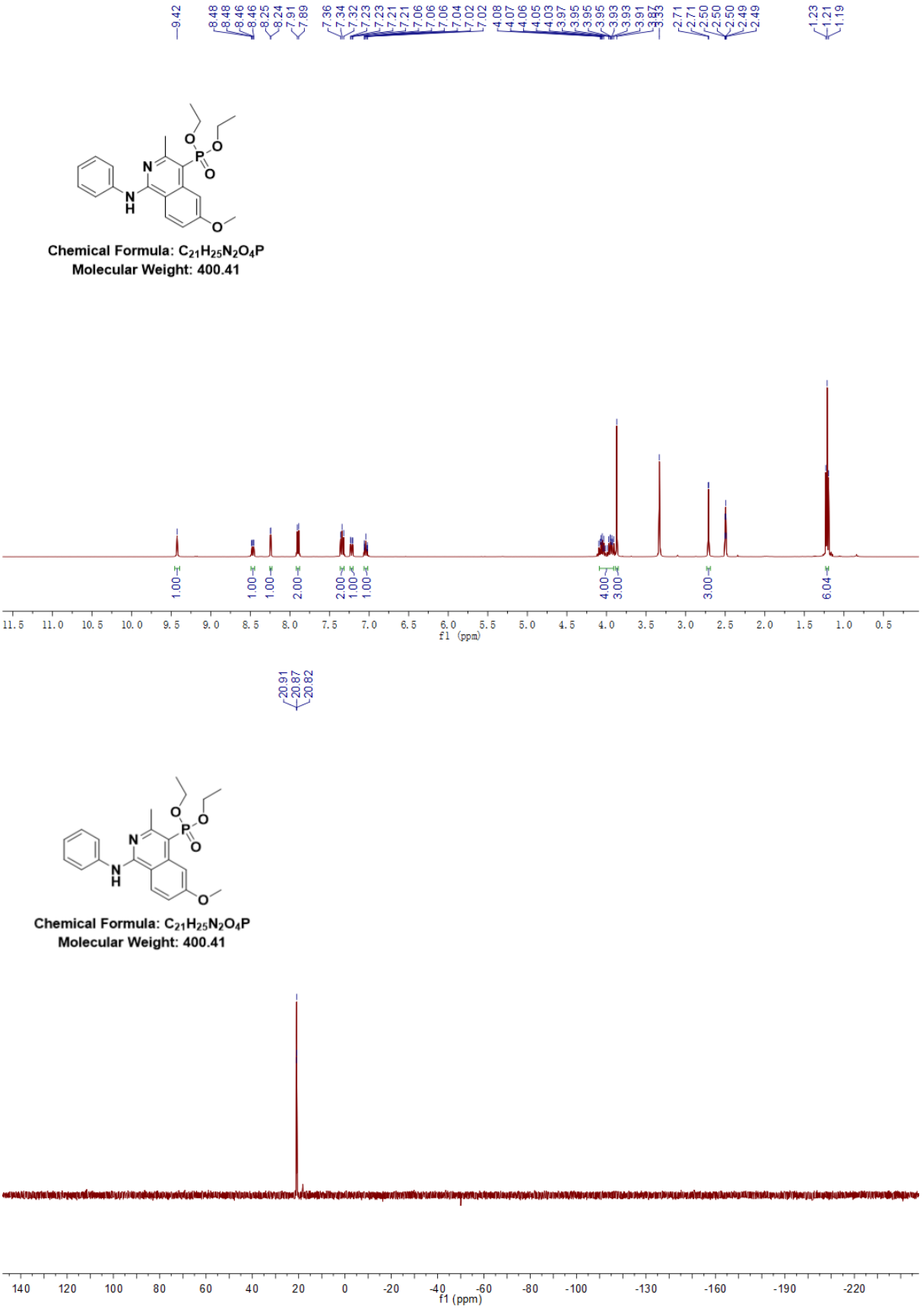


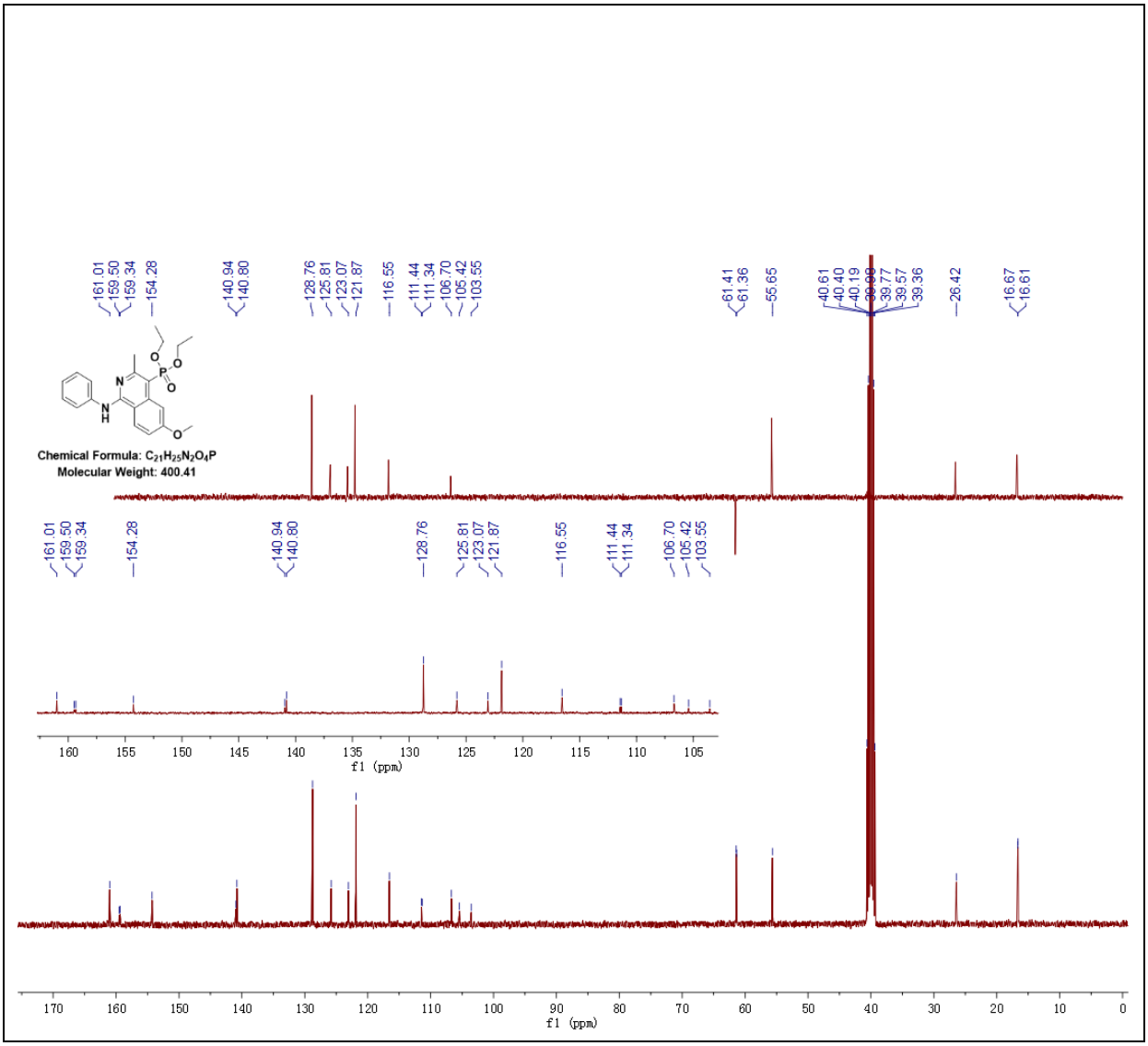
Elemental composition search on mass 385.17

m/z= 380.17-390.17

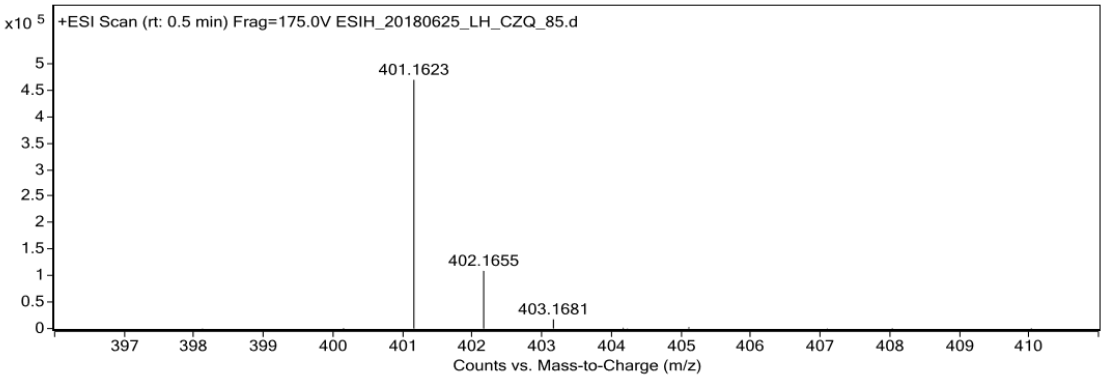
m/z	Theo. Mass	Delta (ppm)	RDB equiv.	Composition
385.1673	385.1676	-0.77	10.5	C21 H26 O3 N2 P

Diethyl (6-methoxy-3-methyl-1-(phenylamino)isoquinolin-4-yl)phosphonate (3i)





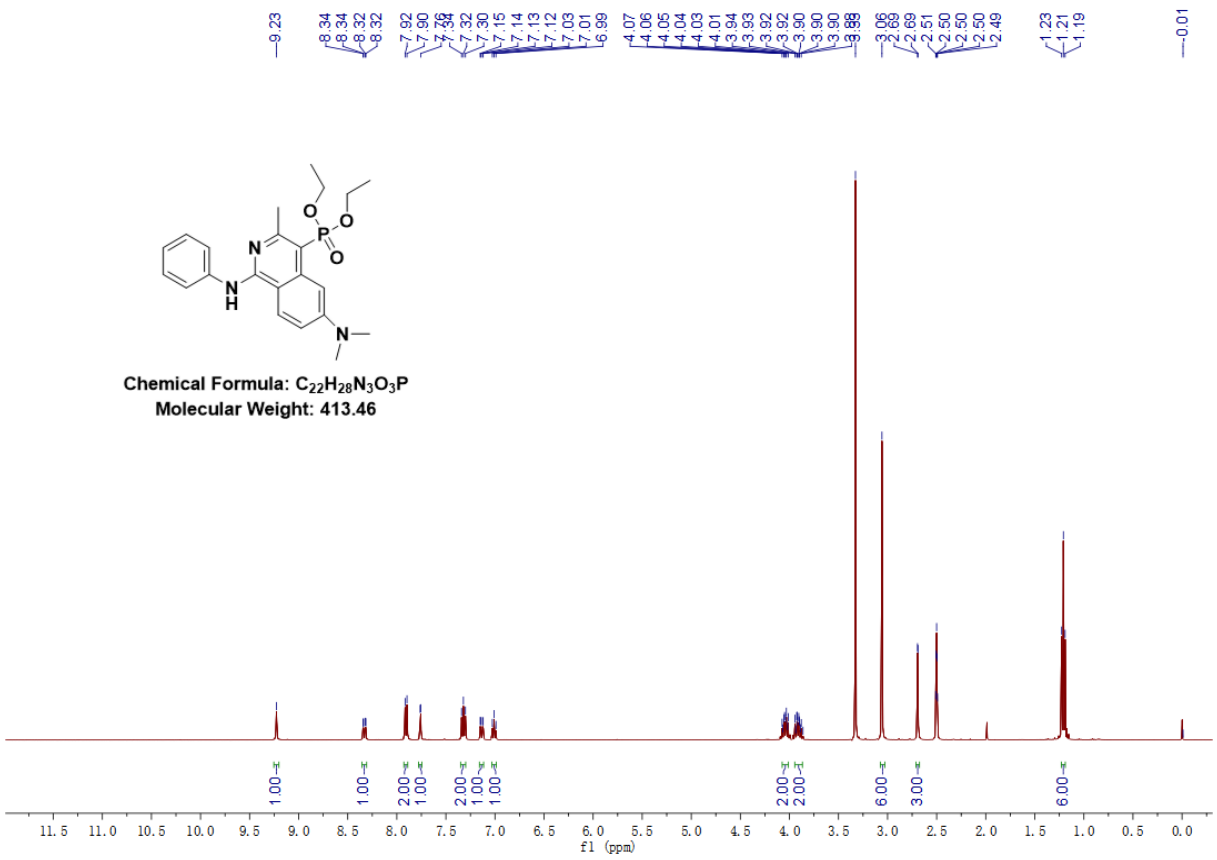
Fragmentor Voltage	Collision Energy	Ionization Mode
175	0	ESI

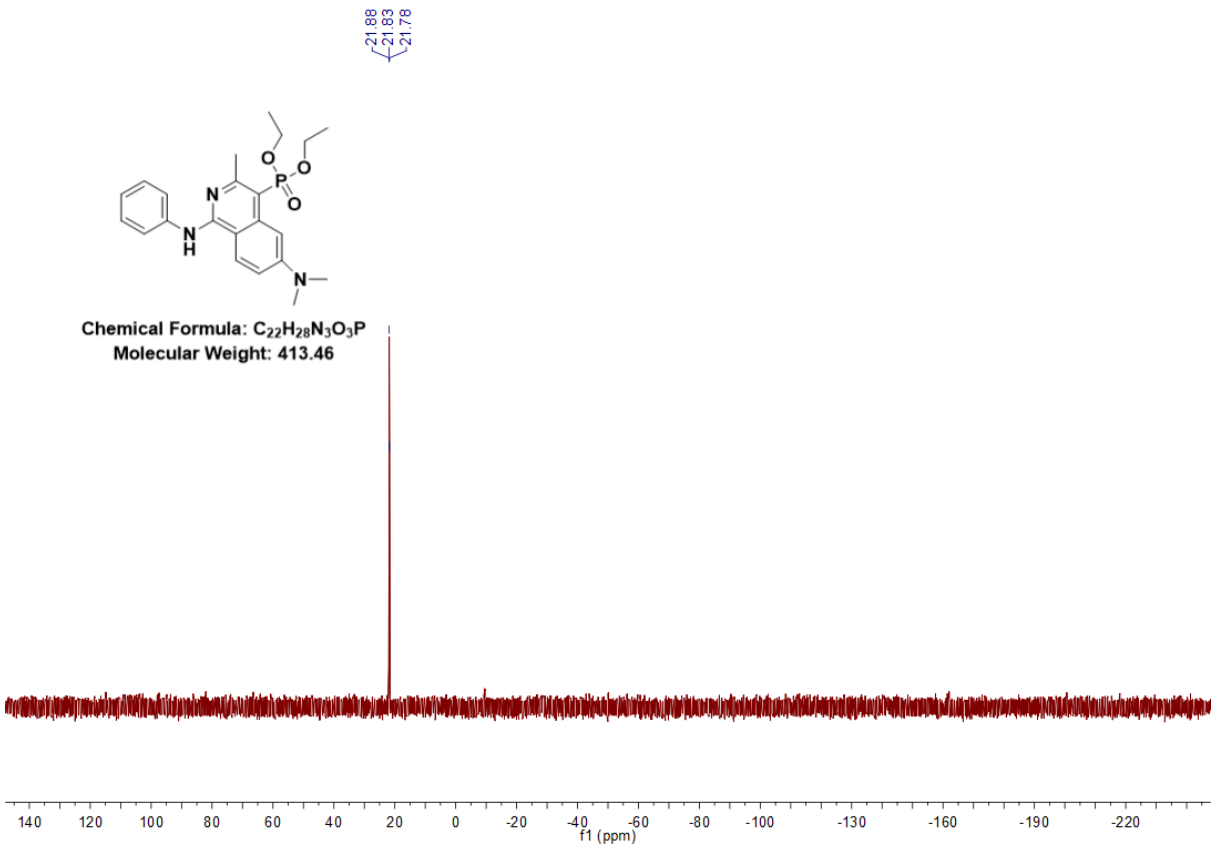


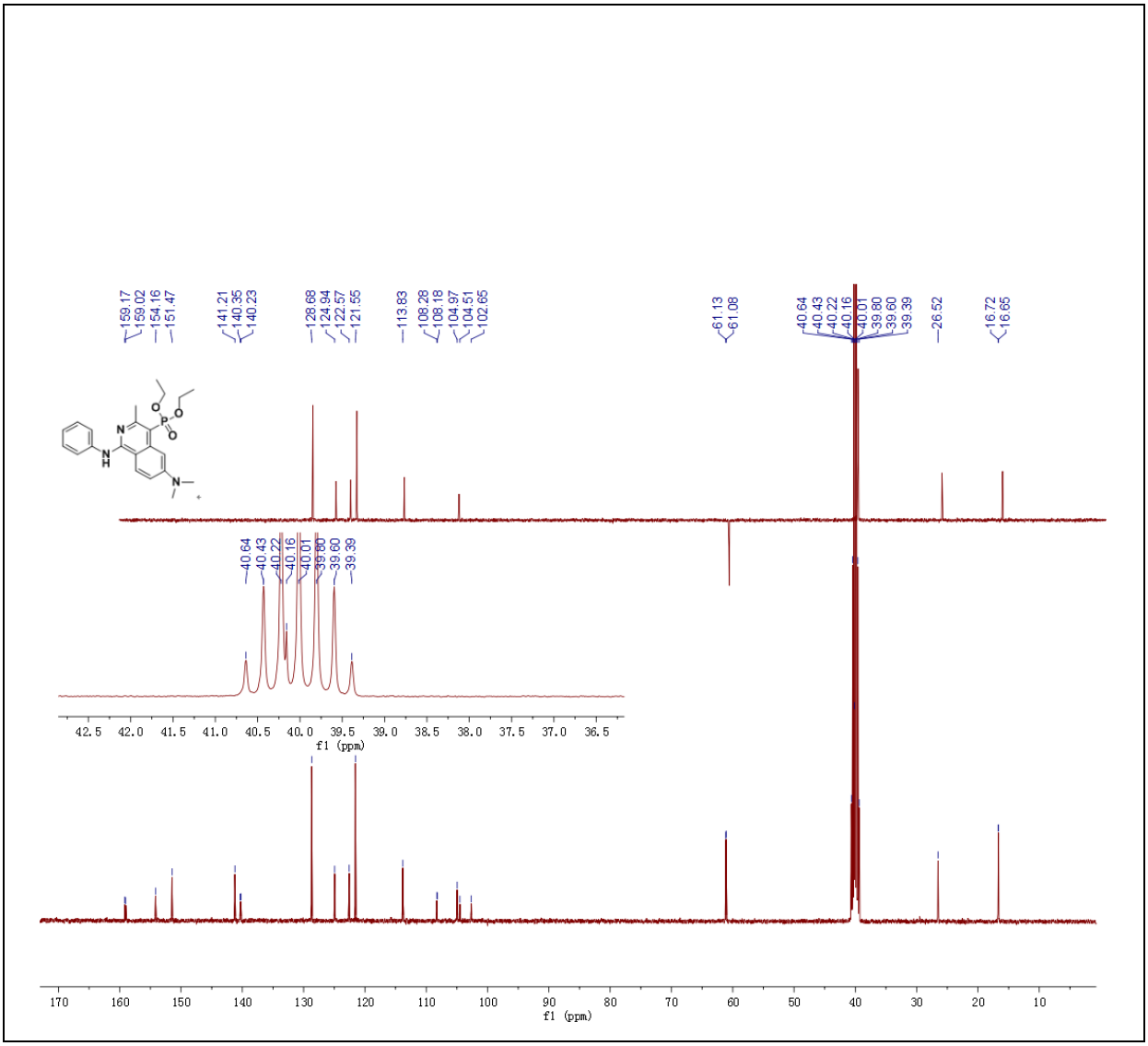
Formula Calculator Results

m/z	Calc m/z	Diff (mDa)	Diff (ppm)	Ion Formula	Ion
401.1623	401.1625	0.15	0.38	C21 H26 N2 O4 P	(M+H)+

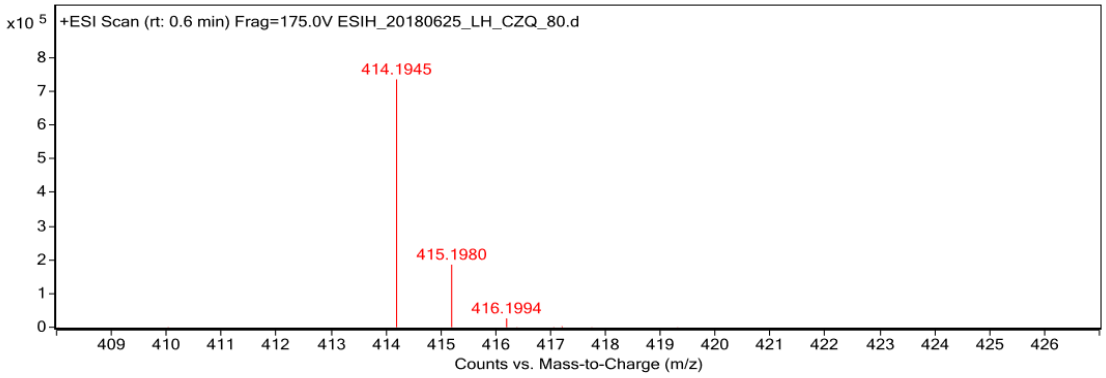
Diethyl(6-(dimethylamino)-3-methyl-1-(phenylamino)isoquinolin-4-yl)phosphonate (3j)







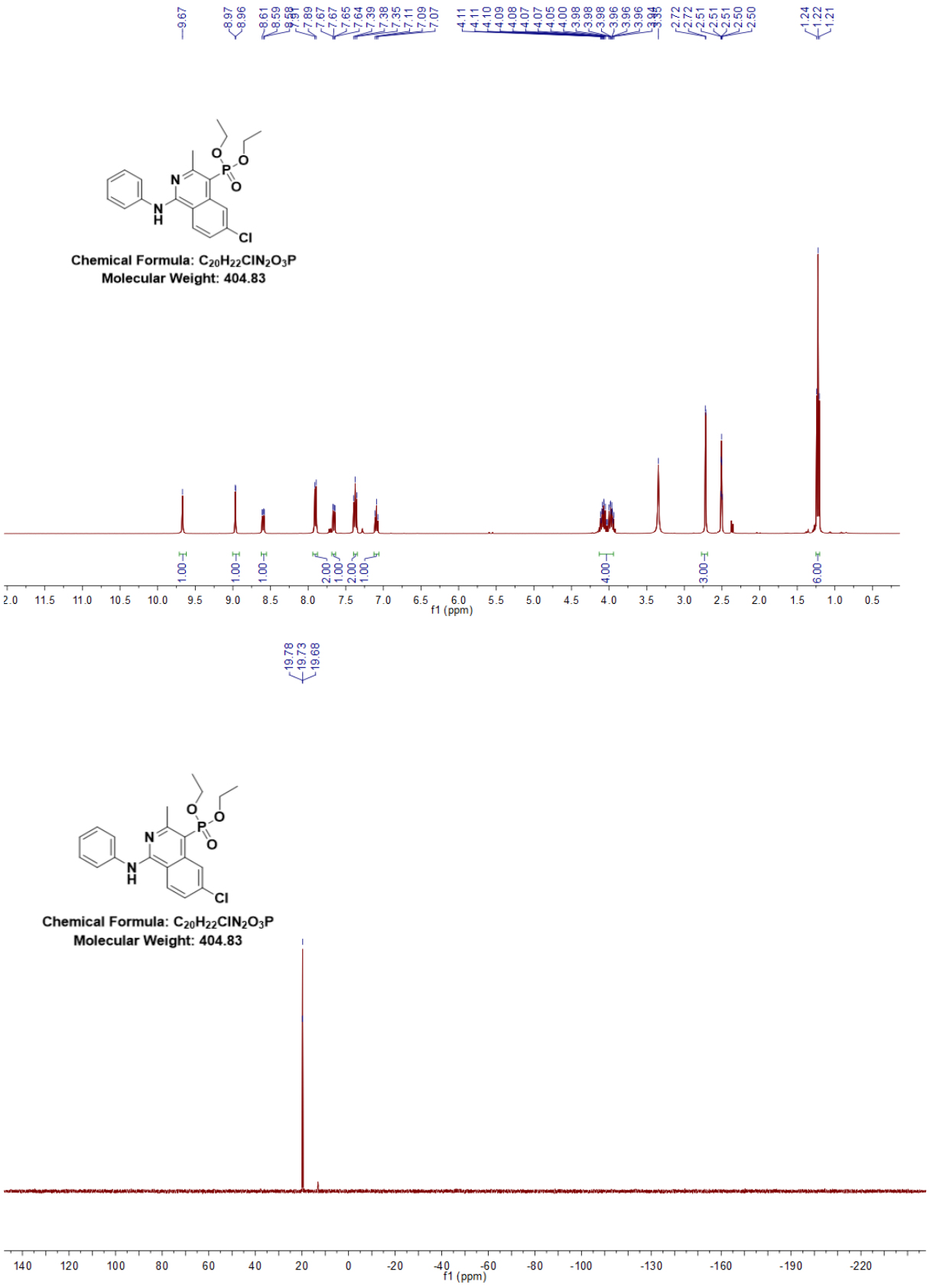
Fragmentor Voltage 175 **Collision Energy** 0 **Ionization Mode** ESI

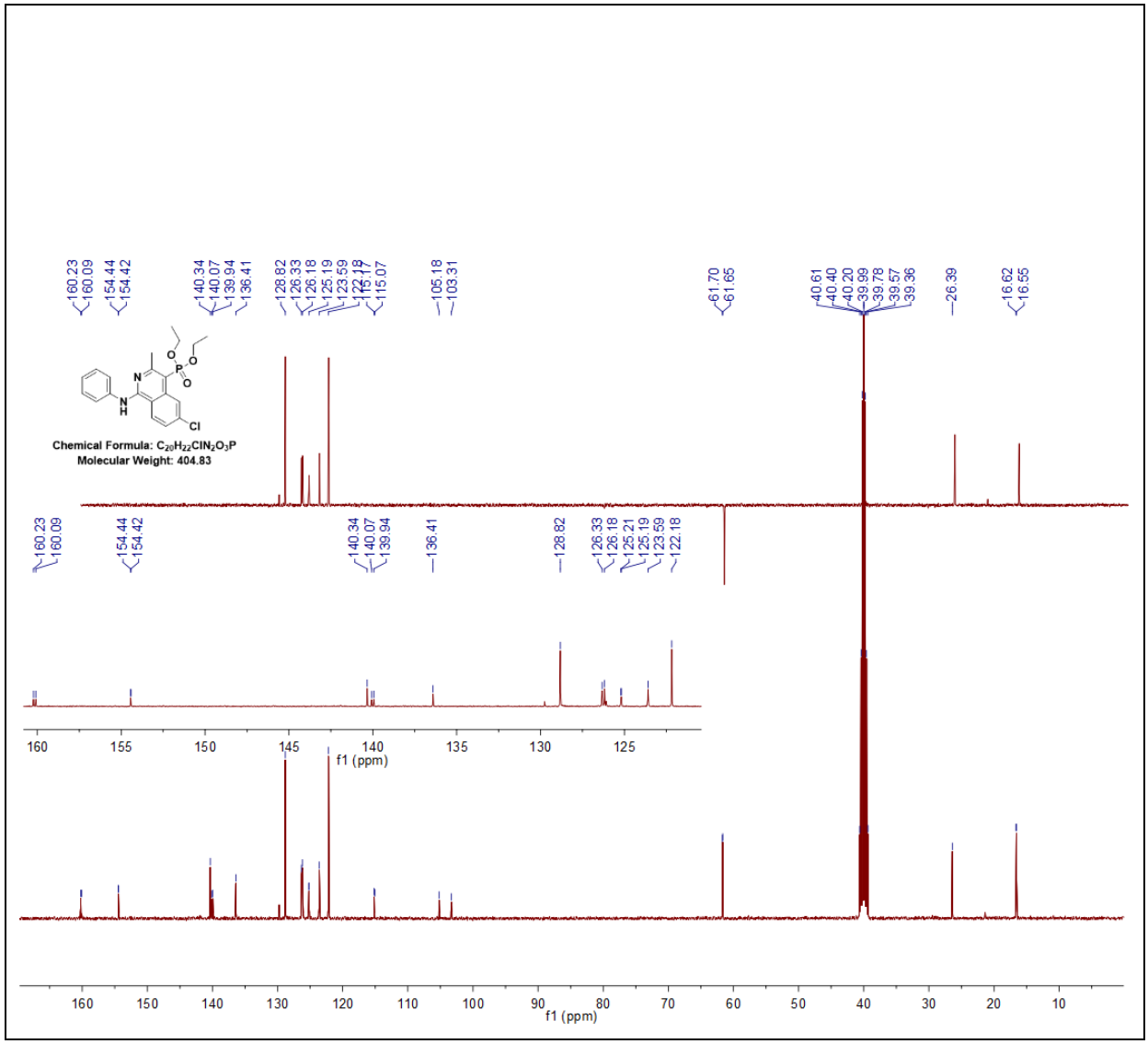


Formula Calculator Results

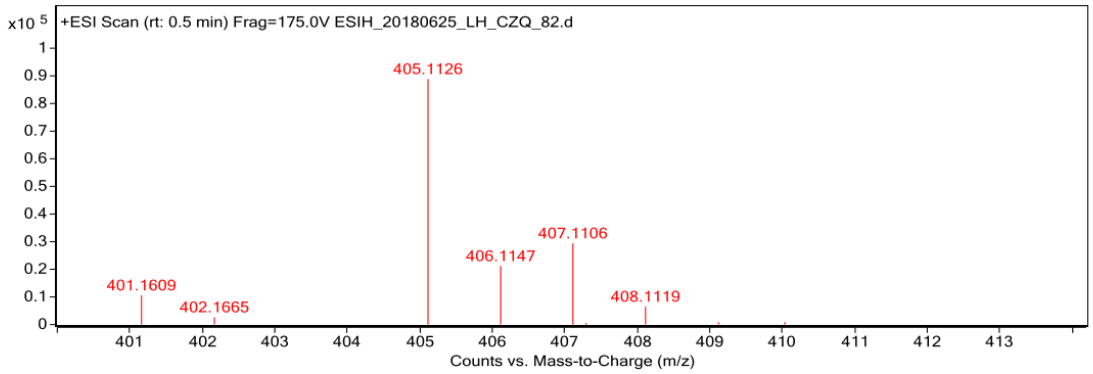
m/z	Calc m/z	Diff (mDa)	Diff (ppm)	Ion Formula	Ion
414.1945	414.1941	-0.38	-0.92	C22 H29 N3 O3 P	(M+H)+

Diethyl (6-chloro-3-methyl-1-(phenylamino)isoquinolin-4-yl)phosphonate (3k)





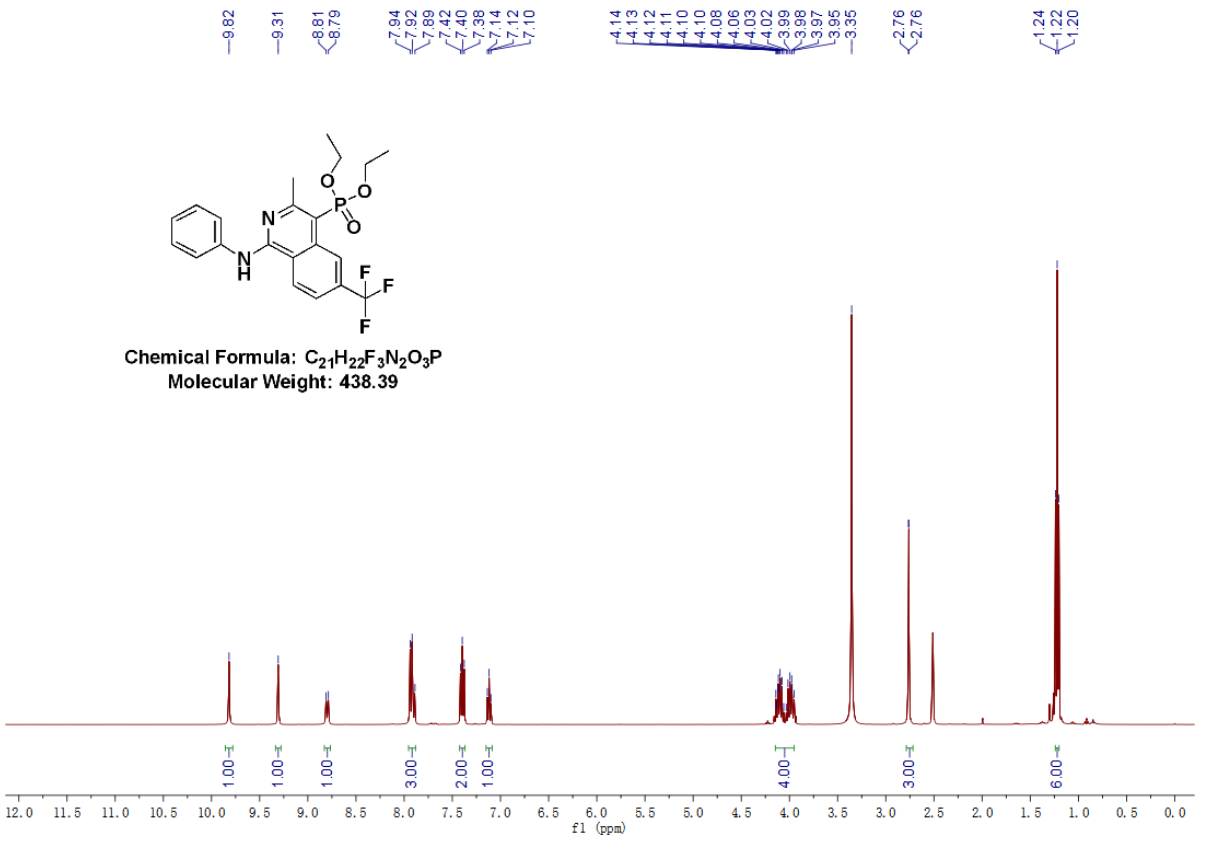
Fragmentor Voltage 175 **Collision Energy** 0 **Ionization Mode** ESI

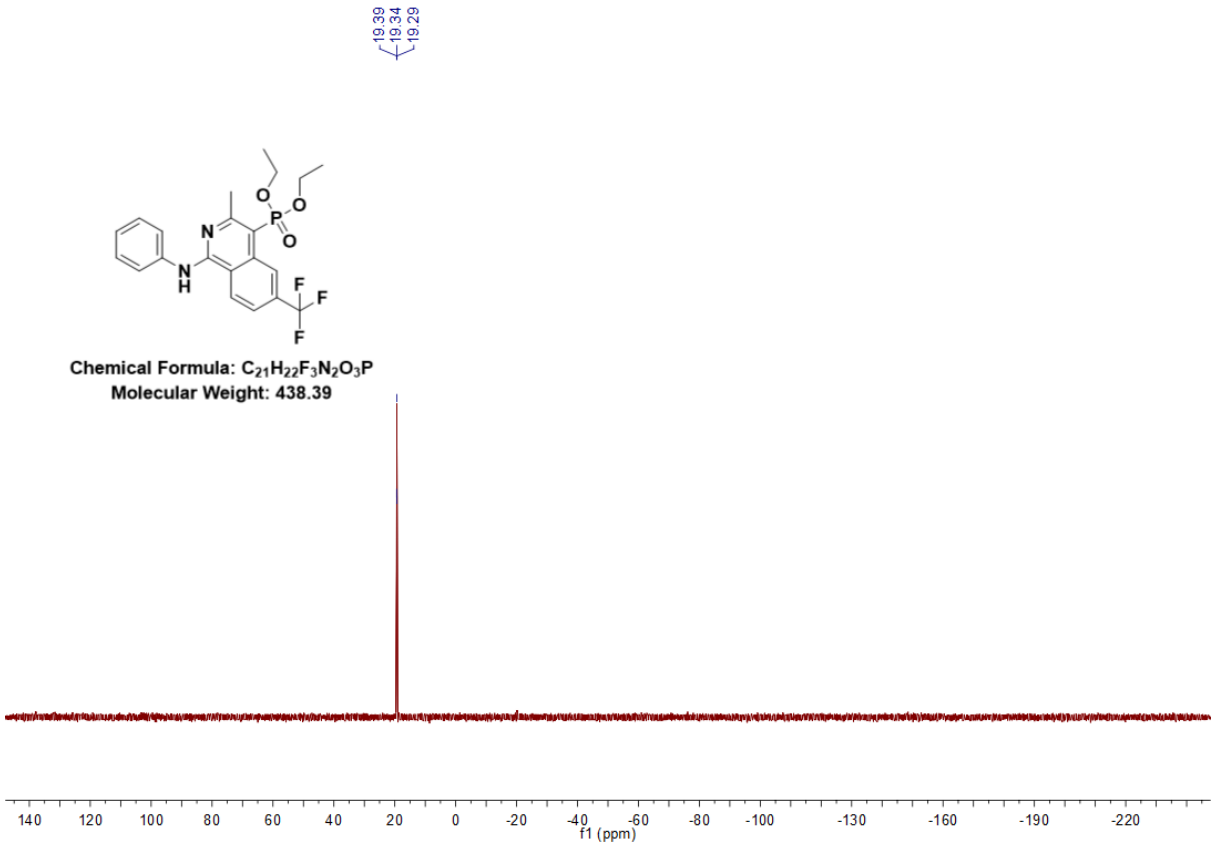


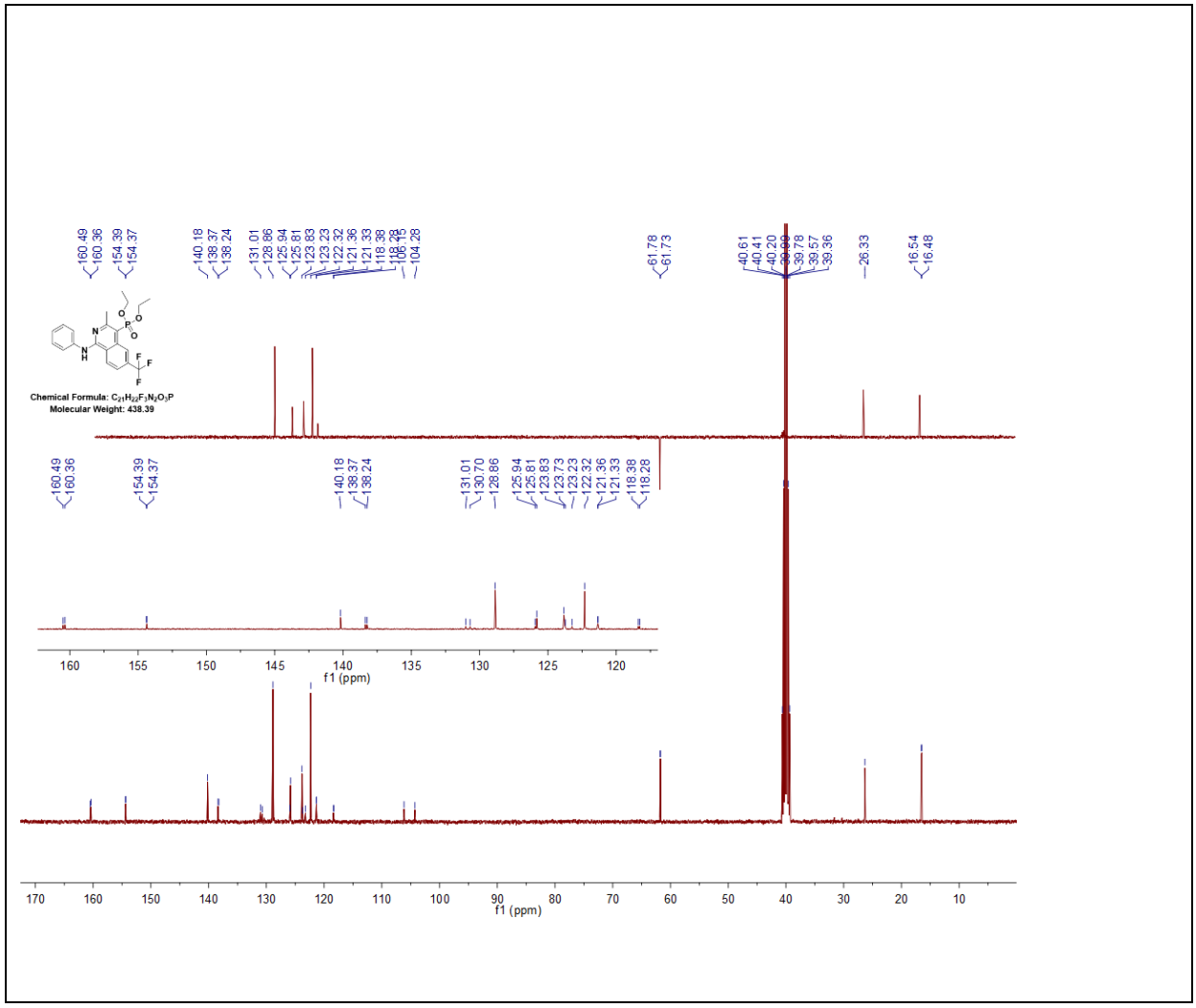
Formula Calculator Results

m/z	Calc m/z	Diff (mDa)	Diff (ppm)	Ion Formula	Ion
405.1126	405.1129	0.3	0.73	C20 H23 Cl N2 O3 P	(M+H)+

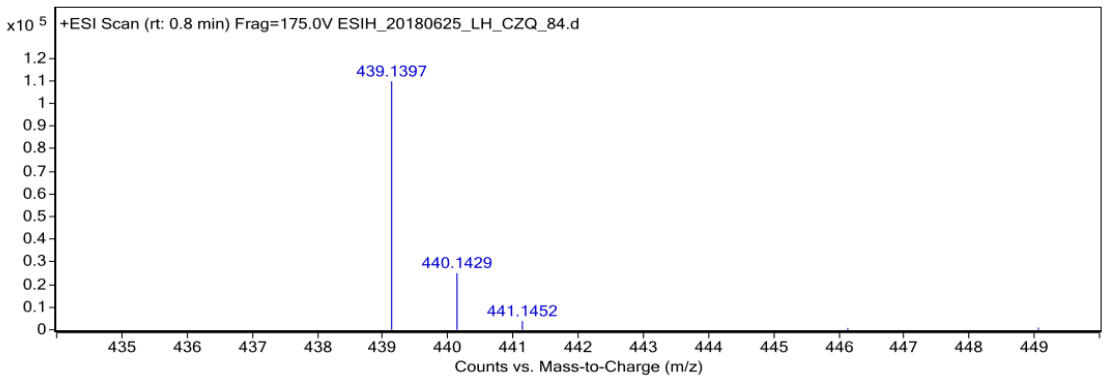
Diethyl (3-methyl-1-(phenylamino)-6-(trifluoromethyl)isoquinolin-4-yl)phosphonate (3l)







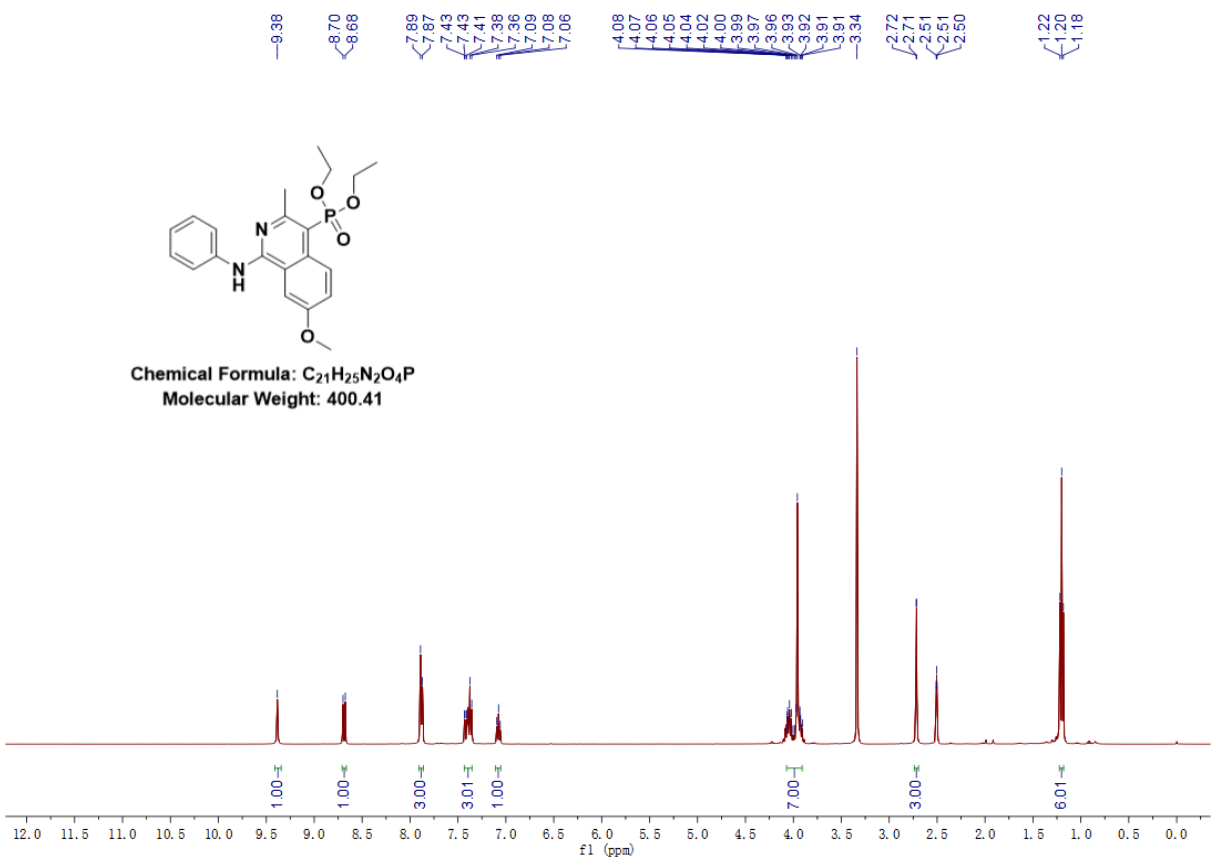
Fragmentor Voltage	Collision Energy	Ionization Mode
175	0	ESI

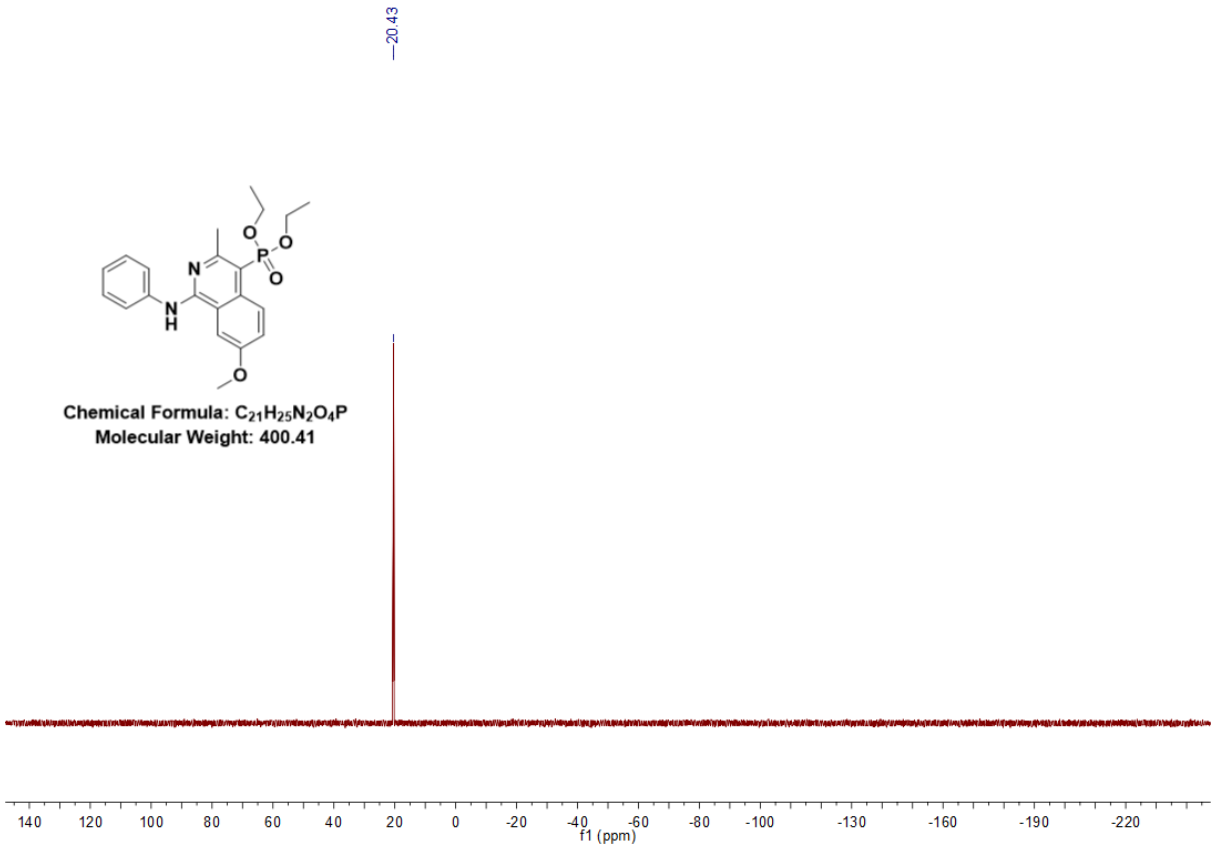


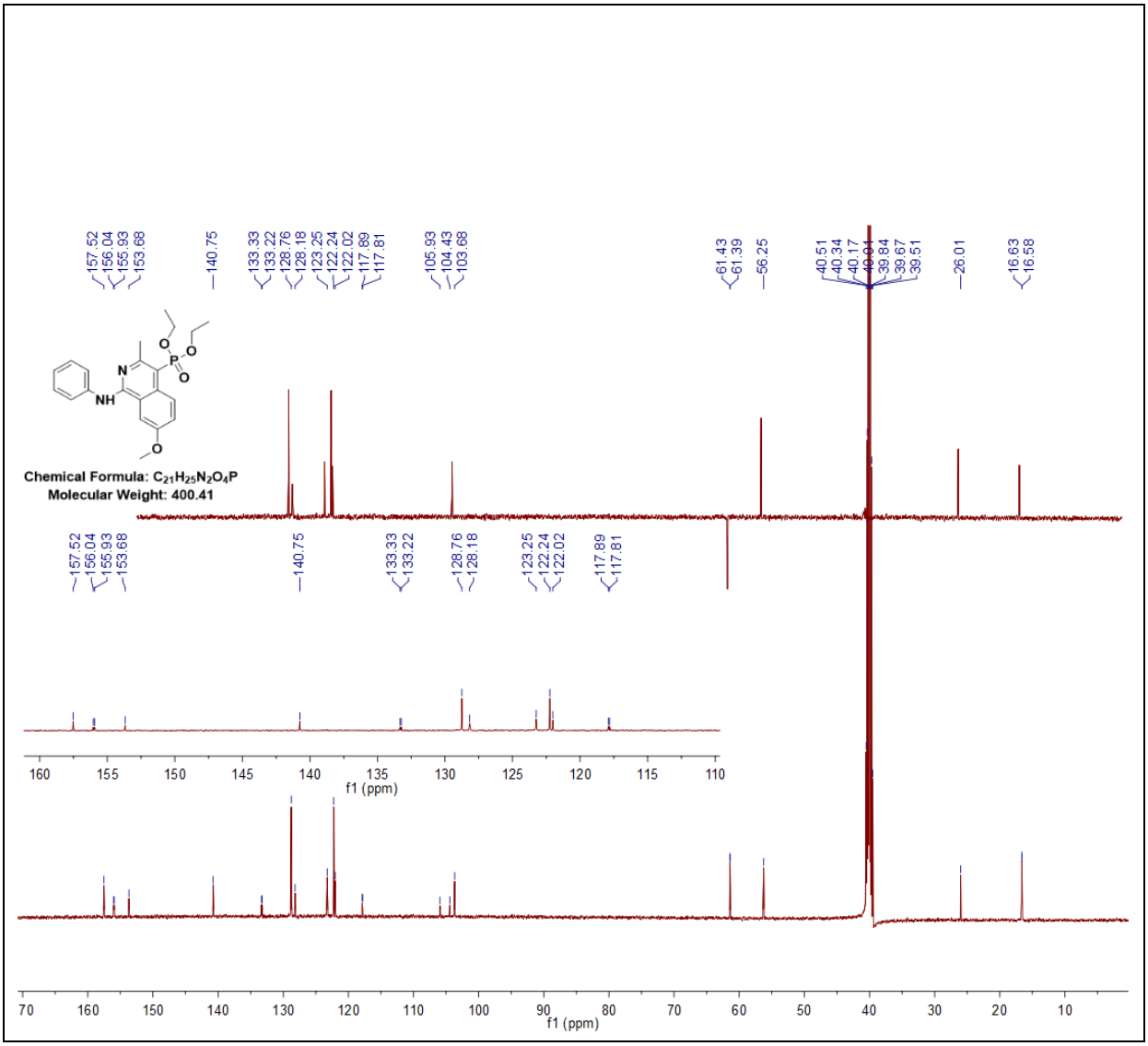
Formula Calculator Results

m/z	Calc m/z	Diff (mDa)	Diff (ppm)	Ion Formula	Ion
439.1397	439.1393	-0.43	-0.98	C21 H23 F3 N2 O3 P	(M+H)+

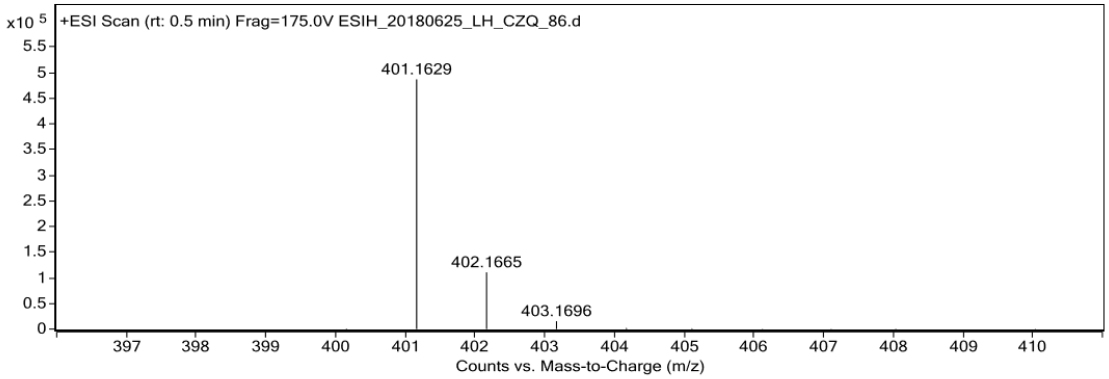
Diethyl (7-methoxy-3-methyl-1-(phenylamino)isoquinolin-4-yl)phosphonate (3m)







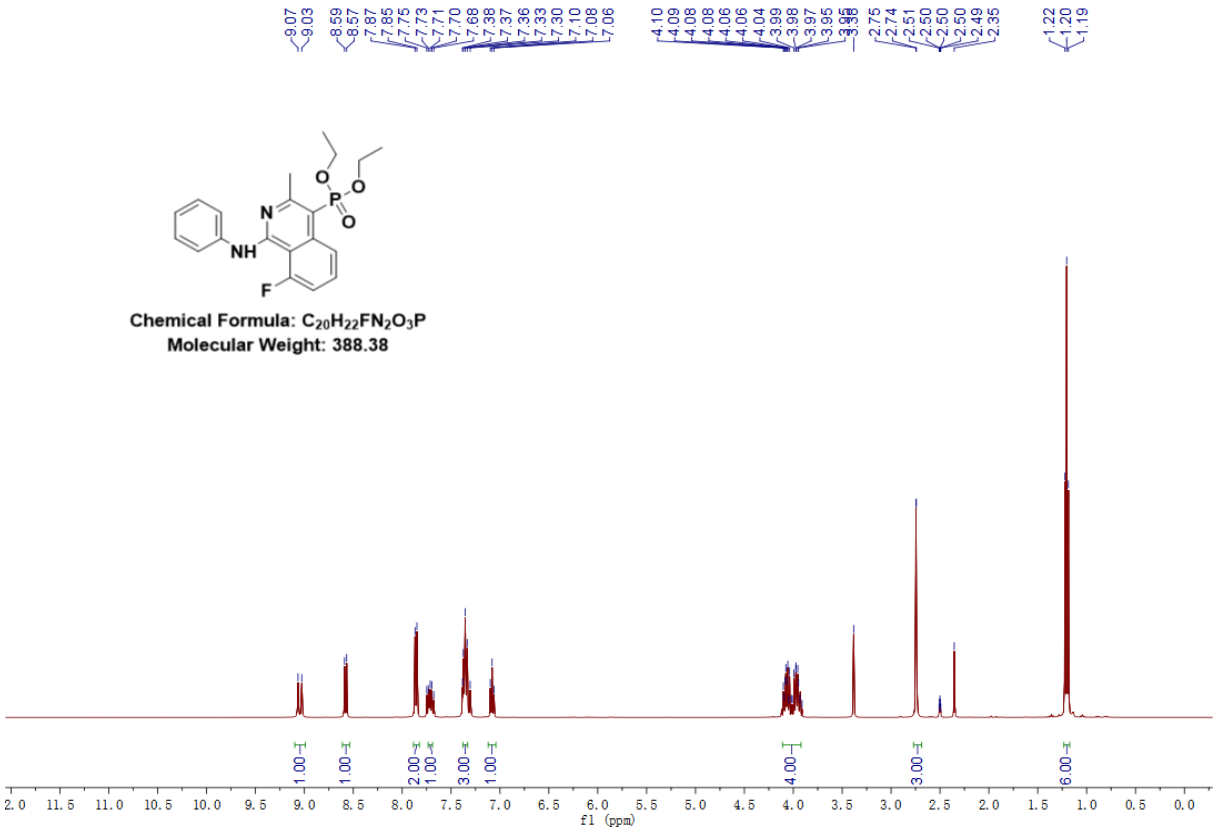
Fragmentor Voltage	Collision Energy	Ionization Mode
175	0	ESI



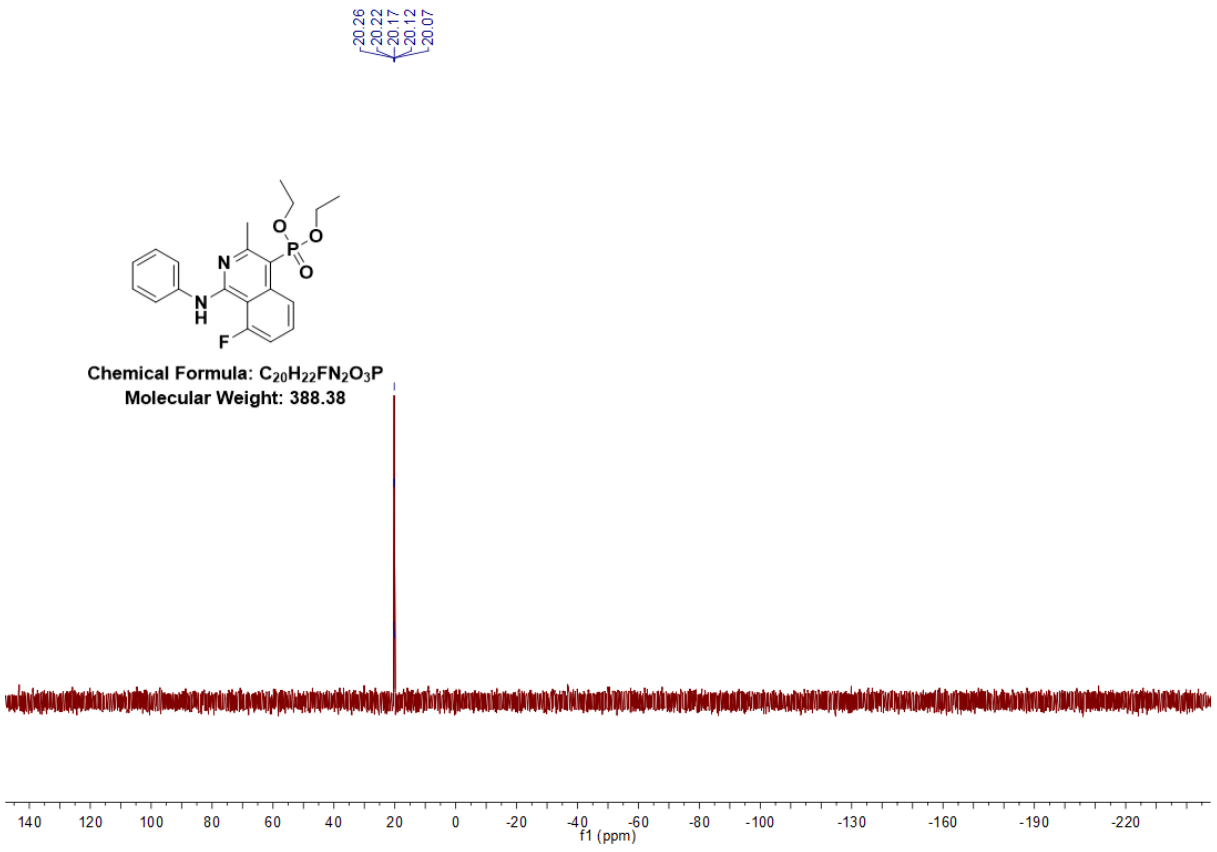
Formula Calculator Results

m/z	Calc m/z	Diff (mDa)	Diff (ppm)	Ion Formula	Ion
401.1629	401.1625	-0.45	-1.13	C21 H26 N2 O4 P	(M+H)+

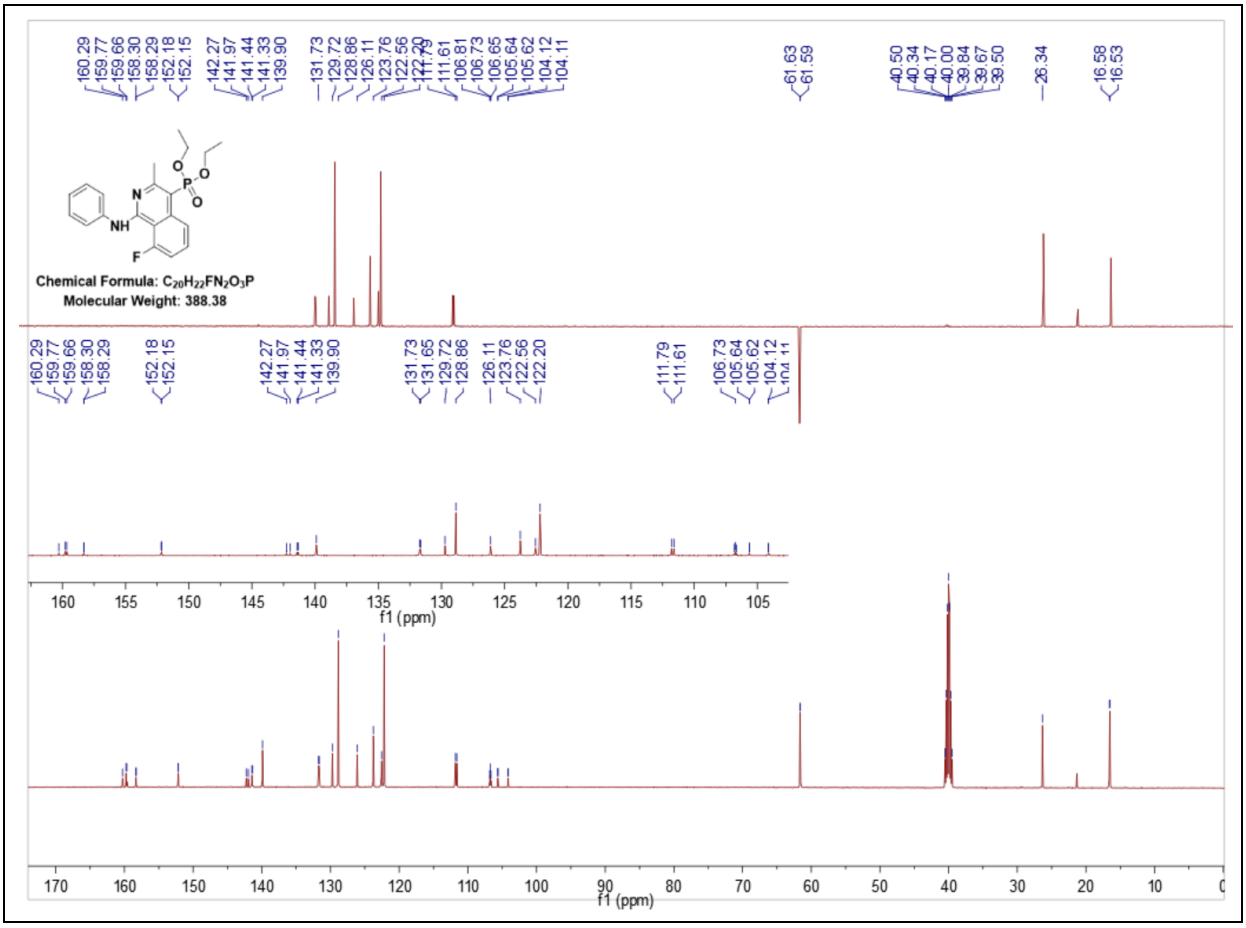
Diethyl (8-fluoro-3-methyl-1-(phenylamino)isoquinolin-4-yl)phosphonate (3n)



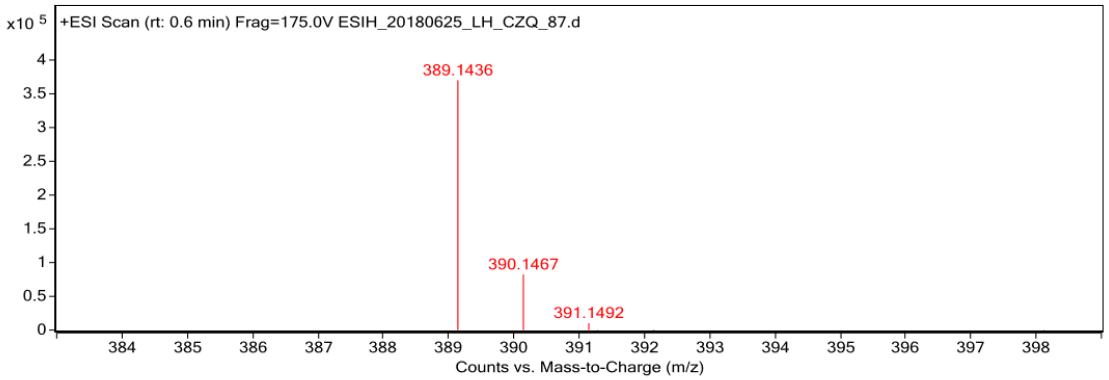
Chemical Formula: $C_{20}H_{22}FN_2O_3P$
Molecular Weight: 388.38



Chemical Formula: $C_{20}H_{22}FN_2O_3P$
Molecular Weight: 388.38



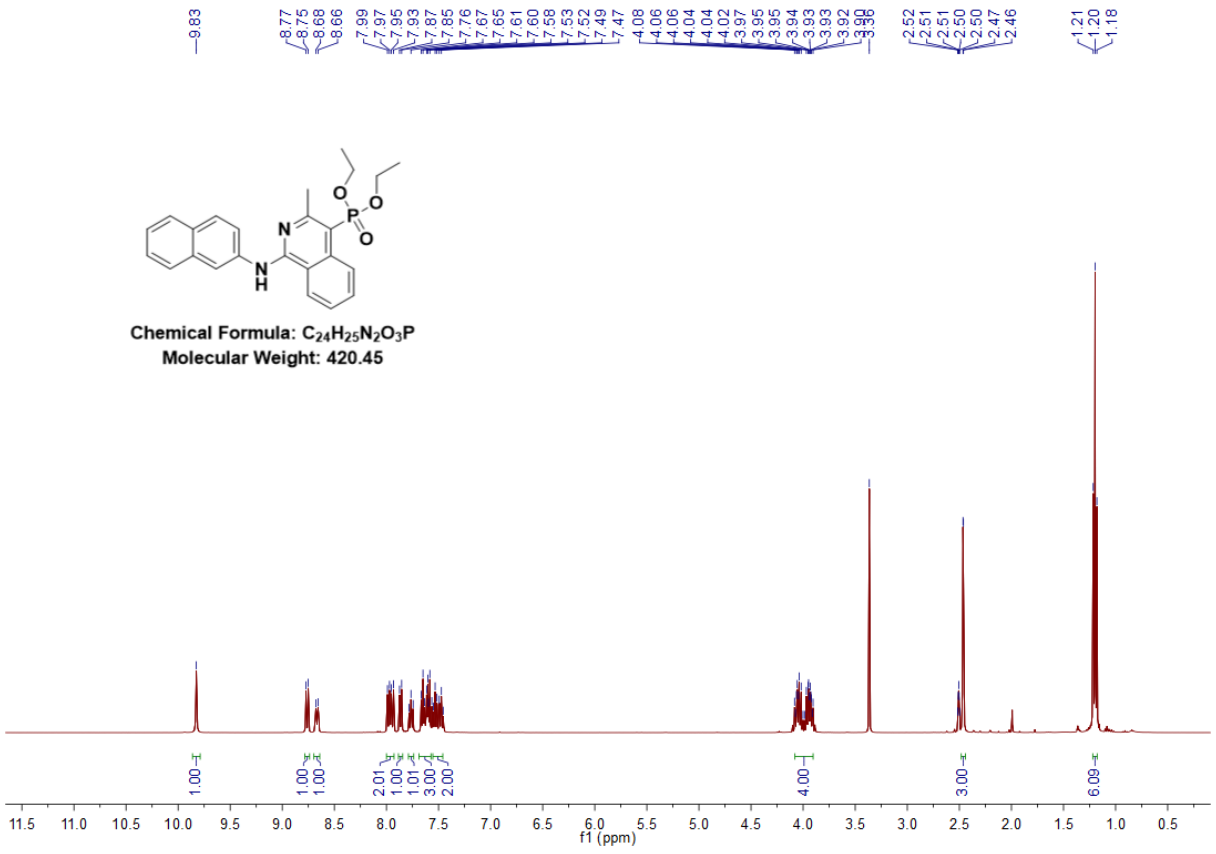
Fragmentor Voltage	Collision Energy	Ionization Mode
175	0	ESI

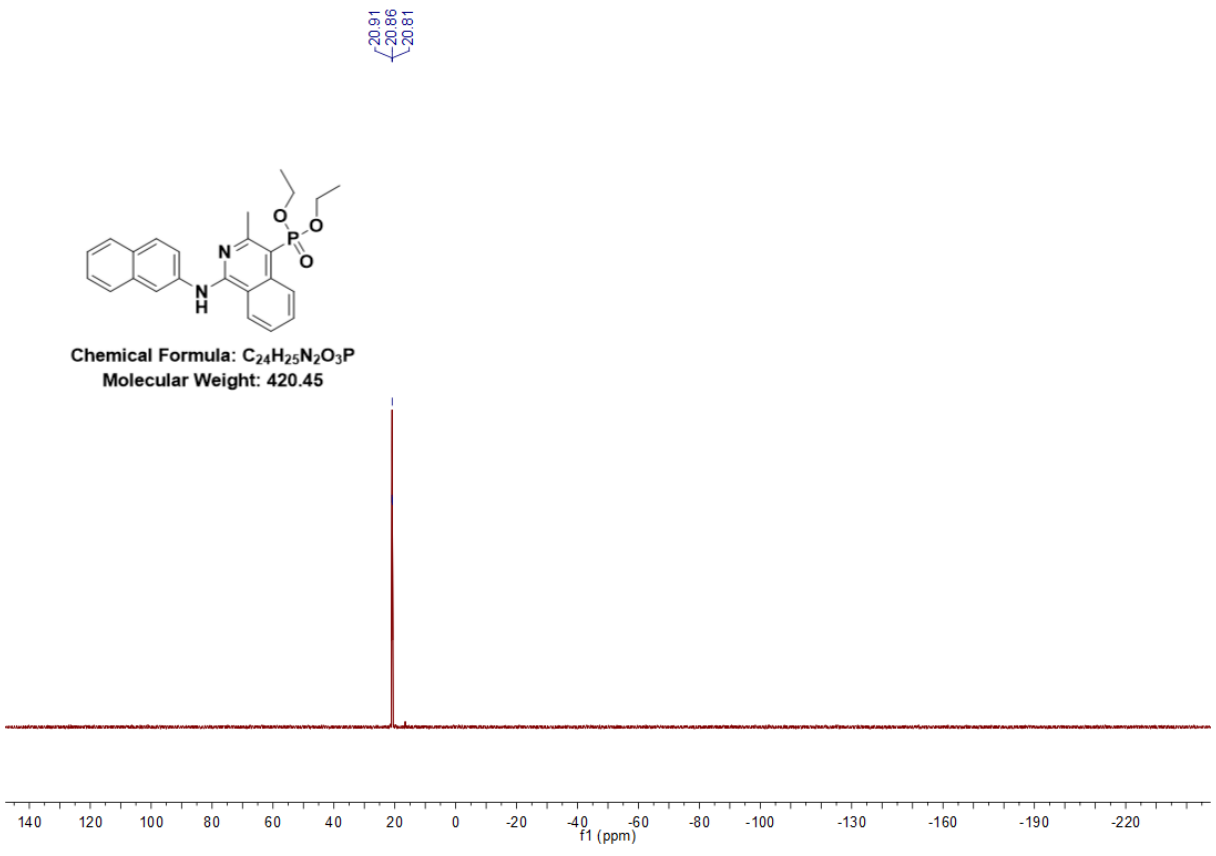


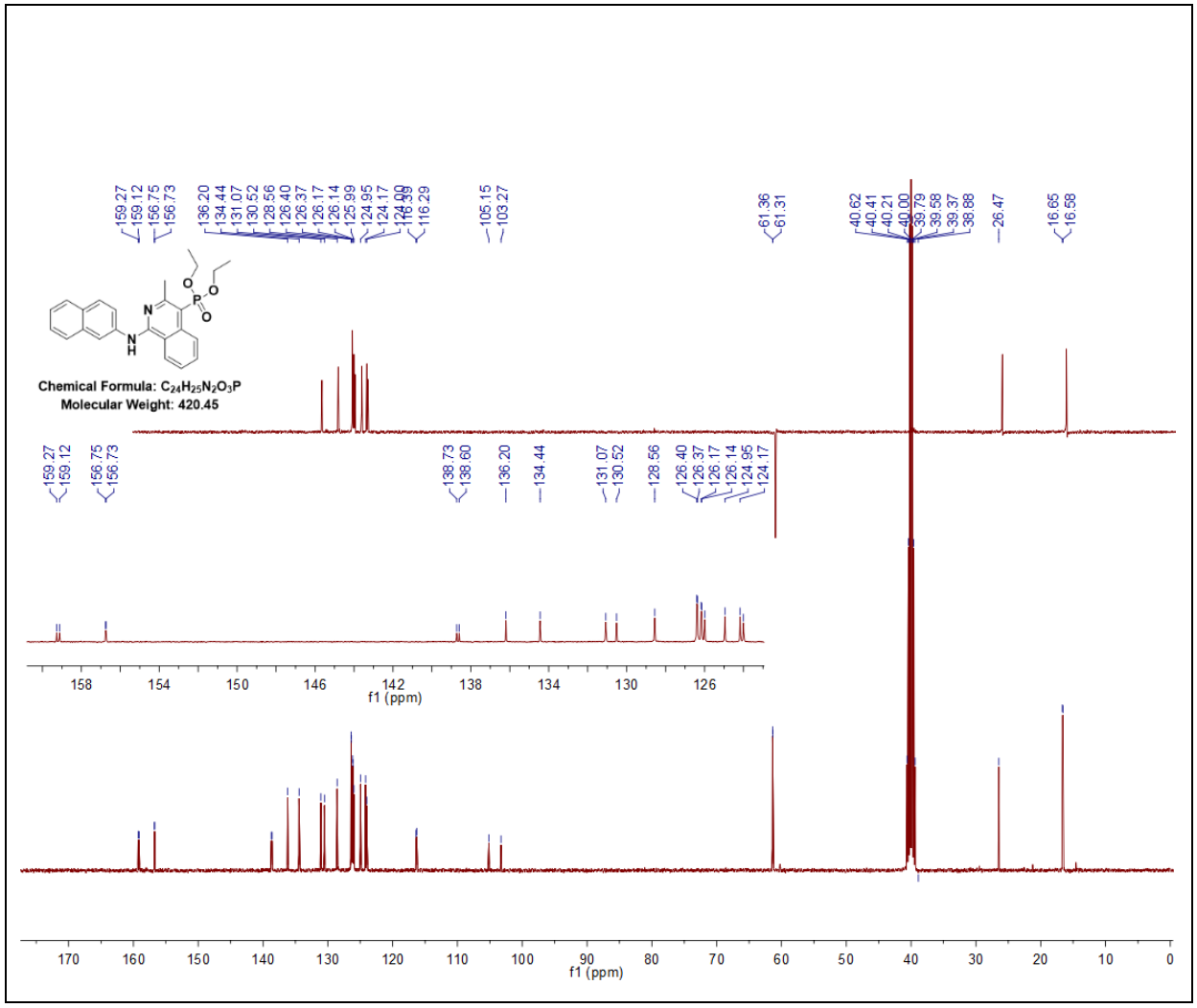
Formula Calculator Results

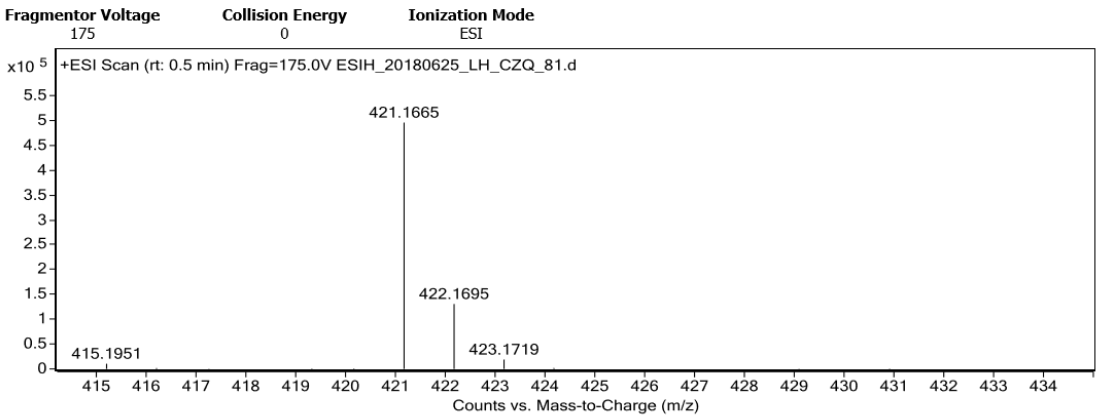
m/z	Calc m/z	Diff (mDa)	Diff (ppm)	Ion Formula	Ion
389.1436	389.1425	-1.16	-2.97	C20 H23 F N2 O3 P	(M+H)+

Diethyl (3-methyl-1-(naphthalen-2-ylamino)isoquinolin-4-yl)phosphonate (3o)





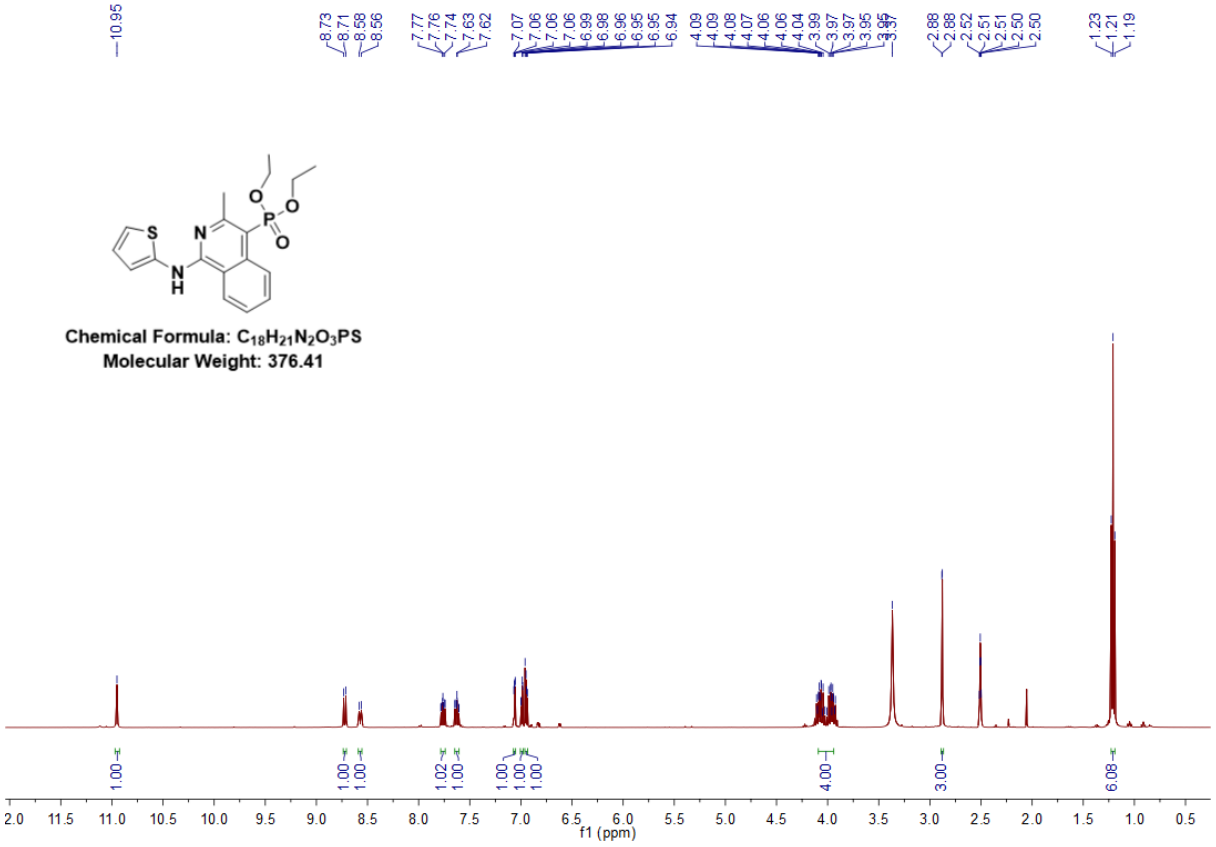


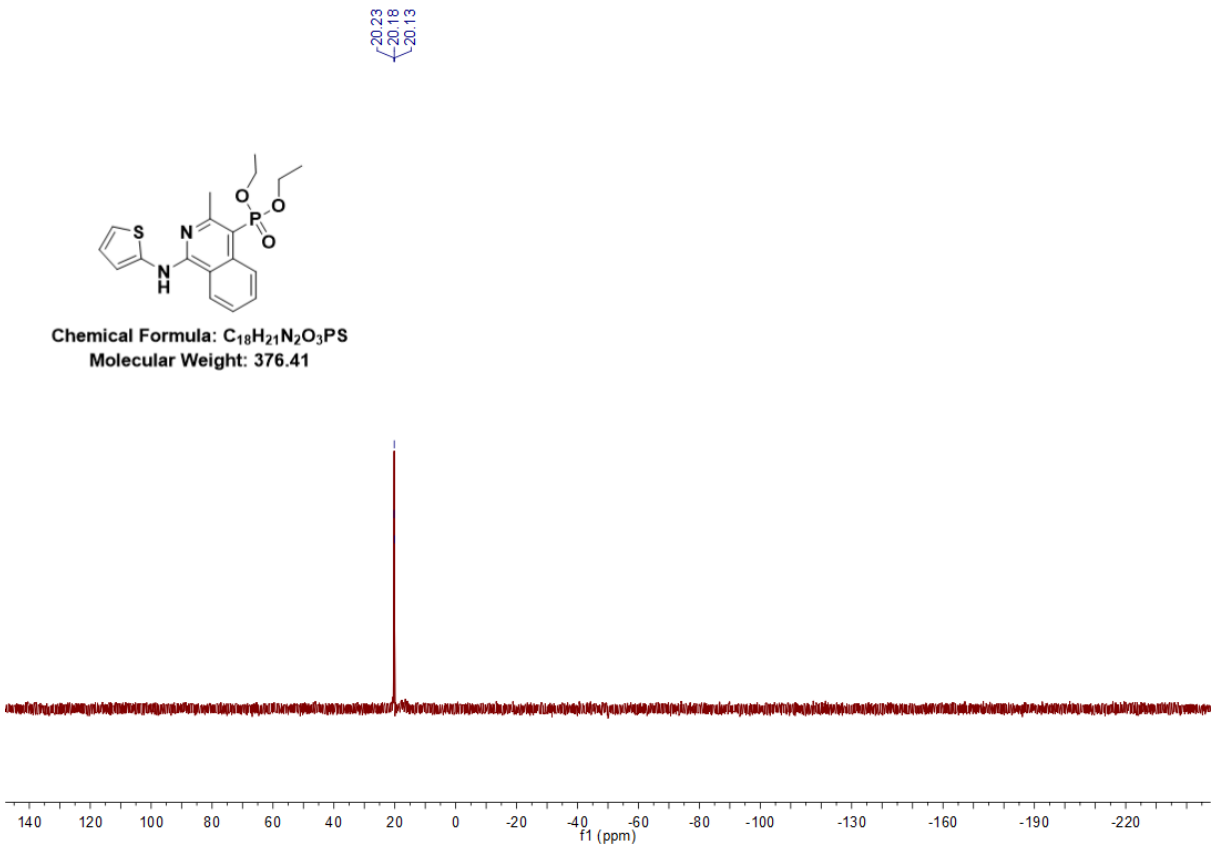


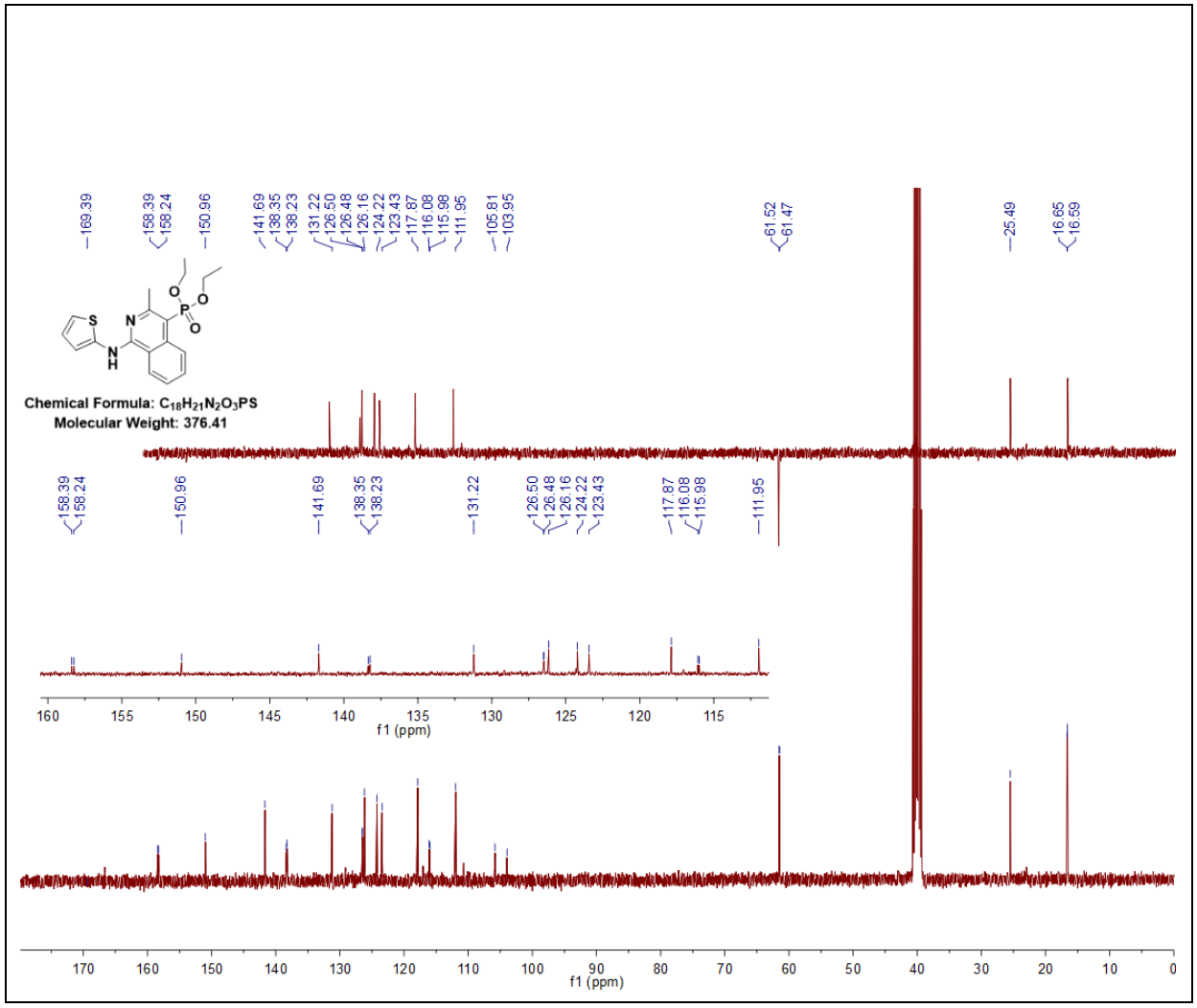
Formula Calculator Results

m/z	Calc m/z	Diff (mDa)	Diff (ppm)	Ion Formula	Ion
421.1665	421.1676	1.06	2.51	C24 H26 N2 O3 P	(M+H)+

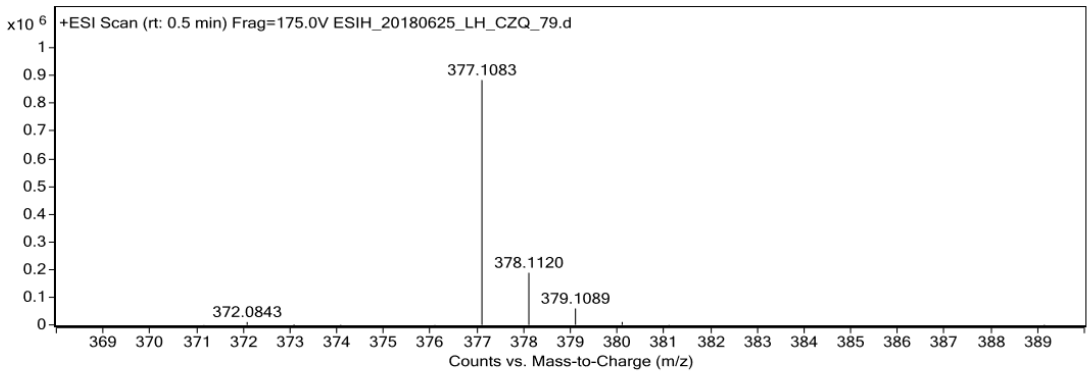
Diethyl (3-methyl-1-(thiophen-2-ylamino)isoquinolin-4-yl)phosphonate (3p)







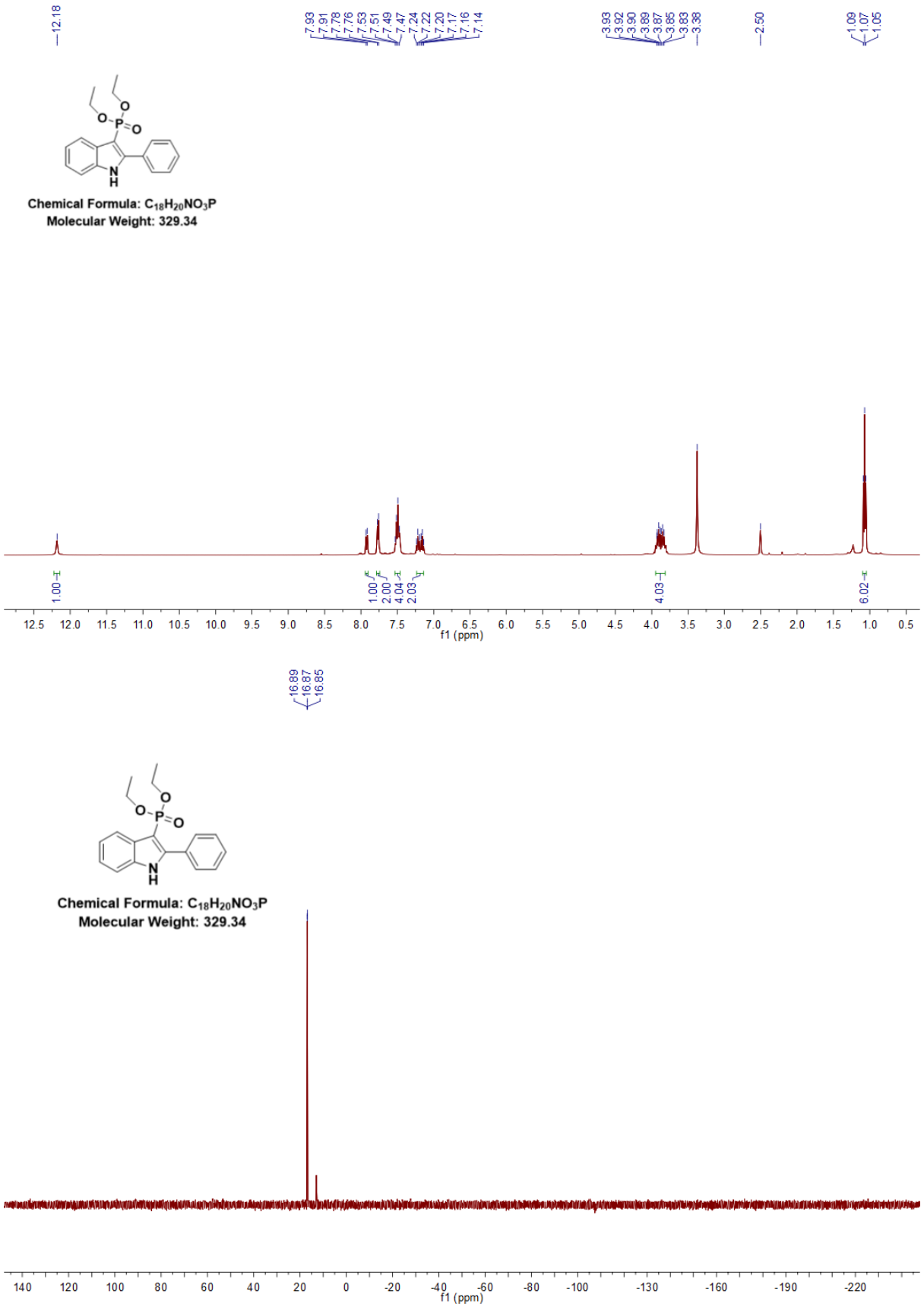
Fragmentor Voltage	Collision Energy	Ionization Mode
175	0	ESI

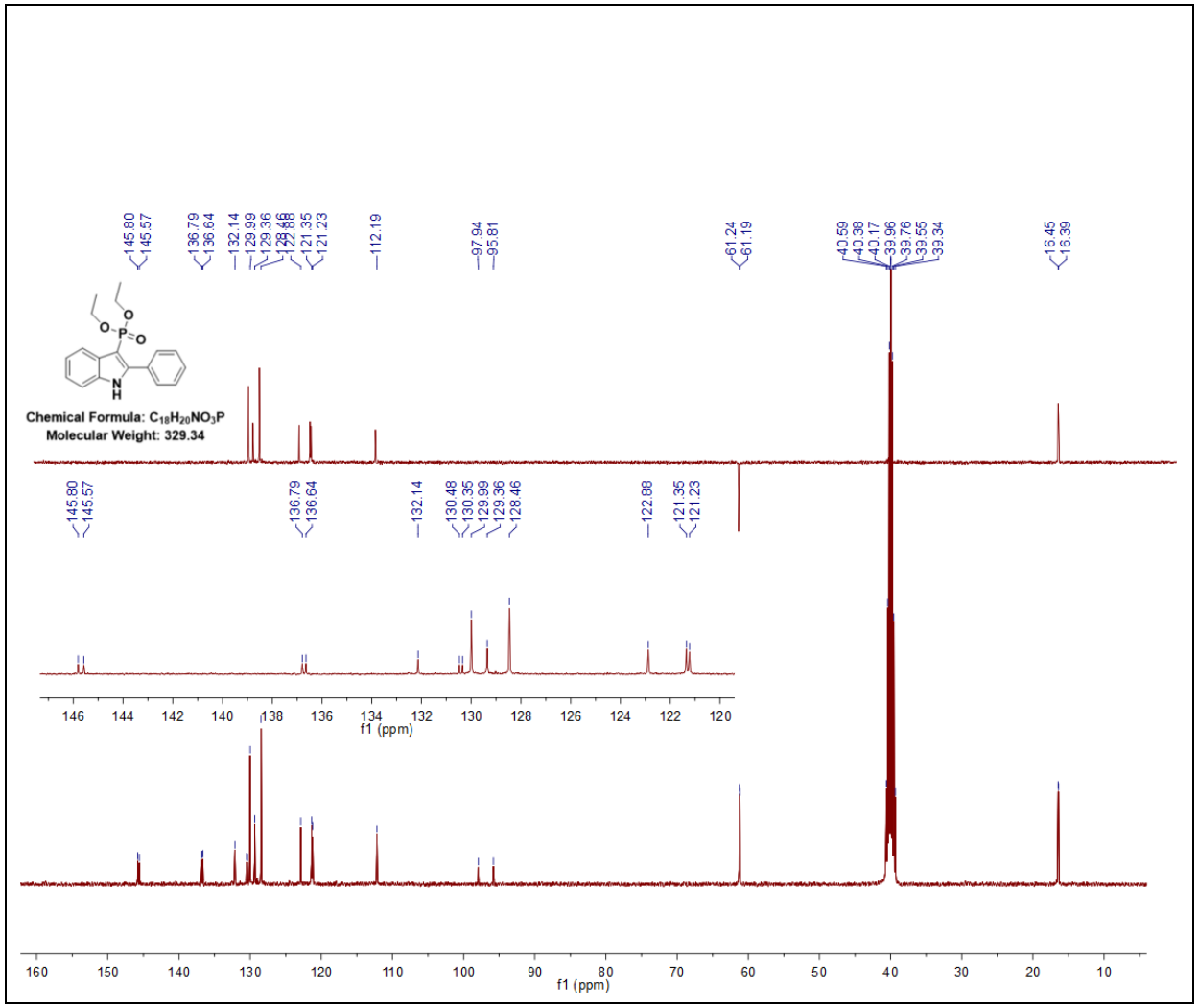


Formula Calculator Results

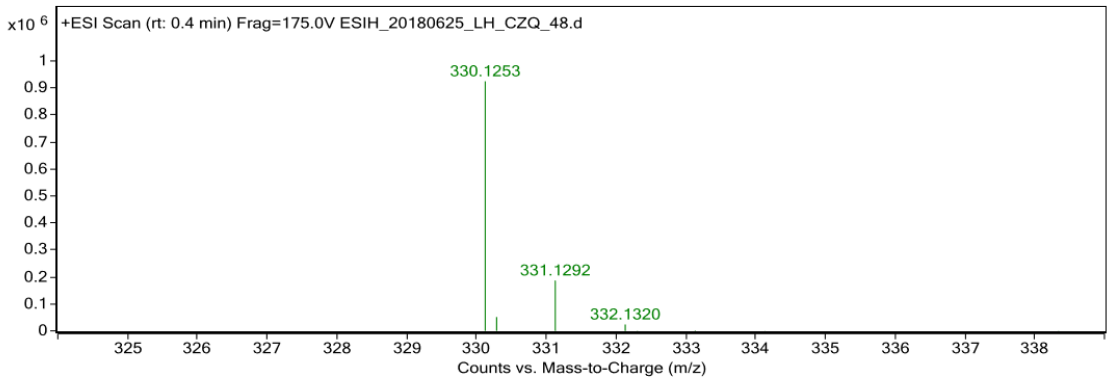
m/z	Calc m/z	Diff (mDa)	Diff (ppm)	Ion Formula	Ion
377.1083	377.1083	0.02	0.05	C18 H22 N2 O3 P S	(M+H)+

Diethyl (2-phenyl-1H-indol-3-yl)phosphonate (4a)





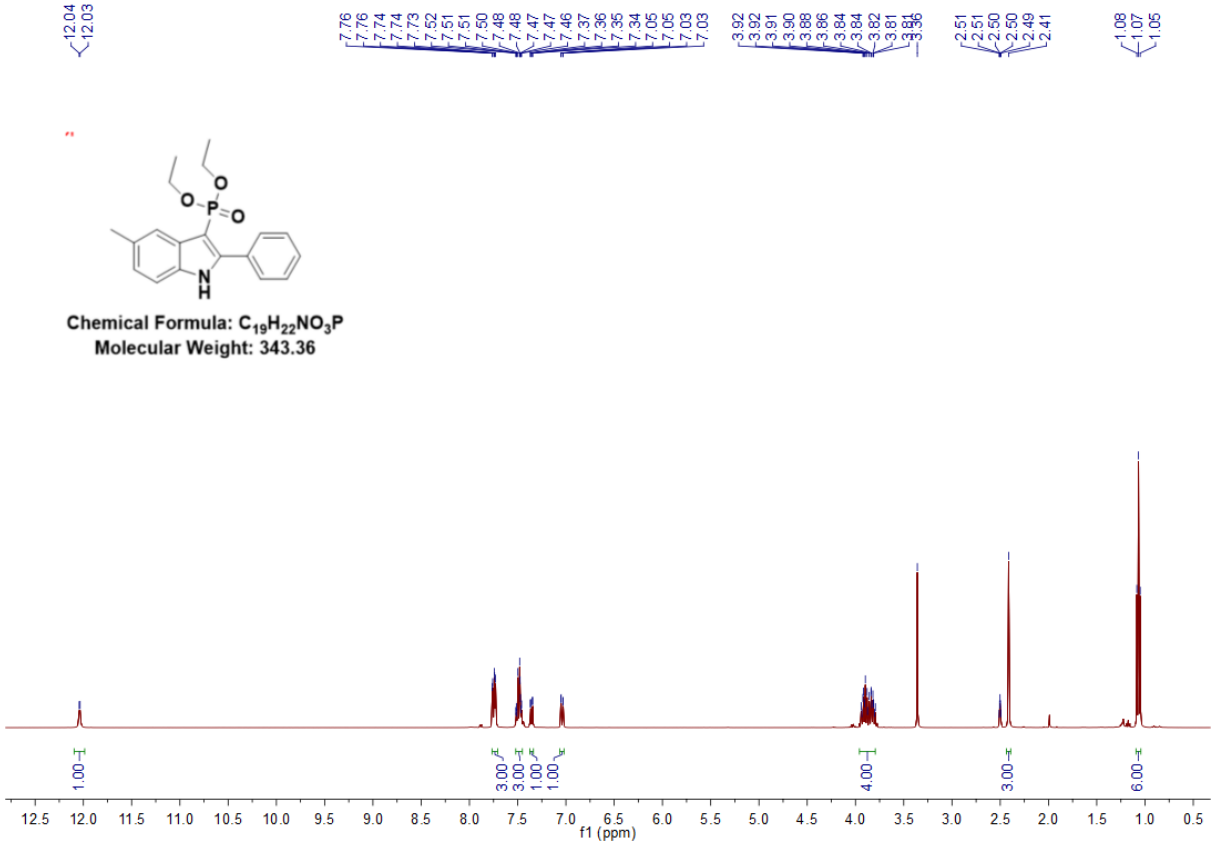
Fragmentor Voltage	Collision Energy	Ionization Mode
175	0	ESI

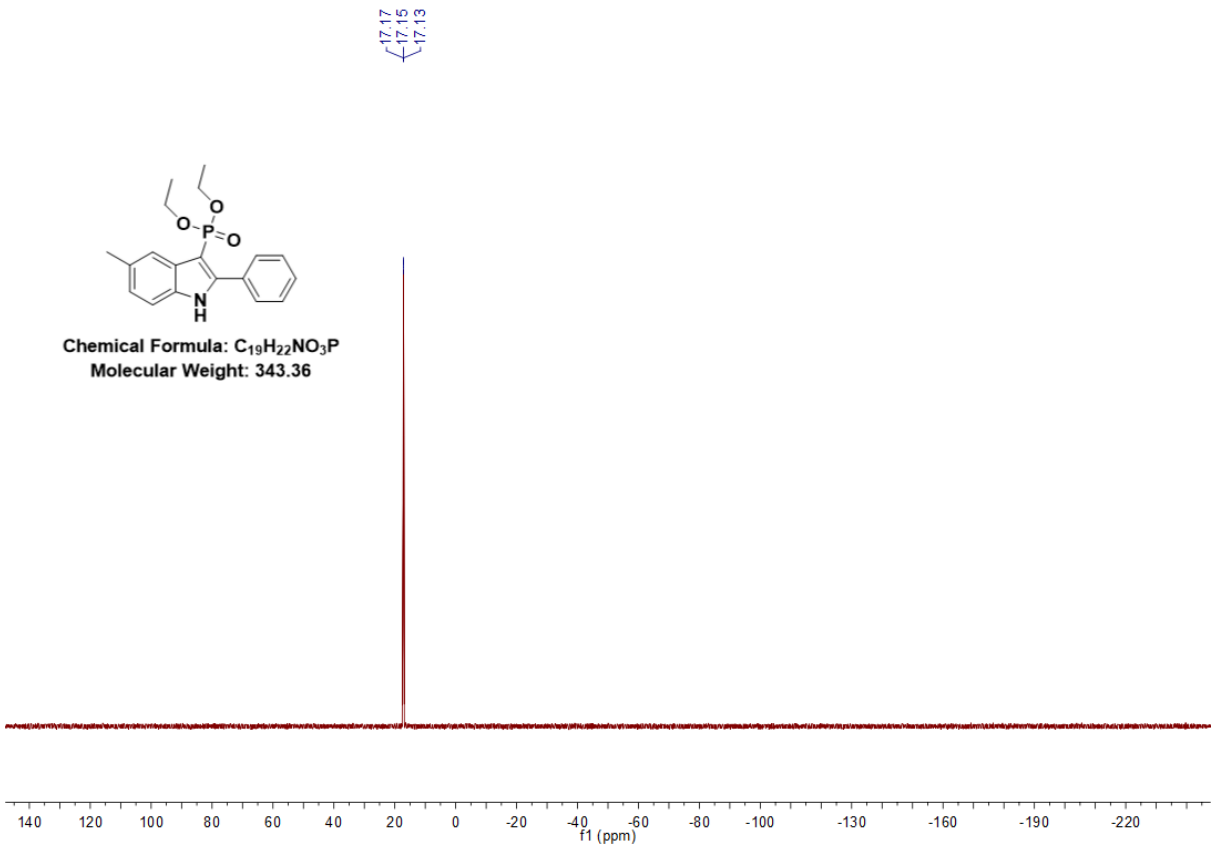


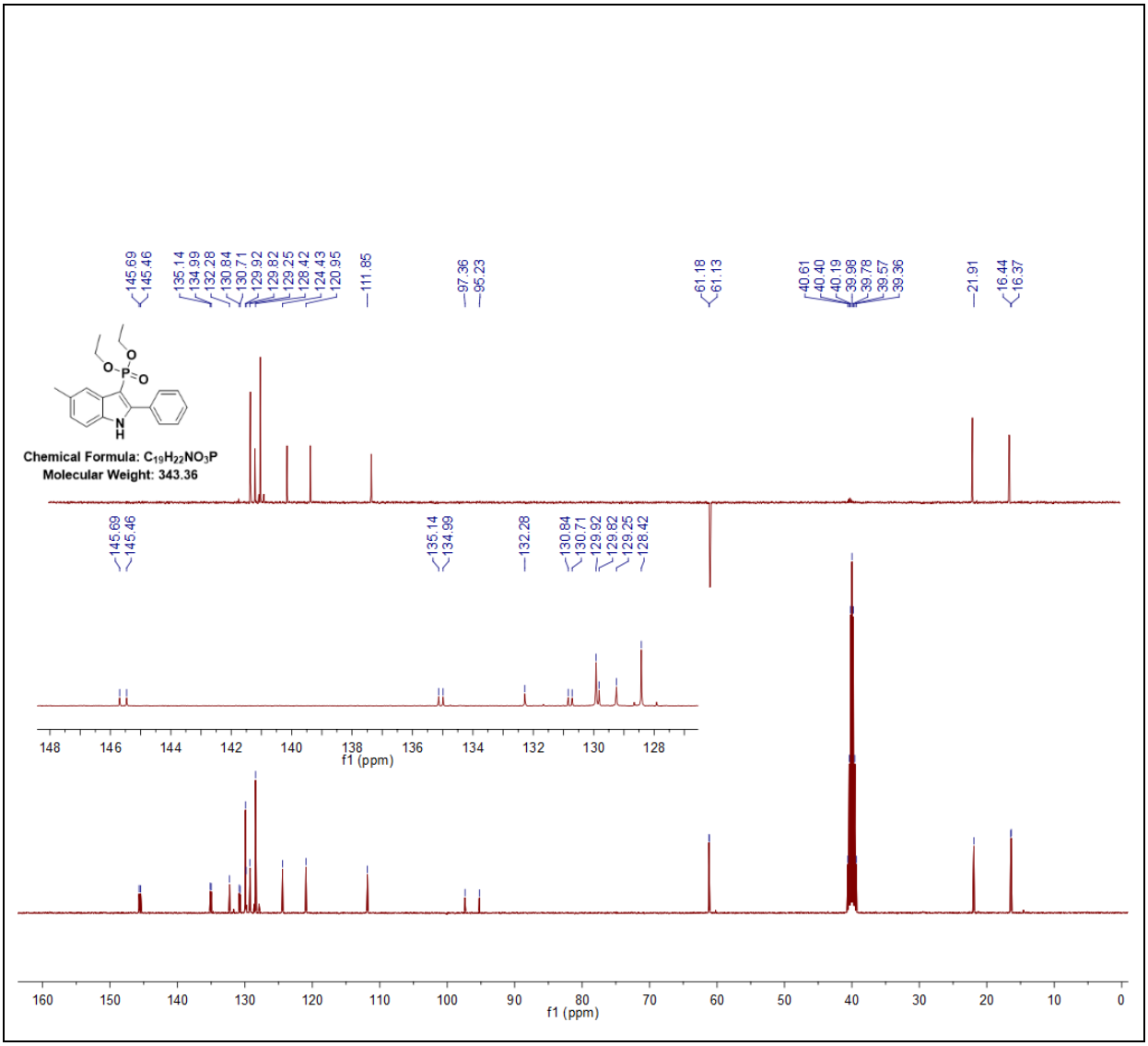
Formula Calculator Results

m/z	Calc m/z	Diff (mDa)	Diff (ppm)	Ion Formula	Ion
330.1253	330.1254	0.06	0.18	C18 H21 N O3 P	(M+H)+

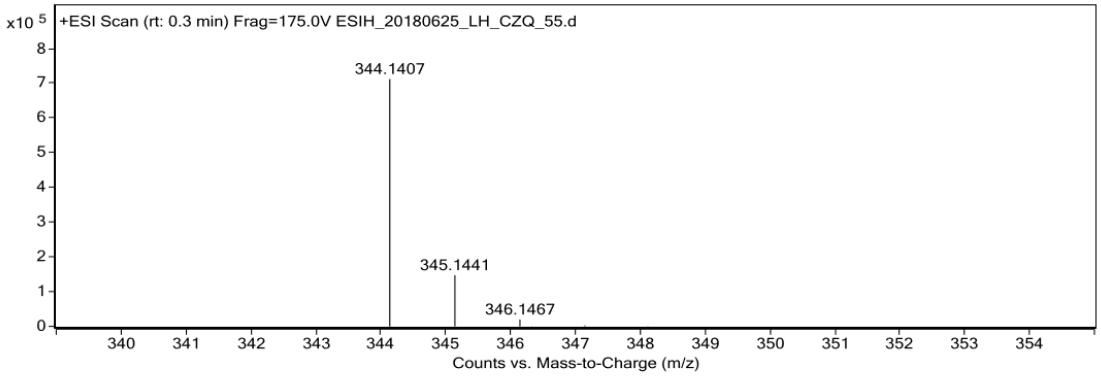
Diethyl (5-methyl-2-phenyl-1H-indol-3-yl)phosphonate (4b)







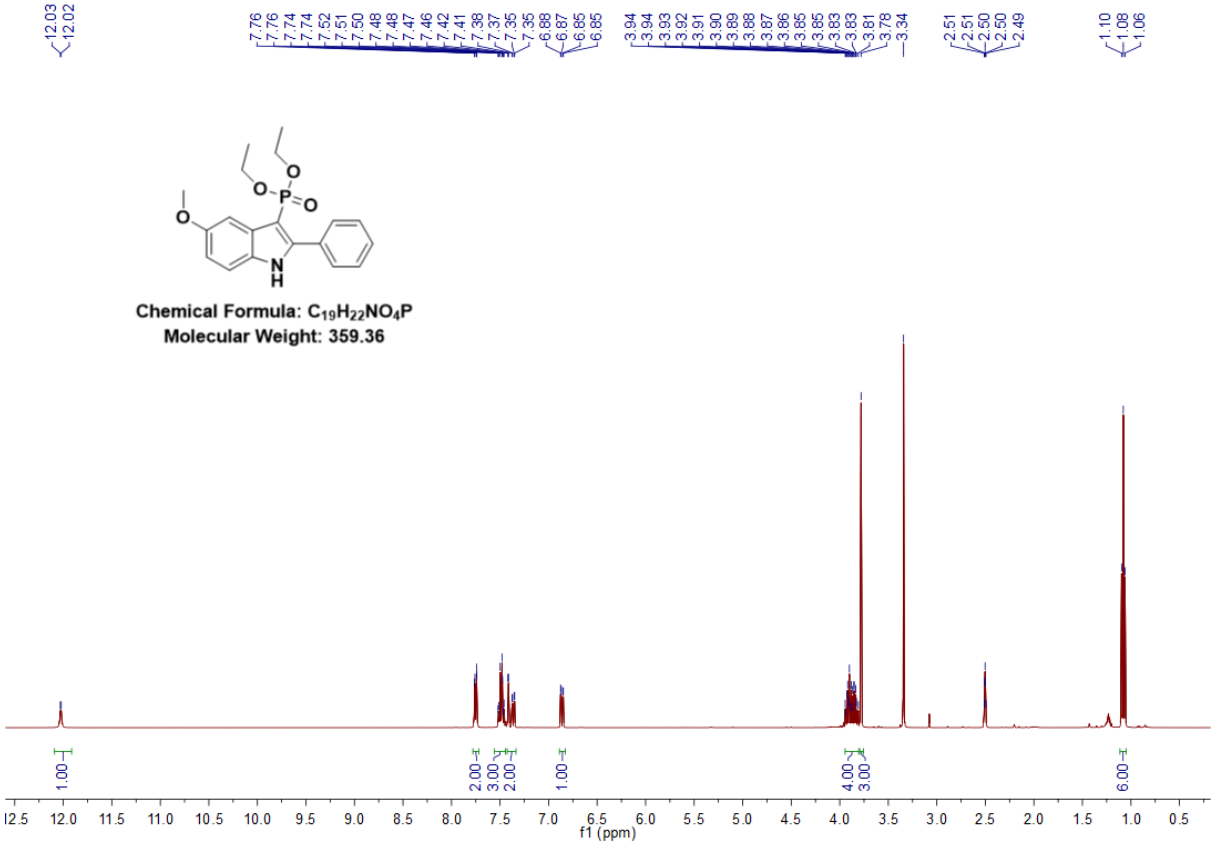
Fragmentor Voltage	Collision Energy	Ionization Mode
175	0	ESI

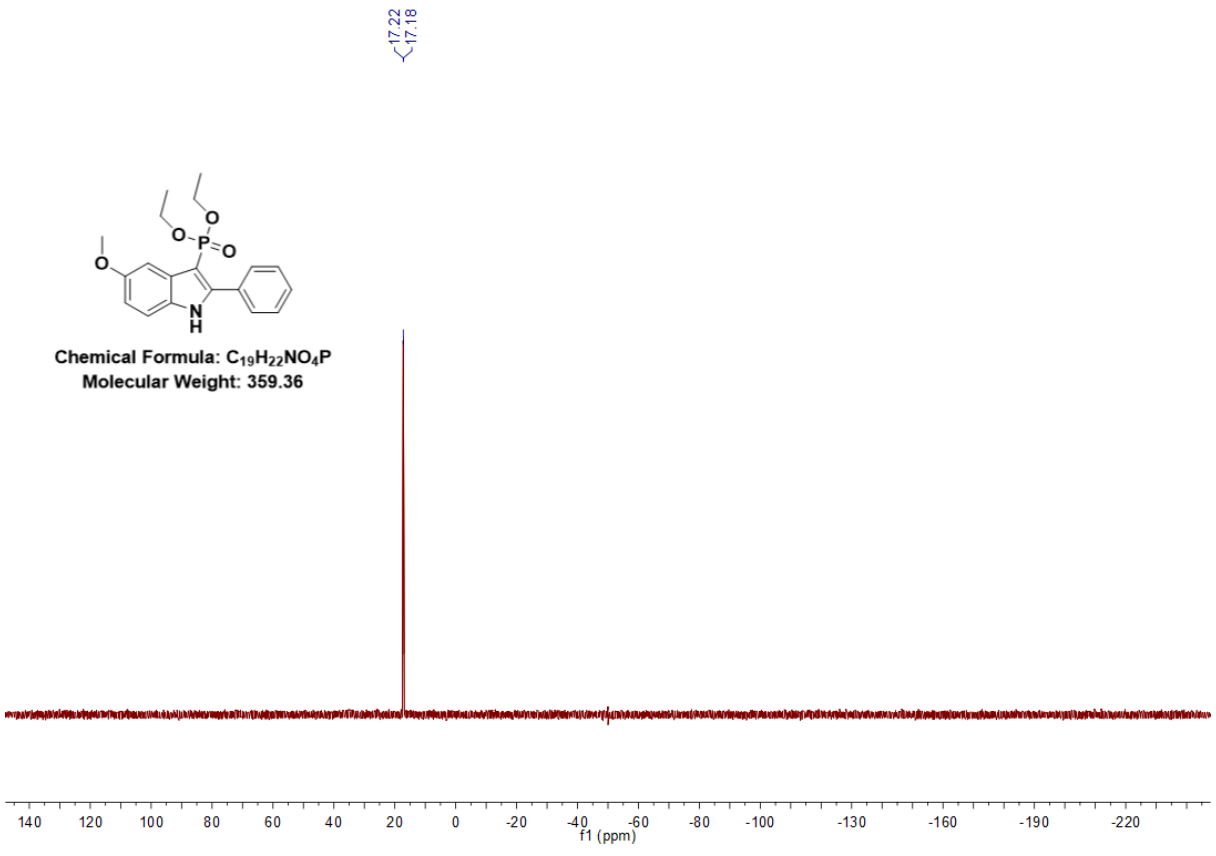


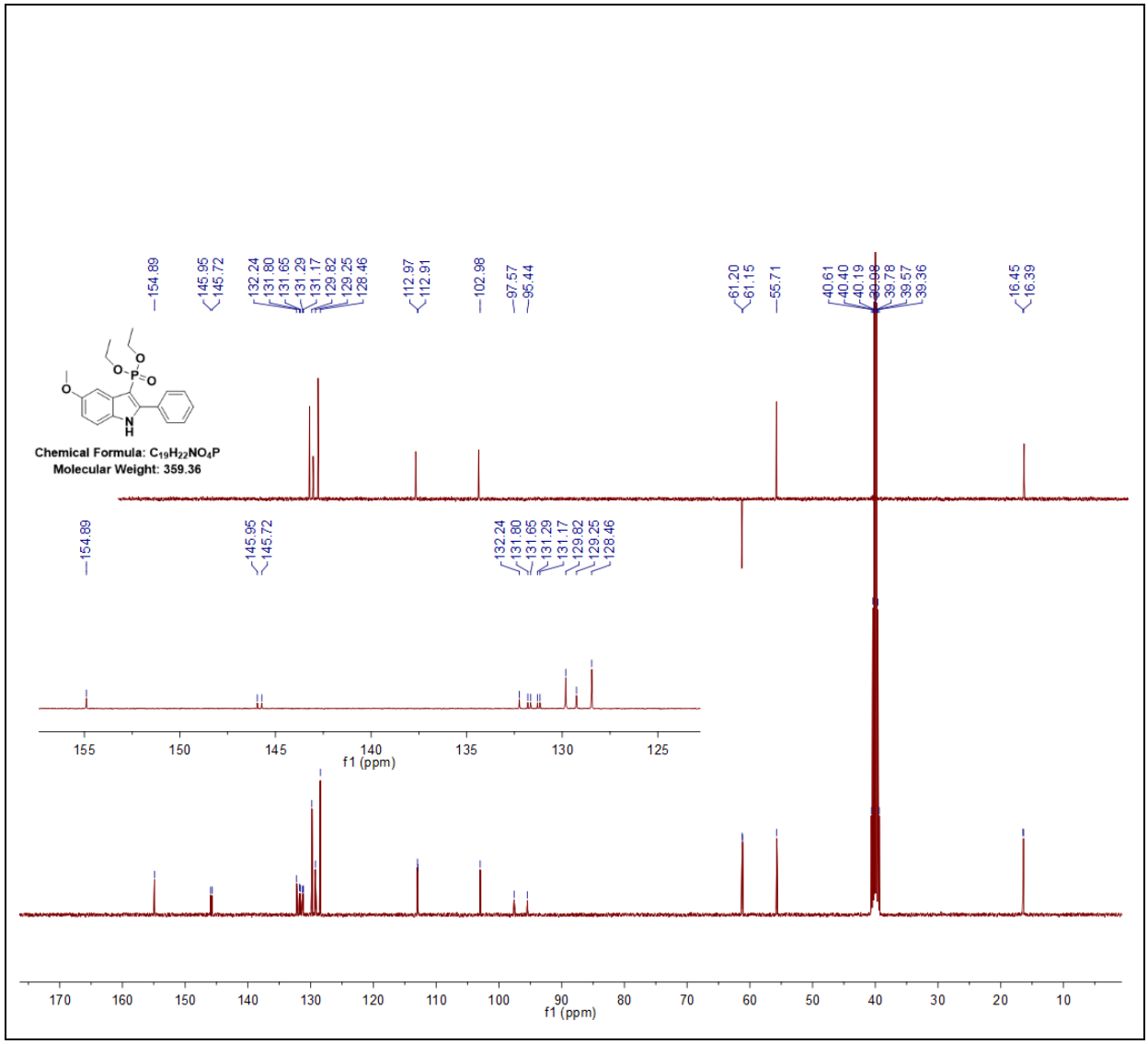
Formula Calculator Results

m/z	Calc m/z	Diff (mDa)	Diff (ppm)	Ion Formula	Ion
344.1407	344.141	0.35	1.03	C19 H23 N O3 P	(M+H)+

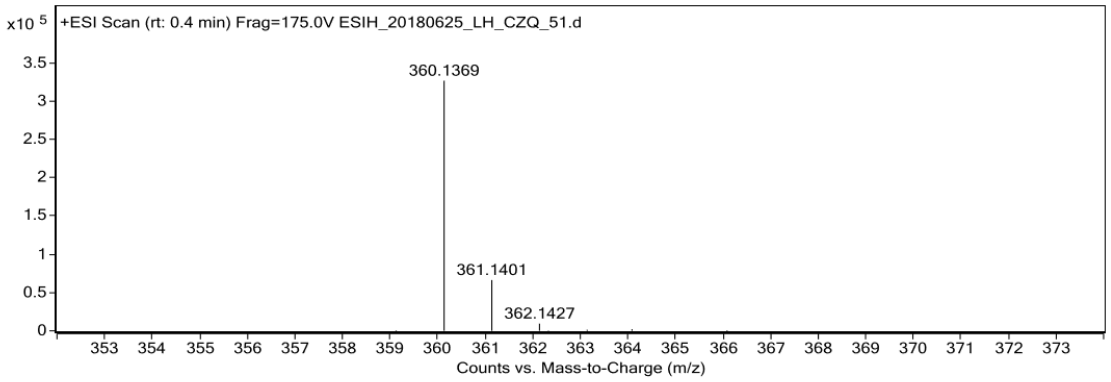
Diethyl (5-methoxy-2-phenyl-1H-indol-3-yl)phosphonate (4c)







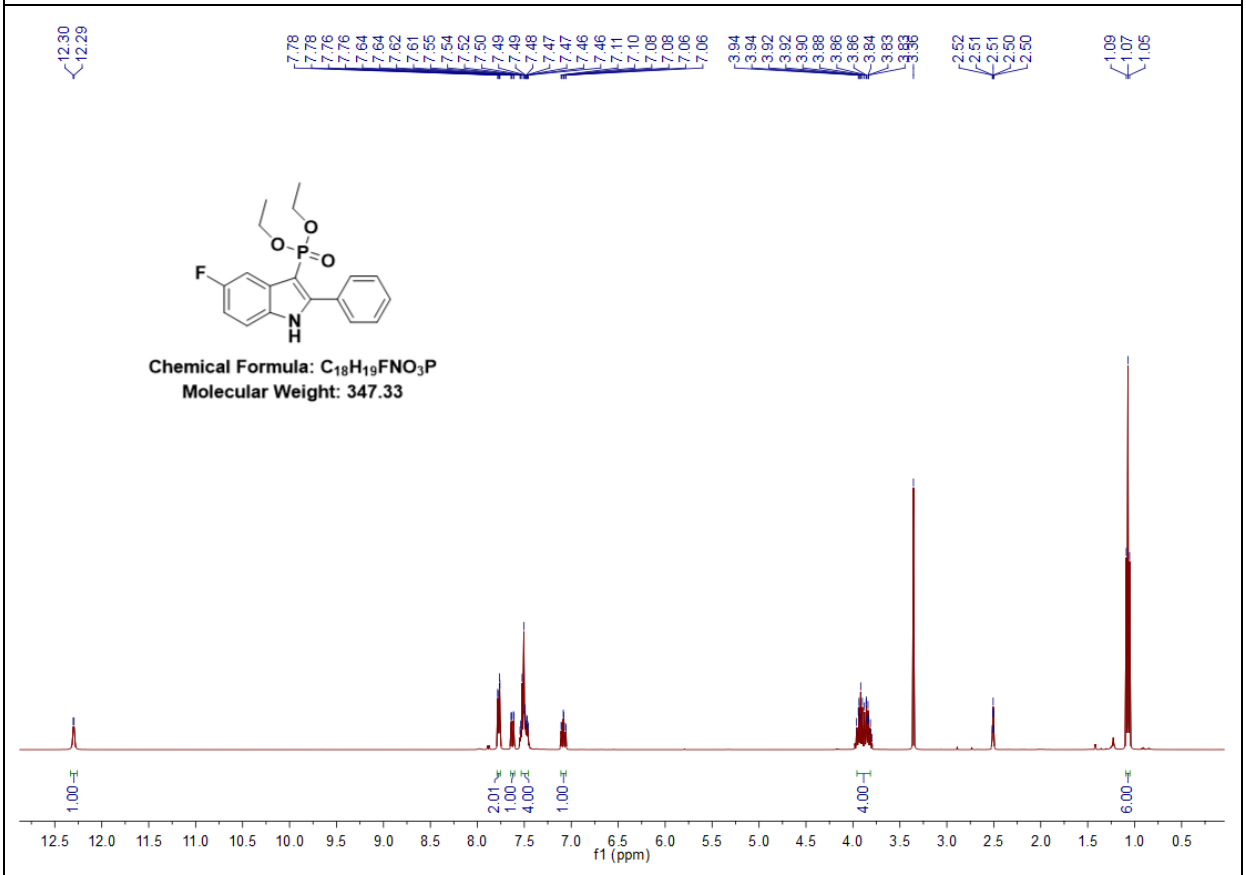
Fragmentor Voltage	Collision Energy	Ionization Mode
175	0	ESI

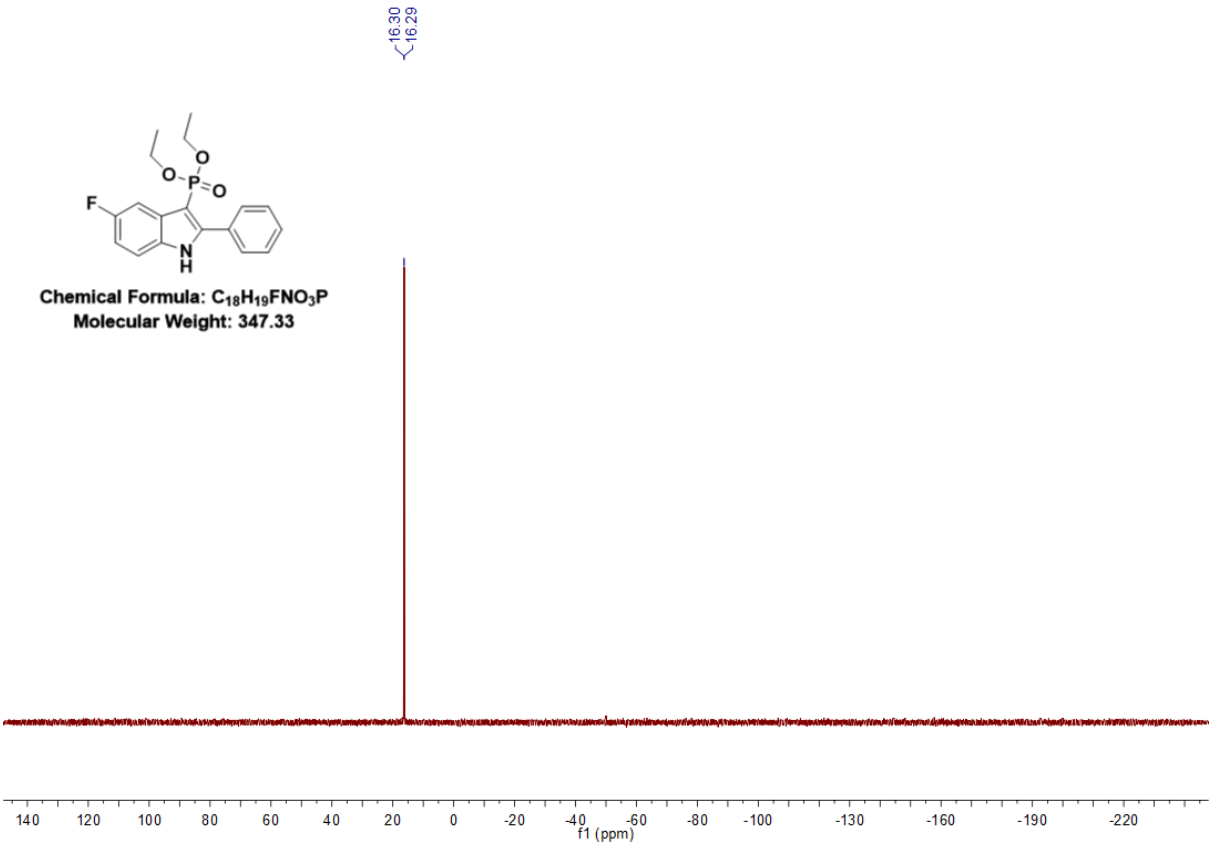


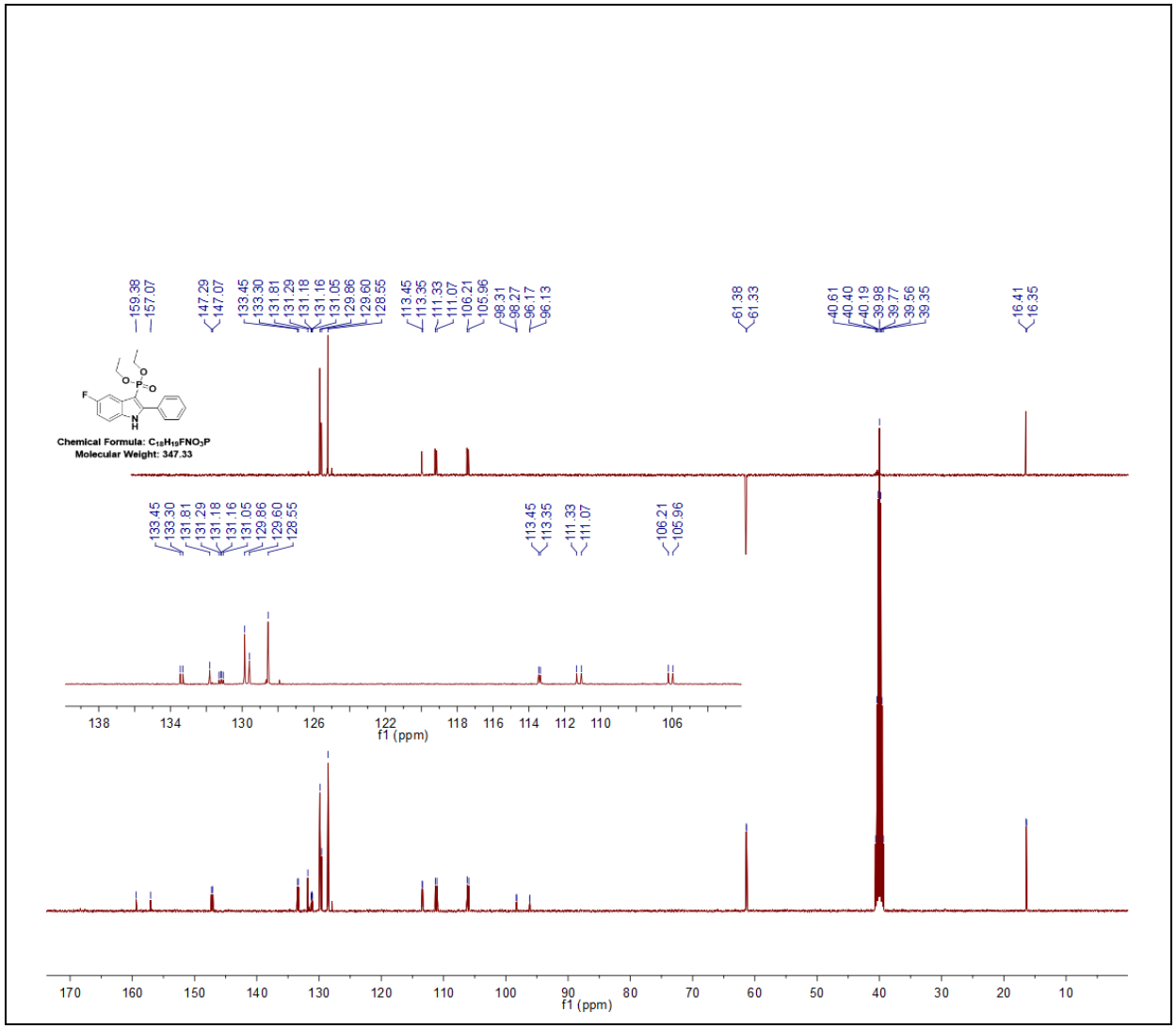
Formula Calculator Results

m/z	Calc m/z	Diff (mDa)	Diff (ppm)	Ion Formula	Ion
360.1369	360.1359	-1.01	-2.82	C19 H23 N O4 P	(M+H)+

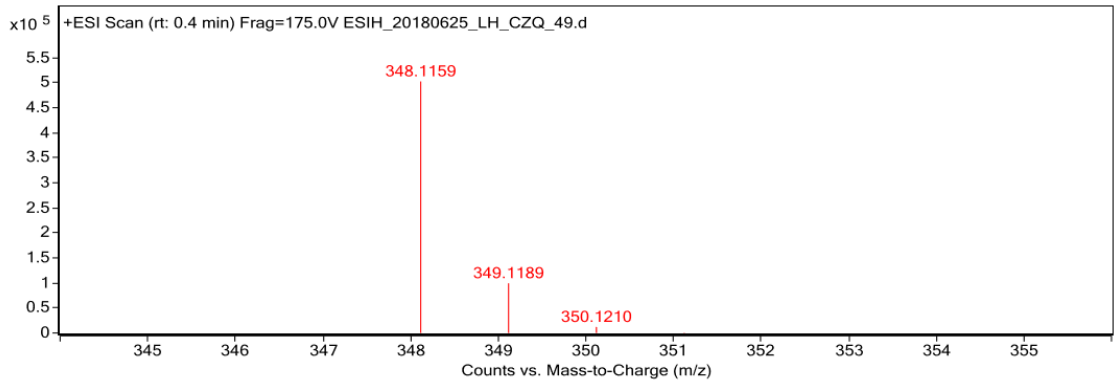
Diethyl (5-fluoro-2-phenyl-1H-indol-3-yl)phosphonate (4d)







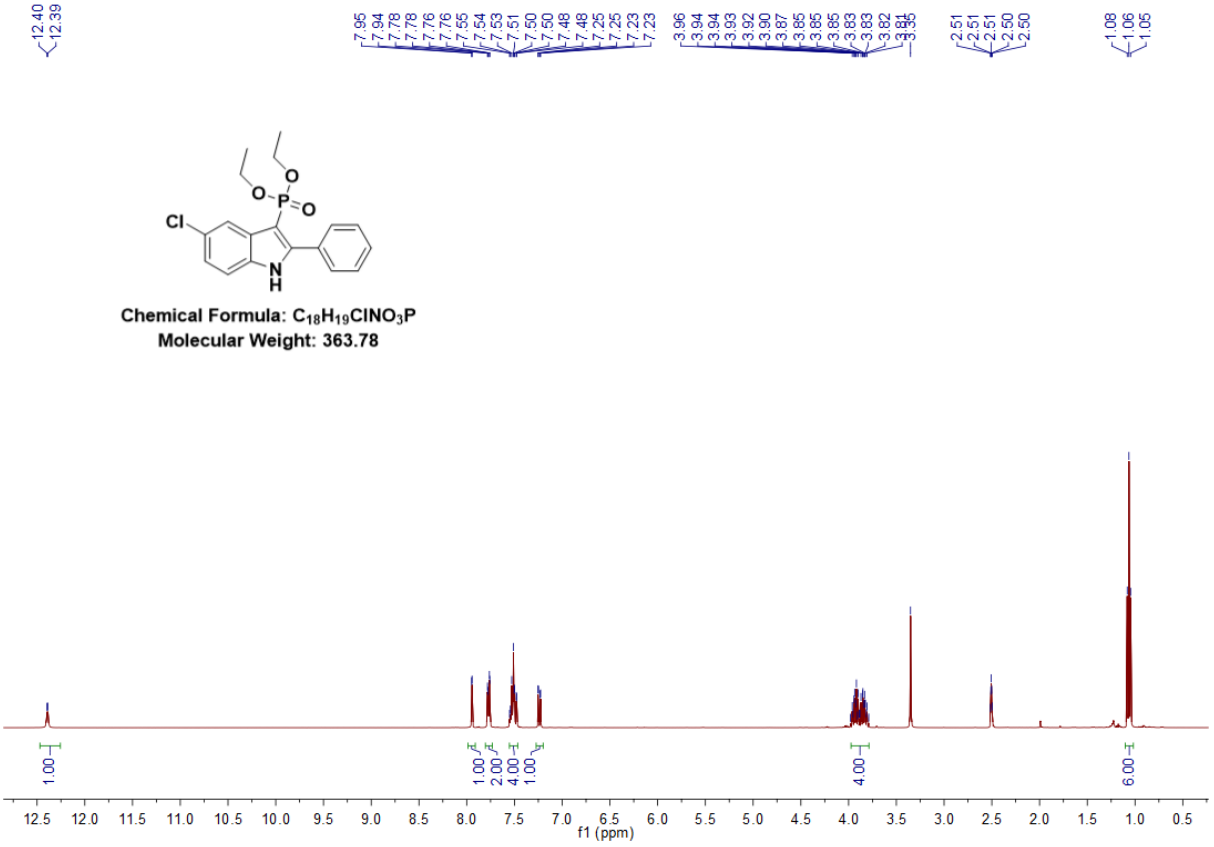
Fragmentor Voltage	Collision Energy	Ionization Mode
175	0	ESI

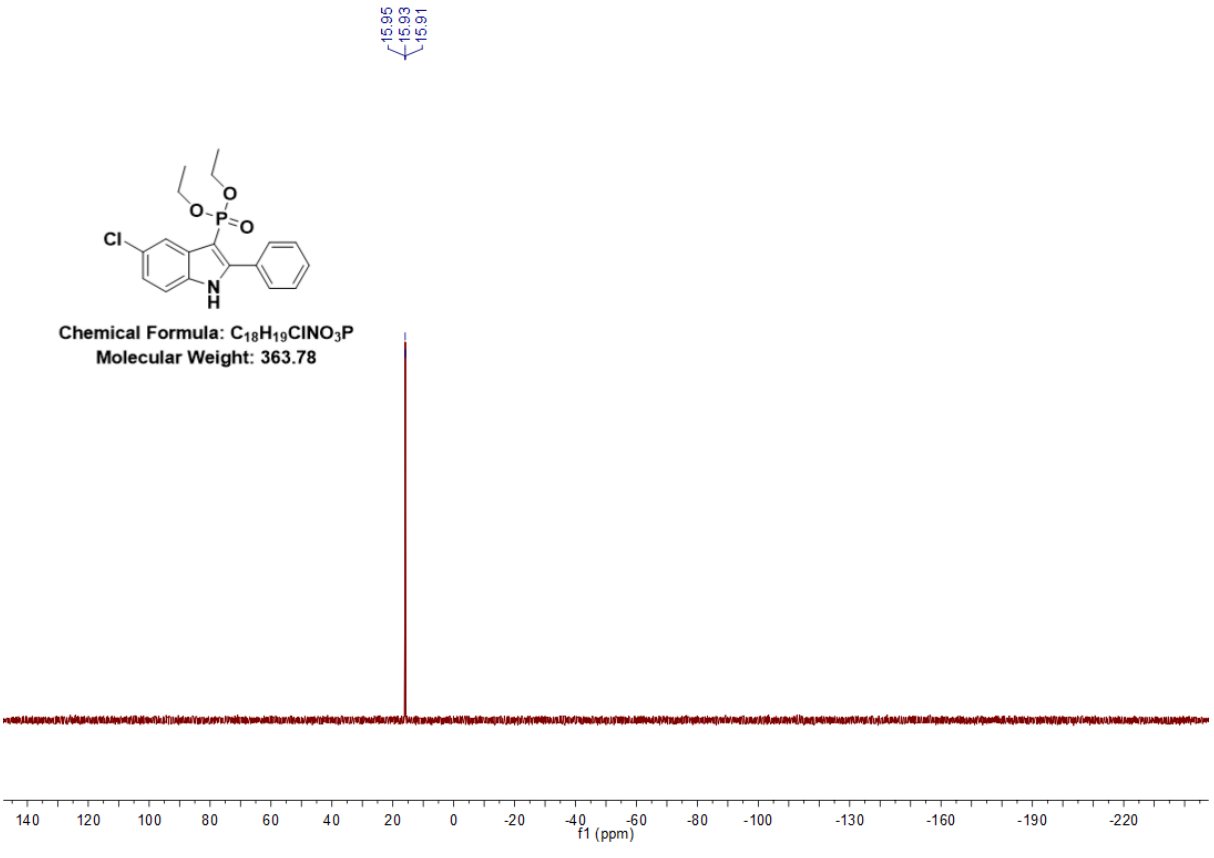


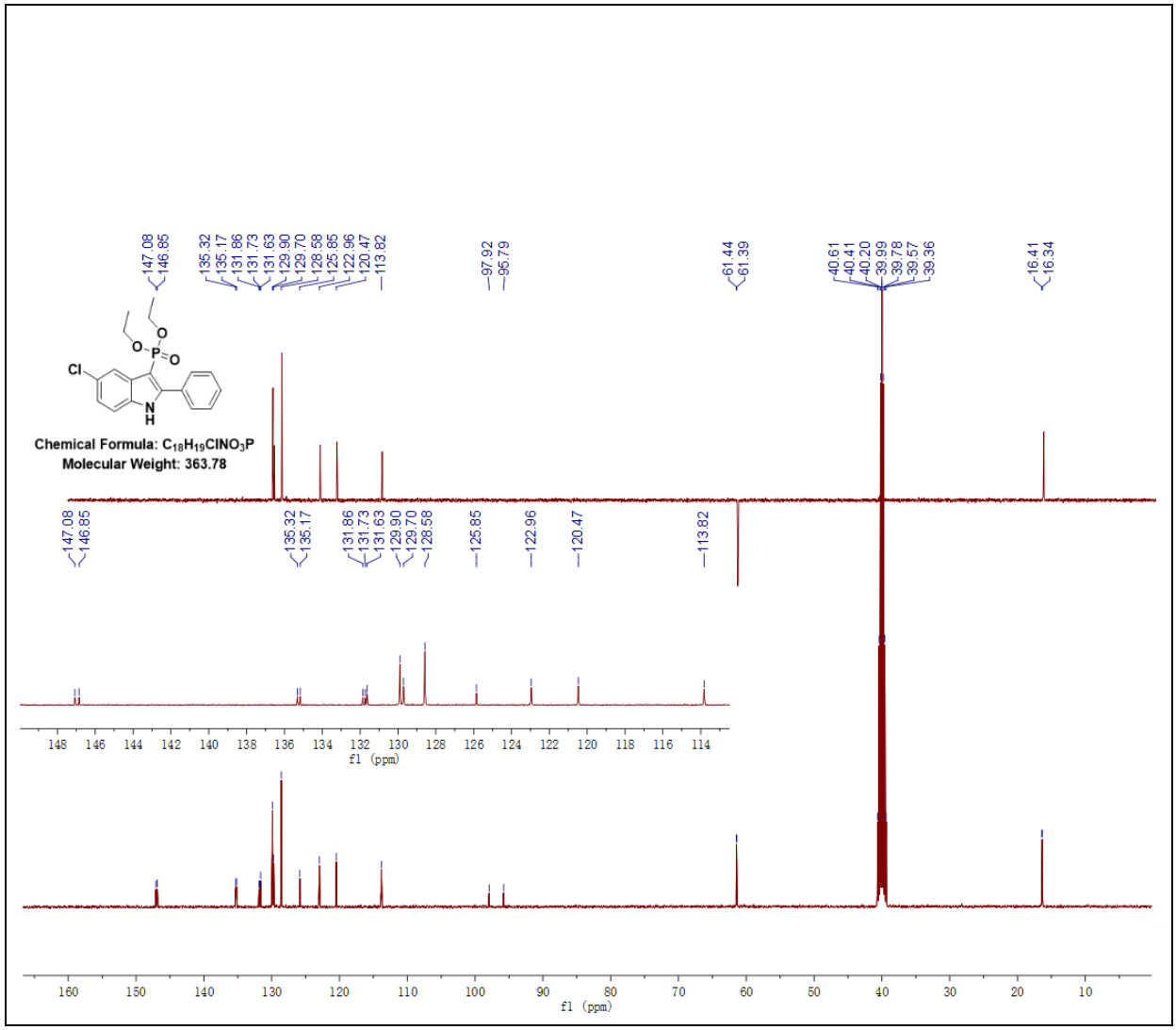
Formula Calculator Results

m/z	Calc m/z	Diff (mDa)	Diff (ppm)	Ion Formula	Ion
348.1159	348.1159	0.06	0.18	C18 H20 F N O3 P	(M+H)+

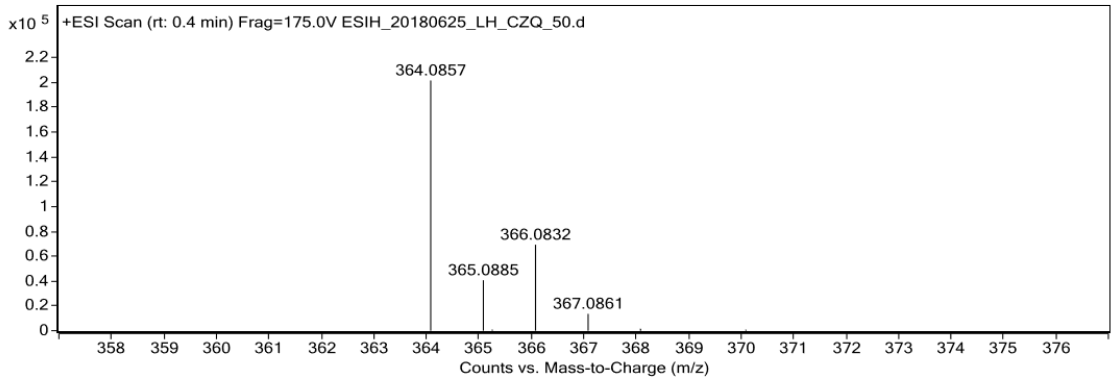
Diethyl (5-chloro-2-phenyl-1H-indol-3-yl)phosphonate (4e)







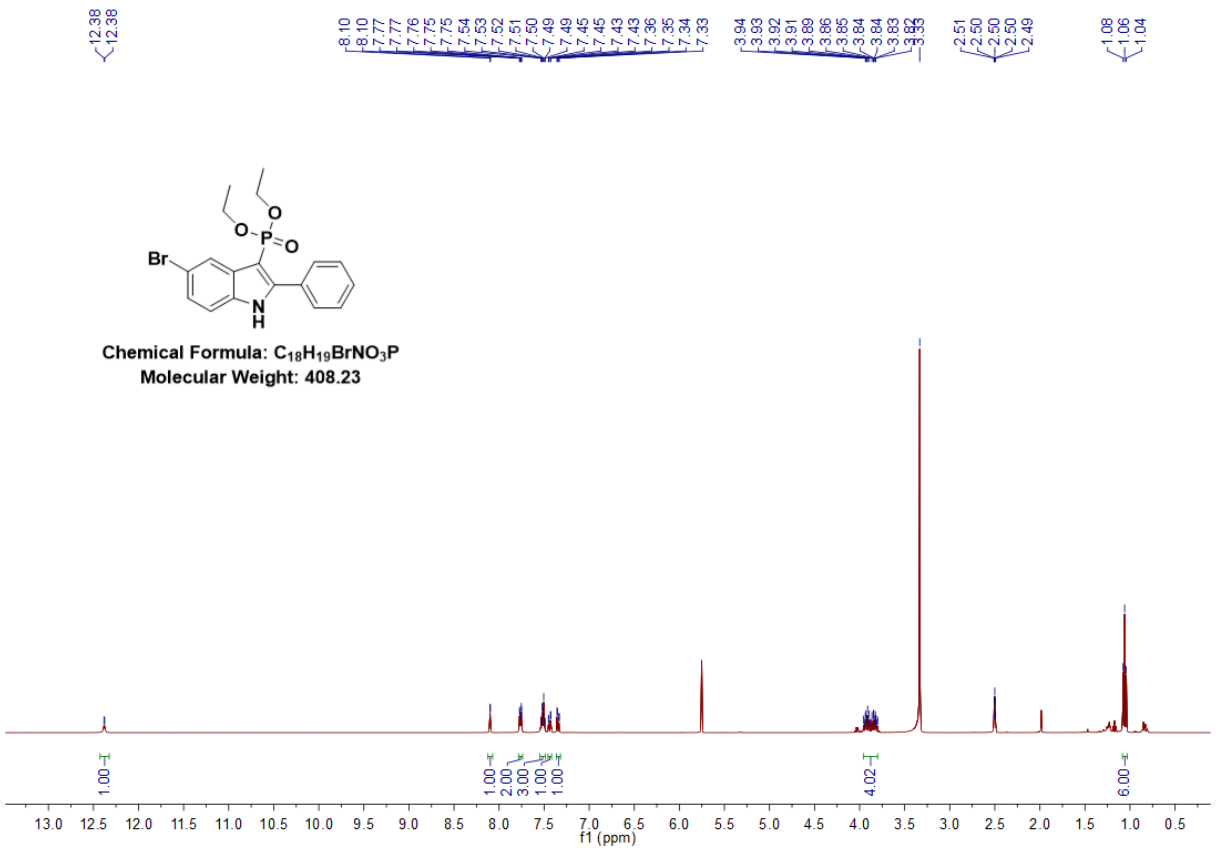
Fragmentor Voltage 175 **Collision Energy** 0 **Ionization Mode** ESI

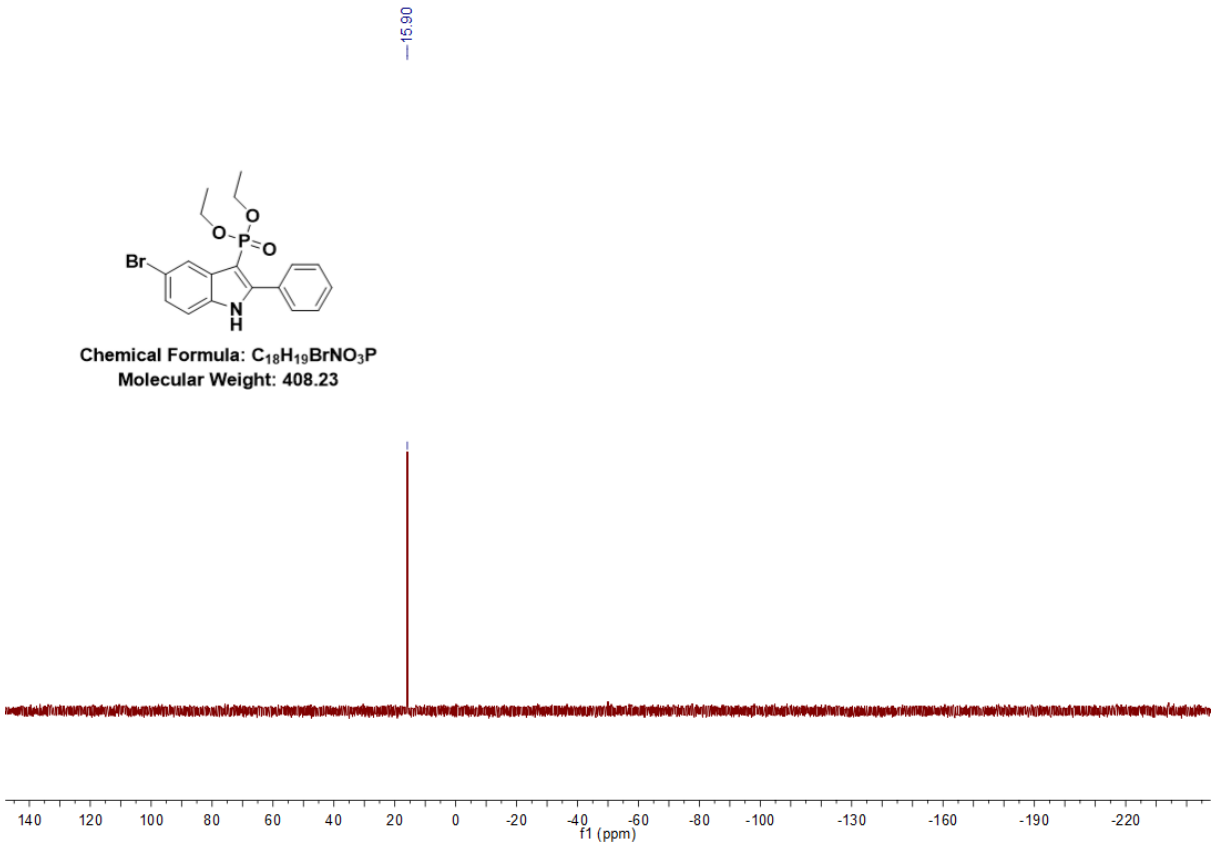


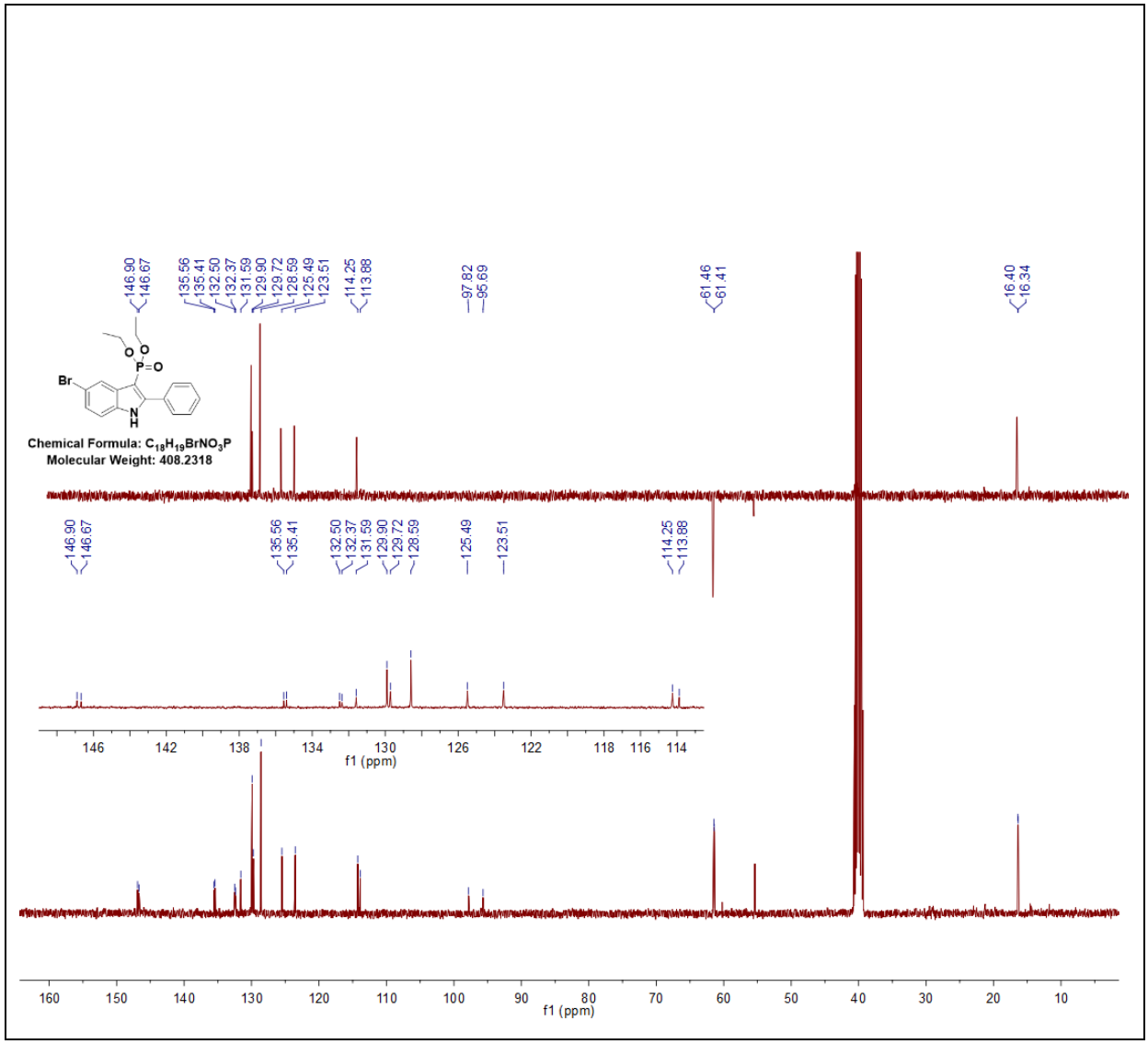
Formula Calculator Results

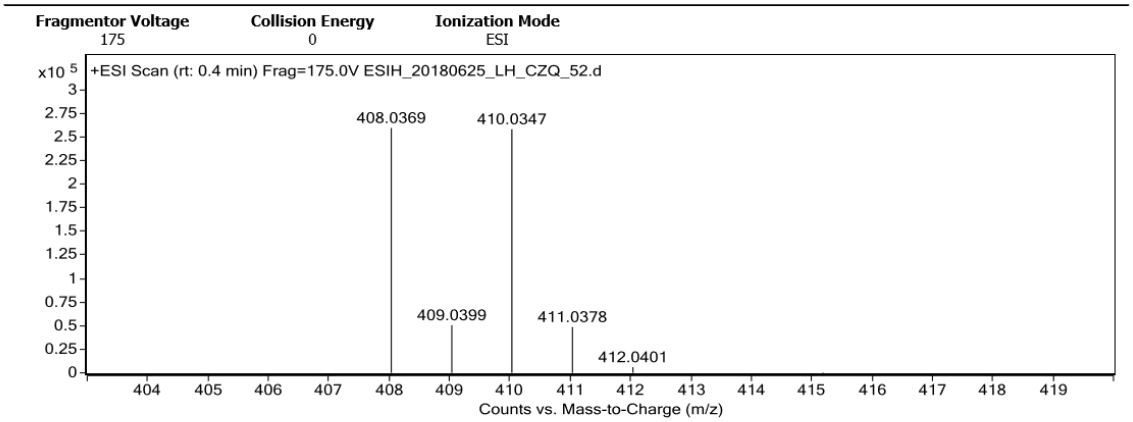
m/z	Calc m/z	Diff (mDa)	Diff (ppm)	Ion Formula	Ion
364.0857	364.0864	0.69	1.89	C18 H20 Cl N O3 P	(M+H)+

Diethyl (7-bromo-2-phenyl-1H-indol-3-yl)phosphonate (4f)





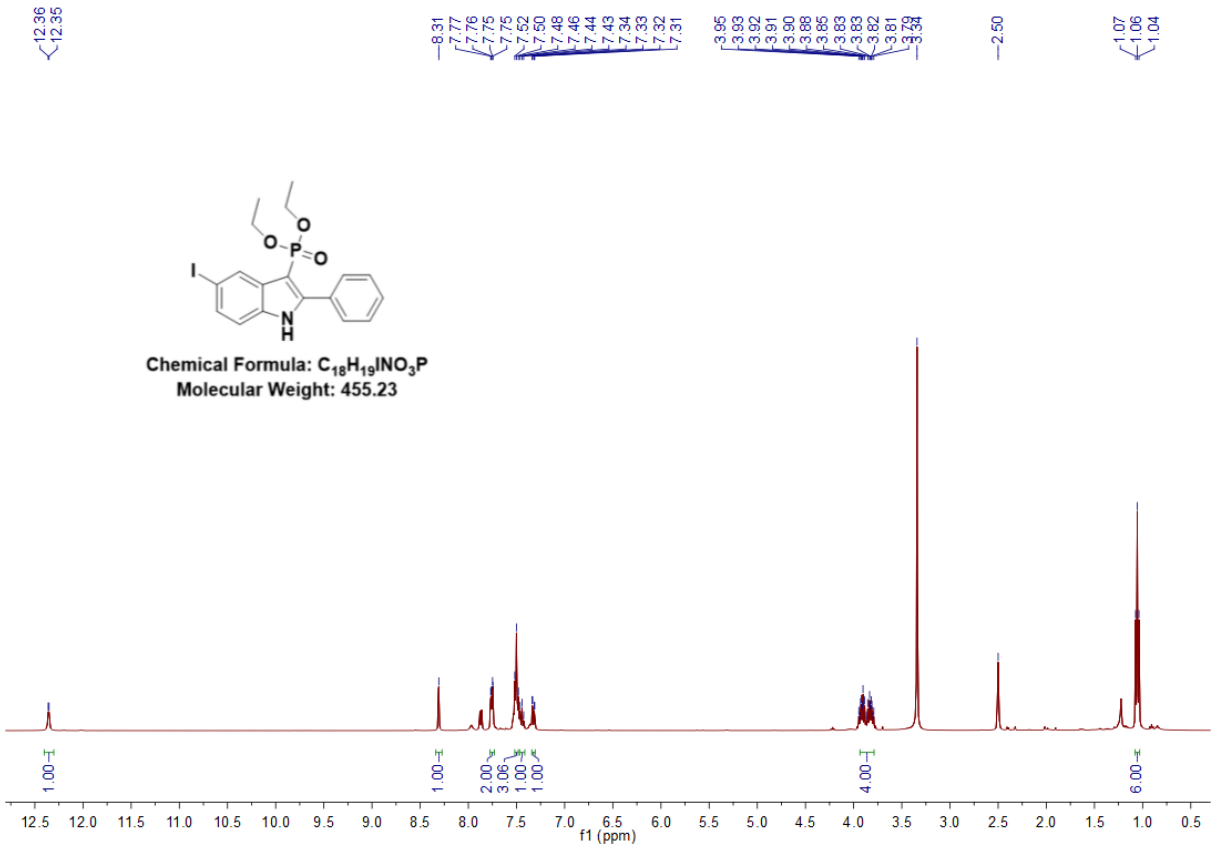


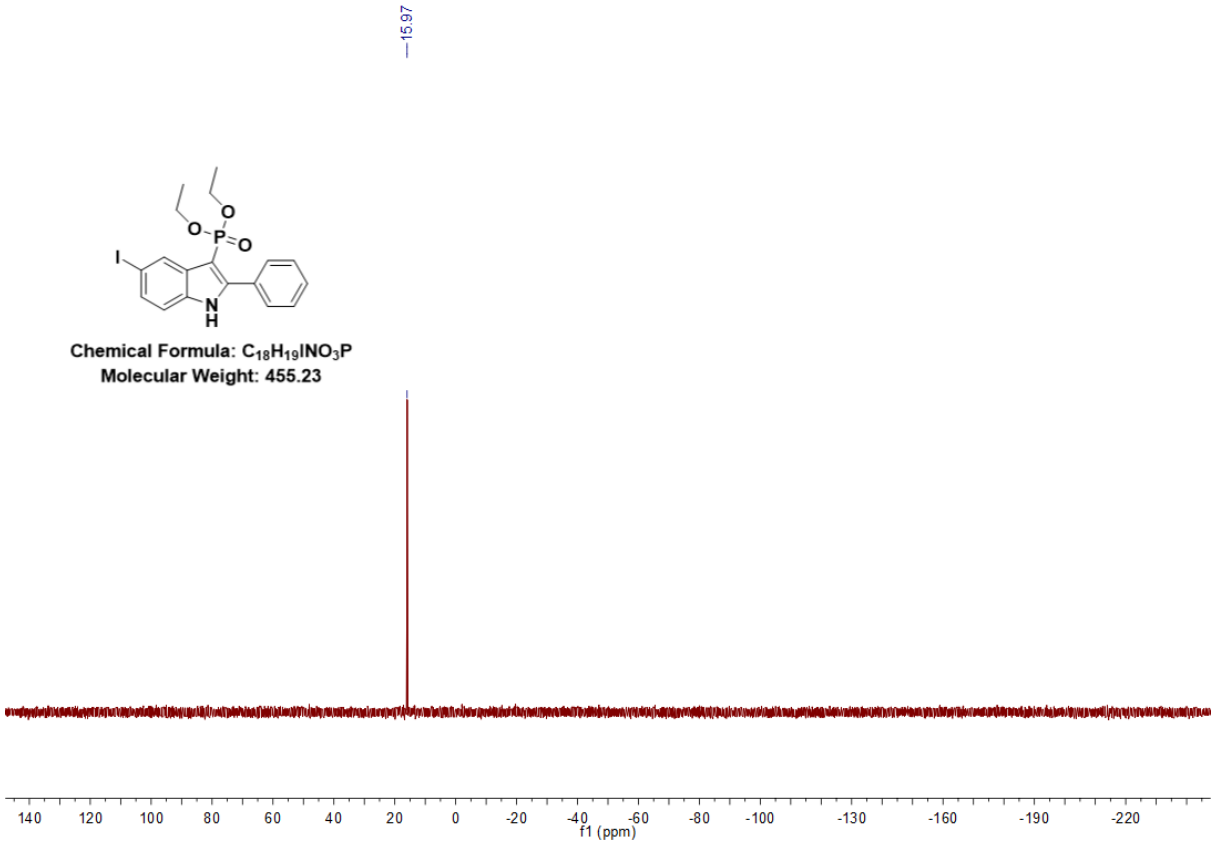


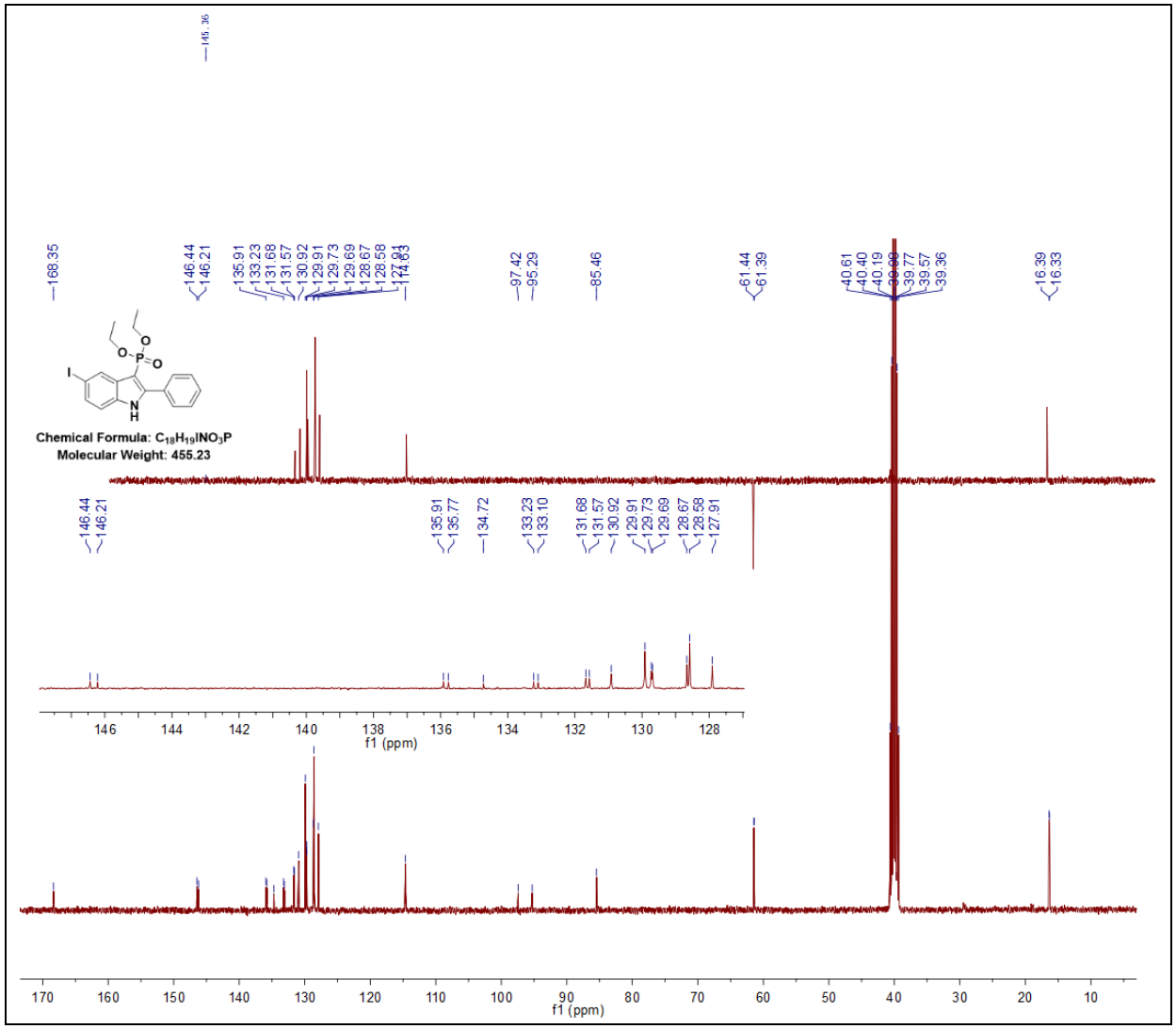
Formula Calculator Results

m/z	Calc m/z	Diff (mDa)	Diff (ppm)	Ion Formula	Ion
408.0369	408.0359	-0.99	-2.44	C18 H20 Br N O3 P	(M+H)+

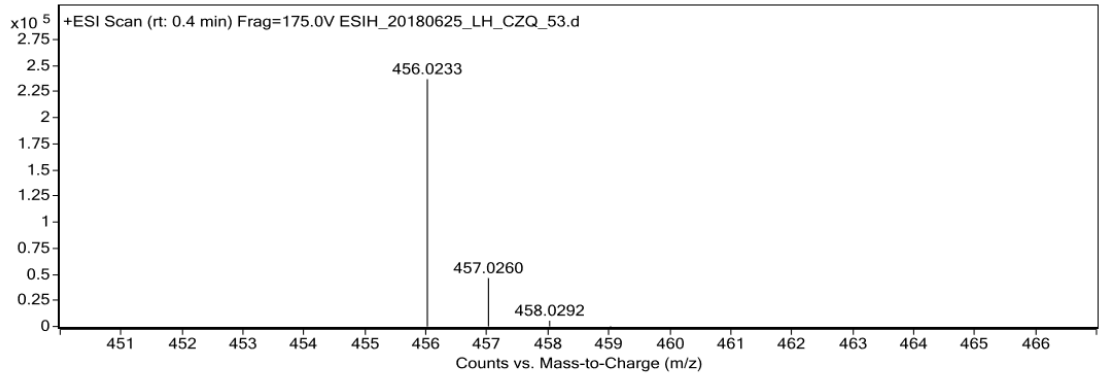
Diethyl (5-iodo-2-phenyl-1H-indol-3-yl)phosphonate (4g)







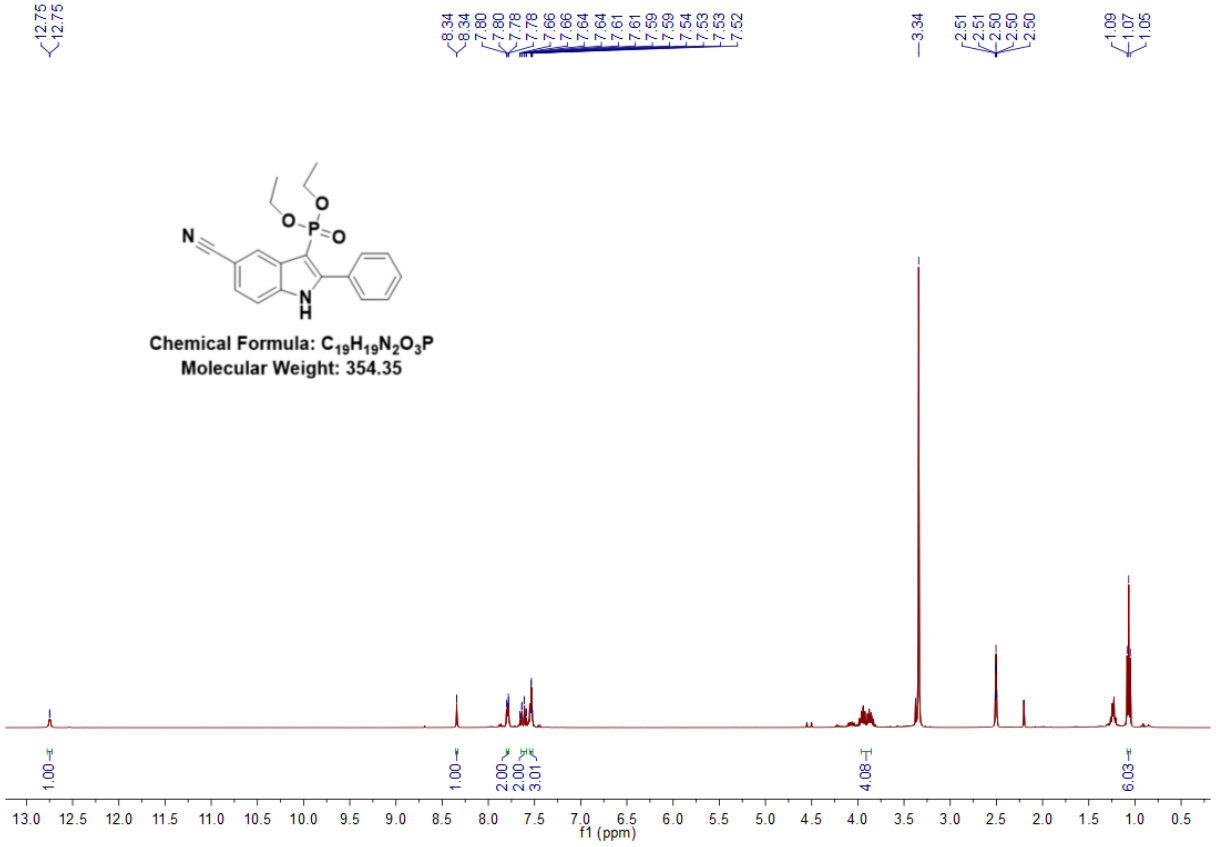
Fragmentor Voltage	Collision Energy	Ionization Mode
175	0	ESI



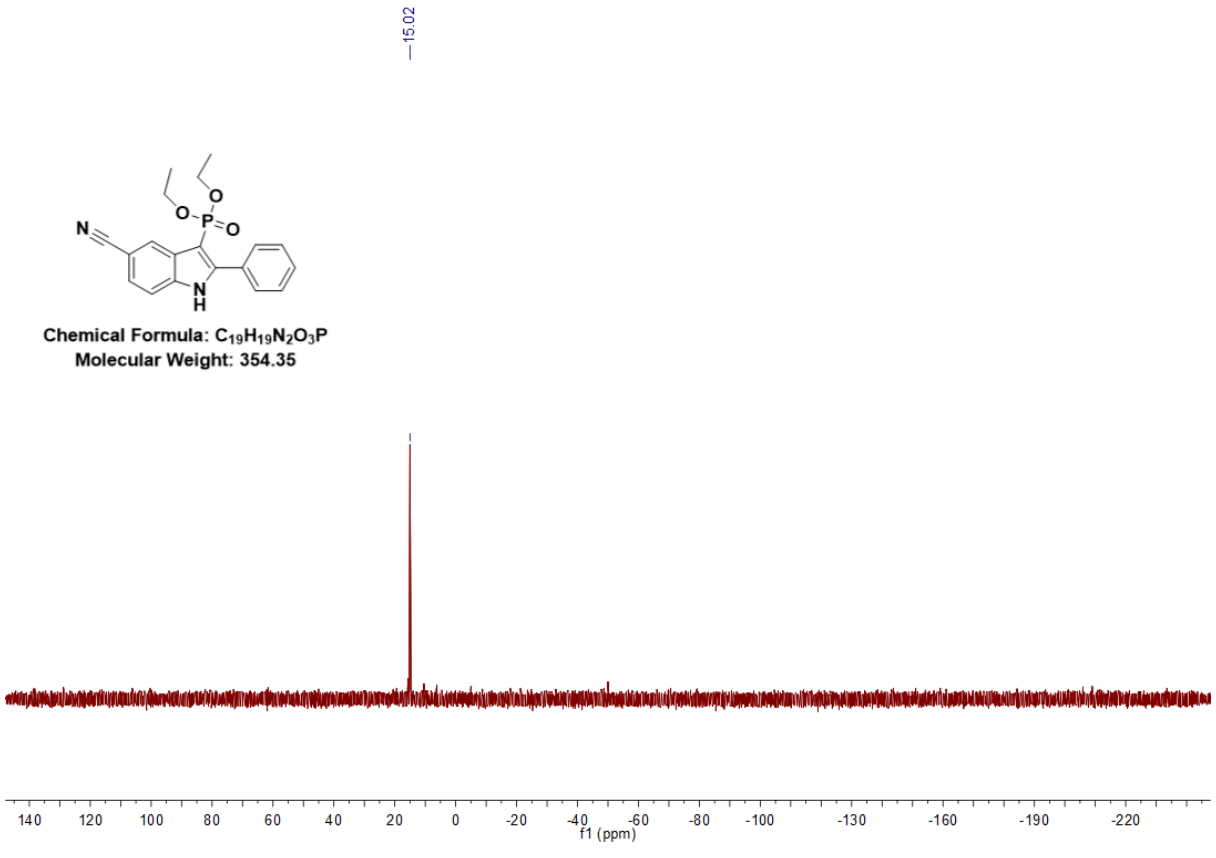
Formula Calculator Results

m/z	Calc m/z	Diff (mDa)	Diff (ppm)	Ion Formula	Ion
456.0233	456.022	-1.26	-2.77	C18 H20 I N O3 P	(M+H)+

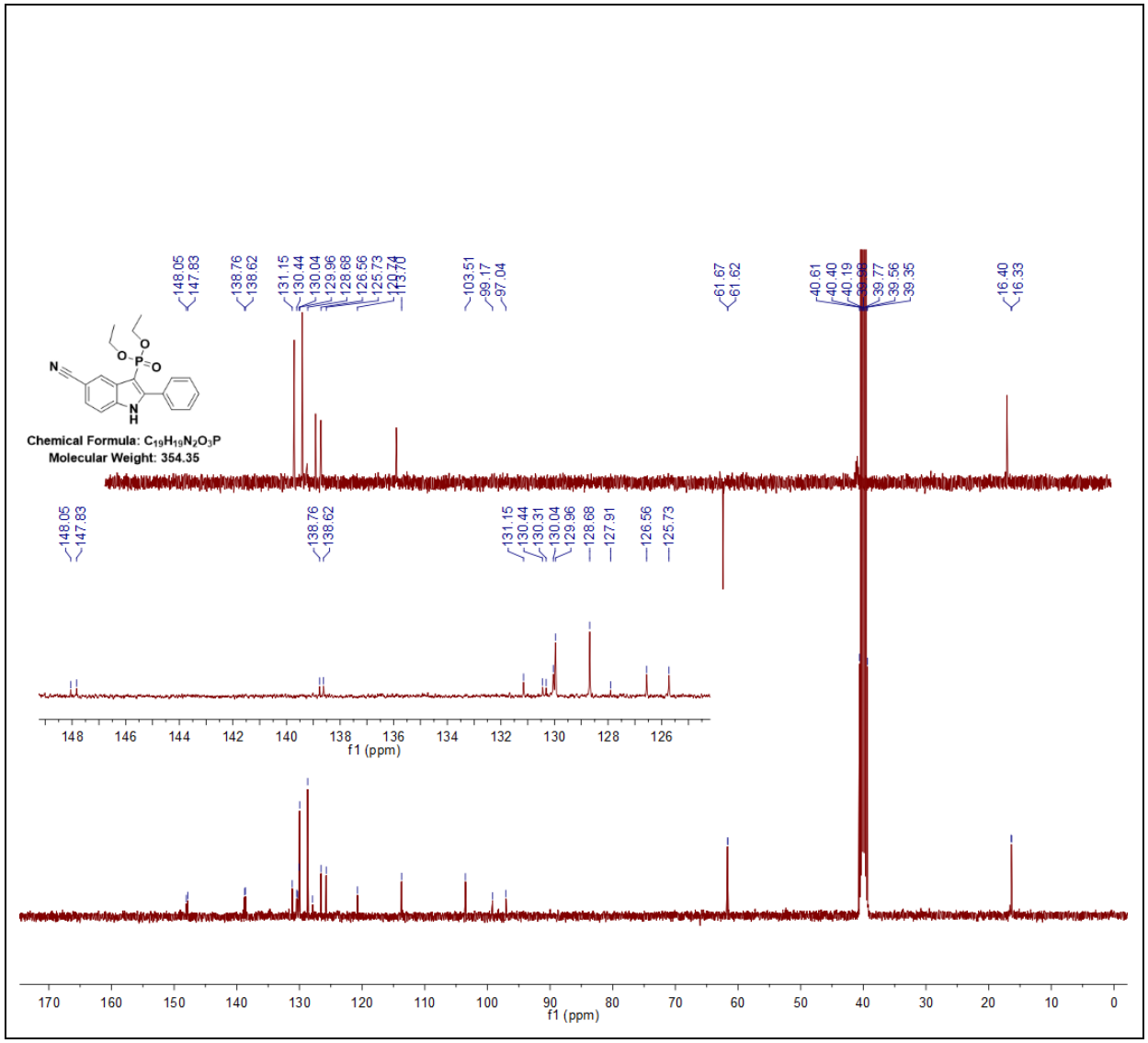
Diethyl (5-cyano-2-phenyl-1H-indol-3-yl)phosphonate (4h)

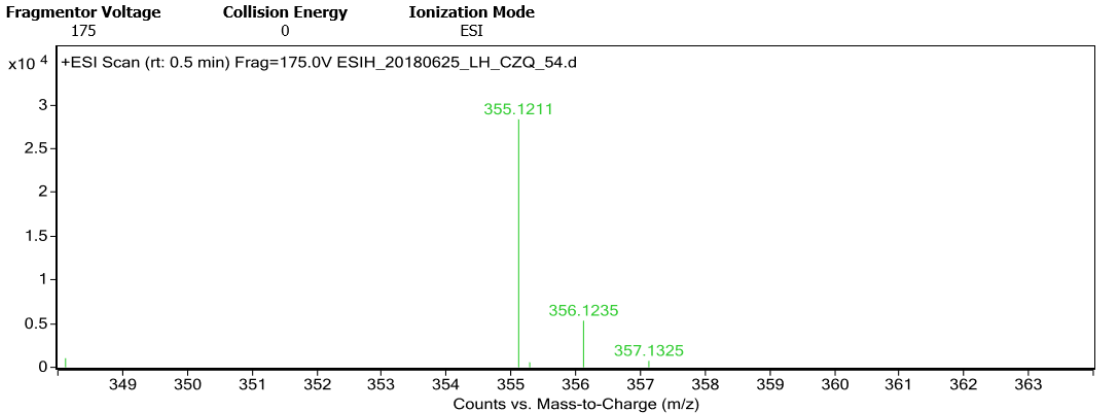


Chemical Formula: $C_{19}H_{19}N_2O_3P$
Molecular Weight: 354.35



Chemical Formula: $C_{19}H_{19}N_2O_3P$
Molecular Weight: 354.35

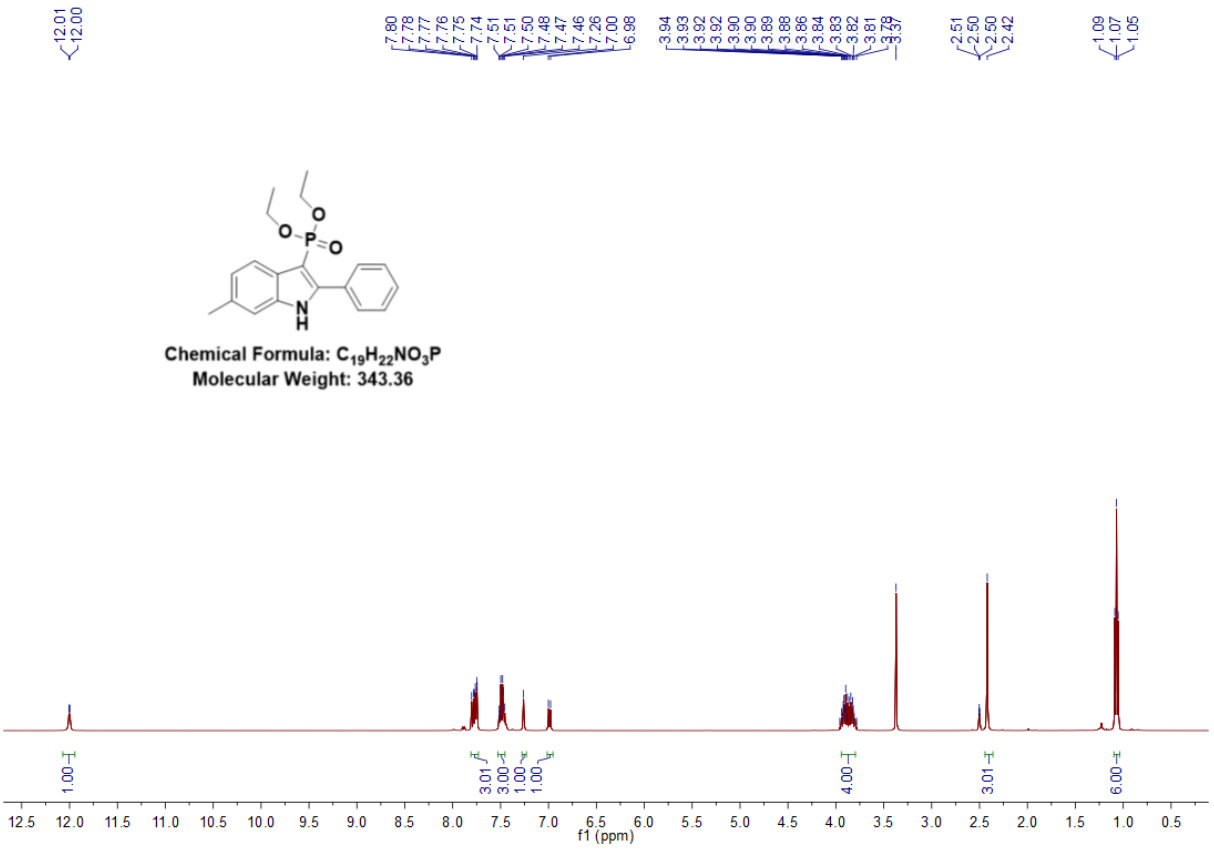


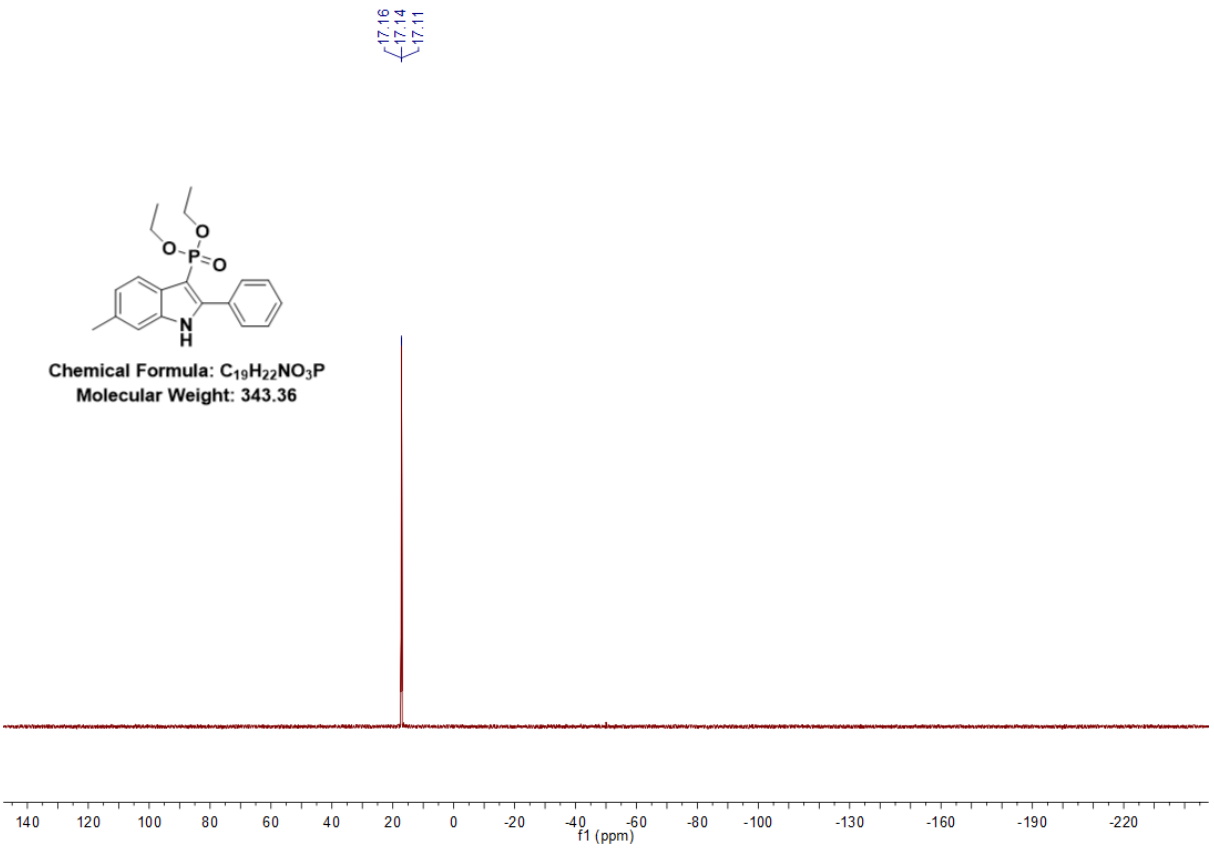


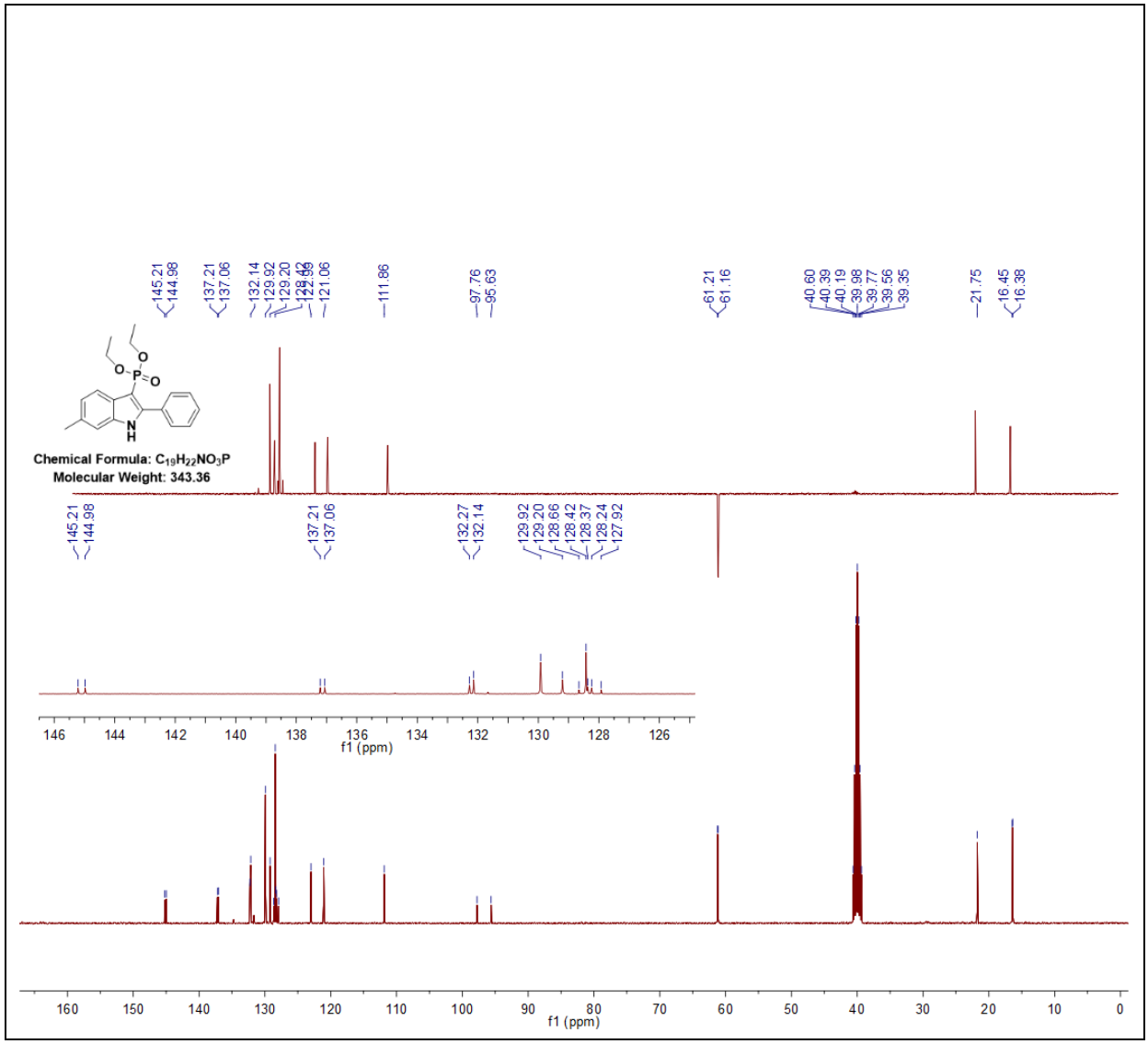
Formula Calculator Results

m/z	Calc m/z	Diff (mDa)	Diff (ppm)	Ion Formula	Ion
355.1211	355.1206	-0.5	-1.41	C19 H20 N2 O3 P	(M+H)+

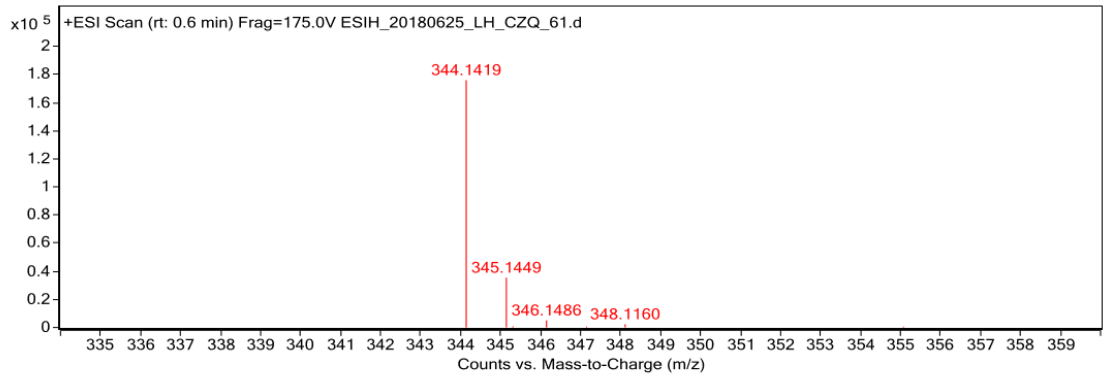
Diethyl (6-methyl-2-phenyl-1H-indol-3-yl)phosphonate (4i)







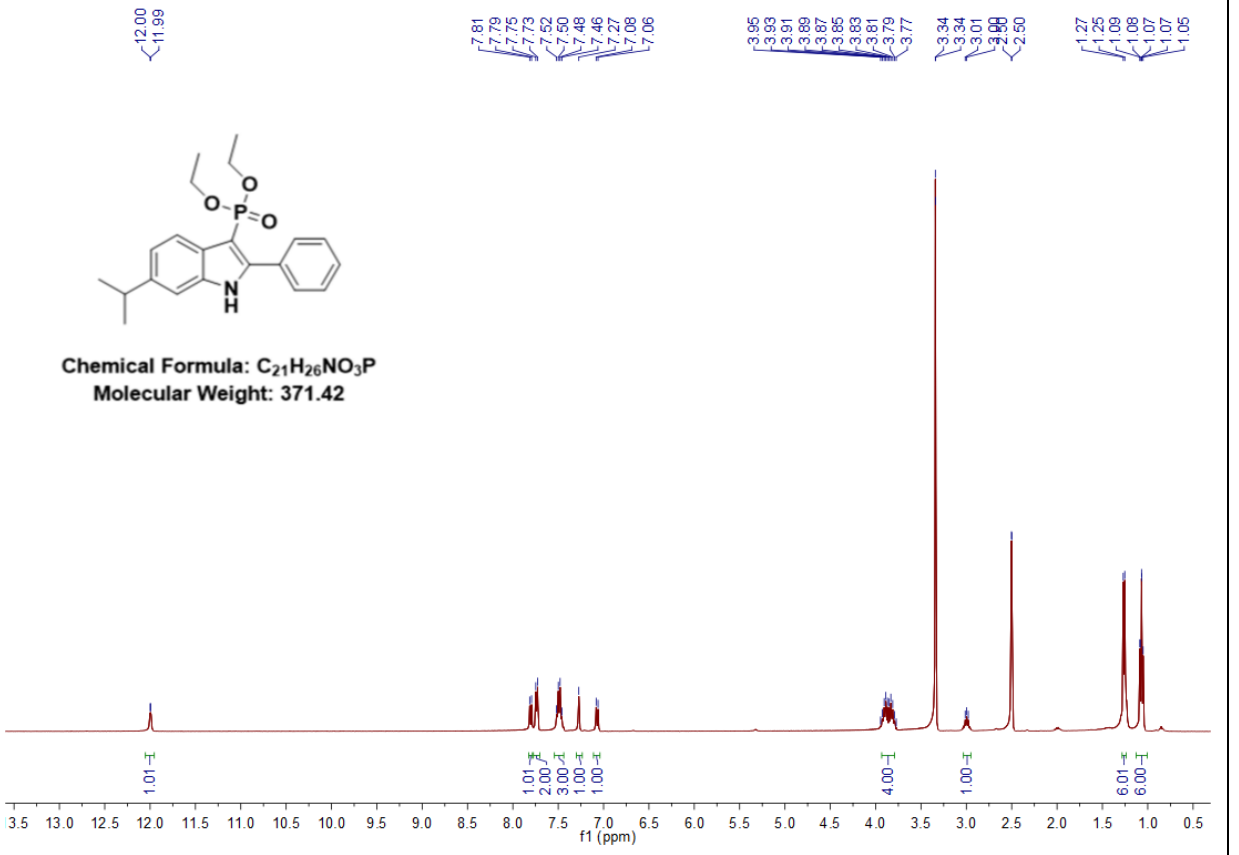
Fragmentor Voltage 175 **Collision Energy** 0 **Ionization Mode** ESI



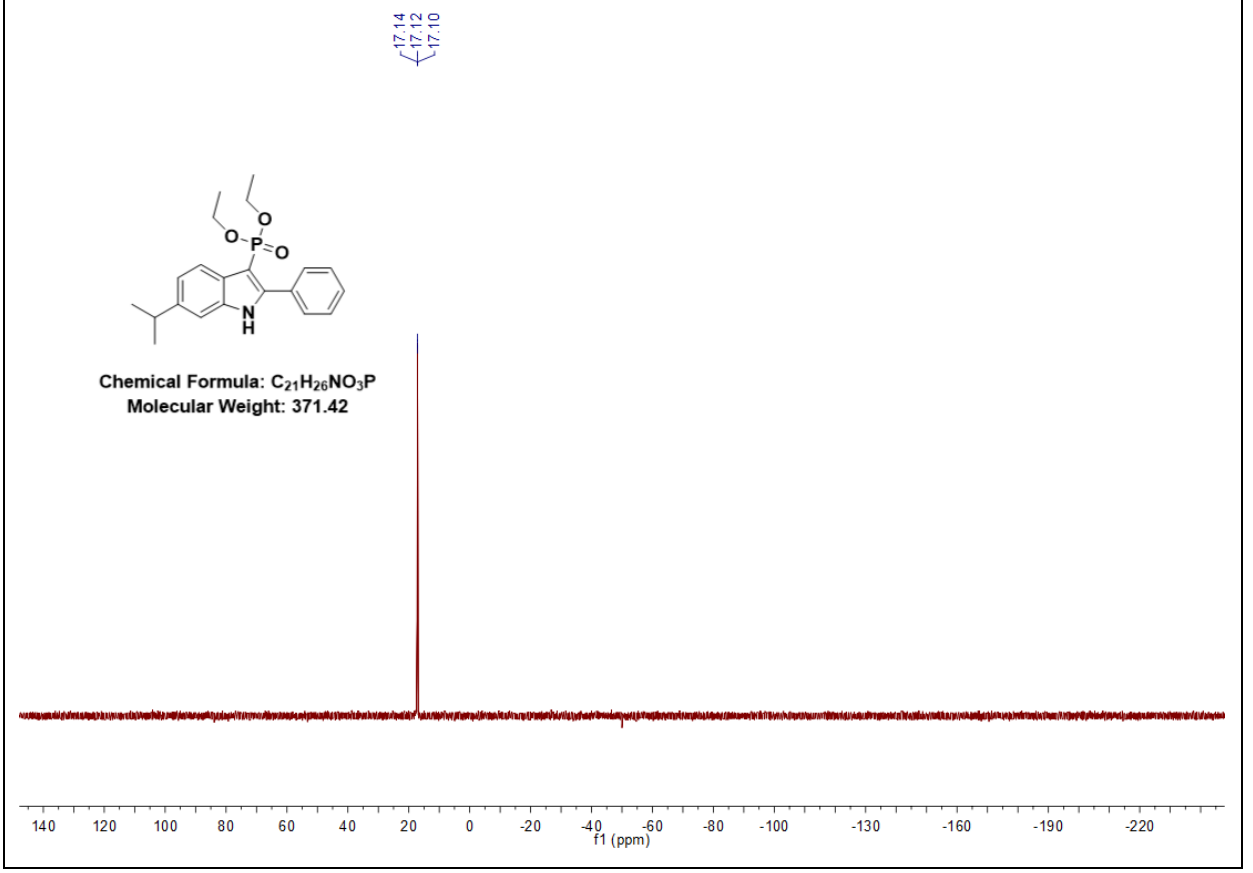
Formula Calculator Results

m/z	Calc m/z	Diff (mDa)	Diff (ppm)	Ion Formula	Ion
344.1419	344.141	-0.89	-2.58	C19 H23 N O3 P	(M+H)+

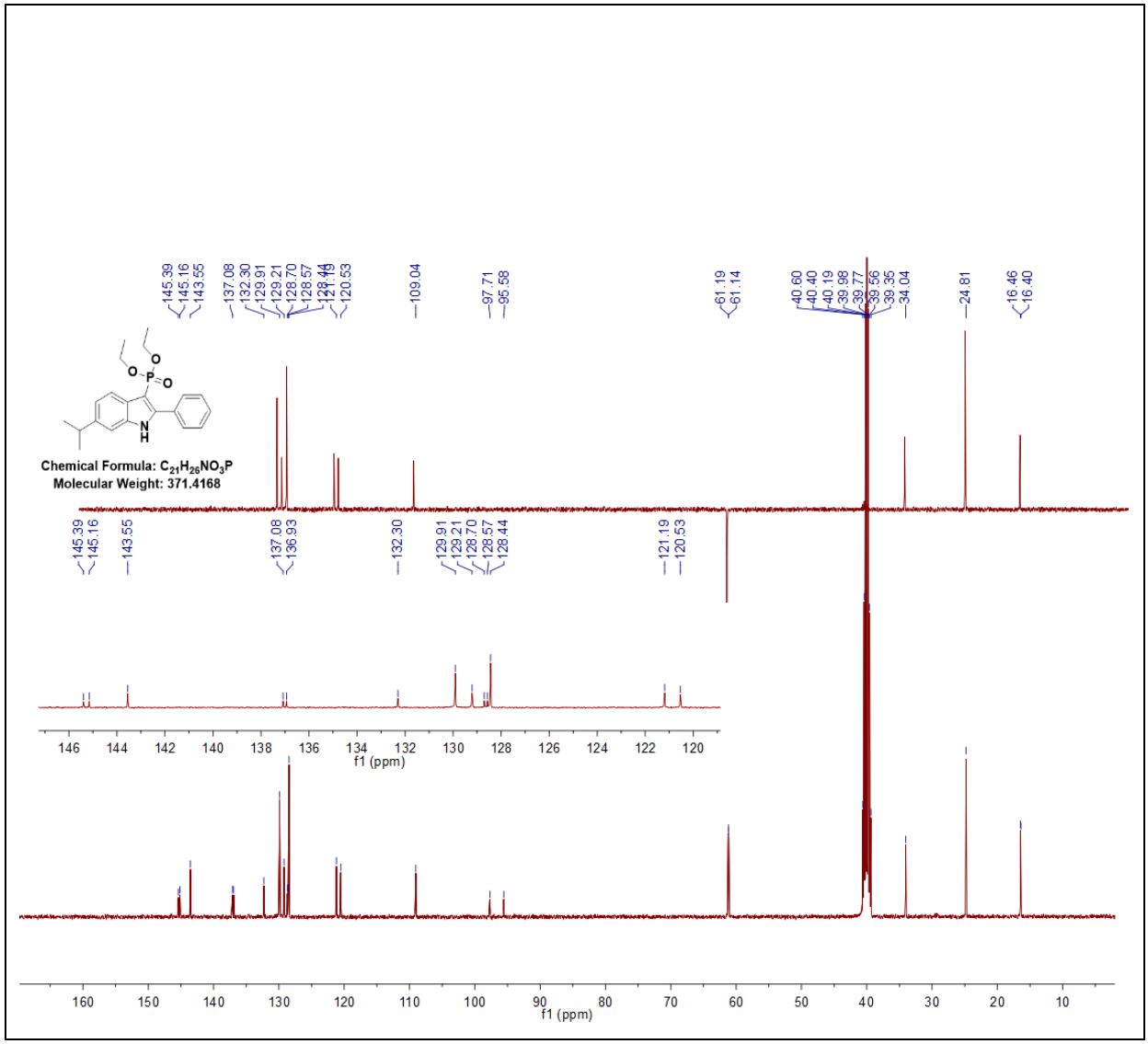
Diethyl (6-isopropyl-2-phenyl-1H-indol-3-yl)phosphonate (4j)

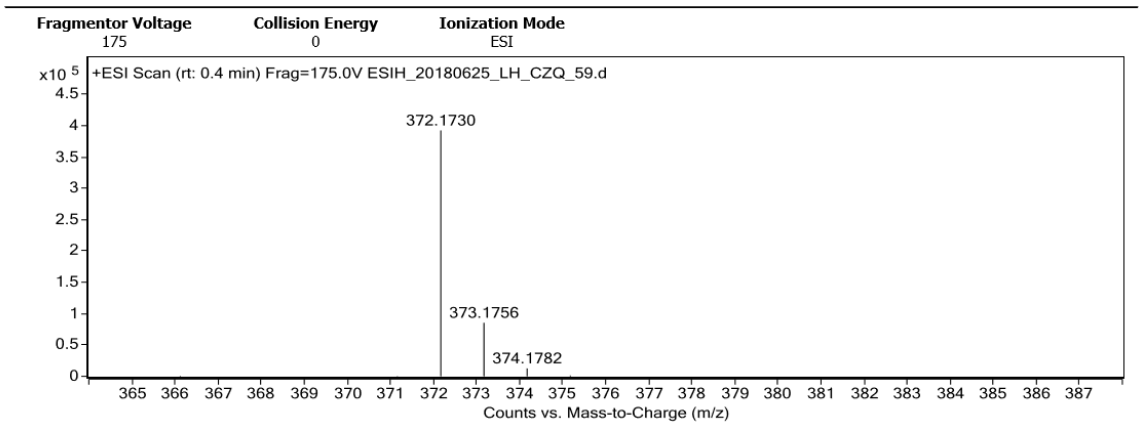


Chemical Formula: $C_{21}H_{26}NO_3P$
Molecular Weight: 371.42



Chemical Formula: $C_{21}H_{26}NO_3P$
Molecular Weight: 371.42

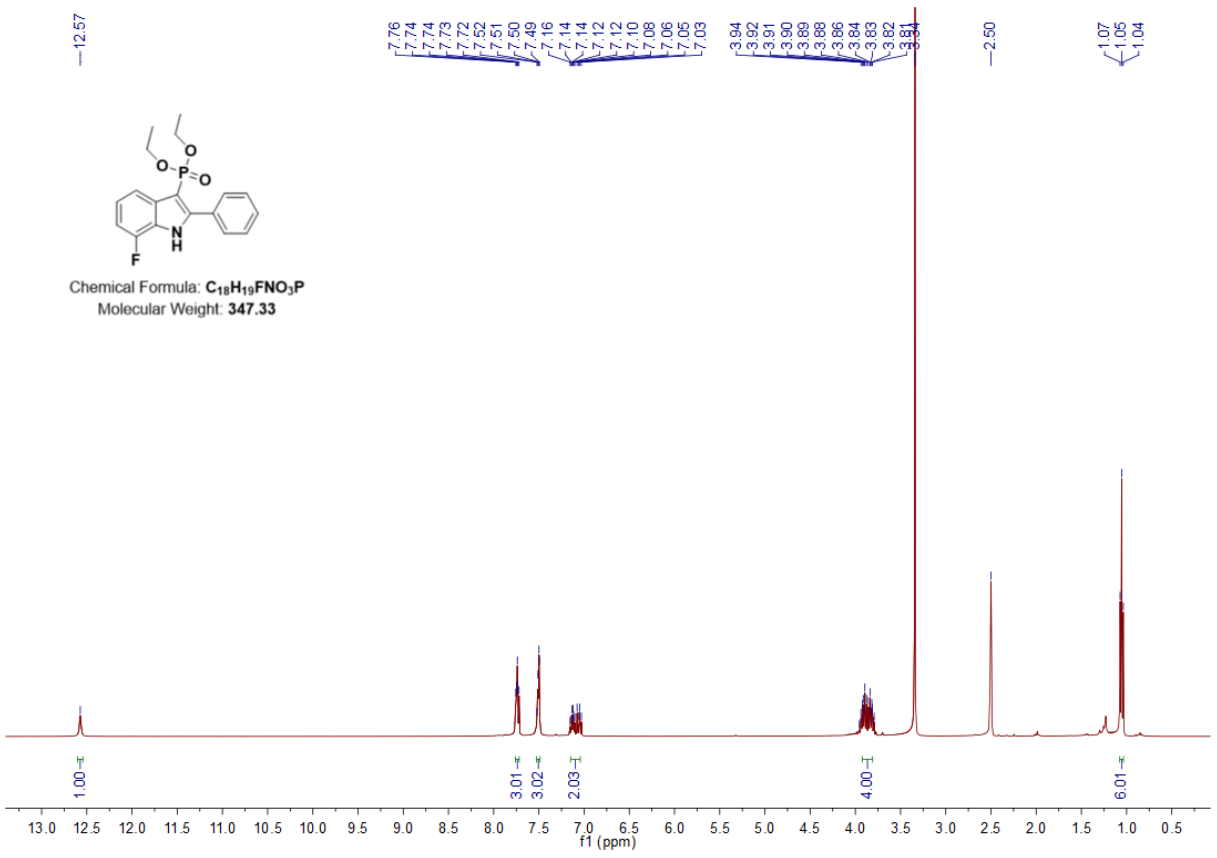


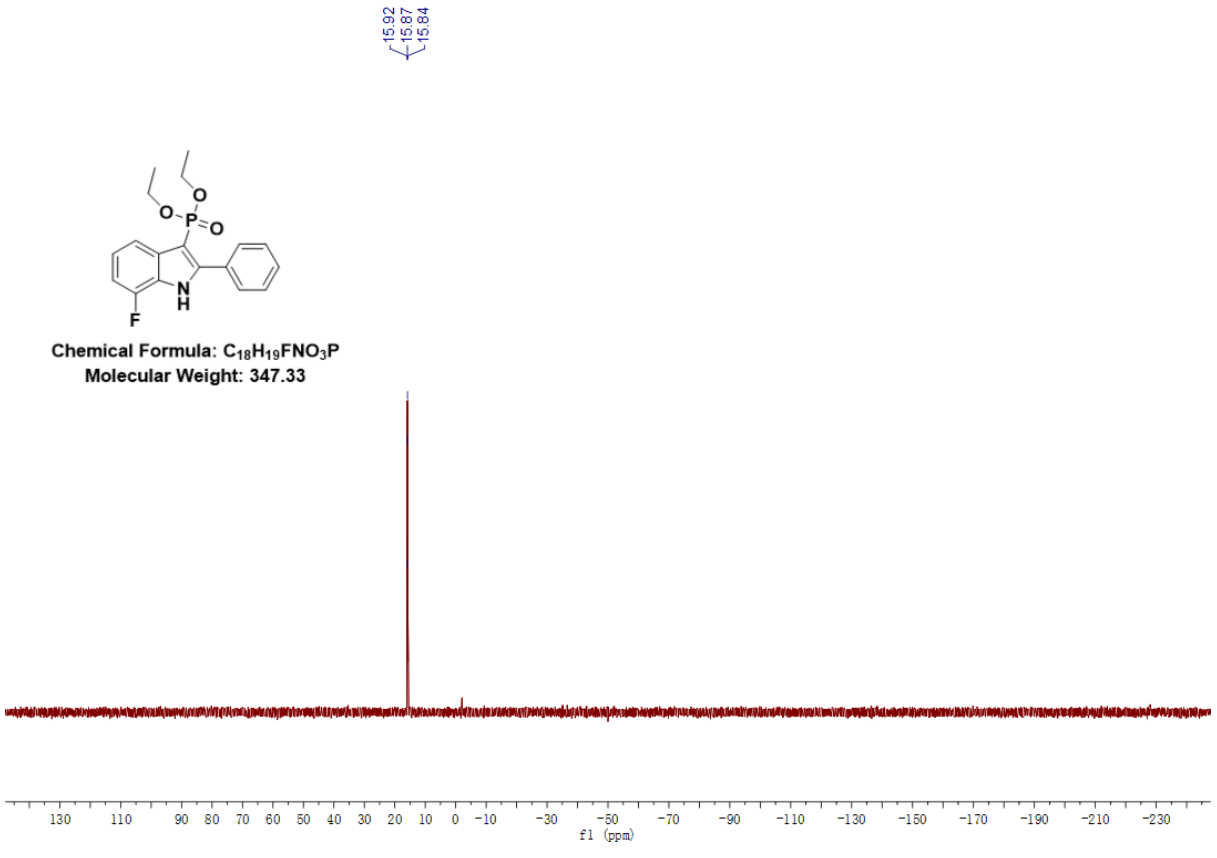


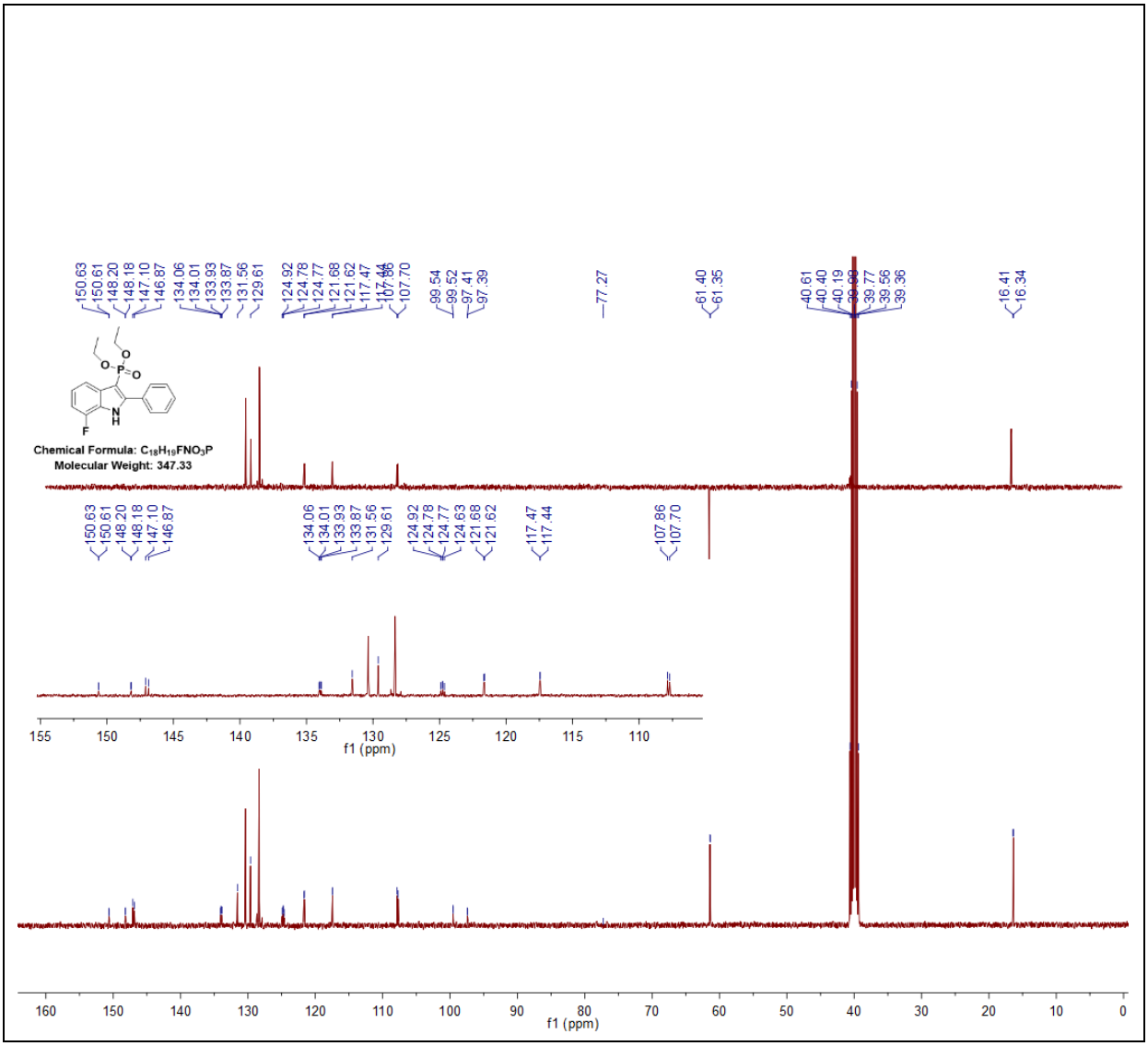
Formula Calculator Results

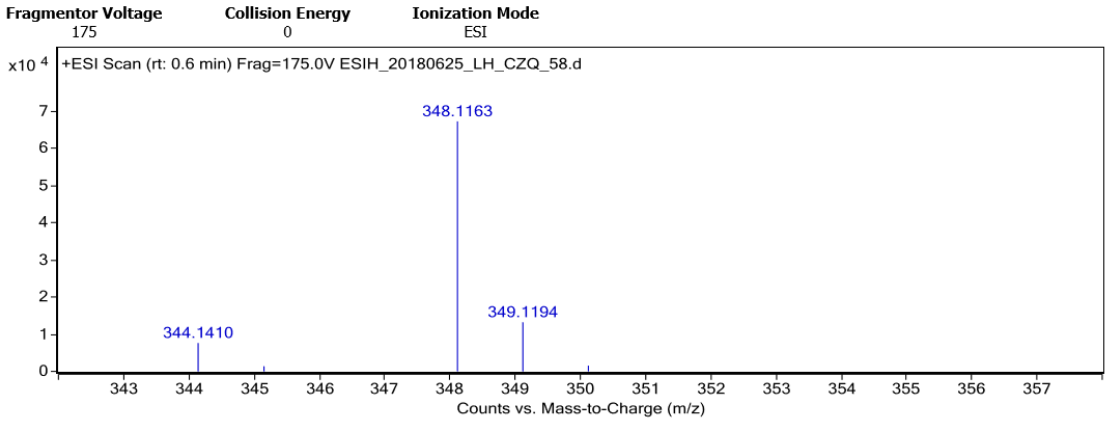
m/z	Calc m/z	Diff (mDa)	Diff (ppm)	Ion Formula	Ion
372.173	372.1723	-0.68	-1.82	C21 H27 N O3 P	(M+H)+

Diethyl (7-fluoro-2-phenyl-1H-indol-3-yl)phosphonate (4k)





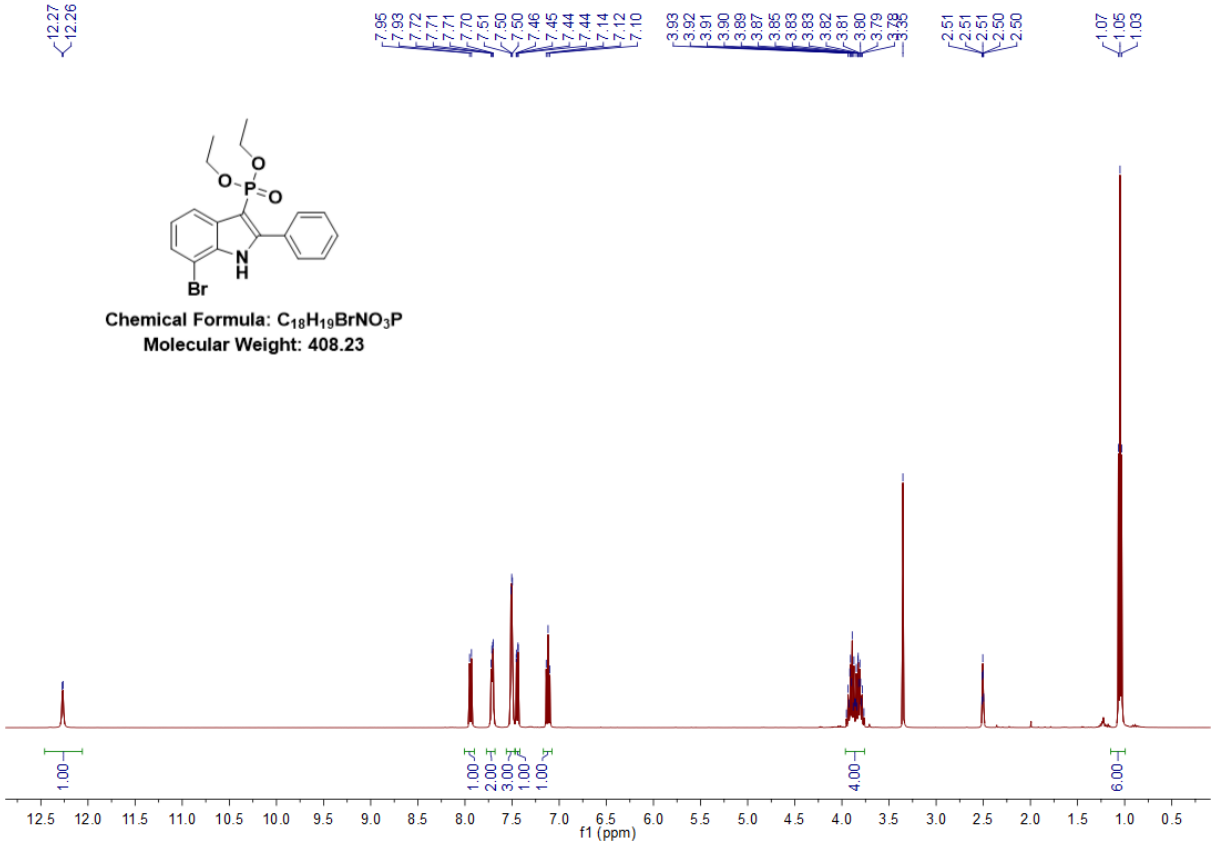


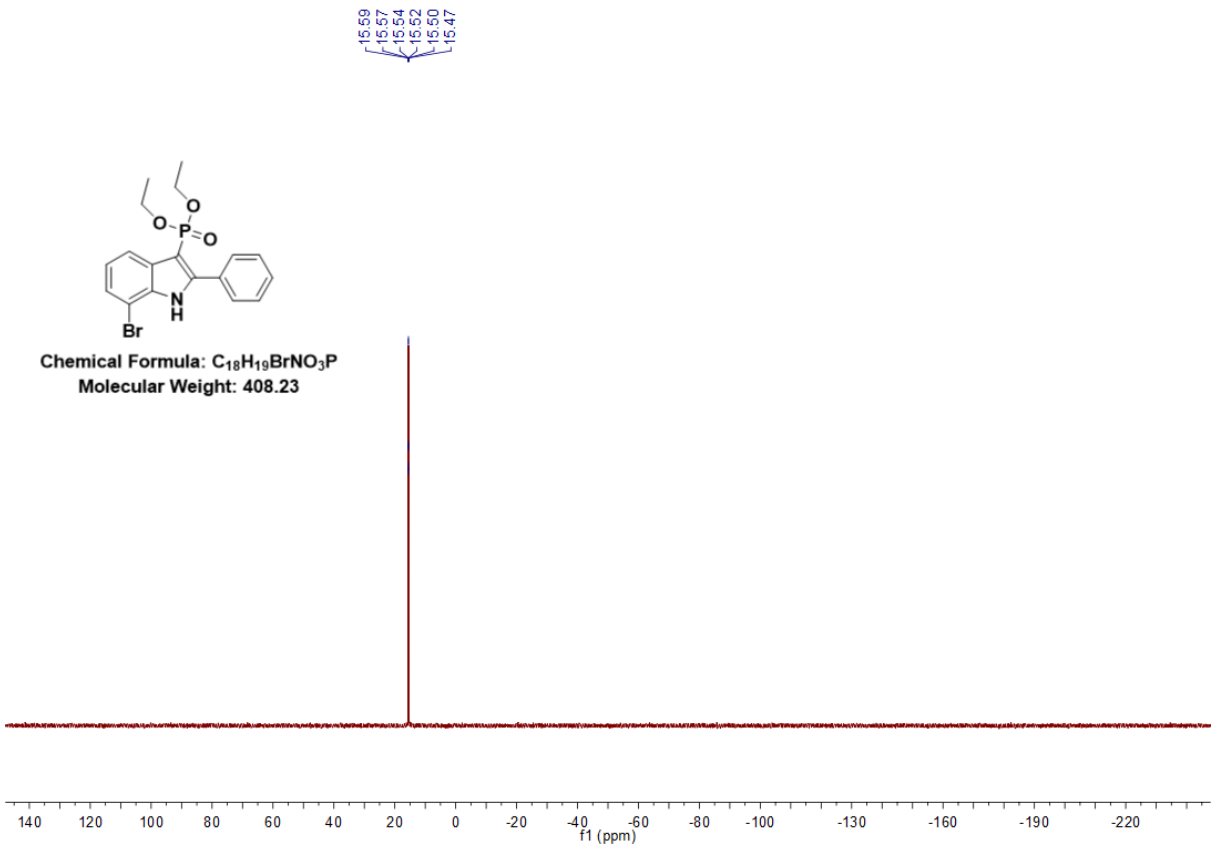


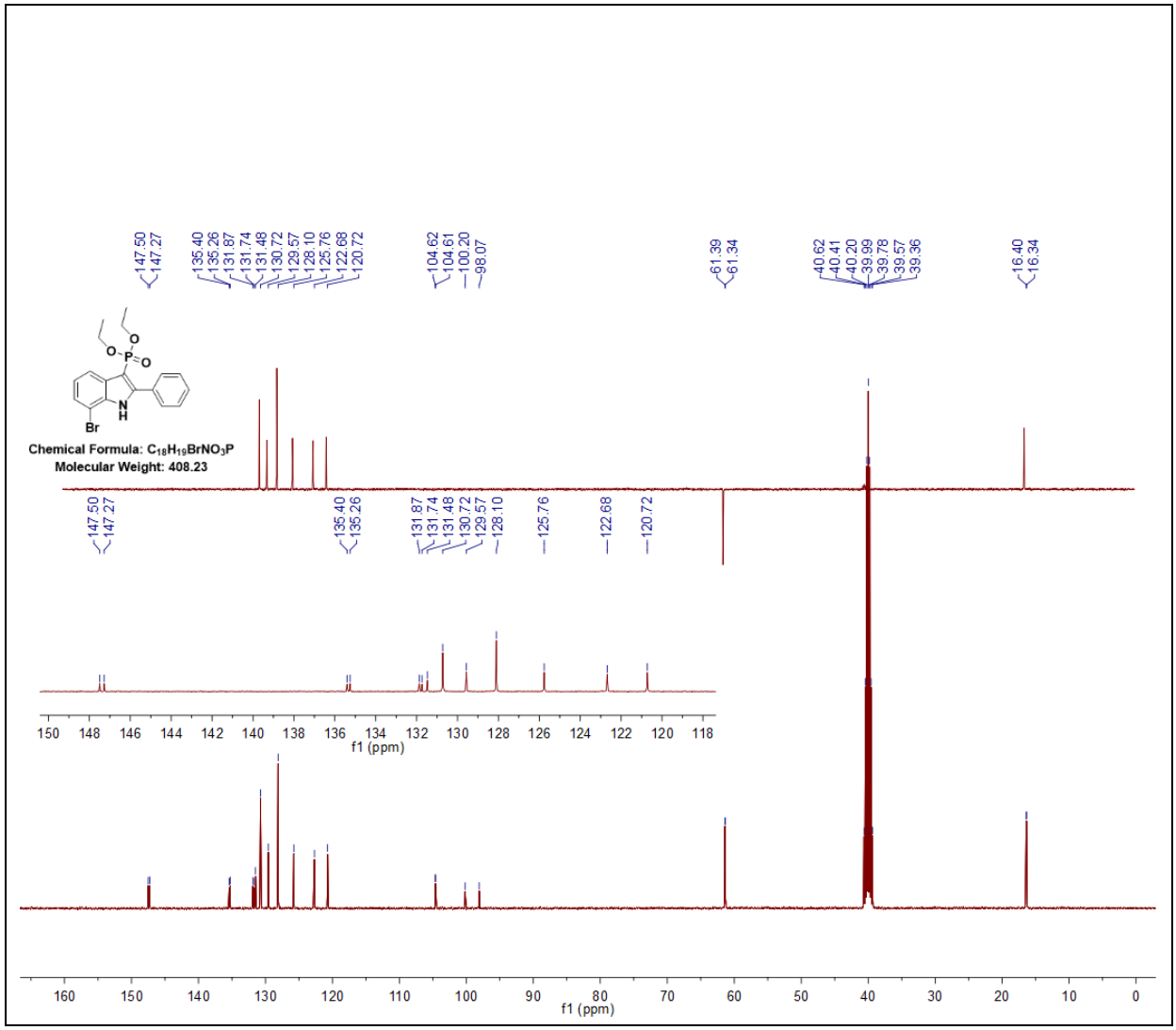
Formula Calculator Results

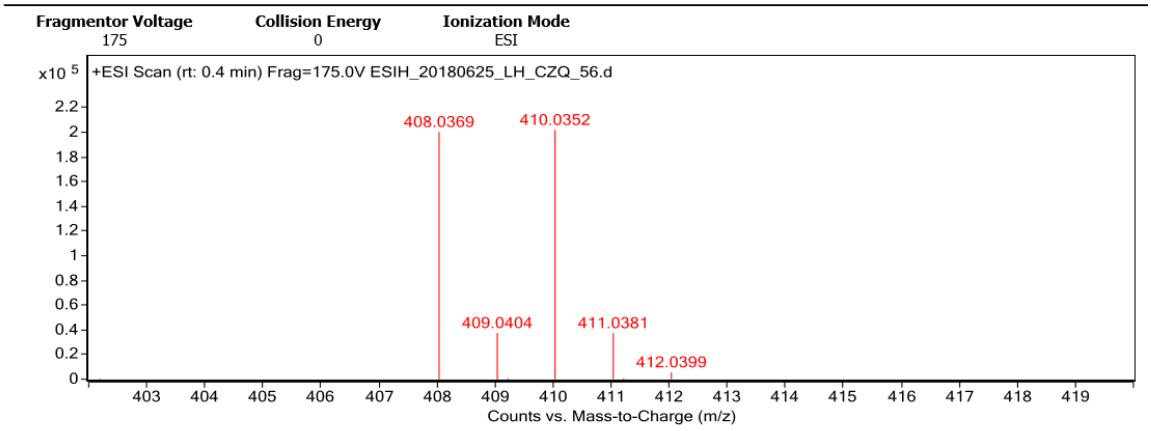
m/z	Calc m/z	Diff (mDa)	Diff (ppm)	Ion Formula	Ion
348.1163	348.1159	-0.38	-1.1	C18 H20 F N O3 P	(M+H)+

Diethyl (7-bromo-2-phenyl-1H-indol-3-yl)phosphonate (4l)





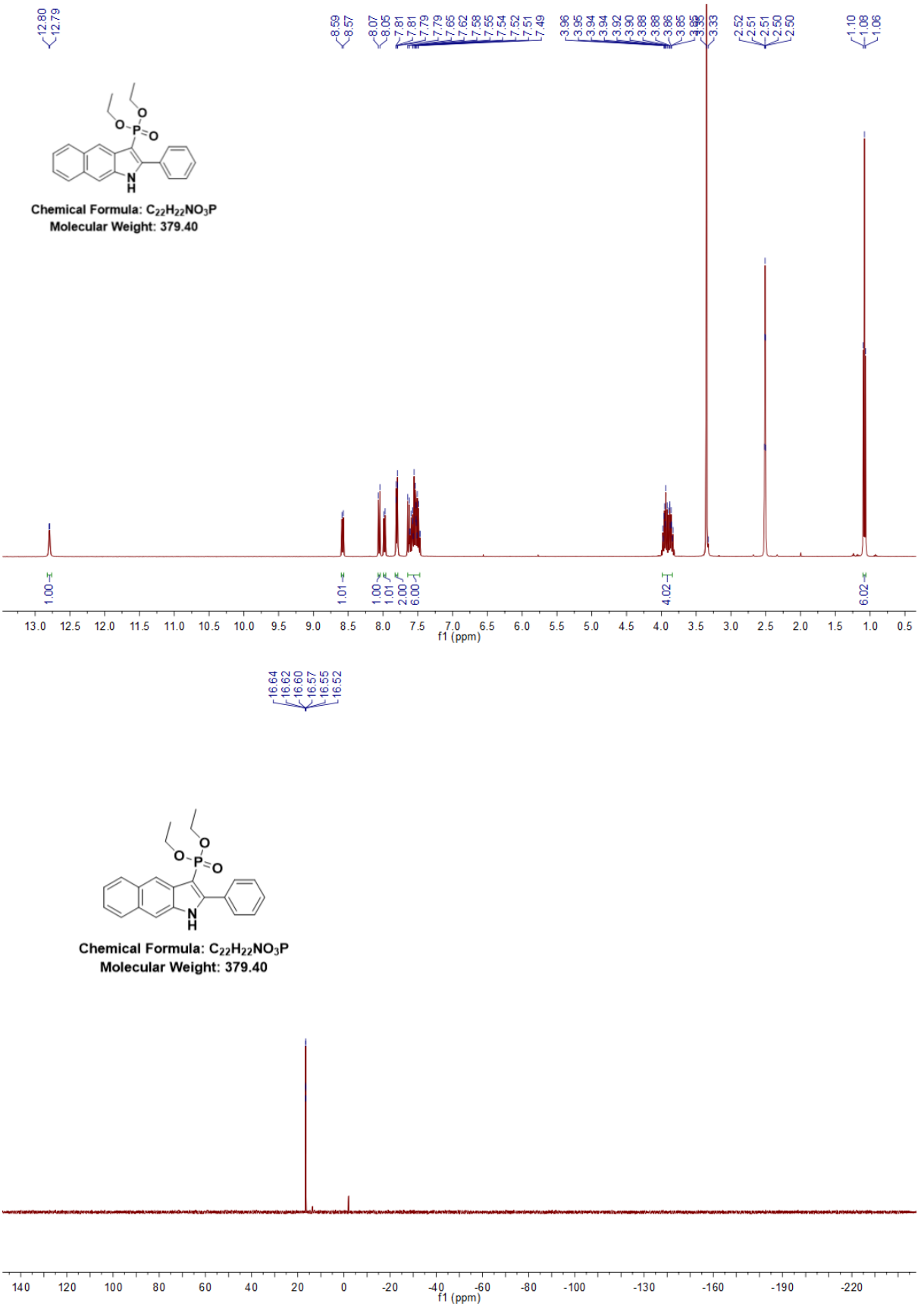


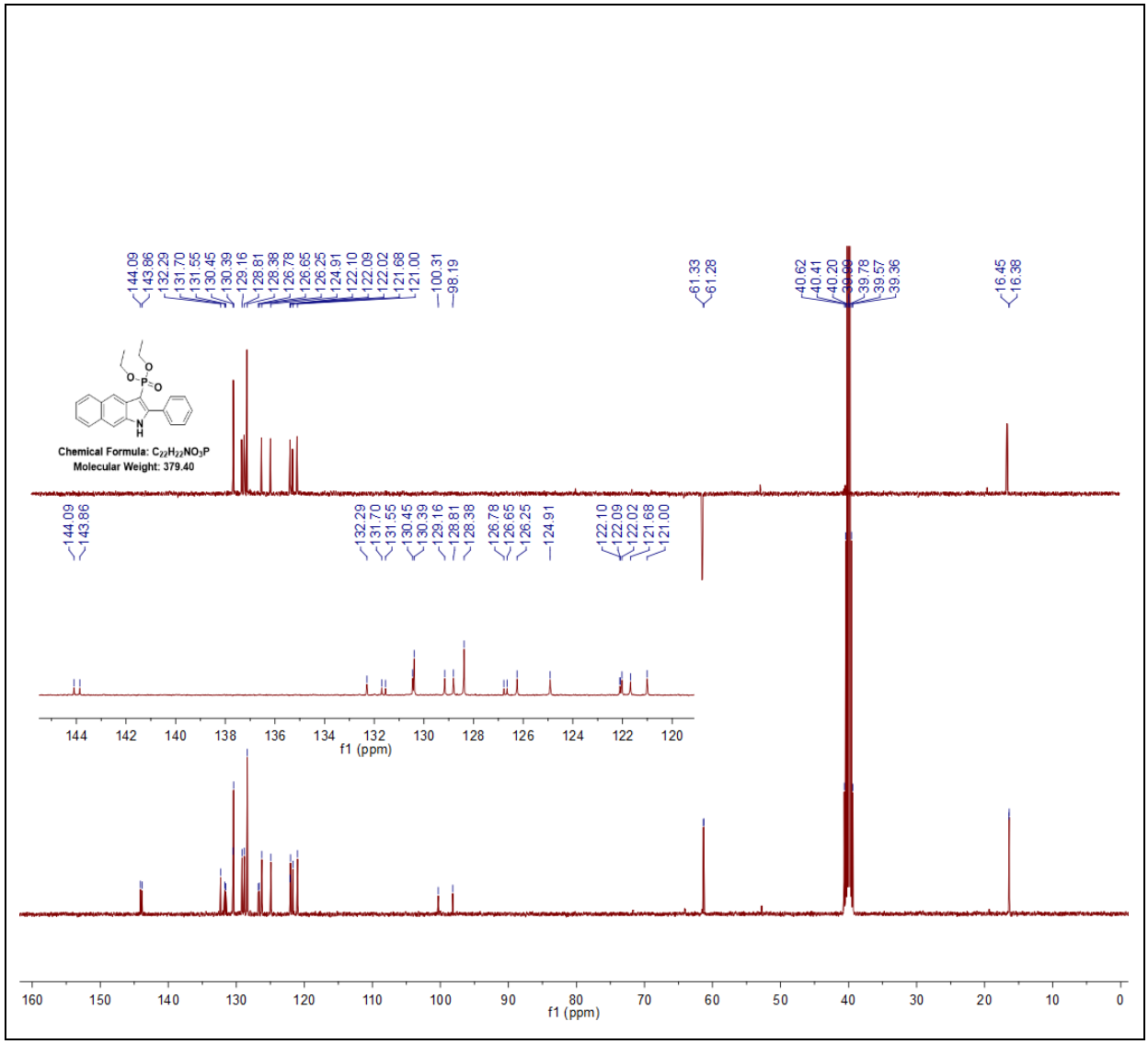


Formula Calculator Results

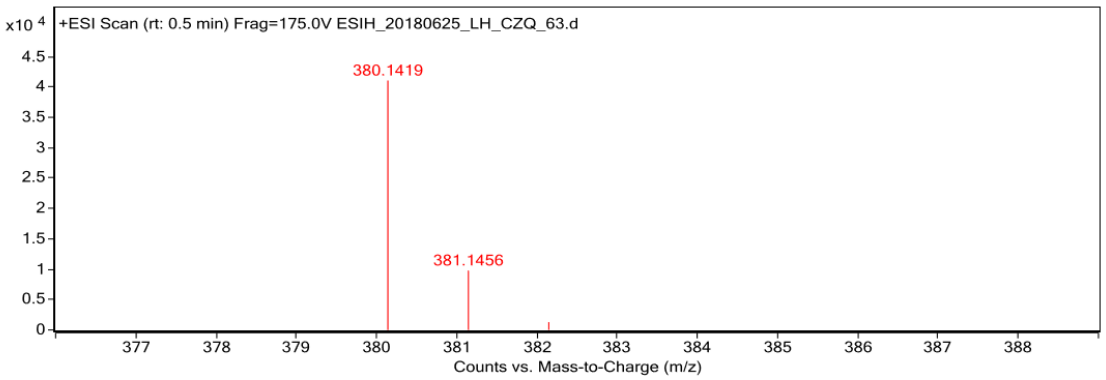
m/z	Calc m/z	Diff (mDa)	Diff (ppm)	Ion Formula	Ion
408.0369	408.0359	-1.04	-2.55	C18 H20 Br N O3 P	(M+H)+

Diethyl (2-phenyl-1H-benzo[f]indol-3-yl)phosphonate (4m)





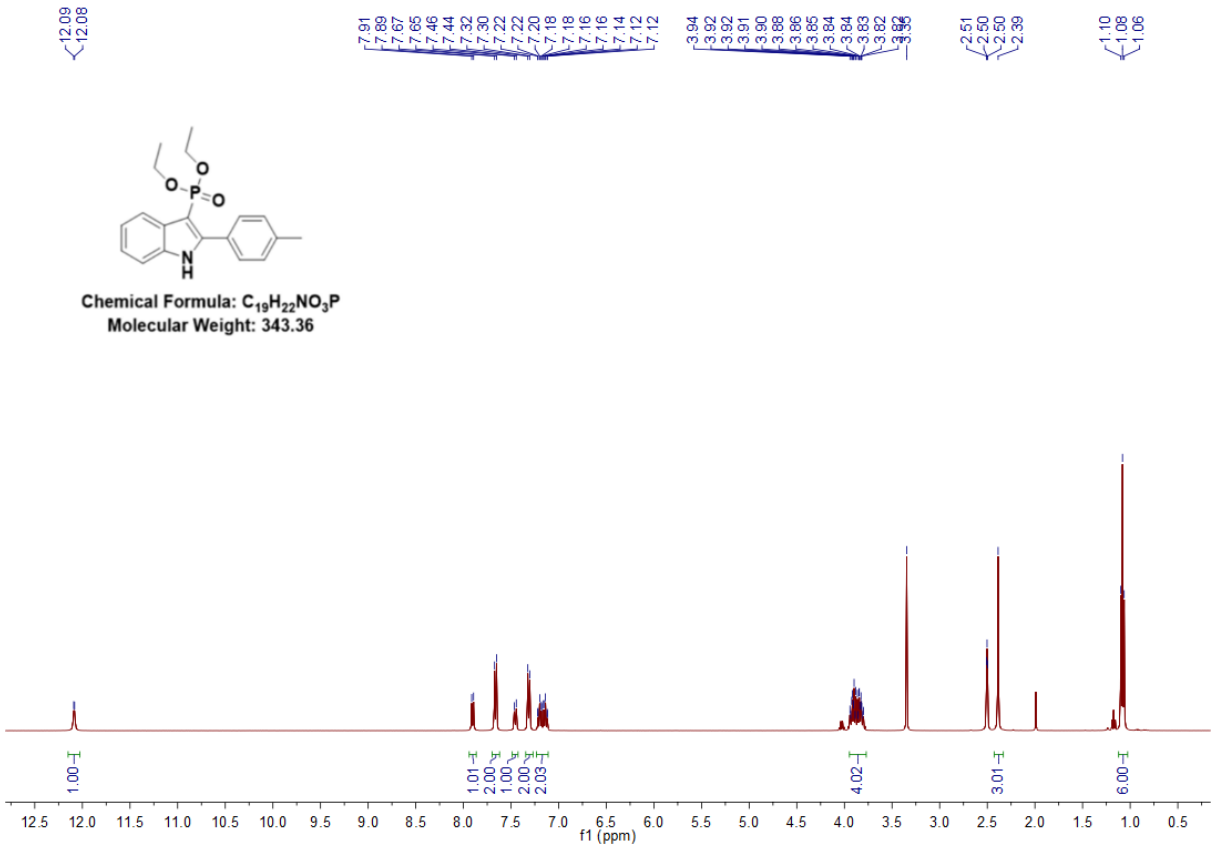
Fragmentor Voltage 175 **Collision Energy** 0 **Ionization Mode** ESI

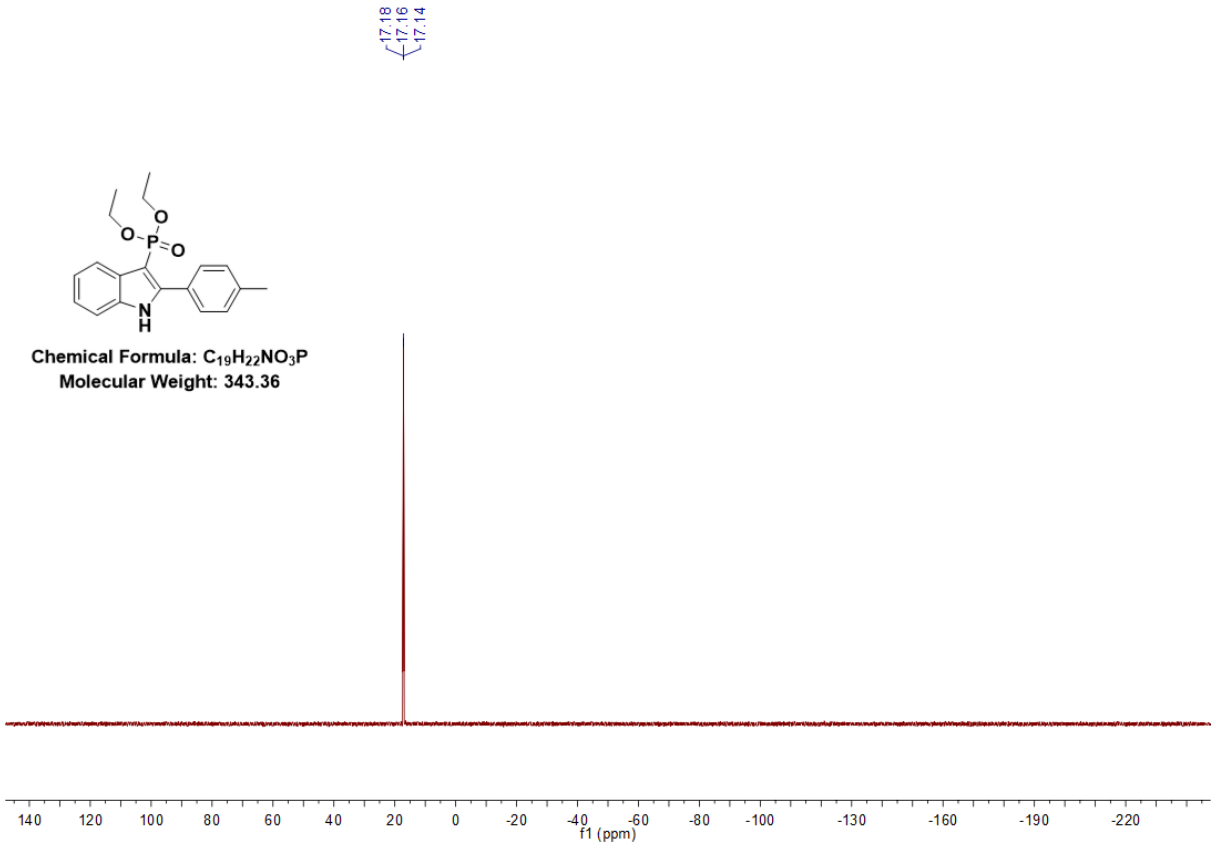


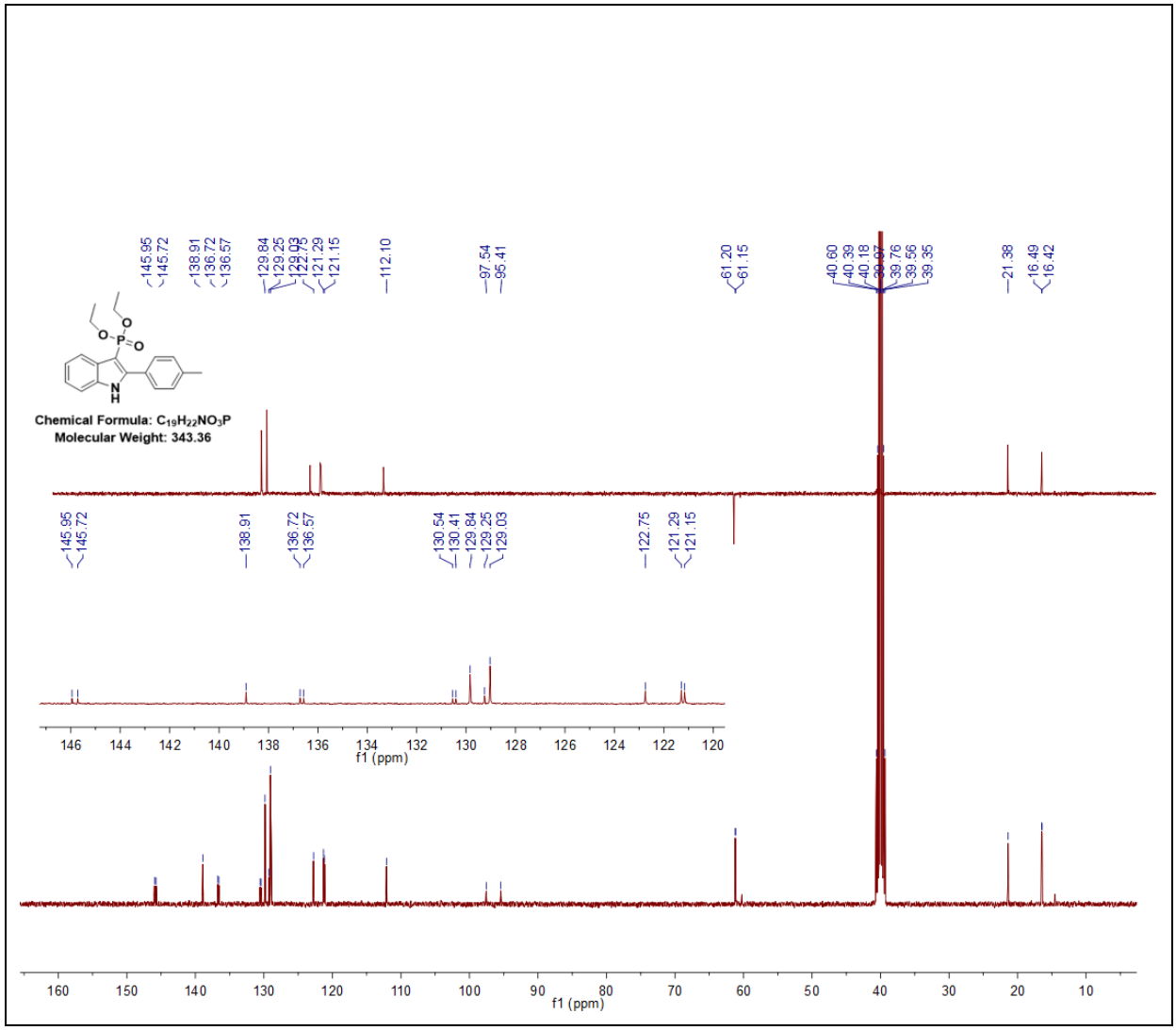
Formula Calculator Results

m/z	Calc m/z	Diff (mDa)	Diff (ppm)	Ion Formula	Ion
380.1419	380.141	-0.86	-2.25	C22 H23 N O3 P	(M+H)+

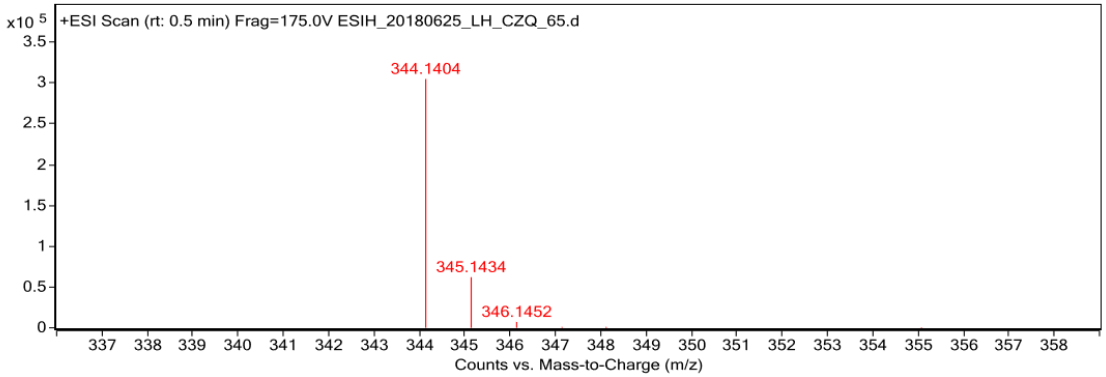
Diethyl (2-(p-tolyl)-1H-indol-3-yl)phosphonate (4n)







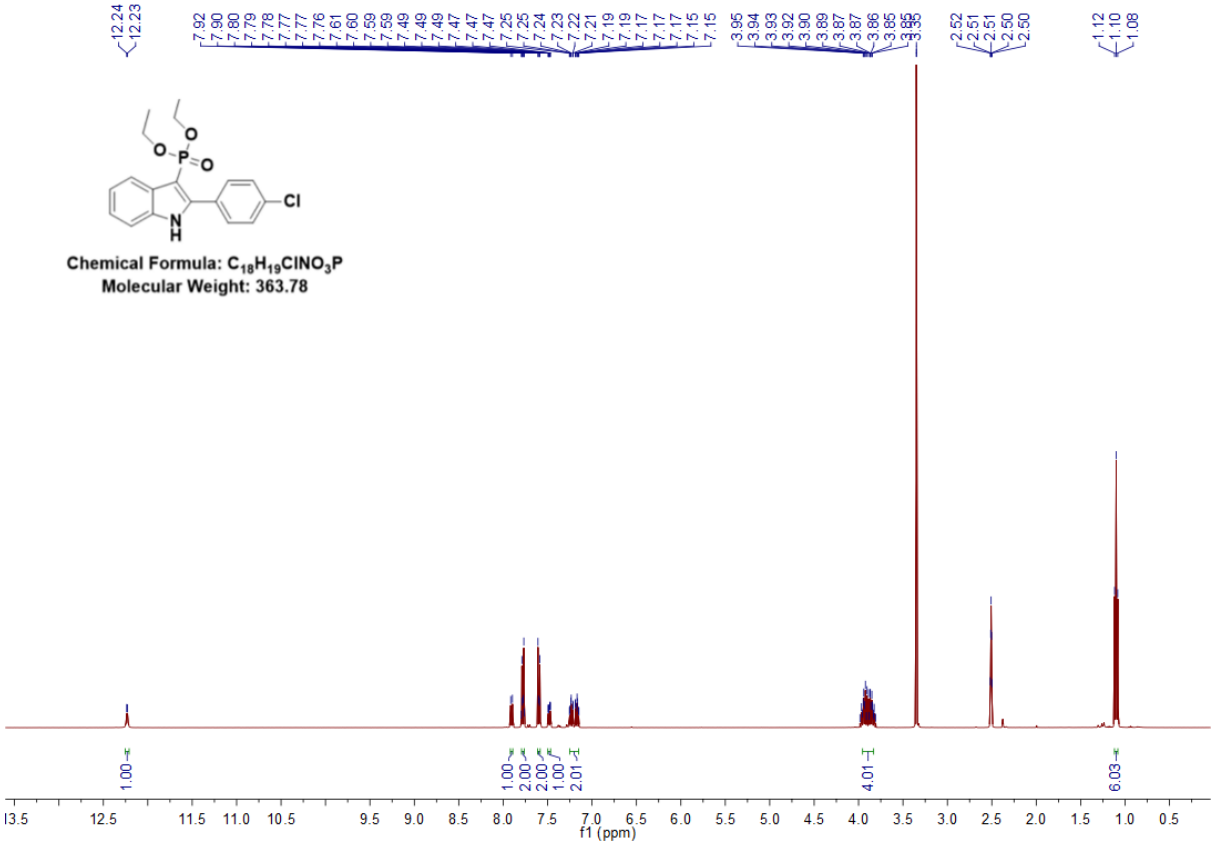
Fragmentor Voltage	Collision Energy	Ionization Mode
175	0	ESI

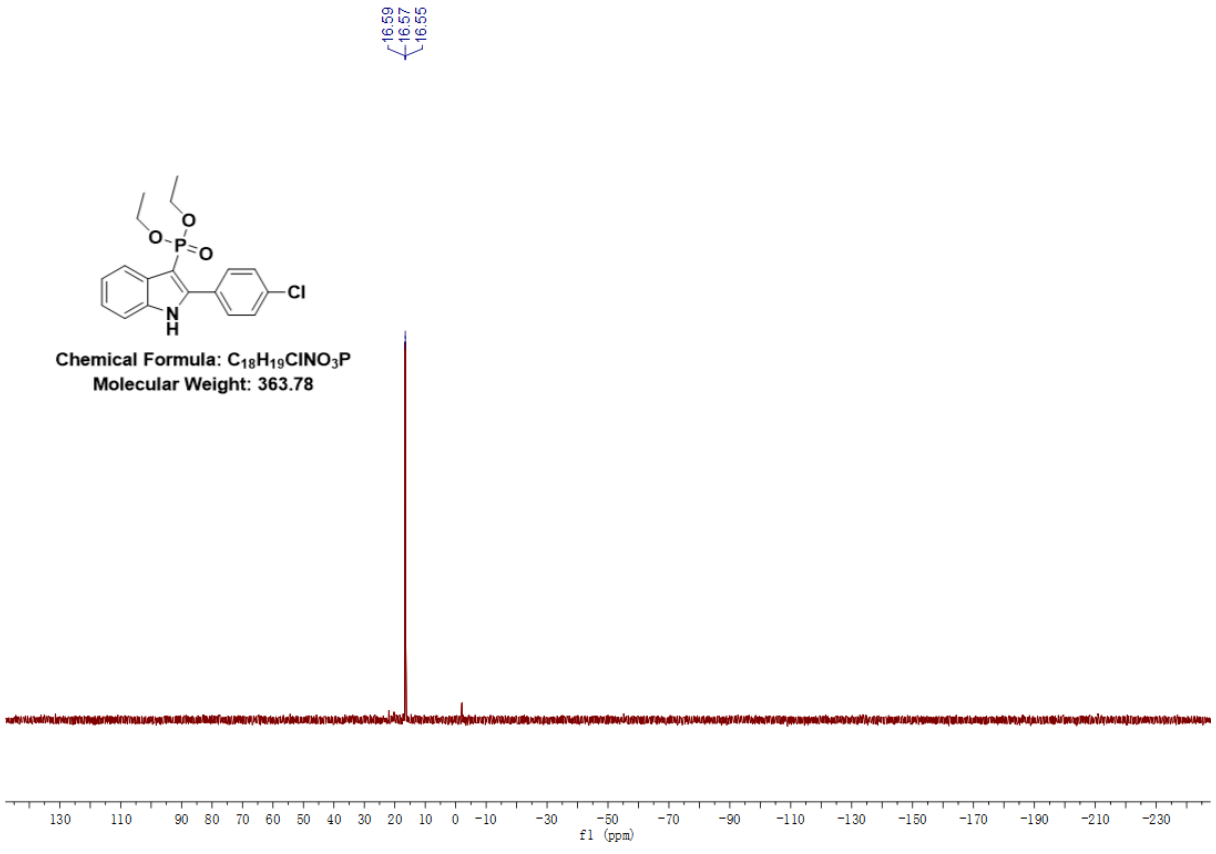


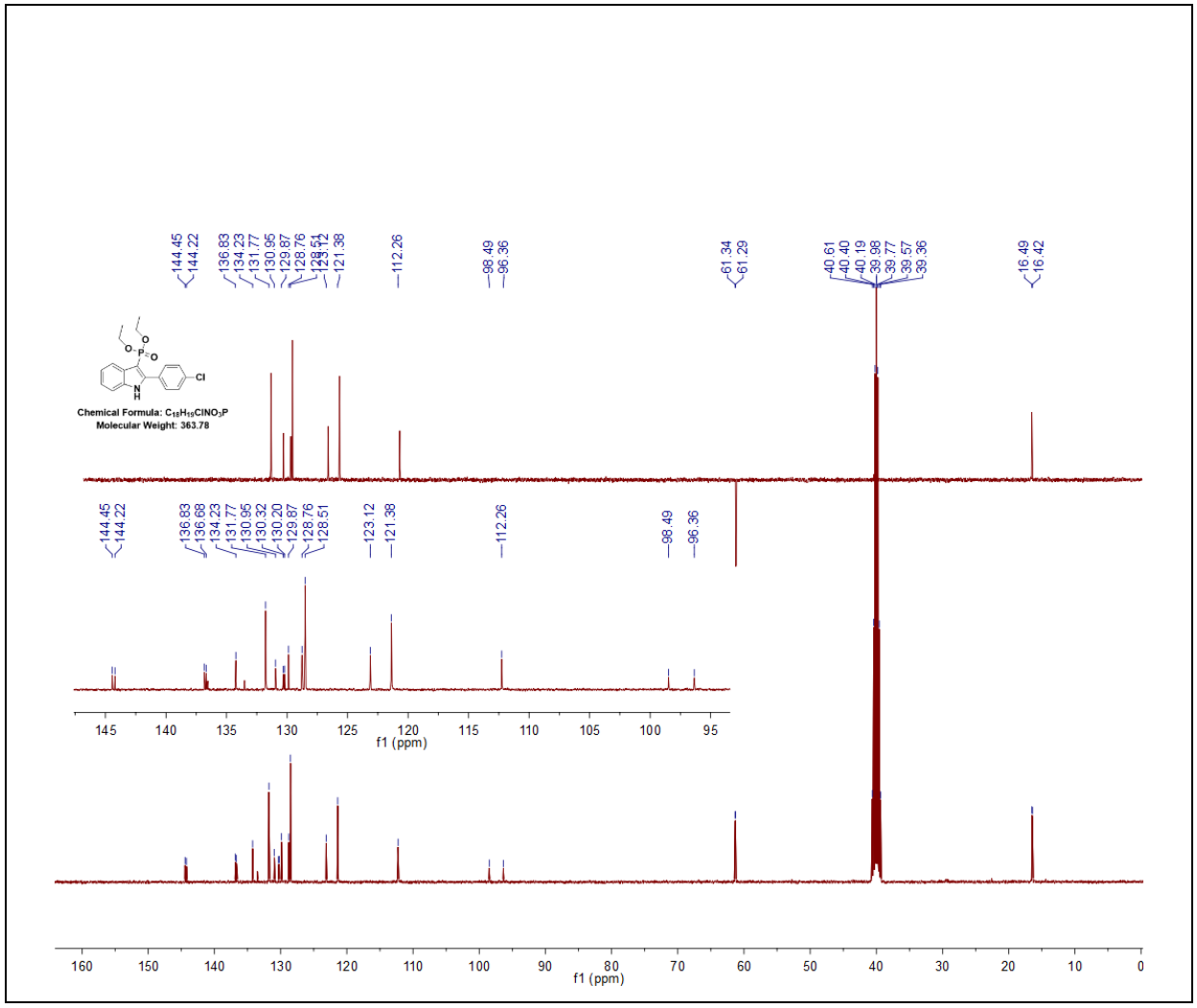
Formula Calculator Results

m/z	Calc m/z	Diff (mDa)	Diff (ppm)	Ion Formula	Ion
344.1404	344.141	0.62	1.79	C19 H23 N O3 P	(M+H)+

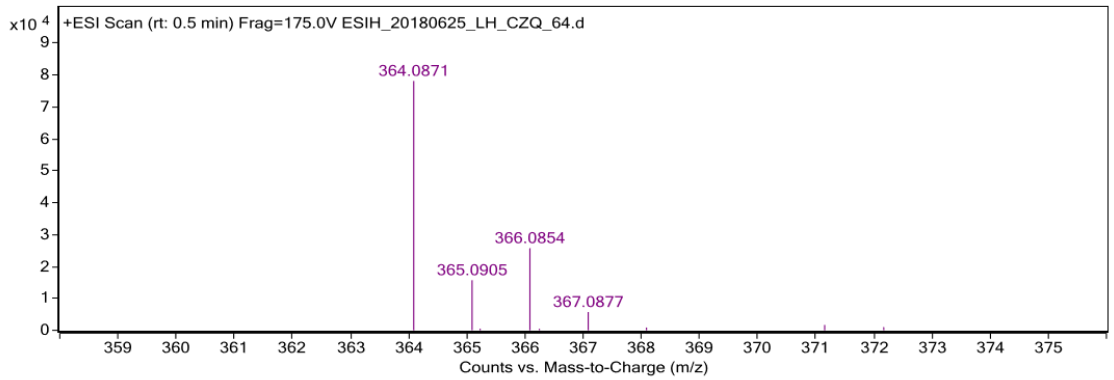
Diethyl (2-(4-chlorophenyl)-1H-indol-3-yl)phosphonate (4o)







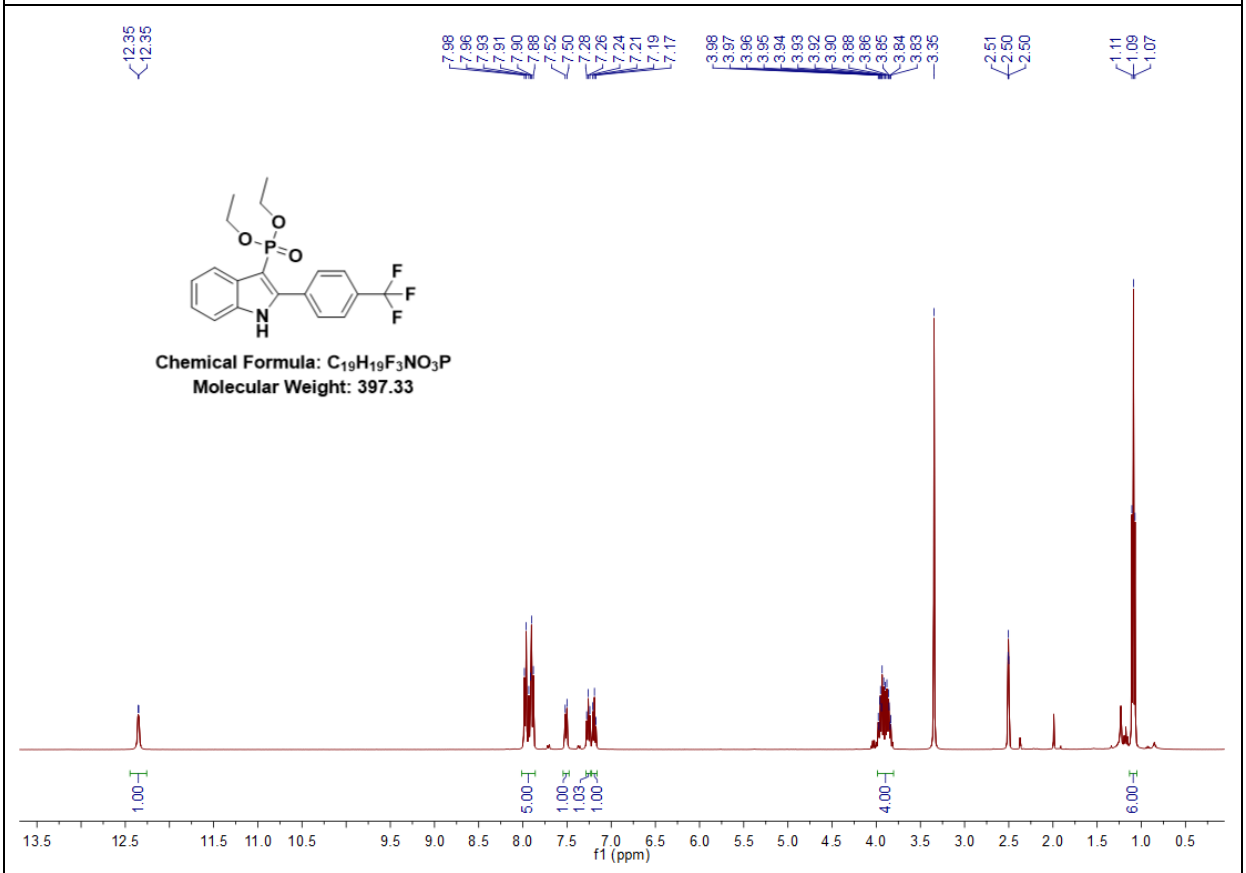
Fragmentor Voltage 175 **Collision Energy** 0 **Ionization Mode** ESI

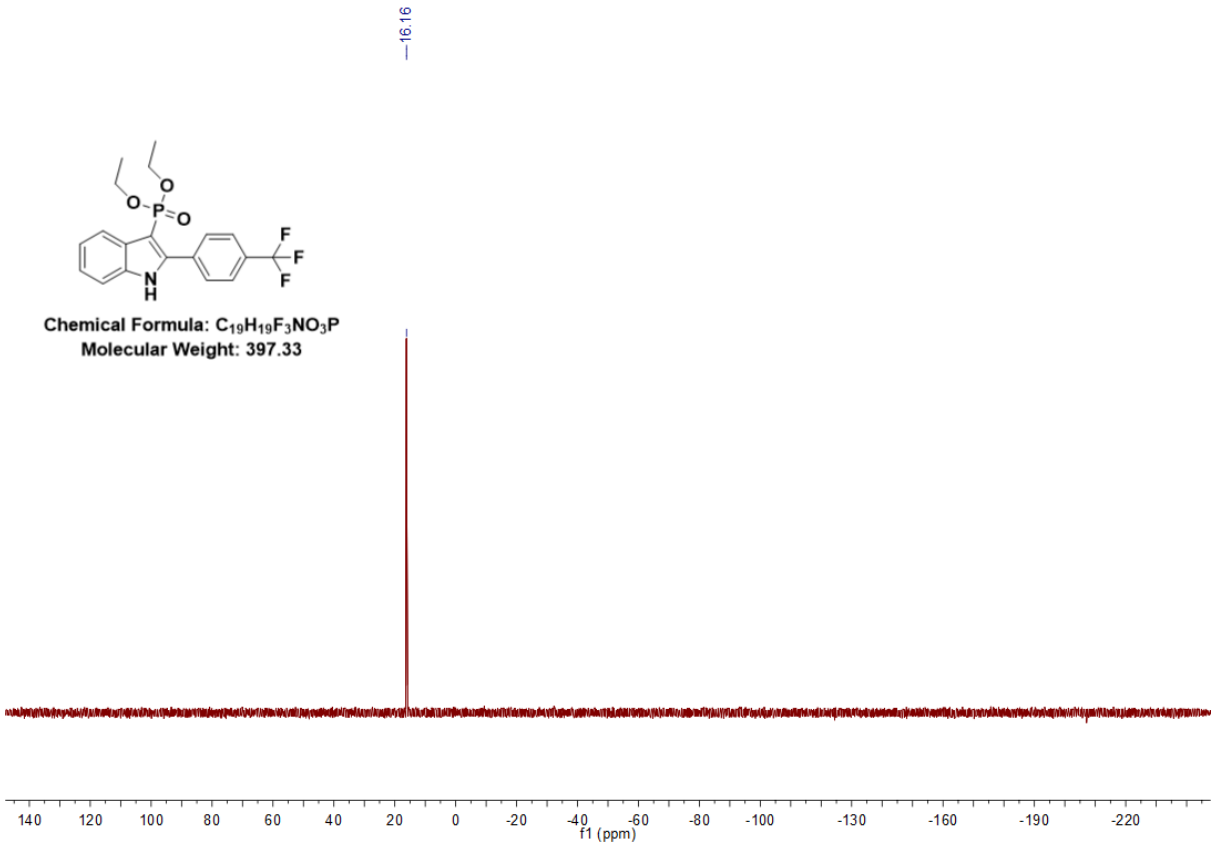


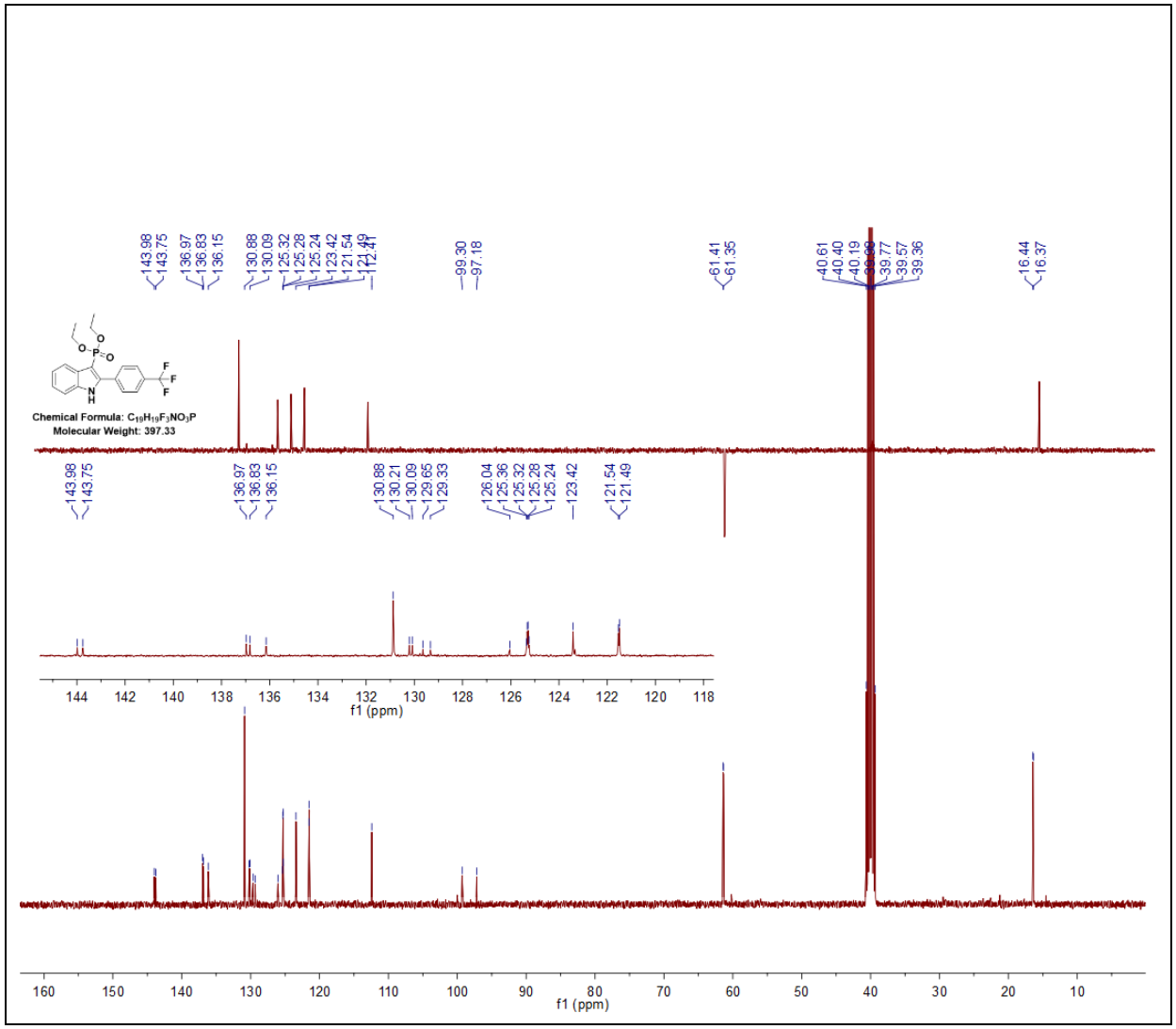
Formula Calculator Results

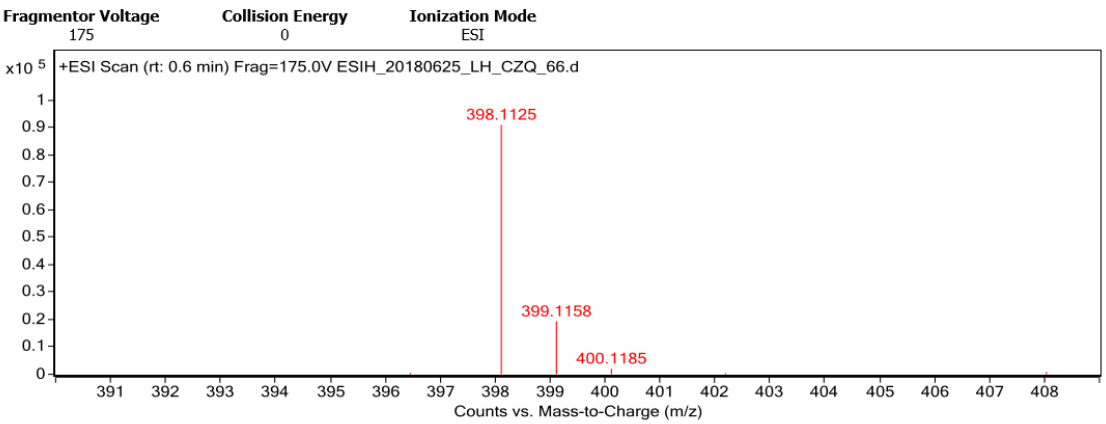
m/z	Calc m/z	Diff (mDa)	Diff (ppm)	Ion Formula	Ion
364.0871	364.0864	-0.71	-1.94	C18 H20 Cl N O3 P	(M+H)+

Diethyl (2-(4-(trifluoromethyl)phenyl)-1H-indol-3-yl)phosphonate (4p)





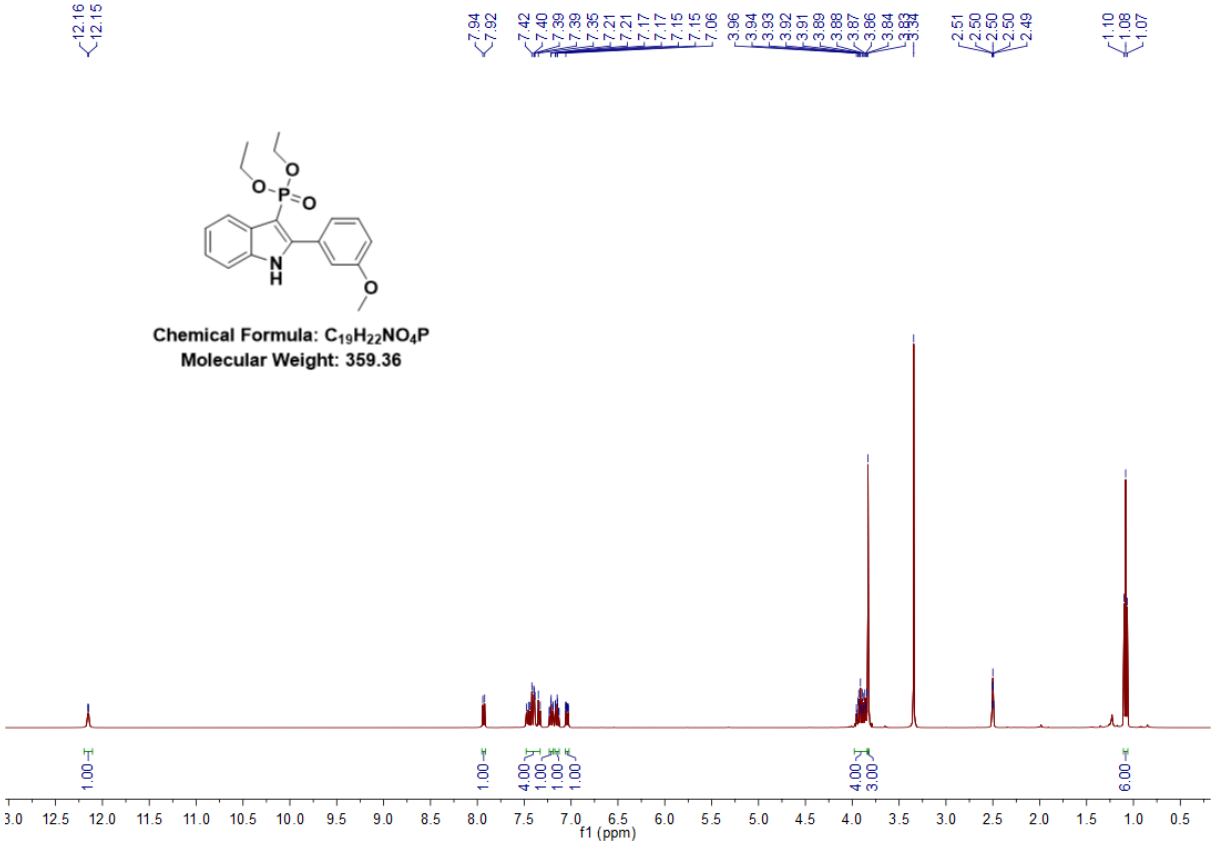


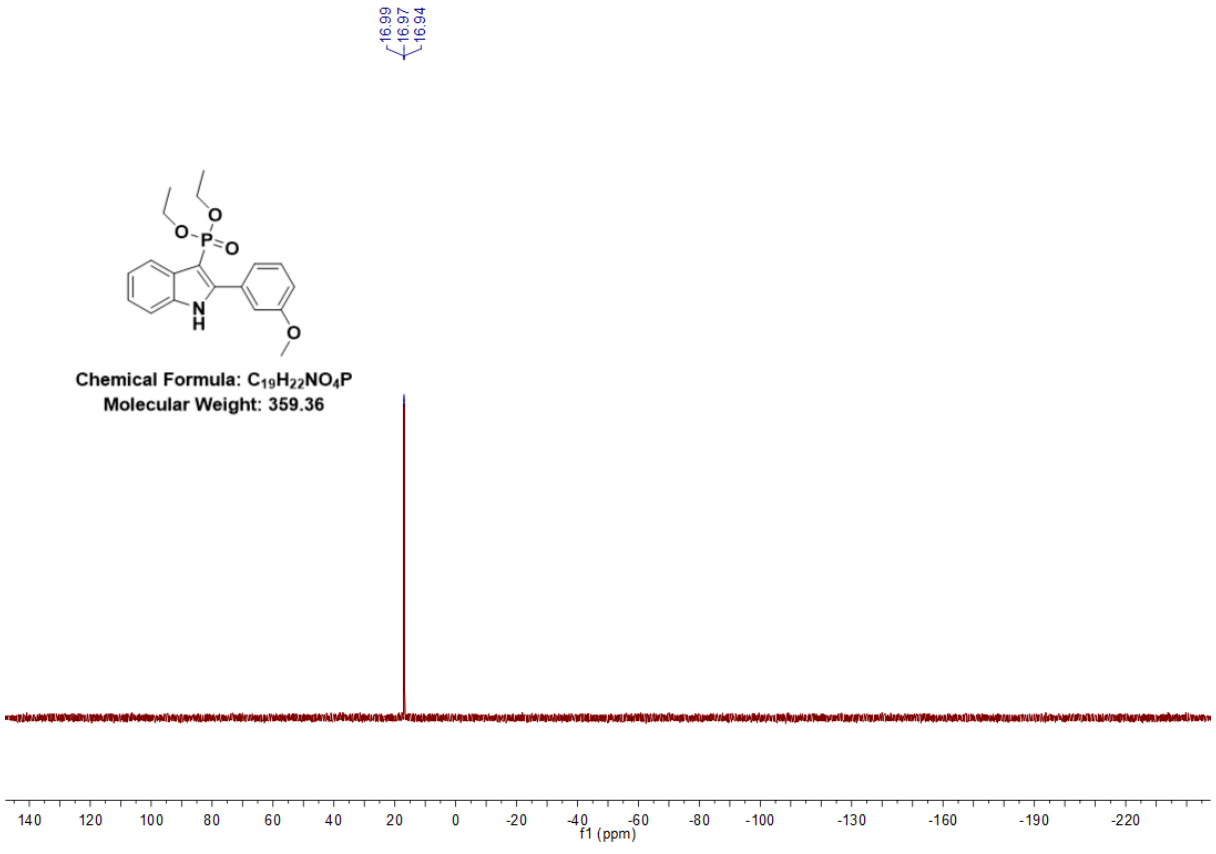


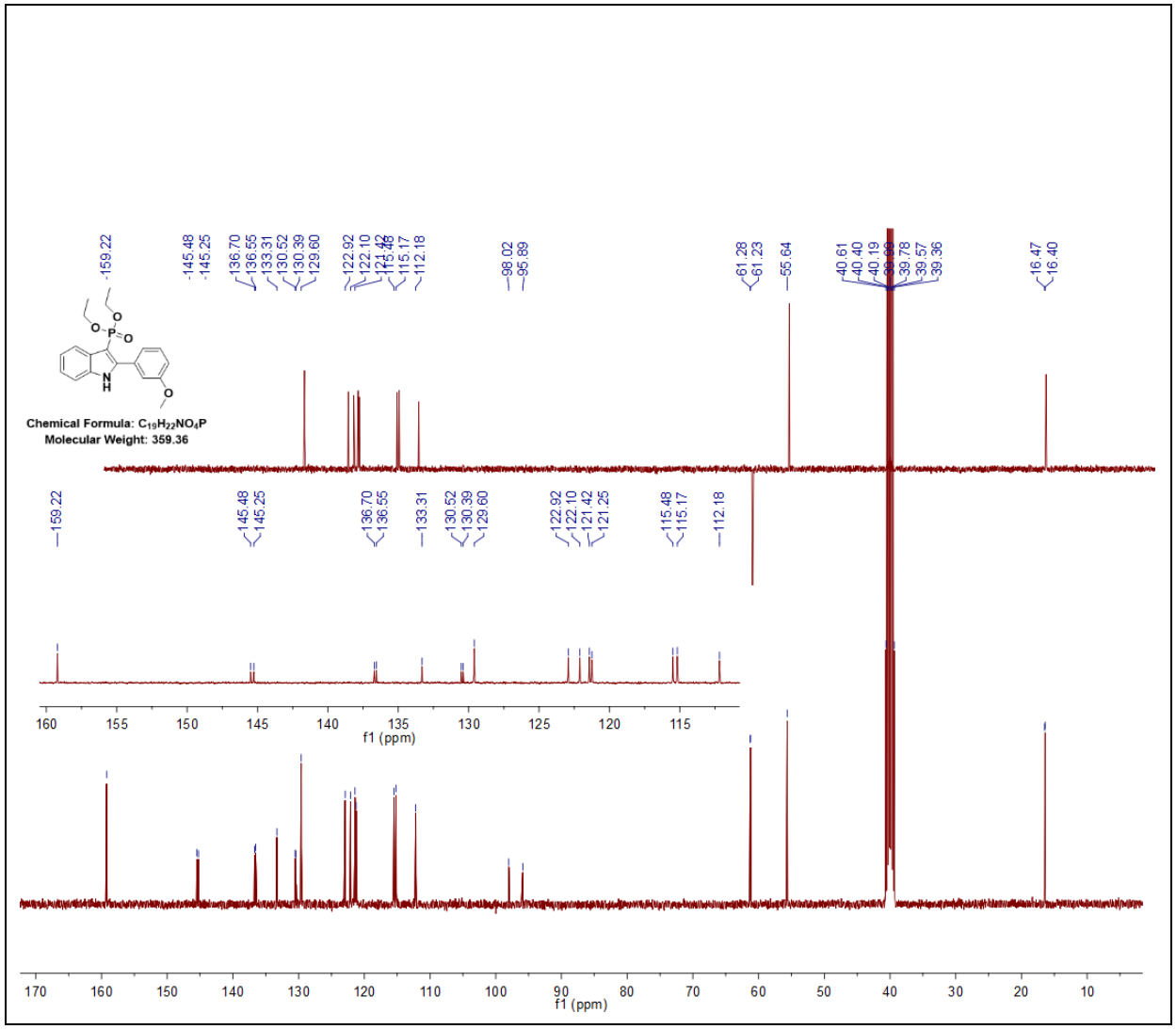
Formula Calculator Results

m/z	Calc m/z	Diff (mDa)	Diff (ppm)	Ion Formula	Ion
398.1125	398.1127	0.21	0.53	C19 H20 F3 N O3 P	(M+H)+

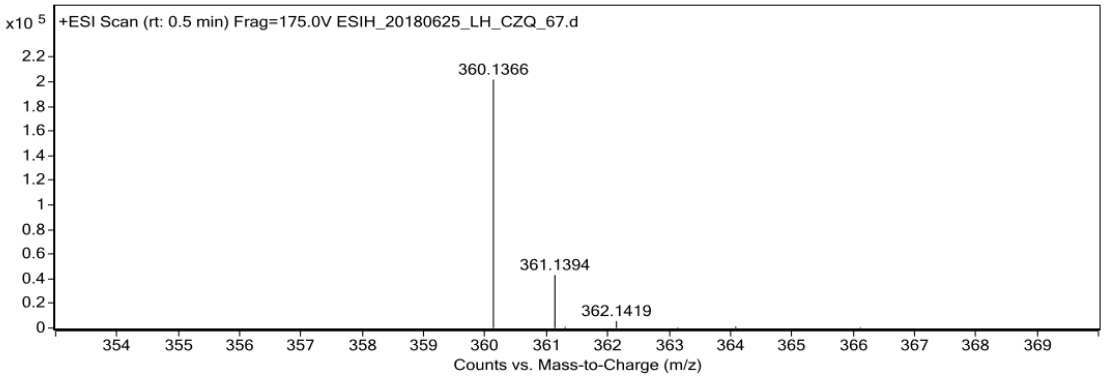
Diethyl (2-(3-methoxyphenyl)-1H-indol-3-yl)phosphonate (4q)







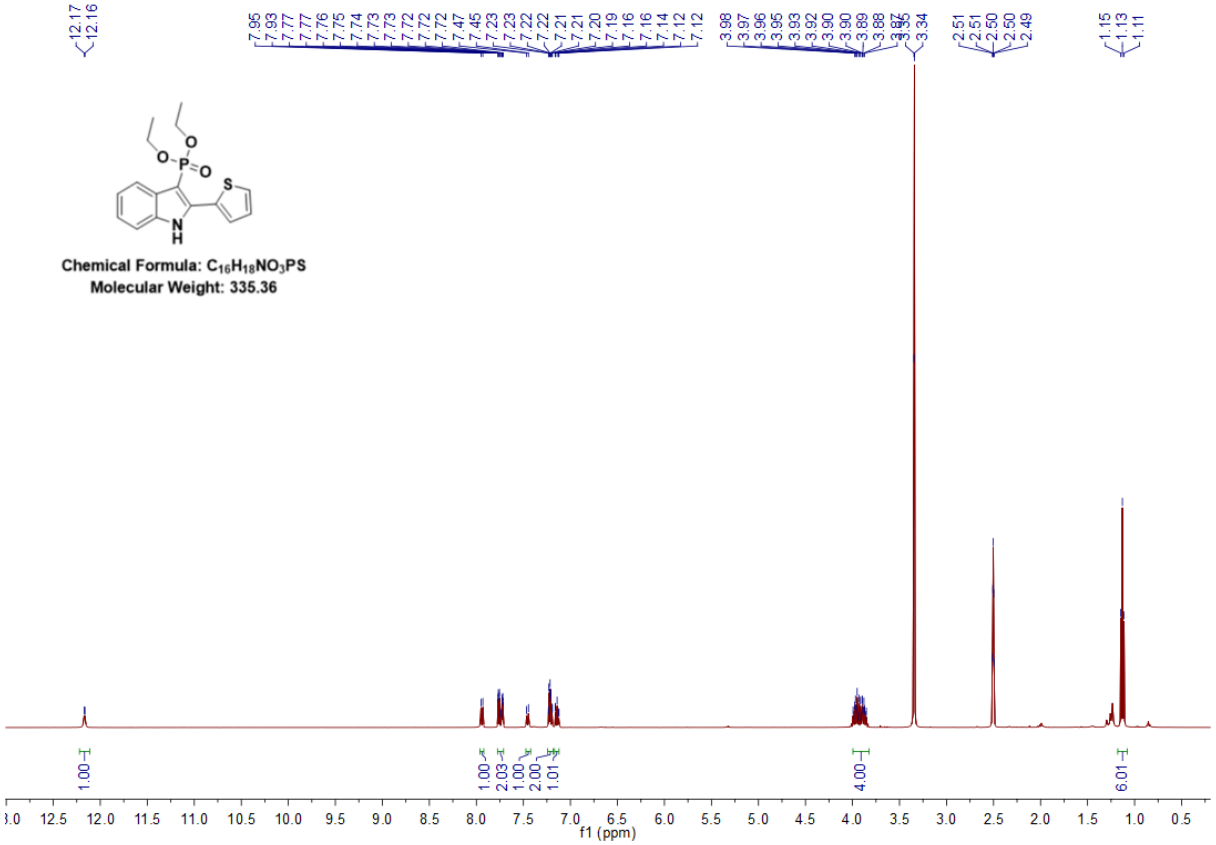
Fragmentor Voltage	Collision Energy	Ionization Mode
175	0	ESI

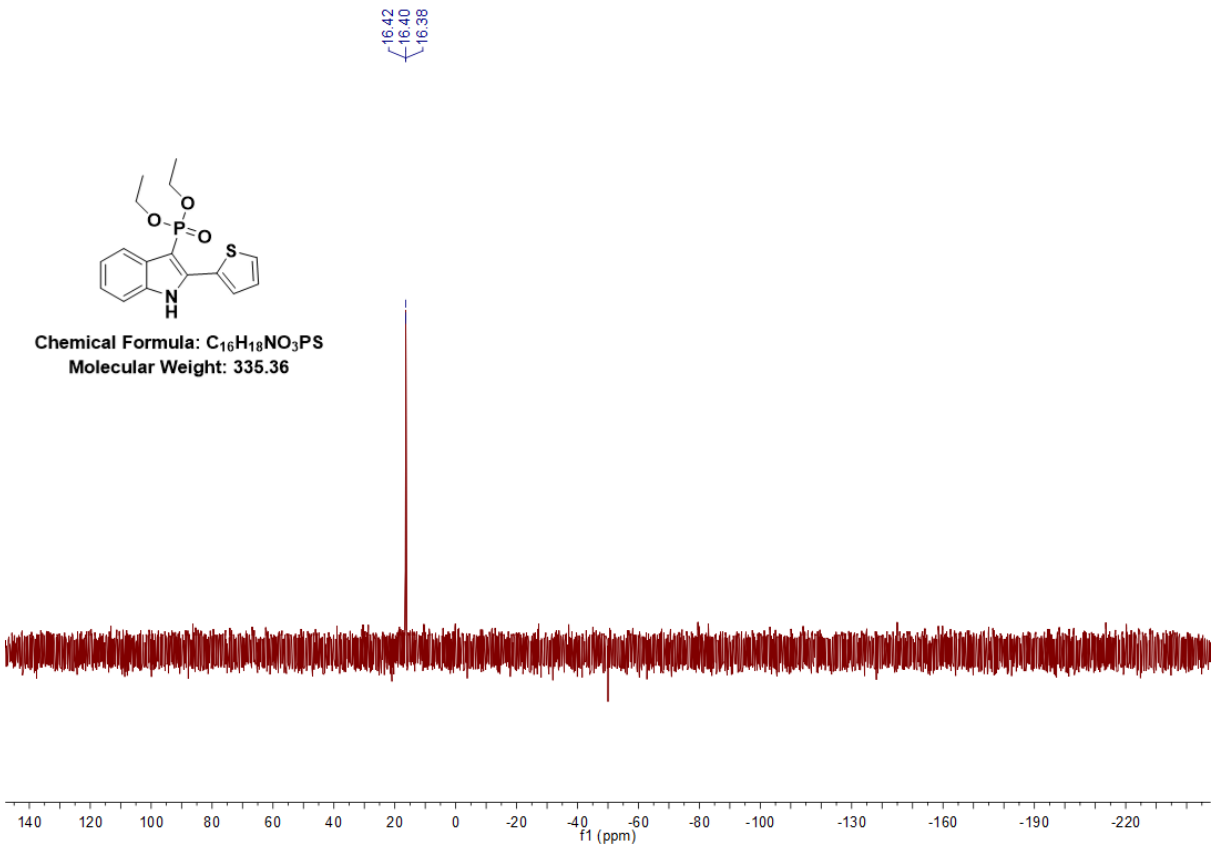


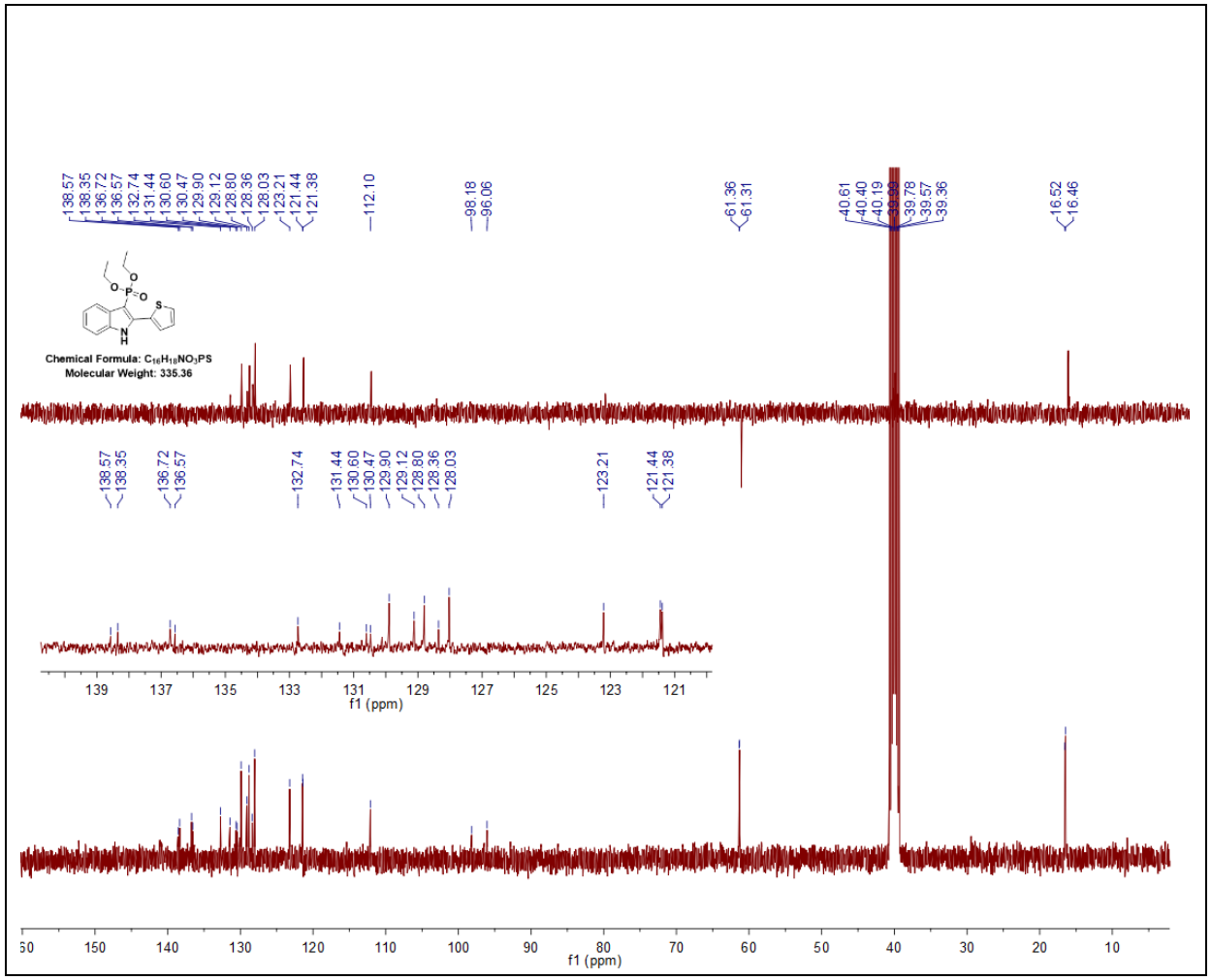
Formula Calculator Results

m/z	Calc m/z	Diff (mDa)	Diff (ppm)	Ion Formula	Ion
360.1366	360.1359	-0.66	-1.83	C19 H23 N O4 P	(M+H)+

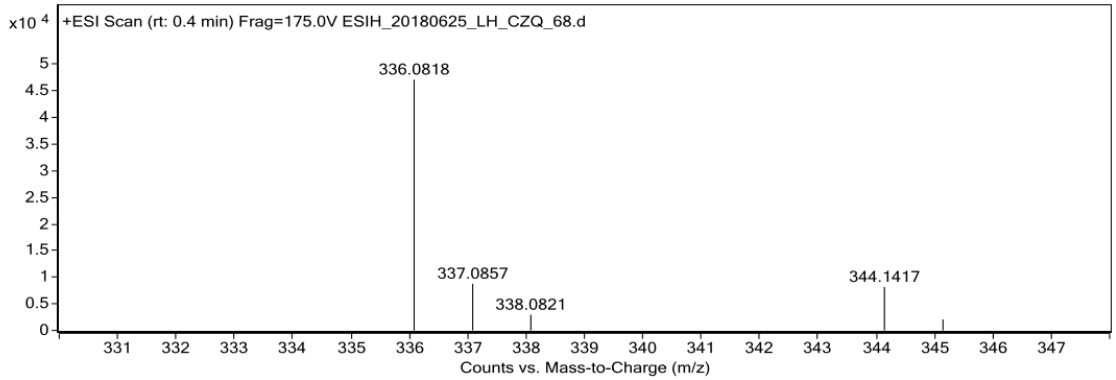
Diethyl (2-(thiophen-2-yl)-1H-indol-3-yl)phosphonate (4r)







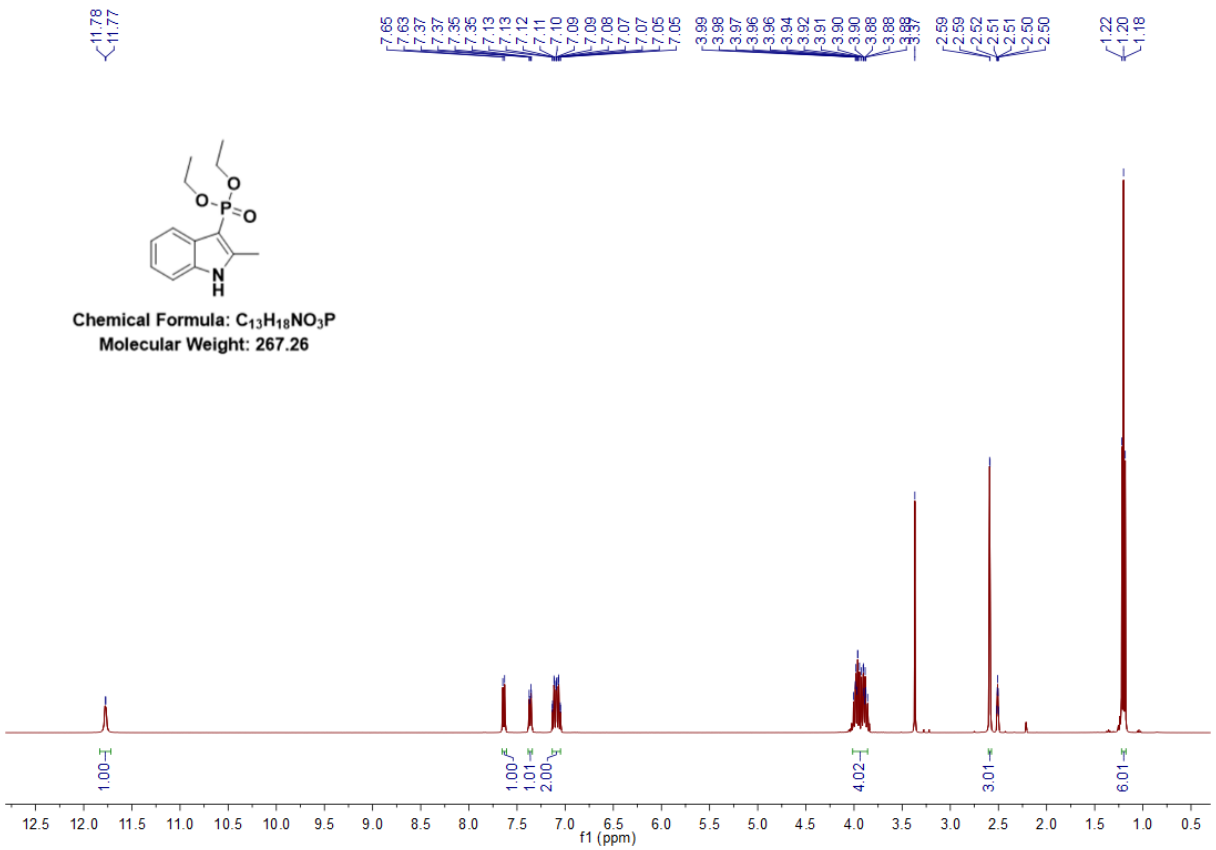
Fragmentor Voltage	Collision Energy	Ionization Mode
175	0	ESI

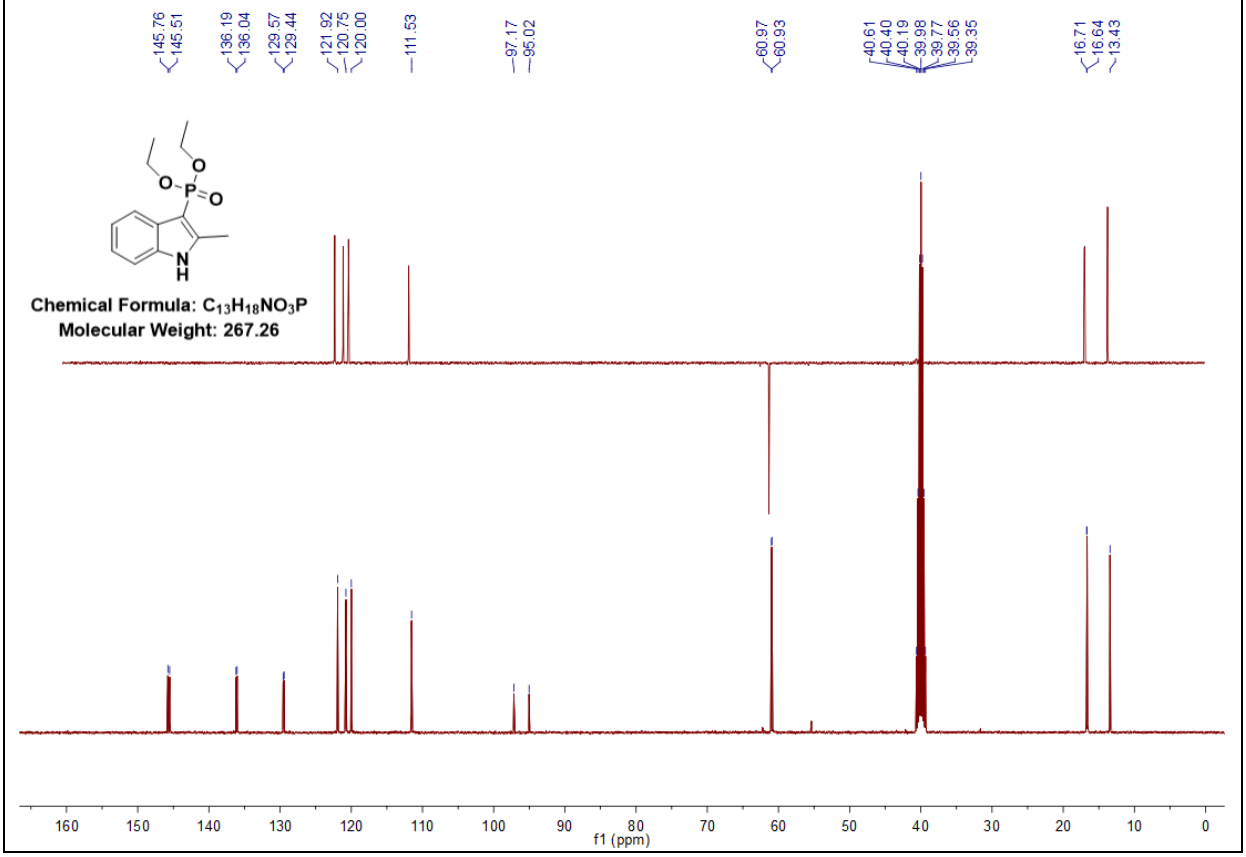


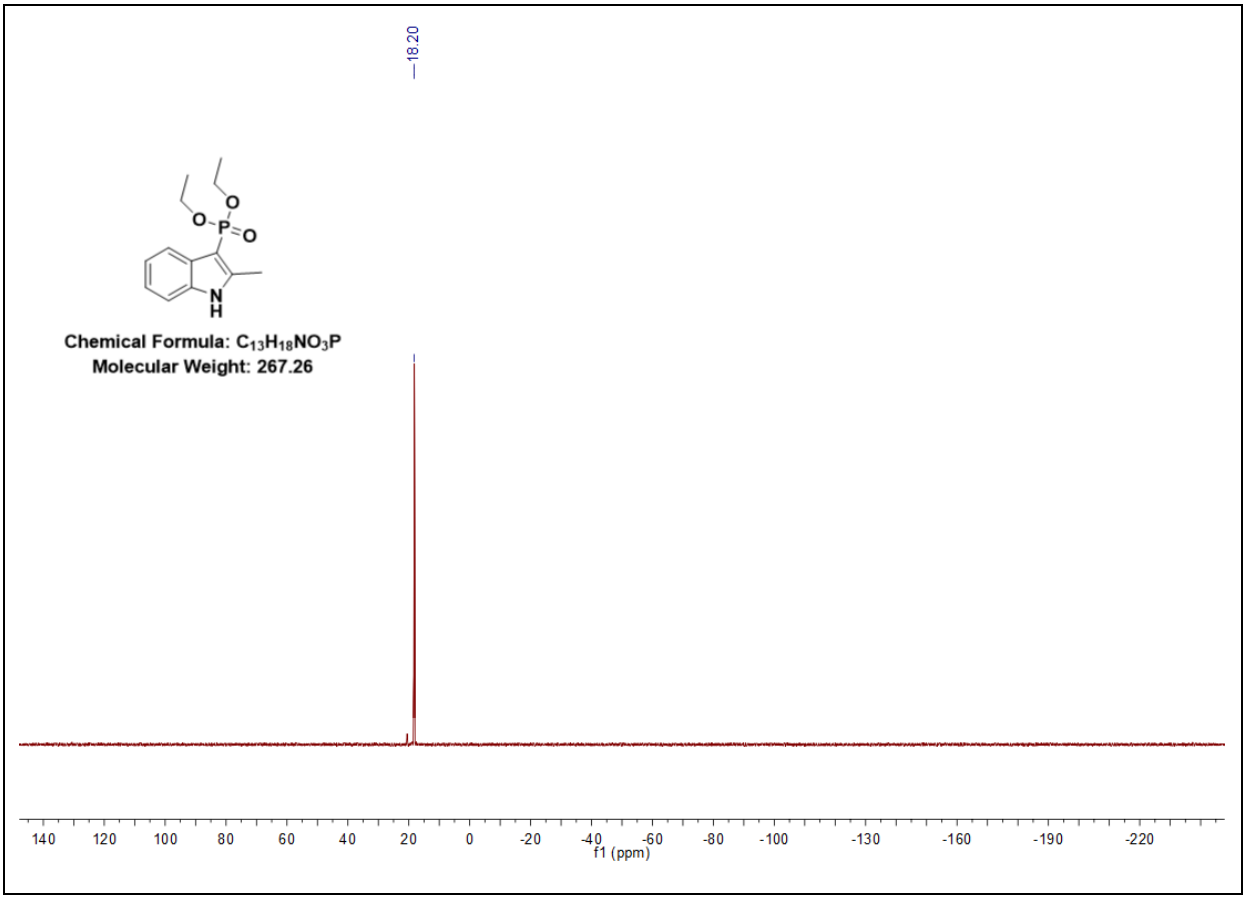
Formula Calculator Results

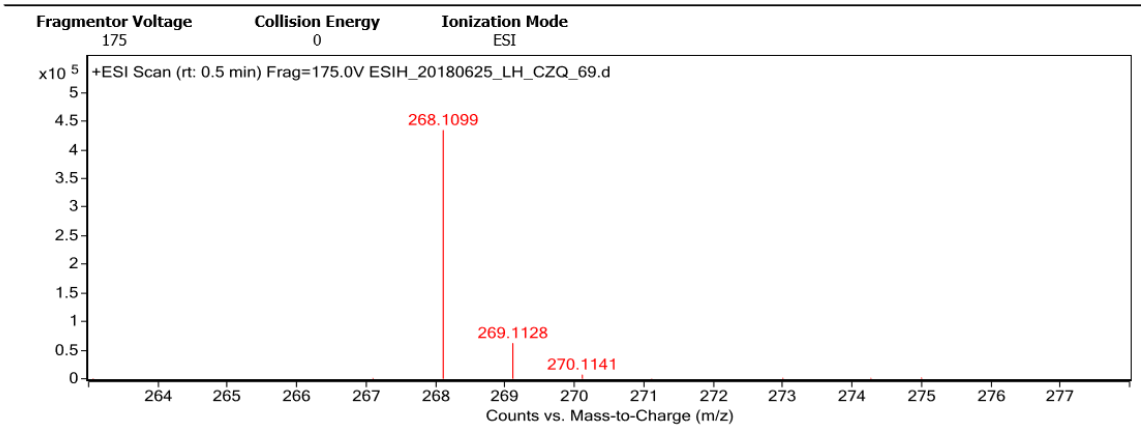
m/z	Calc m/z	Diff (mDa)	Diff (ppm)	Ion Formula	Ion
336.0818	336.0818	-0.03	-0.09	C16 H19 N O3 P S	(M+H)+

Diethyl (2-methyl-1H-indol-3-yl) phosphite (4s)





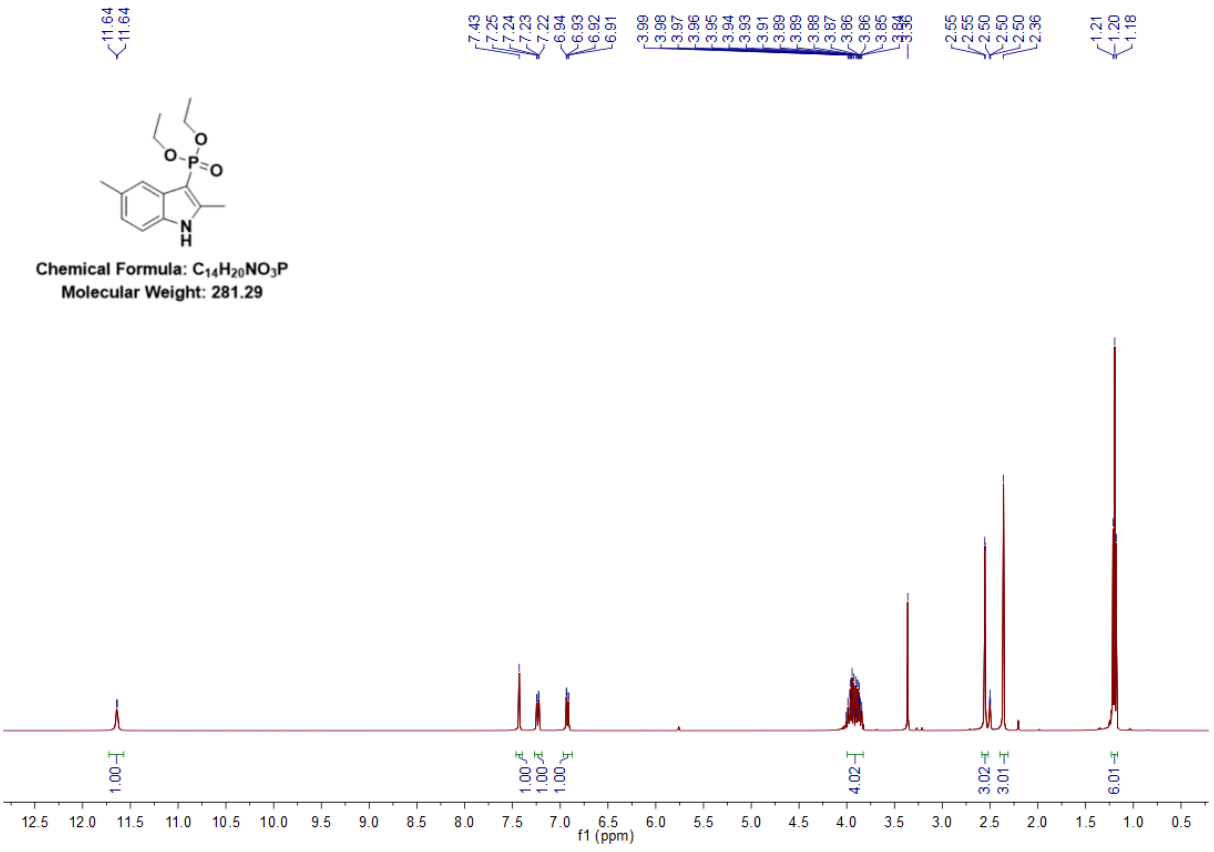


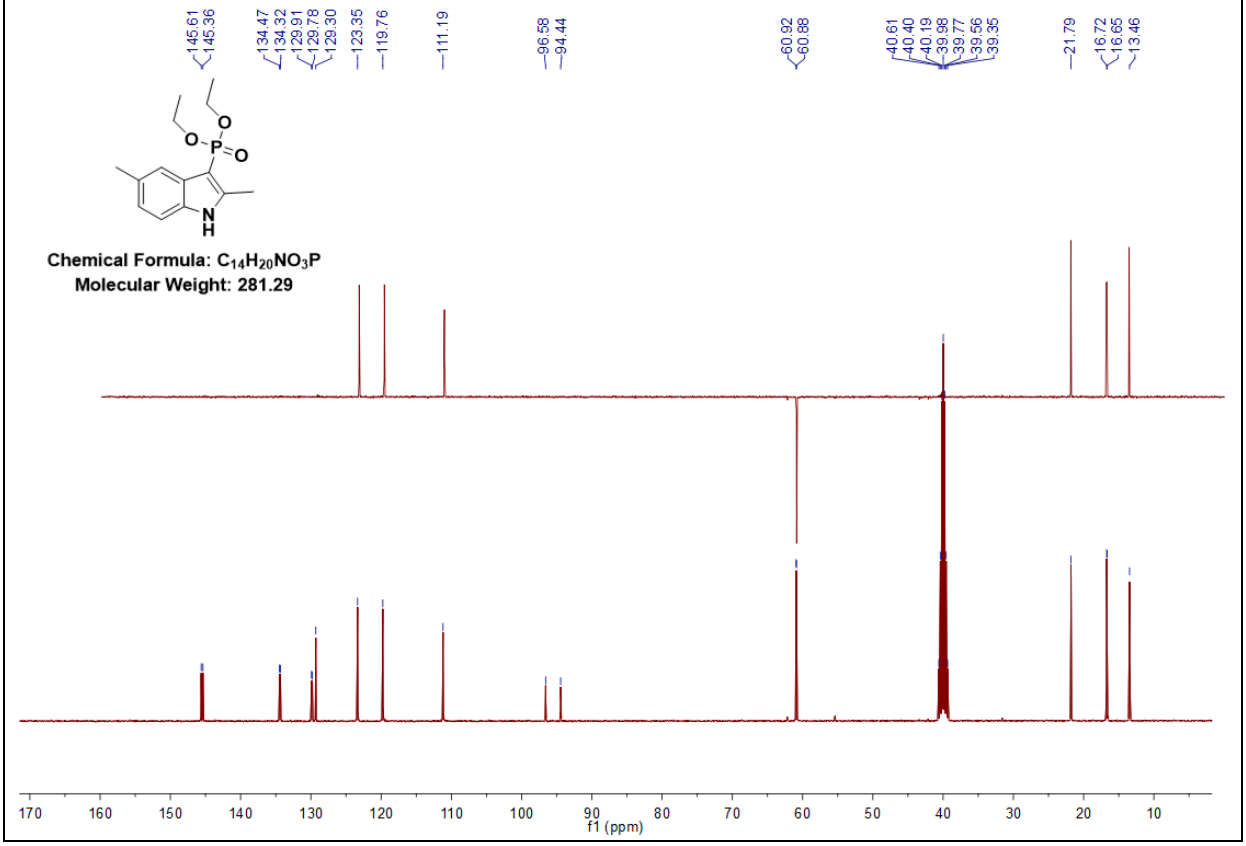


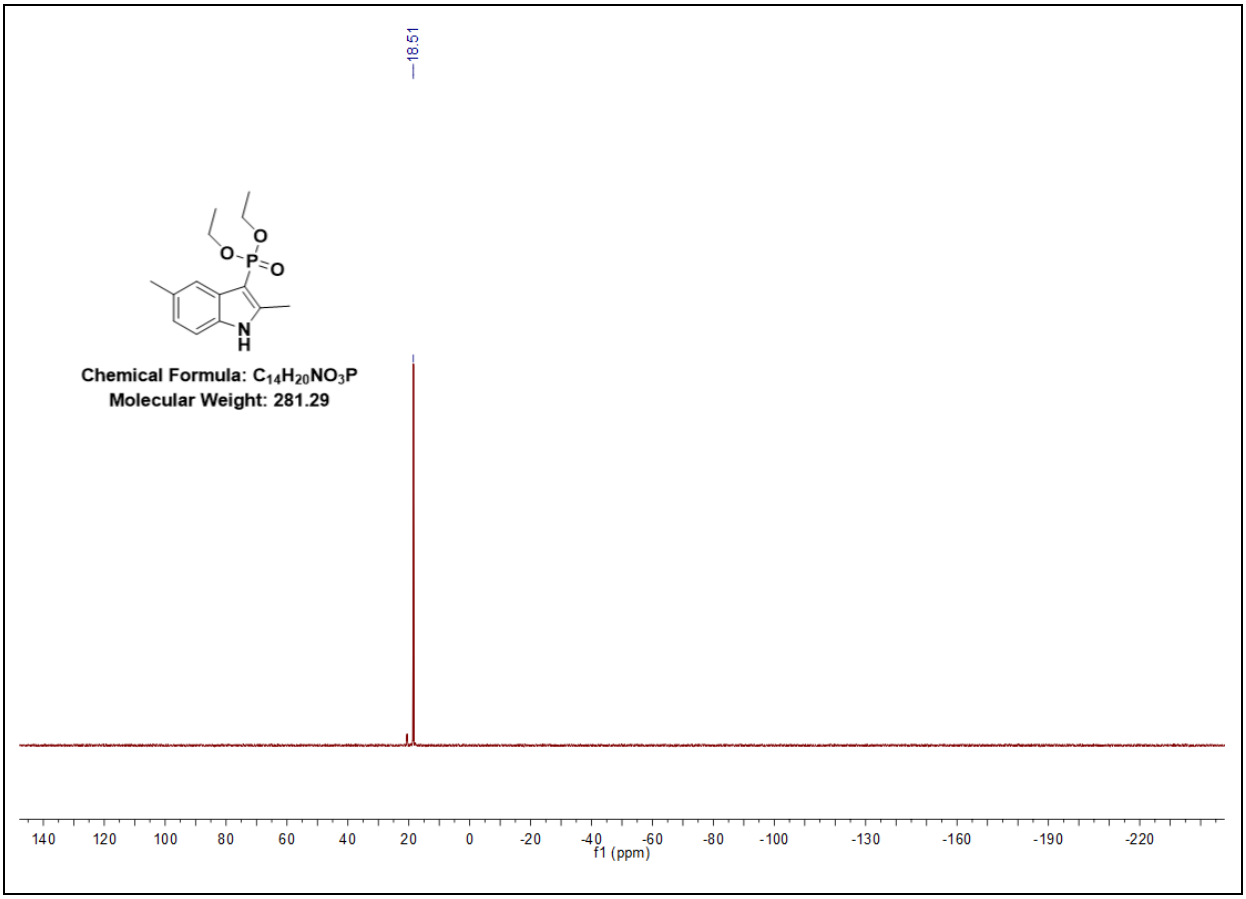
Formula Calculator Results

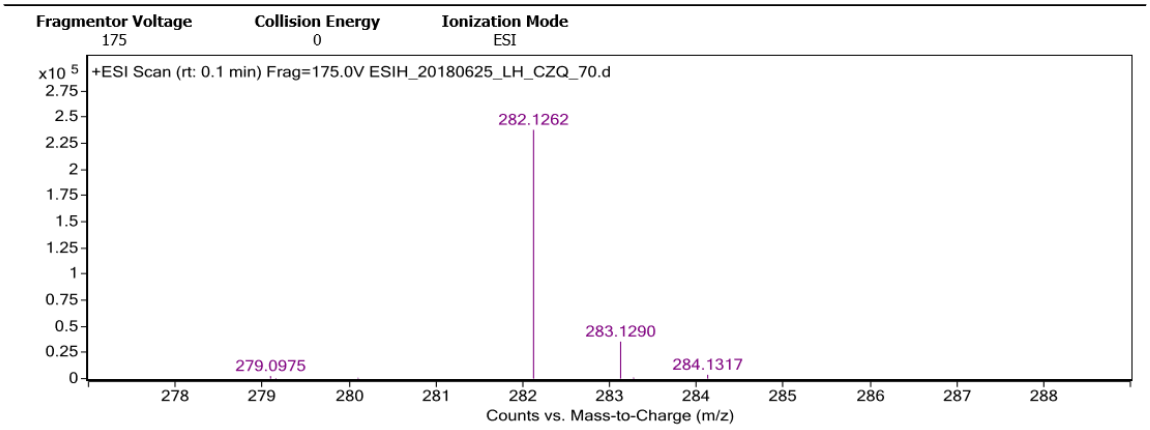
m/z	Calc m/z	Diff (mDa)	Diff (ppm)	Ion Formula	Ion
268.1099	268.1097	-0.19	-0.73	C13 H19 N O3 P	(M+H)+

2,5-Dimethyl-1H-indol-3-yl diethyl phosphite (4t)





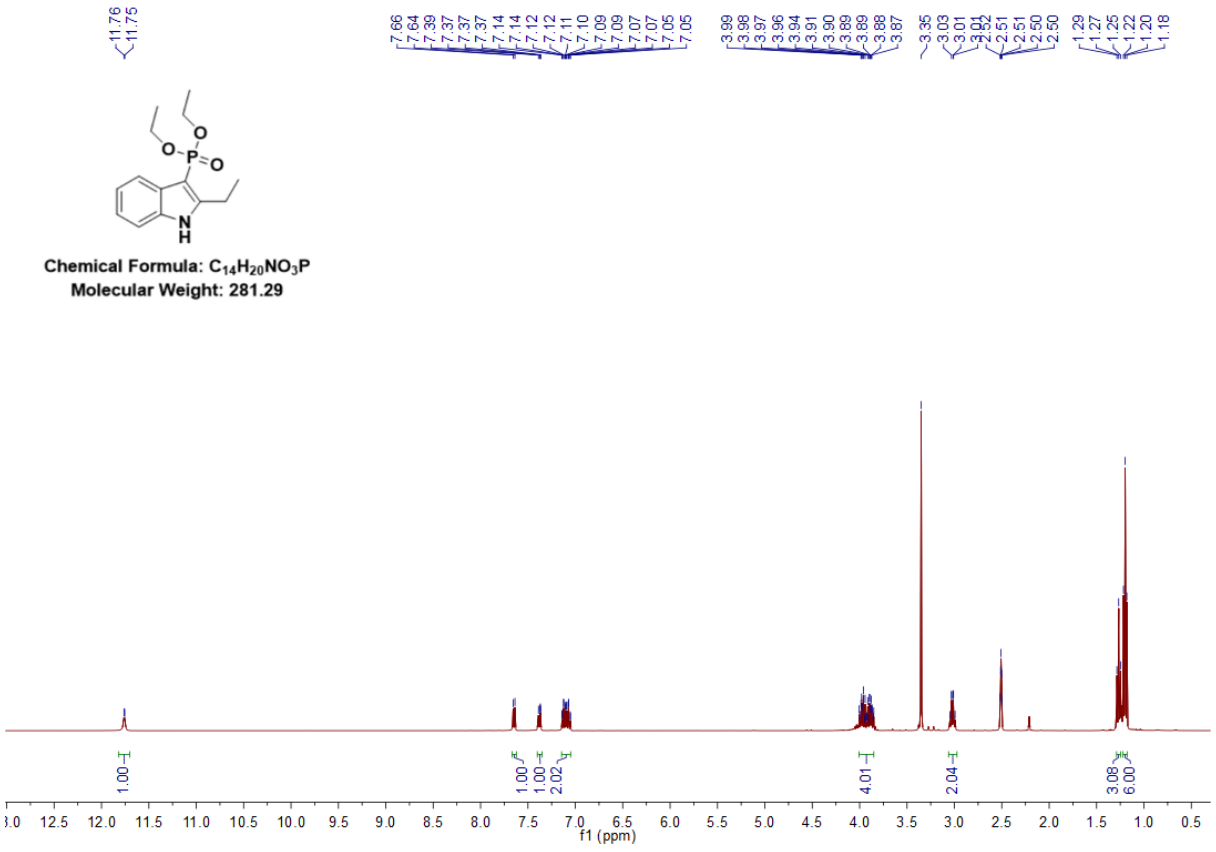


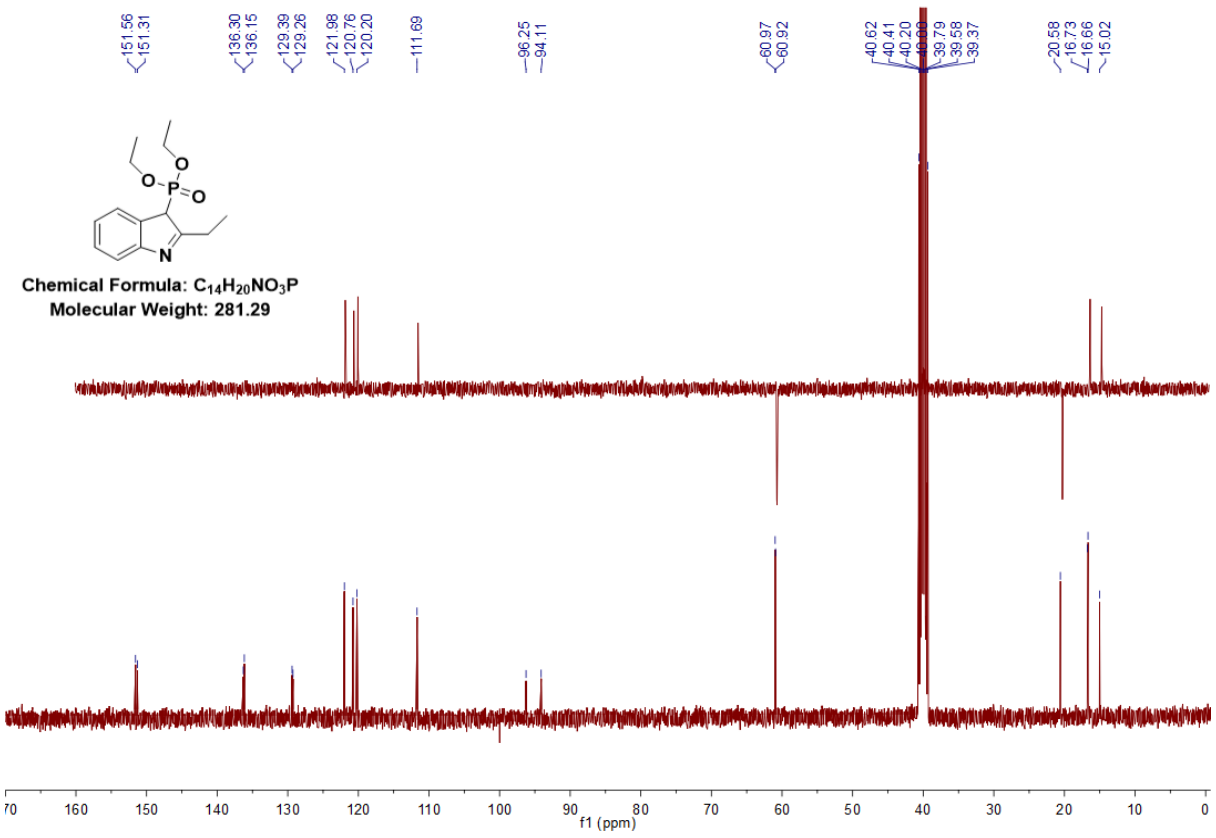


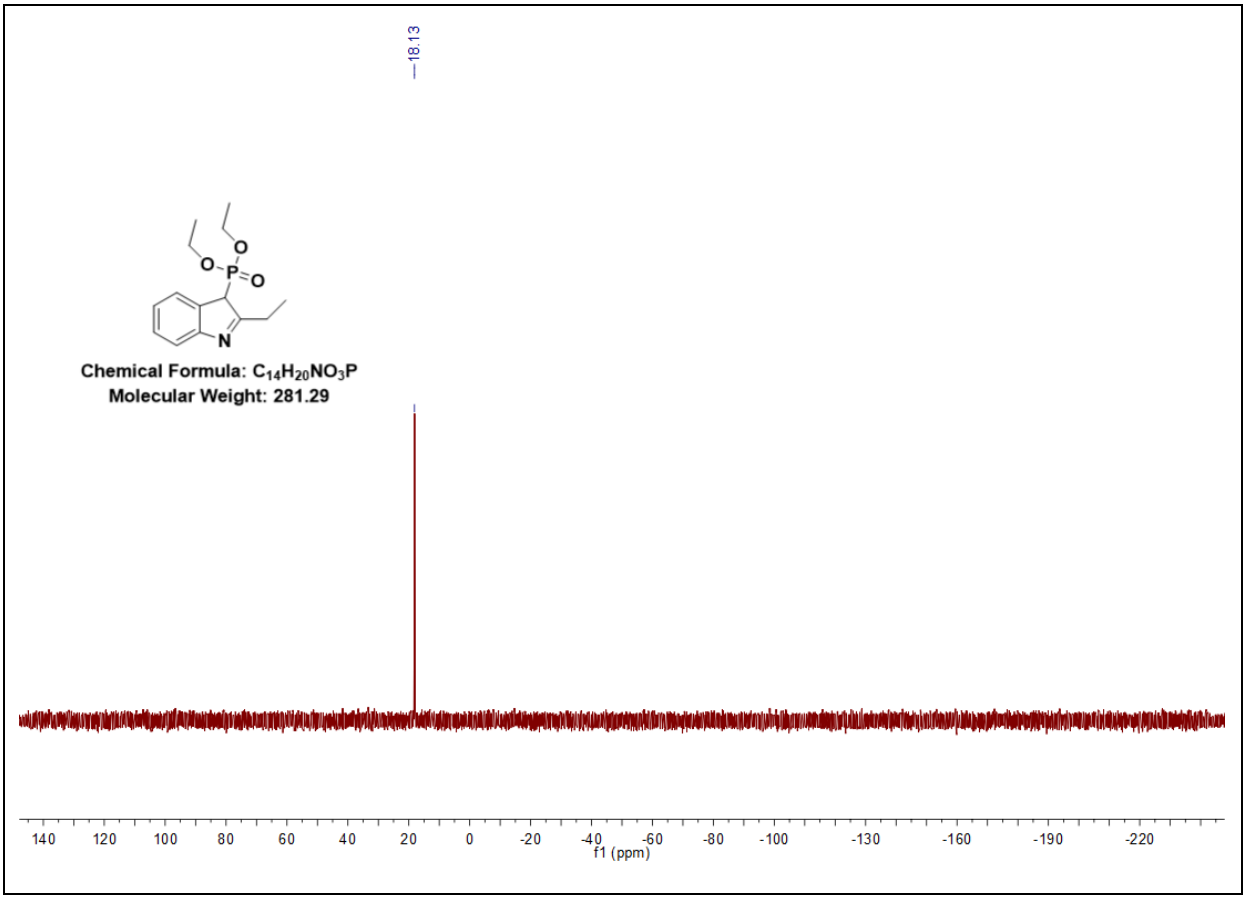
Formula Calculator Results

m/z	Calc m/z	Diff (mDa)	Diff (ppm)	Ion Formula	Ion
282.1262	282.1254	-0.89	-3.14	C14 H21 N O3 P	(M+H)+

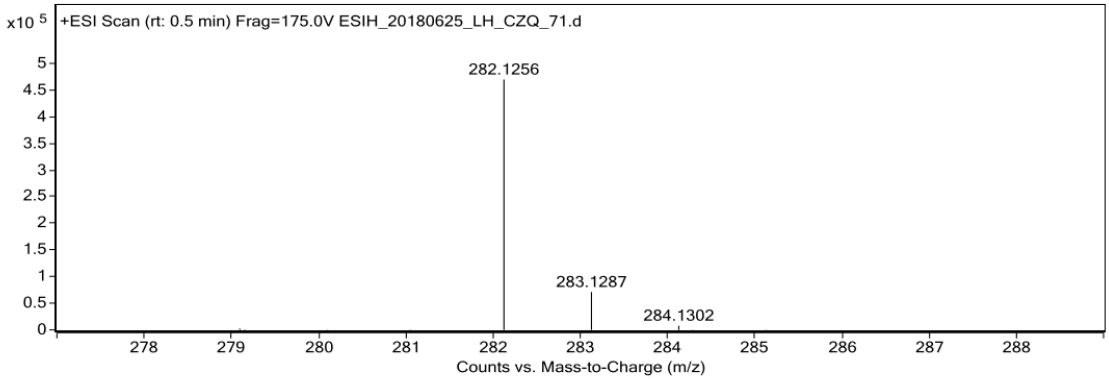
Diethyl (2-ethyl-1H-indol-3-yl) phosphite (4u)







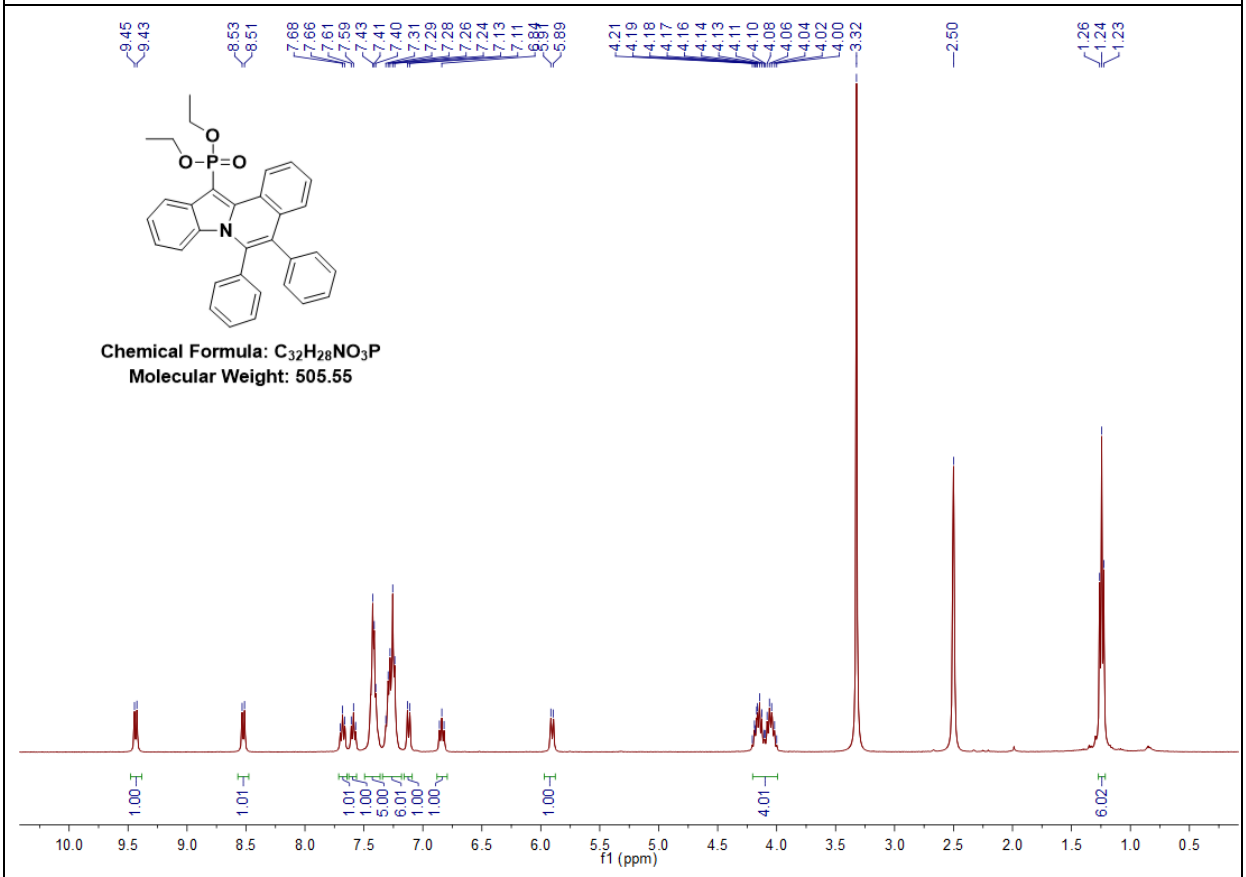
Fragmentor Voltage 175 **Collision Energy** 0 **Ionization Mode** ESI

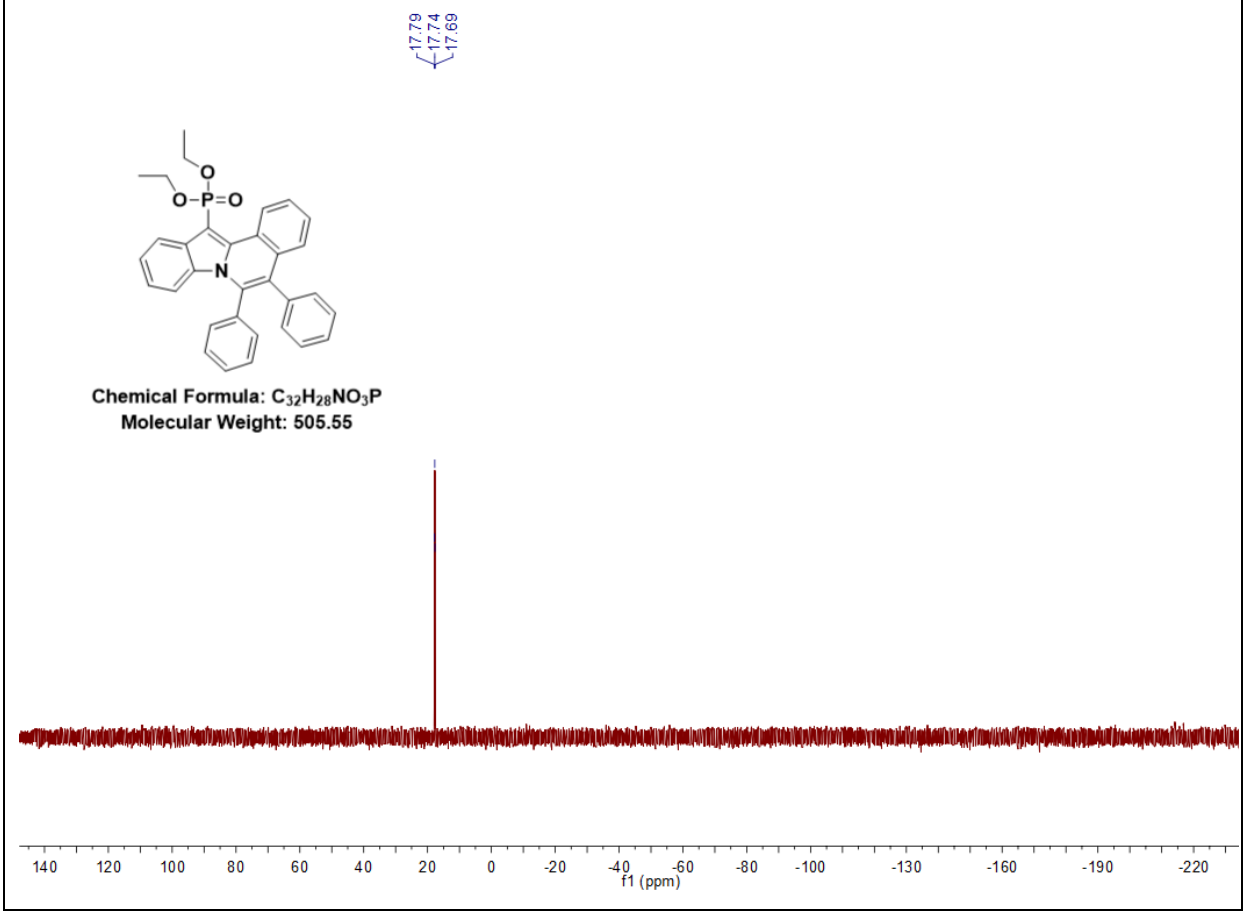


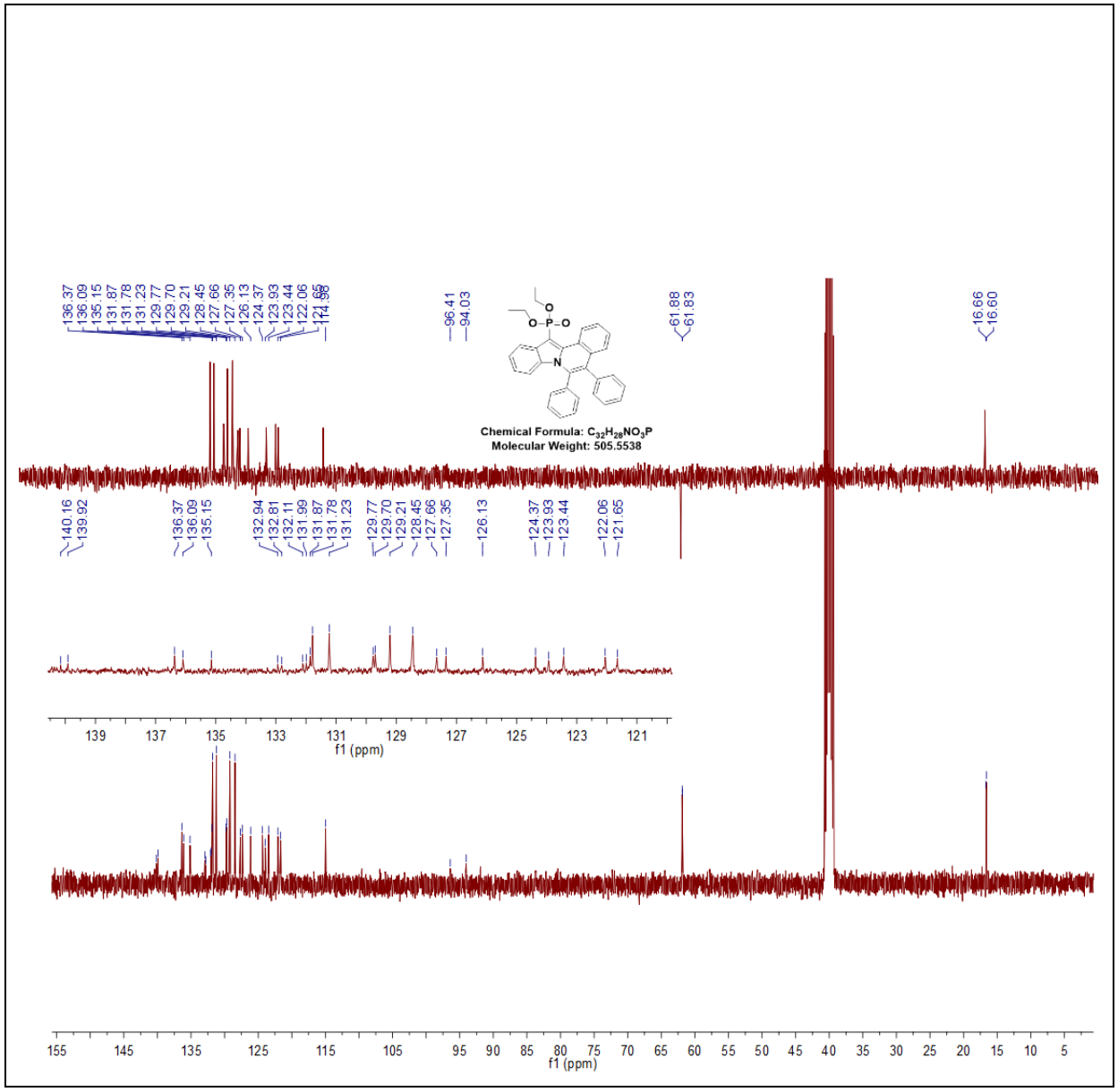
Formula Calculator Results

m/z	Calc m/z	Diff (mDa)	Diff (ppm)	Ion Formula	Ion
282.1256	282.1254	-0.2	-0.7	C14 H21 N O3 P	(M+H)+

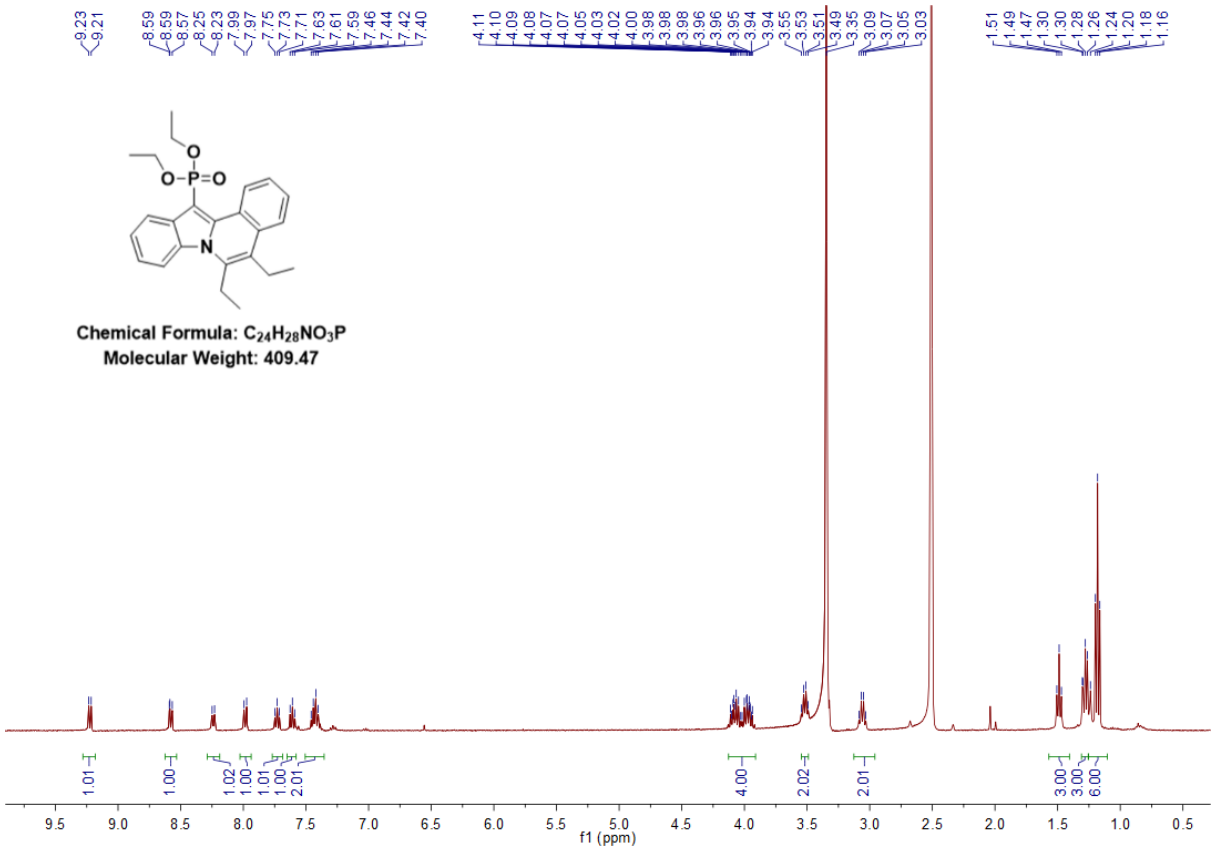
Diethyl (5,6-diphenylindolo[2,1-a]isoquinolin-12-yl)phosphonate (6)

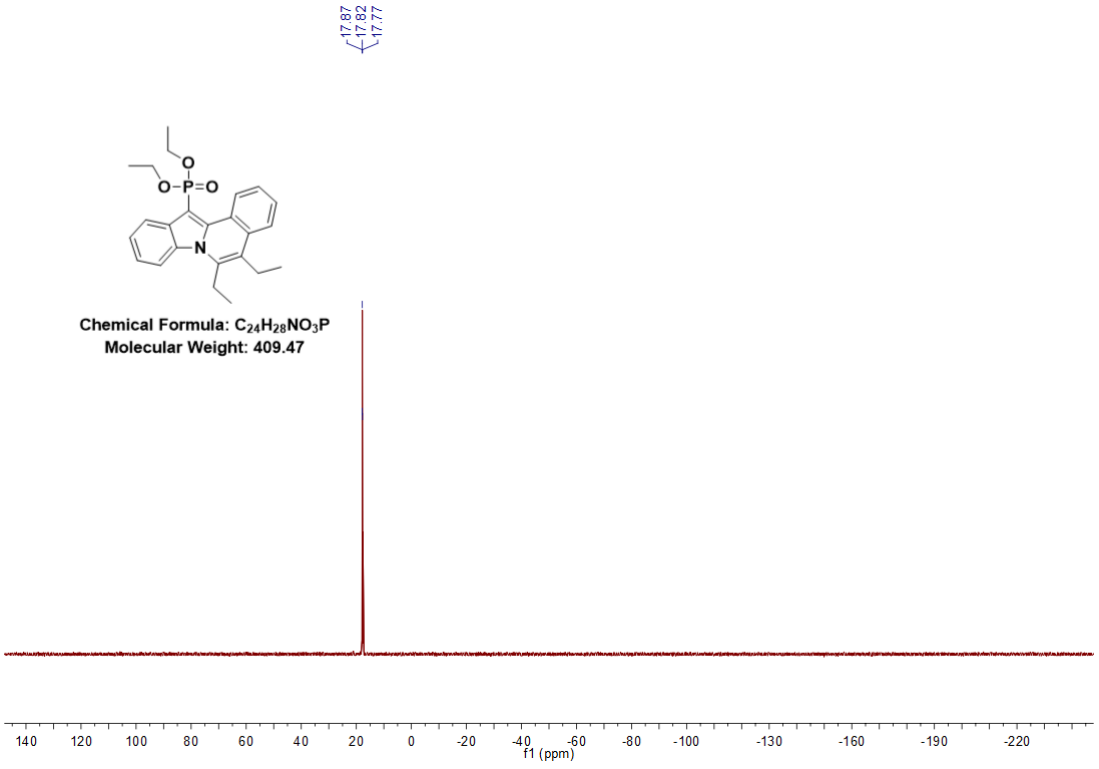





136.37
136.09
135.15
131.87
131.78
131.23
129.77
129.70
129.21
128.45
127.66
127.35
126.13
124.37
123.93
123.44
122.06
96.41
94.03
61.88
61.83
16.66
16.60
Chemical Formula: C32H28NO3P
Molecular Weight: 505.5538
140.16
139.92
136.37
136.09
135.15
132.94
132.81
132.11
131.99
131.87
131.78
131.23
129.77
129.70
129.21
128.45
127.66
127.35
126.13
124.37
123.93
123.44
122.06
121.65
139 137 135 133 131 129 127 125 123 121
f1 (ppm)
155 145 135 125 115 105 95 90 85 80 75 70 65 60 55 50 45 40 35 30 25 20 15 10 5
f1 (ppm)

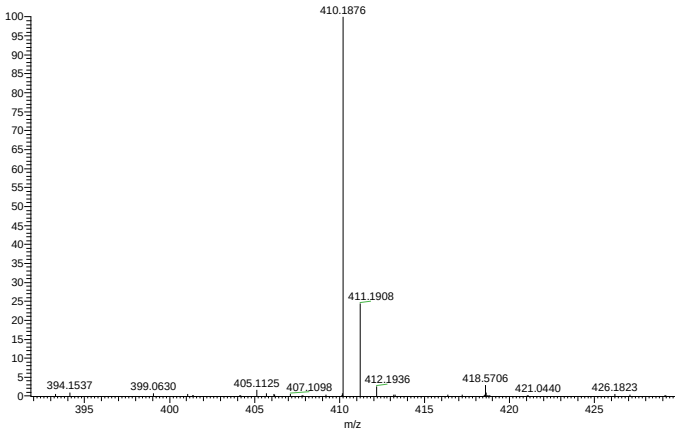
diethyl (5,6-diethylindolo[2,1-a]isoquinolin-12-yl)phosphonate (7)





C:\XCALIBUR\...\ESIH_2018829_LH_LLJ_53 8/29/2018 8:25:01 PM yql-et

ESIH_2018829_LH_LLJ_53 #32 RT: 0.28 AV: 1 NL: 3.43E6
T: FTMS + c ESI Full ms [50.00-2000.00]



Elemental composition search on mass 410.19

m/z= 405.19-415.19

m/z	Theo. Mass	Delta (ppm)	RDB equiv.	Composition
410.1876	410.1880	-0.82	11.5	$C_{24}H_{29}O_3NP$