Supporting Information

Purple light-induced Ritter-type reaction on diazophosphonates: access to α-amido-β-keto phosphonates

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1. General Information

^{1}H NMR and ^{13}C NMR spectra were recorded on a Bruker AVANCE III spectrometer 300 and 400 MHz (300 and 400 MHz for ^{1}H NMR; 75 MHz, 100 MHz for ^{13}C NMR and 162 MHz for ^{31}P NMR with TMS as internal reference, and chemical shift (δ) and coupling constant (*J*) were expressed in ppm and Hz, respectively. HRMS analysis was obtained on Xevo G2S Q-TOF spectrometer with ESI ionization method. TLC was performed on using Merck pre-coated TLC plates (Merck 60 F_{254}) and detected under UV light. All the solvents are commercially available analytically pure. Column chromatography was carried out by using silica gel (100-200 mesh). Reagents and solvents were purified as per standard procedures.

Details of light source: Manufacturer: Kessil; Model: PR160L; Wavelength: 390 nm, Distance: 6 cm.

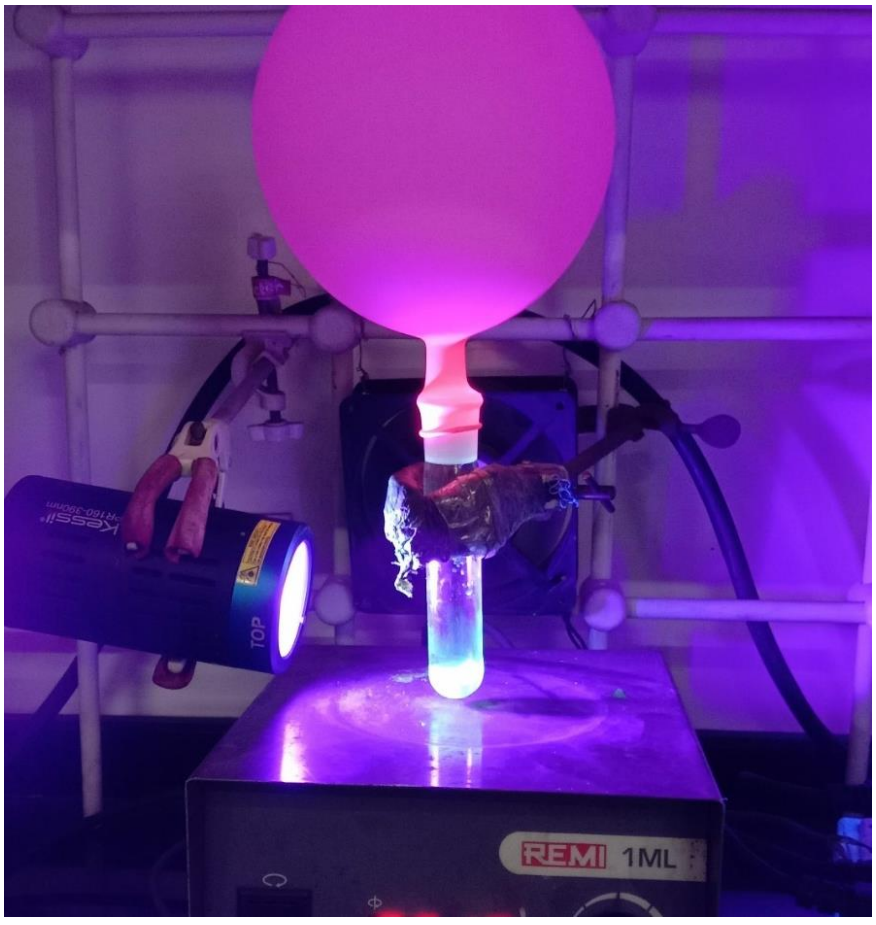
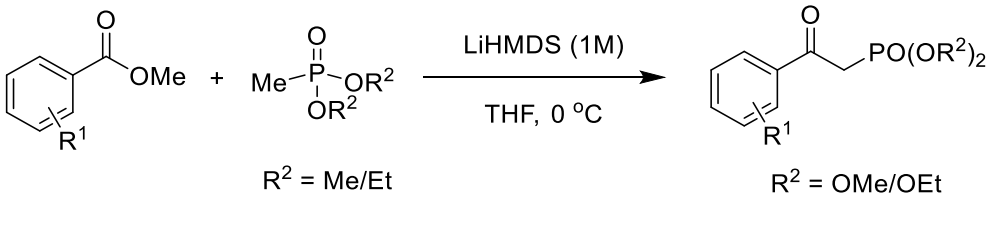


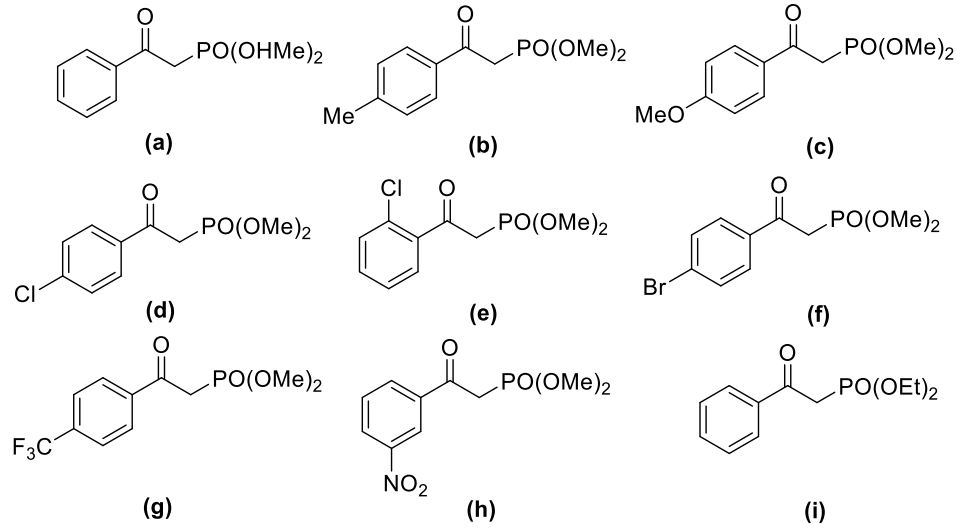
Figure S1 Reaction setup with kessil PR160L- Purple LED 390 nm

2. General Procedures

2.1. General procedure A for synthesis of β-Ketophosphonates:[1]

To a solution of LiHMDS (9.80 g, 42 mmol) in THF (1.0 M) cooled in an ice bath and dimethyl methyl phosphonate (2.72 g, 22 mmol) was added. To this mixture was added the aryl ester (2.72 g, 20 mmol) (either neat or dissolved in a minimal amount of THF) drop-wise, maintaining the internal temperature of the reaction below 5 °C. The reaction was stirred at 0°C until complete consumption of the ester as determined by TLC. The mixture was partitioned between saturated NH_4Cl and EtOAc, the aqueous layer was extracted with EtOAc (20 mL x 3). The combined organic layer was washed with water (20 mL x 2), brine (20 mL x 2), dried over Na_2SO_4 and the solvent removed in vacuo. Crude product as such used for further reaction.

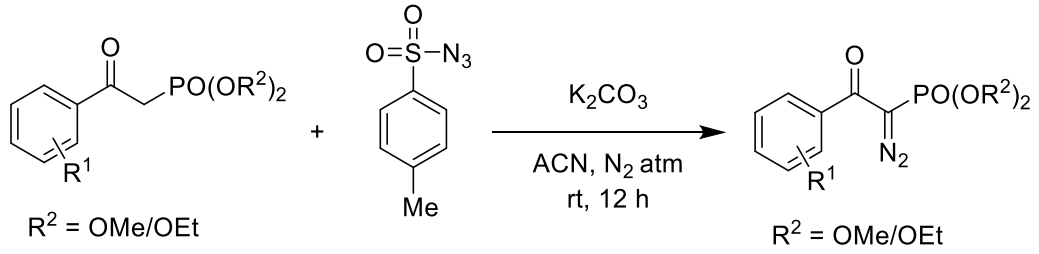


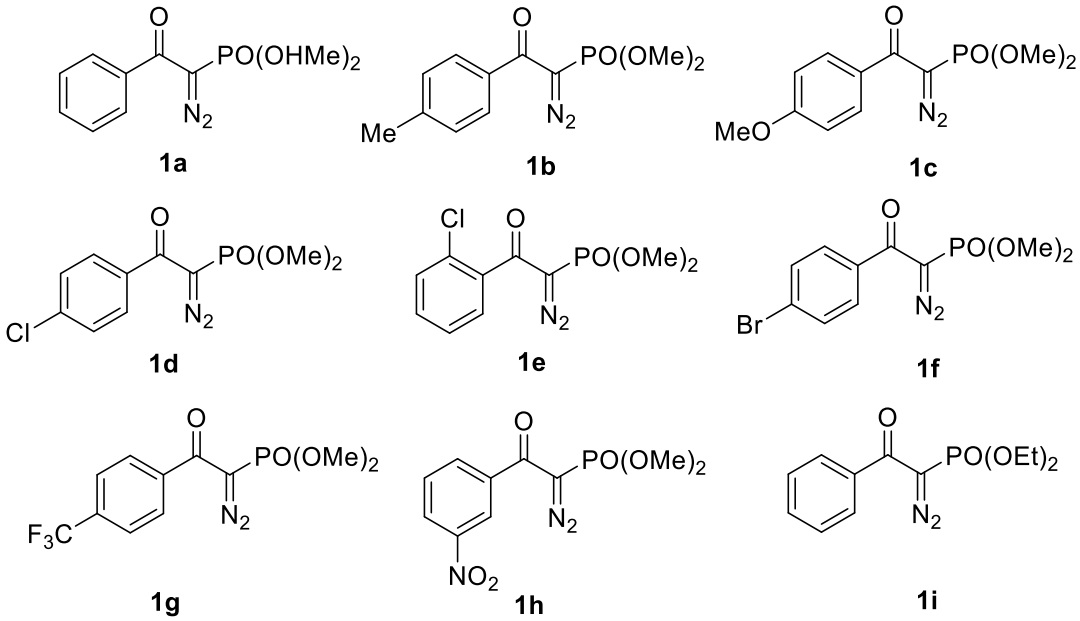


2.2. General procedure B for synthesis of diazo phosphonate derivatives[1a, 2]

To a stirred solution of phosphonate ester (2.28 g, 10 mmol) and TsN_3 (2.16g, 11 mmol) in acetonitrile was added K_2CO_3 (2.07 g, 15 mmol) and the resulting mixture was stirred at room temperature for overnight. The reaction mixture was filtered through a pad of Celite and washed with EtOAc (20 mL x 3). The solvent was evaporated under reduce pressure and

the residue was purified by column chromatography using EtOAc/petroleum ether as eluent to furnish the pure diazo compound **1**.





2.3 General procedure C for the synthesis of α-amido-β-keto phosphonates

The reaction tube was charged with diazo-phosphonate (0.10 g, 0.39 mmol) and nitrile (7.86 mmol) in DCM (4 mL). The mixture was stirred under irradiation of light (390 nm) for 2 hours. After the completion of the reaction was confirmed by TLC, the solvent was evaporated under reduced pressure. The crude was purified by column chromatography using EtOAc/Hexanes as an eluent to furnish the corresponding α-amido-β-keto phosphonates.

3. Mechanistic Studies:

3.1 Reaction without nitrile

The reaction tube was charged with diazo-phosphonate **1a** (0.39 mmol) in DCM (4 mL) was allowed to stir under purple LED (390 nm) for 2 hours. The formation of the β-keto-phosphonate ester **1a'** was initially confirmed by TLC, after purified by column

chromatography (65% yield) was further confirmed by ^{1}H and ^{13}C NMR spectroscopy is shown below (Figure S2).

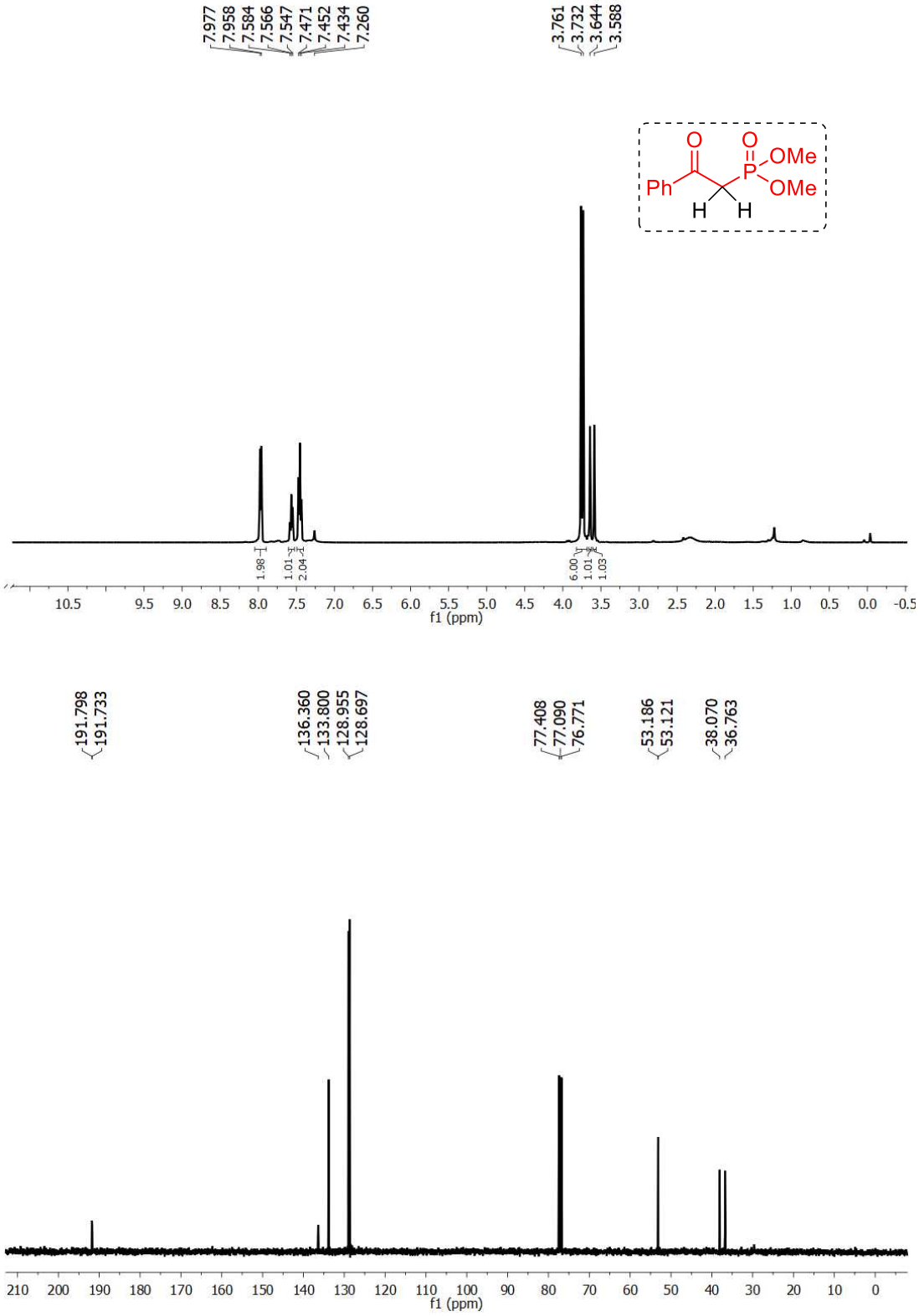


Figure S2: ^{1}H and ^{13}C NMR spectrum of compound 1a'

3.2 Reaction with dry DCM

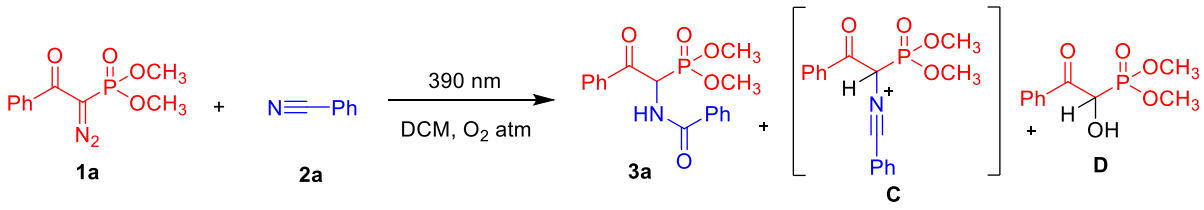
The reaction tube was charged with diazo-phosphonate **1a** (0.39 mmol) in dry DCM (2 mL) purged with nitrogen was allowed to stir under purple LED (390 nm) for 2 hours under oxygen atmosphere. After two hours, the expected β-keto-phosphonate ester **1a'** was not formed and the starting material diazophosphonate **1a** was completely decomposed.

3.3 Reaction with benzamide

The reaction tube was charged with diazophosphonate **1a** (0.39 mmol) and benzamide **2a'** (0.81 mmol) in DCM (4 mL) was added and allowed to stir under purple LED (390 nm) for 2 hours. After two hours the expected product **3a** was not formed and the starting material **2a'** was recovered completely.

3.4 Analysis of reaction mixture

The reaction tube was charged with diazophosphonate **1a** (0.39 mmol) and benzonitrile **2a** (7.86 mmol) in DCM (4 mL). The mixture was stirred under irradiation of light (390 nm) for half an hour. Then the reaction mixture was analysed with HRMS immediately, for the detection of intermediates formed during reaction (Scheme S3-S5).



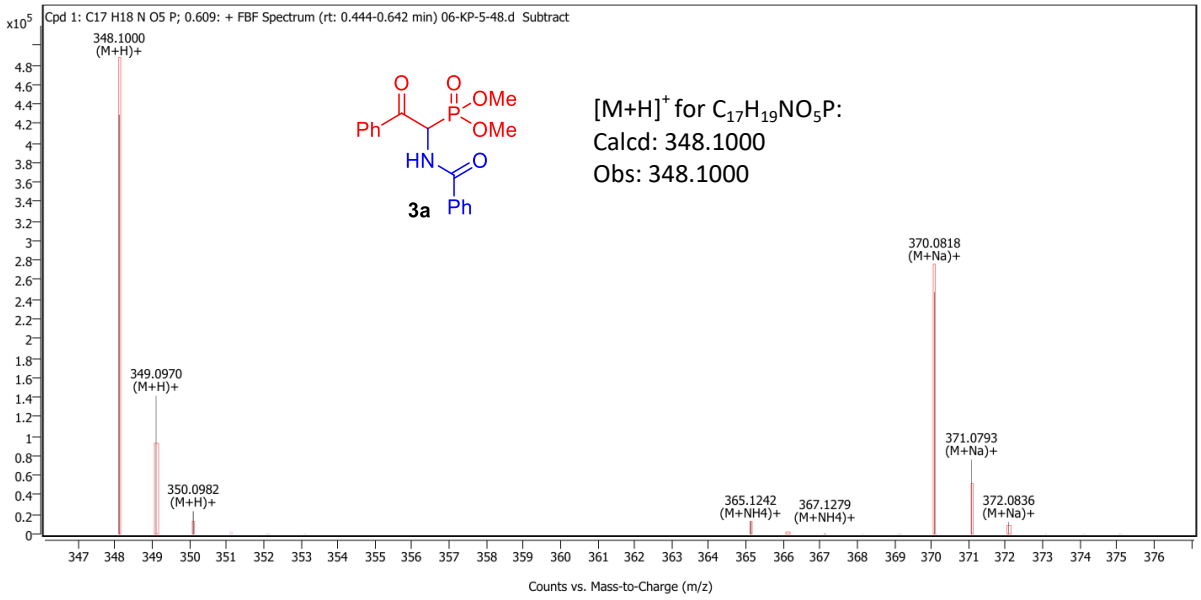


Figure S3: HRMS spectrum of intermediate 3a: Calcd. $[M+H]^+$ for $C_{17}H_{19}NO_5P$: 348.1000; Obs: 348.1000.

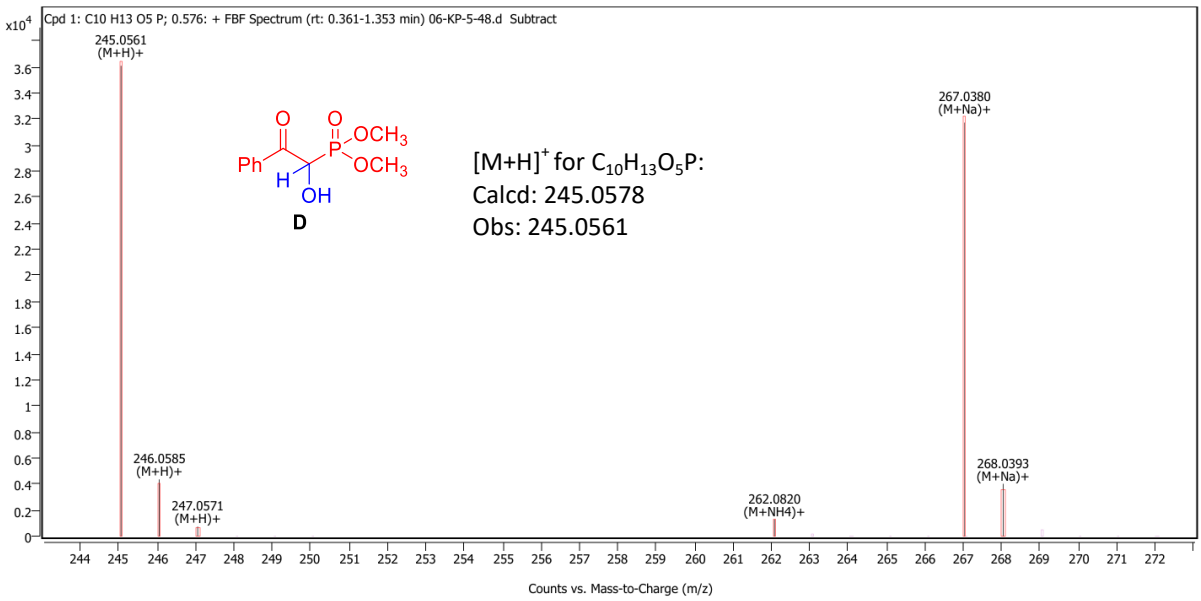


Figure S4: HRMS spectrum of intermediate D: Calcd. $[M+H]^+$ for $C_{10}H_{13}O_5P$: 245.0578; Obs: 245.0561

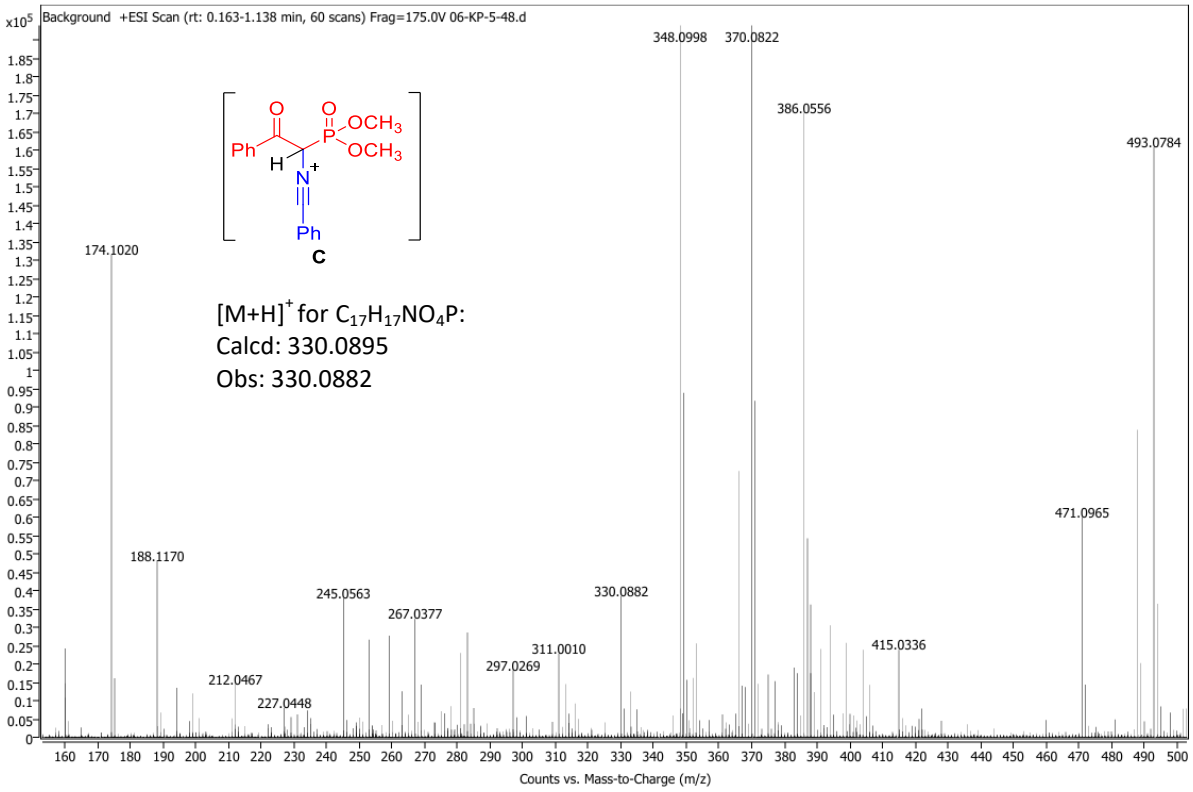
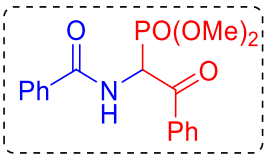


Figure S5: HRMS spectrum of intermediate C: Calcd. $[M+]^+$ for $C_{17}H_{17}NO_4P$: 330.0895; Obs: 330.0882.

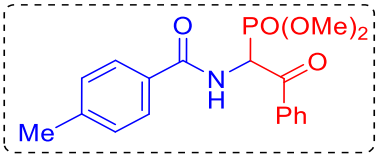
4. Characterization of Products

Dimethyl (1-benzamido-2-oxo-2-phenylethyl)phosphonate (3a)[3]



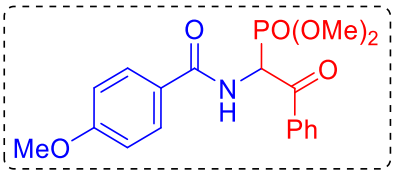
3a (66 mg) was synthesized following general procedure C; White solid; 70% yield (eluent: EtOAc/Hexanes = 2:3); ^{1}H NMR (300 MHz, $CDCl_3$): δ_H 8.13 (d, *J* = 7.8 Hz, 2H), 7.88 (d, *J* = 7.8 Hz, 2H), 7.64 (t, *J* = 7.2 Hz, 1H), 7.55-7.44 (m, 5H), 6.45 (dd, J = 8.4 Hz, 8.4 Hz, 1H), 3.78-3.72 (m, 6H); ^{13}C NMR (75 MHz, $CDCl_3$): δ_C 192.5, 166.6, 134.9, 134.3, 133.4, 132.0, 129.5, 129.4, 128.7, 127.3, 54.3 (t, *J* = 36 Hz), 53.9 (d, *J* = 6.0 Hz), 52.6.

Dimethyl (1-(4-methylbenzamido)-2-oxo-2-phenylethyl)phosphonate (3b)[4]



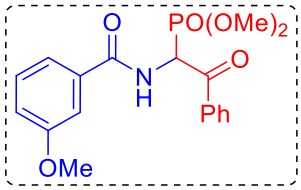
3b (71 mg) was synthesized following general procedure C; White solid; 72% yield (eluent: EtOAc/Hexanes = 2:3); ^{1}H NMR (300 MHz, $CDCl_3$): δ_H 8.13 (d, *J* = 7.8 Hz, 2H), 7.78 (d, *J* = 8.1 Hz, 2H), 7.66-7.61 (m, 1H), 7.54-7.45 (m, 3H), 7.27 (d, *J* = 5.1 Hz, 2H), 6.46 (dd, *J* = 8.4 Hz, *J* = 8.4 Hz, 1H), 3.77-3.72 (m, 6H), 2.41 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ_C 192.5, 166.5 (d, *J* = 3.7 Hz), 142.7, 134.8, 134.5, 130.4, 129.4 (t, *J* = 6.0 Hz), 128.8, 127.5, 127.4, 54.2 (d, *J* = 14.2 Hz), 54.0 (d, *J* = 7.5 Hz), 52.5, 21.6; ^{31}P NMR (162 MHz, $CDCl_3$) δ_P 18.38.

Dimethyl (1-(4-methoxybenzamido)-2-oxo-2-phenylethyl)phosphonate (3c)



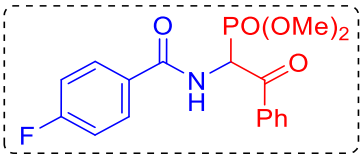
3c (77 mg) was synthesized following general procedure C; White solid; 75% yield (eluent: EtOAc/Hexanes = 2:3); ^{1}H NMR (300 MHz, $CDCl_3$): δ_H 8.12 (d, *J* = 7.2 Hz, 2H), 7.83 (d, *J* = 8.7 Hz, 2H), 7.65-7.60 (m, 1H), 7.54-7.49 (m, 1H), 6.95 (d, *J* = 8.7 Hz, 2H), 7.25 (s, 2H), 6.43 (dd, *J* = 8.4 Hz, 8.4 Hz, 1H), 3.86 (s, 3H), 3.77-3.70 (m, 6H); ^{13}C NMR (75 MHz, $CDCl_3$): δ_C 193.4, 163.1, 135.1, 134.2, 129.4, 129.2, 128.7, 125.7, 114.0, 55.4, 54.5, 53.9 ($J_{c\text{-}p}$ = 6.7 Hz), 52.6; HRMS: $[M+H]^+$ calculated for $C_{18}H_{21}NO_6P$: 378.1106, Found: 378.1103.

Dimethyl (1-(3-methoxybenzamido)-2-oxo-2-phenylethyl)phosphonate (3d)



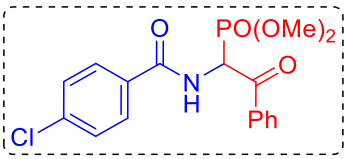
3d (73 mg) was synthesized following general procedure C; White solid; 71% yield (eluent: EtOAc/Hexanes = 2:3); ^{1}H NMR (300 MHz, $CDCl_3$): δ_H 8.13 (d, *J* = 7.8 Hz, 2H), 7.65 (t, *J* = 7.2 Hz, 1H); 7.54 (d, *J* = 7.5 Hz, 1H), 7.50 (d, *J* = 4.5 Hz, 1H), 7.46-7.40 (m, 3H), 7.36 (d, *J* = 8.4 HZ, 1H), 7.08 (d, *J* = 7.8 Hz, 1H), 6.45 (dd, *J* = 8.4 Hz, *J* = 8.4 Hz, 1H), 3.86 (s, 3H), 3.78-3.73 (m, 6H); ^{13}C NMR (75 MHz, $CDCl_3$): δ_C 192.3, 166.5, 166.4, 159.9, 134.6 (d, *J* = 3.0 Hz), 134.5, 129.7, 129.4, 128.7, 119.1, 118.4, 112.5, 55.5, 54.1 ($J_{c\text{-}p}$ = 6.7 Hz), 52.5; HRMS: $[M+H]^+$ calculated for $C_{18}H_{21}NO_6P$: 378.1106, Found: 378.1107.

Dimethyl (1-(4-fluorobenzamido)-2-oxo-2-phenylethyl)phosphonate (3e)



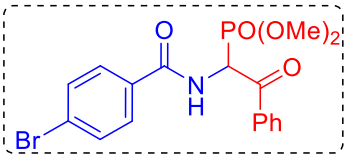
3e (52 mg) was synthesized following general procedure C; White solid; 52% yield (eluent: EtOAc/Hexanes = 2:3); ^{1}H NMR (300 MHz, $CDCl_3$): δ_H 8.12 (d, *J* = 7.8 Hz, 2H), 7.92-788 (m, 2H), 7.68-7.63 (m, 1H), 7.55-7.50 (m, 2H), 7.44 (d, *J* = 8.4 Hz, 1H), 7.17-7.12 (m, 2H), 6.43 (dd, *J* = 8.7 Hz, *J* = 8.1 Hz, 1H), 3.77-3.71 (m, 6H); ^{13}C NMR (75 MHz, $CDCl_3$): δ_C 192.3, 165.5 (d, *J* = 3.7 Hz), 165.1 (d, *J* = 252 Hz), 134.6, 134.5, 129.8, 129.7, 129.4, 128.7, 115.9, 115.6, 54.0 ($J_{c\text{-}p}$ = 6.0 Hz), 52.5; ^{19}F NMR (303 MHz, $CDCl_3$) δ_F -106.95.

Dimethyl (1-(4-chlorobenzamido)-2-oxo-2-phenylethyl)phosphonate (3f)



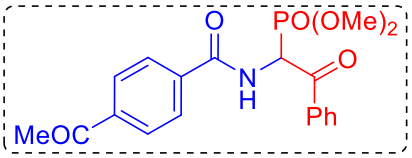
3f (72 mg) was synthesized following general procedure C; White solid; 69% yield (eluent: EtOAc/Hexanes = 2:3); ^{1}H NMR (300 MHz, $CDCl_3$): δ_H 8.13 (d, *J* = 7.5 Hz, 2H), 7.82 (d, *J* = 8.4 Hz, 2H), 7.68-7.63 (m, 1H), 7.56-7.51 (m, 2H), 7.45 (d, *J* = 8.4 Hz, 2H), 7.40 (s, 1H), 6.42 (dd, *J* = 8.4 Hz, *J* = 8.4 Hz, 1H), 3.77-3.70 (m, 6H); ^{13}C NMR (75 MHz, $CDCl_3$): δ_C 192.4, 165.5 (d, *J* = 4.5 Hz), 138.5, 134.6, 131.6, 129.4, 129.0, 128.8, 128.7, 54.1 ($J_{c\text{-}p}$ = 6.7 Hz), 52.5; ^{31}P NMR (162 MHz, $CDCl_3$) δ_P 18.06; HRMS: $[M+H]^+$ calculated for $C_{17}H_{18}ClNO_5P$: 382.0611, Found: 382.0622.

Dimethyl (1-(4-bromobenzamido)-2-oxo-2-phenylethyl)phosphonate (3g)



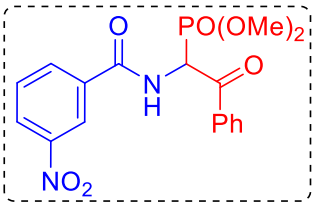
3g (76 mg) was synthesized following general procedure C; White solid; 65% yield (eluent: EtOAc/Hexanes = 2:3); ^{1}H NMR (300 MHz, $CDCl_3$): δ_H 8.12 (d, *J* = 7.5 Hz, 2H), 7.76 (d, *J* = 8.4 Hz, 2H), 7.68-7.60 (m, 3H), 7.53 (t, *J* = 7.8 Hz, 2H), 7.44 (d, *J* = 7.5 Hz, 1H), 6.42 (dd, *J* = 8.4 Hz, *J* = 8.7 Hz, 1H), 3.77-3.71 (m, 6H); ^{13}C NMR (75 MHz, $CDCl_3$): δ_C 192.2, 165.6 (d, *J* = 3.7 Hz), 134.6, 134.5, 132.1, 132.0, 129.4, 128.9, 128.8, 127.0, 54.1 ($J_{c\text{-}p}$ = 7.5 Hz), 52.5; ^{31}P NMR (162 MHz, $CDCl_3$) δ_P 18.03; HRMS: $[M+H]^+$ calculated for $C_{17}H_{18}BrNO_5P$: 425.0105, Found: 425.0105.

Dimethyl (1-(4-acetylbenzamido)-2-oxo-2-phenylethyl)phosphonate (3h)



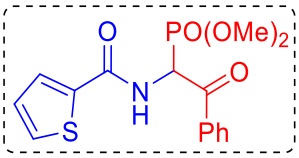
3h (62 mg) was synthesized following general procedure C; White solid; 58% yield (eluent: EtOAc/Hexanes = 2:3); ^{1}H NMR (300 MHz, $CDCl_3$): δ_H 8.13 (d, *J* = 7.2 Hz, 2H), 8.05 (d, *J* = 8.1 Hz, 2H), 7.98 (d, *J* = 8.1 Hz, 2H), 7.66 (t, *J* = 7.5 Hz, 1H), 7.59-7.51 (m, 3H), 6.44 (dd, *J* = 8.7 Hz, *J* = 8.4 Hz, 1H), 3.78-3.72 (m, 6H), 2.65 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ_C 197.3, 192.1, 165.7 (d, *J* = 4.5 Hz), 139.6, 137.0, 134.6, 134.5, 129.4, 128.8, 128.6, 127.6, 54.1 ($J_{c\text{-}p}$ = 6.7 Hz), 52.6, 26.8; ^{31}P NMR (162 MHz, $CDCl_3$) δ_P 18.01; HRMS: $[M+H]^+$ calculated for $C_{19}H_{21}NO_6P$: 390.1106, Found: 390.1108.

Dimethyl (1-(3-nitrobenzamido)-2-oxo-2-phenylethyl)phosphonate (3i)



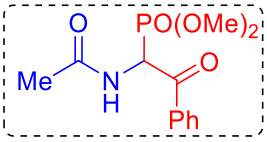
3i (60 mg) was synthesized following general procedure C; White solid; 56% yield (eluent: EtOAc/Hexanes = 2:3); ^{1}H NMR (300 MHz, $CDCl_3$): δ_H 8.74 (s, 1H), 8.41 (d, *J* = 8.1 Hz, 1H), 8.22 (d, *J* = 7.8 Hz, 1H), 8.14 (d, *J* = 7.2 Hz, 2H), 7.72-7.52 (m, 5H), 6.45 (d, *J* = 8.4 Hz, *J* = 8.4 Hz, 1H), 3.79-3.73 (m, 6H); ^{13}C NMR (75 MHz, $CDCl_3$): δ_C 191.9, 164.2, 148.4, 134.9, 134.7, 134.4, 133.1, 129.9, 129.5, 128.8, 126.6, 122.5, 54.2 ($J_{c\text{-}p}$ = 6.7 Hz), 52.7; HRMS: $[M+H]^+$ calculated for $C_{17}H_{18}N_2O_7P$: 393.0857, Found: 393.0855.

Dimethyl (2-oxo-2-phenyl-1-(thiophene-2-carboxamido)ethyl)phosphonate (3j)



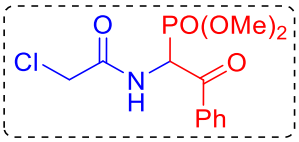
3j (61 mg) was synthesized following general procedure C; White solid; 63% yield (eluent: EtOAc/Hexanes = 2:3); ^{1}H NMR (300 MHz, $CDCl_3$): δ_H 8.11 (d, *J* = 9.0 Hz, 2H), 7.68-7.62 (m, 2H), 7.55-7.49 (m, 3H), 7.34 (d, *J* = 8.1 Hz, 1H), 7.13-7.09 (m, 1H), 6.40 (dd, *J* = 8.1 Hz, *J* = 8.4 Hz, 1H), 3.77-3.72 (m, 6H); ^{13}C NMR (75 MHz, $CDCl_3$): δ_C 192.3 (d, *J* = 0.7 Hz), 161.08, 161.03, 137.5, 134.6, 134.5, 131.0, 129.4, 129.0, 128.7, 127.8, 54.0 ($J_{c\text{-}p}$ = 6.0 Hz), 52.3; ^{31}P NMR (162 MHz, $CDCl_3$) δ_P 17.9; HRMS: $[M+H]^+$ calculated for $C_{15}H_{17}NO_5PS$: 354.0565, Found: 354.0564.

Dimethyl (1-acetamido-2-oxo-2-phenylethyl)phosphonate (3k)[5]



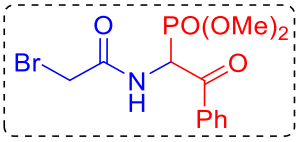
3l (47 mg) was synthesized following general procedure C; White solid; 61% yield (eluent: EtOAc/Hexanes = 2:3); ^{1}H NMR (400 MHz, $CDCl_3$): δ_H 8.07 (d, *J* = 7.2 Hz, 2H), 7.64-7.61 (m, 1H), 7.52-7.48 (m, 2H), 6.98 (d, *J* = 8.0 Hz, 1H), 6.26 (dd, *J* = 8.8 Hz, *J* = 8.8 Hz, 1H), 3.76-3.69 (m, 6H), 2.11 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$): δ_C 192.5, 169.4 (d, *J* = 4.4 Hz), 134.7, 134.3, 129.3, 128.7, 53.9 (d, *J* = 7.0 Hz), 53.7 (d, *J* = 27.2 Hz), 52.1, 22.9. HRMS: $[M+H]^+$ calculated for $C_{12}H_{17}NO_5P$: 286.0844, Found: 286.0837.

Dimethyl (1-(2-chloroacetamido)-2-oxo-2-phenylethyl)phosphonate (3l)



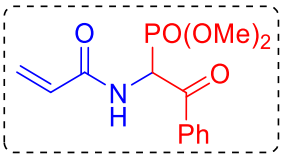
3m (51 mg) was synthesized following general procedure C; White solid; 58% yield (eluent: EtOAc/Hexanes = 2:3); ^{1}H NMR (300 MHz, $CDCl_3$): δ_H 8.08 (d, *J* = 7.2 Hz, 2H), 7.80 (d, *J* = 7.5 Hz, 1H), 7.65 (t, *J* = 6.6 Hz, 1H), 7.52 (t, *J* = 7.5 Hz, 2H), 6.17 (dd, *J* = 8.4 Hz, 8.7 Hz, 1H), 4.15-4.07 (m, 2H), 3.75 (d, *J* = 11.1 Hz, 6H); ^{13}C NMR (75 MHz, $CDCl_3$): δ_C 191.5, 165.7 (d, *J* = 3.7 Hz), 134.7, 134.5, 129.5, 128.9, 54.4 (d, *J* = 6.0 Hz), 51.2 (d, *J* = 6.7 Hz), 52.5, 42.5; ^{31}P NMR (162 MHz, $CDCl_3$) δ_P 17.27; HRMS: $[M+H]^+$ calculated for $C_{12}H_{16}ClNO_5P$: 320.0454, Found: 320.0454.

Dimethyl (1-(2-bromoacetamido)-2-oxo-2-phenylethyl)phosphonate (3m)



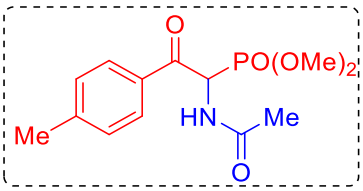
3n (60 mg) was synthesized following general procedure C; White solid; 60% yield (eluent: EtOAc/Hexanes = 2:3); ^{1}H NMR (300 MHz, $CDCl_3$): δ_H 8.07 (d, *J* = 7.5 Hz, 2H), 7.84 (d, *J* = 7.8 Hz, 1H), 7.64 (t, *J* = 7.2 Hz, 1H), 7.54-7.49 (m, 2H), 6.19 (dd, J = 8.7 Hz, 8.7 Hz, 1H), 3.95 (d, *J* = 2.7 Hz, 2H), 3.86-3.71 (m, 6H); ^{13}C NMR (75 MHz, $CDCl_3$): δ_C 191.5, 165.54, 165.49, 134.6, 134.4, 129.4, 128.8, 54.3 ($J_{c\text{-}p}$ = 9.0 Hz), 52.6, 28.2; HRMS: $[M+H]^+$ calculated for $C_{12}H_{16}BrNO_5P$: 363.9949, Found: 363.9947.

Dimethyl (1-acrylamido-2-oxo-2-phenylethyl)phosphonate (3n)



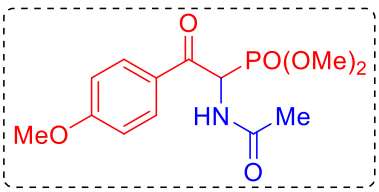
3o (49 mg) was synthesized following general procedure C; White solid; 61% yield (eluent: EtOAc/Hexanes = 2:3); ^{1}H NMR (300 MHz, $CDCl_3$): δ_H 8.07 (d, *J* = 8.1 Hz, 2H), 7.66-7.61 (m, 1H), 7.53-7.48 (m, 2H), 7.33-7.28 (m, 1H), 6.42-6.29 (m, 2H), 5.74 (dd, *J* = 1.8 Hz, 2.1 Hz, 1H), 3.78-3.68 (m, 6H); ^{13}C NMR (75 MHz, $CDCl_3$): δ_C 192.4, 164.8 (d, *J* = 4.5 Hz), 134.6, 134.4, 129.7, 129.3, 128.7, 128.1, 54.1 (d, *J* = 6.7 Hz), 53.7, 51.8; HRMS: $[M+H]^+$ calculated for $C_{13}H_{17}NO_5P$: 298.0844, Found: 298.0844.

Dimethyl (1-acetamido-2-oxo-2-(p-tolyl)ethyl)phosphonate (4a)[3]



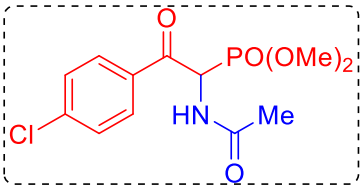
4a (55 mg) was synthesized following general procedure C; White solid; 71% yield (eluent: EtOAc/Hexanes = 2:3); ^{1}H NMR (400 MHz, $CDCl_3$): δ_H 7.90 (d, *J* = 6.8 Hz, 2H), 7.23 (d, *J* = 6.4 Hz, 2H), 6.76 (d, *J* = 7.2 Hz, 1H), 6.15 (dd, *J* = 7.2 Hz, *J* = 6.8 Hz, 1H), 3.67-3.62 (m, 6H), 2.35 (s, 3H), 2.03 (d, *J* = 0.8 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$): δ_C 191.8, 169.33, 169.29, 145.6, 132.1, 129.5, 129.4, 53.8 ($J_{c\text{-}p}$ = 12.1 Hz), 52.0, 23.0, 21.8.

Dimethyl (1-acetamido-2-(4-methoxyphenyl)-2-oxoethyl)phosphonate (4b)[3]



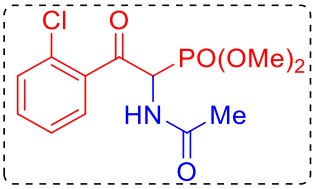
4b (57 mg) was synthesized following general procedure C; White solid; 74% yield (eluent: EtOAc/Hexanes = 2:3); ^{1}H NMR (300 MHz, $CDCl_3$): δ_H 8.06 (d, *J* = 9.0 Hz, 2H), 7.05 (d, *J* = 8.7 Hz, 1H), 6.97 (d, *J* = 9.0 Hz, 2H), 6.21 (dd, *J* = 8.7 Hz, *J* = 8.7 Hz, 1H), 3.89 (s, 3H), 3.76-3.71 (m, 6H), 2.10 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ_C 190.5, 169.8 (d, *J* = 4.5Hz), 164.7, 131.9, 127.5, 114.0, 55.6, 53.9 ($J_{c\text{-}p}$ = 6.7 Hz), 51.4, 22.9; ^{31}P NMR (162 MHz, CDCl3) δ_P 19.01.

Dimethyl (1-acetamido-2-(4-chlorophenyl)-2-oxoethyl)phosphonate (4c)[3]



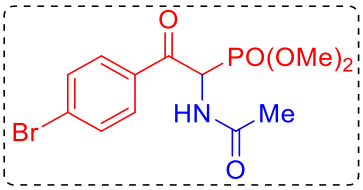
4c (49 mg) was synthesized following general procedure C; White solid; 62% yield (eluent: EtOAc/Hexanes = 2:3); ^{1}H NMR (400 MHz, $CDCl_3$): δ_H 7.93 (d, *J* = 6.8 Hz, 2H), 7.65 (d, *J* = 6.8 Hz, 2H), 6.97 (d, *J* = 6.4 Hz, 1H), 6.19 (dd, *J* = 6.8 Hz, *J* = 7.2 Hz, 1H), 3.76-3.72 (m, 6H), 2.11 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$): δ_C 191.7, 169.5, 169.4, 133.4, 132.0, 130.7, 129.9, 53.9 ($J_{c\text{-}p}$ = 7.0 Hz), 52.2, 22.9.

Dimethyl (1-acetamido-2-(2-chlorophenyl)-2-oxoethyl)phosphonate (4d)



4d (46 mg) was synthesized following general procedure C; White solid; 60% yield (eluent: EtOAc/Hexanes = 2:3); ^{1}H NMR (300 MHz, $CDCl_3$): δ_H 7.70 (d, *J* = 7.8 Hz, 1H), 7.46 (d, *J* = 3.6 Hz, 2H), 7.42-7.35 (m, 1H), 6.93 (d, *J* = 8.4 Hz, 1H), 6.26 (dd, *J* = 8.7 Hz, *J* = 9.0 Hz, 1H), 3.75-3.64 (m, 6H), 2.12 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ_C 194.2 (d, *J* = 2.2 Hz), 169.77, 169.70, 136.3, 132.8, 132.0, 130.8, 130.2, 126.8, 54.0 ($J_{c\text{-}p}$ = 6.7 Hz), 45.3, 22.9; HRMS: $[M+H]^+$ calculated for $C_{12}H_{16}ClNO_5P$: 320.0454, Found: 320.0450.

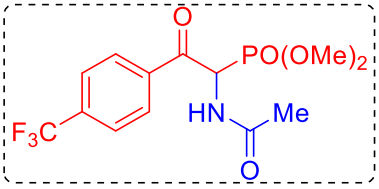
Dimethyl (1-acetamido-2-(4-bromophenyl)-2-oxoethyl)phosphonate (4e)[3]



4e (48 mg) was synthesized following general procedure C; White solid; 63% yield (eluent: EtOAc/Hexanes = 2:3); ^{1}H NMR (400 MHz, $CDCl_3$): δ_H 8.03-8.00 (m, 2H), 7.47 (d, *J* = 8.4 Hz, 2H), 6.96 (d, *J* = 8.4 Hz, 1H), 6.19 (dd, *J* = 8.8 Hz, *J* = 8.8 Hz, 1H), 3.76-3.72 (m, 6H),

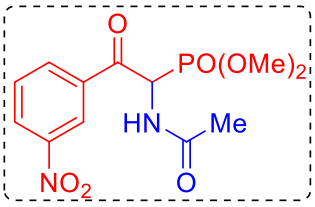
2.10 (d, J = 0.8 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$): δ_C 191.4, 169.5, 169.4, 141.0, 133.0, 130.7, 129.0, 53.9 ($J_{c\text{-}p}$ = 7.0 Hz), 52.2, 22.9.

Dimethyl (1-acetamido-2-oxo-2-(4-(trifluoromethyl)phenyl)ethyl)phosphonate (4f)[3]



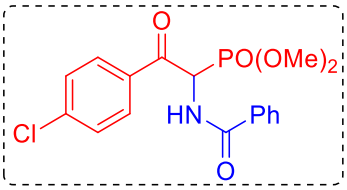
4f (43 mg) was synthesized following general procedure C; White solid; 57% yield (eluent: EtOAc/Hexanes = 2:3); ^{1}H NMR (300 MHz, $CDCl_3$): δ_H 8.18 (d, J = 7.8 Hz, 2H), 7.77 (d, J = 8.1 Hz, 2H), 6.94 (d, J = 7.8 Hz, 1H), 6.23 (dd, J = 8.7 Hz, J = 8.7 Hz, 1H), 3.78-3.73 (m, 6H), 2.12 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ_C 192.0, 169.5, 137.4, 129.6, 125.79, 125.74, 54.1 ($J_{c\text{-}p}$ = 9.7 Hz), 52.3 (d, J = 7.0 Hz), 22.9; ^{19}F NMR (303 MHz, $CDCl_3$) δ_F -63.31.

Dimethyl (1-acetamido-2-(3-nitrophenyl)-2-oxoethyl)phosphonate (4g)



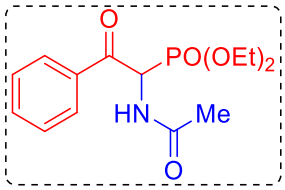
4g (43 mg) was synthesized following general procedure C; White solid; 56% yield (eluent: EtOAc/Hexanes = 2:3); ^{1}H NMR (300 MHz, $CDCl_3$): δ_H 8.90 (s, 1H), 8.49-8.41 (m, 2H), 7.73 (t, J = 8.1Hz, 1H), 6.98 (d, J = 8.1Hz, 1H), 6.24 (dd, J = 8.4 Hz, J = 8.4 Hz, 1H), 3.78 (d, J = 11.1 Hz, 6H), 2.13 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ_C 190.9, 169.7, 169.6, 148.4, 136.0, 134.8, 129.9, 128.3, 124.1, 54.3 ($J_{c\text{-}p}$ = 13.5 Hz), 52.5, 22.8; HRMS: $[M+H]^+$ calculated for $C_{12}H_{16}N_2O_7P$: 331.0695, Found: 331.0695.

Dimethyl (1-benzamido-2-(4-chlorophenyl)-2-oxoethyl)phosphonate (4h)



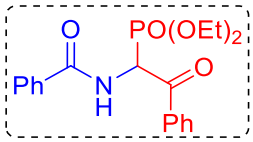
4h (60 mg) was synthesized following general procedure C; White solid; 65% yield (eluent: EtOAc/Hexanes = 2:3); ^{1}H NMR (300 MHz, $CDCl_3$): δ_H 8.08 (d, J = 8.4 Hz, 2H), 7.87 (d, J = 7.2 Hz, 2H), 7.53-7.45 (m, 5H), 6.40 (dd, J = 8.4 Hz, J = 8.4 Hz, 1H), 3.80-3.71 (m, 6H); ^{13}C NMR (75 MHz, $CDCl_3$): δ_C 191.3, 166.68, 166.63, 141.1, 133.1, 132.9, 132.2, 130.8, 129.1, 128.7, 127.3, 54.1 ($J_{c\text{-}p}$ = 6.0 Hz), 52.5; HRMS: $[M+H]^+$ calculated for $C_{13}H_{18}NO_5P$: 382.0611, Found: 382.0622.

Diethyl (1-acetamido-2-oxo-2-phenylethyl)phosphonate (4i)



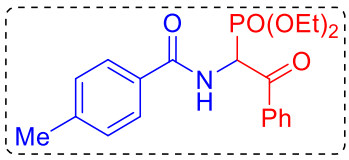
4i (54 mg) was synthesized following general procedure C; White solid; 68% yield (eluent: EtOAc/Hexanes = 2:3); ^{1}H NMR (300 MHz, $CDCl_3$): δ_H 8.06 (d, *J* = 7.5 Hz, 2H), 7.64-7.59 (m, 1H), 7.51-7.46 (m, 2H), 7.16 (d, *J* = 8.4 Hz, 1H), 6.26 (dd, *J* = 8.7 Hz, *J* = 9.0 Hz, 1H), 4.16-3.99 (m, 4H), 2.11 (s, 3H), 1.26 (t, *J* = 7.2 Hz, 3H), 1.14 (t, *J* = 6.9 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ_C 192.8 (d, *J* = 1.5 Hz), 169.57, 169.51, 135.0, 134.1, 129.2, 128.5, 63.6 ($J_{c\text{-}p}$ = 4.5 Hz), 54.2, 52.3, 22.9, 16.2 ($J_{c\text{-}p}$ = 6.0 Hz); HRMS: $[M+H]^+$ calculated for $C_{14}H_{21}NO_5P$: 314.1157, Found: 314.1160.

Diethyl (1-benzamido-2-oxo-2-phenylethyl)phosphonate (4j)



4j (65 mg) was synthesized following general procedure C; White solid; 70% yield (eluent: EtOAc/Hexanes = 2:3); ^{1}H NMR (300 MHz, $CDCl_3$): δ_H 8.13 (d, *J* = 7.8 Hz, 2H), 7.89 (m, 2H), 7.66-7.61(m, 1H), 7.55-7.45 (m, 5Hz, 5H), 6.44 (dd, *J* = 8.7 Hz, *J* = 8.7 Hz, 1H), 4.16-4.11 (m, 4H), 1.25 (t, *J* = 6.9 Hz, 3H), 1.16 (t, *J* = 6.9 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ_C 192.7, 166.7, 166.6, 134.9, 134.3, 133.3, 132.0 (d, *J* = 13.5), 129.4, 128.6 (t, J = 4.5 Hz), 127.3 (d, *J* = 11.2 Hz), 63.7 ($J_{c\text{-}p}$ = 4.5 Hz), 54.8, 52.9, 16.1 ($J_{c\text{-}p}$ = 6.7 Hz).

Diethyl (1-(4-methylbenzamido)-2-oxo-2-phenylethyl)phosphonate (4k)

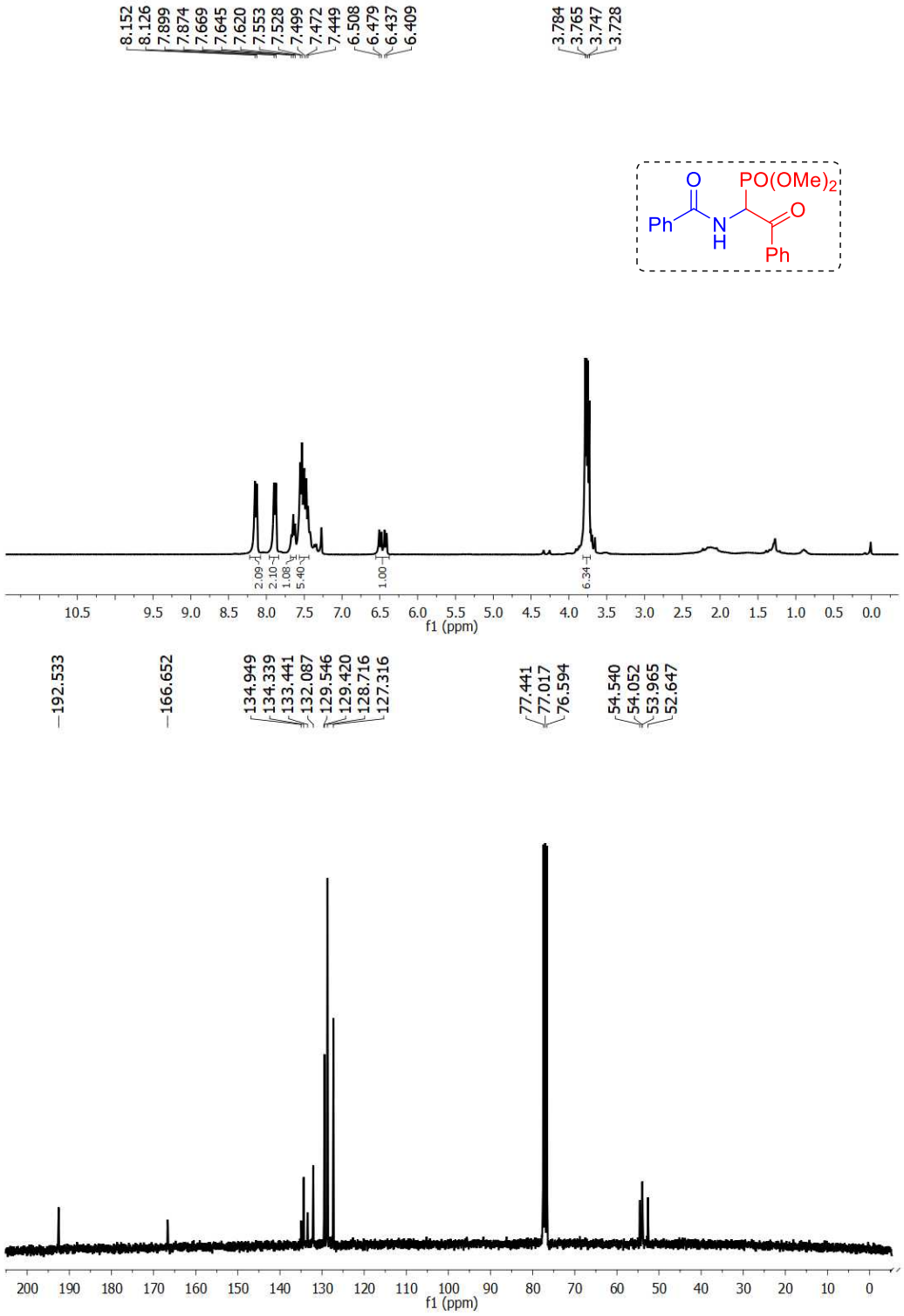


4k (71 mg) was synthesized following general procedure C; White solid; 74% yield (eluent: EtOAc/Hexanes = 2:3); ^{1}H NMR (300 MHz, $CDCl_3$): δ_H 8.12 (d, *J* = 7.8 Hz, 2H), 7.78 (d, *J* = 7.8 Hz, 2H), 7.62 (d, *J* = 7.2 Hz, 1H), 7.54-7.49 (m, 2H), 7.41 (d, *J* = 8.4 Hz, 1H), 7.28-7.25 (m, 2H), 6.44 (dd, *J* = 8.7 Hz, *J* = 8.4 Hz, 1H), 4.15-4.07 (m, 4H), 2.41 (s, 3H), 1.24 (t, *J* = 7.2 Hz, 3H), 1.15 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ_C 192.8, 166.6, 166.5, 142.6, 135.0, 134.2, 130.5, 129.4, 129.3, 128.6, 127.3, 63.7 ($J_{c\text{-}p}$ = 6.7 Hz), 54.7, 52.9, 21.5, 16.2 ($J_{c\text{-}p}$ = 6.0 Hz); HRMS: $[M+H]^+$ calculated for $C_{20}H_{25}NO_5P$: 390.1470, Found: 390.1472.

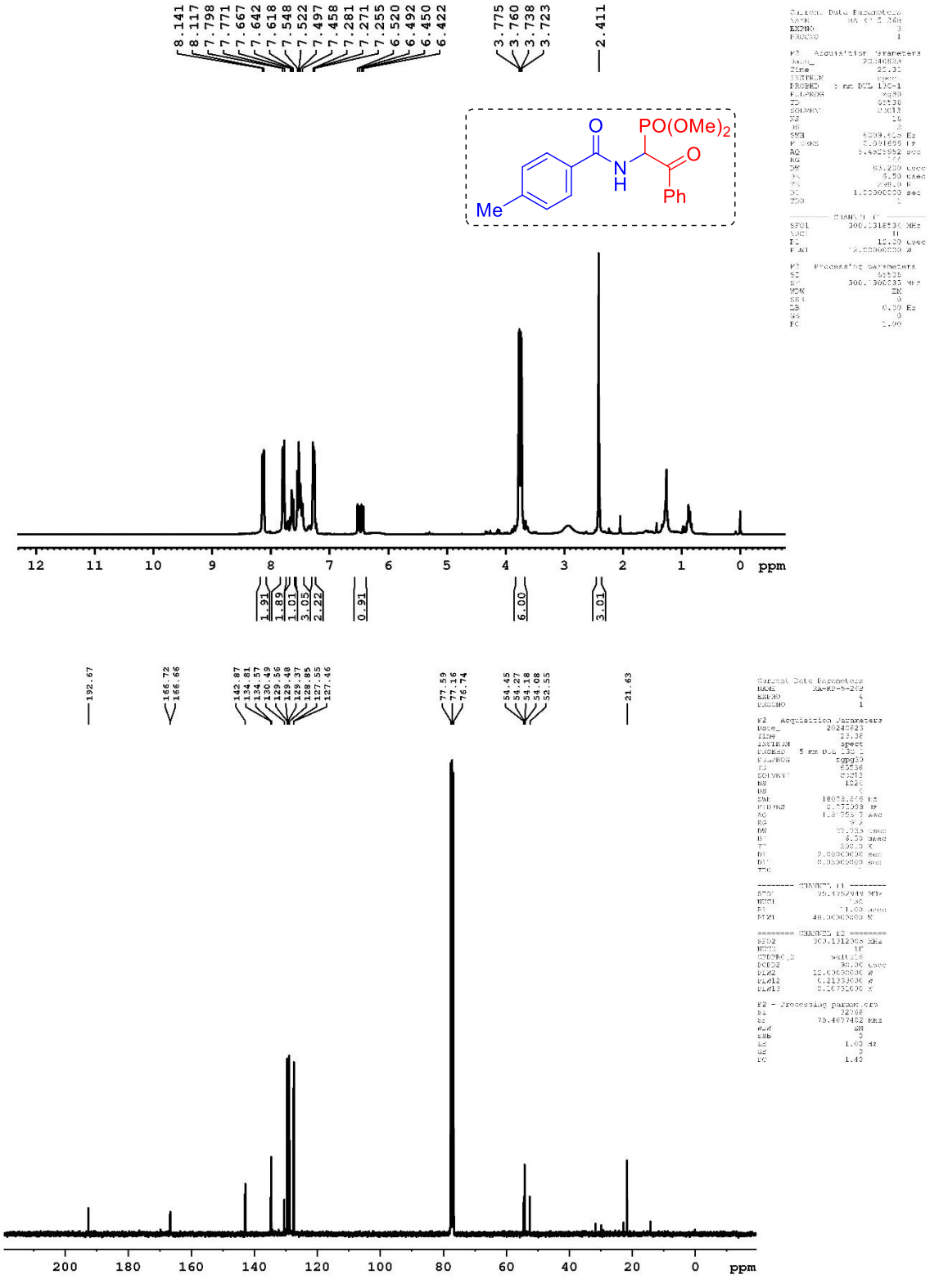
5. References

1. (a) R. S. Phatake, V. Mullapudi, V. C. Wakchaure and C. V. Ramana, Fluoride-Mediated Dephosphonylation of α-Diazo-β-carbonyl Phosphonates, *Org. Lett.,* 2017, **19**, 372; (b) R. R. Milburn, K. McRae, J. Chan, J. Tedrow, R. Larsen and M. Faul, A practical preparation of aryl β-ketophosphonates, *Tetrahedron Lett.,* 2009, **50**, 870; (c) K. M. Maloney and J. Y. L. Chung, A General Procedure for the Preparation of β-Ketophosphonates, *J. Org. Chem.,* 2009, **74**, 7574.
2. D. F. Taber, S. Bai and P.-f. Guo, A convenient reagent for aldehyde to alkyne homologation, *Tetrahedron Lett.,* 2008, **49**, 6904.
3. X. Tao, W. Li, X. Li, X. Xie and Z. Zhang, Diastereo- and Enantioselective Asymmetric Hydrogenation of α-Amido-β-keto Phosphonates via Dynamic Kinetic Resolution, *Org. Lett.,* 2013, **15**, 72.
4. A. G. Belyuga, V. S. Brovarets and B. S. Drach, Convenient Synthetic Approach to (2-Aryl-5-phenyl-1,3-oxazol-4-yl)phosphonic Acids and Their Functional Derivatives, *Russ. J. Gen. Chem.,* 2005, **75**, 523.
5. M. Kitamura, M. Tokunaga, T. Pham, W. D. Lubell and R. Noyori, Asymmetric synthesis of α-amino β-hydroxy phosphonic acids via BINAP-ruthenium catalyzed hydrogenation, *Tetrahedron Lett.,* 1995, **36**, 5769.

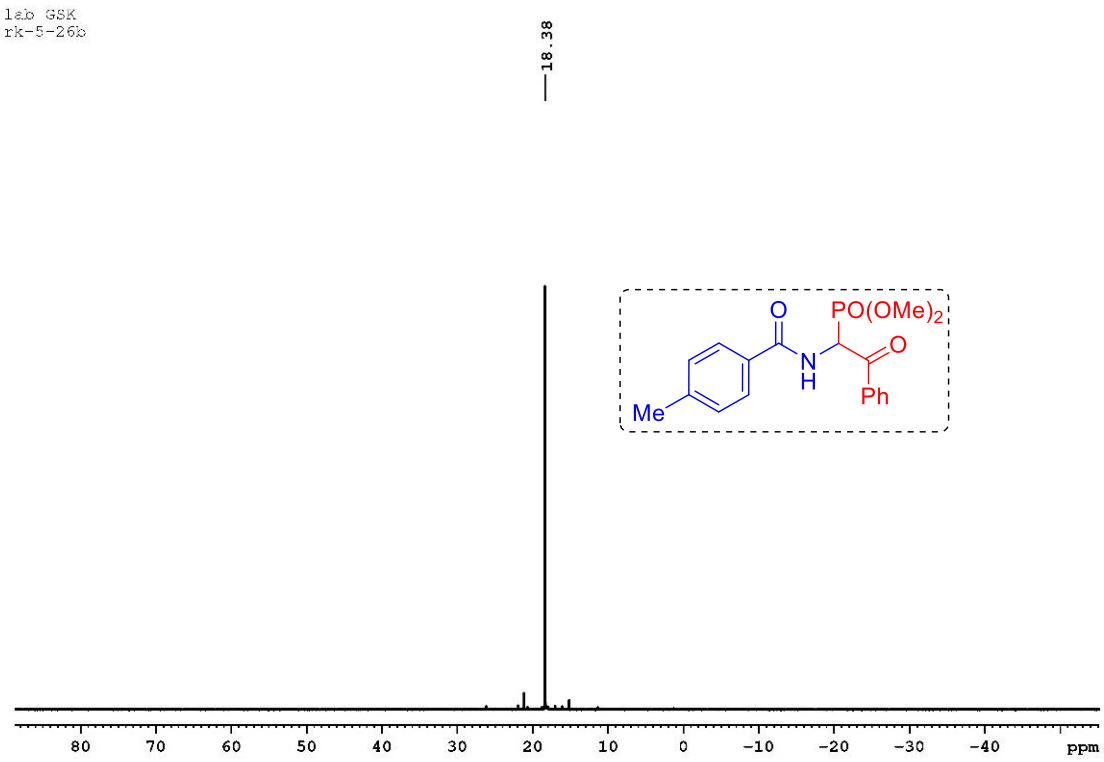
6. ^{1}H, ^{13}C NMR and HRMS Spectra of Products



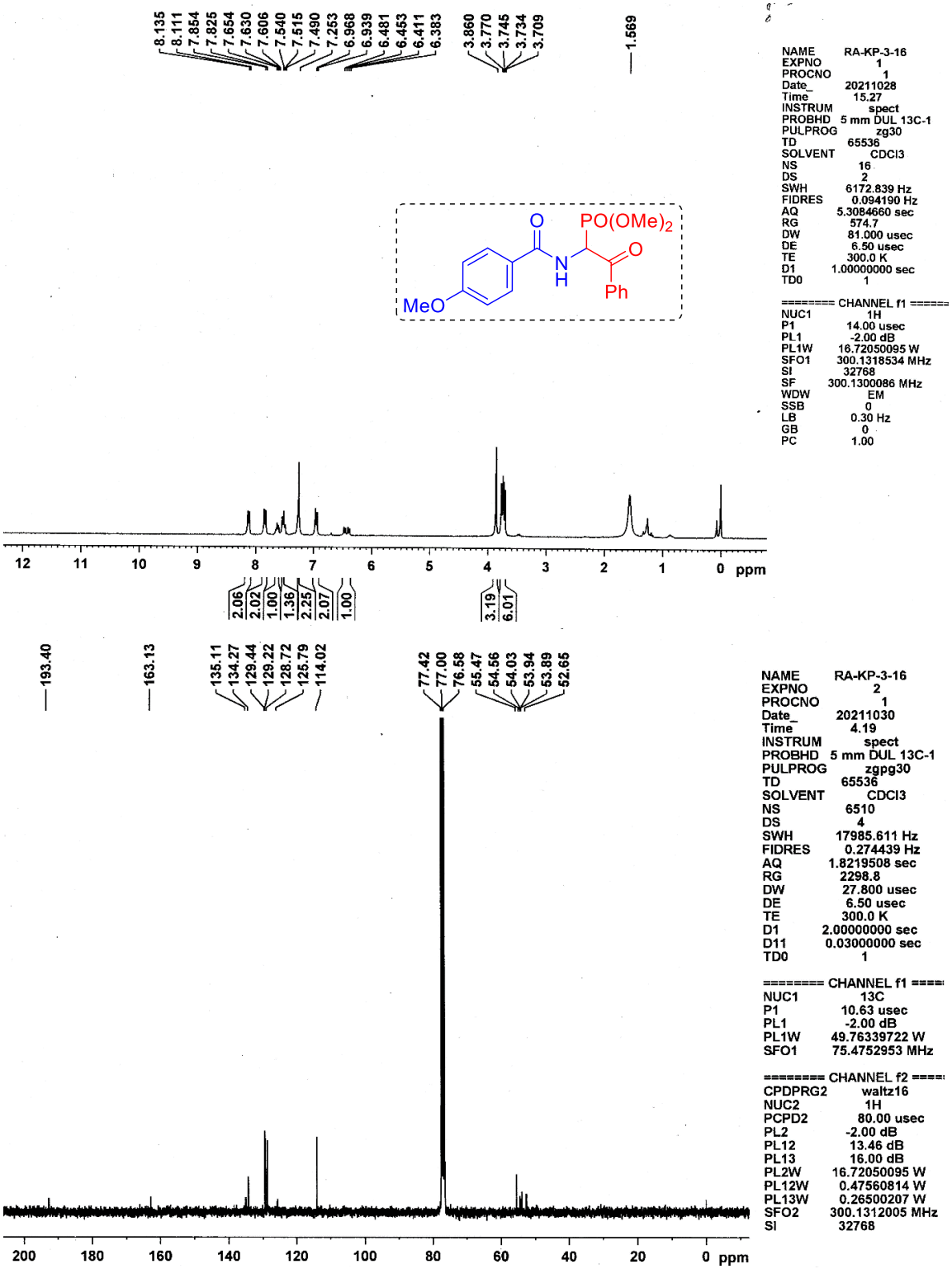
^{1}H and ^{13}C NMR spectra of compound 3a



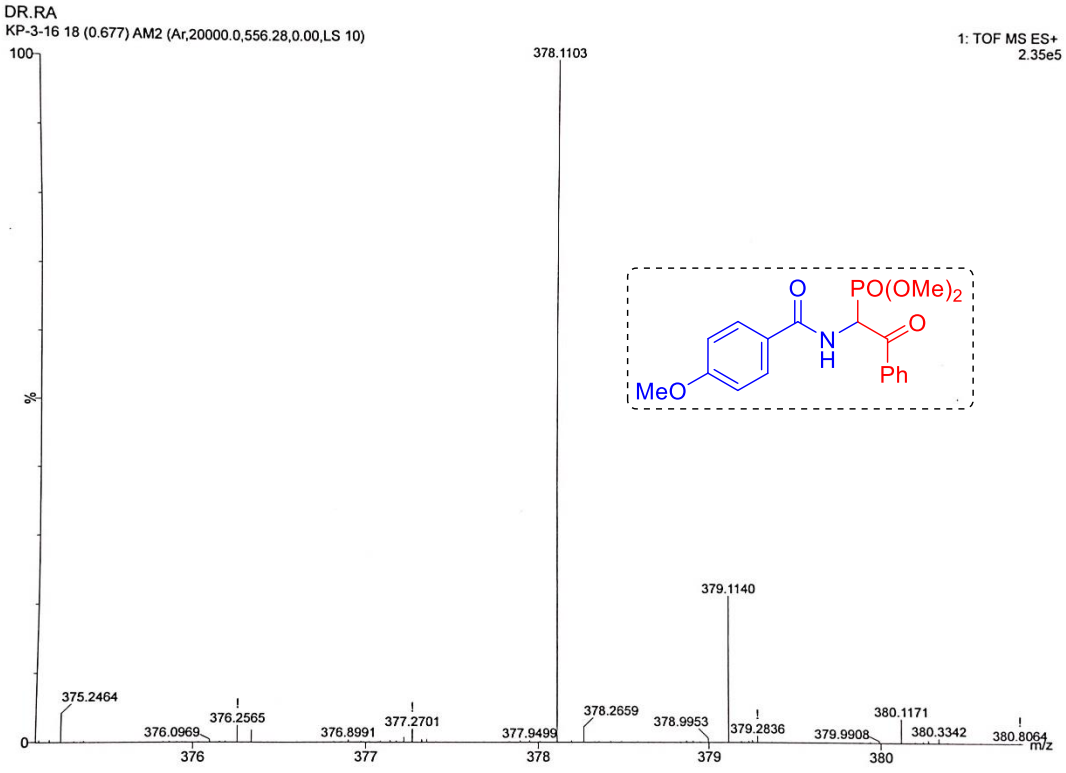
^{1}H and ^{13}C NMR spectra of compound 3b



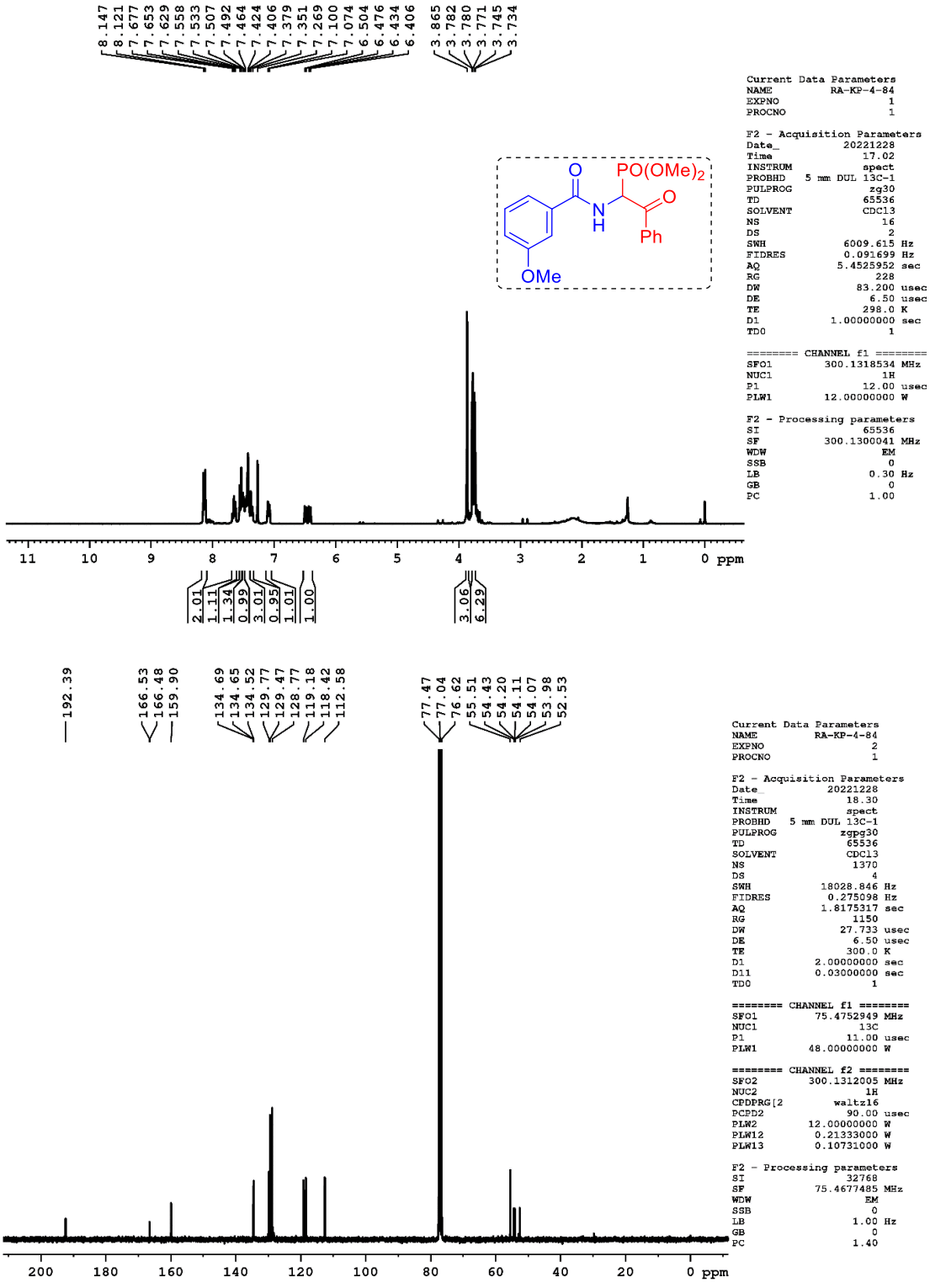
^{31}P NMR spectrum of compound 3b



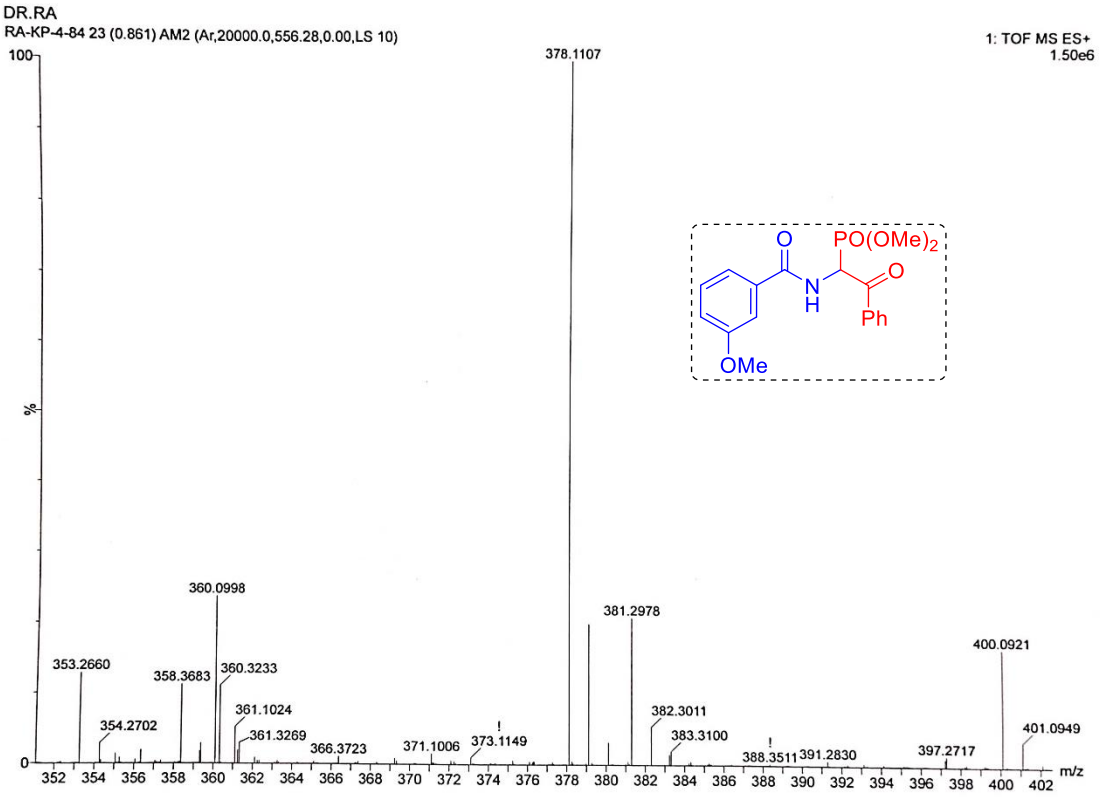
^{1}H and ^{13}C NMR spectra of compound 3c



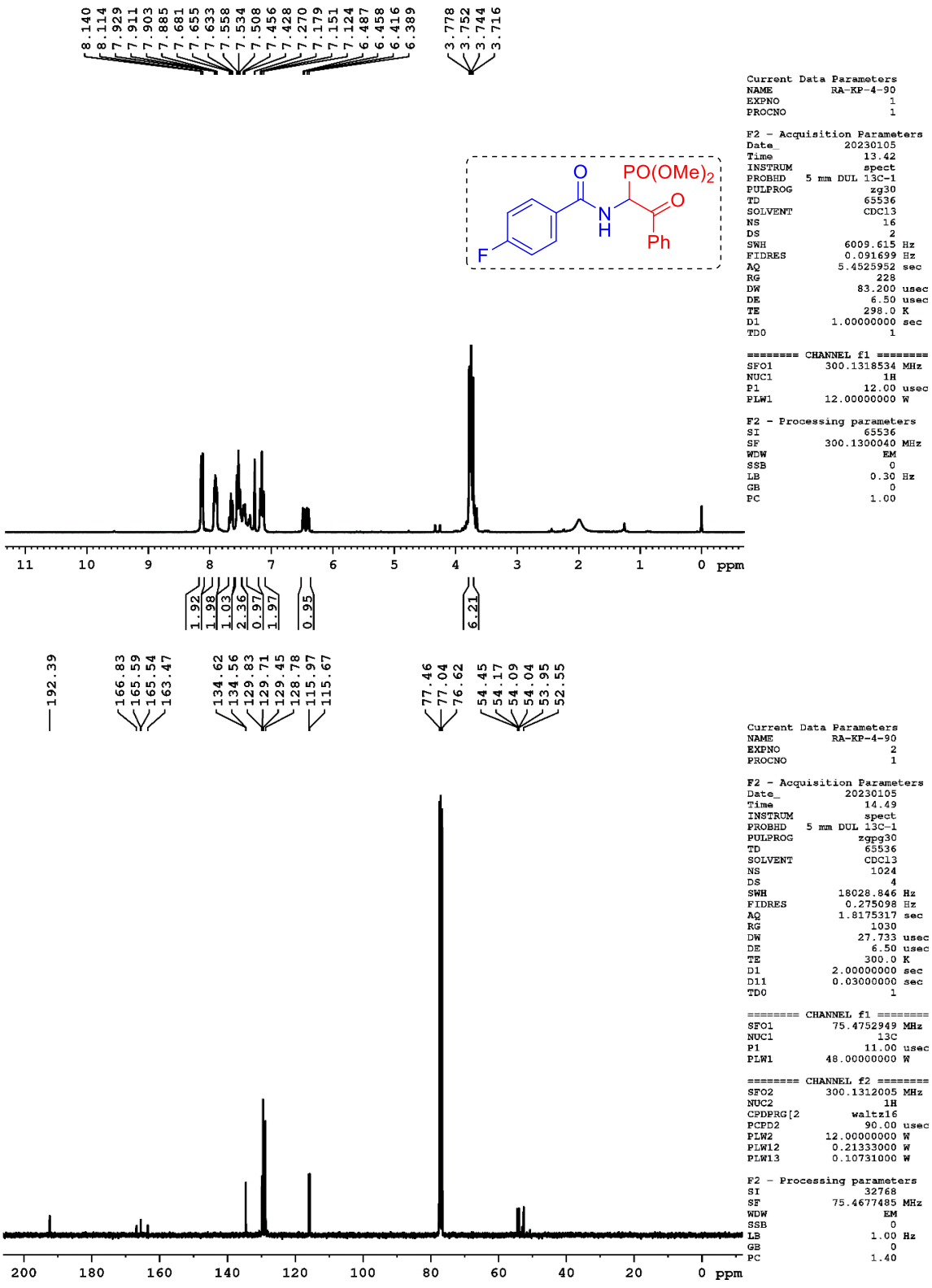
HRMS spectrum of compound 3c



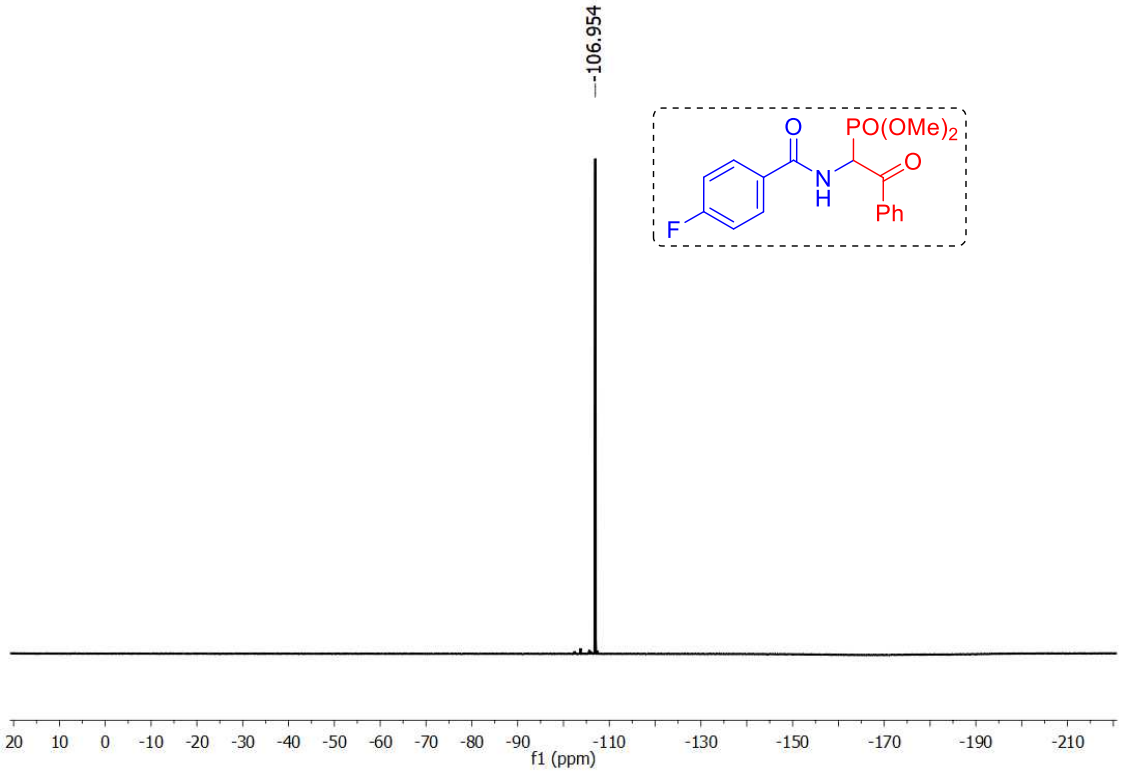
^{1}H and ^{13}C NMR spectra of compound 3d



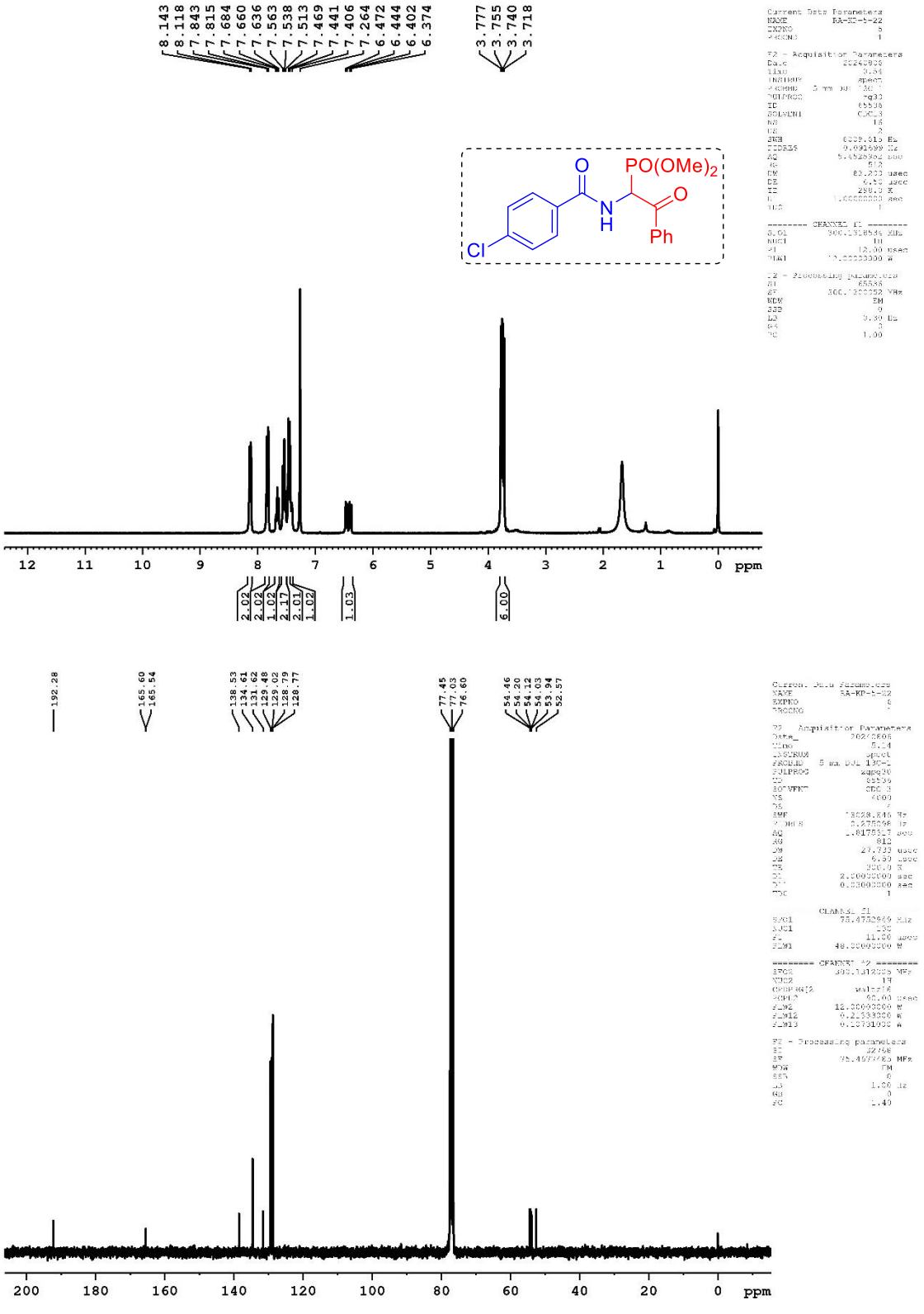
HRMS spectrum of compound 3d



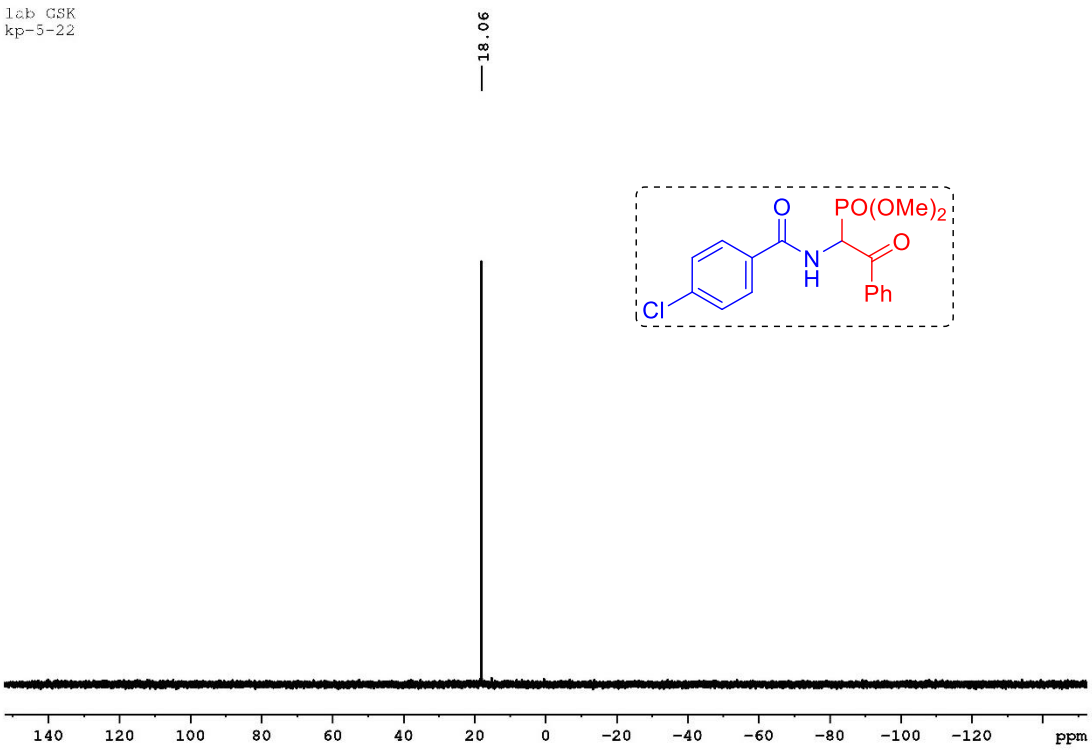
^{1}H and ^{13}C NMR spectra of compound 3e



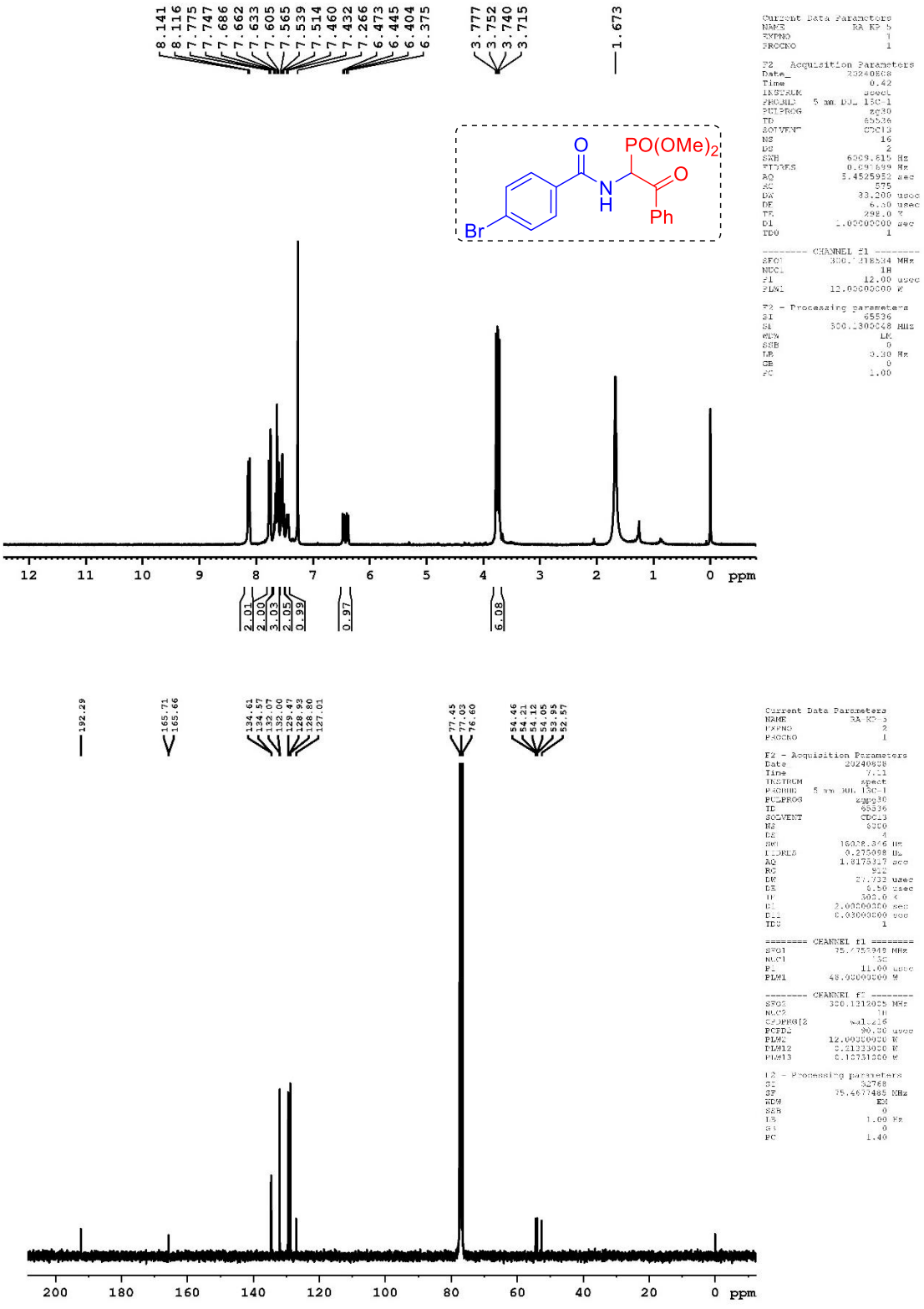
^{19}F NMR spectrum of compound 3e



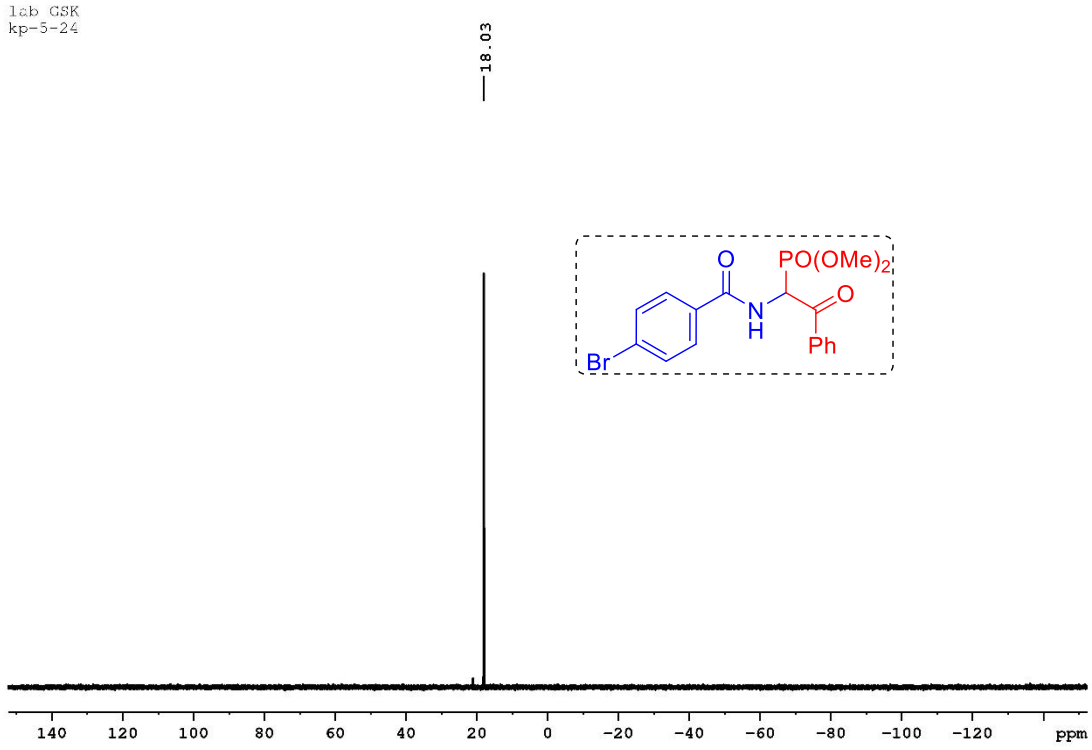
^{1}H and ^{13}C NMR spectra of compound 3f



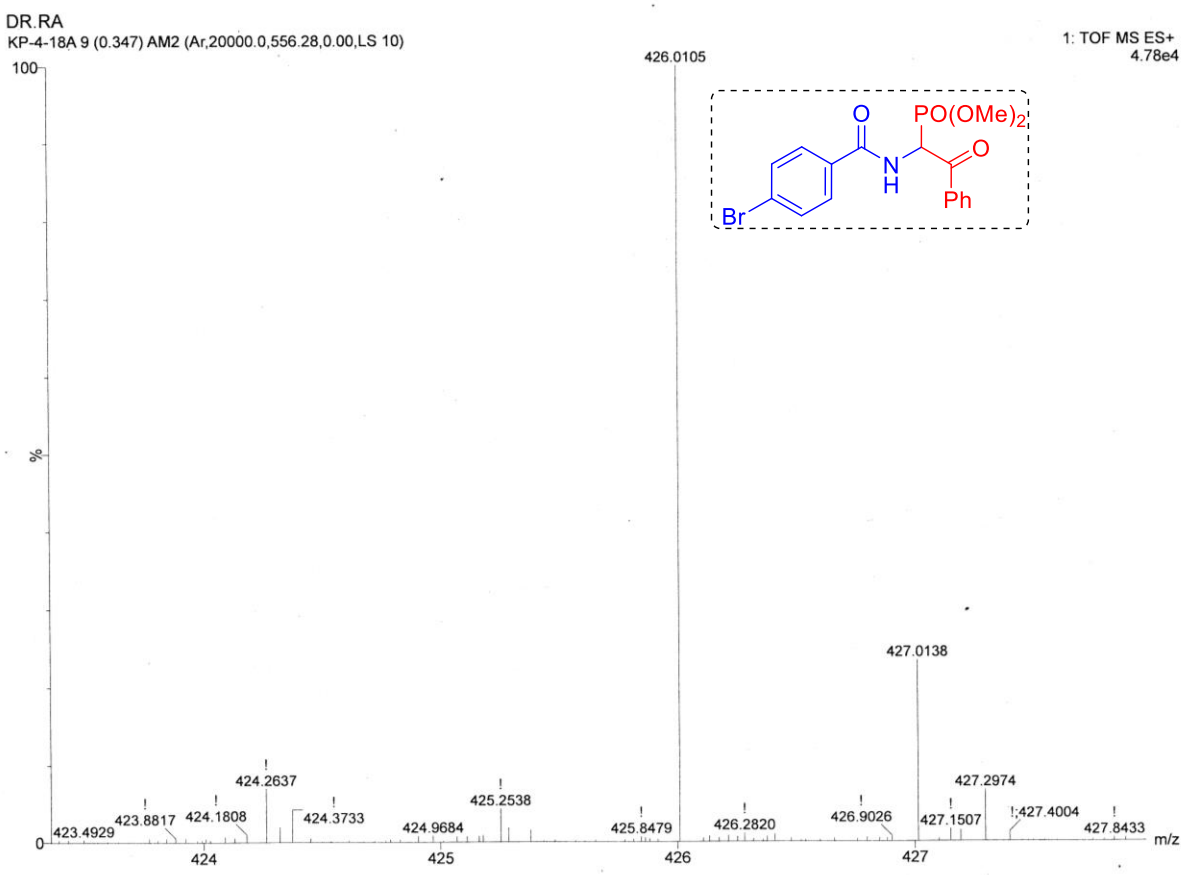
^{31}P NMR spectrum of compound 3f



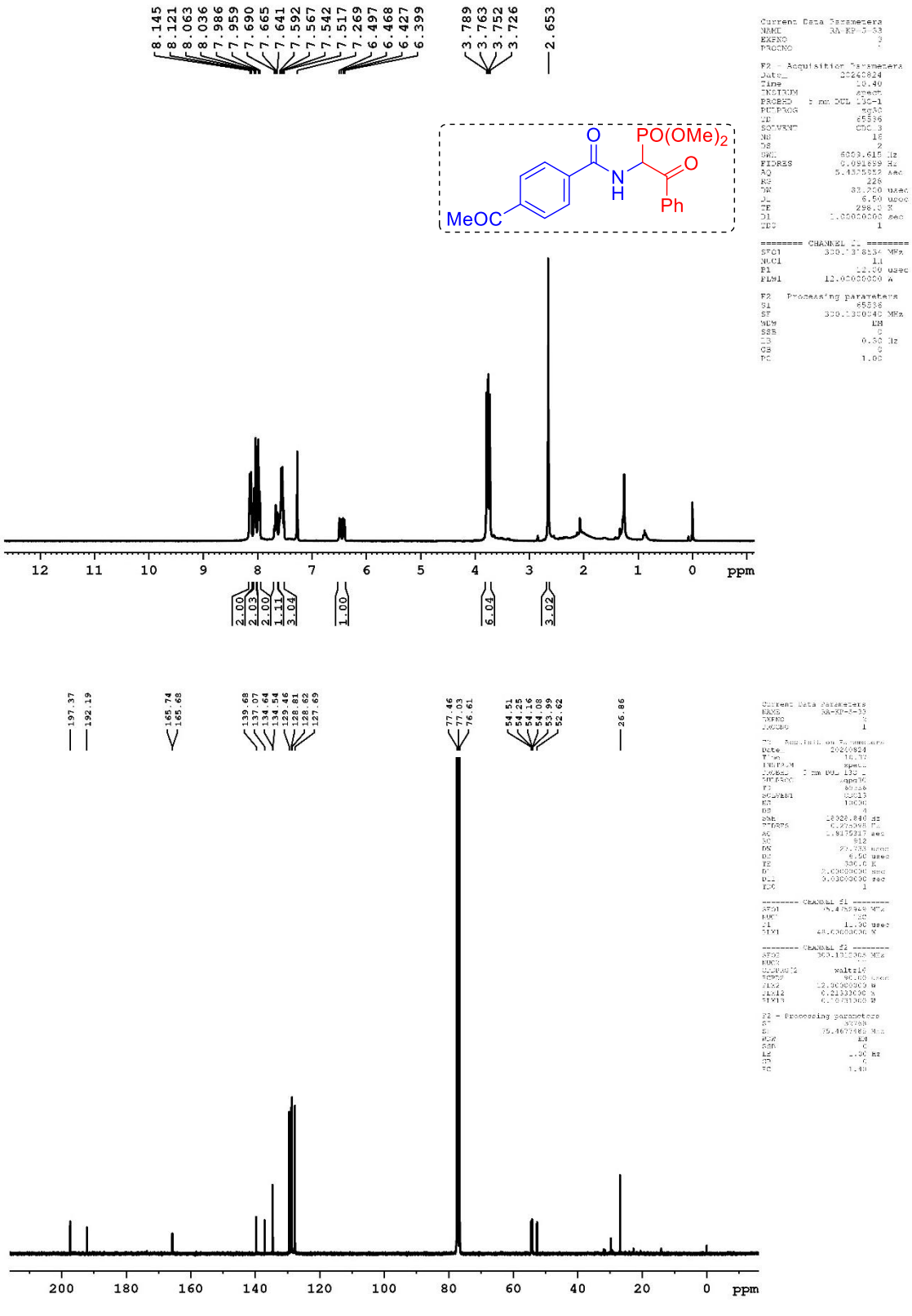
^{1}H and ^{13}C NMR spectra of compound 3g



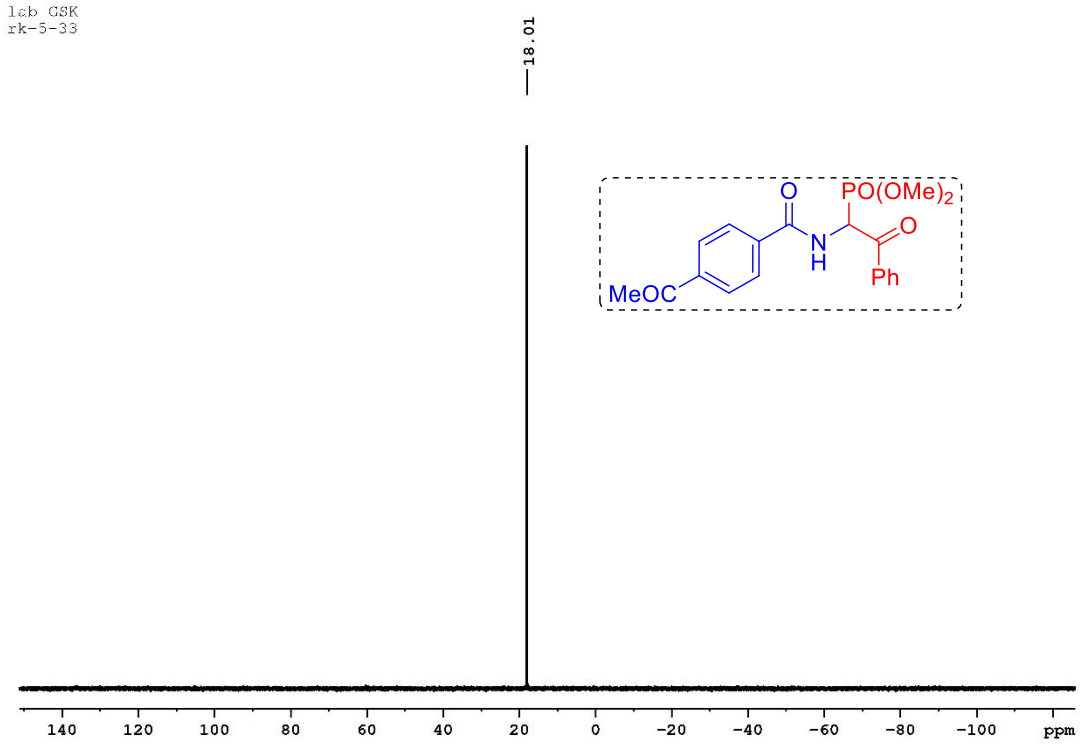
^{31}P NMR spectrum of compound 3g



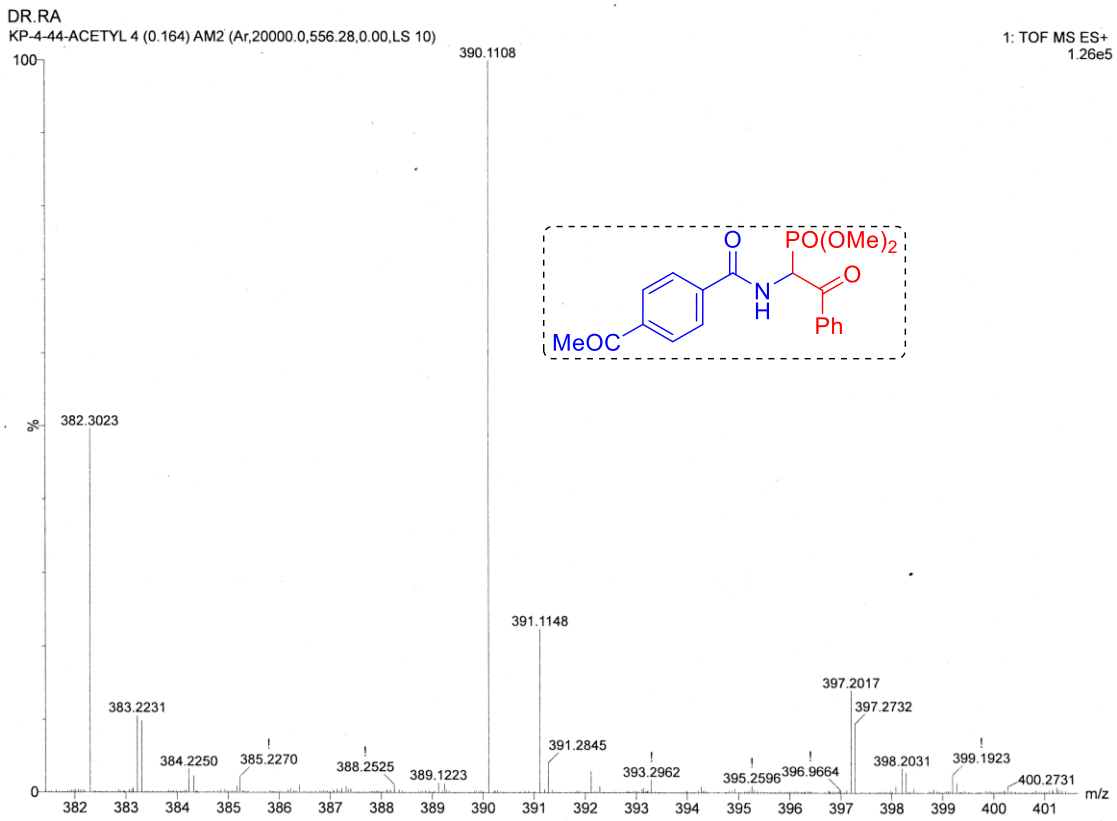
HRMS spectrum of compound 3g



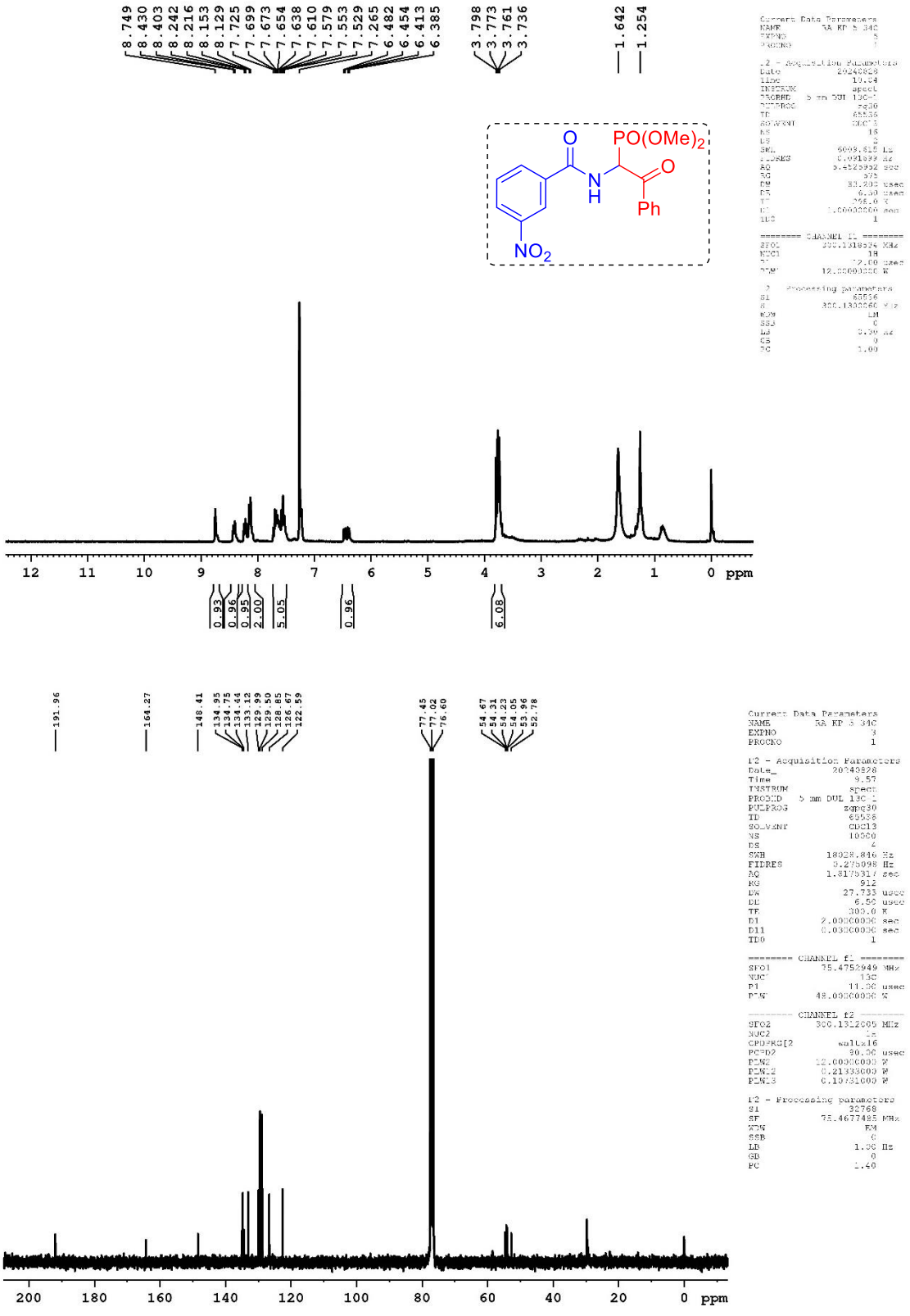
^{1}H and ^{13}C NMR spectra of compound 3h



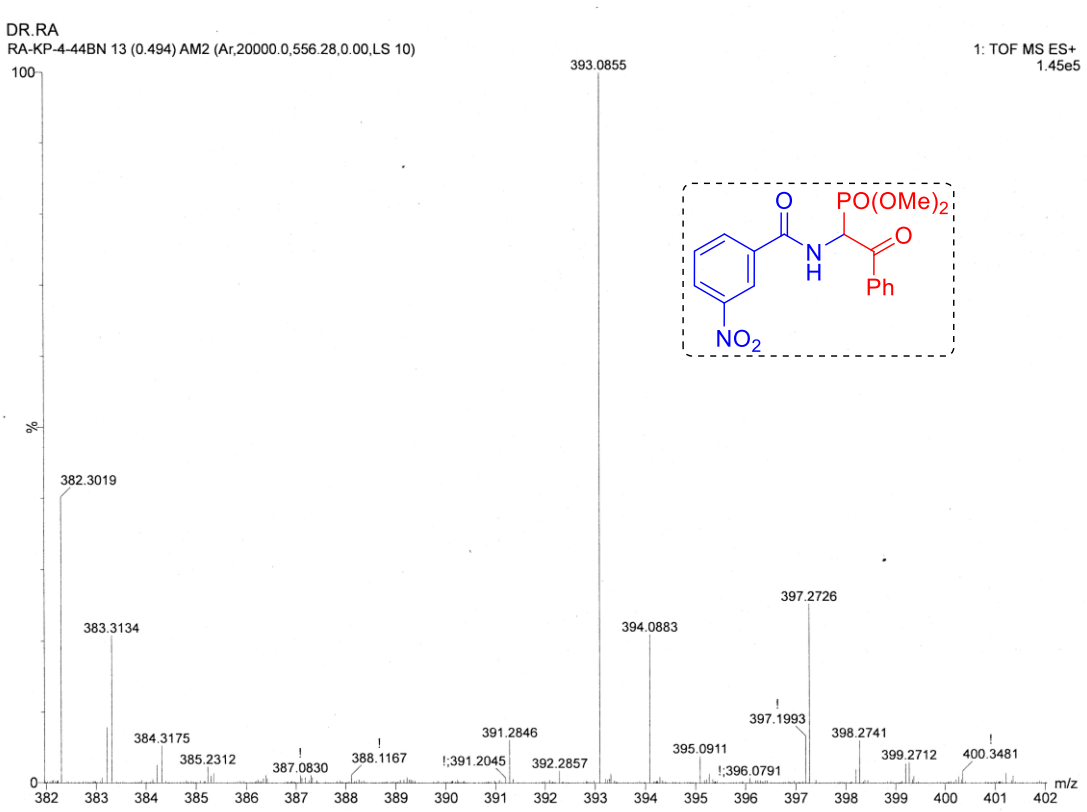
^{31}P NMR spectrum of compound 3h



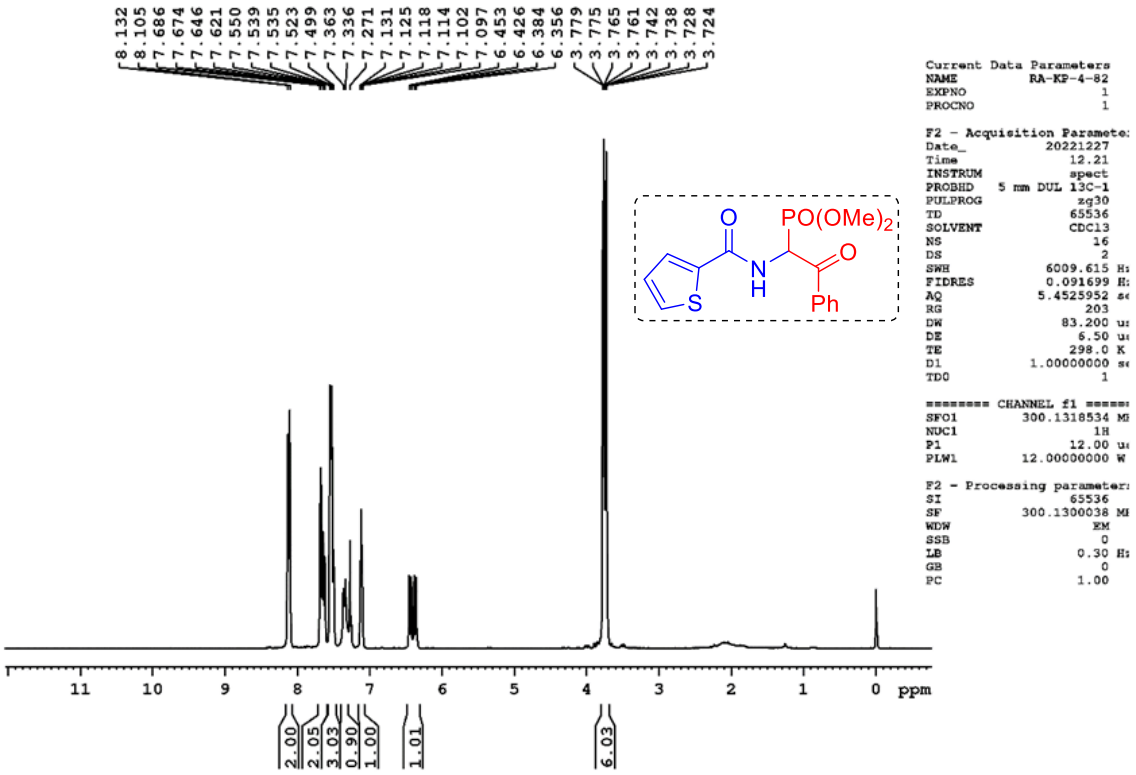
HRMS spectrum of compound 3h

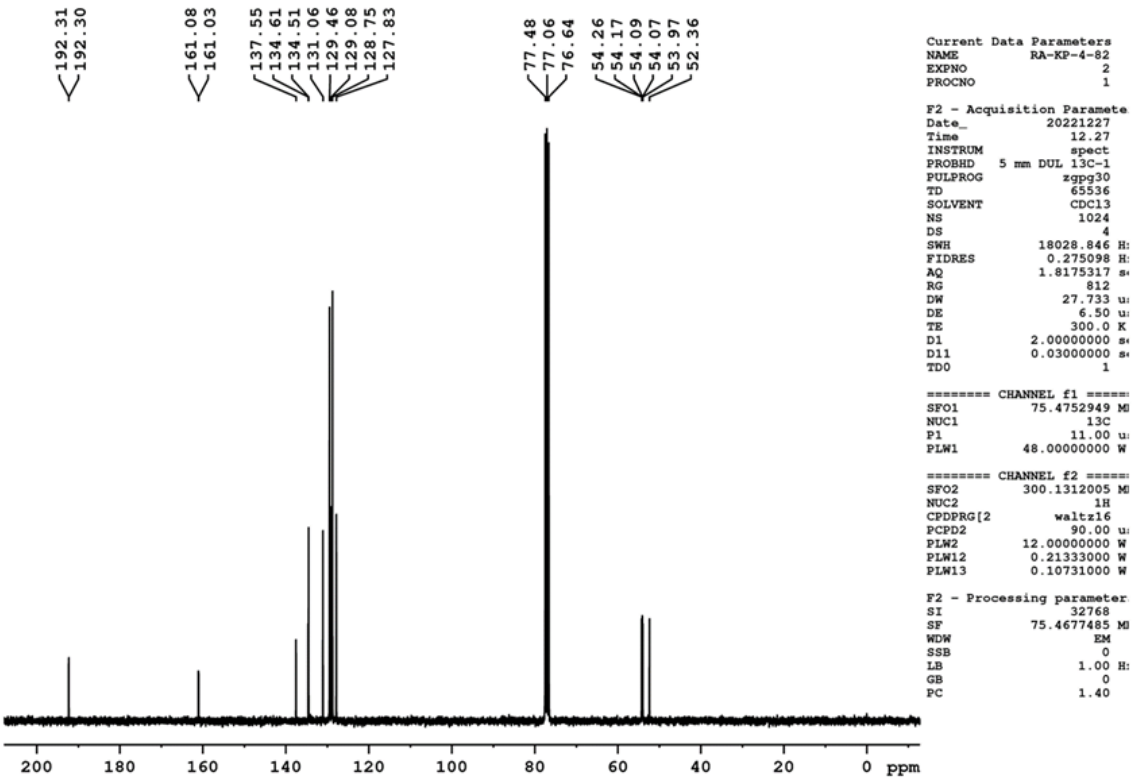


^{1}H and ^{13}C NMR spectra of compound 3i

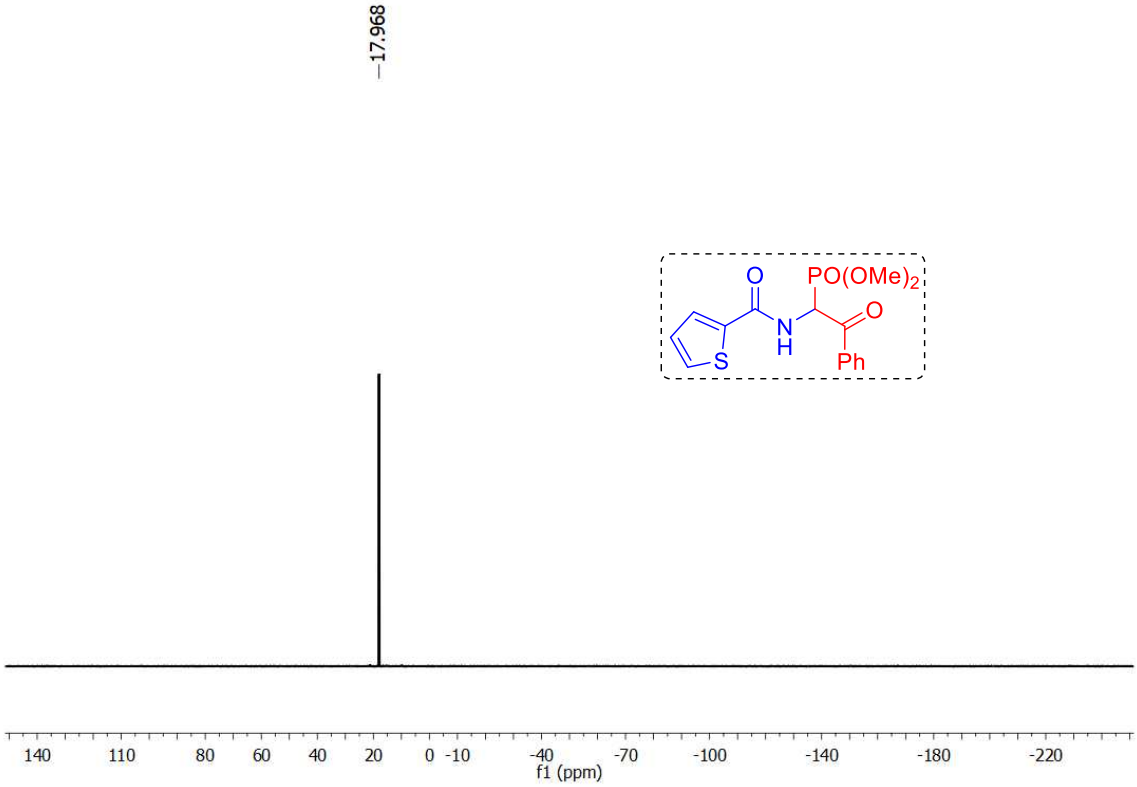


HRMS spectrum of compound 3i

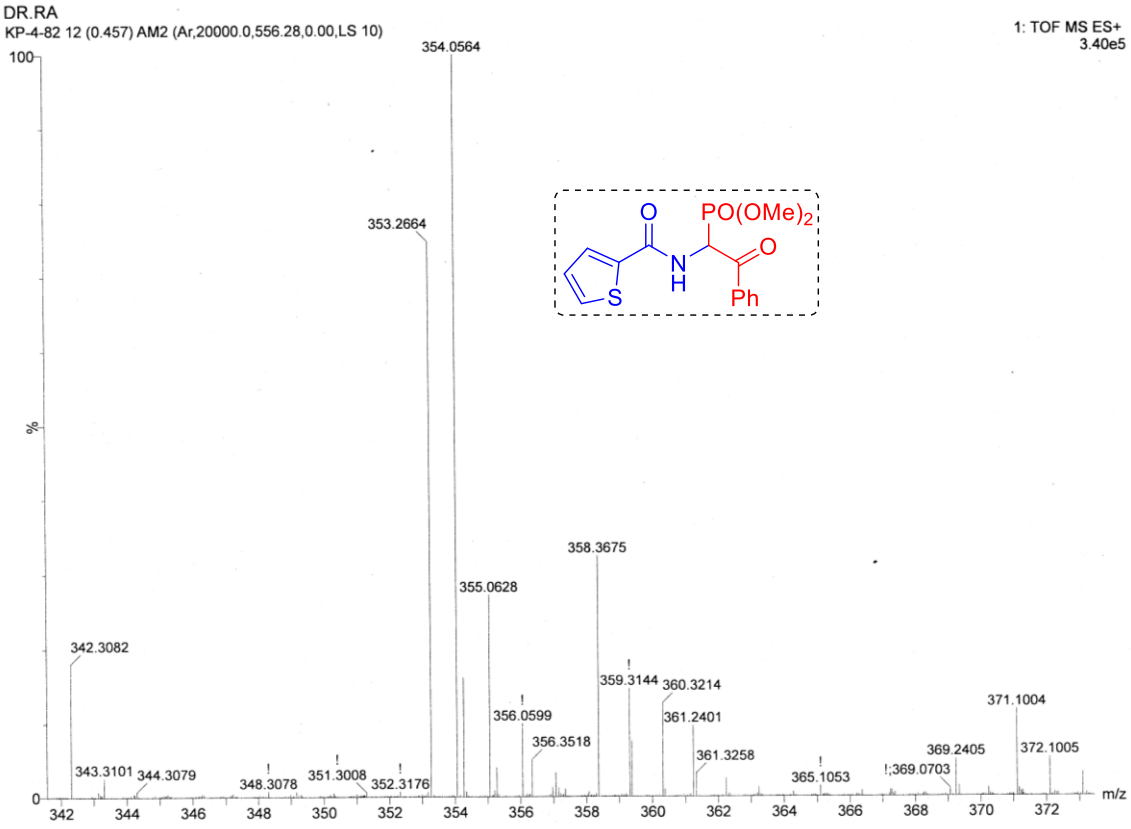




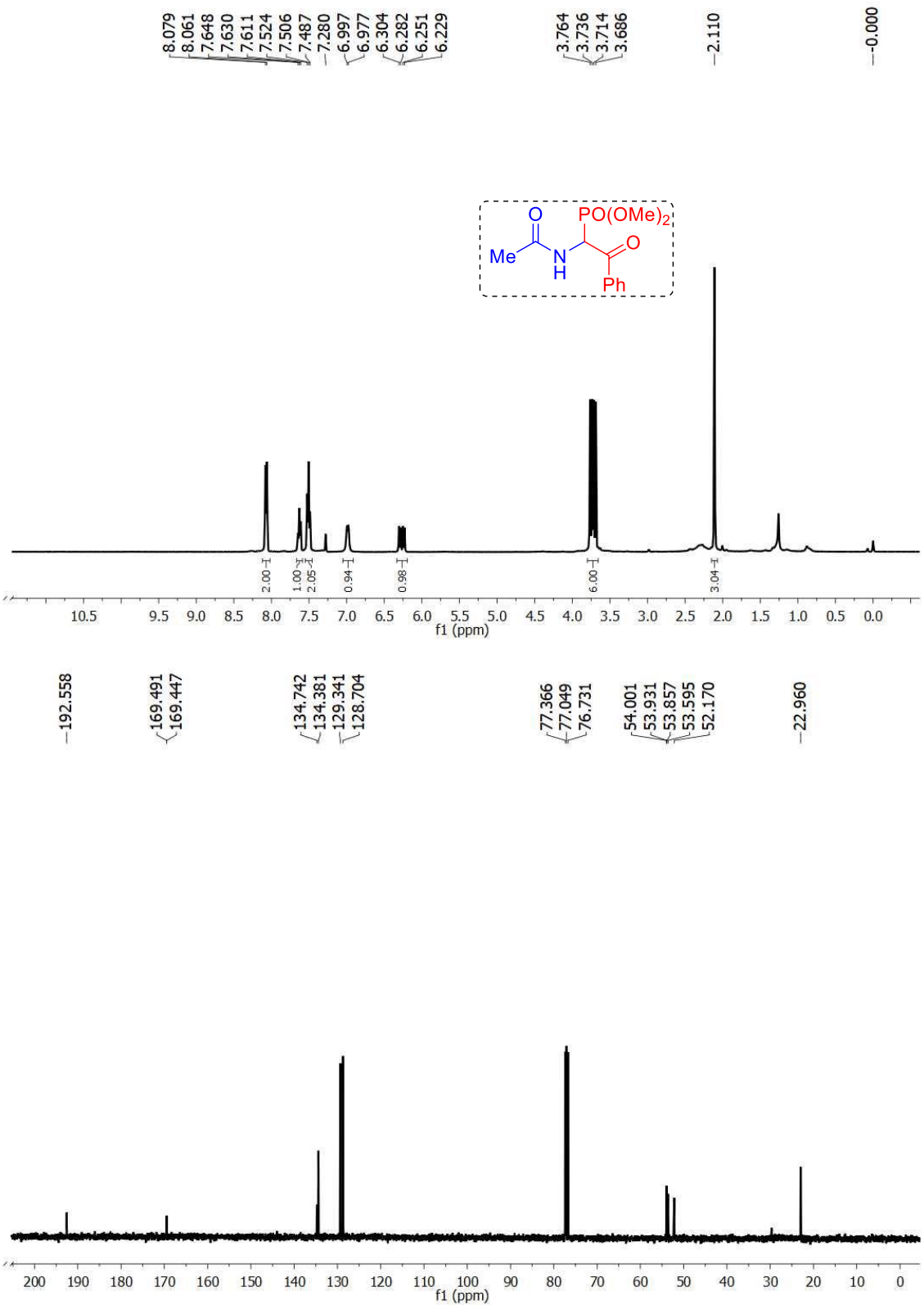
^{1}H and ^{13}C NMR spectra of compound 3j



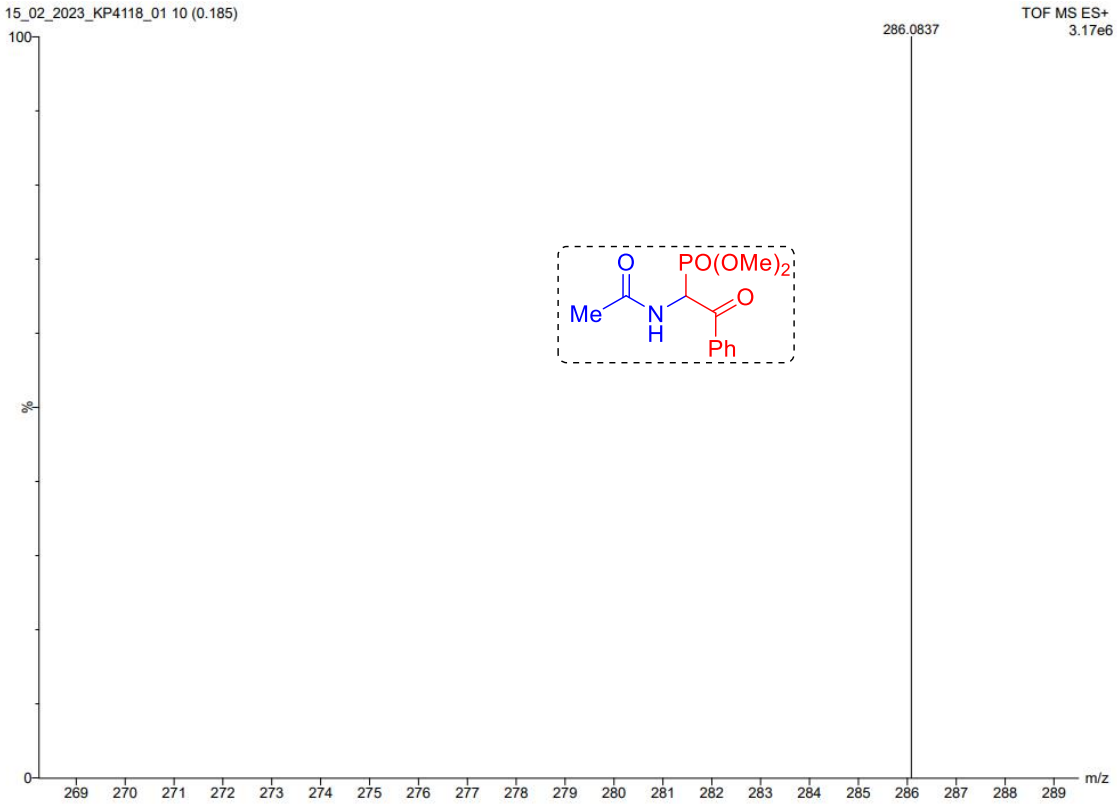
^{31}P NMR spectrum of compound 3j



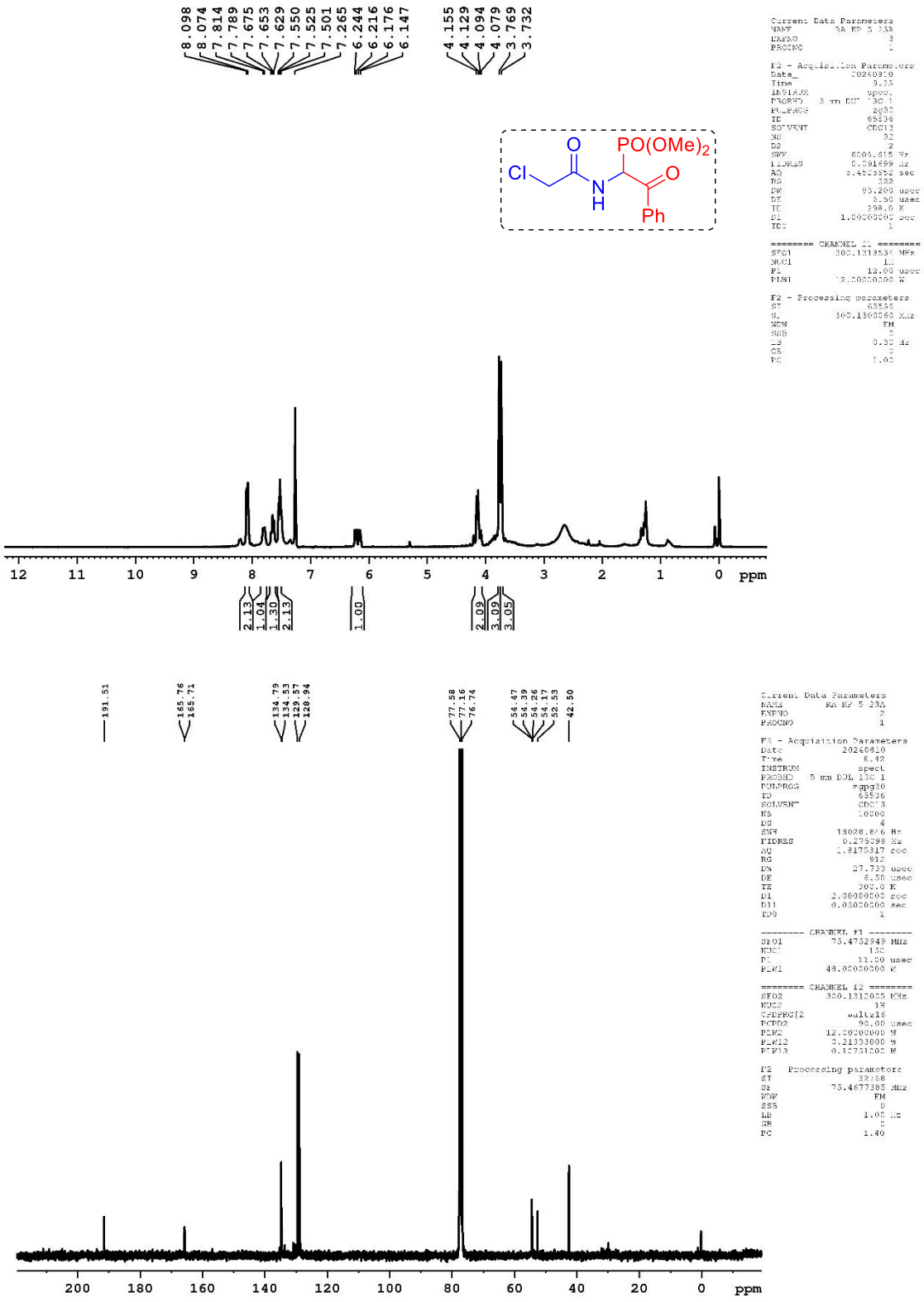
HRMS spectrum of compound 3j



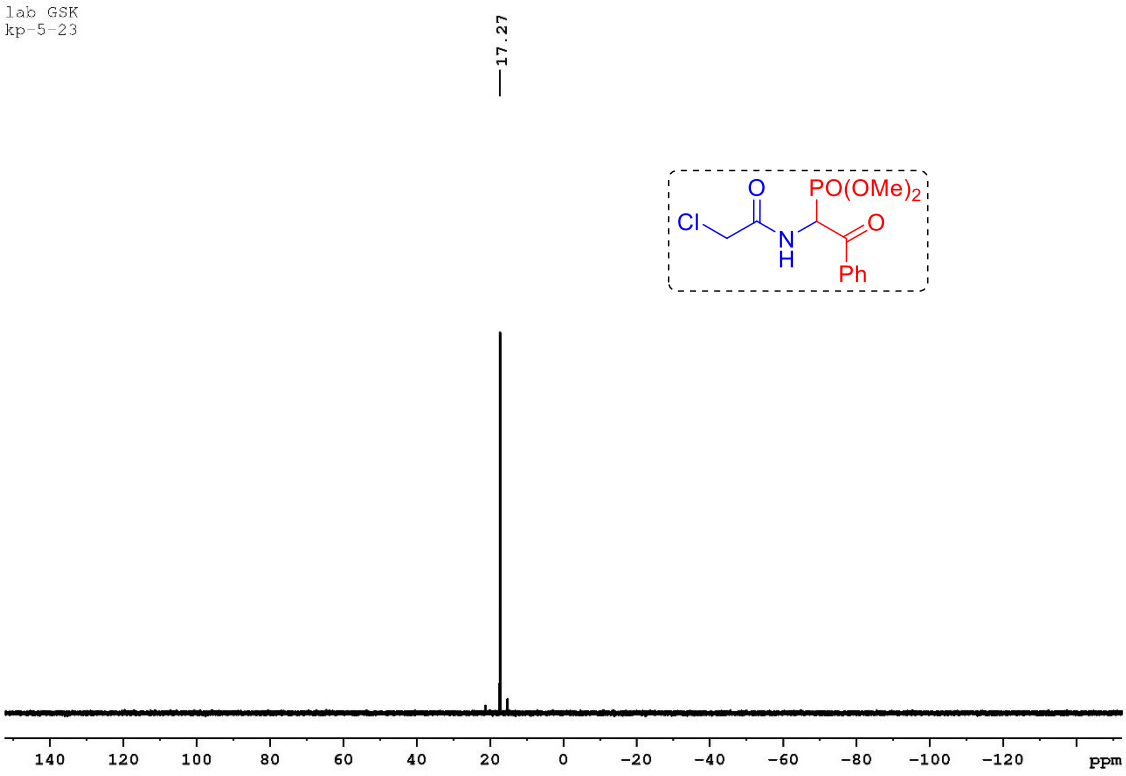
^{1}H and ^{13}C NMR spectra of compound 3k



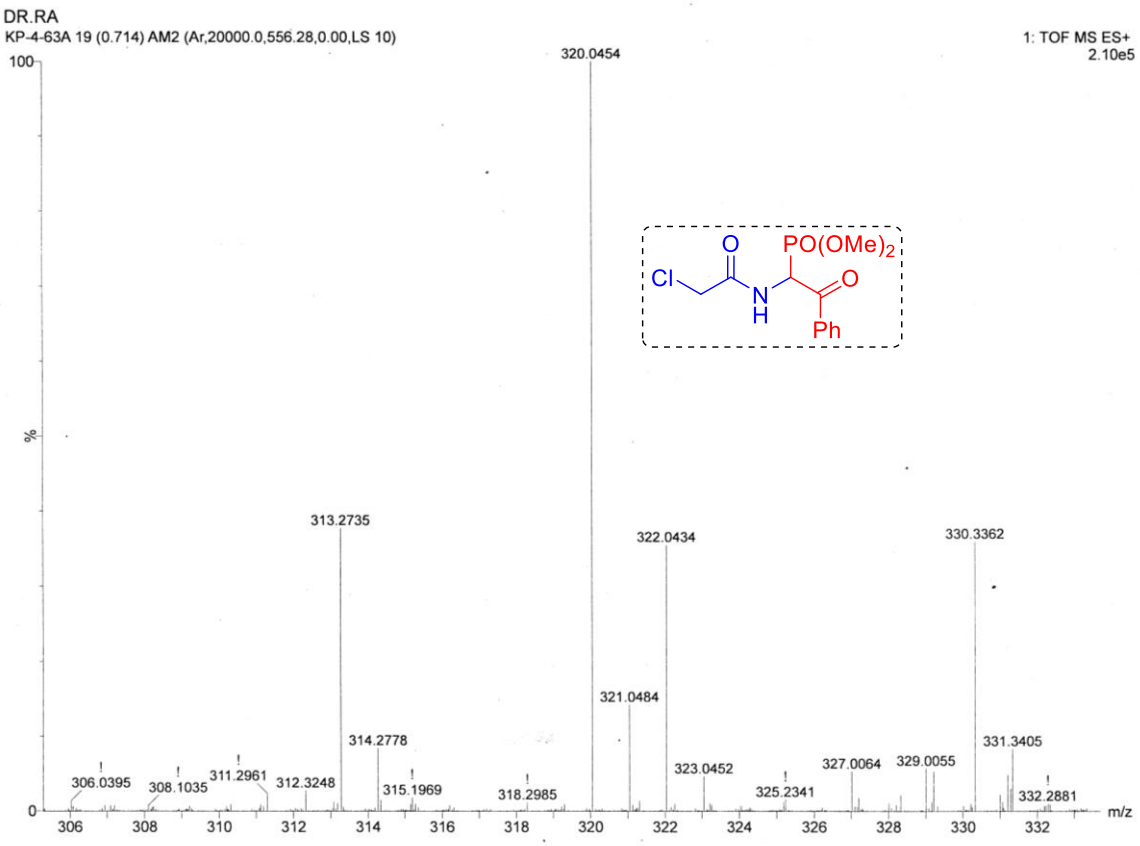
HRMS spectrum of compound 3k



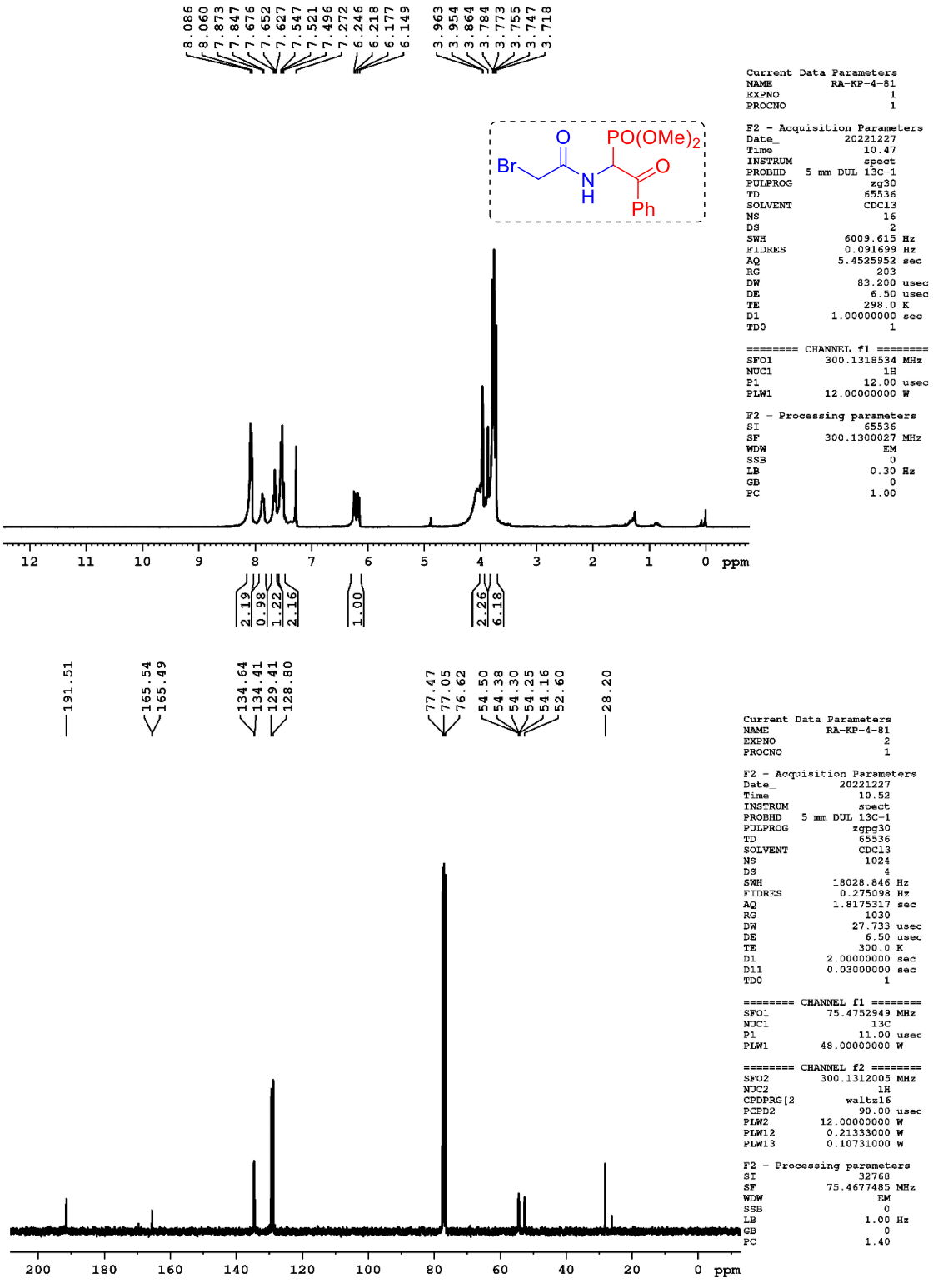
^{1}H and ^{13}C NMR spectra of compound 3l



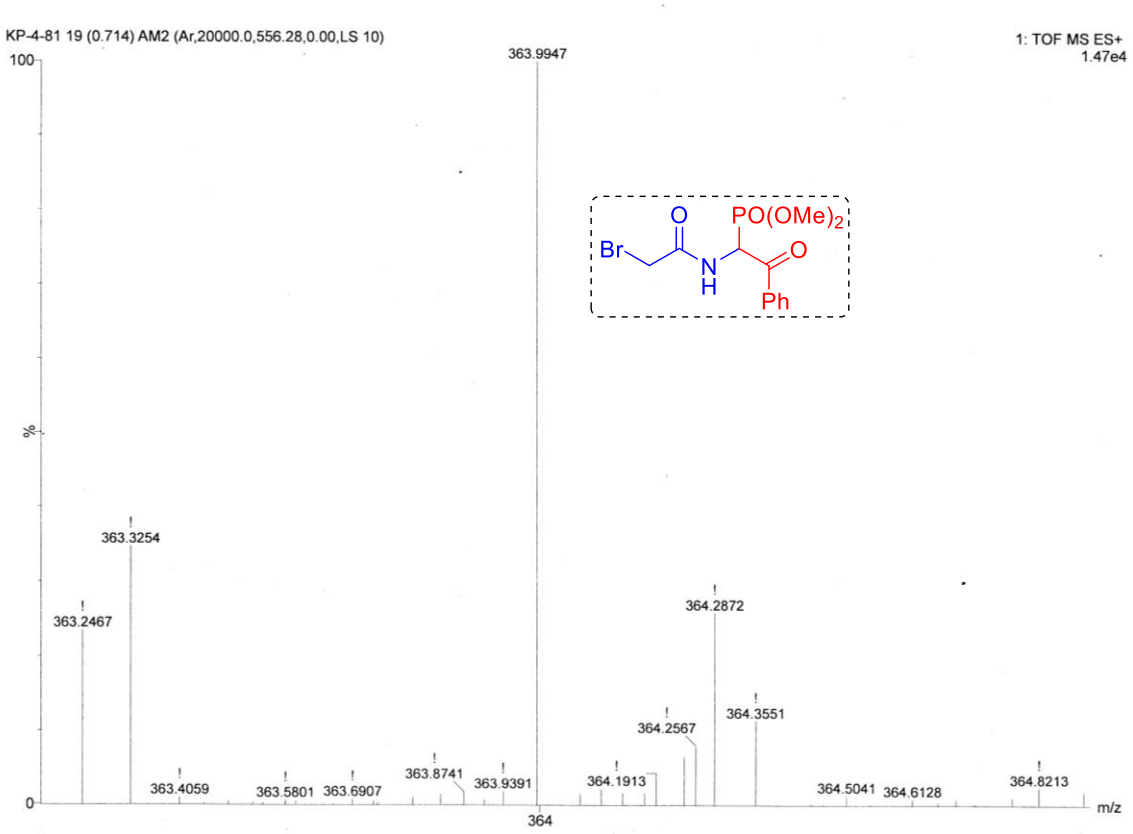
^{31}P NMR spectrum of compound 3l



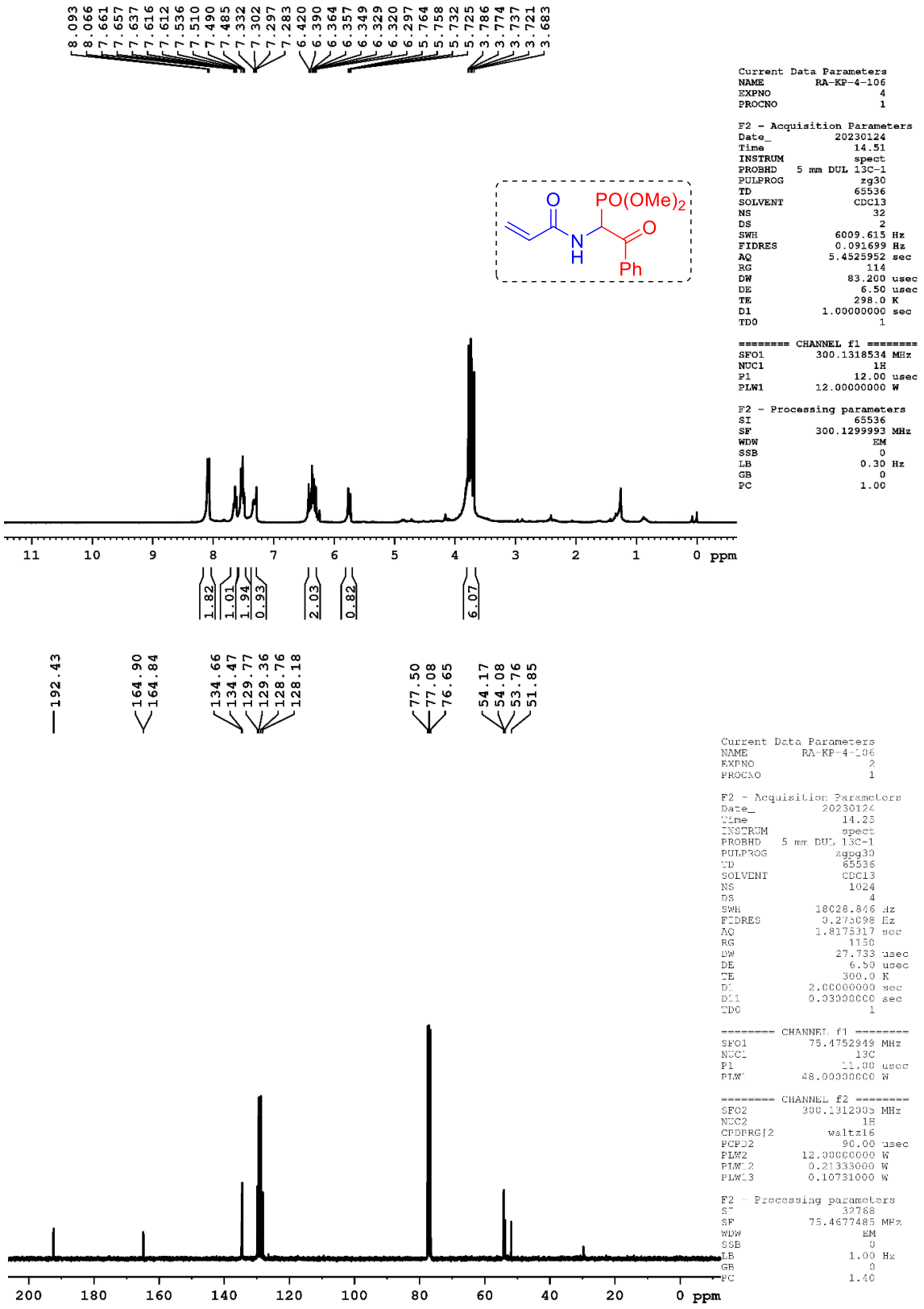
HRMS spectrum of compound 3l



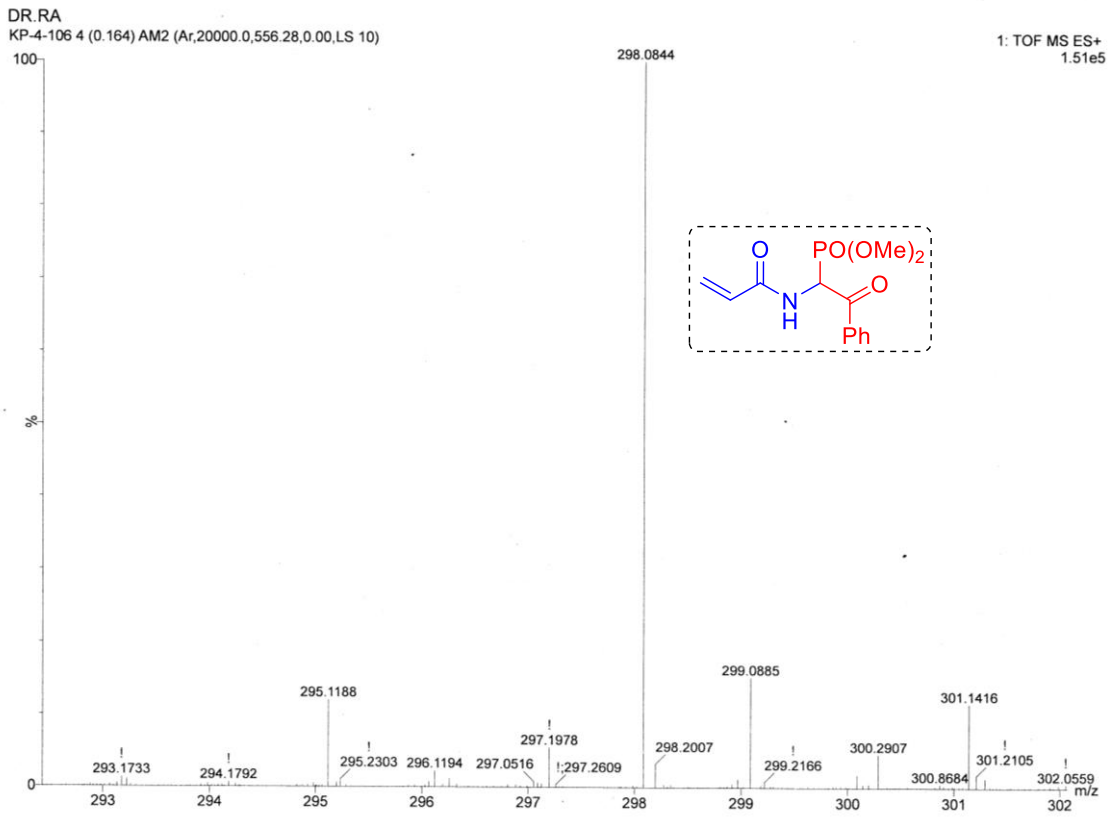
^{1}H and ^{13}C NMR spectra of compound 3m



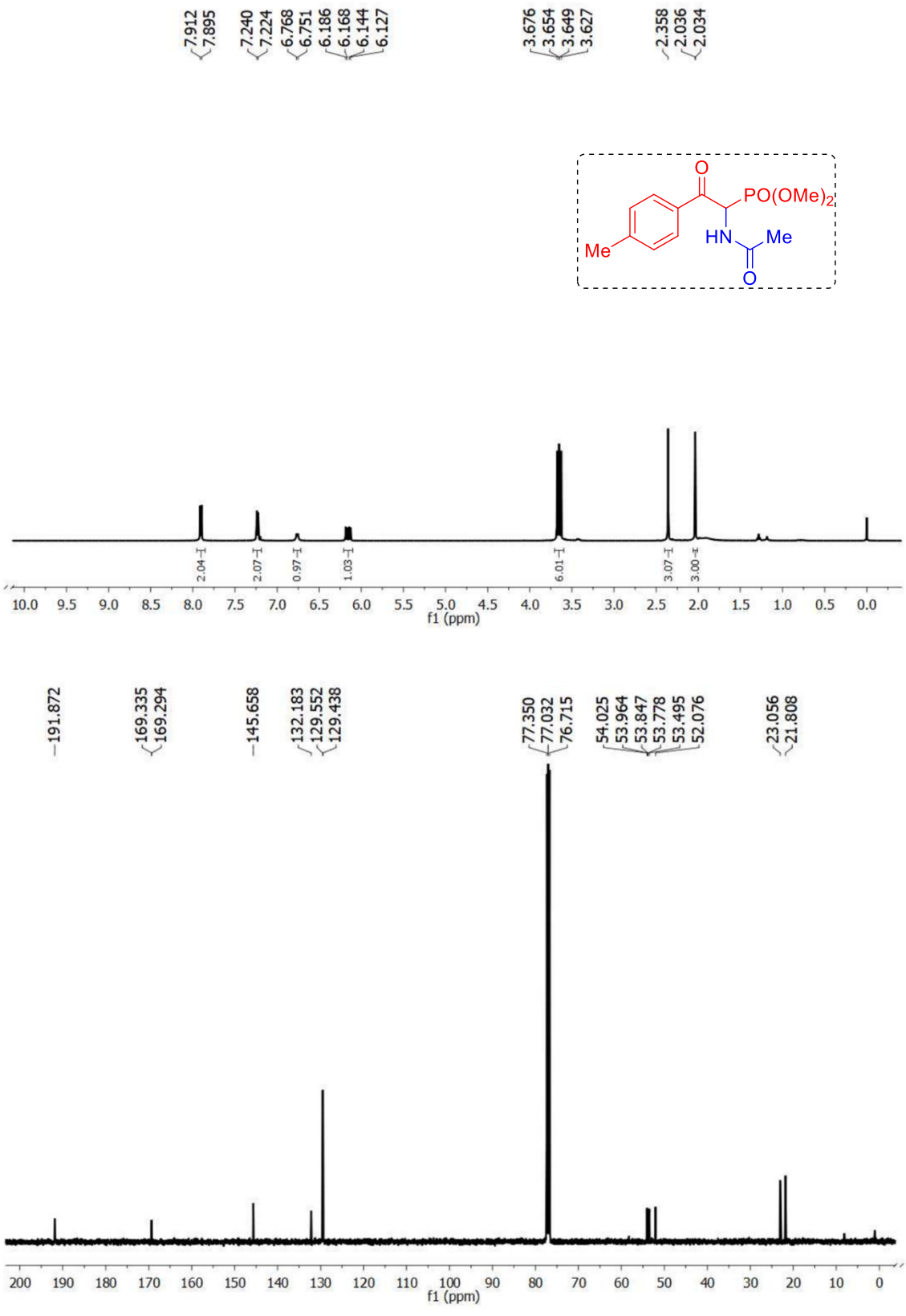
HRMS spectrum of compound 3m



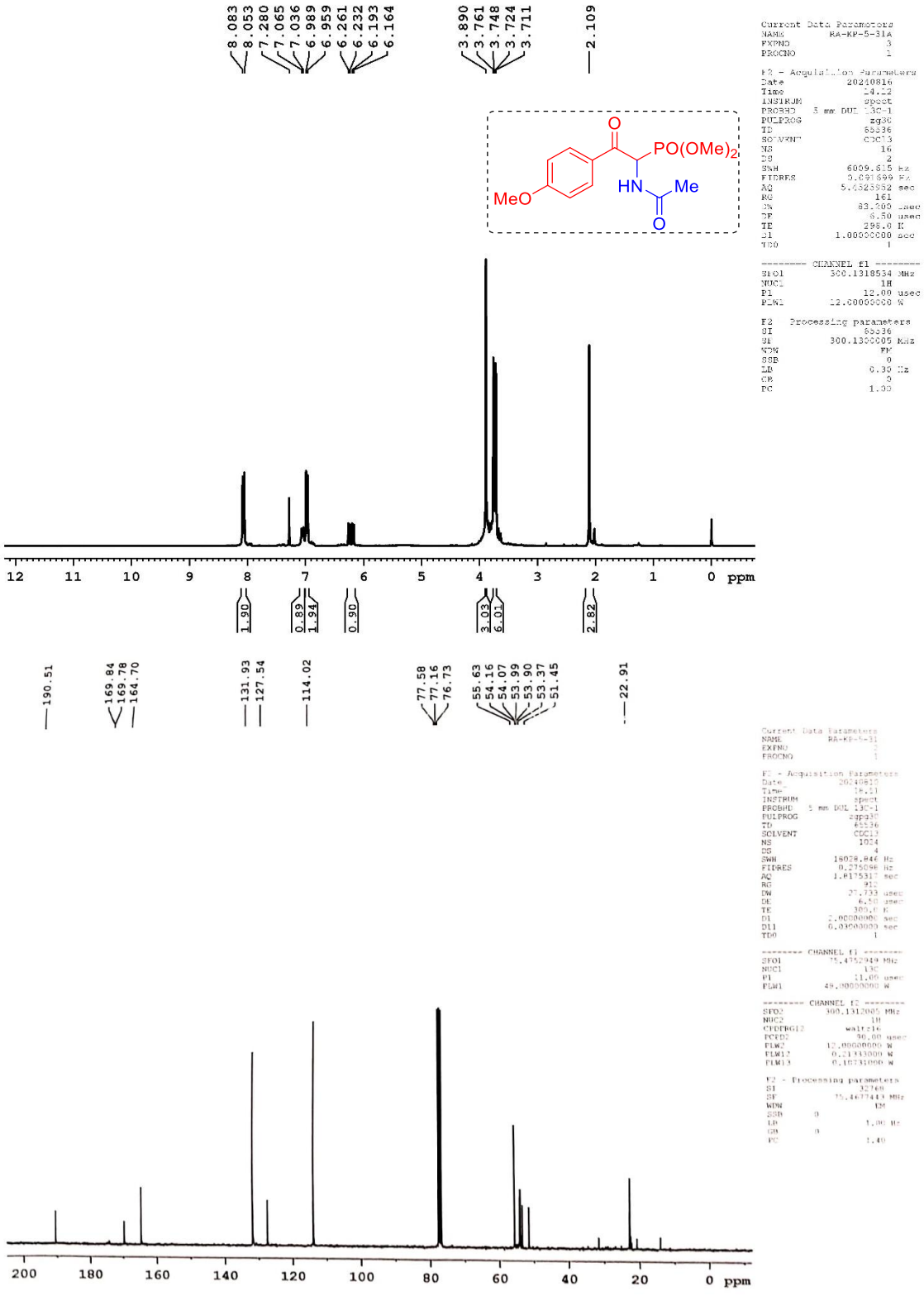
^{1}H and ^{13}C NMR spectra of compound 3n



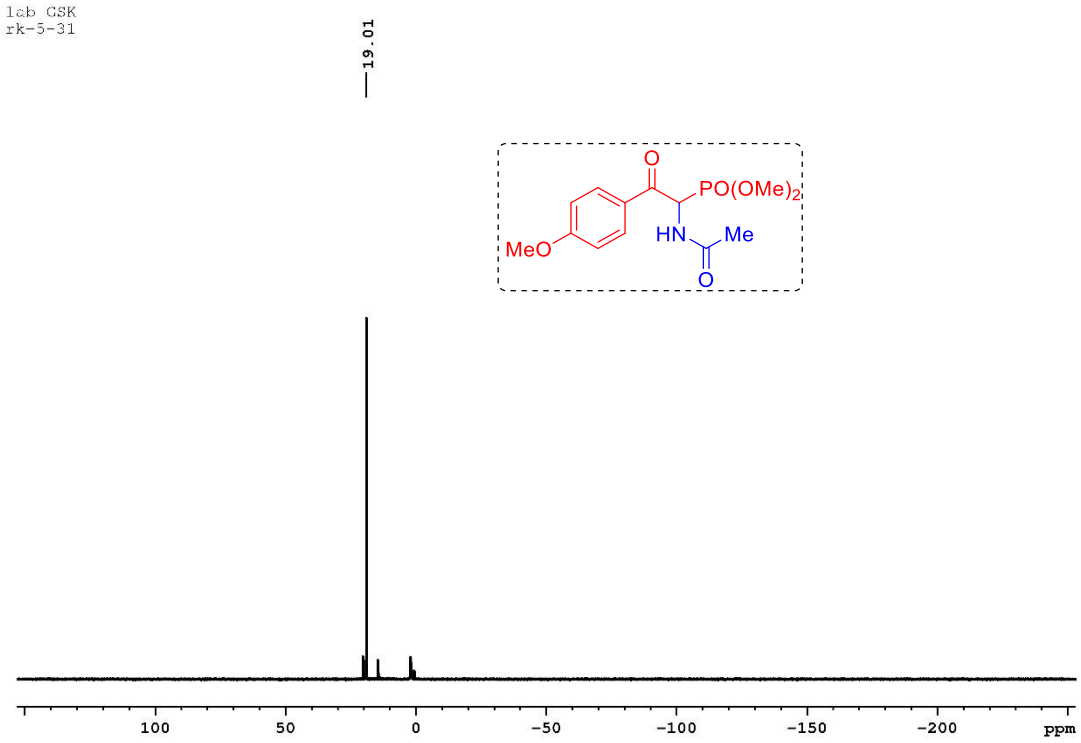
HRMS spectrum of compound 3n



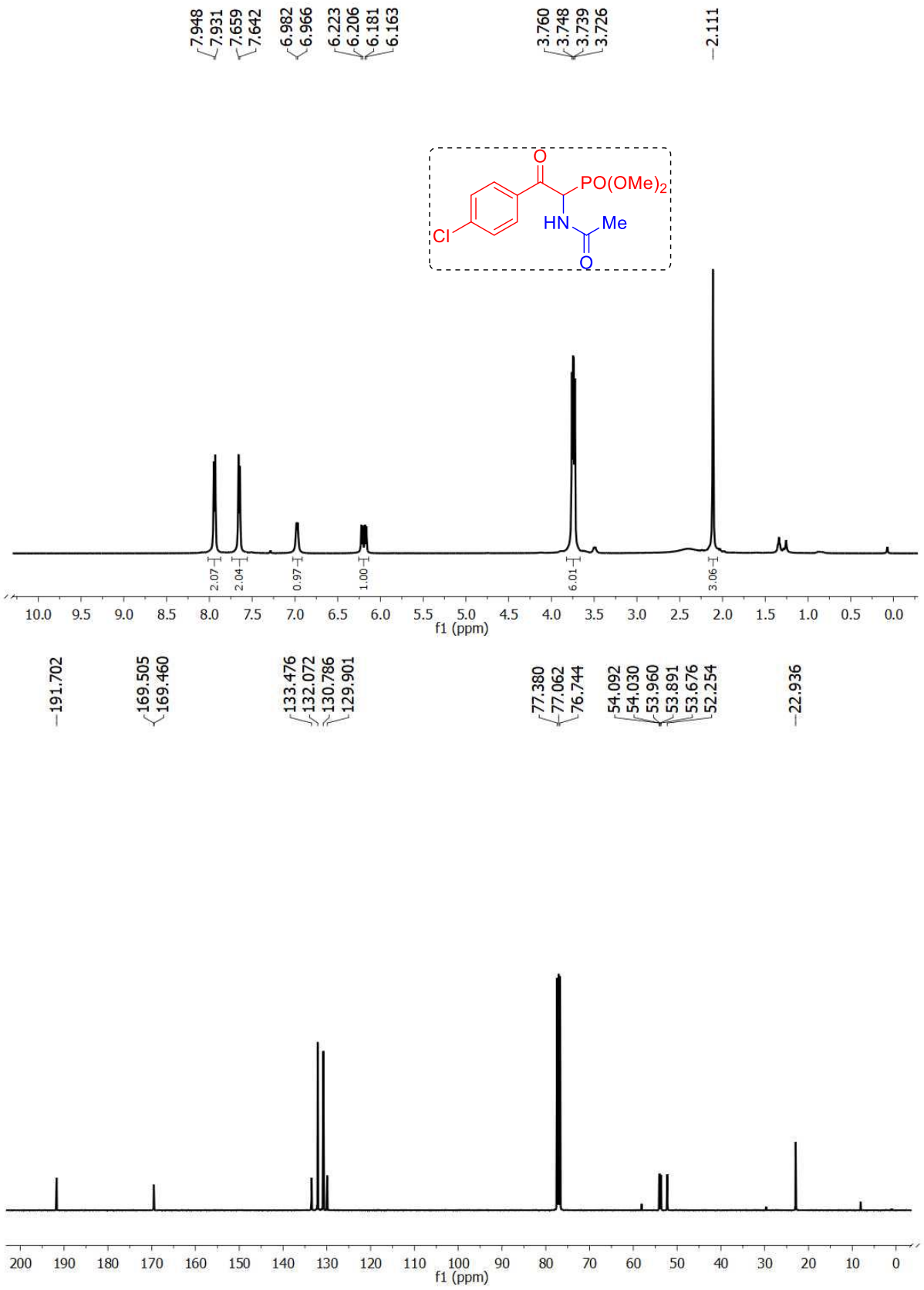
^{1}H and ^{13}C NMR spectra of compound 4a



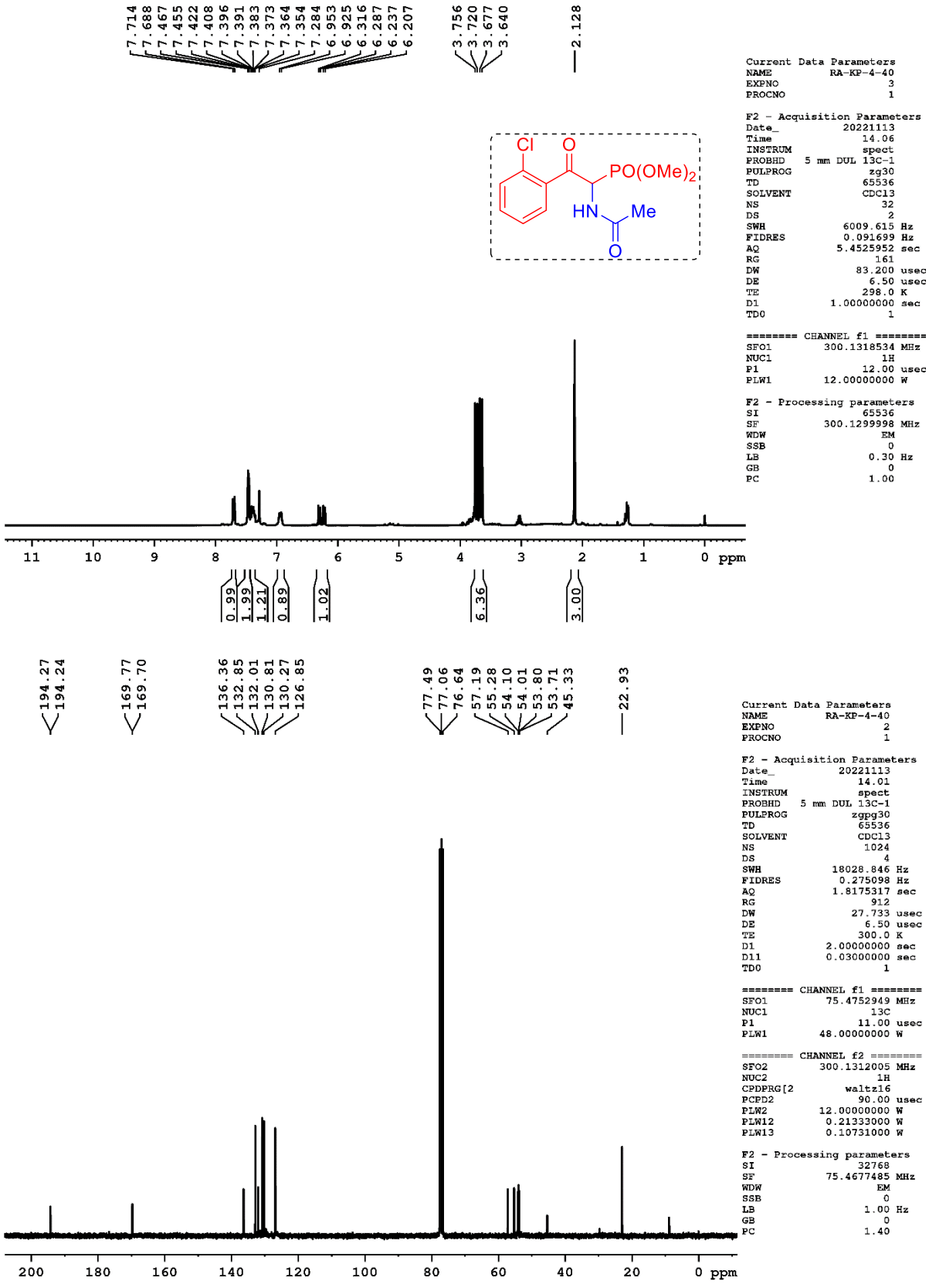
^{1}H and ^{13}C NMR spectra of compound 4b



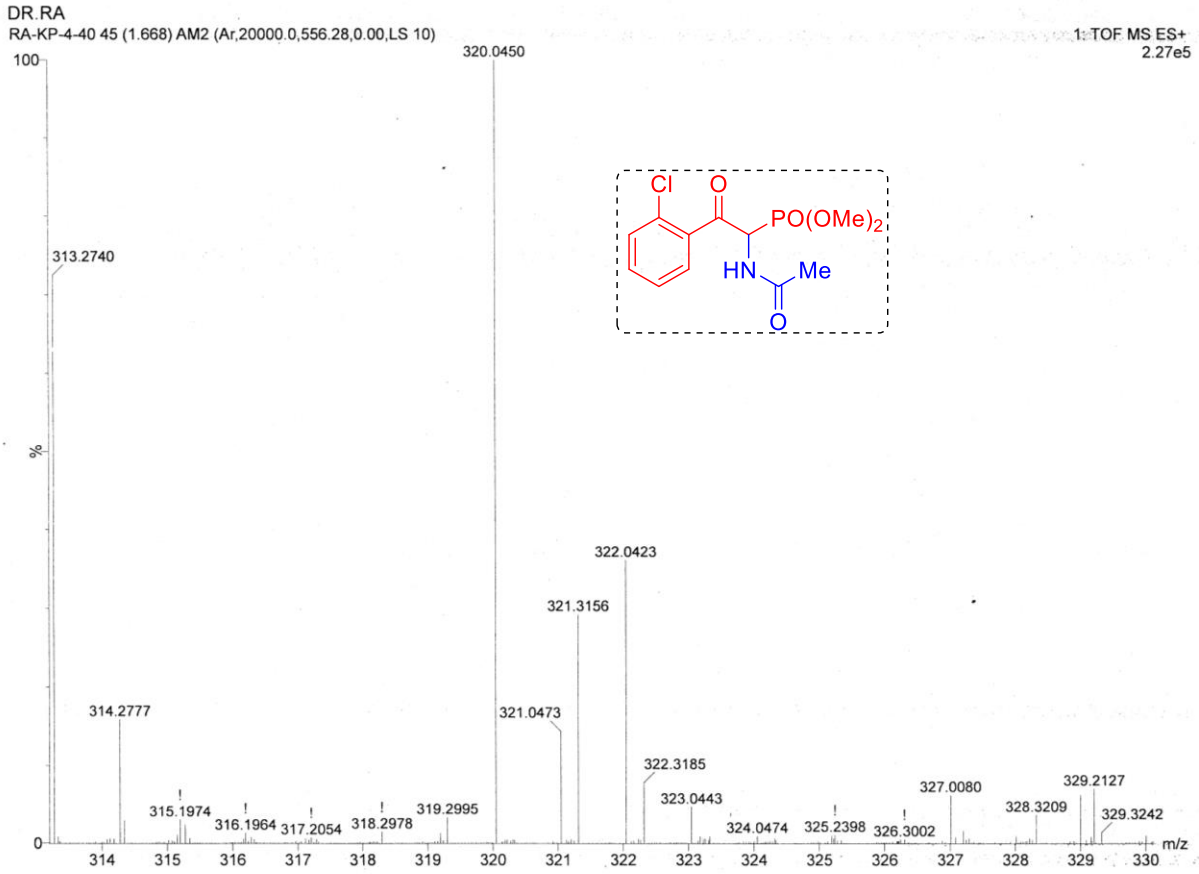
^{31}P NMR spectrum of compound 4b



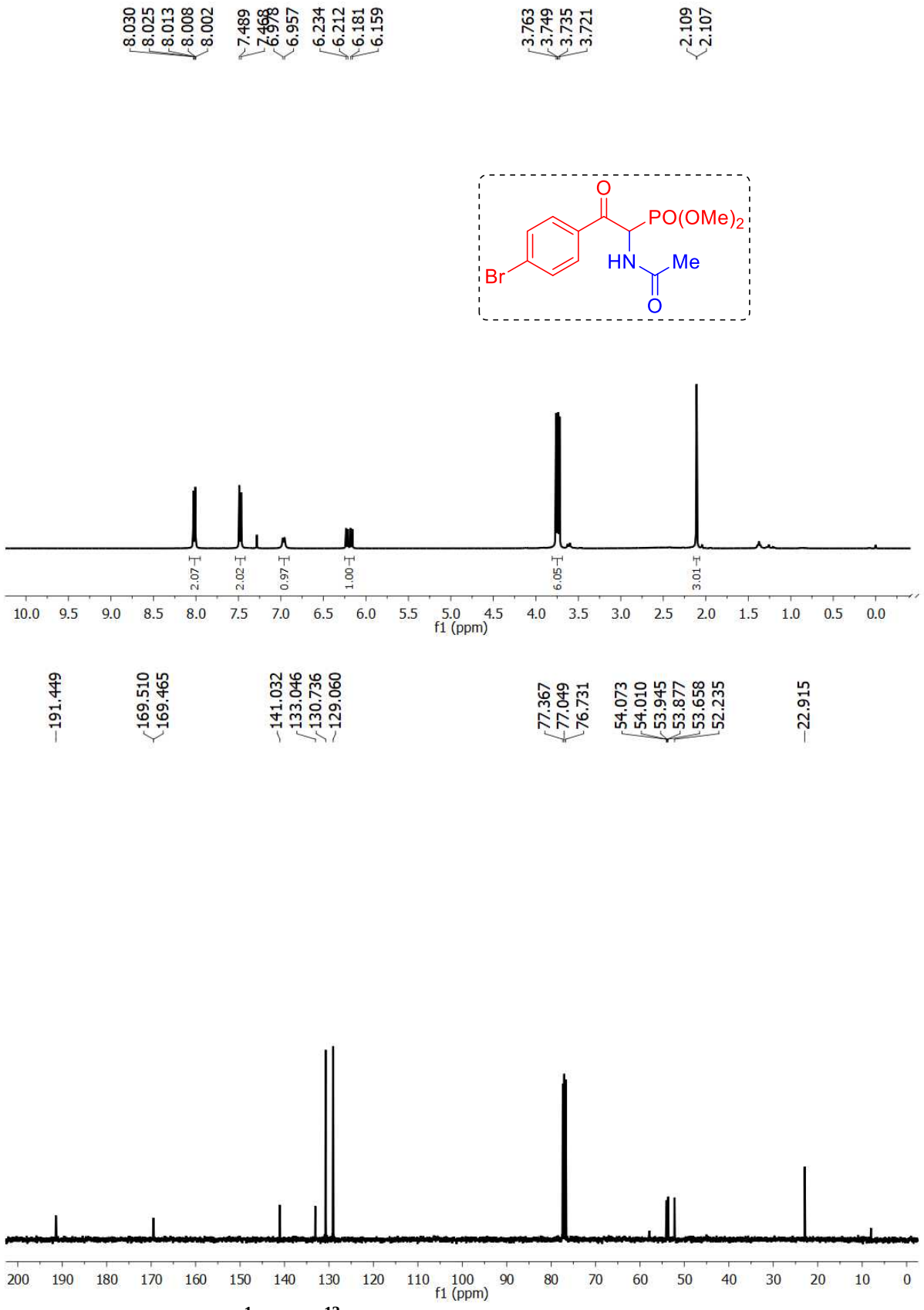
^{1}H and ^{13}C NMR spectra of compound 4c



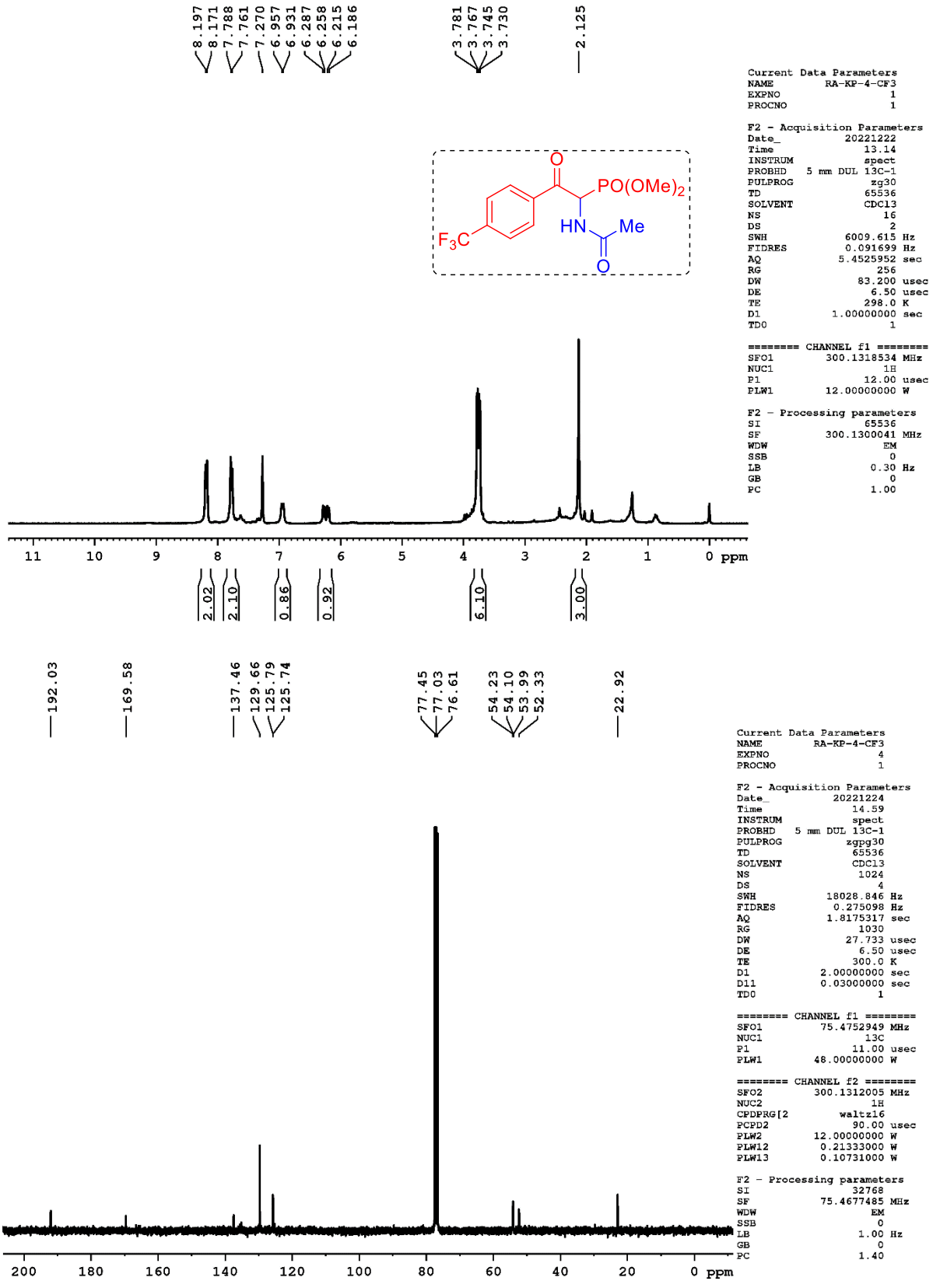
^{1}H and ^{13}C NMR spectra of compound 4d



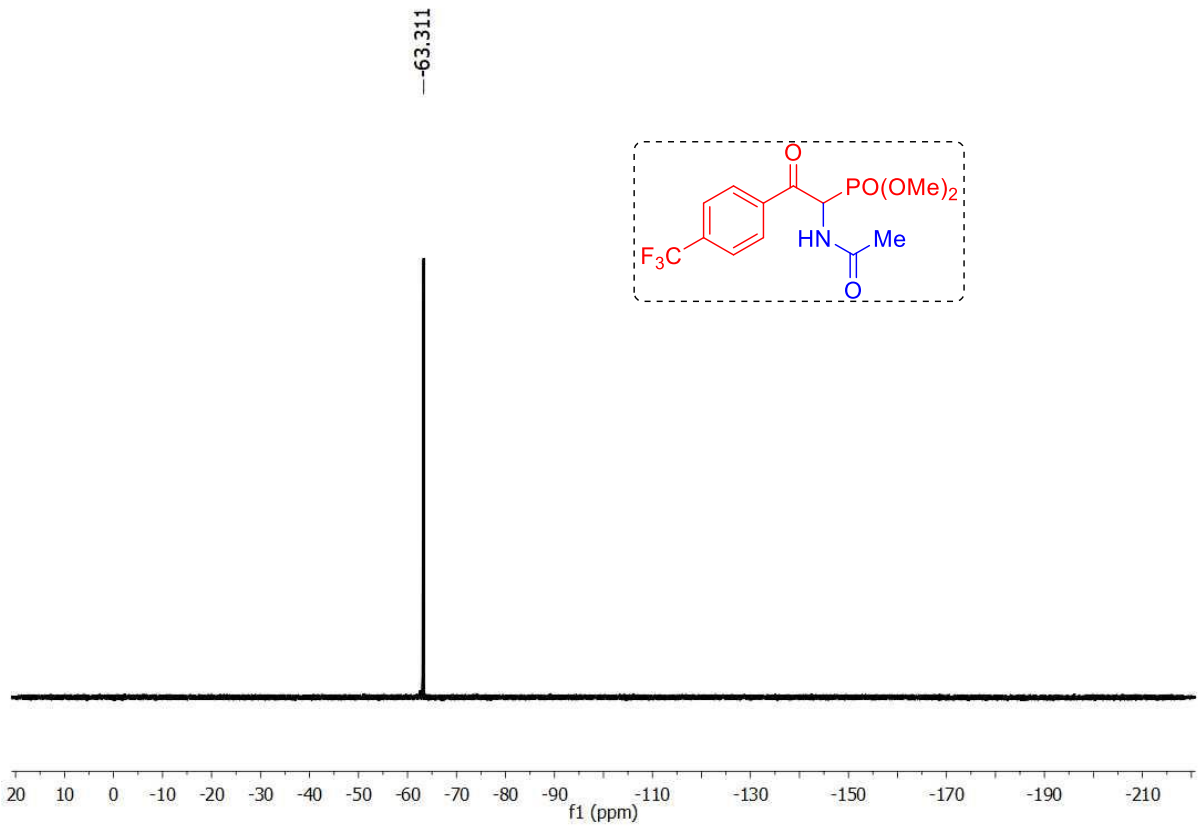
HRMS spectrum of compound 4d



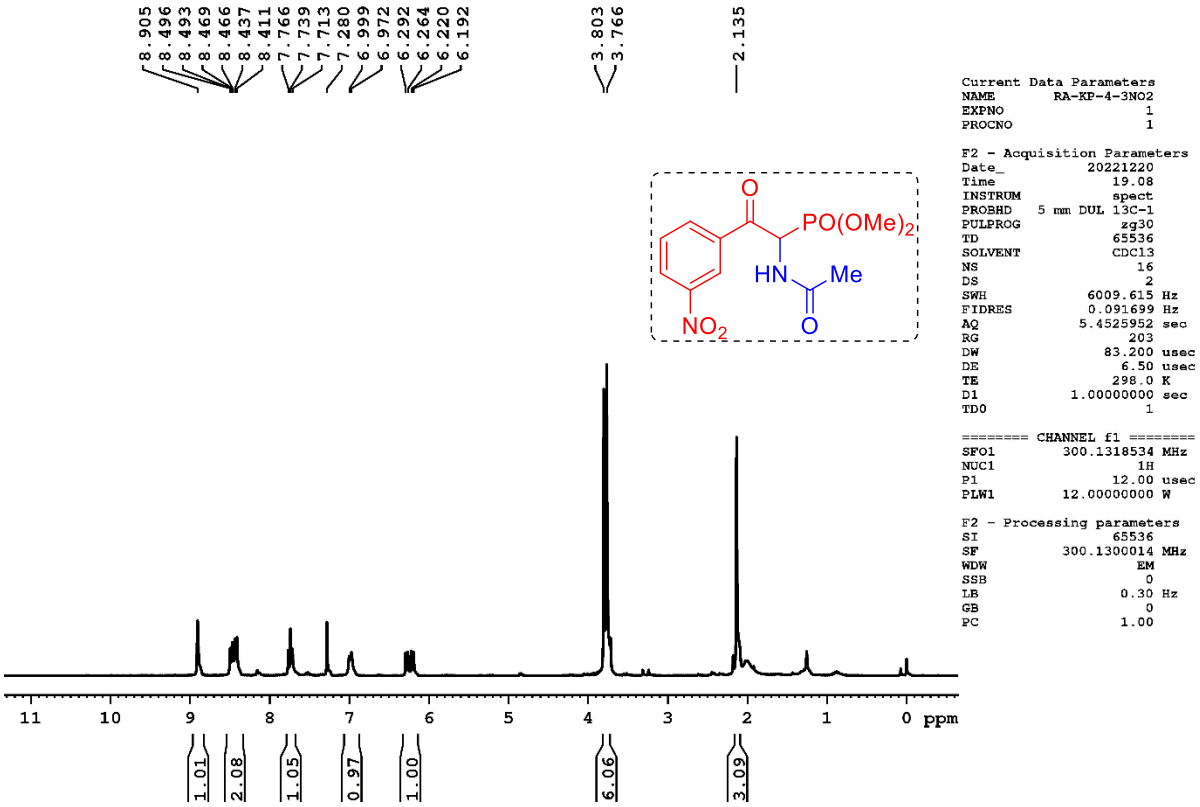
^{1}H and ^{13}C NMR spectra of compound 4e



^{1}H and ^{13}C NMR spectra of compound 4f



^{19}F NMR spectrum of compound 4f

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PROCNO                  1

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DS                     2
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FIDRES          0.091699 Hz
AQ              5.4525952 sec
RG                   203
DW                83.200 usec
DE                 6.50 usec
TE                298.0 K
D1             1.00000000 sec
TD0                    1

======== CHANNEL f1 ========
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NUC1                  1H
P1                 12.00 usec
PLW1          12.00000000 W

F2 - Processing parameters
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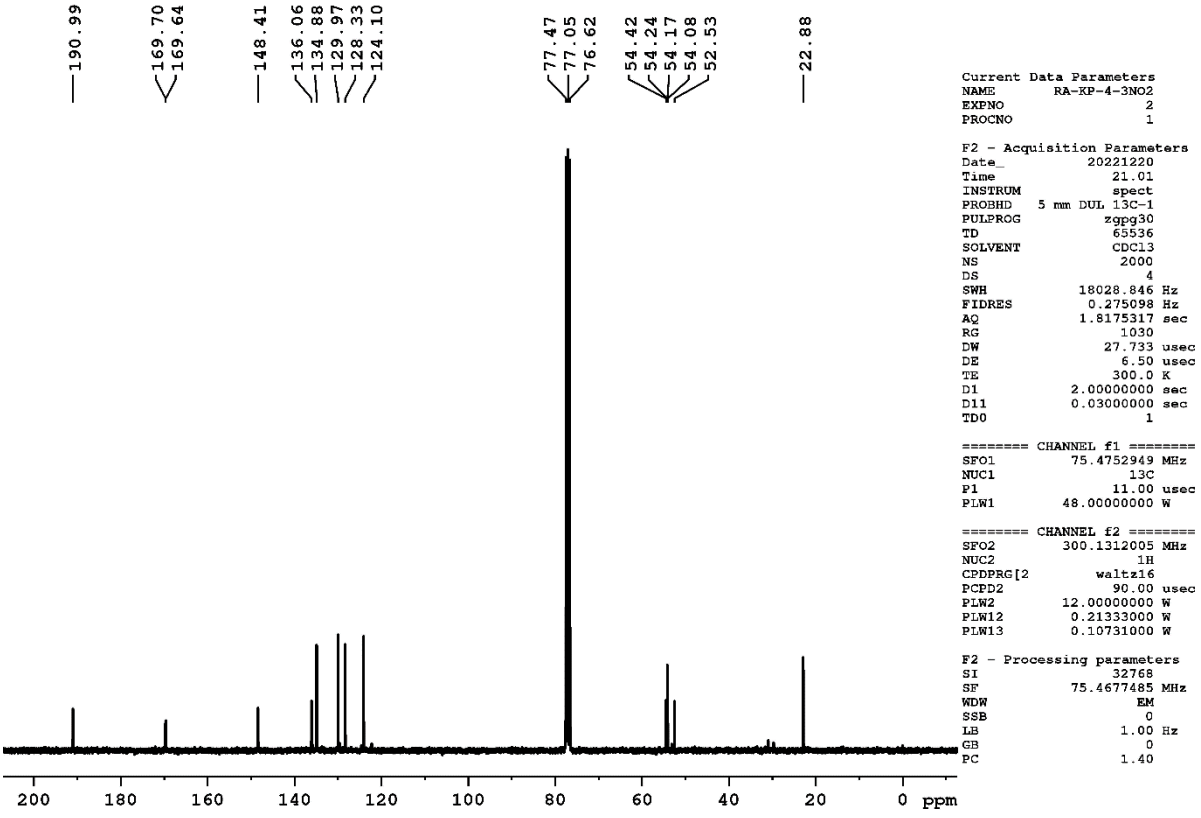


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PROCNO                  1

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NS                  2000
DS                     4
SWH            18028.846 Hz
FIDRES          0.275098 Hz
AQ              1.8175317 sec
RG                  1030
DW                27.733 usec
DE                 6.50 usec
TE                300.0 K
D1             2.00000000 sec
D11            0.03000000 sec
TD0                    1

======== CHANNEL f1 ========
SFO1           75.4752949 MHz
NUC1                  13C
P1                 11.00 usec
PLW1          48.00000000 W

======== CHANNEL f2 ========
SFO2          300.1312005 MHz
NUC2                  1H
CPDPRG[2          waltz16
PCPD2              90.00 usec
PLW2          12.00000000 W
PLW12          0.21333000 W
PLW13          0.10731000 W

F2 - Processing parameters
SI                 32768
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SSB                    0
LB                  1.00 Hz
GB                     0
PC                  1.40
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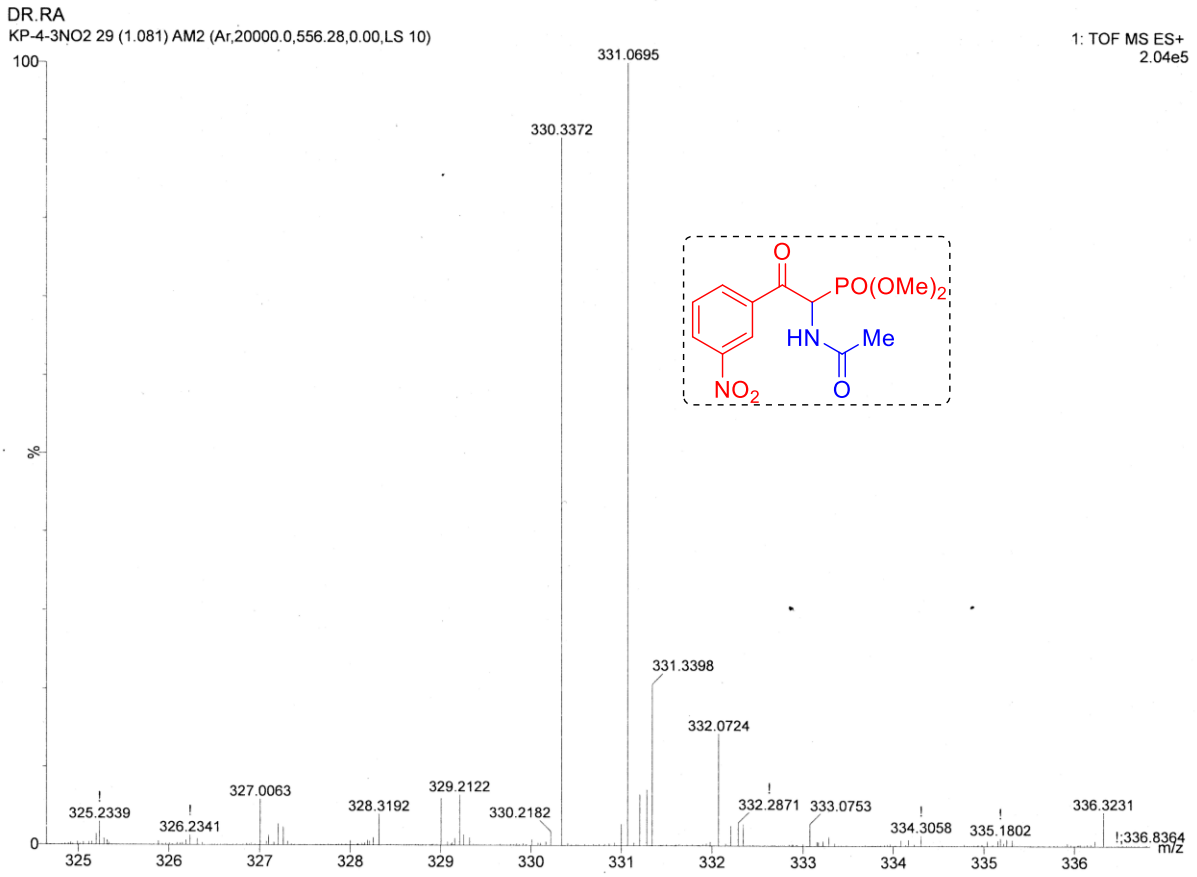
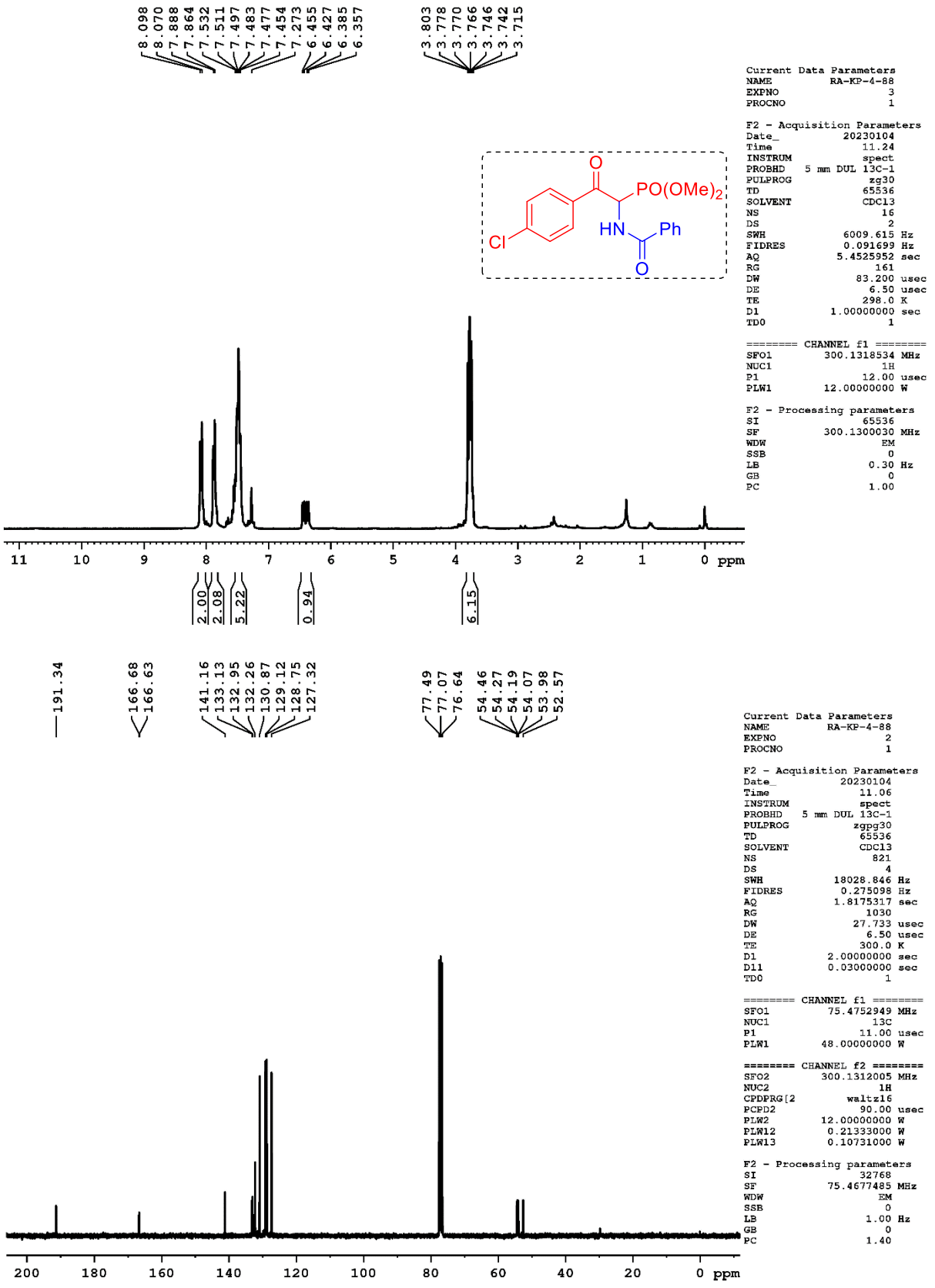
^{1}H and ^{13}C NMR spectra of compound 4g



HRMS spectrum of compound 4g



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PROCNO 1

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SWH 6009.615 Hz
FIDRES 0.091699 Hz
AQ 5.4525952 sec
RG 161
DW 83.200 usec
DE 6.50 usec
TE 298.0 K
D1 1.00000000 sec
TD0 1

======== CHANNEL f1 ========
SFO1 300.1318534 MHz
NUC1 1H
P1 12.00 usec
PLW1 12.00000000 W

F2 - Processing parameters
SI 65536
SF 300.1300030 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00

Current Data Parameters
NAME RA-KP-4-88
EXPNO 2
PROCNO 1

F2 - Acquisition Parameters
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Time 11.06
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PULPROG zgpg30
TD 65536
SOLVENT CDCl3
NS 821
DS 4
SWH 18028.846 Hz
FIDRES 0.275098 Hz
AQ 1.8175317 sec
RG 1030
DW 27.733 usec
DE 6.50 usec
TE 300.0 K
D1 2.00000000 sec
D11 0.03000000 sec
TD0 1

======== CHANNEL f1 ========
SFO1 75.4752949 MHz
NUC1 13C
P1 11.00 usec
PLW1 48.00000000 W

======== CHANNEL f2 ========
SFO2 300.1312005 MHz
NUC2 1H
CPDPRG[2 waltz16
PCPD2 90.00 usec
PLW2 12.00000000 W
PLW12 0.21333000 W
PLW13 0.10731000 W

F2 - Processing parameters
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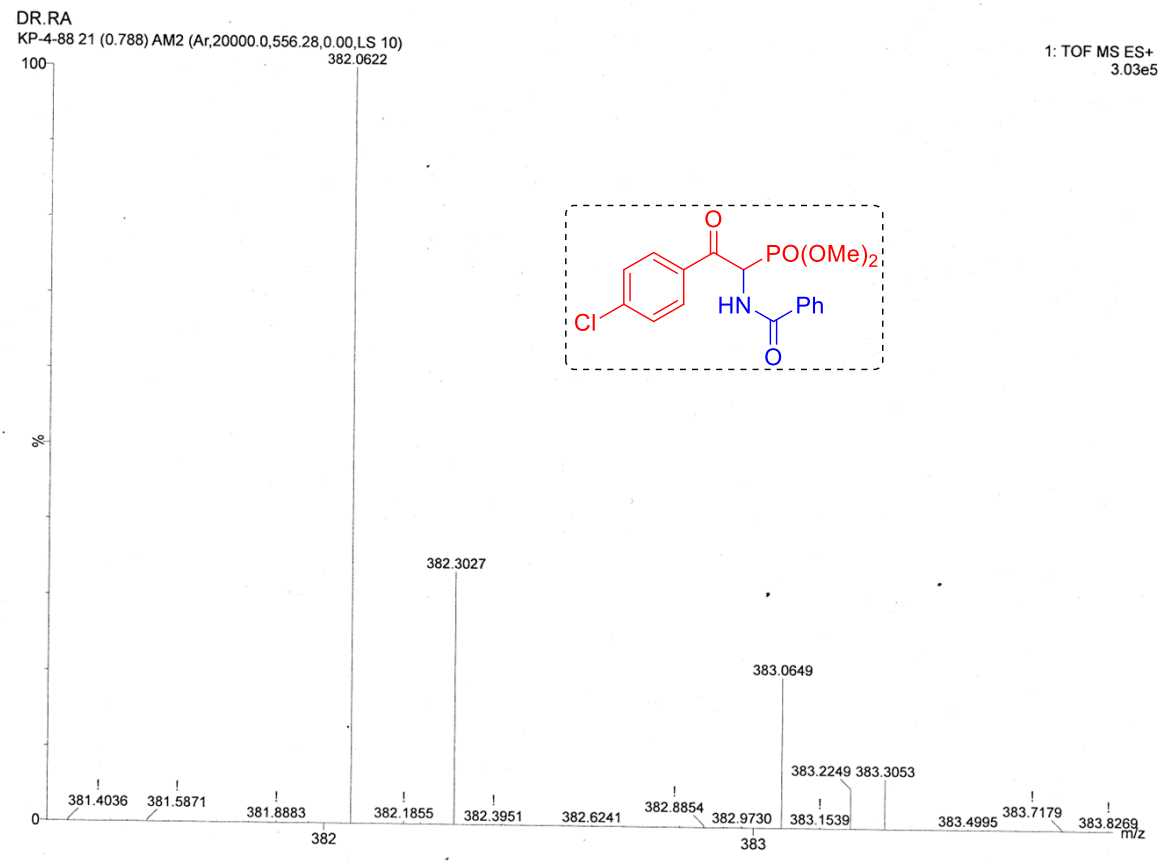
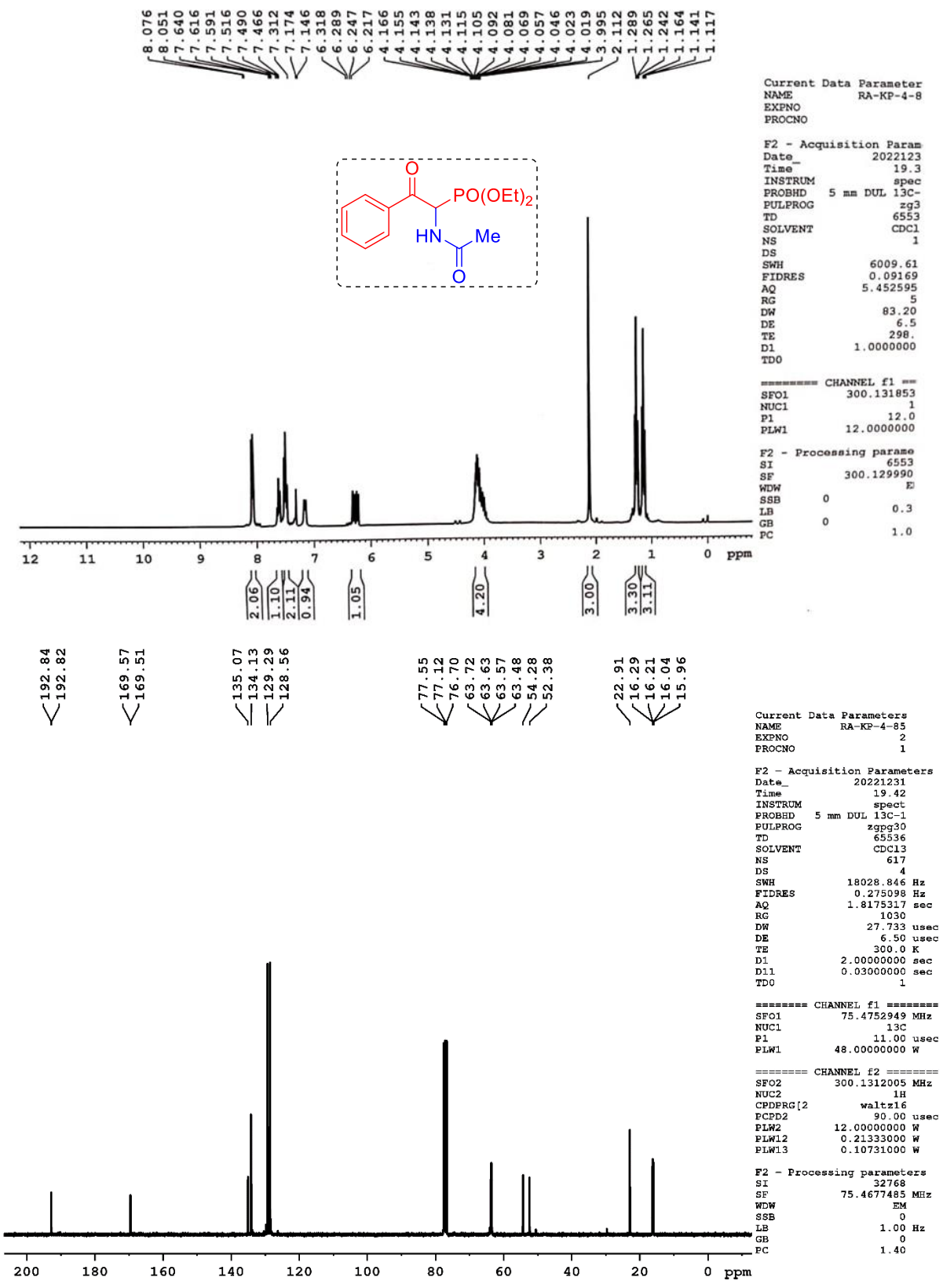
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 1.40

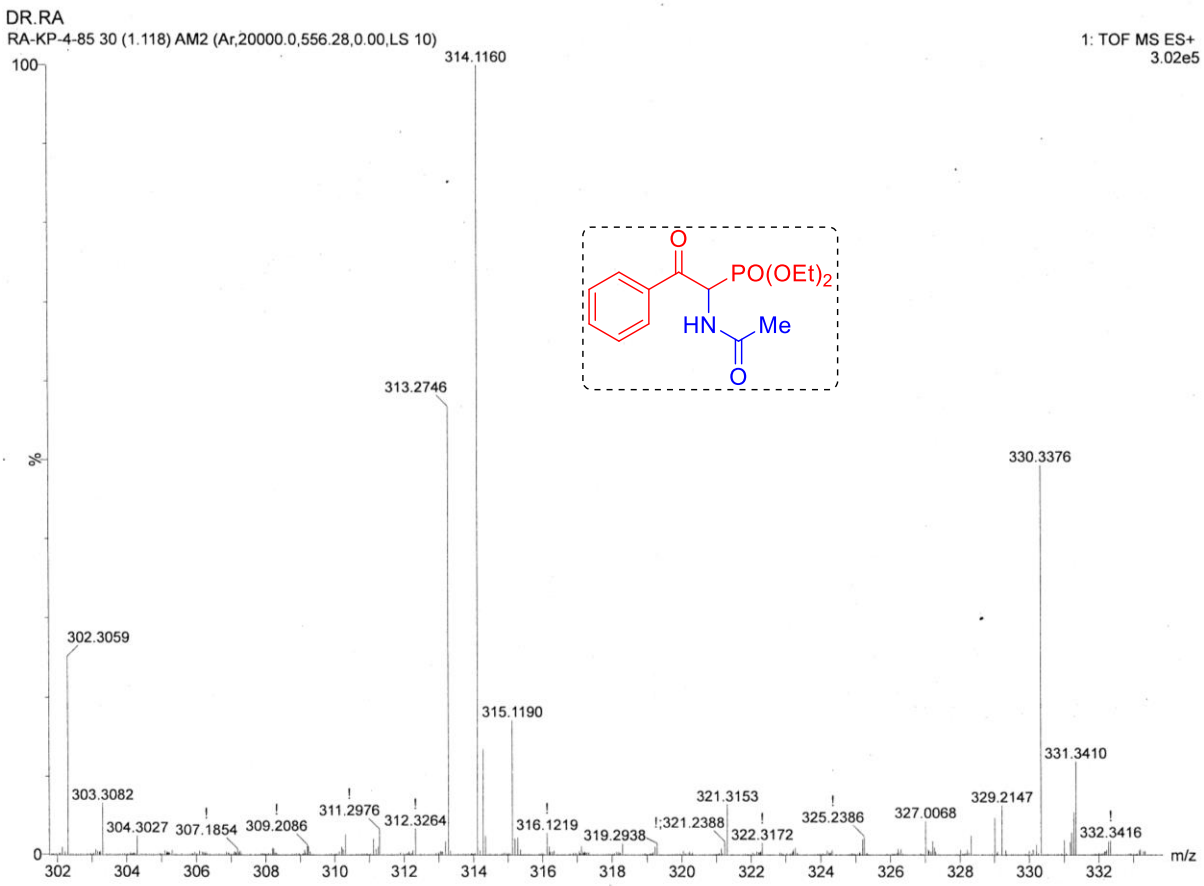
^{1}H and ^{13}C NMR spectra of compound 4h



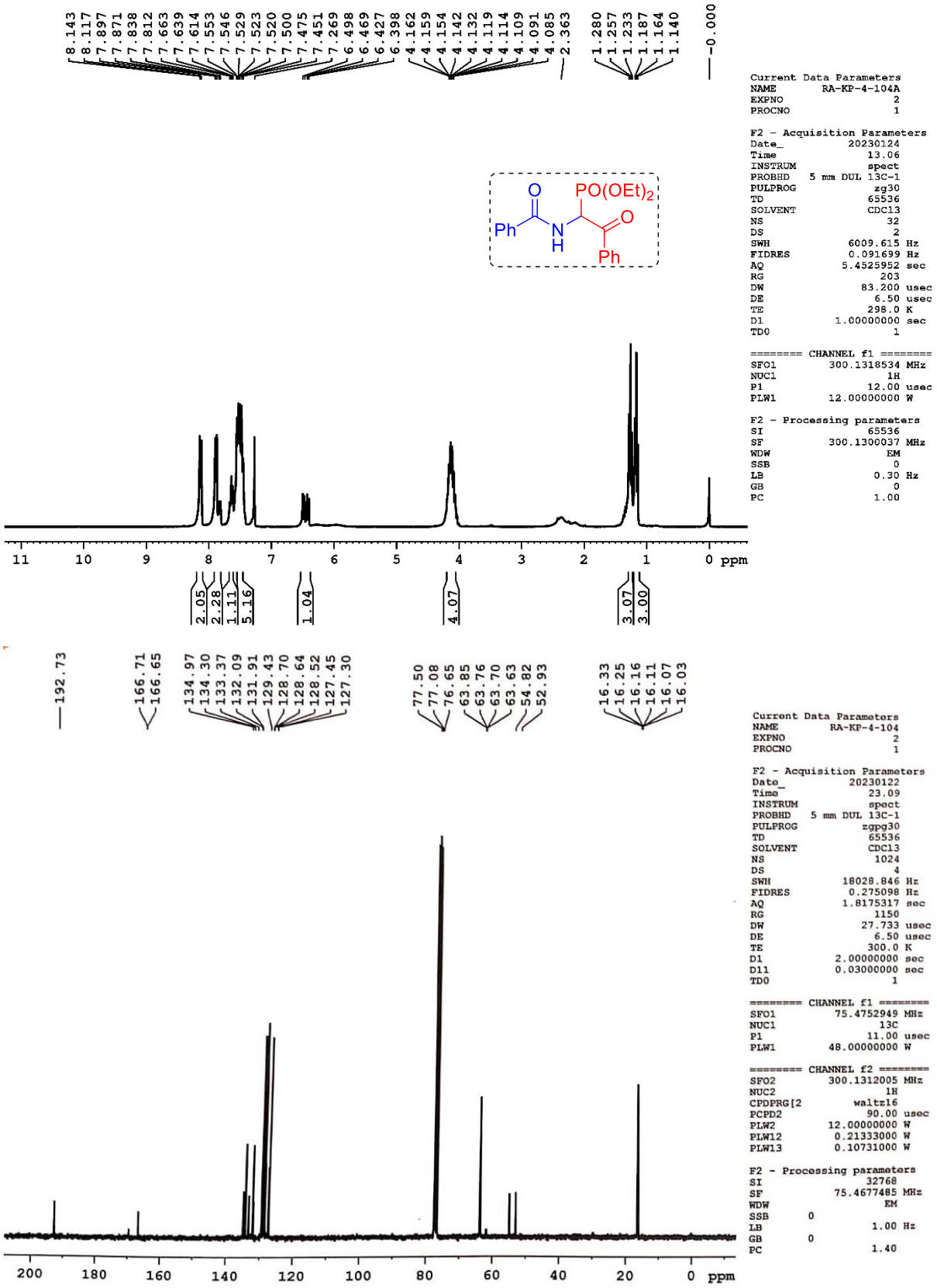
HRMS spectrum of compound 4h



^{1}H and ^{13}C NMR spectra of compound 4i



HRMS spectrum of compound 4i



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PROCNO 1

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SWH 6009.615 Hz
FIDRES 0.091699 Hz
AQ 5.4525952 sec
RG 203
DW 83.200 usec
DE 6.50 usec
TE 298.0 K
D1 1.00000000 sec
TD0 1

======== CHANNEL f1 ========
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NUC1 1H
P1 12.00 usec
PLW1 12.00000000 W

F2 - Processing parameters
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WDW EM
SSB 0
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PC 1.00

Current Data Parameters
NAME RA-KP-4-104
EXPNO 2
PROCNO 1

F2 - Acquisition Parameters
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Time 23.09
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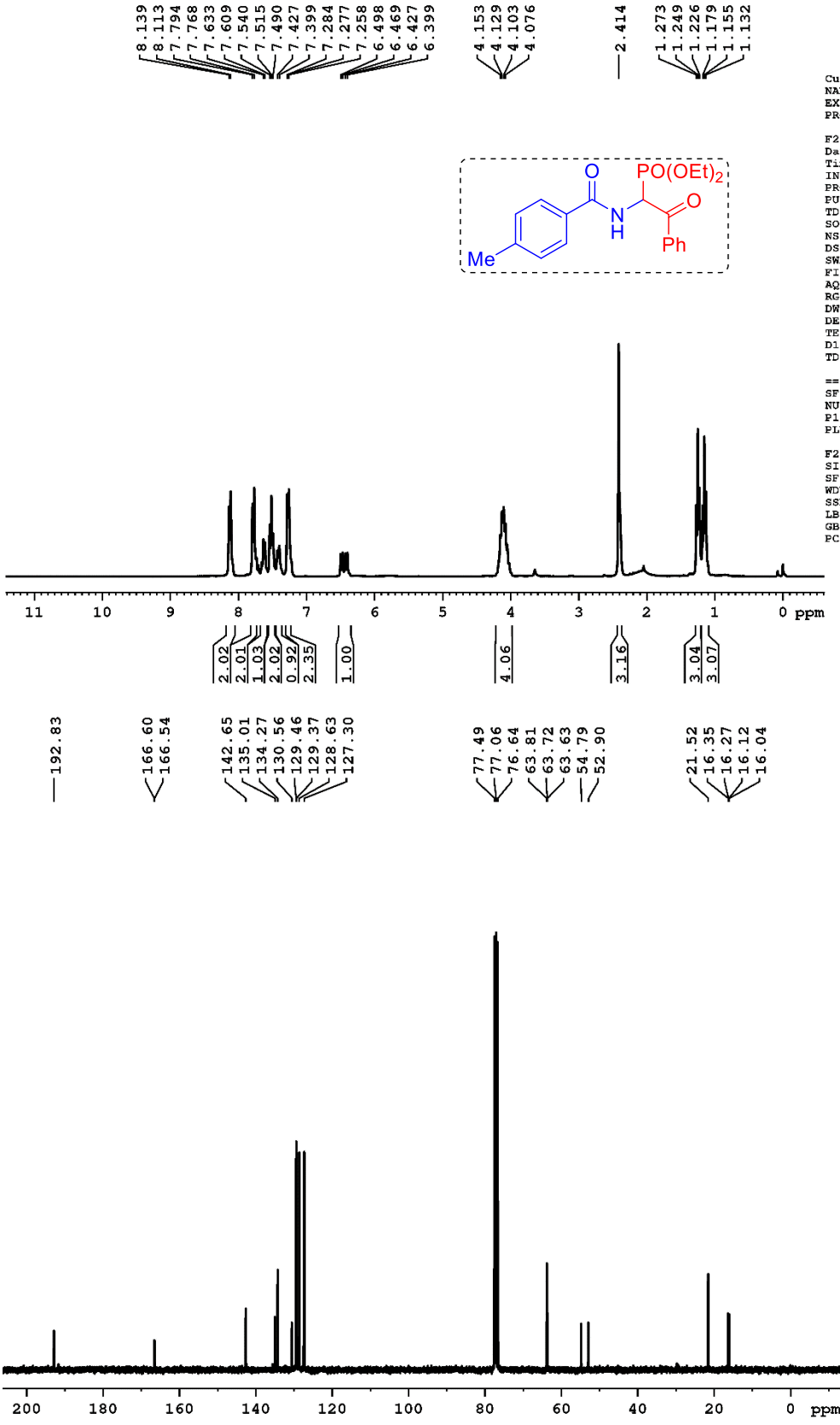
TD 65536
SOLVENT CDCl3
NS 1024
DS 4
SWH 18028.846 Hz
FIDRES 0.275098 Hz
AQ 1.8175317 sec
RG 1150
DW 27.733 usec
DE 6.50 usec
TE 300.0 K
D1 2.00000000 sec
D11 0.03000000 sec
TD0 1

======== CHANNEL f1 ========
SFO1 75.4752949 MHz
NUC1 13C
P1 11.00 usec
PLW1 48.00000000 W

======== CHANNEL f2 ========
SFO2 300.1312005 MHz
NUC2 1H
CPDPRG[2 waltz16
PCPD2 90.00 usec
PLW2 12.00000000 W
PLW12 0.21333000 W
PLW13 0.10731000 W

F2 - Processing parameters
SI 32768
SF 75.4677485 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 1.40

^{1}H and ^{13}C NMR spectra of compound 4j



Current Data Parameters
NAME RA-KP-4-108A
EXPNO 5
PROCNO 1

F2 - Acquisition Parameters
Date_ 20230208
Time 22.52
INSTRUM spect
PROBHD 5 mm DUL 13C-1
PULPROG zg30
TD 65536
SOLVENT CDCl3
NS 16
DS 2
SWH 6009.615 Hz
FIDRES 0.091699 Hz
AQ 5.4525952 sec
RG 144
DW 83.200 usec
DE 6.50 usec
TE 298.0 K
D1 1.00000000 sec
TD0 1

======== CHANNEL f1 ========
SFO1 300.1318534 MHz
NUC1 1H
P1 12.00 usec
PLW1 12.00000000 W

F2 - Processing parameters
SI 65536
SF 300.1300031 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00

Current Data Parameters
NAME RA-KP-4-108A
EXPNO 6
PROCNO 1

F2 - Acquisition Parameters
Date_ 20230208
Time 23.51
INSTRUM spect
PROBHD 5 mm DUL 13C-1
PULPROG zgpg30
TD 65536
SOLVENT CDCl3
NS 1024
DS 4
SWH 18028.846 Hz
FIDRES 0.275098 Hz
AQ 1.8175317 sec
RG 1030
DW 27.733 usec
DE 6.50 usec
TE 300.0 K
D1 2.00000000 sec
D11 0.03000000 sec
TD0 1

======== CHANNEL f1 ========
SFO1 75.4752949 MHz
NUC1 13C
P1 11.00 usec
PLW1 48.00000000 W

======== CHANNEL f2 ========
SFO2 300.1312005 MHz
NUC2 1H
CPDPRG[2 waltz16
PCPD2 90.00 usec
PLW2 12.00000000 W
PLW12 0.21333000 W
PLW13 0.10731000 W

F2 - Processing parameters
SI 32768
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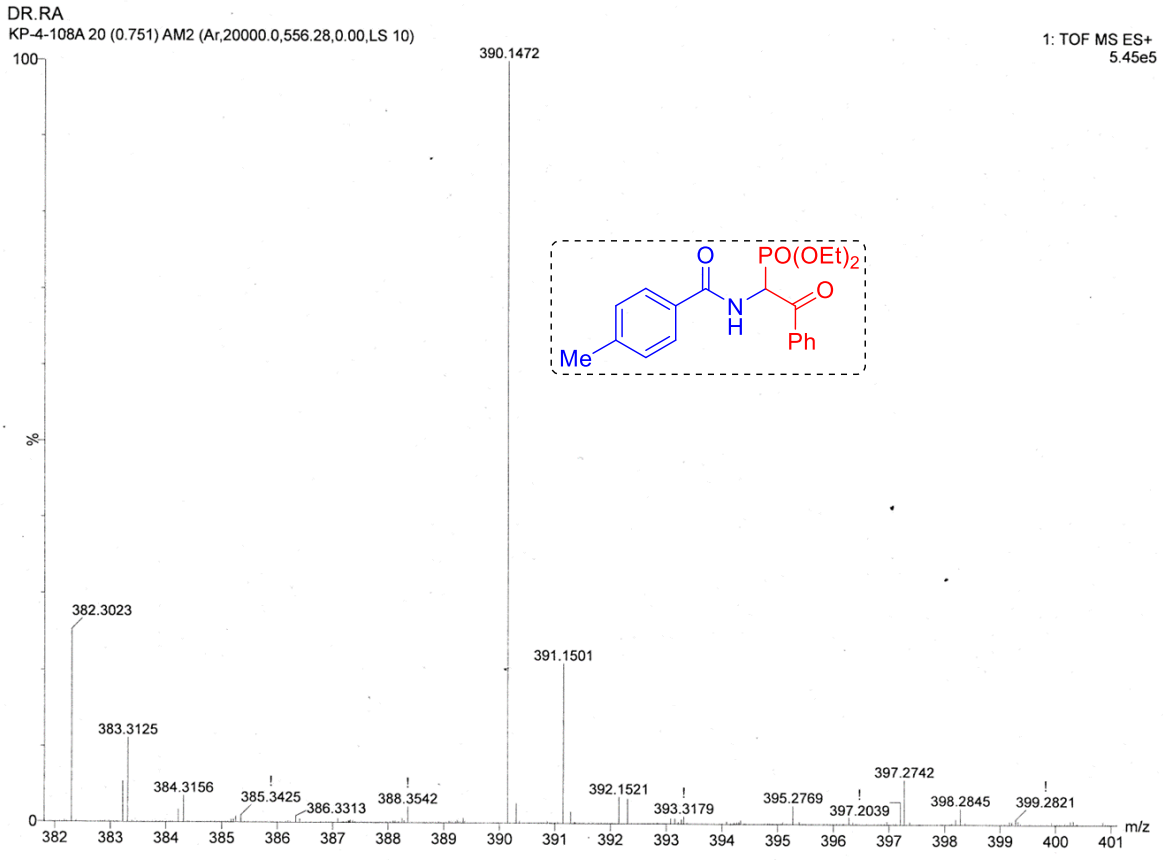
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 1.40

^{1}H and ^{13}C NMR spectra of compound 4k



HRMS spectrum of compound 4k