Supporting Information for

Chemoselective Synthesis of α-Amino-α-cyanophosphonates by Reductive Gem-Cyanation-Phosphonylation of Secondary Amides

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1. General Information

Unless otherwise stated, reactions were performed in oven-dried glassware under a nitrogen atmosphere using standard Schlenk techniques. Commercially available reagents were purchased from Enery, TCI, Acros, Sigma-Aldrich, J&K, Aladdin, Sinoreagent and used as received unless otherwise noted. Dichloromethane was distilled over calcium hydride under a nitrogen atmosphere. Silica gel (300-400 mesh) was used for flash column chromatography, eluting with ethyl acetate (EtOAc)/hexane mixture. Trifluoromethanesulfonic anhydride (Tf_2O) was distilled over phosphorous pentoxide and stored for no more than one week before redistilling.

Melting points were determined on a Büchi M560 Automatic Melting Point apparatus. Infrared spectra were measured with a Nicolet Avatar 330 FT-IR spectrometer using film KBr pellet techniques.). NMR spectra were recorded in $CDCl_3$ on a Bruker Av 400 or 500 spectrometer (400 MHz or 500 MHz for ^1H NMR, 101 MHz or 125 MHz for ^{13}C NMR and 202 MHz for ^{31}P NMR). Chemical shifts (δ) are reported in ppm and referenced to internal standard (Me_4Si, 0 ppm for ^1H NMR), solvent signal ($CDCl_3$, 77.0 ppm for ^{13}C NMR) and external standard (85% H_3PO_4, 0 ppm for ^{31}P NMR), respectively. HRMS spectra were recorded on an ESI-TOF mass spectrometer.

2. Preparation of Amides

General Procedure[1]

To a solution of the amine (5.00 mmol) and Et_3N (6.00 mmol) in DCM (0.10 M), was added the corresponding acyl chloride (5.00 mmol) dropwise at 0 °C. The resulting reaction mixture was allowed to warm to room temperature and stirred for 6 h. Saturated aqueous $NaHCO_3$ solution was then added and the biphasic system was separated. The aqueous phase was extracted with DCM (3 × 20 mL) and the organic phases were combined and dried over anhydrous $MgSO_4$, filtered and concentrated under reduced pressure. The residue was purified by flash column chromatography on silica gel (elution: hexane/EtOAc) to afford the desired amide.

***N*-Isopropylbenzamide (2a)**[2]

98% yield. All analytical data were in good accordance with reported data.

***N*-Isopropyl-4-methylbenzamide (2b)**[3]

95% yield. All analytical data were in good accordance with reported data.

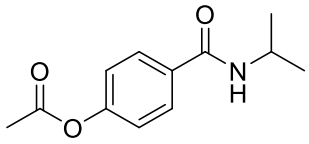
***N*-Isopropyl-2-methylbenzamide (2c)**[4]

92% yield. All analytical data were in good accordance with reported data.

***N*-Isopropyl-4-methoxybenzamide (2d)**[5]

92% yield. All analytical data were in good accordance with reported data.

4-(Isopropylcarbamoyl)phenyl acetate (2e)



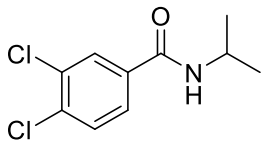
92% yield. White solid. MP: 141–142 °C. IR (film): 3314, 2976, 1760, 1632, 1538, 1191, 914, 749 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.87–7.69 (m, 2H), 7.20–7.01 (m, 2H), 6.37–6.09 (m, 1H), 4.33–4.16 (m, 1H), 2.34–2.27 (m, 3H), 1.28–1.18 (m, 6H) ppm; ^{13}C NMR (101 MHz, $CDCl_3$) δ 169.0, 165.8, 152.8, 132.5, 128.2, 121.5, 41.9,

22.6, 21.0 ppm; HRMS (ESI) calcd for $C_{12}H_{15}NO_3Na$ [M+Na^+]: 244.0939, found: 244.0945.

4-Chloro-*N*-isopropylbenzamide (2f)[6]

96% yield. All analytical data were in good accordance with reported data.

3,4-Dichloro-*N*-isopropylbenzamide (2g)

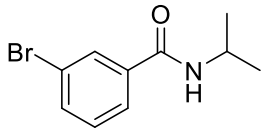


95% yield. White solid. MP: 128–129 °C. IR (film): 3283, 2975, 1630, 1544, 1453, 1365, 1131, 899, 705 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.88–7.80 (m, 1H), 7.62–7.54 (m, 1H), 7.49–7.43 (m, 1H), 6.30 (d, *J* = 7.6 Hz, 1H), 4.38–4.13 (m, 1H), 1.33–1.18 (m, 6H) ppm; ^{13}C NMR (101 MHz, $CDCl_3$) δ 164.5, 135.5, 134.7, 132.8, 130.4, 129.1, 126.1, 42.2, 22.6 ppm; HRMS (ESI) calcd for $C_{10}H_{11}Cl_2NONa$ [M+Na^+]: 254.0104, found: 254.0101.

2-Chloro-*N*-isopropylbenzamide (2h)[7]

97% yield. All analytical data were in good accordance with reported data.

3-Bromo-*N*-isopropylbenzamide (2i)



97% yield. White solid. MP: 83–84 °C. IR (film): 3293, 2973, 1634, 1540, 1276, 1173, 748, 706 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.95–7.84 (m, 1H), 7.81–7.62 (m, 1H), 7.62–7.47 (m, 1H), 7.29–7.20 (m, 1H), 6.43 (s, 1H), 4.40–3.91 (m, 1H), 1.27–1.21 (m, 6H) ppm; ^{13}C NMR (101 MHz, $CDCl_3$) δ 165.3, 136.9, 134.0, 130.0, 129.9, 125.4, 122.5, 42.0, 22.6 ppm; HRMS (ESI) calcd for $C_{10}H_{12}BrNONa$ [M+Na^+]: 263.9989, found: 263.9968.

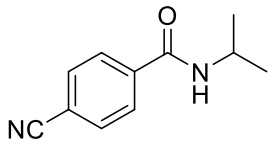
***N*-Isopropyl-4-(trifluoromethyl)benzamide (2j)**[8]

92% yield. All analytical data were in good accordance with reported data.

***N*-Isopropyl-4-nitrobenzamide (2k)**[9]

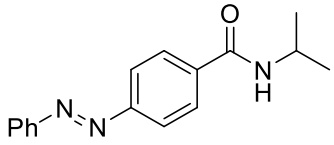
92% yield. All analytical data were in good accordance with reported data.

4-Cyano-*N*-isopropylbenzamide (2l)



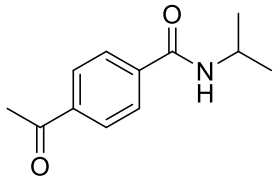
91% yield. White solid. MP: 153–154 °C. IR (film): 3308, 2974, 1633, 1537, 1296, 1160, 856, 684, 569 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.89–7.81 (m, 2H), 7.75–7.69 (m, 2H), 6.06 (s, 1H), 4.38–4.18 (m, 1H), 1.33–1.21 (m, 6H) ppm; ^{13}C NMR (101 MHz, $CDCl_3$) δ 164.8, 138.8, 132.1, 127.6, 117.9, 114.4, 42.2, 22.4 ppm; HRMS (ESI) calcd for $C_{11}H_{13}N_2O$ [M+H^+]: 189.1017, found: 189.1023.

(*E*)-*N*-Isopropyl-4-(phenyldiazenyl)benzamide (2m)



91% yield. White solid. MP: 193–194 °C. IR (film): 3300, 2972, 1629, 1534, 1290, 859, 691 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.99–7.86 (m, 6H), 7.58–7.43 (m, 3H), 6.17 (d, *J* = 7.5 Hz, 1H), 4.40–4.21 (m, 1H), 1.35–1.24 (m, 6H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ 166.0, 154.0, 152.5, 136.7, 131.5, 129.1, 127.8, 123.0, 122.8, 42.1, 22.8 ppm; HRMS (ESI) calcd for $C_{16}H_{17}N_3ONa$ [M+Na^+]: 290.1264, found: 290.1261.

4-Acetyl-*N*-isopropylbenzamide (2n)



92% yield. White solid. MP: 163–164 °C. IR (film): 3317, 2977, 1682, 1537, 1362, 1141, 852, 667 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.07–7.94 (m, 2H), 7.87–7.79 (m, 2H), 6.04 (s, 1H), 4.38–4.21 (m, 1H), 2.63 (s, 3H), 1.32–1.26 (m, 6H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ 197.4, 165.7, 139.0, 138.9, 128.5, 127.1, 42.2, 26.8, 22.8 ppm; HRMS (ESI) calcd for $C_{12}H_{15}NO_2Na$ [M+Na^+]: 228.0995, found: 228.0985.

Methyl 4-(isopropylcarbamoyl)benzoate (2o)[10]

93% yield. All analytical data were in good accordance with reported data.

***N*-Isopropyl-2-naphthamide (2p)**[6]

92% yield. All analytical data were in good accordance with reported data.

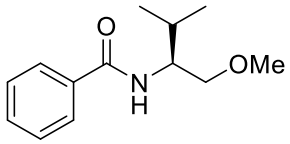
***N*-Cyclohexylbenzamide (2q)**[2]

90% yield. All analytical data were in good accordance with reported data.

***N*-Cyclopropylbenzamide (2r)**[11]

90% yield. All analytical data were in good accordance with reported data.

(*S*)-*N*-(1-Methoxy-3-methylbutan-2-yl)benzamide (2s)



Following the General Procedure, (*S*)-*N*-(1-hydroxy-3-methylbutan-2-yl)benzamide was prepared, which without purification was subjected to methylation:[12] To the solution of the above amide (5.00 mmol) in THF (0.10 M) was added NaH (60% dispersion in mineral oil, 600 mg, 15.0 mmol) at 0 °C and stirred for 30 min. Then MeI (93.3 μL, 15.0 mmol) was added dropwise and the reaction mixture was allowed warm to room temperature and stirred for 10 h. Saturated aqueous NH_4Cl solution was then added and the aqueous phase was extracted with EtOAc (3 × 20 mL). The organic phases were combined and dried over anhydrous $MgSO_4$, filtered and concentrated under reduced pressure. The residue was purified by flash column chromatography on silica gel (elution: hexane/EtOAc = 1:2) to afford the desired amide. 85% yield for 2 steps. White solid. MP: 76–77 °C. IR (film): 3307, 2921, 1653, 1540, 1322, 1114, 694 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.82–7.75 (m, 2H), 7.52–7.38 (m, 3H), 6.46 (d, *J* = 9.3 Hz, 1H), 4.13–3.99 (m, 1H), 3.65–3.54 (m, 1H), 3.50–3.40 (m, 1H), 3.34 (s, 3H), 2.08–1.88 (m, 1H), 1.04–0.93 (m, 6H) ppm; ^{13}C NMR (101 MHz, $CDCl_3$) δ 167.1, 134.8, 131.2, 128.4, 126.8, 72.5, 59.0, 54.4, 29.6, 19.5, 19.1 ppm; HRMS (ESI) calcd for $C_{13}H_{19}NO_2Na$ [M+Na^+]: 244.1308, found: 244.1311.

***N*-Ethylbenzamide (2t)**[13]

90% yield. All analytical data were in good accordance with reported data.

***N*-(3-Methoxypropyl)benzamide (2u)**[14]

Following the General Procedure, *N*-(3-hydroxypropyl)benzamide was prepared,

which without purification was subjected to a methylation:[12] To the solution of the above amide (5.00 mmol) in THF (0.10 M) was added NaH (60% dispersion in mineral oil, 600 mg, 15.0 mmol) at 0 °C and stirred for 30 min. Then MeI (93.3 μL, 15.0 mmol) was added dropwise and the reaction mixture was allowed warm to room temperature and stirred for 10 h. Saturated aqueous NH_4Cl solution was then added and the aqueous phase was extracted with EtOAc (3 × 20 mL). The organic phases were combined and dried over anhydrous $MgSO_4$, filtered and concentrated under reduced pressure. The residue was purified by flash column chromatography on silica gel (elution: hexane/EtOAc = 1:2) to afford the desired amide. 82% yield for 2 steps. All analytical data were in good accordance with reported data.

Methyl 3-benzamidopropanoate (2v)[15]

90% yield. All analytical data were in good accordance with reported data.

***N*-(2-Chloroethyl)benzamide (2w)**[16]

89% yield. All analytical data were in good accordance with reported data.

***N*-(2-Bromoethyl)benzamide (2x)**[17]

93% yield. All analytical data were in good accordance with reported data.

***N*-(4-Bromobutyl)benzamide (2y)**[18]

Following the General Procedure, *N*-(4-hydroxybutyl)benzamide was prepared, which without purification was subjected to bromination:[19] To the solution of the above amide (5.00 mmol) and carbon tetrabromide (1.99 g, 6.00 mmol) in DCM (0.20 M) was added triphenylphosphine (1.83 g, 6.00 mmol) over 30 minutes at 0 °C. The reaction was allowed to warm to room temperature and subsequently heated to 50 ºC and stirred for 6 hours. The reaction was cooled to room temperature, diluted with ethyl acetate, and washed with saturated $Na_2S_2O_3$. The aqueous phase was extracted with EtOAc (3 × 20 mL). The organic phases were combined and dried over anhydrous $MgSO_4$, filtered and concentrated under reduced pressure. The residue was purified by flash column chromatography on silica gel (elution: hexane/EtOAc = 1:2) to afford the desired amide. 80% yield for 2 steps. All analytical data were in good accordance with reported data.

***N*-Benzylbenzamide (2z)**[14]

90% yield. All analytical data were in good accordance with reported data.

***N*-Allylbenzamide (2aa)**[20]

90% yield. All analytical data were in good accordance with reported data.

***N*-(Tert-butyl)benzamide (2ab)**[21]

90% yield. All analytical data were in good accordance with reported data.

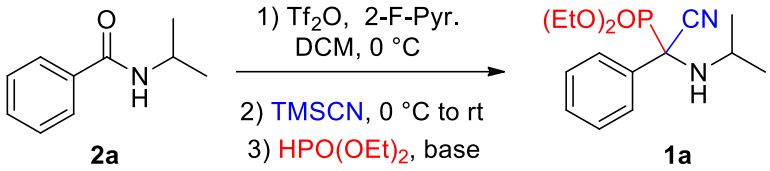
***N*-Phenylbenzamide (2ac)**[22]

92% yield. All analytical data were in good accordance with reported data.

***N*-Isopropylpivalamide (2ad)**[23]

91% yield. All analytical data were in good accordance with reported data.

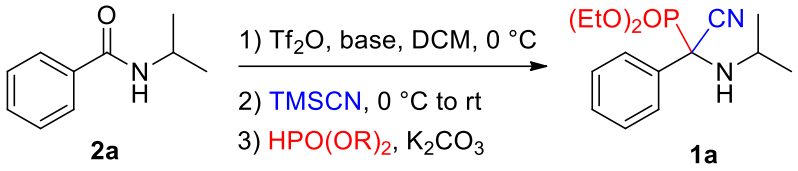
3. Table S1. Reaction Optimization on Reductive Geminal Cyanation/Phosphonylation[a]



Entry	TMSCN (equiv)	Phosphite (equiv)	Base	Temp (°C)	Yield (%)[b]
1	1.2	2.0	None	0 to rt	81 (73[c])
2	1.0	2.0	None	rt	47
3	1.2	2.0	None	rt	81
4	1.5	2.0	None	rt	78
5	1.2	2.0	None	45	55
6	1.2	2.0	NEt_3 (2.0 equiv)	rt	40
7	1.2	2.0	*i*Pr_2NEt (2.0 equiv)	rt	70
8	1.2	2.0	DABCO (2.0 equiv)	rt	81
9	1.2	2.0	DBU (2.0 equiv)	rt	90
10	1.2	2.0	NaOH (2.0 equiv)	rt	89
11	1.2	2.0	K_3PO_4 (2.0 equiv)	rt	85
12	1.2	2.0	Li_2CO_3 (2.0 equiv)	rt	84
13	1.2	2.0	Cs_2CO_3 (2.0 equiv)	rt	89
14	1.2	2.0	K_2CO_3 (2.0 equiv)	rt	96 (90[c])
15	1.2	2.0	Na_2CO_3 (2.0 equiv)	rt	96 (89[c])
16	1.2	1.5	K_2CO_3 (2.0 equiv)	rt	96 (92[c])
17	1.2	1.3	K_2CO_3 (2.0 equiv)	rt	95 (92[c])
18	1.2	1.3	Na_2CO_3 (2.0 equiv)	rt	93(85[c])
19	1.2	1.1	K_2CO_3 (2.0 equiv)	rt	94 (88[c])
20	1.2	1.3	K_2CO_3 (1.8 equiv)	rt	95 (90[c])
21	1.2	1.3	K_2CO_3 (1.5 equiv)	rt	93 (88[c])

[a] Reaction conditions: amide **2a** (0.500 mmol), Tf_2O (0.550 mmol), 2-F-Pyr. (0.600 mmol), CH_2Cl_2 (0.20 M), 0 °C, 10 min.; TMSCN (0.600 mmol), 0 °C to rt, 3 h; $HPO(OEt)_2$, base, 10 h. [b] Determined by ^1H NMR with 1,3,5-trimethoxybenzene as internal standard.

4. Table S2. Base Optimization in Amide Activation[a]



Entry	Base	Yield (%)[b]
1	Et_3N	59
2	Pyridine	76
3	2-Cl-Pyr.[c]	78
4	DTBMP[d]	45
5	2-F-Pyr.[e]	95

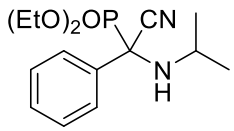
[a] Reaction conditions: amide **2a** (0.500 mmol), Tf_2O (0.550 mmol), base (0.600 mmol), CH_2Cl_2 (0.20 M), 0 °C, 10 min.; TMSCN (0.600 mmol), 0 °C to rt, 3 h; $HPO(OEt)_2$, K_2CO_3 (1.00 mmol), 10 h. [b] Determined by ^1H NMR with 1,3,5-trimethoxybenzene as internal standard. [c]Abbreviation for 2-chloropyridine. [d]Abbreviation for 2,6-di-*tert*-butyl-4-methyl pyridine. [e]Abbreviation for 2-fluoropyridine.

5. Transformation of Amides into α-Amino-α-cyanophosphonates

General Procedure

Trifluoromethanesulfonic anhydride (Tf_2O, 100 μL, 0.550 mmol) was added dropwise to a cooled solution of amides (0.500 mmol) and 2-fluoropyridine (50.0 μL, 0.600 mmol) in dichloromethane (0.20 M) at 0 °C. After the mixture was stirred for 10 min, TMSCN (75.0 μL, 0.600 mmol) was added dropwise at 0 °C. The resulting mixture was warmed to rt and stirred for 3 h. $HPO(OR)_2$ (0.650 mmol) and K_2CO_3 (138 mg, 1.00 mmol) were then added to the above mixture and stirred for 10 h. The reaction was quenched with saturated aqueous $NaHCO_3$ solution (1 mL) at room temperature. The organic layer was separated and the aqueous phase was extracted with dichloromethane (3 × 10 mL). The combined organic layers were washed with brine (3 × 3 mL), dried over anhydrous $MgSO_4$, filtered and concentrated under reduced pressure. The residue was purified by flash column chromatography on silica gel (elution: hexane/EtOAc) to afford the desired α-amino-α-cyanophosphonates.

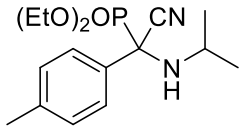
Diethyl (cyano(isopropylamino)(phenyl)methyl)phosphonate (1a)



Following the general procedure , the reaction of amide **2a** (81.6 mg, 0.500 mmol) with TMSCN (75.0 μL, 0.600 mmol) and $HPO(OEt)_2$ (83.0 μL, 0.650 mmol) afforded the α-amino-α-cyanophosphonate **1a** (143 mg, yield: 92%) after flash column chromatography on silica gel (elution with EtOAc/hexane = 1:2) as a pale yellow oil. IR (film): 3295, 2978, 2373, 1253, 1021, 700, 581 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.76–7.73 (m, 2H), 7.46–7.34 (m, 3H), 4.31–4.13 (m, 2H), 4.05–3.92 (m, 1H), 3.90–3.79 (m, 1H), 3.01–2.92 (m, 1H), 2.10 (br s, 1H), 1.36 (t, *J* = 7.1 Hz, 3H), 1.22 (d, *J* = 6.4 Hz, 3H), 1.16 (t, *J* = 7.1 Hz, 3H), 0.93 (d, *J* = 6.5 Hz, 3H) ppm; ^{13}C NMR

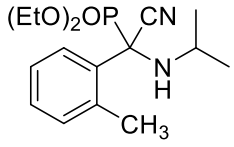
(125 MHz, $CDCl_3$) δ 132.6 (d, $J_{C\text{-}P}$ = 8.2 Hz), 129.0 (d, $J_{C\text{-}P}$ = 3.2 Hz), 128.3 (d, $J_{C\text{-}P}$ = 2.7 Hz), 127.9 (d, $J_{C\text{-}P}$ = 4.7 Hz), 118.1 (d, $J_{C\text{-}P}$ = 4.9 Hz), 65.2 (d, $J_{C\text{-}P}$ = 7.4 Hz), 62.7 (d, $J_{C\text{-}P}$ = 154.8 Hz), 46.9 (d, $J_{C\text{-}P}$ = 13.2 Hz), 24.7, 23.7, 16.2 (d, $J_{C\text{-}P}$ = 5.6 Hz) 16.1 (d, $J_{C\text{-}P}$ = 5.7 Hz) ppm; ^{31}P NMR (202 MHz, $CDCl_3$) δ 14.5 ppm; HRMS (ESI) calcd for $C_{15}H_{23}N_2O_3PNa$ [M+Na^+]: 333.1339, found: 333.1340.

Diethyl (cyano(isopropylamino)(*p*-tolyl)methyl)phosphonate (1b)



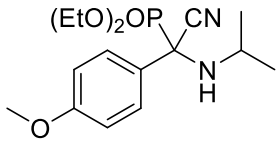
Following the general procedure , the reaction of amide **2b** (88.5 mg, 0.500 mmol) with TMSCN (75.0 μL, 0.600 mmol) and $HPO(OEt)_2$ (83.0 μL, 0.650 mmol) afforded the α-amino-α-cyanophosphonate **1b** (146 mg, yield: 90%) after flash column chromatography on silica gel (elution with EtOAc/hexane = 1:2) as a pale yellow oil. IR (film): 3324, 2968, 2358, 1603, 1255, 1152, 1021, 816, 578 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.63–7.52 (m, 2H), 7.24–7.18 (m, 2H), 4.31–4.15 (m, 2H), 4.05–3.80 (m, 1H), 3.02–2.89 (m, 1H), 2.37 (s, 3H), 2.16–2.00 (m, 1H), 1.36 (t, *J* = 7.1 Hz, 3H), 1.21 (d, *J* = 6.3 Hz, 3H), 1.17 (t, *J* = 7.1 Hz, 3H), 0.93 (d, *J* = 6.4 Hz, 3H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ 139.0 (d, $J_{C\text{-}P}$ = 3.2 Hz), 129.4 (d, $J_{C\text{-}P}$ = 8.3 Hz), 129.1 (d, $J_{C\text{-}P}$ = 2.8 Hz), 127.8 (d, $J_{C\text{-}P}$ = 4.7 Hz), 118.3 (d, $J_{C\text{-}P}$ = 4.6 Hz), 65.3 (d, $J_{C\text{-}P}$ = 7.2 Hz), 65.2 (d, $J_{C\text{-}P}$ = 7.7 Hz), 62.4 (d, $J_{C\text{-}P}$ = 156.1 Hz), 46.8 (d, $J_{C\text{-}P}$ = 13.4 Hz), 24.8, 23.6, 21.1, 16.3 (d, $J_{C\text{-}P}$ = 5.7 Hz), 16.1 (d, $J_{C\text{-}P}$ = 5.7 Hz) ppm; ^{31}P NMR (202 MHz, $CDCl_3$) δ 14.7 ppm; HRMS (ESI) calcd for $C_{16}H_{25}N_2O_3PNa$ [M+Na^+]: 347.1495, found: 347.1497.

Diethyl (cyano(isopropylamino)(o-tolyl)methyl)phosphonate (1c)



Following the general procedure, the reaction of amide **2c** (88.5 mg, 0.500 mmol) with TMSCN (75.0 μL, 0.600 mmol) and $HPO(OEt)_2$ (83.0 μL, 0.650 mmol) afforded the α-amino-α-cyanophosphonate **1c** (115 mg, yield: 71%) after flash column chromatography on silica gel (elution with EtOAc/hexane = 1:2) as a pale yellow oil. IR (film): 3310, 2967, 2257, 1647, 1429, 1279, 1023, 738, 582 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.85–7.80 (m, 1H), 7.28–7.16 (m, 3H), 4.24–4.09 (m, 2H), 4.04–3.94 (m, 1H), 3.91–3.80 (m, 1H), 3.14–3.03 (m, 1H), 2.75 (d, J_{P-H} = 1.8 Hz, 3H), 2.06 (s, 1H), 1.35 (t, J = 7.1 Hz, 3H), 1.24 (d, J = 6.3 Hz, 3H), 1.18 (t, J = 7.1 Hz, 3H), 0.96 (d, J = 6.4 Hz, 3H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ 138.3 (d, J_{C-P} = 4.5 Hz), 133.0 (d, J_{C-P} = 3.1 Hz), 129.6 (d, J_{C-P} = 4.6 Hz), 128.8 (d, J_{C-P} = 3.2 Hz), 125.7 (d, J_{C-P} = 3.0 Hz), 118.5 (d, J_{C-P} = 5.2 Hz), 65.1 (d, J_{C-P} = 6.5 Hz), 65.1 (d, J_{C-P} = 7.0 Hz), 62.7 (d, J_{C-P} = 154.2 Hz), 47.2 (d, J_{C-P} = 13.0 Hz), 23.9, 23.6, 21.8, 16.3 (d, J_{C-P} = 5.6 Hz), 16.1 (d, J_{C-P} = 5.5 Hz) ppm; ^{31}P NMR (202 MHz, $CDCl_3$) δ 15.3 ppm; HRMS (ESI) calcd for $C_{16}H_{24}NO_3P$ [M-HCN+H^+]: 298.1567, found: 298.1566.

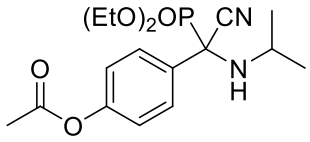
Diethyl (cyano(isopropylamino)(4-methoxyphenyl)methyl)phosphonate (1d)



Following the general procedure, the reaction of amide **2d** (96.6 mg, 0.500 mmol) with TMSCN (75.0 μL, 0.600 mmol) and $HPO(OEt)_2$ (83.0 μL, 0.650 mmol) afforded the α-amino-α-cyanophosphonate **1d** (153 mg, yield: 90%) after flash column chromatography on silica gel (elution with EtOAc/hexane = 1:2) as a pale yellow soild. MP: 72–73 °C; IR (film): 3311, 2977, 2222, 1607, 1509, 1253, 1023, 838, 579 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.72–7.59 (m, 2H), 6.98–6.87 (m, 2H), 4.29–4.13 (m, 2H), 4.05–3.94 (m, 1H), 3.91–3.78 (m, 4H), 3.05–2.88 (m, 1H), 2.12–1.99 (m, 1H), 1.36 (t, J = 7.1 Hz, 3H), 1.21 (d, J = 6.3 Hz, 3H), 1.18 (t, J = 7.1 Hz, 3H), 0.92 (d, J = 6.4 Hz, 3H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ 160.1 (d, J_{C-P} = 2.7 Hz), 129.3 (d, J_{C-P} = 4.7 Hz), 124.1 (d, J_{C-P} = 8.5 Hz), 118.3 (d, J_{C-P} = 4.1 Hz), 113.7 (d, J_{C-P} = 2.7 Hz), 65.2 (d, J_{C-P} = 7.2 Hz), 65.1 (d, J_{C-P} = 7.7 Hz), 62.0 (d, J_{C-P} = 157.5

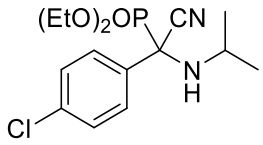
Hz), 55.3, 46.7 (d, $J_{C\text{-}P}$ = 13.5 Hz), 24.8, 23.6, 16.3 (d, $J_{C\text{-}P}$ = 5.7 Hz), 16.2 (d, $J_{C\text{-}P}$ = 5.5 Hz) ppm; ^{31}P NMR (202 MHz, $CDCl_3$) δ 14.7 ppm; HRMS (ESI) calcd for $C_{16}H_{25}N_2O_4PNa$ [M+Na^+]: 363.1444, found: 363.1450.

4-(Cyano(diethoxyphosphoryl)(isopropylamino)methyl)phenyl acetate (1e)



Following the general procedure, the reaction of amide **2e** (111 mg, 0.500 mmol) with TMSCN (75.0 μL, 0.600 mmol) and $HPO(OEt)_2$ (83.0 μL, 0.650 mmol) afforded the α-amino-α-cyanophosphonate **1e** (180 mg, yield: 98%) after flash column chromatography on silica gel (elution with EtOAc/hexane = 1:2) as a pale yellow soild. MP: 74–76 °C; IR (film): 3355, 2978, 2361, 1762, 1200, 1018, 850, 583 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.90–7.68 (m, 2H), 7.26–7.08 (m, 2H), 4.28–4.15 (m, 2H), 4.06–3.96 (m, 1H), 3.95–3.82 (m, 1H), 3.05–2.90 (m, 1H), 2.31 (s, 3H), 2.14 – 2.05 (m, 1H), 1.36 (t, J = 7.1 Hz, 3H), 1.23 (d, J = 6.3 Hz, 3H), 1.18 (t, J = 7.1 Hz, 3H), 0.93 (d, J = 6.4 Hz, 3H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ 169.0, 151.2 (d, $J_{C\text{-}P}$ = 3.4 Hz), 130.1 (d, $J_{C\text{-}P}$ = 8.5 Hz), 129.1 (d, $J_{C\text{-}P}$ = 4.6 Hz), 121.5 (d, $J_{C\text{-}P}$ = 2.8 Hz), 118.0 (d, $J_{C\text{-}P}$ = 4.7 Hz), 65.4 (d, $J_{C\text{-}P}$ = 3.7 Hz), 65.3 (d, $J_{C\text{-}P}$ = 4.0 Hz), 62.2 (d, $J_{C\text{-}P}$ = 155.6 Hz), 46.9 (d, $J_{C\text{-}P}$ = 13.1 Hz), 24.8, 23.5, 21.1, 16.3 (d, $J_{C\text{-}P}$ = 5.6 Hz), 16.1 (d, $J_{C\text{-}P}$ = 5.6 Hz) ppm; ^{31}P NMR (202 MHz, $CDCl_3$) δ 14.3 ppm; HRMS (ESI) calcd for $C_{17}H_{25}N_2O_5PNa$ [M+Na^+]: 391.1393, found: 391.1398.

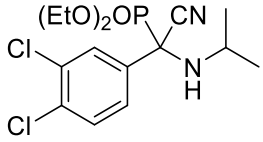
Diethyl ((4-chlorophenyl)(cyano)(isopropylamino)methyl)phosphonate (1f)



Following the general procedure, the reaction of amide **2f** (98.5 mg, 0.500 mmol) with TMSCN (75.0 μL, 0.600 mmol) and $HPO(OEt)_2$ (83.0 μL, 0.650 mmol) afforded the α-amino-α-cyanophosphonate **1f** (155 mg, yield: 90%) after flash column

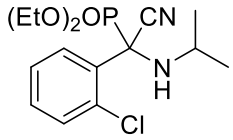
chromatography on silica gel (elution with EtOAc/hexane = 1:2) as a pale yellow soild. MP: 80–81 °C; IR (film): 3262, 2976, 2363, 1487, 1252, 1022, 838, 581 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.72–7.65 (m, 2H), 7.41–7.36 (m, 2H), 4.30–4.16 (m, 2H), 4.10–4.00 (m, 1H), 3.98–3.89 (m, 1H), 3.01–2.91 (m, 1H), 2.14–2.03 (m, 1H), 1.36 (t, *J* = 7.0 Hz, 3H), 1.26–1.16 (m, 6H), 0.91 (d, *J* = 6.4 Hz, 3H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ 135.1 (d, $J_{C\text{-}P}$ = 3.8 Hz), 131.5 (d, $J_{C\text{-}P}$ = 8.6 Hz), 129.3 (d, $J_{C\text{-}P}$ = 4.6 Hz), 128.5 (d, $J_{C\text{-}P}$ = 2.8 Hz), 117.6 (d, $J_{C\text{-}P}$ = 4.9 Hz), 65.3 (d, $J_{C\text{-}P}$ = 7.4 Hz), 62.1 (d, $J_{C\text{-}P}$ = 154.9 Hz), 47.0 (d, $J_{C\text{-}P}$ = 13.1 Hz), 24.6, 23.5, 16.2 (d, $J_{C\text{-}P}$ = 5.6 Hz), 16.1 (d, $J_{C\text{-}P}$ = 5.5 Hz) ppm; ^{31}P NMR (202 MHz, $CDCl_3$) δ 14.1 ppm; HRMS (ESI) calcd for $C_{15}H_{22}ClN_2O_3PNa$ [M+Na^+]: 367.0949, found: 367.0954.

Diethyl (cyano(3,4-dichlorophenyl)(isopropylamino)methyl)phosphonate (1g)



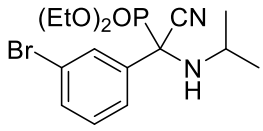
Following the general procedure, the reaction of amide **2g** (116 mg, 0.500 mmol) with TMSCN (75.0 μL, 0.600 mmol) and $HPO(OEt)_2$ (83.0 μL, 0.650 mmol) afforded the α-amino-α-cyanophosphonate **1g** (151 mg, yield: 80%) after flash column chromatography on silica gel (elution with EtOAc/hexane = 1:2) as a pale yellow soild. MP: 95–96 °C; IR (film): 3437, 2976, 2930, 2225, 1590, 1466, 1384, 1256, 1141, 1021, 972, 592 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.84–7.77 (m, 1H), 7.60–7.52 (m, 1H), 7.51–7.43 (m, 1H), 4.31–4.14 (m, 2H), 4.13–3.95 (m, 2H), 3.02–2.87 (m, 1H), 2.18–2.01 (m, 1H), 1.34 (t, *J* = 7.1 Hz, 3H), 1.28–1.16 (m, 6H), 0.90 (d, *J* = 6.4 Hz, 3H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ 133.6 (d, $J_{C\text{-}P}$ = 8.7 Hz), 133.3 (d, $J_{C\text{-}P}$ = 3.8 Hz), 132.7 (d, $J_{C\text{-}P}$ = 3.2 Hz), 130.2 (d, $J_{C\text{-}P}$ = 2.8 Hz), 129.9 (d, $J_{C\text{-}P}$ = 4.6 Hz), 127.2 (d, $J_{C\text{-}P}$ = 4.5 Hz), 117.1 (d, $J_{C\text{-}P}$ = 4.8 Hz), 65.6 (d, $J_{C\text{-}P}$ = 6.4 Hz), 65.5 (d, $J_{C\text{-}P}$ = 7.1 Hz), 61.9 (d, $J_{C\text{-}P}$ = 153.9 Hz), 47.3 (d, $J_{C\text{-}P}$ = 13.0 Hz), 24.7, 23.5, 16.2 (d, $J_{C\text{-}P}$ = 5.8 Hz), 16.1 (d, $J_{C\text{-}P}$ = 5.8 Hz) ppm; ^{31}P NMR (202 MHz, $CDCl_3$) δ 13.6 ppm; HRMS (ESI) calcd for $C_{15}H_{21}N_2Cl_2O_3PNa$ [M+Na^+]: 401.0559, found: 401.0559.

Diethyl ((2-chlorophenyl)(cyano)(isopropylamino)methyl)phosphonate (1h)



Following the general procedure, the reaction of amide **2h** (98.5 mg, 0.500 mmol) with TMSCN (75.0 μL, 0.600 mmol) and $HPO(OEt)_2$ (83.0 μL, 0.650 mmol) afforded the α-amino-α-cyanophosphonate **1h** (138 mg, yield: 80%) after flash column chromatography on silica gel (elution with EtOAc/hexane = 1:2) as a pale yellow oil. IR (film): 3100, 2972, 2929, 1616, 1467, 1254, 1027, 970, 763, 564 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.99–7.92 (m, 1H), 7.43–7.38 (m, 1H), 7.35–7.27 (m, 2H), 4.42–4.28 (m, 2H), 4.09–3.99 (m, 1H), 3.98–3.88 (m, 1H), 3.18–3.01 (m, 1H), 2.63–2.52 (m, 1H), 1.40 (t, *J* = 7.1 Hz, 3H), 1.25 (d, *J* = 6.3 Hz, 3H), 1.16 (t, *J* = 7.1 Hz, 3H), 0.98 (d, *J* = 6.4 Hz, 3H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ 133.2 (d, J_{C-P} = 5.0 Hz), 132.0 (d, J_{C-P} = 2.7 Hz), 131.6 (d, J_{C-P} = 4.6 Hz), 130.0 (d, J_{C-P} = 2.9 Hz), 129.9 (d, J_{C-P} = 7.0 Hz), 117.1 (d, J_{C-P} = 8.3 Hz), 65.7 (d, J_{C-P} = 7.2 Hz), 65.1 (d, J_{C-P} = 7.4 Hz), 62.3 (d, J_{C-P} = 150.7 Hz), 47.4 (d, J_{C-P} = 12.8 Hz), 24.0, 23.4, 16.3 (d, J_{C-P} = 5.6 Hz), 16.0 (d, J_{C-P} = 5.7 Hz) ppm; ^{31}P NMR (202 MHz, $CDCl_3$) δ 13.6 ppm; HRMS (ESI) calcd for $C_{14}H_{21}ClNO_3PNa$ [M-HCN+Na^+]: 340.0840, found: 340.0789.

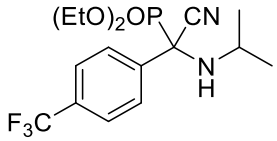
Diethyl ((3-bromophenyl)(cyano)(isopropylamino)methyl)phosphonate (1i)



Following the general procedure, the reaction of amide **2i** (121 mg, 0.500 mmol) with TMSCN (75.0 μL, 0.600 mmol) and $HPO(OEt)_2$ (83.0 μL, 0.650 mmol) afforded the α-amino-α-cyanophosphonate **1i** (159 mg, yield: 82%) after flash column chromatography on silica gel (elution with EtOAc/hexane = 1:2) as a pale yellow soild. MP: 93–94 °C; IR (film): 3292, 2977, 2222, 1470, 1255, 1021, 789, 584 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.91–7.87 (m, 1H), 7.71–7.65 (m, 1H), 7.54–7.49 (m, 1H), 7.32–7.26 (m, 1H), 4.31–4.15 (m, 2H), 4.11–3.93 (m, 2H), 3.03–2.91 (m, 1H), 2.18–2.06 (m, 1H), 1.36 (t, *J* = 7.0 Hz, 3H), 1.25–1.19 (m, 6H), 0.93 (d, *J* = 6.3 Hz,

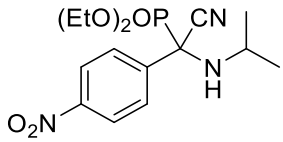
3H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ 135.4 (d, J_{C-P} = 8.6 Hz), 132.2 (d, J_{C-P} = 3.0 Hz), 130.9 (d, J_{C-P} = 4.5 Hz), 129.8 (d, J_{C-P} = 2.8 Hz), 126.6 (d, J_{C-P} = 4.6 Hz), 122.4 (d, J_{C-P} = 3.4 Hz), 117.4 (d, J_{C-P} = 4.9 Hz), 65.5 (d, J_{C-P} = 5.5 Hz), 65.4 (d, J_{C-P} = 5.3 Hz), 62.2 (d, J_{C-P} = 153.7 Hz), 47.2 (d, J_{C-P} = 13.0 Hz), 24.7, 23.5, 16.2 (d, J_{C-P} = 5.7 Hz), 16.1 (d, J_{C-P} = 5.8 Hz) ppm; ^{31}P NMR (202 MHz, $CDCl_3$) δ 13.9 ppm; HRMS (ESI) calcd for $C_{15}H_{22}BrN_2O_3PNa$ [M+Na^+]: 411.0444, found: 411.0451.

Diethyl (cyano(isopropylamino)(4-(trifluoromethyl)phenyl)methyl)phosphonate (1j)



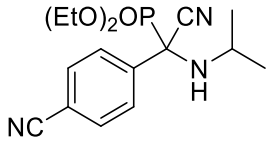
Following the general procedure, the reaction of amide **2j** (116 mg, 0.500 mmol) with TMSCN (75.0 μL, 0.600 mmol) and $HPO(OEt)_2$ (83.0 μL, 0.650 mmol) afforded the α-amino-α-cyanophosphonate **1j** (170 mg, yield: 90%) after flash column chromatography on silica gel (elution with EtOAc/hexane = 1:2) as a pale yellow soild. MP: 62–63 °C; IR (film): 3297, 2980, 2230, 1618, 1327, 1256, 1128, 1018, 846, 806, 577 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.92–7.86 (m, 2H), 7.70–7.66 (m, 2H), 4.32–4.18 (m, 2H), 4.13–3.92 (m, 2H), 3.04–2.88 (m, 1H), 2.22–2.11 (m, 1H), 1.37 (t, J = 7.1 Hz, 3H), 1.24 (d, J = 6.3 Hz, 3H), 1.21 (t, J = 7.1 Hz, 3H), 0.91 (d, J = 6.5 Hz, 3H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ 137.5 (d, J_{C-P} = 8.7 Hz), 131.4 (qd, J_{C-F} = 32.8, J_{C-P} = 3.3 Hz), 128.6 (d, J_{C-P} = 4.3 Hz), 125.7–125.3 (m), 123.9 (q, J_{C-F} = 272.2 Hz), 117.6 (d, J_{C-P} = 5.2 Hz), 65.7 (d, J_{C-P} = 7.6 Hz), 65.6 (d, J_{C-P} = 7.3 Hz), 62.7 (d, J_{C-P} = 153.1 Hz), 47.5 (d, J_{C-P} = 13.1 Hz), 24.8, 23.7, 16.4 (d, J_{C-P} = 5.6 Hz), 16.3 (d, J_{C-P} = 5.5 Hz); ^{31}P NMR (202 MHz, $CDCl_3$) δ 13.8 ppm; ^{19}F NMR (471 MHz, $CDCl_3$) δ -62.7 ppm; HRMS (ESI) calcd for $C_{16}H_{22}F_3N_2O_3PNa$ [M+Na^+]: 401.1212, found: 401.1218.

Diethyl (cyano(isopropylamino)(4-nitrophenyl)methyl)phosphonate (1k)



Following the general procedure, the reaction of amide **2k** (104 mg, 0.500 mmol) with TMSCN (75.0 μL, 0.600 mmol) and $HPO(OEt)_2$ (83.0 μL, 0.650 mmol) afforded the α-amino-α-cyanophosphonate **1k** (163 mg, yield: 92%) after flash column chromatography on silica gel (elution with EtOAc/hexane = 1:2) as a pale yellow soild. MP: 95–96 °C; IR (film): 3266, 2973, 2227, 1525, 1347, 1252, 1022, 855, 582 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 8.32–8.21 (m, 2H), 7.99–7.91 (m, 2H), 4.33–4.19 (m, 2H), 4.16–3.97 (m, 2H), 3.06–2.92 (m, 1H), 2.27–2.15 (m, 1H), 1.37 (t, *J* = 7.0 Hz, 3H), 1.27–1.21 (m, 6H), 0.90 (d, *J* = 6.6 Hz, 3H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ 148.3 (d, $J_{C\text{-}P}$ = 3.5 Hz), 140.7 (d, $J_{C\text{-}P}$ = 8.7 Hz), 129.0 (d, $J_{C\text{-}P}$ = 4.4 Hz), 123.3 (d, $J_{C\text{-}P}$ = 2.9 Hz), 116.9 (d, $J_{C\text{-}P}$ = 5.7 Hz), 65.7 (d, $J_{C\text{-}P}$ = 7.7 Hz), 65.6 (d, $J_{C\text{-}P}$ = 7.3 Hz), 62.6 (d, $J_{C\text{-}P}$ = 151.2 Hz), 47.8 (d, $J_{C\text{-}P}$ = 12.8 Hz), 24.8, 23.7, 16.4 (d, $J_{C\text{-}P}$ = 5.6 Hz), 16.3 (d, $J_{C\text{-}P}$ = 5.8 Hz) ppm; ^{31}P NMR (202 MHz, $CDCl_3$) δ 13.4 ppm; HRMS (ESI) calcd for $C_{15}H_{22}N_3O_5PNa$ [M+Na^+]: 378.1189, found: 378.1194.

Diethyl (cyano(4-cyanophenyl)(isopropylamino)methyl)phosphonate (1l)

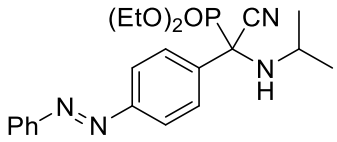


Following the general procedure, the reaction of amide **2l** (94.0 mg, 0.500 mmol) with TMSCN (75.0 μL, 0.600 mmol) and $HPO(OEt)_2$ (83.0 μL, 0.650 mmol) afforded the α-amino-α-cyanophosphonate **1l** (149 mg, yield: 89%) after flash column chromatography on silica gel (elution with EtOAc/hexane = 1:2) as a pale yellow soild. MP: 69–70 °C; IR (film): 3318, 2978, 2230, 1500, 1258, 1019, 844, 584 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.94–7.85 (m, 2H), 7.77–7.68 (m, 2H), 4.33–4.17 (m, 2H), 4.14–3.95 (m, 2H), 3.03–2.91 (m, 1H), 2.23–2.14 (m, 1H), 1.36 (t, *J* = 7.1 Hz, 3H), 1.26–1.19 (m, 6H), 0.89 (d, *J* = 6.7 Hz, 3H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ

138.7 (d, $J_{C\text{-}P}$ = 8.8 Hz), 131.9 (d, $J_{C\text{-}P}$ = 3.0 Hz), 128.7 (d, $J_{C\text{-}P}$ = 4.5 Hz), 118.0 (d, $J_{C\text{-}P}$ = 1.9 Hz), 116.9 (d, $J_{C\text{-}P}$ = 5.5 Hz), 113.0 (d, $J_{C\text{-}P}$ = 3.3 Hz), 65.6 (d, $J_{C\text{-}P}$ = 7.6 Hz), 65.5 (d, $J_{C\text{-}P}$ = 7.4 Hz), 62.6 (d, $J_{C\text{-}P}$ = 151.8 Hz), 47.4 (d, $J_{C\text{-}P}$ = 12.8 Hz), 24.5, 23.5, 16.2 (d, $J_{C\text{-}P}$ = 5.8 Hz), 16.1 (d, $J_{C\text{-}P}$ = 5.7 Hz) ppm; ^{31}P NMR (202 MHz, $CDCl_3$) δ 13.5 ppm; HRMS (ESI) calcd for $C_{16}H_{22}N_3O_3PNa$ [M+Na^+]: 358.1291, found: 358.1295.

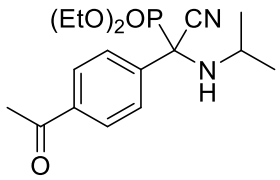
Diethyl (*E*)-(cyano(isopropylamino)(4-(phenyldiazenyl)phenyl)methyl)phosphora

te (1m)



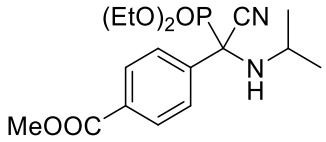
Following the general procedure, the reaction of amide **2m** (134 mg, 0.500 mmol) with TMSCN (75.0 μL, 0.600 mmol) and $HPO(OEt)_2$ (83.0 μL, 0.650 mmol) afforded the α-amino-α-cyanophosphonate **1m** (174 mg, yield: 84%) after flash column chromatography on silica gel (elution with EtOAc/hexane = 1:2) as a pale yellow soild. MP: 91–92 °C; IR (film): 3410, 2975, 1609, 1439, 1255, 1141, 635, 585 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.02–7.87 (m, 6H), 7.58–7.44 (m, 3H), 4.33–4.17 (m, 2H), 4.12–3.89 (m, 2H), 3.08–2.97 (m, 1H), 2.21–2.16 (m, 1H), 1.38 (t, *J* = 7.1 Hz, 3H), 1.25 (d, *J* = 6.2 Hz, 3H), 1.20 (t, *J* = 7.1 Hz, 3H), 0.95 (d, *J* = 6.4, 3H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ 152.8 (d, $J_{C\text{-}P}$ = 3.7 Hz), 152.5, 135.5 (d, $J_{C\text{-}P}$ = 8.8 Hz), 131.3, 129.1, 128.8 (d, $J_{C\text{-}P}$ = 4.8 Hz), 122.9, 122.6 (d, $J_{C\text{-}P}$ = 3.0 Hz), 117.8 (d, $J_{C\text{-}P}$ = 5.1 Hz), 65.5 (d, $J_{C\text{-}P}$ = 7.4 Hz) 62.7 (d, $J_{C\text{-}P}$ = 153.9 Hz), 47.2 (d, $J_{C\text{-}P}$ = 13.2 Hz), 24.7, 23.6, 16.3 (d, $J_{C\text{-}P}$ = 5.7 Hz), 16.2 (d, $J_{C\text{-}P}$ = 5.6 Hz) ppm; ^{31}P NMR (202 MHz, $CDCl_3$) δ 14.1 ppm; HRMS (ESI) calcd for $C_{21}H_{27}N_4O_3PNa$ [M+Na^+]: 437.1713, found: 437.1713.

Diethyl ((4-acetylphenyl)(cyano)(isopropylamino)methyl)phosphonate (1n)



Following the general procedure, the reaction of amide **2n** (103 mg, 0.500 mmol) with TMSCN (75.0 μL, 0.600 mmol) and $HPO(OEt)_2$ (83.0 μL, 0.650 mmol) afforded the α-amino-α-cyanophosphonate **1n** (162 mg, yield: 92%) after flash column chromatography on silica gel (elution with EtOAc/hexane = 1:2) as a pale yellow soild. MP: 82–83 °C; IR (film): 3300, 2978, 2351, 1687, 1261, 1048, 841, 599 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 8.04–7.96 (m, 2H), 7.89–7.81 (m, 2H), 4.32–4.18 (m, 2H), 4.11–4.01 (m, 1H), 4.01–3.91 (m, 1H), 3.02–2.92 (m, 1H), 2.63 (s, 3H), 2.22–2.11 (m, 1H), 1.37 (t, *J* = 7.1 Hz, 3H), 1.24 (d, *J* = 6.3 Hz, 3H), 1.20 (t, *J* = 7.1 Hz, 3H), 0.91 (d, *J* = 6.4 Hz, 3H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ 197.3, 138.1 (d, J_{C-P} = 8.6 Hz), 137.5 (d, J_{C-P} = 3.0 Hz), 128.2 (d, J_{C-P} = 4.5 Hz), 128.2 (d, J_{C-P} = 2.8 Hz), 117. 5 (d, J_{C-P} = 5.4 Hz), 65.5 (d, J_{C-P} = 7.4 Hz), 65.5 (d, J_{C-P} = 7.1 Hz), 62.7 (d, J_{C-P} = 152.9 Hz), 47.2 (d, J_{C-P} = 13.1 Hz), 26.6, 24.6, 23.5, 16.2 (d, J_{C-P} = 5.6 Hz), 16.1 (d, J_{C-P} = 5.6 Hz) ppm; ^{31}P NMR (202 MHz, $CDCl_3$) δ 13.8 ppm; HRMS (ESI) calcd for $C_{17}H_{25}N_2O_4PNa$ [$M+Na^+$]: 375.1444, found: 375.1451.

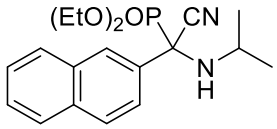
Methyl 4-(cyano(diethoxyphosphoryl)(isopropylamino)methyl)benzoate (1o)



Following the general procedure, the reaction of amide **2o** (111 mg, 0.500 mmol) with TMSCN (75.0 μL, 0.600 mmol) and $HPO(OEt)_2$ (83.0 μL, 0.650 mmol) afforded the α-amino-α-cyanophosphonate **1o** (161 mg, yield: 87%) after flash column chromatography on silica gel (elution with EtOAc/hexane = 1:2) as a pale yellow soild. MP: 78–79 °C; IR (film): 3325, 2978, 2216, 1726, 1437, 1280, 1019, 767, 581 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 8.10–8.02 (m, 2H), 7.83–7.78 (m, 2H), 4.27–4.12 (m, 2H), 4.05–3.95 (m, 1H), 3.95–3.85 (m, 4H), 2.99–2.88 (m, 1H), 2.17–2.10 (m, 1H), 1.33 (t, *J* = 7.1 Hz, 3H), 1.20 (d, *J* = 6.3 Hz, 3H), 1.16 (t, *J* = 7.0 Hz, 3H), 0.87

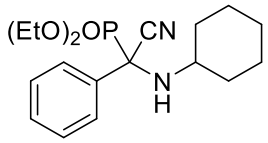
(d, J = 6.4, 3H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ 166.3, 138.0 (d, $J_{C\text{-}P}$ = 8.5 Hz), 130.8 (d, $J_{C\text{-}P}$ = 3.0 Hz), 129.4 (d, $J_{C\text{-}P}$ = 2.8 Hz), 128.0 (d, $J_{C\text{-}P}$ = 4.5 Hz), 117.5 (d, $J_{C\text{-}P}$ = 5.3 Hz), 65.5 (d, $J_{C\text{-}P}$ = 7.6 Hz), 65.5 (d, $J_{C\text{-}P}$ = 7.2 Hz), 62.7 (d, $J_{C\text{-}P}$ = 152.7 Hz), 52.2, 47.2 (d, $J_{C\text{-}P}$ = 13.1 Hz), 24.6, 23.5, 16.2 (d, $J_{C\text{-}P}$ = 5.7 Hz), 16.1 (d, $J_{C\text{-}P}$ = 5.6 Hz) ppm; ^{31}P NMR (202 MHz, $CDCl_3$) δ 13.9 ppm; HRMS (ESI) calcd for $C_{17}H_{25}N_2O_5PNa$ [M+Na^+]: 391.1393, found: 391.1399.

Diethyl (cyano(isopropylamino)(naphthalen-2-yl)methyl)phosphonate (1p)



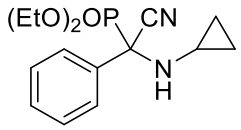
Following the general procedure, the reaction of amide **2p** (107 mg, 0.500 mmol) with TMSCN (75.0 μL, 0.600 mmol) and $HPO(OEt)_2$ (83.0 μL, 0.650 mmol) afforded the α-amino-α-cyanophosphonate **1p** (159 mg, yield: 88%) after flash column chromatography on silica gel (elution with EtOAc/hexane = 1:2) as a pale yellow soild. MP: 71–72 °C; IR (film): 3295, 2977, 2219, 1367, 1255, 1022, 750, 571 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.25–8.20 (m, 1H), 7.94–7.82 (m, 4H), 7.55–7.51 (m, 2H), 4.34–4.16 (m, 2H), 4.06–3.94 (m, 1H), 3.90–3.81 (m, 1H), 3.06–2.94 (m, 1H), 2.24–2.16 (m, 1H), 1.36 (t, J = 7.0 Hz, 3H), 1.24 (d, J = 6.3 Hz, 3H), 1.13 (t, J = 7.0 Hz, 3H), 0.93 (d, J = 6.4 Hz, 3H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ 133.4 (d, $J_{C\text{-}P}$ = 2.3 Hz), 132.7 (d, $J_{C\text{-}P}$ = 2.7 Hz), 130.1 (d, $J_{C\text{-}P}$ = 8.6 Hz), 128.3, 128.0 (d, $J_{C\text{-}P}$ = 2.4 Hz), 127.8 (d, $J_{C\text{-}P}$ = 6.6 Hz), 127.5, 126.5, 124.9 (d, $J_{C\text{-}P}$ = 3.2 Hz), 118.2 (d, $J_{C\text{-}P}$ = 4.6 Hz), 65.3 (d, $J_{C\text{-}P}$ = 7.5 Hz), 62.9 (d, $J_{C\text{-}P}$ = 155.0 Hz), 47.0 (d, $J_{C\text{-}P}$ = 13.4 Hz), 24.7, 23.6, 16.3 (d, $J_{C\text{-}P}$ = 5.6 Hz), 16.1 (d, $J_{C\text{-}P}$ = 5.7 Hz) ppm; ^{31}P NMR (202 MHz, $CDCl_3$) δ 14.5 ppm; HRMS (ESI) calcd for $C_{19}H_{25}N_2O_3PNa$ [M+Na^+]: 383.1495, found: 383.1502.

Diethyl (cyano(cyclohexylamino)(phenyl)methyl)phosphonate (1q)



Following the general procedure, the reaction of amide **2q** (102 mg, 0.500 mmol) with TMSCN (75.0 μL, 0.600 mmol) and $HPO(OEt)_2$ (83.0 μL, 0.650 mmol) afforded the α-amino-α-cyanophosphonate **1q** (149 mg, yield: 85%) after flash column chromatography on silica gel (elution with EtOAc/hexane = 1:2) as a pale yellow soild. MP: 55–56 °C; IR (film): 3853, 3362, 2927, 2215, 1448, 1254, 1021, 800, 699, 583 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.79–7.71 (m, 2H), 7.47–7.34 (m, 3H), 4.31–4.14 (m, 2H), 4.02–3.92 (m, 1H), 3.90–3.79 (m, 1H), 2.67–2.54 (m, 1H), 2.18–2.10 (m, 2H), 1.73–1.64 (m, 1H), 1.63–1.44 (m, 3H), 1.35 (t, J = 7.1 Hz, 3H), 1.31–0.99 (m, 8H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ 132.8 (d, $J_{C\text{-}P}$ = 8.3 Hz), 129.1 (d, $J_{C\text{-}P}$ = 3.2 Hz), 128.3 (d, $J_{C\text{-}P}$ = 2.8 Hz), 128.0 (d, $J_{C\text{-}P}$ = 4.6 Hz), 118.2 (d, $J_{C\text{-}P}$ = 4.8 Hz), 65.3 (d, $J_{C\text{-}P}$ = 7.4 Hz), 62.5 (d, $J_{C\text{-}P}$ = 154.7 Hz), 54.4 (d, $J_{C\text{-}P}$ = 12.6 Hz), 35.2, 34.1, 25.6, 25.1 (d, $J_{C\text{-}P}$ = 9.5 Hz), 16.3 (d, $J_{C\text{-}P}$ = 5.8 Hz), 16.2 (d, $J_{C\text{-}P}$ = 5.7 Hz) ppm; ^{31}P NMR (202 MHz, $CDCl_3$) δ 14.5 ppm; HRMS (ESI) calcd for $C_{18}H_{27}N_2O_3PNa$ [M+Na^+]: 373.1652, found: 373.1655.

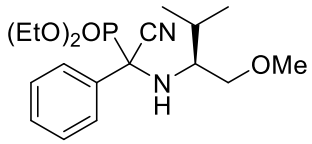
Diethyl (cyano(cyclopropylamino)(phenyl)methyl)phosphonate (1r)



Following the general procedure, the reaction of amide **2r** (80.5 mg, 0.500 mmol) with TMSCN (75.0 μL, 0.600 mmol) and $HPO(OEt)_2$ (83.0 μL, 0.650 mmol) afforded the α-amino-α-cyanophosphonate **1r** (125 mg, yield: 81%) after flash column chromatography on silica gel (elution with EtOAc/hexane = 1:2) as a pale yellow oil. IR (film): 3280, 2982, 1599, 1449, 1391, 1252, 1195, 1019, 972, 699, 580 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.78–7.68 (m, 2H), 7.47–7.35 (m, 3H), 4.30–4.18 (m, 2H), 3.98–3.87 (m, 1H), 3.81–3.67 (m, 1H), 2.91–2.80 (m, 1H), 2.18–2.07 (m, 1H), 1.36 (t, J = 7.1 Hz, 3H), 1.10 (t, J = 7.0 Hz, 3H), 0.72–0.63 (m, 1H), 0.55–0.43 (m, 1H),

0.38–0.27 (m, 2H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ 132.2 (d, $J_{C\text{-}P}$ = 6.6 Hz), 129.1 (d, $J_{C\text{-}P}$ = 2.9 Hz), 128.5 (d, $J_{C\text{-}P}$ = 2.5 Hz), 127.9 (d, $J_{C\text{-}P}$ = 4.6 Hz), 117.2 (d, $J_{C\text{-}P}$ = 6.3 Hz), 65.3 (d, $J_{C\text{-}P}$ = 7.5 Hz), 65.1 (d, $J_{C\text{-}P}$ = 7.3 Hz), 63.6 (d, $J_{C\text{-}P}$ = 153.5 Hz), 27.1 (d, $J_{C\text{-}P}$ = 16.0 Hz), 16.3 (d, $J_{C\text{-}P}$ = 5.7 Hz), 16.0 (d, $J_{C\text{-}P}$ = 5.6 Hz), 6.3, 6.1 ppm; ^{31}P NMR (202 MHz, $CDCl_3$) δ 14.2 ppm; HRMS (ESI) calcd for $C_{15}H_{21}N_2O_3PNa$ [M+Na^+]: 331.1182, found: 331.1182.

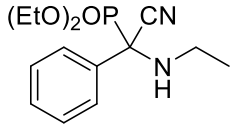
Diethyl (cyano(((S)-1-methoxy-3-methylbutan-2-yl)amino)(phenyl)methyl)phosphonate (1s)



Following the general procedure, the reaction of amide **2s** (111 mg, 0.500 mmol) with TMSCN (75.0 μL, 0.600 mmol) and $HPO(OEt)_2$ (83.0 μL, 0.650 mmol) afforded the α-amino-α-cyanophosphonate **1s** (149 mg, yield: 81%, dr = 1:1.5) after flash column chromatography on silica gel (elution with EtOAc/hexane = 1:2) as a pale yellow oil. IR (film): 3331, 2962, 2222, 1448, 1257, 1049, 1022, 700, 581 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.84–7.71 (m, 2H), 7.45–7.33 (m, 3H), 4.42–4.27 (m, 1H), 4.26–4.17 (m, 1H), 4.09–3.99 (m, 0.6H), 3.97–3.85 (m, 1H), 3.76–3.66 (m, 0.4H), 3.65–3.56 (m, 0.6H), 3.44–3.32 (m, 2.2H), 3.12–3.02 (m, 1.8H), 2.97–2.90 (m, 0.4H), 2.79–2.69 (m, 1.4H), 2.64–2.56 (m, 0.6H), 2.10–2.00 (m, 0.4H), 1.69–1.58 (m, 0.6 H), 1.40 (t, *J* = 7.1 Hz, 1.2H), 1.35 (t, *J* = 7.1 Hz, 1.8H), 1.18 (t, *J* = 7.1 Hz, 1.8H), 1.08 (t, *J* = 7.1 Hz, 1.2H), 0.97 (d, *J* = 6.9 Hz, 1.2H), 0.94 (d, *J* = 6.9 Hz, 1.2H), 0.88 (d, *J* = 7.0 Hz, 1.8H), 0.81 (d, *J* = 6.9 Hz, 1.8H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ 133.5 (d, $J_{C\text{-}P}$ = 5.6 Hz), 131.8 (d, $J_{C\text{-}P}$ = 8.7 Hz), 129.2 (d, $J_{C\text{-}P}$ = 3.0 Hz), 129.0 (d, $J_{C\text{-}P}$ = 2.7 Hz), 128.4 (d, $J_{C\text{-}P}$ = 4.9 Hz), 128.3 (d, $J_{C\text{-}P}$ = 2.4 Hz), 128.3 (d, $J_{C\text{-}P}$ = 2.8 Hz), 127.8 (d, $J_{C\text{-}P}$ = 4.9 Hz), 118.5 (d, $J_{C\text{-}P}$ = 3.3 Hz), 117.5 (d, $J_{C\text{-}P}$ = 8.8 Hz), 71.5, 70.2, 65.5 (d, $J_{C\text{-}P}$ = 7.3 Hz), 65.3 (d, $J_{C\text{-}P}$ = 7.2 Hz), 65.0 (d, $J_{C\text{-}P}$ = 7.8 Hz), 65.0 (d, $J_{C\text{-}P}$ = 7.3 Hz), 63.0 (d, $J_{C\text{-}P}$ = 153.0 Hz), 62.4 (d, $J_{C\text{-}P}$ = 157.2 Hz), 59.8 (d, $J_{C\text{-}P}$ = 12.4 Hz), 58.9 (d,

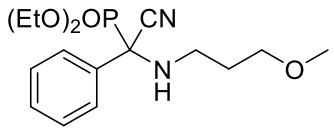
$J_{C\text{-}P}$ = 12.6 Hz), 58.6, 58.5, 30.4, 29.7, 18.8 (d, $J_{C\text{-}P}$ = 106.4 Hz), 18.6 (d, $J_{C\text{-}P}$ = 119.6 Hz), 16.4 (d, $J_{C\text{-}P}$ = 6.0 Hz), 16.3 (d, $J_{C\text{-}P}$ = 5.7 Hz), 16.2 (d, $J_{C\text{-}P}$ = 5.6 Hz), 16.0 (d, $J_{C\text{-}P}$ = 5.6 Hz) ppm; ^{31}P NMR (202 MHz, $CDCl_3$) δ 14.7, 14.5 ppm; HRMS (ESI) calcd for $C_{18}H_{29}N_2O_4PNa$ [M+Na^+]: 391.1757, found: 391.1762.

Diethyl (cyano(ethylamino)(phenyl)methyl)phosphonate (1t)



Following the general procedure, the reaction of amide **2t** (74.5 mg, 0.500 mmol) with TMSCN (75.0 μL, 0.600 mmol) and $HPO(OEt)_2$ (83.0 μL, 0.650 mmol) afforded the α-amino-α-cyanophosphonate **1t** (136 mg, yield: 92%) after flash column chromatography on silica gel (elution with EtOAc/hexane = 1:2) as a pale yellow soild. MP: 69–70 °C; IR (film): 3283, 2978, 2219, 1448, 1254, 1020, 793, 700, 581 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.74–7.64 (m, 2H), 7.47–7.35 (m, 3H), 4.25–4.12 (m, 2H), 4.08–3.90 (m, 2H), 2.85–2.70 (m, 1H), 2.54–2.38 (m, 1H), 2.22–2.10 (m, 1H), 1.34 (t, J = 7.1 Hz, 3H), 1.20 (t, J = 7.1 Hz, 3H), 1.16 (t, J = 7.1 Hz, 3H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ 131.8 (d, $J_{C\text{-}P}$ = 8.7 Hz), 129.3 (d, $J_{C\text{-}P}$ = 3.2 Hz), 128.7 (d, $J_{C\text{-}P}$ = 3.0 Hz), 127.9 (d, $J_{C\text{-}P}$ = 4.5 Hz), 117.5 (d, $J_{C\text{-}P}$ = 2.8 Hz), 65.2 (d, $J_{C\text{-}P}$ = 7.1 Hz), 65.1 (d, $J_{C\text{-}P}$ = 7.5 Hz), 64.0 (d, $J_{C\text{-}P}$ = 157.6 Hz), 39.4 (d, $J_{C\text{-}P}$ = 13.1 Hz), 16.3 (d, $J_{C\text{-}P}$ = 5.7 Hz), 16.2 (d, $J_{C\text{-}P}$ = 5.6 Hz), 15.1 ppm; ^{31}P NMR (202 MHz, $CDCl_3$) δ 14.3 ppm; HRMS (ESI) calcd for $C_{14}H_{21}N_2O_3PNa$ [M+Na^+]: 319.1182, found: 319.1183.

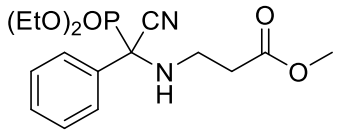
Diethyl (cyano((3-methoxypropyl)amino)(phenyl)methyl)phosphonate (1u)



Following the general procedure, the reaction of amide **2u** (96.5 mg, 0.500 mmol) with TMSCN (75.0 μL, 0.600 mmol) and $HPO(OEt)_2$ (83.0 μL, 0.650 mmol) afforded

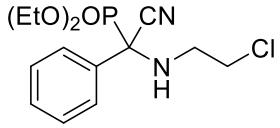
the α-amino-α-cyanophosphonate **1u** (151 mg, yield: 89%) after flash column chromatography on silica gel (elution with EtOAc/hexane = 1:2) as a pale yellow soild. MP: 75–76 °C; IR (film): 3312, 2928, 2216, 1655, 1448, 1257, 1021, 793, 700, 581 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.71–7.63 (m, 2H), 7.45–7.35 (m, 3H), 4.22–4.12 (m, 2H), 4.08–3.88 (m, 2H), 3.51–3.44 (m, 2H), 3.33 (s, 3H), 2.83–2.75 (m, 1H), 2.62–2.48 (m, 2H), 1.87–1.76 (m, 2H), 1.34 (t, J = 7.0 Hz, 3H), 1.20 (t, J = 7.0 Hz, 3H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ 131.5 (d, $J_{C\text{-}P}$ = 8.6 Hz), 129.1 (d, $J_{C\text{-}P}$ = 3.2 Hz), 128.5 (d, $J_{C\text{-}P}$ = 2.8 Hz), 127.7 (d, $J_{C\text{-}P}$ = 4.4 Hz), 117.3 (d, $J_{C\text{-}P}$ = 2.9 Hz), 71.3, 65.2 (d, $J_{C\text{-}P}$ = 7.1 Hz), 65.1 (d, $J_{C\text{-}P}$ = 7.5 Hz), 63.8 (d, $J_{C\text{-}P}$ = 157.6 Hz), 58.6, 42.7 (d, $J_{C\text{-}P}$ = 13.3 Hz), 29.5, 16.2 (d, $J_{C\text{-}P}$ = 5.7 Hz), 16.2 (d, $J_{C\text{-}P}$ = 5.7 Hz) ppm; ^{31}P NMR (202 MHz, $CDCl_3$) δ 14.2 ppm; HRMS (ESI) calcd for $C_{16}H_{25}N_2O_4PNa$ [M+Na^+]: 363.1444, found: 363.1448.

Methyl 3-((cyano(diethoxyphosphoryl)(phenyl)methyl)amino)propanoate (1v)



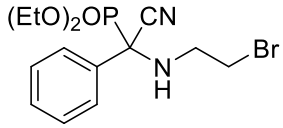
Following the general procedure, the reaction of amide **2v** (104 mg, 0.500 mmol) with TMSCN (75.0 μL, 0.600 mmol) and $HPO(OEt)_2$ (83.0 μL, 0.650 mmol) afforded the α-amino-α-cyanophosphonate **1v** (151 mg, yield: 85%) after flash column chromatography on silica gel (elution with EtOAc/hexane = 1:2) as a pale yellow soild. MP: 71–72 °C; IR (film): 3283, 2984, 2219, 1737, 1439, 1257, 1020, 756, 699, 581 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.70–7.64 (m, 2H), 7.44–7.35 (m, 3H), 4.19–4.11 (m, 2H), 4.05–3.85 (m, 2H), 3.68 (s, 3H), 3.07–2.95 (m, 1H), 2.81–2.72 (m, 1H), 2.70–2.59 (m, 1H), 2.54 (t, J = 6.2 Hz, 2H), 1.32 (t, J = 7.1 Hz, 3H), 1.17 (t, J = 7.1 Hz, 3H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ 172.3, 131.2 (d, $J_{C\text{-}P}$ = 8.2 Hz), 129.2 (d, $J_{C\text{-}P}$ = 3.1 Hz), 128.6 (d, $J_{C\text{-}P}$ = 2.8 Hz), 127.7 (d, $J_{C\text{-}P}$ = 4.4 Hz), 117.0 (d, $J_{C\text{-}P}$ = 3.4 Hz), 65.3 (d, $J_{C\text{-}P}$ = 7.7 Hz), 65.2 (d, $J_{C\text{-}P}$ = 8.2 Hz), 63.5 (d, $J_{C\text{-}P}$ = 157.5 Hz), 51.7, 40.0 (d, $J_{C\text{-}P}$ = 14.0 Hz), 34.1, 16.2 (d, $J_{C\text{-}P}$ = 5.6 Hz), 16.1 (d, $J_{C\text{-}P}$ = 5.8 Hz) ppm; ^{31}P NMR (202 MHz, $CDCl_3$) δ 13.9 ppm; HRMS (ESI) calcd for $C_{16}H_{23}N_2O_5PNa$ [M+Na^+]: 377.1237, found: 377.1243.

Diethyl (((2-chloroethyl)amino)(cyano)(phenyl)methyl)phosphonate (1w)



Following the general procedure, the reaction of amide **2w** (88.6 mg, 0.500 mmol) with TMSCN (75.0 μL, 0.600 mmol) and $HPO(OEt)_2$ (83.0 μL, 0.650 mmol) afforded the α-amino-α-cyanophosphonate **1w** (139 mg, yield: 84%) after flash column chromatography on silica gel (elution with EtOAc/hexane = 1:2) as a pale yellow soild. MP: 73–74 °C; IR (film): 3255, 2983, 2201, 1599, 1488, 1259, 1022, 758, 699, 581 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.75–7.67 (m, 2H), 7.49–7.37 (m, 3H), 4.26–4.14 (m, 2H), 4.11–3.89 (m, 2H), 3.73–3.61 (m, 2H), 3.15–3.03 (m, 1H), 2.85–2.71 (m, 2H), 1.35 (t, J = 7.1 Hz, 3H), 1.21 (t, J = 7.1 Hz, 3H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ 131.1 (d, $J_{C\text{-}P}$ = 8.2 Hz), 129.4 (d, $J_{C\text{-}P}$ = 3.1 Hz), 128.7 (d, $J_{C\text{-}P}$ = 2.7 Hz), 127.6 (d, $J_{C\text{-}P}$ = 4.3 Hz), 116.9 (d, $J_{C\text{-}P}$ = 3.2 Hz), 65.3 (d, $J_{C\text{-}P}$ = 7.2 Hz), 65.2 (d, $J_{C\text{-}P}$ = 7.6 Hz), 63.0 (d, $J_{C\text{-}P}$ = 157.8 Hz), 45.8 (d, $J_{C\text{-}P}$ = 13.4 Hz), 44.0, 16.2 (d, $J_{C\text{-}P}$ = 5.7 Hz), 16.1 (d, $J_{C\text{-}P}$ = 5.7 Hz) ppm; ^{31}P NMR (202 MHz, $CDCl_3$) δ 13.7 ppm; HRMS (ESI) calcd for $C_{14}H_{20}ClN_2O_3PNa$ [$M+Na^+$]: 353.0792, found: 353.0797.

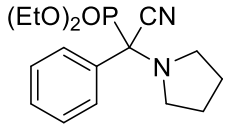
Diethyl (((2-bromoethyl)amino)(cyano)(phenyl)methyl)phosphonate (1x)



Following the general procedure, the reaction of amide **2x** (114 mg, 0.500 mmol) with TMSCN (75.0 μL, 0.600 mmol) and $HPO(OEt)_2$ (83.0 μL, 0.650 mmol) afforded the α-amino-α-cyanophosphonate **1x** (153 mg, yield: 82%) after flash column chromatography on silica gel (elution with EtOAc/hexane = 1:2) as a pale yellow soild. MP: 99–100 °C; IR (film): 3307, 2980, 1251, 1032, 697, 579 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.73–7.67 (m, 2H), 7.48–7.37 (m, 3H), 4.25–4.15 (m, 2H),

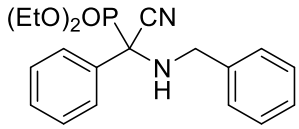
4.13–3.90 (m, 2H), 3.59–3.45 (m, 2H), 3.20–3.09 (m, 1H), 2.91–2.81 (m, 1H), 2.81–2.71 (m, 1H), 1.35 (t, J = 7.1 Hz, 3H), 1.21 (t, J = 7.0 Hz, 3H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ 131.2 (d, $J_{C\text{-}P}$ = 8.3 Hz), 129.4 (d, $J_{C\text{-}P}$ = 3.0 Hz), 128.7 (d, $J_{C\text{-}P}$ = 2.8 Hz), 127.6 (d, $J_{C\text{-}P}$ = 4.4 Hz), 116.9 (d, $J_{C\text{-}P}$ = 3.5 Hz), 65.4 (d, $J_{C\text{-}P}$ = 7.3 Hz), 65.3 (d, $J_{C\text{-}P}$ = 7.6 Hz), 63.0 (d, $J_{C\text{-}P}$ = 157.6 Hz), 45.7 (d, $J_{C\text{-}P}$ = 13.5 Hz), 32.3, 16.2 (d, $J_{C\text{-}P}$ = 5.6 Hz), 16.1 (d, $J_{C\text{-}P}$ = 5.7 Hz) ppm; ^{31}P NMR (202 MHz, $CDCl_3$) δ 13.7 ppm; HRMS (ESI) calcd for $C_{14}H_{20}BrN_2O_3PNa$ [M+Na$^+$]: 397.0287, found: 397.0297.

Diethyl (cyano(phenyl)(pyrrolidin-1-yl)methyl)phosphonate (1y)



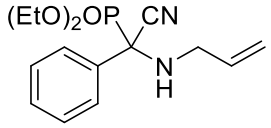
Following the general procedure, the reaction of amide **2y** (128 mg, 0.500 mmol) with TMSCN (75.0 μL, 0.600 mmol) and $HPO(OEt)_2$ (83.0 μL, 0.650 mmol) afforded the α-amino-α-cyanophosphonate **1y** (106 mg, yield: 66%) after flash column chromatography on silica gel (elution with EtOAc/hexane = 1:2) as a pale yellow oil. IR (film): 2973, 2843, 1489, 1261, 1032, 697, 578 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.88–7.70 (m, 2H), 7.43–7.36 (m, 3H), 4.28–4.15 (m, 2H), 3.85–3.69 (m, 1H), 3.39–3.25 (m, 1H), 2.86–2.75 (m, 2H), 2.72–2.60 (m, 2H), 1.88–1.76 (m, 4H), 1.37 (t, J = 7.0 Hz, 3H), 1.05 (td, J = 7.1, $J_{P\text{-}H}$ = 0.8 Hz, 3H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ 133.2 (d, $J_{C\text{-}P}$ = 8.7 Hz), 129.1 (d, $J_{C\text{-}P}$ = 3.0 Hz), 128.4 (d, $J_{C\text{-}P}$ = 2.6 Hz), 128.2 (d, $J_{C\text{-}P}$ = 4.6 Hz), 114.7, 69.4 (d, $J_{C\text{-}P}$ = 164.9 Hz), 64.9 (d, $J_{C\text{-}P}$ = 7.2 Hz), 64.1 (d, $J_{C\text{-}P}$ = 8.5 Hz), 50.1 (d, $J_{C\text{-}P}$ = 6.5 Hz), 23.4, 16.2 (d, $J_{C\text{-}P}$ = 6.0 Hz), 16.0 (d, $J_{C\text{-}P}$ = 5.6 Hz) ppm; ^{31}P NMR (202 MHz, $CDCl_3$) δ 13.5 ppm; HRMS (ESI) calcd for $C_{16}H_{23}N_2O_3PNa$ [M+Na$^+$]: 345.1339, found: 345.1351.

Diethyl ((benzylamino)(cyano)(phenyl)methyl)phosphonate (1z)



Following the general procedure, the reaction of amide **2z** (106 mg, 0.500 mmol) with TMSCN (75.0 μL, 0.600 mmol) and $HPO(OEt)_2$ (83.0 μL, 0.650 mmol) afforded the α-amino-α-cyanophosphonate **1z** (150 mg, yield: 84%) after flash column chromatography on silica gel (elution with EtOAc/hexane = 1:2) as a pale yellow soild. MP: 70–71 °C; IR (film): 3282, 2925, 2359, 1455, 1255, 1020, 698, 583 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.86–7.71 (m, 2H), 7.49–7.39 (m, 3H), 7.39–7.31 (m, 4H), 7.30–7.25 (m, 1H), 4.26–4.12 (m, 2H), 4.12–3.91 (m, 2H), 3.85 (dd, *J* = 12.3, 4.3 Hz, 1H), 3.63 – 3.57 (m, 1H), 2.60–2.45 (m, 1H), 1.34 (t, *J* = 7.1 Hz, 3H), 1.21 (t, *J* = 7.1 Hz, 3H) ppm; ^{13}C NMR (126 MHz, $CDCl_3$) δ 138.2, 131.3 (d, J_{C-P} = 8.6 Hz), 129.3 (d, J_{C-P} = 3.2 Hz), 128.7 (d, J_{C-P} = 2.8 Hz), 128.5, 128.3, 127.7 (d, J_{C-P} = 4.5 Hz), 127.5, 117.1 (d, J_{C-P} = 3.1 Hz), 65.3 (d, J_{C-P} = 7.2 Hz), 65.2 (d, J_{C-P} = 7.6 Hz), 63.7 (d, J_{C-P} = 157.5 Hz), 48.9 (d, J_{C-P} = 13.5 Hz), 16.3 (d, J_{C-P} = 5.6 Hz), 16.2 (d, J_{C-P} = 5.8 Hz) ppm; ^{31}P NMR (202 MHz, $CDCl_3$) δ 13.9 ppm; HRMS (ESI) calcd for $C_{19}H_{23}N_2O_3PNa$ [$M+Na^+$]: 381.1339, found: 381.1342.

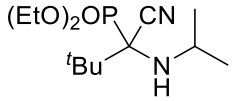
Diethyl ((allylamino)(cyano)(phenyl)methyl)phosphonate (1aa)



Following the general procedure, the reaction of amide **2aa** (80.5 mg, 0.500 mmol) with TMSCN (75.0 μL, 0.600 mmol) and $HPO(OEt)_2$ (83.0 μL, 0.650 mmol) afforded the α-amino-α-cyanophosphonate **1aa** (137 mg, yield: 89%) after flash column chromatography on silica gel (elution with EtOAc/hexane = 1:2) as a pale yellow soild. MP: 69–70 °C; IR (film): 3280, 2984, 2222, 1255, 1021, 758, 698, 580 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.74–7.63 (m, 2H), 7.47–7.35 (m, 3H), 5.99–5.82 (m, 1H), 5.33–5.22 (m, 1H), 5.19–5.09 (m, 1H), 4.22–4.13 (m, 2H), 4.10–3.91 (m, 2H),

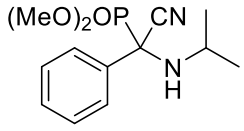
3.39–3.28 (m, 1H), 3.12–3.01 (m, 1H), 2.45–2.20 (m, 1H), 1.34 (t, J = 7.0 Hz, 3H), 1.21 (t, J = 7.0 Hz, 3H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ 134.7, 131.3 (d, $J_{C\text{-}P}$ = 8.4 Hz), 129.2 (d, $J_{C\text{-}P}$ = 3.2 Hz), 128.6 (d, $J_{C\text{-}P}$ = 2.7 Hz), 127.6 (d, $J_{C\text{-}P}$ = 4.4 Hz), 117.1 (d, $J_{C\text{-}P}$ = 2.9 Hz), 117.0, 65.3 (d, $J_{C\text{-}P}$ = 7.1 Hz), 65.2 (d, $J_{C\text{-}P}$ = 7.5 Hz), 63.4 (d, $J_{C\text{-}P}$ = 157.4 Hz), 47.2 (d, $J_{C\text{-}P}$ = 13.3 Hz), 16.2 (d, $J_{C\text{-}P}$ = 5.6 Hz), 16.2 (d, $J_{C\text{-}P}$ = 5.6 Hz) ppm; ^{31}P NMR (202 MHz, $CDCl_3$) δ 14.0 ppm; HRMS (ESI) calcd for $C_{15}H_{21}N_2O_3PNa$ [M+Na^+]: 331.1182, found: 331.1185.

Methyl 3-((cyano(diethoxyphosphoryl)(phenyl)methyl)amino)propanoate (1ad)



Following the general procedure, the reaction of amide **2ad** (43.0 mg, 0.500 mmol) with TMSCN (75.0 μL, 0.600 mmol) and $HPO(OEt)_2$ (83.0 μL, 0.650 mmol) afforded the α-amino-α-cyanophosphonate **1ad** (98.7 mg, yield: 68%) after flash column chromatography on silica gel (elution with EtOAc/hexane = 1:2) as a pale yellow oil. IR (film): 3310, 2927, 2355, 1666, 1462, 1396, 1201, 1055, 997, 753, 546 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 4.32–4.15 (m, 4H), 3.32–3.24 (m, 1H), 1.40–1.34 (m, 6H), 1.18 (s, 9H), 1.14 (t, J = 6.3 Hz, 6H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ 117.1 (d, $J_{C\text{-}P}$ = 4.6 Hz), 64.5 (d, $J_{C\text{-}P}$ = 148.3 Hz), 64.3 (d, $J_{C\text{-}P}$ = 8.1 Hz), 63.9 (d, $J_{C\text{-}P}$ = 7.8 Hz), 47.9 (d, $J_{C\text{-}P}$ = 1.9 Hz), 39.8 (d, $J_{C\text{-}P}$ = 4.0 Hz), 26.2 (d, $J_{C\text{-}P}$ = 4.5 Hz), 24.9 (d, $J_{C\text{-}P}$ = 1.8 Hz), 24.6, 16.4 (d, $J_{C\text{-}P}$ = 5.6 Hz), 16.3 (d, $J_{C\text{-}P}$ = 5.8 Hz) ppm; ^{31}P NMR (202 MHz, $CDCl_3$) δ 18.0 ppm; HRMS (ESI) calcd for $C_{13}H_{27}N_2O_3PNa$ [M+Na^+]: 313.1652, found: 313.1660.

Dimethyl (cyano(isopropylamino)(phenyl)methyl)phosphonate (1ae)



Following the general procedure, the reaction of amide **2a** (81.6 mg, 0.500 mmol) with TMSCN (75.0 μL, 0.600 mmol) and $HPO(OMe)_2$ (60.0 μL, 0.650 mmol) afforded the α-amino-α-cyanophosphonate **1ae** (130 mg, yield: 92%) after flash column chromatography on silica gel (elution with EtOAc/hexane = 1:2) as a pale yellow oil. IR (film): 3302, 2964, 2857, 2359, 2341, 1782, 1693, 1385, 1033, 839, 699, 580 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.77–7.70 (m, 2H), 7.45–7.36 (m, 3H), 3.89–3.82 (m, 3H), 3.61–3.55 (m, 3H), 3.00–2.89 (m, 1H), 2.15–2.06 (m, 1H), 1.23 (d, J = 6.3 Hz, 3H), 0.92 (d, J = 6.4 Hz, 3H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ 132.2 (d, $J_{C\text{-}P}$ = 8.2 Hz), 129.2 (d, $J_{C\text{-}P}$ = 3.1 Hz), 128.5 (d, $J_{C\text{-}P}$ = 2.8 Hz), 127.9 (d, $J_{C\text{-}P}$= 4.6 Hz), 117.9 (d, $J_{C\text{-}P}$ = 4.7 Hz), 62.4 (d, $J_{C\text{-}P}$ = 156.1 Hz), 55.6 (d, $J_{C\text{-}P}$ = 7.2 Hz), 55.5 (d, $J_{C\text{-}P}$ = 7.4 Hz), 46.8 (d, $J_{C\text{-}P}$ = 13.3 Hz), 24.7, 23.5 ppm; ^{31}P NMR (202 MHz, $CDCl_3$) δ 16.8 ppm; HRMS (ESI) calcd for $C_{13}H_{19}N_2O_3PNa$ [M+Na^+]: 305.1026, found: 305.1030.

Diisopropyl (cyano(isopropylamino)(phenyl)methyl)phosphonate (1af)

Following the general procedure, the reaction of amide **2a** (81.6 mg, 0.500 mmol) with TMSCN (75.0 μL, 0.600 mmol) and $HPO(O^iPr)_2$ (106 μL, 0.650 mmol) afforded the α-amino-α-cyanophosphonate **1af** (144 mg, yield: 85%) after flash column chromatography on silica gel (elution with EtOAc/hexane = 1:2) as a pale yellow oil. IR (film): 3316, 2979, 2357, 1639, 1385, 1250, 1009, 697, 584 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.76–7.69 (m, 2H), 7.41–7.32 (m, 3H), 4.87–4.74 (m, 1H), 4.54–4.39 (m, 1H), 3.05–2.86 (m, 1H), 2.15–2.02 (m, 1H), 1.39 (d, J = 6.2 Hz, 3H), 1.33 (d, J = 6.2 Hz, 3H), 1.24–1.18 (m, 6H), 1.03 (d, J = 6.2 Hz, 3H), 0.89 (d, J = 6.4 Hz, 3H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ 132.9 (d, $J_{C\text{-}P}$ = 7.9 Hz), 128.9 (d, $J_{C\text{-}P}$ = 3.1 Hz), 128.1 (d, $J_{C\text{-}P}$ = 2.7 Hz), 128.1 (d, $J_{C\text{-}P}$ = 4.8 Hz), 118.3 (d, $J_{C\text{-}P}$ = 5.3 Hz), 74.2 (d, $J_{C\text{-}P}$ = 5.2 Hz), 74.1 (d, $J_{C\text{-}P}$ = 5.4 Hz), 62.9 (d, $J_{C\text{-}P}$ = 156.2 Hz), 46.9 (d, $J_{C\text{-}P}$ = 13.5 Hz),

24.7, 24.0 (d, $J_{C\text{-}P}$ = 3.2 Hz), 23.9 (d, $J_{C\text{-}P}$ = 3.3 Hz), 23.6, 23.5 (d, $J_{C\text{-}P}$ = 5.9 Hz), 23.1 (d, $J_{C\text{-}P}$ = 6.2 Hz) ppm; ^{31}P NMR (202 MHz, $CDCl_3$) δ 12.9 ppm; HRMS (ESI) calcd for $C_{17}H_{27}N_2O_3PNa$ [M+Na^+]: 361.1652, found: 361.1660.

6. Gram-scale Synthesis of 1z

Trifluoromethanesulfonic anhydride (Tf_2O, 1.00 mL, 5.50 mmol) was added dropwise to a cooled solution of amides **2z** (1.06 g, 5.00 mmol) and 2-fluoropyridine (500 μL, 6.00 mmol) in dichloromethane (0.20 M) at 0 °C. After the mixture was stirred for 10 min, TMSCN (750 μL, 6.00 mmol) was added dropwise at 0 °C. The resulting mixture was warmed to rt and stirred for 3 h. $HPO(OEt)_2$ (830 μL,, 6.50 mmol) and K_2CO_3 (1.38 g, 10.0 mmol) were then added to the above mixture and stirred for 10 h. The reaction was quenched with saturated aqueous $NaHCO_3$ solution (10 mL) at room temperature. The organic layer was separated and the aqueous phase was extracted with dichloromethane (3 × 30 mL). The combined organic layers were washed with brine (3 × 10 mL), dried over anhydrous $MgSO_4$, filtered and concentrated under reduced pressure. The residue was purified by flash column chromatography on silica gel (elution: hexane/EtOAc) to afford the desired α-amino-α-cyanophosphonates **1z** (1.43 g, yield: 80%).

7. References

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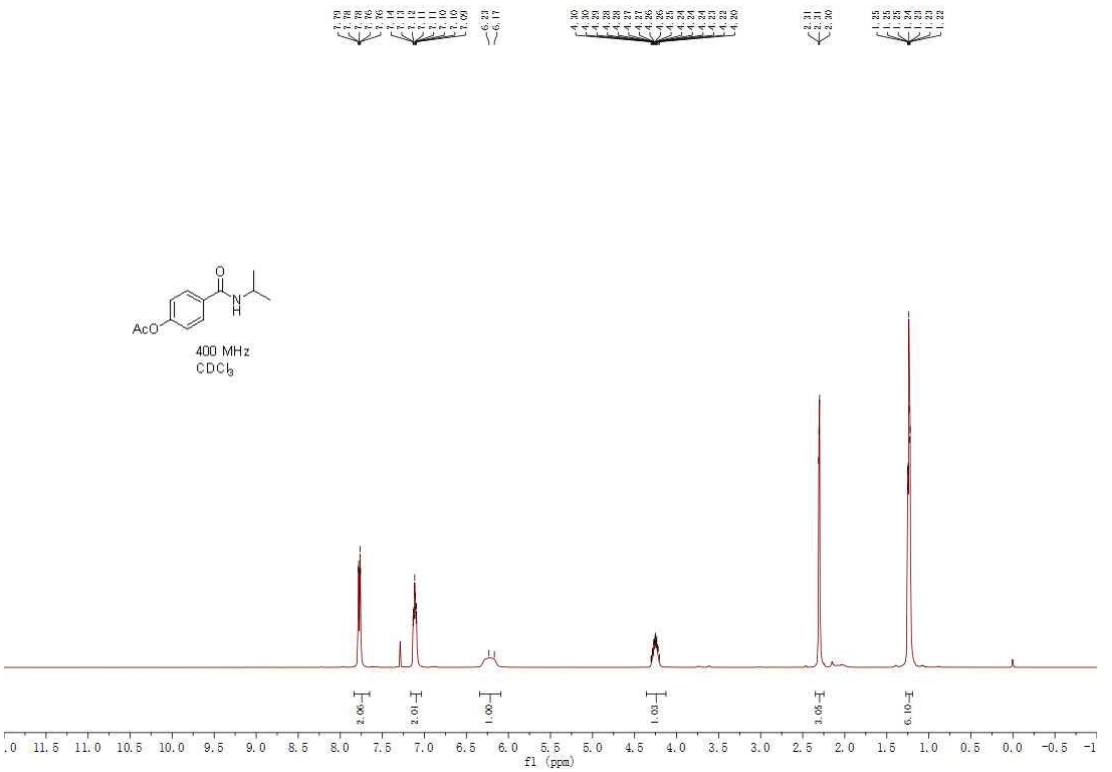
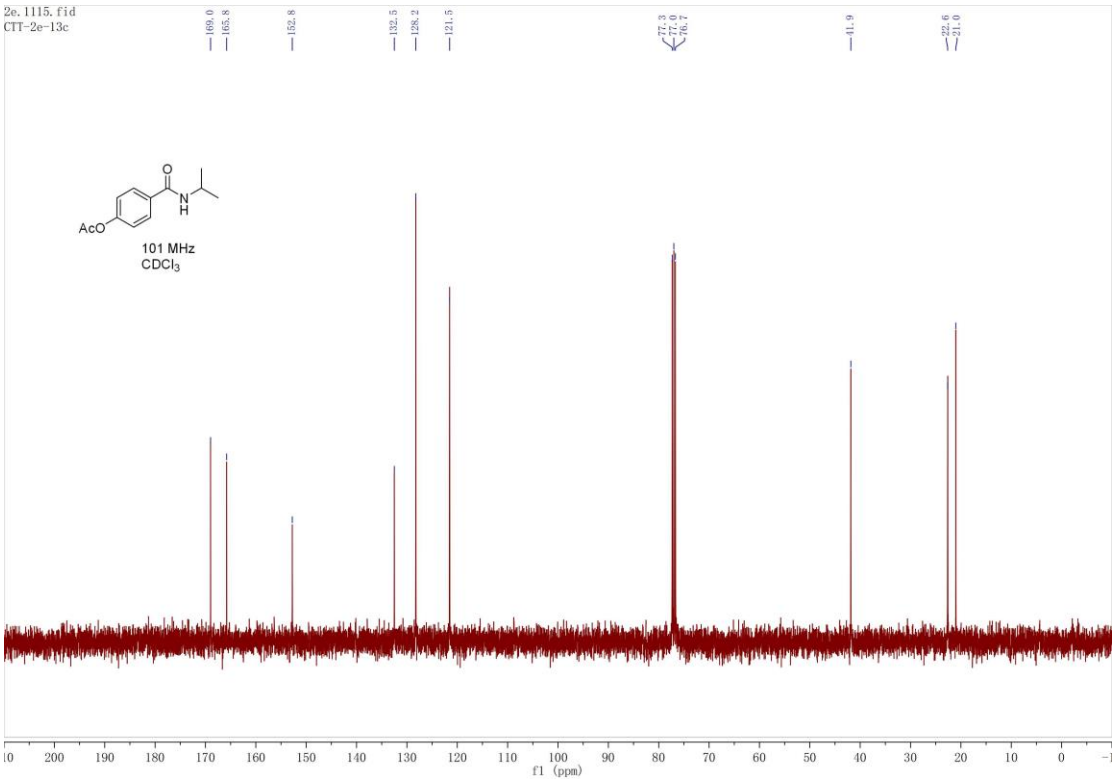
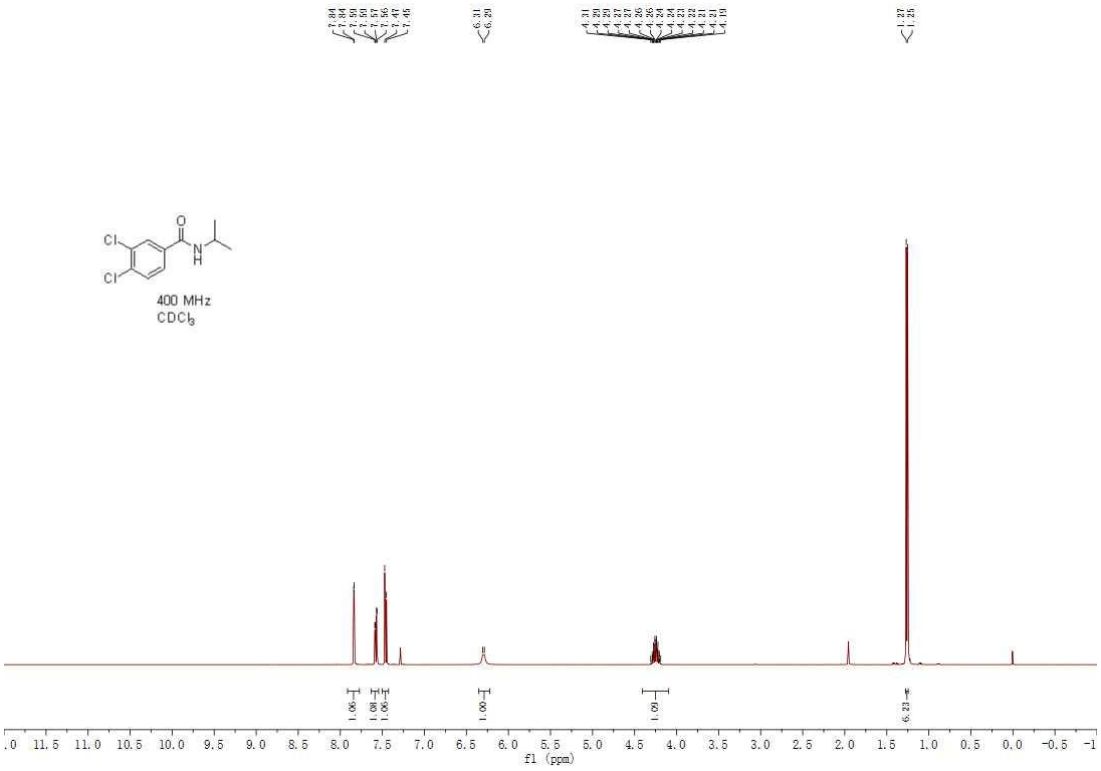
8. $^{1}H/ ^{13}C/ ^{31}P/ ^{19}F$ NMR Spectra of New Compounds

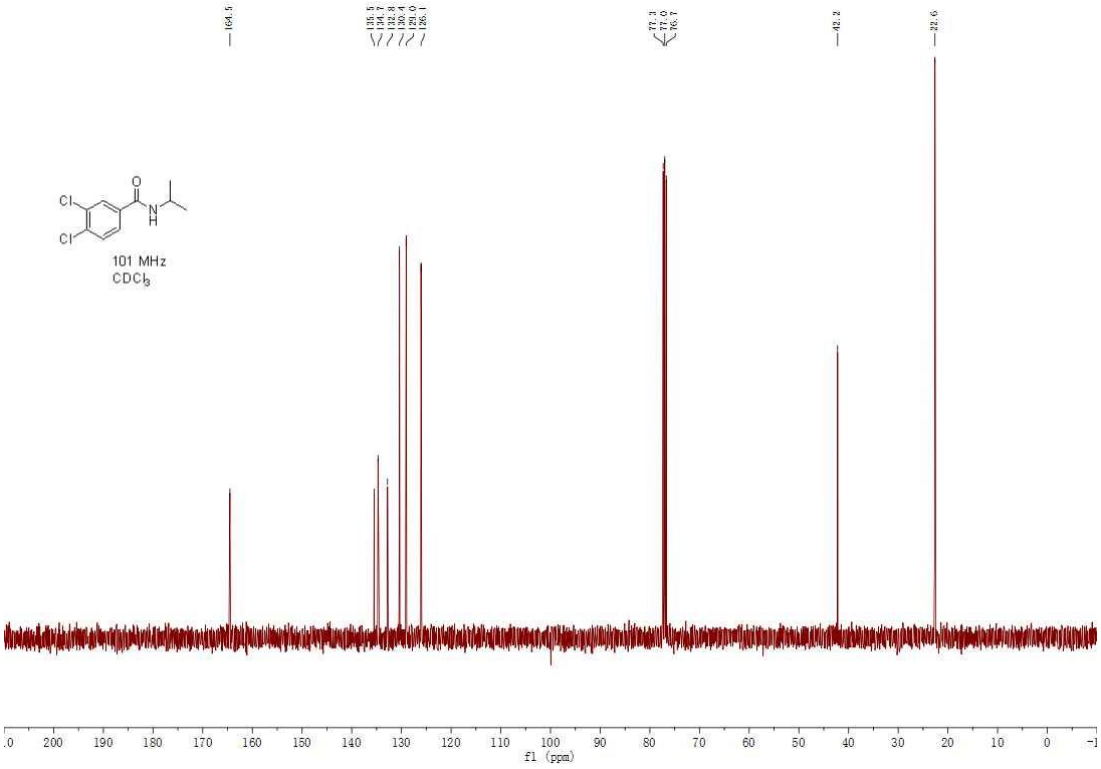
4-(Isopropylcarbamoyl)phenyl acetate (2e)



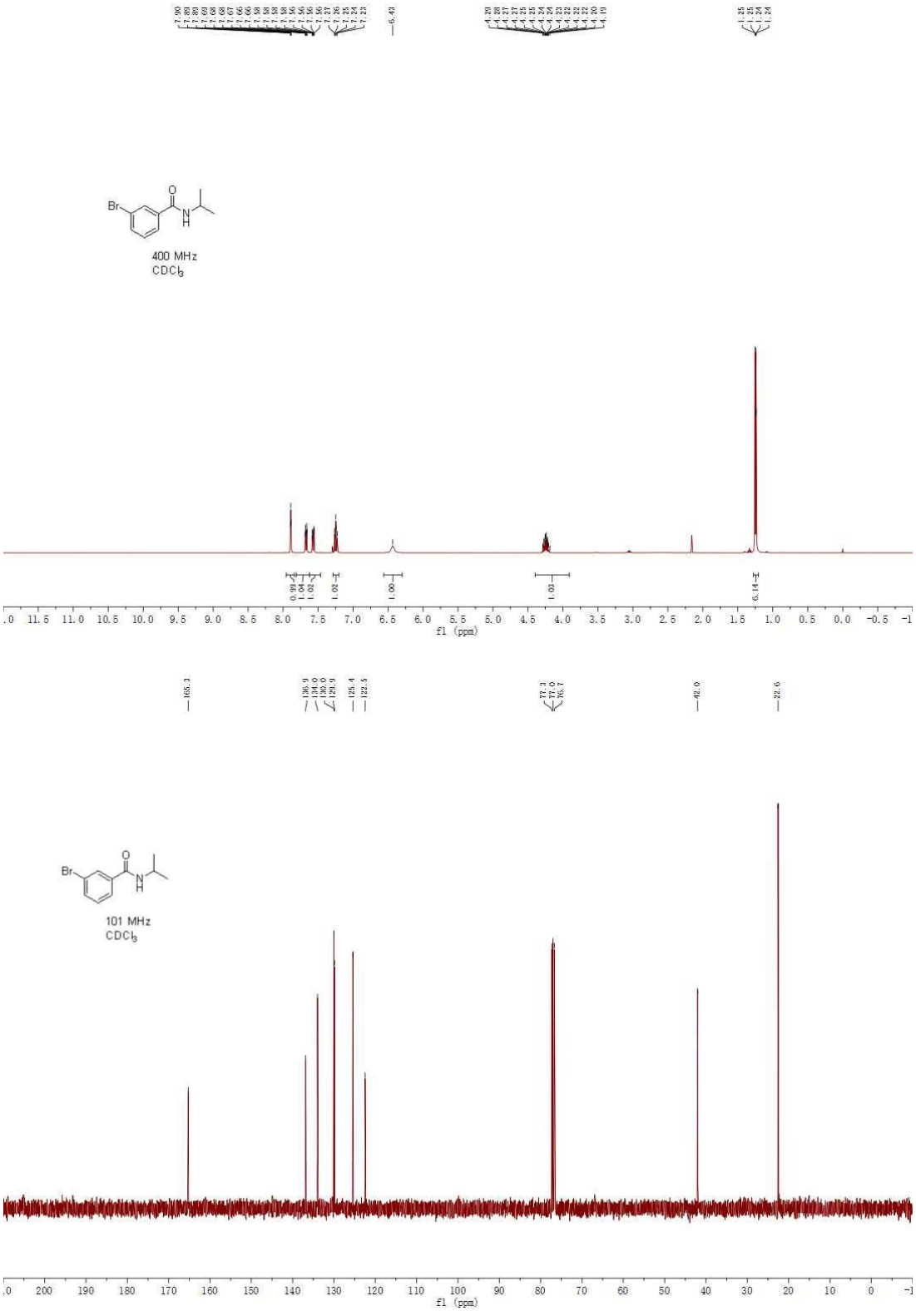


3,4-Dichloro-N-isopropylbenzamide (2g)

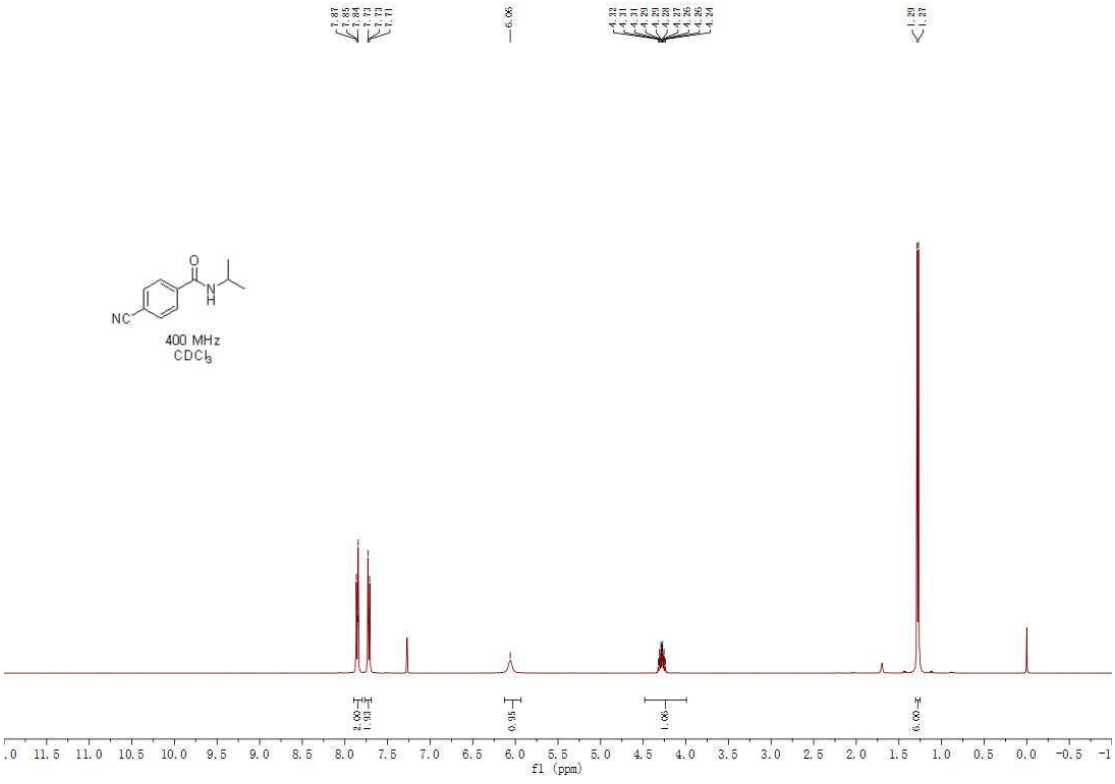


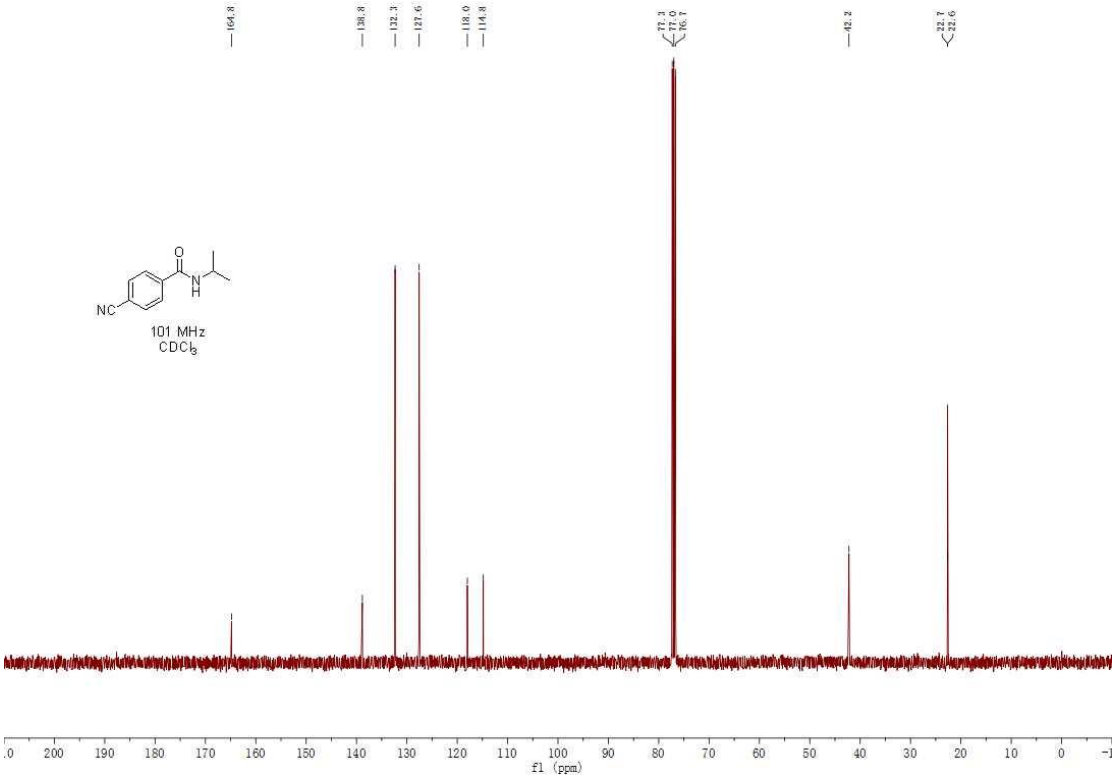


3-Bromo-*N*-isopropylbenzamide (2i)

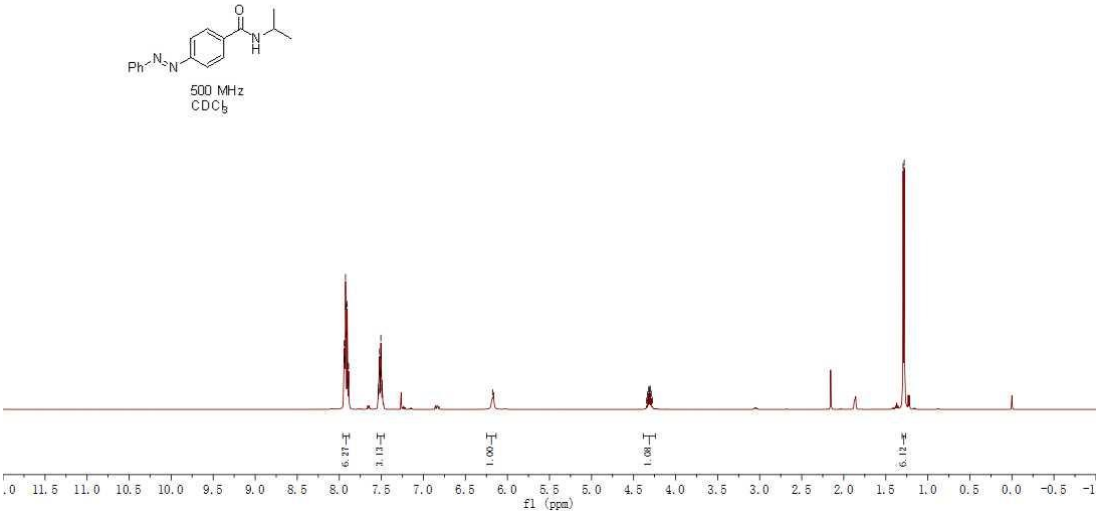


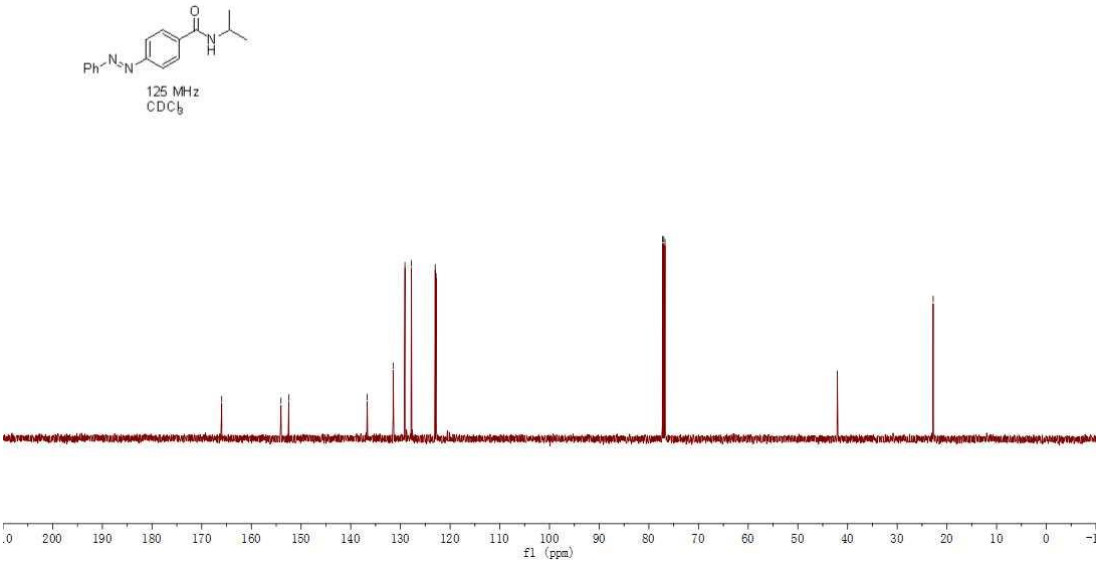
4-Cyano-*N*-isopropylbenzamide (2l)



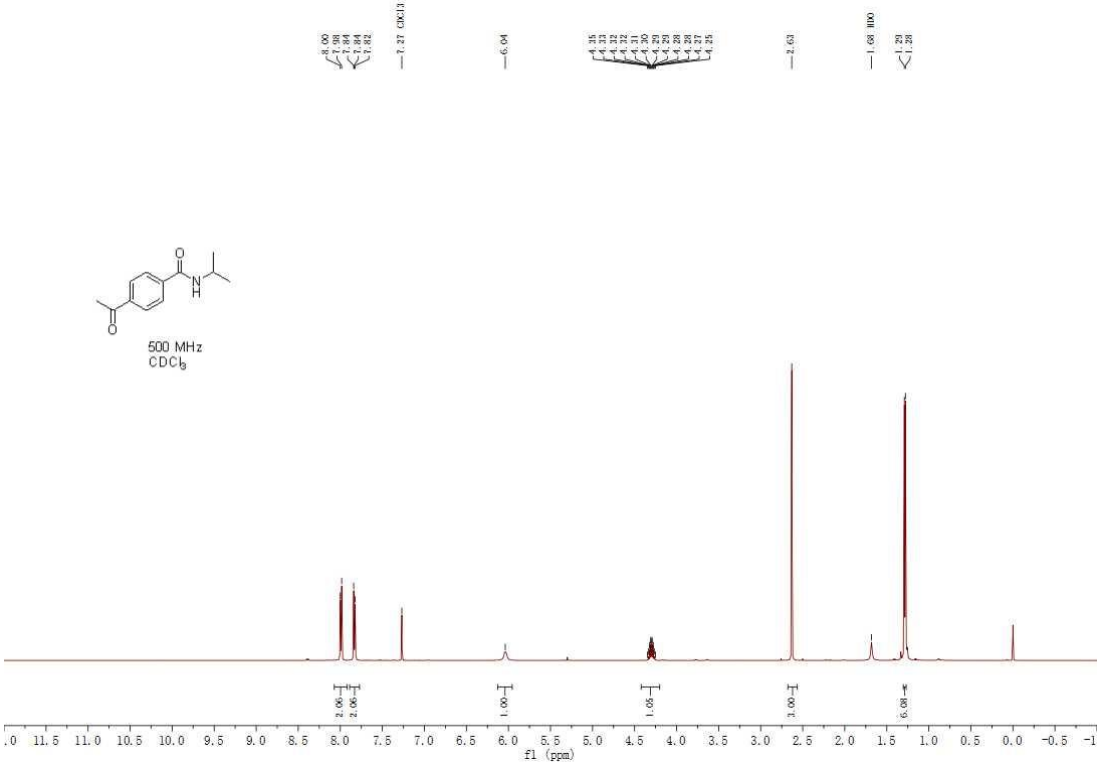


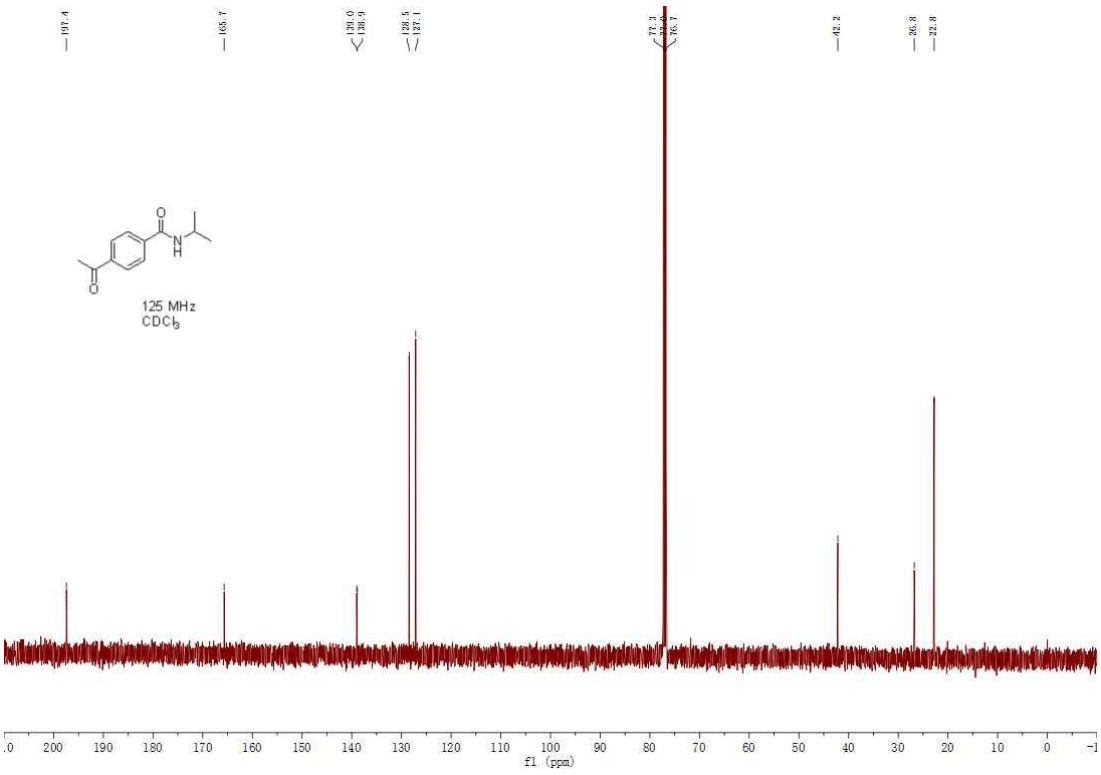
(*E*)-*N*-Isopropyl-4-(phenyldiazenyl)benzamide (2m)



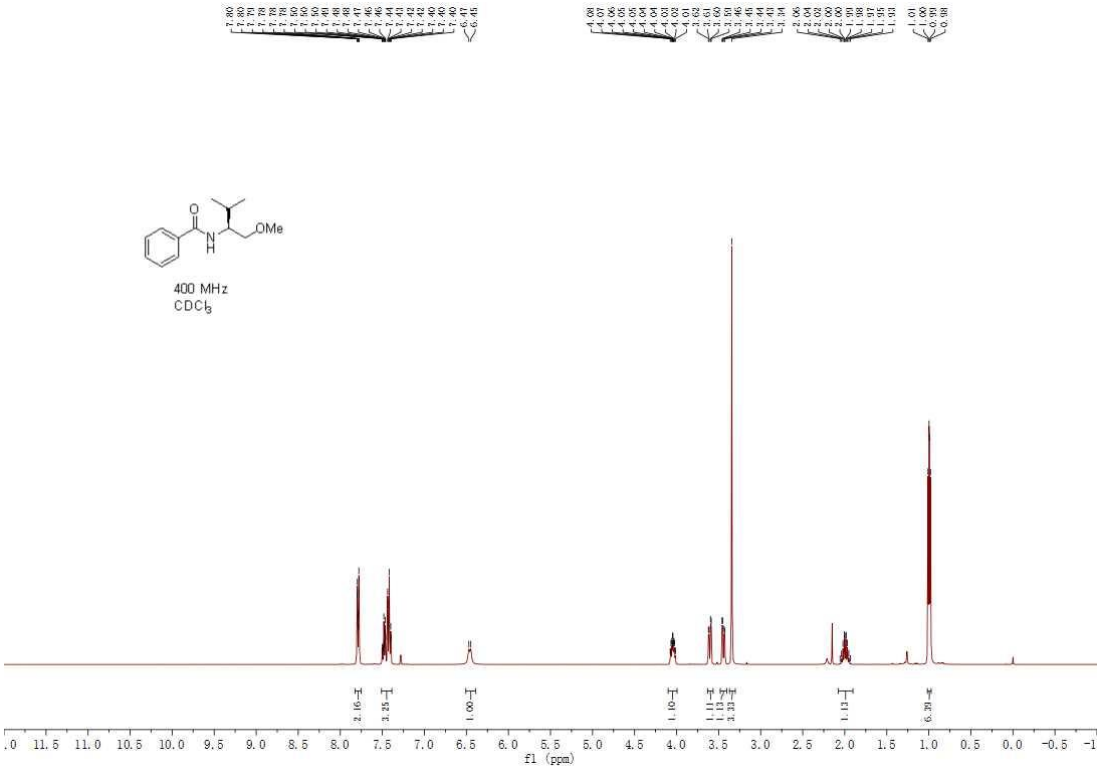


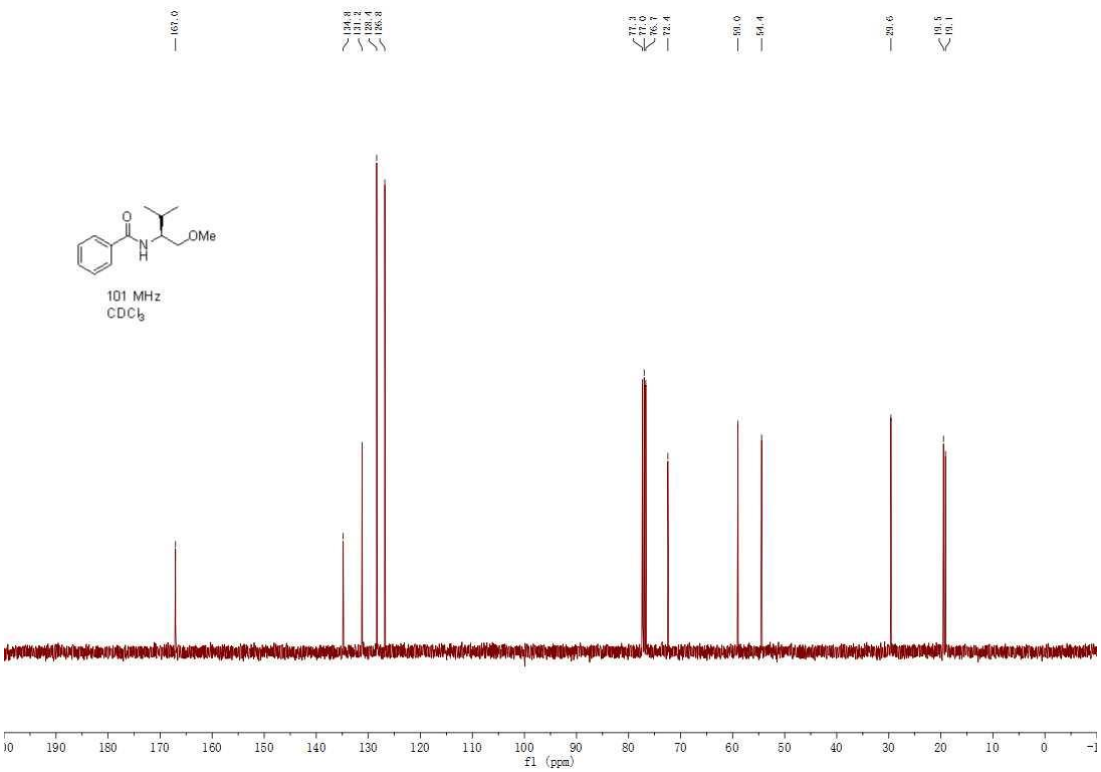
4-Acetyl-*N*-isopropylbenzamide (2n)



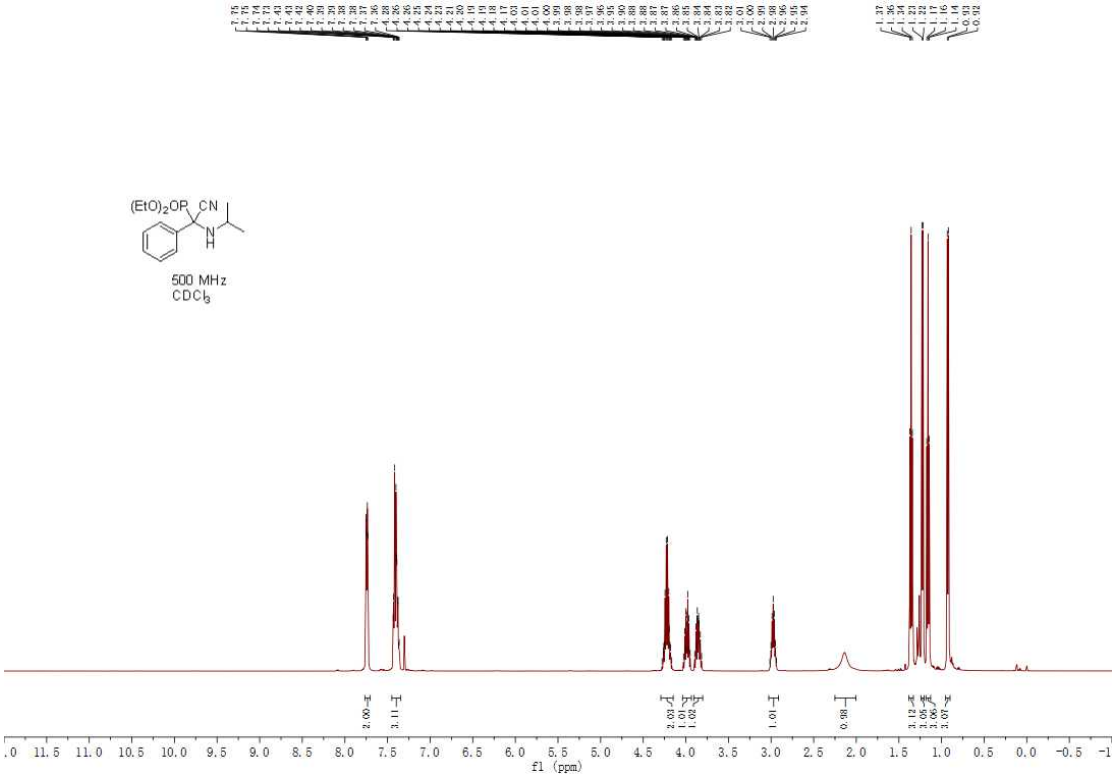


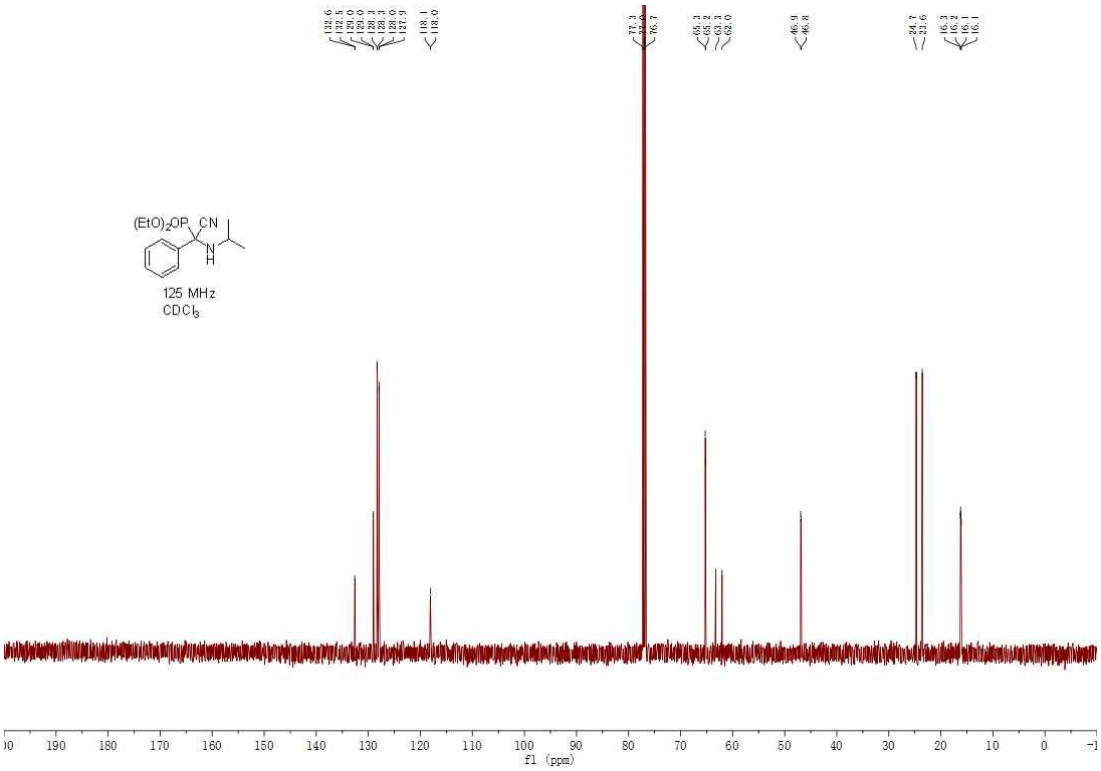
(*S*)-*N*-(1-Methoxy-3-methylbutan-2-yl)benzamide (2s)

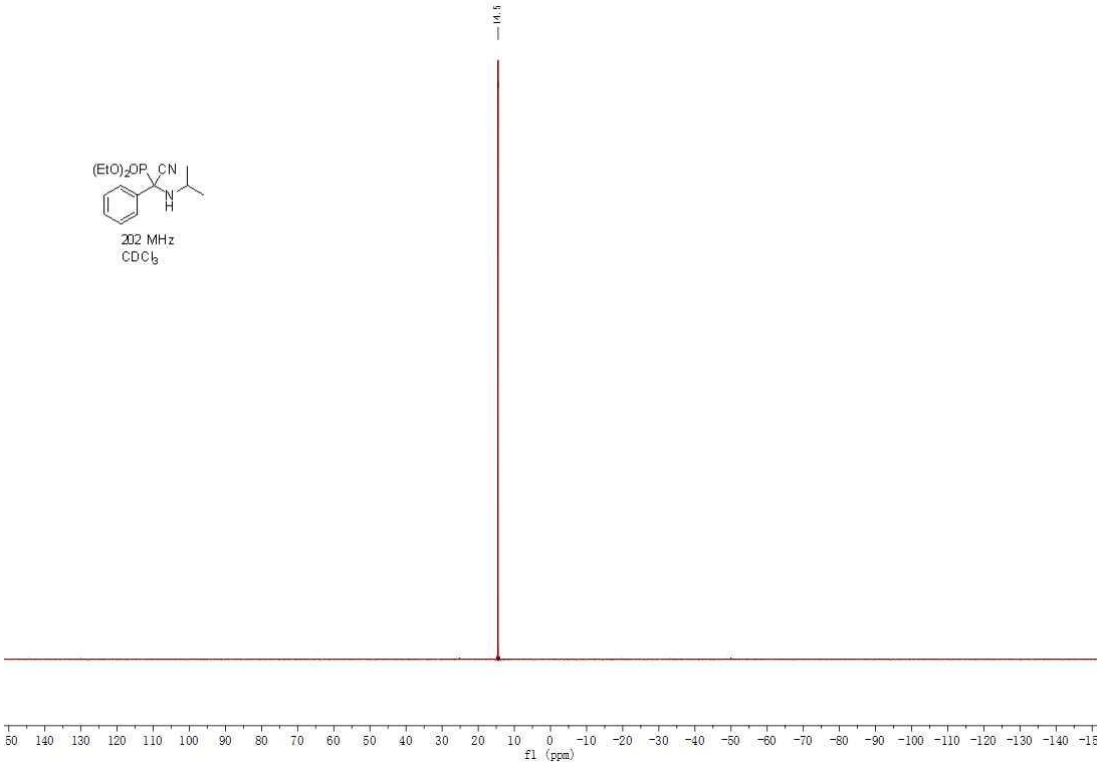




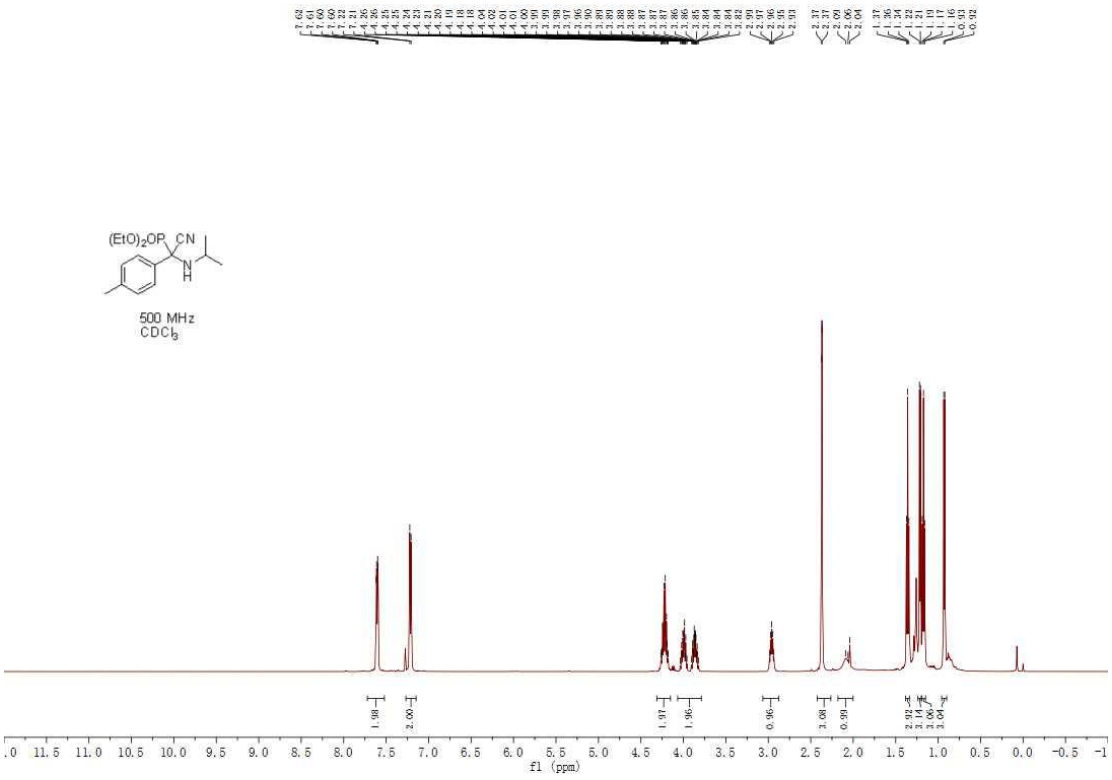
Diethyl (cyano(isopropylamino)(phenyl)methyl)phosphonate (1a)

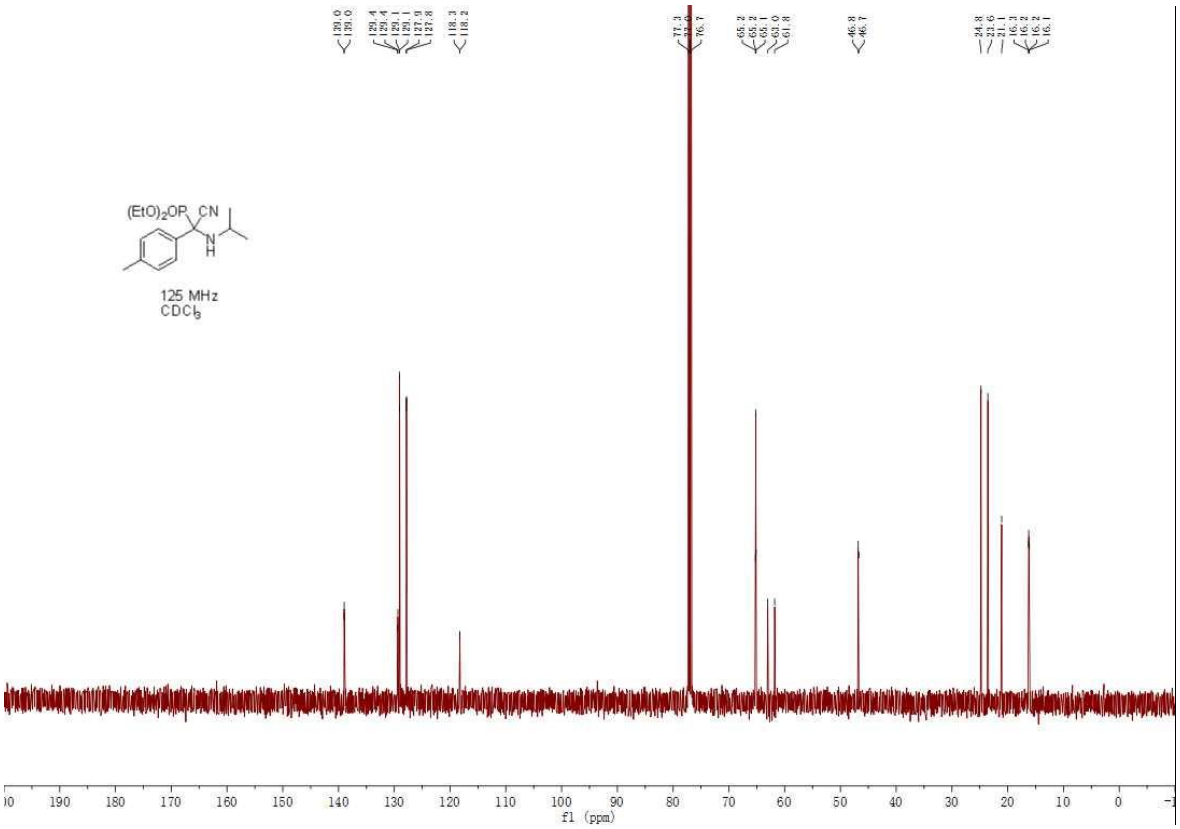






Diethyl (cyano(isopropylamino)(*p*-tolyl)methyl)phosphonate (1b)

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N
H
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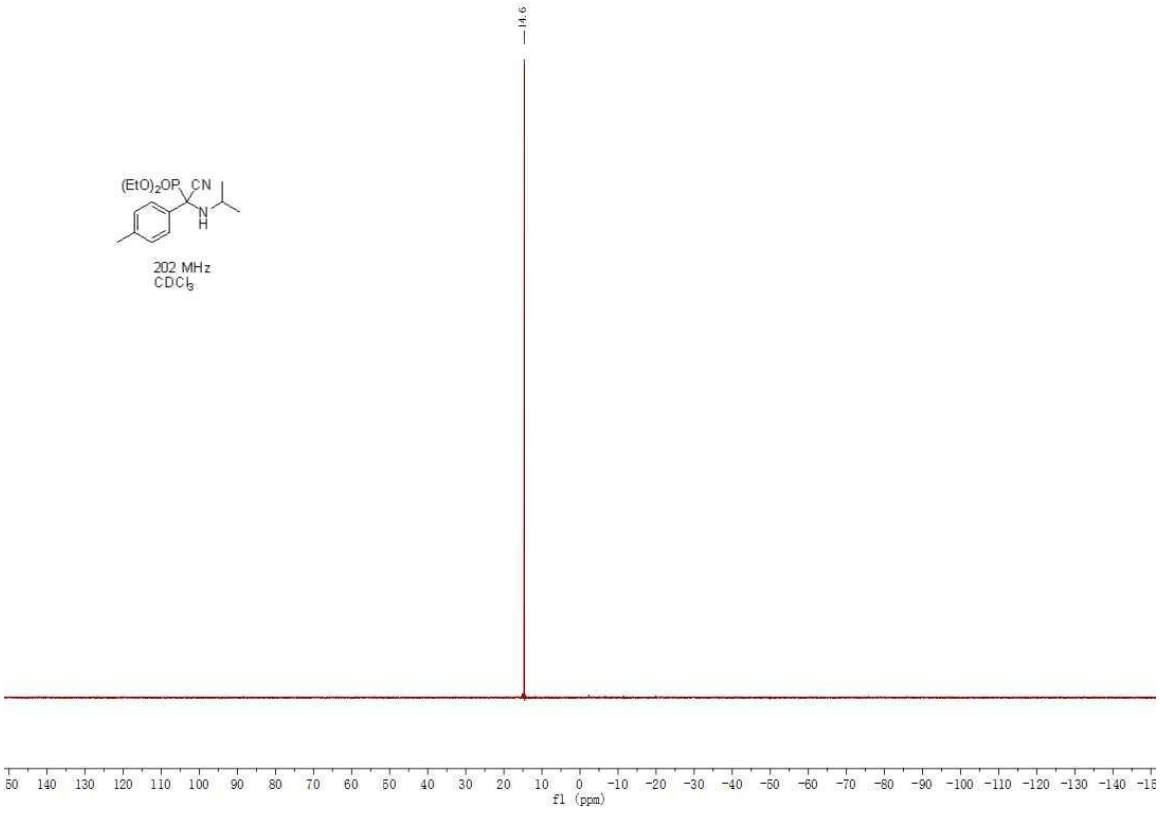
CDCl3
f1 (ppm)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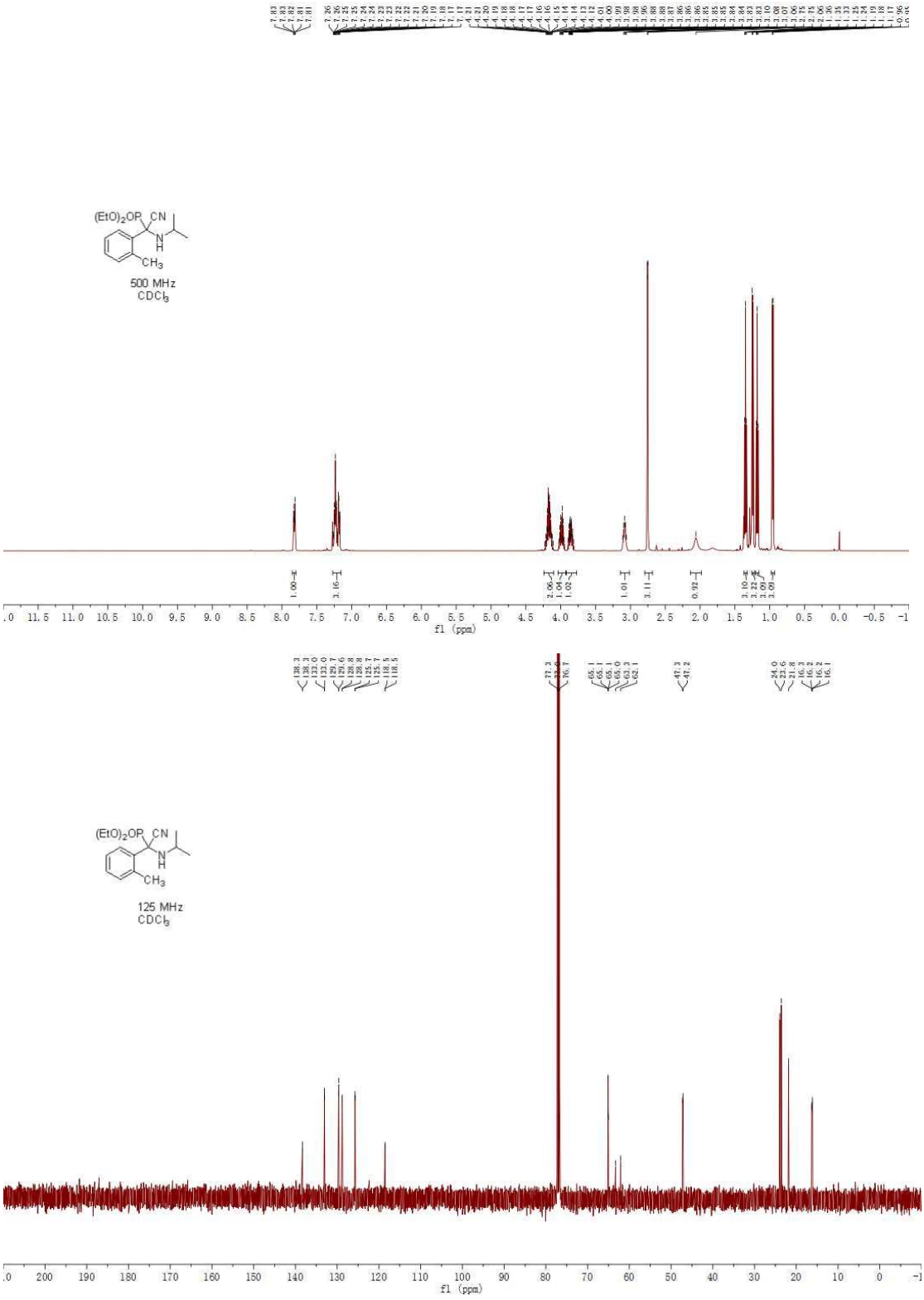
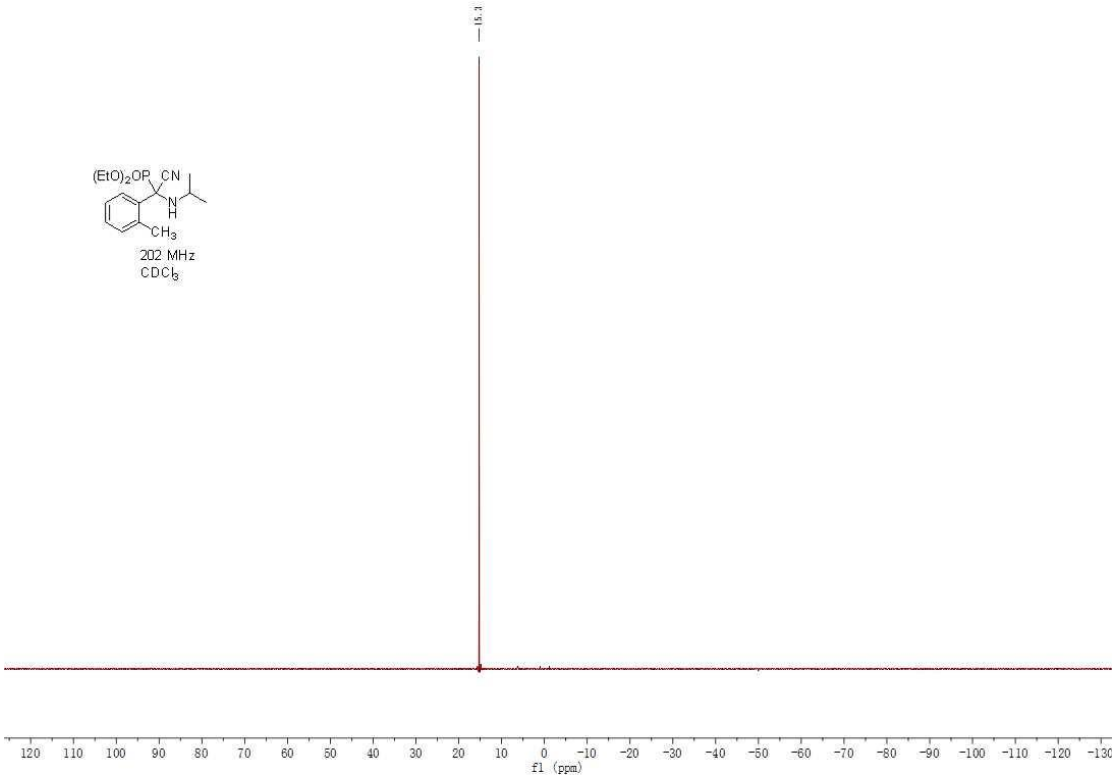
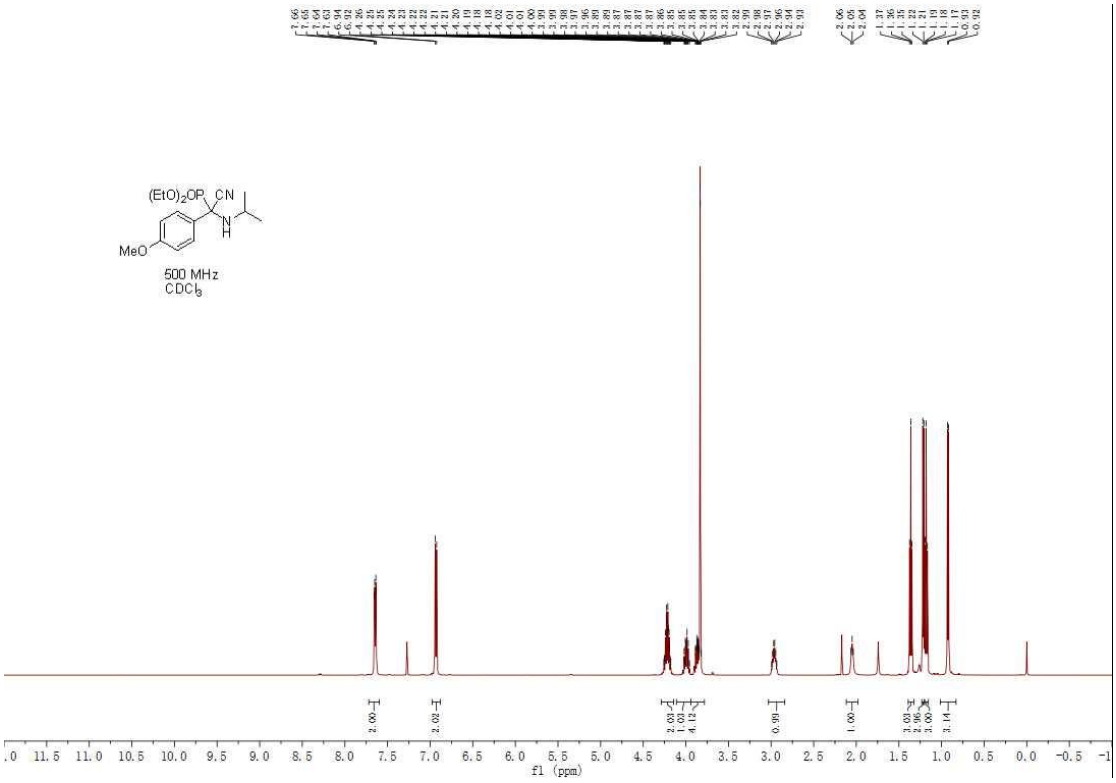
N
H
202 MHz
CDCl3
f1 (ppm)

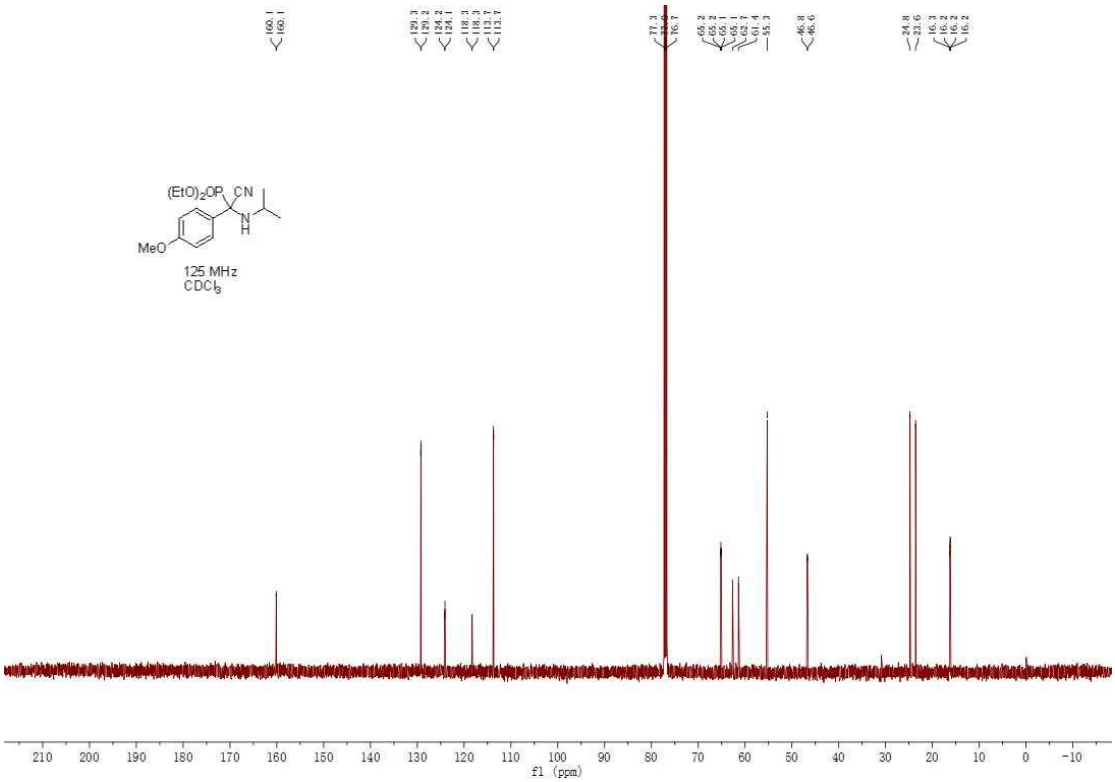
Diethyl (cyano(isopropylamino)(o-tolyl)methyl)phosphonate (1c)





Diethyl (cyano(isopropylamino)(4-methoxyphenyl)methyl)phosphonate (1d)

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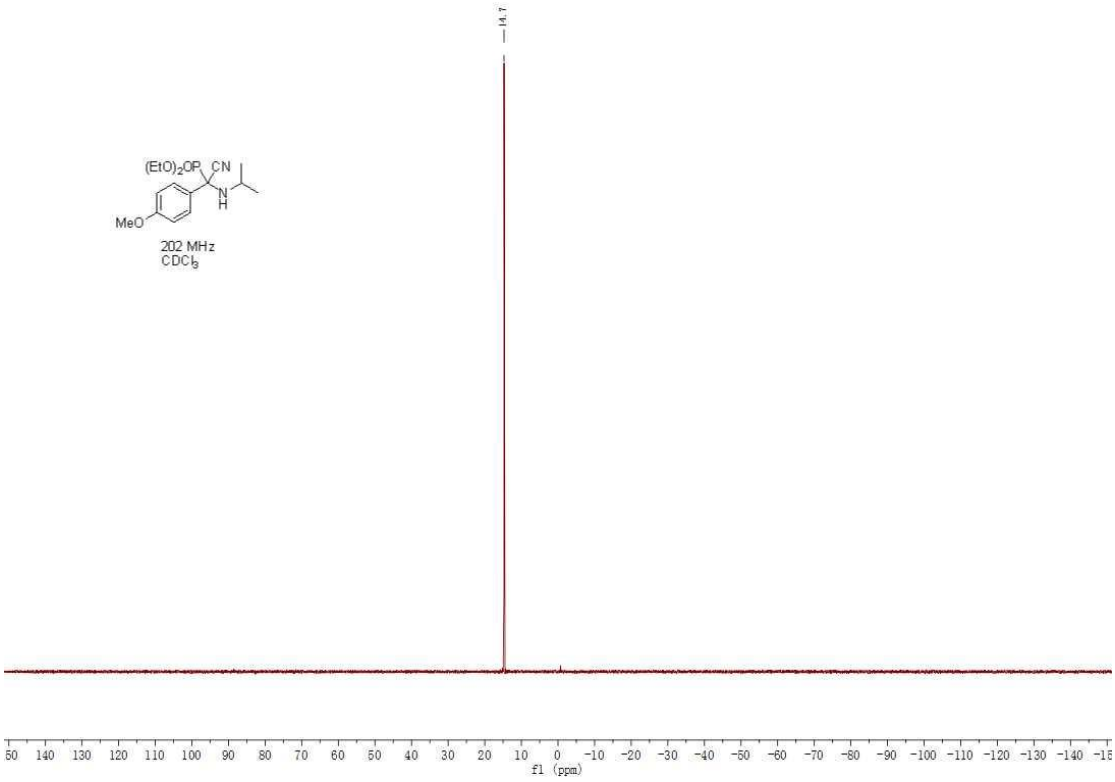
160.1
129.3
129.2
124.2
124.1
118.3
118.3
113.7
113.7
77.3
77.0
76.7
65.2
65.2
65.1
65.1
63.7
63.7
61.4
55.3
46.8
46.6
24.8
23.6
16.3
16.2
16.2
16.2
(EtO)2OP
CN
N
H
MeO
125 MHz
CDCl3
f1 (ppm)


14.7
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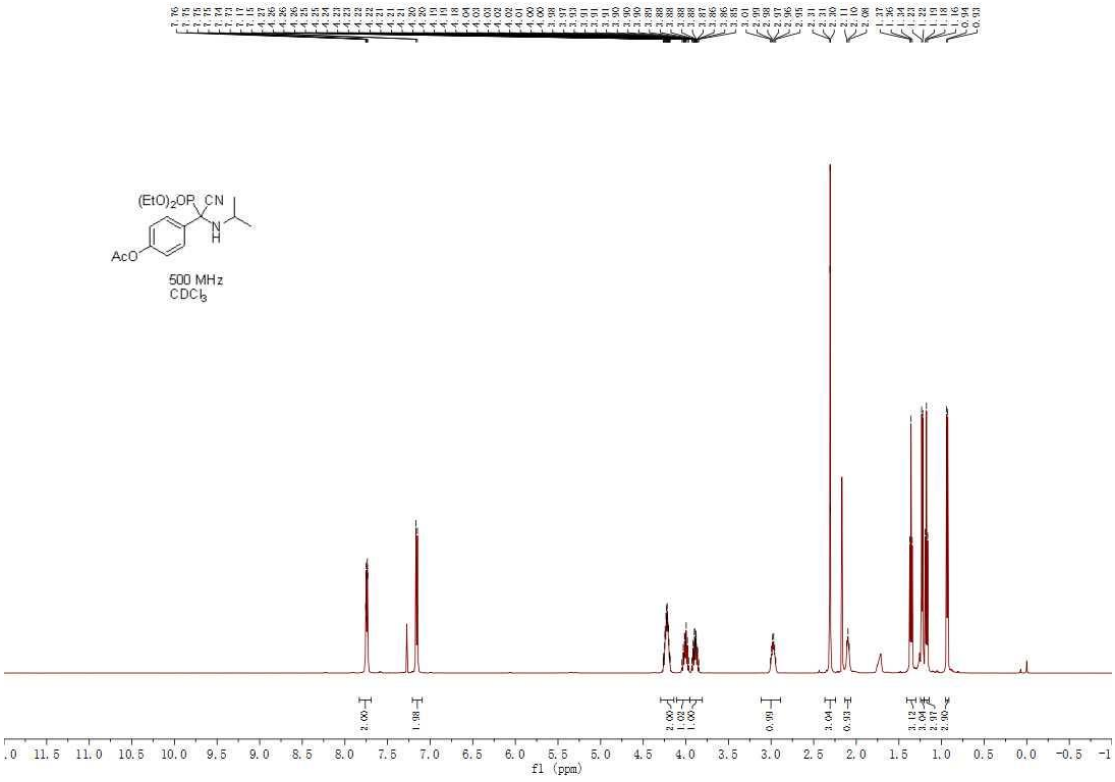
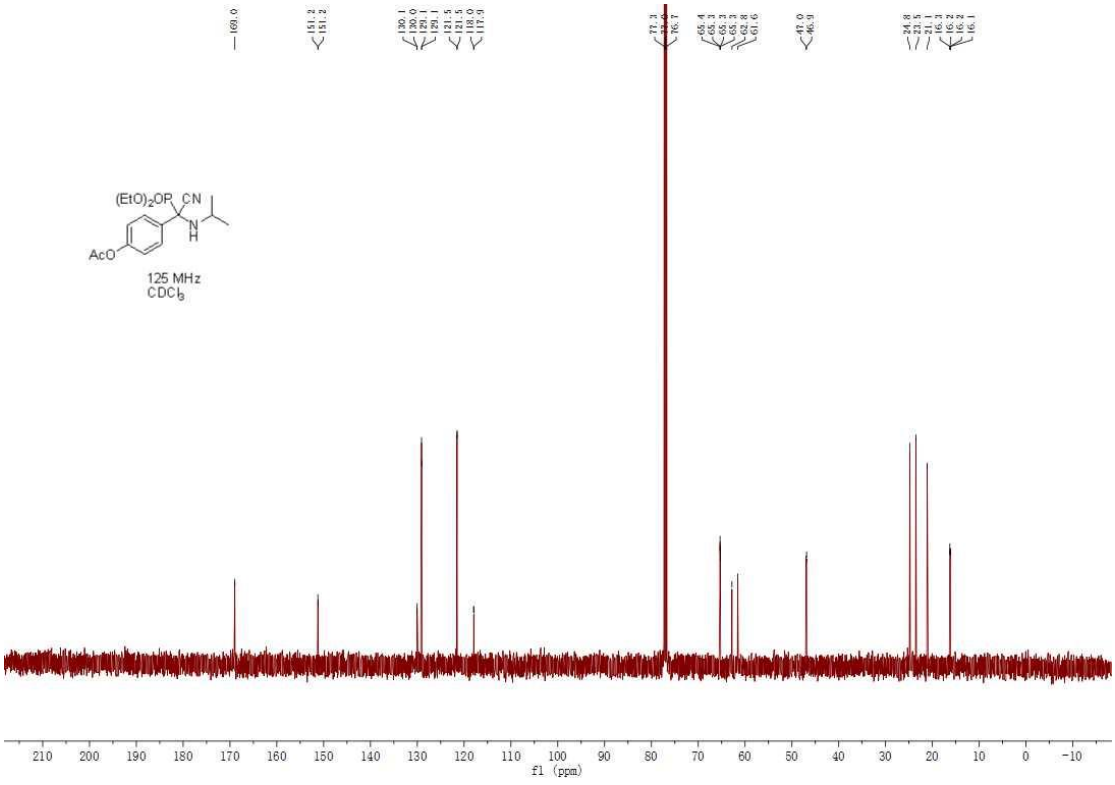
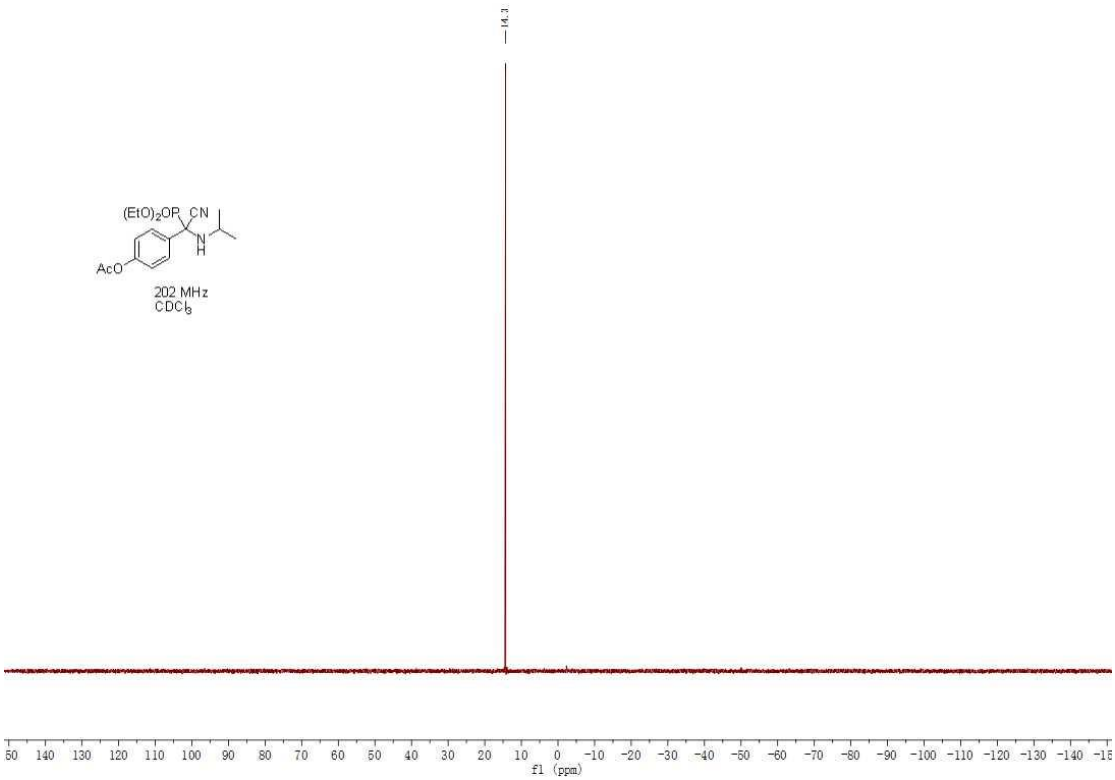
N
H
MeO
202 MHz
CDCl3
f1 (ppm)

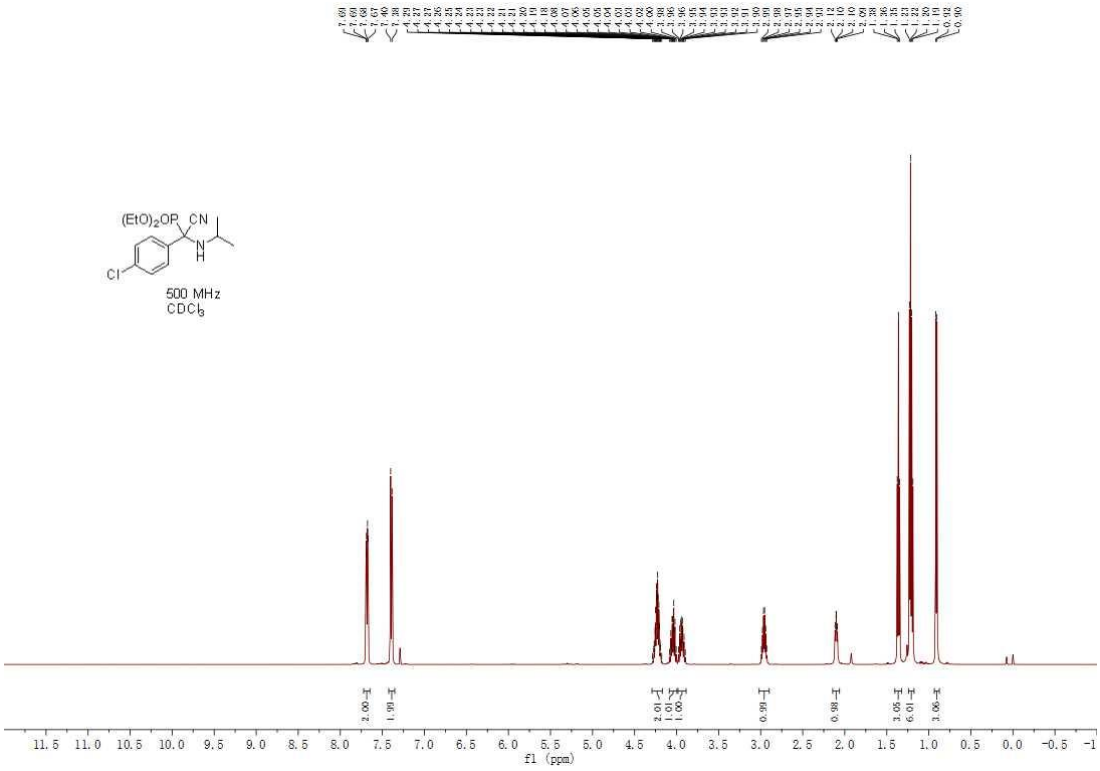
4-(Cyano(diethoxyphosphoryl)(isopropylamino)methyl)phenyl acetate (1e)

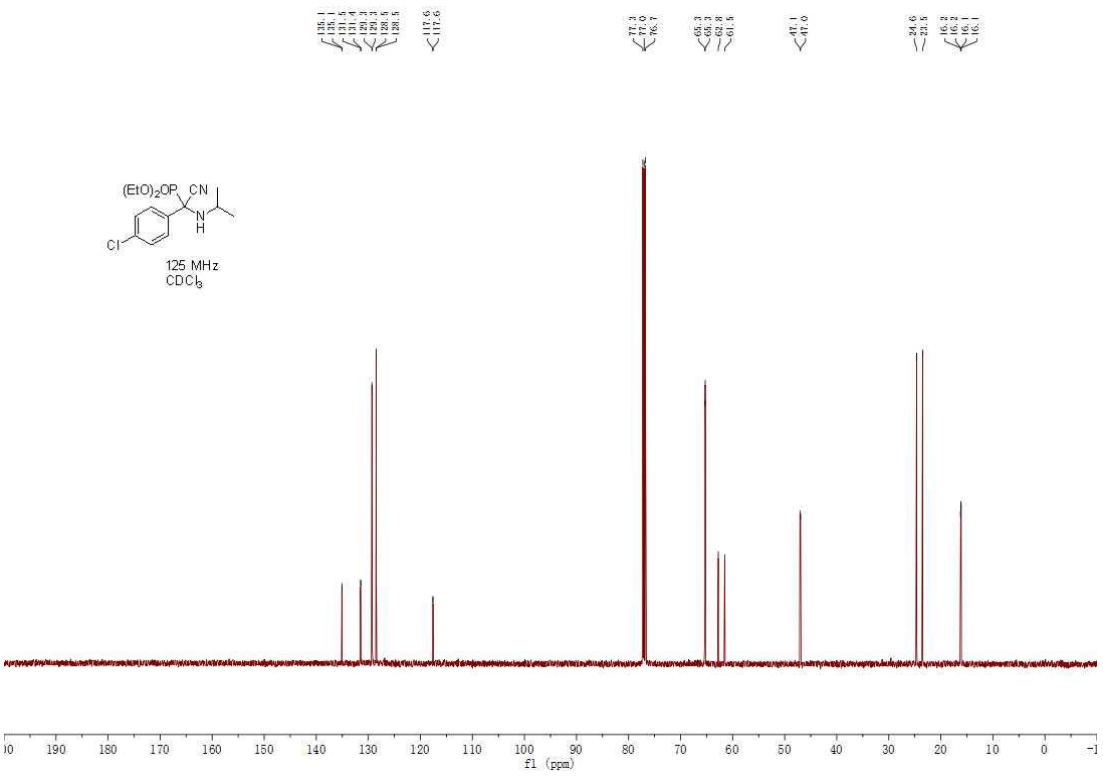






Diethyl ((4-chlorophenyl)(cyano)(isopropylamino)methyl)phosphonate (1f)

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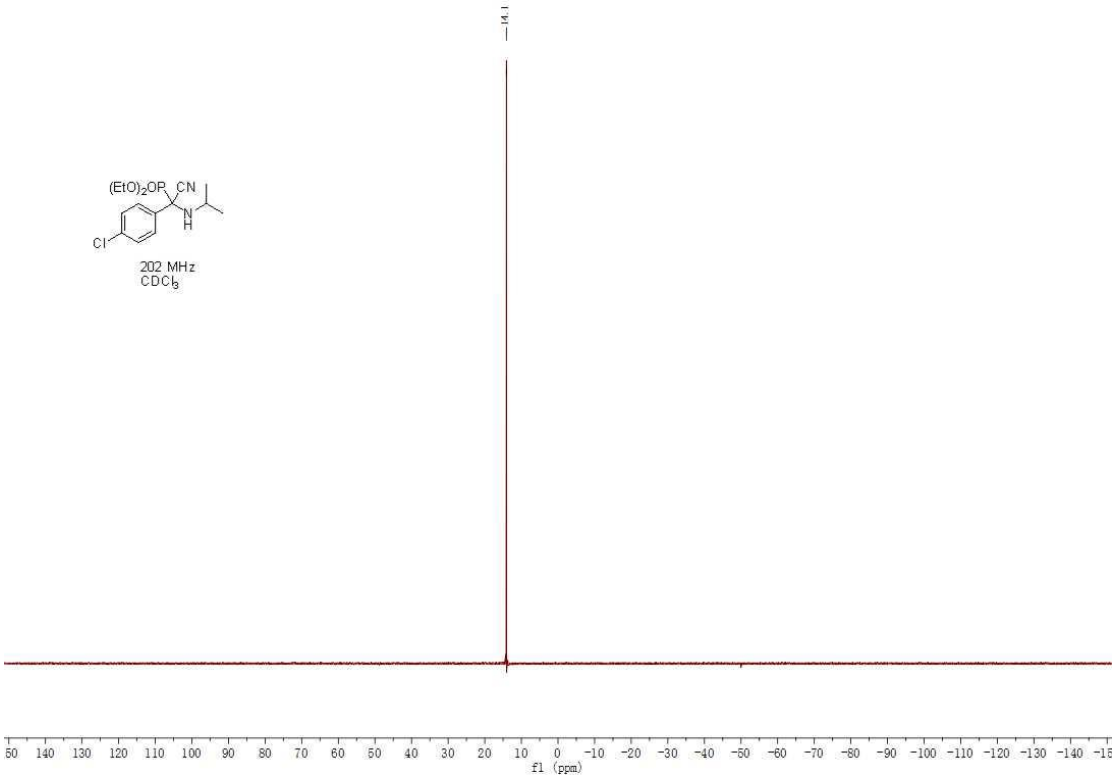
129.3
128.5
117.6
77.3
77.0
76.7
65.3
62.8
61.5
47.1
34.6
23.5
16.2
16.1
(EtO)2OP CN
N
H
Cl
125 MHz
CDCl3
f1 (ppm)


14.1
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H
Cl
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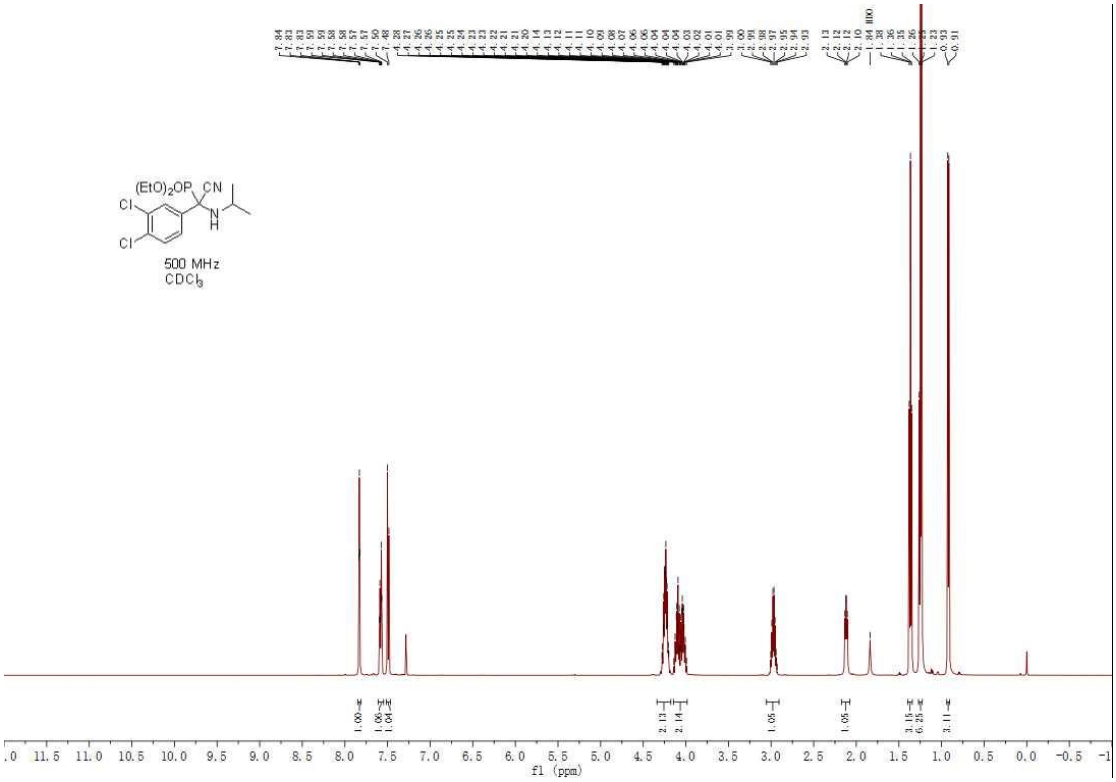
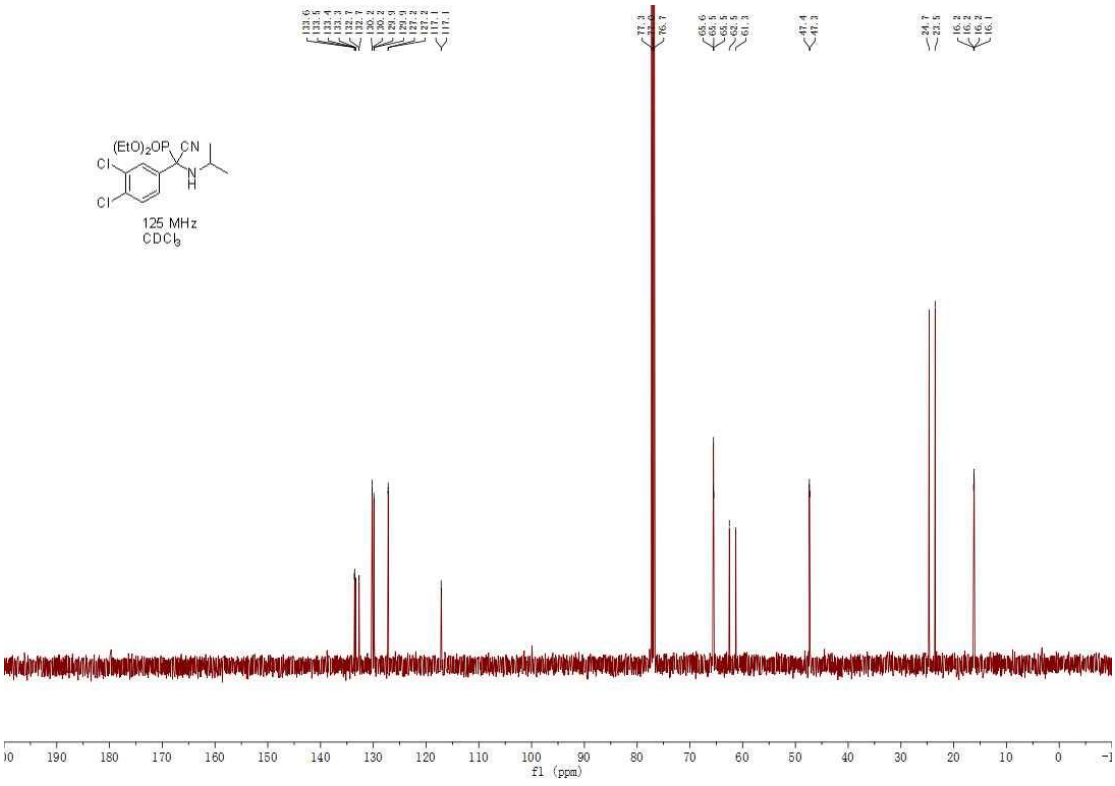
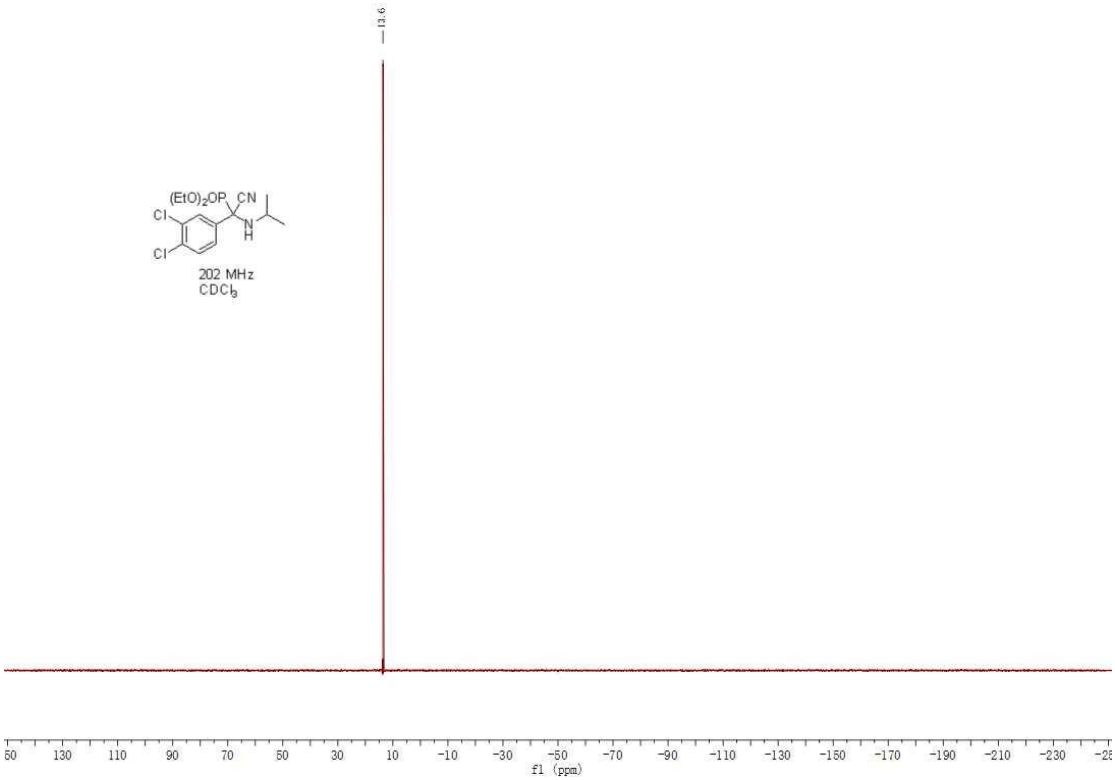
CDCl3
f1 (ppm)

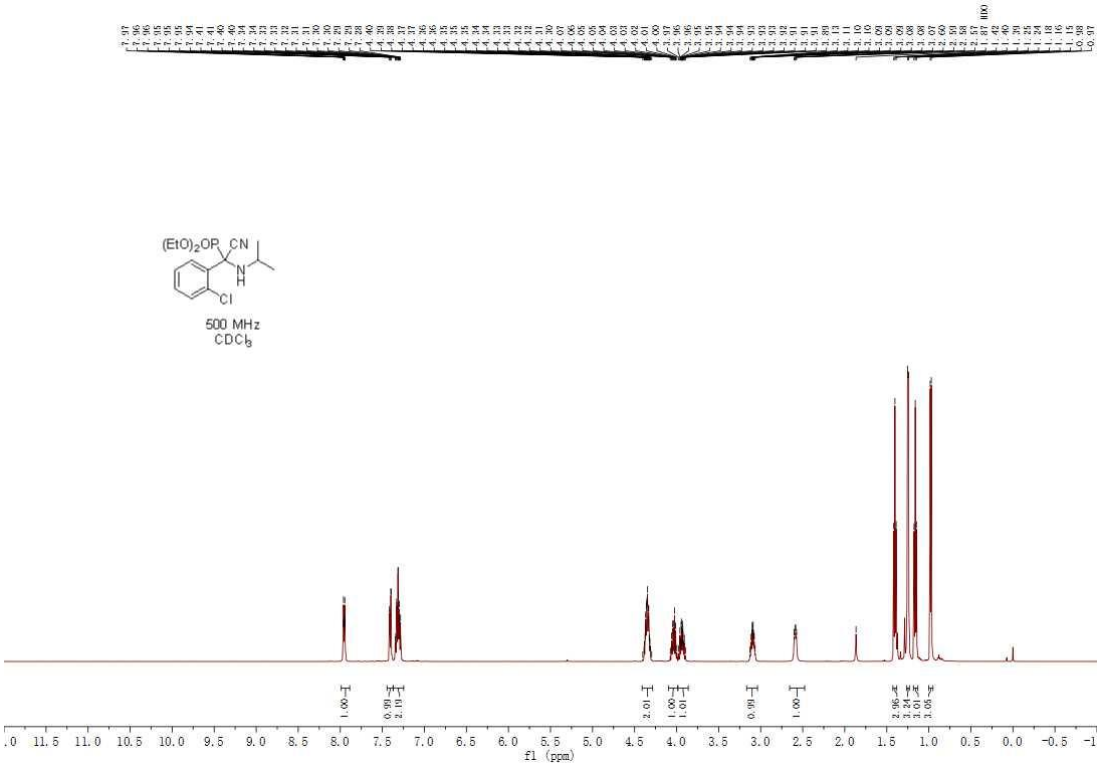
Diethyl (cyano(3,4-dichlorophenyl)(isopropylamino)methyl)phosphonate (1g)

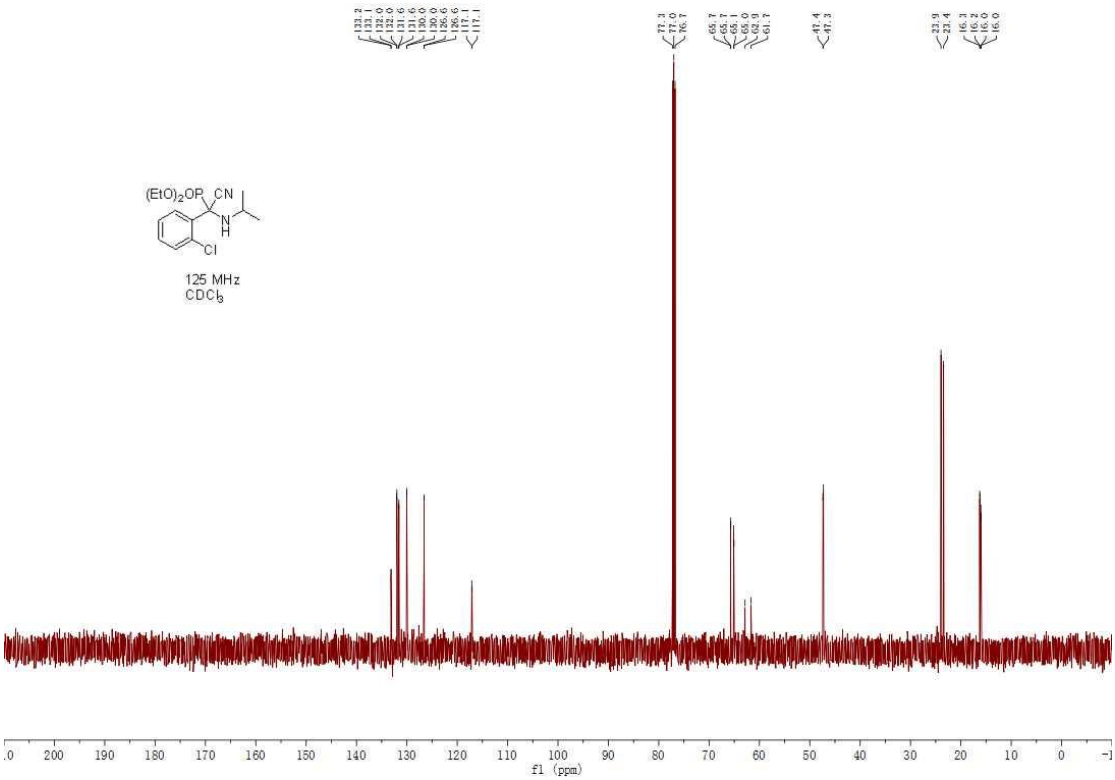






Diethyl ((2-chlorophenyl)(cyano)(isopropylamino)methyl)phosphonate (1h)

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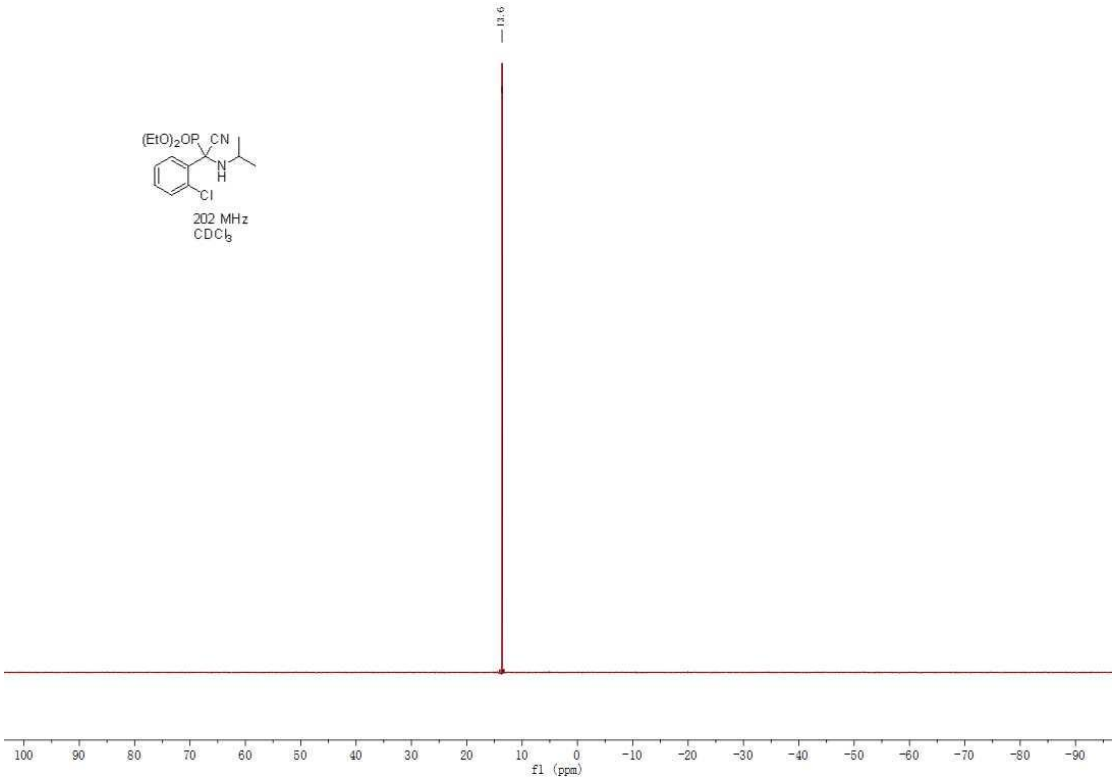
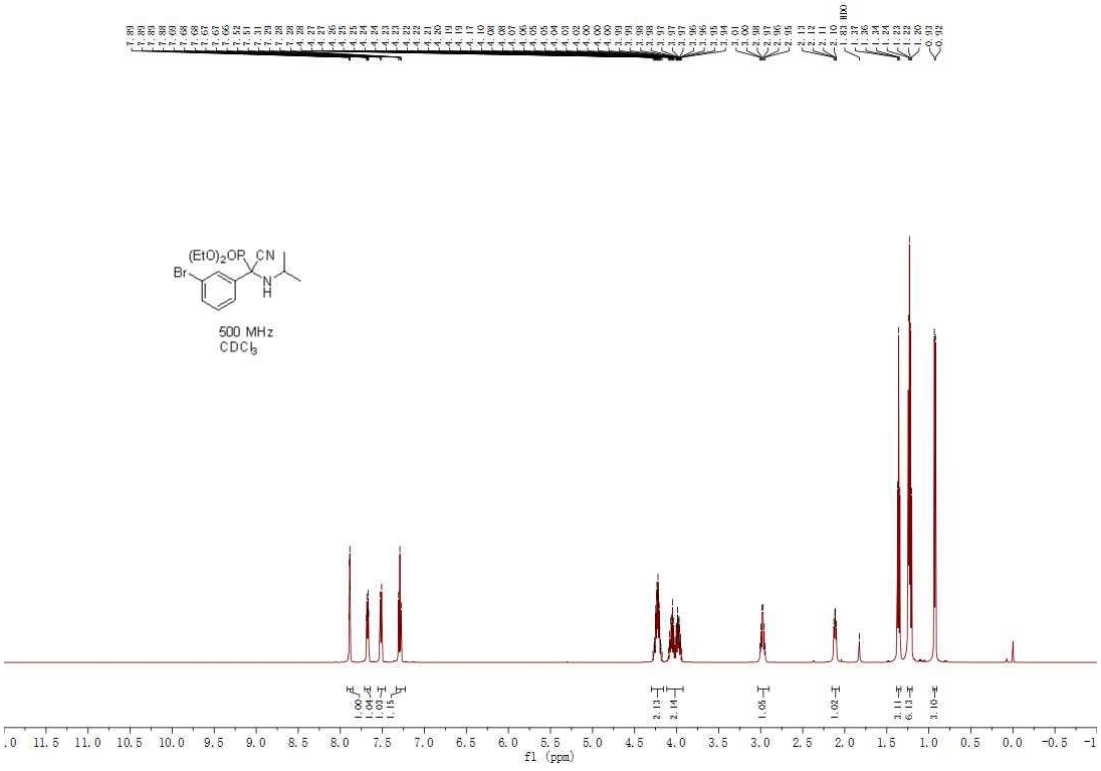
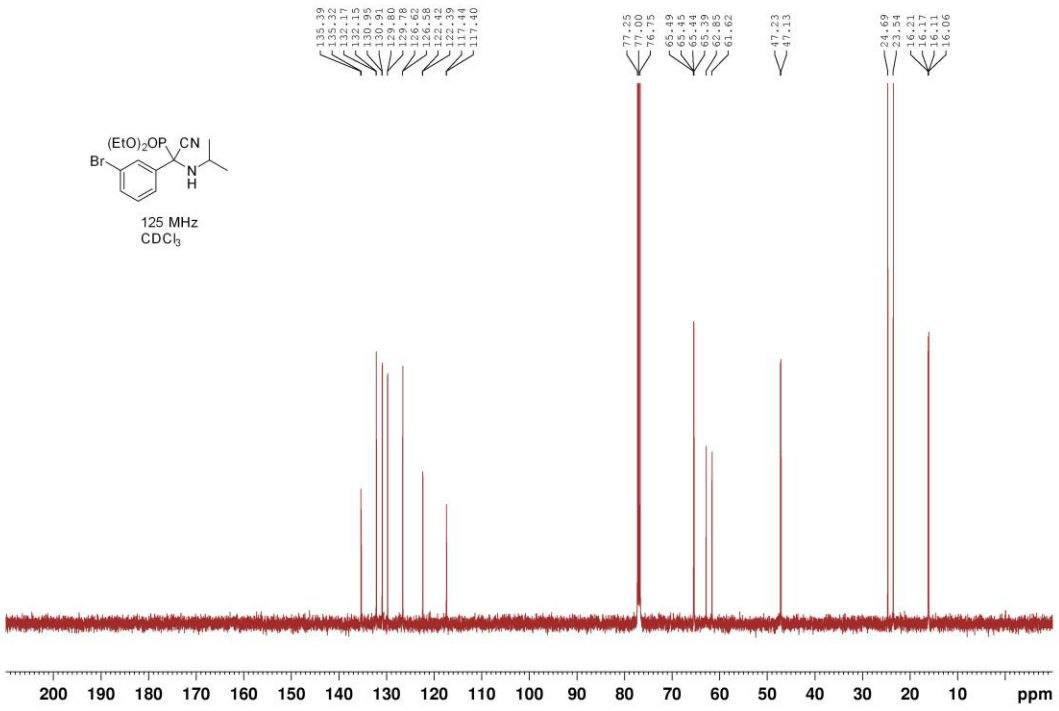
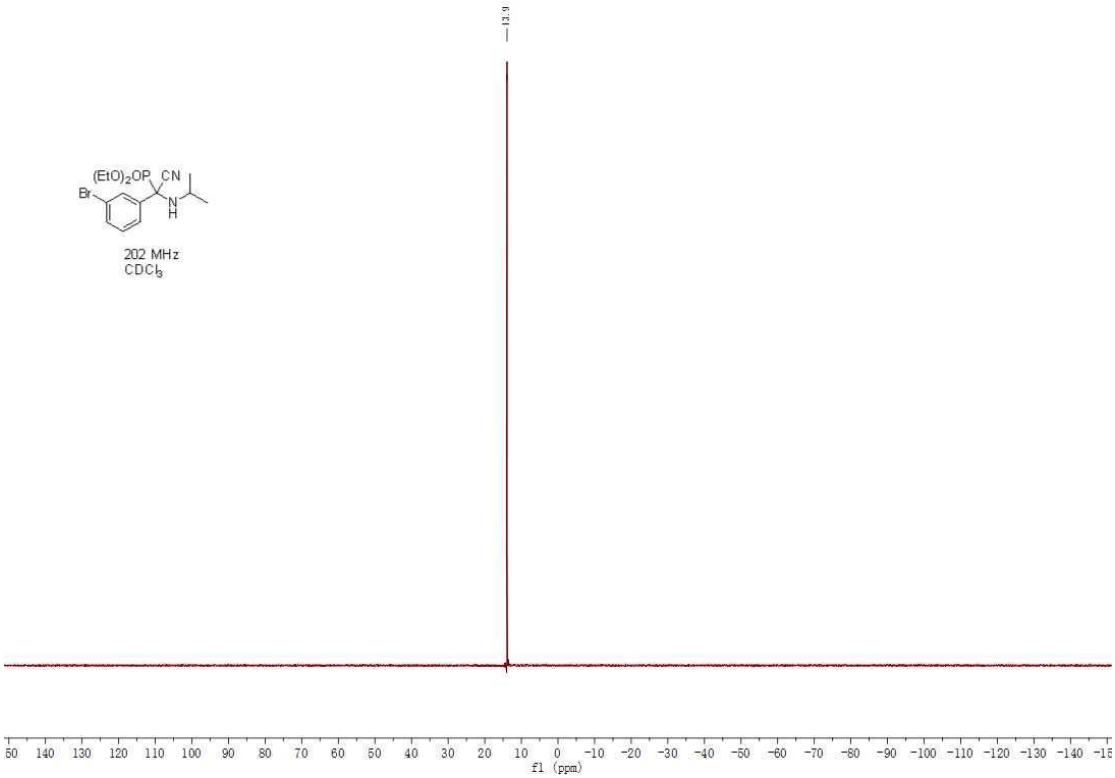
CN
N
H
Cl
125 MHz
CDCl3
f1 (ppm)


13.6
(EtO)2OP
CN
N
H
Cl
202 MHz
CDCl3
f1 (ppm)

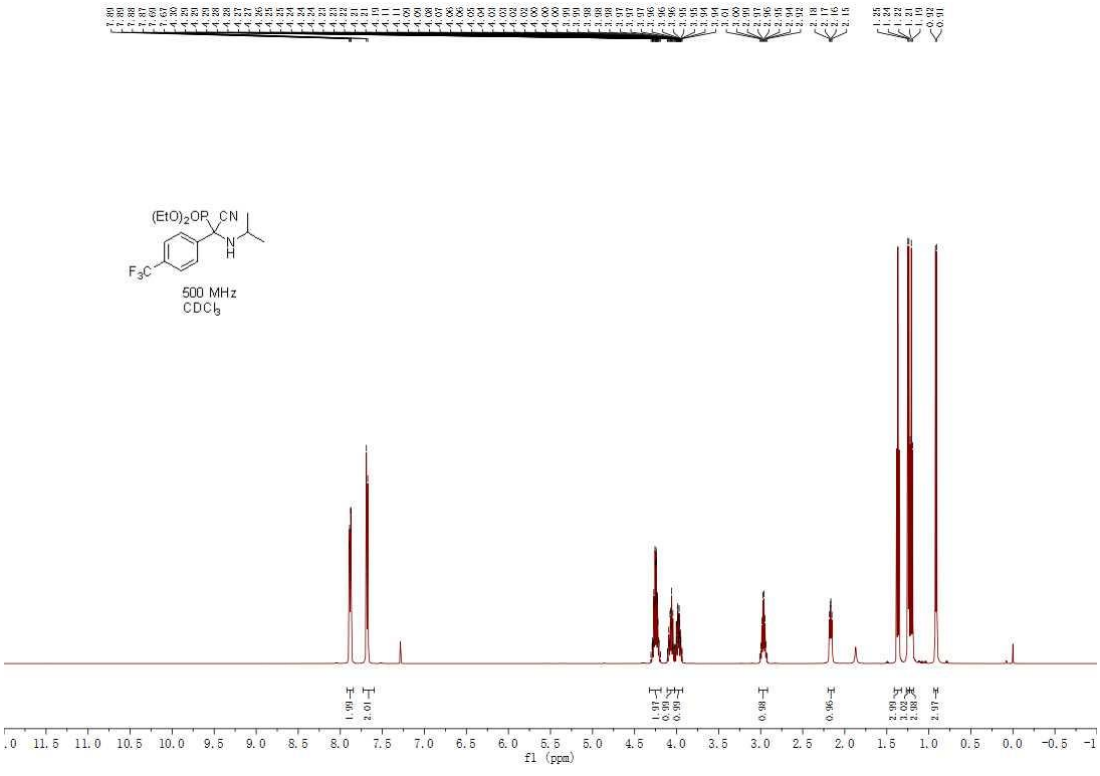
Diethyl ((3-bromophenyl)(cyano)(isopropylamino)methyl)phosphonate (1i)

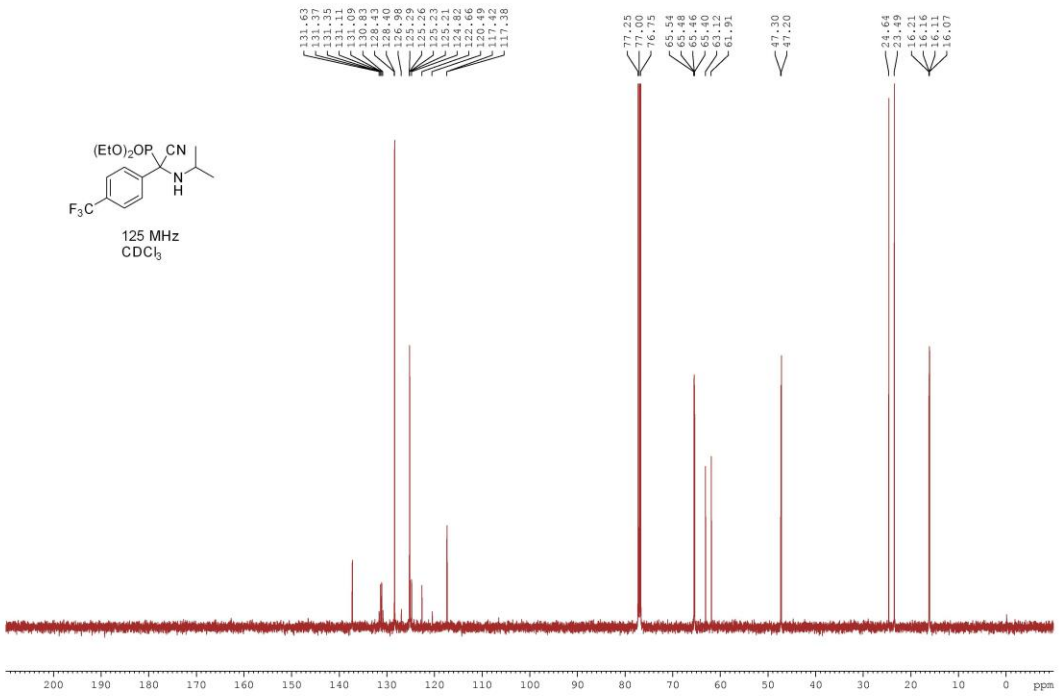






Diethyl (cyano(isopropylamino)(4-(trifluoromethyl)phenyl)methyl)phosphonate (1j)

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131.11
131.09
130.83
128.43
128.40
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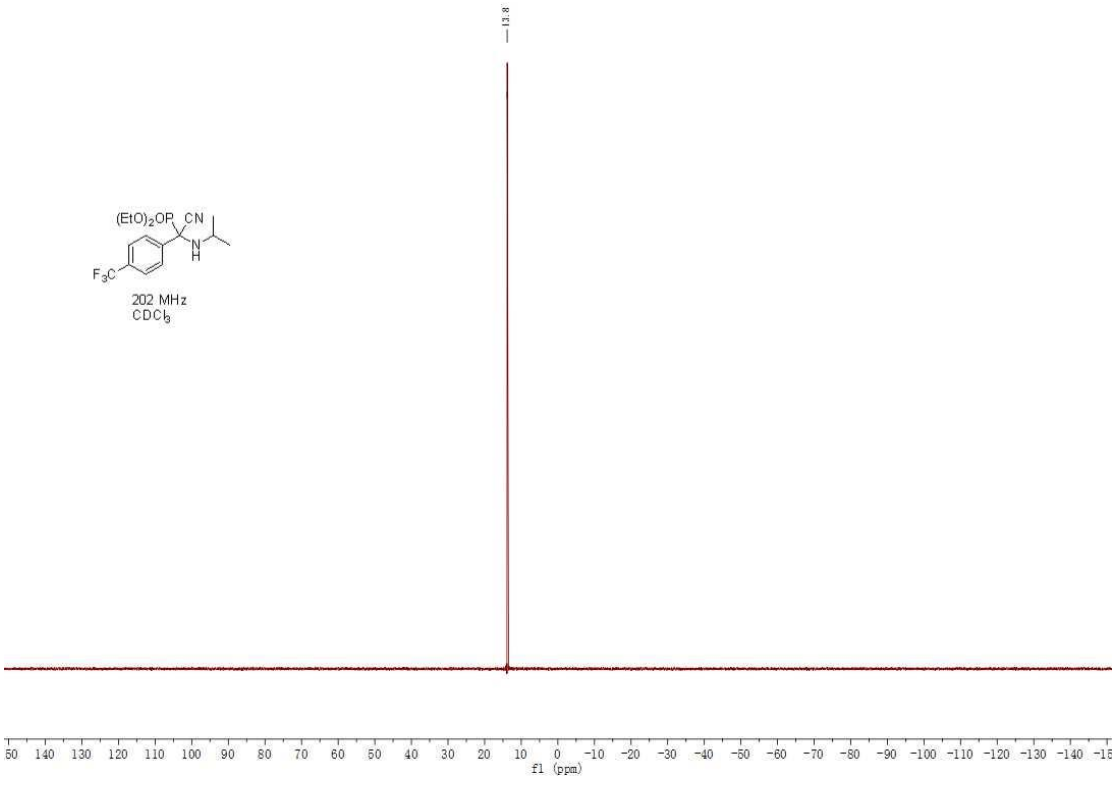
126.96
125.29
125.26
125.23
125.21
124.82
122.66
120.49
117.42
117.38
77.25
77.00
76.75
65.54
65.48
65.46
65.40
63.22
61.91
47.30
47.20
24.64
23.49
16.21
16.16
16.11
16.07
(EtO)2OP
CN
N
H
F3C
125 MHz
CDCl3
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm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CN
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H
F3C
202 MHz
CDCl3
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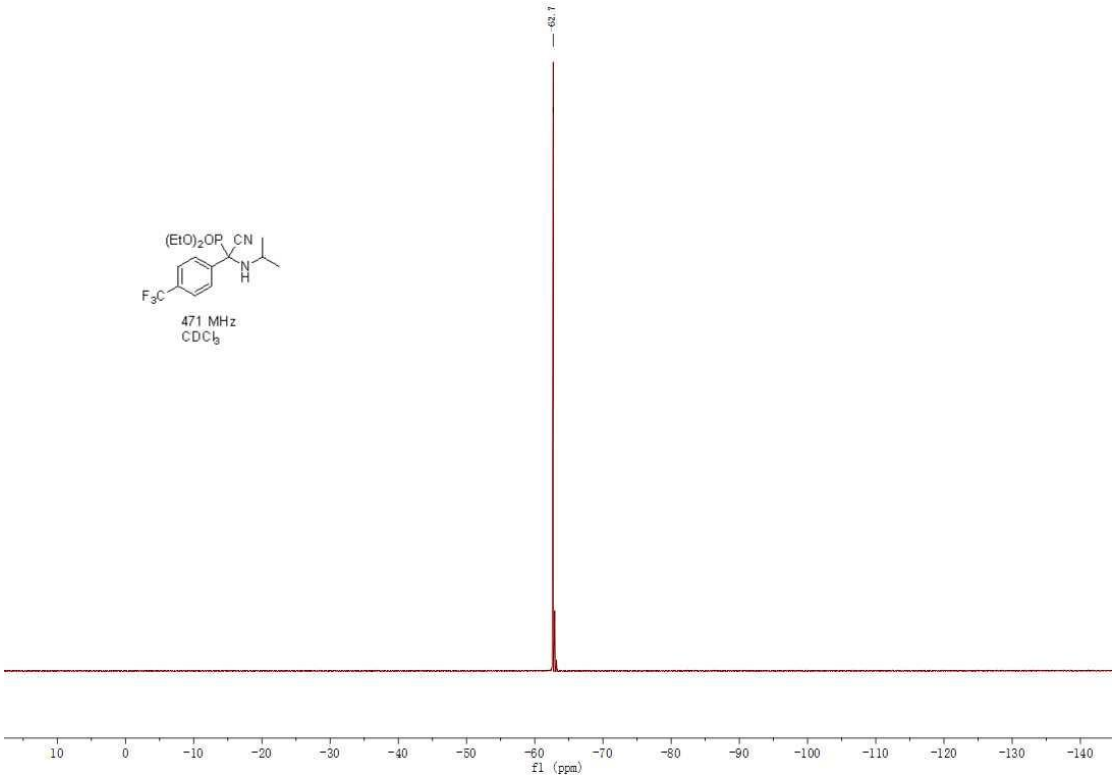
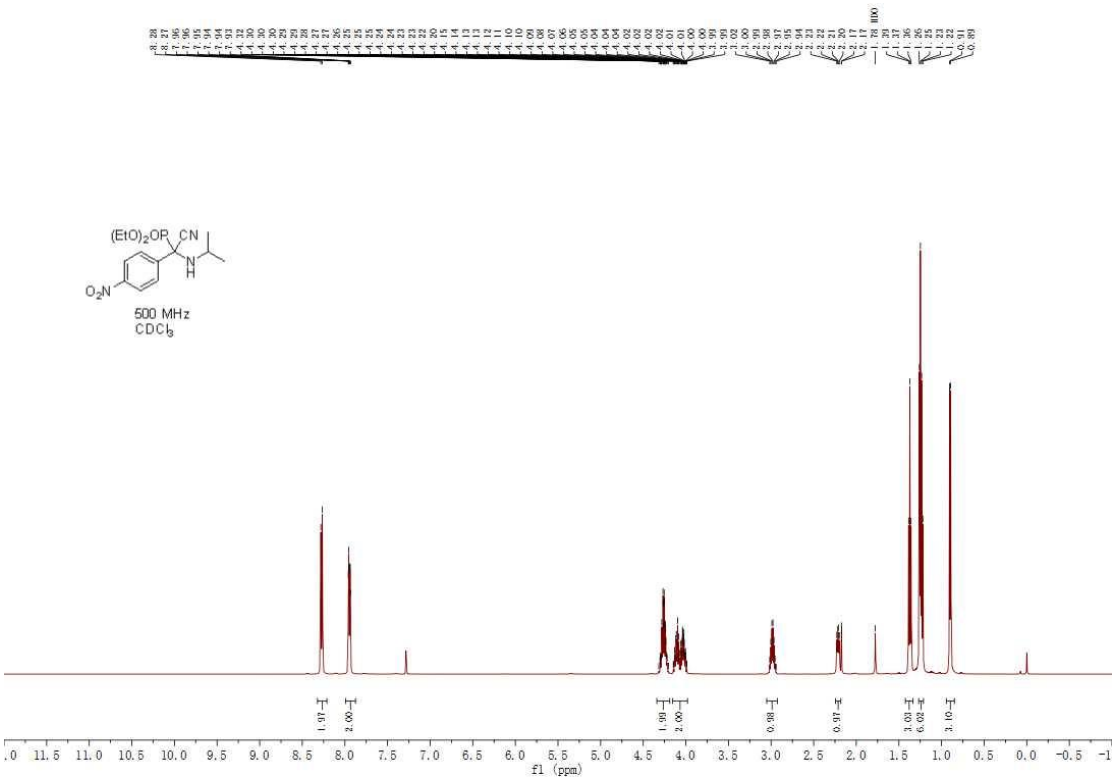
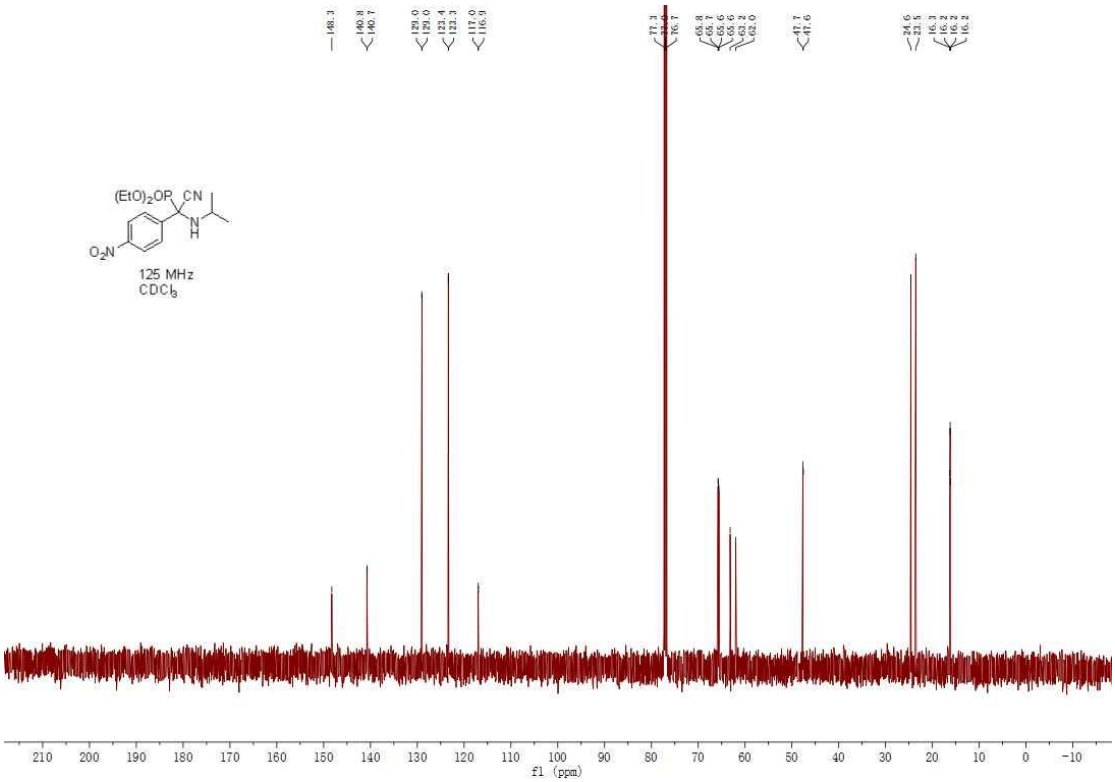
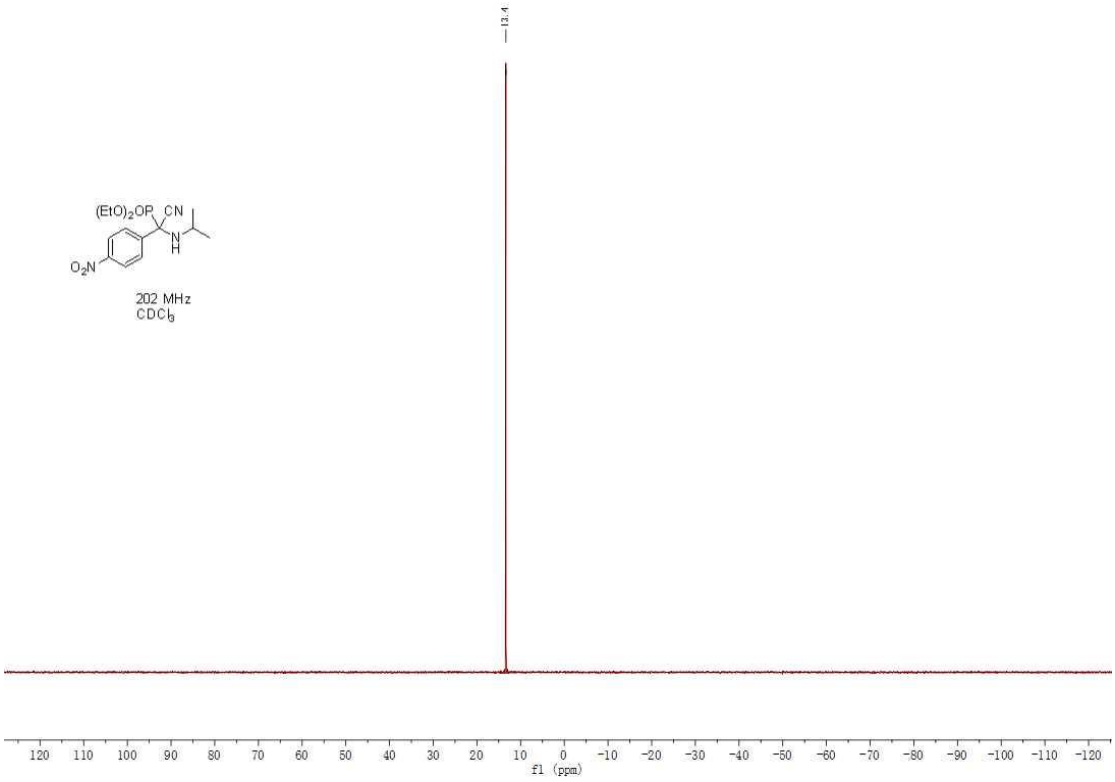
f1 (ppm)



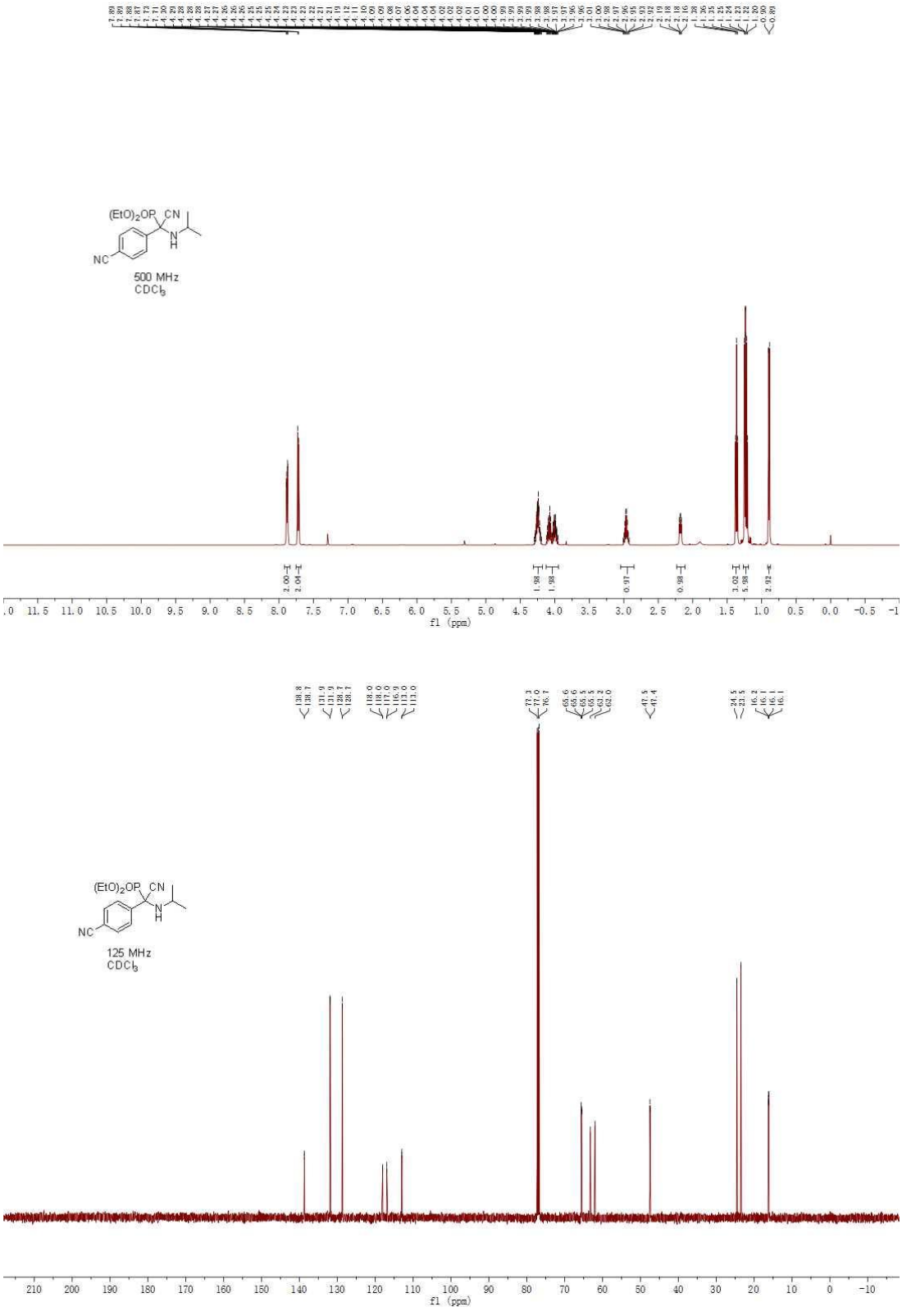
Diethyl (cyano(isopropylamino)(4-nitrophenyl)methyl)phosphonate (1k)

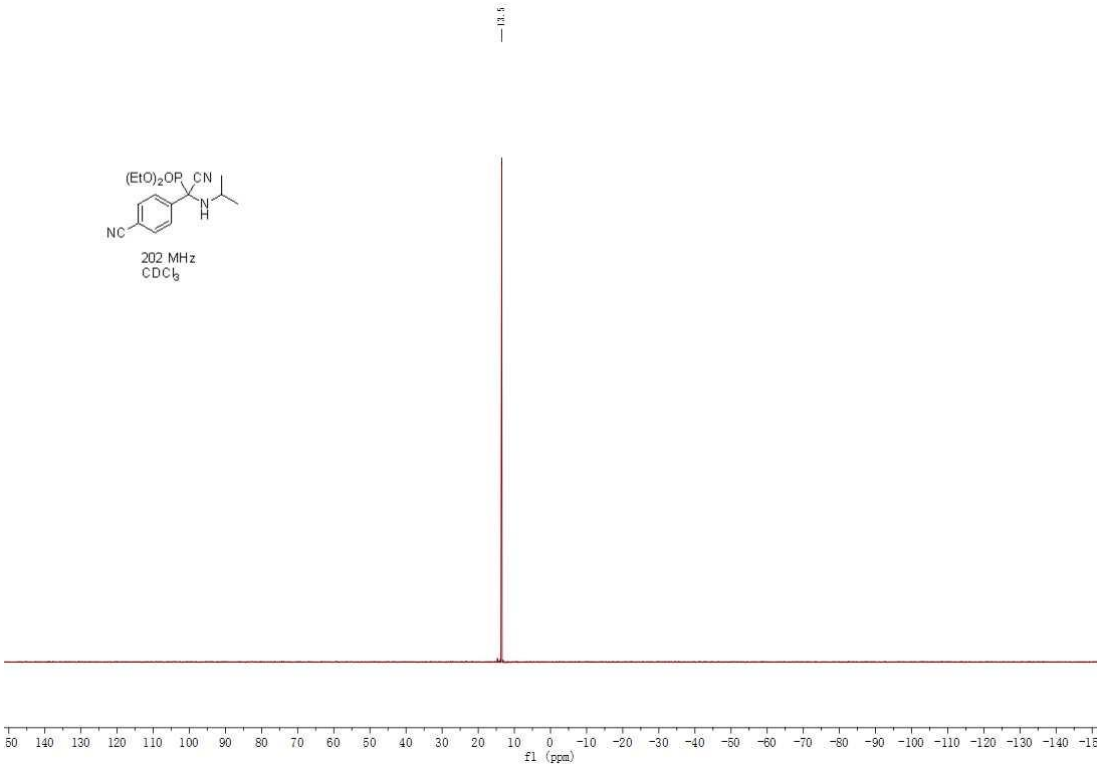



148.3
140.8
140.7
129.0
129.0
123.4
123.3
117.0
116.9
77.3
77.0
76.7
65.8
65.7
65.6
65.5
63.2
62.9
62.0
47.7
41.6
24.6
23.5
16.3
16.2
16.2
16.2
(EtO)2OP
CN
N
H
O2N
125 MHz
CDCl3
f1 (ppm)

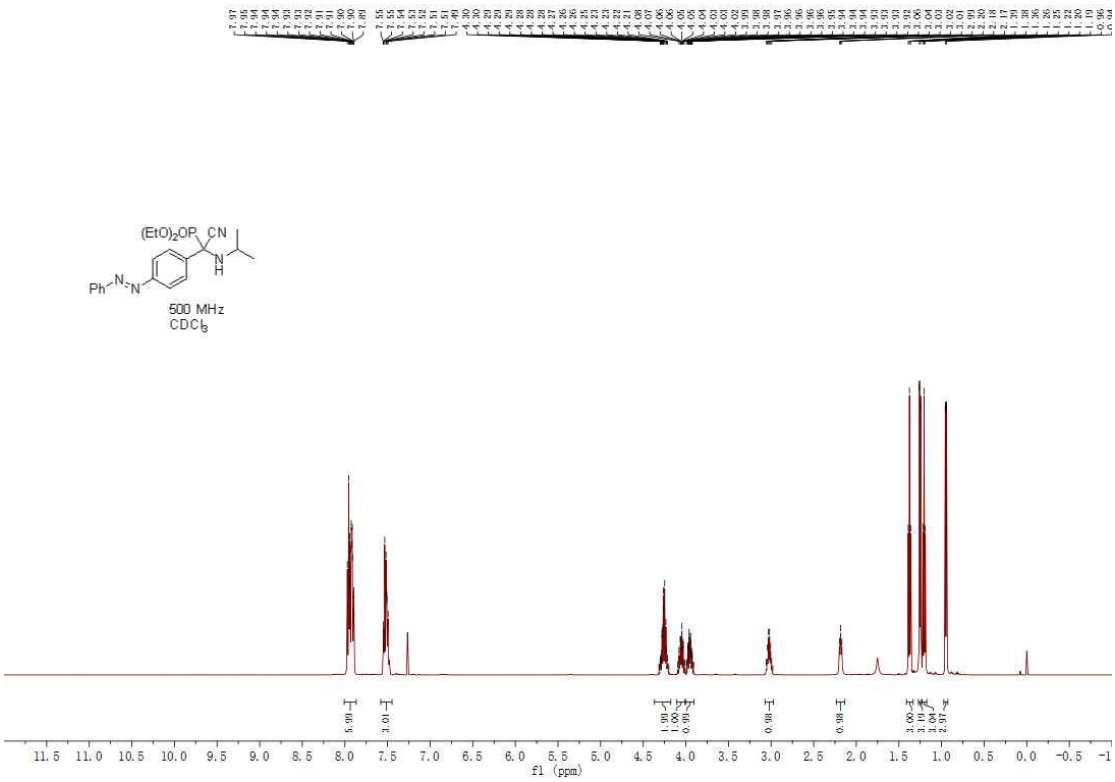

13.4
(EtO)2OP
CN
N
H
O2N
202 MHz
CDCl3
f1 (ppm)

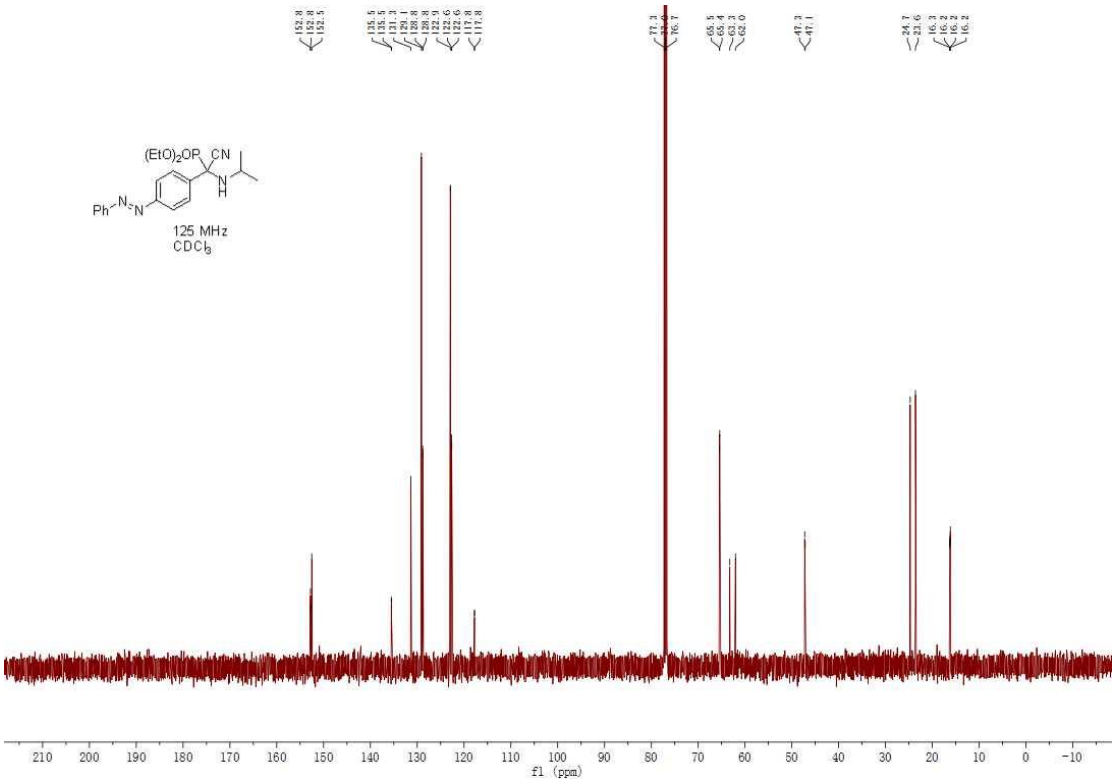
Diethyl (cyano(4-cyanophenyl)(isopropylamino)methyl)phosphonate (1l)

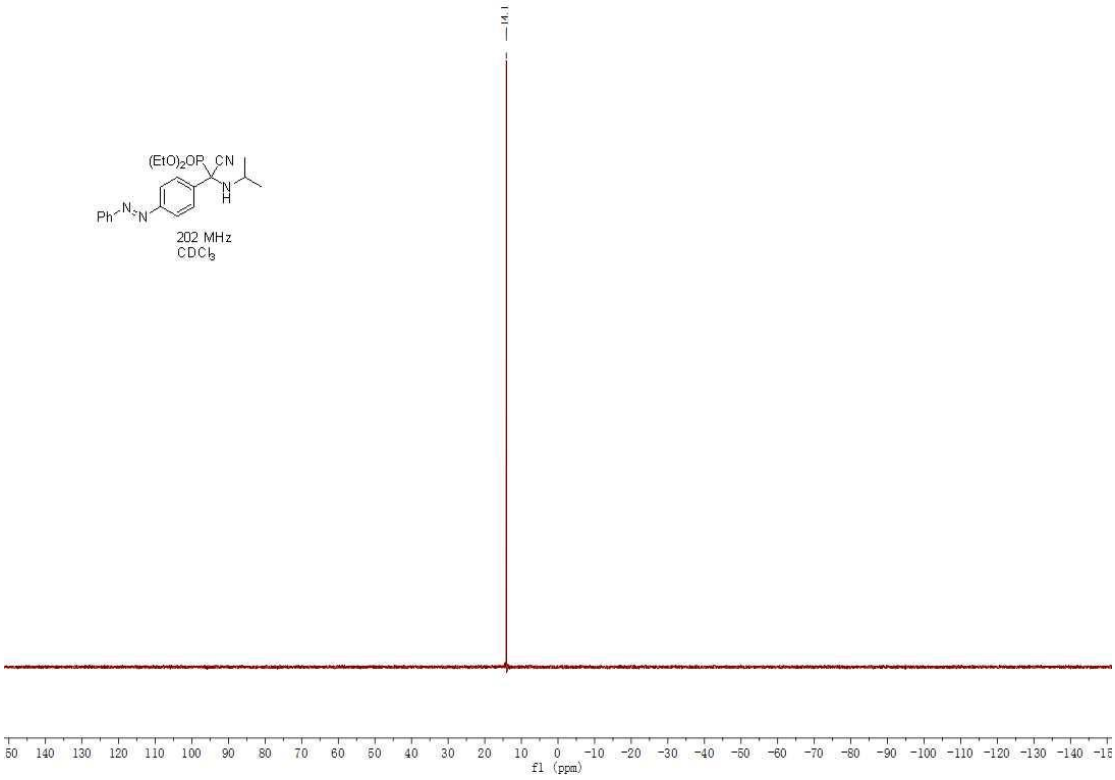




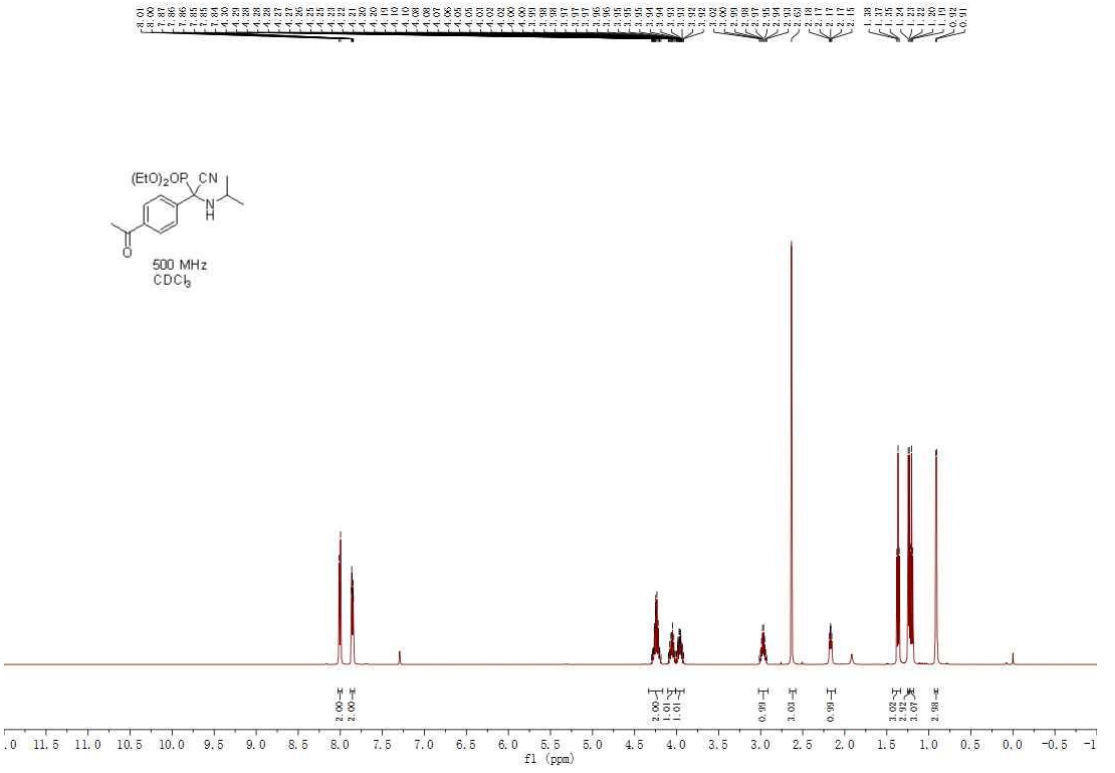
Diethyl (*E*)-(cyano(isopropylamino)(4-(phenyldiazenyl)phenyl)methyl)phosphon ate (1m)

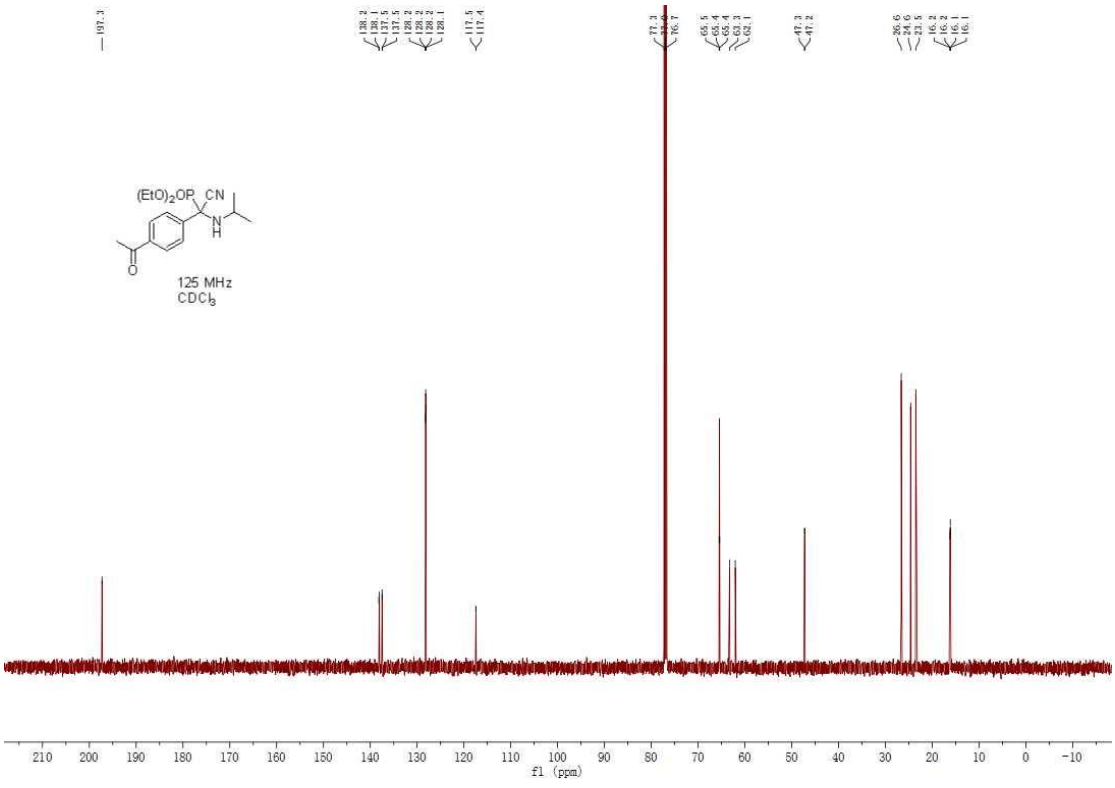


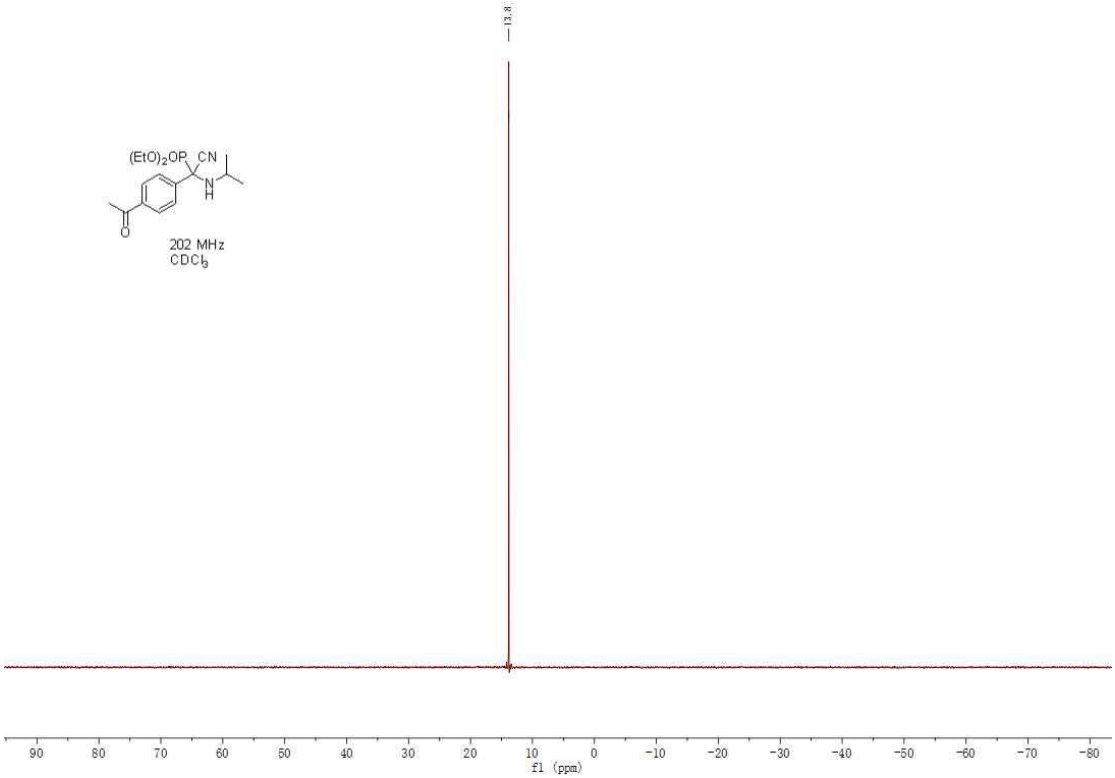

(EtO)2OP CN
Ph N=N
125 MHz
CDCl3
f1 (ppm)


(EtO)2OP CN
Ph N=N
202 MHz
CDCl3
f1 (ppm)

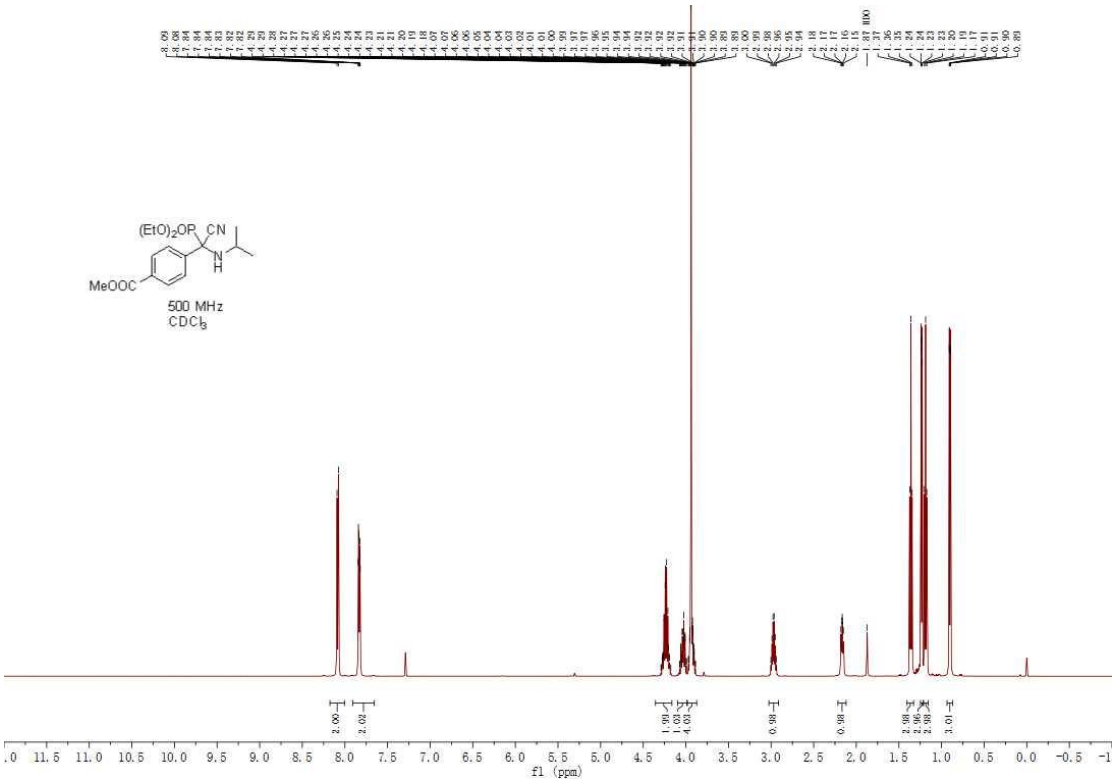
Diethyl ((4-acetylphenyl)(cyano)(isopropylamino)methyl)phosphonate (1n)

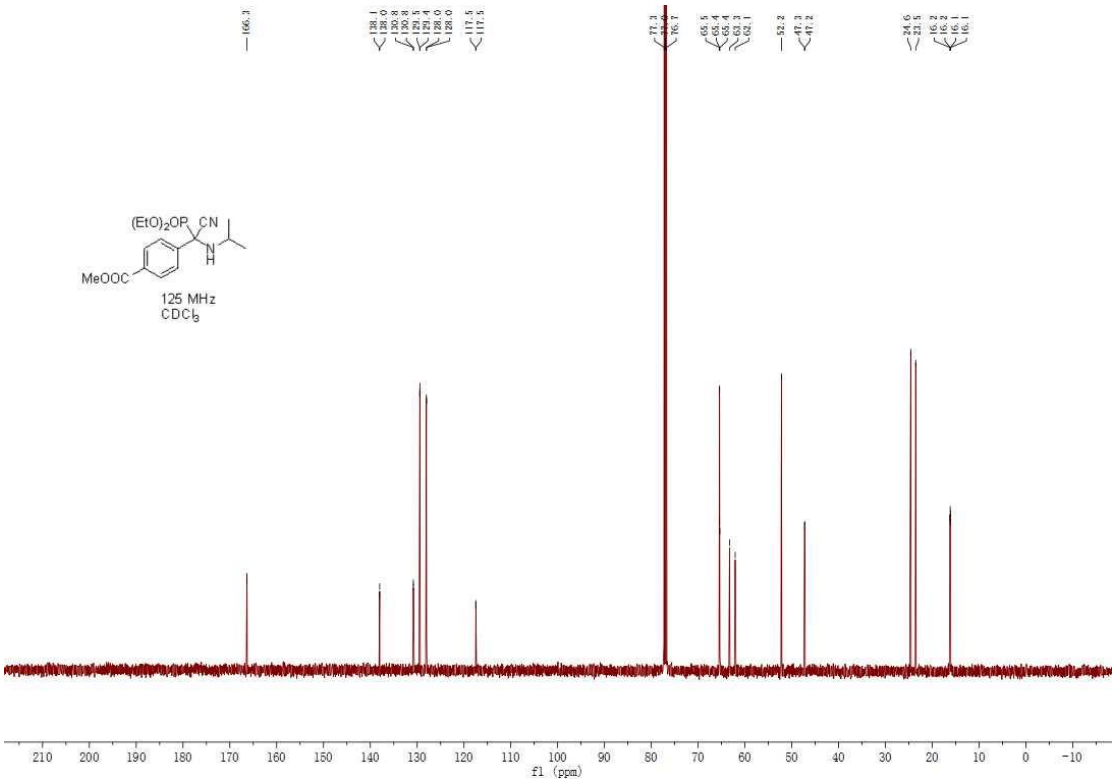


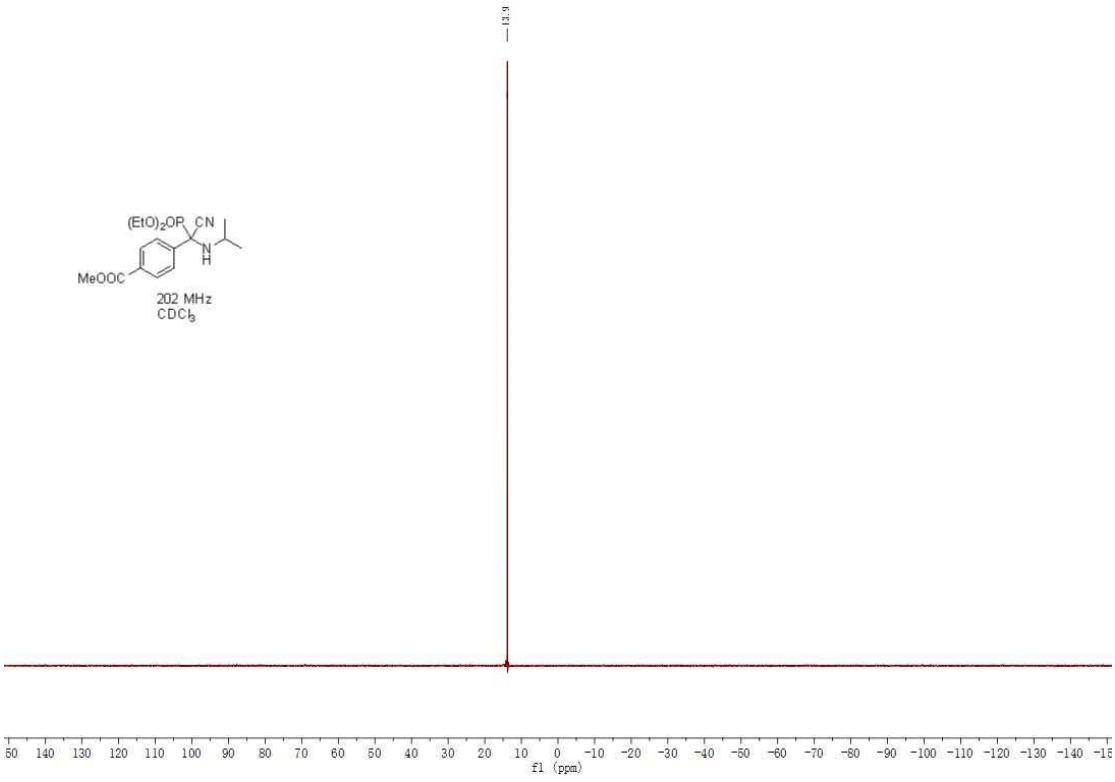




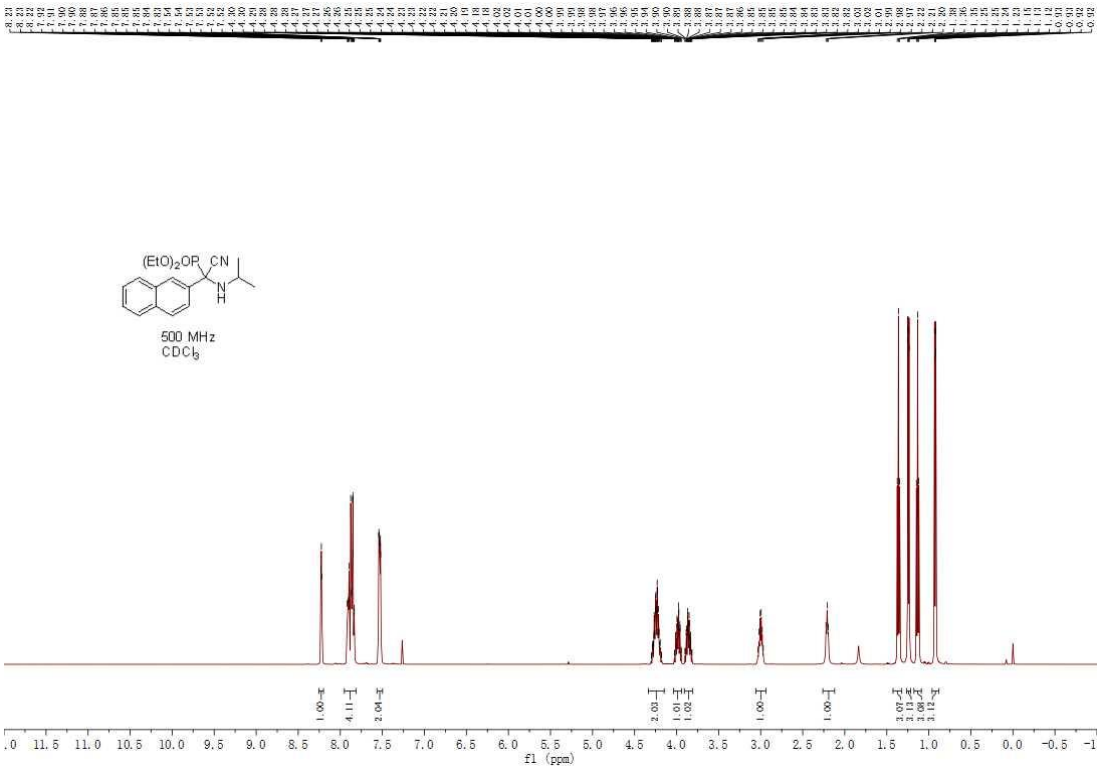
Methyl 4-(cyano(diethoxyphosphoryl)(isopropylamino)methyl)benzoate (1o)

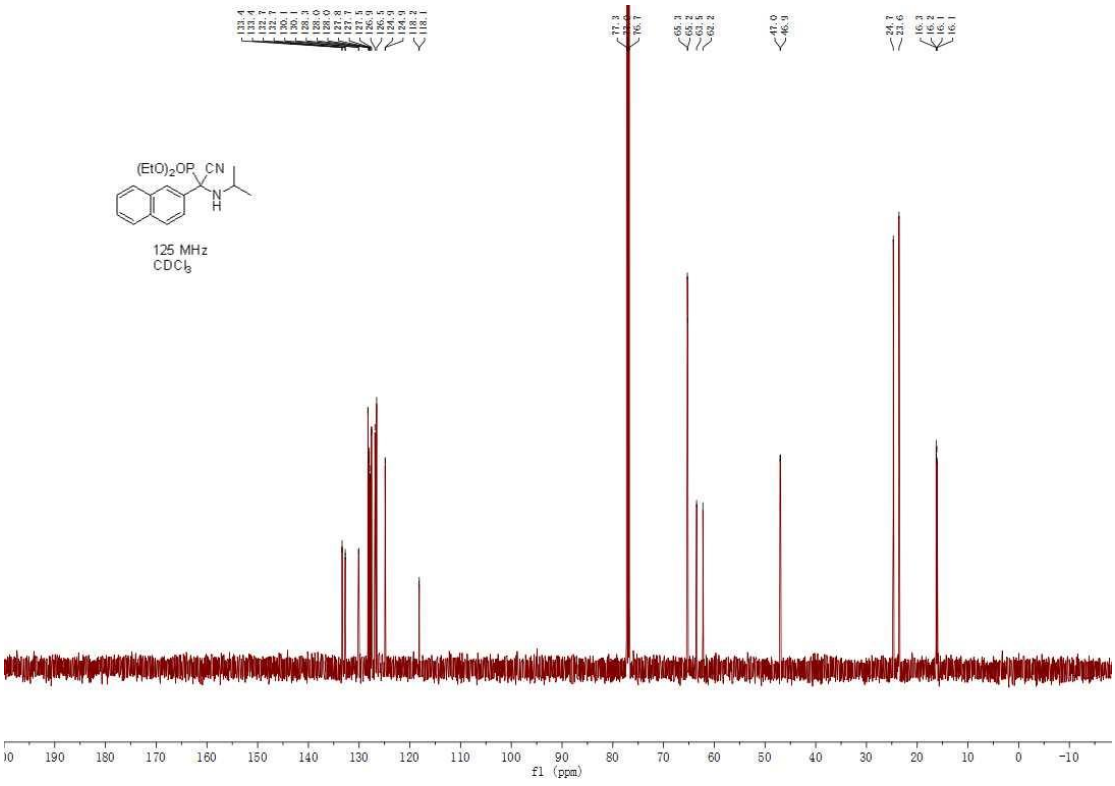


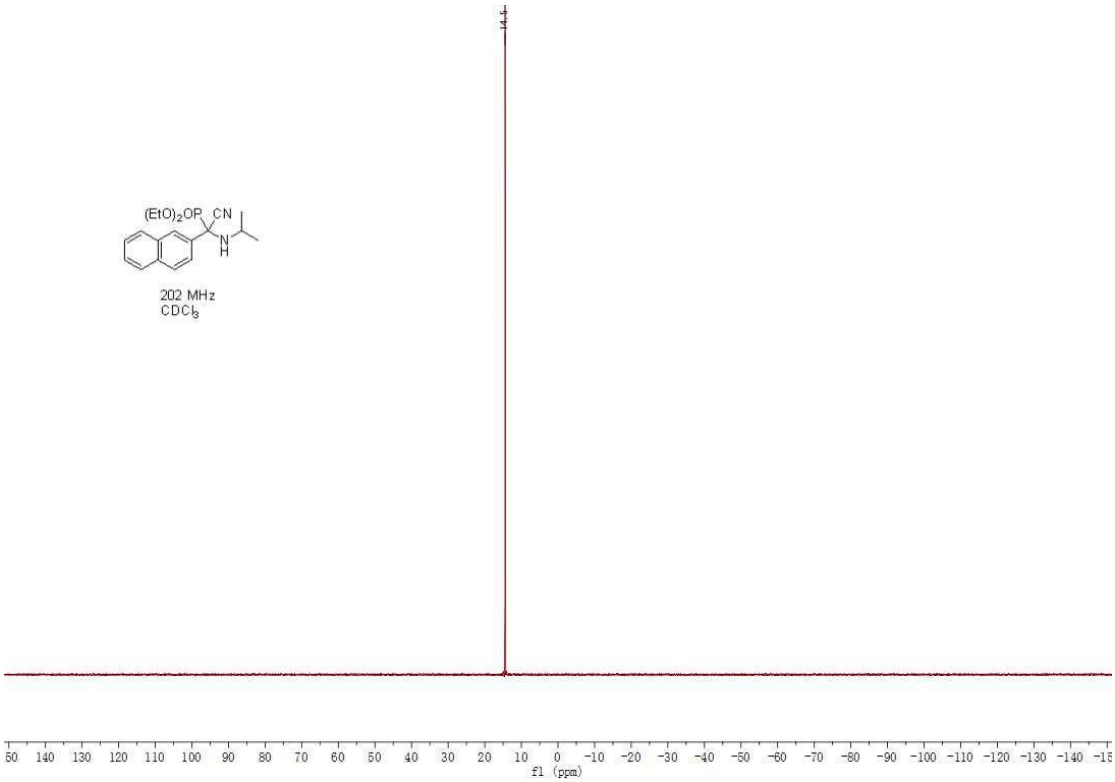

(EtO)2OP CN
MeOOC
125 MHz
CDCl3
f1 (ppm)


(EtO)2OP CN
MeOOC
202 MHz
CDCl3
f1 (ppm)

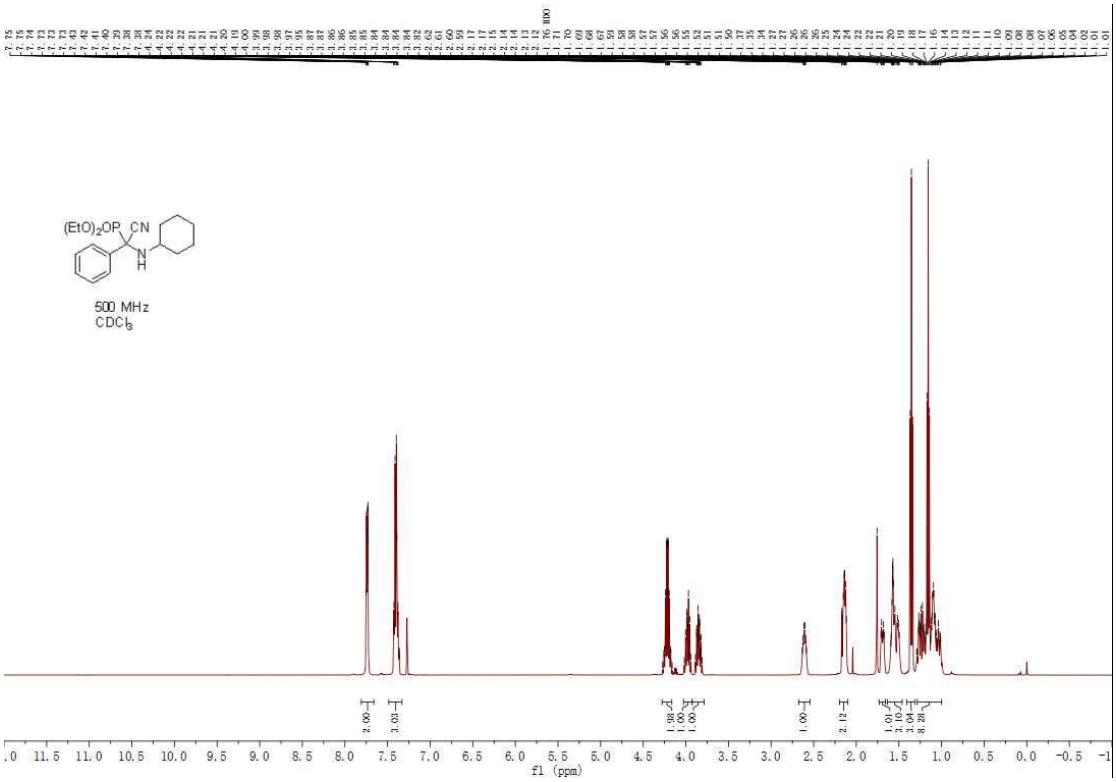
Diethyl (cyano(isopropylamino)(naphthalen-2-yl)methyl)phosphonate (1p)

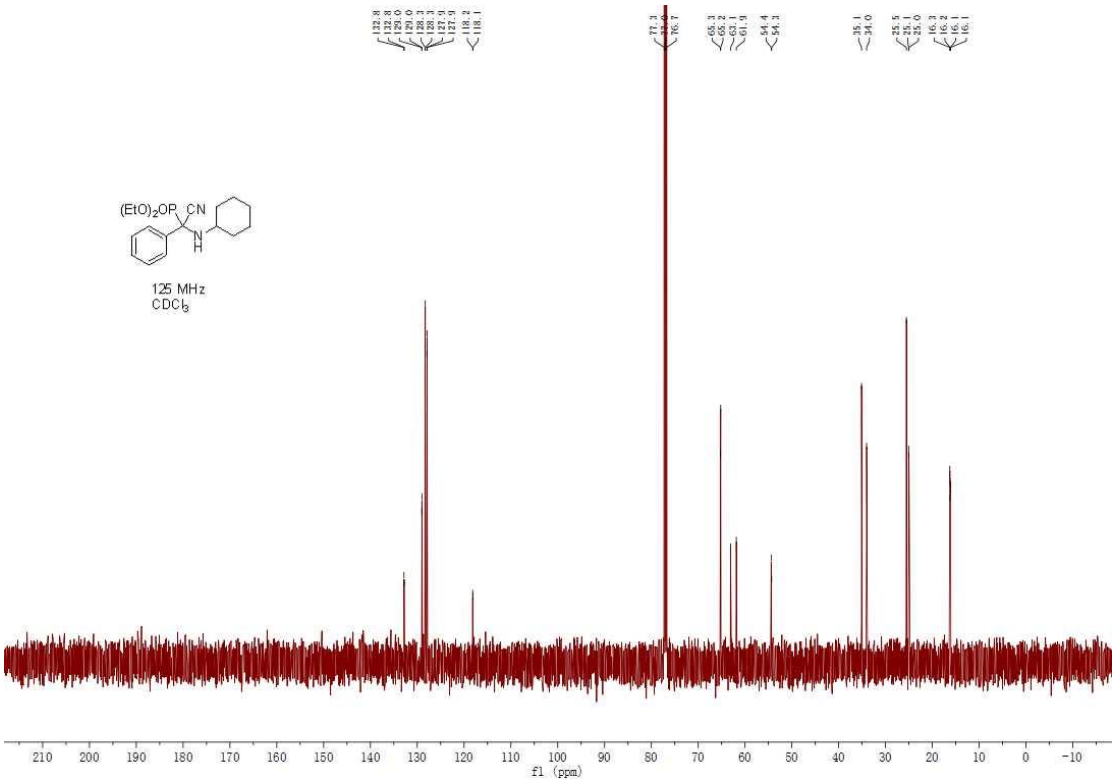


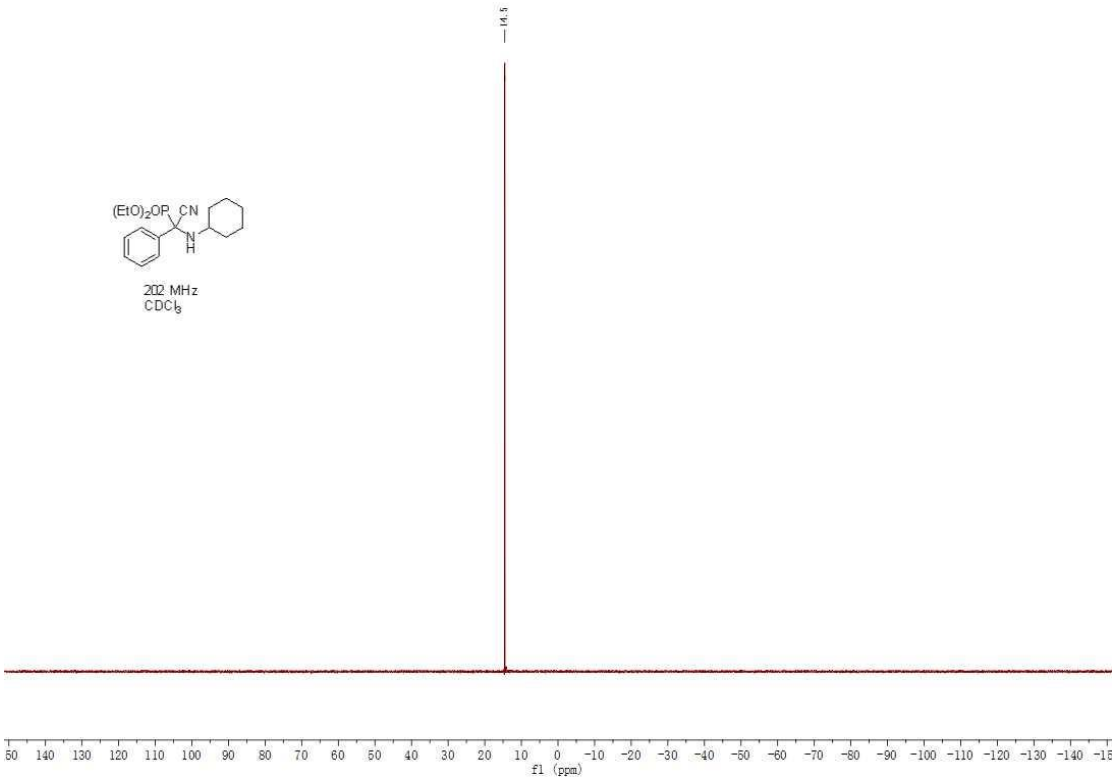




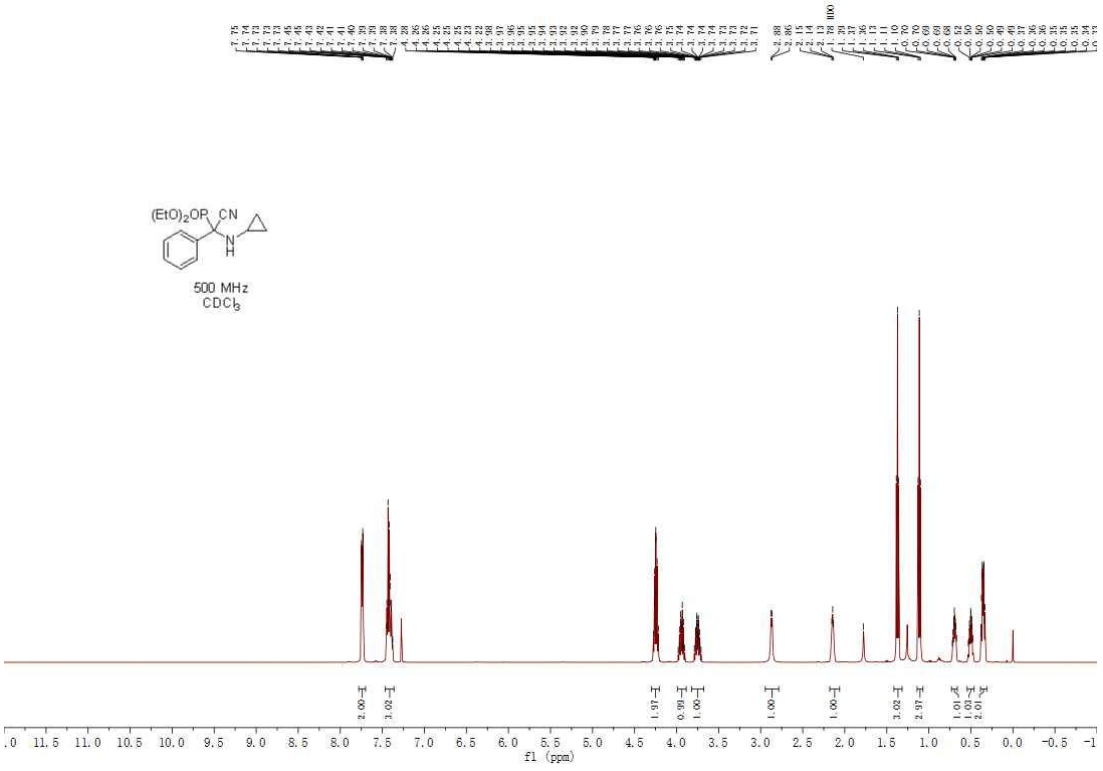
Diethyl (cyano(cyclohexylamino)(phenyl)methyl)phosphonate (1q)

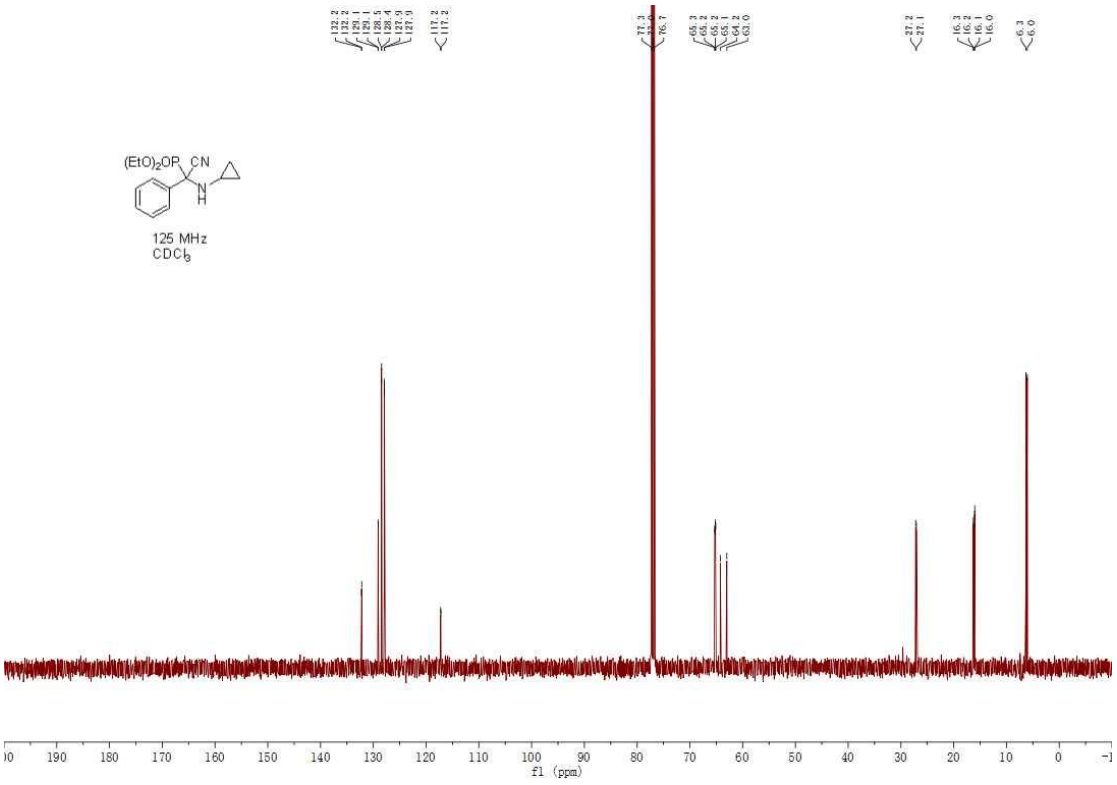


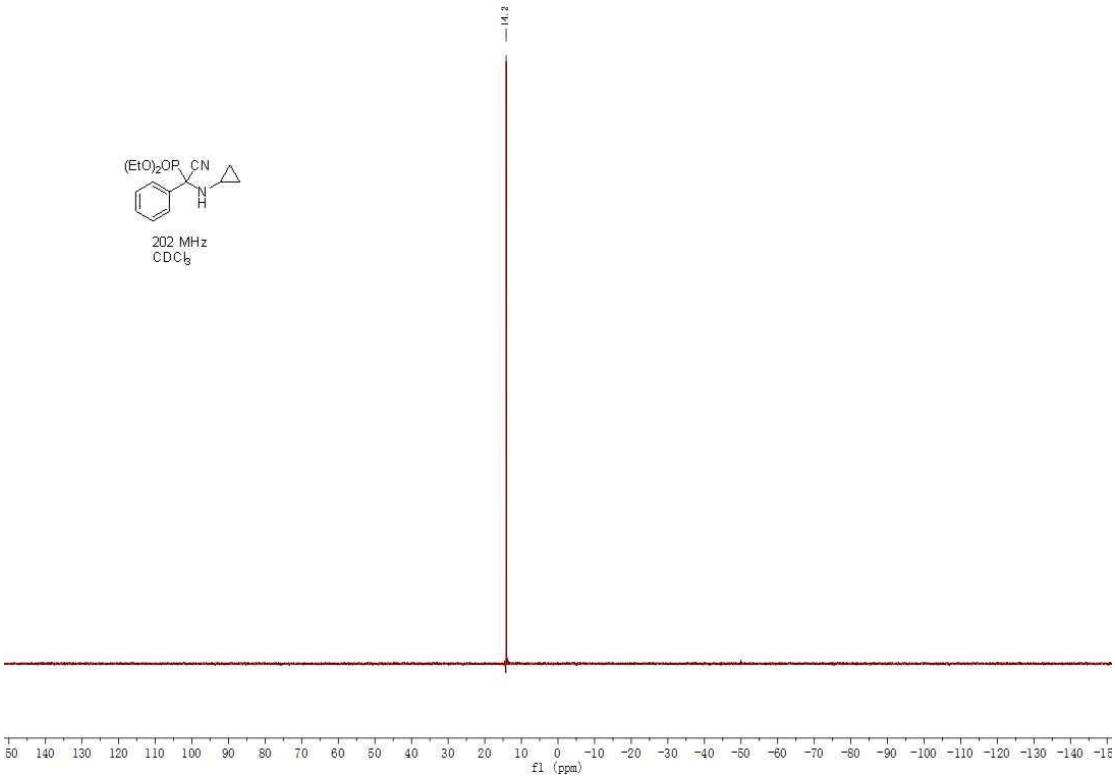

(EtO)2OP CN
H
125 MHz
CDCl3
f1 (ppm)


(EtO)2OP CN
H
202 MHz
CDCl3
f1 (ppm)

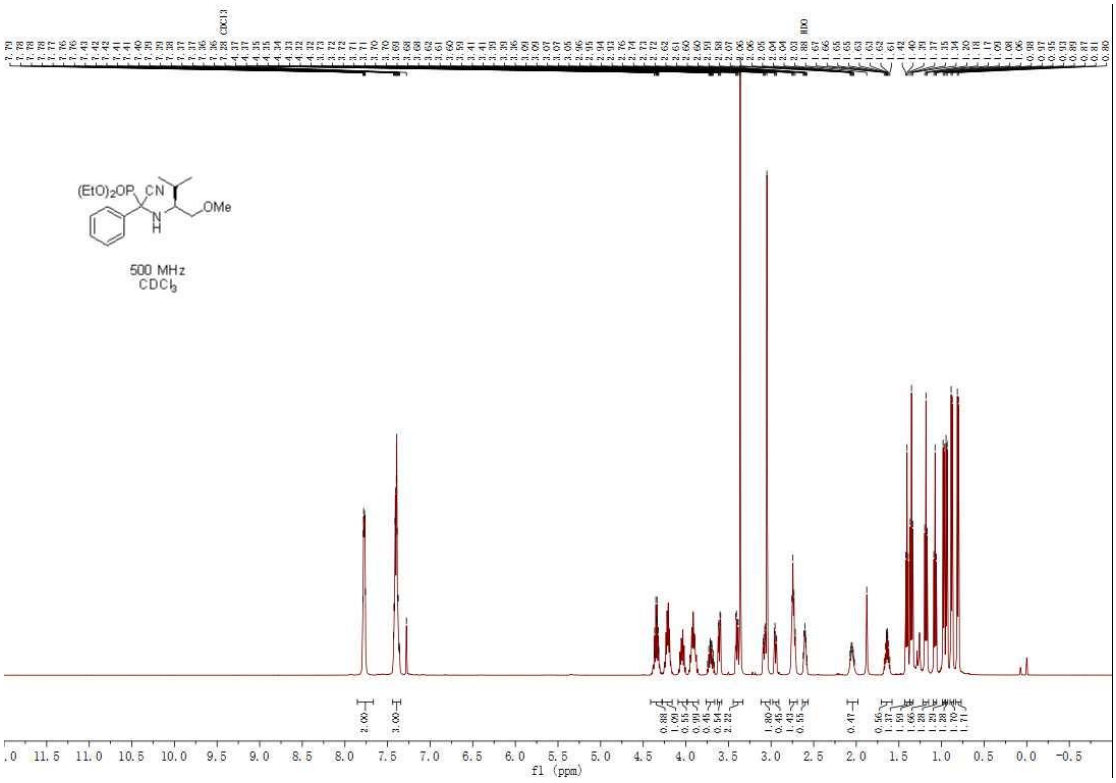
Diethyl (cyano(cyclopropylamino)(phenyl)methyl)phosphonate (1r)

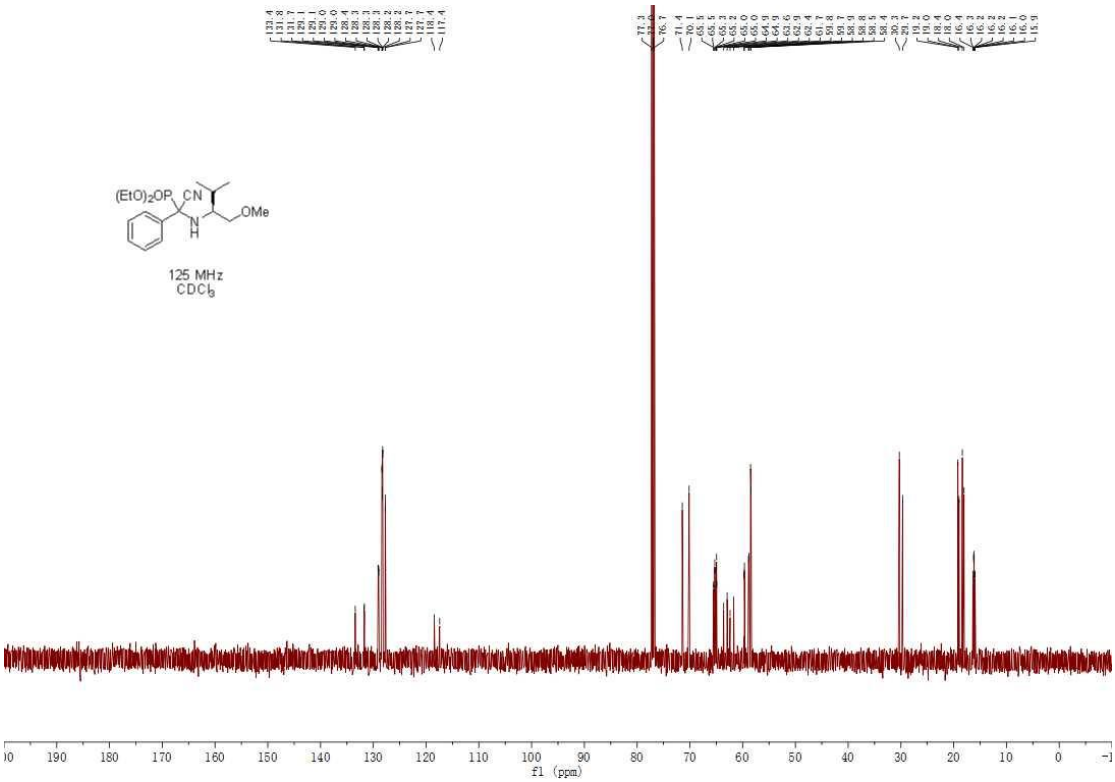


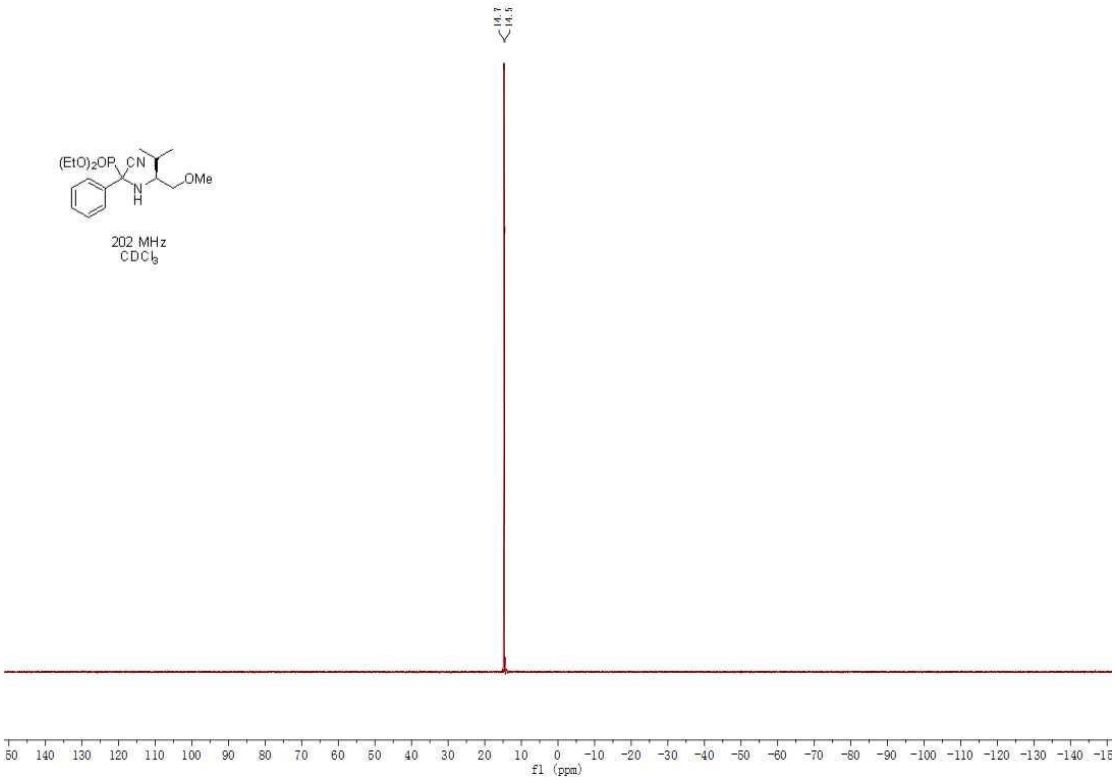




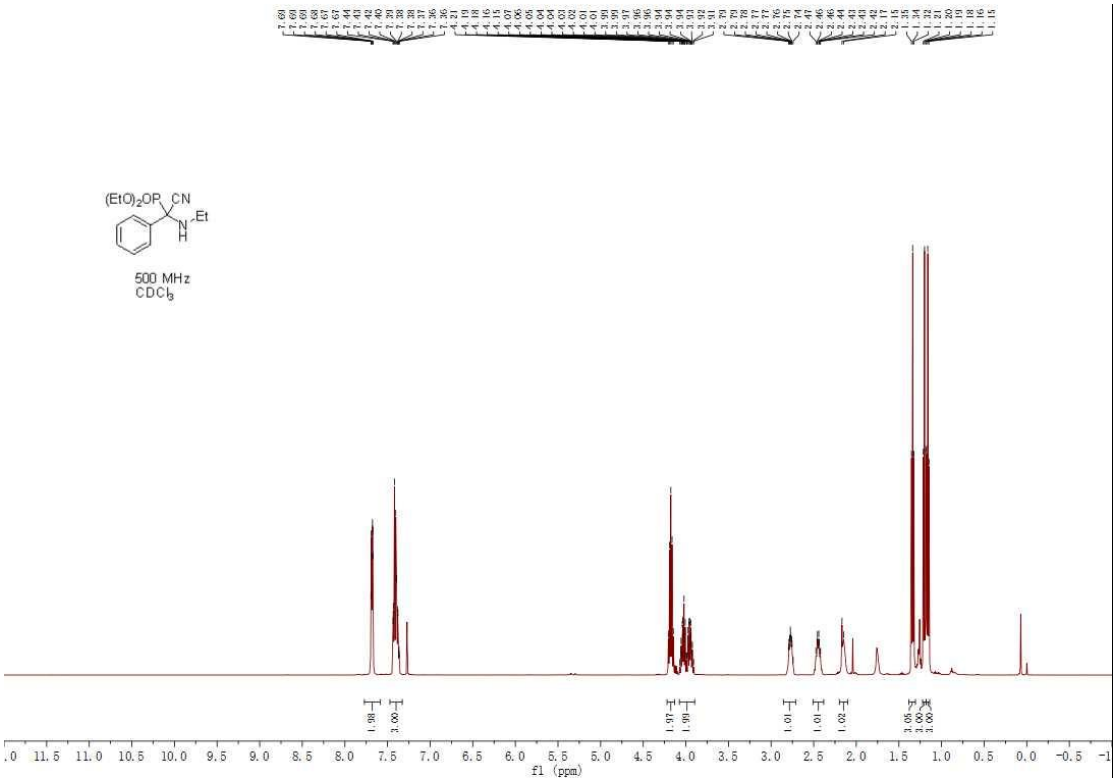
Diethyl (cyano(((S)-1-methoxy-3-methylbutan-2-yl)amino)(phenyl)methyl)phosphonate (1s)

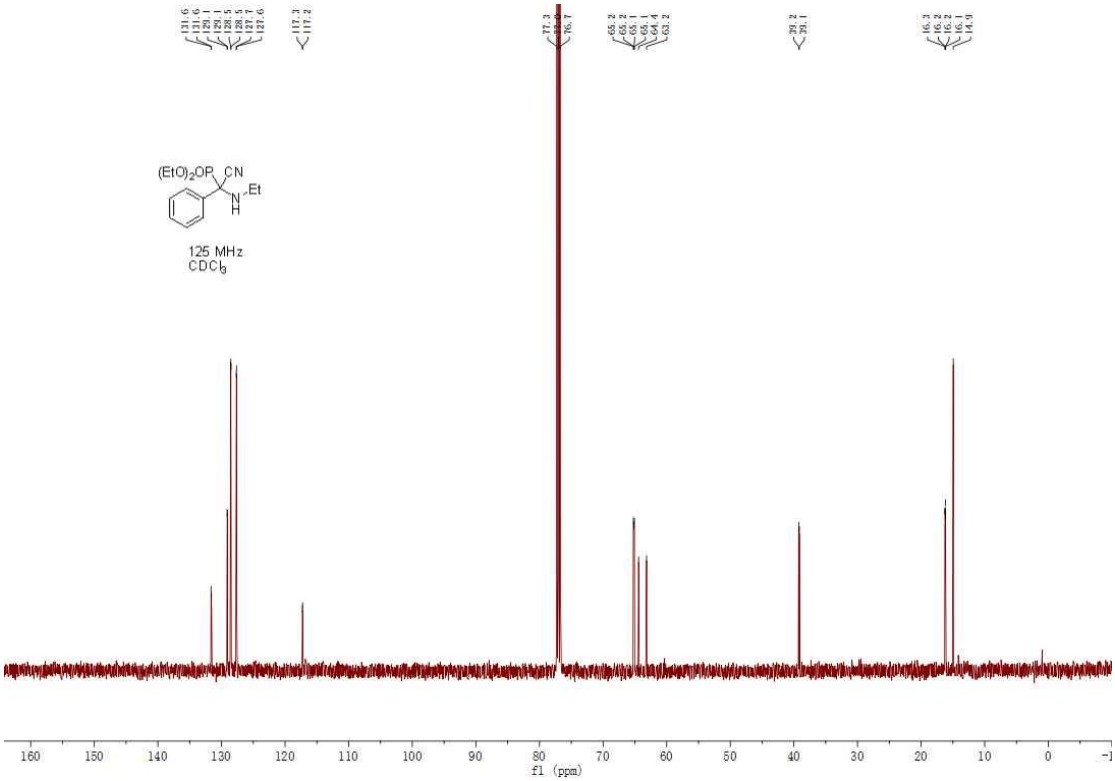


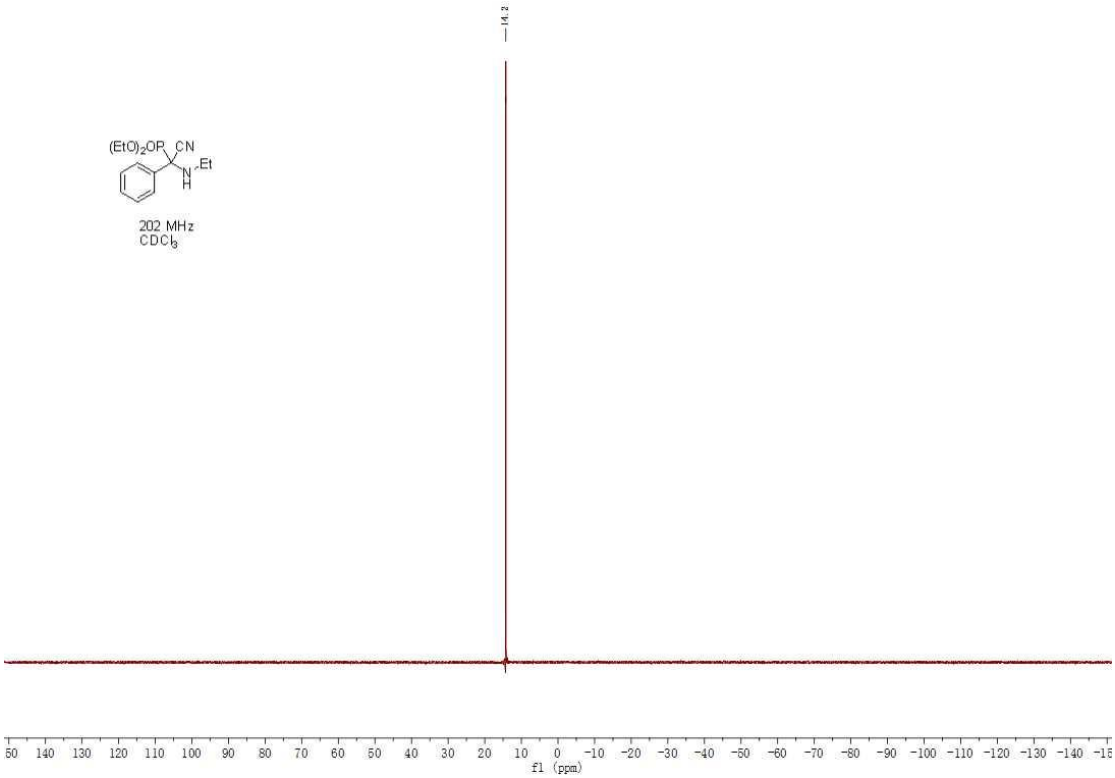

(EtO)2OP
CN
OMe
125 MHz
CDCl3
f1 (ppm)


(EtO)2OP
CN
OMe
202 MHz
CDCl3
f1 (ppm)

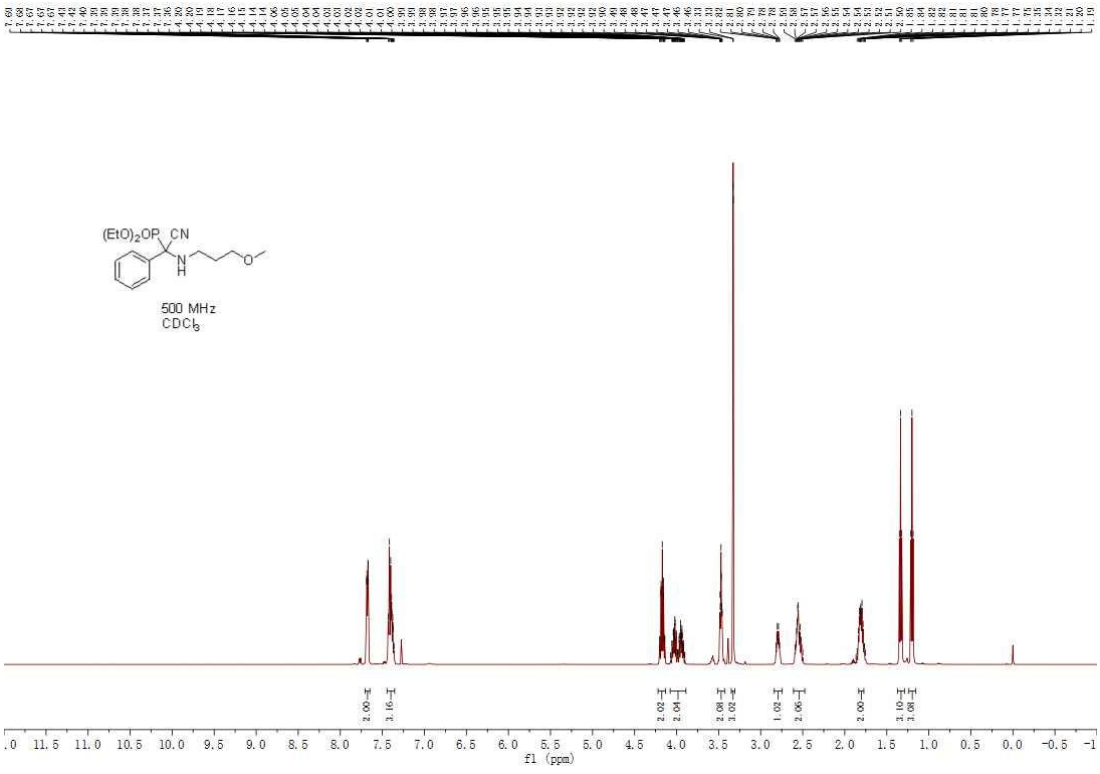
Diethyl (cyano(ethylamino)(phenyl)methyl)phosphonate (1t)

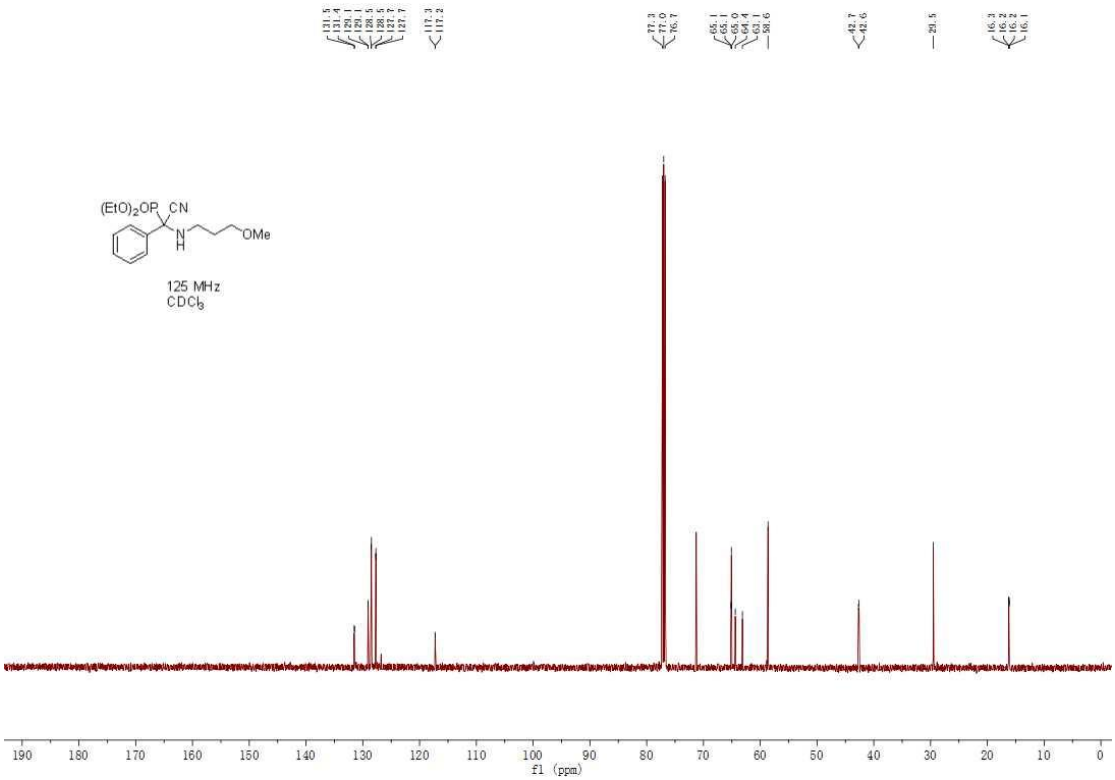


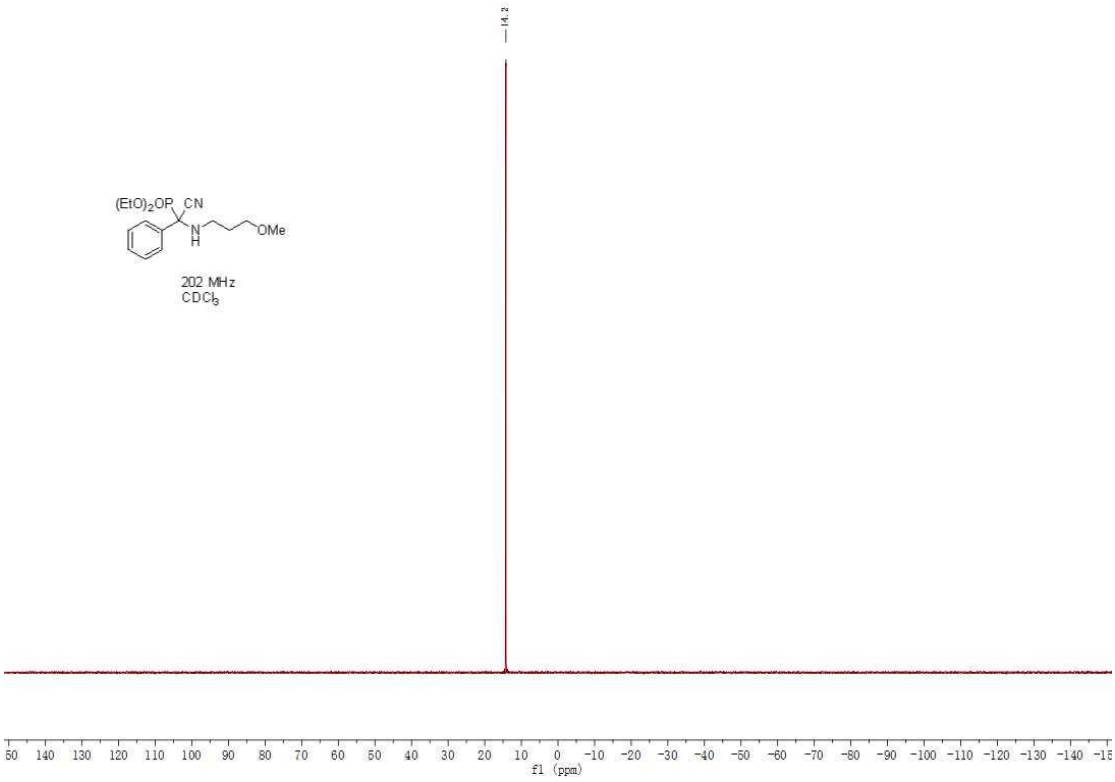




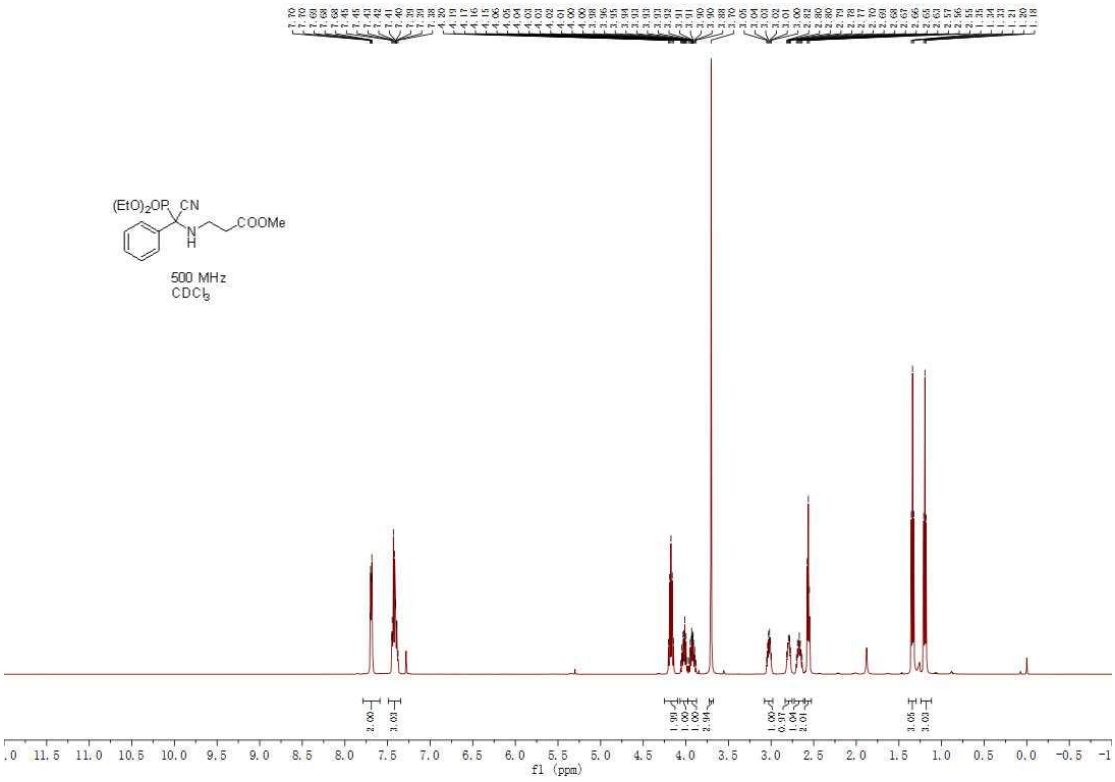
Diethyl (cyano((3-methoxypropyl)amino)(phenyl)methyl)phosphonate (1u)

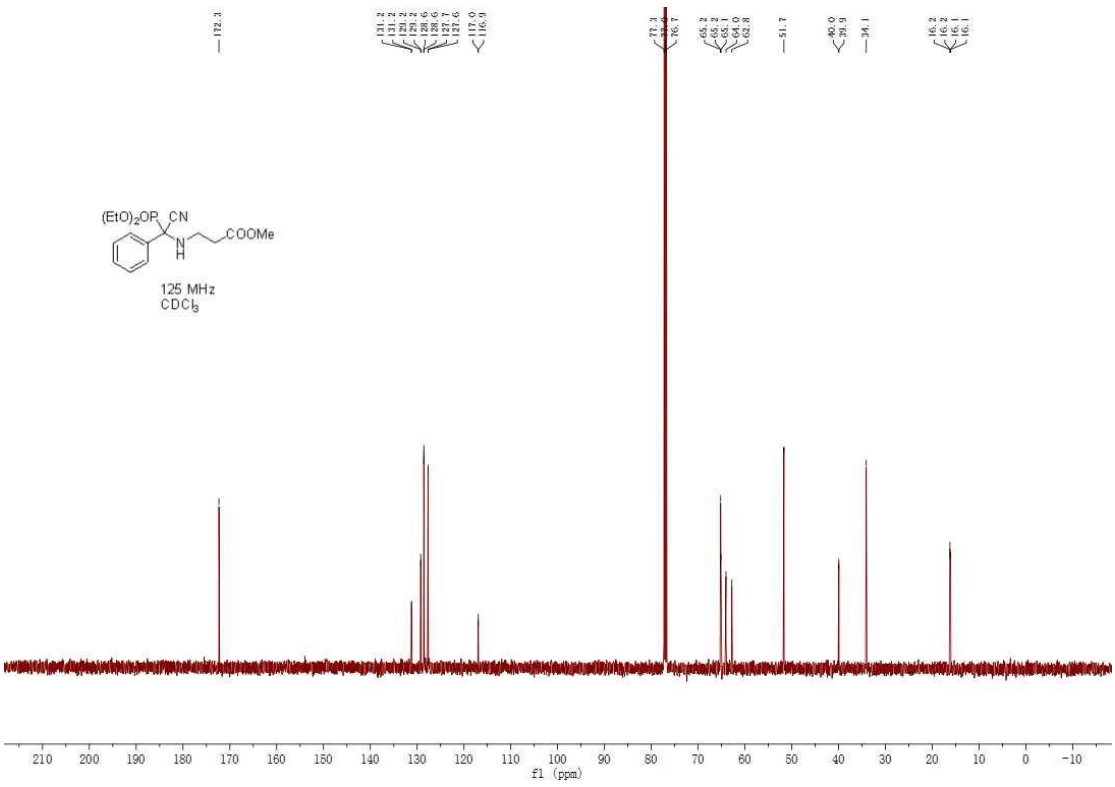


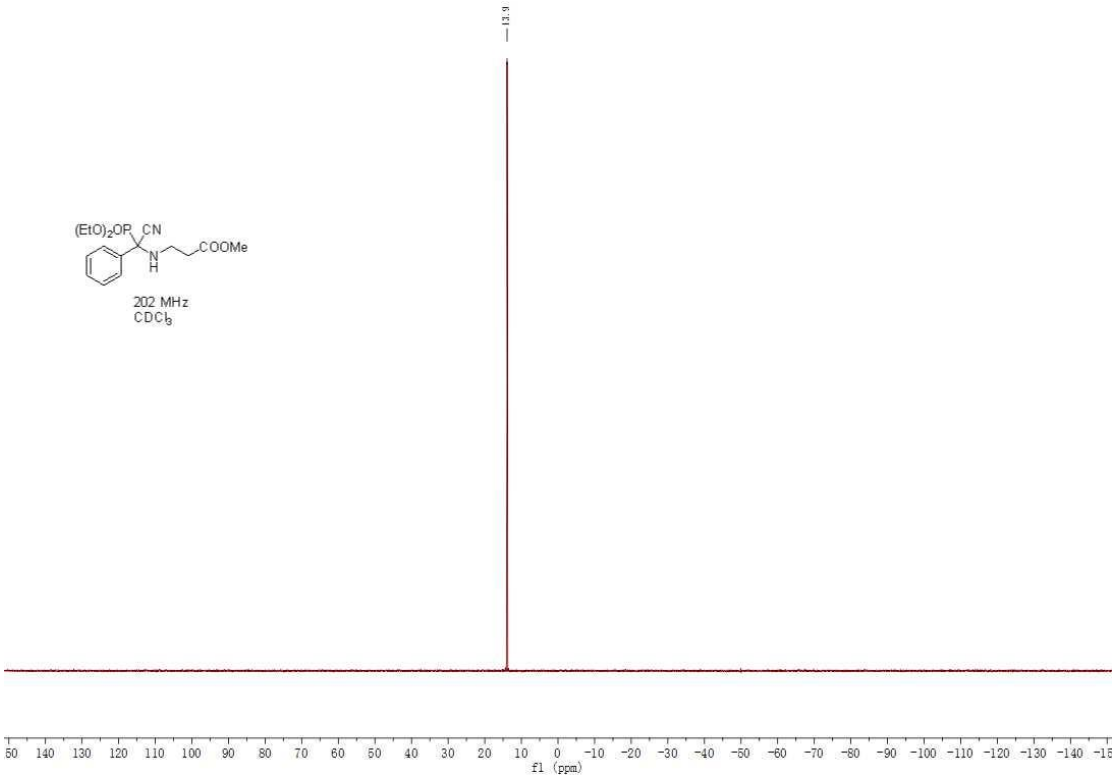

131.5
131.4
129.1
129.1
128.5
128.5
127.7
127.7
117.3
117.2
77.3
77.0
76.7
65.1
65.1
64.9
64.4
63.1
58.6
42.7
42.6
29.5
16.3
16.2
16.2
16.1
(EtO)2OP
CN
N
H
OMe
125 MHz
CDCl3
f1 (ppm)


14.2
(EtO)2OP
CN
N
H
OMe
202 MHz
CDCl3
f1 (ppm)

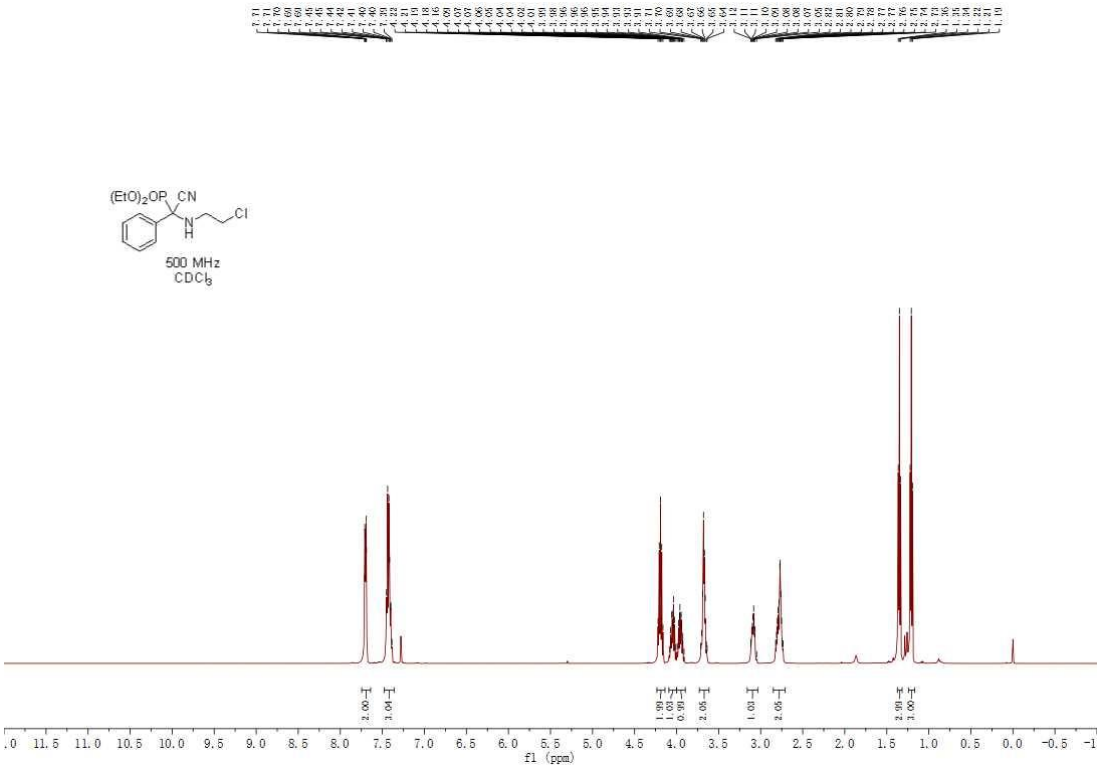
Methyl 3-((cyano(diethoxyphosphoryl)(phenyl)methyl)amino)propanoate (1v)

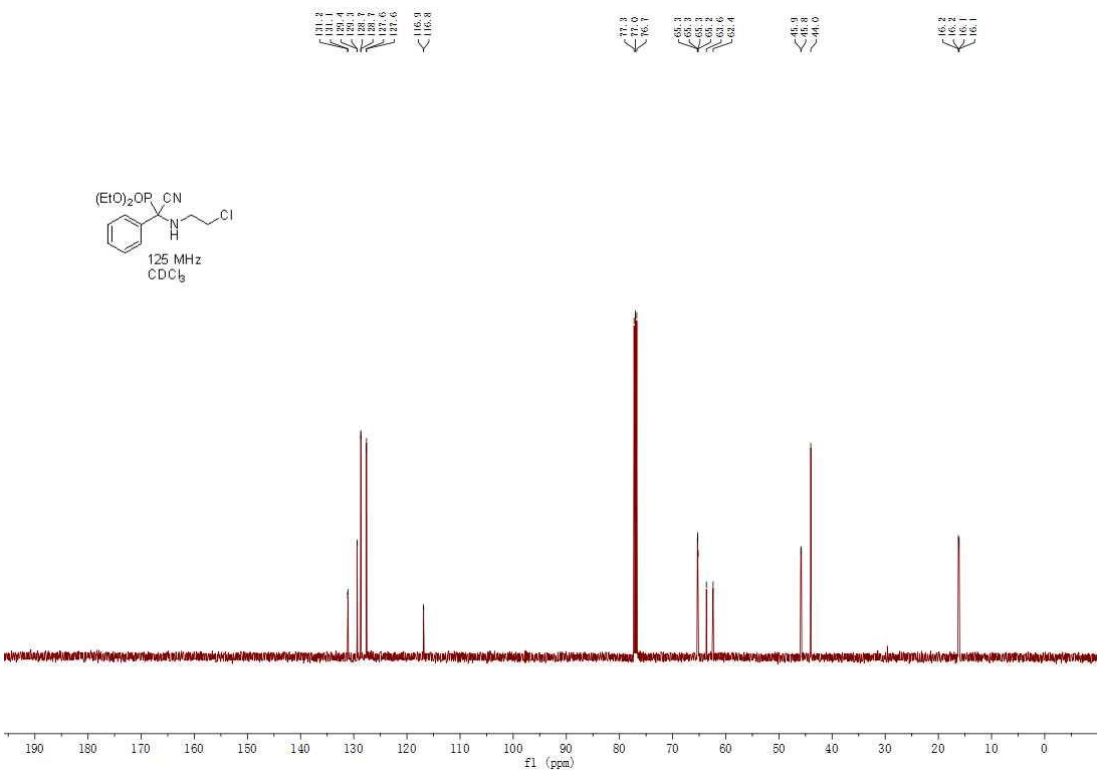


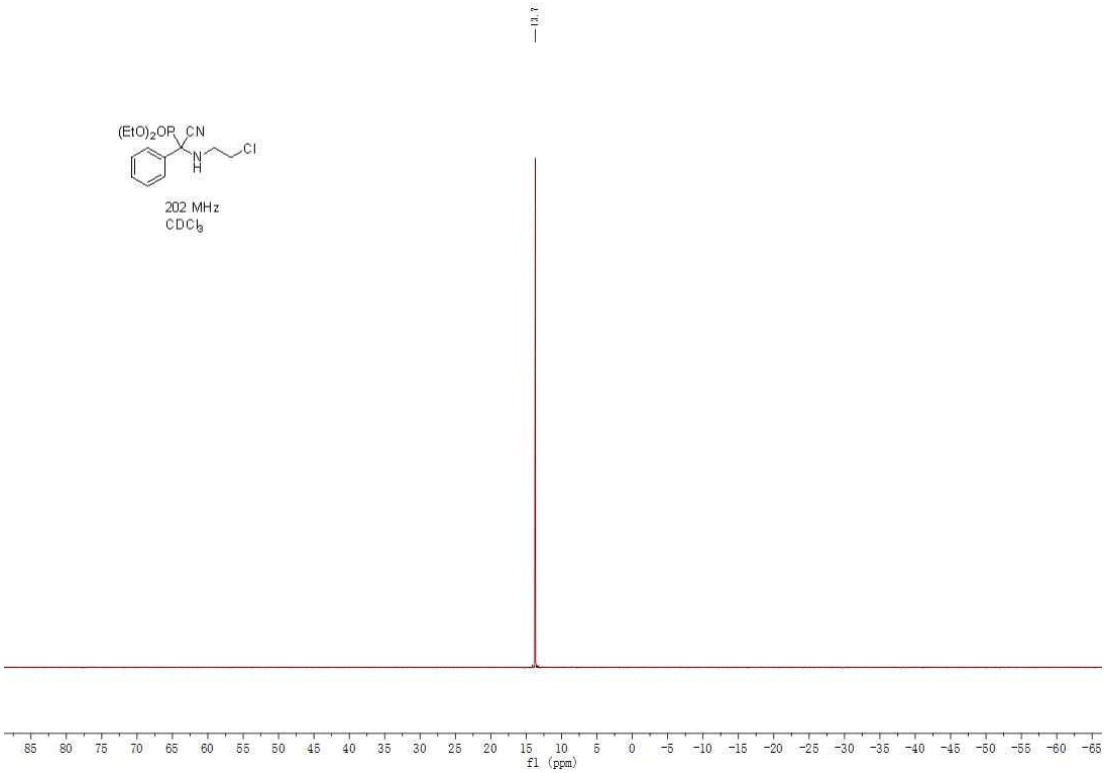




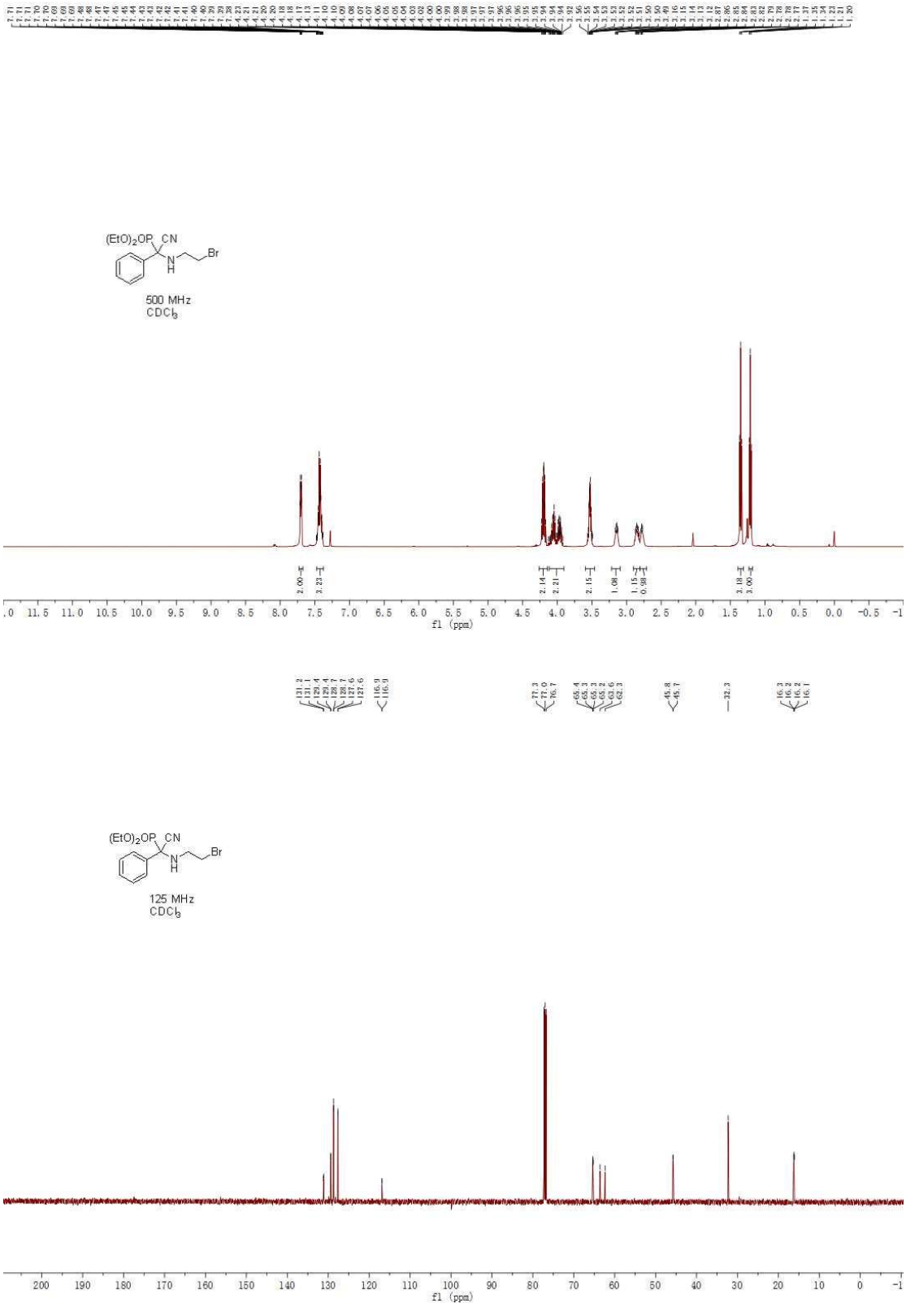
Diethyl (((2-chloroethyl)amino)(cyano)(phenyl)methyl)phosphonate (1w)

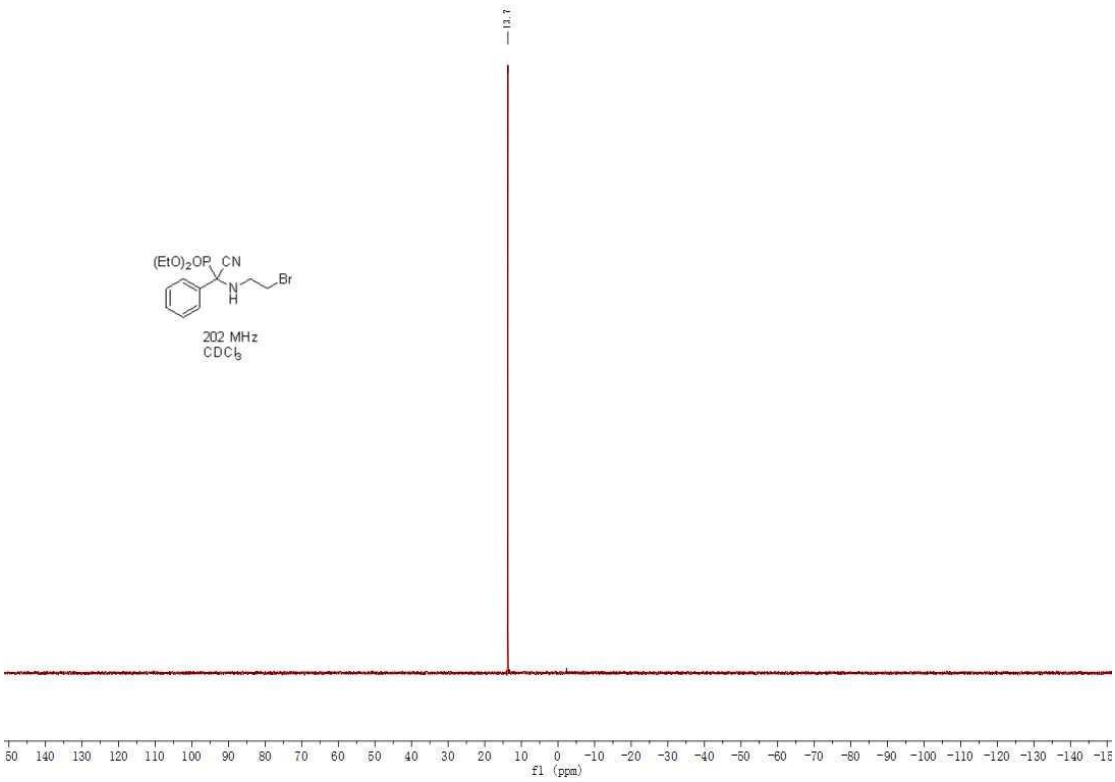



131.2
131.1
129.4
129.3
128.7
127.6
127.6
116.9
116.8
77.3
77.0
76.7
65.3
65.3
65.3
65.2
63.6
62.4
45.9
45.8
44.0
16.2
16.2
16.1
16.1
(EtO)2OP
CN
N
H
Cl
125 MHz
CDCl3
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

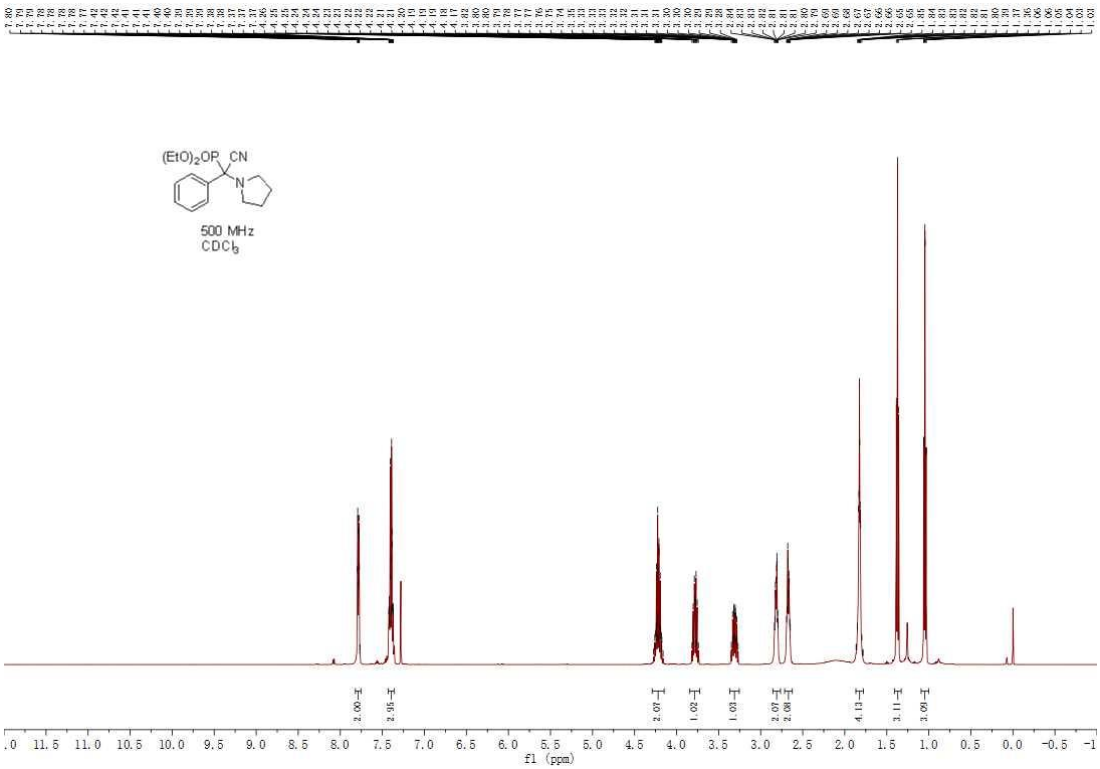

13.7
(EtO)2OP
CN
N
H
Cl
202 MHz
CDCl3
85 80 75 70 65 60 55 50 45 40 35 30 25 20 15 10 5 0 -5 -10 -15 -20 -25 -30 -35 -40 -45 -50 -55 -60 -65
f1 (ppm)

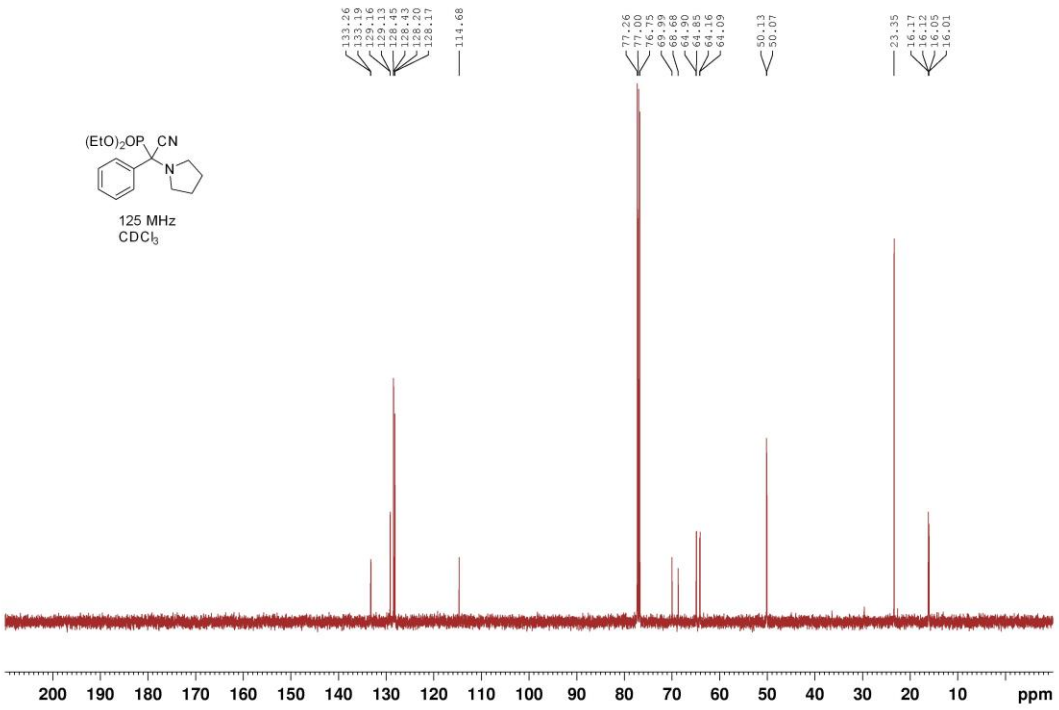
Diethyl (((2-bromoethyl)amino)(cyano)(phenyl)methyl)phosphonate (1x)

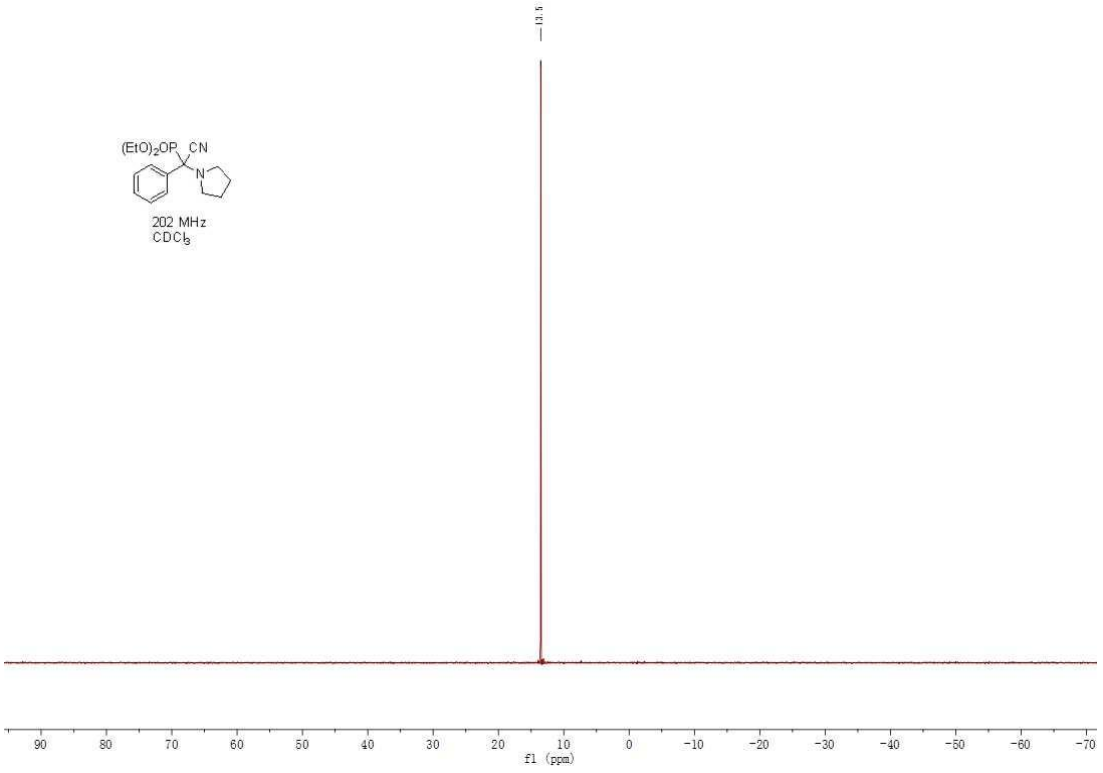




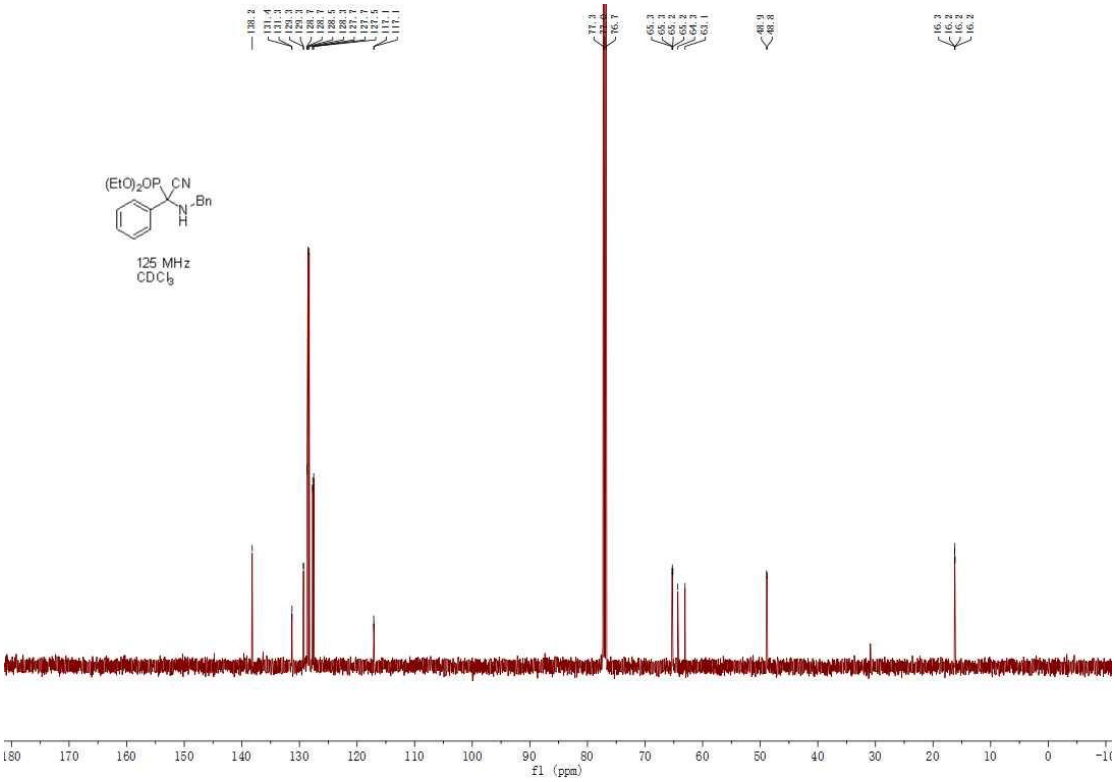
Diethyl (cyano(phenyl)(pyrrolidin-1-yl)methyl)phosphonate (1y)

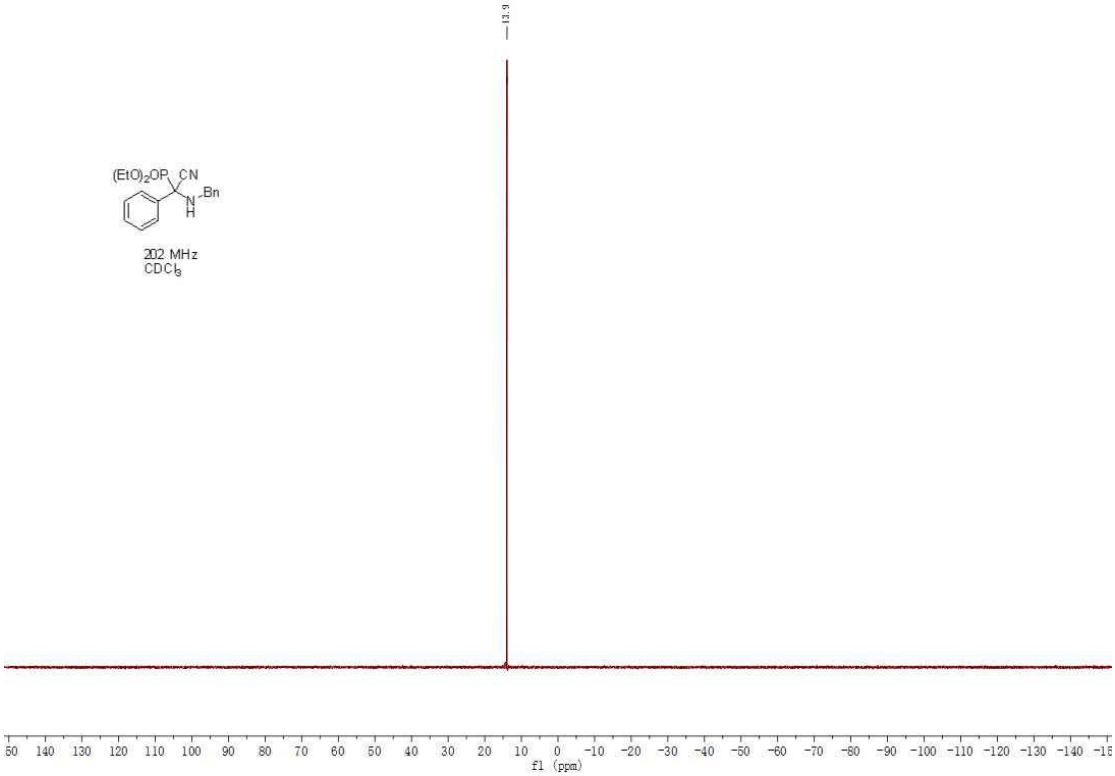



133.26
131.19
129.16
129.13
128.45
128.43
128.20
128.17
114.68
77.26
77.00
76.75
69.99
68.68
64.90
64.85
64.16
64.09
50.13
50.07
23.35
16.17
16.12
16.05
16.01
(EtO)2OP CN
N
125 MHz
CDCl3
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm

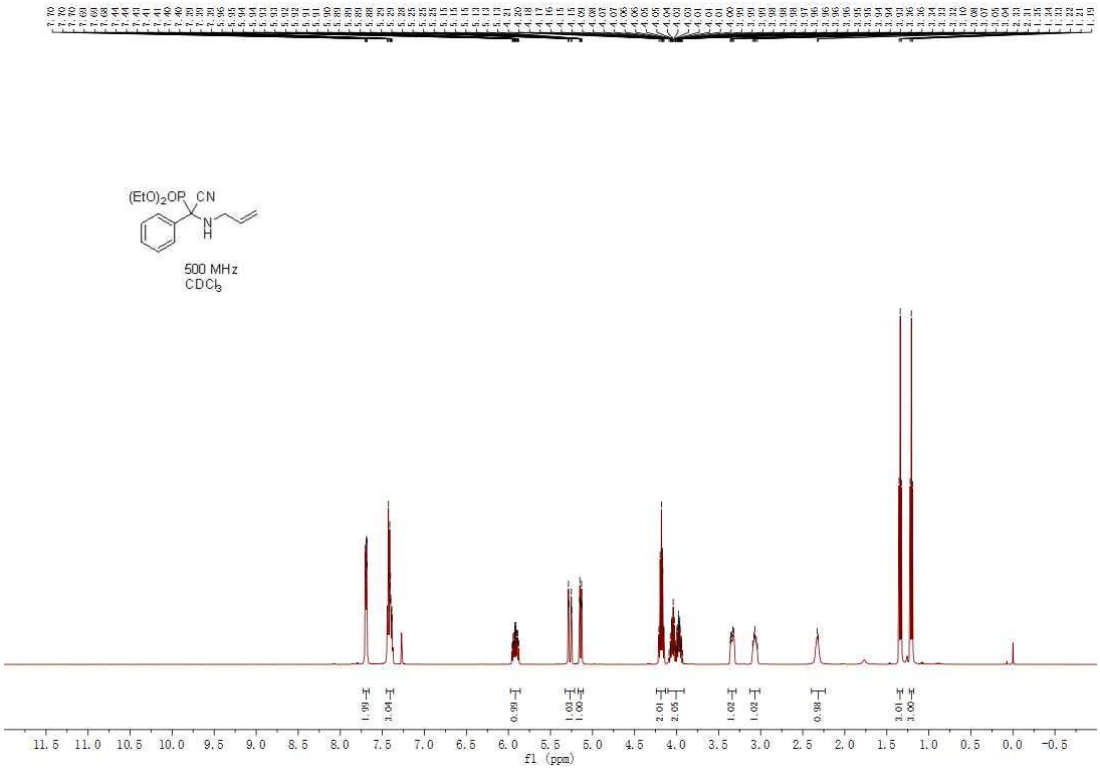

13.5
(EtO)2OP CN
N
202 MHz
CDCl3
90 80 70 60 50 40 30 20 10 0 -10 -20 -30 -40 -50 -60 -70
f1 (ppm)

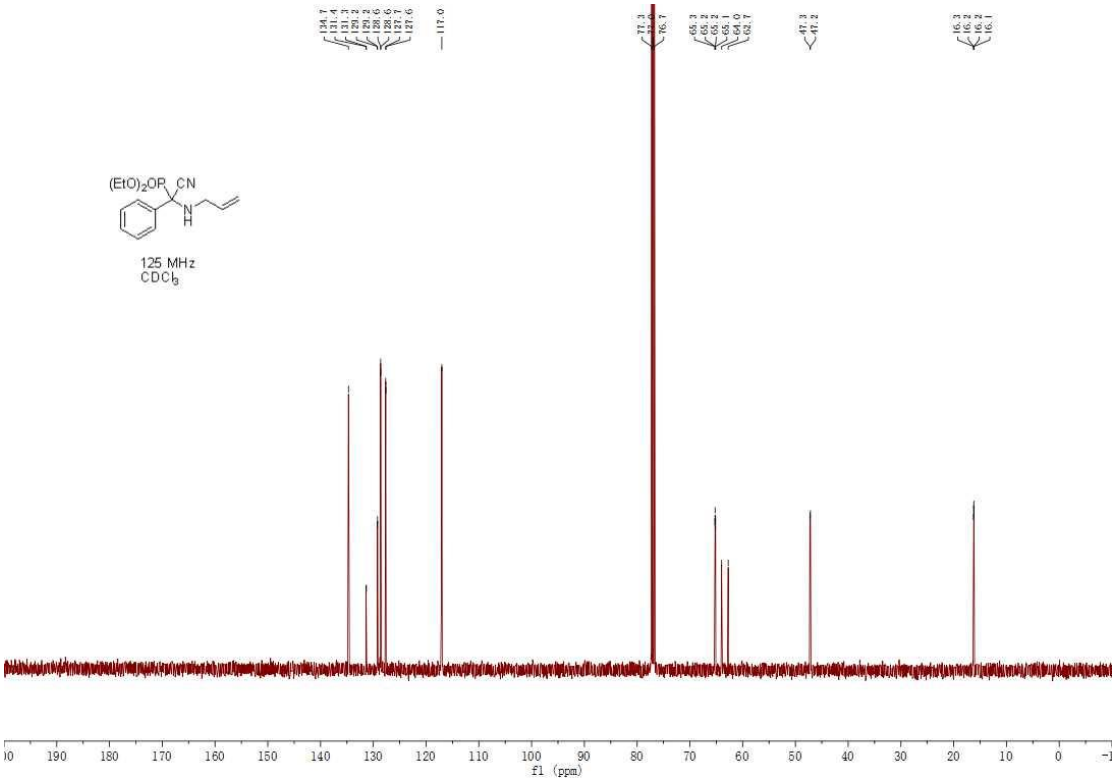
Diethyl ((benzylamino)(cyano)(phenyl)methyl)phosphonate (1z)

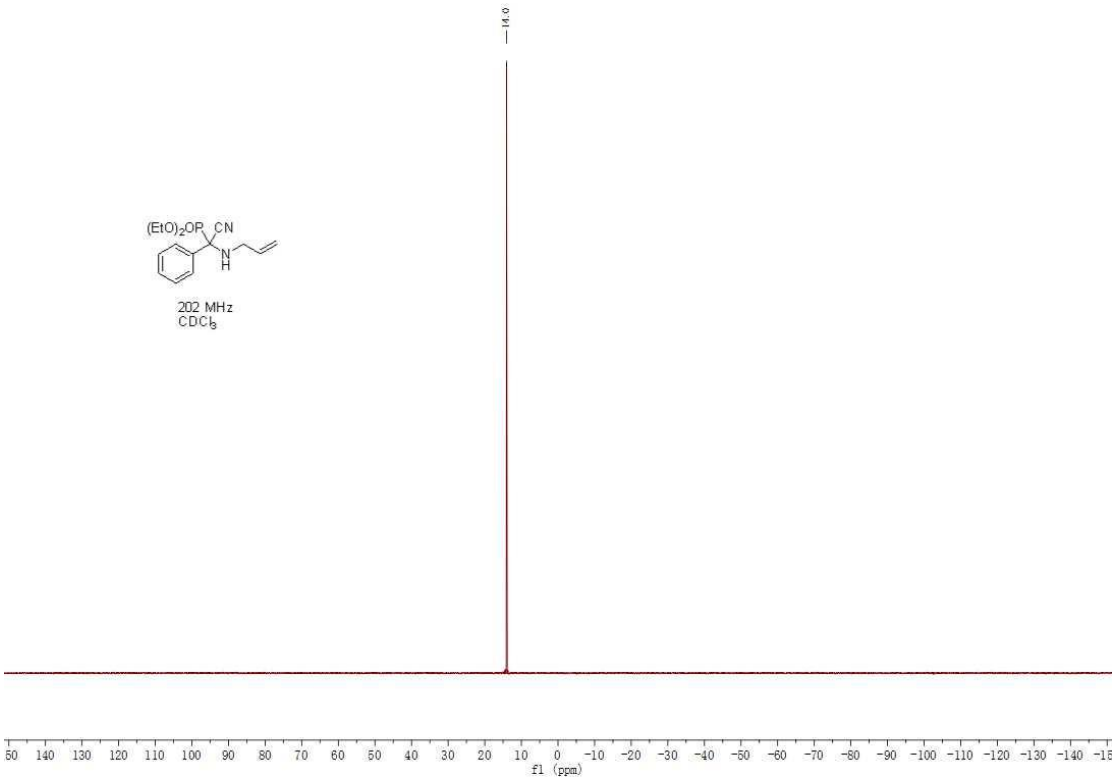




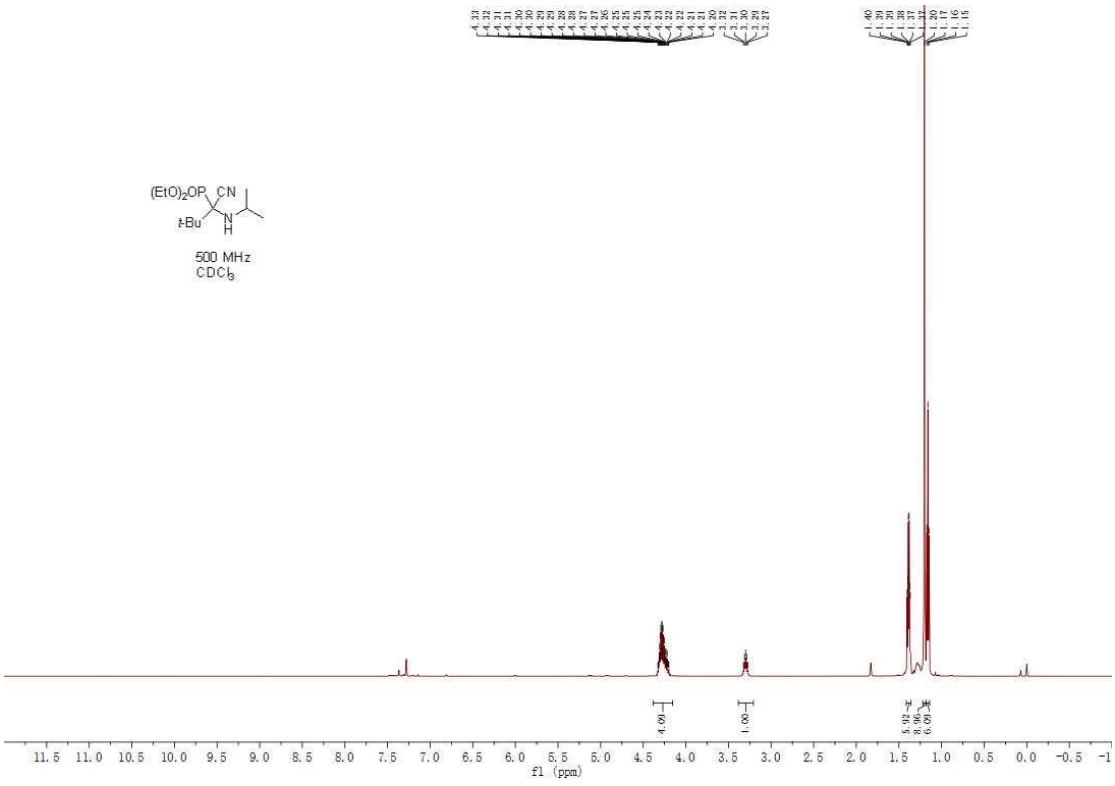
Diethyl ((allylamino)(cyano)(phenyl)methyl)phosphonate (1aa)

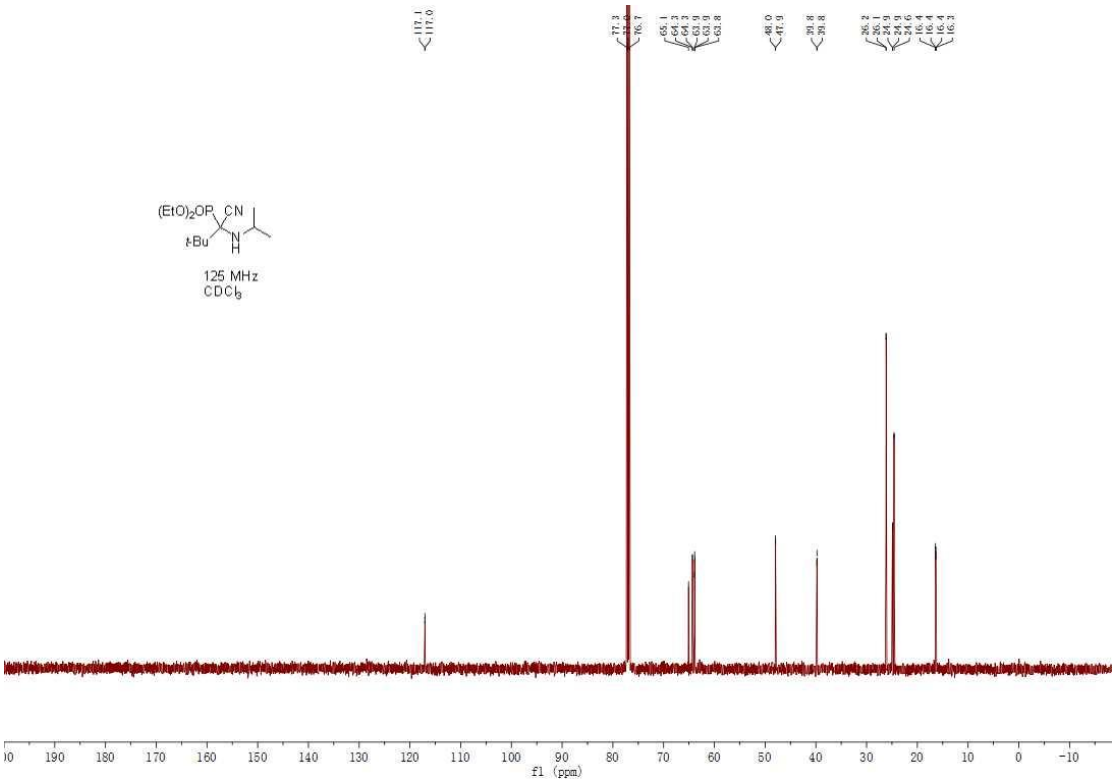


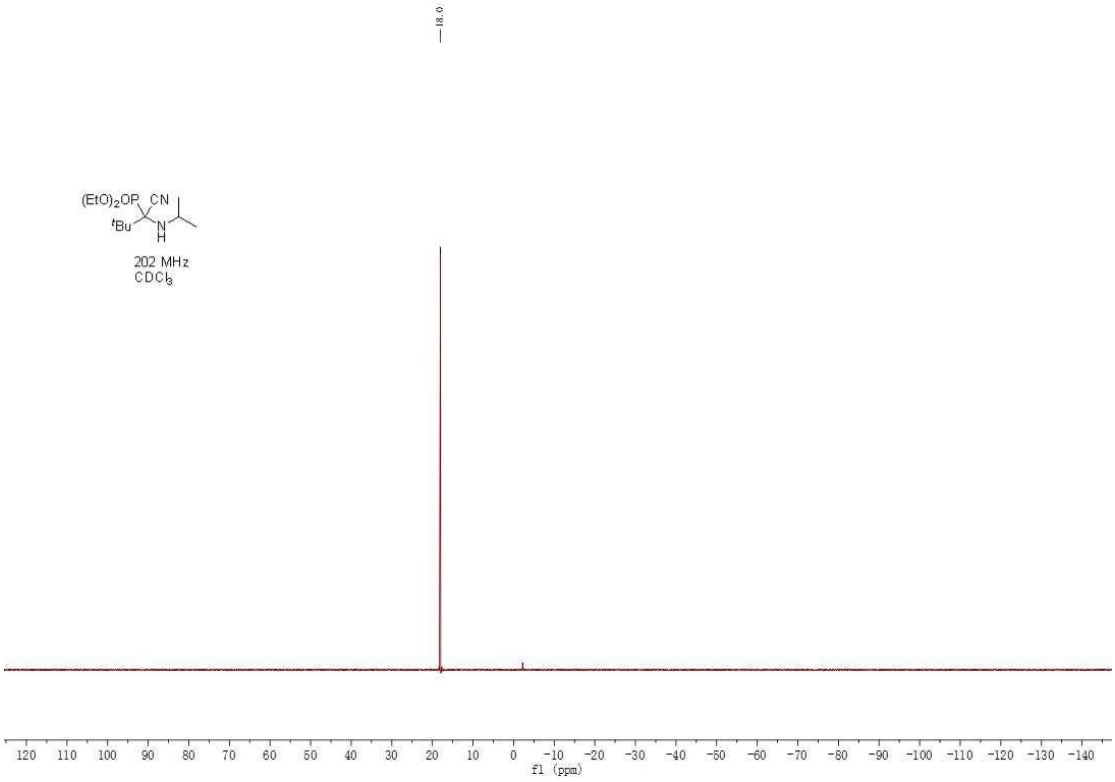




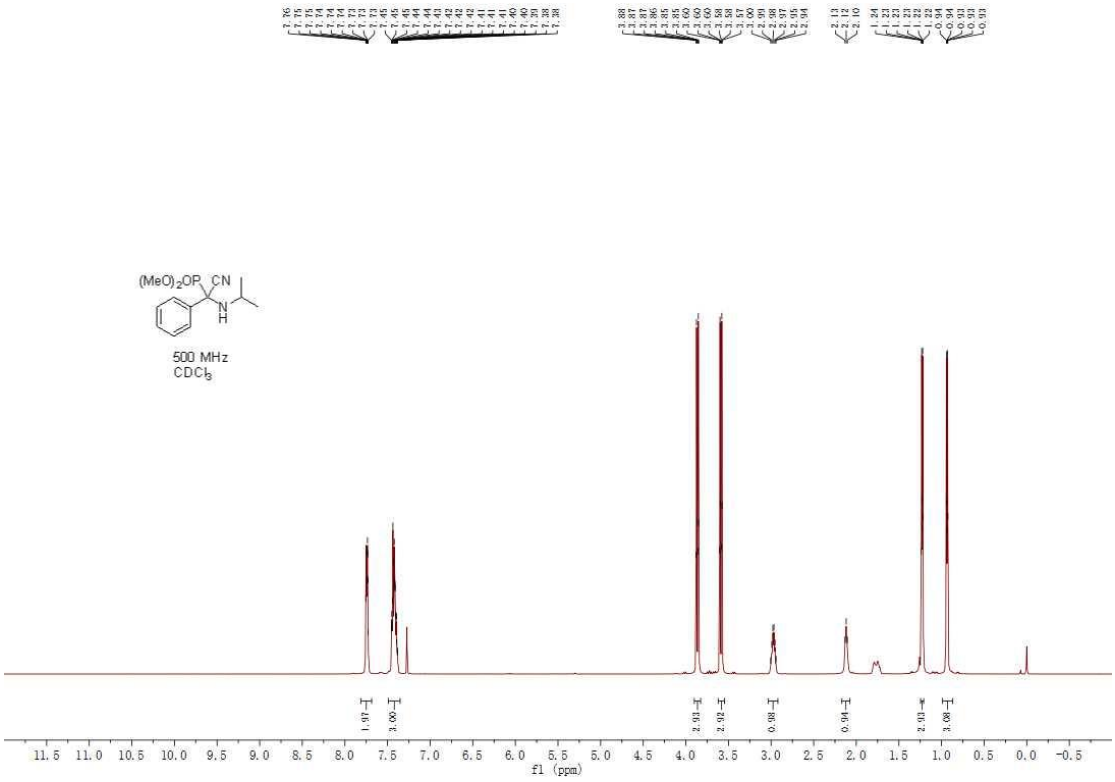
Diethyl (1-cyano-1-(isopropylamino)-2,2-dimethylpropyl)phosphonate (1ad)

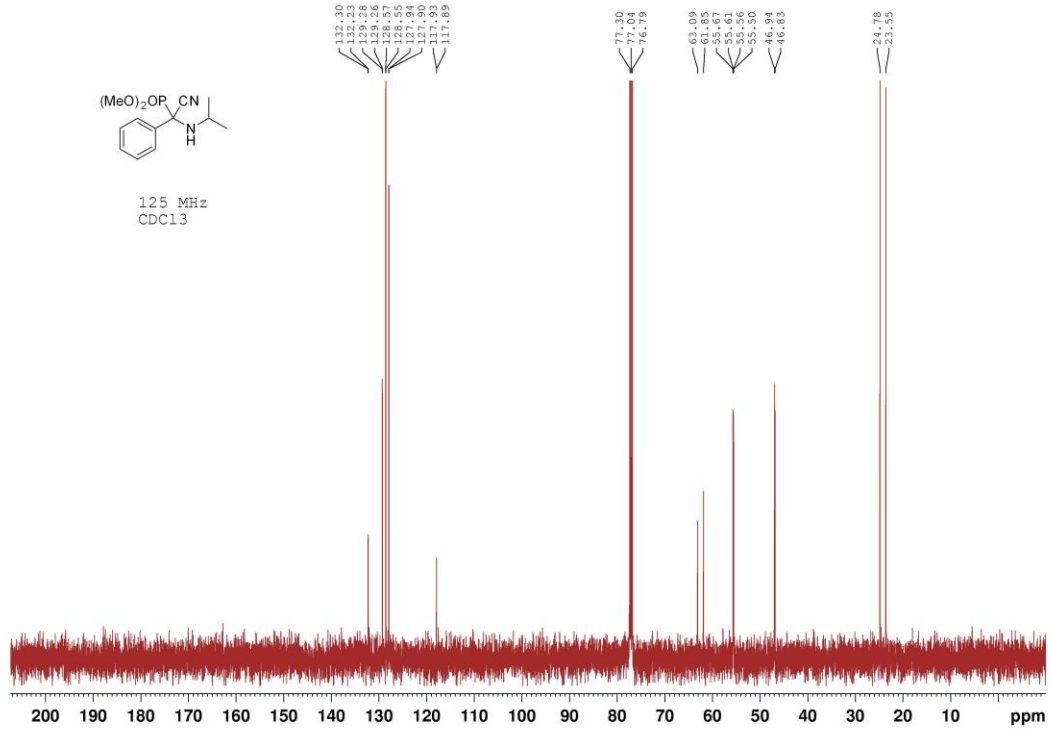


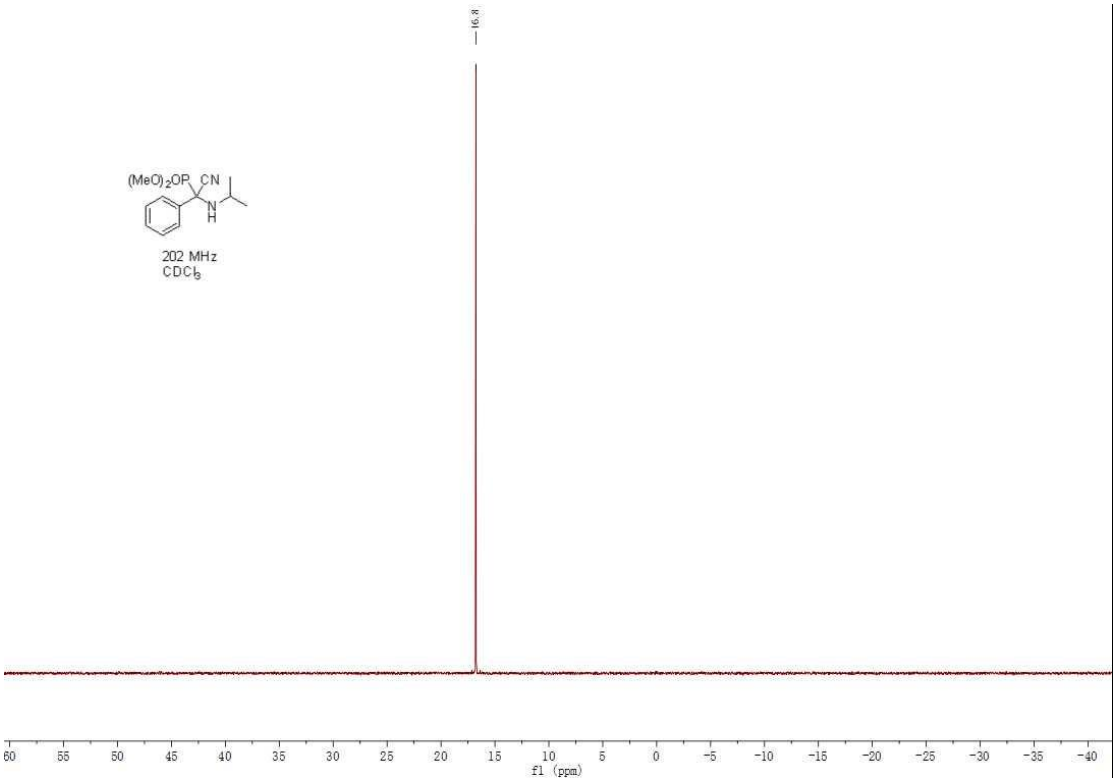

(EtO)2OP CN
tBu N H
125 MHz
CDCl3
117.1
117.0
77.3
76.7
65.1
64.3
63.9
63.8
48.0
47.9
31.8
29.8
26.2
26.1
24.9
24.6
16.4
16.3
f1 (ppm)


18.0
(EtO)2OP CN
tBu N H
202 MHz
CDCl3
f1 (ppm)

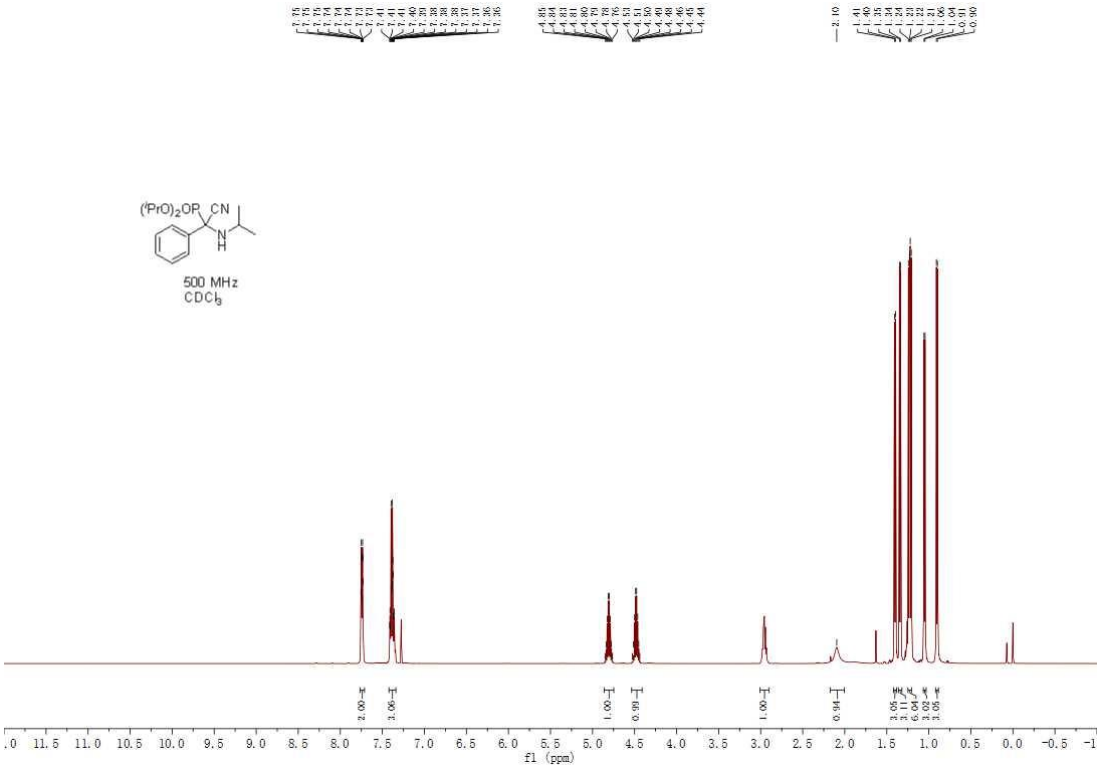
Dimethyl (cyano(isopropylamino)(phenyl)methyl)phosphonate (1ae)

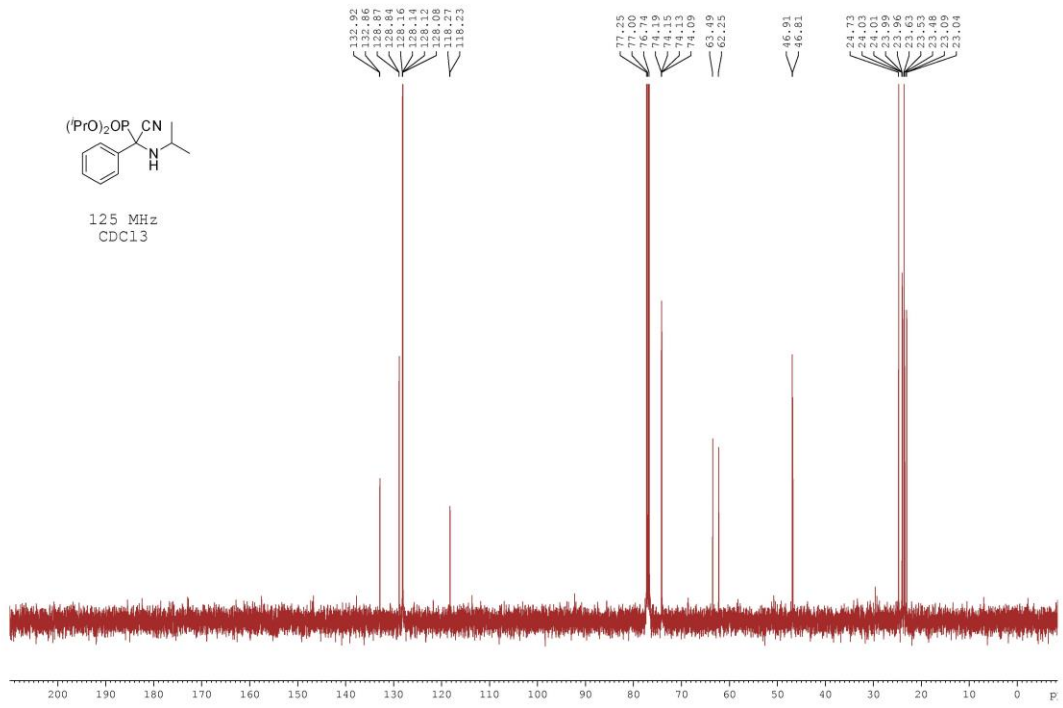


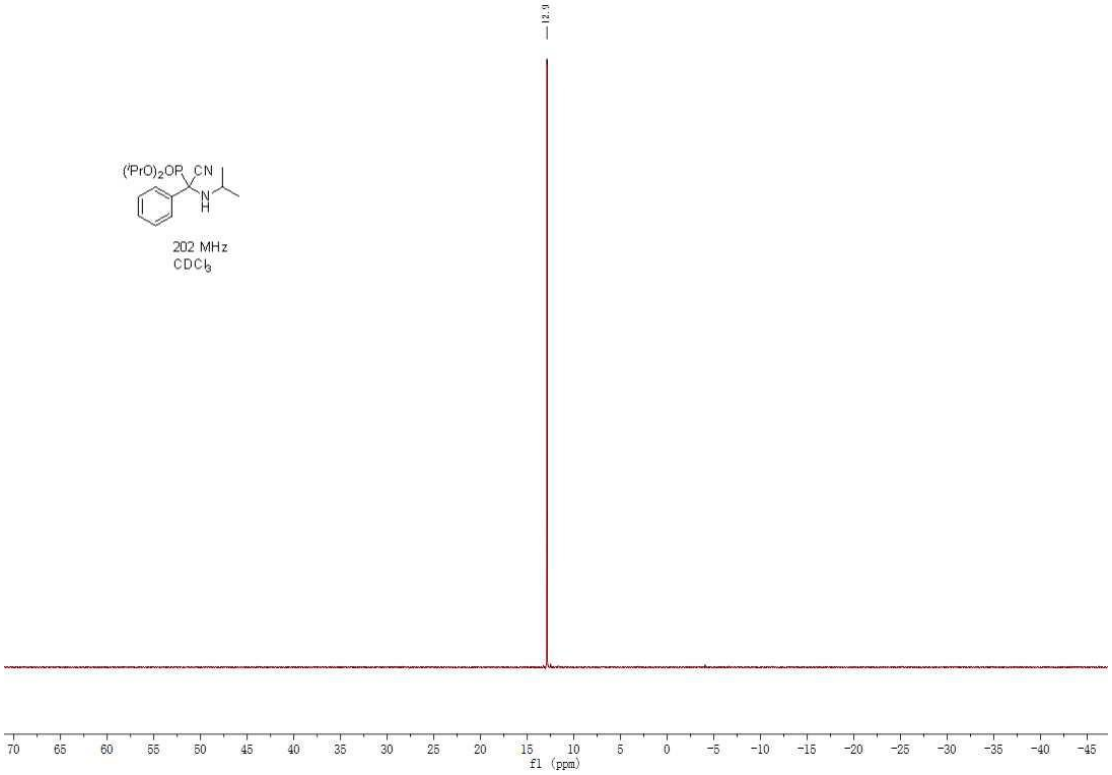




Diisopropyl (cyano(isopropylamino)(phenyl)methyl)phosphonate (1af)




132.92
132.86
128.87
128.84
128.16
128.14
128.12
128.08
118.27
118.23
77.25
77.00
76.74
74.19
74.15
74.13
74.09
63.49
62.25
46.91
46.81
24.73
24.03
24.01
23.99
23.96
23.63
23.53
23.48
23.09
23.04
(iPrO)2OP CN
N
H
125 MHz
CDCl3
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 p


12.9
(iPrO)2OP CN
N
H
202 MHz
CDCl3
70 65 60 55 50 45 40 35 30 25 20 15 10 5 0 -5 -10 -15 -20 -25 -30 -35 -40 -45
f1 (ppm)