

Synthesis of 2-C-substituted benzothiazoles via a copper-promoted domino condensation/S-arylation/heterocyclization process

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General information

All reactions were carried out in oven-dried round-bottom flask (5 mL) under argon atmosphere.

All reactions were magnetically stirred and monitored by analytical thin layer chromatography (TLC) using Yantai Huiyou pre-coated silica gel glass plates (0.15-0.20mm) with F254 indicator.

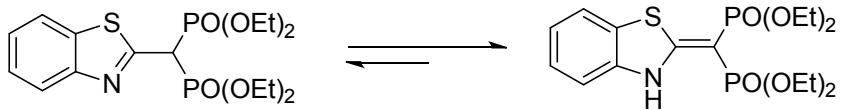
Unless otherwise noted, all solvents and other reagents are commercially available and used without further purification. ^1H , ^{13}C and ^{31}P NMR spectra were recorded on Varian Mercury-300/400 and Varian Mercury-400/500 spectrometers. Tetramethylsilane (TMS) was used as internal standard (^1H NMR: TMS at 0.00 ppm; CHCl_3 at 7.26 ppm; DMSO at 2.50 ppm; ^{13}C NMR: CDCl_3 at 77.0 ppm; DMSO-d_6 at 39.6 ppm). ^{31}P NMR was recorded as spin coupled spectrum and 85 % H_3PO_4 was used as the external reference. Low and high-resolution mass spectra (LRMS and HRMS) were recorded on a Finnigan/MAT-95 (EI), Finnigan LCQ/DECA and Micromass Ultra Q-TOF (ESI) spectrometer. Melting points were measured by Büchi 510 melting point apparatus without further correction.

Typical experimental procedure:

A mixture of commercially available tetraethyl methylenebis(phosphonate)/phenylacetonitrile (0.375 mmol), t-BuOK (0.75 mmol) in DMF (1 mL, anhydrous) was stirred at room temperature for 5 mins. Then CS_2 (0.3 mmol), 2-iodoaniline (0.25 mmol) and CuCl_2 (0.25 mmol) was added to the reaction flask successively. The mixture was evacuated and backfilled with argon three times.

The resulting mixture was stirred at 30 °C pre-heated by an oil bath under argon overnight. The cooled solution was partitioned between ethyl acetate and water. The combined organic layer was washed with water and brine, and then dried over Na_2SO_4 . After removal of the solvent under reduced pressure, the residue was purified by column chromatography to give the desired

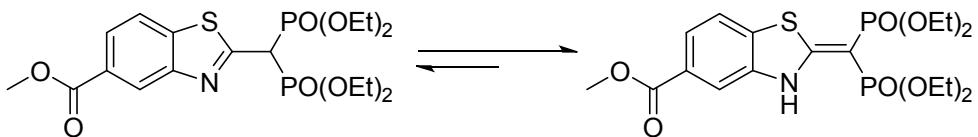
benzothiazoles.



White solid; HRMS (EI): m/z calcd for $C_{16}H_{25}NO_6P_2S$ [M $^+$]: 421.0878; found: 421.0877.

Tetraethyl (benzo[*d*]thiazol-2-ylmethylene)bis(phosphonate): 1H NMR (300 MHz, CDCl₃) δ 8.02 (d, J = 8.1 Hz, 1 H), 7.87 (d, J = 8.1 Hz, 1 H), 7.50 – 7.37 (m, 2 H), 4.60 (t, J = 24.0 Hz, 1 H), 4.29 – 4.16 (m, 8 H), 1.31 – 1.22 (m, 12 H); ^{13}C NMR (126 MHz, CDCl₃) δ 126.0, 125.3, 123.1, 121.5, 63.9 (d, J = 6.3 Hz, POCH₂), 63.8 (d, J = 6.3 Hz, POCH₂), 16.3 (d, J = 7.6 Hz, POCH₂CH₃), 16.2 (d, J = 7.6 Hz, POCH₂CH₃); ^{31}P NMR (202 MHz, CDCl₃) δ 14.75 (dp, J = 30.3, 6.1 Hz).

Tetraethyl (benzo[*d*]thiazol-2(3*H*)-ylidenemethylene)bis(phosphonate): 1H NMR (300 MHz, CDCl₃) δ 7.45 (dd, J = 7.5, 0.6 Hz, 1 H), 7.28 – 7.13 (m, 2 H), 7.10 (td, J = 7.5, 0.9 Hz, 1 H), 4.16 – 4.02 (m, 8 H), 1.37 – 1.31 (m, 12 H); ^{13}C NMR (126 MHz, CDCl₃) δ 172.5 (t, J = 10.1 Hz, PCC), 152.4, 138.7, 126.5, 126.4, 122.8, 121.2, 111.8, 62.0 (d, J = 6.3 Hz, POCH₂), 61.6 (d, J = 6.3 Hz, POCH₂), 16.3 (d, J = 7.6 Hz, POCH₂CH₃), 16.2 (d, J = 7.6 Hz, POCH₂CH₃); ^{31}P NMR (202 MHz, CDCl₃) δ 24.20 (dp, J = 30.3, 6.1 Hz), 22.49 (dp, J = 30.3, 6.1 Hz).

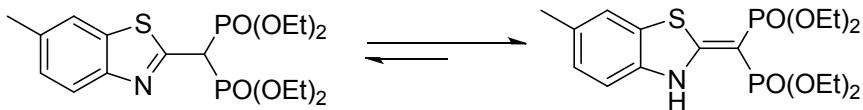


Colorless oil; HRMS (EI): m/z calcd for $C_{18}H_{27}NO_8P_2S$ [M $^+$]: 479.0933; found: 479.0928.

Methyl 2-(bis(diethoxyphosphoryl)methyl)benzo[*d*]thiazole-5-carboxylate: 1H NMR (300 MHz, CDCl₃) δ 8.68 (s, 1 H), 8.08 (d, J = 6.9 Hz, 1 H), 7.93 (d, J = 8.1 Hz, 1 H), 4.28 – 4.18 (m, 9 H),

3.96 (s, 3 H), 1.30 – 1.24 (m, 12 H); ^{13}C NMR (126 MHz, CDCl_3) δ 166.8, 146.1, 141.0, 128.5, 126.0, 124.7, 121.5, 65.4 (s, POCH_2), 65.3 (s, POCH_2), 52.4, 16.3 (d, $J = 6.3$ Hz, POCH_2CH_3), 16.2 (d, $J = 6.3$ Hz, POCH_2CH_3); ^{31}P NMR (202 MHz, CDCl_3) δ 14.53 (s).

Methyl 2-(bis(diethoxyphosphorylmethylene)-2,3-dihydrobenzo[*d*]thiazole-5-carboxylate: ^1H NMR (300 MHz, CDCl_3) δ 12.61 (s, 1 H), 7.83 (s, 1 H), 7.79 (dd, $J = 8.4, 1.5$ Hz, 1 H), 7.49 (d, $J = 8.1$ Hz, 1 H), 4.19 – 4.05 (m, 8 H), 3.92 (s, 3 H), 1.37 – 1.30 (m, 12 H); ^{13}C NMR (151 MHz, CDCl_3) δ 172.7 (t, $J = 10.6$ Hz, PCC), 166.4, 152.2, 139.0, 132.0, 128.7, 124.1, 121.0, 112.6, 62.2 (d, $J = 6.3$ Hz, POCH_2), 61.8 (d, $J = 6.3$ Hz, POCH_2), 52.4, 16.3 (d, $J = 7.6$ Hz, POCH_2CH_3), 16.3 (d, $J = 7.6$ Hz, POCH_2CH_3); ^{31}P NMR (202 MHz, CDCl_3) δ 23.39 (dp, $J = 28.3.0, 7.3$ Hz), 22.05 (dp, $J = 30.3, 6.1$ Hz).

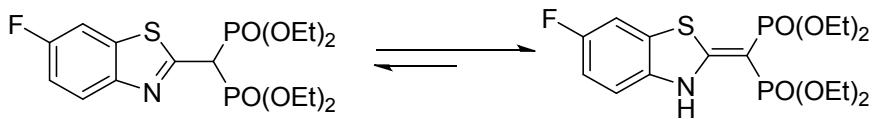


Colorless oil; HRMS (EI): m/z calcd for $\text{C}_{17}\text{H}_{27}\text{NO}_6\text{P}_2\text{S} [\text{M}^+]$: 435.1034; found: 435.1038.

Tetraethyl ((6-methylbenzo[*d*]thiazol-2-yl)methylene)bis(phosphonate): ^1H NMR (300 MHz, CDCl_3) δ 7.87 (d, $J = 8.7$ Hz, 1 H), 7.65 (s, 1 H), 7.27 (d, $J = 8.7$ Hz, 1 H), 4.56 (t, $J = 24.0$ Hz, 1 H), 4.27 – 4.12 (m, 8 H), 2.43 (s, 3 H), 1.30 – 1.21 (m, 12 H); ^{13}C NMR (101 MHz, CDCl_3) δ 136.0, 135.0, 127.2, 122.1, 120.7, 63.5 (d, $J = 6.1$ Hz, POCH_2), 63.3 (d, $J = 6.1$ Hz, POCH_2), 45.6 (t, $J = 112.1$ Hz, PCHP), 21.1, 15.9 (d, $J = 5.1$ Hz, POCH_2CH_3), 15.8 (d, $J = 5.1$ Hz, POCH_2CH_3); ^{31}P NMR (202 MHz, CDCl_3) δ 14.85 (d, $J = 24.2$ Hz).

Tetraethyl ((6-methylbenzo[*d*]thiazol-2(3*H*)-ylidene)methylene)bis(phosphonate): ^1H NMR (300 MHz, CDCl_3) δ 12.45 (s, 1 H), 7.25 (dd, $J = 8.7, 0.6$ Hz, 1 H), 7.08 – 7.02 (m, 2 H), 4.15 – 4.03 (m, 8 H), 2.36 (s, 3 H), 1.36 – 1.27 (m, 12 H); ^{13}C NMR (101 MHz, CDCl_3) δ 172.0 (t, $J = 10.1$ Hz,

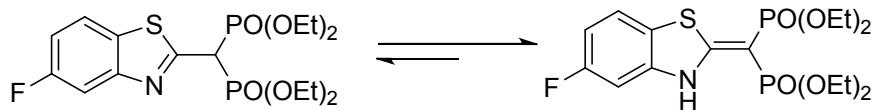
PCC), 150.1, 136.2, 132.3, 127.0, 126.2, 120.8, 111.1, 61.6 (d, $J = 5.1$ Hz, POCH_2), 61.2 (d, $J = 5.1$ Hz, POCH_2), 20.7, 15.9 (d, $J = 5.1$ Hz, POCH_2CH_3), 15.8 (d, $J = 5.1$ Hz, POCH_2CH_3); ^{31}P NMR (202 MHz, CDCl_3) δ 24.48 (d, $J = 30.3$ Hz), 22.69 (dp, $J = 30.3, 6.1$ Hz).



White solid; HRMS (EI): m/z calcd for $\text{C}_{16}\text{H}_{24}\text{FNO}_6\text{P}_2\text{S} [\text{M}^+]$: 439.0784; found: 439.0788.

Tetraethyl ((6-fluorobenzo[*d*]thiazol-2-yl)methylene)bis(phosphonate): ^1H NMR (300 MHz, CDCl_3) δ 7.96 (dd, $J = 9.0, 4.8$ Hz, 1 H), 7.54 (dd, $J = 8.4, 2.4$ Hz, 1 H), 7.23 – 7.15 (m, 1 H), 4.55 (t, $J = 24.3$ Hz, 1 H), 4.30 – 4.17 (m, 8 H), 1.32 – 1.23 (m, 12 H); ^{13}C NMR (151 MHz, CDCl_3) δ 160.6 (d, $J = 246.1$ Hz, FC), 149.0, 137.3 (d, $J = 11.1$ Hz, FCCC), 128.0 (d, $J = 10.1$ Hz, FCCC), 114.8 (d, $J = 24.6$ Hz, FCC), 107.6 (d, $J = 26.7$ Hz, FCC), 64.0 (d, $J = 6.6$ Hz, POCH_2), 63.9 (d, $J = 6.6$ Hz, POCH_2), 46.1 (t, $J = 131.4$ Hz, PCHP), 16.3 (d, $J = 7.4$ Hz, POCH_2CH_3), 16.3 (d, $J = 7.2$ Hz, POCH_2CH_3); ^{31}P NMR (202 MHz, CDCl_3) δ 14.66 (dp, $J = 24.2, 8.1$ Hz).

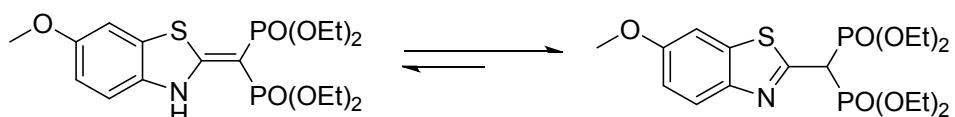
Tetraethyl ((6-fluorobenzo[*d*]thiazol-2(3*H*)-ylidene)methylene)bis(phosphonate): ^1H NMR (300 MHz, CDCl_3) δ 12.51 (s, 1 H), 7.23 – 7.15 (m, 1 H), 7.10 (dd, $J = 9.0, 4.2$ Hz, 1 H), 6.97 (td, $J = 9.0, 2.4$ Hz, 1 H), 4.17 – 4.01 (m, 8 H), 1.39 – 1.29 (m, 12 H); ^{13}C NMR (151 MHz, CDCl_3) δ 172.8 (t, $J = 10.2$ Hz, PCC), 159.3, 158.8 (d, $J = 242.7$ Hz, FC), 135.2, 124.1 (d, $J = 9.3$ Hz, FCCC), 113.9 (d, $J = 24.4$ Hz, FCC), 112.4 (d, $J = 8.8$ Hz, FCCC), 108.4 (d, $J = 27.2$ Hz, FCC), 62.2 (d, $J = 5.2$ Hz, POCH_2), 61.7 (d, $J = 5.3$ Hz, POCH_2), 16.3 (d, $J = 7.4$ Hz, POCH_2CH_3), 16.3 (d, $J = 7.2$ Hz, POCH_2CH_3); ^{31}P NMR (202 MHz, CDCl_3) δ 22.50 (d, $J = 28.3$ Hz), 23.90 (d, $J = 28.3$ Hz).



White solid; HRMS (EI): *m/z* calcd for C₁₆H₂₄FNO₆P₂S [M⁺]: 439.0784; found: 439.0778.

Tetraethyl ((5-fluorobenzo[*d*]thiazol-2-yl)methylene)bis(phosphonate): ¹H NMR (300 MHz, CDCl₃) δ 7.80 (dd, *J* = 9.3, 4.8 Hz, 1 H), 7.71 (td, *J* = 9.3, 2.4 Hz, 1 H), 7.17 (td, *J* = 9.3, 2.1 Hz, 1 H), 4.57 (t, *J* = 23.7 Hz, 1 H), 4.30 – 4.17 (m, 8 H), 1.29 – 1.18 (m, 12 H); ¹³C NMR (126 MHz, CDCl₃) δ 161.6 (d, *J* = 243.2 Hz, FC), 131.7, 122.2 (d, *J* = 9.8 Hz, FCCC), 114.1 (d, *J* = 25.2 Hz, FCC), 113.4 (d, *J* = 22.5 Hz, FCC), 109.5, 64.0 (d, *J* = 6.8 Hz, POCH₂), 63.8 (d, *J* = 6.8 Hz, POCH₂), 46.2 (t, *J* = 131.9 Hz, PCHP), 16.3 (d, *J* = 6.9 Hz, POCH₂CH₃), 16.2 (d, *J* = 6.9 Hz, POCH₂CH₃); ³¹P NMR (202 MHz, CDCl₃) δ 14.52 (dt, *J* = 24.0, 8.6 Hz).

Tetraethyl ((5-fluorobenzo[*d*]thiazol-2(3H)-ylidene)methylene)bis(phosphonate): ¹H NMR (300 MHz, CDCl₃) δ 12.60 (s, 1 H), 7.35 (dd, *J* = 8.5, 5.0 Hz, 1 H), 6.90 (dd, *J* = 8.9, 2.2 Hz, 1 H), 6.83 (td, *J* = 8.8, 2.3 Hz, 1 H), 4.17 – 4.02 (m, 8 H), 1.39 – 1.27 (m, 12 H); ¹³C NMR (126 MHz, CDCl₃) δ 173.7 (t, *J* = 9.9 Hz, PCC), 161.9 (d, *J* = 244.3 Hz, FC), 153.2, 121.9 (d, *J* = 9.9 Hz, FCCC), 121.8, 109.3, 109.2 (d, *J* = 23.2 Hz, FC), 99.6 (d, *J* = 27.5 Hz, FC), 62.1 (d, *J* = 5.4 Hz, POCH₂), 61.7 (d, *J* = 5.3 Hz, POCH₂), 16.3 (d, *J* = 6.9 Hz, POCH₂CH₃), 16.2 (d, *J* = 6.9 Hz, POCH₂CH₃); ³¹P NMR (202 MHz, CDCl₃) δ 23.70 (dt, *J* = 28.8, 8.2 Hz), 22.02 (dt, *J* = 28.8, 7.9 Hz).

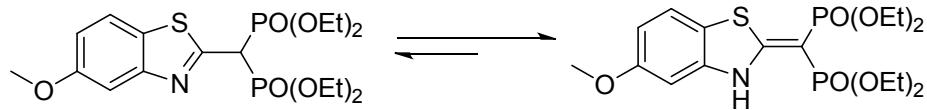


White solid; HRMS (EI): *m/z* calcd for C₁₇H₂₇NO₇P₂S [M⁺]: 451.0983; found: 451.0985.

Tetraethyl ((6-methoxybenzo[*d*]thiazol-2-yl)methylene)bis(phosphonate): ¹H NMR (300 MHz,

CDCl_3) δ 7.89 (d, $J = 8.7$ Hz, 1H), 7.30 (d, $J = 2.4$ Hz, 1H), 7.07 (dd, $J = 9.3, 2.4$ Hz, 1H), 4.53 (t, $J = 24.0$ Hz, 1H), 4.27 – 4.14 (m, 8 H), 3.87 (s, 3H), 1.28 – 1.22 (m, 12 H); ^{13}C NMR (151 MHz, CDCl_3) δ 172.3, 157.8, 146.9, 137.7, 127.9, 113.6, 105.8, 64.0 (d, $J = 6.7$ Hz, POCH_2), 63.8 (d, $J = 6.7$ Hz, POCH_2), 55.8, 45.9 (t, $J = 131.6$ Hz, PCHP), 16.3 (d, $J = 7.8$ Hz, POCH_2CH_3), 16.3 (d, $J = 7.8$ Hz, POCH_2CH_3); ^{31}P NMR (202 MHz, CDCl_3) δ 14.94 (s).

Tetraethyl ((6-methoxybenzo[*d*]thiazol-2(3H)-ylidene)methylene)bis(phosphonate): ^1H NMR (300 MHz, CDCl_3) δ 12.41 (s, 1H), 7.08 (d, $J = 9.0$ Hz, 1H), 6.98 (d, $J = 2.4$ Hz, 1H), 6.83 (dd, $J = 8.7, 2.4$ Hz, 1H), 4.18 – 4.03 (m, 8 H), 3.80 (s, 3H), 1.37 – 1.31 (m, 12 H); ^{13}C NMR (151 MHz, CDCl_3) δ 172.3 (t, $J = 10.1$ Hz, PCC), 156.6, 156.0, 132.8, 123.6, 115.6, 112.4, 103.7, 62.1, 62.0 (d, $J = 7.5$ Hz, POCH_2), 61.6 (d, $J = 7.5$ Hz, POCH_2), 16.3 (d, $J = 7.8$ Hz, POCH_2CH_3), 16.3 (d, $J = 7.8$ Hz, POCH_2CH_3); ^{31}P NMR (202 MHz, CDCl_3) δ 24.69 (s), 22.96 (s).

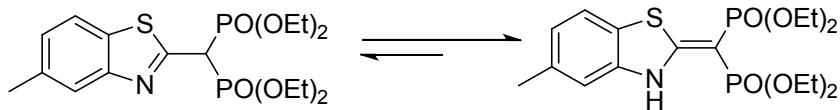


Colorless oil; HRMS (EI): m/z calcd for $\text{C}_{17}\text{H}_{27}\text{NO}_7\text{P}_2\text{S} [\text{M}^+]$: 451.0983; found: 451.0990.

Tetraethyl ((5-methoxybenzo[*d*]thiazol-2-yl)methylene)bis(phosphonate): ^1H NMR (300 MHz, CDCl_3) δ 7.70 (d, $J = 8.7$ Hz, 1H), 7.50 (d, $J = 2.4$ Hz, 1H), 7.08 – 6.99 (dd, $J = 8.7, 2.4$ Hz, 1H), 4.54 (t, $J = 24.3$ Hz, 1H), 4.25 – 4.14 (m, 8 H), 3.87 (s, 3H), 1.29 – 1.21 (m, 12 H); ^{13}C NMR (151 MHz, CDCl_3) δ 121.7, 117.9, 115.7, 105.4, 64.0 (d, $J = 6.7$ Hz, POCH_2), 63.8 (d, $J = 6.7$ Hz, POCH_2), 55.6, 16.4 (d, $J = 7.5$ Hz, POCH_2CH_3), 16.3 (d, $J = 7.4$ Hz, POCH_2CH_3); ^{31}P NMR (202 MHz, CDCl_3) δ 14.82 (dt, $J = 24.2, 8.4$ Hz).

Tetraethyl ((5-methoxybenzo[*d*]thiazol-2(3H)-ylidene)methylene)bis(phosphonate): ^1H NMR (300 MHz, CDCl_3) δ 12.51 (s, 1H), 7.29 (d, $J = 8.4$ Hz, 1H), 6.74 (d, $J = 2.4$ Hz, 1H), 6.69 (dd, $J =$

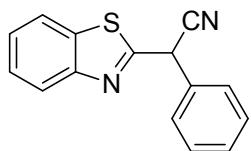
8.4, 2.4 Hz, 1H), 4.22 – 4.04 (m, 8 H), 3.78 (s, 3 H), 1.36 – 1.30 (m, 12 H); ^{13}C NMR (151 MHz, CDCl_3) δ 173.6, 159.2, 139.9, 121.7, 110.4, 97.3, 62.1 (d, $J = 5.2$ Hz, POCH_2), 61.7 (d, $J = 5.2$ Hz, POCH_2), 55.7, 16.4 (d, $J = 7.5$ Hz, POCH_2CH_3), 16.3 (d, $J = 7.5$ Hz, POCH_2CH_3); ^{31}P NMR (202 MHz, CDCl_3) δ 24.33 (dp, $J = 30.3, 7.7$ Hz), 22.41 (dp, $J = 30.4, 7.6$ Hz).



Colorless oil; HRMS (EI): m/z calcd for $\text{C}_{17}\text{H}_{27}\text{NO}_6\text{P}_2\text{S} [\text{M}^+]$: 435.1034; found: 435.1039.

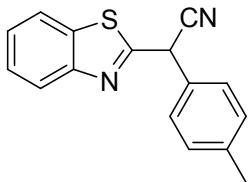
Tetraethyl ((5-methylbenzo[*d*]thiazol-2-yl)methylene)bis(phosphonate): ^1H NMR (300 MHz, CDCl_3) δ 7.82 (s, 1H), 7.74 (d, $J = 8.1$ Hz, 1 H), 7.25 (d, $J = 8.1$ Hz, 1 H), 4.57 (t, $J = 23.9$ Hz, 1H), 4.30 – 4.15 (m, 8 H), 2.49 (s, 3 H), 1.31 – 1.22 (m, 12 H); ^{13}C NMR (151 MHz, CDCl_3) δ 136.1, 133.3, 127.0, 123.1, 121.0, 64.0 (d, $J = 6.7$ Hz, POCH_2), 63.8 (d, $J = 6.7$ Hz, POCH_2), 46.1 (t, $J = 131.4$ Hz, PCHP), 21.5, 16.3 (d, $J = 7.2$ Hz, POCH_2CH_3), 16.3 (d, $J = 7.2$ Hz, POCH_2CH_3); ^{31}P NMR (202 MHz, CDCl_3) δ 14.80 (dt, $J = 24.2, 8.2$ Hz).

Tetraethyl ((5-methylbenzo[*d*]thiazol-2-yl)methylene)bis(phosphonate): ^1H NMR (300 MHz, CDCl_3) δ 12.46 (s, 1 H), 7.74 (d, $J = 8.1$ Hz, 1 H), 7.01 (s, 1 H), 6.93 (d, $J = 7.8$ Hz, 1 H), 4.18 – 4.01 (m, 8 H), 2.37 (s, 3 H), 1.37 – 1.31 (m, 12 H); ^{13}C NMR (151 MHz, CDCl_3) δ 172.8 (t, $J = 9.8$ Hz, PCC), 152.8, 139.0, 136.8, 124.0, 123.4, 120.8, 62.1 (d, $J = 5.3$ Hz, POCH_2), 61.6 (d, $J = 5.2$ Hz, POCH_2), 21.5, 16.3 (d, $J = 7.2$ Hz, POCH_2CH_3), 16.3 (d, $J = 7.4$ Hz, POCH_2CH_3); ^{31}P NMR (202 MHz, CDCl_3) δ 24.35 (dp, $J = 30.3, 7.7$ Hz), 22.61 (dp, $J = 30.4, 7.6$ Hz).

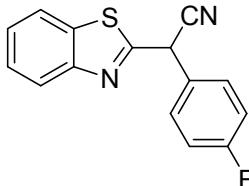


2-(Benzo[*d*]thiazol-2-yl)-2-phenylacetonitrile: Yellow solid. Mp 87 – 88 °C. ^1H NMR (300 MHz,

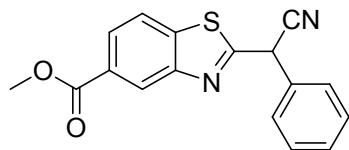
CDCl_3) δ 8.09 (d, $J = 8.1$ Hz, 1 H), 7.82 (d, $J = 7.8$ Hz, 1 H), 7.47 – 7.38 (m, 7 H), 5.64 (s, 1 H); ^{13}C NMR (126 MHz, CDCl_3) δ 164.5, 152.7, 135.6, 132.8, 129.5, 129.2, 127.8, 126.6, 125.9, 123.6, 121.6, 117.0, 42.0; HRMS (EI): m/z calcd for $\text{C}_{15}\text{H}_{10}\text{N}_2\text{S} [\text{M}^+]$: 250.0565; found: 250.0558.



2-(Benzo[*d*]thiazol-2-yl)-2-(p-tolyl)acetonitrile: Yellow solid. Mp 92 – 93 °C. ^1H NMR (300 MHz, CDCl_3) δ 8.07 (dd, $J = 7.5, 0.6$ Hz, 1 H), 7.82 (dd, $J = 7.5, 0.6$ Hz, 1 H), 7.51 (td, $J = 8.1, 0.9$ Hz, 1 H), 7.44 – 7.38 (m, 3 H), 7.24 (d, $J = 8.7$ Hz, 2 H), 5.60 (s, 1 H), 2.37 (s, 3 H); ^{13}C NMR (126 MHz, CDCl_3) δ 164.5, 152.3, 139.0, 135.3, 129.7, 129.5, 127.3, 126.2, 125.4, 123.3, 121.2, 116.8, 41.3, 20.7; HRMS (EI): m/z calcd for $\text{C}_{16}\text{H}_{12}\text{N}_2\text{S} [\text{M}^+]$: 264.0721; found: 264.0723.

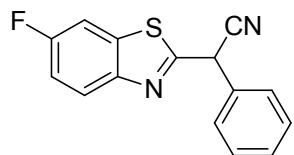


2-(Benzo[*d*]thiazol-2-yl)-2-(4-fluorophenyl)acetonitrile: Yellow solid. Mp 97 – 98 °C. ^1H NMR (300 MHz, CDCl_3) δ 8.07 (td, $J = 7.8, 0.9$ Hz, 1 H), 7.85 (td, $J = 7.8, 0.6$ Hz, 1 H), 7.56 – 7.50 (m, 3 H), 7.42 (td, $J = 8.1, 0.9$ Hz, 1 H), 7.13 (t, $J = 8.4$ Hz, 2 H), 5.62 (s, 1 H); ^{13}C NMR (126 MHz, CDCl_3) δ 163.8, 162.7 (d, $J = 249.7$ Hz, FC), 152.3, 135.2, 129.4 (d, $J = 10.2$, Hz FCCC), 1283 (d, $J = 3.4$ Hz, FCCCC), 126.3, 125.6, 123.3, 121.3, 116.5, 116.2 (d, $J = 27.9$, FCC), 40.9; HRMS (EI): m/z calcd for $\text{C}_{15}\text{H}_9\text{FN}_2\text{S} [\text{M}^+]$: 268.0470; found: 268.0466.

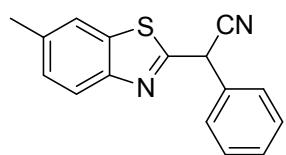


Methyl 2-(cyano(phenyl)methyl)benzo[d]thiazole-5-carboxylate: Yellow solid. Mp 128 – 129 °C.

¹H NMR (300 MHz, CDCl₃) δ 8.74 (d, *J* = 0.9 Hz, 1 H), 8.10 (dd, *J* = 8.4, 1.8 Hz, 1 H), 7.88 (d, *J* = 8.1 Hz, 1 H), 7.58 – 7.54 (m, 2 H), 7.46 – 7.42 (m, 3 H), 5.57 (s, 1 H), 3.97 (s, 3 H); ¹³C NMR (126 MHz, CDCl₃) δ 166.1, 165.6, 152.2, 139.9, 132.1, 129.2, 129.1, 128.6, 127.5, 126.1, 124.9, 121.3, 116.4, 52.1, 41.7; HRMS (EI): *m/z* calcd for C₁₇H₁₂N₂O₂S [M⁺]: 308.0619; found: 308.0615.

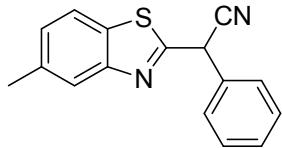


2-(6-Fluorobenzo[d]thiazol-2-yl)-2-phenylacetonitrile: Yellow solid. Mp 82 – 83 °C. ¹H NMR (300 MHz, CDCl₃) δ 8.02 (dd, *J* = 8.7, 4.5 Hz, 1 H), 7.56 – 7.41 (m, 6 H), 7.25 (td, *J* = 8.4, 2.7 Hz, 1 H), 5.61 (s, 1 H); ¹³C NMR (126 MHz, CDCl₃) δ 164.3, 160.7 (d, *J* = 247.5 Hz, FCC), 149.4, 136.8 (d, *J* = 11.3 Hz, FCCC), 132.6, 129.6, 129.4, 127.9, 124.8 (d, *J* = 9.4 Hz, FCCC), 116.9, 115.5 (d, *J* = 24.8, FCC), 107.9 (d, *J* = 26.7, FCC), 42.0; HRMS (EI): *m/z* calcd for C₁₅H₉FN₂S [M⁺]: 268.0470; found: 268.0474.

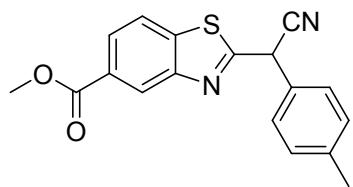


2-(6-Methylbenzo[d]thiazol-2-yl)-2-phenylacetonitrile: White solid. Mp 88 – 89 °C. ¹H NMR (300 MHz, CDCl₃) δ 7.94 (d, *J* = 8.4 Hz, 1 H), 7.61 (s, 1 H), 7.54 (dd, *J* = 7.8, 1.8 Hz, 2 H), 7.49 – 7.37 (m, 3 H), 7.31 (dd, *J* = 8.4, 1.5 Hz, 1 H), 5.62 (s, 1 H), 2.47 (s, 3 H); ¹³C NMR (126 MHz,

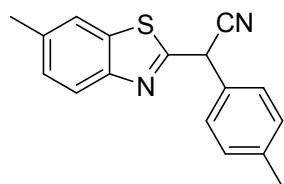
CDCl_3) δ 162.9, 150.4, 135.8, 135.5, 132.5, 129.1, 128.8, 127.8, 127.4, 122.7, 120.9, 116.7, 41.6, 21.1; HRMS (EI): m/z calcd for $\text{C}_{16}\text{H}_{12}\text{N}_2\text{S} [\text{M}^+]$: 264.0721; found: 264.0715.



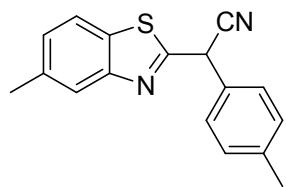
2-(5-Methylbenzo[*d*]thiazol-2-yl)-2-phenylacetonitrile: Yellow solid. Mp 84 – 85 °C. ^1H NMR (400 MHz, CDCl_3) δ 7.94 (d, J = 0.8 Hz, 1 H), 7.69 (d, J = 8.0 Hz, 1 H), 7.54 (dd, J = 8.0, 1.6 Hz, 2 H), 7.46 – 7.40 (m, 3 H), 7.24 (dd, J = 8.0, 1.6 Hz, 1 H), 5.62 (s, 1 H), 2.50 (s, 3 H); ^{13}C NMR (126 MHz, CDCl_3) δ 164.6, 153.2, 136.9, 133.0, 132.7, 129.5, 129.3, 127.9, 127.6, 123.7, 121.2, 117.1, 42.0, 21.5; HRMS (EI): m/z calcd for $\text{C}_{16}\text{H}_{12}\text{N}_2\text{S} [\text{M}^+]$: 264.0721; found: 264.0714.



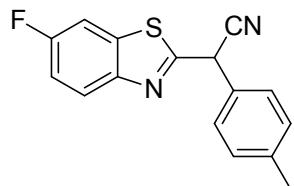
Methyl 2-(cyano(p-tolyl)methyl)benzo[*d*]thiazole-5-carboxylate: Yellow solid. Mp 138 – 139 °C. ^1H NMR (300 MHz, CDCl_3) δ 8.73 (d, J = 1.5 Hz, 1 H), 8.08 (dd, J = 8.7, 1.5 Hz, 1 H), 7.86 (d, J = 8.7 Hz, 1 H), 7.42 (d, J = 8.1 Hz, 2 H), 7.25 (d, J = 7.8 Hz, 2 H), 5.61 (s, 1 H), 3.97 (s, 3 H), 2.37 (s, 3 H); ^{13}C NMR (126 MHz, CDCl_3) δ 166.1, 152.2, 139.9, 139.2, 129.8, 129.1, 128.5, 127.3, 126.0, 124.8, 121.2, 116.5, 52.0, 41.3, 20.7; HRMS (EI): m/z calcd for $\text{C}_{18}\text{H}_{14}\text{N}_2\text{O}_2\text{S} [\text{M}^+]$: 322.0776; found: 322.0772.



2-(6-Methylbenzo[*d*]thiazol-2-yl)-2-(p-tolyl)acetonitrile: Yellow solid. Mp 110 – 111 °C. ¹H NMR (300 MHz, CDCl₃) δ 7.93 (d, *J* = 8.4 Hz, 1 H), 7.60 (s, 1 H), 7.42 (d, *J* = 7.8 Hz, 2 H), 7.30 (dd, *J* = 8.4, 1.5 Hz, 1 H), 7.23 (d, *J* = 7.8 Hz, 2 H), 5.59 (s, 1 H), 2.47 (s, 3 H), 2.37 (s, 3 H); ¹³C NMR (126 MHz, CDCl₃) δ 163.3, 150.4, 138.9, 135.7, 135.5, 129.7, 129.6, 127.8, 127.3, 122.7, 120.9, 116.9, 41.2, 21.1, 20.7; HRMS (EI): *m/z* calcd for C₁₇H₁₄N₂S [M⁺]: 278.0878; found: 278.0876.

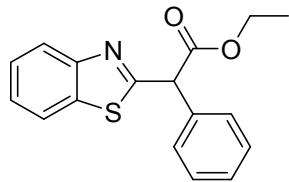


2-(5-Methylbenzo[*d*]thiazol-2-yl)-2-(p-tolyl)acetonitrile: Yellow solid. Mp 131 – 132 °C. ¹H NMR (300 MHz, CDCl₃) δ 7.86 (d, *J* = 1.5 Hz, 1 H), 7.68 (d, *J* = 8.1 Hz, 1 H), 7.42 (d, *J* = 8.1 Hz, 2 H), 7.23 (d, *J* = 8.1 Hz, 3 H), 5.58 (s, 1 H), 2.50 (s, 3 H), 2.36 (s, 3 H); ¹³C NMR (126 MHz, CDCl₃) δ 164.6, 152.7, 138.9, 136.4, 132.3, 129.7, 129.6, 127.3, 127.1, 123.2, 120.7, 116.9, 41.3, 21.1, 20.8; HRMS (EI): *m/z* calcd for C₁₇H₁₄N₂S [M⁺]: 278.0878; found: 278.0872.

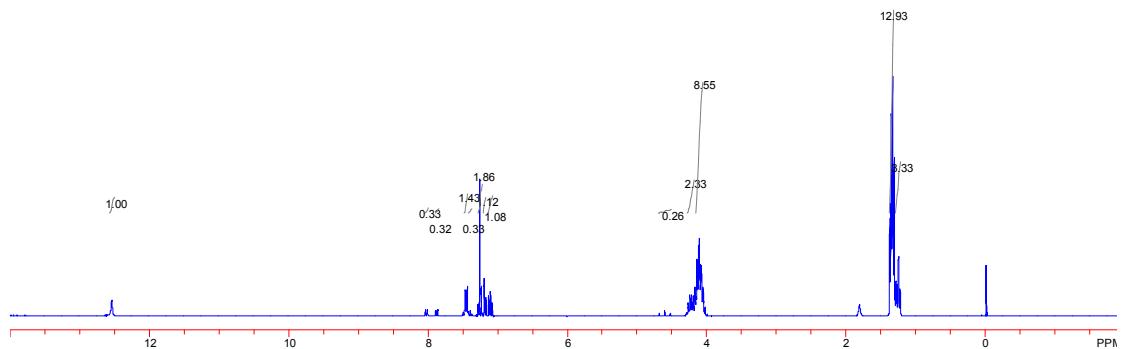
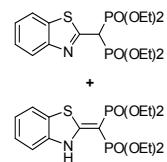
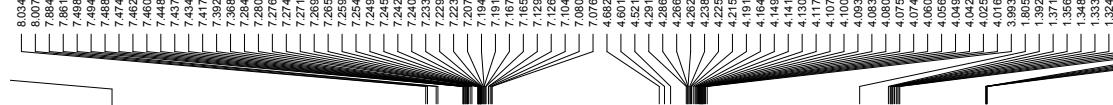


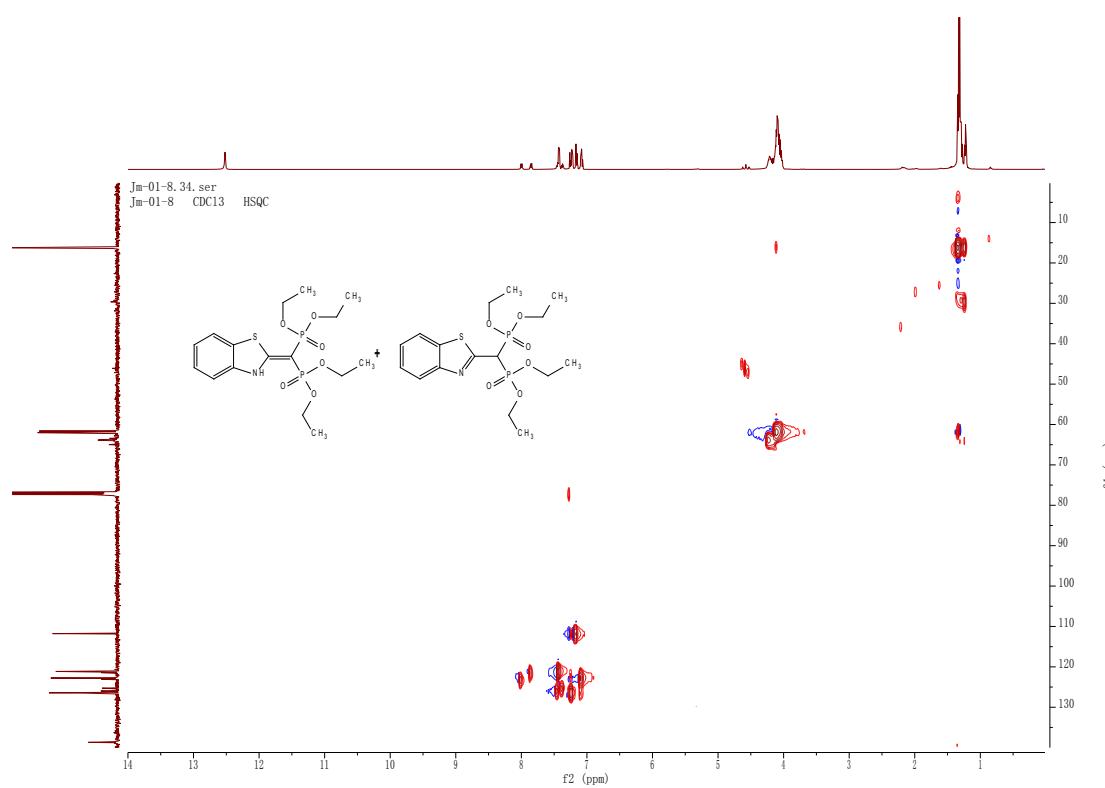
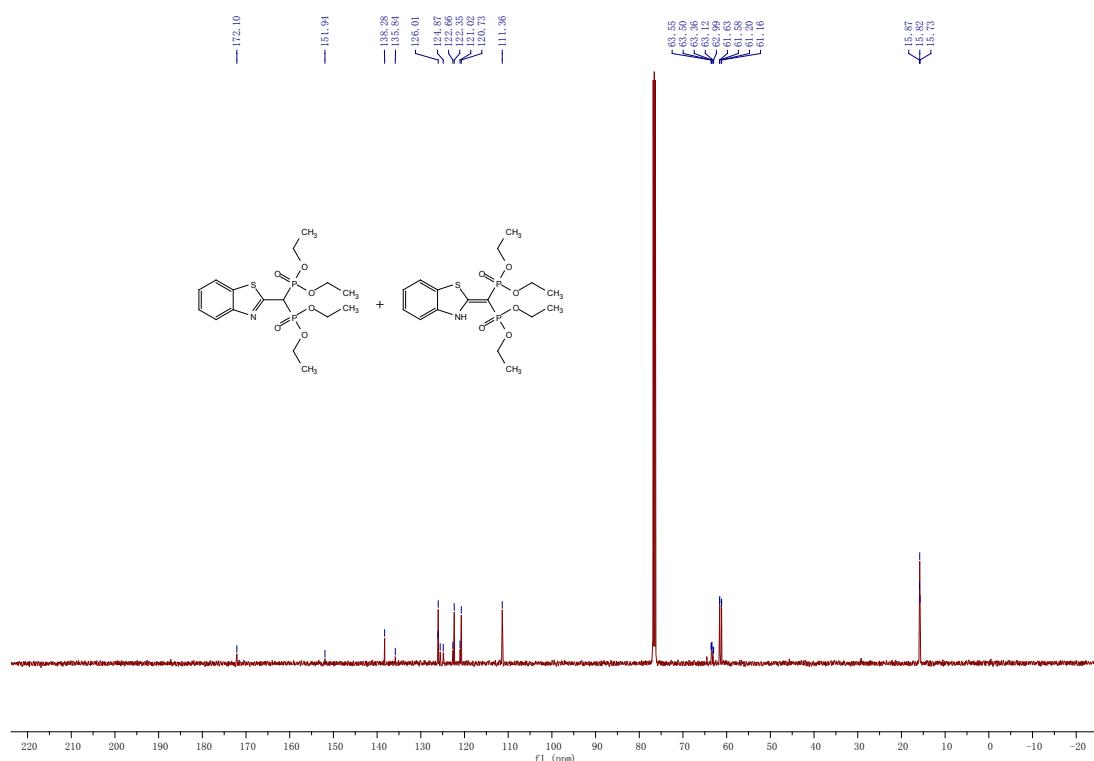
2-(6-Fluorobenzo[*d*]thiazol-2-yl)-2-(p-tolyl)acetonitrile: Yellow solid. Mp 92 – 93 °C. ¹H NMR (300 MHz, CDCl₃) δ 8.01 (dd, *J* = 9.0, 4.5 Hz, 1 H), 7.49 (dd, *J* = 7.8, 2.1 Hz, 1 H), 7.42 (d, *J* = 7.8 Hz, 2 H), 7.27 – 7.21 (m, 3 H), 5.56 (s, 1 H), 2.37 (s, 3 H); ¹³C NMR (126 MHz, CDCl₃) δ 164.7, 160.7 (*J* = 250.2 Hz, FC), 149.4, 139.6, 136.7 (*J* = 11.4 Hz, FCCC), 130.3, 129.7, 127.8,

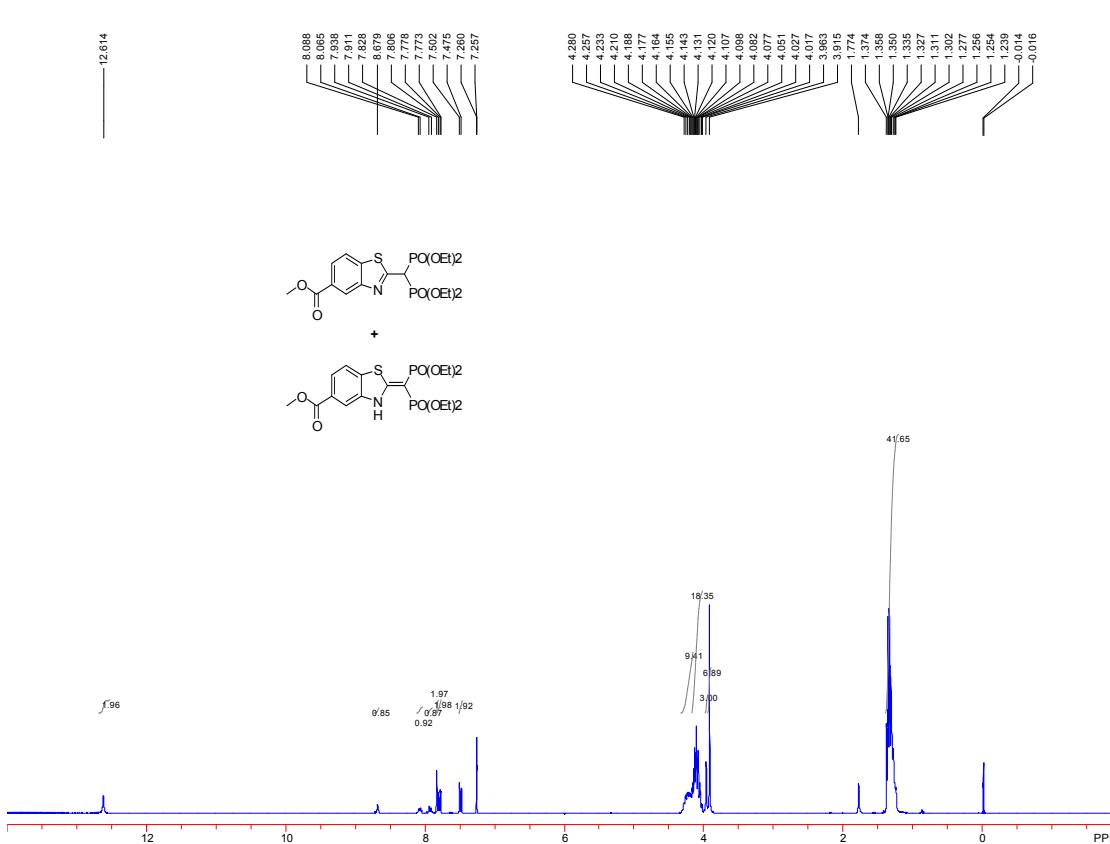
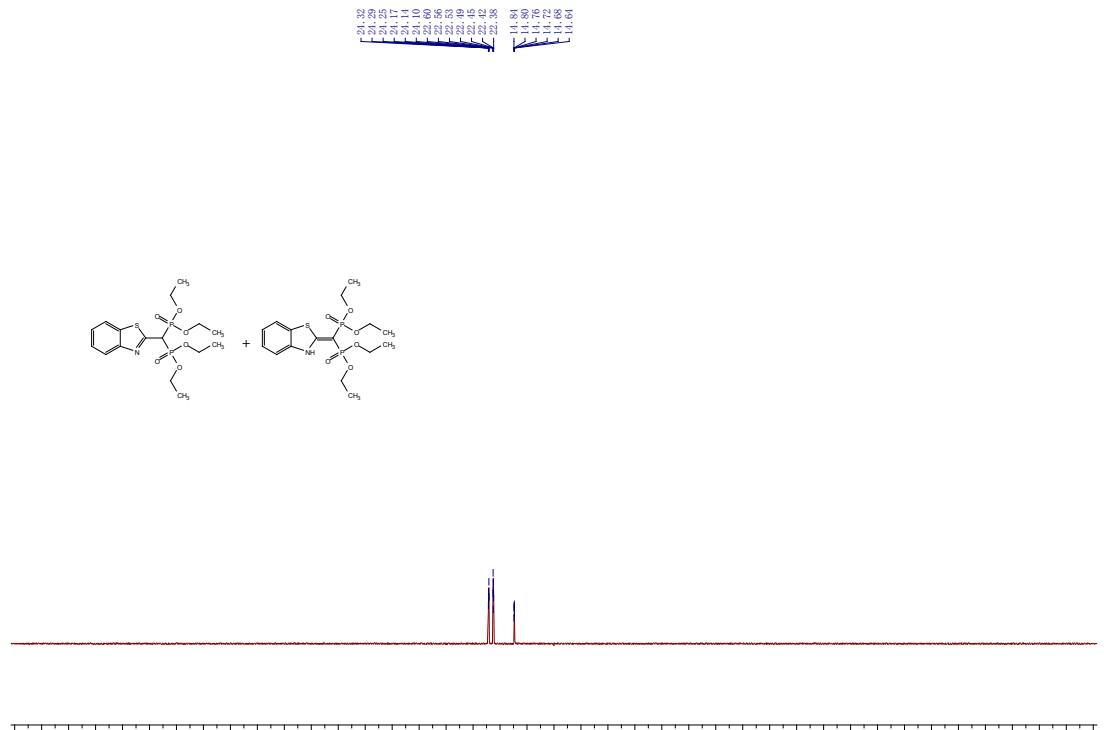
124.8 ($J = 10.2$ Hz, FCCC), 117.0, 115.4 ($J = 25.4$ Hz, FCC), 107.9 ($J = 25.4$ Hz, FCCC), 41.6, 21.2; HRMS (EI): m/z calcd for C₁₆H₁₁FN₂S [M⁺]: 282.0627; found: 282.0620.

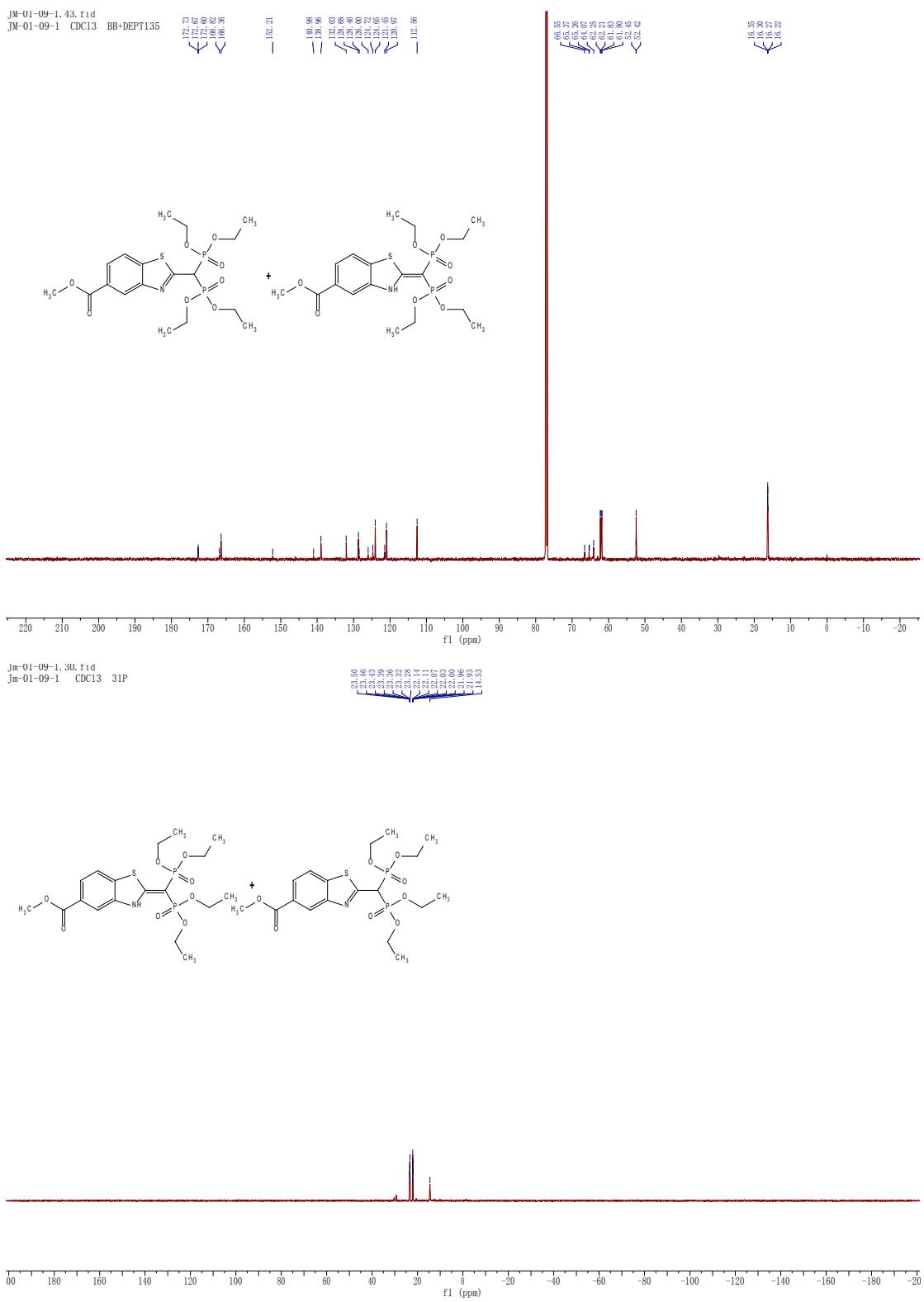


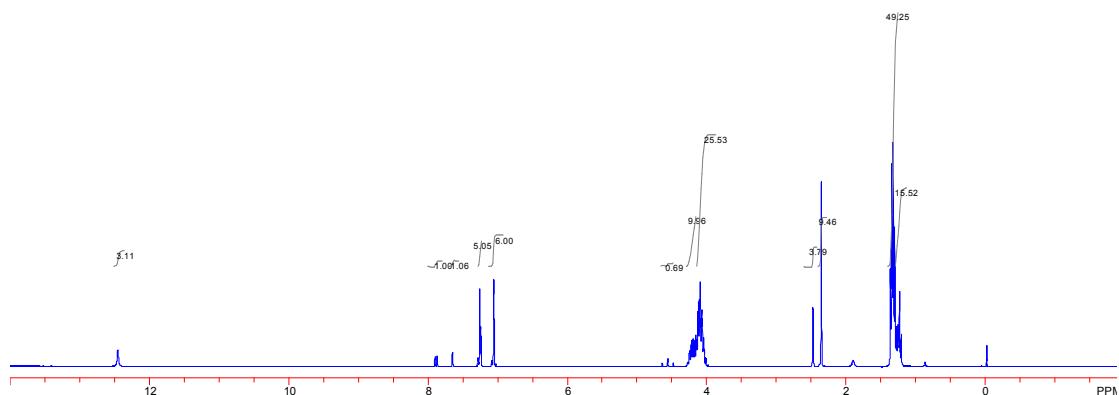
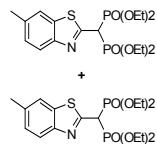
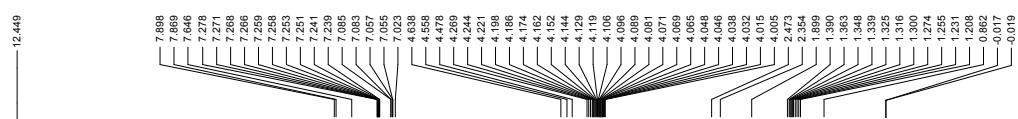
Ethyl 2-(benzo[d]thiazol-2-yl)-2-phenylacetate: Colorless oil. ¹H NMR (300 MHz, CDCl₃) δ 8.10 (d, $J = 7.8$ Hz, 1 H), 7.83 (d, $J = 8.1$ Hz, 1 H), 7.53 – 7.33 (m, 7 H), 5.50 (s, 1 H), 4.34 – 4.22 (m, 2 H), 1.28 (t, $J = 7.2$ Hz, 3 H); ¹³C NMR (101 MHz, CDCl₃) δ 169.6, 167.9, 152.2, 135.3, 128.6, 127.9, 125.6, 124.7, 122.8, 121.1, 61.6, 55.9, 13.6; HRMS (EI): m/z calcd for C₁₇H₁₅NO₂S [M⁺]: 297.0823; found: 297.0825.



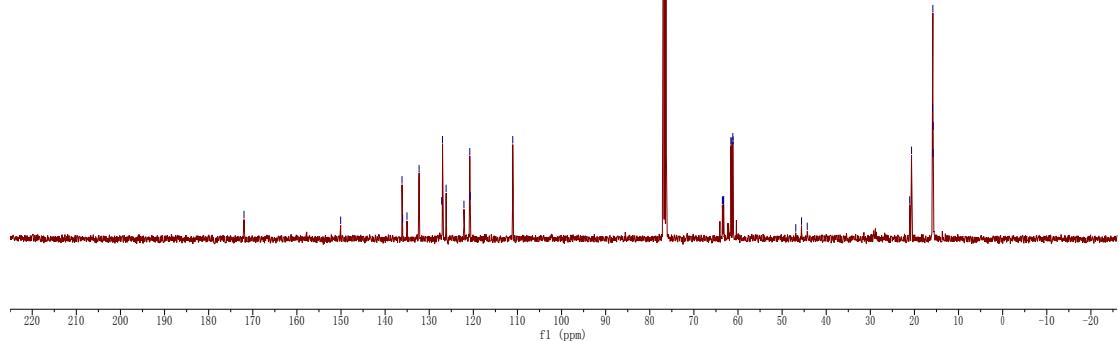
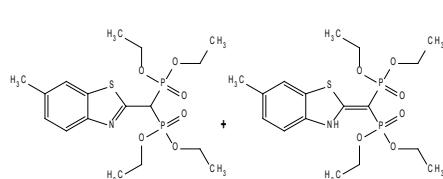




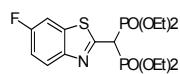
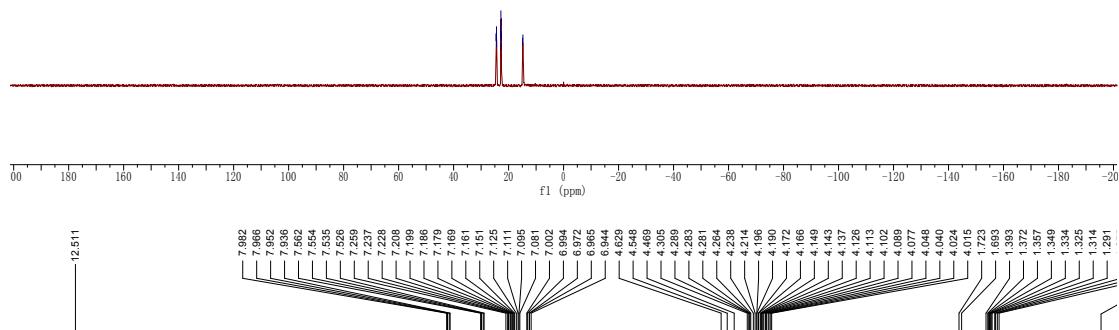
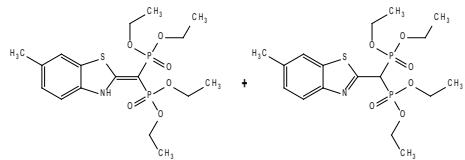




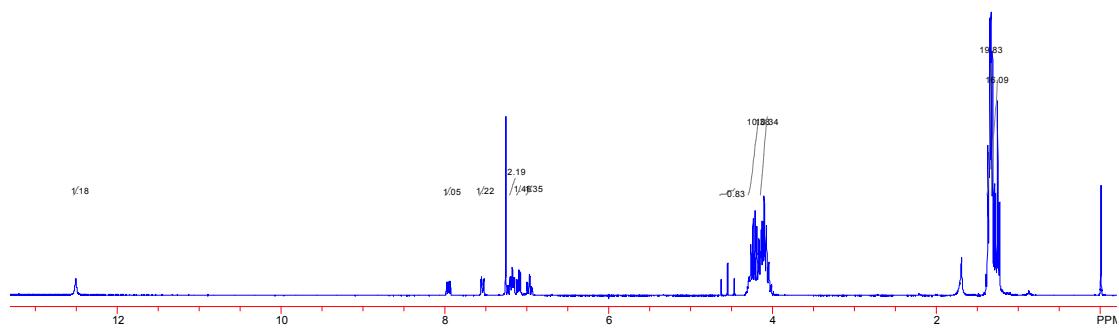
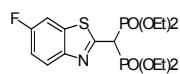
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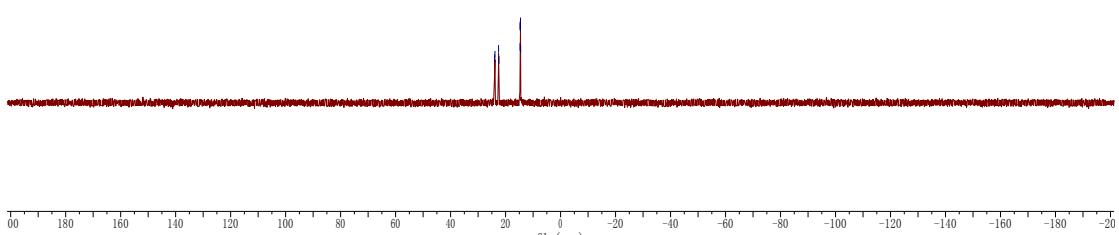
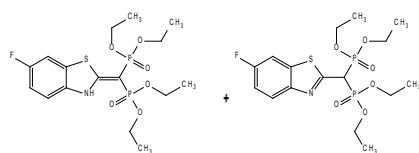
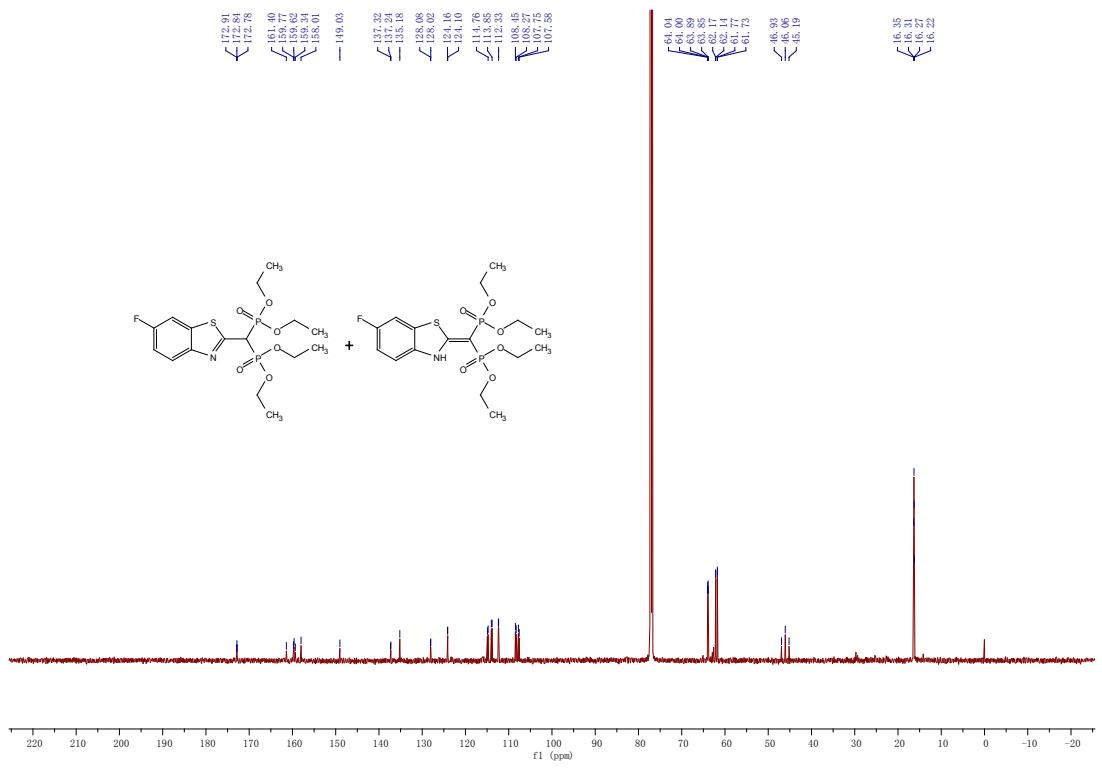


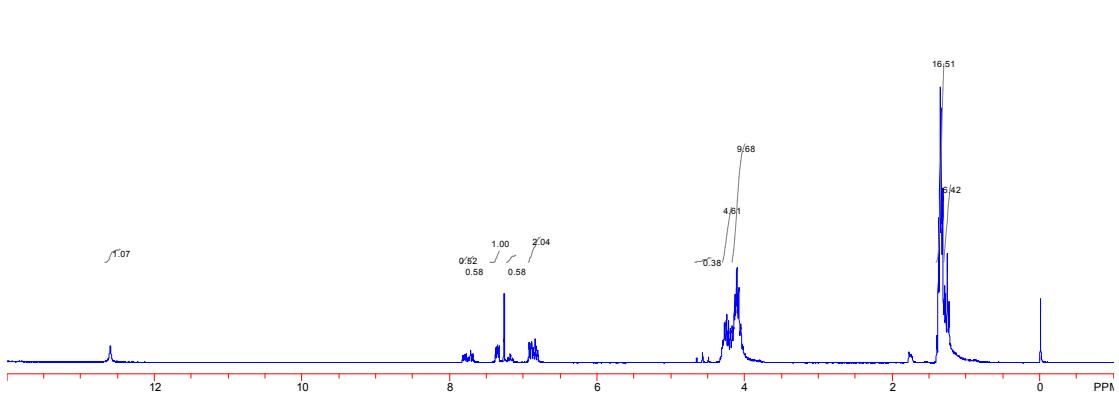
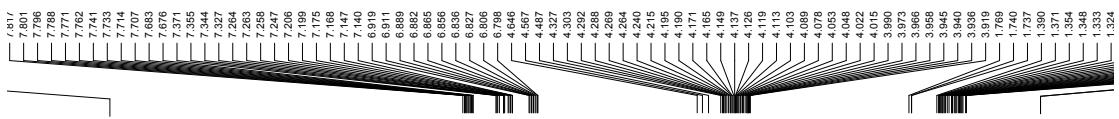
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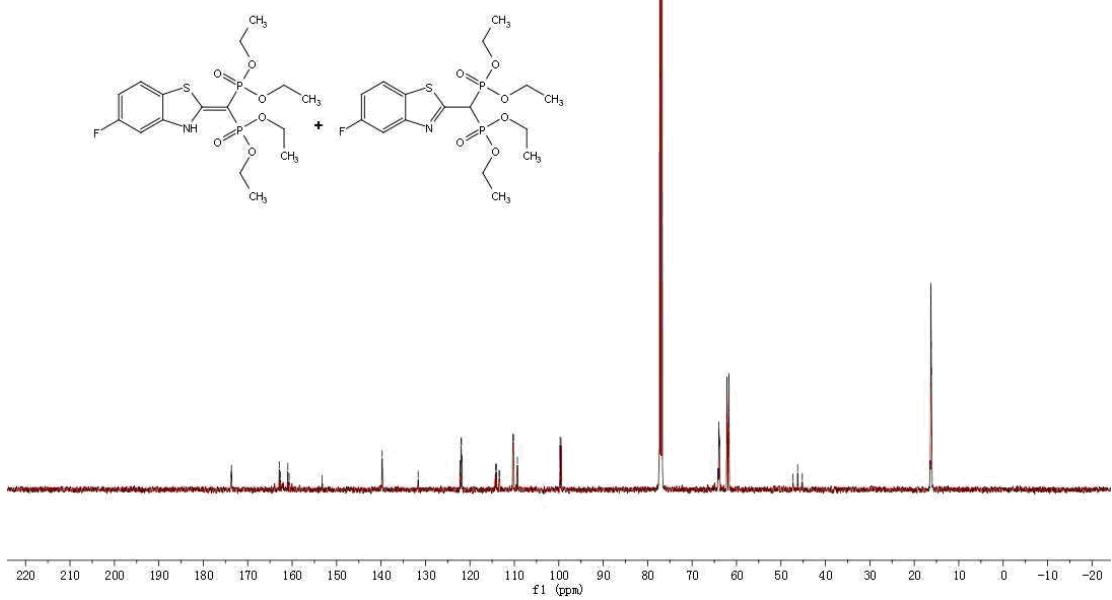
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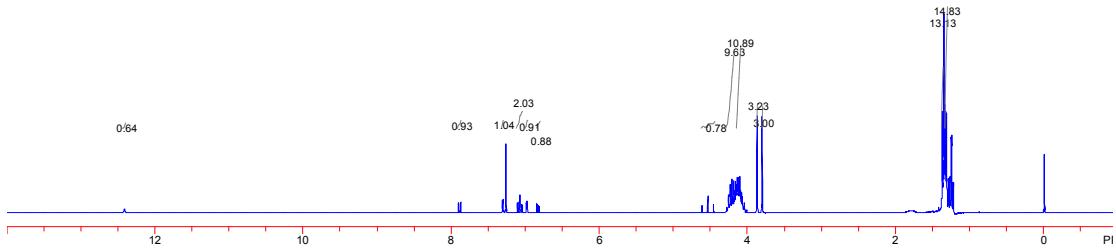
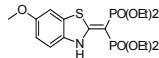
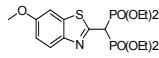
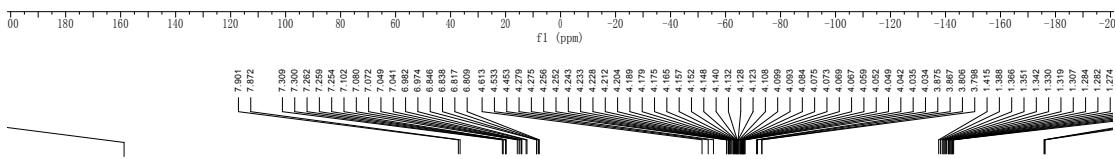
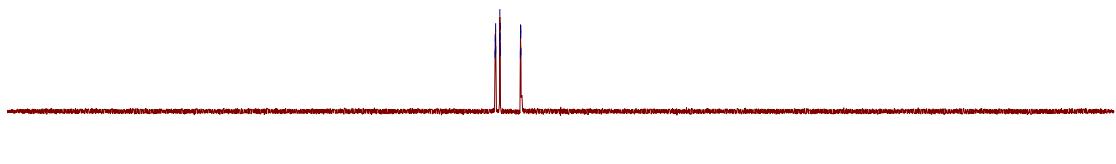
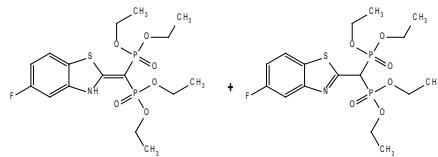


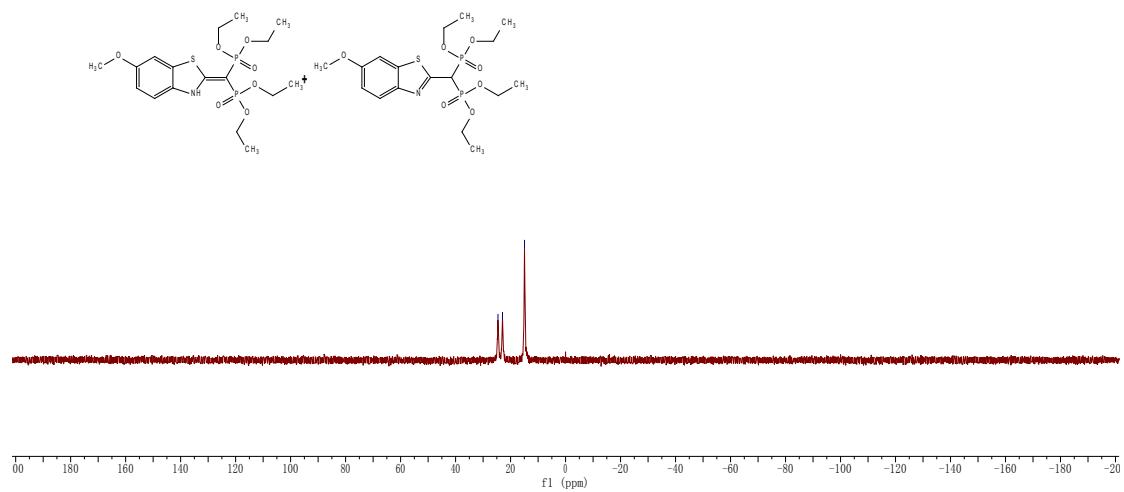
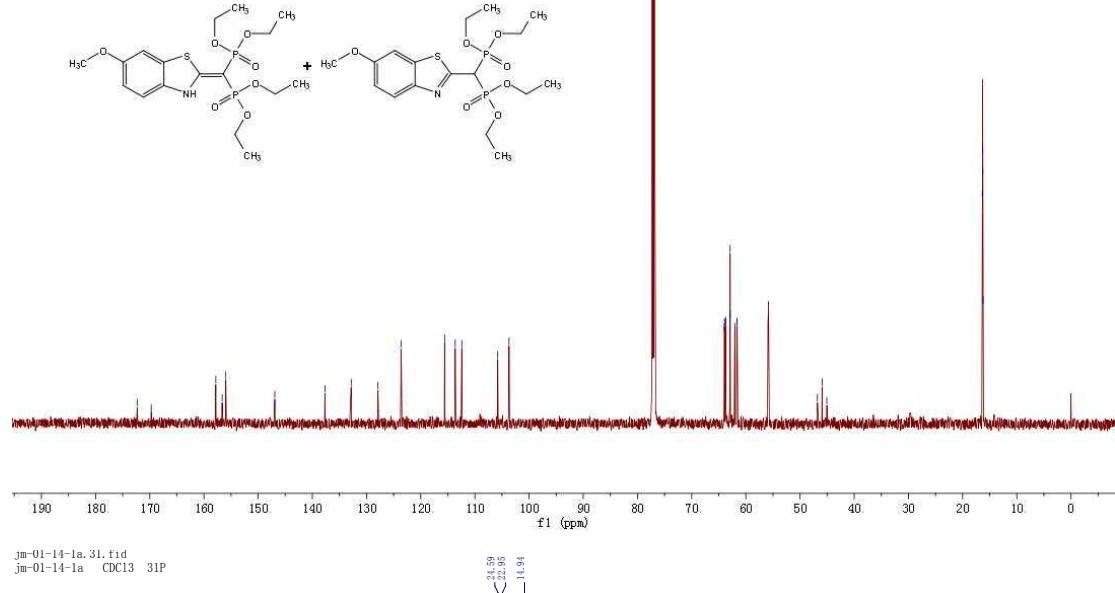


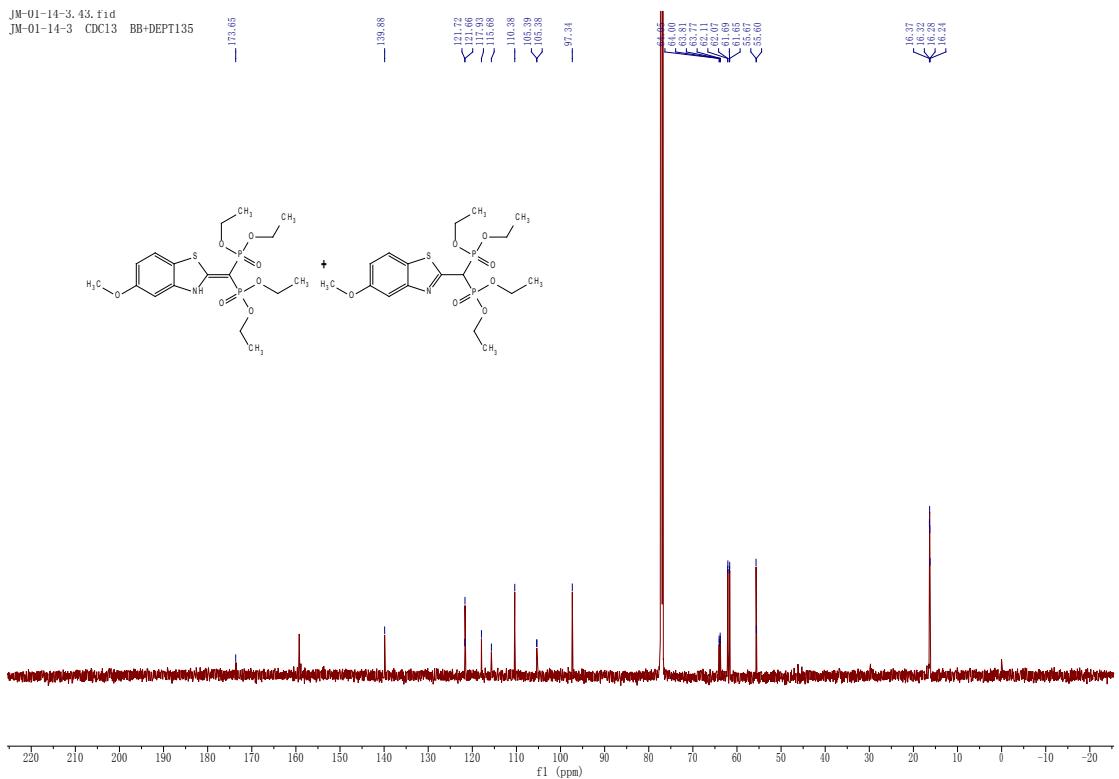
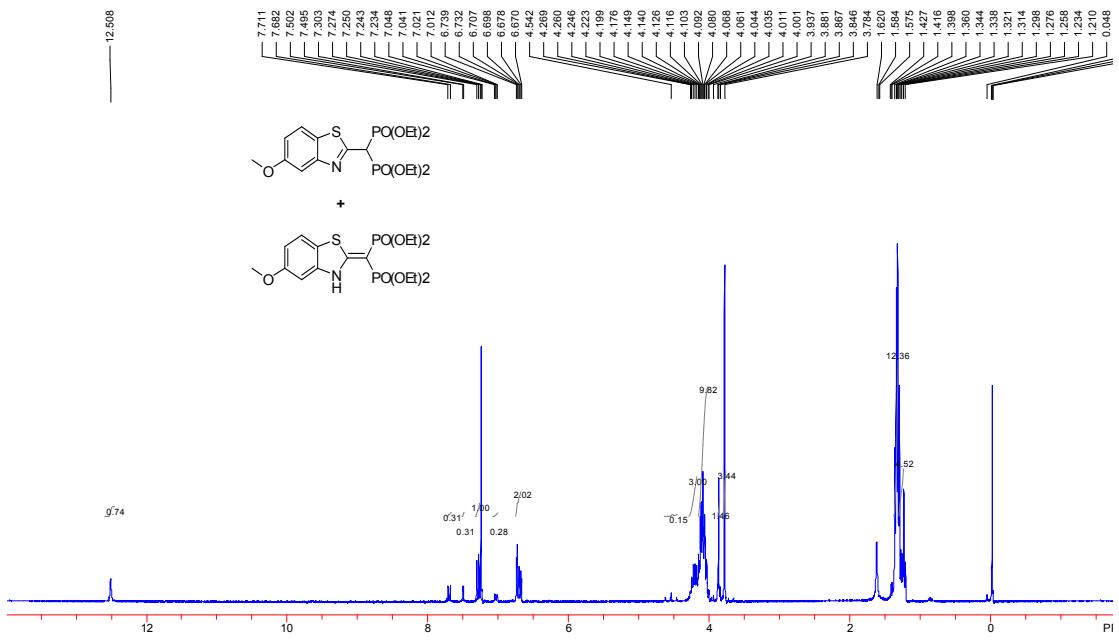
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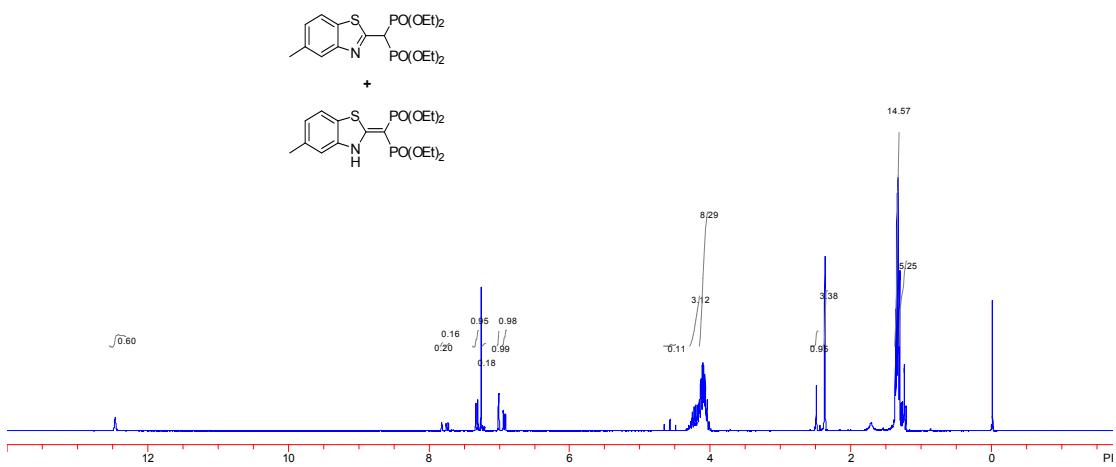
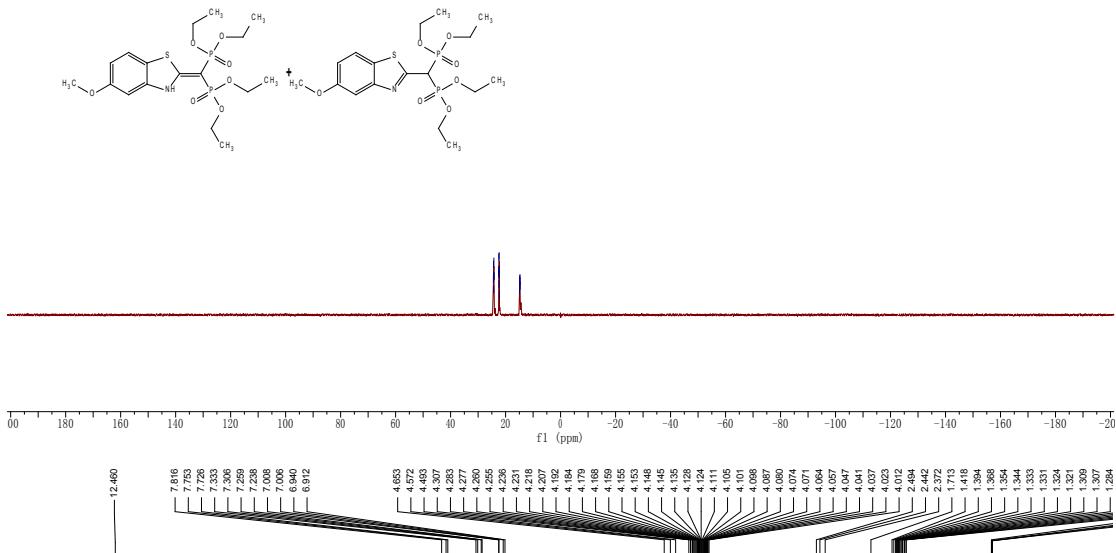
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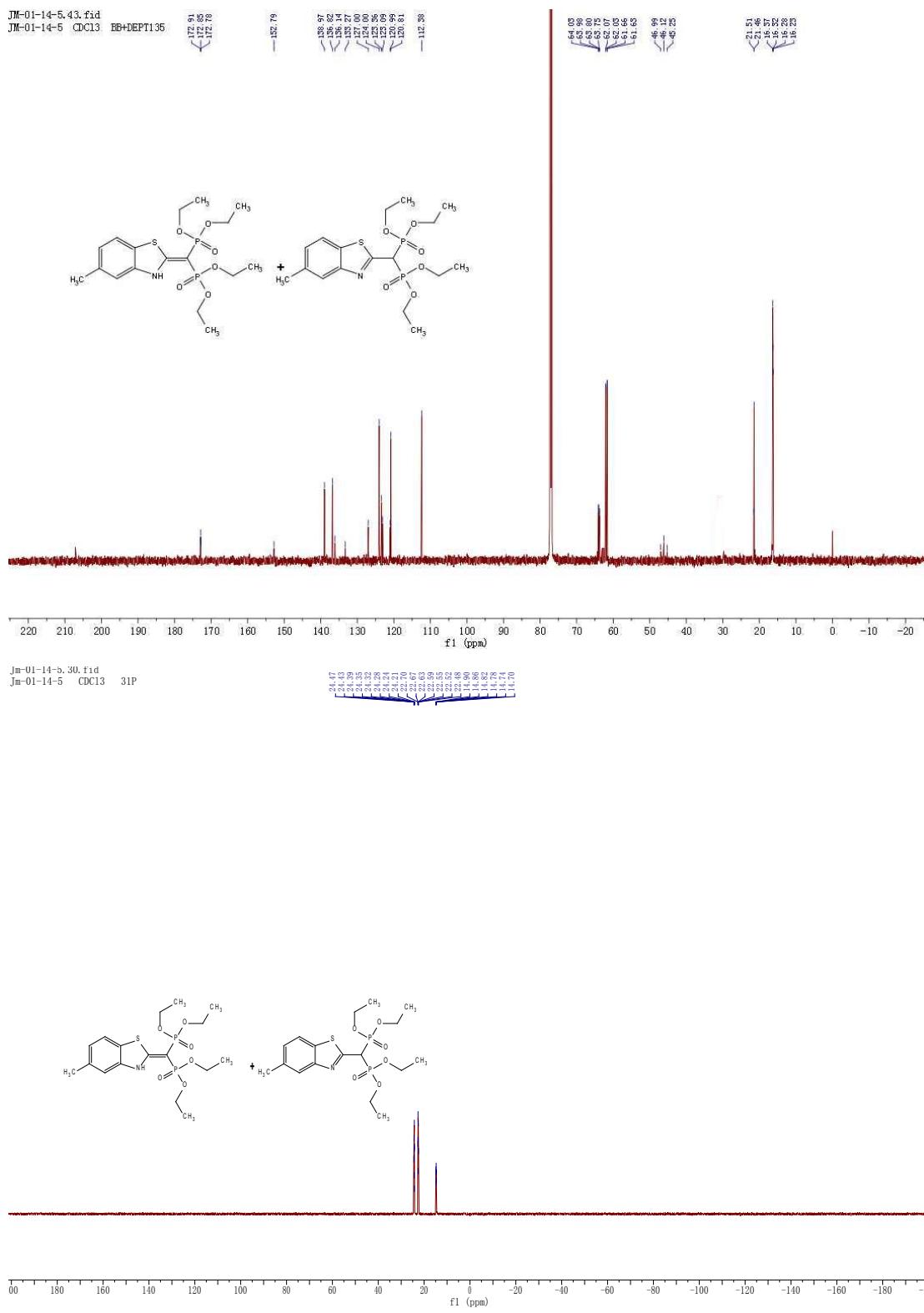


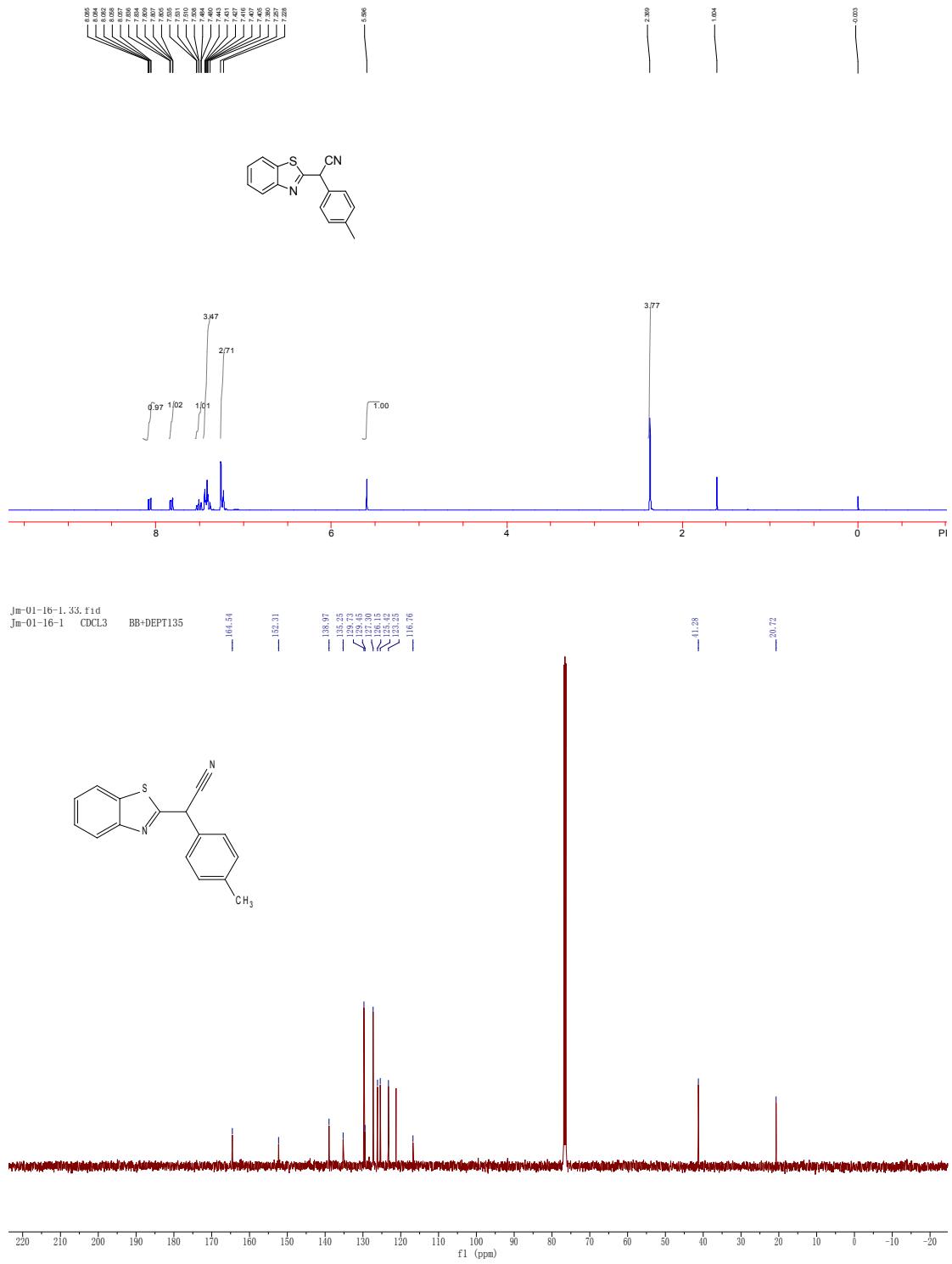


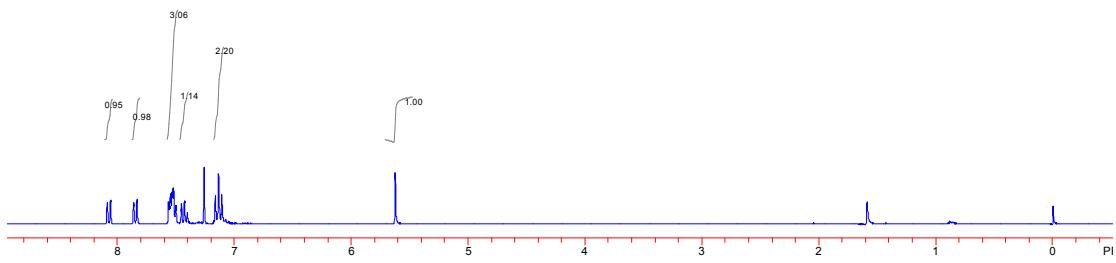
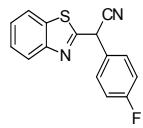


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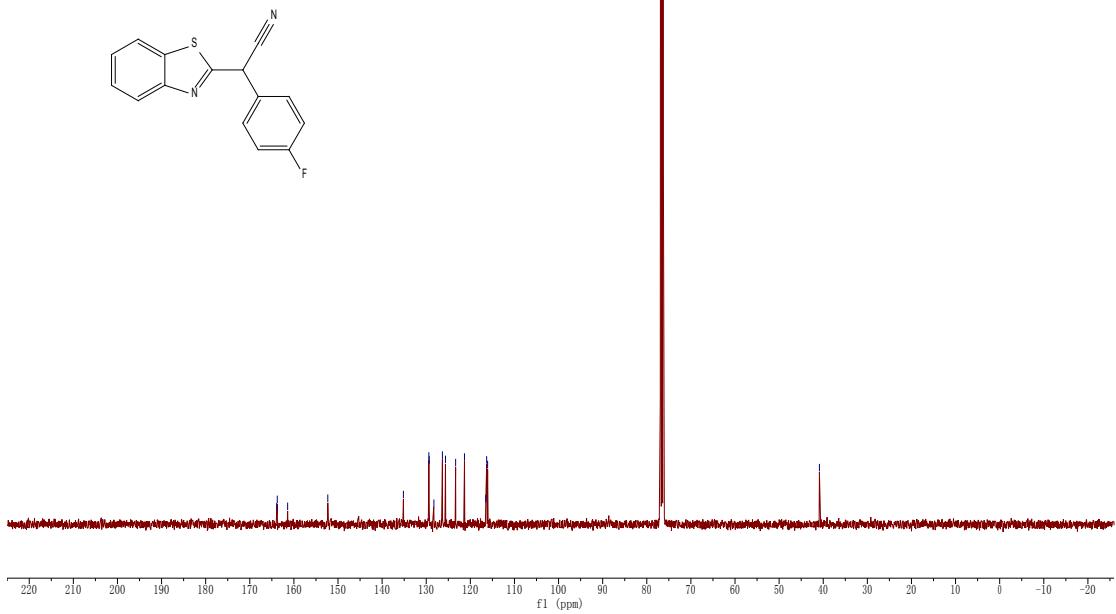


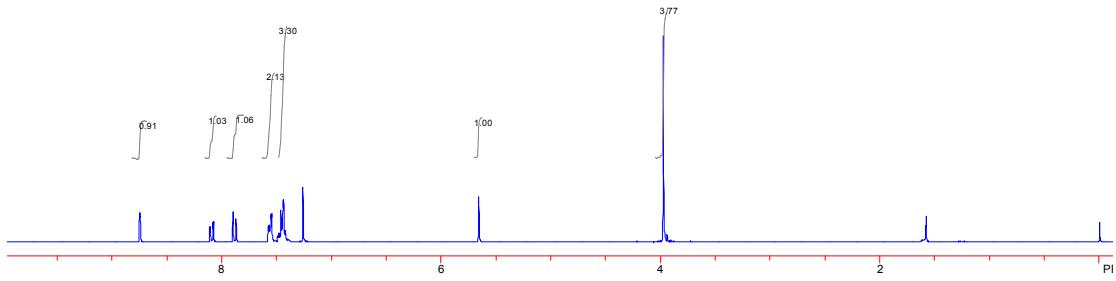
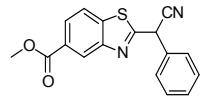




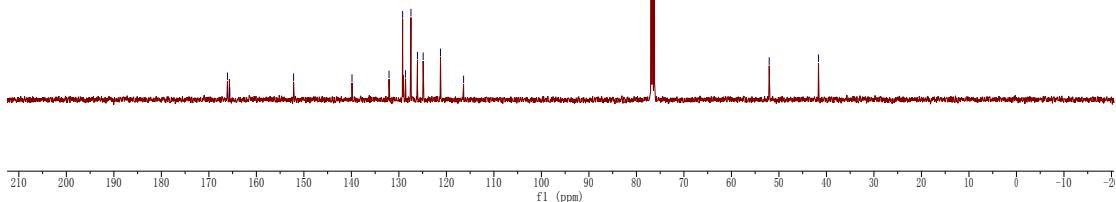
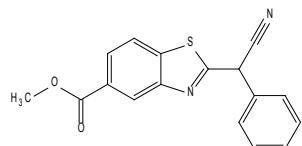


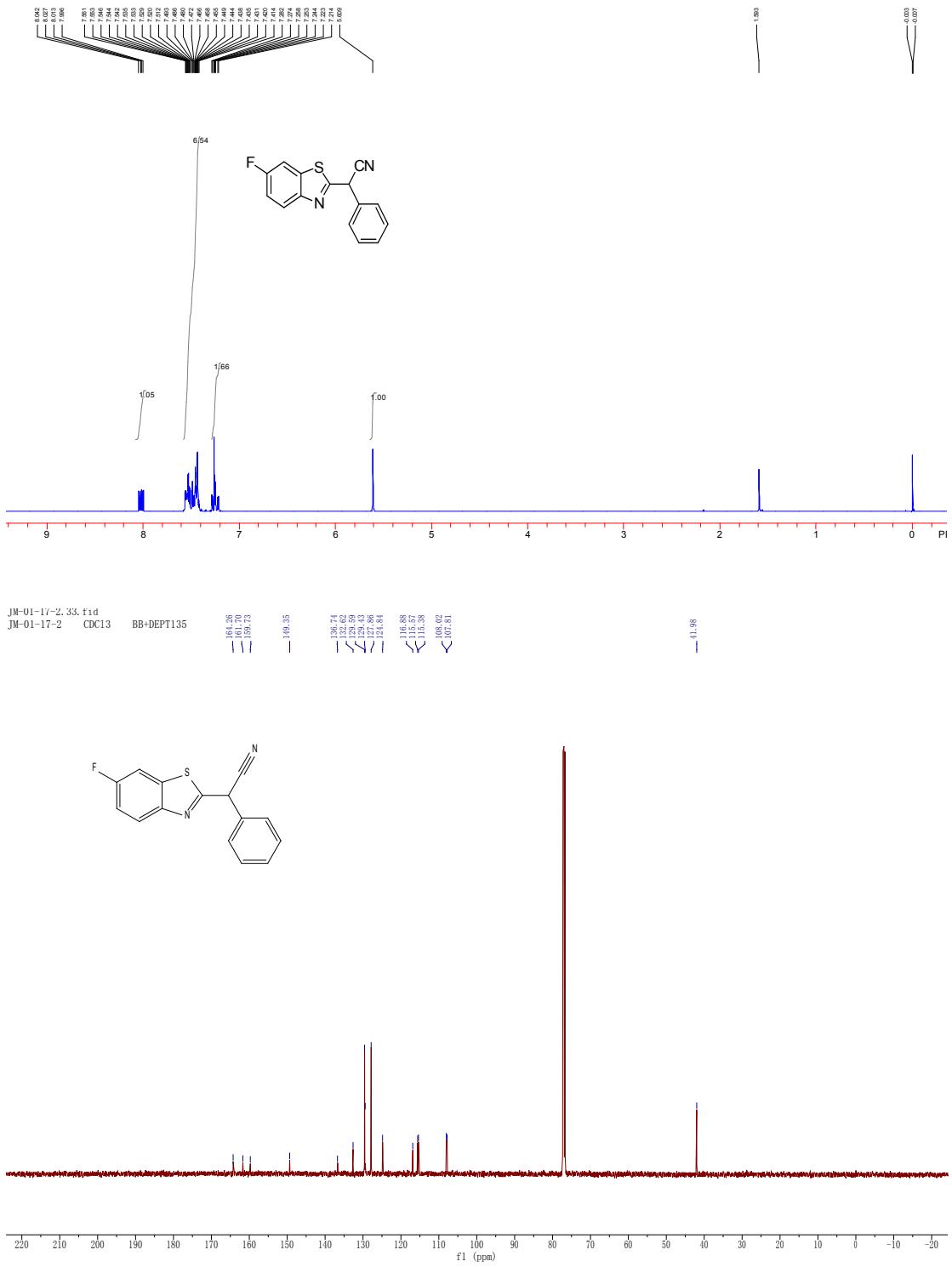
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Jm-01-16-2 CDC13 BB+DEPT135

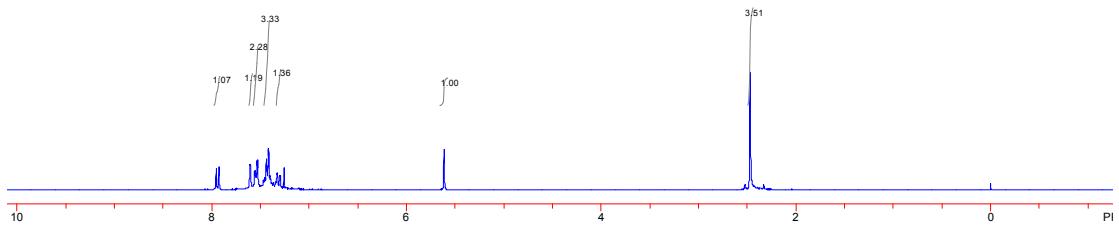
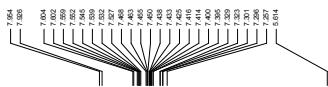




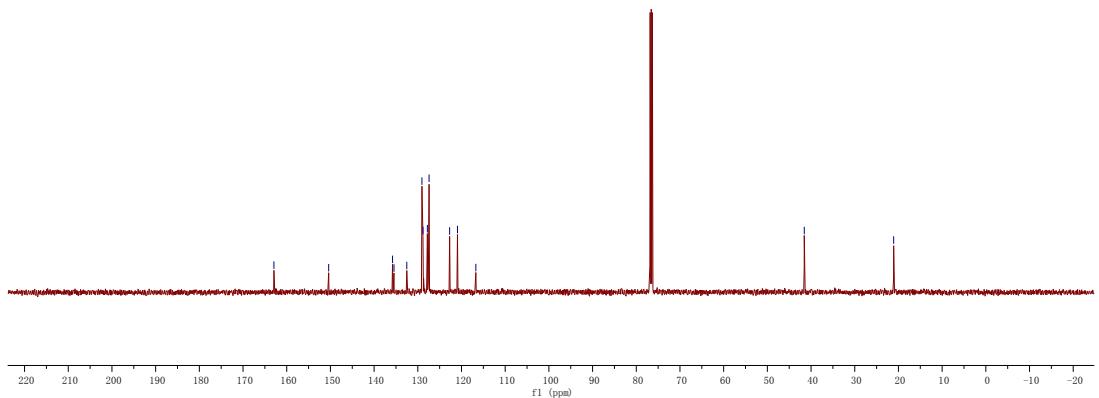
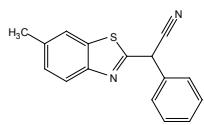
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Jm-01-17-1 CDCl₃ BB+DEPT135
165.88 165.63 152.17
139.87 122.07 129.22 128.60 127.46 125.89 124.89 121.25 116.38
52.65 41.68

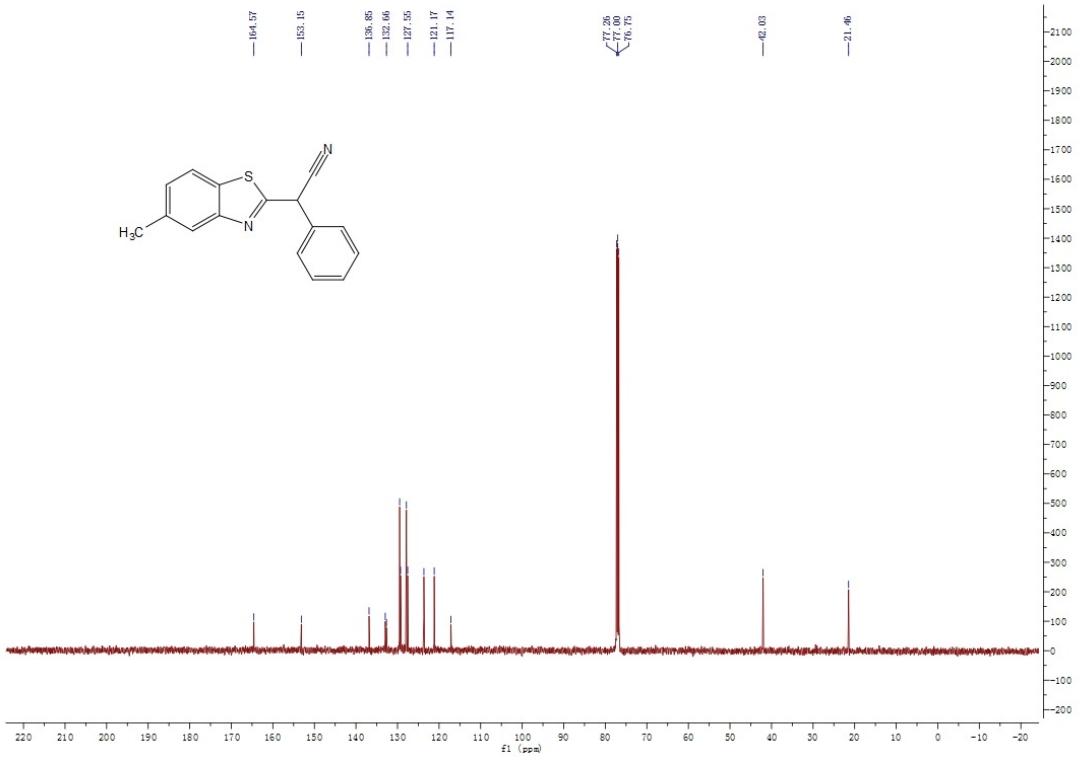
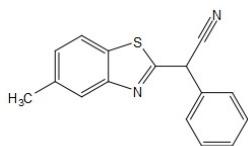
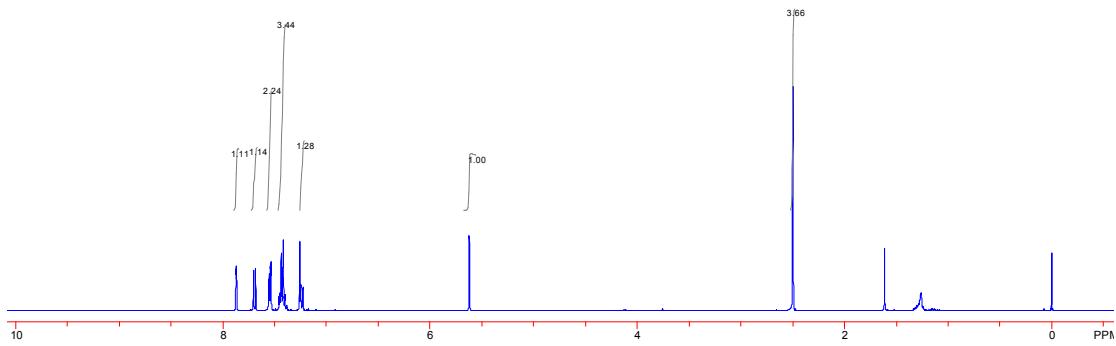
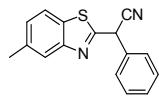


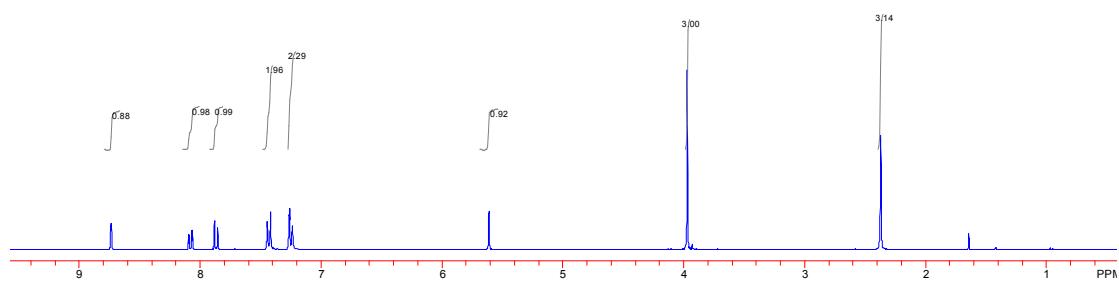




— 162.93
— 159.40
— 135.78
— 135.45
— 132.52
— 127.12
— 120.92
— 116.72
— 41.55
— 21.09

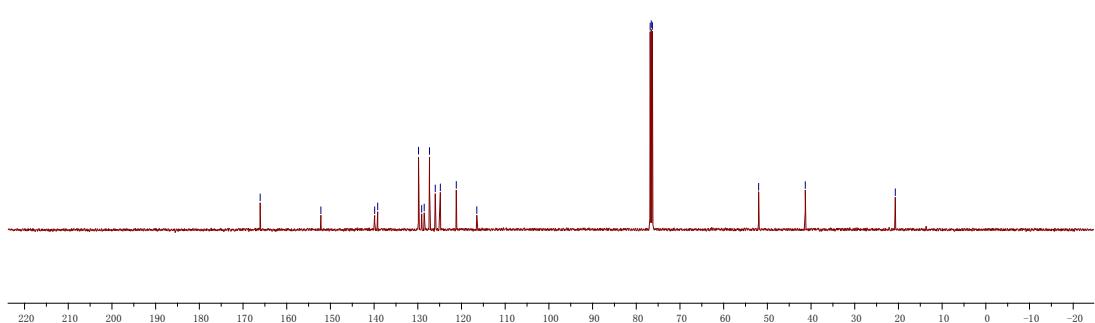
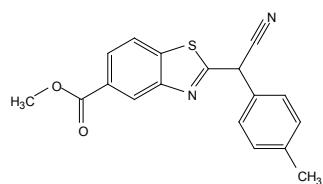


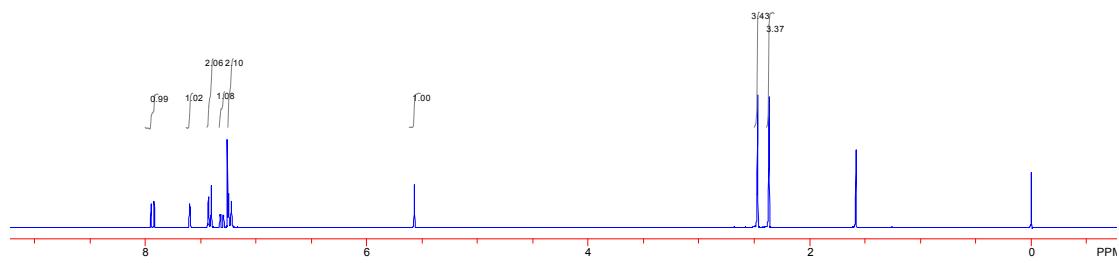
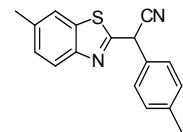




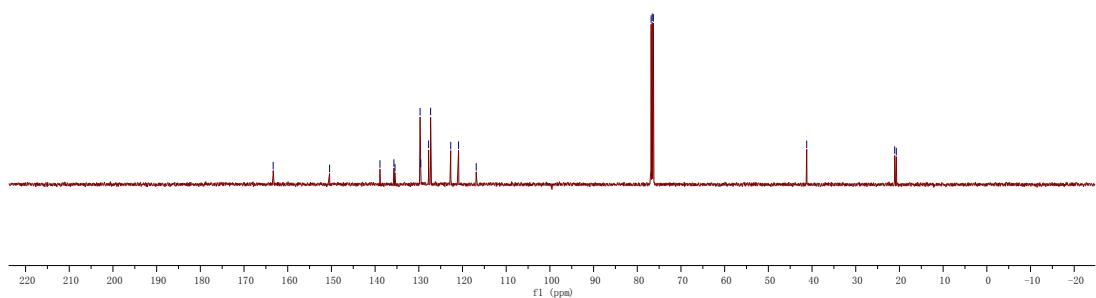
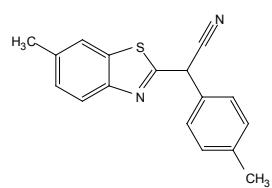
Peak assignments for the ¹H NMR spectrum:

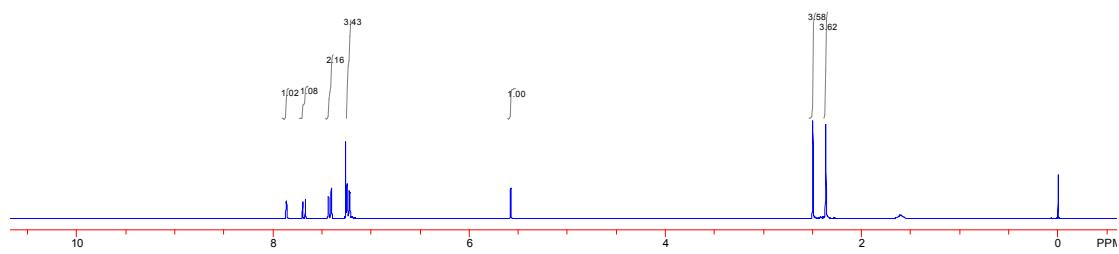
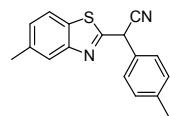
- 152.18
- 166.08
- 139.87, 139.18
- 129.84
- 127.32
- 126.01
- 121.81
- 121.19
- 116.50
- 76.82
- 76.57
- 52.00
- 41.32
- 26.72





— 163.33
— 150.42
— 138.89
— 135.44
— 127.76
— 127.30
— 120.90
— 116.86
— 11.22
— 21.09
— 26.72

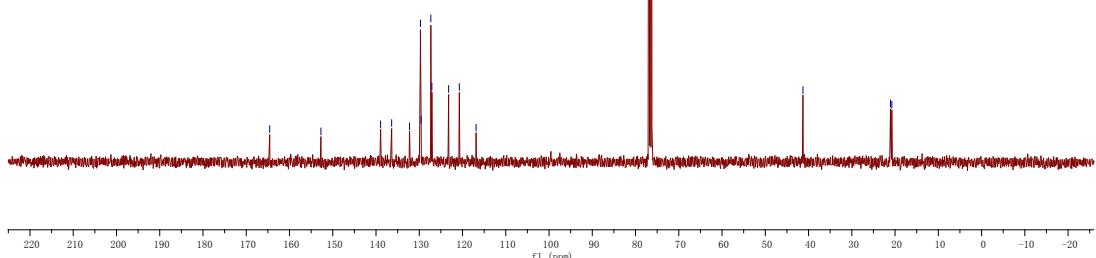
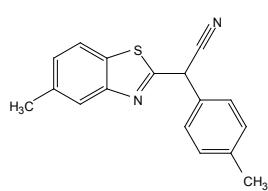


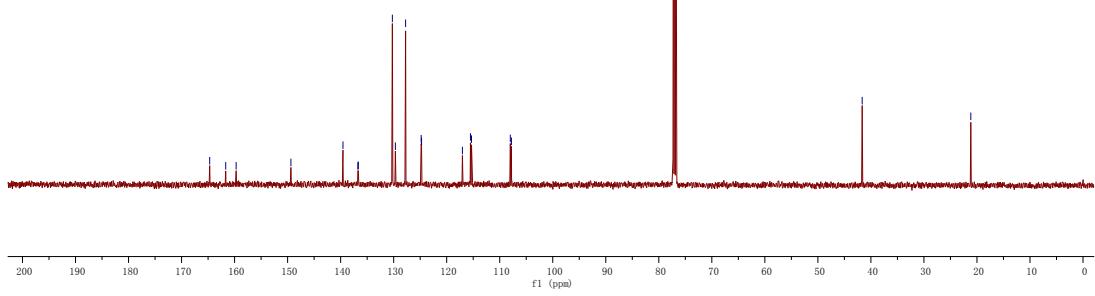
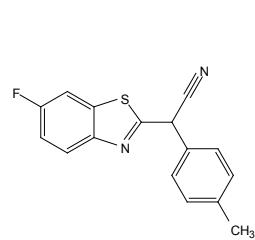
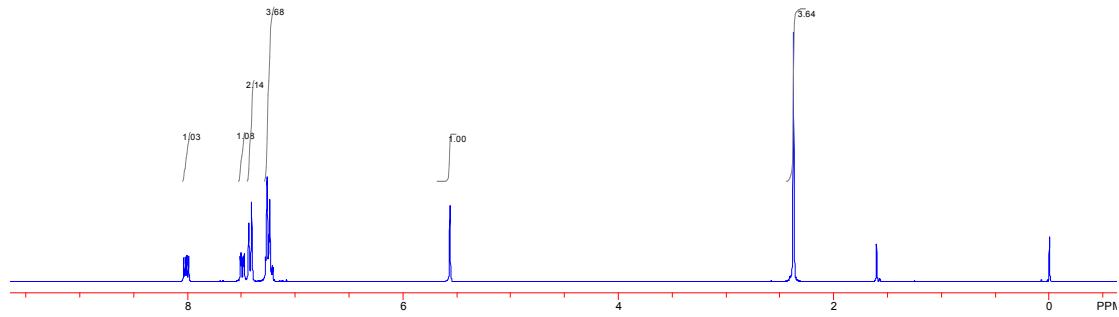
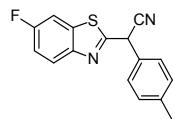


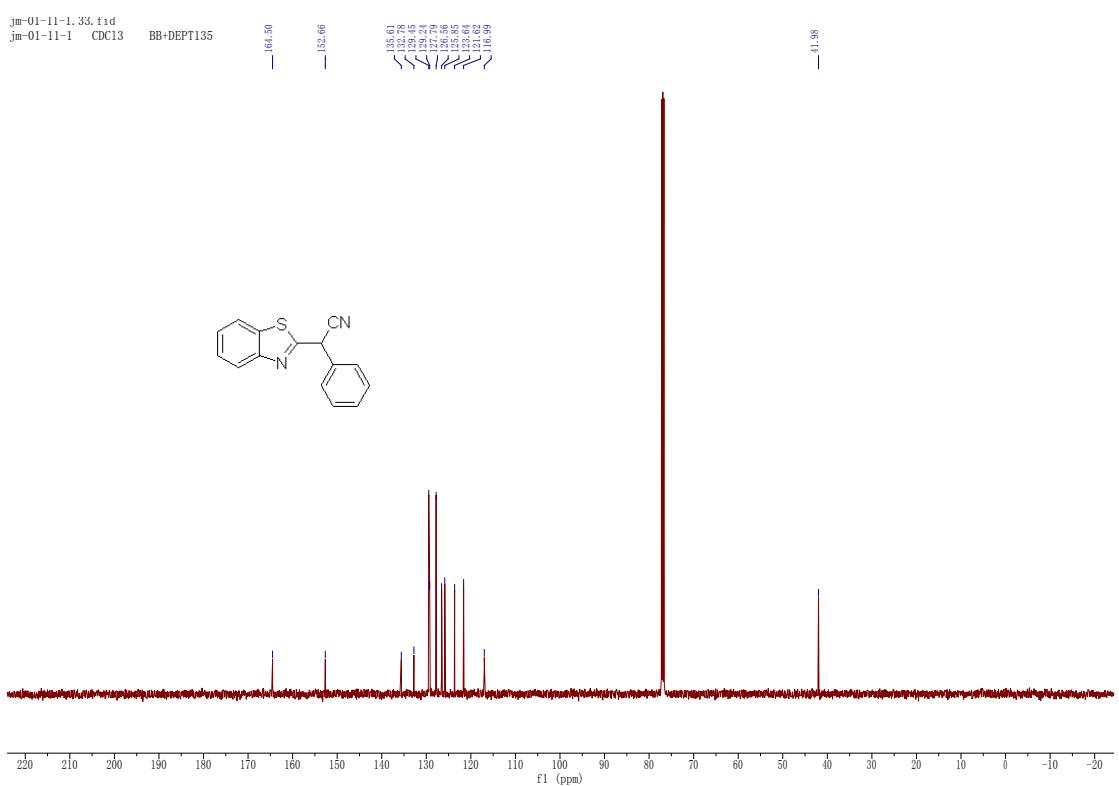
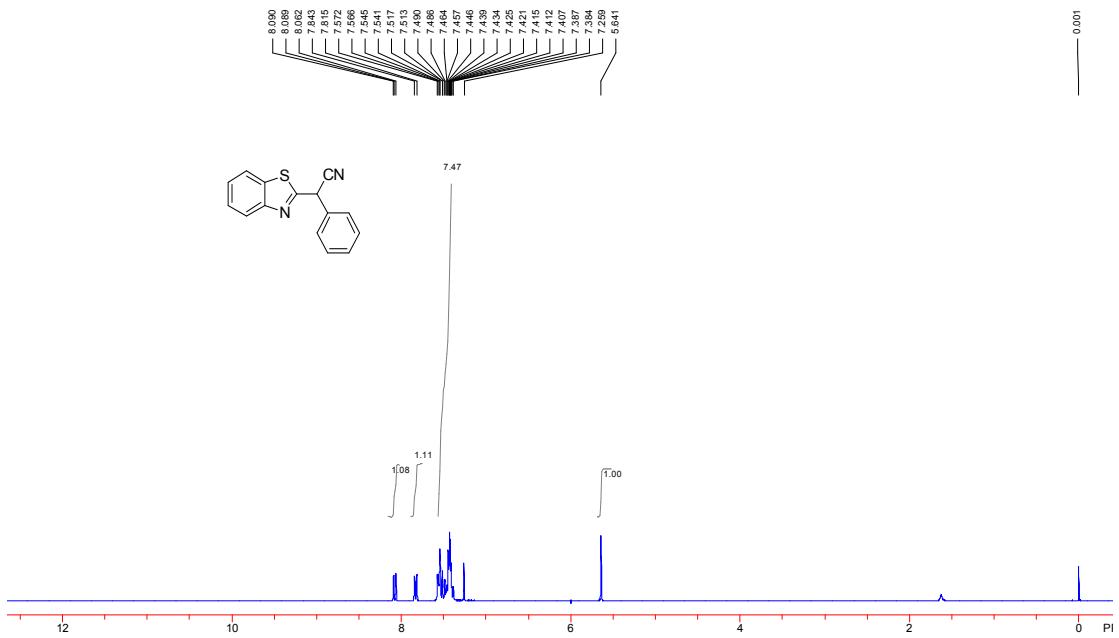
— 164.88
— 152.74
— 138.93
— 135.33
— 127.32
— 127.08
— 120.74
— 116.87

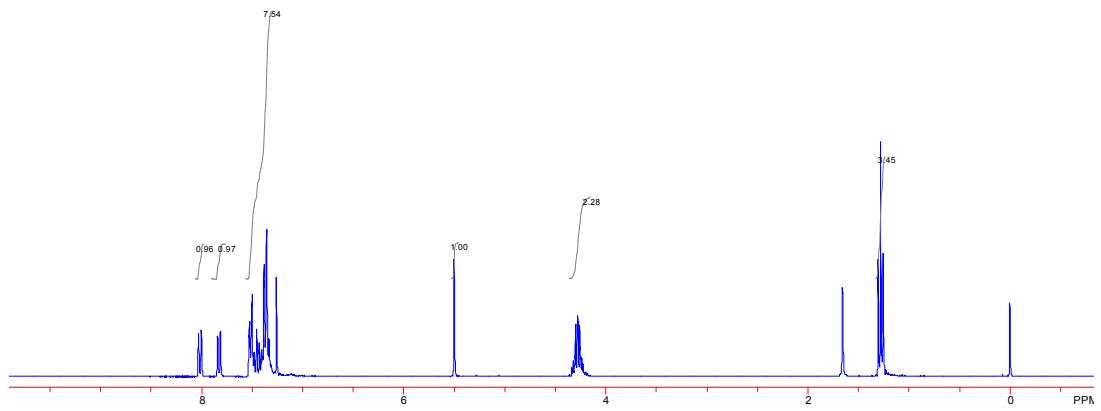
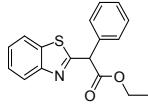
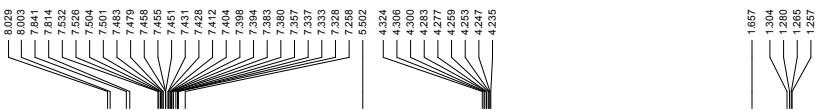
— 76.91
— 76.39

— 41.29
— 21.05
— 20.75









Jm-01-20-1.13.fid
Jm-01-20-1 CDC13 BB+DEPT135

