Cs_2CO_3-promoted defluorination and functionalization of α-CF_3 carbonyl compounds in the presence of N-, O-, and/or S-nucleophiles

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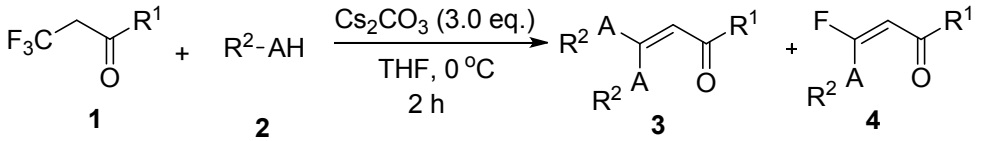
General Experimental:

The chemicals and reagents were purchased from Acros, Alfa Aesar, and National Chemical Reagent Group Co. Ltd., P. R. China, and used without further purification. Anhydrous solvents (THF, MeOH, DMF, DCM, and CH_3CN) used in the reactions were dried and freshly distilled before use. Petroleum ether (PE) used had a boiling range of 60−90 °C. All the reactions were carried out under Ar atmosphere, otherwise stated else. Oxygen and/or moisture sensitive solids and liquids were transferred appropriately. Concentration of solutions in *vacuo* was accomplished using a rotary evaporator fitted with a water aspirator. Residual solvents were removed under high vacuum (0.1-0.2 mm Hg). The progress of the reactions was monitored by TLC (silica-coated glass plates) and visualized under UV light, and by using iodine, ceric ammonium molybdate stain or phosphomolybdic acid. Melting points were measured on a SGW X-4 microscopy melting point apparatus without correction. ^1H NMR and ^{13}C NMR spectra were recorded either on a 400 MHz Varian Instrument at 25 °C or 600 MHz Bruke Instrument at 25 °C, using TMS as an internal standard, respectively. Multiplicity is tabulated as s for singlet, d for doublet, dd for doublet of doublet, t for triplet, and m for multiplet. Coupling constants (J) are reported in Hertz. ^{13}C NMR spectra were completely hetero-decoupled and measured at 150 MHz. HRMS spectra were recorded on Finnigan- Mat-95 mass spectrometer, equipped with ESI source. Single crystal X-ray diffraction measurements were performed with a diffractometer working with graphite-monochromated Cu Kα radiation.

Experimental Procedures:

The preparation of compound 3 or 4 in Table 2:



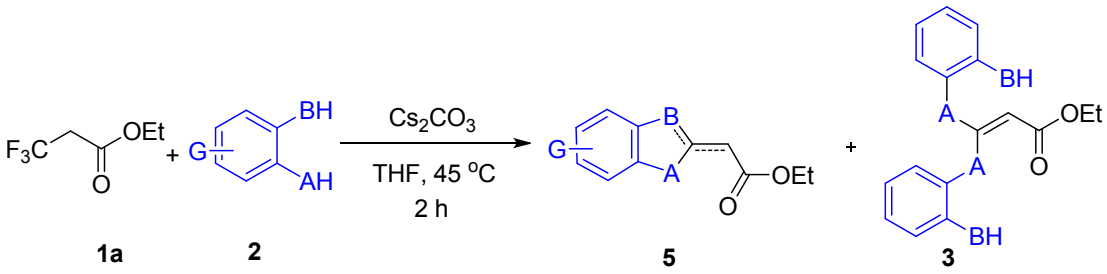
1 **2** **3** **4**

Method a: To a solution of 3,3,3-trifluoropropanoic acid derivatives (1.0 mmol) in THF (5 mL) was added the mono-dentate S-, O-, and N-nucleophiles (2.0 mmol) and Cs_2CO_3 (2.0 mmol)at 0 °C and then stirred for 2 h at under Ar. The reaction was ended with a saturated aqueous ammonium chloride solution (10 mL) and extracted with CH_2Cl_2 (DCM, 20 mL*3). After workup, the product was purified by flash chromatography (Petroleum Ether/Ethyl Acetate, PE/EA).

Method c: To a solution of ethyl 3,3,3-trifluoropropanoate (1.0 mmol) in THF (5 mL), was added the mono-dentate S-, O-, and N-nucleophiles (2.0 mmol) and Cs_2CO_3 (2.0 mmol) at 45 °C for 2 h at under Ar. The reaction was ended with a saturated aqueous ammonium chloride solution (10 mL) and extracted with DCM (20 mL*3). After workup, the product was purified by flash chromatography (PE /EA).

Method d: To a solution of ethyl 3,3,3-trifluoropropanoate (1.0 mmol) in anhydrous DMSO (5 mL), was added the mono-dentate S-, O-, and N-nucleophiles (2.0 mmol) and Cs_2CO_3 (2.0 mmol)at 45 °C for 2 h at under Ar. The reaction was ended with a saturated aqueous ammonium chloride solution (10 mL) and extracted with DCM (20 mL*3). After workup, the product was purified by flash chromatography (PE /EA).

The preparation of the compounds in Table 3:

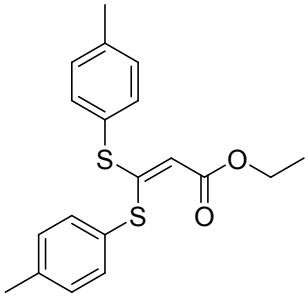


1a **2** **5** **3**

To a solution of ethyl 3,3,3-trifluoropropanoate (1.0 mmol) in THF (5 mL), was added the bidentate nucleophiles (1.0 mmol) and Cs_2CO_3 (2.0 mmol) at 45 °C for 2 h at under Ar. The reaction was ended with a saturated aqueous ammonium chloride solution (10 mL) and extracted with DCM (20 mL*3). After workup, the product was purified by flash chromatography (PE /EA).

Spectral data of all compounds:

Ethyl 3,3-bis(p-tolylthio)acrylate ***(3aa)***.



3aa

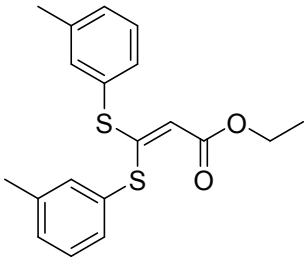
The resultant residue was purified by flash column chromatography (PE/EA=80/1) as a white solid. R_f= 0.20 (PE/EA = 80/1), **Mp** 85-86 °C.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.39 (d, *J* = 7.7 Hz, 2H), 7.09 – 6.88 (m, 6H), 5.03 (s, 1H), 3.92 (q, *J* = 7.1 Hz, 2H), 2.18 (s, 3H), 2.12 (s, 3H), 1.04 – 0.97 (m, 3H).

^{13}C NMR (150 MHz, $CDCl_3$) δ 165.4, 163.0, 140.5, 140.4, 137.0, 135.4, 130.7, 129.6, 126.7, 125.5, 107.1, 59.8, 21.5, 21.4, 14.4.

HRMS-ESI (*m/z*): $[M+H]^+$ calcd for $C_{19}H_{21}O_2S_2$ 345.0978; found 345.0973.

Ethyl 3,3-bis(m-tolylthio)acrylate ***(3ab).***



3ab

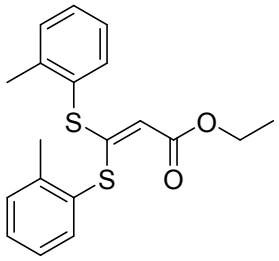
The resultant residue was purified by flash column chromatography (PE/EA=100/1) as a pale yellow liquid. R_f= 0.20 (PE/EA = 100/1).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.36 (d, *J* = 7.5 Hz, 2H), 7.23 – 6.98 (m, 6H), 5.21 (d, *J* = 1.4 Hz, 1H), 4.03 (qd, *J* = 7.1, 1.4 Hz, 2H), 2.26 (s, 3H), 2.21 (s, 3H), 1.12 (td, *J* = 7.1, 1.4 Hz, 4H).

^{13}C NMR (150 MHz, $CDCl_3$) δ 165.5, 161.9, 139.8, 138.7, 137.5, 135.8, 134.1, 132.4, 130.9, 130.9, 130.2, 129.7, 129.0, 128.7, 108.4, 60.1, 21.4, 21.3, 14.5.

HRMS-ESI (*m/z*): $[M + H]^+$ calcd for $C_{19}H_{21}O_2S_2$ 345.0978; found 345.0969.

Ethyl 3,3-bis(o-tolylthio)acrylate ***(3ac)***



3ac

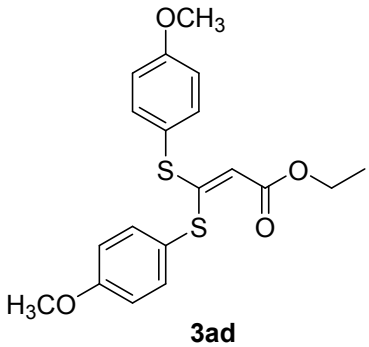
The resultant residue was purified by flash column chromatography (PE/EA=60/1) as a white solid. R_f= 0.20 (PE/EA = 60/1), **Mp** 84-85 °C.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.68 (d, *J* = 7.7 Hz, 1H), 7.47 – 7.08 (m, 7H), 5.11 (s, 1H), 4.13 (q, *J* = 7.1 Hz, 2H), 2.59 (s, 3H), 2.32 (s, 3H), 1.23 (t *J* = 7.1 Hz, 3H).

^{13}C NMR (150 MHz, $CDCl_3$) δ 165.7, 160.9, 144.6, 143.0, 138.2, 136.7, 131.4, 130.9, 130.9, 130.6, 129.4, 128.8, 127.4, 126.6, 106.6, 60.0, 21.4, 20.4, 14.5.

HRMS-ESI (*m/z*): $[M + H]^+$ calcd for $C_{19}H_{21}O_2S_2$ 345.0978; found 345.0974.

Ethyl 3,3-bis((4-methoxyphenyl)thio)acrylate ***(3ad)***



3ad

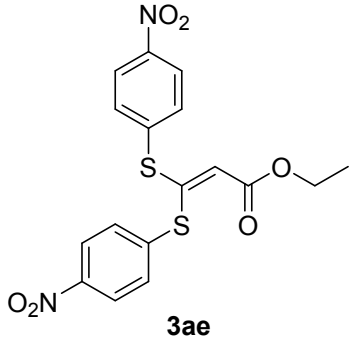
The resultant residue was purified by flash column chromatography (PE/EA=20/1) as a pale yellow liquid. R_f= 0.21 (PE/EA = 20/1).

^{1}H NMR (400 MHz, $CDCl_3$) ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.69 – 7.57 (m, 2H), 7.30 (d, *J* = 8.7 Hz, 2H), 6.99 – 6.84 (m, 4H), 5.14 (s, 1H), 4.13 (q, *J* = 7.1 Hz, 2H), 3.83 (d, *J* = 9.8 Hz, 6H), 1.23 (t, *J* = 7.1 Hz, 3H).

^{13}C NMR (150 MHz, $CDCl_3$) δ 165.7, 164.7, 161.5, 161.2, 138.9, 137.4, 120.8, 119.7, 115.6, 114.5, 106.5, 60.0, 55.5, 14.6.

HRMS-ESI (*m/z*): $[M + H]^+$ calcd for $C_{19}H_{21}O_4S_2$ 377.0876; found 377.0868.

Ethyl 3,3-bis((4-nitrophenyl)thio)acrylate ***(3ae)***



3ae

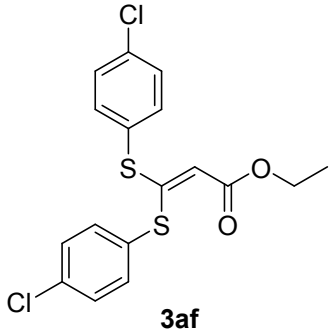
The resultant residue was purified by flash column chromatography (PE/EA=80/1) as a white foamy solid. R_f= 0.20 (PE/EA = 80/1).

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.25 – 8.08 (m, 4H), 7.65 – 7.55 (m, 2H), 7.40 (dd, *J* = 8.9, 2.1 Hz, 2H), 6.10 (s, 1H), 4.23 (q, *J* = 7.1 Hz, 6H), 1.30 (t, *J* = 7.1 Hz, 5H).

^{13}C NMR (150 MHz, $CDCl_3$) δ 164.4, 151.4, 148.3, 147.9, 139.9, 138.8, 135.6, 132.8, 127.0, 124.5, 124.2, 123.6, 119.7, 61.1, 14.4.

HRMS-ESI (*m/z*): $[M + H]^+$ calcd for $C_{17}H_{15}N_2O_6S_2$ 407.0372; found 407.0378.

Ethyl 3,3-bis((4-chlorophenyl)thio)acrylate ***(3af)***



3af

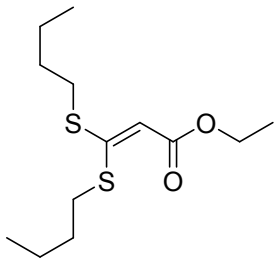
The resultant residue was purified by flash column chromatography (PE/EA=100/1) as a pale yellow liquid. R_f= 0.20 (PE/EA = 100/1).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.69 – 7.44 (d, *J* = 8.0 Hz, 2H), 7.41 – 7.31 (m, 4H), 7.31 – 7.21 (d, *J* = 8.0 Hz, 2H), 5.37 (s, 1H), 4.15 (q, *J* = 7.2 Hz, 2H), 1.24 (t, *J* = 7.2 Hz, 3H).

^{13}C NMR (150 MHz, $CDCl_3$) δ 165.2, 159.6, 138.0, 136.8, 136.6, 136.3, 130.2, 129.2, 128.8, 127.7, 110.1, 60.3, 14.5.

HRMS-ESI (*m/z*): $[M + H]^+$ calcd for $C_{17}H_{15}Cl_2O_2S_2$ 384.9885; found 384.9887.

Ethyl 3,3-bis(butylthio)acrylate ***(3ag)***



3ag

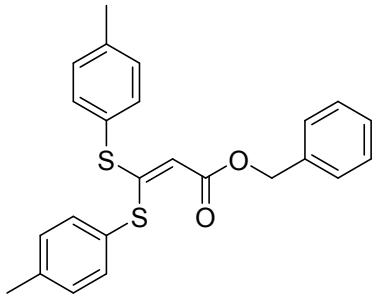
The resultant residue was purified by flash column chromatography (PE/EA=100/1) as a clear liquid. R_f= 0.21 (PE/EA = 100/1).

^{1}H NMR (400 MHz, $CDCl_3$) δ 5.63 (s, 1H), 4.17 (q, *J* = 7.2 Hz, 2H), 3.02 (t, *J* = 6.8 Hz, 2H), 2.87 (t, *J* = 6.8 Hz, 2H), 1.79 – 1.58 (m, 4H), 1.47 (m, 4H), 1.28 (tt, *J* = 7.6, 1.7 Hz, 3H), 0.95 (qd, *J* = 7.6, 3.6 Hz, 6H).

^{13}C NMR (150 MHz, CDCl3) δ 165.3, 160.6, 106.3, 59.9, 33.8, 31.5, 31.4, 29.64, 22.3, 22.2, 14.7, 13.8, 13.8.

HRMS-ESI (*m/z*): $[M + H]^+$ calcd for $C_{13}H_{25}O_2S_2$ 277.1291; found 277.1286.

Benzyl 3,3-bis(p-tolylthio)acrylate ***(3ba)***



3ba

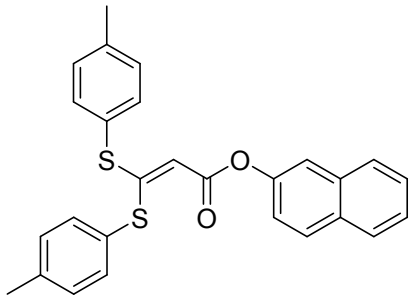
The resultant residue was purified by flash column chromatography (PE/EA=60/1) as a white solid. R_f= 0.25 (PE/EA = 60/1). **Mp** 123-124 °C.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.59 (dd, *J* = 8.1, 2.2 Hz, 2H), 7.40 – 7.06 (m, 11H), 5.24 (s, 1H), 5.11 (s, 2H), 2.40 (s, 3H), 2.34 (s, 3H).

^{13}C NMR (150 MHz, $CDCl_3$) δ 164.6, 163.5, 140.0, 139.9, 136.4, 135.7, 134.8, 130.1, 129.0, 127.9, 127.9, 127.5, 125.8, 124.8, 105.9, 65.1, 20.9, 20.7.

HRMS-ESI (*m/z*): $[M + H]^+$ calcd for $C_{24}H_{23}O_2S_2$ 407.1134; found 407.1130.

Naphthalen-2-yl 3,3-bis(p-tolylthio)acrylate ***(3ca)***



3ca

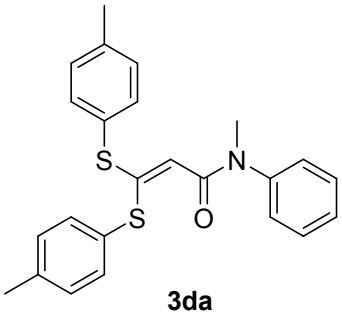
The resultant residue was purified by flash column chromatography (PE/EA=20/1) as a white solid. R_f= 0.20 (PE/EA = 20/1). **Mp** 121-122 °C.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.75 (dd, *J* = 22.1, 8.0 Hz, 2H), 7.52 – 7.45 (m, 2H), 7.41 (d, *J* = 5.5 Hz, 1H), 7.24 – 7.16 (m, 4H), 7.18 – 7.06 (m, 6H), 5.49 (s, 1H), 2.32 (s, 3H), 2.28 (s, 3H).

^{13}C NMR (150 MHz, $CDCl_3$) δ 167.6, 164.0, 148.7, 141.1, 141.0, 137.2, 135.8, 134.0, 131.5, 131.1, 123.0, 129.3, 127.9, 127.8, 126.6, 126.5, 125.6, 125.4, 121.7, 118.8, 105.5, 21.7, 21.6.

HRMS-ESI (*m/z*): $[M + H]^+$ calcd for $C_{27}H_{23}O_2S_2$ 443.1134; found 443.1142.

3,3,3-Trifluoro-N-methyl-N-(p-tolyl)propenamide ***(3da)***



3da

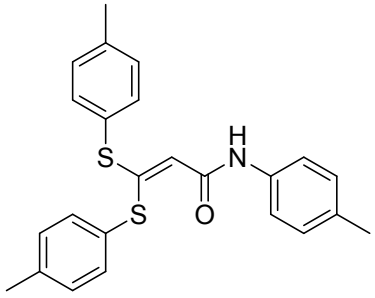
The resultant residue was purified by flash column chromatography (PE/EA=15/1) as a white solid. R_f= 0.20 (PE/EA = 15/1). **Mp** 144-145 °C.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.50 (d, *J* = 7.7 Hz, 2H), 7.11 (d, *J* = 7.7 Hz, 2H), 6.89 (m, 4H), 6.81 (d, *J* = 8.0 Hz, 2H), 6.73 (d, *J* = 7.6 Hz, 2H), 4.98 (s, 1H), 3.15 (s, 3H), 2.31 (s, 3H), 2.27 (s, 3H), 2.20 (s, 3H).

^{13}C NMR (150 MHz, $CDCl_3$) δ 165.5, 157.4, 141.5, 140.2, 139.5, 137.0, 135.3, 130.1, 129.9, 129.6, 127.5, 127.0, 110.2, 36.9, 21.6, 21.5, 21.3.

HRMS-ESI (*m/z*): $[M + H]^+$ calcd for $C_{24}H_{24}NOS_2$ 406.1294; found 406.1319.

N-(p-tolyl)-3,3-bis(p-tolylthio)acrylamide ***(3fa)*****.**



3fa

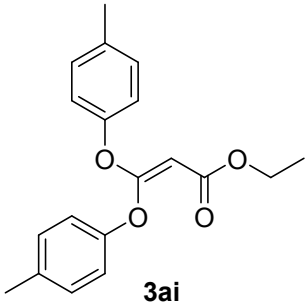
The resultant residue was purified by flash column chromatography (PE/EA=8/1) as a white solid. R_f= 0.21 (PE/EA = 8/1). **Mp** 116-117 °C.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.57 (d, *J* = 7.6 Hz, 2H), 7.39 (s, 2H), 7.25 (dd, *J* = 35.3, 7.6 Hz, 6H), 7.06 (d, *J* = 8.3 Hz, 2H), δ 5.30 (s, 1H), 2.39 (s, 3H), 2.38 (s, 3H), 2.28 (s, 3H).

^{13}C NMR (150 MHz, $CDCl_3$) δ 163.2, 158.0, 140.5, 136.4, 135.8, 135.6, 133.6, 130.8, 129.8, 129.6, 127.5, 119.7, 112.4, 21.6, 21.6, 21.1.

HRMS-ESI (*m/z*): $[M + H]^+$ calcd for $C_{24}H_{24}NOS_2$ 406.1294; found 406.1319.

Ethyl 3,3-bis(p-tolyloxy)acrylate ***(3ai)***



3ai

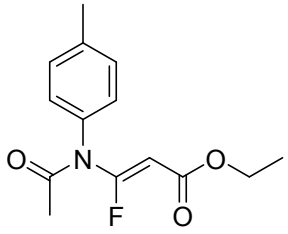
The resultant residue was purified by flash column chromatography (PE/EA=40/1) as a clear liquid. R_f= 0.20 (PE/EA = 40/1).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.21 – 7.03 (m, 6H), 6.93 (d, *J* = 8.3 Hz, 2H), 4.49 (s, 1H), 4.10 (q, *J* = 7.1 Hz, 2H), 2.33 – 2.32 (m, 6H), 1.20 (t, *J* = 7.1 Hz, 3H).

^{13}C NMR (150 MHz, $CDCl_3$) δ 166.4, 166.1, 151.9, 150.5, 136.1, 134.4, 130.7, 130.2, 120.6, 119.0, 80.8, 59.8, 21.1, 21.0, 14.6.

HRMS-ESI (*m/z*): $[M + H]^+$ calcd for $C_{19}H_{21}O_4$ 313.1434; found 313.1441.

Ethyl (Z)-3-fluoro-3-(N-(p-tolyl)acetamido)acrylate ***(4ak)***



4ak

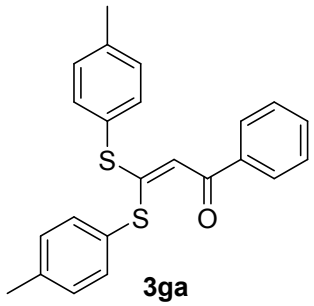
The resultant residue was purified by flash column chromatography (PE/EA=4/1) as a clear liquid. R_f= 0.25 (PE/EA = 4/1).

^{1}H NMR (400 MHz, CDCl) δ 7.26 (d, *J* = 8.2 Hz, 2H), 7.14 (d, *J* = 7.9 Hz, 2H), 5.40 (d, *J* = 27.1 Hz, 1H), 4.18 (q, *J* = 7.2 Hz, 2H), 2.39 (s, 4H), 2.13 (s, 3H), 1.27 (t, *J* = 7.2 Hz, 3H).

^{13}C NMR (150 MHz, $CDCl_3$) δ 170.2, 164.0, 159.1, 157.2, 139.5, 136.1, 130.8, 127.7, 94.7, 94.6, 60.7, 23.9, 23.8, 21.3, 14.4.

HRMS-ESI (*m/z*): $[M + Na]^+$ calcd for $C_{14}H_{16}FNNaO_3$ 288.1006; found 288.0987.

1-Phenyl-3,3-bis(p-tolylthio)prop-2-en-1-one ***(3ga)***



3ga

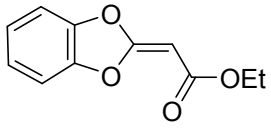
The resultant residue was purified by flash column chromatography (PE/EA=45/1) as a white solid. R_f= 0.20 (PE/EA = 45/1). **Mp** 141-142 °C.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.62 (td, *J* = 5.8, 4.0, 2.0 Hz, 4H), 7.50 – 7.38 (m, 1H), 7.39 – 7.29 (m, 4H), 7.29 – 7.19 (m, 4H), δ 6.41 (s, 1H), 2.41 (s, 3H), 2.40 (s, 3H).

^{13}C NMR (150 MHz, $CDCl_3$) δ 186.3, 167.8, 140.9, 140.8, 139.2, 136.9, 135.7, 131.9, 130.9, 129.9, 128.5, 128.0, 127.4, 126.4, 112.0, 21.7, 21.6.

HRMS-ESI (*m/z*): $[M + H]^+$ calcd for $C_{23}H_{21}OS_2$ 377.1028; found 377.1031.

Ethyl 2-(benzo[d][1,3]dioxol-2-ylidene)acetate ***(5am)***



5am

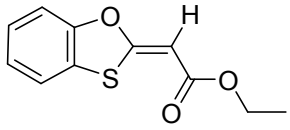
The resultant residue was purified by flash column chromatography (PE /EA = 20/1) as a pale yellow solid. R_f = 0.20 (PE/EA = 20/1), **Mp** 84-85 °C.

^{1}H NMR (400 MHz, CDCl3) δ 7.35 – 7.22 (m, 1H), 7.16 – 7.15 (m, 3H), 5.01 (s, 1H), 4.22 (q, *J* = 7.2 Hz, 2H), 1.31 (t, *J* = 7.2 Hz, 3H).

^{13}C NMR (150 MHz, $CDCl_3$) δ 167.6, 166.4, 145.3, 143.8, 124.8, 124.6, 110.7, 109.9, 70.7, 59.9, 14.7.

HRMS-ESI (*m/z*): $[M + H]^+$ calcd for $C_{11}H_{11}O_4$ 207.0652; found 207.0645.

Ethyl (Z)-2-(benzo[d][1,3]oxathiol-2-ylidene)acetate ***(5an)***



5an

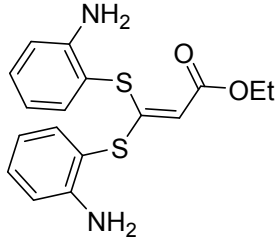
The resultant residue was purified by flash column chromatography (PE/EA=75/1) as a white solid. R_f = 0.23 (PE/EA = 75/1), **Mp** 115-116 °C.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.49 – 7.37 (m, 1H), 7.30 – 7.10 (m, 3H), 5.87 (d, *J* = 1.3 Hz, 1H), 4.25 (q, *J* = 7.1 Hz, 2H), 1.43 – 1.21 (m, 3H).

^{13}C NMR (150 MHz, $CDCl_3$) δ 171.6, 168.5, 152.3, 127.0, 124.7, 124.6, 122.0, 111.3, 89.2, 60.3, 14.7.

HRMS-ESI (*m/z*): $[M + H]^+$ calcd for $C_{11}H_{11}O_3S$ 223.0423; found 223.0422.

Ethyl 3,3-bis((2-aminophenyl)thio)acrylate ***(3ao)***



3ao

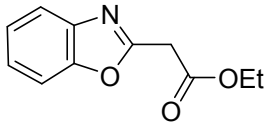
The resultant residue was purified by flash column chromatography (PE/EA=75/1) as a white solid. R_f = 0.23 (PE/EA = 75/1), **Mp** 115-116 °C.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.53 (d, *J* = 7.7 Hz, 1H), 7.28 (dd, *J* = 12.8, 5.5 Hz, 1H), 7.22 (d, *J* = 7.3 Hz, 2H), 6.79 (d, *J* = 7.7 Hz, 2H), 6.70 (q, *J* = 7.7 Hz, 2H), 5.35 (s, 1H), 4.43 (brs, 4H), 4.13 (q, *J* = 7.3 Hz, 2H). 1.24 (t, *J* = 7.1 Hz, 3H).

^{13}C NMR (150 MHz, $CDCl_3$) δ 165.8, 159.2, 150.4, 149.1, 138.5, 137.6, 132.6, 132.5, 119.0, 118.9, 115.8, 115.6, 112.5, 112.0, 107.7, 60.2, 14.6.

HRMS-ESI (*m/z*): $[M + Na]^+$ calcd for $C_{17}H_{18}N_2NaO_2S_2$ 369.0702; found 369.0700.

Ethyl 2-(benzo[d]oxazol-2-yl)acetate ***(5aq)***



5aq

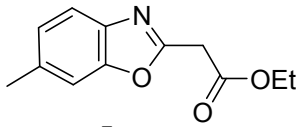
The resultant residue was purified by flash column chromatography (PE/EA=20/1) as a white solid. R_f= 0.20 (PE/EA = 20/1), **Mp** 56-57 °C.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.72 (d, *J* = 3.6 Hz, 1H), 7.71 (d, *J* = 3.6 Hz, 1H), 7.35– 7.10 (m, 2H), 4.25 (q, *J* = 7.1 Hz, 2H), 4.03 (s, 2H), 1.29 (t, *J* = 7.1 Hz, 3H).

^{13}C NMR (150 MHz, $CDCl_3$) δ 167.2, 159.7, 151.3, 141.3, 125.3, 124.6, 120.2, 110.8, 62.1, 35.5, 14.2.

HRMS-ESI (*m/z*): $[M + H]^+$ calcd for $C_{11}H_{12}NO_3$ 206.0812; found 206.0813.

Ethyl 2-(6-methylbenzo[d]oxazol-2-yl)acetate ***(5as)***



5as

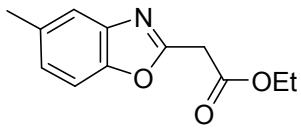
The resultant residue was purified by flash column chromatography (PE/EA=18/1) as a yellow liquid. R_f= 0.20 (PE/EA = 18/1).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.57 – 7.46 (s, 1H), 7.46 – 7.37 (d, *J* = 8.4 Hz, 1H), 7.15 (d, *J* = 8.4 Hz, 1H), 4.40 – 4.13 (q, *J* = 7.2 Hz, 2H), 4.00 (s, 2H), 2.46 (s, 3H), 1.28 (t, *J* = 7.2, Hz, 3H).

^{13}C NMR (150 MHz, $CDCl_3$) δ 167.3, 159.8, 149.6, 141.5, 134.5, 126.4, 120.1, 110.2, 62.1, 35.6, 21.6, 14.3.

HRMS-ESI (*m/z*): $[M + H]^+$ calcd for $C_{12}H_{14}NO_3$ 220.0968; found 220.0967.

Ethyl 2-(5-methylbenzo[d]oxazol-2-yl)acetate ***(5at)***



5at

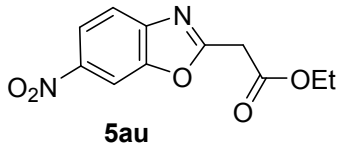
The resultant residue was purified by flash column chromatography (PE/EA=18/1) as a pale yellow solid. R_f= 0.20 (PE/EA = 18/1), **Mp** 58-59 °C.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.49 (s, 1H), 7.39 (d, *J* = 8.4 Hz, 1H), 7.14 (d, *J* = 8.3 Hz, 1H), 4.24 (q, *J* = 7.1 Hz, 2H), 3.99 (s, 2H), 2.46 (s, 3H), 1.28 (t, *J* = 7.1 Hz, 3H).

^{13}C NMR (150 MHz, $CDCl_3$) δ 167.3, 159.2, 151.6, 139.1, 135.7, 125.8, 119.5, 110.9, 62.1, 35.5, 21.9, 14.3.

HRMS-ESI (*m/z*): $[M + H]^+$ calcd for $C_{12}H_{14}NO_3$ 220.0968; found 220.0969.

Ethyl 2-(6-nitrobenzo[d]oxazol-2-yl)acetate ***(5au)***



5au

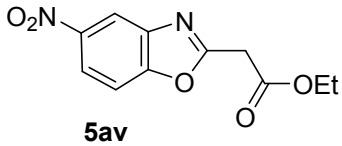
The resultant residue was purified by flash column chromatography (PE/EA=13/1) as a pale yellow solid. R_f = 0.20 (PE/EA = 13/1), **Mp** 77-79 °C.

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.46 (dt, *J* = 6.3, 2.4 Hz, 1H), 8.32 (dq, *J* = 8.9, 1.7 Hz, 1H), 7.83 (dd, *J* = 8.9, 1.7 Hz, 1H), δ 4.28 (q, *J* = 7.0 Hz, 2H), 4.10 (s, 2H), 1.31 (t, *J* = 7.0 Hz, 3H).

^{13}C NMR (150 MHz, $CDCl_3$) δ 166.4, 164.5, 150.4, 146.5, 145.6, 120.8, 120.4, 107.6, 62.5, 35.7, 14.3.

HRMS-ESI (*m/z*): $[M + H]^+$ calcd for $C_{11}H_{11}N_2O_5$ 251.0662; found 251.0665.

Ethyl 2-(5-nitrobenzo[d]oxazol-2-yl)acetate ***(5av)***



5av

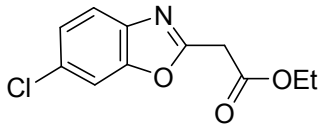
The resultant residue was purified by flash column chromatography (PE/EA=20/1) as a pale yellow solid. R_f = 0.20 (PE/EA = 20/1), **Mp** 87-88 °C.

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.46 (d, *J* = 2.1 Hz, 1H), 8.32 (d, *J* = 8.9 Hz, 1H), 7.91 – 7.78 (m, 1H), 4.27 (q, *J* = 7.0 Hz, 2H), 4.10 (s, 2H), 1.31 (t, *J* = 7.0 Hz, 3H).

^{13}C NMR (150 MHz, $CDCl_3$) δ 166.1, 159.6, 150.6, 139.3, 130.3, 124.6, 120.0, 110.7, 61.4, 34.6, 13.5.

HRMS-ESI (*m/z*): $[M + H]^+$ calcd for $C_{11}H_{10}N_2O_5$ 251.0662; found 251.0663.

Ethyl 2-(6-chlorobenzo[d]oxazol-2-yl)acetate ***(5aw)***



5aw

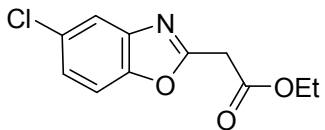
The resultant residue was purified by flash column chromatography (PE/EA=15/1) as a black solid. R_f = 0.21 (PE/EA = 15/1), **Mp** 85-86 °C.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.63 (dt, *J* = 8.5, 1.9 Hz, 1H), 7.55 (q, *J* = 1.9, 1.5 Hz, 1H), 7.33 (dt, *J* = 8.5, 1.5 Hz, 1H), δ 4.25 (q, *J* = 7.1 Hz, 2H), 4.01 (s, 2H), 1.29 (t, *J* = 7.1 Hz, 3H).

^{13}C NMR (150 MHz, $CDCl_3$) δ 166.1, 159.6, 150.6, 139.3, 130.3, 124.6, 120.0, 110.7, 61.4, 34.6, 13.5.

HRMS-ESI (*m/z*): $[M + H]^+$ calcd for $C_{11}H_{11}ClNO_3$ 240.0422; found 240.0419.

Ethyl 2-(5-chlorobenzo[d]oxazol-2-yl)acetate ***(5ax)***



5ax

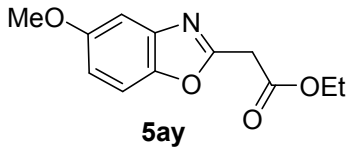
The resultant residue was purified by flash column chromatography (PE/EA=30/1) as a pale yellow solid. R_f = 0.23 (PE/EA = 30/1), **Mp** 85-86 °C.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.70 (q, *J* = 2.0 Hz, 1H), 7.45 (dt, *J* = 8.7, 1.8 Hz, 1H), 7.32 (dq, *J* = 8.7, 2.0 Hz, 1H), 4.25 (q, *J* = 7.1 Hz, 3H), 4.01 (s, 3H), 1.29 (t, *J* = 7.1 Hz, 5H).

^{13}C NMR (150 MHz, $CDCl_3$) δ 166.9, 161.2, 149.9, 142.4, 130.2, 125.7, 120.3, 111.6, 62.3, 35.5, 14.3.

HRMS-ESI (*m/z*): $[M + H]^+$ calcd for $C_{11}H_{11}ClNO_3$ 240.0422; found 240.0419.

Ethyl 2-(5-methoxybenzo[d]oxazol-2-yl)acetate ***(5ay)***



5ay

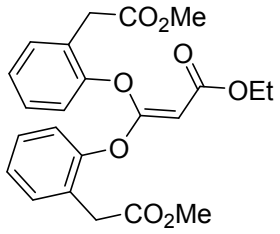
The resultant residue was purified by flash column chromatography (PE/EA=30/1) as a white liquid. R_f = 0.21 (PE/EA = 10/1).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.40 (dd, *J* = 8.9, 1.4 Hz, 1H), 7.19 (d, *J* = 1.4 Hz, 1H), 7.01 – 6.86 (m, 1H), 4.24 (q, *J* = 7.1 Hz, 2H), 3.99 (s, 2H), 3.85 (s, 3H), 1.28 (t, *J* = 7.1 Hz, 3H).

^{13}C NMR (150 MHz, $CDCl_3$) δ 167.2, 160.5, 157.4, 146.0, 142.2, 113.9, 110.9, 103.2, 62.1, 56.1, 35.6, 14.3.

HRMS-ESI (*m/z*): $[M + H]^+$ calcd for $C_{12}H_{14}NO_4$ 236.0917; found 236.0916.

Dimethyl 2,2'-(((3-ethoxy-3-oxoprop-1-ene-1,1-diyl)bis(oxy))bis(2,1-phenylene))diacetate ***(3az)***



3az

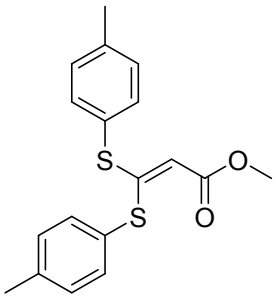
The resultant residue was purified by flash column chromatography (PE/EA=5/1) as a clear liquid. R_f = 0.21 (PE/EA = 5/1).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.48 – 6.83 (m, 8H), δ 4.35 (s, 1H), 4.03 (q, *J* = 7.1 Hz, 2H), 3.72 (s, 2H), 3.60 (s, 3H), 3.53 (s, 3H), 3.44 (s, 2H), 1.12 (t, *J* = 7.1 Hz, 3H).

^{13}C NMR (150 MHz, $CDCl_3$) δ 171.5, 170.9, 165.7, 164.9, 151.8, 150.7, 132.0, 131.4, 129.3, 128.5, 126.7, 126.6, 126.2, 125.4, 121.2, 119.8, 79.9, 59.7, 52.2, 52.1, 35.4, 35.3, 14.5.

HRMS-ESI (*m/z*): $[M + H]^+$ calcd for $C_{23}H_{25}O_8$ 429.1544; found 429.1550.

Methyl 3,3-bis(p-tolylthio)acrylate ***(3ha)***



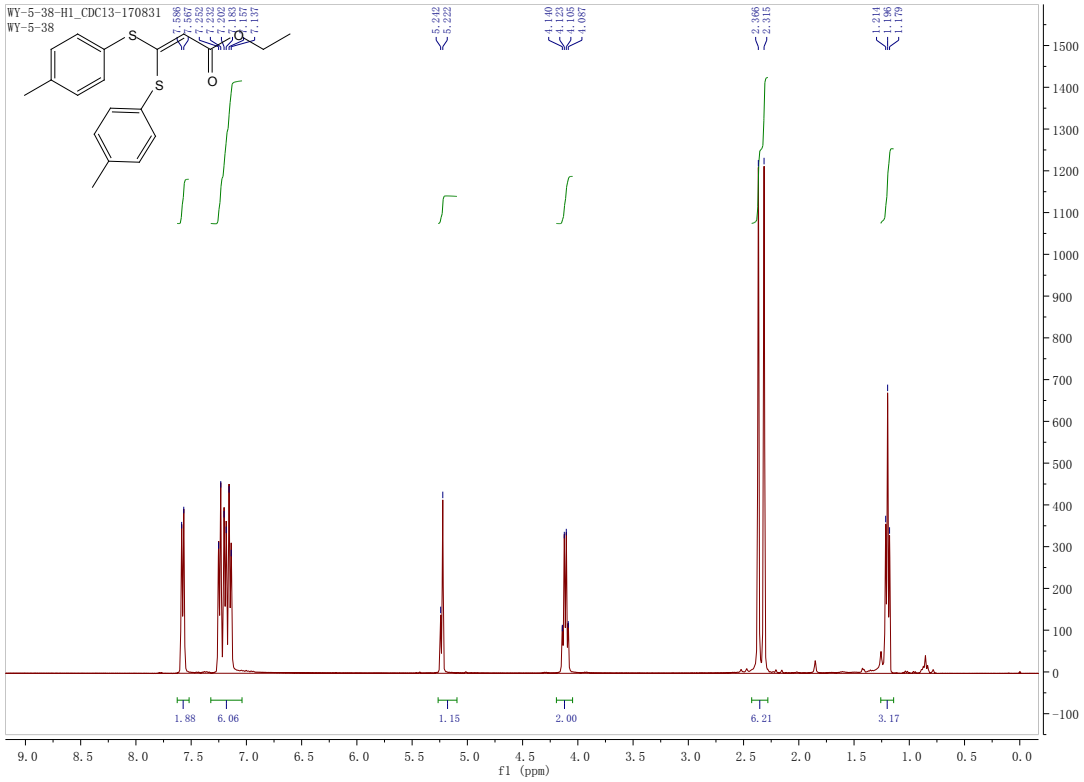
The resultant residue was purified by flash column chromatography (PE/EA=15/1) as a white foamy solid. R_f= 0.21 (PE/EA = 15/1). **Mp** 82-83 °C.

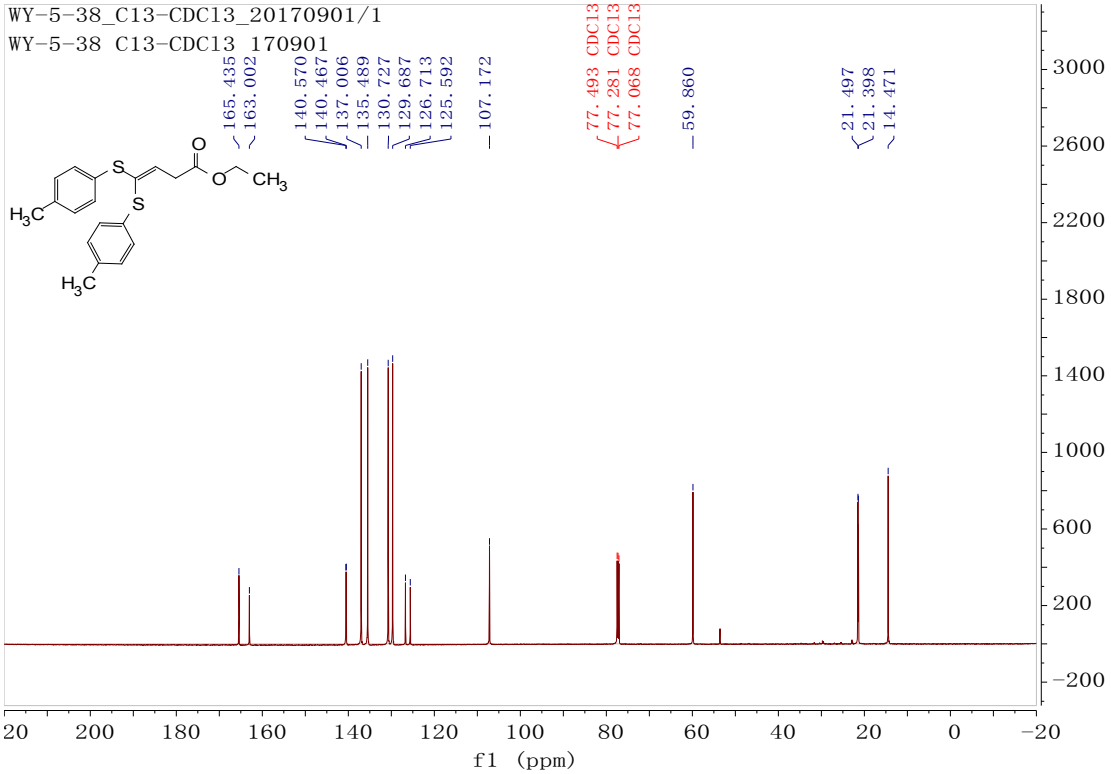
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.59 (d, *J* = 8.1 Hz, 2H), 7.35 – 6.93 (m, 6H), 5.19 (s, 1H), 3.65 (s, 3H), 2.40 (s, 3H), 2.36 (s, 3H).

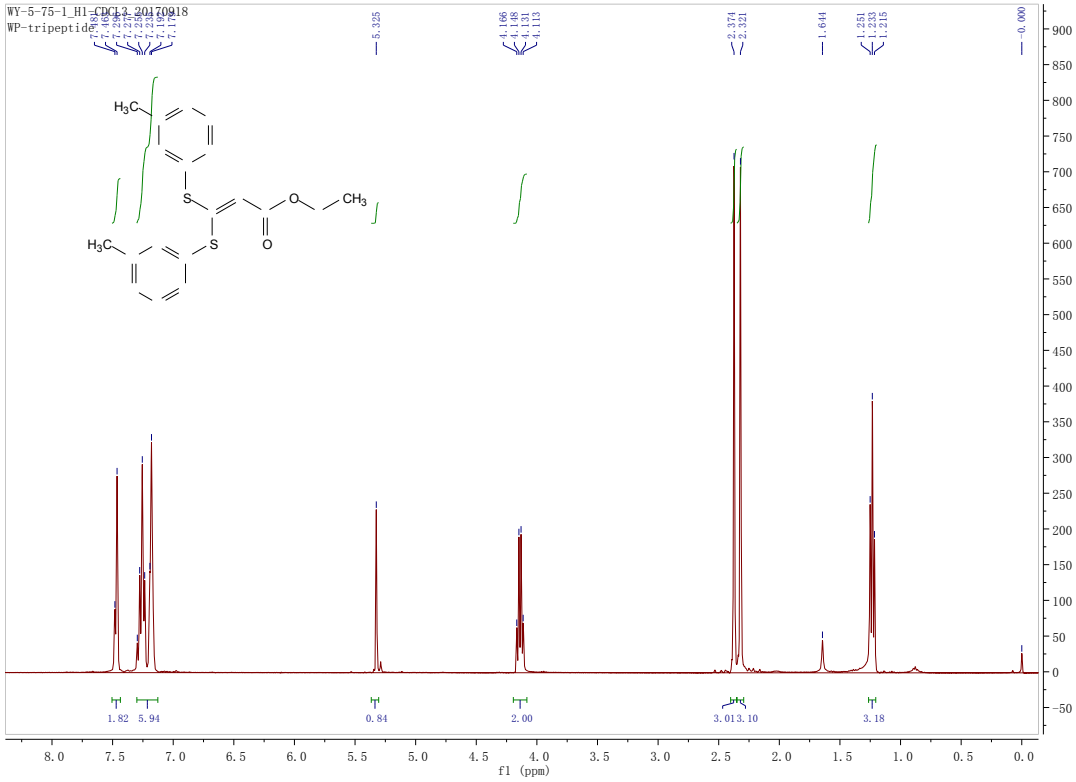
^{13}C NMR (150 MHz, $CDCl_3$) δ 166.0, 163.8, 140.8, 140.7, 137.2, 135.7, 130.9, 129.9, 126.9, 125.6, 106.8, 51.3, 21.7, 21.5.

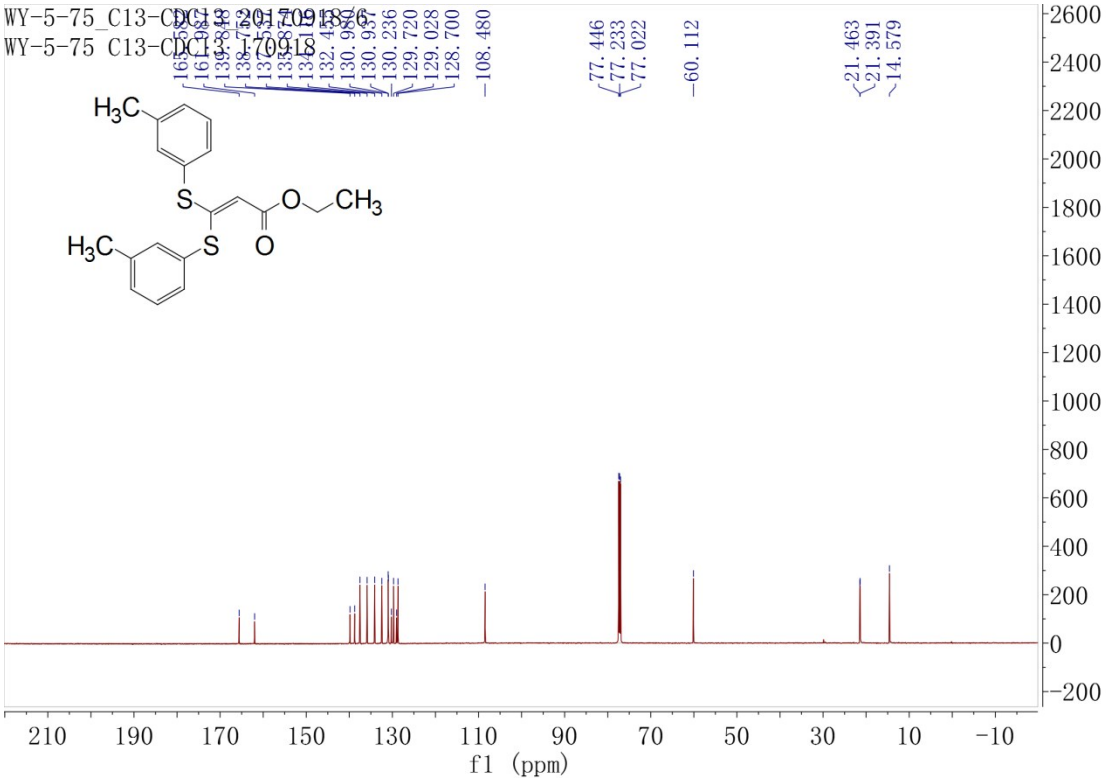
HRMS-ESI (*m/z*): $[M + H]^+$ calcd for $C_{18}H_{19}O_2S_2$ 331.0821; found 331.0826.

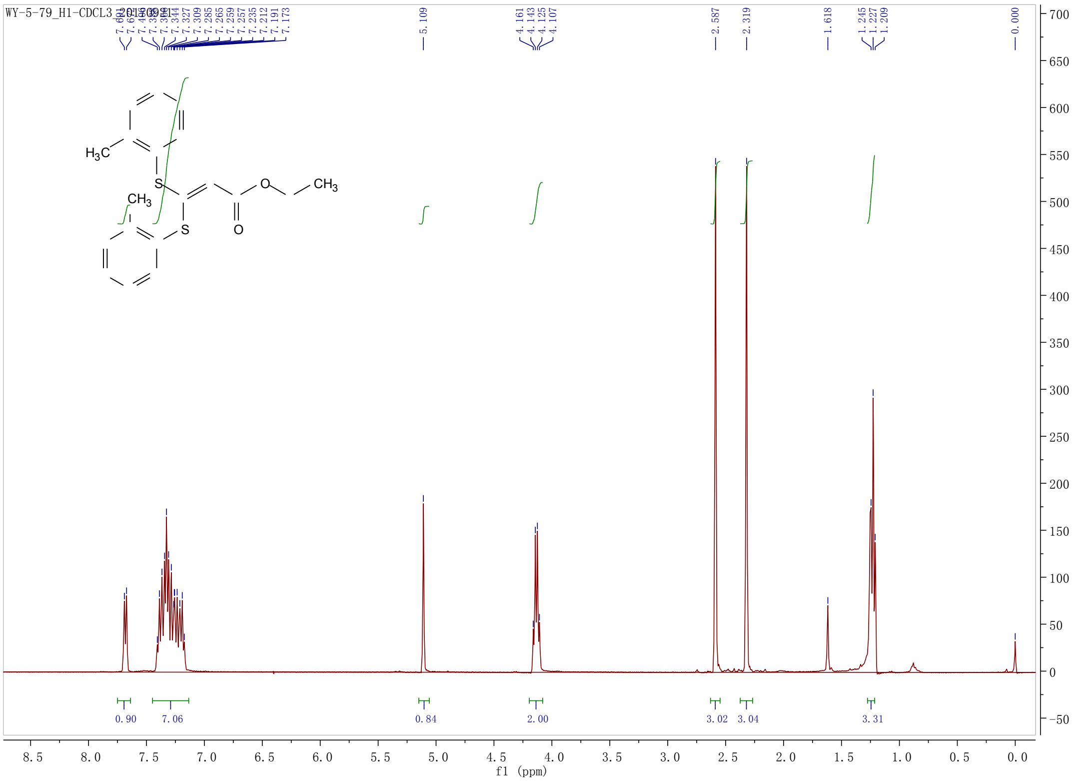
Copies of ^{1}H NMR and ^{13}C NMR spectra of all compound:

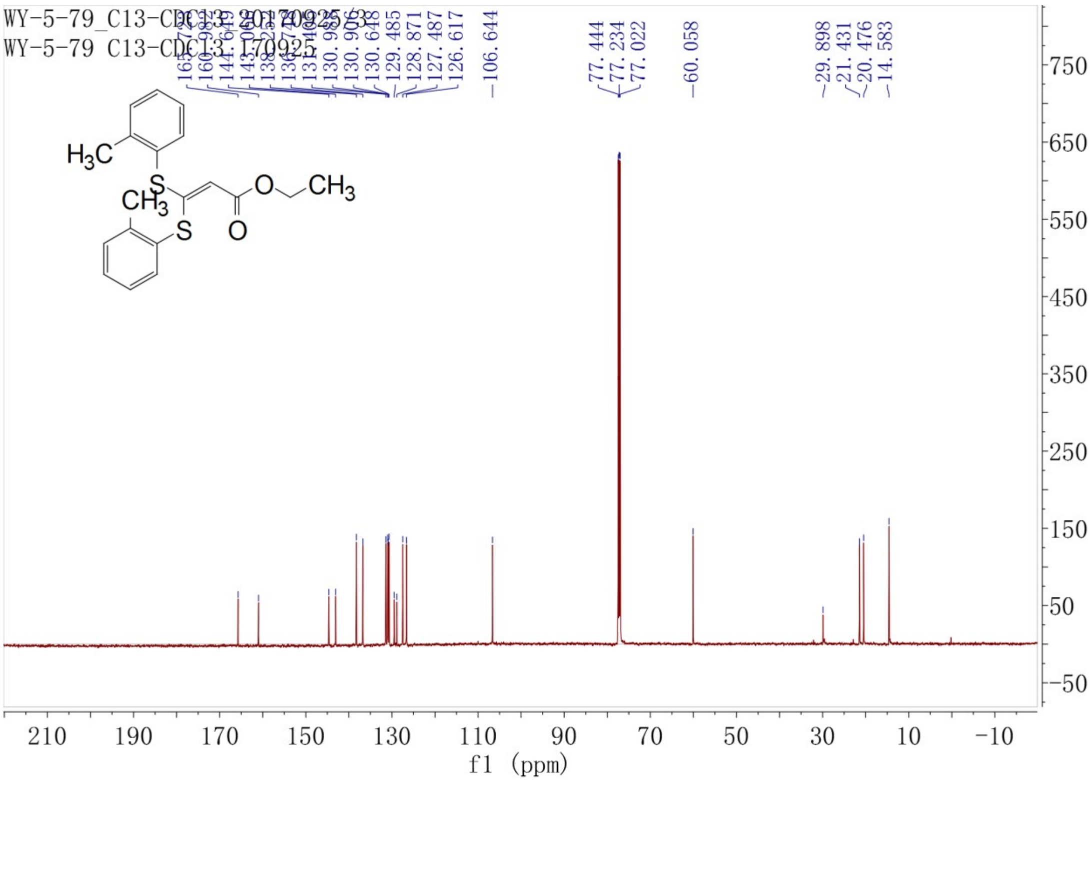


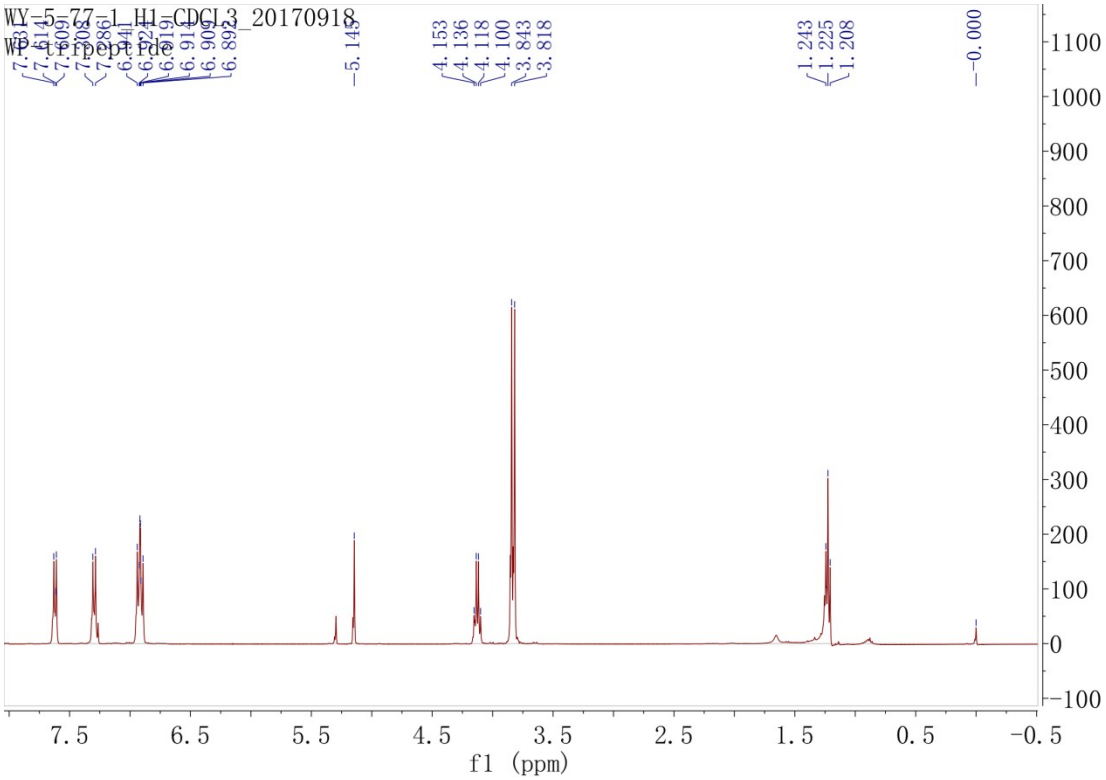


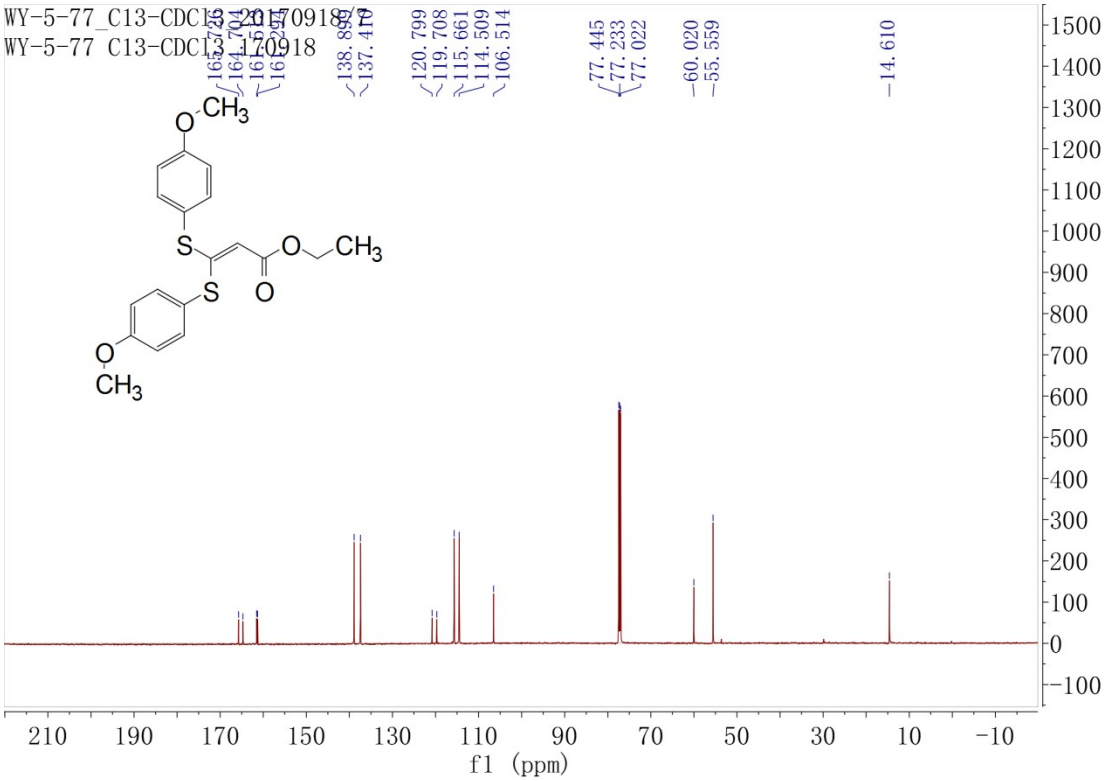

WY-5-75-1_H1-CDCl3_20170918
WP-tripeptide
f1 (ppm)

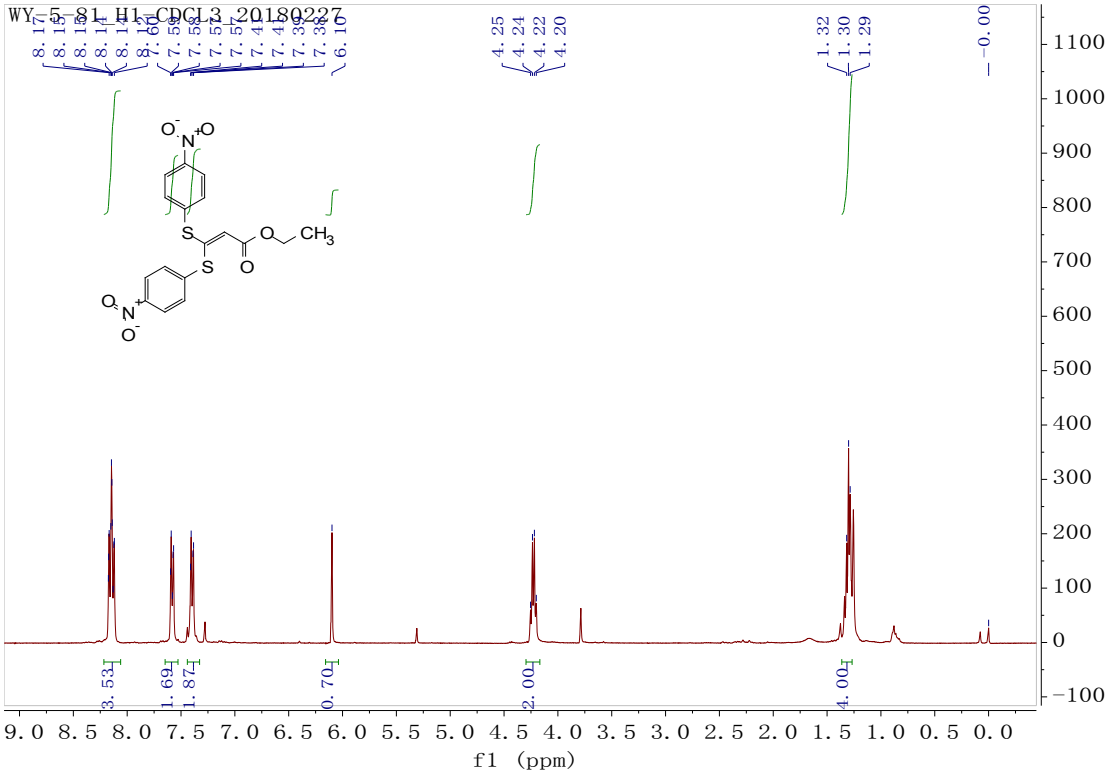

WY-5-75_C13-CDCl3_20170918
f1 (ppm)

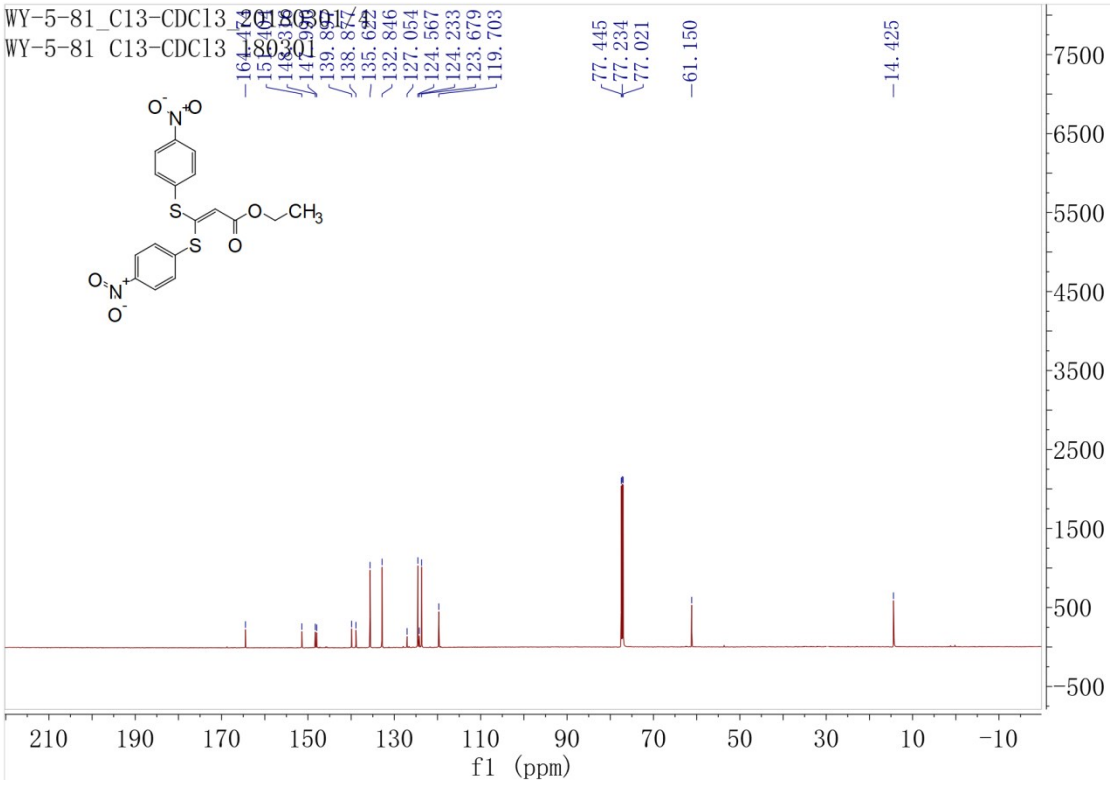

WY-5-79_H1-CDCL3_20170921
5.109
4.161
4.143
4.125
4.107
2.587
2.319
1.618
1.245
1.227
1.209
0.000
0.90
7.06
0.84
2.00
3.02
3.04
3.31
f1 (ppm)

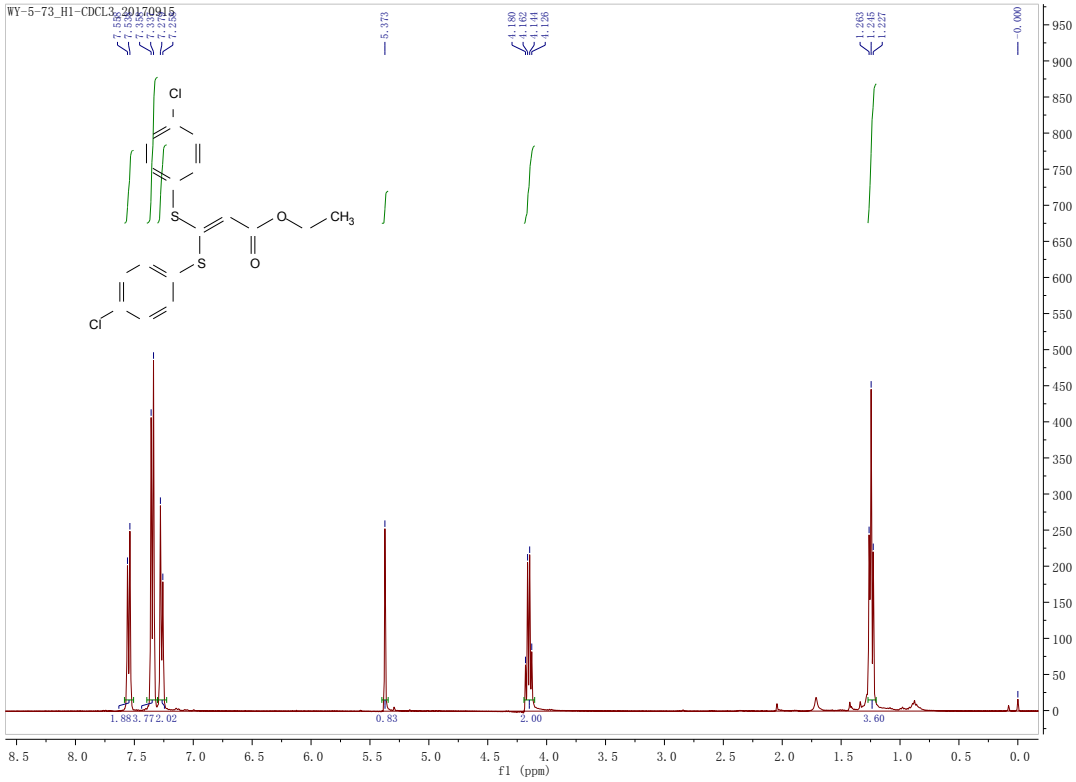

WY-5-79_C13-CDCl3_170925
130.905
130.648
129.485
128.871
127.487
126.617
106.644
77.444
77.234
77.022
60.058
29.898
21.431
20.476
14.583
f1 (ppm)

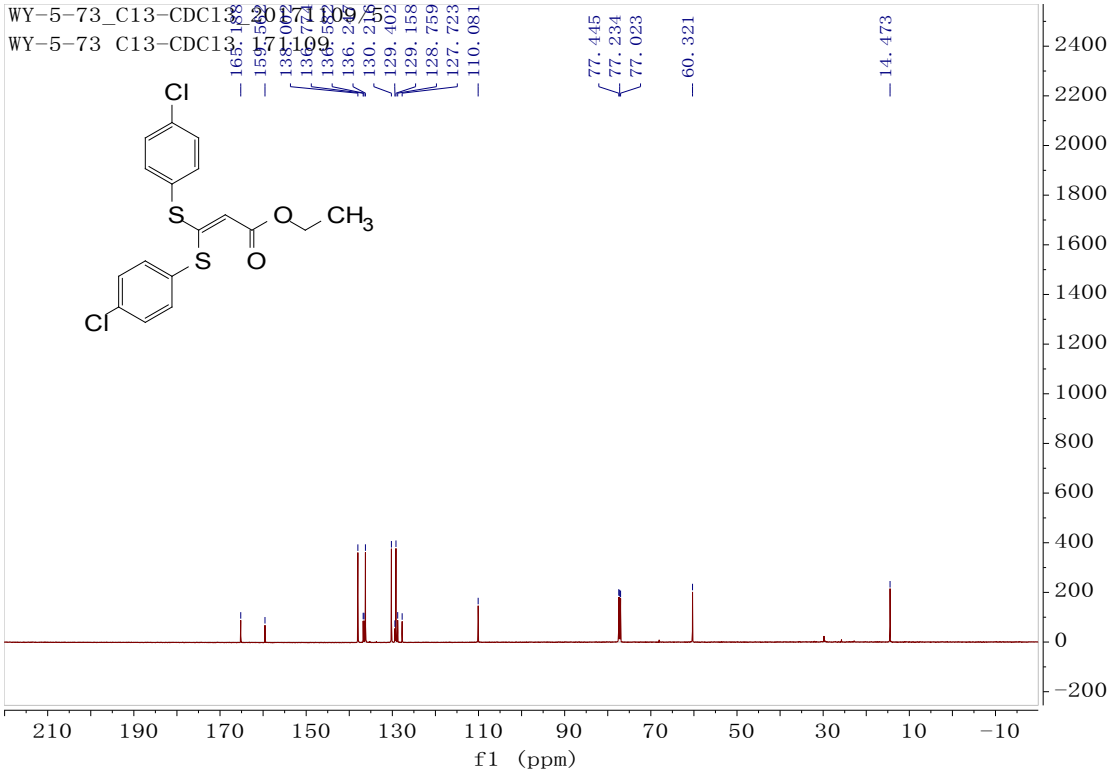

WY-5-77-1_H1-CDCl3_20170918
WP tripeptide
7.414
7.409
7.403
7.386
6.922
6.919
6.914
6.909
6.892
5.143
4.153
4.136
4.118
4.100
3.843
3.818
1.243
1.225
1.208
0.000
f1 (ppm)

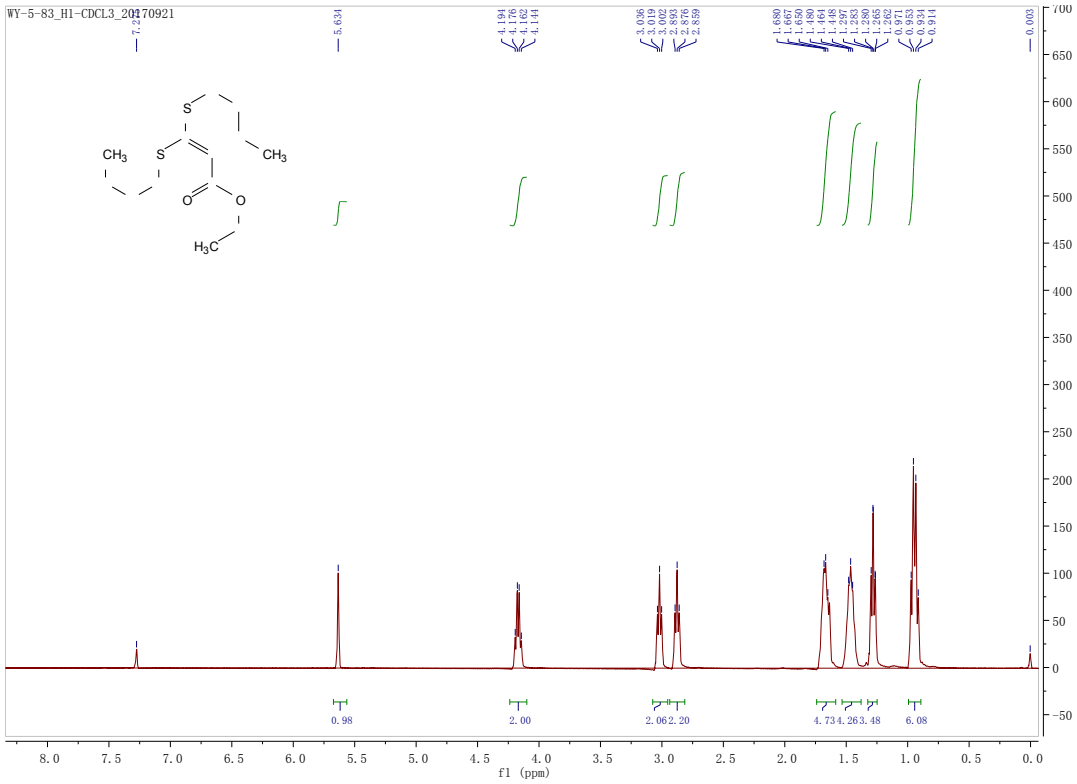

WY-5-77_C13-CDCl3_20170918
WY-5-77 C13-CDCl3 170918
164.704
138.899
137.410
120.799
119.708
115.661
114.509
106.514
77.445
77.233
77.022
60.020
55.559
14.610
O
CH3
S
O
CH3
S
O
O
CH3
f1 (ppm)

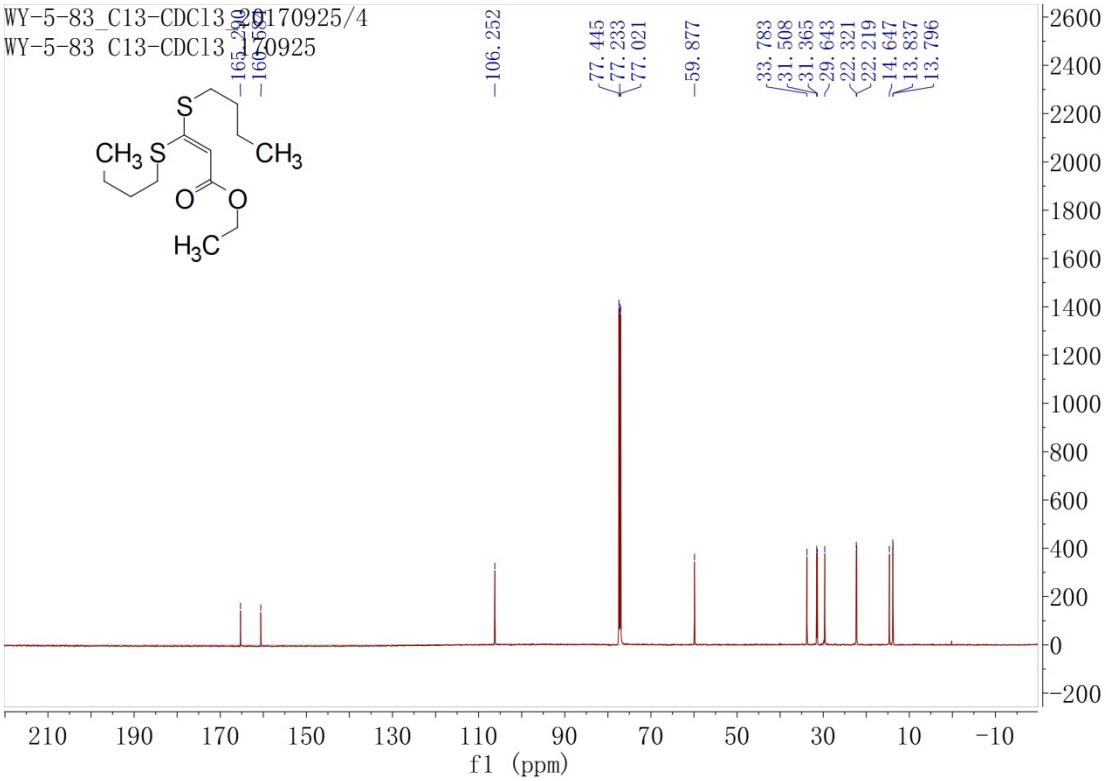

WY-5-81_H1-CDCl3_20180227
f1 (ppm)


WY-5-81_C13-CDCl3_20180227
f1 (ppm)


WY-5-73_H1-CDCL3_20170915
Cl
S
O
CH3
S
O
Cl
1.88
3.77
2.02
0.83
2.00
3.60
f1 (ppm)

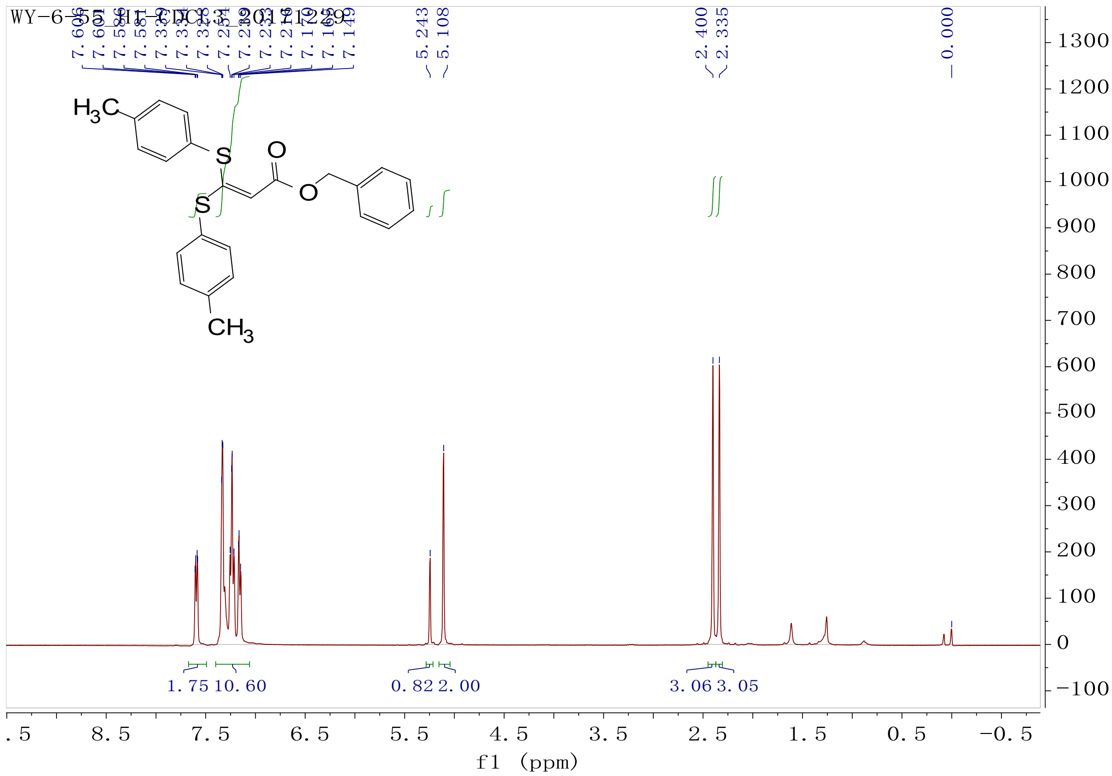

WY-5-73_C13-CDCl3_20171109
WY-5-73 C13-CDCl3 171109
Cl
S
O
CH3
S
O
Cl
f1 (ppm)

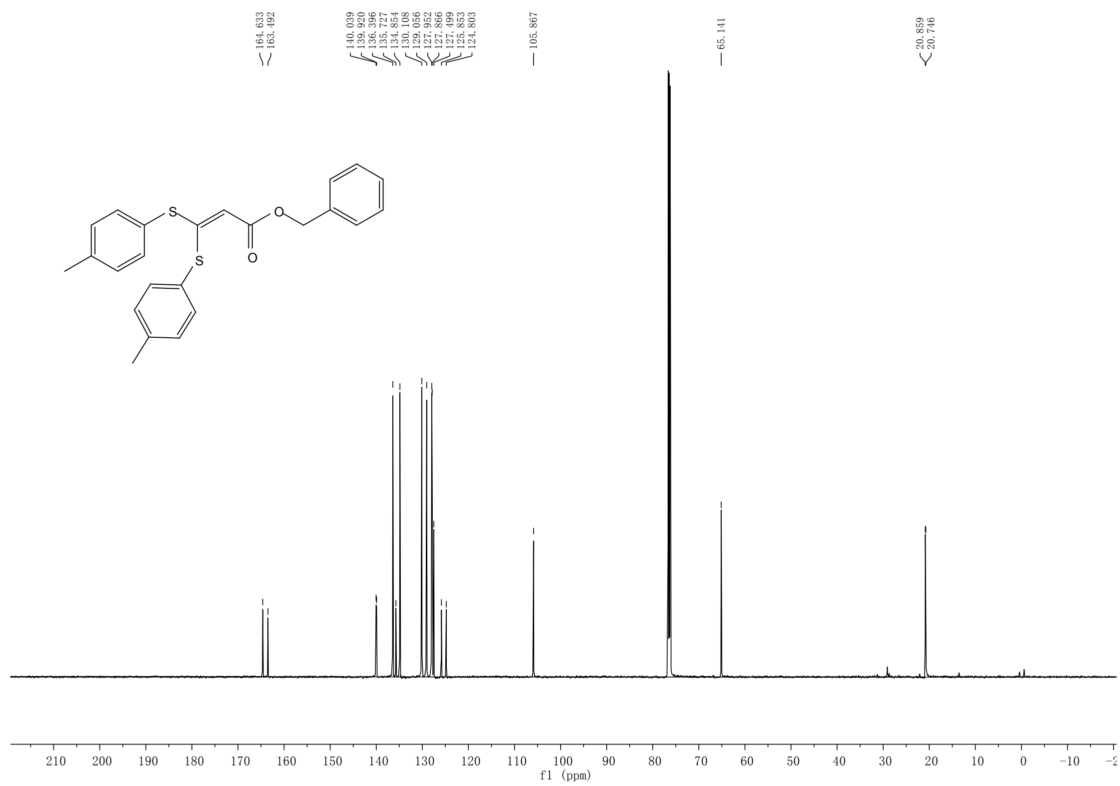

WY-5-83_H1-CDCL3_20170921
f1 (ppm)

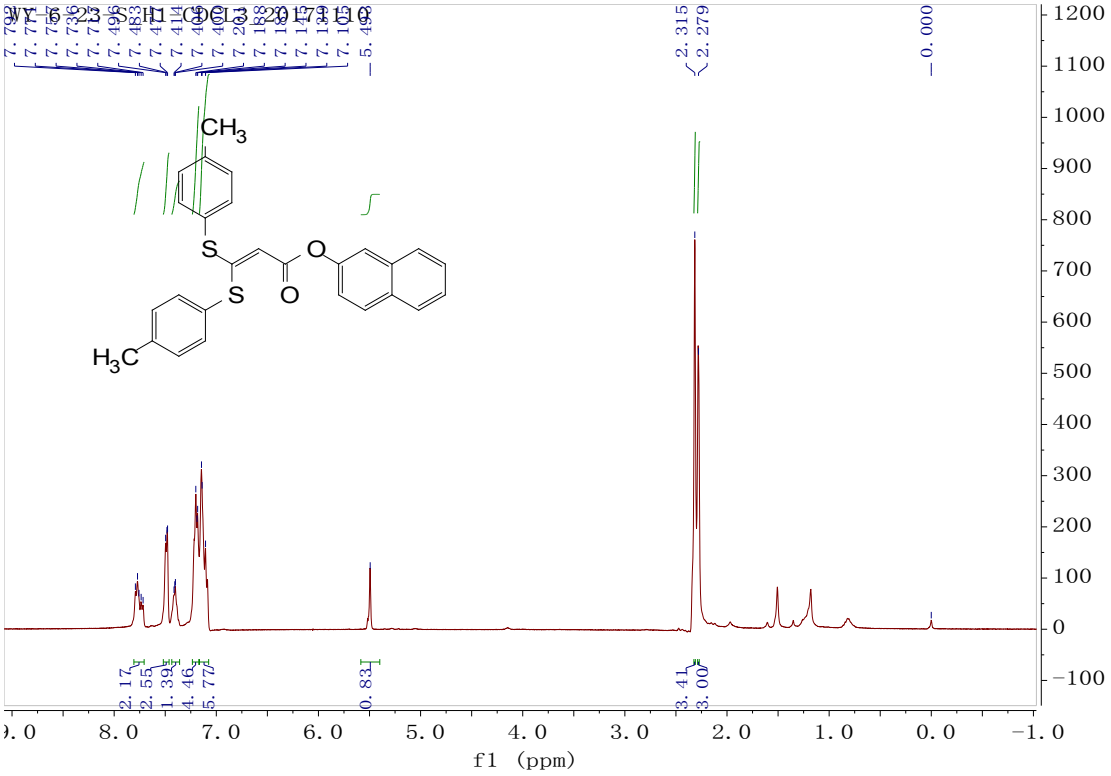

WY-5-83_C13-CDCl3_20170925/4
WY-5-83 C13-CDCl3 20170925
f1 (ppm)

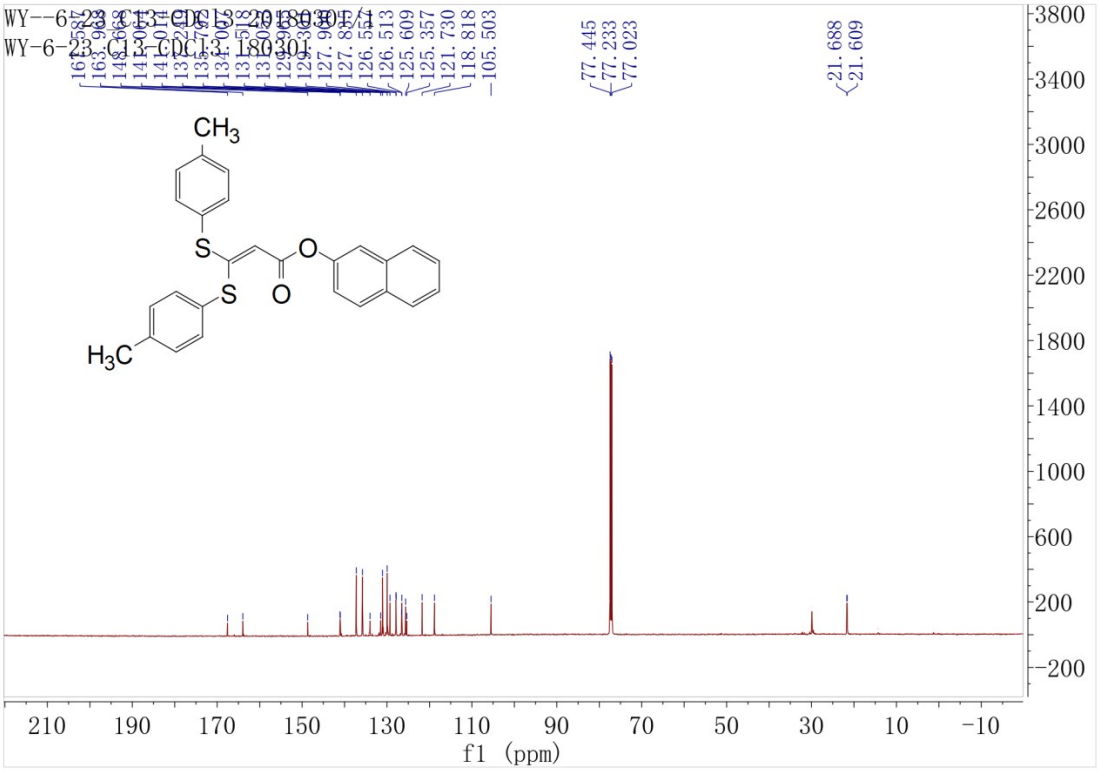
3ah

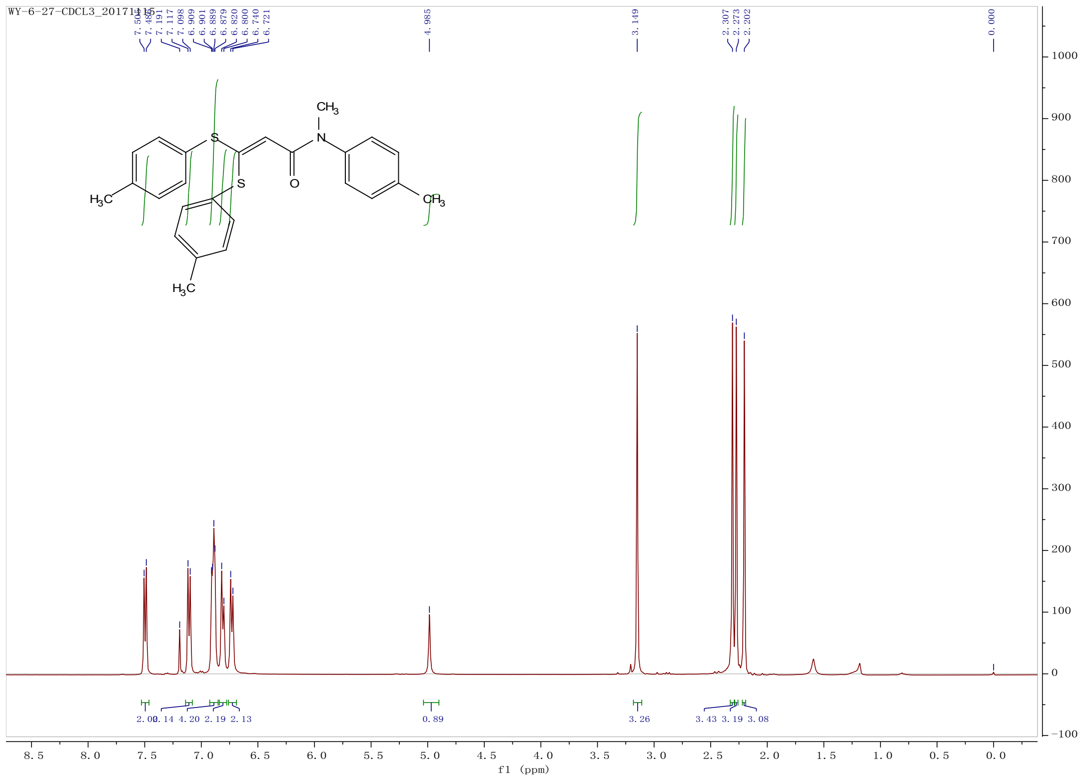
4ah

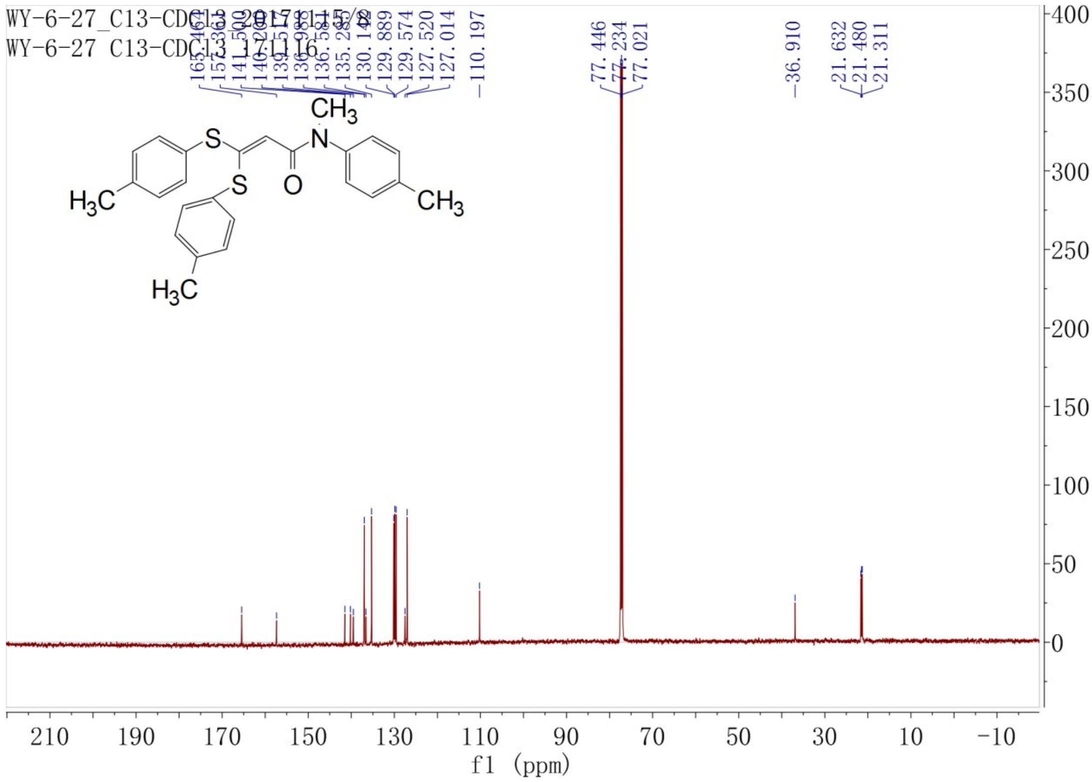


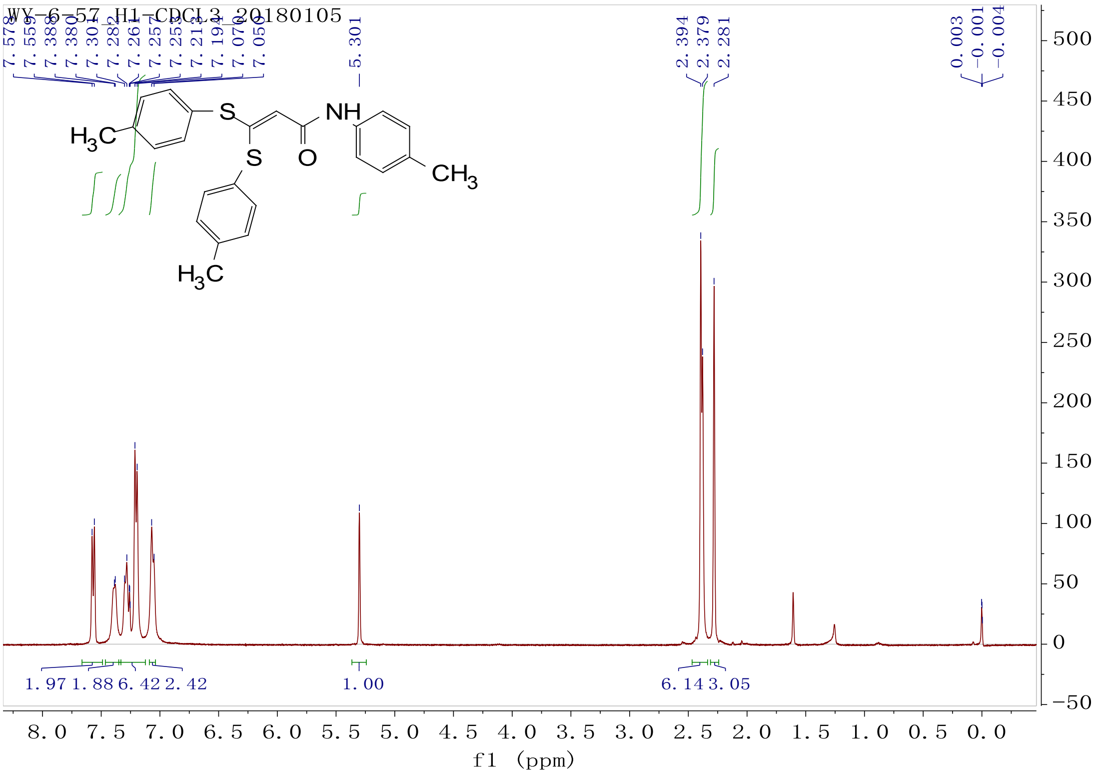



CH3
S
O
S
O
H3C
f1 (ppm)

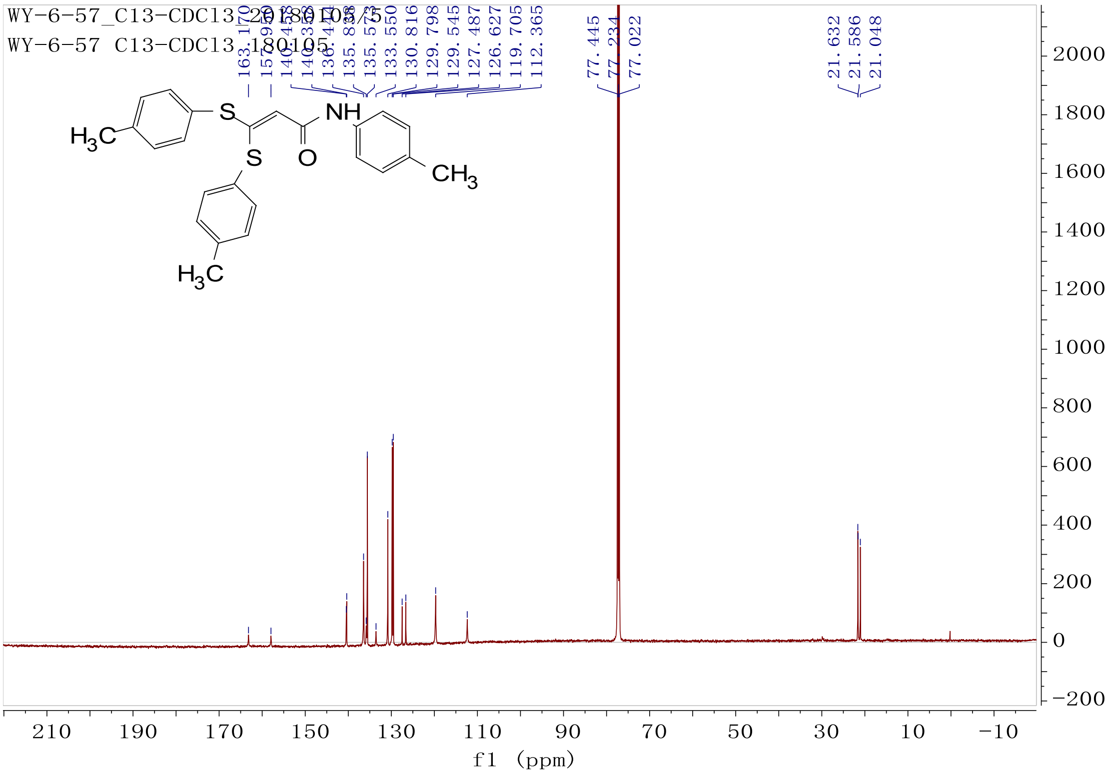

CH3
S
O
S
O
H3C
f1 (ppm)


WY-6-27-CDCL3_20171115
f1 (ppm)

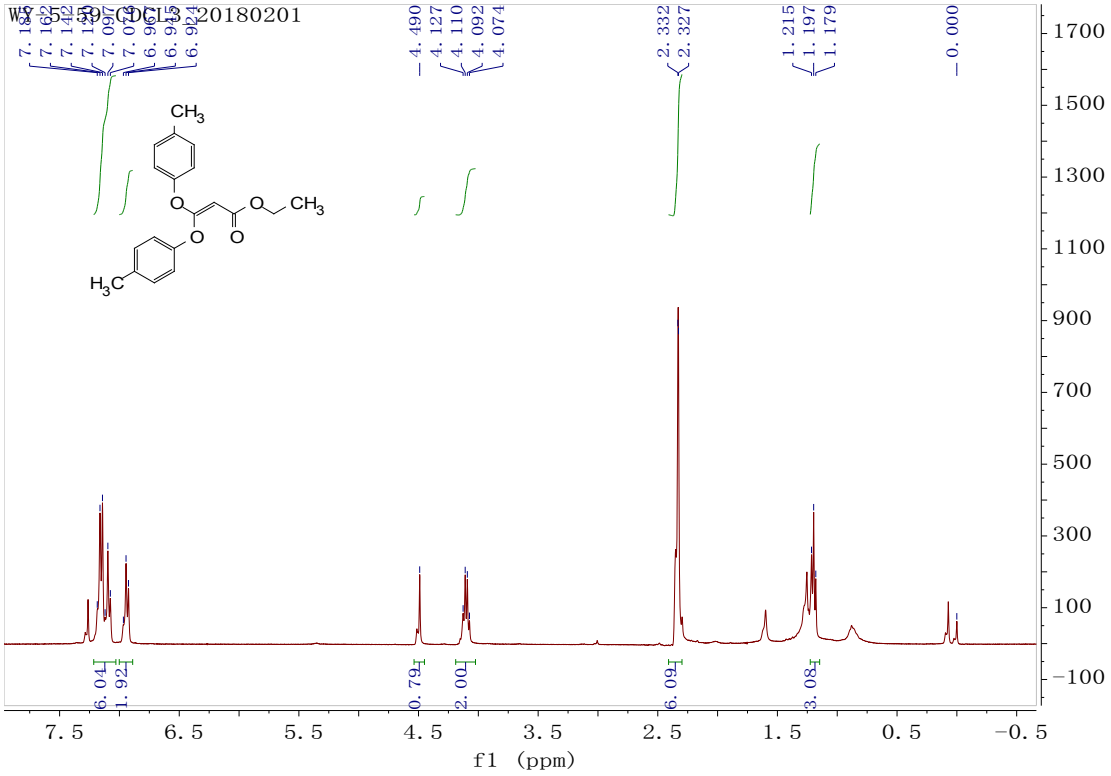

WY-6-27_C13-CDCl3_20171115/8
WY-6-27 C13-CDCl3 171116
f1 (ppm)

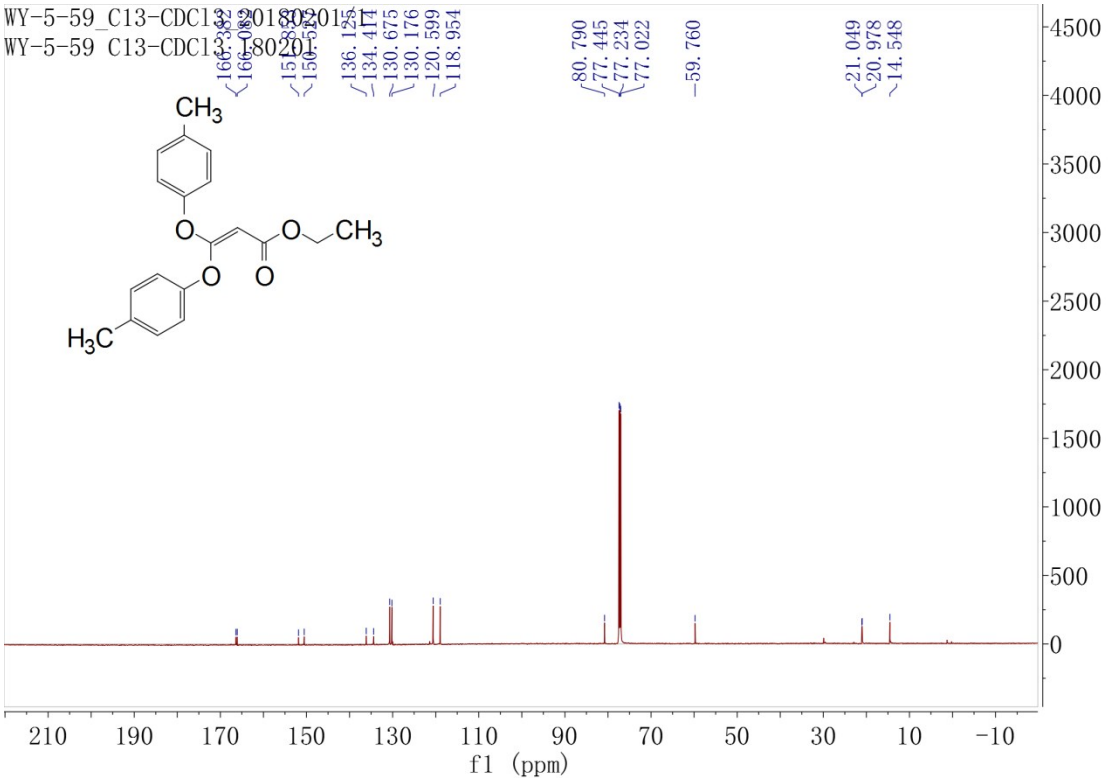


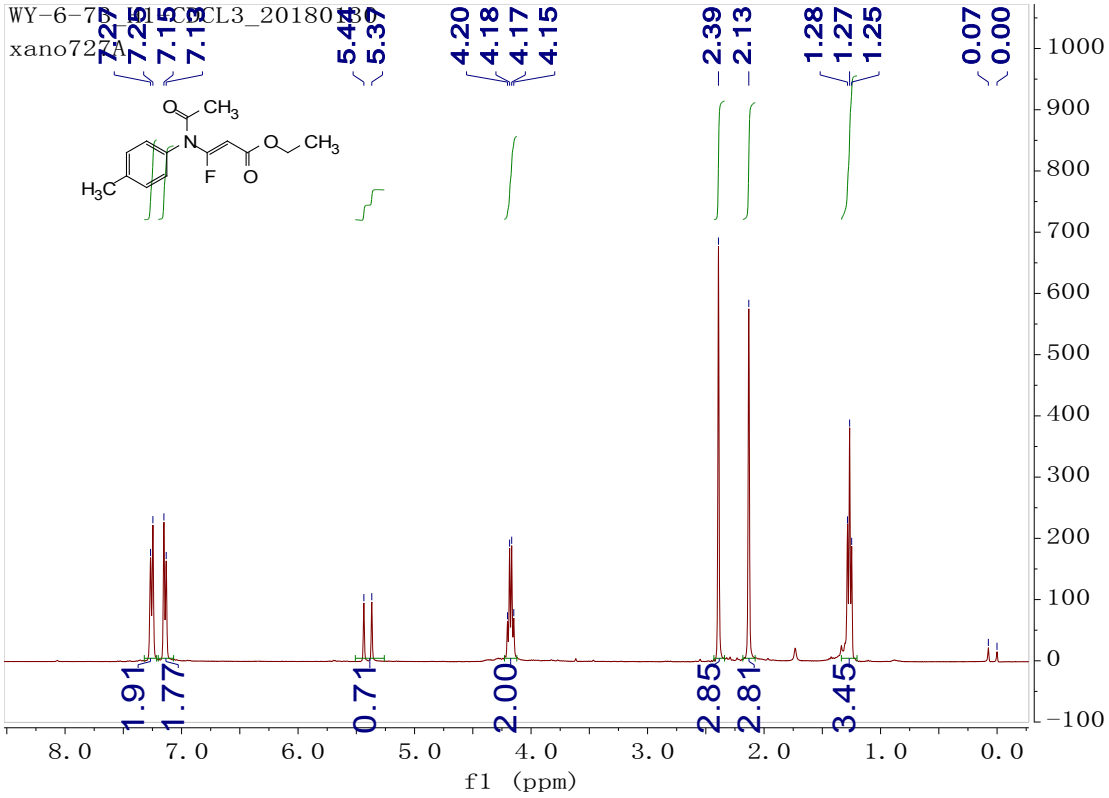
WY-6-57 H1-CDCl3 20180105
7.578
7.559
7.389
7.380
7.301
7.282
7.261
7.257
7.253
7.213
7.194
7.070
7.050
5.301
2.394
2.379
2.281
0.003
-0.001
-0.004
H3C
S
S
NH
O
CH3
H3C
1.97
1.88
6.42
2.42
1.00
6.14
3.05
f1 (ppm)

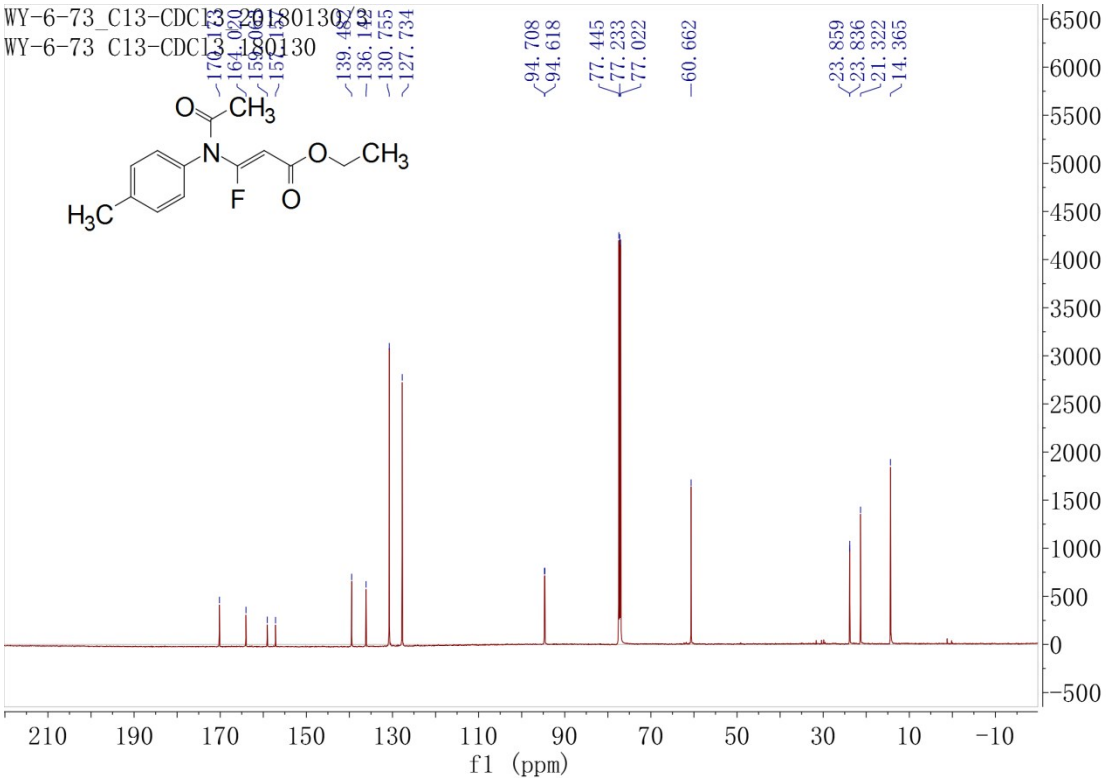


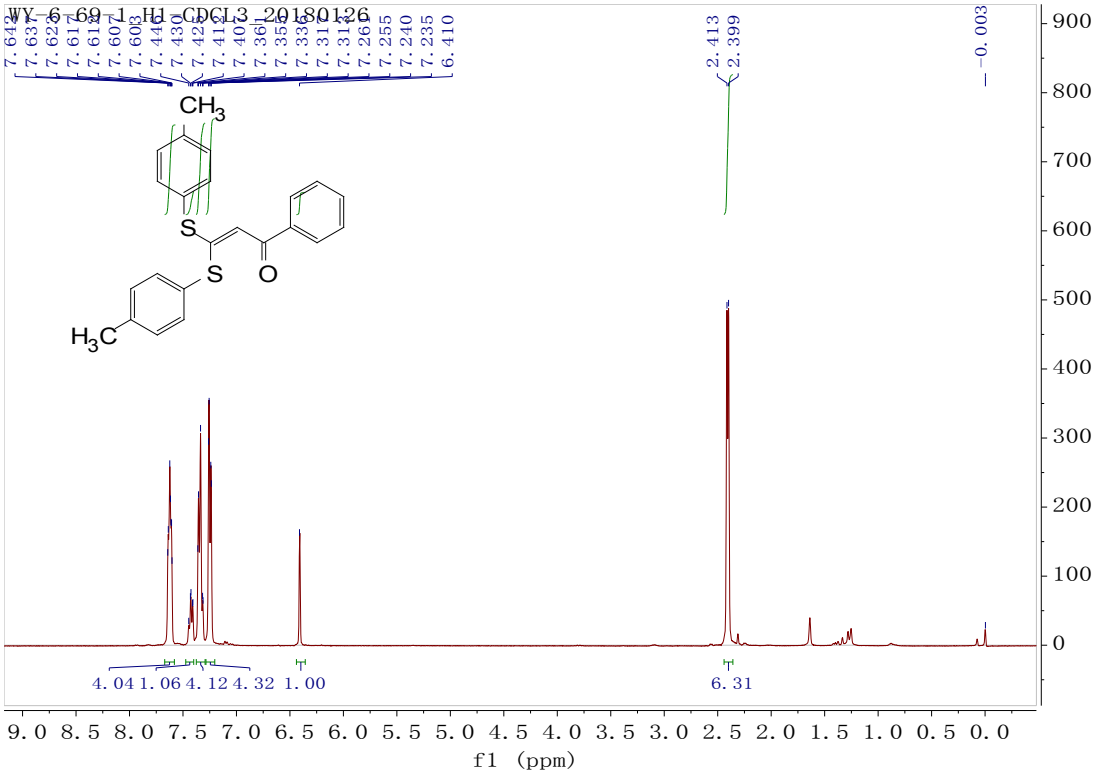
WY-6-57_C13-CDCl3_20180105
WY-6-57 C13-CDCl3 180105
163.170
135.838
135.550
133.550
130.816
129.798
129.545
127.487
126.627
119.705
112.365
77.445
77.234
77.022
21.632
21.586
21.048
H3C
S
S
NH
O
CH3
H3C
f1 (ppm)

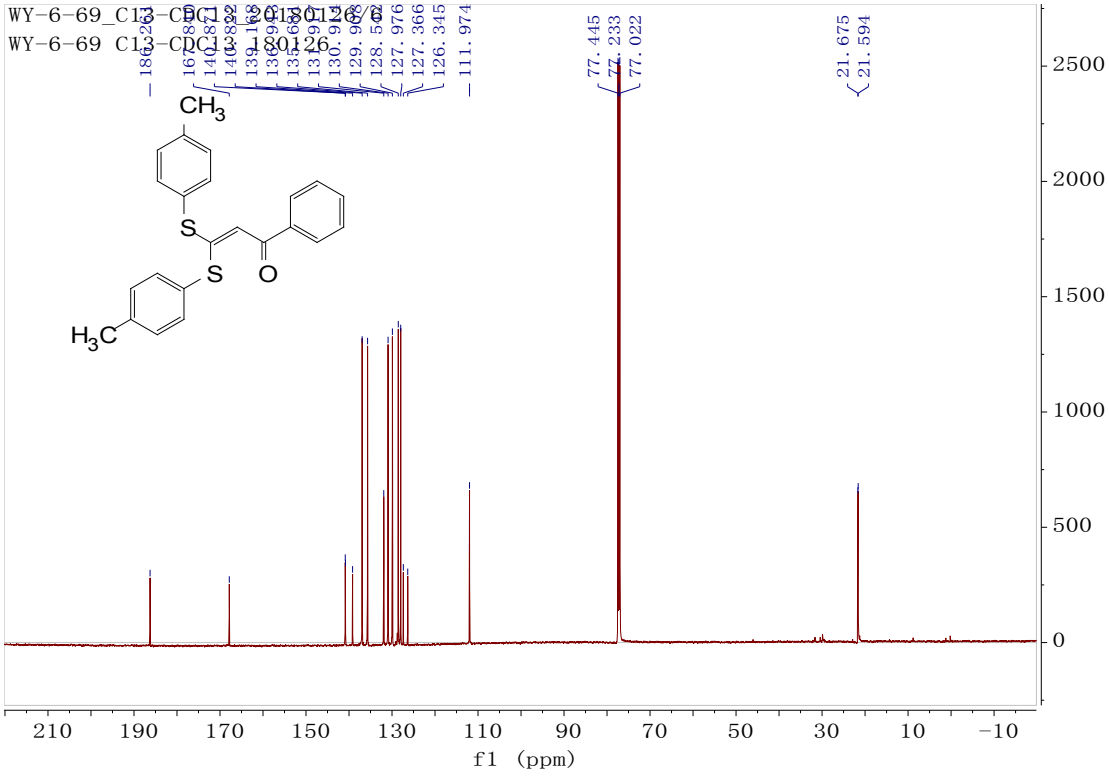

7.162
7.152
7.142
7.139
7.097
7.078
6.961
6.945
6.924
4.490
4.127
4.110
4.092
4.074
2.332
2.327
1.215
1.197
1.179
0.000
6.04
1.92
0.79
2.00
6.09
3.08
f1 (ppm)

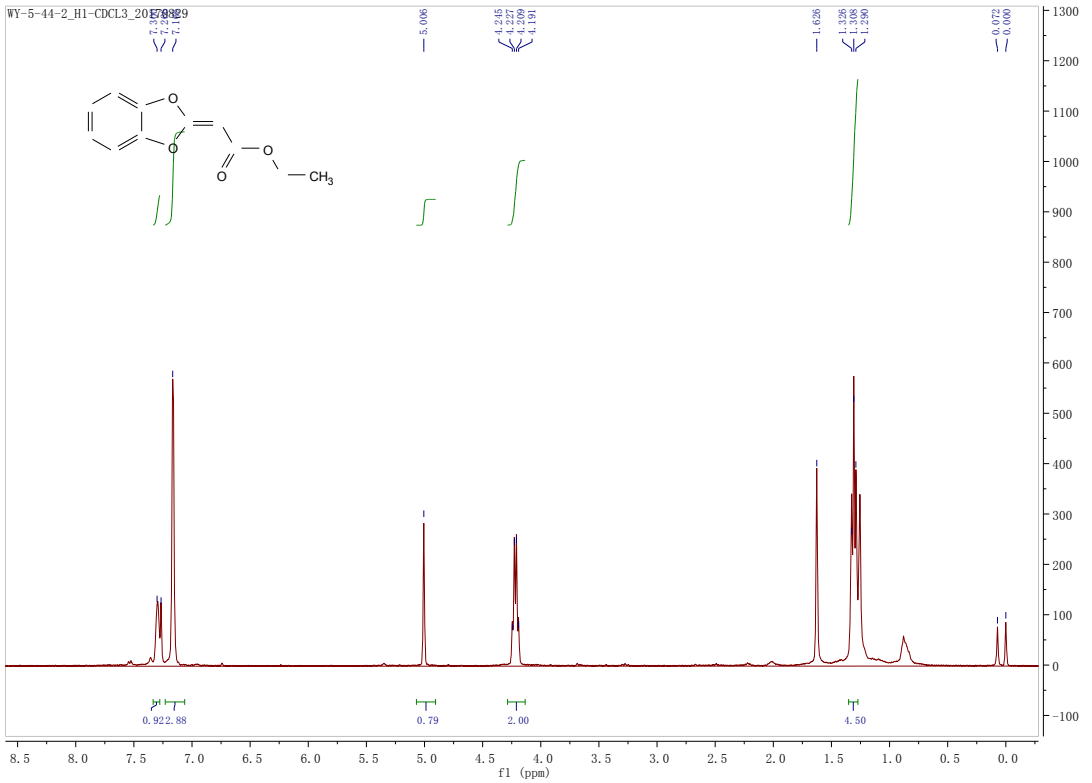

166.382
166.082
153.882
150.532
136.125
134.414
130.675
130.176
120.599
118.954
80.790
77.445
77.234
77.022
59.760
21.049
20.978
14.548
f1 (ppm)

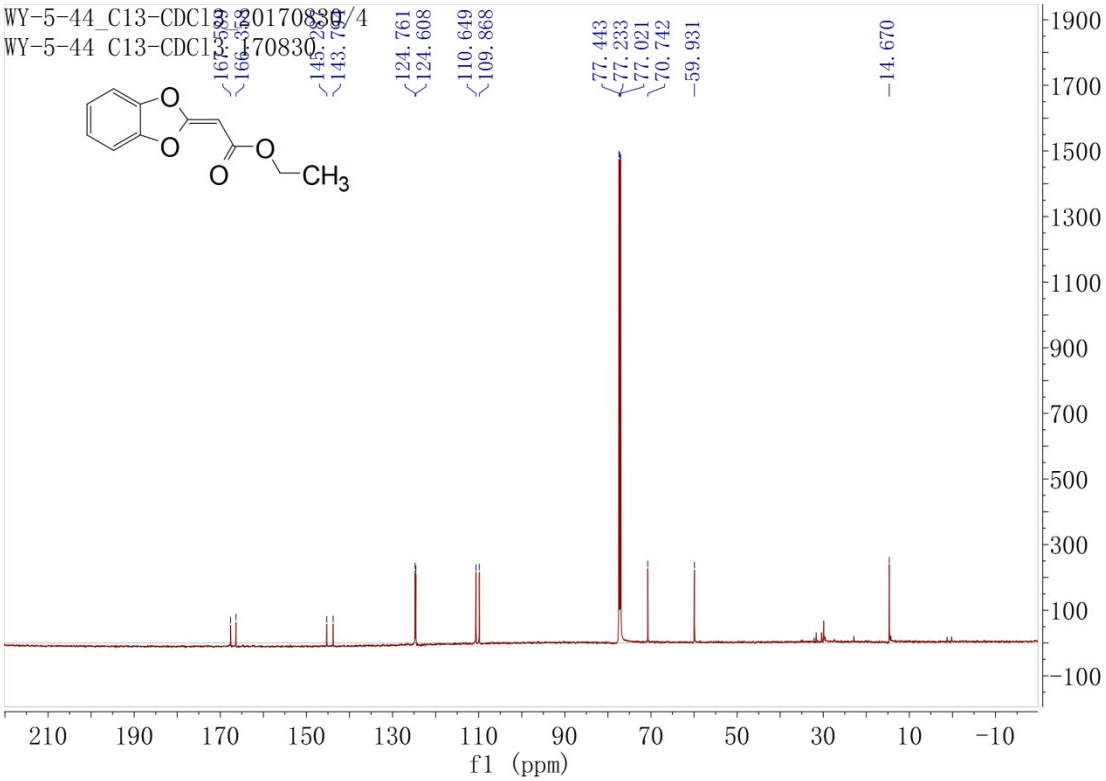

7.27
7.25
7.15
7.13
5.44
5.37
4.20
4.18
4.17
4.15
2.39
2.13
1.28
1.27
1.25
0.07
0.00
1.91
1.77
0.71
2.00
2.85
2.81
3.45
f1 (ppm)

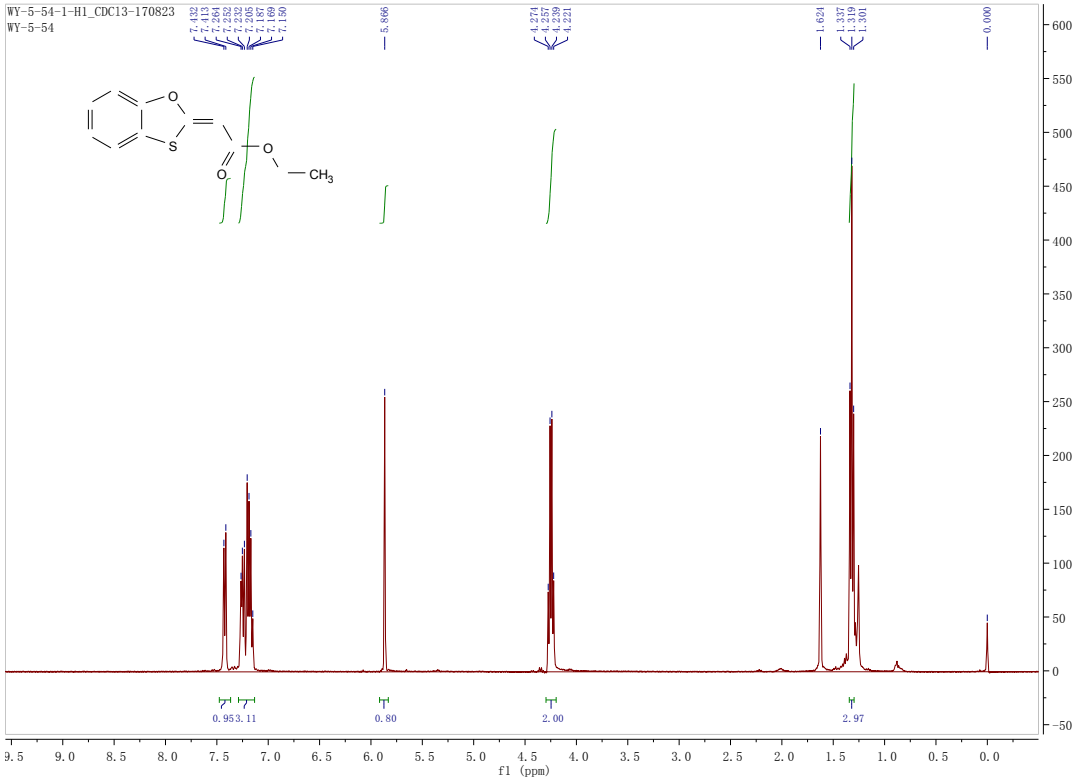

94.708
94.618
77.445
77.233
77.022
60.662
23.859
23.836
21.322
14.365
f1 (ppm)

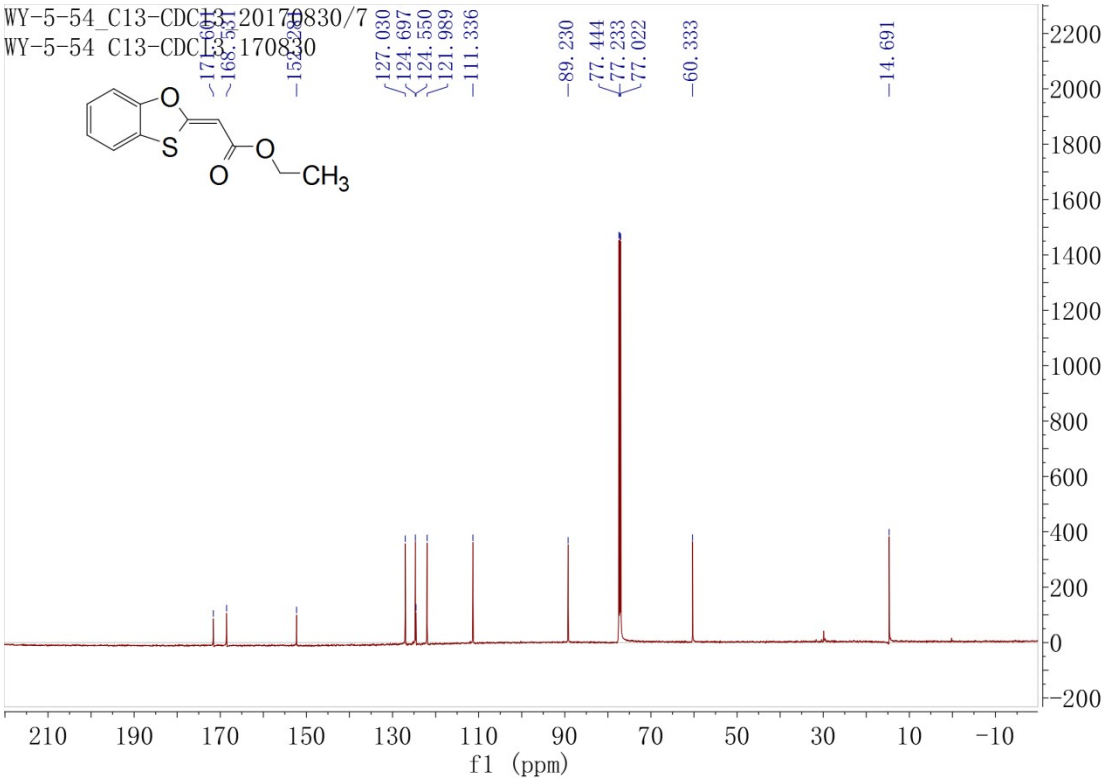

WY-6-69-1-H1-CDCL3-20180126
7.641 7.637 7.627 7.617 7.618 7.607 7.603 7.445 7.430 7.424 7.415 7.401 7.361 7.355 7.336 7.317 7.314 7.261 7.255 7.240 7.235 6.410
2.413 2.399
-0.003
CH3
S
S
O
H3C
4.04 1.06 4.12 4.32 1.00
6.31
900 800 700 600 500 400 300 200 100 0
9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

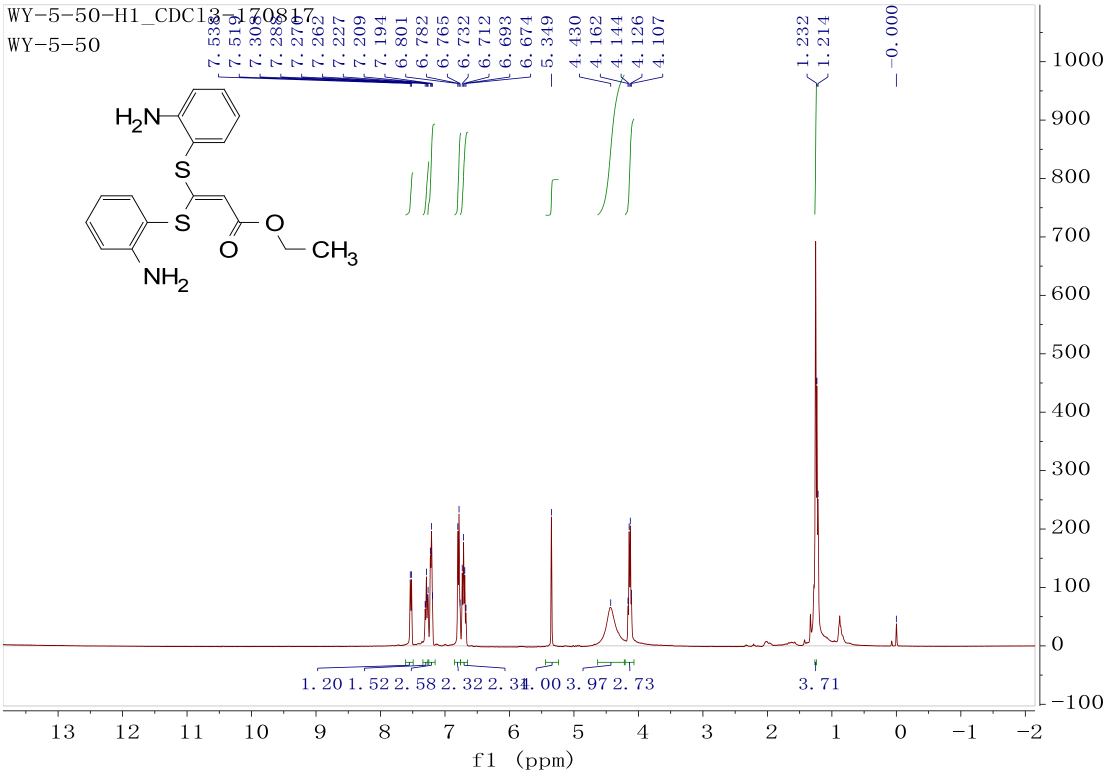

WY-6-69_C13-CDCL3-20180126-6
WY-6-69 C13-CDCl3-180126
186.203 167.787 140.882 140.882 139.168 136.966 135.666 131.941 130.918 129.968 128.582 127.976 127.366 126.345 111.974
77.445 77.233 77.022
21.675 21.594
CH3
S
S
O
H3C
2500 2000 1500 1000 500 0
210 190 170 150 130 110 90 70 50 30 10 -10
f1 (ppm)

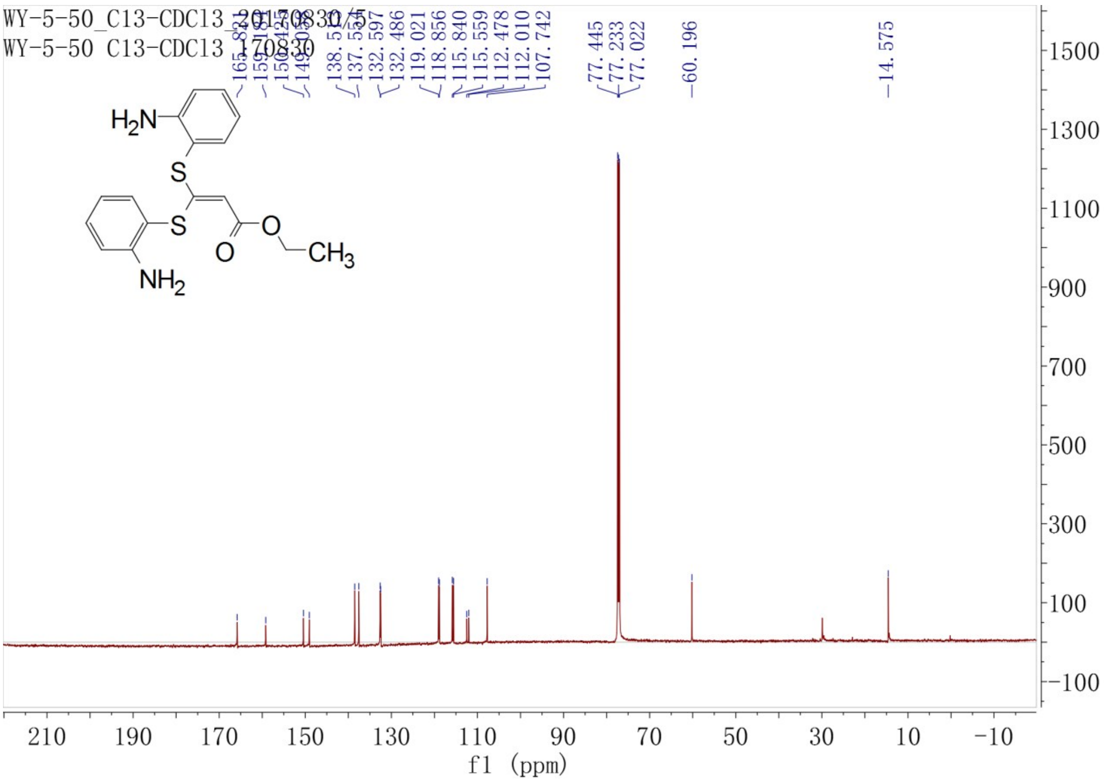

WY-5-44-2_H1-CDCL3_20170829
7.295
7.284
7.142
5.006
4.245
4.227
4.209
4.191
1.626
1.326
1.308
1.290
0.072
0.000
O
O
O
O
CH3
0.92
2.88
0.79
2.00
4.50
f1 (ppm)

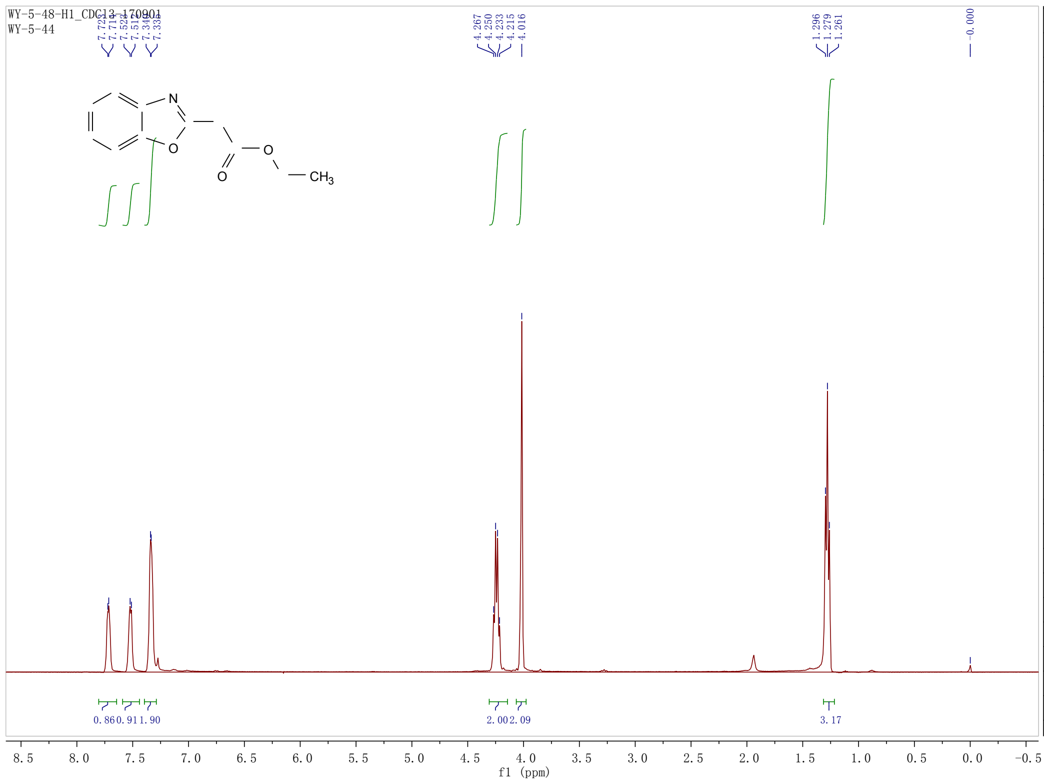

WY-5-44_C13-CDCl3_20170830/4
167.588
166.358
145.288
143.794
124.761
124.608
110.649
109.868
77.443
77.233
77.021
70.742
59.931
14.670
O
O
O
O
CH3
f1 (ppm)

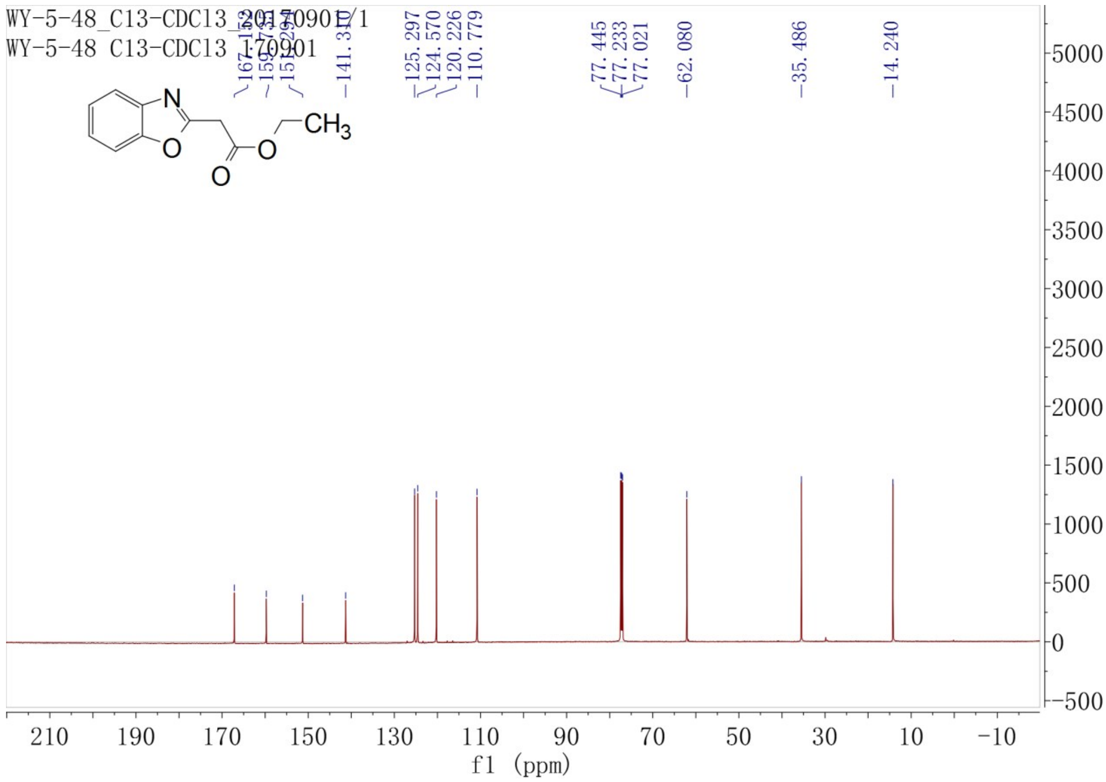

WY-5-54-1-H1_CDC13-170823
WY-5-54
7.432
7.413
7.264
7.252
7.232
7.206
7.187
7.169
7.150
5.866
4.271
4.257
4.239
4.221
1.624
1.337
1.319
1.301
0.000
O
S
O
O
CH3
0.95
3.11
0.80
2.00
2.97
f1 (ppm)

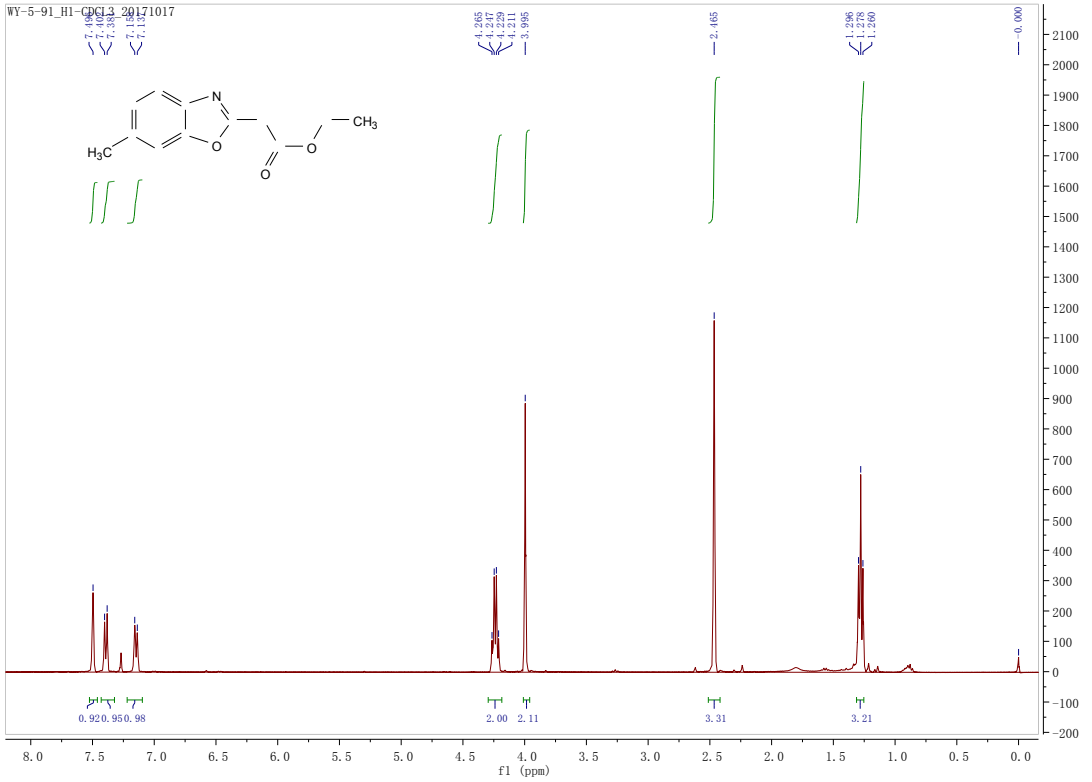

WY-5-54_C13-CDCl3_20170830/7
WY-5-54 C13-CDCl3.170830
171.601
168.351
154.328
127.030
124.697
124.550
121.989
111.336
89.230
77.444
77.233
77.022
60.333
14.691
O
S
O
O
CH3
f1 (ppm)

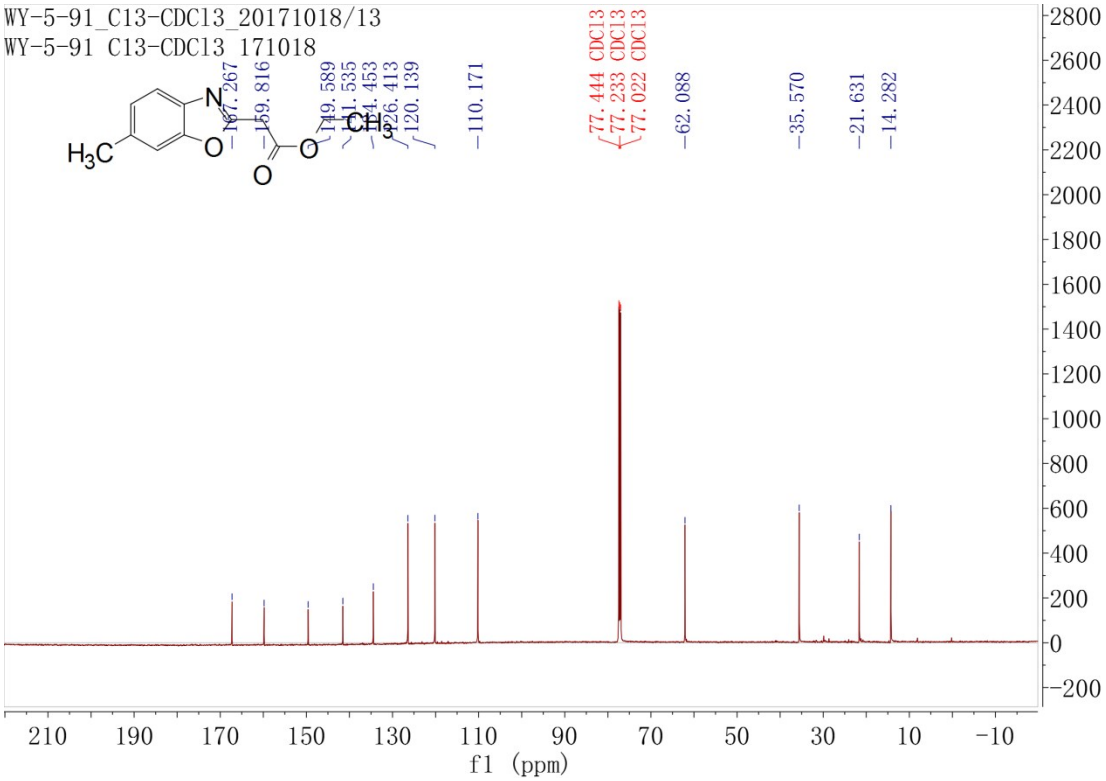

WY-5-50-H1_CDCl3-170817
WY-5-50
7.538
7.519
7.306
7.288
7.276
7.262
7.227
7.209
7.194
6.801
6.782
6.765
6.732
6.712
6.693
6.674
5.349
4.430
4.162
4.144
4.126
4.107
1.232
1.214
-0.000
H2N
S
S
O
O
CH3
NH2
1.20
1.52
2.58
2.32
2.34
1.00
3.97
2.73
3.71
f1 (ppm)

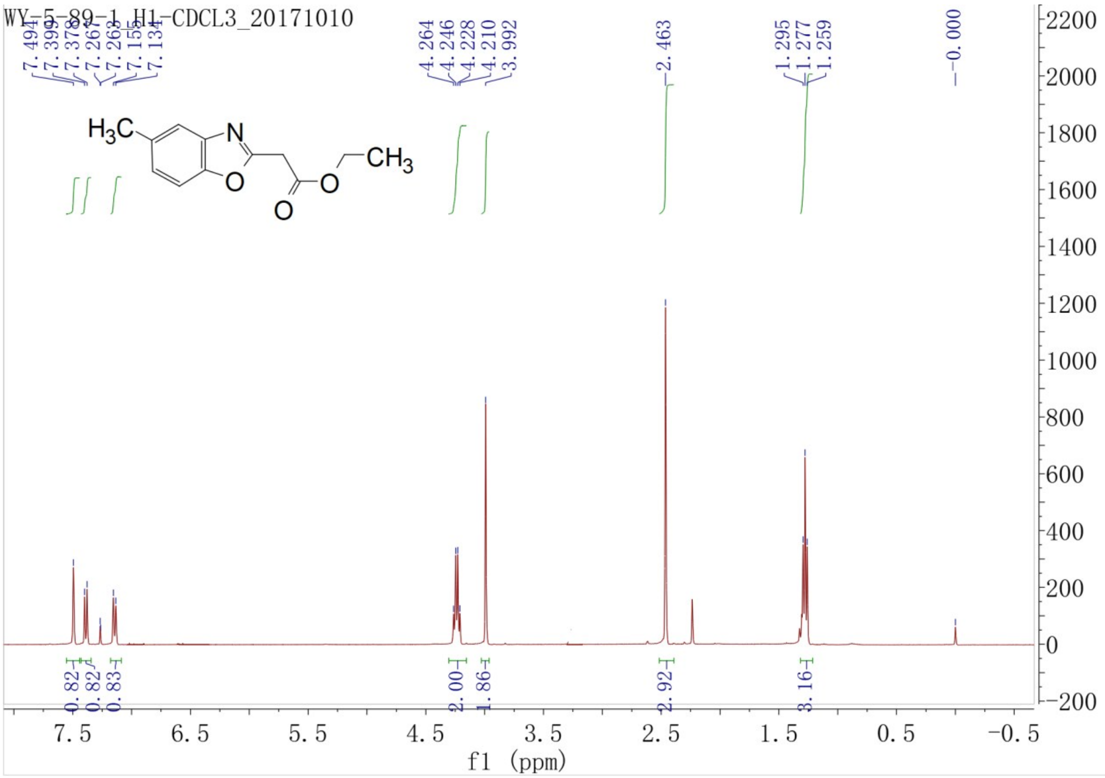

WY-5-50_C13-CDCl3_20170830/5
WY-5-50 C13-CDCl3 170830
138.55
137.53
132.597
132.486
119.021
118.856
115.840
115.559
112.478
112.010
107.742
77.445
77.233
77.022
60.196
14.575
H2N
S
S
O
O
CH3
NH2
f1 (ppm)

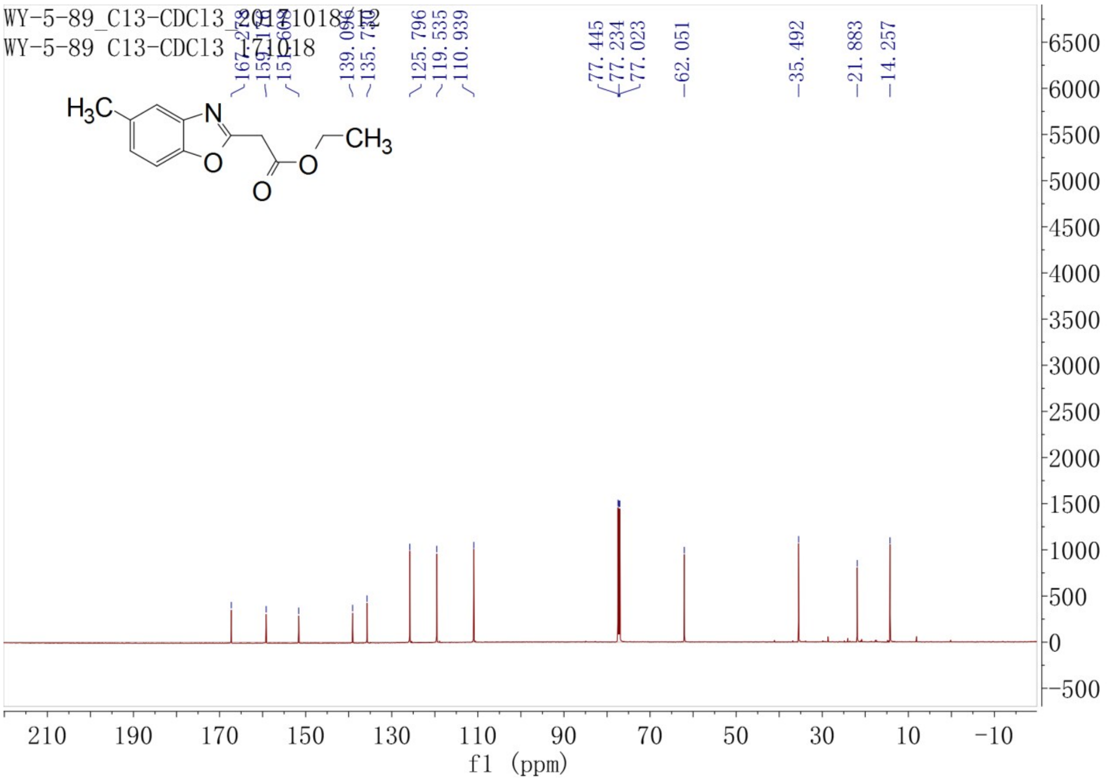


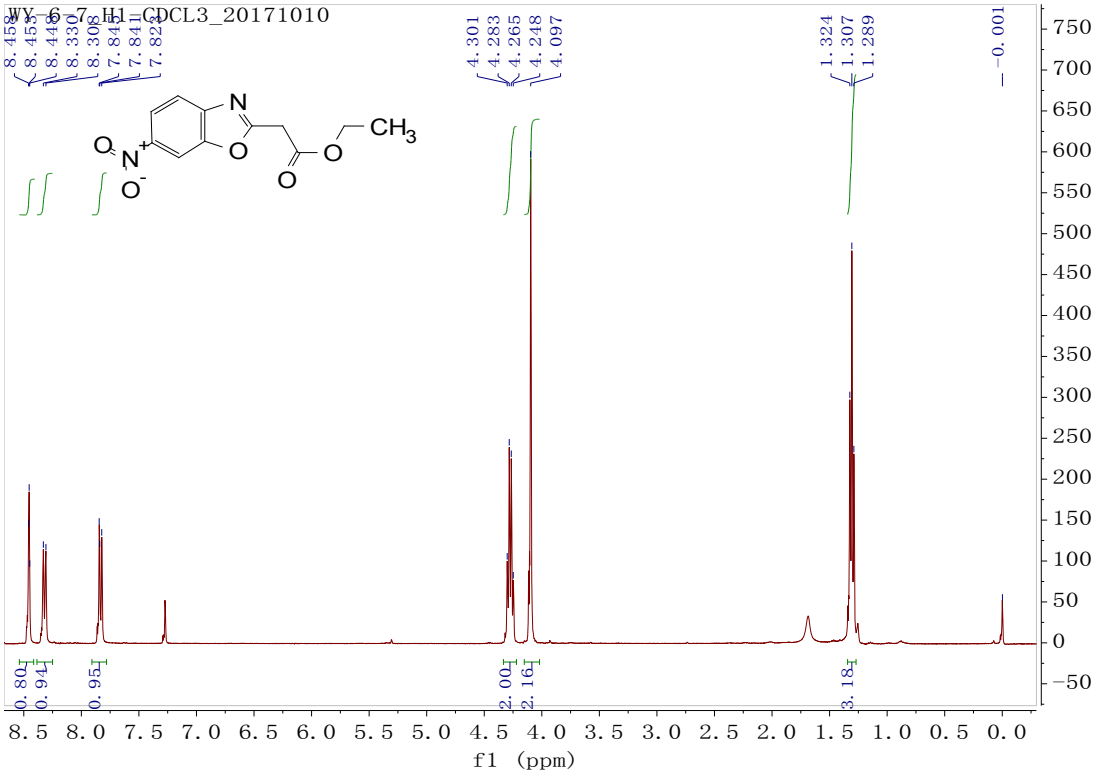


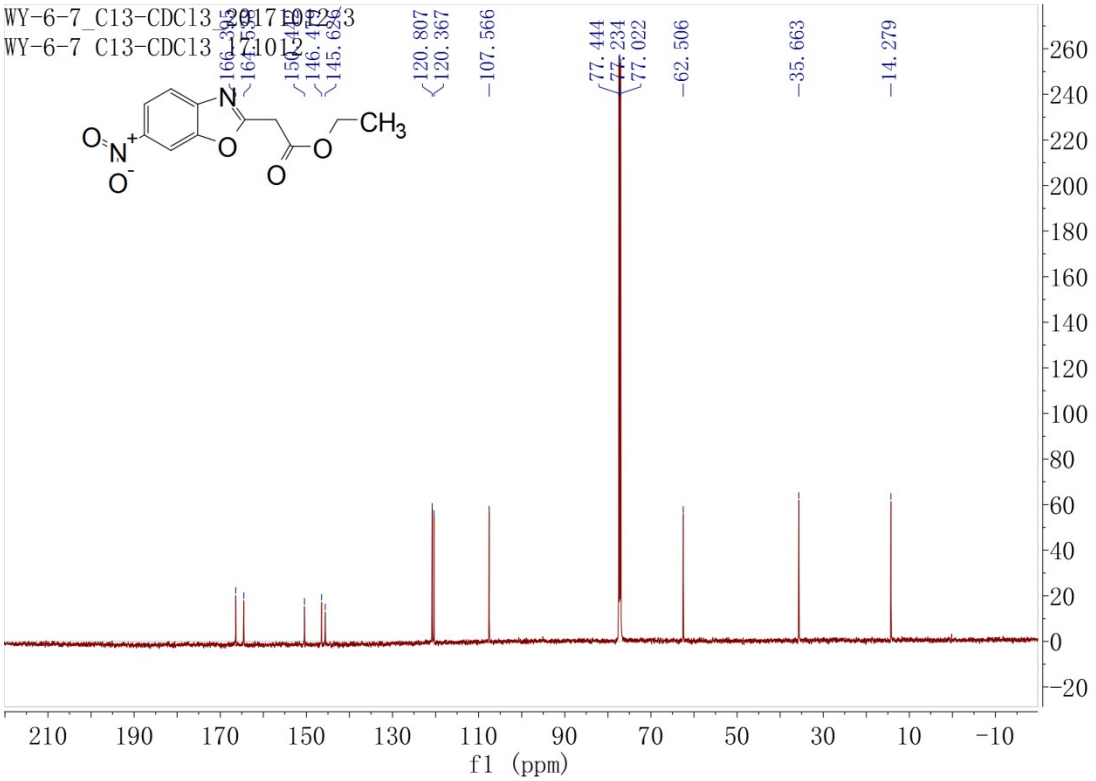

WY-5-91_H1-CDCl3_20171017
f1 (ppm)

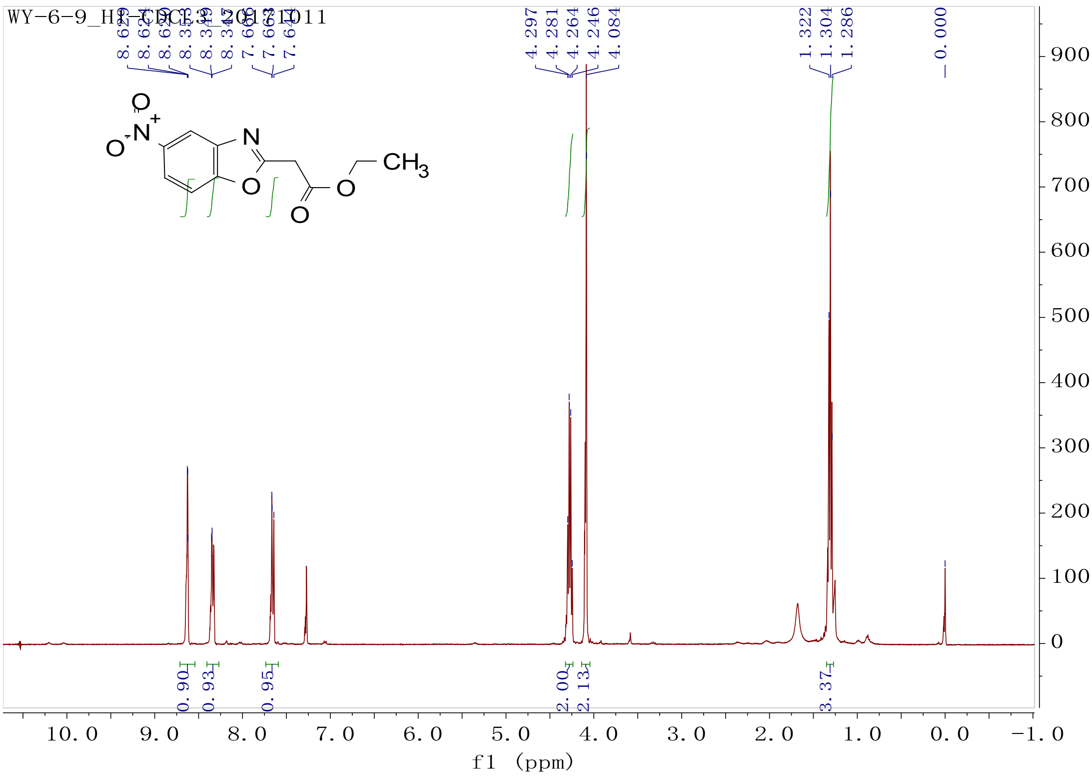

WY-5-91_C13-CDCl3_20171018/13
WY-5-91 C13-CDCl3 171018
f1 (ppm)

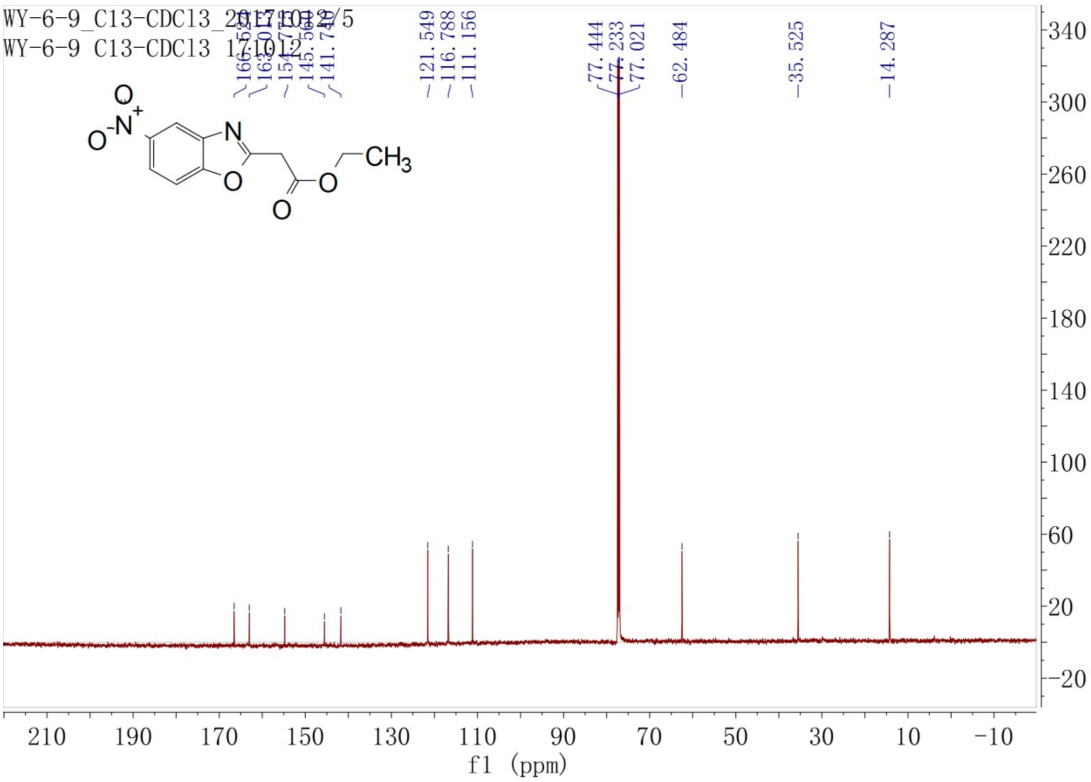

WY-5-89-1 H1-CDCL3_20171010
7.494
7.399
7.378
7.267
7.262
7.155
7.134
4.264
4.246
4.228
4.210
3.992
2.463
1.295
1.277
1.259
-0.000
0.82
0.82
0.83
2.00
1.86
2.92
3.16
f1 (ppm)

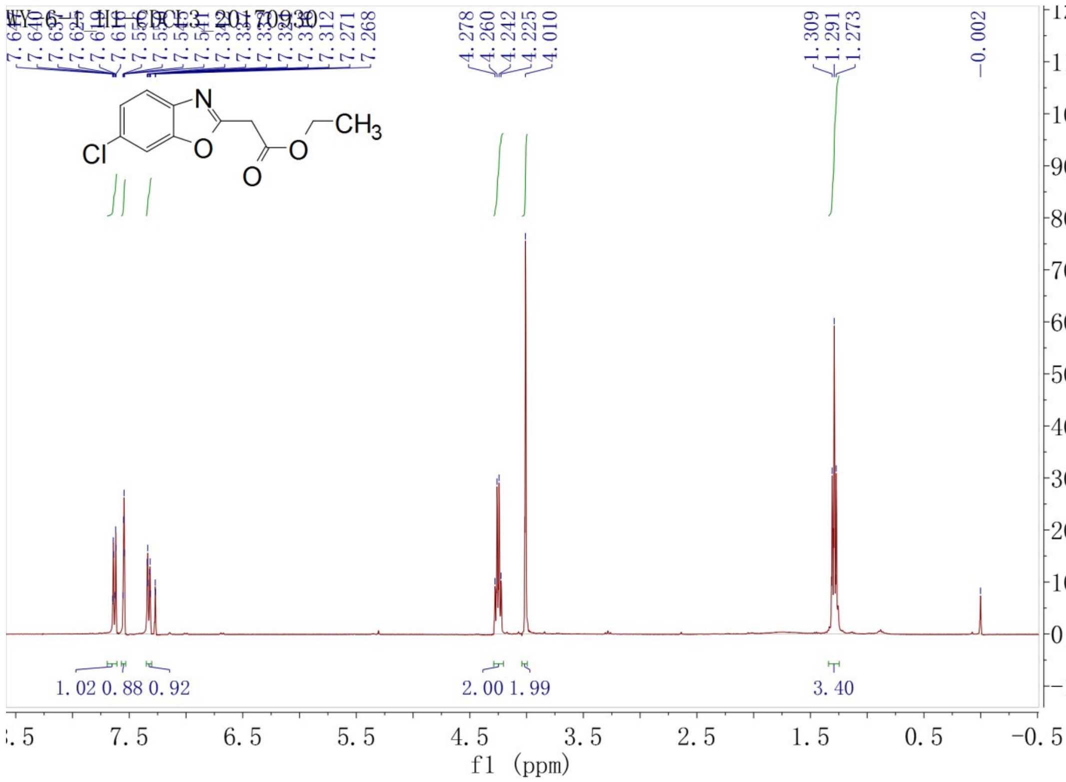

WY-5-89_C13-CDC13_20171018
WY-5-89 C13-CDC13 171018
167.278
159.175
151.609
139.096
135.742
125.796
119.535
110.939
77.445
77.234
77.023
62.051
35.492
21.883
14.257
f1 (ppm)

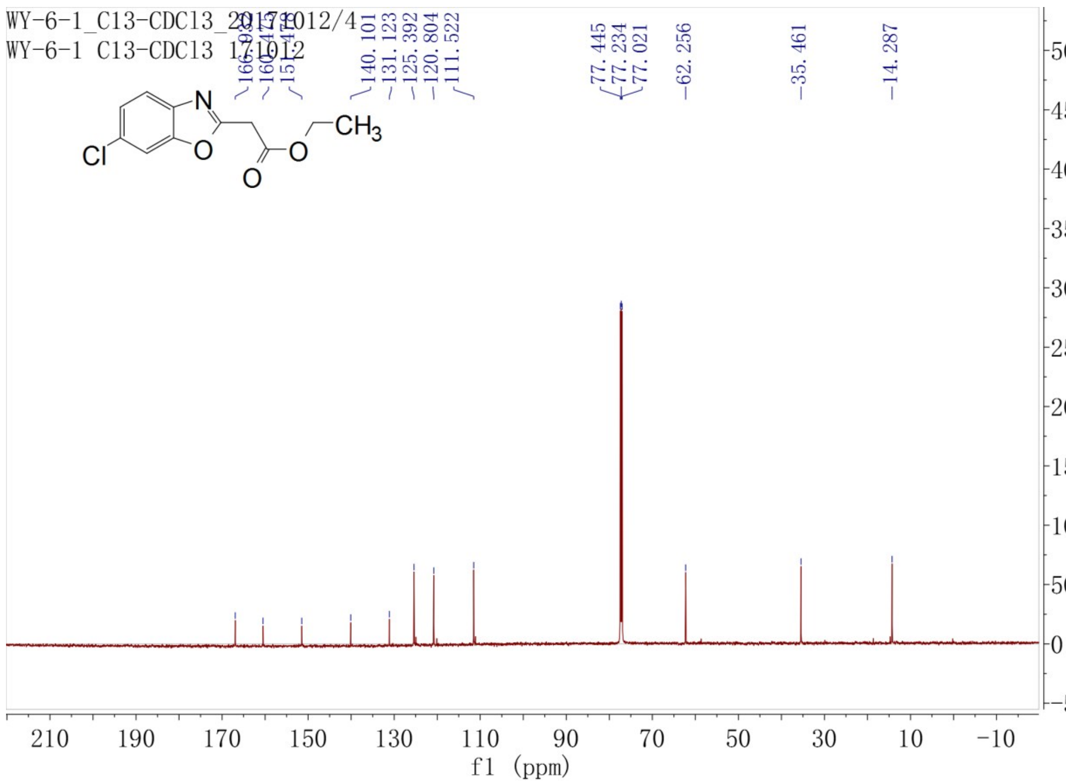

WY-6-7_H1-CDCL3_20171010
8.459
8.453
8.446
8.330
8.308
7.842
7.841
7.824
4.301
4.283
4.265
4.248
4.097
1.324
1.307
1.289
-0.001
0.80
0.94
0.95
2.00
2.16
3.18
f1 (ppm)

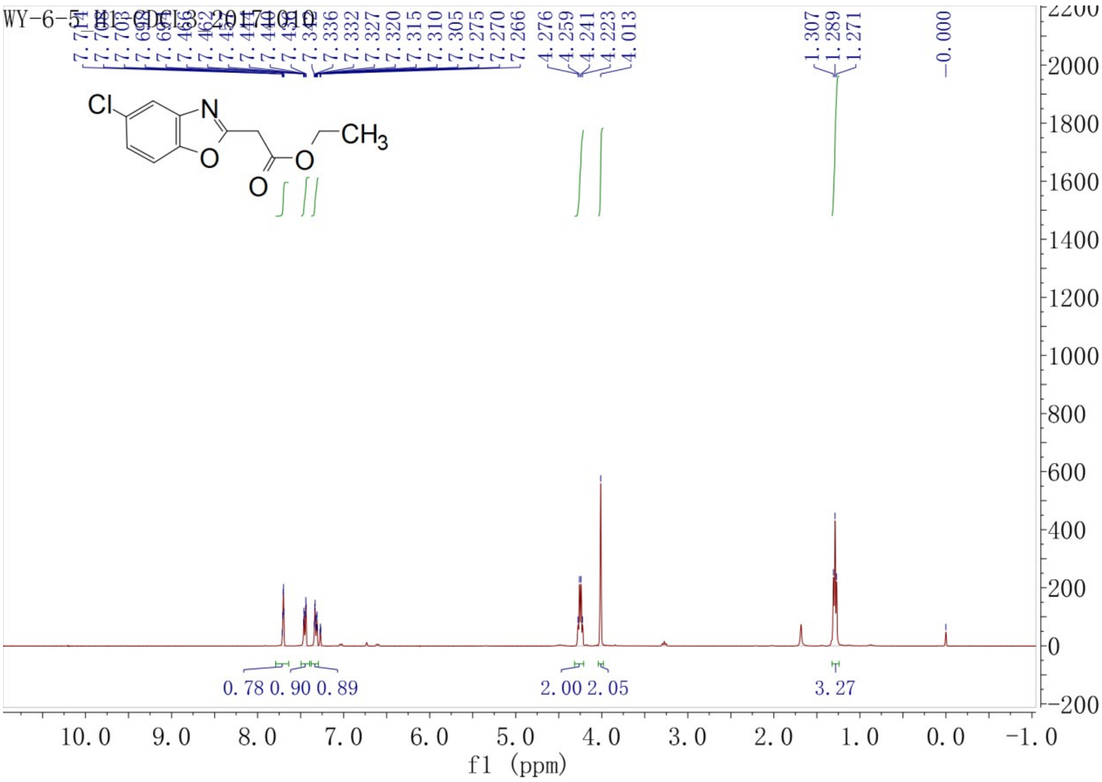

WY-6-7_C13-CDCl3_20171012
WY-6-7 C13-CDCl3
166.395
164.558
150.445
146.472
145.628
120.807
120.367
107.566
77.444
77.234
77.022
62.506
35.663
14.279
f1 (ppm)

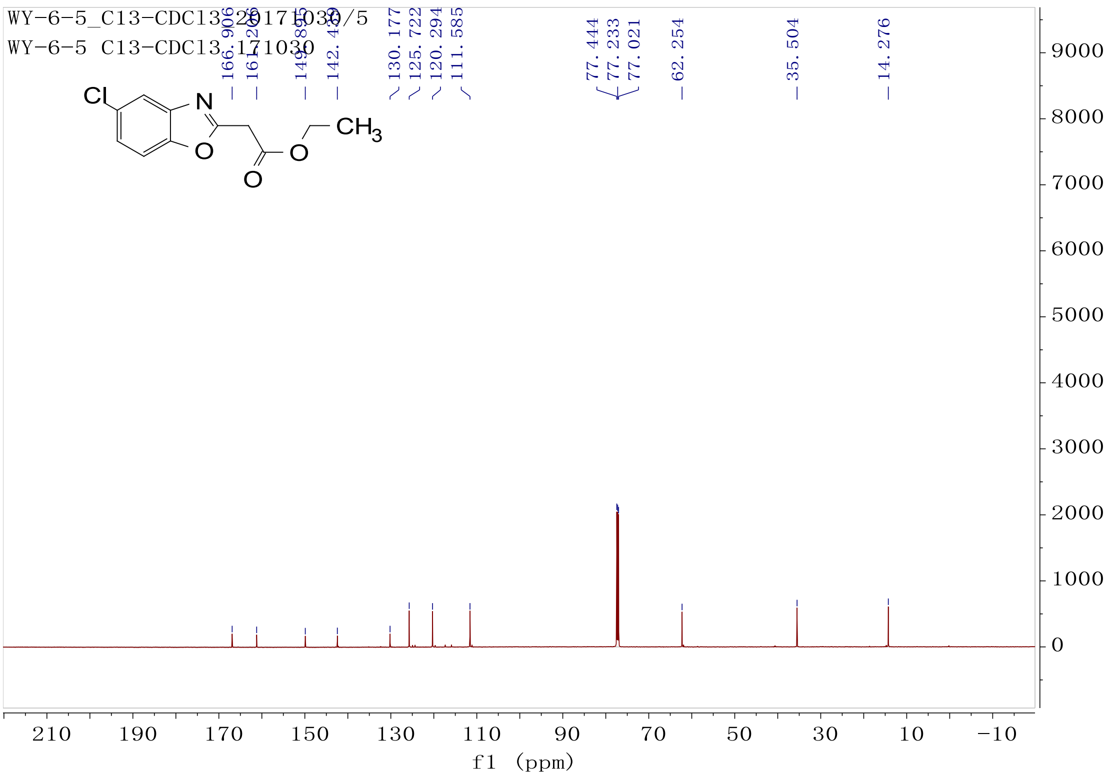

WY-6-9_H1-CDCl3_20171011
4.297
4.281
4.264
4.246
4.084
1.322
1.304
1.286
0.000
0.90
0.93
0.95
2.00
2.13
3.37
f1 (ppm)

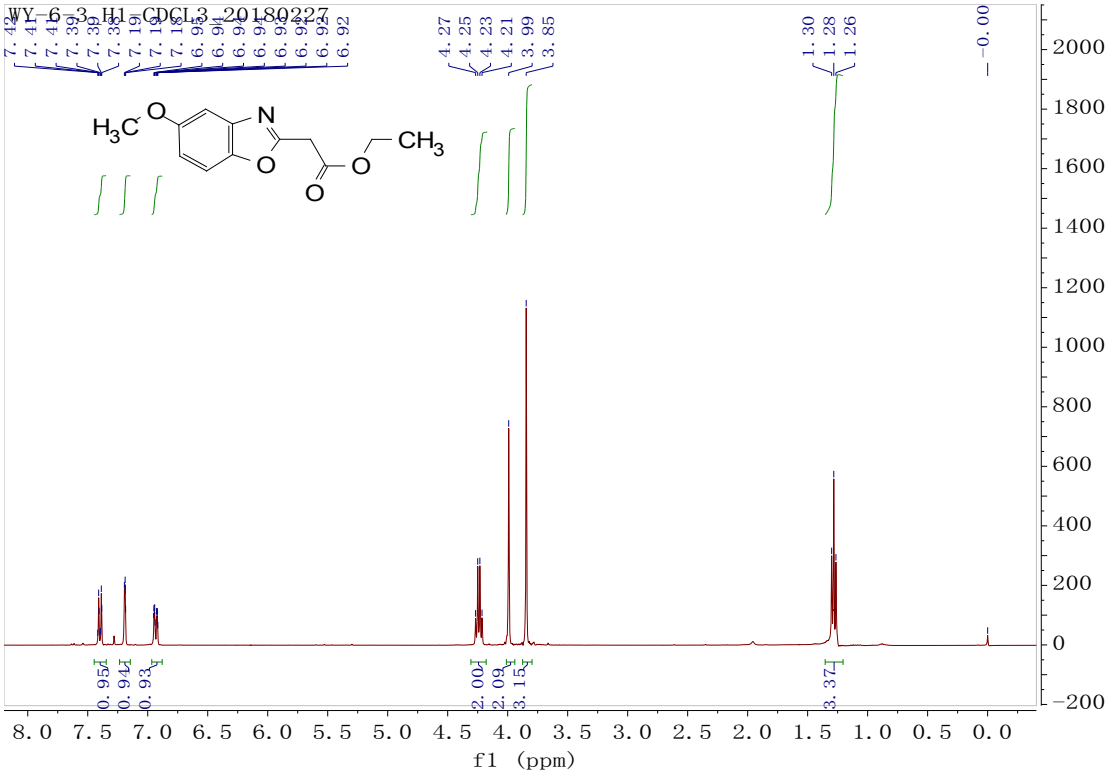

WY-6-9_C13-CDCl3 171012
121.549
116.788
111.156
77.444
77.021
62.484
35.525
14.287
f1 (ppm)

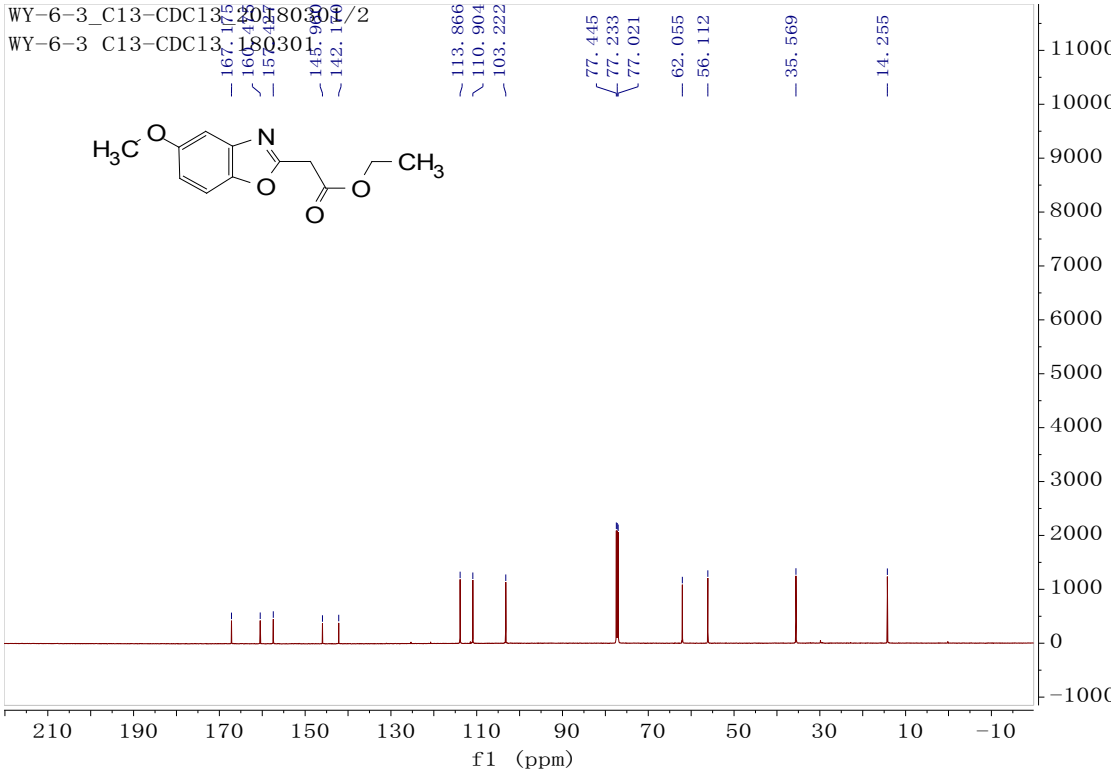

WY-6-1 H1-CDCl3-20170930
7.640
7.612
7.556
7.312
7.271
7.268
4.278
4.260
4.242
4.225
4.010
1.309
1.291
1.273
-0.002
N
O
Cl
O
O
CH3
1.02
0.88
0.92
2.00
1.99
3.40
f1 (ppm)

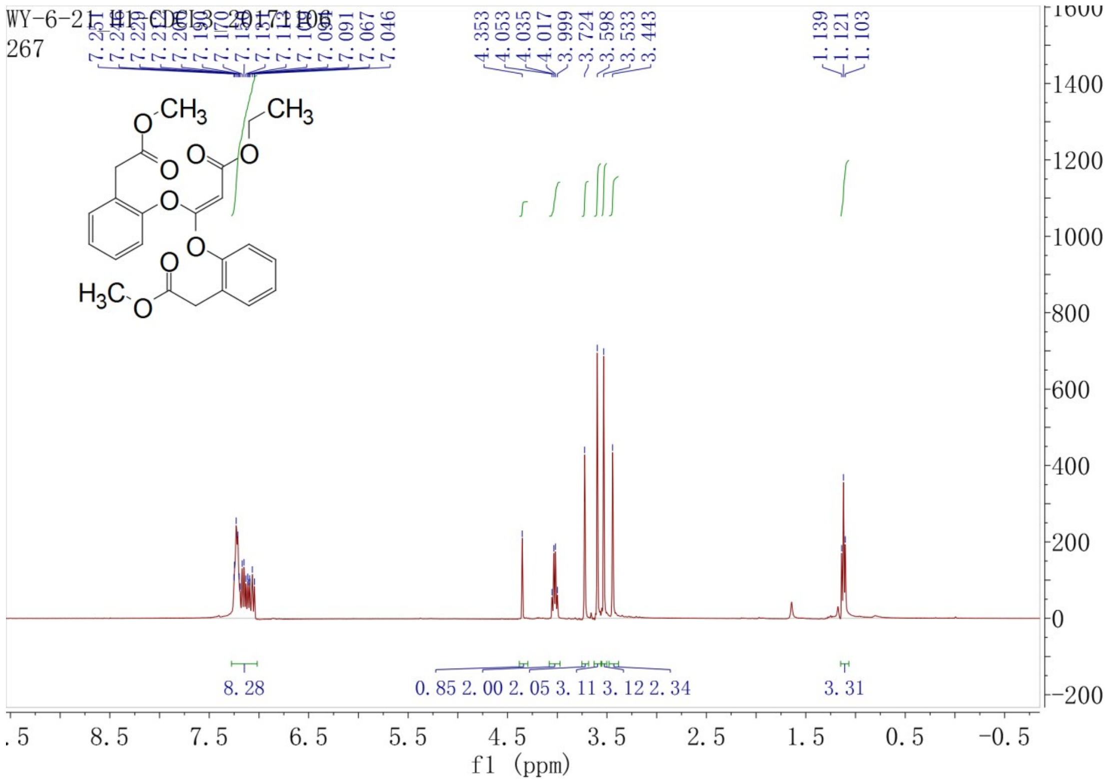

WY-6-1_C13-CDCl3_20171012/4
WY-6-1 C13-CDCl3 171012
140.101
131.123
125.392
120.804
111.522
77.445
77.234
77.021
62.256
35.461
14.287
N
O
Cl
O
O
CH3
f1 (ppm)

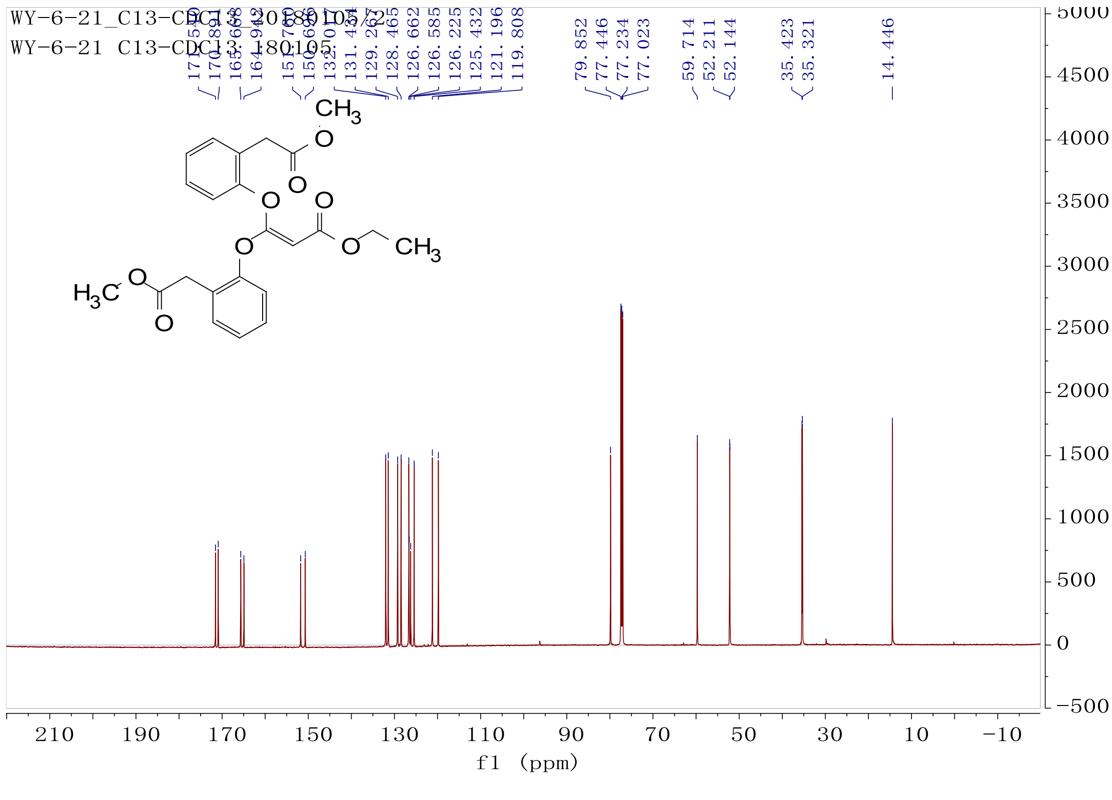

WY-6-5_H1-CDCl3_20171010
4.276
4.259
4.241
4.223
4.013
1.307
1.289
1.271
-0.000
0.78
0.90
0.89
2.00
2.05
3.27
f1 (ppm)

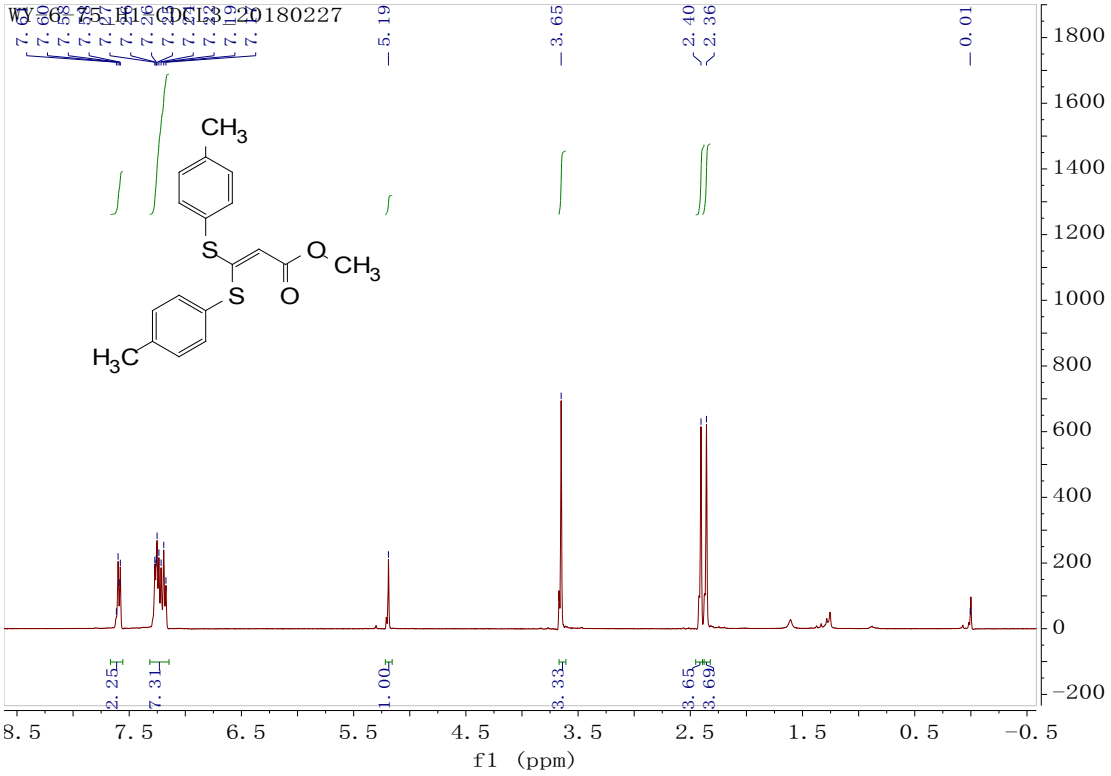

WY-6-5_C13-CDCl3_20171030/5
WY-6-5 C13-CDCl3 171030
130.177
125.722
120.294
111.585
77.444
77.233
77.021
62.254
35.504
14.276
f1 (ppm)

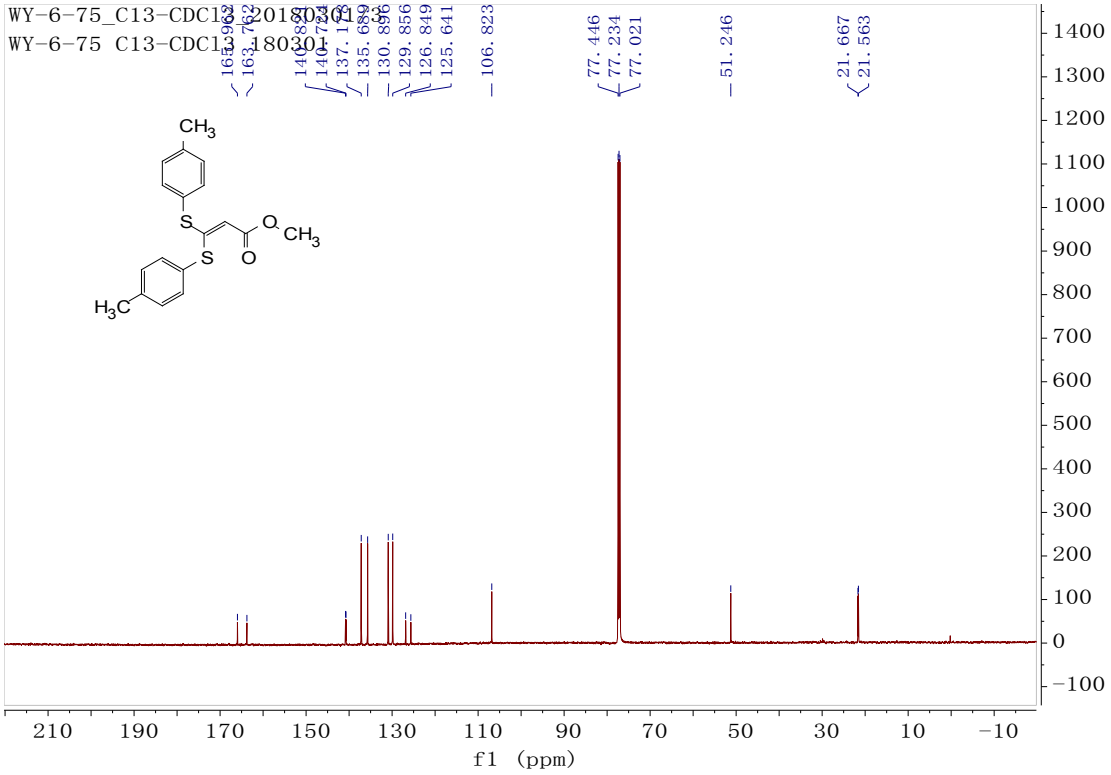

WY-6-3_H1-CDCL3_20180227
f1 (ppm)


WY-6-3_C13-CDC13_20180301/2
WY-6-3 C13-CDC13_180301
f1 (ppm)






WY-6-75 H1-CDCl3-20180227
7.69
7.68
7.55
7.54
7.27
7.26
7.24
7.19
7.17
5.19
3.65
2.40
2.36
0.01
CH3
S
O
CH3
S
O
H3C
2.25
7.31
1.00
3.33
3.65
3.69
f1 (ppm)


WY-6-75_C13-CDCl3_20180301
WY-6-75 C13-CDCl3_180301
165.962
163.762
140.824
140.774
137.119
135.689
130.896
129.856
126.849
125.641
106.823
77.446
77.234
77.021
51.246
21.667
21.563
CH3
S
O
CH3
S
O
H3C
f1 (ppm)