Electronic Supplementary Material (ESI) for ChemComm.

Copper-catalyzed [4 + 2] oxidative annulation of *α,β*-unsaturated ketoxime acetates with ethyl trifluoropyruvate

Huan Yan, Gaochen Xu, Meng Gu, Qinghuan Wu, Sai Zhang, Jingjing Meng, Ning Zhu, Zheng Fang,* Jindian Duan,* and Kai Guo*

College of Biotechnology and Pharmaceutical Engineering, State Key Laboratory of Materials-Oriented Chemical Engineering, Nanjing Tech University, Nanjing 211816, China.

*E-mail: fzcpu@163.com; duanjd@njtech.edu.cn; guok@njtech.edu.cn

Supporting Information

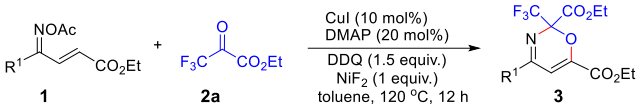
Contents

Experimental section

General

Unless otherwise noted, all experiments were performed under N_2 atmosphere. Commercial solvents and reagents were used without further purification. Thin-layer chromatography (TLC) was performed on silica gel plates (60F-254) using UV-light (254 nm). Flash chromatography was conducted on silica gel (200-300 mesh). NMR (400 MHz for ^{1}H NMR, 100 MHz for ^{13}C NMR) spectra were recorded in $CDCl_3$ with TMS as the internal standard. Chemical shifts are reported in ppm and coupling constants are given in Hz. Data for ^{1}H NMR are recorded as follows: chemical shift (ppm), multiplicity (s, singlet; d, doublet; t, triplet; q, quarter; m, multiplet), coupling constant (Hz), integration. Data for ^{13}C NMR are reported in terms of chemical shift (δ, ppm). High-resolution mass spectra (HRMS) were obtained on an Agilent mass spectrometer using ESI-TOF (electrospray ionization-time of flight). The *α,β*-unsaturated ketoxime acetates were all known compounds and synthesized according to previously reported literature procedures.[1] Ethyl trifluoropyruvate **2a** was purchased and used without additional purification.

General procedure for the synthesis of 3



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

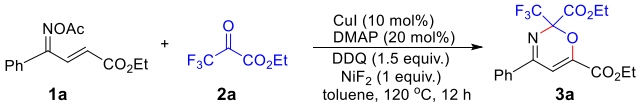
1 (0.3 mmol), **2a** (1.2 mmol), CuI (6 mg, 10 mol%), DDQ (102 mg, 0.45 mmol), DMAP (7 mg, 20 mol%) and NiF_2 (29 mg, 0.3 mmol) were loaded into a 25 mL Schlenk tube equipped with a Teflon-coated magnetic stir bar. The Schlenk tube was placed under vacuum for 1 min and then N_2 was pumped into it. The solvent toluene (3 mL, 0.1 M) was added into the Schlenk tube by syringe. The reaction mixture was stirred at 120 °C for 12 h. After completion of the reaction (detected by TLC), the reaction tube was allowed to cool to room temperature and the reaction solution was concentrated under vacuum. The crude products were purified by column chromatography on silica gel (Petroleum Ether/EtOAc) to give the products **3**.

General procedure for the synthesis of 4

1 **2a** **4**

1 (0.3 mmol), **2a** (1.2 mmol), CuI (6 mg, 10 mol%), DDQ (102 mg, 0.45 mmol), DMAP (7 mg, 20 mol%) and NiF_2 (29 mg, 0.3 mmol) were loaded into a 25 mL Schlenk tube equipped with a Teflon-coated magnetic stir bar. The Schlenk tube was placed under vacuum for 1 min and then N_2 was pumped into it. The solvent toluene (3 mL, 0.1 M) was added into the Schlenk tube by syringe. The reaction mixture was stirred at 120 ℃ (oil bath) for 12 h. After completion of the reaction (detected by TLC), the reaction tube was allowed to cool to room temperature and the reaction solution was concentrated under vacuum. The crude products were purified by column chromatography on silica gel (Petroleum Ether/EtOAc) to give the products **4**.

Scale-up synthesis of compound 3a

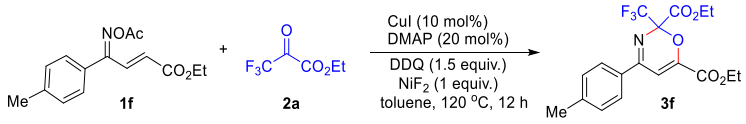


1a **2a** **3a**

1a (1.355 g, 5 mmol), ethyl trifluoropyruvate **2a** (3.402 g, 20 mmol), CuI (0.952 g, 10 mol%), DDQ (1.703 g, 7.5 mmol), DMAP (0.112 g, 20 mol%) and NiF_2 (0.484 g, 5 mmol) were loaded into

a Schlenk tube equipped with a Teflon-coated magnetic stir bar. The Schlenk tube was placed under vacuum for 1 min and then N_2 was pumped into it. The solvent toluene (15 mL) was added into the Schlenk tube by syringe. The reaction mixture was stirred at 120 ℃ (oil bath) for 12 h. Then the reaction tube was allowed to cool to room temperature and the reaction solution was concentrated under reduced pressure. The crude products were purified by column chromatography on silica gel (Petroleum Ether/EtOAc= 10:1) to give the product **3a** 1.207 g (65% yield).

Scale-up synthesis of compound 3f

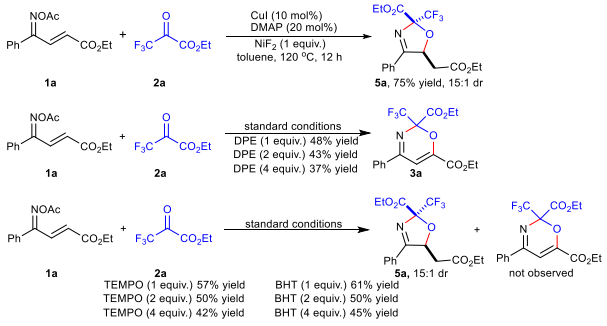


1f (1.376 g, 5 mmol), ethyl trifluoropyruvate **2a** (3.402 g, 20 mmol), CuI (0.952 g, 10 mol%), DDQ (1.703 g, 7.5 mmol), DMAP (0.112 g, 20 mol%) and NiF_2 (0.484 g, 5mmol) were loaded into a Schlenk tube equipped with a Teflon-coated magnetic stir bar. The Schlenk tube was placed under vacuum for 1 min and then N_2 was pumped into it. The solvent toluene (15 mL) was added into the Schlenk tube by syringe. The reaction mixture was stirred at 120 ℃ (oil bath) for 12 h. Then the reaction tube was allowed to cool to room temperature and the reaction solution was concentrated under reduced pressure. The crude products were purified by column chromatography on silica gel (Petroleum Ether/EtOAc= 10:1) to give the product **3f** 1.060 g (55% yield).

Control experiments

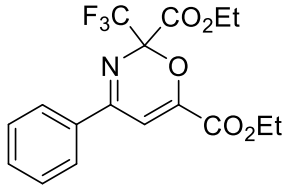
1a (78 mg, 0.3 mmol), ethyl trifluoropyruvate **2a** (204 mg, 1.2 mmol), CuI (6 mg, 10 mol%), DMAP (7 mg, 20 mol%) and NiF_2 (29 mg, 0.3 mmol) were loaded into a Schlenk tube equipped with a Teflon-coated magnetic stir bar. The Schlenk tube was placed under vacuum for 1 min and then N_2 was pumped into it. The solvent toluene (3 mL) was added into the Schlenk tube by syringe. The reaction mixture was stirred at 120 ℃ (oil bath) for 12 h. Then the reaction tube was allowed to cool to room temperature and the reaction solution was concentrated under reduced pressure. The crude products were purified by column chromatography on silica gel (Petroleum Ether/EtOAc= 10:1) to give the product **5a** (84 mg, 75% yield).

1a (78 mg, 0.3 mmol), ethyl trifluoropyruvate **2a** (204 mg, 1.2 mmol), CuI (6 mg, 10 mol%), DDQ (102 mg, 0.45 mmol), DMAP (7 mg, 20 mol%), NiF_2 (29 mg, 0.3 mmol) and radical scavenger (0.3–1.2 mmol) were loaded into a Schlenk tube equipped with a Teflon-coated magnetic stir bar. The Schlenk tube was placed under vacuum for 1 min and then N_2 was pumped into it. The solvent toluene (3 mL) was added into the Schlenk tube by syringe. The reaction mixture was stirred at 120 ℃ (oil bath) for 12 h. Then the reaction tube was allowed to cool to room temperature and the reaction solution was concentrated under reduced pressure. The crude products were purified by column chromatography on silica gel (Petroleum Ether/EtOAc= 10:1) to give the product **3a** or **5a**.



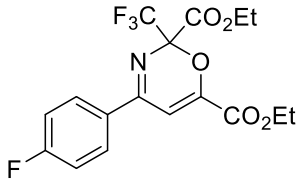
Compounds characterization

Diethyl 4-phenyl-2-(trifluoromethyl)-2*H*-1,3-oxazine-2,6-dicarboxylate (3a)



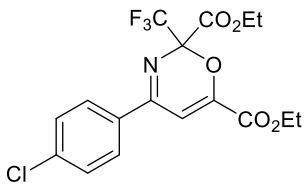
84 mg, 75% yield; White solid; Mp 78–79 °C; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.94 (d, *J* = 7.1 Hz, 2H), 7.54 (t, *J* = 7.3 Hz, 1H), 7.47 (t, *J* = 7.5 Hz, 2H), 6.94 (s, 1H), 4.42–4.27 (m, 4H), 1.39 (t, *J* = 7.1 Hz, 3H), 1.30 (t, *J* = 7.1 Hz, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.5, 162.9, 160.4, 150.2, 134.4, 132.4, 128.9, 127.4, 121.0 (q, *J* = 284.9 Hz), 102.1, 92.2 (q, *J* = 32.0 Hz), 63.5, 62.7, 14.2, 14.0 ppm; ^{19}F NMR (376 MHz, $CDCl_3$) δ -79.3 ppm; HRMS (ESI-TOF): m/z calcd for $C_{17}H_{17}F_3NO_5$ $[M+H]^+$ 372.1053, found 372.1053.

Diethyl 4-(4-fluorophenyl)-2-(trifluoromethyl)-2*H*-1,3-oxazine-2,6-dicarboxylate (3b)



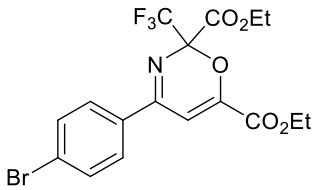
55 mg, 47% yield; Brown solid; Mp 63–65 °C; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.97–7.94 (m, 2H), 7.15 (t, *J* = 8.6 Hz, 2H), 6.89 (s, 1H), 4.42–4.27 (m, 4H), 1.38 (t, *J* = 7.1 Hz, 3H), 1.30 (t, *J* = 7.2 Hz, 3H) ppm; ^{13}C NMR (101 MHz, $CDCl_3$) δ 165.5 (d, *J* = 253.7 Hz), 163.5, 161.8, 160.4, 150.2, 130.7 (d, *J* = 2.9 Hz), 129.9, 129.8, 121.0 (q, *J* = 284.9 Hz), 116.2, 116.0, 101.8, 92.2 (q, *J* = 32.0 Hz), 63.6, 62.8, 14.2, 14.0; ^{19}F NMR (376 MHz, $CDCl_3$) δ -79.4, -106.6 ppm; HRMS (ESI-TOF): m/z calcd for $C_{17}H_{16}F_4NO_5$ $[M+H]^+$ 390.0959, found 390.1010.

Diethyl 4-(4-chlorophenyl)-2-(trifluoromethyl)-2*H*-1,3-oxazine-2,6-dicarboxylate (3c)



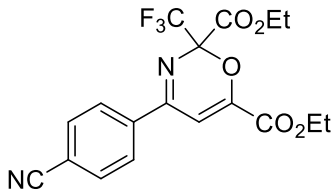
61 mg, 50% yield; White oil; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.88 (d, *J* = 8.6 Hz, 2H), 7.44 (d, *J* = 8.7 Hz, 2H), 6.88 (s, 1H), 4.42–4.27 (m, 4H), 1.38 (t, *J* = 7.1 Hz, 3H), 1.30 (t, *J* = 7.1 Hz, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.4, 161.9, 160.3, 150.3, 138.9, 132.8, 129.2, 128.8, 121.0 (q, *J* = 284.8 Hz), 101.6, 92.2 (q, *J* = 32.1 Hz), 63.6, 62.8, 14.2, 14.0 ppm; ^{19}F NMR (376 MHz, $CDCl_3$) δ -79.3 ppm; HRMS (ESI-TOF): m/z calcd for $C_{17}H_{16}ClF_3NO_5$ $[M+H]^+$ 406.0644, found 406.0658.

Diethyl 4-(4-bromophenyl)-2-(trifluoromethyl)-2*H*-1,3-oxazine-2,6-dicarboxylate (3d)



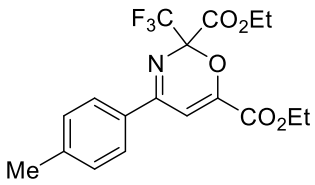
62 mg, 46% yield; White oil; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.80 (d, *J* = 8.6 Hz, 2H), 7.60 (d, *J* = 8.5 Hz, 2H), 6.87 (s, 1H), 4.42 –4.27 (m, 4H), 1.38 (t, *J* = 7.1 Hz, 3H), 1.30 (t, *J* = 7.1 Hz, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.3, 162.1, 160.3, 150.3, 133.3, 132.2, 129.0, 127.4, 120.9 (q, *J* = 284.9 Hz), 101.6, 92.2 (q, *J* = 32.1 Hz), 63.6, 62.9, 14.2, 14.0 ppm; ^{19}F NMR (376 MHz, $CDCl_3$) δ -79.3 ppm; HRMS (ESI-TOF): m/z calcd for $C_{17}H_{16}BrF_3NO_5$ $[M+H]^+$ 450.0158, found 450.0152.

Diethyl 4-(4-cyanophenyl)-2-(trifluoromethyl)-2*H*-1,3-oxazine-2,6-dicarboxylate (3e)



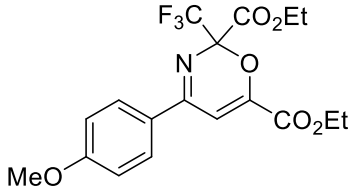
48 mg, 40% yield; Yellow oil; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.04 (d, *J* = 8.5 Hz, 2H), 7.77 (d, *J* = 8.4 Hz, 2H), 6.88 (s, 1H), 4.42–4.27 (m, 4H), 1.38 (t, *J* = 7.1 Hz, 3H), 1.30 (t, *J* = 7.1 Hz, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.1, 161.9, 160.0, 150.8, 138.2, 132.7, 128.0, 120.8 (q, *J* = 285.8Hz), 118.1, 115.8, 101.3, 92.2 (q, *J* = 32.5 Hz), 63.8, 63.0, 14.2, 14.0 ppm; ^{19}F NMR (376 MHz, $CDCl_3$) δ -79.2 ppm; HRMS (ESI-TOF): m/z calcd for $C_{18}H_{16}F_3N_2O_5$ $[M+H]^+$ 397.1006, found 397.1003.

Diethyl 4-(p-tolyl)-2-(trifluoromethyl)-2*H*-1,3-oxazine-2,6-dicarboxylate (3f)



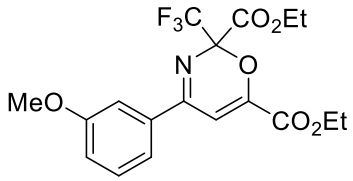
70 mg, 60% yield; Purple oil; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.76 (d, *J* = 8.1 Hz, 2H), 7.19 (d, *J* = 7.9 Hz, 2H), 6.84 (s, 1H), 4.34 – 4.18 (m, 4H), 2.33 (s, 3H), 1.31 (t, *J* = 7.1 Hz, 3H), 1.22 (t, *J* = 7.1 Hz, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.6, 162.5, 160.5, 149.9, 143.2, 131.7, 129.6, 127.4, 121.1 (q, *J* = 284.8 Hz), 102.1, 92.3 (q, *J* = 31.9 Hz), 63.4, 62.7, 21.7, 14.2, 14.0 ppm; ^{19}F NMR (376 MHz, $CDCl_3$) δ -79.4 ppm; HRMS (ESI-TOF): m/z calcd for $C_{18}H_{19}F_3NO_5$ $[M+H]^+$ 386.1210, found 386.1211.

Diethyl 4-(4-methoxyphenyl)-2-(trifluoromethyl)-2*H*-1,3-oxazine-2,6-dicarboxylate (3g)



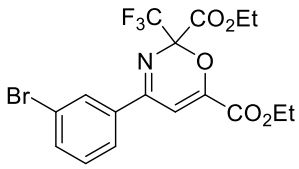
77 mg, 64% yield; Purple oil; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.90 (d, *J* = 8.9 Hz, 2H), 6.96–6.91 (m, 3H), 4.40–4.28 (m, 4H), 3.85 (s, 3H), 1.37 (t, *J* = 7.1 Hz, 3H), 1.28 (t, *J* = 7.1 Hz, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.7, 163.2, 161.7, 160.5, 149.7, 129.3, 126.9, 121.1 (q, *J* = 284.9 Hz), 114.2, 102.0, 92.2 (q, *J* = 31.9 Hz), 63.4, 62.6, 55.5, 14.1, 14.0 ppm; ^{19}F NMR (376 MHz, $CDCl_3$) δ -79.4 ppm; HRMS (ESI-TOF): m/z calcd for $C_{18}H_{19}F_3NO_6$ $[M+H]^+$ 402.1159, found 402.1155.

Diethyl 4-(3-methoxyphenyl)-2-(trifluoromethyl)-2*H*-1,3-oxazine-2,6-dicarboxylate (3h)



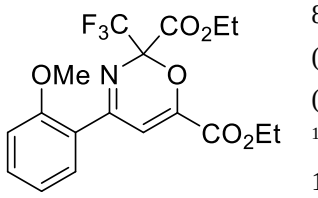
65 mg, 54% yield; Purple oil; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.48–7.46 (m, 2H), 7.37 (t, *J* = 7.9 Hz, 1H), 7.09–7.06 (m, 1H), 6.90 (s, 1H), 4.41–4.24 (m, 4H), 3.85 (s, 3H), 1.38 (t, *J* = 7.1 Hz, 3H), 1.30 (t, *J* = 7.1 Hz, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.5, 162.8, 160.4, 160.1, 145.0, 135.8, 130.0, 121.0 (q, *J* = 286.8 Hz), 120.0, 118.4, 112.3, 102.2, 92.2 (q, *J* = 32.0 Hz), 63.5, 62.7, 55.5, 14.1, 14.0 ppm; ^{19}F NMR (376 MHz, $CDCl_3$) δ -79.3 ppm; HRMS (ESI-TOF): m/z calcd for $C_{18}H_{19}F_3NO_6$ $[M+H]^+$ 402.1159, found 402.1156.

Diethyl 4-(3-bromophenyl)-2-(trifluoromethyl)-2*H*-1,3-oxazine-2,6-dicarboxylate (3i)



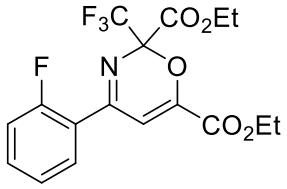
54 mg, 40% yield; Yellow solid; Mp 72–73 ℃; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.08 (s, 1H), 7.83 (d, *J* = 7.9 Hz, 1H), 7.67 (d, *J* = 9.9 Hz, 1H), 7.35 (t, *J* = 7.9 Hz, 1H), 6.86 (s, 1H), 4.43–4.28 (m, 4H), 1.39 (t, *J* = 7.1 Hz, 3H), 1.31 (t, *J* = 7.1 Hz, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.3, 161.9, 160.2, 150.4, 136.4, 135.4, 130.42, 130.40, 126.1, 123.3, 120.9 (q, *J* = 285.9 Hz), 101.7, 92.2 (q, *J* = 32.6 Hz), 63.7, 62.9, 14.2, 14.0 ppm; ^{19}F NMR (376 MHz, $CDCl_3$) δ -79.3 ppm; HRMS (ESI-TOF): m/z calcd for $C_{17}H_{16}BrF_3NO_5$ $[M+H]^+$ 450.0158, found 450.0147.

Diethyl 4-(2-methoxyphenyl)-2-(trifluoromethyl)-2*H*-1,3-oxazine-2,6-dicarboxylate (3j)



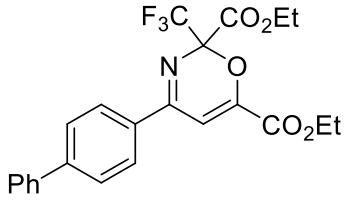
84 mg, 70% yield; Purple oil; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.70 (d, *J* = 7.7 Hz, 1H), 7.44 (t, *J* = 7.0 Hz, 1H), 7.05–6.90 (m, 3H), 4.38–4.31 (m, 4H), 3.86 (s, 3H), 1.36 (t, *J* = 7.1 Hz, 3H), 1.30 (t, *J* = 7.1 Hz, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.8, 163.7, 160.7, 158.5, 147.6, 133.1, 130.4, 124.8, 121.2, 121.0 (q, *J* = 285.8 Hz), 111.5, 107.0, 91.6 (q, *J* = 32.0 Hz), 63.4, 62.4, 55.7, 14.1, 14.0 ppm; ^{19}F NMR (376 MHz, $CDCl_3$) δ -79.3 ppm; HRMS (ESI-TOF): m/z calcd for $C_{18}H_{19}F_3NO_6$ $[M+H]^+$ 402.1159, found 402.1157.

Diethyl 4-(2-fluorophenyl)-2-(trifluoromethyl)-2*H*-1,3-oxazine-2,6-dicarboxylate (3k)



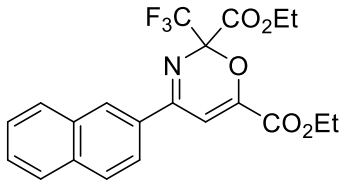
49 mg, 42% yield; Yellow oil; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.90 (t, *J* = 8.6 Hz, 1H), 7.53–7.48 (m, 1H), 7.25 (t, *J* = 7.7 Hz, 1H), 7.17–7.12 (m, 1H), 6.92 (d, *J* = 2.9 Hz, 1H), 4.41–4.30 (m, 4H), 1.38 (t, *J* = 7.1 Hz, 3H), 1.32 (t, *J* = 7.1 Hz, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.4, 161.9, 161.7 (d, *J* = 254.5 Hz), 160.2, 149.2 (d, *J* = 1.8 Hz), 133.9 (d, *J* = 8.8 Hz), 130.5 (d, *J* = 2.5 Hz), 124.9 (d, *J* = 3.5 Hz), 123.3 (d, *J* = 10.8 Hz), 120.9 (q, *J* = 285.8 Hz), 116.6 (d, *J* = 22.3 Hz), 105.4 (d, *J* = 10.1 Hz), 91.6 (q, *J* = 32.2 Hz), 63.6, 62.7, 14.2, 14.0 ppm; ^{19}F NMR (376 MHz, $CDCl_3$) δ -79.3, -112.7 ppm; HRMS (ESI-TOF): m/z calcd for $C_{17}H_{16}F_4NO_5$ $[M+H]^+$ 390.0959, found 390.0957.

Diethyl 4-([1,1'-biphenyl]-4-yl)-2-(trifluoromethyl)-2*H*-1,3-oxazine-2,6-dicarboxylate (3l)



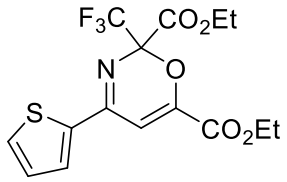
89 mg, 66% yield; Purple oil; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.03 (d, *J* = 8.2 Hz, 2H), 7.70 (d, *J* = 8.4 Hz, 2H), 7.63 (d, *J* = 7.4 Hz, 2H), 7.50–7.46 (m, 2H), 7.42–7.39 (m, 1H), 6.99 (s, 1H), 4.44–4.30 (m, 4H), 1.41 (t, *J* = 7.1 Hz, 3H), 1.32 (t, *J* = 7.1 Hz, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.6, 162.4, 160.5, 150.0, 145.2, 134.0, 133.2, 129.1, 128.3, 128.0, 127.5, 127.3, 121.1 (q, *J* = 285.0 Hz), 102.0, 92.3 (q, *J* = 32.0 Hz), 63.5, 62.8, 14.2, 14.0 ppm; ^{19}F NMR (376 MHz, $CDCl_3$) δ -79.3 ppm; HRMS (ESI-TOF): m/z calcd for $C_{23}H_{21}F_3NO_5$ $[M+H]^+$ 448.1366, found 448.1360.

Diethyl 4-(naphthalen-2-yl)-2-(trifluoromethyl)-2*H*-1,3-oxazine-2,6-dicarboxylate (3m)



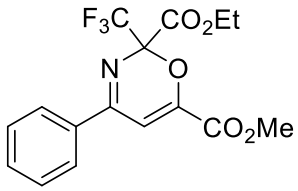
57 mg, 45% yield; White solid; Mp 77–78 °C; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.35 (s, 1H), 8.13–8.11 (m, 1H), 7.97–7.87 (m, 3H), 7.61–7.53 (m, 2H), 7.11 (s, 1H), 4.46–4.30 (m, 4H), 1.42 (t, *J* = 7.1 Hz, 3H), 1.32 (t, *J* = 7.1 Hz, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.6, 162.7, 160.6, 150.0, 135.3, 132.8, 131.8, 129.3, 128.9, 128.6, 128.3, 127.9, 127.0, 121.1 (q, *J* = 285.8 Hz), 123.6, 102.1, 92.4 (q, *J* = 32.0 Hz), 63.6, 62.8, 14.3, 14.0 ppm; ^{19}F NMR (376 MHz, $CDCl_3$) δ -79.2 ppm; HRMS (ESI-TOF): m/z calcd for $C_{21}H_{19}F_3NO_5$ $[M+H]^+$ 422.1210, found 422.1202.

Diethyl 4-(thiophen-2-yl)-2-(trifluoromethyl)-2*H*-1,3-oxazine-2,6-dicarboxylate (3n)



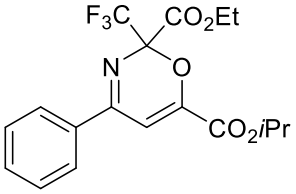
52 mg, 46% yield; Purple oil; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.63 (d, *J* = 3.8 Hz, 1H), 7.59 (d, *J* = 5.0 Hz, 1H), 7.14–7.12 (m, 1H), 6.81 (s, 1H), 4.42–4.27 (m, 4H), 1.39 (t, *J* = 7.1 Hz, 3H), 1.30 (t, *J* = 7.1 Hz, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.5, 160.4, 157.3, 149.6, 140.4, 132.7, 130.8, 128.2, 121.0 (q, *J* = 285.1 Hz), 101.8, 91.8 (q, *J* = 32.1 Hz), 63.5, 62.8, 14.2, 14.0 ppm; ^{19}F NMR (376 MHz, $CDCl_3$) δ -79.4 ppm; HRMS (ESI-TOF): m/z calcd for $C_{15}H_{15}F_3NO_5S$ $[M+H]^+$ 378.0618, found 378.0614.

2-Ethyl 6-methyl 4-phenyl-2-(trifluoromethyl)-2*H*-1,3-oxazine-2,6-dicarboxylate (3o)



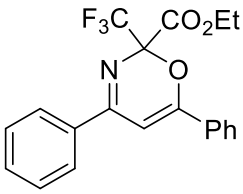
68 mg, 63% yield; White solid; Mp 91–93 °C; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.94 (d, *J* = 7.3 Hz, 2H), 7.54 (t, *J* = 7.4 Hz, 1H), 7.47 (t, *J* = 7.6 Hz, 2H), 6.96 (s, 1H), 4.39–4.27 (m, 2H), 3.93 (s, 3H), 1.30 (t, *J* = 7.1 Hz, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.5, 162.8, 160.9, 149.7, 134.3, 132.5, 128.9, 127.4, 121.0 (q, *J* = 284.9 Hz), 102.3, 92.3 (q, *J* = 32.1 Hz), 63.6, 53.3, 14.0 ppm; ^{19}F NMR (376 MHz, $CDCl_3$) δ -79.3 ppm; HRMS (ESI-TOF): m/z calcd for $C_{16}H_{15}F_3NO_5$ $[M+H]^+$ 358.0897, found 358.0893.

2-Ethyl 6-isopropyl 4-phenyl-2-(trifluoromethyl)-2*H*-1,3-oxazine-2,6-dicarboxylate (3p)



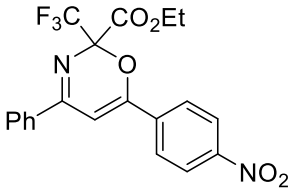
58 mg, 50% yield; Yellow oil; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.93 (d, *J* = 7.2 Hz, 2H), 7.56–7.45 (m, 3H), 6.90 (s, 1H), 5.26–5.20 (m, 1H), 4.38–4.27 (m, 2H), 1.38–1.36 (m, 6H), 1.30 (t, *J* = 7.1 Hz, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.6, 163.0, 159.9, 150.3, 134.5, 132.4, 128.9, 127.4, 121.1 (q, *J* = 284.9 Hz), 101.9, 92.2 (q, *J* = 32.0 Hz), 70.9, 63.4, 21.8, 14.0 ppm; ^{19}F NMR (376 MHz, $CDCl_3$) δ -79.3 ppm; HRMS (ESI-TOF): m/z calcd for $C_{18}H_{19}F_3NO_5$ $[M+H]^+$ 386.1210, found 386.1204.

Ethyl 4,6-diphenyl-2-(trifluoromethyl)-2*H*-1,3-oxazine-2-carboxylate (4a)



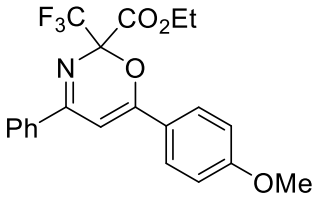
90 mg, 80% yield; White solid; Mp 74–76 °C; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.01 (d, *J* = 7.1 Hz, 2H), 7.92 (d, *J* = 7.0 Hz, 2H), 7.56–7.47 (m, 6H), 6.63 (s, 1H), 4.37–4.27 (m, 2H), 1.28 (t, *J* = 7.1 Hz, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.0, 164.5, 160.7, 135.8, 132.0, 131.7, 131.2, 128.9, 128.8, 127.4, 127.0, 121.6 (q, *J* = 284.2 Hz), 95.1, 91.7 (q, *J* = 31.7 Hz), 63.3, 14.0 ppm; ^{19}F NMR (376 MHz, $CDCl_3$) δ -79.3 ppm; HRMS (ESI-TOF): m/z calcd for $C_{20}H_{17}F_3NO_3$ $[M+H]^+$ 376.1155, found 376.1152.

Ethyl 6-(4-nitrophenyl)-4-phenyl-2-(trifluoromethyl)-2*H*-1,3-oxazine-2-carboxylate (4b)



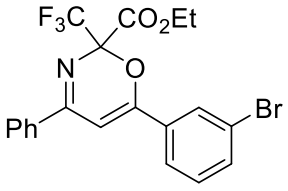
79 mg, 63% yield; Yellow solid; Mp 137–138 °C; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.32 (d, *J* = 8.6 Hz, 2H), 8.07 (d, *J* = 8.6 Hz, 2H), 7.98 (d, *J* = 7.4 Hz, 2H), 7.57–7.47 (m, 3H), 6.73 (s, 1H), 4.39–4.27 (m, 2H), 1.29 (t, *J* = 7.1 Hz, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.4, 163.6, 158.0, 149.6, 137.0, 135.1, 132.1, 128.9, 127.6, 127.4, 124.0, 121.3 (q, *J* = 285.8 Hz), 97.2, 91.9 (q, *J* = 32.0 Hz), 63.6, 14.0 ppm; ^{19}F NMR (376 MHz, $CDCl_3$) δ -79.3 ppm; HRMS (ESI-TOF): m/z calcd for $C_{20}H_{16}F_3N_2O_5$ $[M+H]^+$ 421.1006, found 421.1009.

Ethyl 6-(4-methoxyphenyl)-4-phenyl-2-(trifluoromethyl)-2*H*-1,3-oxazine-2-carboxylate (4c)



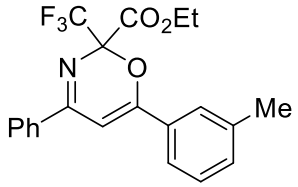
97 mg, 80% yield; Yellow solid; Mp 105–106 °C; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.98 (d, *J* = 8.6 Hz, 2H), 7.91 (d, *J* = 6.9 Hz, 2H), 7.53–7.47 (m, 3H), 6.97 (d, *J* = 8.5 Hz, 2H), 6.60 (s, 1H), 4.35–4.25 (m, 2H), 3.86 (s, 3H), 1.27 (t, *J* = 7.1 Hz, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.2, 163.4, 162.6, 160.4, 131.9, 131.4, 129.2, 128.9, 128.3, 126.9, 121.6 (q, *J* = 284.3 Hz), 114.0, 94.9, 91.7 (q, *J* = 31.6 Hz), 63.2, 55.5, 14.0 ppm; ^{19}F NMR (376 MHz, $CDCl_3$) δ -79.4 ppm; HRMS (ESI-TOF): m/z calcd for $C_{21}H_{19}F_3NO_4$ $[M+H]^+$ 406.1261, found 406.1258.

Ethyl 6-(3-bromophenyl)-4-phenyl-2-(trifluoromethyl)-2*H*-1,3-oxazine-2-carboxylate (4d)



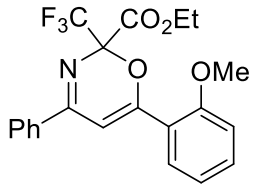
61 mg, 45% yield; Yellow solid; Mp 104–106 °C; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.08–7.92 (m, 3H), 7.83 (d, *J* = 7.9 Hz, 1H), 7.65 (d, *J* = 6.8 Hz, 1H), 7.56–7.47 (m, 3H), 7.36 (t, *J* = 7.9 Hz, 1H), 6.59 (s, 1H), 4.37–4.26 (m, 2H), 1.29 (t, *J* = 7.1 Hz, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.7, 164.1, 159.1, 135.5, 134.8, 133.3, 131.9, 130.5, 129.7, 128.8, 127.4, 125.5, 123.1, 121.4 (q, *J* = 284.8 Hz), 95.8, 91.8 (q, *J* = 31.9 Hz), 63.4, 14.0 ppm; ^{19}F NMR (376 MHz, $CDCl_3$) δ -79.3 ppm; HRMS (ESI-TOF): m/z calcd for $C_{20}H_{16}BrF_3NO_3$ $[M+H]^+$ 454.0260, found 454.0251.

Ethyl 4-phenyl-6-(m-tolyl)-2-(trifluoromethyl)-2*H*-1,3-oxazine-2-carboxylate (4e)



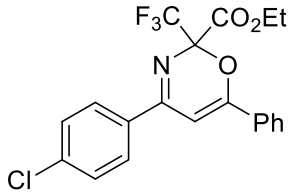
84 mg, 72% yield; Yellow solid; Mp 61–63 °C; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.93 (d, *J* = 6.4 Hz, 2H), 7.85 (s, 1H), 7.77 (d, *J* = 7.2 Hz, 1H), 7.54–7.49 (m, 3H), 7.40–7.34 (m, 2H), 6.63 (s, 1H), 4.38–4.27 (m, 2H), 2.45 (s, 3H), 1.29 (t, *J* = 7.1 Hz, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.0, 164.7, 160.5, 138.6, 135.7, 132.5, 132.0, 131.2, 128.9, 128.6, 127.9, 126.9, 124.6, 121.6 (q, *J* = 285.8 Hz), 95.3, 91.7 (q, *J* = 31.7 Hz), 63.2, 21.5, 14.0 ppm; ^{19}F NMR (376 MHz, $CDCl_3$) δ -79.3 ppm; HRMS (ESI-TOF): m/z calcd for $C_{21}H_{19}F_3NO_3$ $[M+H]^+$ 390.1312, found 390.1311.

Ethyl 6-(2-methoxyphenyl)-4-phenyl-2-(trifluoromethyl)-2*H*-1,3-oxazine-2-carboxylate (4f)



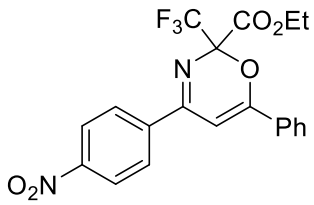
45 mg, 37% yield; Yellow oil; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.08 (d, *J* = 9.6 Hz, 1H), 7.98 (d, *J* = 6.6 Hz, 2H), 7.52–7.46 (m, 4H), 7.16–7.06 (m, 2H), 7.00 (d, *J* = 7.4 Hz, 1H), 4.34–4.23 (m, 2H), 3.97 (s, 3H), 1.24 (d, *J* = 7.1 Hz, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.4, 165.1, 159.1, 157.2, 135.9, 133.1, 131.8, 130.4, 130.1, 130.0, 128.8, 127.8, 121.5 (q, *J* = 285.8 Hz), 121.2, 119.5, 111.4, 100.9, 90.7 (q, *J* = 31.6 Hz), 63.3, 56.0, 14.1 ppm; ^{19}F NMR (376 MHz, $CDCl_3$) δ -79.2 ppm; HRMS (ESI-TOF): m/z calcd for $C_{21}H_{19}F_3NO_5$ $[M+H]^+$ 406.1261, found 406.1257.

Ethyl 4-(4-chlorophenyl)-6-phenyl-2-(trifluoromethyl)-2*H*-1,3-oxazine-2-carboxylate (4g)



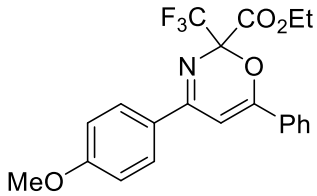
69 mg, 56% yield; Yellow solid; Mp 134–135 °C; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.95–7.90 (m, 4H), 7.54–7.44 (m, 5H), 6.57 (s, 1H), 4.36–4.26 (m, 2H), 1.27 (t, *J* = 7.1 Hz, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.8, 163.4, 161.1, 137.6, 133.6, 132.2, 131.0, 129.0, 129.0, 128.8, 127.0, 121.5 (q, *J* = 284.2 Hz), 94.6, 91.7 (q, *J* = 31.9 Hz), 63.3, 14.0 ppm; ^{19}F NMR (376 MHz, $CDCl_3$) δ -79.3 ppm; HRMS (ESI-TOF): m/z calcd for $C_{20}H_{16}ClF_3NO_3$ $[M+H]^+$ 410.0765, found 410.0761.

Ethyl 4-(4-nitrophenyl)-6-phenyl-2-(trifluoromethyl)-2*H*-1,3-oxazine-2-carboxylate (4h)



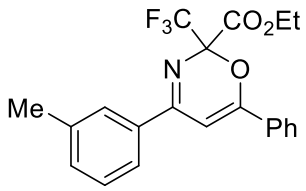
96 mg, 76% yield; Orange solid; Mp 136–138 °C; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.31 (d, *J* = 8.6 Hz, 2H), 8.07 (d, *J* = 8.6 Hz, 2H), 7.98 (d, *J* = 7.3 Hz, 2H), 7.57–7.47 (m, 3H), 6.73 (s, 1H), 4.39–4.27 (m, 2H), 1.29 (t, *J* = 7.1 Hz, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.4, 163.6, 158.0, 149.6, 137.0, 135.1, 132.1, 128.9, 127.6, 127.4, 124.0, 121.3 (q, *J* = 285.8 Hz), 97.2, 91.9 (q, *J* = 32.0 Hz), 63.6, 14.0 ppm; ^{19}F NMR (376 MHz, $CDCl_3$) δ -79.3 ppm; HRMS (ESI-TOF): m/z calcd for $C_{20}H_{16}F_3N_2O_5$ $[M+H]^+$ 421.1006, found 421.1001.

Ethyl 4-(4-methoxyphenyl)-6-phenyl-2-(trifluoromethyl)-2*H*-1,3-oxazine-2-carboxylate (4i)



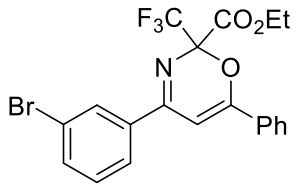
106 mg, 87% yield; Yellow solid; Mp 103–105 °C; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.99 (d, *J* = 6.5 Hz, 2H), 7.87 (d, *J* = 8.8 Hz, 2H), 7.52–7.45 (m, 3H), 6.99 (d, *J* = 8.8 Hz, 2H), 6.52 (s, 1H), 4.35–4.25 (m, 2H), 3.87 (s, 3H), 1.27 (t, *J* = 7.1 Hz, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.2, 164.8, 162.8, 160.7, 136.0, 131.5, 128.9, 128.7, 127.4, 123.5, 121.6 (q, *J* = 284.8 Hz), 114.3, 93.9, 91.6 (q, *J* = 31.7 Hz), 63.2, 55.6, 14.0 ppm; ^{19}F NMR (376 MHz, $CDCl_3$) δ -79.3 ppm; HRMS (ESI-TOF): m/z calcd for $C_{21}H_{19}F_3NO_4$ $[M+H]^+$ 406.1261, found 406.1258.

Ethyl 6-phenyl-4-(m-tolyl)-2-(trifluoromethyl)-2*H*-1,3-oxazine-2-carboxylate (4j)



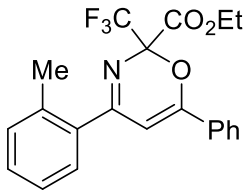
84 mg, 72% yield; Yellow solid; Mp 90–91 °C; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.02 (d, *J* = 6.8 Hz, 2H), 7.73 (s, 2H), 7.54–7.47 (m, 3H), 7.41–7.34 (m, 2H), 6.62 (s, 1H), 4.38–4.27 (m, 2H), 2.45 (s, 3H), 1.29 (t, *J* = 7.1 Hz, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.0, 164.5, 160.9, 138.7, 135.8, 132.9, 131.7, 131.1, 128.8, 128.7, 127.4, 127.4, 124.2, 121.6 (q, *J* = 284.8 Hz), 95.0, 91.7 (q, *J* = 31.7 Hz), 63.2, 21.5, 14.0 ppm; ^{19}F NMR (376 MHz, $CDCl_3$) δ -79.3 ppm; HRMS (ESI-TOF): m/z calcd for $C_{21}H_{19}F_3NO_3$ $[M+H]^+$ 390.1312, found 390.1311.

Ethyl 4-(3-bromophenyl)-6-phenyl-2-(trifluoromethyl)-2*H*-1,3-oxazine-2-carboxylate (4k)



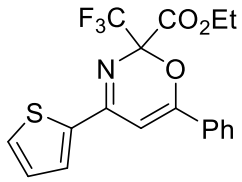
80 mg, 55% yield; Yellow solid; Mp 108–110 °C; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.12 (t, *J* = 1.9 Hz, 1H), 7.97–7.82 (m, 3H), 7.65 (d, *J* = 7.9 Hz, 1H), 7.55–7.48 (m, 3H), 7.36 (t, *J* = 7.9 Hz, 1H), 6.54 (s, 1H), 4.36–4.25 (m, 2H), 1.27 (t, *J* = 7.1 Hz, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.7, 163.4, 161.2, 137.7, 134.6, 132.3, 130.9, 130.4, 130.3, 128.9, 127.0, 126.0, 123.0, 118.6 (q, *J* = 284.9 Hz), 94.7, 91.6 (q, *J* = 31.9 Hz), 63.4, 14.0 ppm; ^{19}F NMR (376 MHz, $CDCl_3$) δ -79.3 ppm; HRMS (ESI-TOF): m/z calcd for $C_{20}H_{16}BrF_3NO_3$ $[M+H]^+$ 454.0260, found 454.0251.

Ethyl 6-phenyl-4-(o-tolyl)-2-(trifluoromethyl)-2*H*-1,3-oxazine-2-carboxylate (4l)



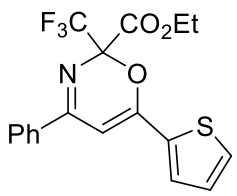
53 mg, 45% yield; Yellow oil; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.86 (d, *J* = 7.0 Hz, 2H), 7.54–7.43 (m, 4H), 7.36–7.25 (m, 3H), 6.29 (s, 1H), 4.38–4.30 (m, 2H), 2.51 (s, 3H), 1.30 (t, *J* = 7.1 Hz, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.1, 164.9, 159.8, 137.0, 136.6, 132.1, 131.4, 130.9, 130.0, 129.0, 128.2, 127.0, 126.1, 121.4 (q, *J* = 284.8 Hz), 98.5, 91.3 (q, *J* = 31.7 Hz), 63.3, 20.3, 14.1 ppm; ^{19}F NMR (376 MHz, $CDCl_3$) δ -79.3 ppm; HRMS (ESI-TOF): m/z calcd for $C_{21}H_{19}F_3NO_3$ $[M+H]^+$ 390.1312, found 390.1307.

Ethyl 6-phenyl-4-(thiophen-2-yl)-2-(trifluoromethyl)-2*H*-1,3-oxazine-2-carboxylate (4m)



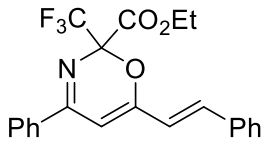
86 mg, 75% yield; Yellow solid; Mp 83–84 °C; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.89 (d, *J* = 7.1 Hz, 2H), 7.68 (d, *J* = 3.7 Hz, 1H), 7.55–7.41 (m, 4H), 7.14 (t, *J* = 4.4 Hz, 1H), 6.54 (s, 1H), 4.31 (m, 2H), 1.28 (t, *J* = 7.1 Hz, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.8, 160.4, 158.8, 141.2, 132.0, 131.4, 131.0, 129.5, 128.9, 127.9, 126.8, 121.4 (q, *J* = 284.4 Hz), 94.5, 91.4 (q, *J* = 31.8 Hz), 63.3, 14.0 ppm; ^{19}F NMR (376 MHz, $CDCl_3$) δ -79.4 ppm; HRMS (ESI-TOF): m/z calcd for $C_{18}H_{15}F_3NO_3S$ $[M+H]^+$ 382.0719, found 382.0716.

Ethyl 4-phenyl-6-(thiophen-2-yl)-2-(trifluoromethyl)-2*H*-1,3-oxazine-2-carboxylate (4n)



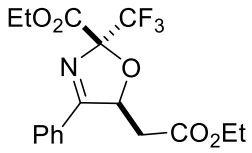
95 mg, 83% yield; Yellow solid; Mp 63–65 °C; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.97 (d, *J* = 7.6 Hz, 2H), 7.74 (d, *J* = 3.7 Hz, 1H), 7.56–7.46 (m, 4H), 7.20–7.13 (m, 1H), 6.48 (s, 1H), 4.37–4.27 (m, 2H), 1.28 (t, *J* = 7.1 Hz, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.7, 164.3, 155.7, 135.6, 134.7, 131.7, 130.4, 129.5, 128.7, 128.4, 127.4, 121.4 (q, *J* = 284.3 Hz), 93.9, 91.6 (q, *J* = 31.7 Hz), 63.3, 14.0 ppm; ^{19}F NMR (376 MHz, $CDCl_3$) δ -79.3 ppm; HRMS (ESI-TOF): m/z calcd for $C_{18}H_{15}F_3NO_3S$ $[M+H]^+$ 382.0719, found 382.0714.

Ethyl (E)-4-phenyl-6-styryl-2-(trifluoromethyl)-2*H*-1,3-oxazine-2-carboxylate (4o)



75 mg, 62% yield; Yellow oil; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.95 (d, *J* = 6.8 Hz, 2H), 7.59–7.54 (m, 3H), 7.52–7.45 (m, 3H), 7.42–7.36 (m, 3H), 6.65 (d, *J* = 15.9 Hz, 1H), 6.17 (s, 1H), 4.41–4.26 (m, 2H), 1.30 (t, *J* = 7.1 Hz, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.8, 164.2, 158.8, 137.5, 135.7, 135.3, 131.6, 129.8, 129.0, 128.7, 127.9, 127.3, 121.6 (q, *J* = 284.8 Hz), 119.3, 98.4, 91.4 (q, *J* = 31.4 Hz), 63.2, 14.0 ppm; ^{19}F NMR (376 MHz, $CDCl_3$) δ -79.3 ppm; HRMS (ESI-TOF): m/z calcd for $C_{22}H_{19}F_3NO_3$ $[M+H]^+$ 402.1312, found 402.1310.

Ethyl-5-(2-ethoxy-2-oxoethyl)-4-phenyl-2-(trifluoromethyl)-2,5-dihydrooxazole-2-carboxylate (5a)



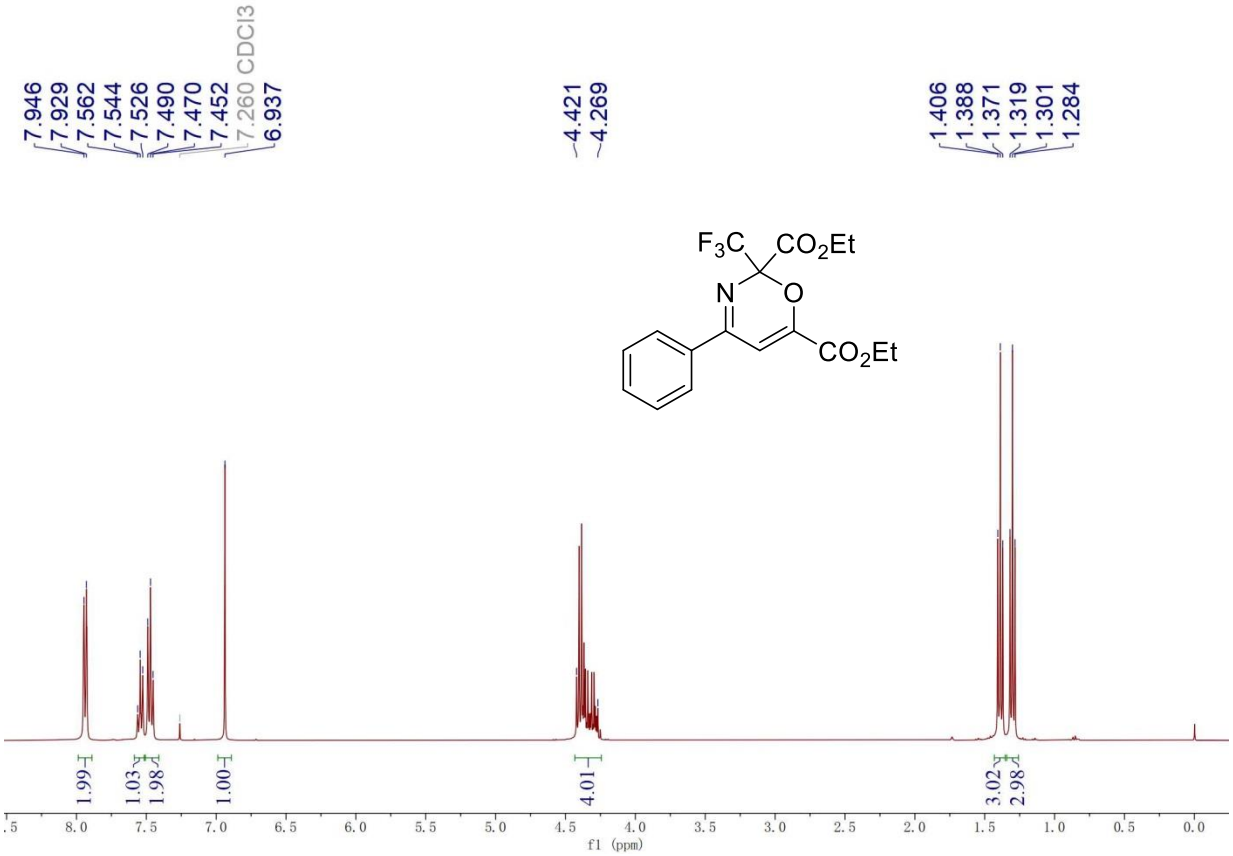
White oil; dr 15:1; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.75 (d, *J* = 7.4 Hz, 2H), 7.51–7.47 (m, 1H), 7.41 (t, *J* = 7.3 Hz, 2H), 5.96 (dd, *J* = 7.6, 3.8 Hz, 1H), 4.27 (q, *J* = 7.0 Hz, 2H), 4.10 (q, *J* = 7.0 Hz, 2H), 2.89–2.78 (m, 2H), 1.28 (t, *J* = 7.0 Hz, 3H), 1.17 (t, *J* = 7.0 Hz, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 176.5, 169.5, 164.2, 132.9, 129.1, 128.8, 121.6 (q, *J* = 285.9 Hz), 106.6 (q, *J* = 30.8 Hz), 85.5, 63.0, 61.3, 39.1, 14.0, 13.9 ppm; ^{19}F NMR (376 MHz, Chloroform-*d*) δ -78.6 ppm; HRMS (ESI-TOF): m/z calcd for $C_{17}H_{19}F_3NO_5$ $[M+H]^+$ 374.1215, found 374.1230.

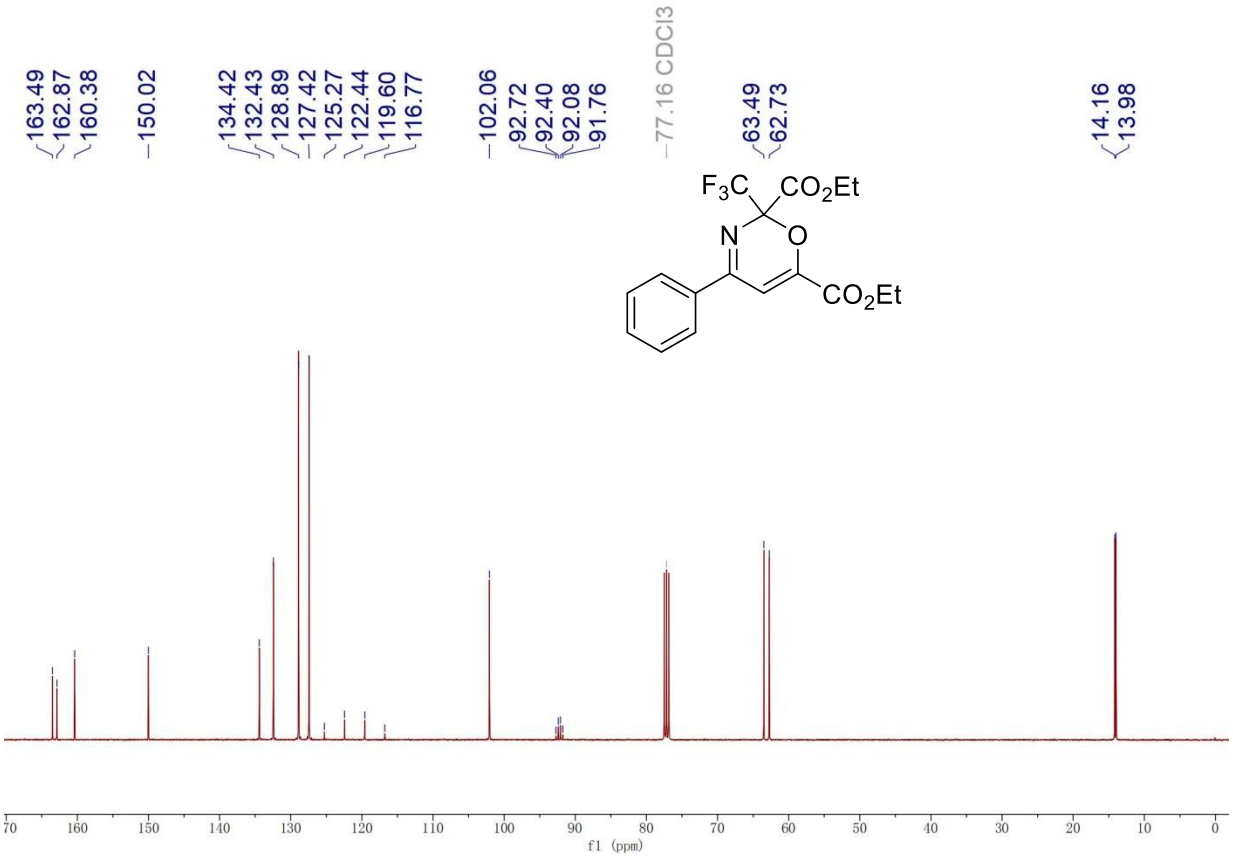
References

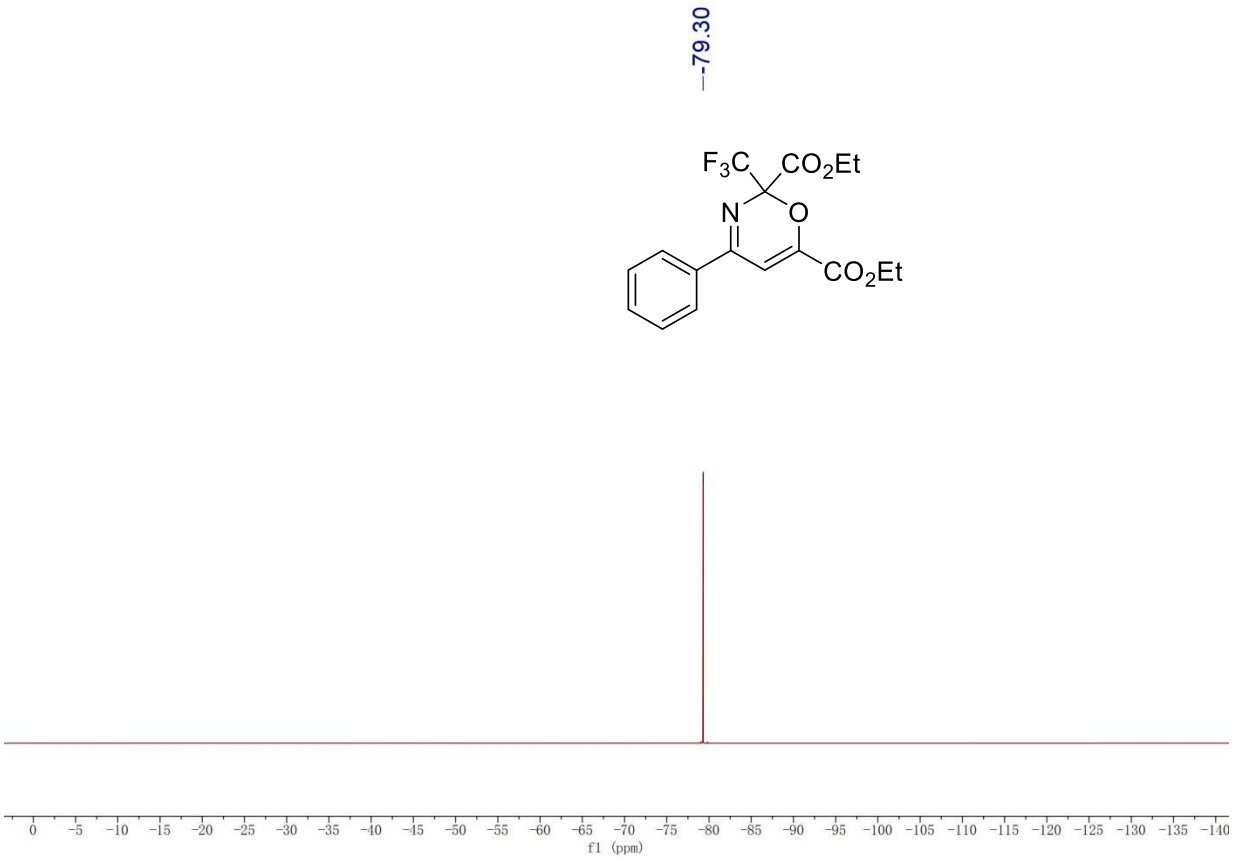
(1) (a) Zhang, L.; Duan, J.; Xu, G.; Ding, X.; Mao, Y.; Rong, B.; Zhu, N.; Fang, Z.; Li, Z.; Guo, K. *J. Org. Chem*. **2020**, *85*, 2532. (b) Duan, J.; Zhang, L.; Xu, G.; Chen, H.; Ding, X.; Mao, Y.; Rong, B.; Zhu, N.; Guo, K. *J. Org. Chem*. **2020**, *85*, 8157. (c) Rong, B.; Xu, G.; Yan, H.; Zhang, S.; Wu, Q.; Zhu, N.; Fang, Z.; Duan, J.; Guo, K. *Org. Chem. Front*. **2021**, *8*, 2939.

NMR Spectra of compounds

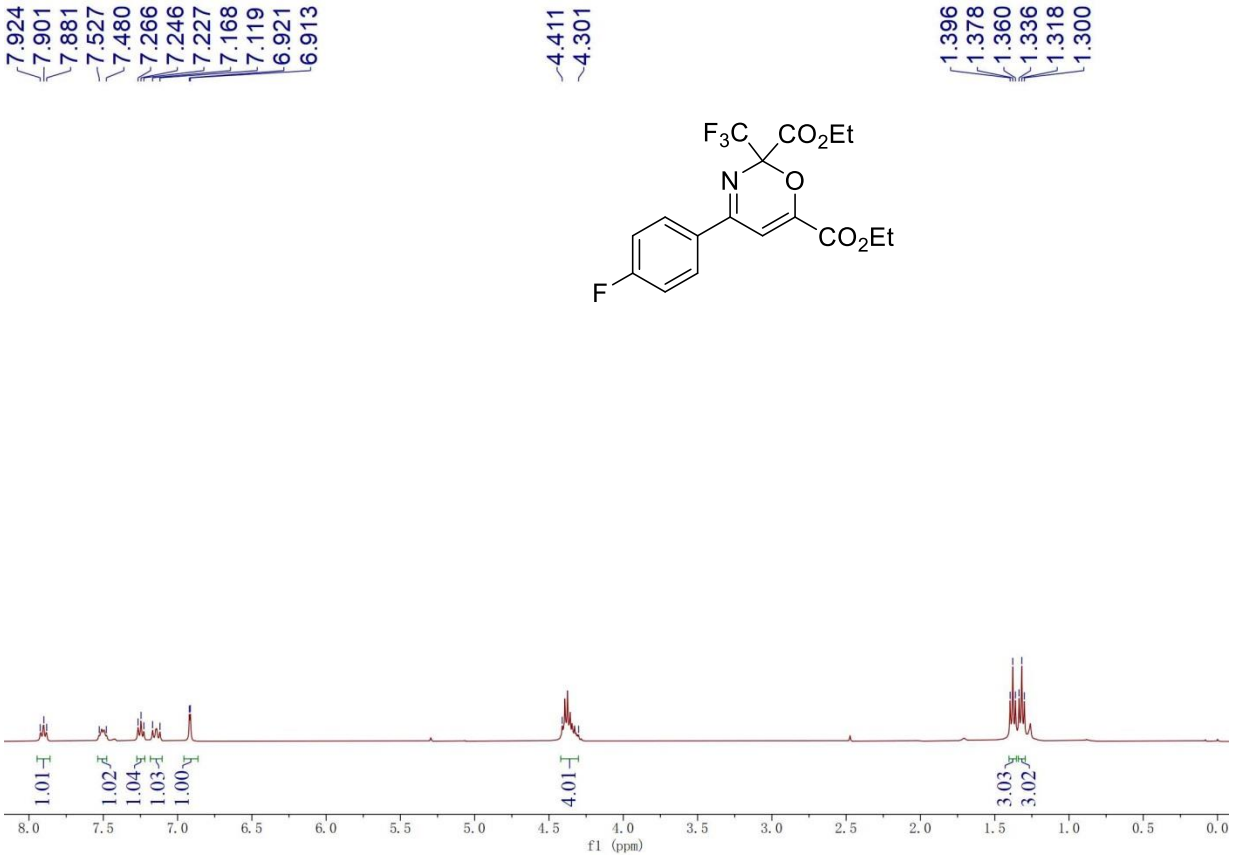
Diethyl 4-phenyl-2-(trifluoromethyl)-2*H*-1,3-oxazine-2,6-dicarboxylate (3a)

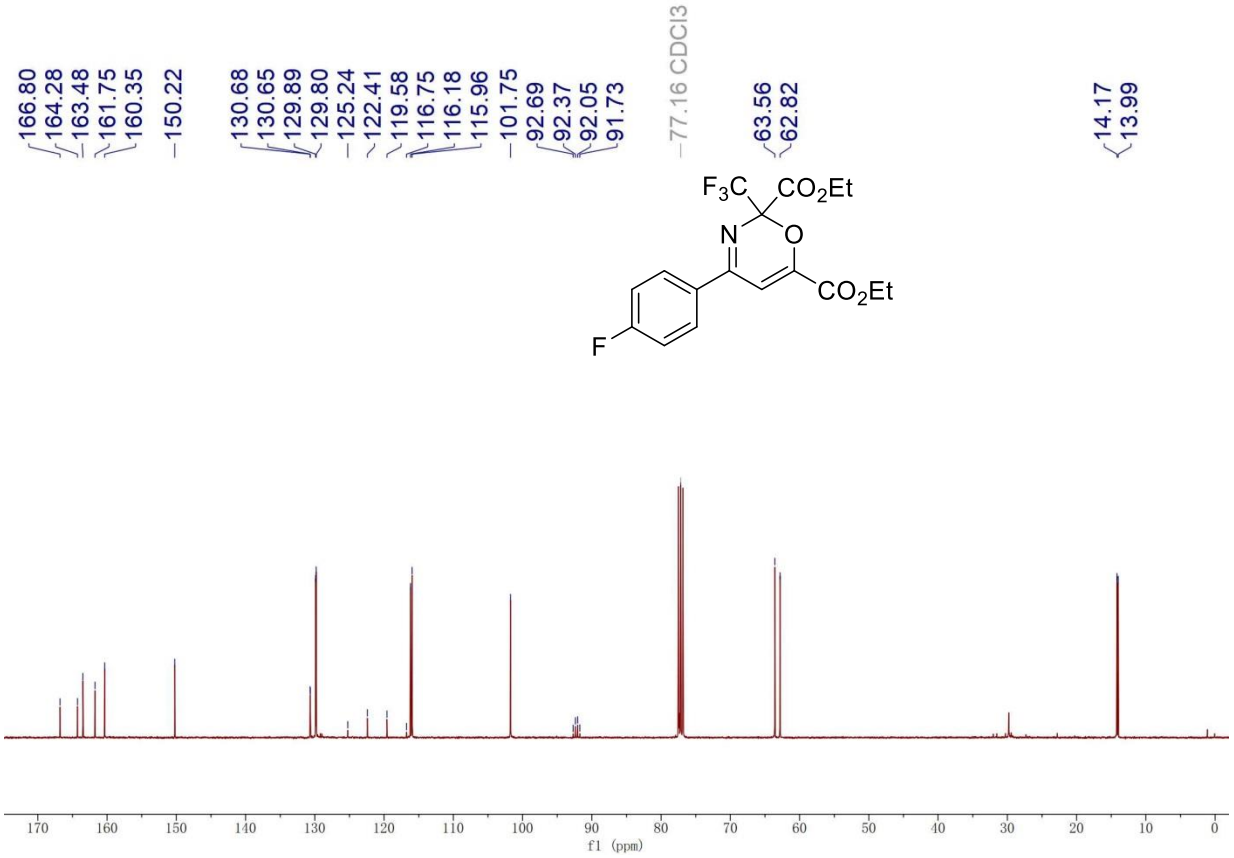






Diethyl 4-(4-fluorophenyl)-2-(trifluoromethyl)-2*H*-1,3-oxazine-2,6-dicarboxylate (3b)

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164.28
163.48
161.75
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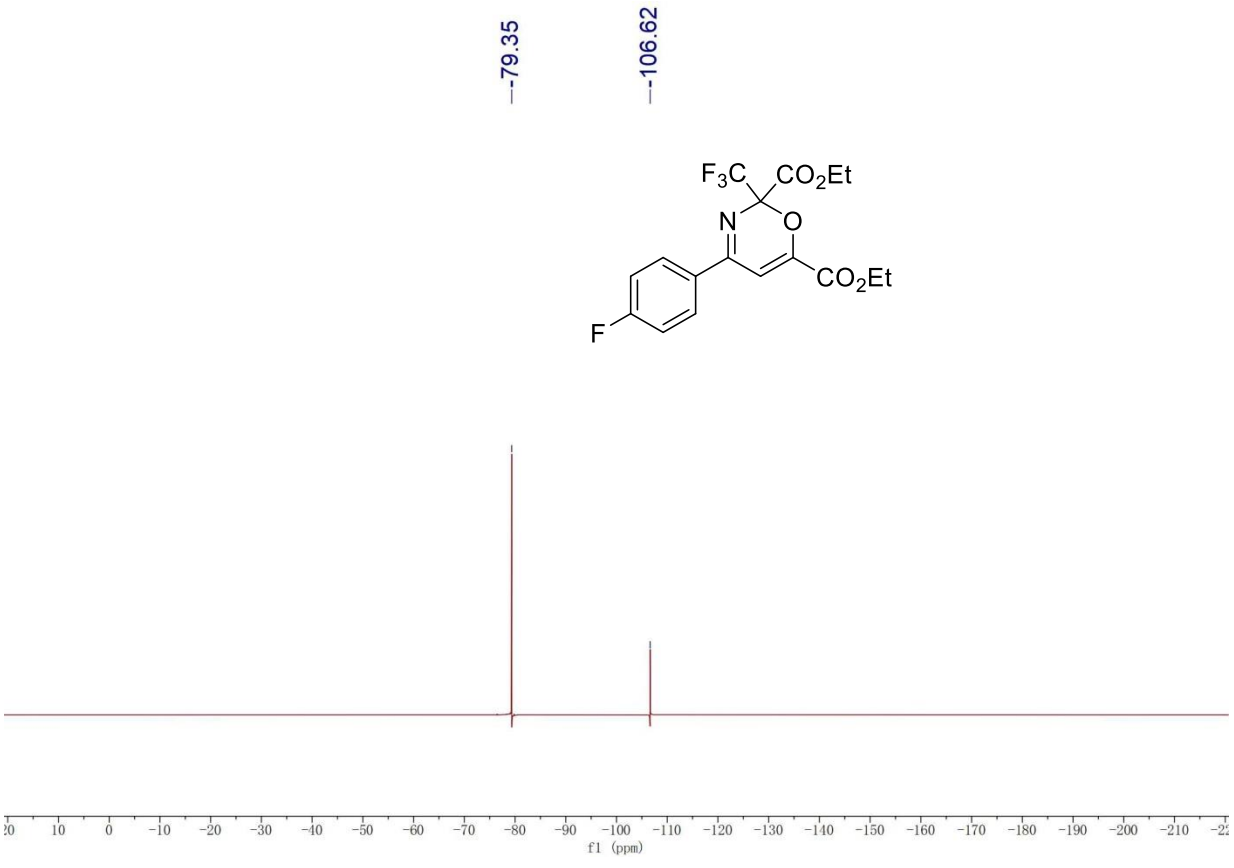
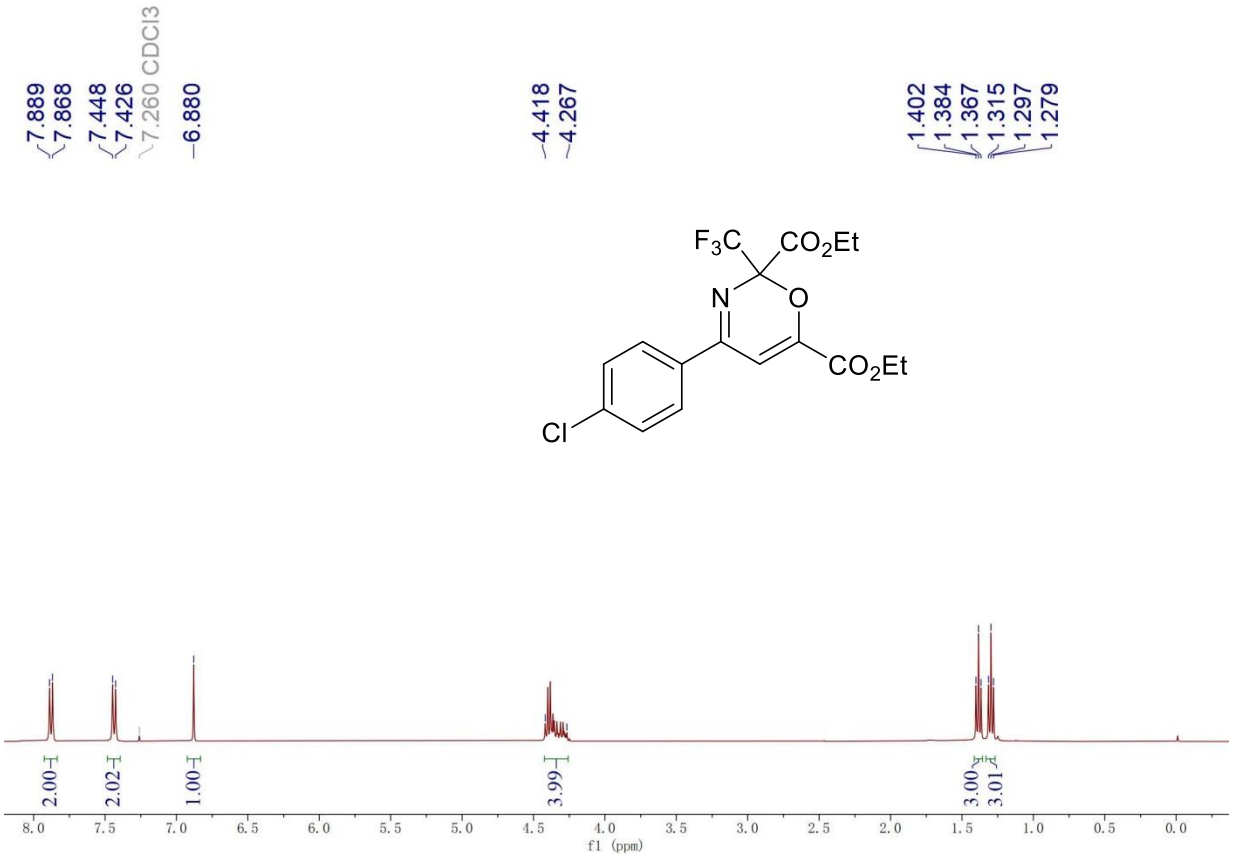
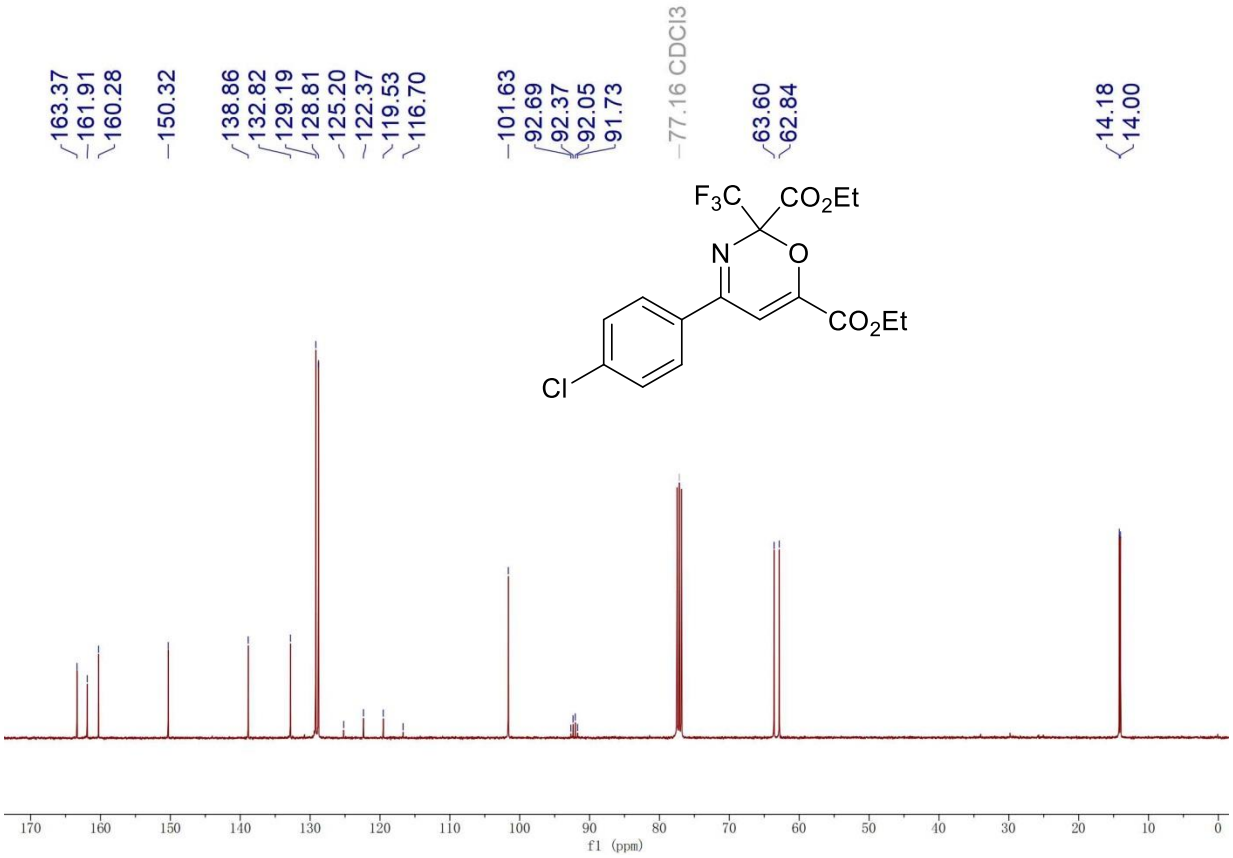
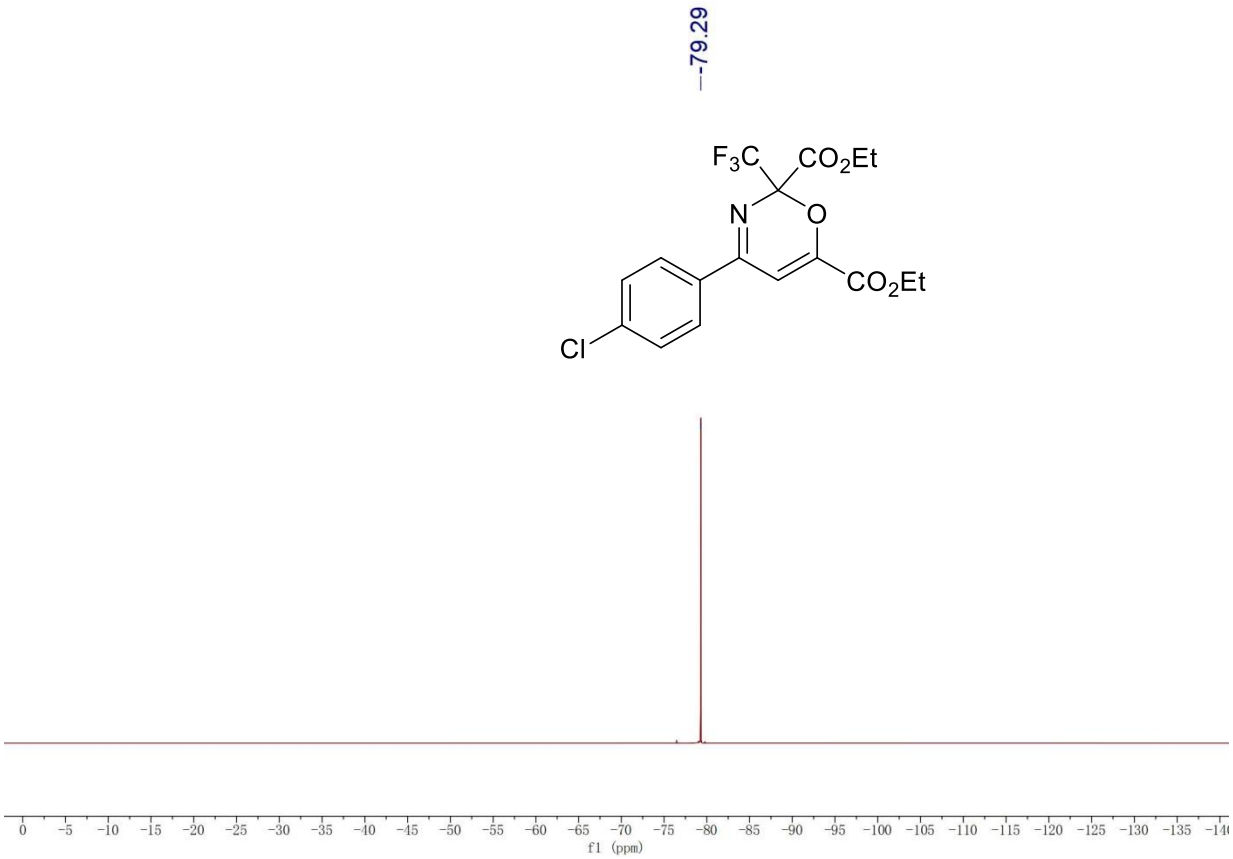
150.22
130.68
130.65
129.89
129.80
125.24
122.41
119.58
116.75
116.18
115.96
101.75
92.69
92.37
92.05
91.73
77.16 CDCl3
63.56
62.82
14.17
13.99
F3C
CO2Et
N
O
CO2Et
F
f1 (ppm)


-79.35
-106.62
F3C
CO2Et
N
O
CO2Et
F
f1 (ppm)

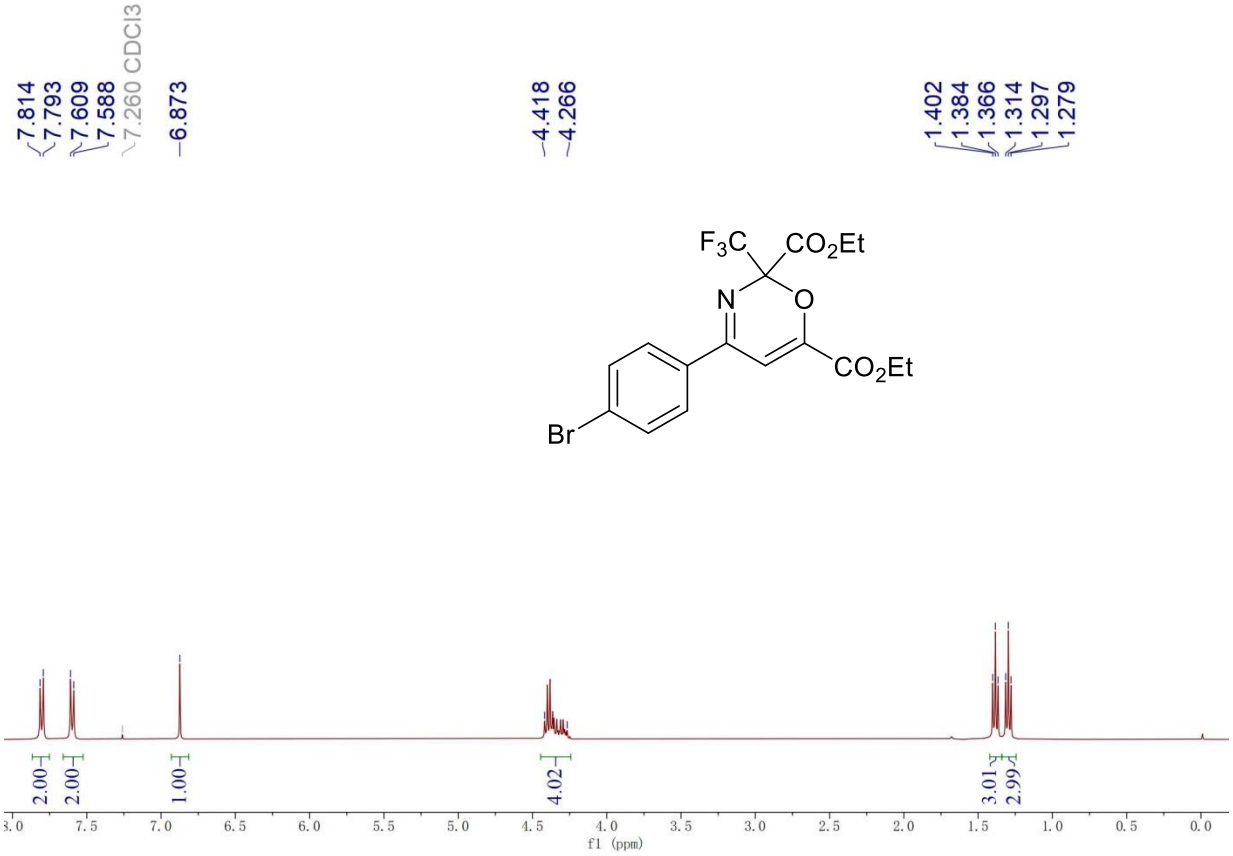
Diethyl 4-(4-chlorophenyl)-2-(trifluoromethyl)-2*H*-1,3-oxazine-2,6-dicarboxylate (3c)

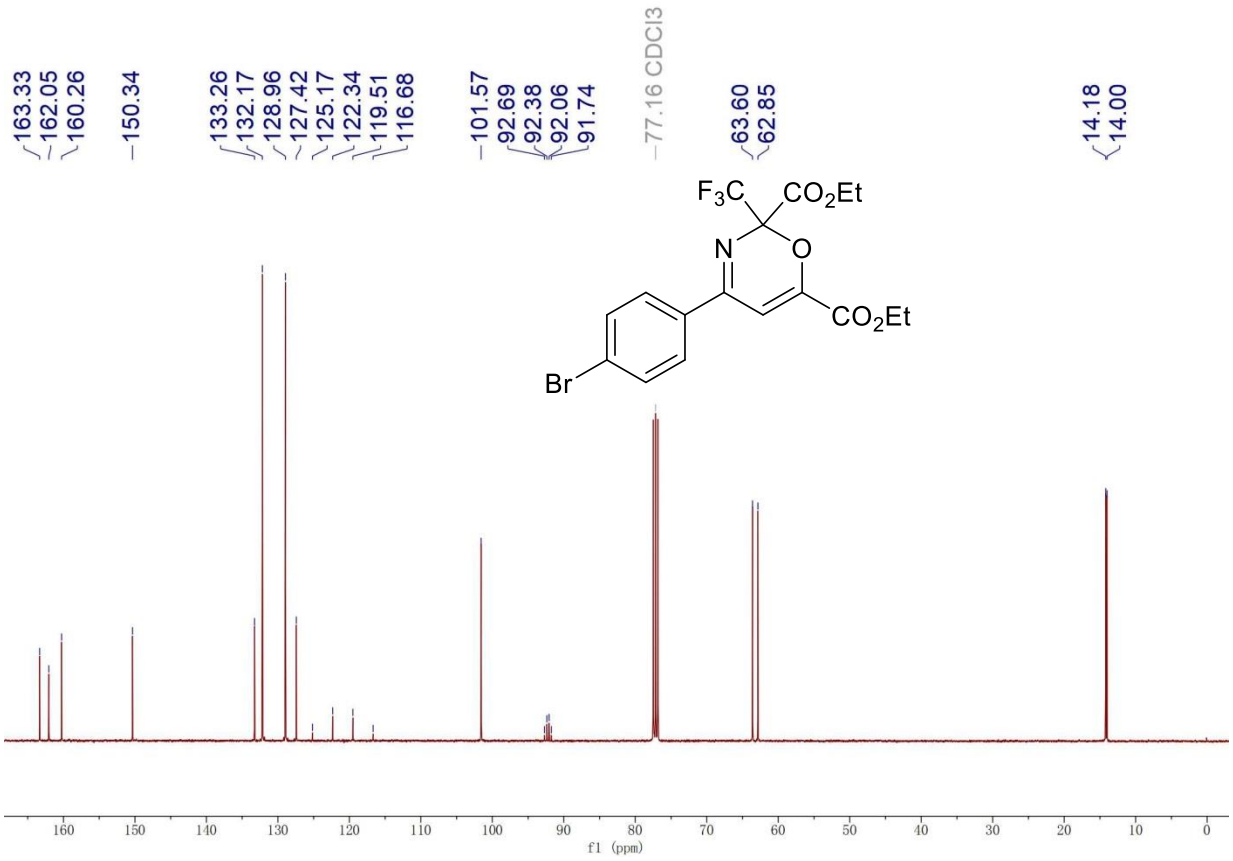






Diethyl 4-(4-bromophenyl)-2-(trifluoromethyl)-2*H*-1,3-oxazine-2,6-dicarboxylate (3d)

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160.26
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132.17
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127.42
125.17
122.34
119.51
116.68
101.57
92.69
92.38
92.06
91.74
77.16 CDCl3
63.60
62.85
14.18
14.00
F3C
CO2Et
N
O
CO2Et
Br
160
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130
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110
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90
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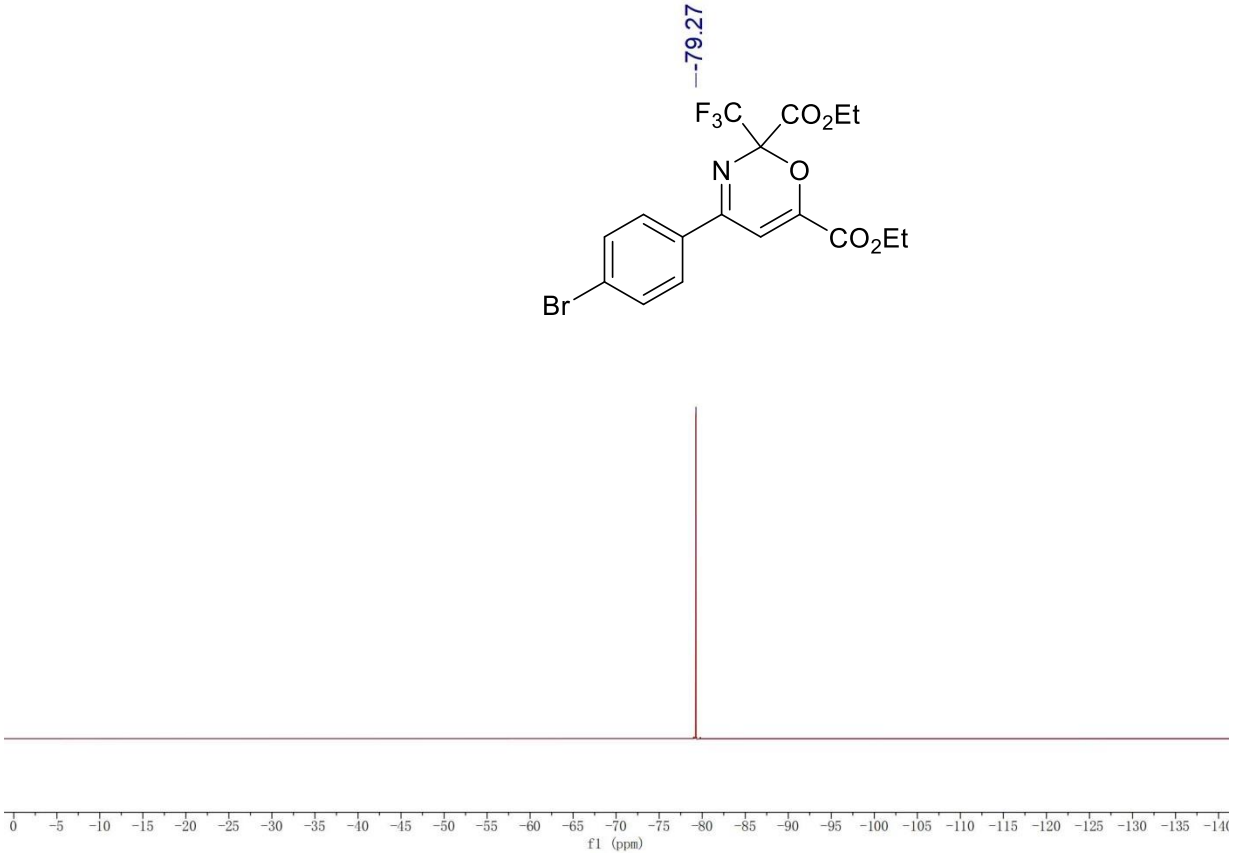
70
60
50
40
30
20
10
0
f1 (ppm)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CO2Et
N
O
CO2Et
Br
0
-5
-10
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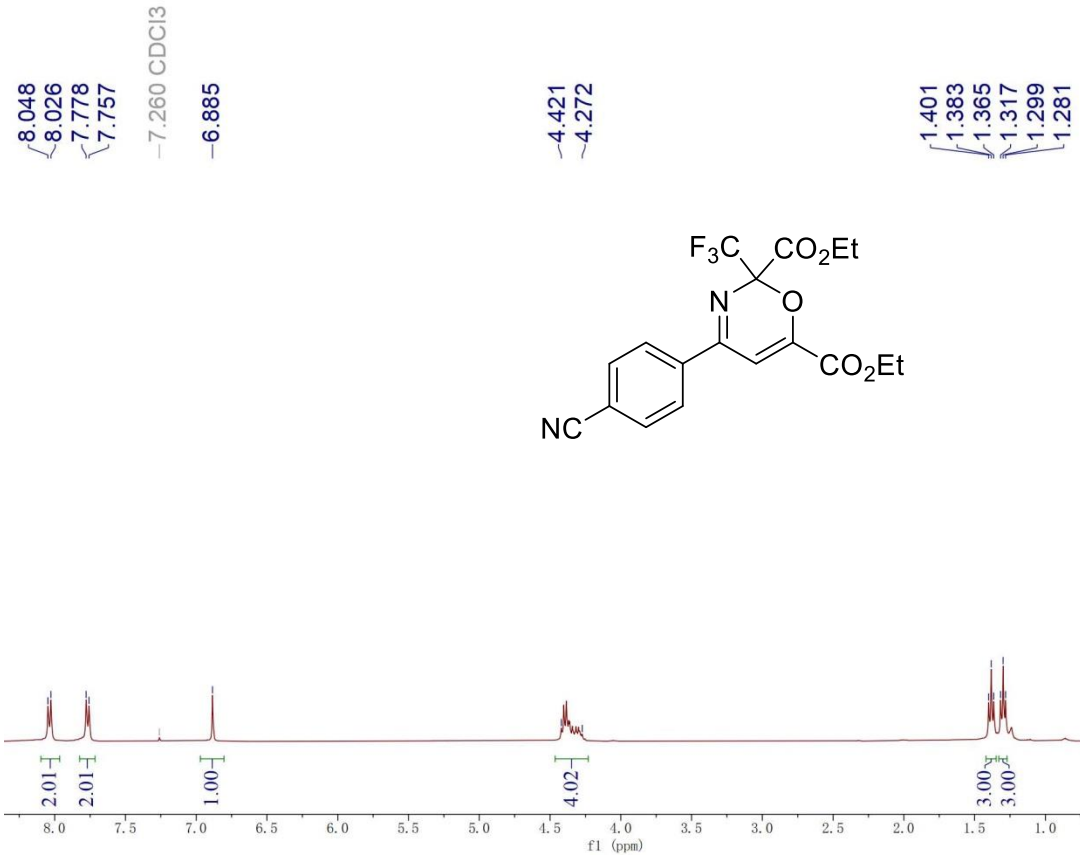
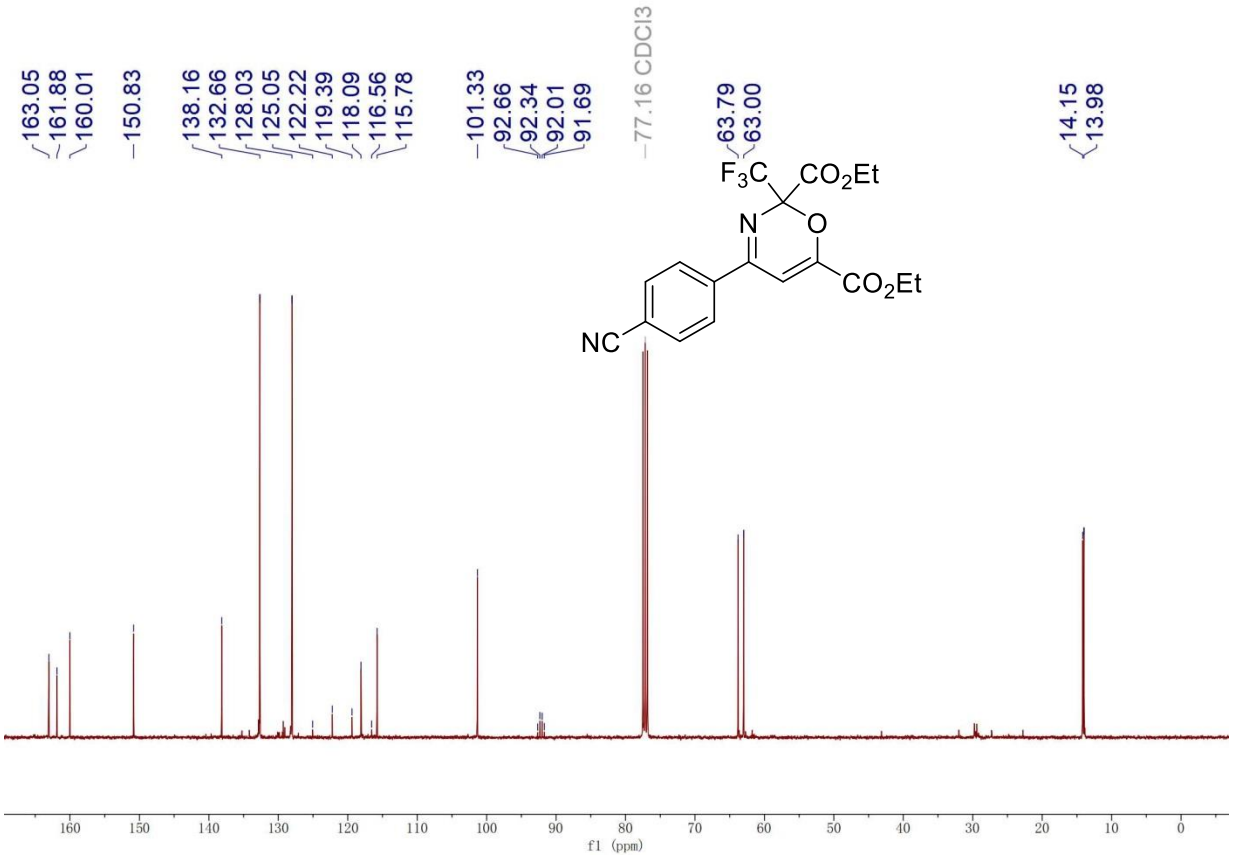
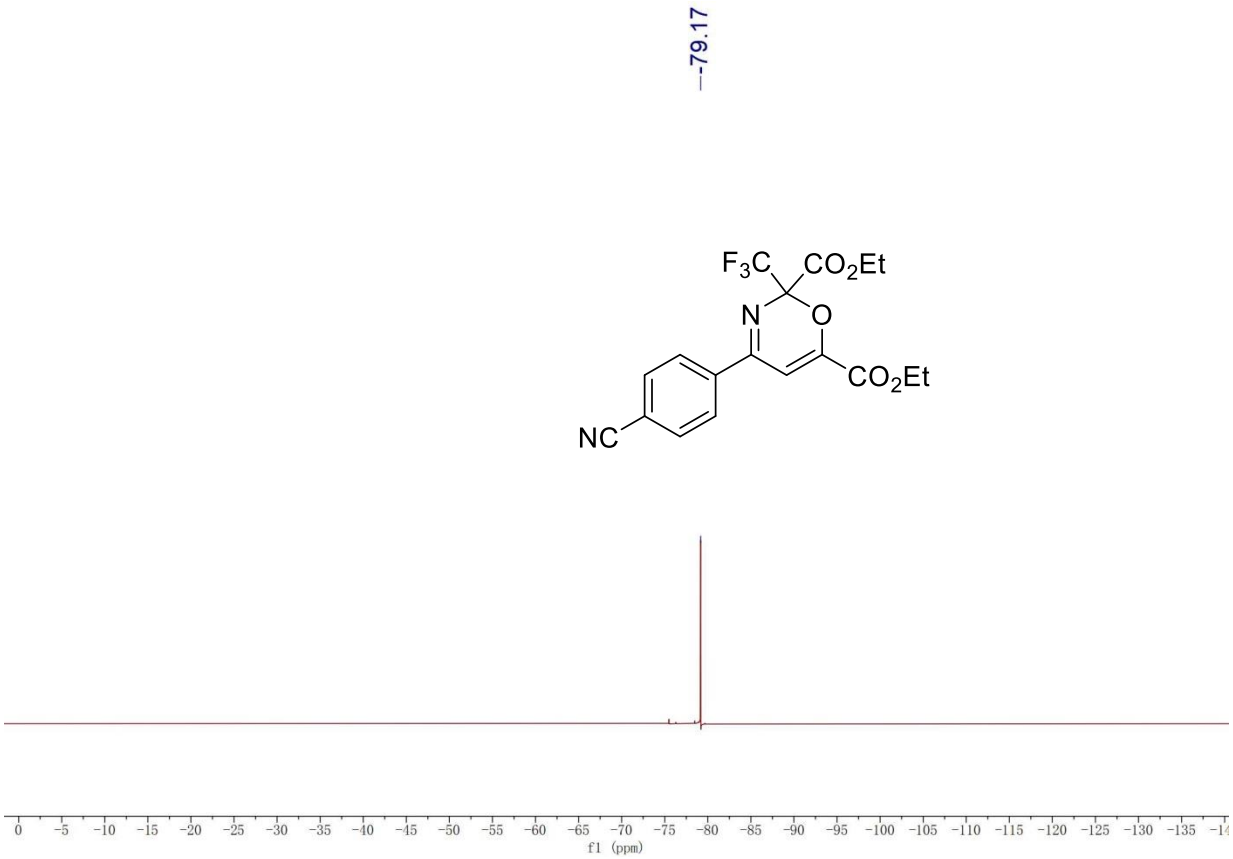
-50
-55
-60
-65
-70
-75
-80
-85
-90
-95
-100
-105
-110
-115
-120
-125
-130
-135
f1 (ppm)

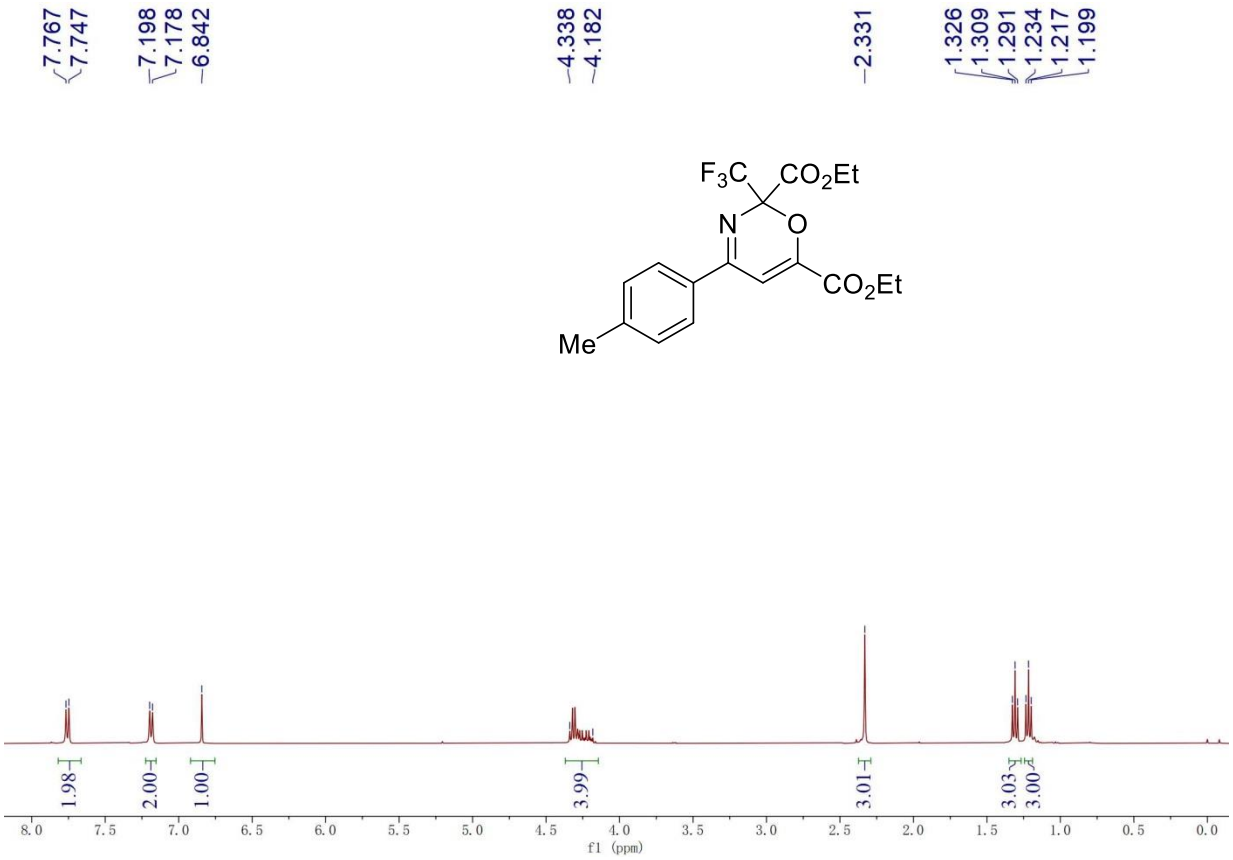
Diethyl 4-(4-cyanophenyl)-2-(trifluoromethyl)-2*H*-1,3-oxazine-2,6-dicarboxylate (3e)

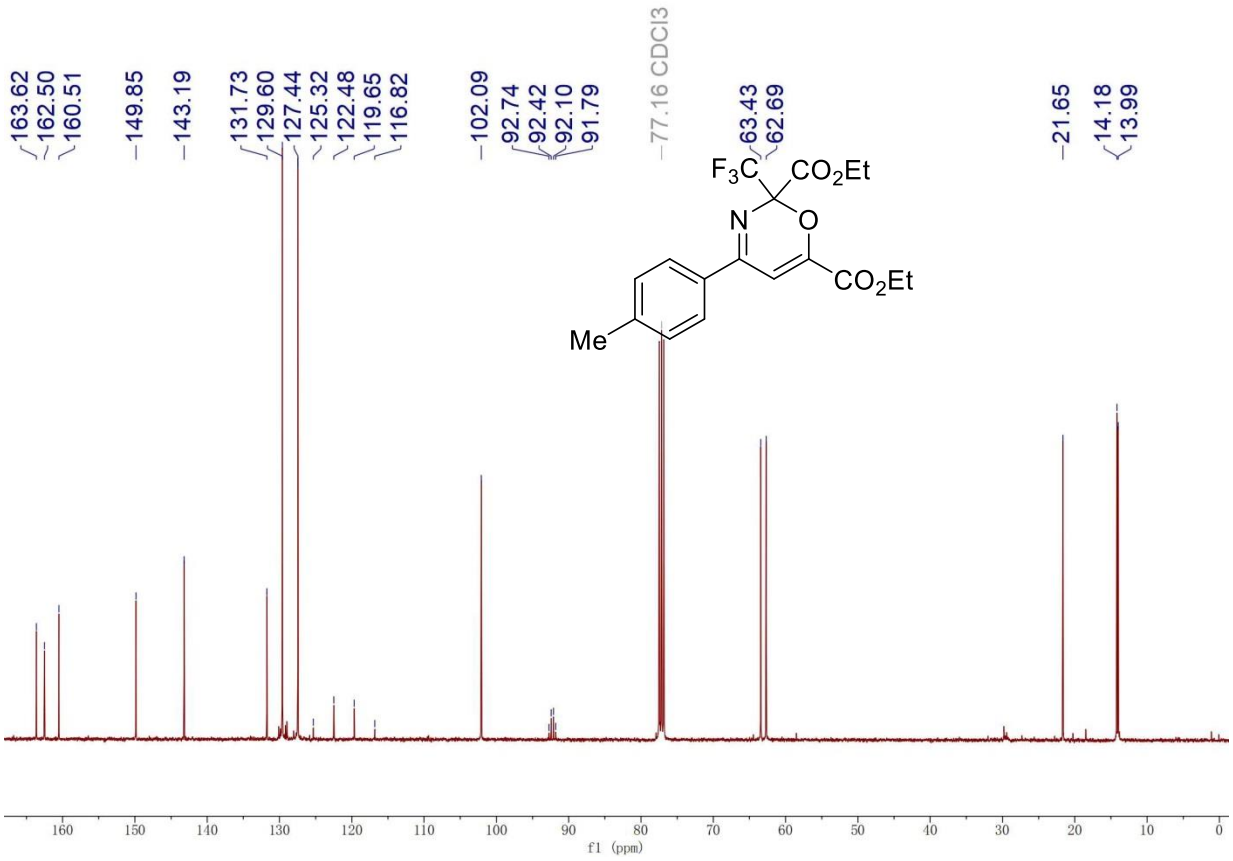






Diethyl 4-(p-tolyl)-2-(trifluoromethyl)-2*H*-1,3-oxazine-2,6-dicarboxylate (3f)

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127.44
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119.65
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92.42
92.10
91.79
77.16 CDCl3
63.43
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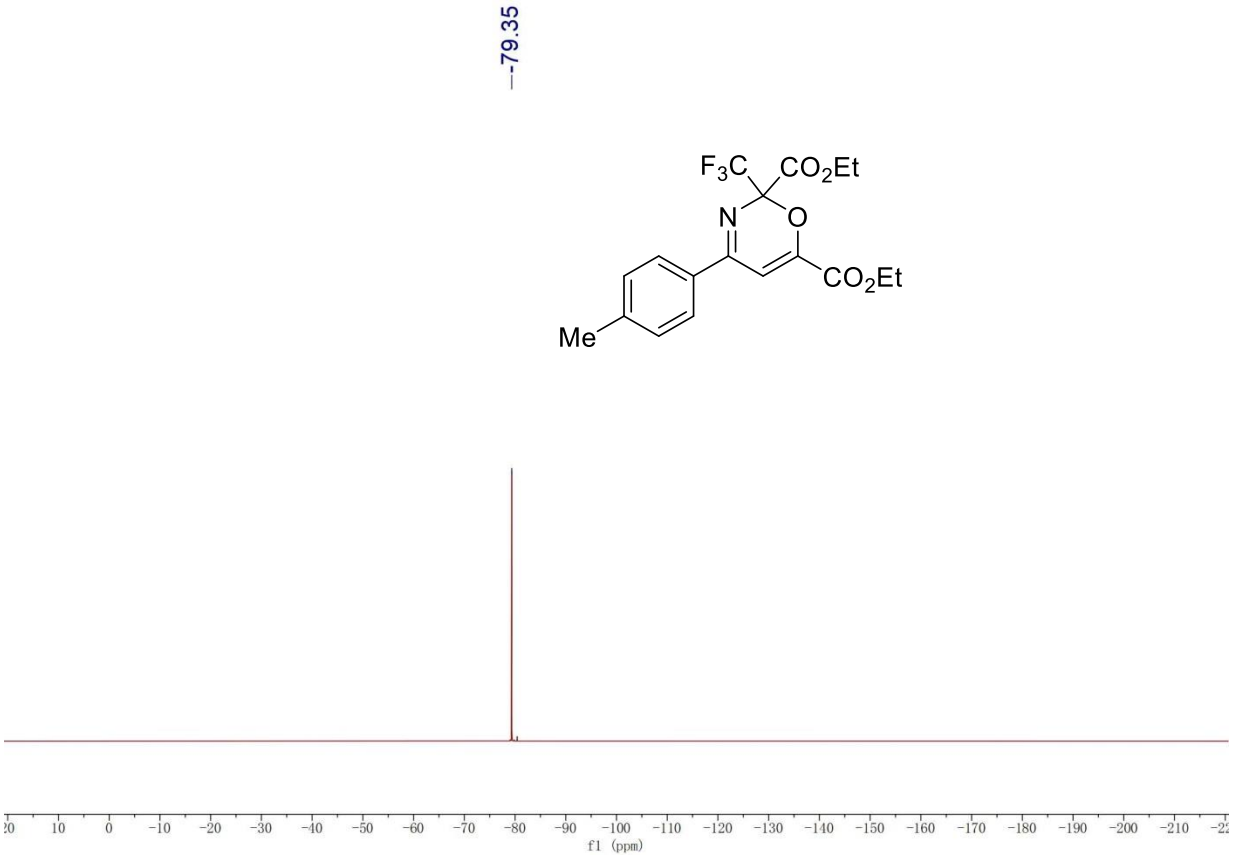
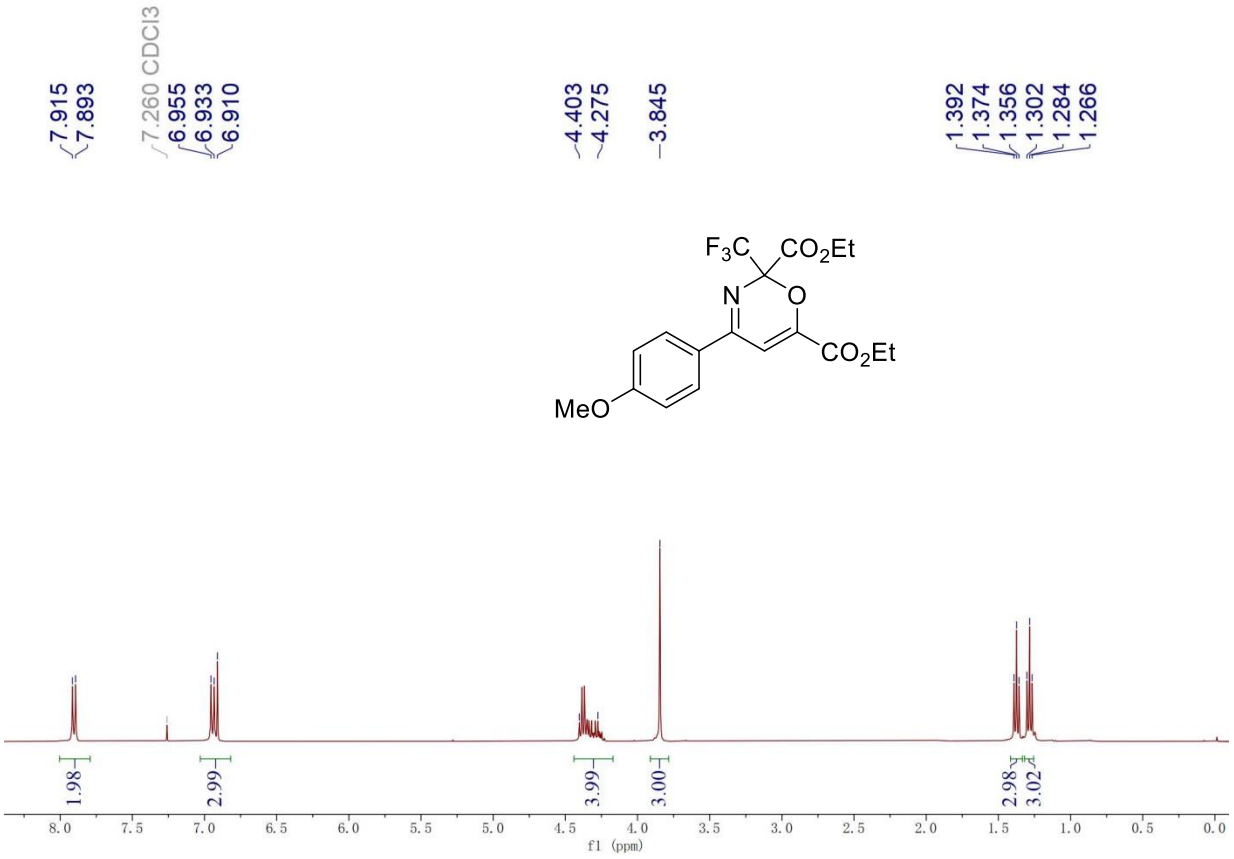
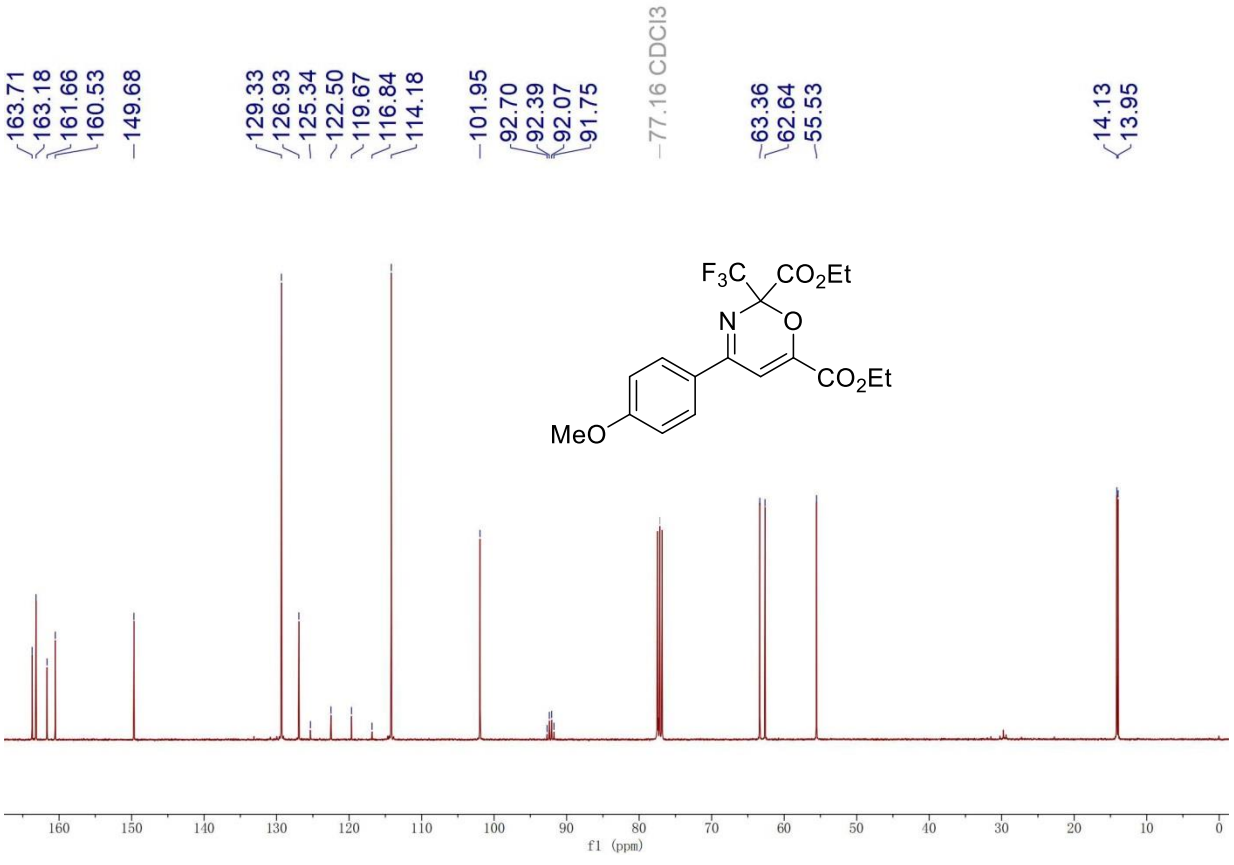
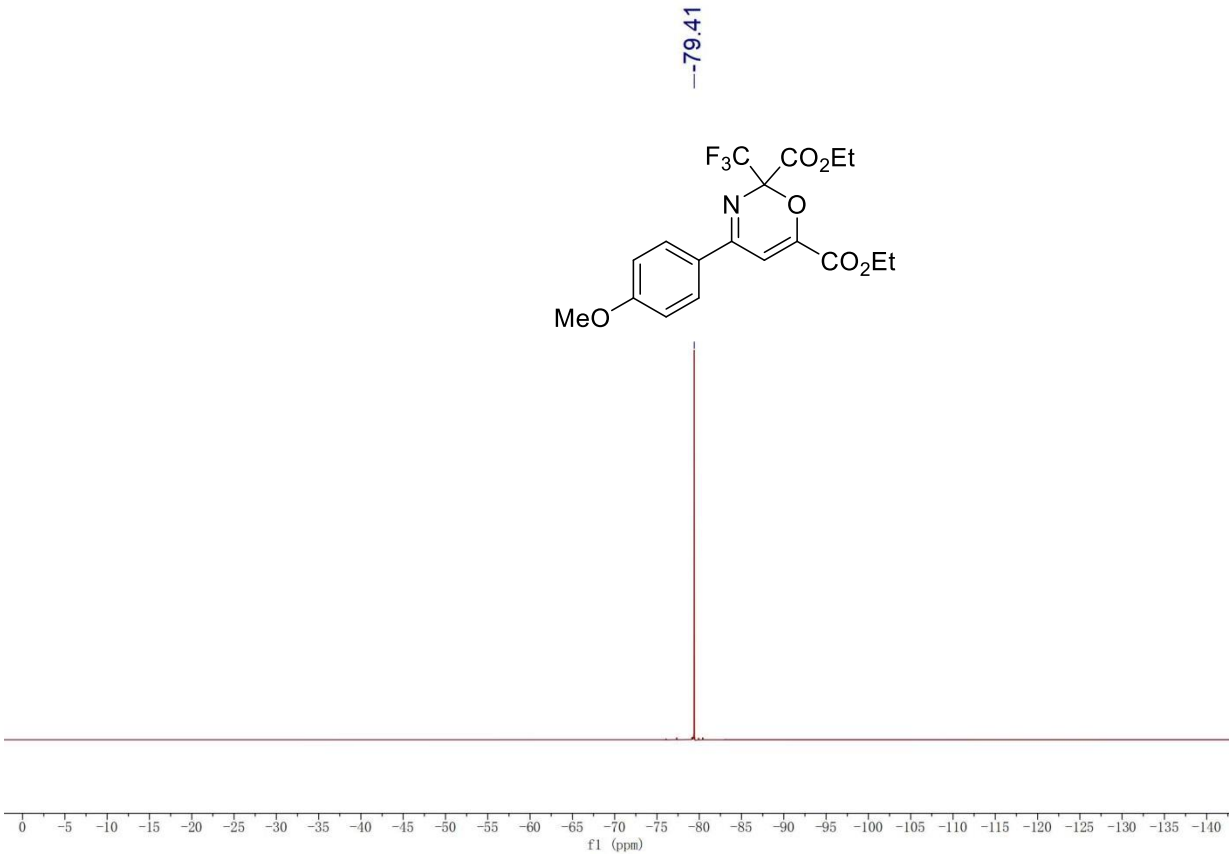
13.99
F3C
CO2Et
N
O
CO2Et
Me
f1 (ppm)


-79.35
F3C
CO2Et
N
O
CO2Et
Me
f1 (ppm)

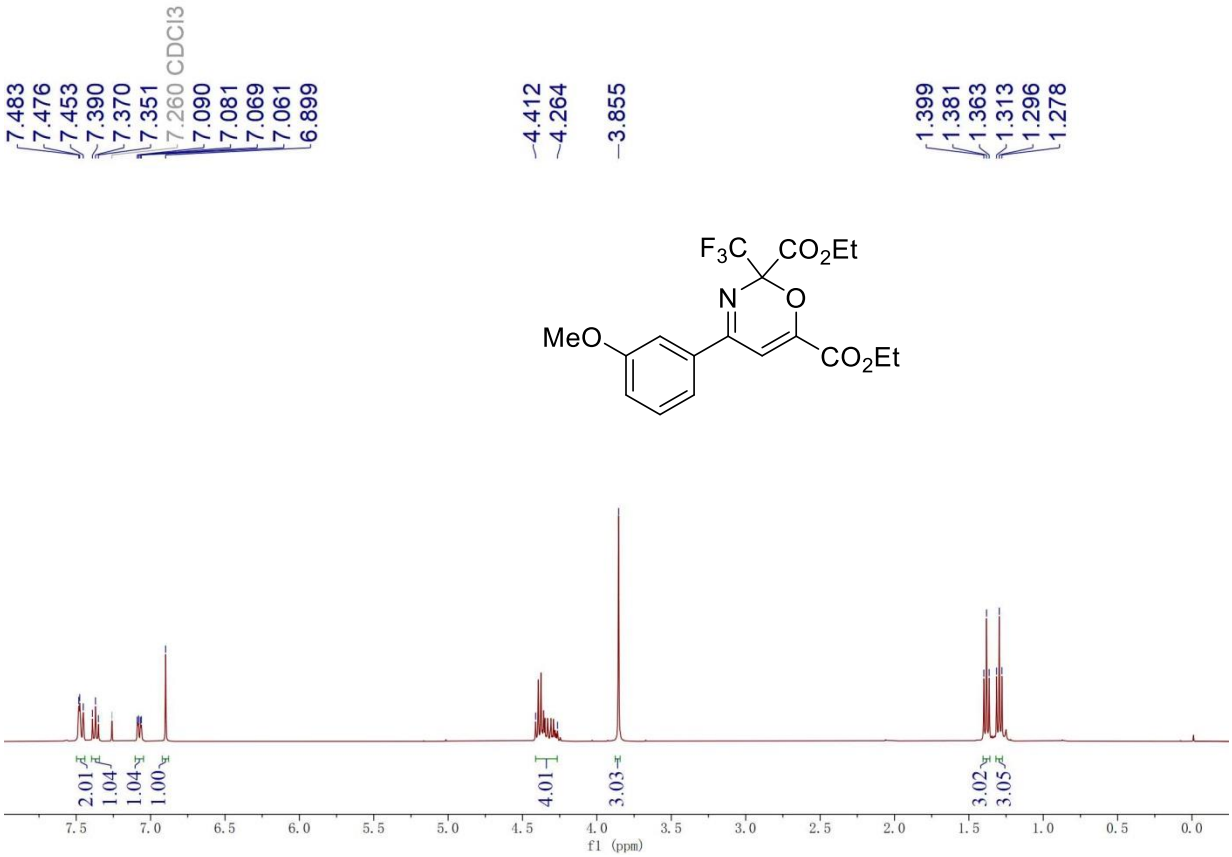
Diethyl 4-(4-methoxyphenyl)-2-(trifluoromethyl)-2*H*-1,3-oxazine-2,6-dicarboxylate (3g)







Diethyl 4-(3-methoxyphenyl)-2-(trifluoromethyl)-2*H*-1,3-oxazine-2,6-dicarboxylate (3h)

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91.73
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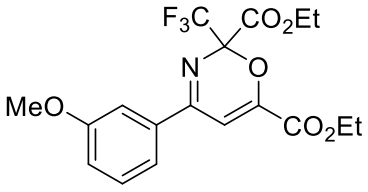
13.96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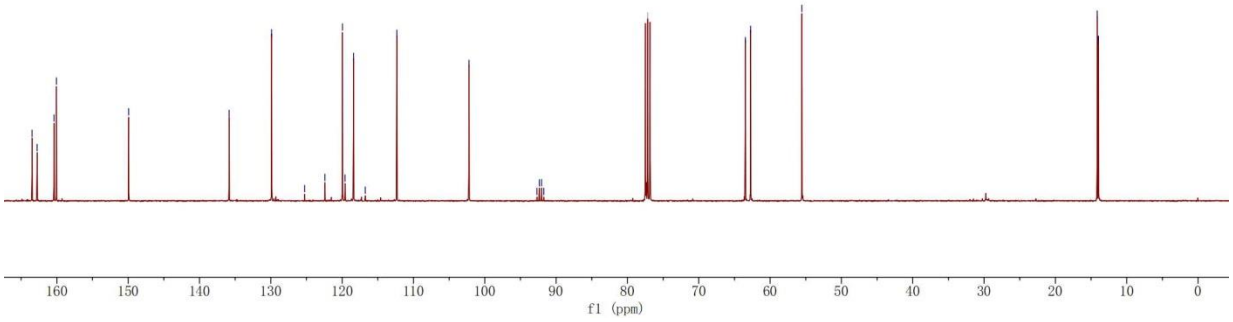
CO2Et
N
O
MeO
CO2Et


160
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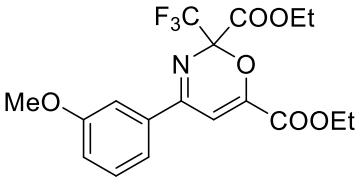
f1 (ppm)


-79.29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N
O
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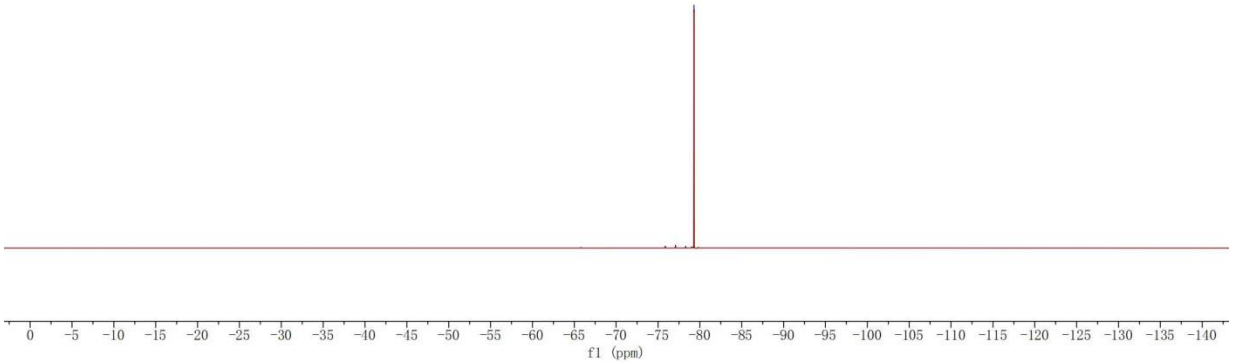
COOEt


0
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-85
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-95
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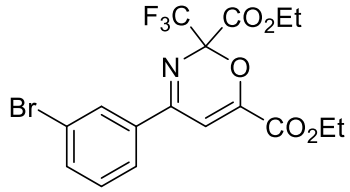
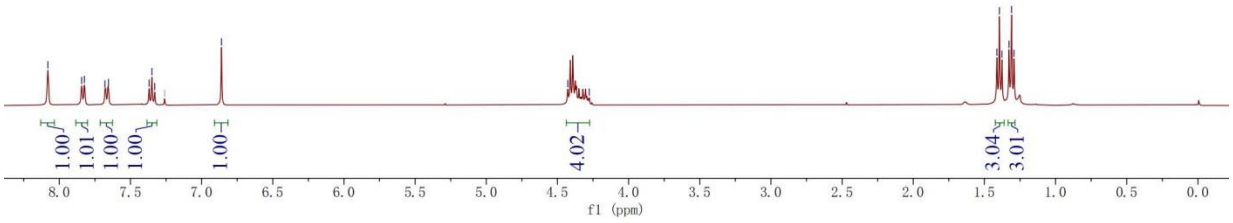
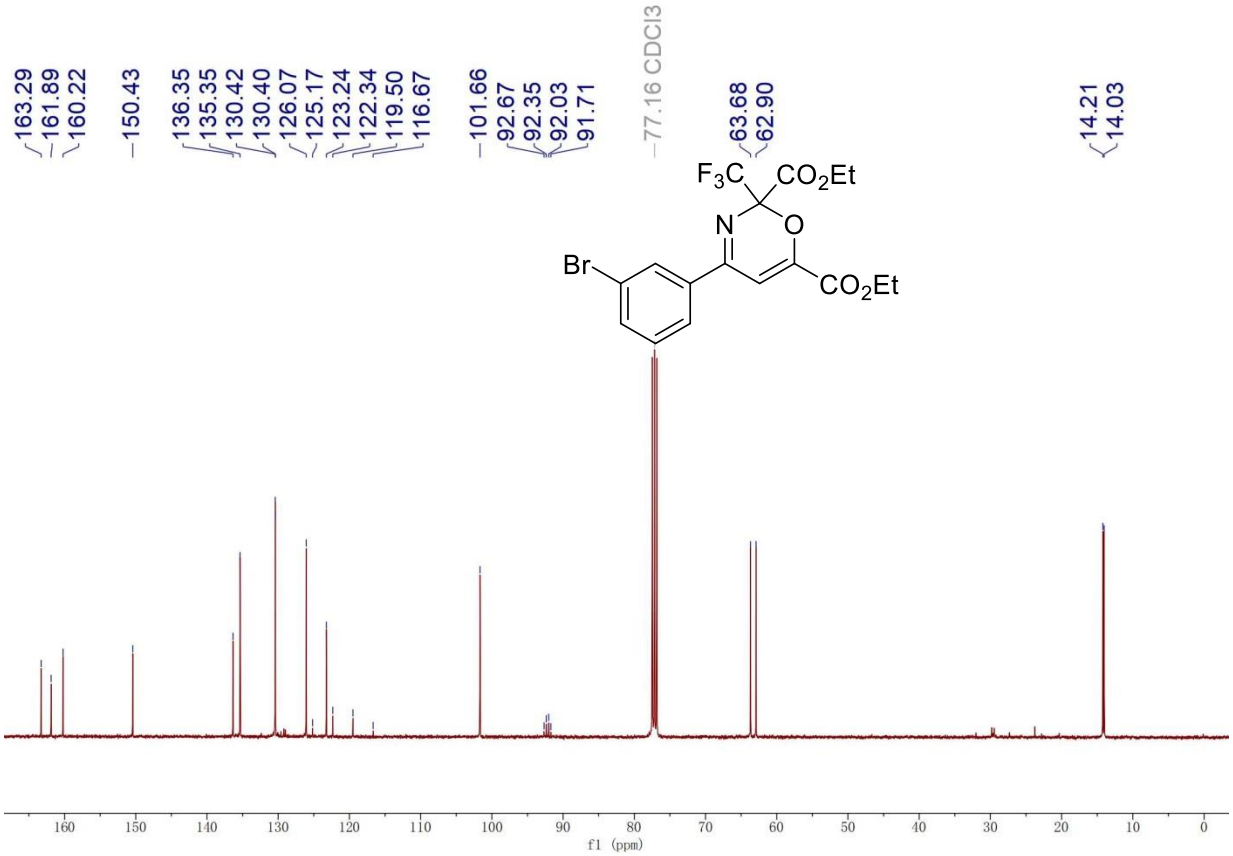
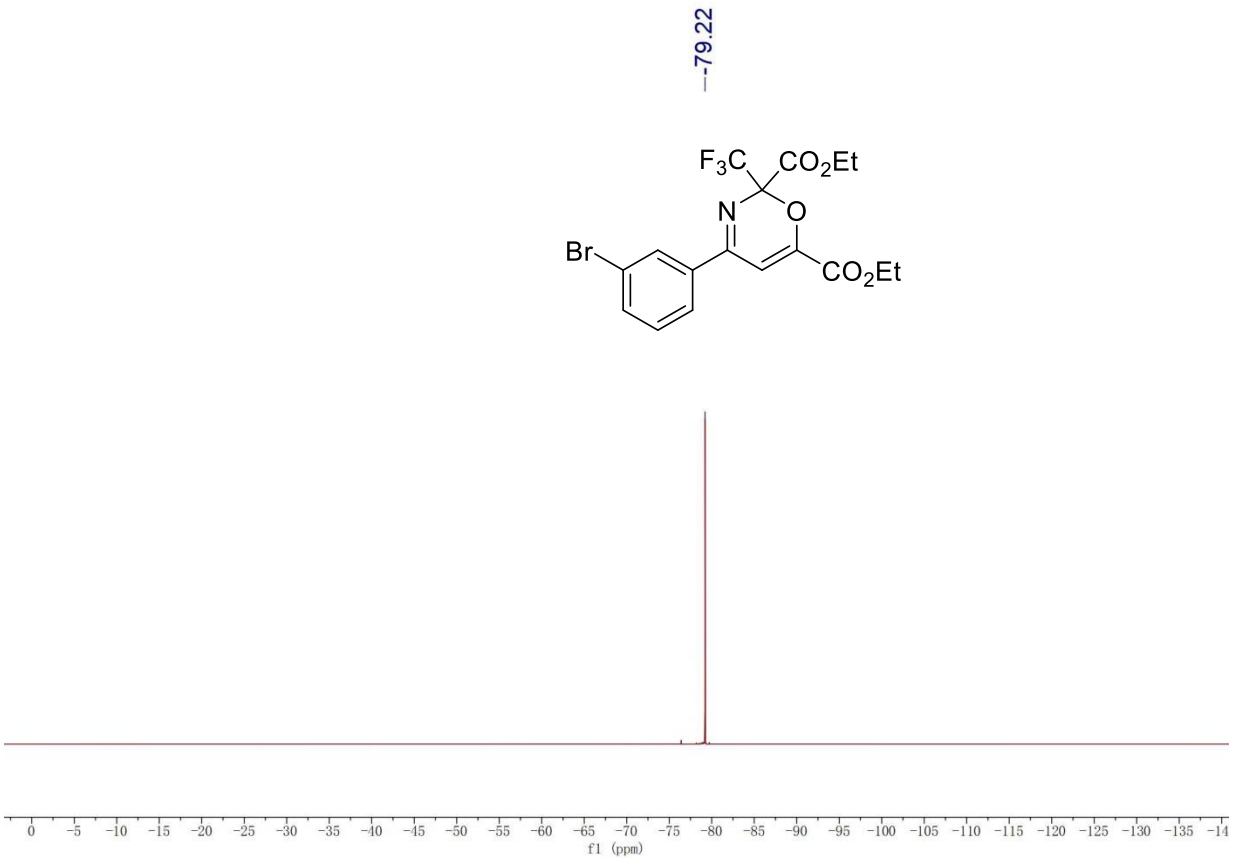
-105
-110
-115
-120
-125
-130
-135
-140
f1 (ppm)

Diethyl 4-(3-bromophenyl)-2-(trifluoromethyl)-2*H*-1,3-oxazine-2,6-dicarboxylate (3i)

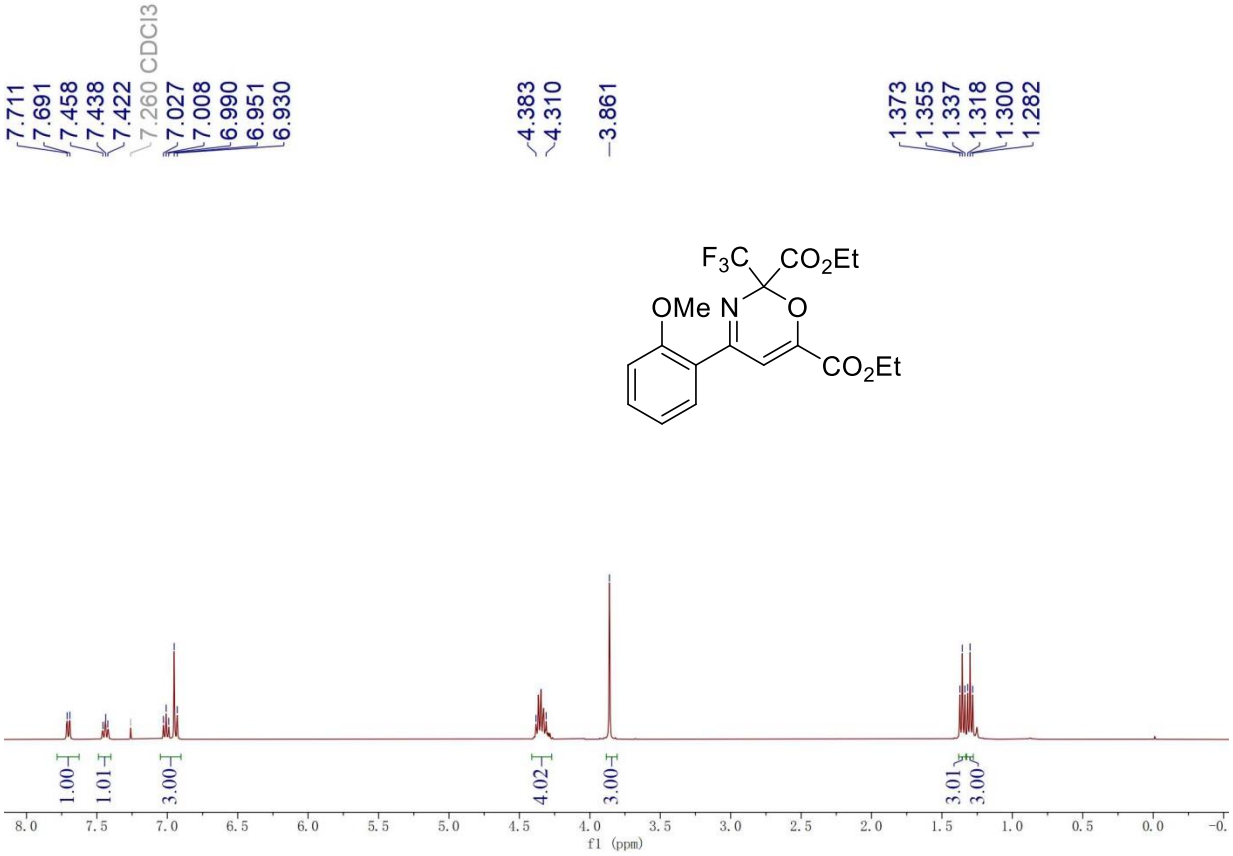


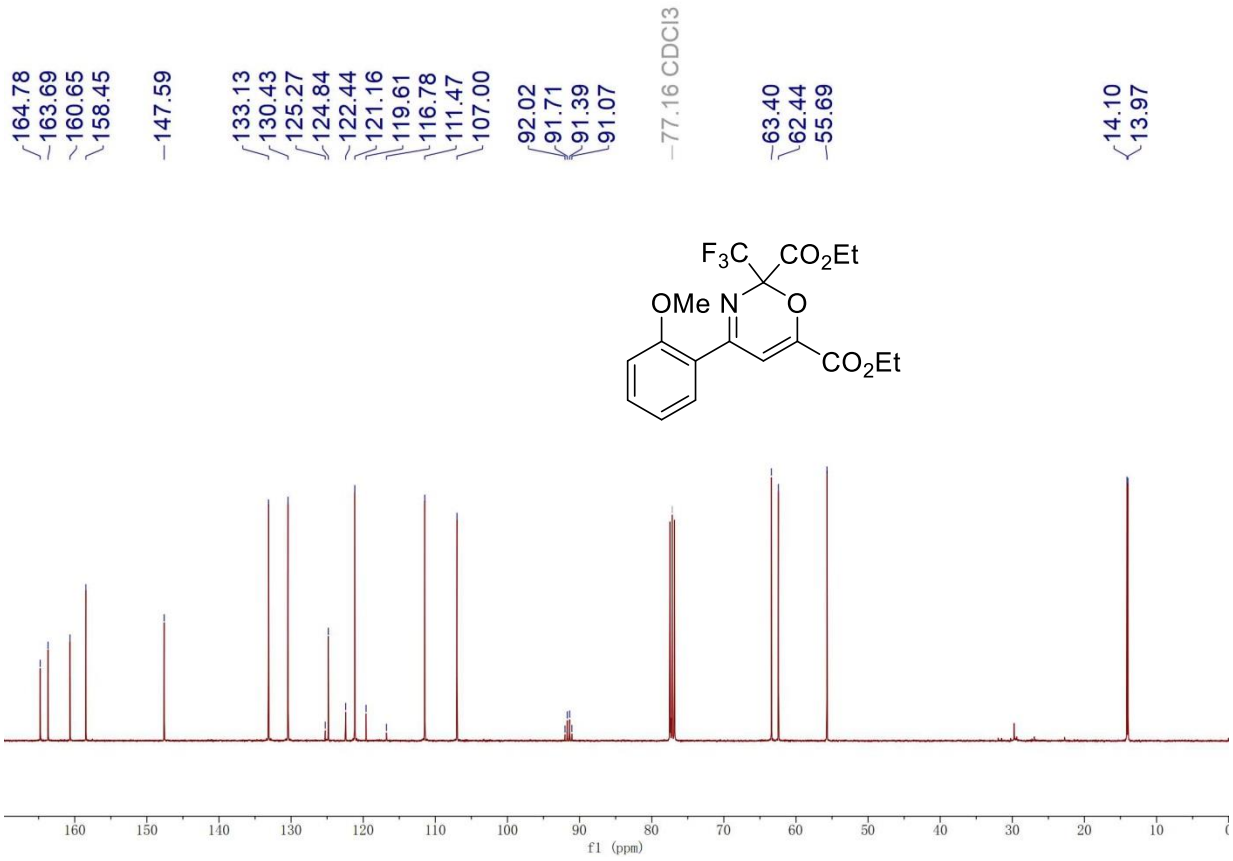






Diethyl 4-(2-methoxyphenyl)-2-(trifluoromethyl)-2*H*-1,3-oxazine-2,6-dicarboxylate (3j)

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163.69
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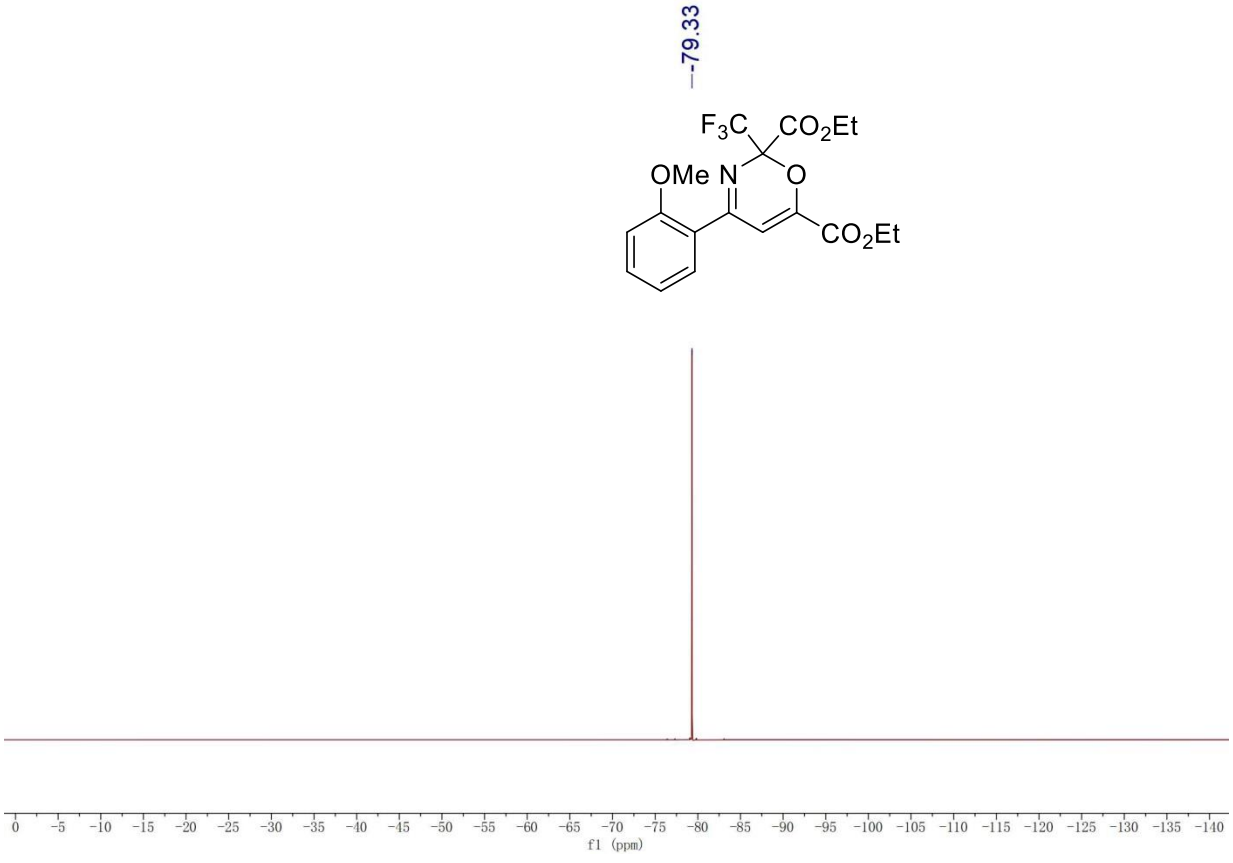
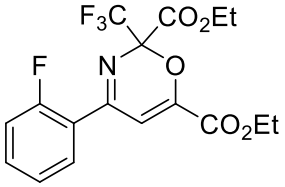
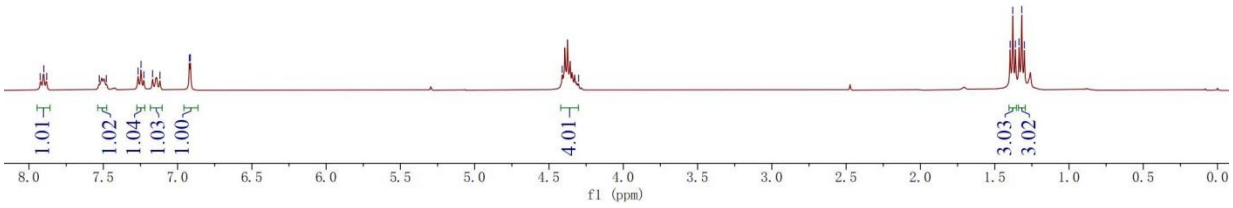
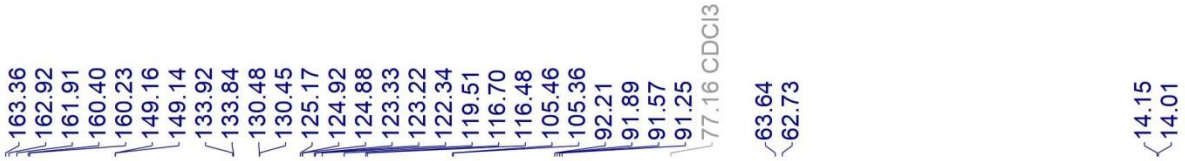
147.59
133.13
130.43
125.27
124.84
122.44
121.16
119.61
116.78
111.47
107.00
92.02
91.71
91.39
91.07
77.16 CDCl3
63.40
62.44
55.69
14.10
13.97
F3C
CO2Et
OMe
N
O
CO2Et
f1 (ppm)

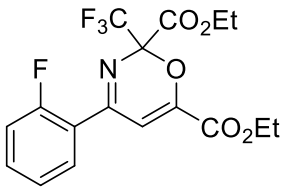

-79.33
F3C
CO2Et
OMe
N
O
CO2Et
f1 (ppm)

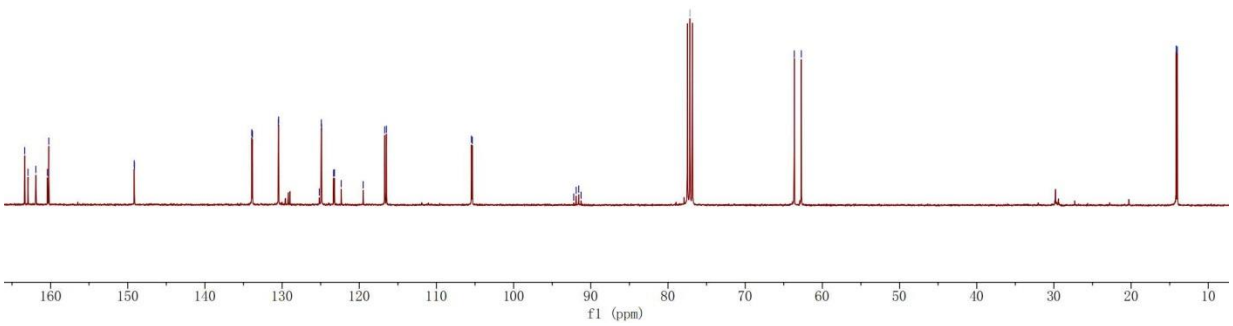
Diethyl 4-(2-fluorophenyl)-2-(trifluoromethyl)-2*H*-1,3-oxazine-2,6-dicarboxylate (3k)

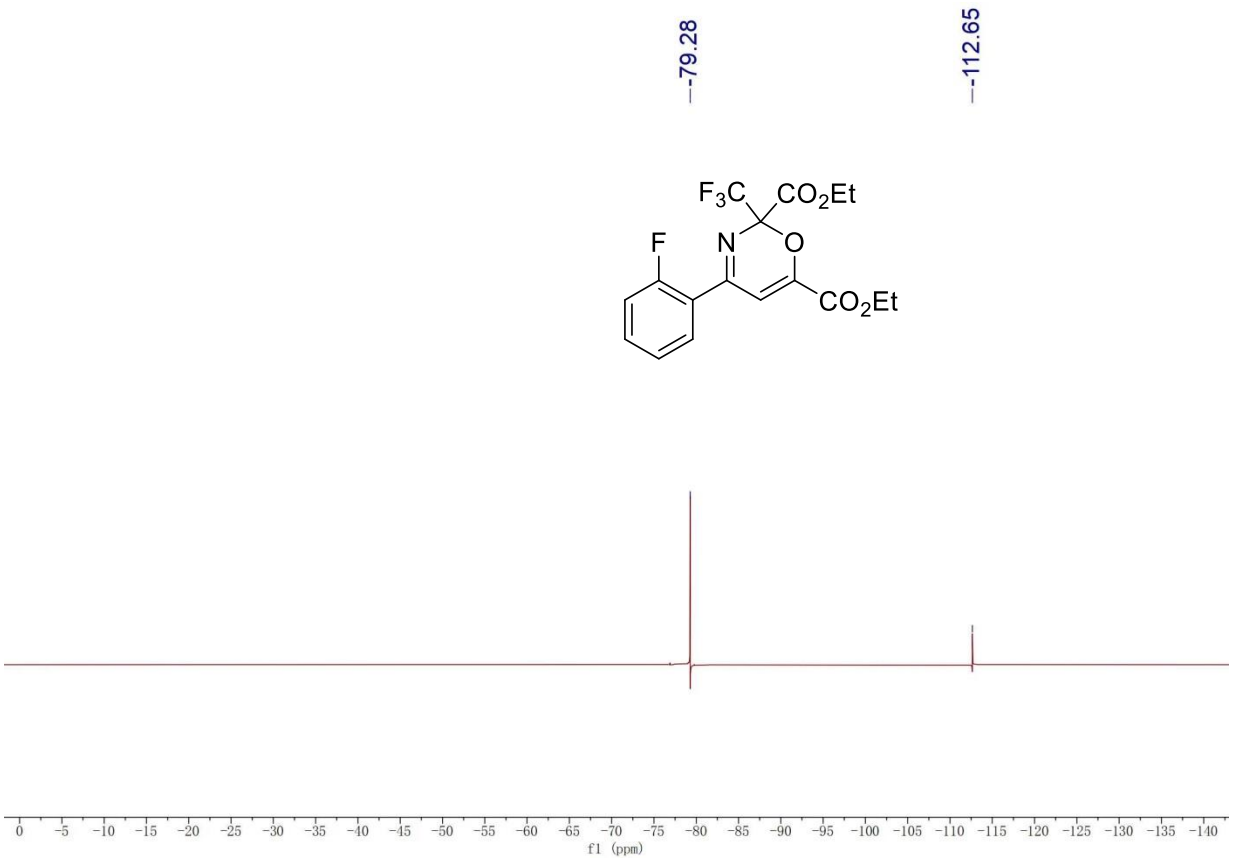




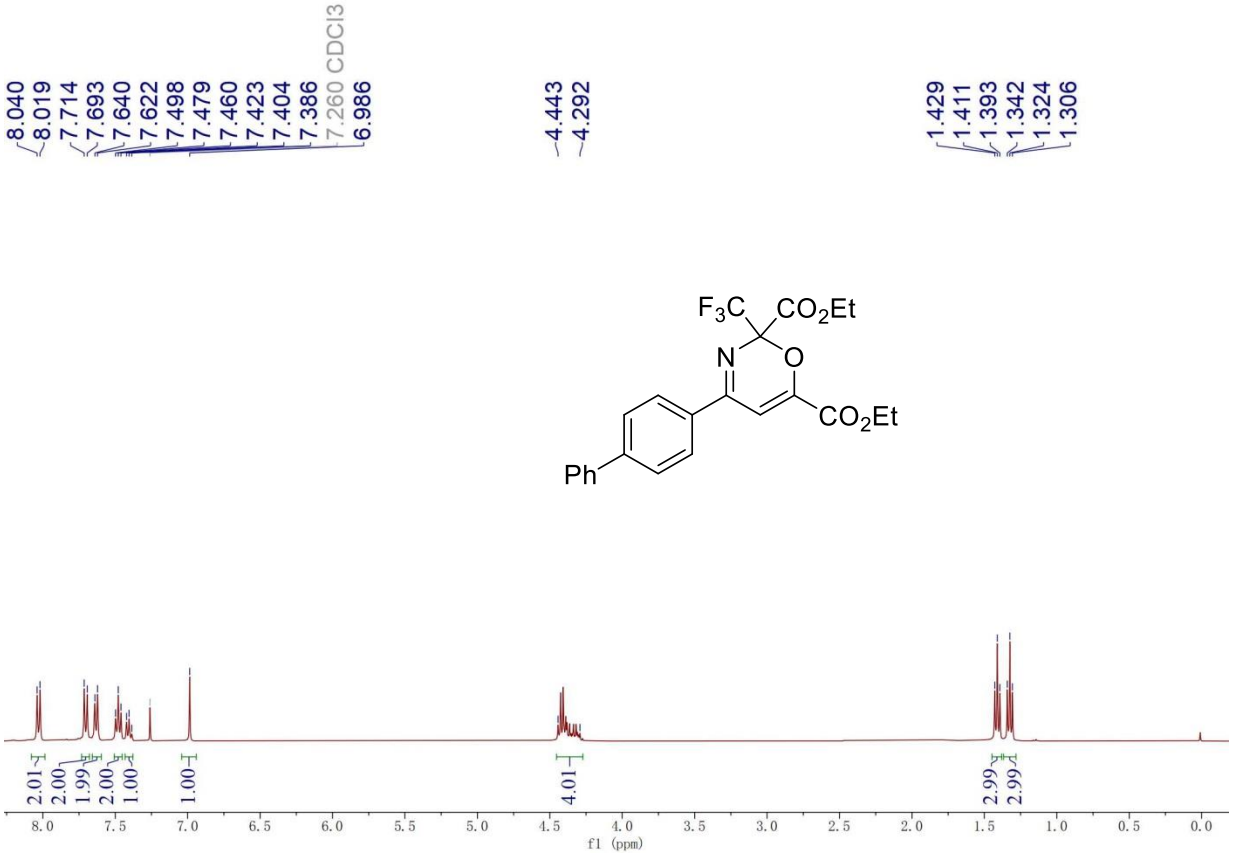


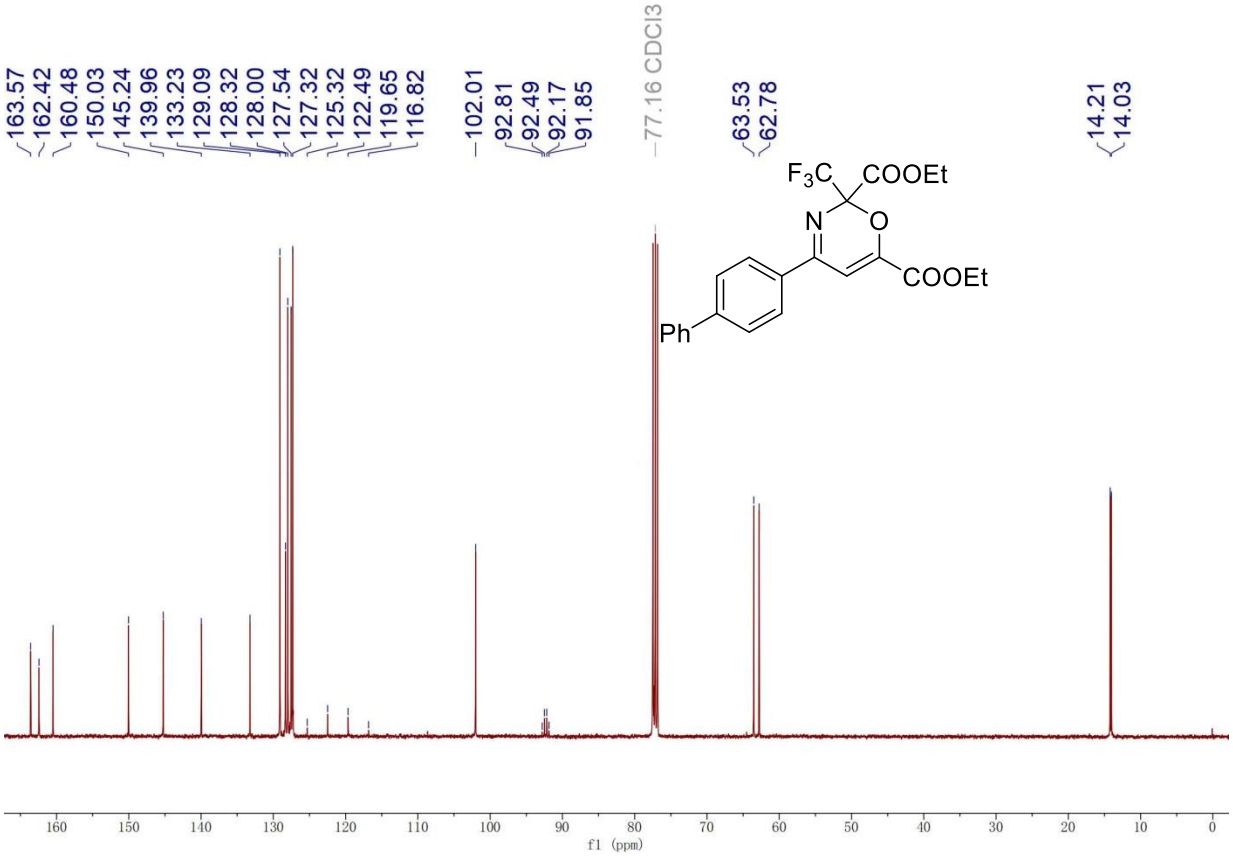






Diethyl 4-([1,1'-biphenyl]-4-yl)-2-(trifluoromethyl)-2*H*-1,3-oxazine-2,6-dicarboxylate (3l)

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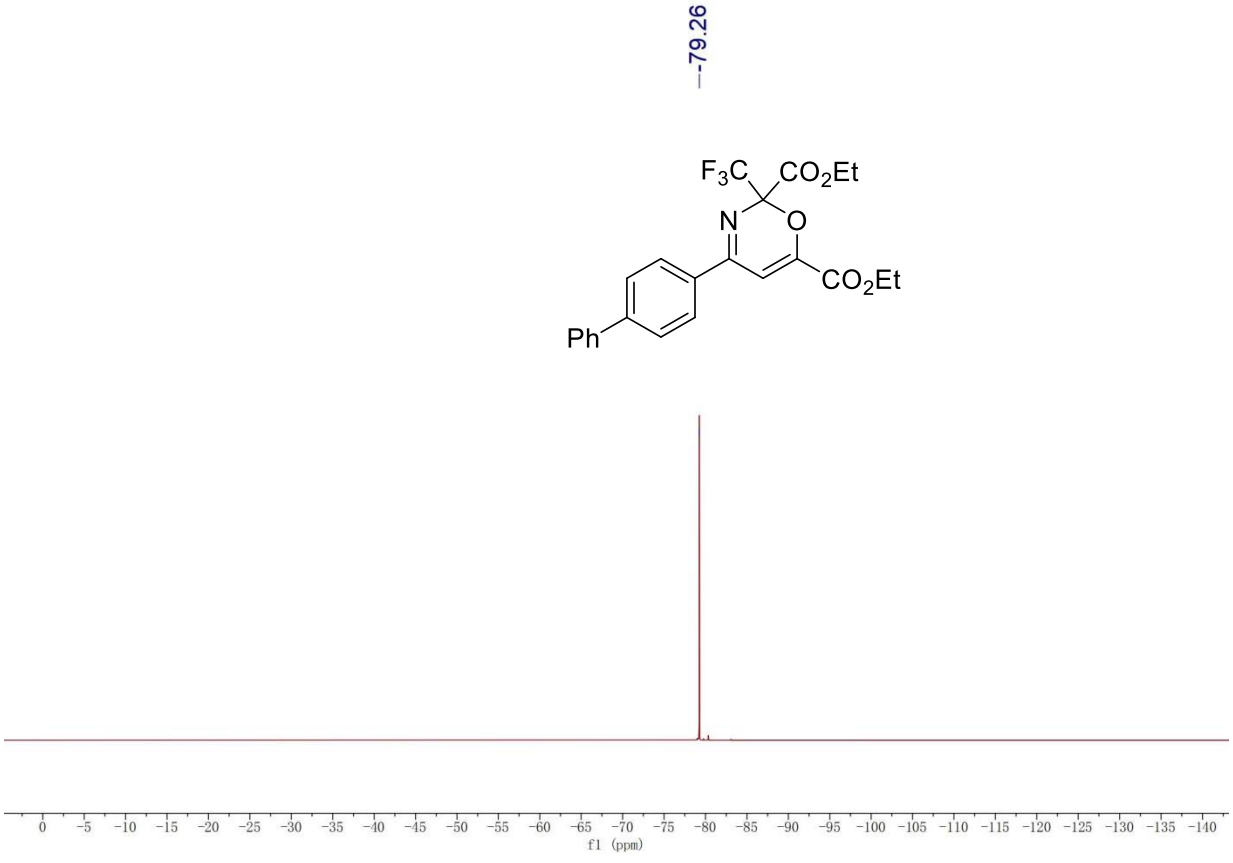
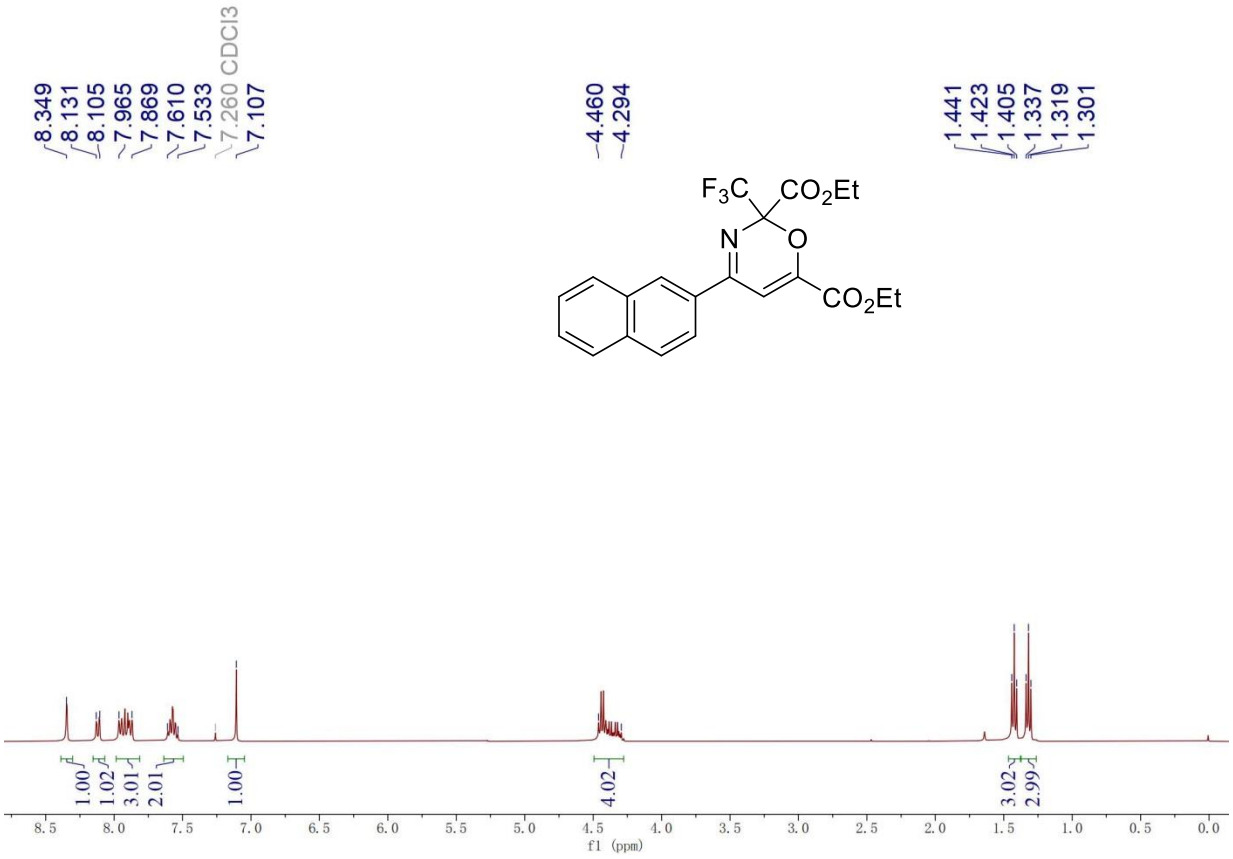
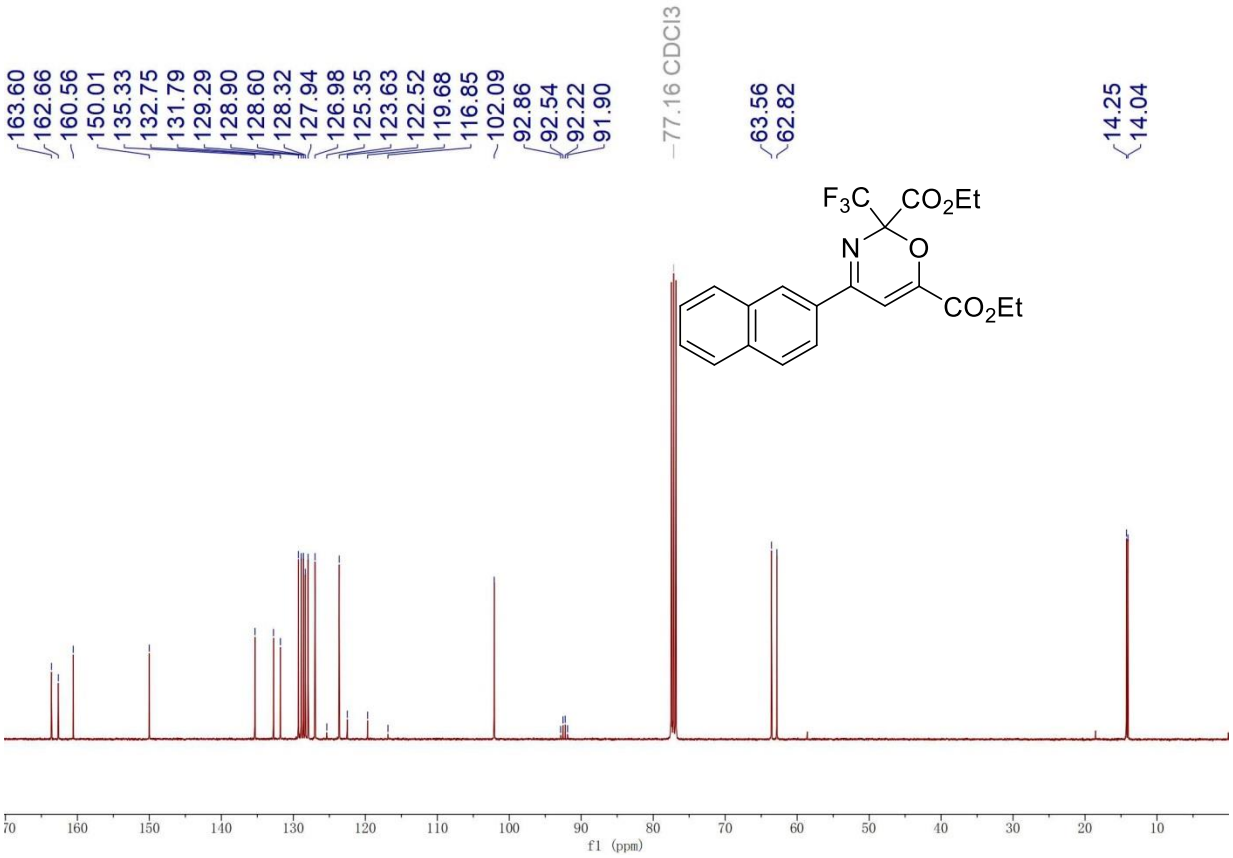
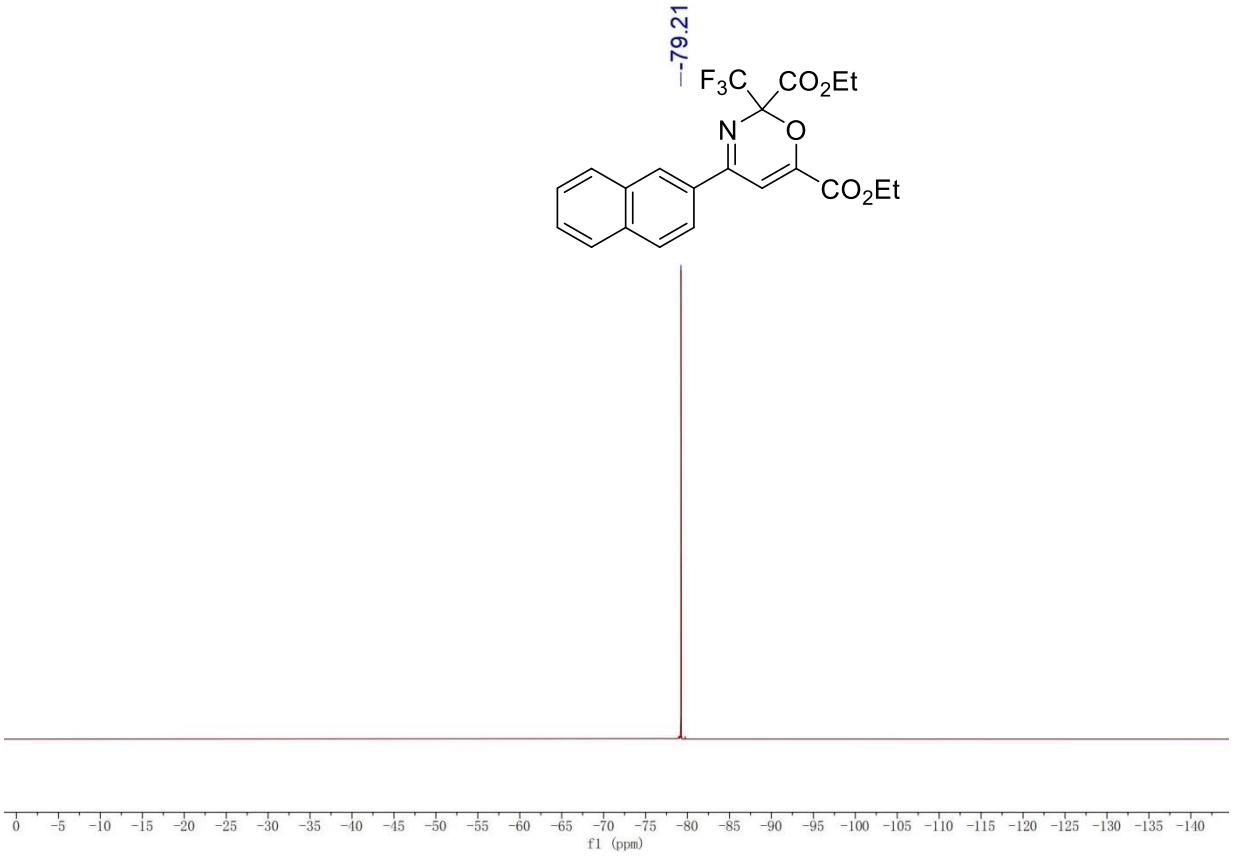
162.42
160.48
150.03
145.24
139.96
133.23
129.09
128.32
128.00
127.54
127.32
125.32
122.49
119.65
116.82
102.01
92.81
92.49
92.17
91.85
77.16 CDCl3
63.53
62.78
14.21
14.03
F3C
COOEt
N
O
COOEt
Ph
f1 (ppm)


-79.26
F3C
CO2Et
N
O
CO2Et
Ph
f1 (ppm)

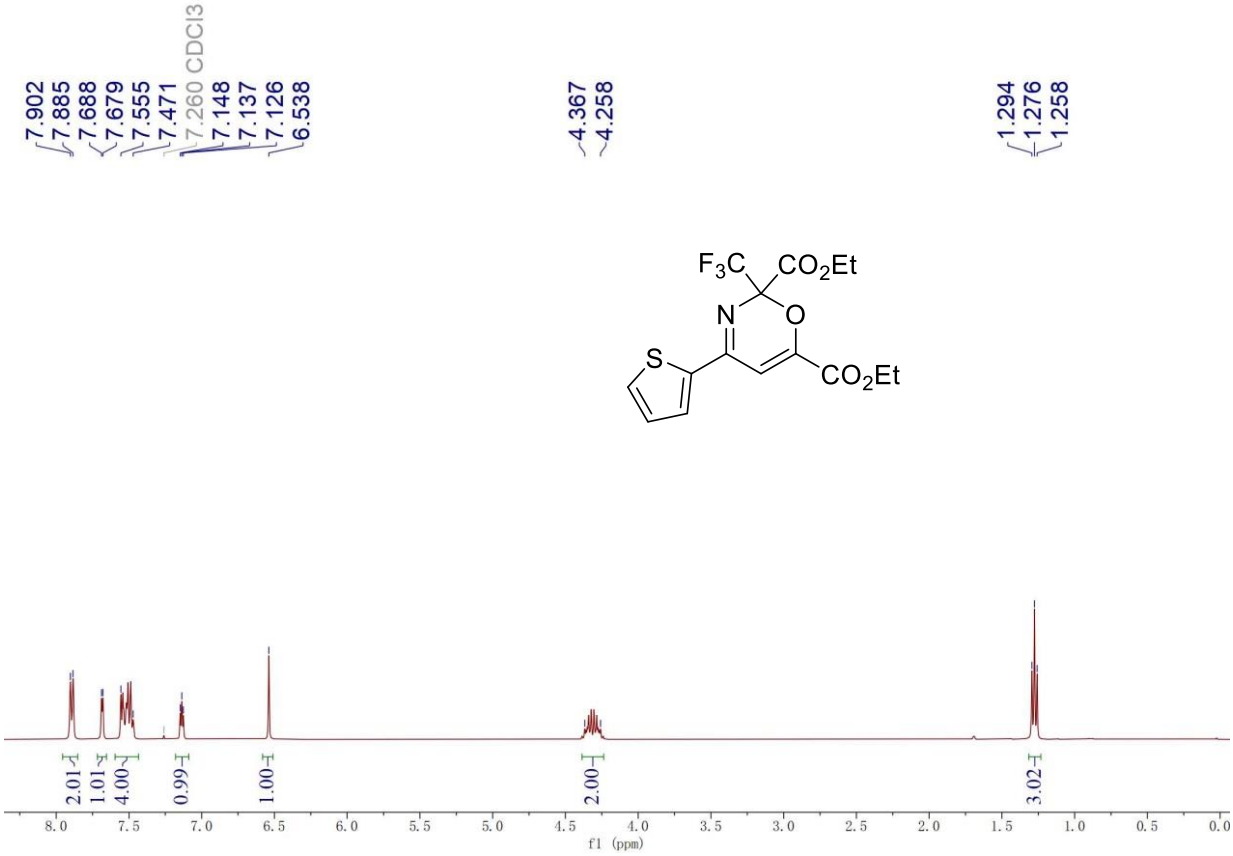
Diethyl 4-(naphthalen-2-yl)-2-(trifluoromethyl)-2*H*-1,3-oxazine-2,6-dicarboxylate (3m)

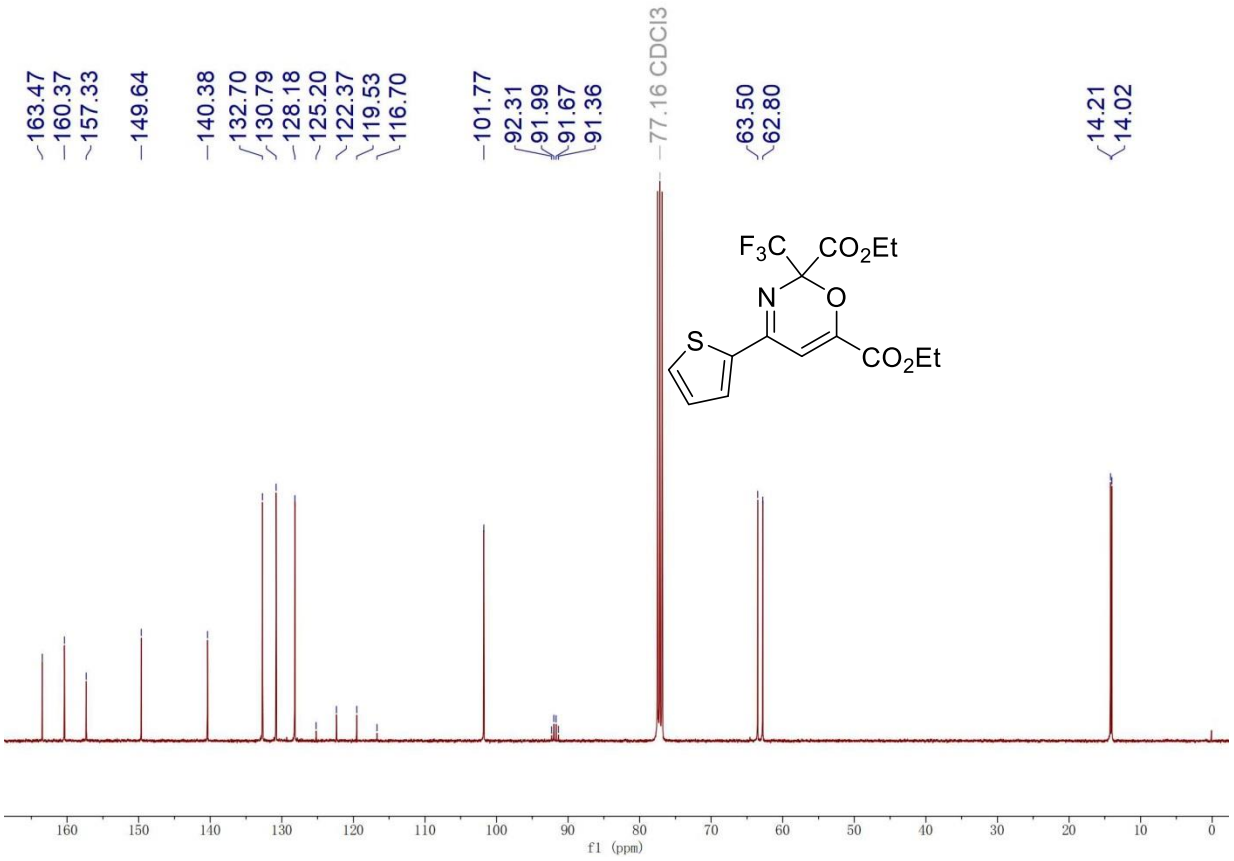


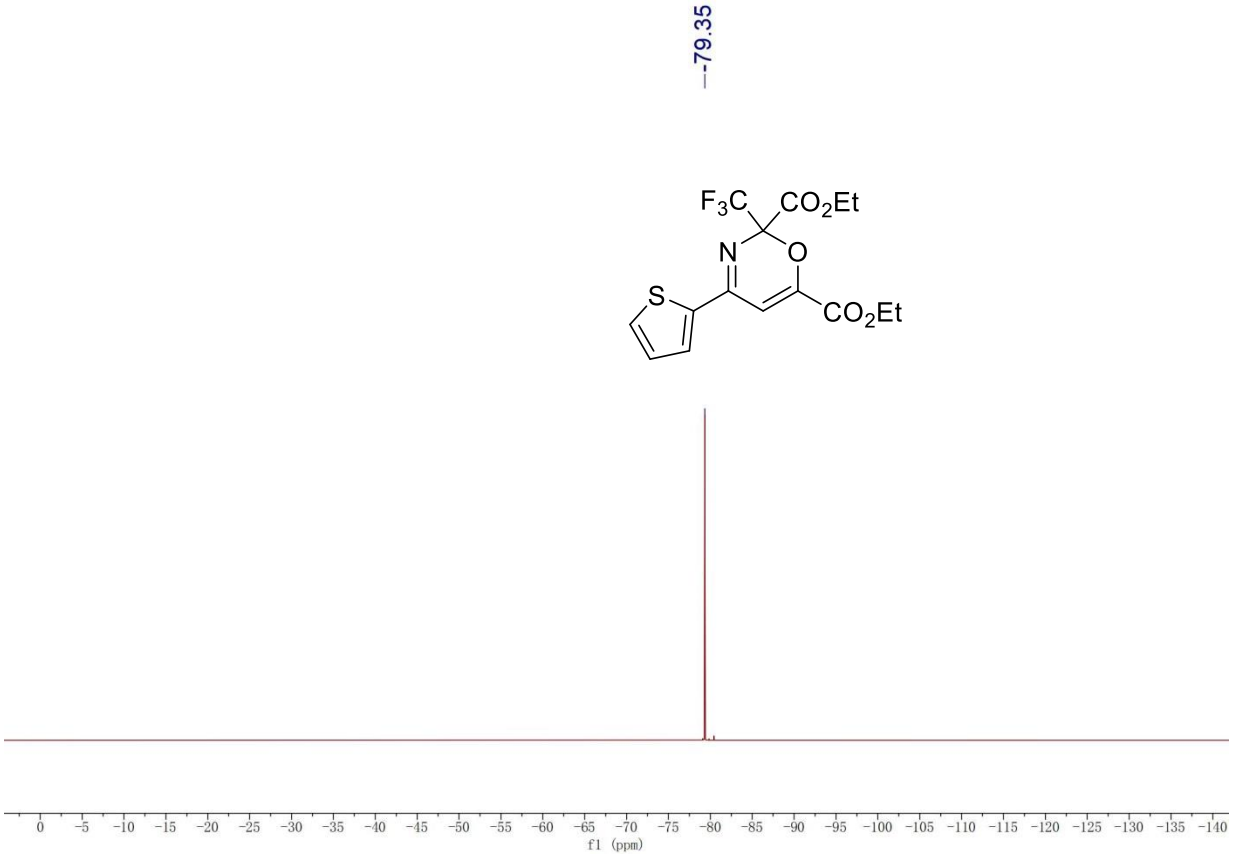




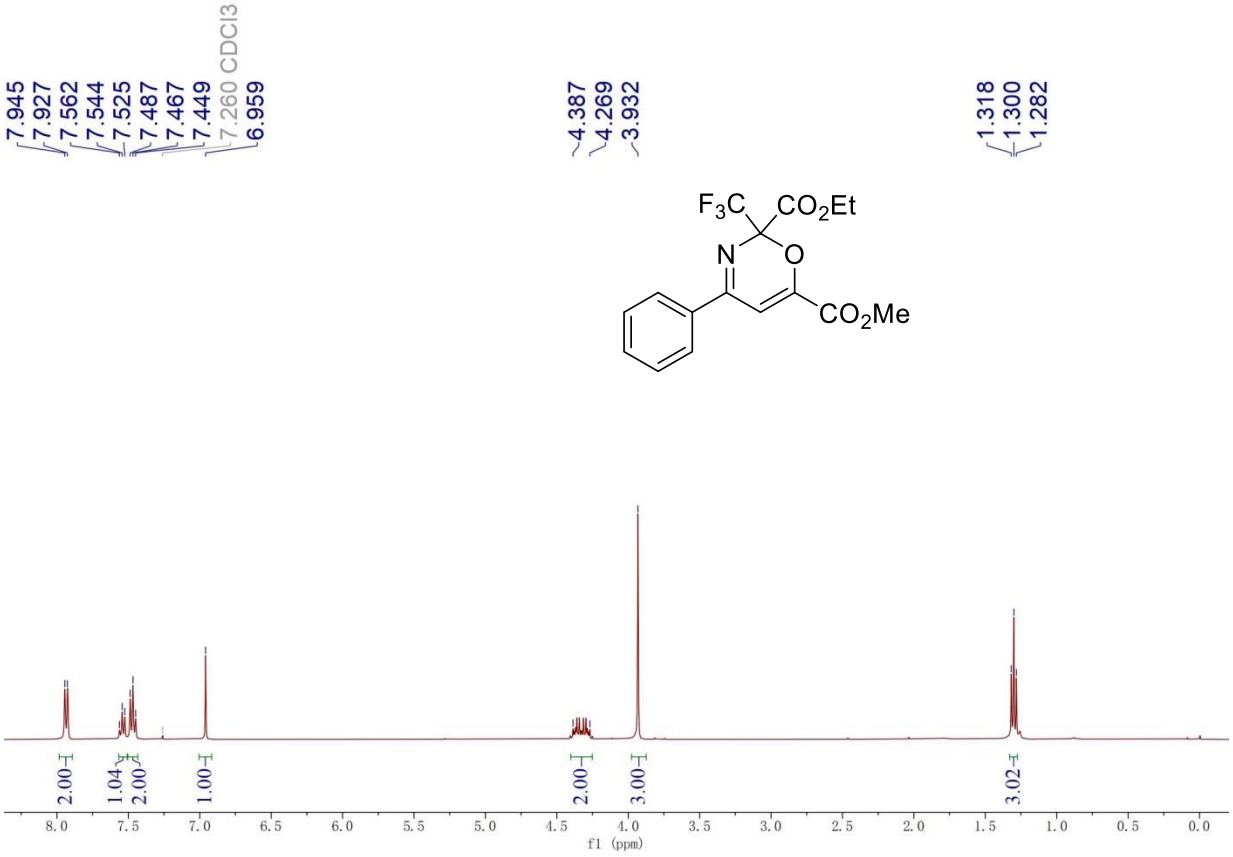
Diethyl 4-(thiophen-2-yl)-2-(trifluoromethyl)-2*H*-1,3-oxazine-2,6-dicarboxylate (3n)

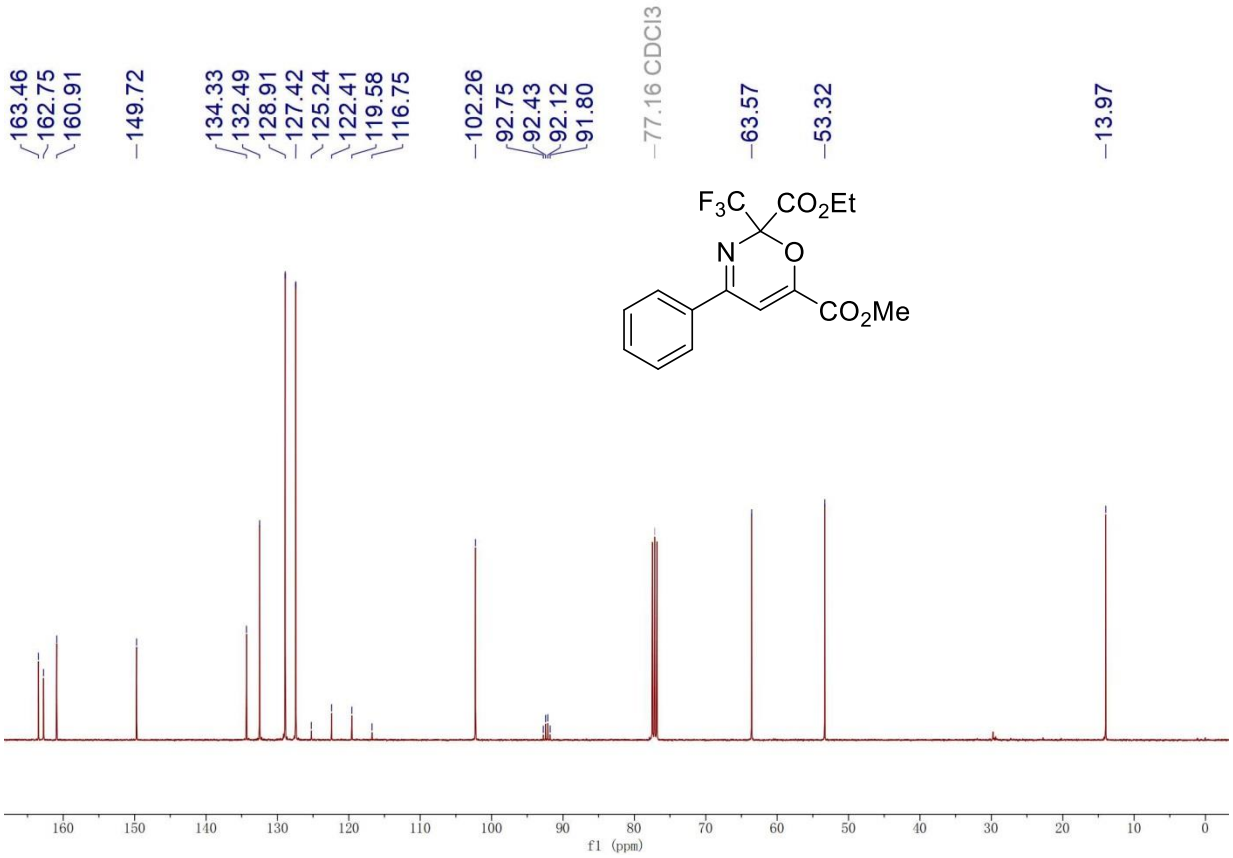


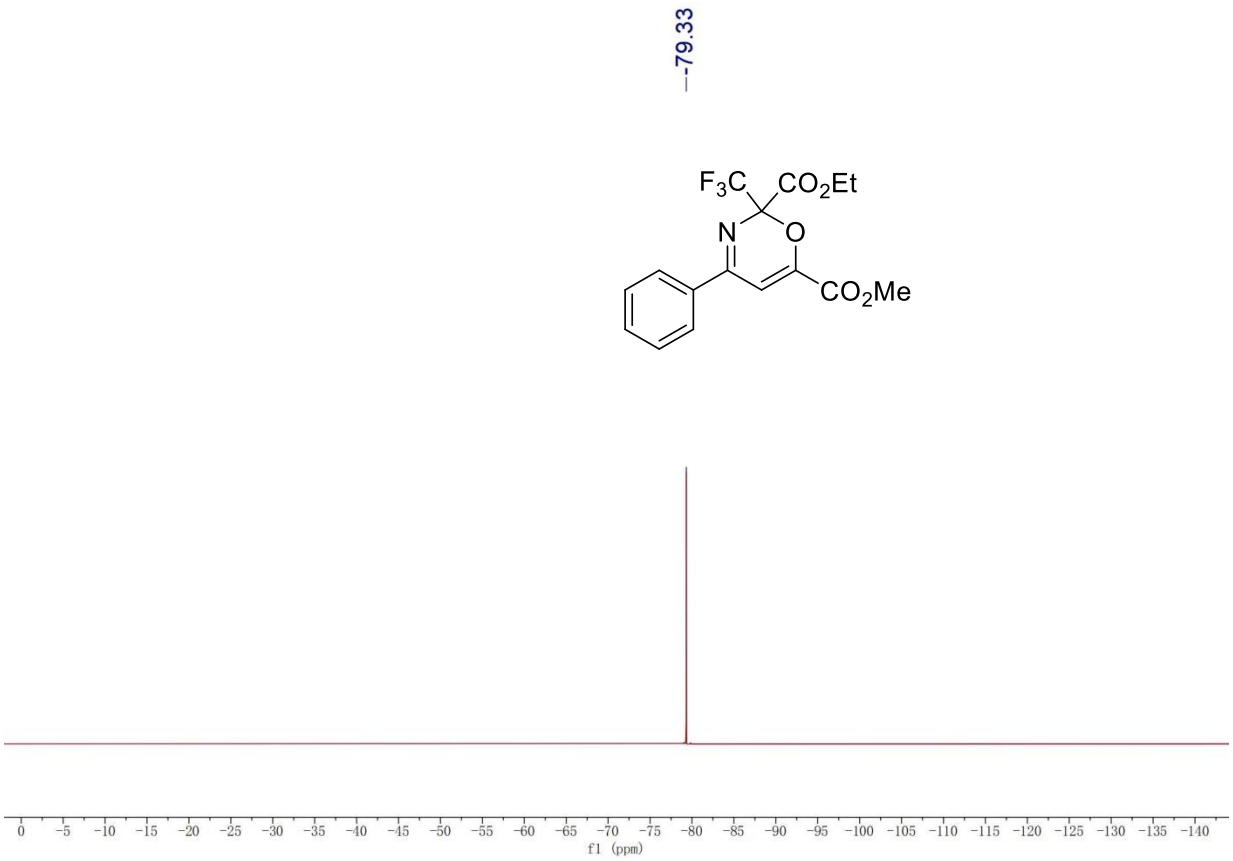

163.47
160.37
157.33
149.64
140.38
132.70
130.79
128.18
125.20
122.37
119.53
116.70
101.77
92.31
91.99
91.67
91.36
77.16 CDCl3
63.50
62.80
14.21
14.02
F3C
CO2Et
N
O
S
CO2Et
f1 (ppm)


-79.35
F3C
CO2Et
N
O
S
CO2Et
f1 (ppm)

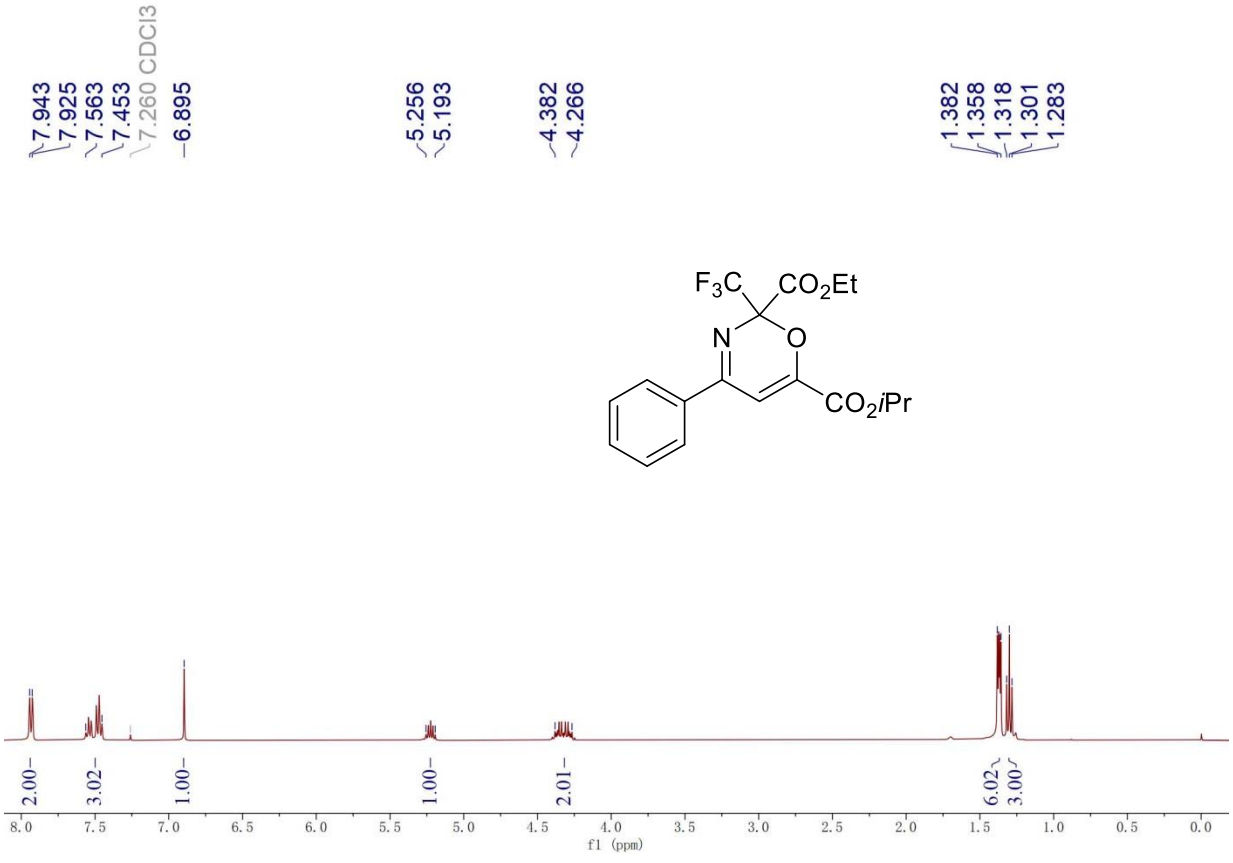
2-Ethyl 6-methyl 4-phenyl-2-(trifluoromethyl)-2*H*-1,3-oxazine-2,6-dicarboxylate (3o)

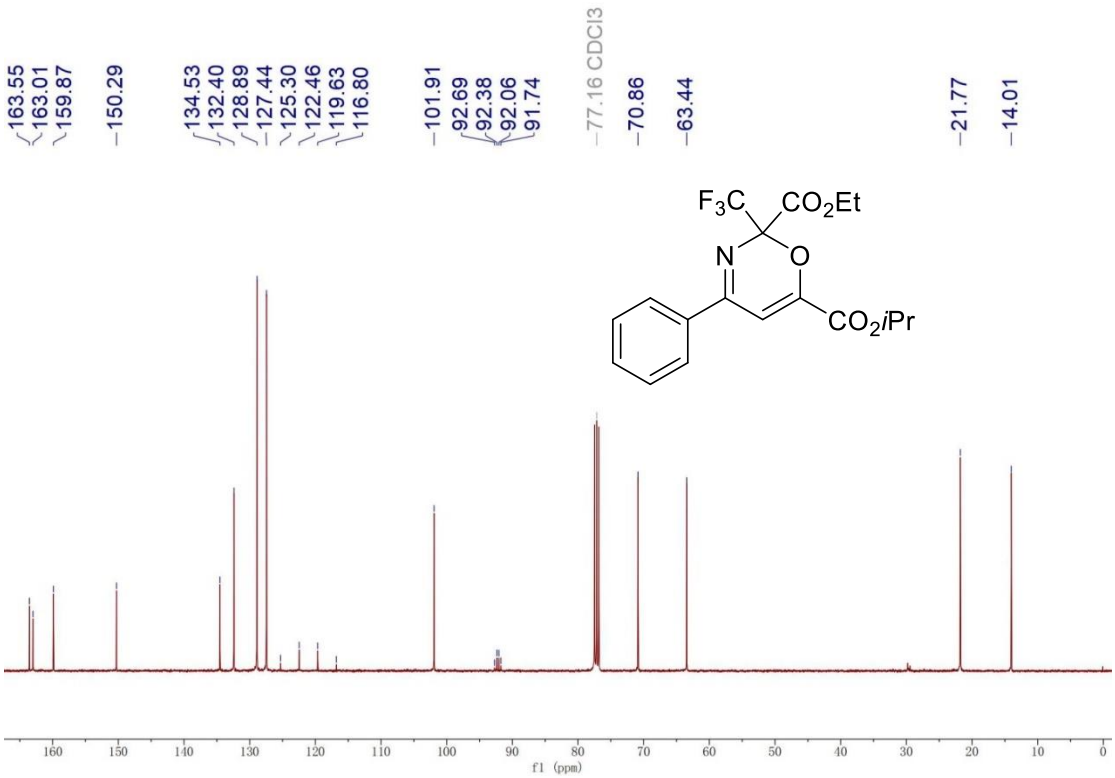


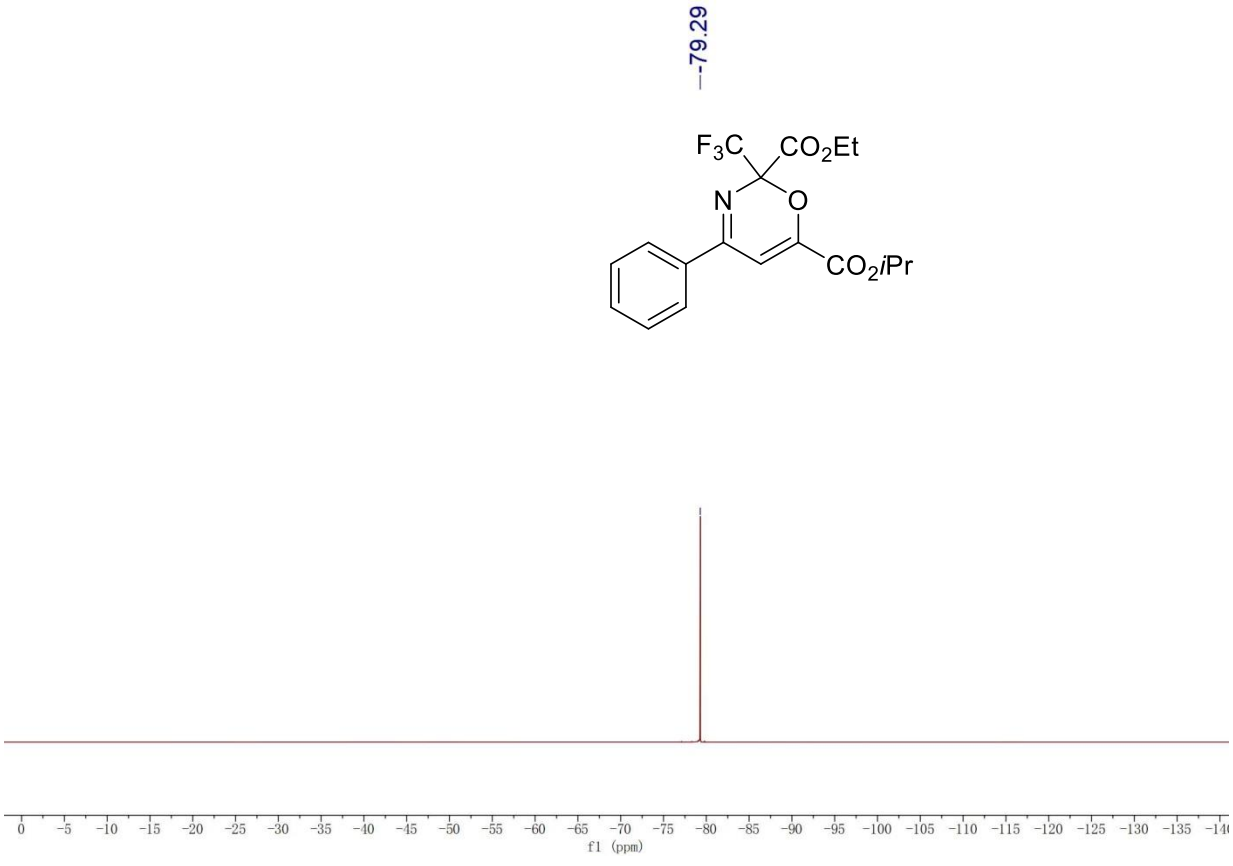




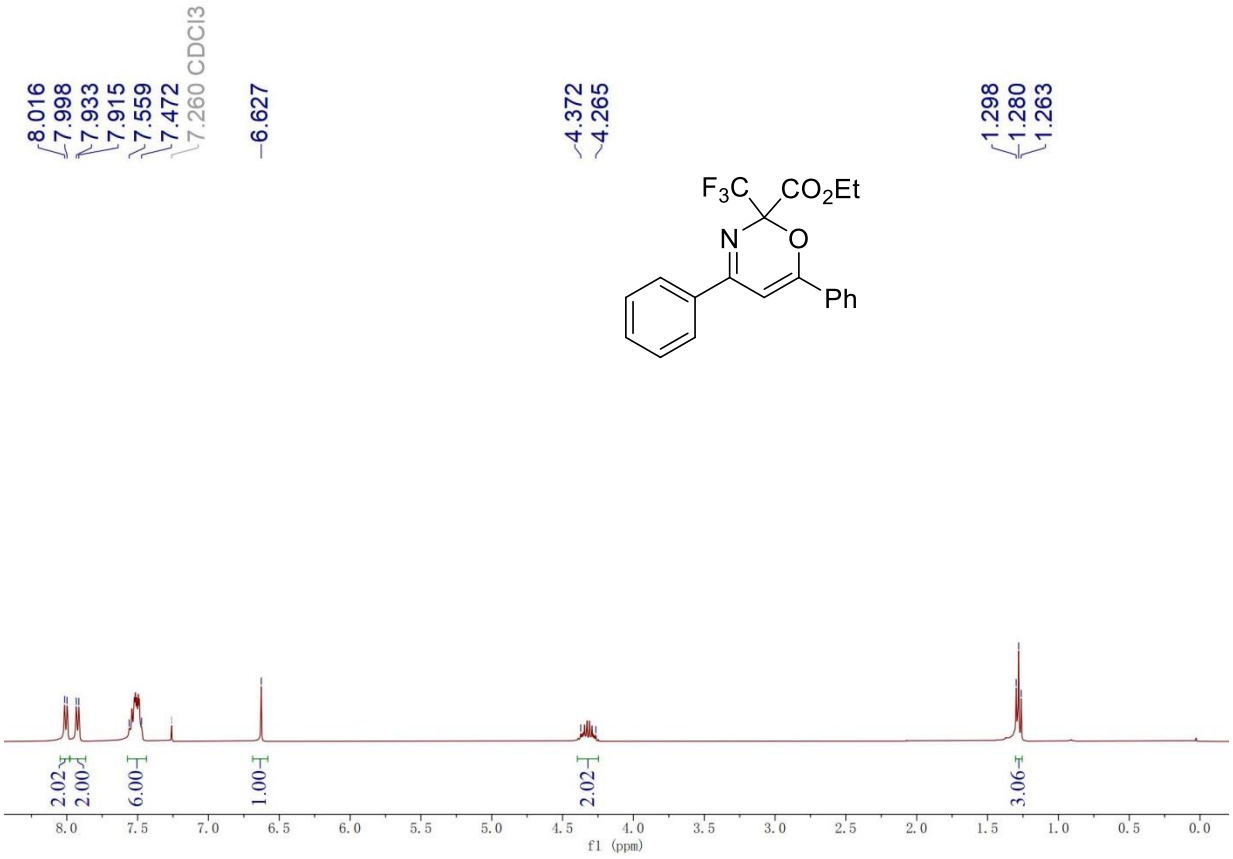
2-Ethyl 6-isopropyl 4-phenyl-2-(trifluoromethyl)-2*H*-1,3-oxazine-2,6-dicarboxylate (3p)

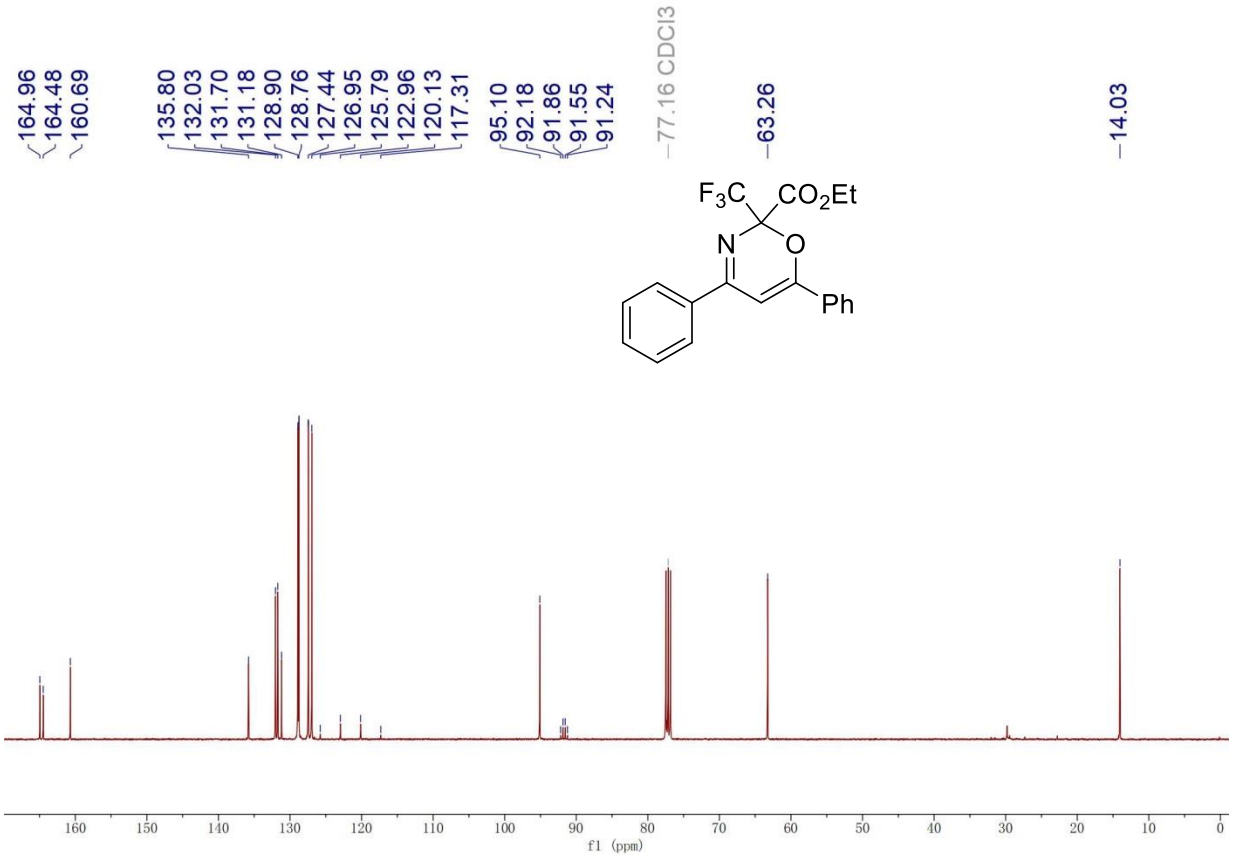


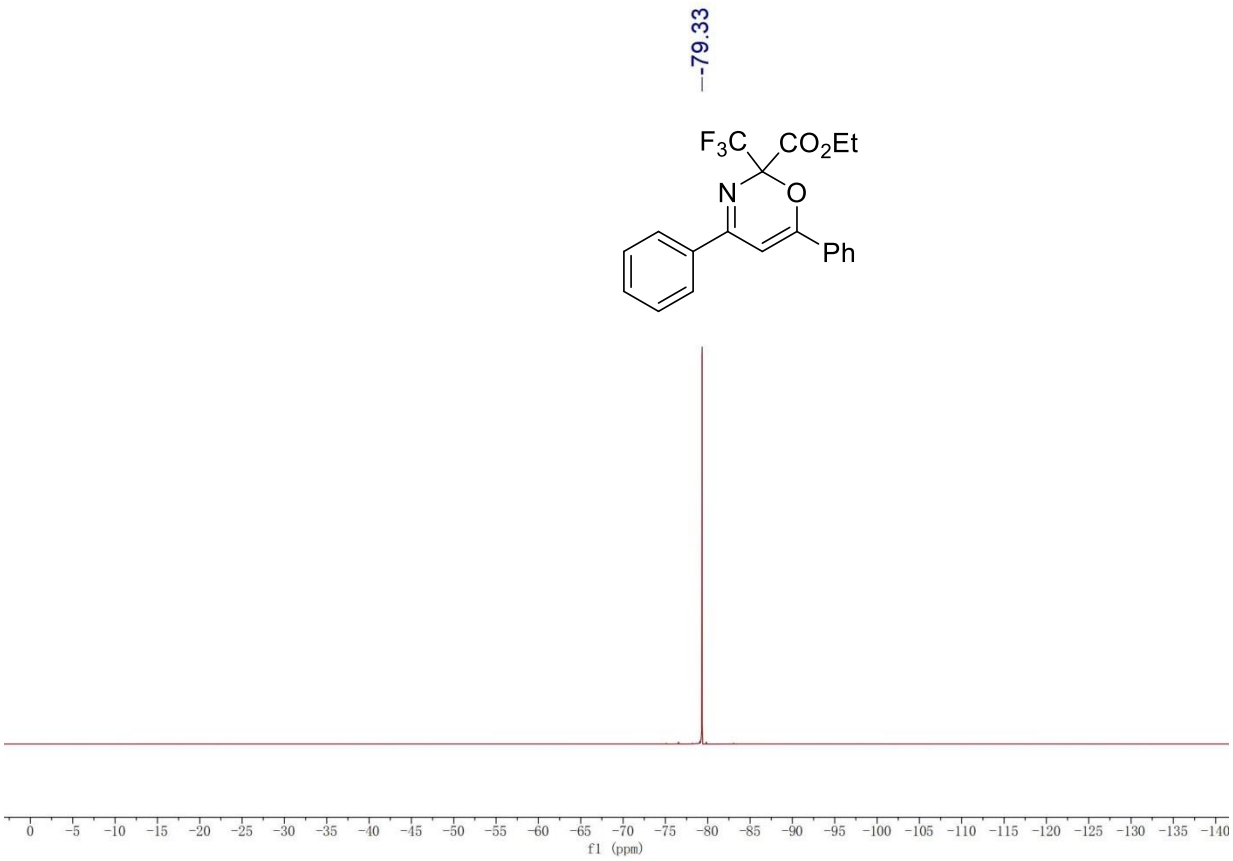

163.55
163.01
159.87
150.29
134.53
132.40
128.89
127.44
125.30
122.46
119.63
116.80
101.91
92.69
92.38
92.06
91.74
77.16 CDCl3
70.86
63.44
21.77
14.01
F3C
CO2Et
N
O
CO2iPr
f1 (ppm)


-79.29
F3C
CO2Et
N
O
CO2iPr
f1 (ppm)

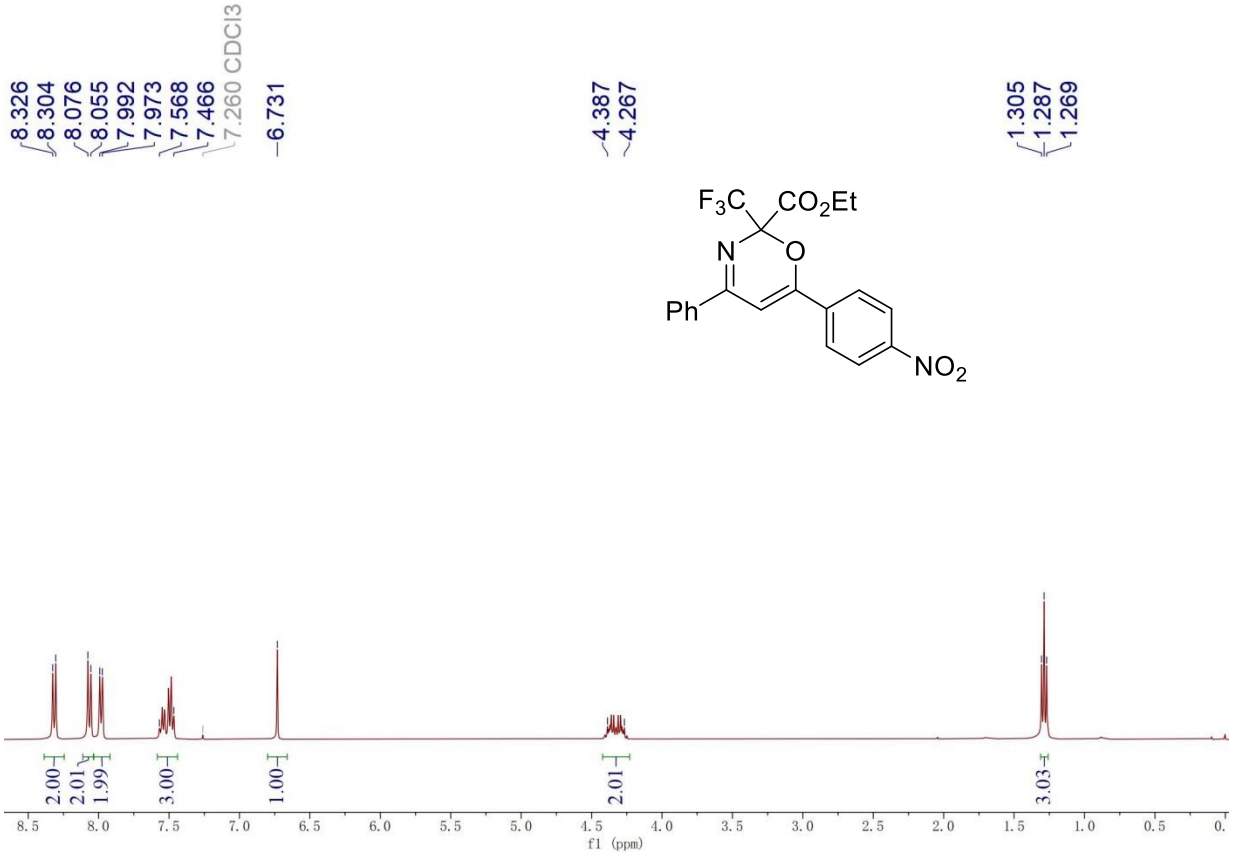
Ethyl 4,6-diphenyl-2-(trifluoromethyl)-2*H*-1,3-oxazine-2-carboxylate (4a)

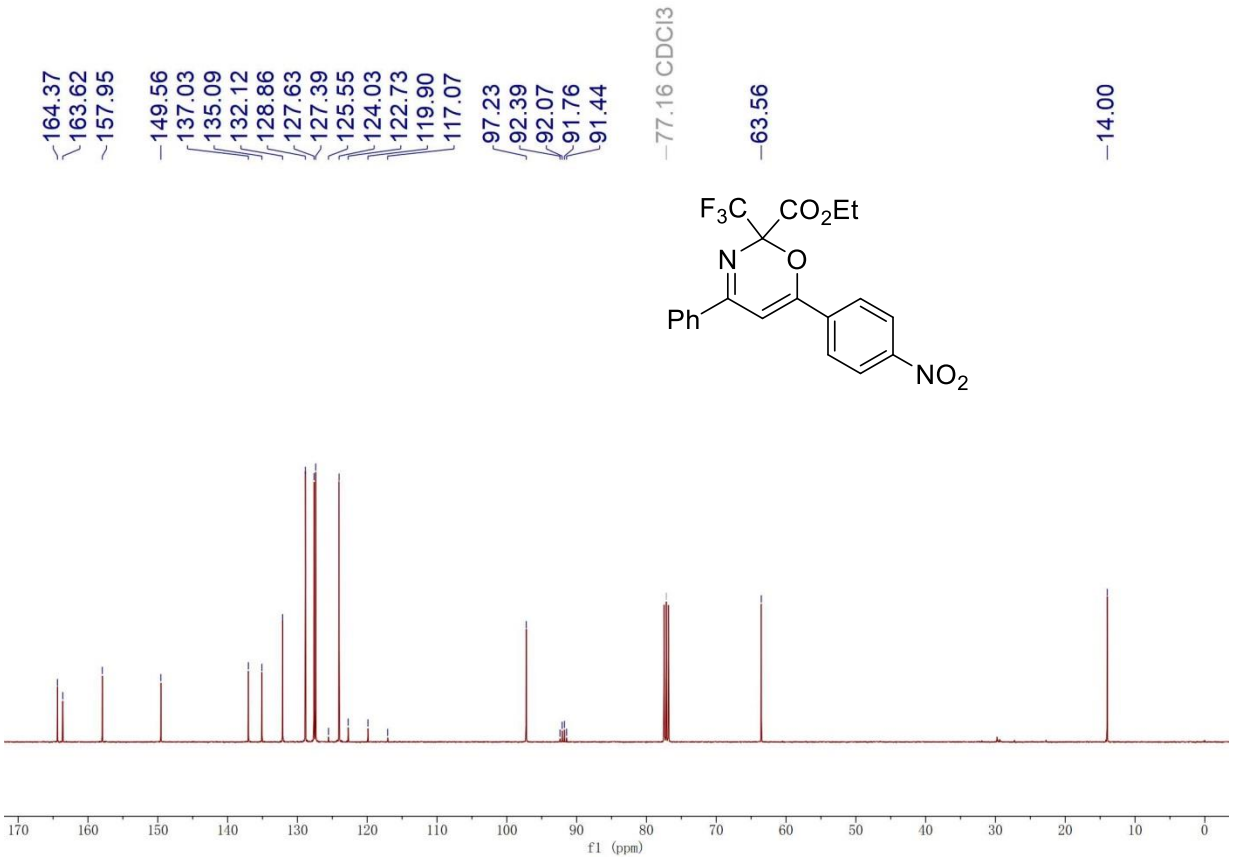


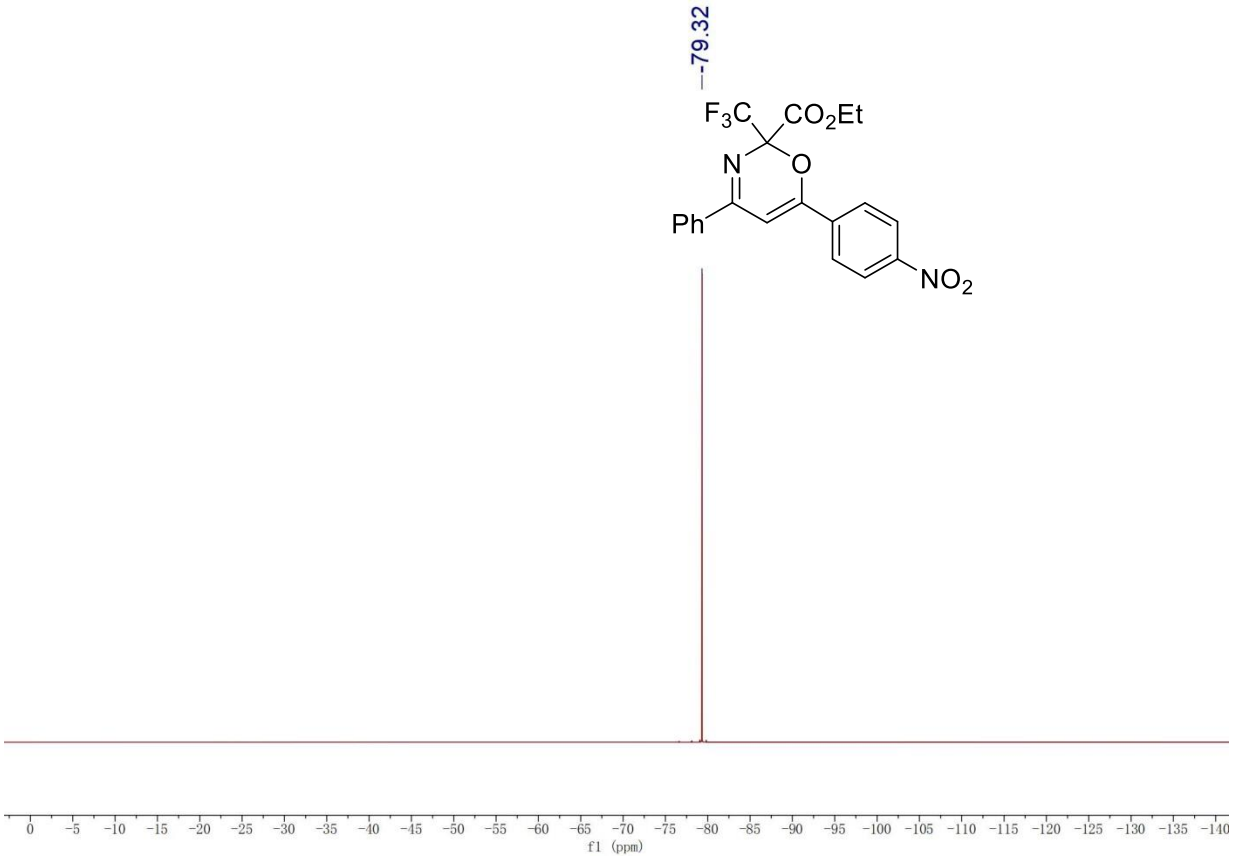




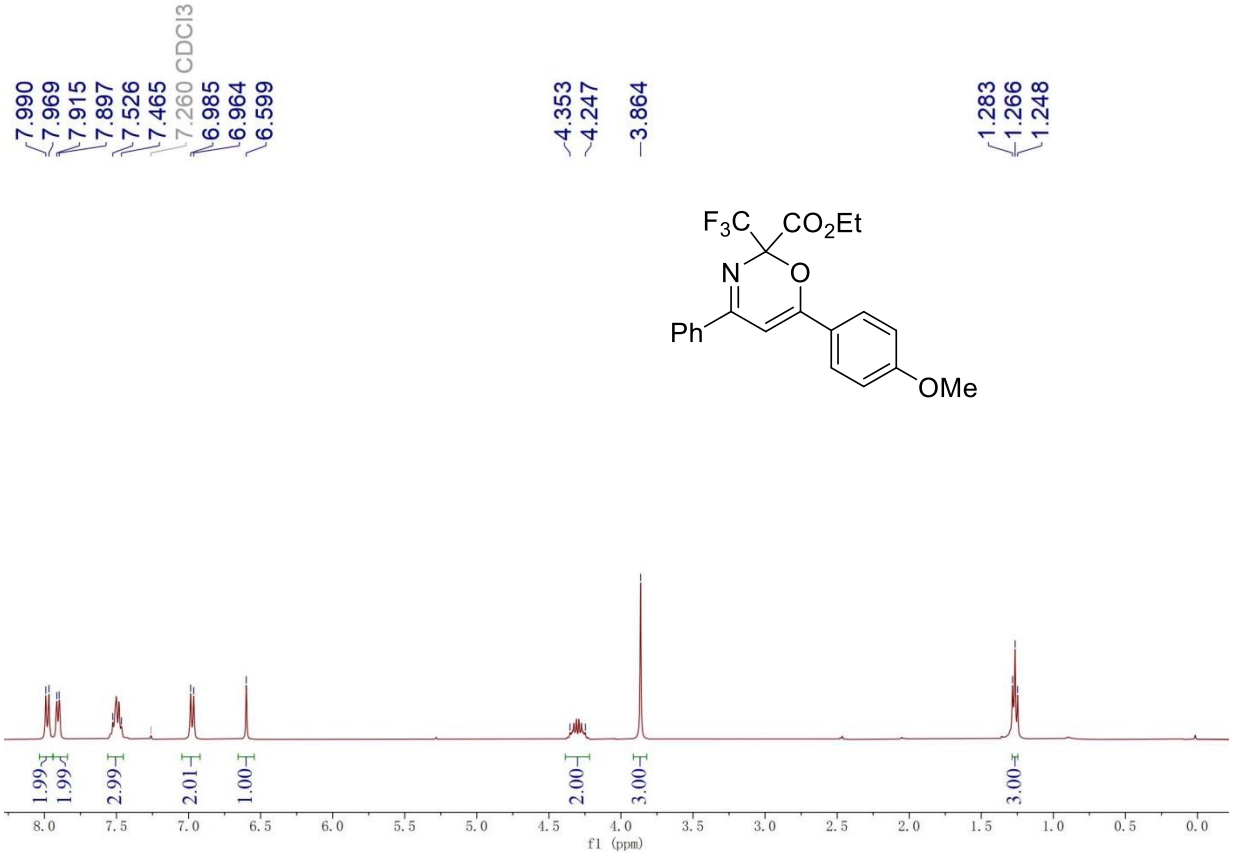
Ethyl 6-(4-nitrophenyl)-4-phenyl-2-(trifluoromethyl)-2*H*-1,3-oxazine-2-carboxylate (4b)

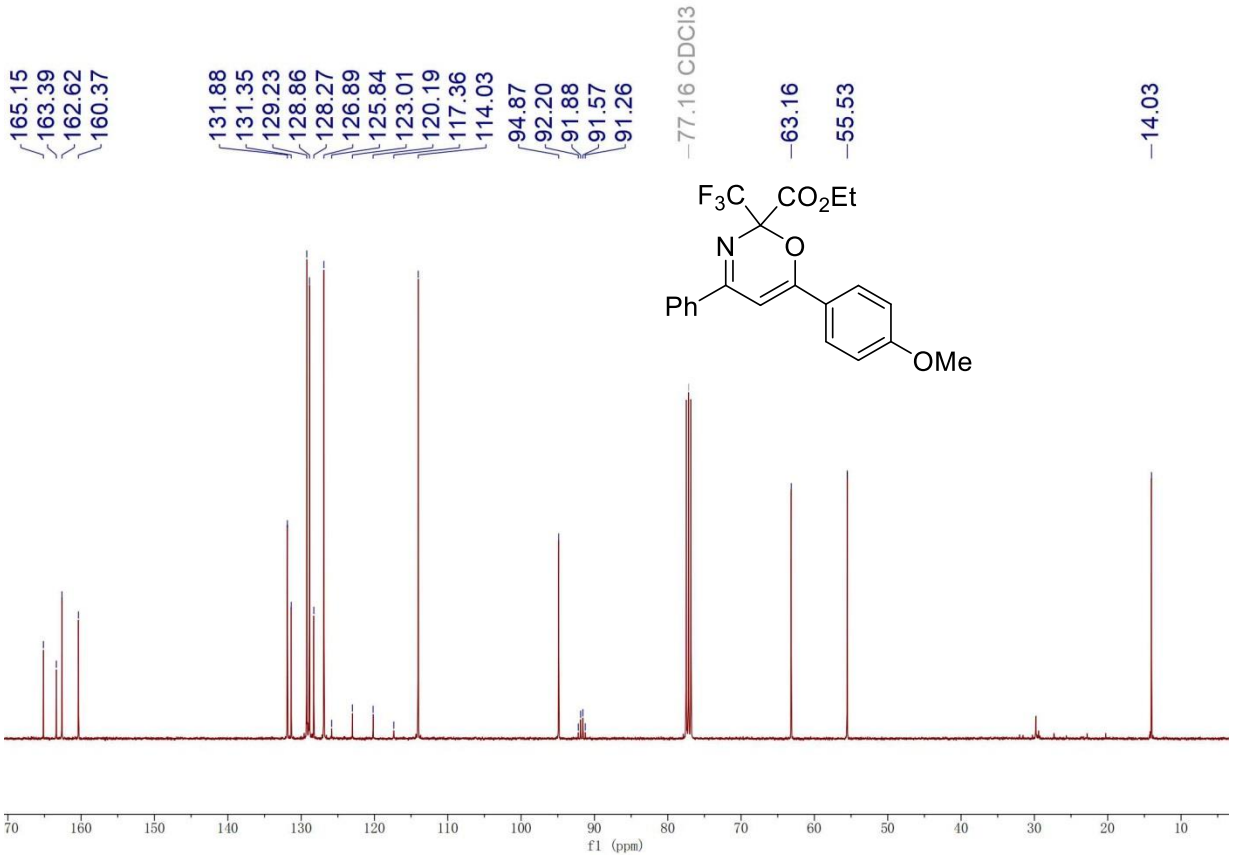


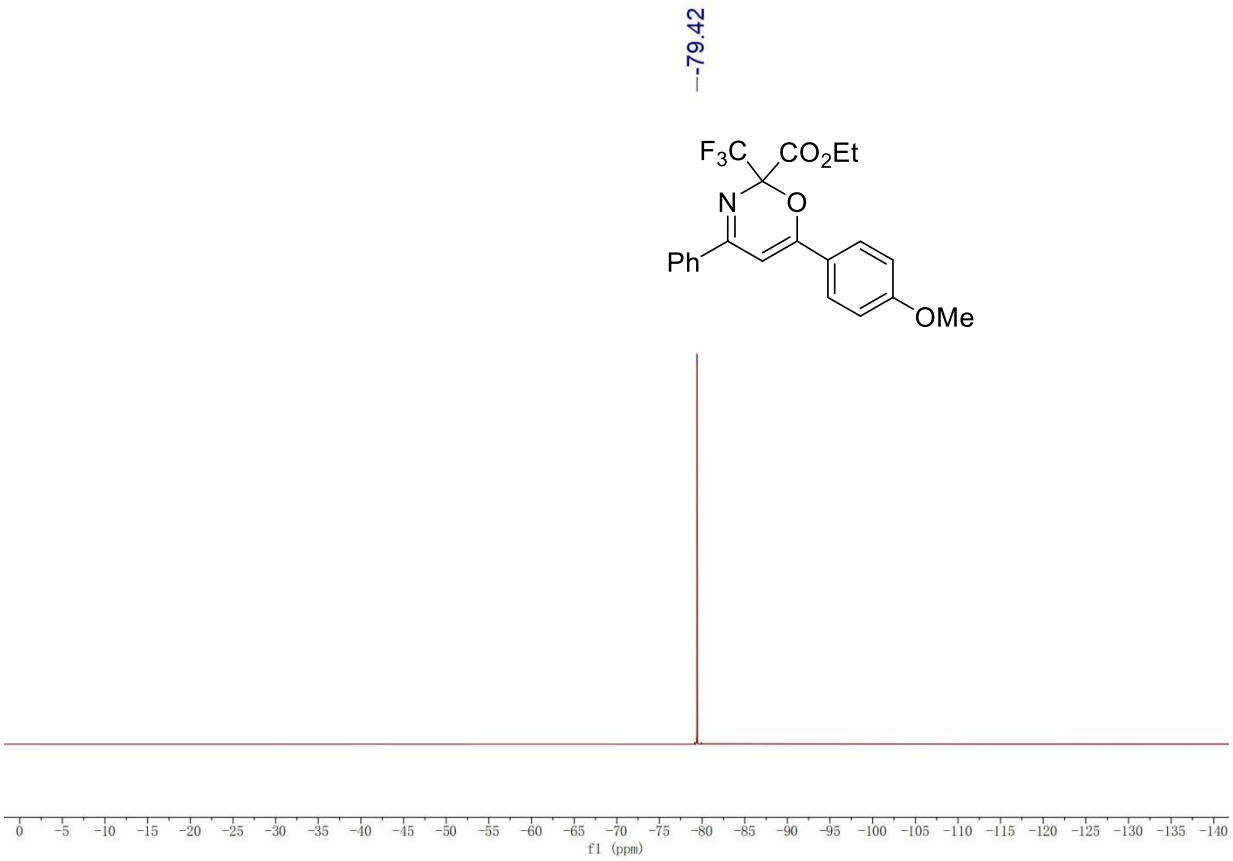

164.37
163.62
157.95
149.56
137.03
135.09
132.12
128.86
127.63
127.39
125.55
124.03
122.73
119.90
117.07
97.23
92.39
92.07
91.76
91.44
77.16 CDCl3
63.56
14.00
F3C
CO2Et
N
O
Ph
NO2
f1 (ppm)


-79.32
F3C
CO2Et
N
O
Ph
NO2
f1 (ppm)

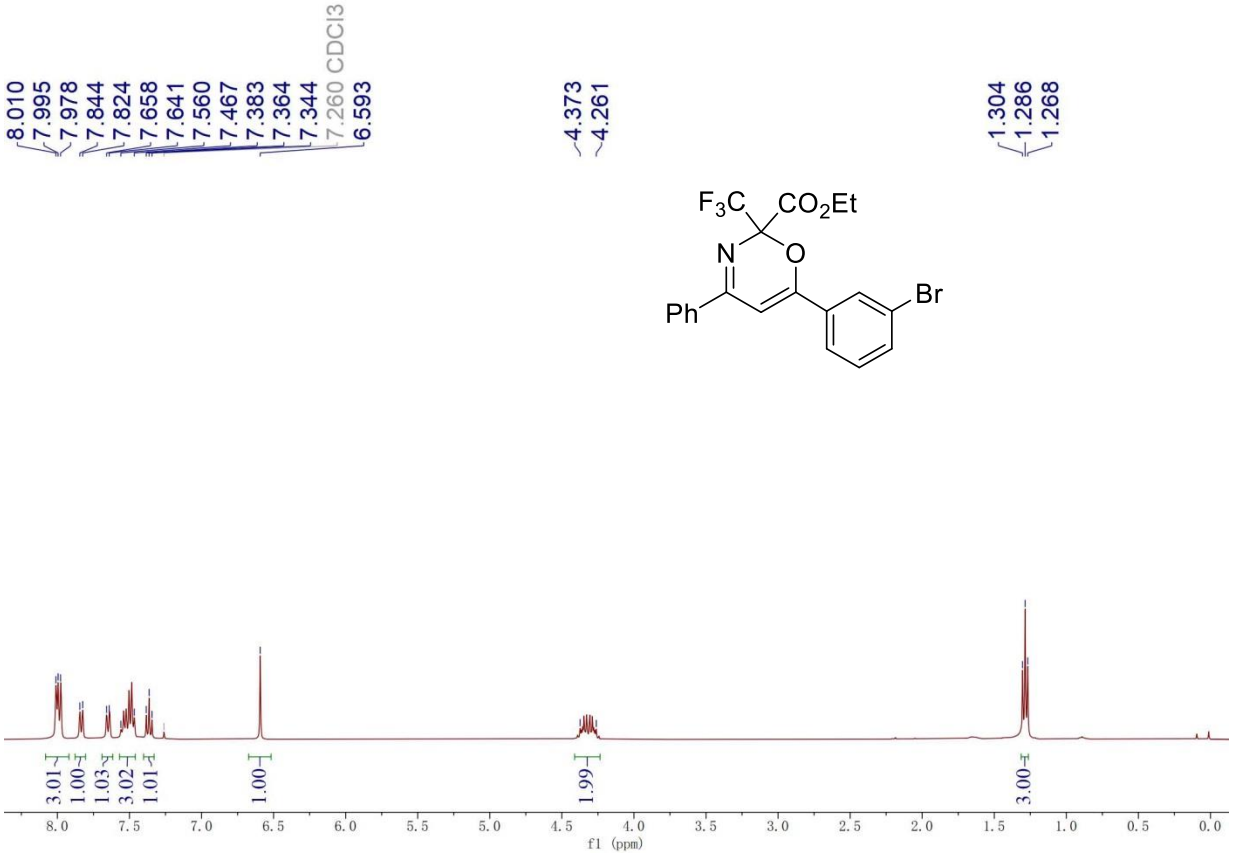
Ethyl 6-(4-methoxyphenyl)-4-phenyl-2-(trifluoromethyl)-2*H*-1,3-oxazine-2-carboxylate (4c)

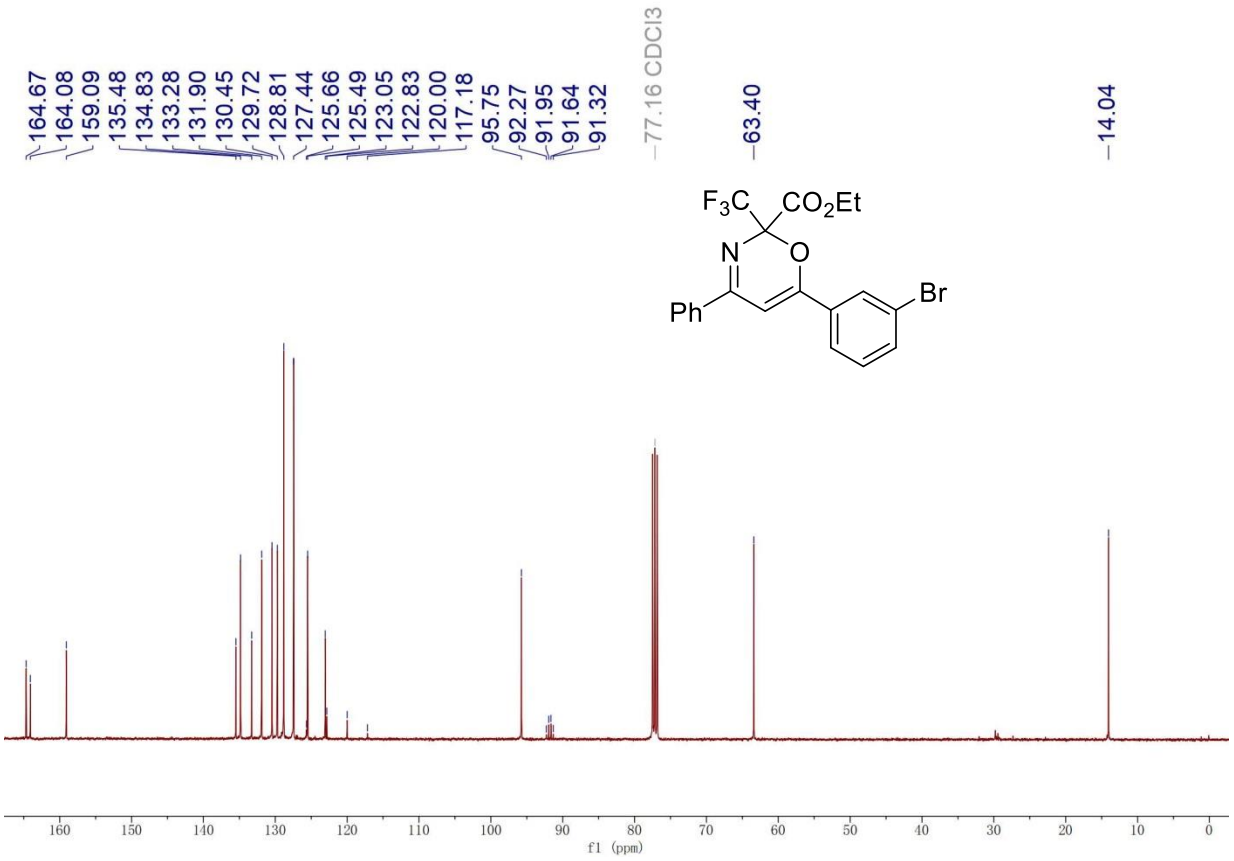






Ethyl 6-(3-bromophenyl)-4-phenyl-2-(trifluoromethyl)-2*H*-1,3-oxazine-2-carboxylate (4d)




164.67
164.08
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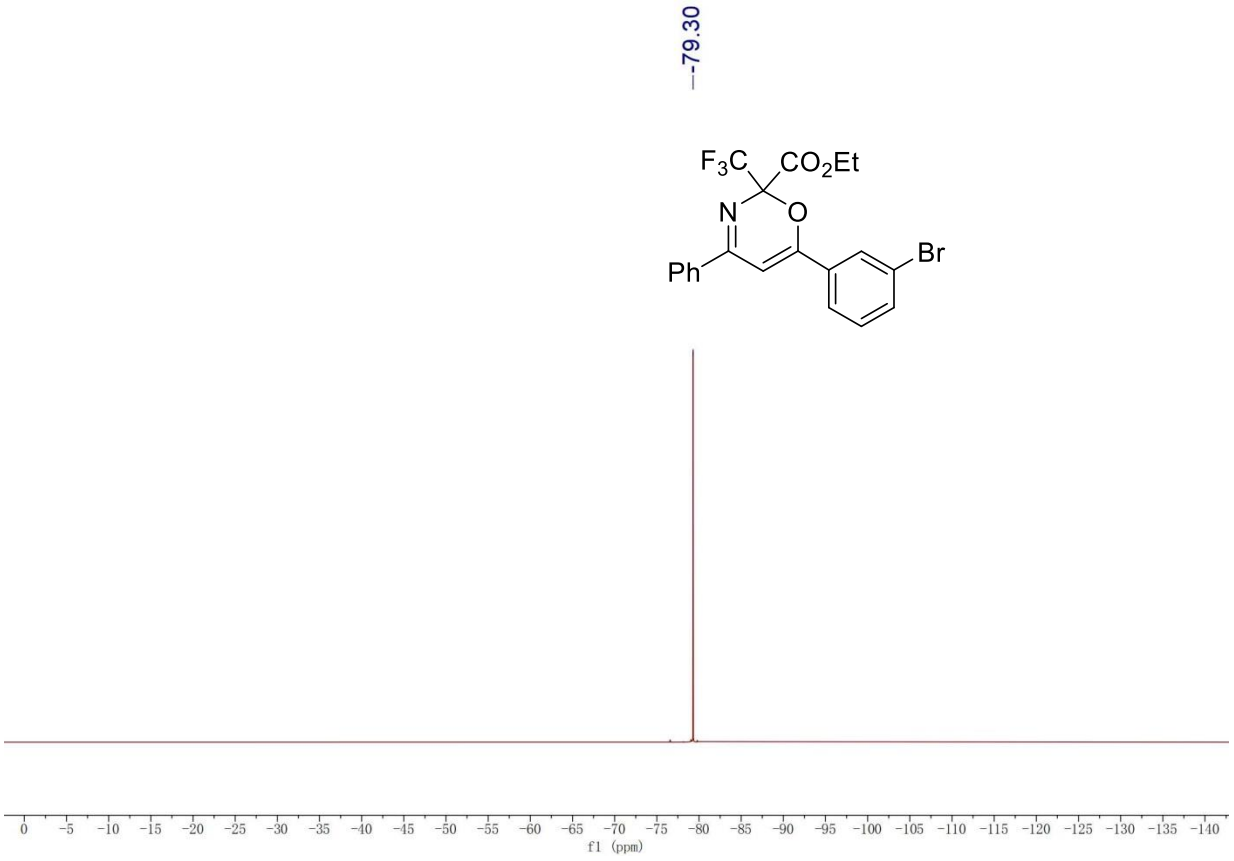
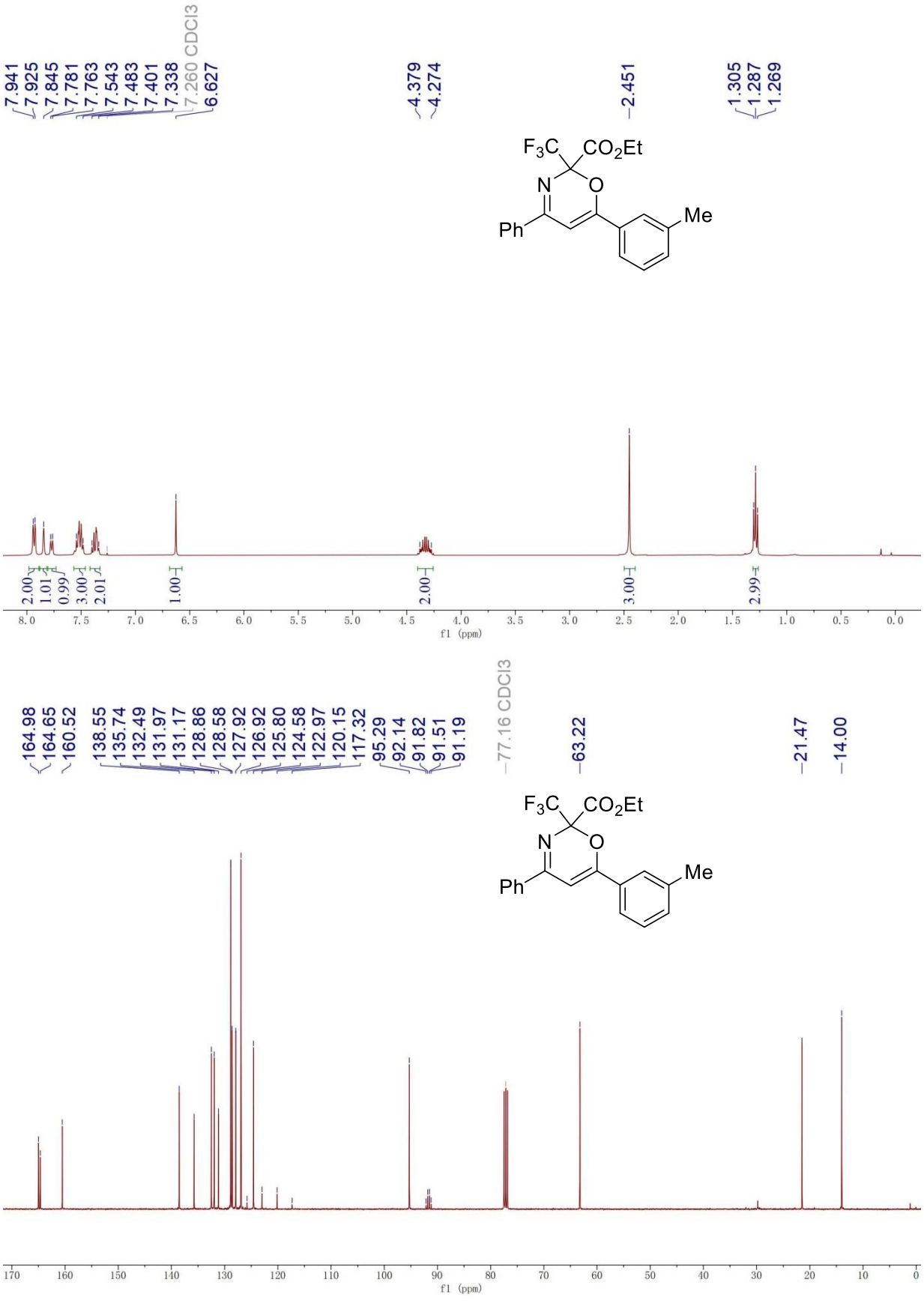
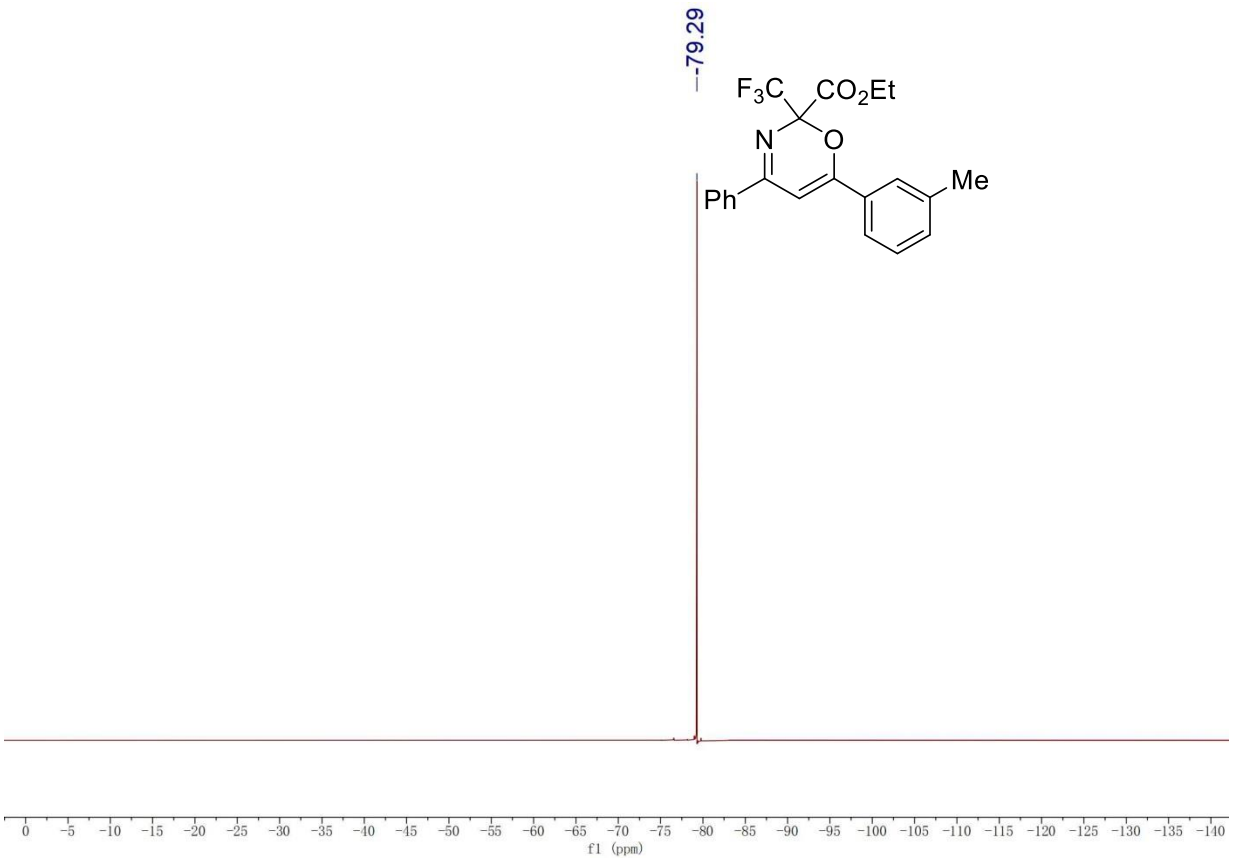
133.28
131.90
130.45
129.72
128.81
127.44
125.66
125.49
123.05
122.83
120.00
117.18
95.75
92.27
91.95
91.64
91.32
77.16 CDCl3
63.40
14.04
F3C
CO2Et
N
O
Ph
Br
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

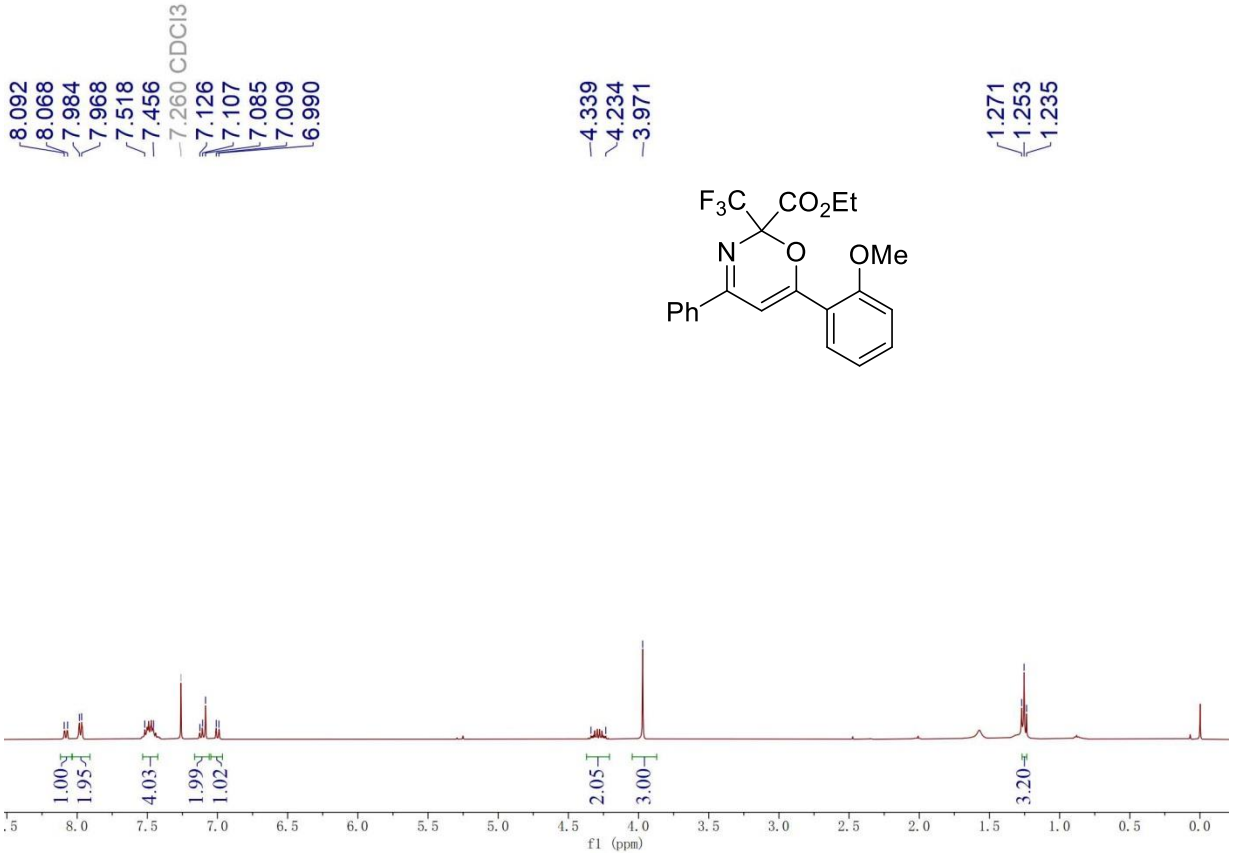

-79.30
F3C
CO2Et
N
O
Ph
Br
0
-5
-10
-15
-20
-25
-30
-35
-40
-45
-50
-55
-60
-65
-70
-75
-80
-85
-90
-95
-100
-105
-110
-115
-120
-125
-130
-135
-140
f1 (ppm)

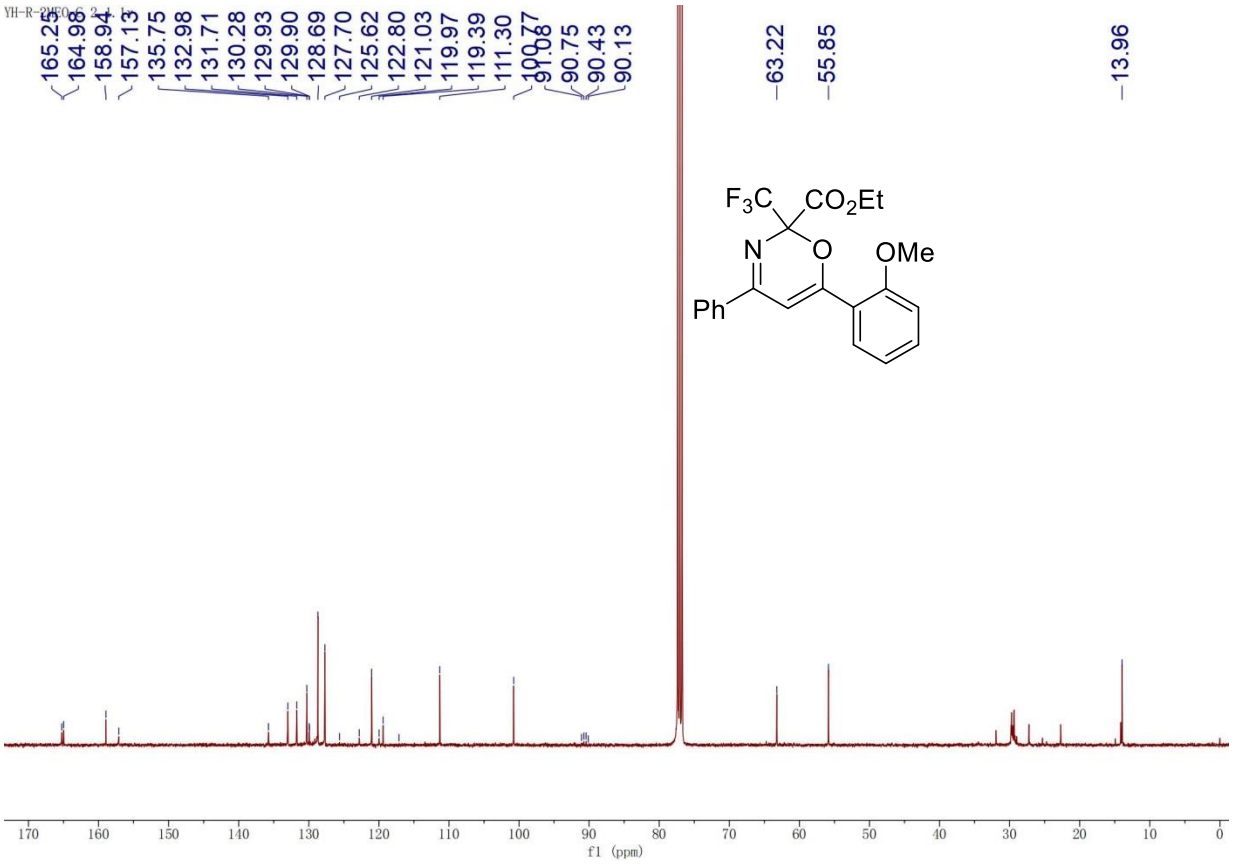
Ethyl 4-phenyl-6-(m-tolyl)-2-(trifluoromethyl)-2*H*-1,3-oxazine-2-carboxylate (4e)





Ethyl 6-(2-methoxyphenyl)-4-phenyl-2-(trifluoromethyl)-2*H*-1,3-oxazine-2-carboxylate (4f)




165.25
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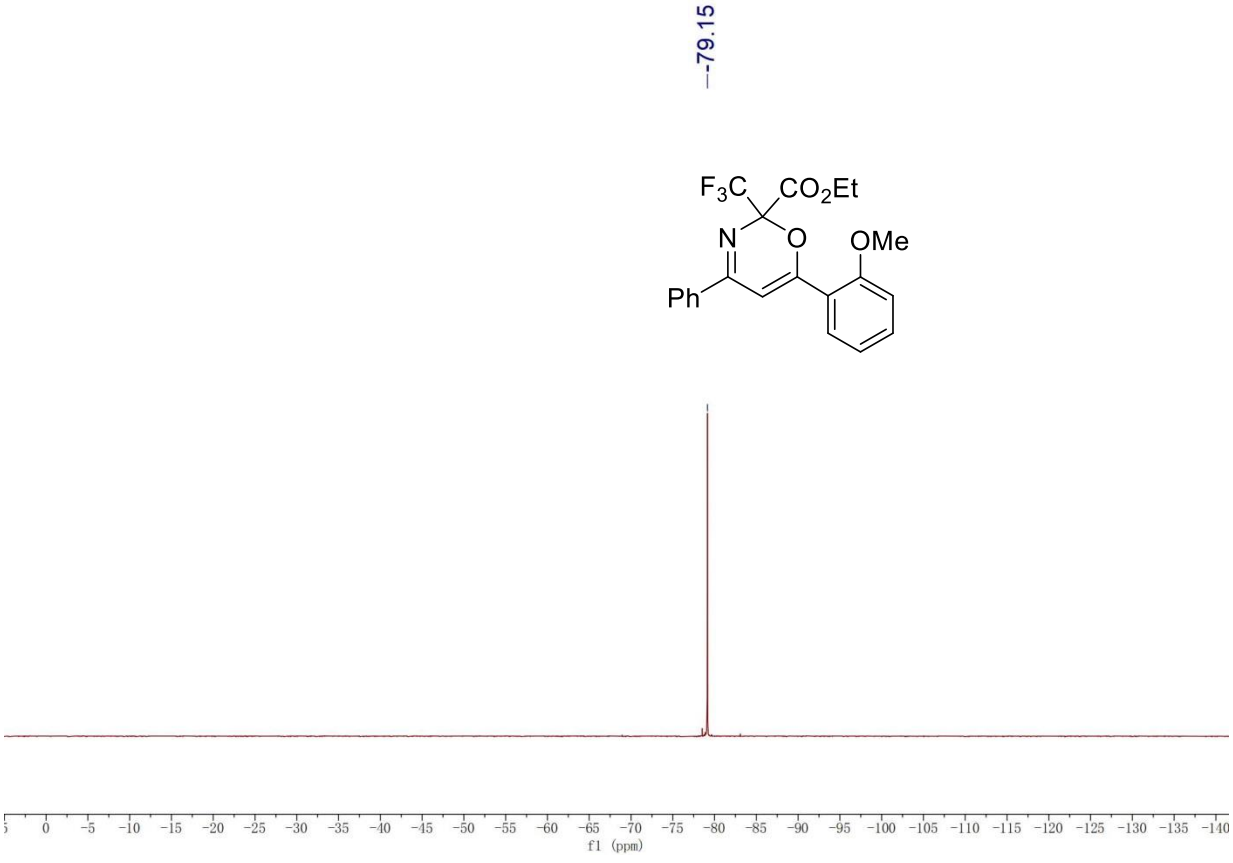
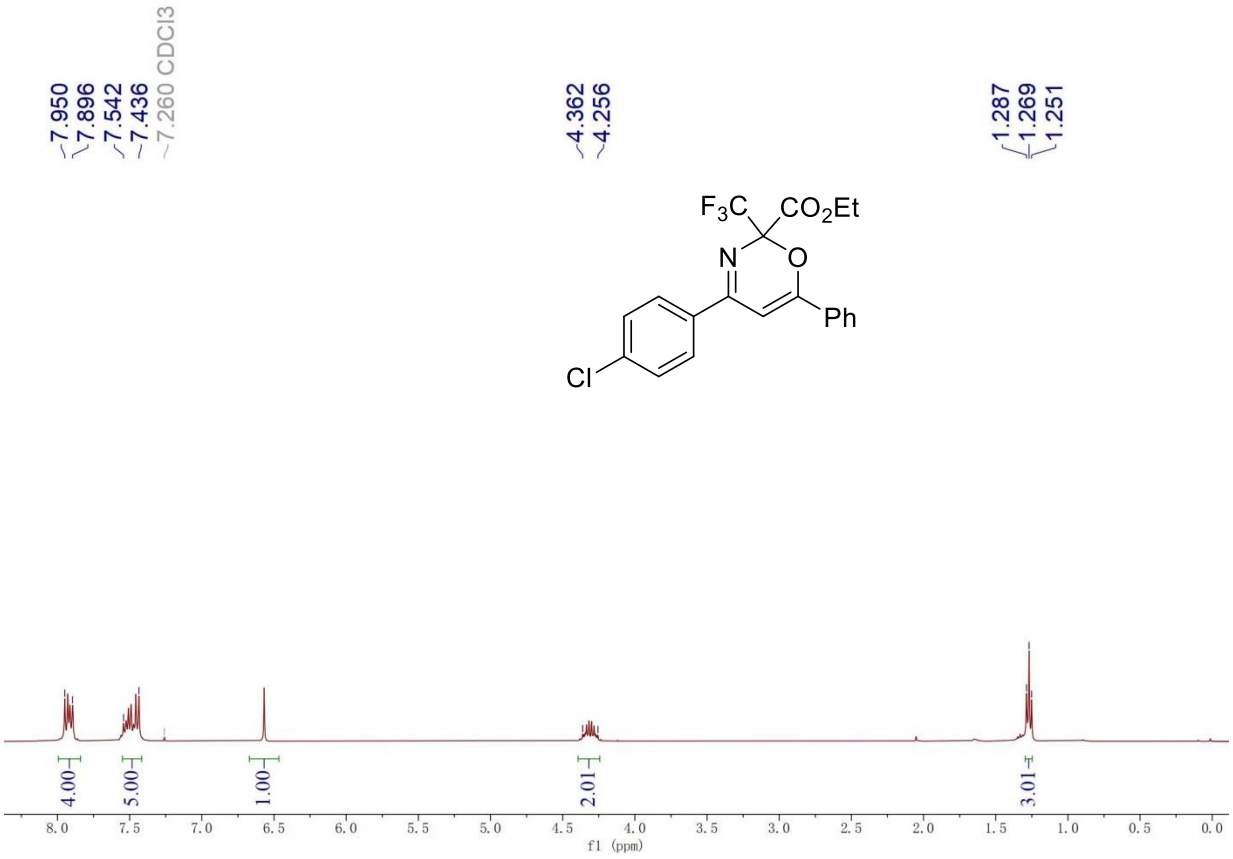
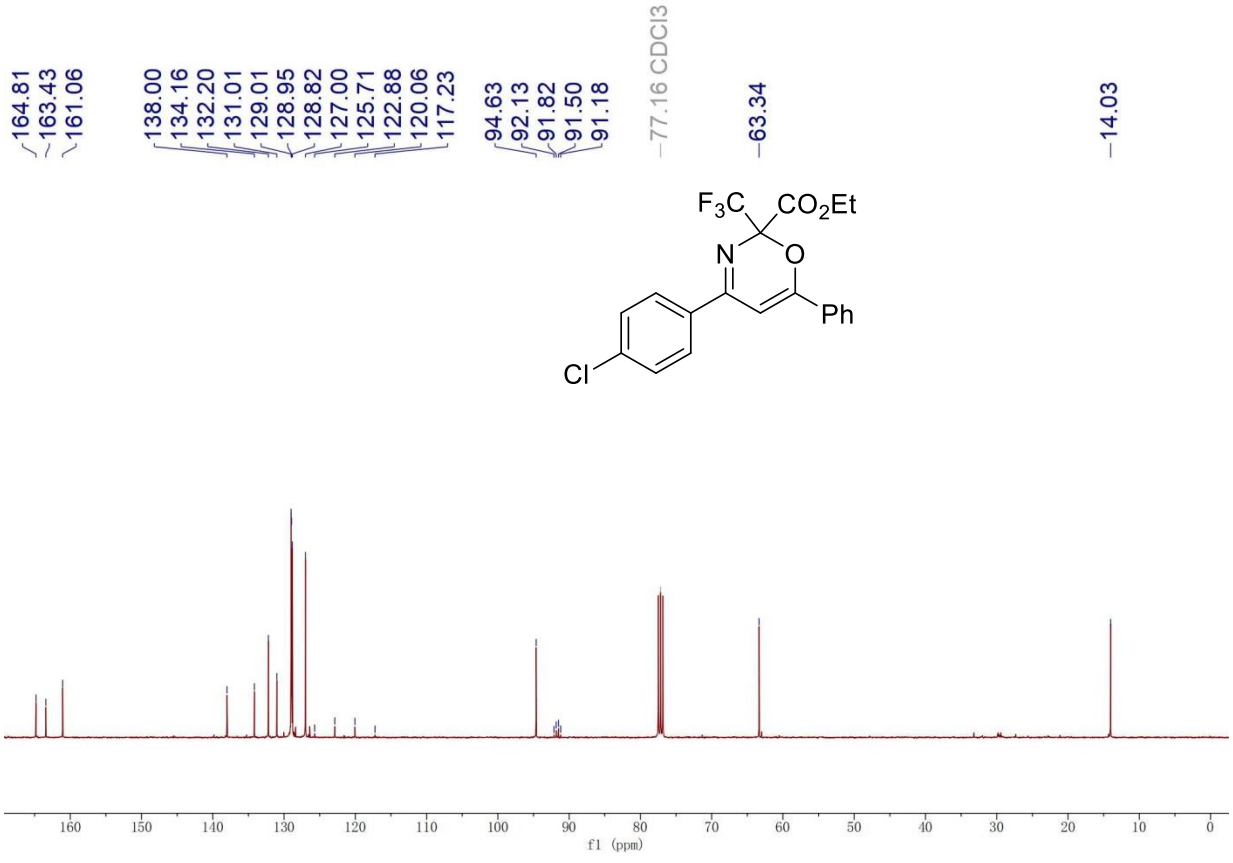
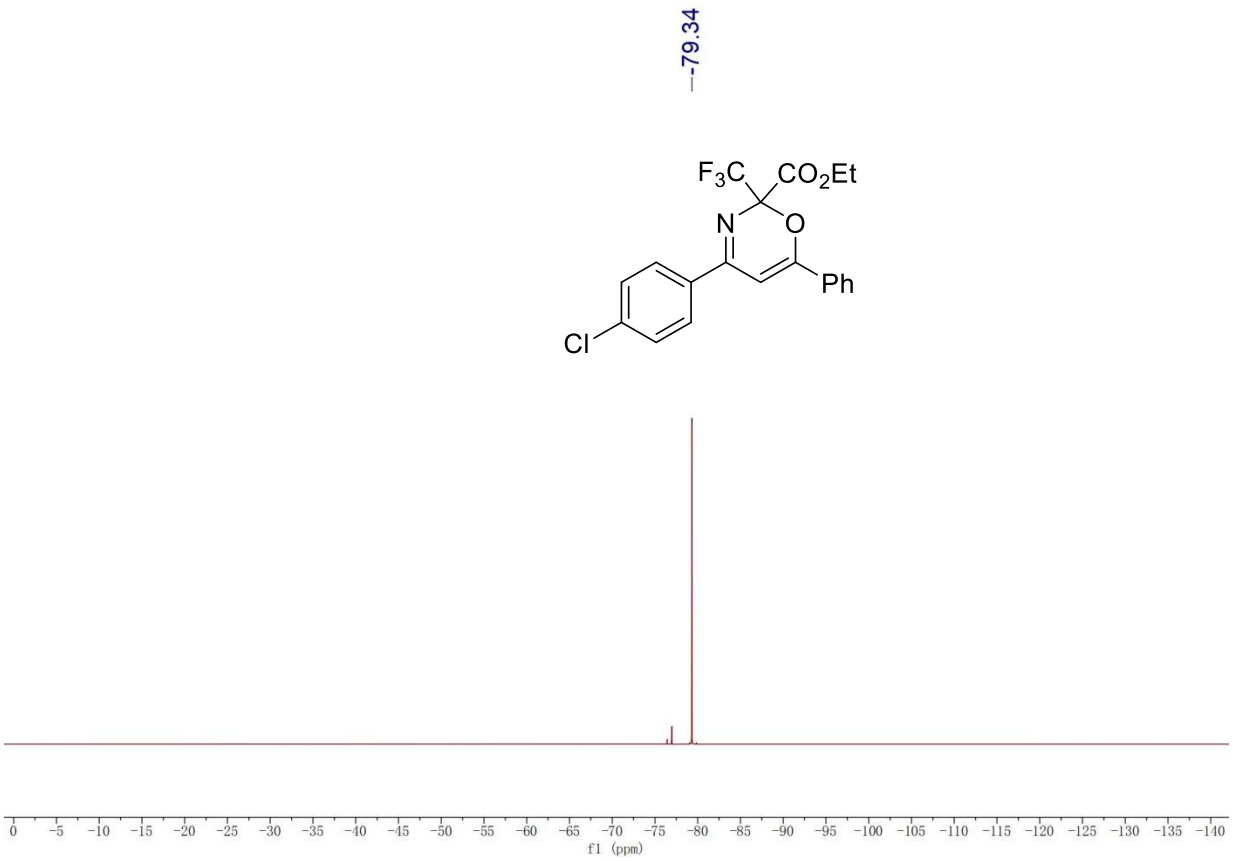
132.98
131.71
130.28
129.93
129.90
128.69
127.70
125.62
122.80
121.03
119.97
119.39
111.30
100.77
91.08
90.75
90.43
90.13
63.22
55.85
13.96
F3C
CO2Et
N
O
OMe
Ph
f1 (ppm)


-79.15
F3C
CO2Et
N
O
OMe
Ph
f1 (ppm)

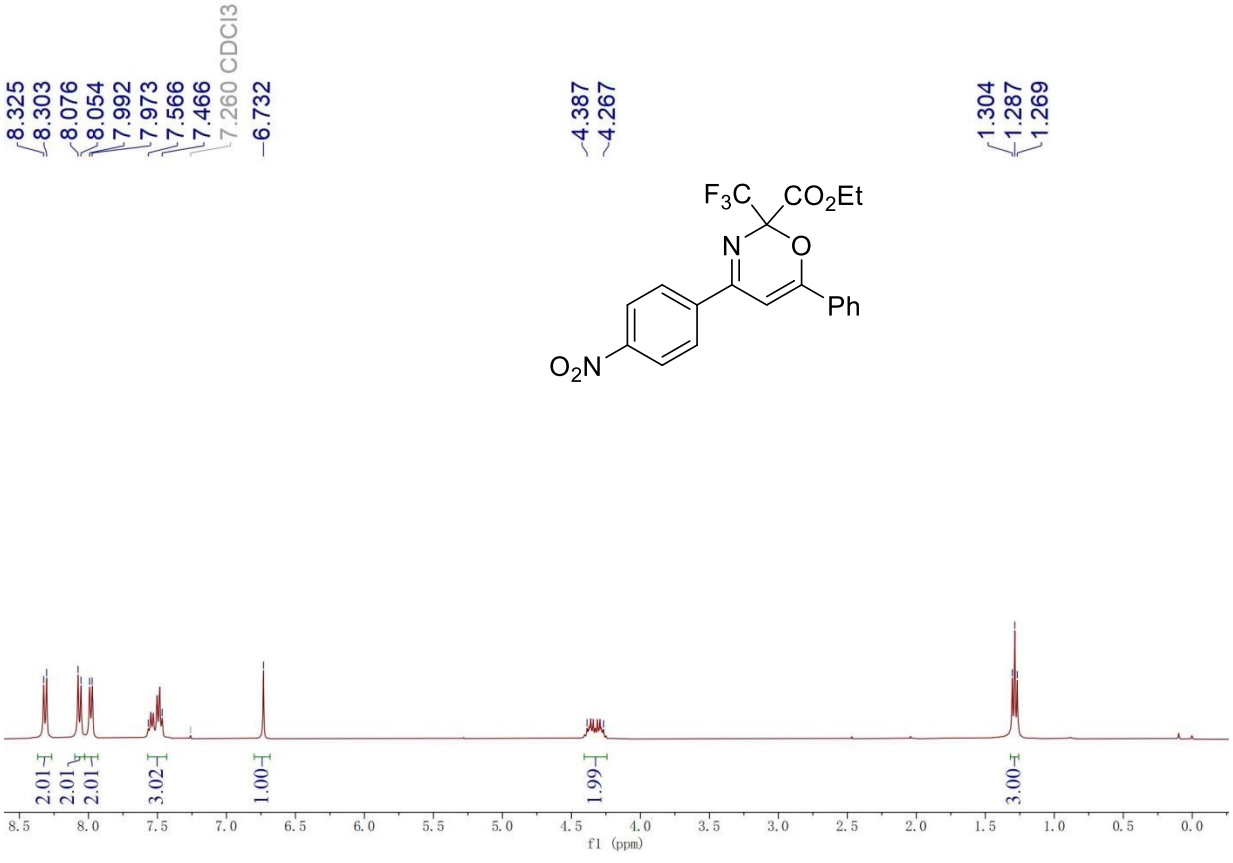
Ethyl 4-(4-chlorophenyl)-6-phenyl-2-(trifluoromethyl)-2*H*-1,3-oxazine-2-carboxylate (4g)

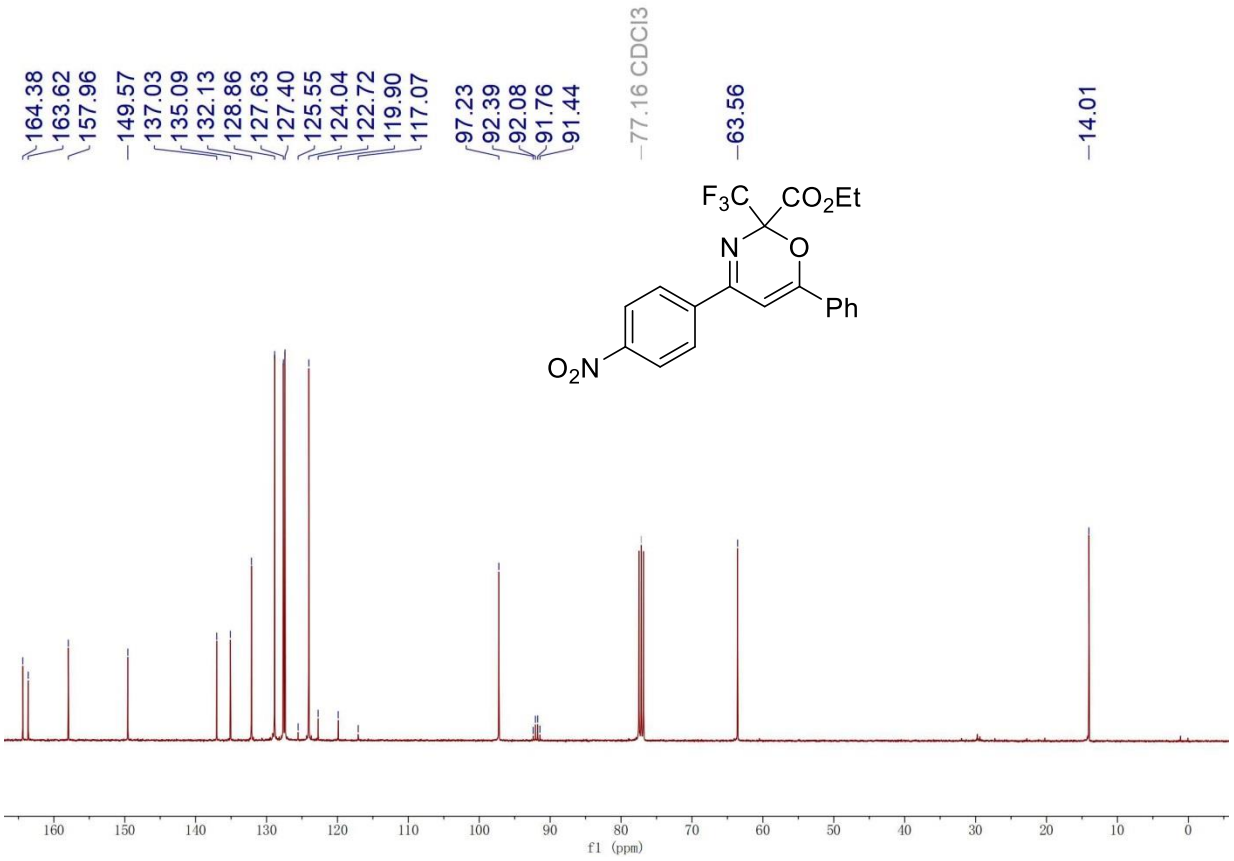


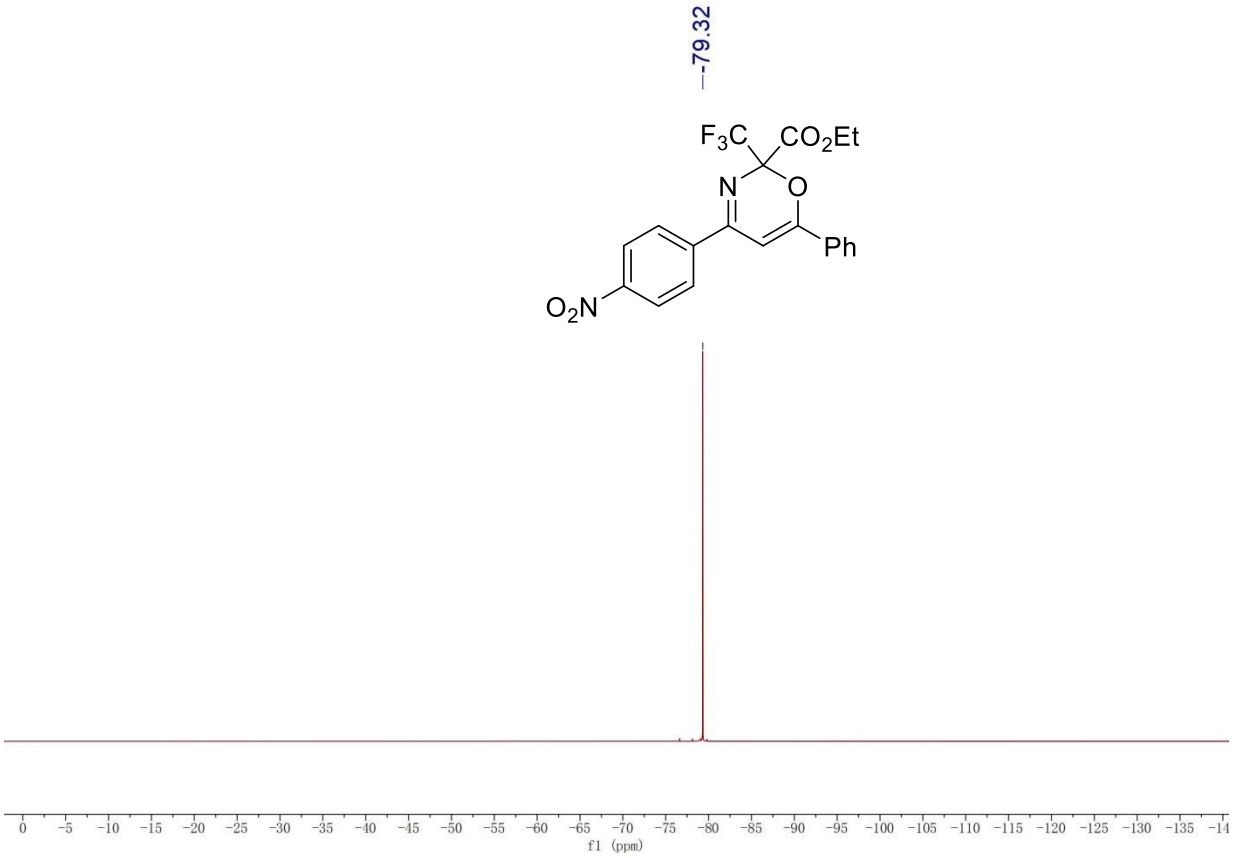




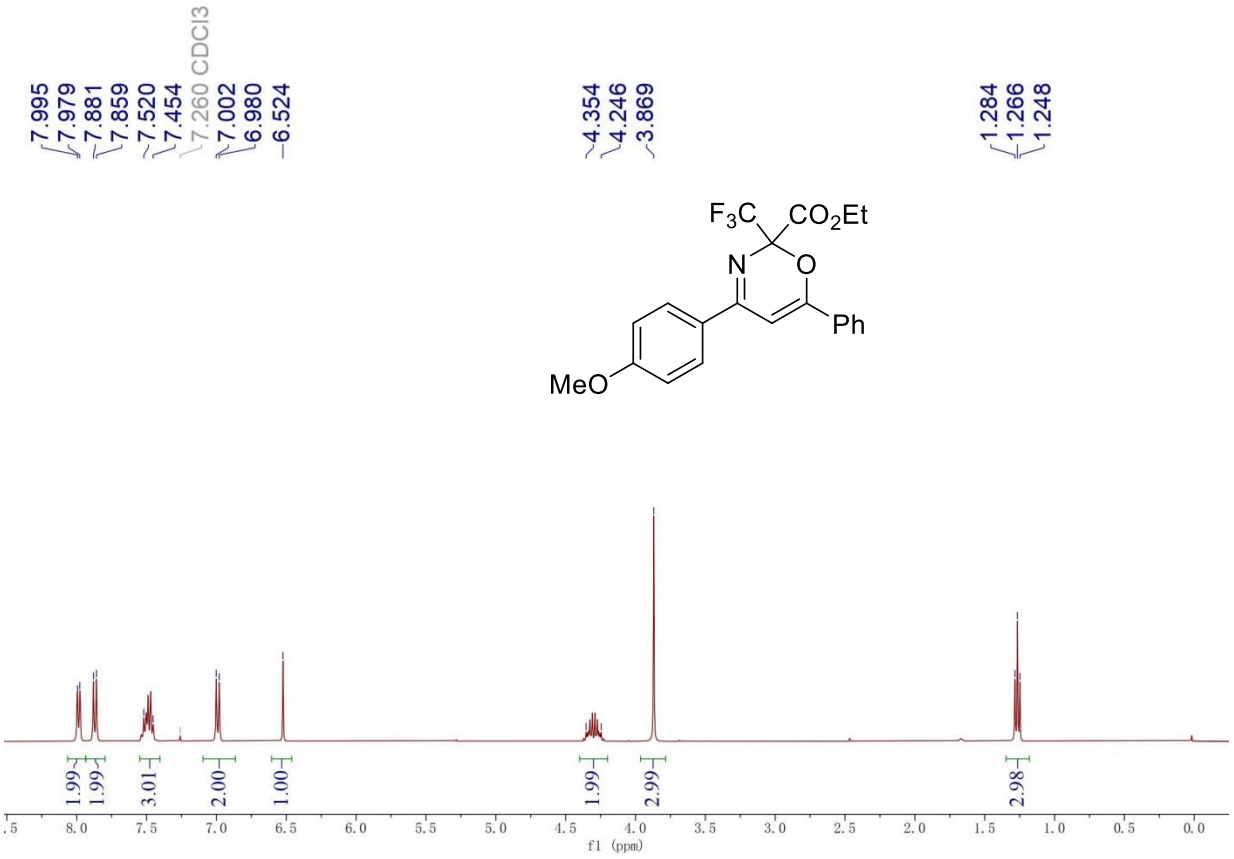
Ethyl 4-(4-nitrophenyl)-6-phenyl-2-(trifluoromethyl)-2*H*-1,3-oxazine-2-carboxylate (4h)

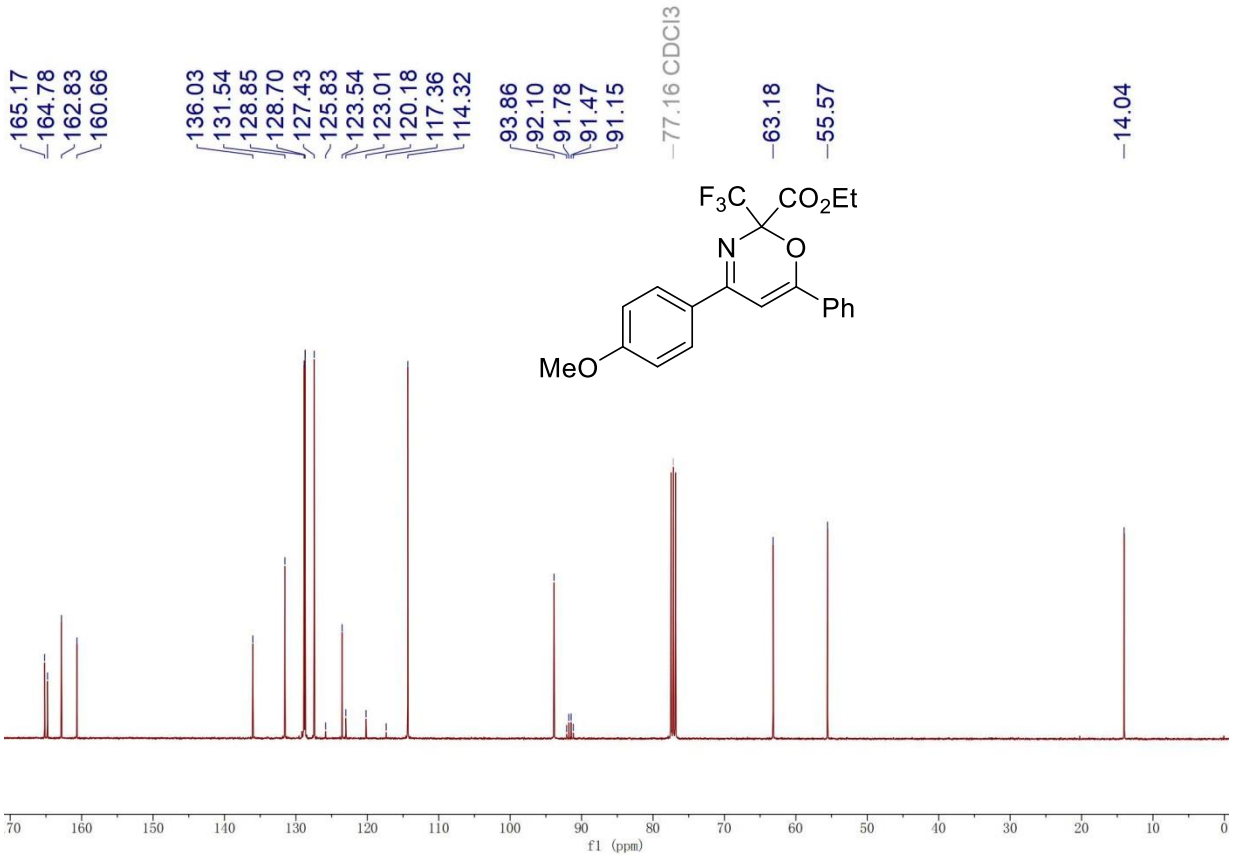


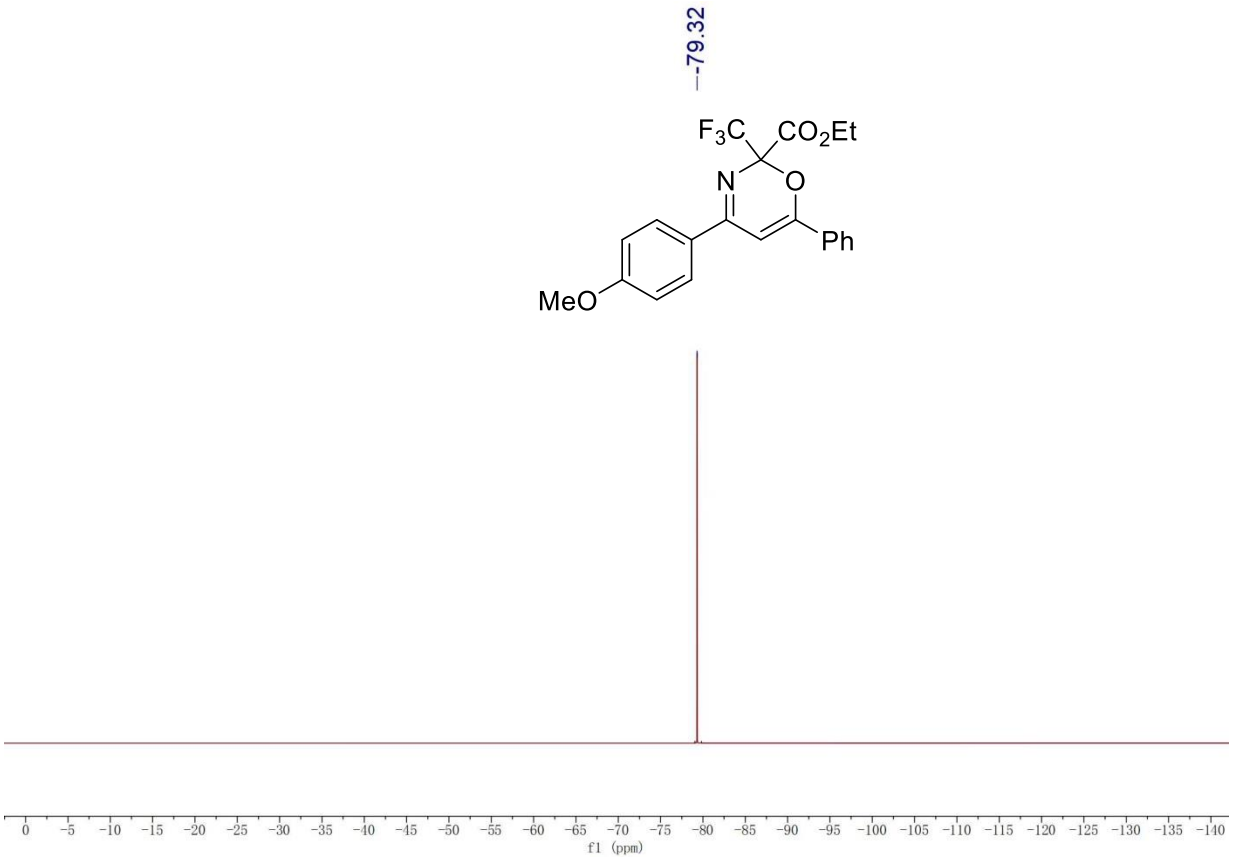

164.38
163.62
157.96
149.57
137.03
135.09
132.13
128.86
127.63
127.40
125.55
124.04
122.72
119.90
117.07
97.23
92.39
92.08
91.76
91.44
77.16 CDCl3
63.56
14.01
F3C
CO2Et
N
O
Ph
O2N
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


-79.32
F3C
CO2Et
N
O
Ph
O2N
0
-5
-10
-15
-20
-25
-30
-35
-40
-45
-50
-55
-60
-65
-70
-75
-80
-85
-90
-95
-100
-105
-110
-115
-120
-125
-130
-135
f1 (ppm)

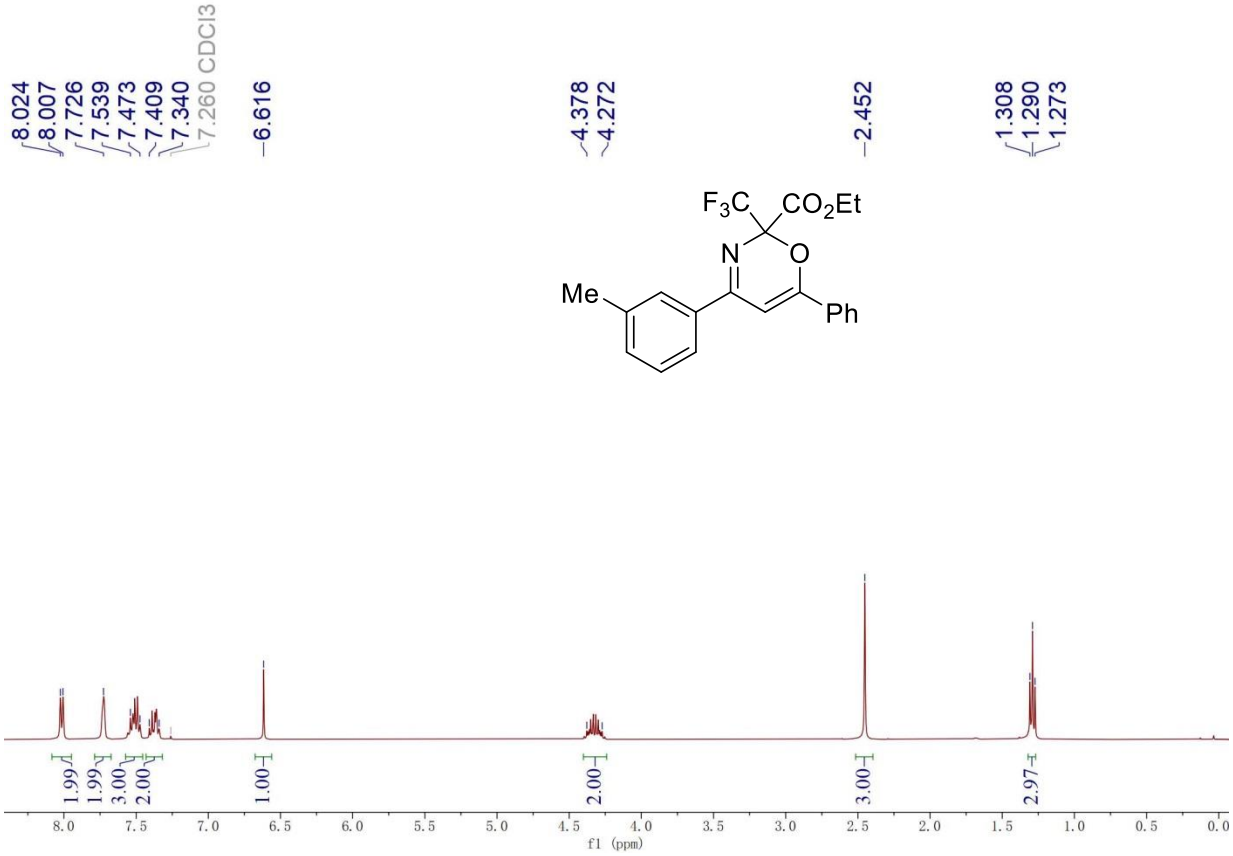
Ethyl 4-(4-methoxyphenyl)-6-phenyl-2-(trifluoromethyl)-2*H*-1,3-oxazine-2-carboxylate (4i)

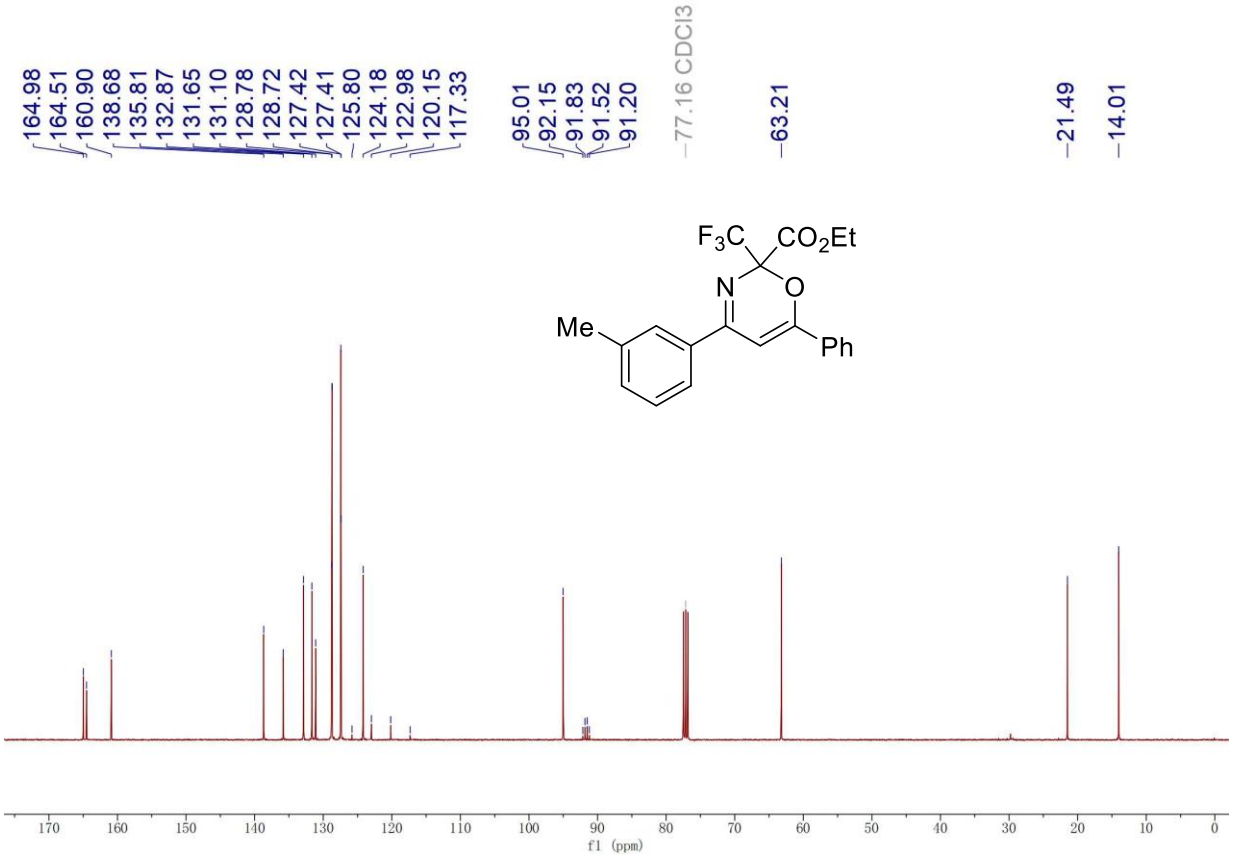


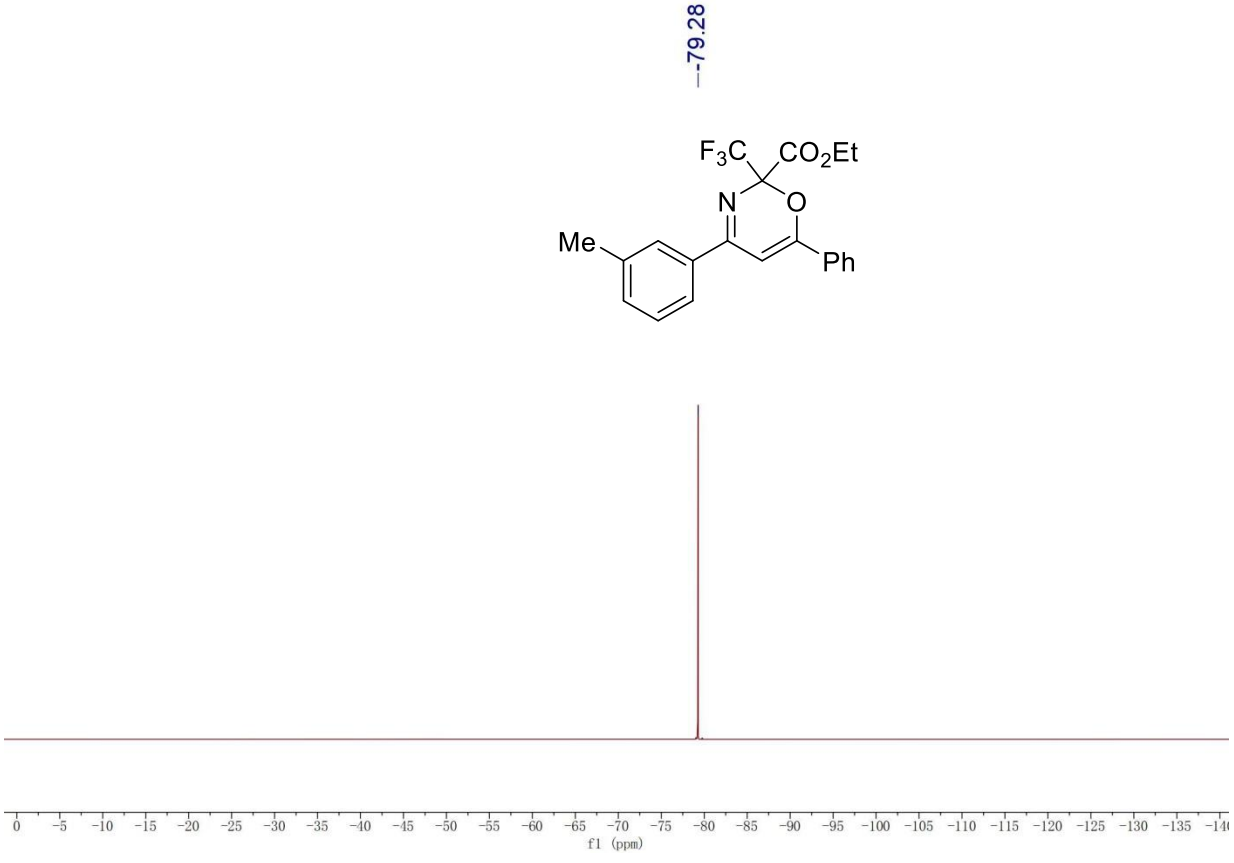




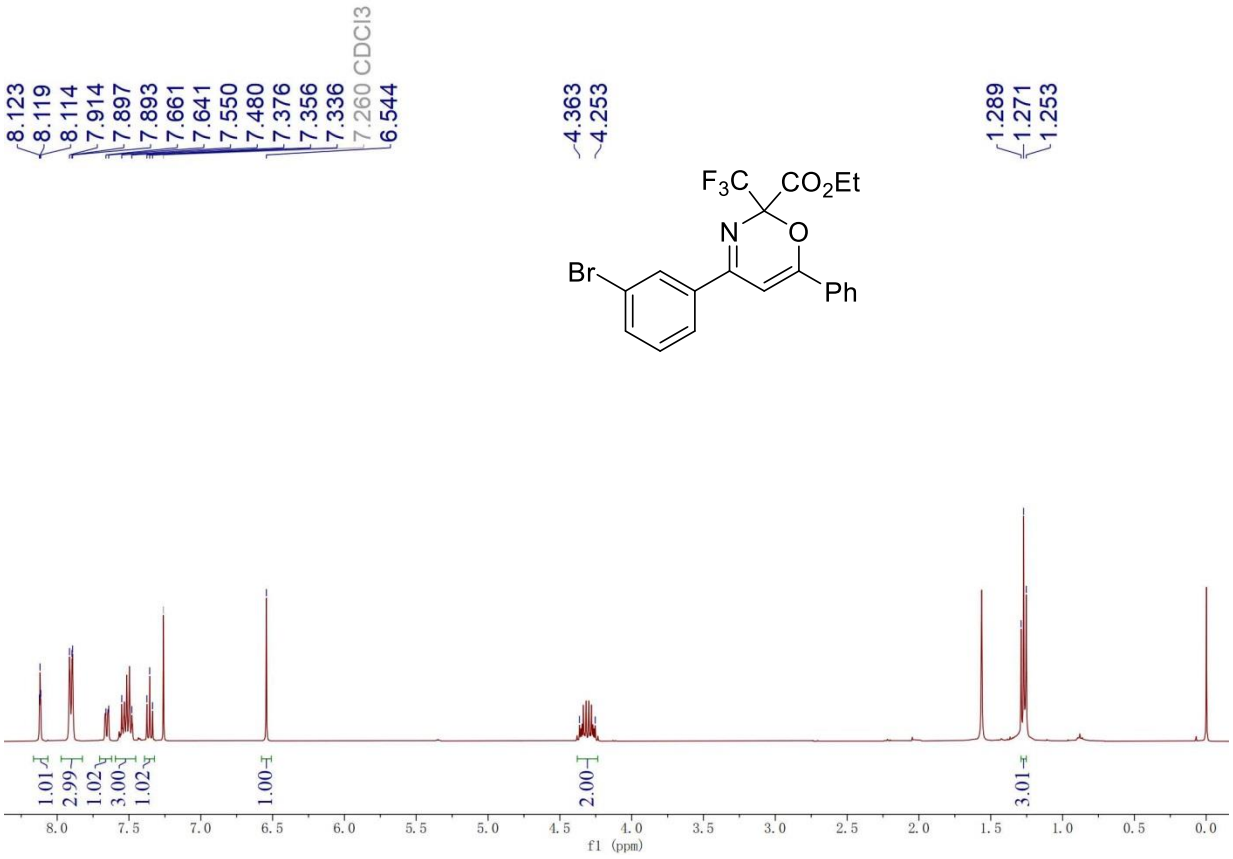
Ethyl 6-phenyl-4-(m-tolyl)-2-(trifluoromethyl)-2*H*-1,3-oxazine-2-carboxylate (4j)

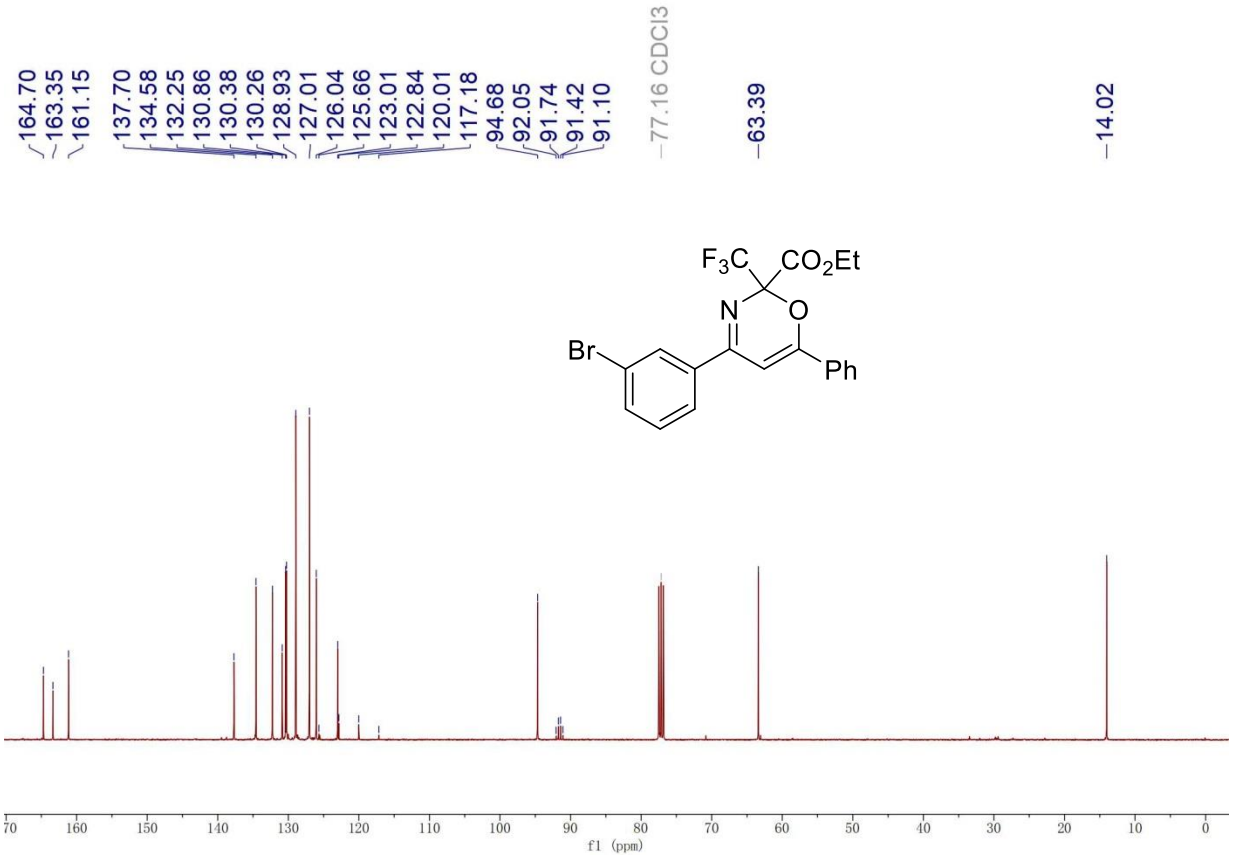


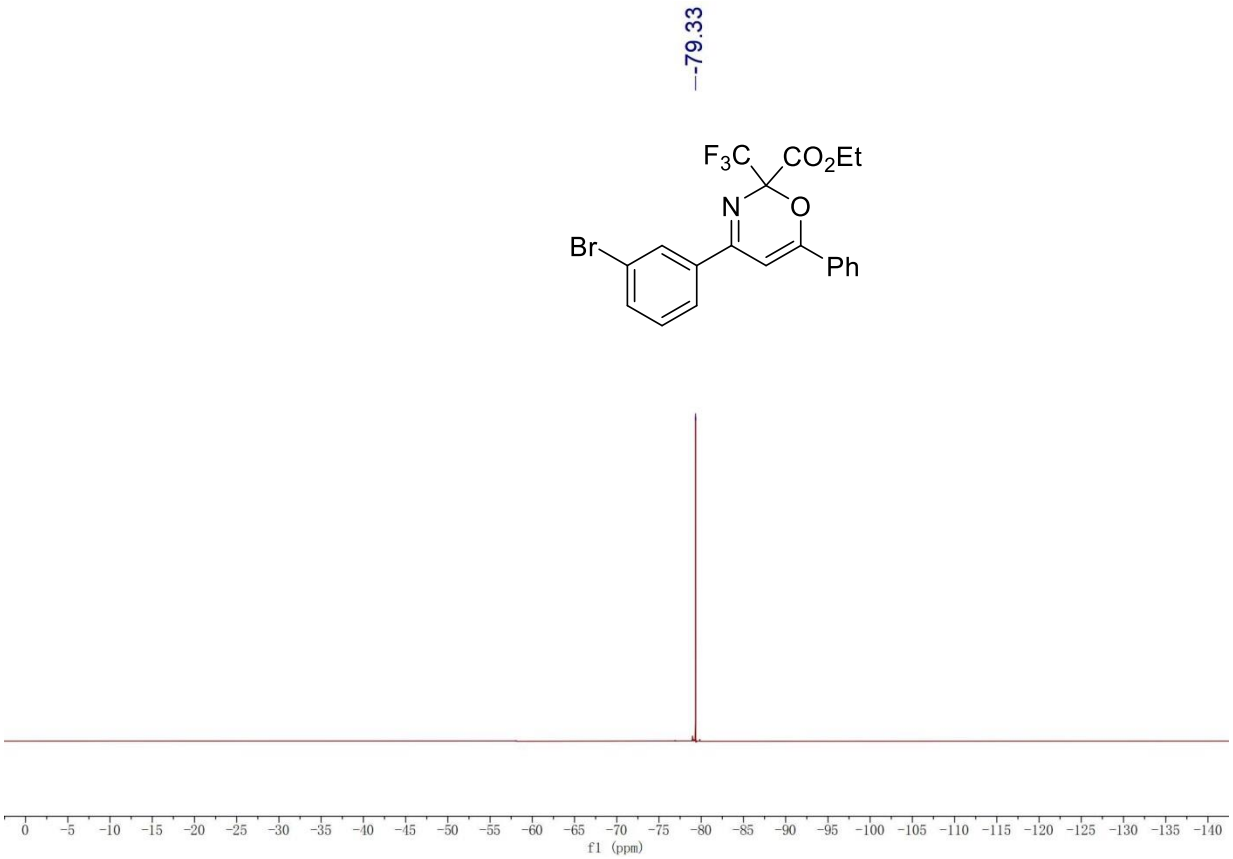

164.98
164.51
160.90
138.68
135.81
132.87
131.65
131.10
128.78
128.72
127.42
127.41
125.80
124.18
122.98
120.15
117.33
95.01
92.15
91.83
91.52
91.20
77.16 CDCl3
63.21
21.49
14.01
F3C
CO2Et
N
O
Me
Ph
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


-79.28
F3C
CO2Et
N
O
Me
Ph
0
-5
-10
-15
-20
-25
-30
-35
-40
-45
-50
-55
-60
-65
-70
-75
-80
-85
-90
-95
-100
-105
-110
-115
-120
-125
-130
-135
f1 (ppm)

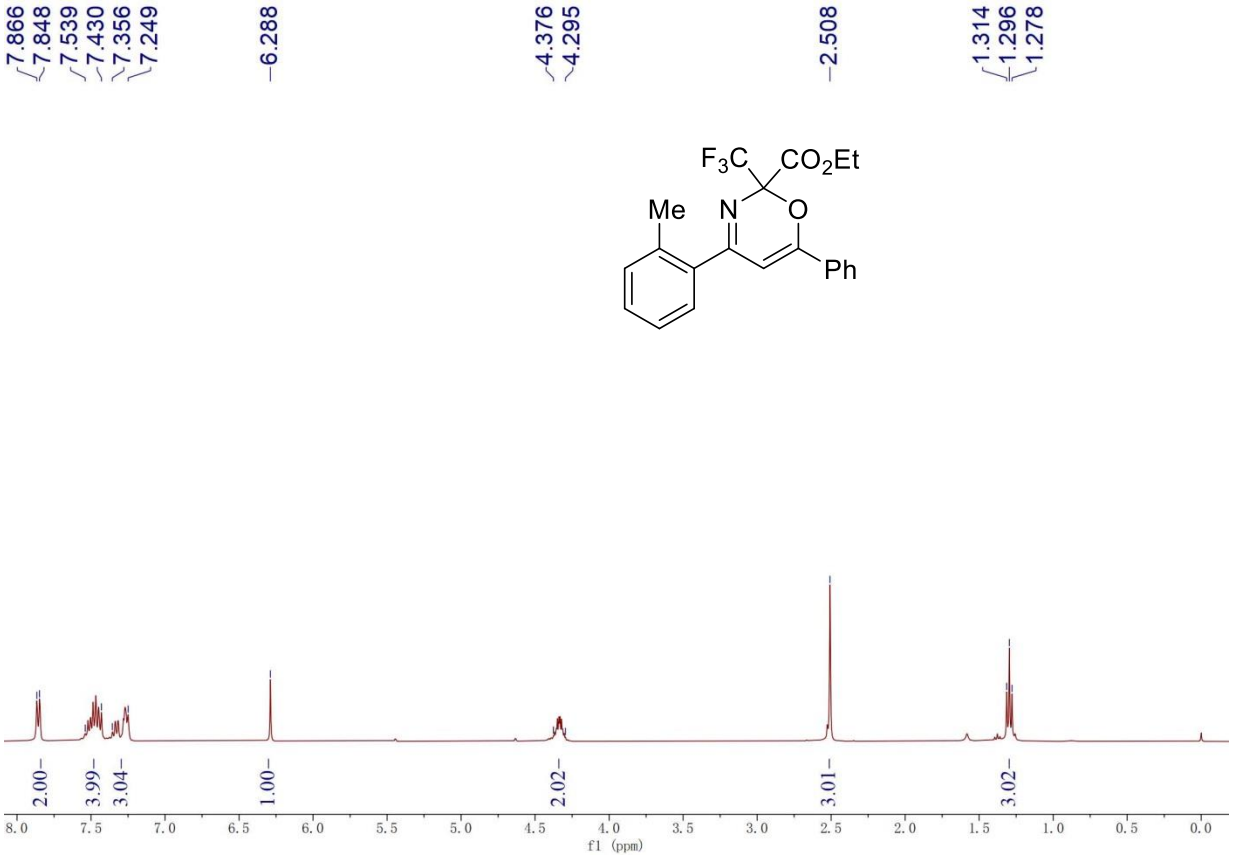
Ethyl 4-(3-bromophenyl)-6-phenyl-2-(trifluoromethyl)-2*H*-1,3-oxazine-2-carboxylate (4k)

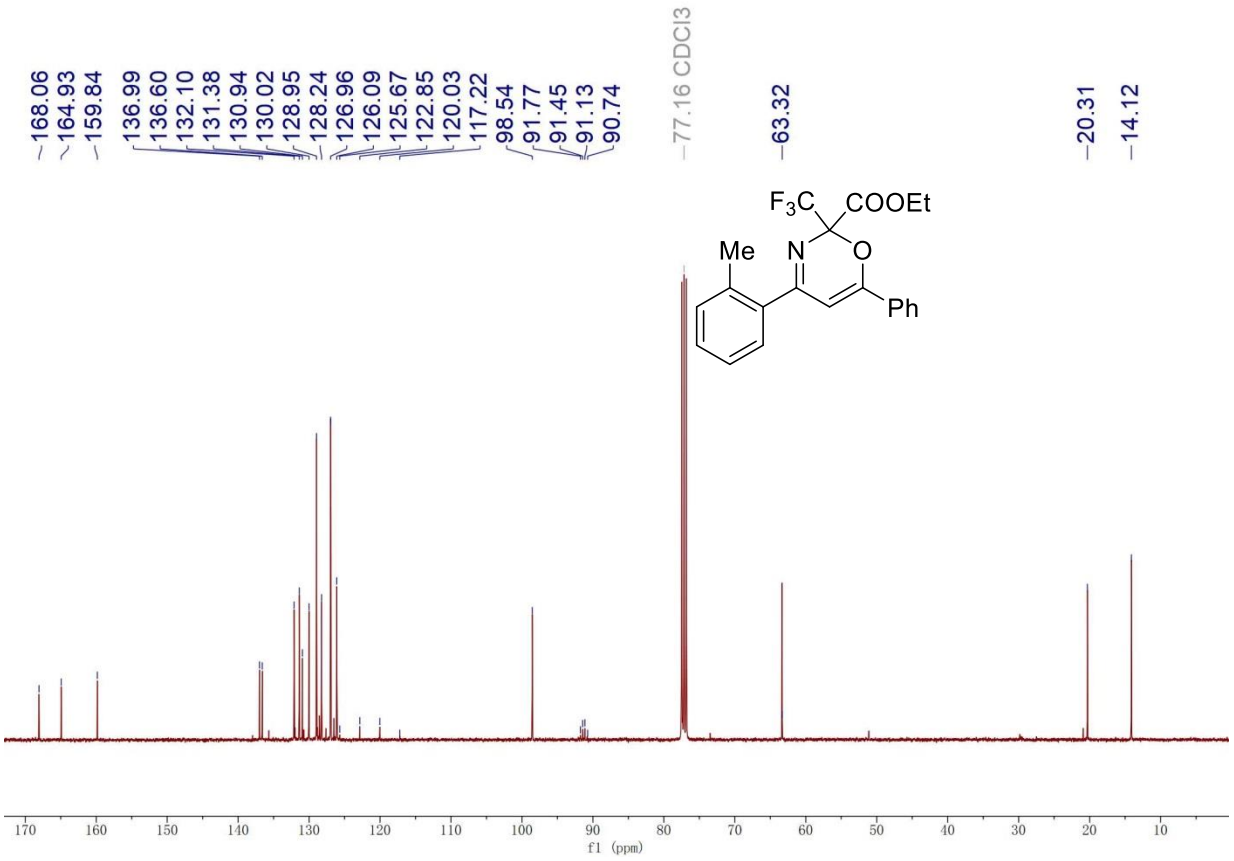


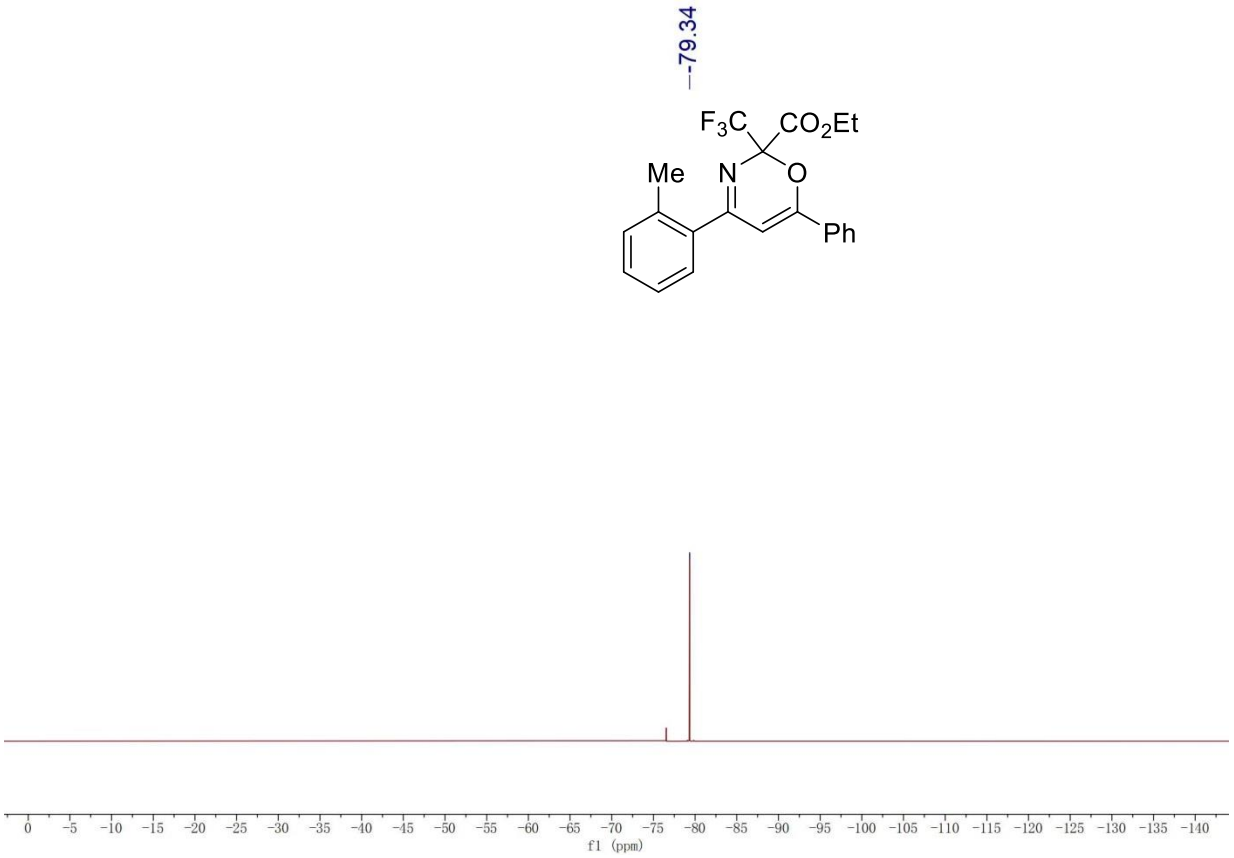




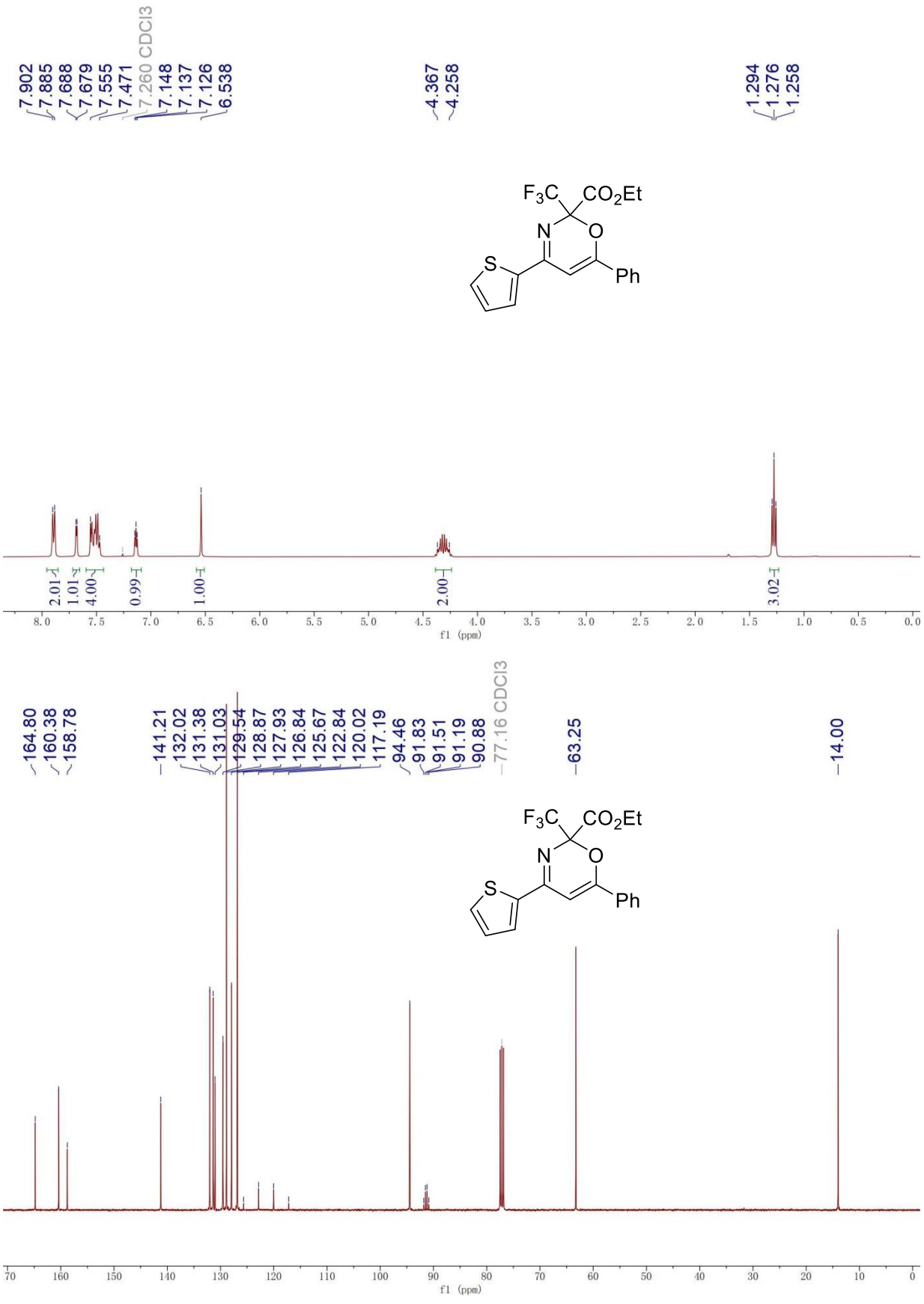
Ethyl 6-phenyl-4-(o-tolyl)-2-(trifluoromethyl)-2*H*-1,3-oxazine-2-carboxylate (4l)

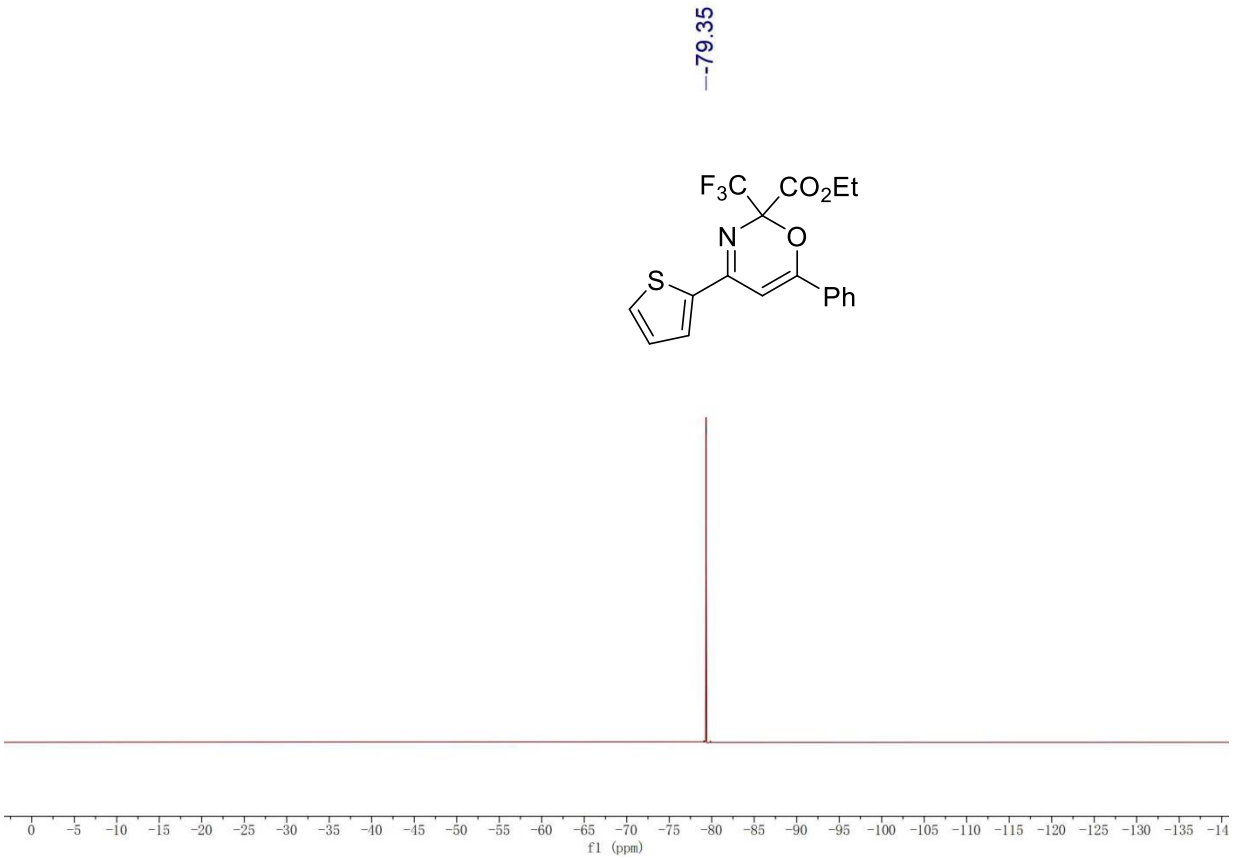



168.06
164.93
159.84
136.99
136.60
132.10
131.38
130.94
130.02
128.95
128.24
126.96
126.09
125.67
122.85
120.03
117.22
98.54
91.77
91.45
91.13
90.74
77.16 CDCl3
63.32
20.31
14.12
F3C
COOEt
Me
N
O
Ph
f1 (ppm)

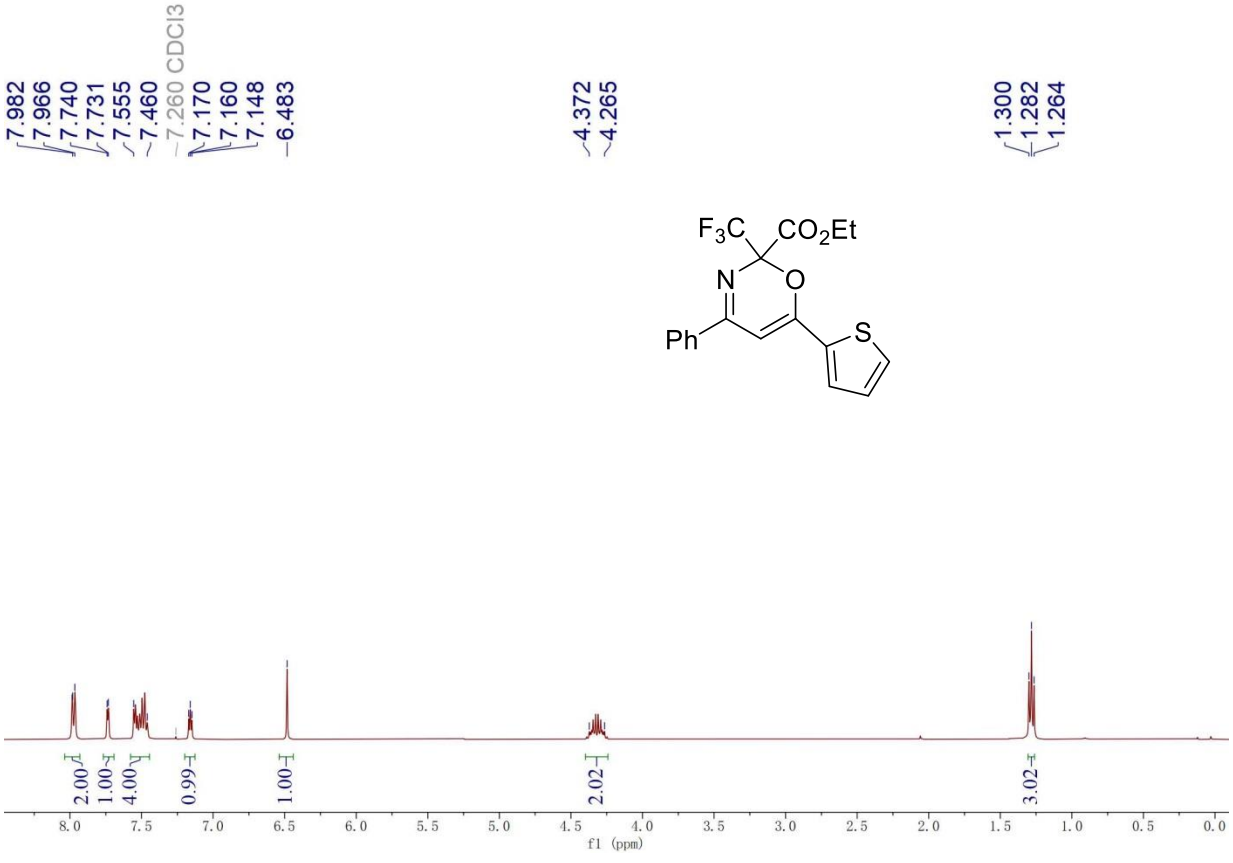

-79.34
F3C
CO2Et
Me
N
O
Ph
f1 (ppm)

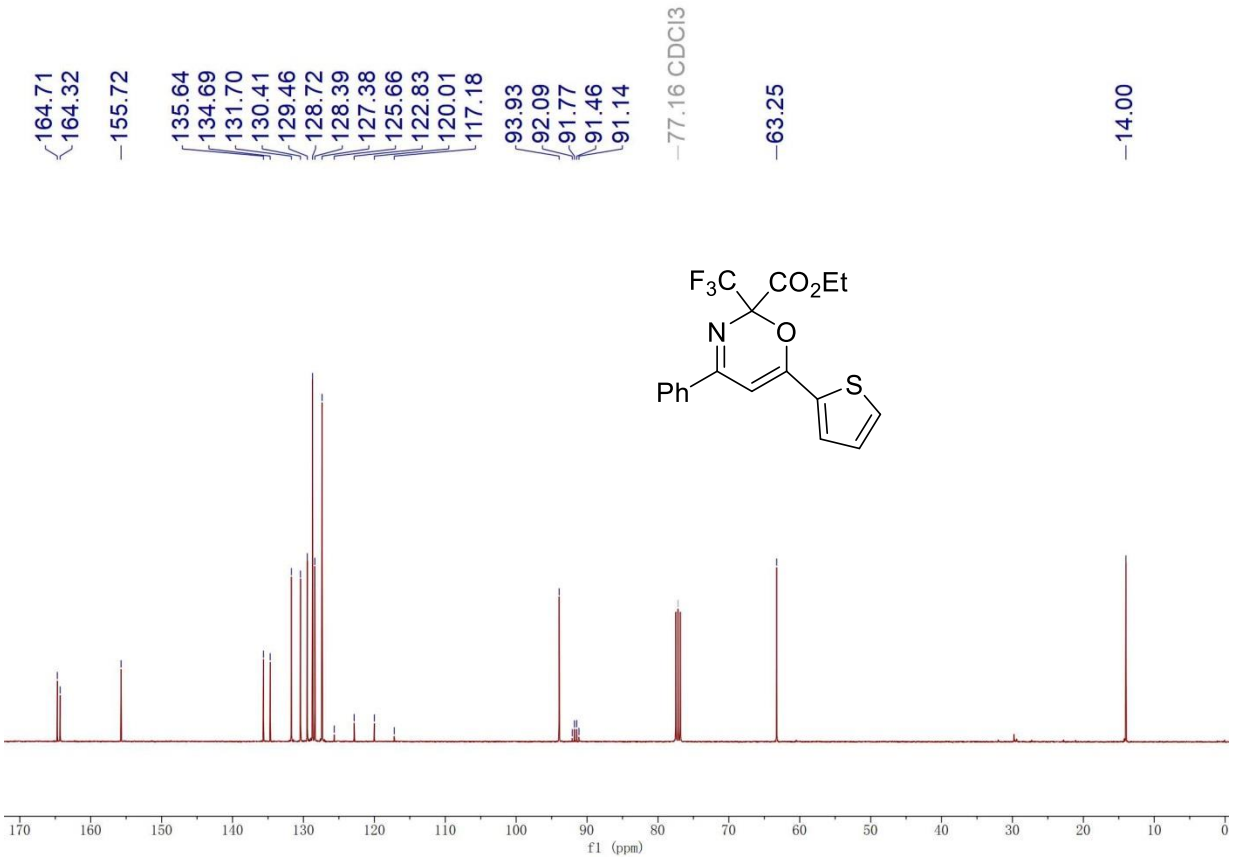
Ethyl 6-phenyl-4-(thiophen-2-yl)-2-(trifluoromethyl)-2*H*-1,3-oxazine-2-carboxylate (4m)

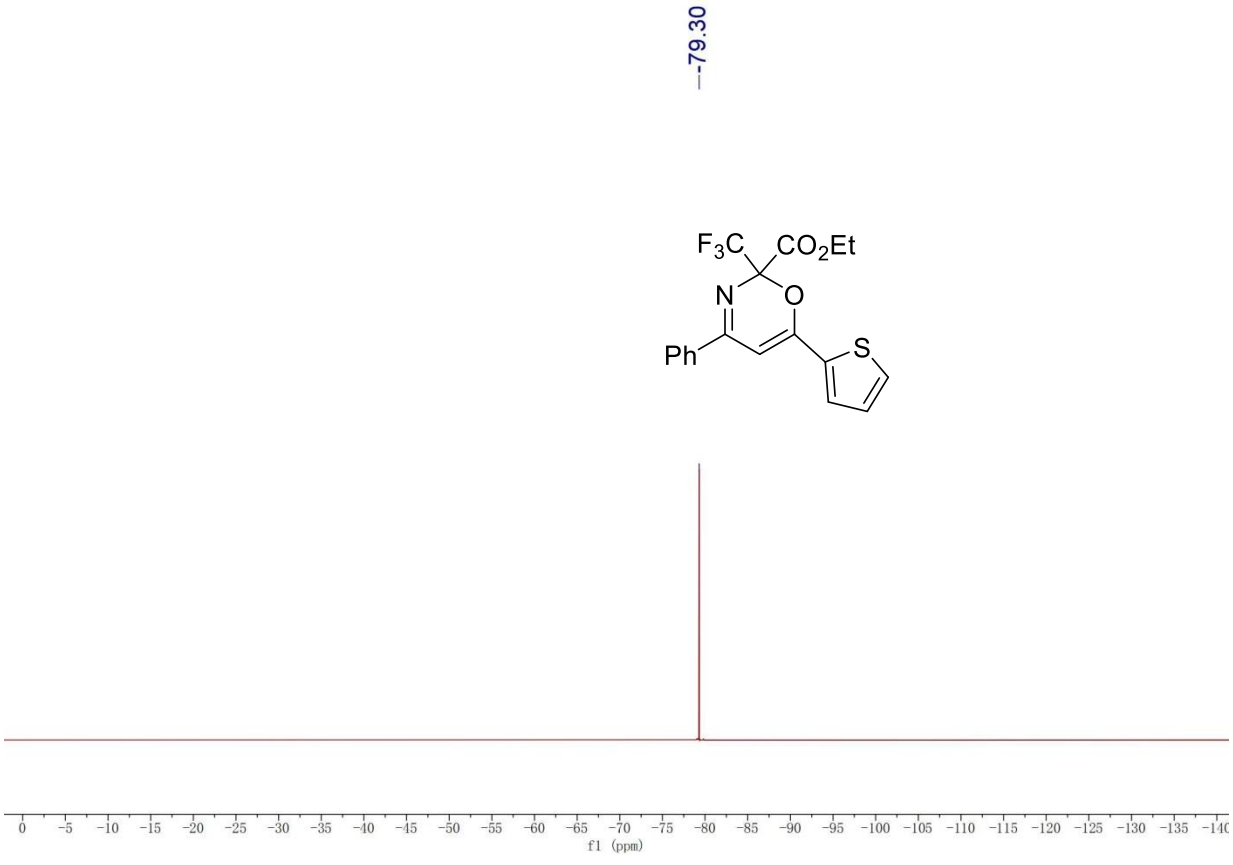




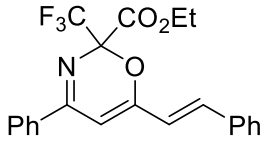
Ethyl 4-phenyl-6-(thiophen-2-yl)-2-(trifluoromethyl)-2*H*-1,3-oxazine-2-carboxylate (4n)

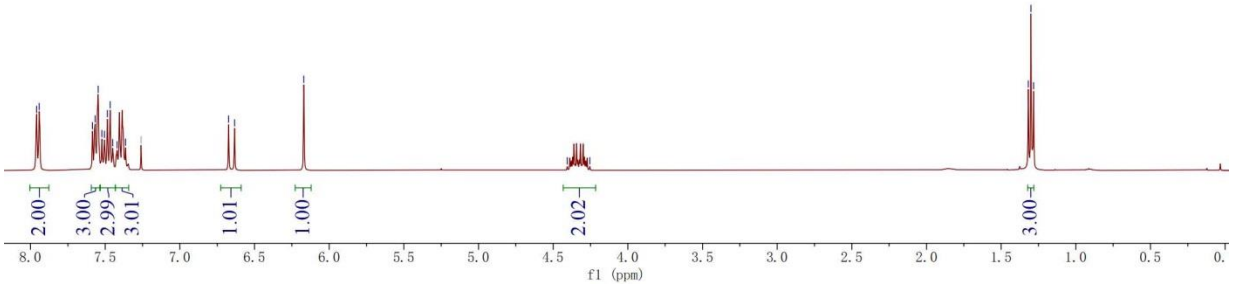


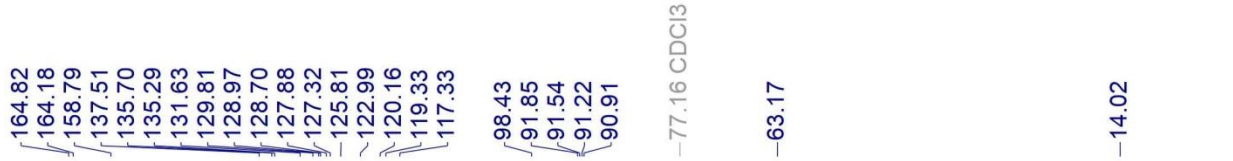

164.71
164.32
155.72
135.64
134.69
131.70
130.41
129.46
128.72
128.39
127.38
125.66
122.83
120.01
117.18
93.93
92.09
91.77
91.46
91.14
77.16 CDCl3
63.25
14.00
F3C
CO2Et
N
O
Ph
S
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

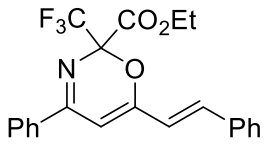

-79.30
F3C
CO2Et
N
O
Ph
S
0
-5
-10
-15
-20
-25
-30
-35
-40
-45
-50
-55
-60
-65
-70
-75
-80
-85
-90
-95
-100
-105
-110
-115
-120
-125
-130
-135
f1 (ppm)

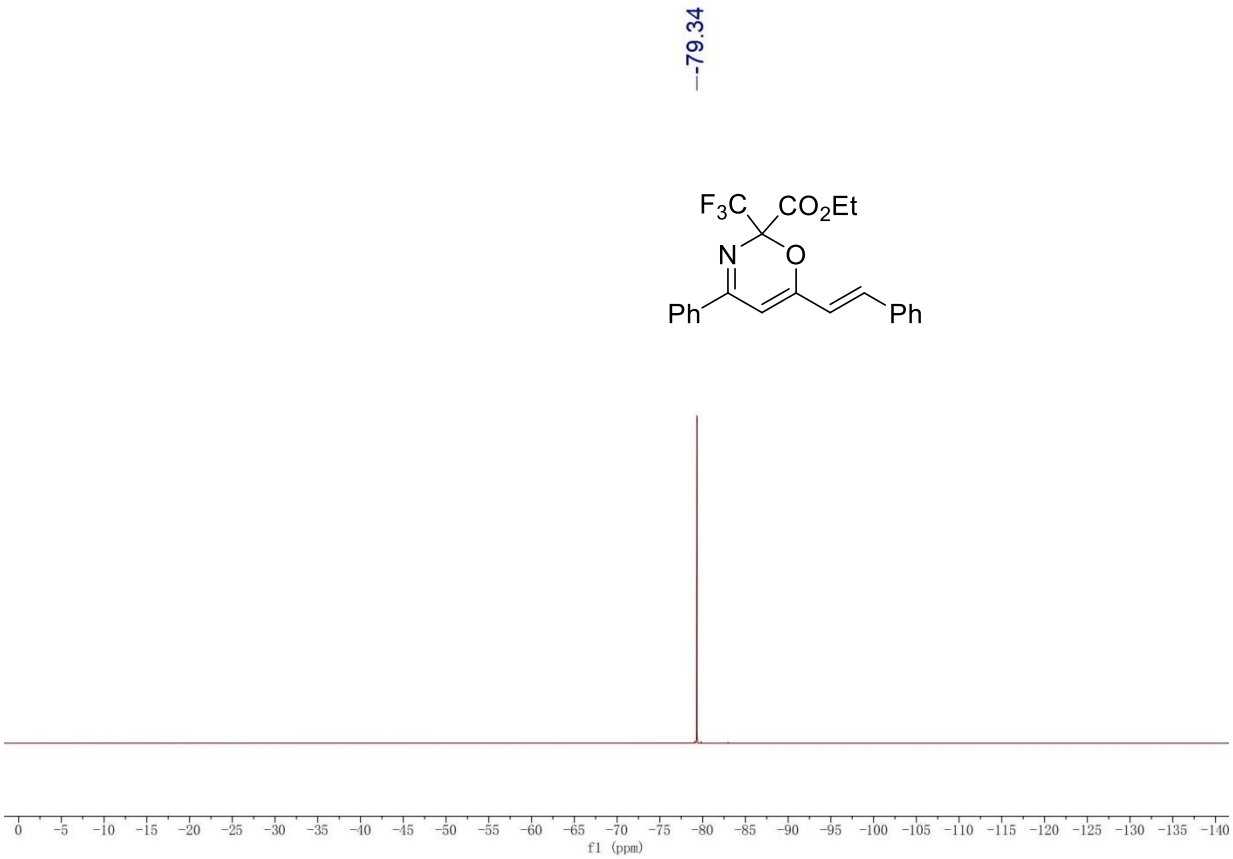
Ethyl (E)-4-phenyl-6-styryl-2-(trifluoromethyl)-2*H*-1,3-oxazine-2-carboxylate (4o)



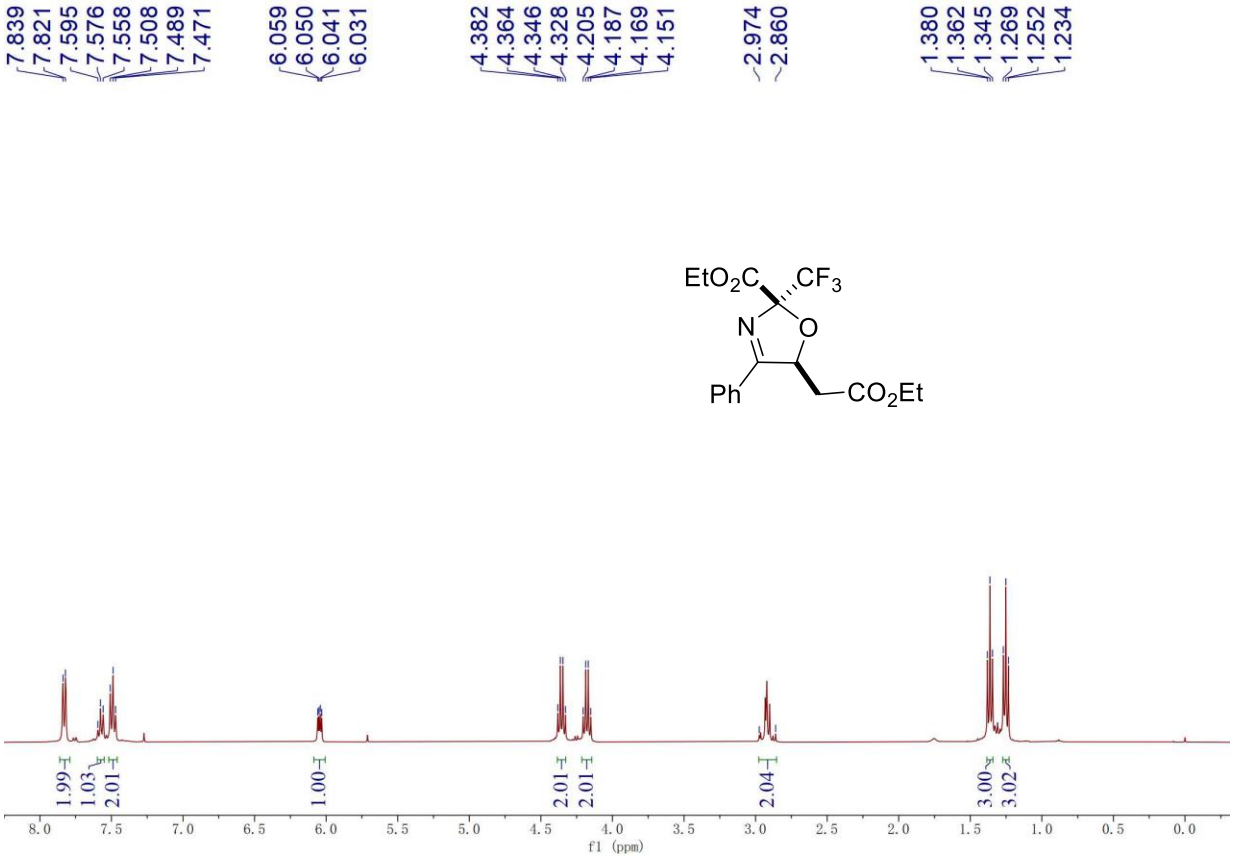


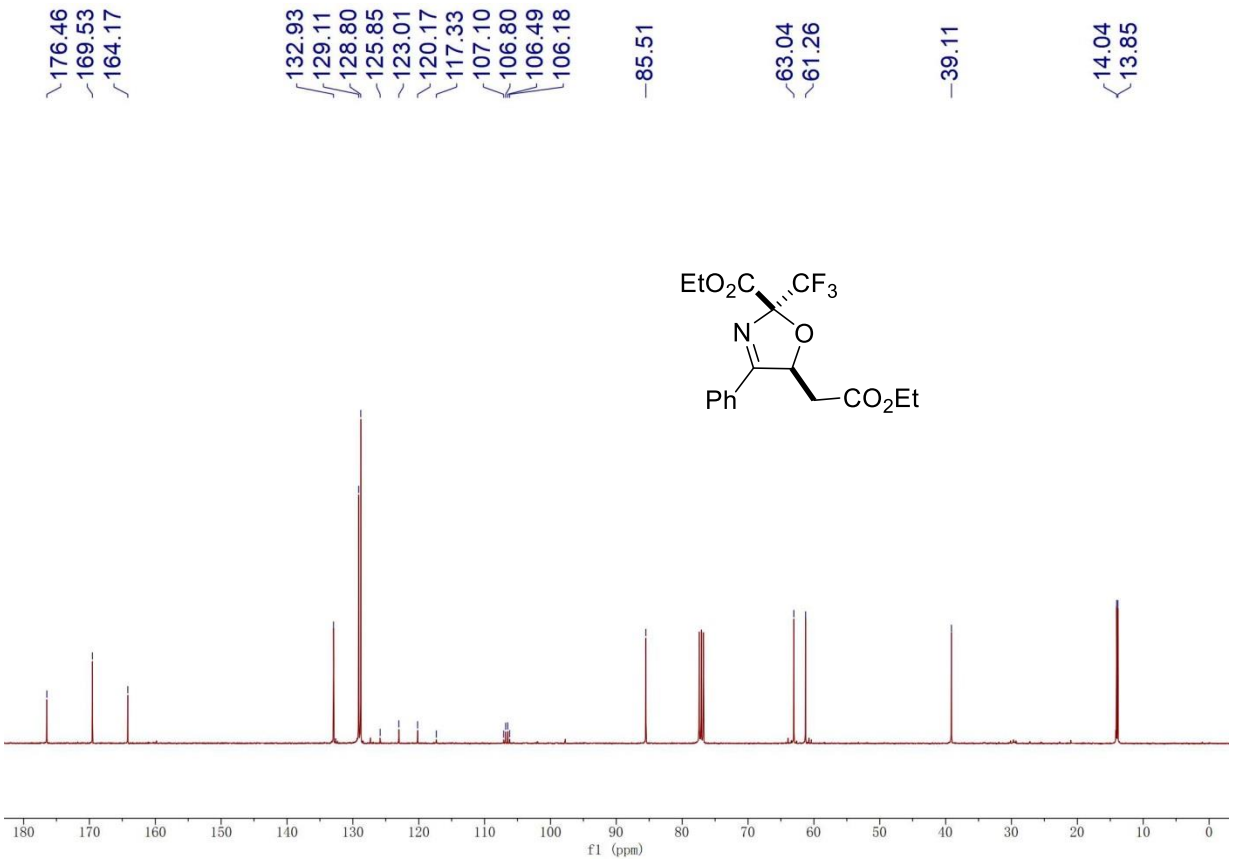


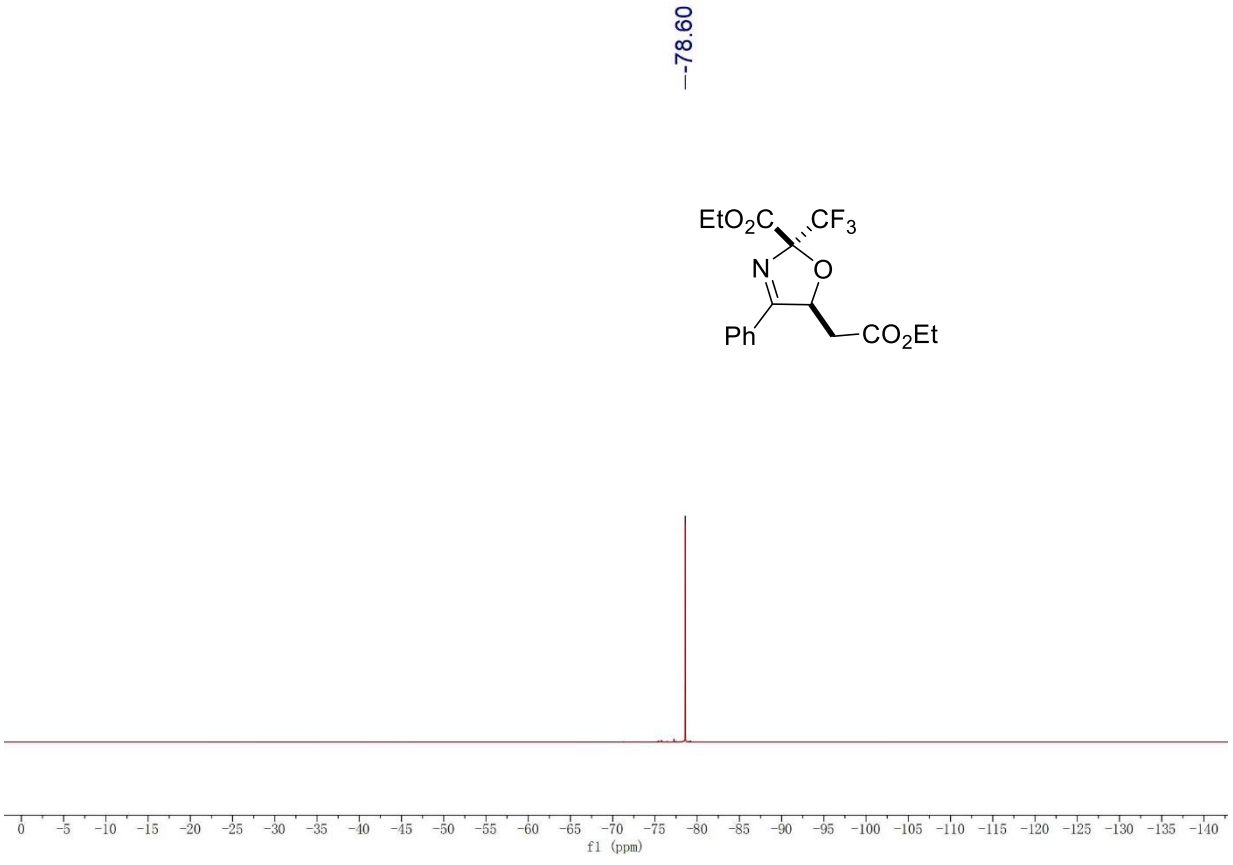




Ethyl-5-(2-ethoxy-2-oxoethyl)-4-phenyl-2-(trifluoromethyl)-2,5-dihydrooxazole-2-carboxylate (5a)




176.46
169.53
164.17
132.93
129.11
128.80
125.85
123.01
120.17
117.33
107.10
106.80
106.49
106.18
85.51
63.04
61.26
39.11
14.04
13.85
EtO2C
CF3
N
O
Ph
CO2Et
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


-78.60
EtO2C
CF3
N
O
Ph
CO2Et
0
-5
-10
-15
-20
-25
-30
-35
-40
-45
-50
-55
-60
-65
-70
-75
-80
-85
-90
-95
-100
-105
-110
-115
-120
-125
-130
-135
-140
f1 (ppm)

Crystal structure and data for compound 3o

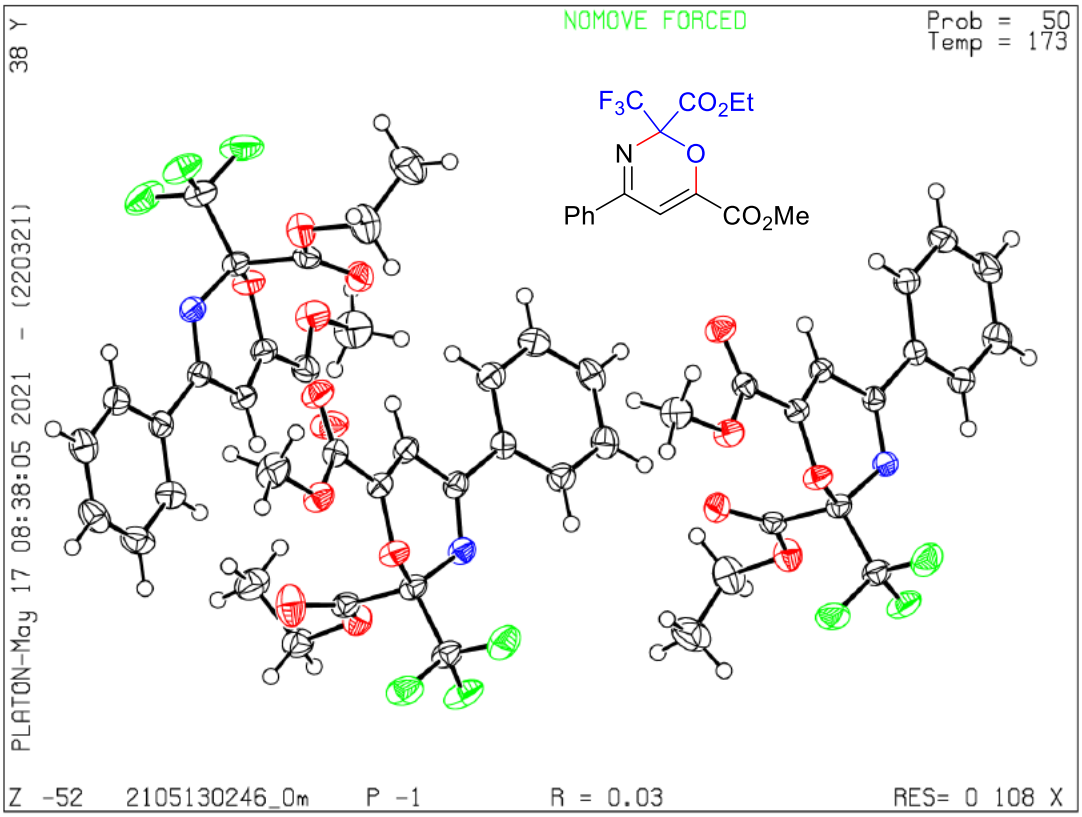


Table 1. Crystal data and structure refinement for 2105130246_0m.

Identification code	2105130246_0m	
Empirical formula	$C_{16}H_{14}F_3NO_5$	
Formula weight	357.28	
Temperature	172.99 K	
Wavelength	1.34139 Å	
Crystal system	Triclinic	
Space group	P-1	
Unit cell dimensions	a = 12.9185(2) Å	a= 85.1240(10)°.
	b = 14.1732(2) Å	b= 79.5830(10)°.
	c = 14.4149(2) Å	g = 67.9670(10)°.
Volume	2405.81(6) $Å^3$	
Z	6	
Density (calculated)	1.480 Mg/m^3	
Absorption coefficient	0.740 mm^{-1}	
F(000)	1104	
Crystal size	0.05 x 0.03 x 0.03 mm^3	
Theta range for data collection	2.927 to 54.928°.	
Index ranges	-15<=h<=15, -17<=k<=16, -15<=l<=17	
Reflections collected	31488	
Independent reflections	9074 [R(int) = 0.0311]	
Completeness to theta = 53.594°	98.9 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	0.7508 and 0.6553	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	9074 / 0 / 682	
Goodness-of-fit on F^2	1.026	
Final R indices [I>2sigma(I)]	R1 = 0.0345, wR2 = 0.0914	
R indices (all data)	R1 = 0.0367, wR2 = 0.0935	
Extinction coefficient	n/a	
Largest diff. peak and hole	0.287 and -0.218 e.$Å^{-3}$	

HRMS (ESI-TOF) analysis of the reaction mixture