Thio-Michael Addition of Thioamides and Allenes for the Selective Construction of Polysubstituted 2-Arylthiophenes via TBAI/H2O2 Promoted Tandem Oxidative Annulation and 1,2-Sulfur Migration

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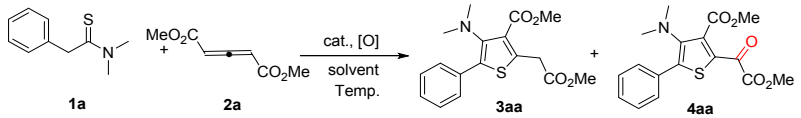
Contents

1. General information

Commercial reagents were used without further purification, unless otherwise noted. Melting points were obtained in open capillary tubes using SGW X-4 micro melting point apparatus which was uncorrected. The mass spectra were recorded on a TOF mass spectrometer using the EI method. ^{1}H NMR spectra were recorded using Bruker DPX 400 M spectrometer at ambient temperatures and the $CDCl_3$ as the solvent. Chemical shifts (in ppm) with internal TMS signal is 0.0 ppm as standard are reported as (s = singlet, d = doublet, t = triplet, q = quartet, and m = multiplet).^{13}C NMR spectra were recorded on a 100 MHz spectrometer by broadband spin decoupling for $CDCl_3$ at ambient temperatures. The standard of chemical shifts (in ppm) is the signal of internal chloroform which at 77.0 ppm. TLC was performed by using commercially prepared 100−400 mesh silica gel plates, and visualization was effected at 254 or 365 nm.

2. Optimization of oxidative annulation reaction of 1a with 2a

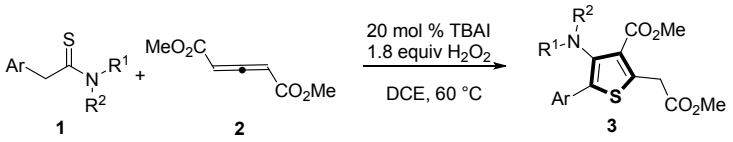


1a 2a 3aa 4aa

Entry	cat.	[O]	Solvent	Temp (°C)	Yield 3aa[%][a]	Yield 4aa[%][a]
1	TBAI	TBHP (2 equiv.)	1,4-dioxane	60	-	40
2	TBAI	TBHP (1 equiv.)	1,4-dioxane	60	30	23
3	TBAI	TBHP (1 equiv.)	DCE	60	34	20
4	TBAI	TBHP (1 equiv.)	toluene	60	20	25
5	TBAI	TBHP (1 equiv.)	THF	60	24	trace
6	TBAI	TBHP (1 equiv.)	EtOAc	60	26	trace
7	TBAI	TBHP (1 equiv.)	CH_3CN	60	20	trace
8	TBAI	TBHP (1 equiv.)	EtOH	60	trace	-
7	TBAI	H_2O_2 (1 equiv.)	DCE	60	50	trace
8	TBAI	mCPBA (1 equiv.)	DCE	60	41	trace
9	TBAI	TBPB(1 equiv.)	DCE	60	20	-
10	TBAI	$K_2S_2O_8$ (1 equiv.)	DCE	60	trace	-
11	TBAI	DTBP(1 equiv.)	DCE	60	22	trace
12	TBAI	H_2O_2 (1 equiv.)	DCE	55	48	trace
13	TBAI	H_2O_2 (1 equiv.)	DCE	50	46	trace
14	TBAI	H_2O_2 (1 equiv.)	DCE	45	43	trace
15	TBAI	H_2O_2 (1 equiv.)	DCE	40	44	trace
16	TBAI	H_2O_2 (1 equiv.)	DCE	25	48	trace
17	TBAI	H_2O_2 (1 equiv.)	DCE	70	40	trace
18	NIS	H_2O_2 (1 equiv.)	DCE	60	30	trace
19	KI	H_2O_2 (1 equiv.)	DCE	60	26	trace
20	I_2	H_2O_2 (1 equiv.)	DCE	60	38	trace
21[c]	TBAI	H_2O_2 (1 equiv.)	DCE	60	53	trace
22[d]	TBAI	H_2O_2 (1 equiv.)	DCE	60	50	trace
23[c]	TBAI	H_2O_2 (1.2 equiv.)	DCE	60	46	trace
24[c]	TBAI	H_2O_2 (1.5 equiv.)	DCE	60	54	trace
25[c]	TBAI	H_2O_2 (1.8 equiv.)	DCE	60	58	trace
26[c]	TBAI	H_2O_2 (2.0 equiv.)	DCE	60	45	trace
27[c]	TBAI	TBHP (1.8 equiv.)	DCE	60	42	trace
28[c]	TBAI	TBPB (1.8 equiv.)	DCE	60	trace	-
29[c]	TBAI	DTBP (1.8 equiv.)	DCE	60	trace	-
30[c]	TBAI	m-CPBA (1.8 equiv.)	DCE	60	trace	-
31[c]	TBAI	Ag_2O (1.8 equiv.)	DCE	60	-	-
32[c]	TBAI	oxone (1.8 equiv.)	DCE	60	-	-
33[c]	TBAI	$PhI(OAc)_2$ (1.8 equiv.)	DCE	60	12	35
34[c]	TBAI	$FeCl_3$ (1.8 equiv.)	DCE	60	40	trace
35[c]	TBAI	$K_2O_8S_2$ (1.8 equiv.)	DCE	60	38	-

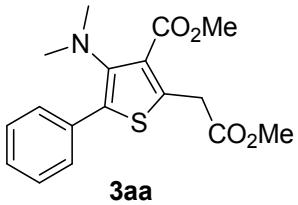
[a]Reaction conditions: **1a** (0.2 mmol), **2a** (0.2 mmol), cat. (0.04 mmol), oxidant (0.4 mmol), solvent (1 mL), under air atmosphere, 7h. [b]Isolated yield. [c]**1a** (0.24 mmol), **2a** (0.2 mmol). [d]**1a** (0.3 mmol), **2a** (0.2 mmol).

3. Preparation and characterization data of polysubstituted thiophenes (3aa-3ab).



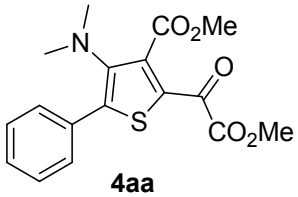
1 2 3

General procedure: Thioamides compounds **1** (0.24 mmol), allene **2** (0.2 mmol), and H_2O_2 (0.36 mmol) were added to a solution of TBAI (0.04 mmol) in 1,2-dichloroethane (1 mL) under an air atmosphere. The mixture was then stirred at 60 °C until the reaction was nearly completed monitored by the TLC. The resulting mixture was concentrated in vacuum and then purified by column chromatography on 100−200 mesh silica gel to afford the desired products **3**.



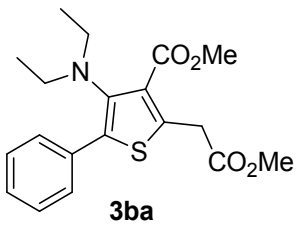
3aa

Methyl 4-(dimethylamino)-2-(2-methoxy-2-oxoethyl)-5-phenylthiophene-3-carboxylate (3aa). A yellow solid (38.6 mg, 58% yield), Mp: 57-59 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.58- 7.54 (m, 2H, Ar*H*), 7.41-7.33 (m, 2H, Ar*H*), 7.33-7.28 (m, 1H, Ar*H*), 3.95 (s, 2H, CH_2), 3.87 (s, 3H, CO_2CH_3), 3.74 (s, 3H, CO_2CH_3), 2.69 (s, 6H, N(CH_3)$_2$). ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.3 (*C*=O), 164.7 (*C*=O), 146.9 (Ar*C*), 138.2 (Ar*C*), 133.7 (Ar*C*), 130.9 (Ar*C*), 128.8 (Ar*C*), 128.7 (2×Ar*C*), 128.3 (2×Ar*C*), 127.5 (Ar*C*), 52.3 (CO_2CH_3), 51.7 (CO_2CH_3), 43.4 (N(CH_3)$_2$), 35.4 (CH_2). HRMS (EI-TOF) calcd for $C_{17}H_{19}NO_4S$ [M]$^+$: 333.1029, found: 333.1036.



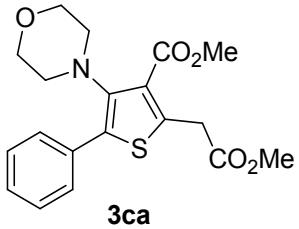
4aa

The further oxidation product of 3aa (4aa). A yellow solid (27.8 mg, 40% yield), Mp: 86-88 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.75-7.59 (m, 2H, Ar*H*), 7.53-7.36 (m, 3H, Ar*H*), 4.23-3.81 (m, 6H, 2×CO_2CH_3), 2.69 (s, 6H, N(CH_3)$_2$). ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.9 (*C*=O), 166.2 (*C*=O), 161.7 (*C*=O), 147.6 (Ar*C*), 144.7 (Ar*C*), 139.5 (Ar*C*), 132.5 (Ar*C*), 129.8 (Ar*C*), 129.2 (Ar*C*), 128.7 (2×Ar*C*), 128.6 (2×Ar*C*), 53.4 (CO_2CH_3), 53.0 (CO_2CH_3), 43.5 (N(CH_3)$_2$). HRMS (EI-TOF) calcd for $C_{17}H_{17}NO_5S$ [M]$^+$: 347.0822, found: 347.0828.



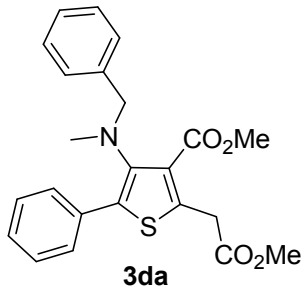
3ba

Methyl 4-(diethylamino)-2-(2-methoxy-2-oxoethyl)-5-phenylthiophene-3-carboxylate (3ba) A yellow solid (31.8 mg, 44% yield), Mp: 61-63 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.67-7.63 (m, 2H, Ar*H*), 7.41-7.32 (m, 2H, Ar*H*), 7.31-7.27 (m, 1H, Ar*H*), 3.95 (s, 2H, CH_2), 3.85 (s, 3H, CO_2CH_3), 3.74 (s, 3H, CO_2CH_3), 2.98 (q, J = 7.2 Hz, 4H, N(CH_2CH_3)$_2$), 0.95 (t, J = 7.2 Hz, 6H, N(CH_2CH_3)$_2$). ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.4 (*C*=O), 165.1 (*C*=O), 144.5 (Ar*C*), 137.4 (Ar*C*), 133.9 (Ar*C*), 133.8 (Ar*C*), 130.1 (Ar*C*), 128.7 (2×Ar*C*), 128.1 (2×Ar*C*), 127.4 (Ar*C*), 52.3 (CO_2CH_3), 51.6 (CO_2CH_3), 47.6 (N(CH_2CH_3)$_2$), 35.4 (CH_2), 14.0 (N(CH_2CH_3)$_2$). HRMS (EI-TOF) calcd for $C_{19}H_{23}NO_4S$ [M]$^+$: 361.1342, found: 361.1346.



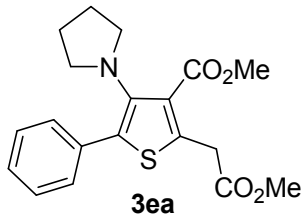
3ca

Methyl 2-(2-methoxy-2-oxoethyl)-4-morpholino-5-phenylthiophene-3-carboxylate (3ca). A yellow solid (34.5 mg, 46% yield), Mp: 112-114 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.55-7.50 (m, 2H, Ar*H*), 7.43-7.31 (m, 3H, Ar*H*), 3.95 (s, 2H, CH_2), 3.88 (s, 3H, CO_2CH_3), 3.74 (s, 3H, CO_2CH_3), 3.68-3.63 (m, 4H, N(CH_2CH_2)$_2$O), 3.00-2.94 (m, 4H, N(CH_2CH_2)$_2$O).^{13}C NMR (100 MHz, $CDCl_3$) δ 170.3 (*C*=O), 164.6 (*C*=O), 145.2 (Ar*C*), 138.5 (Ar*C*), 133.4 (Ar*C*), 131.9 (Ar*C*), 129.6 (2×Ar*C*), 128.9 (Ar*C*), 128.3 (2×Ar*C*), 127.9 (Ar*C*), 67.5 (N(CH_2CH_2)$_2$O), 52.3 (CO_2CH_3), 51.7 (CO_2CH_3), 51.6 (N(CH_2CH_2)$_2$O), 35.3 (CH_2). HRMS (EI-TOF) calcd for $C_{19}H_{21}NO_5S$ [M]$^+$: 375.1135, found: 375.1143.



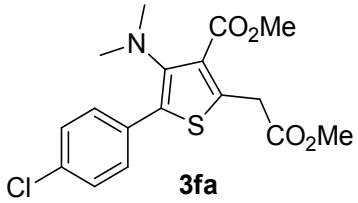
3da

Methyl 4-(benzyl(methyl)amino)-2-(2-methoxy-2-oxoethyl)-5-phenylthiophene-3-carboxylate (3da) A yellow solid (38.5 mg, 47% yield), Mp: 66-68 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.46-7.42 (m, 2H, Ar*H*), 7.39-7.31 (m, 3H, Ar*H*), 7.20-7.16 (m, 3H, Ar*H*), 7.14-7.09 (m, 2H, Ar*H*), 4.00 (s, 2H, ArCH_2), 3.97 (s, 2H, CH_2C=O), 3.88 (s, 3H, CO_2CH_3), 3.75 (s, 3H, CO_2CH_3), 2.66 (s, 3H, NCH_3). ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.3 (*C*=O), 164.8 (*C*=O), 146.5 (Ar*C*), 139.1 (Ar*C*), 138.6 (Ar*C*), 133.5 (Ar*C*), 132.8 (Ar*C*), 129.4 (2×Ar*C*), 129.0 (Ar*C*), 128.6 (2×Ar*C*), 128.2 (2×Ar*C*), 127.9 (2×Ar*C*), 127.7 (Ar*C*), 126.7 (Ar*C*), 60.3 (ArCH_2), 52.3 (CO_2CH_3), 51.7 (CO_2CH_3), 41.0 (NCH_3), 35.5 (CH_2C=O). HRMS (EI-TOF) calcd for $C_{23}H_{23}NO_4S$ [M]$^+$: 409.1342, found: 409.1347.



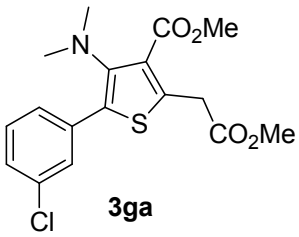
3ea

Methyl 2-(2-methoxy-2-oxoethyl)-5-phenyl-4-(pyrrolidin-1-yl) thiophene-3-carboxylate (3ea) A yellow oil (34.5 mg, 48% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.59-7.53 (m, 2H, Ar*H*), 7.38-7.33 (m, 2H, Ar*H*), 7.31-7.27 (m, 1H, Ar*H*), 3.95 (s, 2H, CH_2), 3.85 (s, 3H, CO_2CH_3), 3.74 (s, 3H, CO_2CH_3), 3.15-3.04 (m, 4H, N(CH_2CH_2)$_2$), 1.91-1.77 (m, 4H, N(CH_2CH_2)$_2$). ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.4 (*C*=O), 164.9 (*C*=O), 143.1 (Ar*C*), 138.1 (Ar*C*), 133.9 (Ar*C*), 131.0 (Ar*C*), 128.6 (Ar*C*), 128.6 (2×Ar*C*), 128.2 (2×Ar*C*), 127.3 (Ar*C*), 52.3 (CO_2CH_3), 51.7 (CO_2CH_3), 51.3 (N(CH_2CH_2)$_2$), 35.4 (CH_2), 26.0 ((N(CH_2CH_2)$_2$). HRMS (EI-TOF) calcd for $C_{19}H_{21}NO_4S$ [M]$^+$: 359.1186, found: 359.1192.



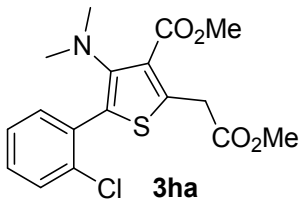
3fa

Methyl 5-(4-chlorophenyl)-4-(dimethylamino)-2-(2-methoxy-2-oxoethyl) thiophene-3-carboxylate (3fa) A yellow solid (44.7 mg, 61% yield), Mp: 70-72 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.54-7.50 (m, 2H, Ar*H*), 7.38-7.31 (m, 2H, Ar*H*), 3.94 (s, 2H, CH_2), 3.88 (s, 3H, CO_2CH_3), 3.74 (s, 3H, CO_2CH_3), 2.69 (s, 6H, N(CH_3)$_2$). ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.3 (*C*=O), 164.7 (*C*=O), 147.2 (Ar*C*), 138.4 (Ar*C*), 133.2 (Ar*C*), 132.1 (Ar*C*), 129.8 (Ar*C*), 129.6 (2×Ar*C*), 129.0 (Ar*C*), 128.5 (2×Ar*C*), 52.4 (CO_2CH_3), 51.7 (CO_2CH_3), 43.2 (N(CH_3)$_2$), 35.4 (CH_2). HRMS (EI-TOF) calcd for $C_{17}H_{18}ClNO_4S$ [M]$^+$: 367.0640, found: 367.0644.



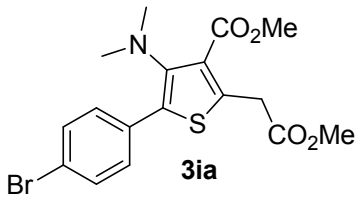
3ga

Methyl 5-(3-chlorophenyl)-4-(dimethylamino)-2-(2-methoxy-2-oxoethyl) thiophene-3-carboxylate (3ga) A yellow oil (40.4mg, 55% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.61-7.59 (m, 1H, Ar*H*), 7.49-7.42 (m, 1H, Ar*H*), 7.28-7.24 (m, 2H, Ar*H*), 3.95 (s, 2H, CH_2), 3.88 (s, 3H, CO_2CH_3), 3.74 (s, 3H, CO_2CH_3), 2.70 (s, 6H, N(CH_3)$_2$). ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.2 (*C*=O), 164.6 (*C*=O), 147.5 (Ar*C*), 138.7 (Ar*C*), 135.4 (Ar*C*), 134.2 (Ar*C*), 129.5 (Ar*C*), 129.2 (Ar*C*), 128.9 (Ar*C*), 128.3 (Ar*C*), 127.4 (Ar*C*), 126.5 (Ar*C*), 52.3 (CO_2CH_3), 51.7 (CO_2CH_3), 43.2 (N(CH_3)$_2$), 35.3 (CH_2). HRMS (EI-TOF) calcd for $C_{17}H_{18}ClNO_4S$ [M]$^+$: 367.0640, found: 367.0648.



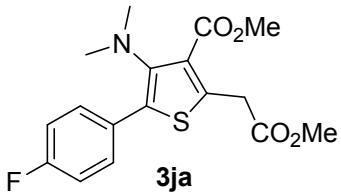
3ha

Methyl 5-(2-chlorophenyl)-4-(dimethylamino)-2-(2-methoxy-2-oxoethyl) thiophene-3-carboxylate (3ha) A yellow oil (28.7 mg, 39% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.46-7.42 (m, 1H, Ar*H*), 7.38 (dd, *J* = 7.1, 2.2 Hz, 1H, Ar*H*), 7.33-7.27 (m, 2H, Ar*H*), 3.96 (s, 2H, CH_2), 3.87 (s, 3H, CO_2CH_3), 3.74 (s, 3H, CO_2CH_3), 2.61 (s, 6H, N(CH_3)$_2$). ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.2 (*C*=O), 164.5 (*C*=O), 148.6 (Ar*C*), 139.8 (Ar*C*), 135.1 (Ar*C*), 133.3 (Ar*C*), 133.0 (Ar*C*), 129.5 (Ar*C*), 129.5 (Ar*C*), 127.2 (Ar*C*), 126.3 (Ar*C*), 123.2 (Ar*C*), 52.3 (CO_2CH_3), 51.7 (CO_2CH_3), 43.5 (N(CH_3)$_2$), 35.5 (CH_2). HRMS (EI-TOF) calcd for $C_{17}H_{18}ClNO_4S$ [M]$^+$: 367.0640, found: 367.0643.



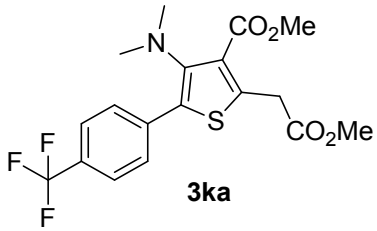
3ia

Methyl 5-(4-bromophenyl)-4-(dimethylamino)-2-(2-methoxy-2-oxoethyl) thiophene-3-carboxylate (3ia) A yellow solid (37.9 mg, 46% yield), Mp: 70-72 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.57-7.38 (m, 4H, Ar*H*), 3.94 (s, 2H, CH_2), 3.88 (s, 3H, CO_2CH_3), 3.74 (s, 3H, CO_2CH_3), 2.69 (s, 6H, N(CH_3)$_2$). ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.2 (*C*=O), 164.6 (*C*=O), 147.2 (Ar*C*), 138.5 (Ar*C*), 132.6 (Ar*C*), 131.5 (2×Ar*C*), 129.9 (2×Ar*C*), 129.8 (Ar*C*), 129.0 (Ar*C*), 121.4 (Ar*C*), 52.3 (CO_2CH_3), 51.7 (CO_2CH_3), 43.2 (N(CH_3)$_2$), 35.3 (CH_2). HRMS (ESI-TOF) calcd for $C_{17}H_{18}BrNO_4S$ [M]$^+$: 411.0134, found: 411.0142.



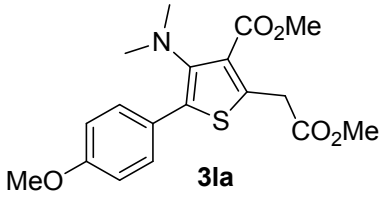
3ja

Methyl 4-(dimethylamino)-5-(4-fluorophenyl)-2-(2-methoxy-2-oxoethyl) thiophene-3-carboxylate (3ja) A yellow solid (29.5 mg, 42% yield), Mp: 60-62 °C.^{1}H NMR (400 MHz, $CDCl_3$) δ 7.62-7.46 (m, 2H, Ar*H*), 7.18-6.90 (m, 2H, Ar*H*), 3.94 (s, 2H, CH_2), 3.87 (s, 3H, CO_2CH_3), 3.74 (s, 3H, CO_2CH_3), 2.68 (s, 6H, N(CH_3)$_2$).^{13}C NMR (100 MHz, $CDCl_3$) δ 170.3 (*C*=O), 164.7 (*C*=O), 162.2 (d, $^1J_{CF}$ = 246.0 Hz, Ar*C*), 146.9 (Ar*C*), 138.1 (Ar*C*), 130.3 (d, $^3J_{CF}$ = 7.9 Hz, 2×Ar*C*), 130.1 (Ar*C*), 129.7 (d, $^4J_{CF}$ = 3.4 Hz, Ar*C*), 128.9 (Ar*C*), 115.3 (d, $^2J_{CF}$ = 21.4 Hz, 2×Ar*C*), 52.3 (CO_2CH_3), 51.7 (CO_2CH_3), 43.3 (N(CH_3)$_2$), 35.3 (CH_2). HRMS (EI-TOF) calcd for $C_{17}H_{18}FNO_4S$ [M]$^+$: 351.0935, found: 351.0943.



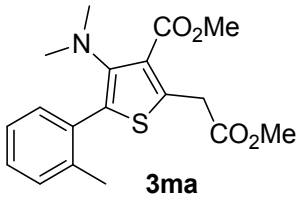
3ka

Methyl 4-(dimethylamino)-2-(2-methoxy-2-oxoethyl)-5-(4-(trifluoromethyl) phenyl) thiophene-3-carboxylate (3ka) A yellow solid (32.1 mg, 40% yield), Mp: 72-75 °C.^{1}H NMR (400 MHz, $CDCl_3$) δ 7.71 (d, *J* = 8.2 Hz, 2H, Ar*H*), 7.62 (d, *J* = 8.3 Hz, 2H, Ar*H*), 3.96 (s, 2H, CH_2), 3.89 (s, 3H, CO_2CH_3), 3.75 (s, 3H, CO_2CH_3), 2.71 (s, 6H, $N(CH_3)_2$). ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.1 (*C*=O), 164.6 (*C*=O), 148.0 (Ar*C*), 139.2 (Ar*C*), 137.2 (Ar*C*), 129.2 (Ar*C*), 129.1 (Ar*C*), 129.1 (q, $^{2}J_{CF}$ = 86.1 Hz, Ar*C*), 128.4 (2×Ar*C*), 125.3 (q, $^{3}J_{CF}$ = 3.8 Hz, 2×Ar*C*), 124.2 (q, $^{1}J_{CF}$ = 270.3 Hz, *C*F_3), 52.4 (CO_2CH_3), 51.8 (CO_2CH_3), 43.1 ($N(CH_3)_2$), 35.3 (CH_2). HRMS (EI-TOF) calcd for $C_{18}H_{18}F_3NO_4S$ $[M]^+$: 401.0903, found: 401.0908.



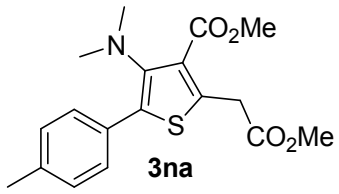
3la

Methyl 4-(dimethylamino)-2-(2-methoxy-2-oxoethyl)-5-(4-methoxyphenyl) thiophene-3-carboxylate (3la) A yellow oil (40.7 mg, 56% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.53-7.45 (m, 2H, Ar*H*), 6.93-6.86 (m, 2H, Ar*H*), 3.93 (s, 2H, CH_2), 3.87 (s, 3H, CO_2CH_3), 3.83 (s, 3H, $ArOCH_3$), 3.73 (s, 3H, CO_2CH_3), 2.68 (s, 6H, $N(CH_3)_2$).^{13}C NMR (100 MHz, $CDCl_3$) δ 170.4 (*C*=O), 164.8 (*C*=O), 159.0 (Ar*C*), 146.2 (Ar*C*), 137.4 (Ar*C*), 131.2 (Ar*C*), 129.9 (2×Ar*C*) , 128.8 (Ar*C*), 126.1 (Ar*C*), 113.7 (2×Ar*C*), 55.2 ($ArOCH_3$), 52.3 (CO_2CH_3), 51.6 (CO_2CH_3), 43.4 ($N(CH_3)_2$), 35.4 (CH_2). HRMS (EI-TOF) calcd for $C_{18}H_{21}NO_5S$ $[M]^+$: 363.1135, found: 363.1141.



3ma

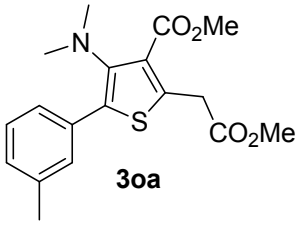
Methyl 4-(dimethylamino)-2-(2-methoxy-2-oxoethyl)-5-(o-tolyl) thiophene-3-carboxylate (3ma) A yellow oil (26.4 mg, 38% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.30-7.14 (m, 4H, Ar*H*), 3.94 (s, 2H, CH_2), 3.87 (s, 3H, CO_2CH_3), 3.74 (s, 3H, CO_2CH_3), 2.57 (s, 6H, $N(CH_3)_2$), 2.26 (s, 3H, $ArCH_3$). ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.4 (*C*=O), 164.8 (*C*=O), 147.5 (Ar*C*), 138.7 (Ar*C*), 138.0 (Ar*C*), 133.3 (Ar*C*), 131.9 (Ar*C*), 129.9 (Ar*C*), 128.3 (Ar*C*), 127.5 (Ar*C*), 126.7 (Ar*C*), 125.3 (Ar*C*), 52.3 (CO_2CH_3), 51.7 (CO_2CH_3), 43.7 ($N(CH_3)_2$), 35.4 (CH_2), 20.5 ($ArCH_3$). HRMS (EI-TOF) calcd for $C_{18}H_{21}NO_4S$ $[M]^+$: 347.1186, found: 347.1194.



3na

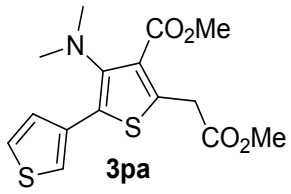
Methyl 4-(dimethylamino)-2-(2-methoxy-2-oxoethyl)-5-(p-tolyl) thiophene-3-carboxylate (3na) A yellow solid (36.8 mg, 53% yield), Mp: 97-99 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.44 (d, *J* = 8.1 Hz, 2H, Ar*H*), 7.18 (d, *J* = 8.0 Hz, 2H, Ar*H*), 3.94 (s, 2H, CH_2), 3.87 (s, 3H, CO_2CH_3), 3.74 (s, 3H, CO_2CH_3), 2.69 (s, 6H, $N(CH_3)_2$), 2.37 (s, 3H, $ArCH_3$). ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.4 (*C*=O), 164.8 (*C*=O), 146.6 (Ar*C*), 137.8 (Ar*C*), 137.3 (Ar*C*), 131.2

(Ar*C*), 130.8 (Ar*C*), 129.0 (2×Ar*C*), 128.8(Ar*C*), 128.6 (2×Ar*C*), 52.3 (CO_2CH_3), 51.6 (CO_2CH_3), 43.4 ($N(CH_3)_2$), 35.4 (CH_2), 21.2 ($ArCH_3$). HRMS (EI-TOF) calcd for $C_{18}H_{21}NO_4S$ $[M]^+$: 347.1186, found: 347.1193.



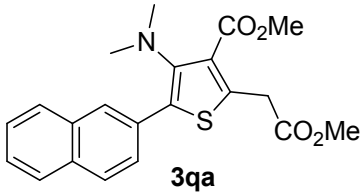
3oa

Methyl 4-(dimethylamino)-2-(2-methoxy-2-oxoethyl)-5-(m-tolyl) thiophene-3-carboxylate (3oa) A yellow oil (34.7 mg, 50% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.40-7.30 (m, 2H, Ar*H*), 7.28-7.20 (m, 1H, Ar*H*), 7.17-7.06 (m, 1H, Ar*H*), 3.94 (s, 2H, CH_2), 3.87 (s, 3H, CO_2CH_3), 3.74 (s, 3H, CO_2CH_3), 2.69 (s, 6H, $N(CH_3)_2$), 2.38 (s, 3H, $ArCH_3$).^{13}C NMR (100 MHz, $CDCl_3$) δ 170.4 (*C*=O), 164.7 (*C*=O), 146.8 (Ar*C*), 138.1 (Ar*C*), 137.8 (Ar*C*), 133.6 (Ar*C*), 131.0 (Ar*C*), 129.4 (Ar*C*), 128.8 (Ar*C*), 128.2 (Ar*C*), 128.1 (Ar*C*), 125.8 (Ar*C*), 52.3 (CO_2CH_3), 51.6 (CO_2CH_3), 43.5 ($N(CH_3)_2$), 35.4 (CH_2), 21.5 ($ArCH_3$). HRMS (EI-TOF) calcd for $C_{18}H_{21}NO_4S$ $[M]^+$: 347.1186, found: 347.1196.



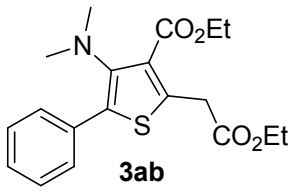
3pa

Methyl 3-(dimethylamino)-5-(2-methoxy-2-oxoethyl)-[2,3'-bithiophene]-4-carboxylate (3pa) A yellow oil (33.9 mg, 50% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.62 (dd, *J* = 3.0, 1.3 Hz, 1H, Ar*H*), 7.39 (dd, *J* = 5.0, 1.3 Hz, 1H, Ar*H*), 7.31 (dd, *J* = 5.0, 3.0 Hz, 1H, Ar*H*), 3.94 (s, 2H, CH_2), 3.88 (s, 3H, CO_2CH_3), 3.74 (s, 3H, CO_2CH_3), 2.74 (s, 6H, $N(CH_3)_2$). ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.3 (*C*=O), 164.8 (*C*=O), 146.6 (Ar*C*), 137.1 (Ar*C*), 133.4 (Ar*C*), 129.0 (Ar*C*), 128.2 (Ar*C*), 127.3 (Ar*C*), 125.1 (Ar*C*), 121.8 (Ar*C*), 52.3 (CO_2CH_3), 51.7 (CO_2CH_3), 42.8 ($N(CH_3)_2$), 35.3 (CH_2). HRMS (EI-TOF) calcd for $C_{15}H_{17}NO_4S_2$ $[M]^+$: 339.0594, found: 339.0600.



3qa

Methyl 4-(dimethylamino)-2-(2-methoxy-2-oxoethyl)-5-(naphthalen-2-yl) thiophene-3-carboxylate (3qa) A yellow solid (43.7 mg, 57% yield), Mp: 106-108 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.99-7.96 (m, 1H, Ar*H*), 7.86-7.81 (m, 3H, Ar*H*), 7.77-7.70 (m, 1H, Ar*H*), 7.52-7.46 (m, 2H, Ar*H*), 3.98 (s, 2H, CH_2), 3.89 (s, 3H, CO_2CH_3), 3.75 (s, 3H, CO_2CH_3), 2.73 (s, 6H, $N(CH_3)_2$). ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.3 (*C*=O), 164.8 (*C*=O), 147.2 (Ar*C*), 138.4 (Ar*C*), 133.2 (Ar*C*), 132.6 (Ar*C*), 131.2 (Ar*C*), 130.8 (Ar*C*), 128.9 (Ar*C*), 128.1 (Ar*C*), 127.8 (Ar*C*), 127.6 (Ar*C*), 127.3 (Ar*C*), 126.8 (Ar*C*), 126.3 (Ar*C*), 126.1 (Ar*C*), 52.3 (CO_2CH_3), 51.7 (CO_2CH_3), 43.4 ($N(CH_3)_2$), 35.4 (CH_2). HRMS (EI-TOF) calcd for $C_{21}H_{21}NO_4S$ $[M]^+$: 383.1186, found: 383.1192.

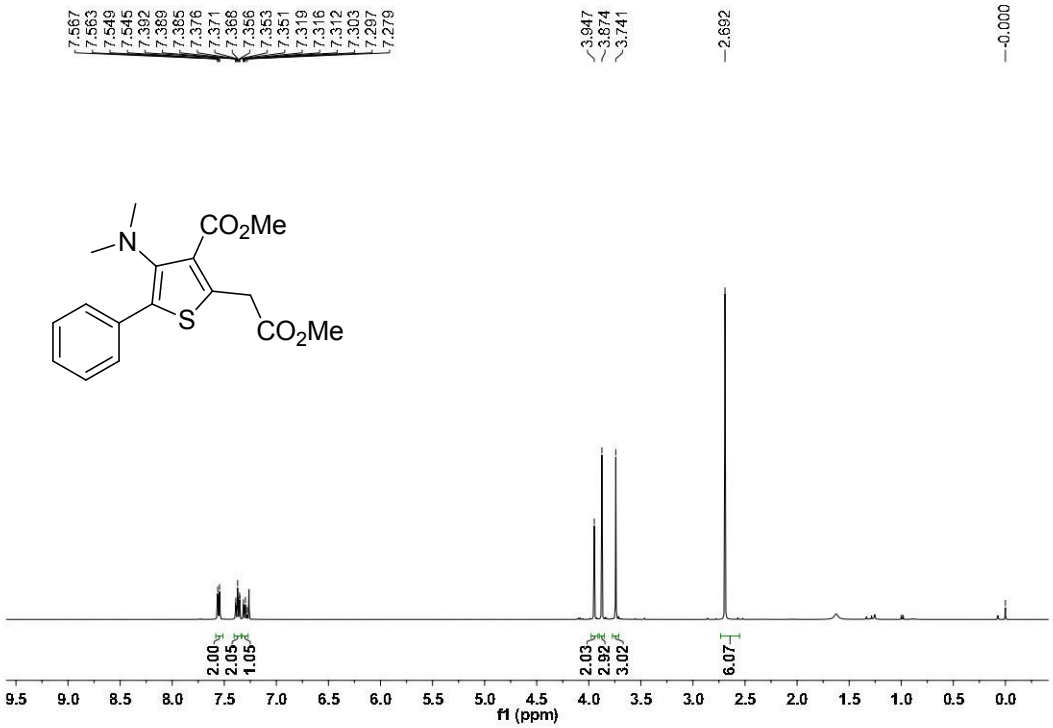


3ab

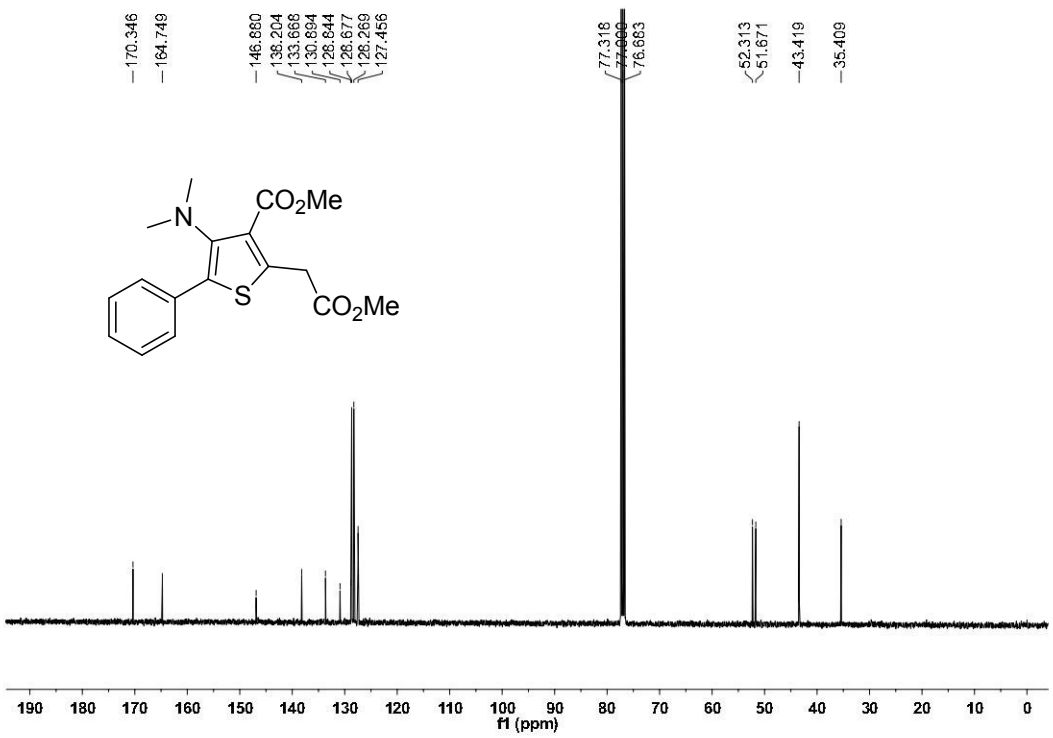
Ethyl 4-(dimethylamino)-2-(2-ethoxy-2-oxoethyl)-5-phenylthiophene-3-carboxylate (3ab) A yellow oil (37.5 mg, 52% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.59-7.53 (m, 2H, Ar*H*), 7.41-7.33 (m, 2H, Ar*H*), 7.33-7.27 (m, 1H, Ar*H*), 4.34 (q, *J* = 7.2 Hz, 2H, OC*H*$_2$CH$_3$), 4.19 (q, *J* = 7.2 Hz, 2H, OC*H*$_2$CH$_3$), 3.95 (s, 2H, C*H*$_2$), 2.70 (s, 6H, N(C*H*$_3$)$_2$), 1.39 (t, *J* = 7.1 Hz, 3H, OCH$_2$C*H*$_3$), 1.28 (t, *J* = 7.2 Hz, 3H, OCH$_2$C*H*$_3$). ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.9 (*C*=O), 164.4 (*C*=O), 146.8 (Ar*C*), 137.9 (Ar*C*), 133.8 (Ar*C*), 131.0 (Ar*C*), 129.4 (Ar*C*), 128.6 (2×Ar*C*), 128.3 (2×Ar*C*), 127.4 (Ar*C*), 61.2 (O*C*H$_2$CH$_3$), 60.8 (O*C*H$_2$CH$_3$), 43.4 (N(*C*H$_3$)$_2$), 35.6 (*C*H$_2$), 14.2 (OCH$_2$*C*H$_3$), 14.1 (OCH$_2$*C*H$_3$). HRMS (EI-TOF) calcd for $C_{19}H_{23}NO_4S$ $[M]^+$: 361.1342, found: 361.1350.

4. ^{1}H NMR and ^{13}C NMR spectra

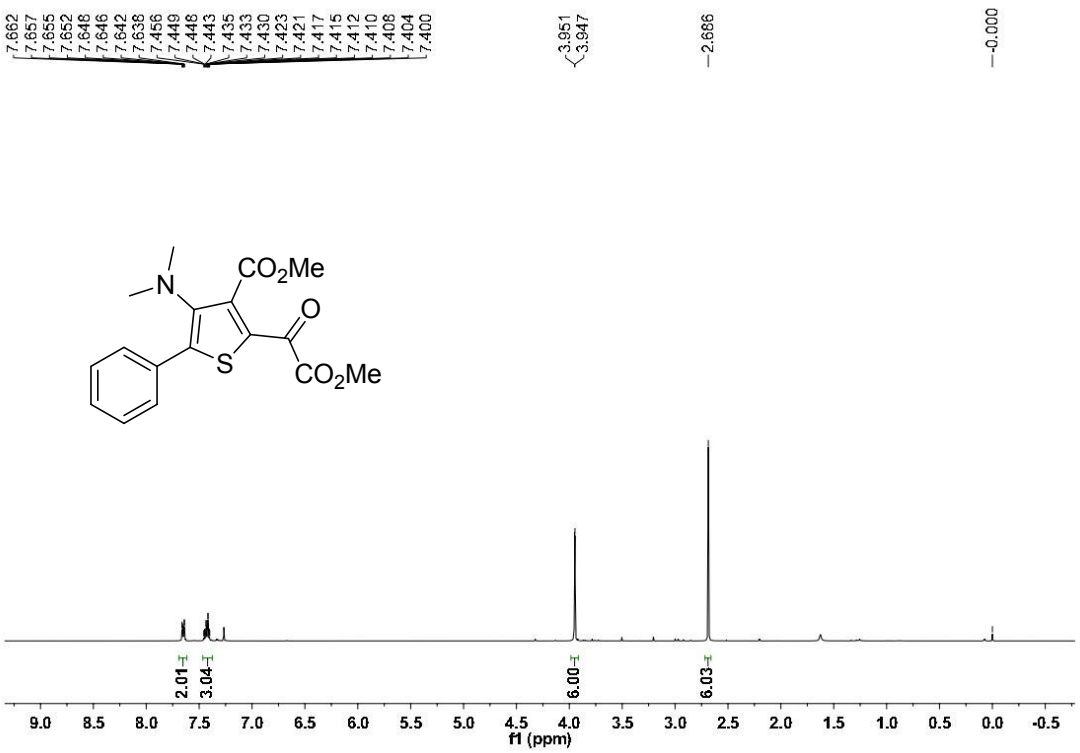
^{1}H NMR spectrum of compound **3aa** ($CDCl_3$)



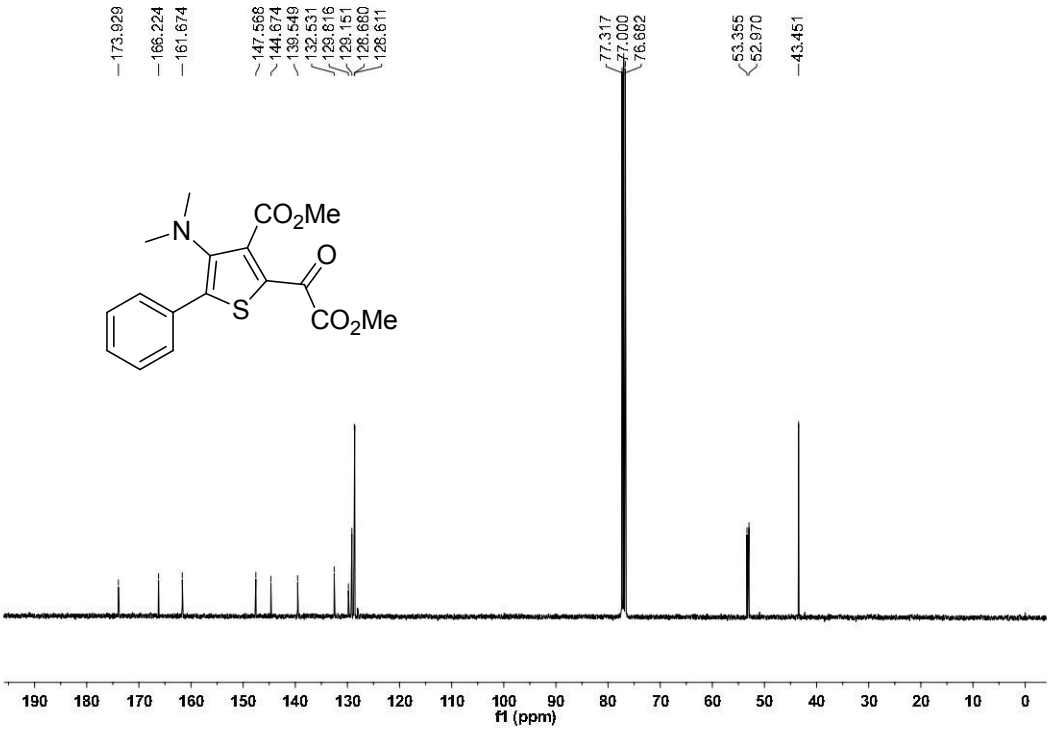
^{13}C NMR spectrum of compound **3aa** ($CDCl_3$)



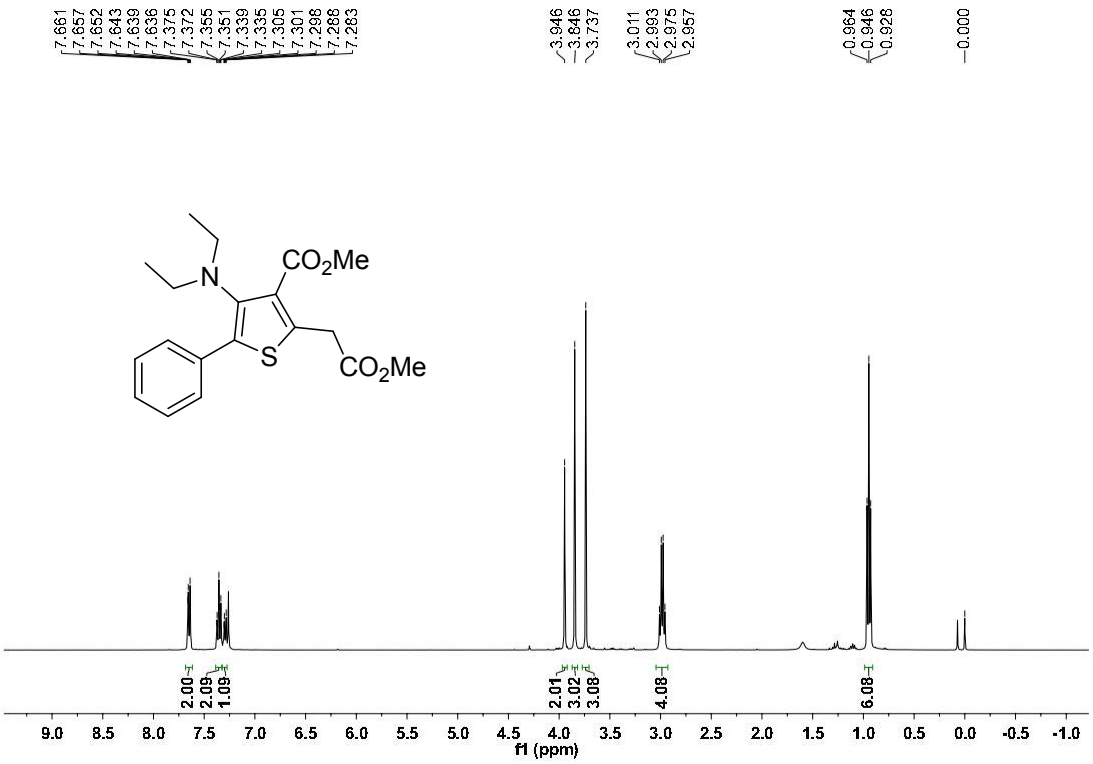
^{1}H NMR spectrum of compound **4aa** ($CDCl_3$)



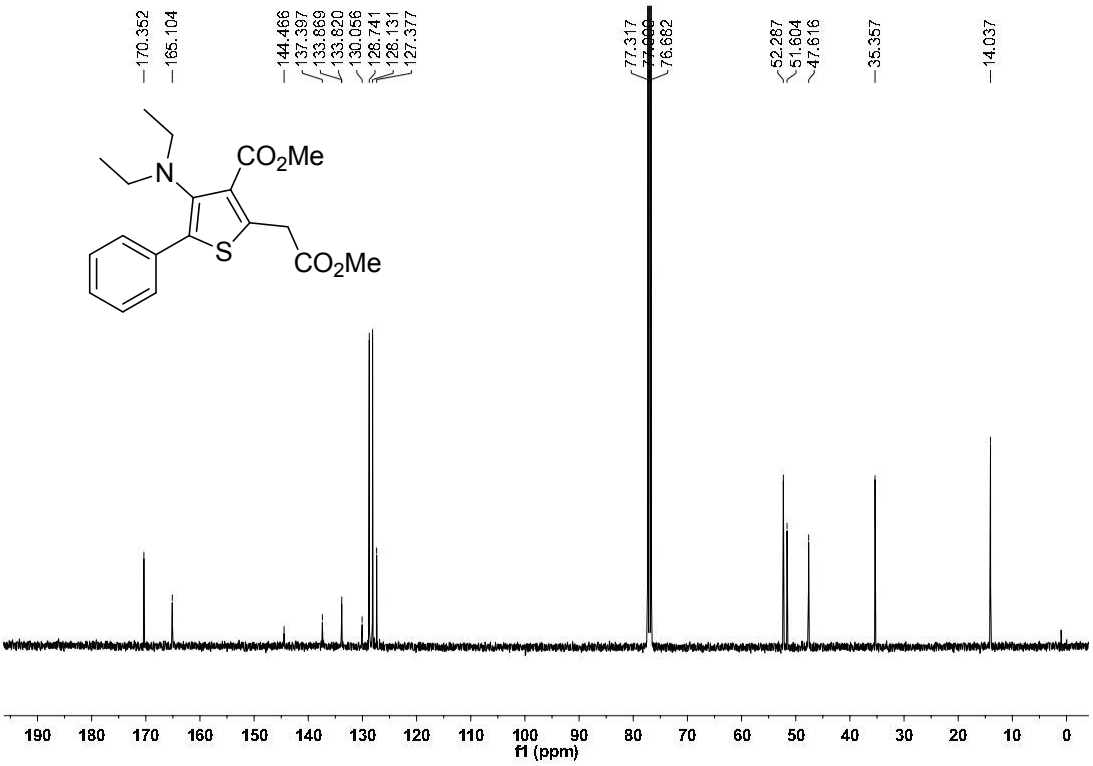
^{13}C NMR spectrum of compound **4aa**($CDCl_3$)



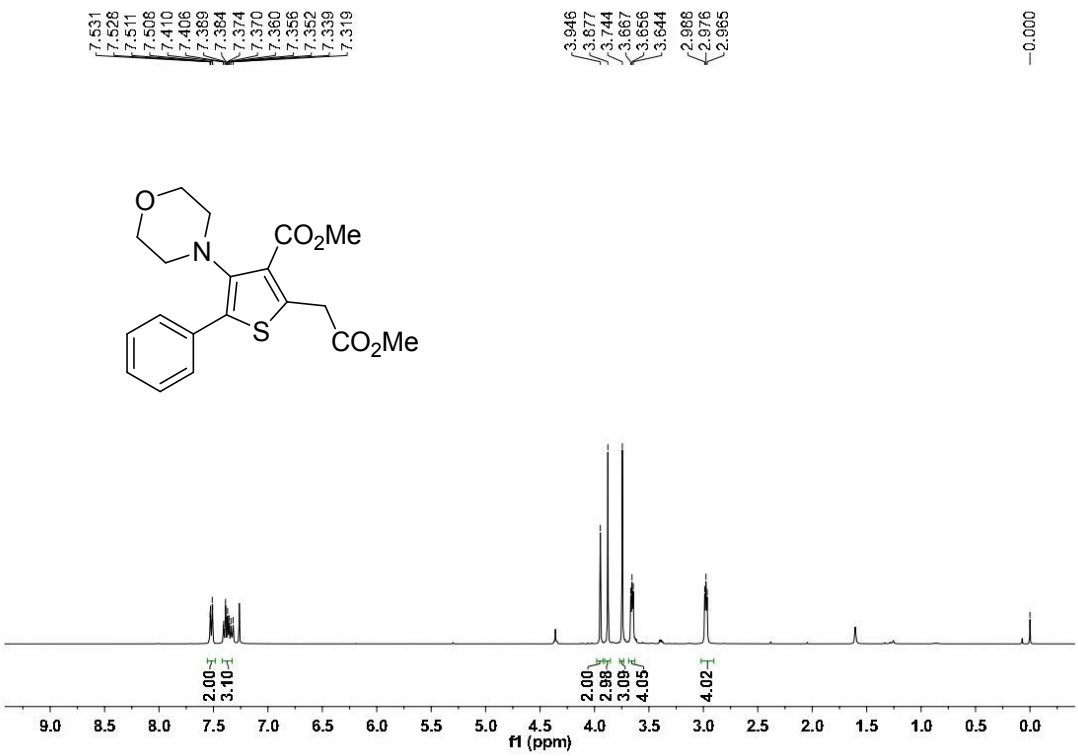
^{1}H NMR spectrum of compound **3ba** ($CDCl_3$)



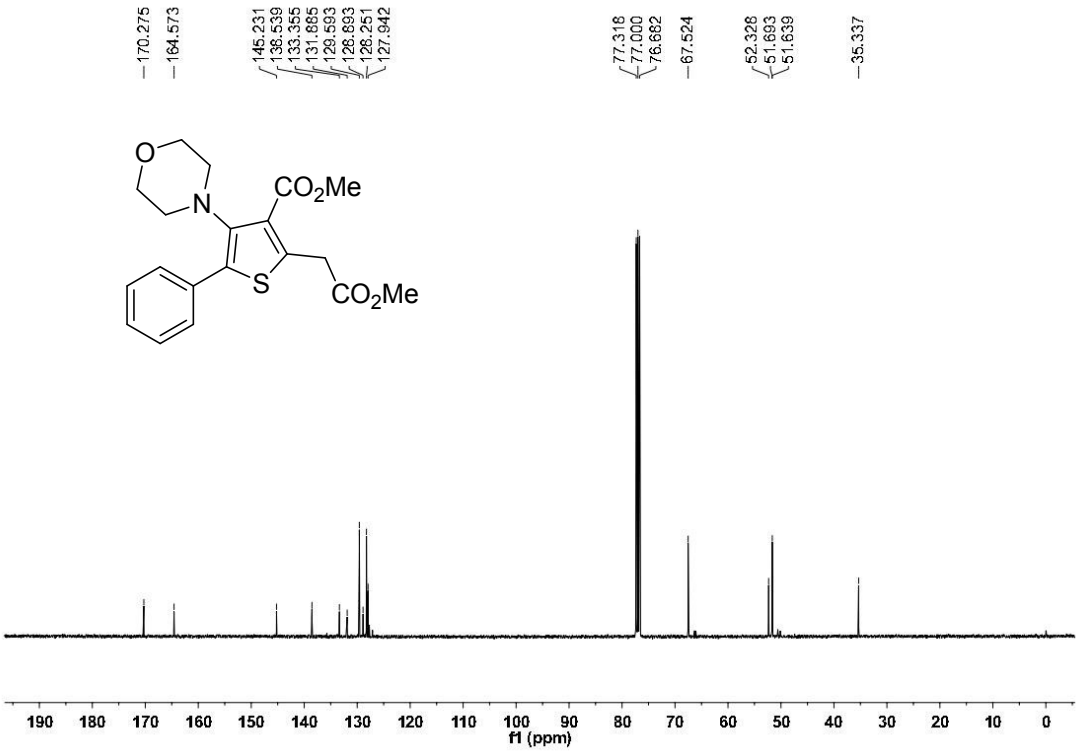
^{13}C NMR spectrum of compound **3ba** ($CDCl_3$)



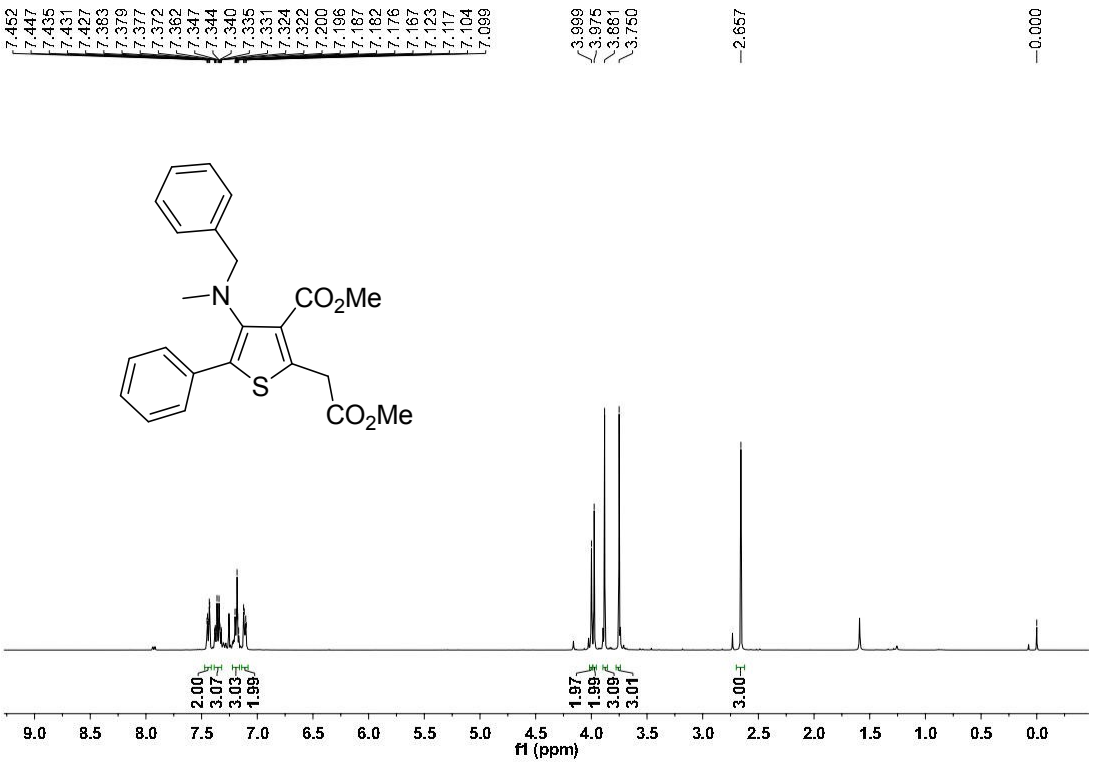
^{1}H NMR spectrum of compound **3ca** ($CDCl_3$)



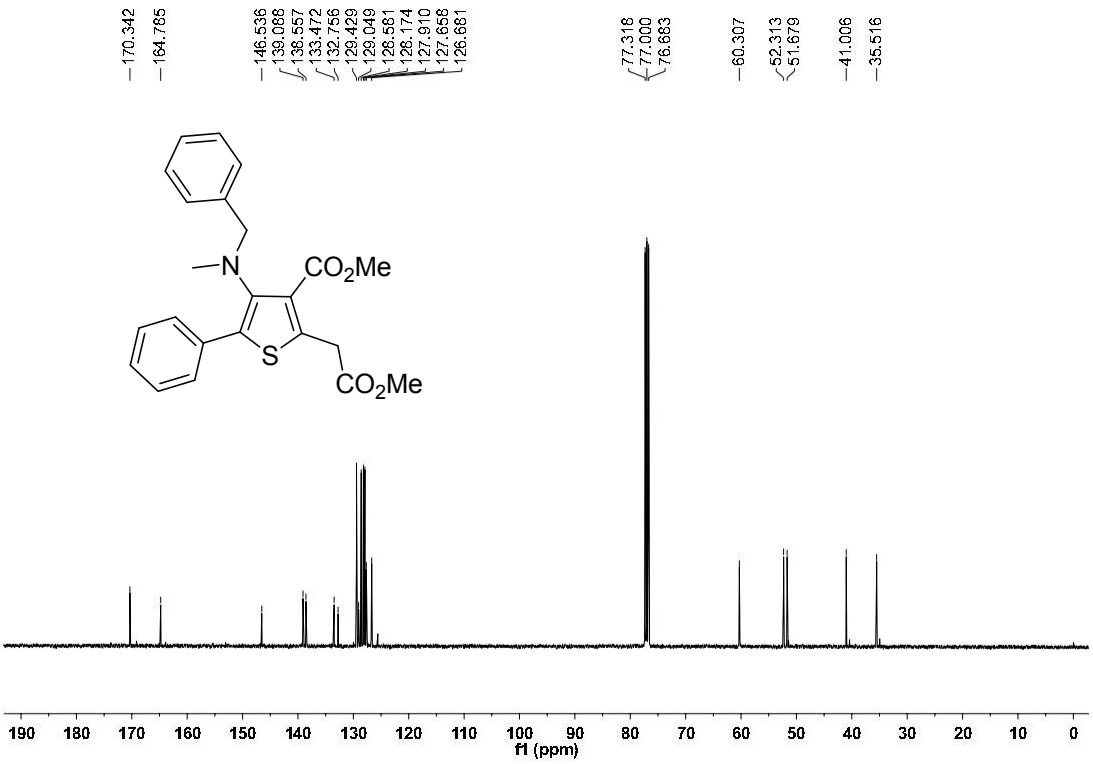
^{13}C NMR spectrum of compound **3ca** ($CDCl_3$)



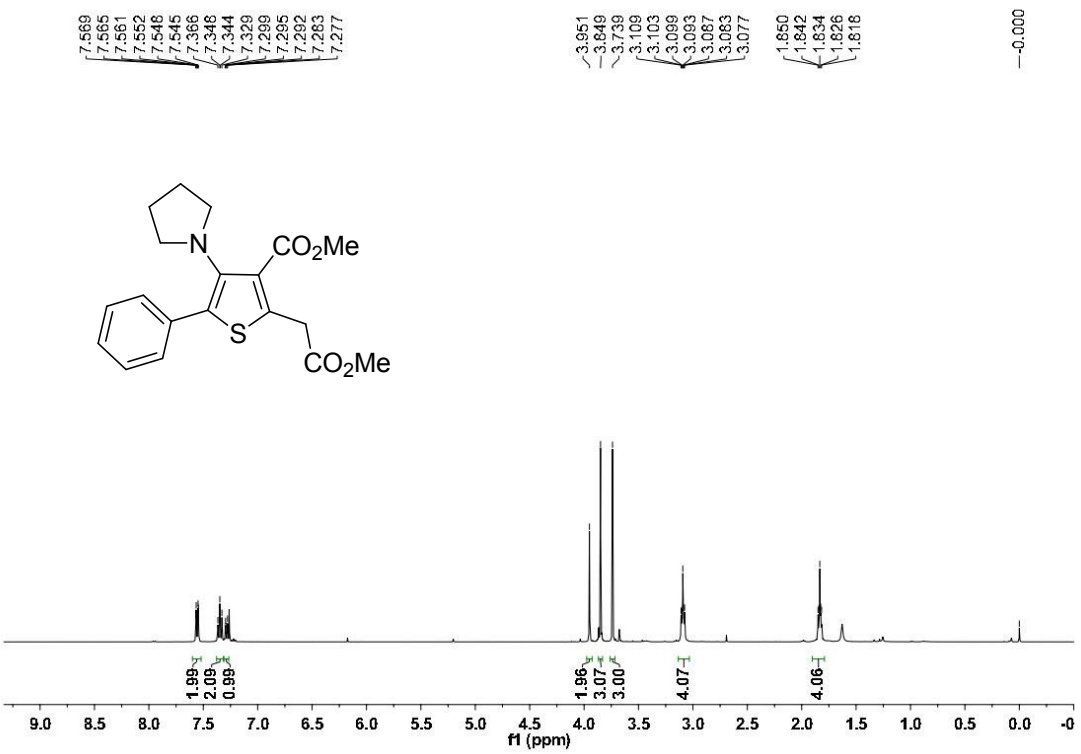
^{1}H NMR spectrum of compound **3da** ($CDCl_3$)



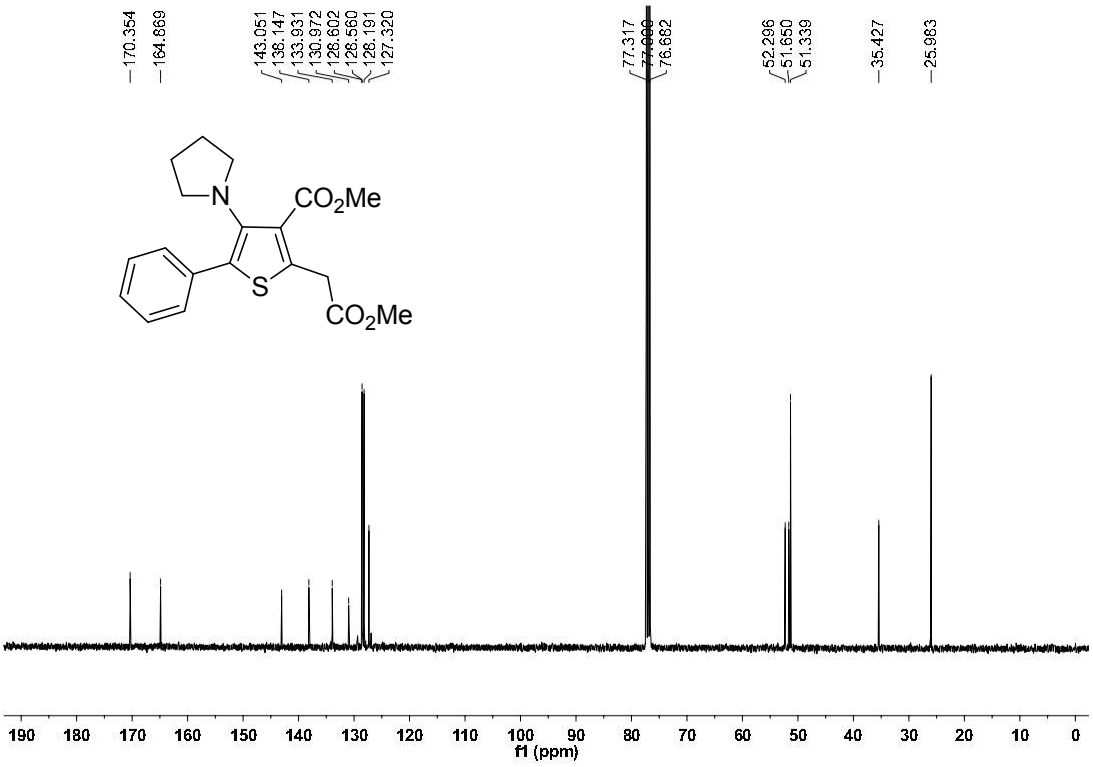
^{13}C NMR spectrum of compound **3da**($CDCl_3$)



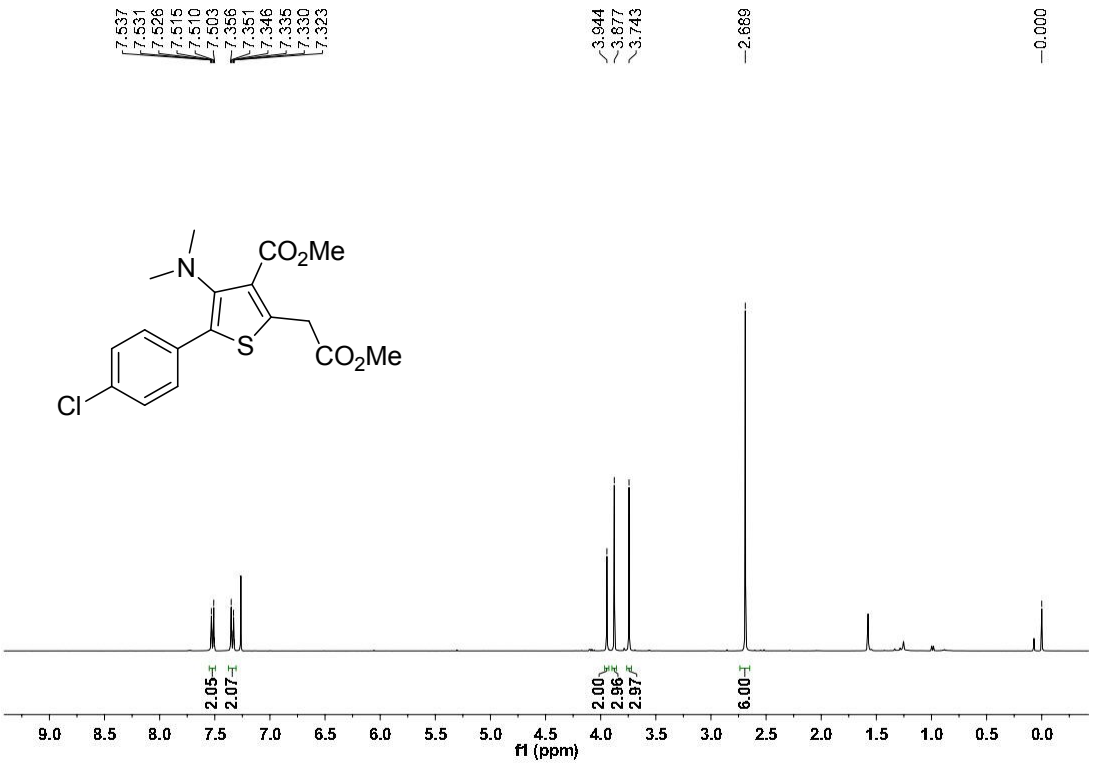
^{1}H NMR spectrum of compound **3ea** ($CDCl_3$)



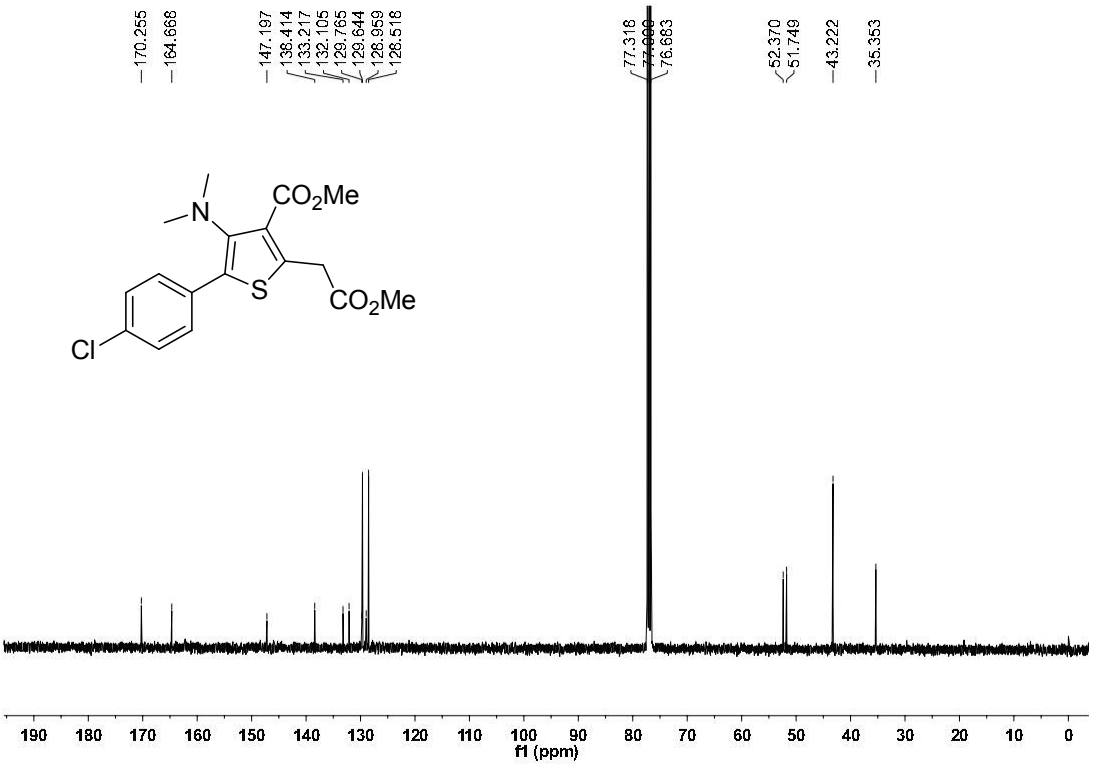
^{13}C NMR spectrum of compound **3ea** ($CDCl_3$)



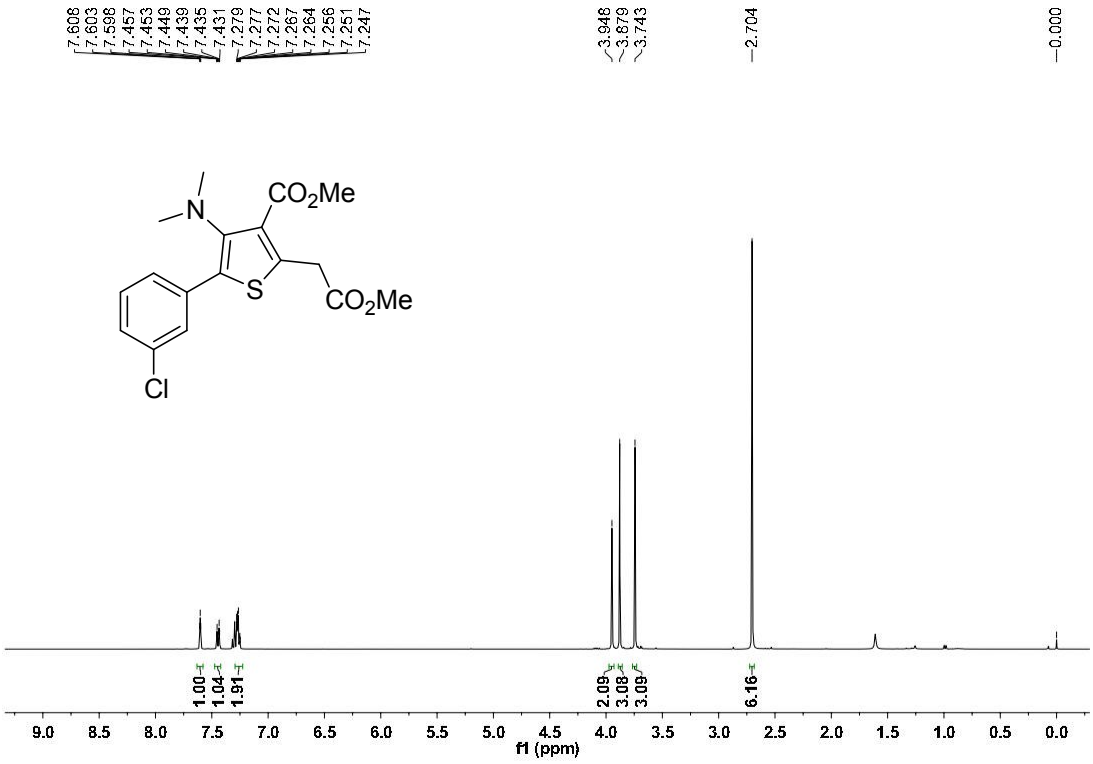
^{1}H NMR spectrum of compound **3fa** ($CDCl_3$)



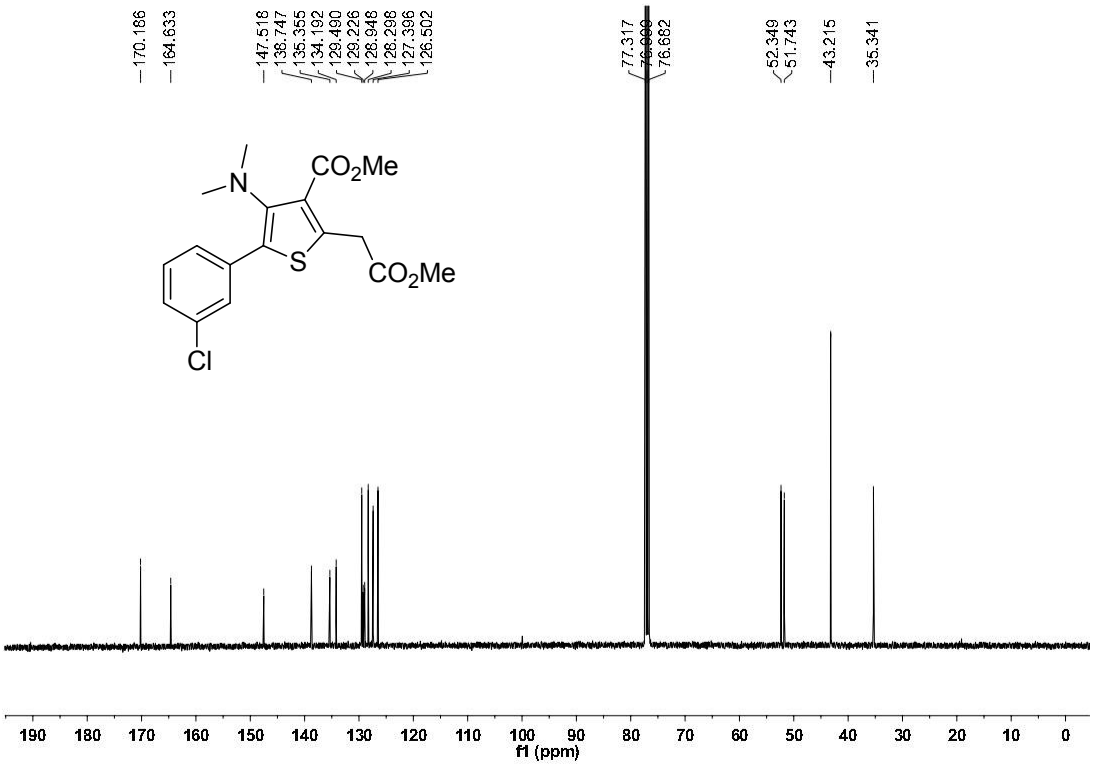
^{13}C NMR spectrum of compound **3fa**($CDCl_3$)



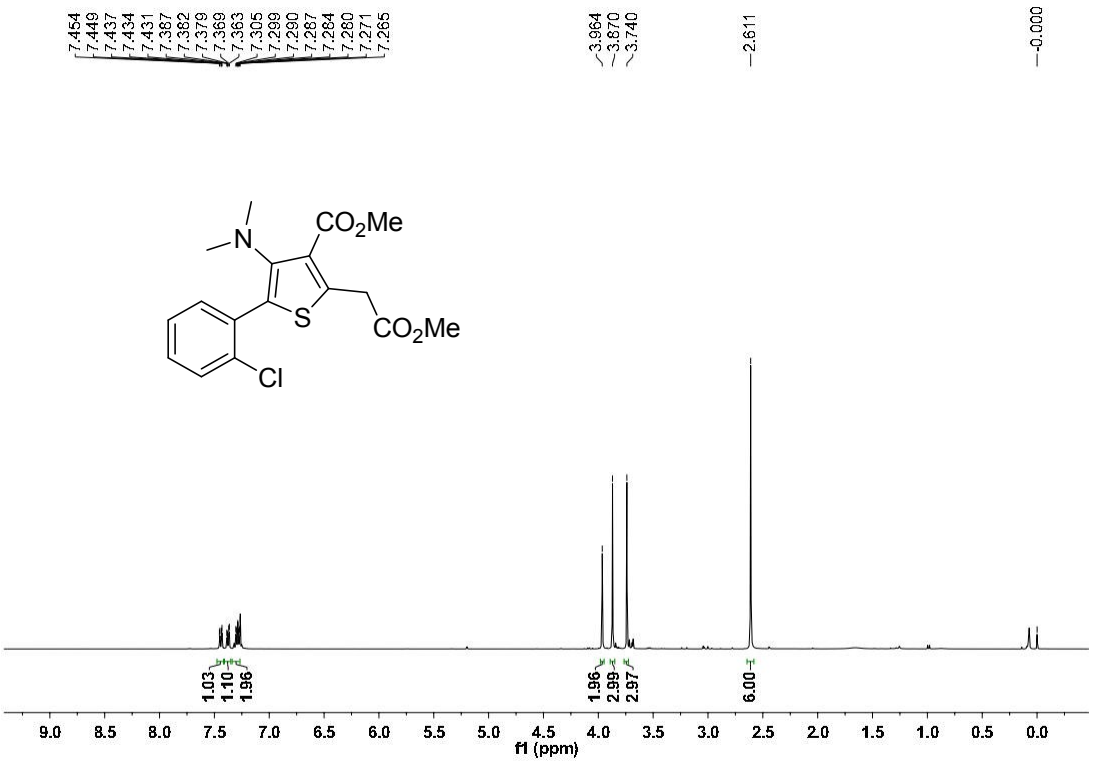
^{1}H NMR spectrum of compound **3ga** ($CDCl_3$)



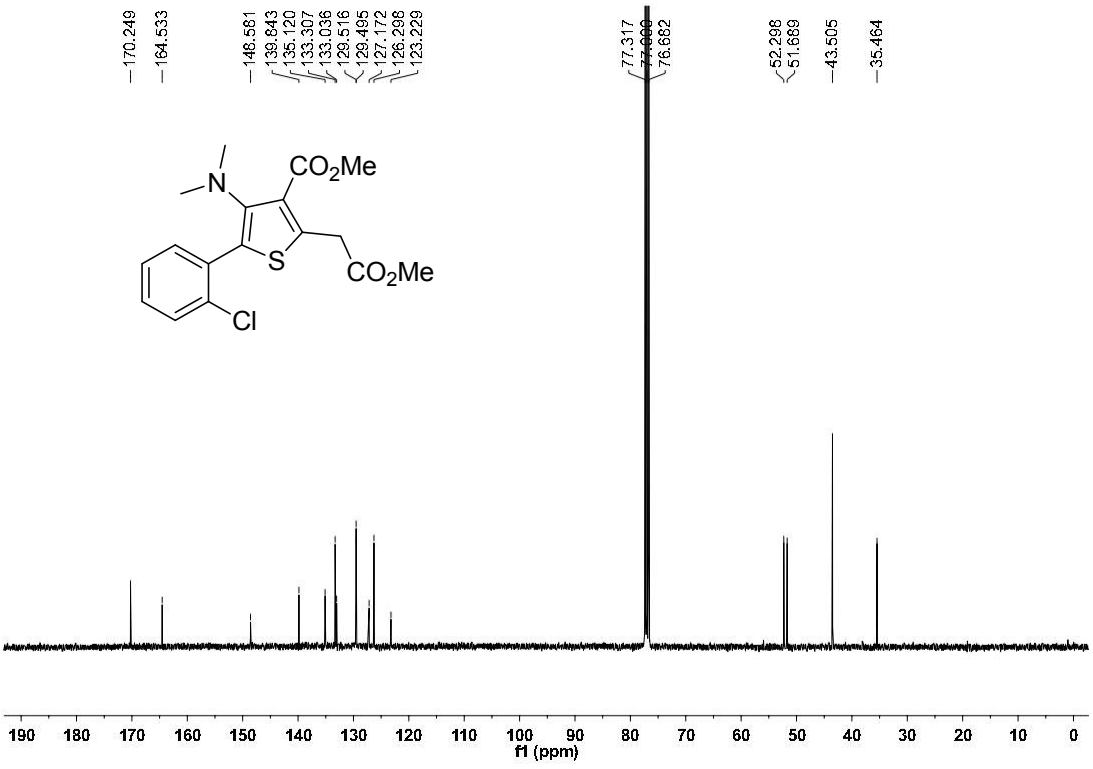
^{13}C NMR spectrum of compound **3ga**($CDCl_3$)



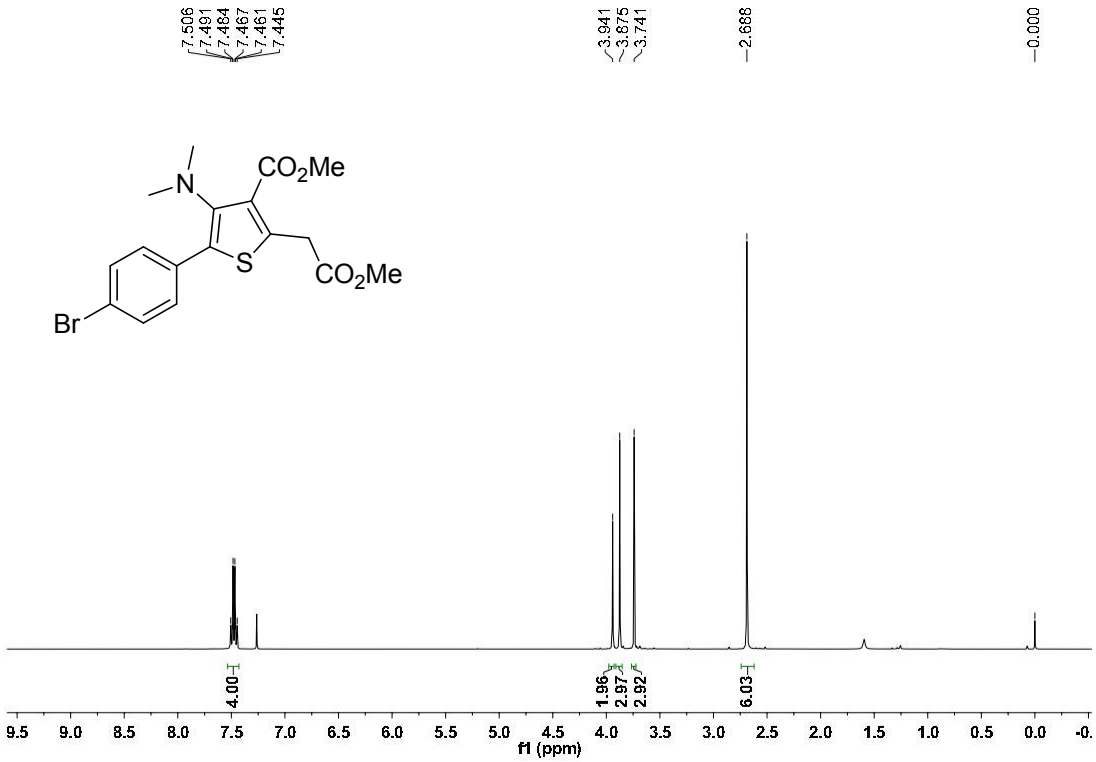
^{1}H NMR spectrum of compound **3ha** ($CDCl_3$)



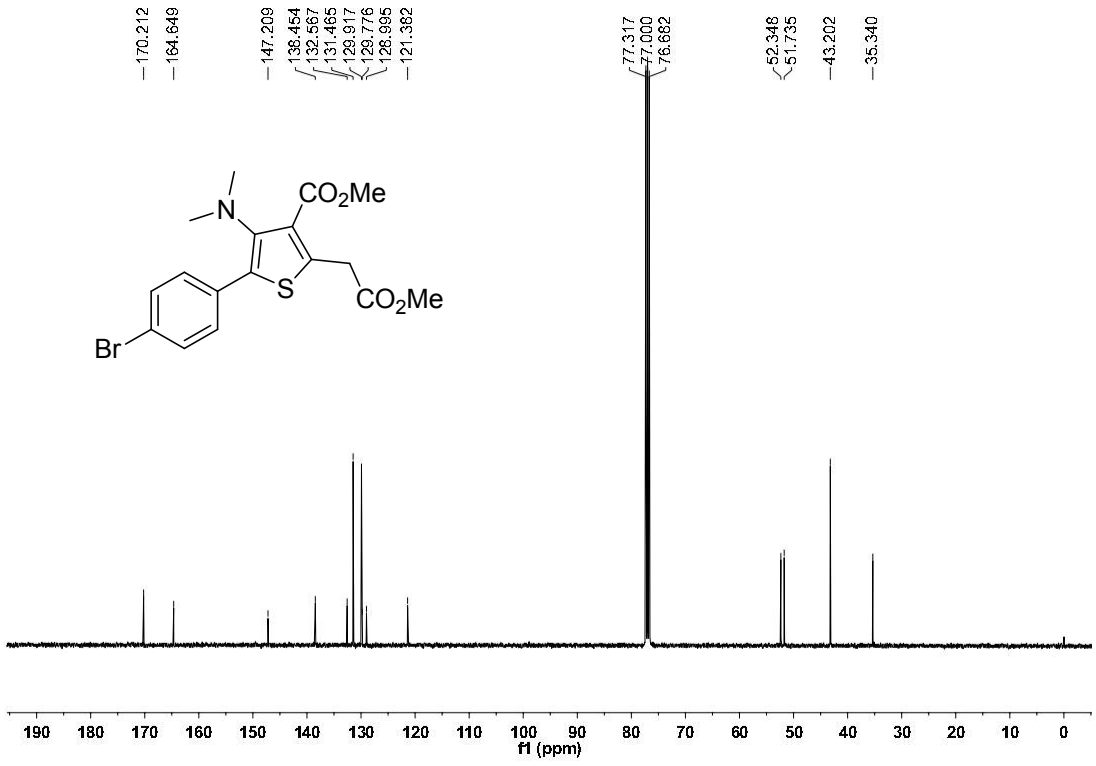
^{13}C NMR spectrum of compound **3ha** ($CDCl_3$)



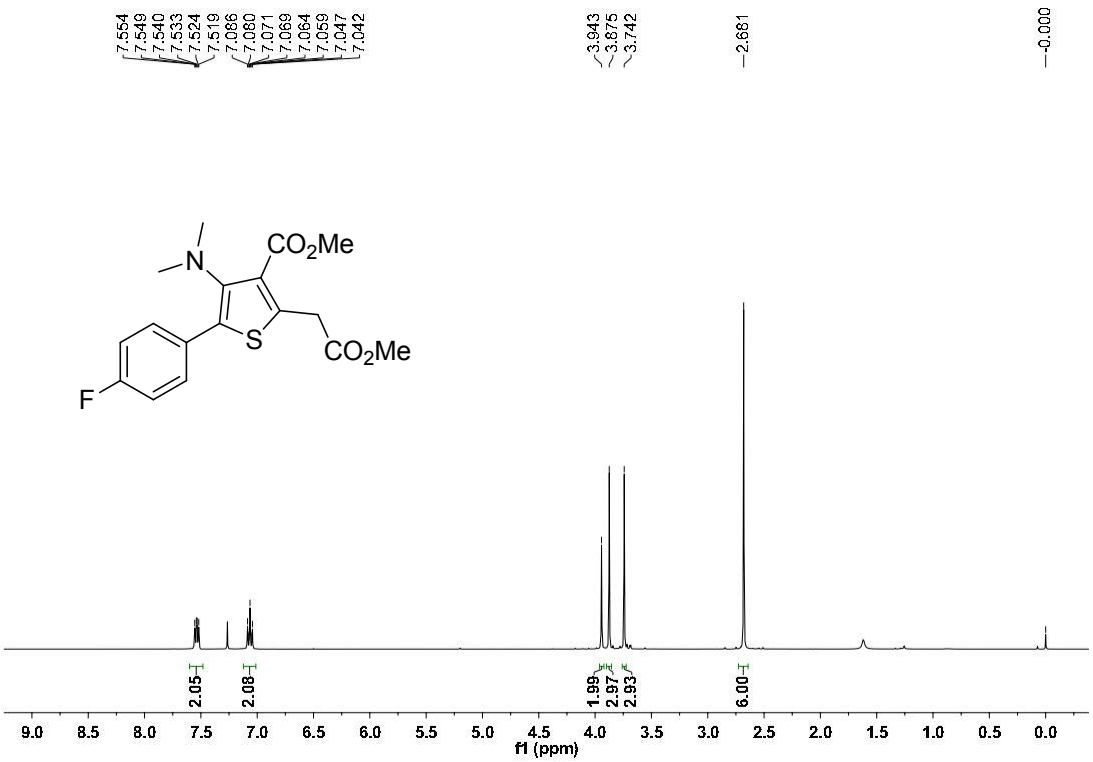
^{1}H NMR spectrum of compound **3ia**($CDCl_3$)



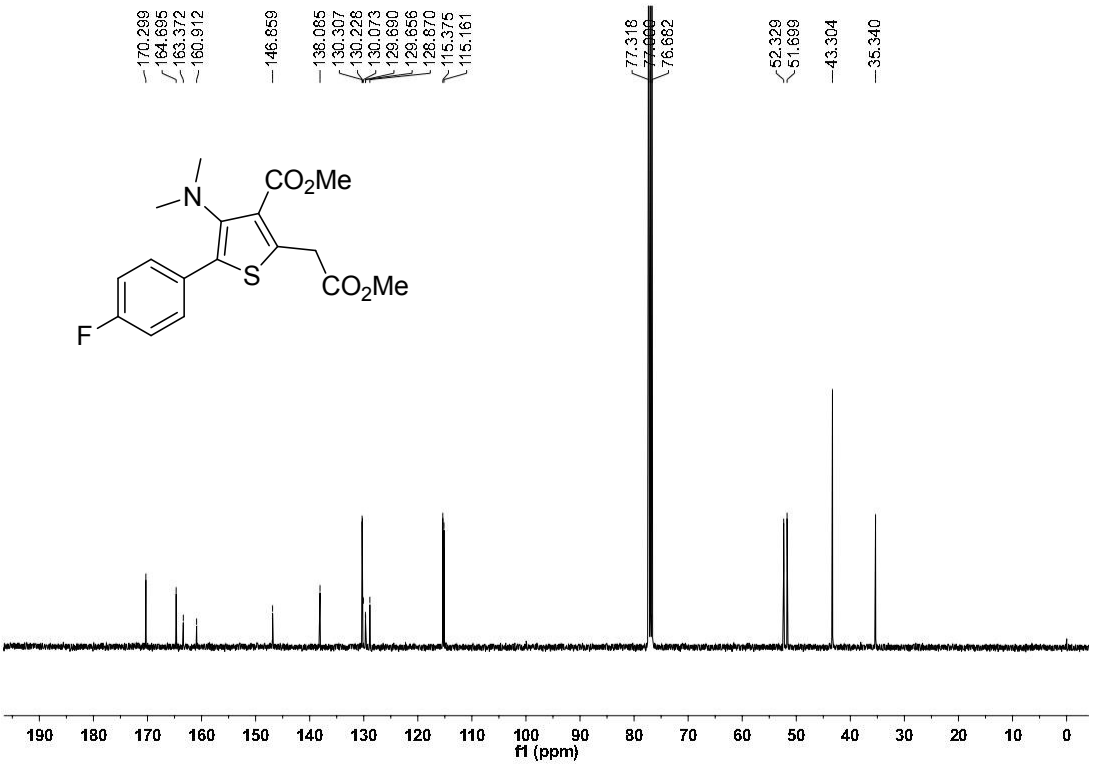
^{13}C NMR spectrum of compound **3ia** ($CDCl_3$)



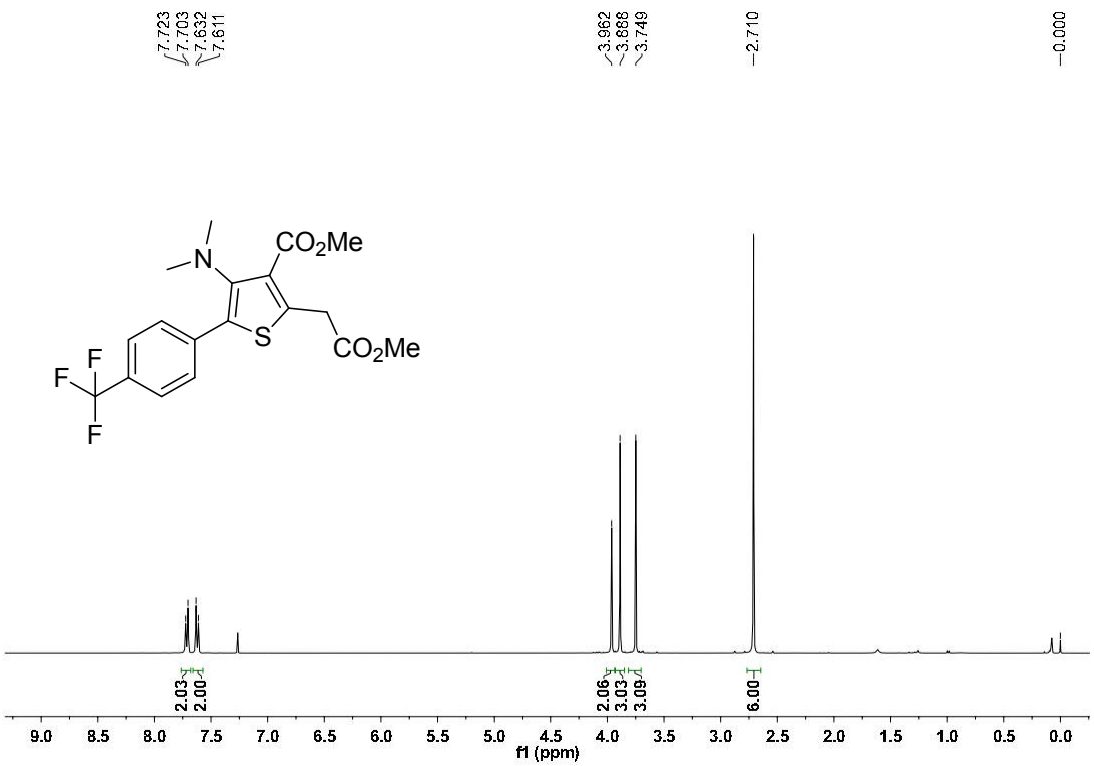
^{1}H NMR spectrum of compound **3ja**($CDCl_3$)



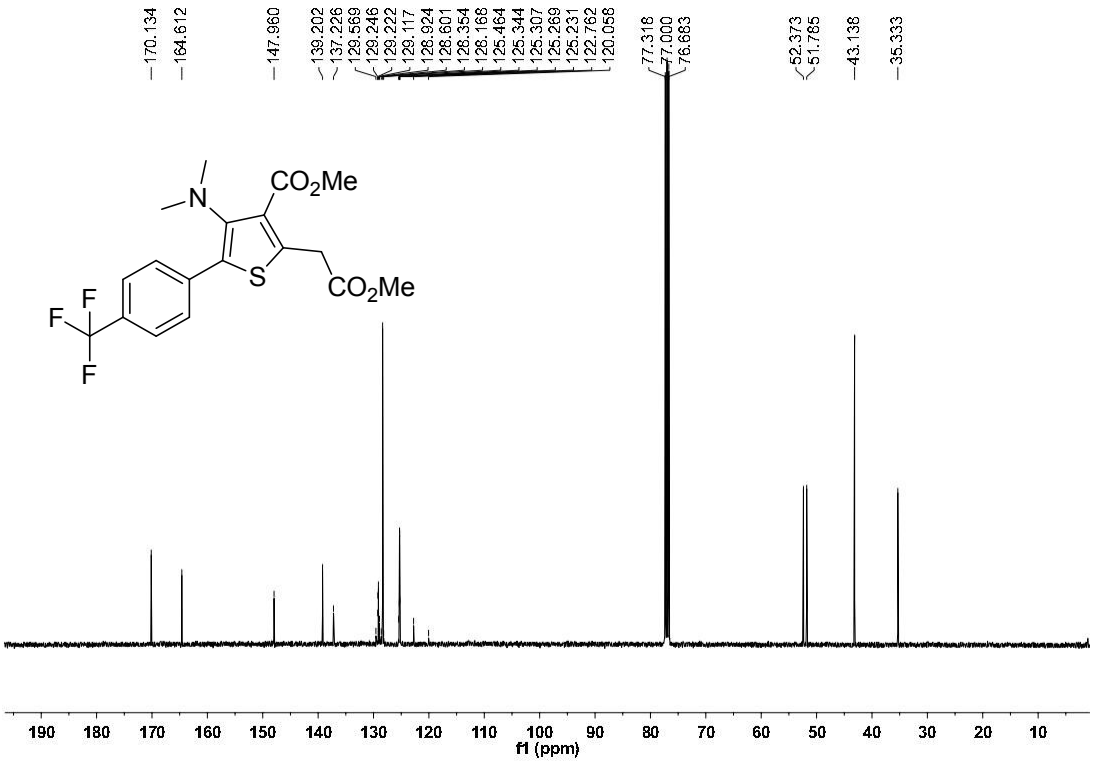
^{13}C NMR spectrum of compound **3ja** ($CDCl_3$)



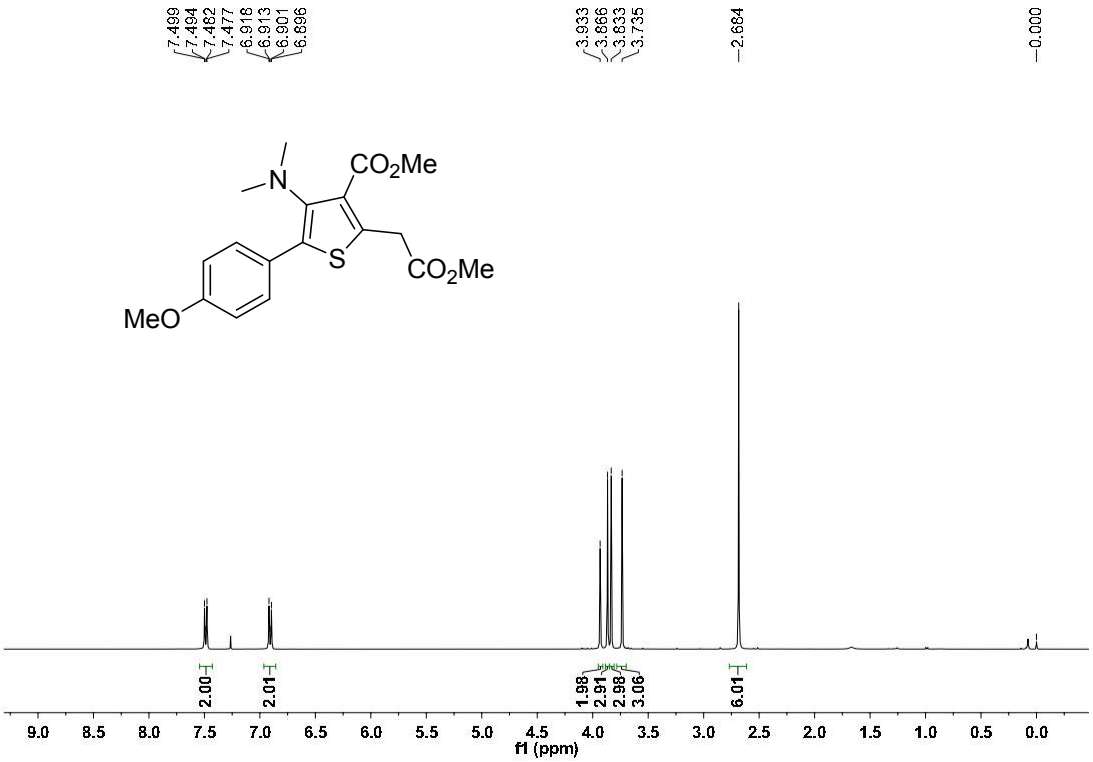
^{1}H NMR spectrum of compound **3ka** ($CDCl_3$)



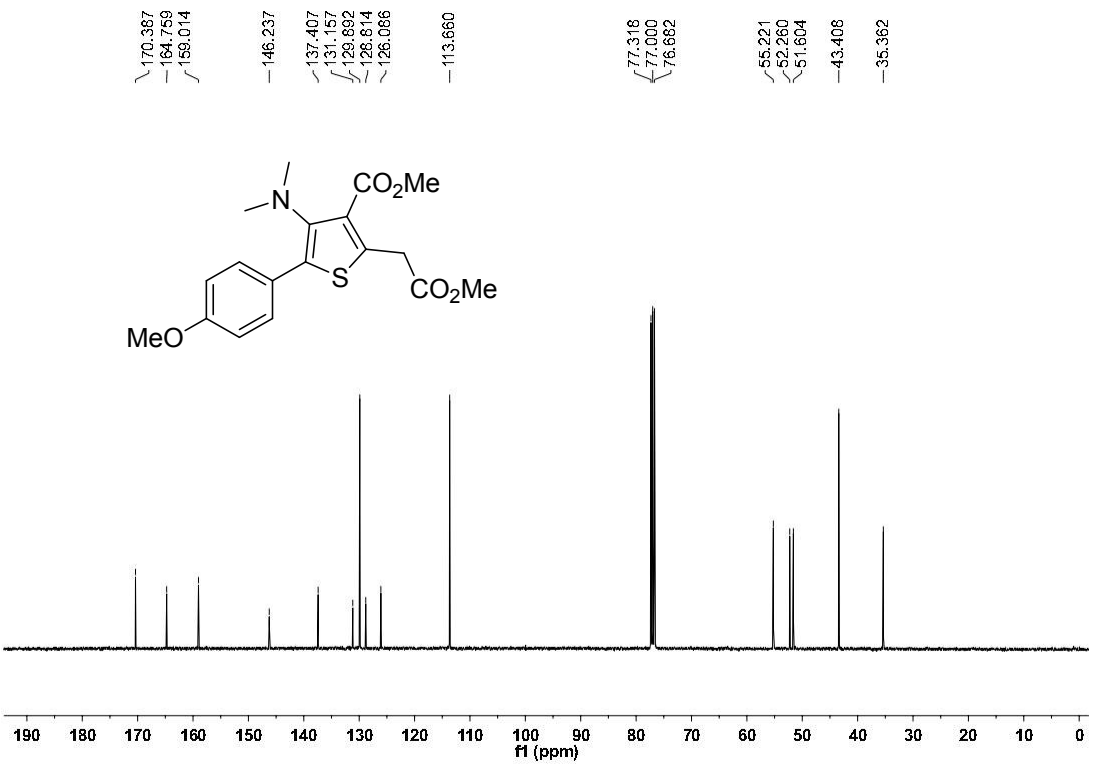
^{13}C NMR spectrum of compound **3ka** ($CDCl_3$)



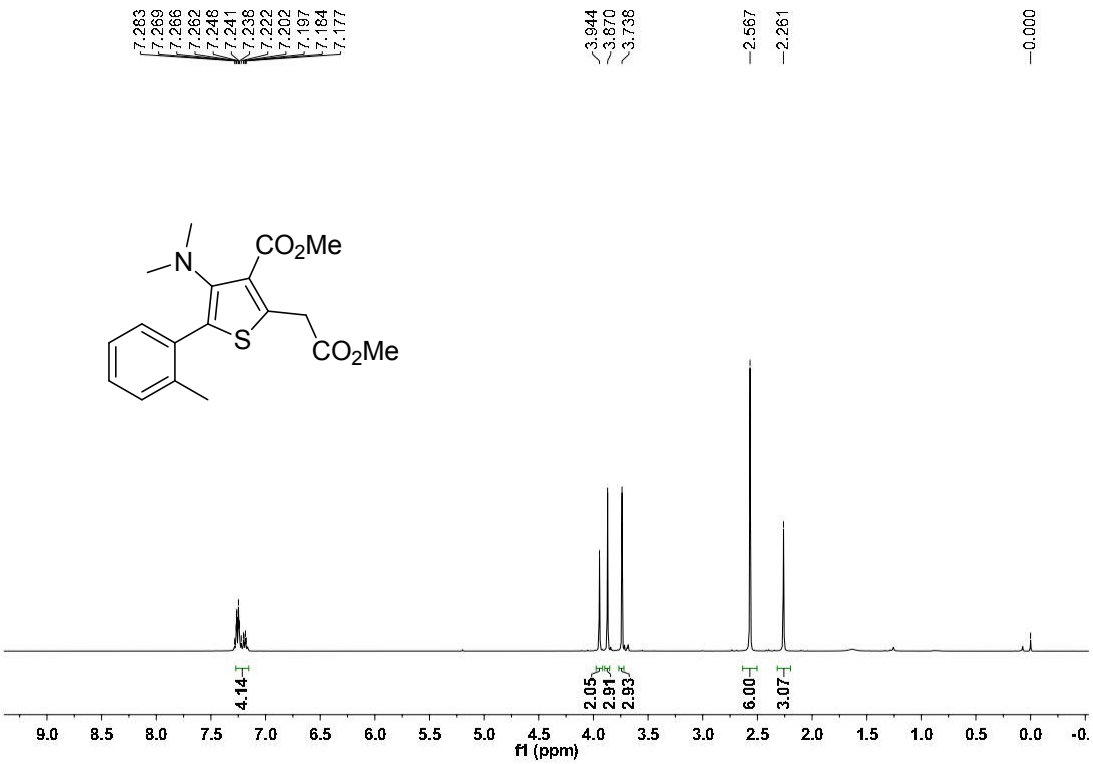
^{1}H NMR spectrum of compound **3la** ($CDCl_3$)



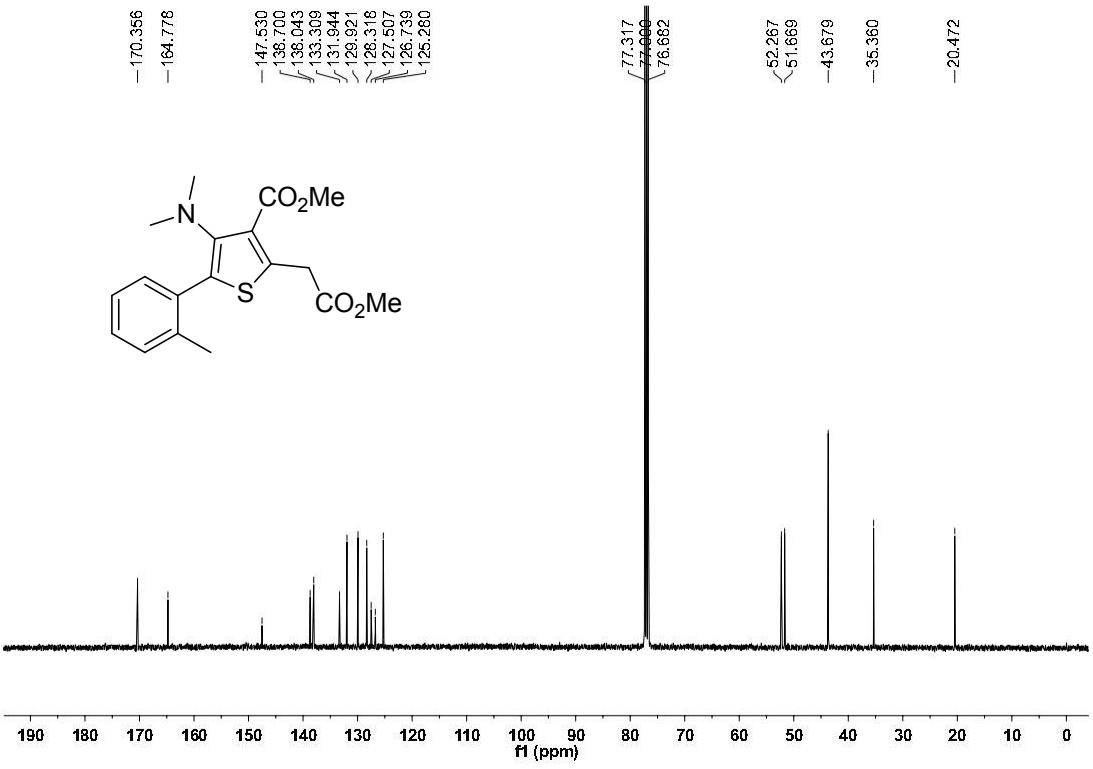
^{13}C NMR spectrum of compound **3la** ($CDCl_3$)



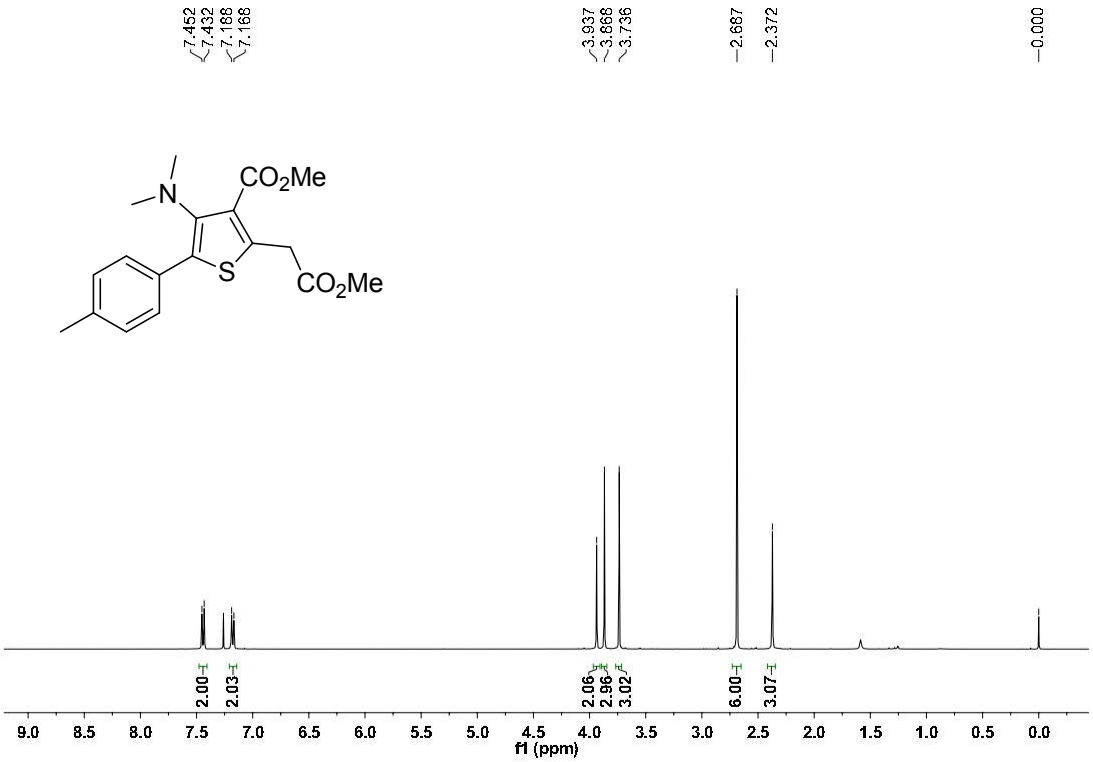
^{1}H NMR spectrum of compound **3ma** ($CDCl_3$)



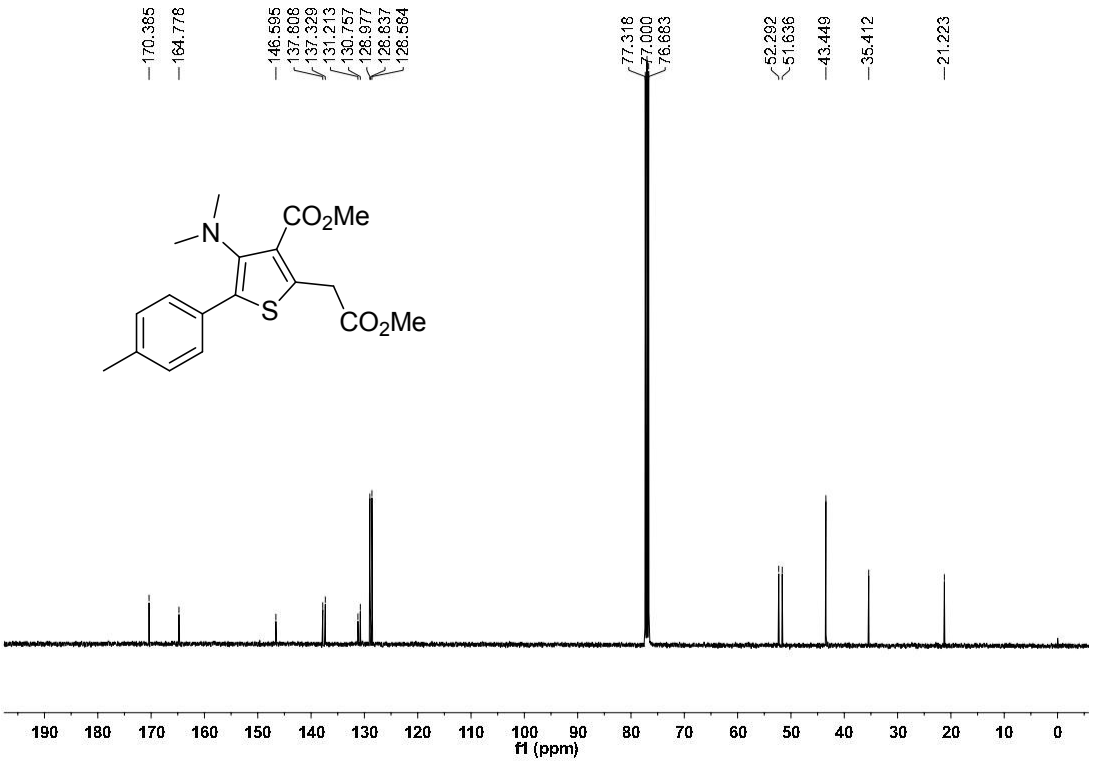
^{13}C NMR spectrum of compound **3ma** ($CDCl_3$)



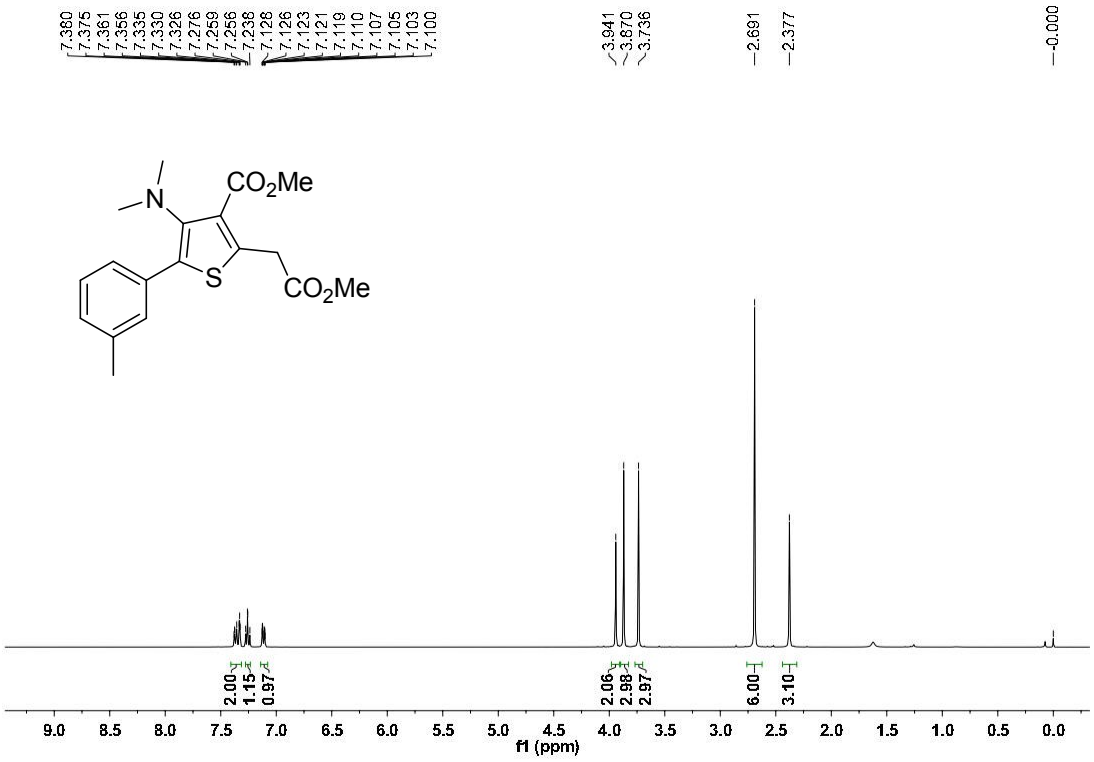
^{1}H NMR spectrum of compound **3na** ($CDCl_3$)



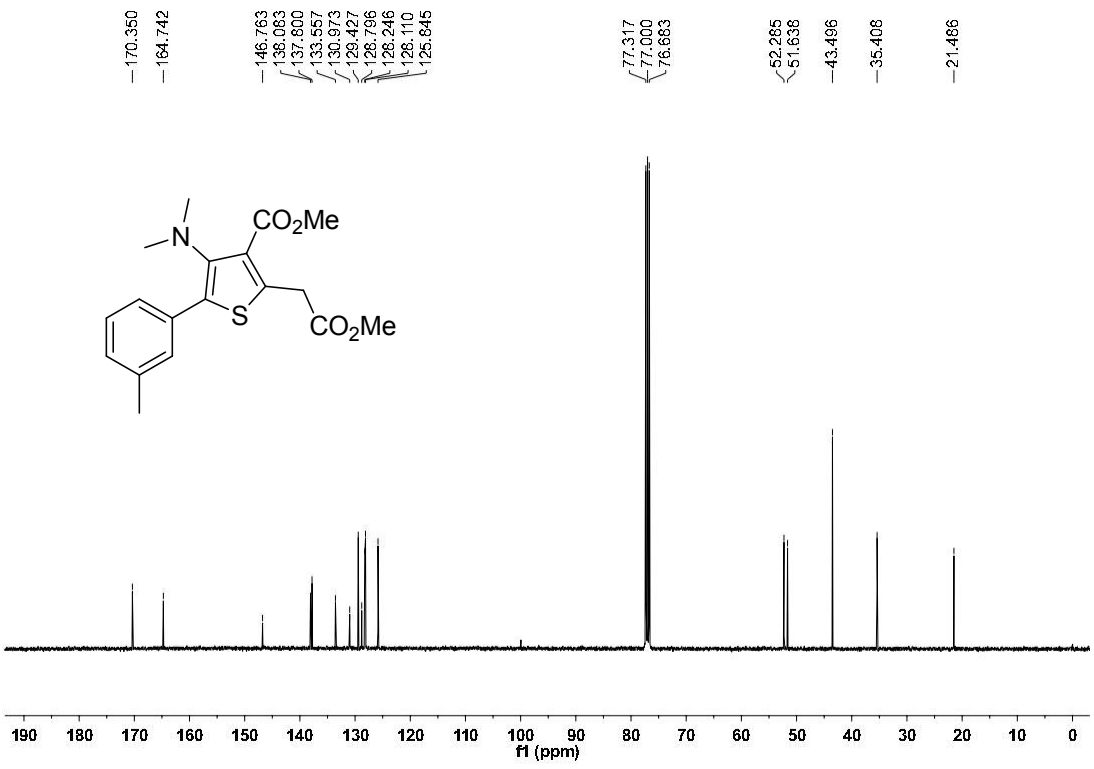
^{13}C NMR spectrum of compound **3na** ($CDCl_3$)



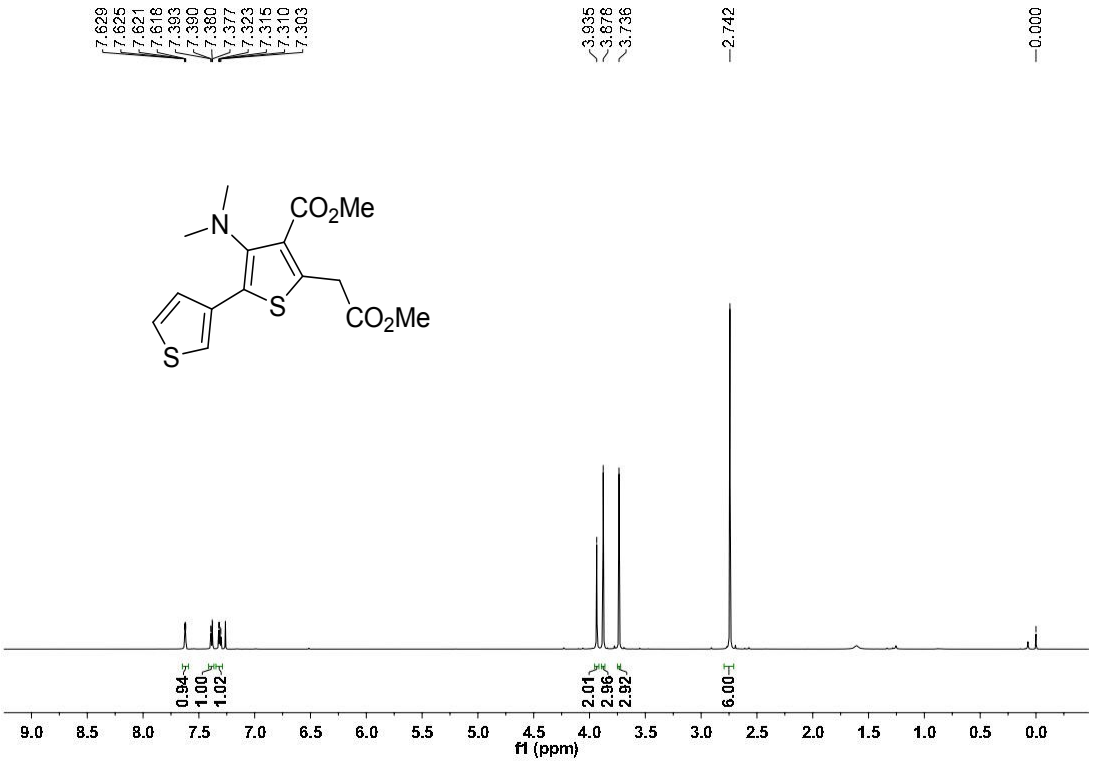
^{1}H NMR spectrum of compound **3oa** ($CDCl_3$)



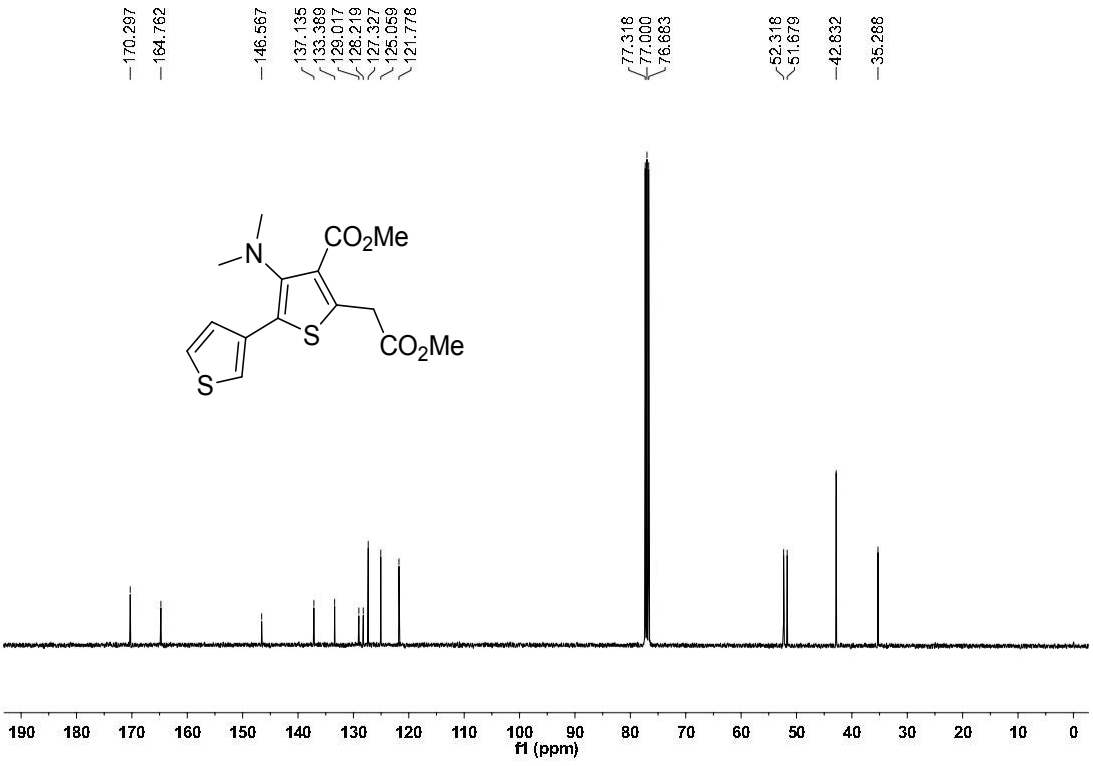
^{13}C NMR spectrum of compound **3oa** ($CDCl_3$)



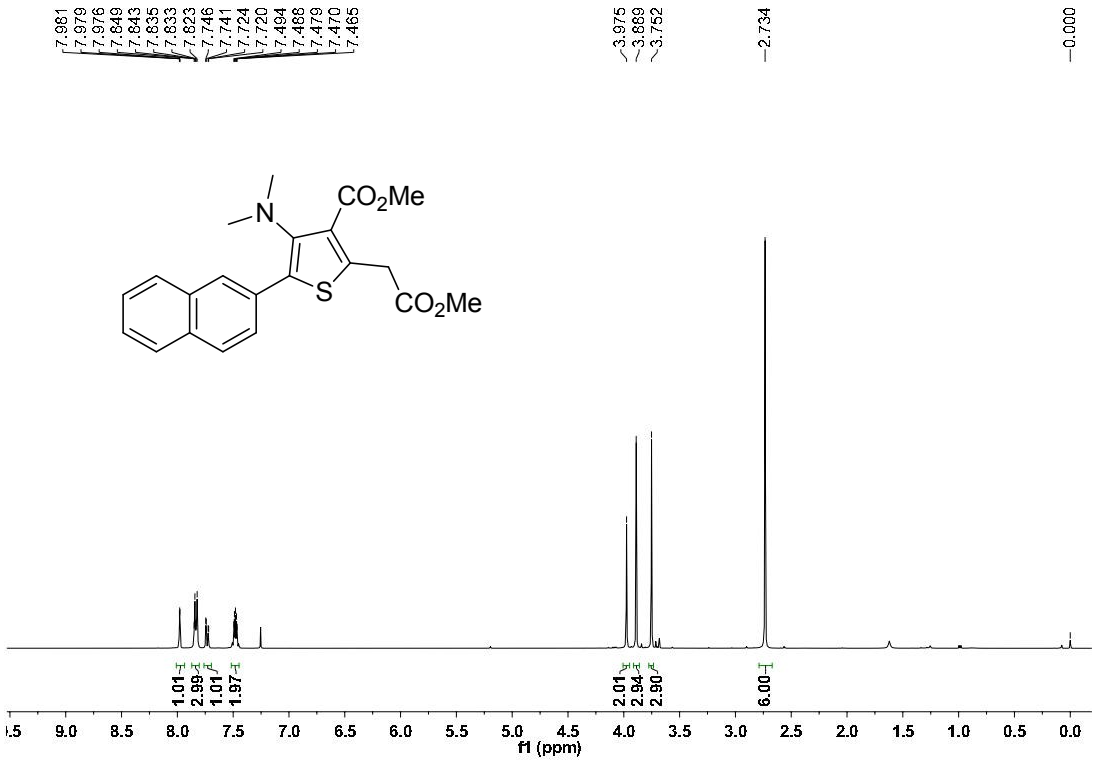
^{1}H NMR spectrum of compound **3pa** ($CDCl_3$)



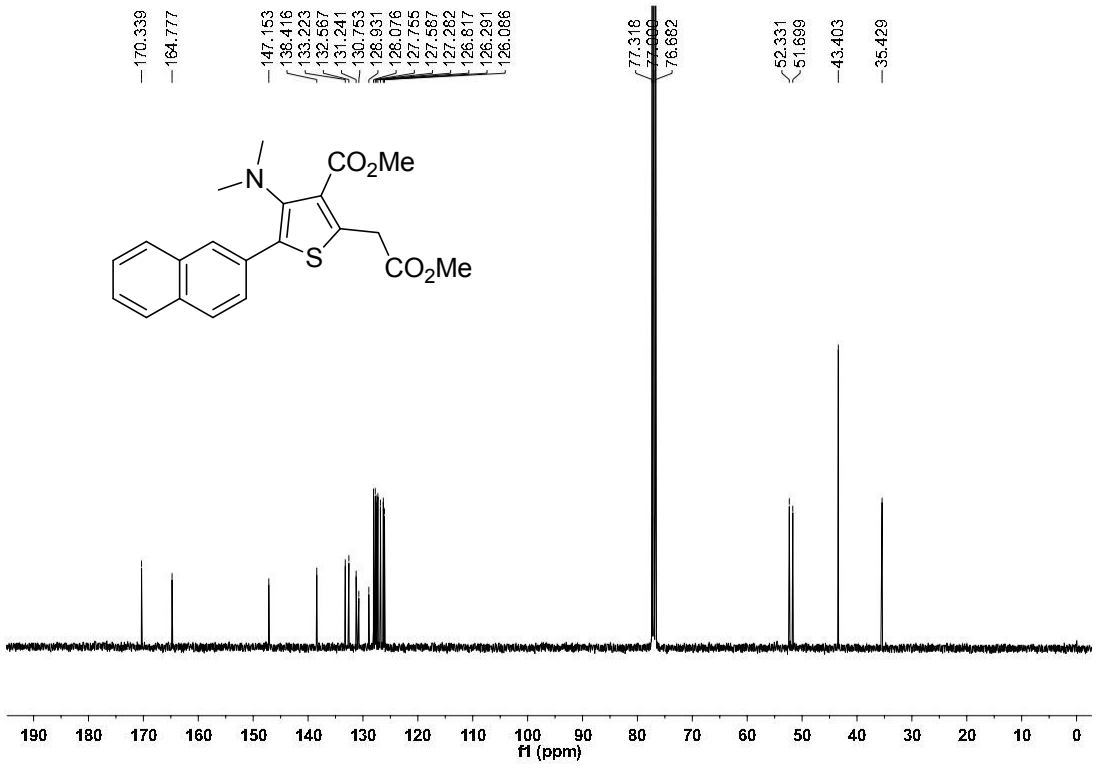
^{13}C NMR spectrum of compound **3pa** ($CDCl_3$)



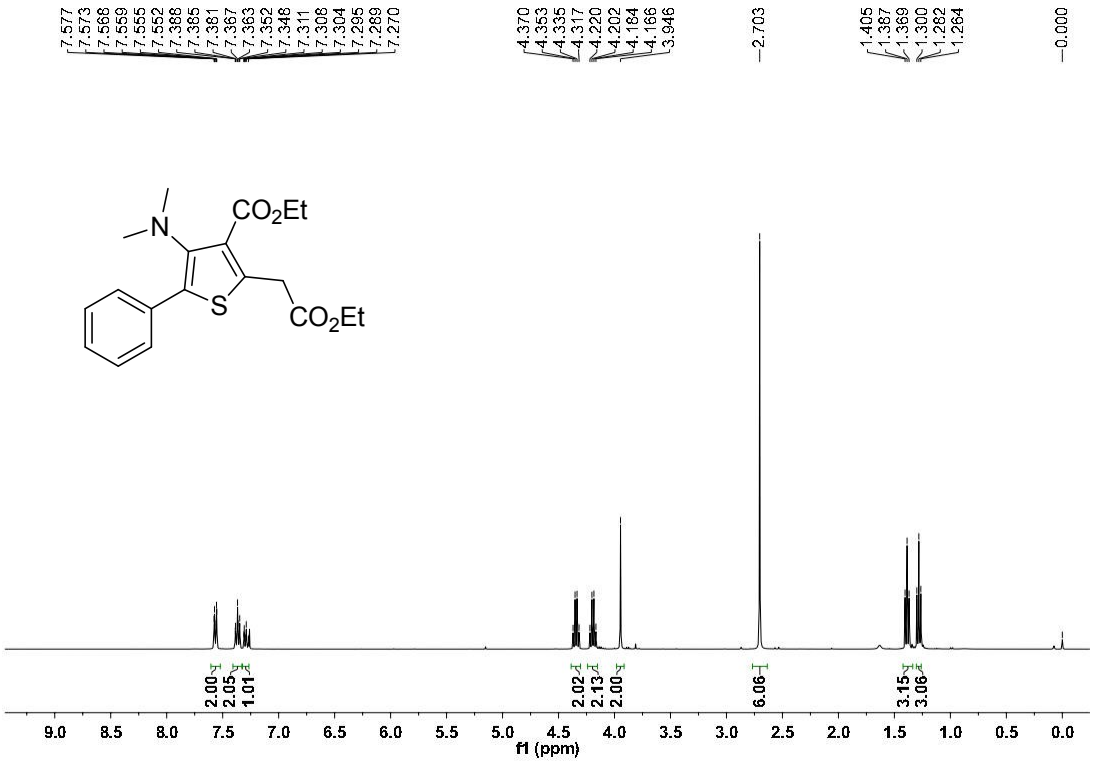
^{1}H NMR spectrum of compound **3qa** ($CDCl_3$)



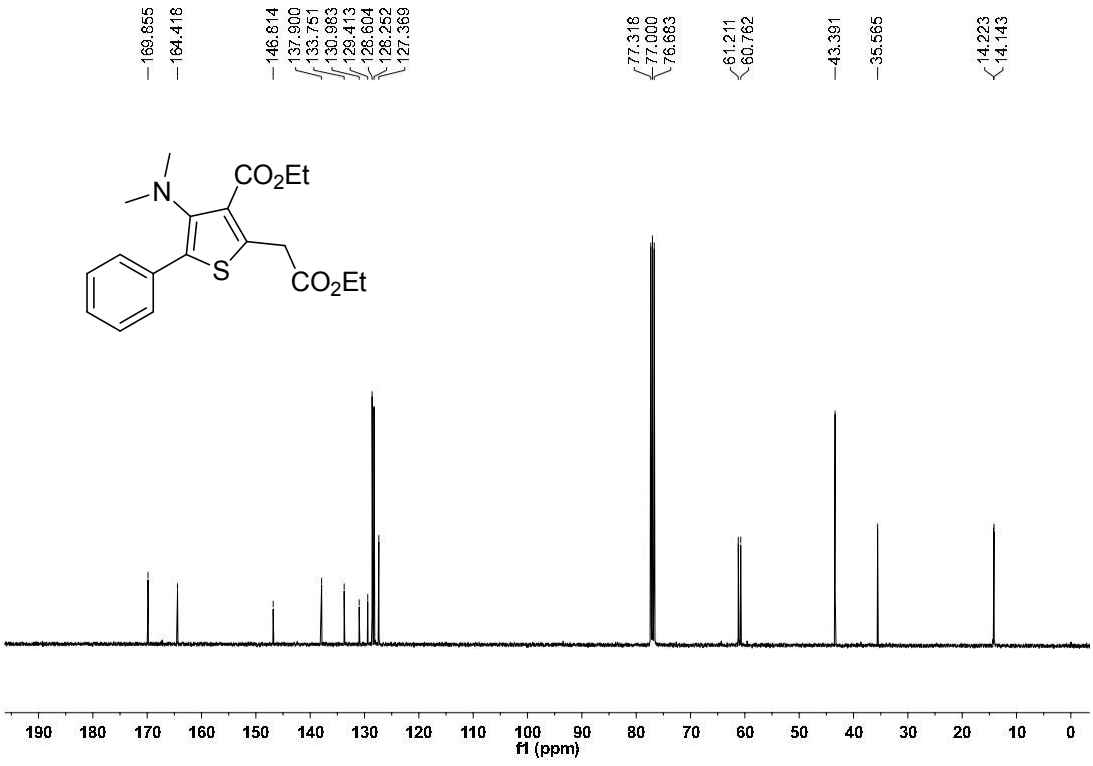
^{13}C NMR spectrum of compound **3qa** ($CDCl_3$)



^{1}H NMR spectrum of compound **3ab** ($CDCl_3$)



^{13}C NMR spectrum of compound **3ab** ($CDCl_3$)



5. X-ray structure for 3aa

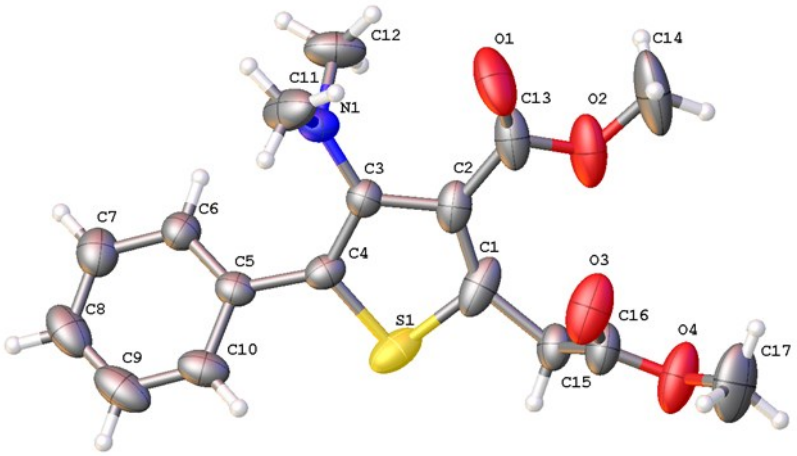


Fig. X-ray structure of **3aa**. Ellipsoids are drawn at the 30% probability level.

Crystal data and structure refinement for dm17469.

Identification code	dm17469	
Empirical formula	C17 H19 N O4 S	
Formula weight	333.39	
Temperature	296 K	
Wavelength	0.71073 Å	
Crystal system	Monoclinic	
Space group	C 1 2/c 1	
Unit cell dimensions	a = 15.538(5) Å	a= 90°.
	b = 6.0233(19) Å	b= 96.818(12)°.
	c = 37.422(12) Å	g = 90°.
Volume	3477.7(19) Å3	
Z	8	
Density (calculated)	1.274 Mg/m3	
Absorption coefficient	0.204 mm-1	
F(000)	1408	
Crystal size	0.12 x 0.1 x 0.05 mm3	
Theta range for data collection	2.192 to 25.997°.	
Index ranges	-11<=h<=18, -7<=k<=7, -46<=l<=46	
Reflections collected	12121	
Independent reflections	3425 [R(int) = 0.0424]	
Completeness to theta = 25.242°	99.9 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	0.7456 and 0.6659	
Refinement method	Full-matrix least-squares on F2	
Data / restraints / parameters	3425 / 0 / 249	
Goodness-of-fit on F2	1.190	

Final R indices [I>2sigma(I)]	R1 = 0.0706, wR2 = 0.1855
R indices (all data)	R1 = 0.1174, wR2 = 0.2104
Extinction coefficient	n/a
Largest diff. peak and hole	0.192 and -0.377 e.Å-3

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