

Electronic Supplementary Information

**Catalytic site-specific and regioselective
(3 + 2) transannulations between 1,2,3-
thiadiazoles and allenates**

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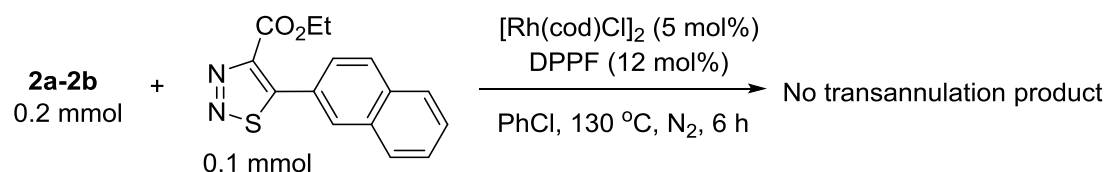
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1. General information and starting materials

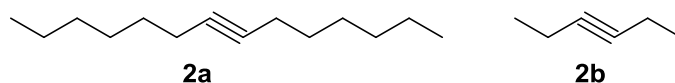
1.1 General information

Unless otherwise noted, all materials were purchased from commercial suppliers. Dichloromethane (DCM) and chlorobenzene were refluxed over CaH₂; tetrahydrofuran (THF) was refluxed over lithium aluminum hydride. The solvents were freshly distilled prior to use. Column chromatography was performed on silica gel (normal phase, 200-300 mesh) from Anhui Liangchen Silicon Material Co., Ltd, with petroleum ether (PE, bp. 60 – 90 °C) and ethyl acetate (EA) as eluent. Reactions were monitored by thin-layer chromatography (TLC) on GF₂₅₄ silica gel plates (0.2 mm) from Anhui Liangchen Silicon Material Co., Ltd. The plates were visualized by UV light, and other TLC stains (1% potassium permanganate in water; 10 g of iodine absorbed on 30 g of silica gel). ¹H and ¹³C NMR spectra were recorded on a Bruker 400 MHz spectrometer, usually in CDCl₃ as an internal standard, and the chemical shifts (δ) were reported in parts per million (ppm). Multiplicities are indicated as s (singlet), d (doublet), t (triplet), q (quartet), dd (double doublet), m (multiplet), and b (broad). Coupling constants (J) are reported in Hertz (Hz). HRMS measurements were carried out on an Agilent LC/MSD TOF mass spectrometer. GC-MS measurements were carried out on a Trace 1300 GC/ISQ QD mass spectrometer. Melting points were obtained on a Yanaco MP-500 melting point apparatus and are uncorrected. X-ray diffraction data were collected on a Rigaku Gemin E diffractometer. IR spectra (KBr pellets, ν (cm⁻¹)) were taken on a Bruker Tensor 27 spectrometer. All thiadiazoles **1** were previously synthesized in our previous publications.¹

1.2 Unsuccessful transannulation of 1,2,3-thiadiazoles with internal alkynes or allenates



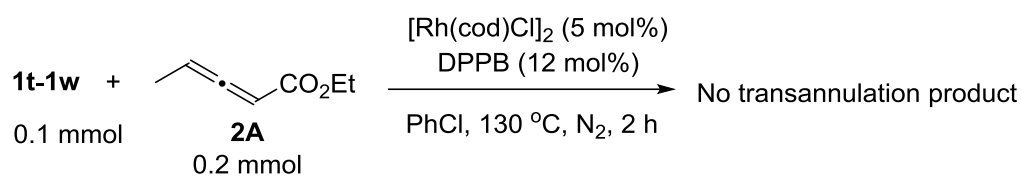
The following internal alkynes were reacted with **1a**



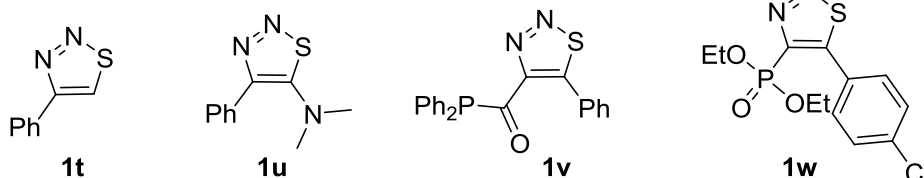
Scheme S1. Reaction of 1,2,3-thiadiazoles with internal alkynes

Procedure: To an oven-dried reaction tube equipped with a magnetic stirring bar was added 1,2,3-thiadiazole **1a** (28.4 mg, 0.1 mmol, 1.0 equiv), alkyne **2** (0.2 mmol, 2.0 equiv), [Rh(cod)Cl]₂ (2.5 mg, 0.005 mmol) and DPPF (6.7 mg, 0.012 mmol). The tube was sealed immediately with a rubber stopper and protected with a nitrogen balloon by evacuation-backfill operations for three times, then dry PhCl (1 mL) was injected to the

tube. The mixture was heated at 130 °C for 6 h. The mixture was detected by TLC and was analyzed by GC-MS.



The following 1,2,3-thiadiazoles were reacted with **2A**



Scheme S2. Reaction of 1,2,3-thiadiazoles with allenates

1.3 Heat of hydrogenation of allenes, alkynes, and alkenes

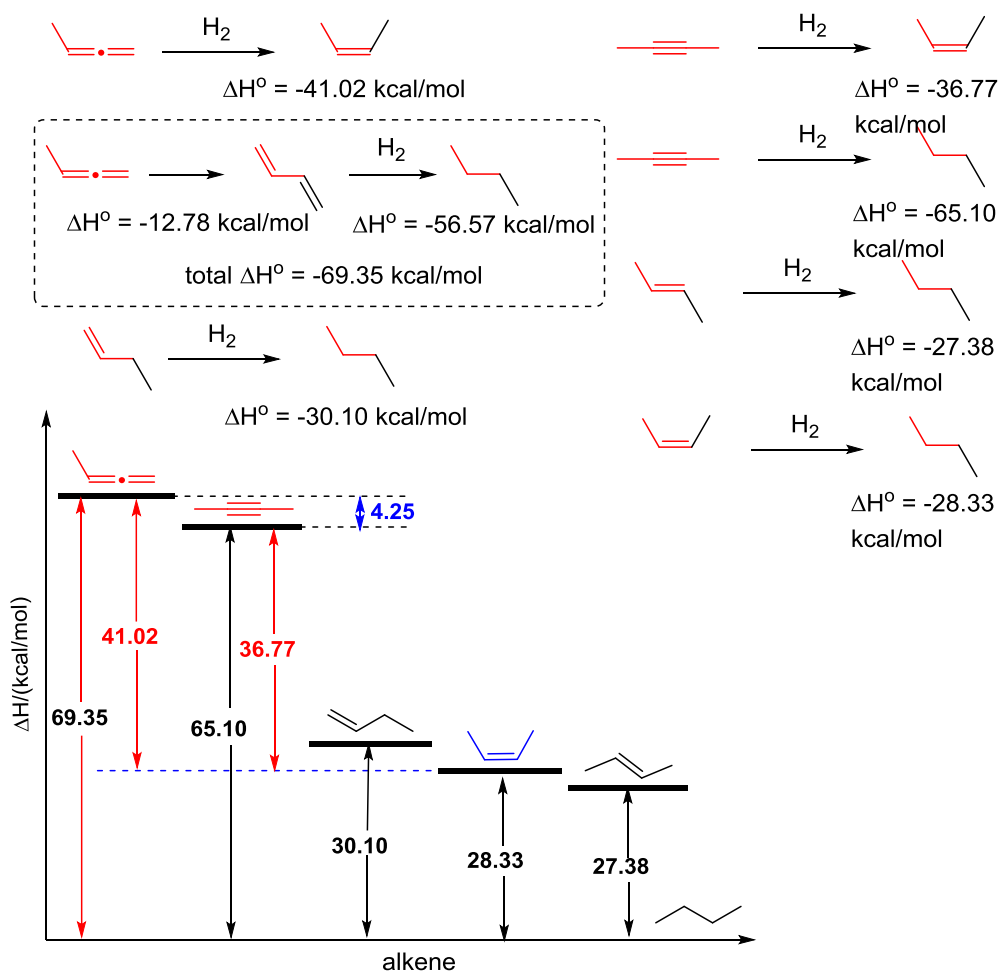


Figure S1. Heat of hydrogenation of allenes, alkynes, and alkenes

The data are obtained on [NIST Chemistry WebBook \(https://webbook.nist.gov/chemistry/\)](https://webbook.nist.gov/chemistry/), and the scientific references are included in the websites.

Heat of isomerization of buta-1,2-diene to buta-1,3-diene: $\Delta H^\circ = -12.78$ kcal/mol
<https://webbook.nist.gov/cgi/cbook.cgi?ID=C590192&Units=CAL&Mask=8>

Heat of hydrogenation of buta-1,3-diene to butane: $\Delta H^\circ = -56.57$ kcal/mol
<https://webbook.nist.gov/cgi/cbook.cgi?ID=C106990&Units=CAL&Mask=8>

Heat of hydrogenation of but-1-ene to butane: $\Delta H^\circ = -30.10$ kcal/mol
<https://webbook.nist.gov/cgi/cbook.cgi?ID=C106989&Units=CAL&Mask=8>

Heat of hydrogenation of but-2-yne to butane: $\Delta H^\circ = -65.10$ kcal/mol
<https://webbook.nist.gov/cgi/cbook.cgi?ID=C503173&Units=CAL&Mask=8>

Heat of hydrogenation of *trans*-but-2-ene to butane: $\Delta H^\circ = -27.38$ kcal/mol
<https://webbook.nist.gov/cgi/cbook.cgi?ID=C624646&Units=CAL&Mask=8>

Heat of hydrogenation of *cis*-but-2-ene to butane: $\Delta H^\circ = -28.33$ kcal/mol
<https://webbook.nist.gov/cgi/cbook.cgi?ID=C590181&Units=CAL&Mask=8>

1.4 Synthesis and Characterization of Substrates

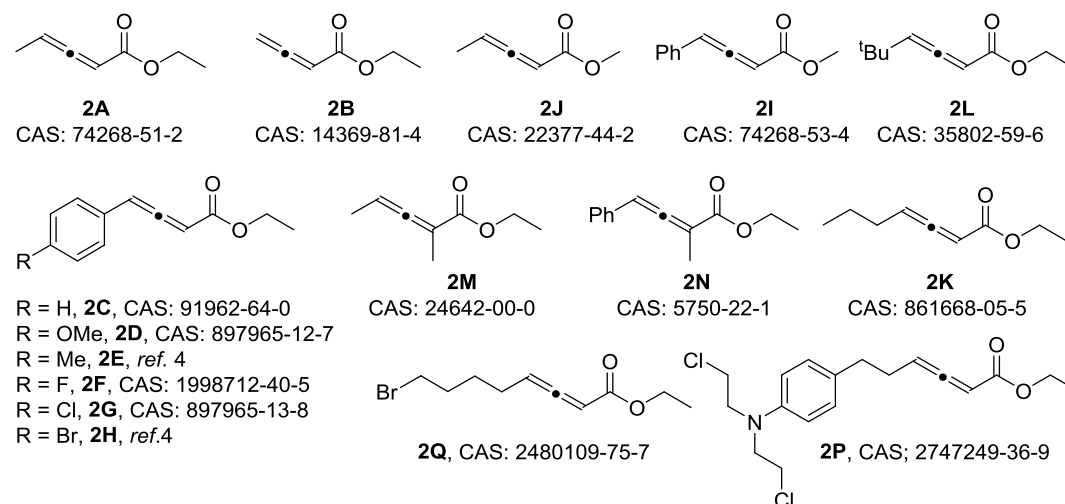
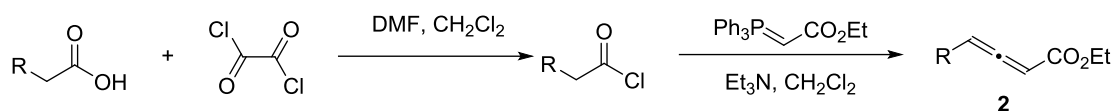


Figure S2. The allenes substrates

2A, **2B**, **2D**, **2M** were prepared according to Guo and coworkers' procedure.² **2E**, **2F**, **2G**, **2H** were prepared according to Zhao and coworkers' procedure.³ **2M**, **2N** were prepared according to List and coworkers' procedure.⁴ **2C**, **2I**, **2L** were prepared according to Robert and coworkers' procedure.⁵ **2J**⁶ and **2K**⁷ were prepared according to the corresponding literature.

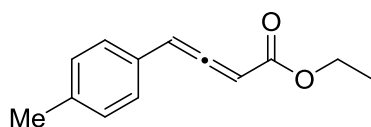


Scheme S3. Synthesis of allenes **2E**, **2H** and **2Q**

(1) Carboxylic acid (5 mmol, 1.0 equiv) was dissolved in 25 mL of CH_2Cl_2 in a 50 mL round-bottom flask with a magnetic stirring bar. One drop of DMF was added, followed by slow addition of $(\text{COCl})_2$ (635 mg, 7.5 mmol, 1.5 equiv) to the mixture at room temperature. The obtained solution was stirred for 4 h at room temperature. The acyl chloride was obtained after evaporating the solvent and used directly in next step without further purification.

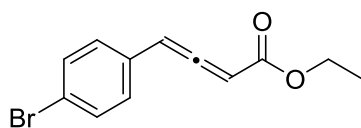
(2) Phosphorus ylide (1.74 g, 5 mmol, 1.0 equiv) and Et_3N (0.7 mL, 5 mmol, 1.0 equiv) were successively dissolved in 15 mL of CH_2Cl_2 in a 50-mL round-bottom flask with a stir bar. To the stirring mixture, a solution of acyl chloride (5 mmol, 1.0 equiv) in 10 mL of CH_2Cl_2 was slowly added at room temperature. After the addition was finished, the reaction mixture was stirred for further 2 h at room temperature. The solvent was evaporated under reduced pressure, and the crude mixture was treated with petroleum ether (25 mL) and was allowed to sit undisturbed for 30 min. The mixture was filtered and the filtrate was evaporated. The crude residue was purified by column chromatography on silica gel to afford allenic ester.

Ethyl 4-(*p*-tolyl)buta-2,3-dienoate (**2E**)



Yellow oil, 420 mg, yield 42%, $R_f = 0.73$ (PE/EA = 10:1, *v/v*). $^1\text{H NMR}$ (400 MHz, CDCl_3) δ 7.20 (d, $J = 8.1$ Hz, 2H), 7.15 (d, $J = 8.0$ Hz, 2H), 6.60 (d, $J = 6.3$ Hz, 1H), 6.01 (d, $J = 6.3$ Hz, 1H), 4.23 (q, $J = 7.1$ Hz, 2H), 2.35 (s, 3H), 1.29 (t, $J = 7.1$ Hz, 3H). $^{13}\text{C NMR}$ (101 MHz, CDCl_3) δ 214.6, 165.1, 138.0, 129.5, 128.0, 127.3, 98.4, 91.8, 61.0, 21.2, 14.2. **GC-MS** (EI, *m/z*, rel. intensity) 202.33 (22.00), 174.25 (21.03), 158.26 (13.61), 129.25 (100.00), 115.21 (10.39), 91.20 (5.81). **IR**(KBr) ν (cm^{-1}): 1731, 1265, 1180.

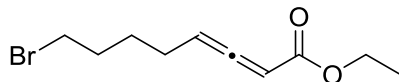
Ethyl 4-(4-bromophenyl)buta-2,3-dienoate (**2H**)



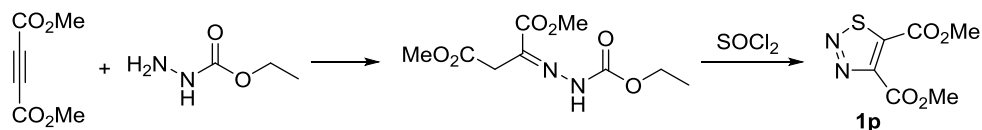
Known compound reported by List and coworkers.⁴ Yellow oil, 336 mg, yield 25%, $R_f = 0.68$ (PE/EA = 5:1, *v/v*). $^1\text{H NMR}$ (400 MHz, CDCl_3) δ 7.46 (d, $J = 8.5$ Hz, 2H), 7.17 (d, $J = 8.4$ Hz, 2H), 6.56 (d, $J = 6.4$ Hz, 1H), 6.01 (d, $J = 6.4$ Hz, 1H), 4.23 (q, $J = 7.1$ Hz, 2H), 1.29 (t, $J = 7.1$ Hz, 3H). $^{13}\text{C NMR}$ (101

MHz, CDCl₃) δ 214.5, 164.7, 132.0, 130.2, 128.9, 122.0, 97.9, 92.3, 61.2, 14.2. **GC-MS** (EI, m/z, rel. intensity) 268.26 (17.04), 266.28 (15.55), 195.19 (99.10), 193.20 (100.00), 187.32 (22.71), 114.24 (92.90). **IR**(KBr) ν (cm⁻¹): 1731, 1072.

Ethyl 8-bromoocta-2,3-dienoate (2Q)

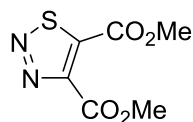


Known compound reported by Mohanan and coworkers.⁸ Yellow oil, 601 mg, yield 49%, R_f = 0.62 (PE/EA = 10:1, v/v). **¹H NMR** (400 MHz, CDCl₃) δ 5.65 – 5.51 (m, 2H), 4.19 (qd, J = 7.2, 1.9 Hz, 2H), 3.47 (dt, J = 52.1, 6.6 Hz, 2H), 2.17 (tt, J = 7.1, 5.1 Hz, 2H), 2.01 – 1.78 (m, 2H), 1.68– 1.57 (m, 2H), 1.28 (t, J = 7.1 Hz, 3H). **¹³C NMR** (101 MHz, CDCl₃) δ 212.2, 166.1, 94.6, 88.6, 60.8, 33.3, 31.7, 27.0, 26.5, 14.2. **IR**(KBr) ν (cm⁻¹): 1710, 1255, 1177.



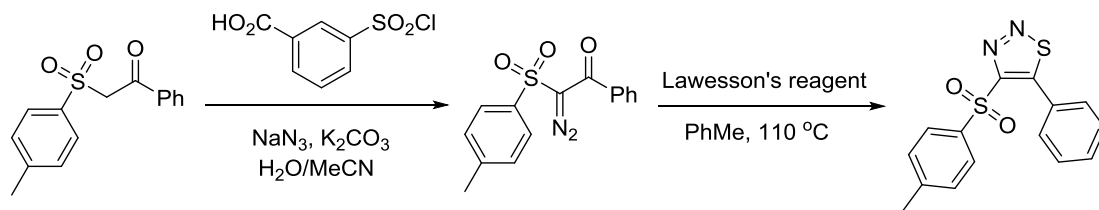
- 1) To a 50 mL round-bottom flask equipped with a magnetic stirring bar was added a solution of ethyl hydrazinecarboxylate (1.04 g, 10 mmol, 1.0 equiv) in methanol (20 mL), then dimethyl acetylenedicarboxylate (1.3 mL, 10 mmol, 1.0 equiv) was added dropwise at 0 °C. The reaction mixture was stirred at room temperature overnight and then concentrated in vacuo. The crude hydrazone was washed with methanol, dried in the air and used for the next step without further purification.
- 2) To a solution of hydrazone (ca. 10 mmol) in CH₂Cl₂ (10 mL) SOCl₂ (3.6 mL, 50 mmol, 5.0 equiv) was added dropwise at 0 °C. The reaction mixture was stirred at room temperature overnight and then concentrated in vacuo. The residue was dissolved in CH₂Cl₂ (10 mL) and washed with 5% NaHCO₃ solution (3 × 10 mL). The combined organic layer was dried over anhydrous magnesium sulfate and concentrated in vacuo. The crude product was purified by column chromatography on silica gel to afford 1,2,3-thiadiazole **1p**.

Dimethyl 1,2,3-thiadiazole-4,5-dicarboxylate (1p)⁹



CAS: 4100-15-6

White solid, 1.1 g, yield 54%, m. p. 40 – 42 °C, R_f = 0.43 (PE/EA = 5:1, v/v). **¹H NMR** (400 MHz, CDCl₃) δ 4.04 (s, 3H), 3.98 (s, 3H). **¹³C NMR** (101 MHz, CDCl₃) δ 159.9, 158.9, 152.8, 148.2, 54.1, 53.5. **HRMS** (ESI): m/z [M+H]⁺ calcd for C₆H₇N₂O₄S⁺ 203.0121, found 203.0122, [M+Na]⁺ calcd for C₆H₆N₂NaO₄S⁺ 224.9940, found 224.9942. **IR**(KBr) ν (cm⁻¹): 1736, 1508, 1438, 1334, 1330, 1280, 1230, 1175, 1091, 1014.

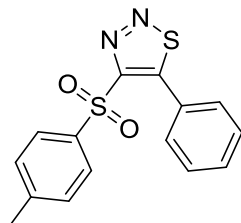


The crude diazo compound was prepared according to Krasavin's procedure.¹⁰

1) To a solution of sodium azide (390 mg, 6 mmol, 2.0 eq.) and potassium carbonate (1.1 g, 8 mmol, 2.67 eq.) in water (8 mL) and acetonitrile (4 mL) was added 3-(chlorosulfonyl)benzoic acid (882 mg, 4 mmol, 1.33 eq.) and 1-phenyl-2-tosylethan-1-one (823 mg, 3 mmol, 1.0 eq.). The mixture was stirred vigorously at room temperature overnight and then extracted with chloroform (4 mL \times 3). The combined organic layers dried over anhydrous Na_2SO_4 . After filtration and removing the solvent in vacuum, the crude product was used for the next step without further purification.

2) To a 48 mL-heavy-walled pressure tube equipped with a magnetic stirring bar was added crude 2-diazo-1-phenyl-2-tosylethan-1-one (796 mg, 2.65 mmol, 1.0 eq.), Lawesson's reagent (1.18 g, 2.92 mmol, 1.1 eq.) and toluene (12 mL). The tube was sealed and stirred at 110 °C (oil bath) for 8 h. Then, after cooling to room temperature and removing the volatiles in vacuum, the residue was purified by column chromatography on silica gel afforded the 5-phenyl-4-tosyl-1,2,3-thiadiazole (**1s**) in 88% yield.

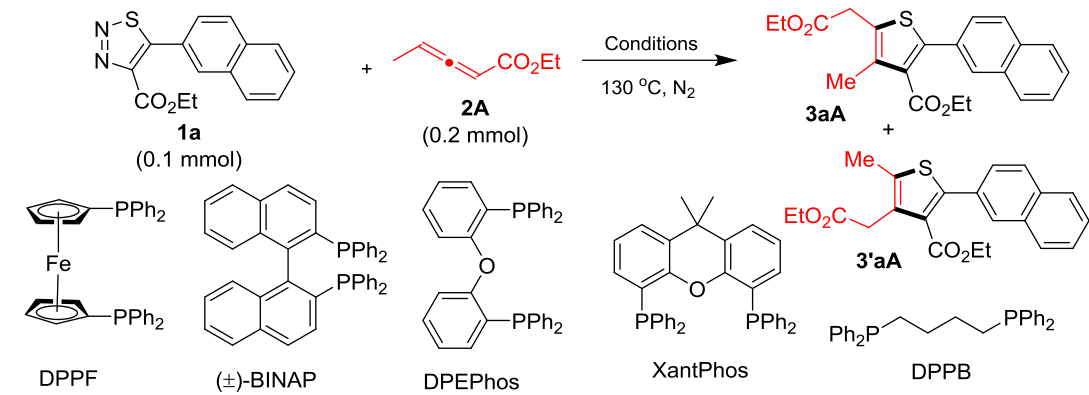
Ethyl 5-phenyl-4-tosyl-1,2,3-thiadiazole (**1s**)



White solid, 835 mg, yield 88%, m. p. 102 – 105 °C, $R_f = 0.43$ (PE/EA = 5:1, v/v). $^1\text{H NMR}$ (400 MHz, CDCl_3) δ 7.83 (d, $J = 8.0$ Hz, 2H), 7.60 – 7.46 (m, 5H), 7.30 (d, $J = 8.0$ Hz, 2H), 2.41 (s, 3H). $^{13}\text{C NMR}$ (101 MHz, CDCl_3) δ 159.7, 156.7, 145.5, 136.8, 131.0, 130.0, 129.8, 128.64, 128.57, 124.2, 21.6. **HRMS** (ESI): m/z $[\text{M}+\text{H}]^+$ calcd for $\text{C}_{15}\text{H}_{13}\text{N}_2\text{O}_2\text{S}_2^+$ 317.0413, found 317.0424. **IR** (KBr) ν (cm^{-1}): 1337, 1153.

2. Optimization Studies

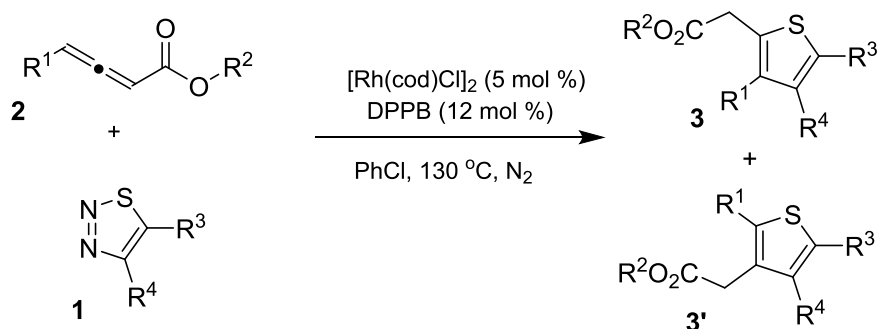
Table S1. Complete optimization of the reaction conditions.^a



entry	catalyst (mol %)	ligand (mol %)	solvent	temperature (°C)	yield ^a (3:3') (%)
1	[Rh(cod)Cl] ₂ (5)	DPPF (12)	PhCl	130	70 (74:26)
2	[Ir(cod)Cl] ₂ (5)	DPPF (12)	PhCl	130	30 (80:20)
3	[Cp*RhCl ₂] ₂ (5)	DPPF (12)	PhCl	130	55 (67:33)
4	[Cp*IrCl ₂] ₂ (5)	DPPF (12)	PhCl	130	7 (78:22)
5	Cu(OAc) ₂ · H ₂ O (10)	Xantphos (10)	PhCl	130	0 (-)
6	[Ni(cod)] (5)	DPPF (12)	PhCl	130	0 (-)
7	<i>trans</i> -Pd(Ph ₃ P) ₂ Cl ₂ (5)	DPPF (12)	PhCl	130	0 (-)
8	Co ₂ (CO) ₈ (5)	DPPF (12)	PhCl	130	0 (-)
9	Mn(CO) ₅ Br (5)	DPPF (12)	PhCl	130	0 (-)
10	[Rh(cod)Cl] ₂ (5)	(±)-BINAP (12)	PhCl	130	31 (32:68)
11	[Rh(cod)Cl] ₂ (5)	DPEPhos (12)	PhCl	130	66 (73:27)
12	[Rh(cod)Cl] ₂ (5)	XantPhos (12)	PhCl	130	0 (-)
13	[Rh(cod)Cl] ₂ (5)	DPPB (12)	PhCl	130	88 (84:16)
14	[Rh(cod)Cl] ₂ (3)	DPPB (7.2)	PhCl	130	69 (82:18)
15	[Rh(cod)Cl] ₂ (1)	DPPB (2.4)	PhCl	130	10 (77:23)
16	[Rh(cod)Cl] ₂ (5)	none	PhCl	130	0 (-)
17	none	DPPB (7.2)	PhCl	130	0 (-)
18	[Rh(cod)Cl] ₂ (5)	DPPB (12)	PhCl	100	40 (87:13)
19	[Rh(cod)Cl] ₂ (5)	DPPB (12)	PhCl	60	45 (100:0)
20	[Rh(cod)Cl] ₂ (5)	DPPB (12)	C ₂ Cl ₄	120	84 (85:15)
21	[Rh(cod)Cl] ₂ (5)	DPPB (12)	CHCl ₂	40	40 (100:0)
23	[Rh(cod)Cl] ₂ (5)	DPPB (12)	PhMe	110	83 (87:13)
24	[Rh(cod)Cl] ₂ (5)	DPPB (12)	DCE	80	24 (100:0)
25	CoCl ₂ (5)	DPPB (12)	PhCl	130	0 (-)

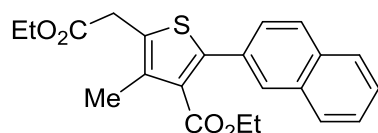
3. Procedures and analytical data for (3 + 2) transannulations, product derivatization, and mechanistic studies

3.1 Synthesis and Characterization of Products 3 and 3'



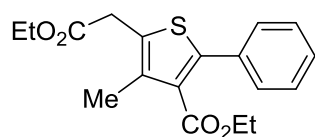
To an oven-dried reaction tube equipped with a magnetic stirring bar was added 1,2,3-thiadiazole **1** (0.1 mmol, 1.0 equiv), allene **2** (0.2 mmol, 2.0 equiv), [Rh(cod)Cl]₂ (2.5 mg, 0.005 mmol, 5 mol %), and DPPB (5.1 mg, 0.012 mmol, 12 mol %). The tube was sealed immediately with a rubber stopper and protected with a nitrogen balloon by evacuation-backfill operations for three times; then PhCl (1 mL) was injected to the tube. The mixture was heated at 130 °C in a heating block for 2 h. When the reaction was finished, as detected by TLC, the solvent was evaporated under reduced pressure. A small portion of the crude reaction mixture was submitted to ¹H NMR test to determine the regioselective ratios. After NMR test, the combined crude reaction mixture was subjected to column chromatography on silica gel, affording the corresponding major products **3**. In some cases, the other regioisomer was also separated, if its yield was enough high.

Ethyl 5-(2-ethoxy-2-oxoethyl)-4-methyl-2-(naphthalen-2-yl)thiophene-3-carboxylate (3aA)



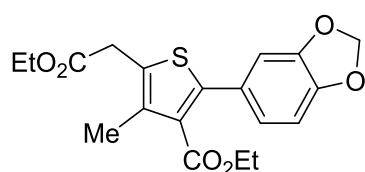
Yellow oil, 24 mg, yield 72%, *R_f* = 0.41 (DCM/PE = 2:1, *v/v*). ¹H NMR (400 MHz, CDCl₃) δ 7.99 – 7.73 (m, 4H), 7.51 – 7.49 (m, 3H), 4.21 (q, *J* = 7.1 Hz, 2H), 4.14 (q, *J* = 7.1 Hz, 2H), 3.78 (s, 3H), 2.33 (s, 2H), 1.30 (t, *J* = 7.1 Hz, 3H), 1.01 (t, *J* = 7.1 Hz, 3H). ¹³C NMR (101 MHz, CDCl₃) δ 170.0, 165.3, 146.1, 136.1, 133.0, 132.9, 131.4, 129.9, 129.1, 128.1, 127.8, 127.64, 127.56, 127.2, 126.39, 126.35, 61.4, 60.6, 33.6, 14.2, 13.8, 13.5. HRMS (ESI): *m/z* [M+H]⁺ calcd for C₂₂H₂₃O₄S⁺ 383.1312, found 383.1313. IR(KBr) *ν* (cm⁻¹): 1736, 1711, 1184.

Ethyl 5-(2-ethoxy-2-oxoethyl)-4-methyl-2-phenylthiophene-3-carboxylate (3bA)



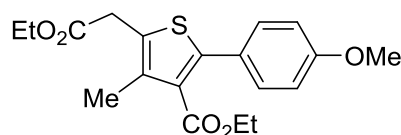
Yellow oil, 23 mg, yield 69%, $R_f = 0.43$ (PE/EA = 10:1, v/v). $^1\text{H NMR}$ (400 MHz, CDCl_3) δ 7.43 – 7.30 (m, 5H), 4.19 (q, $J = 7.2$ Hz, 2H), 4.14 (q, $J = 7.2$ Hz, 2H), 3.74 (s, 2H), 2.29 (s, 3H), 1.29 (t, $J = 7.1$ Hz, 3H), 1.05 (t, $J = 7.1$ Hz, 3H). $^{13}\text{C NMR}$ (101 MHz, CDCl_3) δ 170.0, 165.2, 146.1, 135.8, 134.0, 129.8, 129.0, 128.8, 128.1, 61.3, 60.6, 33.5, 14.1, 13.7, 13.4. **HRMS** (ESI): m/z $[\text{M}+\text{H}]^+$ calcd for $\text{C}_{18}\text{H}_{21}\text{O}_4\text{S}^+$ 333.1155, found 333.1163. **IR**(KBr) ν (cm^{-1}): 1737, 1713, 1184.

Ethyl 2-(benzo[d][1,3]dioxol-5-yl)-5-(2-ethoxy-2-oxoethyl)-4-methylthiophene-3-carboxylate (3cA)



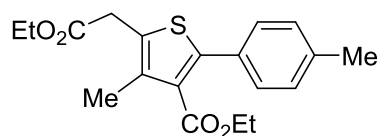
Yellow oil, 22 mg, yield 59%, $R_f = 0.18$ (PE/EA = 10:1, v/v). $^1\text{H NMR}$ (400 MHz, CDCl_3) δ 6.89 – 6.86 (m, 2H), 6.80 (d, $J = 3.6$ Hz, 1H), 5.99 (s, 2H), 4.21 – 4.16 (m, 4H), 3.72 (s, 2H), 2.26 (s, 3H), 1.28 (t, $J = 7.1$ Hz, 3H), 1.14 (t, $J = 7.1$ Hz, 3H). $^{13}\text{C NMR}$ (101 MHz, CDCl_3) δ 170.0, 165.2, 147.7, 147.4, 145.7, 135.7, 129.6, 128.3, 127.6, 122.8, 109.6, 108.0, 101.2, 61.3, 60.6, 33.4, 14.2, 13.9, 13.5. **HRMS** (ESI): m/z $[\text{M}+\text{H}]^+$ calcd for $\text{C}_{19}\text{H}_{21}\text{O}_6\text{S}^+$ 377.1053, found 377.1049. **IR**(KBr) ν (cm^{-1}): 1736, 1713, 1187.

Ethyl 5-(2-ethoxy-2-oxoethyl)-2-(4-methoxyphenyl)-4-methylthiophene-3-carboxylate (3dA)



Yellow oil, 20 mg, yield 55%, $R_f = 0.24$ (PE/EA = 10:1, v/v). $^1\text{H NMR}$ (400 MHz, CDCl_3) δ 7.33 (d, $J = 8.6$ Hz, 2H), 6.89 (d, $J = 8.6$ Hz, 2H), 4.20 (q, $J = 7.2$ Hz, 2H), 4.15 (q, $J = 7.2$ Hz, 2H), 3.83 (s, 3H), 3.72 (s, 2H), 2.27 (s, 3H), 1.28 (t, $J = 7.1$ Hz, 3H), 1.11 (t, $J = 7.1$ Hz, 3H). $^{13}\text{C NMR}$ (101 MHz, CDCl_3) δ 170.1, 165.4, 159.6, 146.1, 135.7, 130.2, 129.2, 128.2, 126.3, 113.5, 61.3, 60.5, 55.3, 33.5, 14.2, 13.9, 13.5. **HRMS** (ESI): m/z $[\text{M}+\text{H}]^+$ calcd for $\text{C}_{19}\text{H}_{22}\text{NaO}_5\text{S}^+$ 385.1080, found 385.1072. **IR**(KBr) ν (cm^{-1}): 1736, 1712, 1179.

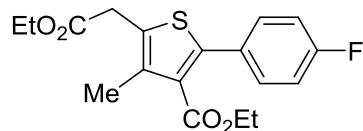
Ethyl 5-(2-ethoxy-2-oxoethyl)-4-methyl-2-(*p*-tolyl)thiophene-3-carboxylate (3eA)



Yellow oil, 20 mg, yield 58%, $R_f = 0.30$ (PE/EA = 10:1, v/v). $^1\text{H NMR}$ (400 MHz, CDCl_3) δ 7.29 (d, $J = 8.1$ Hz, 2H), 7.16 (d, $J = 7.9$ Hz, 2H), 4.20 (q, $J = 7.1$ Hz, 2H), 4.15 (q, $J = 7.1$ Hz, 2H), 3.73 (s, 2H), 2.37 (s, 3H), 2.28 (s, 3H), 1.28 (t, $J = 7.1$ Hz, 3H), 1.10 (t, $J = 7.1$ Hz, 3H). $^{13}\text{C NMR}$ (101 MHz, CDCl_3)

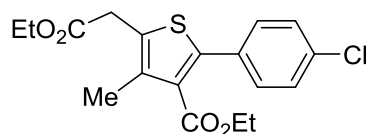
δ 170.0, 165.4, 146.2, 138.0, 135.7, 131.0, 129.5, 128.795, 128.788, 128.5, 61.3, 60.6, 33.5, 21.2, 14.2, 13.8, 13.5. **HRMS** (ESI): m/z $[M+H]^+$ calcd for $C_{19}H_{23}O_4S^+$ 347.1312, found 347.1305. **IR**(KBr) ν (cm^{-1}): 1737, 1713, 1182.

Ethyl 5-(2-ethoxy-2-oxoethyl)-2-(4-fluorophenyl)-4-methylthiophene-3-carboxylate (3fA)



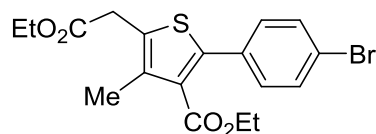
Colorless oil, 27 mg, yield 77%, R_f = 0.43 (PE/EA = 10:1, v/v). **1H NMR** (400 MHz, $CDCl_3$) δ 7.39 – 7.34 (m, 2H), 7.08 – 7.02 (m, 2H), 4.19 (q, J = 7.1 Hz, 2H), 4.14 (q, J = 7.1 Hz, 2H), 3.74 (s, 2H), 2.29 (s, 3H), 1.29 (t, J = 7.1 Hz, 3H), 1.08 (t, J = 7.1 Hz, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 170.0, 165.0, 164.0 (d, J_{C-F} = 248.5 Hz), 145.1, 136.0, 130.8 (d, J_{C-F} = 8.1 Hz), 130.1 (d, J_{C-F} = 3.0 Hz), 129.8, 128.9, 115.2 (d, J_{C-F} = 21.2 Hz), 61.4, 60.6, 33.5, 14.2, 13.8, 13.6. **^{19}F NMR** (377 MHz, $CDCl_3$) δ -113.67. **HRMS** (ESI): m/z $[M+H]^+$ calcd for $C_{18}H_{20}FO_4S^+$ 351.1061, found 351.1051. **IR**(KBr) ν (cm^{-1}): 1736, 1714, 1183.

Ethyl 2-(4-chlorophenyl)-5-(2-ethoxy-2-oxoethyl)-4-methylthiophene-3-carboxylate (3g A)



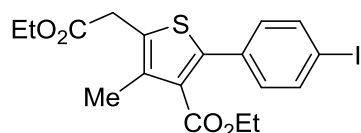
Colorless oil, 29 mg, yield 79%, R_f = 0.45 (PE/EA = 10:1, v/v). **1H NMR** (400 MHz, $CDCl_3$) δ 7.33 (s, 4H), 4.20 (q, J = 7.1 Hz, 2H), 4.15 (q, J = 7.1 Hz, 2H), 3.74 (s, 2H), 2.29 (s, 3H), 1.28 (t, J = 7.1 Hz, 3H), 1.10 (t, J = 7.1 Hz, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 169.9, 164.9, 144.7, 136.1, 134.2, 132.5, 130.3, 130.0, 129.2, 128.3, 61.3, 60.7, 33.4, 14.1, 13.8, 13.6. **HRMS** (ESI): m/z $[M+H]^+$ calcd for $C_{18}H_{20}ClO_4S^+$ 367.0765, found 367.0762. **IR**(KBr) ν (cm^{-1}): 1737, 1714, 1185.

Ethyl 2-(4-bromophenyl)-4-(2-ethoxy-2-oxoethyl)-5-methylthiophene-3-carboxylate (3h A)



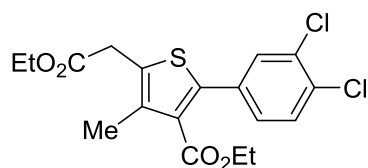
Colorless oil, 26 mg, yield 63%, R_f = 0.33 (PE/EA = 10:1, v/v). **1H NMR** (400 MHz, $CDCl_3$) δ 7.49 (d, J = 8.5 Hz, 2H), 7.26 (d, J = 8.5 Hz, 2H), 4.20 (q, J = 7.1 Hz, 2H), 4.16 (q, J = 7.1 Hz, 2H), 3.74 (s, 2H), 2.29 (s, 3H), 1.28 (t, J = 7.1 Hz, 3H), 1.10 (t, J = 7.1 Hz, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 169.9, 164.9, 144.7, 136.1, 133.0, 131.2, 130.6, 130.0, 129.3, 122.4, 61.4, 60.7, 33.4, 14.2, 13.8, 13.6. **HRMS** (ESI): m/z $[M+H]^+$ calcd for $C_{18}H_{20}BrO_4S^+$ 411.0260, found 411.0252. **IR**(KBr) ν (cm^{-1}): 1736, 1714, 1184.

Ethyl 5-(2-ethoxy-2-oxoethyl)-2-(4-iodophenyl)-4-methylthiophene-3-carboxylate (3iA)



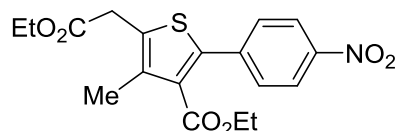
Yellow oil, 21 mg, yield 46%, $R_f = 0.42$ (PE/EA = 10:1, v/v). $^1\text{H NMR}$ (400 MHz, CDCl_3) δ 7.69 (d, $J = 8.4$ Hz, 2H), 7.13 (d, $J = 8.4$ Hz, 2H), 4.20 (q, $J = 7.1$ Hz, 2H), 4.15 (q, $J = 7.1$ Hz, 2H), 3.73 (s, 2H), 2.28 (s, 3H), 1.28 (t, $J = 7.1$ Hz, 3H), 1.11 (t, $J = 7.1$ Hz, 3H). $^{13}\text{C NMR}$ (101 MHz, CDCl_3) δ 169.9, 164.9, 144.8, 137.2, 136.1, 133.5, 130.7, 129.9, 129.3, 94.0, 61.4, 60.7, 33.5, 14.2, 13.8, 13.5. **HRMS** (ESI): m/z $[\text{M}+\text{H}]^+$ calcd for $\text{C}_{18}\text{H}_{20}\text{IO}_4\text{S}^+$ 459.0121, found 459.0115. **IR**(KBr) ν (cm^{-1}): 1736, 1714, 1184.

Ethyl 2-(3,4-dichlorophenyl)-5-(2-ethoxy-2-oxoethyl)-4-methylthiophene-3-carboxylate (3jA)



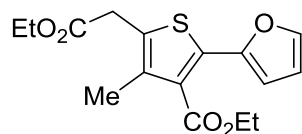
Colorless oil, 29 mg, yield 72%, $R_f = 0.40$ (PE/EA = 10:1, v/v). $^1\text{H NMR}$ (400 MHz, CDCl_3) δ 7.50 (d, $J = 2.0$ Hz, 1H), 7.43 (d, $J = 8.3$ Hz, 1H), 7.23 (dd, $J = 8.3, 2.1$ Hz, 1H), 4.20 (q, $J = 7.2$ Hz, 2H), 4.16 (q, $J = 7.2$ Hz, 2H), 3.74 (s, 2H), 2.29 (s, 3H), 1.29 (t, $J = 7.1$ Hz, 3H), 1.13 (t, $J = 7.2$ Hz, 3H). $^{13}\text{C NMR}$ (101 MHz, CDCl_3) δ 169.8, 164.6, 143.2, 136.3, 133.9, 132.3, 132.1, 130.9, 130.3, 130.0, 129.8, 128.4, 61.4, 60.8, 33.4, 14.2, 13.8, 13.6. **HRMS** (ESI): m/z $[\text{M}+\text{H}]^+$ calcd for $\text{C}_{18}\text{H}_{19}\text{Cl}_2\text{O}_4\text{S}^+$ 401.0376, found 401.0373. **IR**(KBr) ν (cm^{-1}): 1737, 1715, 1185.

Ethyl 5-(2-ethoxy-2-oxoethyl)-4-methyl-2-(4-nitrophenyl)thiophene-3-carboxylate (3kA)



Yellow oil, 21 mg, yield 56%, $R_f = 0.27$ (PE/EA = 10:1, v/v). $^1\text{H NMR}$ (400 MHz, CDCl_3) δ 8.22 (d, $J = 8.8$ Hz, 2H), 7.56 (d, $J = 8.9$ Hz, 2H), 4.22 (q, $J = 6.8$ Hz, 2H), 4.17 (q, $J = 6.8$ Hz, 2H), 3.77 (s, 2H), 2.31 (s, 3H), 1.30 (t, $J = 7.1$ Hz, 3H), 1.11 (t, $J = 7.1$ Hz, 3H). $^{13}\text{C NMR}$ (101 MHz, CDCl_3) δ 169.7, 164.5, 147.3, 143.0, 140.7, 136.6, 131.0, 129.8, 123.4, 61.5, 61.0, 33.5, 14.2, 13.8, 13.6. **HRMS** (ESI): m/z $[\text{M}+\text{H}]^+$ calcd for $\text{C}_{18}\text{H}_{20}\text{NO}_6\text{S}^+$ 378.1006, found 378.1000. **IR**(KBr) ν (cm^{-1}): 1736, 1715, 1519, 1346, 1185.

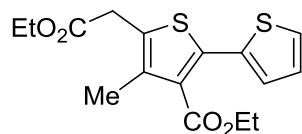
Ethyl 5-(2-ethoxy-2-oxoethyl)-2-(furan-2-yl)-4-methylthiophene-3-carboxylate (3lA)



Yellow oil, 27 mg, yield 84%, $R_f = 0.36$ (PE/EA = 10:1, v/v). $^1\text{H NMR}$ (400 MHz, CDCl_3) δ 7.41 (s, 1H), 6.70 (d, $J = 3.1$ Hz, 1H), 6.44 (s, 1H), 4.32 (q, $J = 7.1$ Hz, 2H), 4.18 (q, $J = 7.2$ Hz, 2H), 3.71 (s, 2H), 2.24 (s, 3H), 1.31 (t, $J = 7.1$ Hz, 3H), 1.26 (t, $J = 7.1$ Hz, 3H). $^{13}\text{C NMR}$ (101 MHz, CDCl_3) δ 169.8,

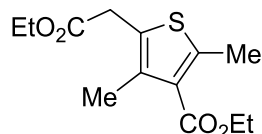
165.1, 147.2, 142.4, 135.6, 134.1, 128.8, 128.7, 111.7, 109.2, 61.3, 60.9, 33.6, 14.2, 14.1, 13.5. **HRMS** (ESI): m/z $[M+H]^+$ calcd for $C_{16}H_{19}O_5S^+$ 323.0948, found 323.0943. **IR**(KBr) ν (cm^{-1}): 1734, 1185.

Ethyl 5-(2-ethoxy-2-oxoethyl)-4-methyl-[2,2'-bithiophene]-3-carboxylate (3mA)



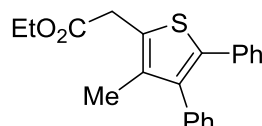
Yellow oil, 22 mg, yield 65%, R_f = 0.40 (PE/EA = 10:1, v/v). **1H NMR** (400 MHz, $CDCl_3$) δ 7.32 (dd, J = 5.1, 1.0 Hz, 1H), 7.18 (dd, J = 3.6, 1.1 Hz, 1H), 7.02 (dd, J = 5.1, 3.6 Hz, 1H), 4.25 (q, J = 7.1 Hz, 2H), 4.19 (q, J = 7.1 Hz, 2H), 3.72 (s, 2H), 2.25 (s, 3H), 1.28 (t, J = 7.1 Hz, 3H), 1.22 (t, J = 7.2 Hz, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 169.8, 165.0, 137.7, 135.8, 134.5, 130.3, 129.1, 127.6, 127.1, 126.6, 61.4, 60.9, 33.4, 14.1, 13.9, 13.5. **HRMS** (ESI): m/z $[M+H]^+$ calcd for $C_{16}H_{19}O_4S_2^+$ 339.0719, found 339.0723. **IR**(KBr) ν (cm^{-1}): 1736, 1712, 1182, 750.

Ethyl 5-(2-ethoxy-2-oxoethyl)-2,4-dimethylthiophene-3-carboxylate (3nA)



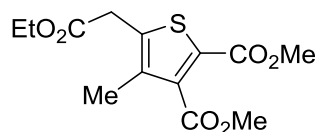
Yellow oil, 21 mg, yield 78%, R_f = 0.45 (PE/EA = 10:1, v/v). **1H NMR** (400 MHz, $CDCl_3$) δ 4.31 (q, J = 7.1 Hz, 2H), 4.16 (q, J = 7.1 Hz, 2H), 3.65 (s, 2H), 2.60 (s, 3H), 2.27 (s, 3H), 1.36 (t, J = 7.1 Hz, 3H), 1.26 (t, J = 7.1 Hz, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 170.3, 164.5, 146.4, 136.3, 128.7, 125.1, 61.2, 60.1, 33.3, 16.0, 14.3, 14.1. **HRMS** (ESI): m/z $[M+H]^+$ calcd for $C_{13}H_{19}O_4S^+$ 271.0999, found 271.0999. **IR**(KBr) ν (cm^{-1}): 1738, 1707, 1180.

Ethyl 2-(3-methyl-4,5-diphenylthiophen-2-yl)acetate (3oA)



Yellow oil, 20 mg, yield 60%, R_f = 0.49 (PE/EA = 10:1, v/v). **1H NMR** (400 MHz, $CDCl_3$) δ 7.37 – 7.28 (m, 3H), 7.23 – 7.10 (m, 7H), 4.08 (q, J = 7.1 Hz, 2H), 3.41 (s, 2H), 2.47 (s, 3H), 1.20 (t, J = 7.1 Hz, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 171.0, 139.2, 136.9, 135.9, 135.1, 134.4, 130.8, 130.3, 128.8, 128.3, 128.1, 127.1, 126.7, 60.7, 33.2, 14.1, 13.6. **HRMS** (ESI): m/z $[M+H]^+$ calcd for $C_{21}H_{21}O_2S^+$ 337.1257, found 337.1255. **IR**(KBr) ν (cm^{-1}): 1735, 1172.

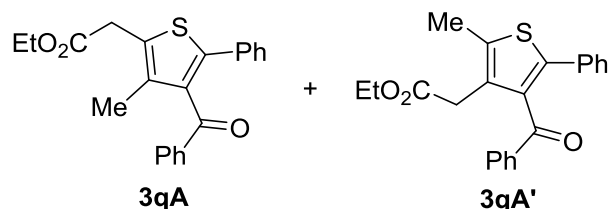
Dimethyl 5-(2-ethoxy-2-oxoethyl)-4-methylthiophene-2,3-dicarboxylate (3pA)



Yellow oil, 27 mg, yield 90%, R_f = 0.25 (PE/EA = 10:1, v/v). **1H NMR** (400 MHz, $CDCl_3$) δ 4.17 (q, J = 7.1 Hz, 2H), 3.92 (s, 3H), 3.83 (s, 3H), 3.72 (s, 2H), 2.12 (s, 3H), 1.26 (t, J = 7.1 Hz, 3H). **^{13}C NMR**

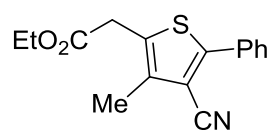
(101 MHz, CDCl₃) δ 169.0, 166.3, 161.3, 139.7, 136.5, 134.7, 128.6, 61.6, 52.7, 52.4, 33.9, 14.1, 12.3.
IR(KBr) ν (cm⁻¹): 1736, 1283, 1243, 1188.

Ethyl 2-(4-benzoyl-3-methyl-5-phenylthiophen-2-yl)acetate (3qA) and ethyl 2-(4-benzoyl-2-methyl-5-phenylthiophen-3-yl)acetate (3qA')



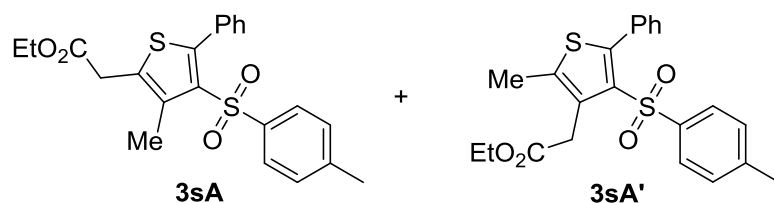
Yellow oil, 31 mg, yield 85%, R_f = 0.33 (PE/EA = 5:1, v/v). Mixture of two regioisomers. **¹H NMR** (400 MHz, CDCl₃) δ 7.74 (d, J = 8.4 Hz, 2.2H), 7.77 (d, J = 8.4 Hz, 1.9H), 7.43 – 7.40 (m, 1.3H), 7.34 – 7.28 (m, 5.3H), 7.22 – 7.07 (m, 10.5H), 4.22 (q, J = 7.2 Hz, 2.4H), 3.92 (q, J = 7.2 Hz, 2H), 3.79 (s, 2.3H), 3.67 (s, 2H), 2.46 (s, 2.9H), 2.08 (s, 3.4H), 1.30 (t, J = 7.2 Hz, 4H), 1.01 (t, J = 7.2 Hz, 3H). **¹³C NMR** (101 MHz, CDCl₃) δ 195.8, 195.4, 170.5, 170.0, 142.3, 142.0, 137.5, 137.4, 137.3, 136.8, 136.4, 135.4, 133.3, 133.2, 132.7, 130.7, 129.9, 129.8, 129.3, 128.8, 128.5, 128.4, 128.3, 128.2, 127.9, 127.8, 127.7, 61.3, 60.7, 33.6, 32.5, 14.2, 13.9, 13.1, 13.0. **HRMS** (ESI): m/z [M+H]⁺ calcd for C₂₂H₂₁O₃S⁺365.1206, found 365.1218. **IR**(KBr) ν (cm⁻¹): 1736, 1655, 1180.

Ethyl 2-(4-cyano-3-methyl-5-phenylthiophen-2-yl)acetate (3rA)



Yellow oil, 22 mg, yield 77%, R_f = 0.51 (PE/EA = 5:1, v/v). **¹H NMR** (400 MHz, CDCl₃) δ 7.73 (dd, J = 8.1, 1.3 Hz, 2H), 7.54 – 7.34 (m, 3H), 4.22 (q, J = 7.1 Hz, 2H), 3.75 (s, 2H), 2.33 (s, 3H), 1.30 (t, J = 7.1 Hz, 3H). **¹³C NMR** (101 MHz, CDCl₃) δ 169.5, 151.7, 137.6, 131.6, 129.5, 129.3, 129.2, 127.5, 115.9, 108.2, 61.6, 33.6, 14.2, 13.2. **HRMS** (ESI): m/z [M+H]⁺ calcd for C₁₆H₁₆NO₂S⁺286.0896, found 286.0901. **IR**(KBr) ν (cm⁻¹): 2218, 1737, 1190.

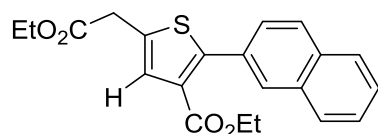
Ethyl 2-(3-methyl-5-phenyl-4-tosylthiophen-2-yl)acetate (3sA) and ethyl 2-(2-methyl-5-phenyl-4-tosylthiophen-3-yl)acetate (3sA')



Yellow oil, 39 mg, yield 94%, R_f = 0.46 (PE/EA = 5:1, v/v). Mixture of two regioisomers. **¹H NMR** (400 MHz, CDCl₃) δ 7.49 (d, J = 8.4 Hz, 0.3H), 7.35 – 7.31 (m, 3.4H), 7.26 – 7.19 (m, 3.9H), 7.15 (d, J = 8.0 Hz, 0.3H), 7.00 (d, J = 8.4 Hz, 1.8H), 4.18 (q, J = 7.2 Hz, 2.2H), 4.00 (s, 1.9H), 3.70 (s, 0.3H), 2.36 (s, 3.2H), 2.34 (s, 0.5H), 2.30 (s, 2.8H), 1.29 (t, J = 7.2 Hz, 3H), 1.26 (t, J = 7.2 Hz, 0.5H). **¹³C NMR** (101 MHz, CDCl₃) δ 170.8, 146.8, 143.2, 139.4, 136.7, 135.1, 131.6, 130.8, 130.6, 129.6, 129.3, 128.8,

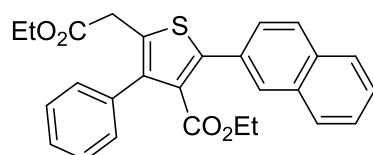
128.7, 127.4, 127.2, 127.1, 60.1, 33.3, 33.0, 21.4, 14.2, 13.1. **HRMS** (ESI): m/z $[M+H]^+$ calcd for $C_{22}H_{23}O_4S_2^+$ 415.1032, found 415.1047. **IR**(KBr) ν (cm^{-1}): 1736, 1316, 1182, 1148.

Ethyl 5-(2-ethoxy-2-oxoethyl)-2-(naphthalen-2-yl)thiophene-3-carboxylate (3aB)



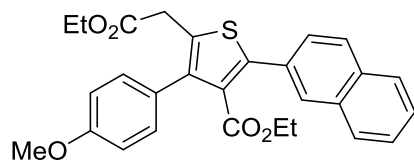
Yellow oil, 9 mg, yield 24%, $R_f = 0.62$ (CH_2Cl_2). **1H NMR** (400 MHz, $CDCl_3$) δ 7.95 (s, 1H), 7.86 – 7.83 (m, 3H), 7.60 (dd, $J = 8.5, 1.7$ Hz, 1H), 7.51 – 7.49 (m, 2H), 7.39 (s, 1H), 4.23 (q, $J = 7.1$ Hz, 2H), 4.16 (q, $J = 7.1$ Hz, 2H), 3.84 (s, 2H), 1.31 (t, $J = 7.1$ Hz, 3H), 1.15 (t, $J = 7.1$ Hz, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 170.0, 163.2, 150.5, 134.0, 133.1, 132.8, 130.9, 129.5, 128.7, 128.2, 127.88, 127.86, 127.7, 127.2, 126.5, 126.3, 61.5, 60.9, 35.5, 14.2, 14.0. **HRMS** (ESI): m/z $[M+H]^+$ calcd for $C_{21}H_{21}O_4S^+$ 369.1155, found 369.1154, $[M+Na]^+$ calcd for $C_{21}H_{20}NaO_4S^+$ 391.0975, found 391.0973. **IR**(KBr) ν (cm^{-1}): 1736, 1703.

Ethyl 5-(2-ethoxy-2-oxoethyl)-2-(naphthalen-2-yl)-4-phenylthiophene-3-carboxylate (3aC)



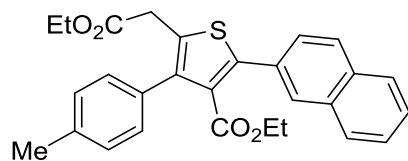
Yellow oil, 28 mg, yield 63%, $R_f = 0.69$ (CH_2Cl_2). **1H NMR** (400 MHz, $CDCl_3$) δ 8.02 (s, 1H), 7.86 (d, $J = 7.6$ Hz, 3H), 7.62 (dd, $J = 8.6, 1.8$ Hz, 1H), 7.55 – 7.46 (m, 2H), 7.46 – 7.30 (m, 5H), 4.18 (q, $J = 7.1$ Hz, 2H), 3.97 (q, $J = 7.1$ Hz, 2H), 3.71 (s, 2H), 1.27 (t, $J = 7.1$ Hz, 3H), 0.83 (t, $J = 7.1$ Hz, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 170.2, 165.2, 145.1, 141.4, 135.3, 133.1, 133.0, 131.2, 130.7, 130.4, 129.4, 128.2, 128.2, 128.0, 127.9, 127.7, 127.6, 126.8, 126.5, 126.4, 61.3, 60.8, 33.9, 14.1, 13.5. **HRMS** (ESI): m/z $[M+H]^+$ calcd for $C_{27}H_{25}O_4S^+$ 445.1468, found 445.1468, $[M+Na]^+$ calcd for $C_{27}H_{24}NaO_4S^+$ 467.1288, found 467.1289. **IR**(KBr) ν (cm^{-1}): 1721, 1184.

Ethyl 5-(2-ethoxy-2-oxoethyl)-4-(4-methoxyphenyl)-2-(naphthalen-2-yl)thiophene-3-carboxylate (3aD)



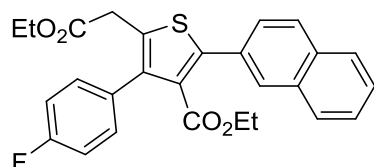
Yellow oil, 46 mg, yield 97%, $R_f = 0.52$ (CH_2Cl_2). **1H NMR** (400 MHz, $CDCl_3$) δ 8.00 (s, 1H), 7.85 (d, $J = 8.3$ Hz, 3H), 7.61 (dd, $J = 8.6, 1.7$ Hz, 1H), 7.50 (dd, $J = 6.2, 3.2$ Hz, 2H), 7.26 (d, $J = 8.4$ Hz, 2H), 6.95 (d, $J = 8.8$ Hz, 2H), 4.19 (q, $J = 7.1$ Hz, 2H), 3.99 (q, $J = 7.1$ Hz, 2H), 3.85 (s, 3H), 3.70 (s, 2H), 1.27 (t, $J = 7.1$ Hz, 3H), 0.87 (t, $J = 7.1$ Hz, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 170.3, 165.4, 159.1, 144.7, 141.1, 133.1, 133.0, 131.1, 130.8, 130.62, 130.55, 128.2, 127.9, 127.8, 127.6, 127.4, 126.8, 126.4, 113.6, 61.3, 60.8, 55.2, 34.0, 14.1, 13.6. **HRMS** (ESI): m/z $[M+H]^+$ calcd for $C_{28}H_{27}O_5S^+$ 475.1574, found 475.1575, $[M+Na]^+$ calcd for $C_{28}H_{26}NaO_5S^+$ 497.1393, found 497.1393. **IR**(KBr) ν (cm^{-1}): 1722, 1184.

Ethyl 5-(2-ethoxy-2-oxoethyl)-2-(naphthalen-2-yl)-4-(*p*-tolyl)thiophene-3-carboxylate (3aE)



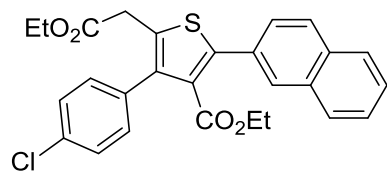
Yellow oil, 38 mg, yield 83%, $R_f = 0.61$ (CH_2Cl_2). $^1\text{H NMR}$ (400 MHz, CDCl_3) δ 8.01 (s, 1H), 7.86 (d, $J = 8.1$ Hz, 3H), 7.62 (dd, $J = 8.5, 1.6$ Hz, 1H), 7.54 – 7.46 (m, 2H), 7.23 (s, 4H), 4.19 (q, $J = 7.1$ Hz, 2H), 3.99 (q, $J = 7.1$ Hz, 2H), 3.71 (s, 2H), 2.41 (s, 3H), 1.28 (t, $J = 7.1$ Hz, 3H), 0.86 (t, $J = 7.1$ Hz, 3H). $^{13}\text{C NMR}$ (101 MHz, CDCl_3) δ 170.3, 165.3, 144.8, 141.5, 137.3, 133.1, 133.0, 132.2, 131.1, 130.8, 130.4, 129.3, 128.9, 128.2, 127.9, 127.6, 126.8, 126.4, 61.3, 60.8, 33.9, 21.3, 14.1, 13.5. **HRMS** (ESI): m/z $[\text{M}+\text{H}]^+$ calcd for $\text{C}_{28}\text{H}_{27}\text{O}_4\text{S}^+$ 459.1625, found 459.1625, $[\text{M}+\text{Na}]^+$ calcd for $\text{C}_{28}\text{H}_{26}\text{NaO}_4\text{S}^+$ 481.1444, found 481.1445. **IR**(KBr) ν (cm^{-1}): 1722, 1184.

Ethyl 5-(2-ethoxy-2-oxoethyl)-4-(4-fluorophenyl)-2-(naphthalen-2-yl)thiophene-3-carboxylate (3aF)



Yellow oil, 37 mg, yield 80%, $R_f = 0.62$ (PE/EA = 5:1, v/v). $^1\text{H NMR}$ (400 MHz, CDCl_3) δ 8.01 (s, 1H), 7.86 (d, $J = 8.6$ Hz, 3H), 7.60 (dd, $J = 8.6, 1.7$ Hz, 1H), 7.51 (dd, $J = 6.2, 3.3$ Hz, 2H), 7.32 (dd, $J = 8.7, 5.4$ Hz, 2H), 7.12 (t, $J = 8.7$ Hz, 2H), 4.19 (q, $J = 7.2$ Hz, 2H), 3.98 (q, $J = 7.1$ Hz, 2H), 3.68 (s, 2H), 1.27 (t, $J = 7.1$ Hz, 3H), 0.86 (t, $J = 7.1$ Hz, 3H). $^{13}\text{C NMR}$ (101 MHz, CDCl_3) δ 170.1, 165.0, 163.6 (d, $J_{\text{C-F}} = 247.8$ Hz), 145.4, 140.4, 133.0 (d, $J_{\text{C-F}} = 3.0$ Hz), 131.5, 131.25, 131.20, 131.17, 130.6, 130.2, 128.8, 128.0, 127.9, 127.6, 126.8, 126.52, 126.49, 115.2 (d, $J_{\text{C-F}} = 21.5$ Hz), 61.4, 60.8, 33.8, 14.1, 13.5. $^{19}\text{F NMR}$ (376 MHz, CDCl_3) δ -114.30. **HRMS** (ESI): m/z $[\text{M}+\text{H}]^+$ calcd for $\text{C}_{27}\text{H}_{24}\text{FO}_4\text{S}^+$ 463.1374, found 463.1376, $[\text{M}+\text{Na}]^+$ calcd for $\text{C}_{27}\text{H}_{23}\text{FNaO}_4\text{S}^+$ 485.1193, found 485.1192. **IR**(KBr) ν (cm^{-1}): 1734, 1721, 1185.

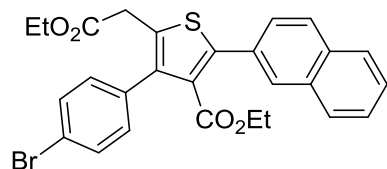
Ethyl 4-(4-chlorophenyl)-5-(2-ethoxy-2-oxoethyl)-2-(naphthalen-2-yl)thiophene-3-carboxylate (3aG)



Yellow oil, 41 mg, yield 86%, $R_f = 0.43$ (PE/EA = 10:1, v/v). $^1\text{H NMR}$ (400 MHz, CDCl_3) δ 8.00 (s, 1H), 7.86 (d, $J = 9.0$ Hz, 3H), 7.60 (dd, $J = 8.5, 1.6$ Hz, 1H), 7.51 (dd, $J = 6.3, 3.2$ Hz, 2H), 7.41 (d, $J = 8.4$ Hz, 2H), 7.28 (d, $J = 8.3$ Hz, 2H), 4.18 (q, $J = 7.1$ Hz, 2H), 3.98 (q, $J = 7.1$ Hz, 2H), 3.67 (s, 2H), 1.27 (t, $J = 7.1$ Hz, 3H), 0.86 (t, $J = 7.1$ Hz, 3H). $^{13}\text{C NMR}$ (101 MHz, CDCl_3) δ 170.0, 164.9, 145.8, 140.2, 133.8, 133.7, 133.0, 131.6, 130.9, 130.6, 130.0, 128.4, 128.2, 128.0, 127.9, 127.7, 126.8, 126.6,

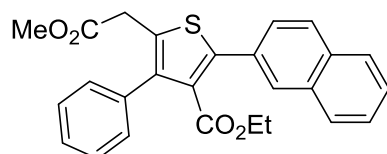
126.5, 61.4, 60.9, 33.8, 14.1, 13.5. **HRMS** (ESI): m/z $[M+H]^+$ calcd for $C_{27}H_{24}ClO_4S^+$ 479.1078, found 479.1080, $[M+Na]^+$ calcd for $C_{27}H_{23}ClNaO_4S^+$ 501.0898, found 501.0898. **IR**(KBr) ν (cm^{-1}): 1734, 1720, 1185.

Ethyl 4-(4-bromophenyl)-5-(2-ethoxy-2-oxoethyl)-2-(naphthalen-2-yl)thiophene-3-carboxylate (3aH)



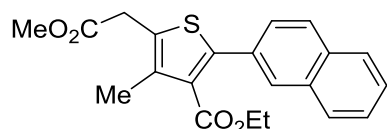
Yellow oil, 44 mg, yield 84%, $R_f = 0.48$ (PE/Ea = 10:1, v/v). **1H NMR** (400 MHz, $CDCl_3$) δ 8.00 (s, 1H), 7.86 (d, $J = 8.7$ Hz, 3H), 7.60 (d, $J = 8.6$ Hz, 1H), 7.56 (d, $J = 8.3$ Hz, 2H), 7.51 (dd, $J = 6.2, 3.2$ Hz, 2H), 7.22 (d, $J = 8.2$ Hz, 2H), 4.19 (q, $J = 7.1$ Hz, 2H), 3.98 (q, $J = 7.1$ Hz, 2H), 3.67 (s, 2H), 1.28 (t, $J = 7.1$ Hz, 3H), 0.86 (t, $J = 7.1$ Hz, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 170.0, 164.8, 145.8, 140.2, 134.2, 133.0, 131.5, 131.3, 131.2, 130.6, 129.9, 128.2, 128.0, 127.9, 127.6, 126.8, 126.53, 126.49, 121.9, 61.4, 60.8, 33.8, 14.1, 13.5. **HRMS** (ESI): m/z $[M+H]^+$ calcd for $C_{27}H_{24}BrO_4S^+$ 523.0573, found 523.0577, $[M+Na]^+$ calcd for $C_{27}H_{23}BrNaO_4S^+$ 545.0393, found 545.0392. **IR**(KBr) ν (cm^{-1}): 1734, 1720, 1185.

Ethyl 5-(2-methoxy-2-oxoethyl)-2-(naphthalen-2-yl)-4-phenylthiophene-3-carboxylate (3aI)



Yellow oil, 36 mg, yield 84%, $R_f = 0.84$ (CH_2Cl_2). **1H NMR** (400 MHz, $CDCl_3$) δ 8.02 (s, 1H), 7.86 (d, $J = 7.8$ Hz, 3H), 7.62 (dd, $J = 8.5, 1.6$ Hz, 1H), 7.51 (dd, $J = 6.0, 3.4$ Hz, 2H), 7.44 – 7.38 (m, 3H), 7.37 – 7.30 (m, 2H), 3.97 (q, $J = 7.1$ Hz, 2H), 3.73 (s, 2H), 3.72 (s, 3H), 0.83 (t, $J = 7.1$ Hz, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 170.7, 165.2, 145.2, 141.5, 135.2, 133.1, 133.0, 131.0, 130.7, 130.4, 129.4, 128.20, 128.17, 128.0, 127.9, 127.6, 126.8, 126.5, 126.4, 60.8, 52.3, 33.6, 13.5. **HRMS** (ESI): m/z $[M+H]^+$ calcd for $C_{26}H_{23}O_4S^+$ 431.1312, found 431.1314, $[M+Na]^+$ calcd for $C_{26}H_{22}NaO_4S^+$ 453, 1131, found 453.1132. **IR**(KBr) ν (cm^{-1}): 1741, 1720.

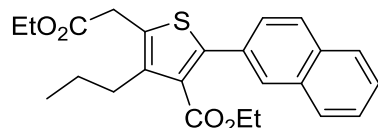
Ethyl 5-(2-methoxy-2-oxoethyl)-4-methyl-2-(naphthalen-2-yl)thiophene-3-carboxylate (3aJ)



Yellow oil, 28 mg, yield 76%, $R_f = 0.62$ (CH_2Cl_2). **1H NMR** (400 MHz, $CDCl_3$) δ 7.89 (s, 1H), 7.87 – 7.79 (m, 3H), 7.54 – 7.46 (m, 3H), 4.15 (q, $J = 7.1$ Hz, 2H), 3.79 (s, 2H), 3.76 (s, 3H), 2.33 (s, 3H), 1.01 (t, $J = 7.1$ Hz, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 170.4, 165.2, 146.1, 136.2, 133.0, 132.9, 131.4, 129.9, 128.9, 128.1, 127.8, 127.62, 127.56, 127.1, 126.39, 126.35, 60.6, 52.3, 33.2, 13.8, 13.5. **HRMS** (ESI):

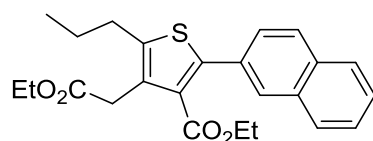
m/z $[M+H]^+$ calcd for $C_{21}H_{21}O_4S^+$ 369.1155, found 369.1156, $[M+Na]^+$ calcd for $C_{21}H_{20}NaO_4S^+$ 391.0975, found 391.0975. **IR**(KBr) ν (cm^{-1}): 1741, 1712, 1182.

Ethyl 5-(2-ethoxy-2-oxoethyl)-2-(naphthalen-2-yl)-4-propylthiophene-3-carboxylate (3aK)



Yellow oil, 35 mg, yield 43%, $R_f = 0.35$ (PE/EA = 10:1, v/v). **1H NMR** (400 MHz, $CDCl_3$) δ 7.90 (s, 1H), 7.87 – 7.78 (m, 3H), 7.55 – 7.45 (m, 3H), 4.22 (q, $J = 7.1$ Hz, 2H), 4.13 (q, $J = 7.1$ Hz, 2H), 3.80 (s, 2H), 2.74 (t, $J = 8.0$ Hz, 2H), 1.63 – 1.53 (m, 2H), 1.31 (t, $J = 7.1$ Hz, 3H), 1.02 (t, $J = 7.2$ Hz, 3H), 0.98 (t, $J = 7.2$ Hz, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 170.2, 161.2, 145.2, 142.9, 133.0, 132.8, 131.4, 129.54, 129.50, 128.1, 127.7, 127.6, 127.0, 126.4, 126.3, 61.3, 60.3, 33.5, 28.5, 24.5, 14.13, 14.10, 12.4. **HRMS** (ESI): m/z $[M+H]^+$ calcd for $C_{24}H_{27}O_4S^+$ 411.1625, found 411.1640. **IR**(KBr) ν (cm^{-1}): 1737, 1708, 1181.

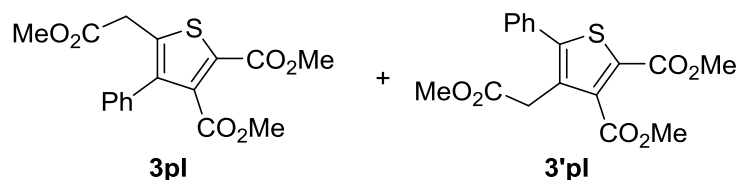
Ethyl 5-(2-ethoxy-2-oxoethyl)-2-(naphthalen-2-yl)-4-propylthiophene-3-carboxylate (3'aK)



Yellow oil, 23 mg, yield 28%, $R_f = 0.25$ (PE/EA = 10:1, v/v). **1H NMR** (400 MHz, $CDCl_3$) δ 7.91 – 7.77 (m, 4H), 7.56 – 7.45 (m, 3H), 4.17 (q, $J = 7.1$ Hz, 2H), 4.10 (q, $J = 7.1$ Hz, 2H), 3.84 (s, 2H), 2.77 (t, $J = 7.6$ Hz, 2H), 1.76 – 1.67 (m, 2H), 1.27 (t, $J = 7.1$ Hz, 3H), 1.02 (t, $J = 7.3$ Hz, 3H), 0.98 (t, $J = 7.1$ Hz, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 171.1, 164.8, 145.7, 142.0, 132.9, 132.8, 131.7, 130.3, 128.9, 128.09, 128.06, 127.62, 127.57, 127.3, 126.3, 60.7, 60.5, 33.1, 29.9, 24.7, 14.2, 13.8, 13.7. **HRMS** (ESI): m/z $[M+H]^+$ calcd for $C_{24}H_{27}O_4S^+$ 411.1625, found 411.1625. **IR**(KBr) ν (cm^{-1}): 1737, 1713, 1182.

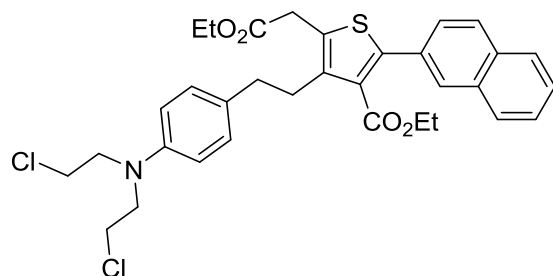
Dimethyl 5-(2-methoxy-2-oxoethyl)-4-phenylthiophene-2,3-dicarboxylate (3pI)

Dimethyl 4-(2-methoxy-2-oxoethyl)-5-phenylthiophene-2,3-dicarboxylate (3'pI)



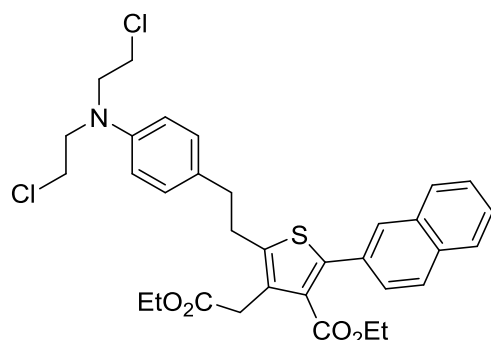
3pI was known compound and reported by Zhai and coworkers.¹¹ These two regioisomers could not be separated, and were isolated as a mixture. Yellow oil, 26 mg, yield 75%, The molar ratio of **3pI**:**3'pI** = 89:11, $R_f = 0.15$ (PE/EA = 10:1, v/v). **1H NMR** (400 MHz, $CDCl_3$) δ 7.45 – 7.37 (m, 4.10H), 7.27 – 7.25 (m, 2.34H), 3.93 (s, 0.47H), 3.885 (s, 0.53H), 3.878 (s, 3H), 3.73 (s, 2H), 3.71 (s, 3H), 3.70 (s, 3H), 3.69 (s, 0.5H), 3.67 (s, 0.28H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 169.8, 165.8, 140.4, 139.6, 138.0, 133.0, 129.5, 129.2, 128.9, 128.8, 128.6, 128.3, 52.6, 52.51, 52.49, 33.9. **IR**(KBr) ν (cm^{-1}): 1736, 1716, 1185.

Ethyl 4-(4-(bis(2-chloroethyl)amino)phenethyl)-5-(2-ethoxy-2-oxoethyl)-2-(naphthalen-2-yl)thiophene-3-carboxylate (3aP)



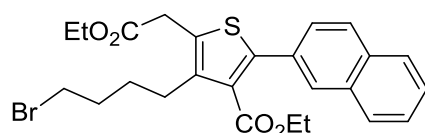
Yellow oil, 30 mg, yield 49%, $R_f = 0.33$ (PE/EA = 10:1, v/v). $^1\text{H NMR}$ (400 MHz, CDCl_3) δ 7.91 (s, 1H), 7.89 – 7.78 (m, 3H), 7.57 – 7.44 (m, 3H), 7.12 (d, $J = 8.6$ Hz, 2H), 6.65 (d, $J = 8.6$ Hz, 2H), 4.21 (q, 7.1 Hz, 2H), 4.14 (q, 7.1 Hz, 2H), 3.74 – 3.70 (t, $J = 6.5$ Hz, 4H), 3.67 – 3.58 (m, 6H), 3.05 – 2.96 (m, 2H), 2.82 – 2.72 (m, 2H), 1.30 (t, $J = 7.1$ Hz, 3H), 1.01 (t, $J = 7.1$ Hz, 3H). $^{13}\text{C NMR}$ (101 MHz, CDCl_3) δ 170.1, 165.3, 146.6, 144.3, 140.0, 133.0, 132.9, 131.5, 130.9, 130.0, 129.8, 129.3, 128.1, 127.8, 127.64, 127.59, 127.1, 126.42, 126.37, 112.2, 61.4, 60.7, 53.6, 40.5, 35.8, 33.3, 30.2, 14.2, 13.8. **HRMS** (ESI): m/z $[\text{M}+\text{H}]^+$ calcd for $\text{C}_{33}\text{H}_{36}\text{Cl}_2\text{NO}_4\text{S}^+$ 612.1737, found 612.1738, $[\text{M}+\text{Na}]^+$ calcd for $\text{C}_{33}\text{H}_{35}\text{Cl}_2\text{NNaO}_4\text{S}^+$ 634.1556, found 634.1558. **IR**(KBr) ν (cm^{-1}): 1735, 1710, 1518, 1182.

Ethyl 5-(4-(bis(2-chloroethyl)amino)phenethyl)-4-(2-ethoxy-2-oxoethyl)-2-(naphthalen-2-yl)thiophene-3-carboxylate (3'aP)



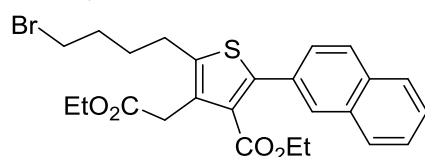
Yellow oil, 24 mg, yield 39%, $R_f = 0.25$ (PE/EA = 10:1, v/v). $^1\text{H NMR}$ (400 MHz, CDCl_3) δ 7.88 (s, 1H), 7.55 – 7.45 (m, 3H), 7.55 – 7.45 (m, 3H), 7.12 (d, $J = 8.6$ Hz, 2H), 6.65 (d, $J = 8.6$ Hz, 2H), 4.17 (q, $J = 7.1$ Hz, 2H), 4.11 (q, $J = 7.1$ Hz, 2H), 3.78 (s, 2H), 3.71 (dt, $J = 7.2, 6.4$ Hz, 4H), 3.63 (dt, $J = 7.2, 6.4$ Hz, 4H), 3.05 (dt, $J = 7.6, 6.0$ Hz, 2H), 2.89 (dt, $J = 7.2, 6.0$ Hz, 2H), 1.27 (t, $J = 7.1$ Hz, 3H), 0.98 (t, $J = 7.1$ Hz, 3H). $^{13}\text{C NMR}$ (101 MHz, CDCl_3) δ 171.0, 164.8, 146.0, 144.6, 141.0, 132.93, 132.88, 131.7, 130.6, 129.8, 129.7, 128.9, 128.1, 127.7, 127.6, 127.4, 126.39, 126.38, 112.3, 60.8, 60.6, 53.6, 40.5, 36.4, 33.1, 30.2, 14.3, 13.7. **HRMS** (ESI): m/z $[\text{M}+\text{H}]^+$ calcd for $\text{C}_{33}\text{H}_{36}\text{Cl}_2\text{NO}_4\text{S}^+$ 612.1737, found 612.1739, $[\text{M}+\text{Na}]^+$ calcd for $\text{C}_{33}\text{H}_{35}\text{Cl}_2\text{NNaO}_4\text{S}^+$ 634.1556, found 634.1558. **IR**(KBr) ν (cm^{-1}): 1734, 1709, 1519, 1180.

Ethyl 4-(4-bromobutyl)-5-(2-ethoxy-2-oxoethyl)-2-(naphthalen-2-yl)thiophene-3-carboxylate (3aQ)



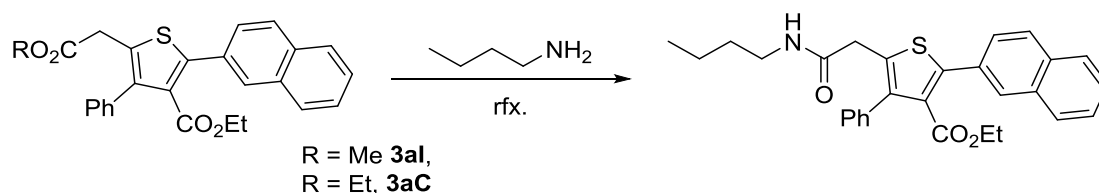
Yellow oil, 23 mg, yield 46%, $R_f = 0.36$ (PE/EA = 10:1, v/v). $^1\text{H NMR}$ (400 MHz, CDCl_3) δ 7.89 (s, 1H), 7.88 – 7.78 (m, 3H), 7.54 – 7.45 (m, 3H), 4.22 (q, $J = 7.1$ Hz, 2H), 4.13 (q, $J = 7.1$ Hz, 2H), 3.80 (s, 2H), 3.51 (dt, $J = 51.7, 6.7$ Hz, 2H), 2.84 – 2.75 (m, 2H), 1.99 – 1.83 (m, 2H), 1.77 – 1.66 (m, 2H), 1.31 (t, $J = 7.1$ Hz, 3H), 0.99 (t, $J = 7.1$ Hz, 3H). $^{13}\text{C NMR}$ (101 MHz, CDCl_3) δ 170.1, 165.4, 146.7, 140.2, 133.0, 132.9, 131.4, 129.8, 129.3, 128.1, 127.8, 127.68, 127.66, 127.1, 126.5, 126.4, 61.5, 60.8, 33.5, 33.5, 32.7, 29.3, 26.8, 14.2, 13.8. **HRMS** (ESI): m/z $[\text{M}+\text{H}]^+$ calcd for $\text{C}_{25}\text{H}_{28}\text{BrO}_4\text{S}^+503.0886$, found 503.0887. **IR**(KBr) ν (cm^{-1}): 1736, 1712, 1183.

Ethyl 5-(4-bromobutyl)-4-(2-ethoxy-2-oxoethyl)-2-(naphthalen-2-yl)thiophene-3-carboxylate (3'aQ)



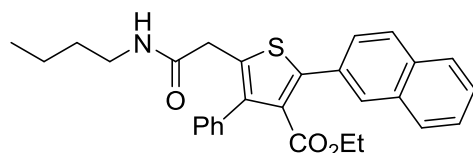
Yellow oil, 14 mg, yield 28%, $R_f = 0.27$ (PE/EA = 10:1, v/v). $^1\text{H NMR}$ (400 MHz, CDCl_3) δ 7.88 (s, 1H), 7.86 – 7.81 (m, 3H), 7.52 – 7.48 (m, 3H), 4.17 (q, $J = 7.1$ Hz, 2H), 4.10 (q, $J = 7.1$ Hz, 2H), 3.83 (s, 2H), 3.51 (dt, $J = 53.5, 6.3$ Hz, 2H), 2.83 (t, $J = 7.5$ Hz, 2H), 2.03 – 1.77 (m, 4H), 1.27 (t, $J = 7.1$ Hz, 3H), 0.98 (t, $J = 7.1$ Hz, 3H). $^{13}\text{C NMR}$ (101 MHz, CDCl_3) δ 171.0, 164.8, 146.0, 141.0, 132.89, 132.87, 131.5, 130.6, 129.0, 128.1, 127.6, 127.5, 127.4, 126.4, 60.9, 60.6, 33.2, 31.9, 29.8, 28.5, 27.0, 14.2, 13.7. **HRMS** (ESI): m/z $[\text{M}+\text{H}]^+$ calcd for $\text{C}_{25}\text{H}_{28}\text{BrO}_4\text{S}^+503.0886$, found 503.0889, $[\text{M}+\text{Na}]^+$ calcd for $\text{C}_{25}\text{H}_{27}\text{BrNaO}_4\text{S}^+525.0706$, found 525.0709. **IR**(KBr) ν (cm^{-1}): 1736, 1708, 1181.

3.2 Synthesis and Characterization of 7aC



Product 3aC or *3aI* (0.2 mmol or 0.11 mmol, 88.8 mg or 46 mg) and butylamine (1.0 mL) were added to a 10 mL-reaction tube. The resulting mixture was stirred for 5 h at 80 °C in a heating block. After evaporation of the solvents in vacuo, the crude product was purified by column chromatography on silica gel using PE/EA = 20:1.

Ethyl 5-(2-(butylamino)-2-oxoethyl)-2-(naphthalen-2-yl)-4-phenylthiophene-3-carboxylate (7aC)



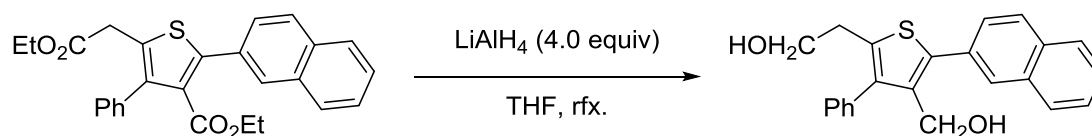
Conditions: 3aC (88.8 mg, 0.2 mmol). Yellow oil, 49 mg, yield 61%, $R_f = 0.36$ (PE/EA = 5:1, v/v).

Conditions: 3aI (46 mg, 0.11 mmol). 42 mg, yield 86%.

$^1\text{H NMR}$ (400 MHz, CDCl_3) δ 8.00 (s, 1H), 7.85 (d, $J = 7.8$ Hz, 3H), 7.60 (dd, $J = 8.5, 1.7$ Hz, 1H), 7.51 (dd, $J = 6.3, 3.2$ Hz, 2H), 7.46 – 7.33 (m, 3H), 7.34 – 7.27 (m, 2H), 5.60 (s, 1H), 3.97 (q, $J = 7.1$ Hz, 2H),

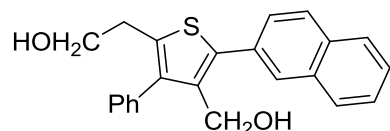
3.60 (s, 2H), 3.21 (q, $J = 7.1$ Hz, 2H), 1.47 – 1.38 (m, 2H), 1.34 – 1.23 (m, 2H), 0.91 (t, $J = 7.3$ Hz, 3H), 0.83 (t, $J = 7.1$ Hz, 3H). $^{13}\text{C NMR}$ (101 MHz, CDCl_3) δ 169.0, 165.2, 145.3, 141.4, 135.1, 133.03, 132.98, 132.1, 130.6, 130.4, 129.2, 128.3, 128.2, 128.0, 127.9, 127.8, 127.6, 126.6, 126.53, 126.49, 60.9, 39.5, 35.8, 31.5, 19.9, 13.7, 13.4. **HRMS** (ESI): m/z $[\text{M}+\text{H}]^+$ calcd for $\text{C}_{29}\text{H}_{30}\text{NO}_3\text{S}^+$ 472.1941, found 472.1942, $[\text{M}+\text{Na}]^+$ calcd for $\text{C}_{29}\text{H}_{29}\text{NNaO}_3\text{S}^+$ 494.1760, found 494.1759. **IR**(KBr) ν (cm^{-1}): 1720, 1650, 1183.

3.3 Synthesis and Characterization of 8aC



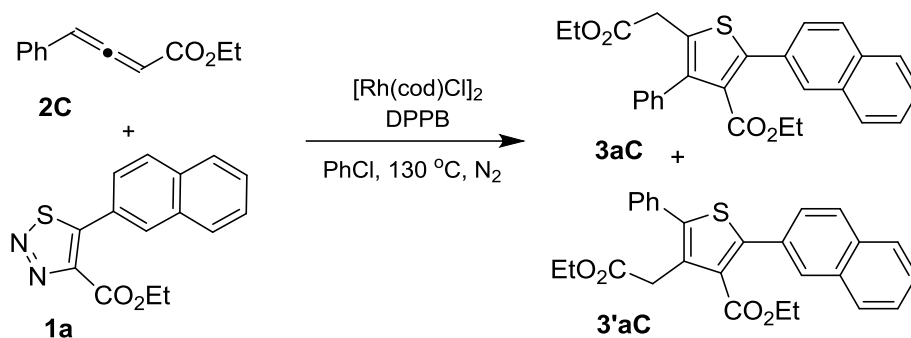
To an oven-dried reaction tube equipped with a magnetic stirring bar was added a solution of *product 3aC* (44.4 mg, 0.1 mmol, 1.0 equiv) in 1 mL of tetrahydrofuran, then a suspension of lithium aluminum hydride (82 mg, 2.18 mmol, 4.0 equiv.) in 0.5 mL of anhydrous tetrahydrofuran was slowly added to the tube under nitrogen atmosphere at 0 °C. The reaction mixture was heated at 70 °C in a heating block for 3 h and then cooled to 0 °C. Water (1.0 mL) was added dropwise, the mixture was dried over sodium sulfate. After celite filtration and evaporation of the solvents in vacuo, the crude product was purified by column chromatography on silica gel using PE/EA = 15:1.

Ethyl 2-(4-(hydroxymethyl)-5-(naphthalen-2-yl)-3-phenylthiophen-2-yl)ethan-1-ol (8aC)

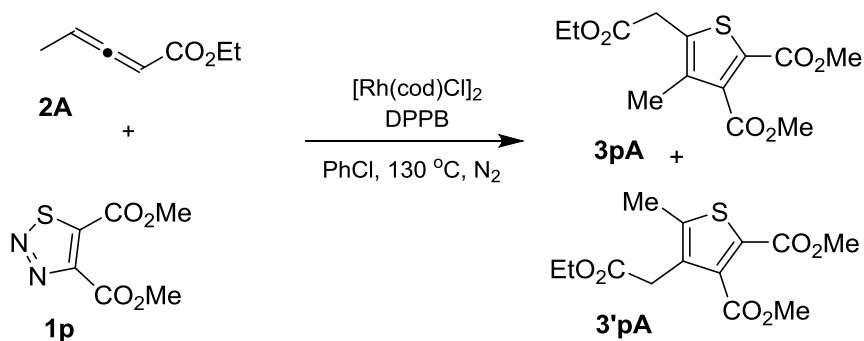


White solid, 34 mg, yield 95%, m. p. 153 – 155 °C, $R_f = 0.44$ (PE/EA = 5:1, ν/ν). $^1\text{H NMR}$ (400 MHz, CDCl_3) δ 8.10 (s, 1H), 7.91 – 7.86 (m, 3H), 7.75 (dd, $J = 8.5, 1.7$ Hz, 1H), 7.55 – 7.43 (m, 4H), 7.45 – 7.36 (m, 3H), 4.44 (d, $J = 4.0$ Hz, 2H), 3.80 (dt, $J = 6.0, 3.6$ Hz, 2H), 2.97 (t, $J = 6.5$ Hz, 2H), 1.58 (s, 1H), 1.52 (s, 1H). $^{13}\text{C NMR}$ (101 MHz, CDCl_3) δ 141.9, 140.8, 136.25, 136.15, 136.1, 133.4, 132.8, 131.3, 130.0, 128.6, 128.33, 128.26, 128.1, 127.7, 127.3, 126.5, 126.3, 63.4, 57.3, 31.8. **HRMS** (ESI): m/z $[\text{M}+\text{Na}]^+$ calcd for $\text{C}_{23}\text{H}_{20}\text{NaO}_2\text{S}^+$ 383.1076, found 383.1074. **IR**(KBr) ν (cm^{-1}): 3440, 2923, 2853, 1725, 1721.

3.4 1-mmol scale reaction

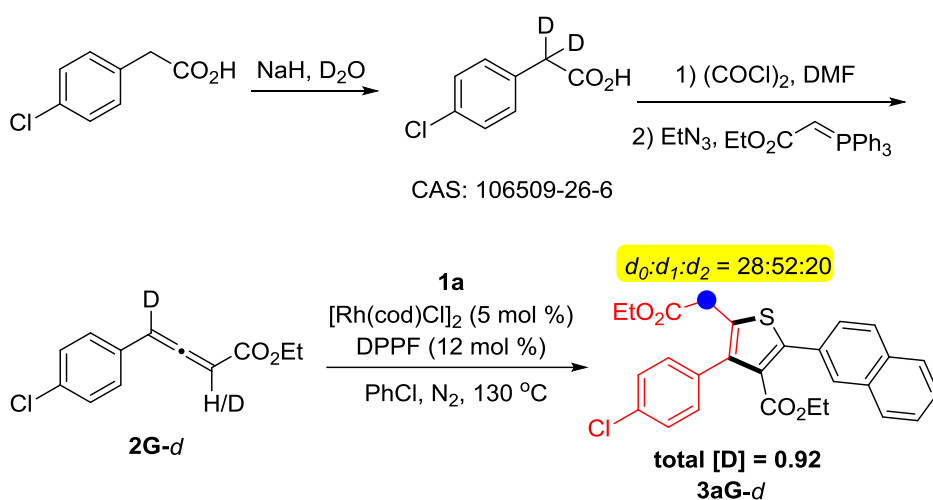


- a) To a dried round-bottom flask equipped with a magnetic stirring bar was added 1,2,3-thiadiazole **1a** (284 mg, 1 mmol, 1.0 equiv), allene **2C** (376 mg, 2 mmol, 2.0 equiv), $[\text{Rh}(\text{cod})\text{Cl}]_2$ (25 mg, 0.05 mmol, 5 mol %), and DPPB (51 mg, 0.12 mmol, 12 mol %). The flask was sealed immediately and protected with a nitrogen balloon by evacuation-backfill operations for three times; then PhCl (6 mL) was injected to the flask. The mixture was heated at 130 °C in an oil-bath for 12 h. When the reaction was finished, as detected by TLC, the solvent was evaporated under reduced pressure. A small portion of the crude reaction mixture was submitted to ^1H NMR test to determine the regioselective ratios. After NMR test, the combined crude reaction mixture was subjected to column chromatography on silica gel, affording the corresponding major products **3aC** (151 mg, 34%).
- b) To a dried round-bottom flask equipped with a magnetic stirring bar was added 1,2,3-thiadiazole **1a** (284 mg, 1 mmol, 1.0 equiv), $[\text{Rh}(\text{cod})\text{Cl}]_2$ (25 mg, 0.05 mmol, 5 mol %), and DPPB (51 mg, 0.12 mmol, 12 mol %). The flask was sealed immediately and protected with a nitrogen balloon by evacuation-backfill operations for three times; then PhCl (6 mL) was injected to the flask. The mixture was heated at 130 °C in an oil-bath. Then allene **2C** (75 mg, 0.4 mmol) was added to the flask every one hour and was repeated five times (total amount: 375 mg, 2 mmol, 2 equiv). Upton the last addition of **2C**, the mixture was stirred for additional 4 h, followed by further addition of $[\text{Rh}(\text{cod})\text{Cl}]_2$ (12.5 mg, 0.025 mmol, 2.5 mol %), and DPPB (26 mg, 0.06 mmol, 6 mol %). After 14 h, the solvent was evaporated under reduced pressure, and the crude mixture was subjected to flash chromatography on silica gel affording the corresponding product **3aC** (204 mg, 46%).



To a dried round-bottom flask equipped with a magnetic stirring bar was added 1,2,3-thiadiazole **1p** (202 mg, 1 mmol, 1.0 equiv), allene **2A** (252 mg, 2 mmol, 2.0 equiv), [Rh(cod)Cl]₂ (25 mg, 0.05 mmol, 5 mol %), and DPPB (51 mg, 0.12 mmol, 12 mol %). The flask was sealed immediately and protected with a nitrogen balloon by evacuation-backfill operations for three times; then PhCl (6 mL) was injected to the flask. The mixture was heated at 130 °C in an oil-bath for 8 h. When the reaction was finished, as detected by TLC, the solvent was evaporated under reduced pressure. A small portion of the crude reaction mixture was submitted to ¹H NMR test to determine the regioselective ratios. After NMR test, the combined crude reaction mixture was subjected to column chromatography on silica gel, affording the corresponding major products **3pA** (280 mg, 93%).

3.5 Deuterium Experiments



Synthesis of 2-(4-Chlorophenyl)acetic-2,2-*d*₂ acid:¹²

In a two-neck flask (10 mL), equipped with a magnetic stir bar and reflux condenser, NaH 60% in mineral oil (504 mg, 35 mmol, 3.5 equiv) was added slowly to D₂O (8 mL) at 0 °C under argon atmosphere. 2-(4-Chlorophenyl)acetic acid (1.7 g, 10 mmol, 1.0 equiv) was added and the mixture was heated at reflux at 100 °C for 12 h. After completion of reaction (as determined by ¹H NMR), the reaction mixture was acidified with 4 N HCl to a pH of 2 and extracted twice with DCM. The combined organic layers were dried over MgSO₄ and concentrated in vacuo to afford crude product (1.6 g, 93% yield) and used for the next step without further purification.

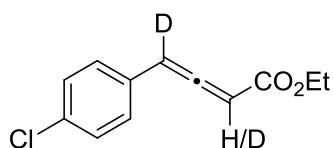
Synthesis of allenic ester **2G-d**:

1) Crude 2-(4-chlorophenyl)acetic-2,2-*d*₂ acid (863 mg, 5 mmol, 1.0 equiv) was dissolved in 25 mL of CH₂Cl₂ in a 50-mL round-bottom flask equipped with a magnetic stirring bar, followed by addition of one drop of DMF and slow addition of (COCl)₂ (634 mg, 7.5 mmol, 1.5 equiv) at room temperature. The solution was stirred for 4 h at

room temperature. The acyl chloride was obtained after evaporating the solvent and used without further purification.

2) Phosphorus ylide (1.74 g, 5 mmol, 1.0 equiv) was dissolved in 15 mL of CH₂Cl₂ in a 50-mL round-bottom flask with a stir bar, followed by addition of Et₃N (0.7 mL, 5 mmol, 1.0 equiv). To the stirring mixture, a solution of acyl chloride (955 mg, 5 mmol, 1.0 equiv) in 10 mL of CH₂Cl₂ was slowly added at room temperature. After the addition was finished, the reaction mixture was stirred for further 2 h at room temperature, then the solvent was evaporated under reduced pressure. The crude mixture was treated with petroleum ether (25 mL), and was allowed to sit undisturbed for 30 min. The mixture was filtered and the filtrate was evaporated. The crude residue was purified by column chromatography on silica gel to afford the title allenic ester **2G-d**.

Ethyl 4-(4-chlorophenyl)buta-2,3-dienoate-2,4-d₂ and 4-(4-chlorophenyl)buta-2,3-dienoate-4-d (2G-d)



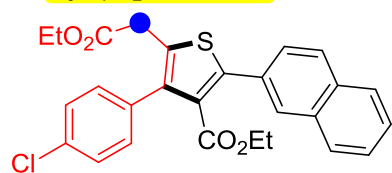
Yellow oil, 220 mg, yield 20%, $R_f = 0.65$ (PE/EA = 10:1, v/v). **¹H NMR** (400 MHz, CDCl₃) δ 7.29 (d, $J = 8.4$ Hz, 2H), 7.22 (d, $J = 8.4$ Hz, 2H), 6.02 (s, 0.51H), 4.22 (q, $J = 7.2$ Hz, 2H), 1.28 (t, $J = 7.2$ Hz, 3H). **¹³C NMR** (101 MHz, CDCl₃) δ 214.6, 164.8, 133.8, 132.9, 129.6, 129.0, 128.6, 92.3, 61.2, 14.2. **GC-MS** (EI, m/z, rel. intensity) 226.31 (3.80), 224.33 (8.52), 223.31 (13.58), 197.25 (6.02), 196.27 (10.53), 195.26 (18.16), 181.25 (4.31), 153.23 (18.45), 152.23 (39.32), 151.23 (57.56), 150.23 (100.00). **IR**(KBr) ν (cm⁻¹): 1670.

Synthesis of product **3aG-d**:

To an oven-dried reaction tube equipped with a magnetic stirring bar was added 1,2,3-thiadiazole **1a** (28.4 mg, 0.100 mmol, 1.0 equiv), allenic ester **2G-d** (44.8 mg, 0.2 mmol, 2 equiv), [Rh(cod)Cl]₂ (2.5 mg, 0.005 mmol, 5 mol %) and DPPB (5.1 mg, 0.012 mmol, 12 mol). The tube was sealed immediately with a rubber stopper and protected with a nitrogen balloon by evacuation-backfill operations for three times; then PhCl (1 mL) was injected to the tube. The mixture was heated at 130 °C in a heating block for 2 h. When the reaction was finished, as detected by TLC, the solvent was evaporated under reduced pressure, and the crude mixture was subjected to column chromatography on silica gel affording the corresponding product **3aG-d**.

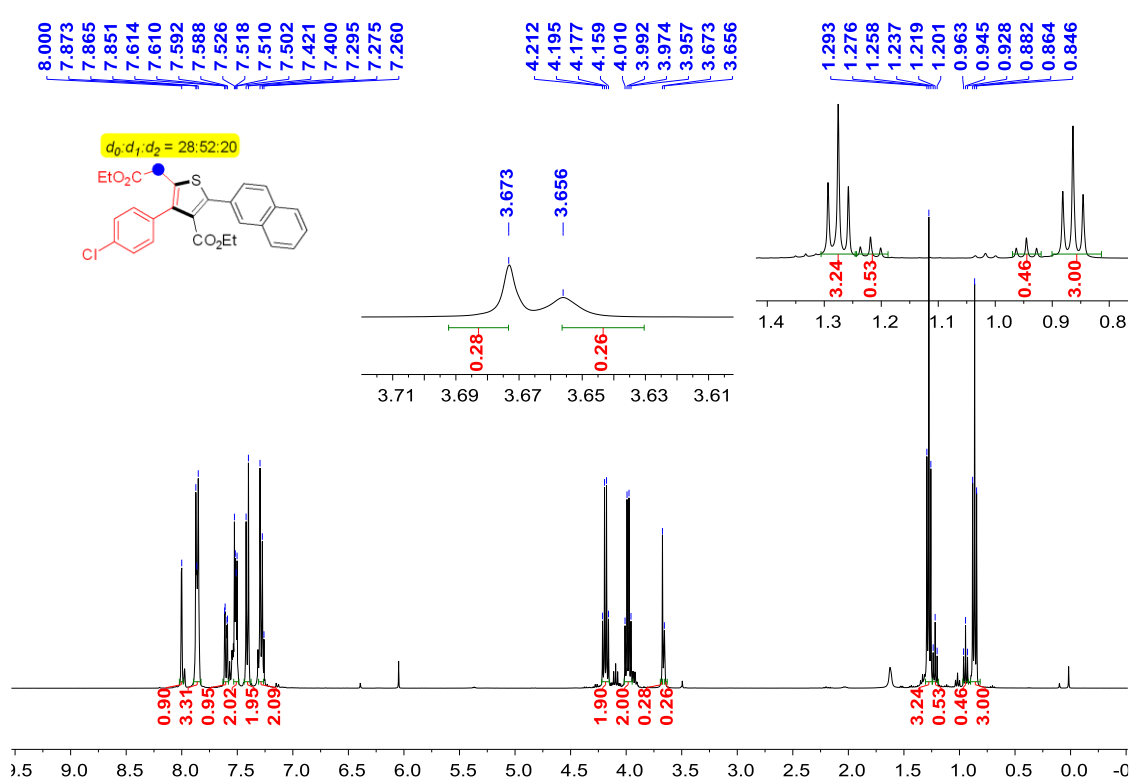
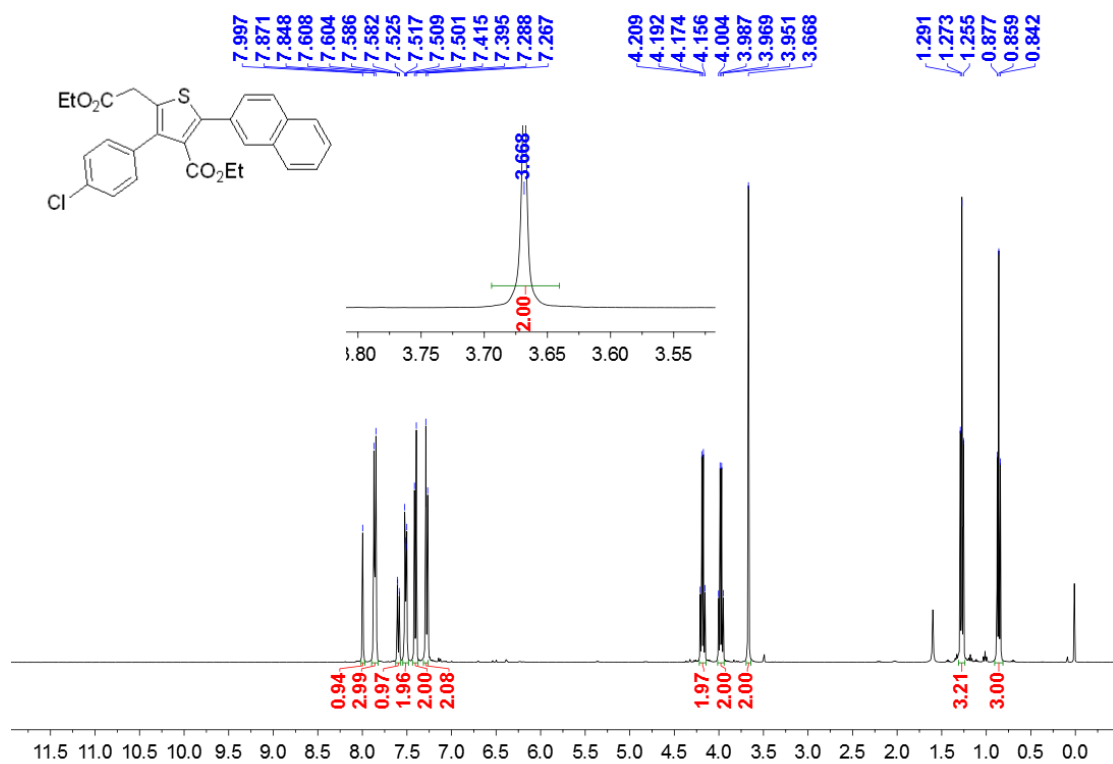
Ethyl 4-(4-chlorophenyl)-5-(2-ethoxy-2-oxoethyl)-2-(naphthalen-2-yl)thiophene-3-carboxylate (3aG-d)

$d_0:d_1:d_2 = 28:52:20$



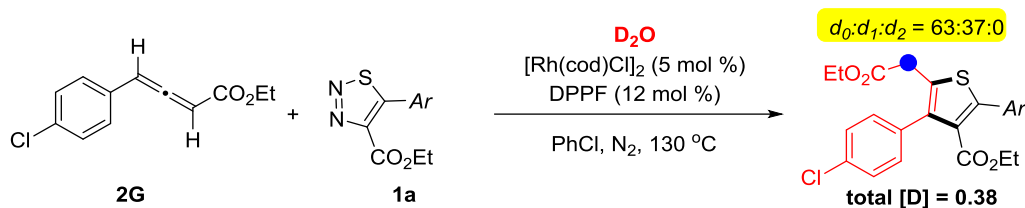
Yellow oil, 36 mg, yield 75%, $R_f = 0.45$ (PE/EA = 10:1, v/v). **$^1\text{H NMR}$** (400 MHz, CDCl_3) δ 8.00 (s, 1H), 7.86 (d, $J = 8.8$ Hz, 3H), 7.60 (dd, $J = 8.8, 1.6$ Hz, 1H), 7.51 (dd, $J = 6.3, 3.2$ Hz, 2H), 7.41 (d, $J = 8.4$ Hz, 2H), 7.28 (d, $J = 8.0$ Hz, 2H), 4.18 (q, $J = 7.1$ Hz, 2H), 3.98 (q, $J = 7.1$ Hz, 2H), 3.67 (s, 0.56H), 3.66 (s, 0.52), 1.27 (t, $J = 7.2$ Hz, 3H), 1.22 (t, $J = 7.2$ Hz, 0.53H), 0.94 (t, $J = 7.2$ Hz, 0.46H), 0.86 (t, $J = 7.2$ Hz, 3H). **$^{13}\text{C NMR}$** (101 MHz, CDCl_3) δ 170.0, 164.9, 145.8, 140.2, 133.7, 133.7, 133.0, 130.8, 130.6, 130.0, 129.7, 128.4, 128.3, 128.2, 128.0, 127.9, 127.6, 126.8, 126.5, 126.5, 61.4, 60.8, 33.8, 14.1, 13.5. **HRMS** (ESI): m/z $[\text{M}+\text{H}]^+$ calcd for $\text{C}_{27}\text{H}_{22}\text{D}_2\text{ClO}_4\text{S}^+$ 481.1204, found 481.1211, $[\text{M}+\text{H}]^+$ calcd for $\text{C}_{27}\text{H}_{23}\text{D}_2\text{ClO}_4\text{S}^+$ 480.1141, found 480.1140, $[\text{M}+\text{Na}]^+$ calcd for $\text{C}_{27}\text{H}_{22}\text{DCINaO}_4\text{S}^+$ 502.0961, found 502.0961. **IR**(KBr) ν (cm^{-1}): 1719, 1185.

¹H NMR (400 MHz, CDCl₃)



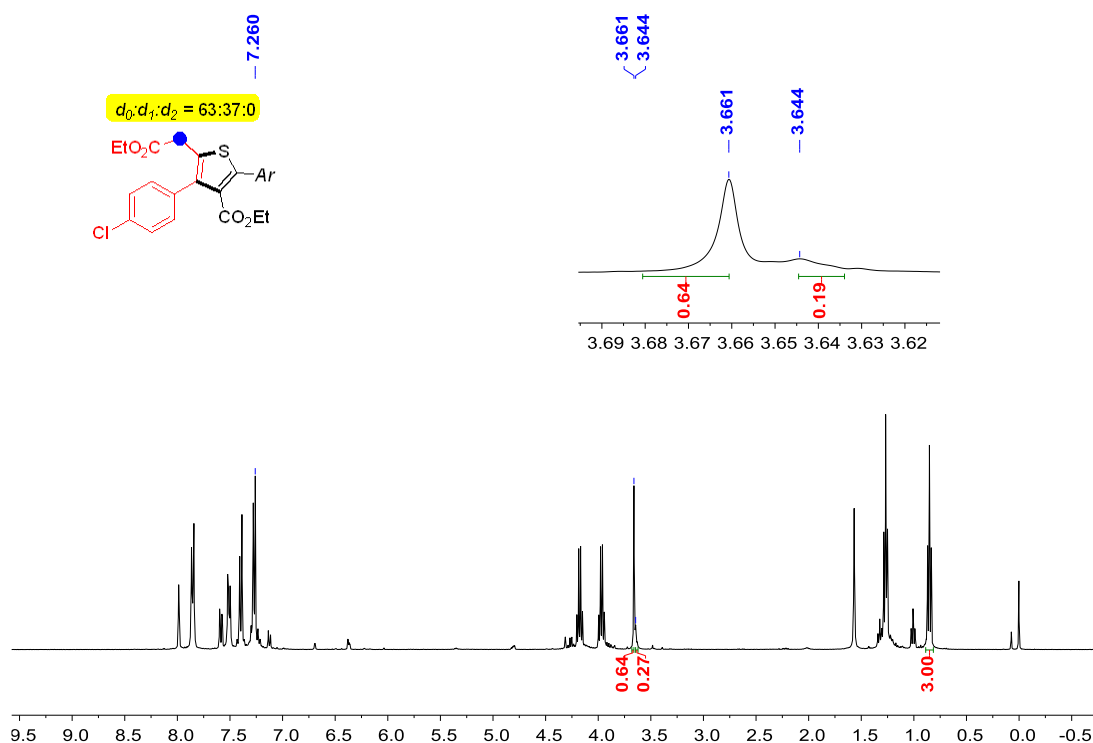
Calculation of the non-, mono-, and dideuterated products (3aG-*d*₀, 3aG-*d*₁, 3aG-*d*₂)

Product	Integral of half-peak	Integral of entire peak	[H]-incorporation	[D]-incorporation	Molar ratio
d ₀ (CH ₂)	0.28	0.56	0.56	0	0.28
d ₁ (CHD)	0.26	0.52	0.52	0.52	0.52
d ₂ (CD ₂)			0	0.40	0.20



To an oven-dried reaction tube equipped with a magnetic stirring bar was added 1,2,3-thiadiazole **1a** (28.4 mg, 0.1 mmol, 1.0 equiv), allenic ester **2G** (44.4 mg, 0.2 mmol, 2.0 equiv), $[\text{Rh}(\text{cod})\text{Cl}]_2$ (2.5 mg, 0.005 mmol, 5 mol %), and DPPB (5.1 mg, 0.012 mmol, 12 mol %). The tube was sealed immediately with a rubber stopper and protected with a nitrogen balloon by evacuation-backfill operations for three times; then PhCl (1 mL) and D_2O (55 μL , 2.5 mmol) were injected to the tube. The mixture was heated at 130 $^\circ\text{C}$ in a heating block for 2 h.

Copies of ^1H NMR of Crude reaction mixtures



Calculation of the non-, mono-, and dideuterated products (3aG- d_0 , 3aG- d_1 , 3aG- d_2)

Product	Integral of half-peak	Integral of entire peak	[H]-incorporation	[D]-incorporation	Molar ratio
d_0 (CH_2)	0.64	1.28	1.28	0	0.63
d_1 (CHD)	0.19	0.38	0.38	0.38	0.37
d_2 (CD_2)			0	0	0

4. X-Ray Crystallographic Analysis



CCDC: 2184292 at 50% probability.

Experimental

Single crystals of $C_{23}H_{20}O_2S$ **8aC** were recrystallised from petroleum ether and tetrahydrofuran and transferred to the cold gas stream of the diffractometer.

Crystal structure determination of **8aC**

Crystal Data. $C_{23}H_{20}O_2S$, $M = 360.45$, monoclinic, $a = 8.7228(5) \text{ \AA}$, $b = 8.0994(4) \text{ \AA}$, $c = 26.1056(16) \text{ \AA}$, $\beta = 97.170(6)^\circ$, $U = 1829.94(18) \text{ \AA}^3$, $T = 113.75(10)$, space group $P2_1/n$ (no. 14), $Z = 4$, $\mu(\text{Mo K}\alpha) = 0.191$, 13871 reflections measured, 3569 unique ($R_{\text{int}} = 0.0527$) which were used in all calculations. The final $wR(F_2)$ was 0.1025 (all data).

Table 1: Crystal data and structure refinement for **8aC**

Identification code	exp_8045
Empirical formula	$C_{23}H_{20}O_2S$
Formula weight	360.45
Temperature / K	113.75(10)
Crystal system	monoclinic
Space group	$P2_1/n$
$a / \text{ \AA}$, $b / \text{ \AA}$, $c / \text{ \AA}$	8.7228(5), 8.0994(4), 26.1056(16)
$\alpha / ^\circ$, $\beta / ^\circ$, $\gamma / ^\circ$	90.00, 97.170(6), 90.00

Volume / Å ³	1829.94(18)
Z	4
ρ _{calc} / mg mm ⁻³	1.308
μ / mm ⁻¹	0.191
F(000)	760
Crystal size / mm ³	0.22 × 0.21 × 0.06
2θ range for data collection	5.94 to 52°
Index ranges	-10 ≤ h ≤ 10, -9 ≤ k ≤ 9, -32 ≤ l ≤ 27
Reflections collected	13871
Independent reflections	3569[R(int) = 0.0527 (inf-0.9Å)]
Data/restraints/parameters	3569/0/237
Goodness-of-fit on F ²	1.043
Final R indexes [I > 2σ (I) i.e. F _o > 4σ (F _o)]	R ₁ = 0.0449, wR ₂ = 0.0913
Final R indexes [all data]	R ₁ = 0.0623, wR ₂ = 0.1025
Largest diff. peak/hole / e Å ⁻³	0.233/-0.304
Flack Parameters	N
Completeness	0.9972

5. References

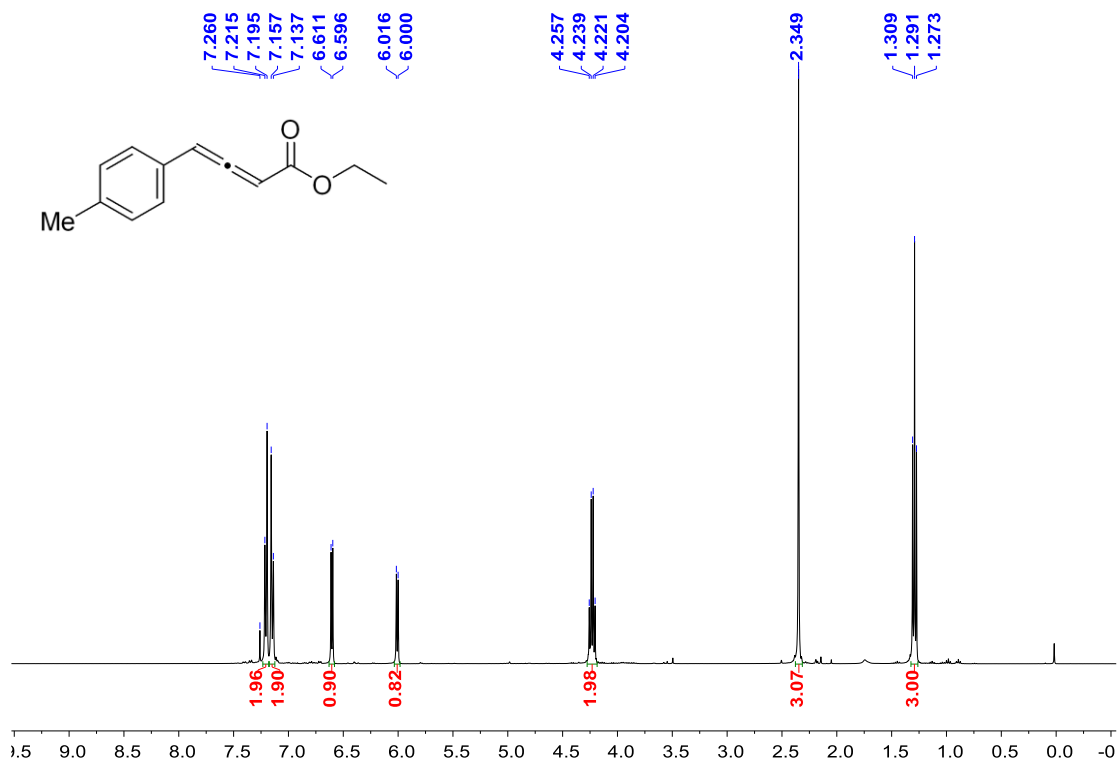
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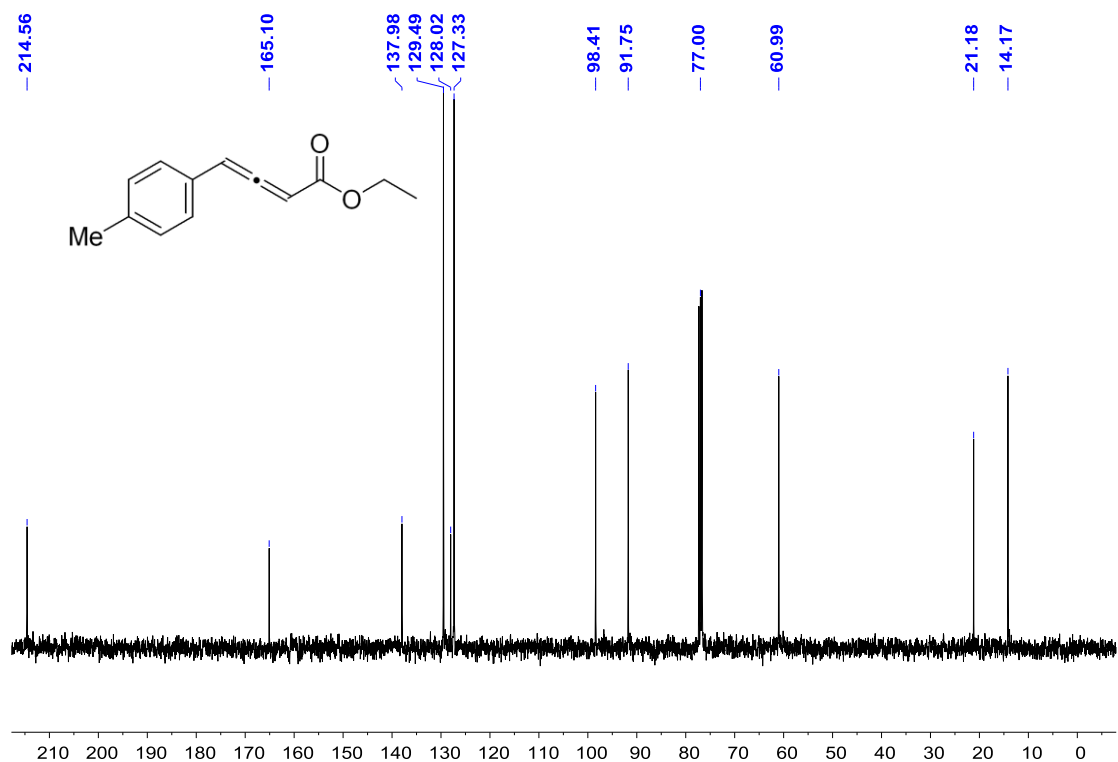
6. Copies of Spectra of Products and Materials

Ethyl 4-(*p*-tolyl)buta-2,3-dienoate (2E)

^1H NMR (400 MHz, CDCl_3)



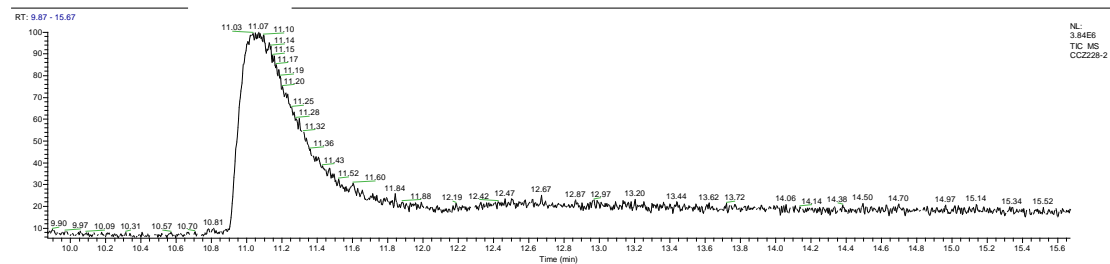
^{13}C NMR (101 MHz, CDCl_3)



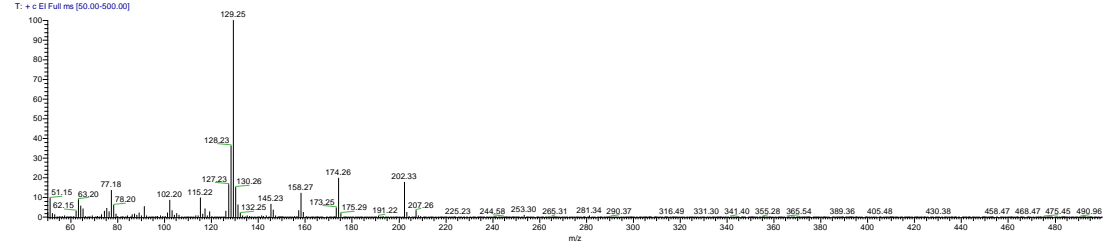
GC-MS (EI)

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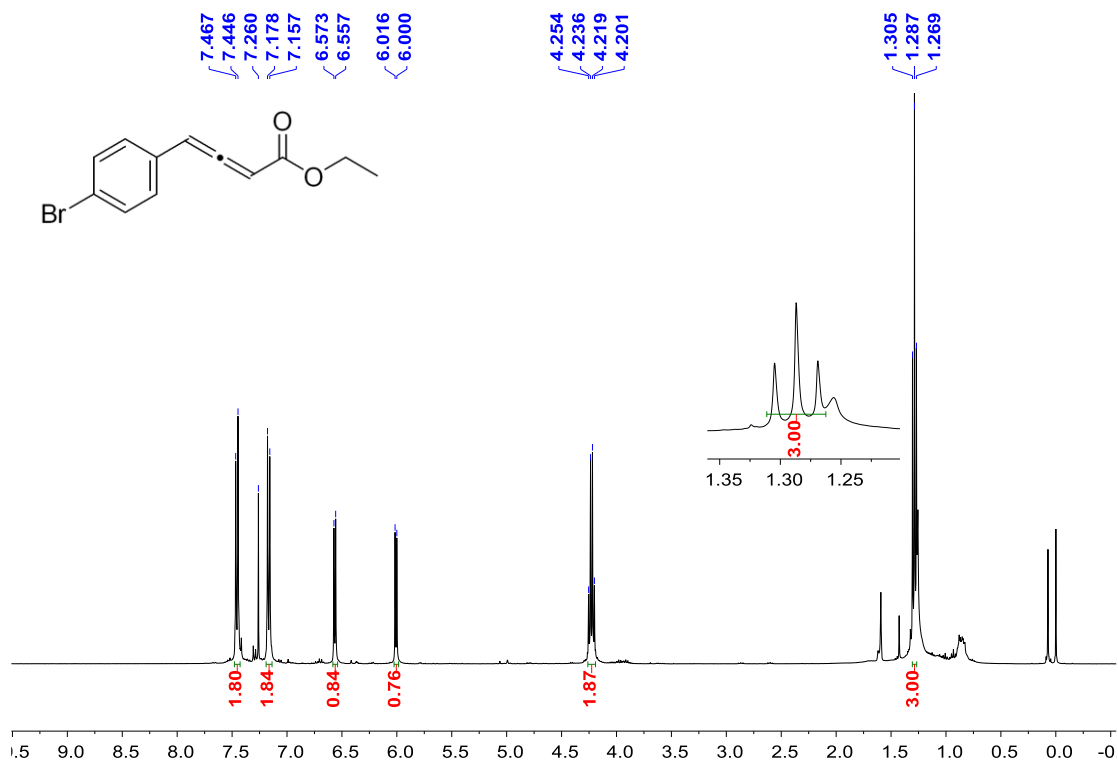


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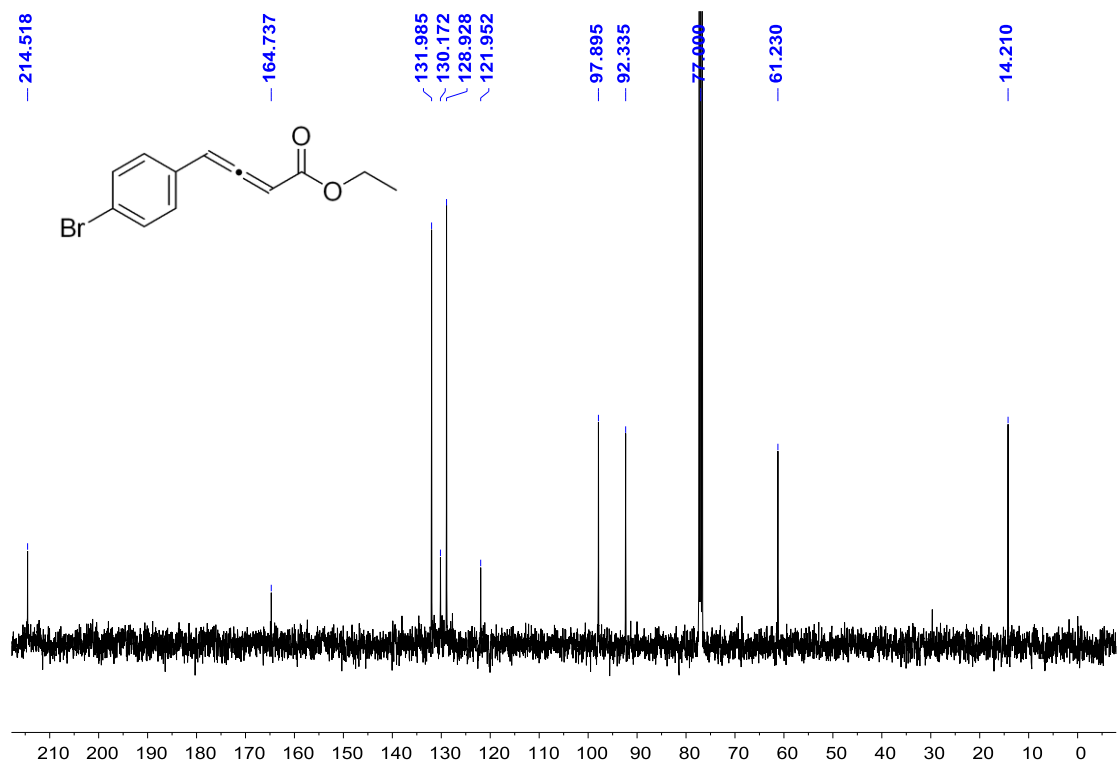


Ethyl 4-(4-bromophenyl)buta-2,3-dienoate (2H)

^1H NMR (400 MHz, CDCl_3)



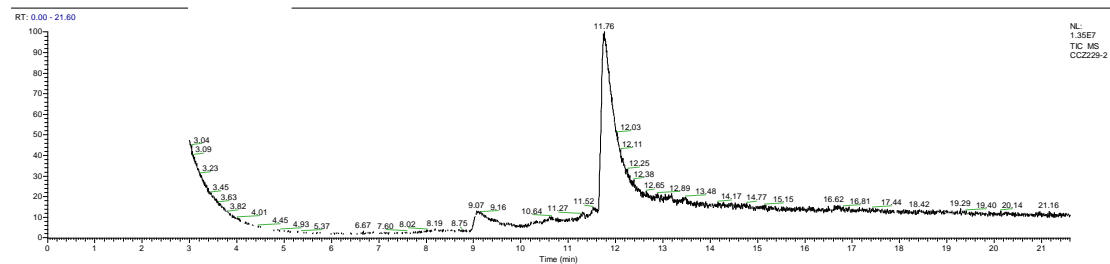
^{13}C NMR (101 MHz, CDCl_3)



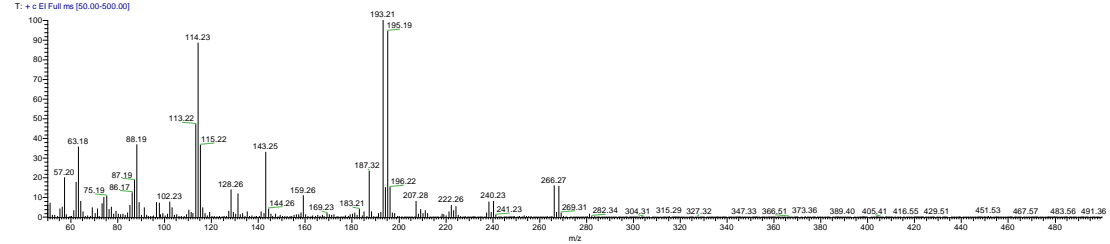
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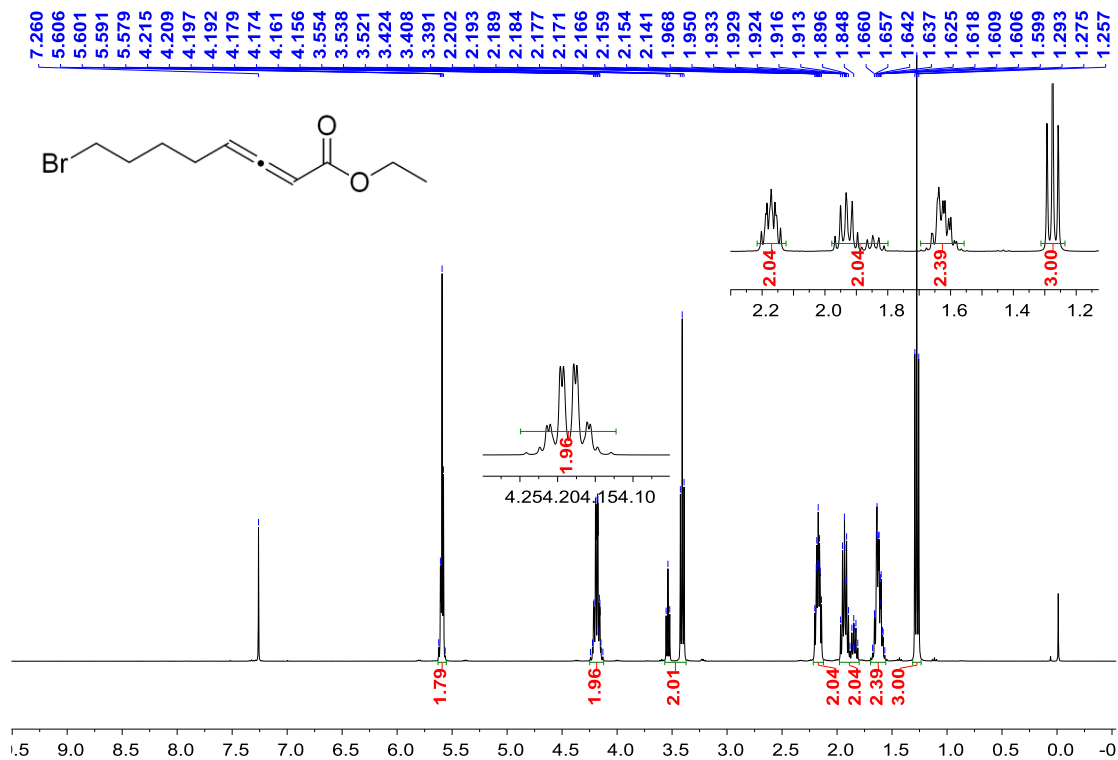


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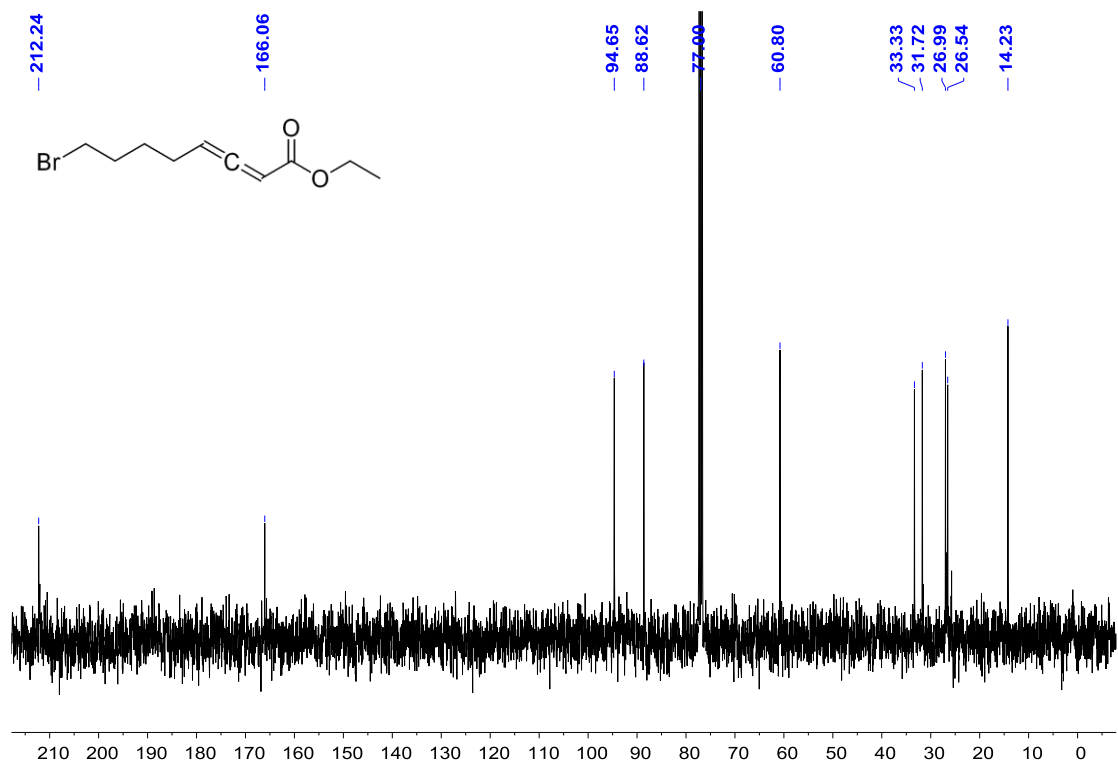


Ethyl 8-bromoocta-2,3-dienoate (2P)

^1H NMR (400 MHz, CDCl_3)

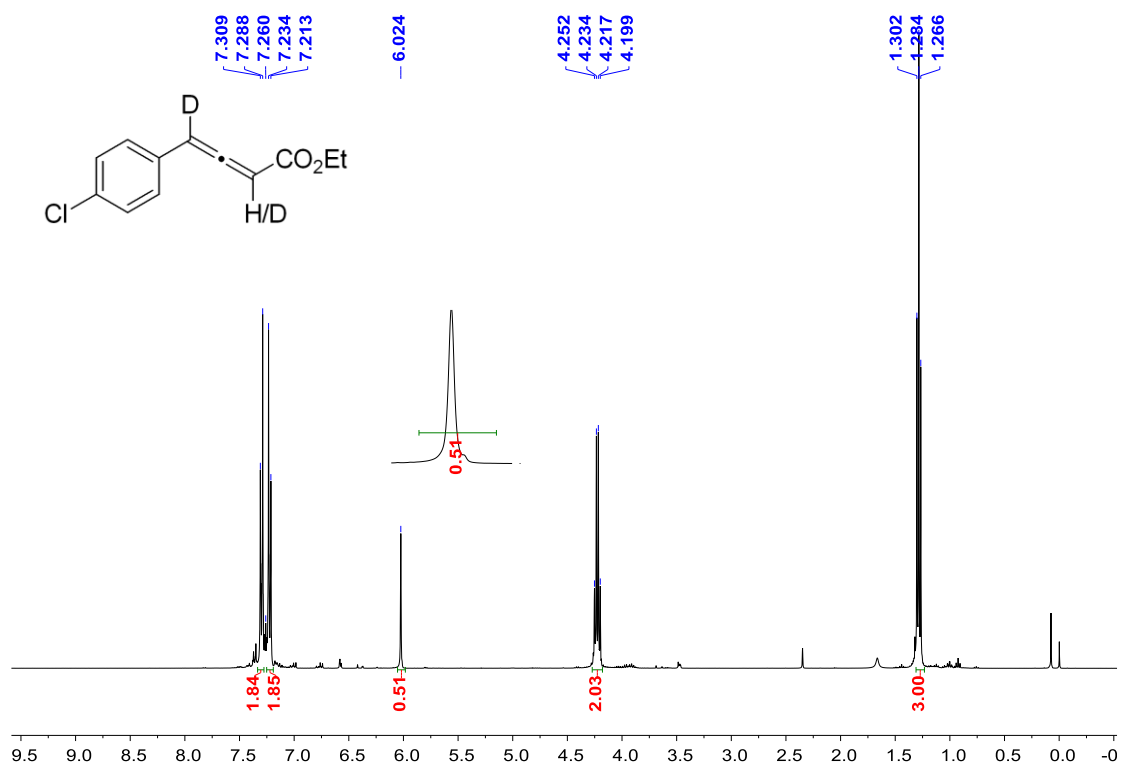


^{13}C NMR (101 MHz, CDCl_3)

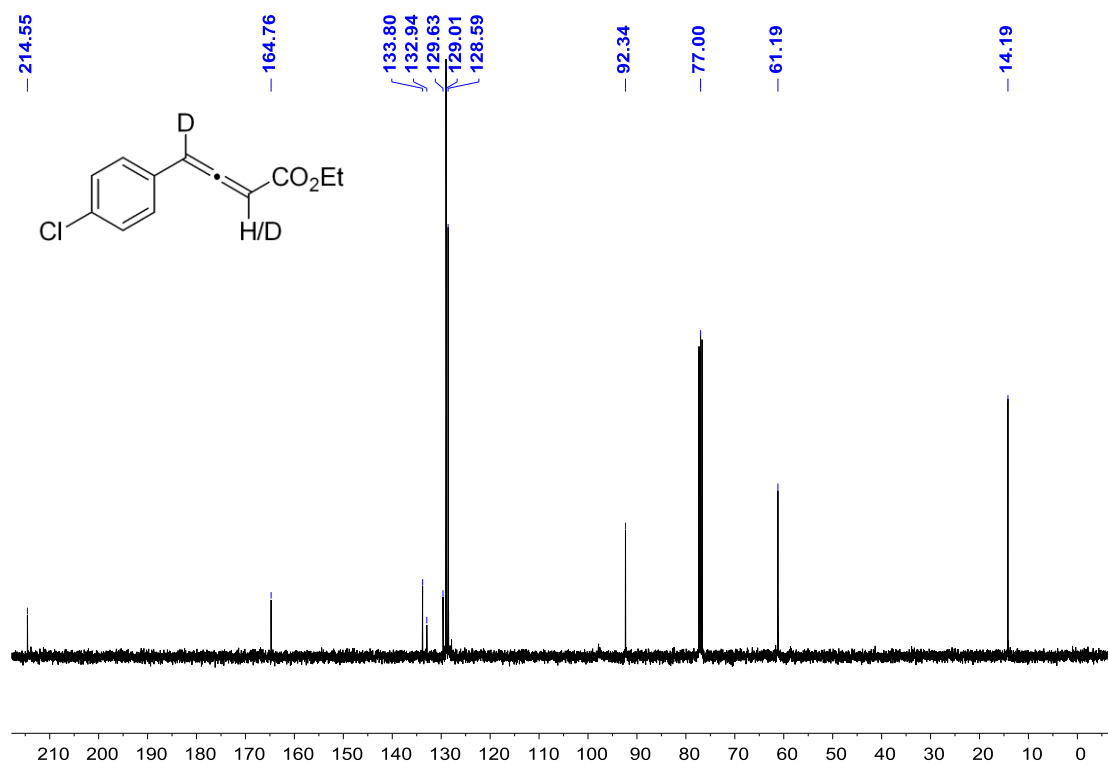


Ethyl 4-(4-chlorophenyl)buta-2,3-dienoate-2,4-*d*₂ and 4-(4-chlorophenyl)buta-2,3-dienoate-4-*d* (2G-*d*)

¹H NMR (400 MHz, CDCl₃)



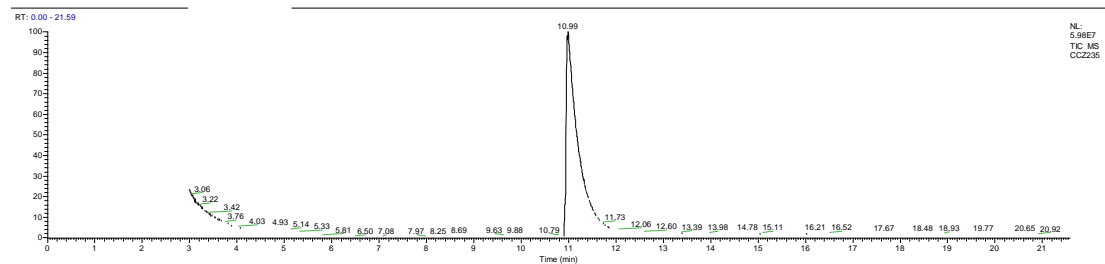
¹³C NMR (400 MHz, CDCl₃)



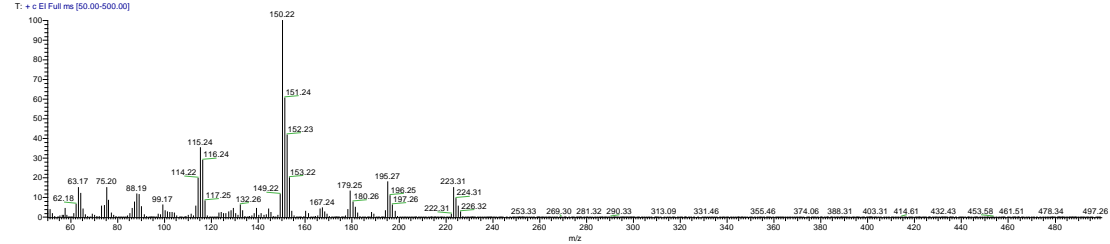
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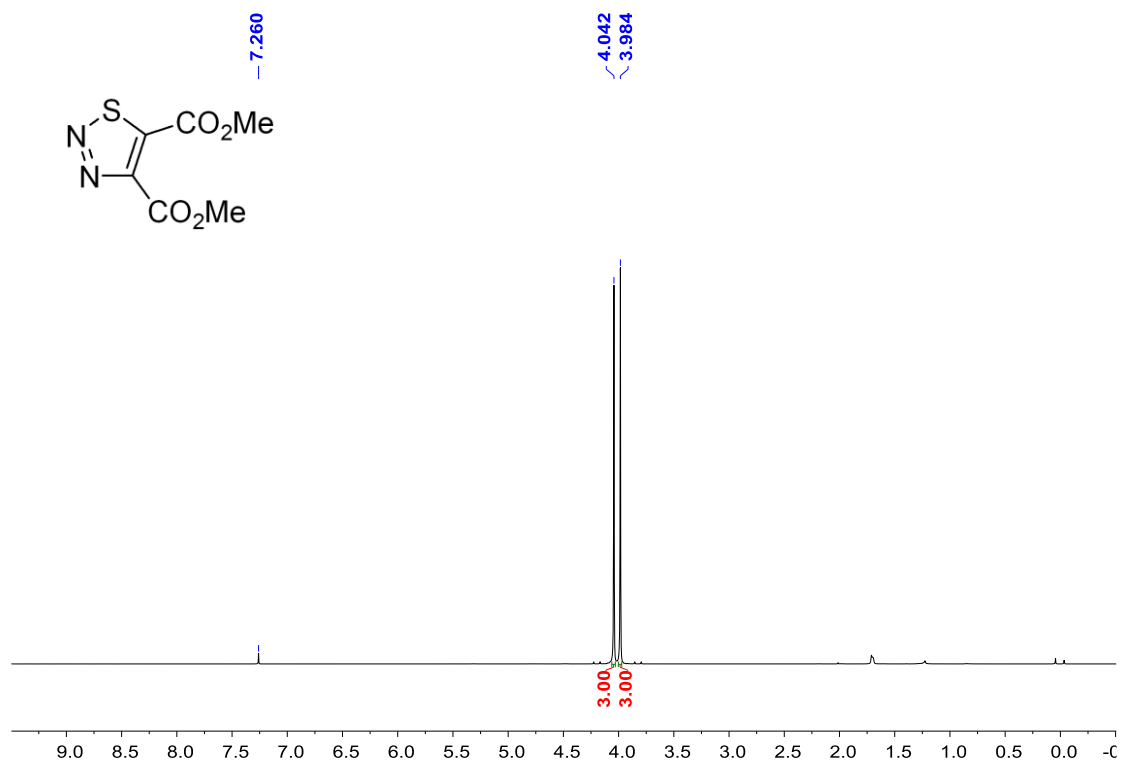


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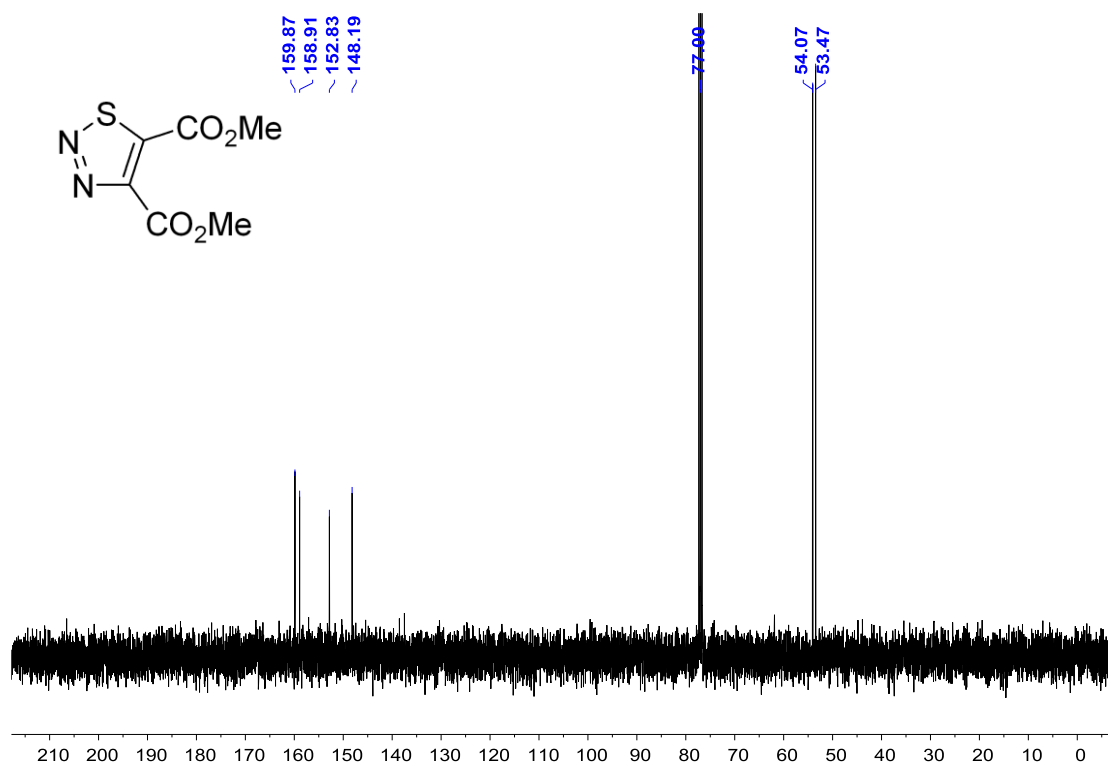


Dimethyl 1,2,3-thiadiazole-4,5-dicarboxylate (1p)

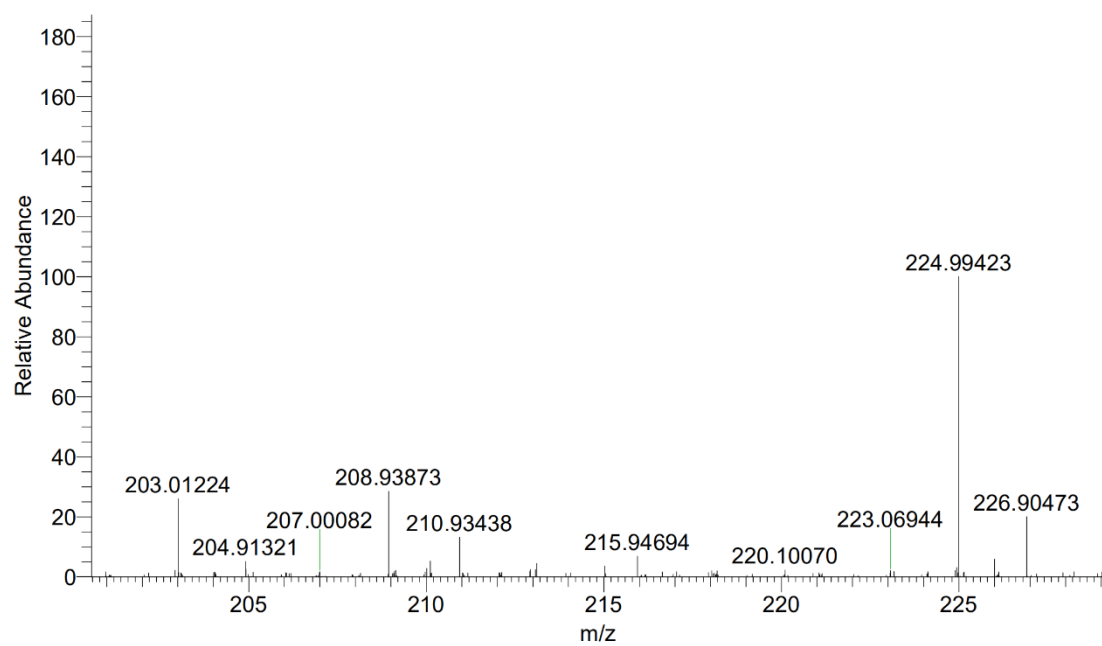
^1H NMR (400 MHz, CDCl_3)



^{13}C NMR (101 MHz, CDCl_3)

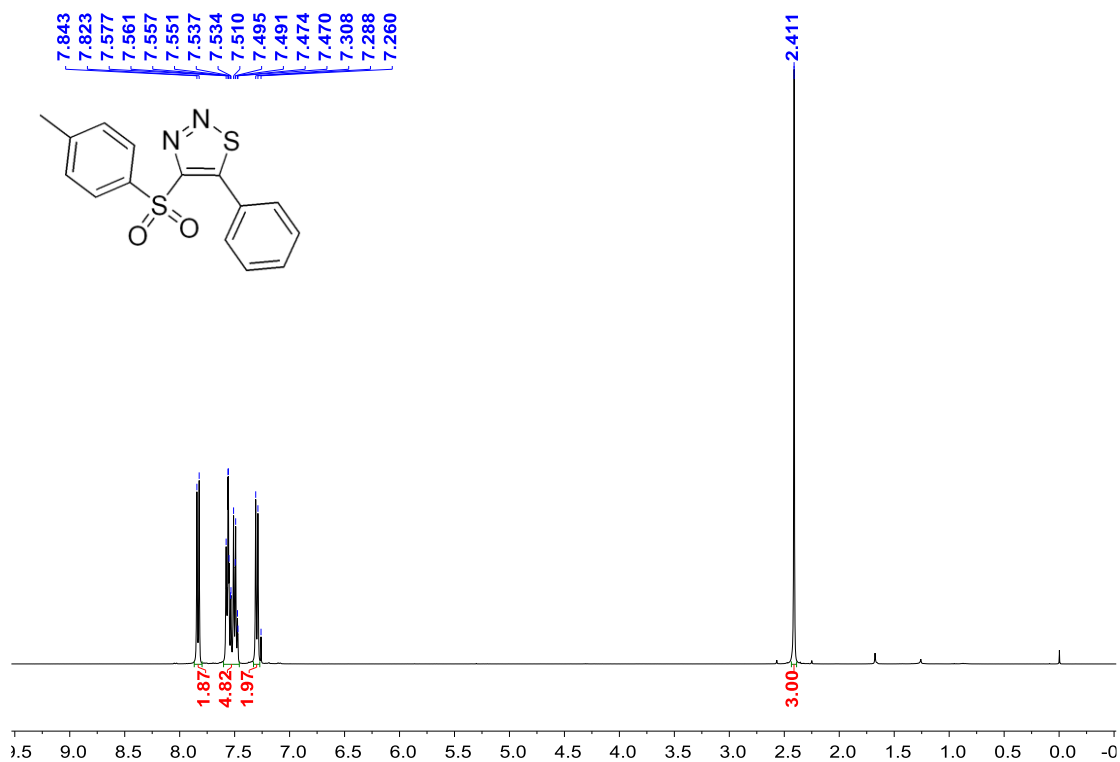


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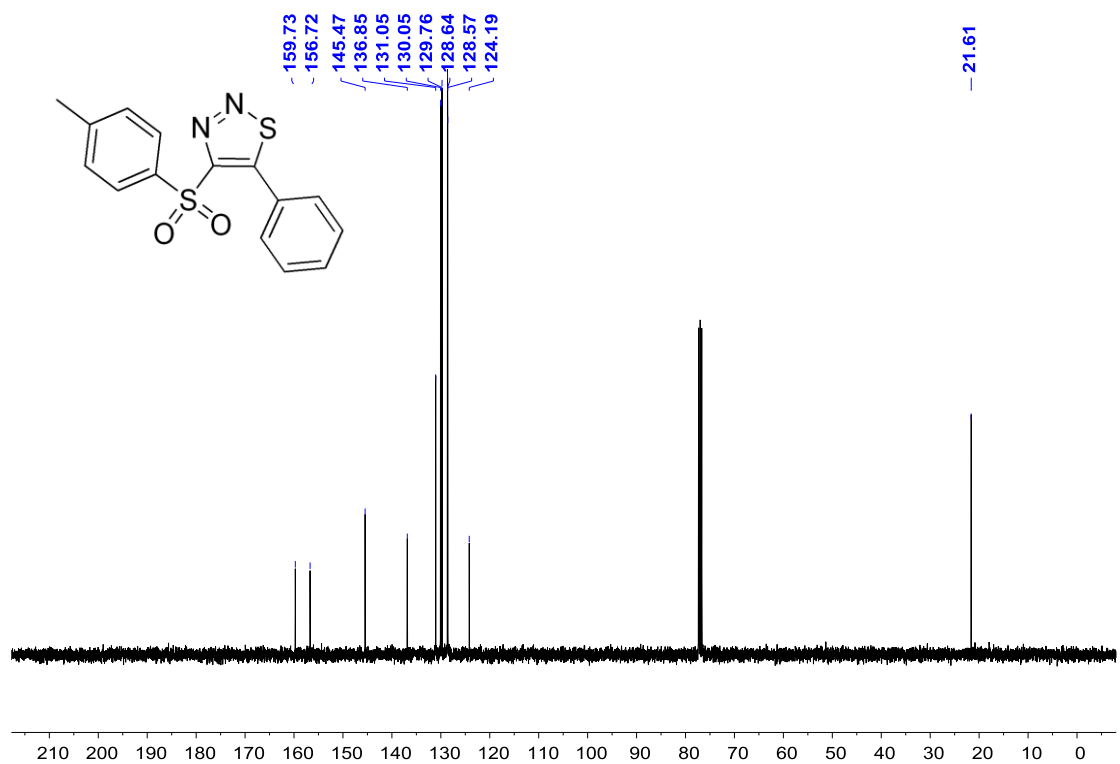


Ethyl 5-phenyl-4-tosyl-1,2,3-thiadiazole (1r)

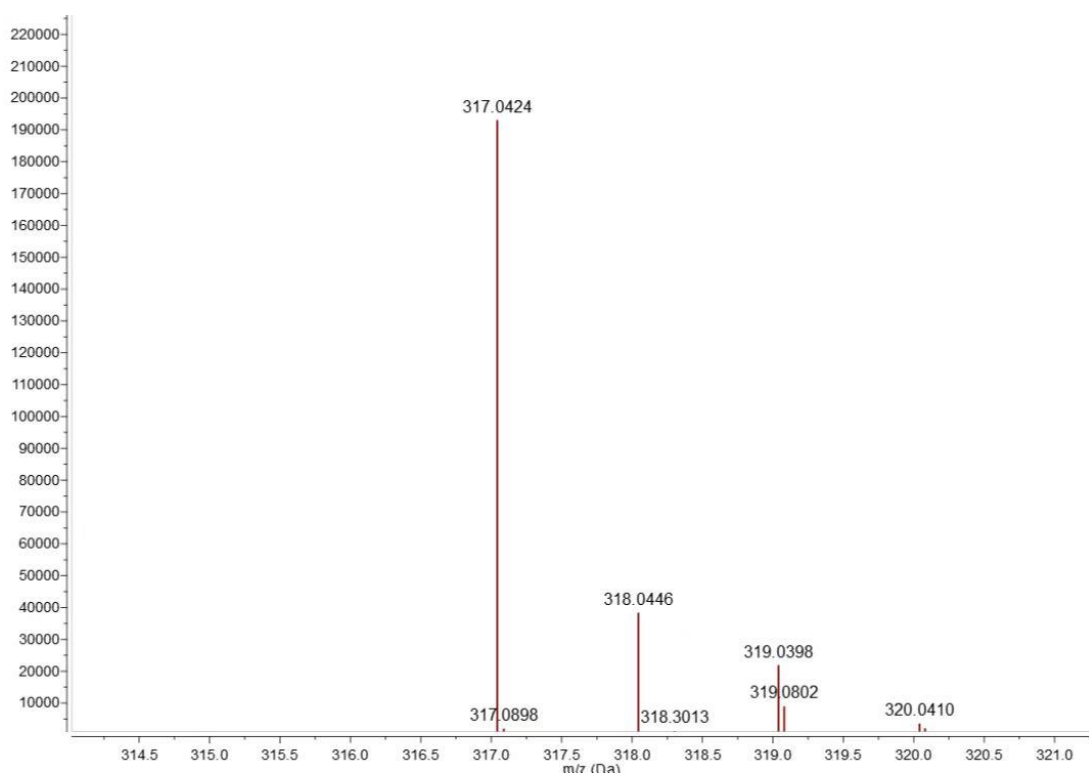
^1H NMR (400 MHz, CDCl_3)



^{13}C NMR (101 MHz, CDCl_3)

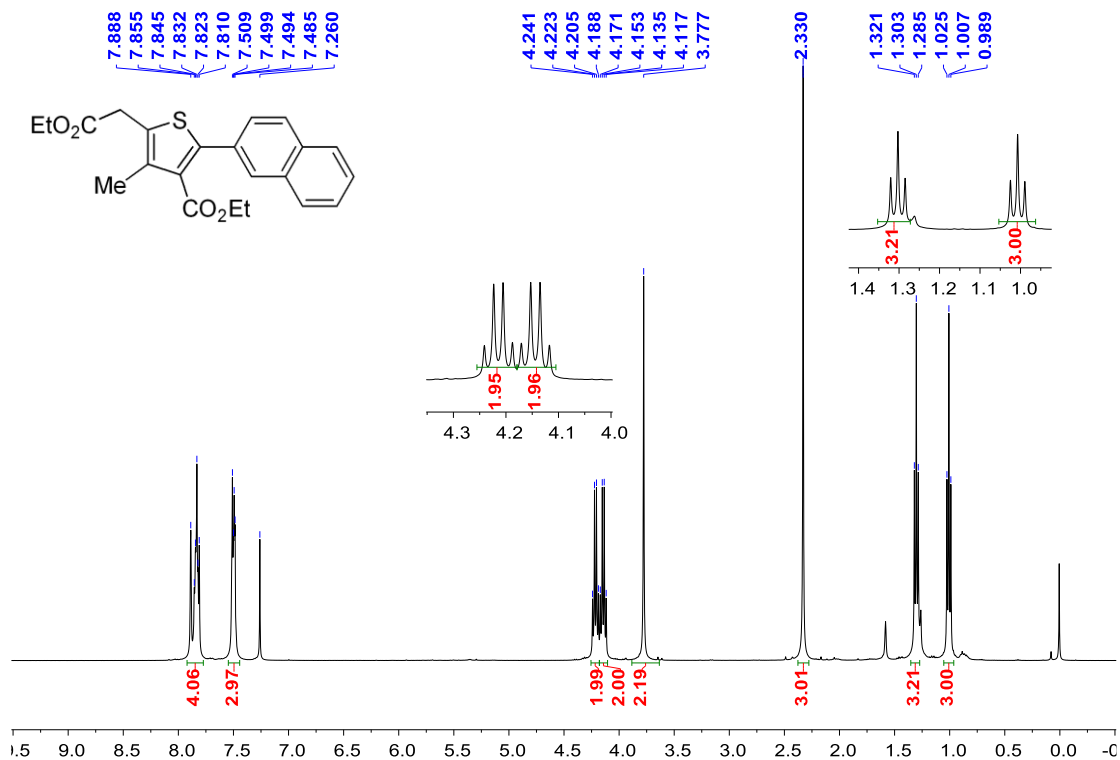


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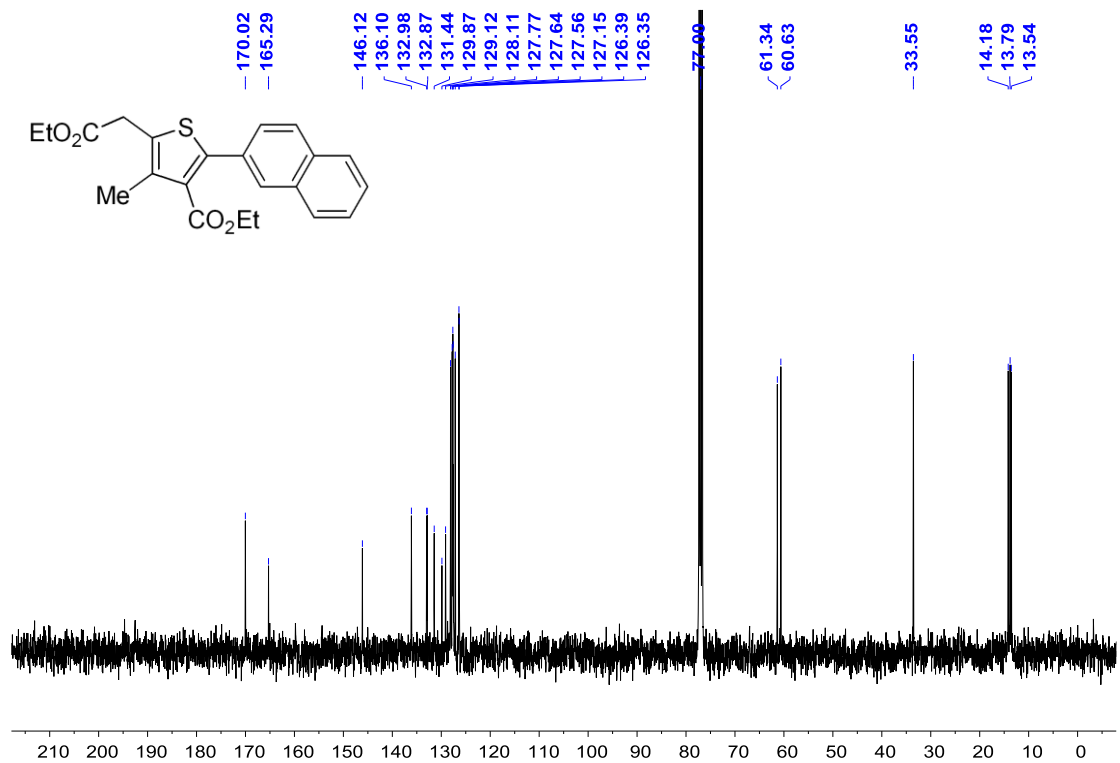


Ethyl 5-(2-ethoxy-2-oxoethyl)-4-methyl-2-(naphthalen-2-yl)thiophene-3-carboxylate (3aA)

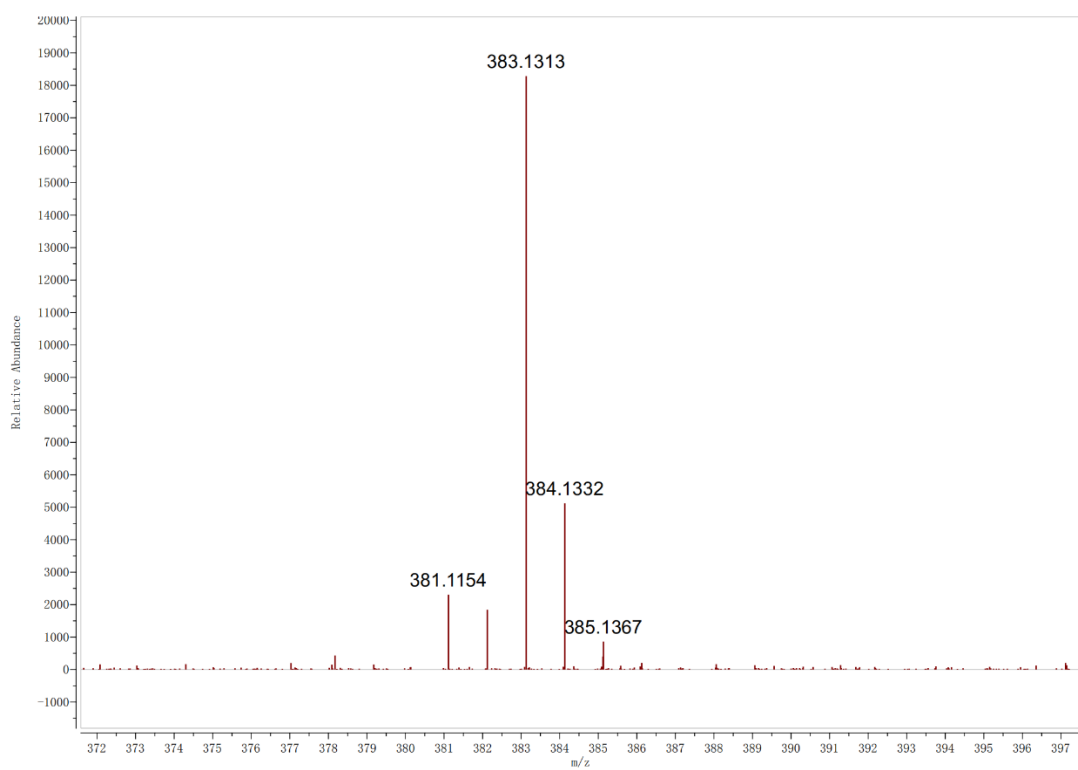
$^1\text{H NMR}$ (400 MHz, CDCl_3)



$^{13}\text{C NMR}$ (101 MHz, CDCl_3)

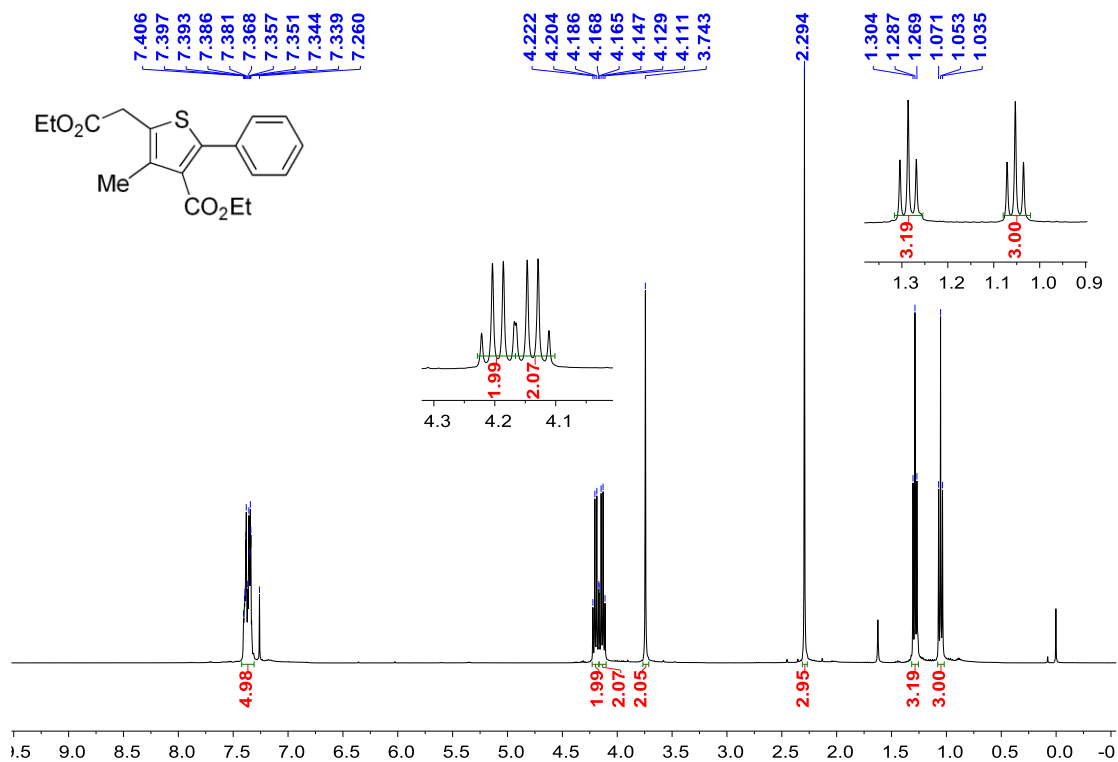


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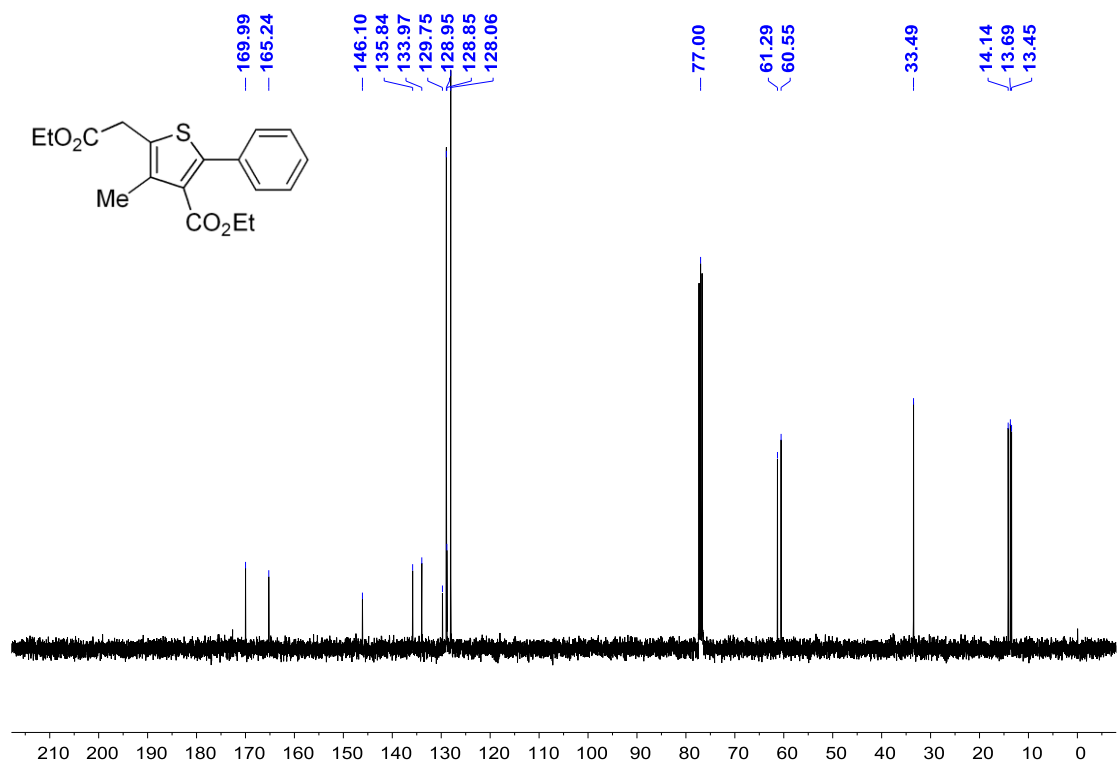


Ethyl 5-(2-ethoxy-2-oxoethyl)-4-methyl-2-phenylthiophene-3-carboxylate (3bA)

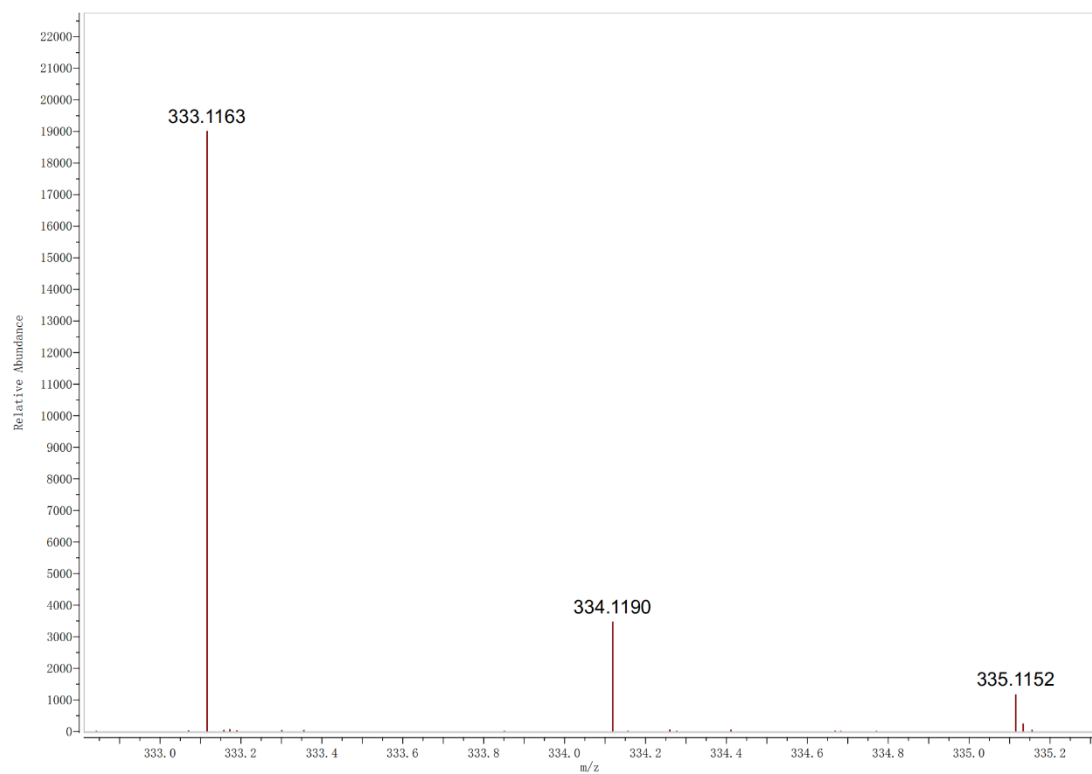
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¹³C NMR (101 MHz, CDCl₃)

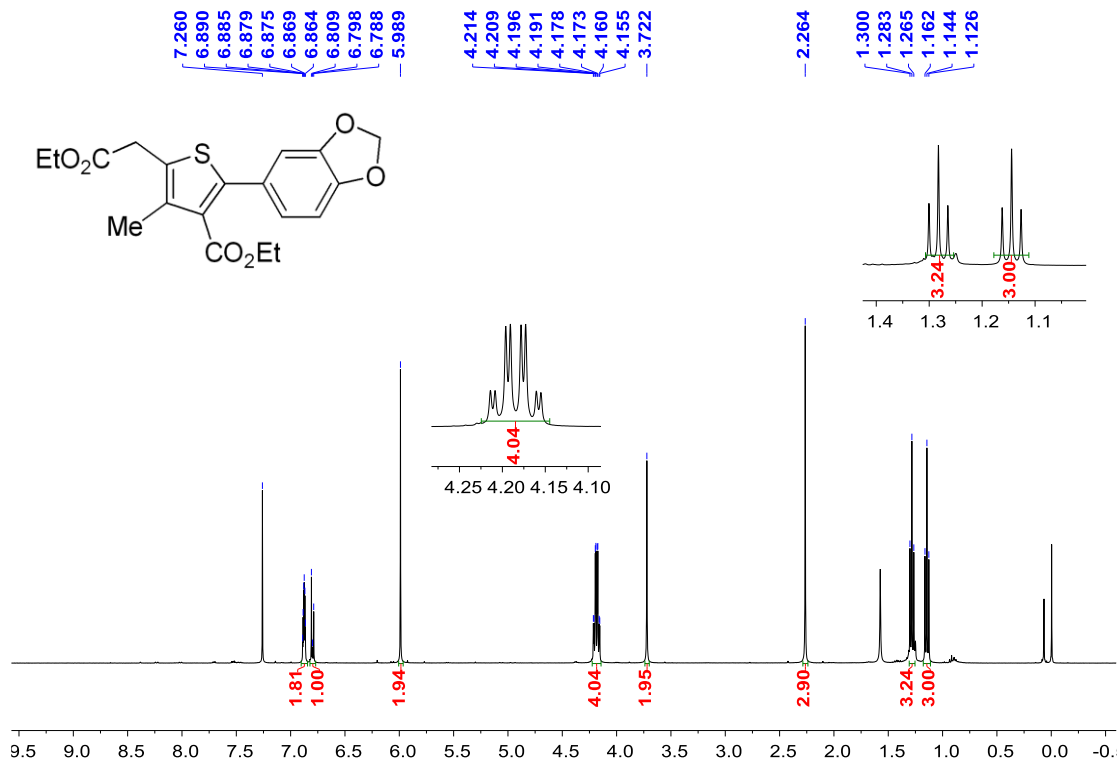


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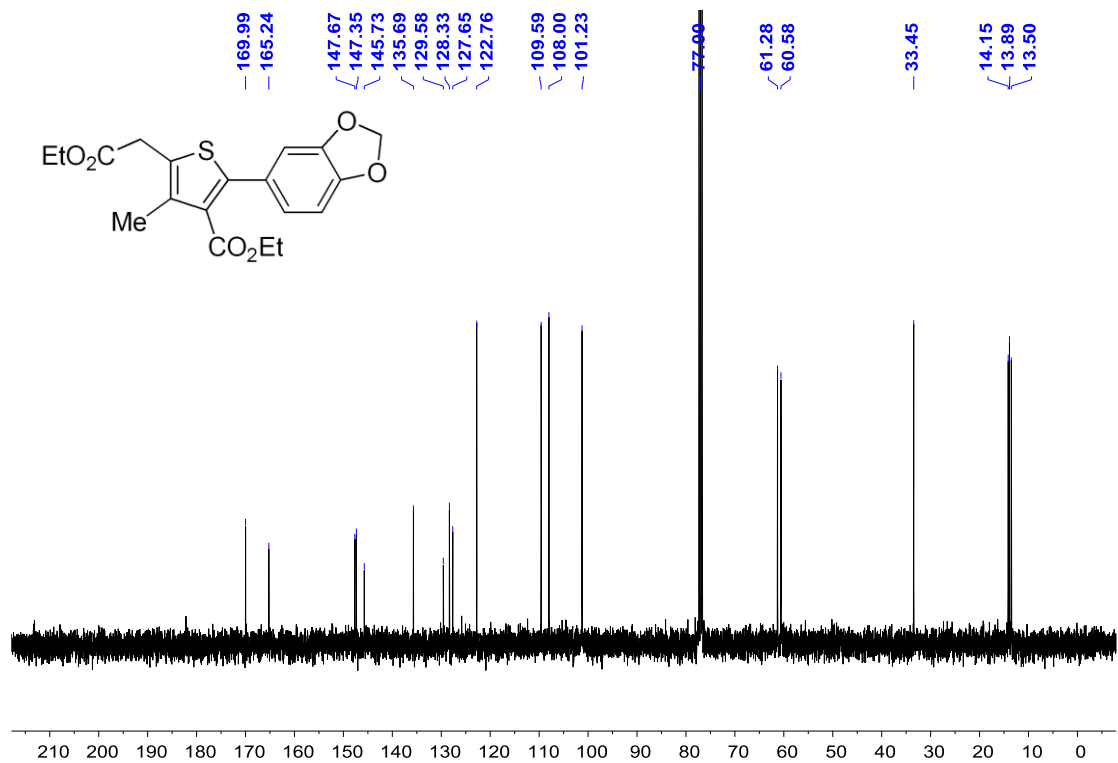


Ethyl 2-(benzo[d][1,3]dioxol-5-yl)-5-(2-ethoxy-2-oxoethyl)-4-methylthiophene-3-carboxylate (3cA)

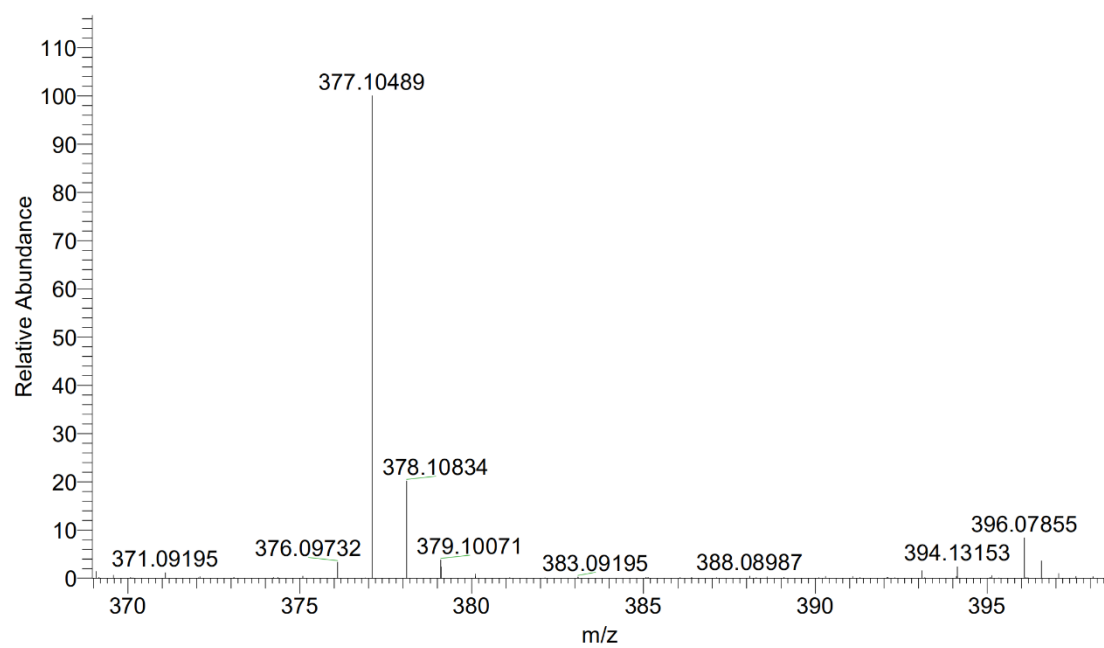
$^1\text{H NMR}$ (400 MHz, CDCl_3)



$^{13}\text{C NMR}$ (101 MHz, CDCl_3)

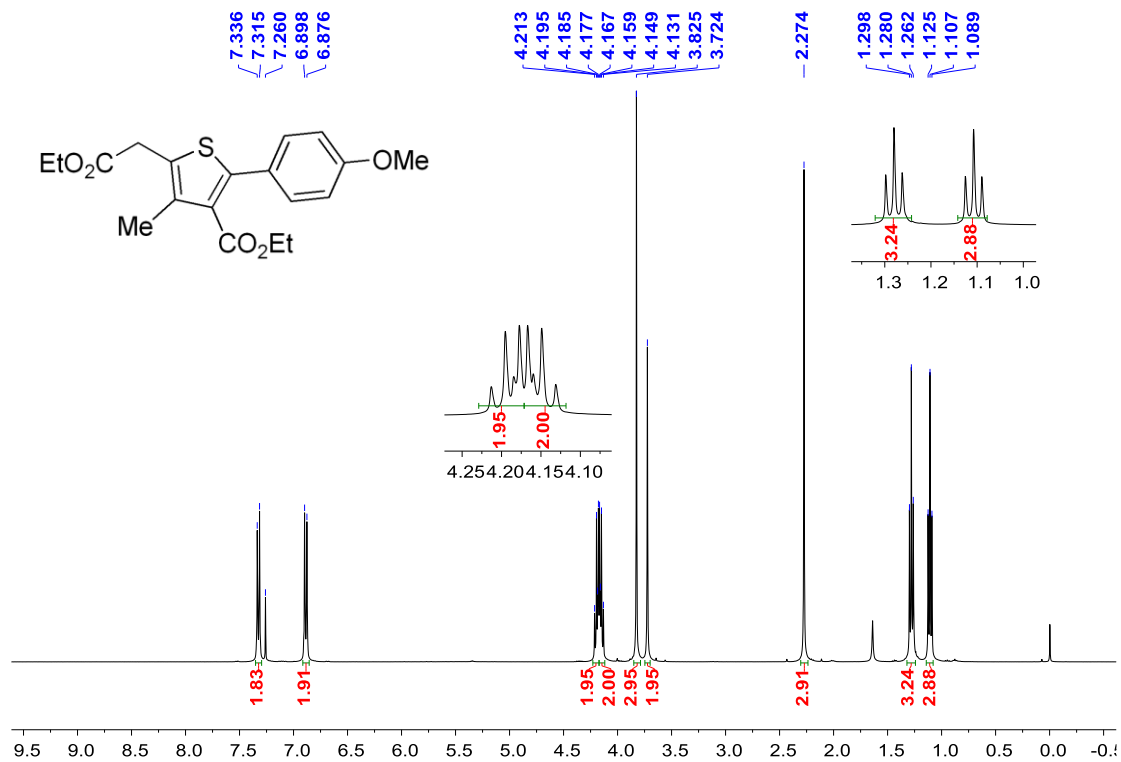


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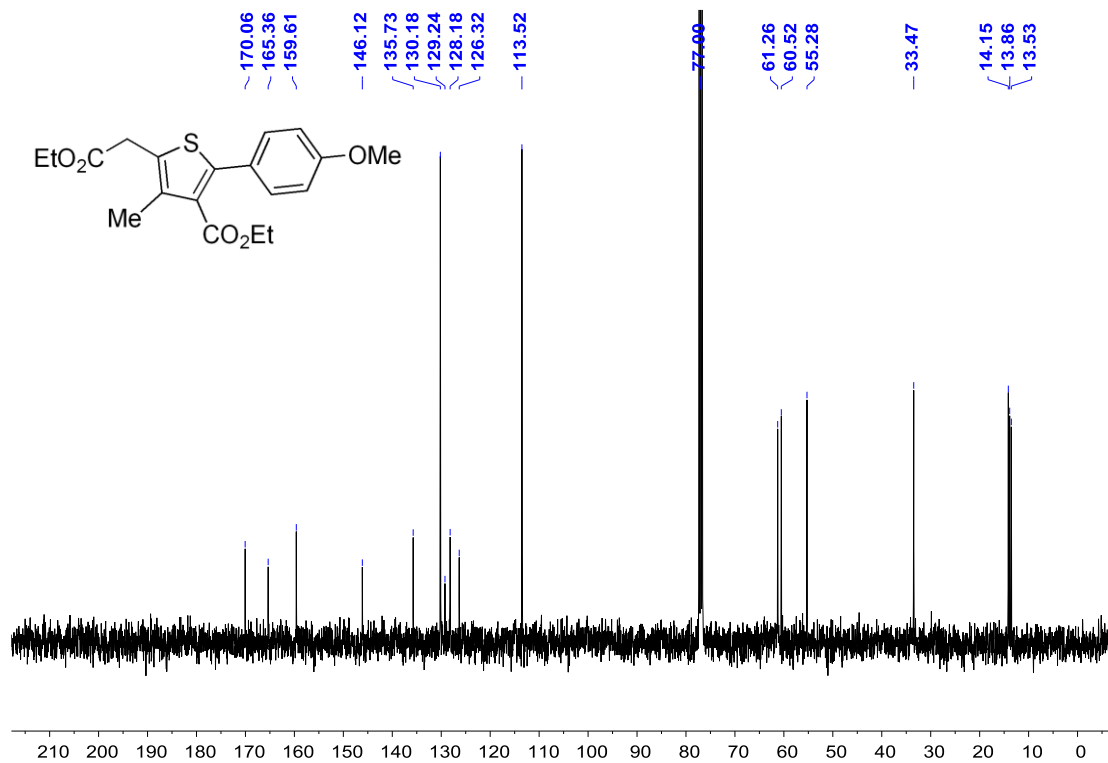


Ethyl 5-(2-ethoxy-2-oxoethyl)-2-(4-methoxyphenyl)-4-methylthiophene-3-carboxylate (3dA)

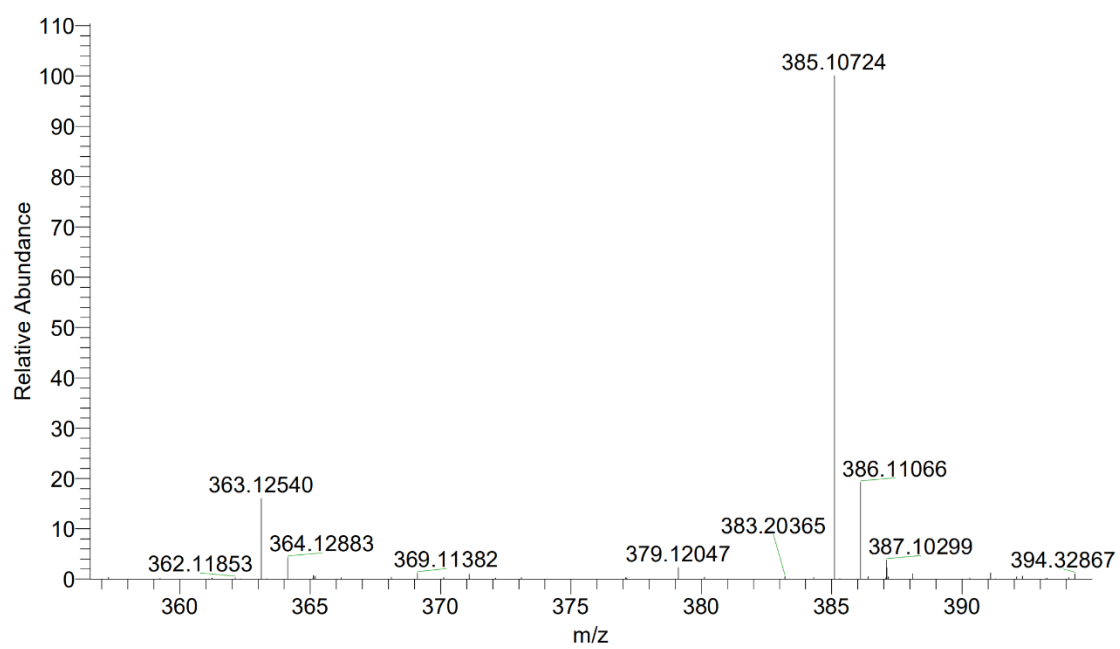
¹H NMR (400 MHz, CDCl₃)



¹³C NMR (101 MHz, CDCl₃)

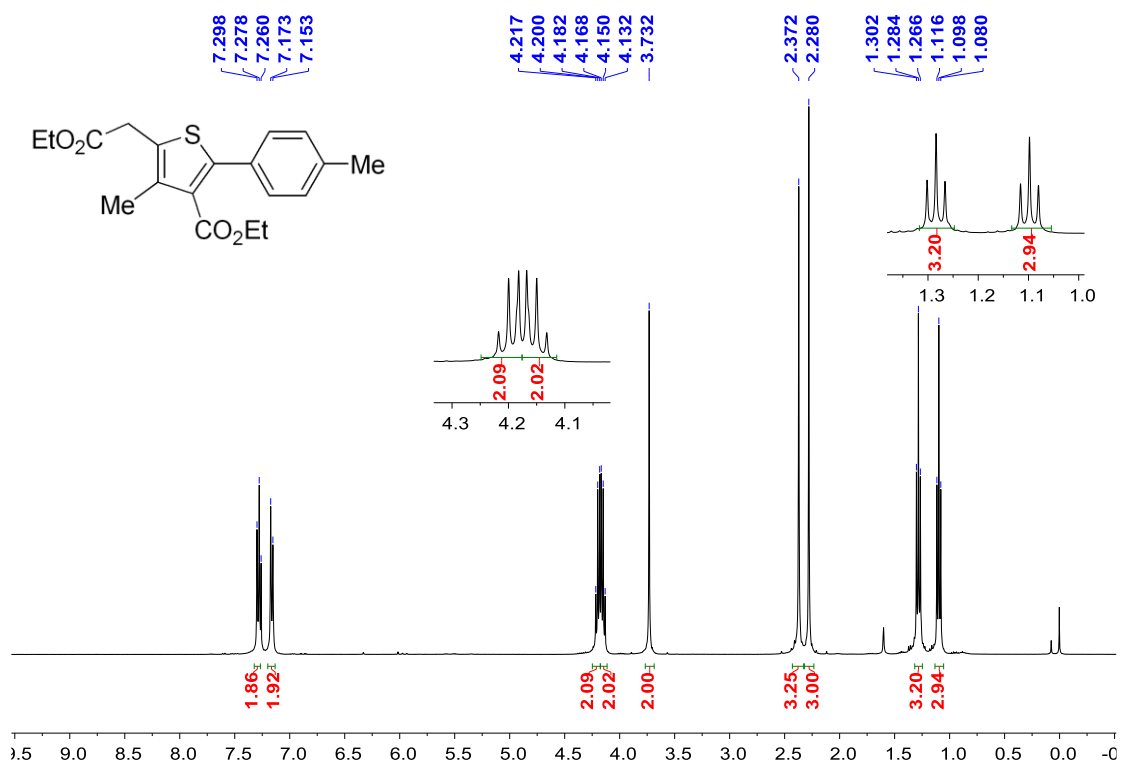


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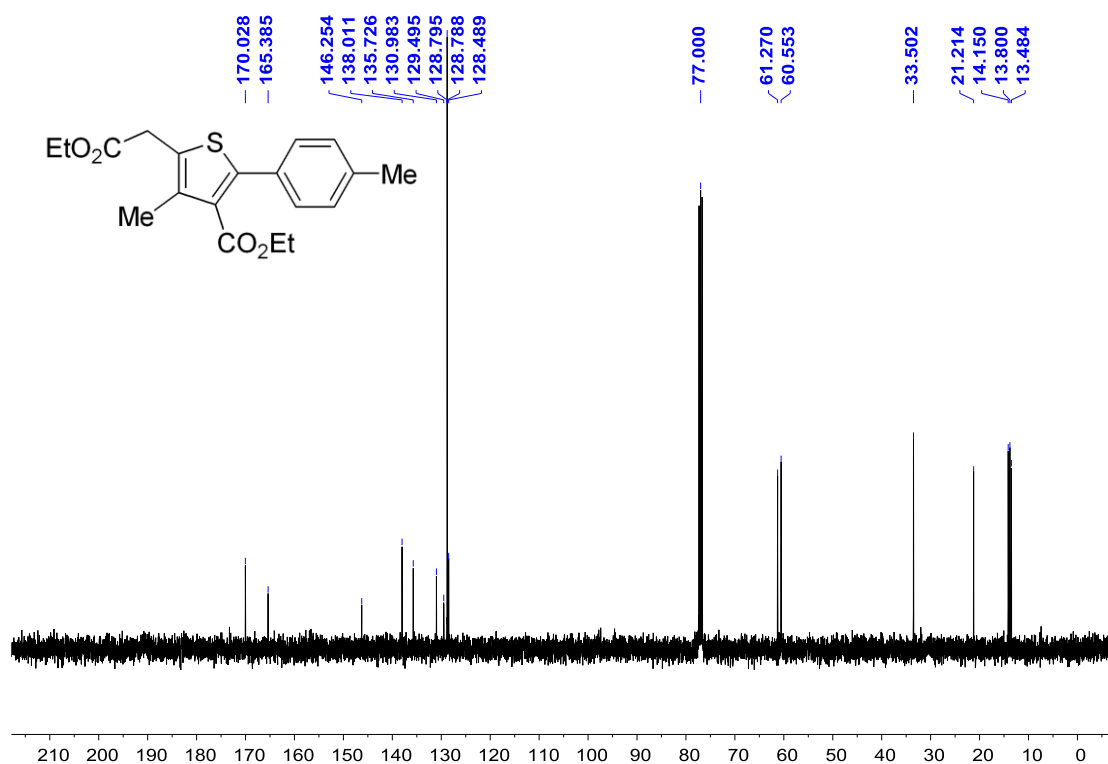


Ethyl 5-(2-ethoxy-2-oxoethyl)-4-methyl-2-(*p*-tolyl)thiophene-3-carboxylate (3eA)

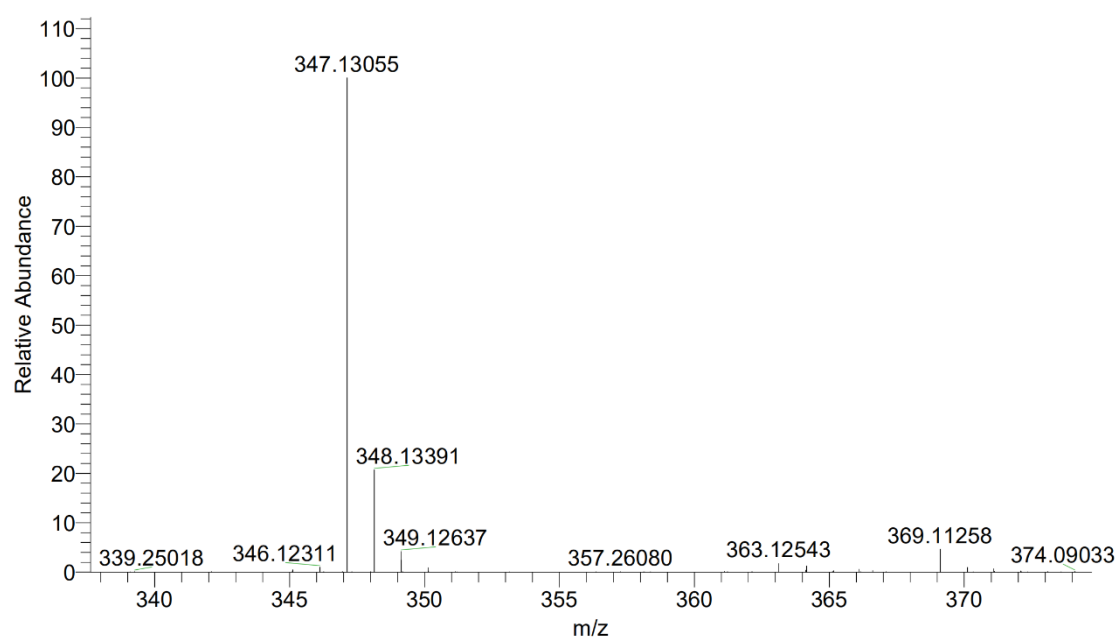
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¹³C NMR (101 MHz, CDCl₃)

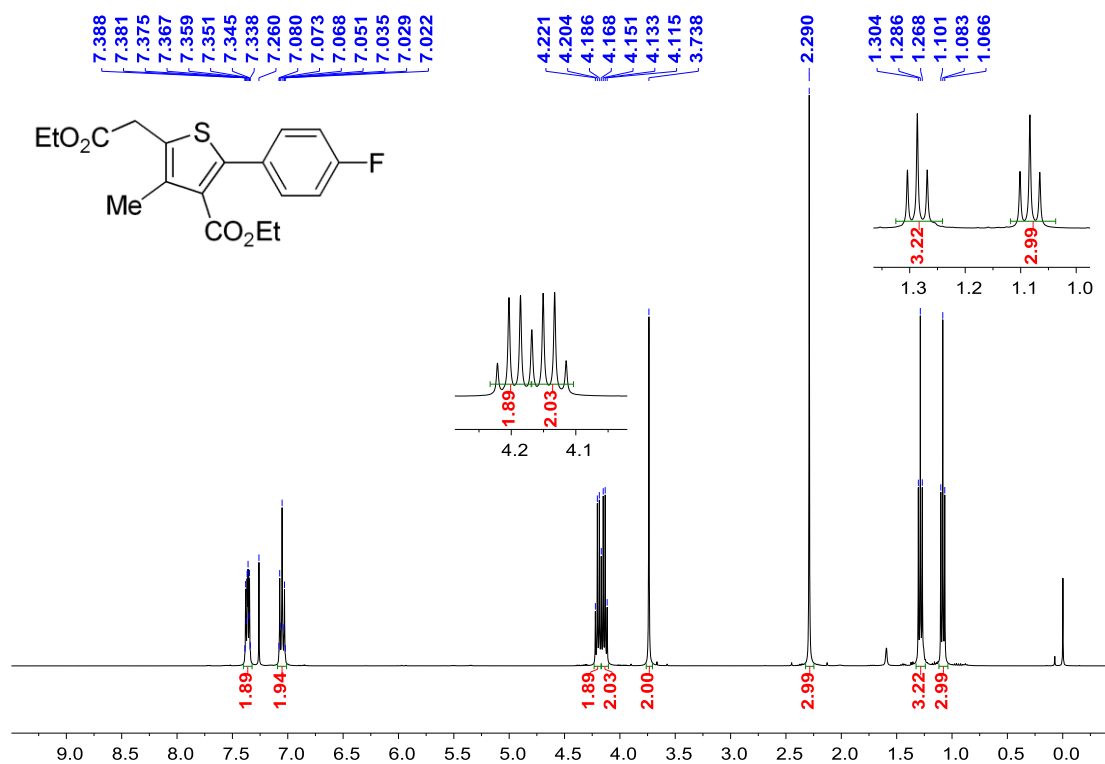


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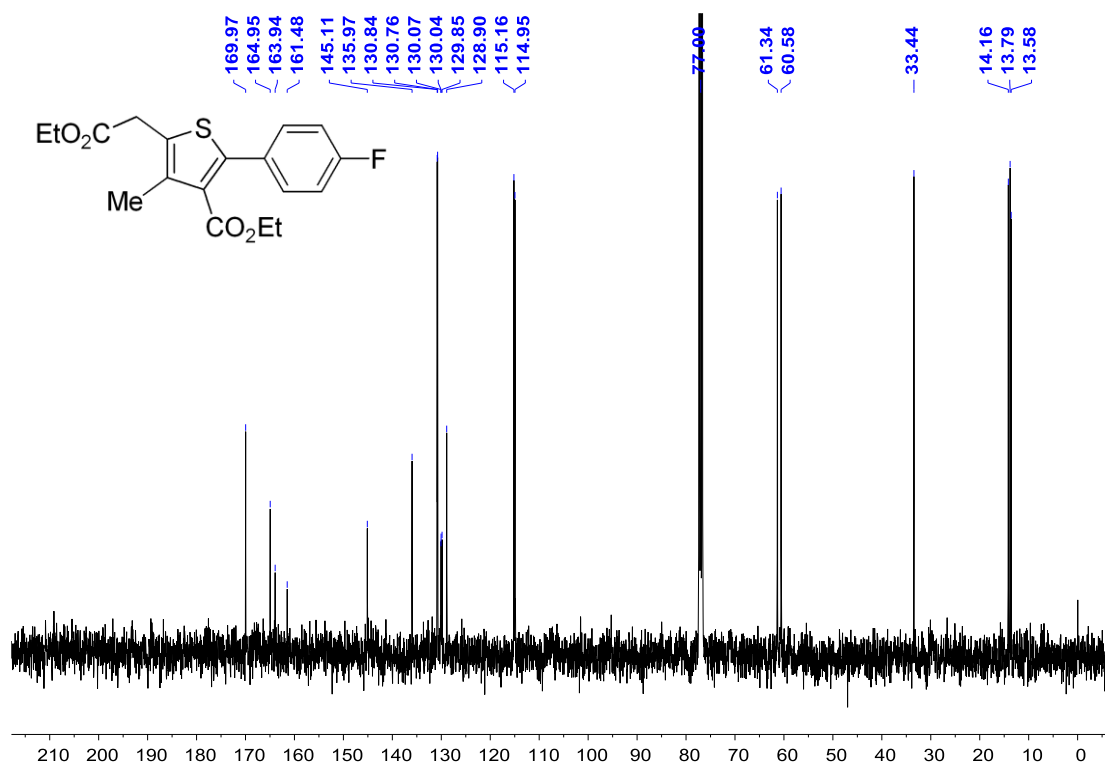


Ethyl 5-(2-ethoxy-2-oxoethyl)-2-(4-fluorophenyl)-4-methylthiophene-3-carboxylate (3fA)

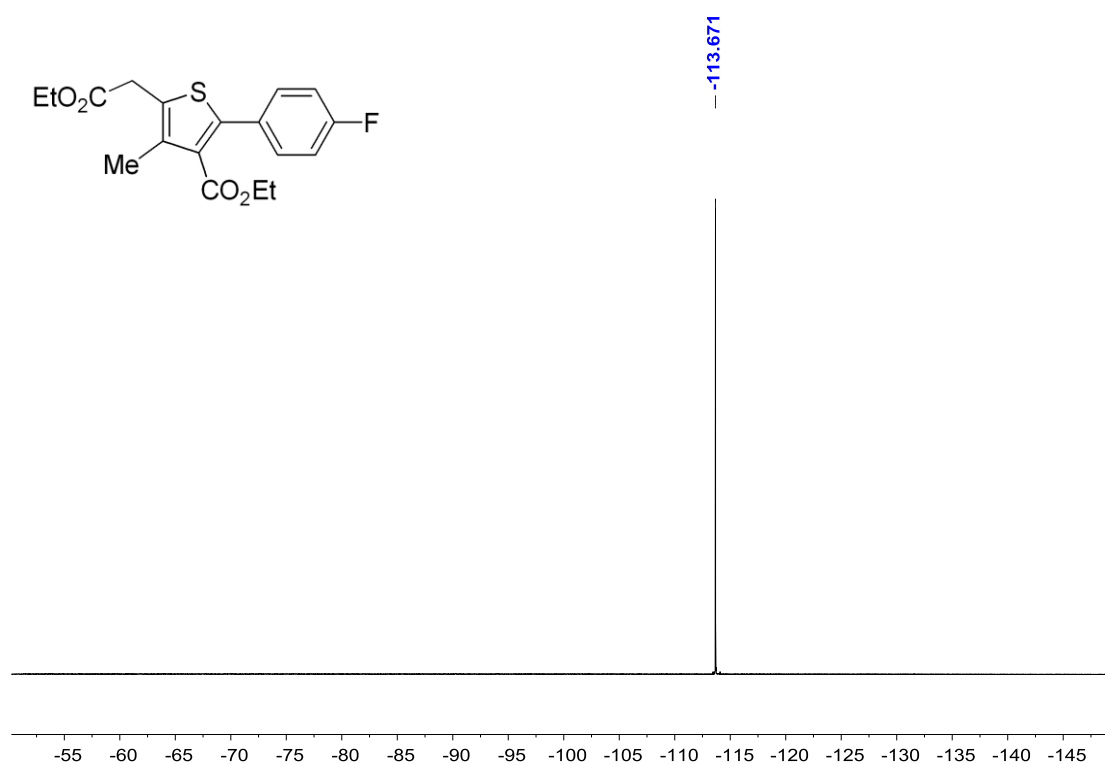
^1H NMR (400 MHz, CDCl_3)



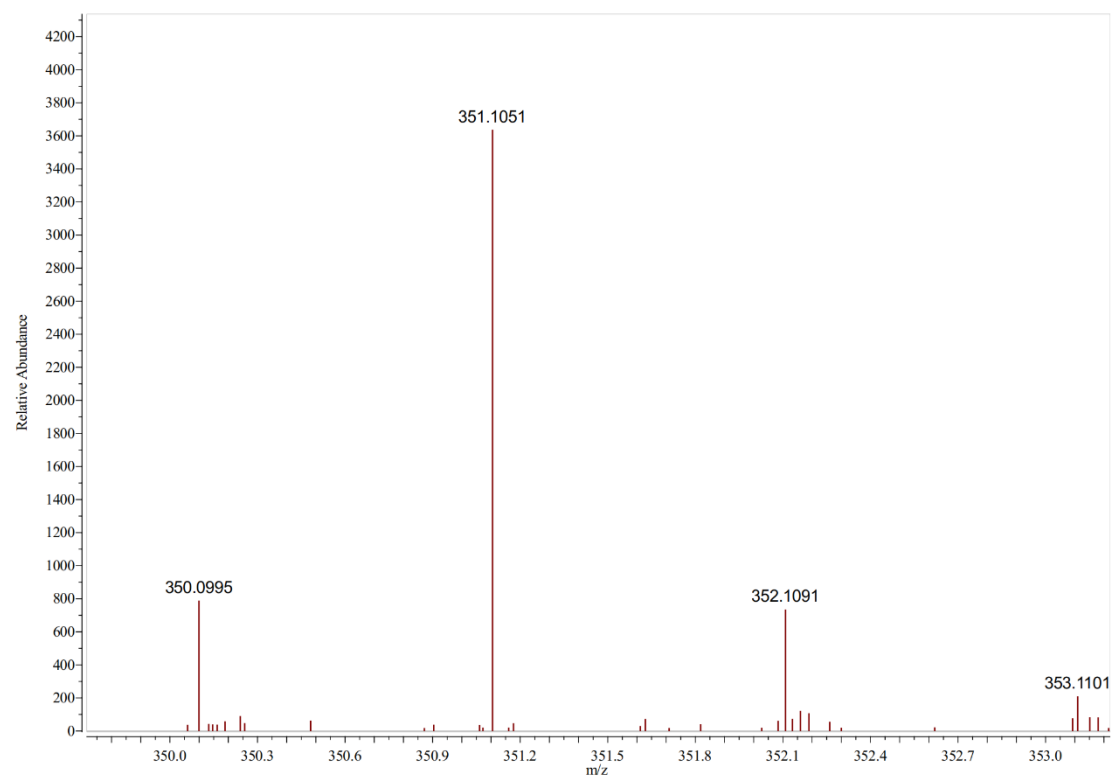
^{13}C NMR (101 MHz, CDCl_3)



¹⁹F NMR (377 MHz, CDCl₃)

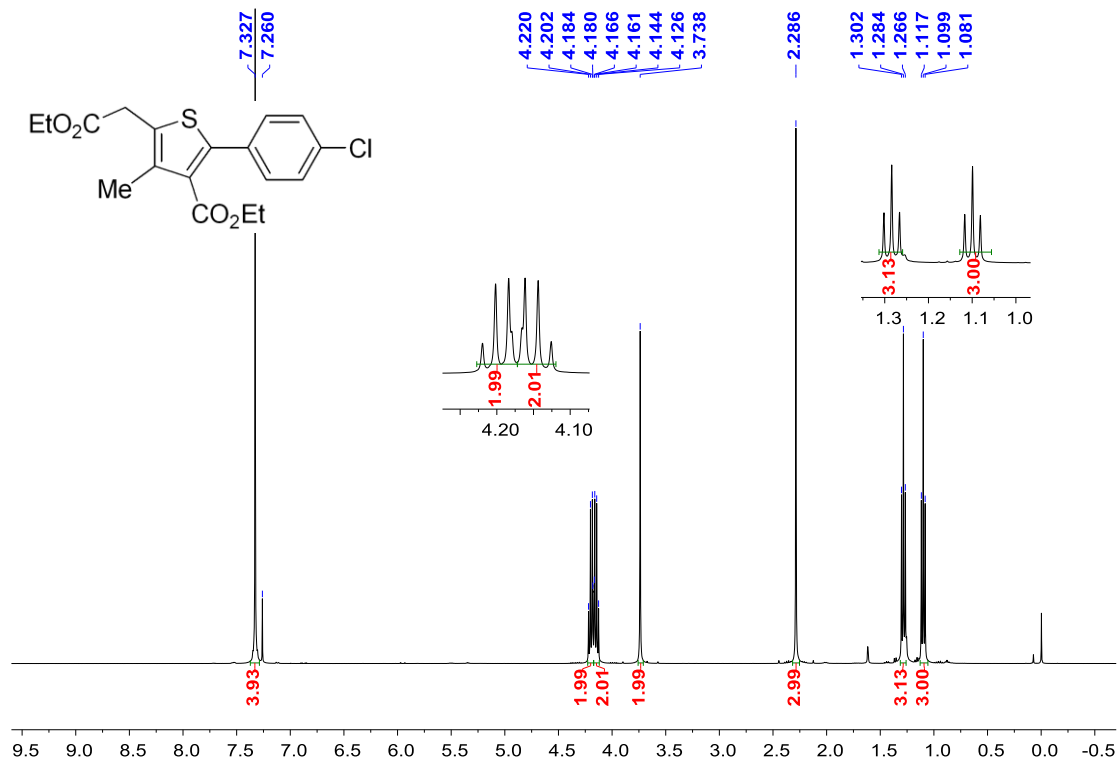


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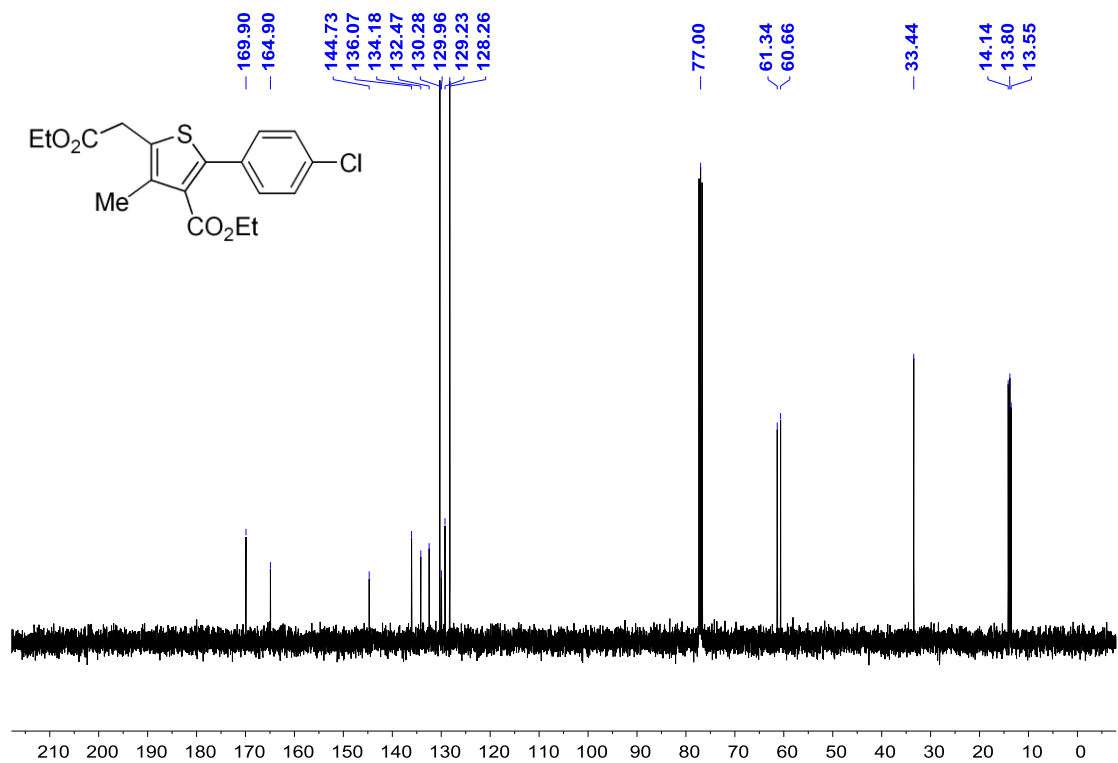


Ethyl 2-(4-chlorophenyl)-5-(2-ethoxy-2-oxoethyl)-4-methylthiophene-3-carboxylate (3gA)

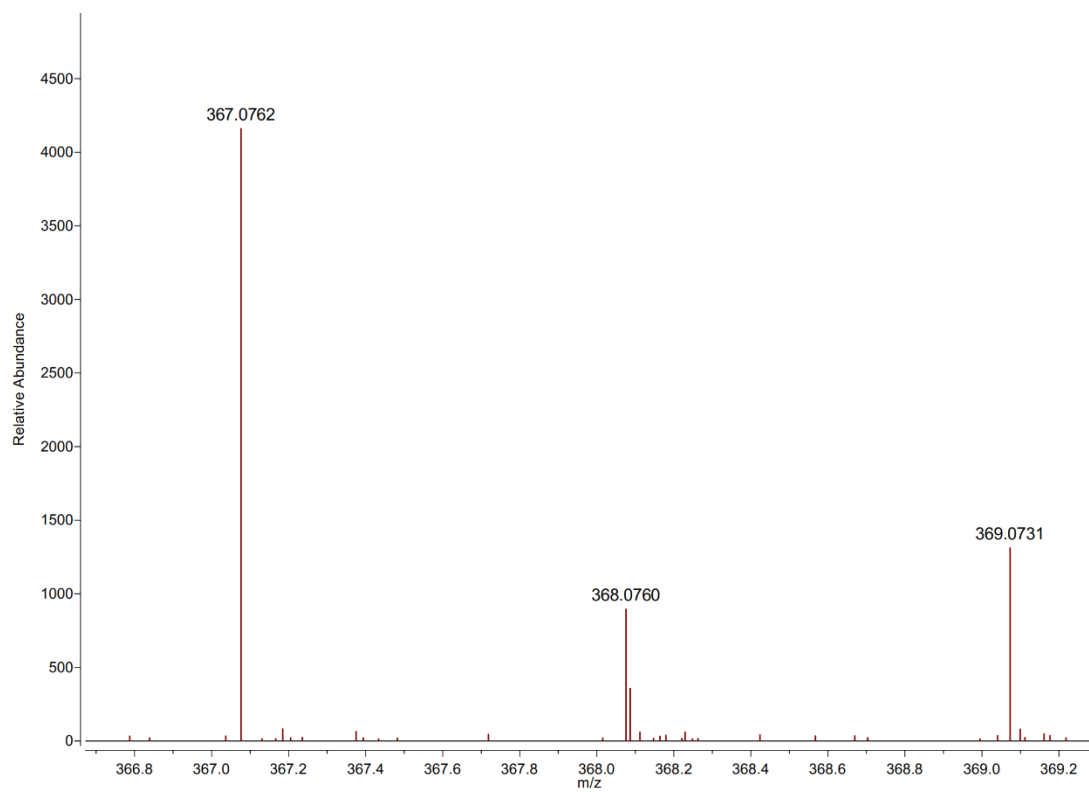
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¹³C NMR (101 MHz, CDCl₃)



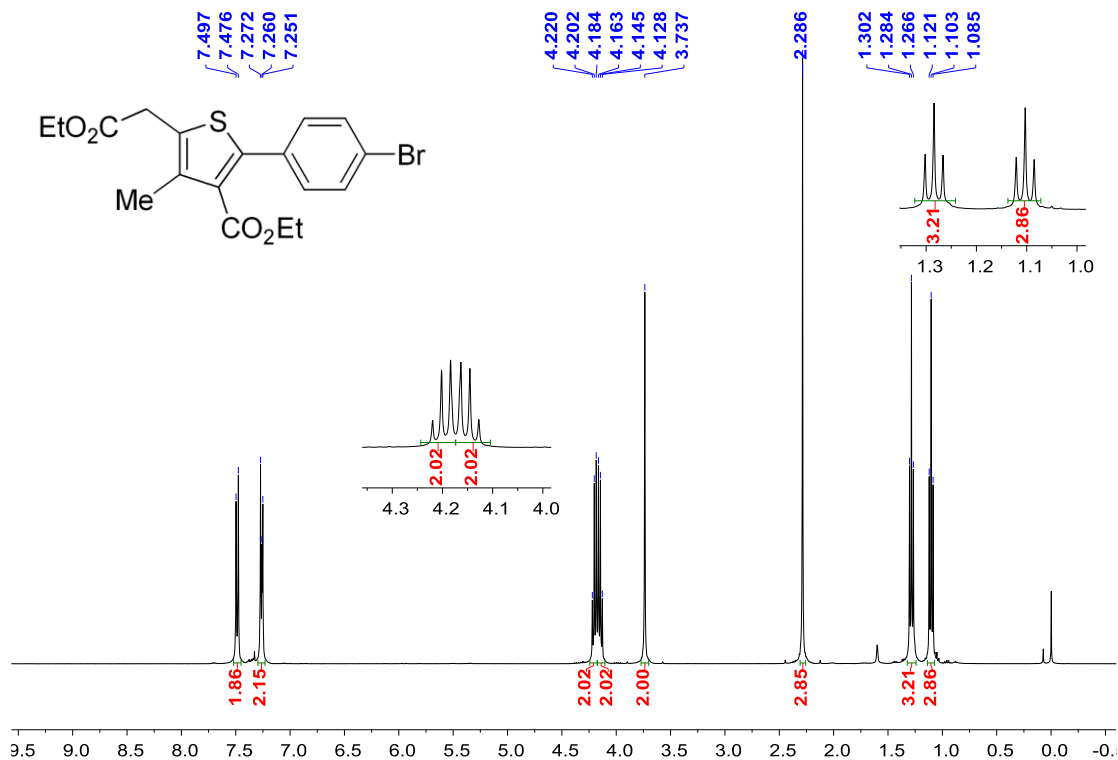
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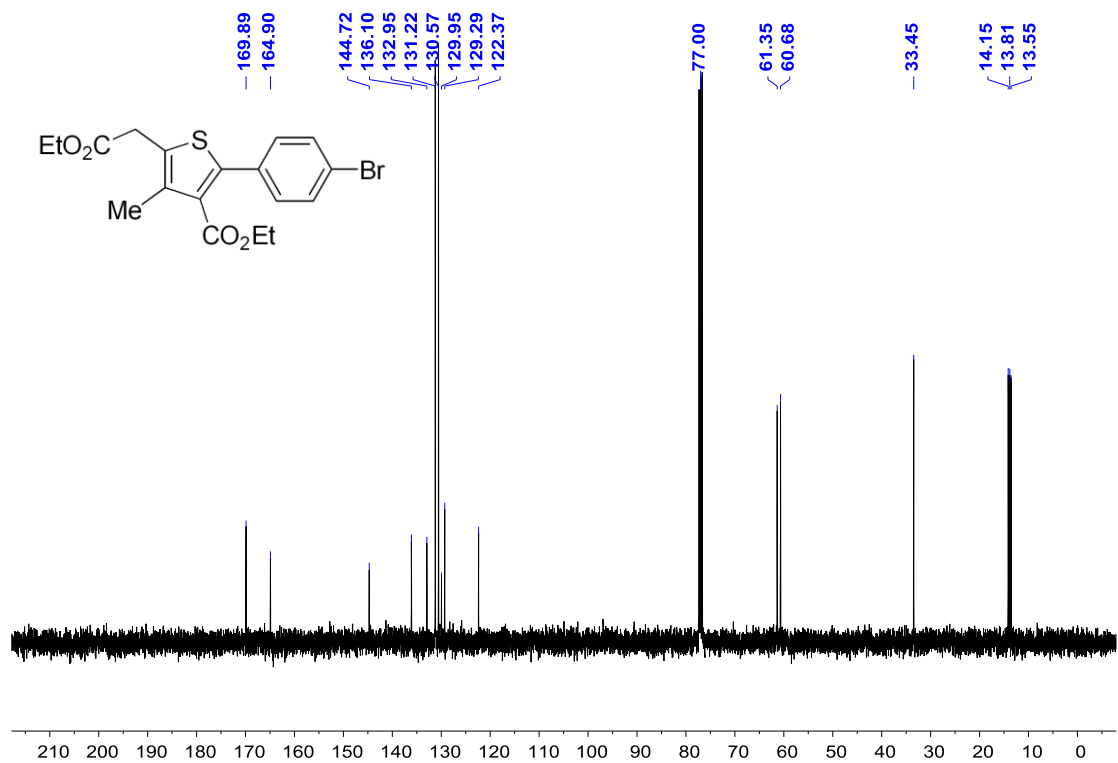
Ethyl 2-(4-bromophenyl)-5-(2-ethoxy-2-oxoethyl)-4-methylthiophene-3-carboxylate (3h)

A)

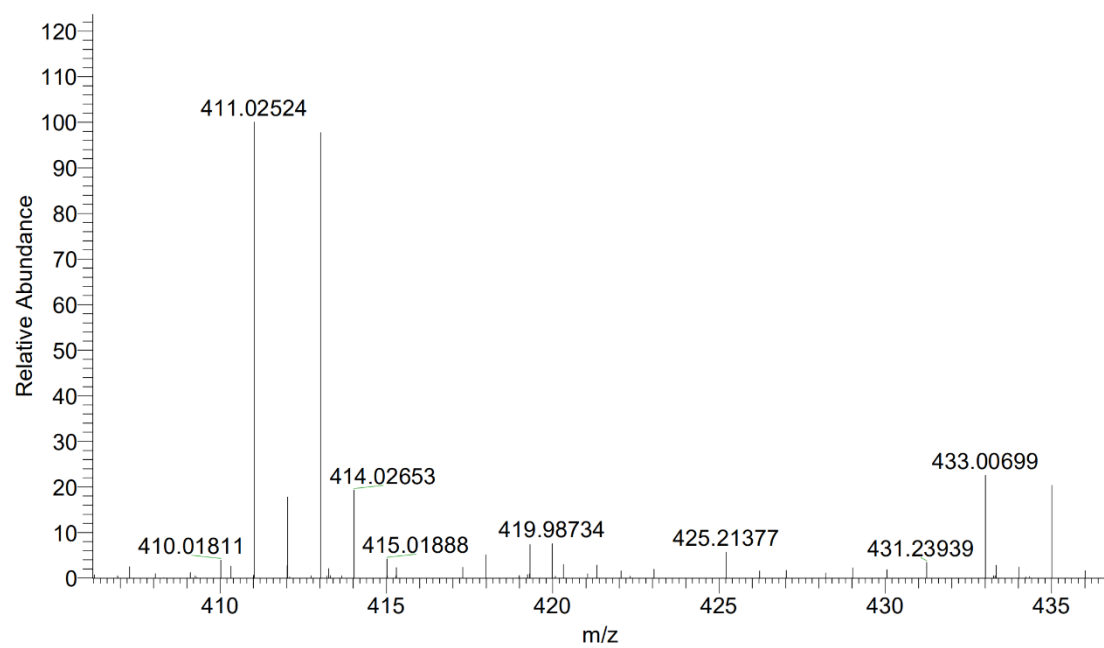
$^1\text{H NMR}$ (400 MHz, CDCl_3)



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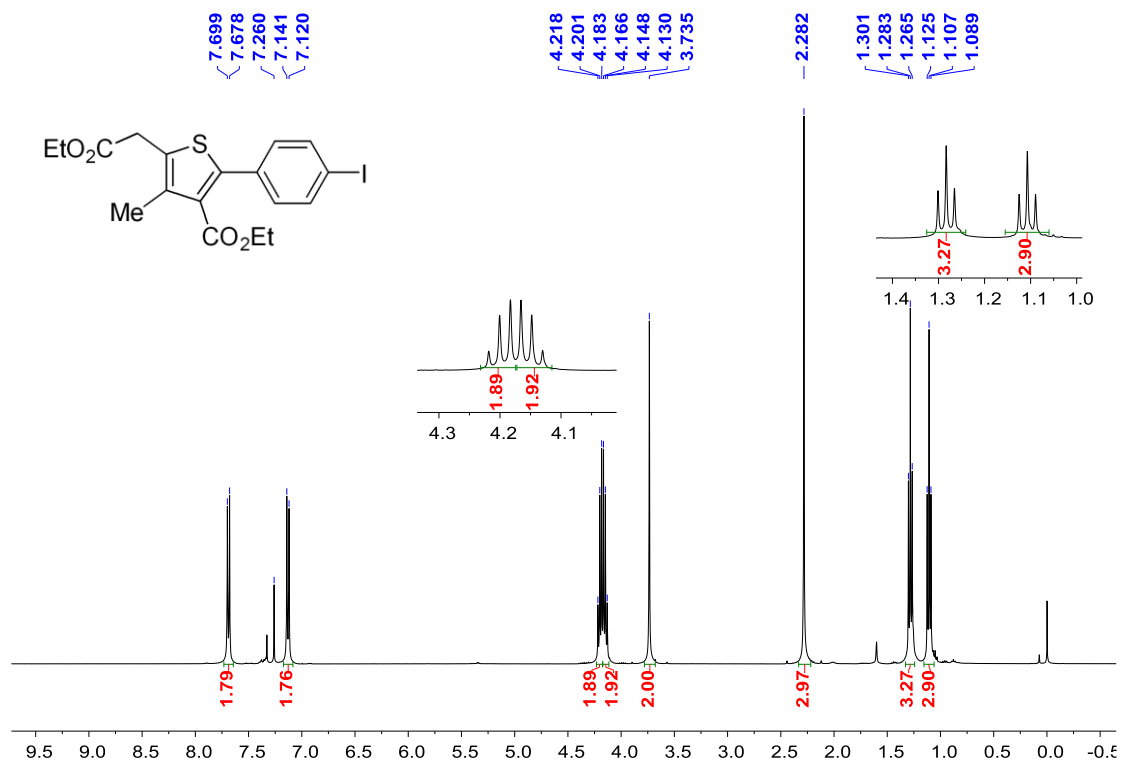


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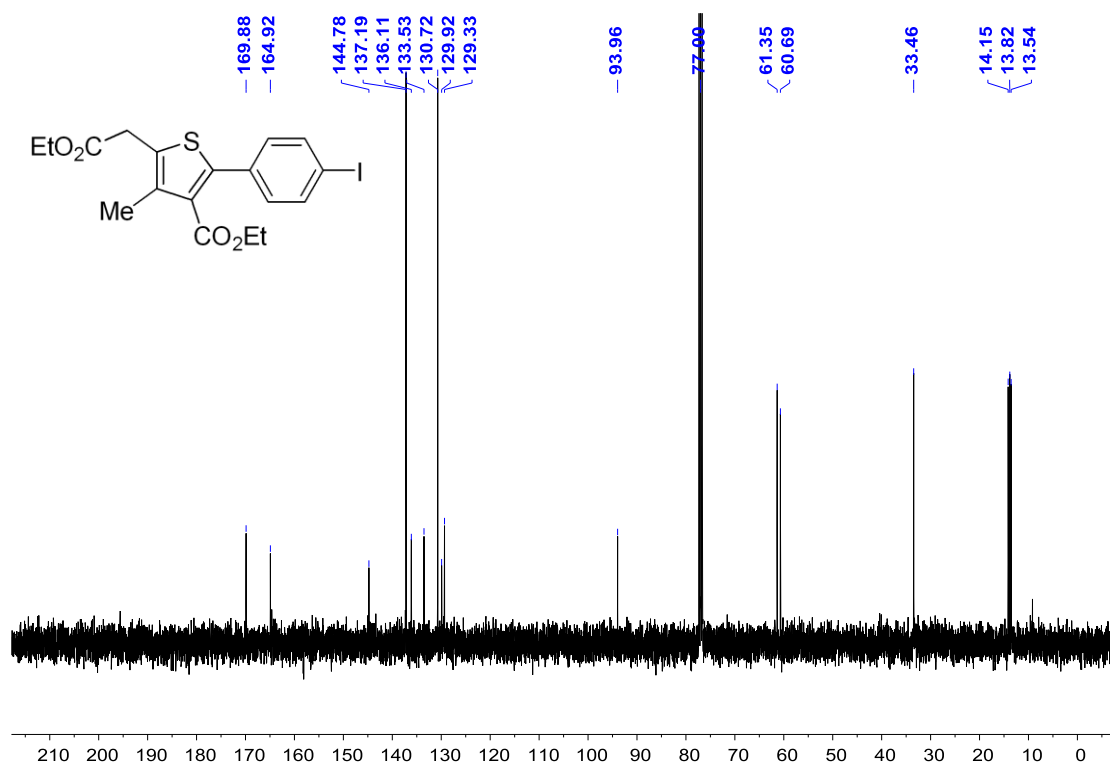


Ethyl 5-(2-ethoxy-2-oxoethyl)-2-(4-iodophenyl)-4-methylthiophene-3-carboxylate (3iA)

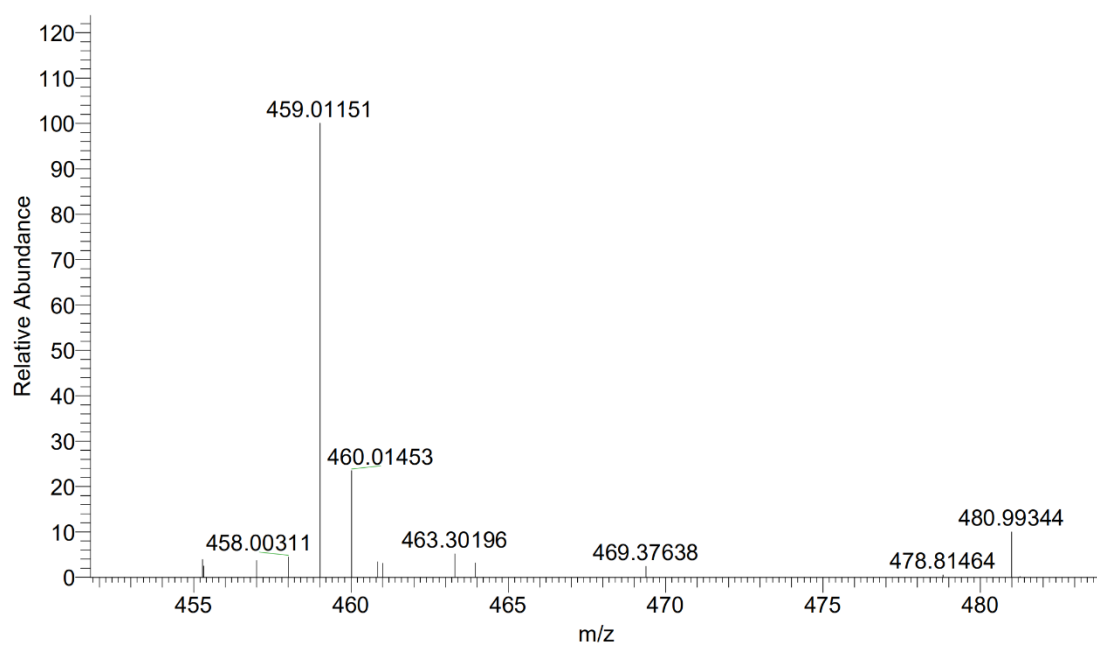
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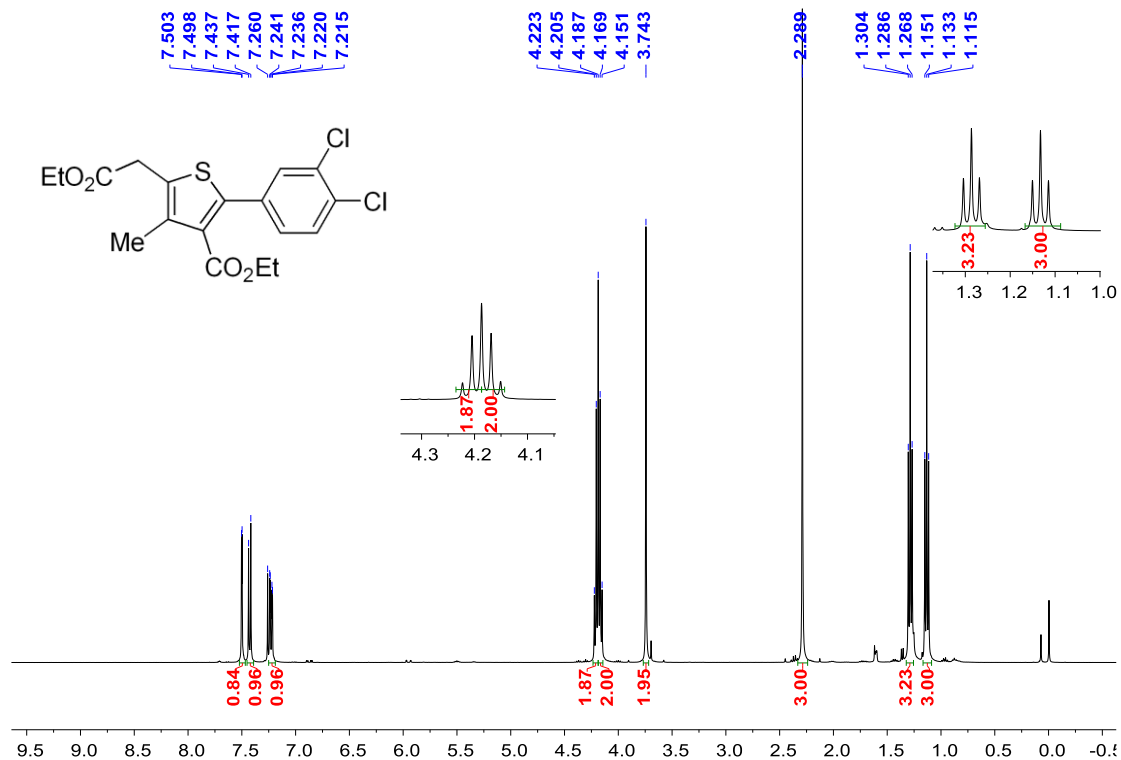


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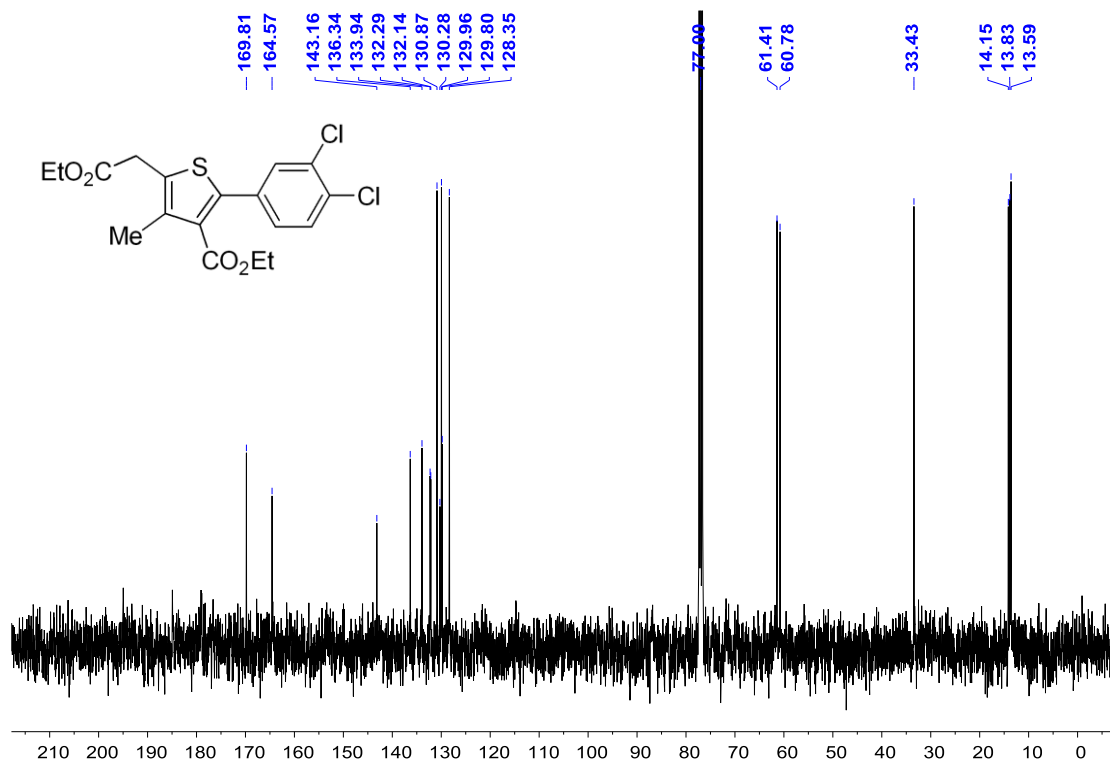


Ethyl 2-(3,4-dichlorophenyl)-5-(2-ethoxy-2-oxoethyl)-4-methylthiophene-3-carboxylate
(3jA)

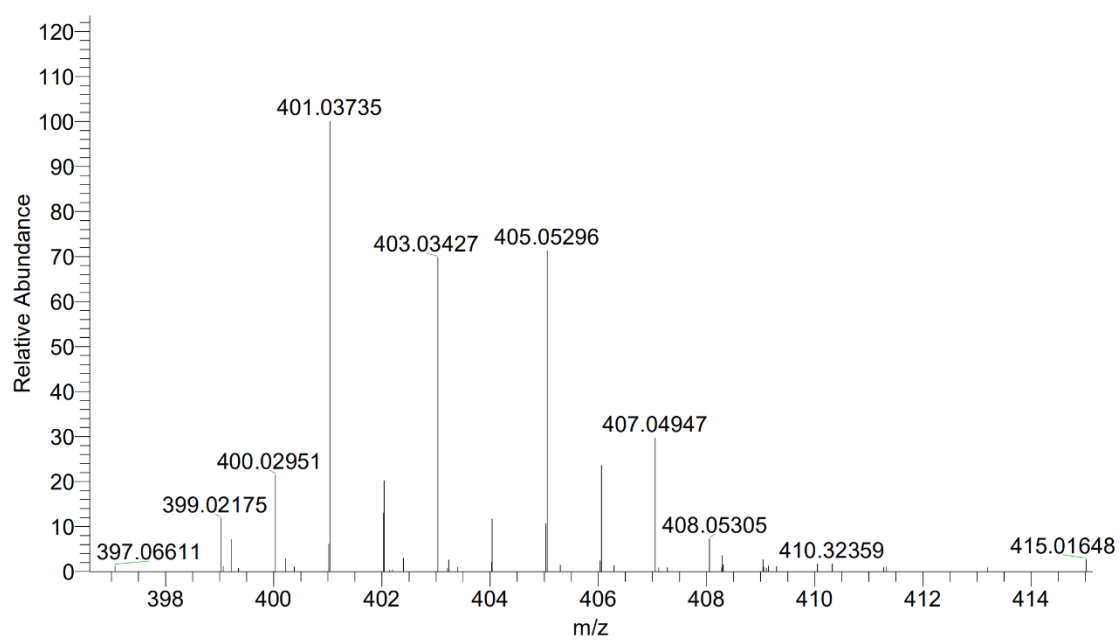
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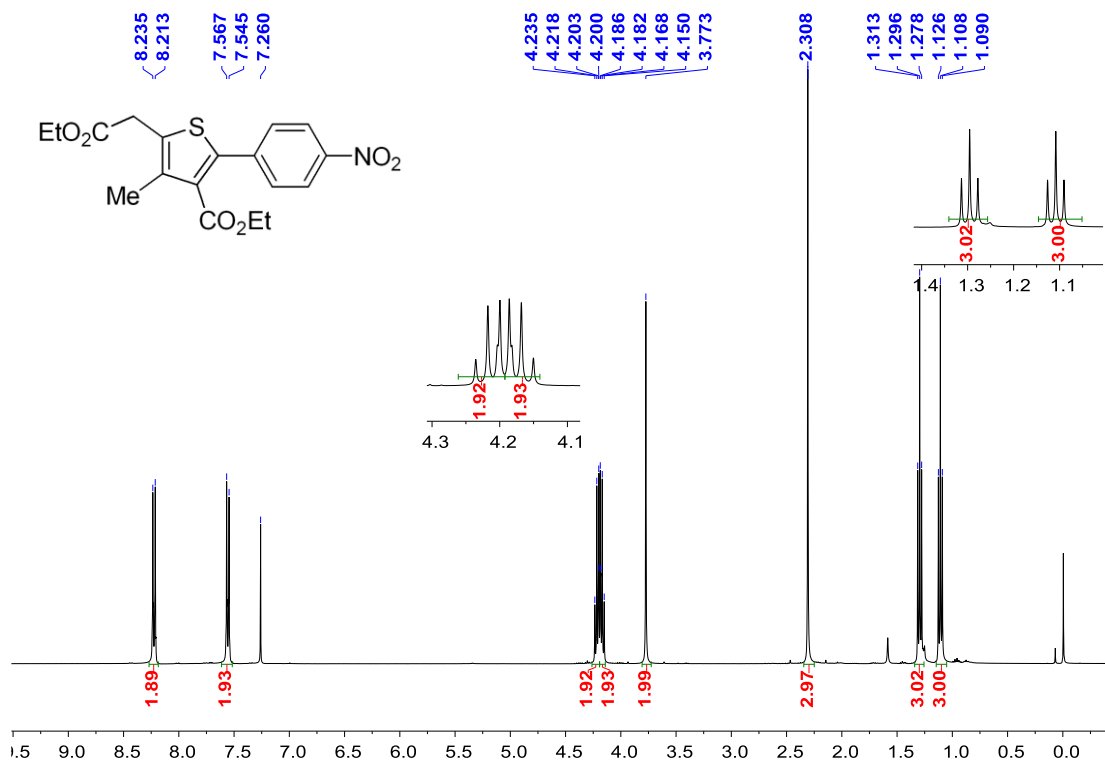


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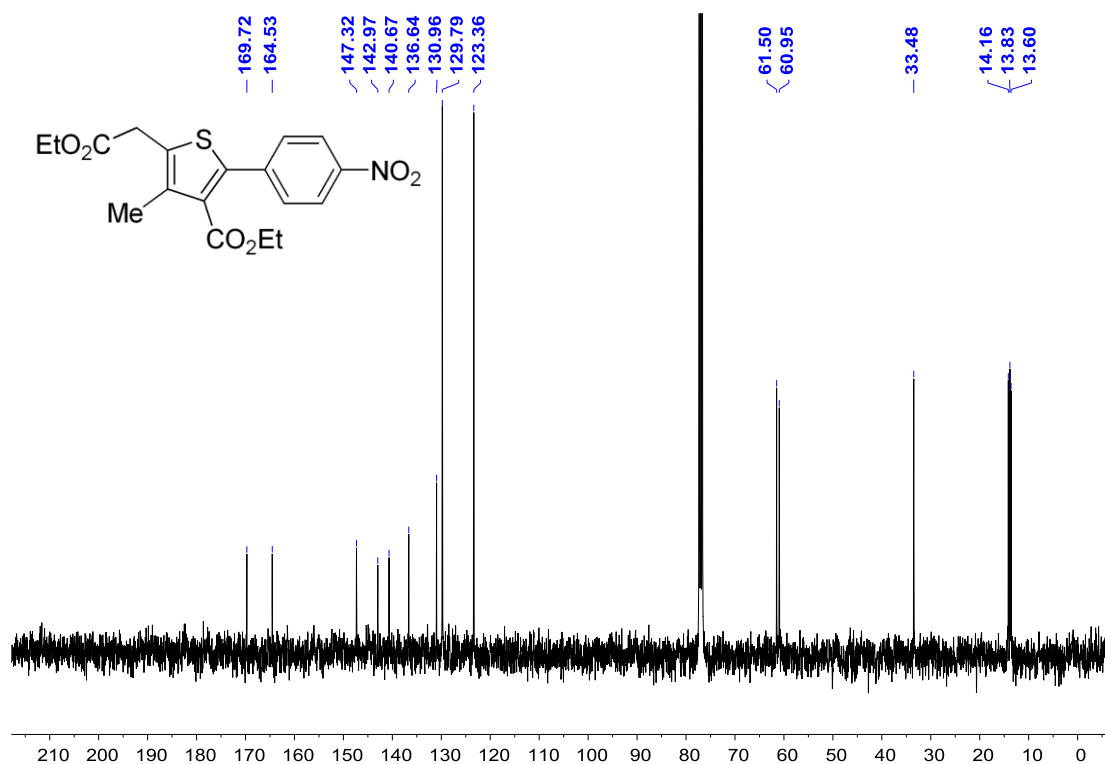


Ethyl 5-(2-ethoxy-2-oxoethyl)-4-methyl-2-(4-nitrophenyl)thiophene-3-carboxylate (3kA)

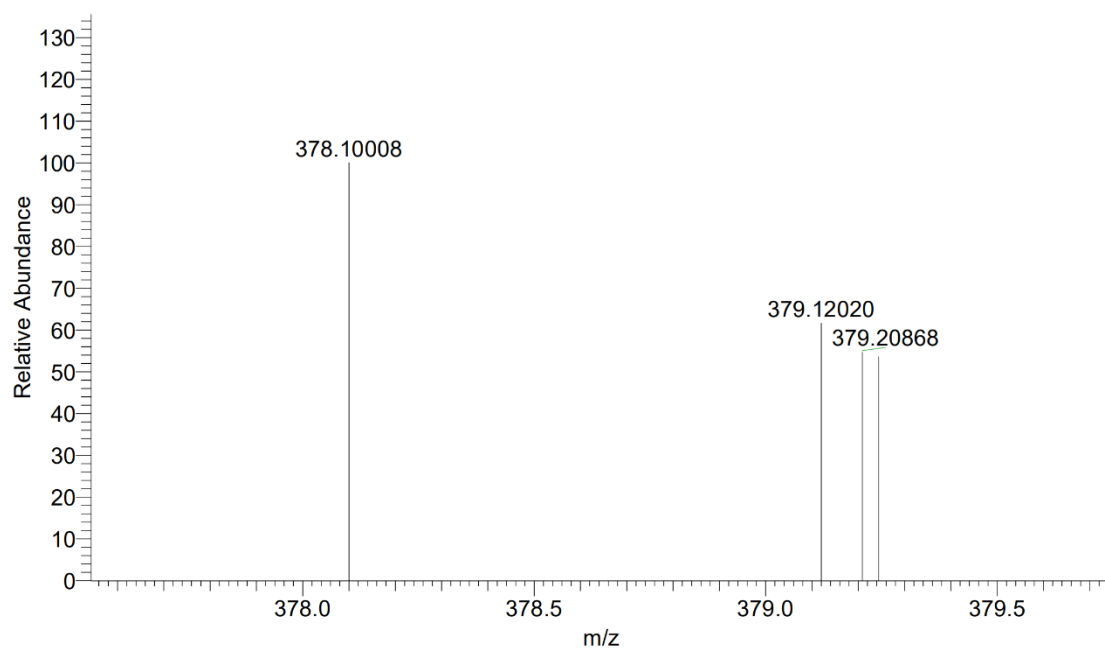
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¹³C NMR (101 MHz, CDCl₃)

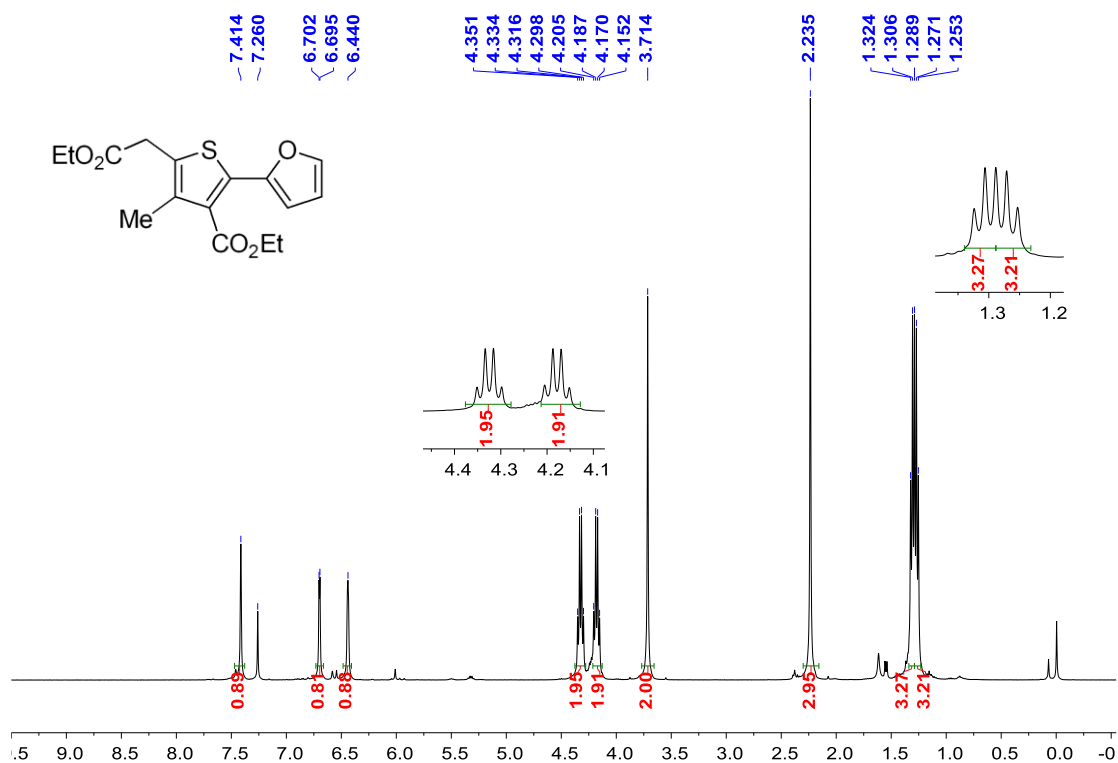


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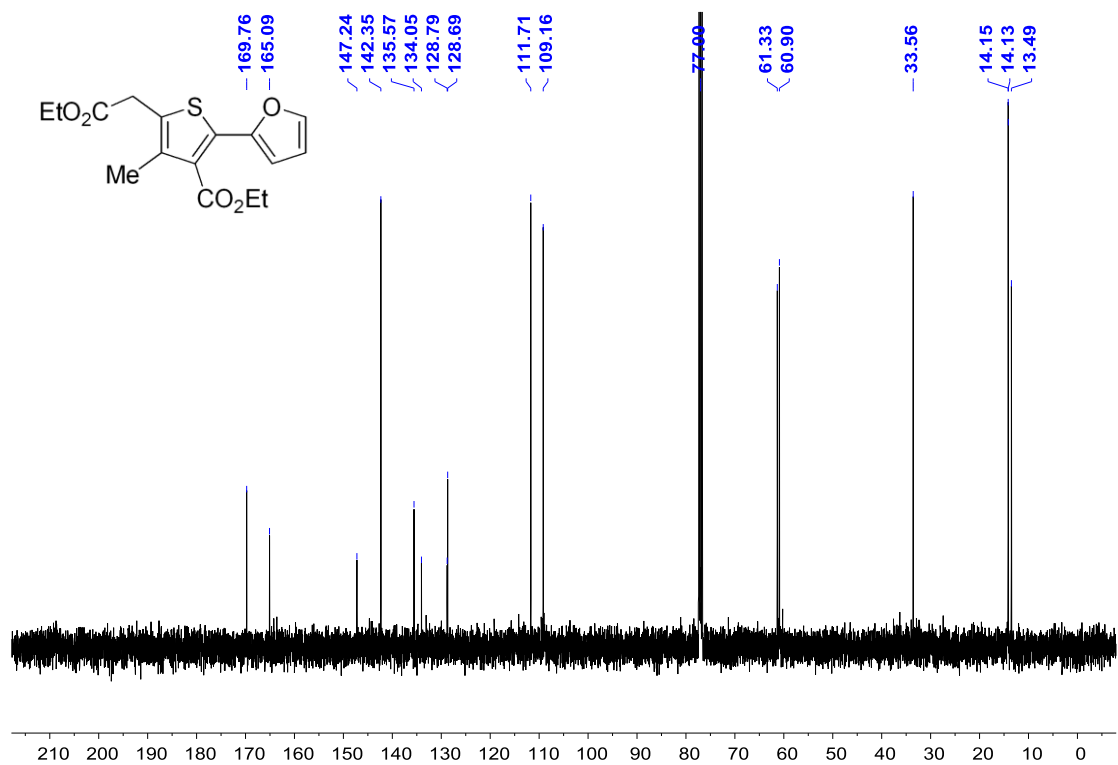


Ethyl 5-(2-ethoxy-2-oxoethyl)-2-(furan-2-yl)-4-methylthiophene-3-carboxylate (31A)

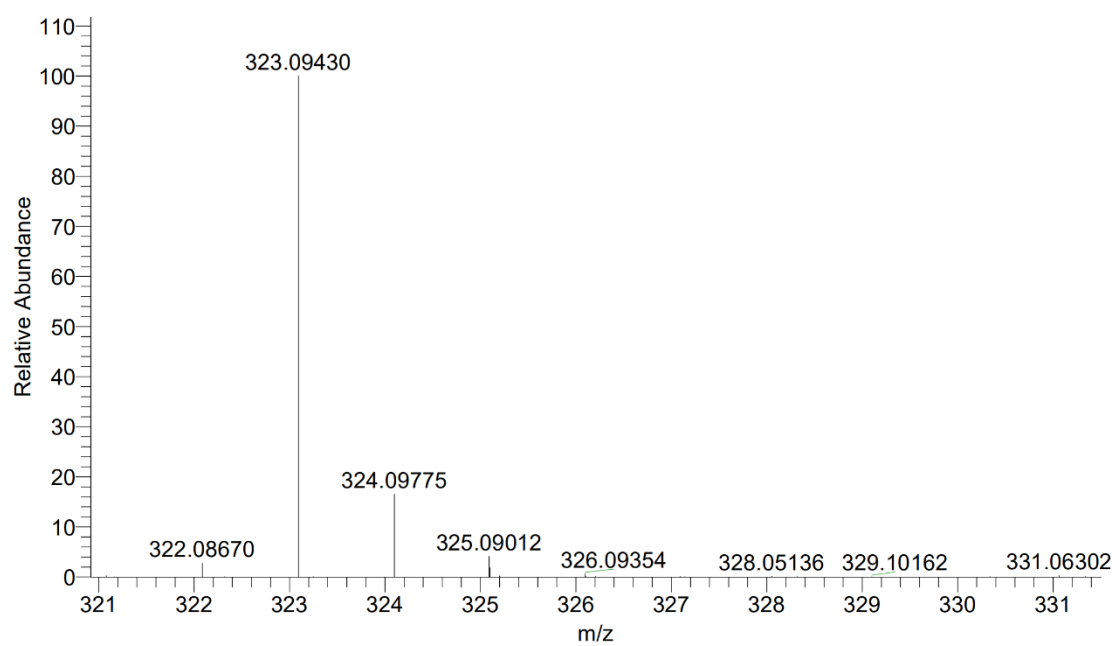
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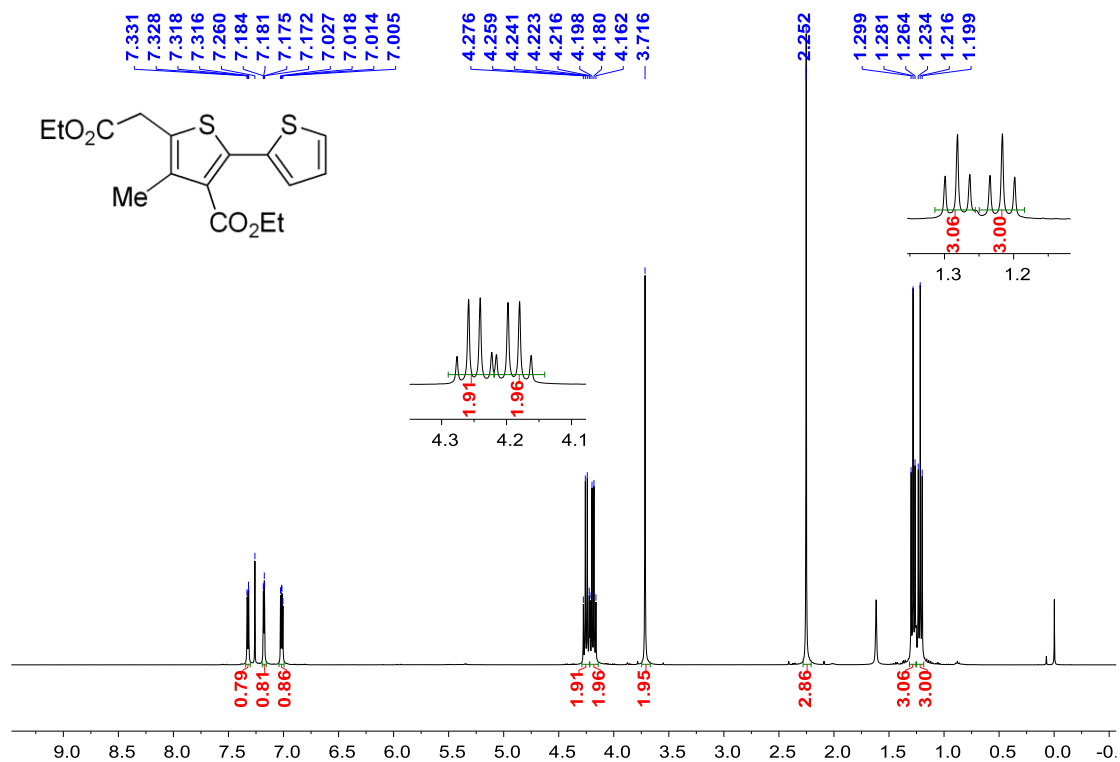


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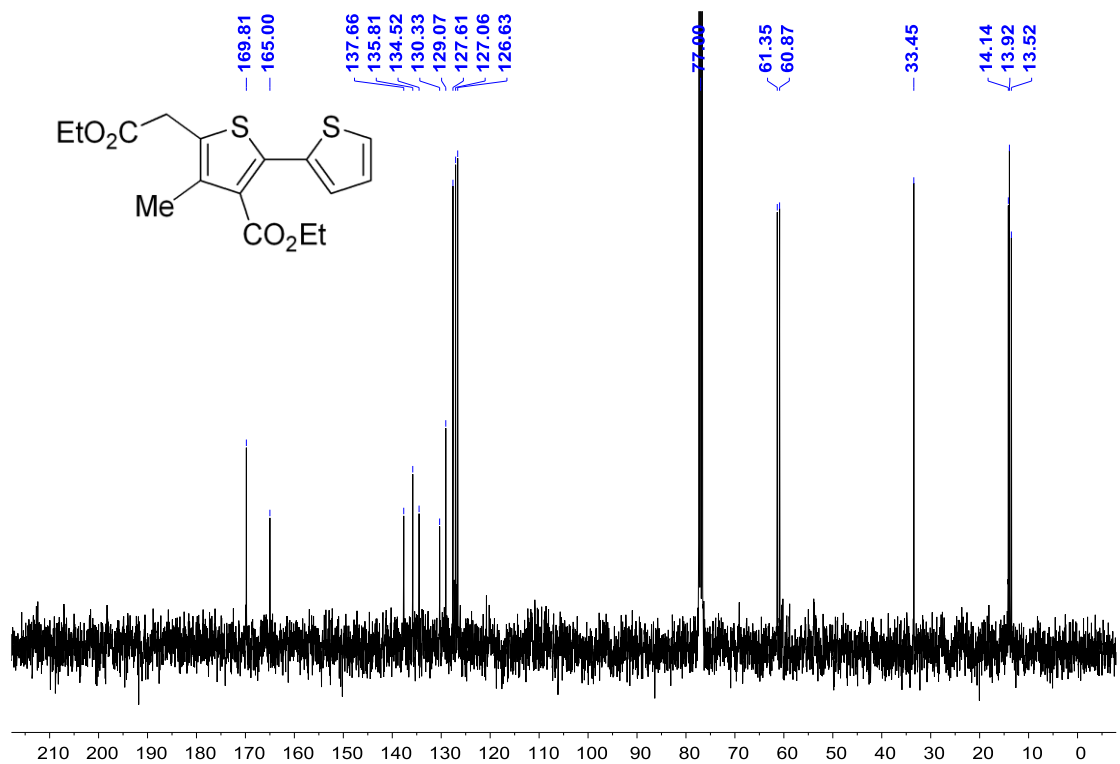


Ethyl 5-(2-ethoxy-2-oxoethyl)-4-methyl-[2,2'-bithiophene]-3-carboxylate (3mA)

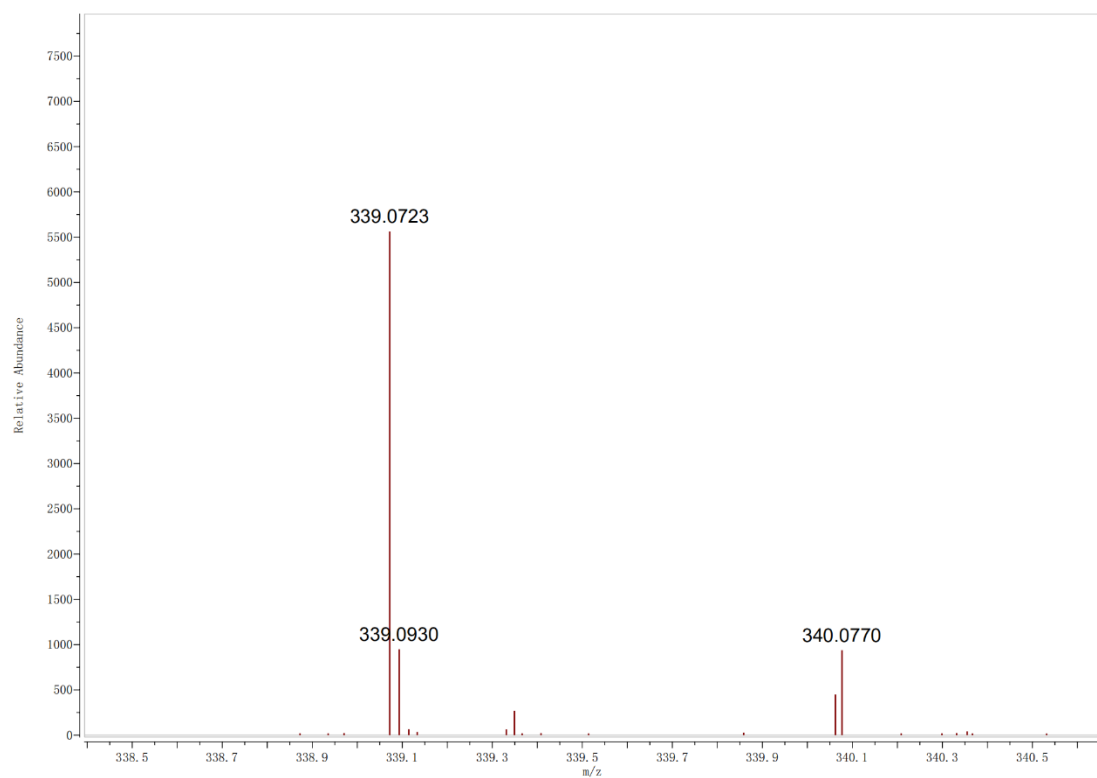
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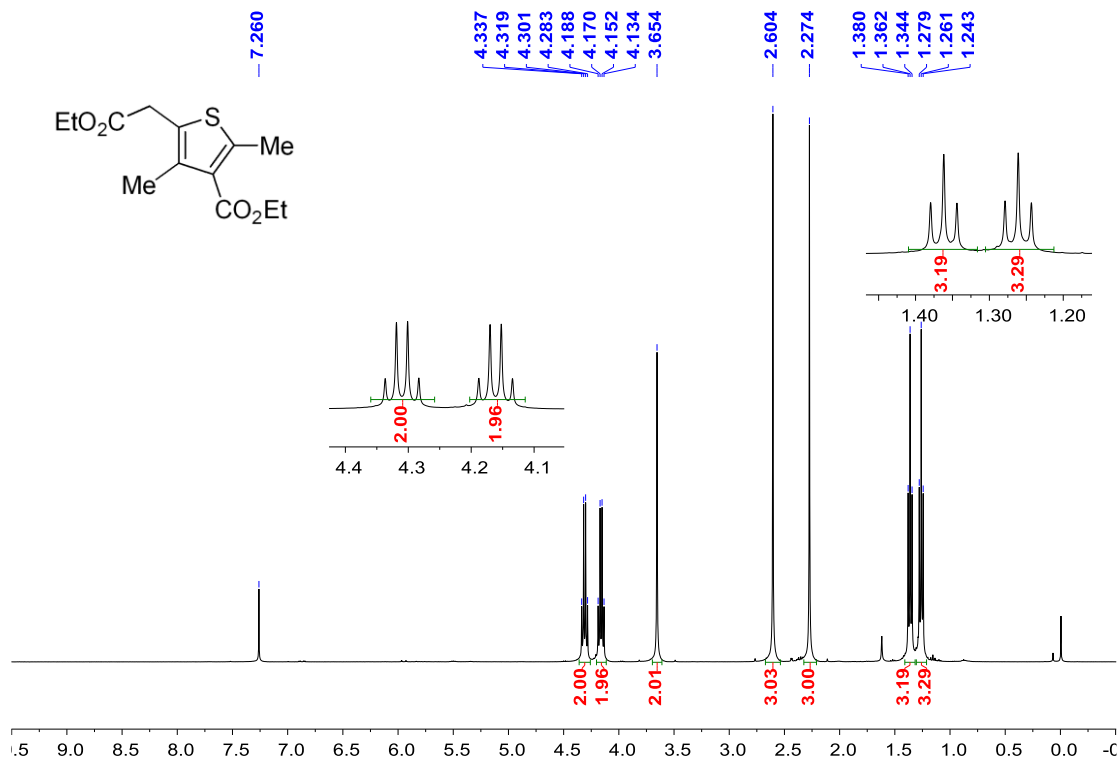


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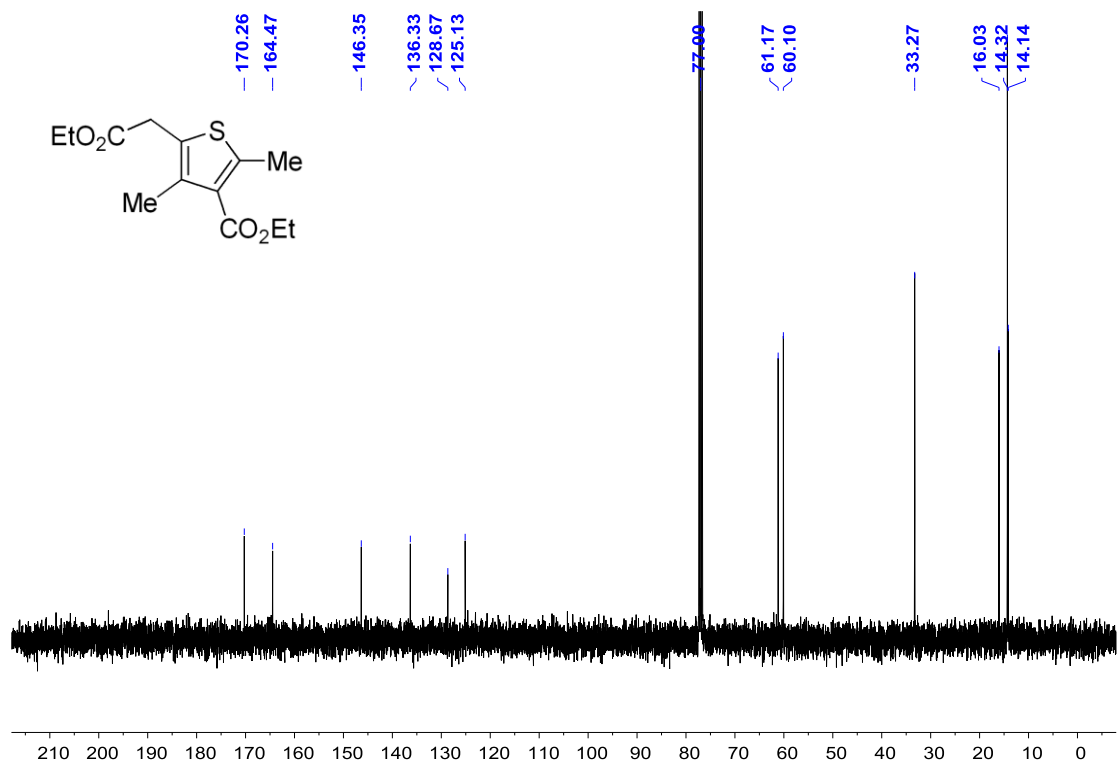


Ethyl 5-(2-ethoxy-2-oxoethyl)-2,4-dimethylthiophene-3-carboxylate (3nA)

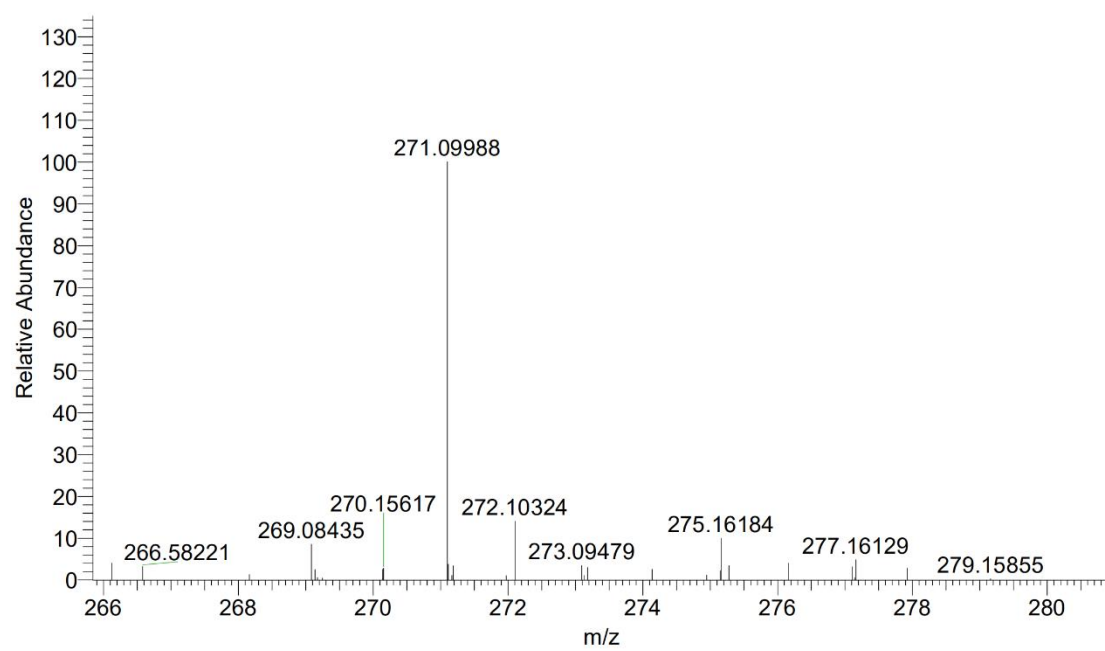
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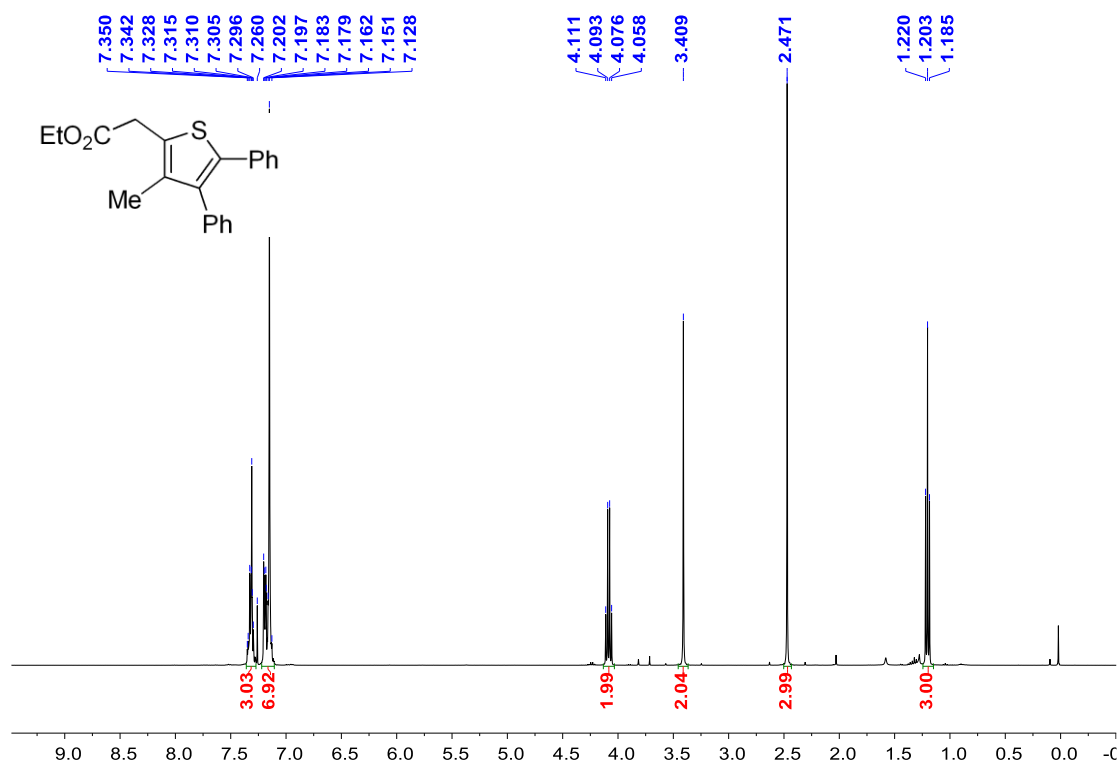


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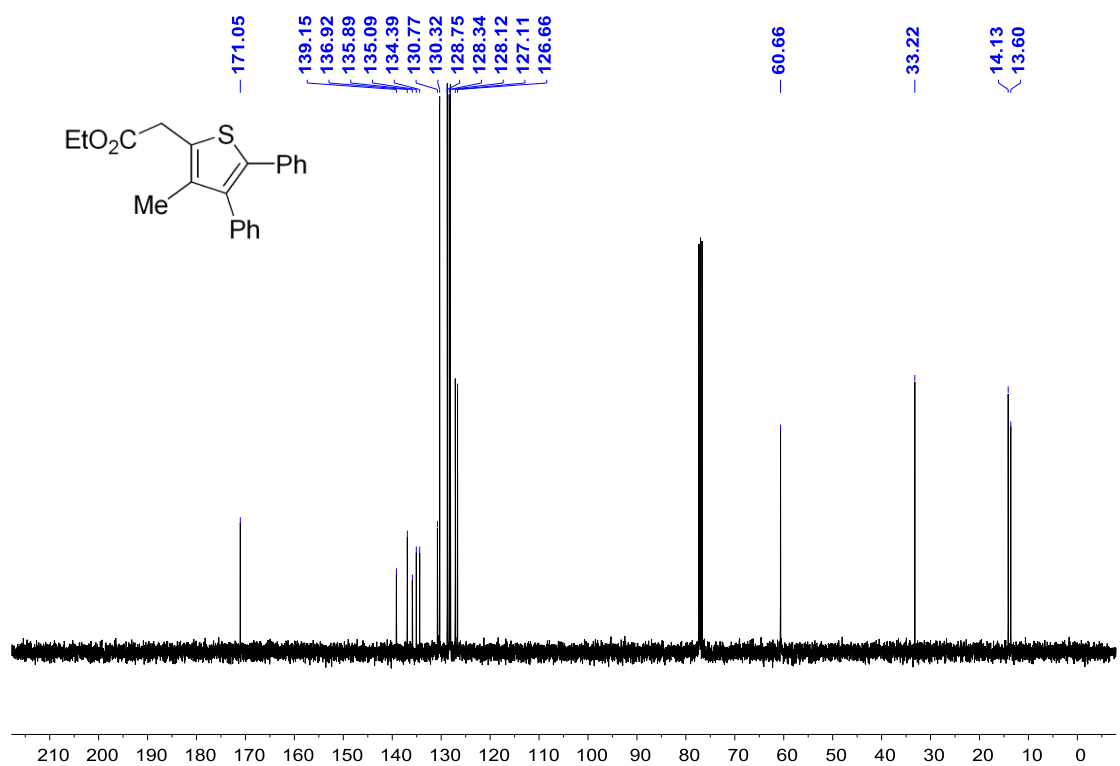


Ethyl 2-(3-methyl-4,5-diphenylthiophen-2-yl)acetate (3oA)

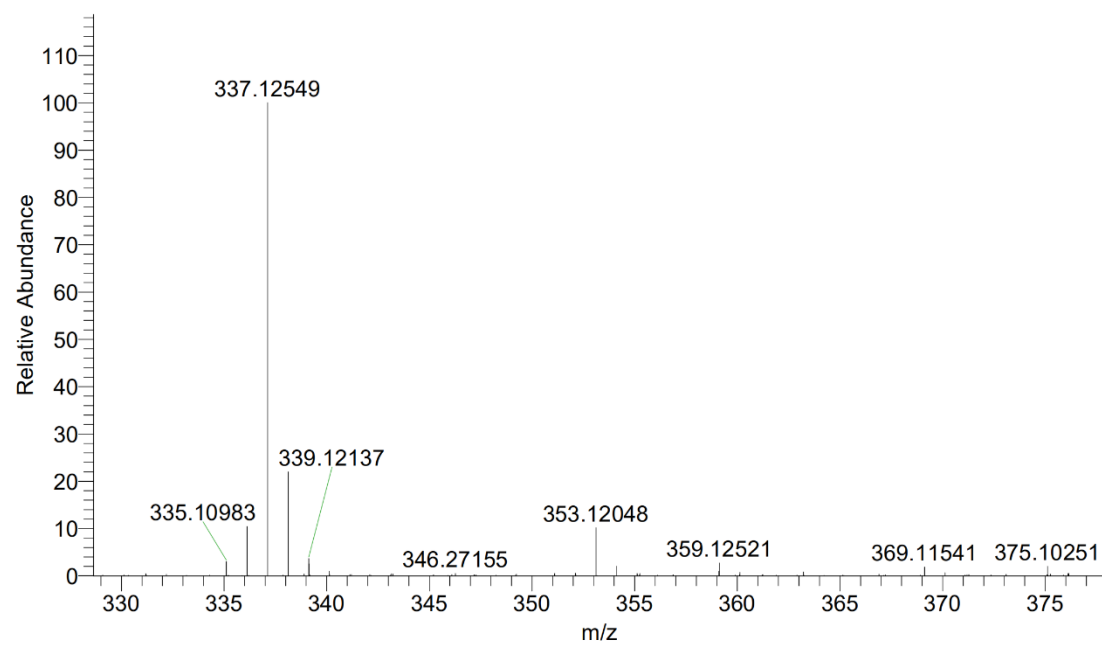
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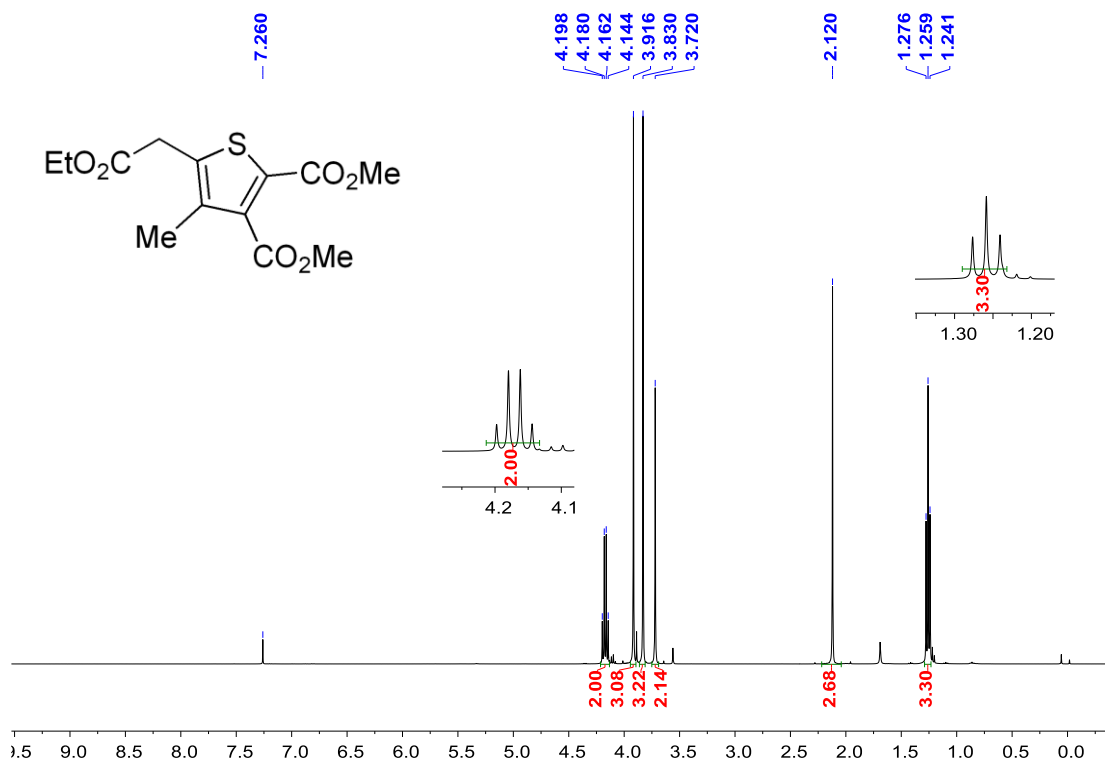


HRMS (ESI)

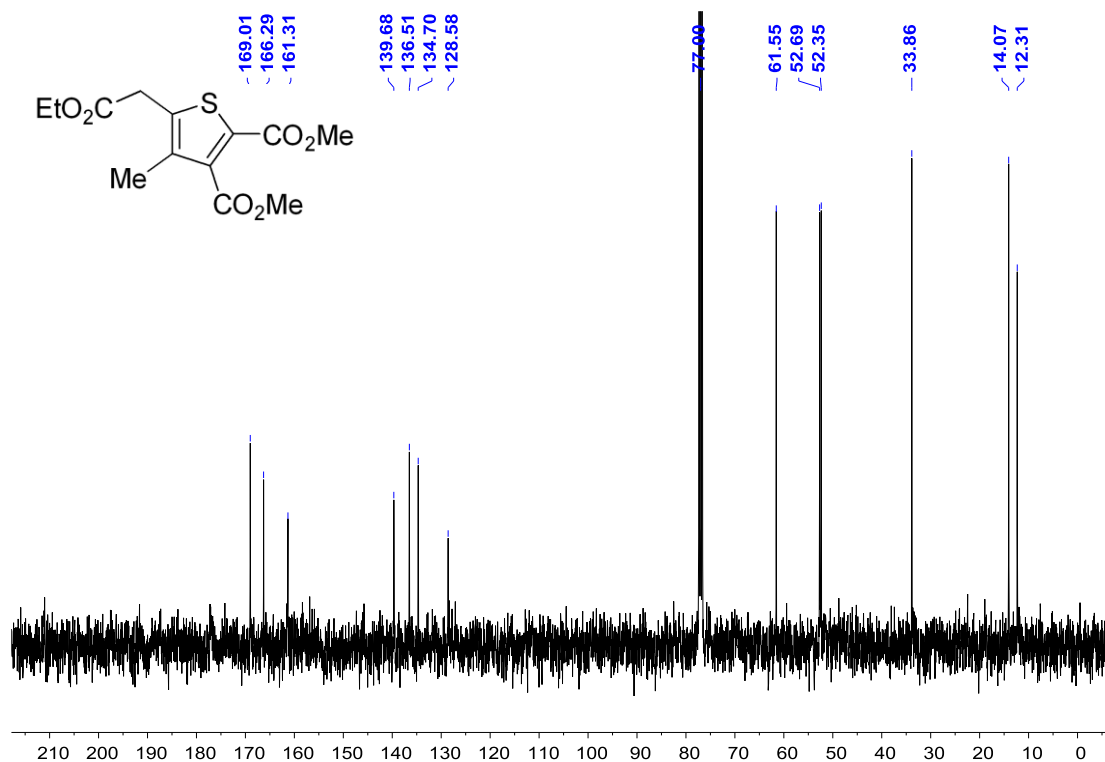


Dimethyl 5-(2-ethoxy-2-oxoethyl)-4-methylthiophene-2,3-dicarboxylate (3pA)

^1H NMR (400 MHz, CDCl_3)

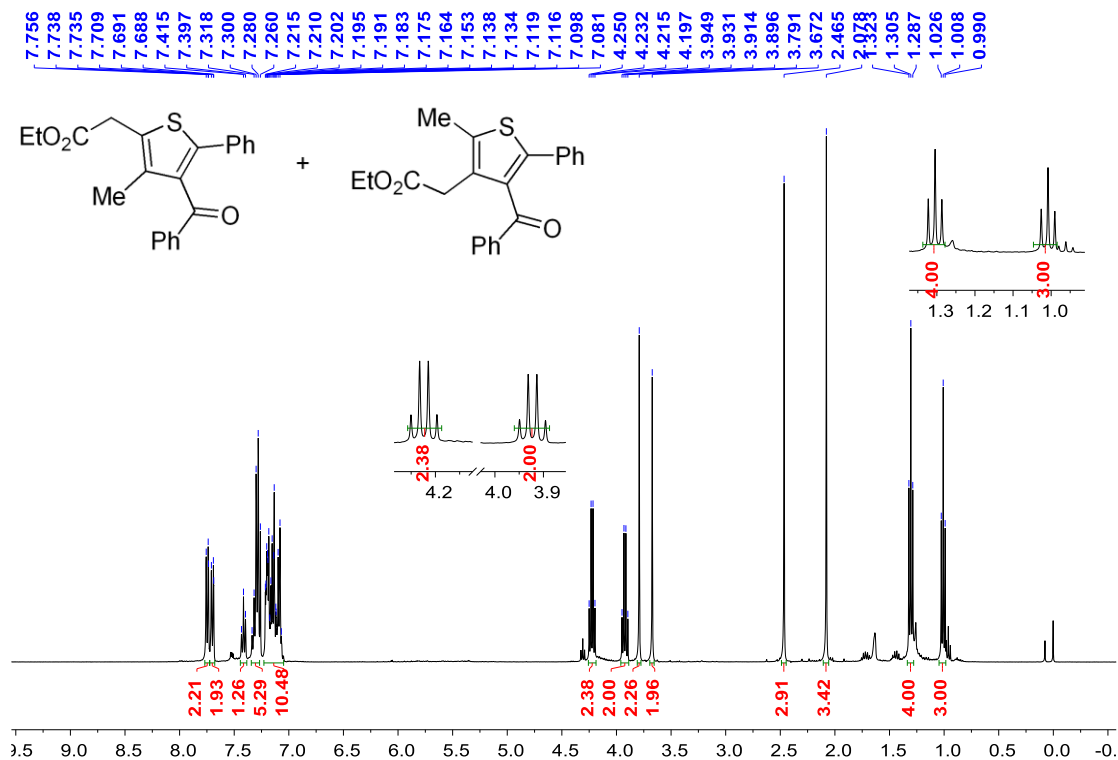


^{13}C NMR (101 MHz, CDCl_3)

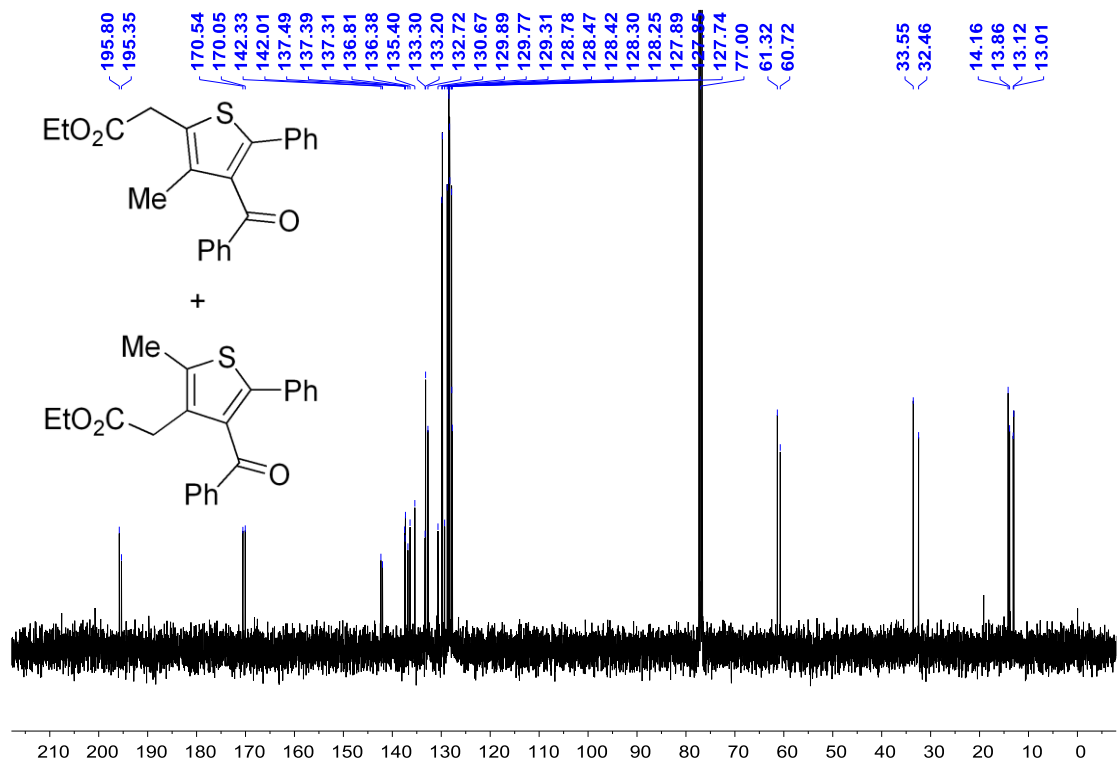


Ethyl 2-(4-benzoyl-3-methyl-5-phenylthiophen-2-yl)acetate (3qA) and ethyl 2-(4-benzoyl-2-methyl-5-phenylthiophen-3-yl)acetate (3qA')

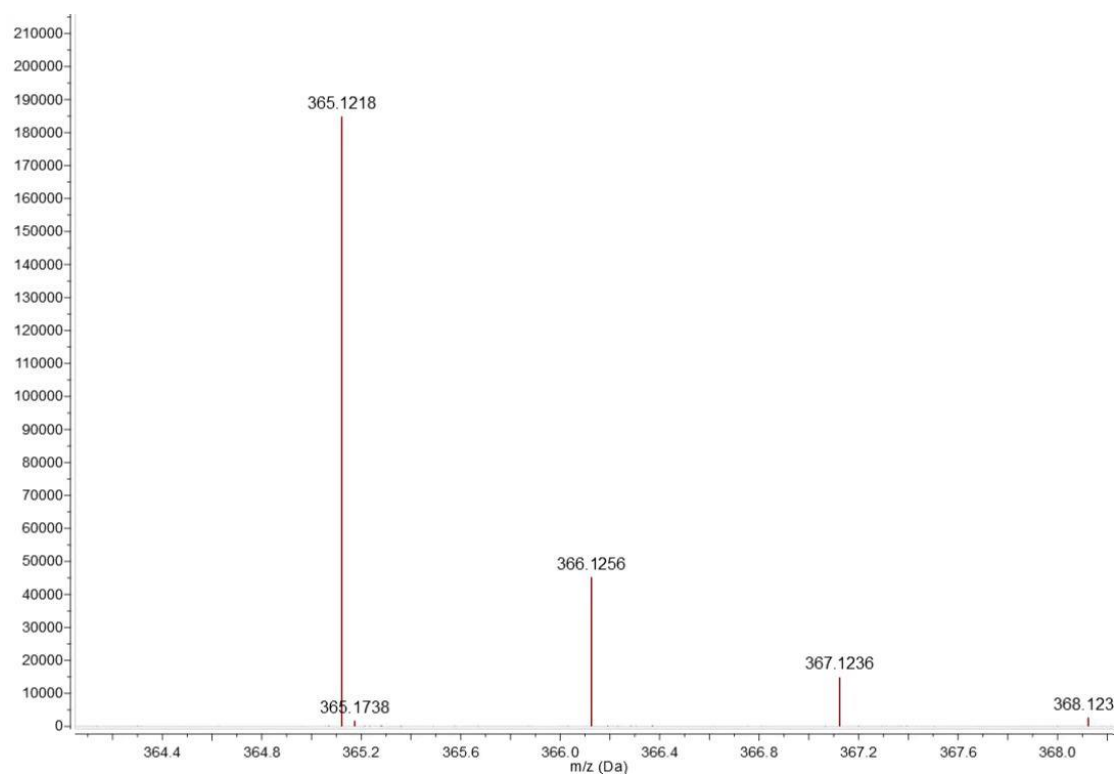
¹H NMR (400 MHz, CDCl₃)



¹³C NMR (101 MHz, CDCl₃)

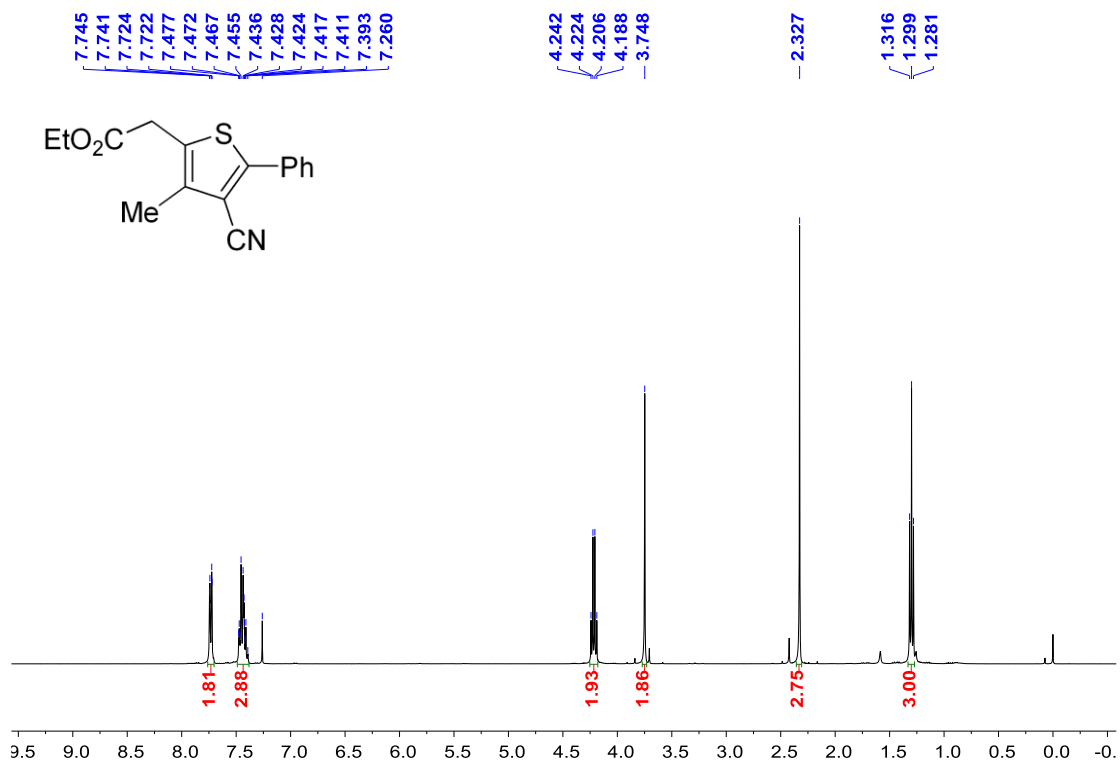


HRMS (ESI)

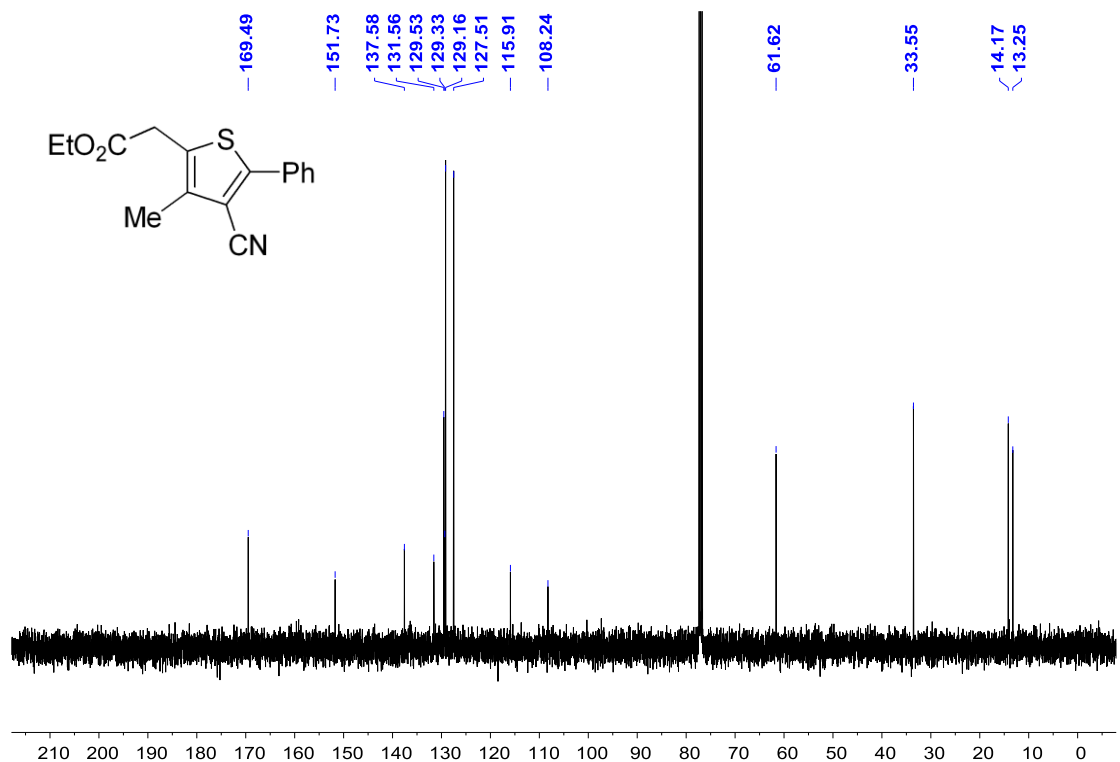


Ethyl 2-(4-cyano-3-methyl-5-phenylthiophen-2-yl)acetate (3rA)

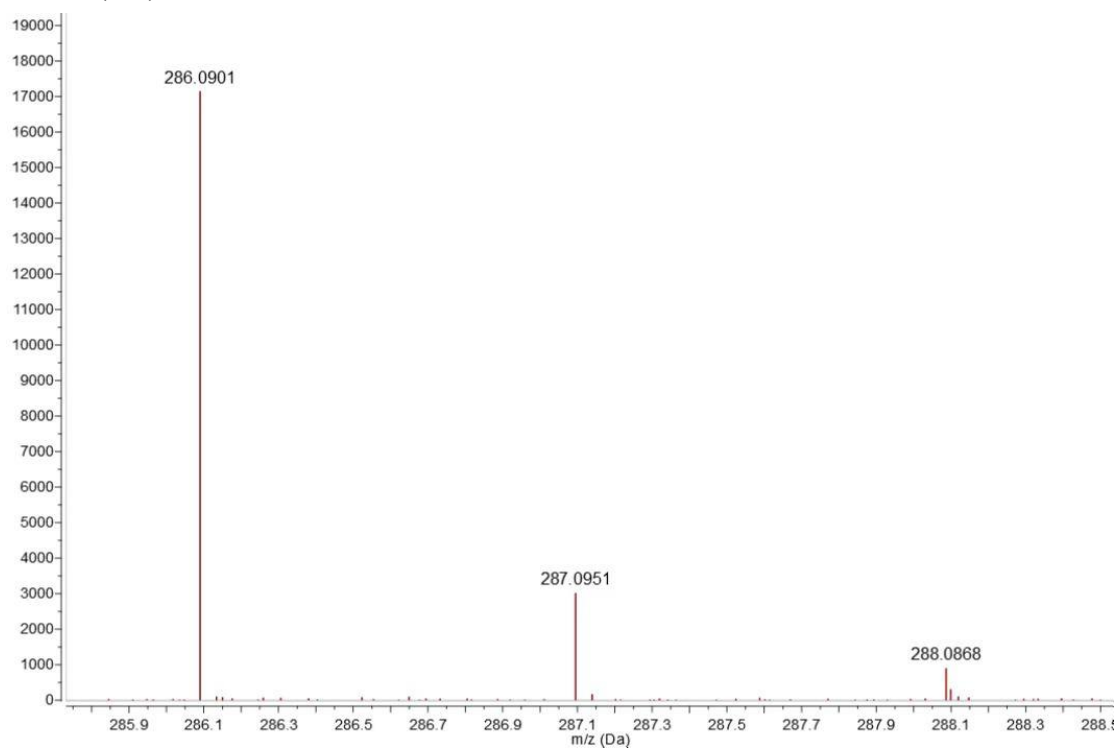
^1H NMR (400 MHz, CDCl_3)



^{13}C NMR (101 MHz, CDCl_3)

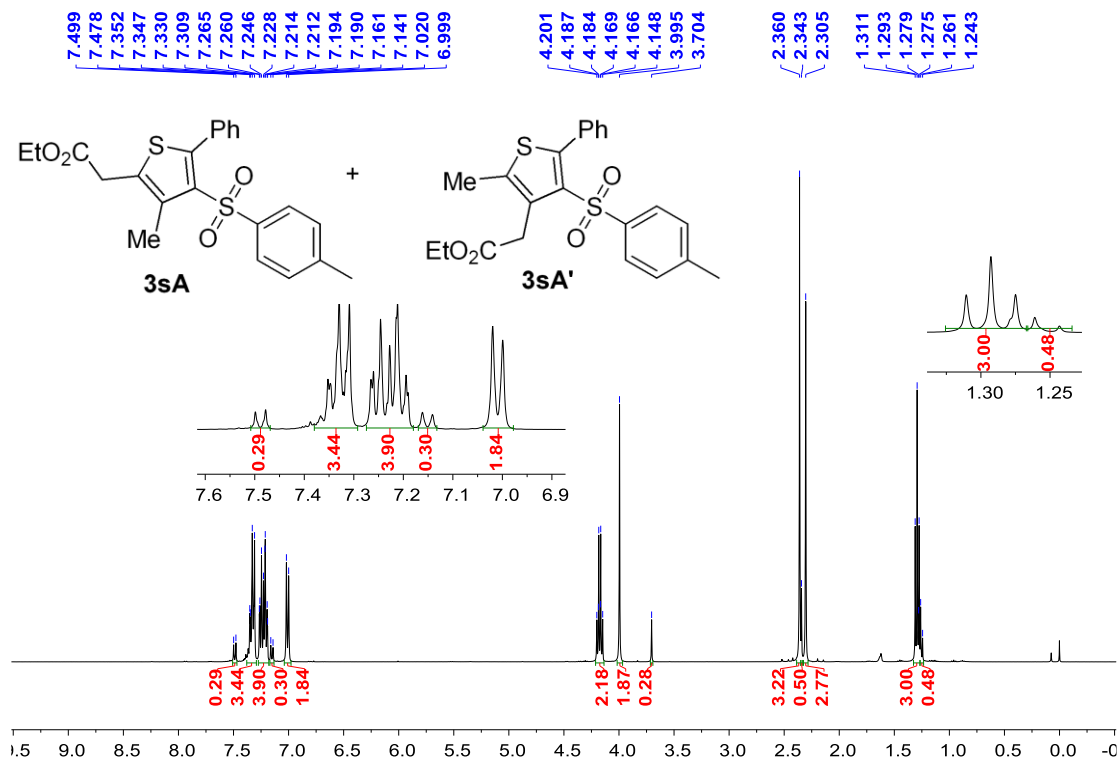


HRMS (ESI)

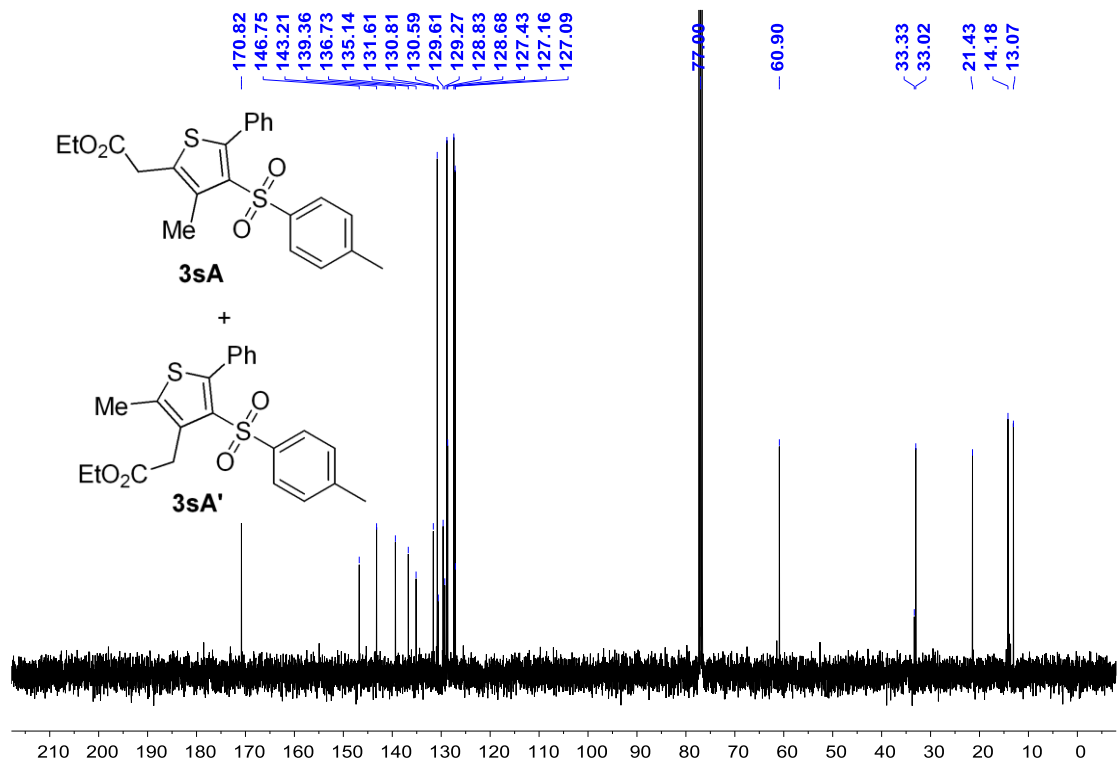


Ethyl 2-(3-methyl-5-phenyl-4-tosylthiophen-2-yl)acetate (3sA) and ethyl 2-(2-methyl-5-phenyl-4-tosylthiophen-3-yl)acetate (3sA')

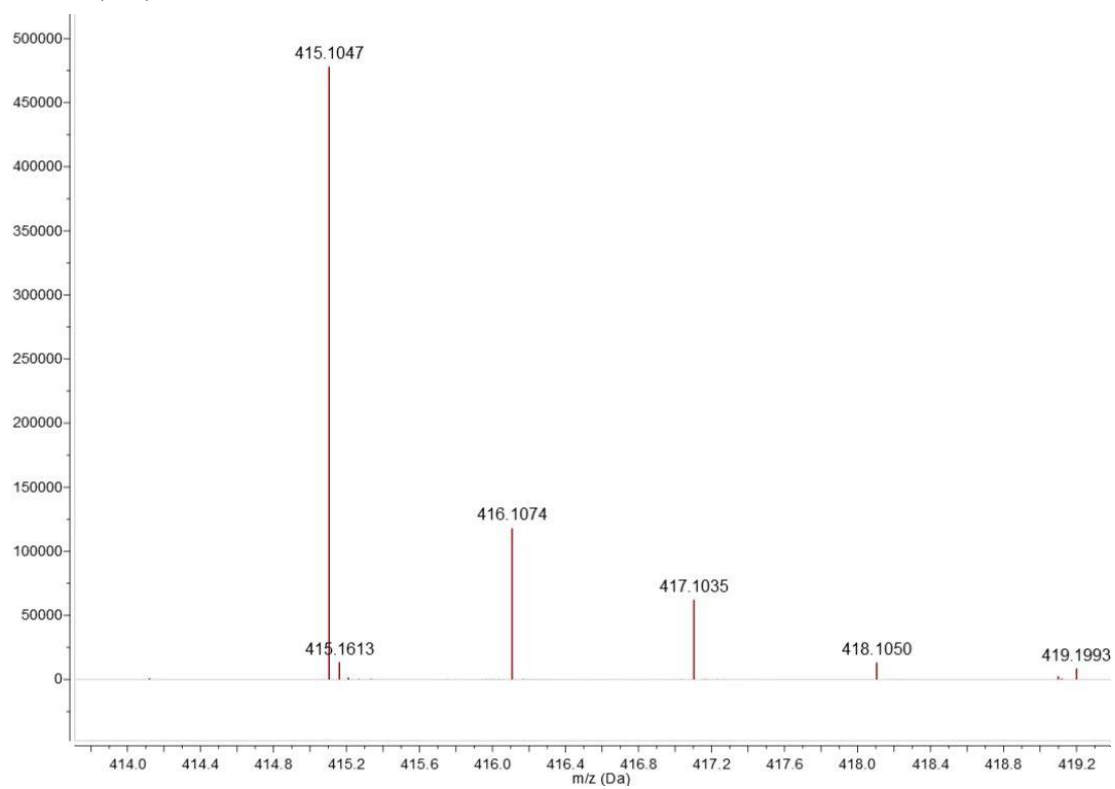
¹H NMR (400 MHz, CDCl₃)



¹³C NMR (101 MHz, CDCl₃)

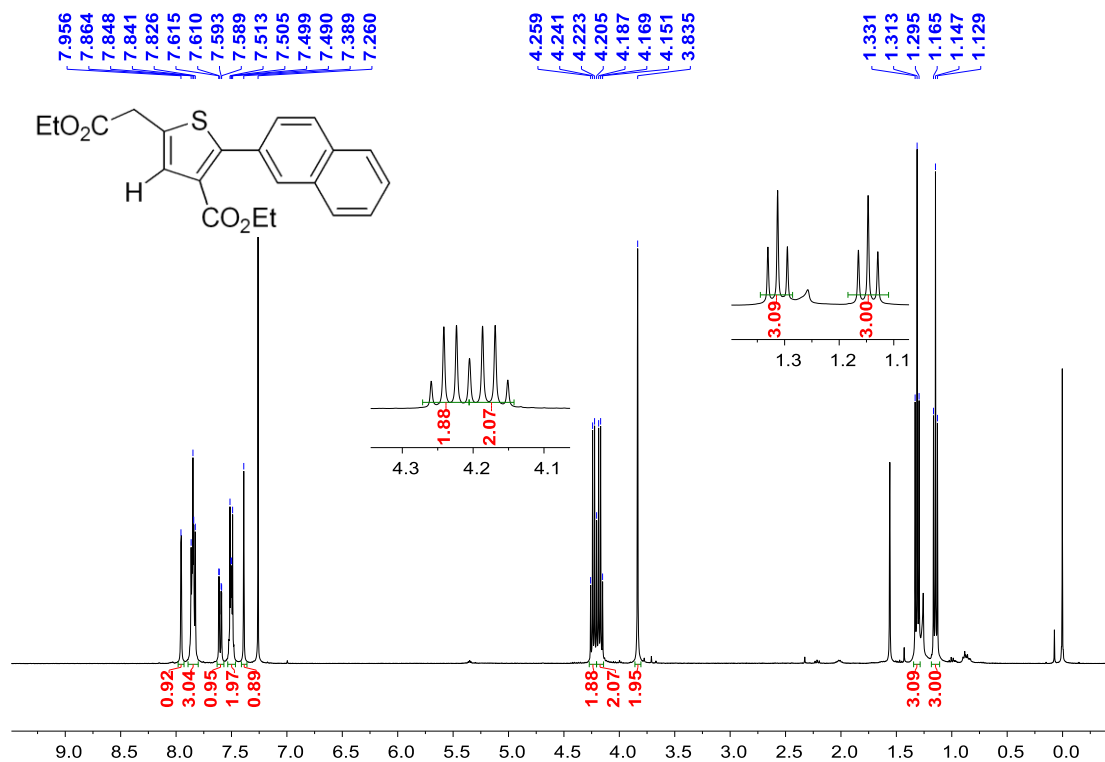


HRMS (ESI)

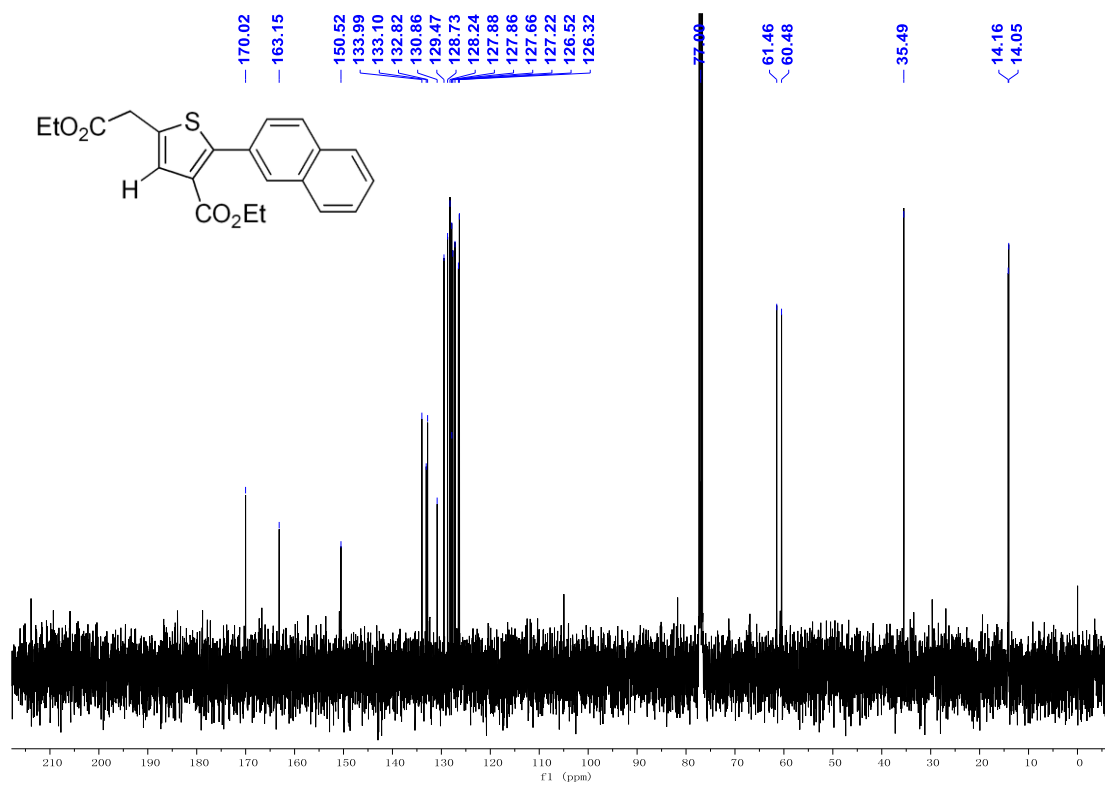


Ethyl 5-(2-ethoxy-2-oxoethyl)-2-(naphthalen-2-yl)thiophene-3-carboxylate (3aB)

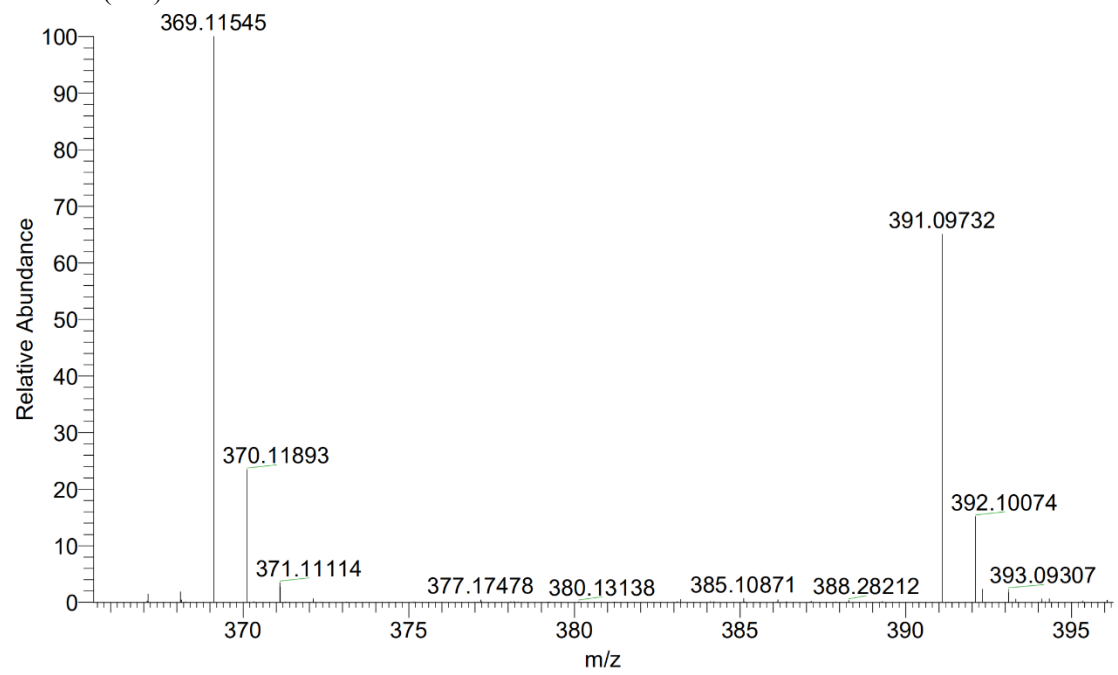
$^1\text{H NMR}$ (400 MHz, CDCl_3)



$^{13}\text{C NMR}$ (101 MHz, CDCl_3)

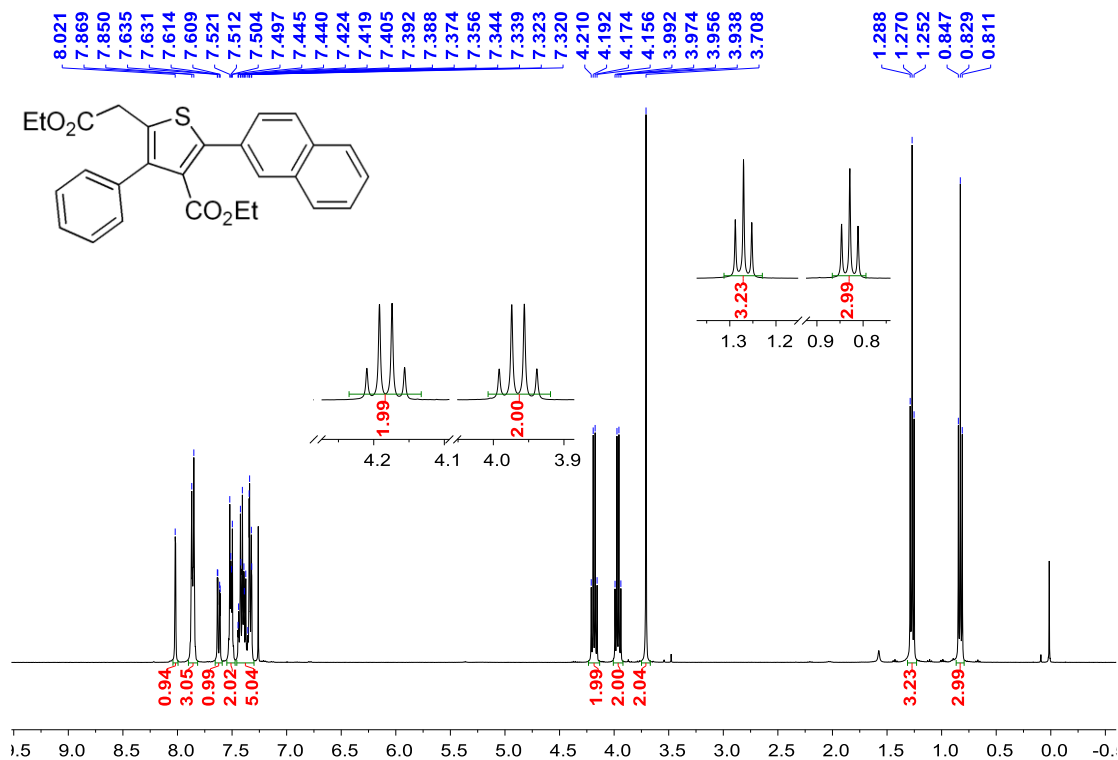


HRMS (ESI)

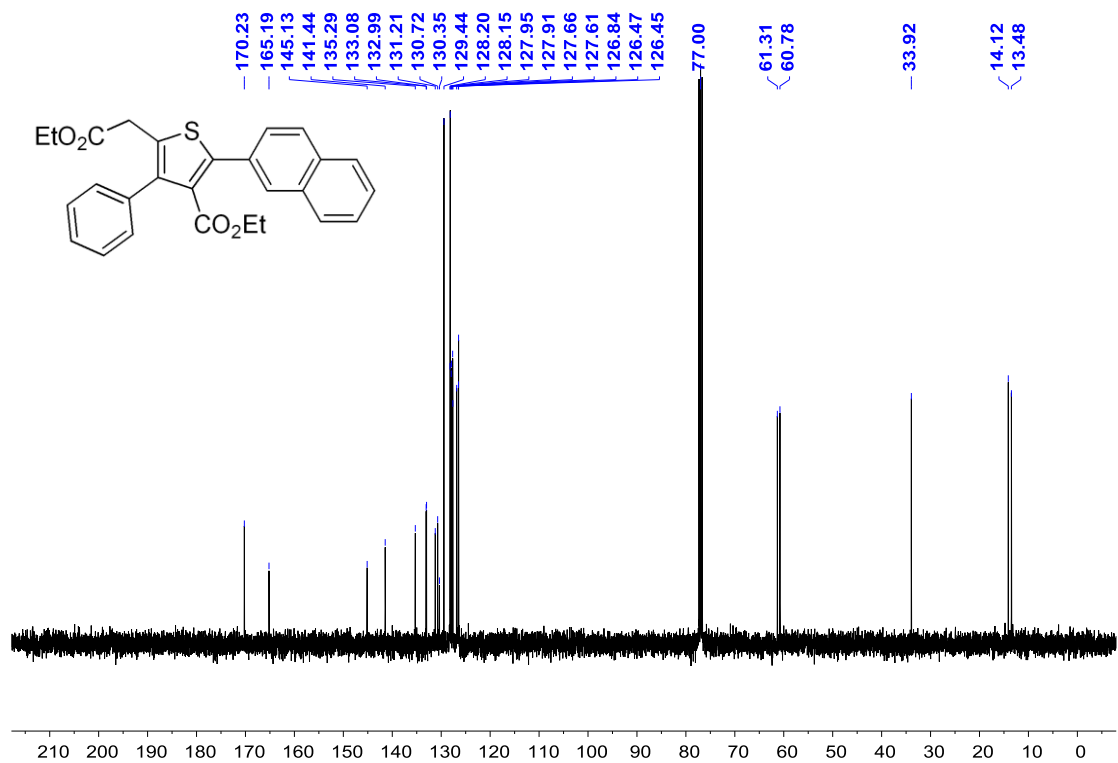


Ethyl 5-(2-ethoxy-2-oxoethyl)-2-(naphthalen-2-yl)-4-phenylthiophene-3-carboxylate (3aC)

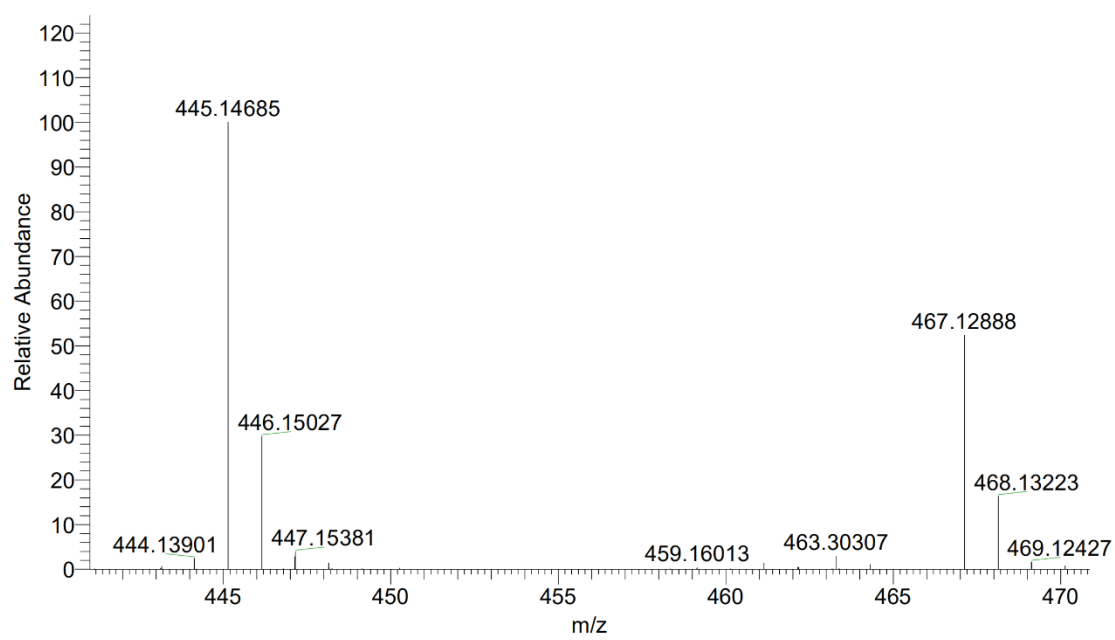
¹H NMR (400 MHz, CDCl₃)



¹³C NMR (101 MHz, CDCl₃)

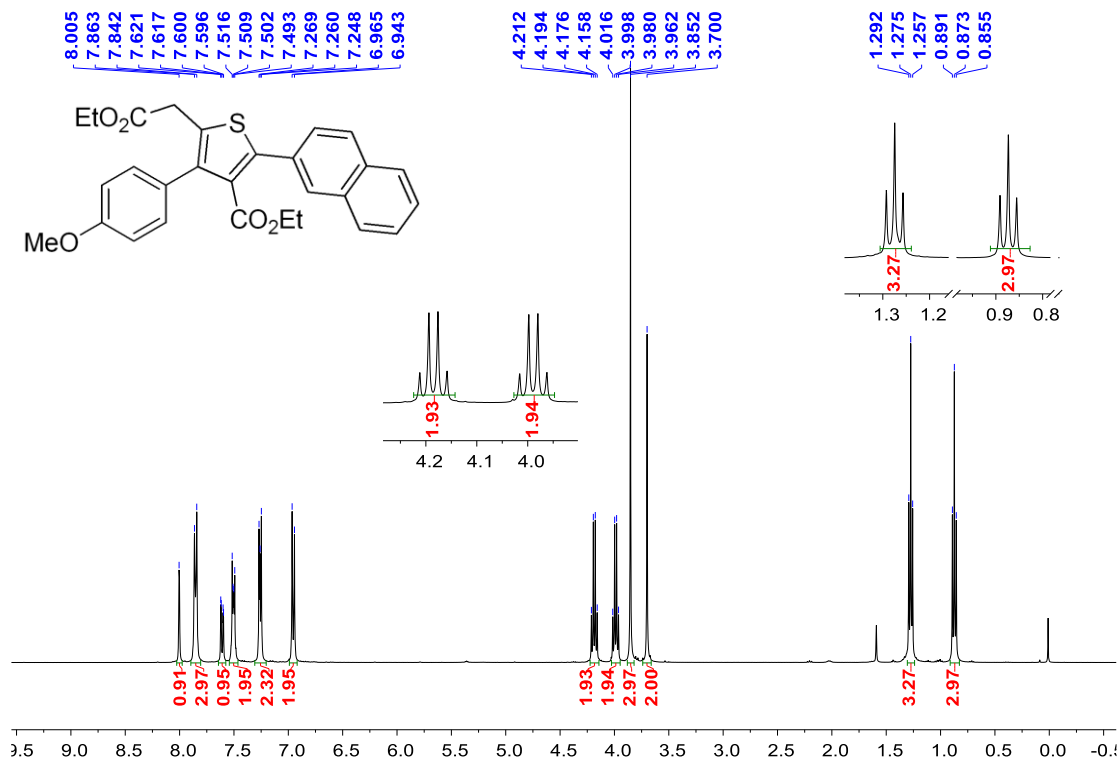


HRMS (ESI)

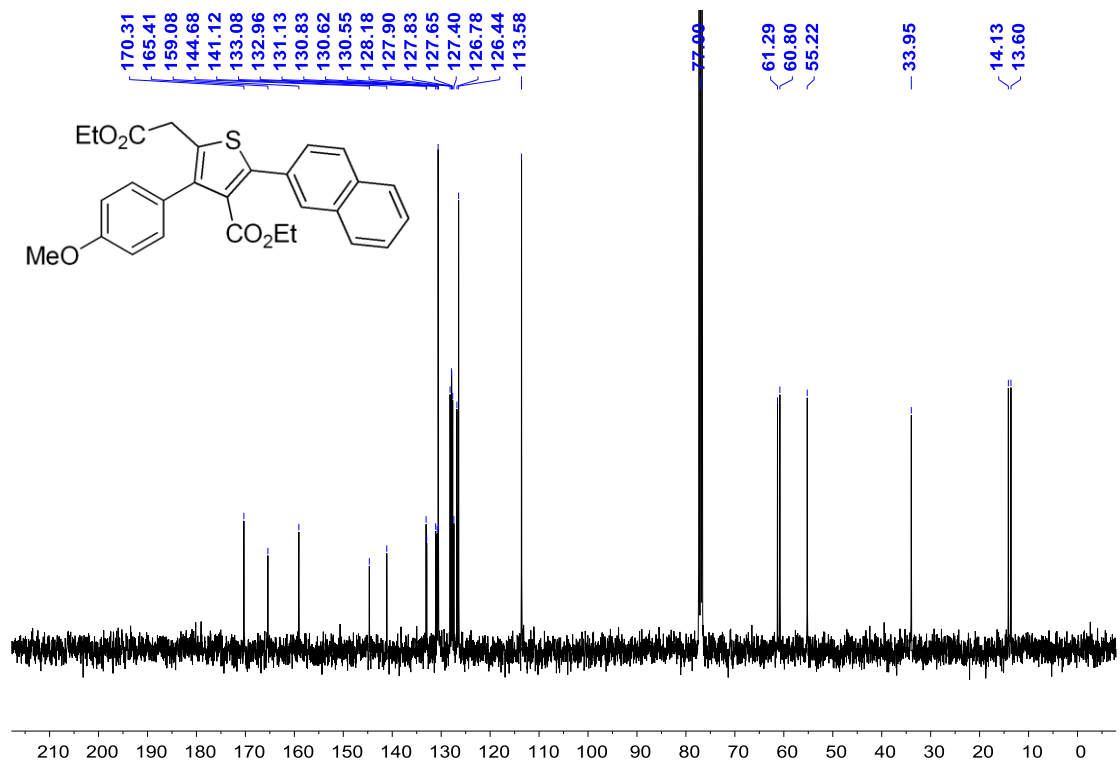


Ethyl 5-(2-ethoxy-2-oxoethyl)-4-(4-methoxyphenyl)-2-(naphthalen-2-yl)thiophene-3-carboxylate (3aD)

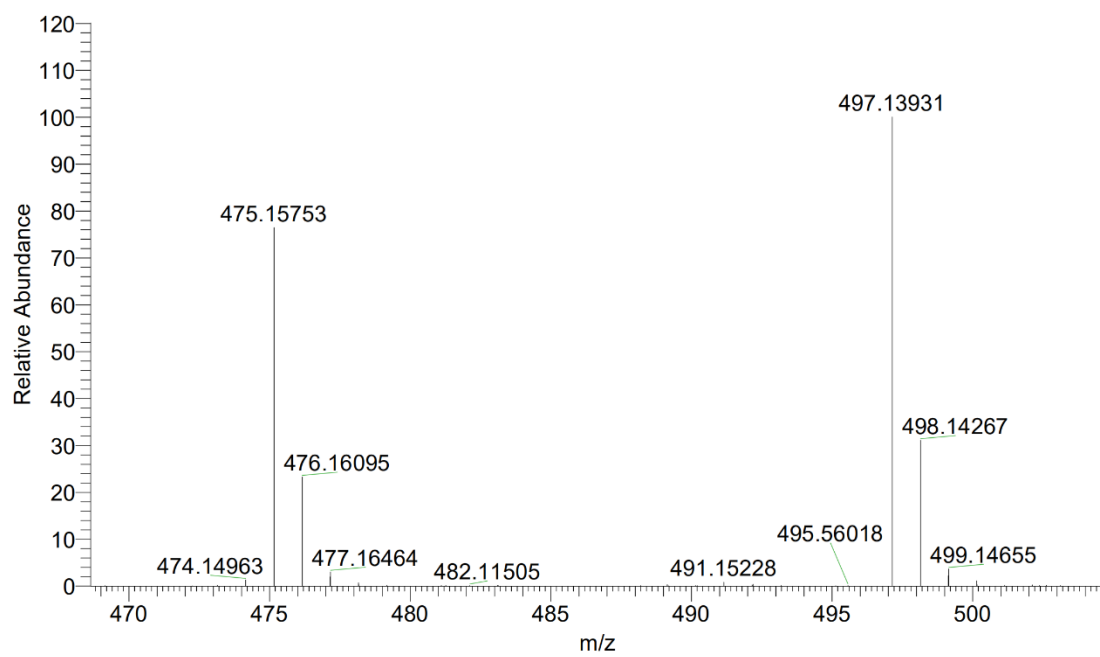
¹H NMR (400 MHz, CDCl₃)



¹³C NMR (101 MHz, CDCl₃)

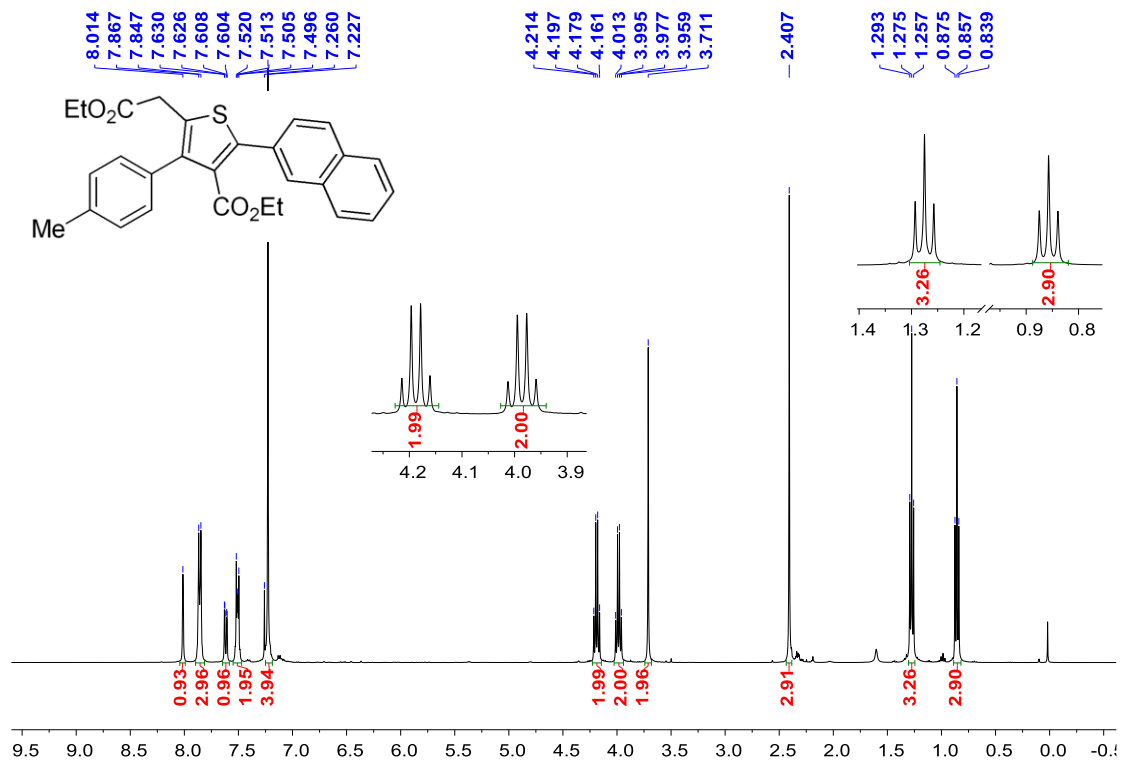


HRMS (ESI)

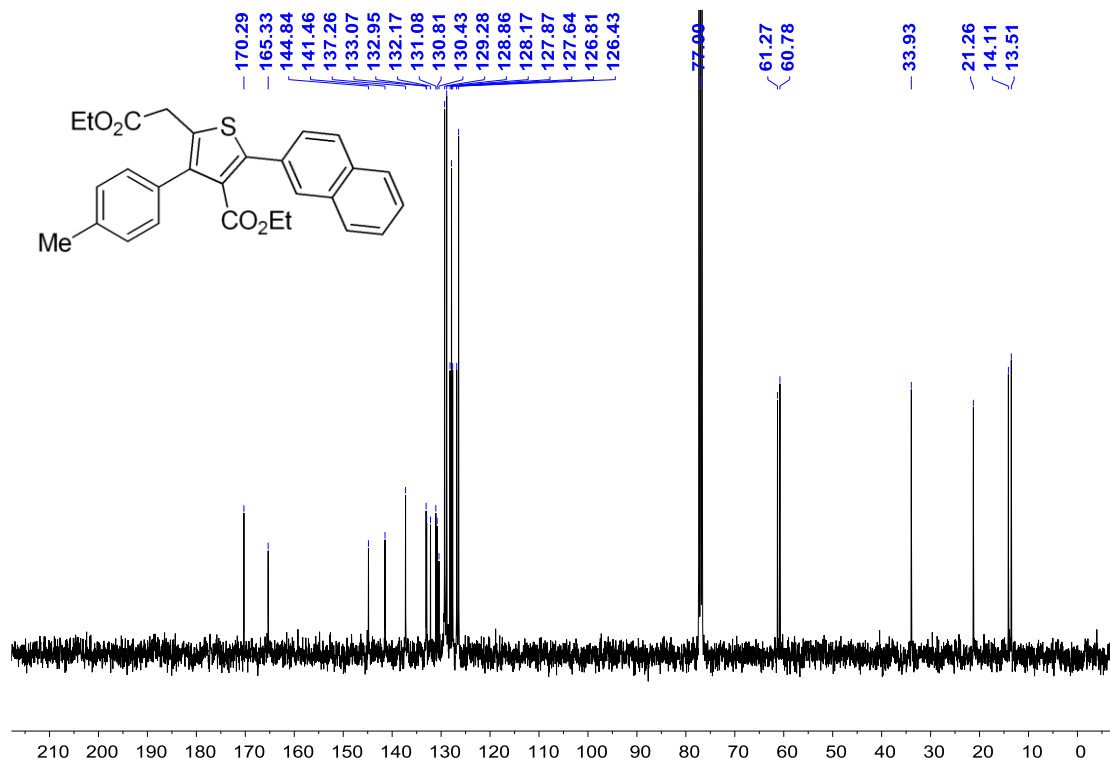


Ethyl 5-(2-ethoxy-2-oxoethyl)-2-(naphthalen-2-yl)-4-(*p*-tolyl)thiophene-3-carboxylate (3aE)

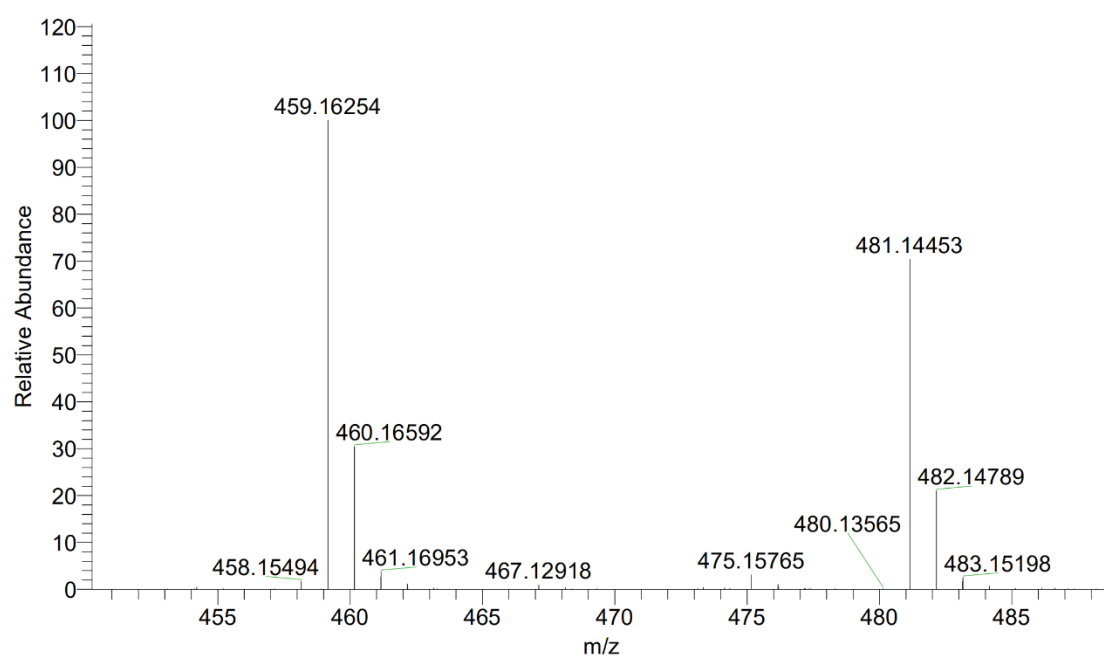
¹H NMR (400 MHz, CDCl₃)



¹³C NMR (101 MHz, CDCl₃)

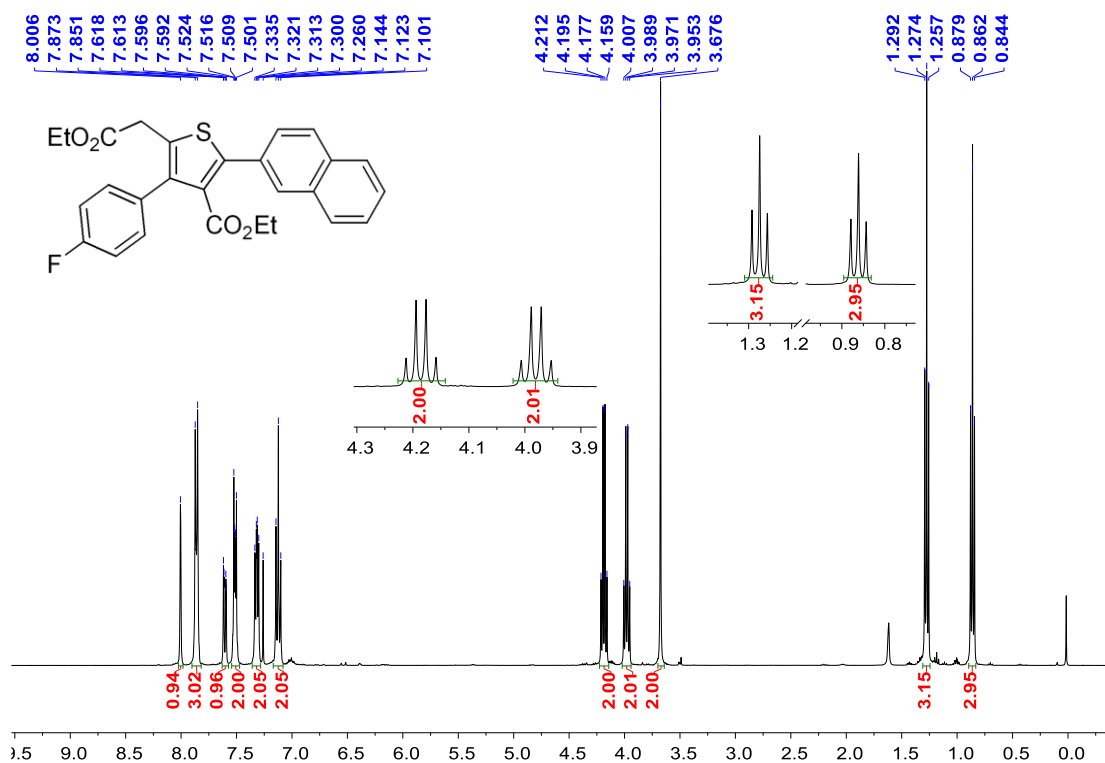


HRMS (ESI)

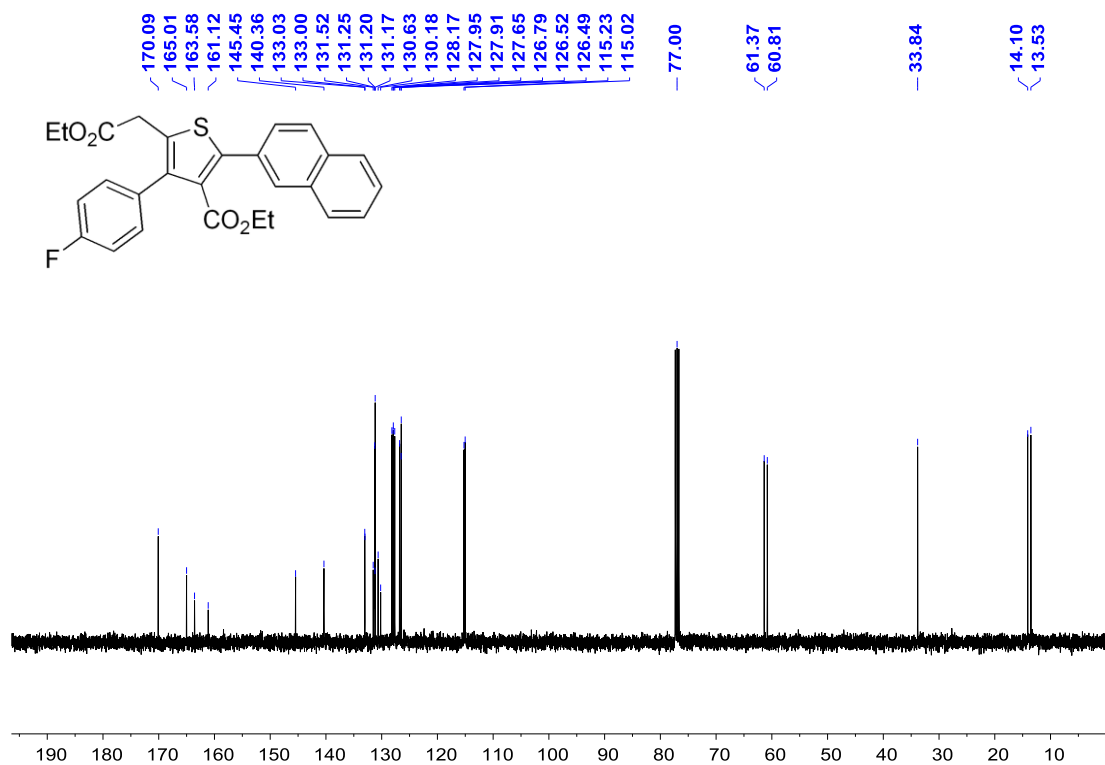


Ethyl 5-(2-ethoxy-2-oxoethyl)-4-(4-fluorophenyl)-2-(naphthalen-2-yl)thiophene-3-carboxylate (3aF)

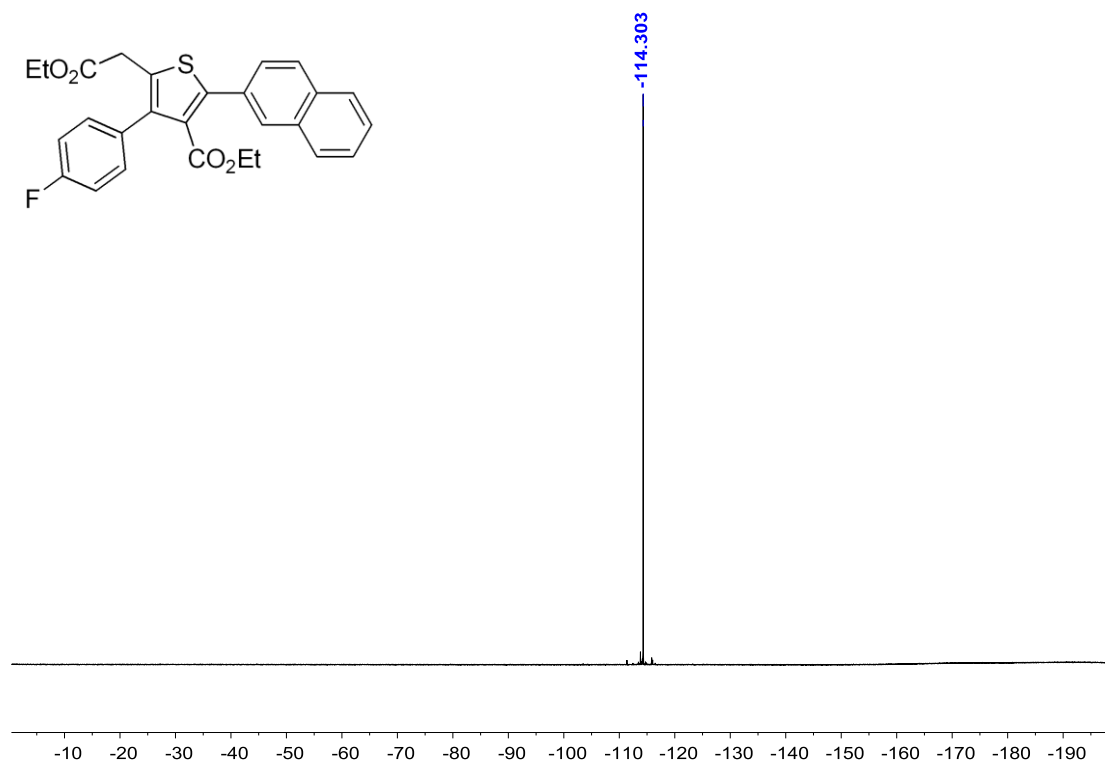
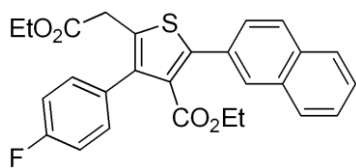
¹H NMR (400 MHz, CDCl₃)



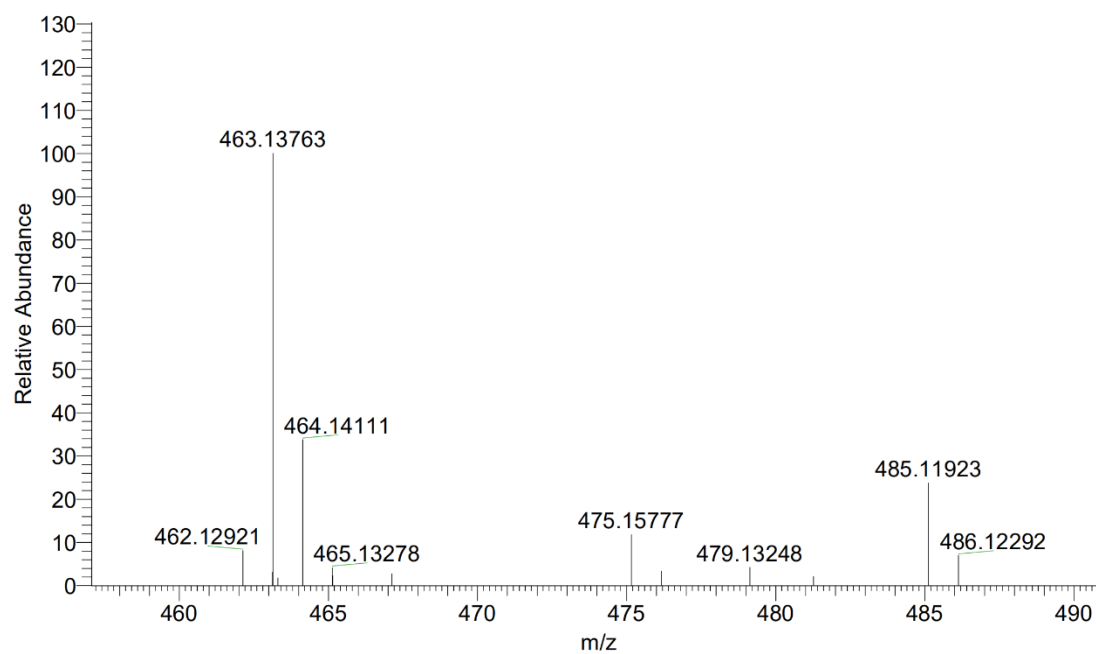
¹³C NMR (101 MHz, CDCl₃)



¹⁹F NMR (376 MHz, CDCl₃)

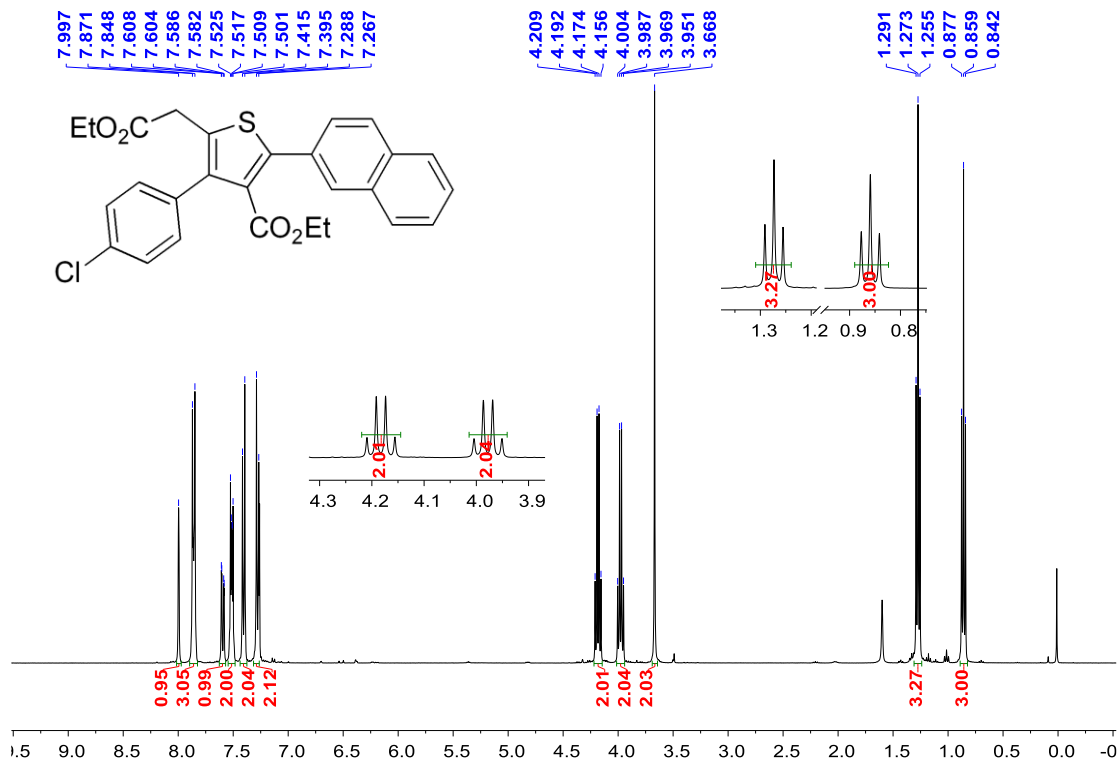


HRMS (ESI)

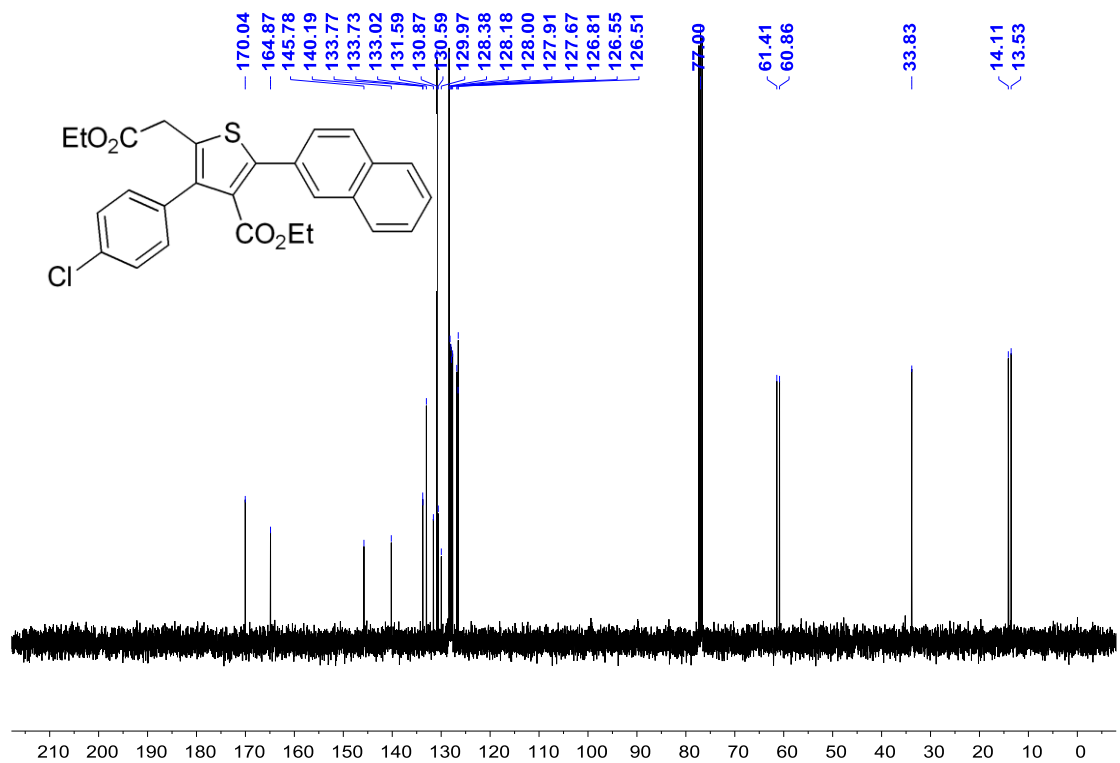


Ethyl 4-(4-chlorophenyl)-5-(2-ethoxy-2-oxoethyl)-2-(naphthalen-2-yl)thiophene-3-carboxylate (3aG)

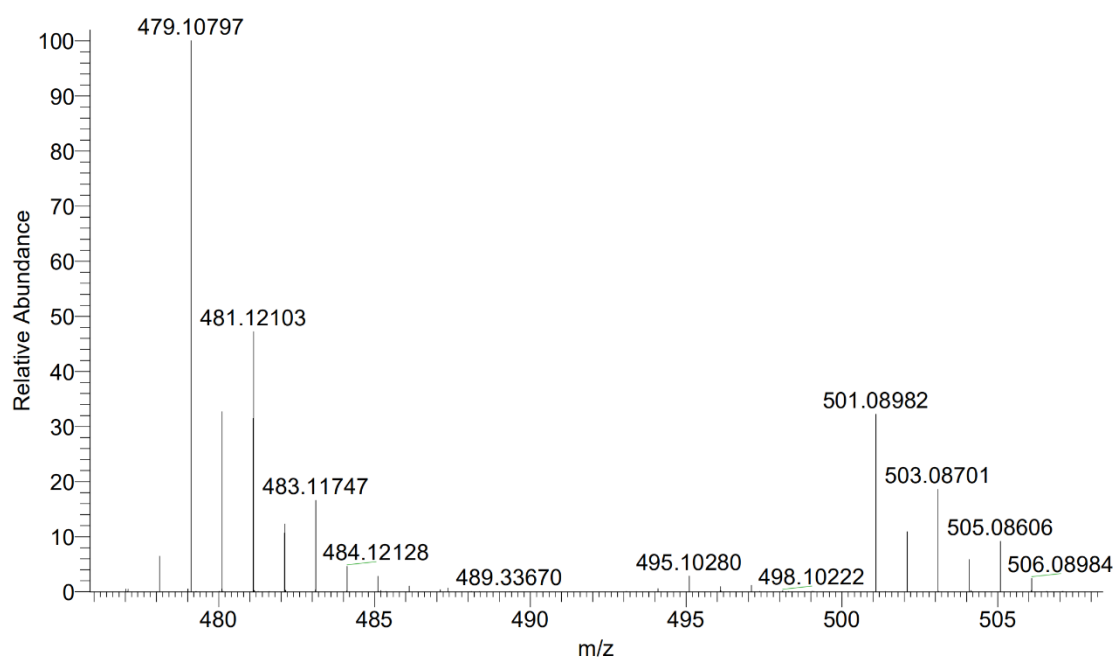
$^1\text{H NMR}$ (400 MHz, CDCl_3)



$^{13}\text{C NMR}$ (101 MHz, CDCl_3)

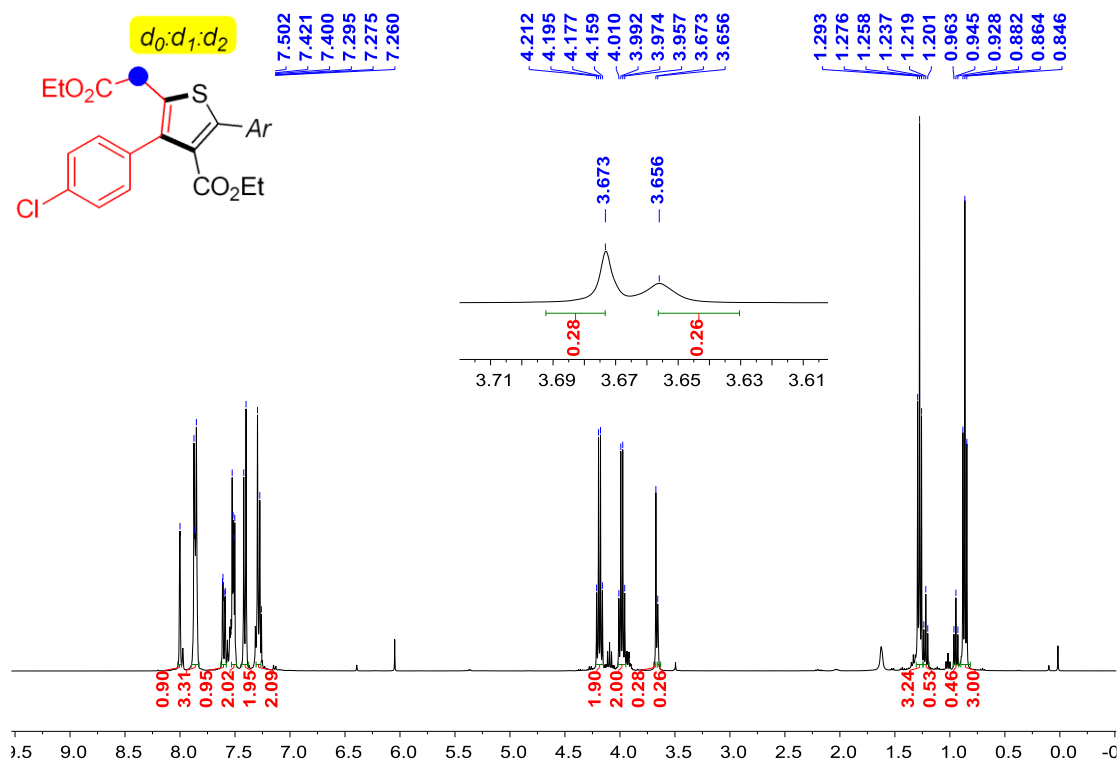


HRMS (ESI)

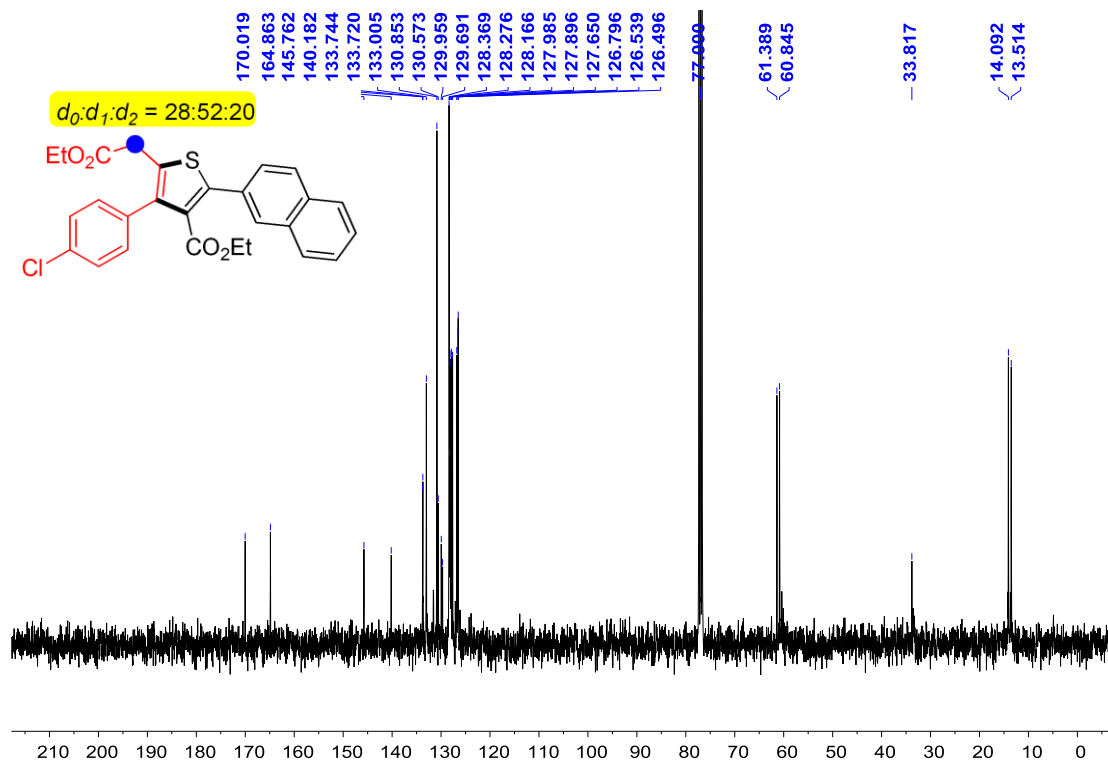


Ethyl 4-(4-chlorophenyl)-5-(2-ethoxy-2-oxoethyl)-2-(naphthalen-2-yl)thiophene-3-carboxylate (3aG-d)

$^1\text{H NMR}$ (400 MHz, CDCl_3)

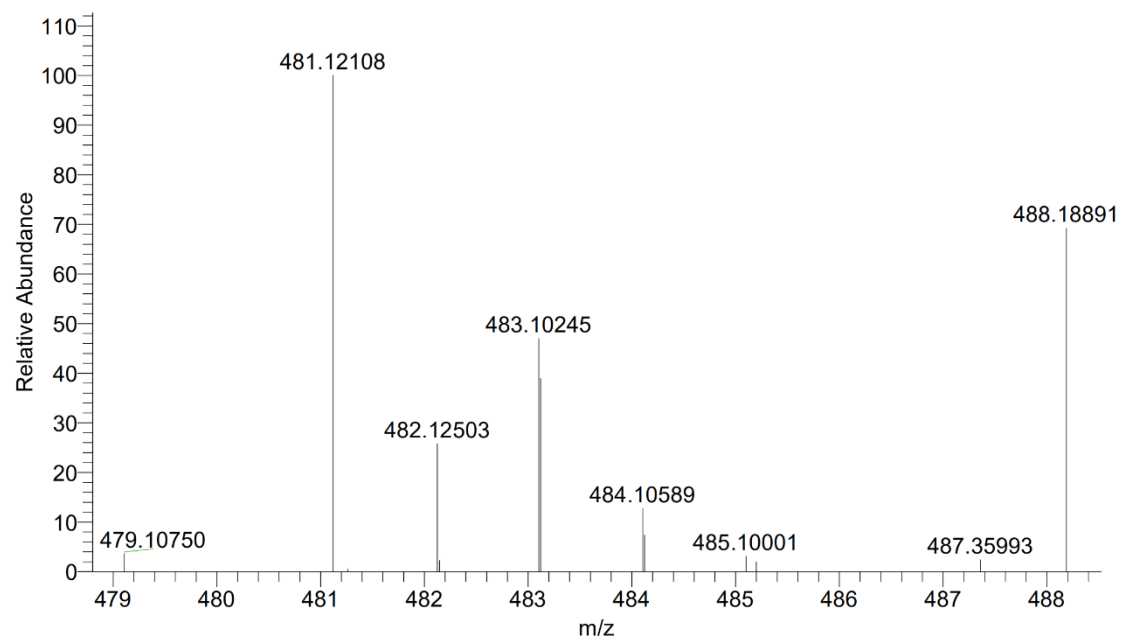


$^{13}\text{C NMR}$ (400 MHz, CDCl_3)



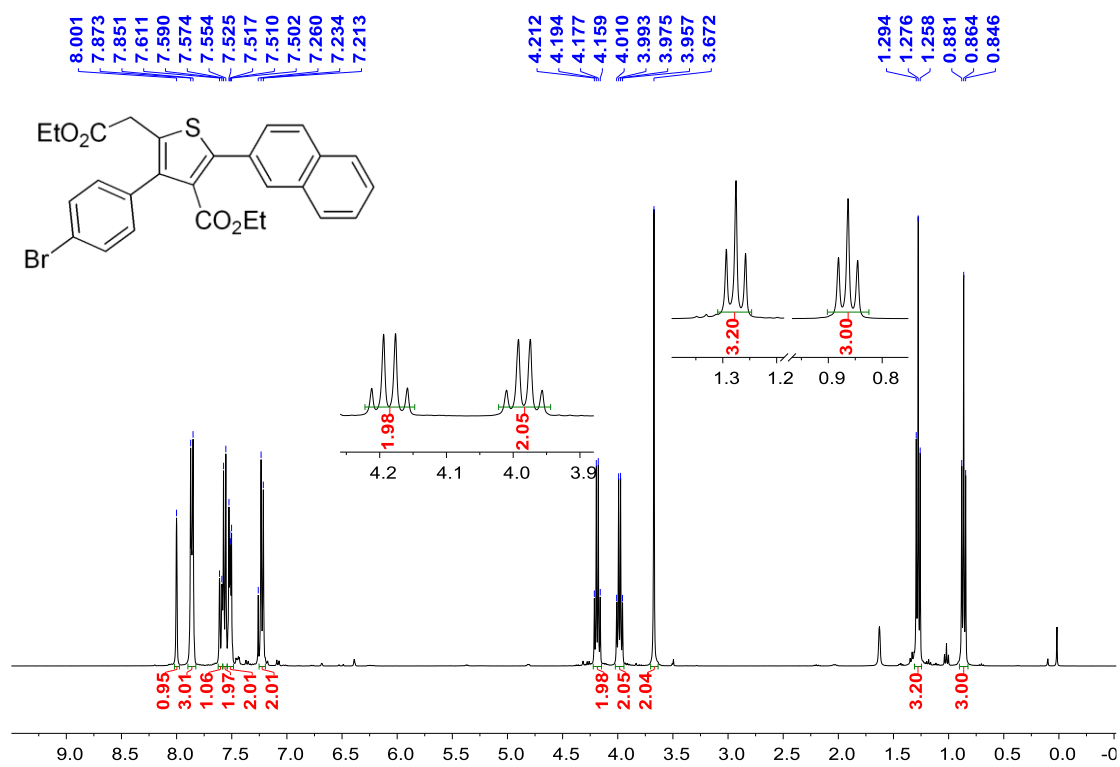
HRMS (ESI)

Ethyl 4-(4-chlorophenyl)-5-(2-ethoxy-2-oxoethyl-1,1-*d*₂)-2-(naphthalen-2-yl)thiophene-3-carboxylate

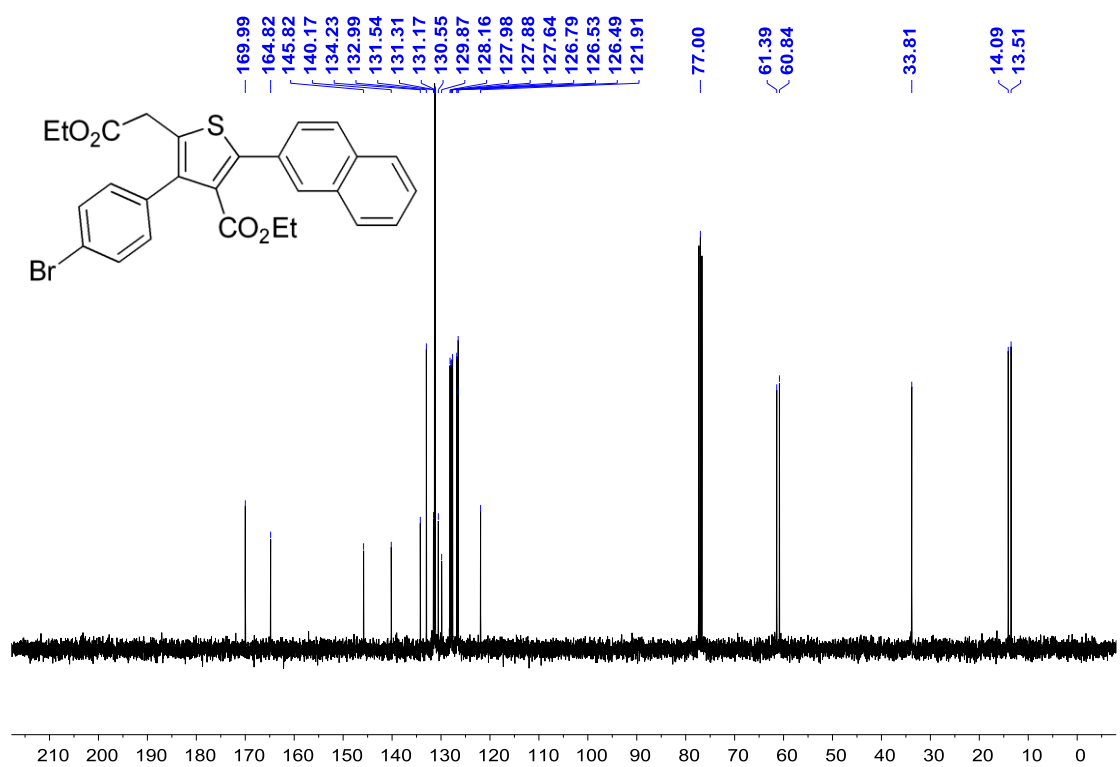


Ethyl 4-(4-bromophenyl)-5-(2-ethoxy-2-oxoethyl)-2-(naphthalen-2-yl)thiophene-3-carboxylate (3aH)

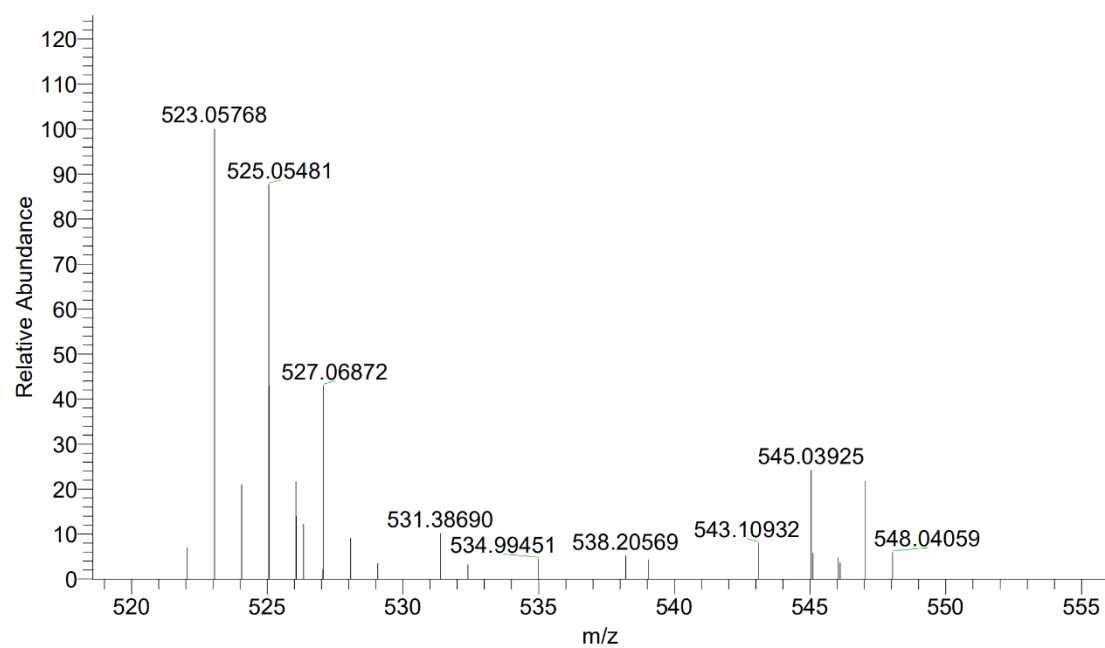
$^1\text{H NMR}$ (400 MHz, CDCl_3)



$^{13}\text{C NMR}$ (101 MHz, CDCl_3)

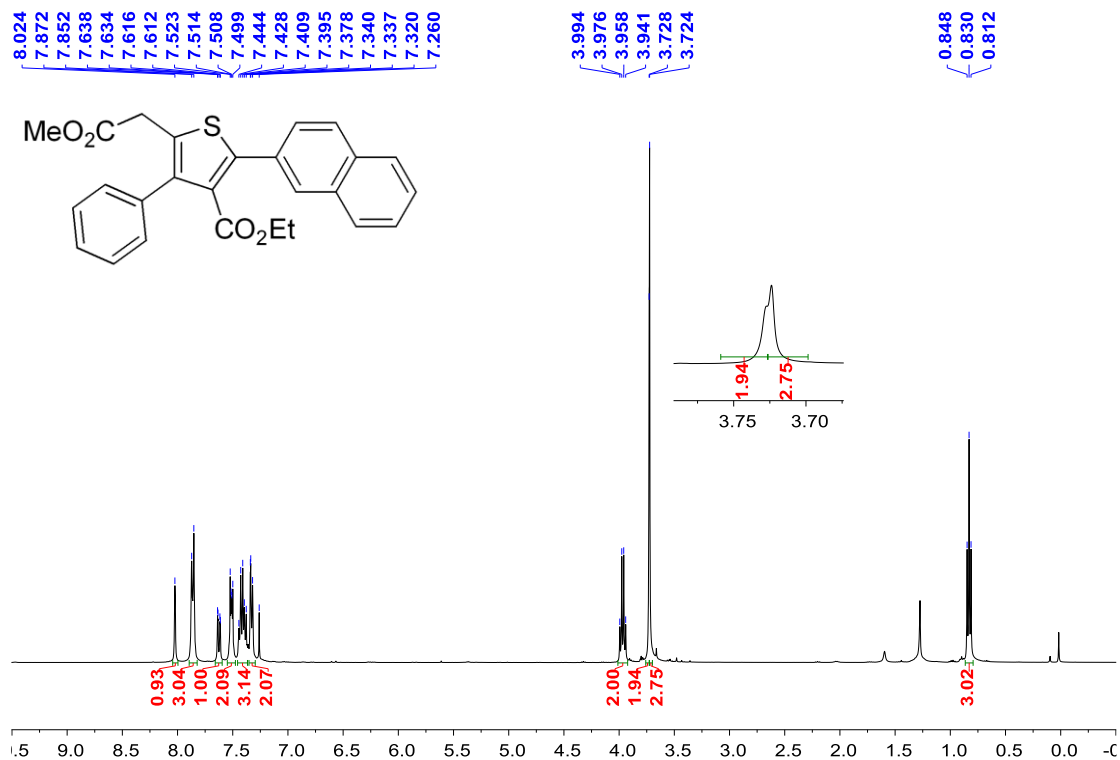


HRMS (ESI)

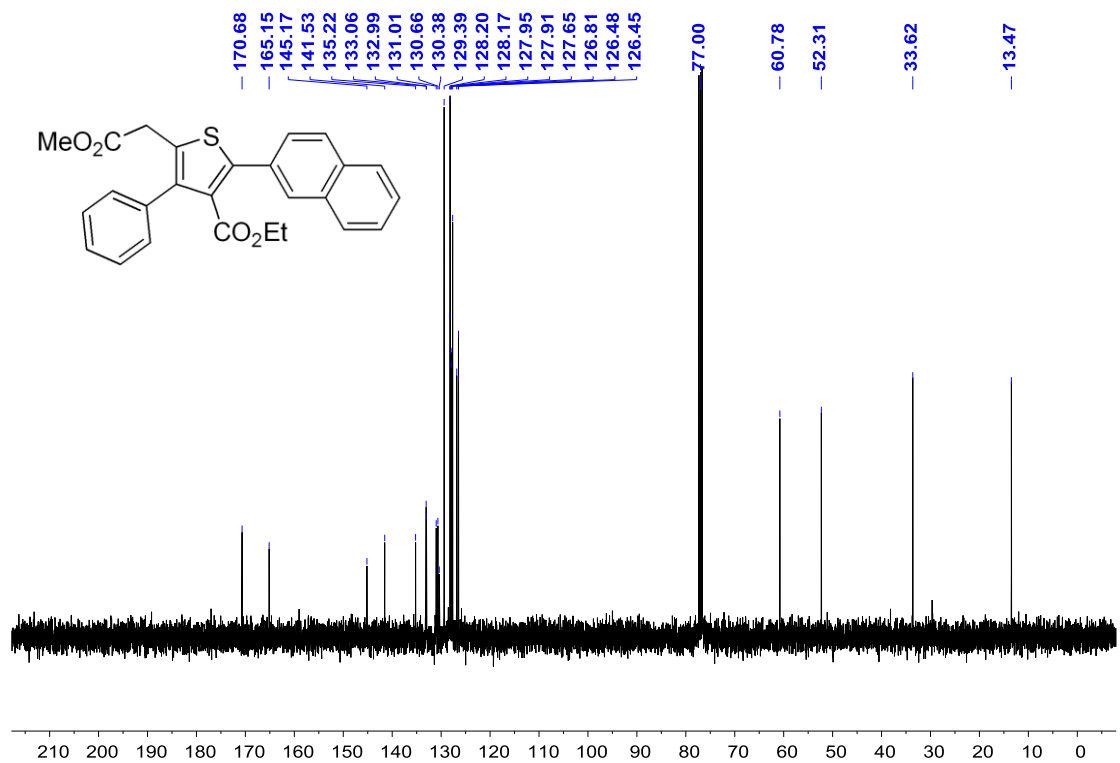


Ethyl 5-(2-methoxy-2-oxoethyl)-2-(naphthalen-2-yl)-4-phenylthiophene-3-carboxylate (3aI)

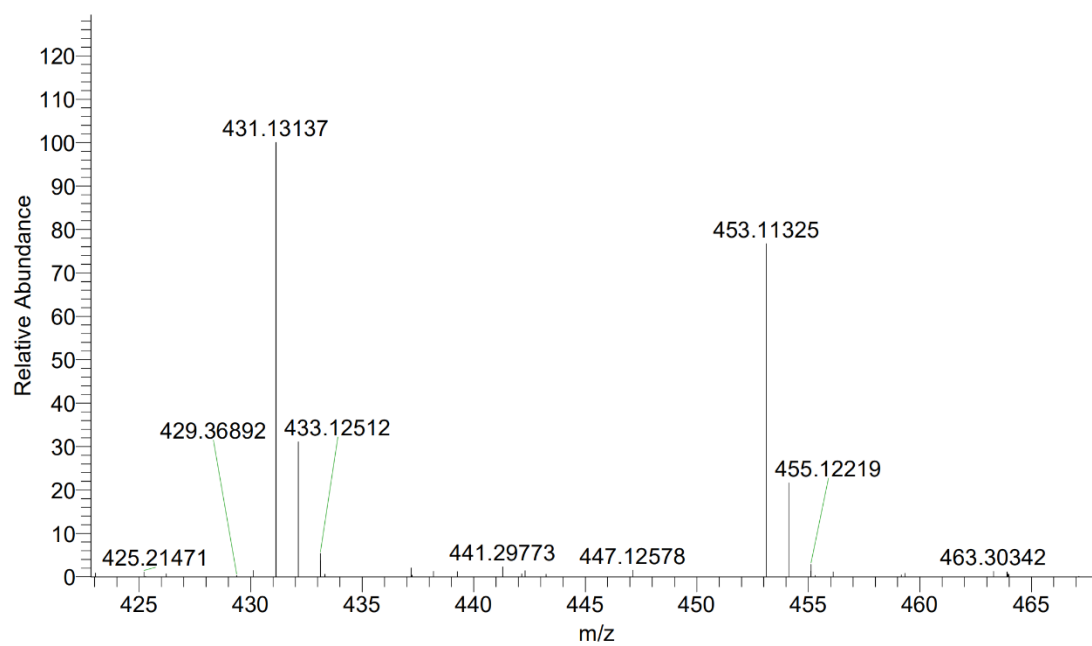
¹H NMR (400 MHz, CDCl₃)



¹³C NMR (101 MHz, CDCl₃)

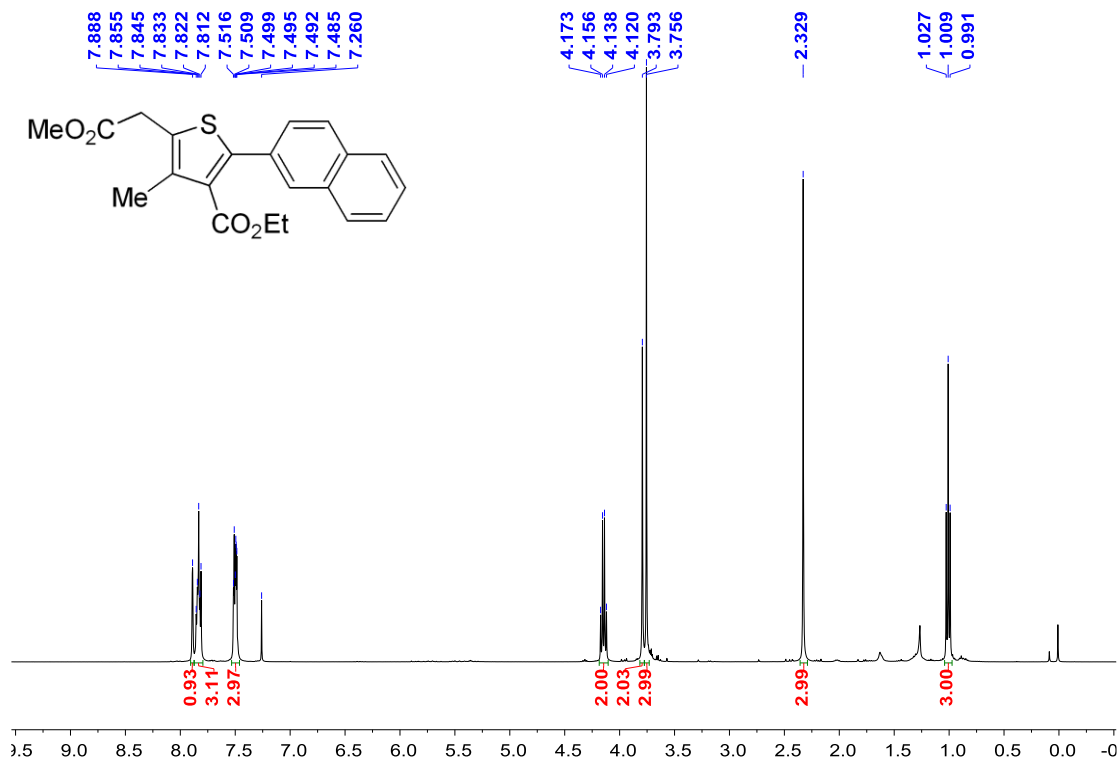


HRMS (ESI)

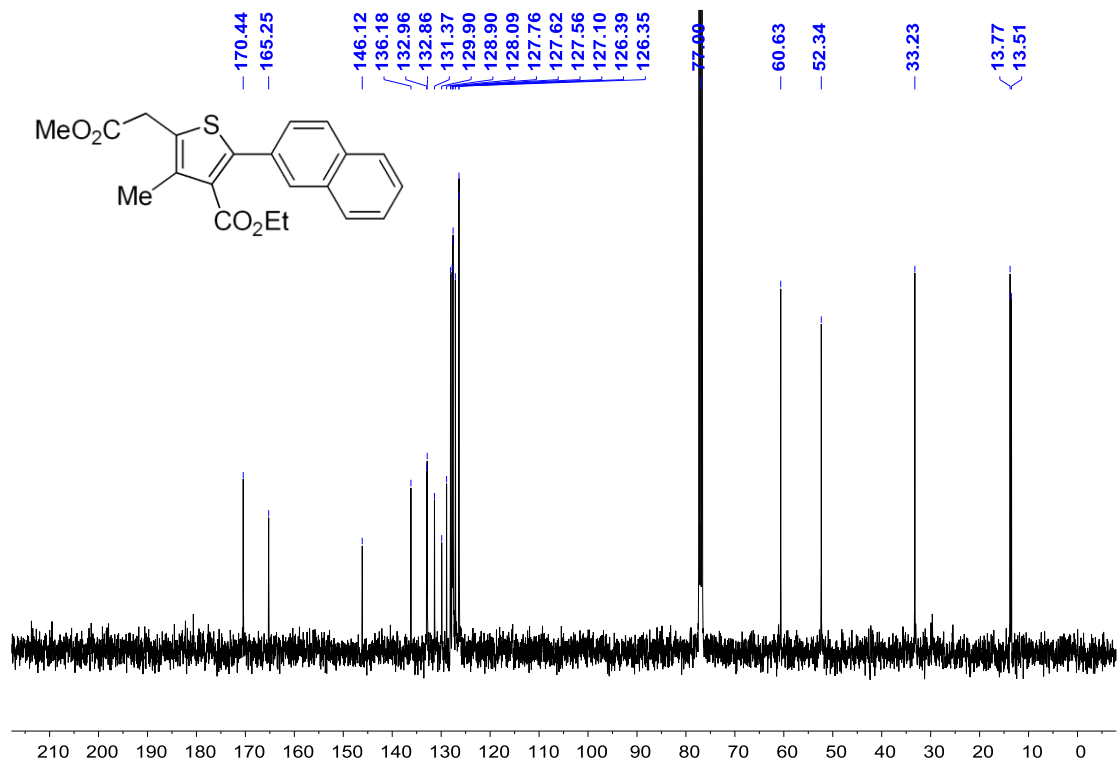


Ethyl 5-(2-methoxy-2-oxoethyl)-4-methyl-2-(naphthalen-2-yl)thiophene-3-carboxylate (3aJ)

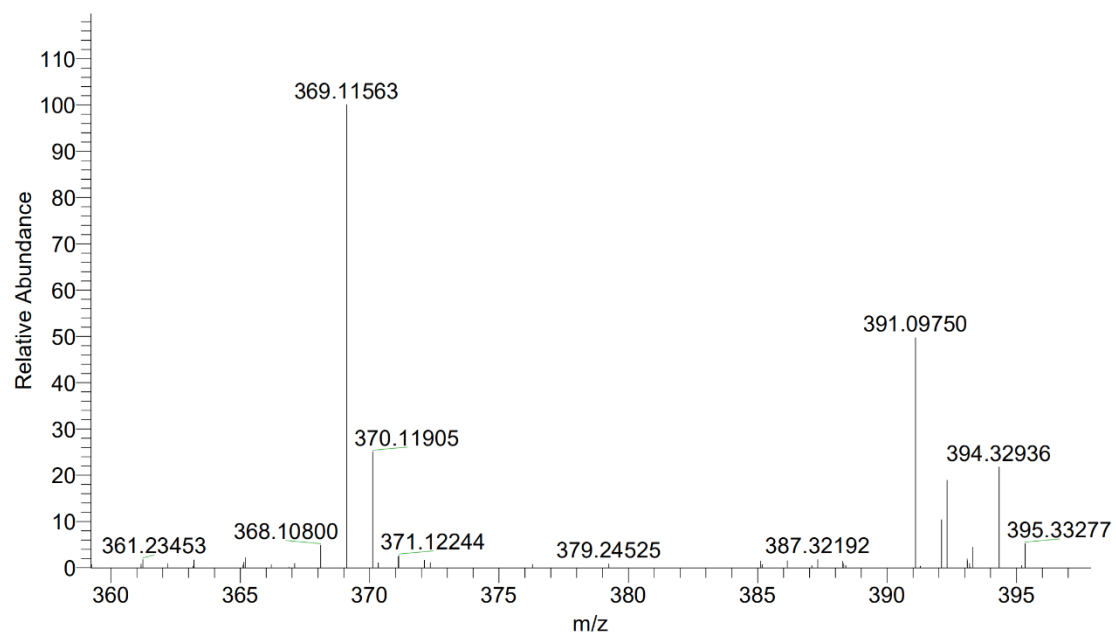
$^1\text{H NMR}$ (400 MHz, CDCl_3)



$^{13}\text{C NMR}$ (101 MHz, CDCl_3)

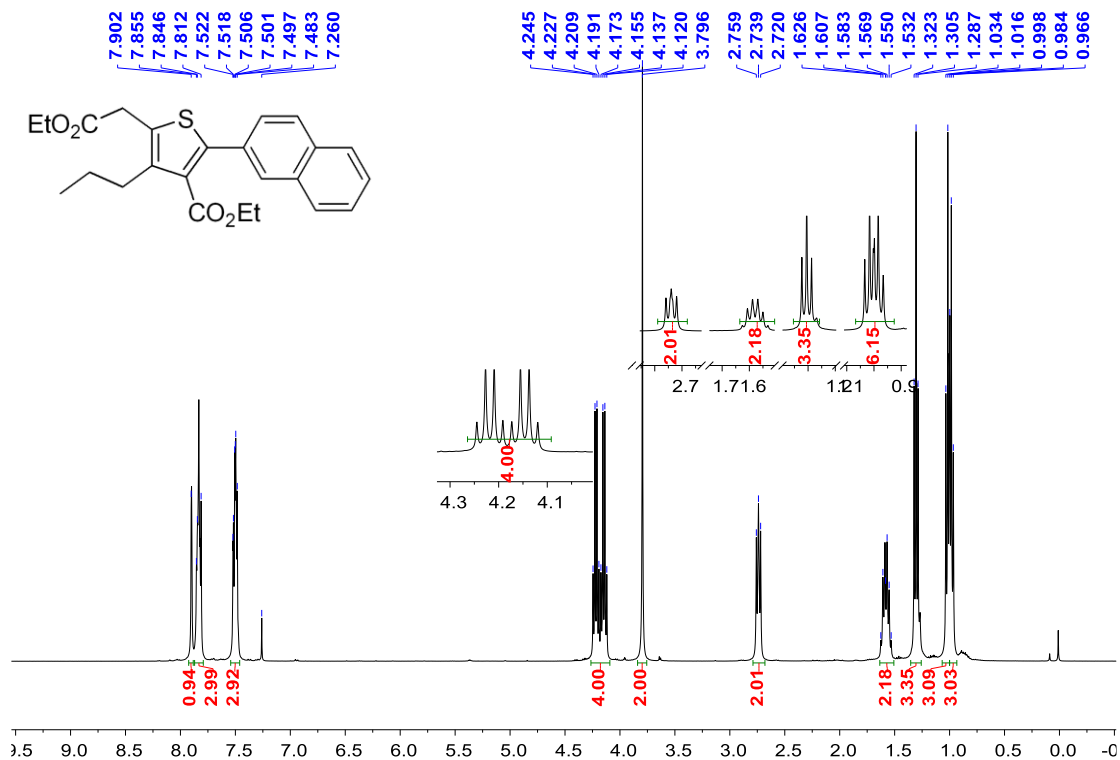


HRMS (ESI)

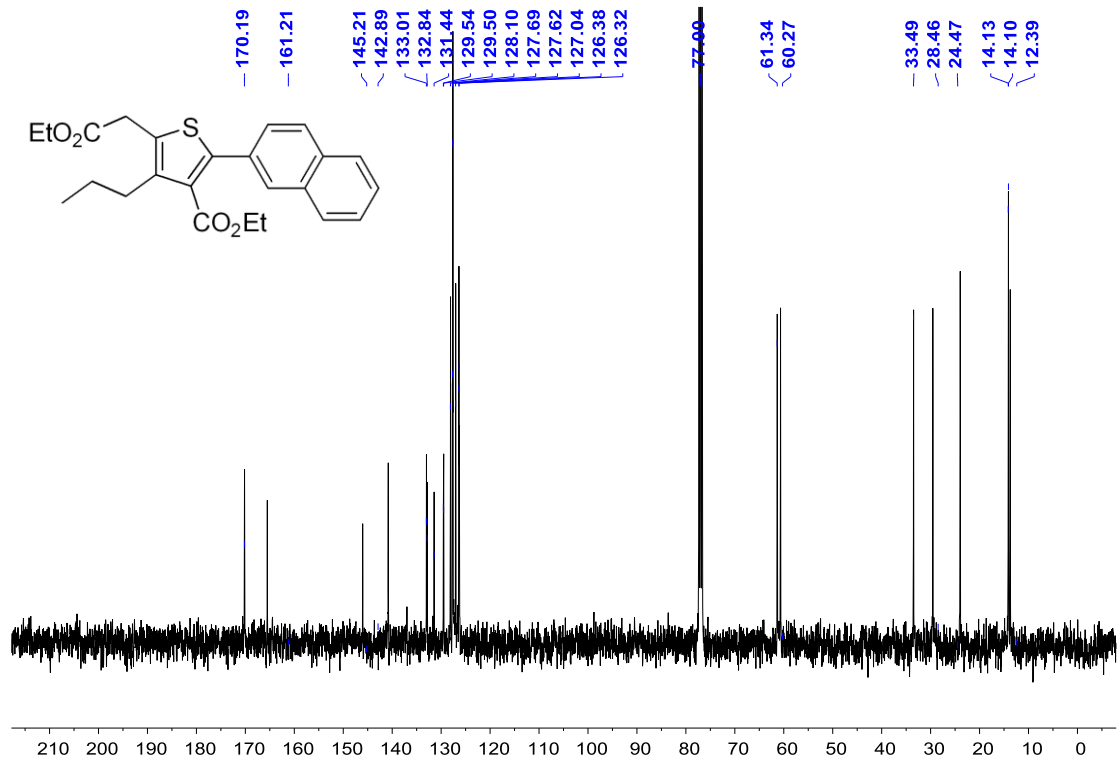


Ethyl 5-(2-ethoxy-2-oxoethyl)-2-(naphthalen-2-yl)-4-propylthiophene-3-carboxylate (3aK)

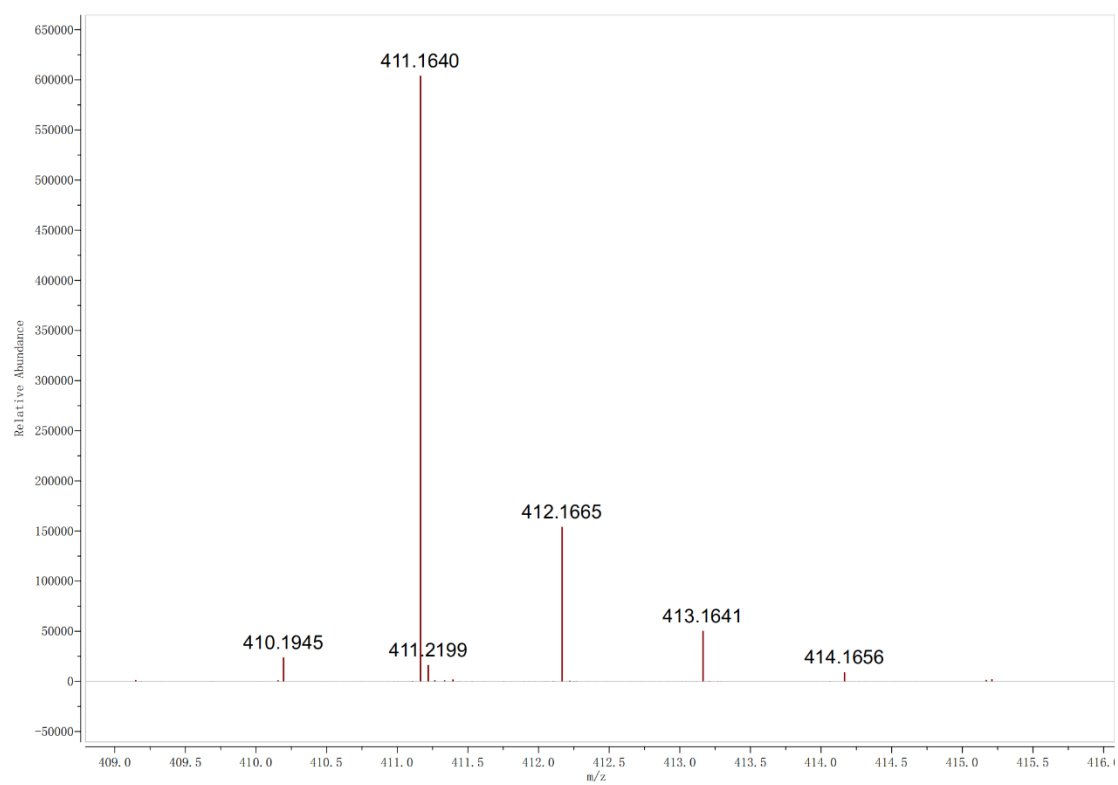
¹H NMR (400 MHz, CDCl₃)



¹³C NMR (101 MHz, CDCl₃)



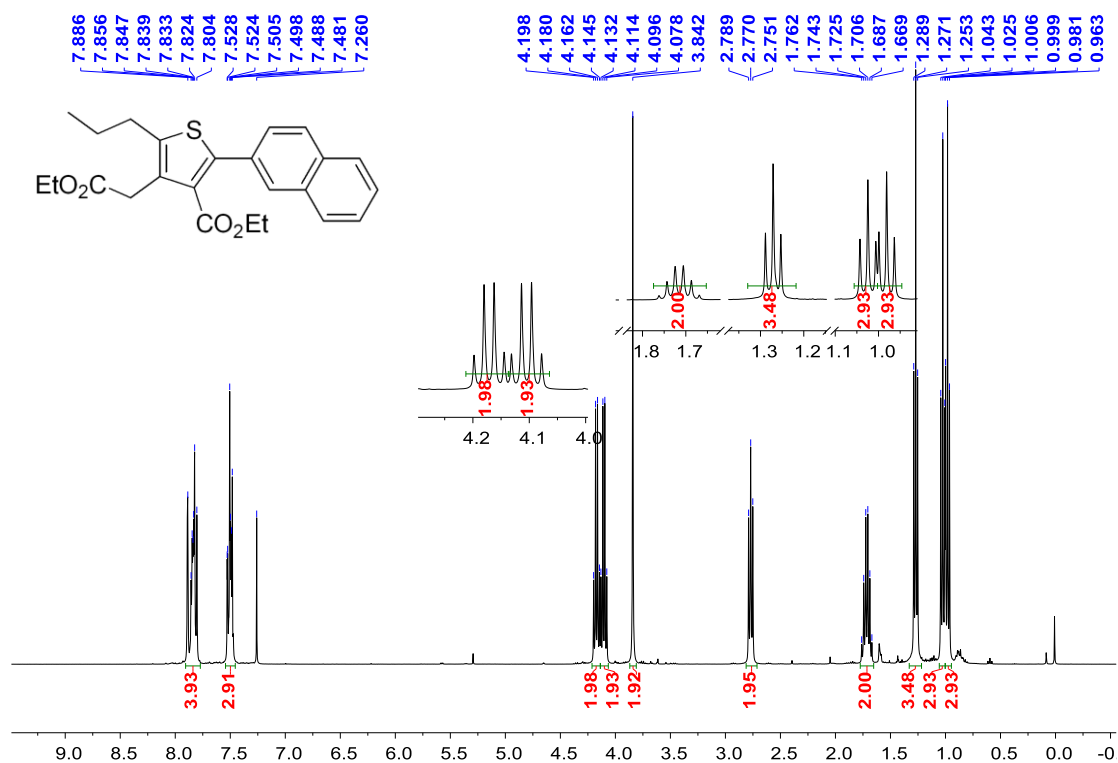
HRMS (ESI)



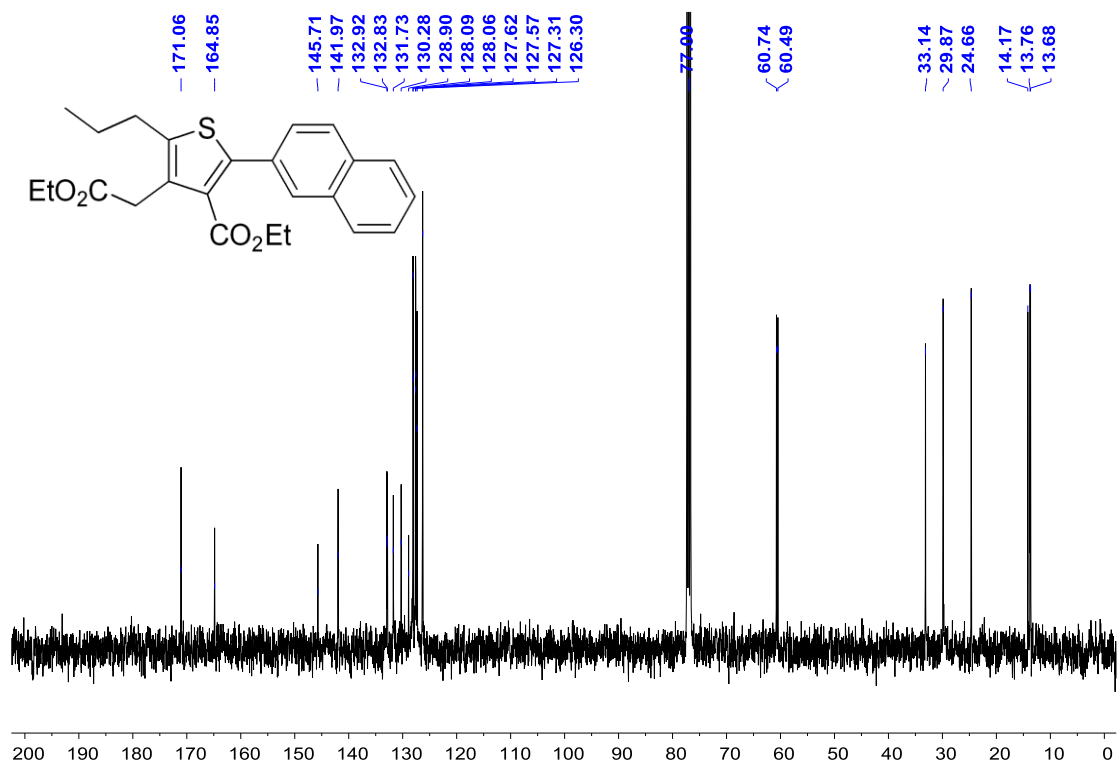
Ethyl 4-(2-ethoxy-2-oxoethyl)-2-(naphthalen-2-yl)-5-propylthiophene-3-carboxylate

(3'aK)

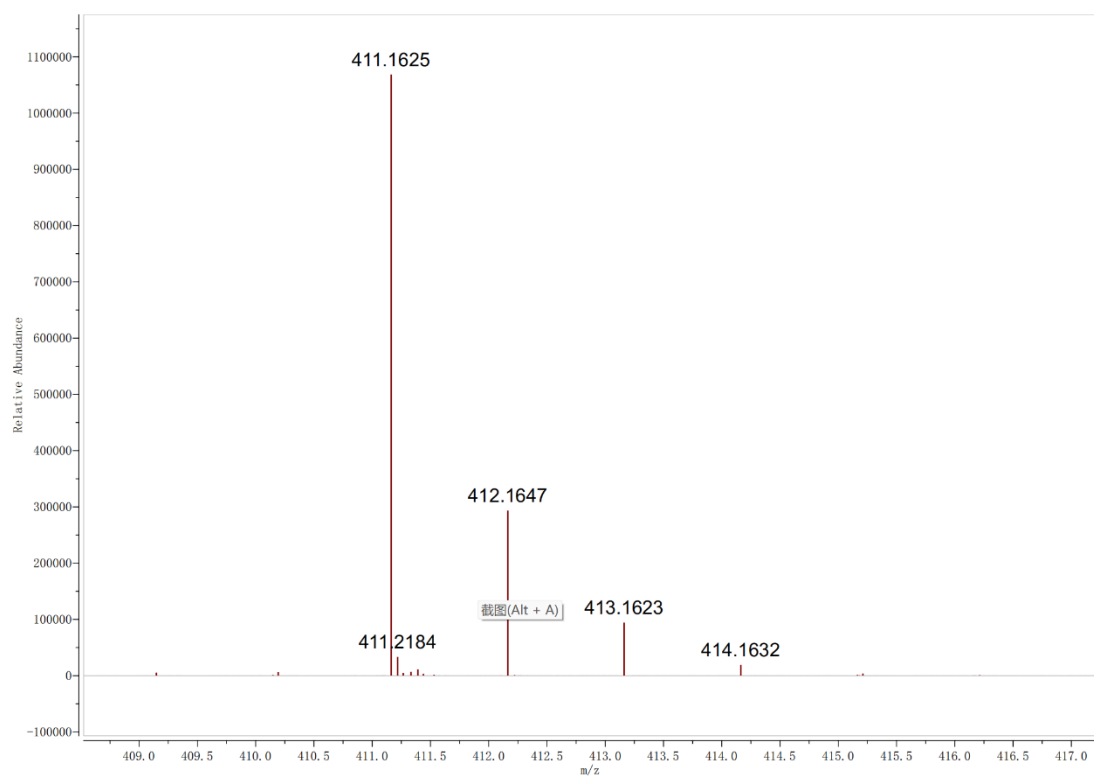
¹H NMR (400 MHz, CDCl₃)



¹³C NMR (101 MHz, CDCl₃)

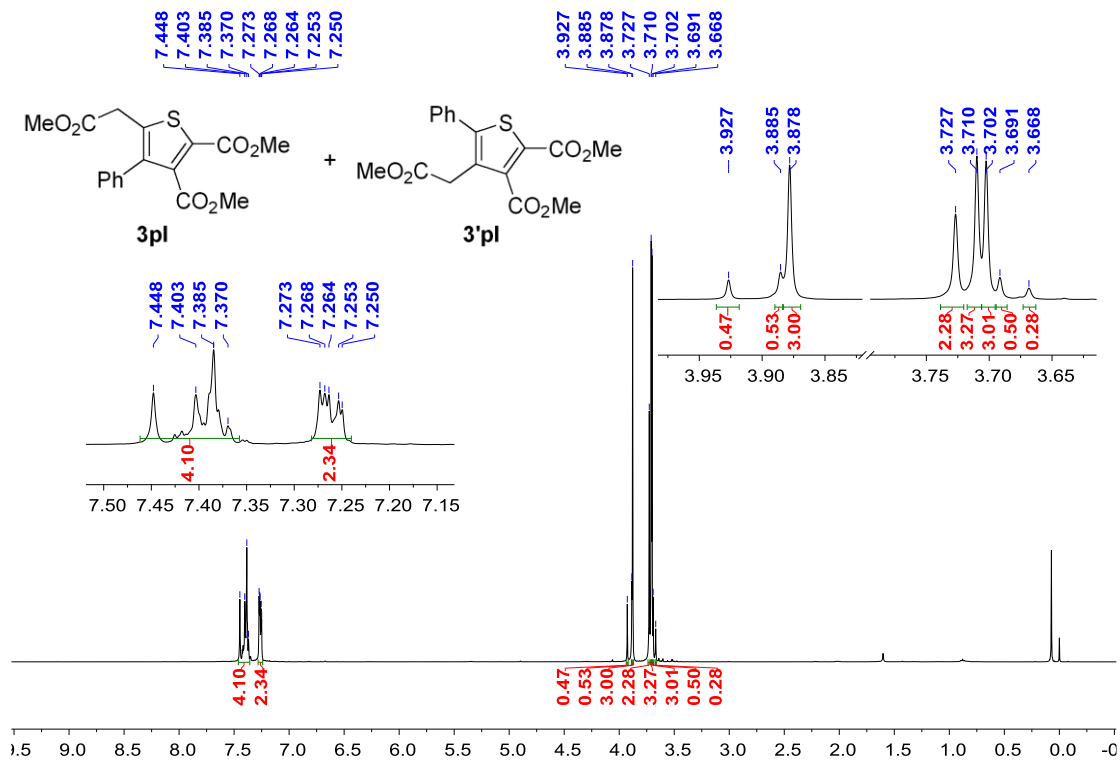


HRMS (ESI)

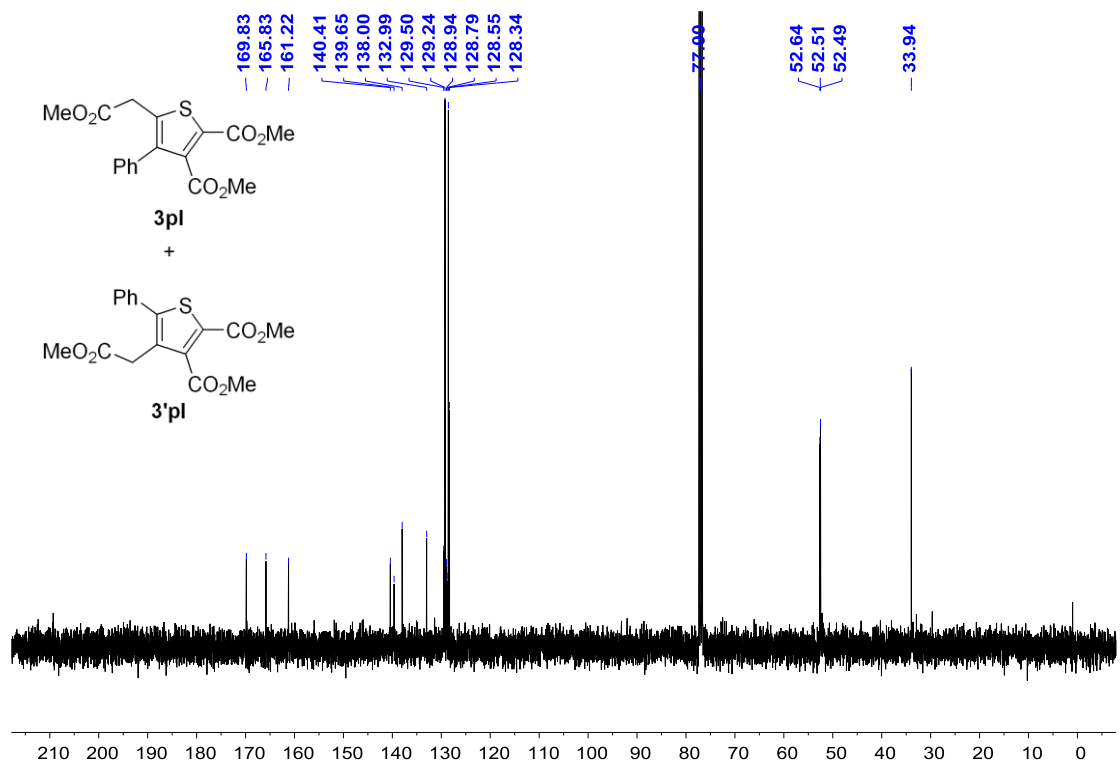


Dimethyl 5-(2-methoxy-2-oxoethyl)-4-phenylthiophene-2,3-dicarboxylate

^1H NMR (400 MHz, CDCl_3)

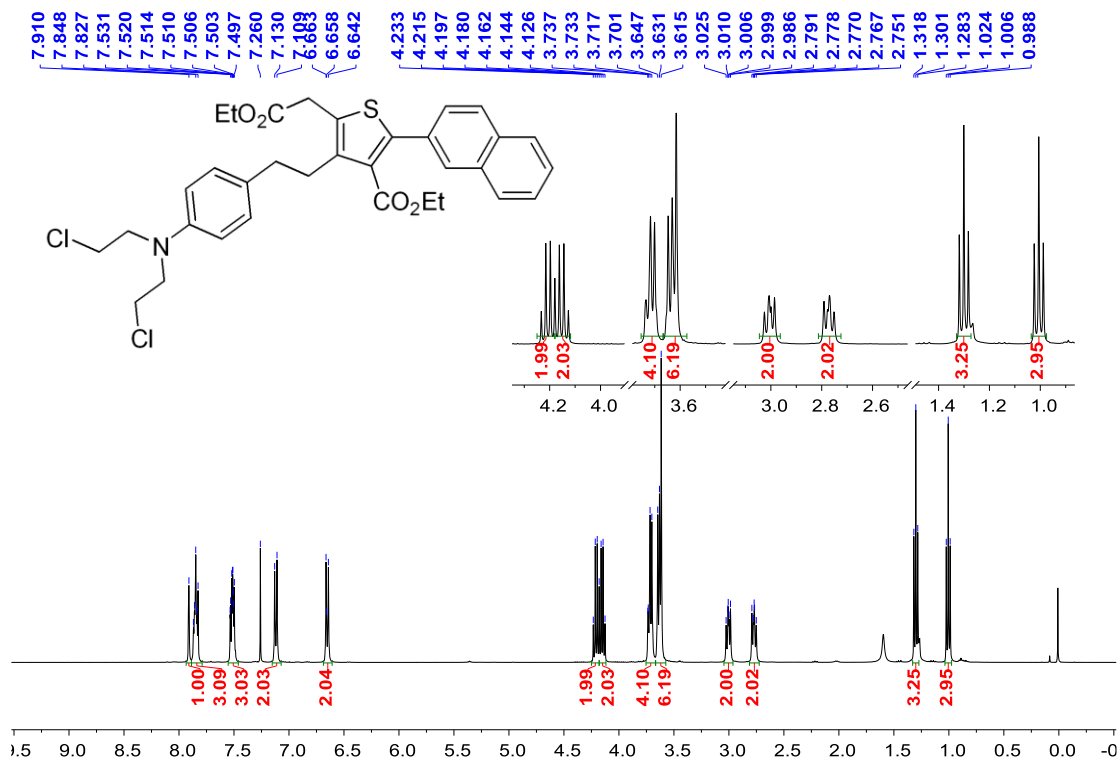


^{13}C NMR (101 MHz, CDCl_3)

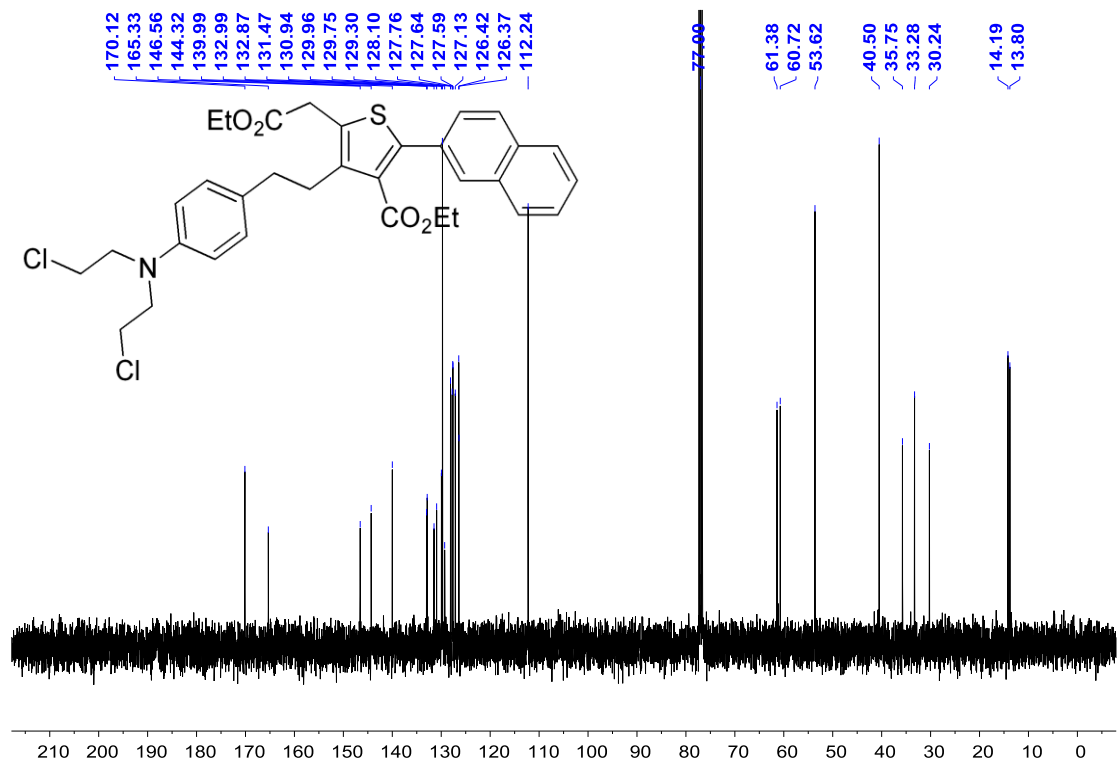


Ethyl 4-(4-(bis(2-chloroethyl)amino)phenethyl)-5-(2-ethoxy-2-oxoethyl)-2-(naphthalen-2-yl)thiophene-3-carboxylate (3aP)

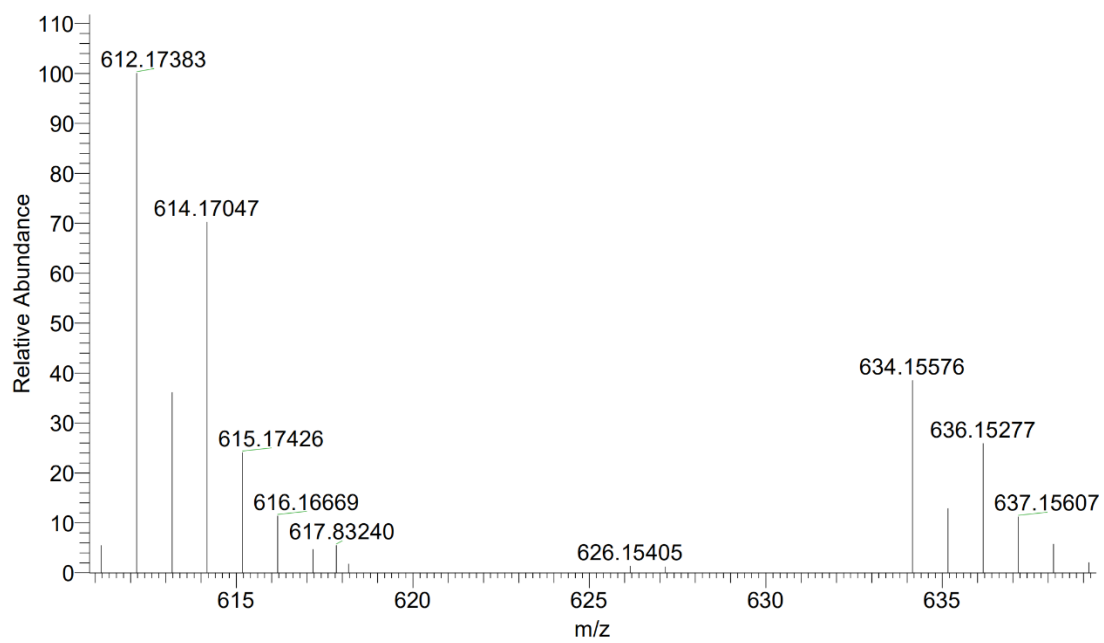
¹H NMR (400 MHz, CDCl₃)



¹³C NMR (101 MHz, CDCl₃)

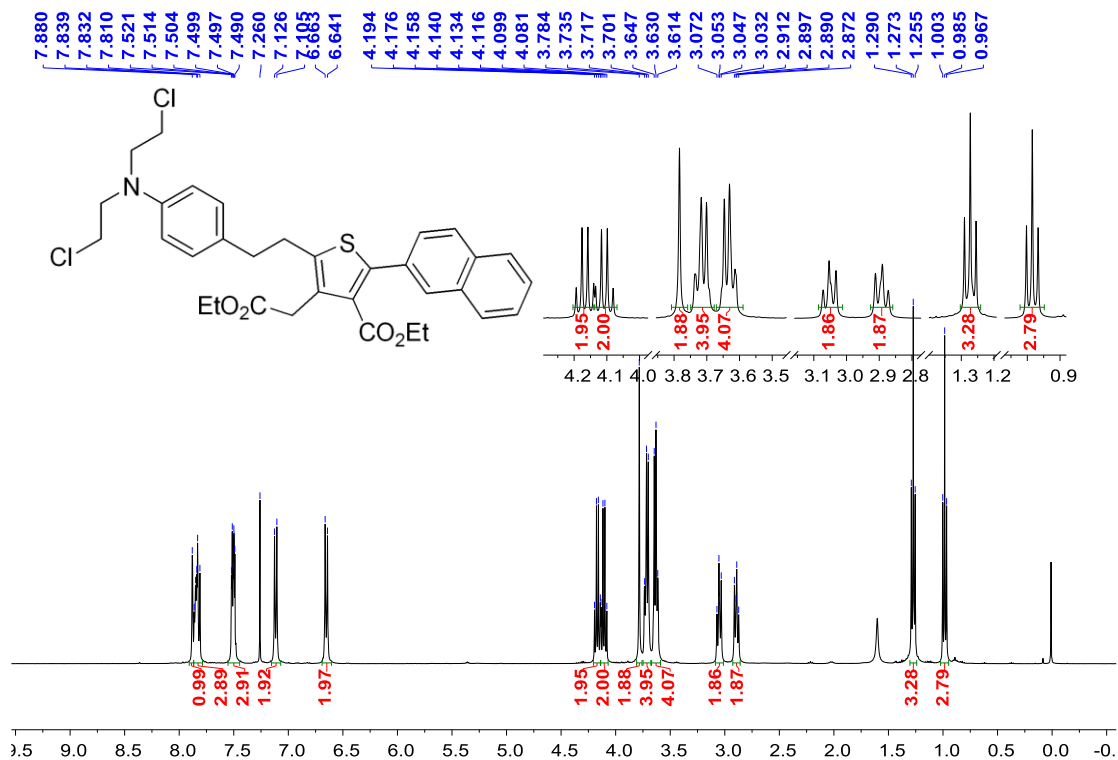


HRMS (ESI)

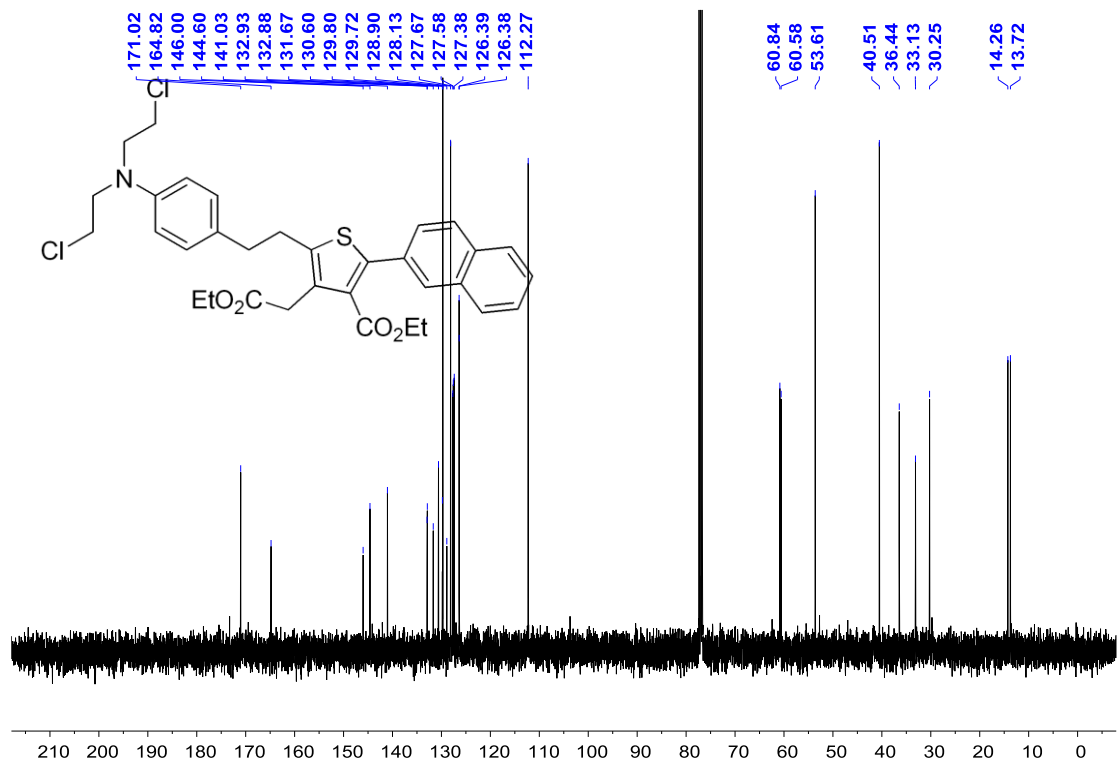


Ethyl 5-(4-(bis(2-chloroethyl)amino)phenethyl)-4-(2-ethoxy-2-oxoethyl)-2-(naphthalen-2-yl)thiophene-3-carboxylate (3'aP)

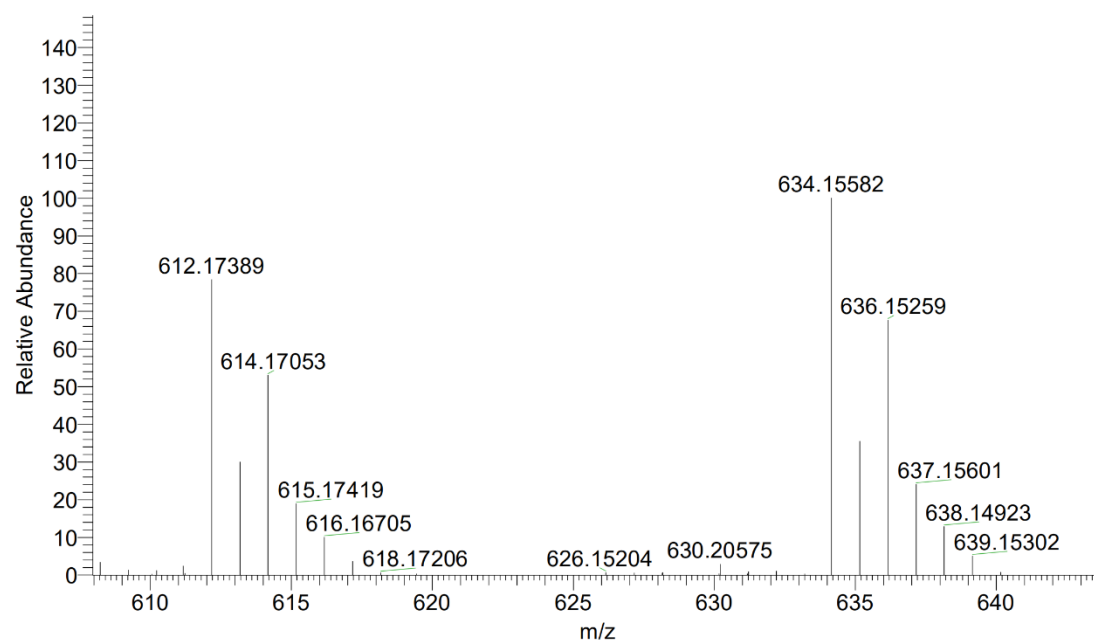
¹H NMR (400 MHz, CDCl₃)



¹³C NMR (101 MHz, CDCl₃)

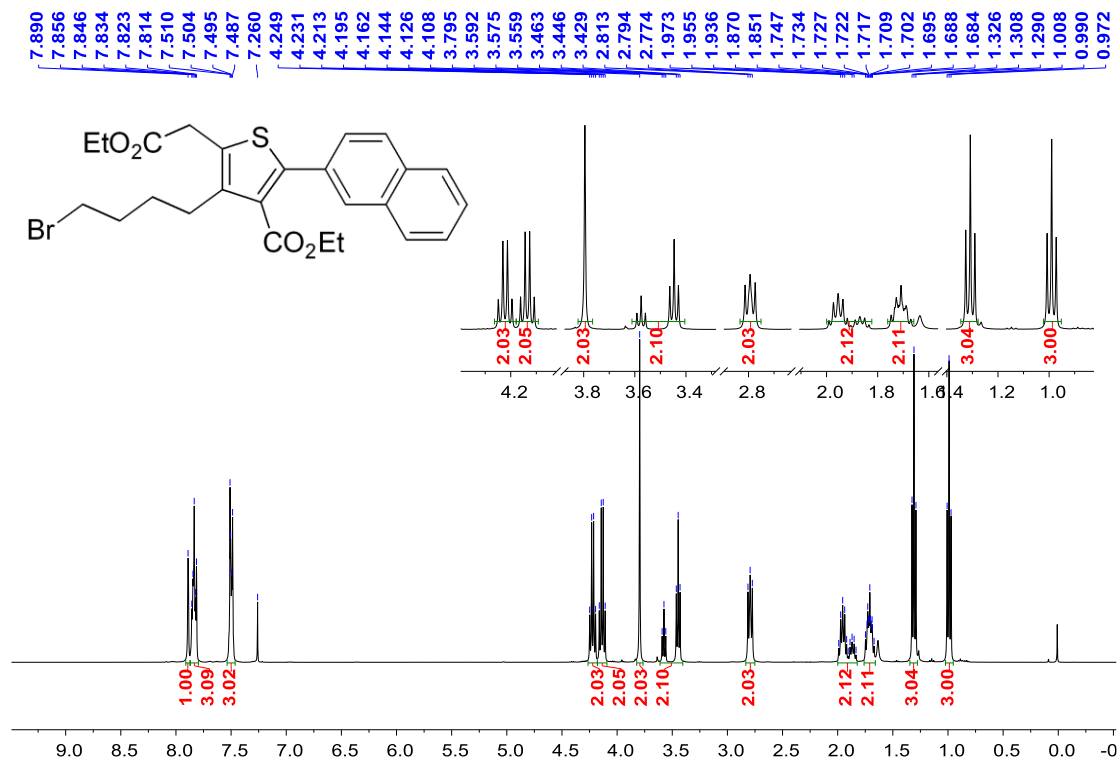


HRMS (ESI)

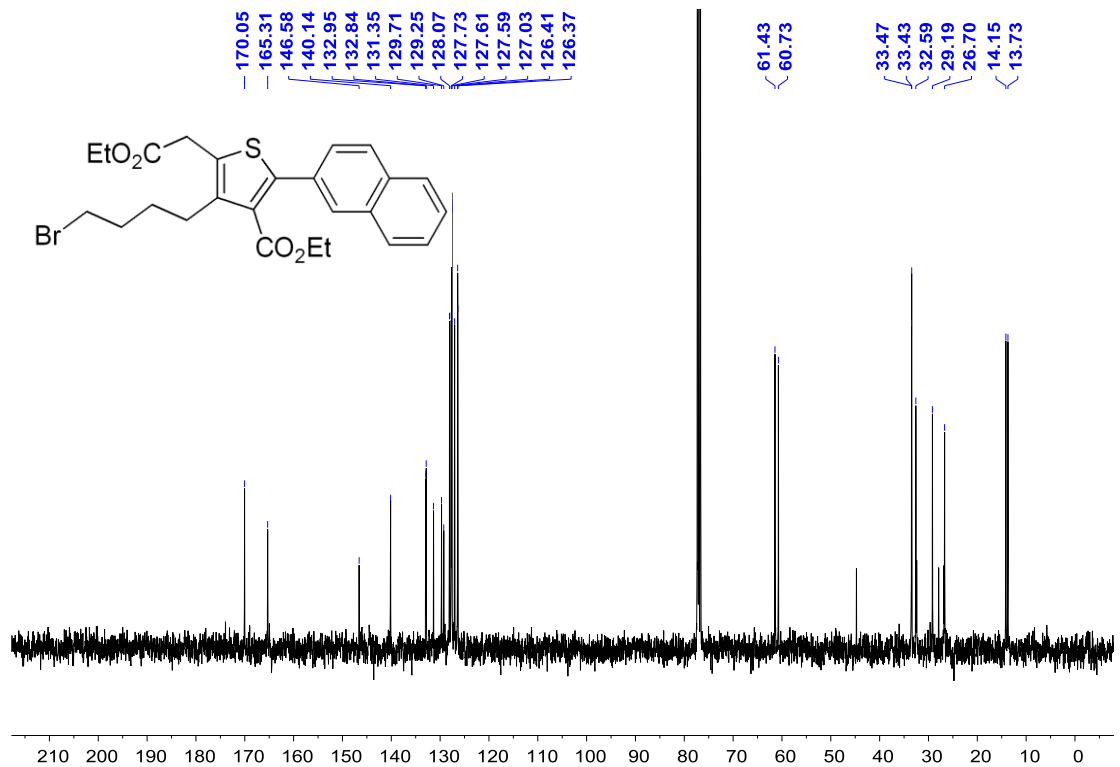


Ehyl 4-(4-bromobutyl)-5-(2-ethoxy-2-oxoethyl)-2-(naphthalen-2-yl)thiophene-3-carboxylate (3aQ)

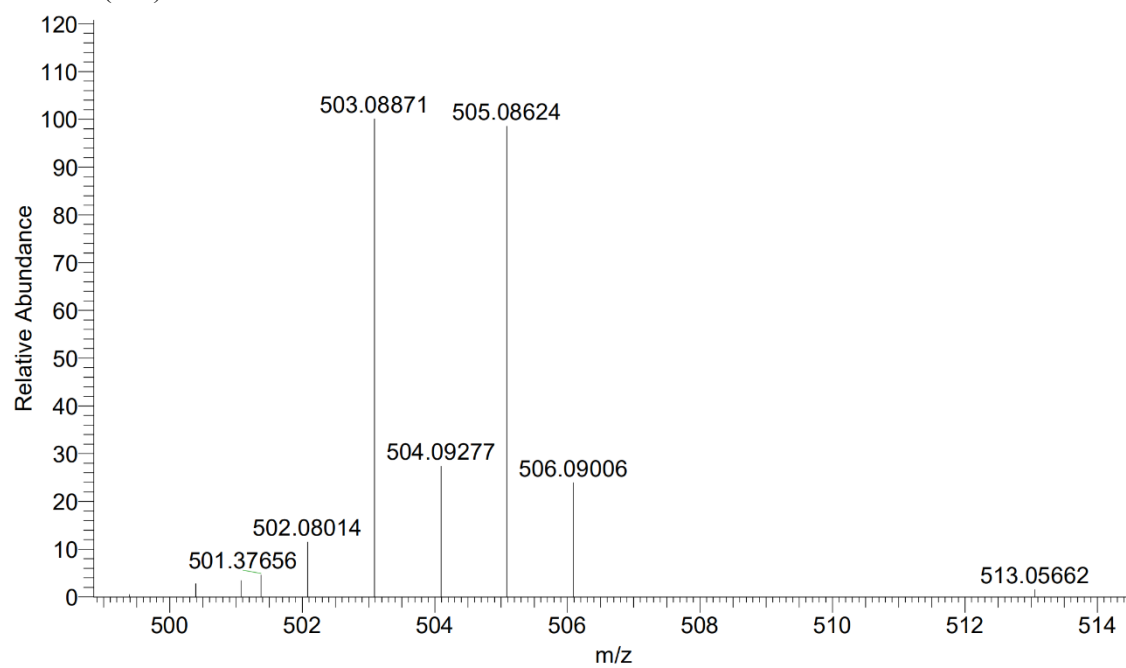
¹H NMR (400 MHz, CDCl₃)



¹³C NMR (101 MHz, CDCl₃)

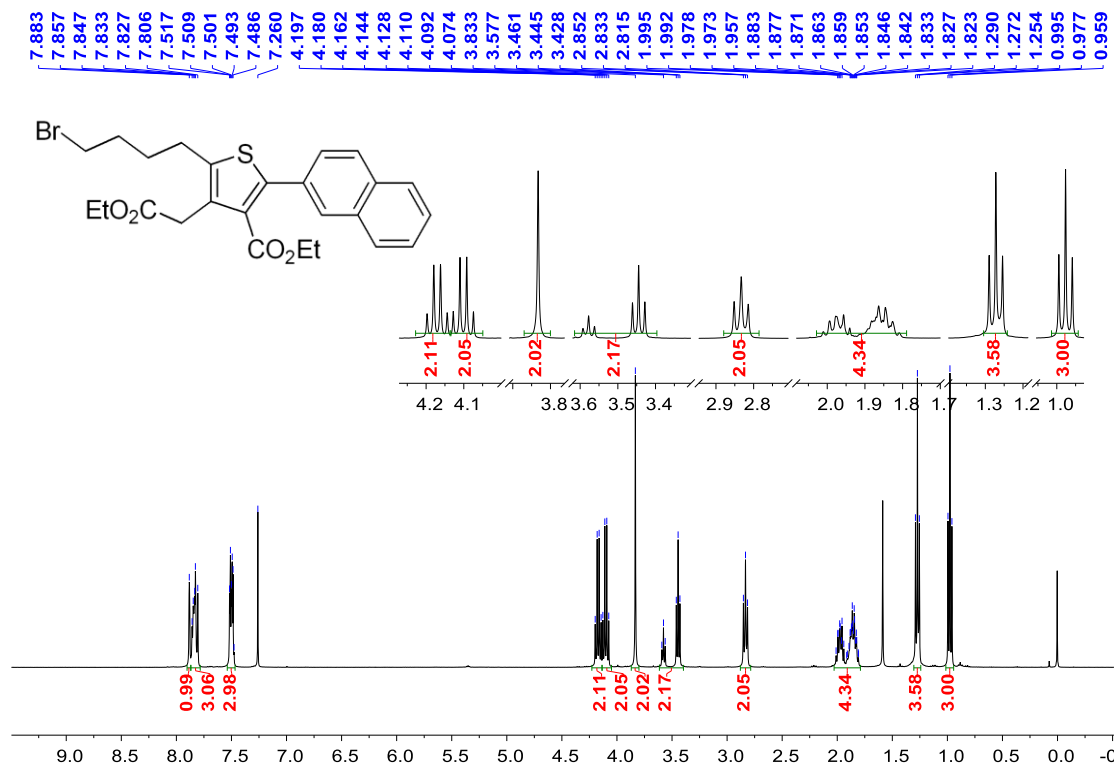


HRMS (ESI)

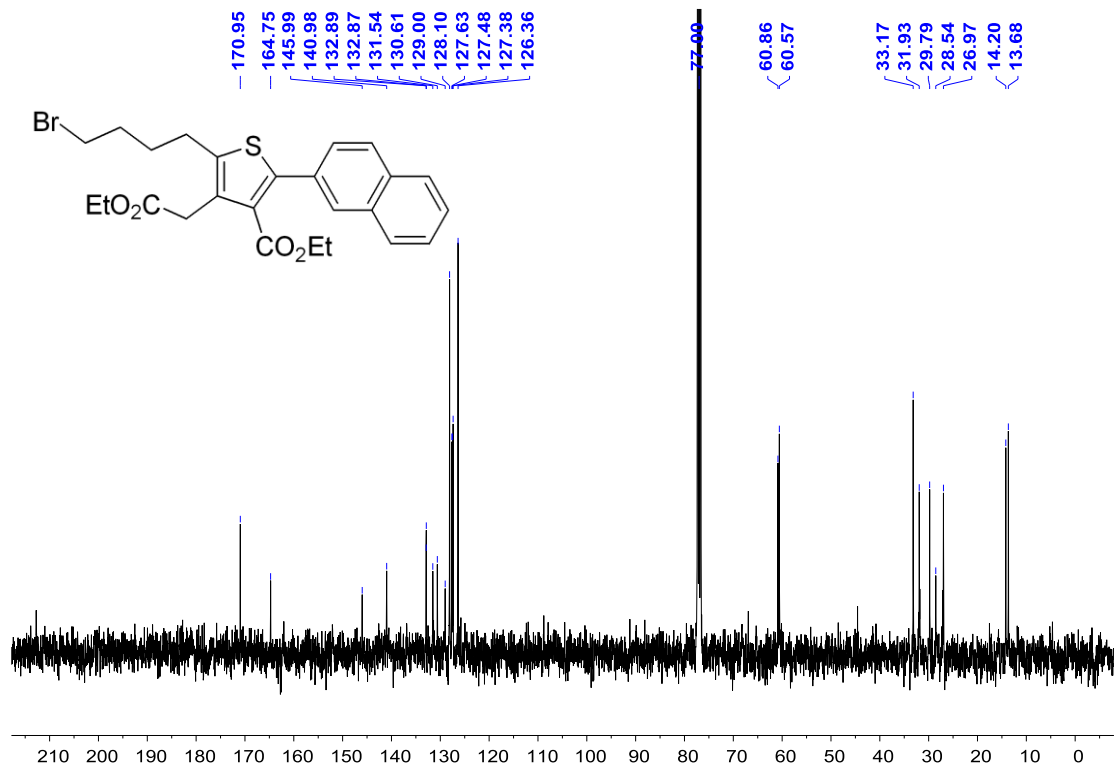


Ethyl 5-(4-bromobutyl)-4-(2-ethoxy-2-oxoethyl)-2-(naphthalen-2-yl)thiophene-3-carboxylate (3'aQ)

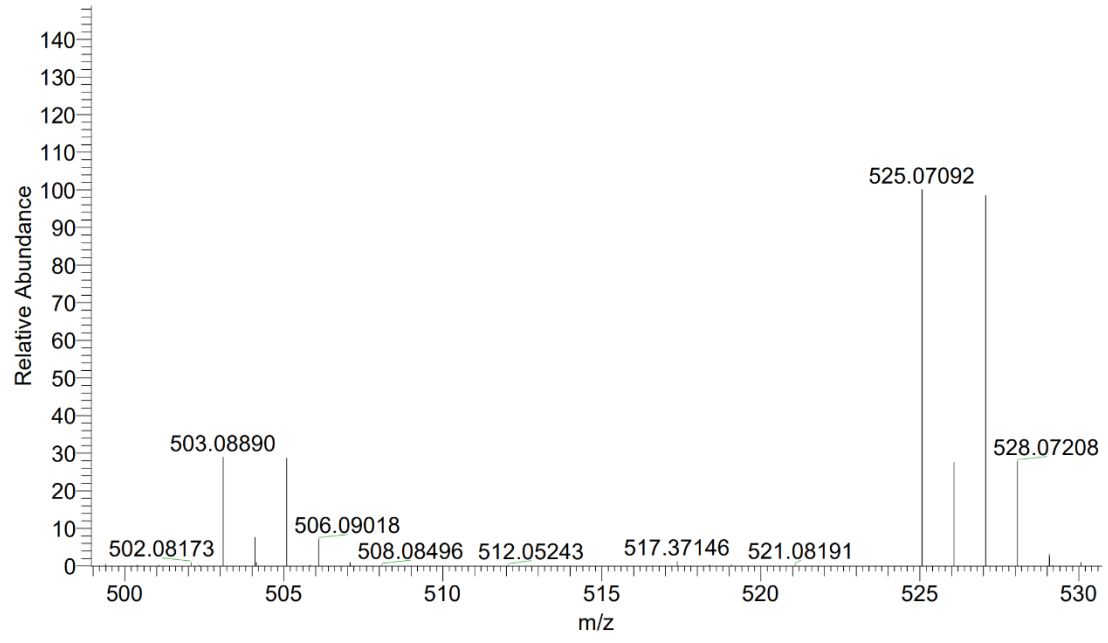
¹H NMR (400 MHz, CDCl₃)



¹³C NMR (101 MHz, CDCl₃)

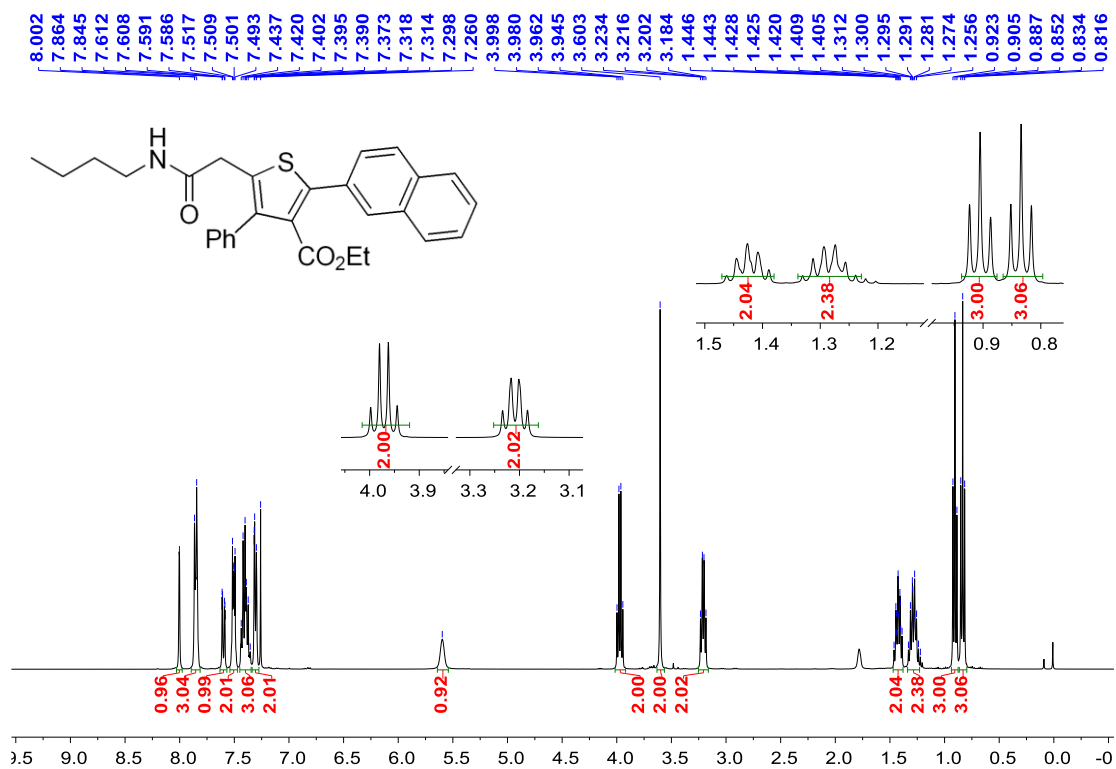


HRMS (ESI)

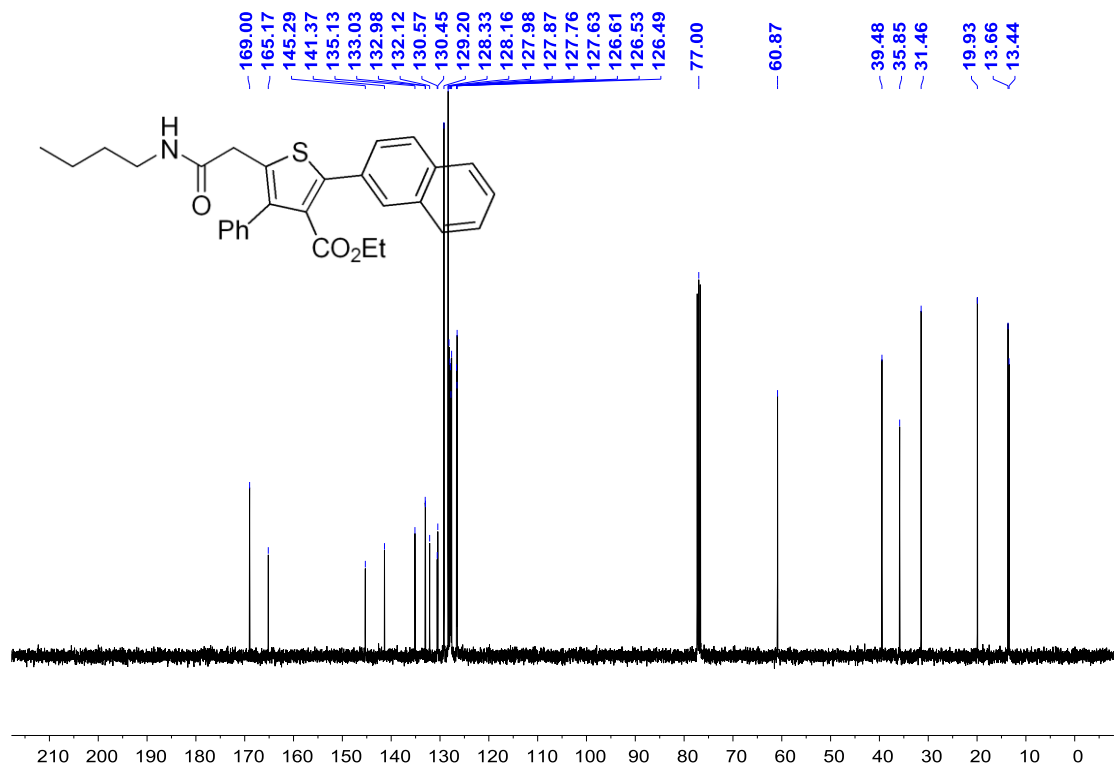


Ethyl 5-(2-(butylamino)-2-oxoethyl)-2-(naphthalen-2-yl)-4-phenylthiophene-3-carboxylate (7aC)

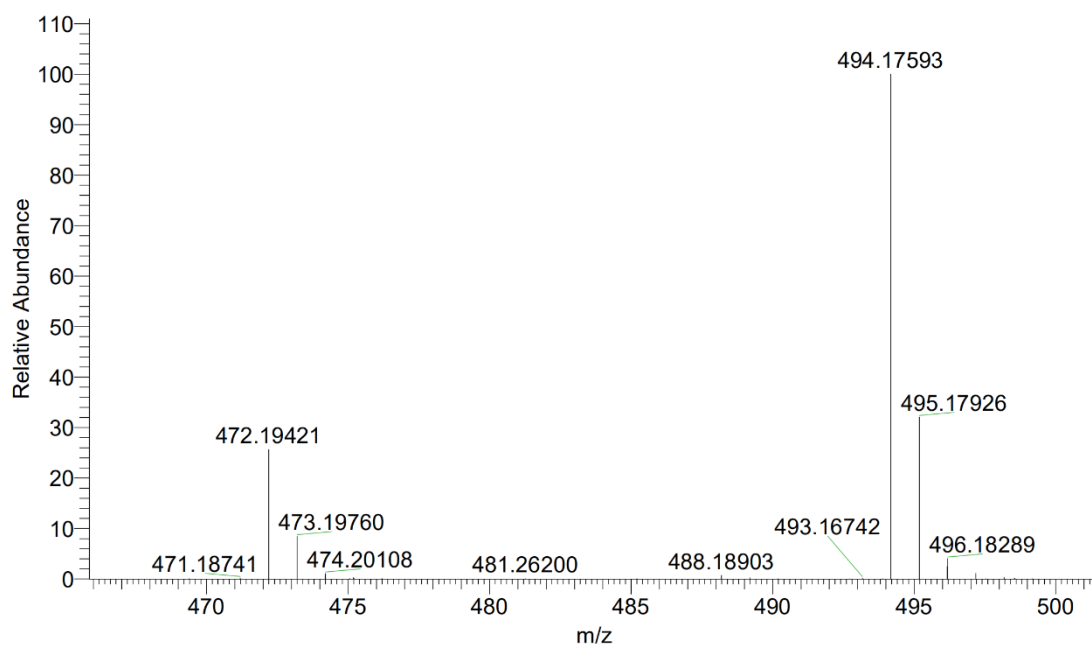
¹H NMR (400 MHz, CDCl₃)



¹³C NMR (101 MHz, CDCl₃)

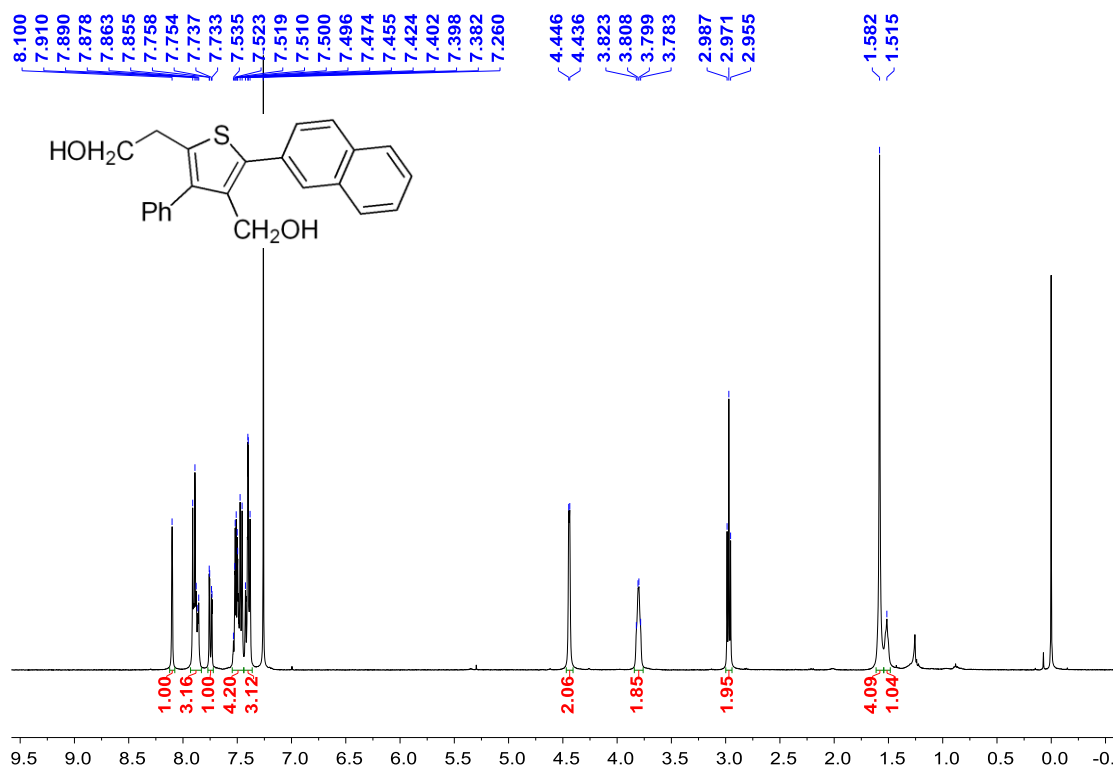


HRMS (ESI)

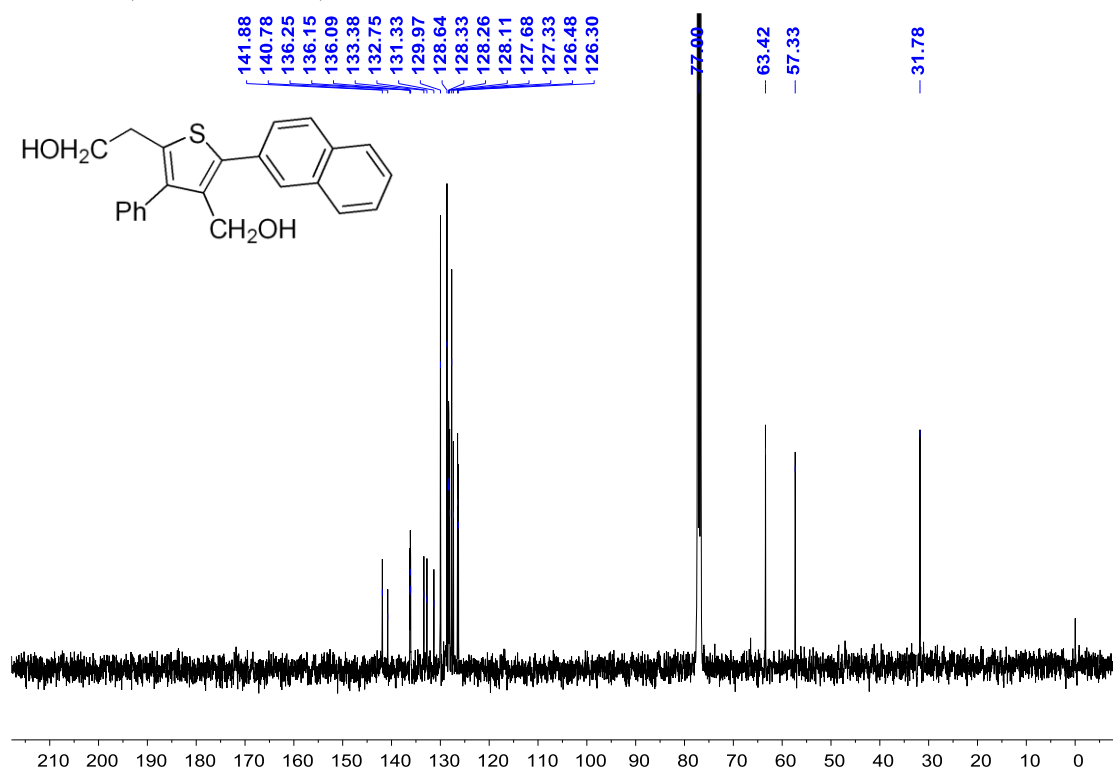


Ethyl 2-(4-(hydroxymethyl)-5-(naphthalen-2-yl)-3-phenylthiophen-2-yl)ethan-1-ol (8aC)

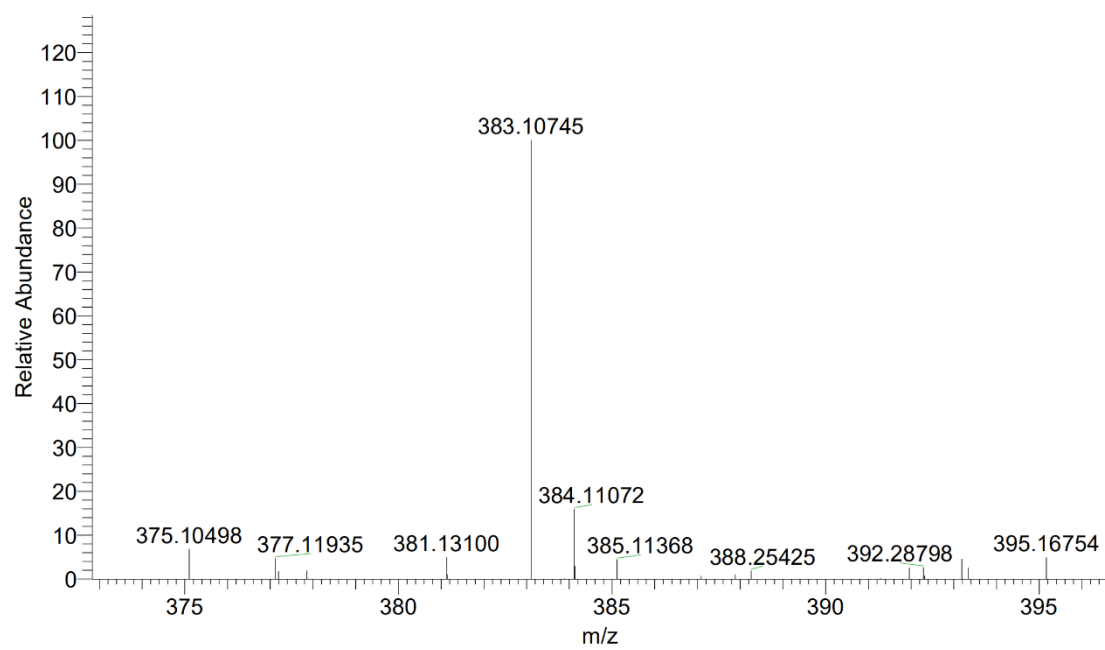
¹H NMR (400 MHz, CDCl₃)



¹³C NMR (101 MHz, CDCl₃)



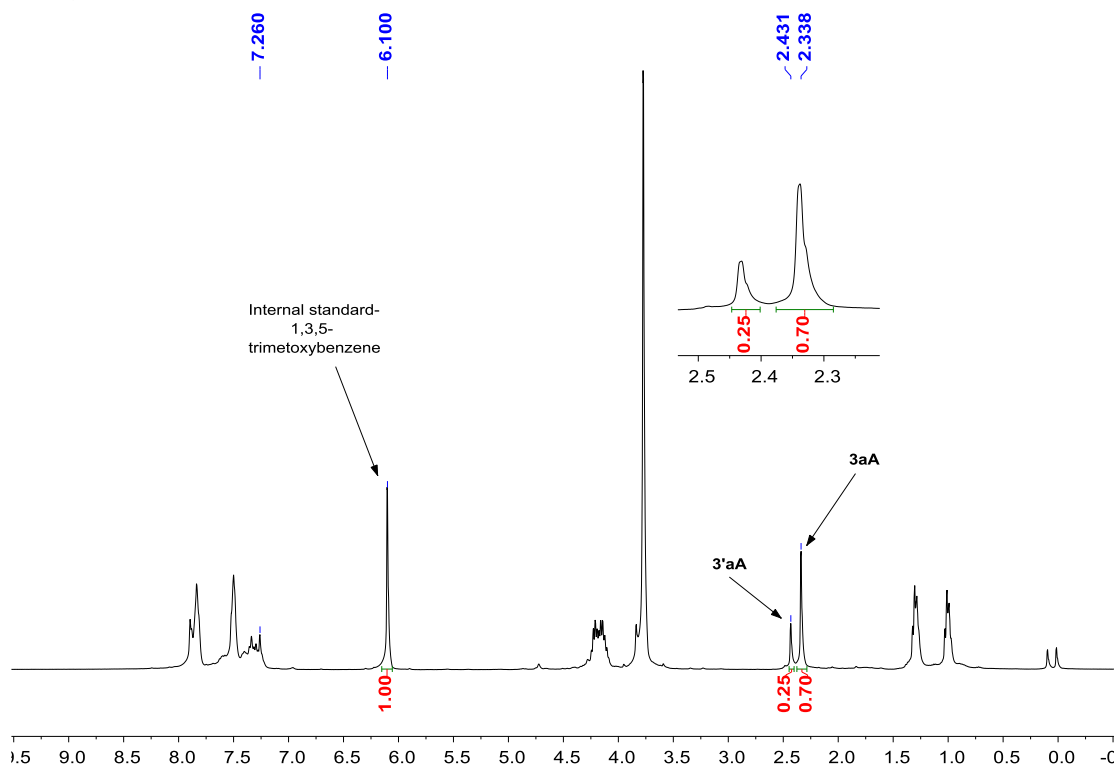
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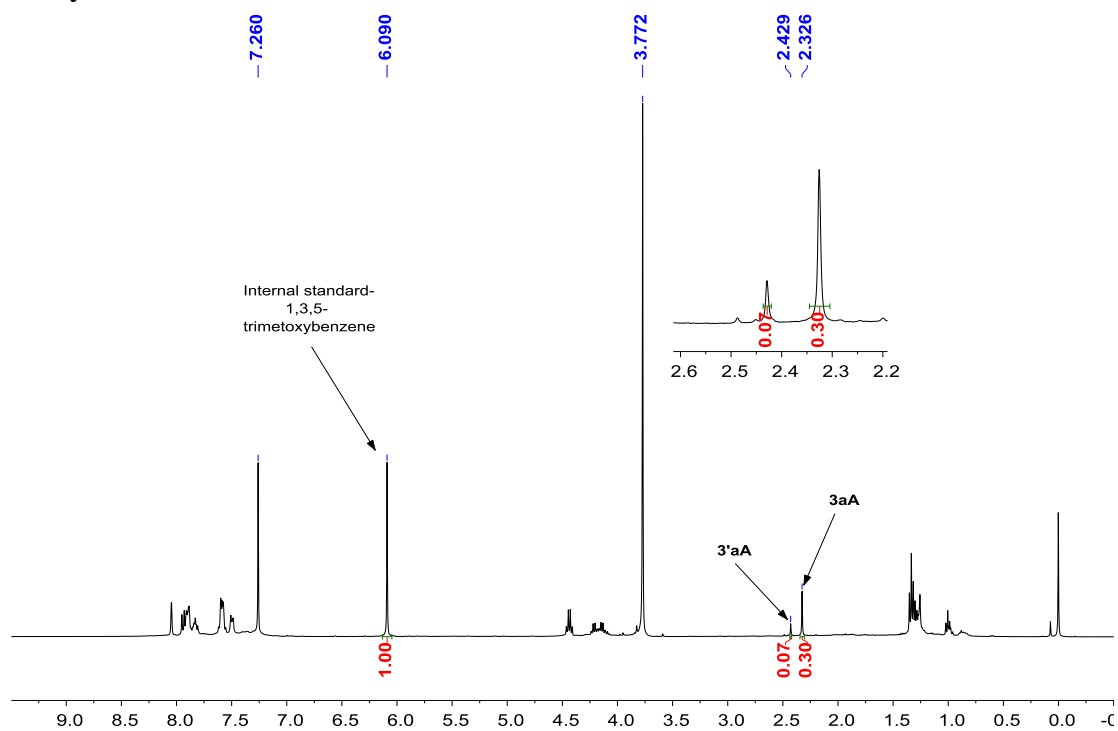
7. Copies of ^1H NMR spectra of Crude reaction mixtures

7.1 Spectra for the reaction condition optimization

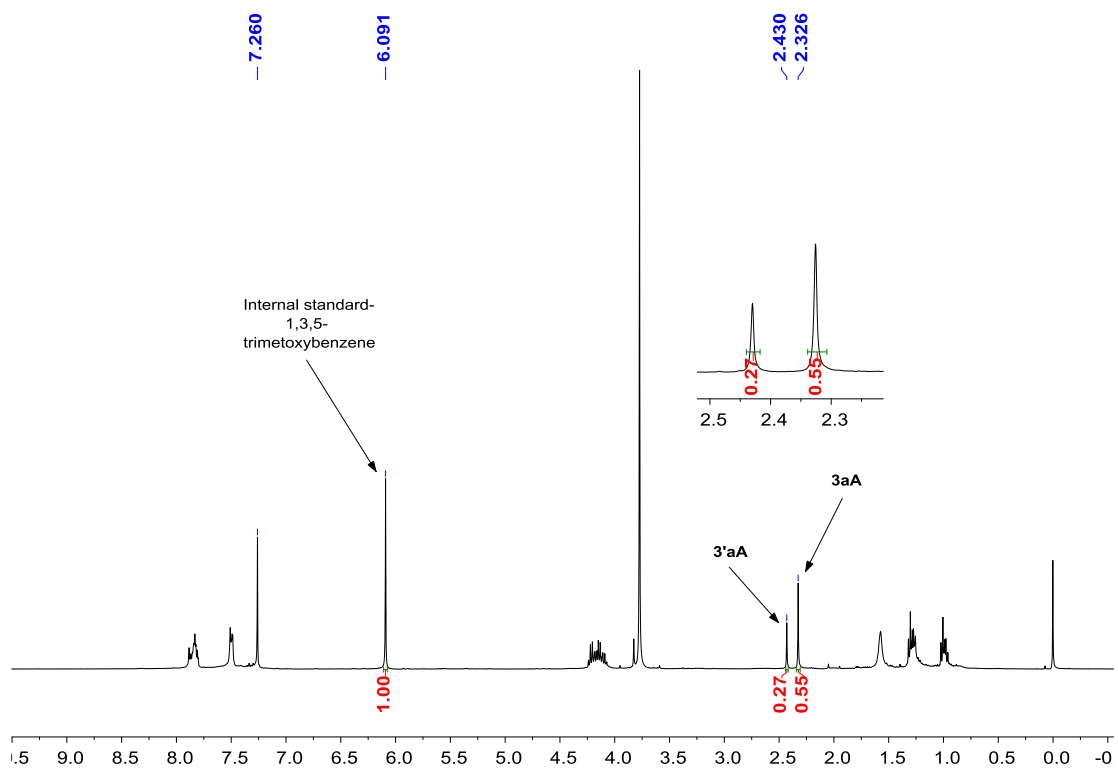
Entry 1



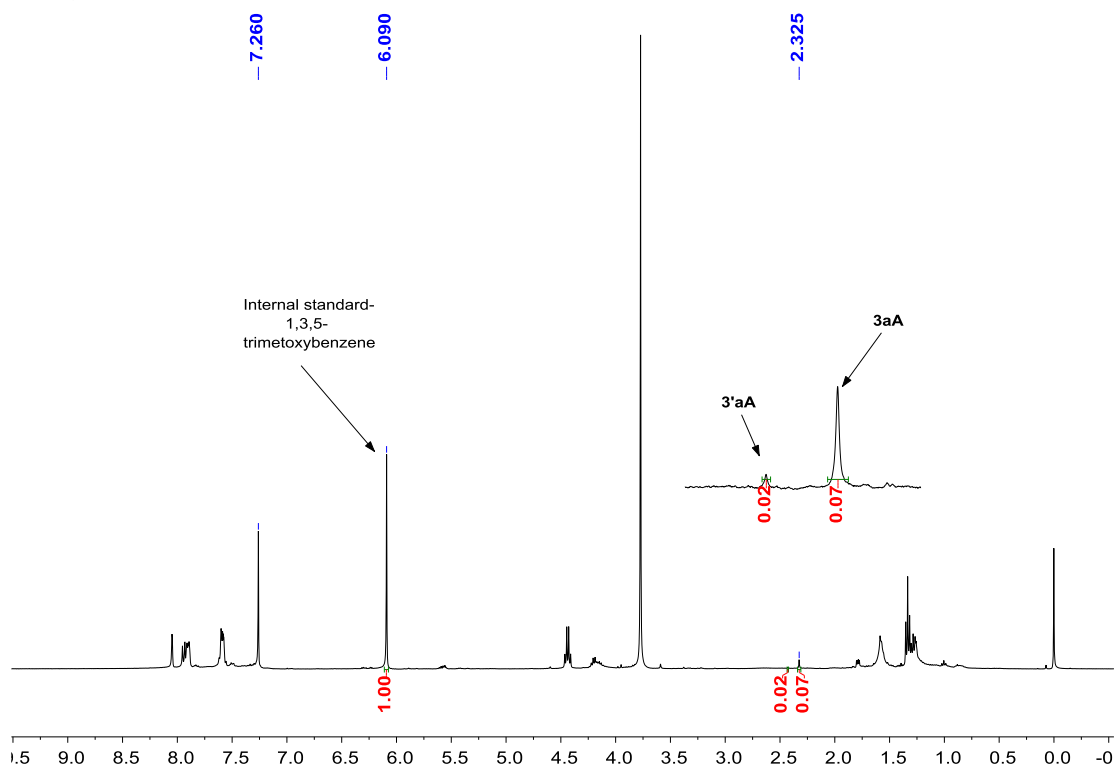
Entry 2



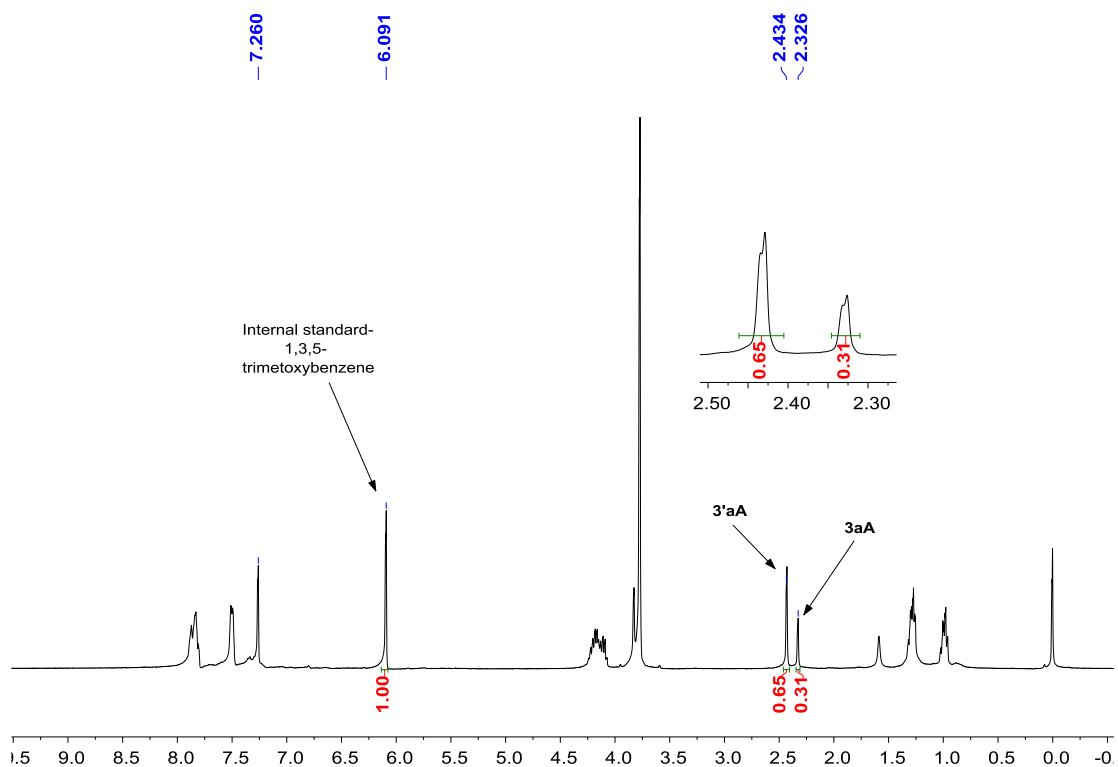
Entry 3



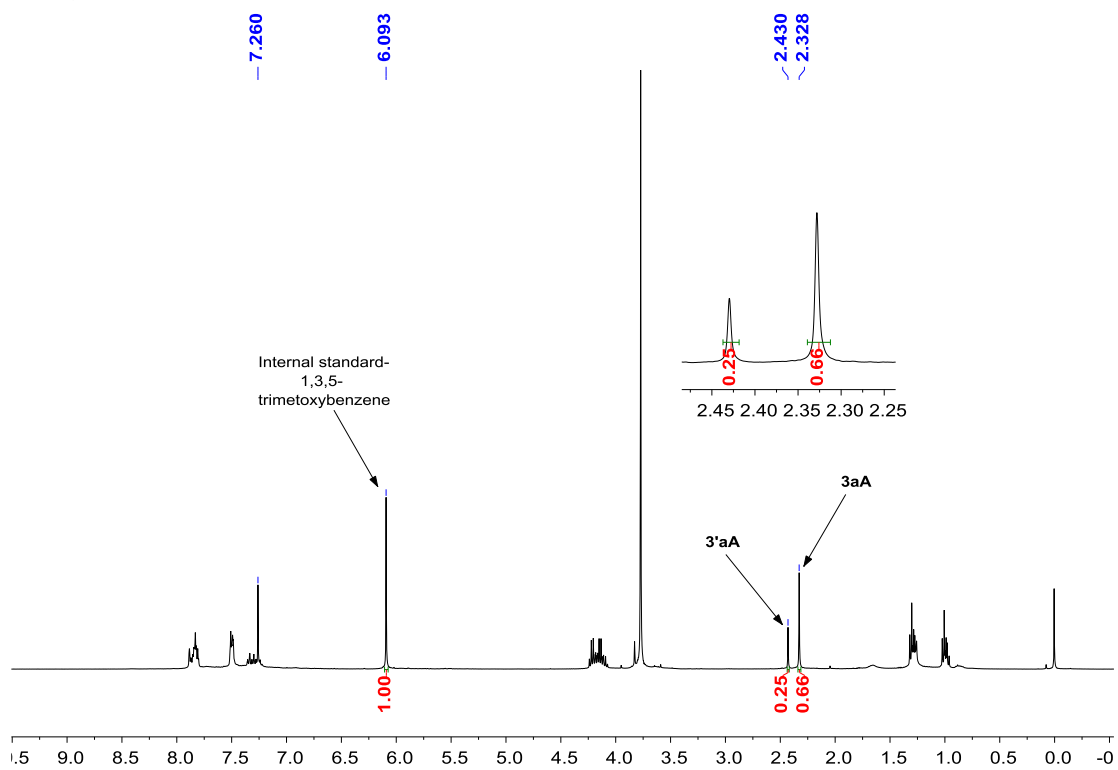
Entry 4



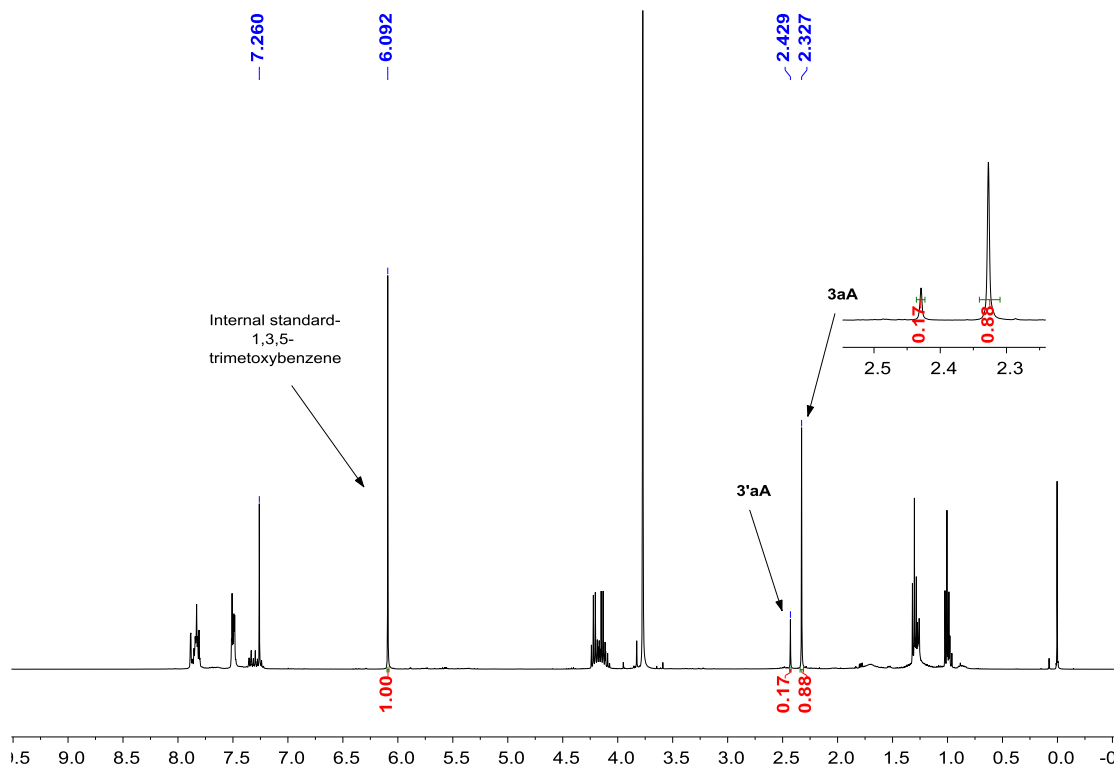
Entry 10



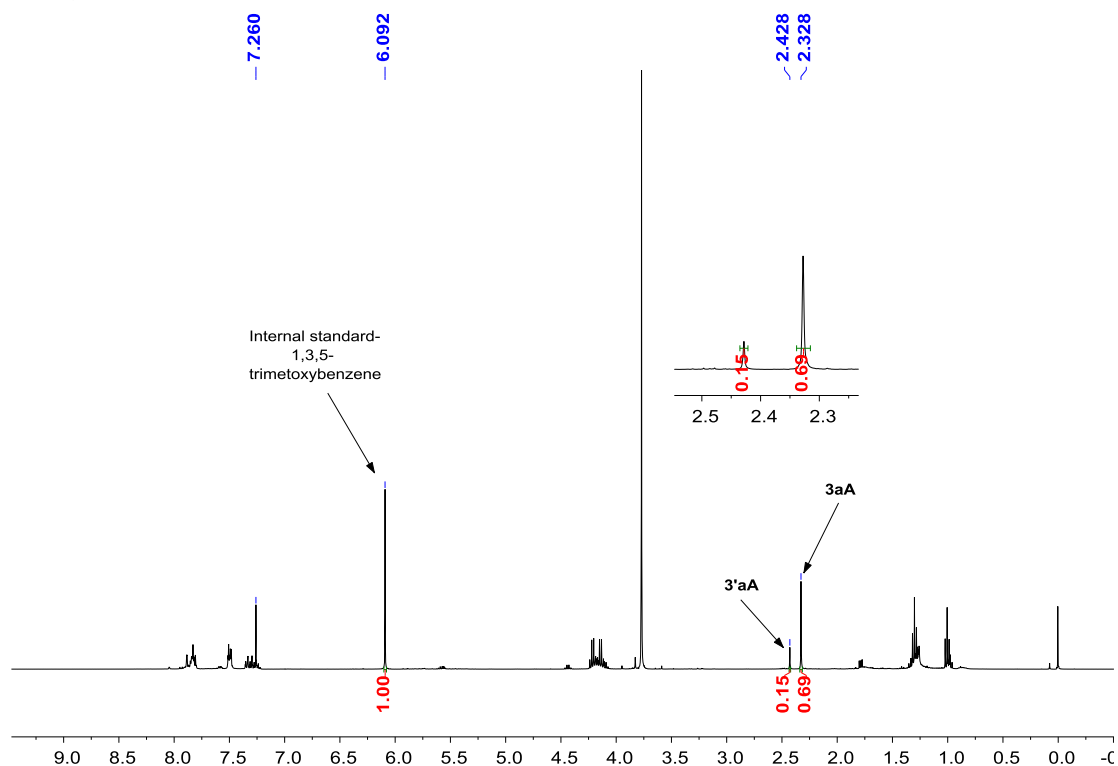
Entry 11



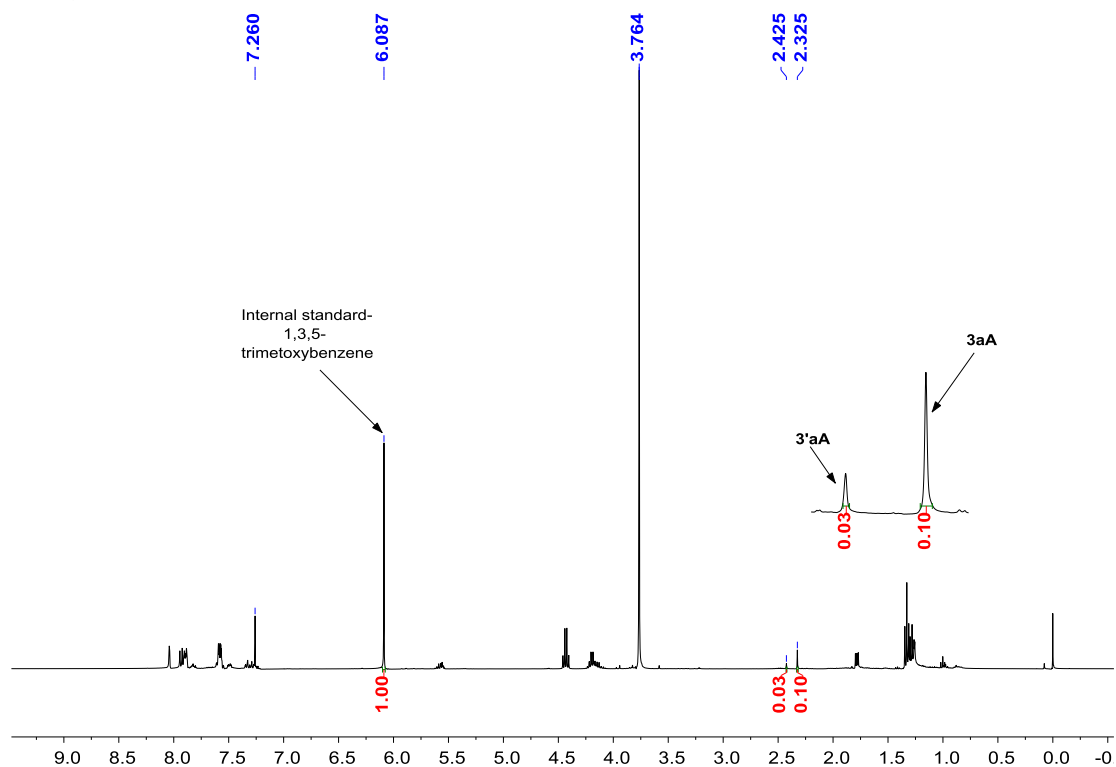
Entry 13



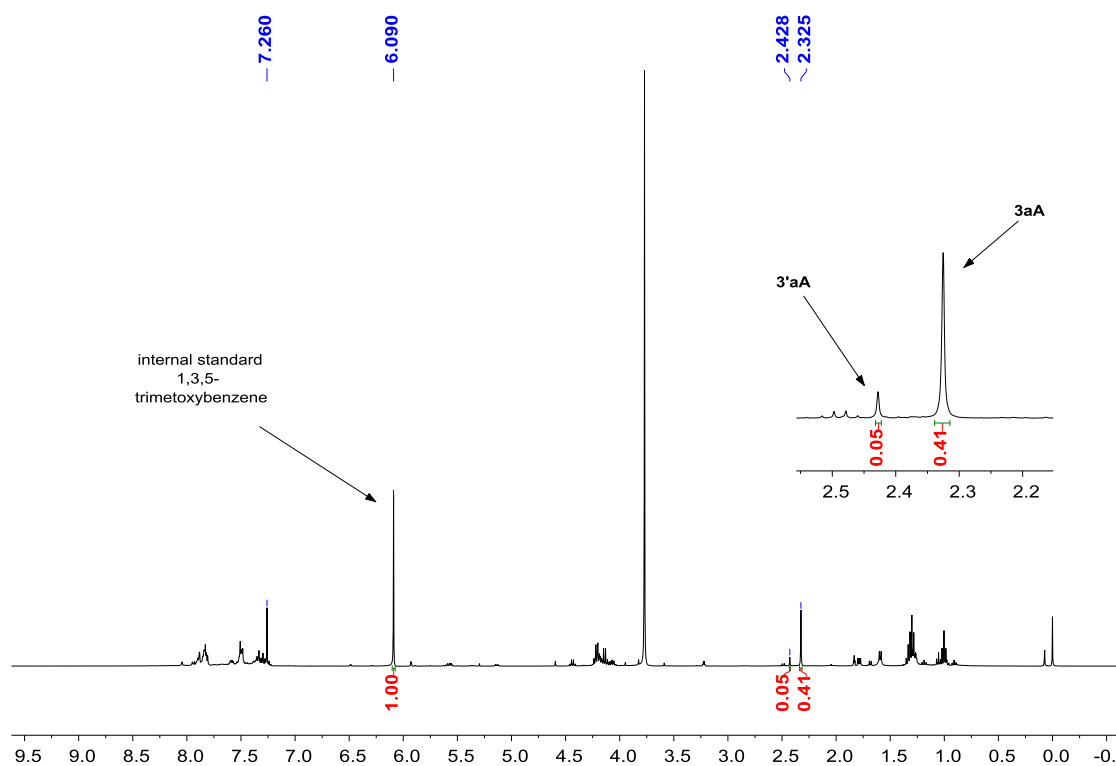
Entry 14



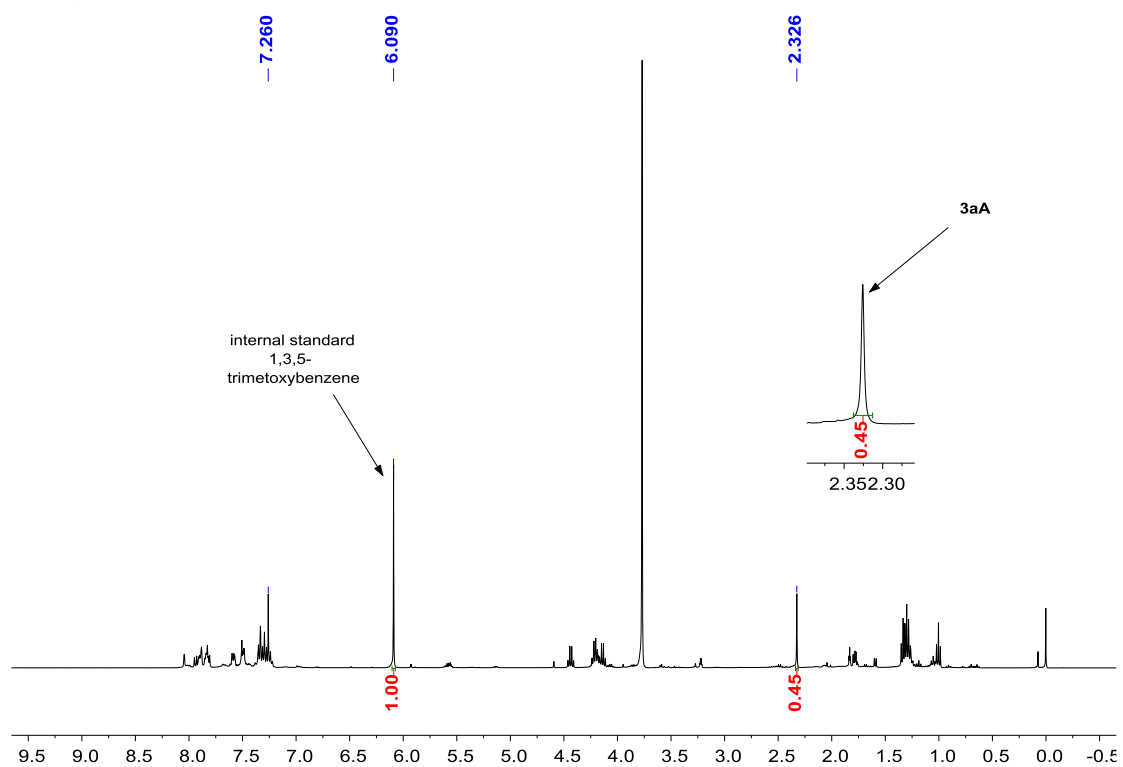
Entry 15



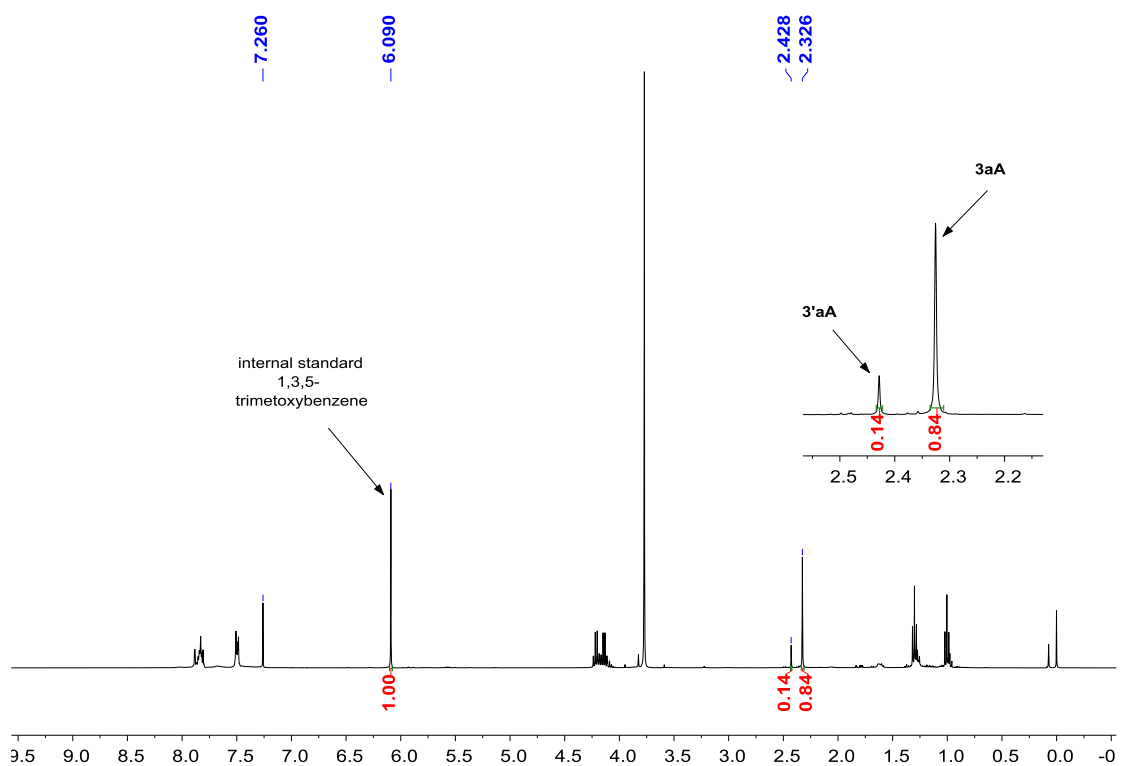
Entry 18



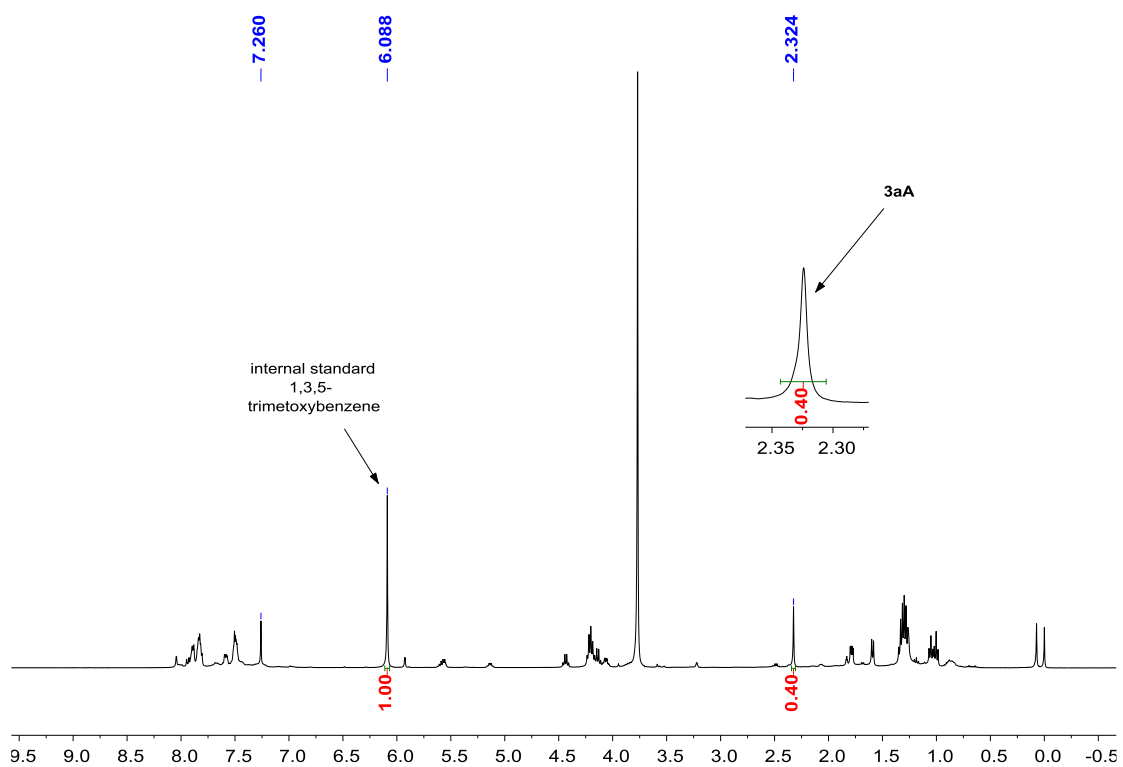
Entry 19



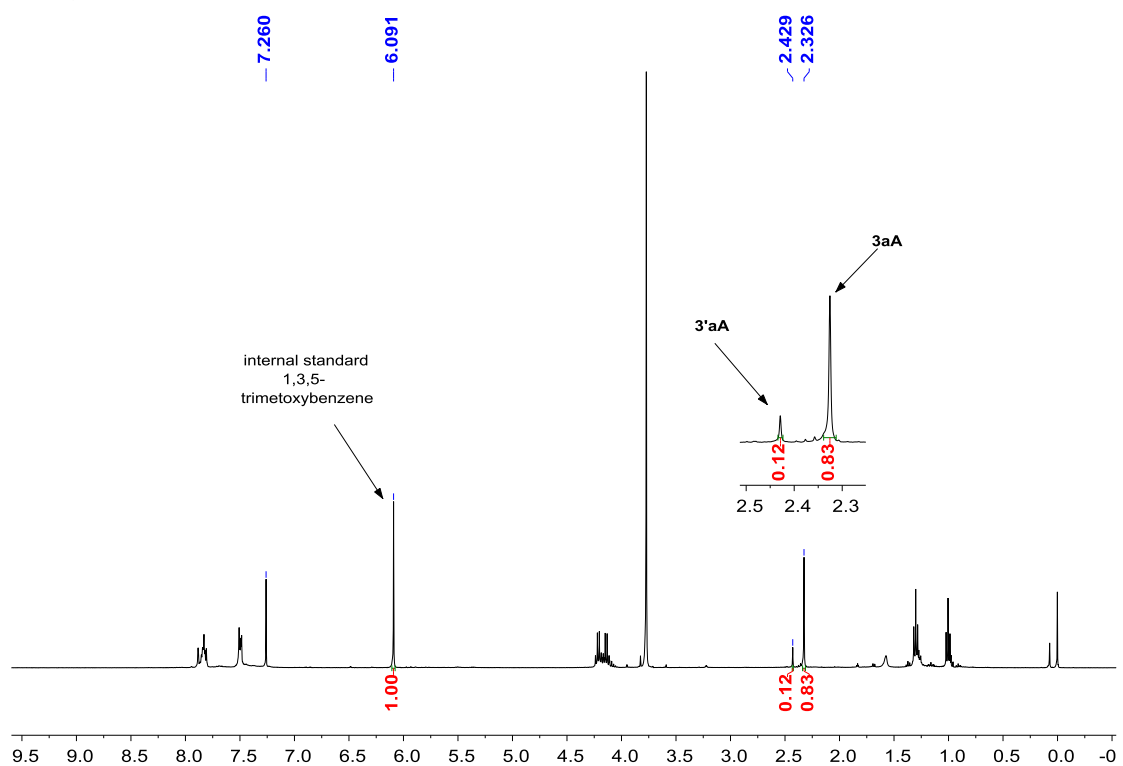
Entry 20



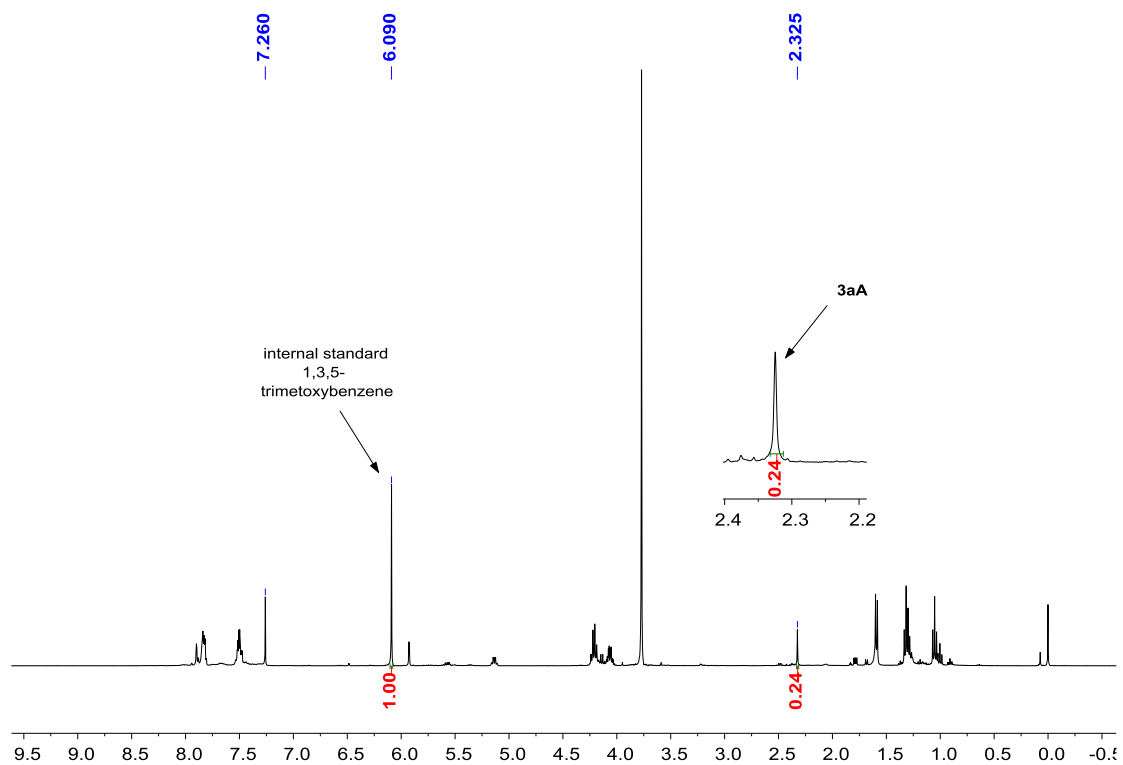
Entry 21



Entry 21

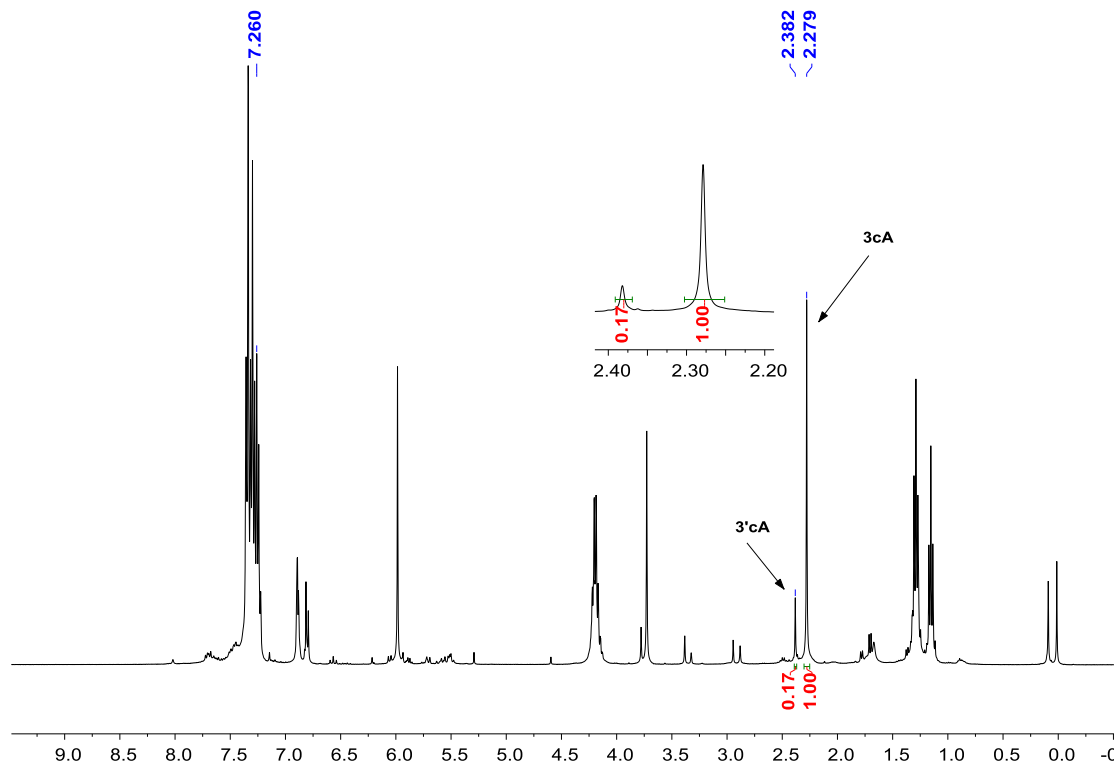


Entry 23

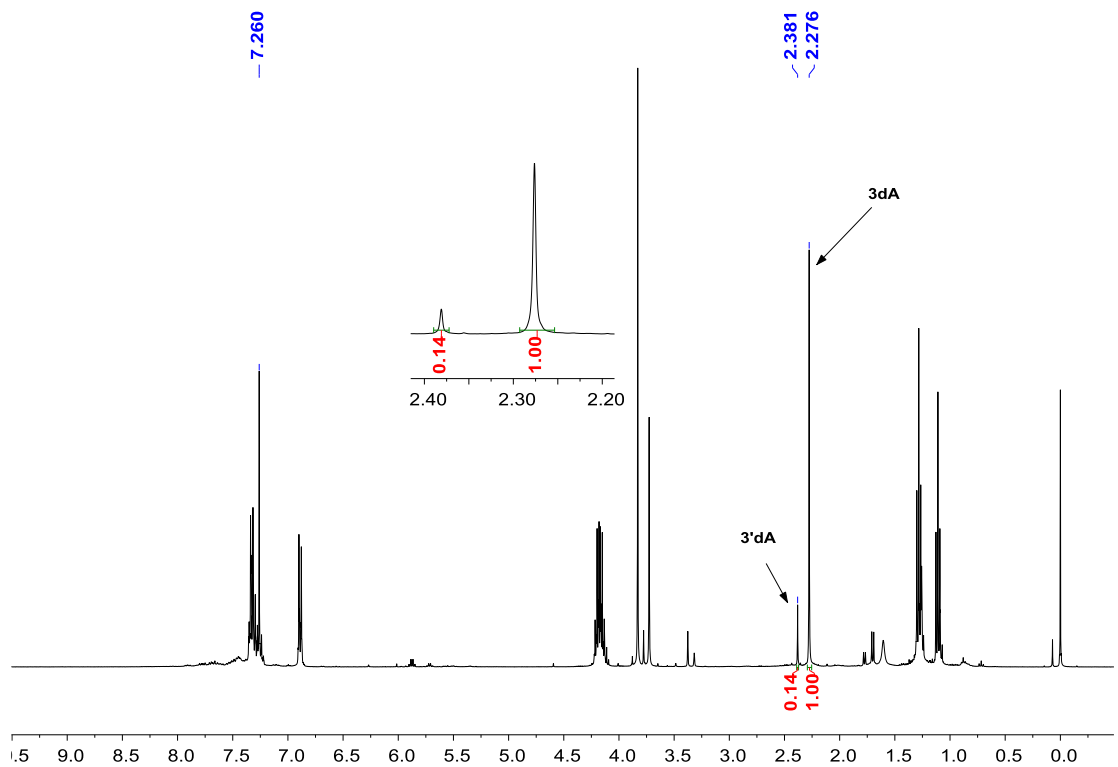


7.2 Spectra for the substrate scope exploration.

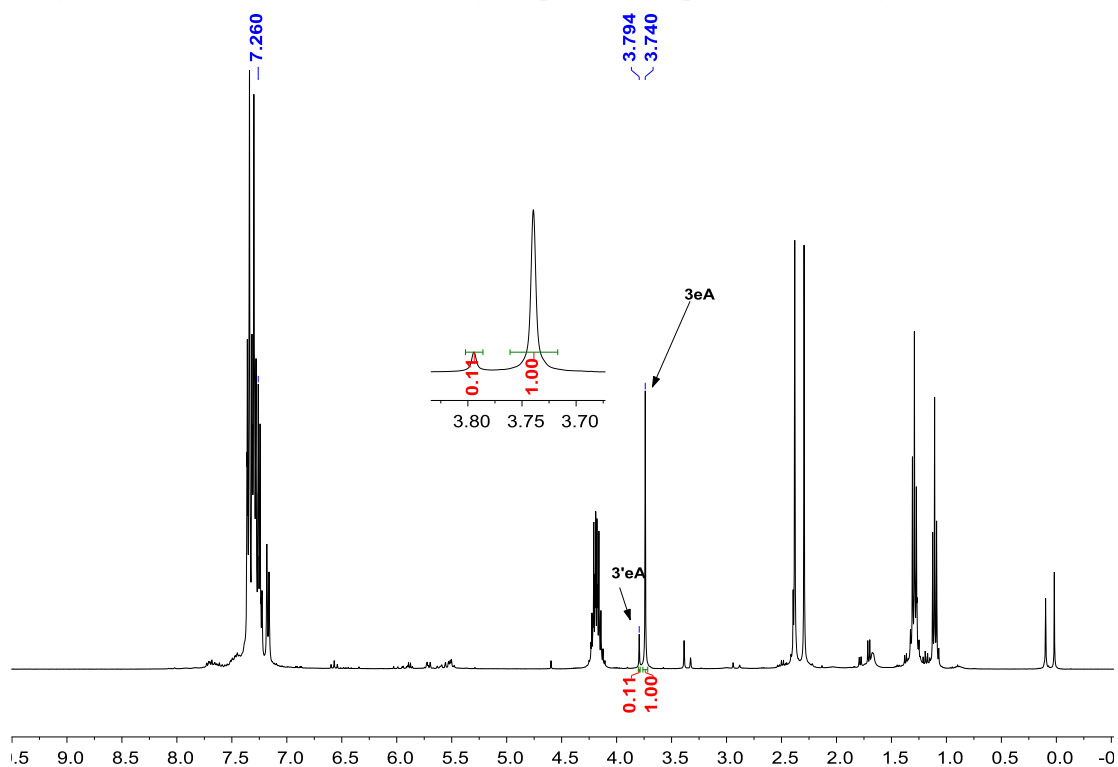
Ethyl 2-(benzo[d][1,3]dioxol-5-yl)-5-(2-ethoxy-2-oxoethyl)-4-methylthiophene-3-carboxylate (3cA)



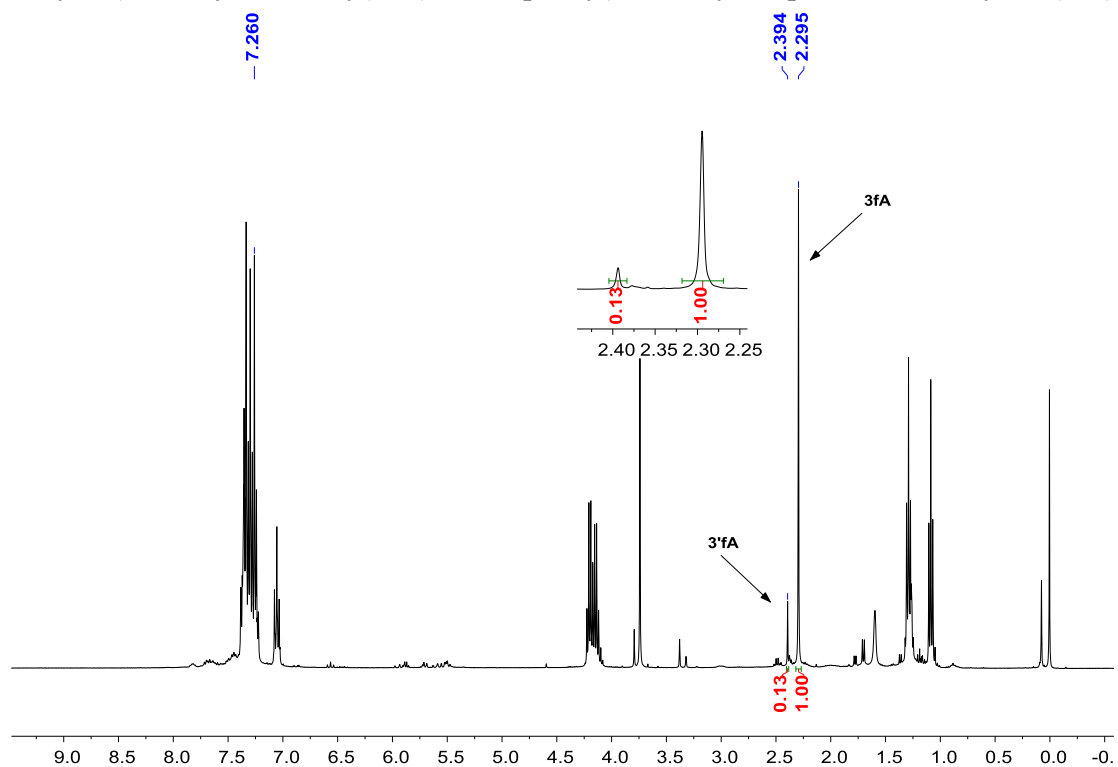
Ethyl 5-(2-ethoxy-2-oxoethyl)-2-(4-methoxyphenyl)-4-methylthiophene-3-carboxylate (3dA)



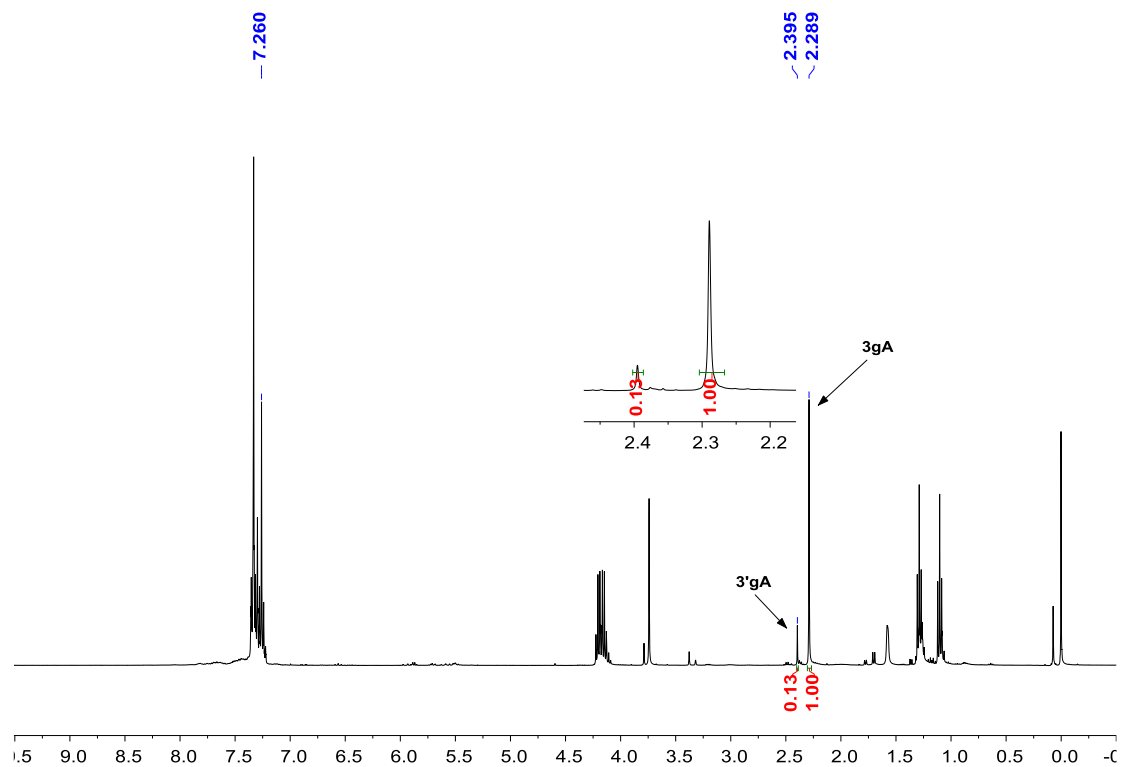
Ethyl 5-(2-ethoxy-2-oxoethyl)-4-methyl-2-(*p*-tolyl)thiophene-3-carboxylate (3eA)



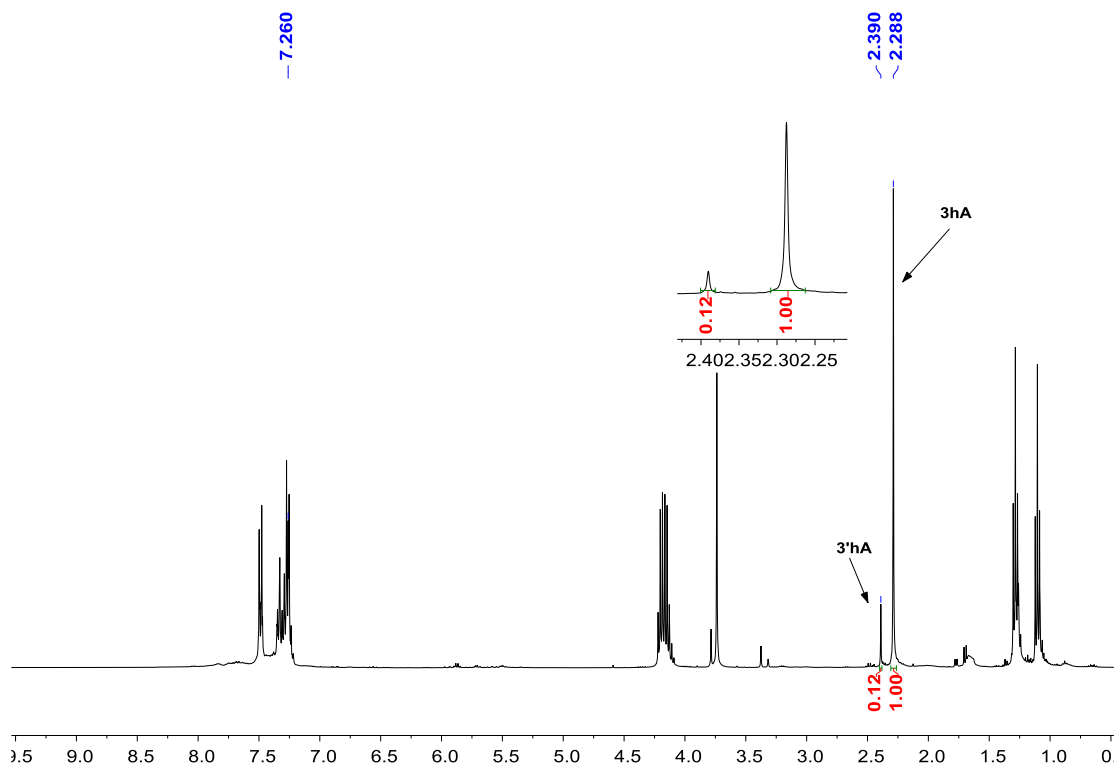
Ethyl 5-(2-ethoxy-2-oxoethyl)-2-(4-fluorophenyl)-4-methylthiophene-3-carboxylate (3fA)



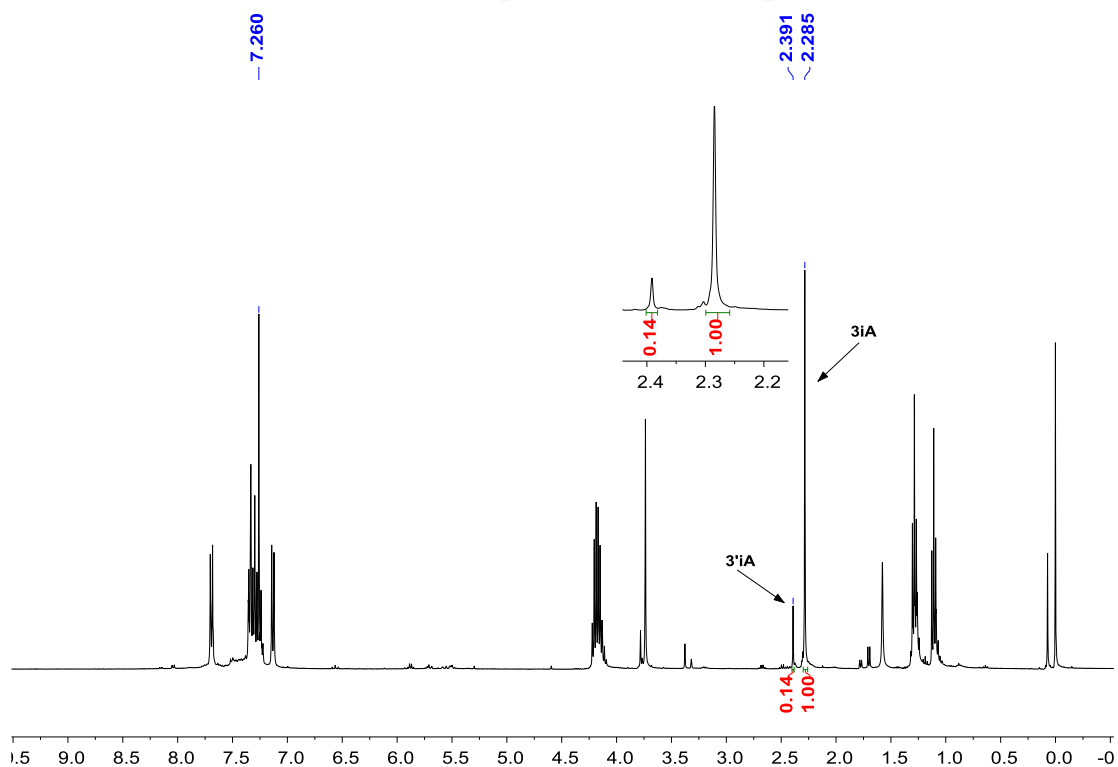
Ethyl 2-(4-chlorophenyl)-5-(2-ethoxy-2-oxoethyl)-4-methylthiophene-3-carboxylate (3gA)



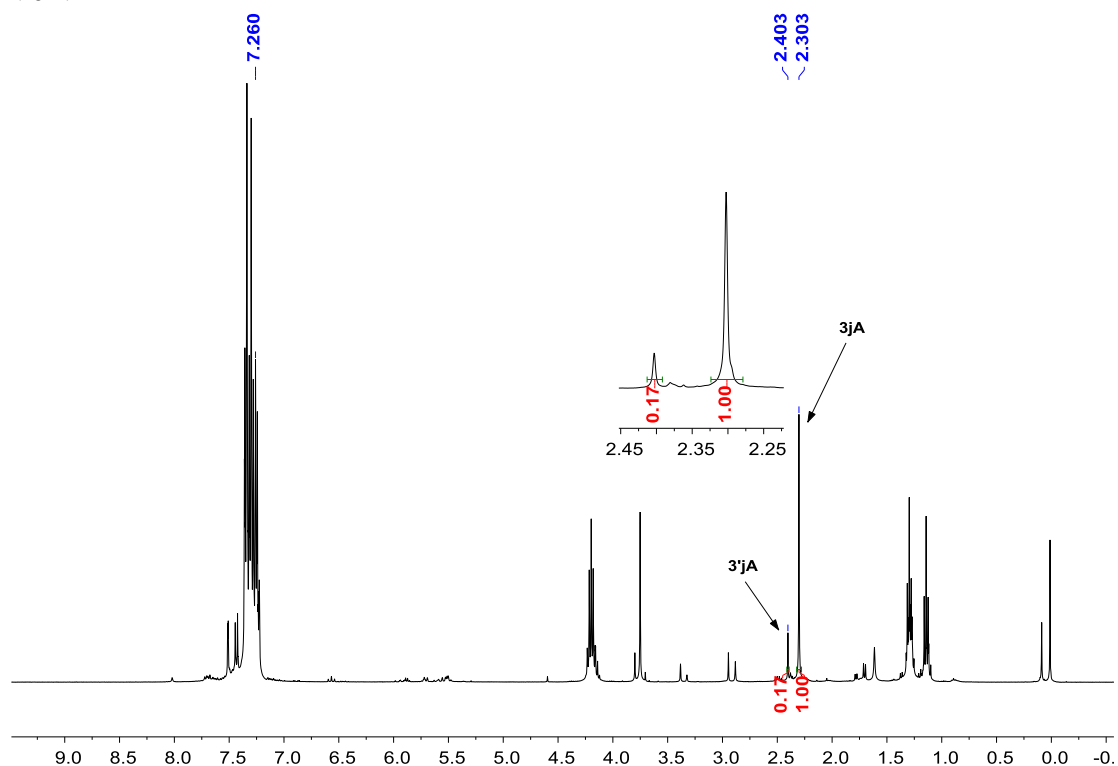
Ethyl 2-(4-bromophenyl)-5-(2-ethoxy-2-oxoethyl)-4-methylthiophene-3-carboxylate (3hA)



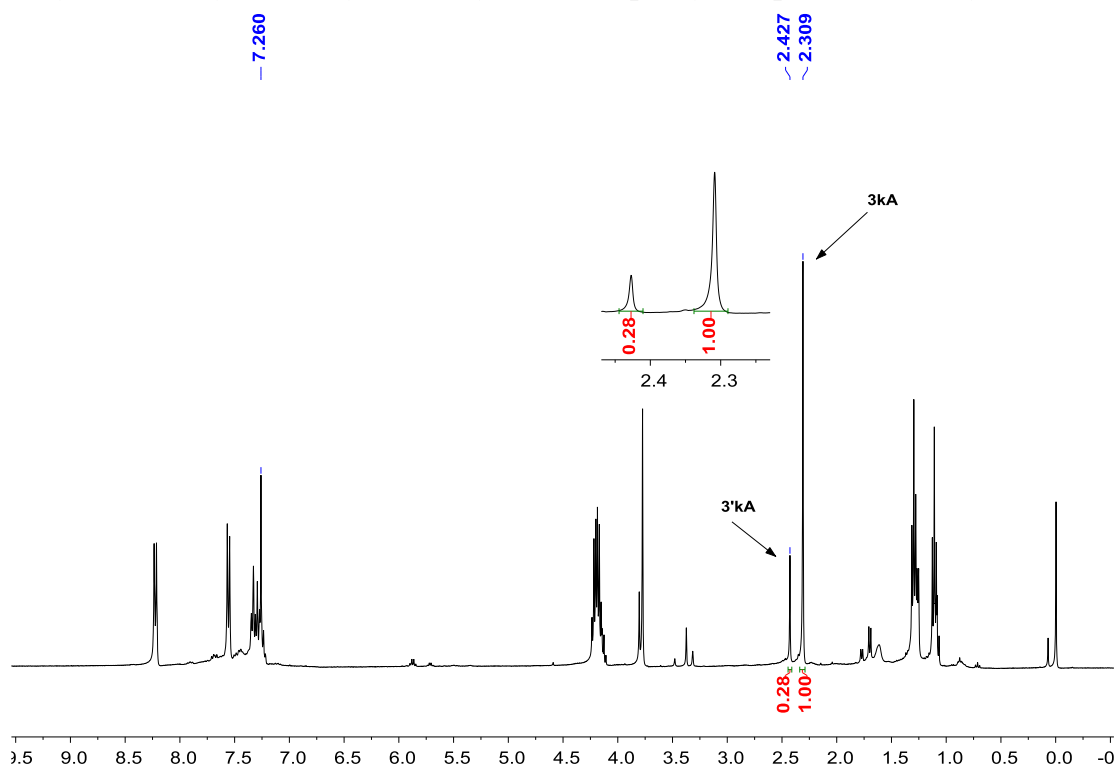
Ethyl 5-(2-ethoxy-2-oxoethyl)-2-(4-iodophenyl)-4-methylthiophene-3-carboxylate (3iA)



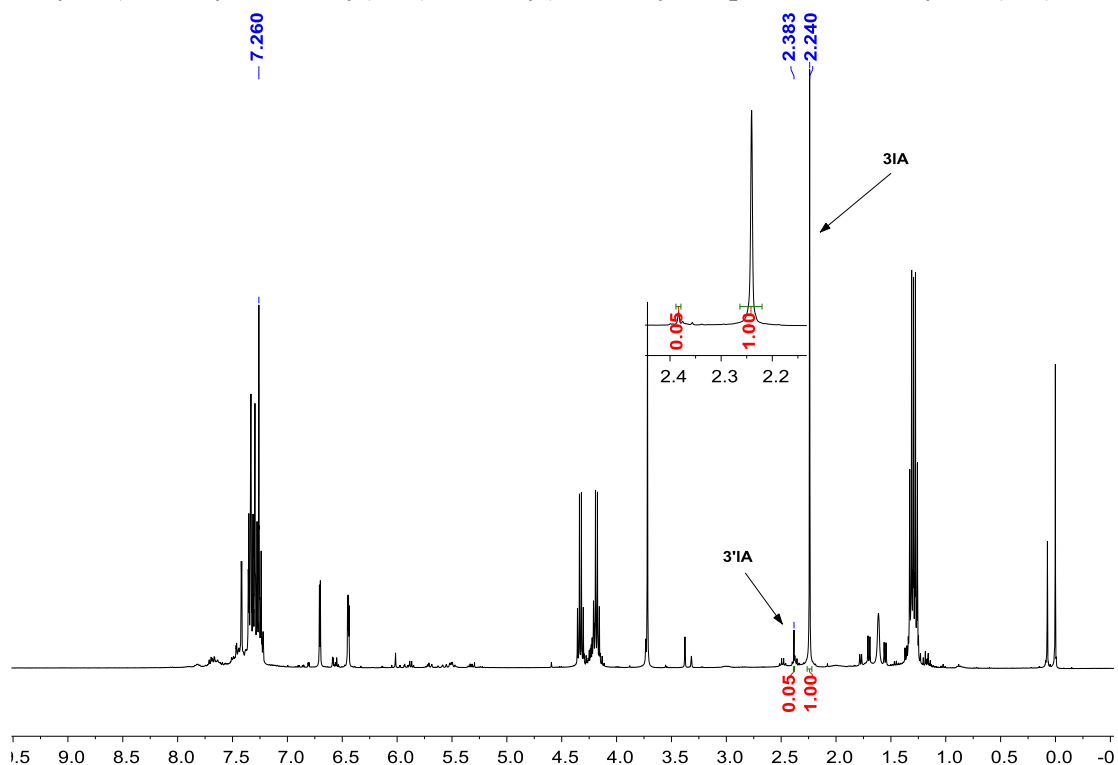
Ethyl 2-(3,4-dichlorophenyl)-5-(2-ethoxy-2-oxoethyl)-4-methylthiophene-3-carboxylate (3jA)



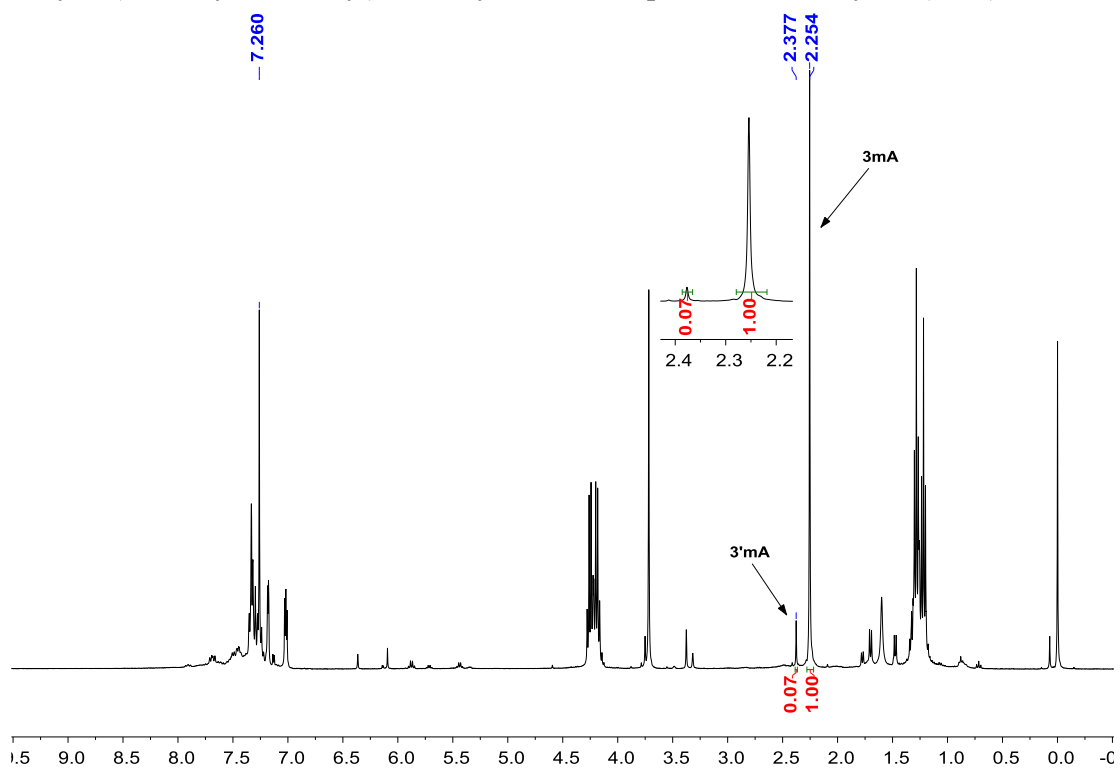
Ethyl 5-(2-ethoxy-2-oxoethyl)-4-methyl-2-(4-nitrophenyl)thiophene-3-carboxylate (3kA)



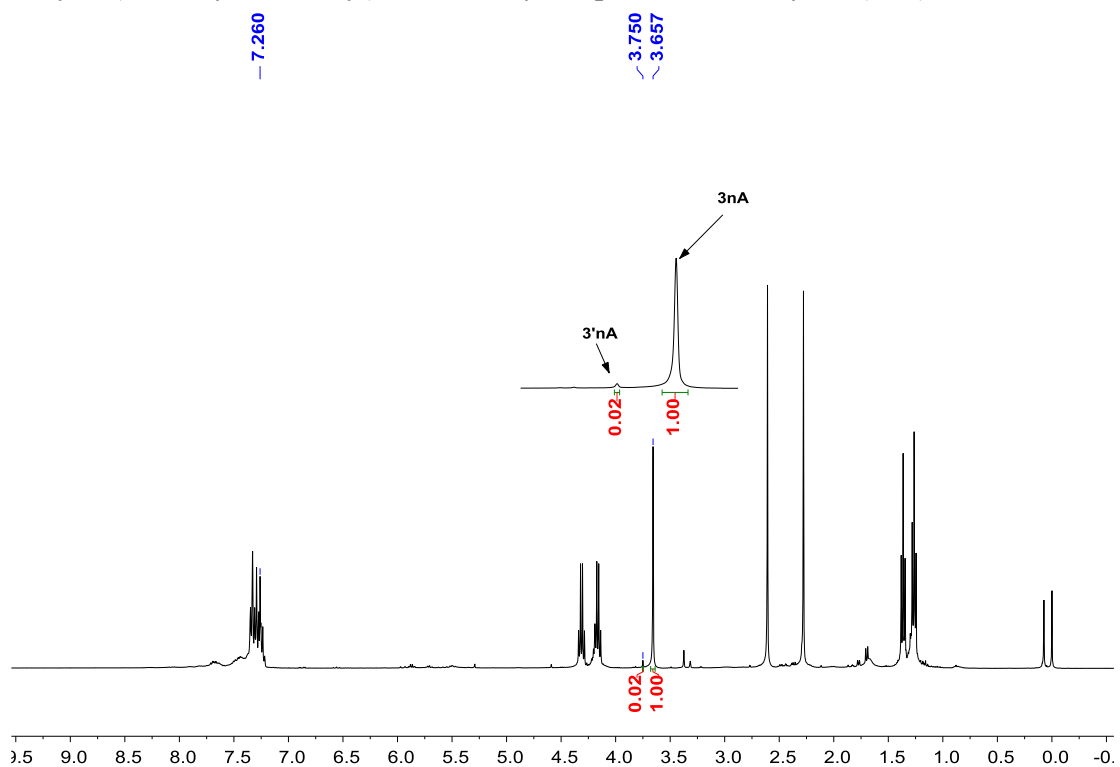
Ethyl 5-(2-ethoxy-2-oxoethyl)-2-(furan-2-yl)-4-methylthiophene-3-carboxylate (3IA)



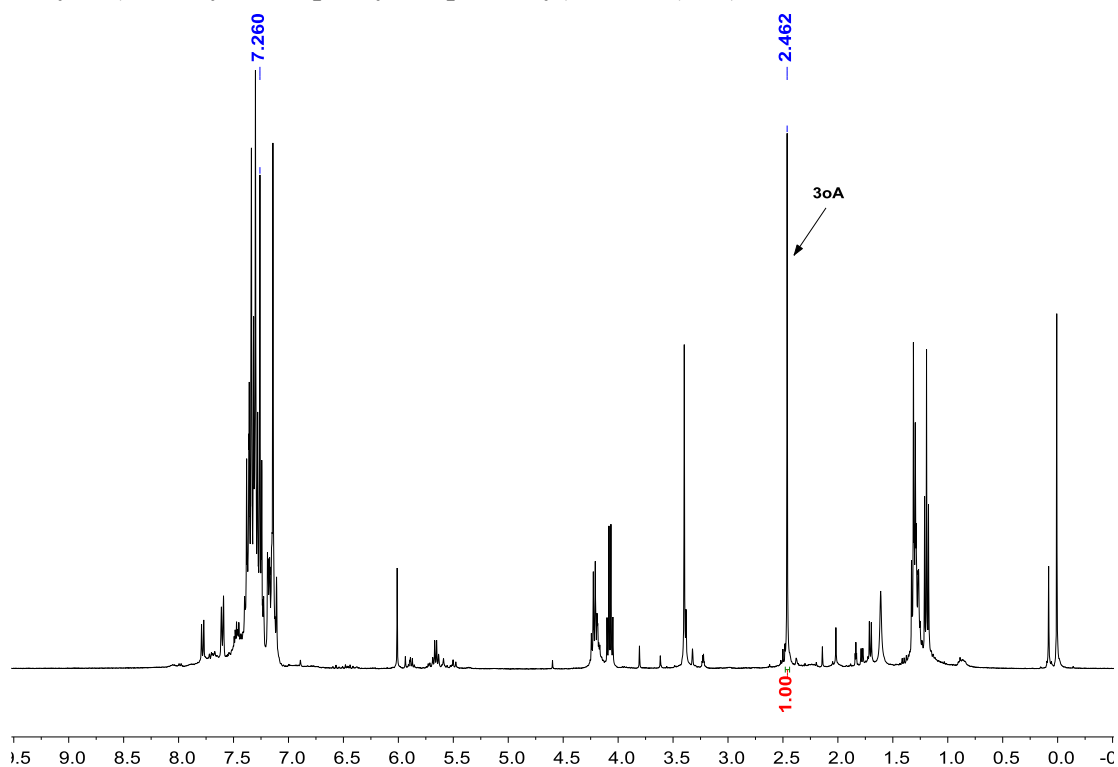
Ethyl 5-(2-ethoxy-2-oxoethyl)-4-methyl-[2,2'-bithiophene]-3-carboxylate (3mA)



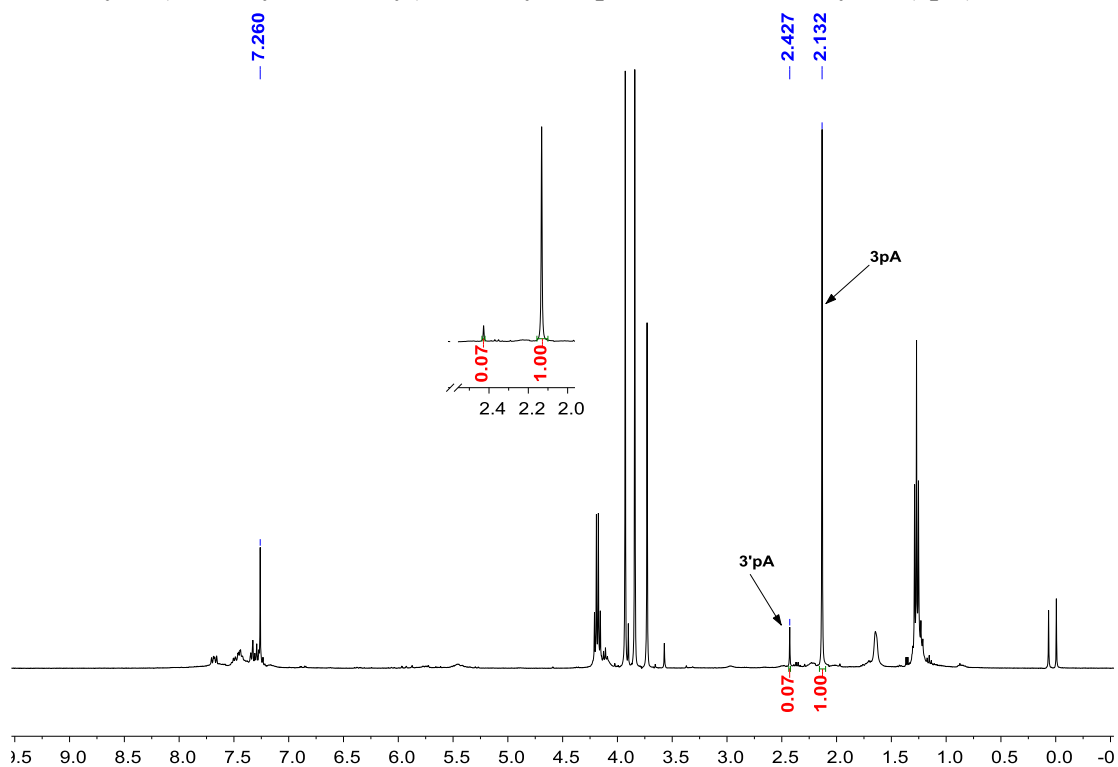
Ethyl 5-(2-ethoxy-2-oxoethyl)-2,4-dimethylthiophene-3-carboxylate (3nA)



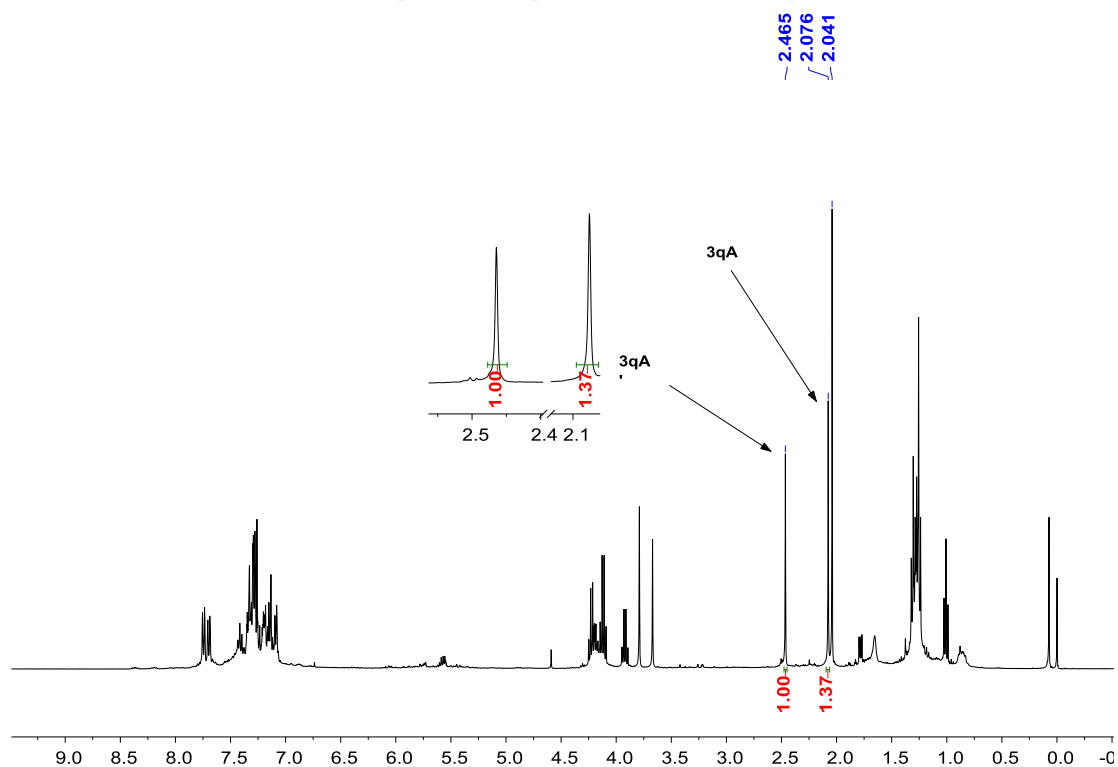
Ethyl 2-(3-methyl-4,5-diphenylthiophen-2-yl)acetate (3oA)



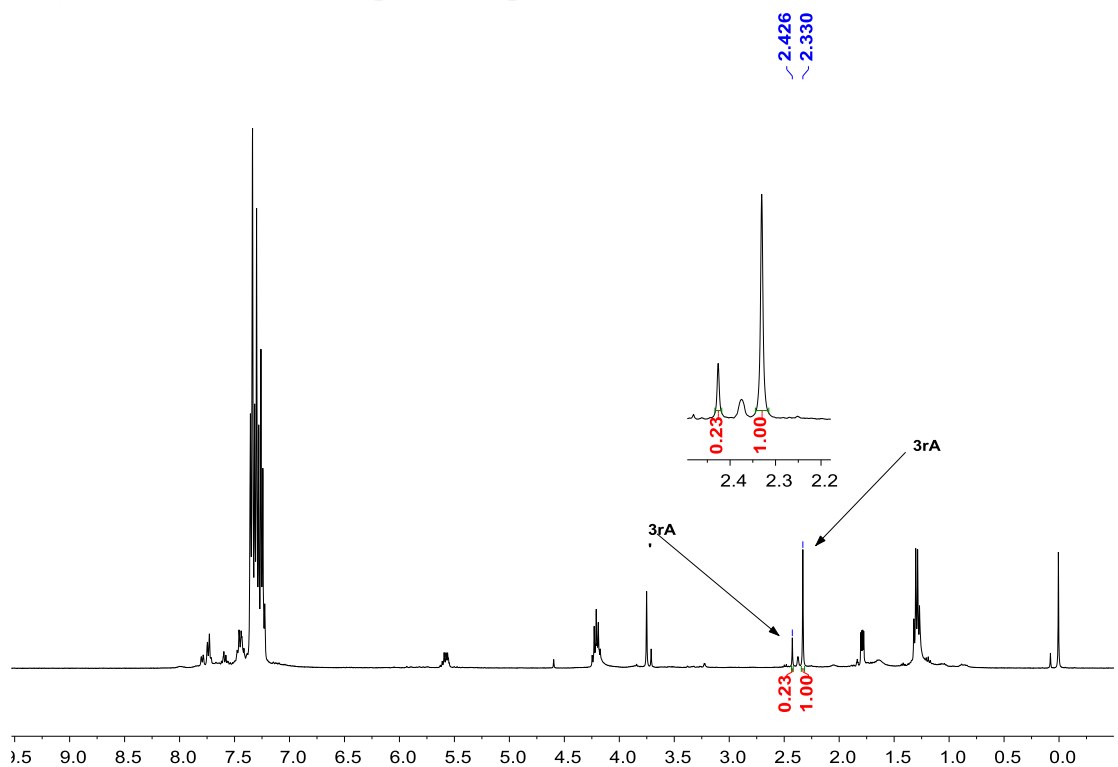
Dimethyl 5-(2-ethoxy-2-oxoethyl)-4-methylthiophene-2,3-dicarboxylate (3pA)



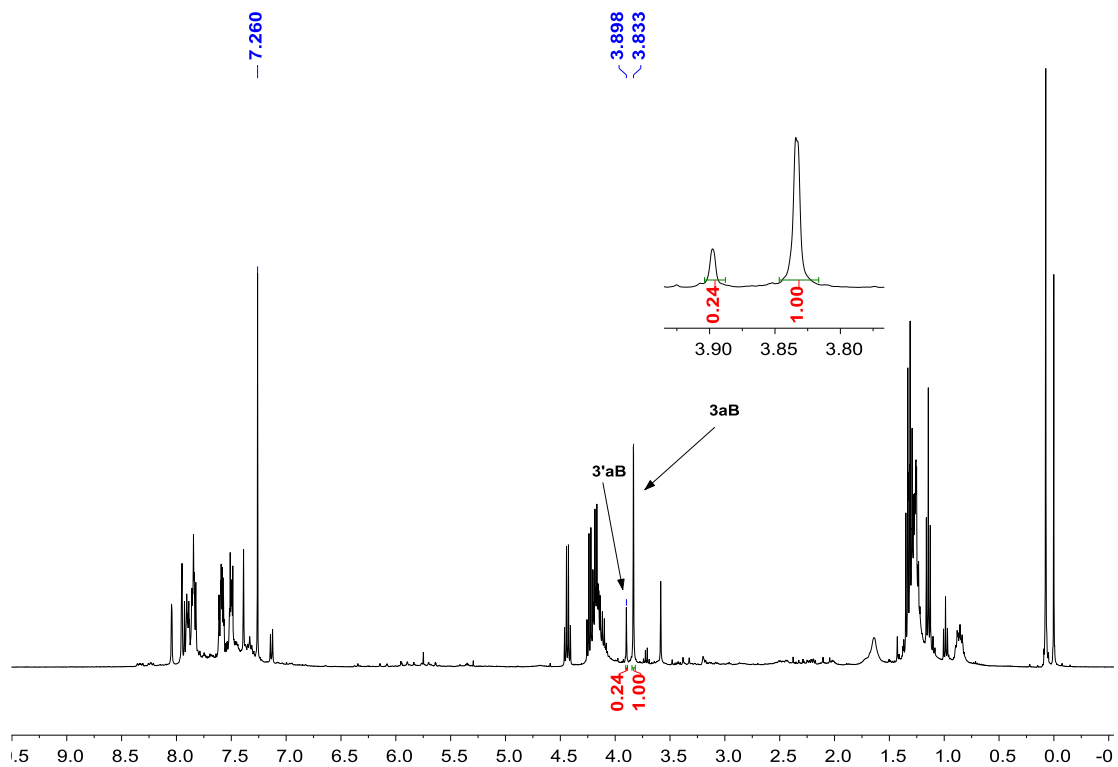
Ethyl 2-(4-benzoyl-3-methyl-5-phenylthiophen-2-yl)acetate (3qA)



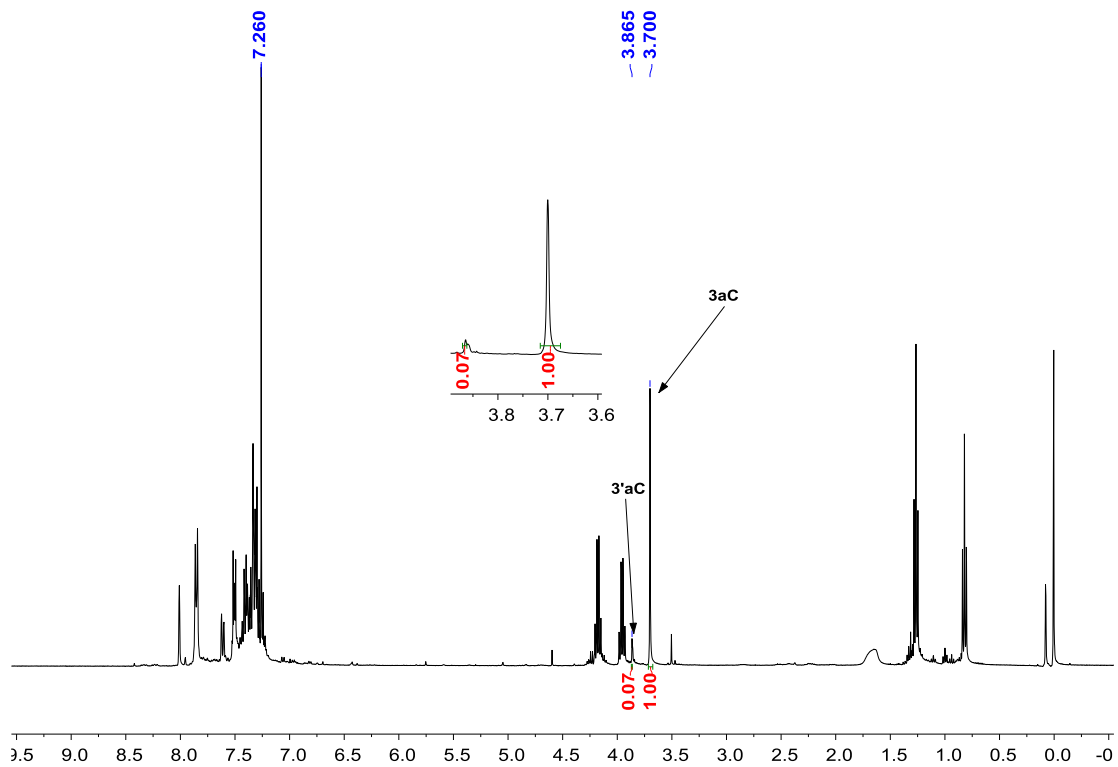
Ethyl 2-(4-cyano-3-methyl-5-phenylthiophen-2-yl)acetate (3rA)



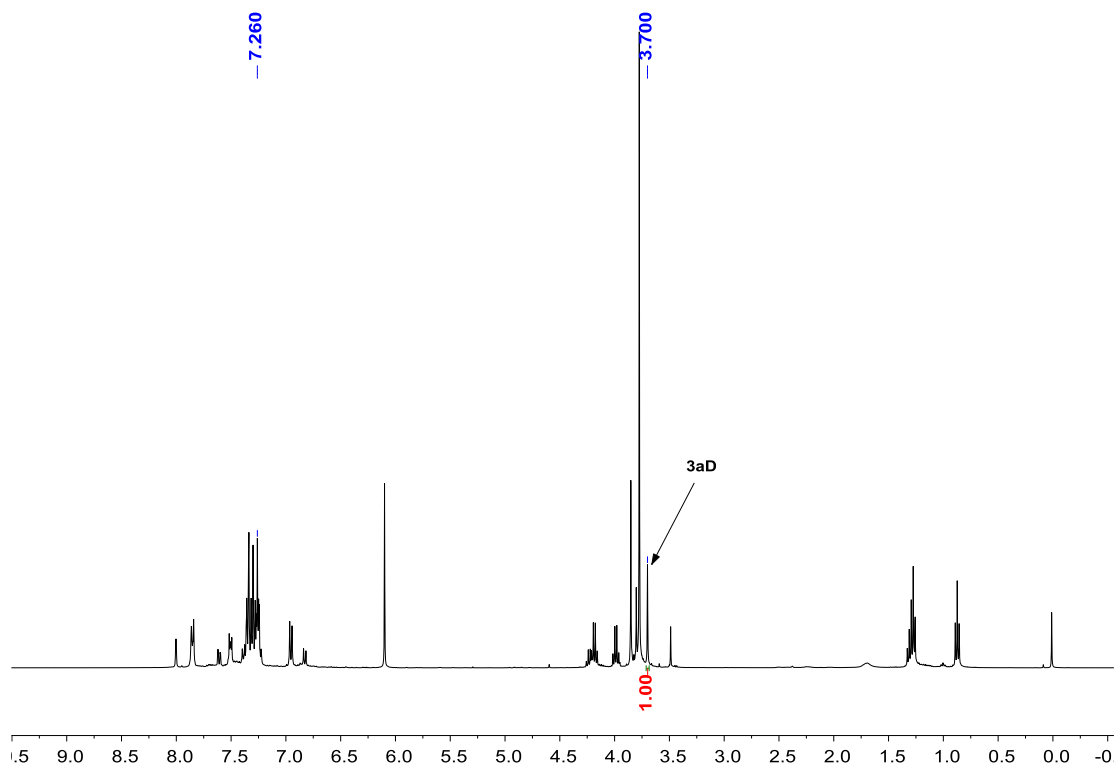
Ethyl 5-(2-ethoxy-2-oxoethyl)-2-(naphthalen-2-yl)thiophene-3-carboxylate (3aB)



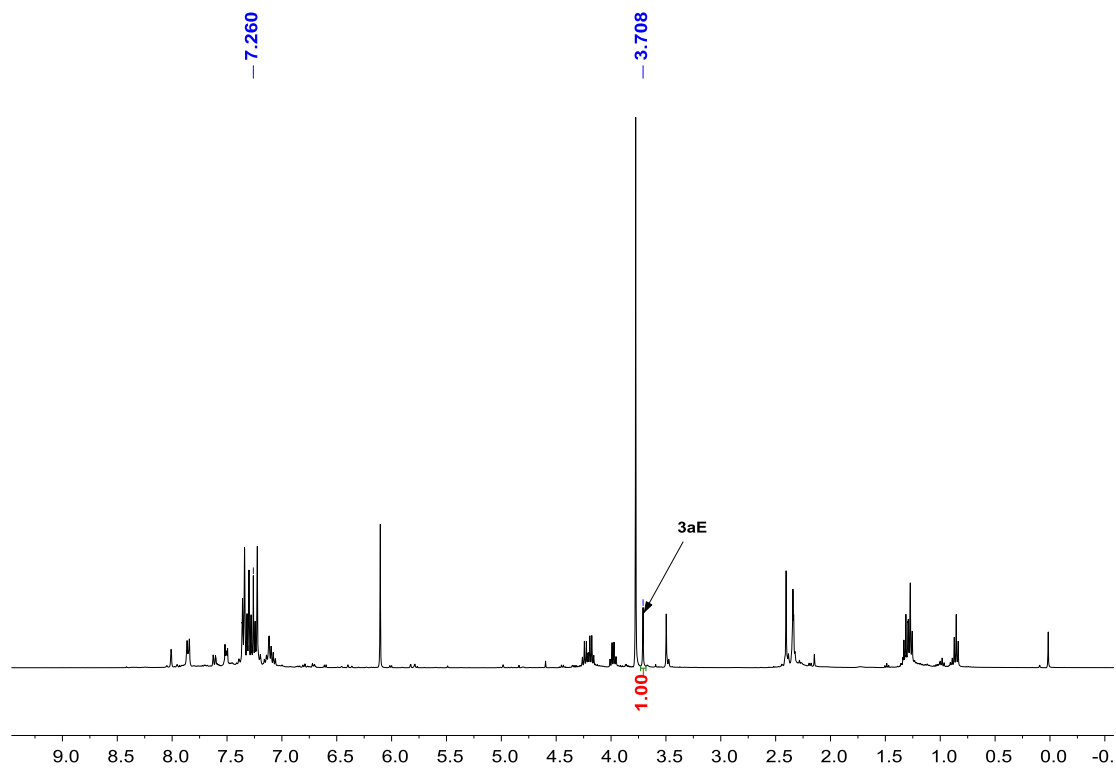
Ethyl 5-(2-ethoxy-2-oxoethyl)-2-(naphthalen-2-yl)-4-phenylthiophene-3-carboxylate (3aC)



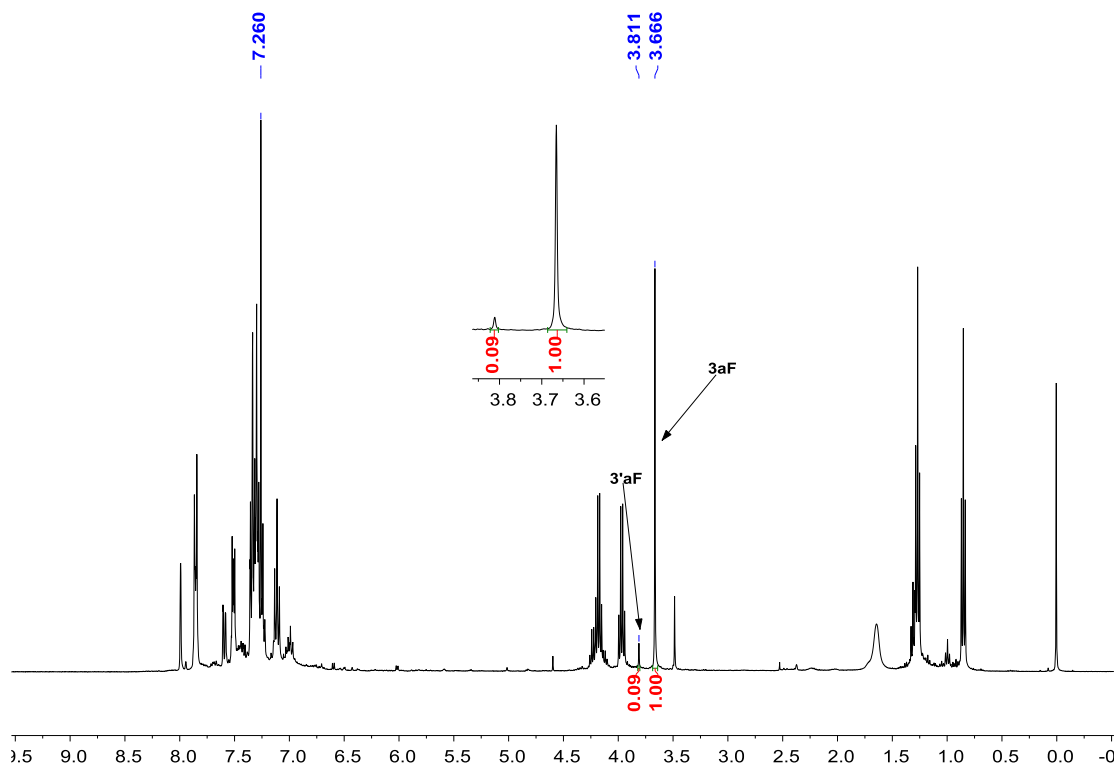
Ethyl 5-(2-ethoxy-2-oxoethyl)-4-(4-methoxyphenyl)-2-(naphthalen-2-yl)thiophene-3-carboxylate (3aD)



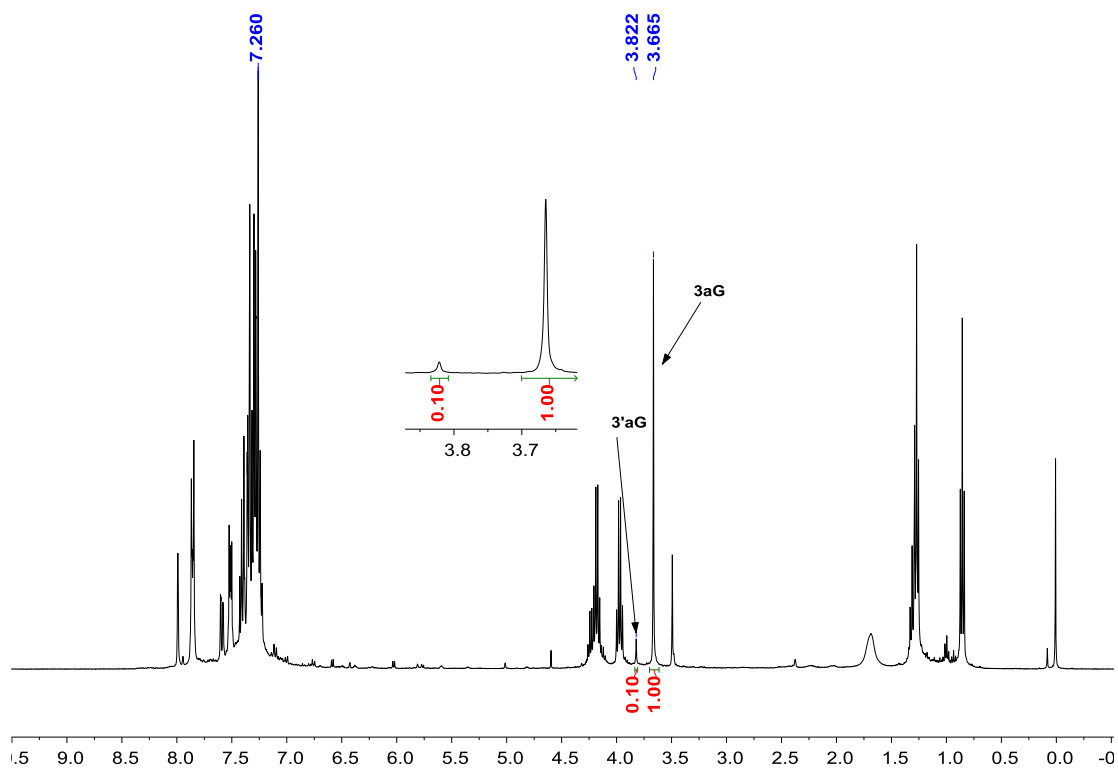
Ethyl 5-(2-ethoxy-2-oxoethyl)-2-(naphthalen-2-yl)-4-(p-tolyl)thiophene-3-carboxylate (3aE)



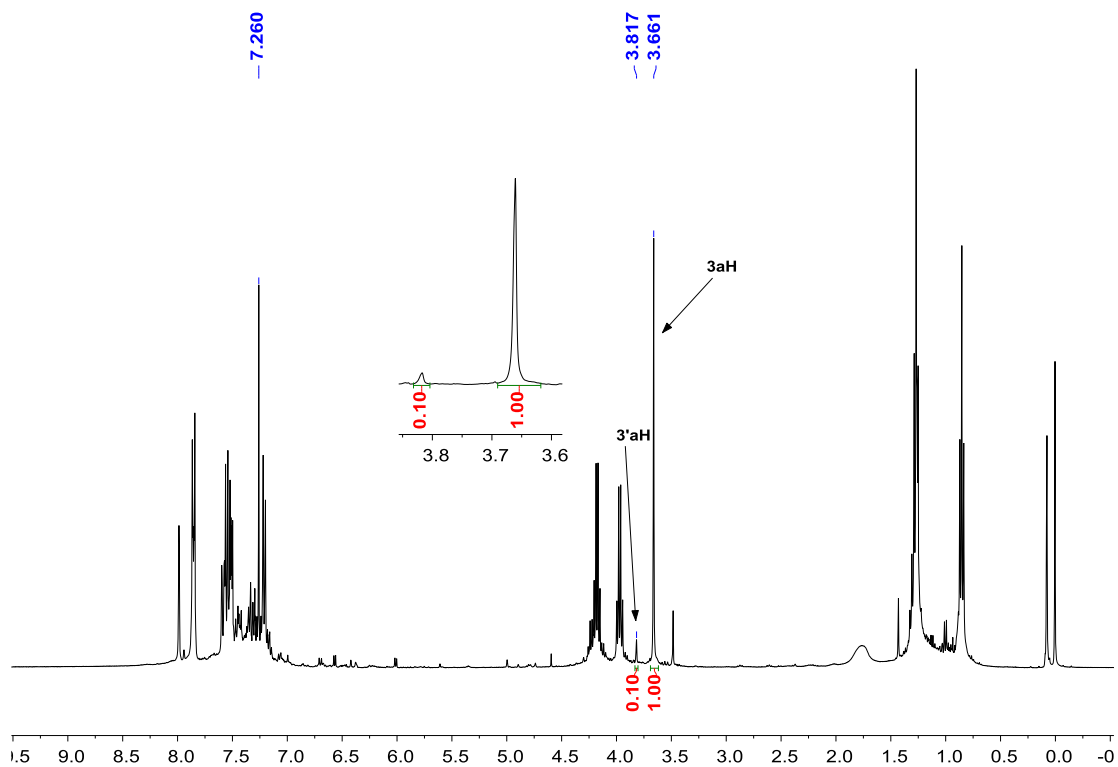
Ethyl 5-(2-ethoxy-2-oxoethyl)-4-(4-fluorophenyl)-2-(naphthalen-2-yl)thiophene-3-carboxylate (3aF)



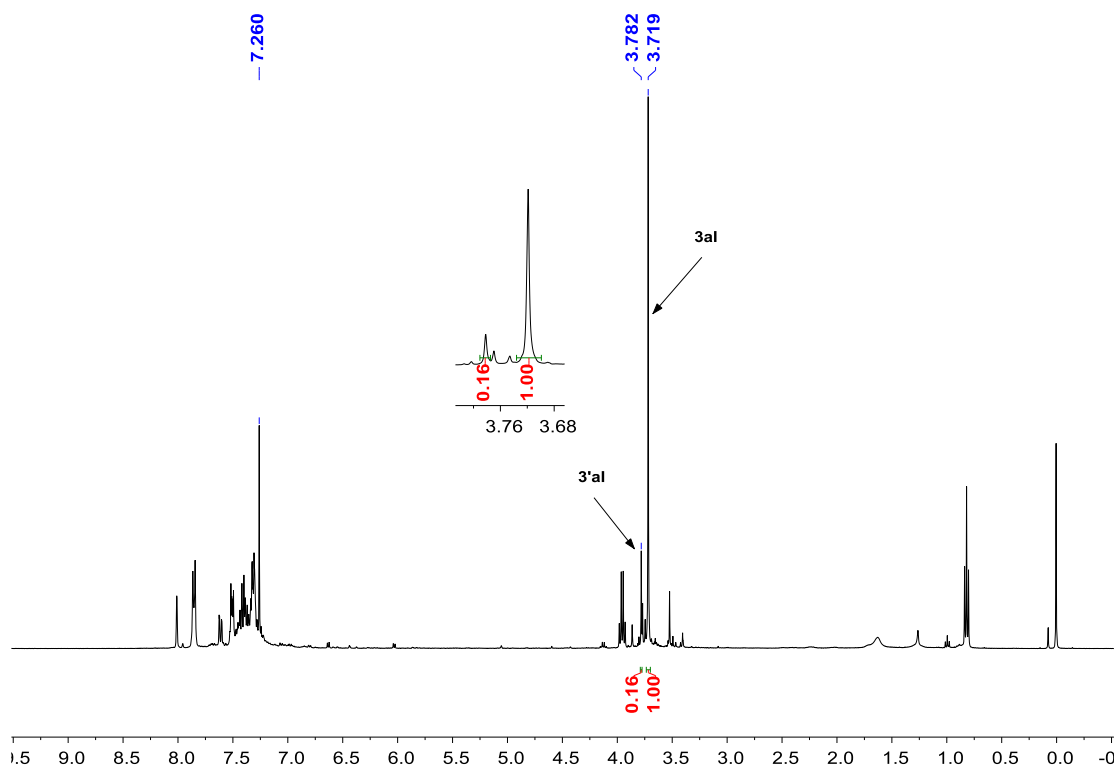
Ethyl 4-(4-chlorophenyl)-5-(2-ethoxy-2-oxoethyl)-2-(naphthalen-2-yl)thiophene-3-carboxylate (3aG)



Ethyl 4-(4-bromophenyl)-5-(2-ethoxy-2-oxoethyl)-2-(naphthalen-2-yl)thiophene-3-carboxylate (3aH)



Ethyl 5-(2-methoxy-2-oxoethyl)-2-(naphthalen-2-yl)-4-phenylthiophene-3-carboxylate (3aI)



Ethyl 5-(2-methoxy-2-oxoethyl)-4-methyl-2-(naphthalen-2-yl)thiophene-3-carboxylate (3aJ)

