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Direct Access to 2-Aryl-3-Cyanothiophenes by Base-Catalyzed Three-component Reaction of Chalcones with Benzoylacetonitriles and Elemental Sulfur

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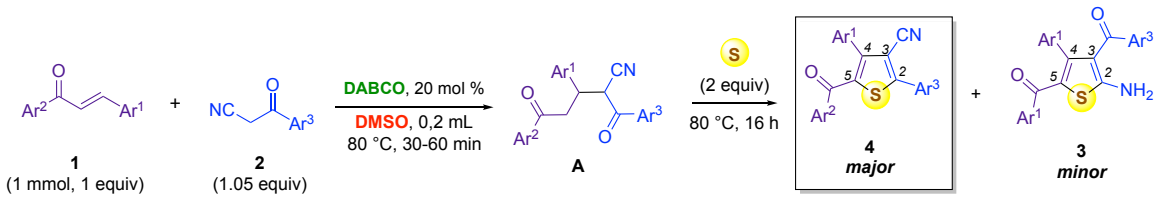
Supporting Information

General Information

Chalcones **1** were prepared as previously described.[1] Other reagents (S_8, DMSO, DABCO as well as other bases, benzoylacetonitriles **2** and ethyl benzoylacetate **5**) were obtained from commercial supplier and used without further purification. Analytical thin layer chromatography (TLC) was purchased from Merck KGaA (silica gel 60 F254). Visualization of the chromatogram was performed by UV light (254 nm) or $KMnO_4$ or vanilline stains. Flash column chromatography was carried out using kieselgel 35-70 µm particle sized silica gel (230-400 mesh). NMR Chemical shifts are reported in (δ) ppm relative to tetramethylsilane (TMS) with the residual solvent as internal reference ($CDCl_3$, δ 7.26 ppm for ^1H and δ 77.0 ppm for ^{13}C; (DMSO-d_6, δ 2.50 ppm for ^1H and δ 39.5 ppm for ^{13}C.). Data are reported as follows: chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet), coupling constants (Hz) and integration.

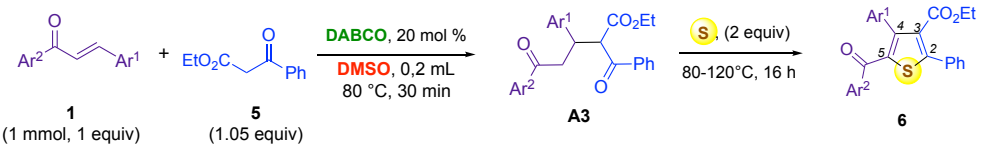
General Protocol for the Synthesis of 2-Aryl-3-cyanothiophenes (4) and 2-Aminothiophene (3)



A mixture of chalcone **1** (1 mmol), benzoylacetonitrile **2** (1.05 mmol) and DABCO (22 mg, 0.2 mmol) in DMSO (0.2 mL) in a 7-mL test tube closed with a rubber septum heated at 80 °C until completion of reaction (followed by ^1H-NMR (30-60 min)). After completion of the Michael addition reaction, sulfur (64 mg, 2 mmol) was added to the reaction mixture in one portion, the tube was closed again without any interruption of stirring and then heated at 80 °C for additional 16 h. The mixture was cooled to room temperature and was purified by column chromatography on silica gel (eluent hexane:ethyl acetate 95:5 to 70:30).

[1] T. B. Nguyen, and P. Retailleau, *Org. Lett.*, 2017, **19**, 3879.

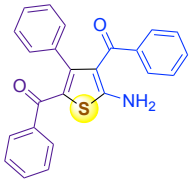
General Protocol for the Synthesis of Ethyl Cyanothiophene-3-carboxylates (6)



A mixture of chalcone **1** (1 mmol), ethyl benzoylacetate **5** (2.2 mg, 1.05 mmol) and DABCO (22 mg, 0.2 mmol) in DMSO (0.2 mL) in a 7-mL test tube closed with a rubber septum heated at 80-120 °C until completion of reaction (followed by ^{1}H-NMR (30 min)). After completion of the Michael addition reaction, sulfur (64 mg, 2 mmol) was added to the reaction mixture in one portion, the tube was closed again without any interruption of stirring and then heated at 80-120 °C for 16 h. The mixture was cooled to room temperature and was purified by column chromatography on silica gel (eluent hexane: ethyl acetate 95:5 to 70:30) to afford the products **6** as pale yellow solids.

Characterization of the thiophene products 3, 4 and 6

(5-Amino-3-phenylthiophene-2,4-diyl)bis(phenylmethanone) (3a)



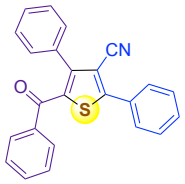
Pale yellow solid (57 mg, 15%).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.28 (d, *J* = 7.3 Hz, 2H), 7.19 (d, *J* = 7.2 Hz, 2H), 7.11 (t, *J* = 7.4 Hz, 1H), 7.05 (t, *J* = 7.4 Hz, 1H), 6.95 (s, *2H-NH₂*), 6.92 (t, *J* = 7.7 Hz, 2H), 6.76 (d, *J* = 7.1 Hz, 2H), 6.67 (t, *J* = 7.4 Hz, 1H), 6.61 (t, *J* = 7.4 Hz, 2H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 194.6, 190.2, 167.8, 147.3, 139.4, 138.3, 134.7, 133.6, 130.9, 130.9, 130.7, 130.1, 128.8, 128.6, 128.5, 127.4, 127.3, 127.1, 121.6, 118.3.

HRMS m/z calculated for $[M+Na]^+$: $C_{24}H_{17}NO_2SNa$ 406.0878. Found 406.0883.

5-Benzoyl-2,4-diphenylthiophene-3-carbonitrile (4a)



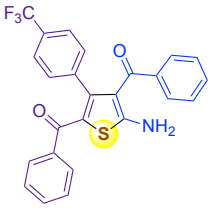
Pale yellow solid (222 mg, 61%).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.92 – 7.83 (m, 2H), 7.61 – 7.48 (m, 5H), 7.39 – 7.28 (m, 3H), 7.25 – 7.11 (m, 5H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 188.9, 157.8, 147.8, 137.7, 136.5, 132.8, 132.4, 130.8, 129.8, 129.5, 129.0, 128.3, 128.1, 128.0, 115.1, 108.9.

HRMS m/z calculated for $[M+Na]^+$: $C_{24}H_{15}NOSNa$ 388.0772. Found 388.0776.

(5-Amino-3-(4-(trifluoromethyl)phenyl)thiophene-2,4-diyl)bis(phenylmethanone) (3b)



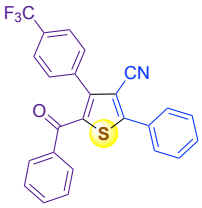
Pale yellow solid (144 mg, 32%).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.29 – 7.22 (m, 2H), 7.18 – 7.14 (m, 3H), 7.11 (s, 2H-*NH*$_2$), 7.06 (t, *J* = 7.4 Hz, 1H), 6.98 (t, *J* = 7.8 Hz, 2H), 6.92 (t, *J* = 7.7 Hz, 2H), 6.85 (s, 2H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 194.4, 189.7, 168.3, 145.7, 139.4, 138.5, 138.1, 131.2, 131.1, 130.9, 129.3, 129.0, 128.6, 128.3, 127.6, 127.5, 123.8, 123.8, 118.0.

HRMS m/z calculated for $[M+Na]^+$: $C_{25}H_{16}F_3NO_2SNa$ 474.0752. Found 474.0759.

5-Benzoyl-2-phenyl-4-(4-(trifluoromethyl)phenyl)thiophene-3-carbonitrile (4b)



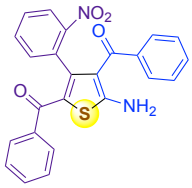
Pale yellow solid (264 mg, 61%).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.87 (dd, *J* = 6.6, 2.9 Hz, 2H), 7.64 – 7.53 (m, 5H), 7.49 (d, *J* = 8.2 Hz, 2H), 7.43 (d, *J* = 8.1 Hz, 2H), 7.39 (t, *J* = 7.5 Hz, 1H), 7.21 (t, *J* = 7.8 Hz, 2H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 188.3, 158.1, 146.3, 138.3, 136.5, 136.0, 133.1, 131.1, 130.8, 130.5, 130.1, 129.6, 129.5, 129.5, 129.5, 129.4, 128.4, 128.3, 128.2, 128.1, 125.3, 125.3, 124.8, 122.6, 114.8, 108.6.

HRMS m/z calculated for $[M+Na]^+$: $C_{25}H_{14}F_3NOSNa$ 456.0646. Found 456.0652.

(5-Amino-3-(2-nitrophenyl)thiophene-2,4-diyl)bis(phenylmethanone) (3c)



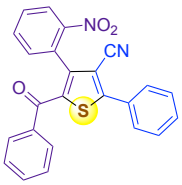
Pale yellow solid (51 mg, 12%).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.49 (d, *J* = 8.0 Hz, 1H), 7.40 (d, *J* = 7.3 Hz, 2H), 7.23 (t, *J* = 7.5 Hz, 1H), 7.15 (d, *J* = 7.3 Hz, 2H), 7.09 (s, 2H-NH_2), 7.09-7.05 (m, 3H), 6.98 (d, *J* = 7.8 Hz, 2H), 6.94 (t, *J* = 7.7 Hz, 2H).

13C NMR (126 MHz, $CDCl_3$) δ 187.4, 157.2, 147.9, 145.2, 137.5, 136.4, 133.4, 133.0, 132.6, 131.1, 130.3, 130.3, 130.2, 129.5, 129.3, 129.0, 128.5, 128.5, 128.4, 128.0, 125.1, 114.2, 109.1.

HRMS m/z calculated for $[M+Na]^+$: $C_{24}H_{16}N_2O_4SNa$: 451.0728. Found 451.0733.

5-Benzoyl-4-(2-nitrophenyl)-2-phenylthiophene-3-carbonitrile (4c)



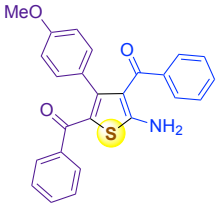
Pale yellow solid (250 mg, 61%).

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.15 (dd, *J* = 7.8, 1.1 Hz, 1H), 7.89 – 7.85 (m, 2H), 7.71 – 7.65 (m, 2H), 7.58 – 7.48 (m, 6H), 7.44 (t, *J* = 7.5 Hz, 1H), 7.33 (dd, *J* = 7.5, 1.3 Hz, 1H), 7.29 (t, *J* = 7.8 Hz, 2H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 187.4, 157.2, 147.9, 145.2, 137.5, 136.4, 133.4, 133.0, 132.6, 131.1, 130.3, 130.3, 130.2, 130.0, 129.5, 129.3, 129.0, 128.5, 128.5, 128.4, 128.0, 125.1, 114.2, 109.1.

HRMS m/z calculated for $[M+Na]^+$: 433.0623 $C_{24}H_{14}N_2O_3SNa$. Found 433.0629.

(5-Amino-3-(4-methoxyphenyl)thiophene-2,4-diyl)bis(phenylmethanone) (3d)



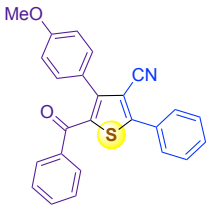
Pale yellow solid (136 mg, 33%).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.32 (d, *J* = 8.8 Hz, 2H), 7.20 (d, *J* = 7.2 Hz, 2H), 7.05 (t, *J* = 7.4 Hz, 1H), 6.93 (d, *J* = 7.7 Hz, 2H), 6.90 (s, 2H-*NH*$_2$), 6.79 (d, *J* = 7.0 Hz, 2H), 6.71 (t, *J* = 7.3 Hz, 1H), 6.65 (t, *J* = 7.3 Hz, 2H), 6.47 (d, *J* = 8.8 Hz, 2H), 3.67 (s, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 194.5, 188.9, 167.2, 162.1, 146.2, 139.4, 135.0, 131.3, 130.8, 130.7, 128.7, 127.3, 127.2, 127.1, 121.5, 118.1, 112.8, 55.3.

HRMS m/z calculated for $[M+Na]^+$: $C_{25}H_{19}NO_3SNa$ 436.0983. Found 436.0991.

5-Benzoyl-4-(4-methoxyphenyl)-2-phenylthiophene-3-carbonitrile (4d)



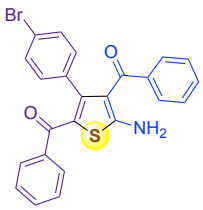
Pale yellow solid (260 mg, 66%).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.91 – 7.80 (m, 2H), 7.61 (d, *J* = 8.8 Hz, 2H), 7.56 – 7.42 (m, 3H), 7.34 (dd, *J* = 6.2, 2.7 Hz, 2H), 7.29 – 7.17 (m, 4H), 6.67 (d, *J* = 8.8 Hz, 2H), 3.77 (s, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 187.3, 163.5, 157.0, 146.8, 137.9, 132.6, 132.2, 130.9, 130.7, 129.7, 129.4, 129.2, 129.1, 128.9, 128.7, 128.4, 128.1, 115.3, 113.4, 108.5, 55.4.

HRMS m/z calculated for $[M+Na]^+$: $C_{25}H_{17}NO_2SNa$ 418.0878. Found 418.0884.

(5-Amino-3-(4-bromophenyl)thiophene-2,4-diyl)bis(phenylmethanone) (3e)



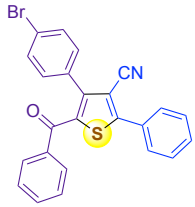
Pale yellow solid (60 mg, 13%).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.27 (d, *J* = 5.6 Hz, 2H), 7.21 (t, *J* = 7.5 Hz, 1H), 7.15 (t, *J* = 8.8 Hz, 2H), 7.02 (t, *J* = 7.8 Hz, 2H), 7.00-6.91 (m, 2H), 6.96 (s, 2H-NH_2), 6.73 (d, *J* = 8.4 Hz, 2H), 6.60 (d, *J* = 8.4 Hz, 2H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 194.4, 189.8, 167.9, 145.9, 139.3, 138.2, 133.8, 132.2, 131.1, 130.8, 130.1, 128.7, 128.5, 127.6, 127.5, 121.7, 118.0.

HRMS m/z calculated for $[M+Na]^+$: $C_{24}H_{16}BrNO_2SNa$ 483.9983. Found 483.9987.

5-Benzoyl-4-(4-bromophenyl)-2-phenylthiophene-3-carbonitrile (4e)



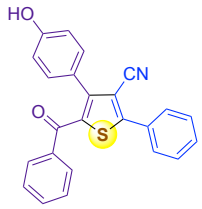
Pale yellow solid (274 mg, 62%).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.86 (dd, *J* = 6.5, 2.7 Hz, 2H), 7.58 (d, *J* = 7.4 Hz, 2H), 7.55 – 7.47 (m, 3H), 7.41 (t, *J* = 7.4 Hz, 1H), 7.35 (d, *J* = 8.4 Hz, 2H), 7.23 (t, *J* = 7.7 Hz, 2H), 7.18 (d, *J* = 8.4 Hz, 2H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 188.5, 157.9, 146.6, 137.7, 136.5, 133.0, 131.6, 131.5, 131.4, 131.4, 131.3, 131.3, 131.2, 131.0, 130.6, 129.5, 129.5, 128.2, 128.1, 123.6, 114.9, 108.6.

HRMS m/z calculated for $[M+Na]^+$: $C_{24}H_{14}BrNOSNa$ 465.9877. Found 465.9882.

5-Benzoyl-4-(4-hydroxyphenyl)-2-phenylthiophene-3-carbonitrile (4f)



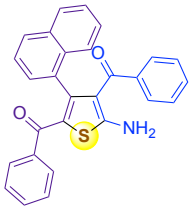
Pale yellow solid (297 mg, 78%).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.86 (dd, *J* = 6.4, 3.0 Hz, 2H), 7.58 (d, *J* = 7.3 Hz, 2H), 7.54 (dd, *J* = 5.0, 1.6 Hz, 3H), 7.37 (t, *J* = 7.4 Hz, 1H), 7.20 (t, *J* = 7.8 Hz, 2H), 7.16 (d, *J* = 8.5 Hz, 1H), 6.63 (d, *J* = 8.5 Hz, 1H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 189.3, 158.0, 156.7, 148.0, 136.9, 136.5, 132.9, 131.3, 130.8, 129.6, 129.5, 128.1, 128.1, 124.6, 115.4, 108.7.

HRMS m/z calculated for $[M+Na]^+$: $C_{24}H_{15}NO_2SNa$ 404.0721. Found 404.0725.

(5-Amino-3-(naphthalen-1-yl)thiophene-2,4-diyl)bis(phenylmethanone) (3g)



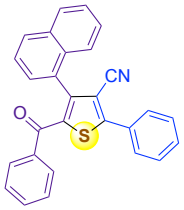
Pale yellow solid (65 mg, 15%).

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.14 – 8.06 (m, 1H), 7.76 (d, *J* = 8.5 Hz, 1H), 7.61 (t, *J* = 7.2, 6.5 Hzi, 1H), 7.48 (t, *J* = 7.8 Hz, 2H), 7.41 – 7.34 (m, 2H), 7.28 (d, *J* = 6.9 Hz, 1H), 7.17 – 7.09 (m, 2H-*NH*$_2$), 7.07 – 7.00 (m, 1H), 6.91 (dd, *J* = 6.0, 1.1 Hz, 1H), 6.85 (t, *J* = 7.7, 7.3 Hz, 1H), 6.83 – 6.79 (m, 1H), 6.78 – 6.70 (m, 1H), 6.59 (t, *J* = 7.8 Hz, 1H), 6.51 (t, *J* = 7.8 Hz, 1H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 195.4, 190.4, 170.8, 168.2, 145.4, 139.1, 138.4, 133.7, 132.8, 132.6, 132.4, 130.6, 130.2, 129.9, 129.9, 128.5, 128.3, 127.8, 127.7, 127.0, 126.7, 126.3, 126.2, 125.3, 125.2, 124.0, 123.1, 118.8.

HRMS m/z calculated for $[M+Na]^+$: $C_{28}H_{19}NO_2SNa$ 456.1034. Found 456.1038.

5-Benzoyl-4-(naphthalen-1-yl)-2-phenylthiophene-3-carbonitrile (4g)



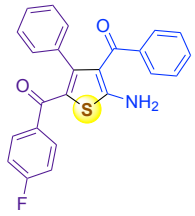
Pale yellow solid (249 mg, 60%).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.99 – 7.89 (m, 2H), 7.75 – 7.70 (m, 2H), 7.68 (d, *J* = 8.1 Hz, 1H), 7.59 – 7.53 (m, 4H), 7.51 – 7.47 (m, 2H), 7.47 – 7.42 (m, 2H), 7.39 (d, *J* = 7.1 Hz, 1H), 7.34 – 7.29 (m, 4H), 7.09 (t, *J* = 6.9 Hz, 1H), 6.84 (t, *J* = 7.1 Hz, 2H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 189.1, 189.1, 158.0, 158.0, 146.6, 146.6, 139.5, 139.5, 136.6, 136.6, 133.3, 132.2, 131.8, 130.9, 130.8, 130.3, 129.7, 129.5, 128.6, 128.4, 128.4, 128.1, 127.2, 126.9, 126.1, 124.8, 124.8, 114.7, 114.7, 110.2, 110.2.

HRMS m/z calculated for $[M+Na]^+$: $C_{28}H_{17}NOSNa$ 438.0929. Found 438.0935.

(5-Amino-4-benzoyl-3-phenylthiophen-2-yl)(4-fluorophenyl)methanone (3h)



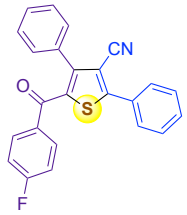
Pale yellow solid (92 mg, 23%).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.31 – 7.27 (m, 2H), 7.19 (d, *J* = 7.2 Hz, 2H), 7.06 (t, *J* = 7.4 Hz, 1H), 6.92 (s, 2H-*NH*$_2$), 6.97 – 6.88 (m, 2H), 6.73 (dd, *J* = 12.4, 7.2 Hz, 3H), 6.66 – 6.63 (m, 2H), 6.61 (t, *J* = 7.7 Hz, 2H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 194.6, 188.7, 167.7, 165.1, 163.1, 147.2, 139.3, 134.7, 134.4, 131.3, 131.2, 130.9, 130.8, 128.6, 127.5, 127.3, 127.2, 121.5, 118.3, 114.5, 114.3.

HRMS m/z calculated for $[M+Na]^+$: $C_{24}H_{16}FNO_2SNa$ 424.0783. Found 424.0791.

5-(4-Fluorobenzoyl)-2,4-diphenylthiophene-3-carbonitrile (4h)



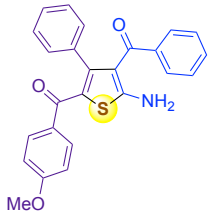
Pale yellow solid (225 mg, 59%).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.91 – 7.83 (m, 2H), 7.58 (dd, *J* = 8.5, 5.4 Hz, 3H), 7.55 (d, *J* = 5.1 Hz, 3H), 7.31 – 7.27 (m, 3H), 7.25 – 7.19 (m, 3H), 6.83 (t, *J* = 8.5 Hz, 2H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 187.5, 166.3, 164.3, 158.0, 147.7, 137.5, 132.7, 132.3, 132.2, 132.1, 130.9, 130.7, 129.9, 129.8, 129.5, 129.4, 129.2, 129.0, 128.8, 128.4, 128.1, 127.9, 115.3, 115.1, 115.1, 108.8.

HRMS m/z calculated for $[M+Na]^+$: $C_{24}H_{14}FNOSNa$ 406.0678. Found 406.0684.

(5-Amino-4-benzoyl-3-phenylthiophen-2-yl)(4-methoxyphenyl)methanone (3i)



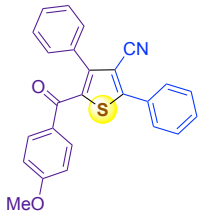
Pale yellow solid (66 mg, 15%).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.31 (d, *J* = 8.7 Hz, 1H), 7.19 (d, *J* = 7.6 Hz, 1H), 7.05 (t, *J* = 7.4 Hz, 1H), 7.00 (s, 2H-NH_2), 6.91 (t, *J* = 7.6 Hz, 2H), 6.78 (d, *J* = 7.2 Hz, 2H), 6.70 (t, *J* = 7.2 Hz, 1H), 6.65 (t, *J* = 7.4 Hz, 2H), 6.46 (d, *J* = 8.7 Hz, 1H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 194.6, 189.0, 167.4, 162.0, 146.4, 139.4, 135.0, 131.3, 130.9, 130.7, 128.7, 127.3, 127.3, 127.2, 121.4, 118.0, 112.8, 55.3.

HRMS m/z calculated for $[M+Na]^+$: $C_{25}H_{19}NO_3SNa$ 436.0983. Found 436.0991.

5-(4-Methoxybenzoyl)-2,4-diphenylthiophene-3-carbonitrile (4i)



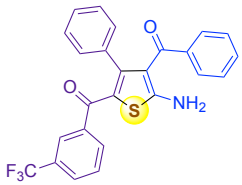
Pale yellow solid (253 mg, 64%).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.94 – 7.84 (m, 3H), 7.63 (d, *J* = 8.8 Hz, 2H), 7.59 – 7.52 (m, 3H), 7.37 (dd, *J* = 6.5, 2.8 Hz, 3H), 7.30 – 7.21 (m, 4H), 6.69 (d, *J* = 8.8 Hz, 2H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 187.4, 163.5, 157.1, 146.8, 137.9, 132.6, 132.2, 130.9, 130.7, 129.7, 129.5, 129.1, 129.0, 128.4, 128.1, 115.3, 113.4, 108.5, 55.5.

HRMS m/z calculated for $[M+Na]^+$: $C_{25}H_{17}NO_2SNa$: 418.0878. Found 418.0886.

(5-Amino-4-benzoyl-3-phenylthiophen-2-yl)(3-(trifluoromethyl)phenyl)methanone (3j)



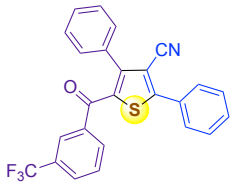
Pale yellow solid (104 mg, 22%).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.47 (d, *J* = 7.6 Hz, 1H), 7.39 (s, 1H), 7.32 (d, *J* = 7.8 Hz, 1H), 7.17 (d, *J* = 7.3 Hz, 2H), 7.11 (t, *J* = 7.8 Hz, 1H), 7.05 (t, *J* = 7.4 Hz, 1H), 7.01 (s, 2H-NH_2), 6.91 (t, *J* = 7.7 Hz, 2H), 6.72 (d, *J* = 7.2 Hz, 2H), 6.66 (t, *J* = 7.4 Hz, 1H), 6.59 (t, *J* = 7.5 Hz, 2H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 194.6, 188.7, 168.3, 148.2, 139.2, 139.1, 134.2, 133.6, 131.6, 130.9, 130.2, 128.5, 128.1, 127.7, 127.3, 127.2, 125.6, 125.5, 118.4.

HRMS m/z calculated for $[M+Na]^+$: $C_{25}H_{16}F_3NO_2SNa$ 474.0752. Found 474.0758.

2,4-Diphenyl-5-(3-(trifluoromethyl)benzoyl)thiophene-3-carbonitrile (4j)



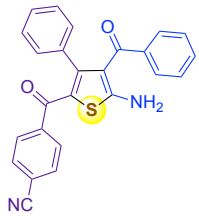
Pale yellow solid (273 mg, 63%).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.85 – 7.78 (m, 2H), 7.66 (d, *J* = 7.7 Hz, 1H), 7.60 (s, 1H), 7.50 – 7.42 (m, 5H), 7.23 (t, *J* = 7.6 Hz, 2H), 7.20 – 7.14 (m, 3H), 7.10 (d, *J* = 6.0 Hz, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 187.8, 158.8, 148.5, 137.3, 137.1, 132.5, 132.2, 132.0, 131.1, 130.6, 130.5, 130.3, 130.1, 130.0, 129.8, 129.7, 129.5, 129.4, 129.3, 129.1, 128.9, 128.9, 128.8, 128.7, 128.6, 128.5, 128.3, 128.2, 128.0, 127.9, 126.3, 126.2, 124.4, 114.9, 109.1.

HRMS m/z calculated for $[M+Na]^+$: $C_{25}H_{14}F_3NOSNa$ 456.0646. Found 456.0652.

4-(5-Amino-4-benzoyl-3-phenylthiophene-2-carbonyl)benzonitrile (3k)



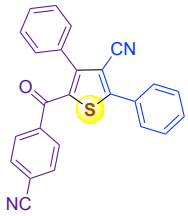
Pale yellow solid (41 mg, 10%).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.24 (d, *J* = 8.4 Hz, 3H), 7.19 (d, *J* = 8.4 Hz, 2H), 7.16 (d, *J* = 7.2 Hz, 2H), 7.07 (d, *J* = 7.4 Hz, 1H), 7.03 (s, 2H-*NH*$_2$), 6.92 (t, *J* = 7.7 Hz, 2H), 6.73 (t, *J* = 7.4 Hz, 1H), 6.69 (d, *J* = 7.2 Hz, 2H), 6.60 (t, *J* = 7.6 Hz, 2H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 194.6, 188.2, 168.7, 148.6, 142.3, 139.1, 134.2, 131.1, 130.9, 128.9, 128.5, 128.0, 127.4, 127.2, 118.1, 113.6.

HRMS m/z calculated for $[M+Na]^+$: $C_{25}H_{16}N_2O_2SNa$ 431.0830. Found 431.0838.

5-(4-Cyanobenzoyl)-2,4-diphenylthiophene-3-carbonitrile (4k)



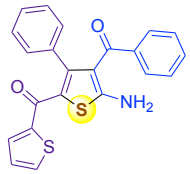
Pale yellow solid (203 mg, 52%).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.83 – 7.78 (m, 2H), 7.50 – 7.43 (m, 7H), 7.33 (d, *J* = 8.4 Hz, 2H), 7.19 – 7.14 (m, 3H), 7.14 – 7.08 (m, 2H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 187.6, 159.2, 148.8, 140.0, 137.1, 132.0, 131.6, 131.2, 130.5, 129.9, 129.6, 129.5, 128.5, 128.1, 117.7, 115.5, 114.7, 109.1.

HRMS m/z calculated for $[M+Na]^+$: $C_{25}H_{14}N_2OSNa$ 413.0725. Found 413.0735.

(5-Amino-4-benzoyl-3-phenylthiophen-2-yl)(thiophen-2-yl)methanone (3l)



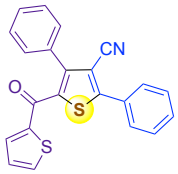
Pale yellow solid (66 mg, 17%).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.36 (d, *J* = 4.2 Hz, 1H), 7.23 (d, *J* = 7.2 Hz, 2H), 7.09 (t, *J* = 7.4 Hz, 1H), 7.01 (d, *J* = 3.0 Hz, 1H), 6.96 (d, *J* = 7.7 Hz, 2H), 6.93 (d, *J* = 6.4 Hz, 3H), 6.80 (dd, *J* = 11.0, 7.0 Hz, 4H), 6.77 (s, 2H-NH_2), 6.66 – 6.62 (m, 1H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 194.5, 181.0, 166.7, 146.2, 143.4, 139.4, 135.2, 133.5, 132.5, 130.8, 130.6, 128.7, 127.5, 127.4, 127.3, 127.1, 120.0, 118.1.

HRMS m/z calculated for $[M+Na]^+$: $C_{22}H_{15}NO_2S_2Na$ 412.0442. Found 412.0449.

2,4-Diphenyl-5-(thiophene-2-carbonyl)thiophene-3-carbonitrile (4l)



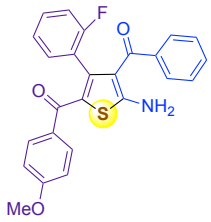
Pale yellow solid (219 mg, 59%).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.91 – 7.82 (m, 2H), 7.61 – 7.50 (m, 4H), 7.49 – 7.43 (m, 2H), 7.38 – 7.30 (m, 4H), 6.86 (t, *J* = 4.4 Hz, 1H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 179.9, 156.8, 147.0, 142.6, 136.5, 135.2, 135.1, 132.6, 130.8, 130.7, 129.7, 129.7, 129.6, 129.6, 129.5, 129.4, 129.4, 129.4, 129.2, 128.8, 128.8, 128.7, 128.6, 128.6, 128.6, 128.2, 127.9, 115.2, 108.8.

HRMS m/z calculated for $[M+Na]^+$: $C_{22}H_{13}NOS_2Na$ 394.0336. Found 394.0339.

(2-Amino-4-(2-fluorophenyl)-5-(4-methoxybenzoyl)thiophen-3-yl)(phenyl)methanone (3m)



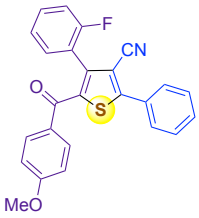
Pale yellow solid (56 mg, 13%).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.38 (d, *J* = 8.8 Hz, 2H), 7.23 (d, *J* = 7.3 Hz, 2H), 7.07 (t, *J* = 7.4 Hz, 1H), 6.96 (t, *J* = 7.6 Hz, 2H), 6.89 (s, 2H-*NH*$_2$), 6.77 (t, *J* = 7.4 Hz, 1H), 6.75 – 6.66 (m, 1H), 6.53 (d, *J* = 8.8 Hz, 2H), 6.31 (t, *J* = 9.0 Hz, 1H), 3.69 (s, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 194.3, 188.6, 167.4, 162.2, 159.7, 157.7, 139.3, 139.1, 132.3, 131.1, 130.7, 130.7, 129.9, 129.8, 128.3, 127.2, 124.0, 123.8, 123.1, 123.1, 122.2, 117.4, 114.7, 114.5, 112.8, 55.3.

HRMS m/z calculated for $[M+Na]^+$: $C_{25}H_{18}FNO_3SNa$ 454.0889. Found 454.0895.

4-(2-Fluorophenyl)-5-(4-methoxybenzoyl)-2-phenylthiophene-3-carbonitrile (4m)



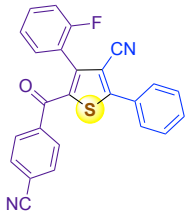
Pale yellow solid (186 mg, 45%).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.87 (dd, *J* = 7.4, 2.0 Hz, 3H), 7.65 (d, *J* = 8.8 Hz, 2H), 7.58 – 7.48 (m, 4H), 7.32 (td, *J* = 7.5, 1.4 Hz, 2H), 7.26 (q, *J* = 7.2, 5.8 Hz, 2H), 7.08 (t, *J* = 7.6 Hz, 1H), 6.97 (t, *J* = 9.2 Hz, 1H), 6.72 (d, *J* = 8.8 Hz, 2H), 3.79 (s, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 186.7, 163.5, 160.3, 158.3, 157.0, 140.4, 139.0, 131.9, 131.4, 131.3, 131.2, 130.7, 130.5, 129.5, 129.2, 128.1, 124.3, 124.2, 121.0, 120.9, 115.9, 115.7, 114.7, 113.9, 113.4, 109.1, 55.5.

HRMS m/z calculated for $[M+Na]^+$: $C_{25}H_{16}FNO_2SNa$ 436.0783. Found 436.0788.

5-(4-Cyanobenzoyl)-4-(2-fluorophenyl)-2-phenylthiophene-3-carbonitrile (4n)



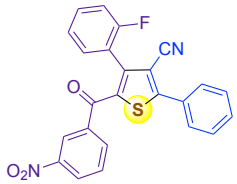
Pale yellow solid (204mg, 50%).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.90 – 7.85 (m, 2H), 7.62 (d, *J* = 8.3 Hz, 2H), 7.59 – 7.53 (m, 4H), 7.47 (d, *J* = 8.3 Hz, 2H), 7.28 (d, *J* = 7.5 Hz, 1H), 7.07 (t, *J* = 8.8 Hz, 1H), 6.88 (t, *J* = 9.0 Hz, 1H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 187.0, 160.0, 159.1, 158.0, 141.9, 140.0, 132.0, 132.0, 131.8, 131.6, 131.4, 131.3, 131.2, 130.3, 129.6, 129.3, 128.1, 124.5, 124.4, 117.7, 115.9, 115.8, 115.7, 114.3, 109.6.

HRMS m/z calculated for $[M+Na]^+$: $C_{25}H_{13}FN_2OSNa$ 431.0630. Found 431.0638.

4-(2-Fluorophenyl)-5-(3-nitrobenzoyl)-2-phenylthiophene-3-carbonitrile (4o)



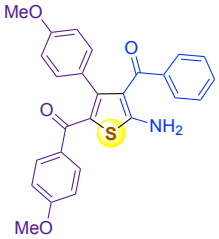
Pale yellow solid (304 mg, 71%).

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.28 (s, 1H), 8.17 (d, *J* = 8.2 Hz, 1H), 7.94 (d, *J* = 7.7 Hz, 1H), 7.89 (dd, *J* = 6.4, 2.9 Hz, 2H), 7.60 – 7.54 (m, 4H), 7.44 (t, *J* = 7.9 Hz, 1H), 7.34 (t, *J* = 7.3 Hz, 1H), 7.19 (q, *J* = 7.0 Hz, 1H), 7.04 (t, *J* = 7.5 Hz, 1H), 6.82 (t, *J* = 9.1 Hz, 1H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 186.1, 159.9, 159.3, 157.9, 147.2, 141.8, 138.0, 137.6, 134.4, 131.9, 131.9, 131.3, 131.2, 130.4, 129.6, 129.3, 128.1, 126.7, 124.5, 124.5, 124.2, 120.5, 115.8, 115.6, 114.3.

HRMS m/z calculated for $[M+Na]^+$: $C_{24}H_{13}FN_2O_3SNa$ 451.0529. Found 451.0536.

(5-Amino-4-benzoyl-3-(4-methoxyphenyl)thiophen-2-yl)(4-methoxyphenyl)methanone (3p)



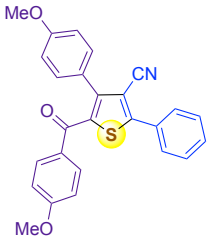
Pale yellow solid (119 mg, 27%).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.31 (d, *J* = 8.7 Hz, 2H), 7.19 (d, *J* = 7.3 Hz, 2H), 7.08 (t, *J* = 7.4 Hz, 1H), 6.94 (t, *J* = 7.7 Hz, 3H), 6.67 (d, *J* = 8.6 Hz, 2H), 6.49 (d, *J* = 8.7 Hz, 2H), 6.18 (d, *J* = 8.6 Hz, 2H), 3.67 (s, 3H), 3.52 (s, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 194.6, 189.0, 167.5, 162.0, 158.7, 146.3, 139.5, 132.1, 131.3, 130.8, 130.6, 130.1, 128.9, 128.7, 128.4, 127.6, 127.3, 121.0, 118.0, 112.8, 55.3, 55.1.

HRMS m/z calculated for $[M+Na]^+$: $C_{26}H_{21}NO_4SNa$ 466.1089. Found 466.1097.

5-(4-methoxybenzoyl)-4-(4-methoxyphenyl)-2-phenylthiophene-3-carbonitrile (4p)



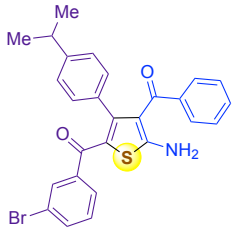
Pale yellow solid (246 mg, 58%).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.91 – 7.84 (m, 3H), 7.65 (d, *J* = 8.8 Hz, 2H), 7.59 – 7.50 (m, 4H), 7.30 (d, *J* = 12.8 Hz, 2H), 6.80 (d, *J* = 8.7 Hz, 2H), 6.72 (d, *J* = 8.8 Hz, 2H), 3.80 (s, 3H), 3.77 (s, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 187.5, 163.5, 160.1, 156.9, 146.6, 137.2, 132.2, 131.1, 131.0, 130.6, 130.3, 129.4, 129.1, 128.1, 125.0, 115.5, 114.0, 113.4, 108.6, 55.5, 55.3.

HRMS m/z calculated for $[M+Na]^+$: $C_{26}H_{19}NO_3SNa$ 448.0983. Found 448.0992.

(5-Amino-4-benzoyl-3-(4-isopropylphenyl)thiophen-2-yl)(3-bromophenyl)methanone (3q)



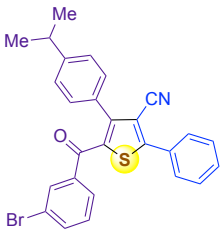
Pale yellow solid (60 mg, 12%).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.24 – 7.18 (m, 2H), 7.17 – 7.09 (m, 3H), 7.04 (s, 2H-NH_2), 7.01 (d, J = 7.5 Hz, 1H), 6.88 (t, J = 8.0 Hz, 2H), 6.85 (t, J = 8.3 Hz, 1H), 6.60 (d, J = 8.0 Hz, 2H), 6.47 (d, J = 7.8 Hz, 2H), 2.51 (p, J = 6.9 Hz, 1H), 0.96 (d, J = 6.9 Hz, 6H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 194.8, 188.6, 168.6, 148.7, 148.2, 140.2, 139.4, 133.3, 131.9, 131.8, 130.8, 130.5, 128.9, 128.5, 127.2, 126.9, 125.2, 121.2, 118.2, 33.7, 23.4.

HRMS m/z calculated for $[M+Na]^+$: $C_{27}H_{22}BrNO_2SNa$ 526.0452. Found 526.0460.

5-(3-Bromobenzoyl)-4-(4-isopropylphenyl)-2-phenylthiophene-3-carbonitrile (4q)



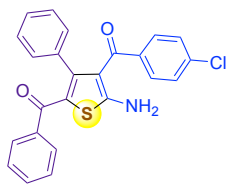
Pale yellow solid (242 mg, 50%).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.92 – 7.82 (m, 2H), 7.58 – 7.50 (m, 3H), 7.49 – 7.41 (m, 2H), 7.36 (dt, J = 8.0, 1.3 Hz, 1H), 7.16 (d, J = 8.1 Hz, 2H), 7.07 – 7.03 (m, 2H), 7.02 (d, J = 7.8 Hz, 1H), 2.80 (p, J = 6.9 Hz, 1H), 1.16 (d, J = 6.9 Hz, 6H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 187.8, 158.7, 150.1, 148.9, 138.2, 137.4, 135.0, 132.5, 131.0, 130.8, 129.8, 129.6, 129.5, 129.5, 128.1, 127.5, 126.5, 121.8, 115.1, 33.9, 23.6

HRMS m/z calculated for $[M+Na]^+$: C27H20BrNOSNa: 508.0347. Found 508.0355.

(5-Amino-4-(4-chlorobenzoyl)-3-phenylthiophen-2-yl)(phenyl)methanone (3r)



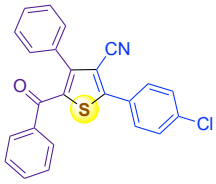
Pale yellow solid (62 mg, 15%).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.28 (dd, *J* = 6.9, 0.9 Hz, 2H), 7.13 (t, *J* = 7.4 Hz, 1H), 7.10 (d, *J* = 8.5 Hz, 2H), 7.01 (s, 2H-*NH*$_2$), 6.96 (t, *J* = 7.8 Hz, 2H), 6.87 (d, *J* = 8.4 Hz, 2H), 6.76 – 6.71 (m, 3H), 6.64 (t, *J* = 7.6 Hz, 2H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 193.2, 190.1, 168.1, 146.9, 138.1, 137.8, 136.7, 134.6, 131.1, 130.9, 129.9, 128.8, 127.5, 127.5, 127.4, 127.2, 121.8, 117.9.

HRMS m/z calculated for $[M+Na]^+$: $C_{24}H_{16}ClNO_2SNa$ 440.0488. Found 440.0492.

5-Benzoyl-2-(4-chlorophenyl)-4-phenylthiophene-3-carbonitrile (4r)



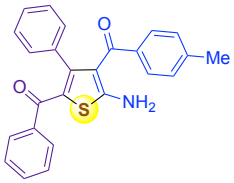
Pale yellow solid (185 mg, 60%).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.87 – 7.78 (m, 2H), 7.60 – 7.54 (m, 2H), 7.54 – 7.49 (m, 2H), 7.34 (td, *J* = 7.6, 1.2 Hz, 1H), 7.31 – 7.27 (m, 2H), 7.20 (dd, *J* = 5.1, 1.6 Hz, 3H), 7.17 (t, *J* = 7.8 Hz, 2H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 188.8, 156.2, 147.8, 138.0, 137.1, 136.3, 132.9, 132.3, 129.8, 129.7, 129.5, 129.3, 129.2, 129.1, 128.4, 128.0, 114.9, 109.1.

HRMS m/z calculated for $[M+Na]^+$: $C_{24}H_{14}ClNOSNa$: 422.0382. Found 422.0393.

(5-Amino-4-(4-methylbenzoyl)-3-phenylthiophen-2-yl)(phenyl)methanone (3s)



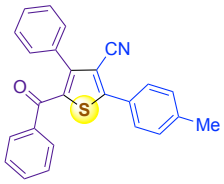
Pale yellow solid (59 mg, 15%).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.28 (d, *J* = 7.8 Hz, 2H), 7.10 (d, *J* = 8.1 Hz, 3H), 6.95 (t, *J* = 7.7 Hz, 2H), 6.86 (s, 2H-*NH*$_2$), 6.76 (d, *J* = 7.5 Hz, 2H), 6.71 (d, *J* = 8.0 Hz, 2H), 6.68 (d, *J* = 7.6 Hz, 1H), 6.61 (t, *J* = 7.6 Hz, 2H), 2.12 (s, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 194.4, 190.2, 167.3, 147.5, 141.3, 138.3, 136.5, 134.8, 130.9, 130.9, 128.9, 128.0, 127.4, 127.2, 127.0, 121.6, 118.6, 21.3.

HRMS m/z calculated for $[M+Na]^+$: $C_{25}H_{19}NO_2SNa$ 420.1034. Found 420.1041.

5-Benzoyl-4-phenyl-2-(p-tolyl)thiophene-3-carbonitrile (4s)



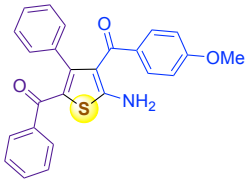
Pale yellow solid (238 mg, 63%).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.78 (d, *J* = 8.2 Hz, 2H), 7.56 (dd, *J* = 8.2, 1.1 Hz, 2H), 7.37 – 7.32 (m, 3H), 7.32 – 7.28 (m, 3H), 7.20 (dt, *J* = 6.0, 3.2 Hz, 3H), 7.16 (t, *J* = 7.8 Hz, 2H), 2.44 (s, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 189.0, 147.9, 147.9, 141.4, 141.4, 137.2, 137.2, 136.6, 136.6, 132.7, 132.5, 130.2, 129.8, 129.5, 129.0, 128.3, 128.0, 128.0, 128.0, 115.3, 115.3, 108.4, 108.4, 21.5.

HRMS m/z calculated for $[M+Na]^+$: $C_{25}H_{17}NOSNa$ 402.0929. Found 402.0936.

(5-Amino-4-(4-methoxybenzoyl)-3-phenylthiophen-2-yl)(phenyl)methanone (3t)



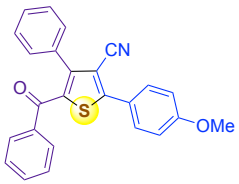
Pale yellow solid (70 mg, 17%).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.29 (dd, *J* = 8.2, 1.2 Hz, 2H), 7.23 (dt, *J* = 8.8, 2.8, 1.9 Hz, 2H), 7.12 (tt, *J* = 7.3, 1.2 Hz, 1H), 6.96 (t, *J* = 7.8 Hz, 1H), 6.81 – 6.75 (m, 2H), 6.75 – 6.69 (m, 1H), 6.65 (t, *J* = 7.4 Hz, 2H), 6.59 (s, 2H-*NH*$_2$), 6.43 (dt, *J* = 8.9, 3.0, 2.0 Hz, 2H), 3.65 (s, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 193.2, 190.1, 166.5, 161.9, 147.2, 138.3, 134.9, 131.8, 131.1, 130.9, 130.8, 128.9, 127.4, 127.1, 121.7, 118.8, 112.7, 55.2.

HRMS m/z calculated for $[M+Na]^+$: $C_{25}H_{19}NO_3SNa$ 436.0983. Found 436.0992.

5-Benzoyl-2-(4-methoxyphenyl)-4-phenylthiophene-3-carbonitrile (4t)



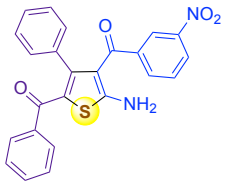
Pale yellow solid (257 mg, 65%).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.85 (dt, *J* = 8.9, 2.9, 2.1 Hz, 2H), 7.55 (dd, *J* = 8.2, 1.2 Hz, 2H), 7.32 (t, *J* = 7.4 Hz, 1H), 7.28 (dd, *J* = 6.6, 3.0 Hz, 3H), 7.22 – 7.18 (m, 3H), 7.15 (t, *J* = 7.8 Hz, 2H), 7.05 (dt, *J* = 8.8, 3.1, 2.1 Hz, 2H), 3.89 (s, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 189.0, 161.7, 158.1, 148.0, 136.6, 132.6, 132.6, 129.8, 129.6, 129.4, 128.9, 128.3, 127.9, 123.3, 115.5, 114.9, 107.8, 55.5.

HRMS m/z calculated for $[M+Na]^+$: $C_{25}H_{17}NO_2SNa$ 418.0878. Found 418.0885.

(5-Amino-4-(3-nitrobenzoyl)-3-phenylthiophen-2-yl)(phenyl)methanone (3u)



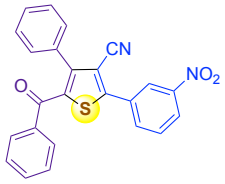
Pale yellow solid (43 mg, 10%).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.88 (ddd, J = 8.2, 2.4, 1.2 Hz, 1H), 7.82 (t, J = 2.0 Hz, 1H), 7.59 (dt, J = 7.7, 1.3 Hz, 1H), 7.23 – 7.14 (m, 3H), 7.14 – 7.08 (m, 1H), 6.96 (t, J = 7.8 Hz, 2H), 6.81 – 6.73 (m, 2H), 6.70 – 6.62 (m, 1H), 6.59 (dd, J = 8.1, 6.6 Hz, 2H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 191.5, 189.9, 169.1, 146.6, 146.2, 140.7, 138.0, 134.5, 133.8, 131.1, 130.8, 128.7, 128.6, 127.8, 127.4, 127.3, 124.8, 123.9, 117.2.

HRMS m/z calculated for $[M+Na]^+$: $C_{24}H_{16}N_2O_4SNa$: 451.0728. Found 451.0732.

5-Benzoyl-2-(3-nitrophenyl)-4-phenylthiophene-3-carbonitrile (4u)



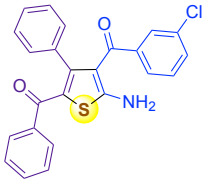
Pale yellow solid (172mg, 42%).

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.68 (t, J = 2.0 Hz, 1H), 8.39 (ddd, J = 8.3, 2.2, 1.0 Hz, 1H), 8.23 (ddd, J = 7.8, 1.8, 1.0 Hz, 1H), 7.77 (t, J = 8.0 Hz, 1H), 7.65 – 7.51 (m, 2H), 7.40 – 7.34 (m, 1H), 7.33 – 7.29 (m, 2H), 7.25 – 7.15 (m, 5H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 188.6, 153.9, 148.8, 147.7, 139.1, 136.1, 133.7, 133.1, 132.4, 131.9, 130.7, 129.7, 129.5, 129.3, 128.5, 128.1, 125.1, 123.2, 114.5, 110.4.

HRMS m/z calculated for $[M+Na]^+$: $C_{24}H_{14}N_2O_3SNa$: 433.0623. Found 433.0631.

(5-Amino-4-(3-chlorobenzoyl)-3-phenylthiophen-2-yl)(phenyl)methanone (3v)



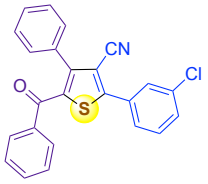
Pale yellow solid (50 mg, 12%).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.28 (d, *J* = 9.3 Hz, 1H), 7.13 – 7.08 (m, 3H), 7.04 (s, 3H), 7.02 – 6.98 (m, 2H), 6.96 (t, *J* = 7.6 Hz, 2H-*NH*$_2$), 6.88 (t, *J* = 7.8 Hz, 1H), 6.78 – 6.73 (m, 2H), 6.70 (d, *J* = 6.8 Hz, 1H), 6.68 (d, *J* = 7.7 Hz, 2H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 192.9, 190.1, 168.4, 147.0, 140.9, 138.1, 134.6, 133.2, 131.0, 130.6, 130.5, 128.9, 128.8, 128.8, 127.6, 127.4, 127.2, 126.4, 121.9, 117.8.

HRMS m/z calculated for $[M+Na]^+$: $C_{24}H_{16}ClNO_2SNa$ 440.0488. Found 440.0497.

5-Benzoyl-2-(3-chlorophenyl)-4-phenylthiophene-3-carbonitrile (4v)



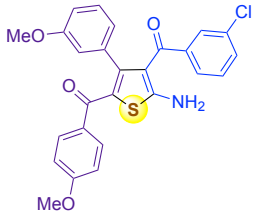
Pale yellow solid (179 mg, 45%).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.82 (d, *J* = 1.8 Hz, 1H), 7.78 (dt, *J* = 6.8, 1.7 Hz, 1H), 7.60 – 7.54 (m, 2H), 7.52 – 7.46 (m, 2H), 7.35 (t, *J* = 7.4 Hz, 1H), 7.29 (dd, *J* = 6.6, 2.9 Hz, 2H), 7.21 (dd, *J* = 4.8, 1.7 Hz, 3H), 7.17 (t, *J* = 7.8 Hz, 2H)

^{13}C NMR (126 MHz, $CDCl_3$) δ 188.8, 155.6, 147.8, 138.3, 136.3, 135.5, 132.9, 132.4, 132.2, 130.8, 130.7, 129.7, 129.5, 129.1, 128.4, 128.2, 128.0, 126.3, 114.7, 109.5.

HRMS m/z calculated for $[M+Na]^+$: $C_{24}H_{14}ClNOSNa$ 422.0382. Found 422.0385.

(5-Amino-4-(3-chlorobenzoyl)-3-(3-methoxyphenyl)thiophen-2-yl)(4-methoxyphenyl) methanone (3x)



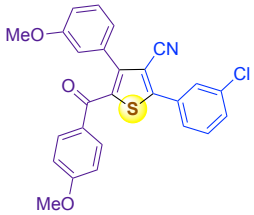
Pale yellow solid (86 mg, 18%).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.35 (d, *J* = 8.8 Hz, 2H), 7.15 (dt, *J* = 7.7, 1.3 Hz, 1H), 7.07 (t, *J* = 1.8 Hz, 1H), 7.03 (dt, *J* = 8.0, 1.4 Hz, 1H), 6.96 (s, 2H-*NH*$_2$), 6.93 (t, *J* = 7.8 Hz, 1H), 6.64 (t, *J* = 7.7 Hz, 1H), 6.53 – 6.45 (m, 2H), 6.41 (d, *J* = 7.7 Hz, 1H), 6.30 (d, *J* = 8.4 Hz, 2H), 3.69 (s, 3H), 3.50 (s, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 192.8, 188.8, 167.8, 162.2, 158.6, 145.5, 141.1, 136.1, 133.1, 131.1, 130.7, 130.5, 128.7, 128.5, 126.1, 123.4, 115.6, 114.1, 112.8, 55.3, 55.0.

HRMS m/z calculated for $[M+Na]^+$: $C_{26}H_{20}ClNO_4SNa$: 500.0699. Found 500.0705.

2-(3-chlorophenyl)-5-(4-methoxybenzoyl)-4-(3-methoxyphenyl)thiophene-3-carbonitrile (4x)



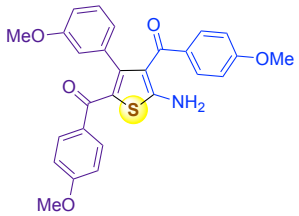
Pale yellow solid (192 mg, 42%).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.81 (d, *J* = 2.2 Hz, 1H), 7.79 – 7.72 (m, 1H), 7.62 (d, *J* = 8.6 Hz, 2H), 7.55 – 7.41 (m, 2H), 7.17 (t, *J* = 7.9 Hz, 1H), 6.94 (d, *J* = 7.4 Hz, 1H), 6.84 (t, *J* = 1.9 Hz, 1H), 6.79 (dd, *J* = 8.2, 2.5 Hz, 1H), 6.70 (d, *J* = 8.6 Hz, 2H), 3.79 (s, 3H), 3.71 (s, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 187.2, 163.7, 159.4, 154.9, 146.4, 135.4, 133.5, 132.5, 132.1, 130.7, 129.6, 129.0, 128.2, 126.3, 122.1, 115.3, 114.9, 114.9, 113.5, 55.5, 55.3

HRMS m/z calculated for $[M+Na]^+$: $C_{26}H_{18}ClNO_3SNa$: 482.0594. Found 482.0599.

(5-Amino-3-(3-methoxyphenyl)thiophene-2,4-diyl)bis((4-methoxyphenyl)methanone) (3y)



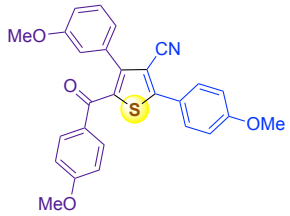
Pale yellow solid (76 mg, 16%).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.35 (d, *J* = 8.6 Hz, 2H), 7.26 (d, *J* = 9.1 Hz), 6.67 (s, 1H), 6.63 (t, 1H), 6.50 (s, 2H-NH_2), 6.46 (d, *J* = 8.8 Hz, 2H), 6.34 (s, 1H), 6.31 (dd, *J* = 8.2, 2.3 Hz, 1H), 3.69 (s, 3H), 3.66 (s, 3H), 3.48 (s, 3H).

^{13}C NMR (126 MHz, CDCl3) δ 193.2, 188.9, 166.1, 161.9, 158.4, 145.9, 136.3, 132.0, 131.8, 131.4, 131.2, 130.9, 130.9, 129.8, 128.4, 123.7, 116.0, 113.8, 112.8, 112.6, 55.3, 55.3, 55.1

HRMS m/z calculated for [M+Na]+:$C_{27}H_{23}NO_5SNa$: 496.1195. Found 496.1203.

5-(4-methoxybenzoyl)-4-(3-methoxyphenyl)-2-(4-methoxyphenyl)thiophene-3-carbonitrile (4y)



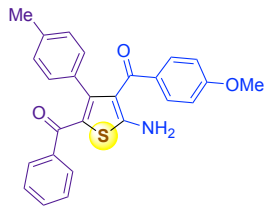
Pale yellow solid (282 mg, 62%).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.82 (d, *J* = 8.6 Hz, 2H), 7.61 (d, *J* = 8.6 Hz, 2H), 7.15 (t, *J* = 7.9 Hz, 1H), 7.04 (d, *J* = 8.6 Hz, 2H), 6.94 (d, *J* = 7.3 Hz, 1H), 6.82 (s, 1H), 6.77 (d, *J* = 8.3 Hz, 1H), 6.67 (d, *J* = 8.6 Hz, 2H), 3.89 (s, 2H), 3.78 (s, 2H), 3.70 (s, 2H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 187.5, 163.4, 161.6, 159.3, 157.3, 146.6, 137.0, 133.8, 132.0, 129.6, 129.5, 129.3, 123.4, 122.2, 115.6, 115.1, 115.0, 114.8, 113.3, 107.4, 77.3, 55.5, 55.5, 55.3.

HRMS m/z calculated for [M+Na]+: $C_{27}H_{21}NO_4SNa$: 478.1089. Found 478.1095.

(5-Amino-4-(4-methoxybenzoyl)-3-(p-tolyl)thiophen-2-yl)(phenyl)methanone (3z)



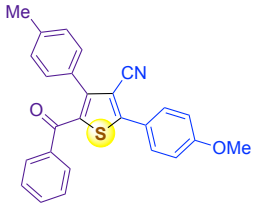
Pale yellow solid (68 mg, 16%).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.28 (d, *J* = 7.5 Hz, 2H), 7.23 (d, *J* = 8.7 Hz, 2H), 7.13 (d, *J* = 7.4 Hz, 1H), 6.97 (t, *J* = 7.7 Hz, 2H), 6.64 (d, *J* = 7.9 Hz, 2H), 6.59 (s, 2H-NH_2), 6.44 (d, *J* = 8.4 Hz, 4H), 3.66 (s, 3H), 1.97 (s, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 193.3, 190.1, 166.6, 161.9, 147.6, 138.4, 137.1, 131.9, 131.8, 131.1, 130.7, 130.6, 128.9, 127.7, 127.3, 121.4, 118.8, 112.6, 55.3, 20.8.

HRMS m/z calculated for $[M+Na]^+$: $C_{26}H_{21}NO_3SNa$ 450.1140. Found 450.1148.

5-Benzoyl-2-(4-methoxyphenyl)-4-(p-tolyl)thiophene-3-carbonitrile (4z)



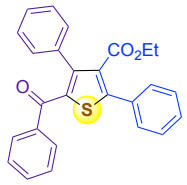
Pale yellow solid (245 mg, 60%).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.84 (d, J = 8.7 Hz, 2H), 7.56 (d, J = 7.5 Hz, 2H), 7.34 (t, J = 7.4 Hz, 1H), 7.22 – 7.12 (m, 4H), 7.04 (d, J = 8.7 Hz, 2H), 6.99 (d, J = 7.9 Hz, 2H), 3.88 (s, 3H), 2.24 (s, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 189.1, 161.7, 157.9, 148.3, 138.9, 136.7, 136.3, 132.5, 129.7, 129.6, 129.6, 129.5, 129.0, 127.9, 123.4, 115.6, 114.9, 107.9, 55.5, 21.2.

HRMS m/z calculated for $[M+Na]^+$: $C_{26}H_{19}NO_2SNa$: 432.1034.

Ethyl 5-benzoyl-2,4-diphenylthiophene-3-carboxylate (6a)



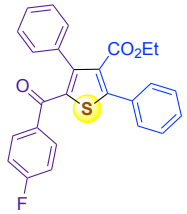
Pale yellow solid (268 mg, 65%).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.62 – 7.56 (m, 5H), 7.44 (dd, J = 5.0, 1.7 Hz, 4H), 7.33 (t, J = 7.4 Hz, 1H), 7.23 – 7.09 (m, 10H), 4.00 (q, J = 7.1 Hz, 2H), 0.88 (t, J = 7.1 Hz, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 189.6, 165.1, 149.5, 145.8, 137.5, 134.7, 133.4, 132.8, 132.4, 132.3, 130.4, 129.9, 129.7, 129.6, 129.5, 129.3, 129.2, 128.8, 128.7, 128.3, 128.0, 127.9, 127.8, 127.8, 127.7, 127.5, 61.3, 13.5.

HRMS m/z calculated for $[M+Na]^+$: $C_{26}H_{20}O_3SNa$ 435.1031. Found 435.1039.

Ethyl 5-(4-fluorobenzoyl)-2,4-diphenylthiophene-3-carboxylate (6b)



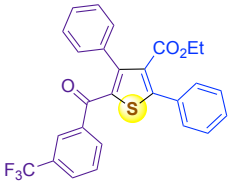
Pale yellow solid (228mg, 53%).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.68 – 7.53 (m, 6H), 7.49 – 7.39 (m, 4H), 7.23 – 7.06 (m, 6H), 6.83 (t, *J* = 8.6 Hz, 2H), 4.00 (q, *J* = 7.1 Hz, 2H), 0.88 (t, *J* = 7.1 Hz, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 188.19, 166.06, 164.54 (d, *J* = 126.3 Hz), 149.65, 145.62, 137.41, 134.52, 133.65, 132.06 (d, *J* = 9.3 Hz), 129.59, 129.40, 128.83, 128.75, 128.07, 127.87, 114.96 (d, *J* = 22.0 Hz), 61.38, 13.48.

HRMS m/z calculated for $[M+Na]^+$: $C_{26}H_{19}FO_3SNa$ 453.0937. Found 453.0944.

Ethyl 2,4-diphenyl-5-(3-(trifluoromethyl)benzoyl)thiophene-3-carboxylate (6c)



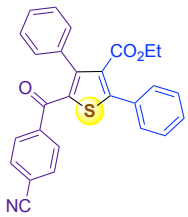
Pale yellow solid (288 mg, 60%).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.66 (d, *J* = 7.8 Hz, 1H), 7.62 (s, 1H), 7.57 – 7.50 (m, 2H), 7.43 (d, *J* = 7.8 Hz, 1H), 7.40 – 7.32 (m, 3H), 7.21 (t, *J* = 7.8 Hz, 1H), 7.11 – 7.04 (m, 2H), 7.01 (d, *J* = 5.2 Hz, 3H), 3.91 (q, *J* = 7.1 Hz, 2H), 0.79 (t, *J* = 7.1 Hz, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 188.5, 164.9, 150.7, 146.3, 138.0, 137.3, 134.2, 132.5, 132.3, 132.2, 130.3, 130.0, 129.7, 129.5, 128.8, 128.8, 128.5, 128.4, 128.4, 128.2, 127.9, 126.2, 126.2, 61.4, 13.5.

HRMS m/z calculated for $[M+Na]^+$: $C_{27}H_{19}F_3O_3SNa$ 503.0905. Found 503.0909.

Ethyl 5-(4-cyanobenzoyl)-2,4-diphenylthiophene-3-carboxylate (6d)



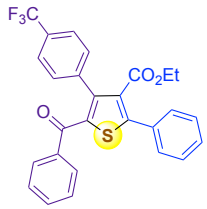
Pale yellow solid (449 mg, 47%).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.63 – 7.57 (m, 2H), 7.55 (d, *J* = 8.2 Hz, 2H), 7.49 – 7.43 (m, 3H), 7.39 (d, *J* = 8.3 Hz, 2H), 7.19 – 7.03 (m, 5H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 188.3, 164.8, 151.2, 146.6, 141.1, 137.1, 134.1, 133.6, 132.6, 132.1, 131.5, 130.1, 129.7, 129.7, 129.4, 128.8, 128.8, 128.4, 128.1, 127.9, 117.9, 115.0, 61.5, 13.5.

HRMS m/z calculated for $[M+Na]^+$: $C_{27}H_{19}NO_3SNa$ 460.0983. Found 460.0987.

Ethyl 5-benzoyl-2-phenyl-4-(4-(trifluoromethyl)phenyl)thiophene-3-carboxylate (6e)



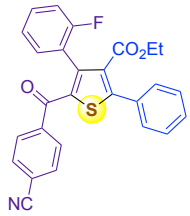
Pale yellow solid (360 mg, 75%).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.63 – 7.56 (m, 5H), 7.48 – 7.42 (m, 6H), 7.38 (t, *J* = 7.5 Hz, 1H), 7.35 (d, *J* = 8.1 Hz, 2H), 7.22 (t, *J* = 7.7 Hz, 2H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 189.0, 164.5, 150.5, 144.5, 138.5, 137.9, 137.6, 132.6, 132.2, 131.9, 130.1, 130.0, 129.9, 129.8, 129.5, 129.3, 129.0, 128.9, 128.8, 128.6, 128.3, 128.0, 124.7, 124.6, 61.4, 13.4.

HRMS m/z calculated for $[M+Na]^+$: $C_{27}H_{19}F_3O_3SNa$ 503.0905. Found 503.0912.

Ethyl 5-(4-cyanobenzoyl)-4-(2-fluorophenyl)-2-phenylthiophene-3-carboxylate (6f)



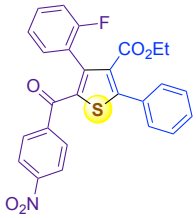
Pale yellow solid (286 mg, 63%).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.62 (d, *J* = 8.2 Hz, 2H), 7.57 (dd, *J* = 6.2, 2.7 Hz, 2H), 7.50 – 7.39 (m, 8H), 7.21 – 7.15 (m, 1H), 7.09 (t, *J* = 7.4 Hz, 1H), 6.92 (t, *J* = 7.5 Hz, 1H), 6.84 (t, *J* = 9.1 Hz, 1H), 3.99 (q, *J* = 7.1 Hz, 2H), 0.87 (t, *J* = 7.1 Hz, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 187.9, 163.8, 160.3, 152.8, 141.1, 140.1, 132.2, 131.6, 130.7, 130.7, 129.7, 129.2, 129.1, 128.6, 123.8, 123.8, 117.9, 115.2, 115.2, 115.1, 61.3, 13.4.

HRMS m/z calculated for $[M+Na]^+$: $C_{27}H_{18}FNO_3SNa$ 478.0889. Found 478.0897.

Ethyl 4-(2-fluorophenyl)-5-(4-nitrobenzoyl)-2-phenylthiophene-3-carboxylate (6g)



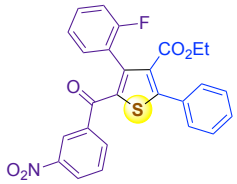
Pale yellow solid (294mg, 62%).

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.01 (d, J = 8.7 Hz, 2H), 7.67 (d, J = 8.6 Hz, 2H), 7.57 (dd, J = 6.1, 2.6 Hz, 3H), 7.51 – 7.38 (m, 4H), 7.20 – 7.12 (m, 1H), 7.10 (t, J = 7.5 Hz, 1H), 6.92 (t, J = 7.4 Hz, 1H), 6.83 (t, J = 9.0 Hz, 1H), 4.00 (q, J = 7.1 Hz, 2H), 0.87 (t, J = 7.1 Hz, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 187.7, 163.8, 160.3, 158.3, 153.1, 149.3, 142.8, 140.3, 137.9, 133.7, 132.1, 131.9, 131.6, 130.7, 130.7, 130.2, 129.7, 129.1, 128.7, 128.5, 123.8, 123.8, 122.9, 122.8, 122.6, 115.3, 115.1, 61.3, 13.4.

HRMS m/z calculated for $[M+Na]^+$: $C_{26}H_{18}FNO_5SNa$ 498.0787. Found 498.0792.

Ethyl 4-(2-fluorophenyl)-5-(3-nitrobenzoyl)-2-phenylthiophene-3-carboxylate (6h)



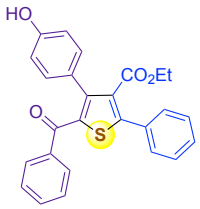
Pale yellow solid (290 mg, 61%).

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.31 (s, 1H), 8.15 (d, J = 8.2 Hz, 1H), 7.94 (d, J = 7.7 Hz, 1H), 7.60 (dd, J = 6.1, 2.5 Hz, 3H), 7.54 – 7.45 (m, 4H), 7.43 (t, J = 7.9 Hz, 1H), 7.16 (t, J = 7.4 Hz, 1H), 7.13 – 7.07 (m, 1H), 6.91 (t, J = 7.5 Hz, 1H), 6.81 (t, J = 9.0 Hz, 1H), 4.02 (q, J = 7.1 Hz, 2H), 0.89 (t, J = 7.1 Hz, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 187.0, 163.8, 160.2, 158.3, 153.0, 147.2, 140.0, 138.6, 137.9, 134.3, 133.6, 132.2, 131.9, 131.5, 130.7, 130.6, 130.1, 129.7, 129.2, 129.1, 128.6, 128.6, 128.5, 126.3, 124.1, 123.8, 123.8, 122.8, 122.7, 115.2, 115.0, 61.3, 13.4.

HRMS m/z calculated for $[M+Na]^+$: $C_{26}H_{18}FNO_5SNa$ 498.0787. Found 498.0791.

Ethyl 5-benzoyl-4-(4-hydroxyphenyl)-2-phenylthiophene-3-carboxylate (6i)



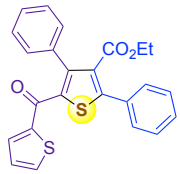
Pale yellow solid (197 mg, 46%).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.62 (d, J = 7.5 Hz, 2H), 7.57 (dd, J = 6.5, 2.7 Hz, 3H), 7.50 – 7.41 (m, 4H), 7.37 (t, J = 7.4 Hz, 1H), 7.21 (t, J = 7.7 Hz, 2H), 7.04 (d, J = 8.4 Hz, 2H), 6.54 (d, J = 8.5 Hz, 2H), 4.04 (q, J = 7.1 Hz, 2H), 0.94 (t, J = 7.1 Hz, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 190.0, 165.6, 155.8, 149.5, 146.0, 137.6, 136.8, 132.4, 130.9, 129.6, 129.3, 128.7, 128.5, 127.9, 126.6, 114.9, 61.6, 13.6.

HRMS m/z calculated for $[M+Na]^+$: $C_{26}H_{20}O_4SNa$ 451.0980. Found 451.0987.

Ethyl 2,4-diphenyl-5-(thiophene-2-carbonyl)thiophene-3-carboxylate (6j)



Pale yellow solid (326 mg, 78%).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.50 (dd, J = 6.4, 2.9 Hz, 2H), 7.46 (d, J = 4.9 Hz, 1H), 7.40 (d, J = 5.3 Hz, 1H), 7.38 – 7.28 (m, 3H), 7.27 – 7.22 (m, 3H), 7.21 – 7.12 (m, 5H), 6.83 – 6.78 (m, 1H), 3.93 (q, J = 7.1 Hz, 1H), 0.80 (t, J = 7.1 Hz, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 180.3, 165.1, 148.4, 145.3, 143.7, 136.0, 134.8, 134.3, 132.3, 129.4, 129.3, 128.9, 128.7, 128.1, 128.0, 128.0, 127.9, 127.9, 127.8, 127.7, 61.4, 13.5.

HRMS m/z calculated for $[M+Na]^+$: $C_{24}H_{18}O_3S_2Na$ 441.0595. Found 441.0598.

Crystallographic data collection, structure determination and refinement

Suitable crystals for single crystal X-ray diffraction (SCXRD) analysis were obtained for the following nine chalcone compounds (see Table S1) after slow concentration in $CDCl_3$ solvent. X-ray diffraction data for all compounds were measured at room temperature using either a RIGAKU *XtaLabPro* diffractometer equipped with a Mo microfocus sealed tube *MM003* generator coupled to a double-bounce confocal Max-Flux® multilayer optic and a HPAD *PILATUS3R 200K* detector (for compounds **3b**, **3p**, **4a**, **4b**, **6e**, **6a**), a Bruker APEX-II / CCD for compounds **4v** and **4r** or a RIGAKU rotating anode *MM007HF* with a CMF optics and a Spider2 Imaging-plate detector for compound **3a**. *CrysAlisPro 1.171.39.46* [1] was employed for the processing of data collected on the *XtaLabPro*, with *SCALE3 ABSPACK* scaling algorithm implemented for the absorption correction combining a numerical approach based on gaussian integration over a multifaceted crystal model and empirical one using spherical harmonics. Regarding **4v** and **3r**, the *SAINT V8.40A* program [2] was used implementing the *SADABS-2016/2* [3] software for the absorption correction. Finally data collection and processing for **3a** were carried out using the *CrystalClear 2.0* suite [4] implementing *ABSCOR* [5] as multi-scan empirical absorption correction method.

All the structures were solved by intrinsic phasing methods (*SHELXT* program),[6] and all were refined by full-matrix least-squares methods on F^2 using *SHELXL*.[7] All non-hydrogen atoms of the molecules of interest improved by anisotropic refinement. Most of their H atoms were clearly identified in difference maps but were positioned geometrically and refined with U_{iso} set to $1.2U_{eq}$(C) of the parent atom (or 1.5 for the methyls in compounds **3p**, **6a** and **6e**). The amine hydrogen parameters were freely refined except similar distance restraints (SADI) in compounds **3b** and **3p**, their U_{iso} were set to 1.2Ueq for compound **6a** or positioned geometrically in compound **3a** with the AFIX 93. All the CF3 groups present in compounds **3b**, **4b**, and **6e** were disordered over two orientations in refined ratio and restrained using DELU and SIMU commands in *SHELXL*. In compound 8 the ethyl carboxylate group was also disordered over two sites with refined occupancy ratio of 0.54(1)/0.46(1) whereas the thiophene groups in the two molecules present in the asymmetric unit of crystal **3a** were swapped with refined occupancies of 0.80(1)/0.20(1) and 0.52(1)/0.48(1) respectively. The poor diffraction of this crystal led us to apply a d_{max}=1.08Å resolution cutoff to the recorded data and to resort to numerous restraints upon atomic displacement parameters and geometric parameters to compensate with a very low observables over parameters ratio.

Crystal data, data collection and structure refinement details are summarized in Table S1.

CCDC 2163444 – 2163449, 2165840, 2165911 and 2166476 contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from the Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

References

1 Rigaku OD (2015). *CrysAlis PRO*. Rigaku Oxford Diffraction, Yarnton, Oxfordshire, England.

2 Bruker (2012). *SAINT*. Bruker AXS Inc., Madison, Wisconsin, USA.

3 Bruker (2001). *SADABS.* Bruker AXS Inc., Madison, Wisconsin, USA.

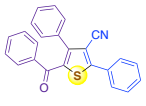
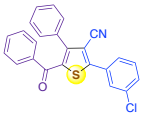
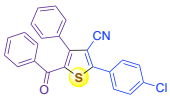
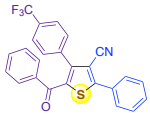
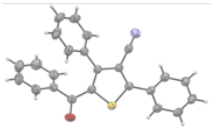
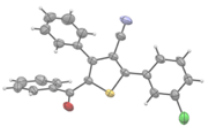
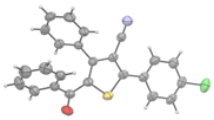
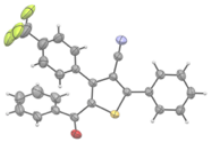
4 Rigaku. (2009) *CrystalClear-SM Expert 2.0 r4* Rigaku Corporation, Tokyo, Japan.

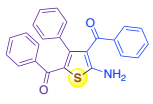
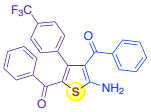
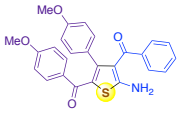
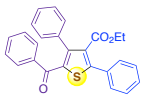
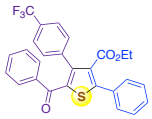
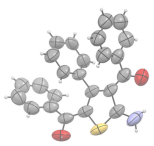
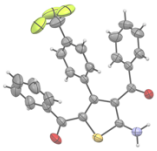
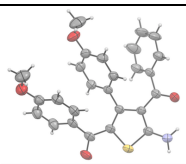
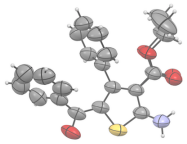
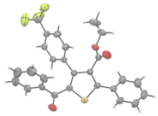
5 Higashi, T. (1995). *ABSCOR*. Rigaku Corporation, Tokyo, Japan.

6 Sheldrick, G. M. (2015). *Acta Crystallogr.,* C**71**, 3-8.

7 Sheldrick, G. M. (2015). *Acta Crystallogr.,* A**71**, 3-8.

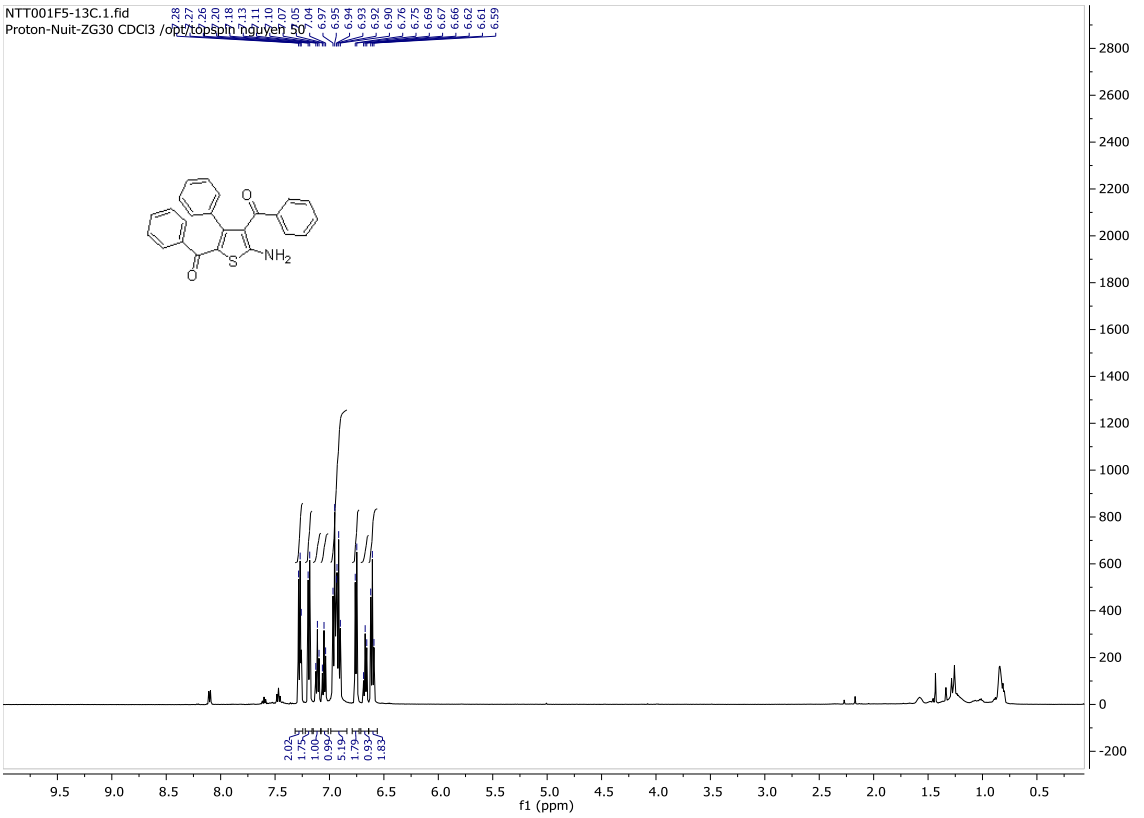
Table S1 Crystal data, data collection and structure refinement details for the thiophene derivatives **4a**, **4v**, **4r**, **4b**, **3b** and **6e**.

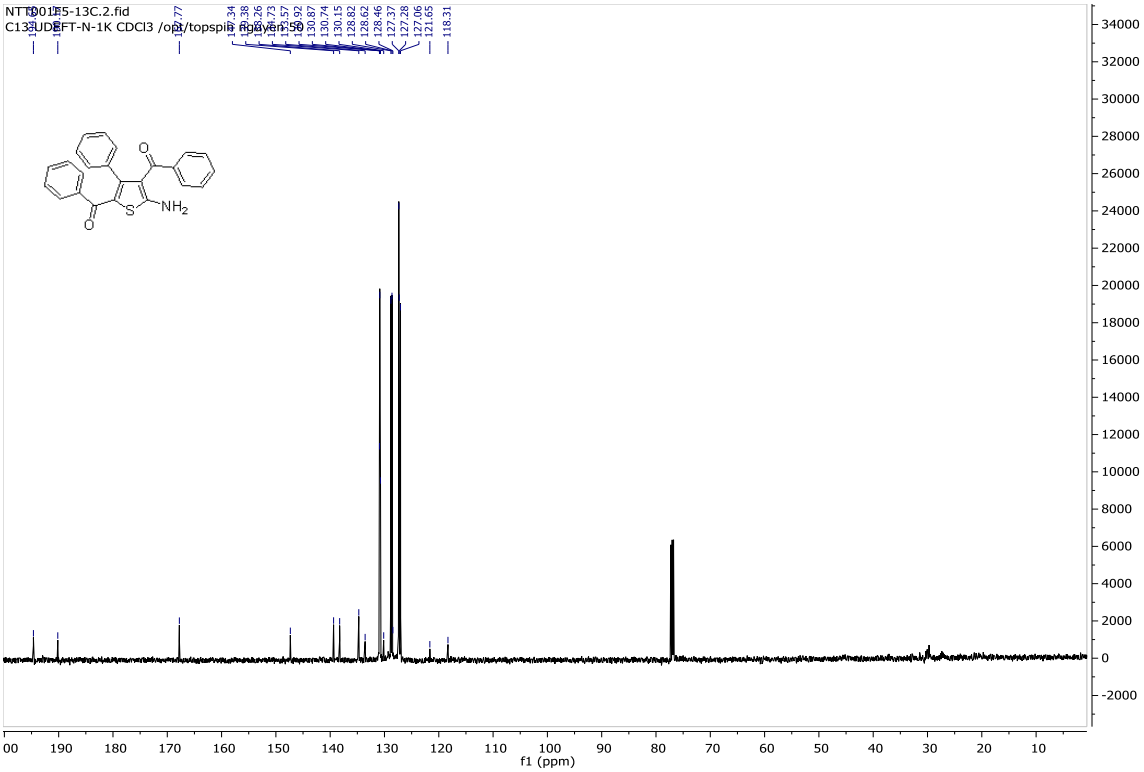
Compound	4a	4v	4r	4b
2D-scheme				
Ortep view. Displacement ellipsoids drawn at the 30% probability level. H atoms shown as small spheres of arbitrary radii.				
Systematic chemical name	5-benzoyl-2,4-diphenylthiophene-3-carbonitrile	5-benzoyl-2-(3-chlorophenyl)-4-phenylthiophene-3-carbonitrile	5-benzoyl-2-(4-chlorophenyl)-4-phenylthiophene-3-carbonitrile	5-benzoyl-2-phenyl-4-(4-(trifluoromethyl)phenyl)thiophene-3-carbonitrile
Empirical formula	$C_{24}H_{15}NOS$	$C_{24}H_{14}ClNOS$	$C_{24}H_{14}ClNOS$	$C_{25}H_{14}F_3NOS$
Formula weight	365.43	399.87	399.87	433.43
Temperature (K)	293(2)	293(2)	293(2)	293(2)
Wavelength (Å)	0.71073	0.71073	0.71073	0.71073
Crystal system, space group	Orthorhombic, Pbca	Triclinic, P-1	Triclinic, P-1	Triclinic, P-1
Unit cell dimensions | (Å) | (°)	7.2549(3) 14.6152(5) 34.7662(13) 90 90 90	7.8592(5) 9.8424(6) 13.5018(8) 109.699(2) 95.917(2) 100.938(2)	9.6404(5) 9.9855(6) 11.0770(7) 70.189(2) 88.960(2) 74.740(2)	7.9211(2) 9.5827(2) 14.7540(3) 99.448(2) 102.525(2) 100.847(2)
Volume ($Å^3$)	3685.2(2)	949.53(10)	964.87(10)	1048.89(4)
Z, Calculated density (Mg/m^3)	8, 1.317	2, 1.399	2, 1.376	2, 1.372
Absorption coefficient (mm^{-1})	0.189	0.326	0.321	0.197
F(000)	1520	412	412	444
Crystal size (mm)	0.26 x 0.10 x 0.04	0.32 x 0.15 x 0.06	0.39 x 0.19 x 0.07	0.29 x 0.17 x 0.14
θ range for data collection (°)	2.787 to 25.350	2.684 to 26.729	2.683 to 26.726	2.373 to 27.103
Limiting indices	$-8 \le h \le 8$, $-17 \le k \le 16$, $-41 \le l \le 27$	$-9 \le h \le 9$, $-12 \le k \le 12$, $-17 \le l \le 17$	$-12 \le h \le 12$, $-12 \le k \le 12$, $-14 \le l \le 14$	$-10 \le h \le 10$, $-12 \le k \le 12$, $-18 \le l \le 18$
Reflections collected / unique [R(int)	18737 / 3373 0.0555	31092 / 3986 0.032	16099 / 4079 0.0378	27479 / 4598 0.0279
Completeness to θ_{full} (%)	99.8	99.4	99.6	99.9
Absorption correction	Gaussian & Semi-empirical from equivalents	Semi-empirical from equivalents	Semi-empirical from equivalents	Gaussian & Semi-empirical from equivalents
Max. and min. transmission	1.000 and 0.562	0.7456 and 0.6443	0.7457 and 0.6711	1.000 and 0.420
Refinement method	Full-matrix least-squares on F^2	Full-matrix least-squares on F^2	Full-matrix least-squares on F^2	Full-matrix least-squares on F^2
Data / restraints / parameters	3371 / 0 / 244	3986 / 0 / 253	4079 / 0 / 253	4598 / 177 / 317
Goodness-of-fit on F^2	1.164	1.110	1.051	1.065
Final R indices R1, $[I>2\sigma(I)]$ wR2	0.0587, 0.1544	0.0514, 0.1016	0.0523, 0.0902	0.0454, 0.1284
R indices R1, (all data) wR2	0.0622, 0.1569	0.0649, 0.1098	0.0883, 0.1058	0.0494, 0.1323
Largest Δ peak and hole ($e.Å^{-3}$)	0.802 and -0.277	0.391 and -0.462	0.303 and -0.247	0.386 and -0.467
CCDC deposit number	2163444	2163445	2163446	2163447

Compound	3a	3b	3p	6a	6e
2D-scheme					
Ortep view. Displacement ellipsoids drawn at the 30% probability level. H atoms shown as small spheres of arbitrary radii.					
Systematic chemical name	(5-amino-3-phenylthiophene-2,4-diyl)bis(phenylmethanone)	5-amino-3-(4-(trifluoromethyl)phenyl)thiophene-2,4-diyl)bis(phenylmethanone)	(5-amino-4-benzoyl-3-(4-methoxyphenyl)thiophen-2-yl)(4-methoxyphenyl)methanone	ethyl 2-amino-5-benzoyl-4-phenylthiophene-3-carboxylate	ethyl 5-benzoyl-2-phenyl-4-(4-(trifluoromethyl)phenyl)thiophene-3-carboxylate
Empirical formula	$C_{24}H_{17}NO_2S$	$C_{25}H_{16}F_3NO_2S$	$C_{26}H_{21}NO_4S$	$C_{20}H_{17}NO_3S$	$C_{27}H_{19}F_3O_3S$
Formula weight	383.44	451.45	443.50	351.40	480.48
Temperature (K)	293(2)	293(2)	293(2)	293(2)	293(2)
Wavelength (Å)	1.54187	0.71073	0.71073	0.71073	0.71073
Crystal system, space group	Orthorhombic, $Pca2_1$	Monoclinic, $P2_1/c$	Monoclinic, $P2_1/c$	Orthorhombic, Pbca	Triclinic, P-1
Unit cell dimensions | (Å) | (°)	34.351(3) 11.9372(10) 9.5653(7) 90 90 90	26.6681(8) 9.3197(2) 18.2235(5) 90 104.917(3) 90	12.6311(2) 9.7581(2) 54.9229(7) 90 95.3721(14) 90	8.3532(10) 19.2461(14) 22.742(3) 90 90 90	9.6201(4) 11.1658(4) 11.4664(4) 95.279(3) 95.489(3) 106.999(4)
Volume ($Å^3$)	3922.4(5)	4376.6(2)	6739.79(2)	3656.1(6)	1163.11(8)
Z, Calculated density (Mg/m^3)	8, 1.299	8, 1.370	12, 1.311	8, 1.277	2, 1.372
Absorption coefficient (mm^{-1})	1.615	0.196	0.177	0.195	0.190
F(000)	1600	1856	2784	1472	496
Crystal size (mm)	0.28 x 0.05 x 0.02	0.35 x 0.19 x 0.12	0.22 x 0.16 x 0.05	0.26 x 0.05x 0.05	0.18 x 0.07 x 0.03
θ range for data collection (°)	2.573 to 45.538	2.313 to 26.0191	2.120 to 26.022	2.773 to 25.025	2.464 to 27.877
Limiting indices	$-30 \le h \le 31$, $-11 \le k \le 10$, $-8 \le l \le 8$	$-32 \le h \le 32$, $-9 \le k \le 11$, $-22 \le l \le 22$	$-15 \le h \le 15$, $-10 \le k \le 12$, $-67 \le l \le 67$	$-9 \le h \le 9$, $-22 \le k \le 22$, $-27 \le l \le 27$	$-12 \le h \le 12$, $-14 \le k \le 14$, $-15 \le l \le 15$
Reflections collected / unique [R(int)	17849 / 3232 0.055	55784 / 8627 0.0268	75512 / 13254 0.040	31779 / 3215 0.055	34665 / 5554 0.0302
Completeness to θ_{full} (%)	99.5	99.9	99.9	99.6	99.9
Absorption correction	Semi-empirical from equivalents	Gaussian & Semi-empirical from equivalents	Gaussian & Semi-empirical from equivalents	Gaussian & Semi-empirical from equivalents	Gaussian & Semi-empirical from equivalents
Max. and min. transmission	1.000 and 0.524	1.000 and 0.763	1.000 and 0.590	1.000 and 0.735	1.000 and 0.716
Refinement method	Full-matrix least-squares on F^2	Full-matrix least-squares on F^2	Full-matrix least-squares on F^2	Full-matrix least-squares on F^2	Full-matrix least-squares on F^2
Data / restraints / parameters	3221 / 1189 / 616	8624 / 327 / 649	13247 / 15 / 895	3208 / 398 / 280	5554 / 105 / 336
Goodness-of-fit on F^2	1.099	1.029	1.025	1.006	1.044
Final R indices [$I>2\sigma(I)$] R1, wR2	0.0964 0.2528	0.0455, 0.1216	0.0433, 0.1080	0.0450, 0.1133	0.0388, 0.1006
R indices (all data) R1, wR2	0.1090 0.2675	0.0527, 0.1265	0.0548, 0.1133	0.0755 0.1349	0.0478, 0.1059
Largest Δ peak and hole ($e.Å^{-3}$)	0.725 and -0.191	0.300 and -0.363	0.194 and -0.209	0.123 and -0.165	0.181 and -0.280
CCDC deposit number	2166476	2163448	2165840	2165911	2163449

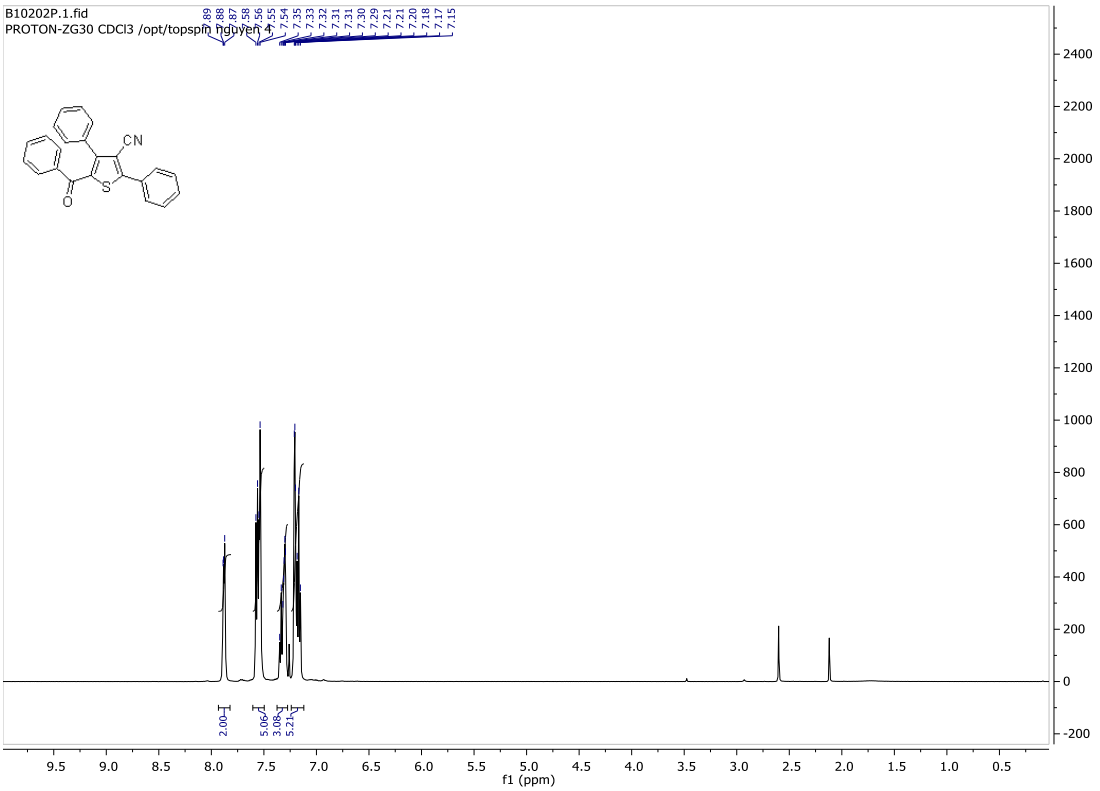
Copies of ^{1}H and ^{13}C spectra of all new compounds

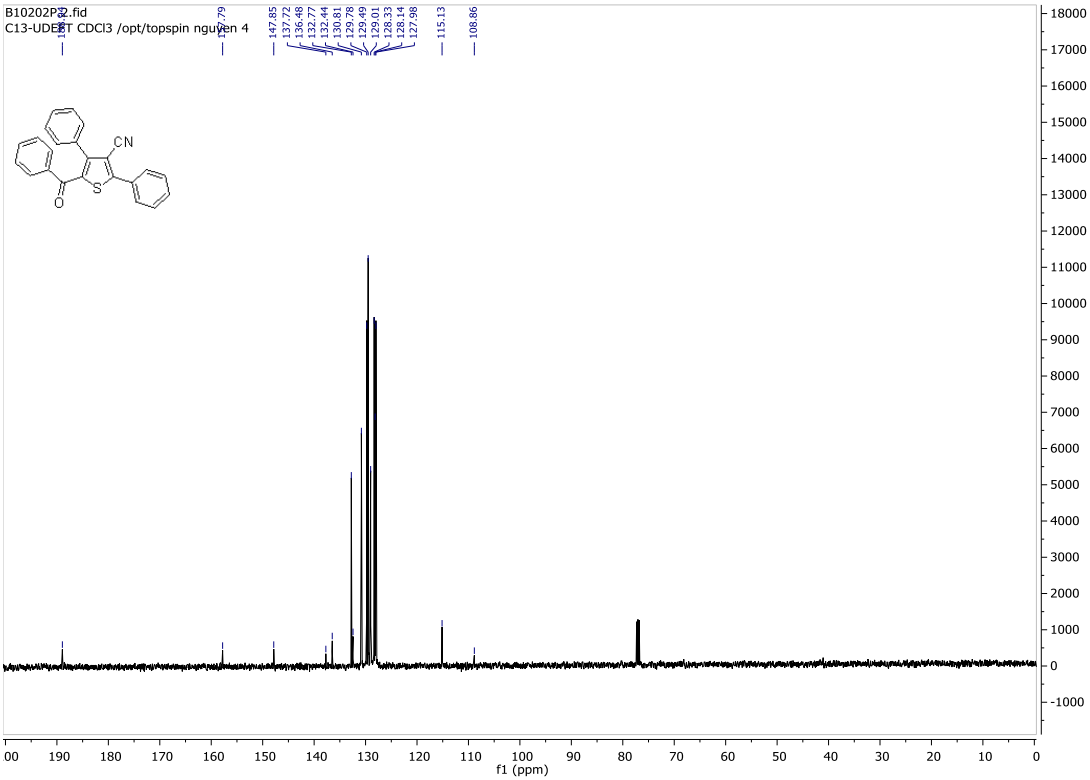
(5-Amino-3-phenylthiophene-2,4-diyl)bis(phenylmethanone) (3a)



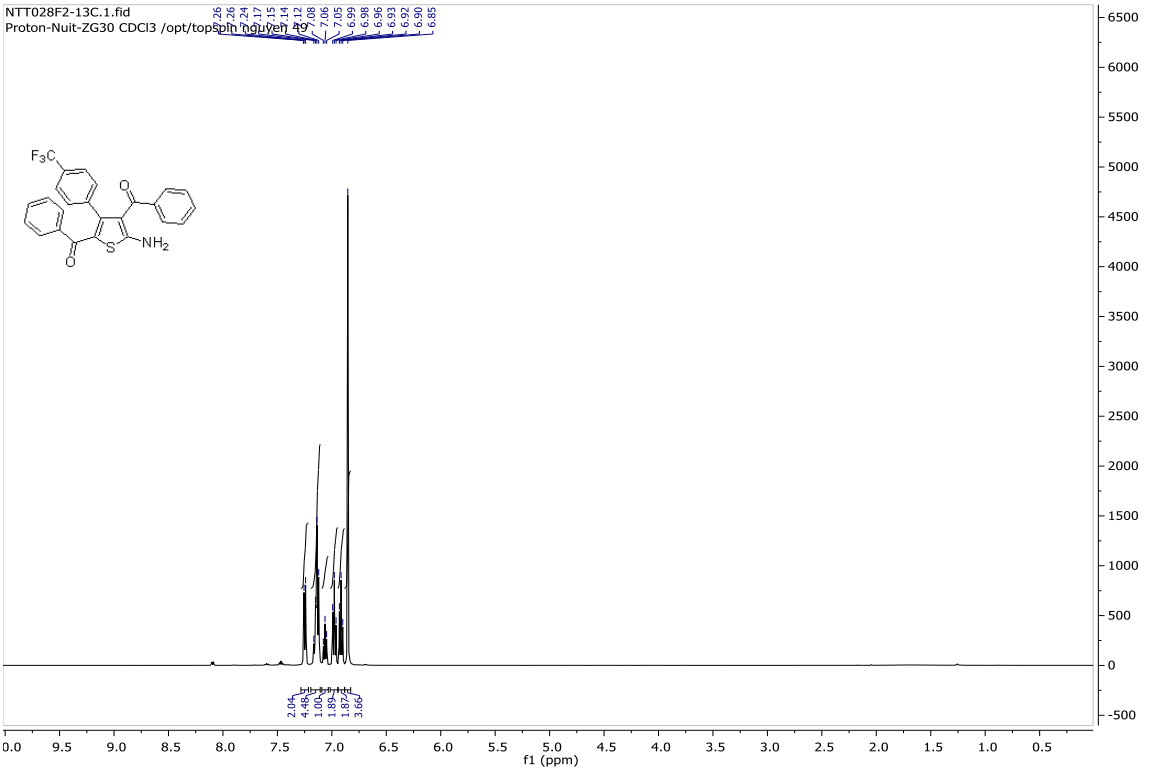


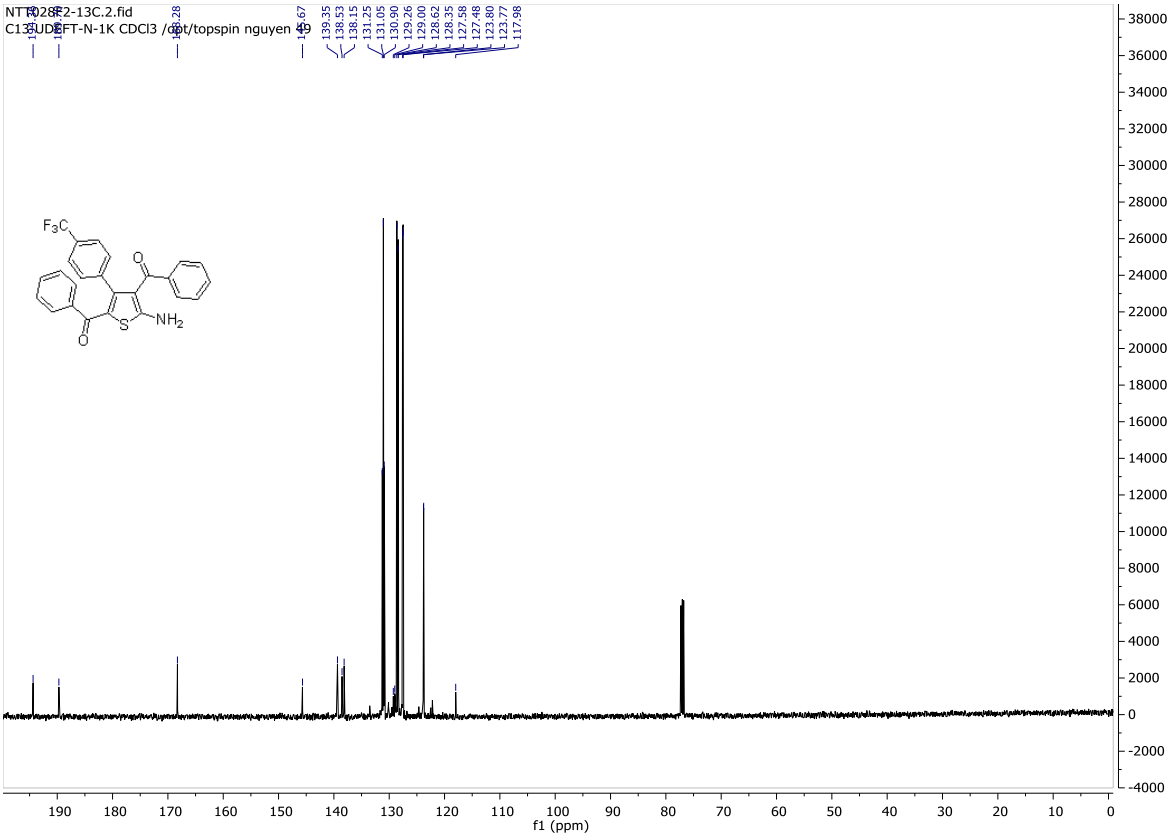
5-Benzoyl-2,4-diphenylthiophene-3-carbonitrile (4a)



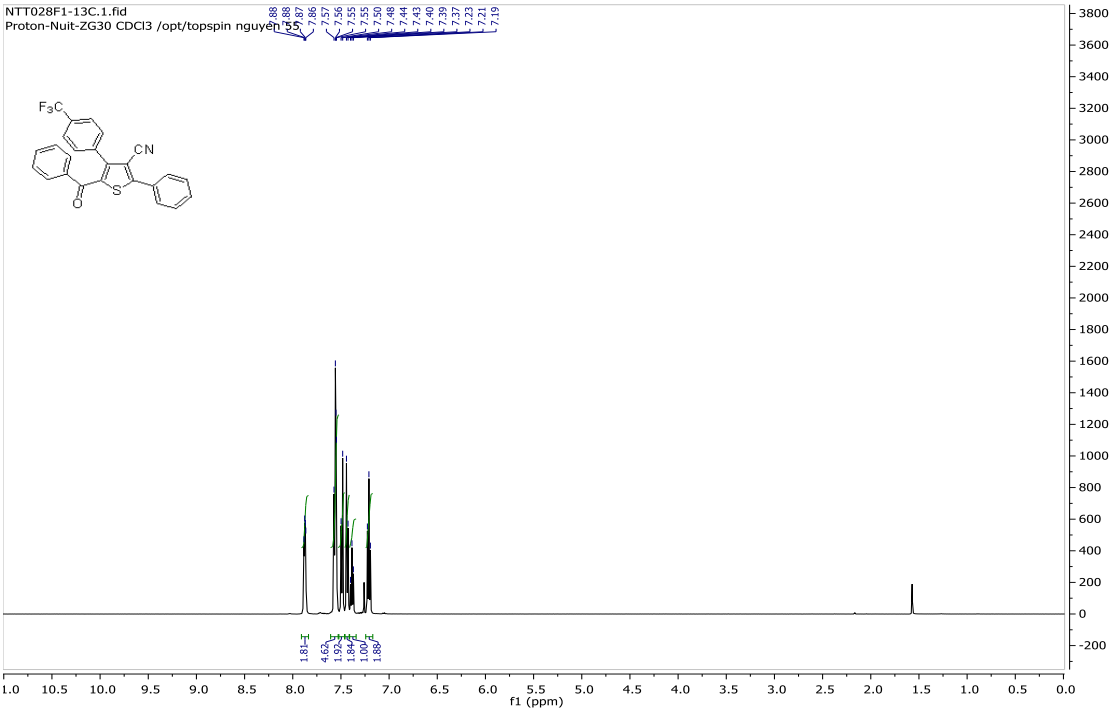


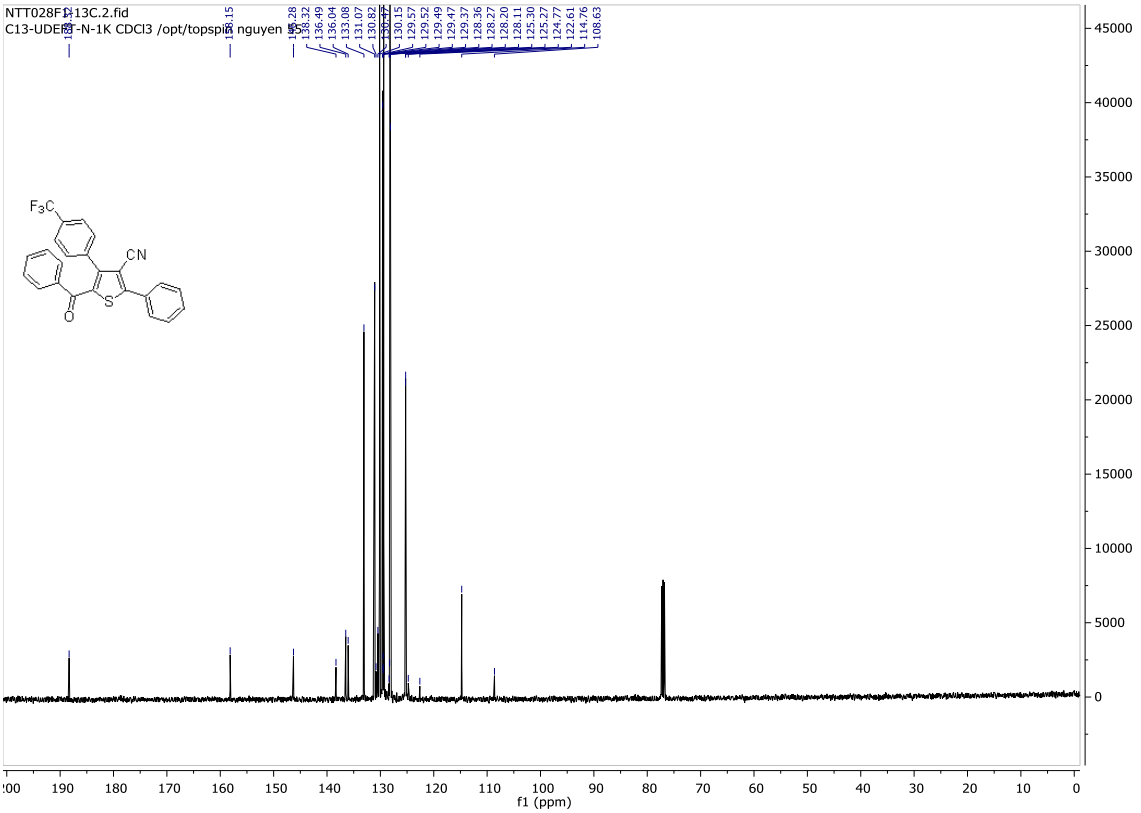
(5-Amino-3-(4-(trifluoromethyl)phenyl)thiophene-2,4-diyl)bis(phenylmethanone) (3b)



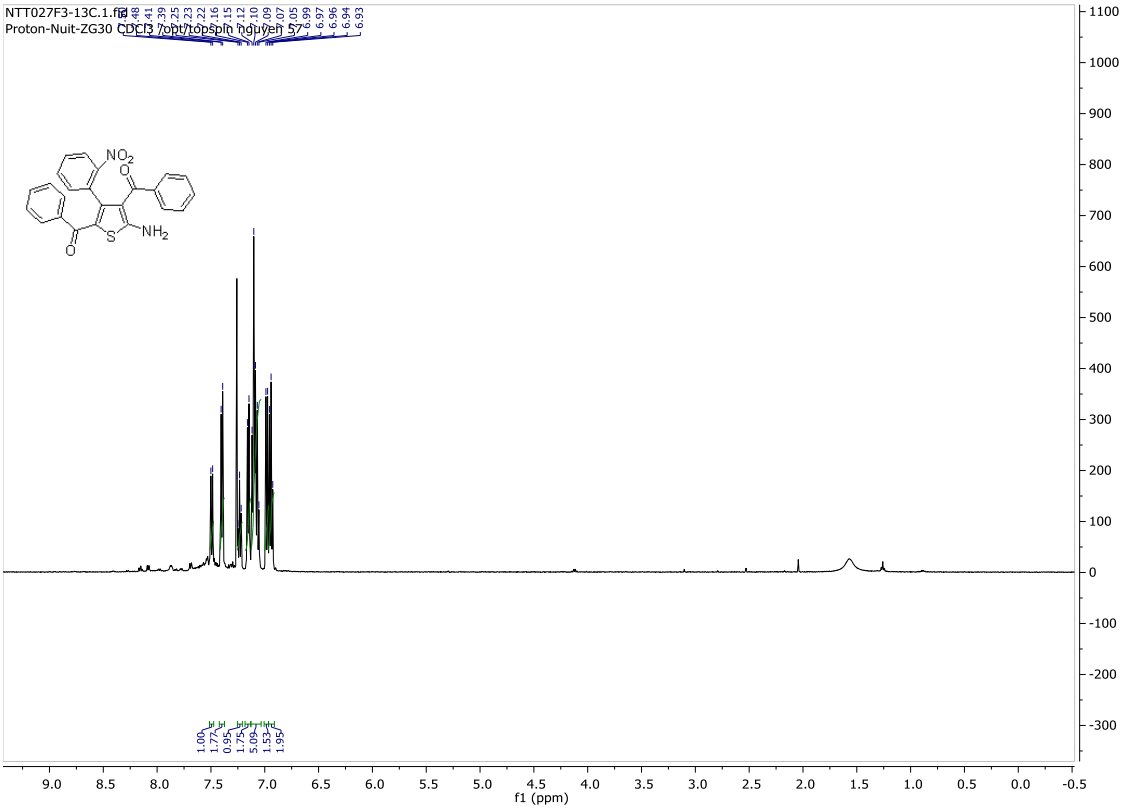


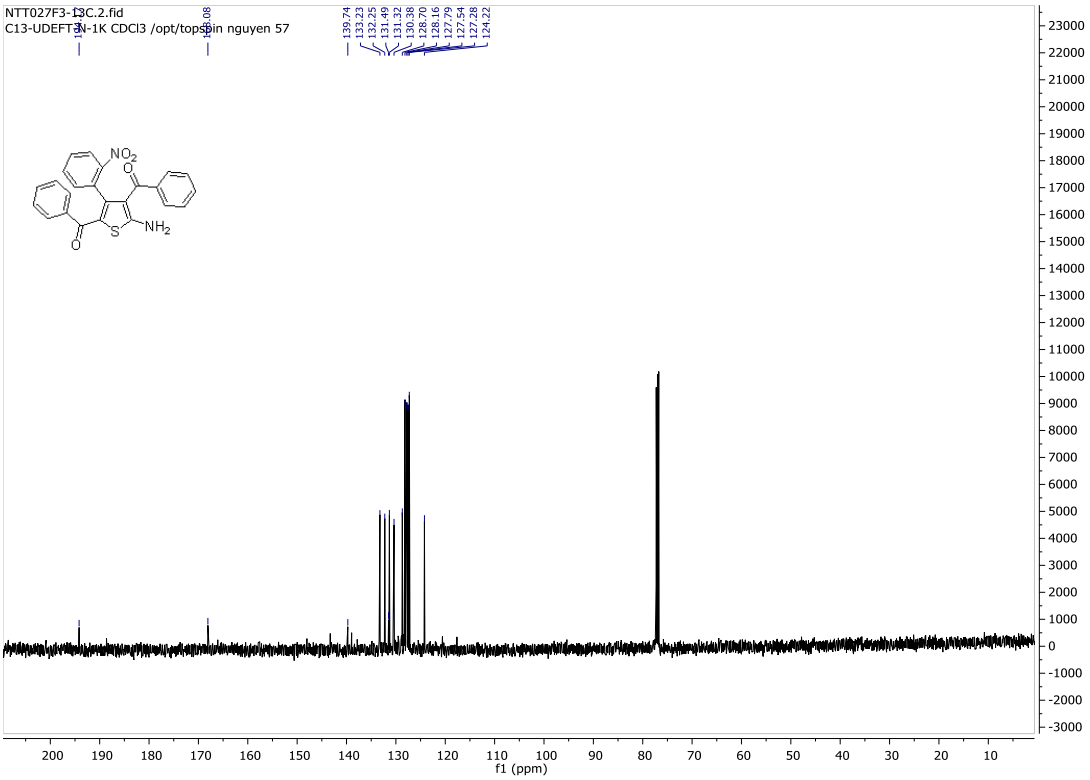
5-Benzoyl-2-phenyl-4-(4-(trifluoromethyl)phenyl)thiophene-3-carbonitrile (4b)



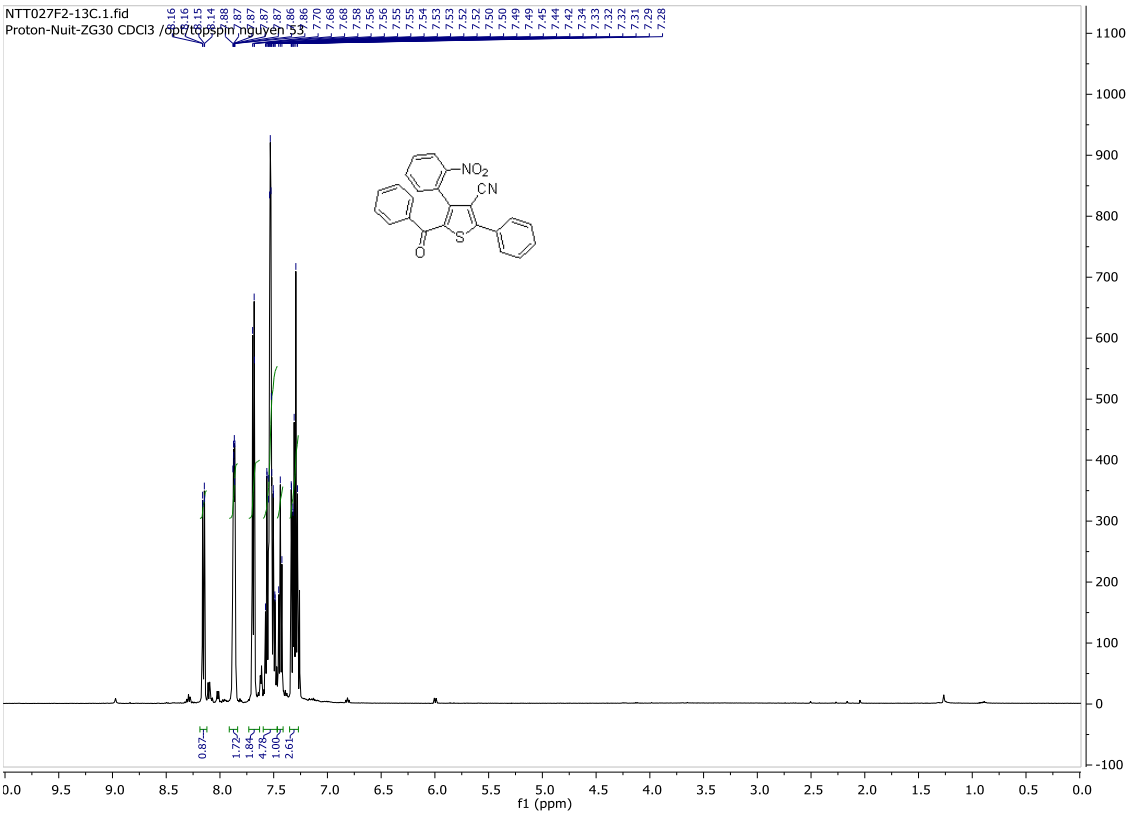


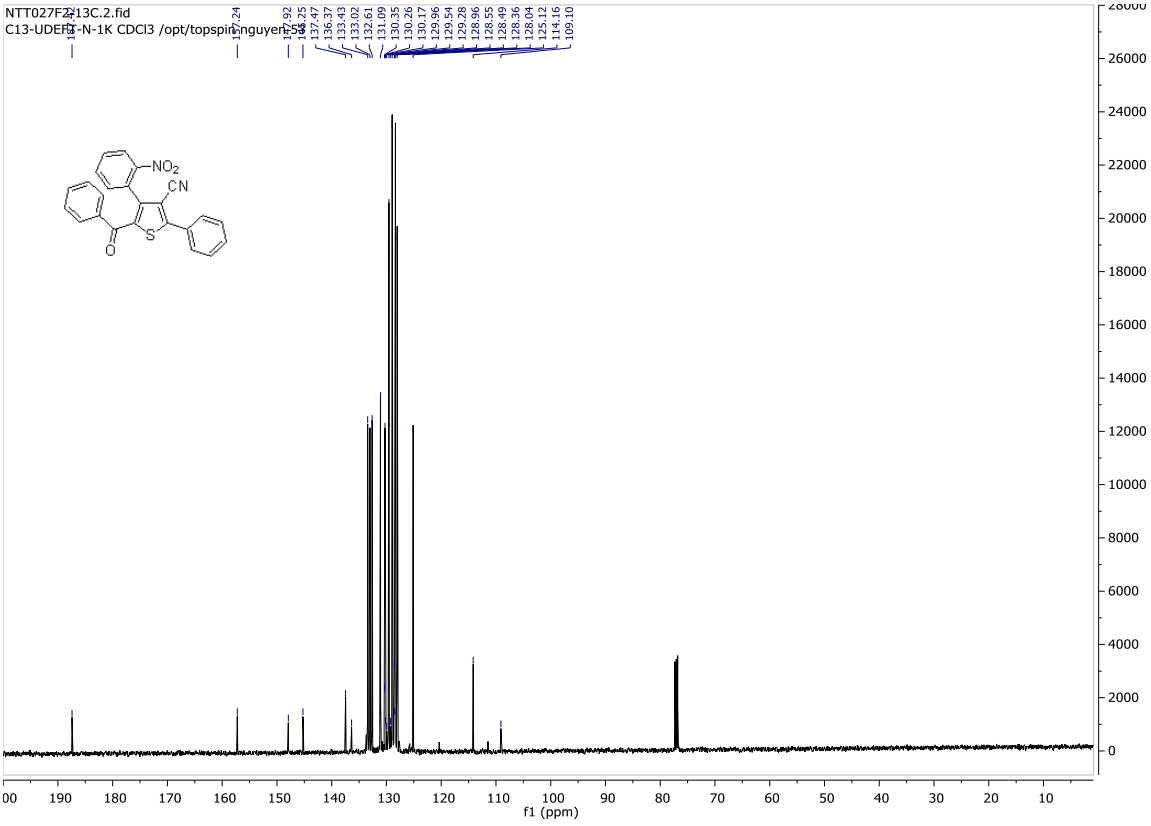
(5-Amino-3-(2-nitrophenyl)thiophene-2,4-diyl)bis(phenylmethanone) (3c)



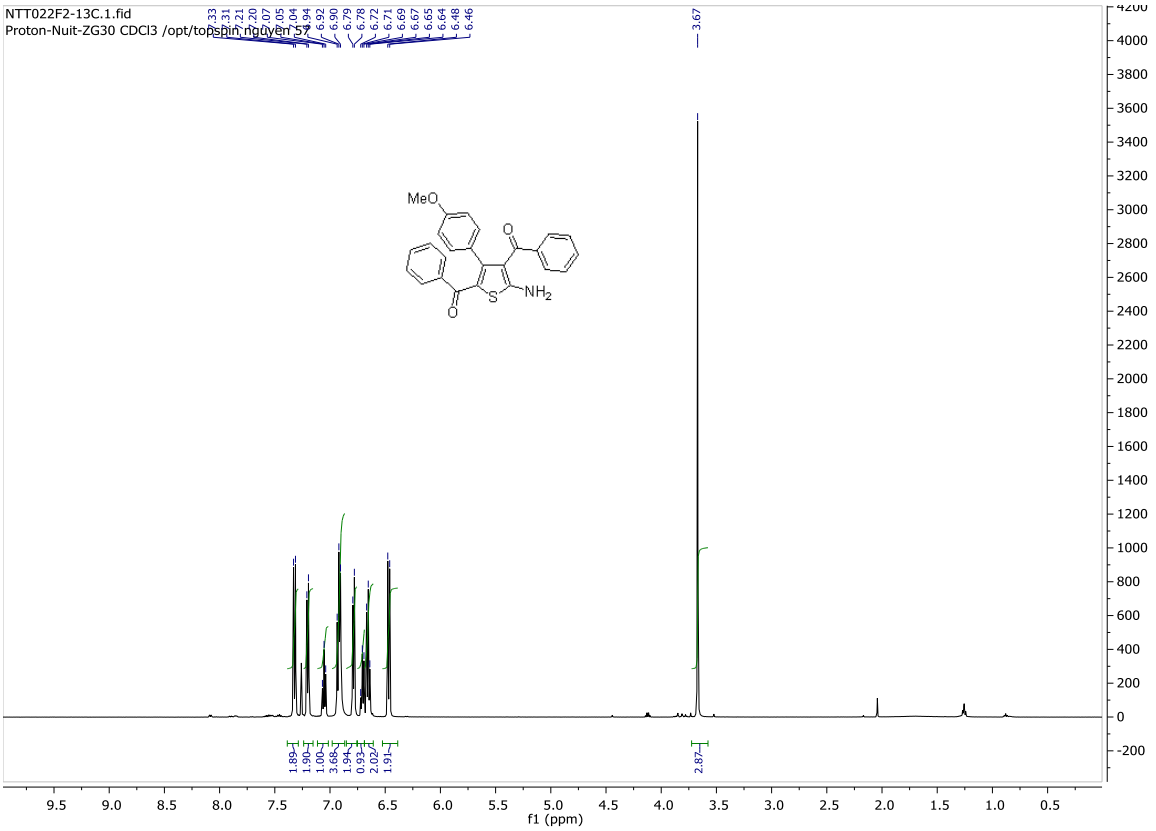


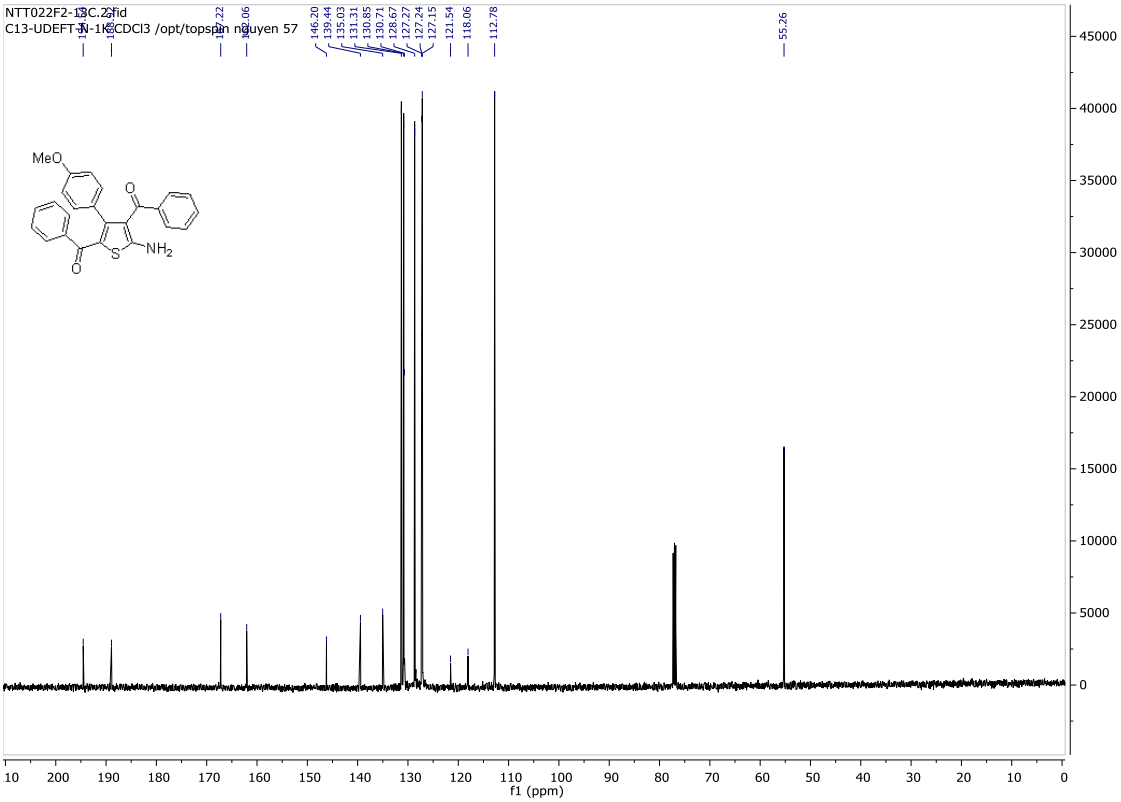
5-Benzoyl-4-(2-nitrophenyl)-2-phenylthiophene-3-carbonitrile (4c)



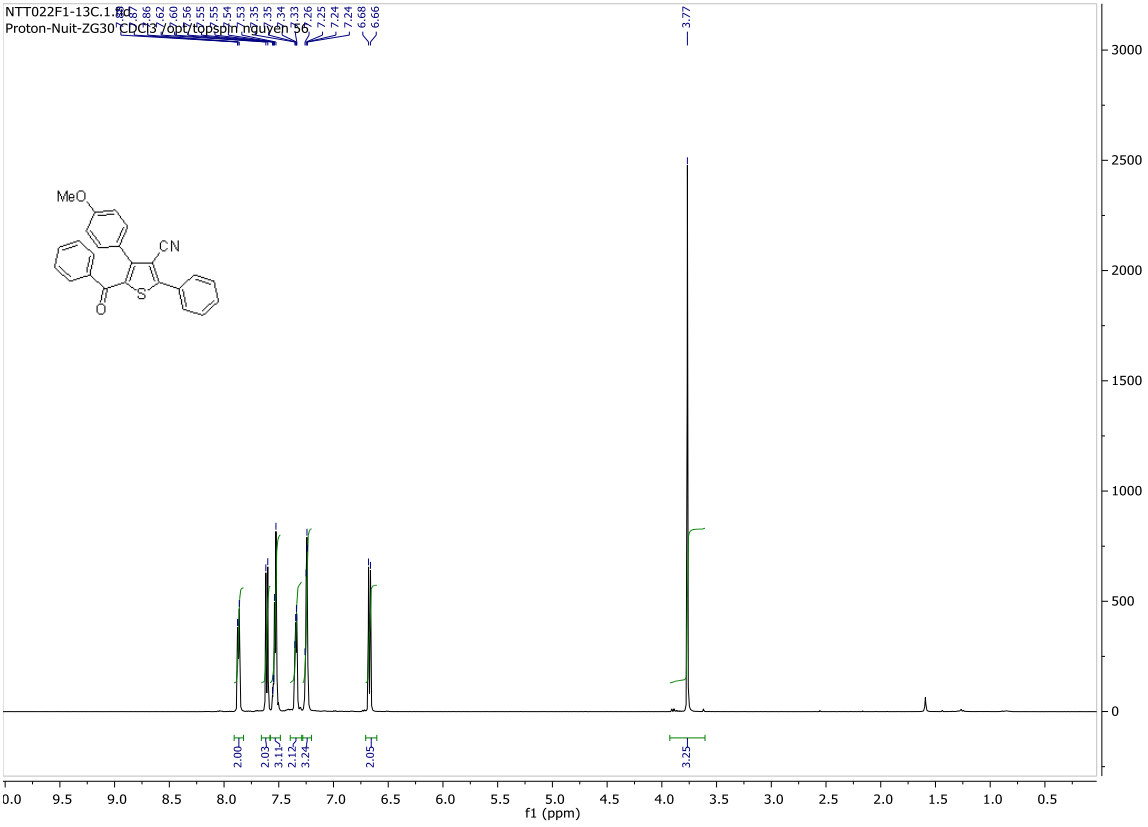


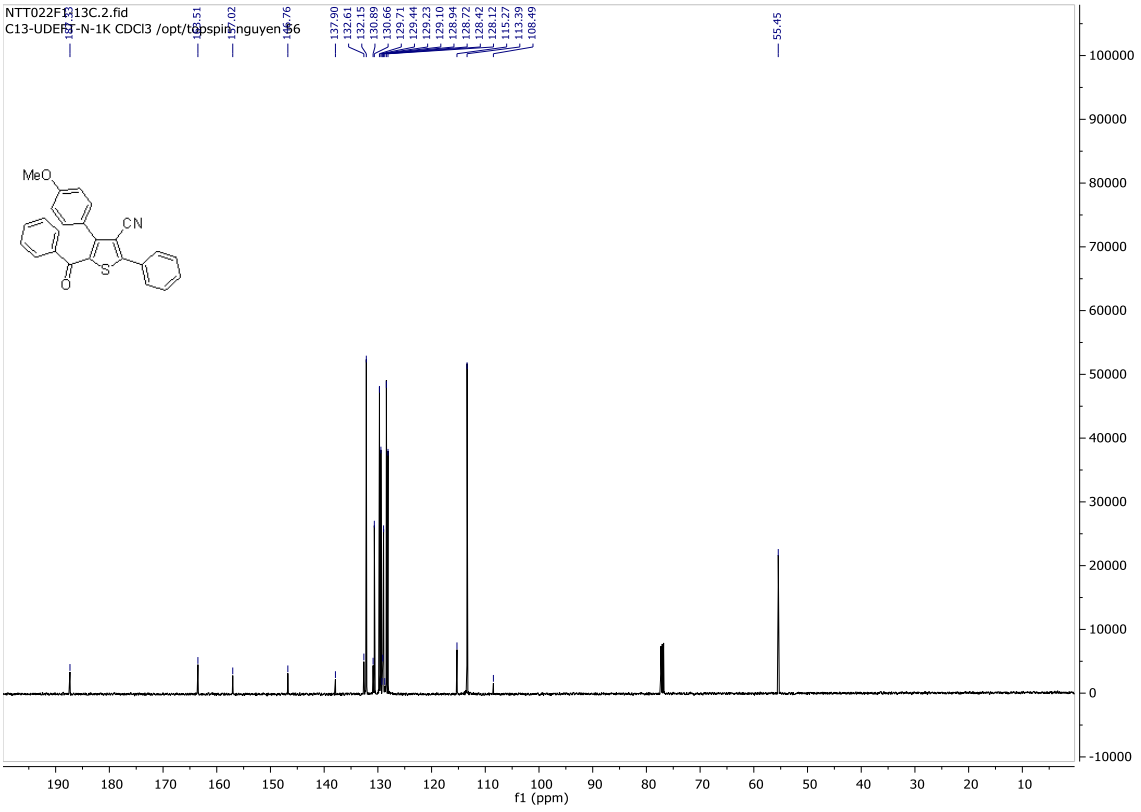
(5-Amino-3-(4-methoxyphenyl)thiophene-2,4-diyl)bis(phenylmethanone) (3d)



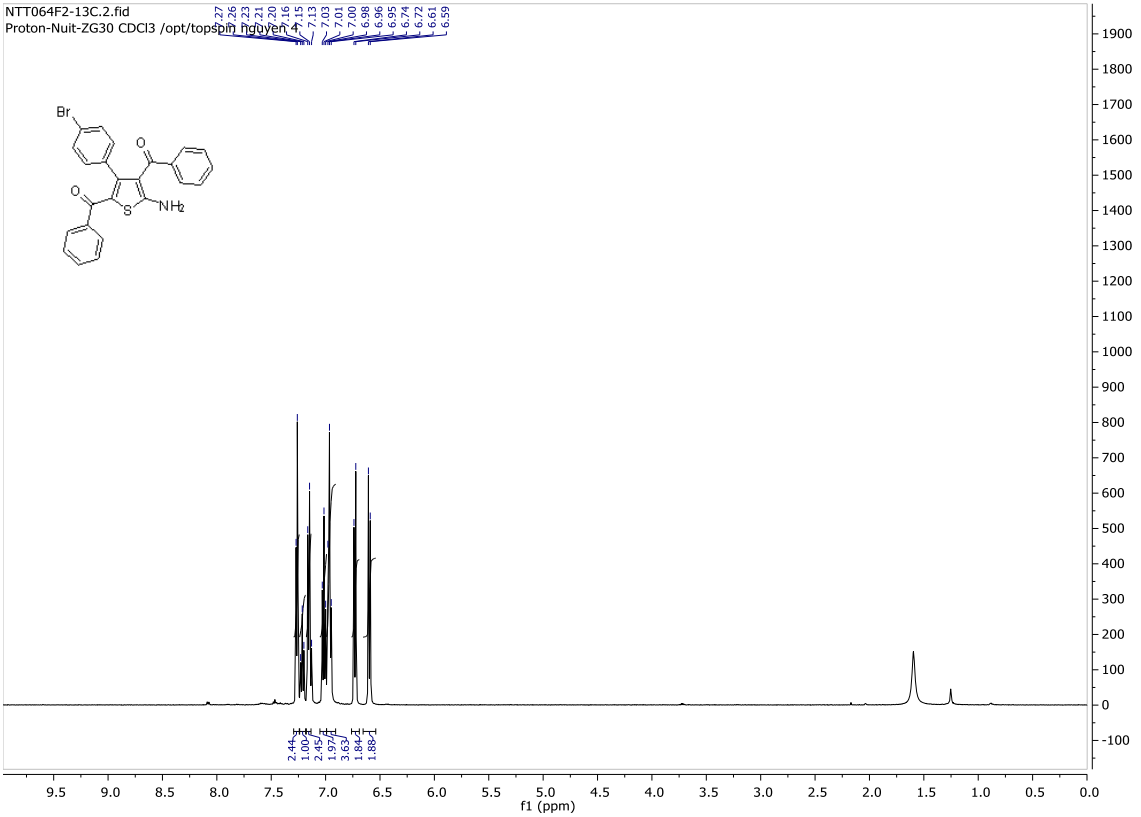


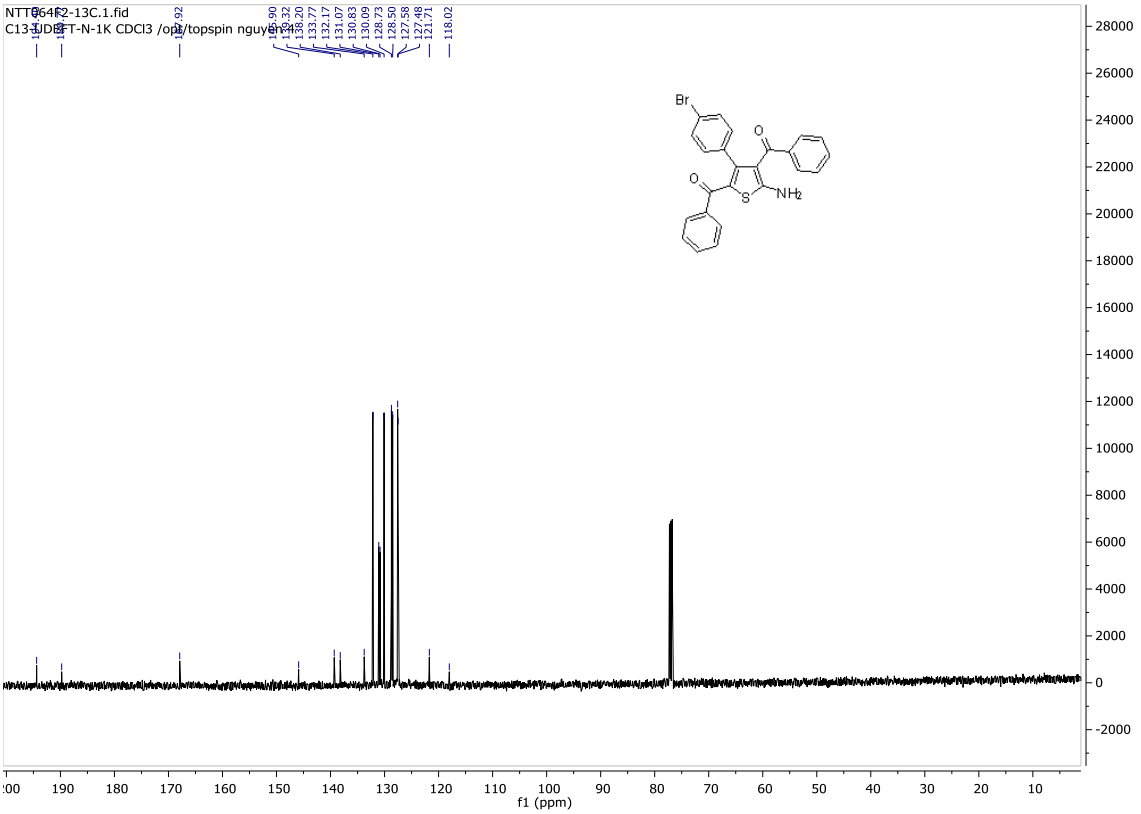
5-Benzoyl-4-(4-methoxyphenyl)-2-phenylthiophene-3-carbonitrile (4d)



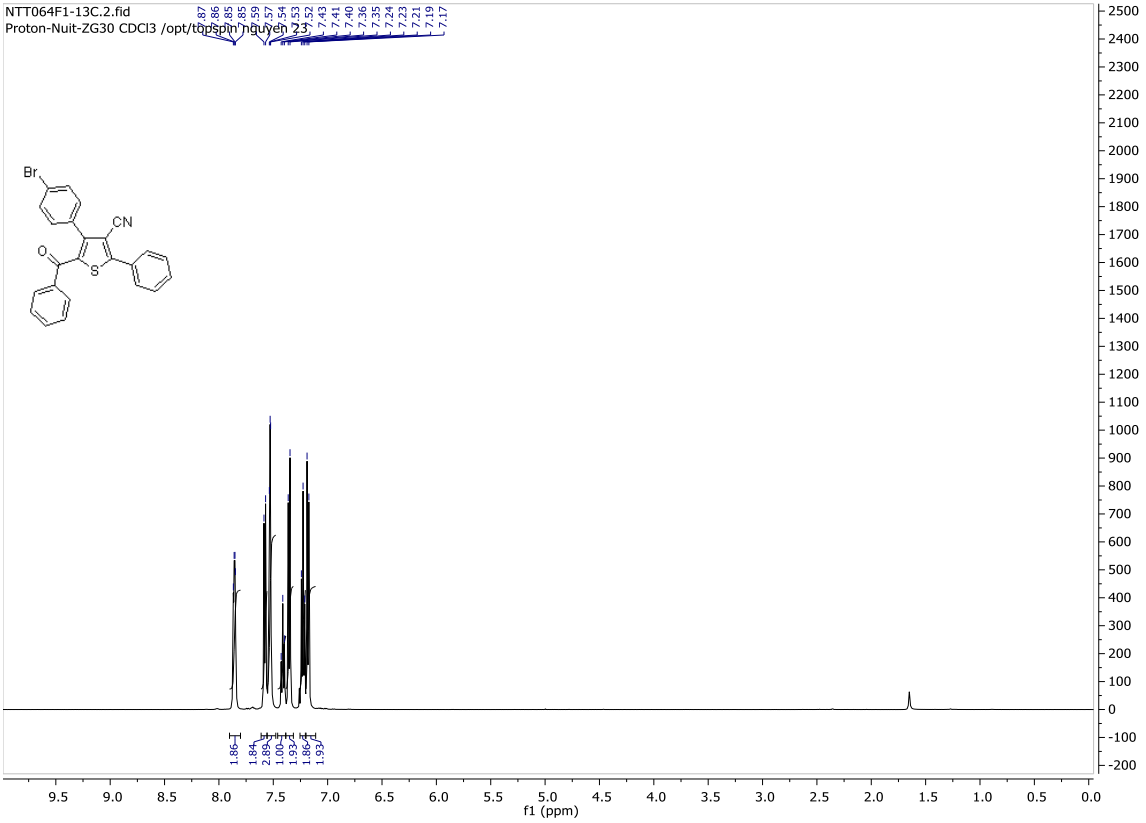


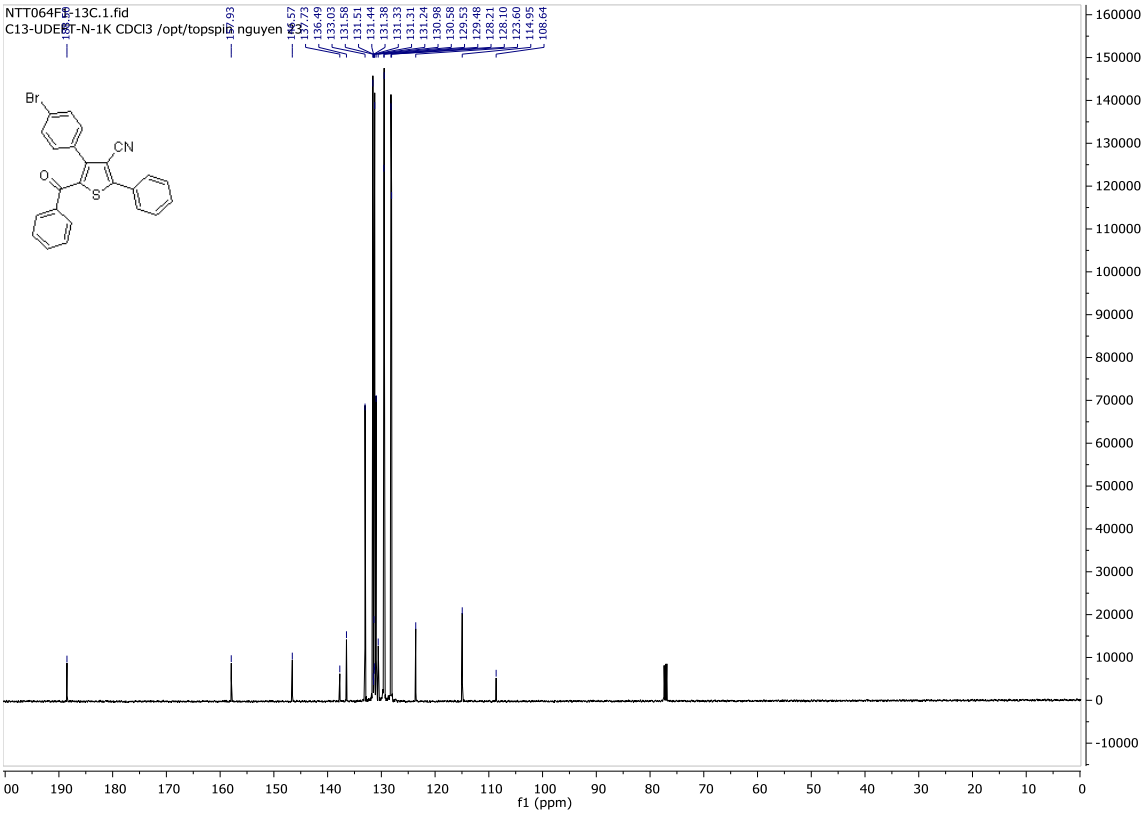
(5-Amino-3-(4-bromophenyl)thiophene-2,4-diyl)bis(phenylmethanone) (3e)



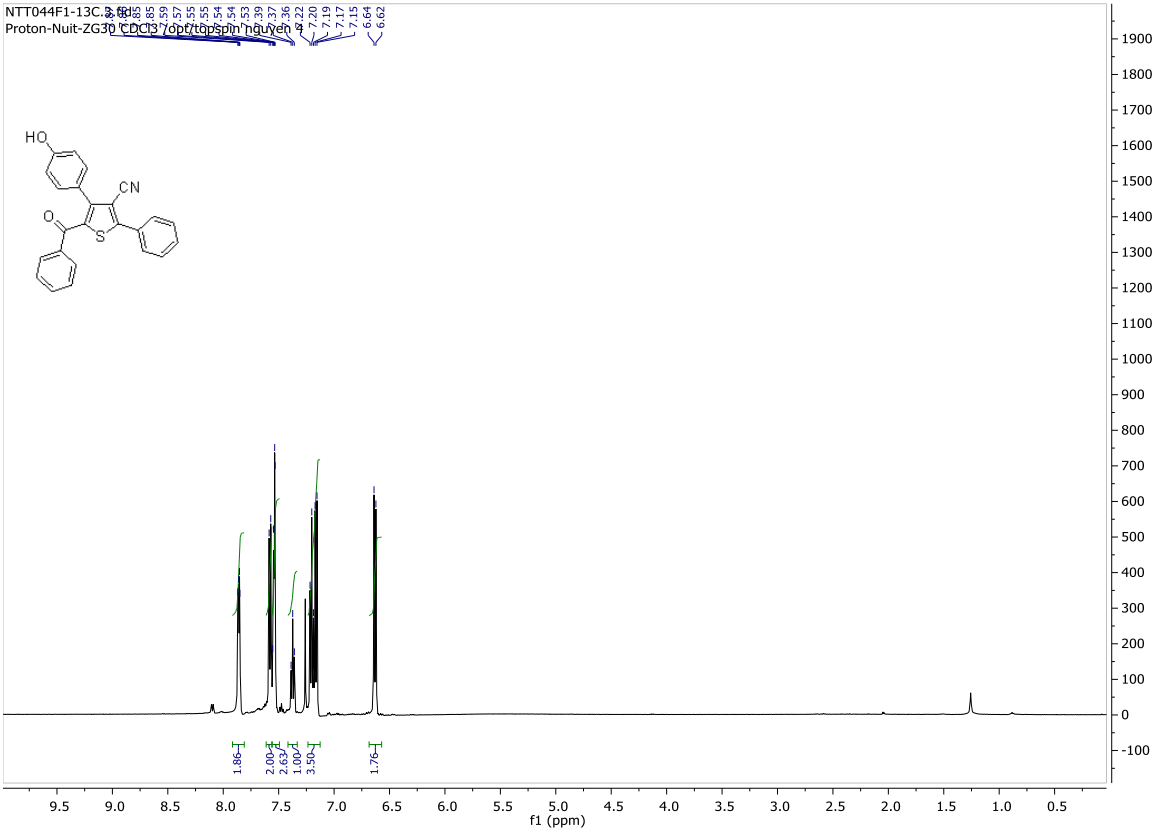


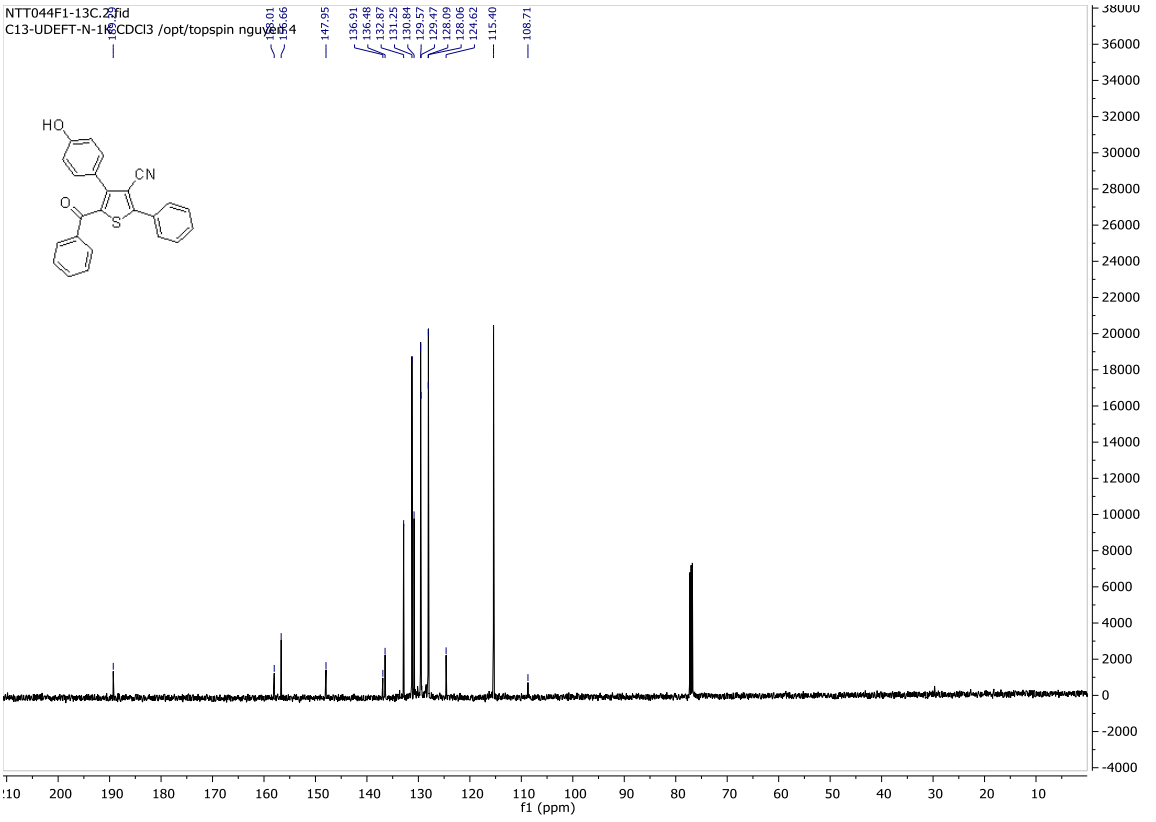
5-Benzoyl-4-(4-bromophenyl)-2-phenylthiophene-3-carbonitrile (4e)



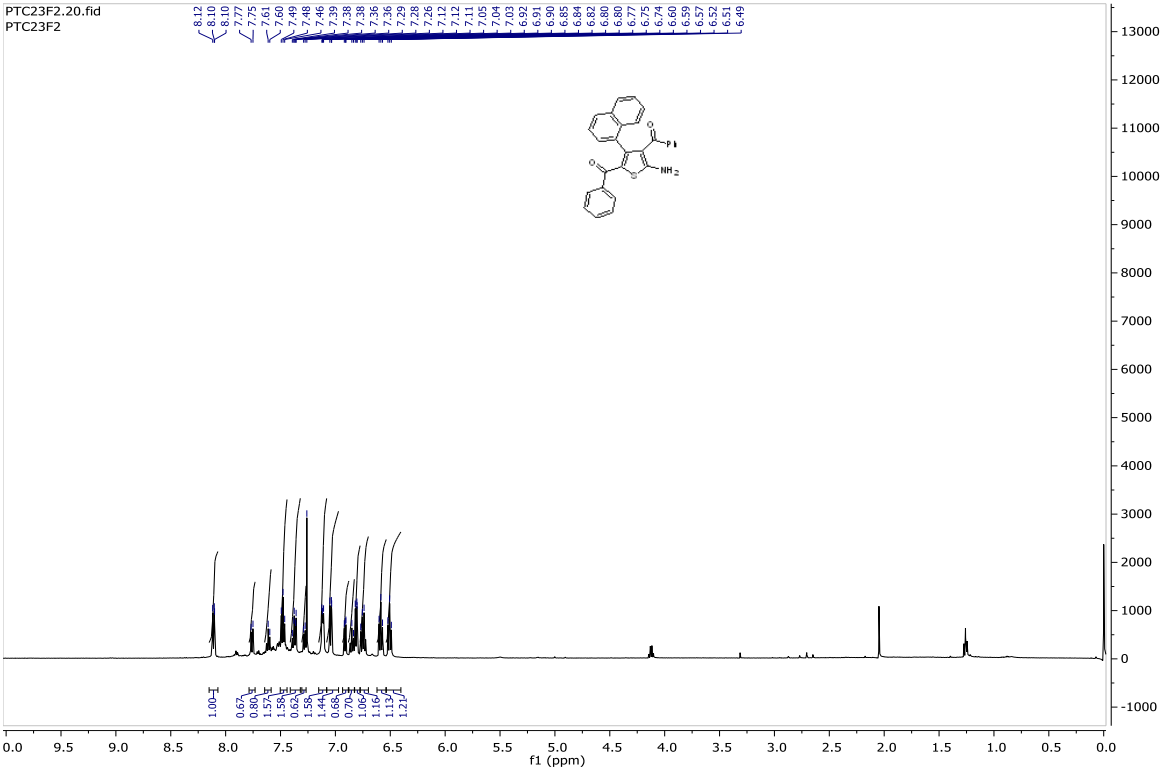


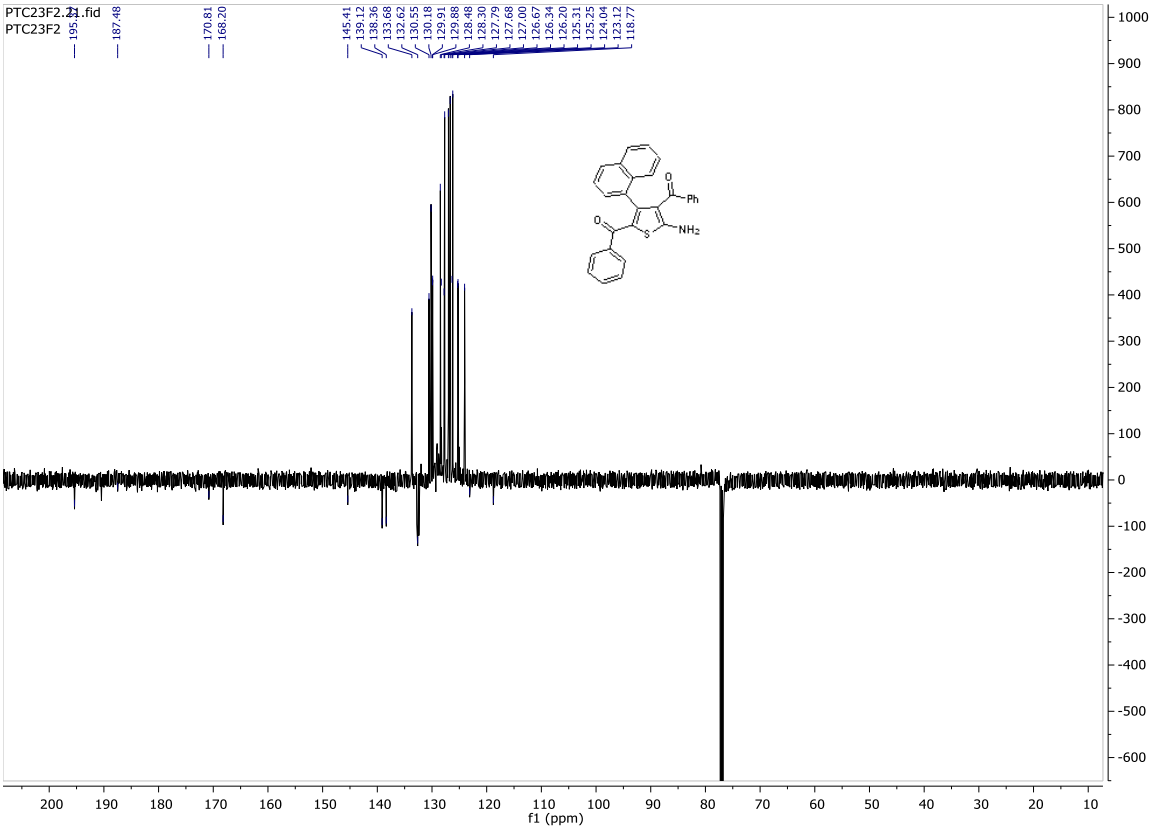
5-Benzoyl-4-(4-hydroxyphenyl)-2-phenylthiophene-3-carbonitrile (4f)



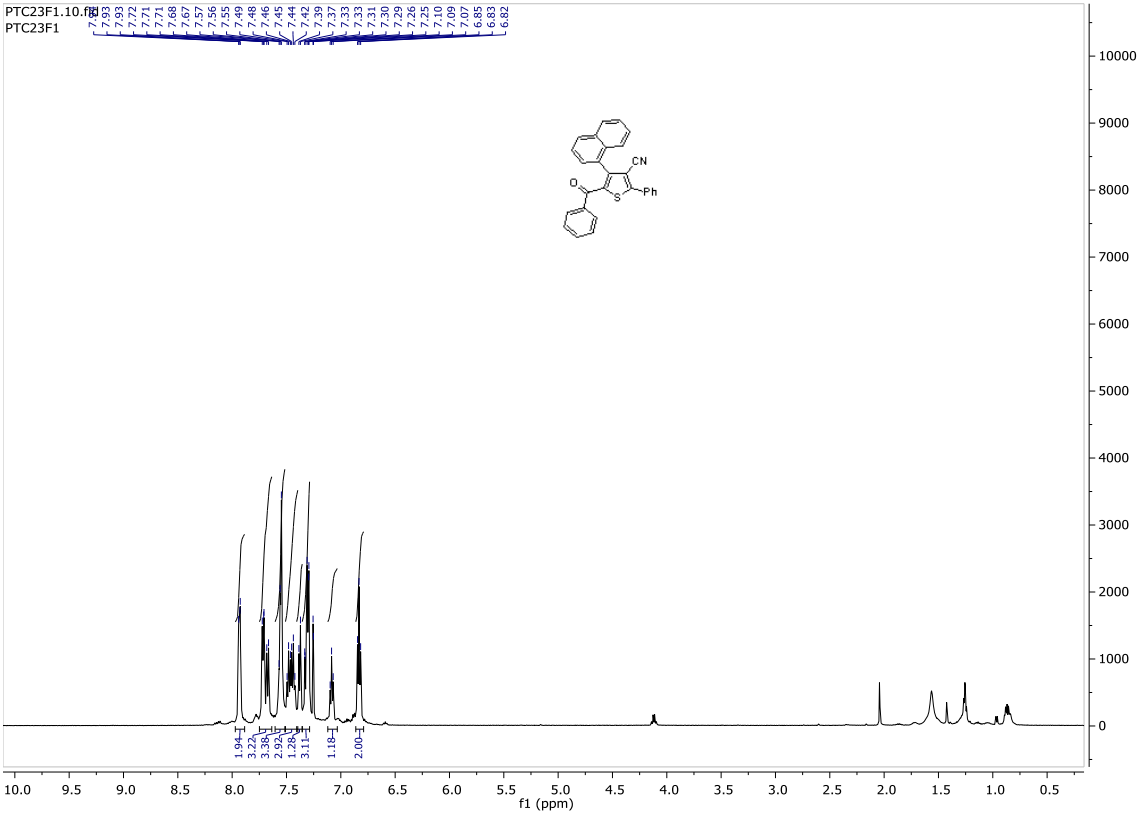


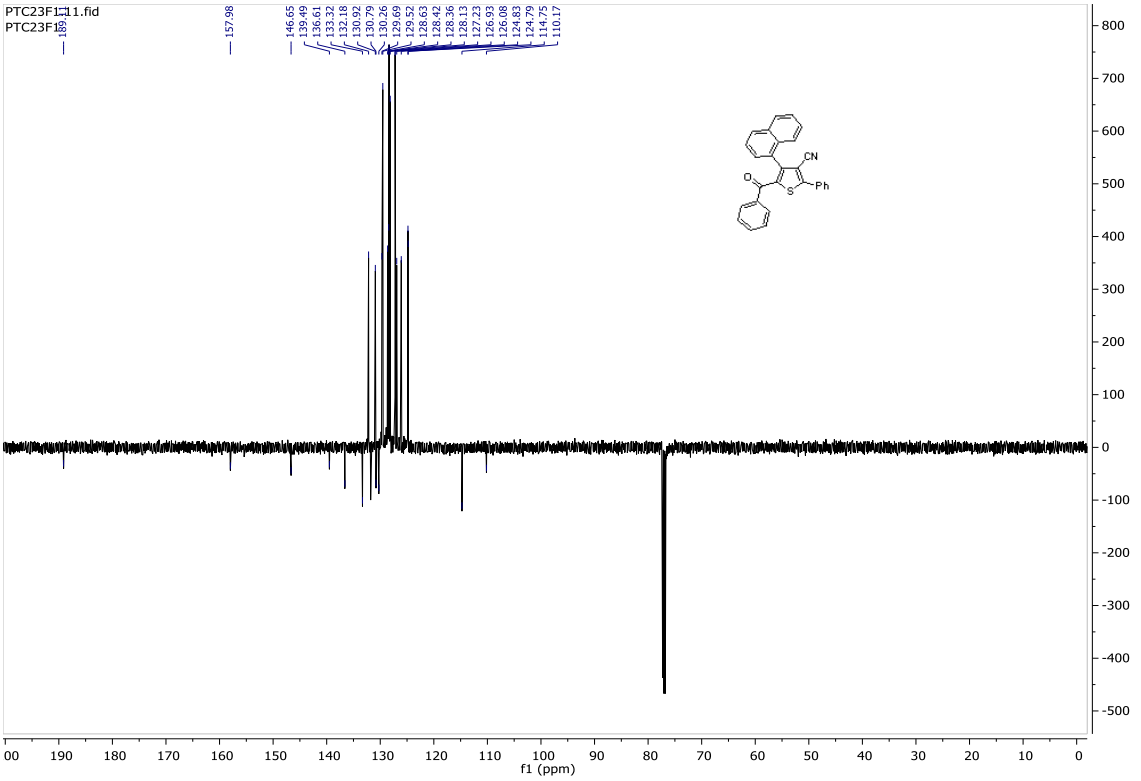
(5-Amino-3-(naphthalen-1-yl)thiophene-2,4-diyl)bis(phenylmethanone) (3g)



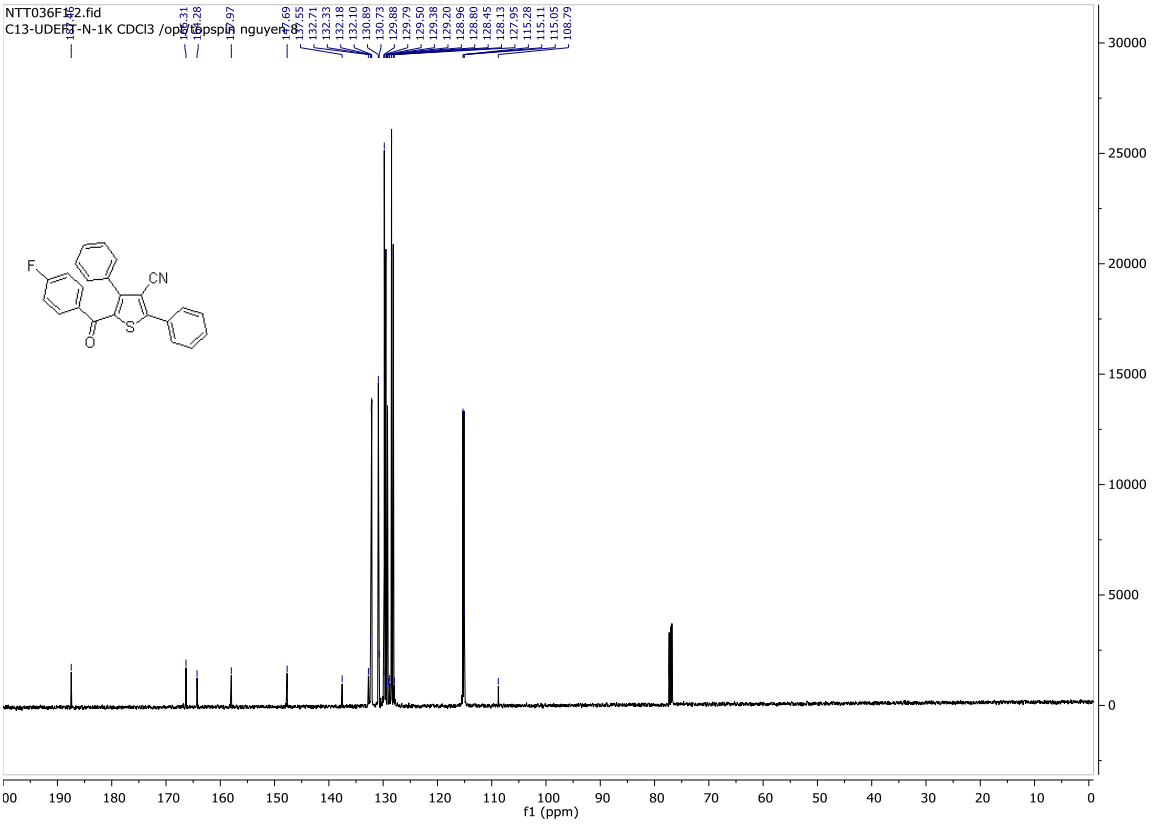


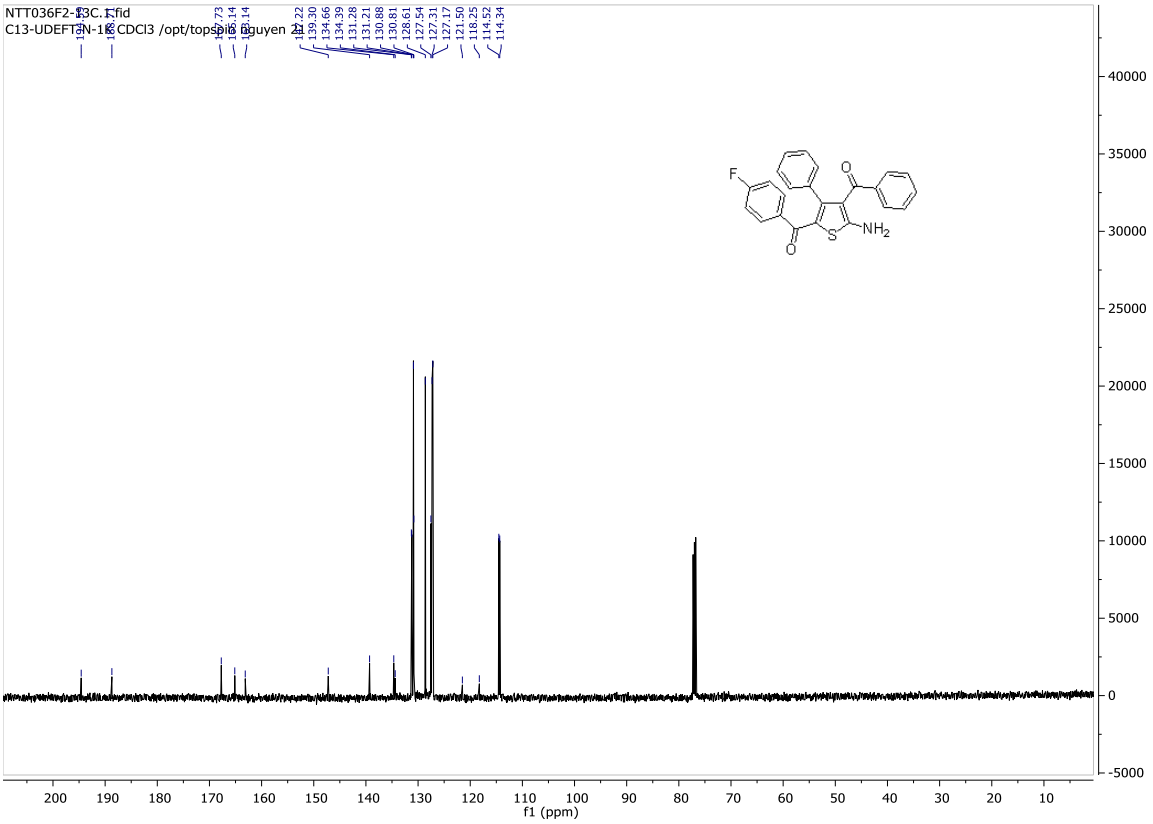
5-Benzoyl-4-(naphthalen-1-yl)-2-phenylthiophene-3-carbonitrile (4g)



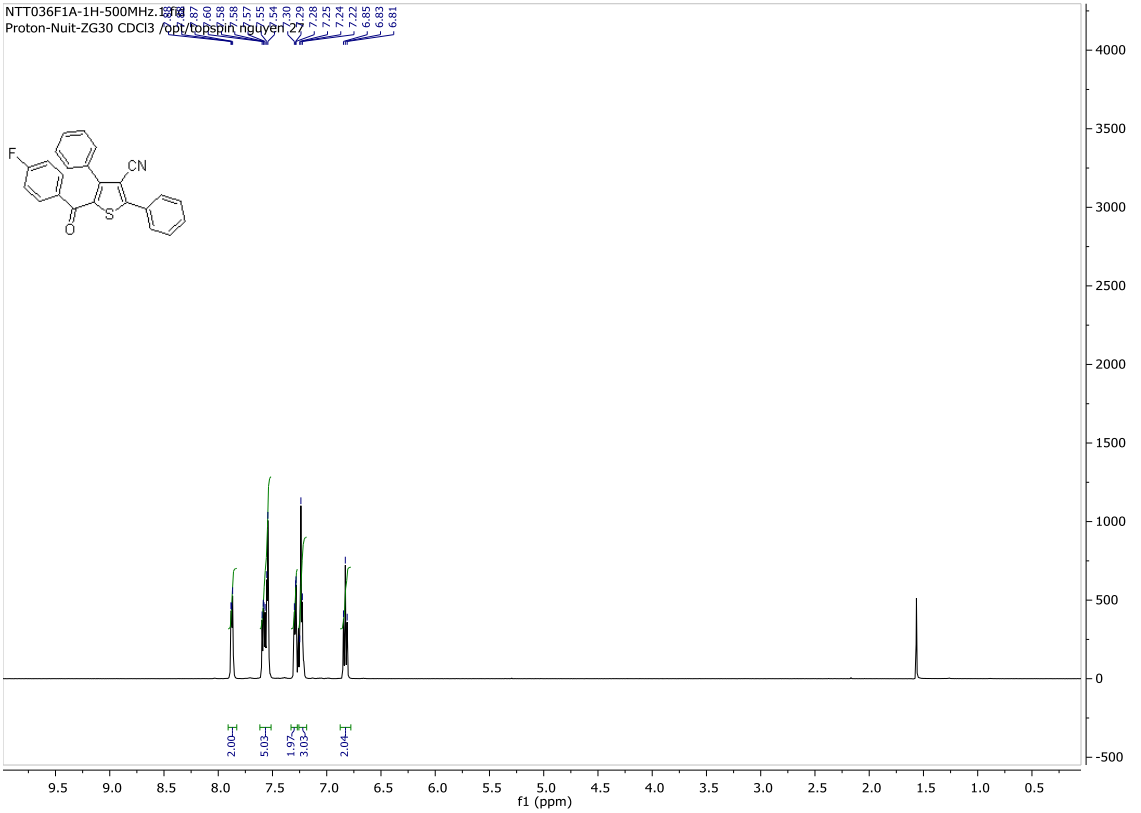


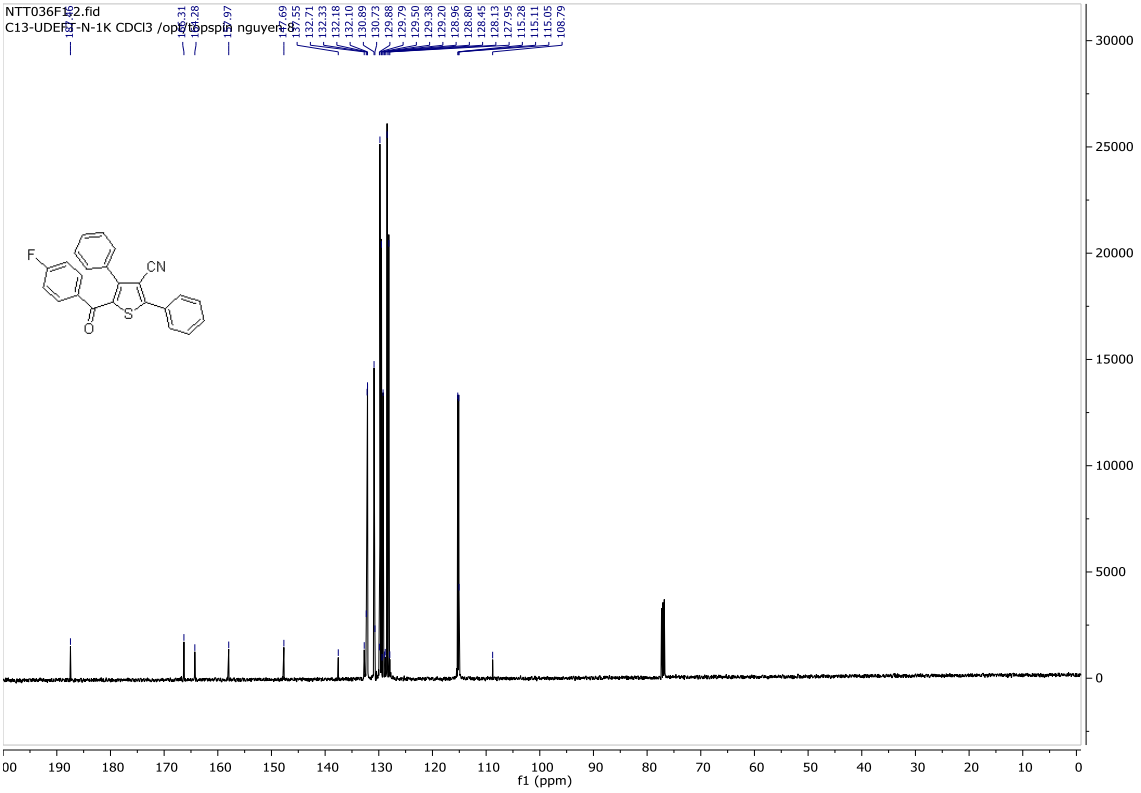
(5-Amino-4-benzoyl-3-phenylthiophen-2-yl)(4-fluorophenyl)methanone (3h)



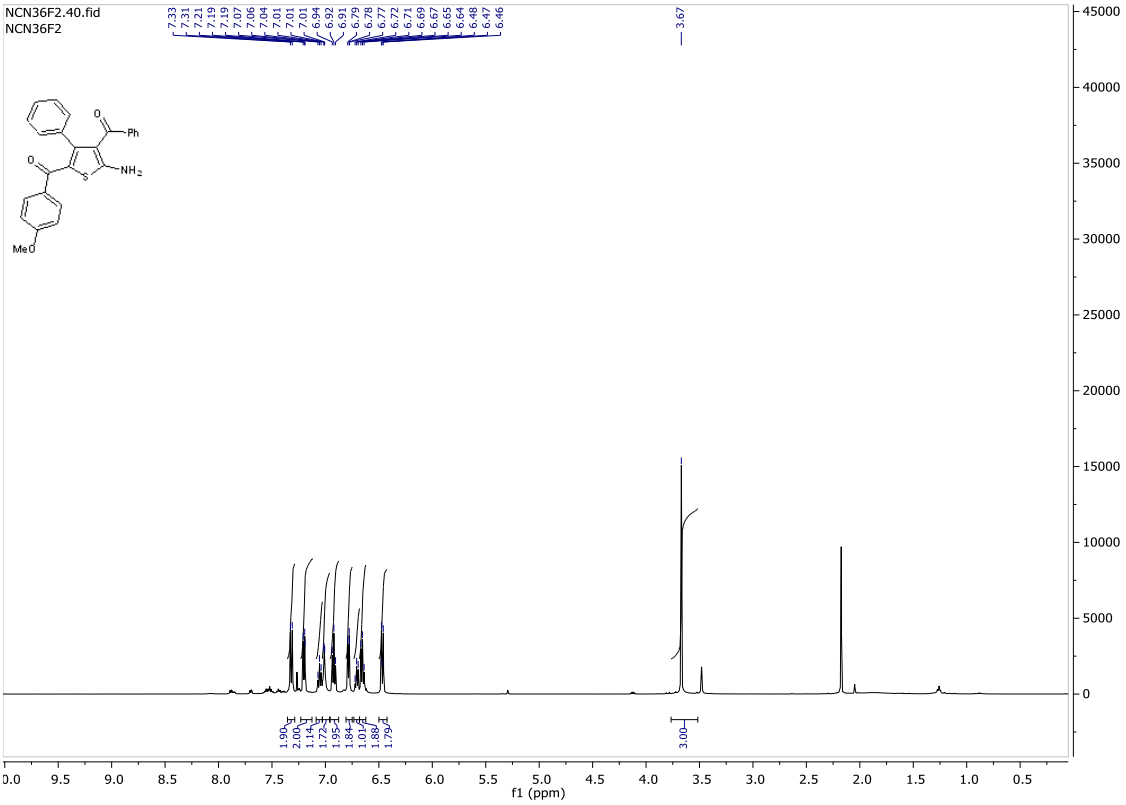


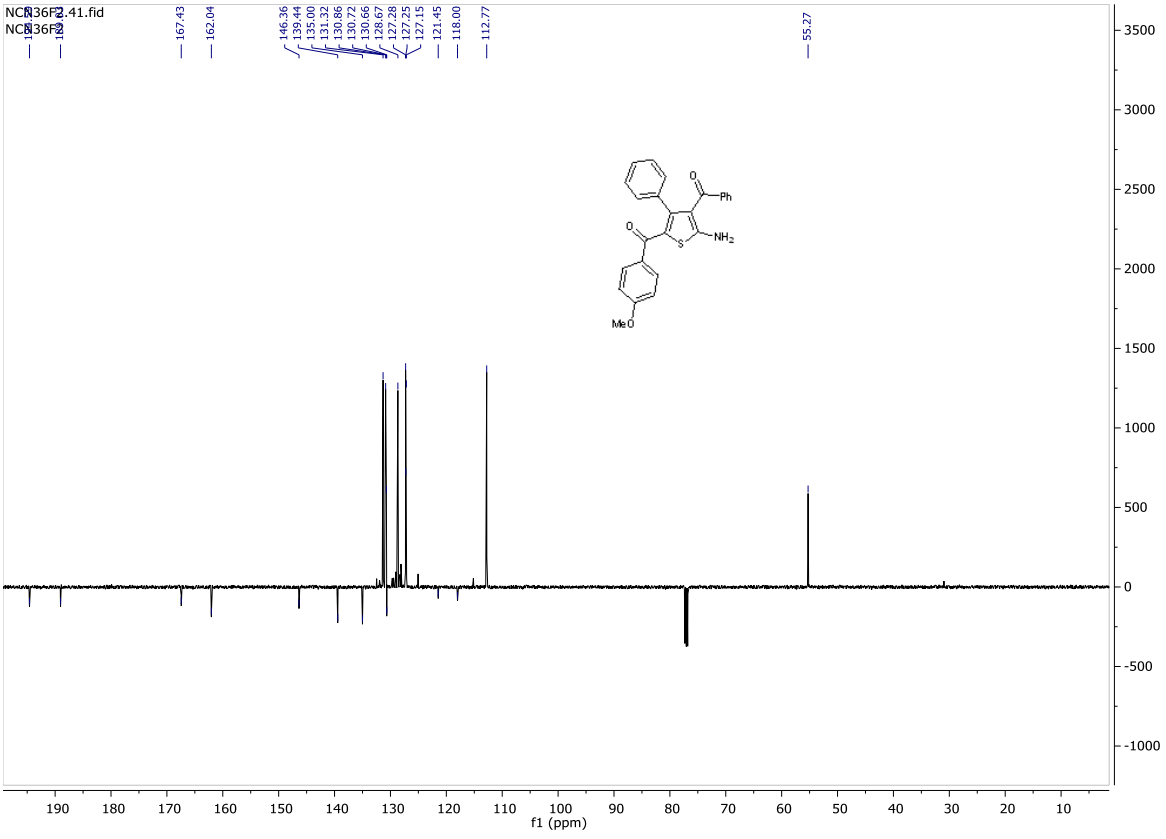
5-(4-Fluorobenzoyl)-2,4-diphenylthiophene-3-carbonitrile (4h)



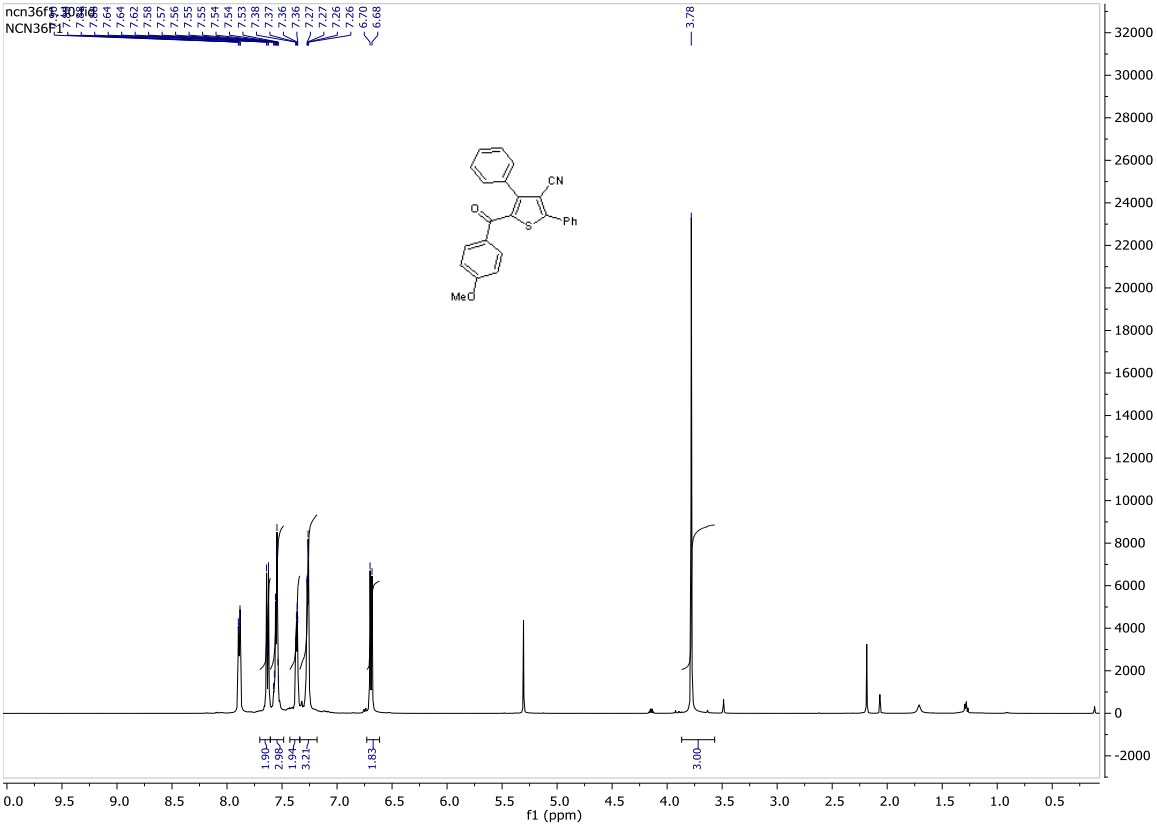


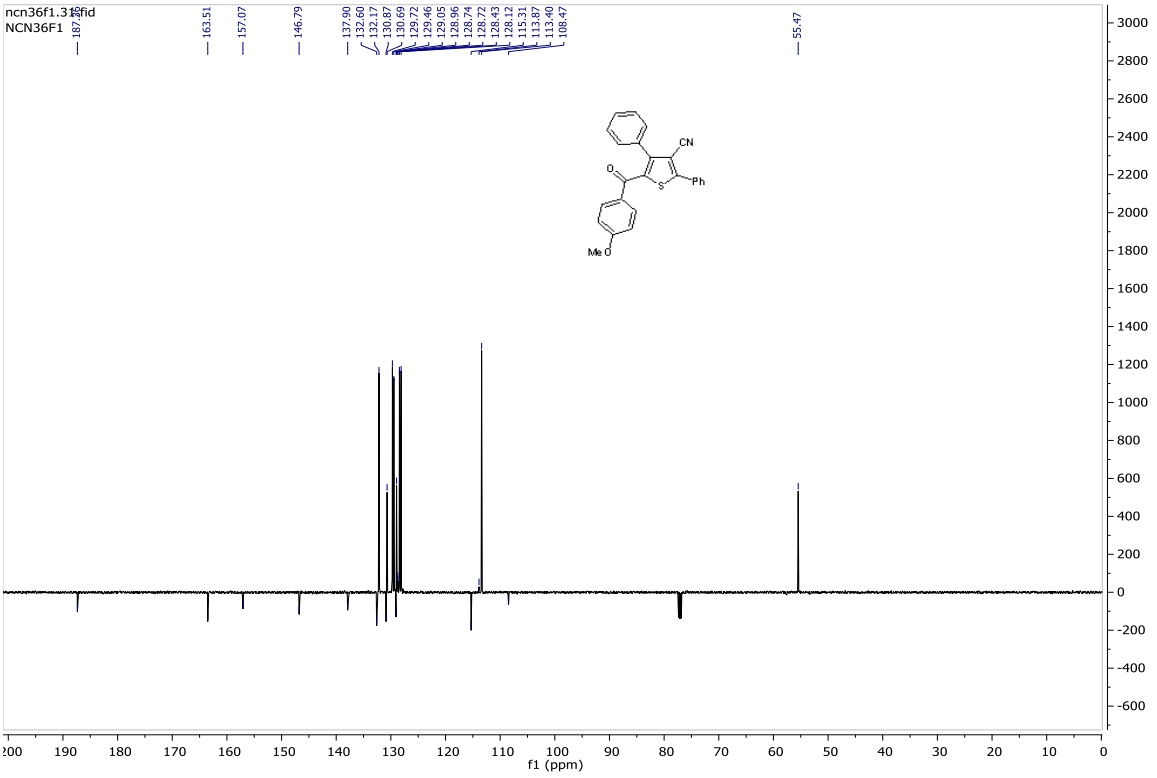
(5-Amino-4-benzoyl-3-phenylthiophen-2-yl)(4-methoxyphenyl)methanone (3i)



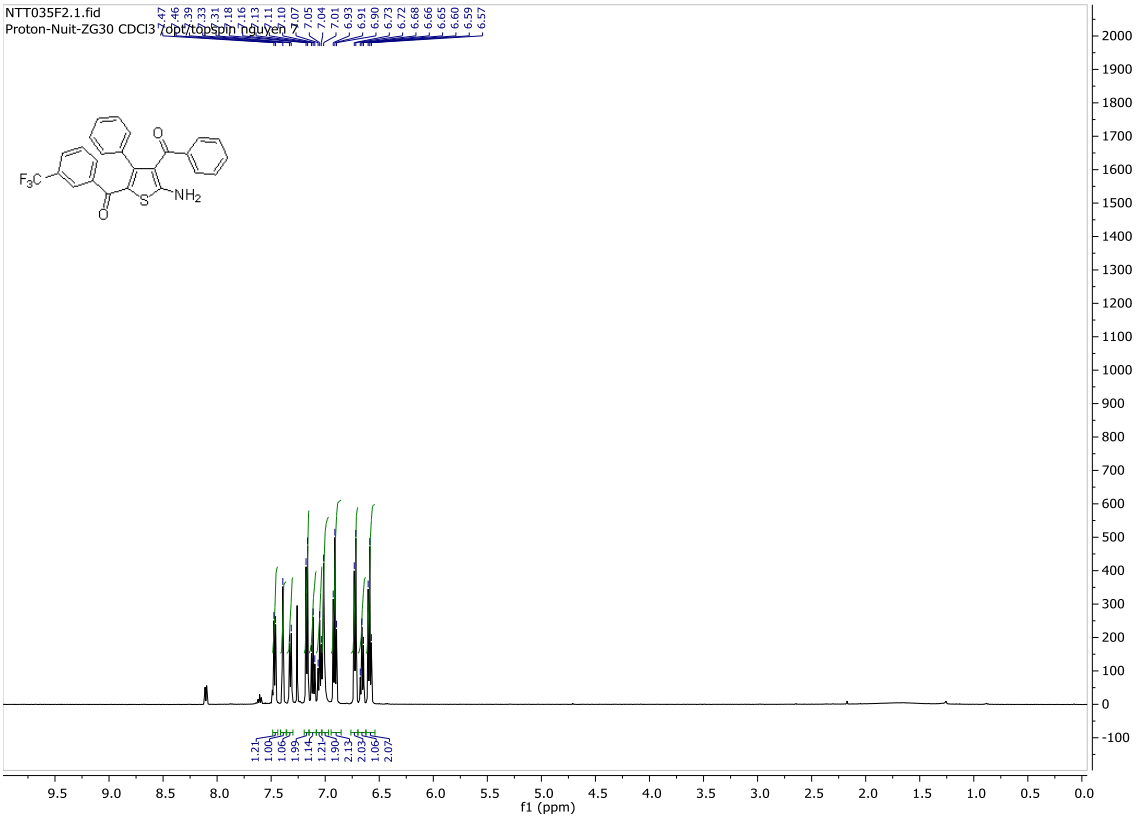


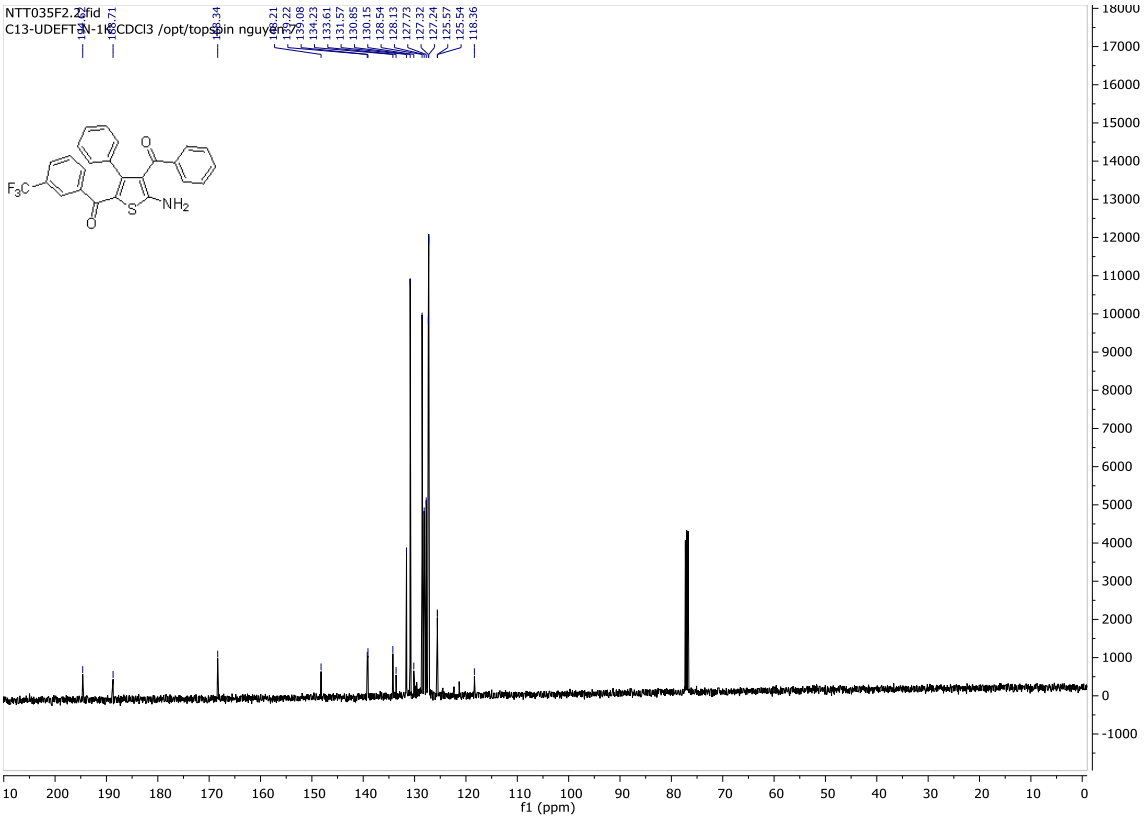
5-(4-Methoxybenzoyl)-2,4-diphenylthiophene-3-carbonitrile (4i)



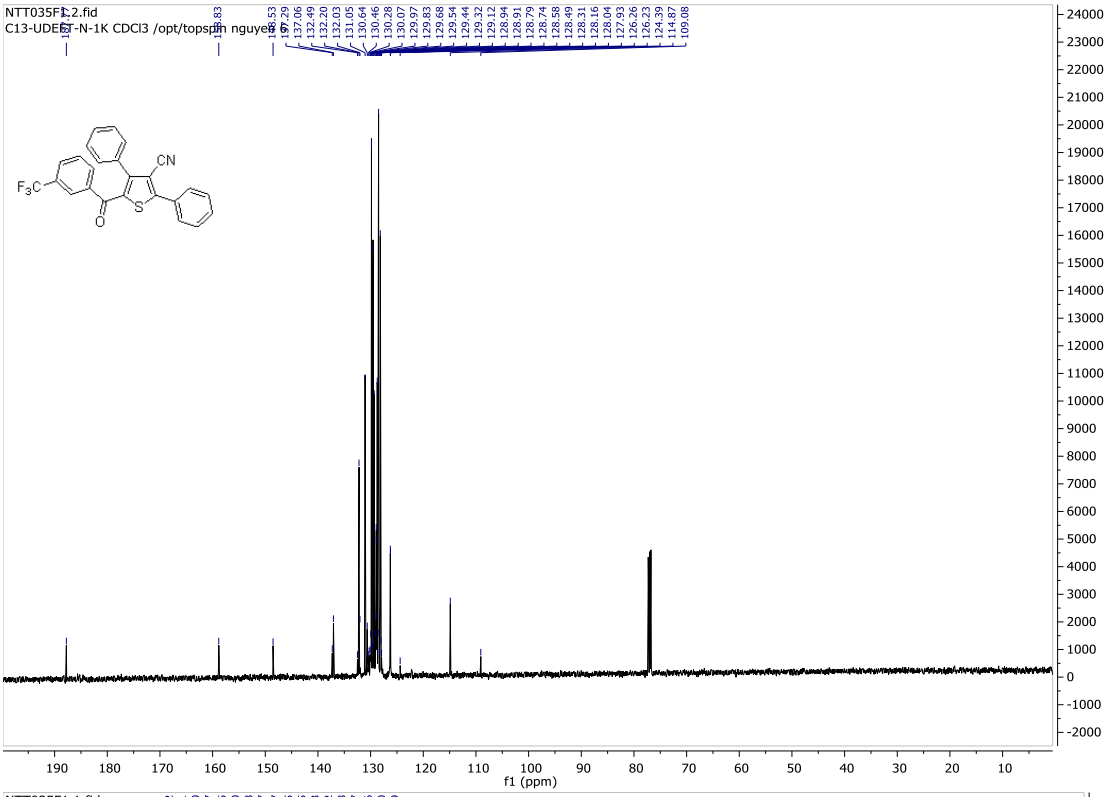


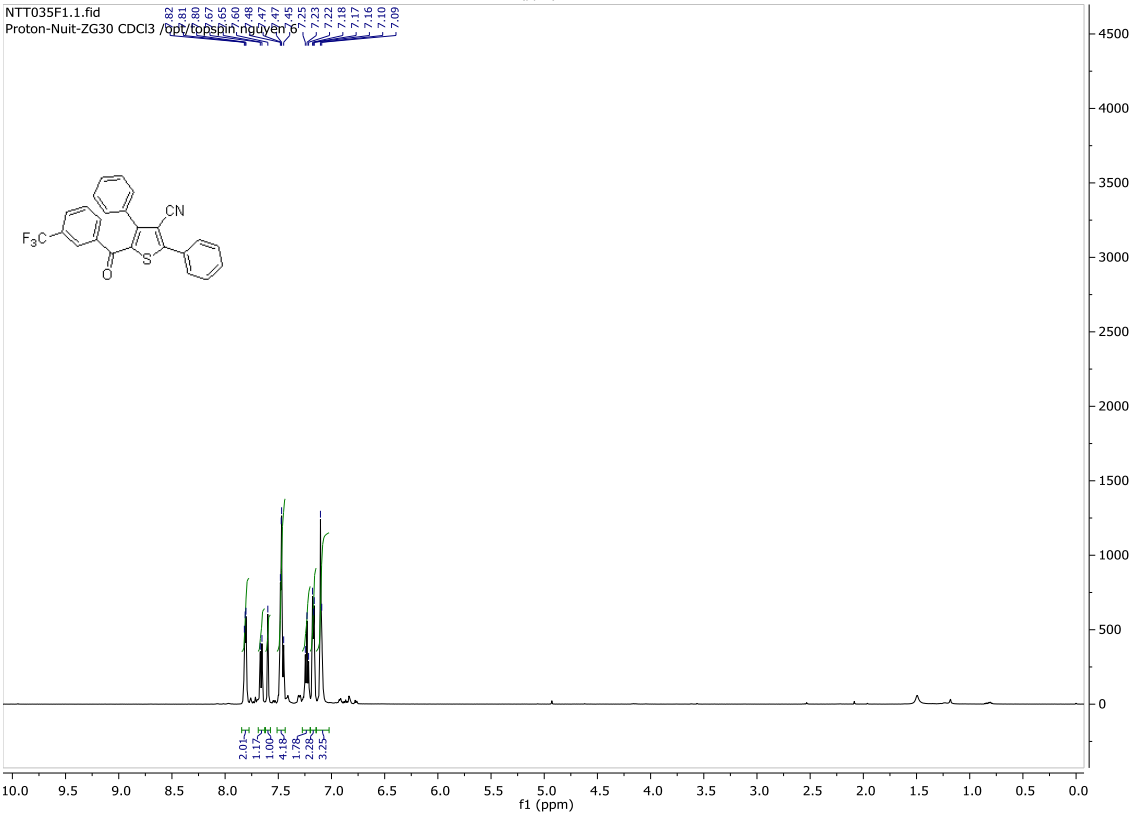
(5-Amino-4-benzoyl-3-phenylthiophen-2-yl)(3-(trifluoromethyl)phenyl)methanone (3j)



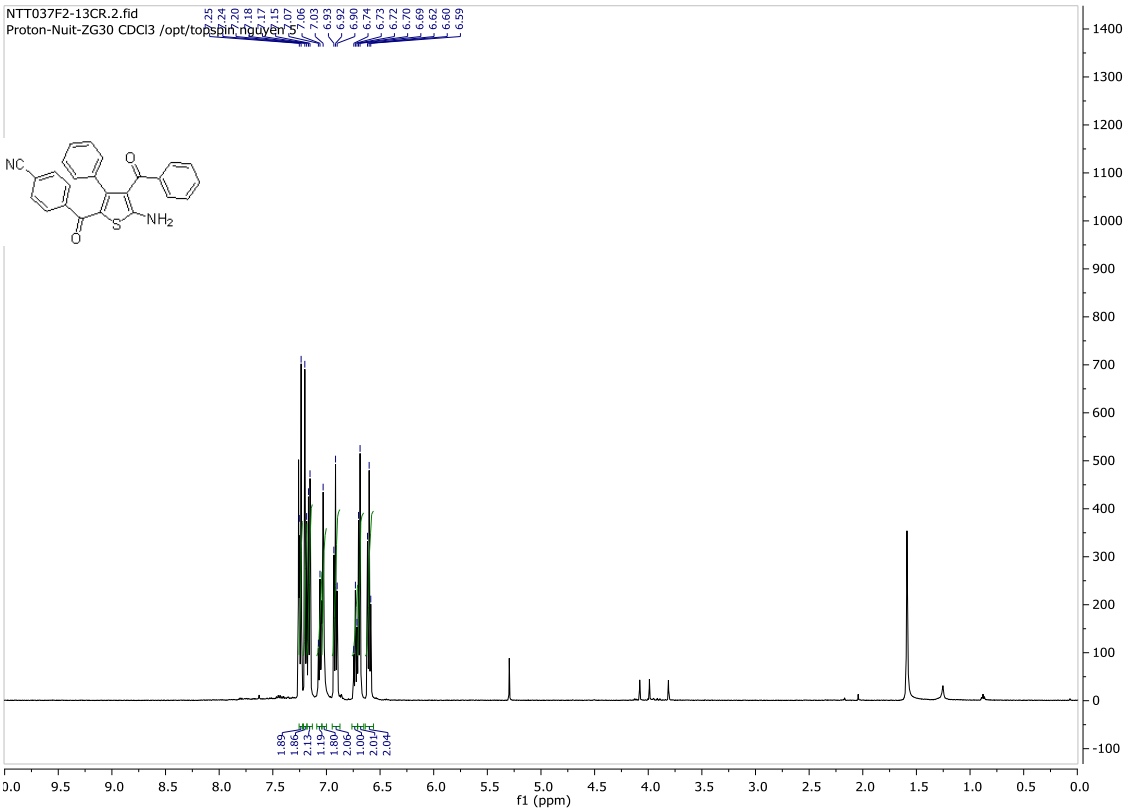


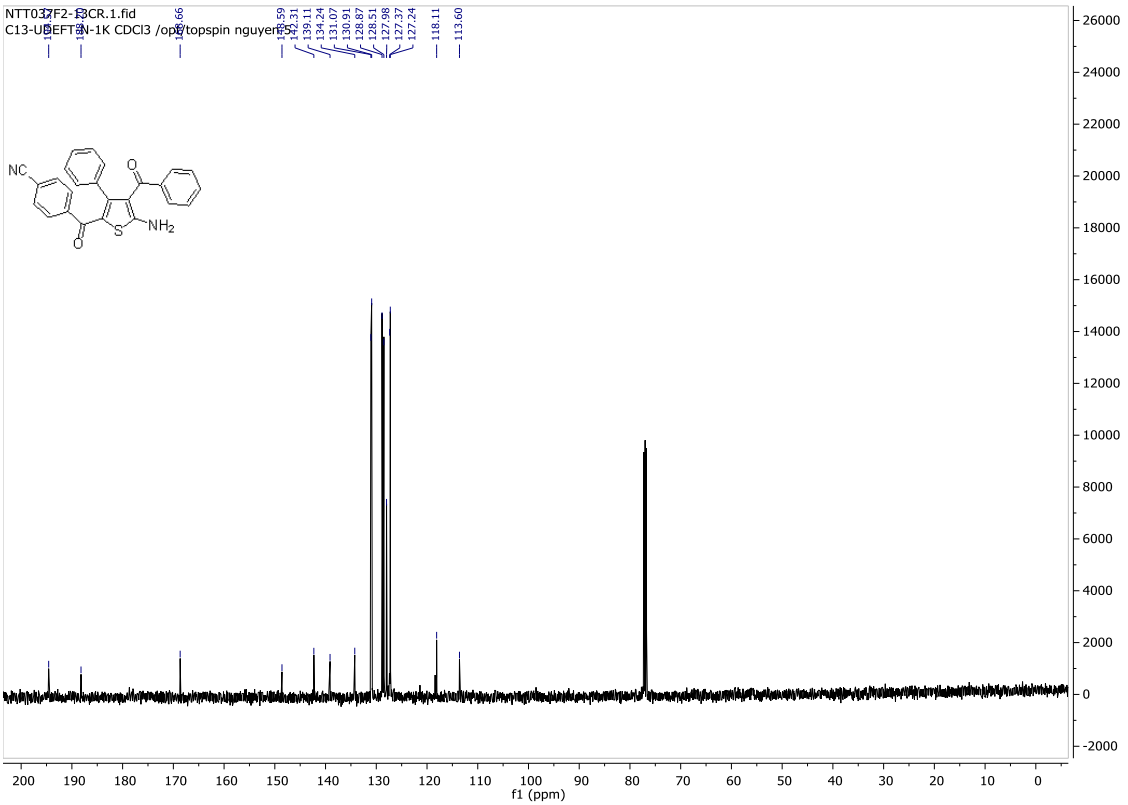
2,4-Diphenyl-5-(3-(trifluoromethyl)benzoyl)thiophene-3-carbonitrile (4j)



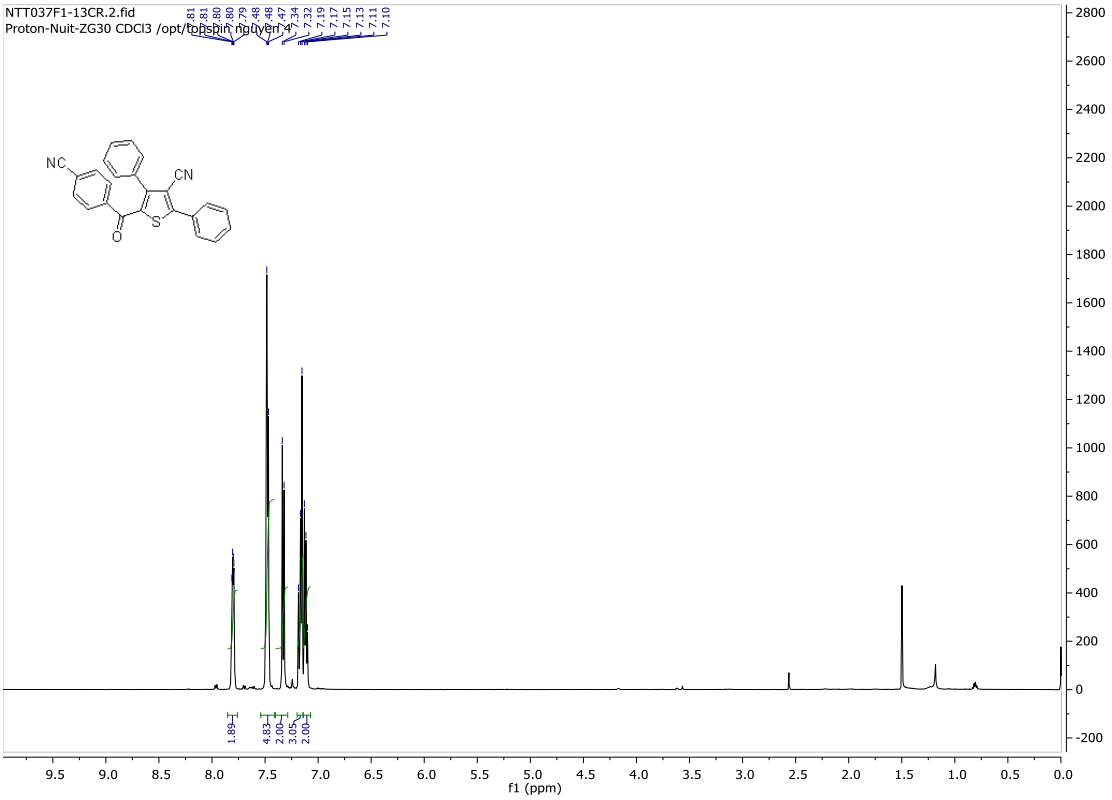


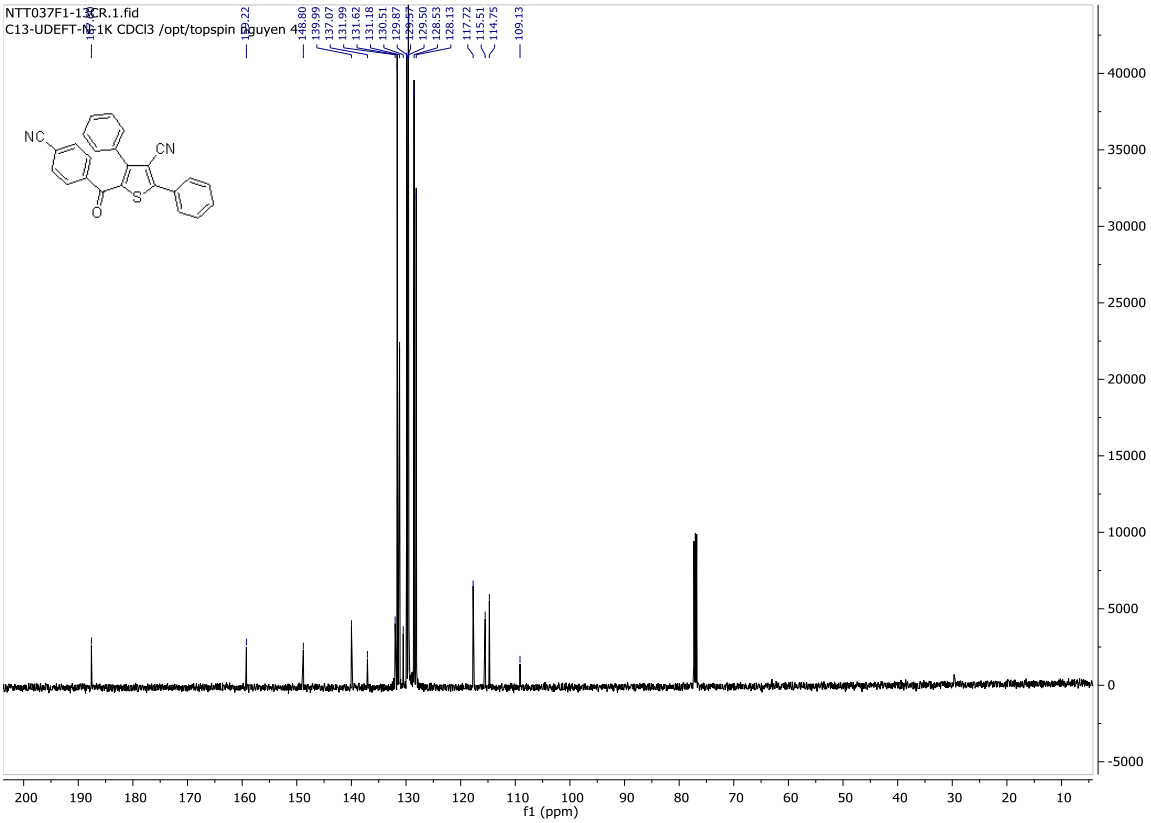
4-(5-Amino-4-benzoyl-3-phenylthiophene-2-carbonyl)benzonitrile (3k)



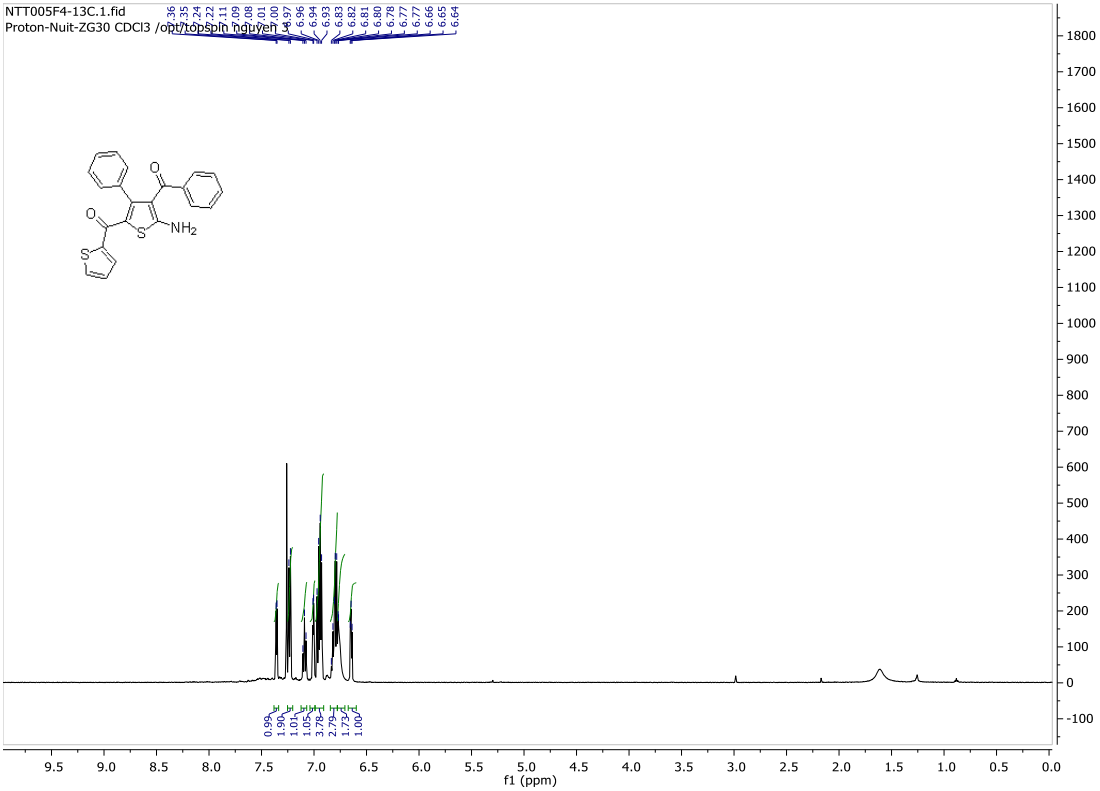


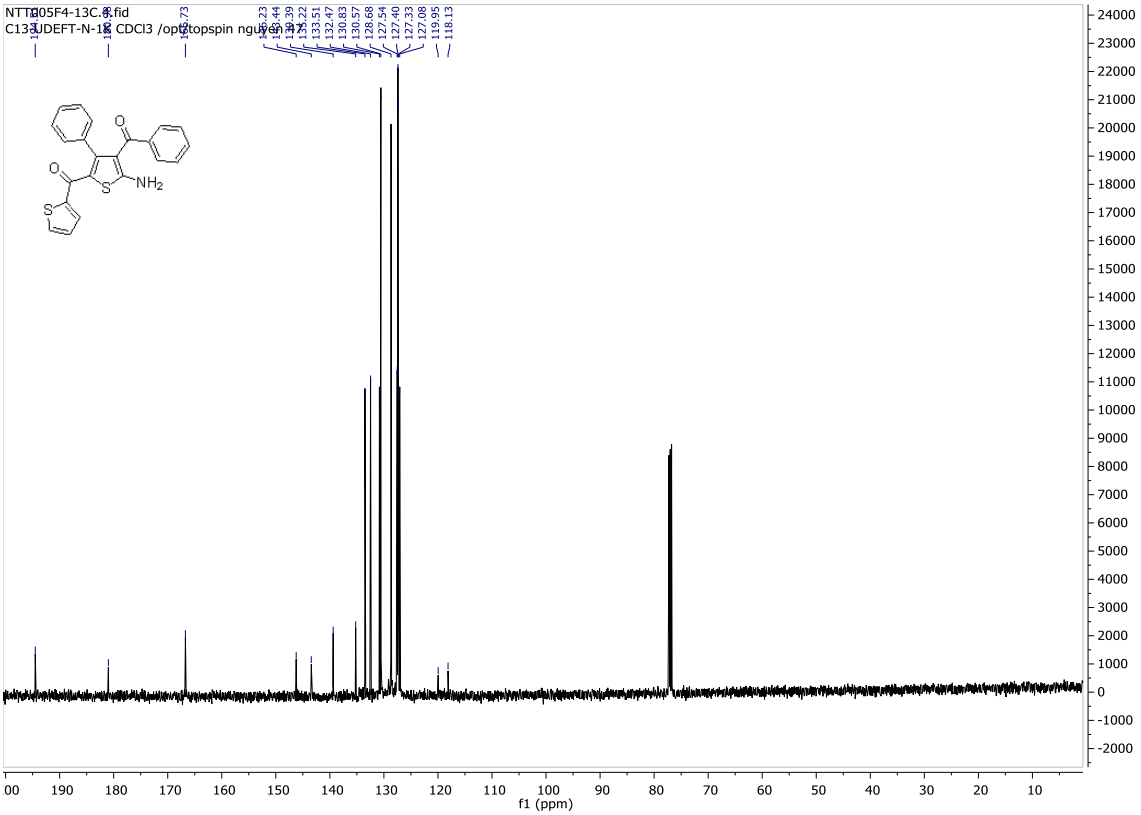
5-(4-Cyanobenzoyl)-2,4-diphenylthiophene-3-carbonitrile (4k)



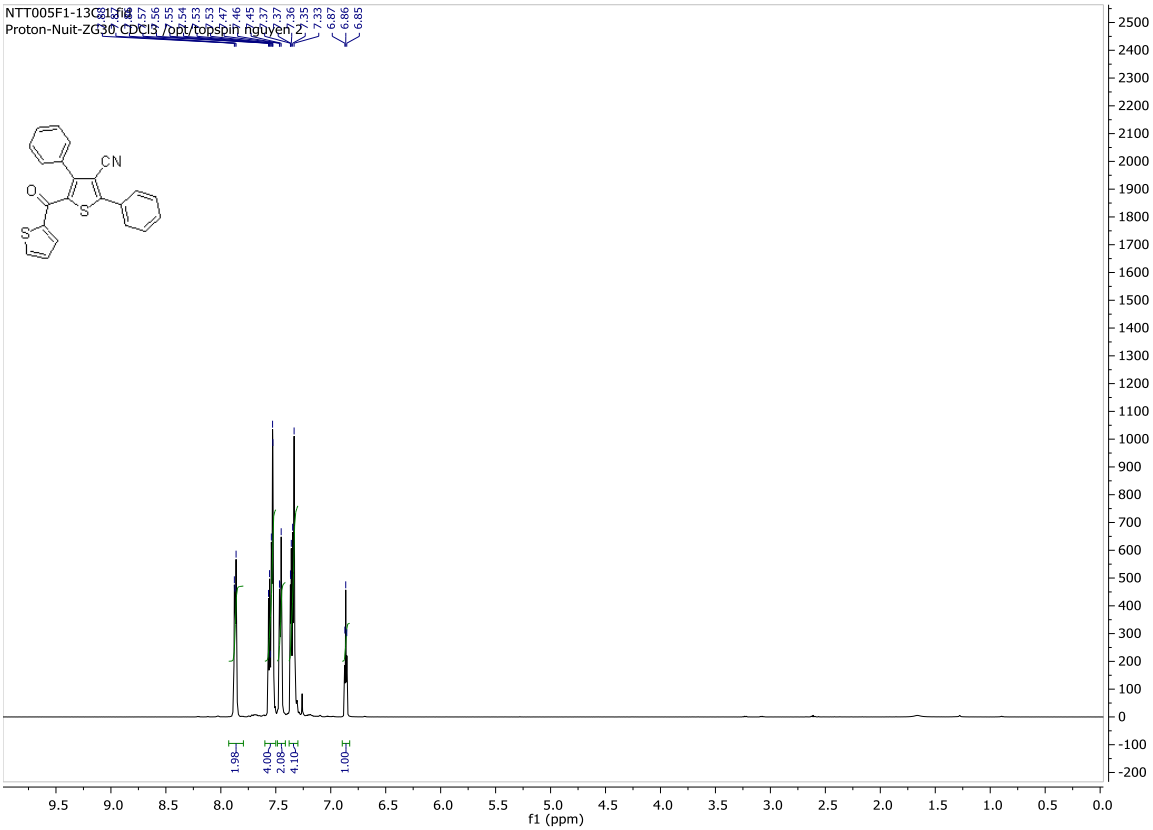


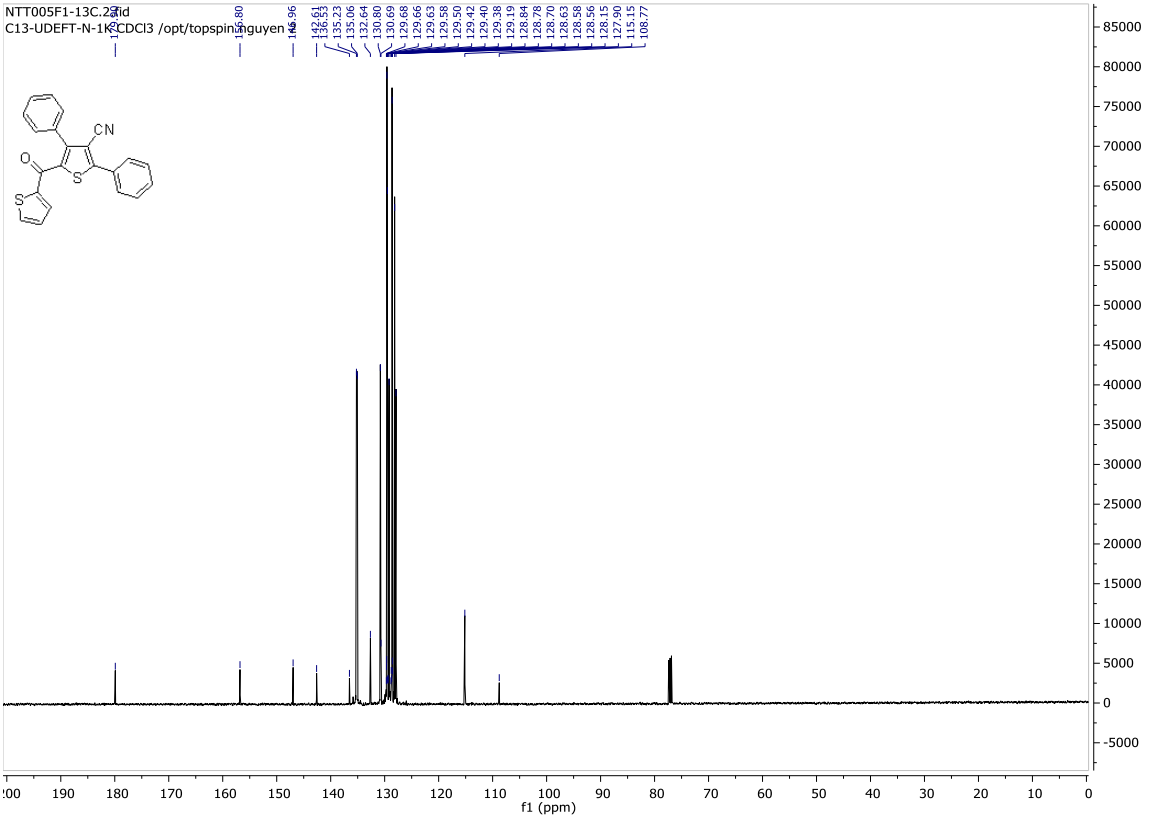
(5-Amino-4-benzoyl-3-phenylthiophen-2-yl)(thiophen-2-yl)methanone (3l)



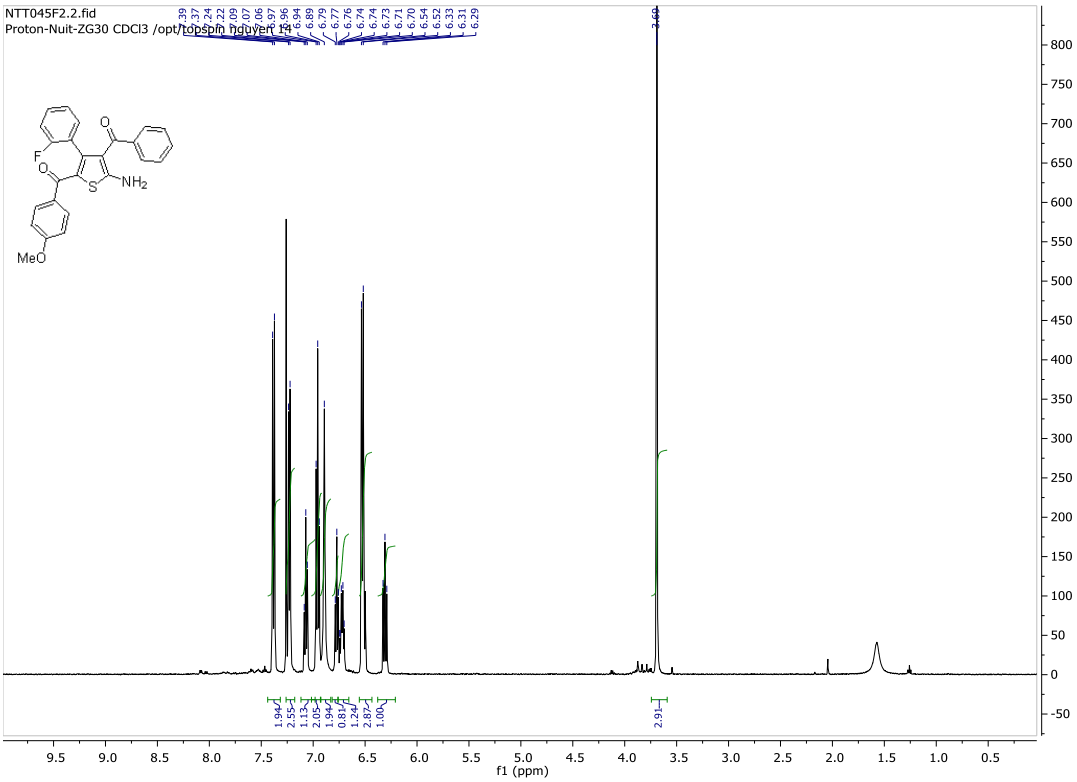


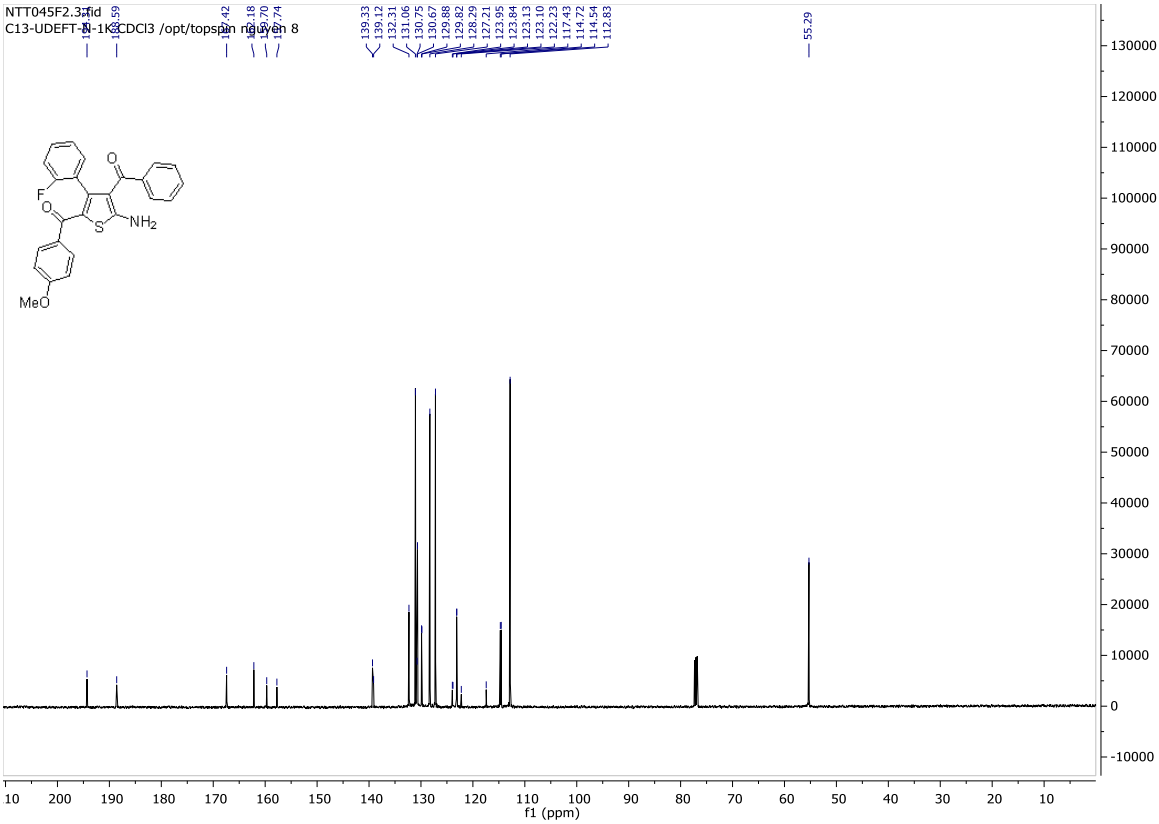
2,4-Diphenyl-5-(thiophene-2-carbonyl)thiophene-3-carbonitrile (4l)



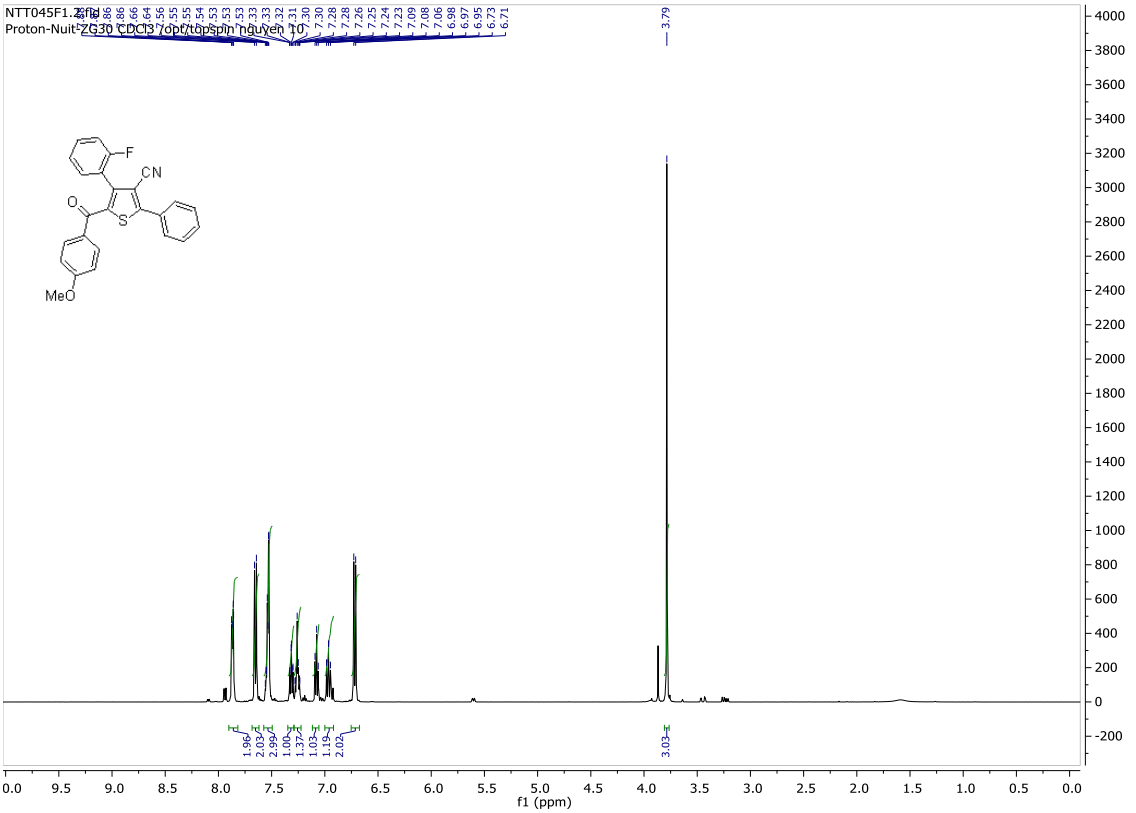


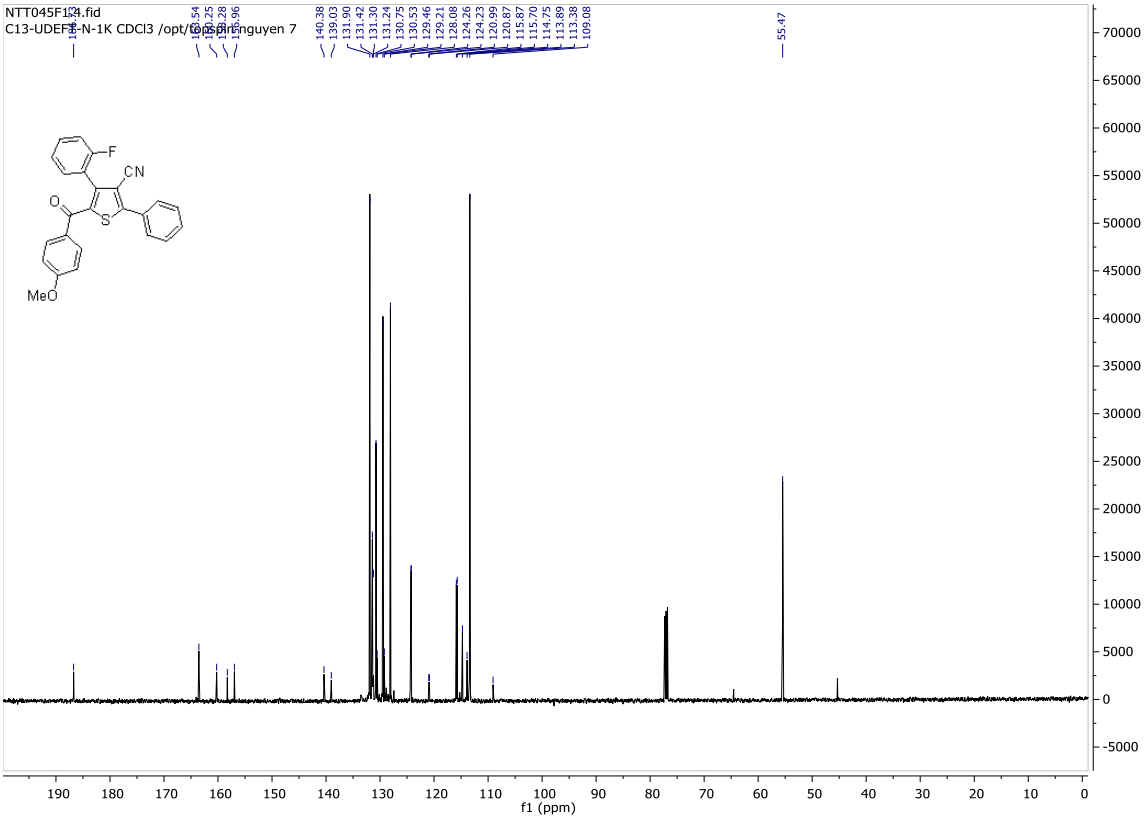
(2-Amino-4-(2-fluorophenyl)-5-(4-methoxybenzoyl)thiophen-3-yl)(phenyl)methanone (3m)



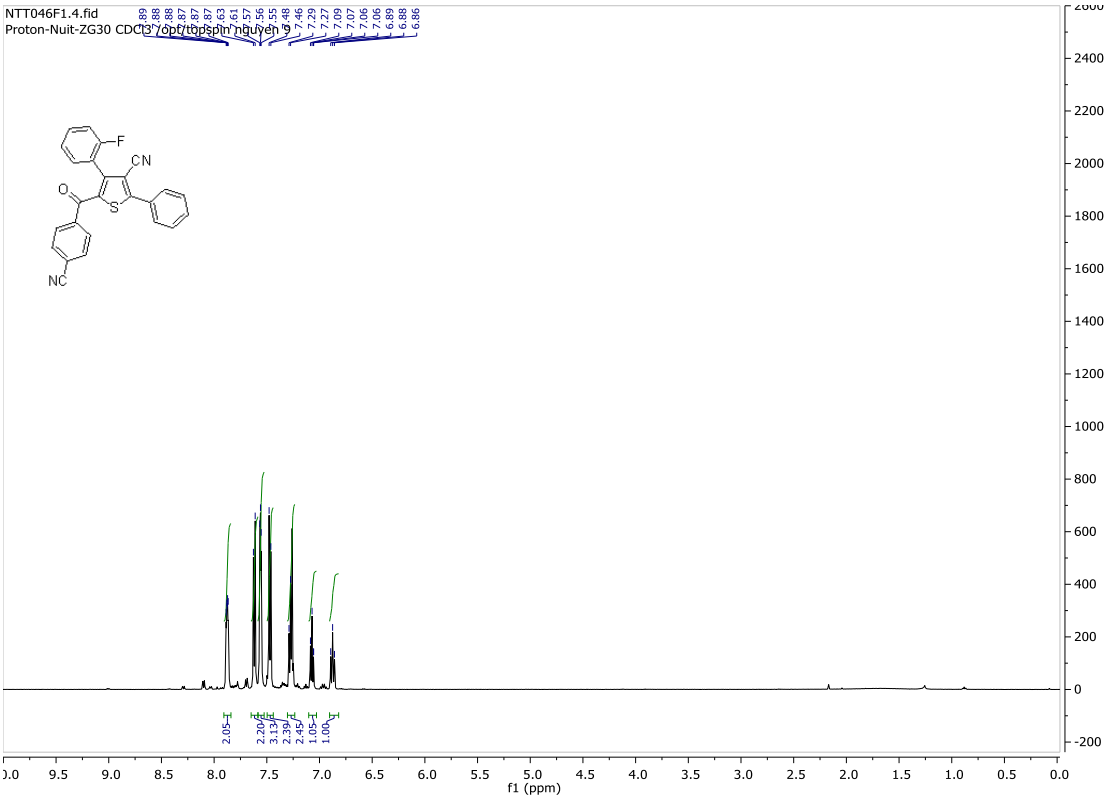


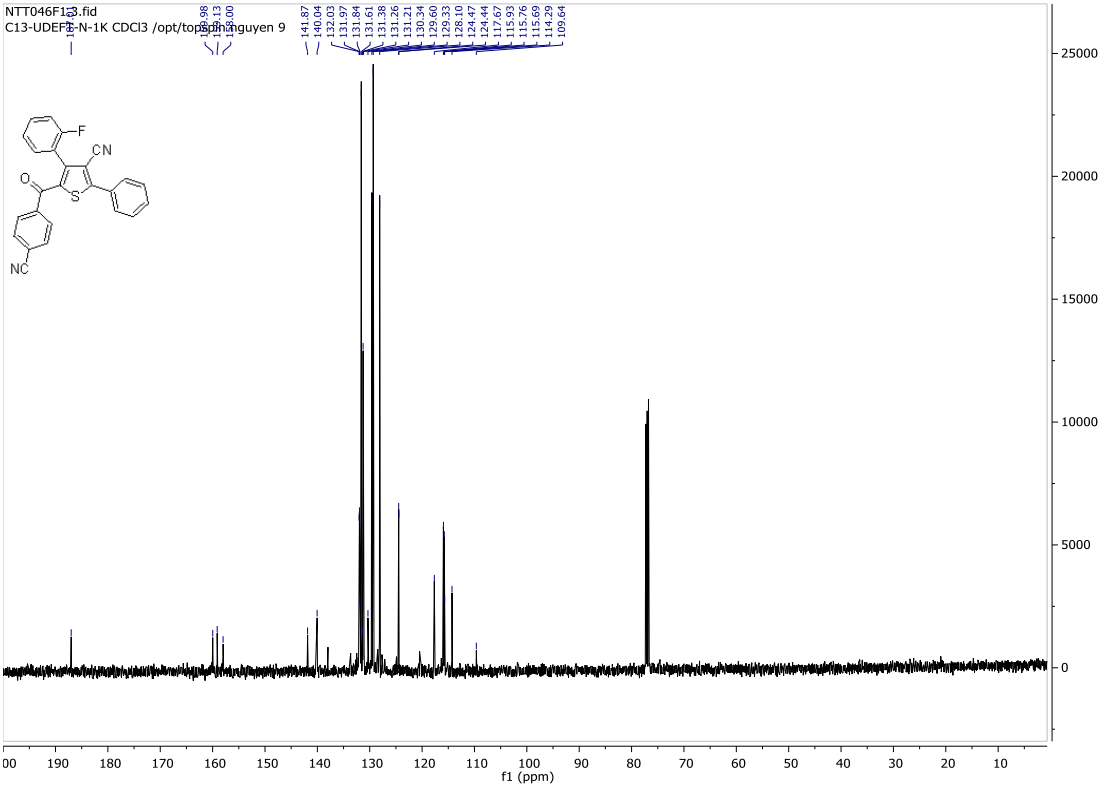
4-(2-Fluorophenyl)-5-(4-methoxybenzoyl)-2-phenylthiophene-3-carbonitrile (4m)



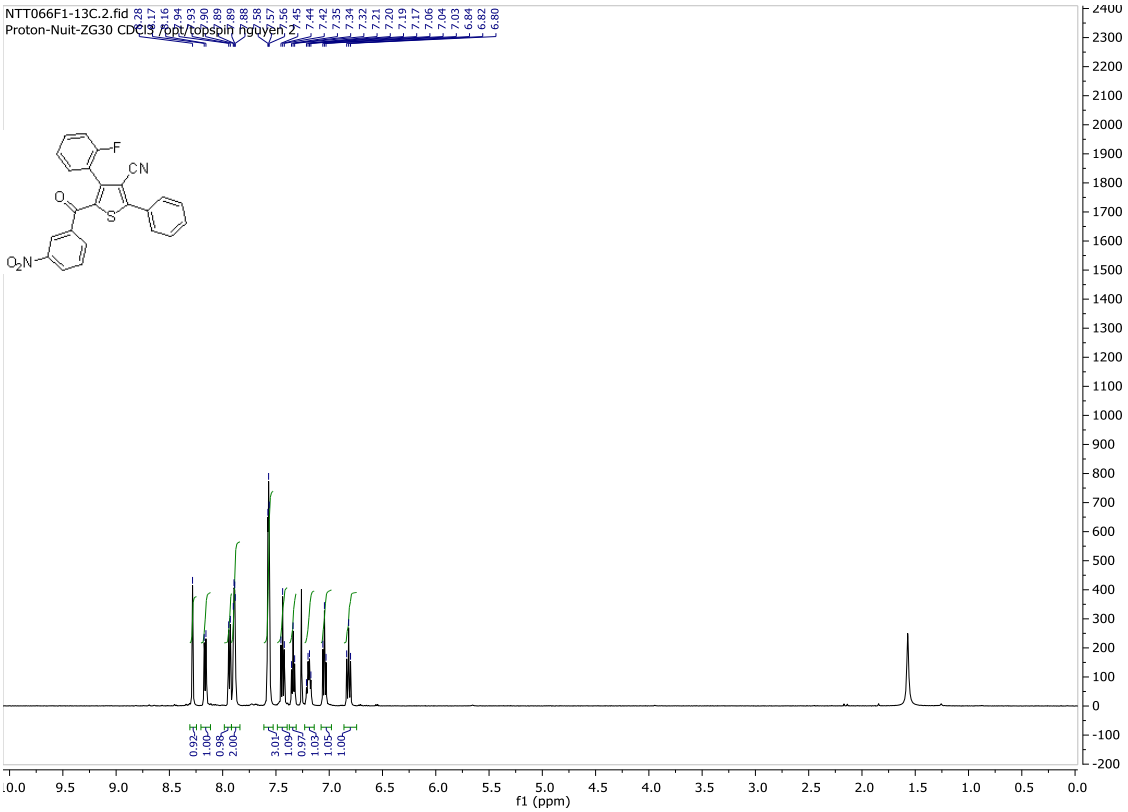


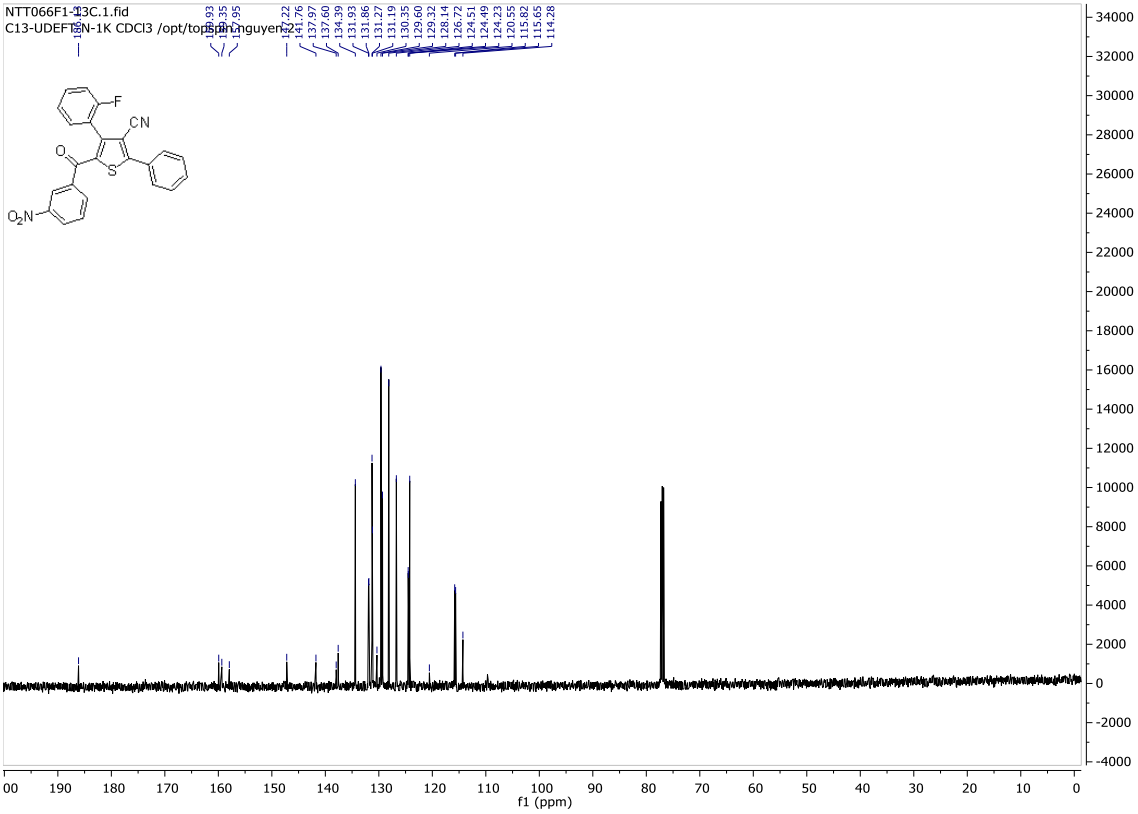
5-(4-Cyanobenzoyl)-4-(2-fluorophenyl)-2-phenylthiophene-3-carbonitrile (4n)



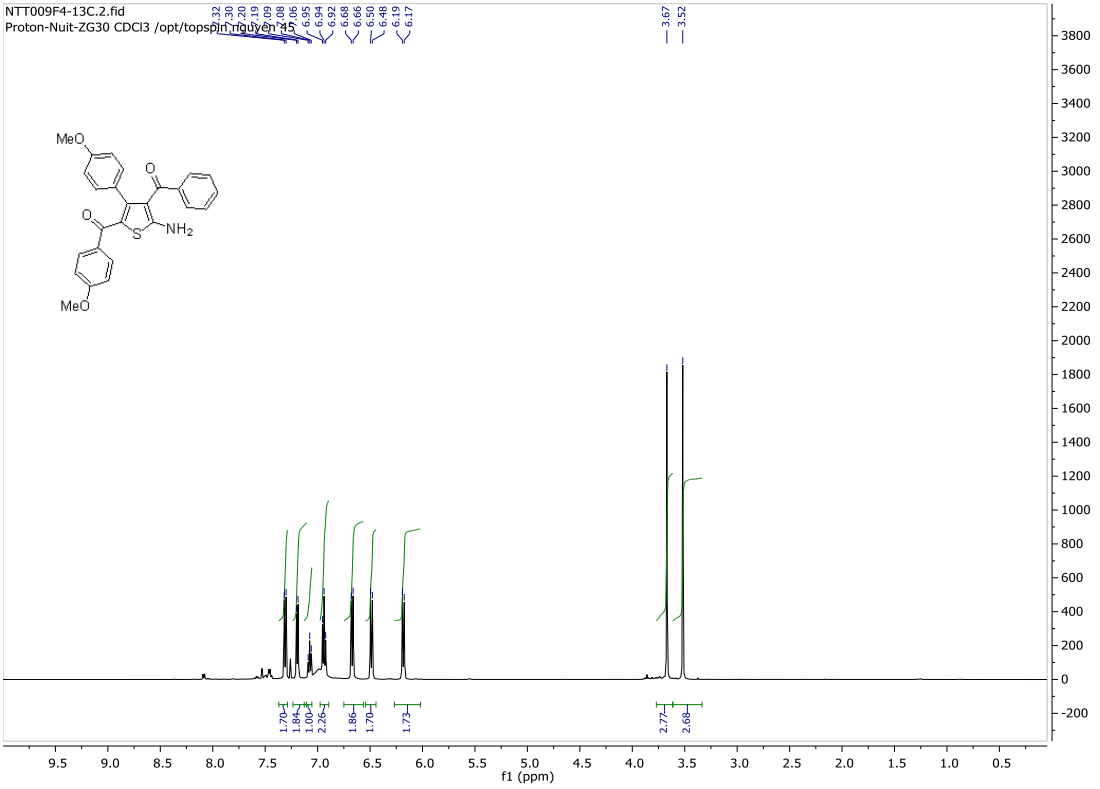


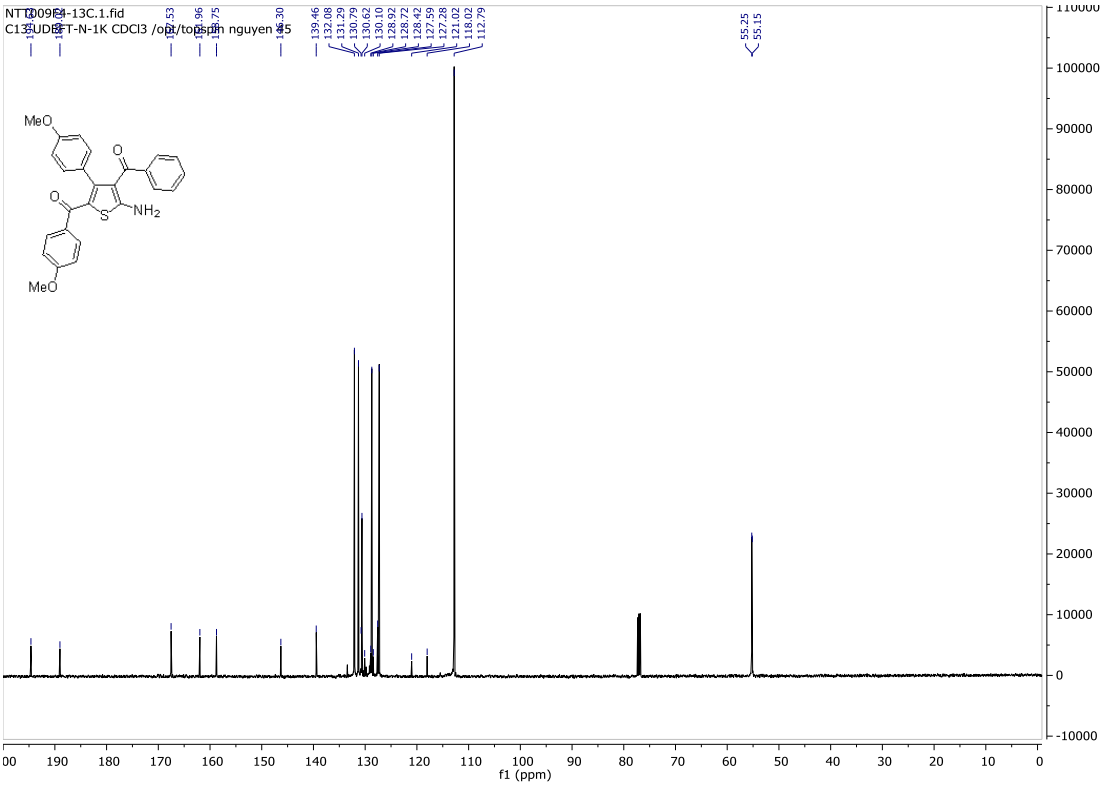
4-(2-Fluorophenyl)-5-(3-nitrobenzoyl)-2-phenylthiophene-3-carbonitrile (4o)



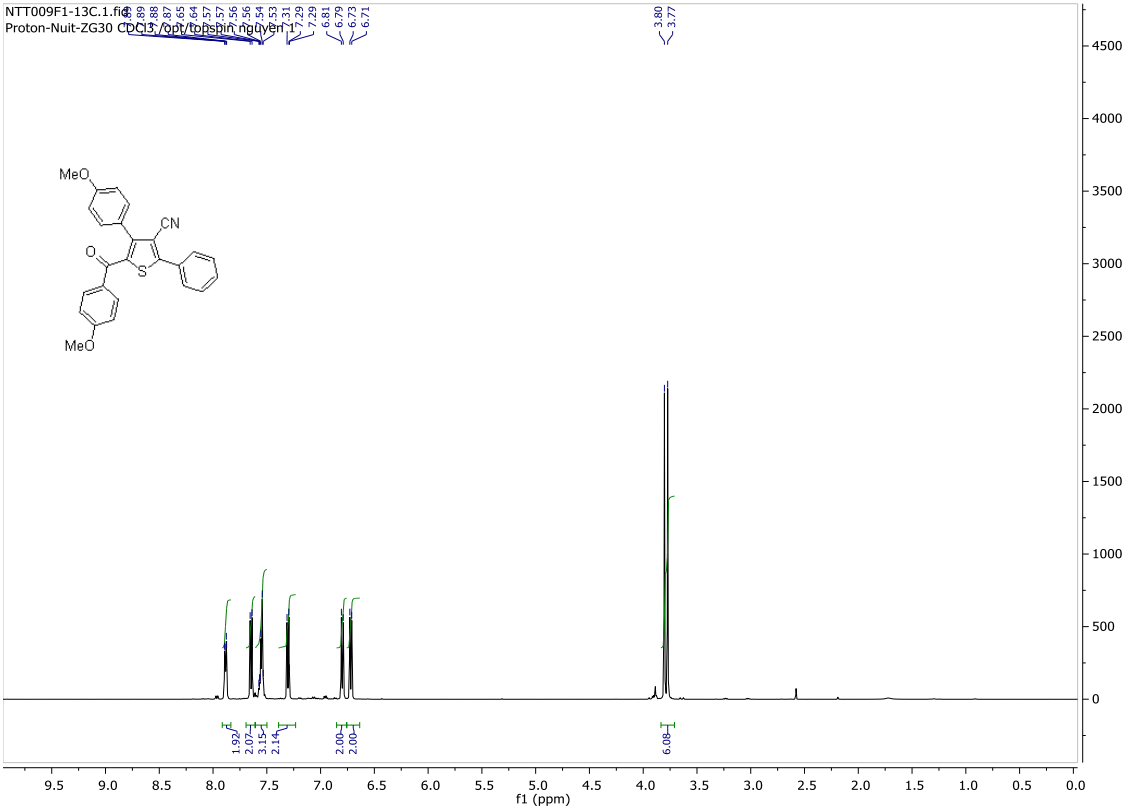


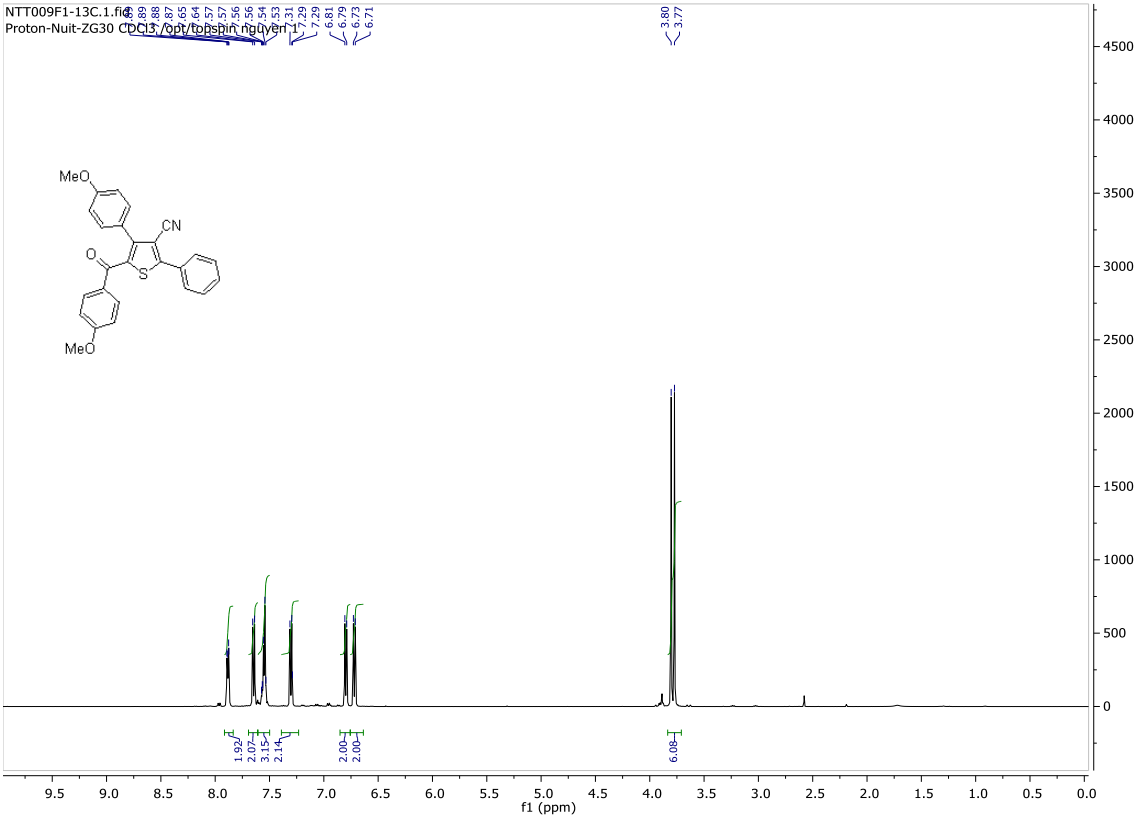
(5-Amino-4-benzoyl-3-(4-methoxyphenyl)thiophen-2-yl)(4-methoxyphenyl)methanone (3p)



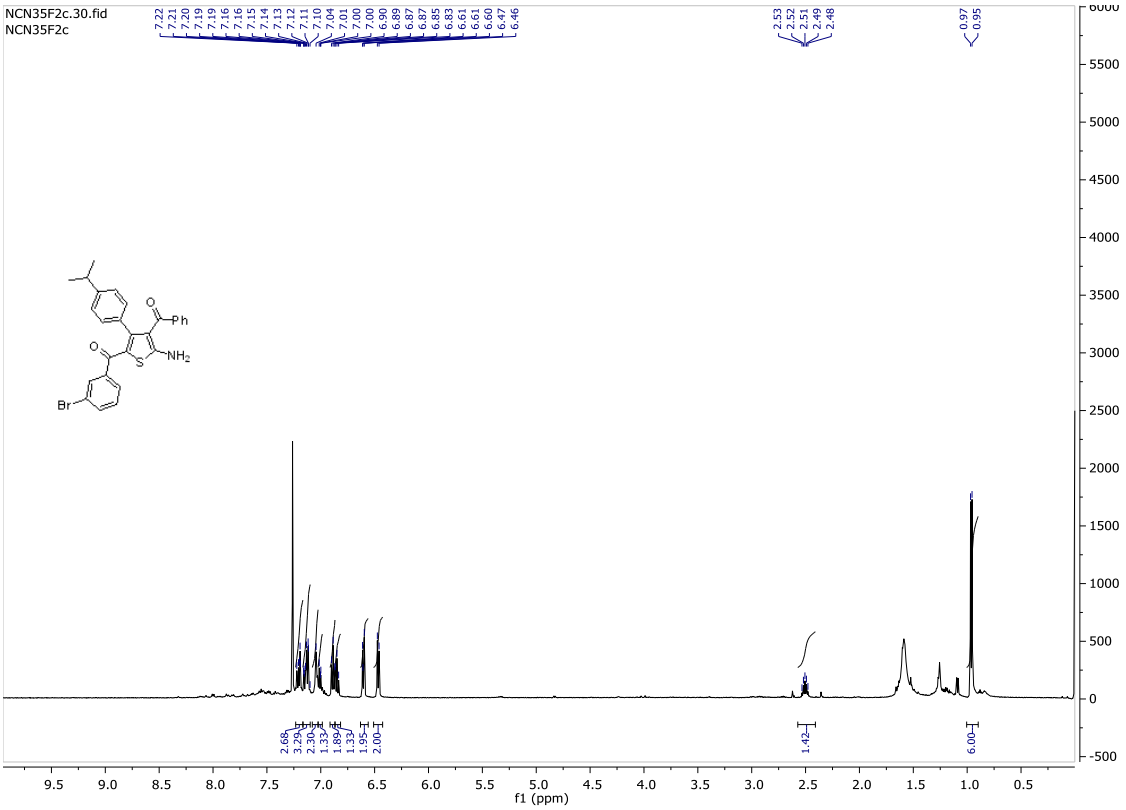


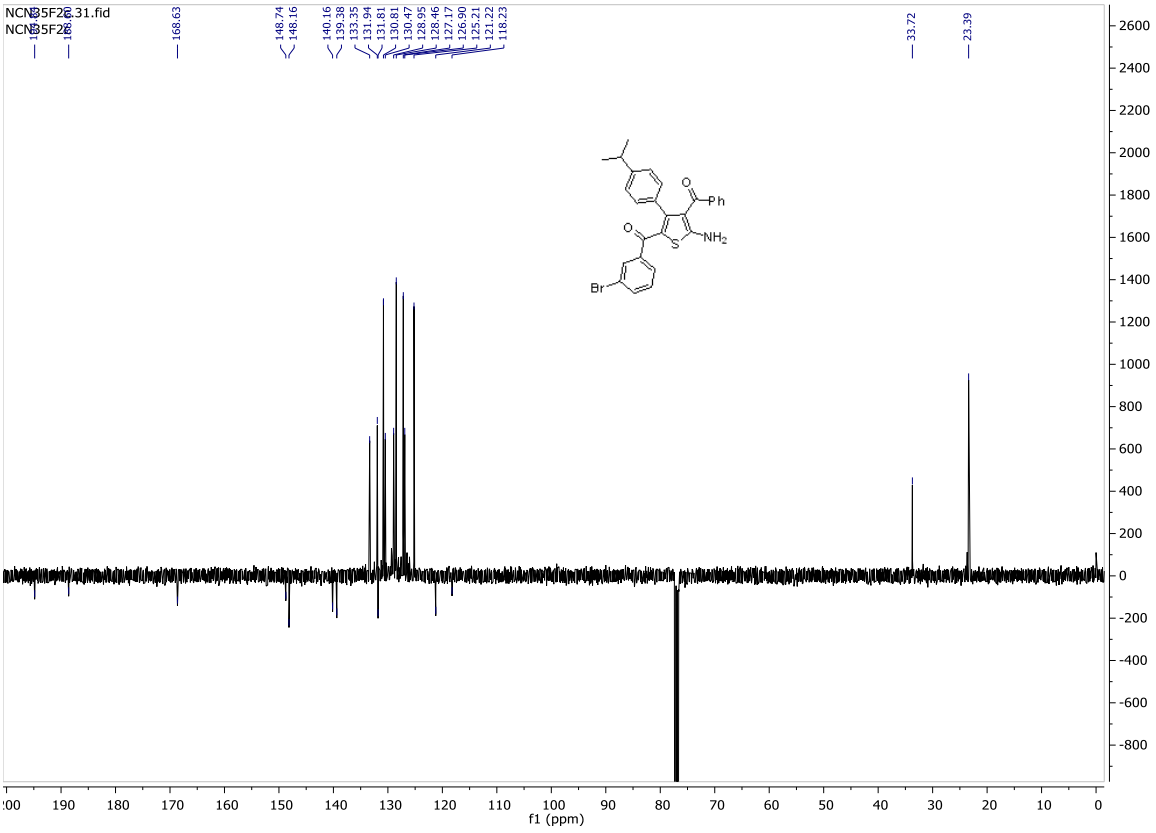
5-(4-Methoxybenzoyl)-4-(4-methoxyphenyl)-2-phenylthiophene-3-carbonitrile (4p)



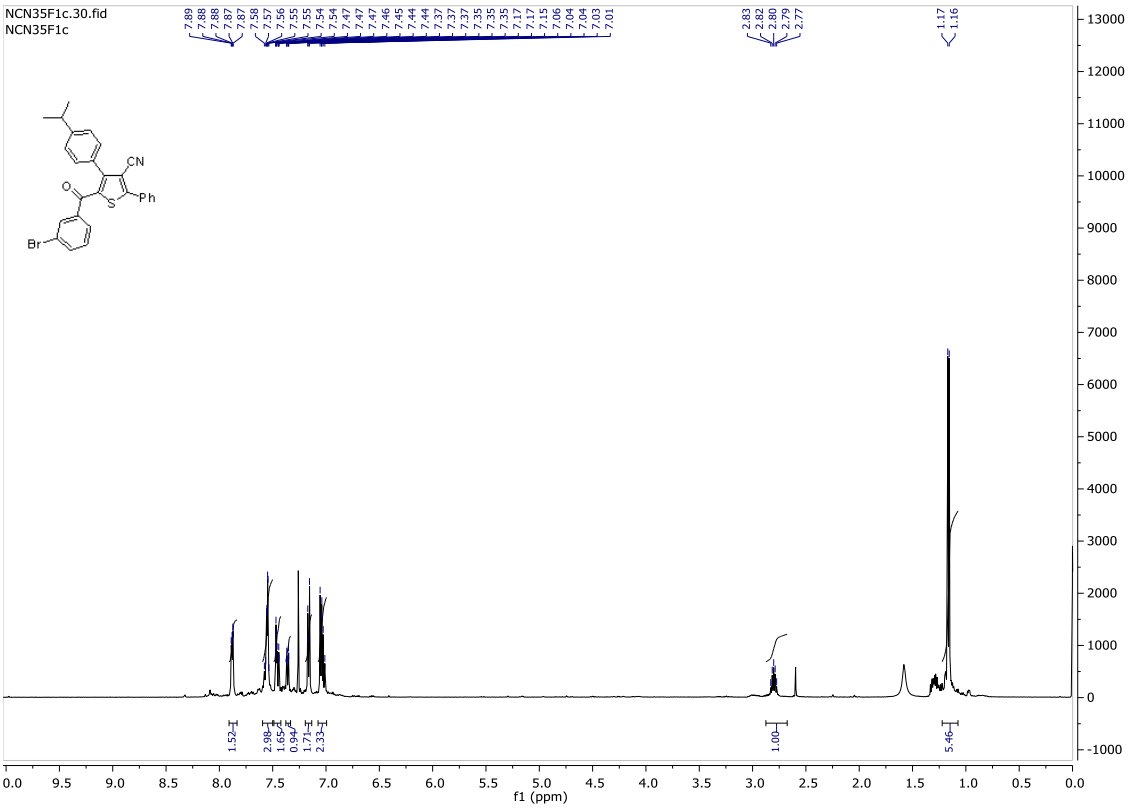


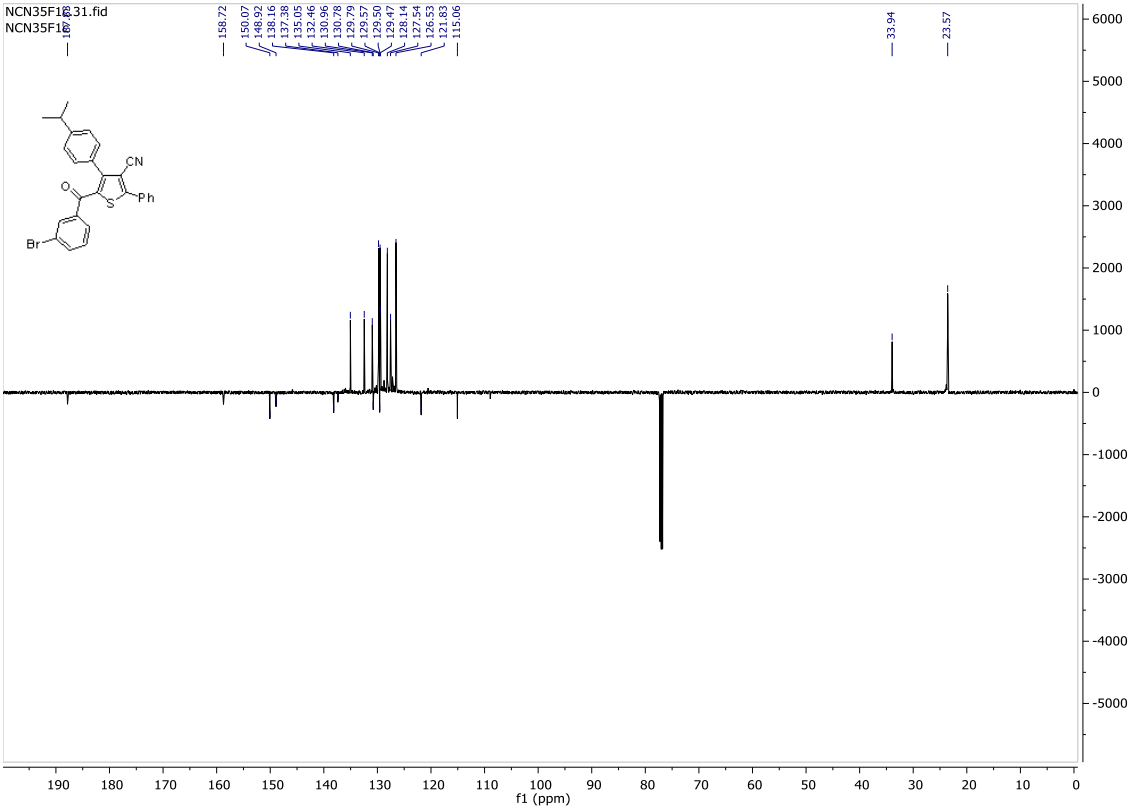
(5-Amino-4-benzoyl-3-(4-isopropylphenyl)thiophen-2-yl)(3-bromophenyl)methanone (3q)



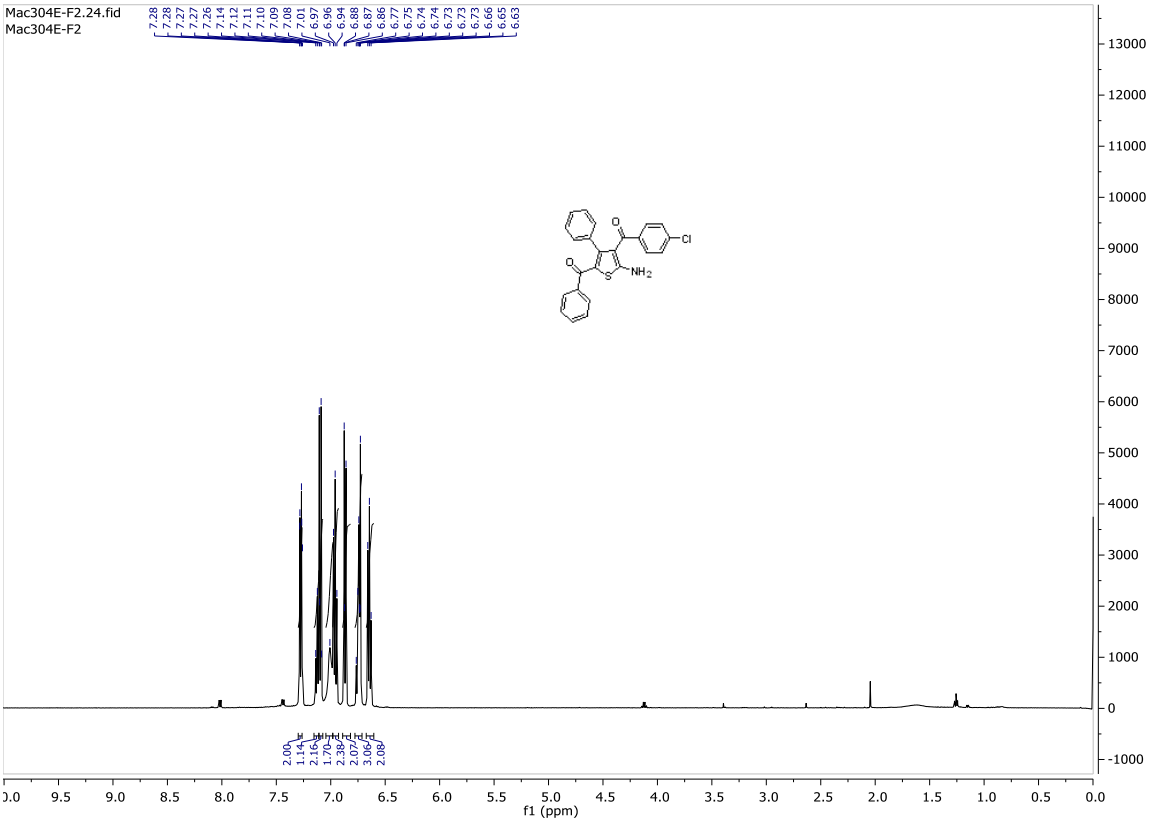


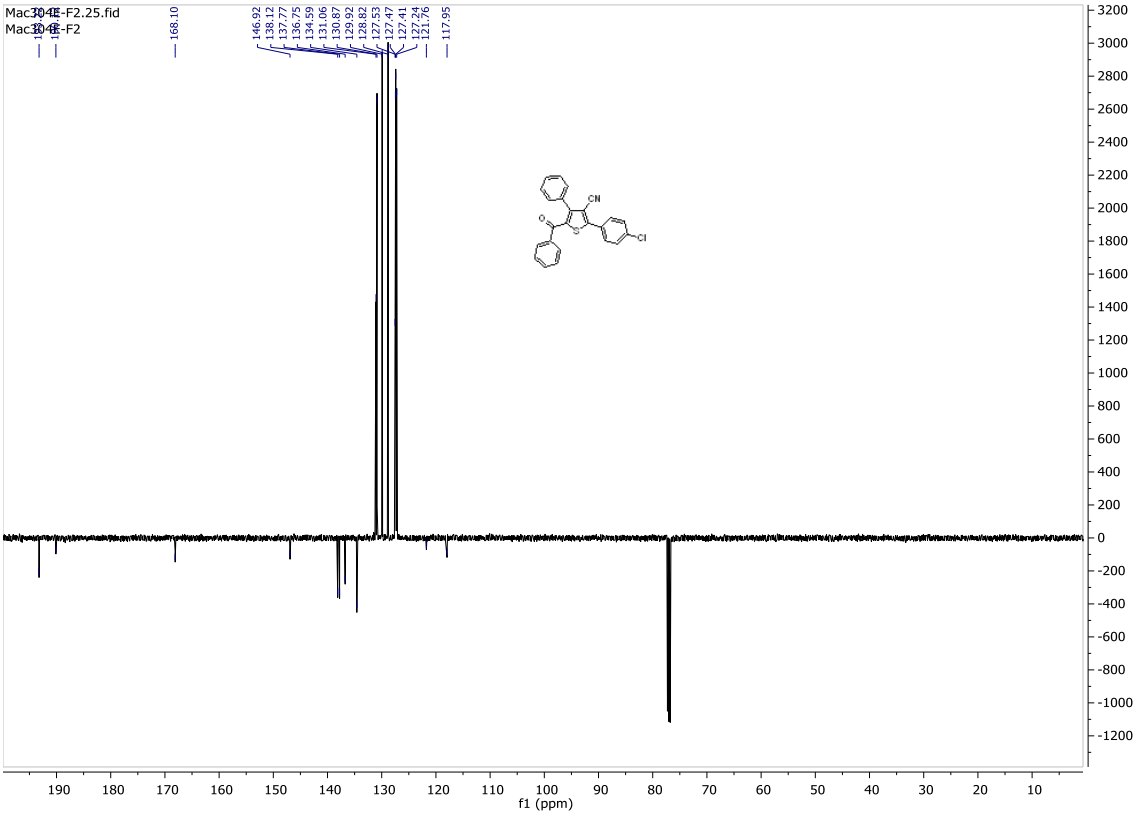
5-(3-Bromobenzoyl)-4-(4-isopropylphenyl)-2-phenylthiophene-3-carbonitrile (4q)



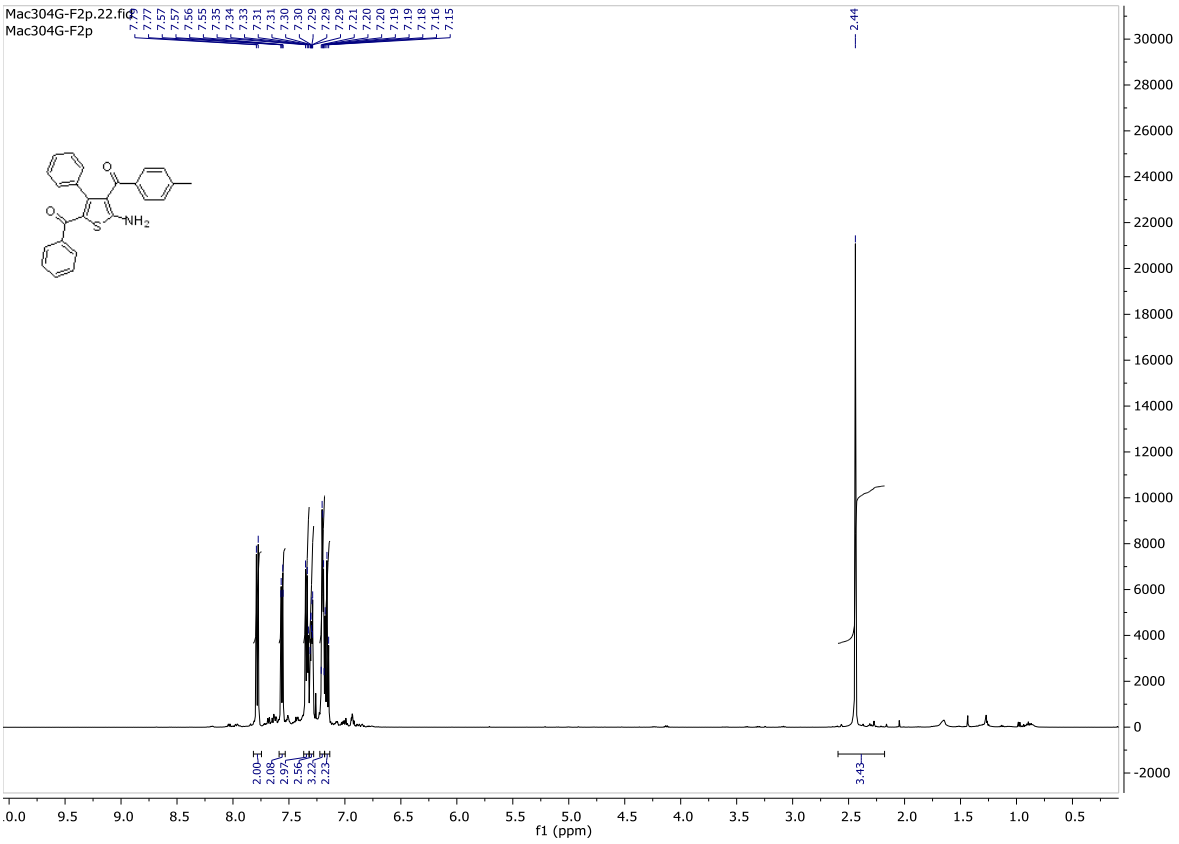


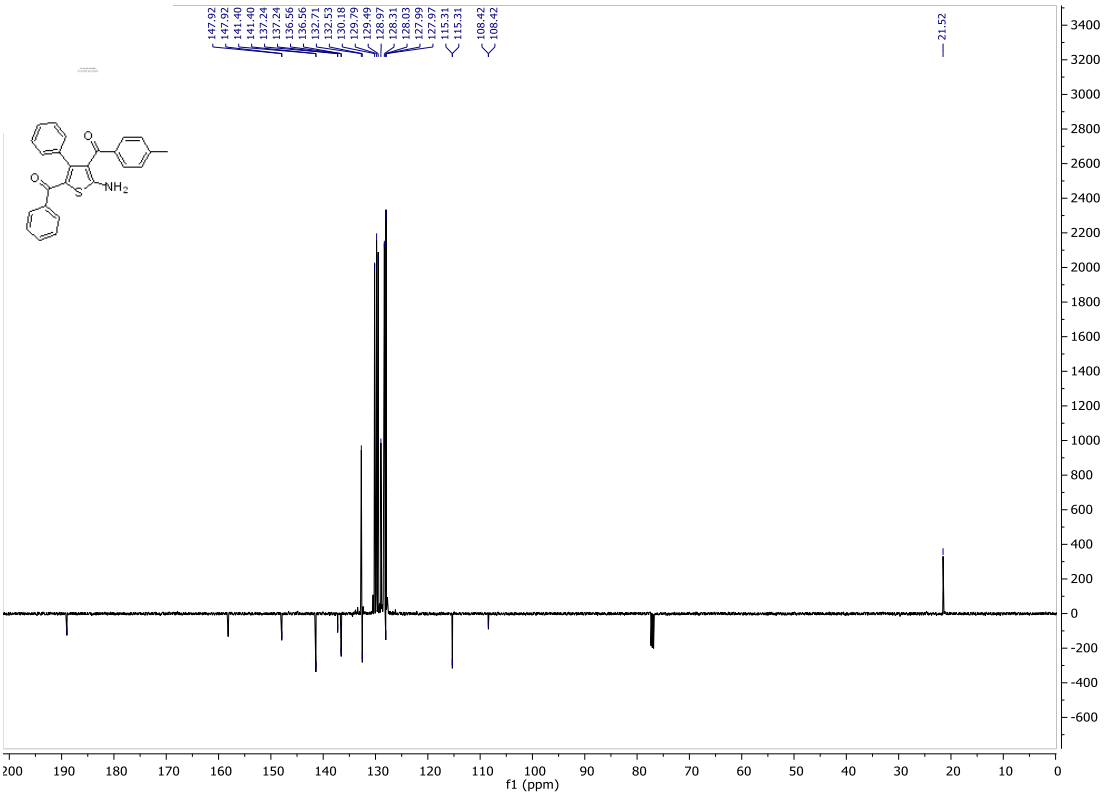
(5-Amino-4-(4-chlorobenzoyl)-3-phenylthiophen-2-yl)(phenyl)methanone (3r)



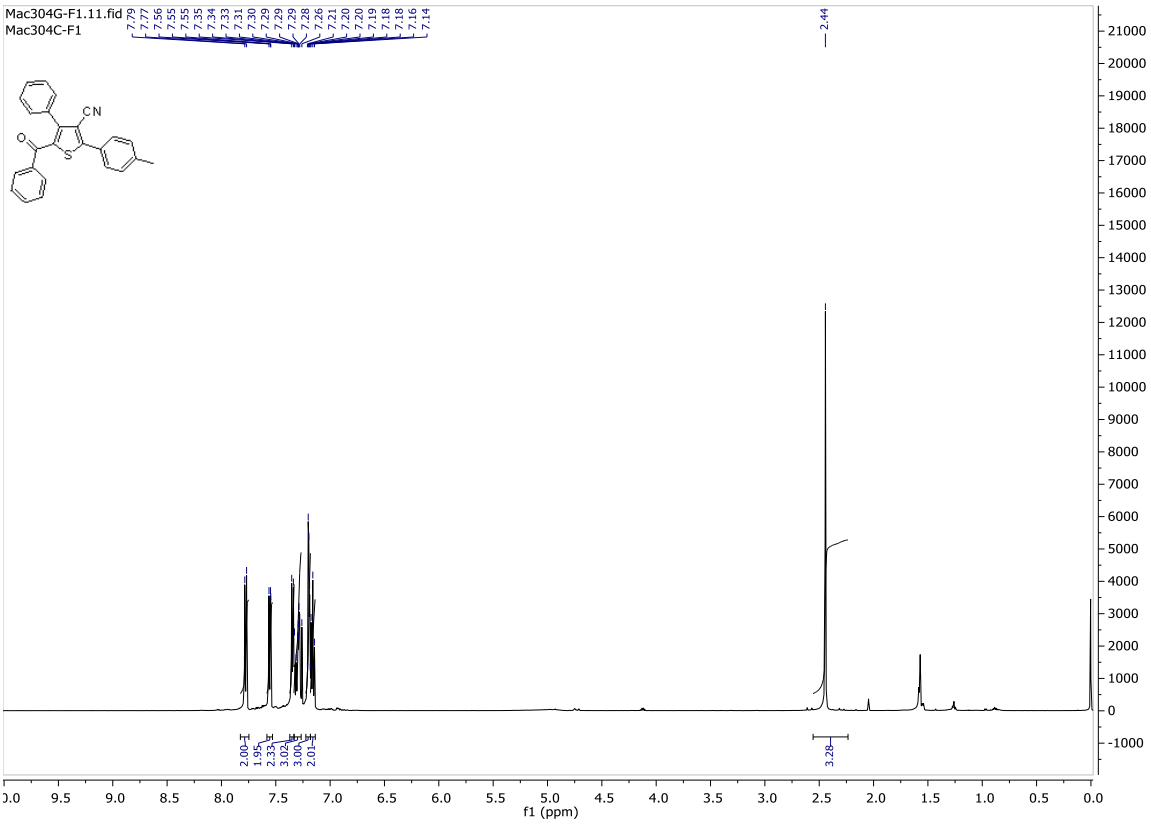


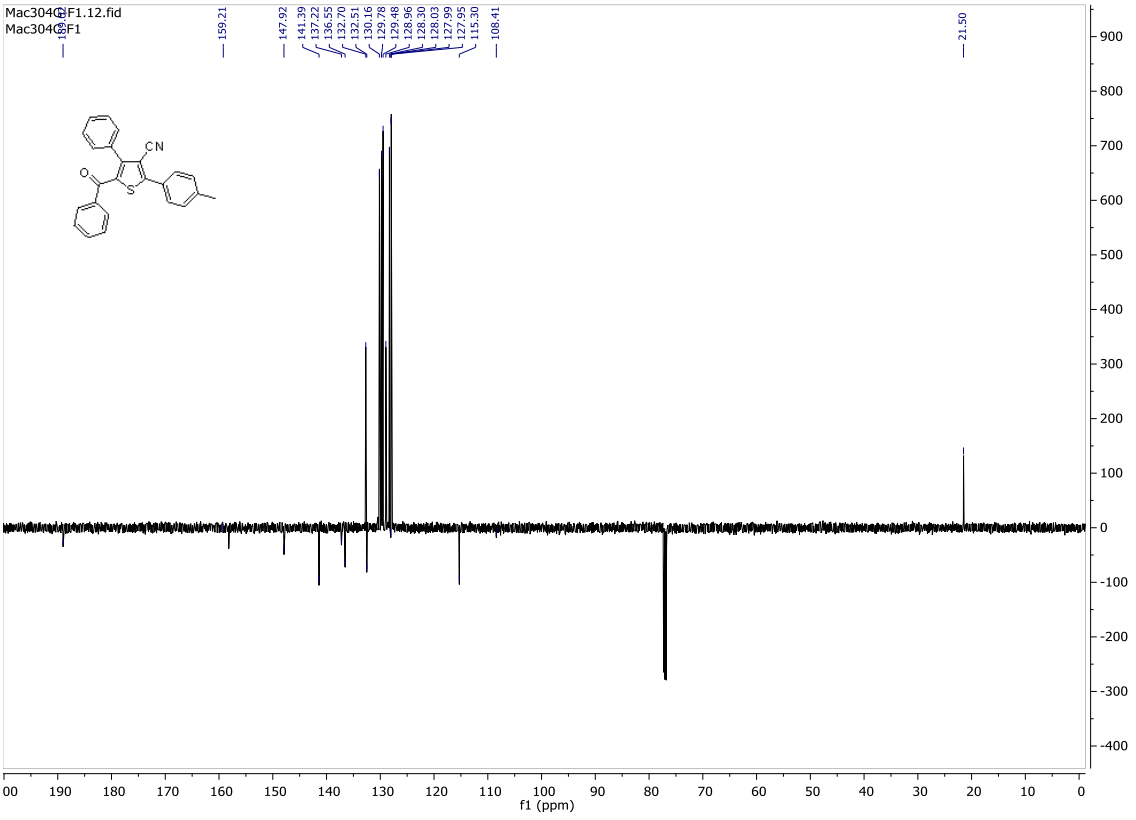
(5-Amino-4-(4-methylbenzoyl)-3-phenylthiophen-2-yl)(phenyl)methanone (3s)



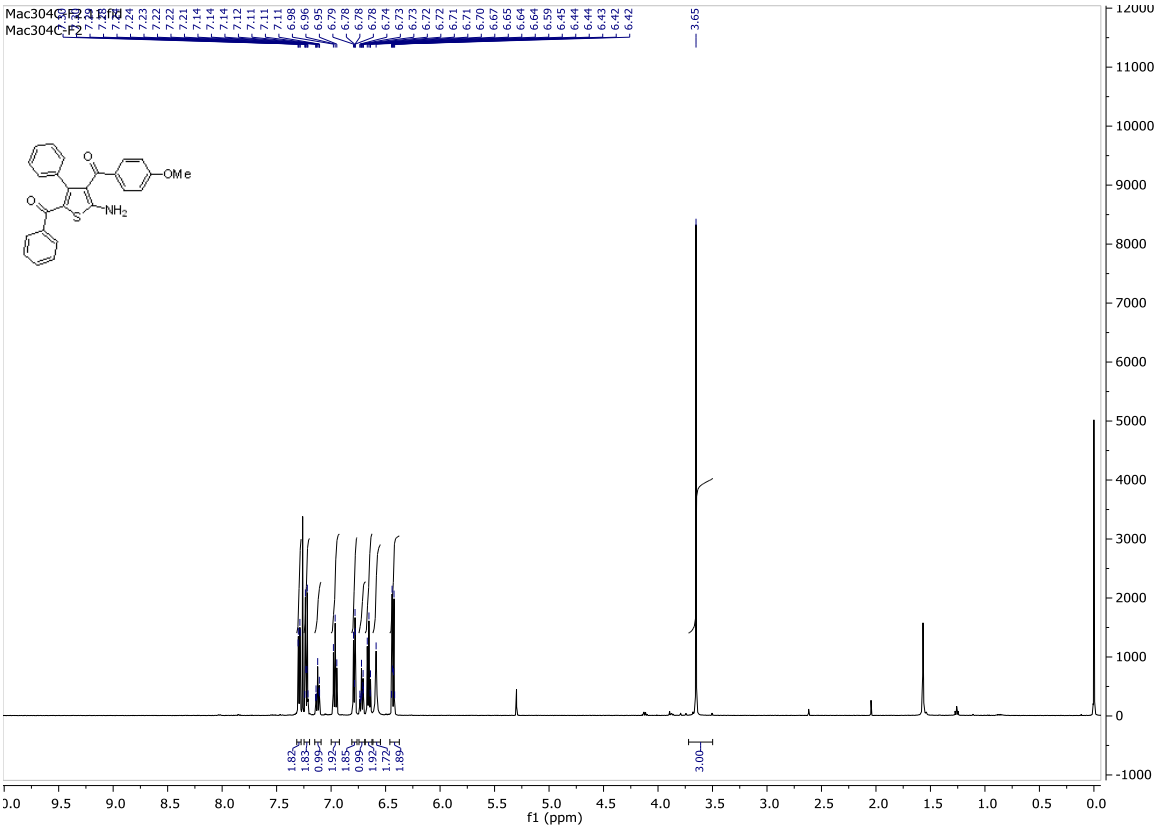


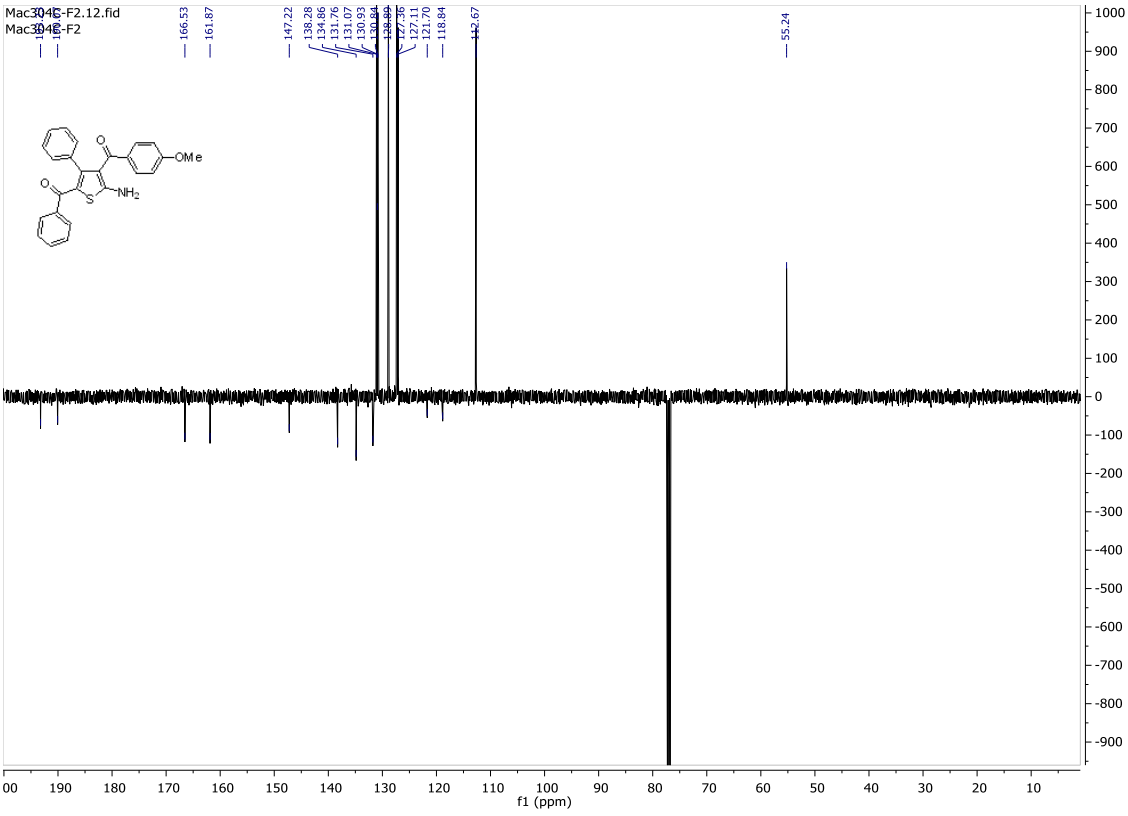
5-Benzoyl-4-phenyl-2-(p-tolyl)thiophene-3-carbonitrile (4s)



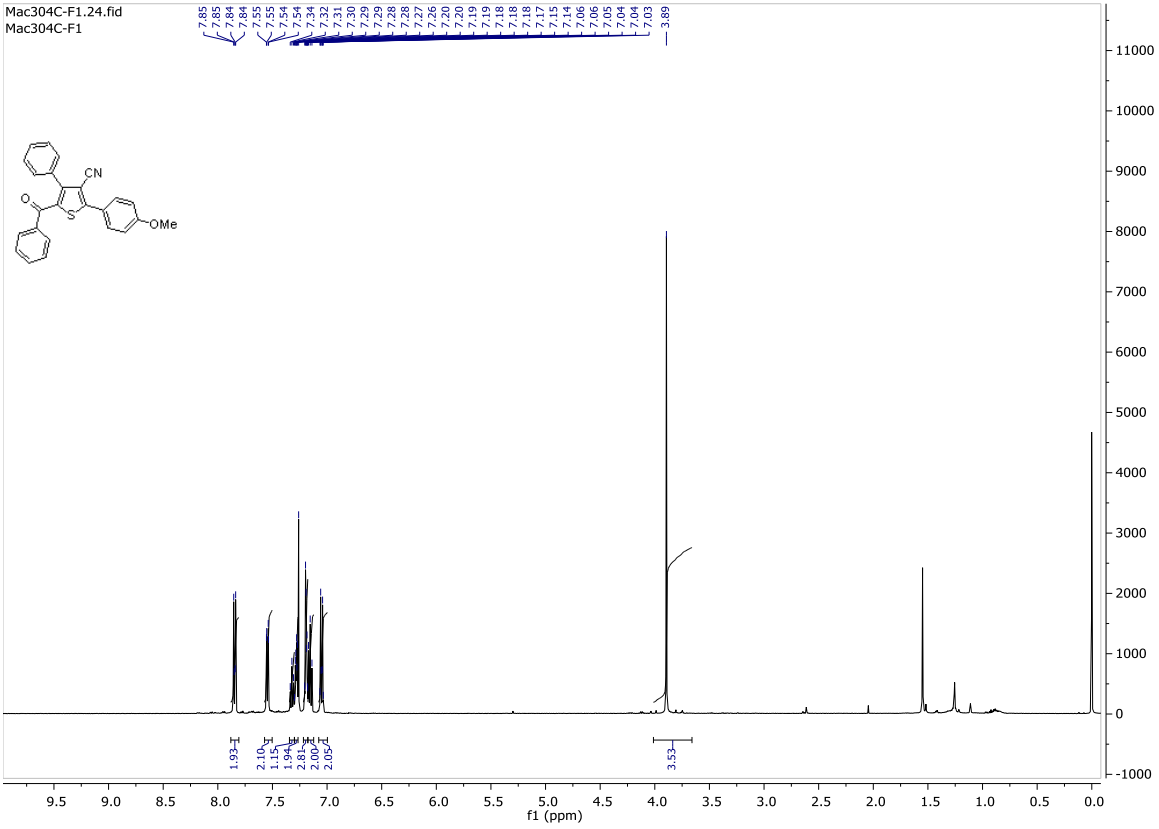


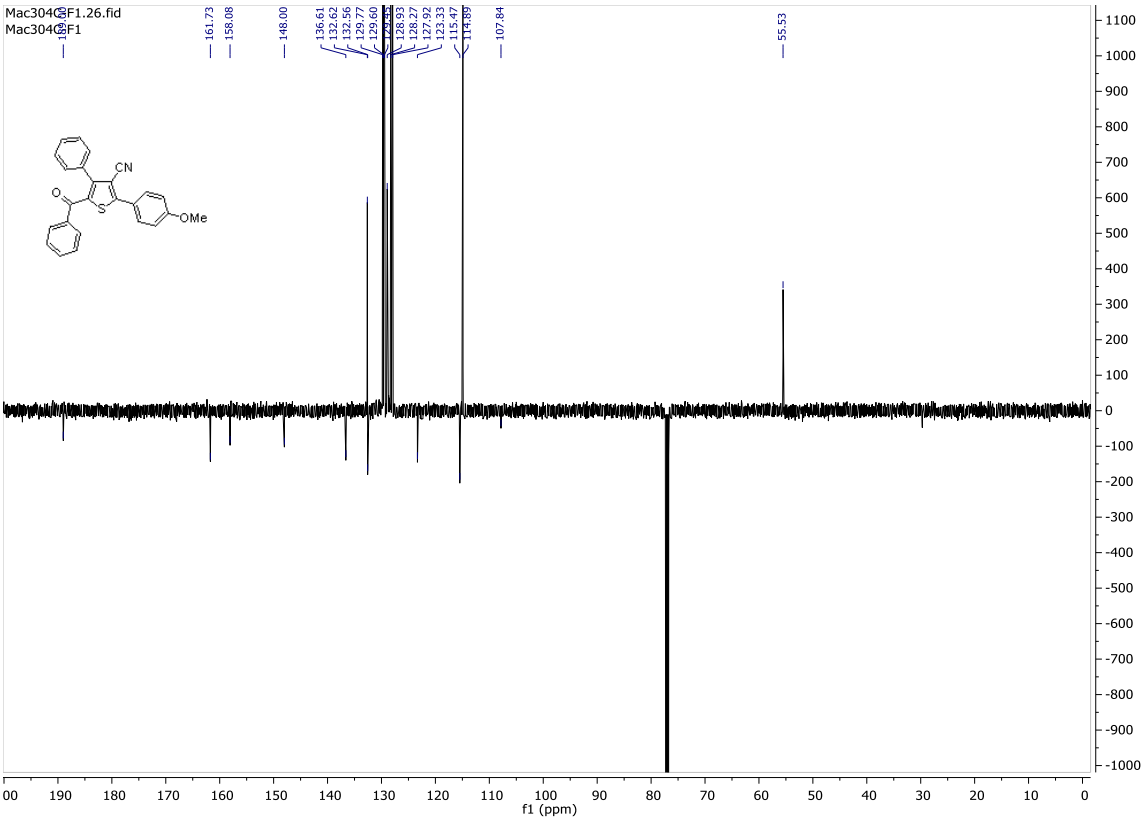
(5-Amino-4-(4-methoxybenzoyl)-3-phenylthiophen-2-yl)(phenyl)methanone (3t)



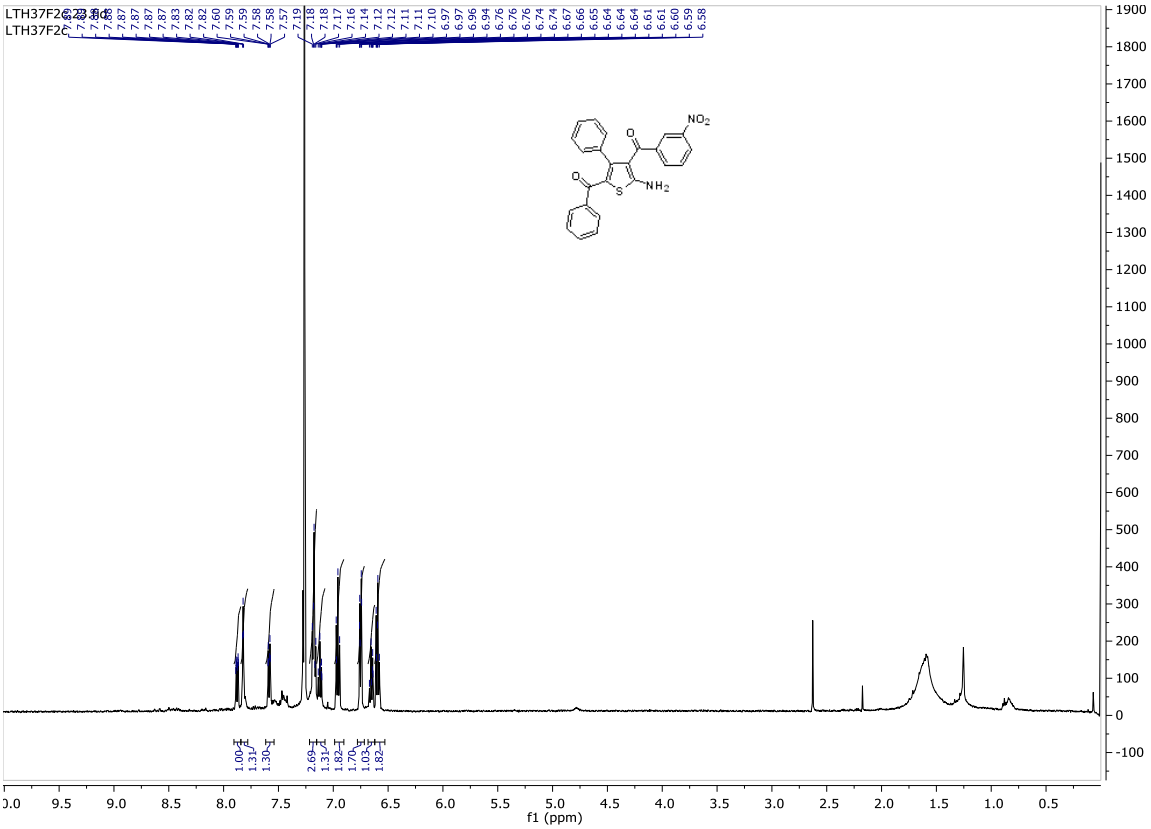


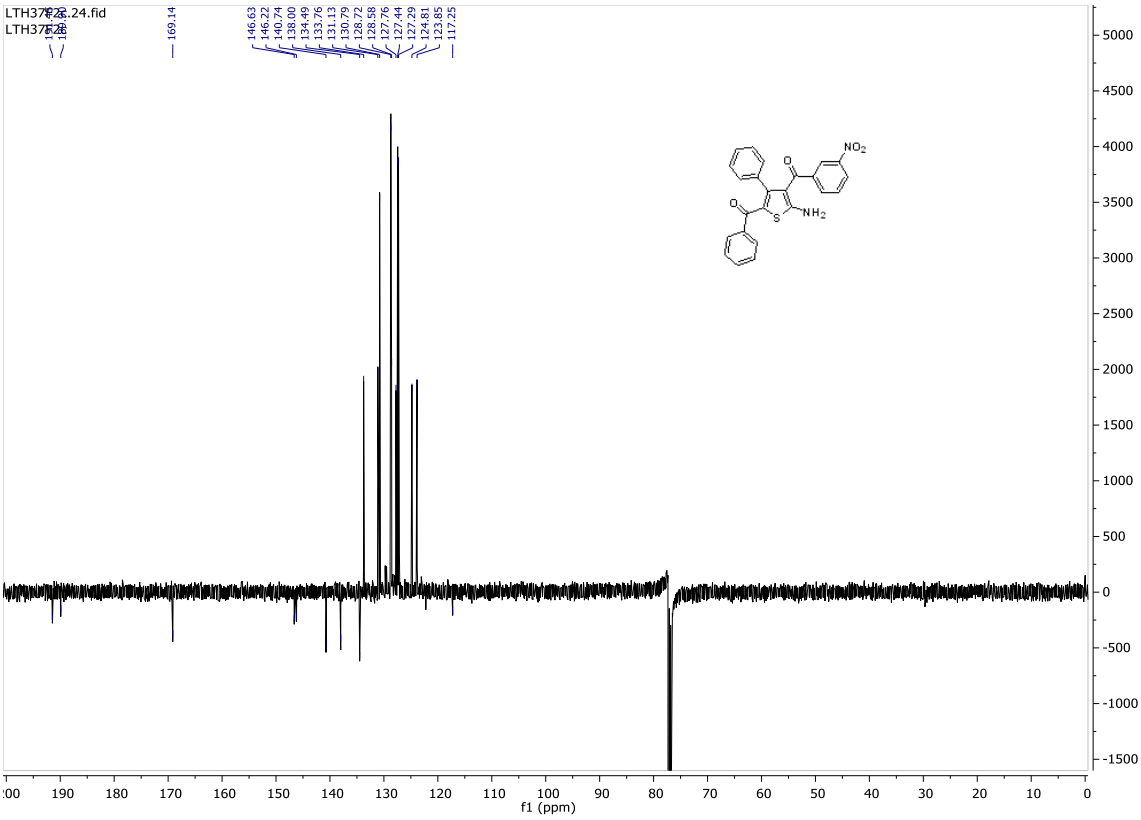
5-Benzoyl-2-(4-methoxyphenyl)-4-phenylthiophene-3-carbonitrile (4t)



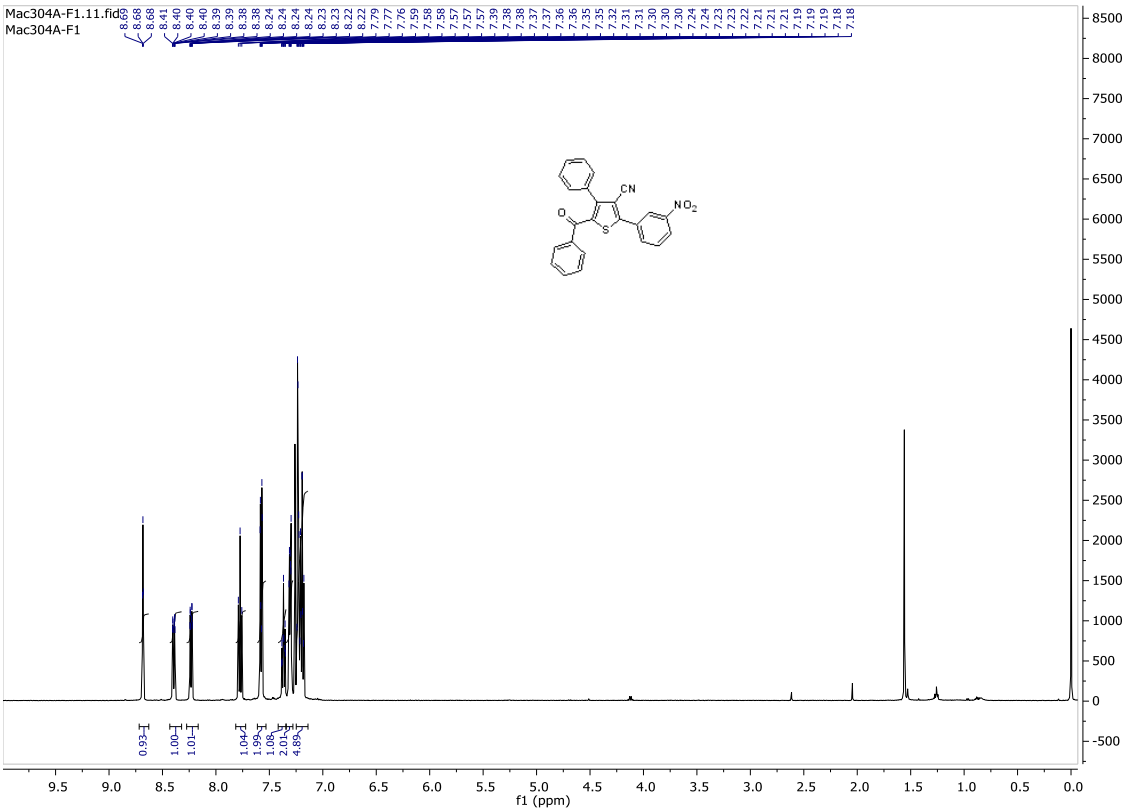


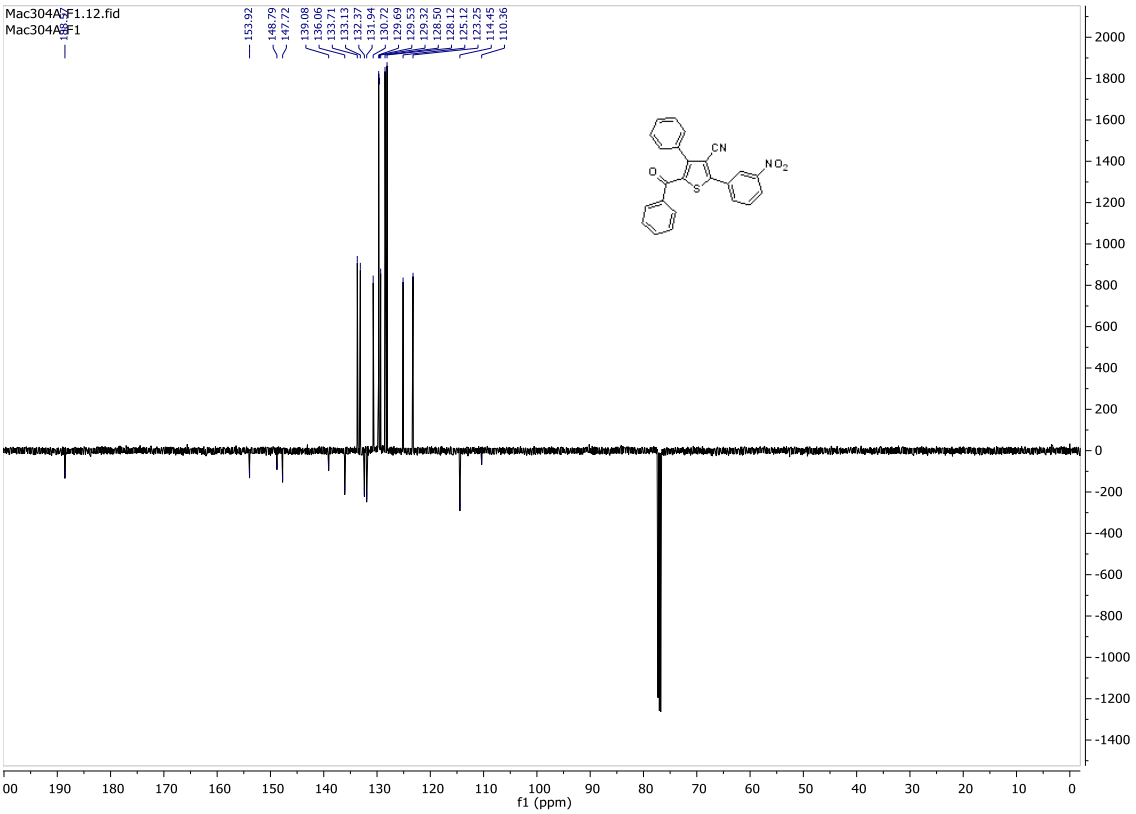
(5-Amino-4-(3-nitrobenzoyl)-3-phenylthiophen-2-yl)(phenyl)methanone (3u)



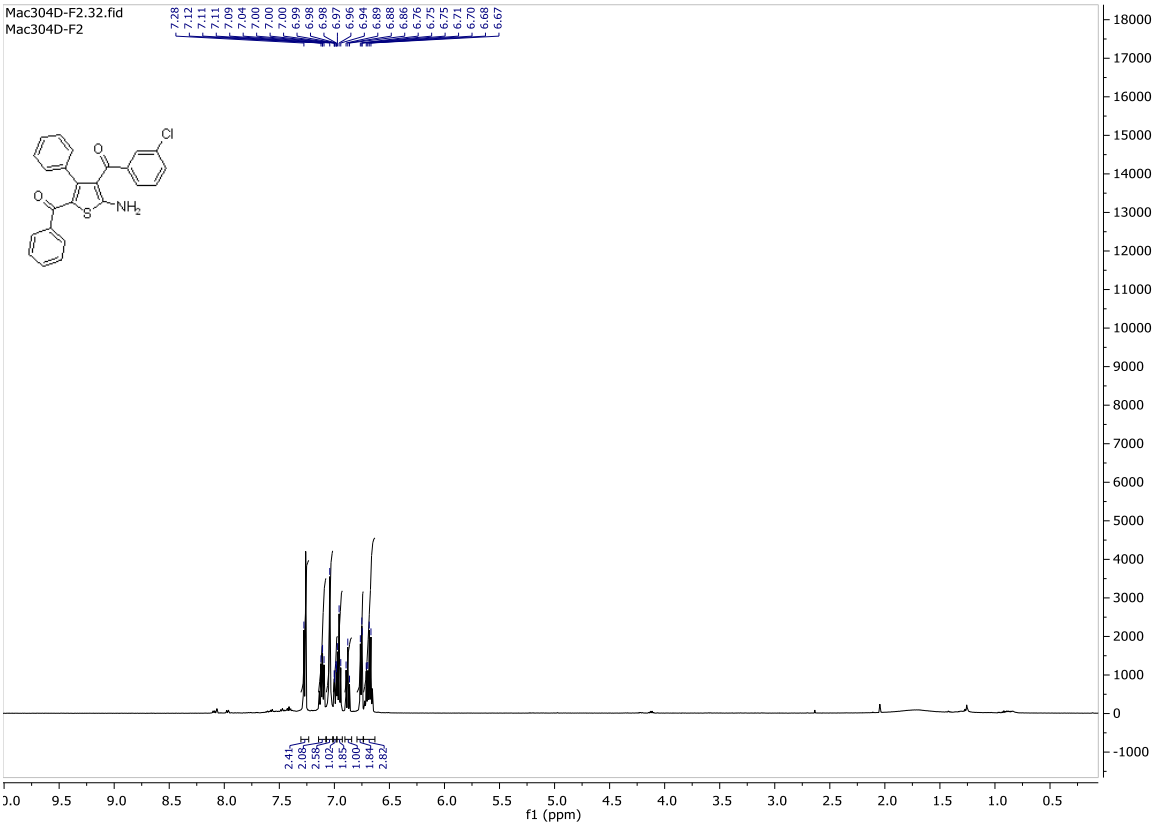


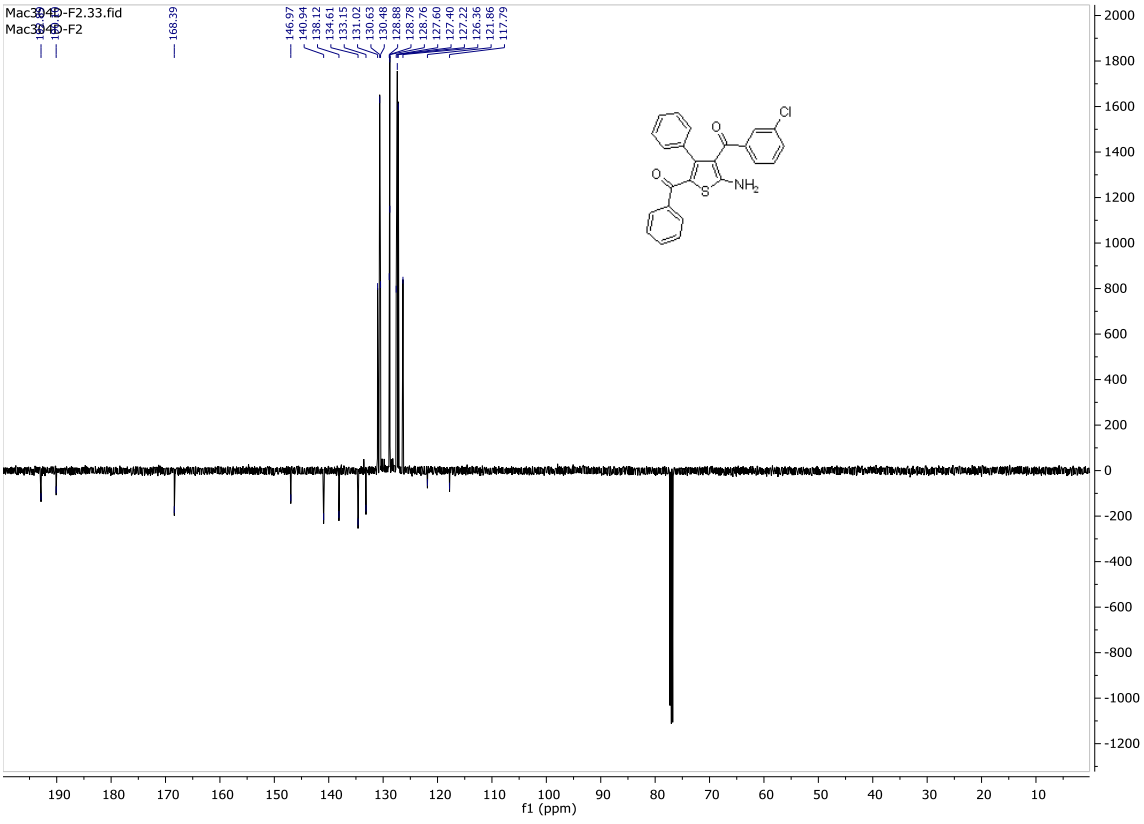
5-Benzoyl-2-(3-nitrophenyl)-4-phenylthiophene-3-carbonitrile (4u)



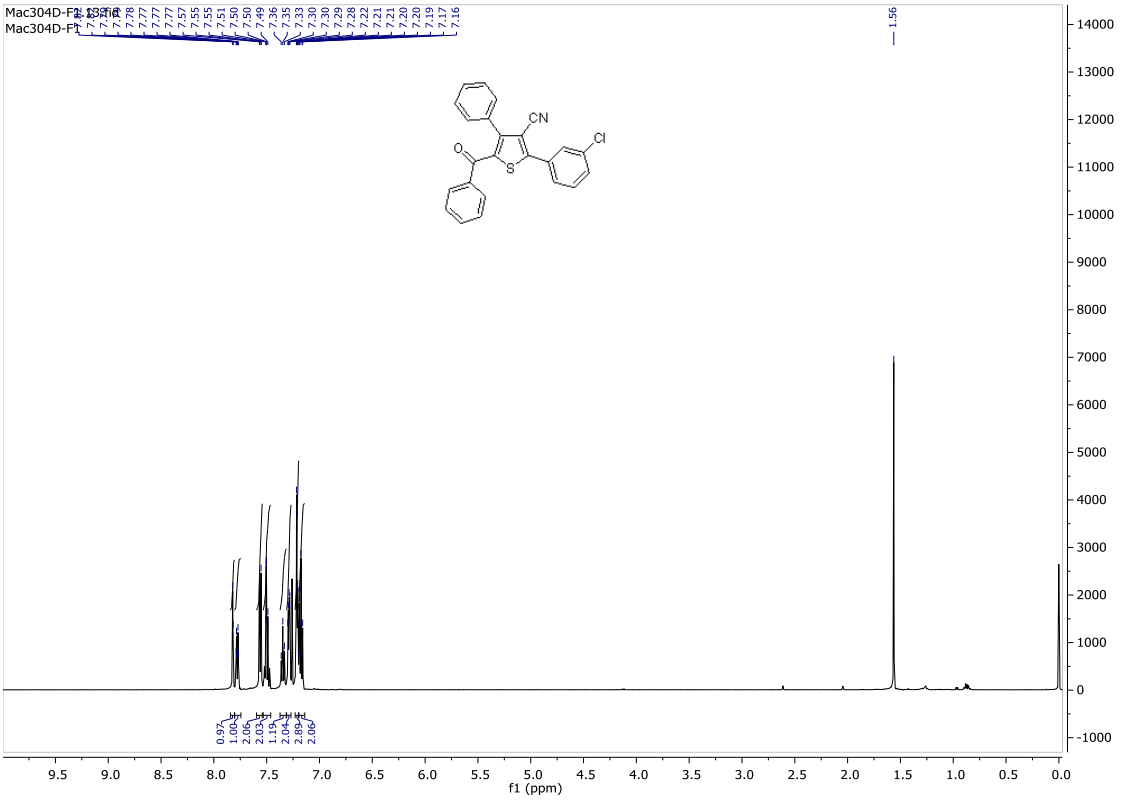


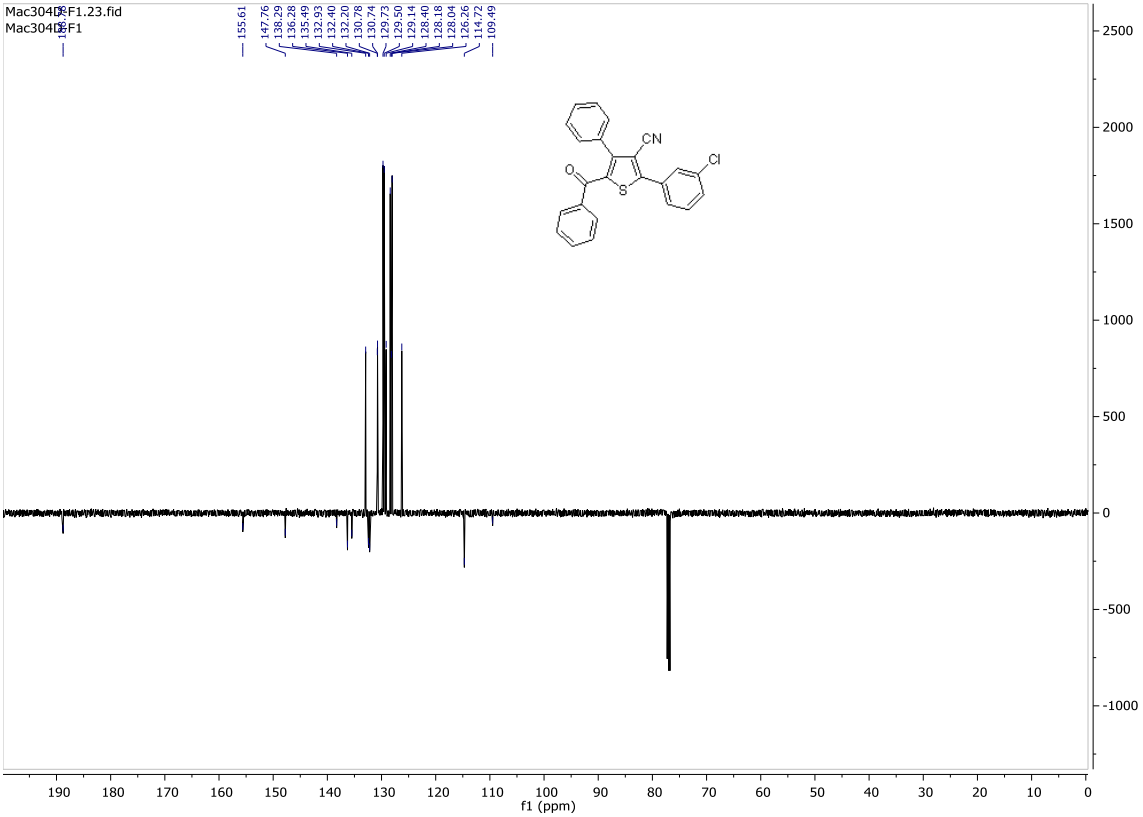
(5-Amino-4-(3-chlorobenzoyl)-3-phenylthiophen-2-yl)(phenyl)methanone (3v)



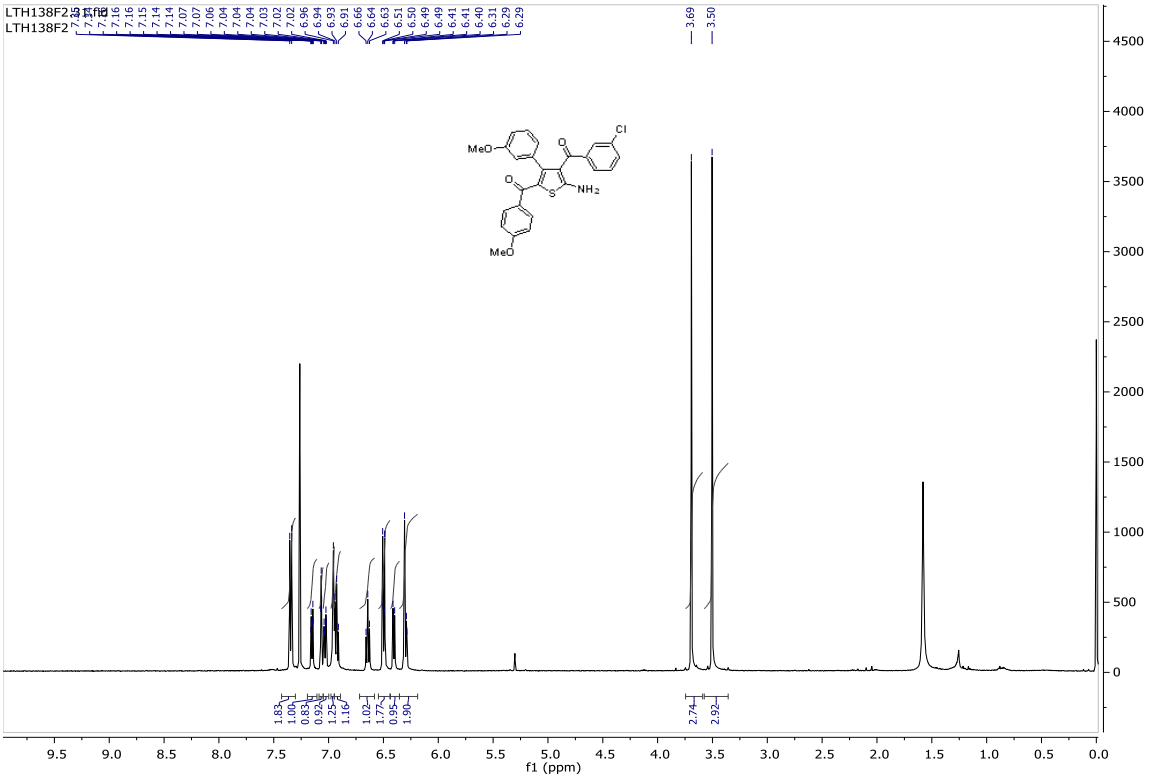


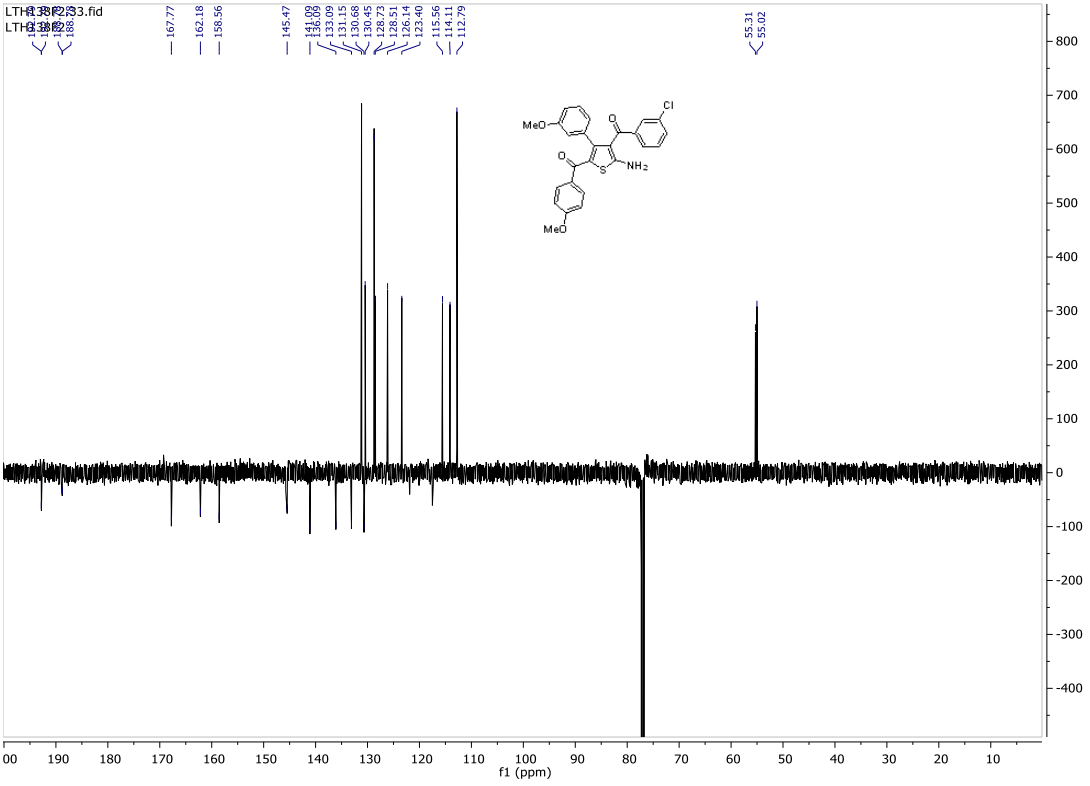
5-Benzoyl-2-(3-chlorophenyl)-4-phenylthiophene-3-carbonitrile (4v)



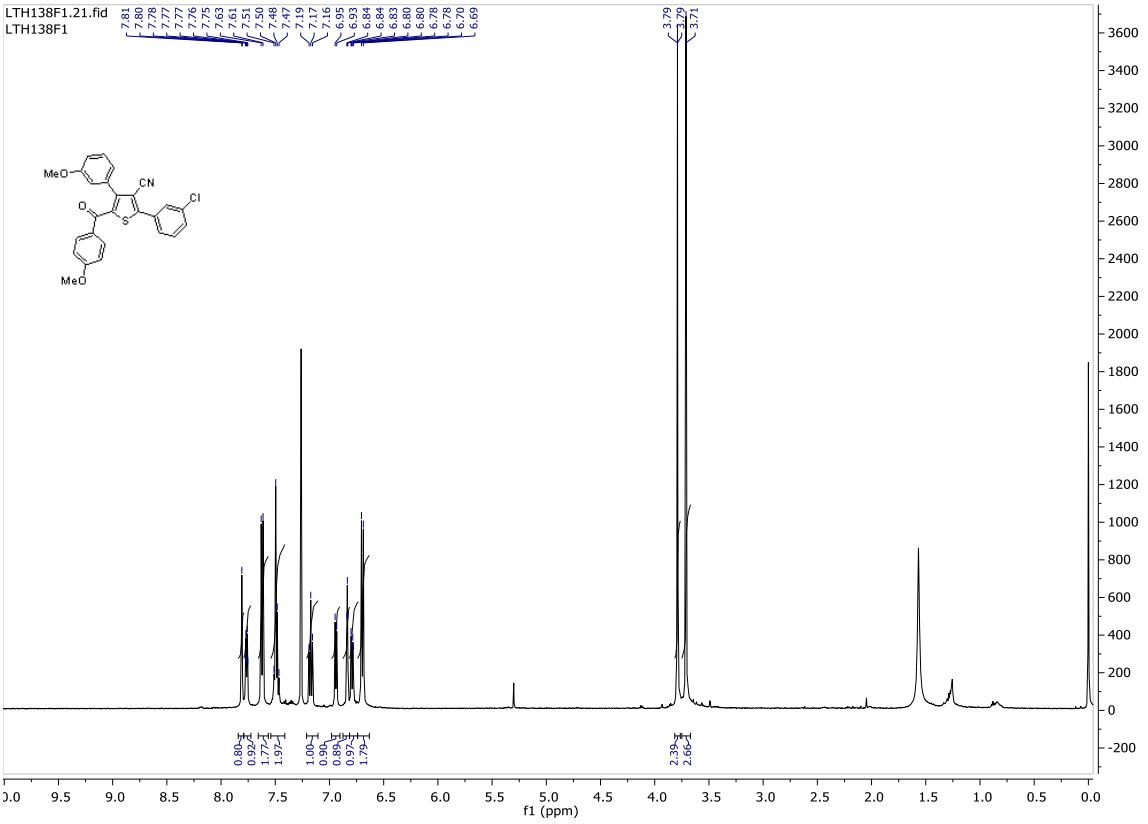


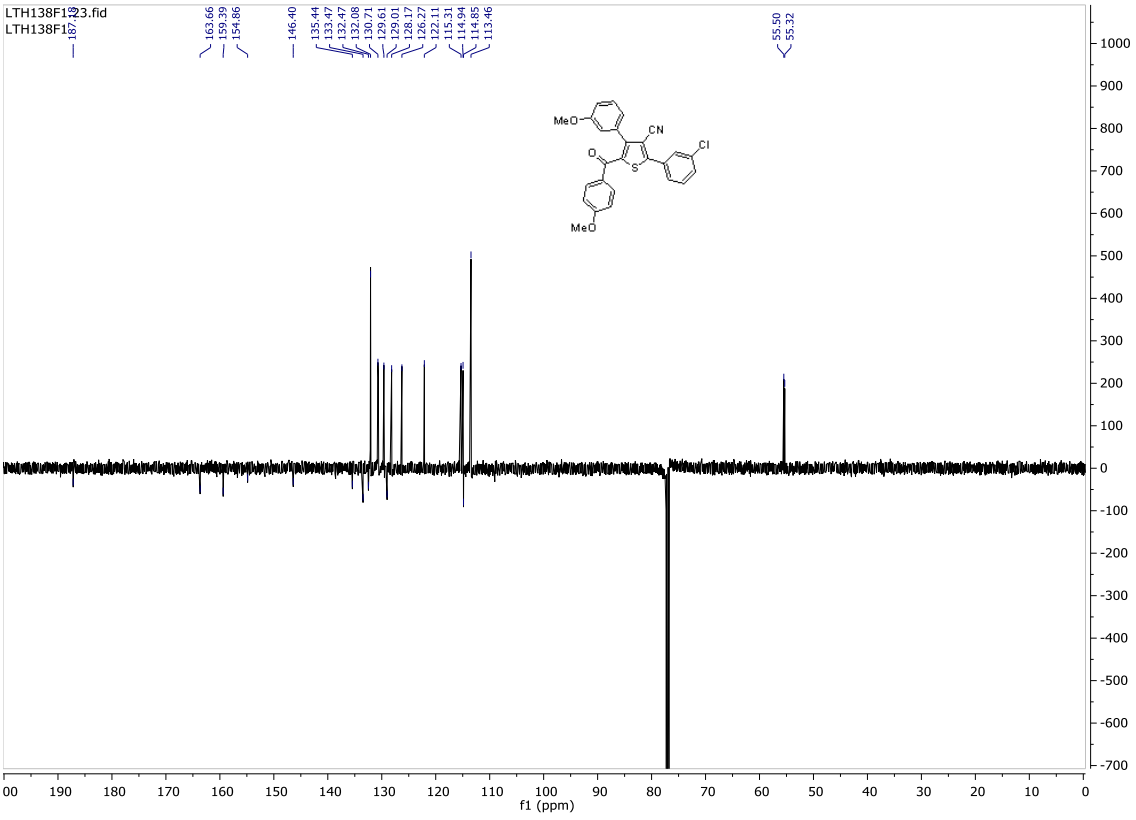
(5-Amino-4-(3-chlorobenzoyl)-3-(3-methoxyphenyl)thiophen-2-yl)(4-methoxyphenyl) methanone (3x)



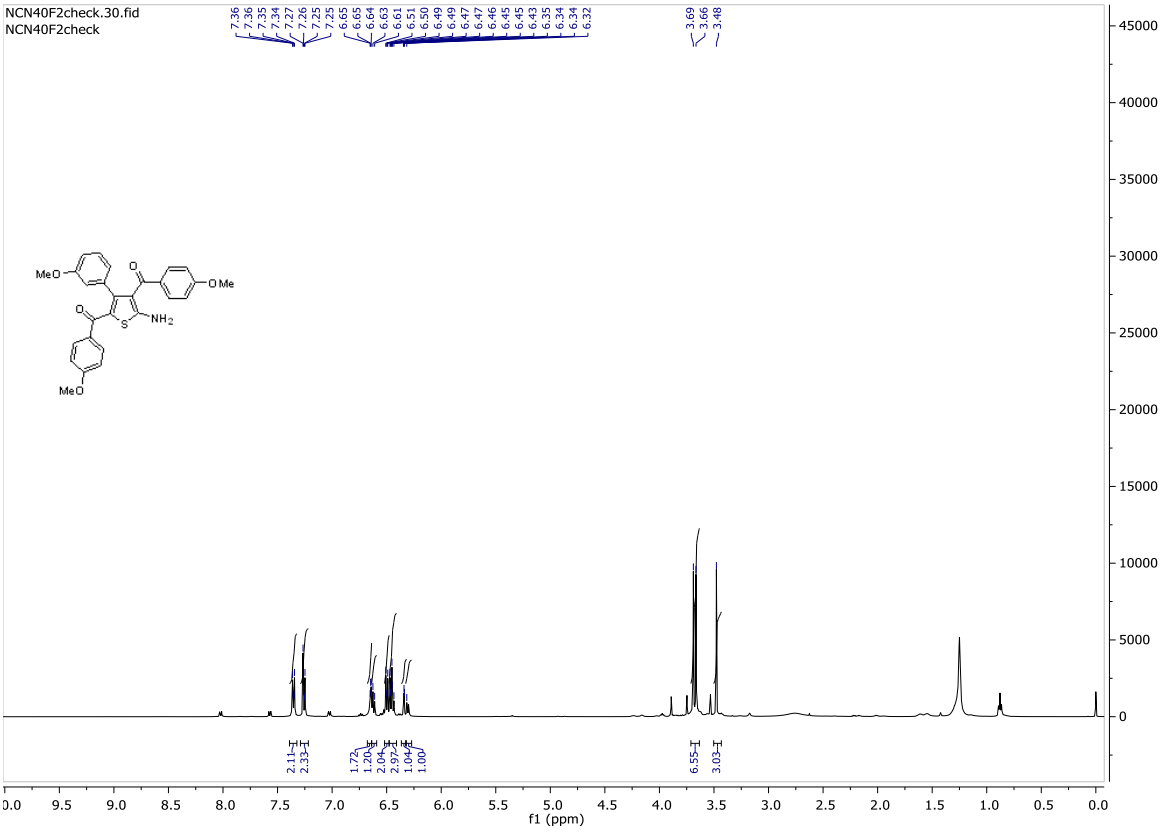


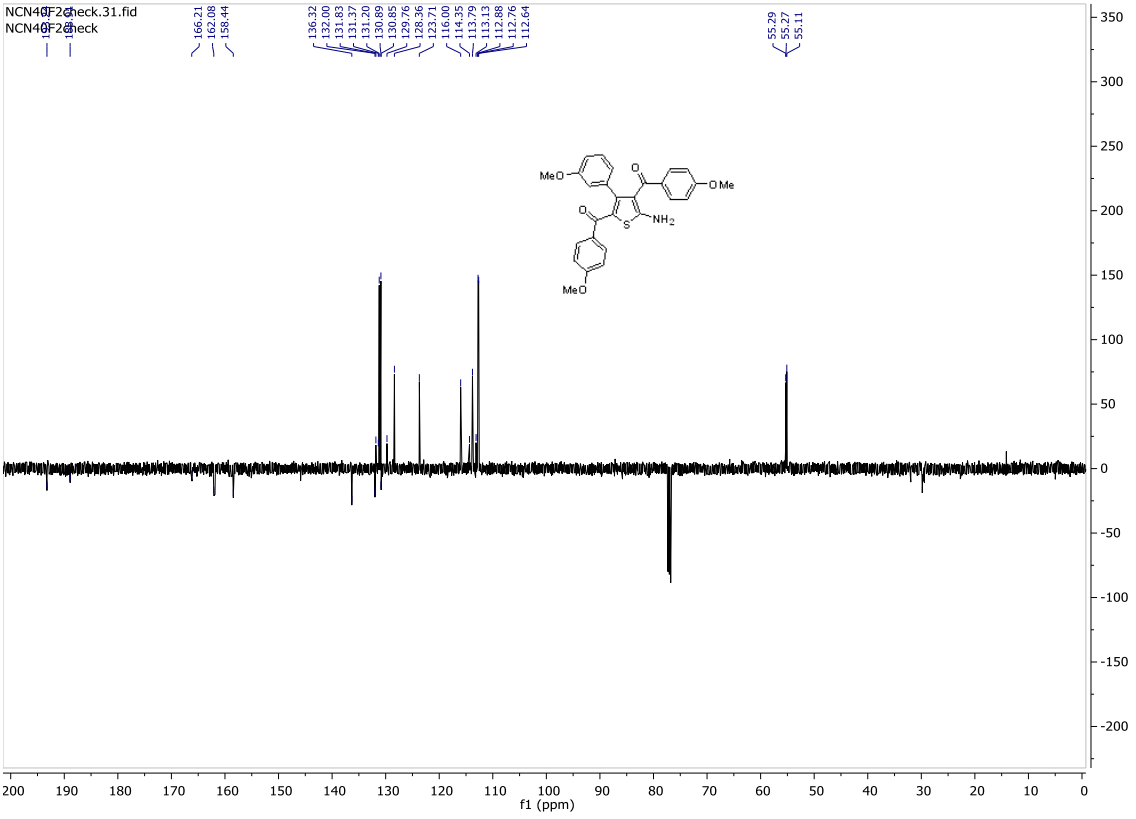
2-(3-Chlorophenyl)-5-(4-methoxybenzoyl)-4-(3-methoxyphenyl)thiophene-3-carbonitrile (4x)



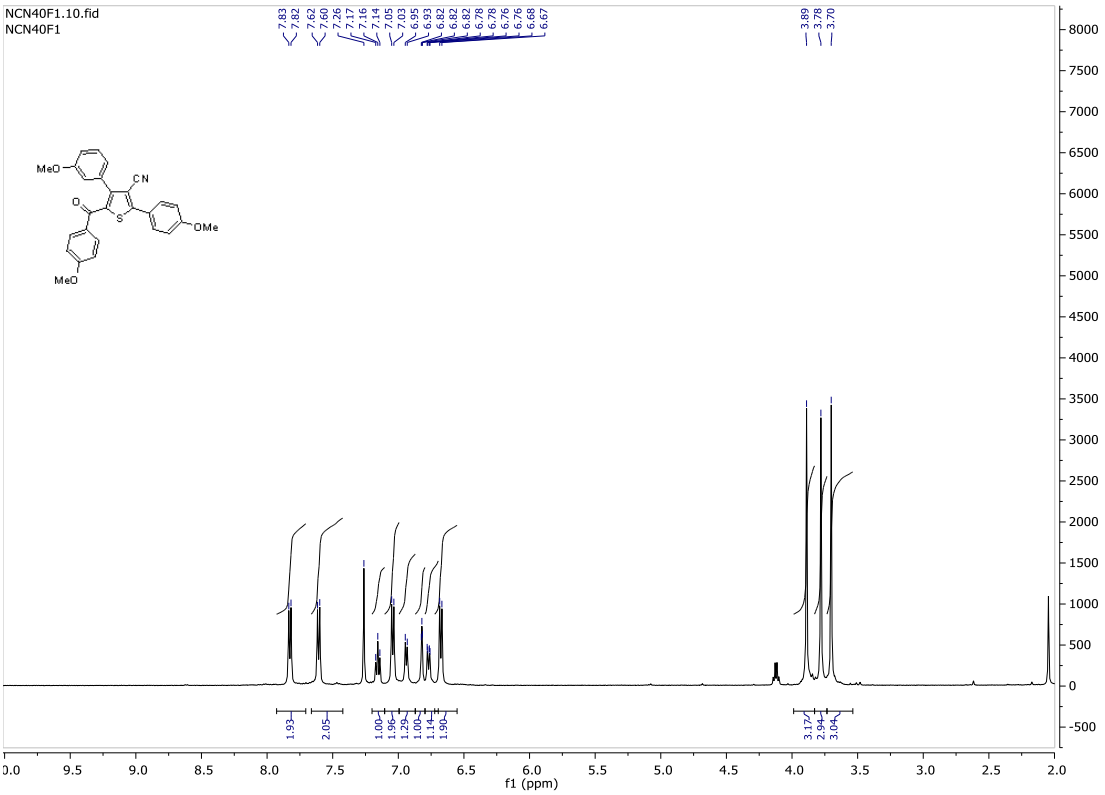


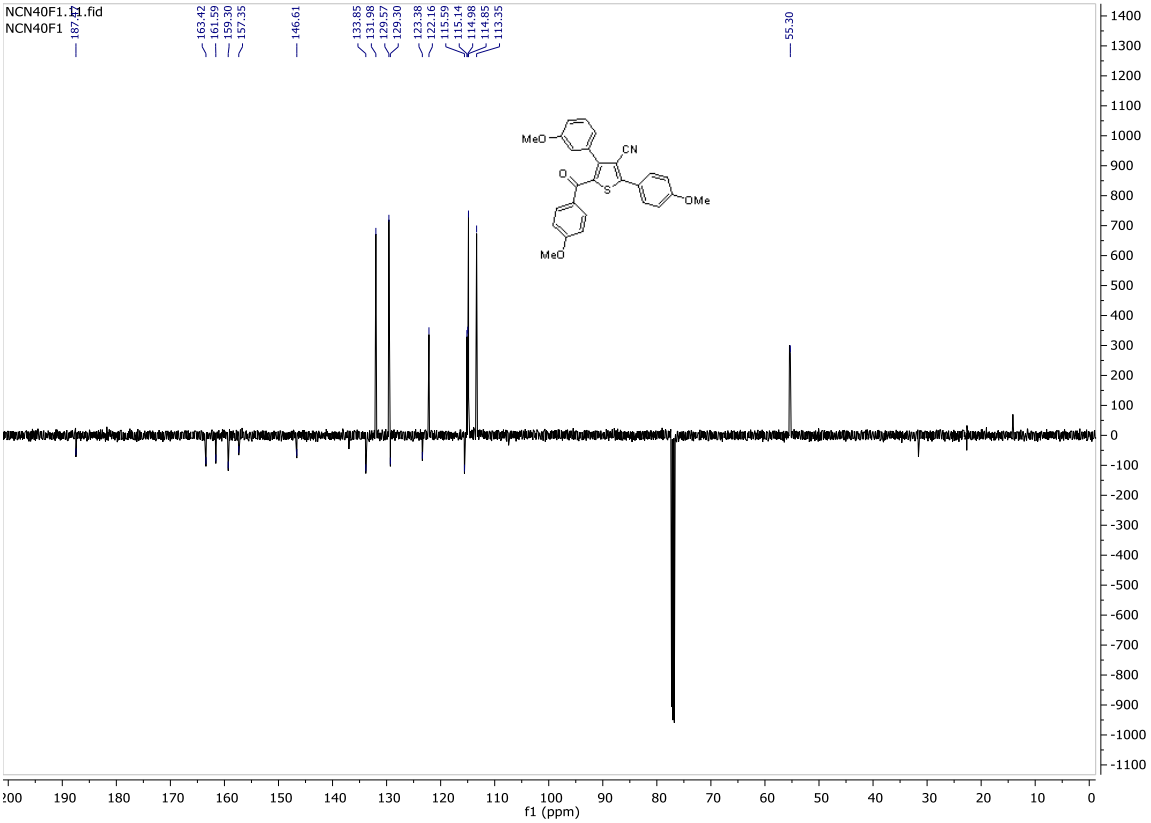
(5-Amino-3-(3-methoxyphenyl)thiophene-2,4-diyl)bis((4-methoxyphenyl)methanone) (3y)



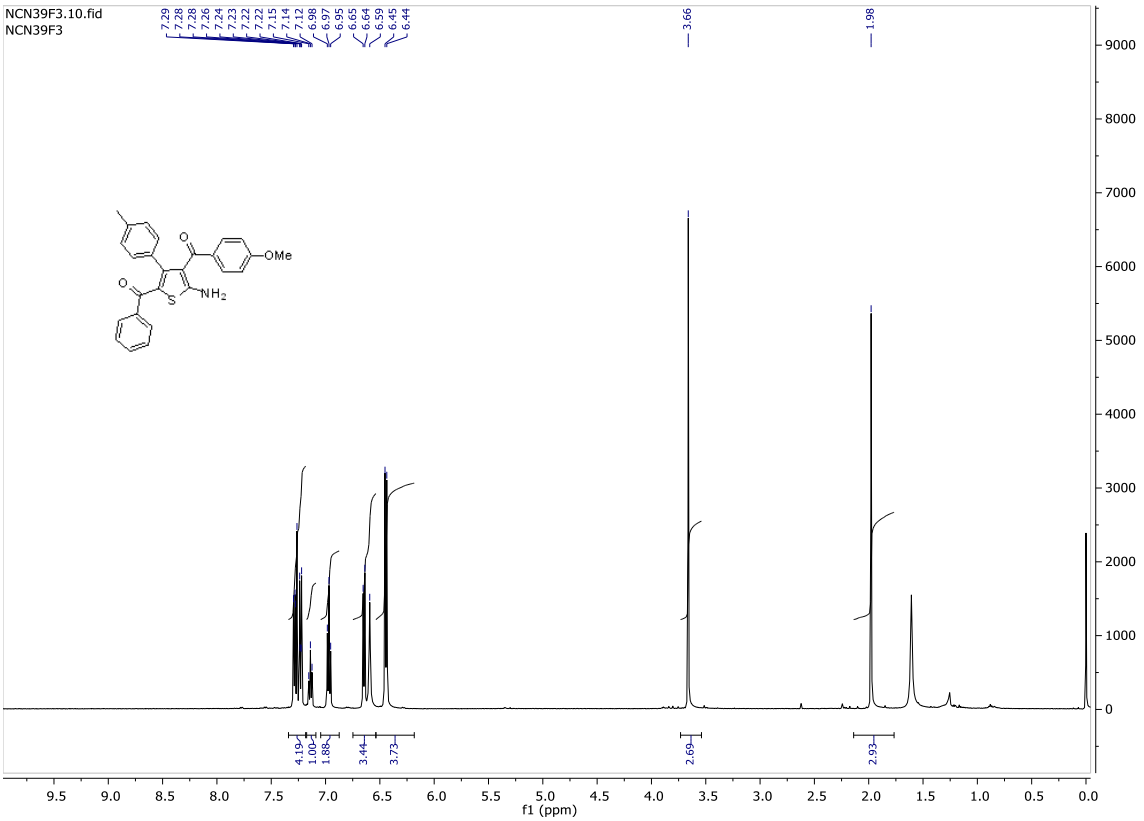


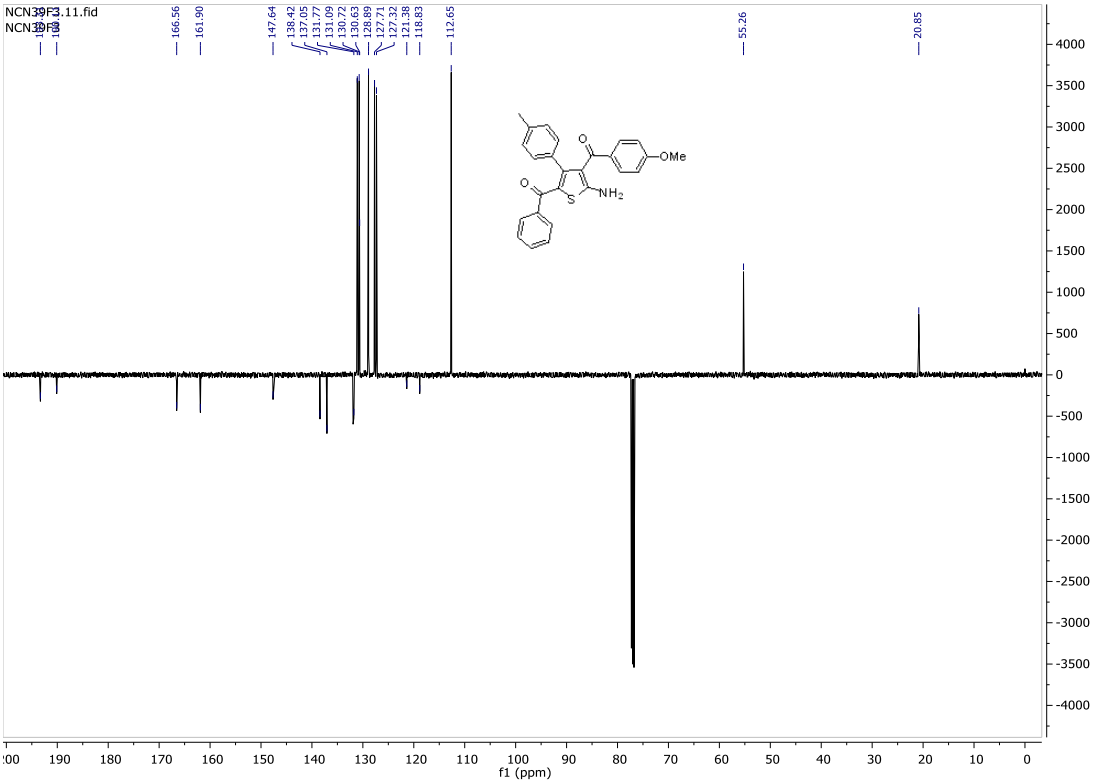
5-(4-Methoxybenzoyl)-4-(3-methoxyphenyl)-2-(4-methoxyphenyl)thiophene-3-carbonitrile (4y)



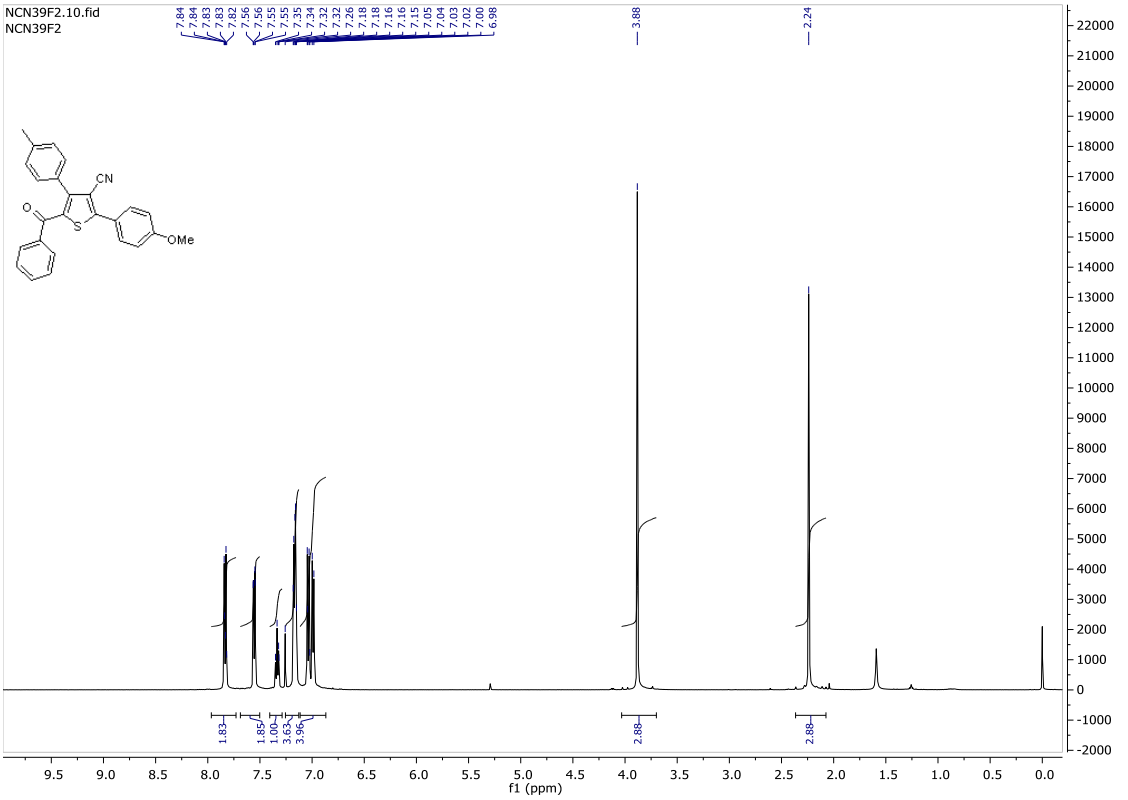


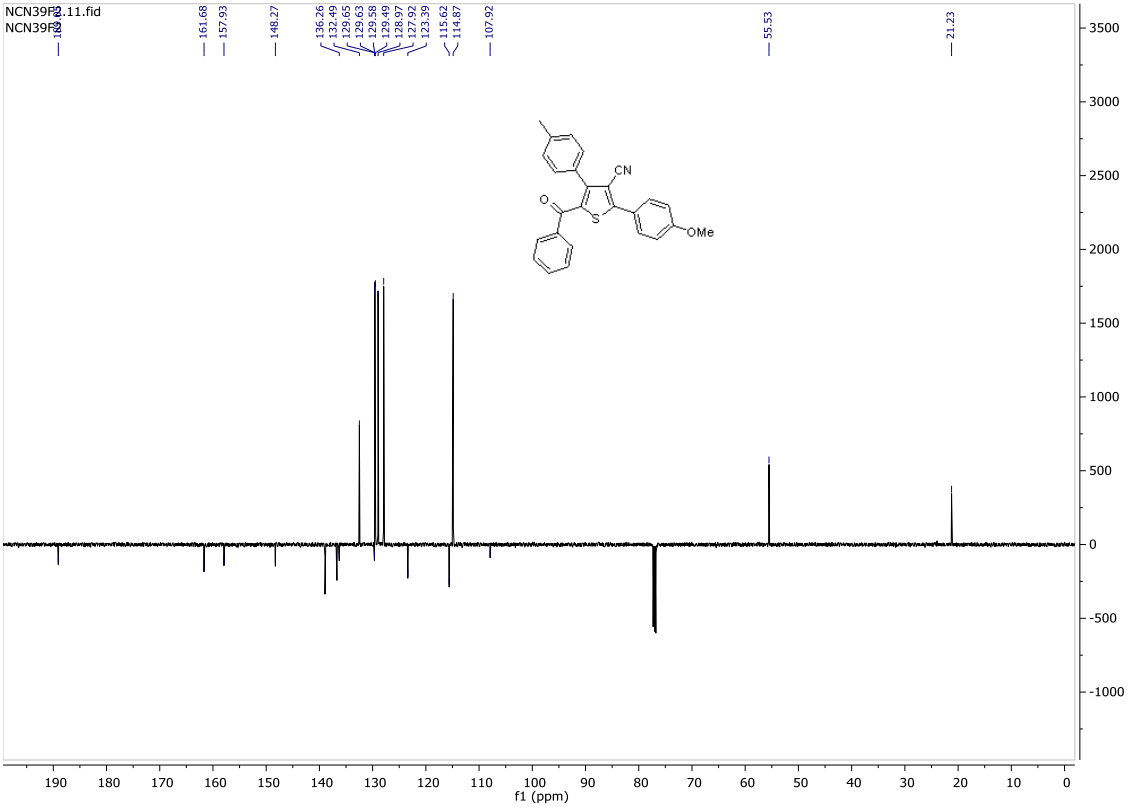
(5-Amino-4-(4-methoxybenzoyl)-3-(p-tolyl)thiophen-2-yl)(phenyl)methanone (3z)



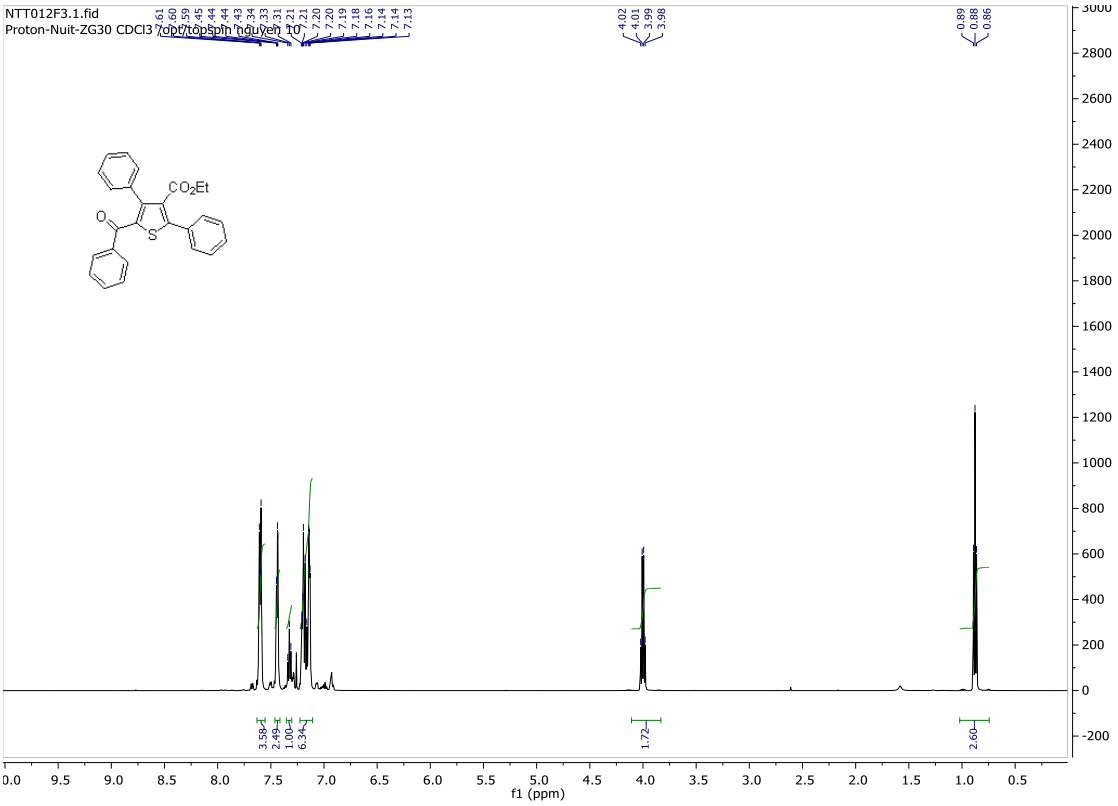


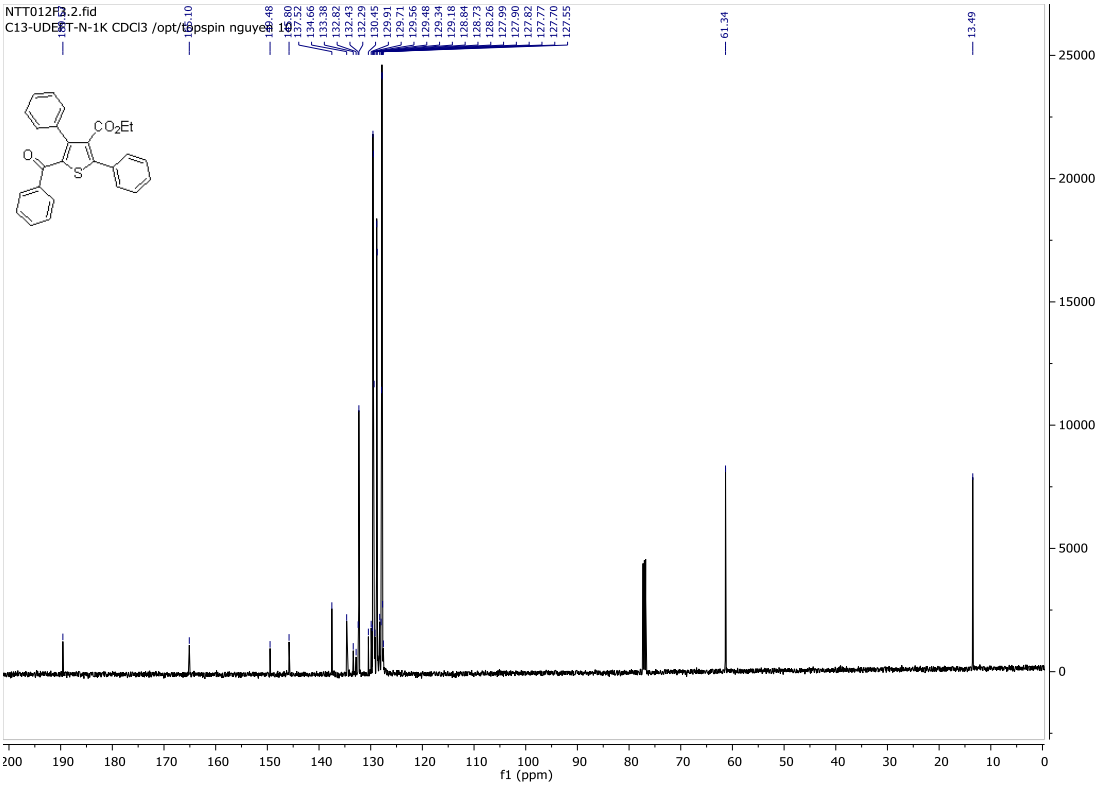
5-Benzoyl-2-(4-methoxyphenyl)-4-(p-tolyl)thiophene-3-carbonitrile (4z)



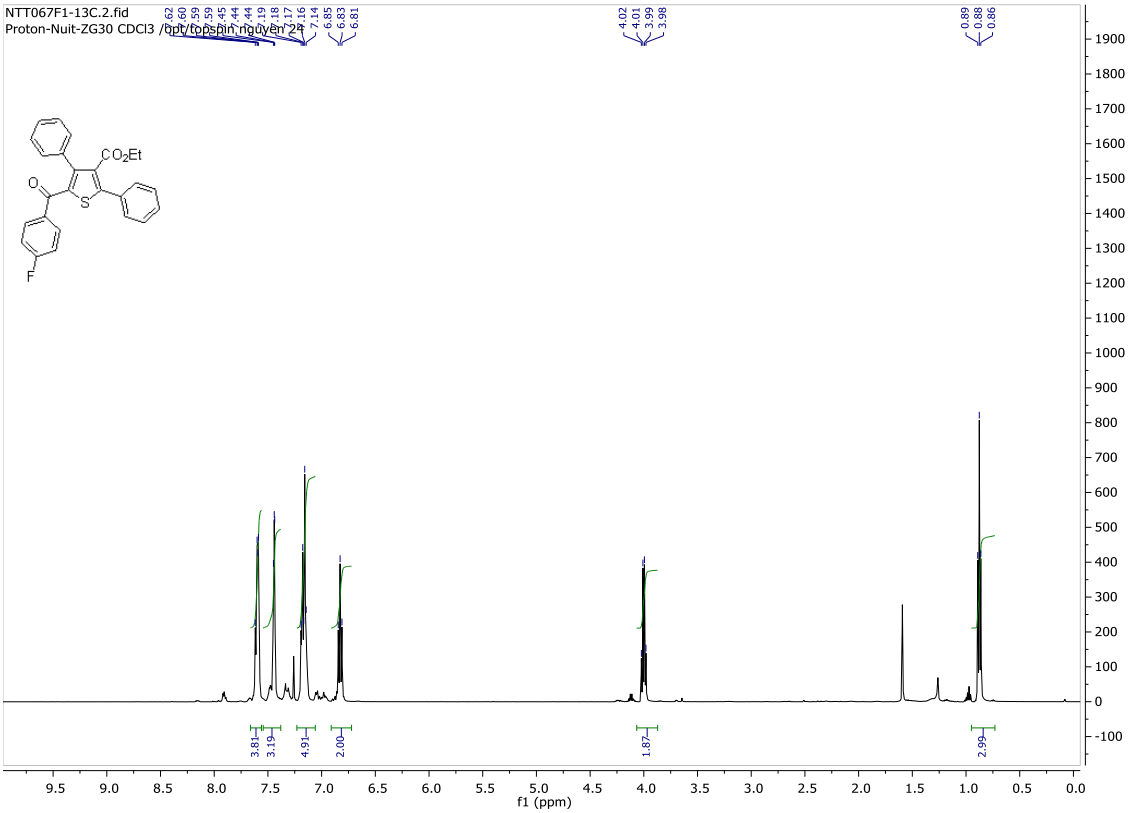


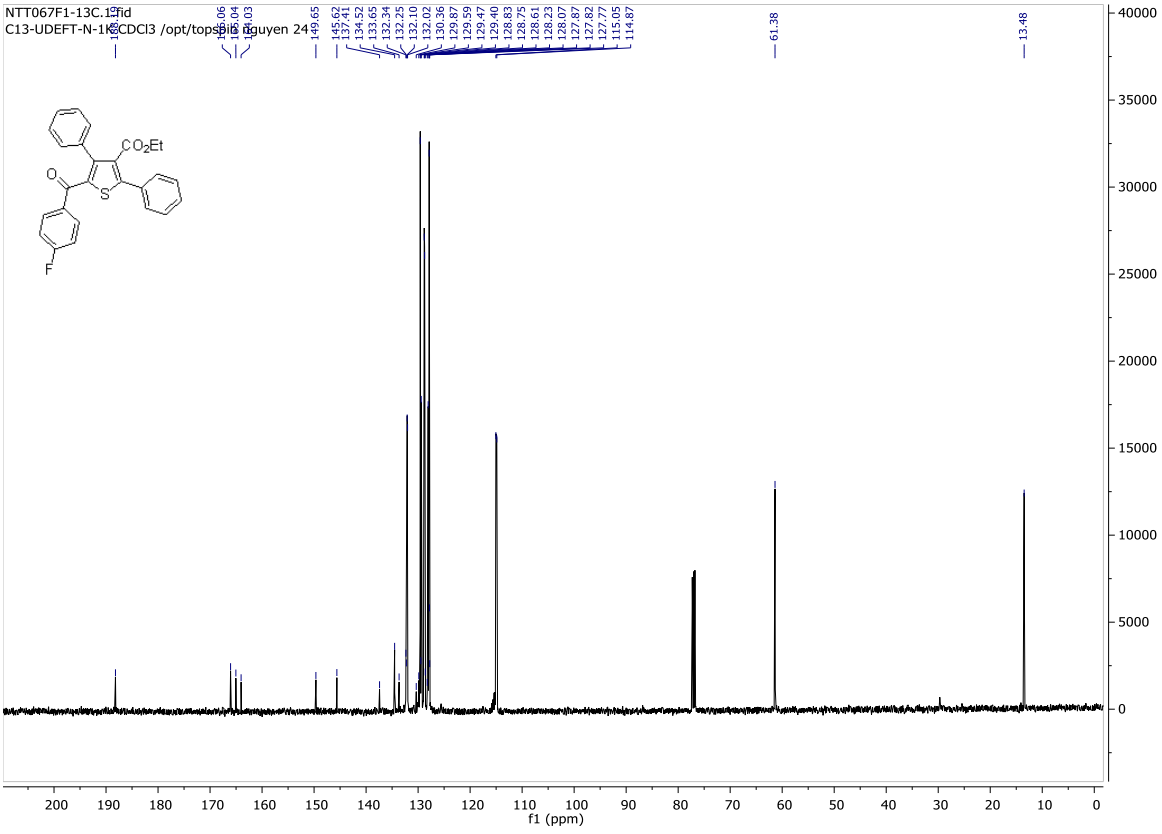
Ethyl 5-benzoyl-2,4-diphenylthiophene-3-carboxylate (6a)



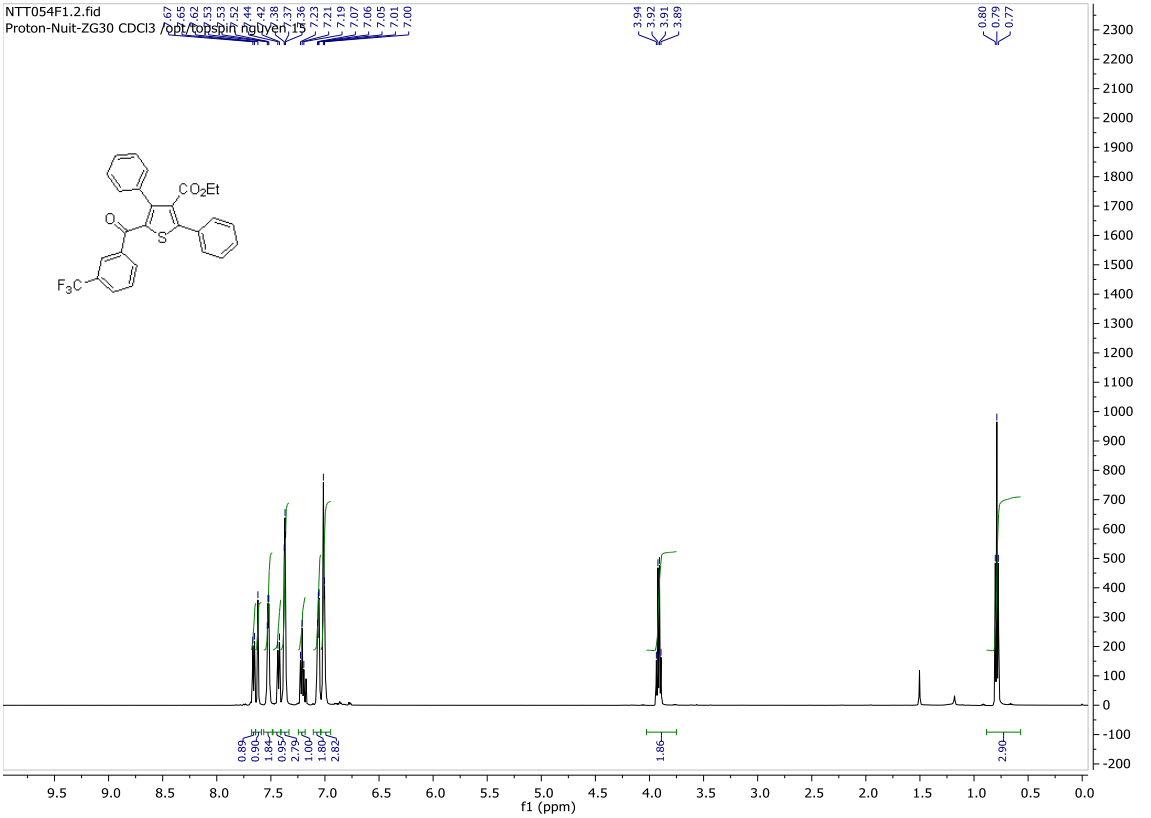


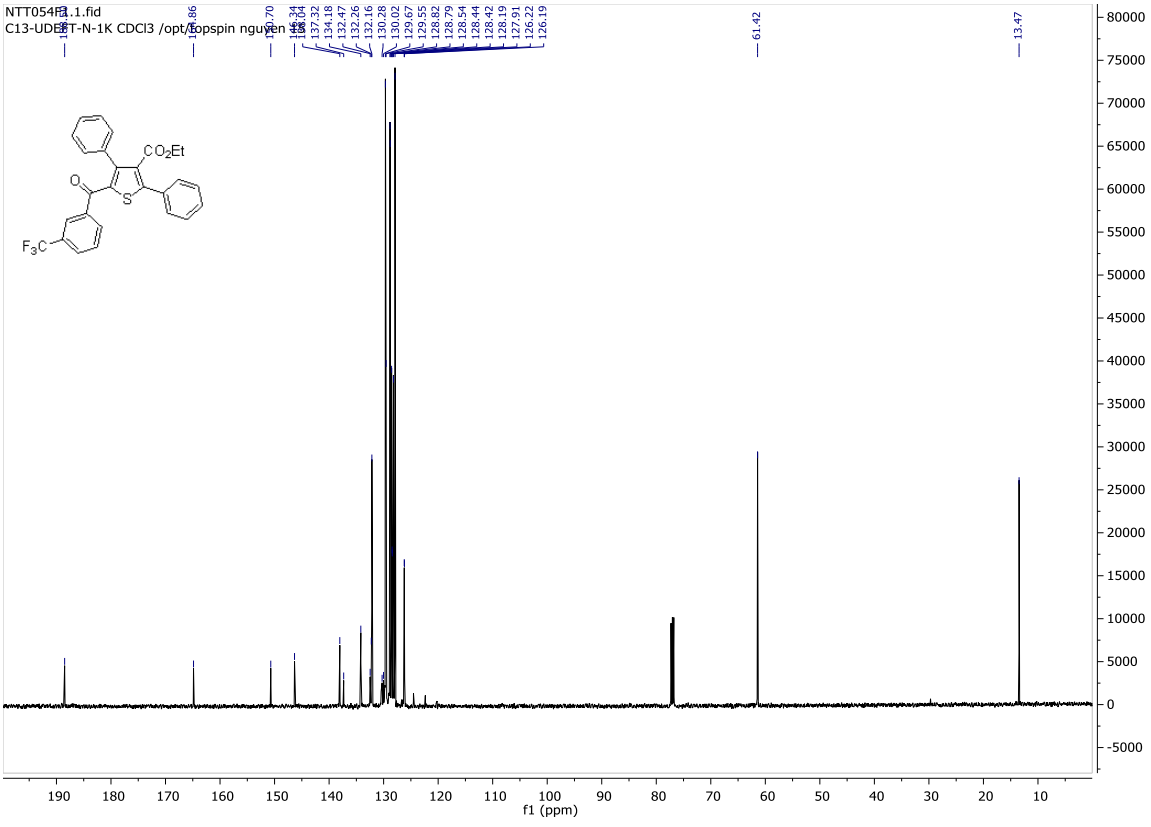
Ethyl 5-(4-fluorobenzoyl)-2,4-diphenylthiophene-3-carboxylate (6b)



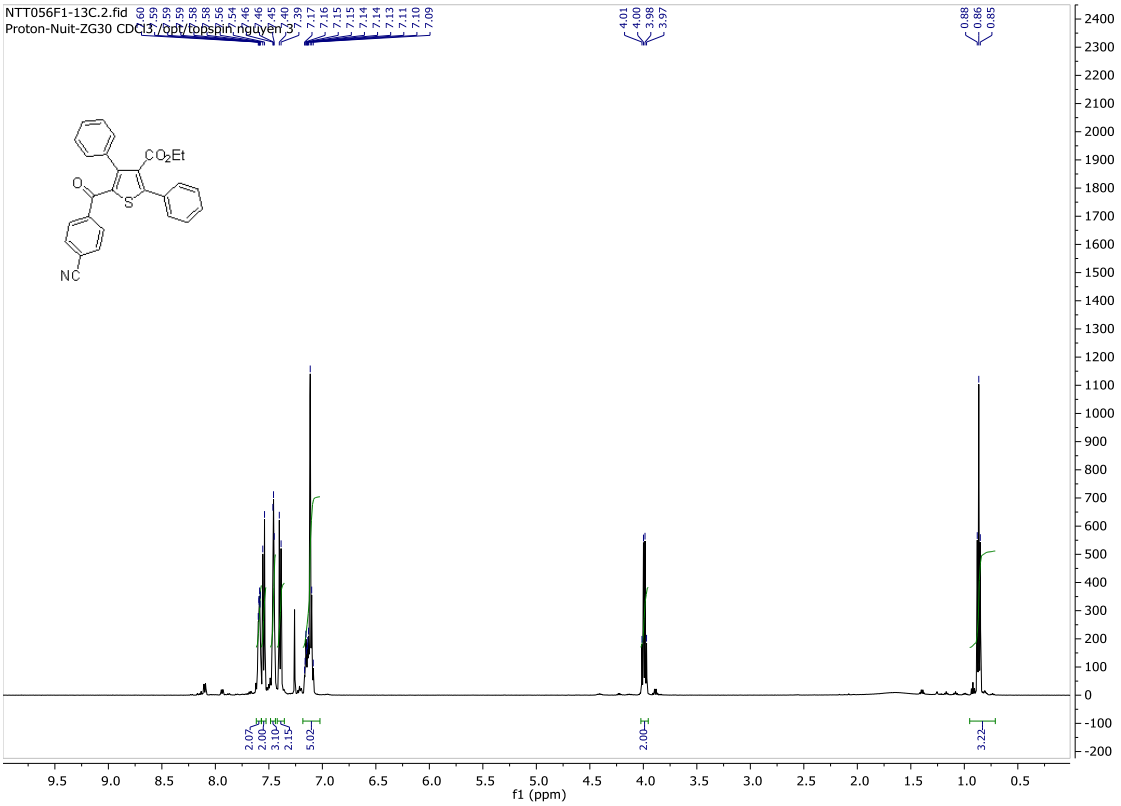


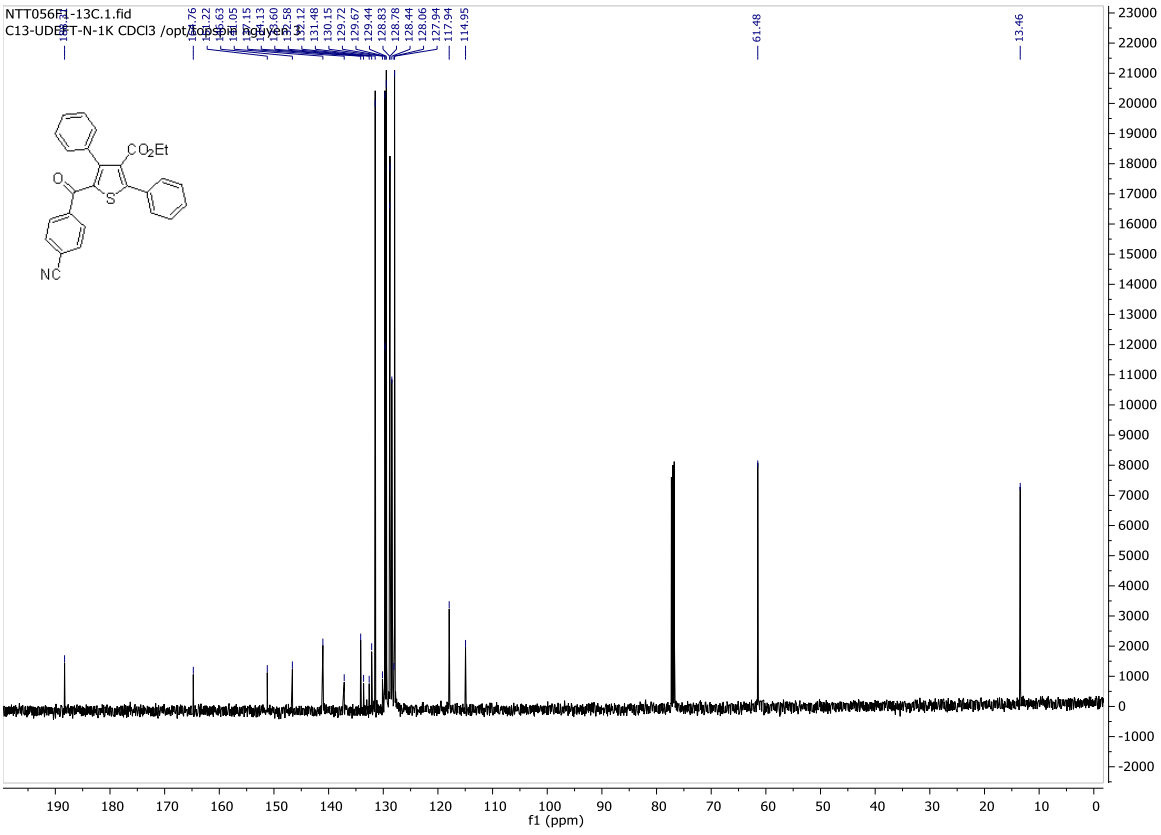
Ethyl 2,4-diphenyl-5-(3-(trifluoromethyl)benzoyl)thiophene-3-carboxylate (6c)



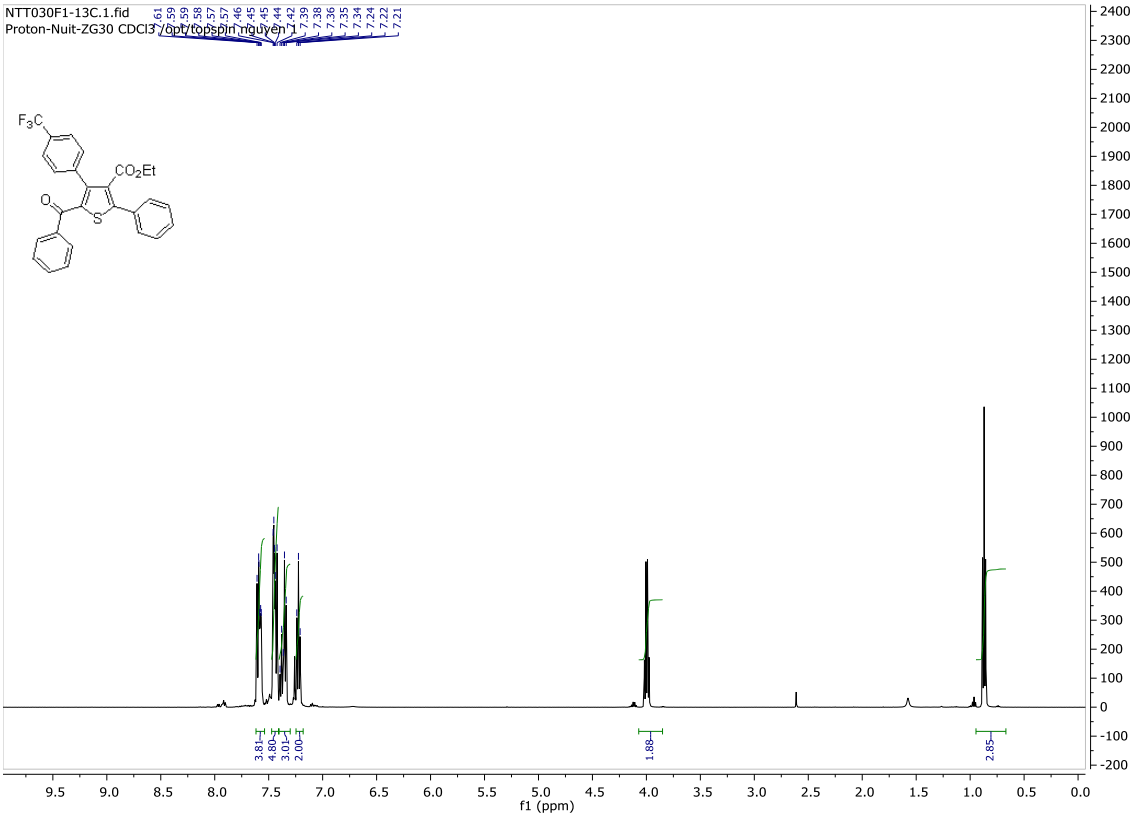


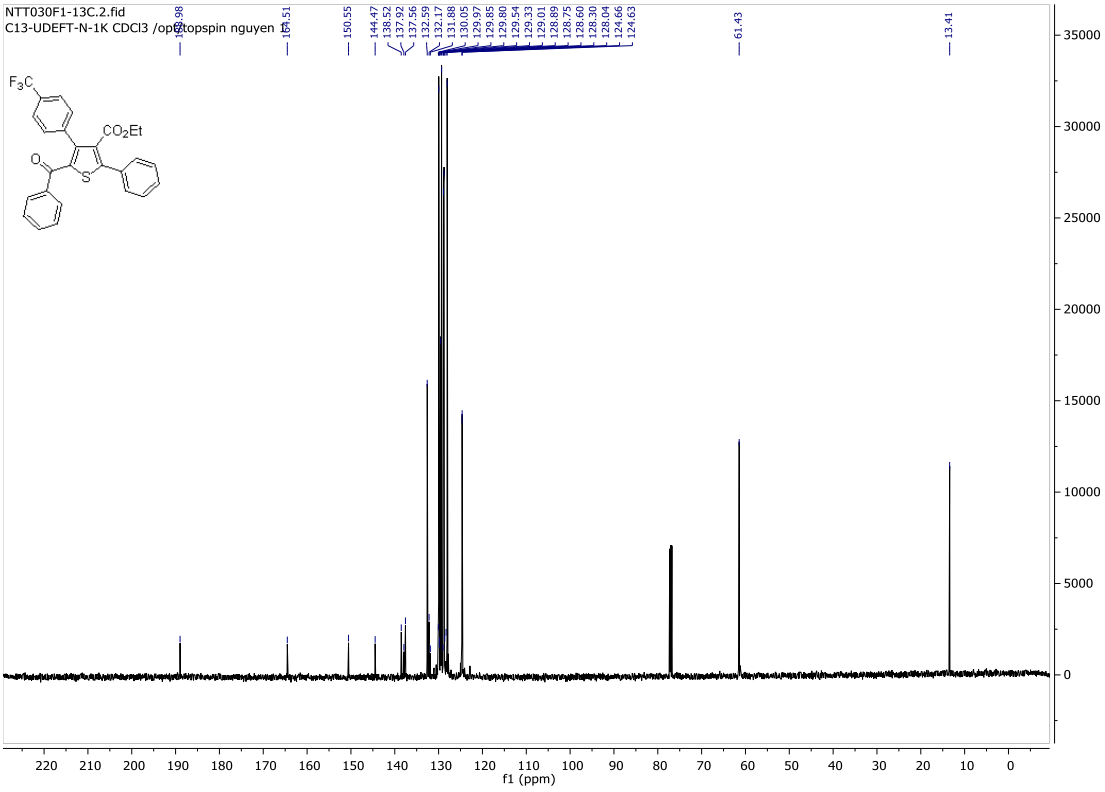
Ethyl 5-(4-cyanobenzoyl)-2,4-diphenylthiophene-3-carboxylate (6d)



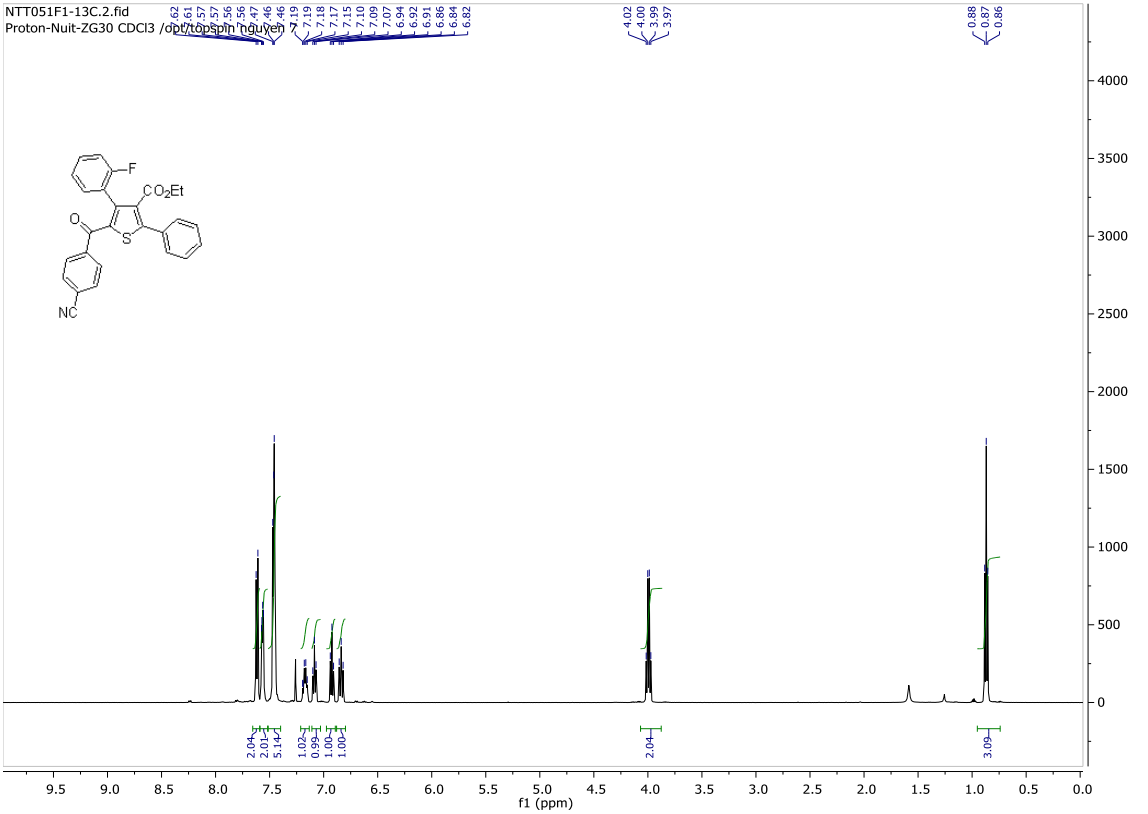


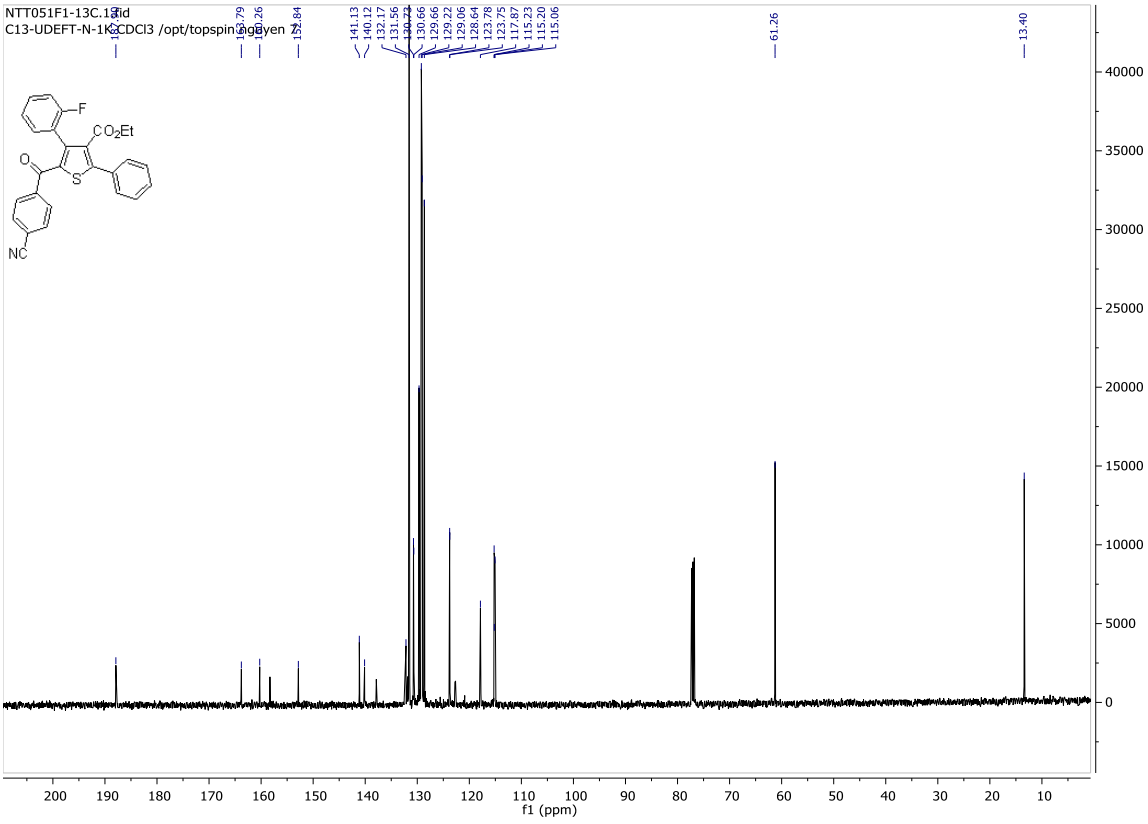
Ethyl 5-benzoyl-2-phenyl-4-(4-(trifluoromethyl)phenyl)thiophene-3-carboxylate (6e)



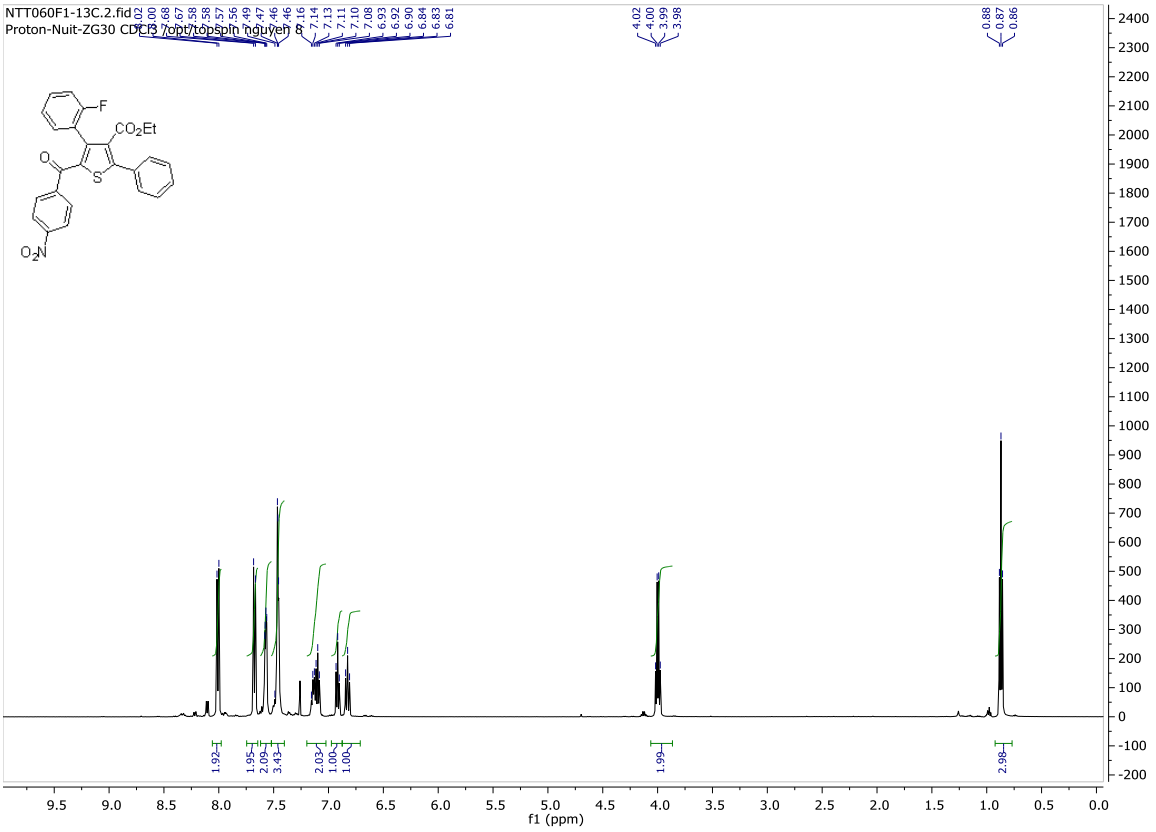


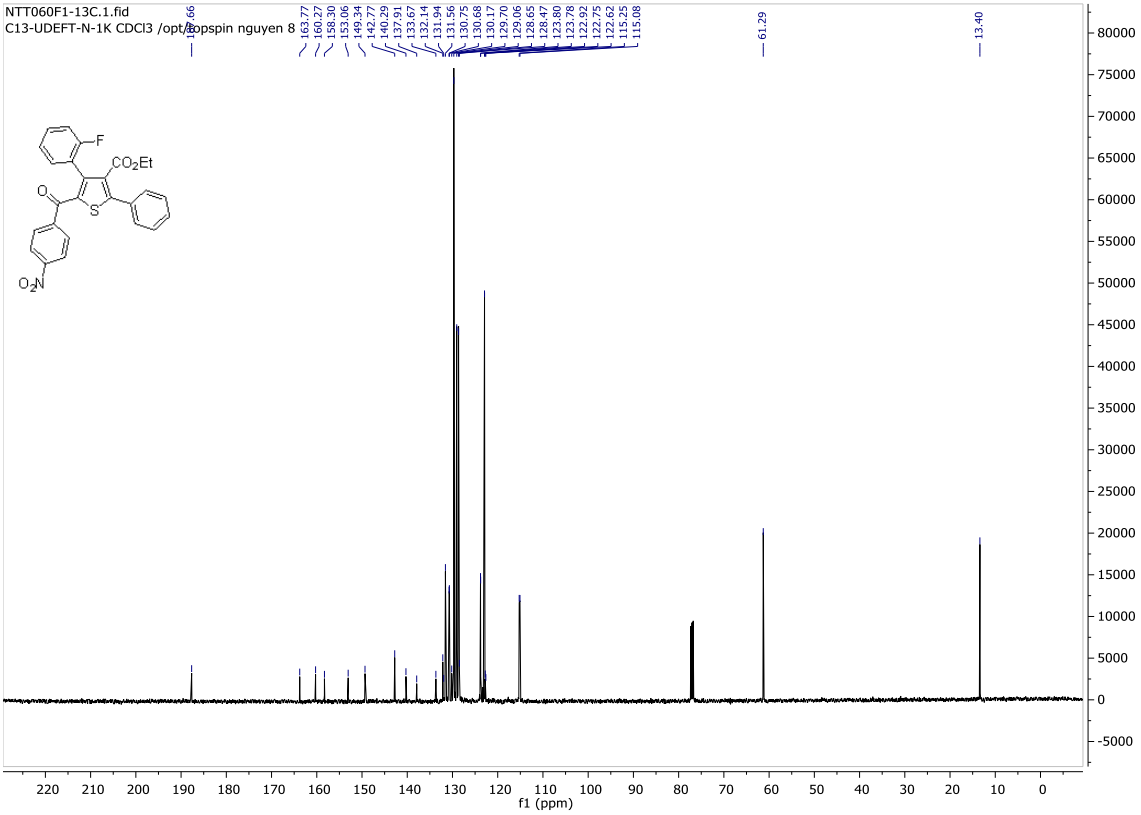
Ethyl 5-(4-cyanobenzoyl)-4-(2-fluorophenyl)-2-phenylthiophene-3-carboxylate (6f)



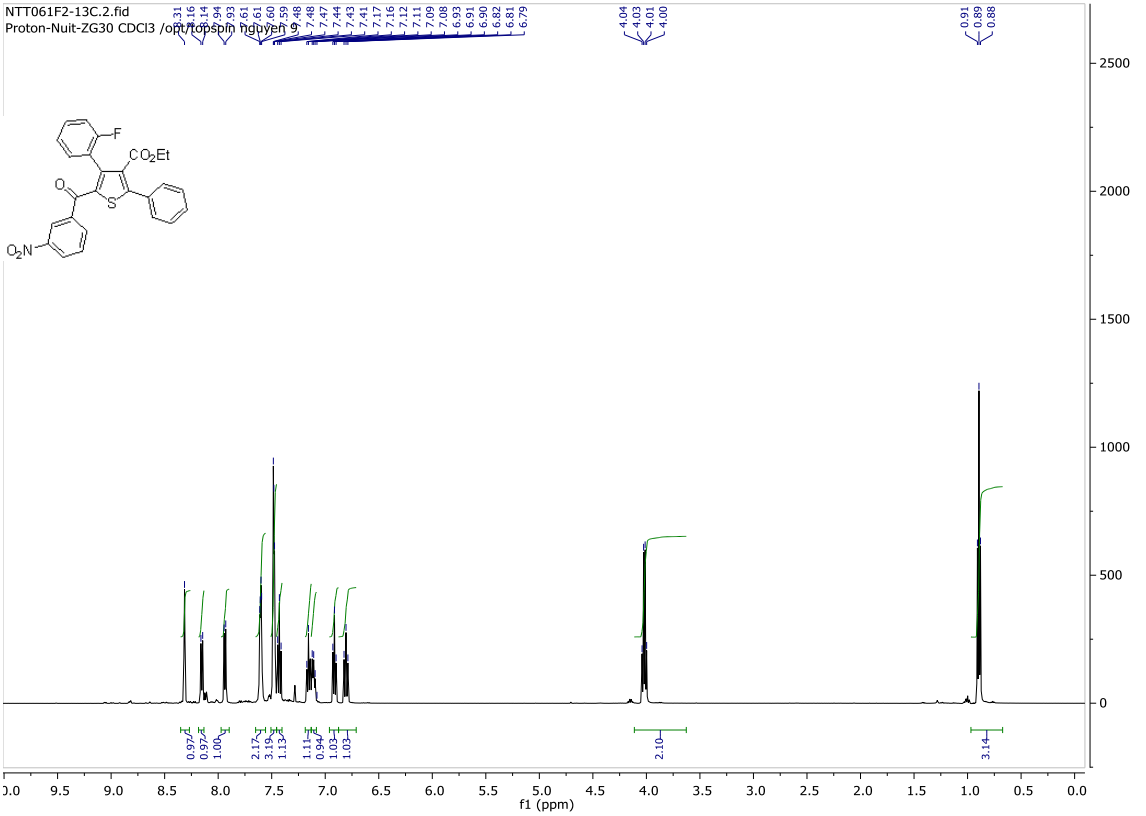


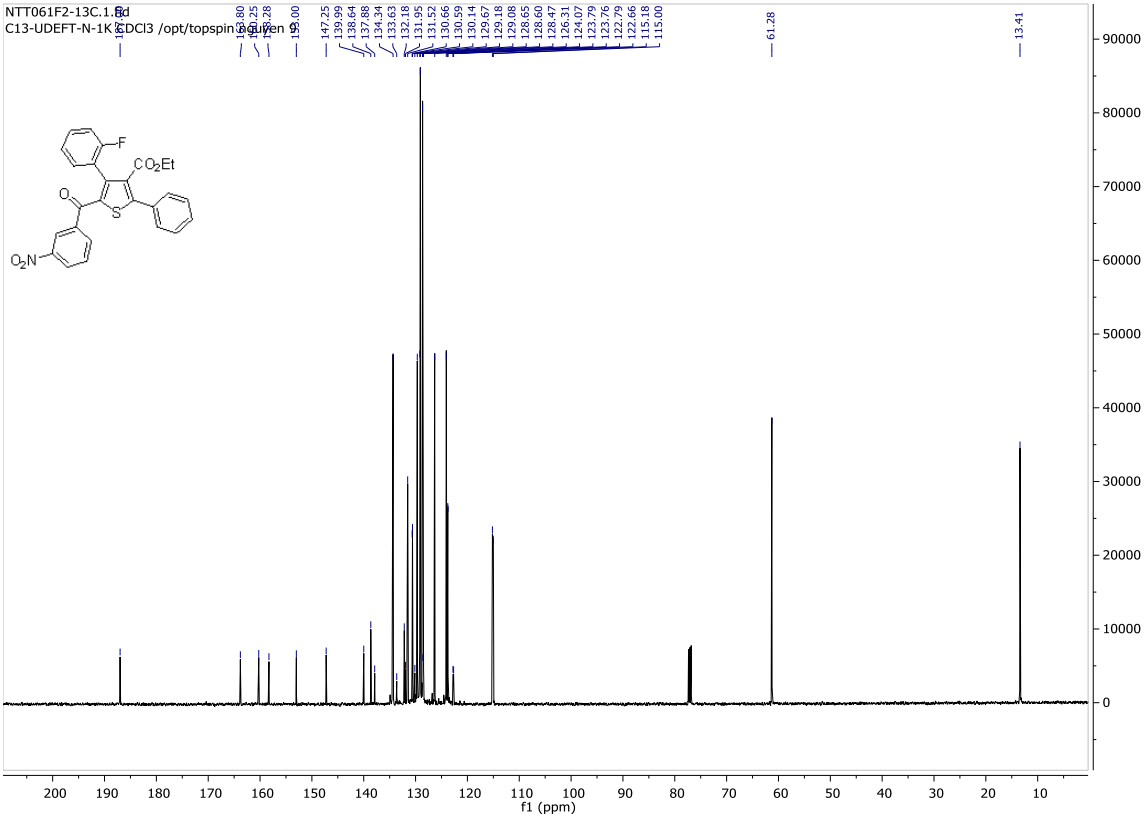
Ethyl 4-(2-fluorophenyl)-5-(4-nitrobenzoyl)-2-phenylthiophene-3-carboxylate (6g)



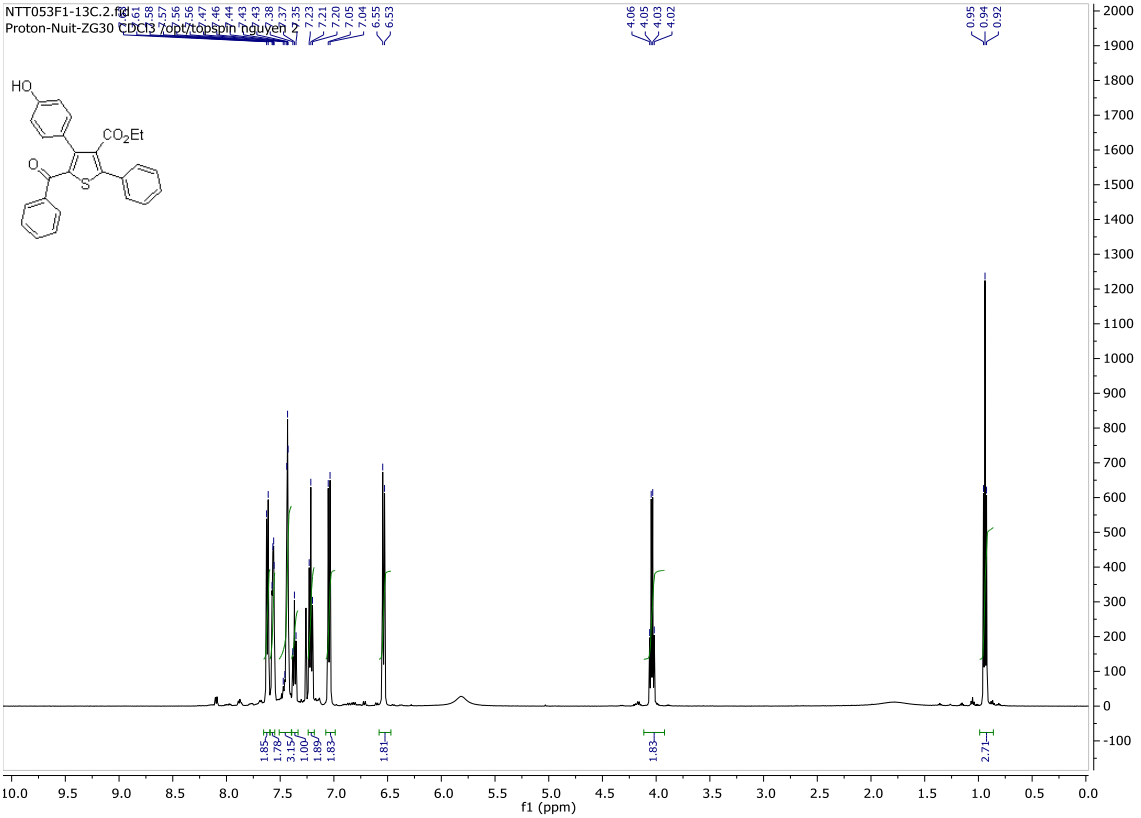


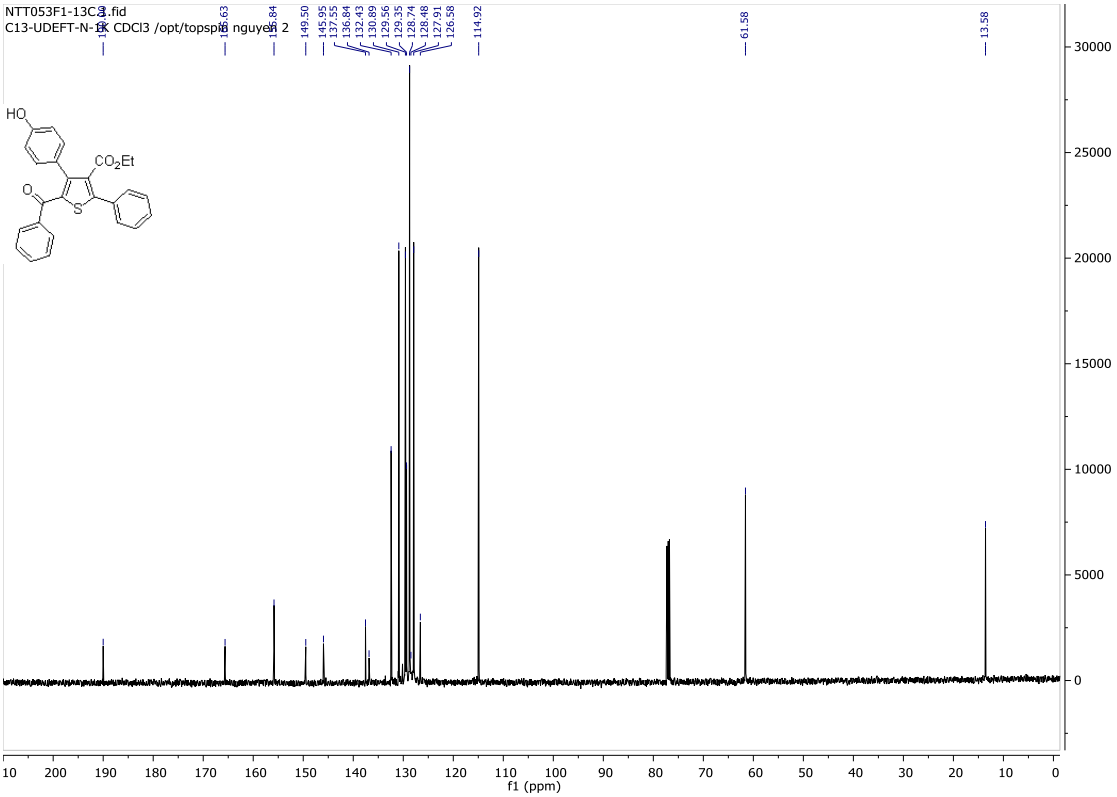
Ethyl 4-(2-fluorophenyl)-5-(3-nitrobenzoyl)-2-phenylthiophene-3-carboxylate (6h)





Ethyl 5-benzoyl-4-(4-hydroxyphenyl)-2-phenylthiophene-3-carboxylate (6i)





Ethyl 2,4-diphenyl-5-(thiophene-2-carbonyl)thiophene-3-carboxylate (6j)