# Assembly of Fully Substituted 2,5-Dihydrothiophenes via a Novel Sequential Multicomponent Reaction

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## SUPPORTING INFORMATION

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## 1. General experimental details.

All the commercially available reagents and solvents were used without further purification. 1,2-Diaza-1,3-dienes **6a–k** were synthesized as a mixture of *E/Z* isomers as previously reported.[1,2] Chromatographic purification of compounds was carried out on silica gel (60–200 μm). TLC analysis was performed on pre-loaded (0.25 mm) glass supported silica gel plates (Kieselgel 60); compounds were visualized by exposure to UV light and by dipping the plates in 1% $Ce(SO_4)\cdot 4H_2O$, 2.5% $(NH_4)_6Mo_7O_{24}\cdot 4H_2O$ in 10% sulphuric acid followed by heating on a hot plate. All $^1H$ NMR and $^{13}C$ NMR spectra were recorded at 400 and 100.56 MHz, respectively. Proton and carbon spectra were referenced internally to solvent signals, using values of δ = 2.49 ppm for proton (middle peak) and δ = 39.50 ppm for carbon (middle peak) in DMSO-$d_6$ and δ = 7.27 ppm for proton and δ = 77.00 ppm for carbon (middle peak) in $CDCl_3$. The following abbreviations are used to describe peak patterns where appropriate: s = singlet, d = doublet, t = triplet q = quartet, sep = septet, m = multiplet and br = broad signal. All coupling constants (*J*) are given in Hz. FT-IR spectra were obtained as Nujol mulls. Mass spectra were obtained by EI (70eV) or by ESI-MS analyses. Elemental analyses were within ± 0.4 of the theoretical values (C, H, N). Melting points were determined in open capillary tubes and are uncorrected.

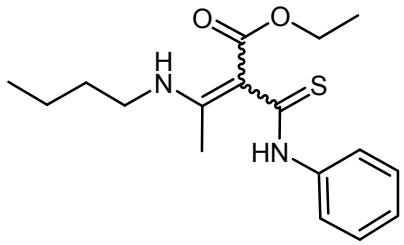
## 2. General procedure for synthesis of ethyl 3-(butylamino)-2-(phenylcarbamothioyl)but-2-enoate 5a under SFC conditions.

*n*-Butyl amine **1a** (0.5 mmol) was added to methyl 3-oxobutanoate **2a** (0.55 mmol) under solvent-free conditions at room temperature and vigorously stirred. After 0.5 h, phenyl isothiocyanate **4a** (0.50 mmol) was added and the reaction was stirred until the disappearance of the enamino ester **3** (6.5 h monitored by TLC). Then, the crude was chromatographed on silica gel column (elution mixture: cyclohexane: ethyl acetate) obtaining the corresponding ethyl 3-(butylamino)-2-(phenylcarbamothioyl)but-2-enoate **5a**.

## 3. General procedure for synthesis of 3-alkylamino-2-(carbamothioyl)but-2-enoates (ACTs) 5a-k

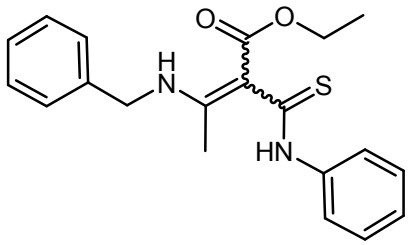
Butyl amine **1a** (0.5 mmol) was added to β-ketoesters **2a-e** (0.55 mmol) under solvent-free conditions at room temperature and vigorously stirred. After 0.5 h aryl isothiocyanates **4a-c** (0.50 mmol) in MeOH (1.5 mL) were added and the reactions were stirred until the disappearance of the enamino esters **3** (6.0-18.0 h monitored by TLC). The compounds **5a,c-j** crystallized directly from the reaction medium and were collected as pure products by filtration. From the mother solution, the methanol was evaporated under reduced pressure and the residue ACTs **5a,c-j** were purified by chromatography on silica gel column (elution mixture: cyclohexane: ethyl acetate) and successively crystallized in methanol. In the other cases, the reaction solvent was evaporated under reduced pressure and the final ACTs **5b,k** were purified by chromatography on silica gel column (elution mixture: cyclohexane: ethyl acetate) and successively crystallized in methanol.

## 4 Spectral data of 3-alkylamino-2-(carbamothioyl)but-2-enoates (ACTs) 5a-m.



**Ethyl 3-(butylamino)-2-(phenylcarbamothioyl)but-2-enoate 5a.**

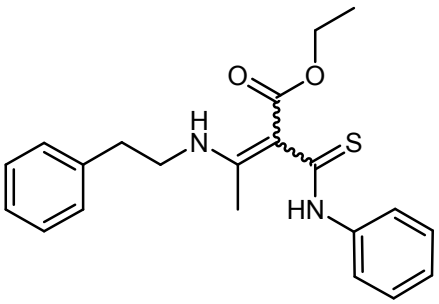
**5a** was isolated by precipitation in methanol in 78% yield. Light yellow solid; mp: 107-109 °C; $^{1}$H NMR (400 MHz, $CDCl_3$, 25 °C): δ = 0.95 (t, 3H, *J*=7,6 Hz, *n*-But), 1.30 (t, 3H, *J*=7,2 Hz, $OCH_2CH_3$), 1.37-1.69 (m, 4H, *n*-But), 2.23 and 2.25 (2s, 3H, $CH_3$), 3.24 and 3.33 (2q, 2H, *J*=6,0 Hz, *J*=6,8 Hz, *n*-But), 3.87 and 4.21 (2q, 2H, *J*=6,8 Hz, *J*=7,2 Hz, $OCH_2CH_3$), 7.03-7.56 (m, 5H, Ph), 9.65, 9.70, 10.58 and 12.07 (4brs, 2H, *NH*); $^{13}$C NMR (100 MHz, $CDCl_3$, 25 °C): δ = 13.6 (q), 14.2 (q), 17.2 (t), 19.4 (t), 19.9 (t), 20.1 (t), 31.2 (q), 31.9 (q), 43.1 (t), 43.7 (t), 59.1 (t), 60.00 (t), 97.8 (s), 100.3 (s), 122.0 (d), 125.0 (d), 125.7 (d), 126.1 (d), 128.6 (d), 129.0 (d), 139.4 (s), 161.9 (s), 165.8 (s), 166.1 (s), 169.5 (s), 191.7 (s), 191.7 (s), 191.8 (s), 201.4 (s); IR (nujol): $\nu_{max}$ = 3232, 3142, 1653, 1634 cm$^{-1}$; MS *m/z* (ESI): 321.26 ($M + H^+$); anal. calcd. for $C_{17}H_{24}N_2O_2S$ (320.45): C 63.72, H 7.55, N 8.74; found: C 63.84, H 7.57, N 8.68.



**Ethyl 3-(benzylamino)-2-(phenylcarbamothioyl)but-2-enoate 5b.**

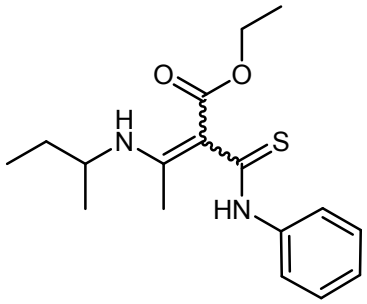
**5b** was purified by chromatography on silica gel column and successively crystallized in methanol with 54% yield. Light yellow solid; mp: 97–98 °C; $^{1}$H NMR (400 MHz, $CDCl_3$, 25 °C): δ = 1.05 and 1.29 (2t, 3H, *J*=6.8 Hz, *J*=7,2 Hz, $OCH_2CH_3$), 2.17 and 2.25 (2s, 3H, $CH_3$), 3.94, and 4.20 (2q, 2H, *J*=6,8 Hz, *J*=7,2 Hz, $OCH_2CH_3$), 4.44 and 4.53 (2d, 2H, *J*=6.0 Hz, *J*=6,0 Hz, $NHCH_2Ph$), 7.05-7.40 (m, 9H,2Ph), 7.61 (d, 1H, *J*=7,6 Hz, Ph), 9.91, 9.93, 10.31, 11.96 (4brs, 2H, *NH*); $^{13}$C NMR (100 MHz, $CDCl_3$, 25 °C): δ = 14.1 (q), 14.2 (q), 17.0 (q), 18.9 (q), 46.9 (t), 47.4 (t), 59.3 (t), 60.0 (t), 99.0 (s), 101.6 (s), 122.4 (d), 124.6 (d), 126.0 (d), 126.2 (d), 126.5 (d), 127.0 (d), 127.4 (d), 127.6 (d), 128.6 (d), 128.7 (d), 128.8 (d), 128.9 (d), 136.8 (s), 137.7 (s), 139.2 (s), 139.3 (s), 161.2 (s), 164.9 (s), 166.1 (s), 169.0 (s), 192.8 (s), 201.3 (s); IR (nujol): $\nu_{max}$ = 3130, 3088, 1648, 1589 cm$^{-1}$; MS *m/z*

(ESI): 355.32 (M + $H^+$); anal. calcd. for $C_{20}H_{22}N_2O_2S$ (354.47): C 67.77, H 6.26, N 7.90; found: C 67.63, H 6.22, N 7.96.



**Ethyl 3-(phenethylamino)-2-(phenylcarbamothioyl)but-2-enoate 5c.**

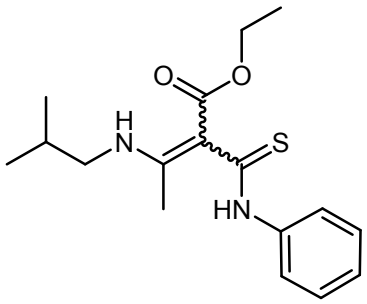
**5c** was isolated by precipitation in methanol in 53% yield. Light yellow solid; mp: 89–91 °C; $^1$H NMR (400 MHz, $CDCl_3$, 25 °C): δ = 0.99 and 1.30 (2t, 3H, *J*=7,2 Hz, *J*=7, Hz, $OCH_2CH_3$), 2.15 and 2.18 (2s, 3H, $CH_3$), 2.87-3.02 (m, 2H, $NCH_2CH_2$), 3.49-3.61 (m, 2H, $NCH_2CH_2$), 3.88 and 4.21 (2q, 2H, *J*=7,2 Hz, *J*=7,2 Hz, $OCH_2CH_3$), 7.02-7.58 (m, 10H, 2Ph), 9.54, 9.76, 10.44 and 12.06 (4brs, 2H, 2*NH*); $^{13}$C NMR (100 MHz, $CDCl_3$, 25 °C): δ = 14.2 (q), 19.0 (q), 36.0 (t), 45.5 (t), 60.0 (t), 82.2 (s), 98.2 (s), 100.9 (s), 122.0 (d), 124.8 (d), 126.1 (d), 126.7 (d), 128.5 (d), 128.6 (d), 128.7 (d), 128.9 (d), 129.4 (d), 137.9 (s), 139.3 (s), 161.4 (s), 165.1 (s), 165.9 (s), 169.2 (s), 170.4 (s), 192.2 (s), 201.2 (s); IR (nujol): $\nu_{max}$ = 3255, 3167, 1622, 1612 $cm^{-1}$; MS *m/z* (ESI): 369.53 (M + $H^+$); anal. calcd. for $C_{21}H_{24}N_2O_2S$ (368.49): C 68.45, H 6.56, N 7.60; found: C 68.59, H 6.61, N 7.52.



**Ethyl 3-(*sec*-butylamino)-2-(phenylcarbamothioyl)but-2-enoate 5d.**

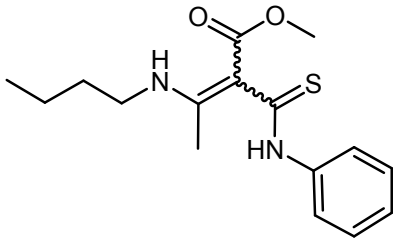
**5d** was isolated by precipitation in methanol in 34% yield. Light yellow solid; mp: 88–90 °C; $^1$H NMR (400 MHz, $DMSO_{d6}$, 25 °C): δ = 0.87-0.97 (m, 3H, $OCH_2CH_3$), 1.10-1.16 (m, 6H $NCH(CH_3)CH_2CH_3$), 1.50-1,53 (m, 2H, $NCH(CH_3)CH_2CH_3$), 2.11 (s, 3H, $CH_3$), 3.61-3.64 (m, 1H, $NCH(CH_3)CH_2CH_3$), 3.97-4.08 (m, 2H, $OCH_2CH_3$), 7.19-7.88 (m, 5H, Ph), 9.38, (brs, 1H, *NH*), 11.51, (brs, 1H, *NH*); $^{13}$C NMR (100 MHz, $DMSO_{d6}$, 25 °C): δ = 10.2 (q), 14.4 (q), 16.2 (q), 21.4 (q), 30.1 (t), 49.4 (d), 58.4 (t), 81.0 (s), 102.7 (s), 122.8 (d), 123.6 (d), 125.6 (d), 125.9 (d), 128.4 (d), 128.4 (d), 129.4 (s), 129.9 (s), 139.4 (s), 140.2(s), 159.5 (s), 161.5 (s), 166.9 (s),168.2 (s), 169.5 (s),

179.6 (s), 196.9 (s); IR (nujol): $\nu_{max}$ = 3257, 3191, 1624, 1615 $cm^{-1}$; MS *m/z* (ESI): 321.19 ($M + H^+$); anal. calcd. for $C_{17}H_{24}N_2O_2S$ (320.45): C 63.72, H 7.55, N 8.74; found: C 63.58, H 7.57, N 8.83.



**Ethyl 3-(isobutylamino)-2-(phenylcarbamothioyl)but-2-enoate 5e.**

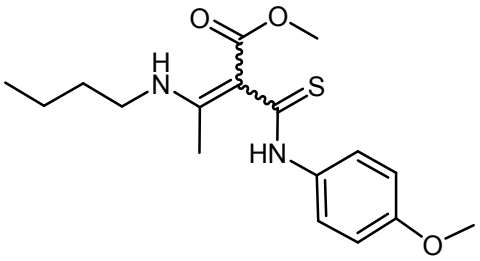
**5e** was isolated by precipitation in methanol in 60% yield. Light yellow solid; mp: 108–110 °C; $^1$H NMR (400 MHz, $CDCl_3$, 25 °C): δ = 0.95-1.02 and 1.04 (m and d, 6H, *J*=6,4 Hz, $NCH_2CH(CH_3)_2$), 1.23-1.28 and 1.31 (m and t, 3H, *J*=7,6 Hz, $OCH_2CH_3$), 1.79-1.83 and 1.95 (m and ept, 1H, *J*=6,8 Hz, $NCH_2CH(CH_3)_2$), 2.21 and 2.25 (2s, 3H, $CH_3$), 3.06-3.18 (m, 2H, $NCH_2CH(CH_3)_2$), 3.84-3.90 and 4.22 (m and q, 2H, $OCH_2CH_3$), 7.03-7.57 (m, 5H, Ph), 9.71, 9.76, 10.57 and 12.18 (4brs, 2H, *NH*); $^{13}$C NMR (100 MHz, $CDCl_3$, 25 °C): δ = 14.2 (t), 20.0 (d), 20.0 (q), 20.4 (q), 51.7 (t), 60.0 (t), 100.4 (s), 122.0 (s), 125.1 (d), 125.7 (d), 126.1 (d), 127.2 (d), 128.6 (d), 129.0 (s), 129.5 (d), 139.5 (s), 161.9 (s), 165.9 (s), 166.1 (s), 169.6 (s), 191.6 (s), 191.6 (s),201.7 (s); IR (nujol): $\nu_{max}$ = 3240, 3141, 1654, 1626 $cm^{-1}$; MS *m/z* (ESI): 321.53 ($M + H^+$); anal. calcd. for $C_{17}H_{24}N_2O_2S$ (320.45): C 63.72, H 7.55, N 8.74; found: C 63.85, H 7.51, N 8.78.



**Methyl 3-(butylamino)-2-(phenylcarbamothioyl)but-2-enoate 5f.**

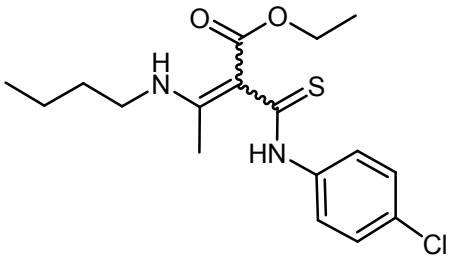
**5f** was isolated by precipitation in methanol in 82% yield. Light yellow solid; mp: 109–110 °C; $^1$H NMR (400 MHz, $CDCl_3$, 25 °C): δ = 0.93 (t, 3H, *J*=7,6 Hz, *n*-But), 1.33-1.64 (m, 4H, *n*-But), 2.18 and 2.21 (2s, 3H, $CH_3$), 3.20 and 3.30 (2q, 2H, *J*=6,0 Hz, *J*=6,8 Hz, *n*-But), 3.40 and 3.71 (2s, 3H, $OCH_3$), 7.02-7.60 (m, 5H, Ph), 9.54, 9.59, 10.40 and 11.69 (4brs, 2H, *NH*); $^{13}$C NMR (100 MHz, $CDCl_3$, 25 °C): δ = 13.6 (q), 17.0 (t), 19.0 (t), 19.8 (t), 20.1 (t), 31.2 (q), 31.8 (q), 43.0 (t), 43.6 (t), 50.3 (q), 51.00 (q), 97.5 (s), 100.3 (s), 122.4 (d), 124.6 (d), 126.1 (d), 128.5 (d), 128.9 (d), 139.2 (s), 139.3 (s), 161.7 (s), 165.3 (s), 166.5 (s), 169.6 (s), 192.2 (s), 192.3 (s), 201.5 (s), 201.5 (s); IR

(nujol): $\nu_{max}$ = 3277, 3246, 1629, 1594 $cm^{-1}$; MS *m/z* (ESI): 307.23 ($M + H^+$); anal. calcd. for $C_{16}H_{22}N_2O_2S$ (306.42): C 62.71, H 7.24, N 9.14; found: C 62.60, H 7.21, N 9.21.



**Methyl 3-(butylamino)-2-((4-methoxyphenyl)carbamothioyl)but-2-enoate 5g.**

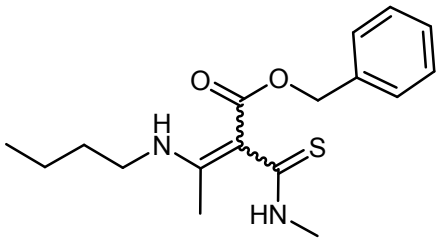
**5g** was isolated by precipitation in methanol in 77% yield. Light yellow solid; mp: 107-109 °C; $^1$H NMR (400 MHz, $CDCl_3$, 25 °C): δ = 0.89-0.95 (m, 3H, *n*-But), 1.33-1.65 (m, 4H, *n*-But), 2.16 and 2.21 (2s, 3H, *CH*$_3$), 3.16-3.22 and 3.36 (m and q, 2H, *J*=5,2 Hz, *n*-But), 3.46, 3.60 and 3.72 (3s, 3H, O*CH*$_3$), 3.76, 3.79 and 3.80 (3s, 3H, O*CH*$_3$), 6.78-7.46 (m, 4H, Ph), 9.46, 9.70, 10.26 and 11.67 (4brs, 2H, *NH*); $^{13}$C NMR (100 MHz, $CDCl_3$, 25 °C): δ = 13.6 (q), 16.9 (q), 18.9 (t), 19.8 (q), 20.1 (q), 31.3 (t), 31.8 (t), 32.3 (t), 42.6 (t), 43.0 (t), 43.5 (t), 49.7 (q), 50.4 (q), 51.0 (q), 55.3 (q), 55.4 (q), 81.2 (s), 97.2 (s), 100.1 (s), 113.8 (d), 114.0 (d), 114.7 (d), 124.3 (s), 126.4 (d), 126.8 (d), 132.4 (s), 157.7 (s), 161.3 (s), 165.1 (s), 166.5 (s), 169.6 (s), 192.6 (s), 201.6 (s); IR (nujol): $\nu_{max}$ = 3257, 3252, 1631, 1597 $cm^{-1}$; MS *m/z* (ESI): 337.21 ($M + H^+$); anal. calcd. for $C_{17}H_{24}N_2O_3S$ (336.45): C 60.69, H 7.19, N 8.33; found: C 60.83, H 7.16, N 8.48.



**Ethyl 3-(butylamino)-2-((4-chlorophenyl)carbamothioyl)but-2-enoate 5h.**

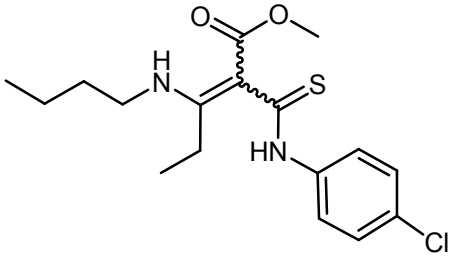
**5h** was isolated by precipitation in methanol in 75% yield. Light yellow solid; mp: 89–92 °C; $^1$H NMR (400 MHz, $CDCl_3$, 25 °C): δ = 0.96 (t, 3H, *J*=7,2 Hz, *n*-But), 1.31 (t, 3H, *J*=7,2 Hz, $OCH_2$*CH*$_3$),1.43-1.70 (m, 4H, *n*-But), 2.26 (s, 3H, *CH*$_3$), 3.36 (q, 2H, *J*=5,6 Hz, *n*-But), 4.22 (q, 2H, O*CH*$_2$$CH_3$), 7.32 (d, 2H, *J*=8.4 Hz, Ph), 7.49 (d, 2H, *J*=8.4 Hz, Ph), 10.86, (brs, 1H, *NH*), 12.49 (brs, 1H, *NH*); $^{13}$C NMR (100 MHz, $CDCl_3$, 25 °C): δ = 13.6 (q), 13.7 (q), 14.2 (q), 14.6 (q), 19.3 (t), 20.0 (t), 20.2 (t), 31.2 (q), 32.4 (q), 42.7 (t), 43.8 (t), 58.2 (t), 60.2 (t), 81.6 (s), 99.9 (s), 126.5 (d), 126.9 (d), 128.7 (d), 130.0 (d), 131.2 (s), 132.9 (s), 138.0 (s), 161.9 (s), 166.7 (s), 169.9 (s), 170.6 (s), 195.9

(s), 206.9 (s); IR (nujol): $\nu_{max}$ = 3257, 3187, 1632, 1602 $cm^{-1}$; MS *m/z* (ESI): 355.33 ($M + H^+$); anal. calcd. for $C_{17}H_{23}ClN_2O_2S$ (354.89): C 57.53, H 6.53, N 7.89; found: C 57.62, H 6.52, N 7.83.



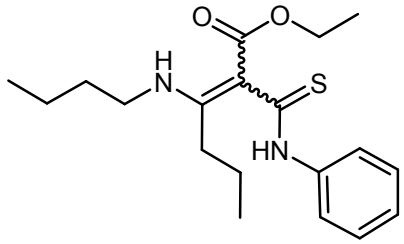
**Benzyl 3-(butylamino)-2-(methylcarbamothioyl)but-2-enoate 5i.**

**5i** was isolated by precipitation in methanol in 13% yield. Light yellow solid; mp: 93–95 °C; $^1$H NMR (400 MHz, $CDCl_3$, 25 °C): δ = 0.93 (t, 3H, *J*=7,2 Hz, *n*-But), 1.39-1.45 (m, 2H, *n*-But), 1.56-1.62 (m, 2H, *n*-But), 2.12 (s, 3H, *CH*$_3$), 3.13 and 3.14 (2s, 3H, N*CH*$_3$), 3.22-3.27 (m, 2H, *n*-But), 5.12 (s, 2H, O*CH*$_2$Ph), 7.26-7.36 (m, 5H, Ph), 8.59, (brs, 1H, *NH*), 11.17 (brs, 1H, *NH*); $^{13}$C NMR (100 MHz, $CDCl_3$, 25 °C): δ = 13.6 (q), 18.5 (t), 20.1 (q), 31.5 (t), 32.5 (t), 43.4 (t), 65.3 (t), 99.3 (s), 127.6 (d), 127.8 (d), 128.4 (d), 136.5 (s), 164.1 (s), 168.4 (s), 195.0 (s), 202.9 (s); IR (nujol): $\nu_{max}$ = 3272, 3163, 1685, 1622 $cm^{-1}$; MS *m/z* (ESI): 321.36 ($M + H^+$); anal. calcd. for $C_{17}H_{24}N_2O_2S$ (320.45): C 63.72, H 6.53, N 8.74; found: C 63.57, H 6.56, N 8.81.



**Methyl 3-(butylamino)-2-((4-chlorophenyl)carbamothioyl)pent-2-enoate 5j.**

**5j** was isolated by precipitation in methanol in 66% yield. Light yellow solid; mp: 102–105 °C; $^1$H NMR (400 MHz, $CDCl_3$, 25 °C): δ = 0.95 (t, 3H, *J*=7,2 Hz, *n*-But), 1.27 (t, 3H, *J*=7,2 Hz, $CH_2$*CH*$_3$),1.47 (sex, 2H, *J*=7,6 Hz, *n*-But),1.63-1.70 (m, 2H, *n*-But), 2.55 (q, 2H, *J*=7,2 Hz, *CH*$_2$$CH_3$), 3.37 (q, 2H, *J*=6,4 Hz, *n*-But), 3.74 (s, 3H, O*CH*$_3$), 7.33 (d, 2H, *J*=8.4 Hz, Ph), 7.53 (d, 2H, *J*=8.4 Hz, Ph), 9.58, 9.63, 10.48 and 11.90 (4brs, 2H, *NH*); $^{13}$C NMR (100 MHz, $CDCl_3$, 25 °C): δ = 12.6 (q), 13.6 (q), 20.0 (t), 20.1 (t), 25.2 (t), 30.8 (q), 31.6 (q), 43.2 (t), 51.1 (q), 51.2 (q), 99.8 (s), 123.4 (d), 126.1 (d), 126.3 (d), 128.6 (d), 130.0 (s), 131.2 (s), 137.9 (s), 166.6 (s), 169.7 (s), 170.0 (s), 180.5 (s), 199.2 (s), 199.2 (s), 201.5 (s); IR (nujol): $\nu_{max}$ = 3289, 3267, 1654, 1632 $cm^{-1}$; MS *m/z* (ESI): 355.58 ($M + H^+$); anal. calcd. for $C_{17}H_{23}ClN_2O_2S$ (354.89): C 57.53, H 6.53, N 7.89; found: C 57.39, H 6.49, N 8.01.



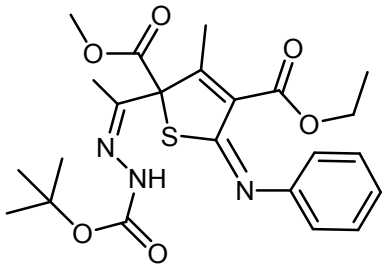
**Ethyl 3-(butylamino)-2-(phenylcarbamothioyl)hex-2-enoate 5k.**

**5k** was purified by chromatography on silica gel column and successively crystallized in methanol with 57% yield. Light yellow solid; mp: 88–91 °C; $^{1}$H NMR (400 MHz, $CDCl_3$, 25 °C): δ = 0.95 (t, 3H, *J*=7,2 Hz, *n*-But), 1.01 (t, 3H, *J*=7,2 Hz, prop), 1.31 (t, 3H, *J*=7,2 Hz, $OCH_2CH_3$), 1.42-1.52 (m, 2H, prop), 1.56-1.74 (m, 4H, *n*-But), 2.51-2.55 (m, 2H, prop), 3.34 (q, 2H, *J*= 5.6 Hz, *n*-But), 3.81-3.84 and 4.20 (m, and q, 2H, *J*=6,8 Hz, $OCH_2CH_3$), 7.04-7.57 (m, 5H, Ph), 9.57, 9.71, 10.27 and 11.71 (4brs, 2H, *NH*); $^{13}$C NMR (100 MHz, $CDCl_3$, 25 °C): δ = 13.7 (q), 14.3 (q), 20.2 (q), 21.9 (t), 31.8 (t), 33.7 (t), 43.2 (t), 60.1 (t), 97.1 (s), 100.4 (s), 121.6 (s), 124.9 (d), 126.2 (s), 128.6 (d), 129.0 (s), 139.4 (s), 165.7 (s), 166.3 (s), 168.0 (s), 169.5 (s), 192.6 (s), 192.7 (s), 192.8 (s), 201.4 (s); IR (nujol): $\nu_{max}$ = 3282, 3214, 1649, 1616 $cm^{-1}$; MS *m/z* (ESI): 349.29 ($M + H^+$);anal. calcd. for $C_{19}H_{28}N_2O_2S$ (348.50): C 65.48, H 8.10, N 8.04; found: C 65.39, H 8.06, N 8.16.

## 5 One-pot procedure for synthesis of 2,5-dihydrothiophenes 7a-w

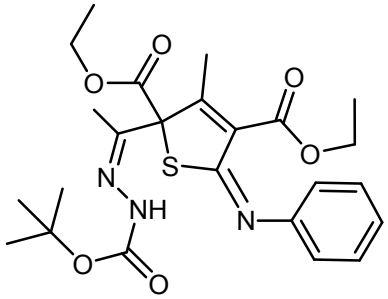
*n*-Butyl amine **1a** (0.5 mmol) was added to β-ketoesters **2a-i** (0.55 mmol) under solvent-free conditions and vigorously stirred at room temperature. After 0.5 h aryl isothiocyanates **4a-c** (0.5mmol) in MeOH (1.5 mL) were added and the reactions were stirred until the disappearance of the enamino esters **3** (6.0-18.0h monitored by TLC). DDs **6a-k** (1.0 mmol) in MeOH (2.0 mL) were added to the reaction medium and magnetically stirred until the complete disappearance of the ACTs **5** (3.0-5.0 h monitored by TLC). Then, the reaction solvent was evaporated under reduced pressure and the desired 2,5-dihydrothiophenes **7a-w** were purified by chromatography on silica gel column (elution mixture: cyclohexane: ethyl acetate).

## 6 Spectral data of 2,5-dihydrothiophenes 7a-w.



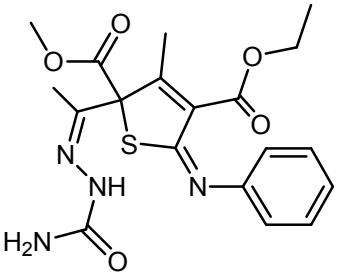
**4-Ethyl-2-methyl 2-(1-(2-*tert*-butoxycarbonyl)hydrazono)ethyl)-3-methyl-5-(phenylimino)-2,5-dihydrothiophene-2,4-dicarboxylate 7a.**

**7a** was isolated by column chromatography on silica gel (ethyl acetate/cyclohexane) in 64% yield. White solid; mp: 136–139 °C; $^{1}$H NMR (400 MHz, DMSO$_{d6}$, 25 °C): δ = 1.30 (t, 3H, *J* = 7.2 Hz OCH$_2$*CH$_3$*), 1.45 (s, 9H, C(*CH$_3$*)$_3$), 1.84 (s, 3H, *CH$_3$*), 2.13 (s, 3H, *CH$_3$*), 3.73 (s, 3H, O*CH$_3$*), 4.33 (q, 2H, *J* = 7.2 Hz, O*CH$_2$*CH$_3$), 6.97 (d, 2H, *J* = 7.2 Hz, Ph), 7.18 (t, 1H, *J* = 7.6 Hz, Ph), 7.40 (t, 2H, *J* = 7.6 Hz, Ph), 9.88 (s, 1H, *NH*); $^{13}$C NMR (100 MHz, DMSO$_{d6}$, 25 °C): δ = 13.4 (q), 13.9 (q), 15.4 (q), 27.9 (q), 53.4 (q), 61.4 (t), 75.4 (s), 79.7 (s), 119.6 (d), 125.2 (d), 129.3 (d), 135.7 (s), 145.9 (s), 150.2 (s), 152.6 (s), 156.5 (s), 163.1 (s), 163.2 (s), 167.8 (s); IR (nujol): $\nu_{max}$ = 3227, 1739, 1695, 1636 cm$^{-1}$; MS *m/z* (ESI): 476.29 (M + H$^+$); anal. calcd. for $C_{23}H_{29}N_3O_6S$ (475.56): C 58.09, H 6.15, N 8.84; found: C 58.21, H 6.17, N 8.70.



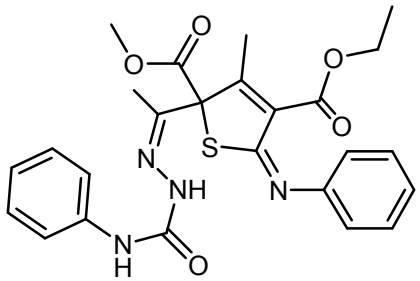
**Diethyl 2-(1-(2(*tert*-butoxycarbonyl)hydrazono)ethyl)-3-methyl-5-(phenylimino)-2,5-dihydrothiophene-2,4-dicarboxylate 7b.**

**7b** was isolated by column chromatography on silica gel (ethyl acetate/cyclohexane) in 60 % yield. White solid; mp: 136–139 °C; $^{1}$H NMR (400 MHz, DMSO$_{d6}$, 25 °C): δ = 1.21 (t, 3H, *J* = 7.2 Hz OCH$_2$*CH$_3$*), 1.29 (t, 3H, *J* = 7.2 Hz OCH$_2$*CH$_3$*), 1.44 (s, 9H, C(*CH$_3$*)$_3$), 1.84 (s, 3H, *CH$_3$*), 2.13 (s, 3H, *CH$_3$*), 4.16-4.24 (m, 2H, O*CH$_2$*CH$_3$), 4.32 (q, 2H, *J* = 7.2 Hz, O*CH$_2$*CH$_3$), 6.98 (d, 2H, *J* = 7.6 Hz, Ph), 7.17 (t, 1H, *J* = 7.6 Hz Ph), 7.40 (t, 2H, *J* = 8.0 Hz, Ph), 9.90 (s, 1H, *NH*); $^{13}$C NMR (100 MHz, DMSO$_{d6}$, 25 °C): δ = 13.5 (q), 13.7 (q), 14.0 (q), 15.5 (q), 27.9 (q), 61.5 (t), .62.5 (t), 75.5 (s), 79.7 (s), 119.6 (d), 125.2 (d), 129.4 (d), 135.7 (s), 145.8 (s), 150.3 (s), 152.6 (s), 156.6 (s), 163.2 (s), 163.3 (s), 167.2 (s); IR (nujol): $\nu_{max}$ = 3230,1731,1693,1622 cm$^{-1}$; MS *m/z* (ESI): 490.59 (M + H$^+$); anal. calcd. for $C_{24}H_{31}N_3O_6S$ (489.58): C 58.88, H 6.38, N 8.58; found: C 58.76, H 6.35, N 8.65.



**4-Ethyl-2-methyl 2-(1-(2-carbamoylhydrazono)ethyl)-3-methyl-5-(phenylimino)-2,5-dihydrothiophene-2,4-dicarboxylate 7c.**

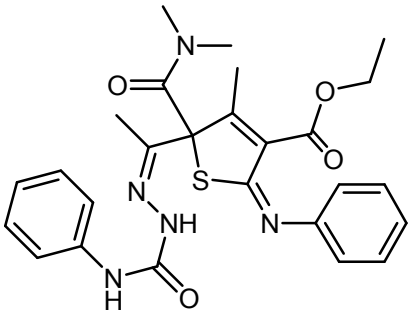
**7c** was isolated by column chromatography on silica gel (ethyl acetate/cyclohexane) in 56 % yield. Pale yellow solid; mp: 165–169 °C; $^{1}$H NMR (400 MHz, DMSO$_{d6}$, 25 °C): δ = 1.29 (t, 3H, *J* = 7.2 Hz OCH$_2$*CH$_3$*), 1.83 (s, 3H, *CH$_3$*), 2.10 (s, 3H, *CH$_3$*), 3.75 (s, 3H, O*CH$_3$*), 4.32 (q, 2H, *J* = 7.2 Hz , O*CH$_2$*CH$_3$), 6.12 (brs, 2H, *NH$_2$*), 6.98 (dd, 2H, *J* = 8.4 Hz, *J* = 1.2 Hz, Ph), 7.18 (t, 1H, *J* = 7.6 Hz, Ph), 7.40 (t, 2H, *J* = 7.6 Hz, Ph), 9.55 (s, 1H, *NH*); $^{13}$C NMR (100 MHz, DMSO$_{d6}$, 25 °C): δ = 13.0 (q), 14.0 (q), 15.3 (q), 53.5 (q), 61.6 (t), 75.2 (s), 119.6 (d), 125.3 (d), 129.4 (d), 135.8 (s), 142.4 (s), 150.2 (s), 156.3 (s), 156.3 (s), 163.1 (s), 163.2 (s), 167.8 (s); IR (nujol): $\nu_{max}$ = 3412, 3278, 3243, 1753, 1644, 1623 cm$^{-1}$; MS *m/z* (ESI): 419.02 (M + H$^+$); anal. calcd. for $C_{19}H_{22}N_4O_5S$ (418.47): C 54.53, H 5.30, N 13.39; found: C 54.63, H 5.33, N 13.27.



**4-Ethyl-2-methyl 3-methyl-2-(1-(2-phenylcarbomoyl)hydrazono)ethyl)-5-(phenylimino)-2,5-dihydrothiophene-2,4-dicarboxylate 7d.**

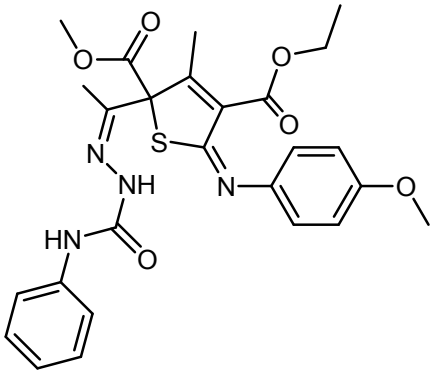
**7d** was isolated by column chromatography on silica gel (ethyl acetate/cyclohexane) in 51 % yield. Pale yellow solid; mp: 137–139 °C; $^{1}$H NMR (400 MHz, DMSO$_{d6}$, 25 °C): δ = 1.30 (t, 3H, *J* = 7.2 Hz OCH$_2$*CH$_3$*), 1.93 (s, 3H, *CH$_3$*), 2.18 (s, 3H, *CH$_3$*), 3.82 (s, 3H, O*CH$_3$*), 4.36 (q, 2H, *J* = 7.2 Hz, O*CH$_2$*CH$_3$), 6.99-7.04 (m, 3H, Ph), 7.18 (t, 1H, *J* = 7.6 Hz, Ph), 7.31 (t, 2H, *J* = 7.6 Hz, Ph), 7.40 (dt, 2H, *J* = 7.6 Hz, *J* = 0.8 Hz,Ph), 7.46 (dd, 2H, *J* = 8.4 Hz, *J* = 0.8 Hz, Ph), 8.28 (s, 1H, *NH*), 10.05 (s, 1H, *NH*); $^{13}$C NMR (100 MHz, DMSO$_{d6}$, 25 °C): δ = 13.5 (q), 14.0 (q), 15.4 (q), 53.7 (q), 61.7 (t), 75.2 (s), 118.5 (d), 119.7 (d), 122.6 (d), 125.3 (d), 128.9 (d), 129.4 (d), 136.0 (s), 138.4 (s), 144.1 (s), 150.3 (s), 152.3 (s), 156.2 (s), 163.1 (s), 163.2 (s), 167.7 (s); IR (nujol): $\nu_{max}$ = 3357, 3241, 1707,

1698, 1653 $cm^{-1}$; MS *m/z* (ESI): 495.76 ($M + H^+$); anal. calcd. for $C_{25}H_{26}N_4O_5S$ (494.56): C 60.71, H 5.30, N 11.33; found: C 60.57, H 5.26, N 11.45.



**Ethyl 5-(dimethylcarbamoyl)-4-methyl-5-(-1-(2(phenylcarbamoyl)hydrazono)ethyl)-2-(phenylimino)-2,5-dihydrothiophene-3-carboxylate 7e.**

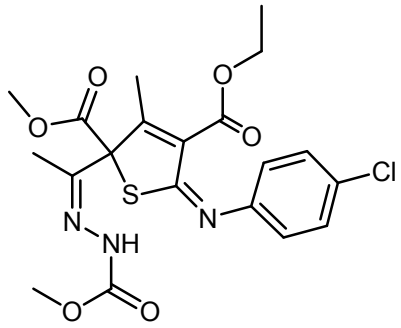
**7e** was isolated by column chromatography on silica gel (ethyl acetate/cyclohexane) in 51 % yield. Pale yellow solid; mp: 125−127 °C; $^1$H NMR (400 MHz, $CDCl_3$, 25 °C): δ = 1.39 (t, 3H, *J* = 7.2 Hz, $OCH_2CH_3$), 2.04 (s, 3H, $CH_3$), 2.23 (s, 3H, $CH_3$), 2.81 (s, 3H, $NCH_3$), 3.05 (s, 3H, $NCH_3$), 4.42 (q, 2H, *J* = 7.2 Hz, $OCH_2CH_3$),7.05 (d, 2H, *J* = 7.6 Hz, Ph), 7.10 (t, 1H, *J* = 7.2 Hz, Ph), 7.17 (t, 1H, *J* = 7.2 Hz, Ph), 7.32-7.40 (m, 4H, Ph), 7.43 (d, 2H, *J* = 7.6 Hz, Ph), 8.01 (s, 1H, *NH*), 9.48 (s, 1H, *NH*); $^{13}$C NMR (100 MHz, $CDCl_3$, 25 °C): δ = 13.3 (q), 14.2 (q), 16.6 (q), 36.8 (q), .39.0 (q), 61.9 (t), 73.8 (s), 119.0 (d), 120.1 (d), 123.7 (d), 125.3 (d), 129.2 (d), 129.2 (d), 135.6 (s), 137.5 (s), 144.7 (s), 150.8 (s), 153.4 (s), 159.2 (s), 163.0 (s), 163.8 (s), 167.2 (s); IR (nujol): $\nu_{max}$ = 3374, 3239, 1754, 1636, 1625 $cm^{-1}$; MS *m/z* (ESI): 508.72 ($M + H^+$); anal. calcd. for $C_{26}H_{29}N_5O_4S$ (507.60): C 61.52, H 5.76, N 13.80; found: C 61.64, H 5.79, N 13.72.



**4-Ethyl 2-methyl 5-((4-methoxyphenyl)imino)-3methyl-1-(2-(phenylcarbamoyl)hydrazono)ethyl)-2,5-dihydrothiophene-2,4-dicarboxylate 7f.**

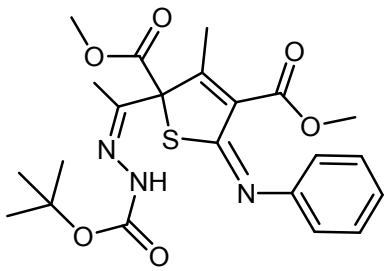
**7f** was isolated by column chromatography on silica gel (ethyl acetate/cyclohexane) in 51 % yield. White solid; mp: 133−139 °C; $^1$H NMR (400 MHz, $DMSO_{d6}$, 25 °C): δ = 1.23 (t, 3H, *J* = 7.2 Hz $OCH_2CH_3$), 1.91 (s, 3H, $CH_3$), 2.15 (s, 3H, $CH_3$), 3.76 (s, 3H, $OCH_3$), 3.86 (s, 3H, $OCH_3$), 4.25-4.31 (q, 2H, *J* = 7.2 Hz $OCH_2CH_3$), 6.96-7.05 (m, 5H, Ph), 7.31 (t, 2H, *J* = 7.6 Hz, Ph), 7.44 (d, 2H, *J* =

7.6 Hz, Ph), 8.27 (s, 1H, *NH*), 10.0 (s, 1H, *NH*); $^{13}$C NMR (100 MHz, DMSO$_{d6}$, 25 °C): δ = 13.5 (q), 13.8 (q), 15.4 (q), 52.7 (q), 55.2 (q), 62.7 (t), 75.3 (s), 114.6 (d), 118.5 (d), 121.4 (d), 122.7 (d), 128.9 (d), 136.0 (s), 138.4 (d), 143.0 (s), 144.2 (s), 152.3 (s), 155.6 (s), 157.0 (s), 161.6 (s), 163.9 (s), 167.2 (s); IR (nujol): $\nu_{max}$ = 3349, 3208, 1733, 1675, 1649 cm$^{-1}$; MS *m/z* (ESI): 525.79 (M + H$^+$); anal. calcd. for $C_{26}H_{28}N_4O_6S$ (524.59): C 59.53, H 5.38, N 10.68; found: C 59.38, H 5.34, N 10.79.



**4-Ethyl-2-methyl 5-((4-chlorophenyl)imino)-2-(1-(2(methoxycarbonyl)hydrazono)ethyl)-3-methyl-2,5-dihydrothiophene-2,4-dicarboxylate 7g.**

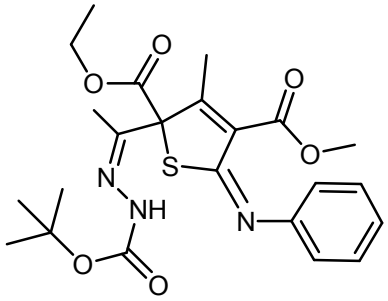
**7g** was isolated by column chromatography on silica gel (ethyl acetate/cyclohexane) in 63 % yield. White solid; mp: 106–109 °C; $^1$H NMR (400 MHz, DMSO$_{d6}$, 25 °C): δ = 1.29 (t, 3H, *J* = 7.6 Hz, OCH$_2$*CH$_3$*), 1.85 (s, 3H, *CH$_3$*), 2.13 (s, 3H, *CH$_3$*), 3.67 (s, 3H, O*CH$_3$*), 3.73 (s, 3H, O*CH$_3$*), 4.33 (q, 2H, *J* = 7.2 Hz, O*CH$_2$*CH$_3$), 7.02 (d, 2H, *J* = 8.8 Hz, Ph), 7.44 (d, 2H, *J* = 8.4 Hz Ph), 10.30 (s, 1H, *NH*); $^{13}$C NMR (100 MHz, DMSO$_{d6}$, 25 °C): δ = 13.3 (q), 14.0 (q), 15.4 (q), 52.1 (q), 53.5 (q), 61.6 (t), 75.6 (s), 121.6 (d), 129.4 (s), 129.4 (d), 135.8 (s), 146.7 (s), 149.0 (s), 154.2 (s), 157.0 (s), 163.0 (s), 164.2 (s), 167.6 (s); IR (nujol): $\nu_{max}$ = 3257, 1749, 1686 cm$^{-1}$; MS *m/z* (ESI): 468.76 (M + H$^+$); anal. calcd. for $C_{20}H_{22}ClN_3O_6S$ (467.92): C 51.34, H 4.74, N 8.98; found: C 51.18, H 4.69, N 9.13.



**Dimethyl 2-(1-(2-*tert*-butoxycarbonyl)hydrazono)ethyl)-3-methyl-5-(phenylimino)-2,5-dihydrothiophene-2,4-dicarboxylate 7h.**

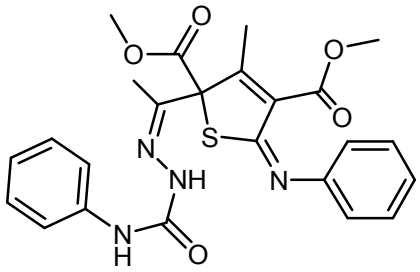
**7h** was isolated by column chromatography on silica gel (ethyl acetate/cyclohexane) in 68% yield. White solid; mp: 151–153 °C; $^1$H NMR (400 MHz, CDCl$_3$, 25 °C): δ = 1.50 (s, 9H, C(*CH$_3$*)$_3$), 1.83 (s, 3H, *CH$_3$*), 2.24 (s, 3H, *CH$_3$*), 3.80 (s, 3H, O*CH$_3$*), 3.93 (s, 3H, O*CH$_3$*), 7.04 (d, 2H, *J* = 8.0 Hz, Ph), 7.15 (t, 1H, *J* = 7.2 Hz, Ph), 7.35 (t, 2H, *J* = 7.6 Hz, Ph), 7.85 (s, 1H, *NH*); $^{13}$C NMR (100 MHz, CDCl$_3$, 25 °C): δ = 12.3 (q), 16.2 (q), 28.2 (q), 52.7 (q), 64.4 (q), 75.1 (s), 81.7 (s), 120.1 (d), 125.2

(d), 129.1 (d), 136.0 (s), 144.6 (s), 150.7 (s), 152.2 (s), 157.7 (s), 163.8 (s), 164.2 (s), 168.1 (s); IR (nujol): $\nu_{max}$ = 3231, 1740, 1698, 1629 $cm^{-1}$; MS *m/z* (ESI): 462.64 ($M + H^+$); anal. calcd. for $C_{22}H_{27}N_3O_6S$ (461.53): C 57.25, H 5.90, N 9.10; found: C 57.16, H 5.87, N 9.16.



**2-Ethyl-4-methyl 2-(1-(2(*tert*-butoxycarbonyl)hydrazono)ethyl)-3-methyl-5-(phenylimino)-2,5-dihydrothiophene-2,4-dicarboxylate 7i.**

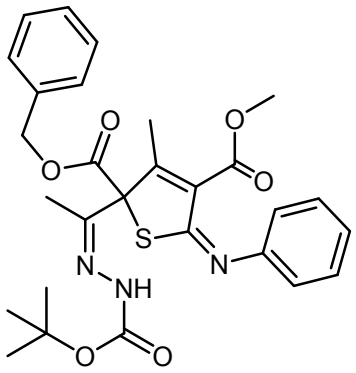
**7i** was isolated by column chromatography on silica gel (ethyl acetate/cyclohexane) in 69 % yield. White solid; mp: 152–156 °C; $^1$H NMR (400 MHz, DMSO$_{d6}$, 25 °C): δ = 1.30 (t, 3H, *J* = 7.2 Hz $OCH_2CH_3$), 1.50 (s, 9H, $C(CH_3)_3$), 1.83 (s, 3H, $CH_3$), 2.24 (s, 3H, $CH_3$), 3.92 (s, 3H, $OCH_3$), 4.26 (q, 2H, *J* = 7.2 Hz, $OCH_2CH_3$), 7.03 (dd, 2H, *J* = 8.4 Hz, *J* = 1.2 Hz, Ph), 7.14 (tt, 1H, *J* = 7.2 Hz, *J* = 1.2 Hz, Ph), 7.35 (t, 2H, *J* = 7.6 Hz, Ph), 7.91 (brs, 1H, *NH*); $^{13}$C NMR (100 MHz, DMSO$_{d6}$, 25 °C): δ = 12.5 (q), 14.0 (q), 16.2 (q), 28.2 (q), 52.6 (q), 62.7 (t), 75.2 (s), 81.6 (s), 120.1 (d), 125.1 (d), 129.1 (d), 135.9 (s), 144.8 (s), 150.9 (s), 152.4 (s), 157.8 (s), 163.8 (s), 164.3 (s), 167.6 (s); IR (nujol): $\nu_{max}$ = 3254, 1713, 1676, 1628 $cm^{-1}$; MS *m/z* (ESI): 476.38 ($M + H^+$); anal. calcd. for $C_{23}H_{29}N_3O_6S$ (475.56): C 58.09, H 6.15, N 8.84; found: C 57.95, H 6.11, N 8.98.



**Dimethyl 3-methyl 2-(1-(2(phenylcarbamoyl)hydrazono)ethyl)-5-(phenylimino)-2,5-dihydrothiophene-2,4-dicarboxylate 7j.**

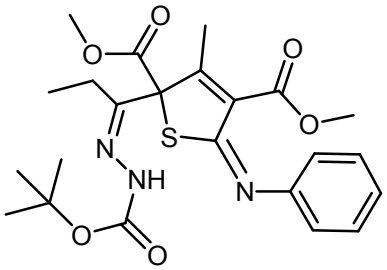
**7j** was isolated by column chromatography on silica gel (ethyl acetate/cyclohexane) in 51 % yield. Pale yellow solid; mp: 126–128 °C; $^1$H NMR (400 MHz, DMSO$_{d6}$, 25 °C): δ = 1.91 (s, 3H, $CH_3$), 2.17 (s, 3H, $CH_3$), 3.81 (s, 3H, $OCH_3$), 3.87 (s, 3H, $OCH_3$), 6.98-7.05 (m, 3H, Ph), 7.19 (t, 1H, *J* = 7.2 Hz, Ph), 7.31 (t, 2H, , *J* = 7.6 Hz, Ph), 7.38-7.46 (m, 4H, Ph), 8.27 (s, 1H, *NH*), 10.02 (s, 1H, *NH*); $^{13}$C NMR (100 MHz, DMSO$_{d6}$, 25 °C): δ = 13.5 (q), 15.5 (q), 52.7 (q), .53.7 (q), 75.1 (s), 118.5

(d), 119.6 (d), 122.6 (d), 125.3 (d), 128.9 (d), 129.4 (d), 135.7 (s), 138.4 (s), 144.1 (s), 150.3 (s), 152.3 (s), 156.9 (s), 163.2 (s), 163.7 (s), 167.7 (s); IR (nujol): $\nu_{max}$ = 3335, 3215, 1712, 1684, 1677 $cm^{-1}$; MS *m/z* (ESI): 481.22 ($M + H^+$); anal. calcd. for $C_{24}H_{24}N_4O_5S$ (480.54): C 59.99, H 5.03, N 11.66; found: C 60.10, H 5.06, N 11.55.



**2-Benzyl-4-methyl 2-(1-(2-*tert*-butoxycarbonyl)hydrazono)ethyl)-3-methyl-5-(phenylimino)-2,5-dihydrothiophene-2,4-dicarboxylate 7k.**

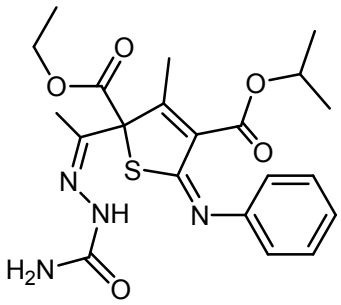
**7k** was isolated by column chromatography on silica gel (ethyl acetate/cyclohexane) in 66 % yield. White solid; mp: 135–137 °C; $^1$H NMR (400 MHz, $DMSO_{d6}$, 25 °C): δ = 1.45 (s, 9H, C(*CH*$_3$)$_3$), 1.85 (s, 3H, *CH*$_3$), 2.11 (s, 3H, *CH*$_3$), 3.85 (s, 3H, O*CH*$_3$), 5.21 (s, 2H, O*CH*$_2$Ph), 6.96 (dd, 2H, *J* = 8.4 Hz, *J* = 1.2 Hz, Ph), 7.16 (t, 1H, *J* = 7.2 Hz, Ph), 7.31-7.41 (m, 7H, Ph), 9.98 (s, 1H, *NH*); $^{13}$C NMR (100 MHz $DMSO_{d6}$, 25 °C): δ = 13.5 (q), 15.6 (q), 27.9 (q), 52.6 (q), 67.8 (t), 75.5 (s), 79.8 (s), 119.5 (d), 125.2 (d), 126.4 (d), 128.1 (d), 128.2 (d), 128.3 (d), 129.4 (d), 135.1 (s), 135.6 (s), 145.8 (s), 150.3 (s), 152.6 (s), 157.2 (s), 163.3 (s), 163.6 (s), 167.2 (s); IR (nujol): $\nu_{max}$ = 3216 ,1735, 1722, 1634 $cm^{-1}$; MS *m/z* (ESI): 538.19 ($M + H^+$); anal. calcd. for $C_{28}H_{31}N_3O_6S$ (537.63): C 62.55, H 5.81, N 7.82; found: C 62.71, H 5.83, N 7.71.



**Dimethyl 2-(1-(2-*tert*-butoxycarbonyl)hydrazono)propyl)-3-methyl-5-(phenylimino)-2,5-dihydrothiophene-2,4-dicarboxylate 7l.**

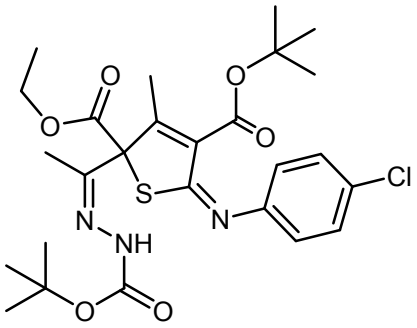
**7l** was isolated by column chromatography on silica gel (ethyl acetate/cyclohexane) in 65% yield. White solid; mp: 120–124 °C; $^1$H NMR (400 MHz, $DMSO_{d6}$, 25 °C): δ = 0.96 (t, 3H, *J* = 7.6 Hz $CH_2$*CH*$_3$), 1.45 (s, 9H, C(*CH*$_3$)$_3$), 2.11 (s, 3H, *CH*$_3$), 2.11.-2.18 (m, 1H, *CH*$_2$$CH_3$), 2.39.-2.47 (m, 1H,

*CH*$_2$CH$_3$), 3.71 (s, 3H, O*CH*$_3$), 3.85 (s, 3H, O*CH*$_3$), 6.97 (dd, 2H, *J* = 8.4 Hz, *J* = 1.2 Hz, Ph), 7.18 (t, 1H, *J* = 7.6 Hz, Ph), 7.40 (t, 2H, *J* = 7.6 Hz, Ph), 10.05 (s, 1H, *NH*); $^{13}$C NMR (100 MHz, DMSO$_{d6}$, 25 °C): δ = 10.5 (q), 15.8 (q), 19.8 (t), 28.0 (q), 52.7 (q), 53.3 (q), 75.3 (s), 79.9 (s), 119.5 (d), 125.2 (d), 129.5 (d), 135.6 (s), 149.0 (s), 150.3 (s), 152.6 (s), 157.2 (s), 163.4 (s), 163.7 (s), 167.9 (s); IR (nujol): $\nu_{max}$ = 3220, 1749, 1715, 1654 cm$^{-1}$; MS *m/z* (ESI): 476.29 (M + H$^+$); anal. calcd. for $C_{23}H_{29}N_3O_6S$ (475.56): C 58.09, H 6.15, N 8.84; found: C 57.96, H 6.12, N 8.96.



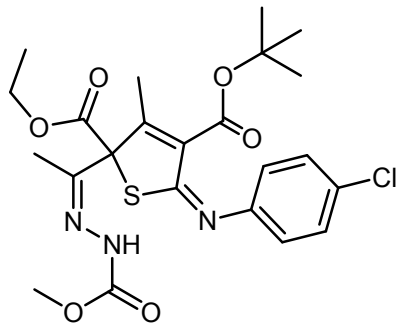
**2-Ethyl 4-*iso*-propyl 2-((1-(2-carbamoylhydrazono)ethyl)-3-methyl-5-((phenyl)imino)-2,5-dihydrothiophene-2,4-dicarboxylate 7m.**

**7m** was isolated by column chromatography on silica gel (ethyl acetate/cyclohexane) in 52 % yield. White solid; mp: 170–173 °C; $^1$H NMR (400 MHz, $CDCl_3$, 25 °C): δ = 1.27 (t, 3H, *J* = 7.2 Hz OCH$_2$*CH*$_3$), 1.35 (d, 6H, *J* = 6.4 Hz, CH(*CH*$_3$)$_2$), 1.90 (s, 3H, *CH*$_3$), 2.16 (s, 3H, *CH*$_3$), 4.23 (q, 2H, *J* = 7.2 Hz O*CH*$_2$CH$_3$), 5.29 (hept, 1H, *J* = 6.4 Hz, C*H*(CH$_3$)$_2$),5.60 and 5.82 (2 brs, 2H, *NH*$_2$), 7.04 (dd, 2H, *J* = 8.8 Hz, *J* = 1.2 Hz, Ph), 7.13 (t, 1H, *J* = 7.2 Hz, Ph), 7.34 (d, 2H, *J* = 8.4 Hz Ph), 9.40 (s, 1H, *NH*); $^{13}$C NMR (100 MHz, $CDCl_3$, 25 °C): δ = 12.8 (q), 14.0 (q), 15.4 (q), 27.8 (q), 62.6 (t), 69.7 (d), 75.3 (s), 120.1 (d), 125.1 (d), 129.1 (d), 136.9 (s), 144.7 (s), 150.6 (s), 155.0 (s), 157.9 (s), 163.1 (s), 163.3 (s), 167.5 (s); IR (nujol): $\nu_{max}$ = 3421, 3264, 3257, 1742, 1613, 1606 cm$^{-1}$; MS *m/z* (ESI): 447.17 (M + H$^+$); anal. calcd. for $C_{21}H_{26}N_4O_5S$ (446.52): C 56.49, H 5.87, N 12.55; found: C 56.37, H 5.89, N 12.68.



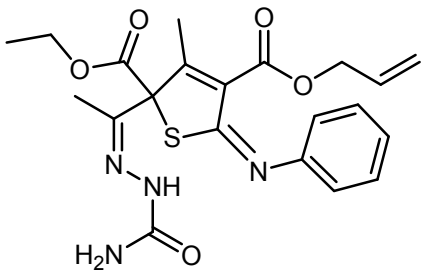
**4-*Tert*-butyl 2-ethyl 2-((1-(2(*tert*-butoxycarbonyl)hydrazono)ethyl)-5-((4-chlorophenyl)imino)--3-methyl-2,5-dihydrothiophene-2,4-dicarboxylate 7n.**

**7n** was isolated by column chromatography on silica gel (ethyl acetate/cyclohexane) in 68 % yield. Pale yellow solid; mp: 120–124 °C; $^{1}$H NMR (400 MHz, $CDCl_3$, 25 °C): δ = 1.28 (t, 3H, *J* = 7.2 Hz $OCH_2\mathit{CH_3}$), 1.47 (s, 9H, $C(\mathit{CH_3})_3$), 1.56 (s, 9H, $C(\mathit{CH_3})_3$), 1.81 (s, 3H, $\mathit{CH_3}$), 2.20 (s, 3H, $\mathit{CH_3}$), 4.23 (q, 2H, *J* = 7.2 Hz $O\mathit{CH_2}CH_3$), 6.96 (d, 2H, *J* = 8.8 Hz, Ph), 7.27 (d, 2H, *J* = 8.8 Hz Ph), 8.46 (brs, 1H, *NH*); $^{13}$C NMR (100 MHz, $CDCl_3$, 25 °C): δ = 12.4 (q), 13.9 (q), 15.8 (q), 28.1 (q), 62.6 (t), 75.4 (s), 81.4 (s), 83.0 (s), 121.4 (d), 129.9 (d), 130.1 (d), 137.1 (s), 144.8 (s), 149.3 (s), 152.7 (s), 155.9 (s), 162.8 (s), 164.4 (s), 167.5 (s); IR (nujol): $\nu_{max}$ = 3255, 1736, 1685, 1624 cm$^{-1}$; MS *m/z* (ESI): 553.04 ($M + H^+$); anal. calcd. for $C_{26}H_{34}ClN_3O_6S$ (552.08): C 56.56, H 6.21, N 7.61; found: C 56.68, H 6.24, N 7.51.



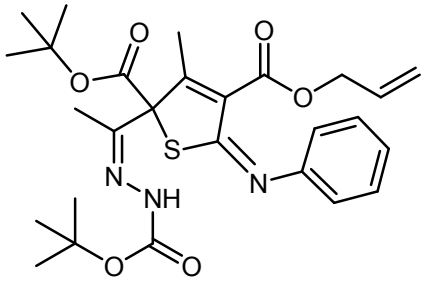
**4-*Tert*-butyl 2-ethyl 5-((4-chlorophenyl)imino)-2-((1-(2(methoxycarbonyl)hydrazono)ethyl)-3-methyl-2,5-dihydrothiophene-2,4-dicarboxylate 7o.**

**7o** was isolated by column chromatography on silica gel (ethyl acetate/cyclohexane) in 65 % yield. White solid; mp: 132–135 °C; $^{1}$H NMR (400 MHz, $CDCl_3$, 25 °C): δ = 1.28 (t, 3H, *J* = 7.2 Hz $OCH_2\mathit{CH_3}$), 1.56 (s, 9H, $C(\mathit{CH_3})_3$), 1.81 (s, 3H, $\mathit{CH_3}$), 2.18 (s, 3H, $\mathit{CH_3}$), 3.75 (s, 3H, $O\mathit{CH_3}$), 4.16-4.34 (m, 2H, $O\mathit{CH_2}CH_3$), 6.95 (d, 2H, *J* = 8.4 Hz, Ph), 7.28 (d, 2H, *J* = 8.8 Hz, Ph), 8.43 (brs, 1H, *NH*); $^{13}$C NMR (100 MHz, $CDCl_3$, 25 °C): δ = 12.0 (q), 13.9 (q), 15.7 (q), 28.2 (q), 53.0 (q), 62.8 (t), 75.4 (s), 83.2 (s), 121.7 (d), 129.2 (s), 130.3 (d), 137.8 (s), 146.2 (s), 149.3 (s), 154.3 (s), 155.4 (s), 162.9 (s), 164.2 (s), 167.4 (s); IR (nujol): $\nu_{max}$ = 3243, 1741, 1703, 1612 cm$^{-1}$; MS *m/z* (ESI): 511.14 ($M + H^+$); anal. calcd. for $C_{23}H_{28}ClN_3O_6S$ (510.00): C 54.17, H 5.53, N 8.24; found: C 54.30, H 5.57, N 8.11.



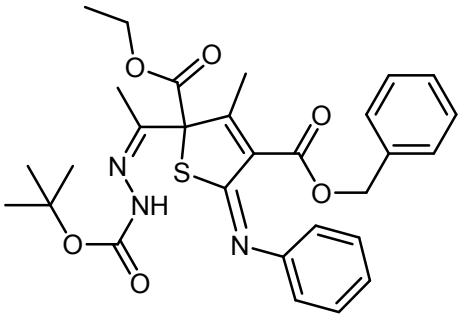
**4-Allyl 2-ethyl-2-(1-(2(carbamoylhydrazono)ethyl)-3-methyl-5-(phenylimino)-2,5-dihydrothiophene-2,4-dicarboxylate 7p.**

**7p** was isolated by column chromatography on silica gel (ethyl acetate/cyclohexane) in 52 % yield. White solid; mp: 155–158 °C; $^{1}$H NMR (400 MHz, DMSO$_{d6}$, 25 °C): δ = 1.19 (t, 3H, *J* = 7.2 Hz $OCH_2\mathit{CH_3}$), 1.84 (s, 3H, $\mathit{CH_3}$), 2.11 (s, 3H, $\mathit{CH_3}$), 4.18-4.26 (m, 2H, $O\mathit{CH_2}CH_3$), 4.82 (dt, 2H, *J* = 5.2 Hz, *J* = 1.6 Hz, $O\mathit{CH_2}CH{=}CH_2$), 5.27 (ddt, 1H, *J* = 10.4 Hz, *J* = 1.6 Hz, *J* = 1.2 Hz,$OCH_2CH{=}\mathit{CH_2}$), 5.46 (ddt, 1H, *J* = 17.2 Hz, *J* = 1.6 Hz, *J* = 1.6 Hz, $OCH_2CH{=}\mathit{CH_2}$), 5.94-6.04 (m, 1H, $OCH_2\mathit{CH}{=}CH_2$), 6.13 (brs, 2H, $NH_2$), 6.99 (dd, 2H, *J* = 8.8 Hz, *J* = 1.2 Hz, Ph), 7.18 (t, 1H, *J* = 7.6 Hz Ph), 7.40 (t, 2H, *J* = 8.0 Hz, Ph), 9.56 (s, 1H, *NH*); $^{13}$C NMR (100 MHz, DMSO$_{d6}$, 25 °C): δ = 13.0 (q), 13.7 (q), 15.4 (q), 62.6 (t), .65.7 (t), 75.4 (s), 118.4 (t), 119.6 (d), 125.3 (d), 129.4 (d), 131.9 (d), 135.5 (s), 142.3 (s), 150.2 (s), 156.3 (s), 157.0 (s), 162.8 (s), 163.1 (s), 167.1 (s); IR (nujol): $\nu_{max}$ = 3476, 3316, 3197, 1739, 1732, 1695 cm$^{-1}$; MS *m/z* (ESI): 445.13 (M + H$^{+}$); anal. calcd. for $C_{21}H_{24}N_4O_5S$ (444.50): C 56.74, H 5.44, N 12.60; found: C 56.63, H 5.40, N 12.71.



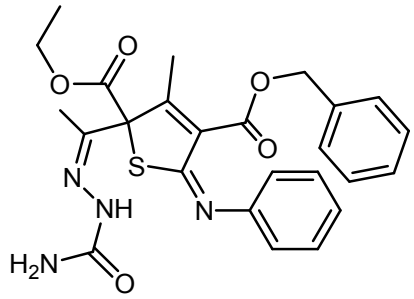

**4-Allyl 2-*tert*-butyl-2-(1-(2-(*tert*-butoxycarbonyl)hydrazono)ethyl)-3-methyl-5-(phenylimino)-2,5-dihydrothiophene-2,4-dicarboxylate 7q.**

**7q** was isolated by column chromatography on silica gel (ethyl acetate/cyclohexane) in 61 % yield. White solid; mp: 121–125 °C; $^{1}$H NMR (400 MHz, DMSO$_{d6}$, 25 °C): δ = 1.43 (s, 9H, $OC(\mathit{CH_3})_3$), 1.44 (s, 9H, $OC(\mathit{CH_3})_3$), 1.83 (s, 3H, $\mathit{CH_3}$), 2.12 (s, 3H, $\mathit{CH_3}$), 4.81 (d, 2H, *J* = 5.2 Hz, $O\mathit{CH_2}CH{=}CH_2$), 5.27 (dd, 1H, *J* = 10.4 Hz, *J* = 1.2 Hz, $OCH_2CH{=}\mathit{CH_2}$), 5.46 (dd, 1H, *J* = 17.2 Hz, *J* = 1.2 Hz, $OCH_2CH{=}\mathit{CH_2}$), 5.94-6.04 (m, 1H, $OCH_2\mathit{CH}{=}CH_2$), 6.97 (d, 2H, *J* = 8.0 Hz, Ph), 7.18 (t, 1H, *J* = 7.6 Hz, Ph), 7.40 (t, 2H, *J* = 7.6 Hz, Ph), 9.82 (s, 1H, *NH*); $^{13}$C NMR (100 MHz, DMSO$_{d6}$, 25 °C): δ = 14.0 (q), 15.7 (q), 27.4 (q), 28.0 (q), 65.7 (t), 76.4 (s), 79.8 (s), 83.8 (s), 118.4 (t), 119.6 (d), 125.2 (d), 129.5 (d), 132.0 (d), 135.2 (s), 146.4 (s), 150.3 (s), 152.7 (s), 163.0 (s), 163.5 (s), 165.9 (s); IR (nujol): $\nu_{max}$ = 3235, 1752, 1727, 1676 cm$^{-1}$; MS *m/z* (ESI): 530.36 (M + H$^{+}$); anal. calcd. for $C_{27}H_{35}N_3O_6S$ (529.65): C 61.23, H 6.66, N 7.93; found: C 61.10, H 6.64, N 8.02.



**4-Benzyl-2-ethyl 2-(1-(2-*tert*-butoxycarbonyl)hydrazono)ethyl)-3-methyl-5-(phenylimino)-2,5-dihydrothiophene-2,4-dicarboxylate 7r.**

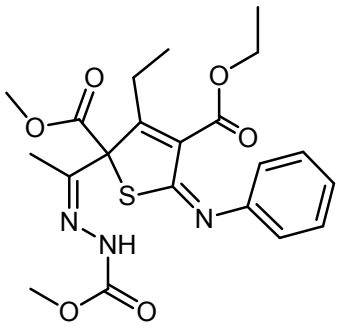
**7r** was isolated by column chromatography on silica gel (ethyl acetate/cyclohexane) in 47% yield. White solid; mp: 109–113 °C; $^1$H NMR (400 MHz, DMSO$_{d6}$, 25 °C): δ = 1.20 (t, 3H, *J* = 7.2 Hz $OCH_2CH_3$), 1.42 (s, 9H, $C(CH_3)_3$), 1.83 (s, 3H, $CH_3$), 2.10 (s, 3H, $CH_3$), 4.19 (q, 2H, *J* = 7.2 Hz, $OCH_2CH_3$), 5.36 (s, 2H, $OCH_2Ph$), 6.99 (dd, 2H, *J* = 8.4 Hz, *J* = 1.2 Hz, Ph), 7.19 (t, 1H, *J* = 7.6 Hz, Ph), 7.34-7.43 (m, 5H, Ph), 7.47 (dd, 2H, *J* = 8.0 Hz, *J* = 1.6 Hz, Ph), 9.88 (s, 1H, *NH*); $^{13}$C NMR (100 MHz, DMSO$_{d6}$, 25 °C): δ = 13.7 (q), 13.7 (q), 15.6 (q), 28.0 (q), 62.6 (t), 66.9 (t), 75.6 (s), 79.8 (s), 119.7 (d), 125.3 (d), 128.1 (d), 128.2 (d), 128.4 (d), 129.5 (d), 135.3 (s), 135.4 (s), 143.7 (s), 150.2 (s), 152.6 (s), 157.3 (s), 163.1 (s), 163.2 (s), 167.1 (s); IR (nujol): $\nu_{max}$ = 3255, 1751, 1681, 1643 cm$^{-1}$; MS *m/z* (ESI): 552.37 (M + H$^+$); anal. calcd. for $C_{29}H_{33}N_3O_6S$ (551.65): C 63.14, H 6.03, N 7.62; found: C 63.02, H 6.00, N 7.74.



**4-Benzyl 2-ethyl 2-((1-(2-carbamoylhydrazono)ethyl)-3-methyl-5-((phenyl)imino)-2,5-dihydrothiophene-2,4-dicarboxylate 7s.**

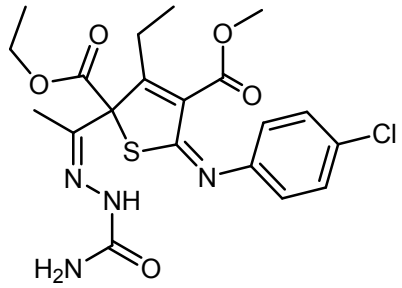
**7s** was isolated by column chromatography on silica gel (ethyl acetate/cyclohexane) in 44 % yield. Pale yellow solid; mp: 148–151 °C; $^1$H NMR (400 MHz, $CDCl_3$, 25 °C): δ = 1.27 (t, 3H, *J* = 7.2 Hz $OCH_2CH_3$), 1.88 (s, 3H, $CH_3$), 2.14 (s, 3H, $CH_3$), 4.22 (dq, 2H, *J* = 7.2 Hz, *J* = 1.6 Hz,$OCH_2CH_3$), 5.38 (AB system, 2H, *J* = 12.4 Hz, $OCH_2Ph$), 5.78 ( brs, 2H, $NH_2$), 7.05 (dd, 2H, *J* = 8.4 Hz, *J* = 1.2 Hz, Ph), 7.16 (t, 1H, *J* = 7.2 Hz, Ph), 7.34-7.40 (m, 5H, Ph), 7.46 (dd, 2H, *J* = 8.0 Hz, *J* = 1.6 Hz, Ph), 9.32 (s, 1H, *NH*); $^{13}$C NMR (100 MHz, $CDCl_3$, 25 °C): δ = 12.9 (q), 14.0 (q), 15.7 (q), 62.6 (t), 67.5 (t), 75.3 (s), 120.1 (d), 125.2 (d), 128.3 (d), 128.4 (d), 128.5 (d), 129.1 (d), 135, 2 (s), 136.2 (s), 144.5 (s), 150.6 (s), 156.5 (s), 157.7 (s), 163.1 (s), 163.6 (s), 167.4 (s); IR (nujol): $\nu_{max}$ = 3470, 3361,

3196, 1732, 1697, 1682 $cm^{-1}$; MS *m/z* (ESI): 495.36 ($M + H^+$); anal. calcd. for $C_{25}H_{26}N_4O_5S$ (494.56): C 60.71, H 5.30, N 11.33; found: C 60.86, H 5.34, N 11.21.



**4-Ethyl-2-methyl 3-ethyl-2-(1-(2(methoxycarbonyl)hydrazono)ethyl)-5-(phenylimino)-2,5-dihydrothiophene-2,4-dicarboxylate 7t.**

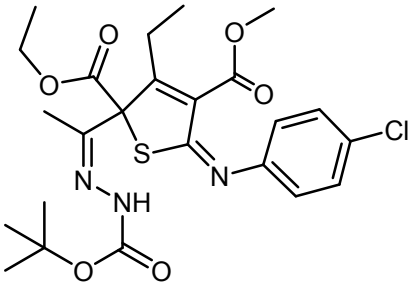
**7t** was isolated chromatography on by column silica gel (ethyl acetate/cyclohexane) in 48 % yield. White solid; mp: 136–139 °C; $^1$H NMR (400 MHz, $DMSO_{d6}$, 25 °C): δ = 1.03 (t, 3H, *J* = 7.6 Hz $CH_2CH_3$), 1.29 (t, 3H, *J* = 7.2 Hz $OCH_2CH_3$), 1.85 (s, 3H, $CH_3$), 2.49-2.54 (m, 2H, $CH_2CH_3$), 3.67 (s, 3H, $OCH_3$), 3.71 (s, 3H, $OCH_3$), 4.33 (q, 2H, *J* = 7.2 Hz $OCH_2CH_3$), 6.98 (dd, 2H, *J* = 8.4 Hz, *J* = 1.2 Hz, Ph), 7.18 (t, 1H, *J* = 7.2 Hz Ph), 7.33 (t, 2H, *J* = 7.6 Hz Ph), 10.33 (s, 1H, *NH*); $^{13}$C NMR (100 MHz, $DMSO_{d6}$, 25 °C): δ = 12.5 (q), 13.9 (q), 14.0 (q), 22.6 (t), 52.1 (q), 53.4 (q), 61.6 (t), 75.5 (s), 119.6 (d), 125.3 (d), 129.5 (d), 135.9 (s), 147.1 (s), 150.4 (s), 154.2 (s), 161.8 (s), 163.5 (s), 163.8 (s), 168.1 (s); IR (nujol): $\nu_{max}$ = 3262, 1732, 1624, 1598 $cm^{-1}$; MS *m/z* (ESI): 448.24 ($M + H^+$); anal. calcd. for $C_{21}H_{25}N_3O_6S$ (447.50): C 56.36, H 5.63, N 9.39; found: C 56.45, H 5.66, N 9.32.



**2-Ethyl-4-methyl 2-(1-(2(carbamoylhydrazono)ethyl)-5-((4-chlorophenyl)imino)-3-ethyl-2,5-dihydrothiophene-2,4-dicarboxylate 7u.**

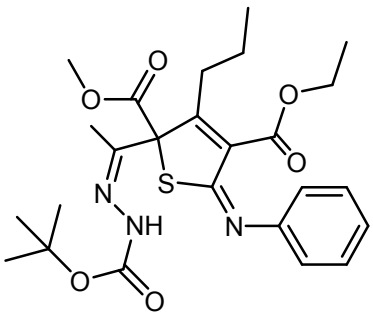
**7u** was isolated by column chromatography on silica gel (ethyl acetate/cyclohexane) in 46 % yield. Pale yellow solid; mp: 158–161 °C; $^1$H NMR (400 MHz, $DMSO_{d6}$, 25 °C): δ = 1.00 (t, 3H, *J* = 7.6 Hz $CH_2CH_3$), 1.19 (t, 3H, *J* = 7.2 Hz $OCH_2CH_3$), 1.84 (s, 3H, $CH_3$), 2.48-2.58 (m, 2H, $CH_2CH_3$), 3.85 (s, 3H, $OCH_3$), 4.17-4.26 (m, 2H, $OCH_2CH_3$), 6.23 (brs, 2H, $NH_2$), 7.02 (d, 2H, *J* = 8.8 Hz, Ph), 7.45 (d, 2H, *J* = 8.8 Hz Ph), 9.62 (s, 1H, *NH*); $^{13}$C NMR (100 MHz, $DMSO_{d6}$, 25 °C): δ = 12.6 (q),

13.5 (q), 13.7 (q), 22.7 (t), 52.7 (q), 62.6 (t), 75.8 (s), 81.6 (s), 121.6 (d), 129.4 (s), 129.4 (d), 135.4 (s), 142.2 (s), 149.0 (s), 156.3 (s), 162.2 (s), 163.8 (s), 164.8 (s), 167.2 (s); IR (nujol): $\nu_{max}$ = 3446, 3321, 3223, 1747, 1730, 1684 $cm^{-1}$; MS *m/z* (ESI): 467.63 ($M + H^+$); anal. calcd. for $C_{20}H_{23}ClN_4O_5S$ (466.94): C 51.44, H 4.96, N 12.00; found: C 51.36, H 4.97, N 12.11.



**2-Ethyl-4-methyl 2-(1-(2(*tert*-butoxycarbonyl)hydrazono)ethyl)-5-((4-chlorophenyl)imino)-3-ethyl-2,5-dihydrothiophene-2,4-dicarboxylate 7v.**

**7v** was isolated by column chromatography on silica gel (ethyl acetate/cyclohexane) in 46 % yield. Pale yellow solid; mp: 107–109 °C; $^1$H NMR (400 MHz, $DMSO_{d6}$, 25 °C): δ = 1.03 (t, 3H, *J* = 7.6 Hz $CH_2CH_3$), 1.21 (t, 3H, *J* = 7.2 Hz $OCH_2CH_3$), 1.44 (s, 9H, $C(CH_3)_3$), 1.85 (s, 3H, $CH_3$), 2.52-2.57 (m, 2H, $CH_2CH_3$), 3.85 (s, 3H, $OCH_3$), 4.17-4.22 (m, 2H, $OCH_2CH_3$), 7.00 (d, 2H, *J* = 8.8 Hz, Ph), 7.44 (d, 2H, *J* = 8.8 Hz Ph), 9.92 (s, 1H, *NH*); $^{13}$C NMR (100 MHz, $DMSO_{d6}$, 25 °C): δ = 12.4 (q), 13.7 (q), 14.0 (q), 22.8 (t), 27.9 (q), 52.6 (q), 62.6 (t), 76.0 (s), 79.8 (s), 122.6 (d), 129.3 (s), 129.4 (d), 135.5 (s), 142.2 (s), 149.1 (s), 152.6 (s), 162.5 (s), 163.9 (s), 164.9 (s), 167.2 (s); IR (nujol): $\nu_{max}$ = 3223, 1717, 1684, 1621 $cm^{-1}$; MS *m/z* (ESI): 524.81 ($M + H^+$); anal. calcd. for $C_{24}H_{30}ClN_3O_6S$ (524.03): C 55.01, H 6.77, N 8.02; found: C 54.95, H 6.79, N 8.15.



**4-Ethyl-2-methyl 2-(1-(2-*tert*-butoxycarbonyl)hydrazono)ethyl)-5-(phenylimino)-3-propyl--2,5-dihydrothiophene-2,4-dicarboxylate 7w.**

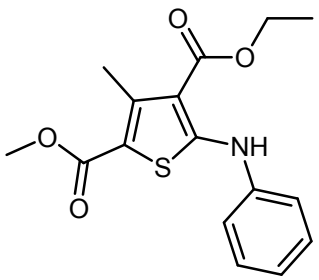
**7w** was isolated by column chromatography on silica gel (ethyl acetate/cyclohexane) in 40% yield. White solid; mp: 142–144 °C; $^1$H NMR (400 MHz, $DMSO_{d6}$, 25 °C): δ = 0.88 (t, 3H, *J* = 7.6 Hz $CH_2CH_2CH_3$), 1.29 (t, 3H, *J* = 7.2 Hz $OCH_2CH_3$), 1.35-1.50 (m, 2H, $CH_2CH_2CH_3$), 1.44 (s, 9H, $C(CH_3)_3$), 1.84 (s, 3H, $CH_3$), 2.42-2.56 (m, 2H, $CH_2CH_2CH_3$), 3.72 (s, 3H, $OCH_3$), 4.32 (q, 2H, *J* =

7.2 Hz, O*CH*$_2$CH$_3$), 6.97 (dd, 2H, *J* = 7.6 Hz, *J* = 0.8 Hz, Ph), 7.18 (t, 1H, *J* = 7.6 Hz, Ph), 7.40 (t, 2H, *J* = 7.6 Hz, Ph), 9.92 (s, 1H, *NH*); $^{13}$C NMR (100 MHz, DMSO$_{d6}$, 25 °C): δ = 13.9 (q), 14.1 (q), 14.4 (q), 21.4 (t), 28.0 (q), 31.6 (t), 53.4 (q), 61.5 (t), 75.6 (s), 79.8 (s), 119.6 (d), 125.2 (d), 129.4 (d), 135.8 (s), 146.2 (s), 150.3 (s), 152.6 (s), 159.4 (s), 163.4 (s), 163.7 (s), 168.0 (s); IR (nujol): $\nu_{max}$ = 3237, 1745, 1695, 1636 cm$^{-1}$; MS *m/z* (ESI): 504.45 (M + H$^+$); anal. calcd. for $C_{25}H_{33}N_3O_6S$ (503.61): C 59.62, H 6.60, N 8.34; found: C 59.49, H 6.56, N 8.48.

## 7 General procedure for synthesis of 5-amino thiophene-2,4-dicarboxylates 8a-j.

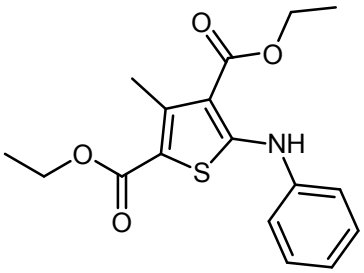
To a solution of 2,5-dihydrothiophenes **7a-d,g-i,k,p-s,u,v** (0.5 mmol) in acetone/water (90/10, 5.0 mL) Amberlyst 15 *H* (4.0 equiv) was added and the reaction mixture was softly stirred at room temperature. At the disappearance of the starting 2,5-dihydrothiophenes **7** (2.0-4.0 h, monitored by TLC) the reaction solvent was evaporated under reduced pressure and the desired 2,5-5-amino thiophene-2,4-dicarboxylates **8a-j** were purified by chromatography on silica gel column (elution mixture: cyclohexane: ethyl acetate).

## 8 Spectral data of 5-amino thiophene-2,4-dicarboxylates 8a-j.




**4-Ethyl-2-methyl 3-methyl-5-(phenylamino)thiophene-2,4-dicarboxylate 8a.**

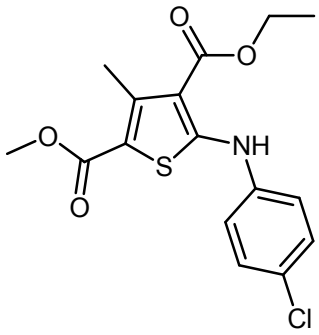
**8a** was isolated by column chromatography on silica gel (ethyl acetate/cyclohexane) in 82% yield from **7a**, in 61% yield from **7c**, and in 64% yield from **7d**. White solid; mp: 136–138 °C; $^{1}$H NMR (400 MHz, $CDCl_3$, 25 °C): δ = 1.42 (t, 3H, *J* = 7.2 Hz $OCH_2\mathit{CH_3}$), 2.77 (s, 3H, $\mathit{CH_3}$), 3.81 (s, 3H, $O\mathit{CH_3}$), 4.36 (q, 2H, *J* = 7.2 Hz, $O\mathit{CH_2}CH_3$), 7.15 (t, 1H, *J* = 7.2 Hz, Ph), 7.33-7.42 (m, 4H, Ph), 10.62 (s, 1H, *NH*); $^{13}$C NMR (100 MHz, $CDCl_3$, 25 °C): δ = 14.3 (q), 16.0 (q), 51.5 (q), 60.4 (t), 108.1 (s), 109.2 (s), 119.9 (d), 124.3 (d), 129.6 (d), 139.8 (s), 147.8 (s), 162.4 (s), 163.2 (s), 166.9 (s); IR (nujol): $\nu_{max}$ = 3217, 1714, 1650 $cm^{-1}$; MS *m/z* (ESI): 320.08 ($M + H^+$); anal. calcd. for $C_{16}H_{17}NO_4S$ (319.38): C 60.17, H 5.37, N 4.39; found: C 60.26, H 5.39, N 4.32.




**Diethyl 3-methyl-5-(phenylamino)thiophene-2,4-dicarboxylate 8b.**

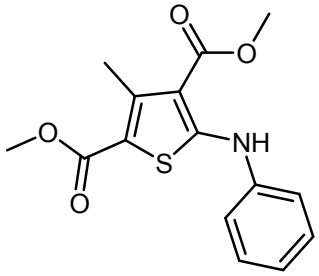
**8b** was isolated by column chromatography on silica gel (ethyl acetate/cyclohexane) in 78% yield from **7b**. White solid; mp: 106–108 °C; $^{1}$H NMR (400 MHz, $CDCl_3$, 25 °C): δ = 1.34 (t, 3H, *J* = 7.2 Hz $OCH_2\mathit{CH_3}$), 1.41 (t, 3H, *J* = 7.2 Hz $OCH_2\mathit{CH_3}$), 2.76 (s, 3H, $\mathit{CH_3}$), 4.28 (q, 2H, *J* = 7.2 Hz, $O\mathit{CH_2}CH_3$), 4.35 (q, 2H, *J* = 7.2 Hz, $O\mathit{CH_2}CH_3$), 7.12-7.41 (m, 5H, Ph), 10.62 (s, 1H, *NH*); $^{13}$C NMR (100 MHz, $CDCl_3$, 25 °C): δ = 14.0 (q), 14.2 (q), 15.7 (q), 60.2 (t), 108.4 (s), 108.9 (s), 119.6 (d), 124.0 (d), 129.3 (d), 139.6 (s), 147.2 (s), 162.0 (s), 162.6 (s), 166.1 (s); IR (nujol): $\nu_{max}$ = 3257, 1749,

1686 $cm^{-1}$; MS *m/z* (ESI): 334.19 ($M + H^+$); anal. calcd. for $C_{17}H_{19}NO_4S$ (333.40): C 61.24, H 5.74, N 4.20; found: C 61.39, H 5.79, N 4.12.



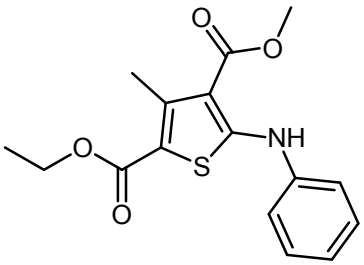

**4-Ethyl 2-methyl 5-((4-chlorophenyl)amino) 3-methylthiophene-2,4-dicarboxylate 8c.**

**8c** was isolated by column chromatography on silica gel (ethyl acetate/cyclohexane) in 81% yield from **7g**. White solid; mp: 140–141 °C; $^1$H NMR (400 MHz, $CDCl_3$, 25 °C): δ = 1.42 (t, 3H, *J* = 7.6 Hz $OCH_2CH_3$), 2.77 (s, 3H, $CH_3$), 3.82 (s, 3H, O $CH_3$), 4.37 (q, 2H, *J* = 7.6 Hz, $OCH_2CH_3$), 7.28 (d, 2H, *J* = 9.6 Hz, Ph), 7.36 (d, 2H, *J* = 9.6 Hz, Ph), 10.62 (s, 1H, *NH*); $^{13}$C NMR (100 MHz, $CDCl_3$, 25 °C): δ = 14.3 (q), 16.0 (q), 51.6 (q), 60.6 (t), 108.6 (s), 109.6 (s), 121.2 (d), 129.4 (s), 129.6 (d), 138.4 (s), 147.8 (s), 162.0 (s), 163.1 (s), 166.9 (s); IR (nujol): $\nu_{max}$ = 3160, 1704, 1652 $cm^{-1}$; MS *m/z* (ESI): 354.13 ($M + H^+$); anal. calcd. for $C_{16}H_{16}ClNO_4S$ (353.82): C 54.31, H 4.56, N 3.96; found: C 54.42, H 4.61, N 3.88.



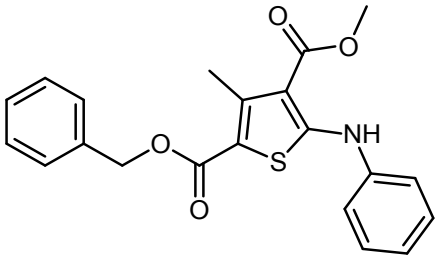

**Dimethyl 3-methyl-5-(phenylamino)thiophene-2,4-dicarboxylate 8d.**

**8d** was isolated by column chromatography on silica gel (ethyl acetate/cyclohexane) in 80% yield from **7h**. White solid; mp: 135–137 °C; $^1$H NMR (400 MHz, $CDCl_3$, 25 °C): δ = 2.75 (s, 3H, $CH_3$), 3.81 (s, 3H, O$CH_3$), 3.90 (s, 3H, O$CH_3$), 7.15 (t, 1H, *J* = 7.2 Hz, Ph), 7.34 (d, 2H, *J* = 7.6 Hz, Ph), 7.40 (t, 2H, *J* = 7.2 Hz, Ph), 10.58 (s, 1H, *NH*); $^{13}$C NMR (100 MHz, $CDCl_3$, 25 °C): δ = 15.9 (q), 51.3 (q), 51.5 (q), 108.2 (s), 109.0 (s), 120.0 (d), 124.4 (d), 129.6 (d), 139.8 (s), 147.7 (s), 162.6 (s), 163.1 (s), 167.3 (s); IR (nujol): $\nu_{max}$ = 3225, 1700, 1662 $cm^{-1}$; MS *m/z* (ESI): 306.18 ($M + H^+$); anal. calcd. for $C_{15}H_{15}NO_4S$ (305.35): C 59.00, H 4.95, N 4.59; found: C 58.88, H 4.92, N 4.70.



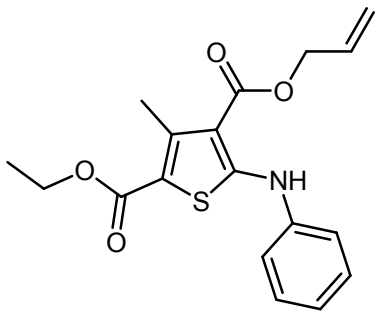
**2-Ethyl-4-methyl 3-methyl-5-(phenylamino)thiophene-2,4-dicarboxylate 8e.**

**8e** was isolated by column chromatography on silica gel (ethyl acetate/cyclohexane) in 78% yield from **7i**. White solid; mp: 128–131 °C; $^{1}$H NMR (400 MHz, $CDCl_3$, 25 °C): δ = 1.35 (t, 3H, *J* = 7.2 Hz $OCH_2CH_3$), 2.76 (s, 3H, $CH_3$), 3.91 (s, 3H, $OCH_3$), 4.29 (q, 2H, *J* = 7.2 Hz, $OCH_2CH_3$), 7.16 (t, 1H, *J* = 7.2 Hz, Ph), 7.35-7.44 (m, 4H, Ph), 10.55 (s, 1H, *NH*); $^{13}$C NMR (100 MHz, $CDCl_3$, 25 °C): δ = 14.4 (q), 15.9 (q), 51.3 (q), 60.5 (t), 108.8 (s), 109.1 (s), 120.1 (d), 124.5 (d), 129.6 (d), 139.9 (s), 147.4 (s), 162.6 (s), 162.8 (s), 167.4 (s); IR (nujol): $\nu_{max}$ = 3163, 1698, 1667 cm$^{-1}$; MS *m/z* (ESI): 320.05 (M + H$^+$); anal. calcd. for $C_{16}H_{17}NO_4S$ (319.38): C 60.17, H 5.37, N 4.39; found: C 60.05, H 5.34, N 4.43.



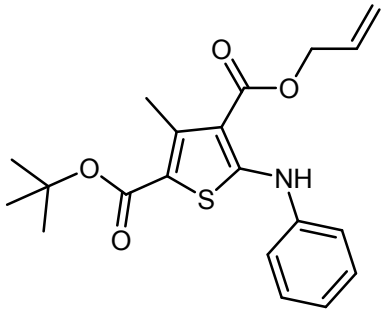
**2-Benzyl 4-methyl 3-methyl-5-(phenylamino)thiophene-2,4-dicarboxylate 8f.**

**8f** was isolated by column chromatography on silica gel (ethyl acetate/cyclohexane) in 81% yield from **7k**. White solid; mp: 116–118 °C; $^{1}$H NMR (400 MHz, $CDCl_3$, 25 °C): δ = 2.78 (s, 3H, $CH_3$), 3.91 (s, 3H, $OCH_3$), 5.29 (s, 2H, $OCH_2$Ph), 7.16 (t, 1H, *J* = 7.2 Hz, Ph), 7.34-7.43 (m, 9H, Ph), 10.59 (s, 1H, *NH*); $^{13}$C NMR (100 MHz, $CDCl_3$, 25 °C): δ = 16.0 (q), 51.4 (q), 66.0 (t), 108.2 (s), 109.2 (s), 120.1 (d), 124.5 (d), 128.0 (d), 128.1 (d), 128.5 (d), 129.6 (d), 136.2 (s), 139.8 (s), 148.1 (s), 162.6 (s), 162.8 (s), 167.3 (s); IR (nujol): $\nu_{max}$ = 3221, 1695, 1666 cm$^{-1}$; MS *m/z* (ESI): 382.52 (M + H$^+$); anal. calcd. for $C_{21}H_{19}NO_4S$ (381.44): C 66.12, H 5.02, N 3.67; found: C 65.98, H 4.98, N 3.72.



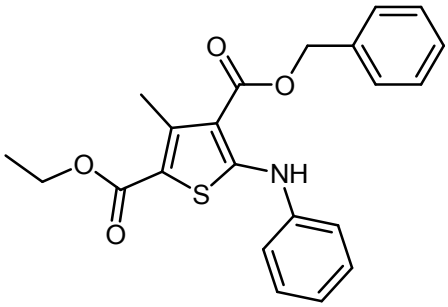
**4-Allyl 2-ethyl 3-methyl-5-(phenylamino)thiophene-2,4-dicarboxylate 8g.**

**8g** was isolated by column chromatography on silica gel (ethyl acetate/cyclohexane) in 83% yield from **7p**. White solid; mp: 70–73 °C; $^{1}$H NMR (400 MHz, $CDCl_3$, 25 °C): δ = 1.35 (t, 3H, *J* = 7.2 Hz $OCH_2\mathit{CH_3}$), 2.79 (s, 3H, $\mathit{CH_3}$), 4.29 (q, 2H, *J* = 7.2 Hz, $O\mathit{CH_2}CH_3$), 4.83 (dt, 2H, *J* = 5.6 Hz, *J* = 1.2 Hz, $O\mathit{CH_2}CH{=}CH_2$), 5.31 (dd, 1H, *J* = 10.4 Hz, *J* = 1.2 Hz, $OCH_2CH{=}\mathit{CH_2}$), 5.46 (dd, 1H, *J* = 17.2 Hz, *J* = 1.2 Hz, $OCH_2CH{=}\mathit{CH_2}$), 6.00-6.10 (m, 1H, $OCH_2\mathit{CH}{=}CH_2$), 7.16 (t, 1H, *J* = 7.2 Hz, Ph), 7.34-7.43 (m, 4H, Ph), 10.56 (s, 1H, *NH*); $^{13}$C NMR (100 MHz, $CDCl_3$, 25 °C): δ = 16.4 (q), 16.1 (q), 60.5 (t), 65.1 (t), 108.8 (s), 108.9 (s), 118.4 (t), 120.1 (d), 124.5 (d), 129.6 (d), 132.2 (d), 139.8 (s), 147.4 (s), 162.7 (s), 162.8 (s), 166.5 (s); IR (nujol): $\nu_{max}$ = 3283, 1708, 1663 cm$^{-1}$; MS *m/z* (ESI): 346.11 (M + H$^+$); anal. calcd. for $C_{18}H_{19}NO_4S$ (345.41): C 62.59, H 5.54, N 4.06; found: C 62.46, H 5.51, N 4.12.



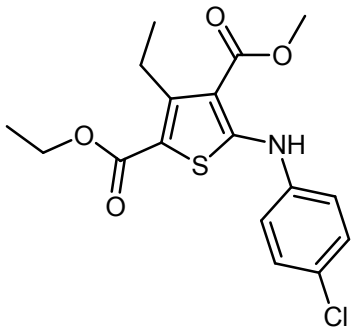

**4-Allyl 2-*tert*-butyl 3-methyl-5-(phenylamino)thiophene-2,4-dicarboxylate 8h.**

**8h** was isolated by column chromatography on silica gel (ethyl acetate/cyclohexane) in 70% yield from **7q**. White solid; mp: 120–124 °C; $^{1}$H NMR (400 MHz, $CDCl_3$, 25 °C): δ = 1.56 (s, 9H, $OC(\mathit{CH_3})_3$), 2.75 (s, 3H, $\mathit{CH_3}$), 4.82 (d, 2H, *J* = 5.2 Hz, $O\mathit{CH_2}CH{=}CH_2$), 5.31 (dd, 1H, *J* = 10.4 Hz, *J* = 0.8 Hz, $OCH_2CH{=}\mathit{CH_2}$), 5.42 (dd, 1H, *J* = 17.2 Hz, *J* = 1.2 Hz, $OCH_2CH{=}\mathit{CH_2}$), 6.00-6.10 (m, 1H, $OCH_2\mathit{CH}{=}CH_2$), 7.15 (t, 1H, *J* = 7.2 Hz, Ph), 7.34-7.42 (m, 4H, Ph), 10.54 (s, 1H, *NH*); $^{13}$C NMR (100 MHz, $CDCl_3$, 25 °C): δ = 15.9 (q), 28.4 (q), 65.0 (s), 81.3 (s), 108.9 (s), 110.6 (s), 118.2 (t), 120.0 (d), 124.3 (d), 129.6 (d), 132. 2 (s), 139.9 (s), 146.2 (s), 162.3 (s), 162.3 (s), 166.6 (s); IR (nujol): $\nu_{max}$ = 3257, 1749, 1686 cm$^{-1}$; MS *m/z* (ESI): 374.23 (M + H$^+$); anal. calcd. for $C_{20}H_{23}NO_4S$ (373.47): C 64.32, H 6.21, N 3.75; found: C 64.39, H 6.24, N 3.77.



**4-Benzyl 2-ethyl 3-methyl-5-(phenylamino)thiophene-2,4-dicarboxylate 8i.**

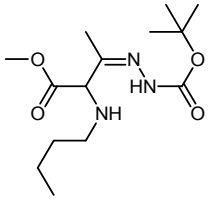
**8i** was isolated by column chromatography on silica gel (ethyl acetate/cyclohexane) in 81% yield from **7r**, and in 65% from **7s**. White solid; mp: 117–119 °C; $^{1}$H NMR (400 MHz, $CDCl_3$, 25 °C): δ = 1.34 (t, 3H, *J* = 7.2 Hz $OCH_2\mathit{CH_3}$), 2.77 (s, 3H, $\mathit{CH_3}$), 4.28 (q, 2H, *J* = 7.2 Hz, $O\mathit{CH_2}CH_3$), 5.38 (s, 2H, $O\mathit{CH_2}Ph$), 7.16 (t, 1H, *J* = 7.2 Hz, Ph), 7.33-7.46 (m, 9H, Ph), 10.54 (s, 1H, *NH*); $^{13}$C NMR (100 MHz, $CDCl_3$, 25 °C): δ = 14.4 (q), 16.2 (q), 60.5 (t), 66.2 (t), 108.8 (s), 108.9 (s), 120.2 (d), 124.5 (d), 128.1 (d), 128.3 (d), 128.7 (d), 129.6 (d), 135.9 (s), 139.8 (s), 147.4 (s), 162.8 (s), 166.6 (s); IR (nujol): $\nu_{max}$ = 3257, 1749, 1686 cm$^{-1}$; MS *m/z* (ESI): 396.38 ($M + H^+$); anal. calcd. for $C_{22}H_{21}NO_4S$ (395.47): C 66.82, H 5.35, N 3.54; found: C 66.95, H 5.38, N 3.59.



**2-Ethyl 4-methyl 5-((4-chlorophenyl)amino) 3-ethylthiophene-2,4-dicarboxylate 8j.**

**8j** was isolated by column chromatography on silica gel (ethyl acetate/cyclohexane) in 68% yield from **7u**, and in 79% from **7v**. White solid; mp: 149–151 °C; $^{1}$H NMR (400 MHz, $CDCl_3$, 25 °C): δ = 1.19 (t, 3H, *J* = 7.6 Hz $CH_2\mathit{CH_3}$), 1.35 (t, 3H, *J* = 7.2 Hz $OCH_2\mathit{CH_3}$), 3.31 (q, 2H, *J* = 7.2 Hz, $\mathit{CH_2}CH_3$), 3.91 (s, 3H, O $\mathit{CH_3}$), 4.30 (q, 2H, *J* = 7.2 Hz, $O\mathit{CH_2}CH_3$), 7.30 (d, 2H, *J* = 8.8 Hz, Ph), 7.37 (d, 2H, *J* = 8.8 Hz, Ph), 10.58 (s, 1H, *NH*); $^{13}$C NMR (100 MHz, $CDCl_3$, 25 °C): δ = 14.4 (q), 14.8 (q), 22.3 (t), 51.5 (q), 60.6 (t), 108.5 (s), 108.8 (s), 121.4 (d), 129.5 (s), 129.7 (d), 138.5 (s), 153.7 (s), 162.3 (s), 162.6 (s), 167.1 (s); IR (nujol): $\nu_{max}$ = 3223, 1696, 1664 cm$^{-1}$; MS *m/z* (ESI): 368.42 ($M + H^+$); anal. calcd. for $C_{17}H_{18}ClNO_4S$ (367.85): C 55.51, H 4.93, N 3.81; found: C 55.37, H 4.97, N 3.89.

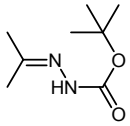
## 9 Spectral data of α-amino hydrazone 11.



***Tert*-butyl 2-(3-(butylamino)-4-methoxy-4-oxobutan-2-ylidene)hydrazinecarboxylate.**

was isolated by crystallization. Pale pink solid; $^{1}$H NMR (400 MHz, DMSO$_{d6}$, 25 °C): δ = 0.84 (q, 3H, *J* = 7.2 Hz, but), 1.24-1.38 (m, 4H, but), 1.44 (s, 9H, C(*CH*$_3$)$_3$), 1.75 (s, 3H, *CH*$_3$), 2.16 (brs, 1H, *NH*), 2.31-2.47 (m, 2H, but), 3.66 (s, 3H, O*CH*$_3$), 3.87 (s, 1H, O*CH*), 9.61 (s, 1H, *NH*); $^{13}$C NMR (100 MHz, DMSO$_{d6}$, 25 °C): δ = 12.9 (q), 13.8 (q), 19.8 (t), 28.1 (q), 31.6 (t), 46.7 (t), 51.9 (q), 67.4 (d), 79.2 (s), 149.6 (s), 153.0 (s), 171.5 (s); IR (nujol): $\nu_{max}$ = 3257, 3107, 1779, 1666 cm$^{-1}$; MS *m/z* (ESI): 302.25 (M + H$^{+}$); anal. calcd. for $C_{14}H_{27}N_3O_4$ (301.38): C 55.79, H 9.03, N 13.94; found: C 55.90, H 9.06, N 13.88.

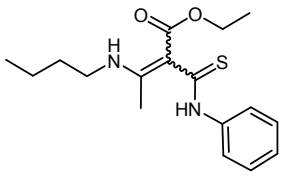
## 10 Spectral data of hydrazone 12.



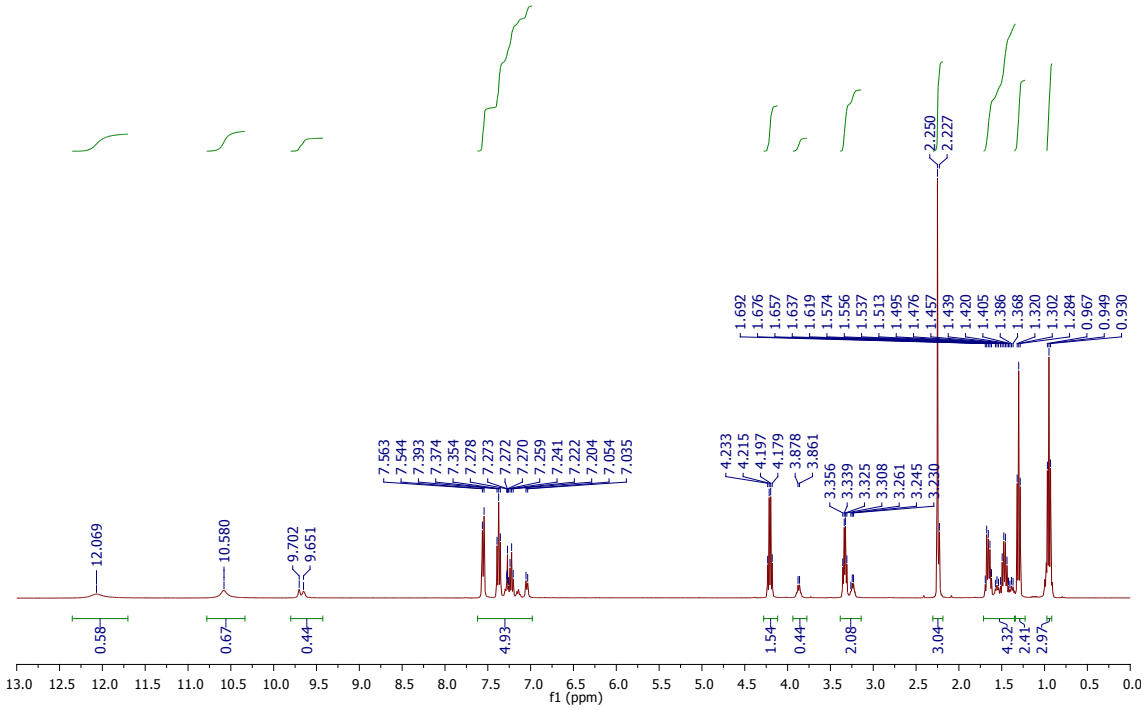
***Tert*-butyl 2-(propan-2-ylidene)hydrazinecarboxylate.**

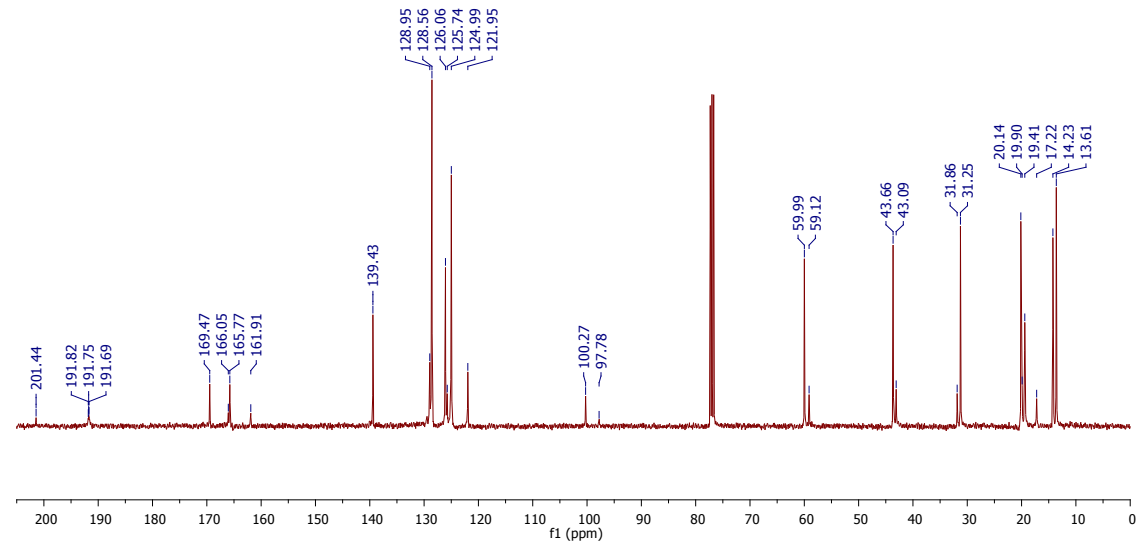
White solid; $^{1}$H NMR (400 MHz, DMSO$_{d6}$, 25 °C): δ = 1.42 (s, 9H, C(*CH*$_3$)$_3$), 1.77 (s, 3H, *CH*$_3$), 1.85 (s, 3H, *CH*$_3$), 9.31 (s, 1H, *NH*); $^{13}$C NMR (100 MHz, DMSO$_{d6}$, 25 °C): δ = 17.1 (q), 24.9 (q), 28.1 (q), 151.1 (s), 153.2 (s), 155.6 (s);

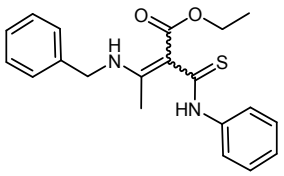
## 11 $^{1}H$ and $^{13}C$ NMR spectra of 3-alkylamino-2-(carbamothioyl)but-2-enoates (ACTs) 5a-m.



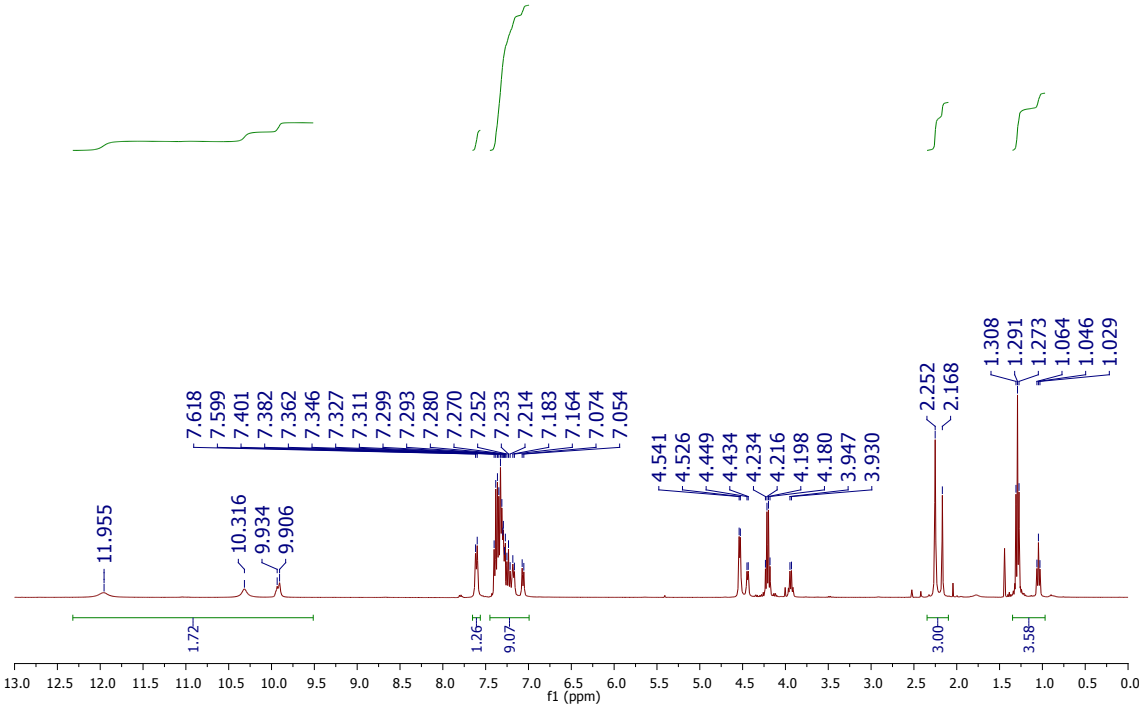
**Ethyl 3-(butylamino)-2-(phenylcarbamothioyl)but-2-enoate 5a.**

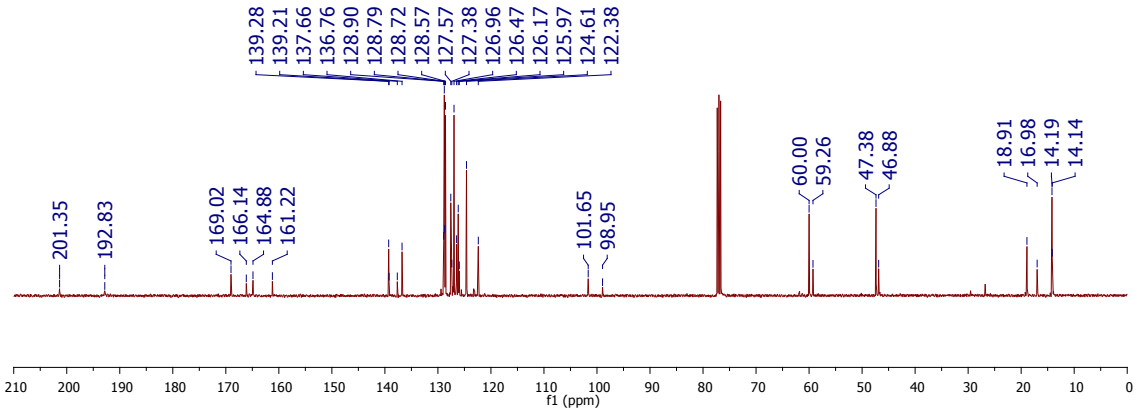


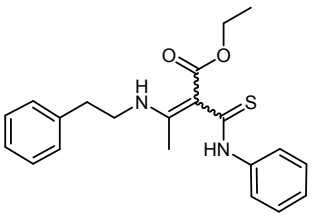





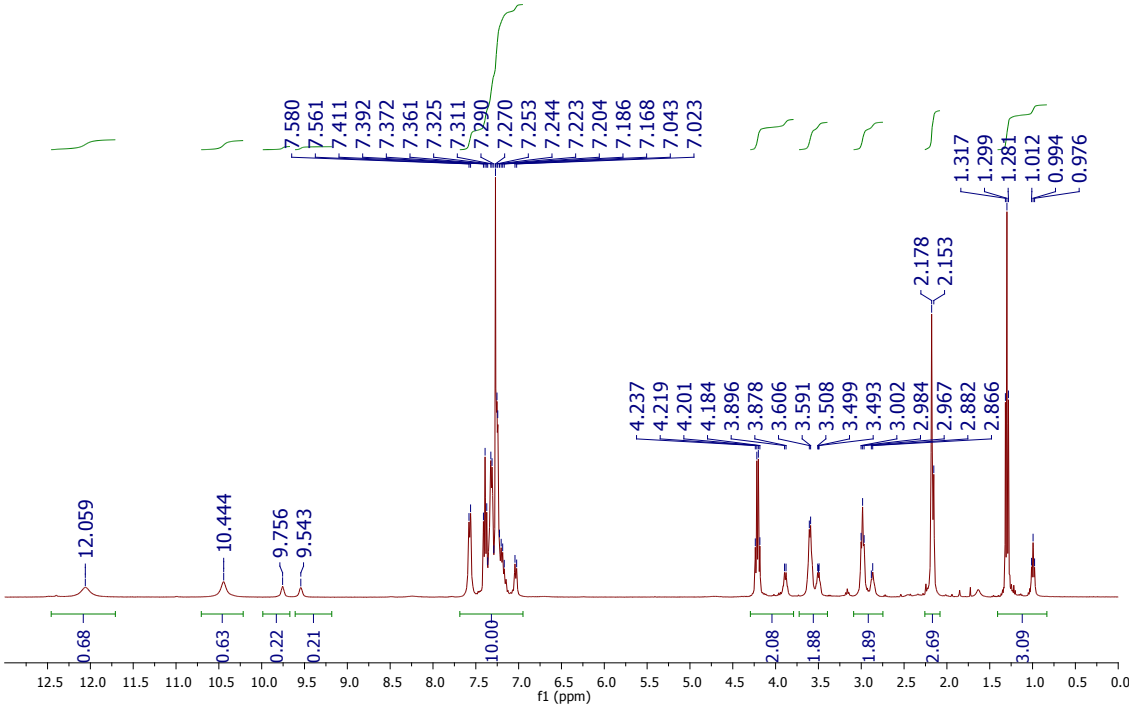
**Ethyl 3-(benzylamino)-2-(phenylcarbamothioyl)but-2-enoate 5b**.

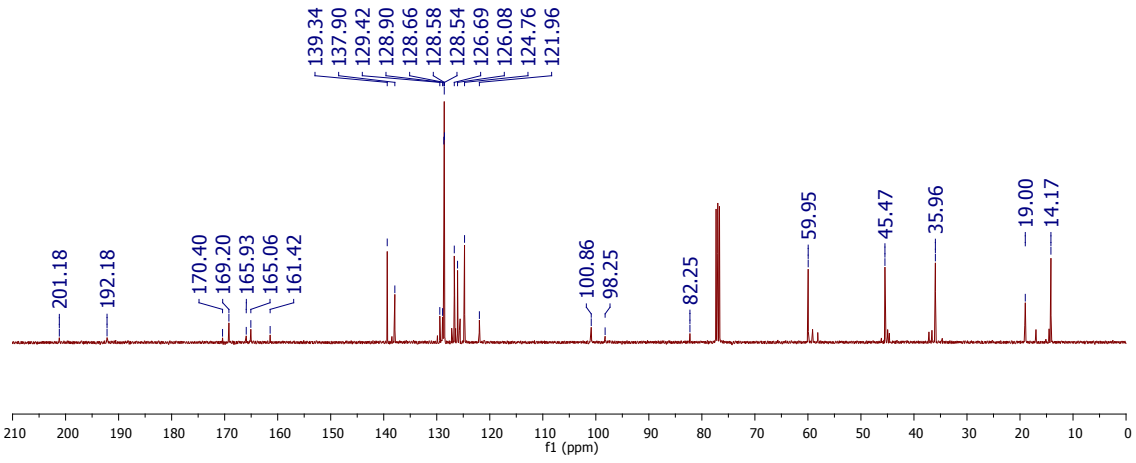


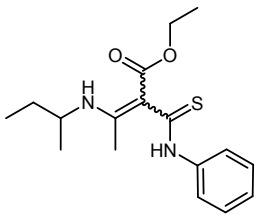





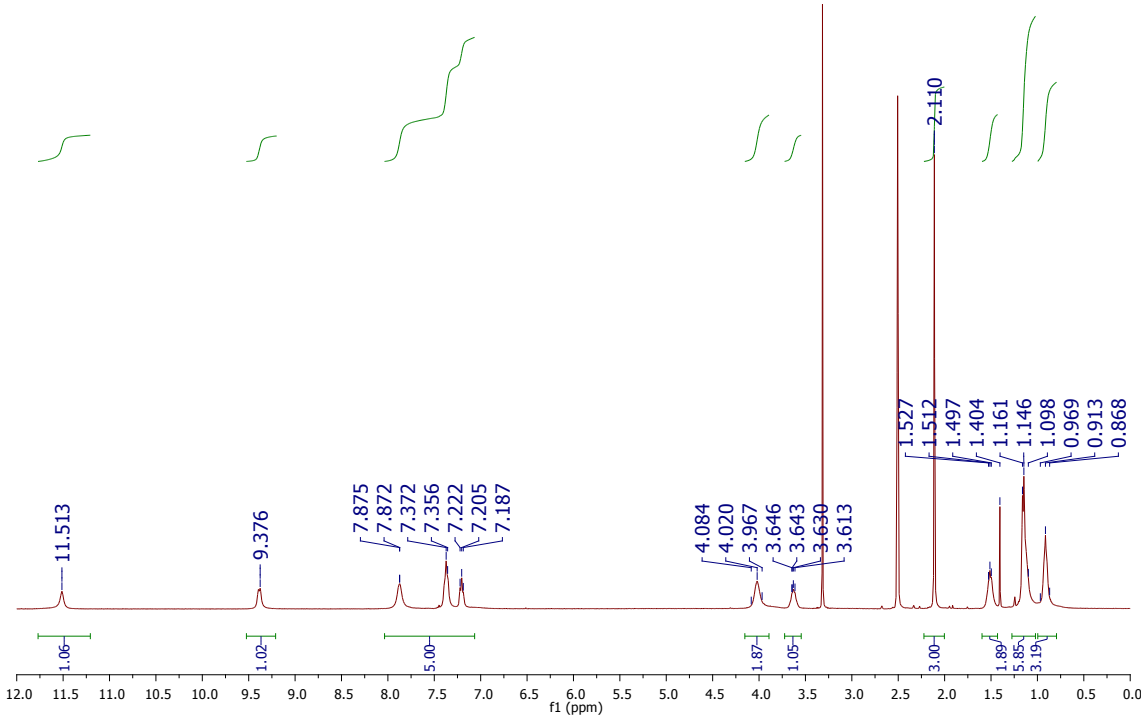
**Ethyl 3-(phenethylamino)-2-(phenylcarbamothioyl)but-2-enoate 5c.**

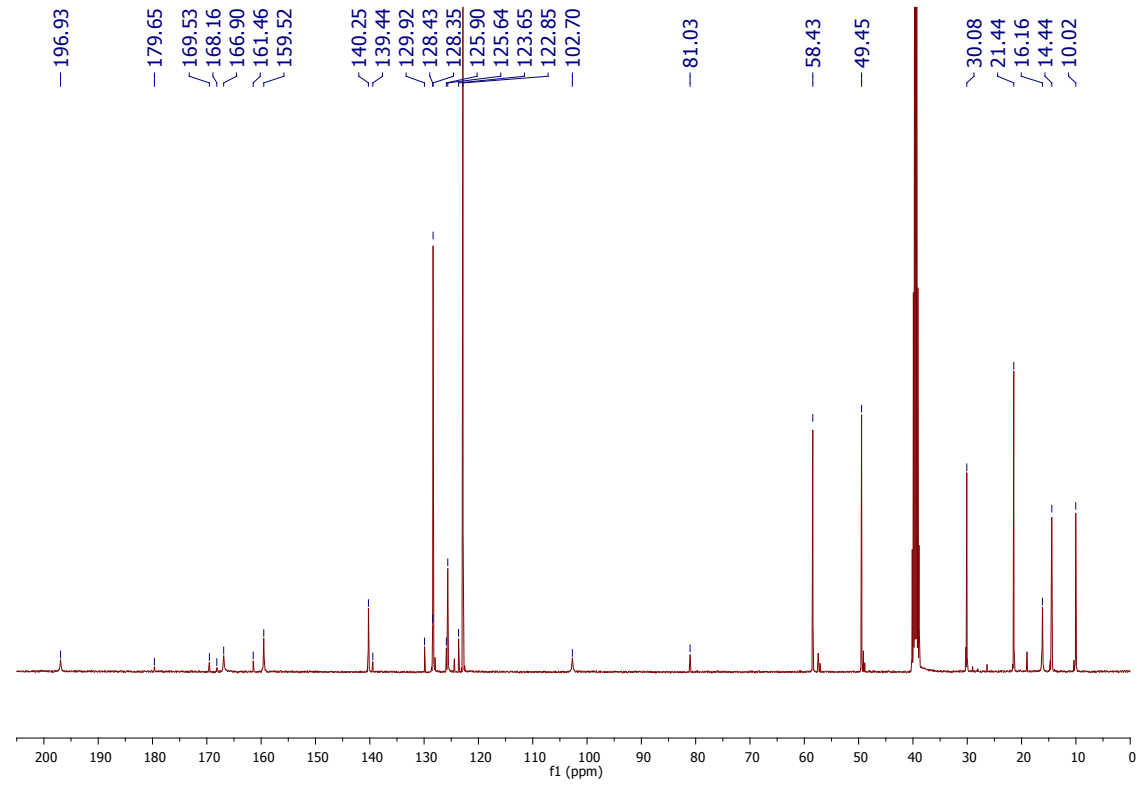


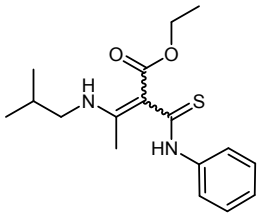





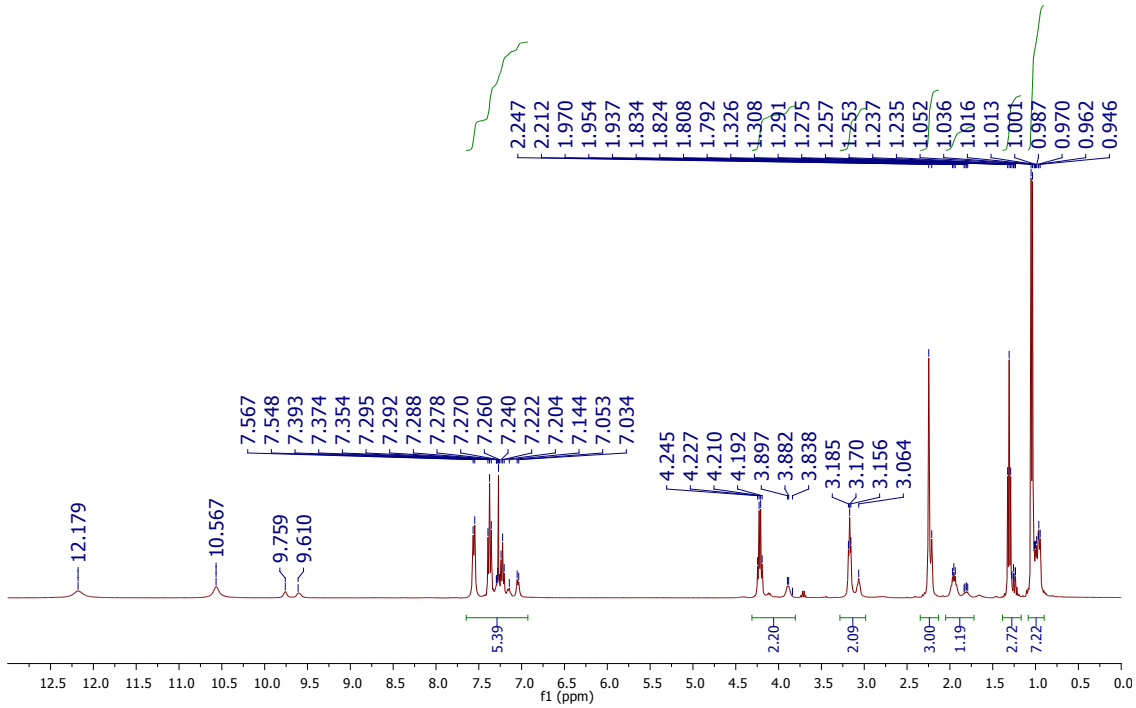

**Ethyl 3-(*sec*-butylamino)-2-(phenylcarbamothioyl)but-2-enoate 5d.**

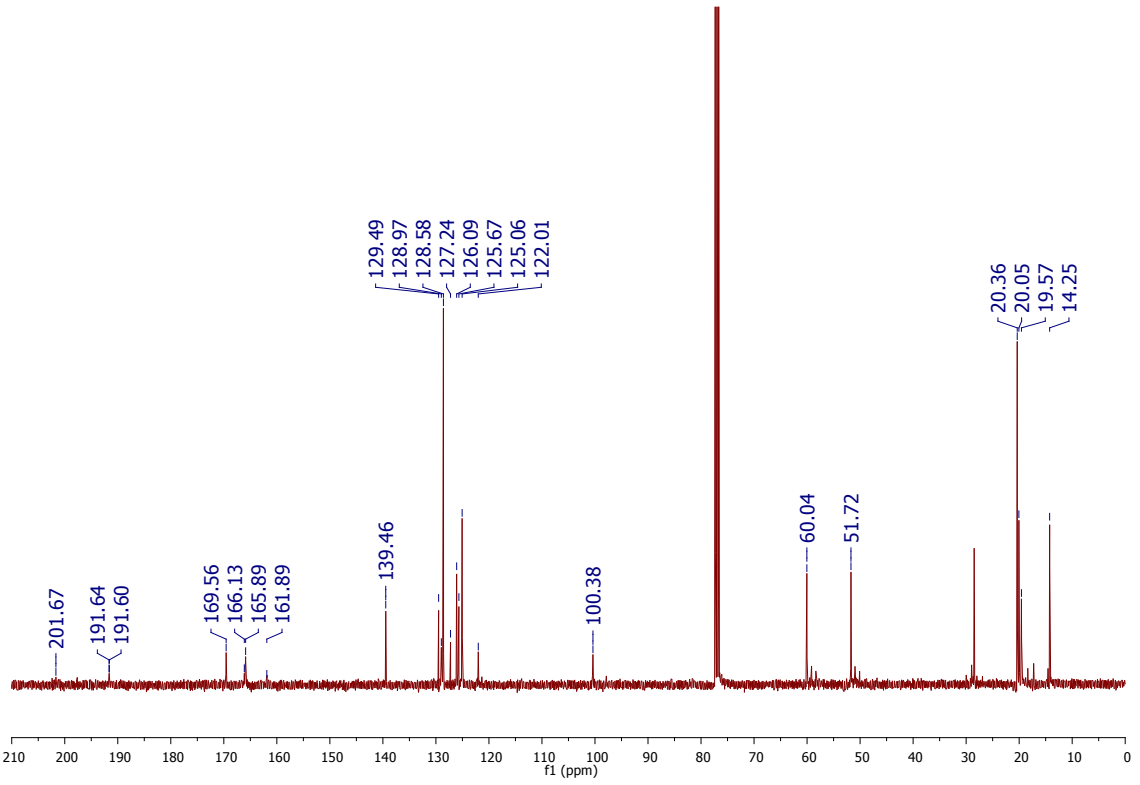


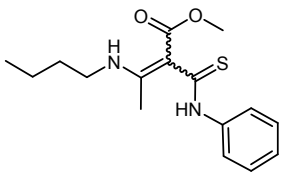





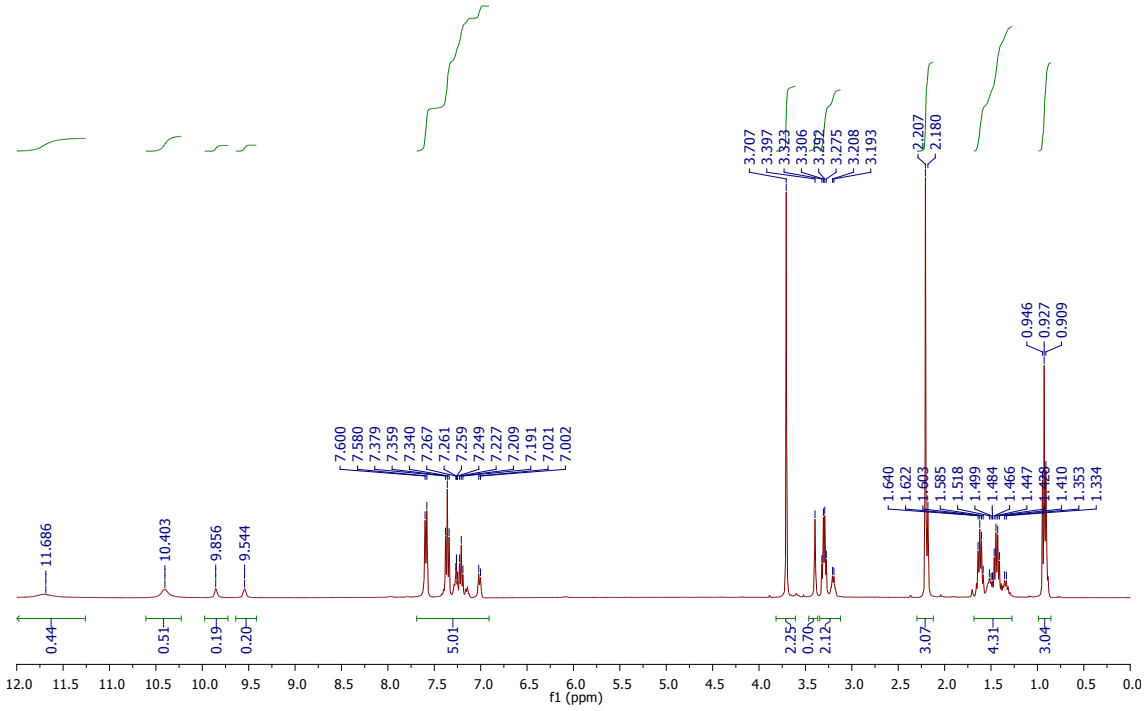

**Ethyl 3-(isobutylamino)-2-(phenylcarbamothioyl)but-2-enoate 5e.**

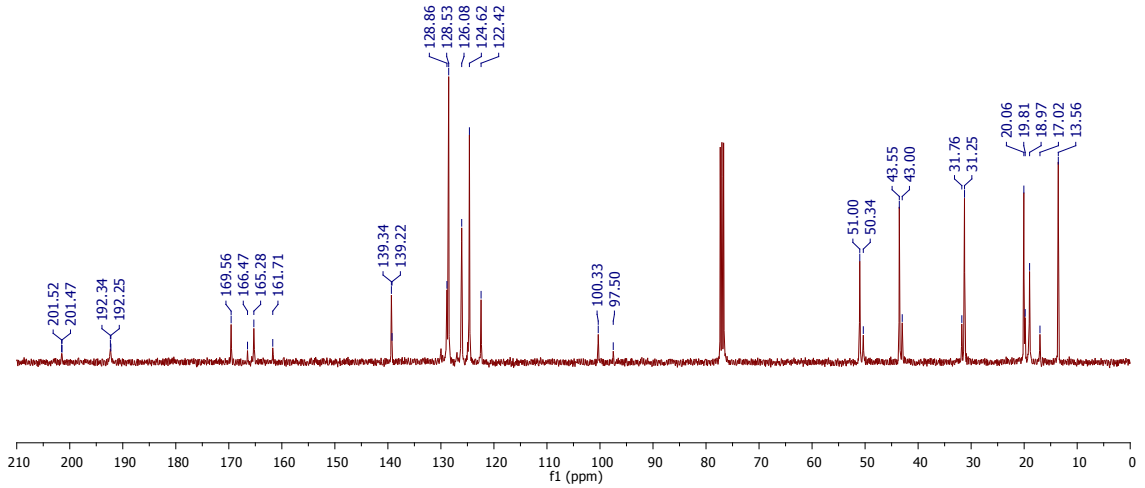


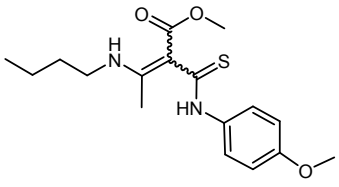





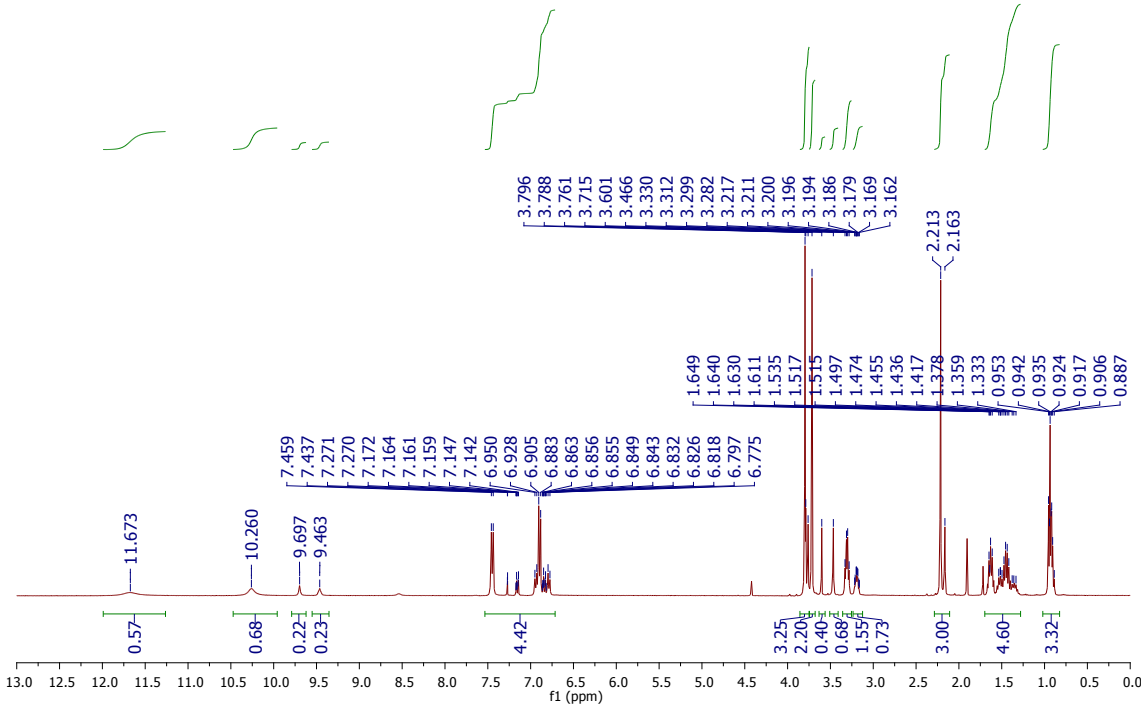
**Methyl 3-(butylamino)-2-(phenylcarbamothioyl)but-2-enoate 5f.**

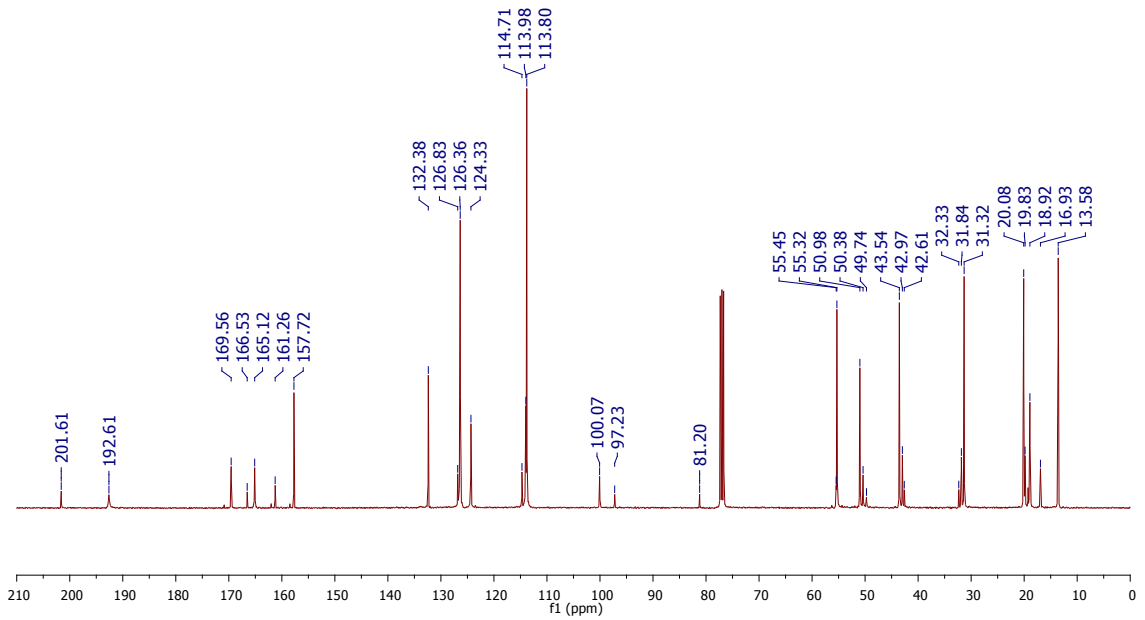


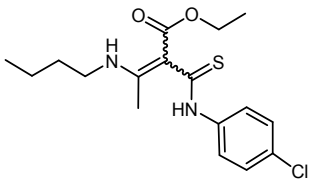





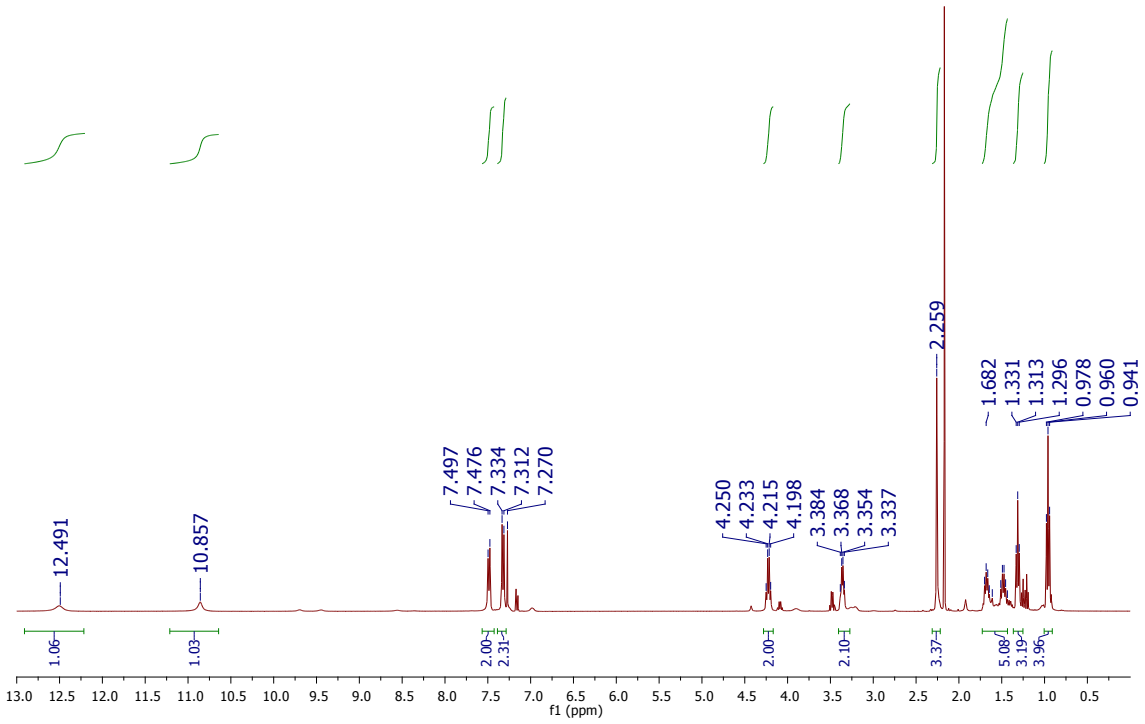
**Methyl 3-(butylamino)-2-((4-methoxyphenyl)carbamothioyl)but-2-enoate 5g**.

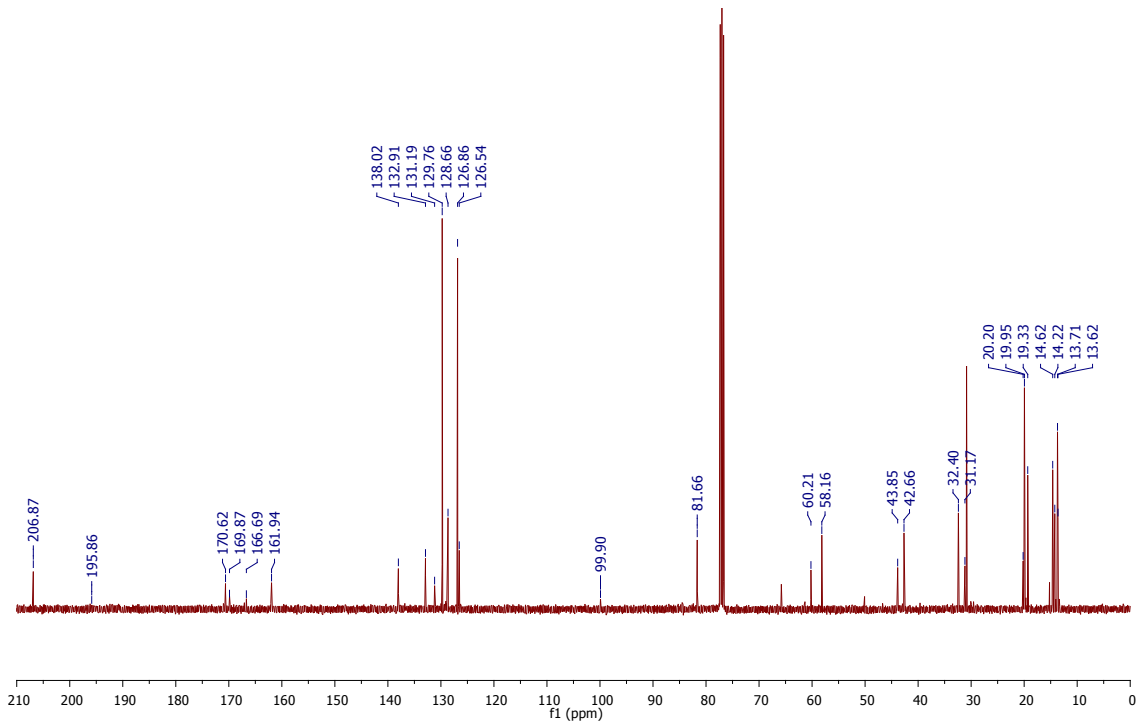


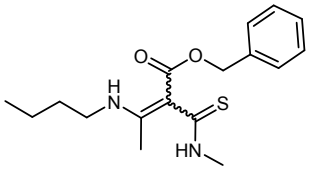





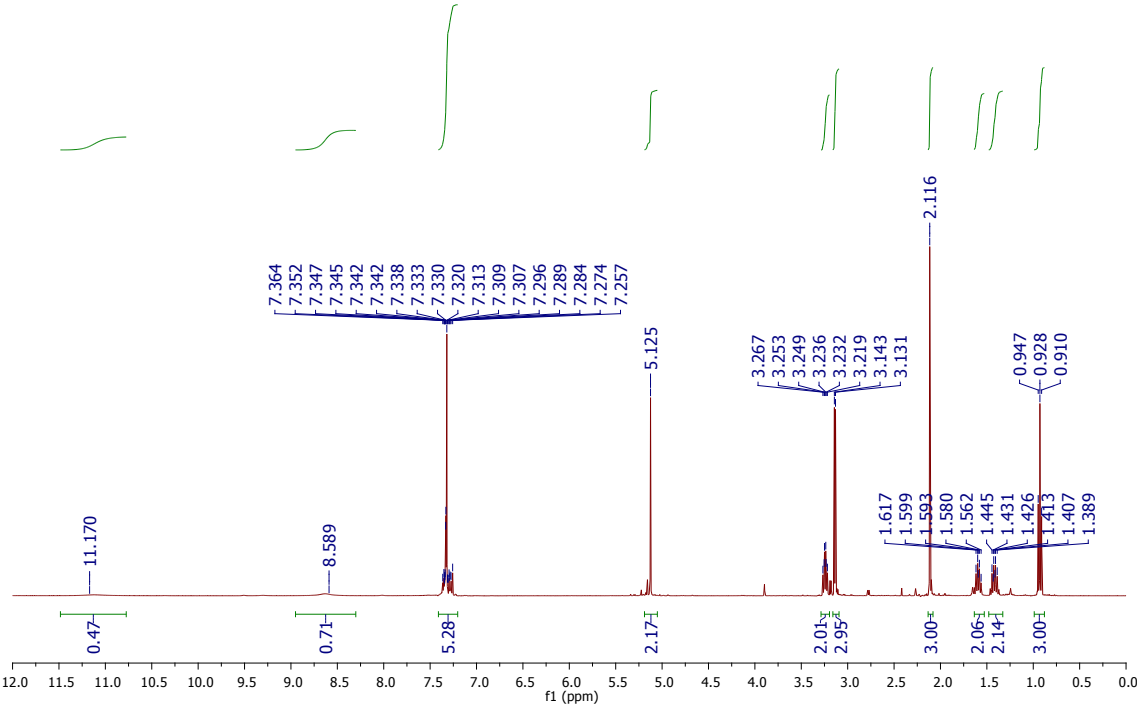
**Ethyl 3-(butylamino)-2-((4-chlorophenyl)carbamothioyl)but-2-enoate 5h.**

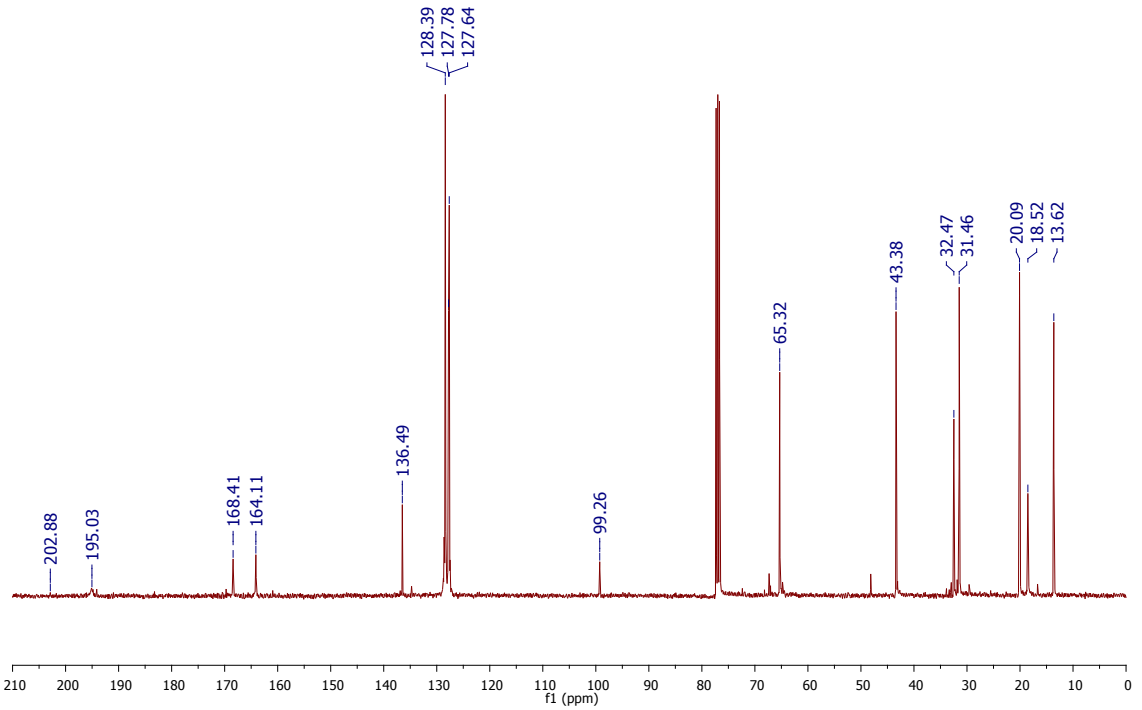


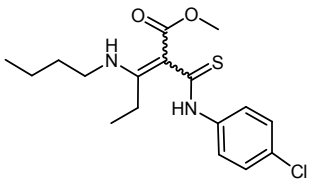





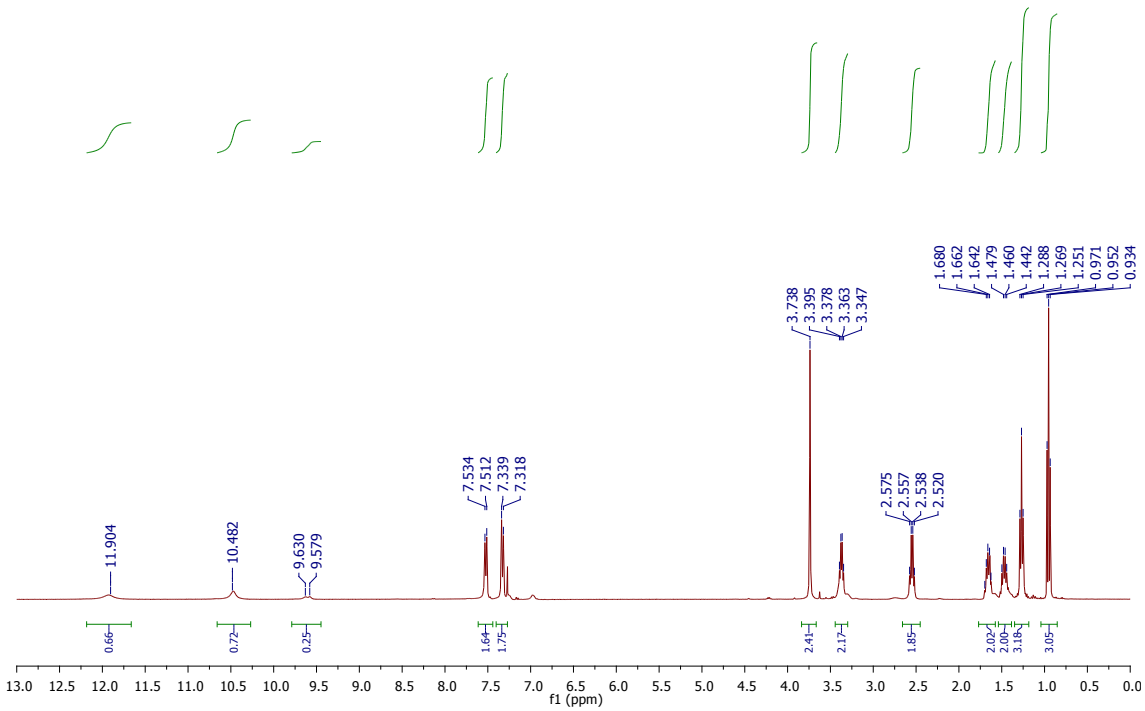
**Benzyl 3-(butylamino)-2-(methylcarbamothioyl)but-2-enoate 5i.**

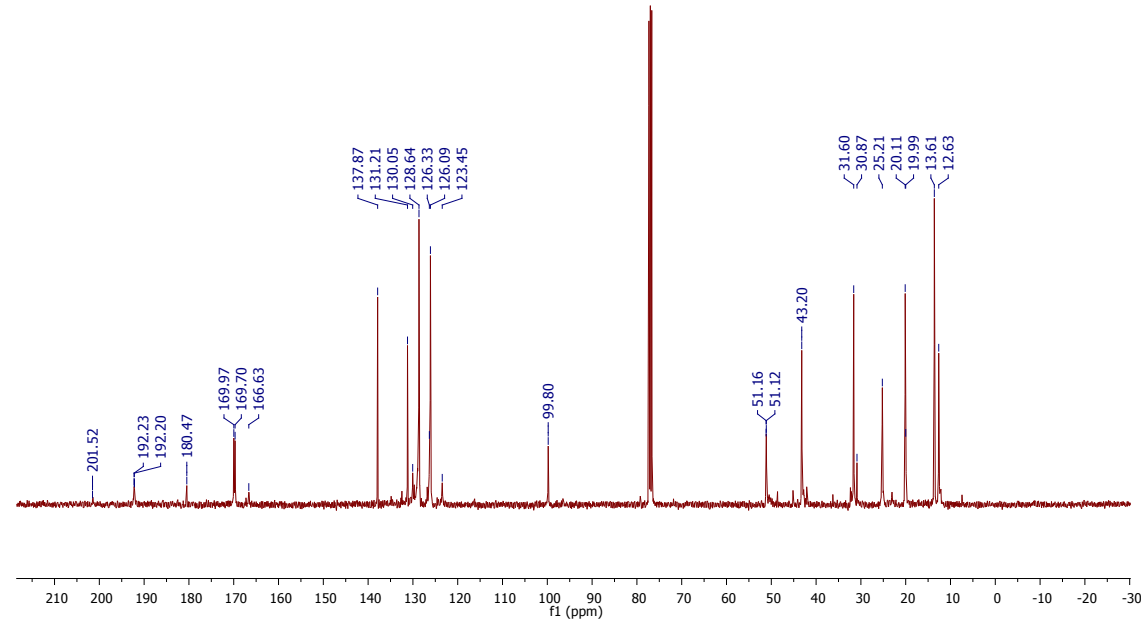


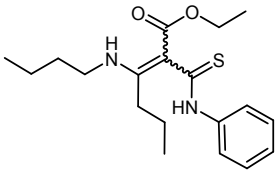





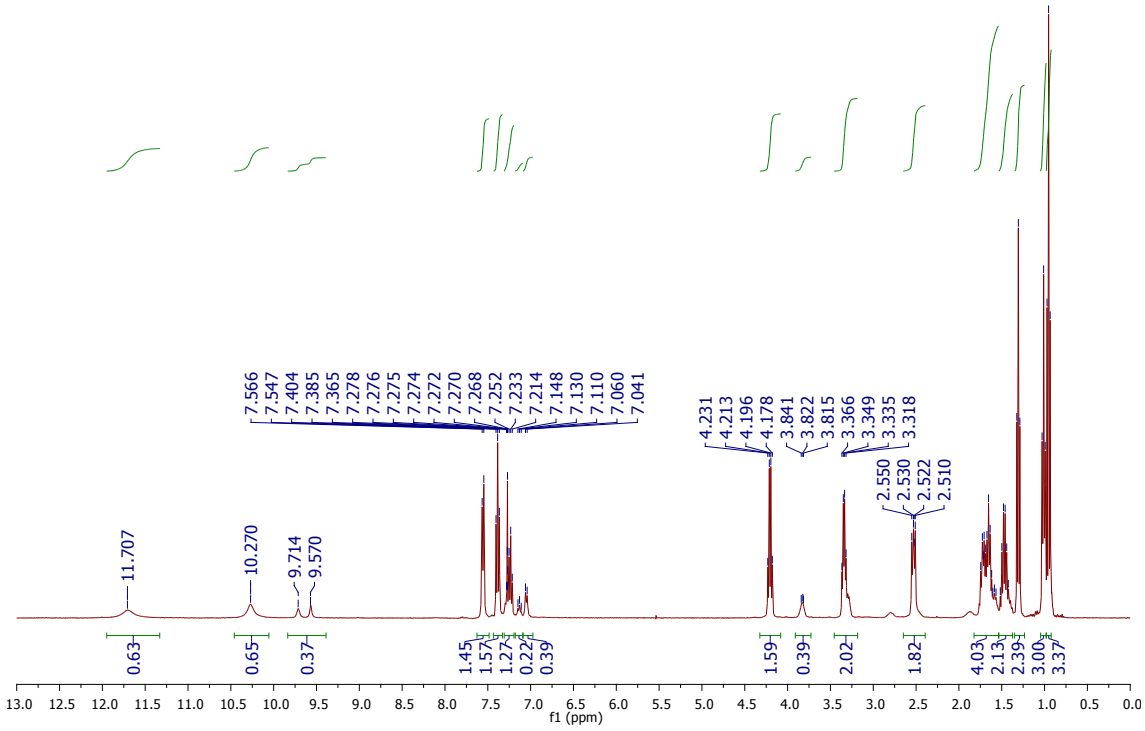
**Methyl 3-(butylamino)-2-((4-chlorophenyl)carbamothioyl)pent-2-enoate 5j.**

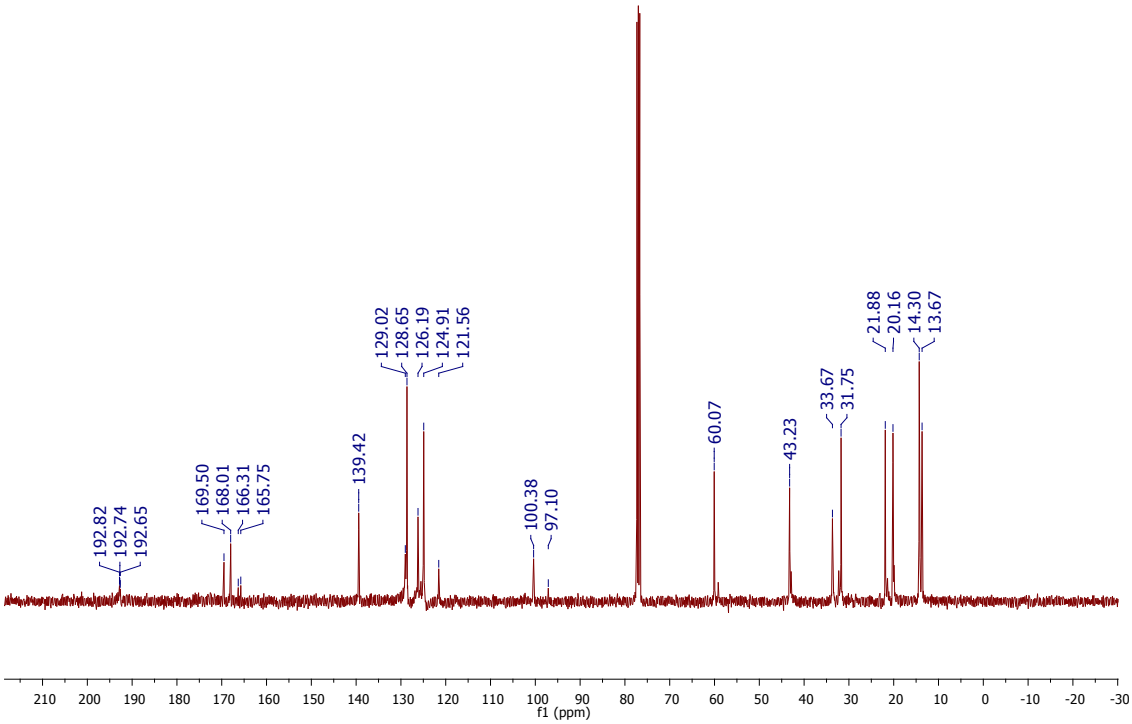


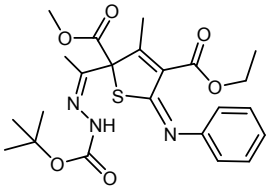


**Ethyl 3-(butylamino)-2-(phenylcarbamothioyl)hex-2-enoate 5k**.

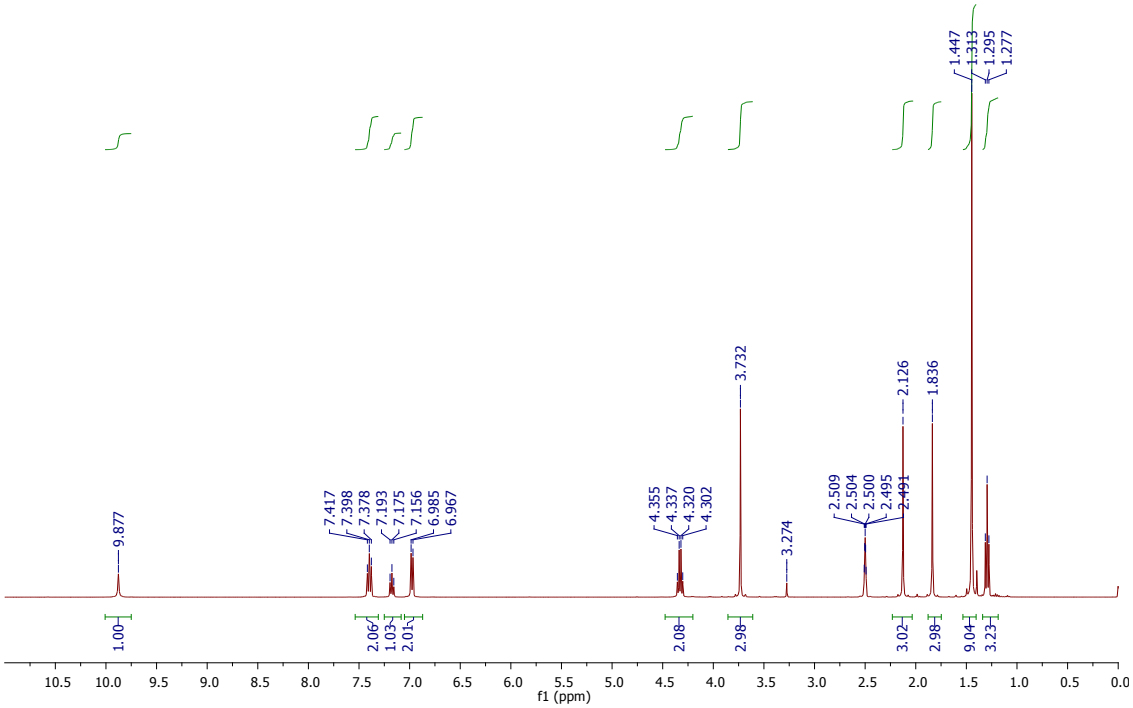


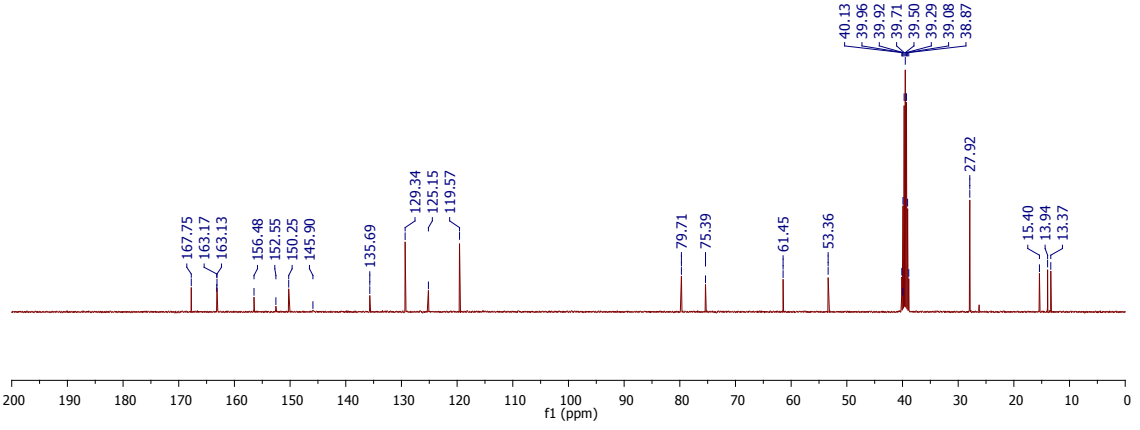



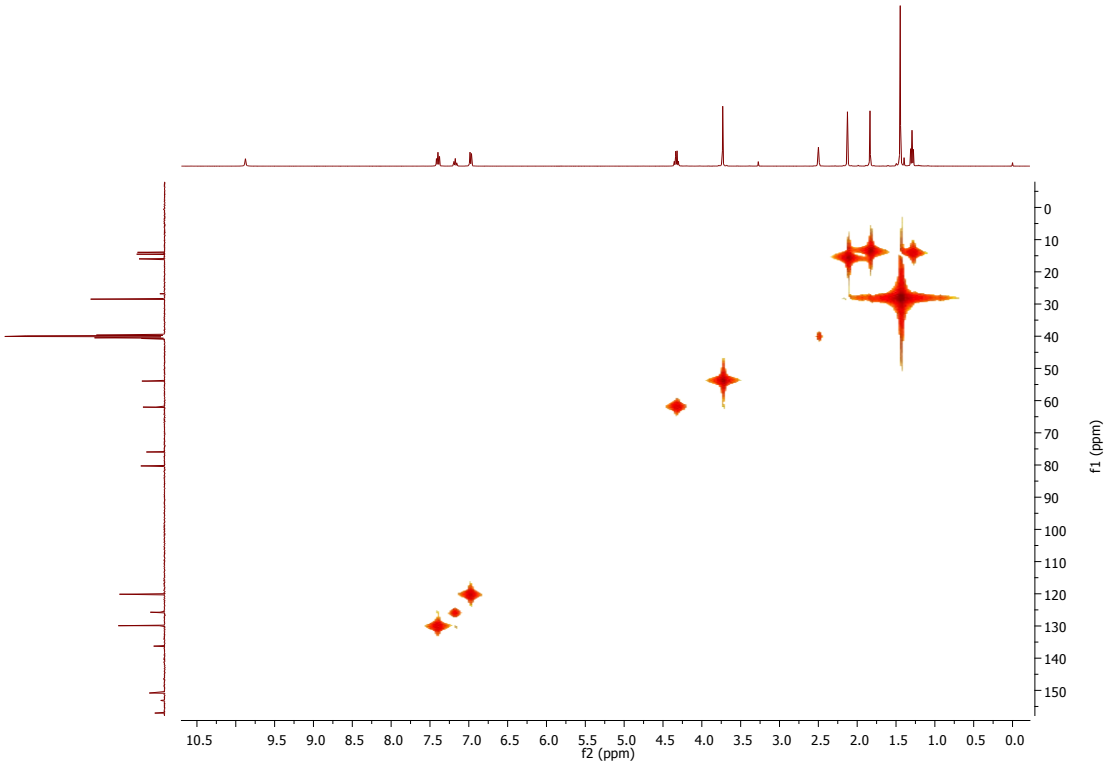
## 12 $^{1}H$ and $^{13}C$ NMR Spectra of 2,5-dihydrothiophenes 7a-w

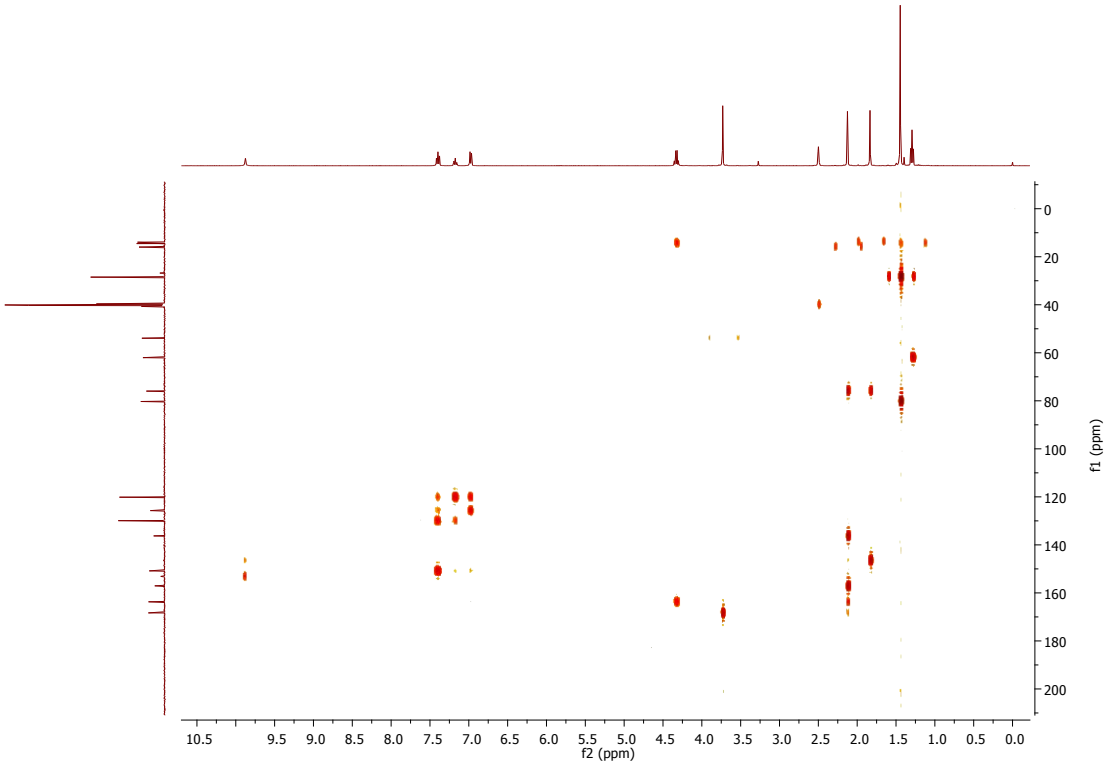


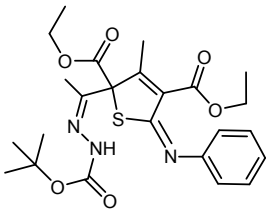
**4-Ethyl-2-methyl 2-(1-(2-*tert*butoxycarbonyl)hydrazono)ethyl)-3-methyl-5-(phenylimino)-2,5-dihydrothiophene-2,4-dicarboxylate 7a.**



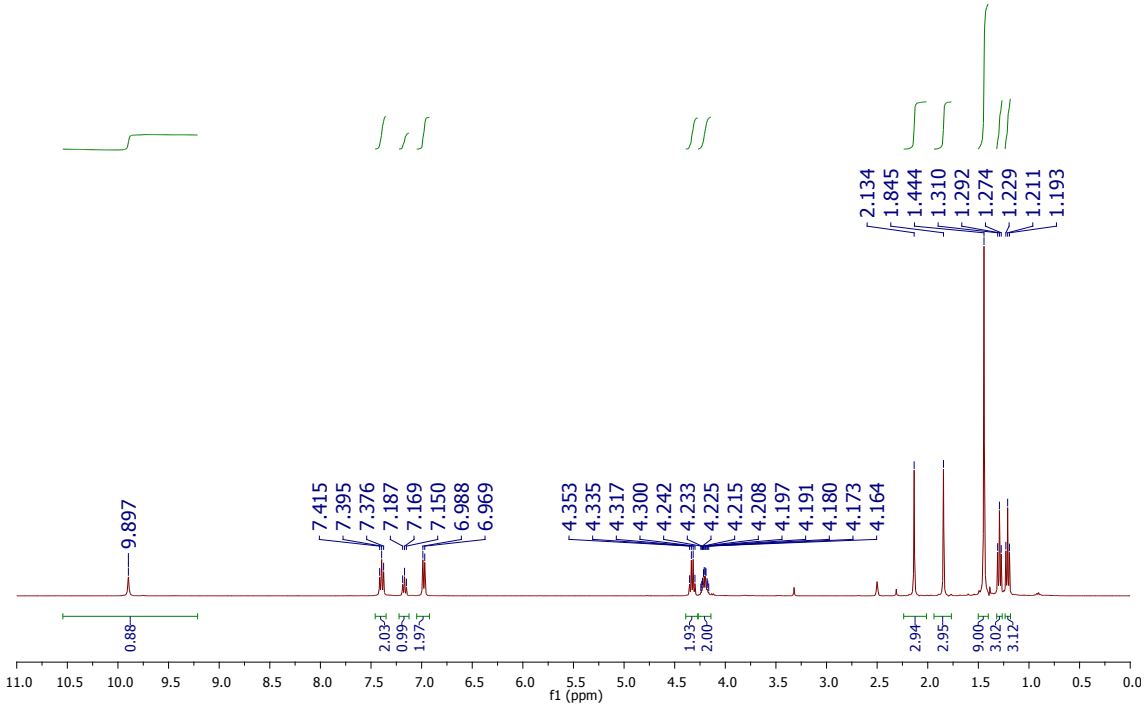



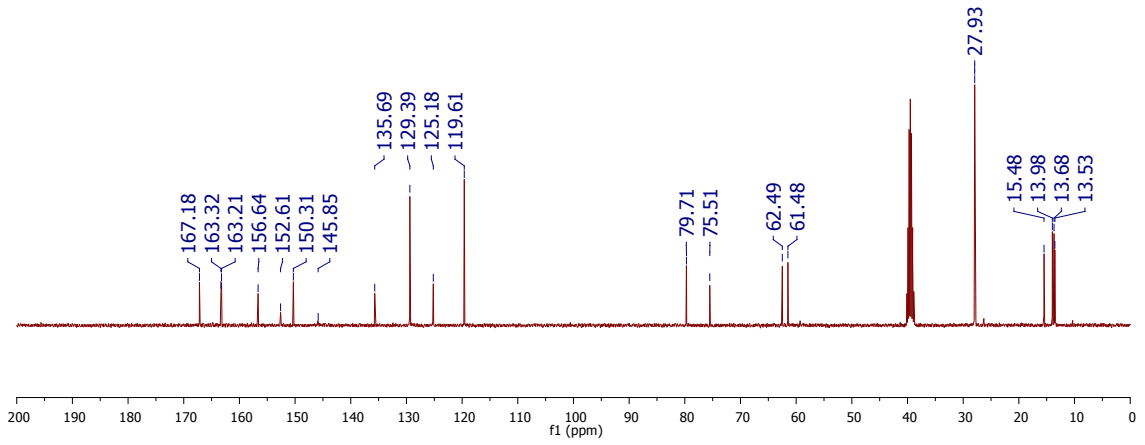

0
10
20
30
40
50
60
70
80
90
100
110
120
130
140
150
f1 (ppm)
10.5
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f2 (ppm)

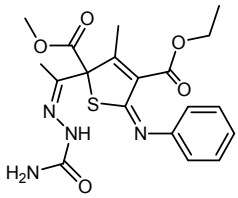

0
20
40
60
80
100
120
140
160
180
200
f1 (ppm)
10.5
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f2 (ppm)



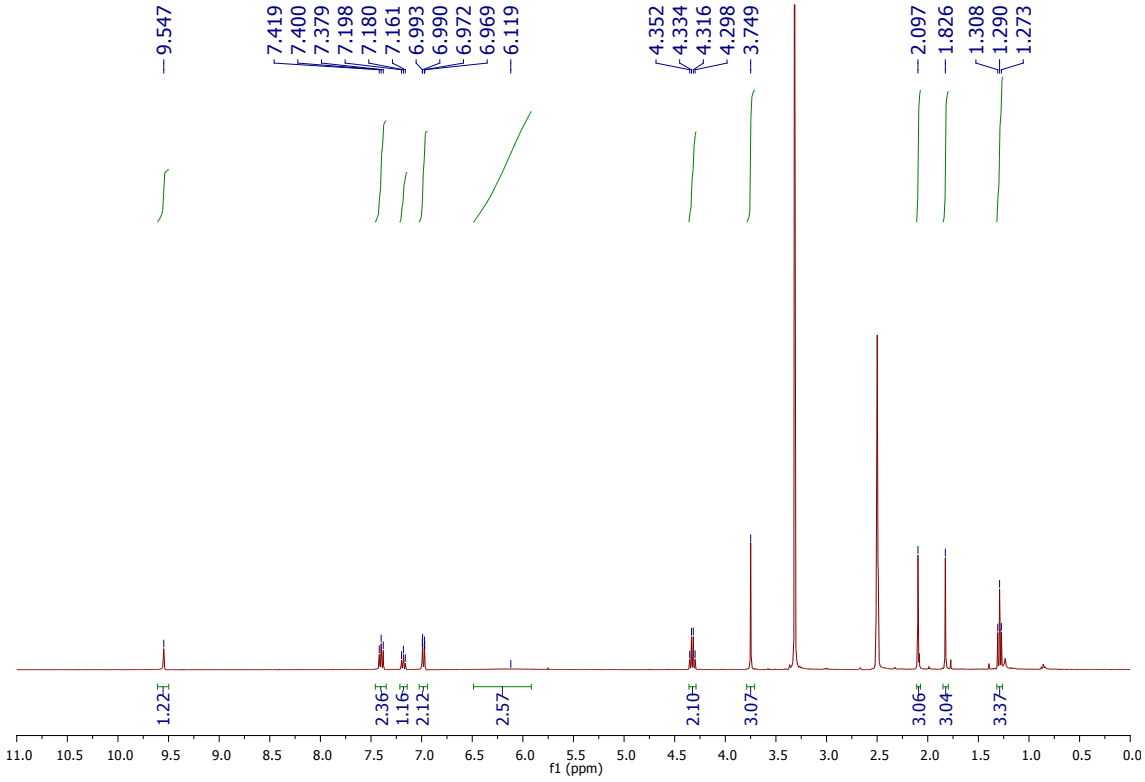
**Diethyl 2-(1-(2(*tert*-butoxycarbonyl)hydrazono)ethyl)-3-methyl-5-(phenylimino)-2,5-dihydrothiophene-2,4-dicarboxylate 7b.**

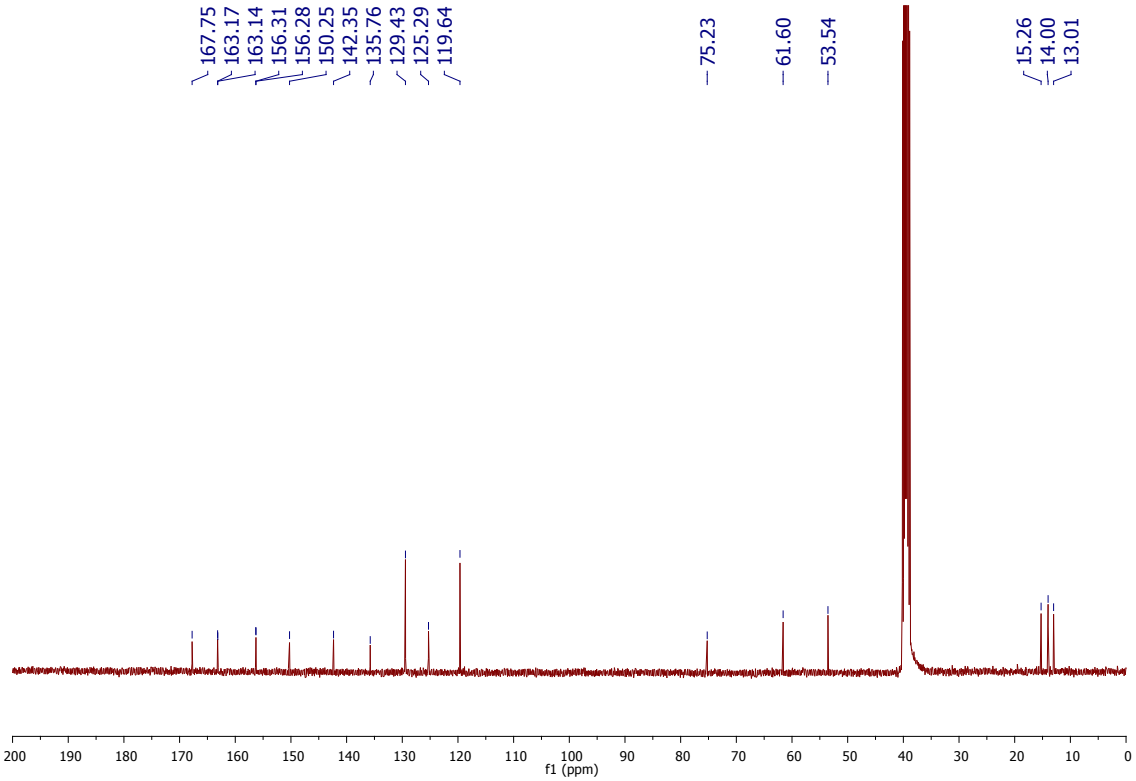


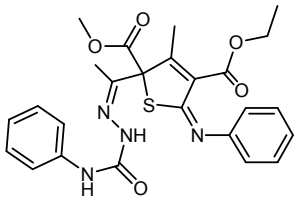





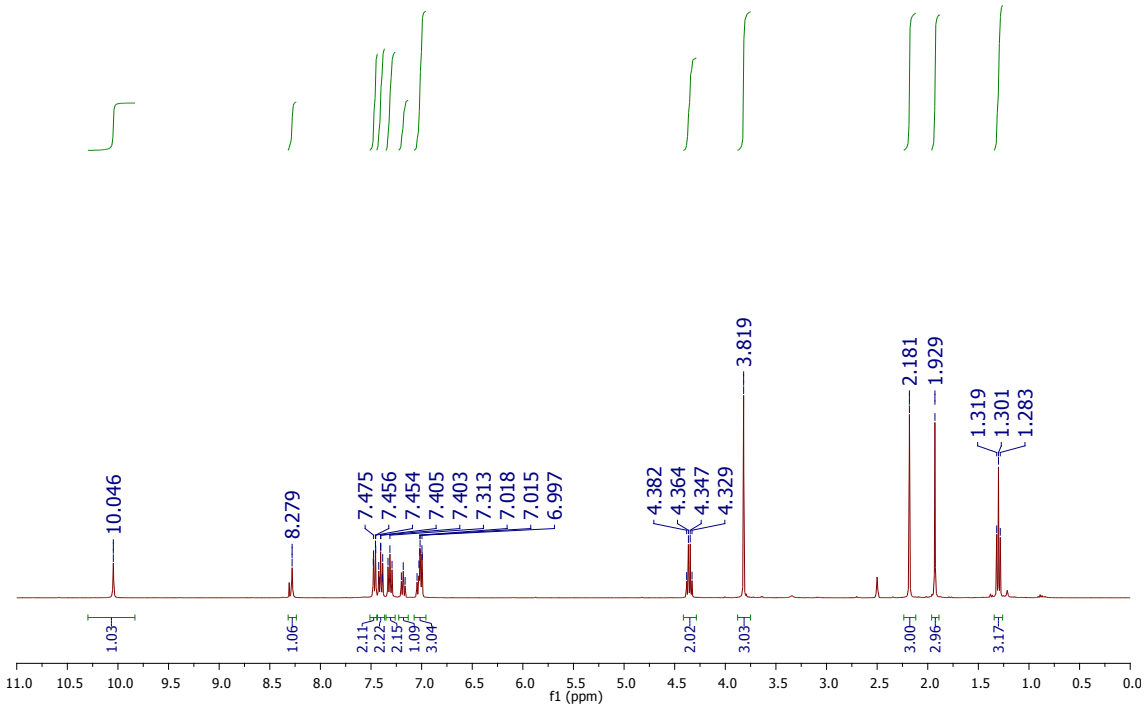
**4-Ethyl-2-methyl 2-(1-(2-carbomoylhydrazono)ethyl)-3-methyl-5-(phenylimino)-2,5-dihydrothiophene-2,4-dicarboxylate 7c.**

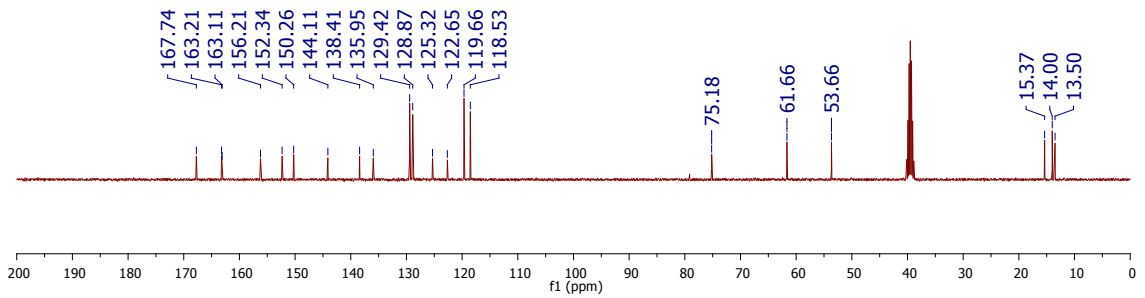


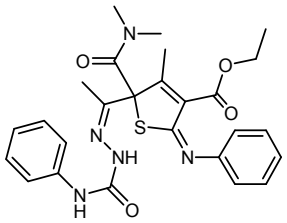





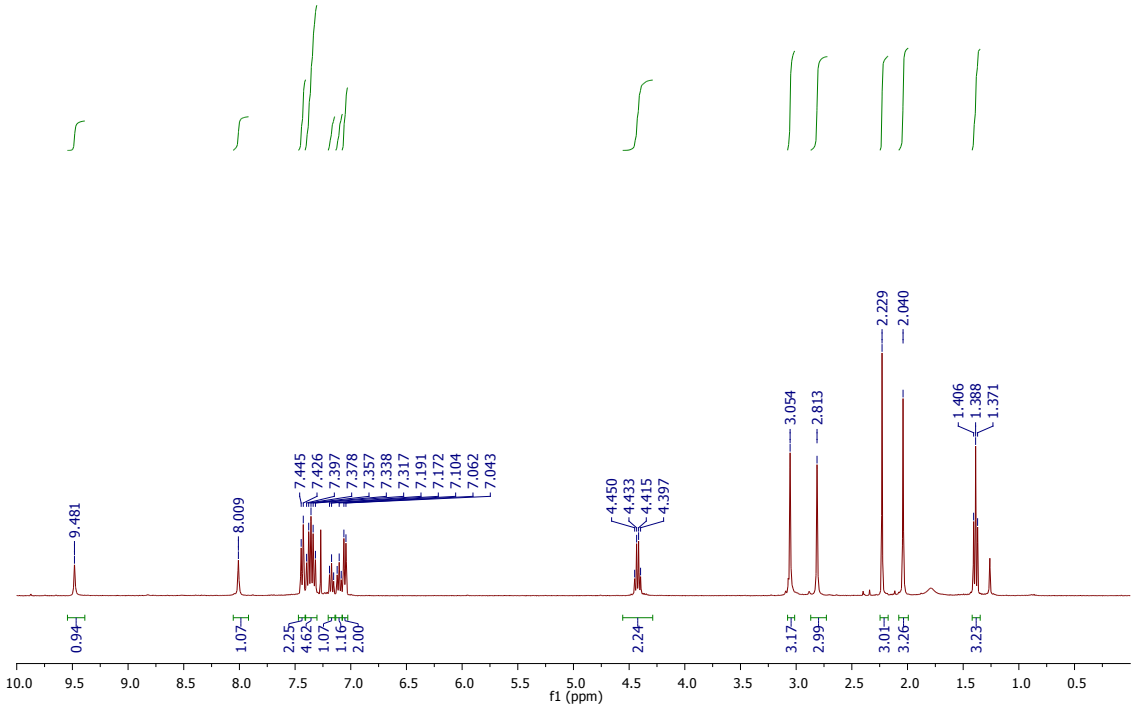
**4-Ethyl-2-methyl 3-methyl-2-(1-(2-phenylcarbomoyl)hydrazono)ethyl)-5-(phenylimino)-2,5-dihydrothiophene-2,4-dicarboxylate 7d.**

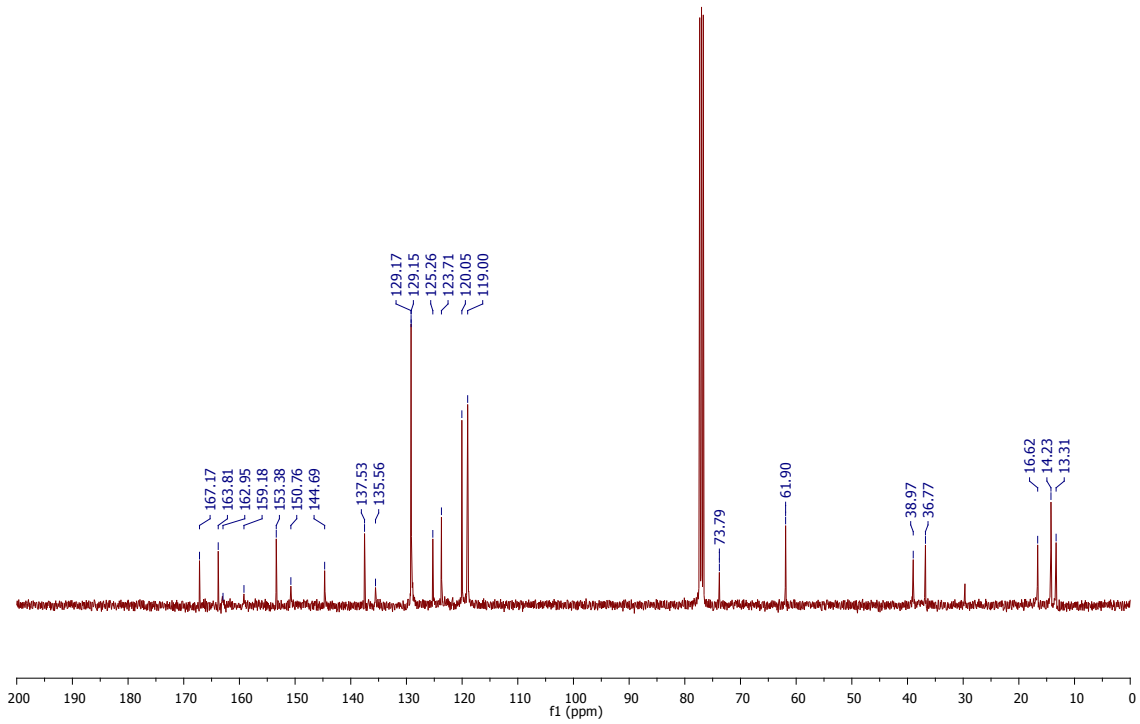


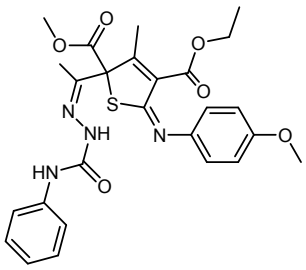





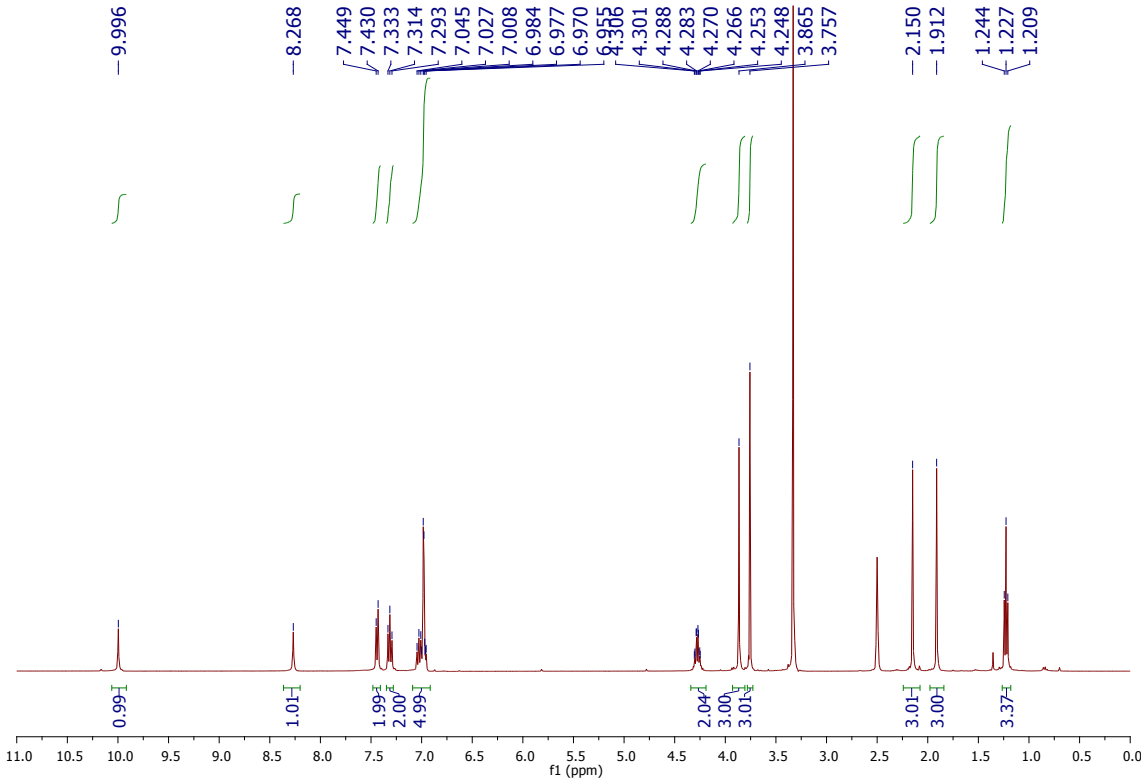
**Ethyl 5-(dimethylcarbamoyl)-4-methyl-5-(-1-(2(phenylcarbamoyl)hydrazono)ethyl)-2-(phenylimino)-2,5-dihydrothiophene-3-carboxylate 7e.**

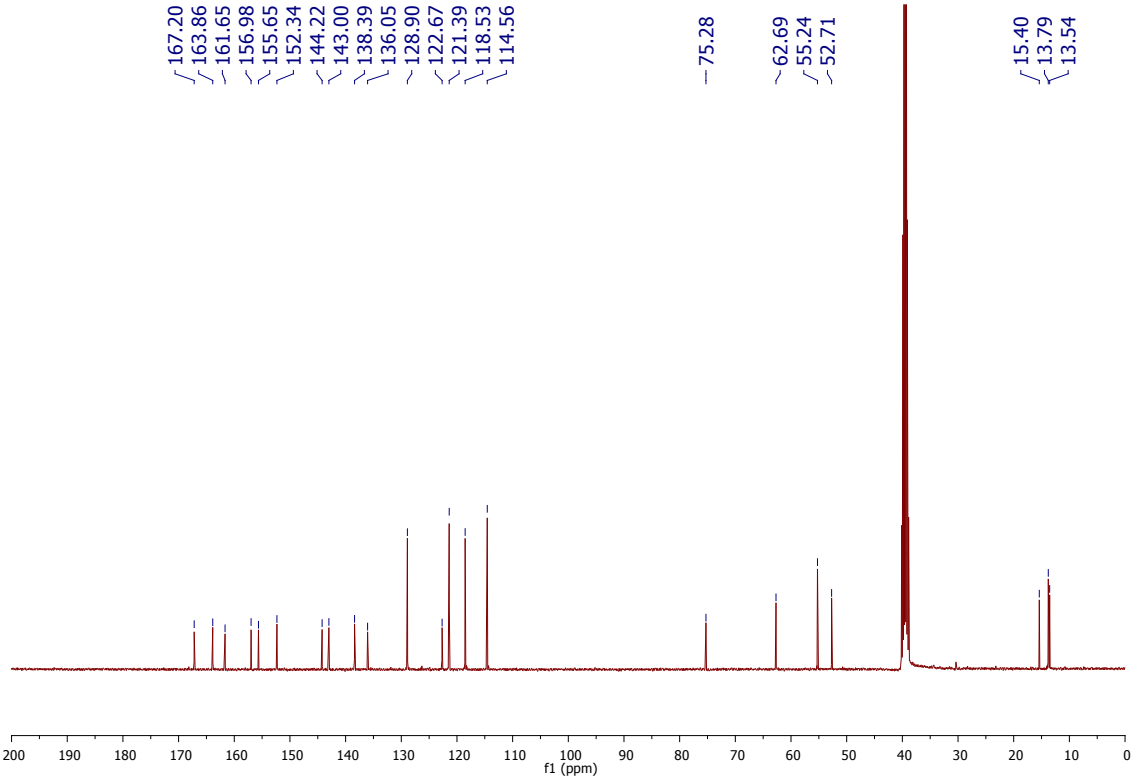


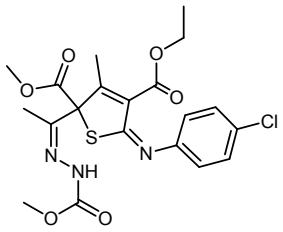





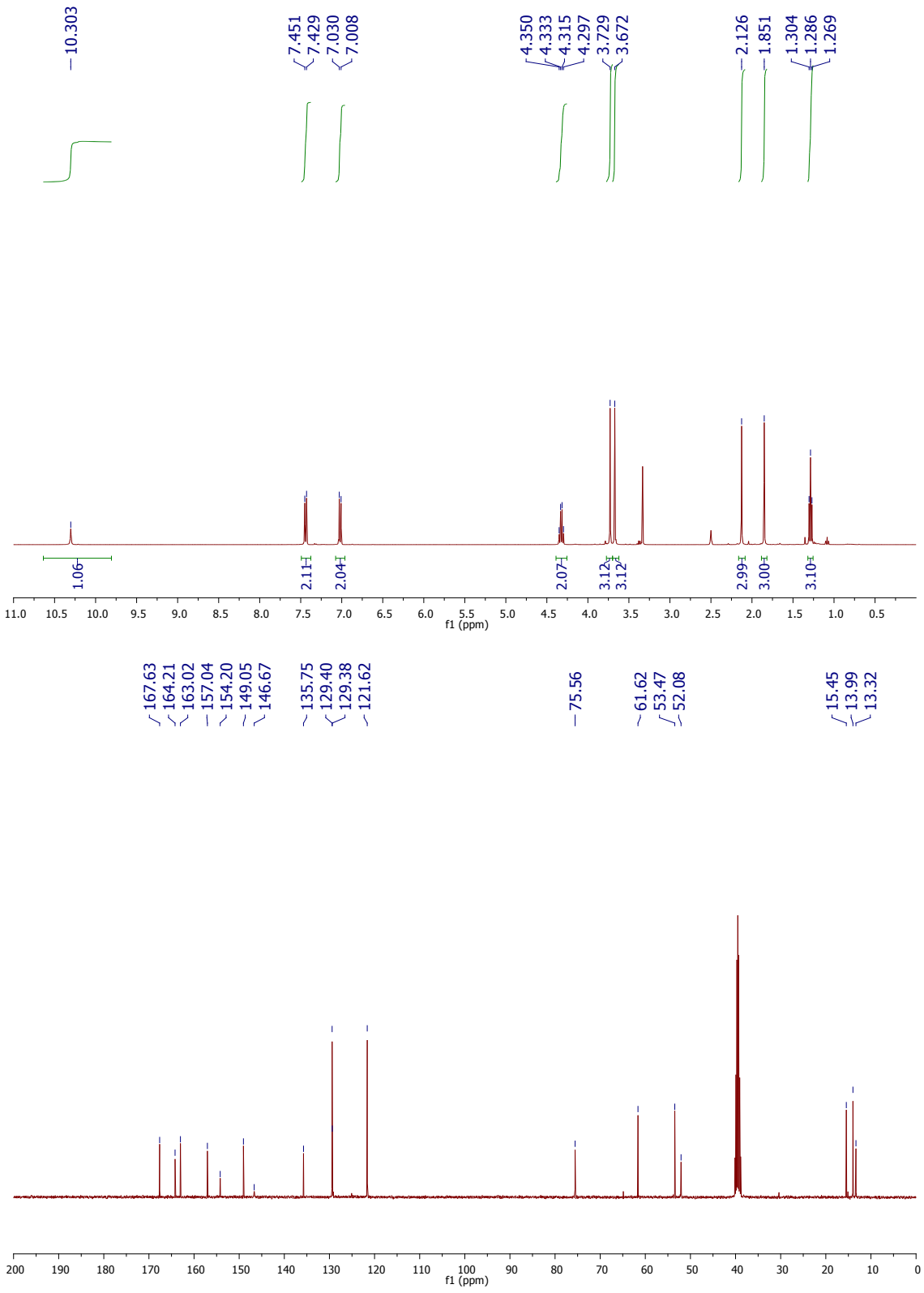
**4-Ethyl 2-methyl 5-((4-methoxyphenyl)imino)-3methyl-1-(2-(phenylcarbamoyl)hydrazono)ethyl)-2,5-dihydrothiophene-2,4-dicarboxylate 7f.**

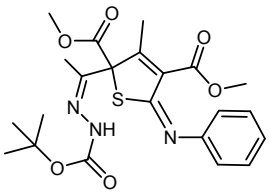


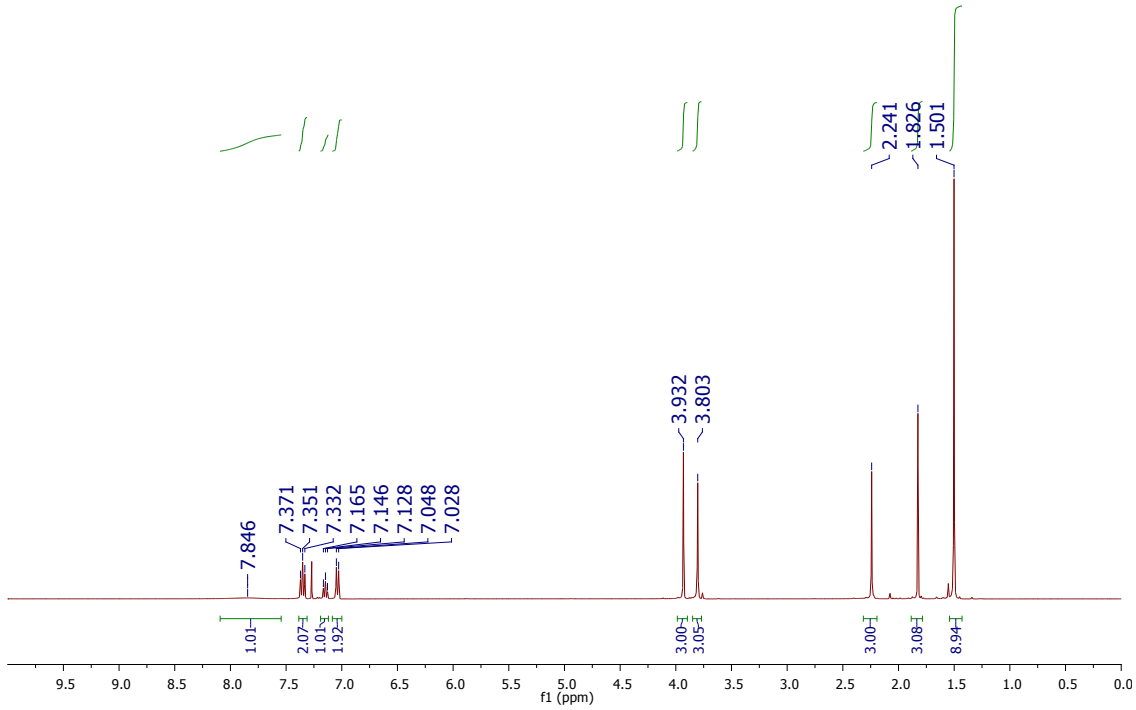


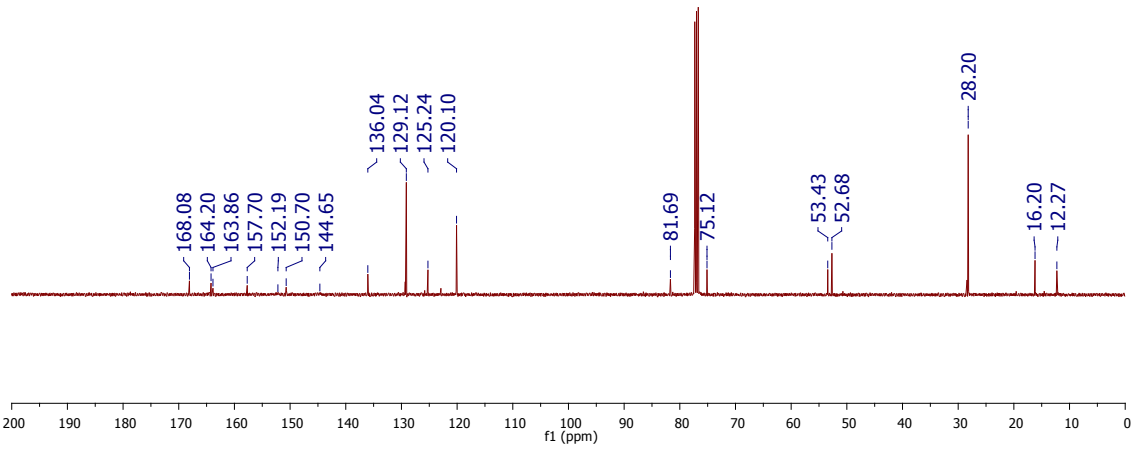
**4-Ethyl-2-methyl 5-((4-chlorophenyl)imino)-2-(1-(2(methoxycarbonyl)hydrazono)ethyl)-3-methyl-2,5-dihydrothiophene-2,4-dicarboxylate 7g.**

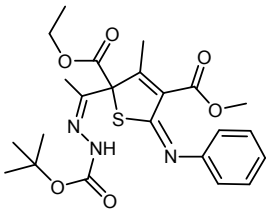




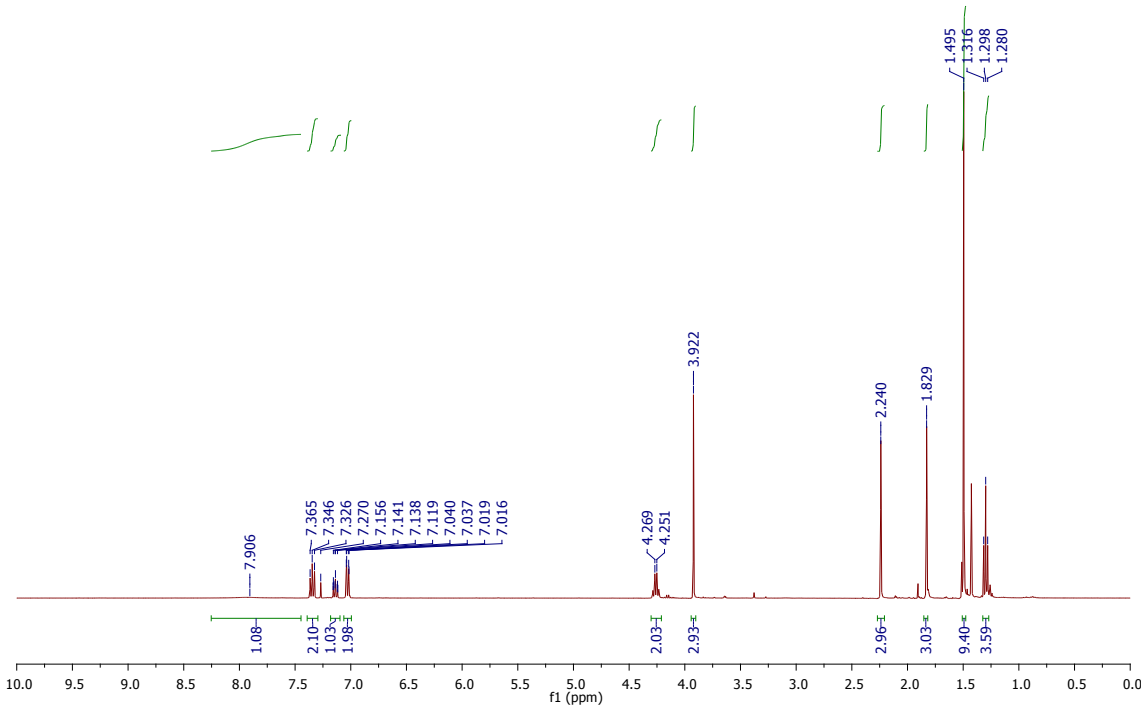
**Dimethyl 2-(1-(2-*tert*-butoxycarbonyl)hydrazono)ethyl)-3-methyl-5-(phenylimino)-2,5-dihydrothiophene-2,4-dicarboxylate 7h.**

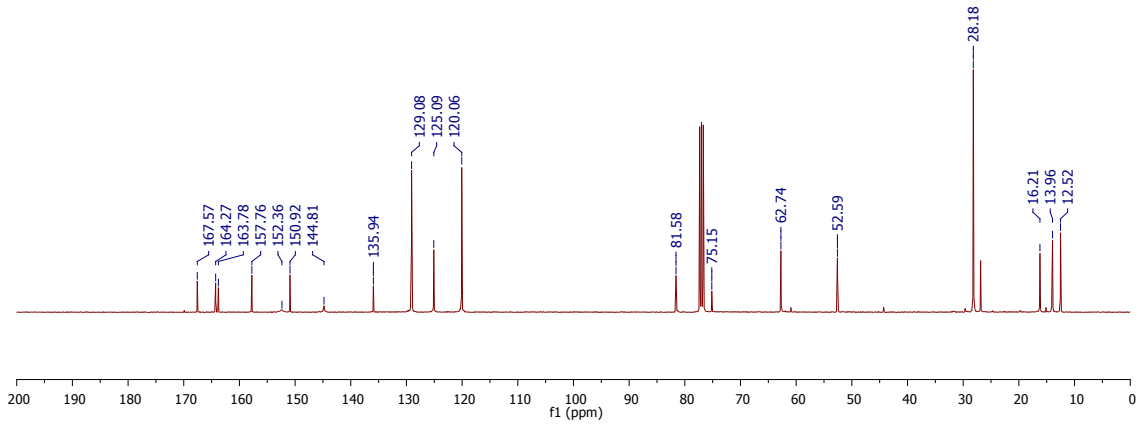


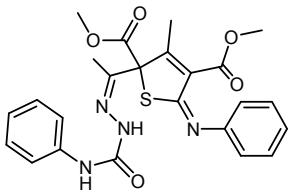





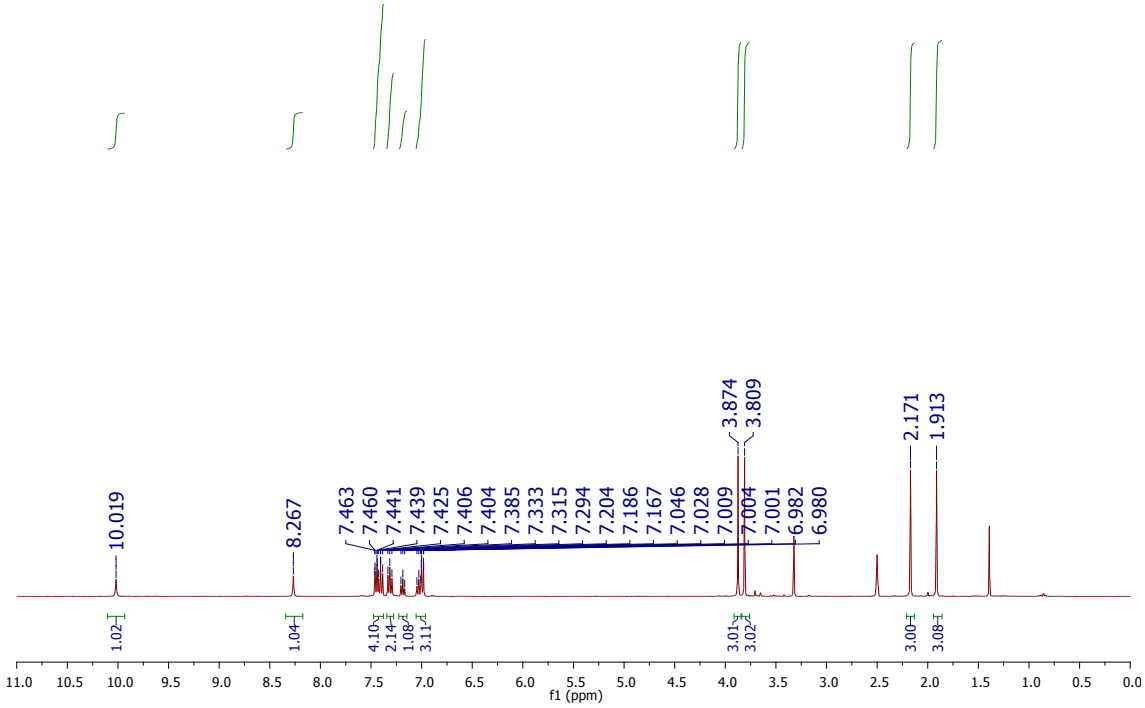
**2-Ethyl-4-methyl 2-(1-(2(*tert*-butoxycarbonyl)hydrazono)ethyl)-3-methyl-5-(phenylimino)-2,5-dihydrothiophene-2,4-dicarboxylate 7i.**

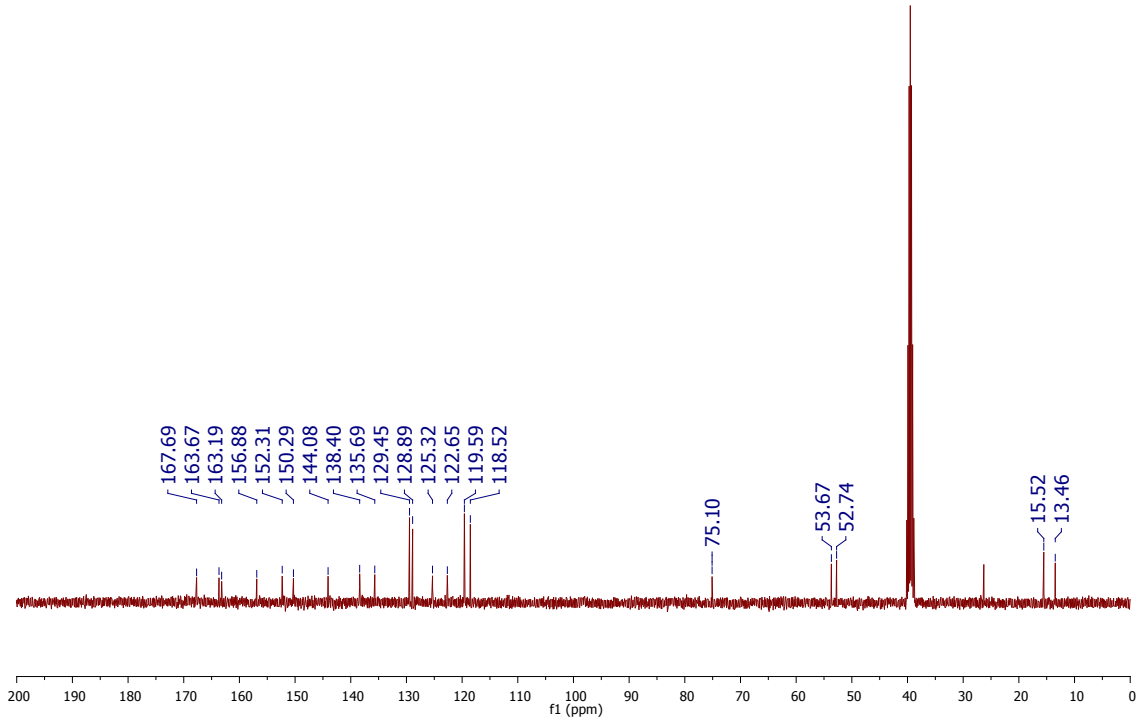


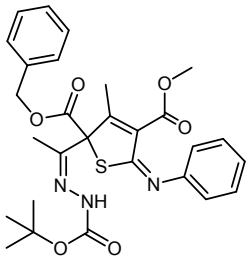





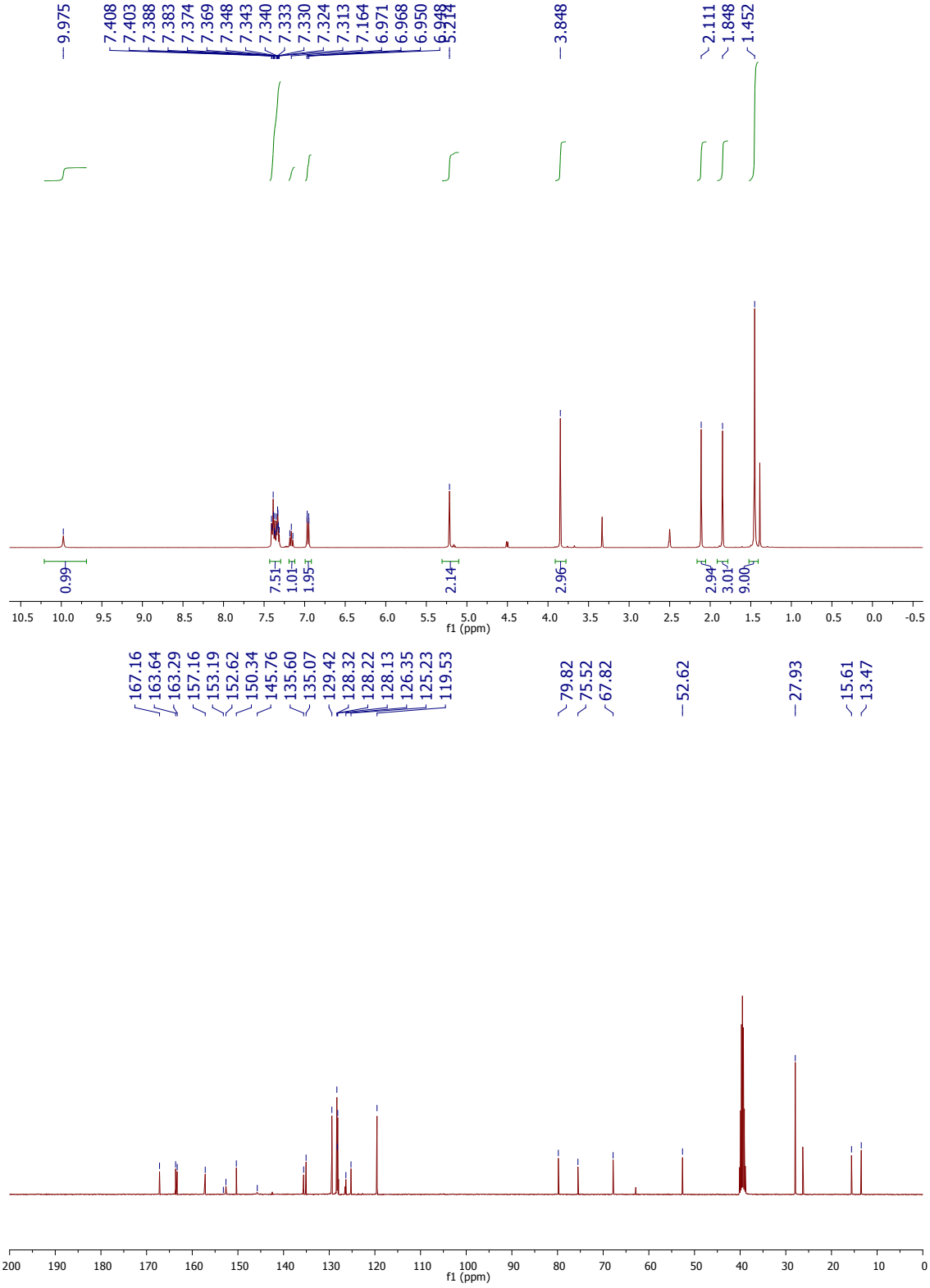
**Dimethyl 3-methyl 2-(1-(2(phenylcarbamoyl)hydrazono)ethyl)-5-(phenylimino)-2,5-dihydrothiophene-2,4-dicarboxylate 7j.**

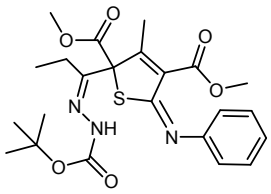


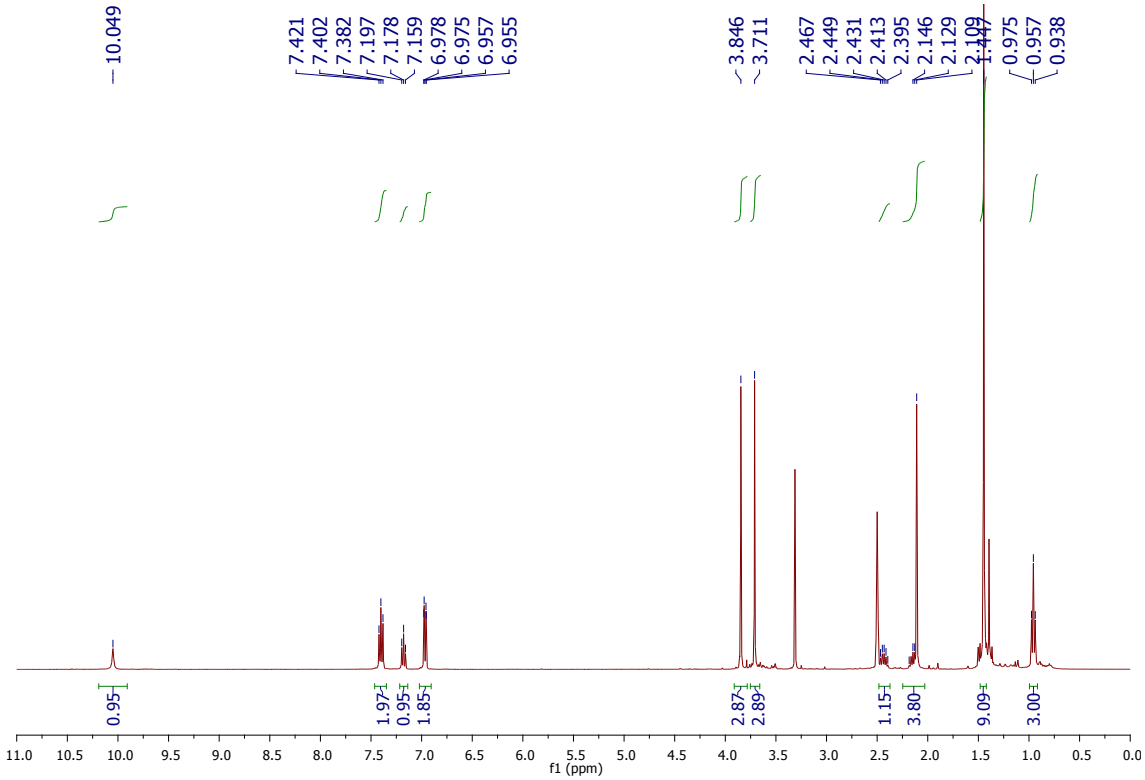


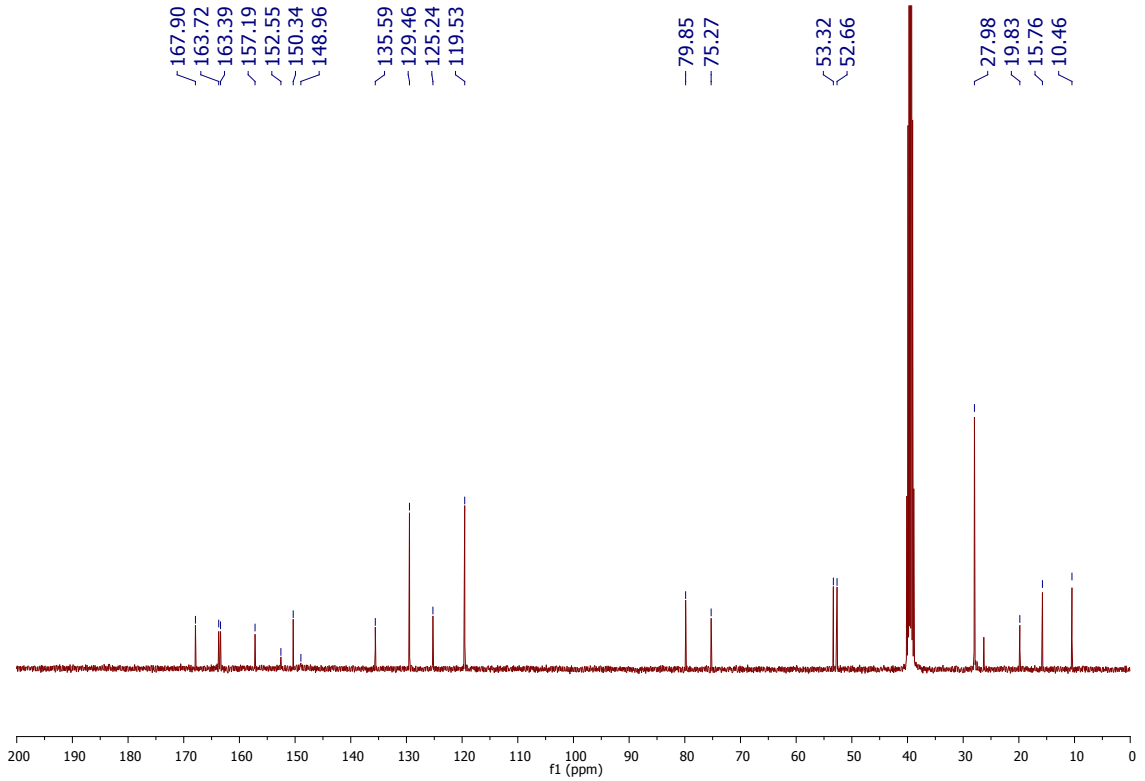
**2-Benzyl-4-methyl 2-(1-(2-*tert*-butoxycarbonyl)hydrazono)ethyl)-3-methyl-5-(phenylimino)-2,5-dihydrothiophene-2,4-dicarboxylate 7k.**

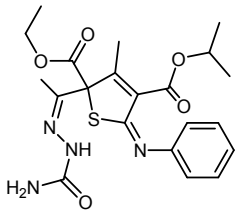




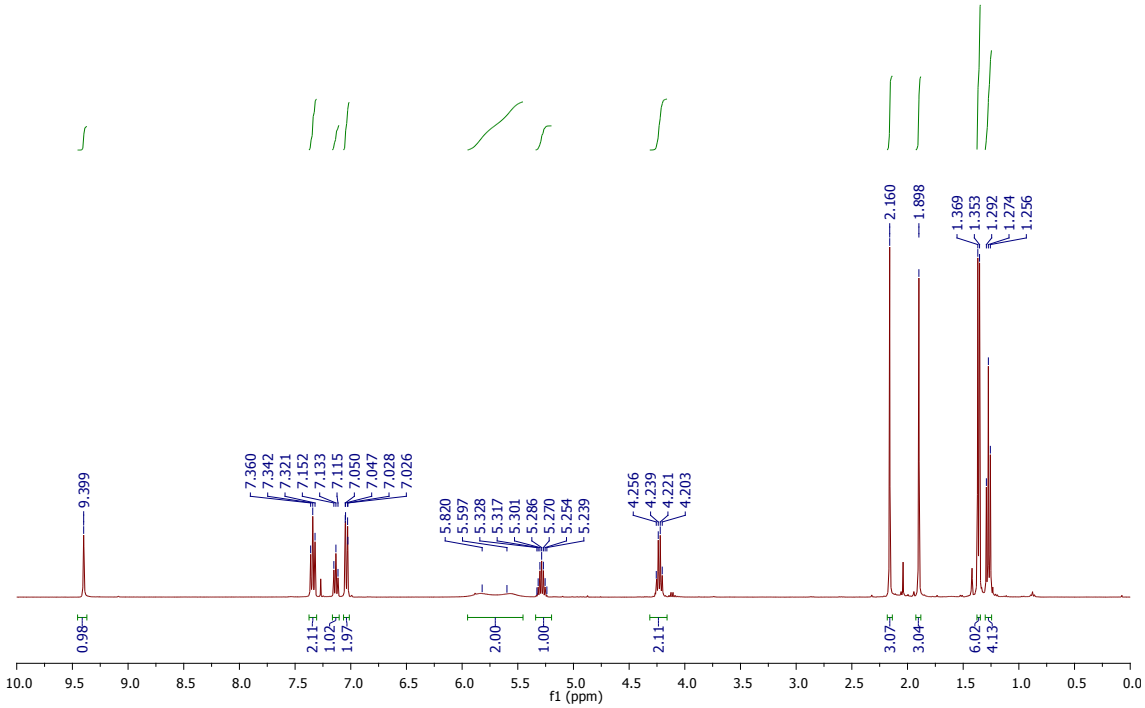
**Dimethyl 2-(1-(2-*tert*-butoxycarbonyl)hydrazono)propyl)-3-methyl-5-(phenylimino)-2,5-dihydrothiophene-2,4-dicarboxylate 7l.**

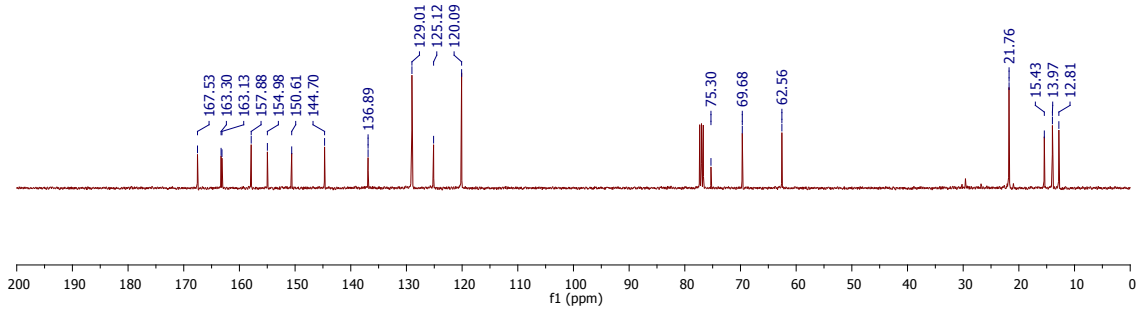


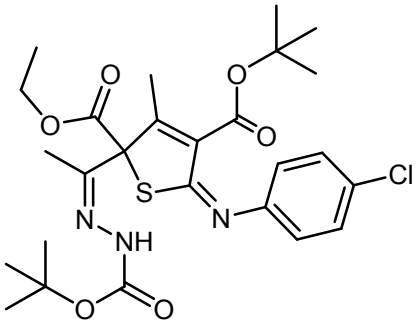





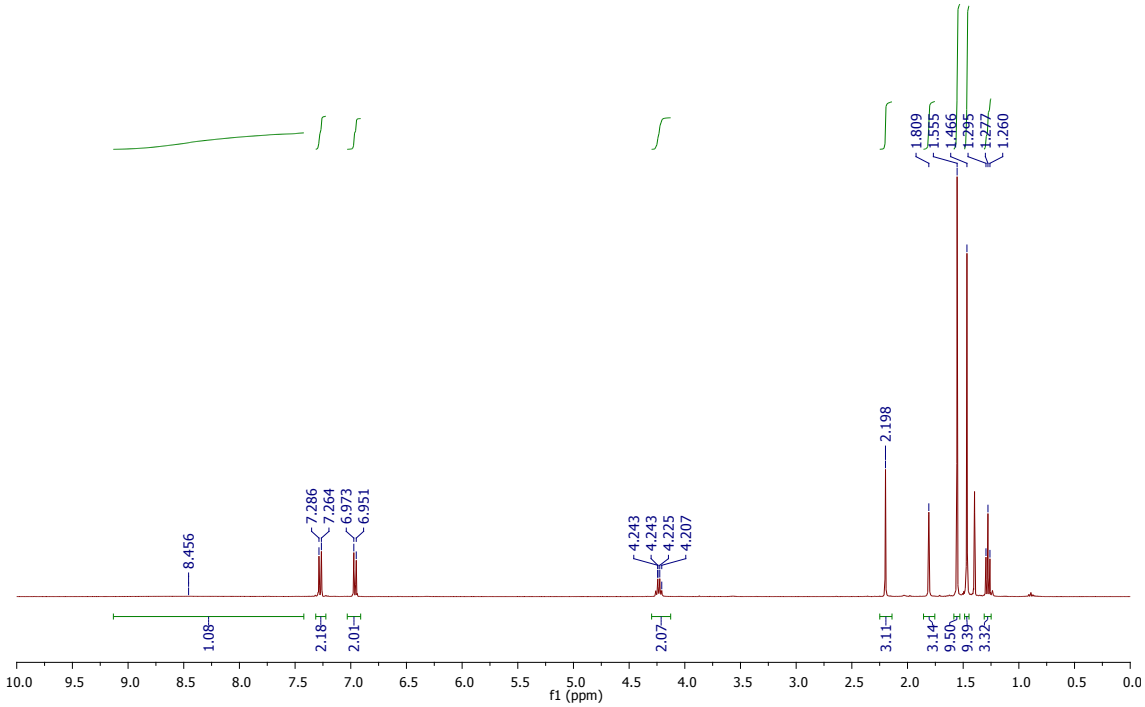
**2-Ethyl 4-*iso*-propyl 2-((1-(2-carbamoylhydrazono)ethyl)-3-methyl-5-((phenyl)imino)-2,5-dihydrothiophene-2,4-dicarboxylate 7m.**

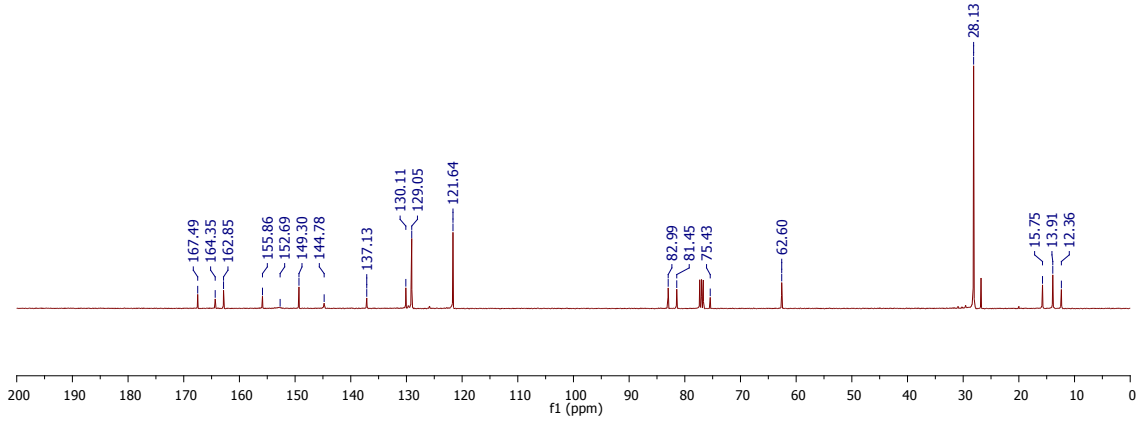


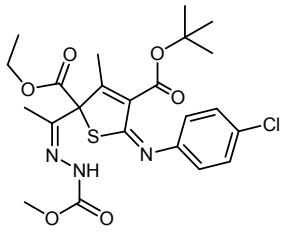





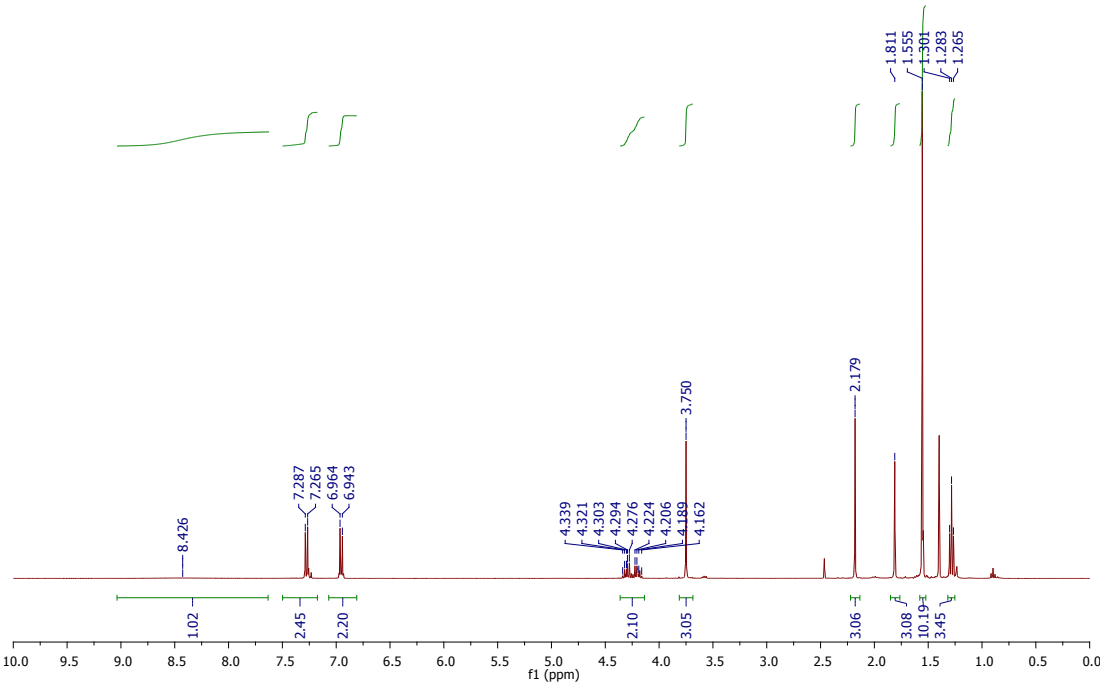
**4-*Tert*-butyl 2-ethyl 2-((1-(2(*tert*-butoxycarbonyl)hydrazono)ethyl)-5-((4-chlorophenyl)imino)--3-methyl-2,5-dihydrothiophene-2,4-dicarboxylate 7n.**

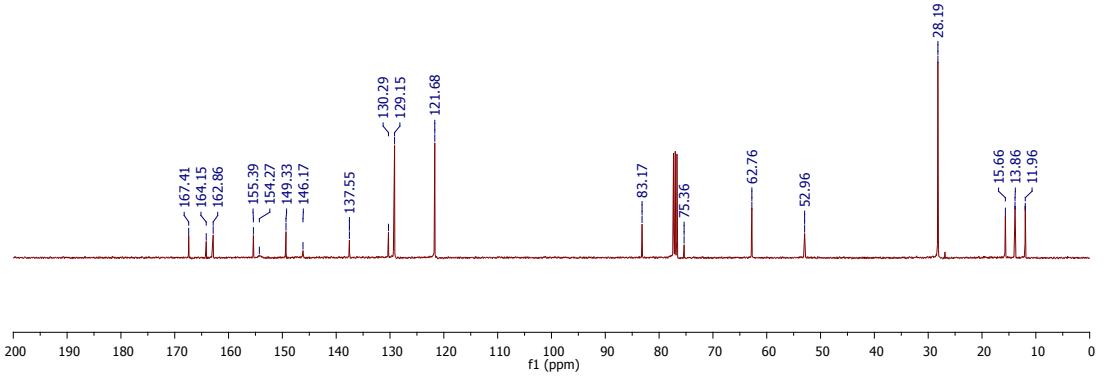


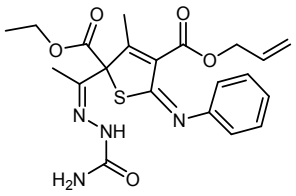





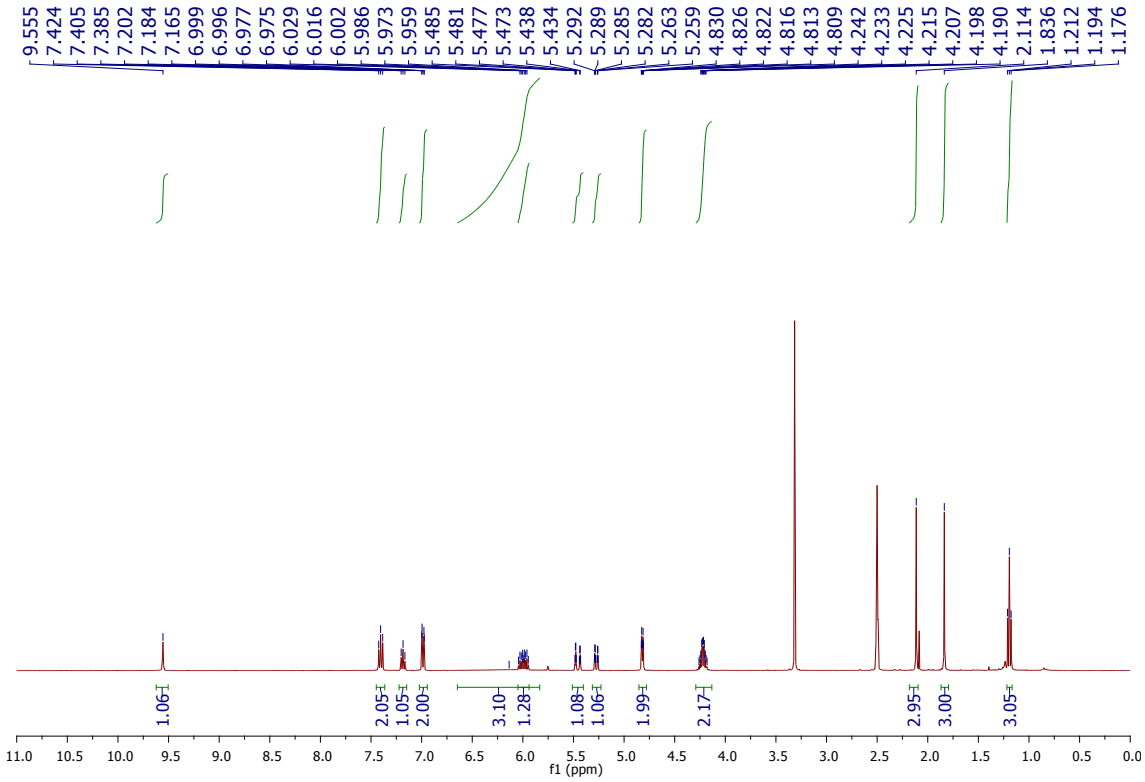
**4-*Tert*-butyl 2-ethyl 5-((4-chlorophenyl)imino)-2-((1-(2(methoxycarbonyl)hydrazono)ethyl)-3-methyl-2,5-dihydrothiophene-2,4-dicarboxylate 7o.**

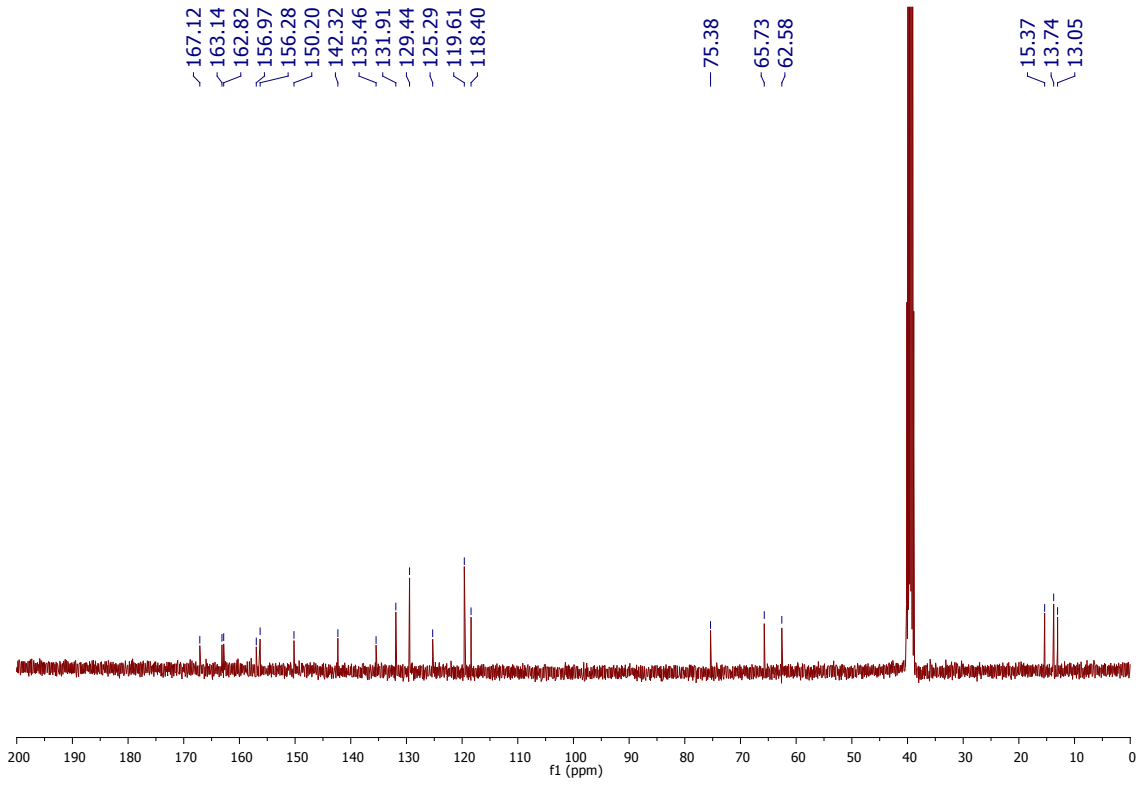


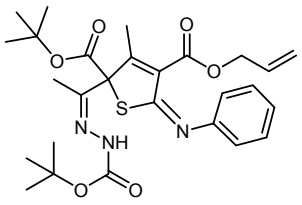





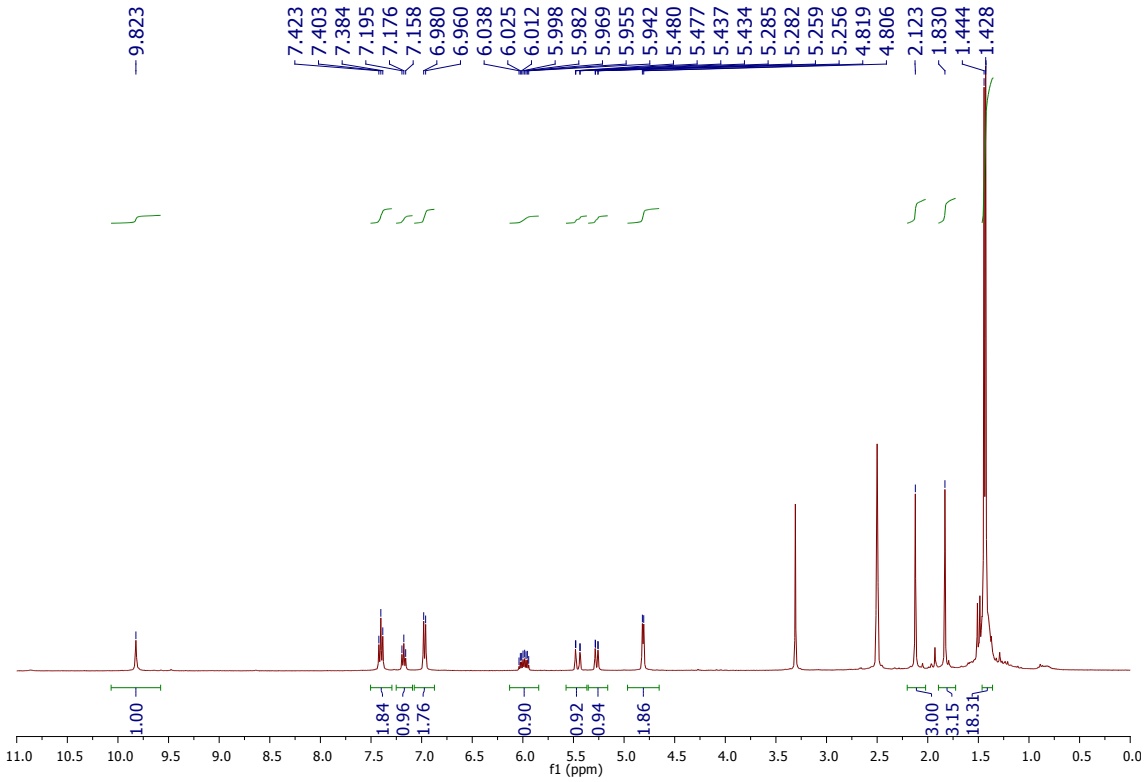
**4-Allyl 2-tert-butyl-2-(1-(2(carbamoylhydrazono)ethyl)-3-methyl-5-(phenylimino)-2,5-dihydrothiophene-2,4-dicarboxylate 7p.**

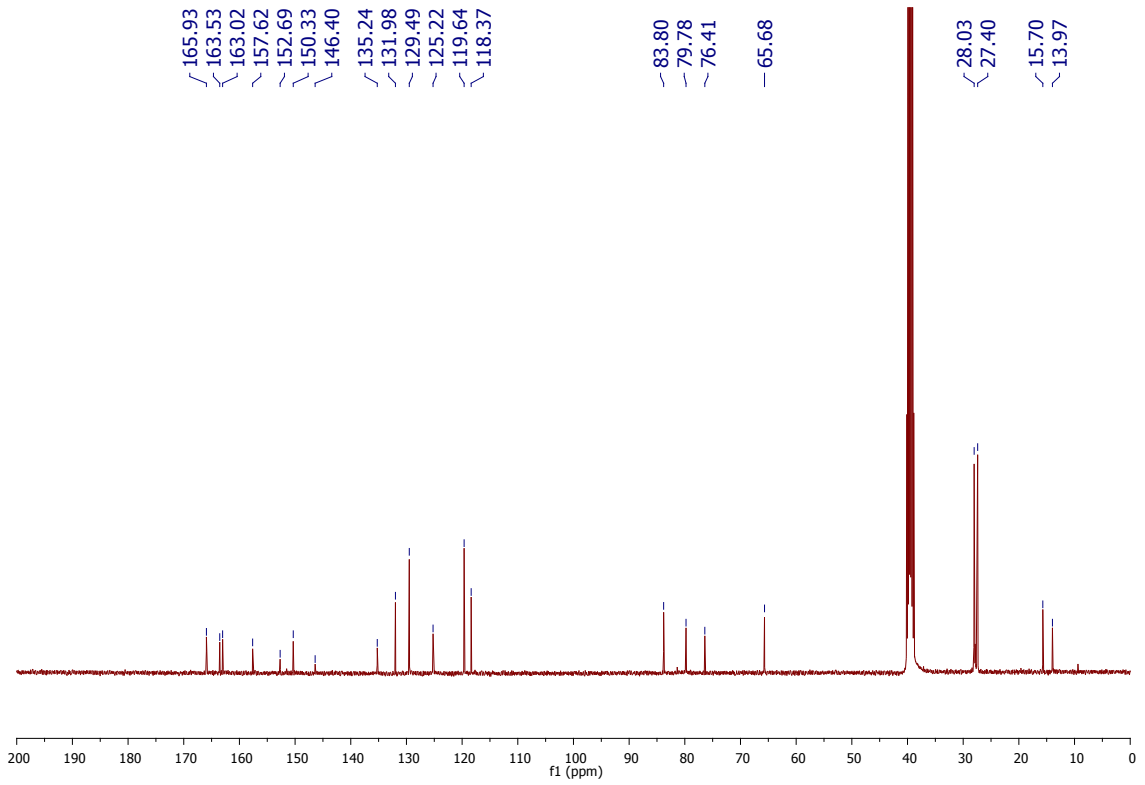


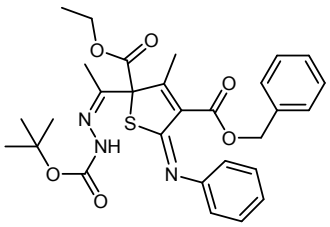





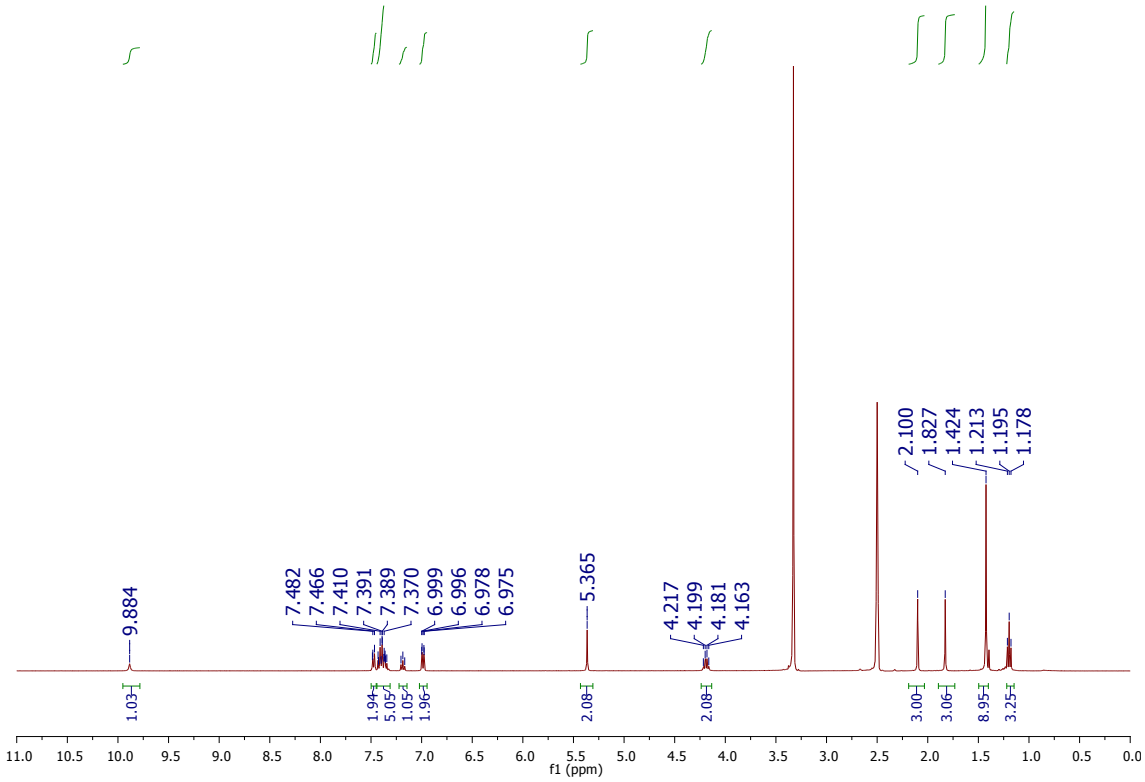
**4-Allyl 2-tert-butyl-2-(1-(2(*tert*-butoxycarbonyl)hydrazono)ethyl)-3-methyl-5-(phenylimino)-2,5-dihydrothiophene-2,4-dicarboxylate 7q.**

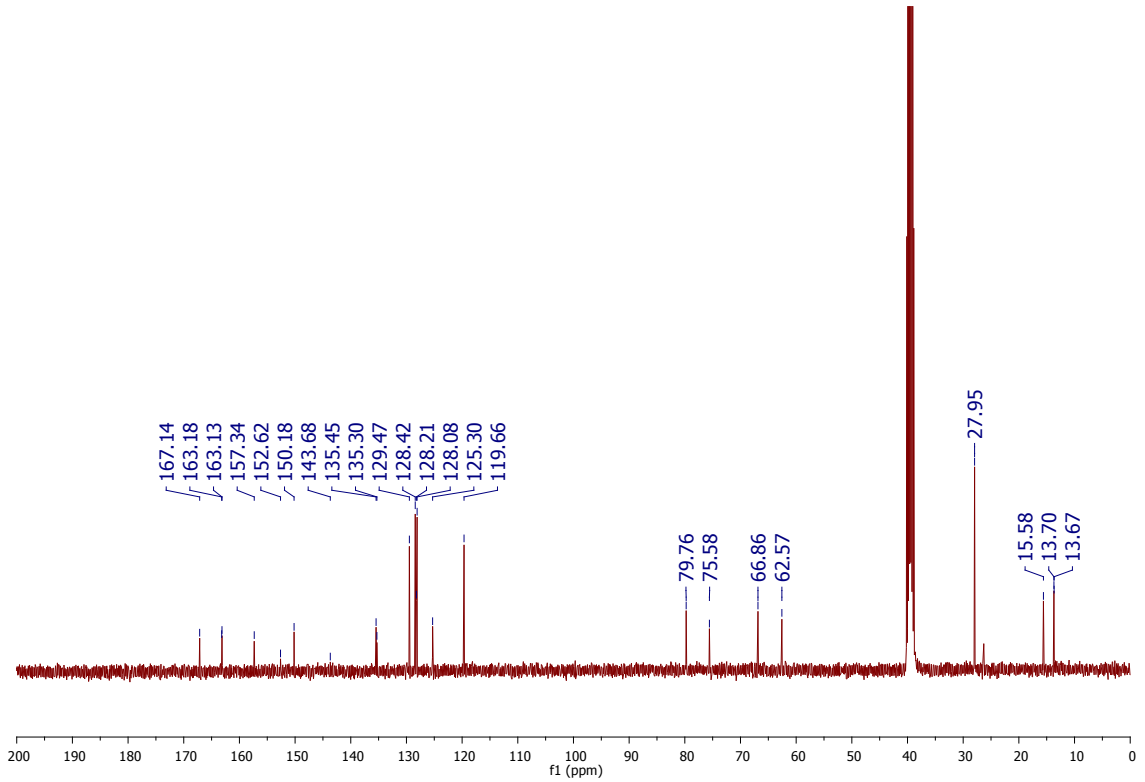


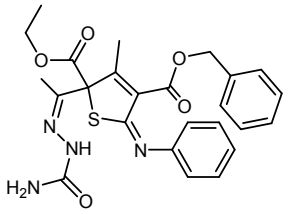





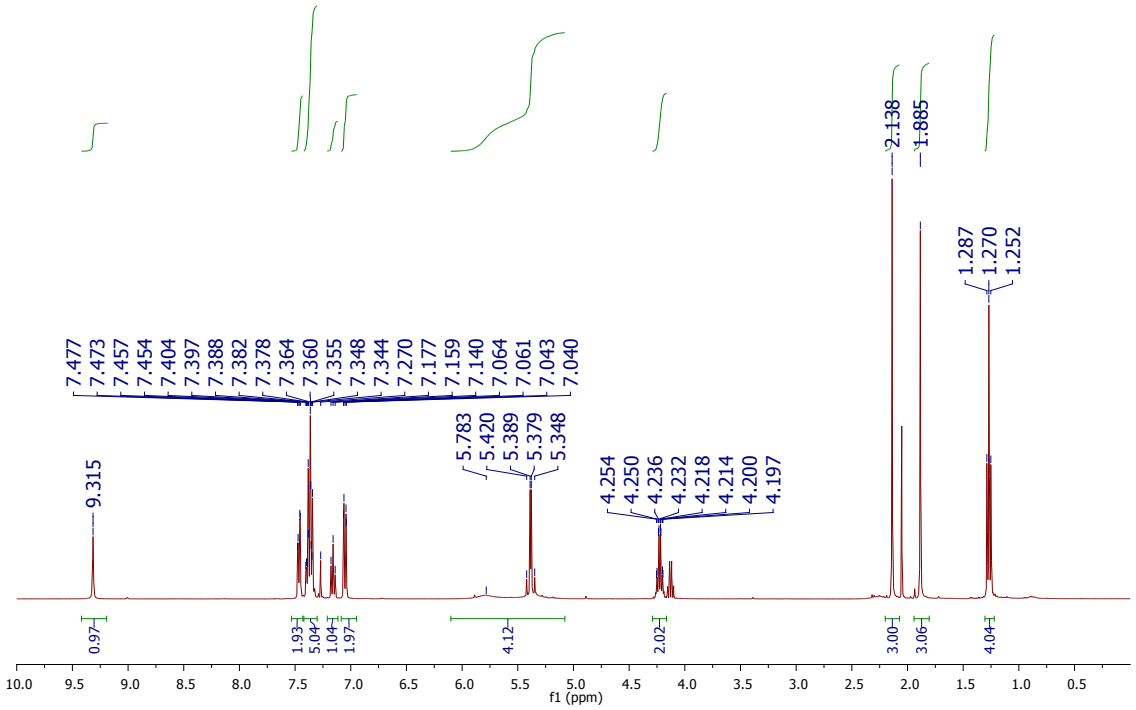
**4-Benzyl-2-ethyl 2-(1-(2-*tert*-butoxycarbonyl)hydrazono)ethyl)-3-methyl-5-(phenylimino)-2,5-dihydrothiophene-2,4-dicarboxylate 7r.**

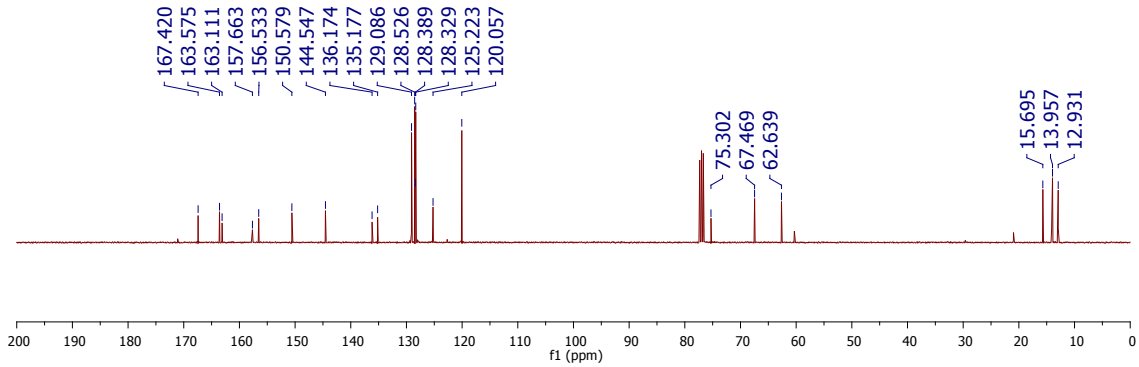


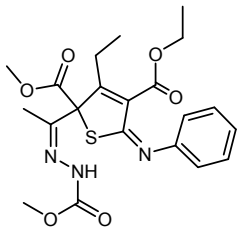





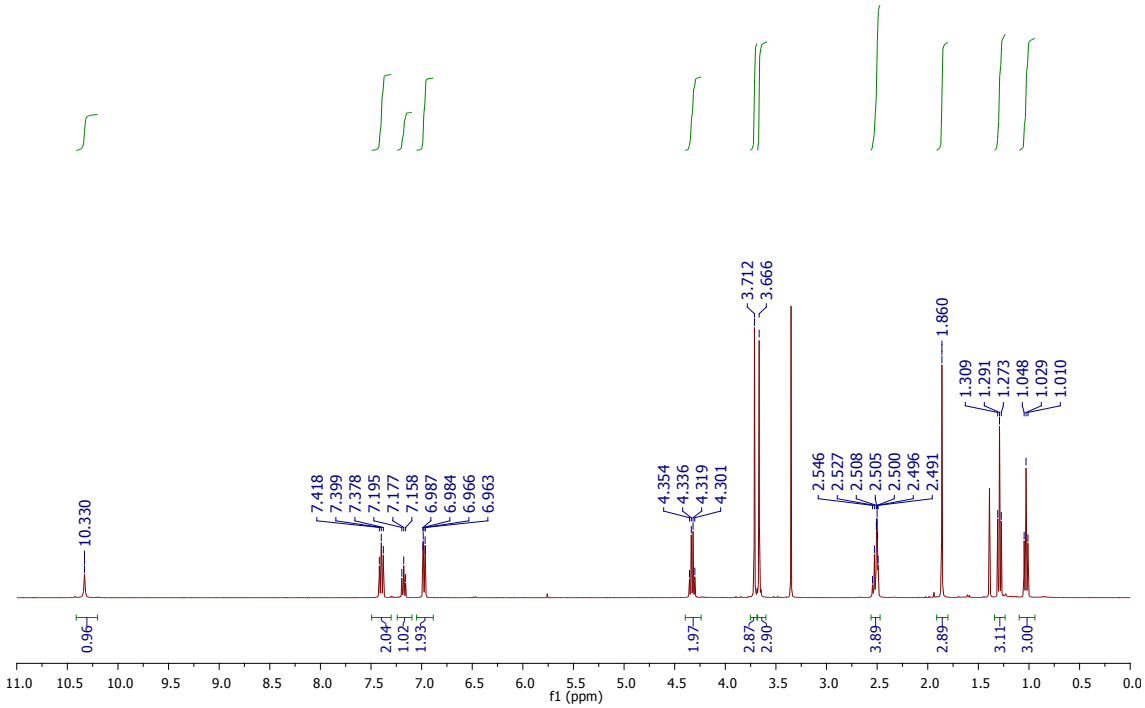
**4-Benzyl 2-ethyl 2-((1-(2-carbamoylhydrazono)ethyl)-3-methyl-5-((phenyl)imino)-2,5-dihydrothiophene-2,4-dicarboxylate 7s.**

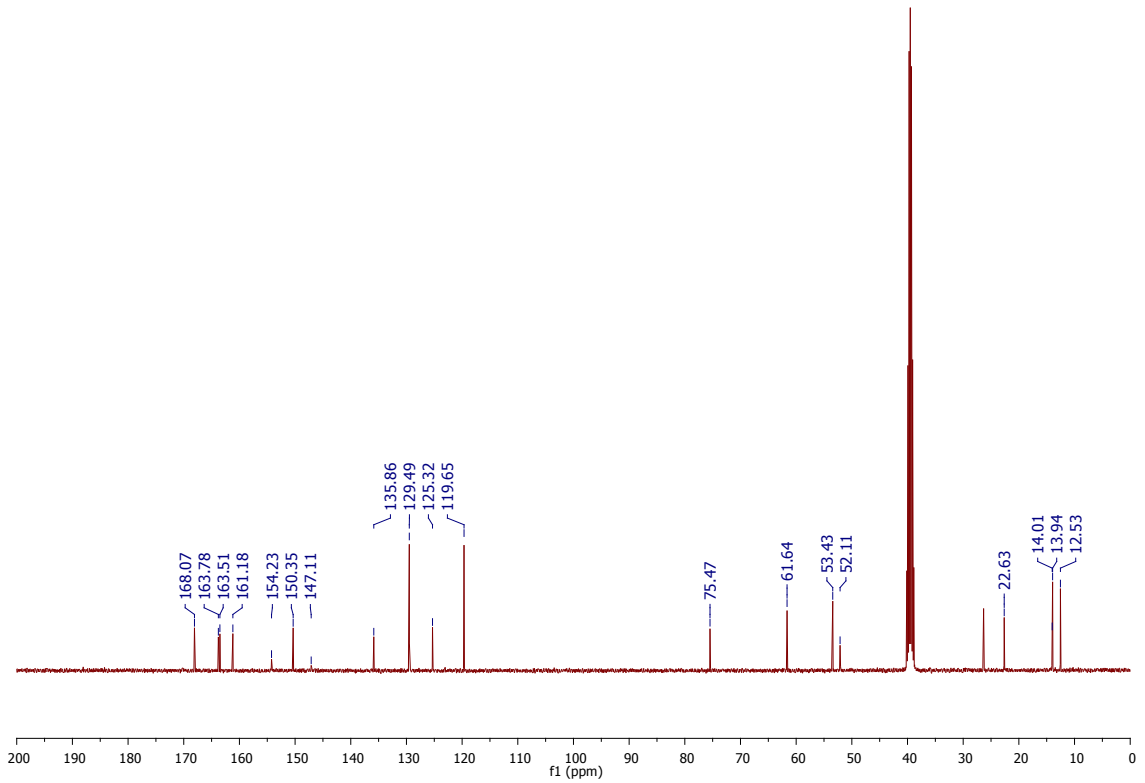


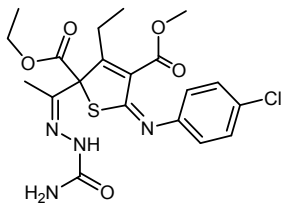





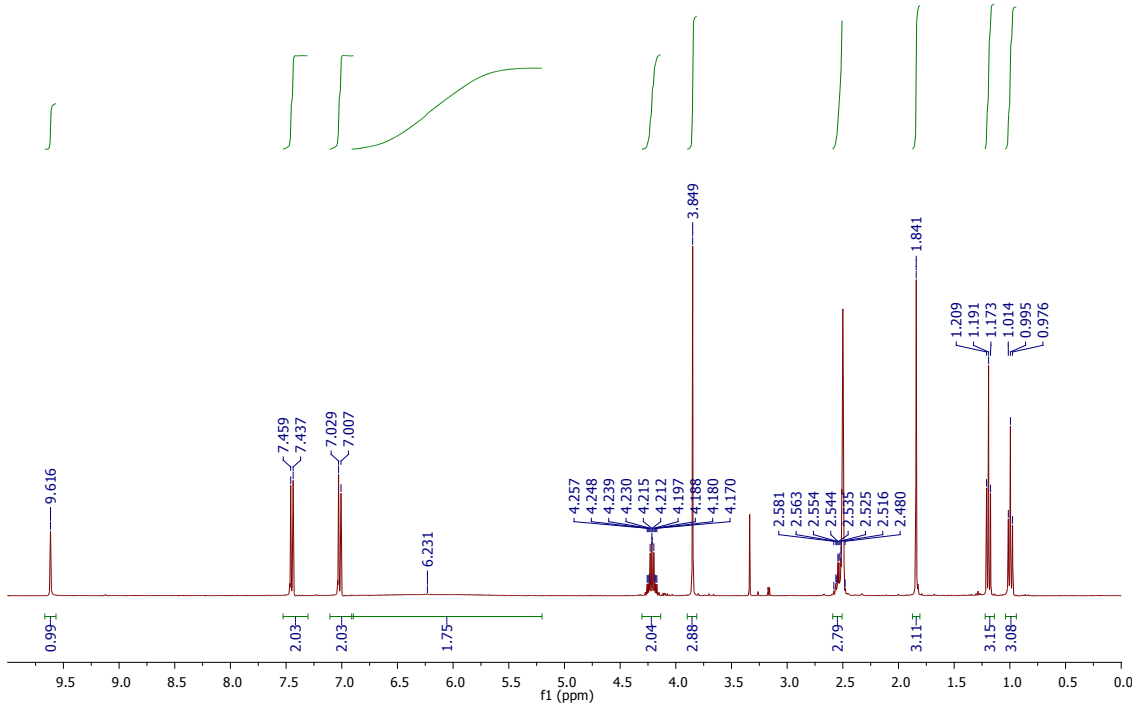
**4-Ethyl-2-methyl 3-ethyl-2-(1-(2(metoxycarbonyl)hydrazono)ethyl)-5-(phenylimino)-2,5-dihydrothiophene-2,4-dicarboxylate 7t.**

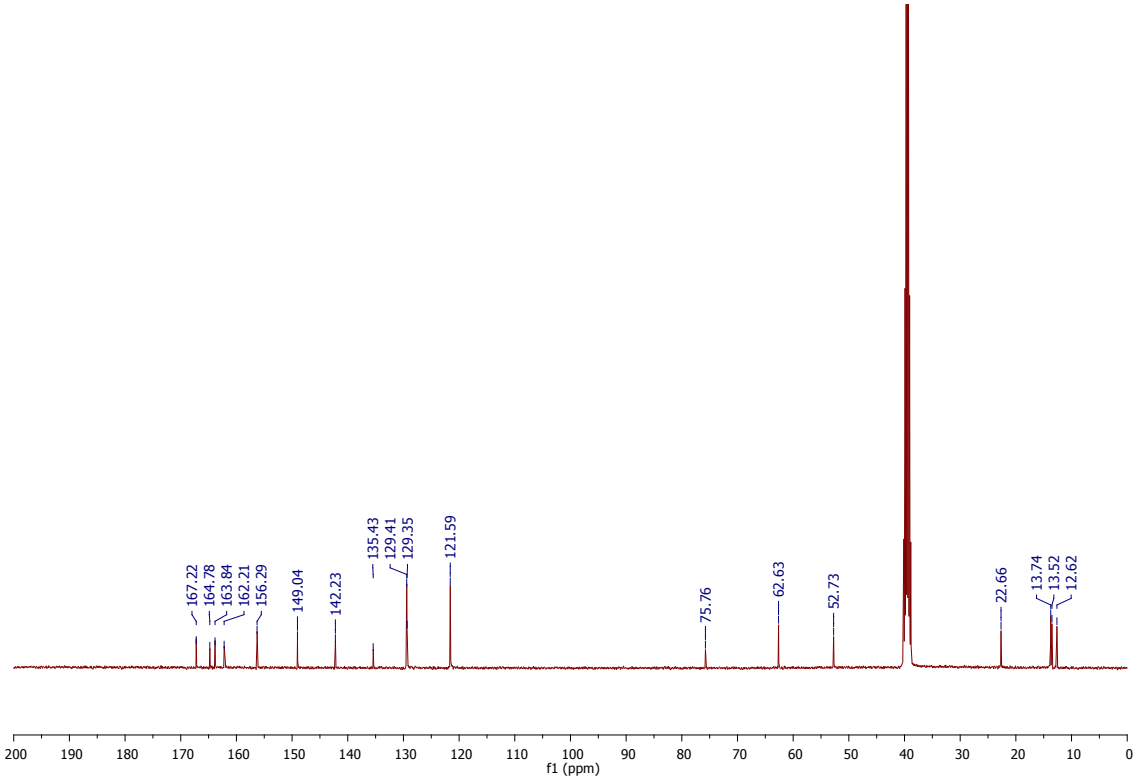


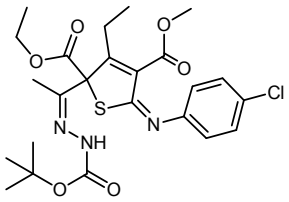





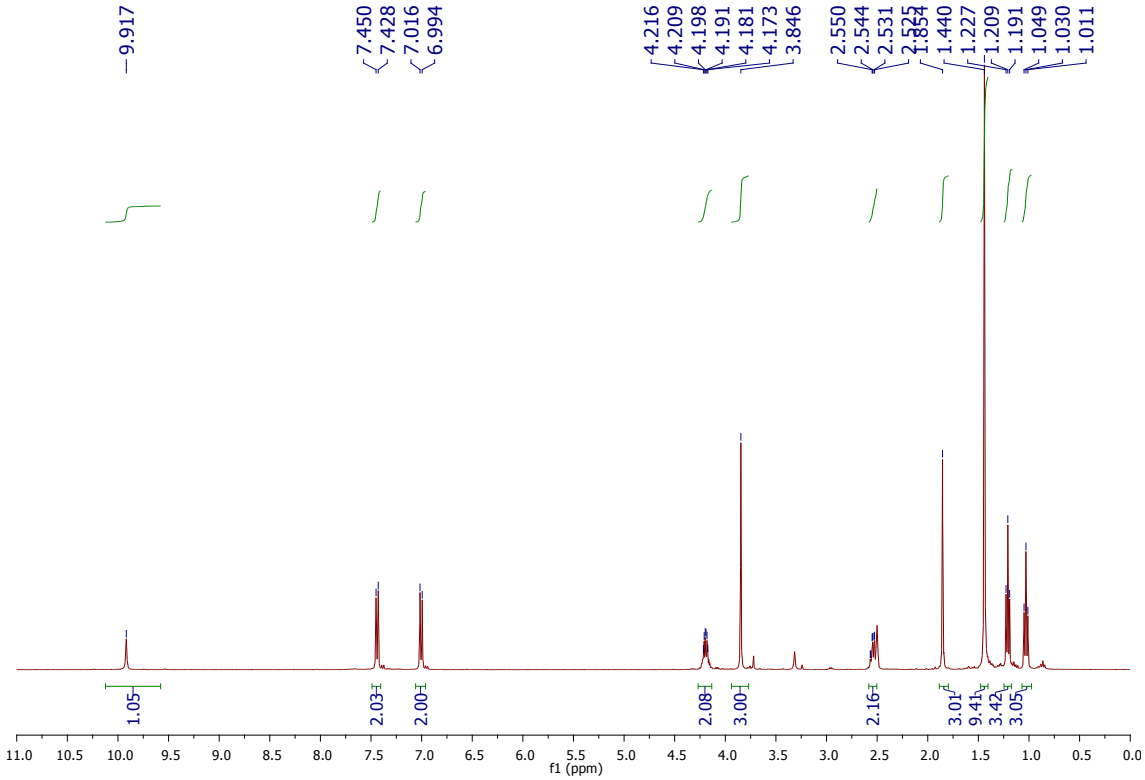
**2-Ethyl-4-methyl 2-(1-(2(carbamoylhydrazono)ethyl)-5-((4-chlorophenyl)imino)-3-ethyl-2,5-dihydrothiophene-2,4-dicarboxylate 7u.**

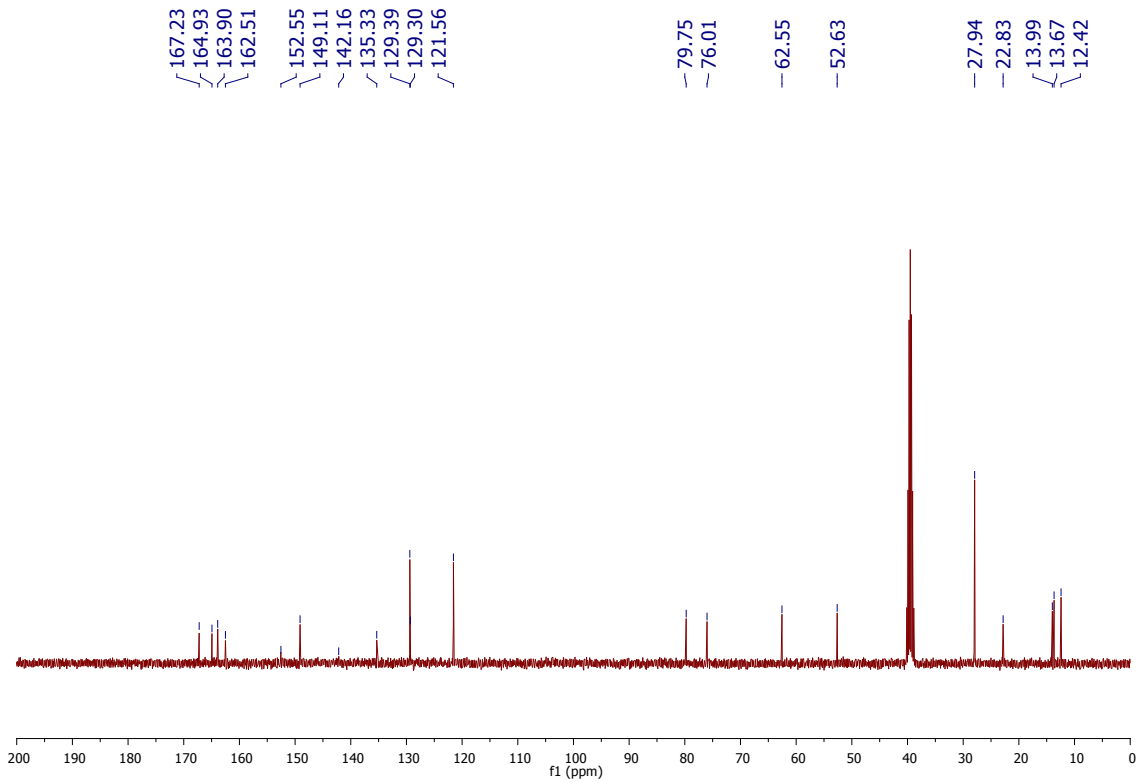


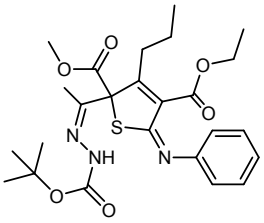





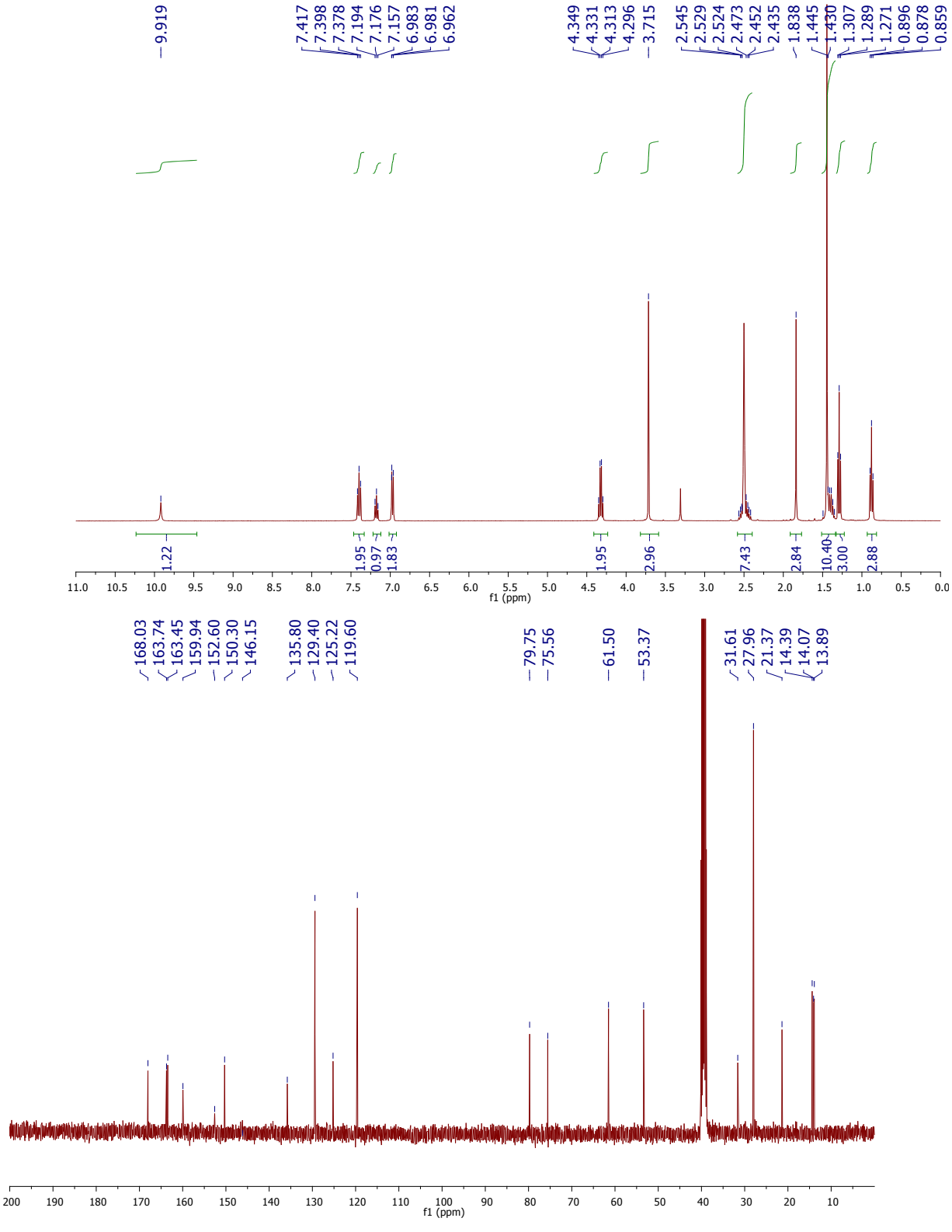
**2-Ethyl-4-methyl 2-(1-(2(*tert*-butoxycarbonyl)hydrazono)ethyl)-5-((4-chlorophenyl)imino)-3-ethyl-2,5-dihydrothiophene-2,4-dicarboxylate 7v.**



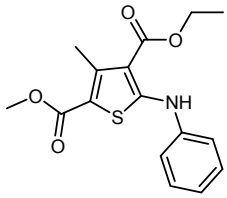





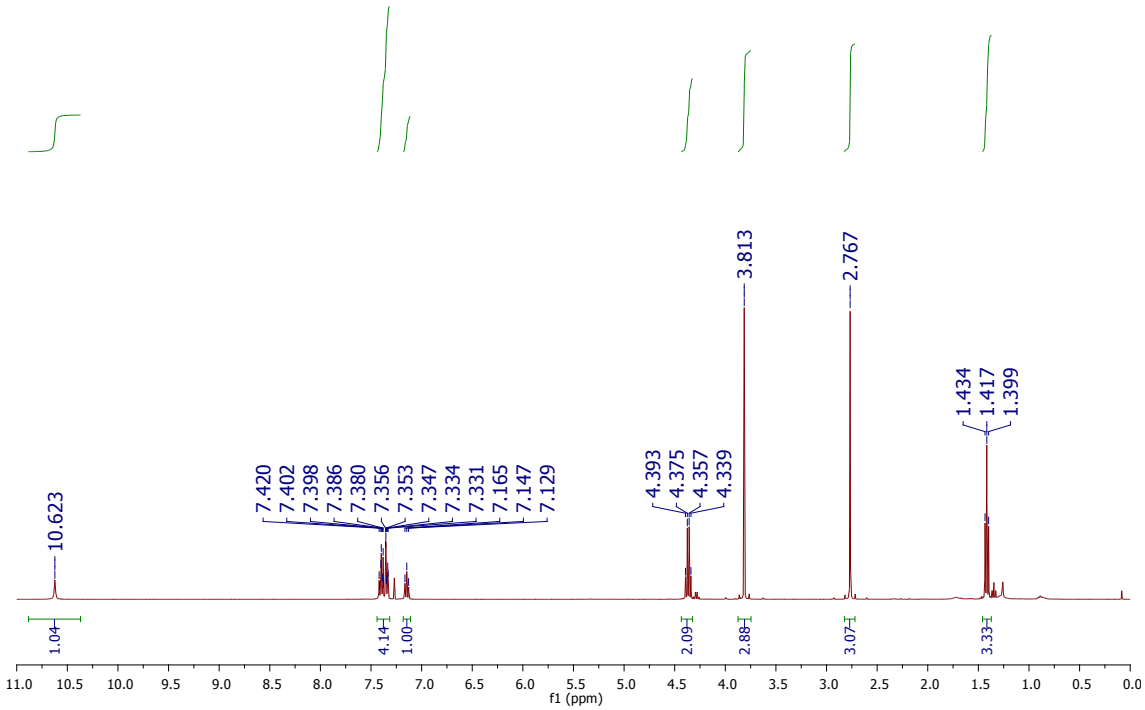
**4-Ethyl-2-methyl 2-(1-(2-*tert*-butoxycarbonyl)hydrazono)ethyl)-5-(phenylimino)-3-propyl--2,5-dihydrothiophene-2,4-dicarboxylate 7w**

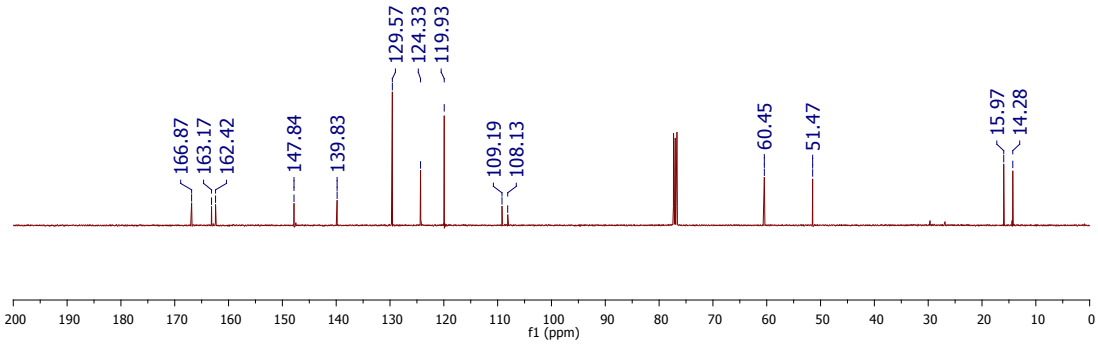


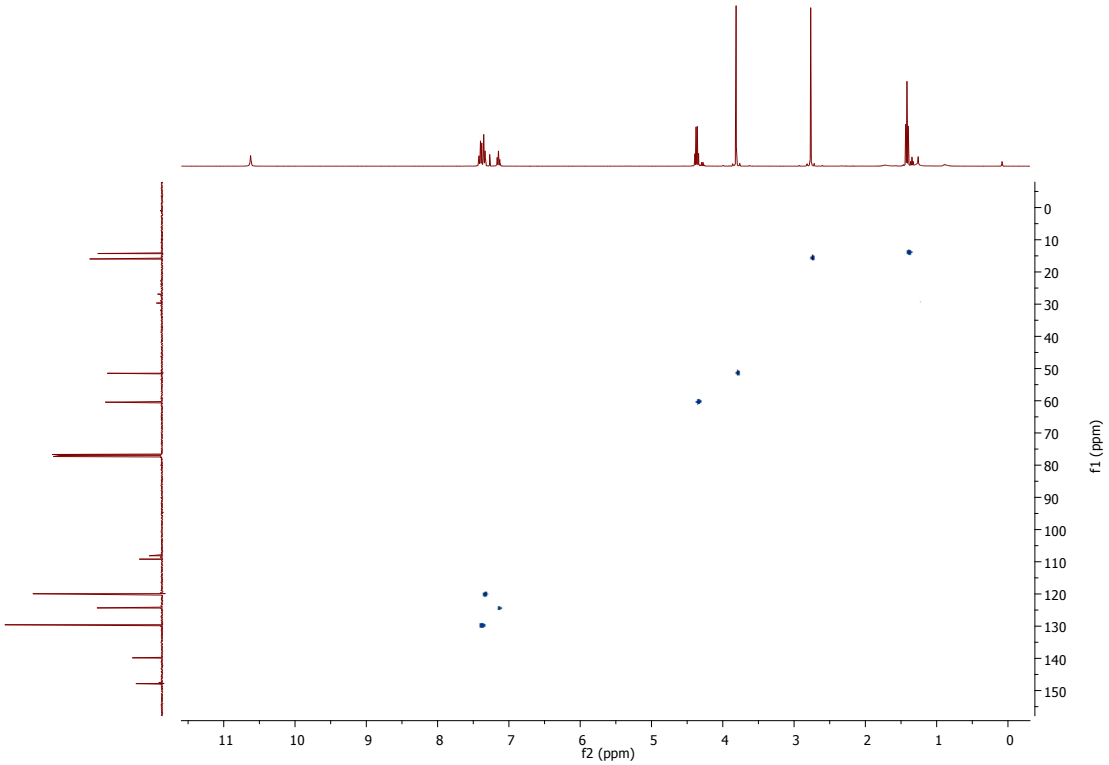
## 13 $^{1}H$ and $^{13}C$ NMR spectra of 5-amino thiophene-2,4-dicarboxylates 8a-j.

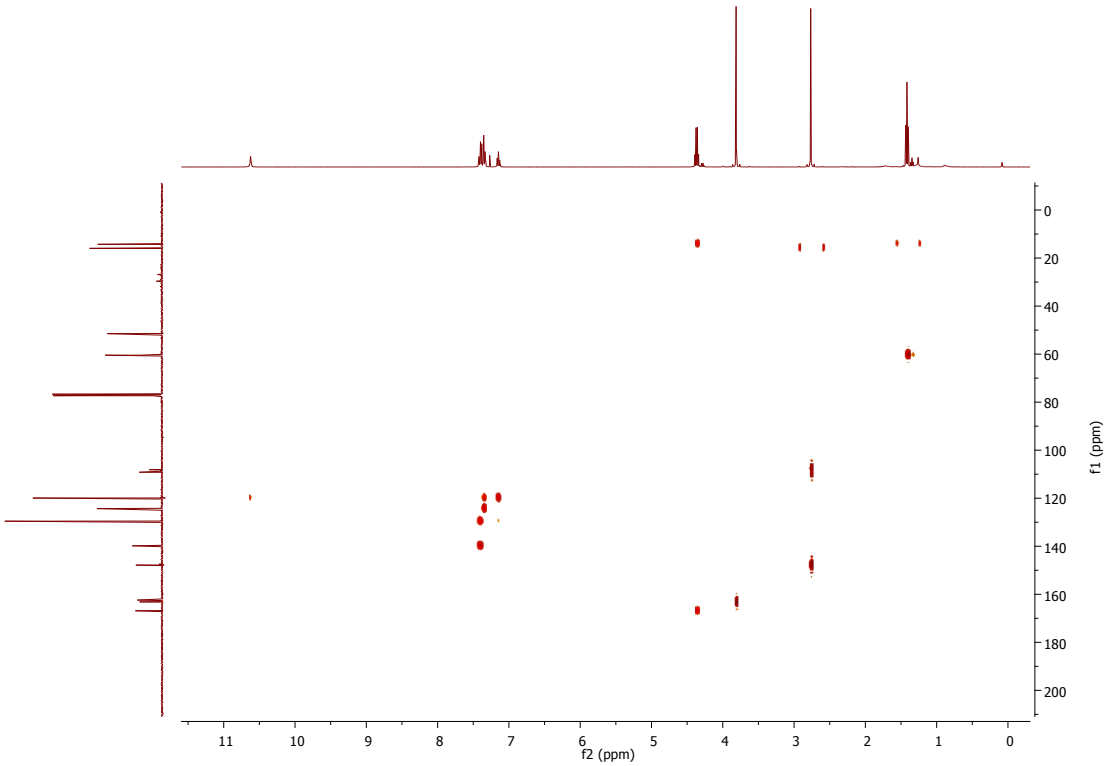


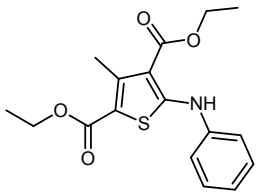

**4-Ethyl-2-methyl 3-methyl-5-(phenylamino)thiophene-2,4-dicarboxylate 8a.**



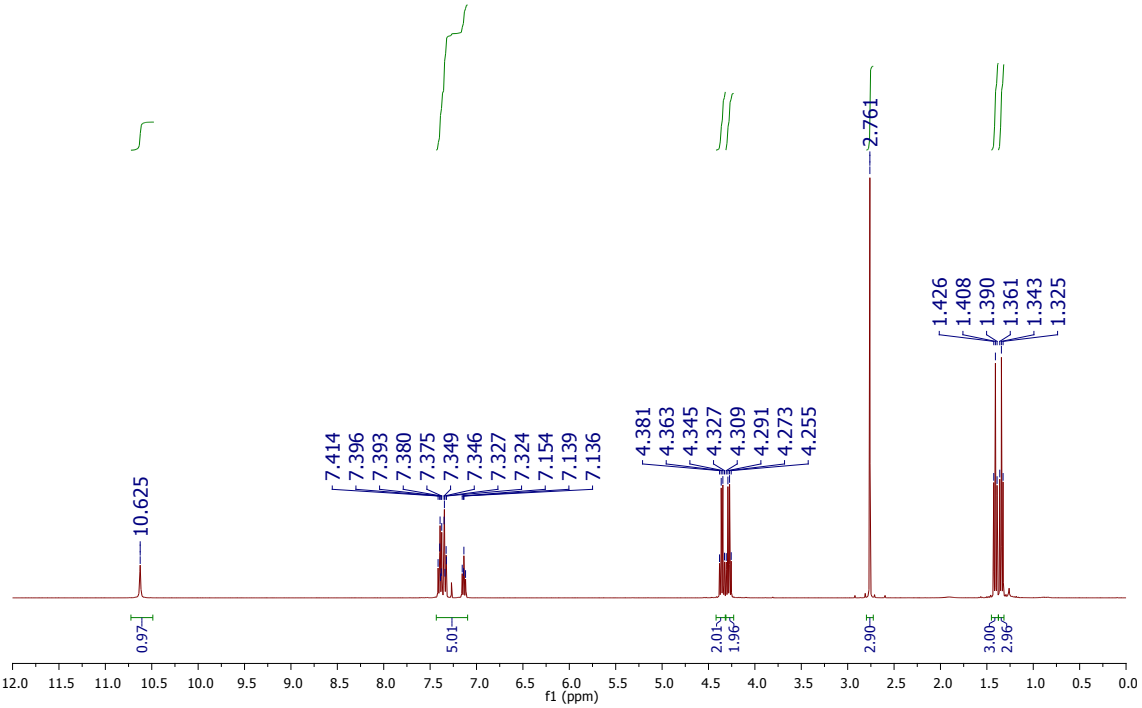



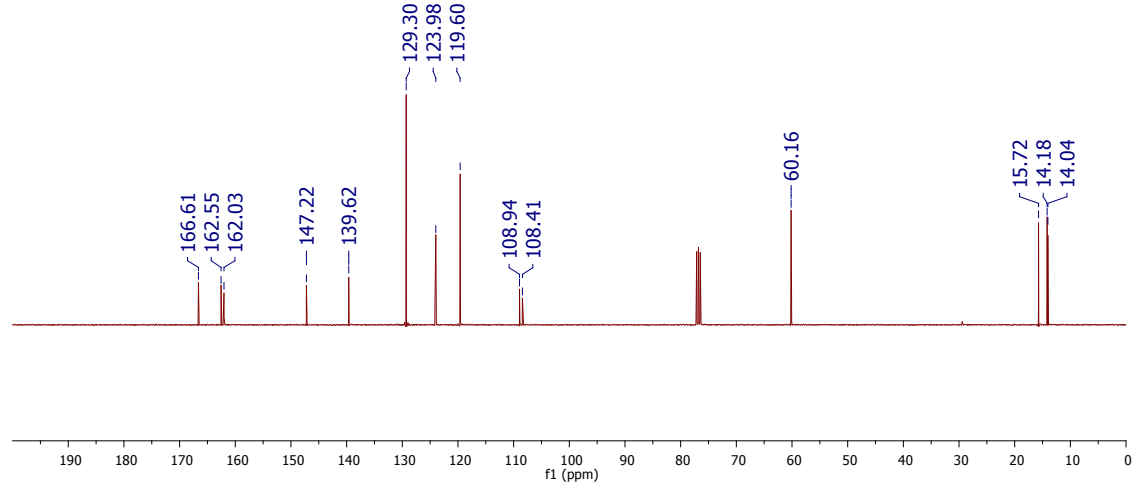

f2 (ppm)
f1 (ppm)

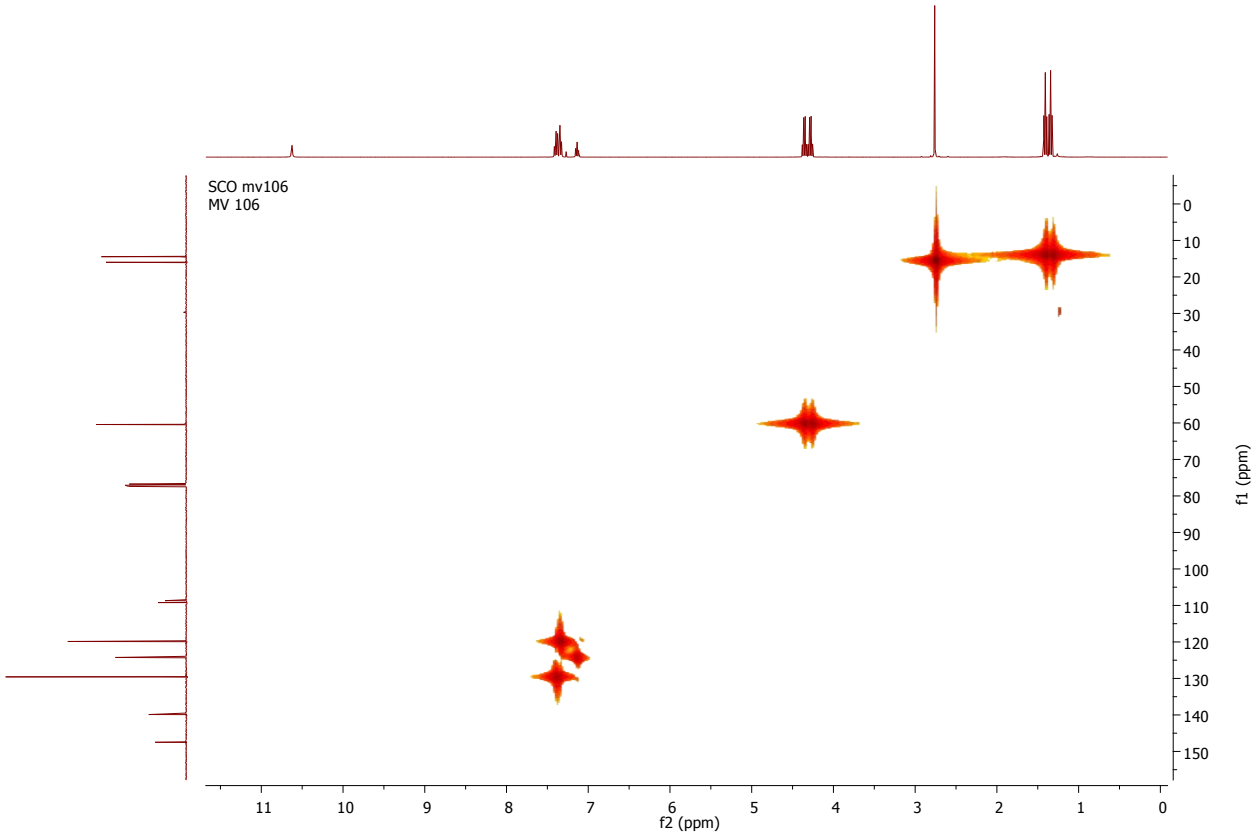

f2 (ppm)
f1 (ppm)

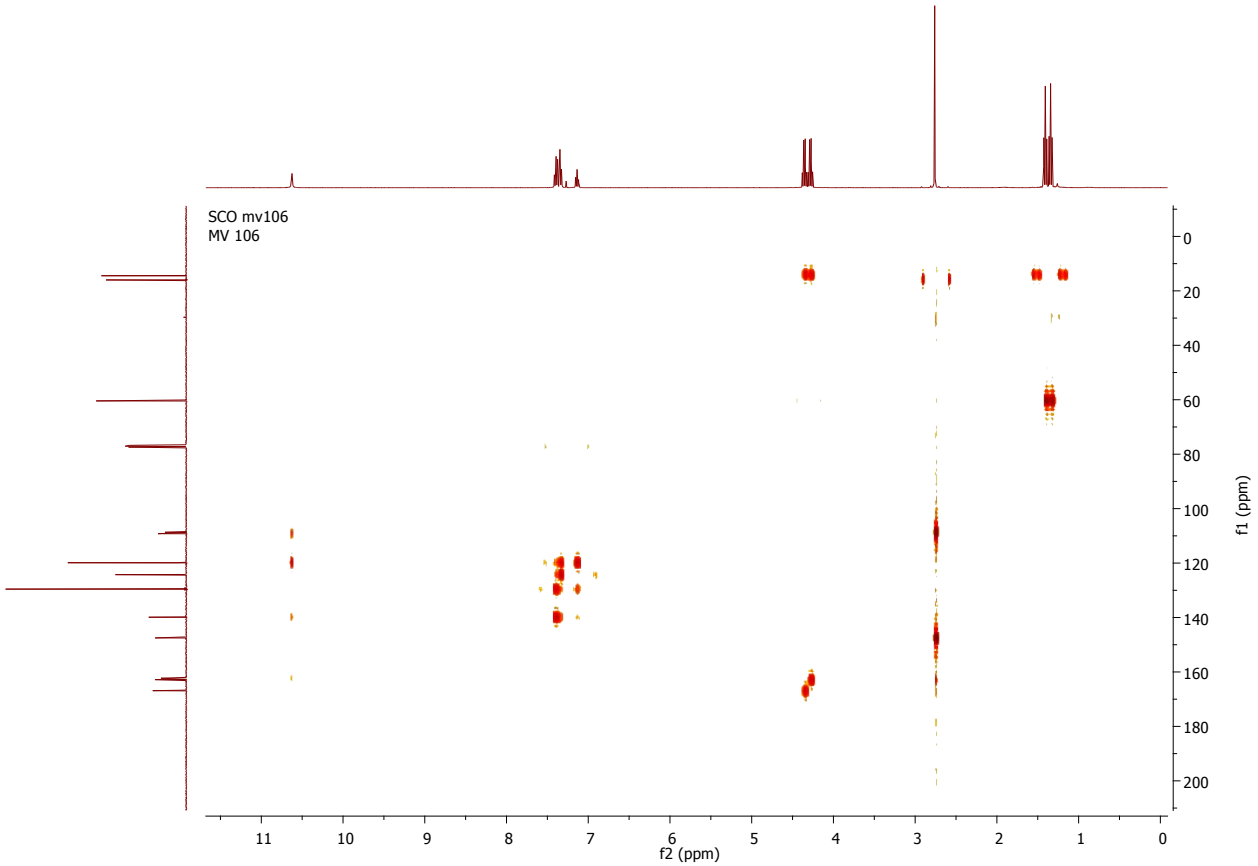


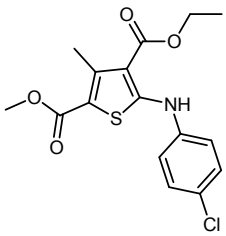
**Diethyl 3-methyl-5-(phenylamino)thiophene-2,4-dicarboxylate 8b.**



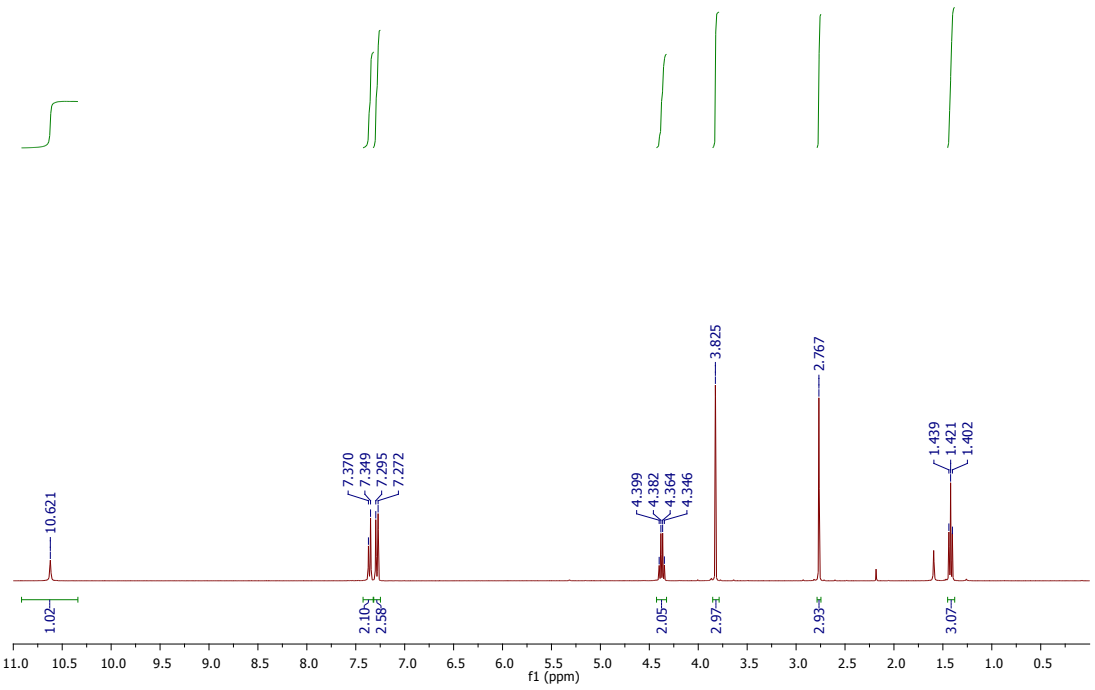



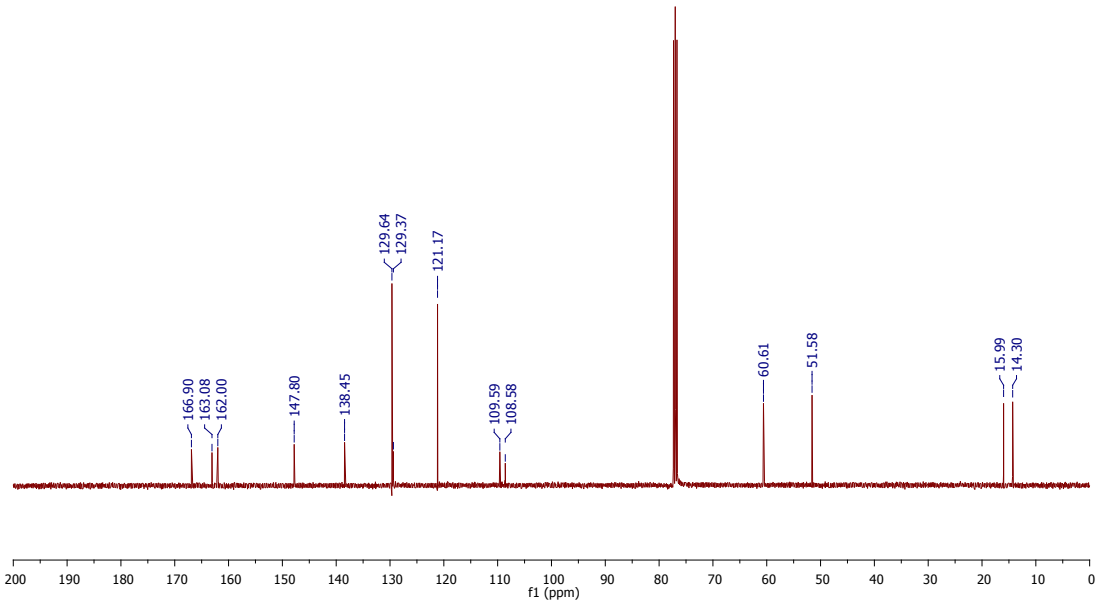

SCO mv106
MV 106
f2 (ppm)
f1 (ppm)

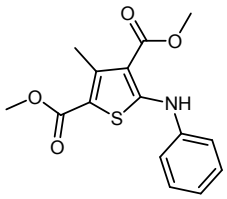

SCO mv106
MV 106
f2 (ppm)
f1 (ppm)



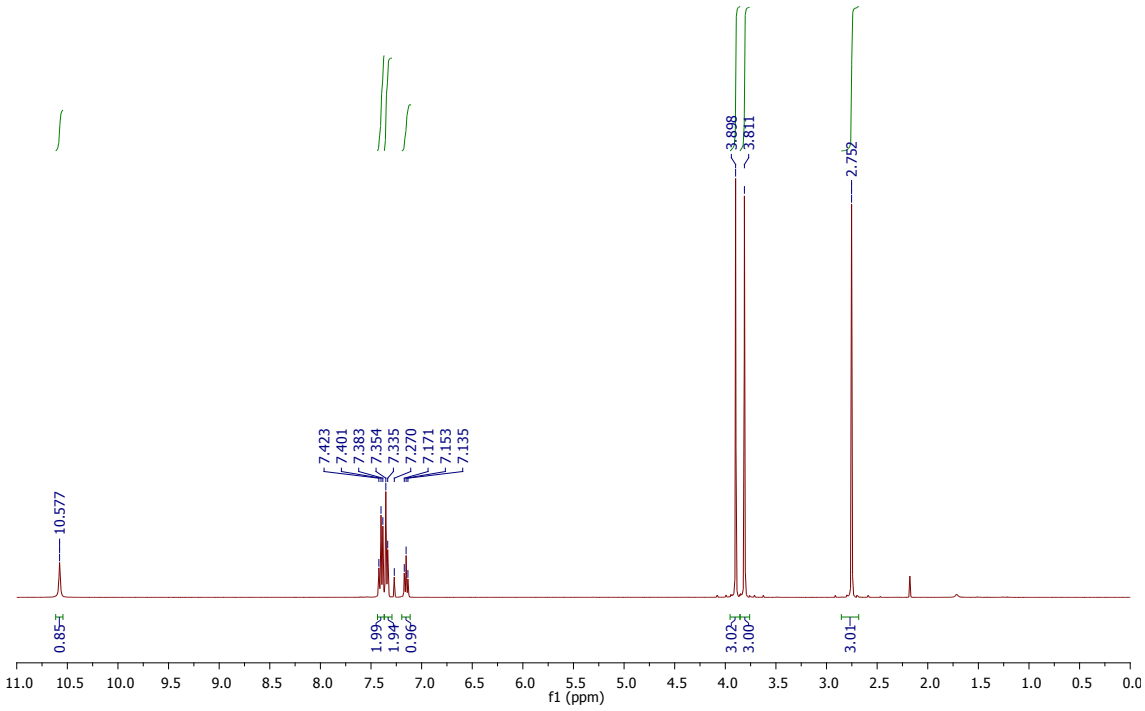

**4-Ethyl 2-methyl 5-((4-chlorophenyl)amino) 3-methylthiophene-2,4-dicarboxylate 8c.**

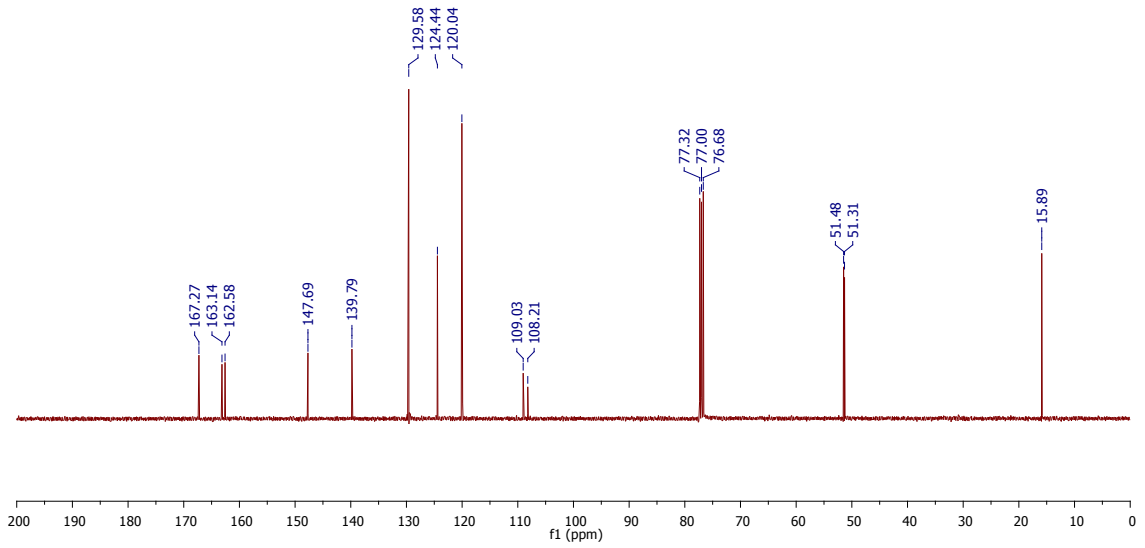


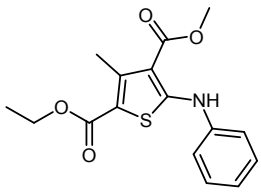





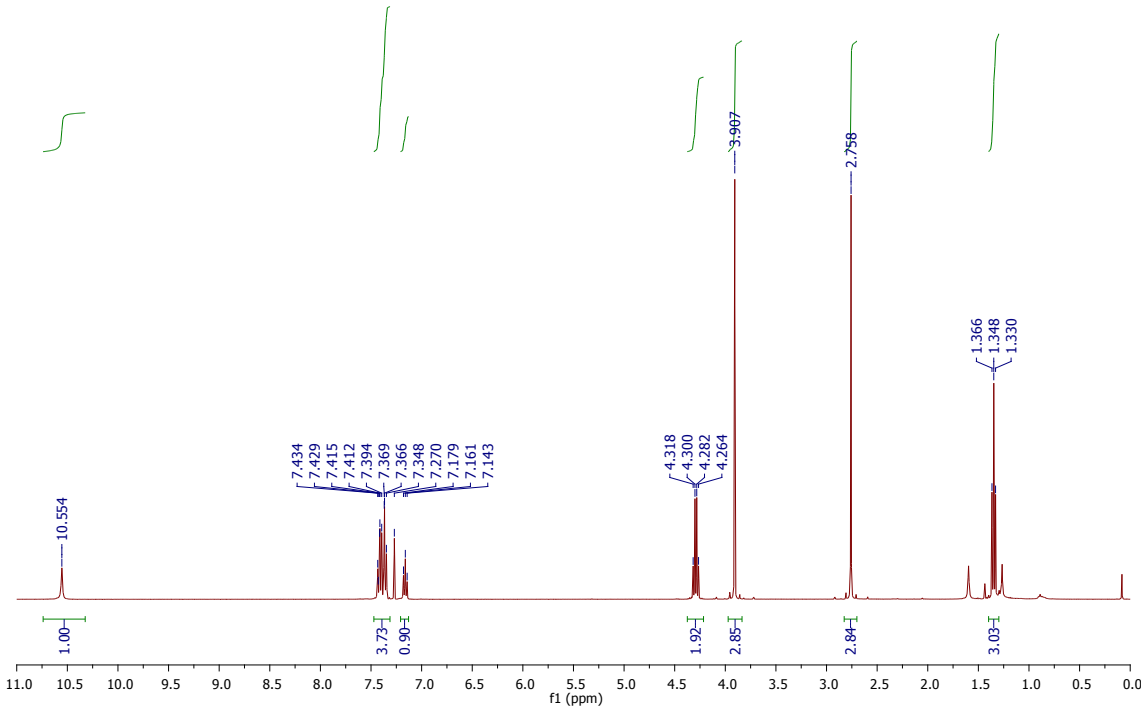
**Dimethyl 3-methyl-5-(phenylamino)thiophene-2,4-dicarboxylate 8d.**

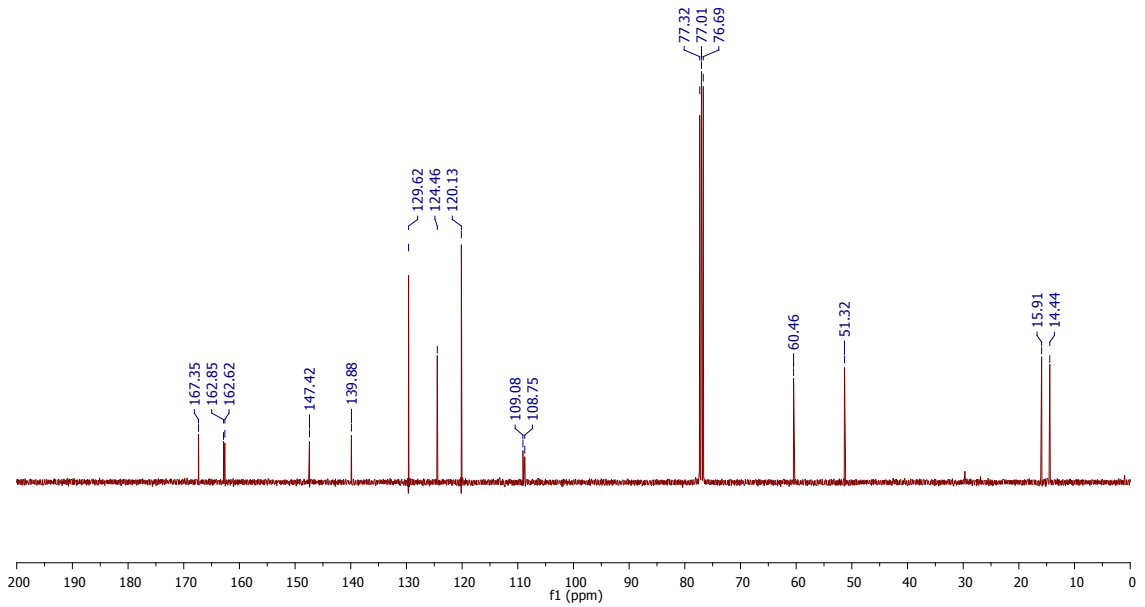


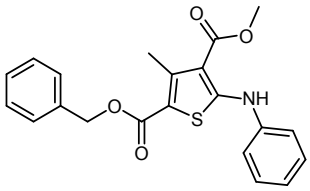





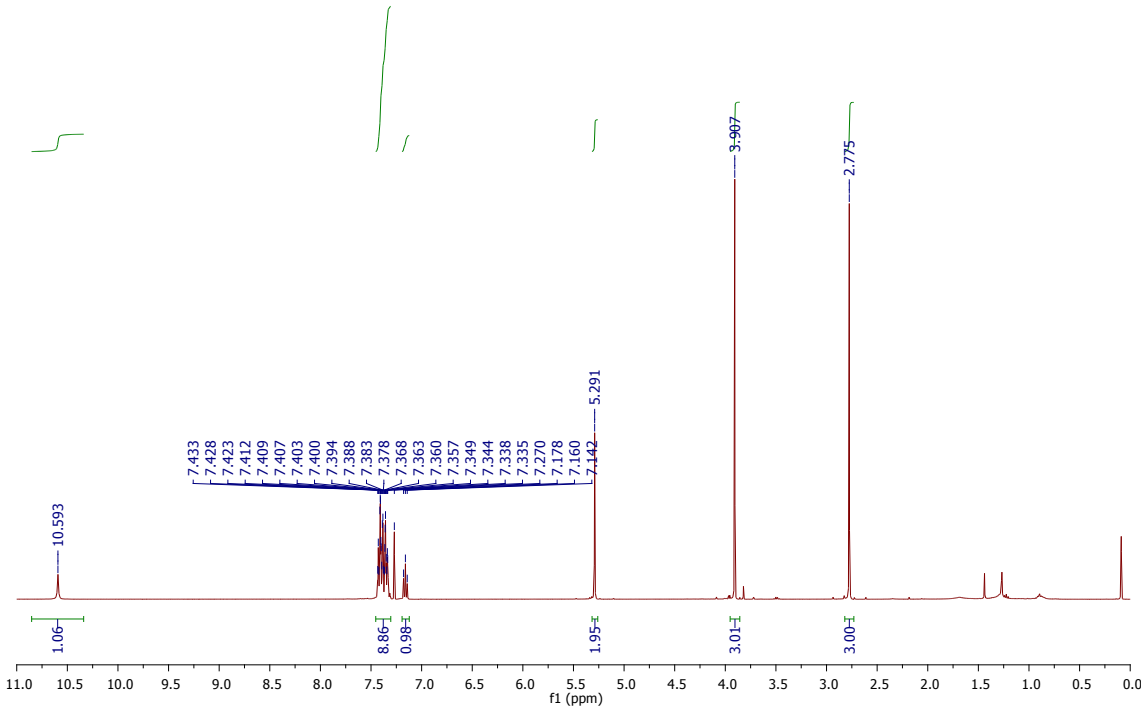

**2-Ethyl-4-methyl 3-methyl-5-(phenylamino)thiophene-2,4-dicarboxylate 8e.**

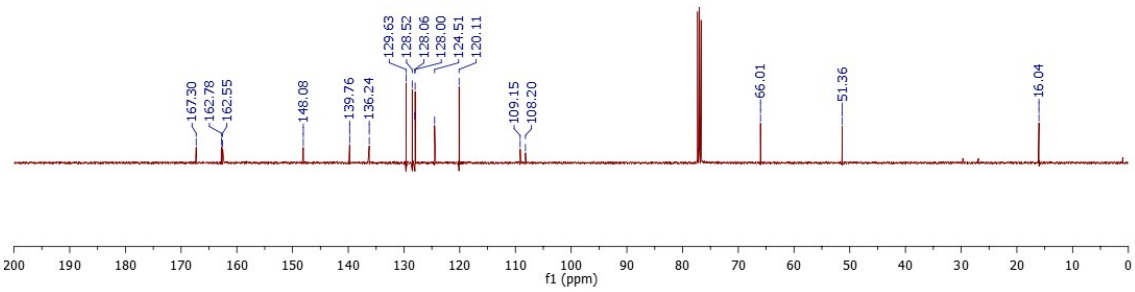


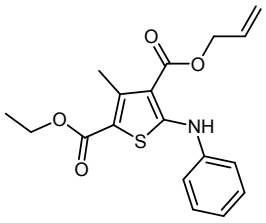





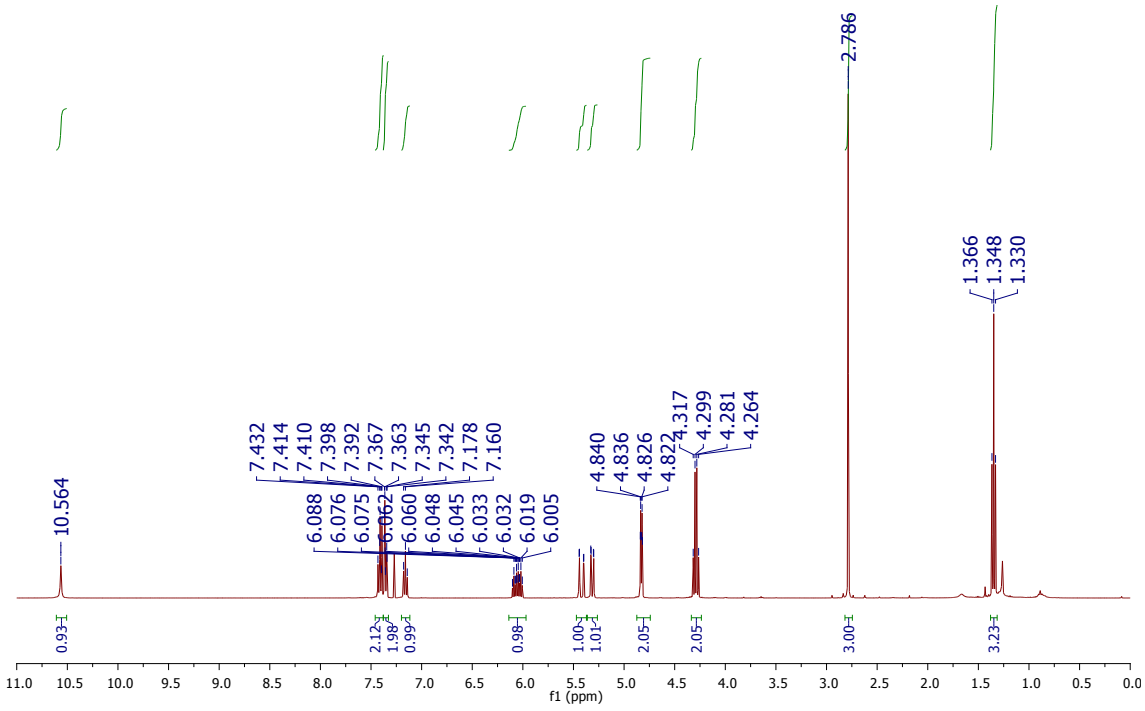
**2-Benzyl 4-methyl 3-methyl-5-(phenylamino)thiophene-2,4-dicarboxylate 8f.**

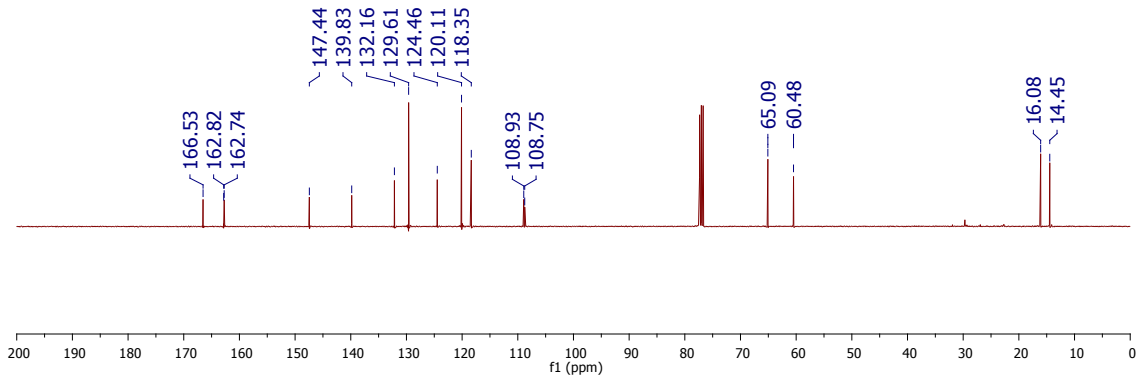


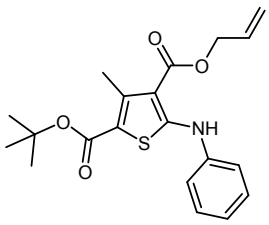





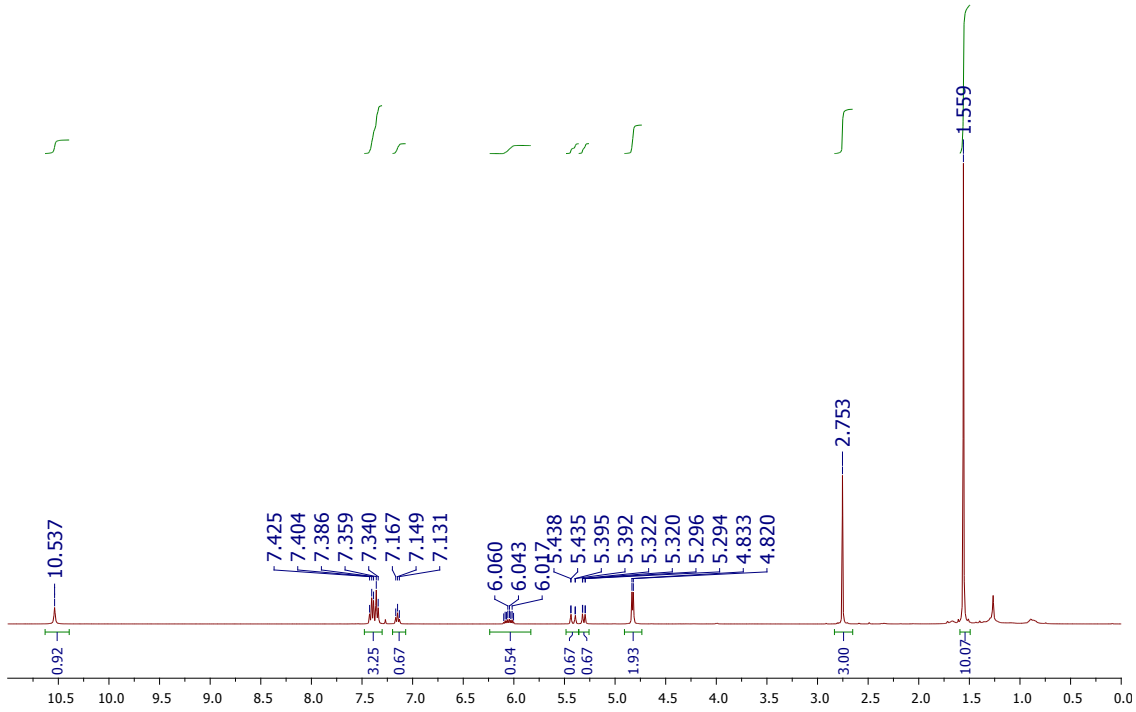

**4-Allyl 2-ethyl 3-methyl-5-(phenylamino)thiophene-2,4-dicarboxylate 8g.**

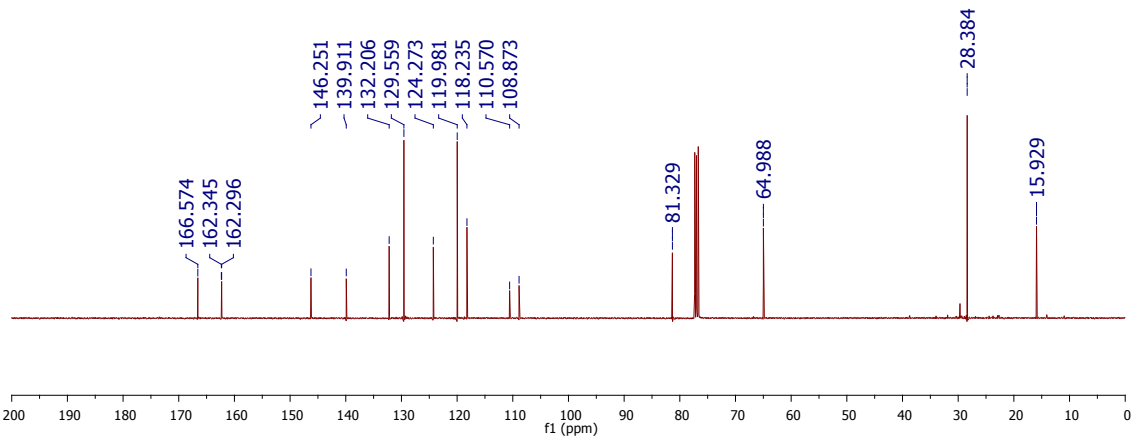


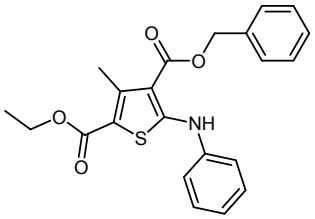





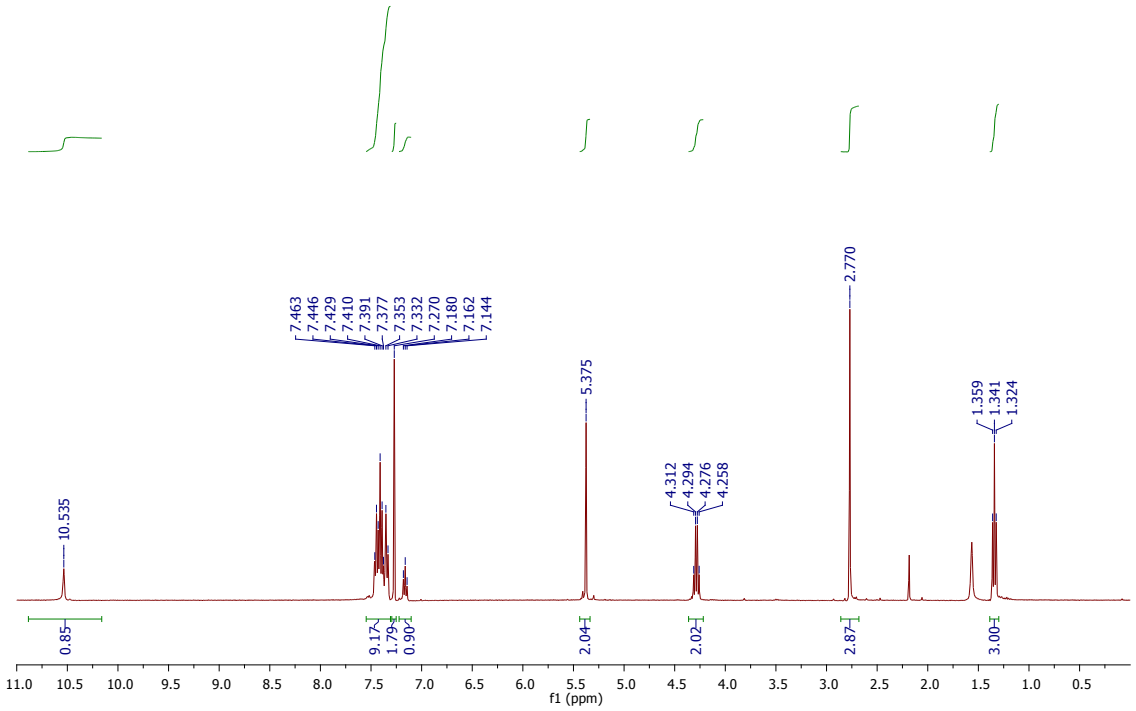

**4-Allyl 2-*tert-but*yl 3-methyl-5-(phenylamino)thiophene-2,4-dicarboxylate 8h.**

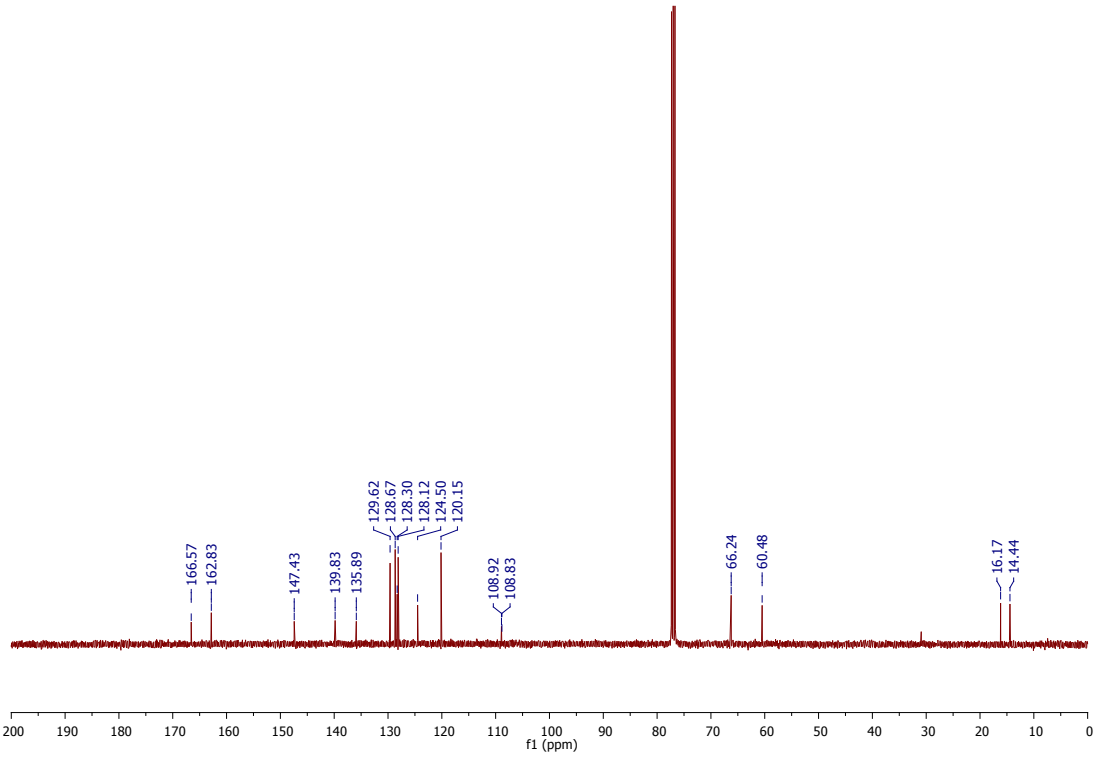


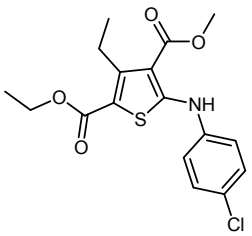





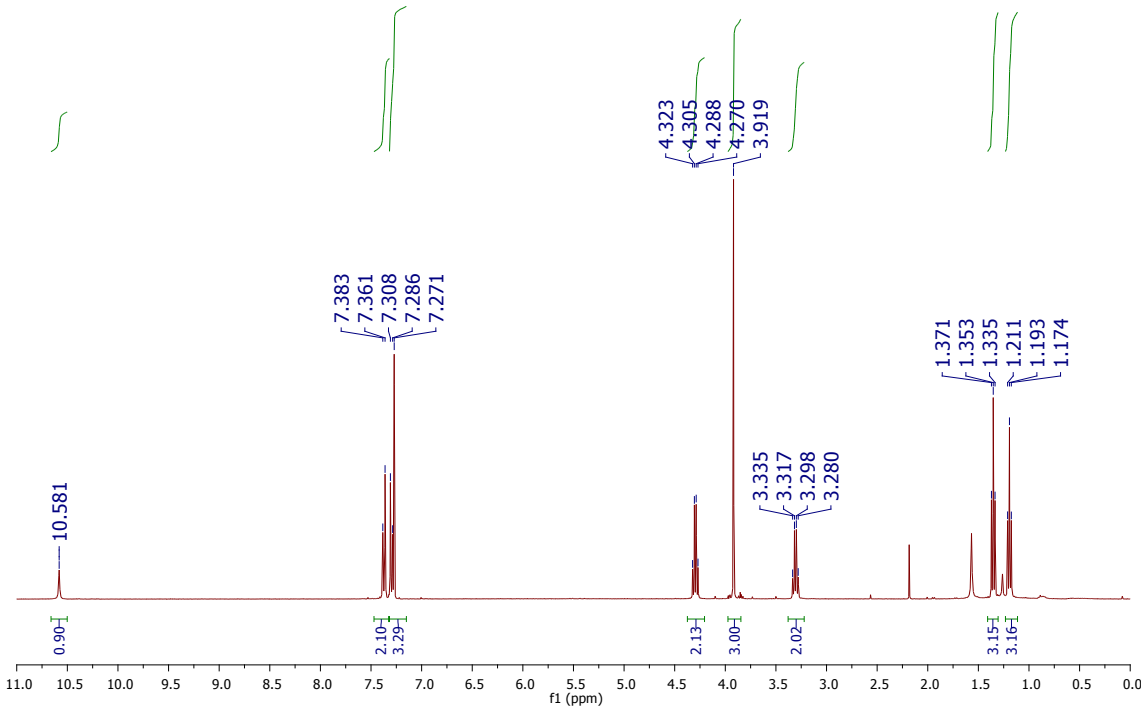

**4-Benzyl 2-ethyl 3-methyl-5-(phenylamino)thiophene-2,4-dicarboxylate 8i.**

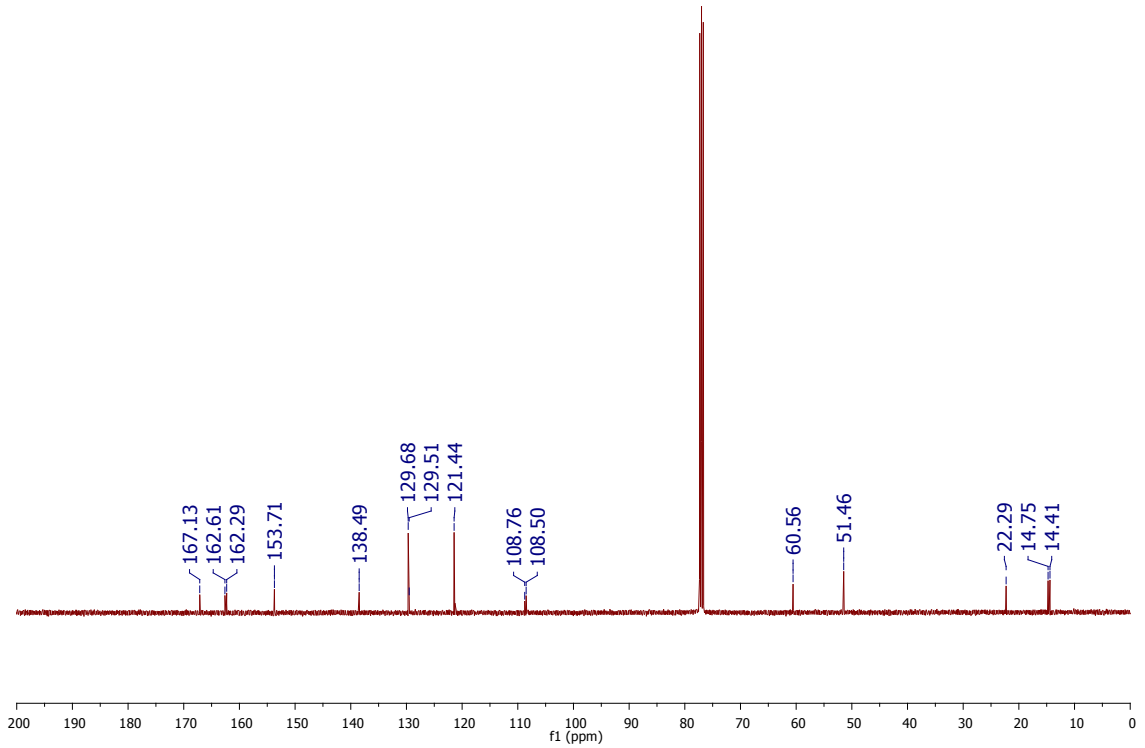


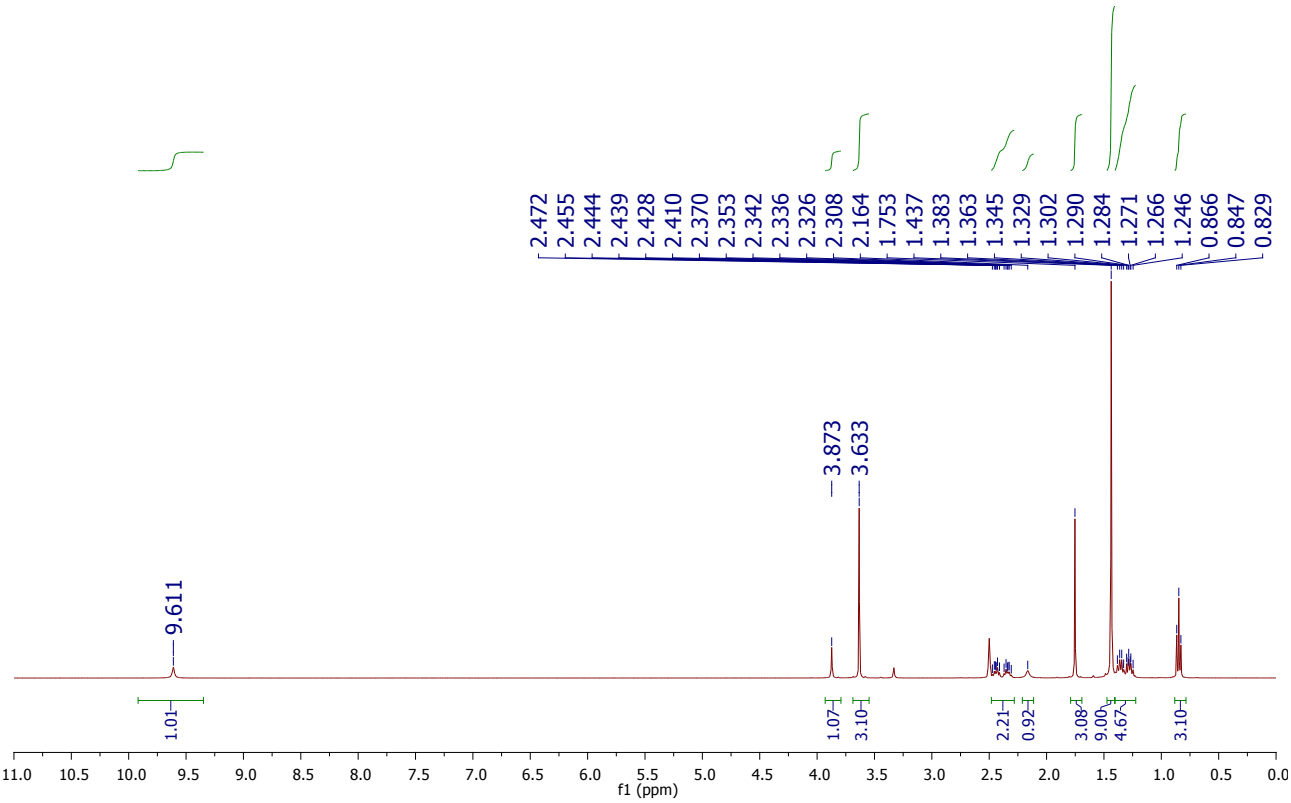


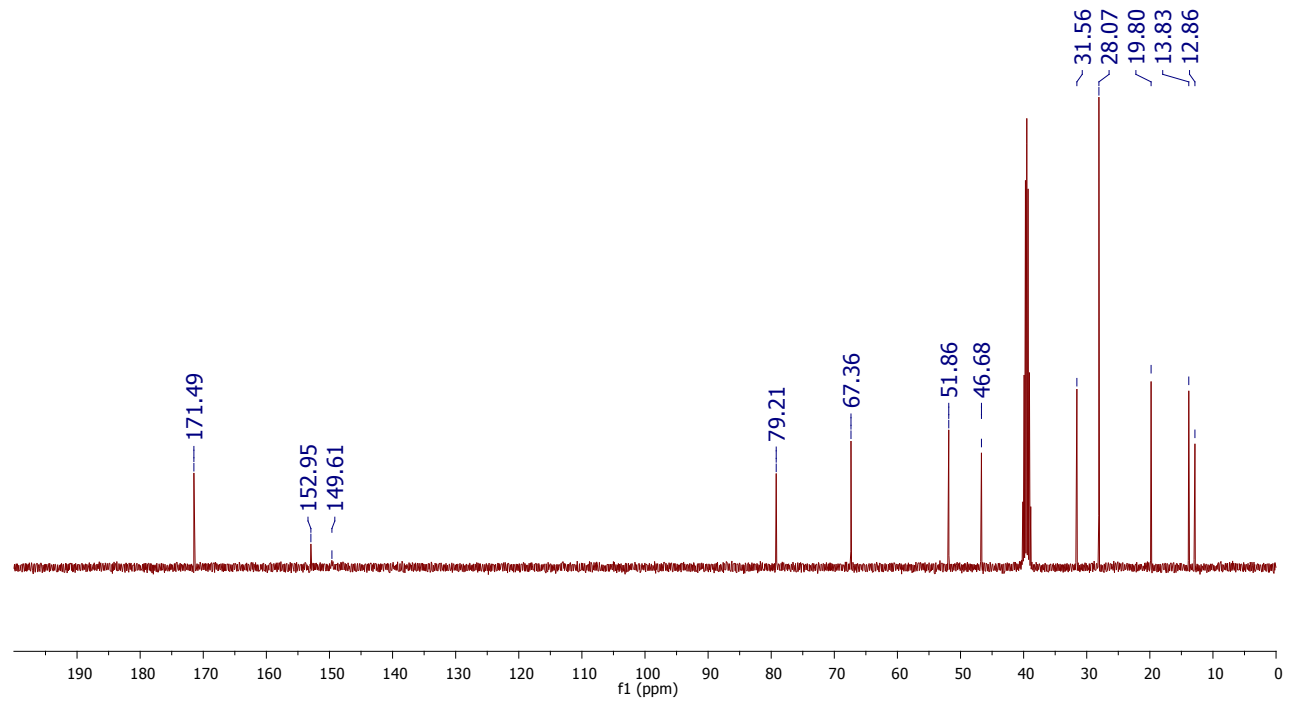

**2-Ethyl 4-methyl 5-((4-chlorophenyl)amino) 3-ethylthiophene-2,4-dicarboxylate 8j.**



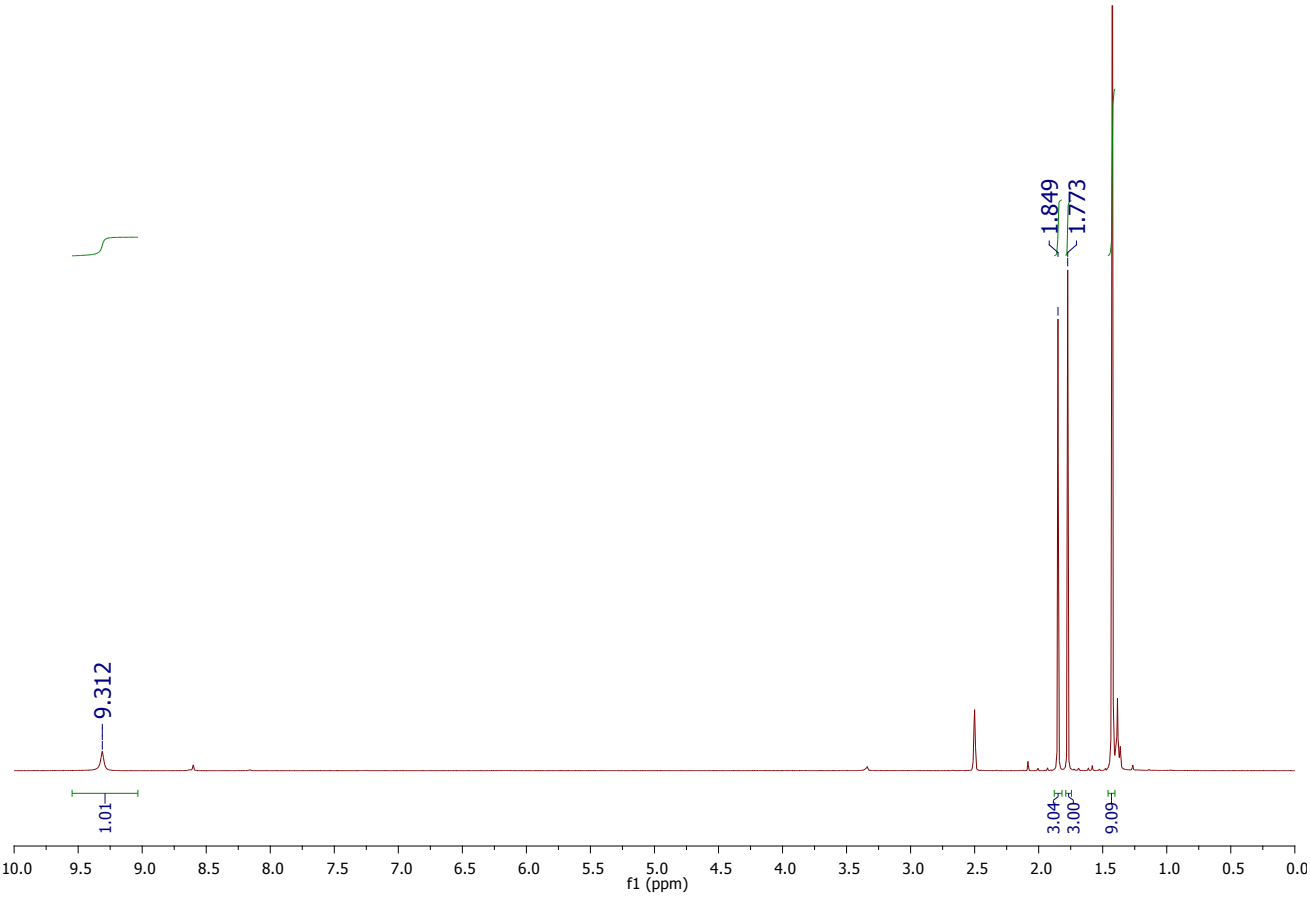



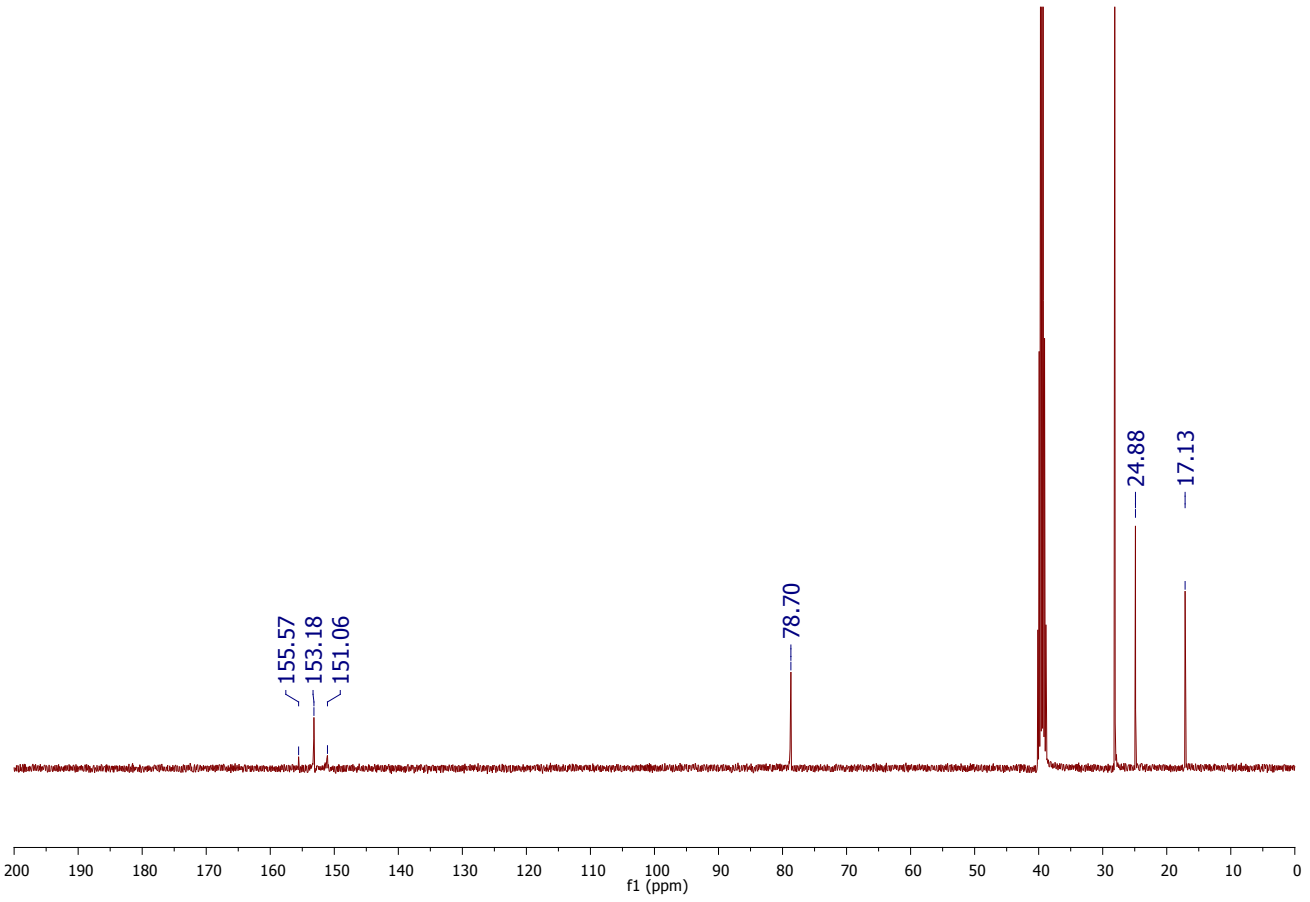
## 14 $^{1}H$ and $^{13}C$ NMR spectra of α-amino hydrazone 11



## 15 $^{1}H$ and $^{13}C$ NMR spectra of hydrazone 12



## 16. References

(1) (a) O. A. Attanasi, P. Filippone, A. Mei, S. Santeusanio, *Synthesis* **1984**, 671; (b) O. A. Attanasi, P. Filippone, A. Mei, S. Santeusanio, *Synthesis* **1984**, 873.

(2) L. Preti, O. A. Attanasi, E. Caselli, G. Favi, C. Ori, P. Davoli, F. Felluga, F. Prati, *Eur. J. Org. Chem.* **2010**, 4312.