# Supporting Information

## for

# An efficient synthesis of N-substituted 3-nitrothiophen-2-amines

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Experimental procedures, characterization data, details of the NMR structural determination of **3c** and copies of $^{1}$H NMR, $^{13}$C NMR and ESI mass spectra of all new compounds **1** and **3**

## 1. Experimental Section

**General experimental information**. Melting points were measured in open capillary tubes and are uncorrected. Infrared spectra were obtained on a Shimadzu 8400S FT-IR Spectrophotometer, in a 4000-400 $cm^{-1}$ spectral window, using neat samples on a KBr disk or KBr pellets. $^{1}H$ NMR, $^{13}C$ NMR, DEPT, H,H-COSY, C,H-COSY and HMBC spectra were recorded on a Bruker (Avance) 300 MHz NMR instrument using TMS as internal standard and $CDCl_3$ as solvent. Standard Bruker software was used throughout. Chemical shifts are given in parts per million (δ scale) and the coupling constants are given in Hertz (Hz). Mass spectra were recorded with a LCQ Fleet mass spectrometer, Thermo Fisher Instruments Limited, US. Electrospray ionization mass spectrometry (ESIMS) analysis was performed in the positive/negative ion mode on a liquid chromatography ion trap. Combustion microanalyses were performed by the CAI de Microanálisis Elemental, Universidad Complutense, using a Leco-932 CHNS microanalyzer. Silica gel-G plates (Merck) were used for TLC analysis with mixtures of petroleum ether (bp 60–80 °C) and ethyl acetate as eluent.

**General procedure for the synthesis of α-nitroketene N,S-arylaminoacetals 1a–1r** [1]. A mixture of 1,1-bis(methylthio)-2-nitroethylene (1 mmol) and the suitable aromatic amine in ethanol was magnetically stirred while heated under reflux for 24 h. After completion of the reaction (TLC), the mixture was cooled to room temperature, and the separated solid was filtered and washed with ethanol to afford the pure *α*-nitroketene *N,S*-arylaminoacetals.

**General procedure for the synthesis of α-nitroketene N,S-alkylaminoacetals 1s–1z** [2]. A mixture of 1,1-bis(methylthio)-2-nitroethylene (1 mmol) and the

suitable aliphatic amine in ethanol was magnetically stirred while heated under reflux for 24 h. After completion of the reaction (TLC), the solvent was removed under reduced pressure and the resulting crude products were purified by flash chromatography eluting with $CHCl_3$/MeOH mixtures to afford the pure α-nitroketene N,S-alkylaminoacetals.

Compounds **1d**, **1g**, **1m**, **1q**, **1w** and **1z** are new and their characterization data follow.

**(*E*)-4-Iodo-*N*-(1-(methylthio)-2-nitrovinyl)aniline (1d):** Isolated as a pale green solid. Yield: 85%; mp = 174–175 °C; IR (KBr) $\nu_{max}$: 3145, 3003, 2954, 2926, 2853,1544, 1460, 1344, 1265, 1168 cm $^{-1}$; H NMR (300 MHz, $CDCl_3$) $\delta_H$: 2.40 (s, 3H, $SCH_3$),6.69 (s, 1H, CH), 7.06 (d, *J* = 8.4 Hz, 2H, Ar-H), 7.75 (d, *J* = 8.7 Hz, 2H, Ar-H), 11.72 (br s, 1H, NH); $^{13}$C NMR (75 MHz, $CDCl_3$) $\delta_c$: 14.7, 93.5, 108.2, 127.6, 135.9, 138.5, 162.8; ESI-MS: m/z. Calcd: 335.94. Found: 334.90 (M-1).

**(*E*)-4-Ethyl-*N*-(1-(methylthio)-2-nitrovinyl)aniline (1g):** Isolated as a yellow solid. Yield: 88%; mp = 111–112 °C; IR (KBr) $\nu_{max}$: 3157, 2997, 2962, 2929, 1560, 1425, 1346, 1265, 1166 cm $^{-1}$; H NMR (300 MHz, $CDCl_3$) $\delta_H$: 2.38 (s, 3H, $SCH_3$), 6.70 (s, 1H, CH), 7.20 (d, *J* = 8.4 Hz, 2H, Ar-H), 7.25 (d, *J* = 6.9 Hz, 2H, Ar-H), 11.78 (br s, 1H, NH); $^{13}$C NMR (75 MHz, $CDCl_3$) $\delta_c$: 14.6, 15.2, 28.3, 107.4, 125.8, 128.7, 133.6, 144.5, 163.9; ESI-MS: m/z. Calcd: 238.08. Found: 239.01 (M+1).

**(*E*)-3-Bromo-*N*-(1-(methylthio)-2-nitrovinyl)aniline (1m):** Isolated as a pale yellow solid. Yield: 83%; mp = 118–119 °C; IR (KBr) $\nu_{max}$: 3152, 3001, 2929, 1547, 1460, 1352, 1247, 1174 cm $^{-1}$; H NMR (300 MHz, $CDCl_3$) $\delta_H$: 2.40 (s, 3H, $SCH_3$), 6.69 (s, 1H, CH), 7.24-7.33 (m, 2H, Ar-H), 7.48-7.51 (m, 2H, Ar-H) 11.74 (br s, 1H, NH); $^{13}$C NMR (75

MHz, $CDCl_3$) $\delta_c$: 14.7, 108.3, 122.7, 124.6, 128.9, 130.6, 131.1, 137.4, 162.9; ESI-MS: m/z. Calcd: 287.96. Found: 286.94 (M-1), 288.91(M+1).

**(*E*)-2,4-Dimethyl-*N*-(1-(methylthio)-2-nitrovinyl)aniline (1q):** Isolated as a yellow solid. Yield: 87%; mp = 132–133 °C; IR (KBr) $\nu_{max}$: 3146, 2995, 2926, 1544,1460, 1325, 1267, 1178 $cm^{-1}$; H NMR (300 MHz, $CDCl_3$) $\delta_H$: 2.26 (s, 3H, $SCH_3$), 2.35 (s, 6H, Ar-$(CH_3)_2$ ) 6.70 (s, 1H, CH), 7.05 (d, J = 7.8 Hz, 1H, Ar-H), 7.11-7.13 (m, 2H, Ar-H) 11.53 (br s, 1H, NH); $^{13}C$ NMR (75 MHz, $CDCl_3$) $\delta_c$: 14.4, 17.7, 21.1, 107.1, 127.2, 127.4, 131.8, 132.3, 134.8, 139.0, 165.0; ESI-MS: m/z. Calcd: 238.08. Found: 239.02 (M+1).

**(*E*)-*N*-(1-(Methylthio)-2-nitrovinyl)cyclopropanamine (1w):** Isolated as a pale yellow solid. Yield: 93%; mp = 85–86 °C; IR (Neat) $\nu_{max}$: 3199, 3169, 3088, 2991, 1564, 1467, 1340, 1230, 1165, 1047 $cm^{-1}$; H NMR (300 MHz, $CDCl_3$) $\delta_H$: 0.81-0.98 (m, 4H, $CH_2$-$CH_2$), 2.42 (s, 3H, $SCH_3$), 2.70-2.73 (m, 1H, CH) 6.55 (s, 1H, CH), 10.34 (br s, 1H, NH); $^{13}C$ NMR (75 MHz, $CDCl_3$) $\delta_c$: 8.3, 14.2, 25.7, 106.1, 167.3; ESI-MS: m/z. Calcd: 174.05. Found: 175.01 (M+1).

**(*R,E*)-1-(Methylthio)-2-nitro-*N*-(1-phenylethyl)ethen-1-amine (1z):** Isolated as a yellow solid. Yield: 90%; mp = 41–42 °C; IR (KBr) $\nu_{max}$: 3146, 3022, 2978, 2928, 1557,1464, 1415, 1325, 1215, 1118, 1080 $cm^{-1}$; H NMR (300 MHz, $CDCl_3$) $\delta_H$: 1.65 (d, *J* = 6.6 Hz, 3H, $CH_3$), 2.36 (s, 3H, $SCH_3$), 4.89-4.96 (m, 1H, CH), 6.56 (s, 1H, CH), 7.26-7.40 (m, 5H, Ar-H) 10.90 (br s, 1H, NH); $^{13}C$ NMR (75 MHz, $CDCl_3$) $\delta_c$: 14.6, 24.0, 54.7, 106.6, 125.8, 128.0, 129.0, 141.6, 164.0; ESI-MS: m/z. Calcd: 238.08. Found: 237.02 (M-1).

**General procedure for the synthesis of 3-nitro-N-arylthiophen-2-amines 3a–r**. A mixture of the suitable α-nitroketene N,S-arylaminoacetal (1 mmol), 1,4-dithiane-2,5-diol (0.5 mmol) and $K_2CO_3$ (25 mol %) in ethanol (6 mL) was heated under reflux for 20–25 min. After completion of the reaction (TLC), the mixture was cooled to room temperature, and the precipitated solid was filtered and washed with ethanol to afford the pure 3-nitro-N-arylthiophen-2-amines **3a–r**.

**General procedure for the synthesis of 3-nitro-*N*-alkylthiophen-2-amines 3s–3z**. A mixture of the suitable α-nitroketene N,S-alkylaminoacetal (1 mmol), 1,4-dithiane-2,5-diol (0.5 mmol) and $K_2CO_3$ (25 mol %) in ethanol (6 mL) was heated under reflux for 3–3.4 h. After completion of the reaction (TLC), the mixture was poured into water and extracted with ethyl acetate. After removal of the solvent, the residue was purified by filtration through a pad of silica gel, eluting with a petroleum ether/ethyl acetate mixture (4:1 v/v), which afforded 3-nitro-N-alkylthiophen-2-amines **3s**–**3z**.

***N*-(4-Fluorophenyl)-3-nitrothiophen-2-amine (3a)**. Isolated as a pale yellow solid. Yield: 90%; mp = 129–130 °C; IR (KBr) $\nu_{max}$: 3261,1560,1508, 1490, 1342, 1226, 1192 $cm^{-1}$. $^1H$ NMR (300 MHz, $CDCl_3$) $\delta_H$: 6.29 (d, $J$ = 6.3 Hz, 1H, H-5), 7.12–7.18 (m, 2H, H-3',5'), 7.34–7.39 (m, 3H, H-4, H-2',6'), 10.16 (br s, 1H, NH); $^{13}C$ NMR (75 MHz, $CDCl_3$) $\delta_c$: 107.0 (C-4), 116.8 (d, $^2J_{C,F}$ = 22.9 Hz, C-3',5'), 121.9 (C-5), 123.4 (d, $^3J_{C,F}$ = 8.3 Hz, C-2',6'), 127.9 (C-1'), 135.2 (C-1), 156.8 (C-3), 160.5 (d, $^1J_{C,F}$ = 245.5 Hz, C4'); ESI-MS: m/z. Calcd: 238.02. Found: 237.08 (M-1). Analysis: Calcd for $C_{10}H_7FN_2O_2S$: C, 50.41; H, 2.96; N, 11.76. Found: C, 49.91; H, H, 2.98; N, 11.60.

***N*-(4-Chlorophenyl)-3-nitrothiophen-2-amine (3b)**. Isolated as a pale yellow solid. Yield: 92%; mp = 161–162 °C. IR (KBr) $\nu_{max}$: 3259, 3116, 3099, 1560, 1508, 1491,

1342, 1261, 1203,1091 $cm^{-1}$. $^{1}H$ NMR (300 MHz, $CDCl_3$) $\delta_H$: 6.33 (d, *J* = 6.0 Hz, 1H, H-5), 7.31–7.43 (m, 5H, H-4, H-2',3',5',6'), 10.29 (br s, 1H, NH); $^{13}C$ NMR (75 MHz, $CDCl_3$) $\delta_c$: 107.4 (C-4), 121.8 , 121.9 (C-2',6'), 128.4 (C-4'), 130.0 (C-3',5'), 131.1 (C-5), 137.6 (C-1'), 155.2 (C-3); ESI-MS: m/z. Calcd: 253.99. Found: 253.00 (M-1), 255.12 (M+2). Analysis: Calcd for $C_{10}H_7ClN_2O_2S$: C, 47.16; H, 2.77; N, 11.00. Found: C, 46.87; H, 2.88; N, 10.80.

***N*-(4-Bromophenyl)-3-nitrothiophen-2-amine (3c)**. Isolated as a pale yellow solid. Yield: 91%; mp = 173–174 °C. IR (KBr) $\nu_{max}$: 3253, 3116, 3099, 1560,1508, 1483, 1340, 1199, 1085 $cm^{-1}$. $^{1}H$ NMR (300 MHz, $CDCl_3$) $\delta_H$: 6.34 (d, *J* = 6.3 Hz, 1H, H-5), 7.26 (d, *J* = 8.7 Hz, 2H, H-3',5'), 7.37 (d, *J* = 6.0 Hz, 1H, H-4), 7.56 (d, *J* = 8.7 Hz, 2H, H-2',6'), 10.30 (br s, 1H, NH); $^{13}C$ NMR (75 MHz, $CDCl_3$) $\delta_c$: 107.4 (C-4), 118.6 (C-2',6'), 121.9 (C-5), 122.0 (C-3',5'), 128.5 (C-4'), 132.9 (C-1'), 138.1 (C-2), 154.9 (C-3); ESI-MS: m/z. Calcd: 297.94. Found: 297.06 (M-1), 299.06 (M+2). Analysis: Calcd for $C_{10}H_7BrN_2O_2S$: C, 40.15; H, 2.36; N, 9.36. Found: C, 39.93; H, 2.88; N, 10.80.

***N*-(4-Iodophenyl)-3-nitrothiophen-2-amine (3d)**. Isolated as a yellow solid. Yield: 93%; mp = 185–186 °C. IR (KBr) $\nu_{max}$: 3209, 3120, 3105, 1560, 1350, 1240, 1195 $cm^{-1}$. $^{1}H$ NMR (300 MHz, $CDCl_3$) $\delta_H$: 6.35 (d, *J* = 6.3 Hz, 1H, H-5), 7.15 (d, *J* = 8.7 Hz, 2H, H-2',6'), 7.37 (d, *J* = 6.0 Hz, 1H, H-4), 7.75 (d, *J* = 8.7 Hz, 2H, H-3',5'), 10.32 (br s, 1H, NH); $^{13}C$ NMR (75 MHz, DMSO-$d^6$) $\delta_c$: 90.7 (C-4'), 109.5 (C-4), 121.5 (C-5), 124.7 (C-3',5'), 127.9 (C-1'), 138.6 (C-2',6'), 140.1 (C-2), 156.5 (C-3); ESI-MS: m/z. Calcd: 345.93. Found: 344.91 (M-1). Analysis: Calcd for $C_{10}H_7IN_2O_2S$: C, 34.70; H, 2.04; N, 8.09. Found: C, 34.73; H, 2.17; N, 8.16.

**3-Nitro-*N*-phenylthiophen-2-amine (3e)**. Isolated as a yellow solid. Yield: 94%; mp = 67–68 °C. IR (KBr) $\nu_{max}$: 3190, 3118, 3099, 1571, 1483, 1348, 1230, 1184 $cm^{-1}$. $^{1}H$ NMR (300 MHz, $CDCl_3$) $\delta_H$: 6.31 (d, *J* = 6.3 Hz, 1H, H-5), 7.22–7.26 (m, 1H, H-4'), 7.35–7.39 (m, 3H, H-4, H-3',5'), 7.42–4.47 (m, 2H, H-2',6'), 10.38 (br s, 1H, NH); $^{13}C$ NMR (75 MHz, $CDCl_3$) $\delta_c$: 107.1 (C-4), 120.2 (C-2',6'), 121.5 (C-4'), 125.6 (C-5), 128.0 (C-1'), 129.7 (C-3',5'), 138.8 (C-1), 155.5 (C-3); ESI-MS: m/z. Calcd: 220.03. Found: 255.26 ($M+Cl^{35}$). Analysis: Calcd for $C_{10}H_8N_2O_2S$: C, 54.53; H, 3.66; N, 12.72. Found: 54.16; H, 3.67; N, 12.61.

**3-Nitro-*N*-(*p*-tolyl)thiophen-2-amine (3f)**. Isolated as a yellow solid. Yield: 94%; mp = 96–97 °C. IR (KBr) $\nu_{max}$: 3244, 3095, 2920, 2853, 1560,1508, 1490, 1390, 1369, 1236,1197 $cm^{-1}$. $^{1}H$ NMR (300 MHz, $CDCl_3$) $\delta_H$: 2.38 (s, 3H, Me), 6.27 (d, *J* = 6.0 Hz, 1H, H-5), 7.19–7.25 (m, 4H, H-2',3',5',6'), 7.34 (d, *J* = 6.3 Hz, 1H, H-4), 10.29 (br s, 1H, NH); $^{13}C$ NMR (75 MHz, $CDCl_3$) $\delta_c$: 20.8 (Me), 107.0 (C-4), 120.7 (C-2',6'), 121.5 (C-4'), 127.7 (C-2), 130.2 (C-3',5'), 135.8 (C-1'), 136.4 (C-5), 156.4 (C-3); ESI-MS: m/z. Calcd: 234.05. Found: 235.10 (M+1). Analysis: Calcd for $C_{11}H_{10}N_2O_2S$: C, 56.39; H, 4.30; N, 11.96. Found: C, 56.01; H, 4.33; N, 11.71.

***N*-(4-Ethylphenyl)-3-nitrothiophen-2-amine (3g)**. Isolated as a pale yellow solid. Yield: 95%; mp = 74–75 °C. IR (KBr) $\nu_{max}$: 3231, 3105, 2962, 2926, 2868, 1544, 1475, 1369,1242,1180 $cm^{-1}$. $^{1}H$ NMR (300 MHz, $CDCl_3$) $\delta_H$: 1.26 (t, *J* = 7.5 Hz, 3H, $CH_2CH_3$), 2.68 (q, *J* = 7.5 Hz, 2H, $CH_2CH_3$), 6.28 (d, *J* = 6.0 Hz, 1H, H-5), 7.26–7.32 (m, 4H, H-2',3',5',6'), 7.35 (d, *J* = 6.3 Hz, 1H, H-4), 10.32 (br s, 1H, NH); $^{13}C$ NMR (75 MHz, $CDCl_3$) $\delta_c$: 15.3 ($\underline{CH_2}\underline{C}H_3$), 28.3 ($\underline{C}\underline{H_2}CH_3$), 107.0 (C-4), 121.0 (C-2',6'), 121.8 (C-5), 127.9 (C-1'), 129.2 (C-3',5'), 136.8 (C-4'), 142.4 (C-2), 156.5 (C-3); ESI-MS: m/z. Calcd:

248.06. Found: 247.12 (M-1). Analysis: Calcd for $C_{12}H_{12}N_2O_2S$: C, 58.05; H, 4.87; N, 11.28. Found: C, 57.84; H, 4.95; N, 11.08.

***N*-(4-Isopropylphenyl)-3-nitrothiophen-2-amine (3h)**. Isolated as a pale yellow solid. Yield: 93%. IR (KBr) $\nu_{max}$: 3230, 2956, 1544,1510, 1465, 1369, 1177 $cm^{-1}$. mp = 90–91 °C; $^1H$ NMR (300 MHz, $CDCl_3$) $\delta_H$: 1.27 (d, *J* = 6.9 Hz, 6H, $CH(CH_3)_2$), 2.94 (sept, *J* = 6.9 Hz, 1H, $CH(CH_3)_2$), 6.28 (dd, *J* = 0.7, 6.1 Hz, 1H, H-5), 7.26–7.34 (m, 4H, H-2',3',5',6'), 7.35 (d, *J* = 6.3 Hz, 1H, H-4), 10.33 (br s, 1H, NH);$^{13}C$ NMR (75 MHz, $CDCl_3$) $\delta_c$: 23.8 ($CH(CH_3)_2$), 33.6 ($CH(CH_3)_2$), 107.0 (C-4), 120.7 (C-2',6'), 121.6 (C-5), 127.7 (C-1' and C-3',5'), 136.6 (C-4'), 146.8 (C-2), 156.3 (C-3); ESI-MS: m/z. Calcd: 262.08. Found: 261.15 (M-1). Analysis: Calcd for $C_{13}H_{14}N_2O_2S$: C, 59.52; H, 5.38; N, 10.68. Found: C, 59.40; H, 5.53; N, 10.62.

***N*-(4-Methoxyphenyl)-3-nitrothiophen-2-amine (3i)**. Isolated as an orange solid. Yield: 96%; mp = 98–99 °C. IR (KBr) $\nu_{max}$: 3228, 3097, 2839, 1560,1508, 1500, 1388, 1224, 1195 $cm^{-1}$. $^1H$ NMR (300 MHz, $CDCl_3$) $\delta_H$: 3.85 (s, 3H, OMe), 6.24 (d, *J* = 6.0 Hz, 1H, H-5), 6.95–6.98 (m, 2H, H-3',5'), 7.26–7.34 (m, 3H, H-4 and H-2',6'), 10.11 (br s, 1H, NH); $^{13}C$ NMR (75 MHz, $CDCl_3$) $\delta_c$: 55.5 (OMe), 106.9 (C-4), 115.0 (C-3',5'), 121.8 (C-5), 123.5 (C-2',6'), 127.4 (C-1'), 132.1 (C-2), 158.0 (C-4'), 158.1 (C-3); ESI-MS: m/z. Calcd: 250.04. Found: 249.12 (M-1). Analysis: Calcd for $C_{11}H_{10}N_2O_3S$: C, 52.79; H, 4.03; N, 11.19. Found: C, ; H, 3.95; N, 10.81.

**3-Nitro-*N*-(*o*-tolyl)thiophen-2-amine (3j)**. Isolated as a pale yellow solid. Yield: 93%; mp = 169–170 °C. IR (KBr) $\nu_{max}$: 3236, 3101, 3118,1544,1465, 1375, 1340, 1227, 1180 $cm^{-1}$. $^1H$ NMR (300 MHz, $CDCl_3$) $\delta_H$: 2.38 (s, 3H, Me), 6.28 (d, *J* = 6.3 Hz, 1H, H-5), 7.18–7.37 (m, 4H, H-3',4',5',6'), 7.51 (d, *J* = 8.1 Hz, 1H, H-4), 10.22 (br s, 1H, NH); $^{13}C$

NMR (75 MHz, $CDCl_3$) $\delta_c$: 17.7 (Me), 107.2 (C-4), 120.9 (C-4'), 121.7 (C-6'), 126.5 (C-5'), 127.3 (C-3'), 127.8 (C-2'), 130.9 (C-1'), 131.4 (C-5), 137.7 (C-2), 157.2 (C-3); ESI-MS: m/z. Calcd: 234.05. Found: 234.99 (M+1). Analysis: Calcd for $C_{11}H_{10}N_2O_2S$: C, 56.40; H, 4.30; N, 11.96. Found: C, 55.95; H, 4.41; N, 11.75.

***N*-(2-Methoxyphenyl)-3-nitrothiophen-2-amine (3k)**. Isolated as a yellow solid. Yield: 91%; mp = 123–124 °C. IR (KBr) $\nu_{max}$: 3228, 3103,1560,1490, 1363, 1388, 1221, 1170 $cm^{-1}$. $^1H$ NMR (300 MHz, $CDCl_3$) $\delta_H$: 3.96 (s, 3H, OMe), 6.35 (d, *J* = 6.0 Hz, 1H, H-5), 6.99 (dd, *J* = 1.2, 8.1 Hz, 1H, H-3'), 7.05 (td, *J* = 1.2, 7.8 Hz, 1H, H-5'), 7.16 (td, *J* = 1.2, 7.8 Hz, 1H, H-4'), 7.40 (d, *J* = 6.0 Hz, 1H, H-4), 7.55 (dd, *J* = 1.3, 7.9 Hz, 1H, H-6'), 10.93 (br s, 1H, NH); $^{13}C$ NMR (75 MHz, $CDCl_3$) $\delta_c$: 55.9 (OMe), 107.2 (C-4), 111.0 (C-3'), 117.1 (C-6'), 120.6 (C-5'), 120.8 (C-4'), 121.7, 125.1 (C-5 and C-1'), 128.5 (C-2), 149.4 (C-2'), 153.8 (C-3); ESI-MS: m/z. Calcd: 250.04. Found: 249.08 (M-1). Analysis: Calcd for $C_{11}H_{10}N_2O_3S$: C, 52.79; H, 4.03; N, 11.19. Found: C, 52.27; H, 4.09; N, 10.95.

***N*-(3-Fluorophenyl)-3-nitrothiophen-2-amine (3l)**. Isolated as a yellow solid. Yield: 94%; mp = 101–102 °C. IR (KBr) $\nu_{max}$: 3327,1560,1508, 1458, 1365, 1149, 1240, 1180 $cm^{-1}$. $^1H$ NMR (300 MHz, $CDCl_3$) $\delta_H$: 6.38 (d, *J* = 6.3 Hz, 1H, H-5), 6.93 (m, 1H, H-4'), 7.11–7.17 (m, 2H, H-4, H-6'), 7.37–7.44 (m, 2H, H-2', H-5'), 10.39 (br s, 1H, NH); $^{13}C$ NMR (75 MHz, $CDCl_3$) $\delta_c$: 107.2 (d, $^2J_{C,F}$ = 25.2 Hz, C-2'), 107.6 (C-4), 112.2 (d, $^2J_{C,F}$ = 21.1 Hz, C-4'), 115.6 (d, $^4J_{C,F}$ = 3.0 Hz, C-6'), 121.7 (C-5), 128.6 (C-2), 131.1 (d, $^3J_{C,F}$ = 9.4 Hz, C-5'), 140.4 (d, $^3J_{C,F}$ =10.0 Hz, C-1'), 154.3 (C-3), 163.2 (d, $^1J_{C,F}$ = 246.4 Hz, C-3'); ESI-MS: m/z. Calcd: 238.02. Found: 251.04 (M+2+Na). Analysis: Calcd for $C_{10}H_7FN_2O_2S$: C, 50.42; H, 2.96; N, 11.76. Found: C, 50.43; H, 3.03; N, 11.71.

***N*-(3-Bromophenyl)-3-nitrothiophen-2-amine (3m)**. Isolated as a pale yellow solid. Yield: 90%; mp = 132–133 °C. IR (KBr) $\nu_{max}$: 3253, 3116, 3099, 1560, 1467, 1340, 1259, 1165, 1080 $cm^{-1}$. $^{1}H$ NMR (300 MHz, $CDCl_3$) $\delta_H$: 6.37 (d, *J* = 6.3 Hz, 1H, H-5), 7.30–7.36 (m, 3H, H-4',5',6'), 7.38 (d, *J* = 6.3 Hz, 1H, H-4), 7.55 (s, 1H, H-2'), 10.31 (br s, 1H, NH); $^{13}C$ NMR (75 MHz, $CDCl_3$) $\delta_c$: 107.6 (C-4), 118.7 (C-2'), 121.8 (C-6'), 123.1 (C-3'), 123.4 (C-4'), 128.5 (C-2), 128.7 (C-5), 131.1 (C-5'), 140.2 (C-1'), 154.4 (C-3); ESI-MS: m/z. Calcd: 297.94. Found: 296.98 (M-1), 298.99 (M+2). Analysis: Calcd for $C_{10}H_7BrN_2O_2S$: C, 40.15; H, 2.36; N, 9.36. Found: 40.17; H, 2.37; N, 11.71.

**3-Nitro-*N*-(3-(trifluoromethyl)phenyl)thiophen-2-amine (3n)**. Isolated as a pale yellow solid. Yield: 89%; mp = 106–107 °C. IR (KBr) $\nu_{max}$: 3257, 3101, 1560,1508, 1491, 1327, 1234, 1205, 1170 $cm^{-1}$. $^{1}H$ NMR (300 MHz, $CDCl_3$) $\delta_H$: 6.39 (d, *J* = 6.3 Hz, 1H, H-5), 7.41 (d, *J* = 6.0 Hz, 1H, H-4), 7.44–7.59 (m, 3H, H-4',5',6'), 7.65 (s, 1H, H-2'), 10.41 (br s, 1H, NH); $^{13}C$ NMR (75 MHz, $CDCl_3$) $\delta_c$: 107.6 (C-4), 116.8 (q, $^{3}J_{C,F}$ = 3.8 Hz, C-2'), 121.6 (C-6'), 121.9, 122.0 (q, $^{3}J_{C,F}$ = 3.6 Hz, C-4'), 123.2 (C-1'), 127.1 (q, $^{1}J_{C,F}$ = 271.5 Hz, $CF_3$), 130.5 (C-5), 132.1(q, $^{2}J_{C,F}$ = 32.7 Hz, C-3'), 139.6 (C-2), 154.2 (C-3); ESI-MS: m/z. Calcd: 288.02. Found: 287.04 (M-1). Analysis: Calcd for $C_{11}H_7F_3N_2O_2S$: C, 45.84; H, 2.45; N, 9.72. Found: C, 45.53, H, 2.52; N, 9.88.

**3-Nitro-*N*-(*m*-tolyl)thiophen-2-amine (3o)**. Isolated as a yellow solid. Yield: 94%; mp = 83–84 °C. IR (KBr) $\nu_{max}$: 3103, 2918, 2852,1572, 1491, 1391, 1357, 1213, 1171 $cm^{-1}$. $^{1}H$ NMR (300 MHz, $CDCl_3$) $\delta_H$: 6.30 (dd, *J* = 0.6, 6.0 Hz, 1H, H-5), 7.06 (m, 1H, H-4'), 7.19 (m, 2H, H-4, H-5'), 7.30–7.37 (m, 2H, H-2',5'), 10.35 (br s, 1H, NH); $^{13}C$ NMR (75 MHz, $CDCl_3$) $\delta_c$: 21.4 (Me), 107.1 (C-4), 117.4 (C-6'), 121.2 (C-4'), 121.7 (C-2'), 126.6 (C-5'), 128.1 (C-2), 129.6 (C-5), 138.9 (C-1'), 140.0 (C-3'), 155.7 (C-3); ESI-MS: m/z.

Calcd: 234.05. Found: 233.13 (M-1). Analysis: Calcd for $C_{11}H_{10}N_2O_2S$: C, 56.40; H, 4.30; N, 11.96. Found: 56.25; H, 4.42; N, 11.67.

***N*-(3-Methoxyphenyl)-3-nitrothiophen-2-amine (3p)**. Isolated as an orange solid. Yield: 95%; mp = 111–112 °C. IR (KBr) $\nu_{max}$: 3157, 3116, 3101,1562, 1508, 1481, 1369, 1355, 1215, 1161 $cm^{-1}$. $^1H$ NMR (300 MHz, $CDCl_3$) $\delta_H$: 3.84 (s, 3H, OMe), 6.32, (d, *J* = 6.0 Hz, 1H, H-5), 6.78 (dd, *J* = 2.4, 8.4 Hz, 1H, H-4'), 6.91 (t, *J* = 2.1 Hz, 1H, H-2'), 6.96 (dd, *J* = 2.2, 7.9 Hz, 1H, H-6'), 7.33 (t, *J* = 8.1 Hz, 1H, H-5'), 7.36 (d, *J* = 6.0 Hz, 1H, H-4), 10.37 (br s, 1H, NH); $^{13}C$ NMR (75 MHz, $CDCl_3$) $\delta_c$: 55.3 (OMe), 106.0 (C-2'), 107.4 (C-4), 111.1 (C-6'), 112.3 (C-4'), 121.5 (C-5), 128.1 (C-1'), 130.5 (C-5'), 139.9 (C-2), 155.2 (C-3), 160.6 (C-3'); ESI-MS: m/z. Calcd: 250.04. Found: 249.10 (M-1). Analysis: Calcd for $C_{11}H_{10}N_2O_3S$: C, 52.79; H, 4.03; N, 11.19. Found: C, 52.63; H, 4.10; N, 11.09.

***N*-(2,4-Dimethylphenyl)-3-nitrothiophen-2-amine (3q)**. Isolated as a yellow solid. Yield: 92%; mp = 114–115 °C. IR (KBr) $\nu_{max}$: 3186, 3122, 3105,1560, 1491, 1377, 1354, 1223, 1167 $cm^{-1}$. $^1H$ NMR (300 MHz, $CDCl_3$) $\delta_H$: 2.33 (s, 3H, Me), 2.36 (s, 3H, Me), 6.24 (dd, *J* = 0.9, 6.3 Hz, 1H, H-5), 7.09–7.14 (m, 2H, H-3' and H-6'), 7.32–7.37 (m, 2H, H-4 and H-5'), 10.08 (br s, 1H, NH); $^{13}C$ NMR (75 MHz, $CDCl_3$) $\delta_c$: 17.6 (Me), 20.9 (Me), 107.1 (C-4), 121.8 (C-6'), 127.4 (C-1'), 127.8 (C-5), 131.3 (C-3'), 132.1 (C-2'), 135.2 (C-4'), 136.9 (C-2), 158.3 (C-3); ESI-MS: m/z. Calcd: 248.06. Found: 249.06 (M+1). Analysis: Calcd for $C_{12}H_{12}N_2O_2S$: C, 58.05; H, 4.87; N, 11.28. Found: C, 58.39; H, 4.63; N, 10.90.

***N*-(Naphthalen-1-yl)-3-nitrothiophen-2-amine (3r)**. Isolated as a yellow solid. Yield: 91%; mp = 153–154 °C. IR (KBr) $\nu_{max}$: 3290, 3109, 3091,1558, 1508, 1458, 1390, 1211, 1182 $cm^{-1}$. $^1H$ NMR (300 MHz, $CDCl_3$) $\delta_H$: 6.28 (d, *J* = 6.3 Hz, 1H, H-

5), 7.38 (d, *J* = 6.0 Hz, 1H, H-4), 7.50–7.56 (m, 1H, H-7'), 7.59–7.64 (m, 2H, H-2',6'), 7.71 (d, *J* = 7.5 Hz, 1H, H-4'), 7.83 (d, *J* = 8.4 Hz, 1H, H-3'), 7.92–7.95 (m, 1H, H-5'), 8.05–8.06 (m, 1H, H-8'), 10.67 (br s, 1H, NH); $^{13}$C NMR (75 MHz, $CDCl_3$) $\delta_c$: 107.4 (C-4), 118.8 (C-2'), 121.0 (C-4'), 121.7 (C-8'), 125.0 (C-8a'), 125.4 (C-7'), 127.0 (C-1'), 127.2 (C-6'), 127.26 (C-3'), 127.28 (C-5), 128.6 (C-5'), 134.4 (C-4a'), 135.1 (C-2), 158.1 (C-3); ESI-MS: m/z. Calcd: 270.05. Found: 271.07 (M+1). Analysis: Calcd for $C_{14}H_{10}N_2O_2S$: C, 62.21; H, 3.73; N, 10.36. Found: 62.48; H, 4.05; N, 9.97.

***N*-Methyl-3-nitrothiophen-2-amine (3s)**. Isolated as a yellow solid. Yield: 93%; mp = 69–70 °C. IR (KBr) $\nu_{max}$: 3327, 2922, 2852, 1560, 1344, 1261, 1195, 1026 cm$^{-1}$. $^1$H NMR (300 MHz, $CDCl_3$) $\delta_H$: 3.14 (d, *J* = 5.4 Hz, 3H, Me), 6.24 (d, *J* = 6.0 Hz, 1H, H-5), 7.27 (d, *J* = 6.3 Hz, 1H, H-4), 8.41 (br s, 1H, NH); $^{13}$C NMR (75 MHz, $CDCl_3$) $\delta_c$: 33.7 (Me), 106.5 (C-4), 122.1 (C-5), 125.5 (C-2), 162.5 (C-3); ESI-MS: m/z. Calcd: 158.01. Found: 158.98 (M+1). Analysis: Calcd for $C_5H_6N_2O_2S$: C, 37.97; H, 3.82; N, 17.71. Found: C, 38.45; H, 3.92; N, 17.37.

**3-Nitro-*N*-propylthiophen-2-amine (3t)**. Isolated as a yellow liquid. Yield: 95%. IR (KBr) $\nu_{max}$: 3308, 3101, 2964, 2931,2874,1572, 1516, 1400, 1336, 1263, 1186, 1084 cm$^{-1}$. $^1$H NMR (300 MHz, $CDCl_3$) $\delta_H$: 1.05 (t, *J* = 7.3 Hz, 3H, $CH_2CH_2CH_3$), 1.80 (sext, *J* = 7.2 Hz, 2H, $CH_2CH_2CH_3$), 3.32 (q, *J* = 6.9 Hz, 2H, $CH_2CH_2CH_3$), 6.21 (dd, *J* = 0.9, 6.0 Hz, 1H, H-5), 7.25 (d, *J* = 6.0 Hz, 1H, H-4), 8.47 (br s, 1H, NH); $^{13}$C NMR (75 MHz, $CDCl_3$) $\delta_c$: 11.2 ($CH_2CH_2CH_3$), 22.0 ($CH_2CH_2CH_3$), 49.7 ($CH_2CH_2CH_3$), 106.4 (C-4), 122.1 (C-5), 125.7 (C-2), 161.5 (C-3); ESI-MS: m/z.

Calcd: 186.05. Found: 187.00 (M+1). Analysis: Calcd for $C_7H_{10}N_2O_2S$: C, 45.15; H, 5.41; N, 15.04. Found: C, 45.50; H, 5.55; N, 14.86.

***N*-Butyl-3-nitrothiophen-2-amine (3u)**. Isolated as a yellow solid. Yield: 92%; mp = 50–51 °C. IR (KBr) $\nu_{max}$: 3331, 2931, 2868, 1570, 1381, 1259, 1055 $cm^{-1}$. $^1H$ NMR (300 MHz, $CDCl_3$) $\delta_H$: 0.98 (t, *J* = 7.3 Hz, 3H, $CH_2CH_2CH_2CH_3$), 1.47 (sext, *J* = 7.4 Hz, 2H, $CH_2CH_2CH_2CH_3$), 1.70–1.80 (m, 2H, $CH_2CH_2CH_2CH_3$), 3.35 (q, *J* = 6.7 Hz, 2H, $CH_2CH_2CH_2CH_3$), 6.21 (dd, *J* = 1.0, 6.1 Hz, 1H, H-5), 7.25 (d, *J* = 6.3 Hz, 1H, H-4), 8.45 (br s, 1H, NH); $^{13}C$ NMR (75 MHz, $CDCl_3$) $\delta_c$: 13.5 ($CH_2CH_2CH_2CH_3$), 19.9 ($CH_2CH_2CH_2CH_3$), 30.6 ($CH_2CH_2CH_2CH_3$), 47.7 ($CH_2CH_2CH_2CH_3$), 106.4 (C-4), 122.1 (C-5), 125.6 (C-2), 161.4 (C-3); ESI-MS: m/z. Calcd: 200.06. Found: 201.02 (M+1). Analysis: Calcd for $C_8H_{12}N_2O_2S$: C, 47.98; H, 6.04; N, 13.99. Found: 48.35; H, 6.01; N, 13.66.

***N*-Isopropyl-3-nitrothiophen-2-amine (3v)**. Isolated as a yellow liquid. Yield: 93%. IR (KBr) $\nu_{max}$: 3302, 3097, 2974, 2928, 1562, 1400, 1334, 1265, 1153 $cm^{-1}$. $^1H$ NMR (300 MHz, $CDCl_3$) $\delta_H$: 1.39 (d, *J* = 6.3 Hz, 6H, $CH(CH_3)_2$), 3.58–3.67 (m, 1H, $CH(CH_3)_2$), 6.22 (d, *J* = 6.3 Hz, 1H, H-5), 7.25 (d, *J* = 6.0 Hz, 1H, H-4), 8.40 (br s, 1H, NH); $^{13}C$ NMR (75 MHz, $CDCl_3$) $\delta_c$: 22.3 ($CH(CH_3)_2$), 50.6 ($CH(CH_3)_2$), 106.4 (C-4), 122.1 (C-5), 125.7 (C-2), 160.1 (C-3); ESI-MS: m/z. Calcd: 186.05. Found: 187.08 (M+1). Analysis: Calcd for $C_7H_{10}N_2O_2S$: C, 45.15; H, 5.41; N, 15.04. Found: C, 45.54; H, 5.56; N, 14.83.

***N*-Cyclopropyl-3-nitrothiophen-2-amine (3w)**. Isolated as a yellow liquid. Yield: 94%. IR (KBr) $\nu_{max}$: 3321, 3100, 3009, 2872, 1562, 1516, 1400, 1332, 1259, 1188, 1084 $cm^{-1}$. $^1H$ NMR (300 MHz, $CDCl_3$) $\delta_H$: 0.79–1.02 (m, 4H, H-2',3'), 2.69–2.76 (m, 1H, H-1'), 6.27 (d, *J* = 6.0 Hz, 1H, H-5), 7.27 (d, *J* = 6.0 Hz, 1H, H-4), 8.38 (br s, 1H, NH); $^{13}C$ NMR (75

MHz, $CDCl_3$) $\delta_c$: 7.7 (C-2',3'), 28.3 (C-1'), 107.6 (C-4), 121.9 (C-5), 125.9 (C-2), 162.3 (C-3); ESI-MS: m/z. Calcd: 184.03. Found: 183.06 (M-1). Analysis: Calcd for $C_7H_8N_2O_2S$: C, 45.64; H, 4.38; N, 15.21. Found: C, 45.29; H, 4.49; N, 14.85.

***N*-Cyclohexyl-3-nitrothiophen-2-amine (3x)**. Isolated as a yellow solid. Yield: 95%; mp = 130–131 °C. IR (KBr) $\nu_{max}$: 3285, 3115, 3096, 2931, 2852, 1570, 1389, 1240, 1076 $cm^{-1}$. $^1H$ NMR (300 MHz, $CDCl_3$) $\delta_H$: 1.29–1.50 (m, 5H, H-3',5',6'), 1.65–1.68 (m, 1H, H-4'), 1.80–1.83 (m, 2H, H-2',6'), 2.09–2.14 (m, 2H, H2',6'), 3.23–3.31 (m, 1H, H-1'), 6.20 (d, *J* = 6.3 Hz, 1H, H-5), 7.24 (d, *J* = 6.0 Hz, 1H, H-4), 8.52 (br s, 1H, NH); $^{13}C$ NMR (75 MHz, $CDCl_3$) $\delta_c$: 24.3 (C-3',5'), 25.1 (C-4'), 32.1 (C-2',6'), 57.4 (C-1'), 106.3 (C-4), 122.0 (C-5), 125.6 (C-2), 160.0 (C-3); ESI-MS: m/z. Calcd: 226.08. Found: 227.10 (M+1). Analysis: Calcd for $C_{10}H_{14}N_2O_2S$: C, 53.08; H, 6.24; N, 12.38. Found: C, 53.33; H, 6.24; N, 12.30.

***N*-Benzyl-3-nitrothiophen-2-amine (3y)**. Isolated as a yellow solid. Yield: 92 %; mp = 55–56 °C; IR (KBr) $\nu_{max}$: 3287, 3115, 3093, 2922, 2954, 1560, 1386, 1219, 1066 $cm^{-1}$. $^1H$ NMR (300 MHz, $CDCl_3$) $\delta_H$: 4.53 (d, *J* = 5.7 Hz, 2H, C$H_2$Ph), 6.22 (d, *J* = 6.0 Hz, 1H, H-5), 7.28 (d, *J* = 6.0 Hz, 1H, H-4), 7.37–7.42 (m, 5H, $CH_2$*Ph*), 8.72 (br s, 1H, NH); $^{13}C$ NMR (75 MHz, $CDCl_3$) $\delta_c$: 51.7 (*C*$H_2$Ph), 106.7 (C-4), 122.3 (C-2 and C-5), 127.6 (C-2',6'), 128.4 (C-4'), 129.0 (C-3',5'), 135.2 (C-1'), 160.8 (C-3); ESI-MS: m/z. Calcd: 234.05. Found: 235.07 (M+1). Analysis: Calcd for $C_{11}H_{10}N_2O_2S$: C, 56.40; H, 4.30; N, 11.96. Found: C, 56.89; H, 4.79; N, 11.83.

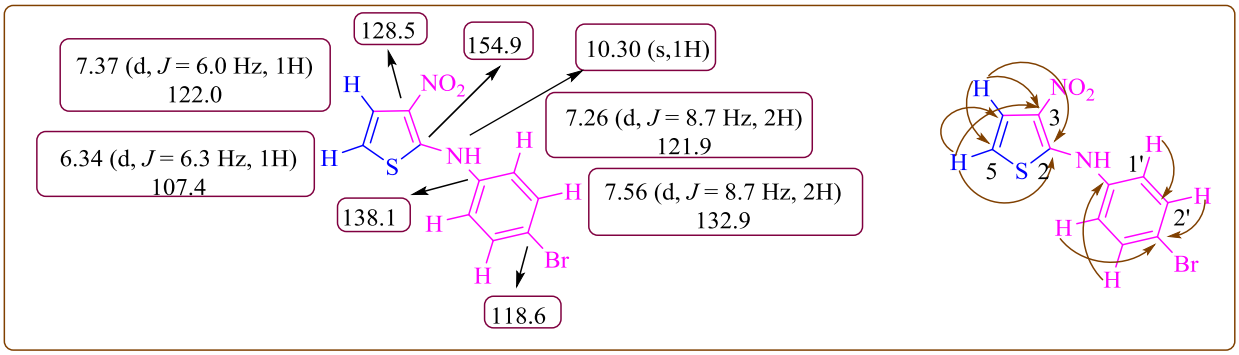
**(*R*)-3-Nitro-*N*-(1-phenylethyl)thiophen-2-amine (3z)**. Isolated as a yellow solid. Yield: 96 %; mp = 71–72 °C. IR (KBr) $\nu_{max}$: 3319, 3120, 3100, 2974, 2926, 1545, 1342, 1254, 1068 $cm^{-1}$. $^1H$ NMR (300 MHz, $CDCl_3$) $\delta_H$: 1.70 (d, *J* = 6.9 Hz, 3H, Me), 4.52 (q, *J* = 6.7

Hz, 1H, C*H*Me), 6.13 (dd, *J* = 0.9, 6.0 Hz, 1H, H-5), 7.23 (d, *J* = 6.0 Hz, 1H, H-4), 8.80 (br s, 1H, NH); $^{13}$C NMR (75 MHz, $CDCl_3$) $\delta_c$: 23.9 (Me), 57.9 (*C*HMe), 107.2 (C-4), 121.7 (C-2 and C-5), 126.1 (C-2',6'), 128.1 (C-4'), 128.9 (C-3',5'), 140.9 (C-1'), 159.8 (C-3); ESI-MS: m/z. Calcd: 248.06. Found: 249.04 (M+1). Analysis: Calcd for $C_{12}H_{12}N_2O_2S$: C, 58.05; H, 4.87; N, 11.28. Found: C, 58.19; H, 4.91; N, 11.29.

## 2. Structure determination of 3c using NMR spectroscopic data

The structure of *N*-(4-bromophenyl)-3-nitrothiophen-2-amine (**3c)** was deduced from one- and two-dimensional NMR spectroscopic data. The structural elucidation of **3c** using NMR spectroscopy is discussed below.

The H-4 appears as a doublet at 7.37 ppm ($J$ = 6.0 Hz), which shows HMBCs with C-2, C-3 and C-5 at 154.9, 128.5 and 107.4 ppm, respectively. Likewise, the H-5 appears as a doublet at 6.34 ppm ($J$ = 6.3 Hz), which shows HMBCs with C-2, C-3, C-4 at 154.9, 128.5 and 122.0 ppm, respectively. The NH peak appears as a broad singlet at 10.30 ppm.



## 3. Copies of spectra

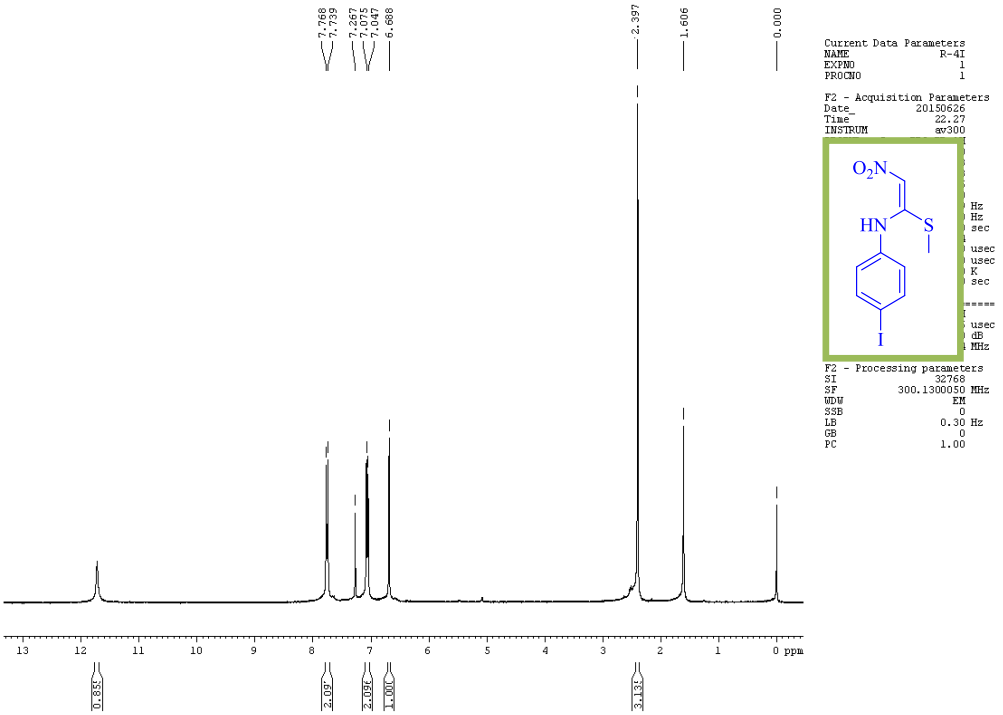



**Figure 1** $^{1}$H NMR Spectrum **1d** ($CDCl_3$)

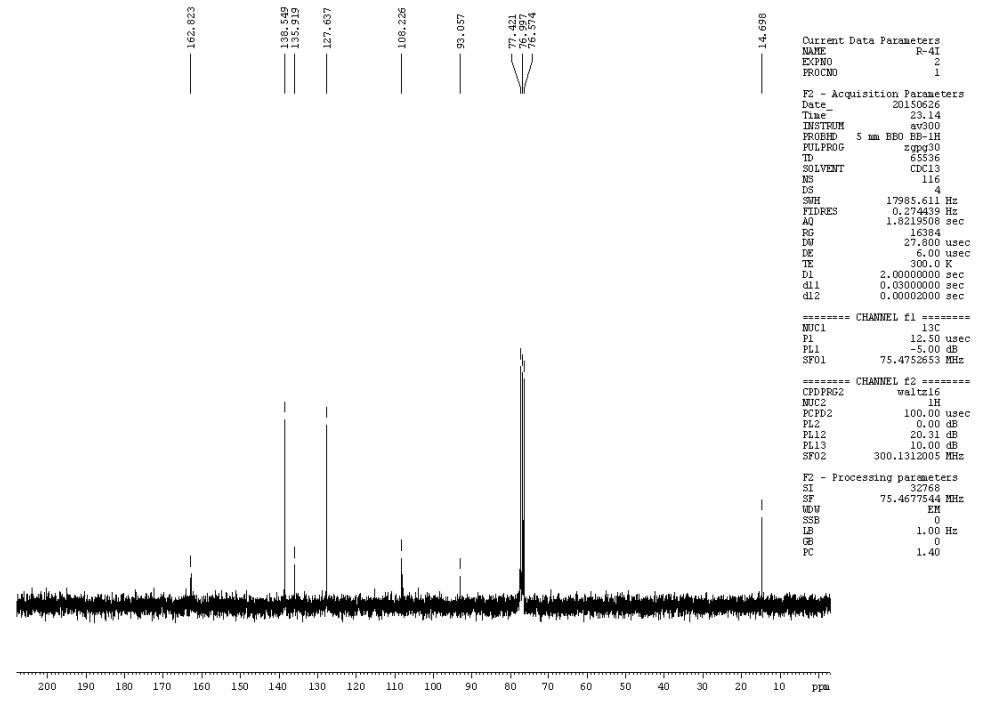



**Figure 2** $^{13}$C NMR Spectrum of **1d** ($CDCl_3$)

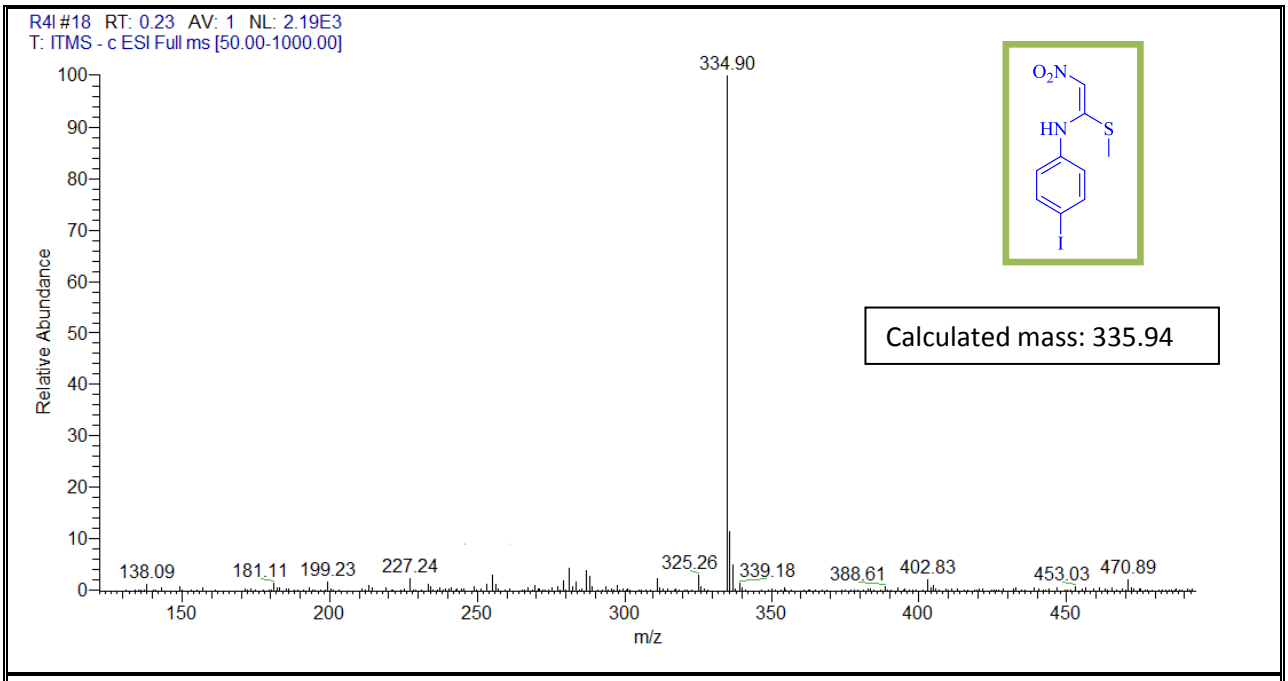



**Figure 3** ESI mass spectrum of **1d**

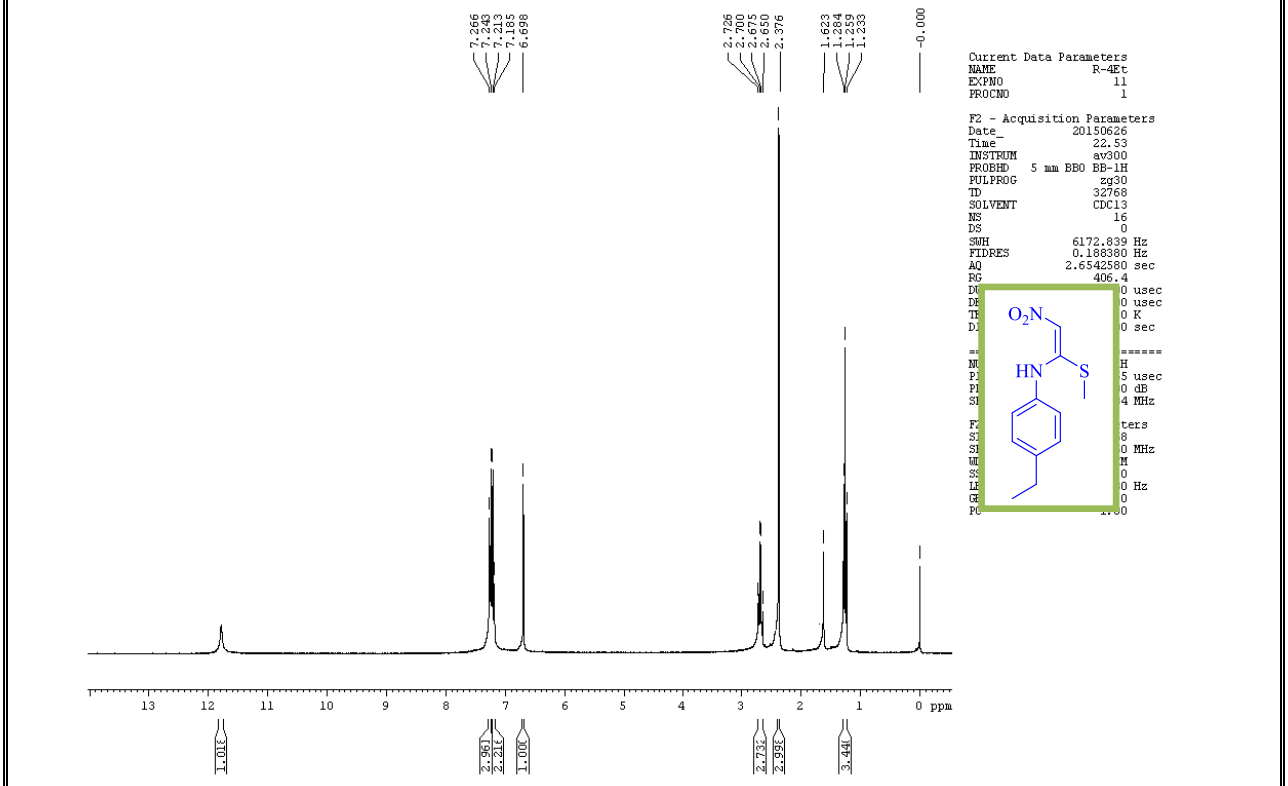



**Figure 4** $^{1}$H NMR Spectrum **1g** ($CDCl_3$)

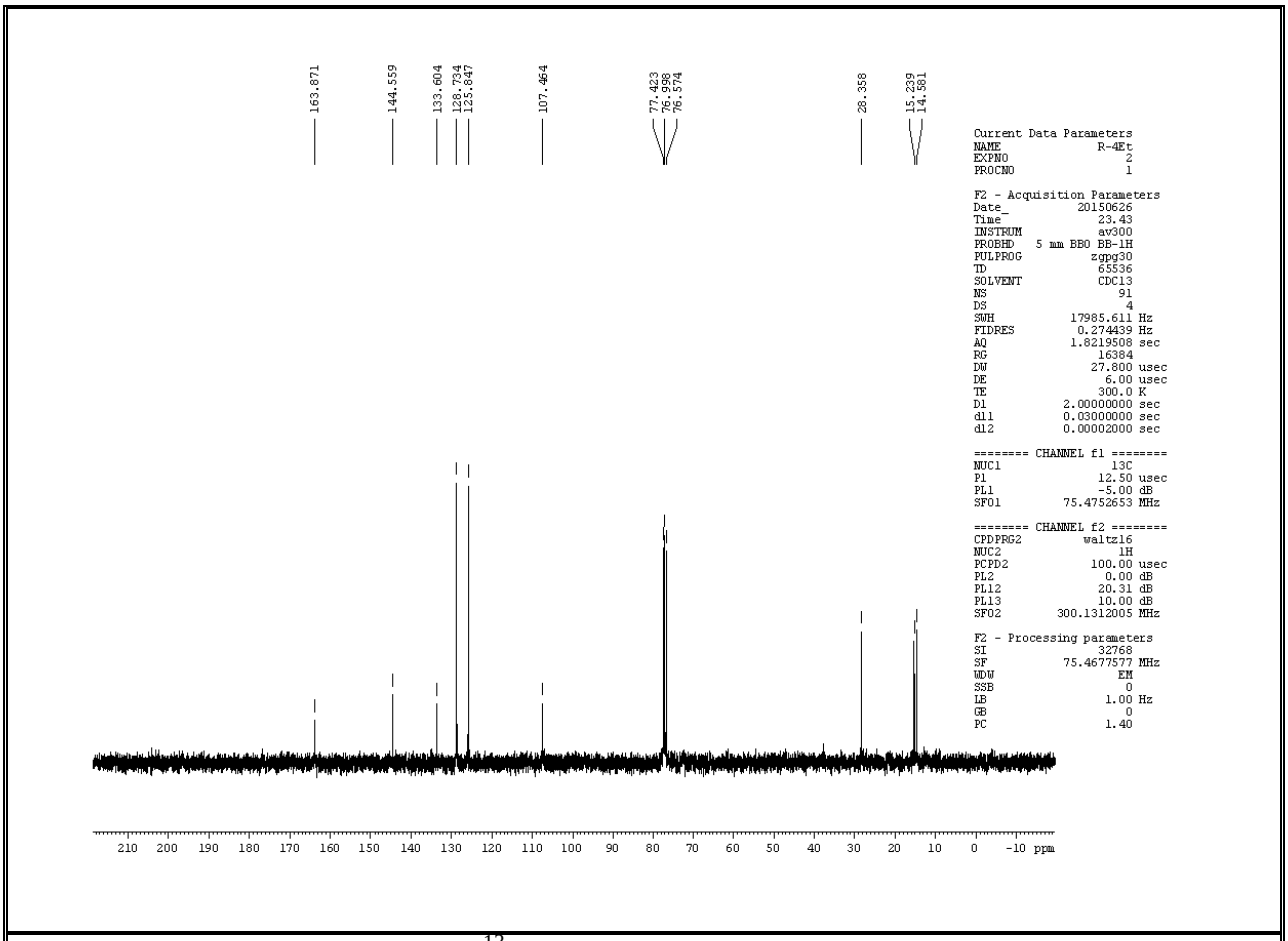



**Figure 5** $^{13}$C NMR Spectrum of **1g** ($CDCl_3$)

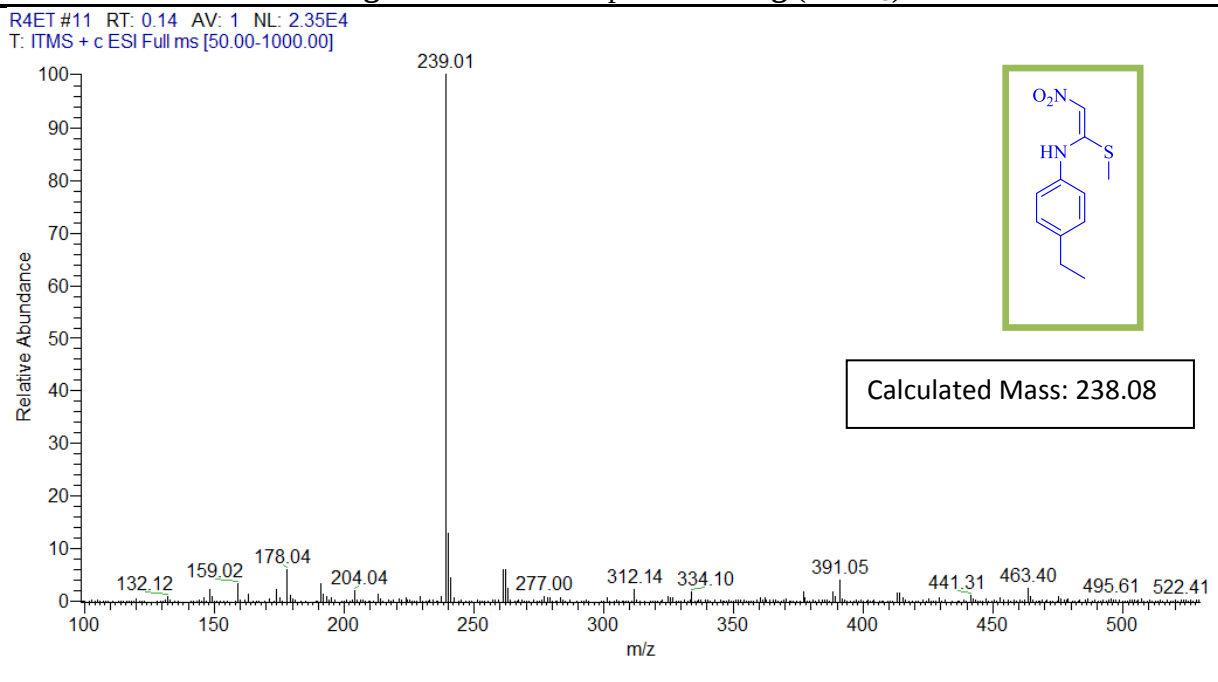



**Figure 6** ESI mass spectrum of **1g**

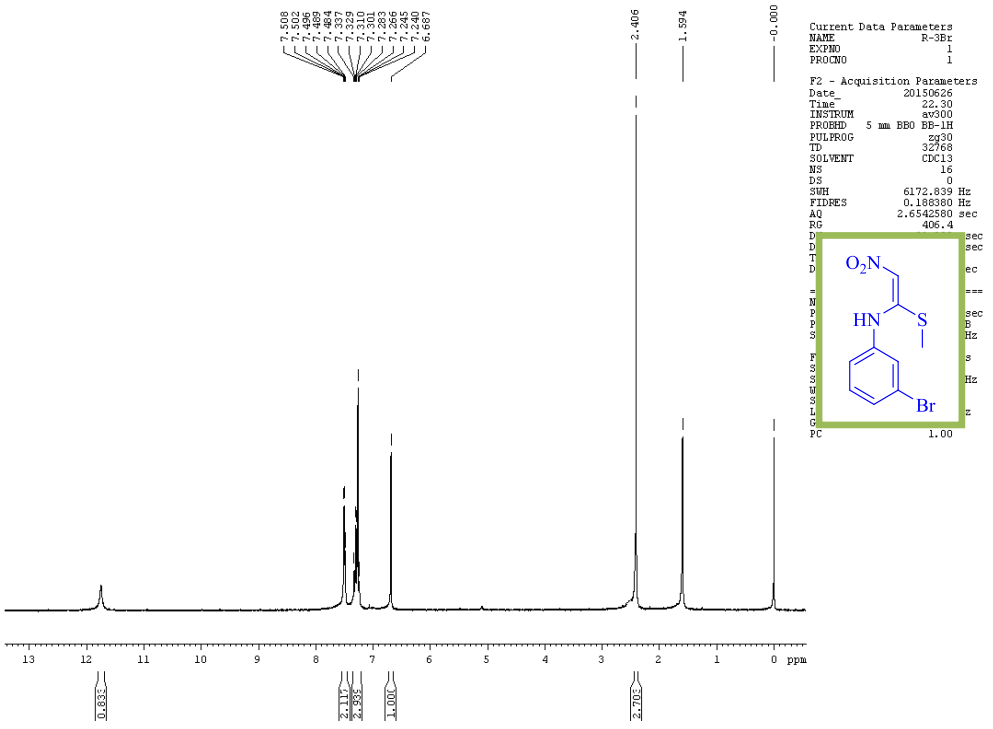



**Figure 7** $^{1}$H NMR Spectrum **1m** ($CDCl_3$)

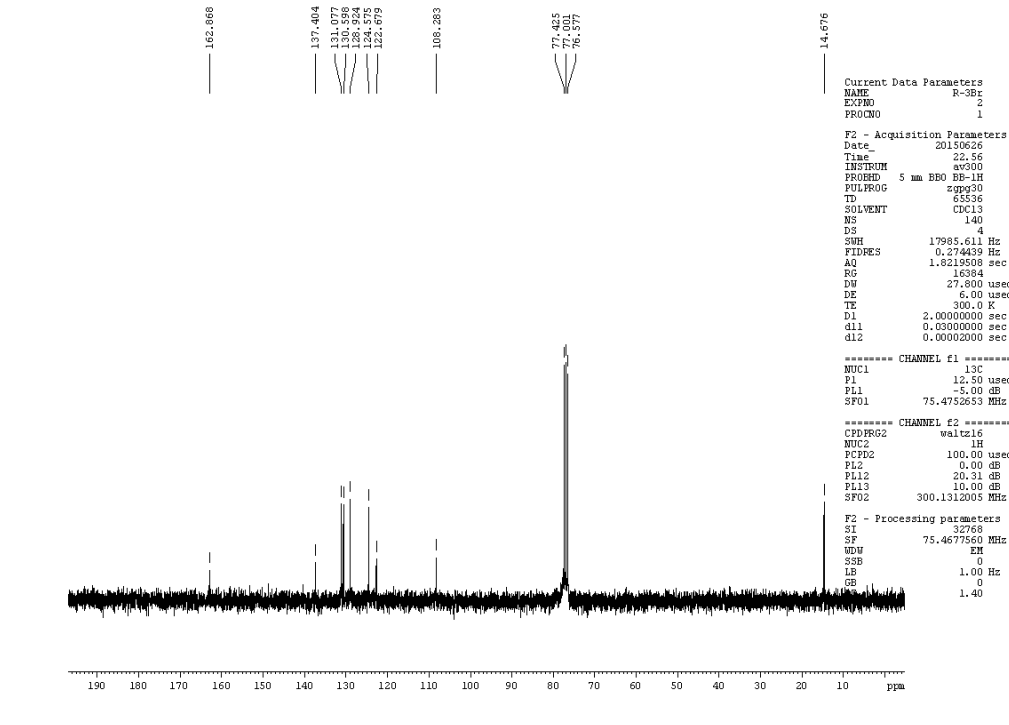



**Figure 8** $^{13}$C NMR Spectrum of **1m** ($CDCl_3$)

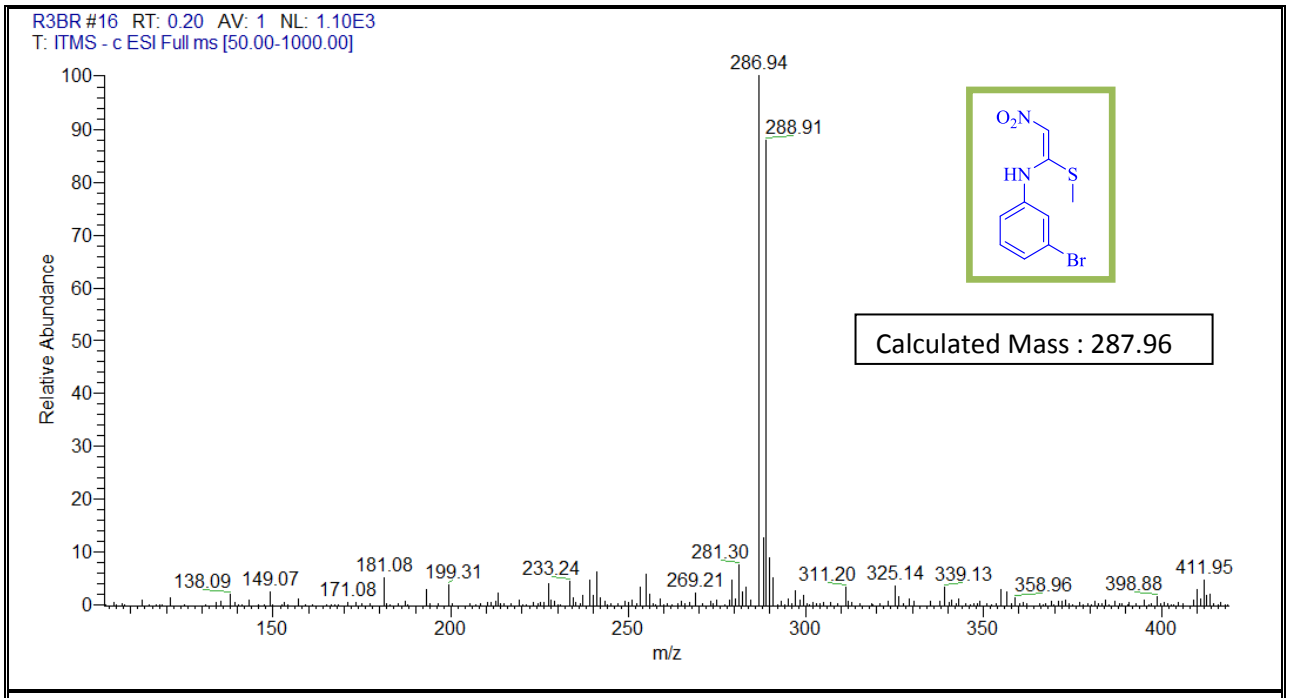



**Figure 9** ESI mass spectrum of Spectrum of **1m**

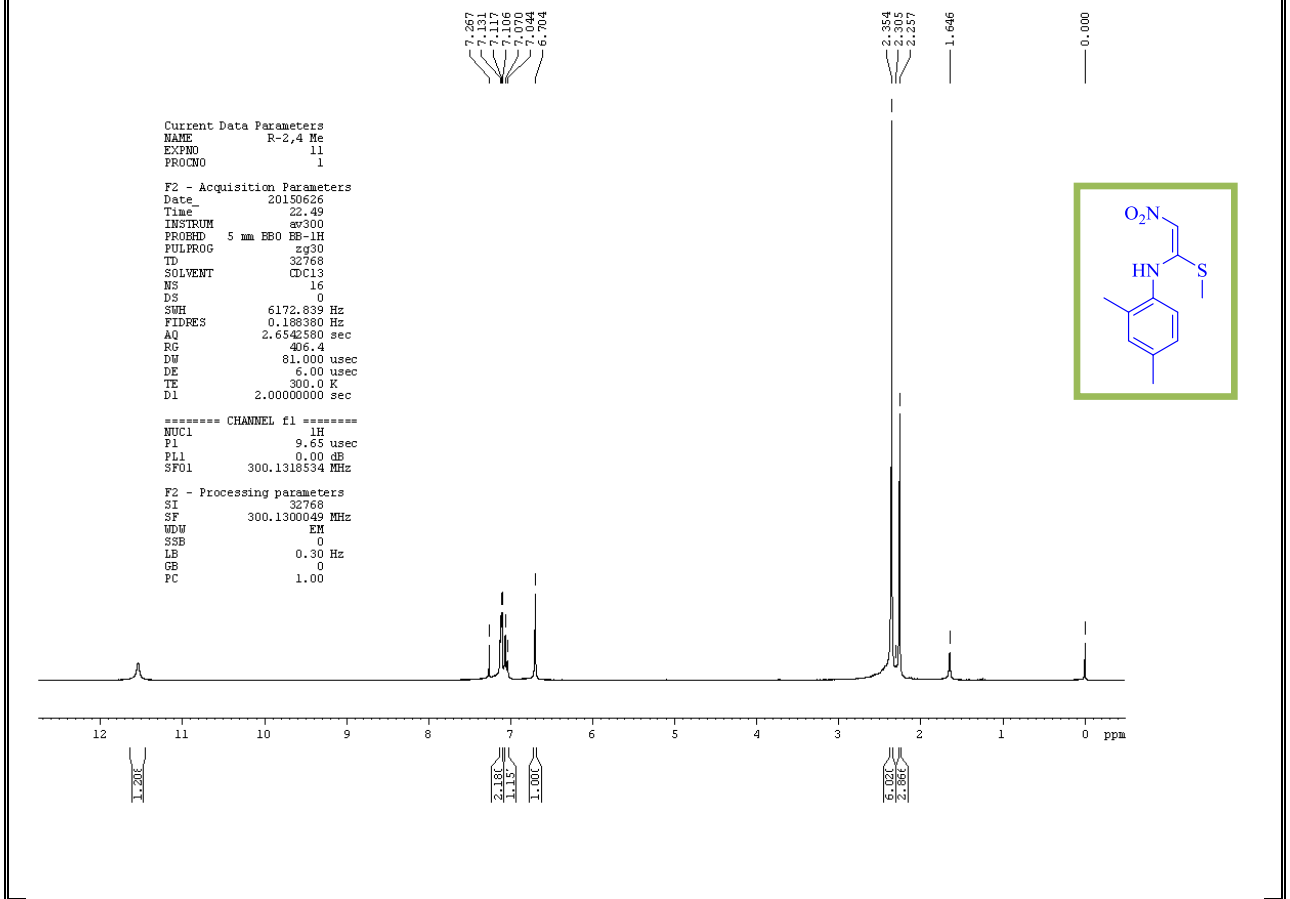



**Figure 10** $^{1}$H NMR Spectrum of **1q** ($CDCl_3$)

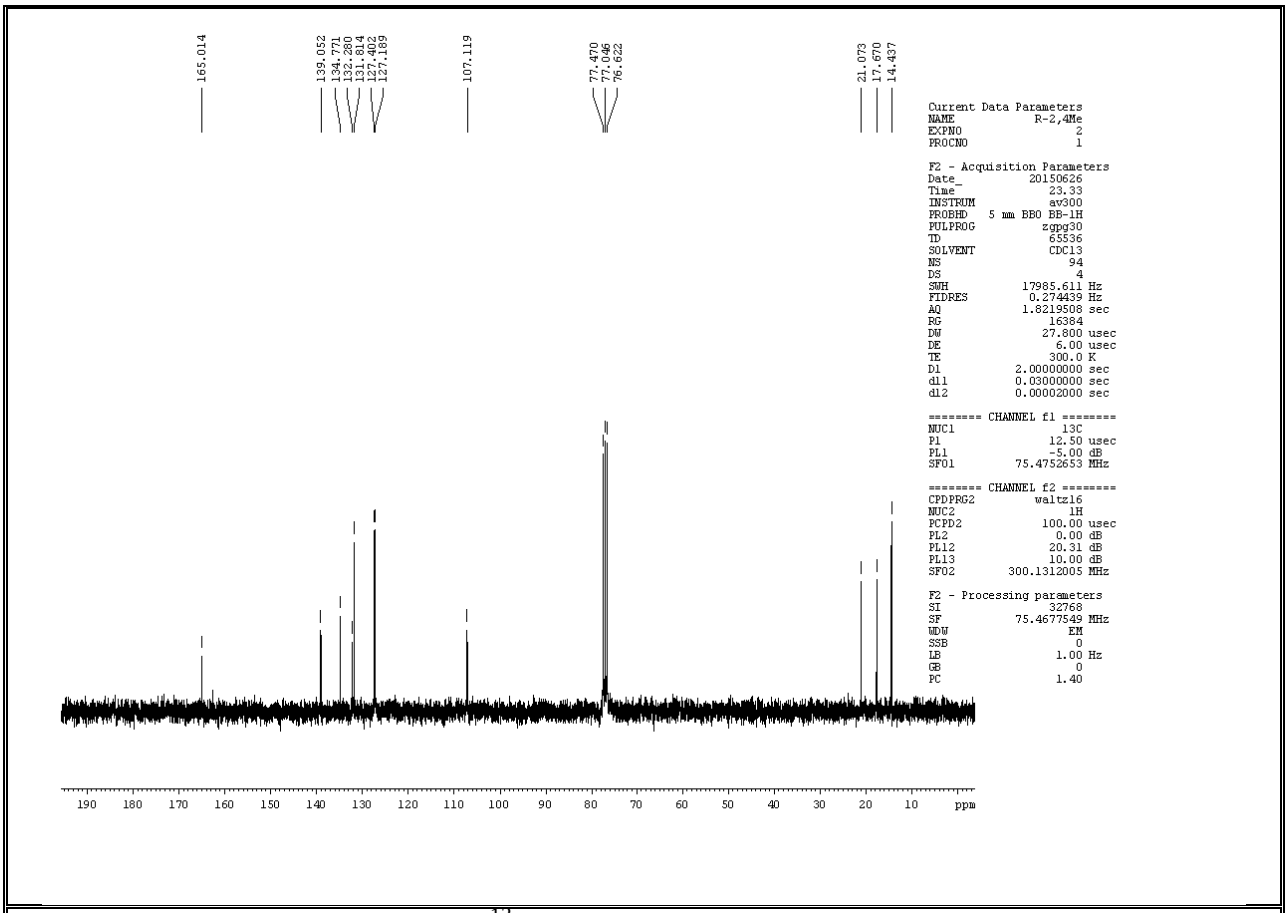



**Figure 11** $^{13}$C NMR Spectrum of **1q** ($CDCl_3$)

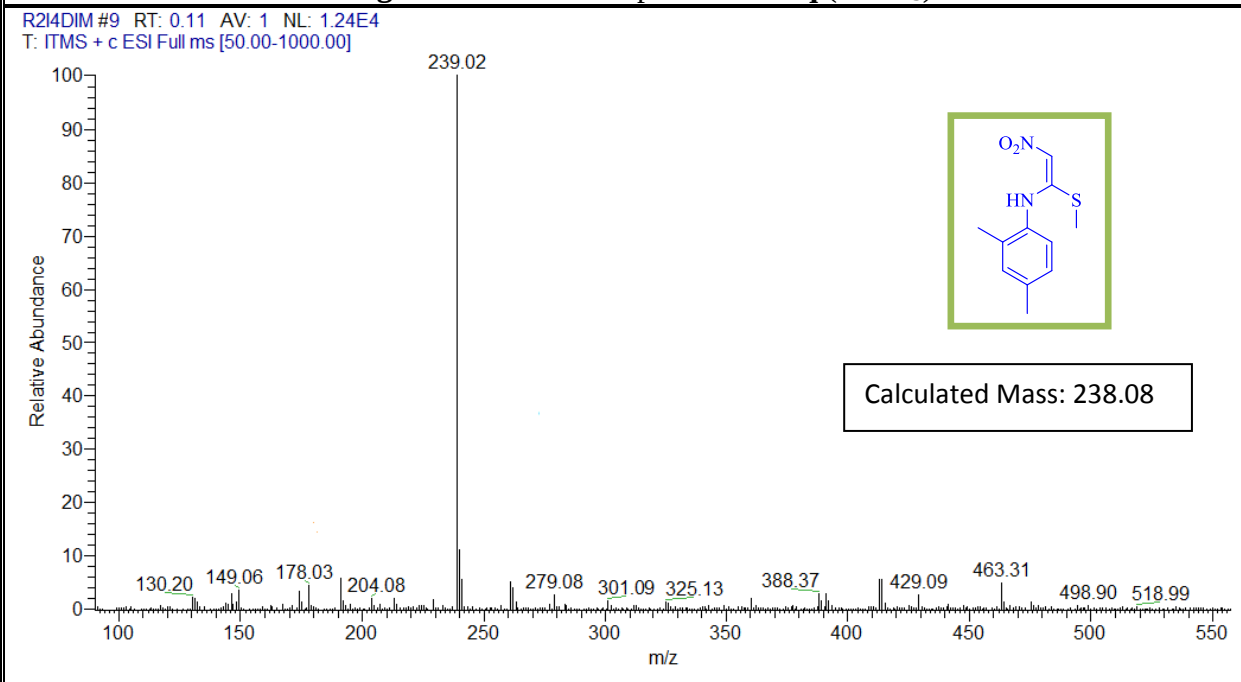



**Figure 12** ESI mass spectrum of **1q**

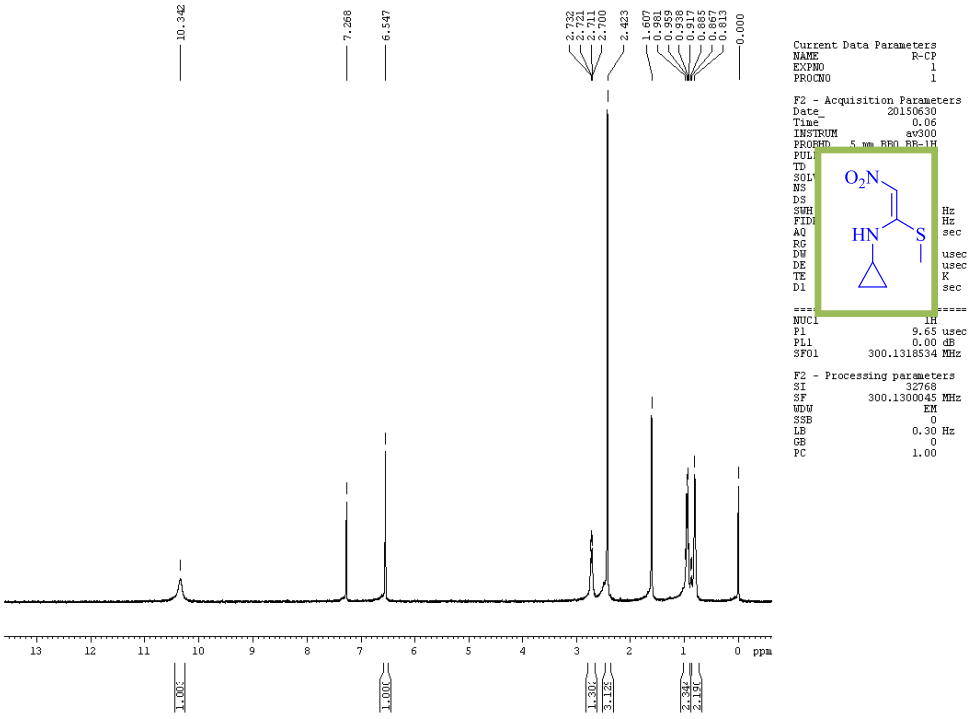



**Figure 13** $^{1}$H NMR Spectrum of **1w** ($CDCl_3$)

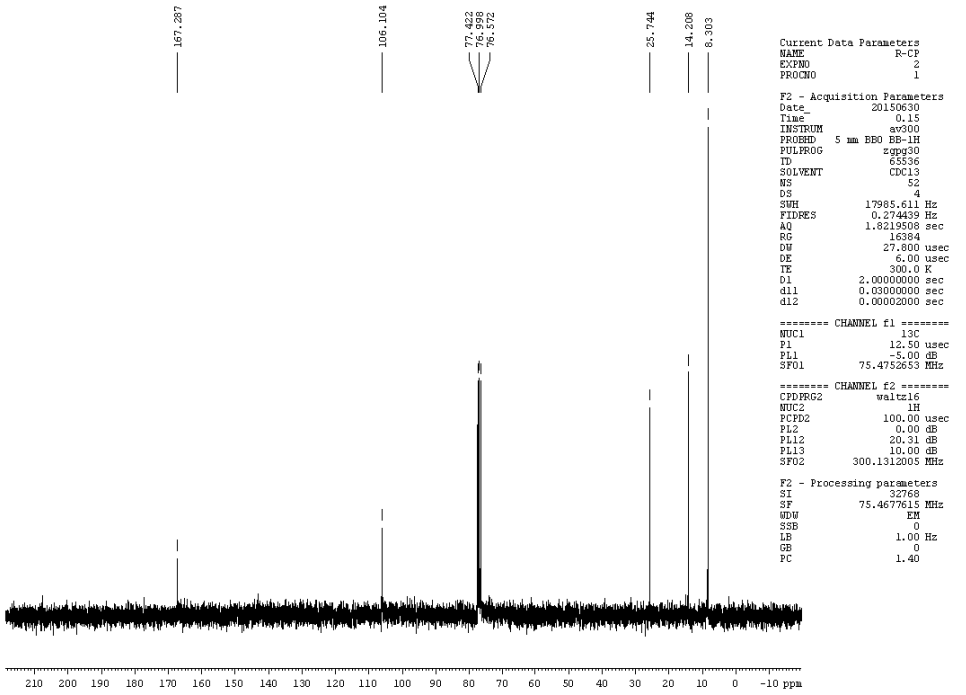



**Figure 14** $^{13}$C NMR Spectrum of **1w** ($CDCl_3$)

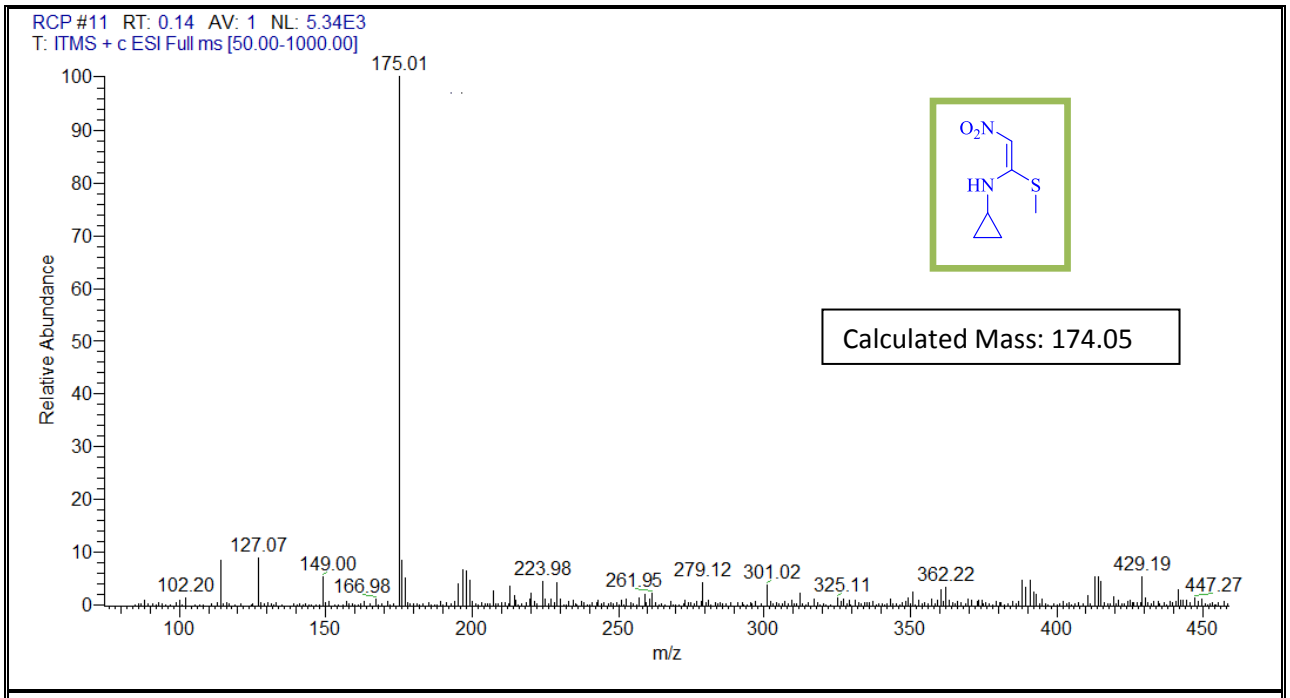



**Figure 15** ESI mass spectrum of **1w**

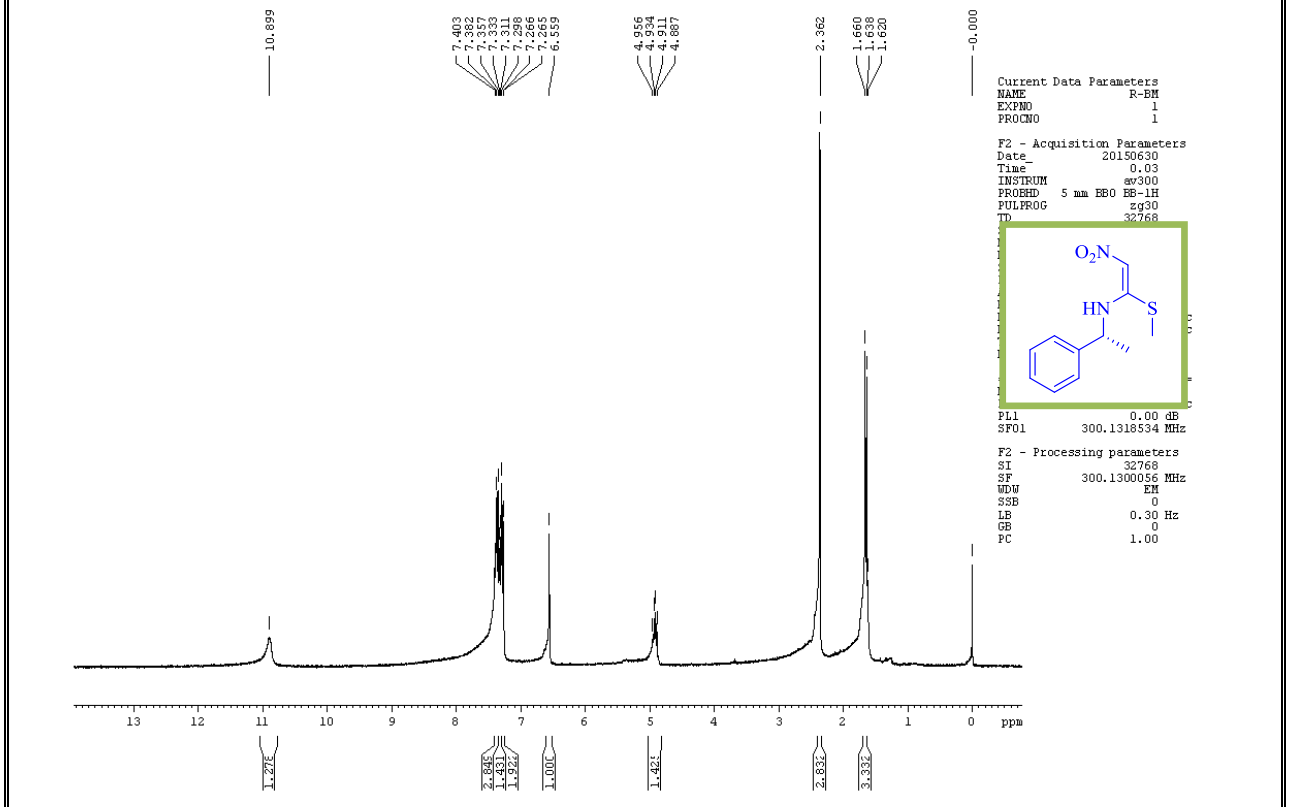



**Figure 16** $^{1}$H NMR Spectrum of **1z** ($CDCl_3$)

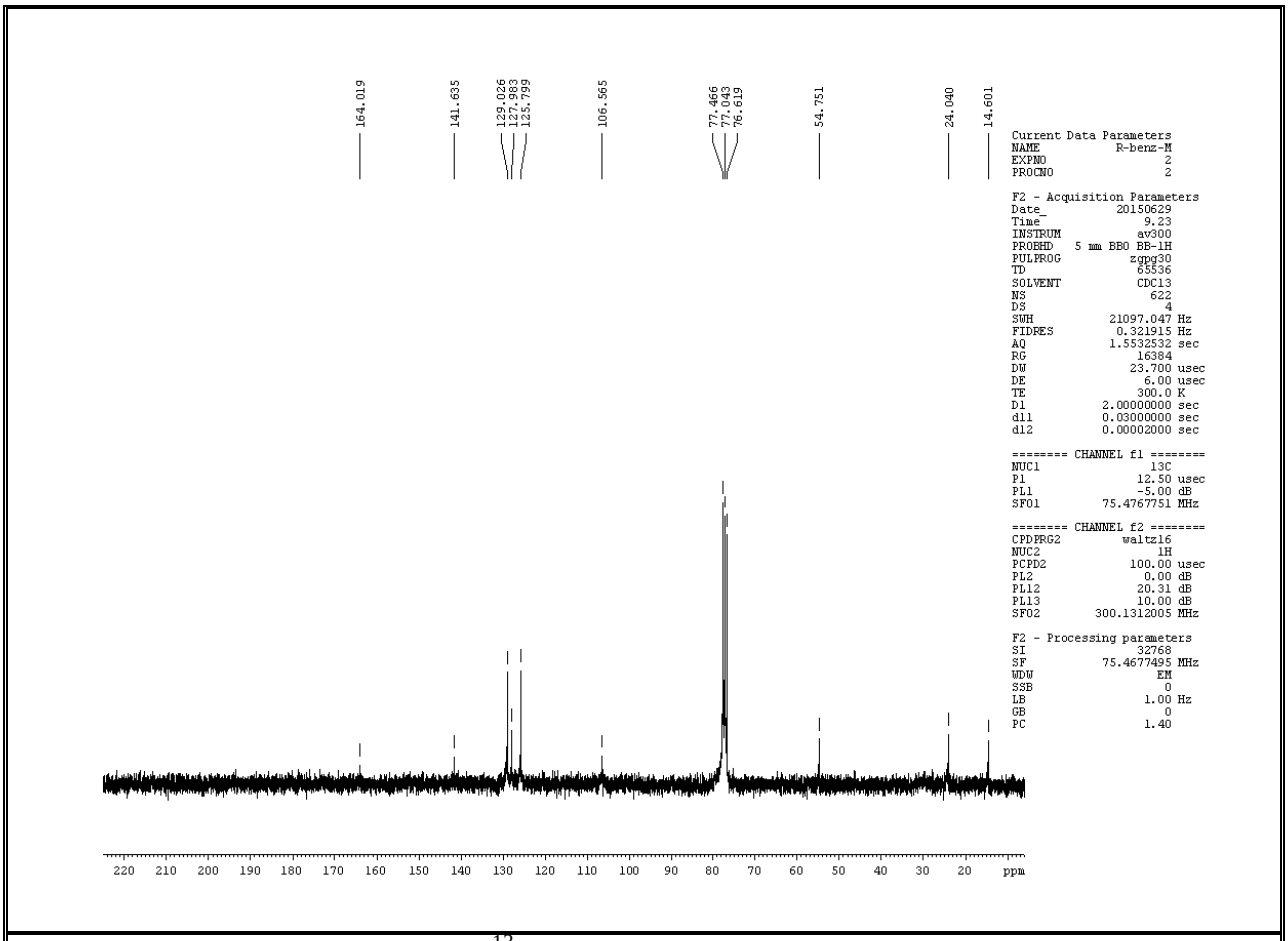



**Figure 17** $^{13}$C NMR Spectrum of **1z** ($CDCl_3$)

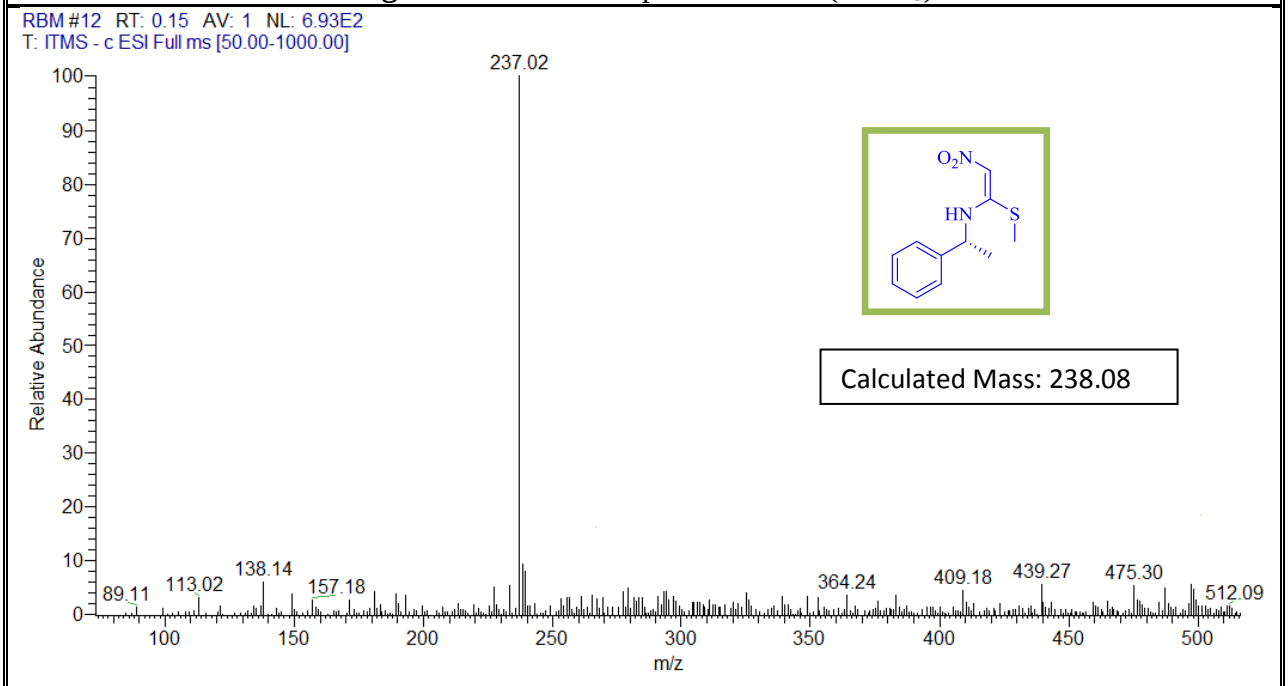



**Figure 18** ESI mass spectrum of Spectrum of **1z**

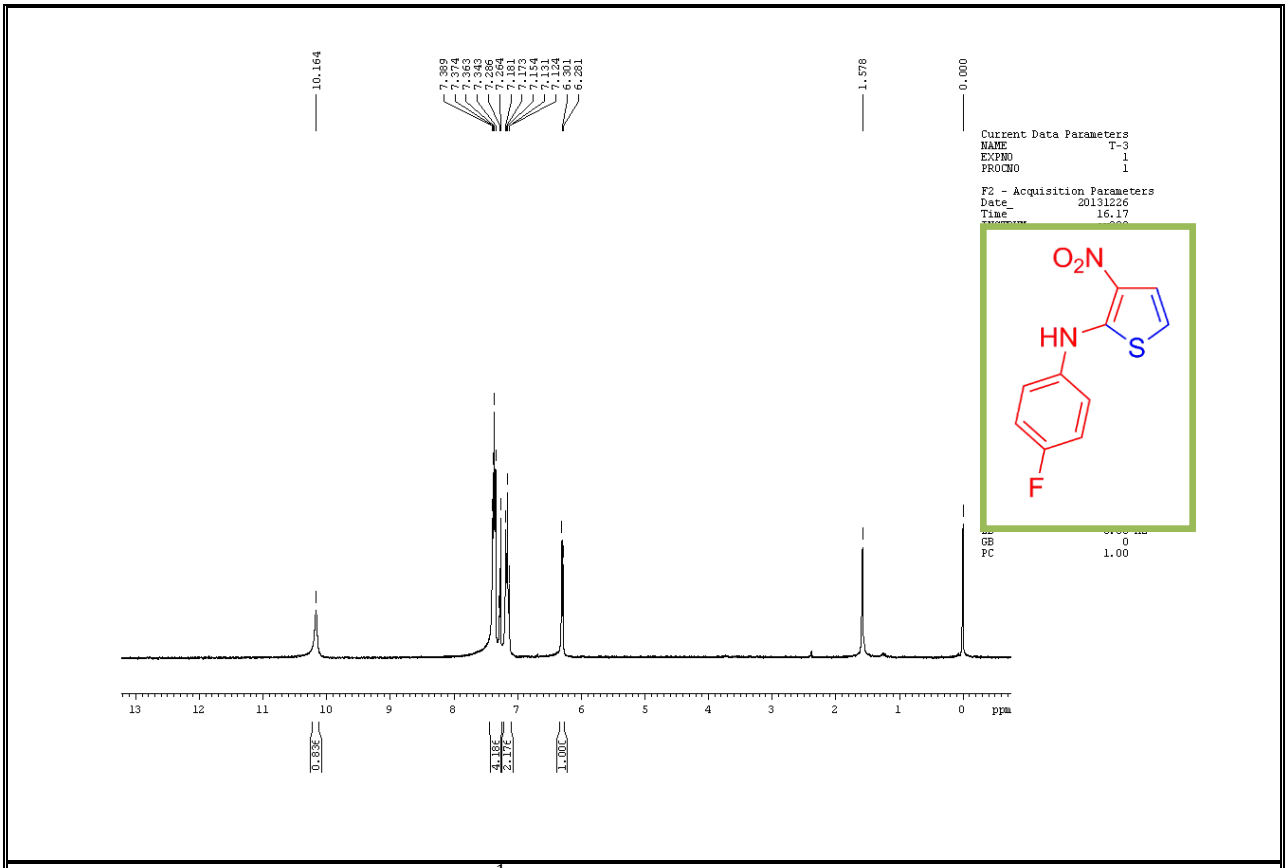



**Figure 19** $^{1}$H NMR Spectrum of **3a** ($CDCl_3$)

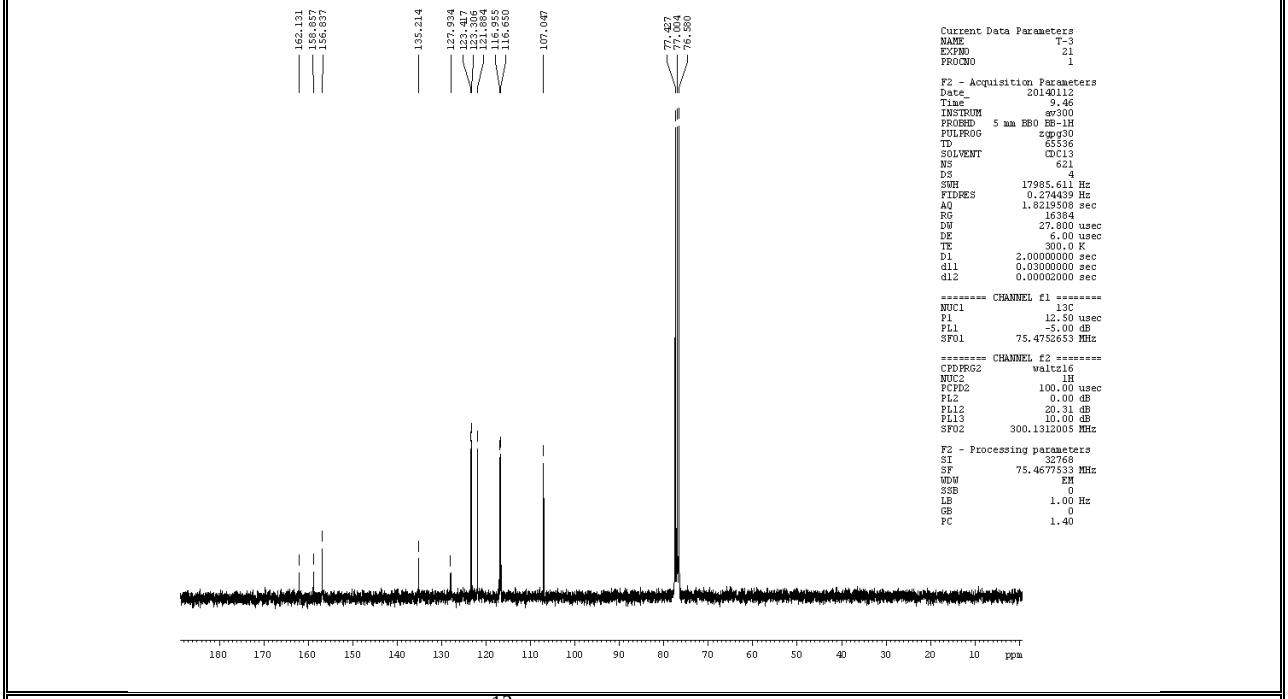



**Figure 20** $^{13}$C NMR Spectrum of **3a** ($CDCl_3$)

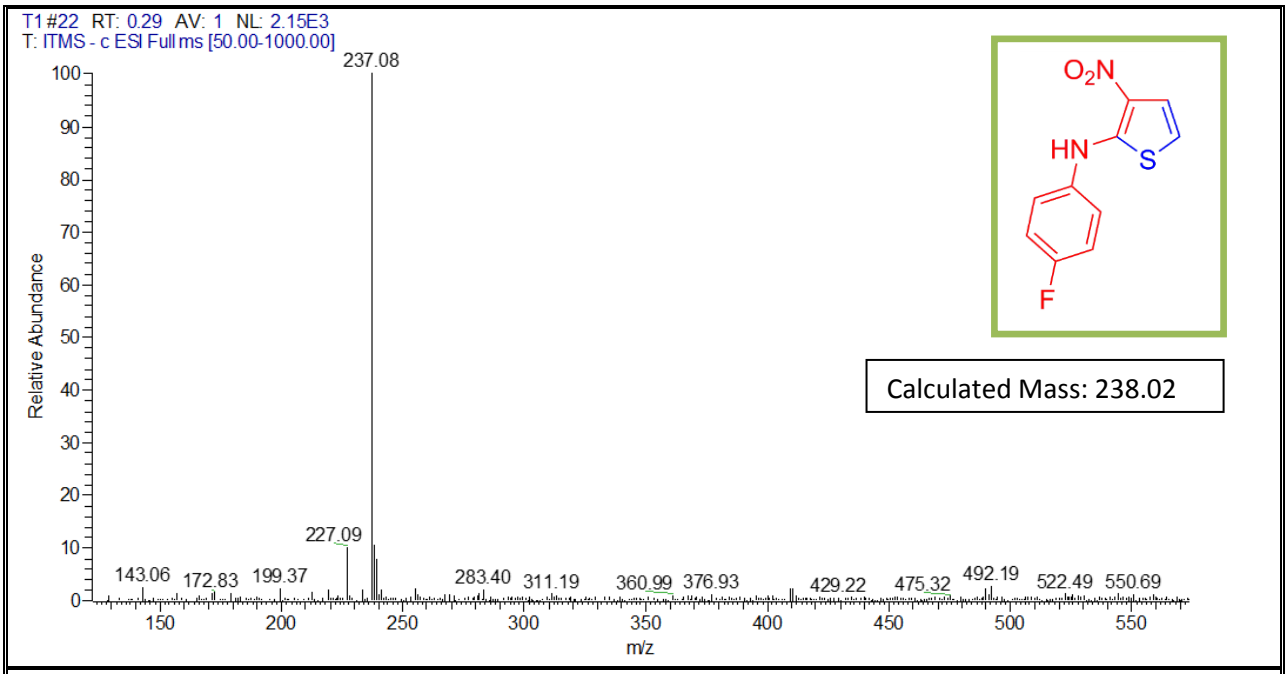



**Figure 21** ESI mass spectrum of Spectrum of **3a**

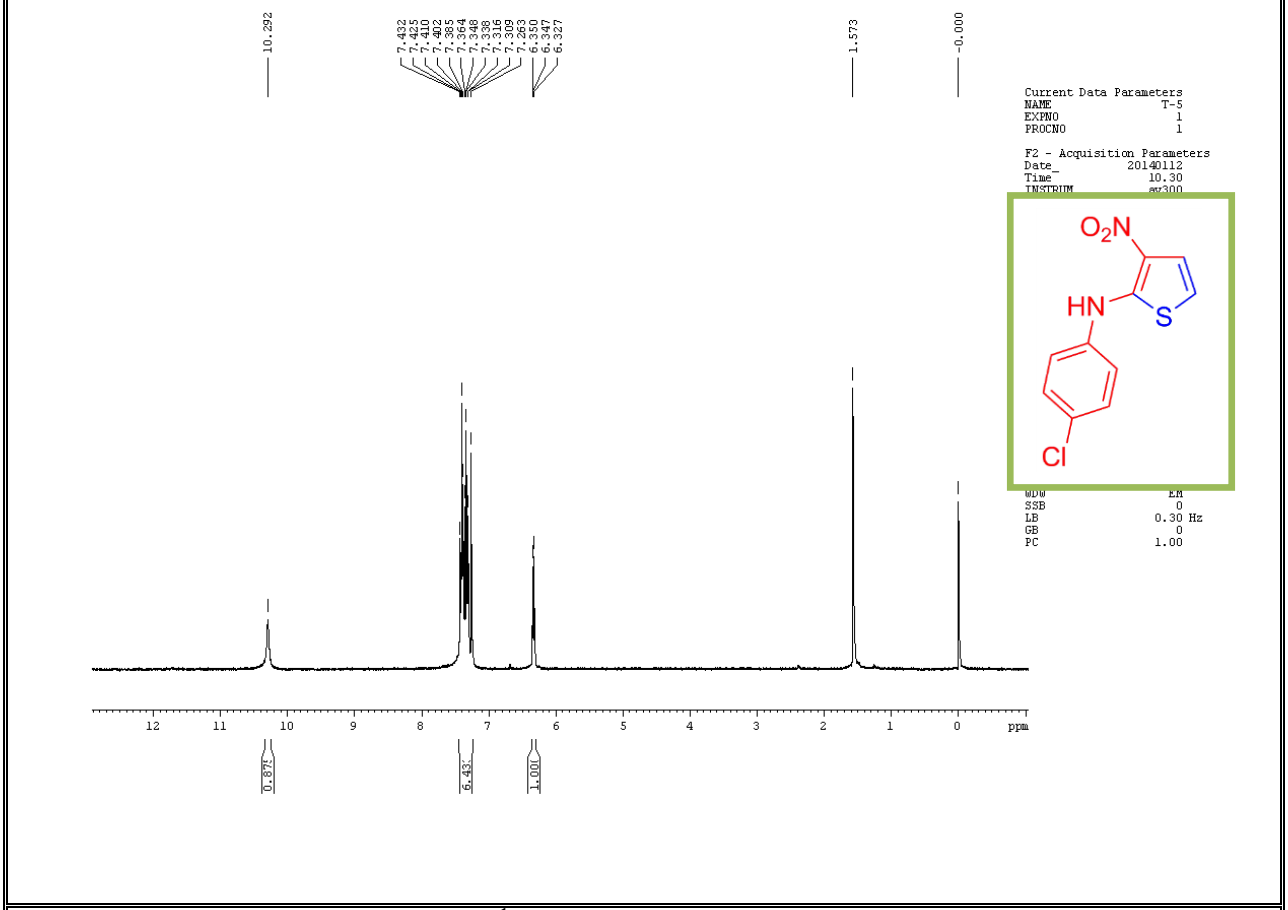



**Figure 22** $^{1}$H NMR Spectrum of **3b**($CDCl_3$)

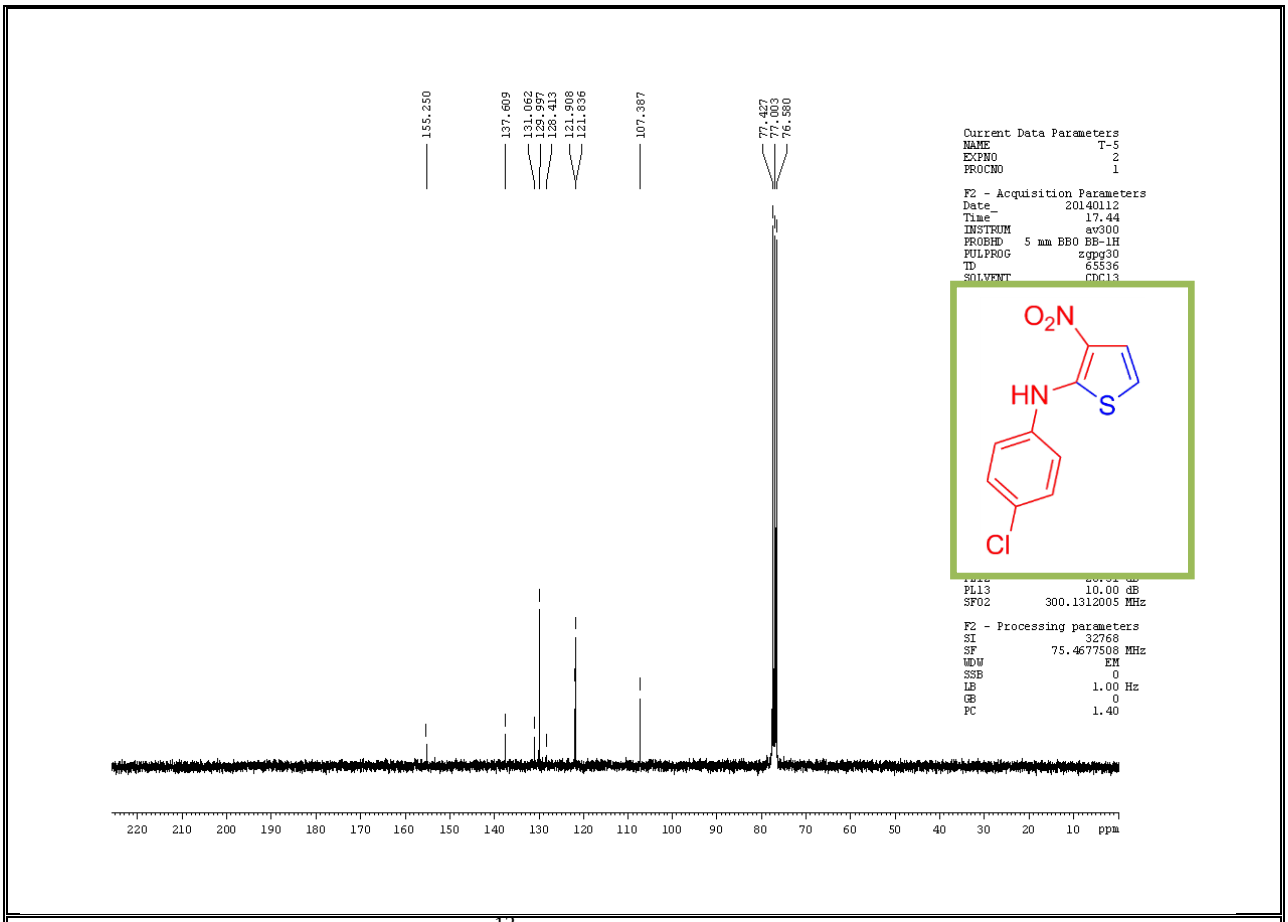



**Figure 23** $^{13}$C NMR Spectrum of **3b**($CDCl_3$)

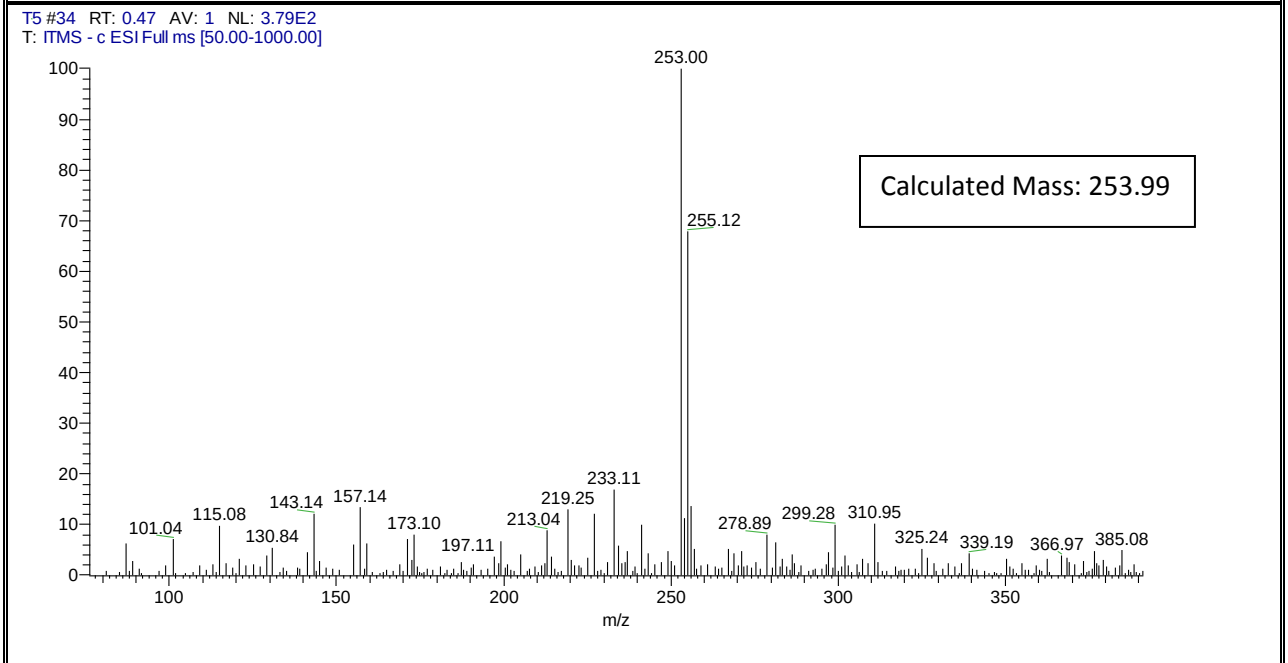



**Figure 24** ESI mass spectrum of Spectrum of **3b**

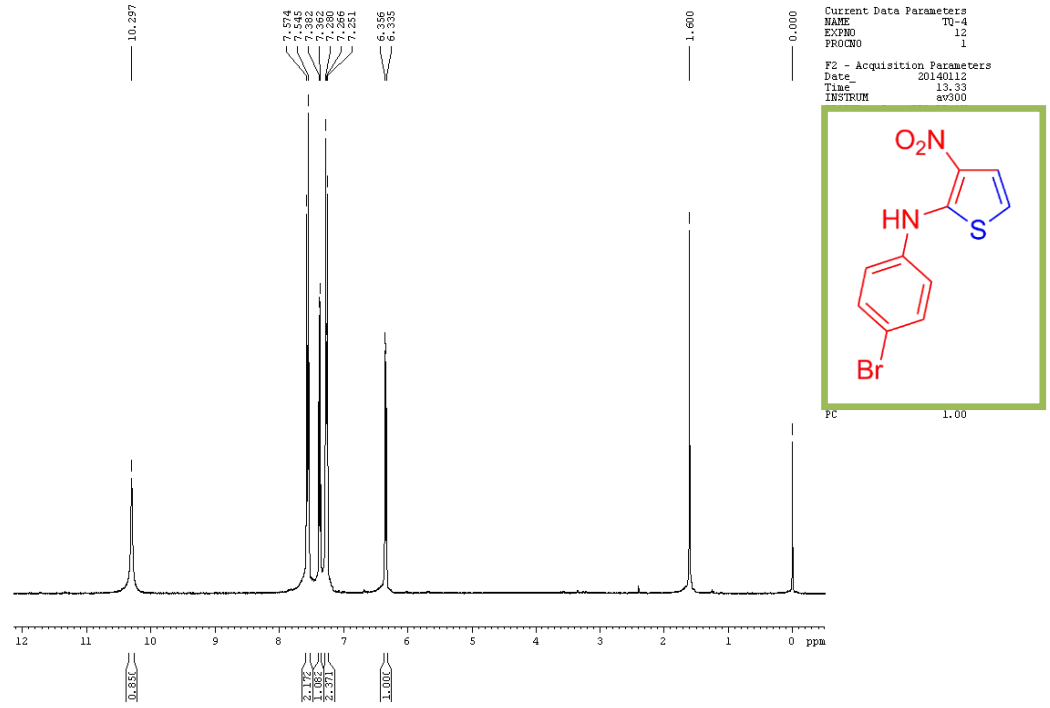



**Figure 25** $^{1}$H NMR Spectrum of **3c**($CDCl_3$)

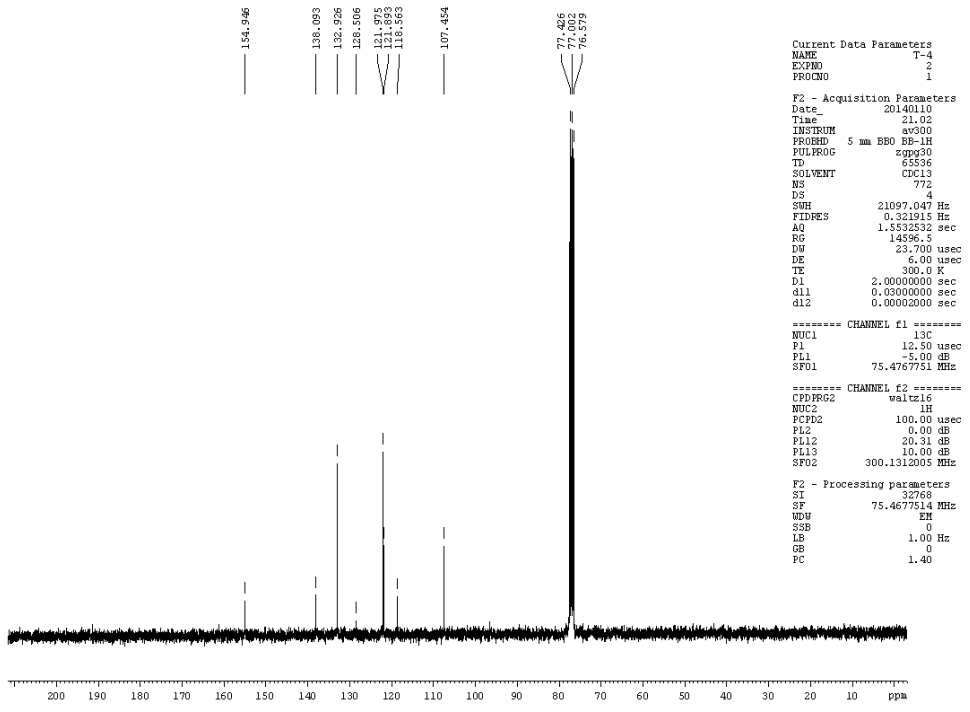



**Figure 26** $^{13}$C NMR Spectrum of **3c**($CDCl_3$)

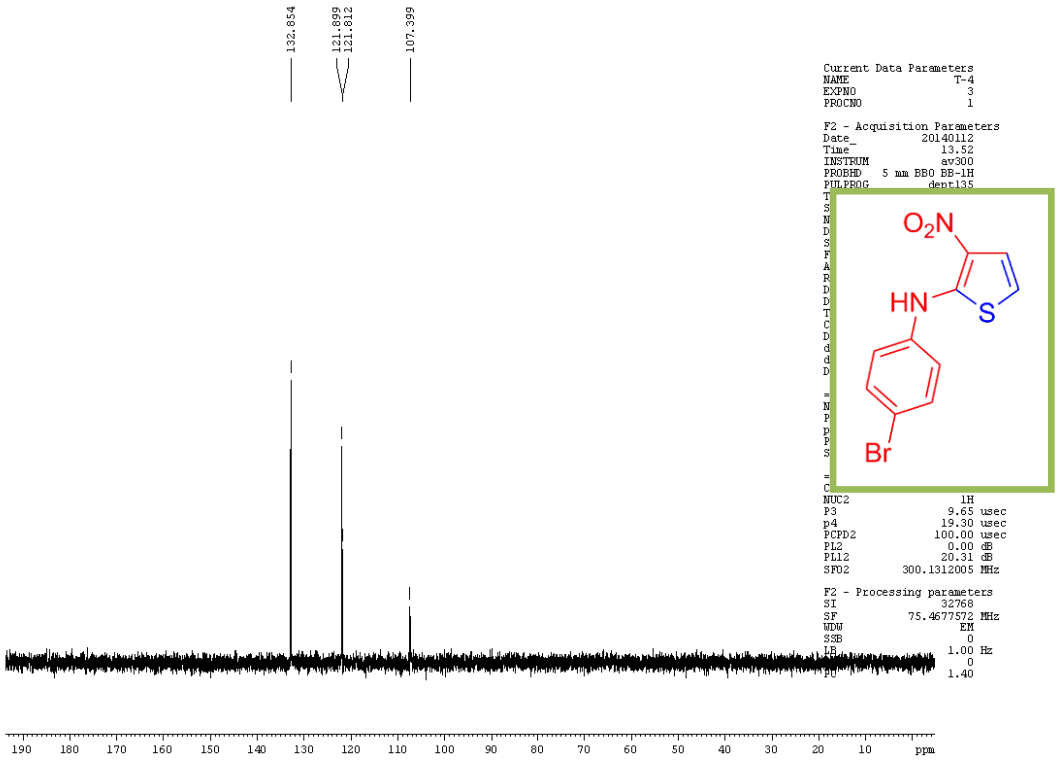



**Figure 27** DEPT Spectrum of **3c** ($CDCl_3$)

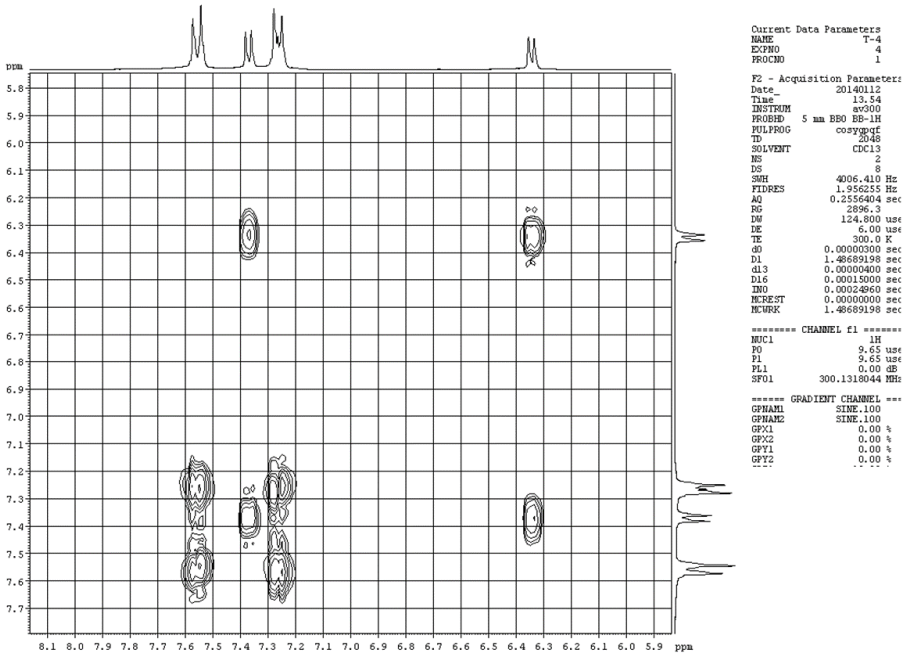



**Figure 28** H, H-COSY Spectrum of **3c** ($CDCl_3$)

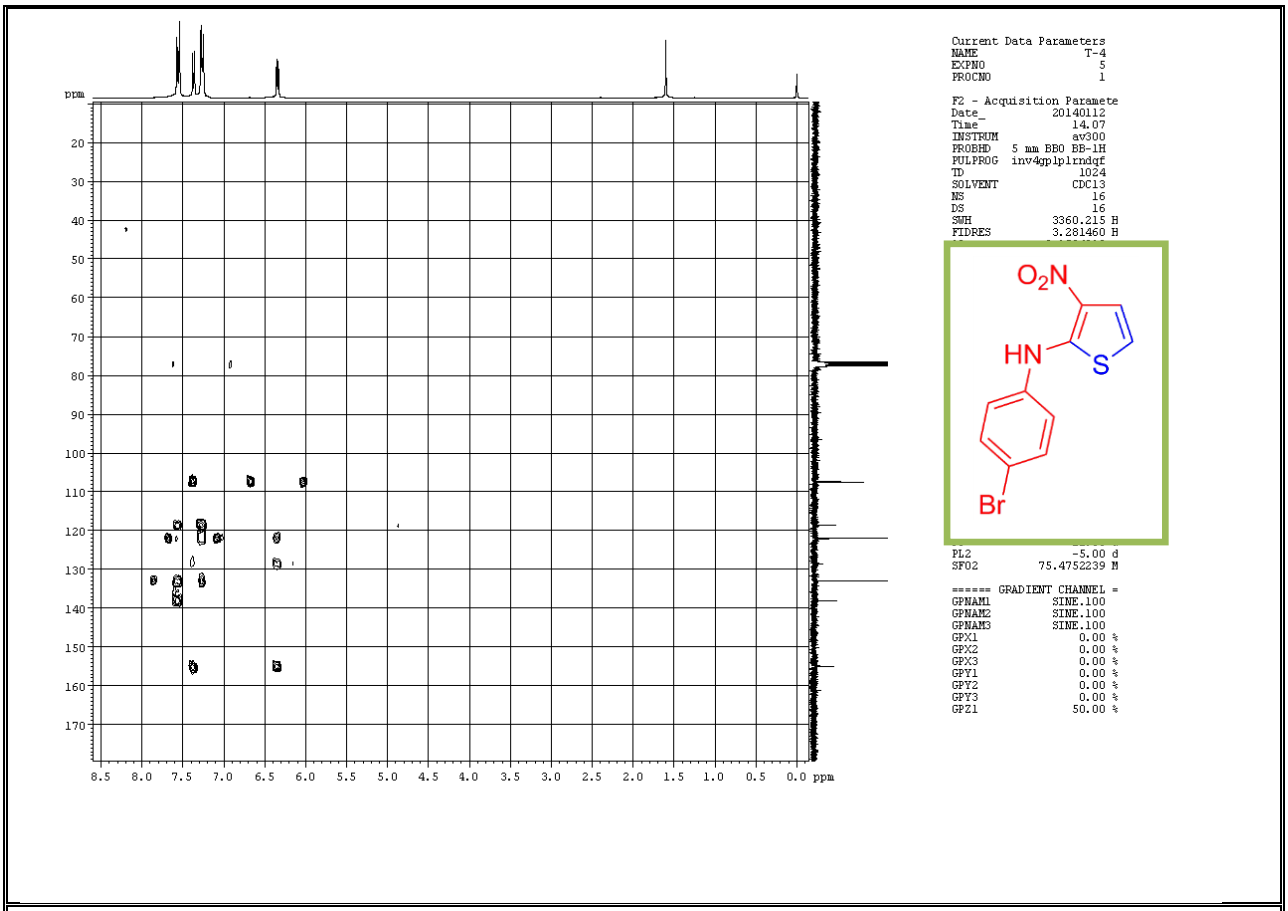



**Figure 29** HMBC Spectrum of **3c** ($CDCl_3$)

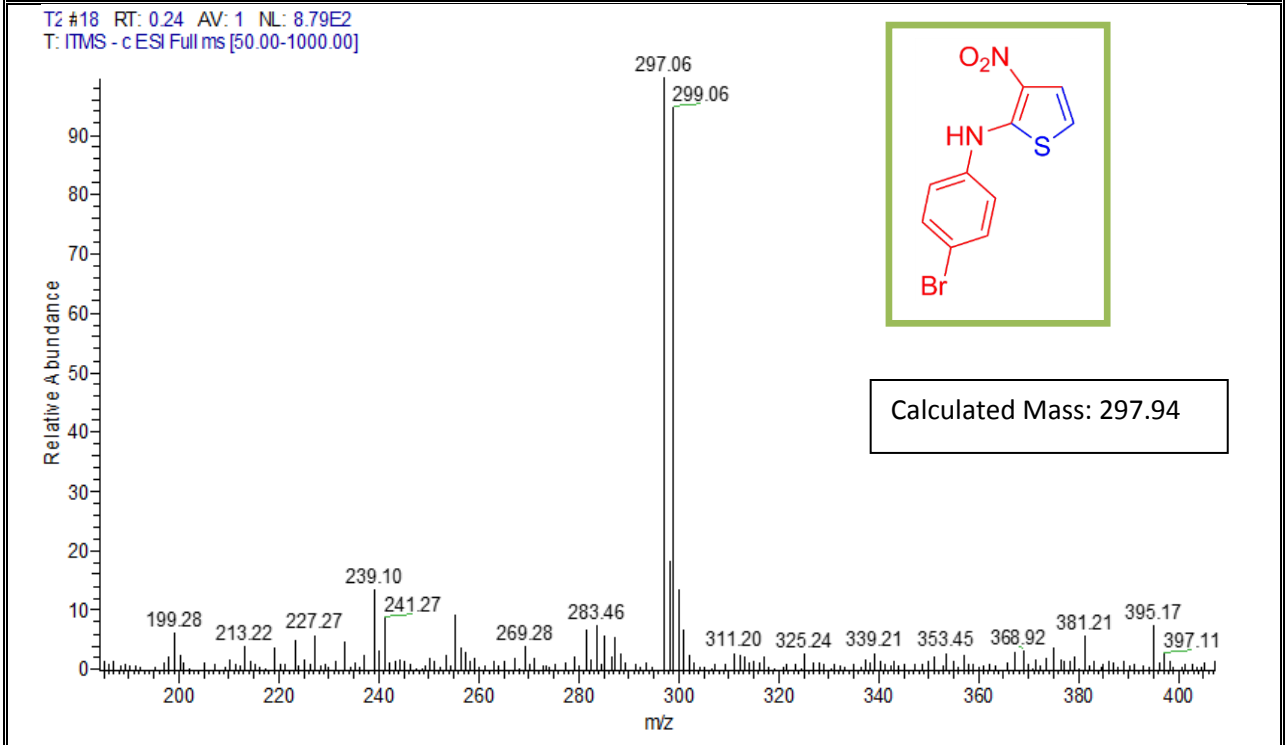



**Figure 30** ESI mass spectrum of Spectrum of **3c**

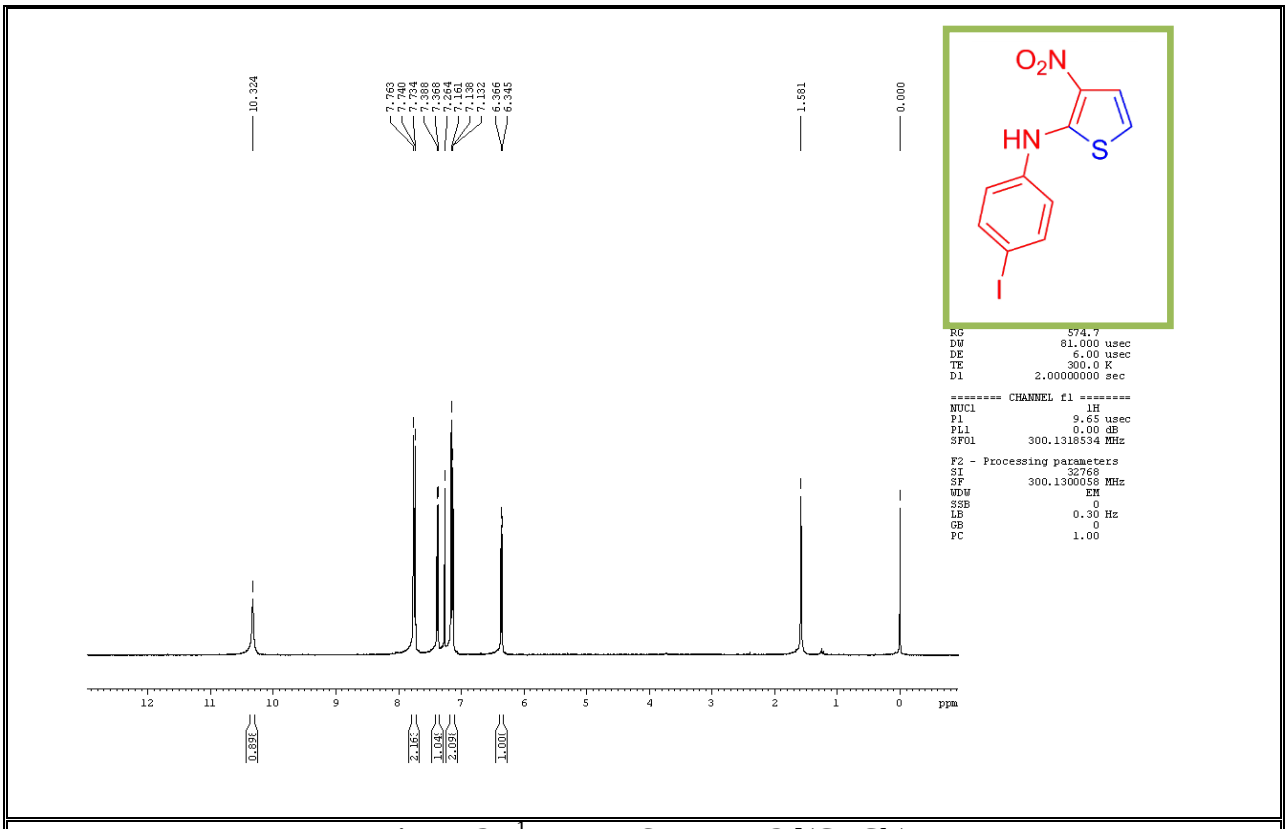



**Figure 31** $^{1}$H NMR Spectrum **3d**($CDCl_3$)

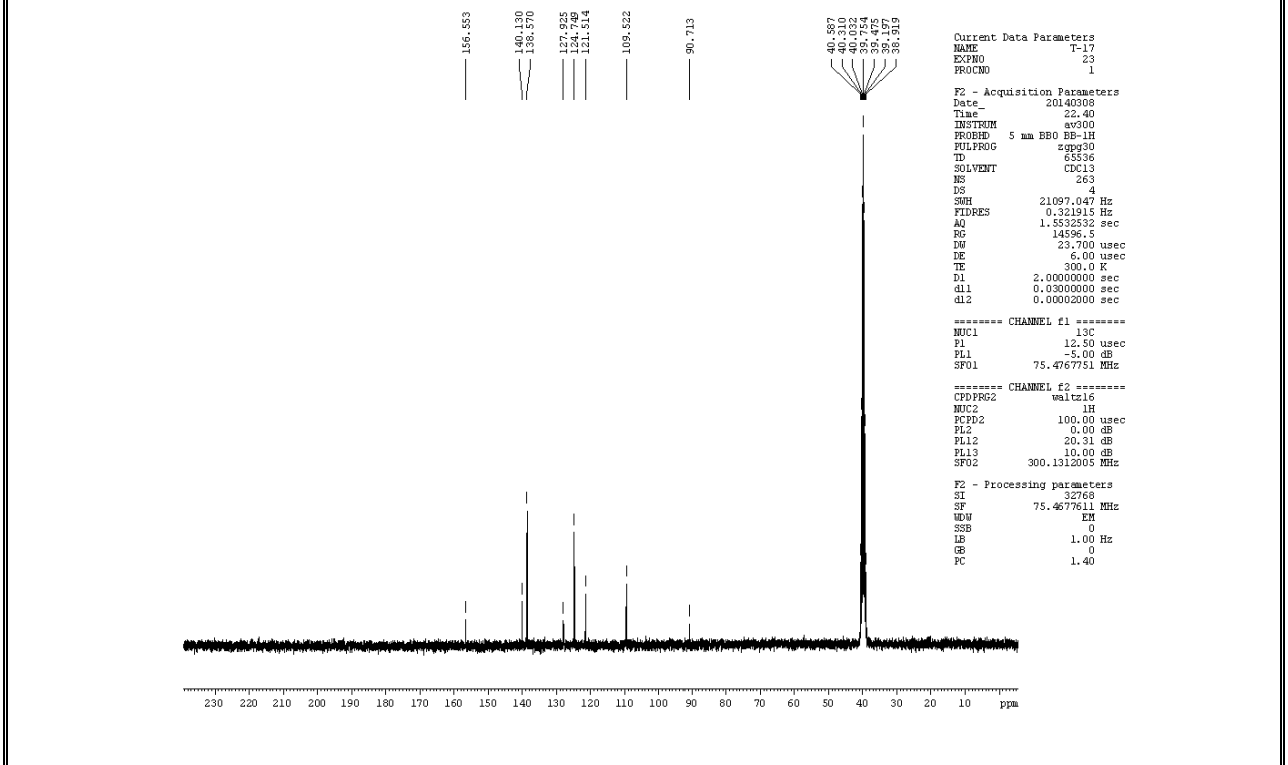



**Figure 32** $^{13}$C NMR Spectrum of **3d** (DMSO-$d^6$)

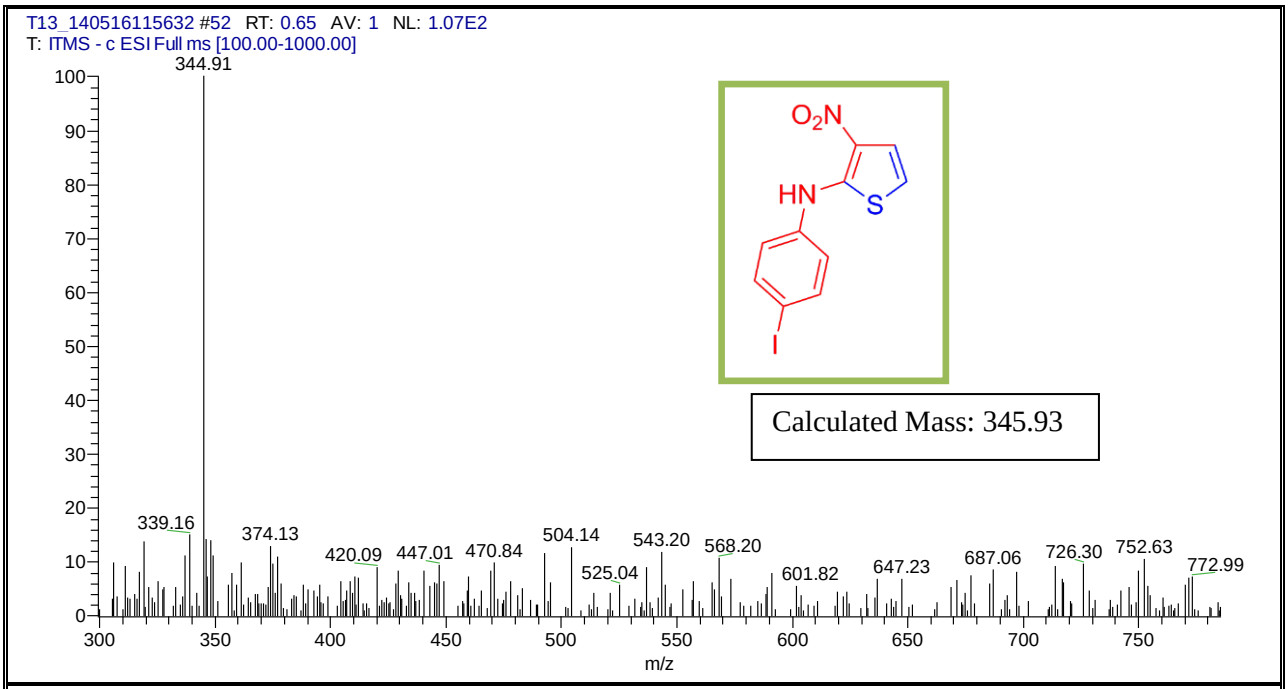



**Figure 33** ESI mass spectrum of **3d**

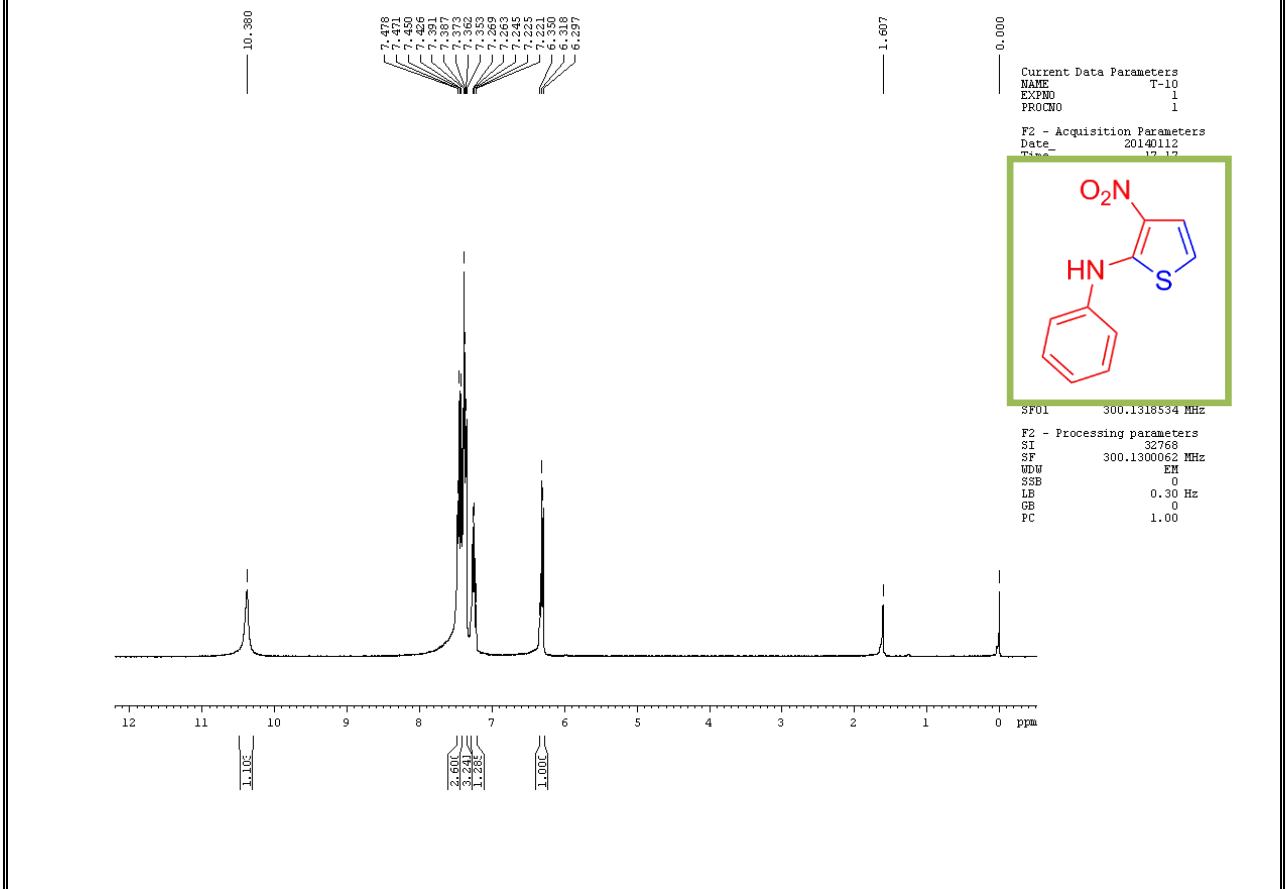



**Figure 34** $^{1}$H NMR Spectrum of **3e** ($CDCl_3$)

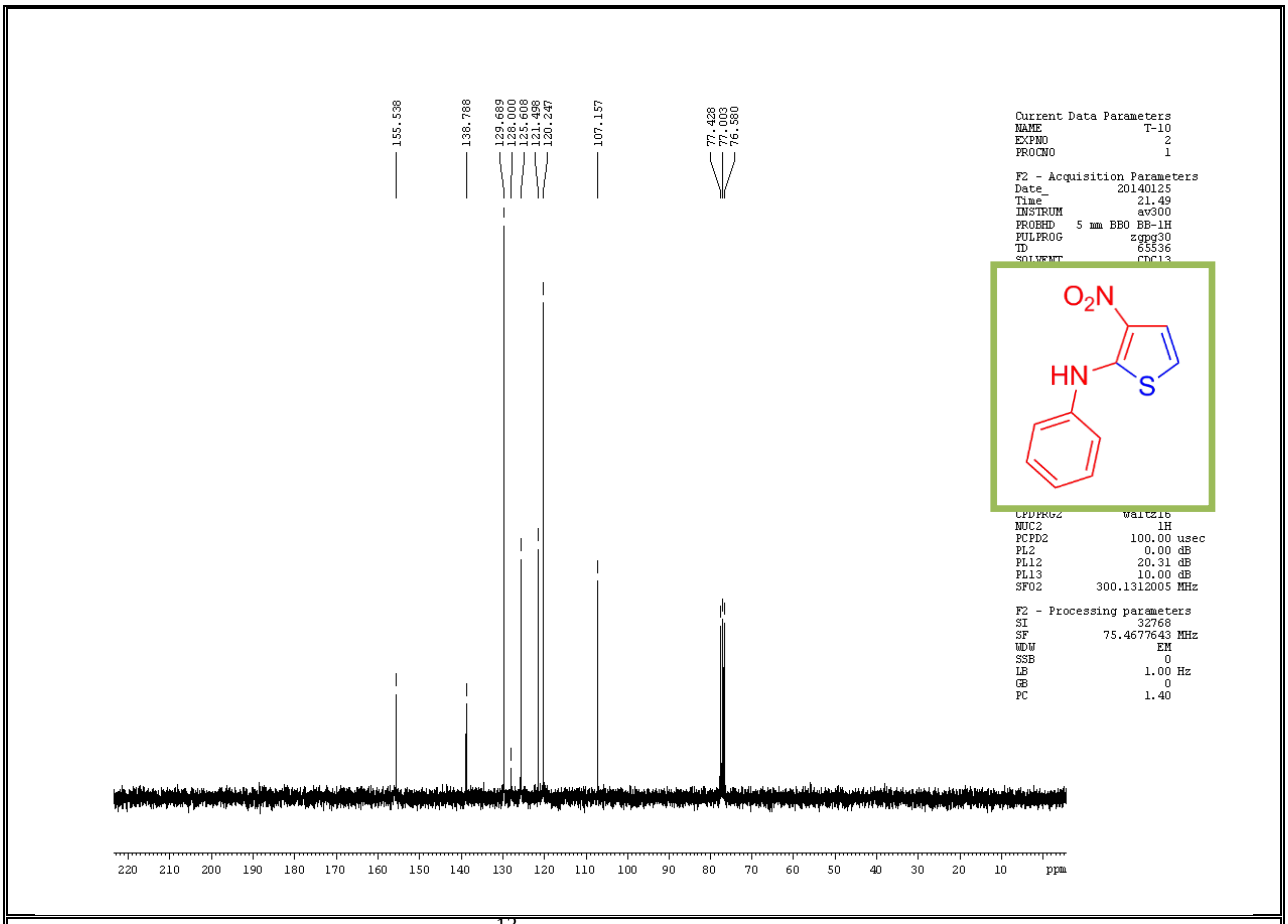



**Figure 35** $^{13}$C NMR Spectrum of **3e**($CDCl_3$)

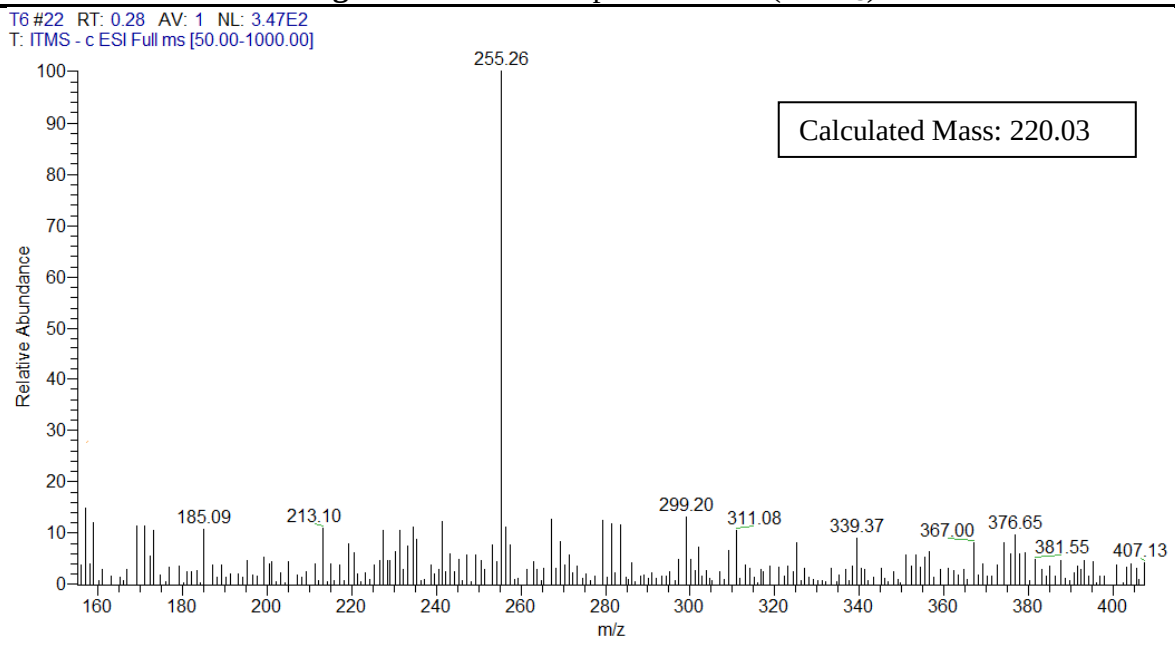



**Figure 36** ESI mass spectrum of Spectrum of **3e**

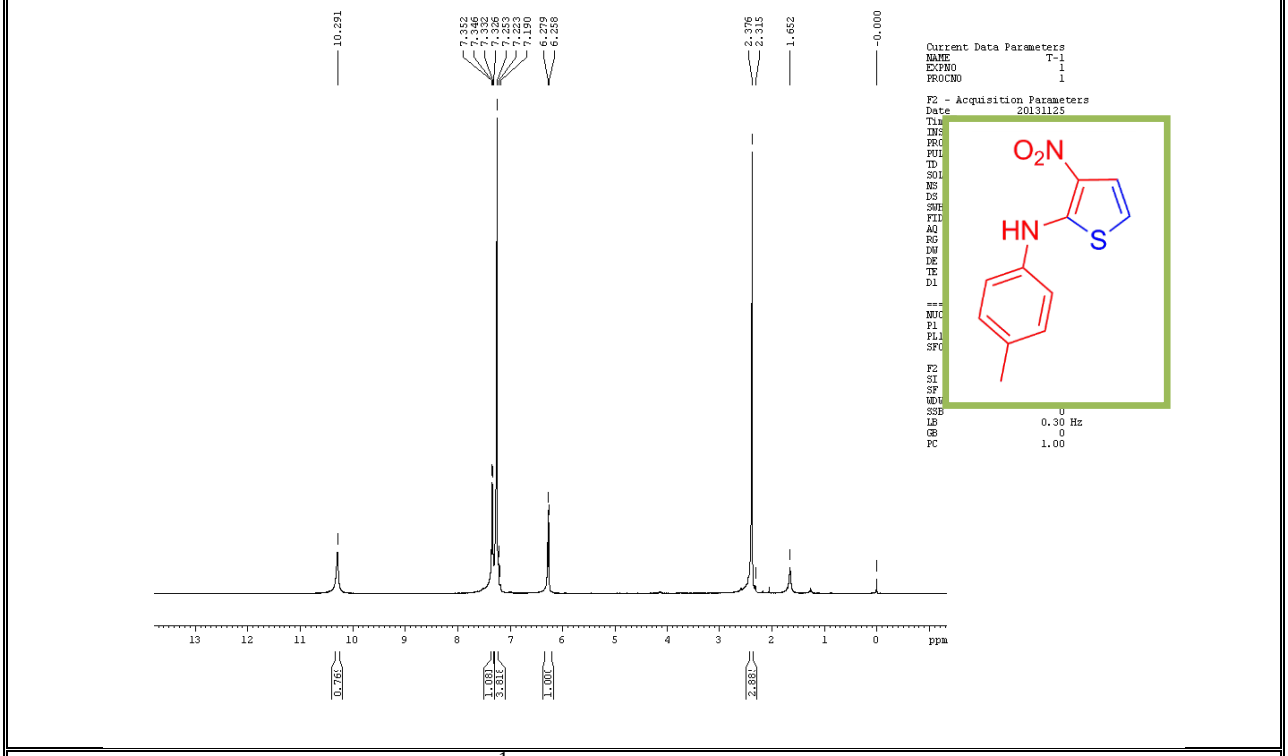



**Figure 37** $^{1}$H NMR Spectrum of **3f** ($CDCl_3$)

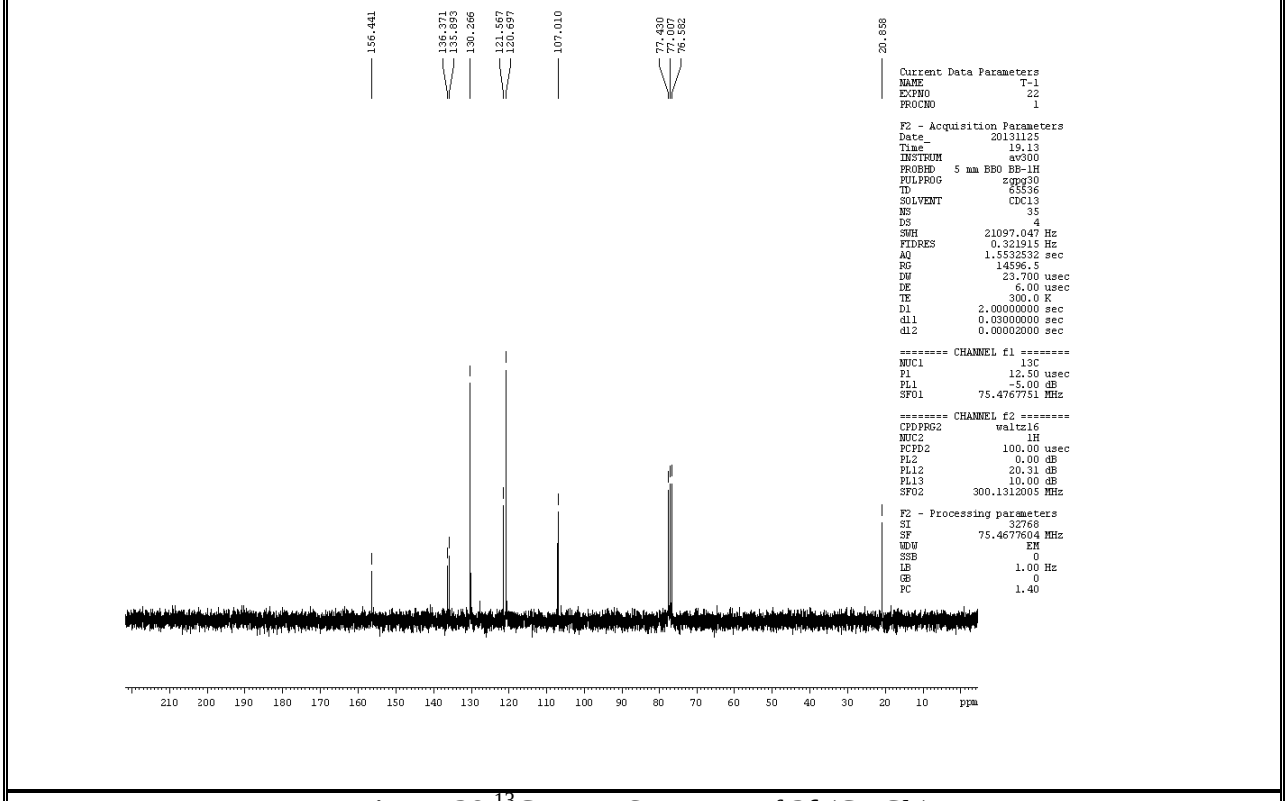



**Figure 38** $^{13}$C NMR Spectrum of **3f** ($CDCl_3$)

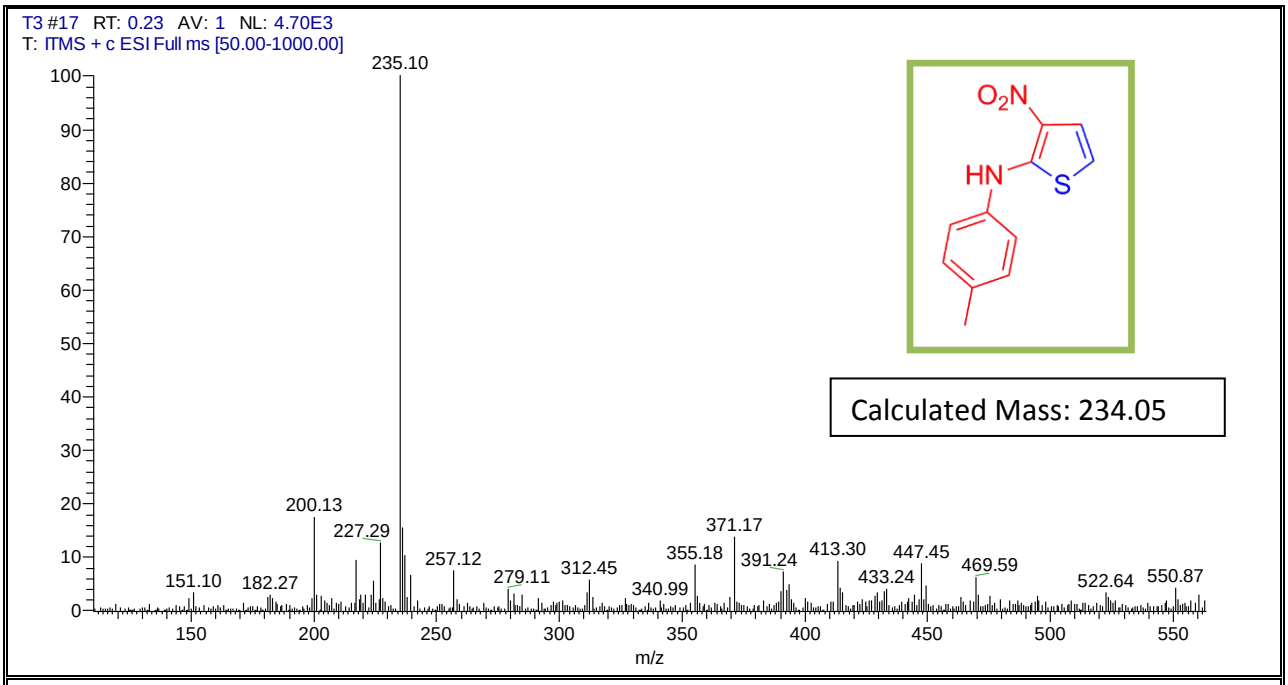



**Figure 39** ESI mass spectrum of Spectrum of **3f**

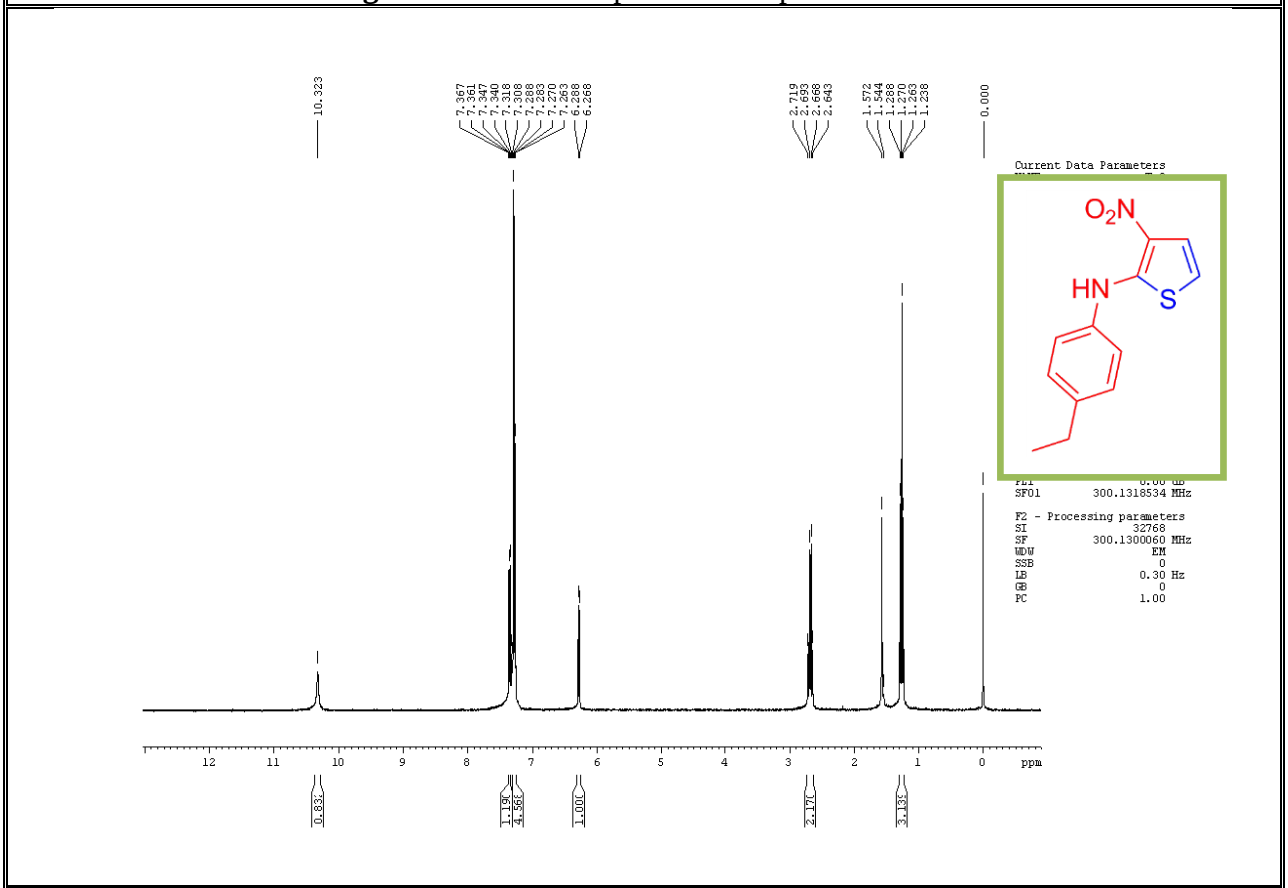



**Figure 40** $^{1}$H NMR Spectrum **3g** ($CDCl_3$)

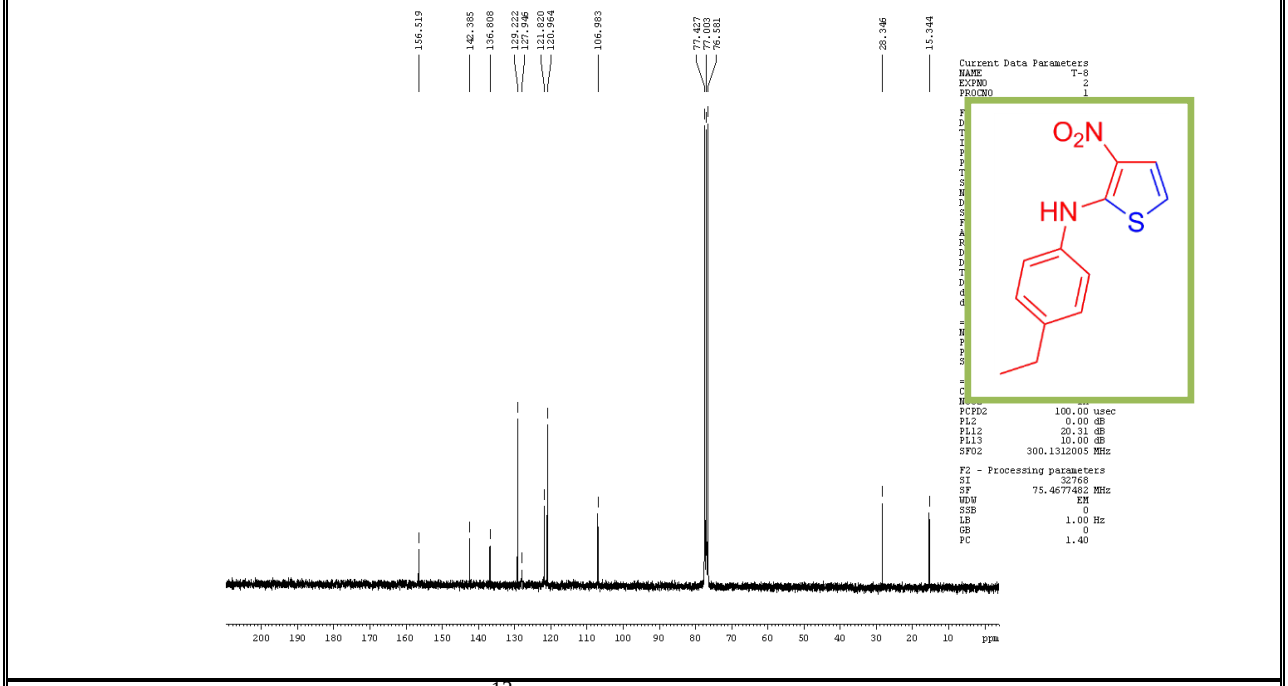



**Figure 41** $^{13}$C NMR Spectrum of **3g** ($CDCl_3$)

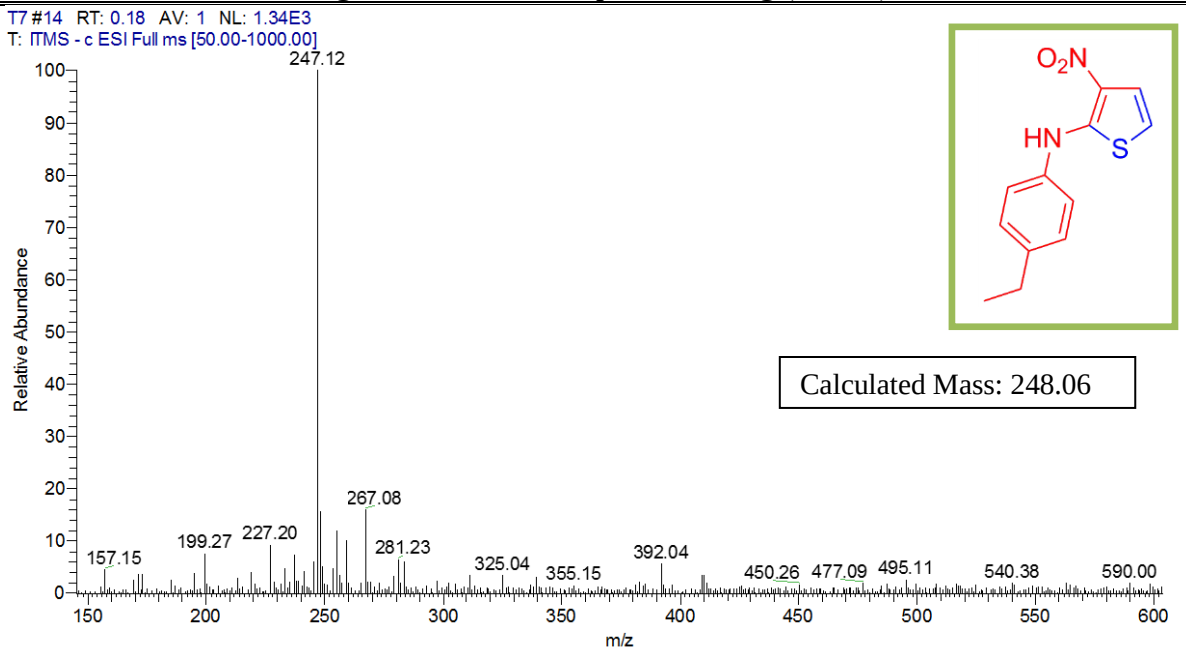



**Figure 42** ESI mass spectrum of Spectrum of **3g**

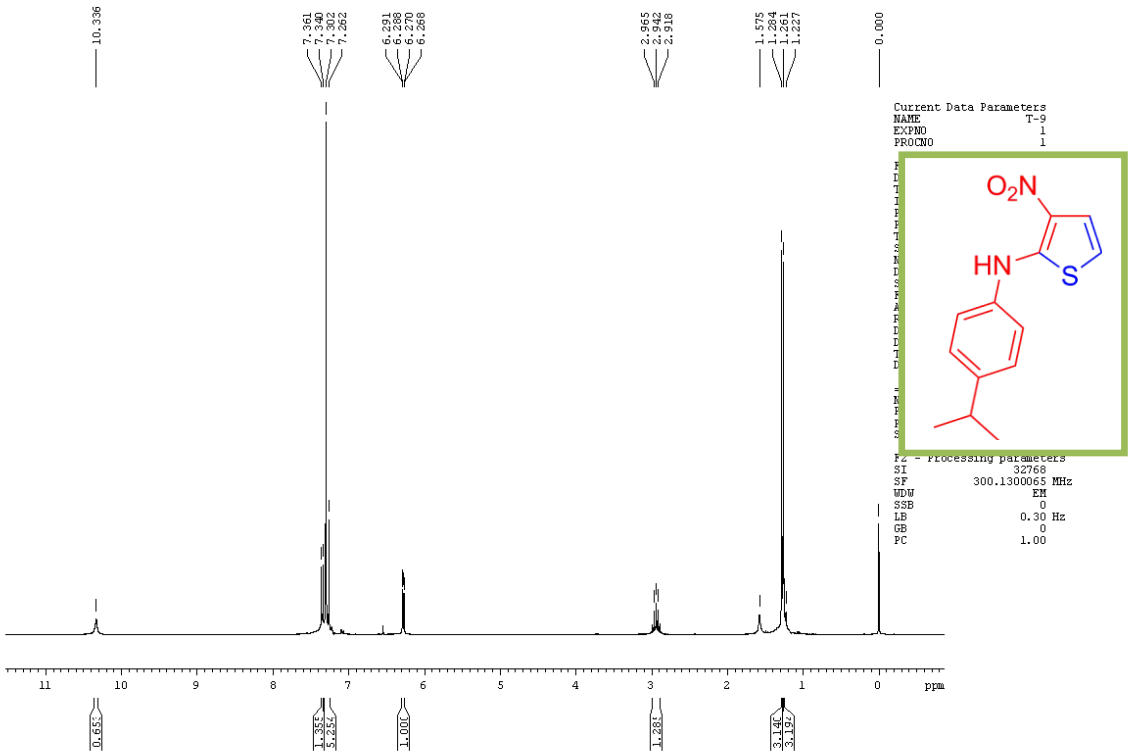



**Figure 43** $^{1}$H NMR Spectrum **3h** ($CDCl_3$)

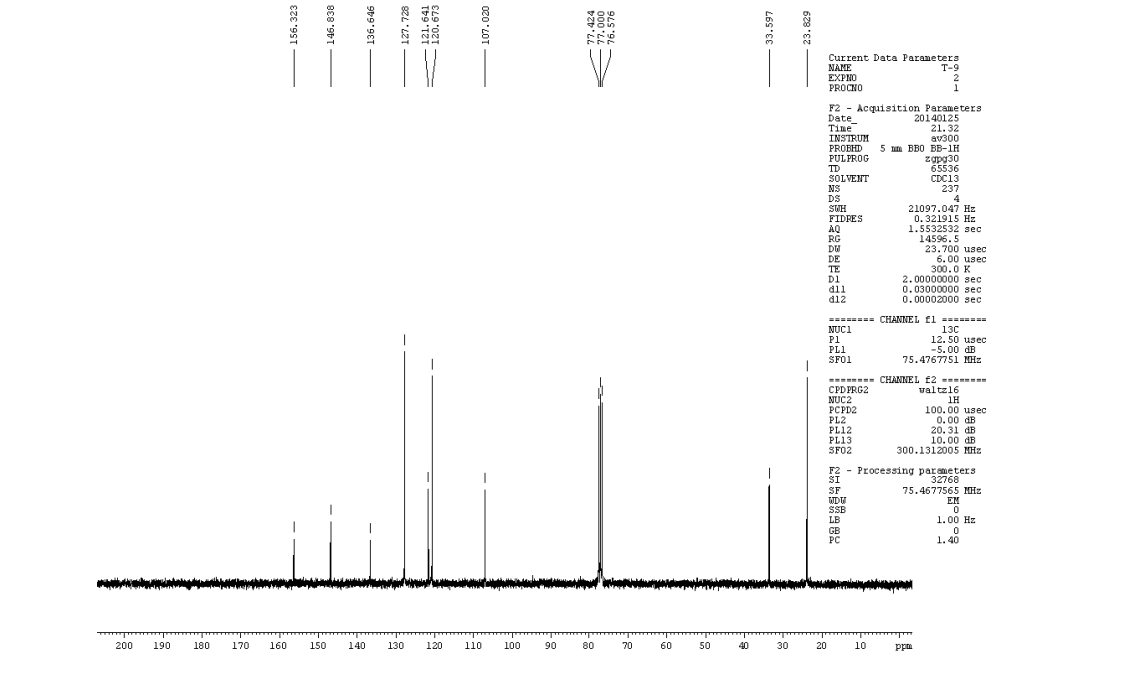



**Figure 44** $^{13}$C NMR Spectrum of **3h** ($CDCl_3$)

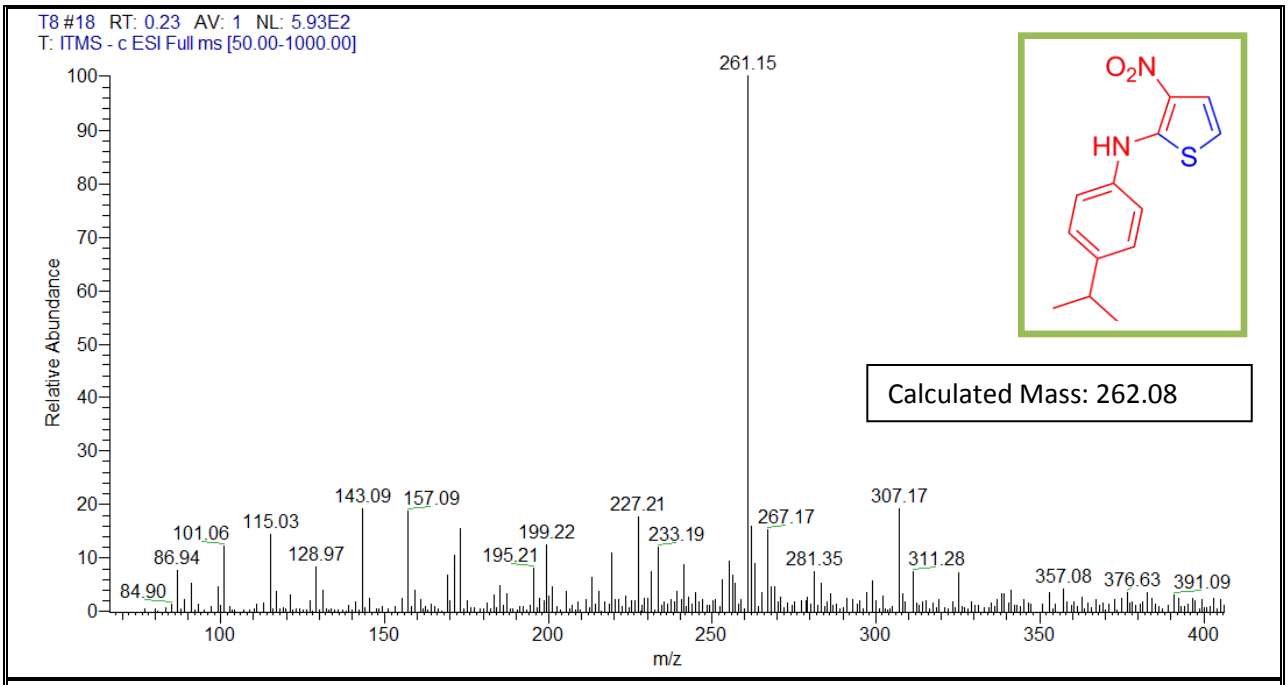



**Figure 45** ESI mass spectrum of Spectrum of **3h**

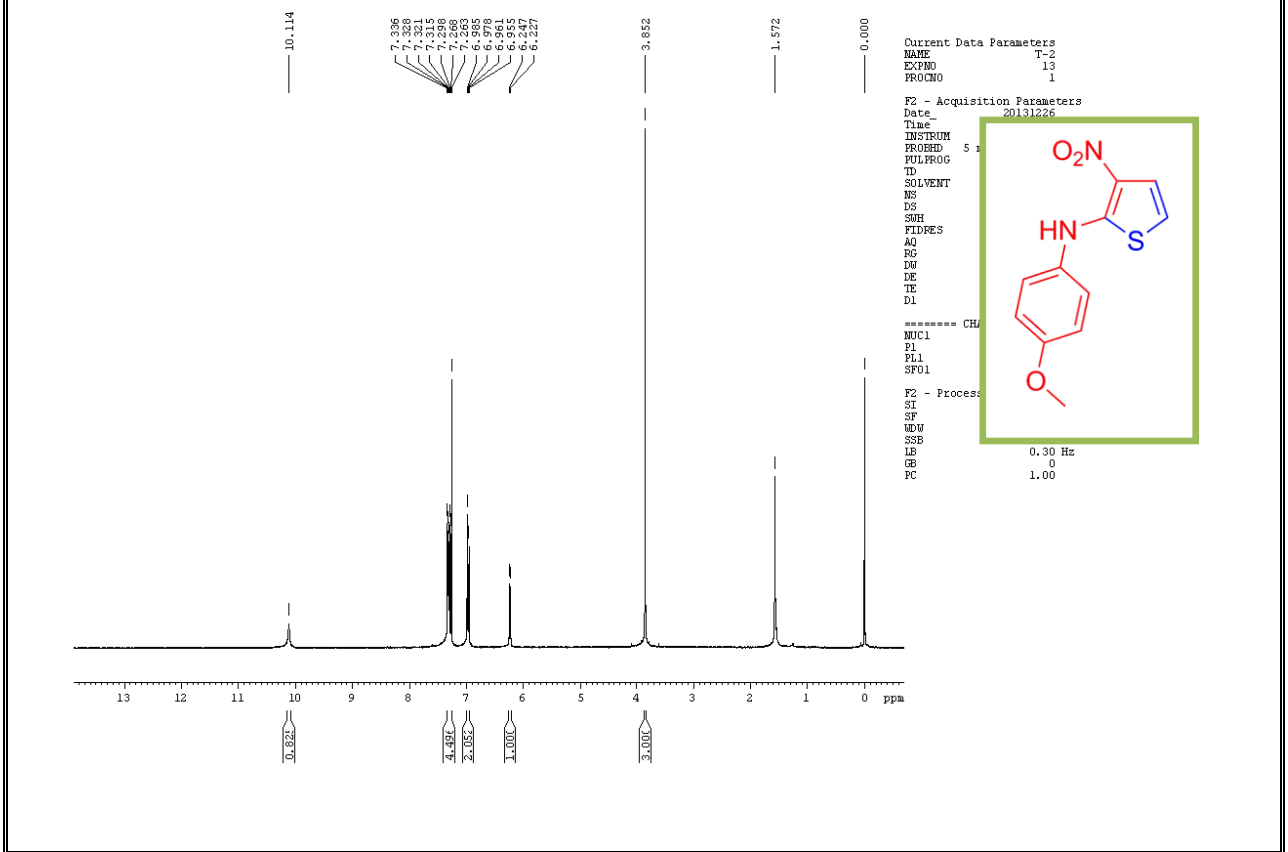



**Figure 46** $^{1}$H NMR Spectrum **3i** ($CDCl_3$)

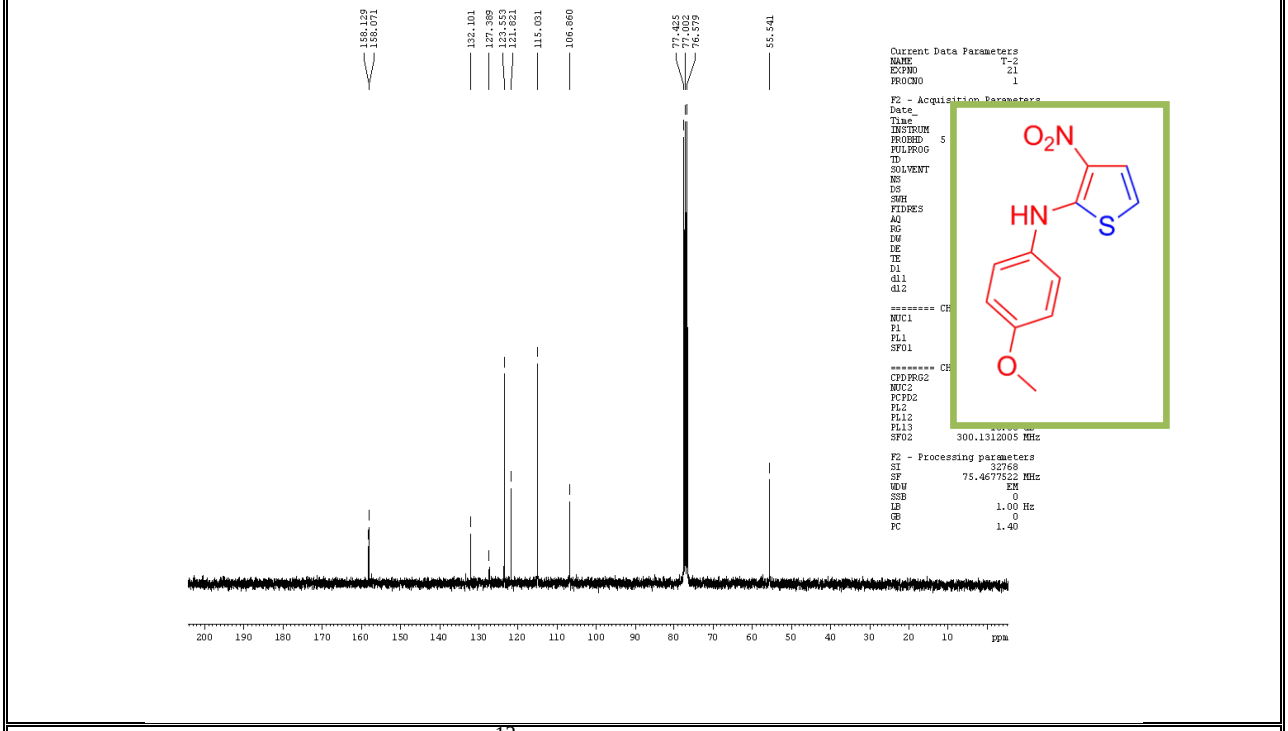



**Figure 47** $^{13}$C NMR Spectrum of **3i** ($CDCl_3$)

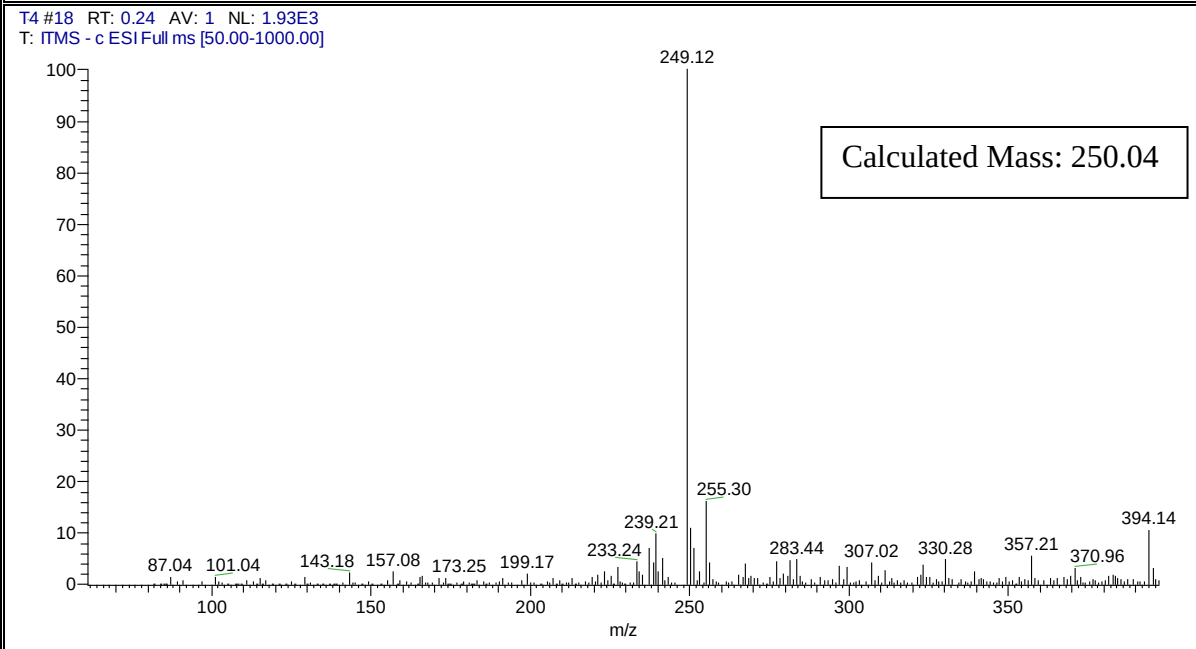



**Figure 48** ESI mass spectrum of Spectrum of **3i**

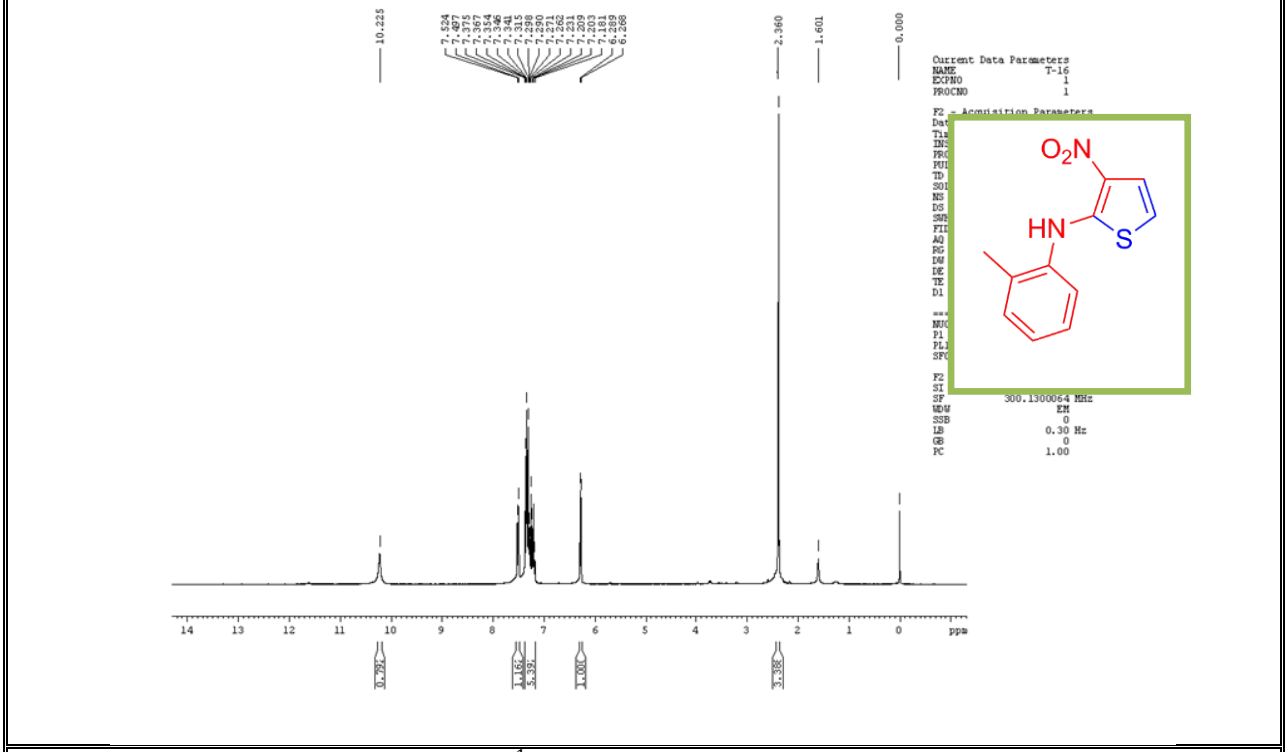



**Figure 49** $^{1}$H NMR Spectrum **3j** ($CDCl_3$)

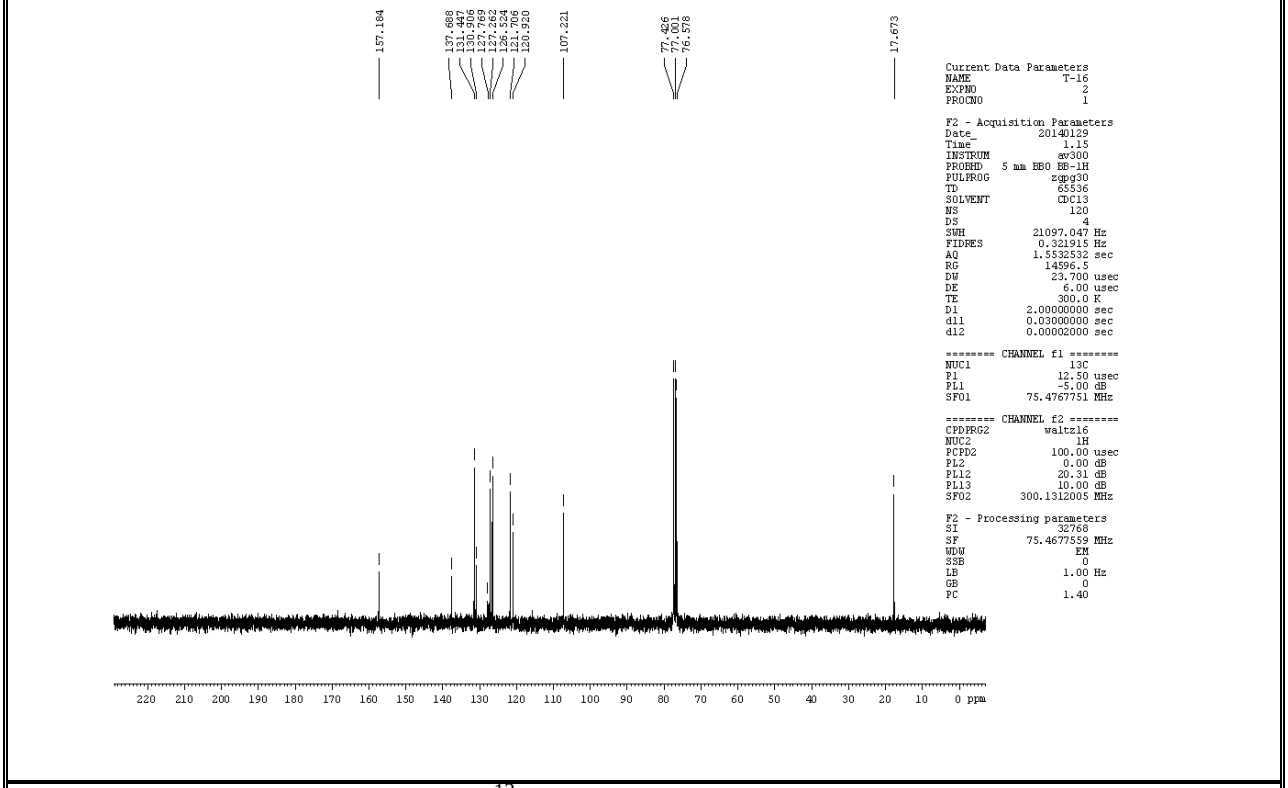



**Figure 50** $^{13}$C NMR Spectrum of **3j** ($CDCl_3$)

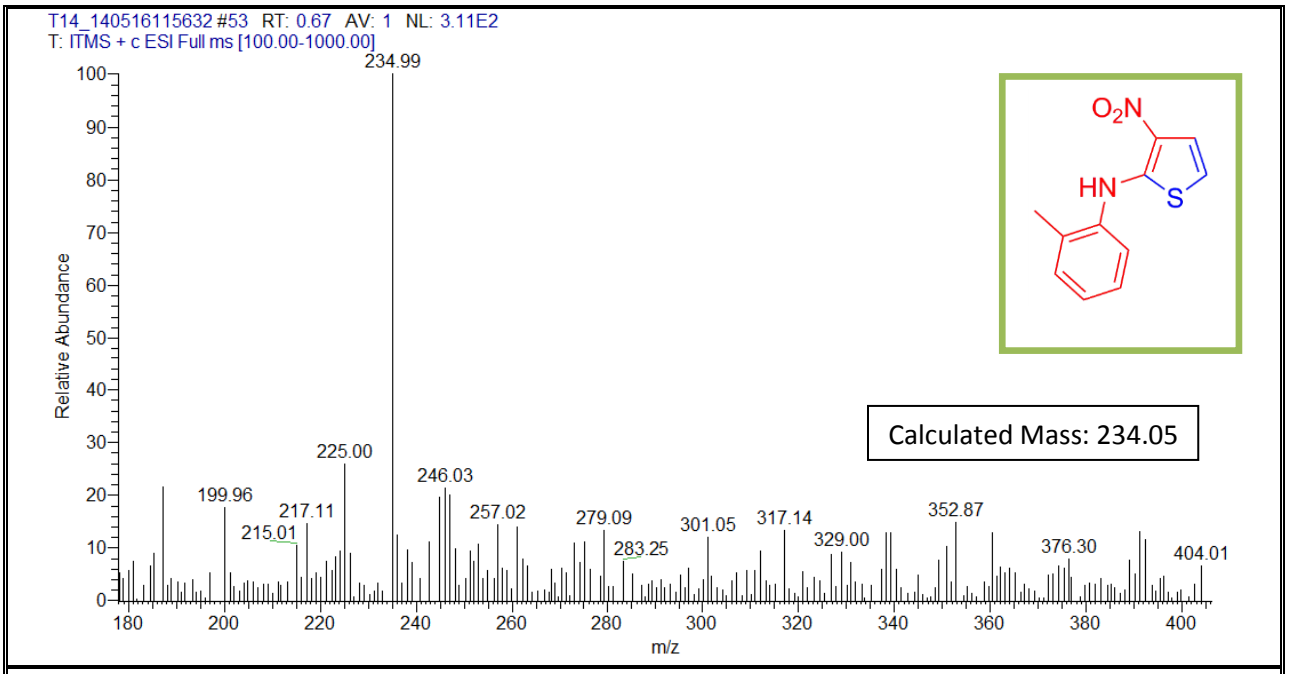



**Figure 51** ESI mass spectrum of Spectrum of **3j**

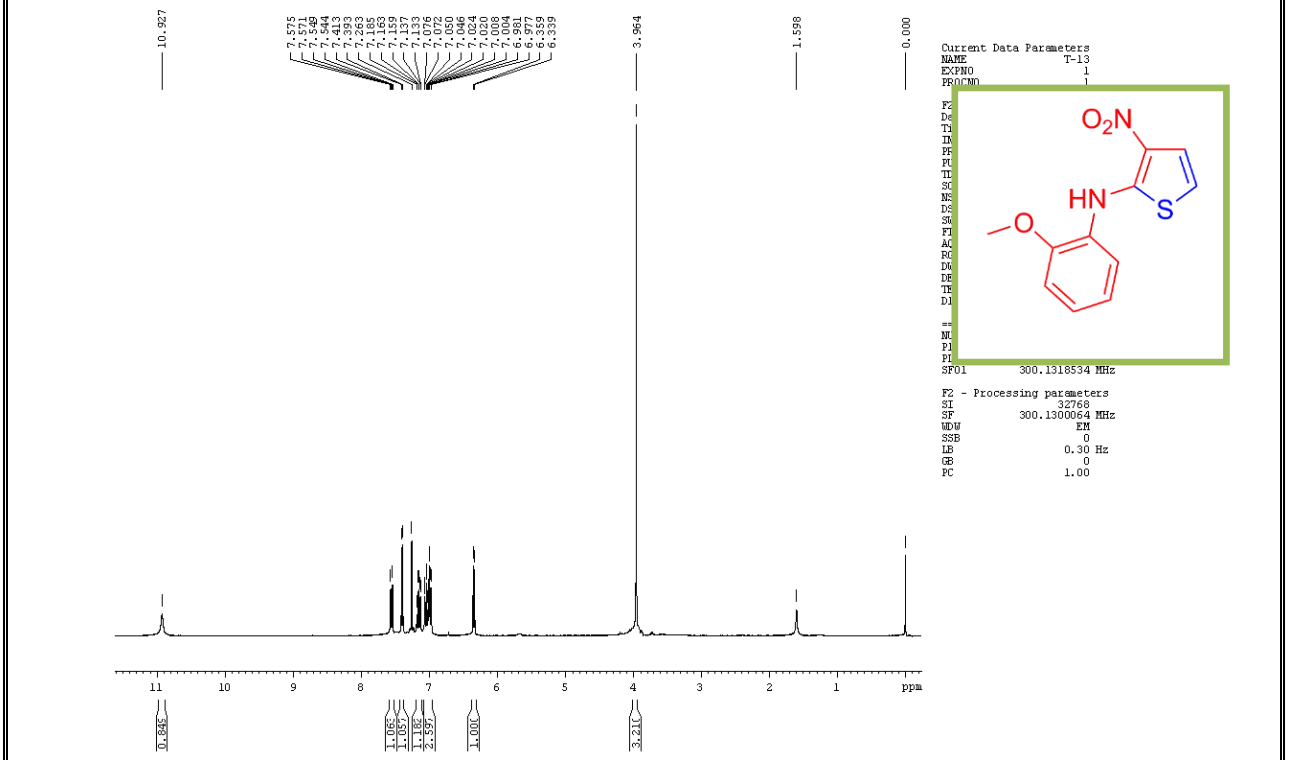



**Figure 52** $^{1}$H NMR Spectrum **3k** ($CDCl_3$)

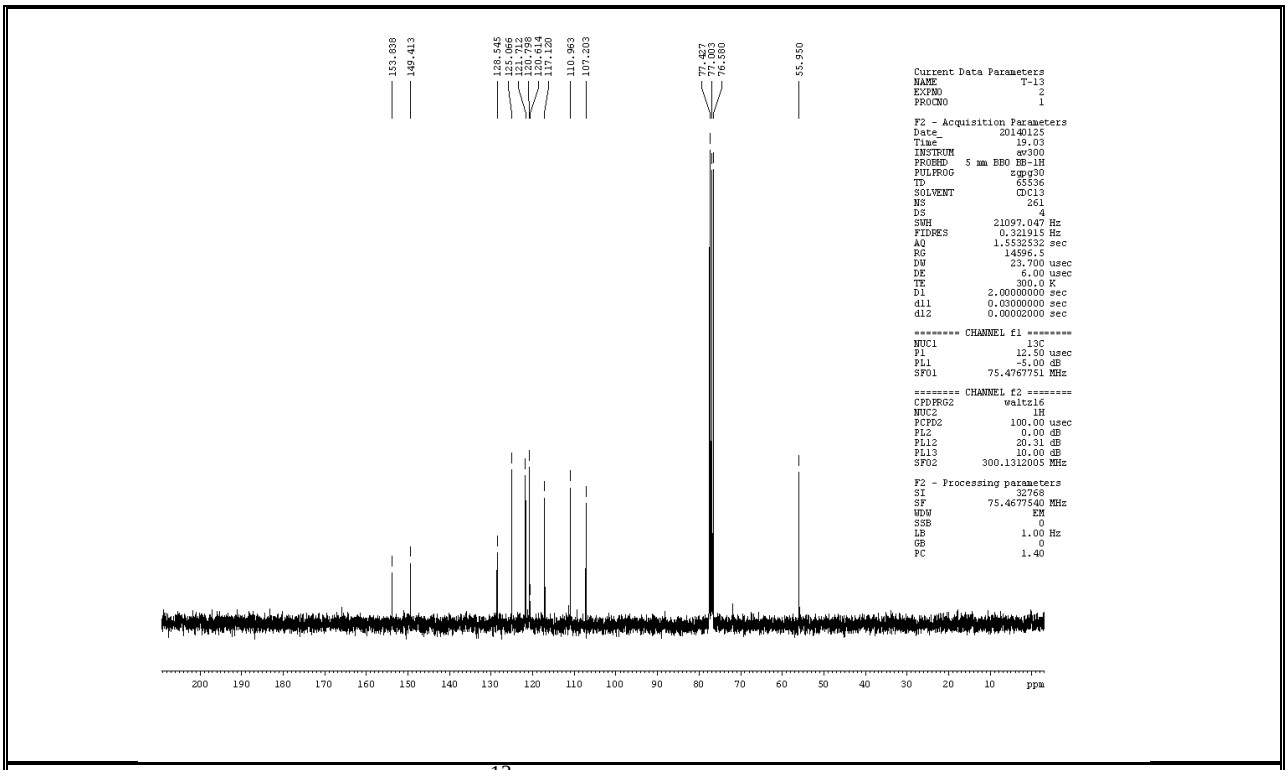



**Figure 53** $^{13}$C NMR Spectrum of **3k** ($CDCl_3$)

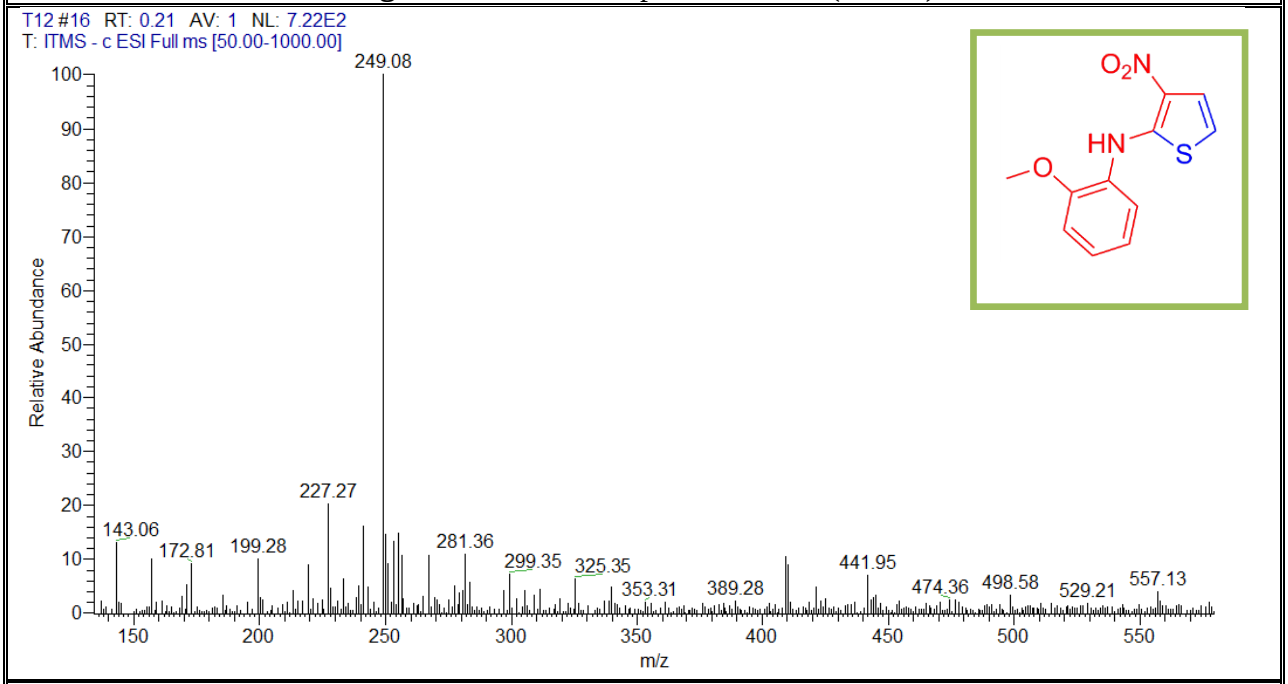



**Figure 54** ESI mass spectrum of Spectrum of **3k**

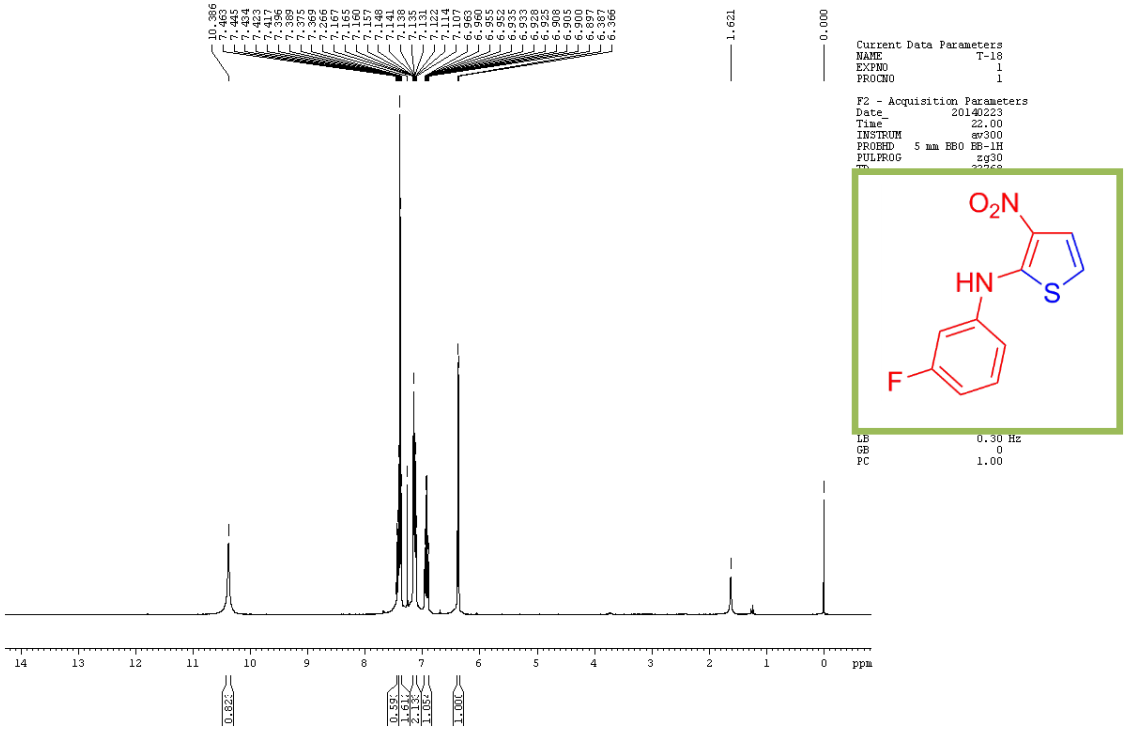



**Figure 55** $^{1}$H NMR Spectrum **3l** ($CDCl_3$)

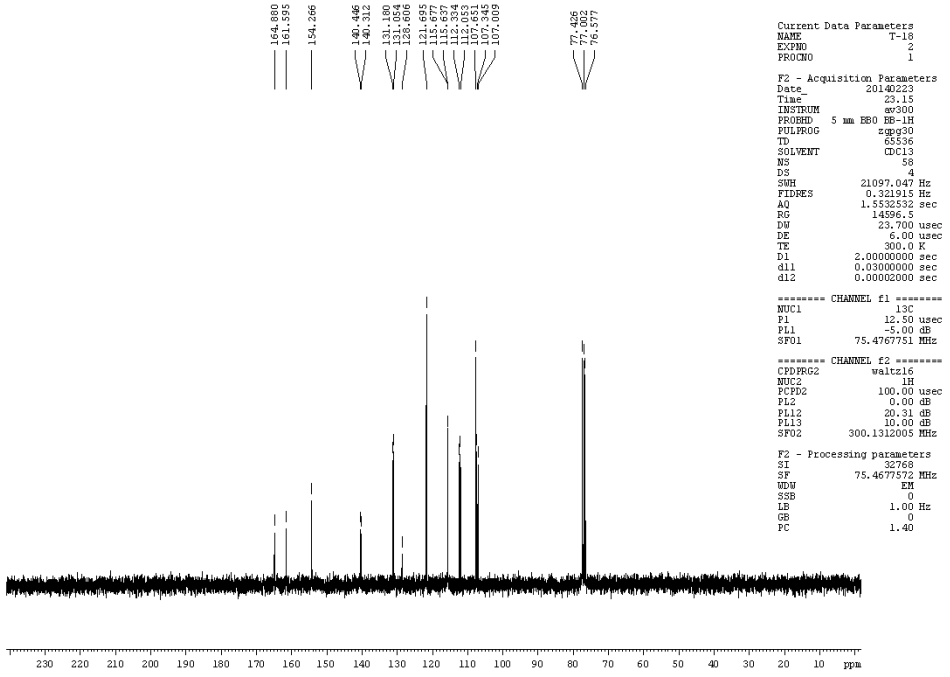



**Figure 56** $^{13}$C NMR Spectrum of **3l** ($CDCl_3$)

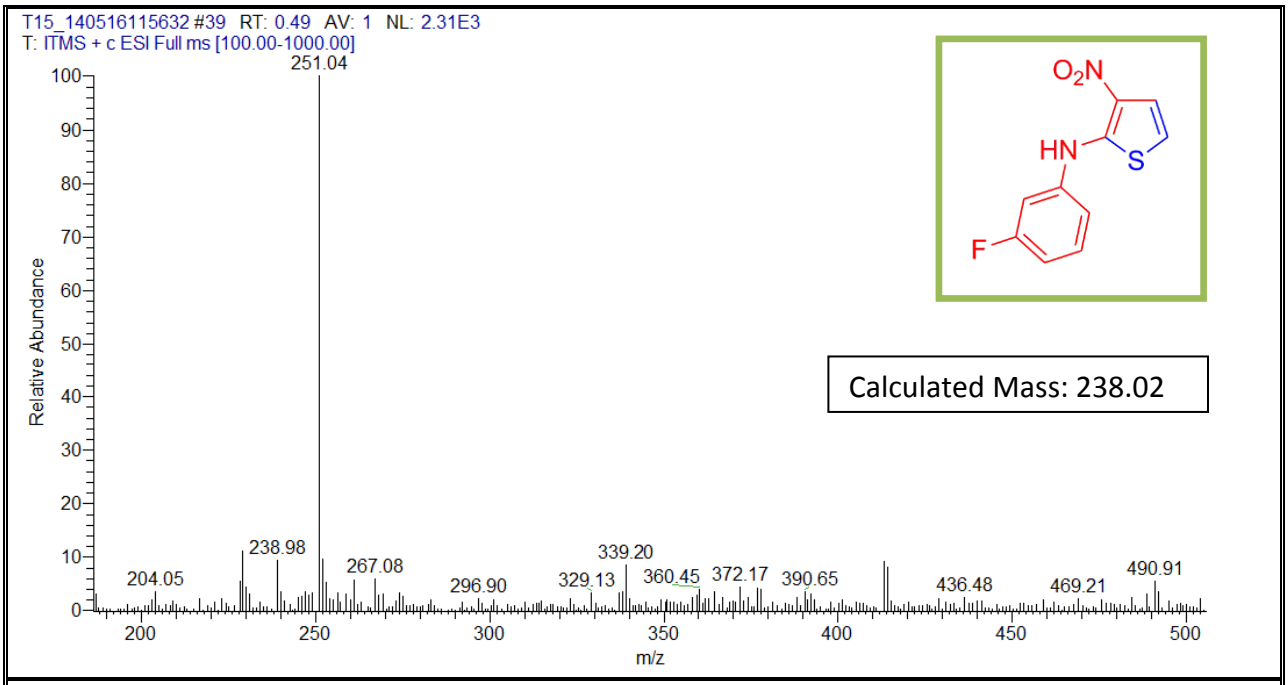



**Figure 57** ESI mass spectrum of Spectrum of **3l**

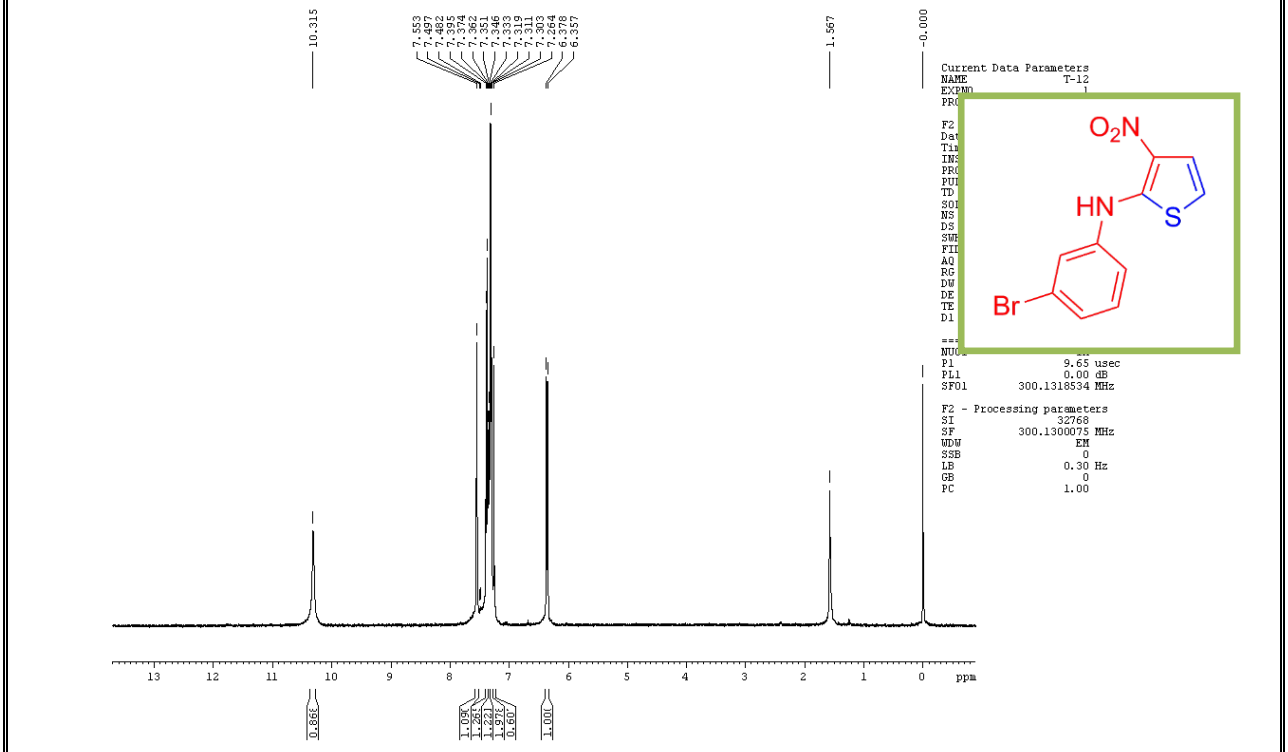



**Figure 58** $^{1}$H NMR Spectrum **3m** ($CDCl_3$)

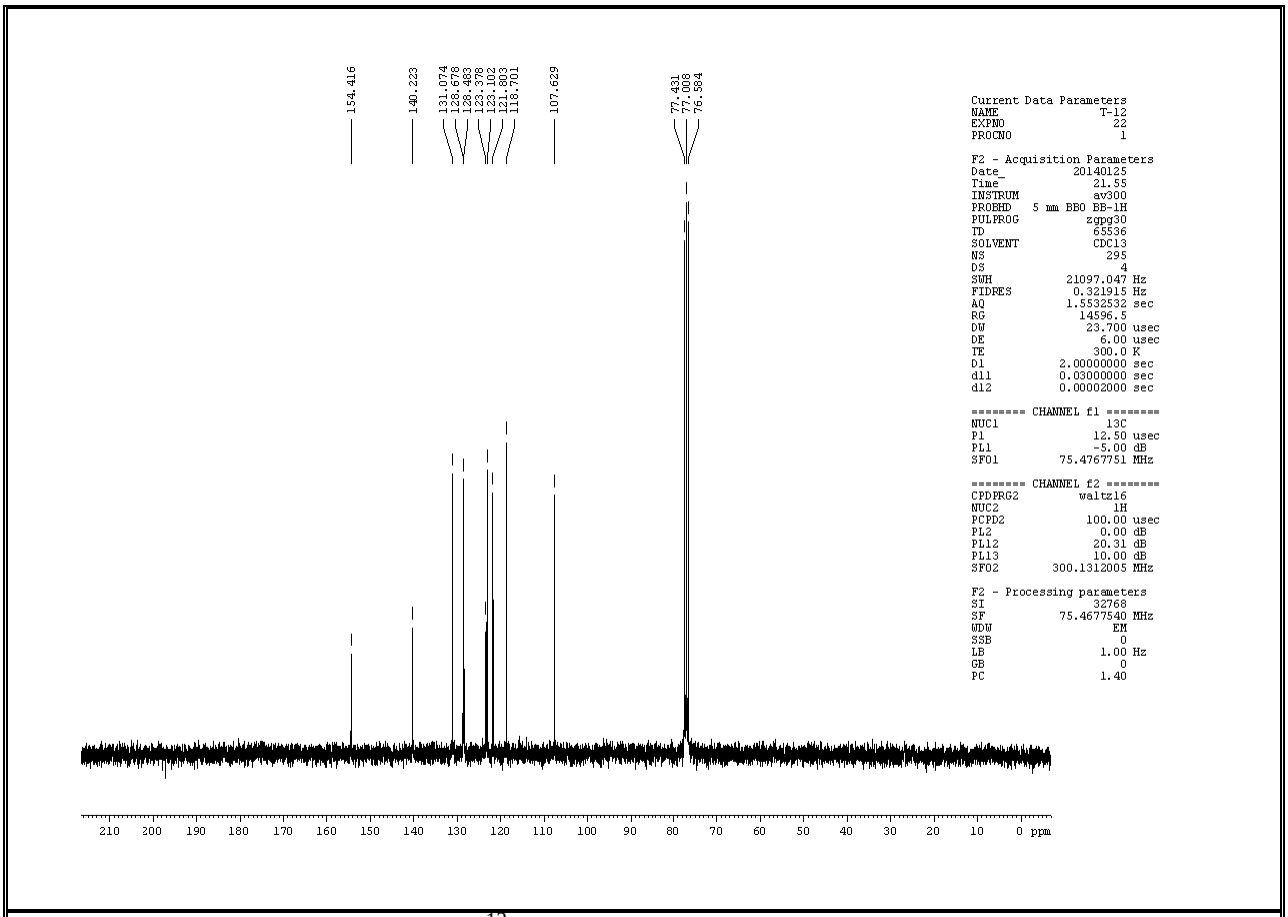



**Figure 59** $^{13}$C NMR Spectrum of **3m** ($CDCl_3$)

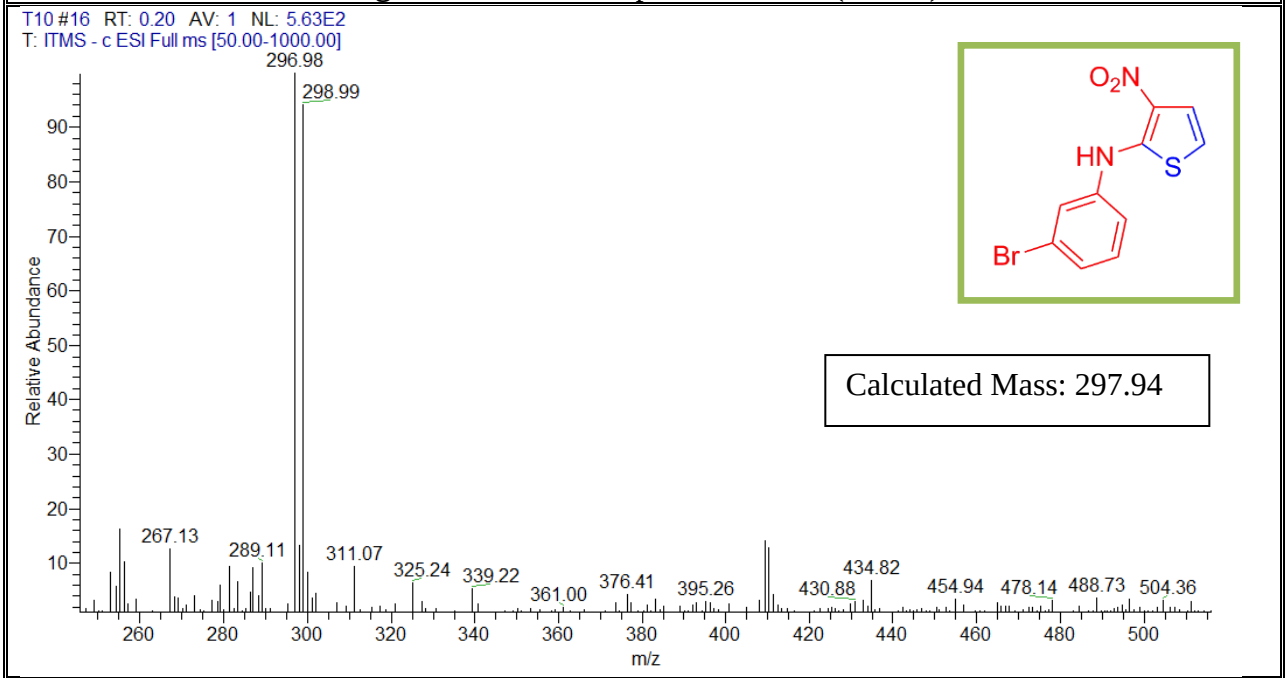



**Figure 60** ESI mass spectrum of Spectrum of **3m**

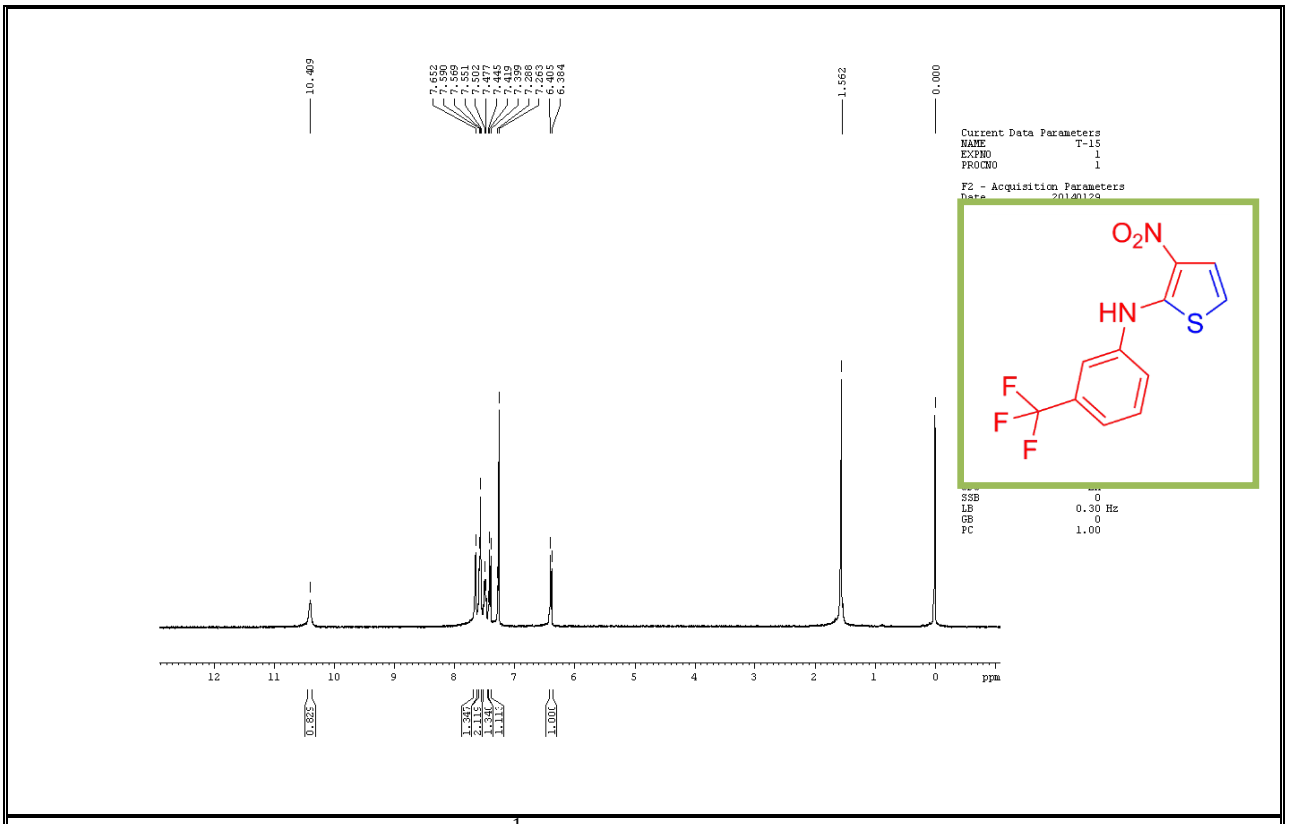



**Figure 61** $^{1}$H NMR Spectrum **3n** ($CDCl_3$)

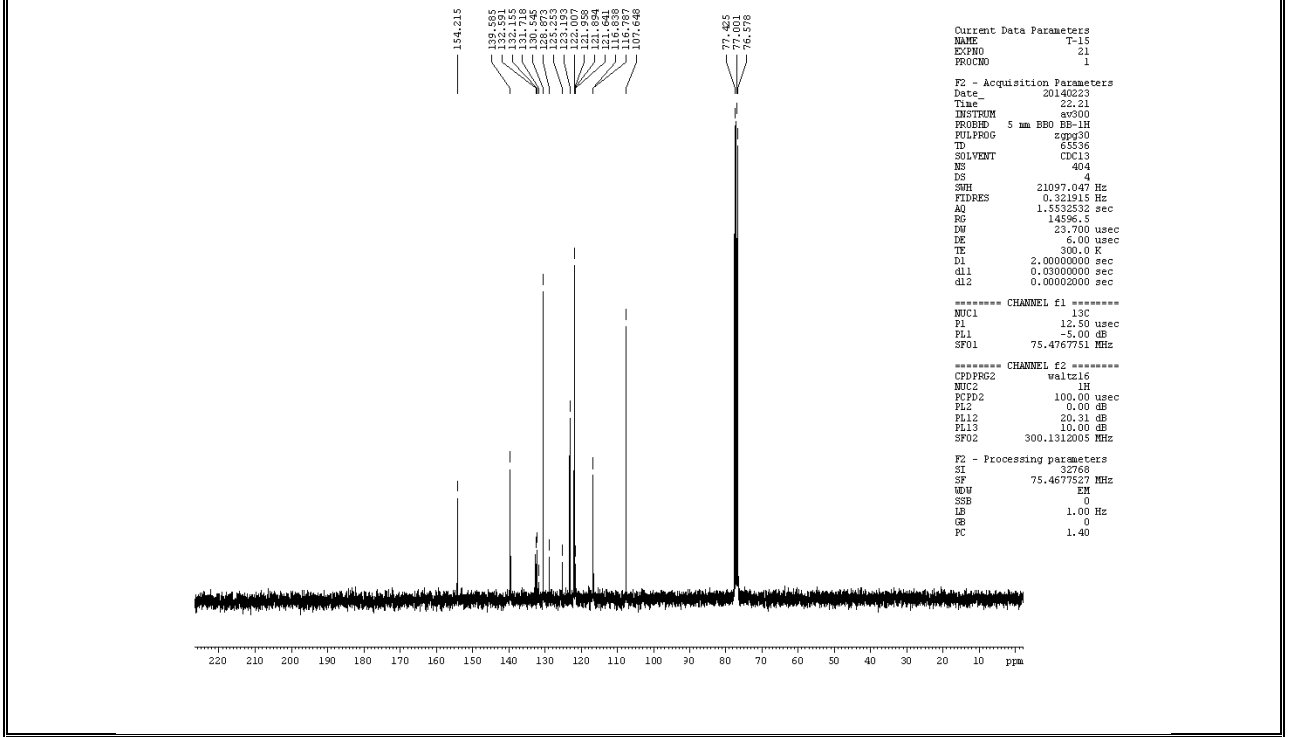



**Figure 62** $^{13}$C NMR Spectrum of **3n** ($CDCl_3$)

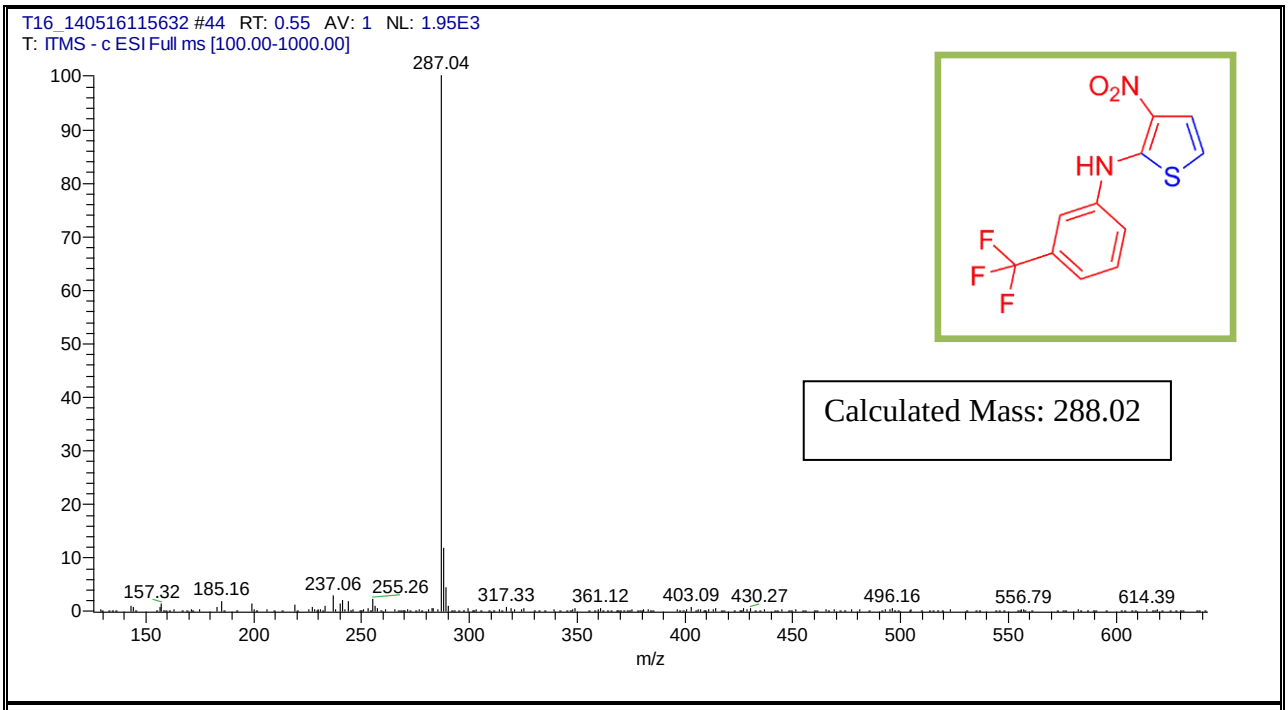



**Figure 63** ESI mass spectrum of Spectrum of **3n**

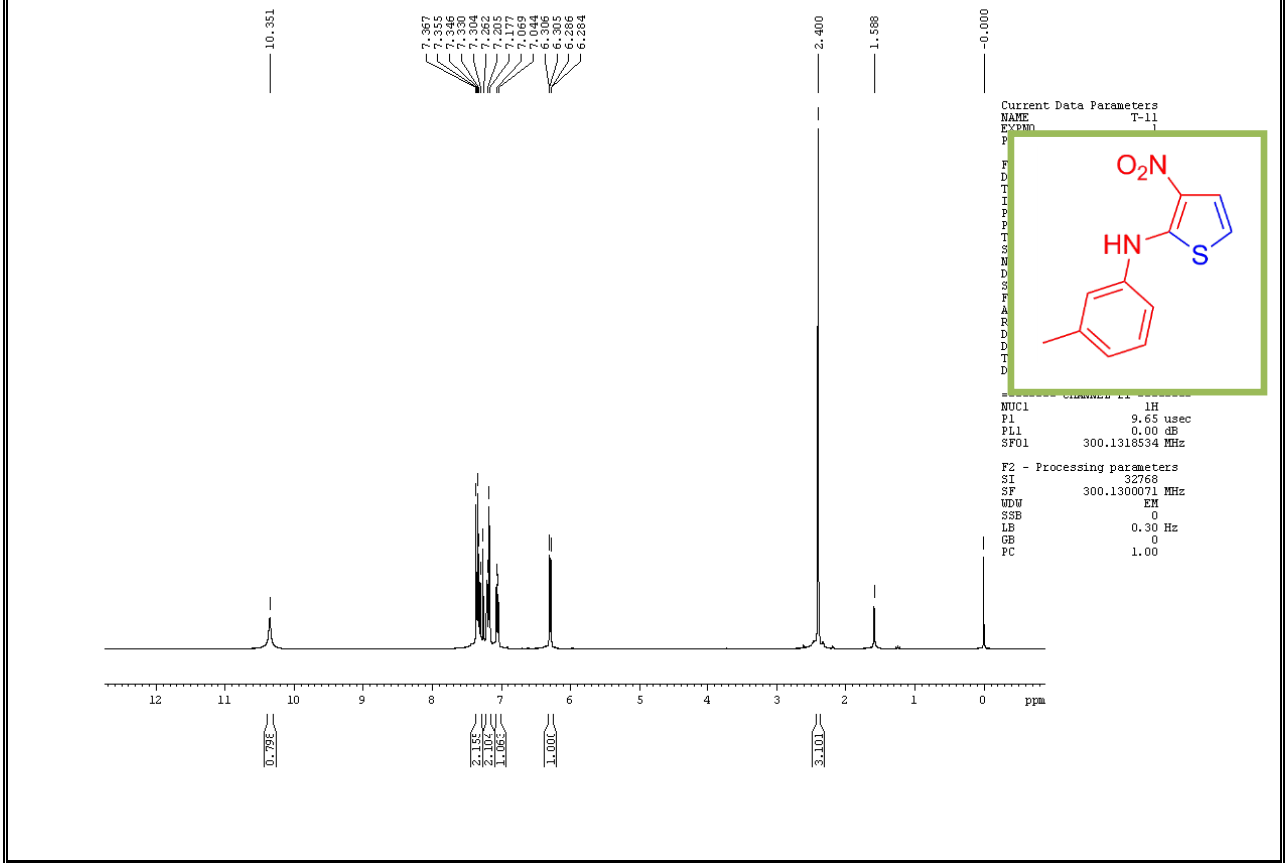



**Figure 64** $^{1}$H NMR Spectrum **3o** ($CDCl_3$)

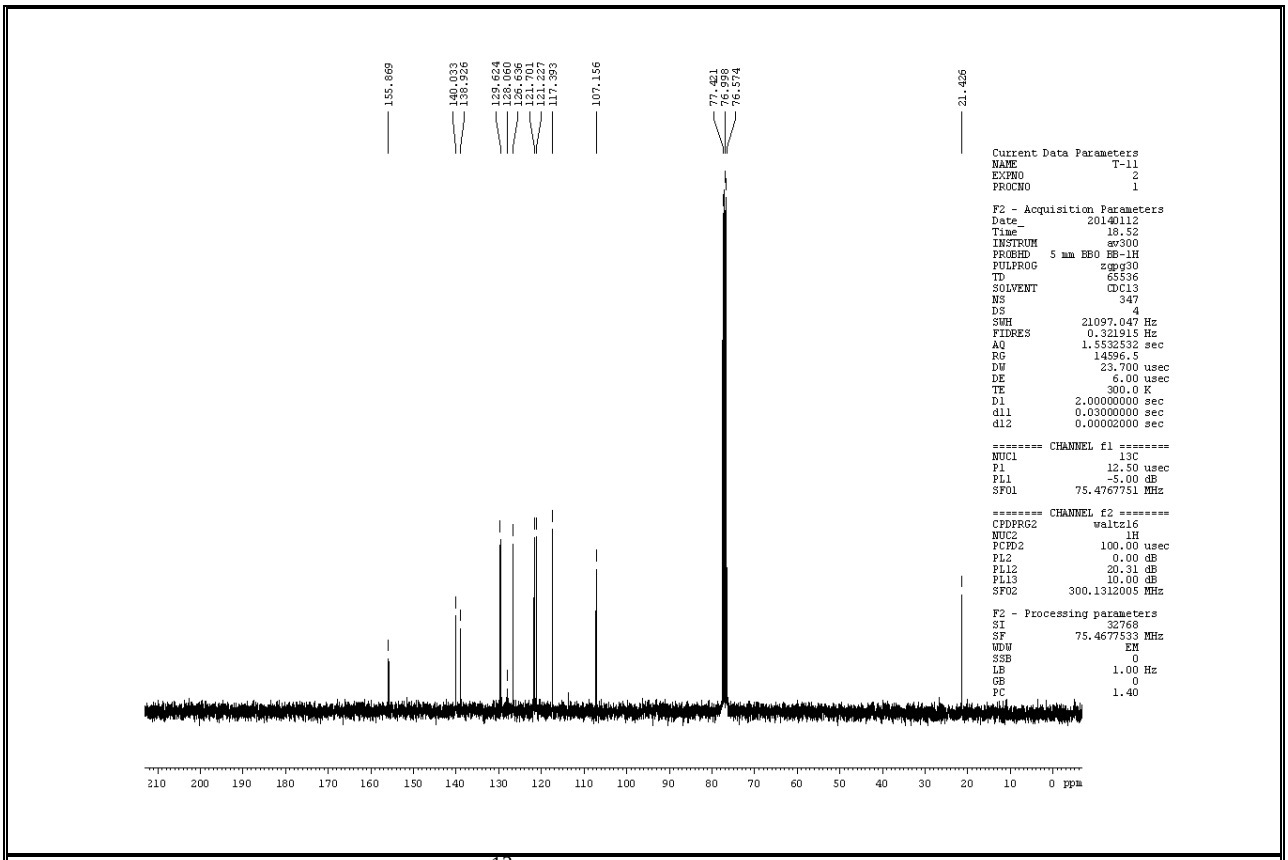



**Figure 65** $^{13}$C NMR Spectrum of **3o** ($CDCl_3$)

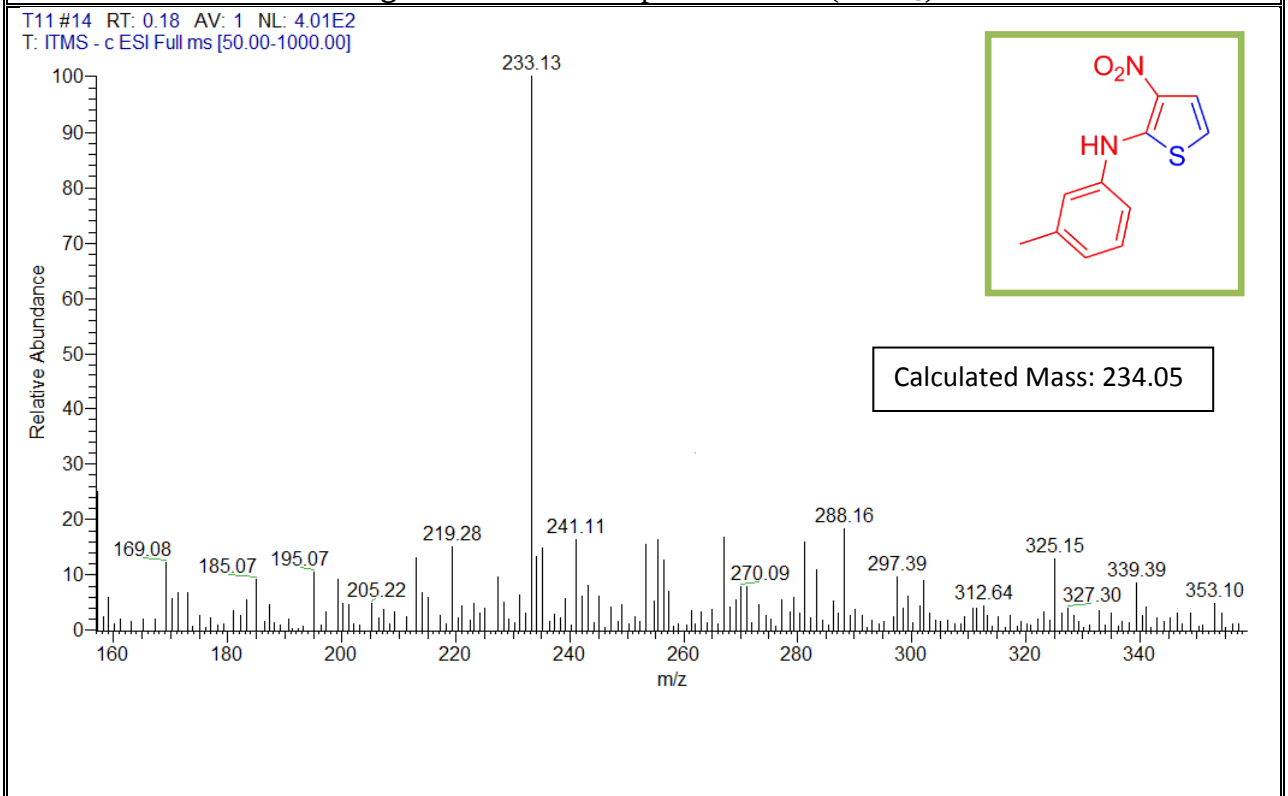



**Figure 66** ESI mass spectrum of Spectrum of **3o**

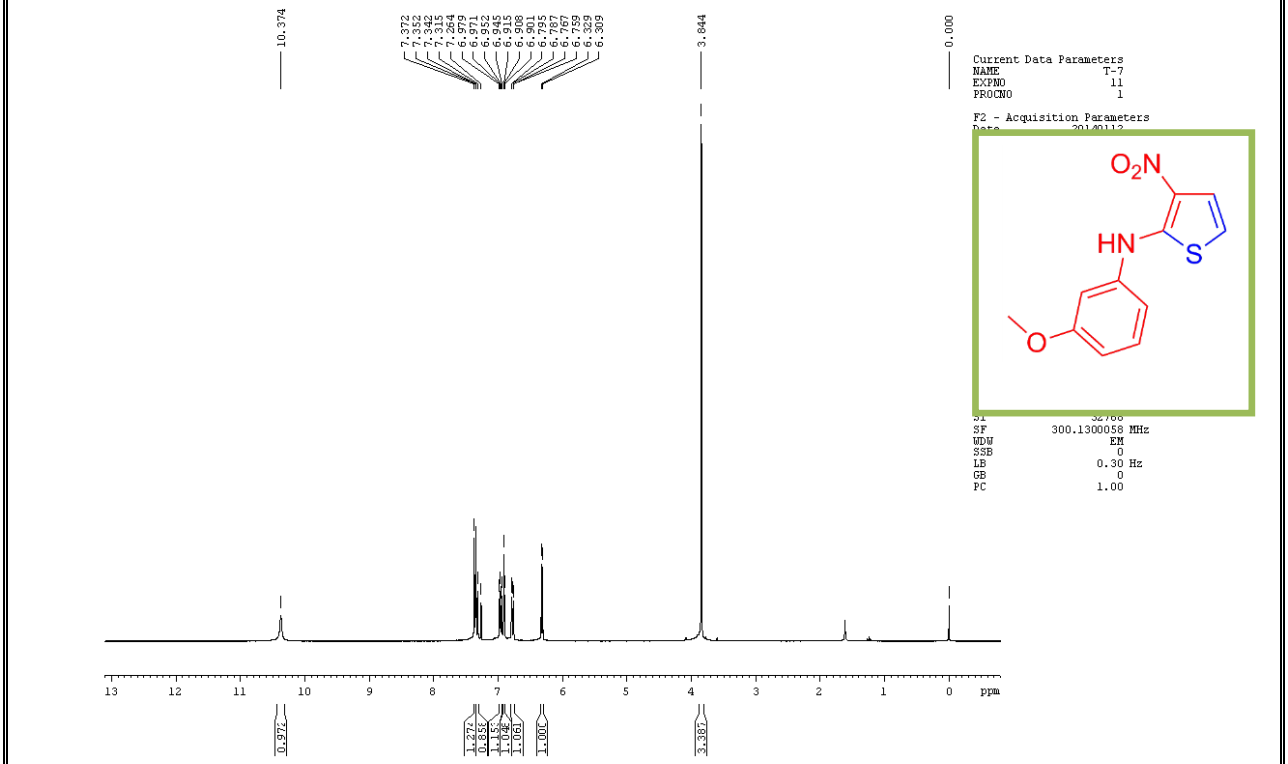



**Figure 67** $^{1}$H NMR Spectrum **3p** ($CDCl_3$)

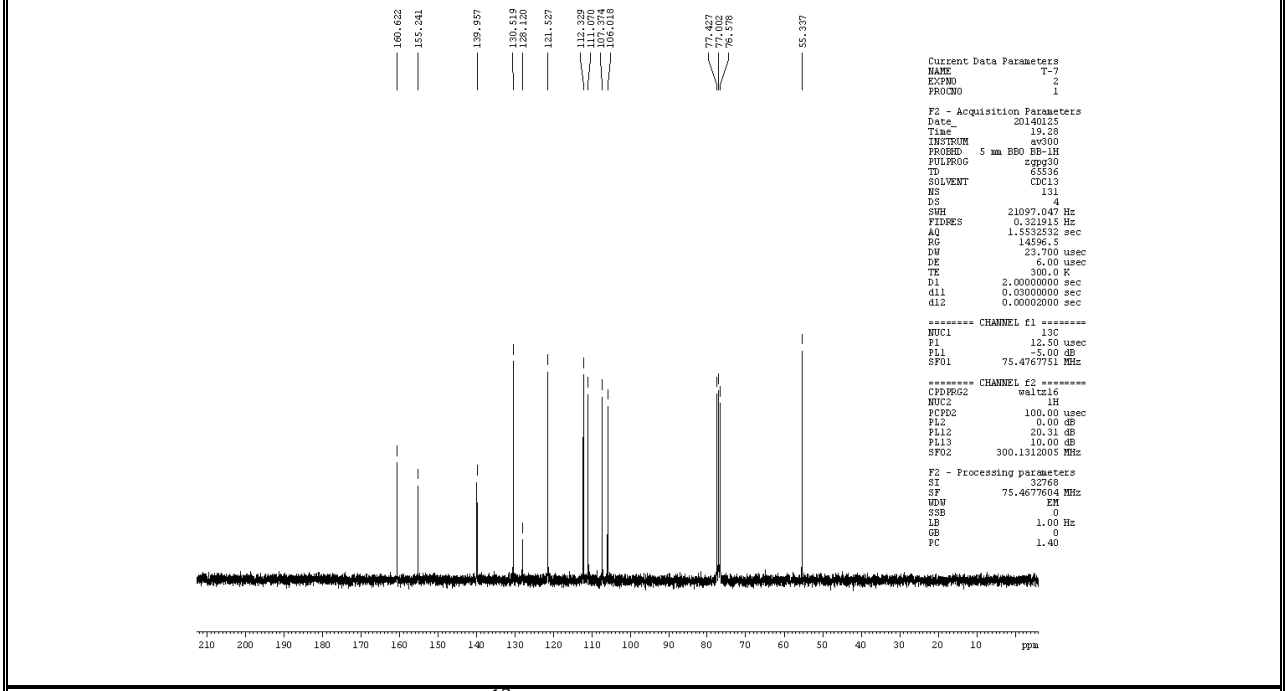



**Figure 68** $^{13}$C NMR Spectrum of **3p** ($CDCl_3$)

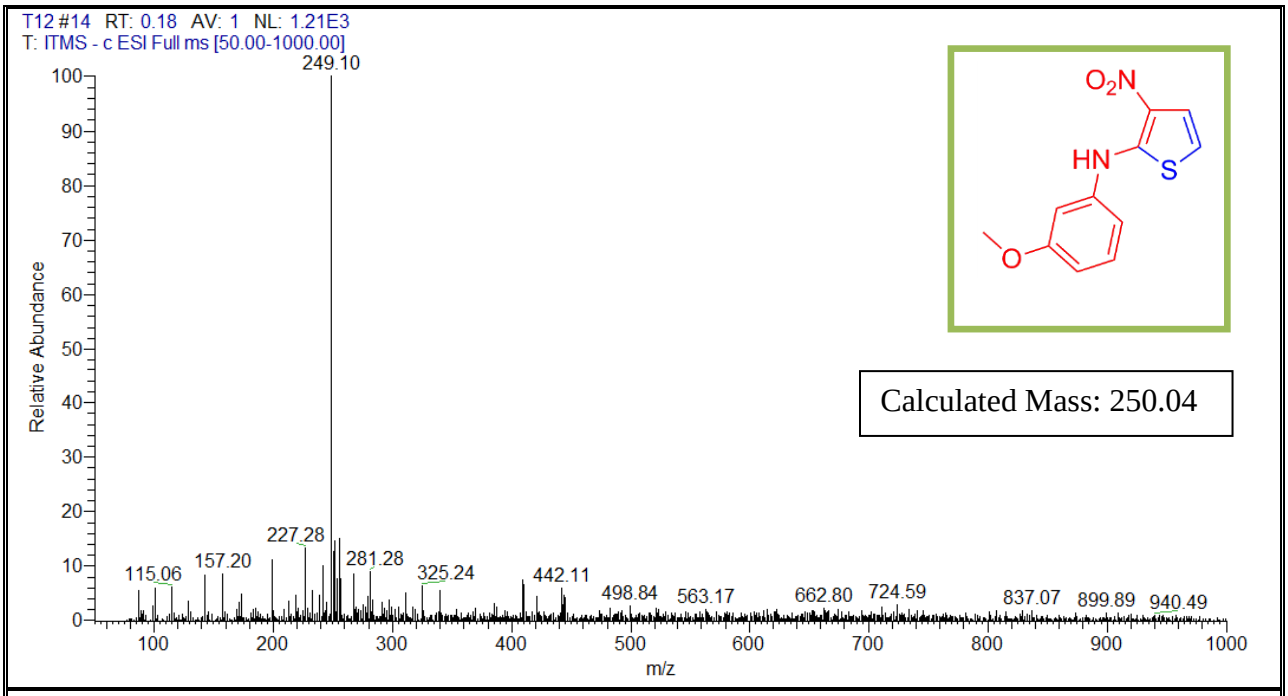



**Figure 69** ESI mass spectrum of Spectrum of **3p**

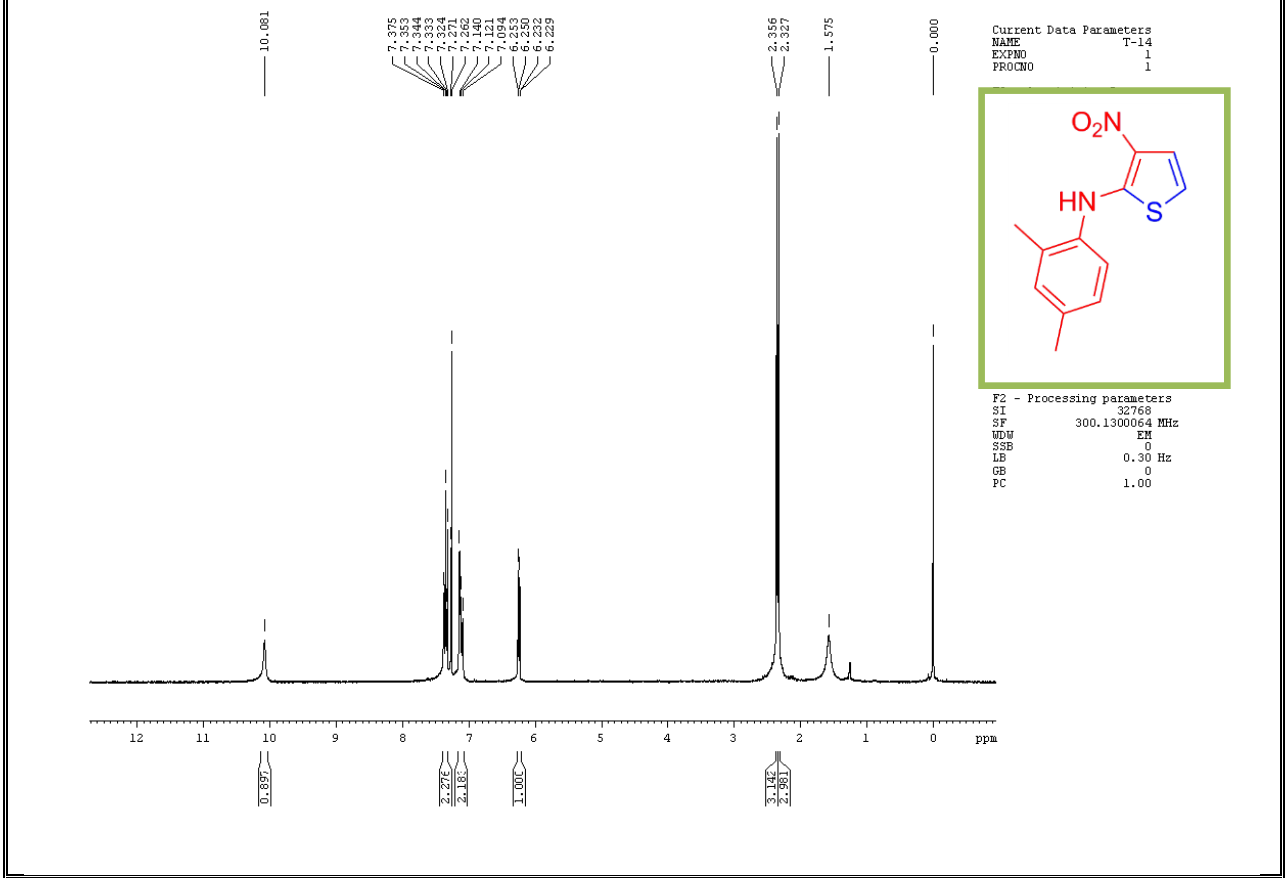



**Figure 70** $^{1}$H NMR Spectrum **3q** ($CDCl_3$)

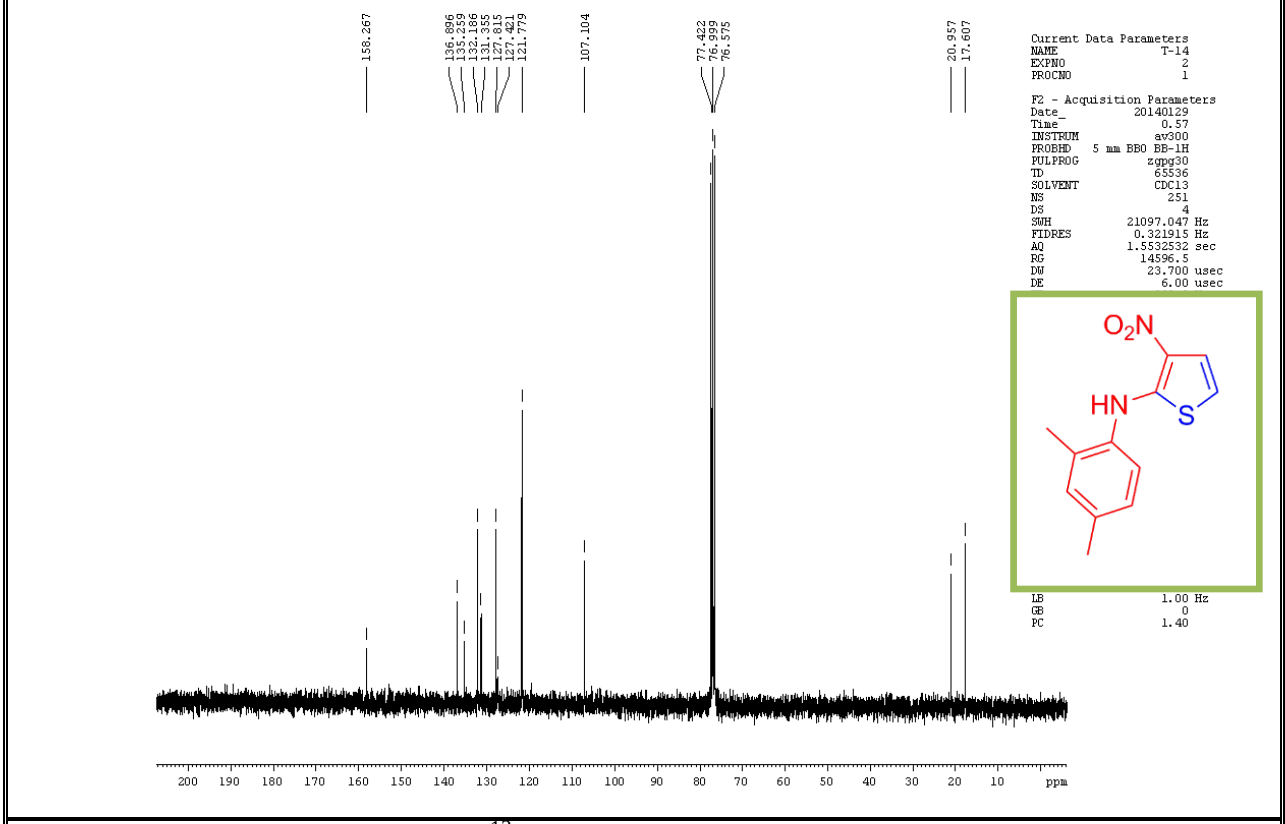



**Figure 71** $^{13}$C NMR Spectrum of **3q** ($CDCl_3$)

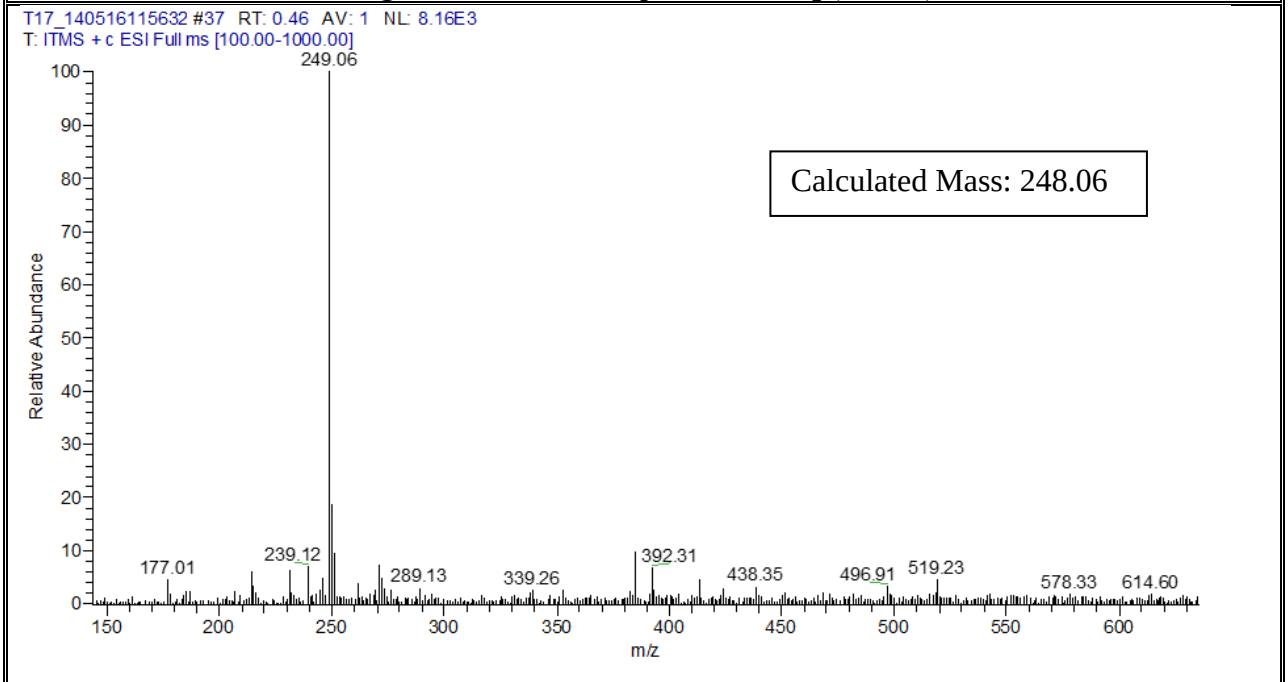



**Figure 72** ESI mass spectrum of Spectrum of **3q**

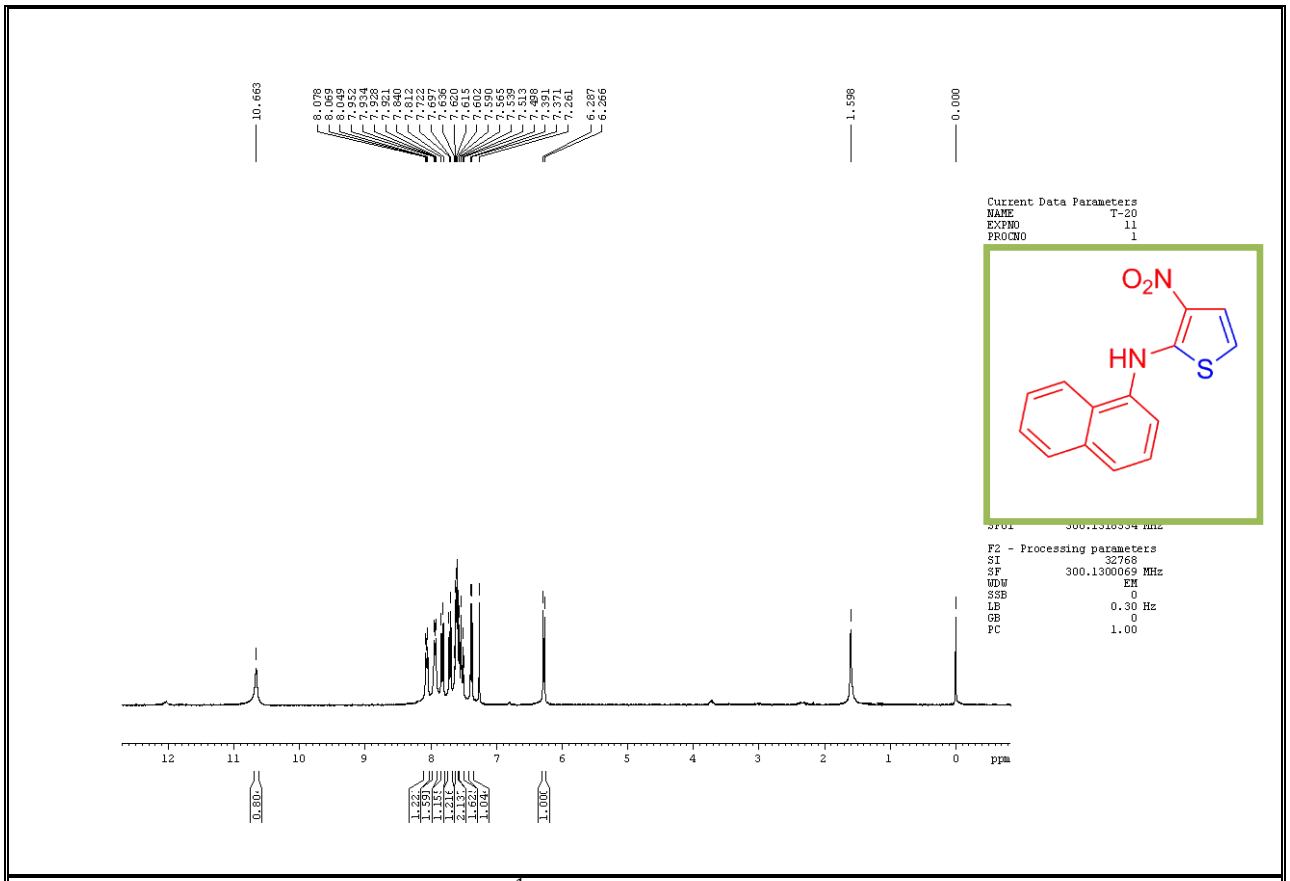



**Figure 73** $^{1}$H NMR Spectrum **3r** ($CDCl_3$)

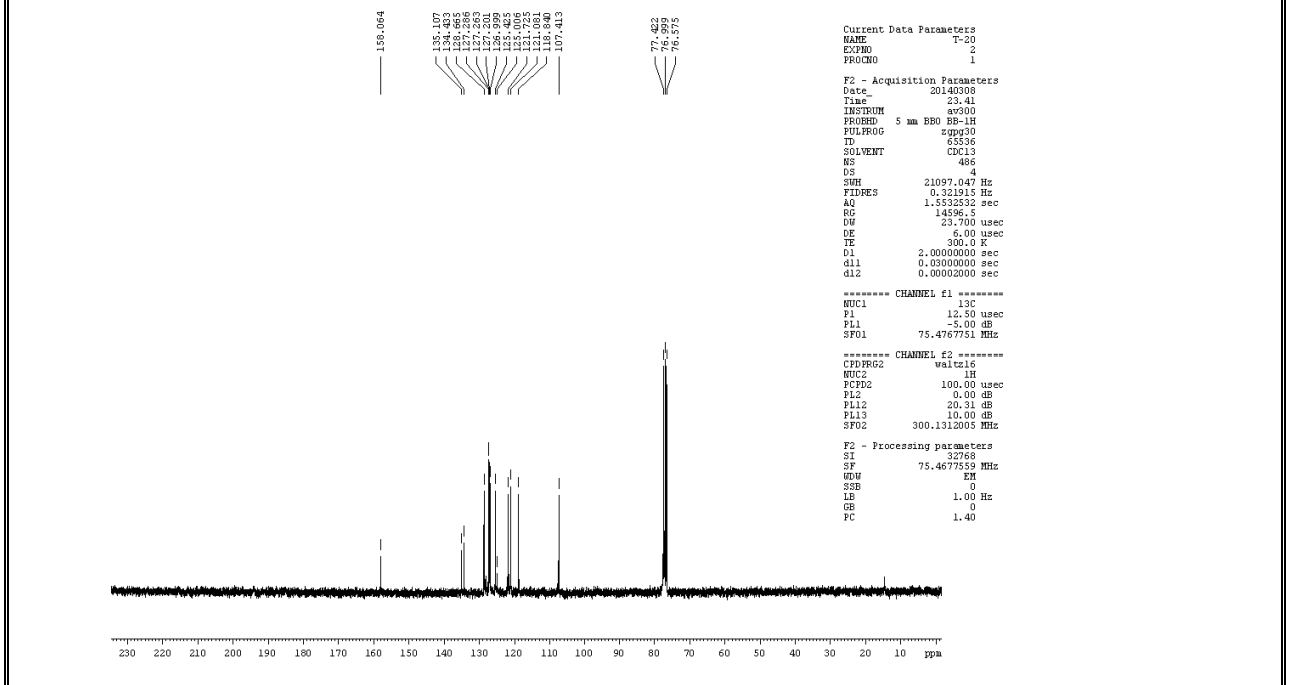



**Figure 74** $^{13}$C NMR Spectrum of **3r** ($CDCl_3$)

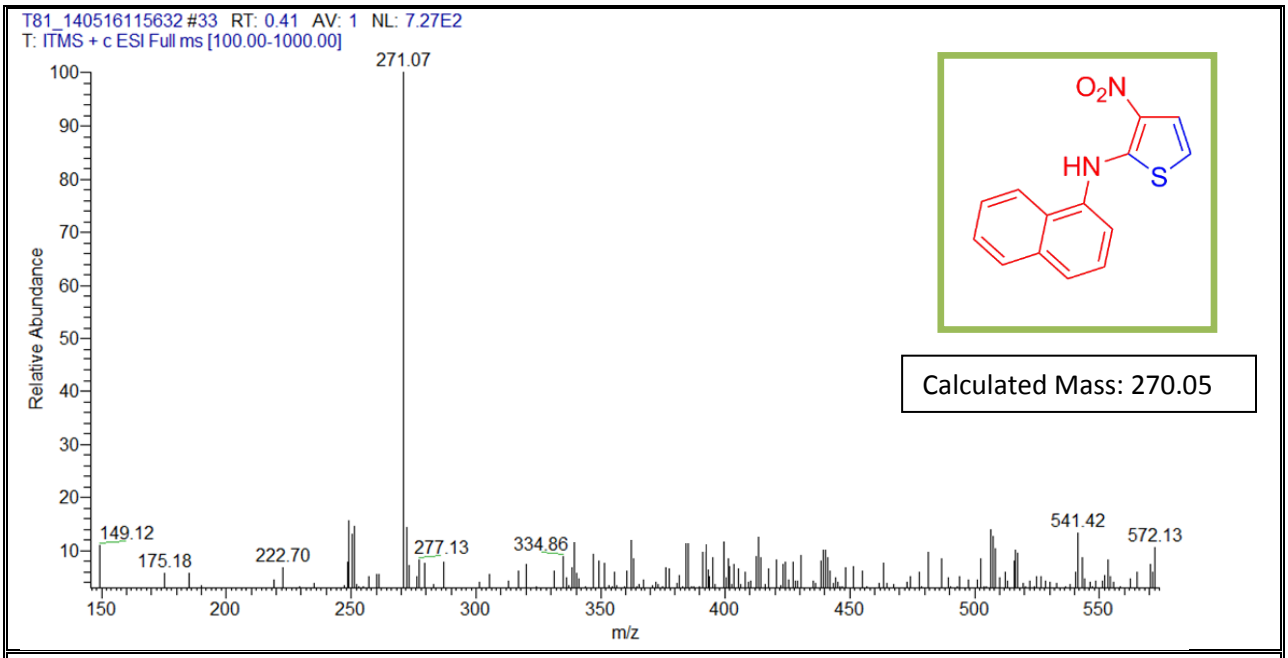



**Figure 75** ESI mass spectrum of Spectrum of **3r**

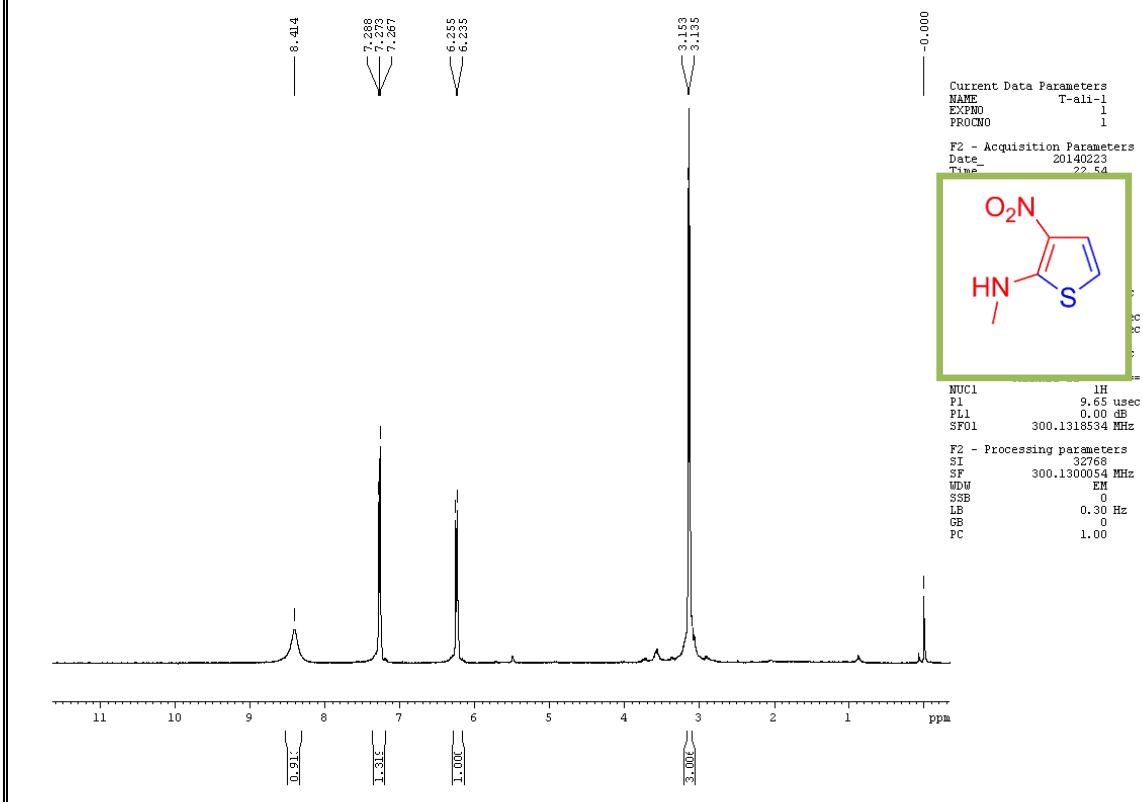



**Figure 76** $^{1}$H NMR Spectrum **3s** ($CDCl_3$)

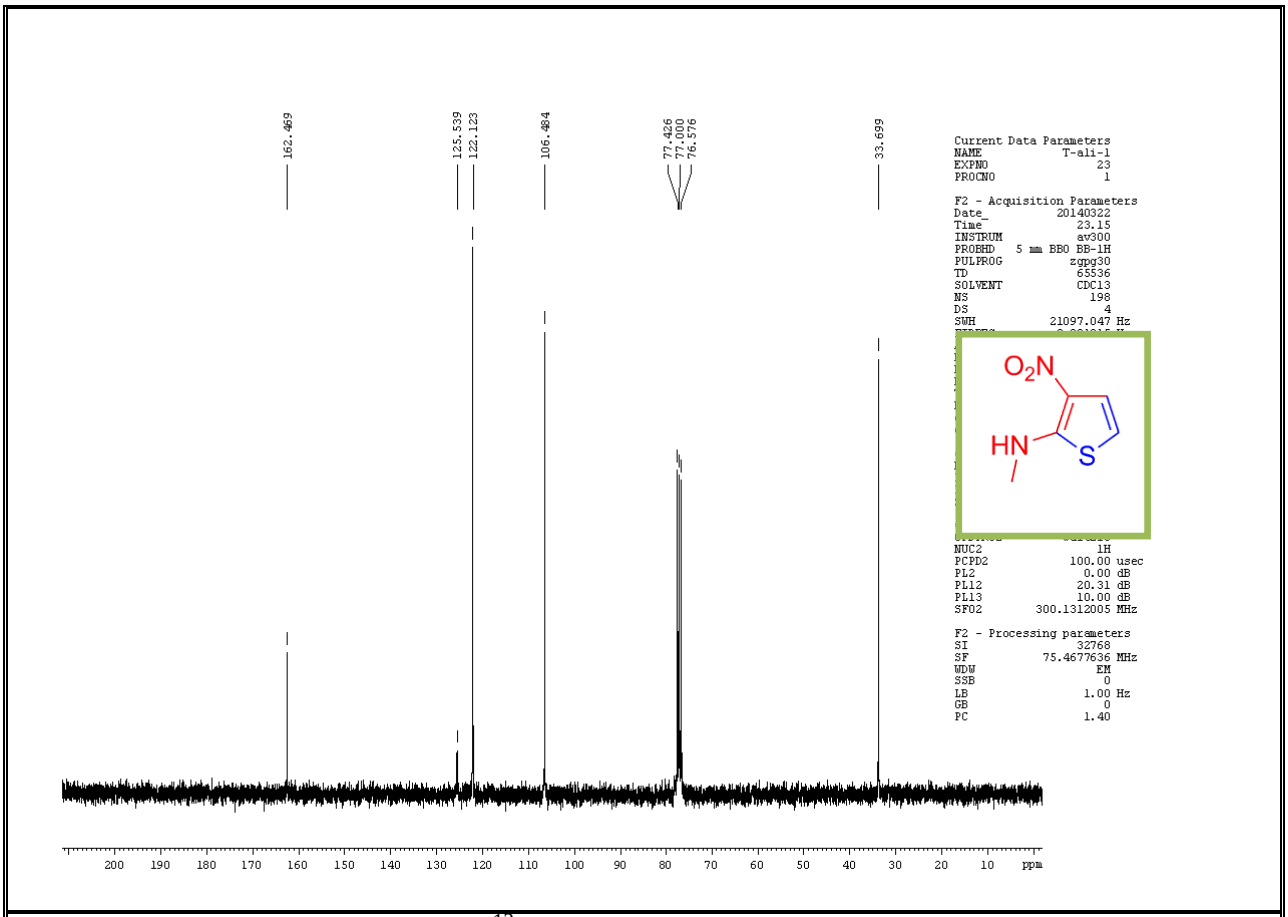



**Figure 77** $^{13}$C NMR Spectrum of **3s** ($CDCl_3$)

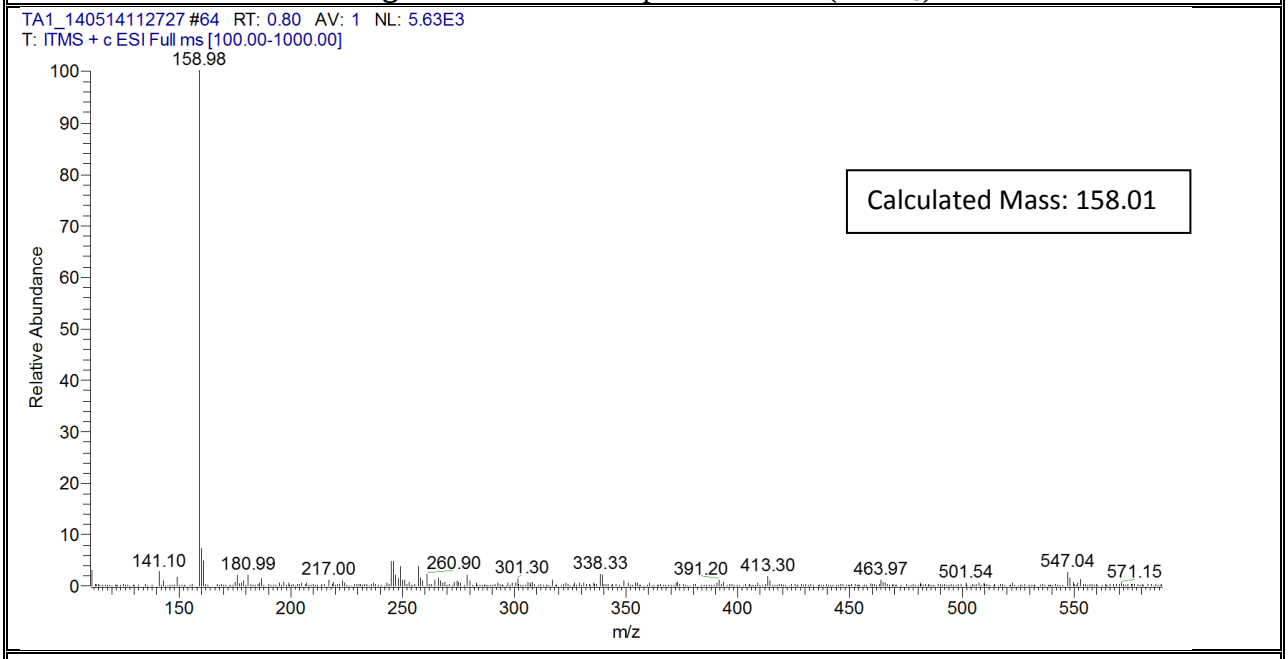



**Figure 78** ESI mass spectrum of Spectrum of **3s**

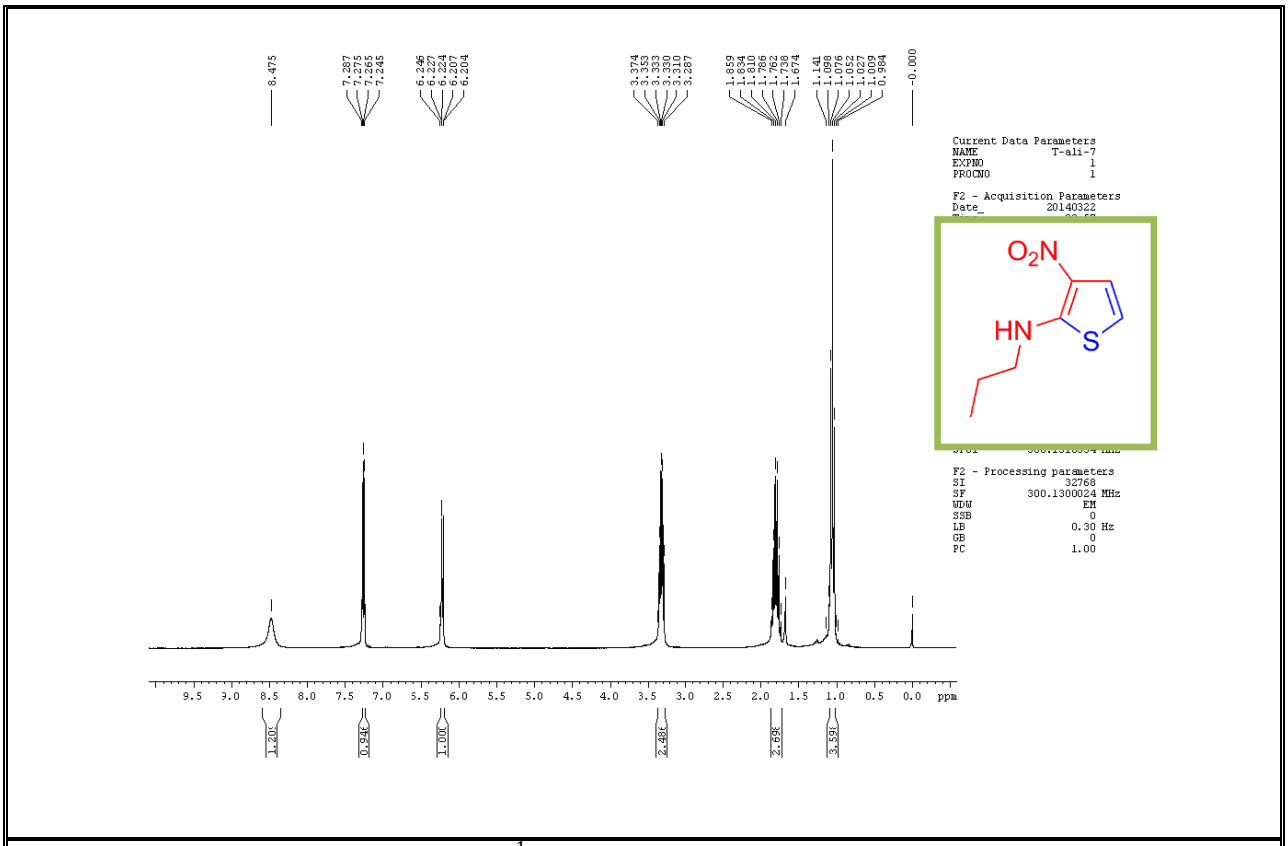



**Figure 79** $^{1}$H NMR Spectrum **3t** ($CDCl_3$)

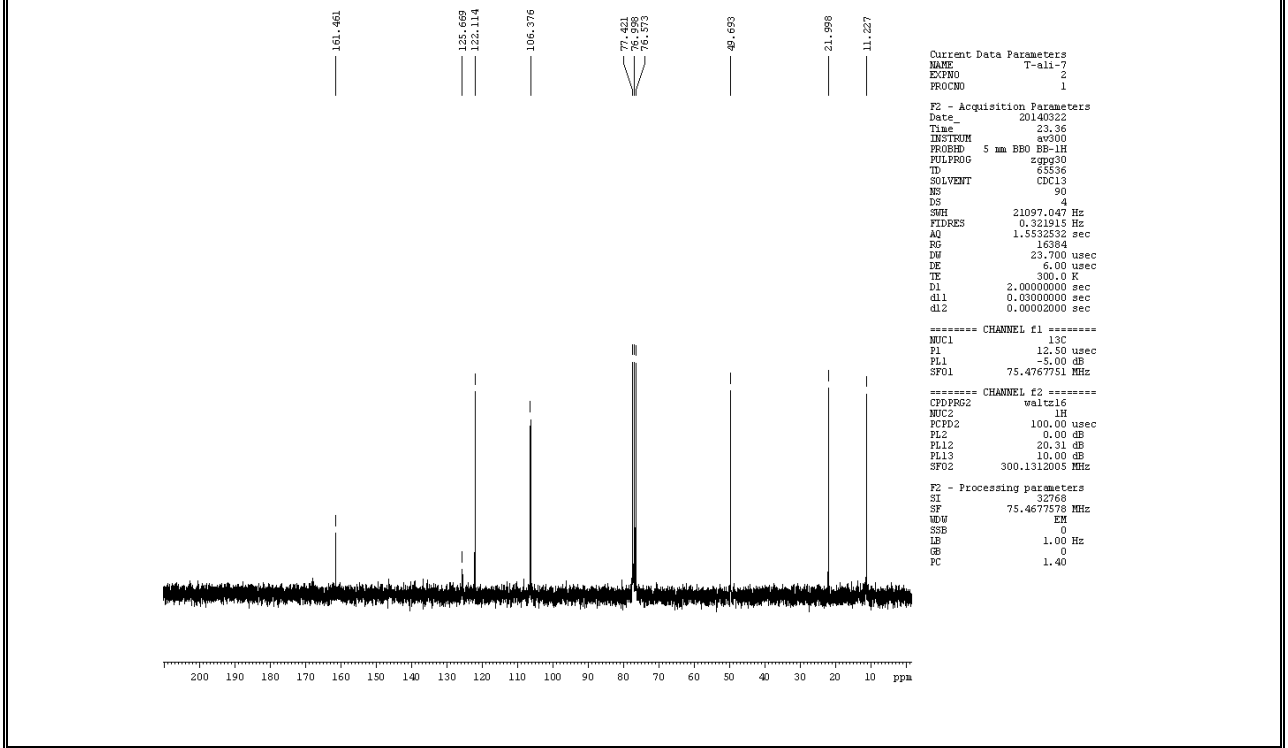



**Figure 80** $^{13}$C NMR Spectrum of **3t** ($CDCl_3$)

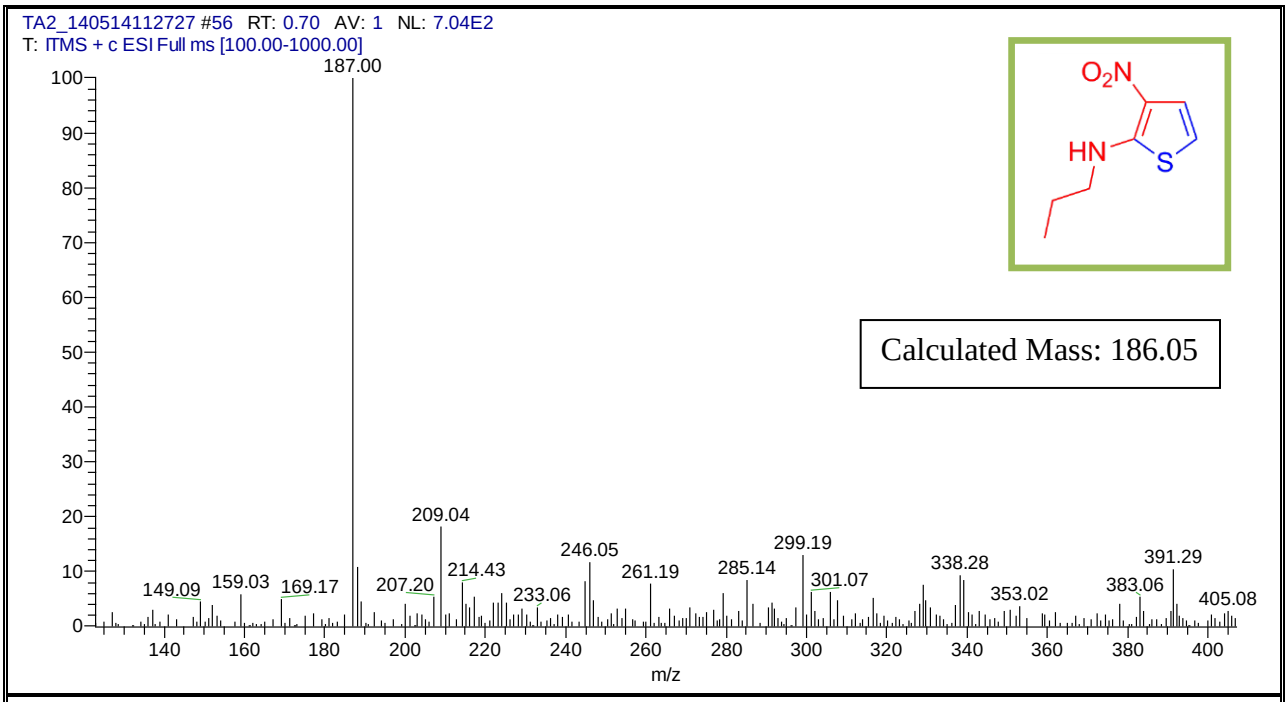



**Figure 81** ESI mass spectrum of Spectrum of **3t**

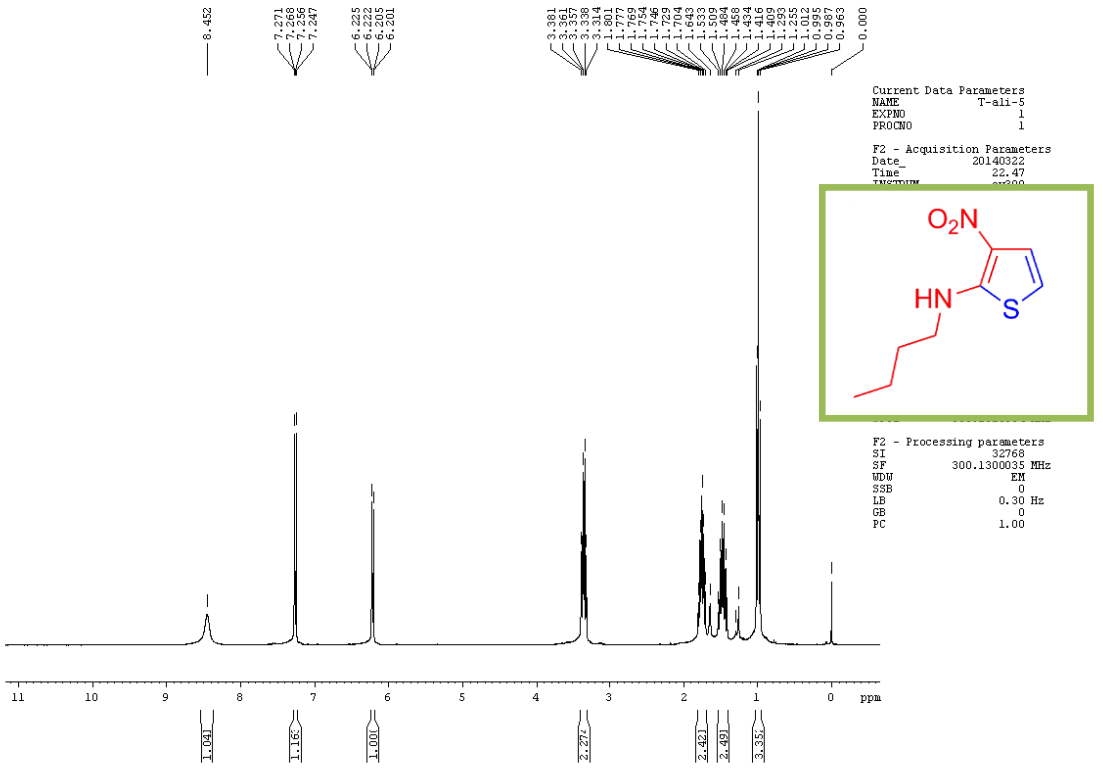



**Figure 82** $^{1}$H NMR Spectrum **3u** ($CDCl_3$)

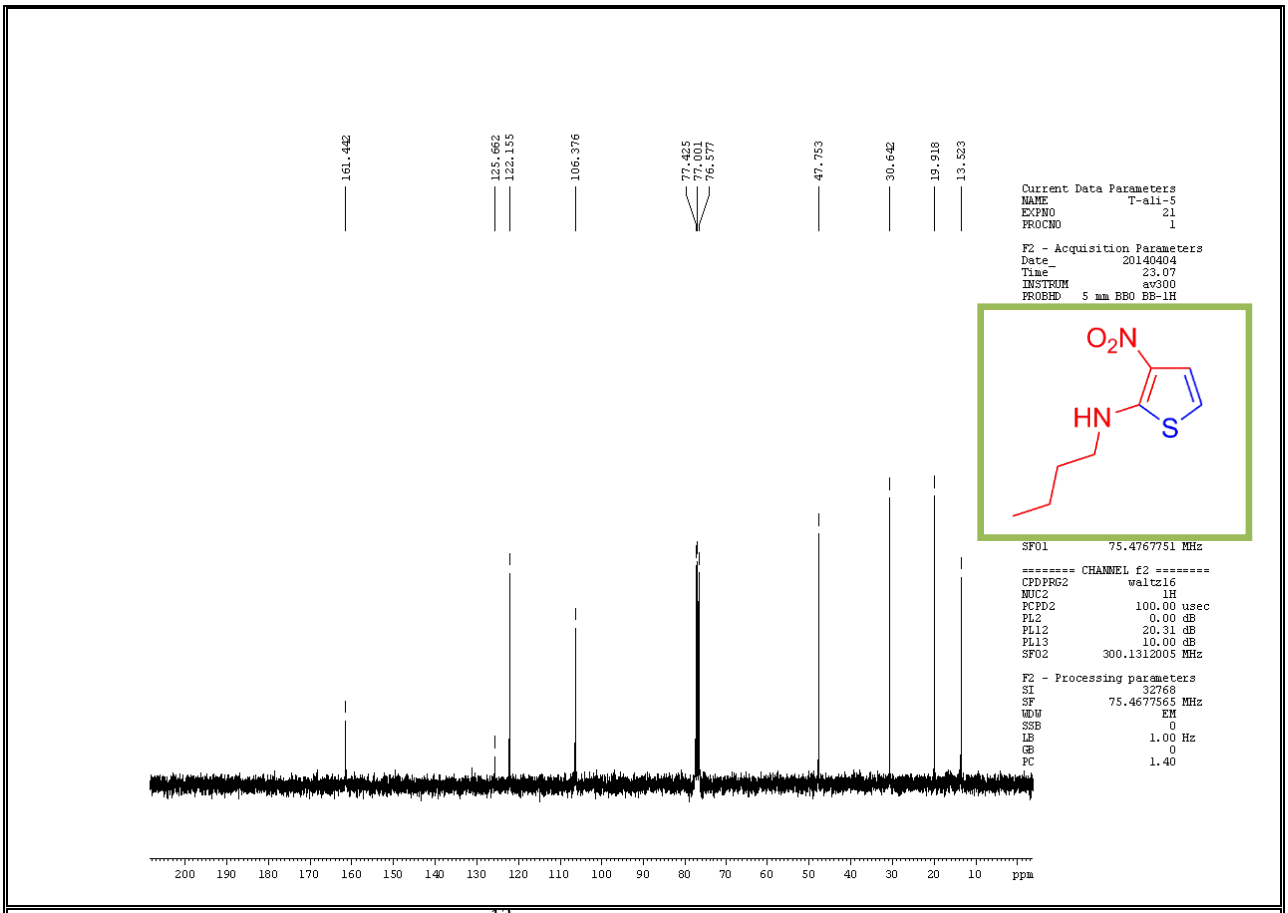



**Figure 83** $^{13}$C NMR Spectrum of **3u** ($CDCl_3$)

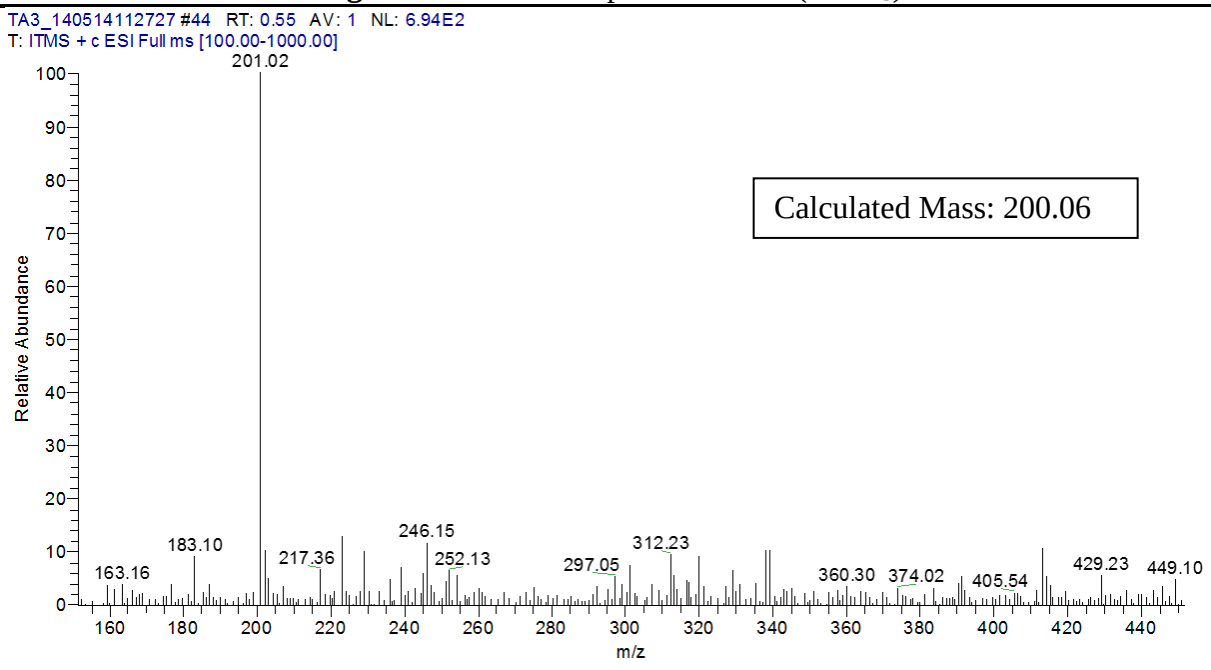



**Figure 84** ESI mass spectrum of Spectrum of **3u**

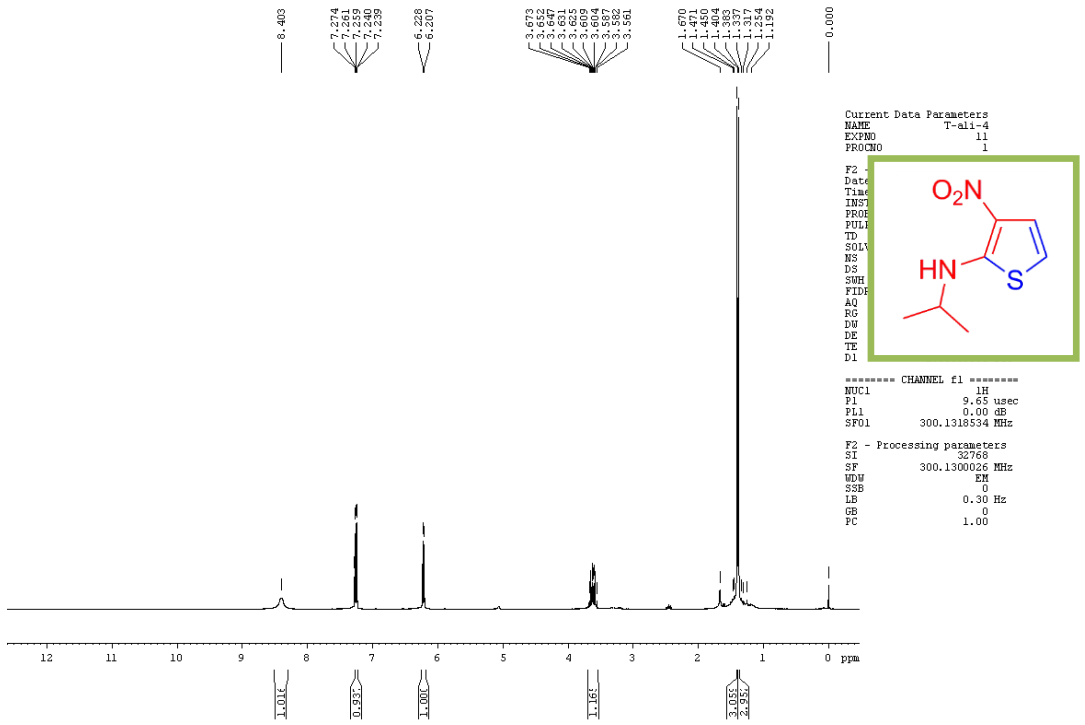



**Figure 85** $^{1}$H NMR Spectrum **3v** ($CDCl_3$)

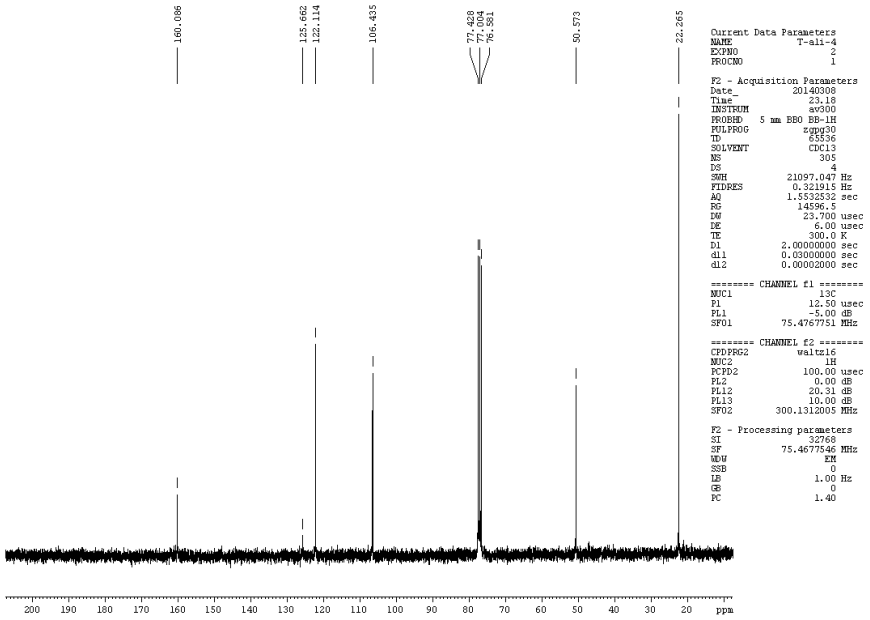



**Figure 86** $^{13}$C NMR Spectrum of **3v** ($CDCl_3$)

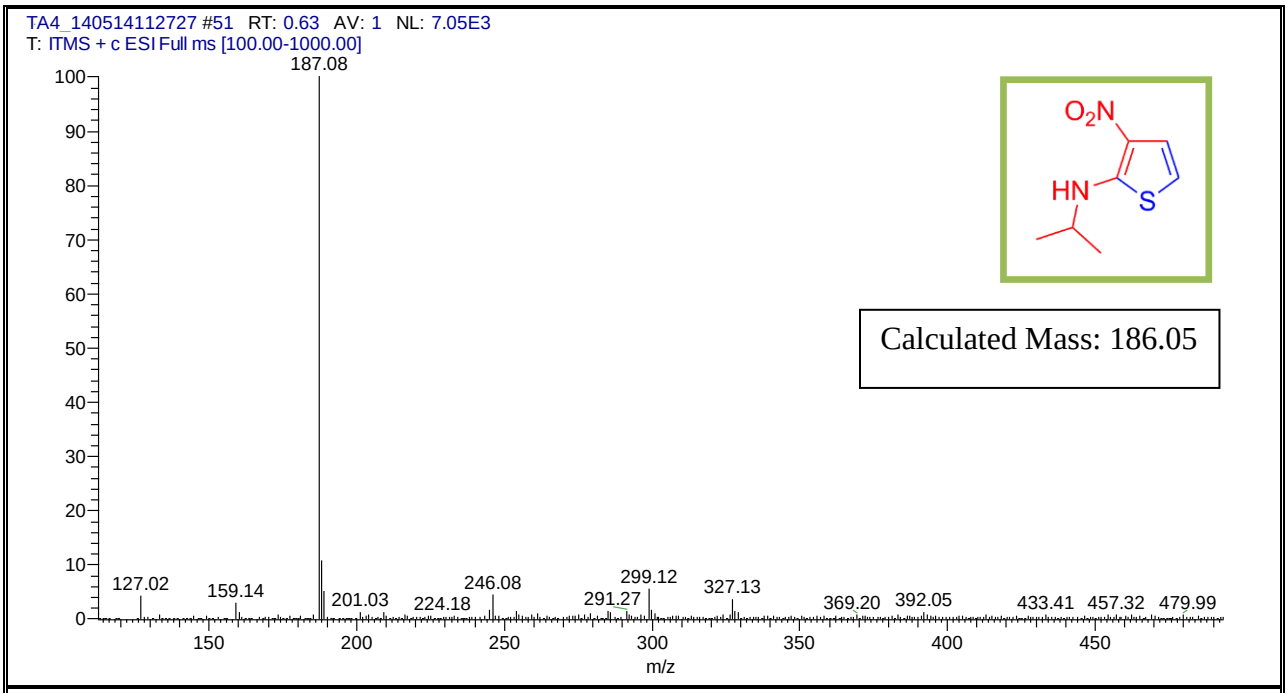



**Figure 87** ESI mass spectrum of Spectrum of **3v**

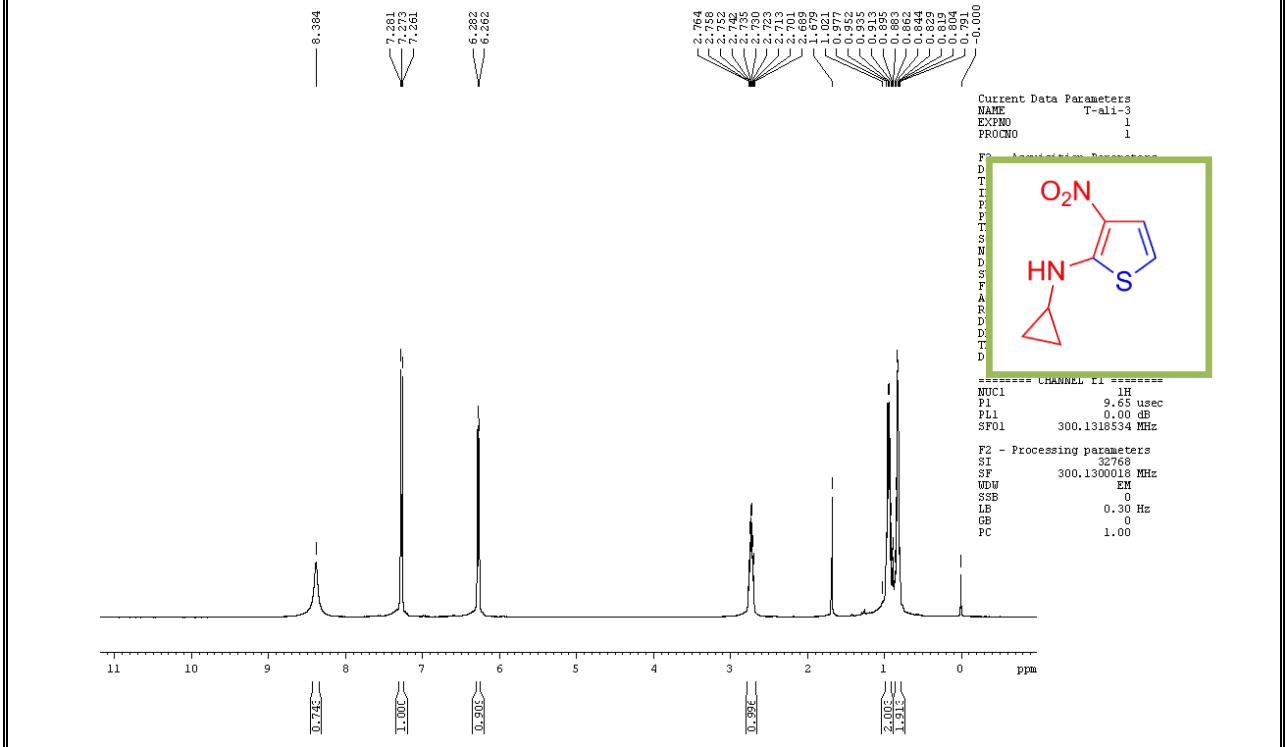



**Figure 88** $^{1}$H NMR Spectrum **3w** ($CDCl_3$)

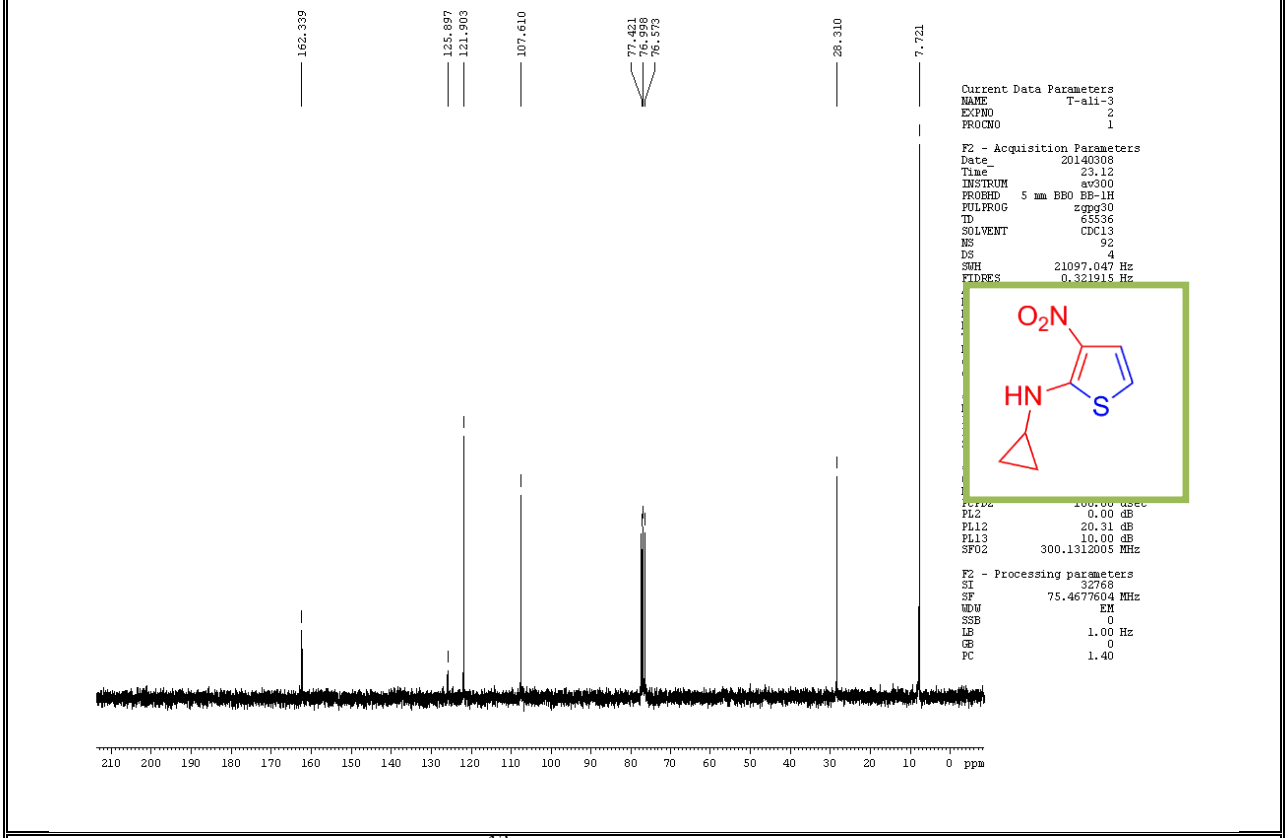



**Figure 89** $^{13}$C NMR Spectrum of **3w** ($CDCl_3$)

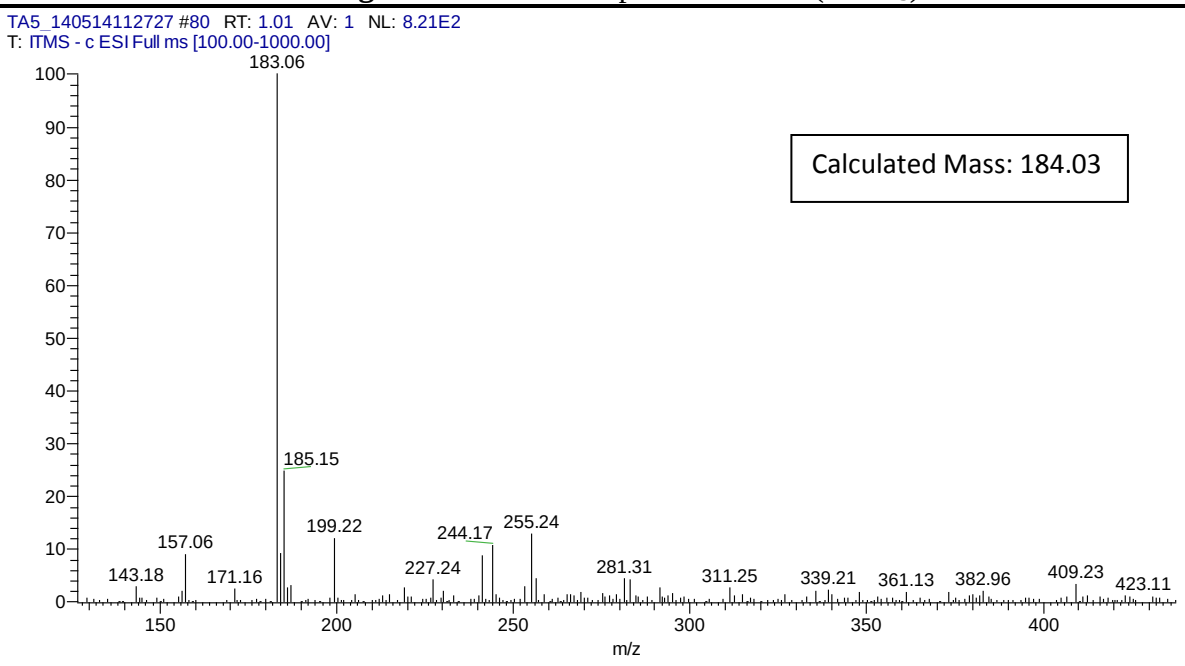



**Figure 90** ESI mass spectrum of Spectrum of **3w**

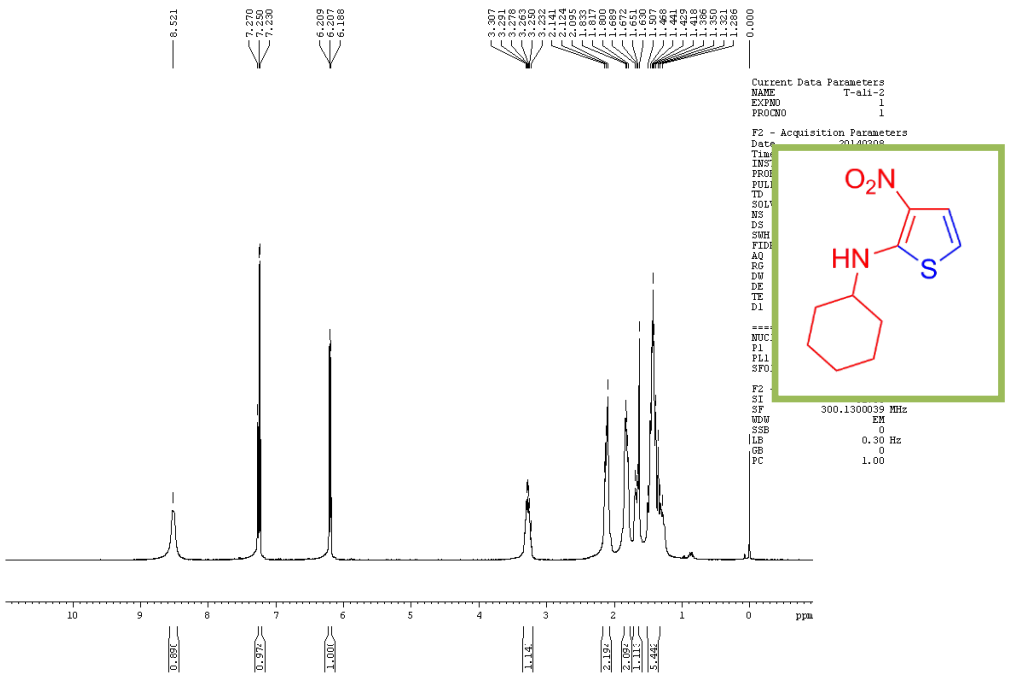



**Figure 91** $^{1}$H NMR Spectrum **3x** ($CDCl_3$)

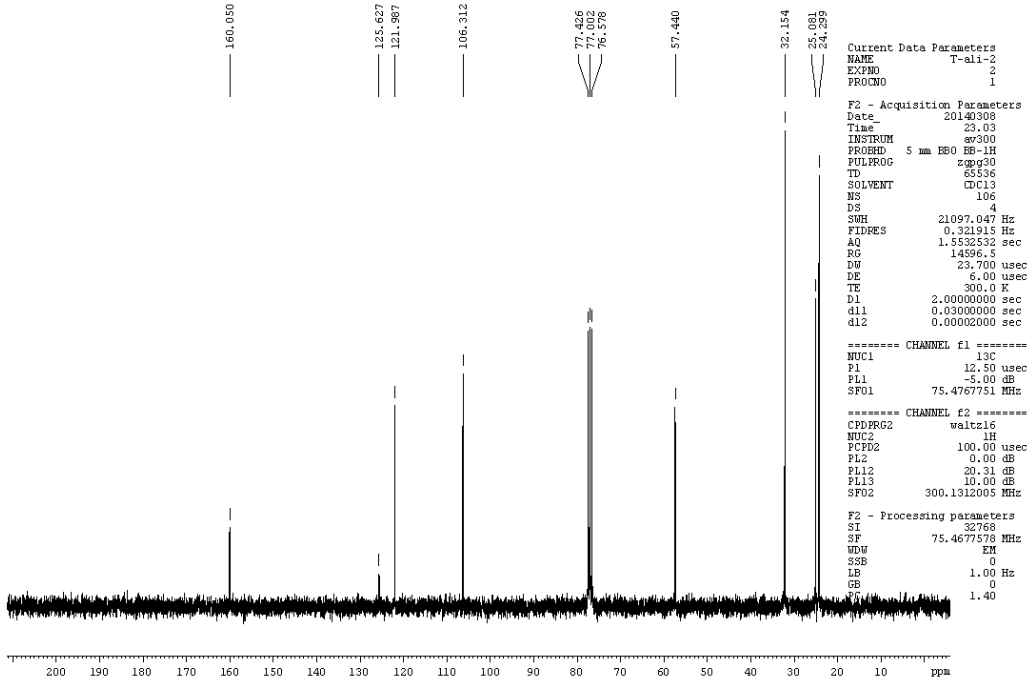



**Figure 92** $^{13}$C NMR Spectrum of **3x** ($CDCl_3$)

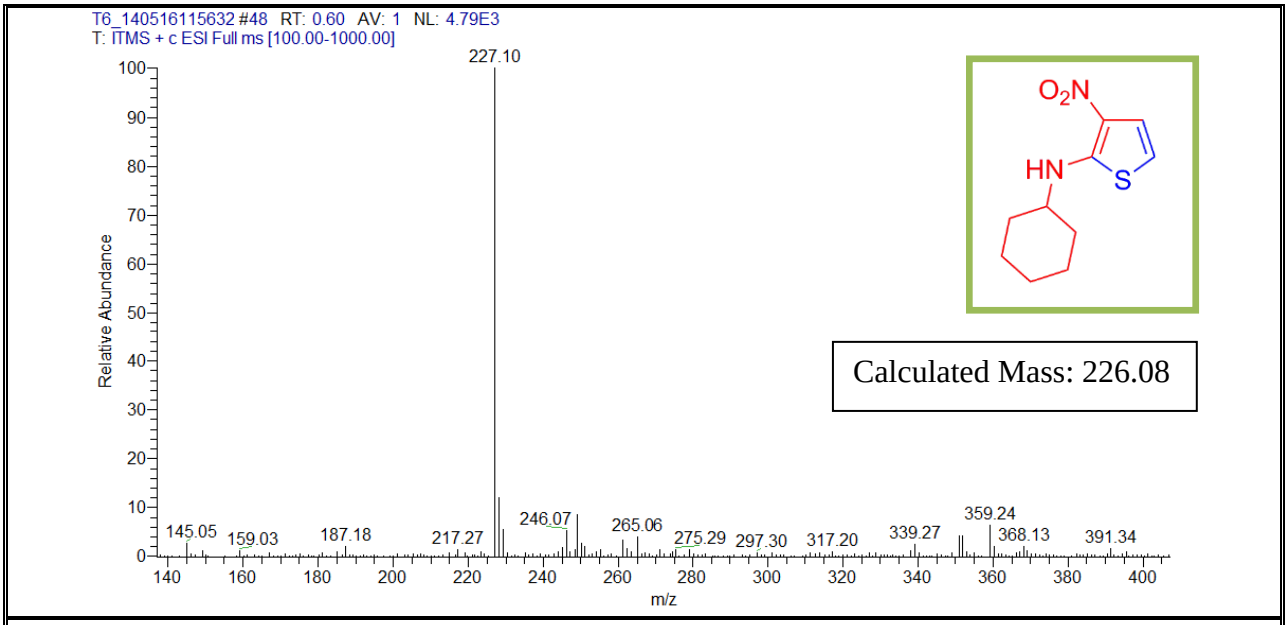



**Figure 93** ESI mass spectrum of Spectrum of **3x**

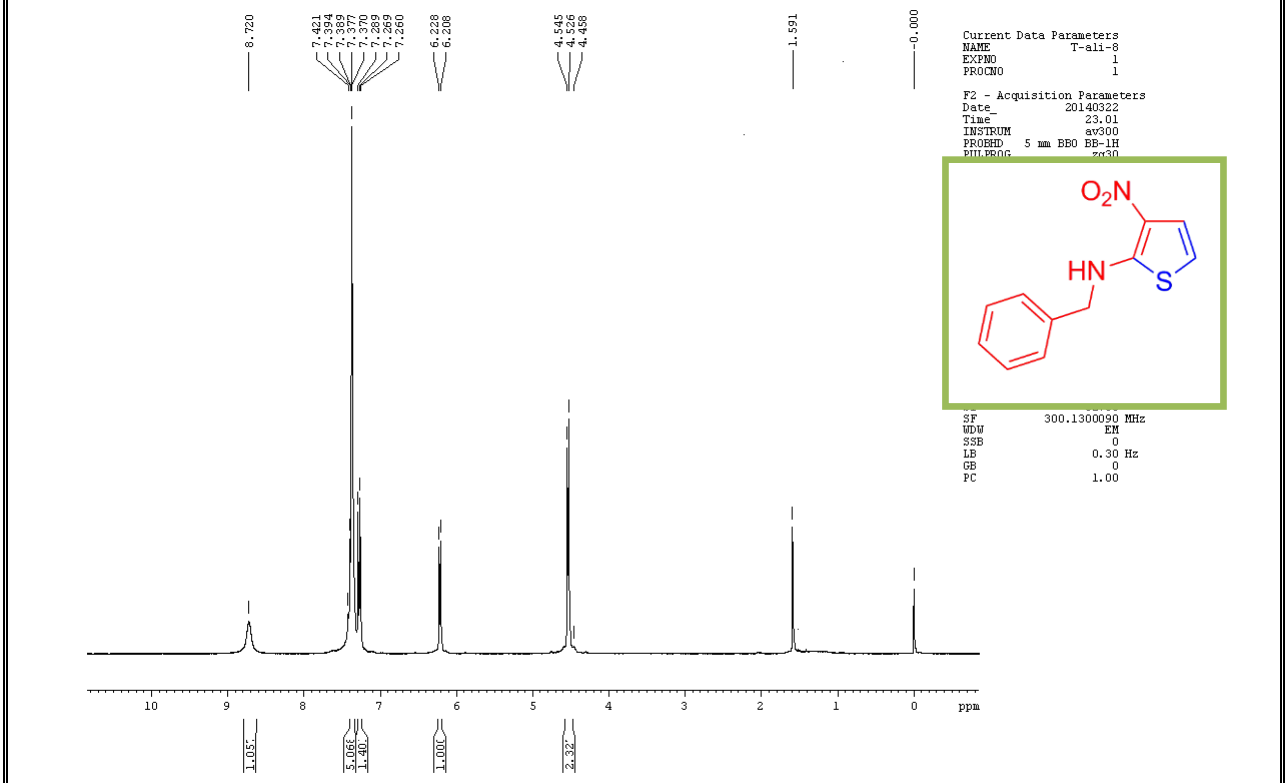



**Figure 94** $^{1}$H NMR Spectrum **3y** ($CDCl_3$)

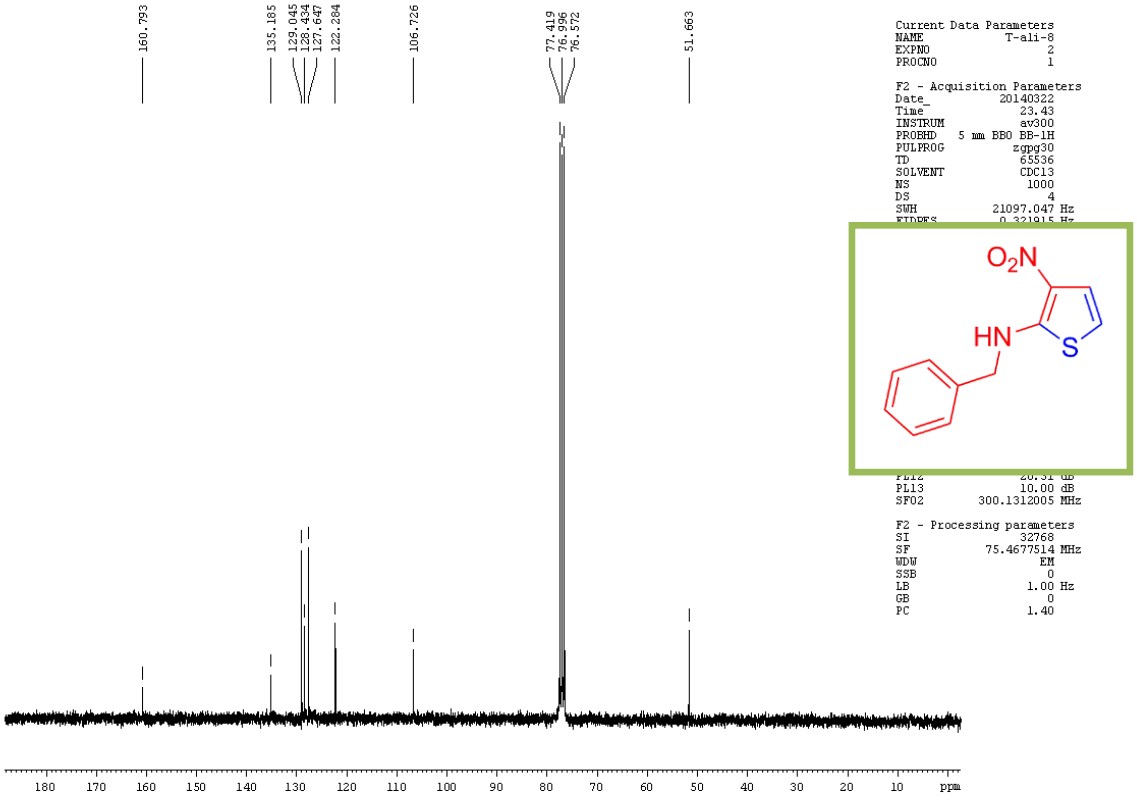



**Figure 95** $^{13}$C NMR Spectrum of **3y** ($CDCl_3$)

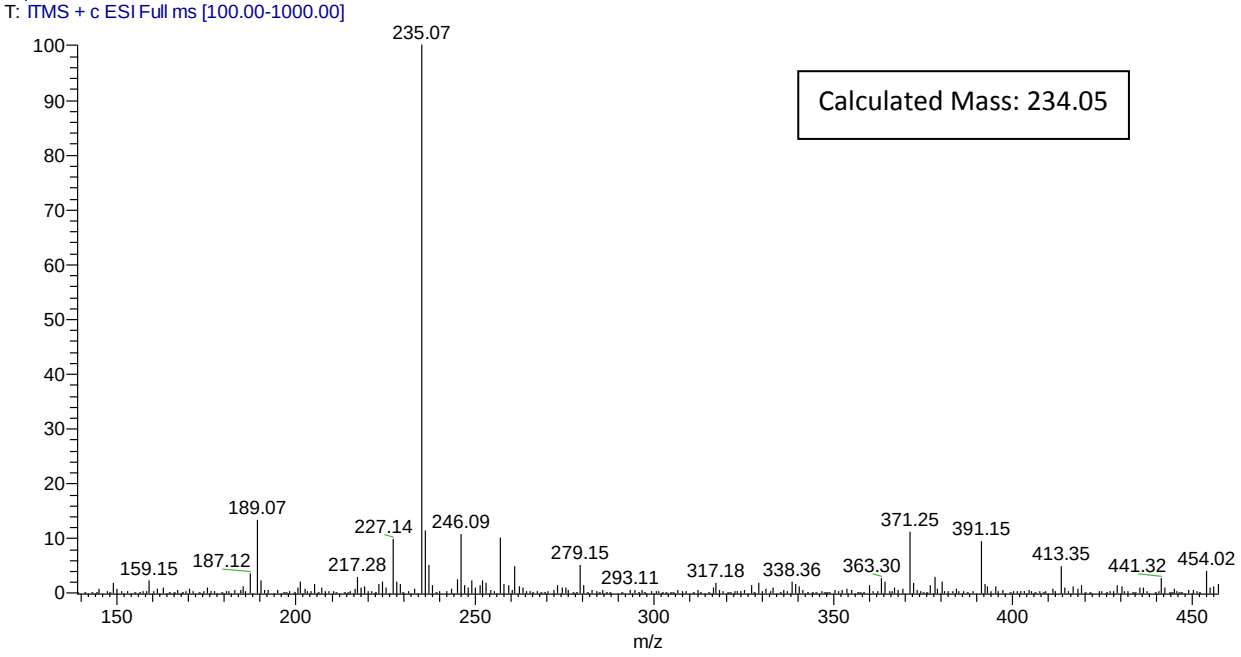



**Figure 96** ESI mass spectrum of Spectrum of **3y**

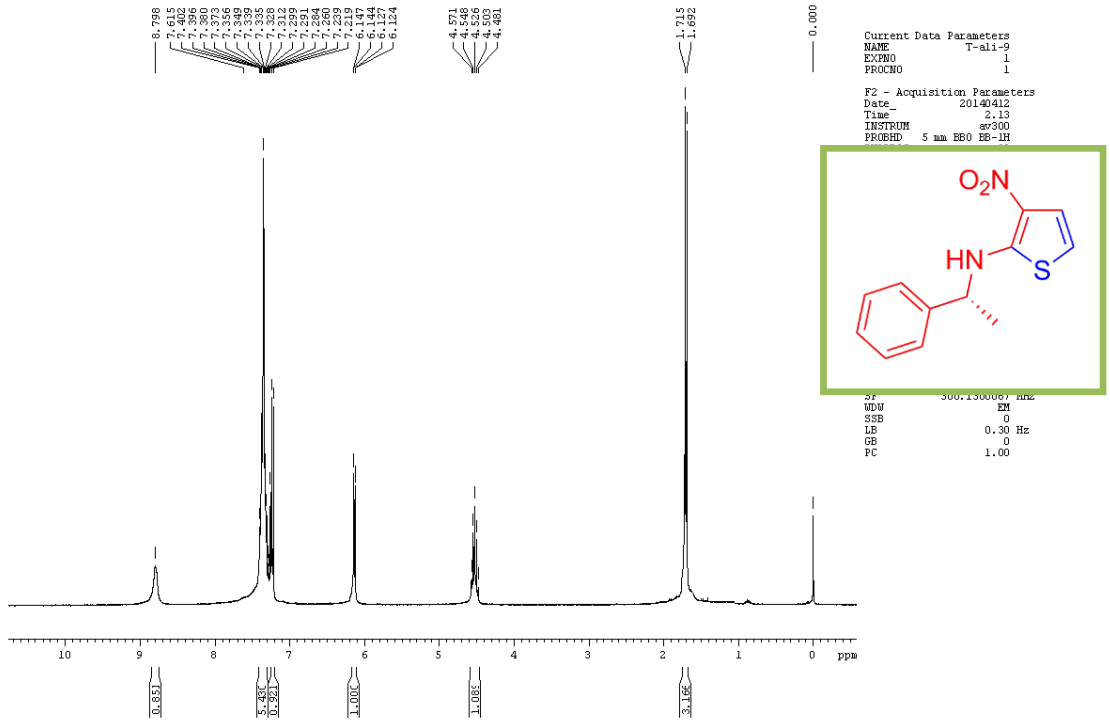



**Figure 97** $^{1}$H NMR Spectrum **3z** ($CDCl_3$)

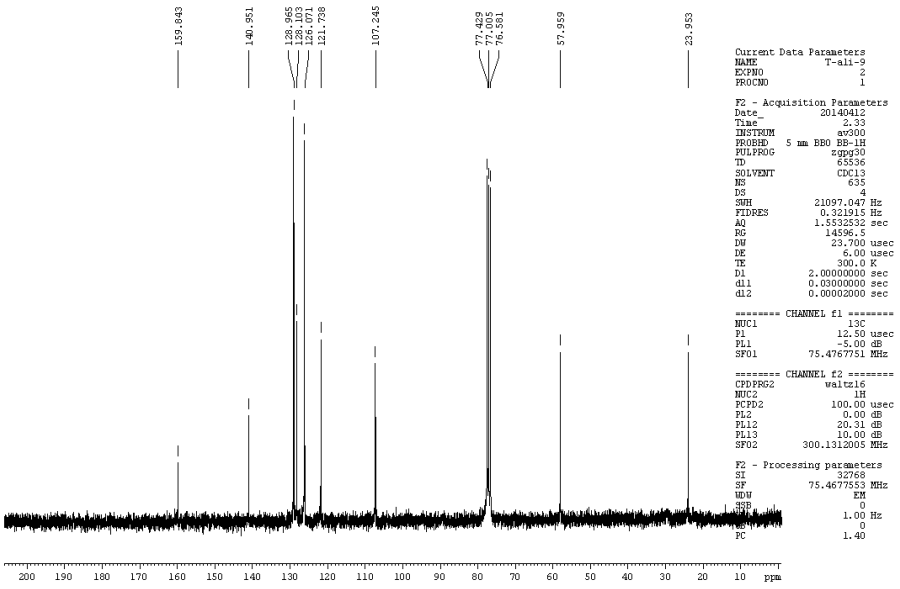



**Figure 98** $^{13}$C NMR Spectrum of **3z** ($CDCl_3$)

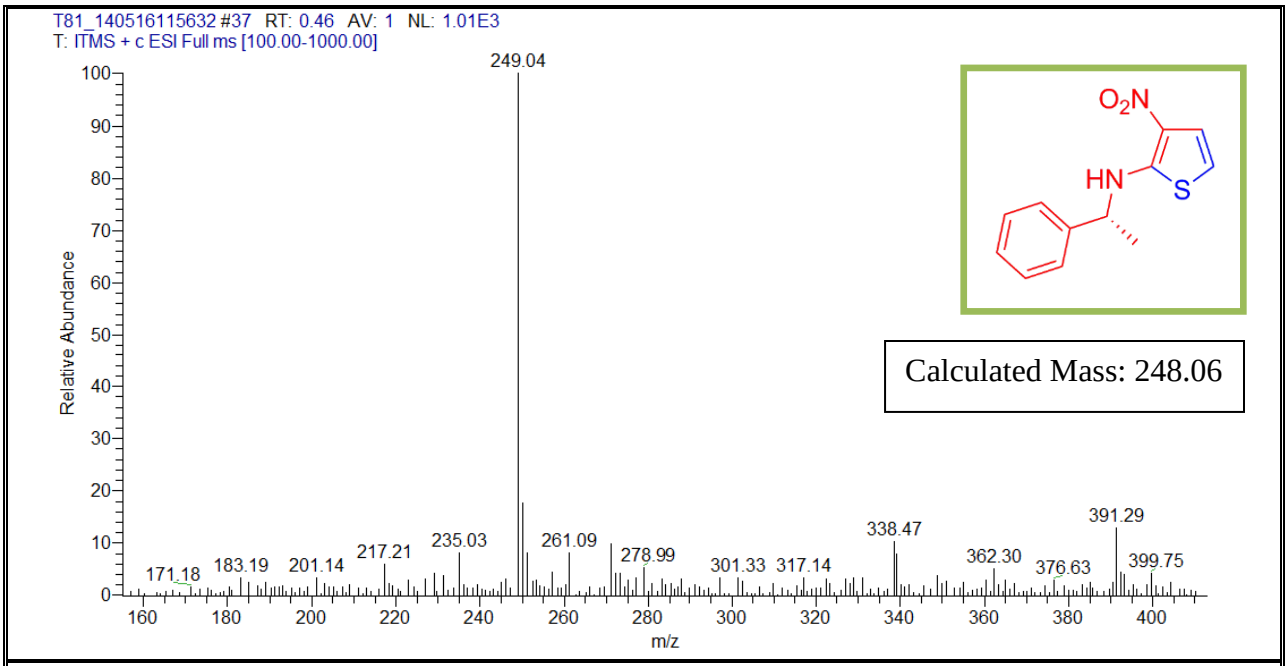



**Figure 99** ESI mass spectrum of Spectrum of **3z**

## References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2. Buchholz, M.; Hamann, A.; Aust, S.; Brandt, W.; Bohme, L.; Hoffmann, T.; Schilling, S.; Demuth, H.-U.; Heiser, U. *J. Med. Chem.* **2009,** *52,* 7069–7080. doi:10.1021/jm900969p