

**Novel sulfamoylbenzoates as antifungal agents against
*Malassezia furfur***

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1. Experimental

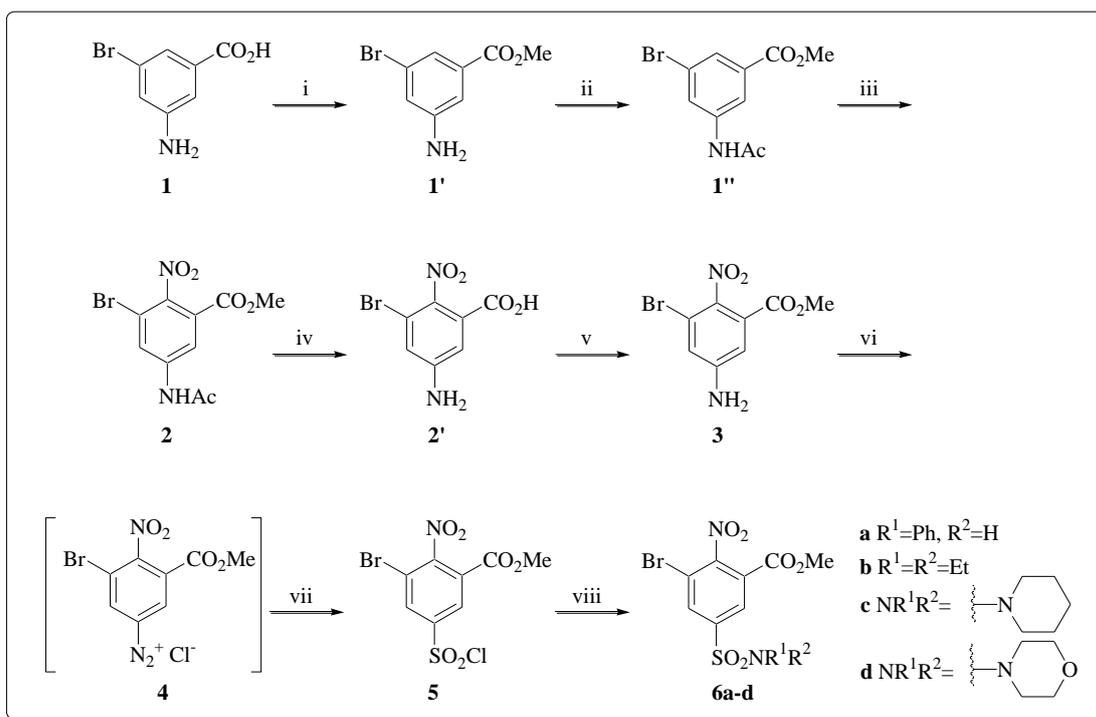
Materials and Methods

The ^1H , $^{13}\text{C}/\text{DEPT}$ and 2D NMR spectra were recorded at 25 °C on Bruker Avance NMR spectrometers (Vernon Hills, IL) operating at 400 and 600 MHz for ^1H , and at 100 and 150 MHz for ^{13}C . The chemical shifts are reported in ppm units (δ) and are referenced to TMS at 0 ppm; the coupling constants J are reported in Hertz. The residual proton signals of the deuterated solvents were used as internal standards in ^1H NMR measurements ($\delta_{\text{H}} = 7.26$ ppm for CDCl_3 and 2.50 ppm $\text{DMSO}-d_6$). In the ^{13}C NMR measurements, the central signals of the deuterated solvents ($\delta_{\text{C}} = 77.1$ ppm for CDCl_3 and 39.5 ppm for $\text{DMSO}-d_6$) were used as internal standards [H. E. Gottlieb, V. Kotlyar and A. Nudelman, *J Org Chem*, 1997, **62**, 7512]. The splitting pattern abbreviations are as follows: s, singlet; d, doublet; t, triplet; q, quartet; qui, quintet; m, unresolved multiplet, and br, broad. High-resolution mass spectra (HRMS) were obtained using a QTOF instrument (Agilent) mass spectrometer in electrospray ionization (ESI) negative mode or a GC-MS instrument (Agilent) mass spectrometer in electron ionization (EI) positive mode. Melting points were measured with a Fisher–Johns melting point apparatus (Waltham, MA, USA) and are uncorrected. Column flash chromatography (FC) from Merck was performed on silica gel 60 (230–400 mesh ASTM). Analytical TLC was carried out on pre-coated silica gel 60 F_{254} (Merck) sheets using UV absorption, iodine, and vanillin physical adsorption for visualization.

Analytical HPLC (Young Lin Instruments, Anyang, Korea) was performed on a LUNA C18(2) (10 μm , 250 mm \times 21.2 mm) column from Phenomenex, Inc. (Torrance, CA). Acetonitrile and doubly distilled water were used as an eluent in different ratios. Dry THF was prepared by distillation from sodium/benzophenone ketyl under N_2 . Other anhydrous solvents and commercially available reagents were purchased from several companies: Sigma-Aldrich, Holand-Moran, Acros Organic, Alfa Aesar, Merck and IU-CHEM LTD, and were used without additional purification.

Malassezia furfur was obtained from the ATCC (14521). It was inoculated and maintained in modified Dixon media in a shaking bacterial incubator at 32 °C. Then, the fungi were diluted to O.D 0.1 and grown in bacterial 96-well plate w/o or with the compound. *Malassezia furfur* growth inhibition was determined as previously reported with a minor modification [C. Leong, A. Buttafuoco, M. Glatz and P. P. Bosshard, *J Clin Microbiol*, 2017, **55**, 1883]. Briefly, in the end of incubation, AlamarBlue (Resazurin) was added at a final concentration of 0.004% and the fluorescence was determined (Excitation 550; Emission 590). The statistics were calculated by Student's T-test and a p-value below 0.05 was considered significant.

Synthetic procedures



Scheme S1 Synthesis of multi-functional arenesulfonamides **6a-d**. *Reagents and conditions:* i, MeOH, SOCl_2 , $0 \rightarrow 25$ °C, then reflux 2 h; ii, Ac_2O , Et_3N , DMAP (cat), THF, 25 °C, overnight; iii, HNO_3 , conc. H_2SO_4 , $0 \rightarrow 25$ °C, then 25 °C 30 min; iv, $\text{Ba}(\text{OH})_2$, MeOH- H_2O , reflux, 18 h; v, MeOH, H_2SO_4 (cat), 25 °C, sonication, 91 h; vi, NaNO_2 , conc. HCl/water , 0 °C, 15 min; vii, SO_2 , CuCl (cat), HCl (aq.), -5 °C, then 0 °C 75 min; viii, $\text{R}^1\text{R}^2\text{NH}$, CH_2Cl_2 , 25 °C, overnight.

Methyl 3-amino-5-bromobenzoate (1'). Thionyl chloride (8.71 g, 5.34 ml, 73.2 mmol) was added dropwise over 20 min to an ice-cold stirred solution of 3-amino-5-bromobenzoic acid (**1**, 10.54 g, 48.8 mmol) in dry methanol (150 ml). The resulting reaction mixture was refluxed for 2 h. After it was cooled, the solvent was evaporated in vacuum, and the residue was suspended in ethyl acetate (200 ml). Next, the suspension was washed with 0.2 M NaOH (2×100 ml), brine (100 ml), dried (Na_2SO_4) and concentrated to afford methyl ester **1'** (10.09 g, 90%) as an off-white solid. The NMR spectra of thus prepared **1'** match those of the literature data [S. R. Inglis, A. Zervosen, E. C. Woon, T. Gerards, N. Teller, D. S. Fischer, A. Luxen and C. J. Schofield, *J Med Chem*, 2009, **52**, 6097; G. Haberhauer, C. Burkhardt, S. Woitschetzki and C. Wolper, *J Org Chem*, 2015, **80**, 1887].

Methyl 3-acetamido-5-bromobenzoate (1''). Acetic anhydride (535 mg, 5.24 mmol) was added dropwise over 5 min to an ice-cooled stirred solution of compound **1'** (1.00 g, 4.35 mmol), triethylamine (955 mg, 9.46 mmol) and DMAP (53 mg, 0.435 mmol) as a catalyst in dry THF (12 ml). The mixture was stirred at 25 °C overnight and concentrated in vacuum. The residue was dissolved in ethyl acetate (60 ml), washed with water (30 ml), 5% NaHCO₃ (2×30 ml) and with brine (30 ml). After it was dried with Na₂SO₄ and the solvent was evaporated, acetanilide **1''** (1.10 g, 93%) was obtained as an off-white solid. The NMR spectra of **1''** match those of the literature data [S. R. Inglis, A. Zervosen, E. C. Woon, T. Gerards, N. Teller, D. S. Fischer, A. Luxen and C. J. Schofield, *J Med Chem*, 2009, **52**, 6097; H. Kakuta, I. Azumaya, H. Masu, M. Matsumura, K. Yamaguchi, H. Kagechika and A. Tanatani, *Tetrahedron*, 2010, **66**, 8254].

Methyl 5-acetamido-3-bromo-2-nitrobenzoate (2) [cf. D. P. Sevbo and O. F. Ginzburg, *Zh. Org. Khim.*, 1976, **12**, 1819]. A mixture of HNO₃ (0.24 g, d 1.42, 0.17 ml) and conc. H₂SO₄ (3 ml) was added to an ice-cooled well-stirred suspension of **1c** (0.50 g, 1.84 mmol) in conc. H₂SO₄ (10 ml, *d* = 1.83). The mixture was allowed to reach 25 °C and was stirred for additional 30 min. The mixture was poured into ice, **which caused** formation of a crystalline precipitate. Finally, the solid was filtered, thoroughly washed with water and dried in vacuum to afford nitrobenzoate **2** (410 mg, 70%) as an off-white solid, mp 164-167 °C. ¹H NMR (400 MHz, DMSO-*d*₆): δ 10.65 (br s, 1H, NH), 8.33 (d, *J* = 2.2 Hz, 1H, C4H), 8.18 (d, *J* = 2.2 Hz, 1H, C6H), 3.87 (s, 3H, OCH₃), 2.12 (s, 3H, CH₃CO). ¹³C NMR (100 MHz, DMSO-*d*₆): δ 169.6 (CH₃CONH), 162.3 (CO₂CH₃), 144.4 (C2), 141.8 (C5), 125.9 (C4H), 124.6 (C1), 119.5 (C6H), 114.2 (C3), 53.5 (OCH₃), 24.2 (CH₃CO). HRMS (ESI, negative mode): *m/z* calcd. for C₁₀H₈⁷⁹BrN₂O₅ [MH⁻] 314.9622, found 314.9630.

5-Amino-3-bromo-2-nitrobenzoic acid (2'). A solution of Ba(OH)₂·8H₂O (0.56 g, 1.78 mmol) in water (4 ml) was added to a solution of acetamido ester **2** (470 mg, 1.48 mmol) in MeOH (4 ml). The mixture was refluxed for 18 h. Methanol was evaporated in vacuum; the residue was acidified with conc. aq. HCl to pH 1-2. The formed precipitate was filtered, thoroughly washed with water and dried in vacuum to afford amino acid **2'** (335 mg, 86%) as yellow crystals, mp 203-208 °C. ¹H NMR (400 MHz, DMSO-*d*₆): δ 6.99 and 6.98 (AB q, *J* = 2.4 Hz, 2H, C6H and C4H), 6.39 (br s, 2H, NH₂). ¹³C NMR (150 MHz, DMSO-*d*₆): δ 164.8 (CO₂H), 151.6 (C5), 138.5 (C2), 128.8 (C1), 118.3 (C4H), 114.9 (C3), 113.4 (C6H). HRMS (ESI, negative mode): *m/z* calcd. for C₇H₄⁷⁹BrN₂O₄ [MH⁻] 258.9360, found 258.9370.

Methyl 5-amino-3-bromo-2-nitrobenzoate (3). A solution of aminobenzoic acid **2'** (400 mg, 1.53 mmol) in dry methanol (25 ml) was placed in a 100 ml corked tube, and 10 N H₂SO₄ (0.75 ml) was added. The mixture was sonicated at 25 °C for 91 h. After methanol was evaporated in vacuum, the residue was dissolved in CH₂Cl₂ (150 ml), washed with 20% NaHCO₃ (2×75 ml), with water (75 ml) and with brine (75 ml). After it was dried over Na₂SO₄, the solution was filtered and evaporated to afford the amino ester **3** (262 mg, 62%) as yellow crystals, mp 96-98 °C, R_f = 0.24 (CH₂Cl₂/hexane, 3:1). ¹H NMR: (600 MHz, CDCl₃): δ 7.07 (d, *J* = 2.5 Hz, 1H, C6H), 6.99 (d, *J* = 2.5 Hz, 1H, C4H), 4.22 (br s, 2H, NH₂), 3.87 (s, 3H, OCH₃). ¹³C NMR: (150 MHz, CDCl₃): δ 163.6 (CO₂CH₃), 148.5 (C5), 141.8 (C2), 127.1 (C1), 120.9 (C4H), 115.7 (C3), 114.9 (C6H), 53.3 (OCH₃). HRMS (ESI, negative mode): *m/z* calcd. for C₈H₆⁷⁹BrN₂O₄ [MH⁻] 272.9516, found 272.9520.

Methyl 3-bromo-5-chlorosulfonyl-2-nitrobenzoate (5). Thionyl chloride (0.52 g, 0.32 ml, 4.38 mmol) was added dropwise to water (4 ml) at 0 °C, and the solution was allowed to warm to 25 °C within 18 h. Cuprous chloride (30 mg, 0.30 mmol) was added to the mixture, and the resulting solution was stirred for 15 min at -5 °C (solution A). A solution of sodium nitrite (90 mg, 1.23 mmol) in water (0.60 ml) was added over 5 min to a cold (0 °C) solution of aniline **3** (300 mg, 1.09 mmol) in 10 M hydrochloric acid (5 ml). The reaction mixture was stirred at -5 to 0 °C for 1 h to afford a solution of diazonium chloride **4** (Solution B). Next, cold (0 °C) solution of diazonium salt **4** (Solution B) was added to solution A at -5 °C over 30 min, and the mixture was stirred at 0 °C for 75 min. The stirring was stopped, and after keeping at 0 °C for additional 30 min the aqueous phase was decanted from heavy orange oil which precipitated at the bottom of the reaction vessel. Finally, the oil was washed with cold (0 °C) water (2 x 3 ml) and dried in vacuum to afford crude sulfonyl chloride **5** (210 mg of *ca.* 70% purity (NMR), ~ 37% yield in 2 steps. ¹H NMR: (400 MHz, CDCl₃): δ 8.61 (d, *J* = 2.0 Hz, 1H, C6H), 8.44 (d, *J* = 2.0 Hz, 1H, C4H), 3.93 (s, 3H, OCH₃). ¹³C NMR: (100 MHz, CDCl₃): δ 160.3 (CO₂CH₃), 153.6 (C2), 145.5 (C5), 135.9 (C4H), 129.0 (C6H), 125.9 (C1), 116.4 (C3), 53.1 (OCH₃).

Crude sulfonyl chloride **5** was used without further purification in the following reaction steps.

General procedure for the synthesis of sulfonamides 6a-d. A solution of crude sulfonyl chloride **5** (0.20 mmol) in dry CH₂Cl₂ (7 ml) was added dropwise to a solution of an appropriate amine (0.22 mmol, see Scheme S1) in dry CH₂Cl₂ (7 ml). The mixture was stirred at 25 °C overnight and concentrated in vacuum. The residue was dissolved in ethyl acetate (60 ml), washed with water (20 ml), brine (20 ml), dried over Na₂SO₄ and evaporated. The residue was subjected to flash chromatography using ethyl acetate/hexane as the eluent to afford sulfonamides **6a-d**.

Methyl 3-bromo-2-nitro-5-(*N*-phenylsulfamoyl)benzoate (6a). Yield 74%, off-white solid, mp 158-162 °C, R_f = 0.33 (ethyl acetate/hexane, 3:7). ¹H NMR (400 MHz, CDCl₃): δ 8.28 (d, *J* = 1.8 Hz, 1H, C6H), 8.09 (d, *J* = 1.8 Hz, 1 H, C4H), 7.29-7.25 (m, 2H, *m*-H_{Ph}), 7.20-7.16 (m, 1H, *p*-H_{Ph}), 7.05-7.02 (m, 2H, *o*-H_{Ph}), 6.62 (br s, 1H, NH), 3.85 (s, 3H, CH₃O). ¹³C NMR (100 MHz, CDCl₃): δ 161.1 (CO₂CH₃), 152.6 (C2), 142.1 (C5), 136.4 (C4H), 134.9 (NC_{Ph}), 130.0 (2 *m*-C_{Ph}H), 129.2 (C6H), 127.2 (*p*-C_{Ph}H), 125.3 (C1), 122.9 (2 *o*-C_{Ph}H), 115.7 (C3), 54.0 (OCH₃). HRMS (ESI, negative mode): *m/z* calcd. for C₁₄H₁₀⁷⁹BrN₂O₆S [MH⁻] 412.9448, found 412.9456.

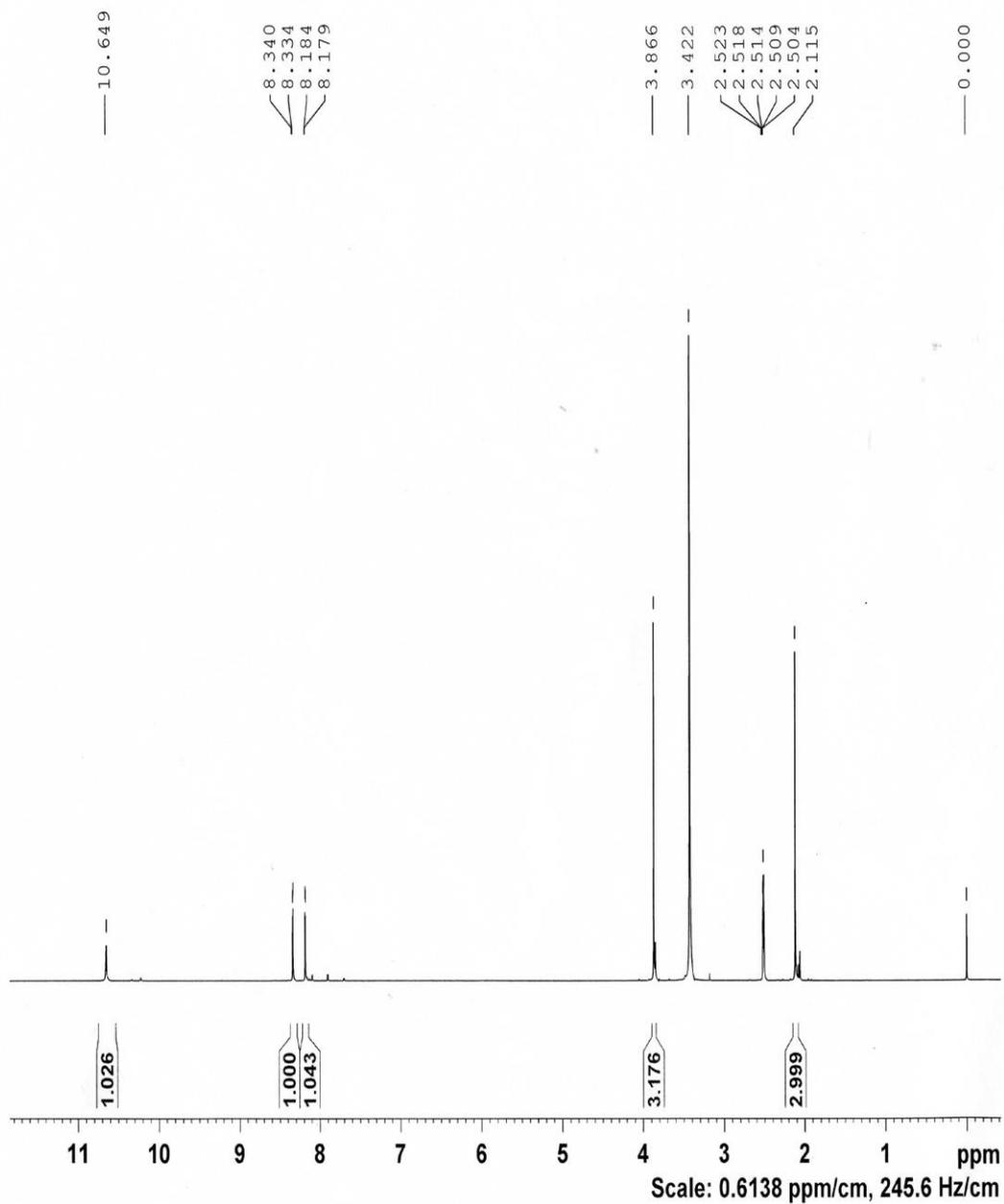
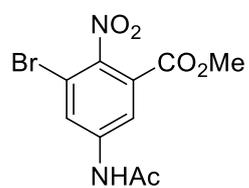
Methyl 3-bromo-5-(*N,N*-diethylsulfamoyl)-2-nitrobenzoate (6b). Yield 94%, colorless solid, mp 110-114 °C, R_f = 0.32 (CH₂Cl₂/toluene, 2:3). ¹H NMR (400 MHz, CDCl₃): δ 8.40 (d, *J* = 1.8 Hz, 1H, C6H), 8.27 (d, *J* = 1.8 Hz, 1H, C4H), 3.96 (s, 3H, CH₃O), 3.31 (q, *J* = 7.2 Hz, 4H, 2 NCH₂), 1.20 (t, *J* = 7.2 Hz, 6H, 2 CH₂CH₃). ¹³C NMR (100 MHz, CDCl₃): δ 161.2 (CO₂CH₃), 152.0 (C2), 143.7 (C5), 135.9 (C4H), 128.6 (C6H), 125.3 (C1), 115.6 (C3), 53.8 (OCH₃), 42.5 (2 NCH₂), 14.3 (2 CH₂CH₃). HRMS (EI, positive mode): *m/z* calcd. for C₁₂H₁₅⁷⁹BrN₂O₆S [M⁺] 393.9829, found 393.9818.

Methyl 3-bromo-2-nitro-5-(piperidin-1-ylsulfonyl)benzoate (6c). Yield 96%, off-white solid, mp 153-156 °C, R_f = 0.36 (CH₂Cl₂/toluene, 2:3). ¹H NMR (400 MHz, CDCl₃): δ 8.34 (d, *J* = 1.8 Hz, 1H, C6H), 8.22 (d, *J* = 1.8 Hz, 1H, C4H), 3.96 (s, 3H, CH₃O), 3.09 (t, *J* = 5.5 Hz, 4H, 2 NCH₂), 1.72-1.66 (m, 4H, 2 NCH₂CH₂), 1.55-1.48 (m, 2H, NCH₂CH₂CH₂). ¹³C NMR (100 MHz, CDCl₃): δ 161.2 (CO₂CH₃), 152.5 (C2), 140.1 (C5), 136.4 (C4H), 129.1 (C6H), 125.3 (C1), 115.6 (C3), 53.9 (OCH₃), 47.0 (2 NCH₂), 25.1 (2 NCH₂CH₂), 23.3 (NCH₂CH₂CH₂). HRMS (EI, positive mode): *m/z* calcd. for C₁₃H₁₅⁷⁹BrN₂O₆S [M⁺] 405.9829, found 405.9822.

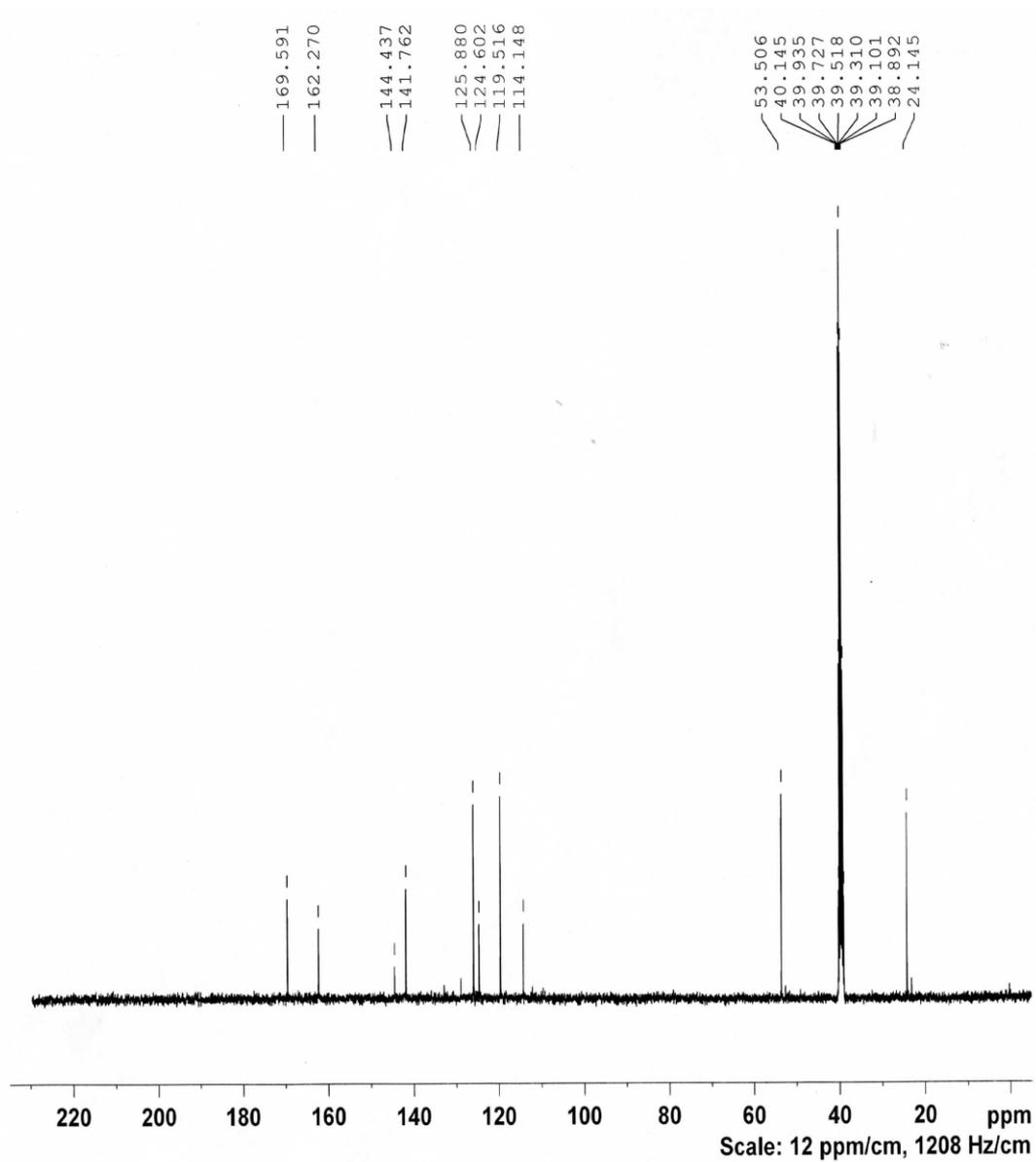
Methyl 3-bromo-5-(morpholinofulfonyl)-2-nitrobenzoate (6d). Yield 44%, yellow solid, mp 153-157 °C, R_f = 0.08 (CH₂Cl₂/toluene, 2:3). ¹H NMR (400 MHz, CDCl₃): δ 8.35 (d, *J* = 1.8 Hz, 1H, C6H), 8.22 (d, *J* = 1.8 Hz, 1H, C4H), 3.97 (s, 3H, CH₃O), 3.79 (t, *J* = 4.6 Hz, 4H, 2 OCH₂), 3.11 (t, *J* = 4.6 Hz, 4H, 2 NCH₂). ¹³C NMR (100 MHz, CDCl₃): δ 161.1 (CO₂CH₃), 152.5 (C2), 139.0 (C5), 136.6 (C4H), 129.4 (C6H), 125.5 (C1), 115.9 (C3), 66.0 (2 OCH₂), 53.9 (OCH₃), 45.9 (2 NCH₂). HRMS (EI, positive mode): *m/z* calcd. for C₁₂H₁₃⁷⁹BrN₂O₇S [M⁺] 407.9621, found 407.9612.

2. NMR spectra images

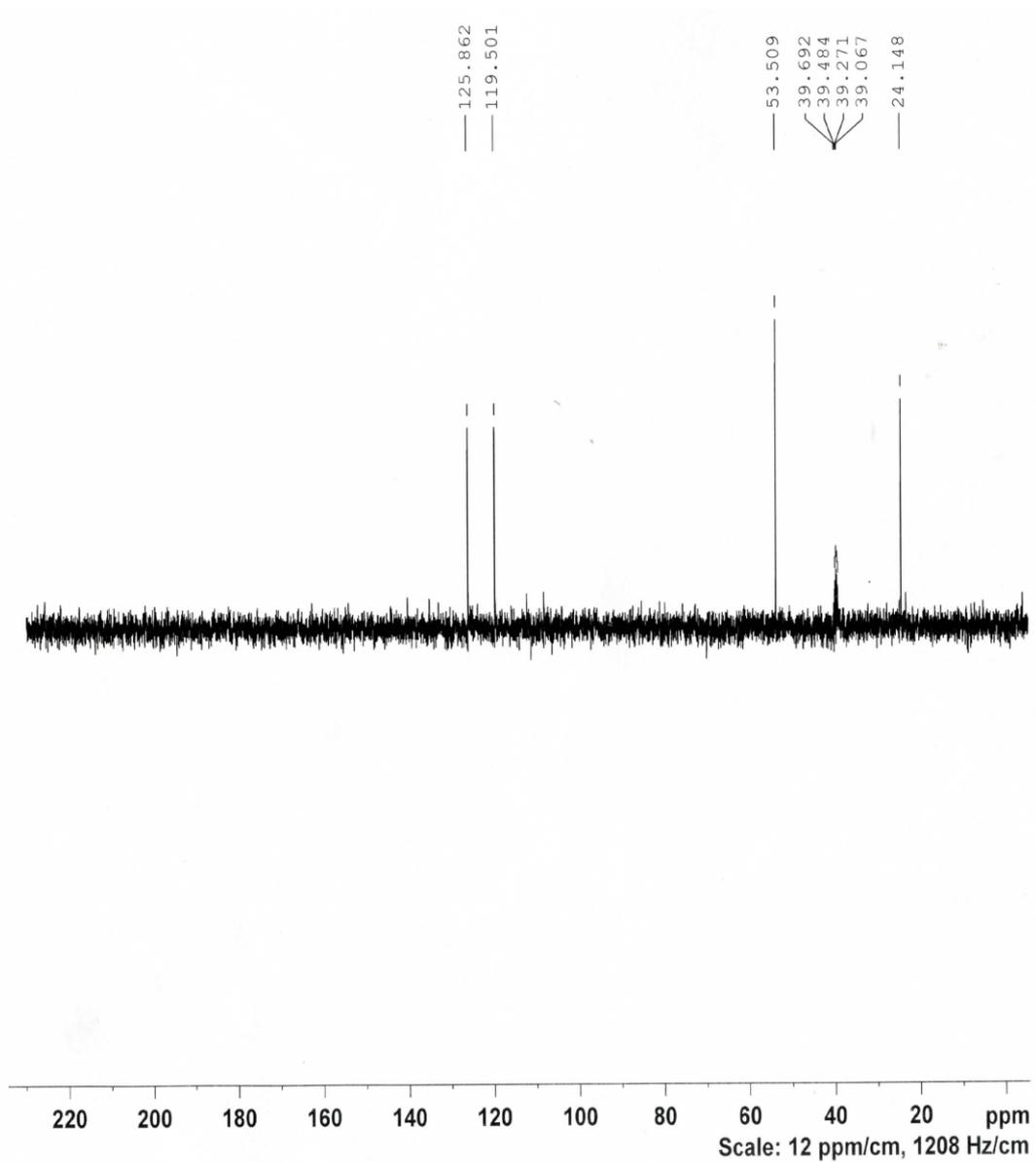
$^1\text{H-NMR}$ (400MHz, DMSO) – 2



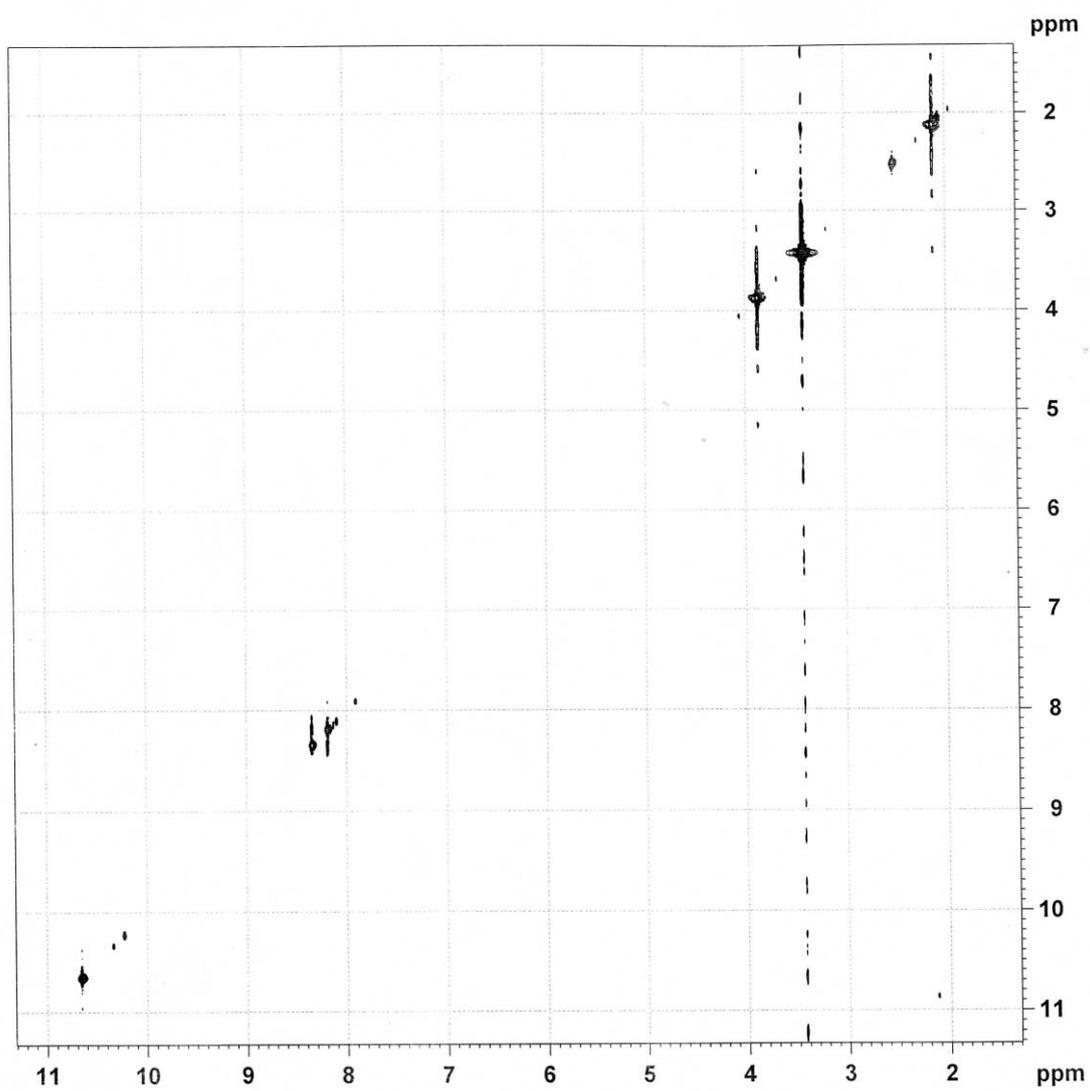
¹³C-NMR (100MHz, DMSO) – 2



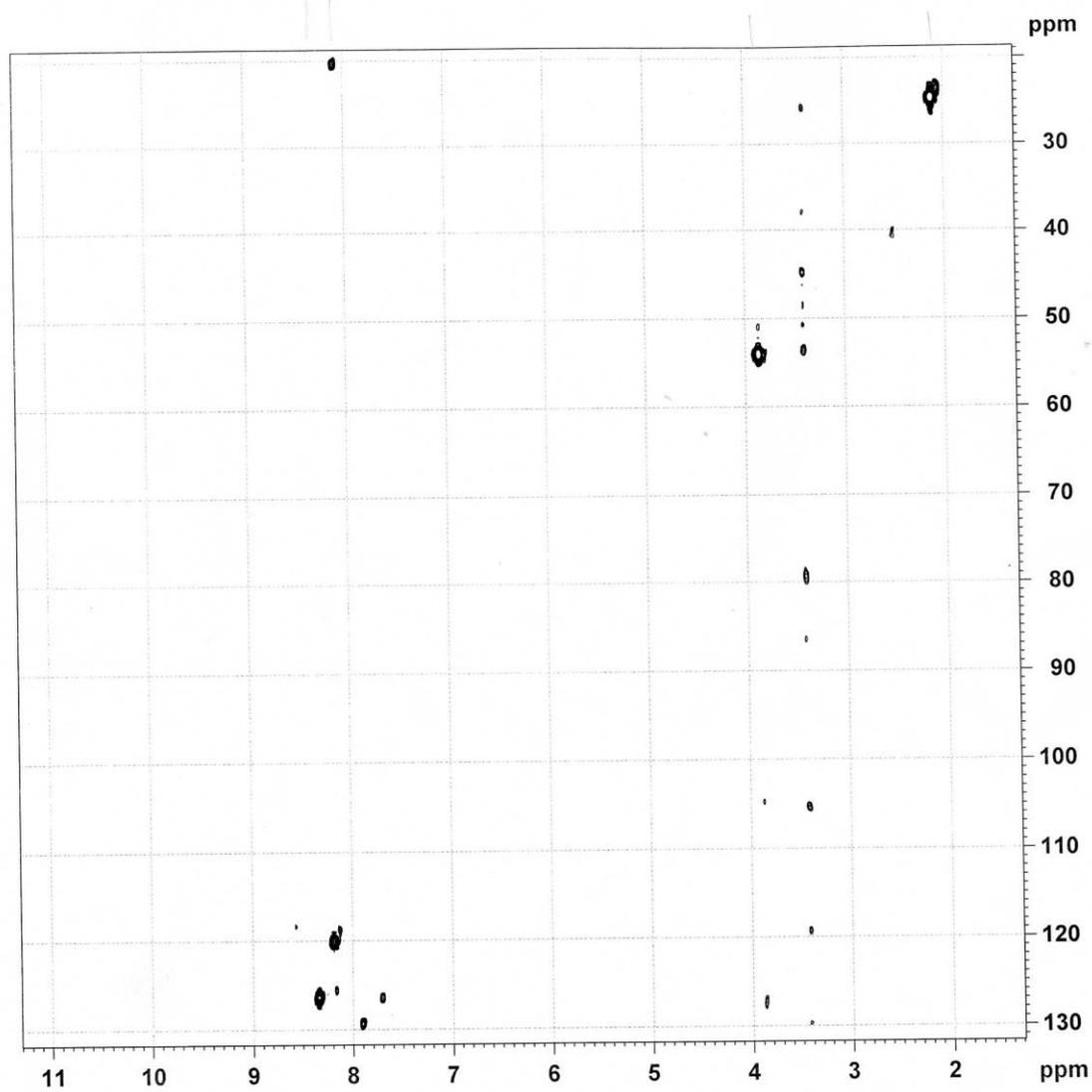
DEPT (100MHz, DMSO) – 2



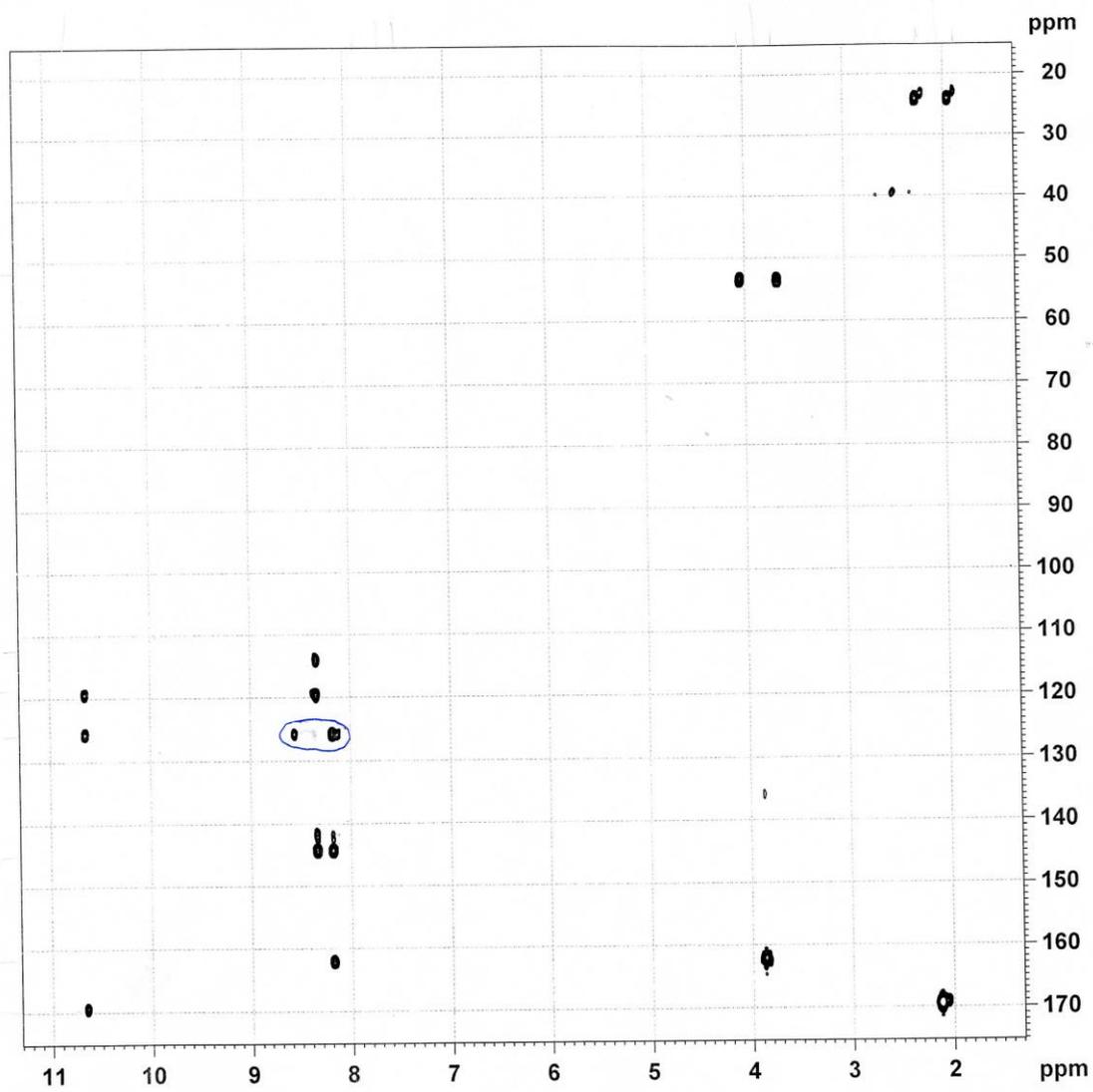
COSY (400MHz, DMSO) – 2



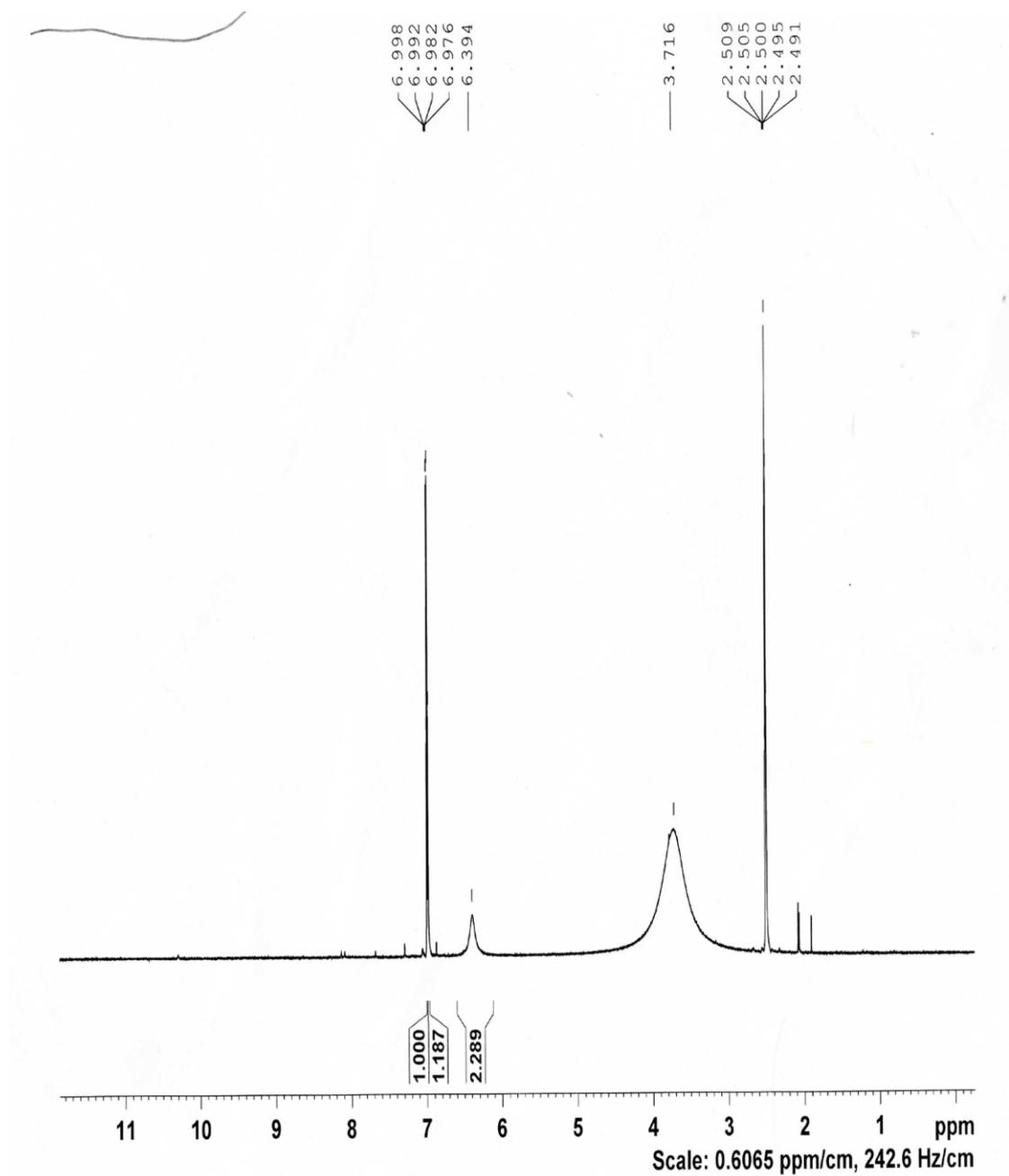
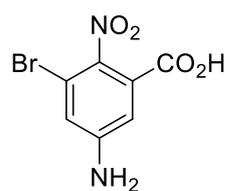
HMQC (100MHz, DMSO) – 2



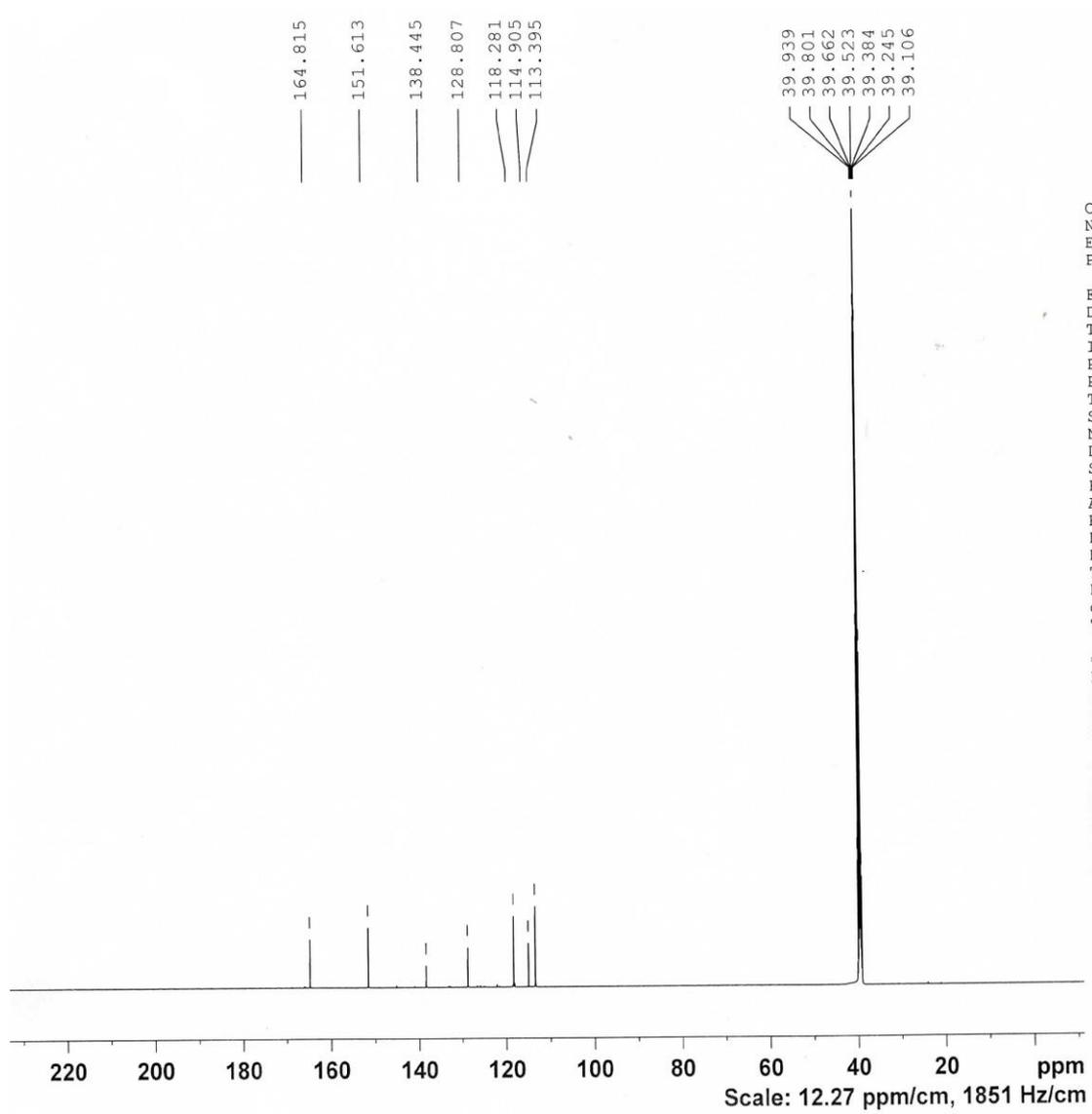
HMBC (100MHz, DMSO) – 2



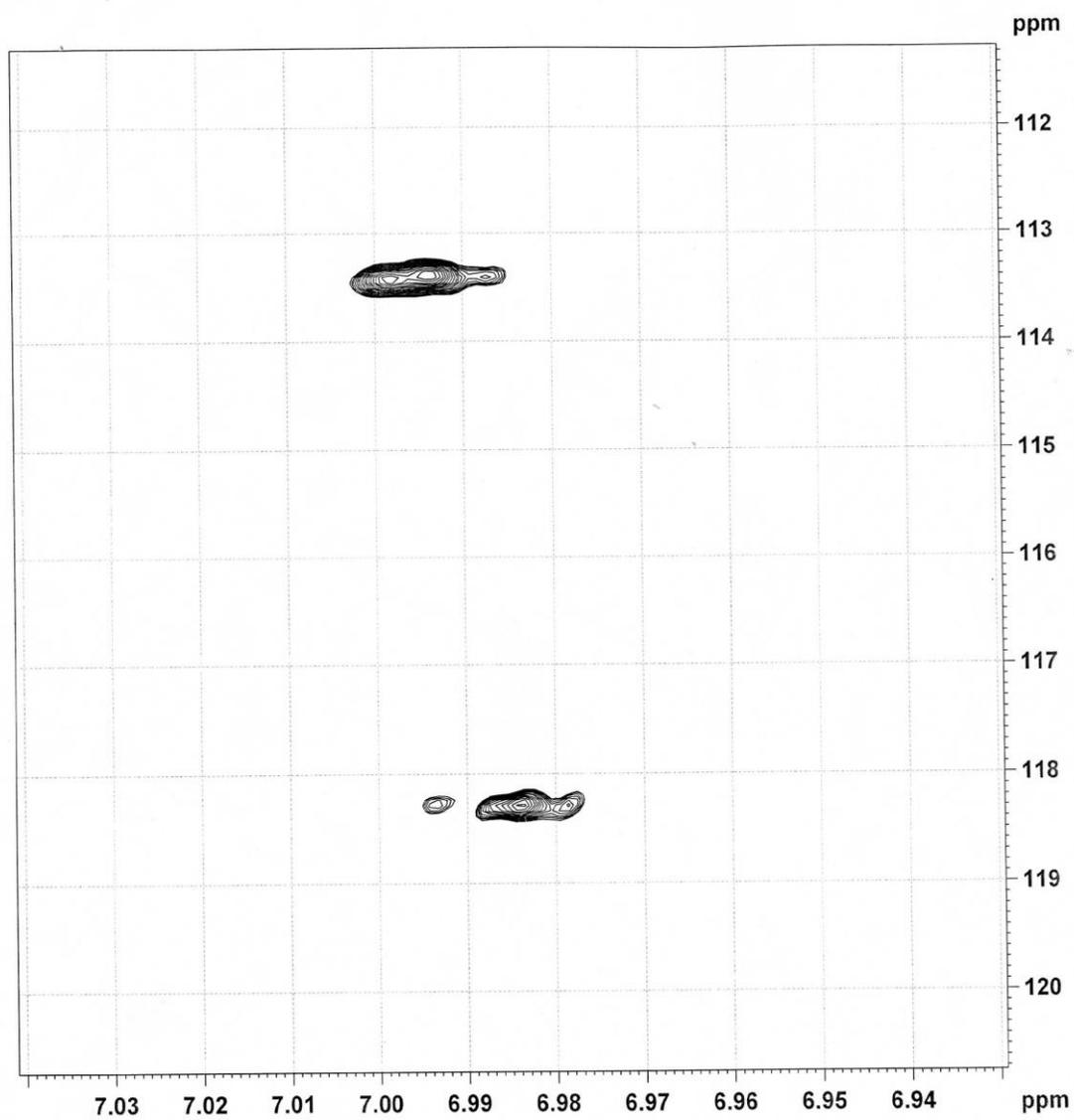
¹H-NMR (400MHz, DMSO) – 2b



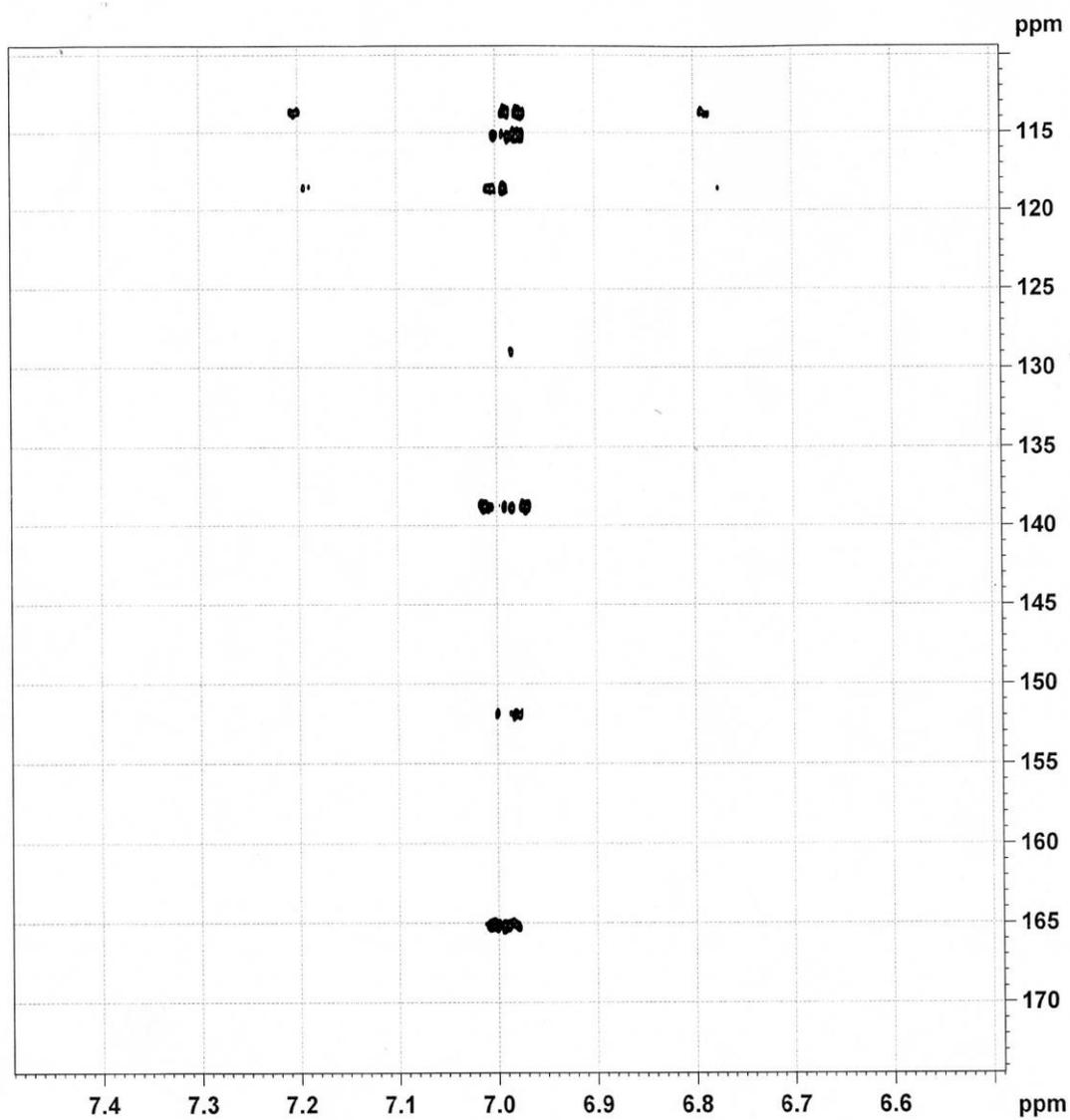
¹³C-NMR (150MHz, DMSO) – **2b**



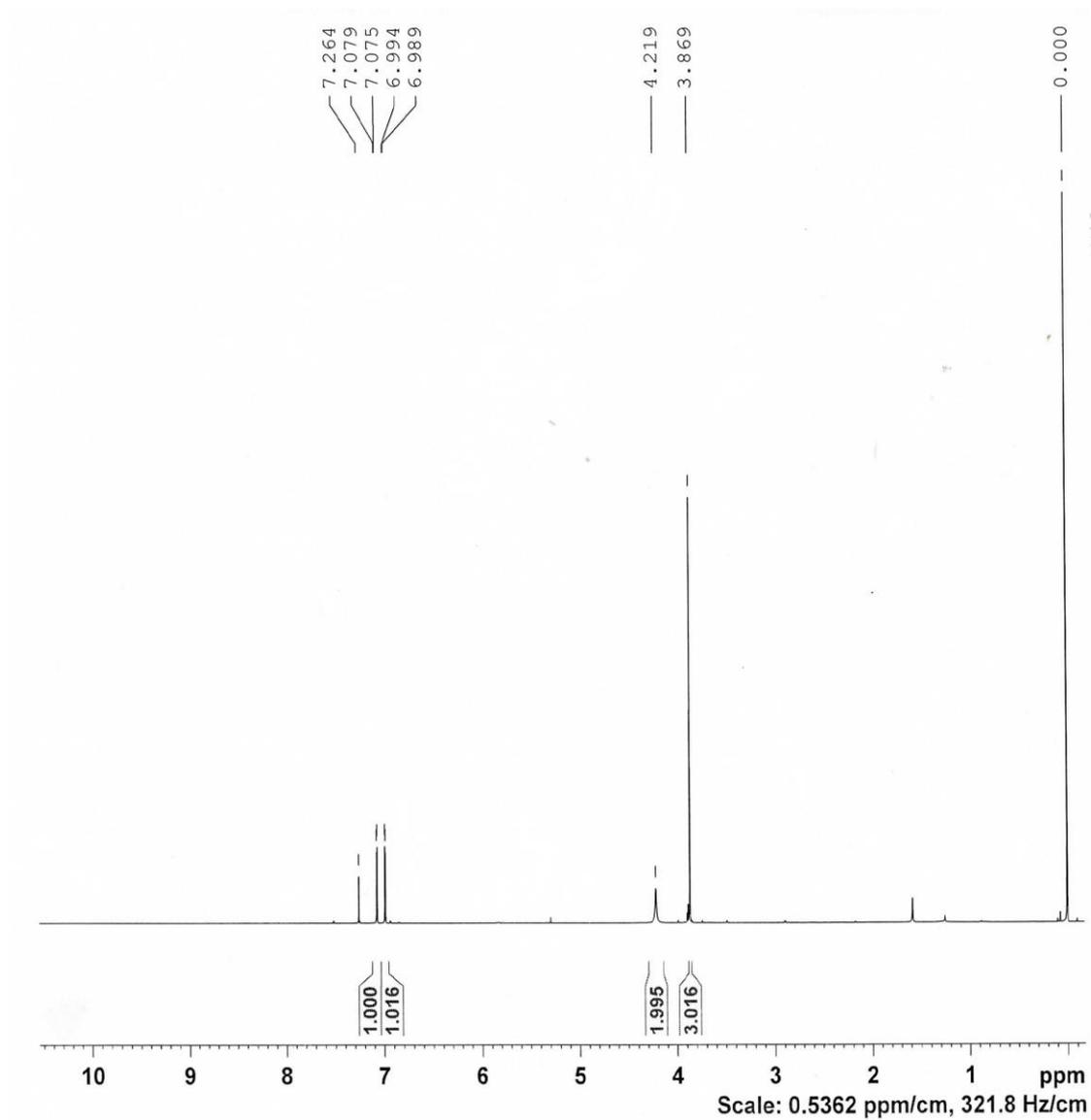
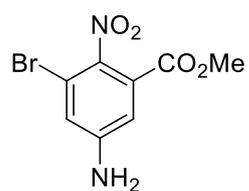
HMQC (100MHz, DMSO) – 2b



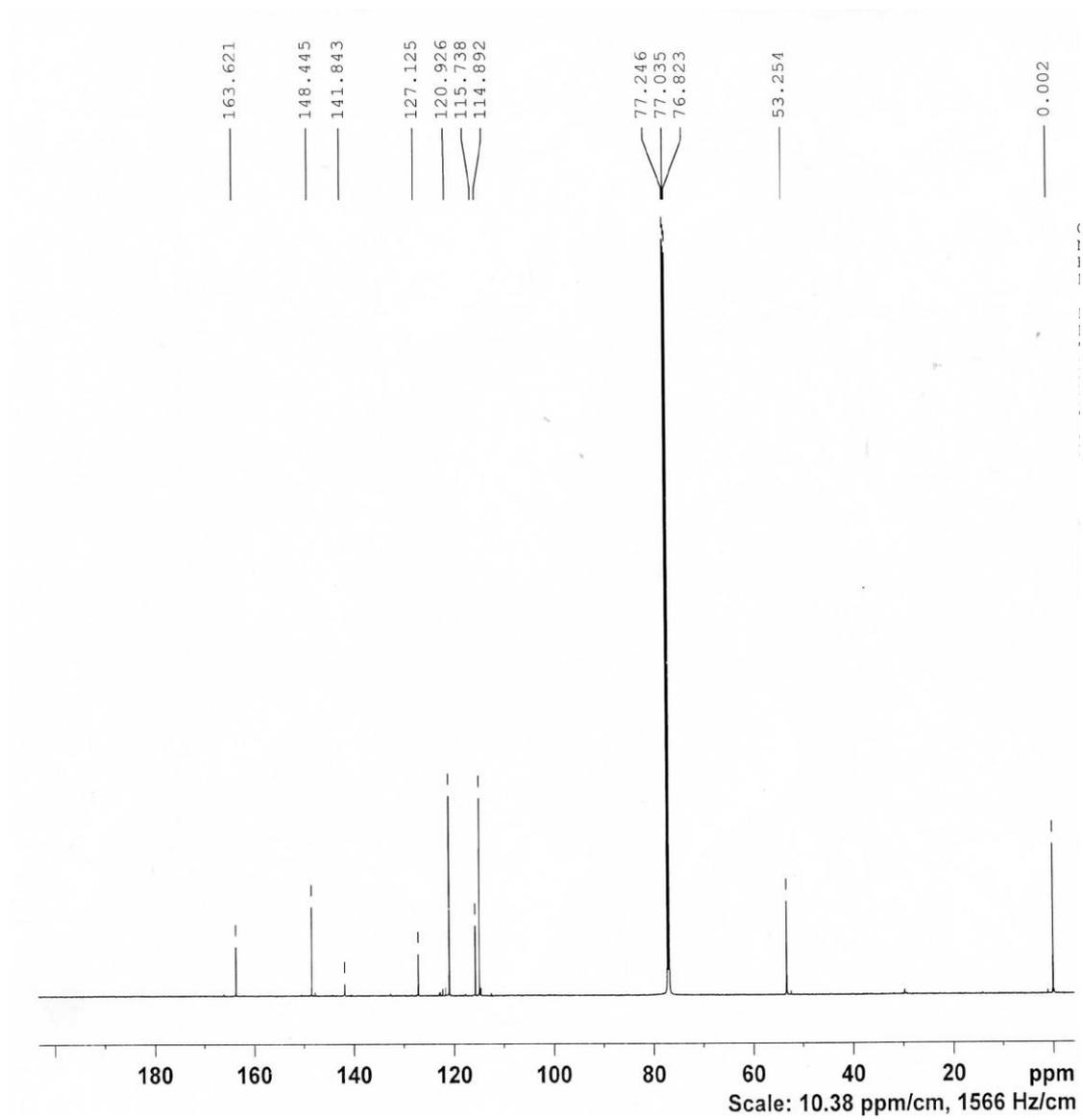
HMBC (100MHz, DMSO) – 2b



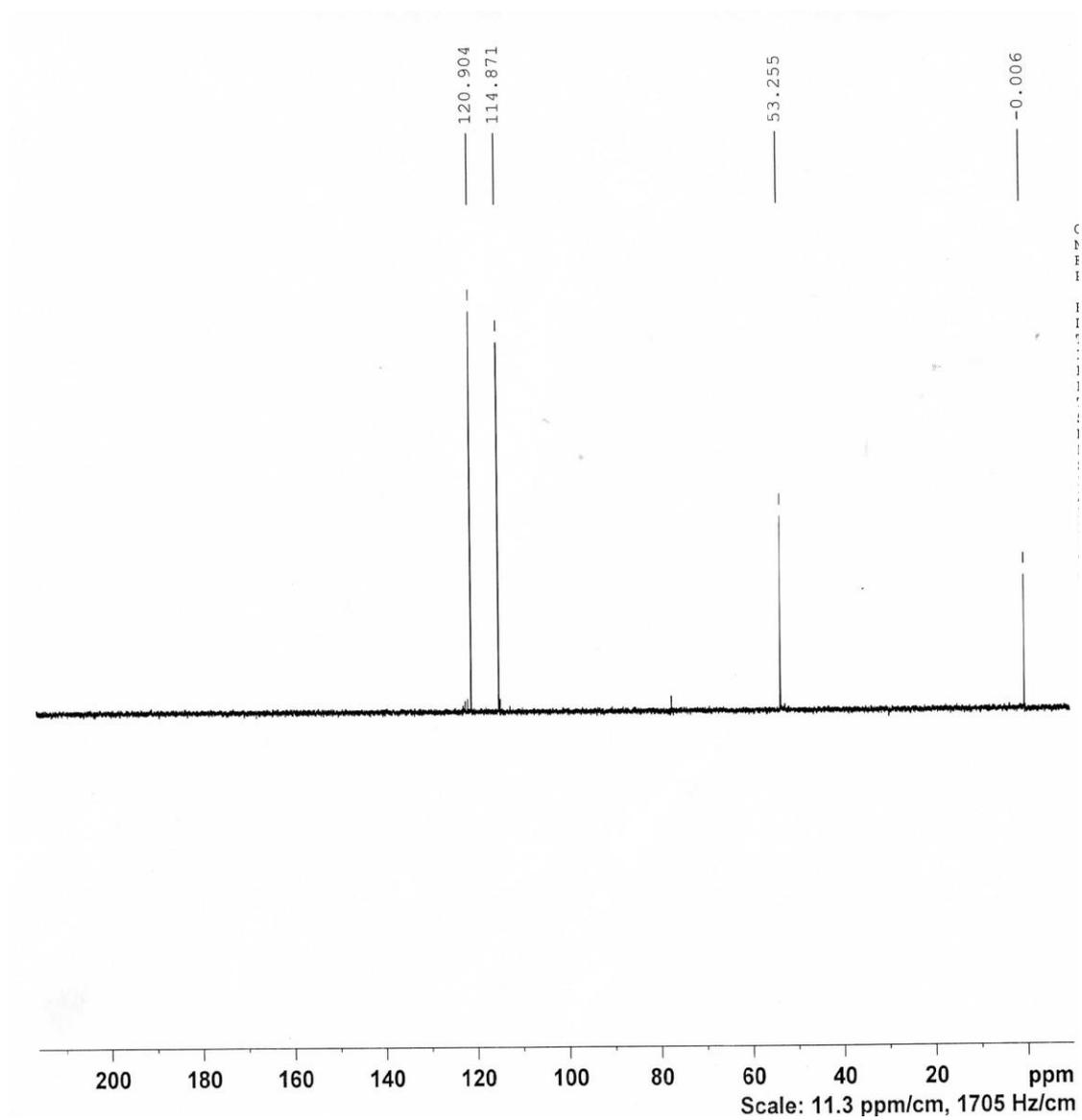
$^1\text{H-NMR}$ (600MHz, CDCl_3) – 3



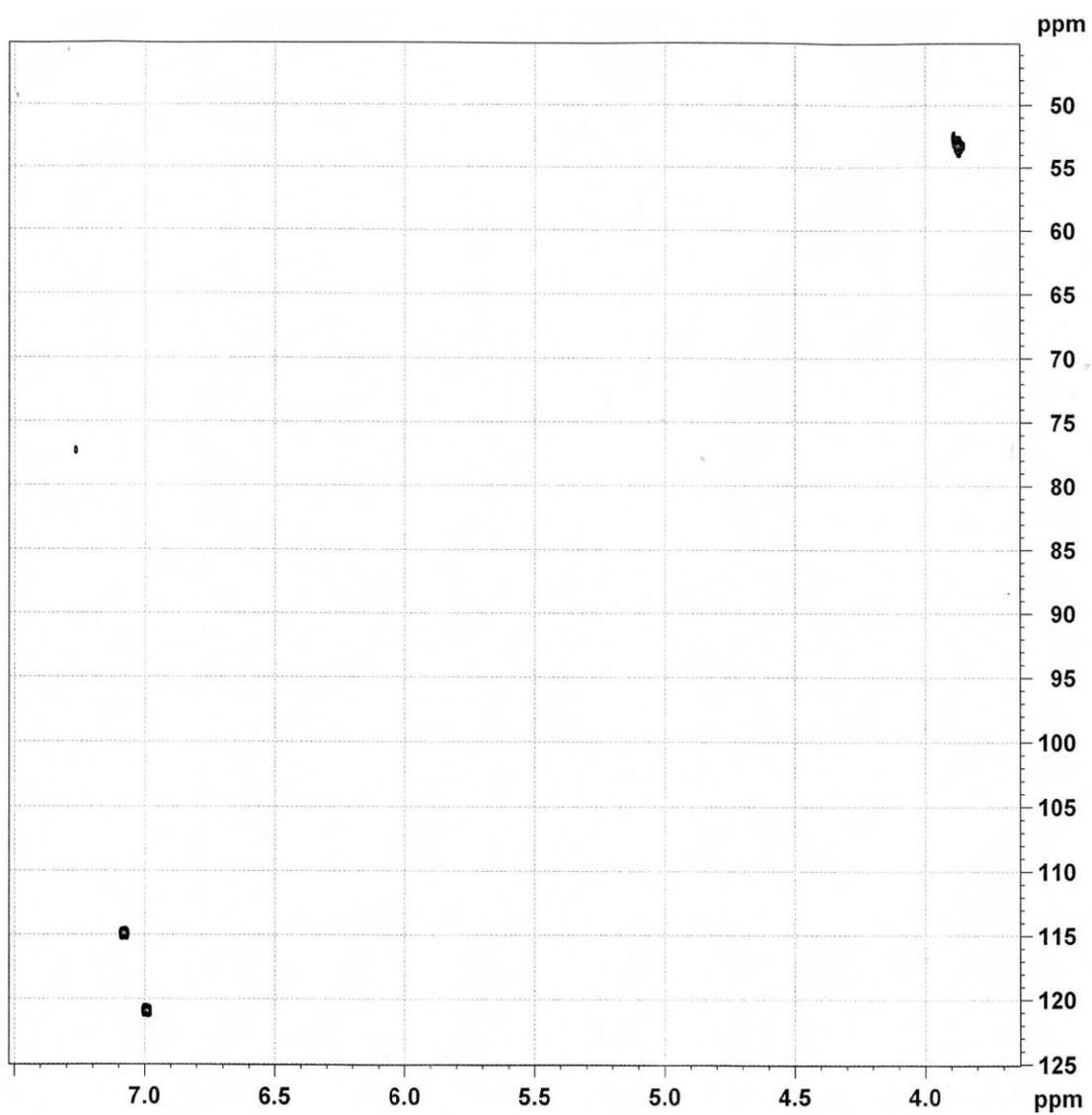
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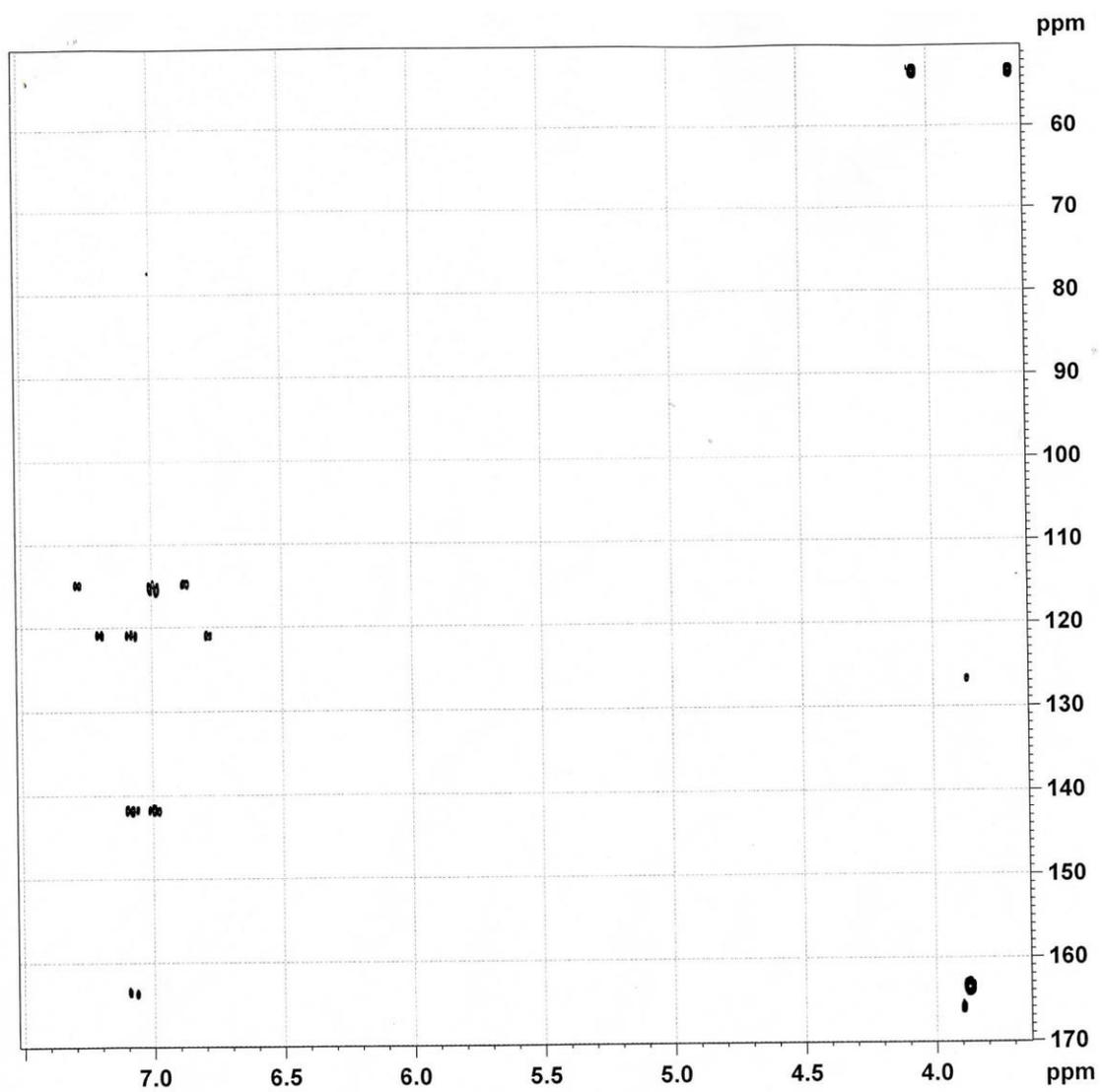
DEPT (100MHz, CDCl₃) – 3



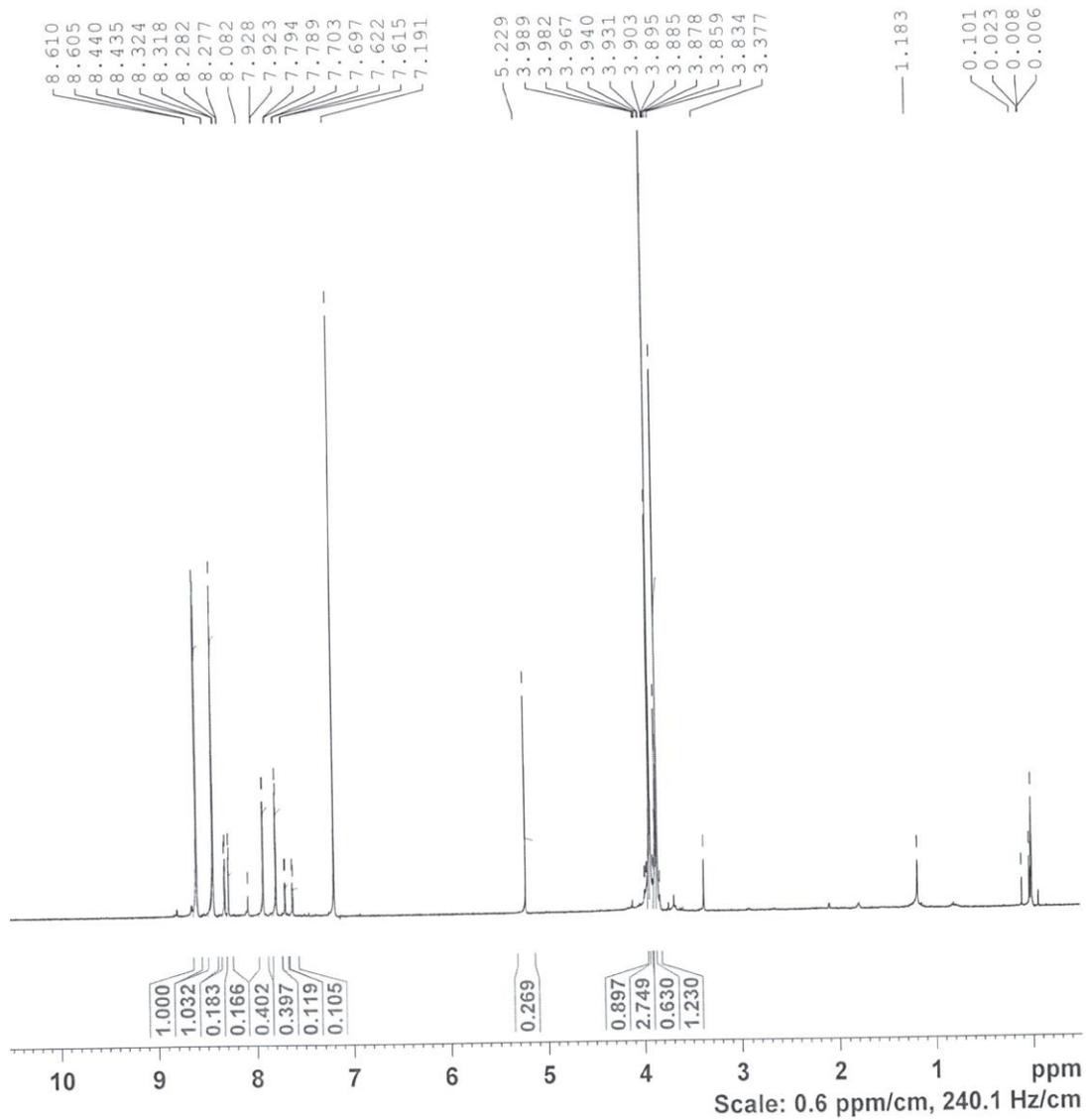
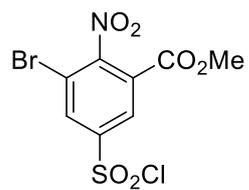
HMQC (100MHz, CDCl₃) – 3



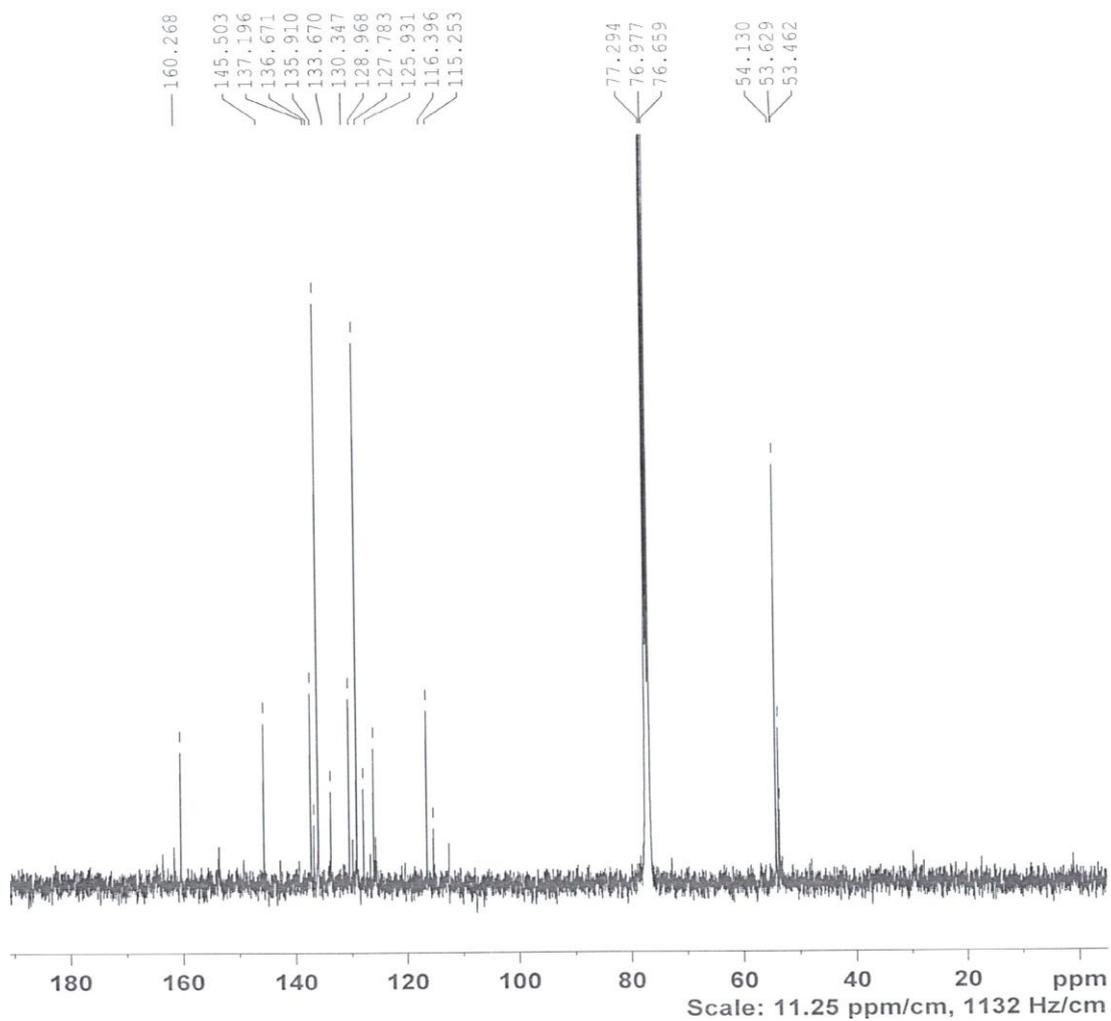
HMBC (100MHz, CDCl₃) – 3



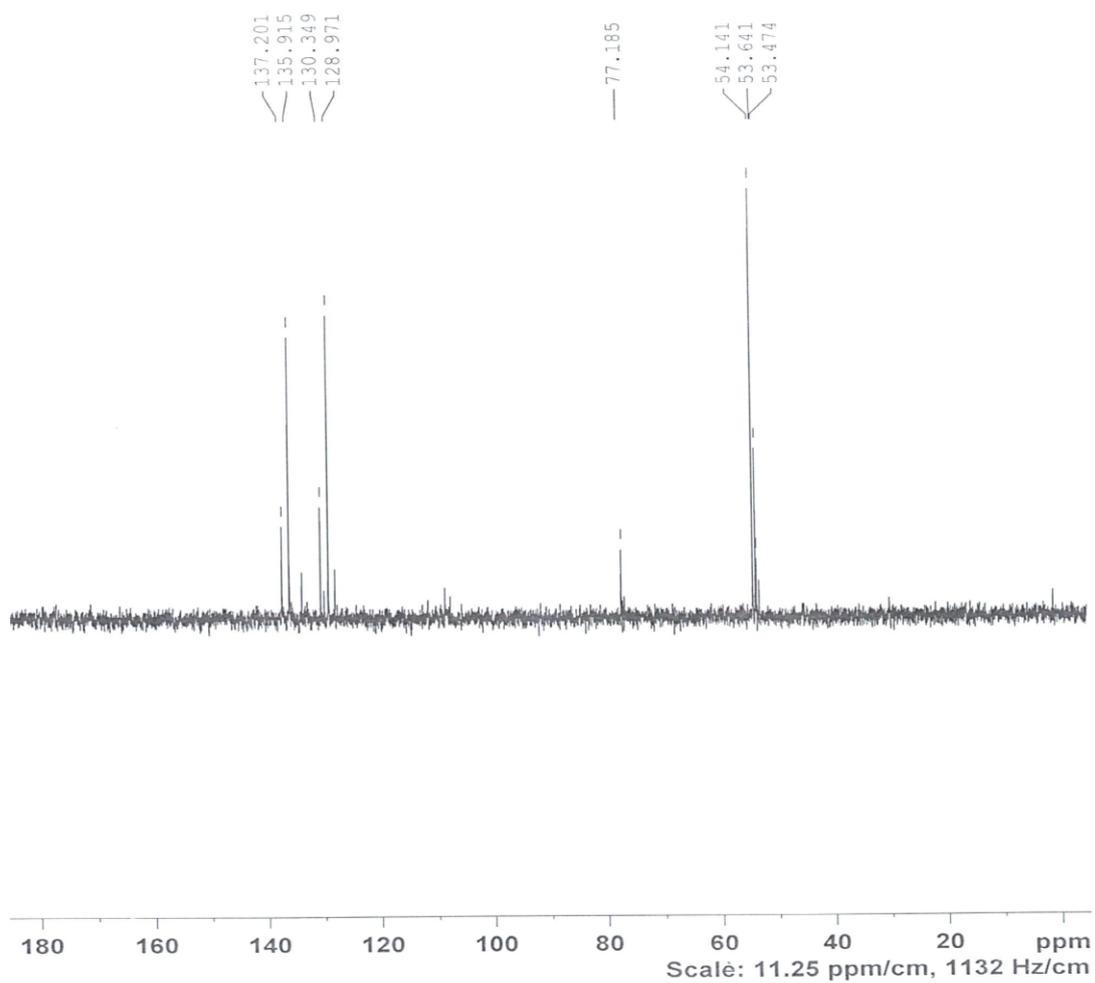
$^1\text{H-NMR}$ (400MHz, CDCl_3) – **5** (crude, 70% purity)



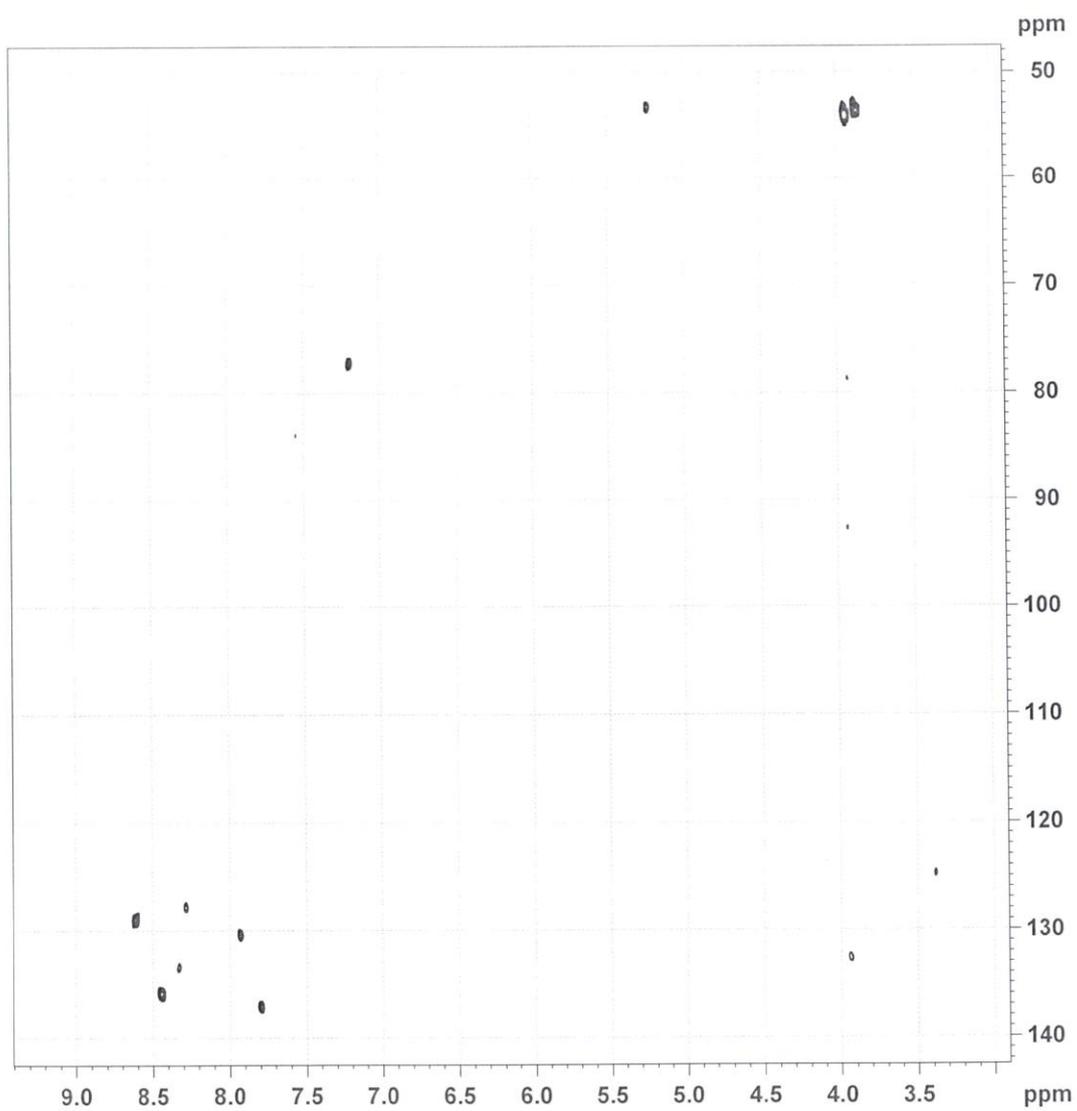
^{13}C -NMR (100MHz, CDCl_3) – 5



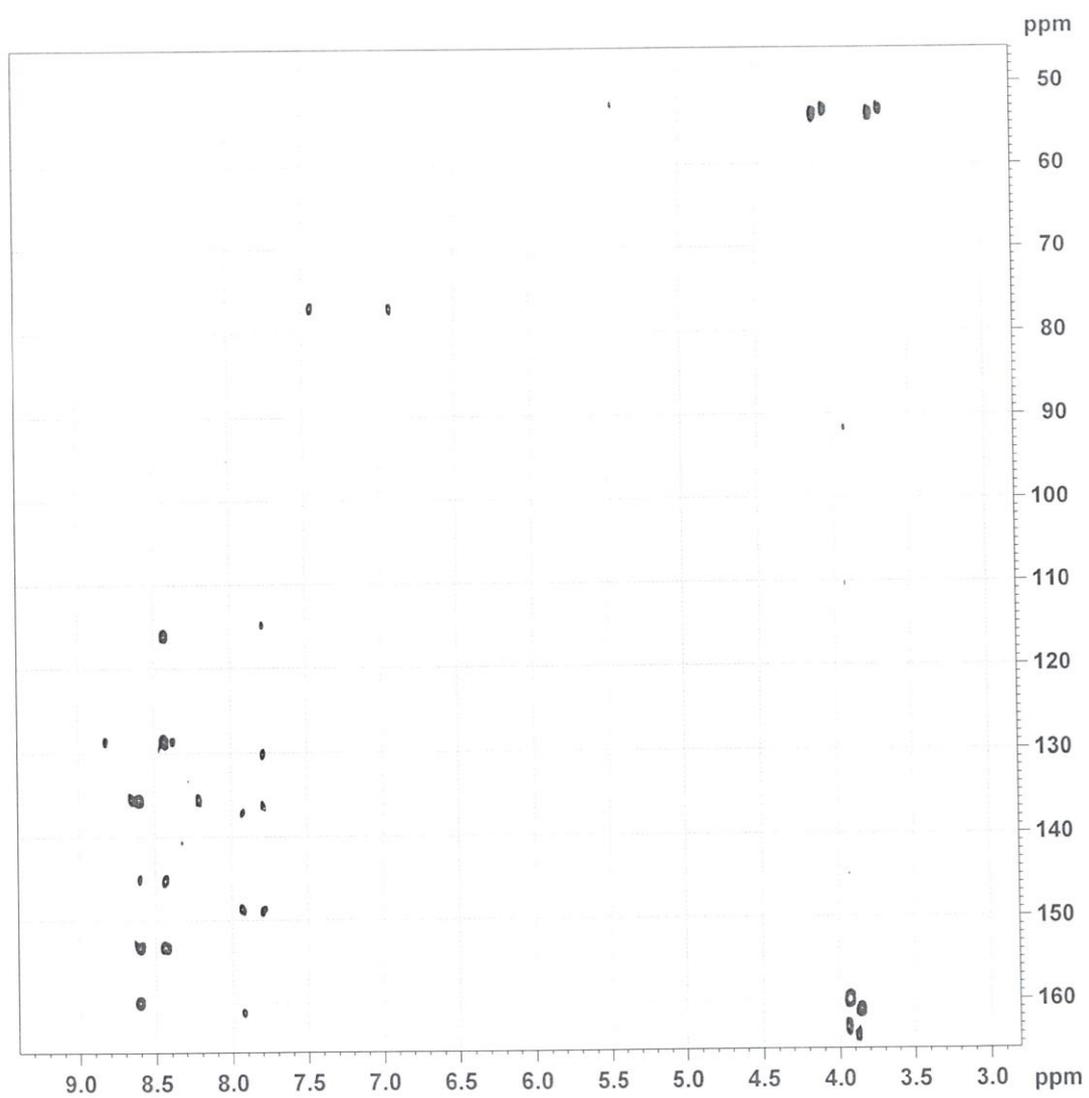
DEPT (100MHz, CDCl₃) – 5



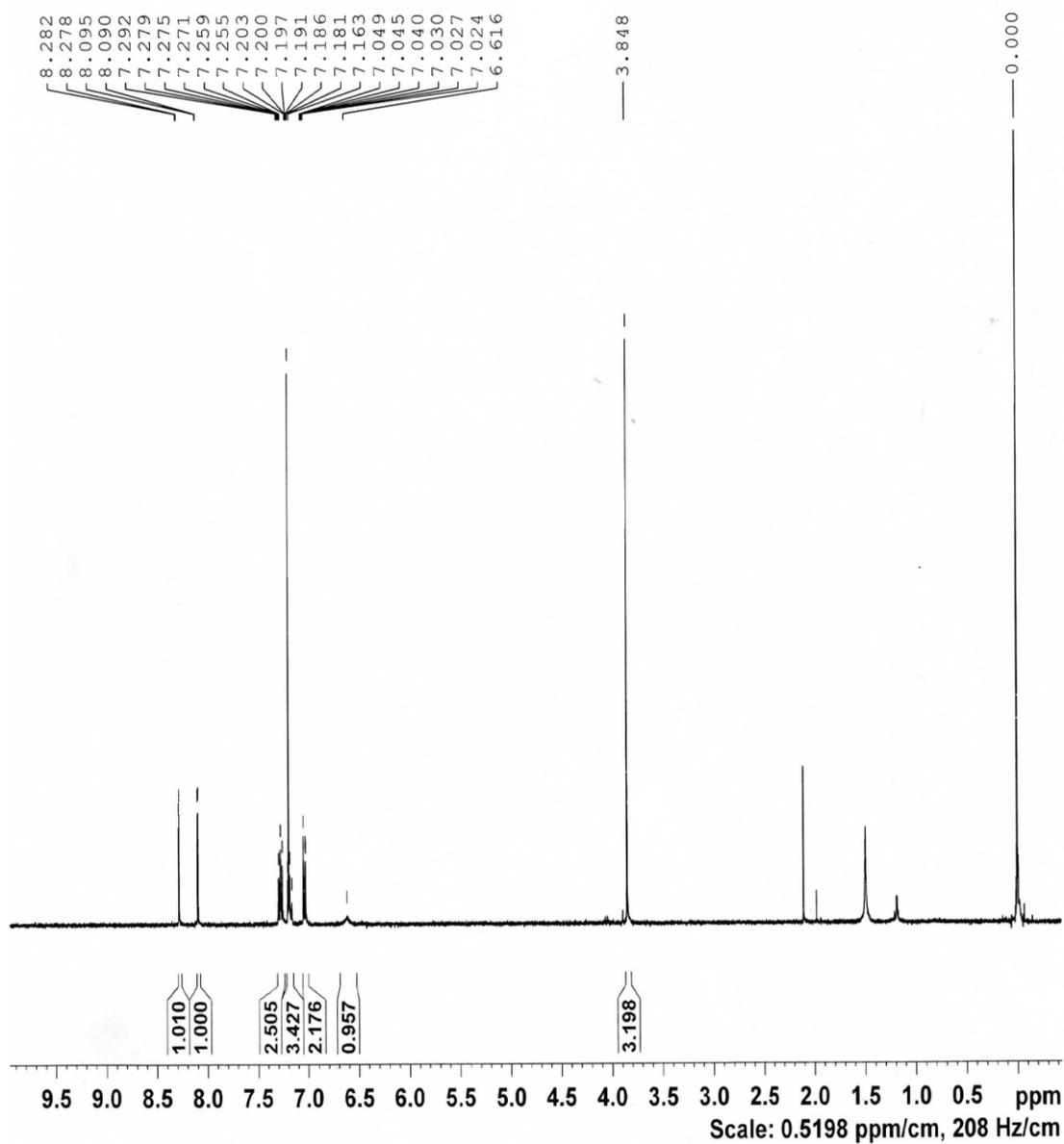
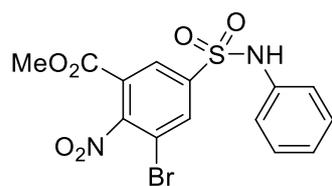
HMQC (100MHz, CDCl₃) – 5



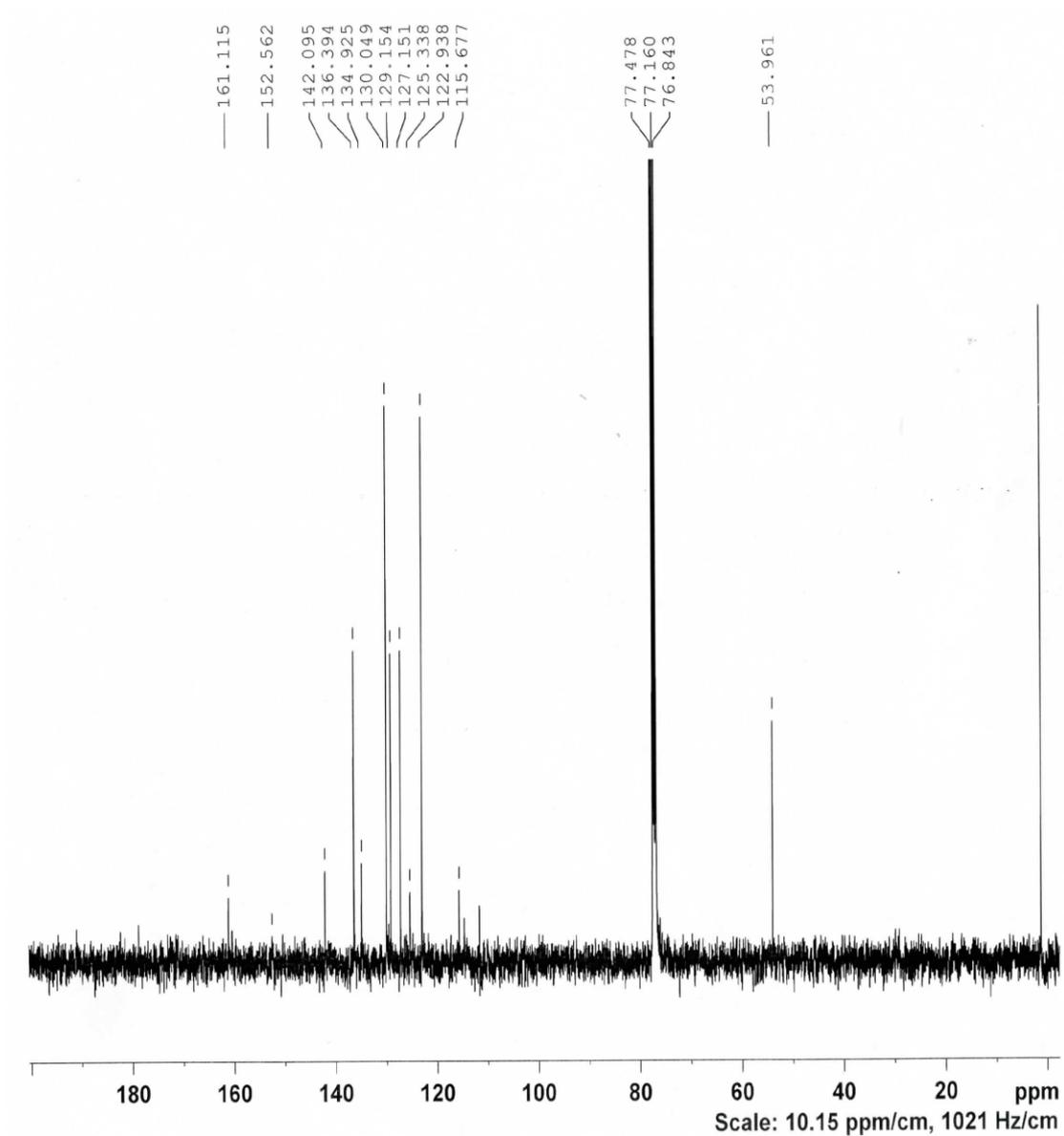
HMBC (100MHz, CDCl₃) – 5



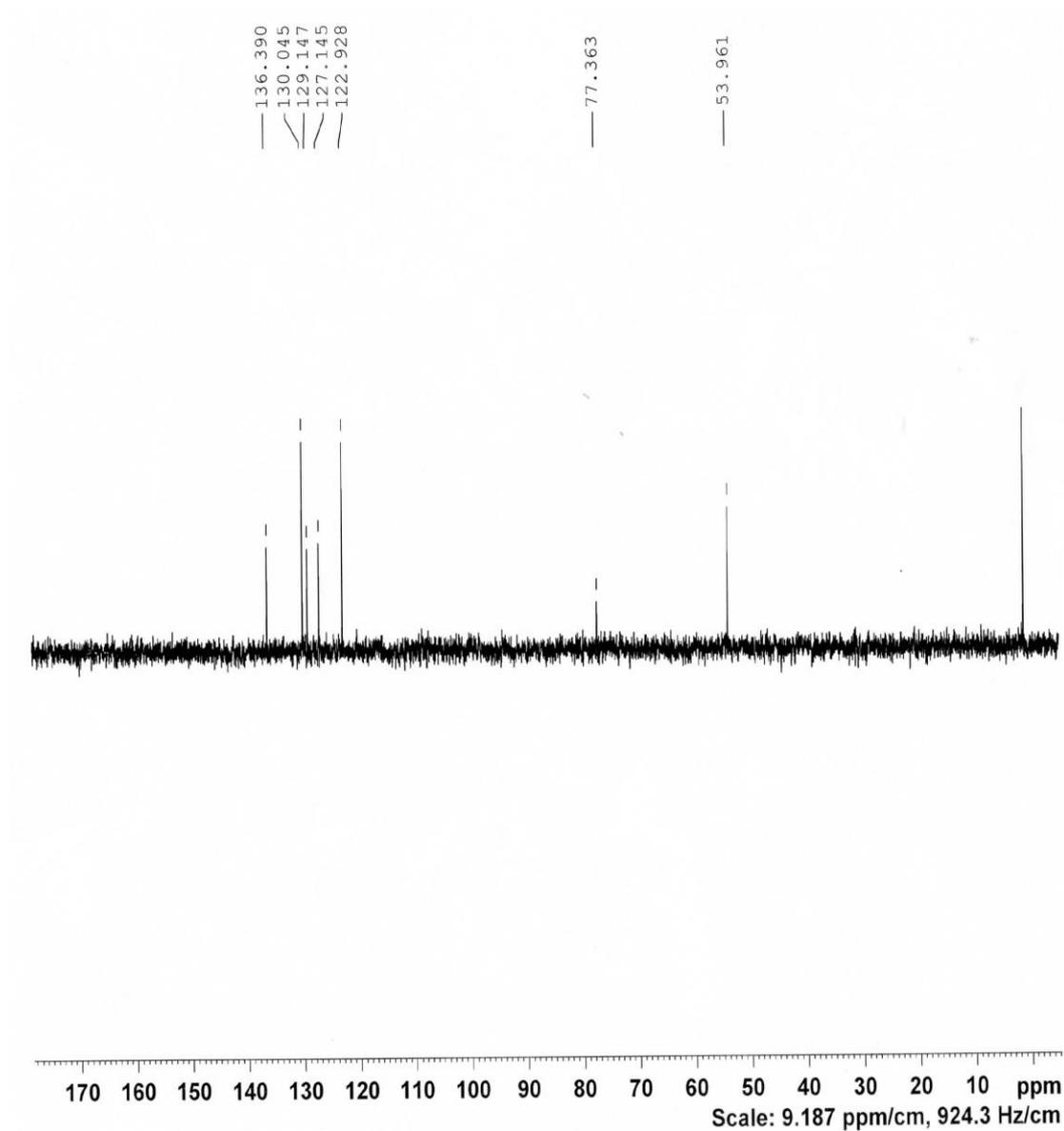
$^1\text{H-NMR}$ (400MHz, CDCl_3) – **6a**



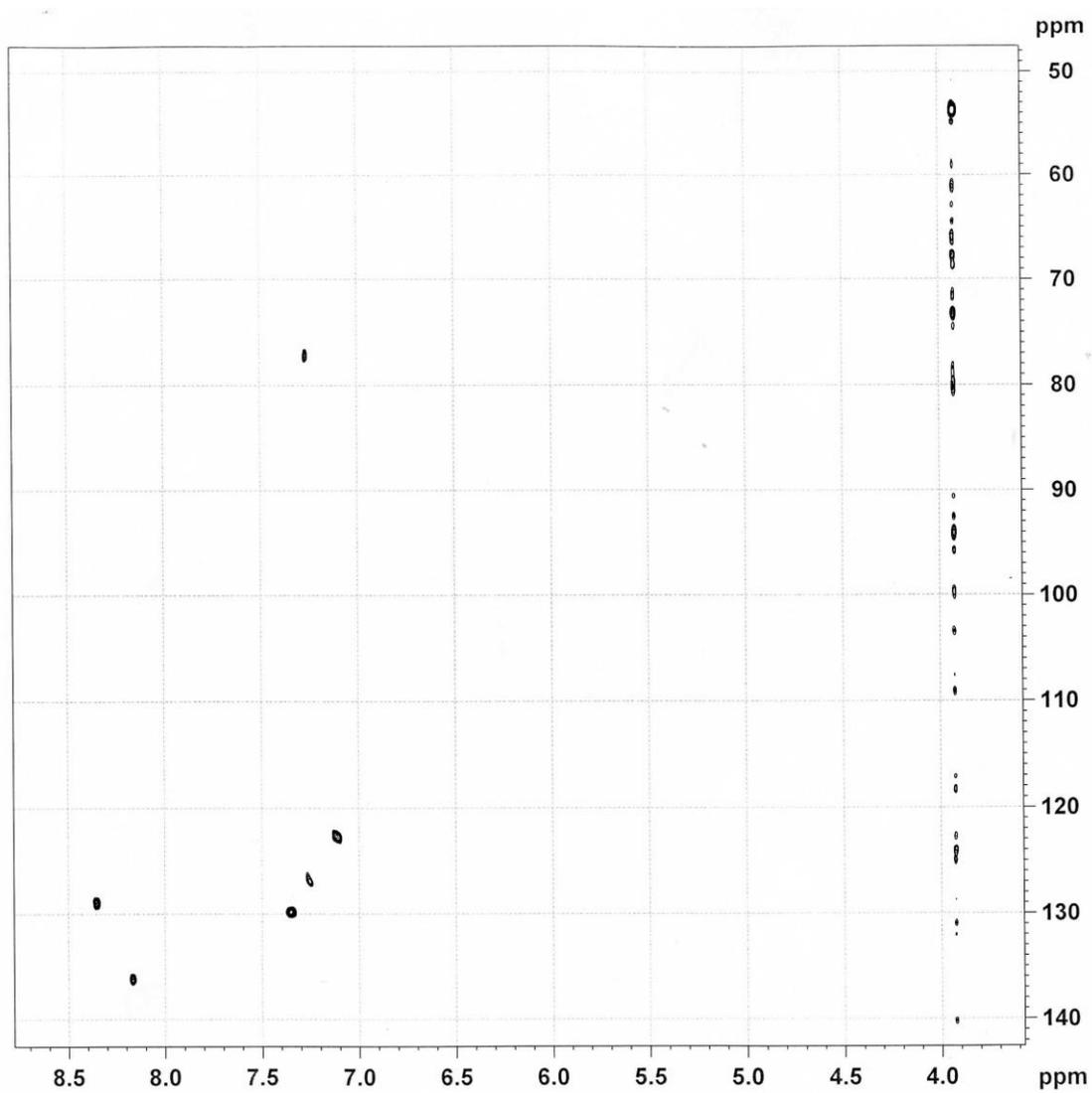
^{13}C -NMR (100MHz, CDCl_3) – **6a**



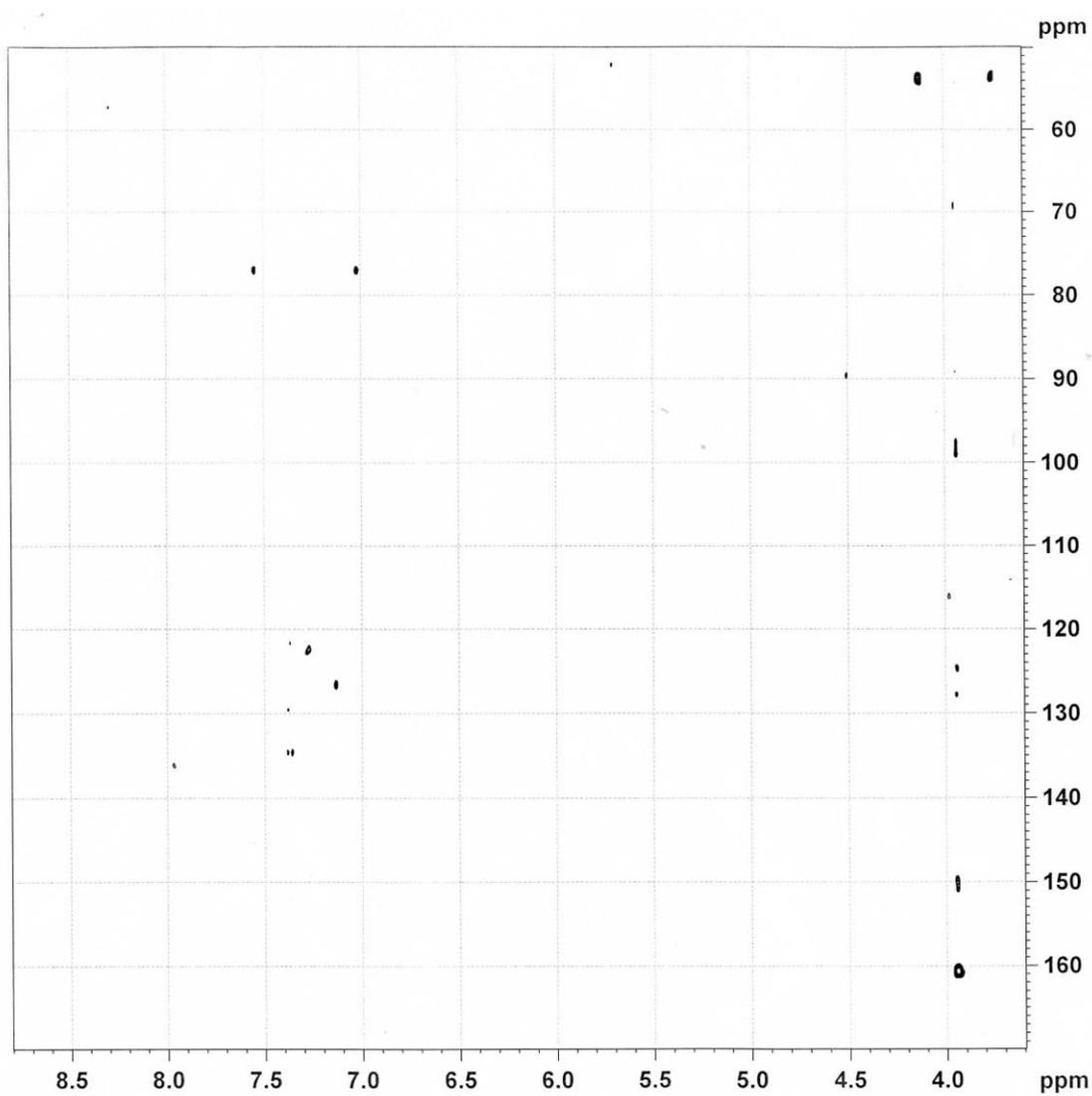
DEPT (100MHz, CDCl₃) – **6a**



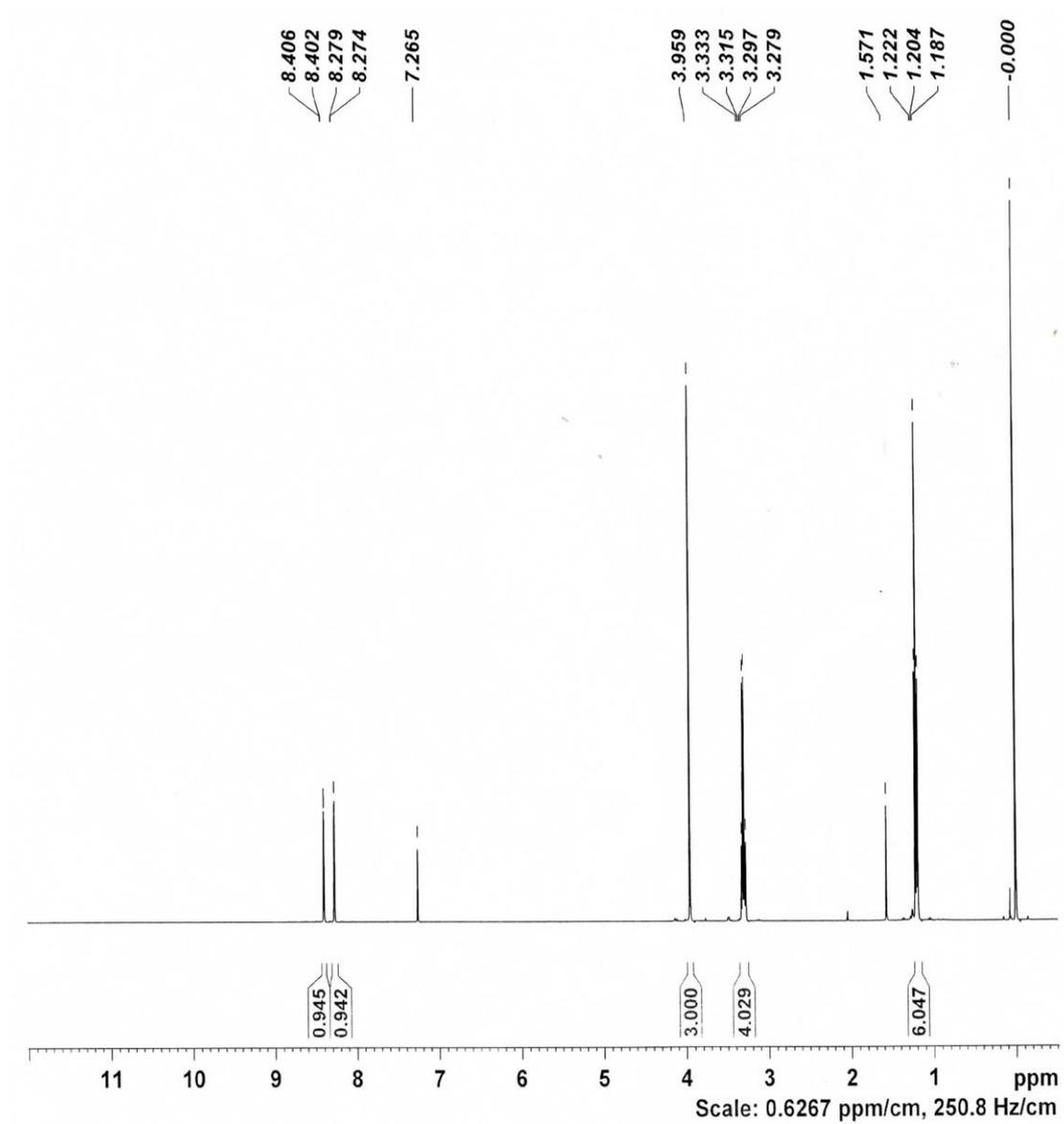
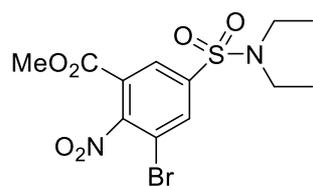
HMQC (100MHz, CDCl₃) – 6a



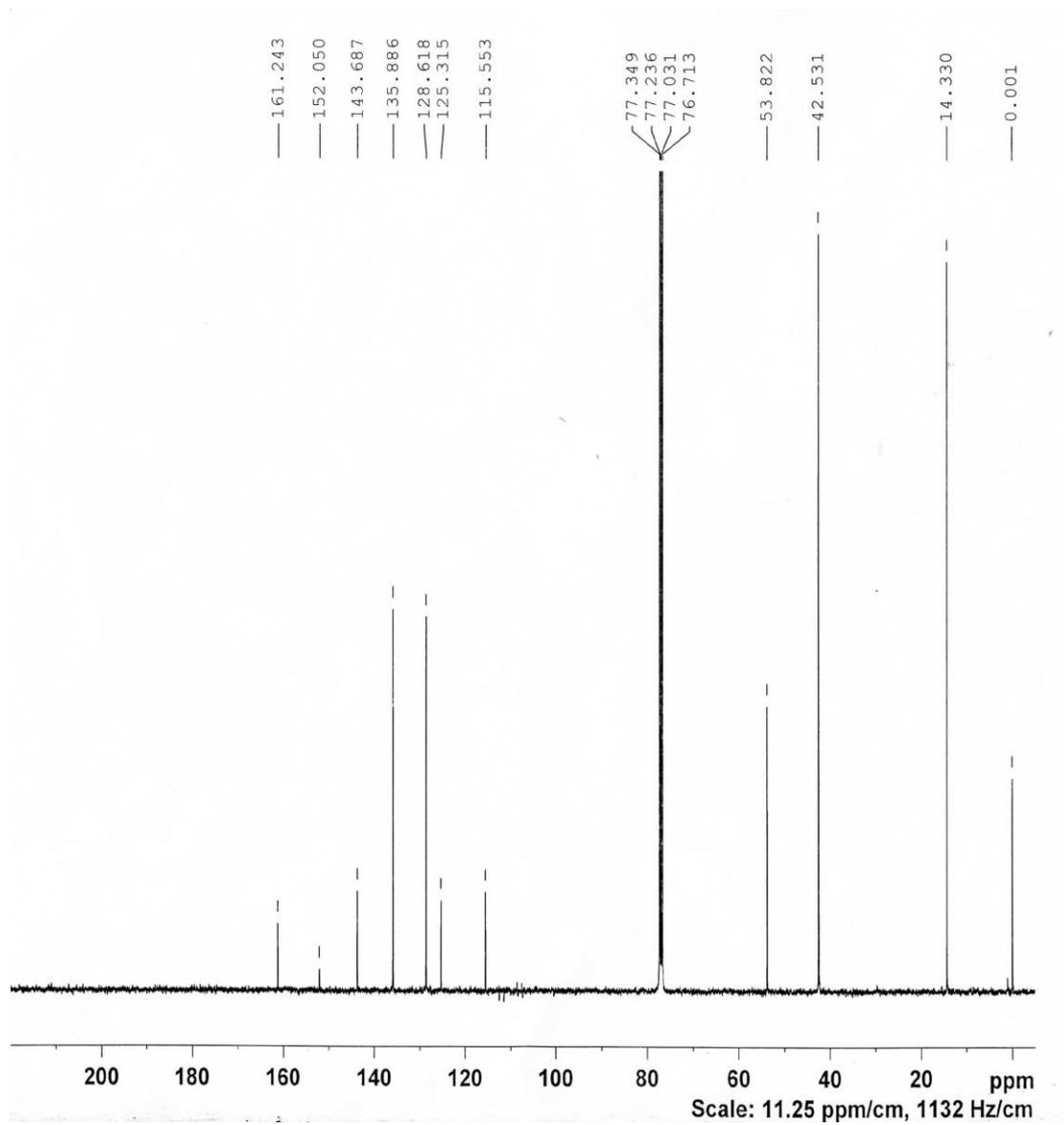
HMBC (100MHz, CDCl₃) – 6a



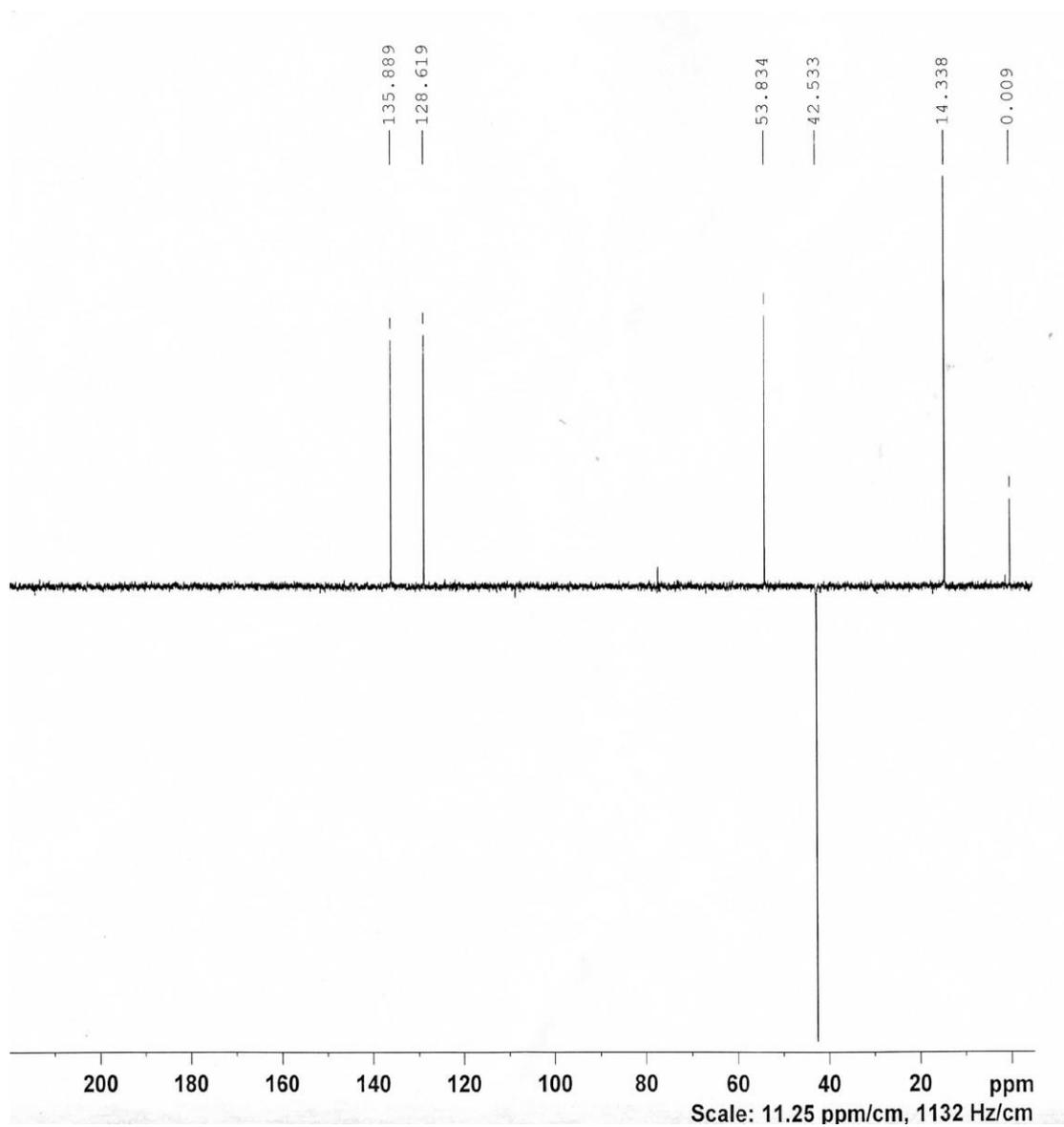
$^1\text{H-NMR}$ (400MHz, CDCl_3) – **6b**



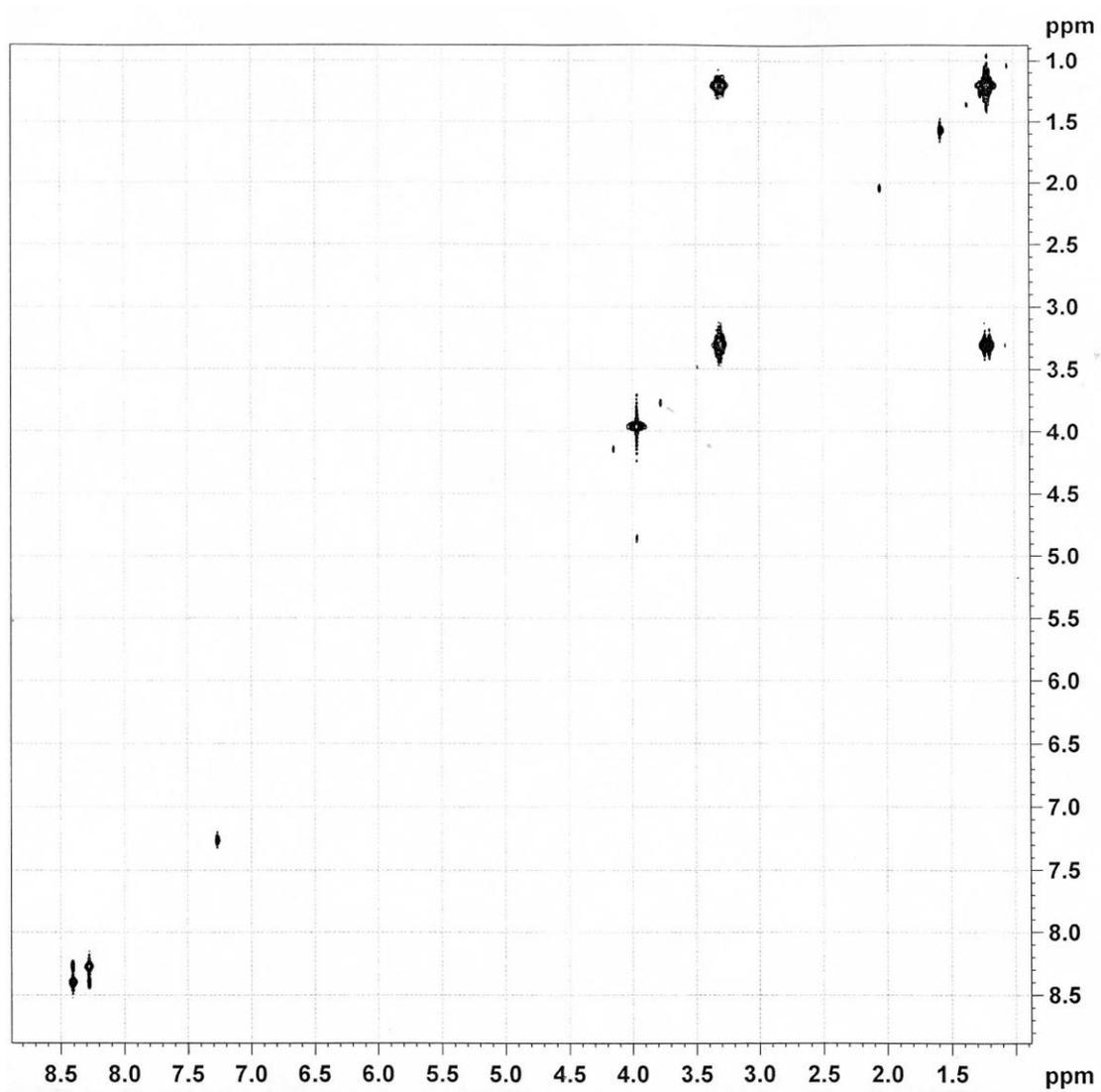
^{13}C -NMR (100MHz, CDCl_3) – **6b**



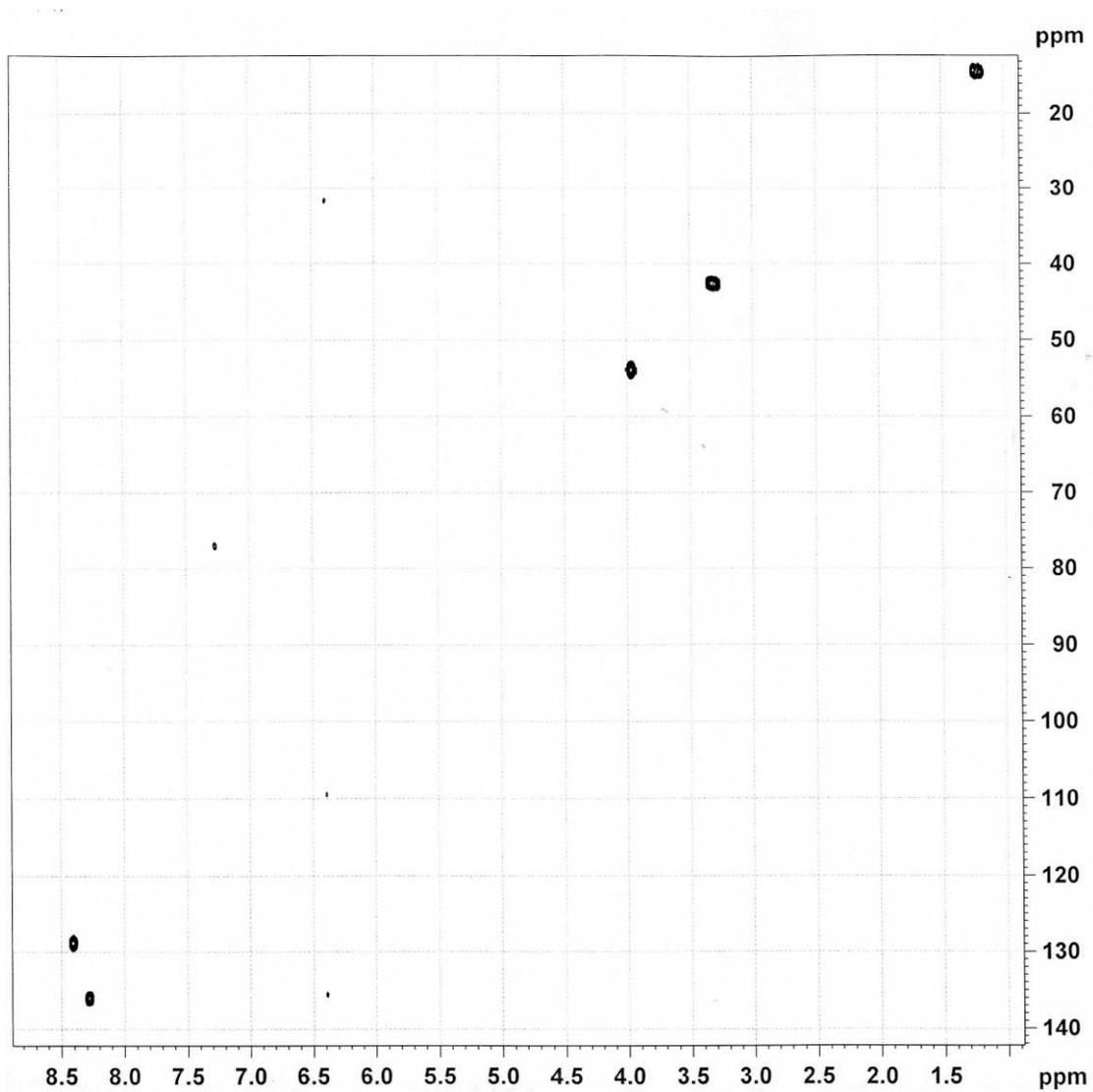
DEPT (100MHz, CDCl₃) – **6b**



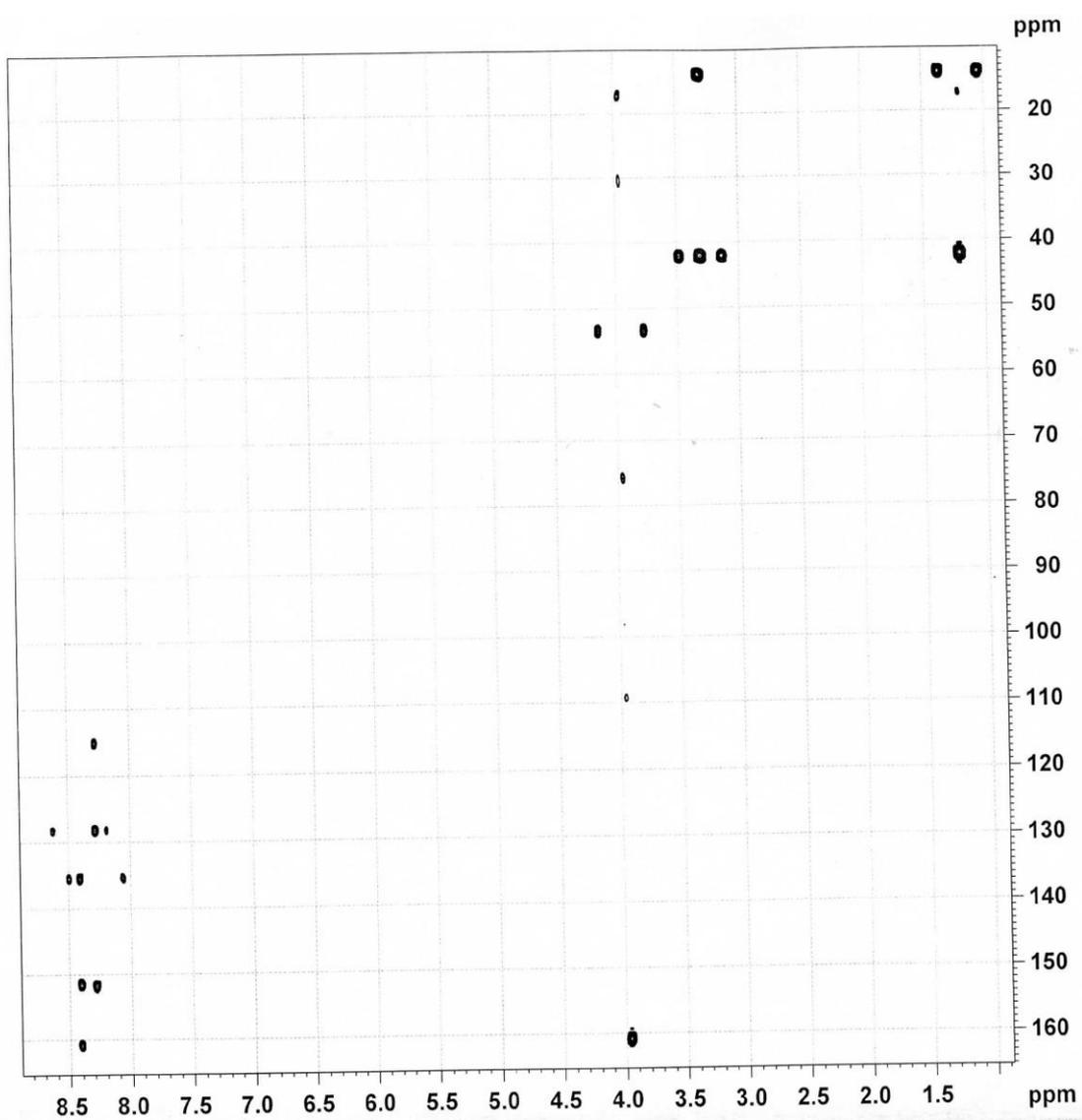
COSY (400MHz, CDCl₃) – **6b**



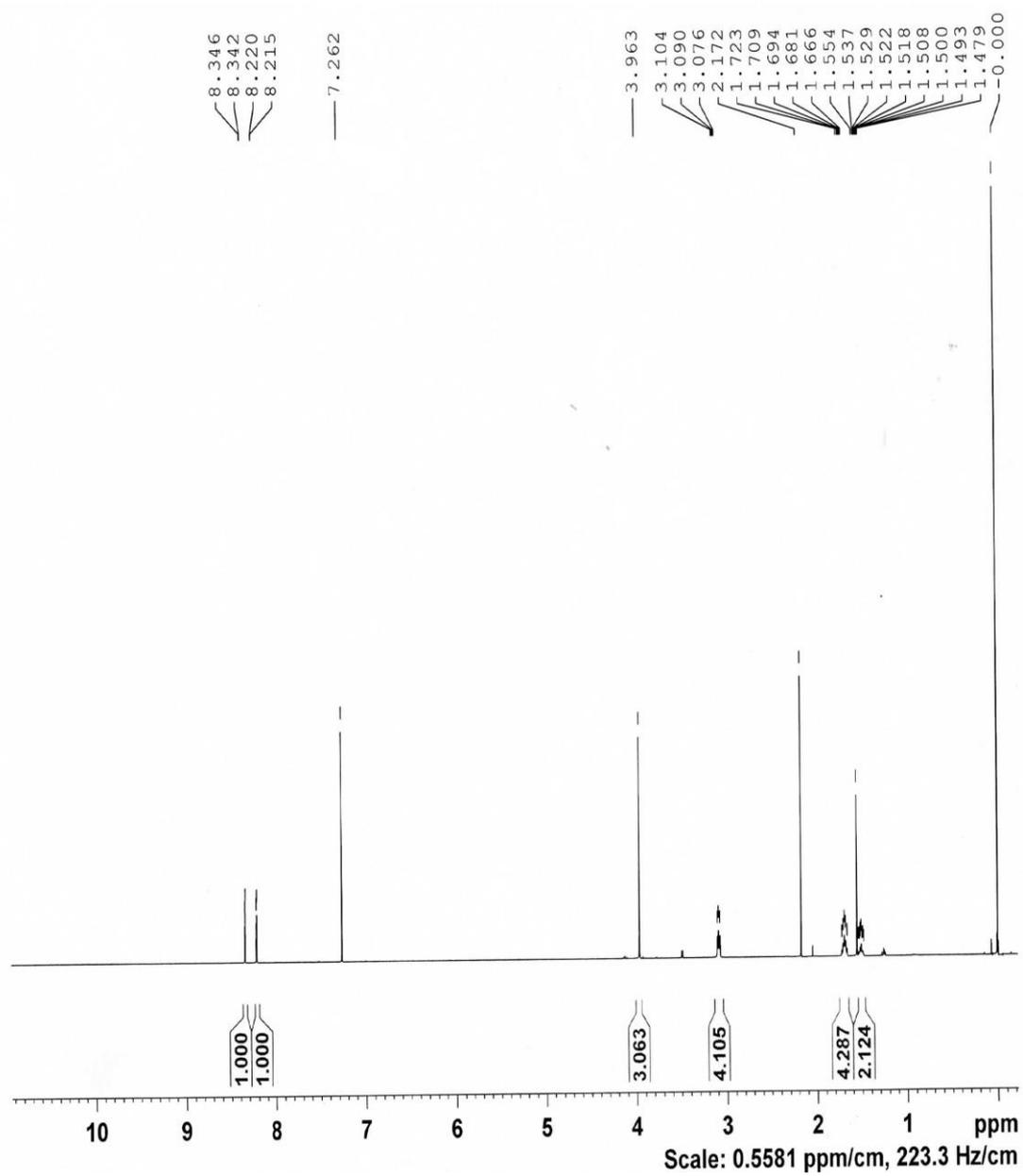
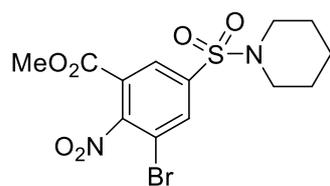
HMQC (100MHz, CDCl₃) – **6b**



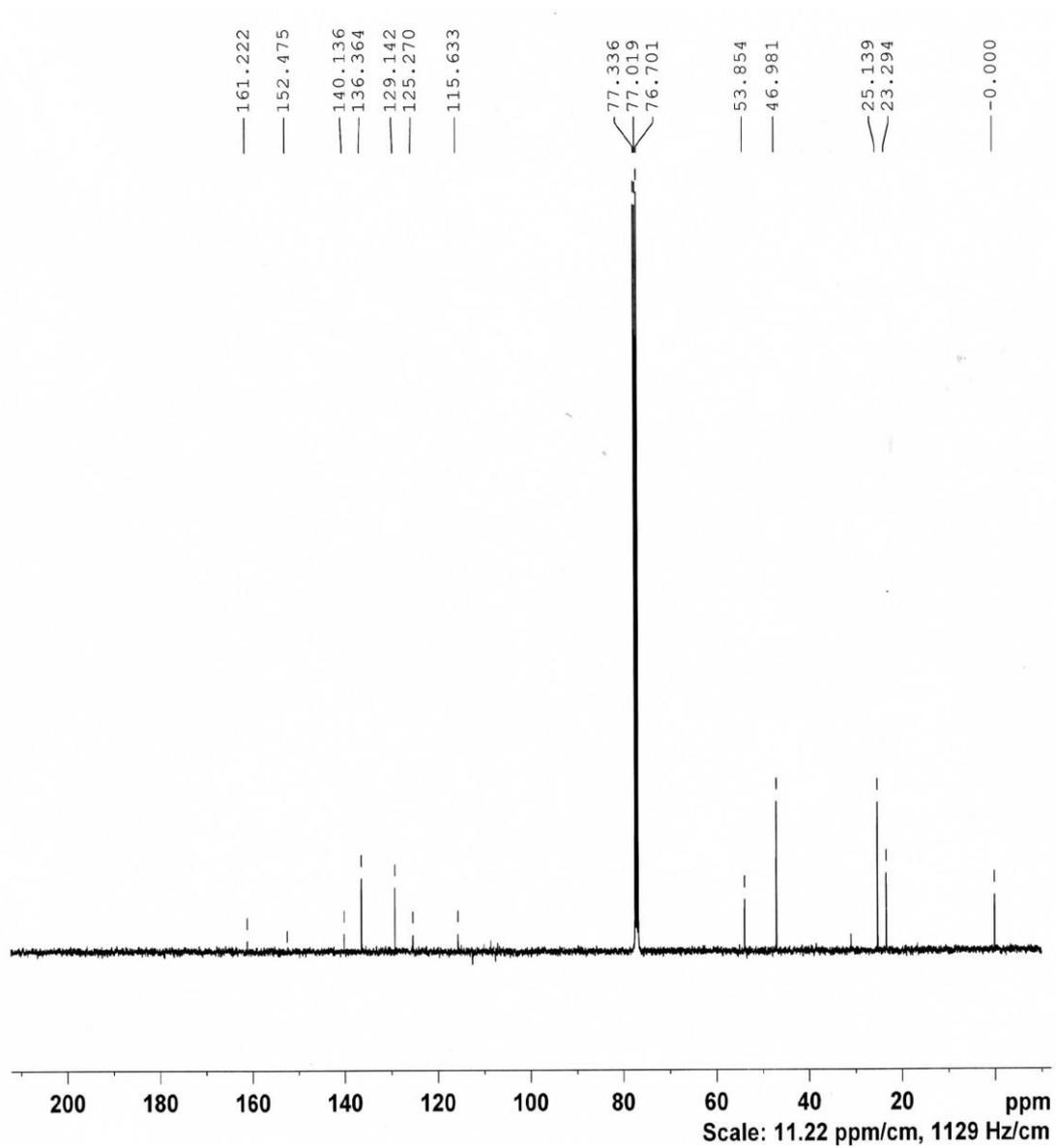
HMBC (100MHz, CDCl₃) – **6b**



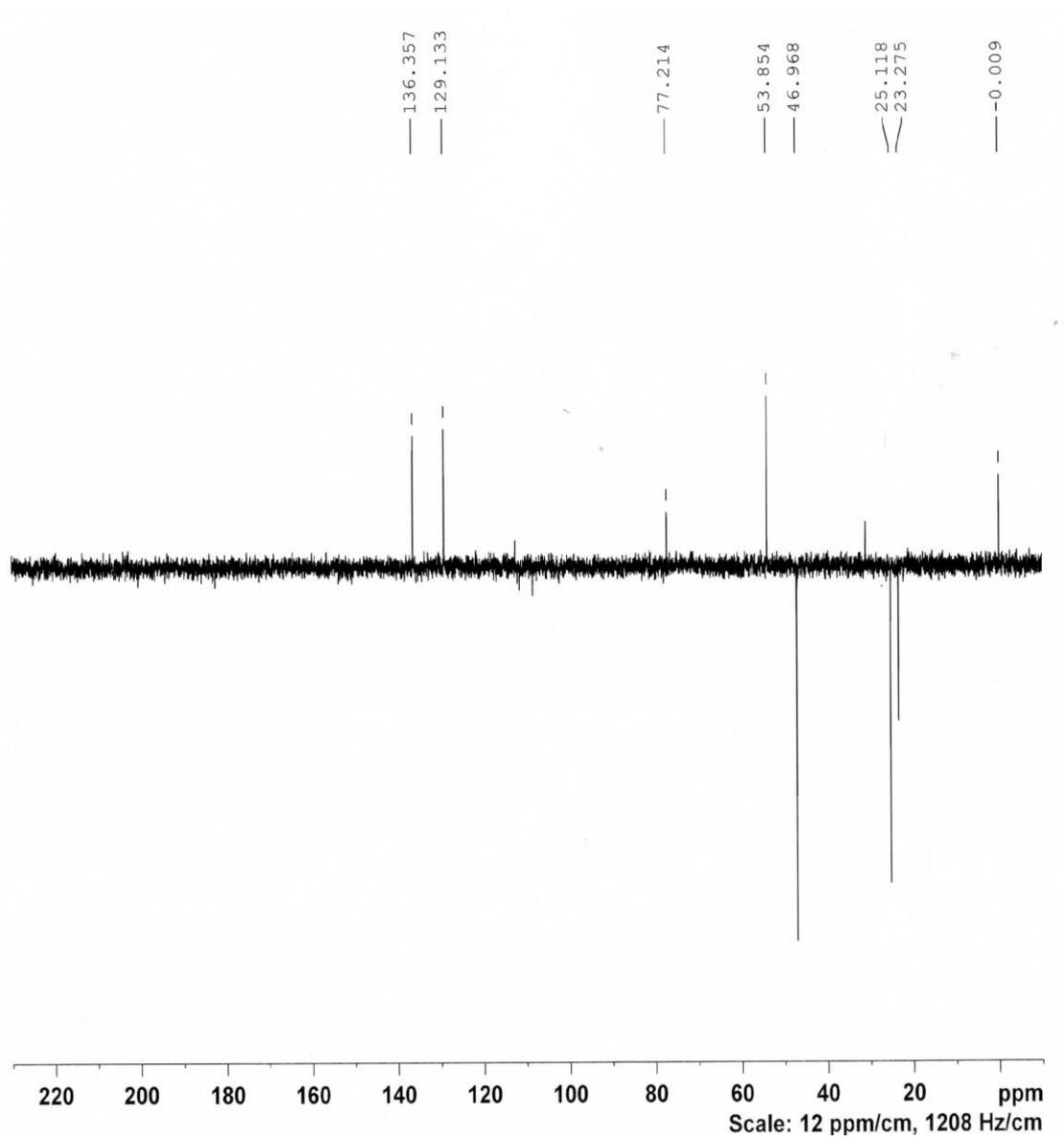
$^1\text{H-NMR}$ (400MHz, CDCl_3) – **6c**



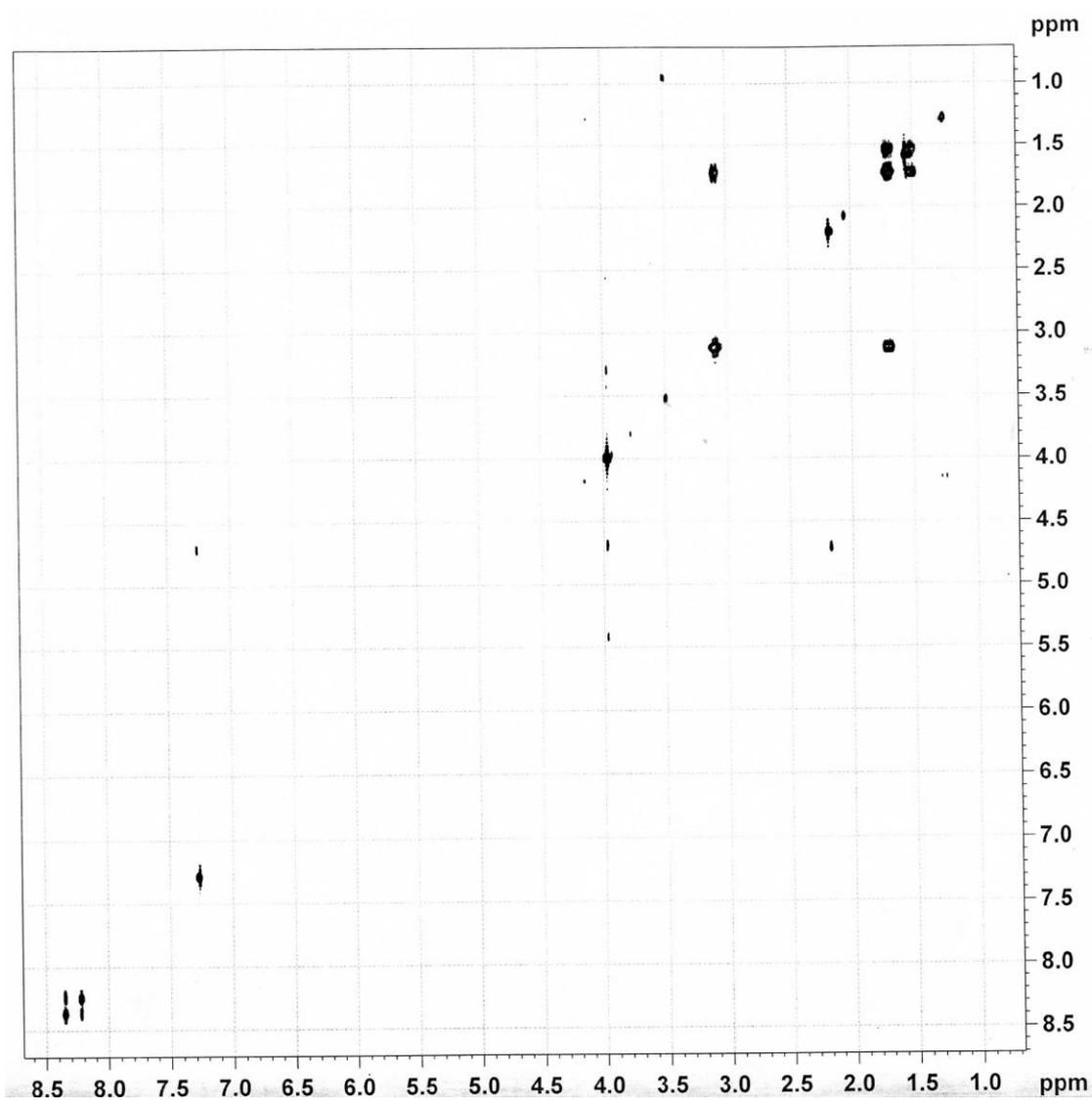
^{13}C -NMR (100MHz, CDCl_3) – **6c**



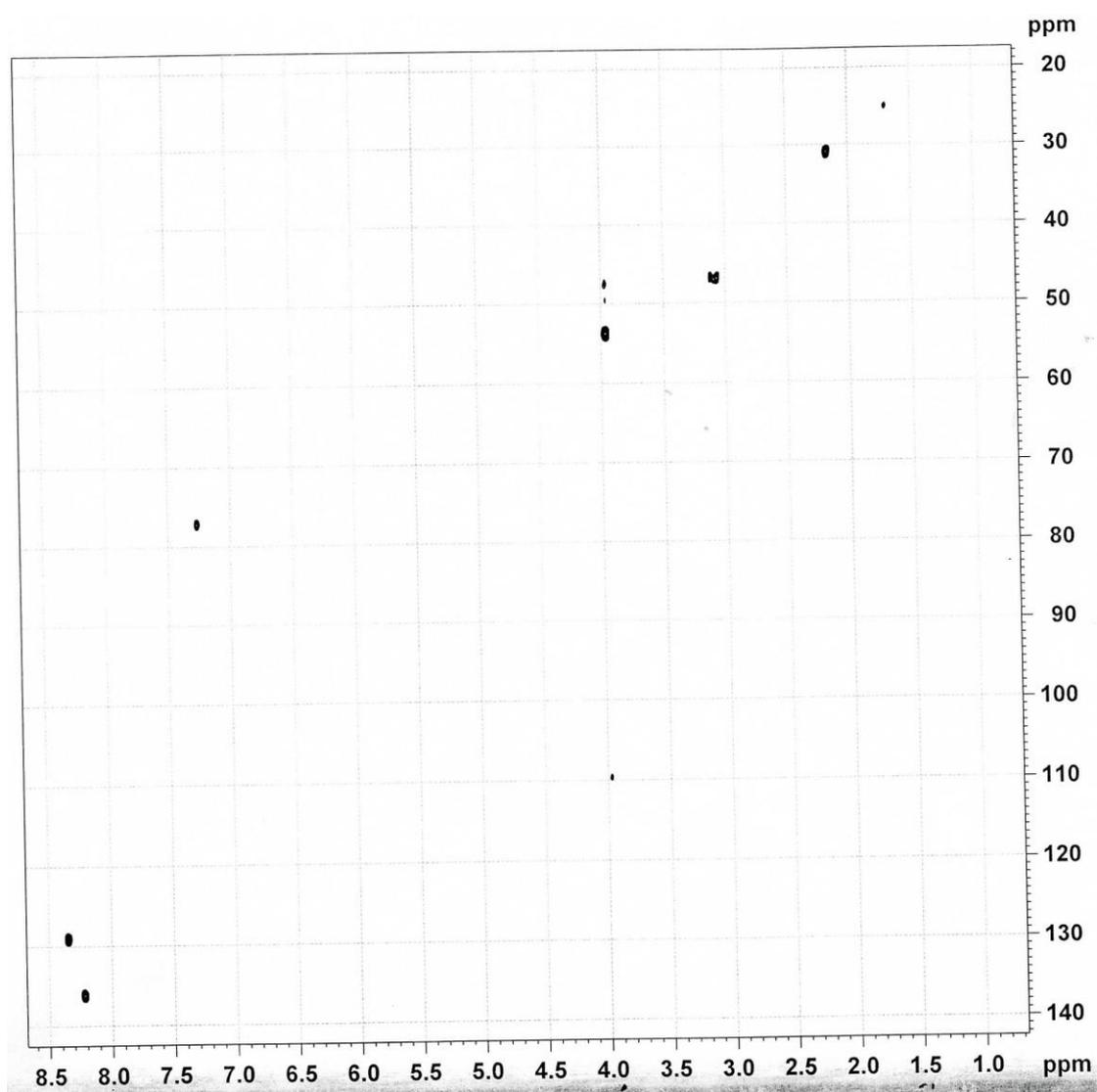
DEPT (100MHz, CDCl₃) – **6c**



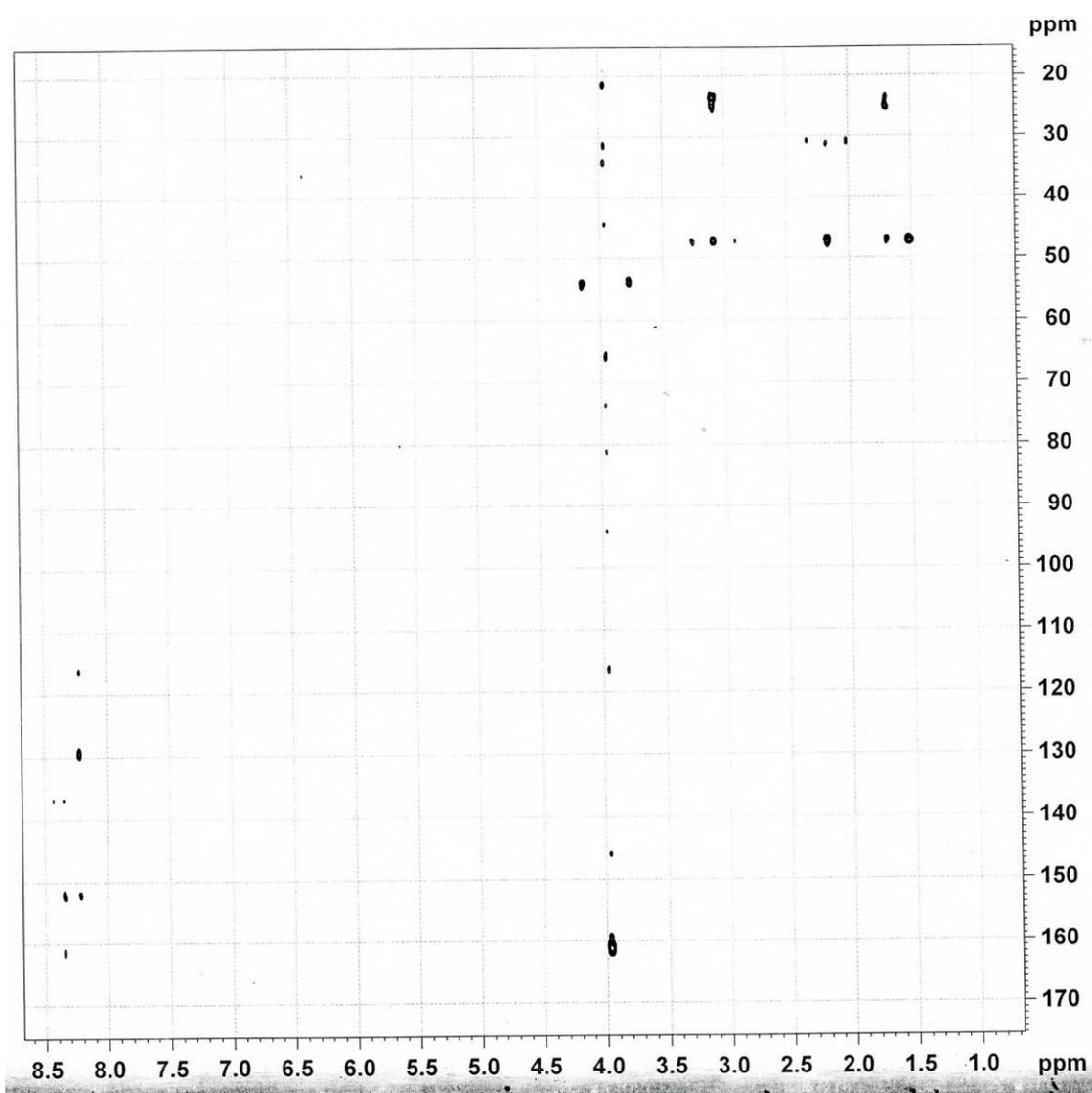
COSY (400MHz, CDCl₃) – 6c



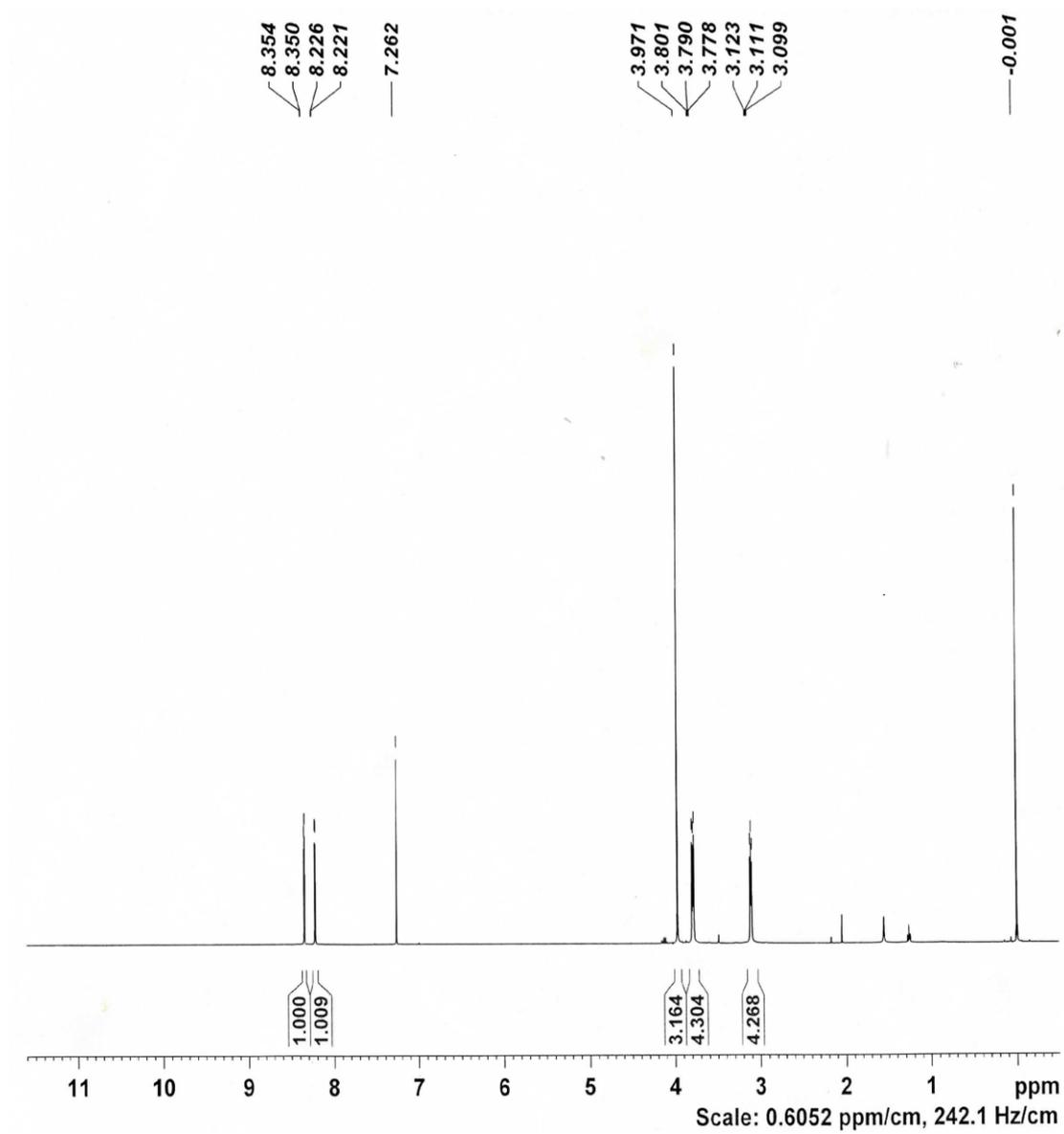
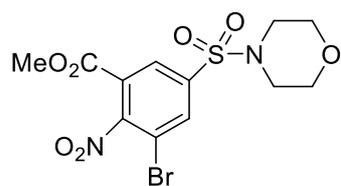
HMQC (100MHz, CDCl₃) – 6c



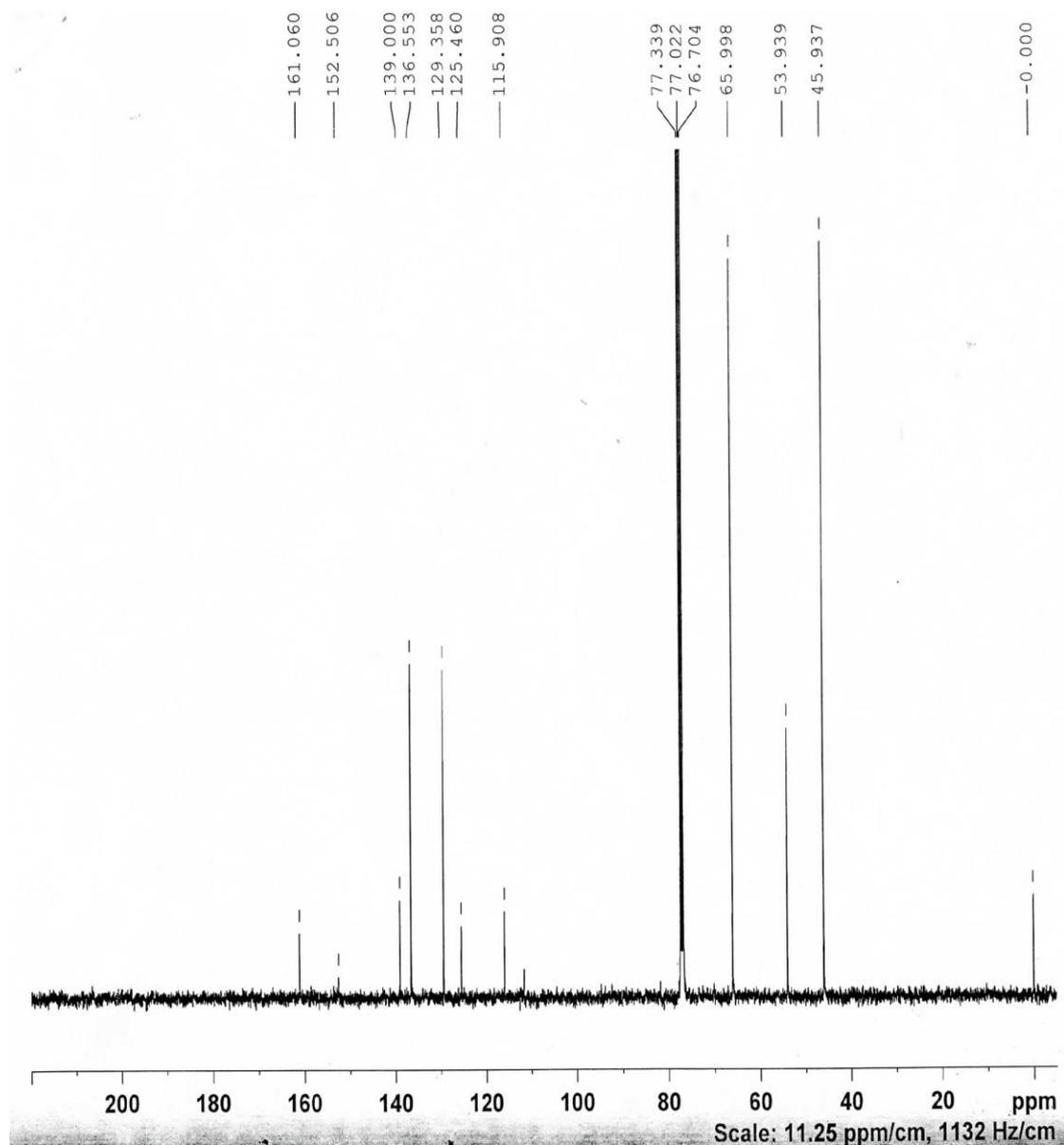
HMBC (100MHz, CDCl₃) – 6c



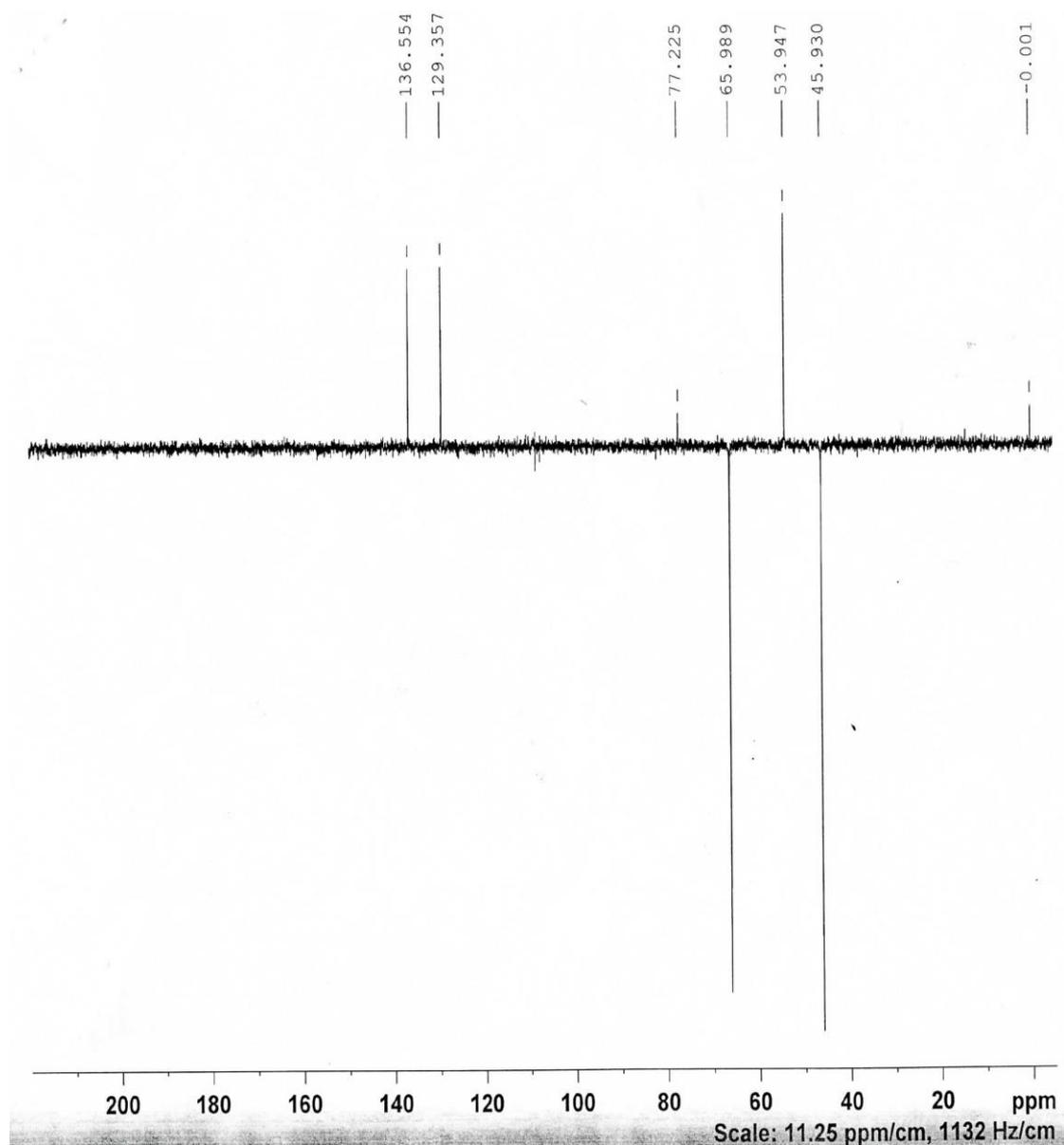
¹H-NMR (400MHz, CDCl₃) – **6d**



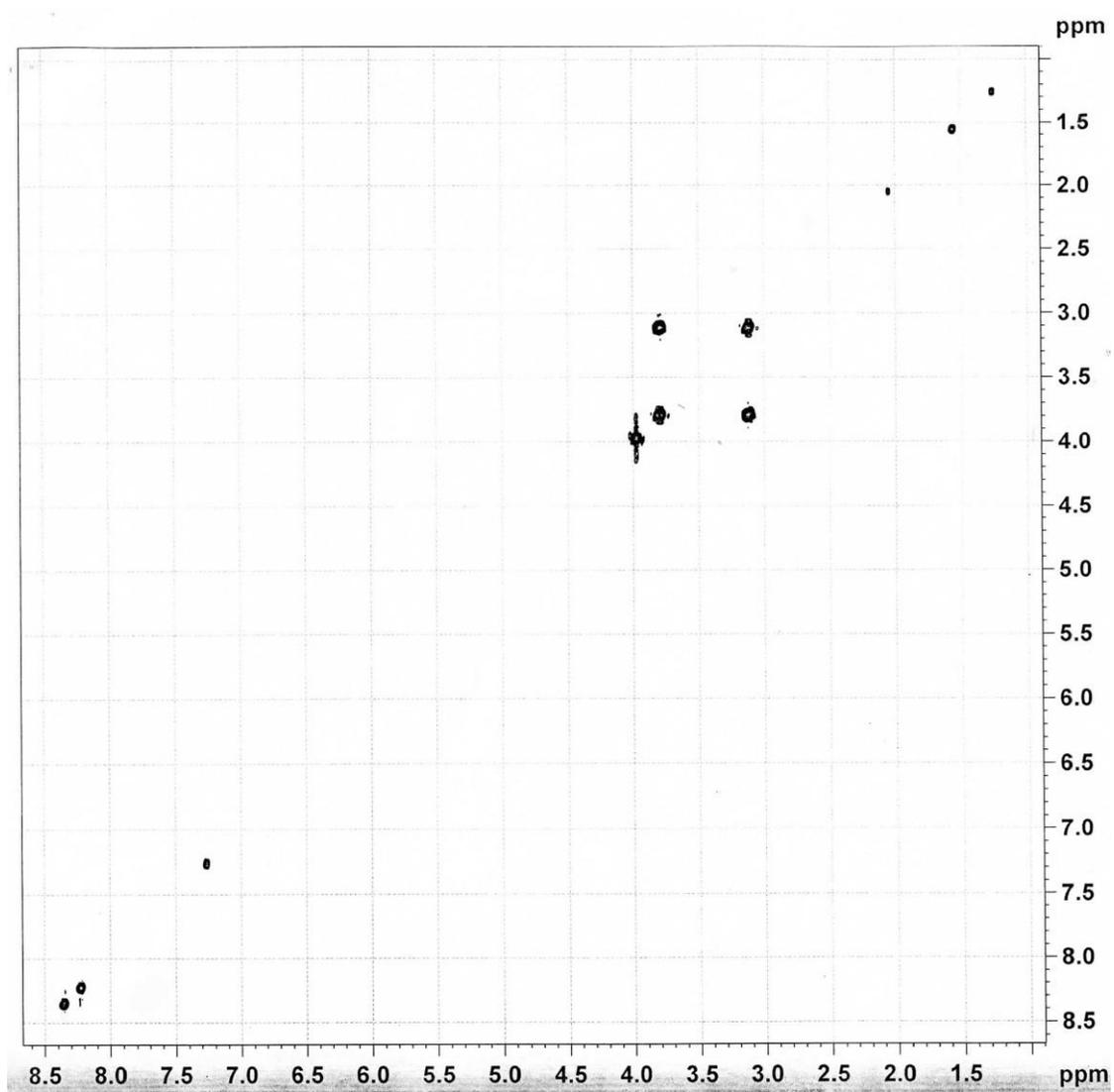
¹³C-NMR (100MHz, CDCl₃) – **6d**



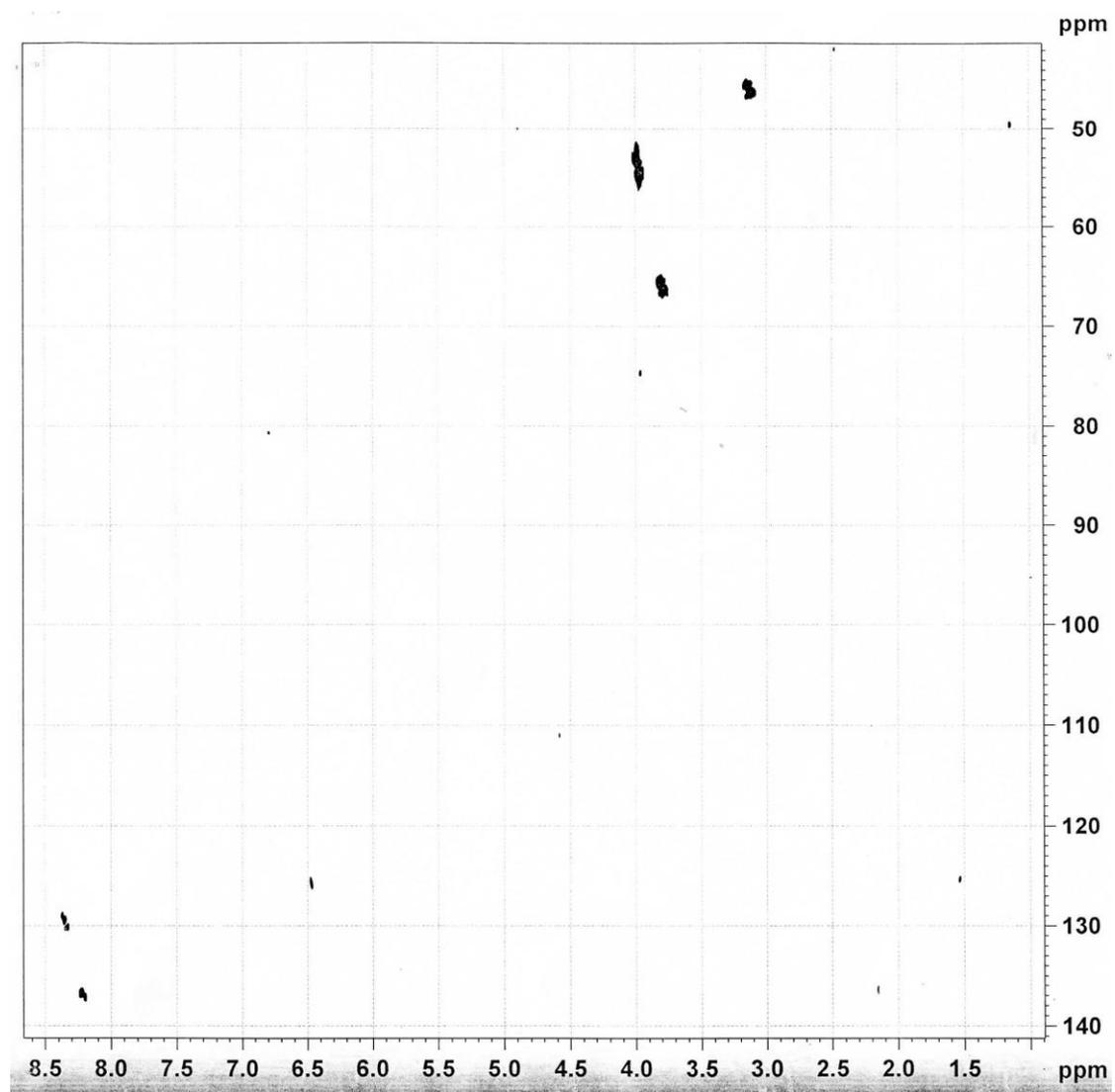
DEPT (100MHz, CDCl₃) – **6d**



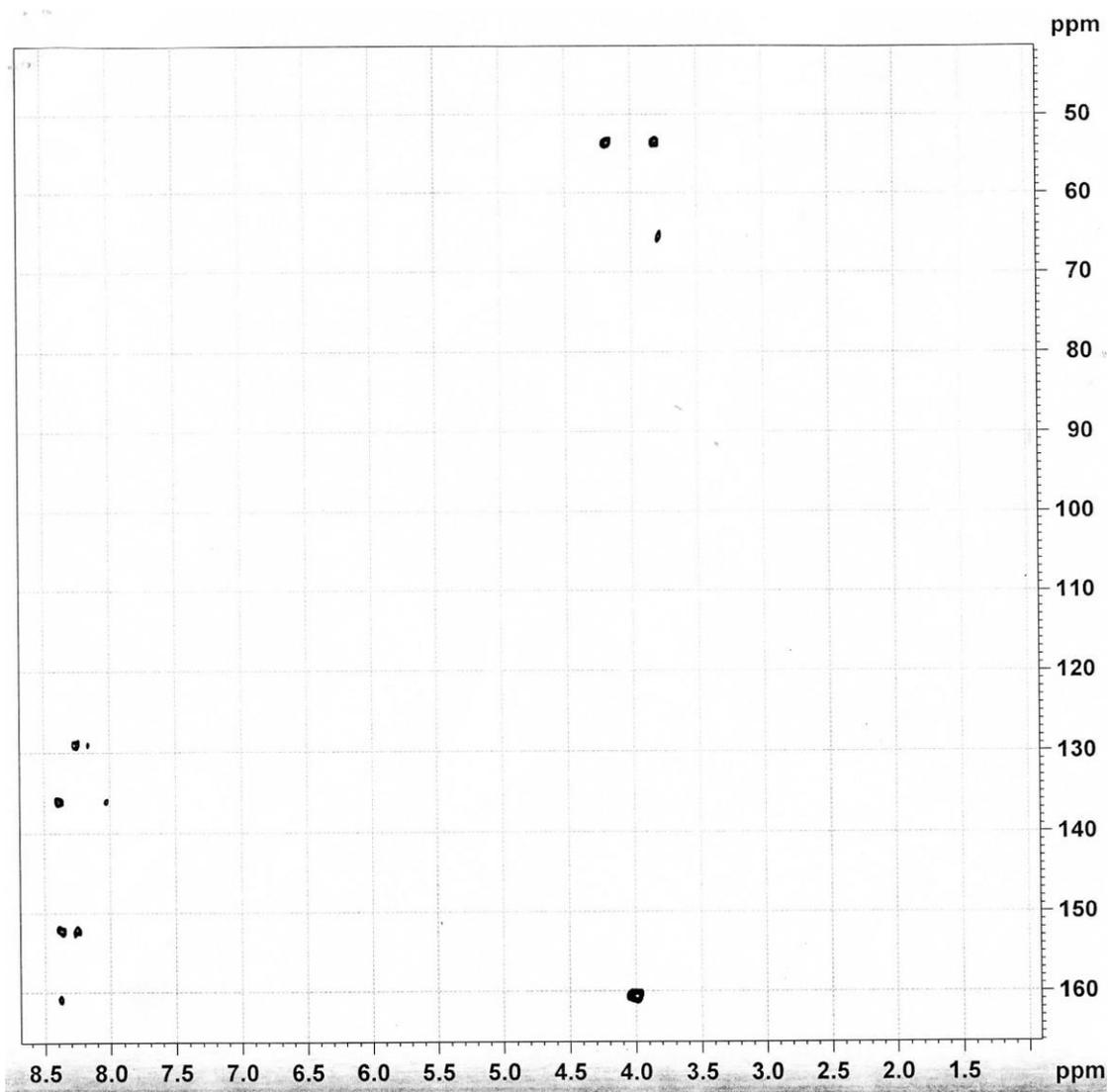
COSY (400MHz, CDCl₃) – 6d



HMQC (100MHz, CDCl₃) – 6d

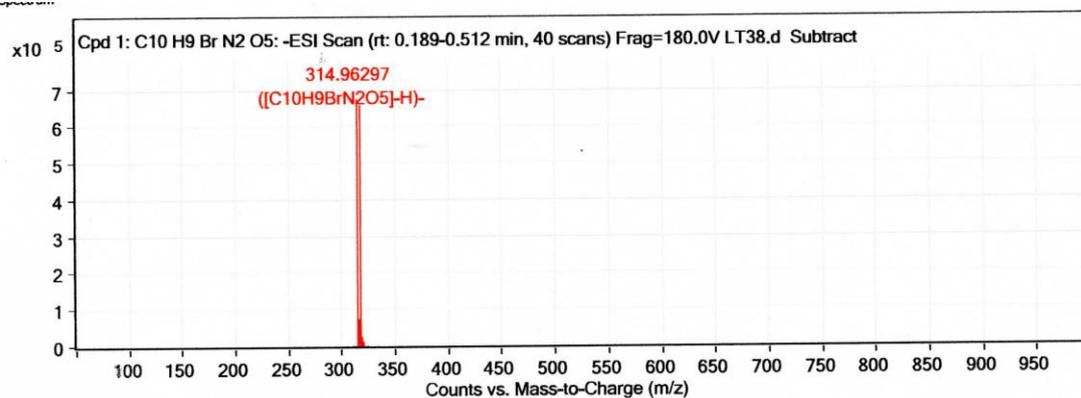


HMBC (100MHz, CDCl₃) – 6d



3. Mass Spectroscopy analytical data

2 –

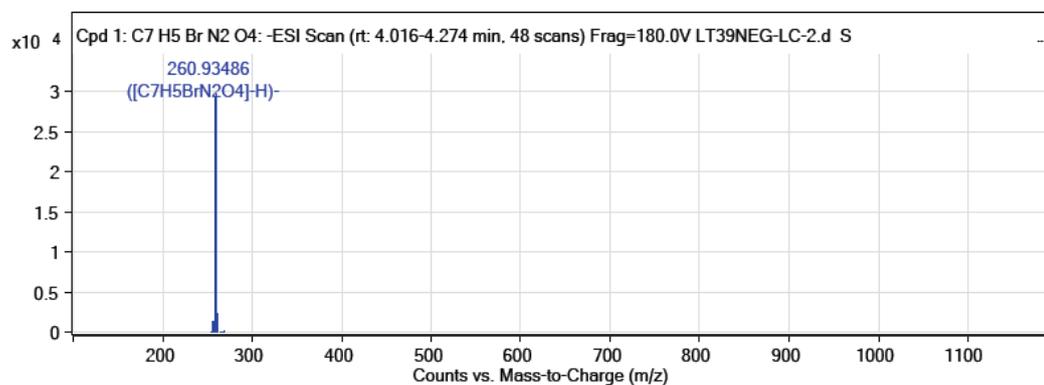


MS Spectrum Peak List

m/z	Calc m/z	Diff(ppm)	z	Abund	Formula	Ion
314.96297	314.96221	-2.43	1	674833.69	C10H9BrN2O5	(M-H)-
315.96613	315.96521	-2.93	1	72014.21	C10H9BrN2O5	(M-H)-
316.96098	316.96028	-2.2	1	660035.63	C10H9BrN2O5	(M-H)-
317.96379	317.96324	-1.73	1	73567.6	C10H9BrN2O5	(M-H)-
318.92623	318.96511	121.91	1	22486.12	C10H9BrN2O5	(M-H)-

--- End Of Report ---

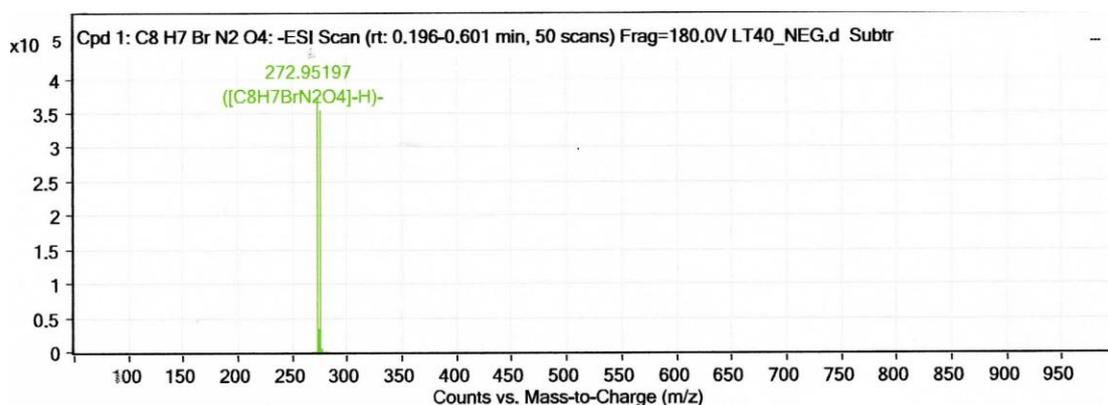
2b –



MS Spectrum Peak List

m/z	Calc m/z	Diff(ppm)	z	Abund	Formula	Ion
258.93702	258.93599	-3.95	1	29516.24	C7H5BrN2O4	(M-H)-
259.93955	259.93884	-2.75	1	2542.68	C7H5BrN2O4	(M-H)-
260.93486	260.93402	-3.22	1	29615.81	C7H5BrN2O4	(M-H)-
261.93733	261.93685	-1.84	1	2396.06	C7H5BrN2O4	(M-H)-
262.93782	262.9386	2.98	1	366.22	C7H5BrN2O4	(M-H)-

3 -

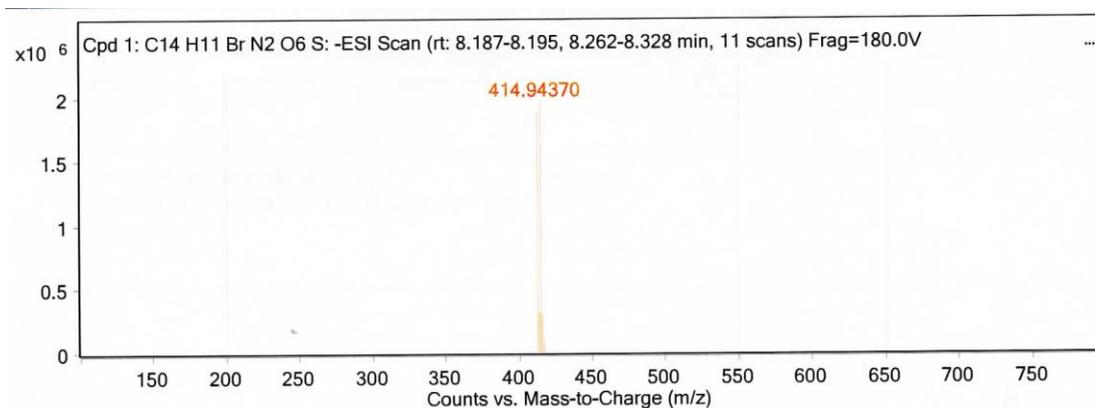


MS Spectrum Peak List

m/z	Calc m/z	Diff(ppm)	z	Abund	Formula	Ion
272.95197	272.95164	-1.19	1	372591.69	C8H7BrN2O4	(M-H)-
273.95489	273.95455	-1.24	1	33507.11	C8H7BrN2O4	(M-H)-
274.94999	274.94968	-1.11	1	354931.25	C8H7BrN2O4	(M-H)-
275.95281	275.95257	-0.89	1	31027.75	C8H7BrN2O4	(M-H)-
276.95452	276.95438	-0.51	1	3977.97	C8H7BrN2O4	(M-H)-
277.95736	277.95693	-1.52	1	252.26	C8H7BrN2O4	(M-H)-

--- End Of Report ---

6a -

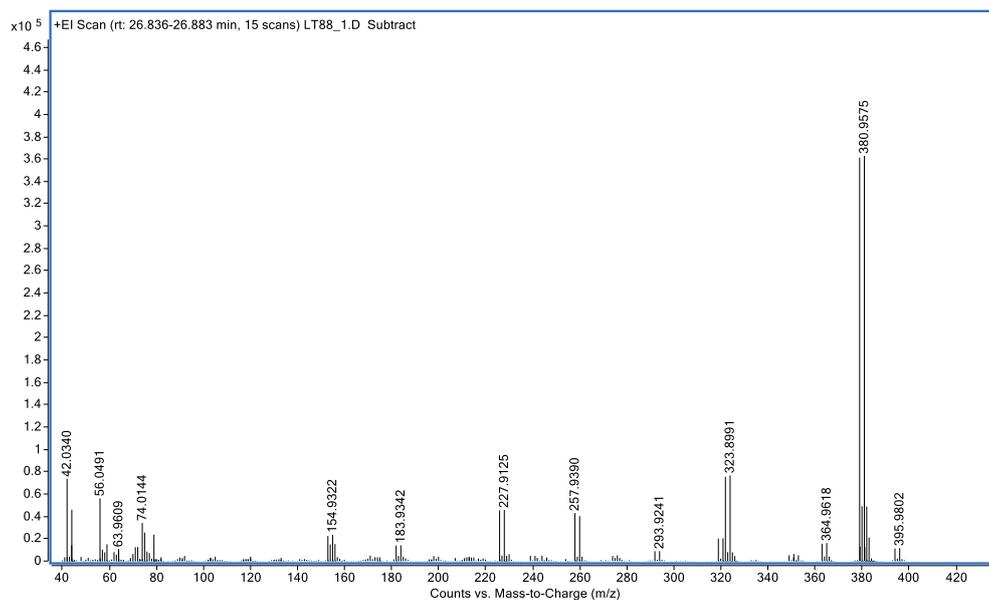


MS Spectrum Peak List

m/z	Calc m/z	Diff(ppm)	z	Abund	Formula	Ion
412.9456	412.94484	-1.83	1	1897143.75	C14H11BrN2O6S	(M-H)-
413.94798	413.94777	-0.5	1	317796.72	C14H11BrN2O6S	(M-H)-
414.9437	414.94288	-1.97	1	1964517.63	C14H11BrN2O6S	(M-H)-
415.94609	415.94575	-0.82	1	310896.44	C14H11BrN2O6S	(M-H)-
416.94277	416.9421	-1.61	1	98066.38	C14H11BrN2O6S	(M-H)-
417.94415	417.94416	0.02	1	13196.55	C14H11BrN2O6S	(M-H)-
418.94452	418.94496	1.05	1	2078.81	C14H11BrN2O6S	(M-H)-
864.85105	864.87164	23.81	1	167.42	C14H11BrN2O6S	(2M+Cl)-

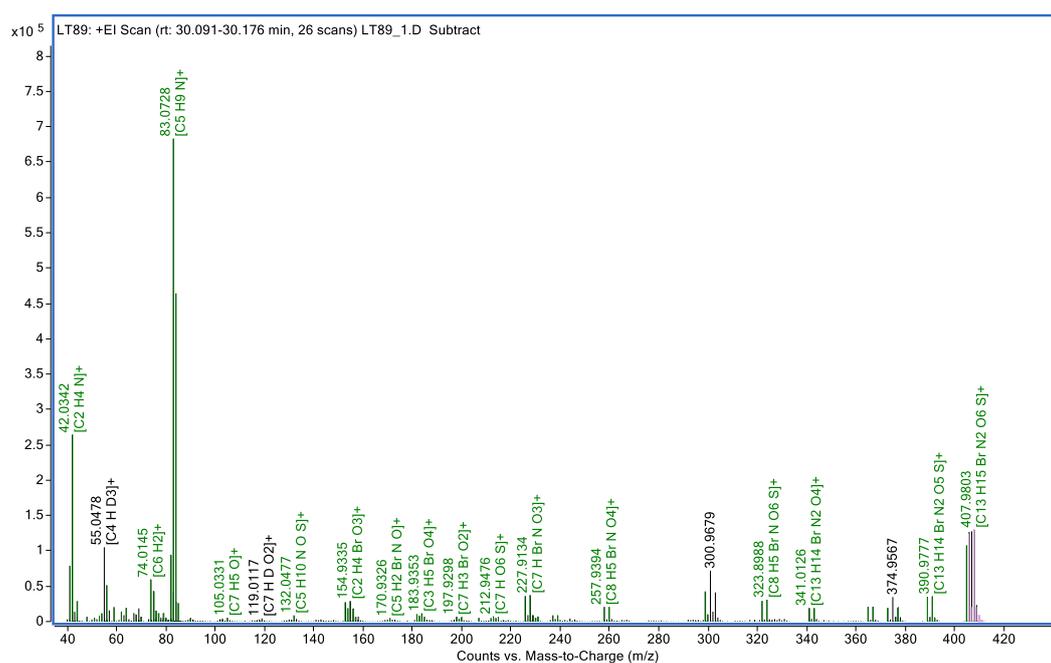
--- End Of Report ---

6b –



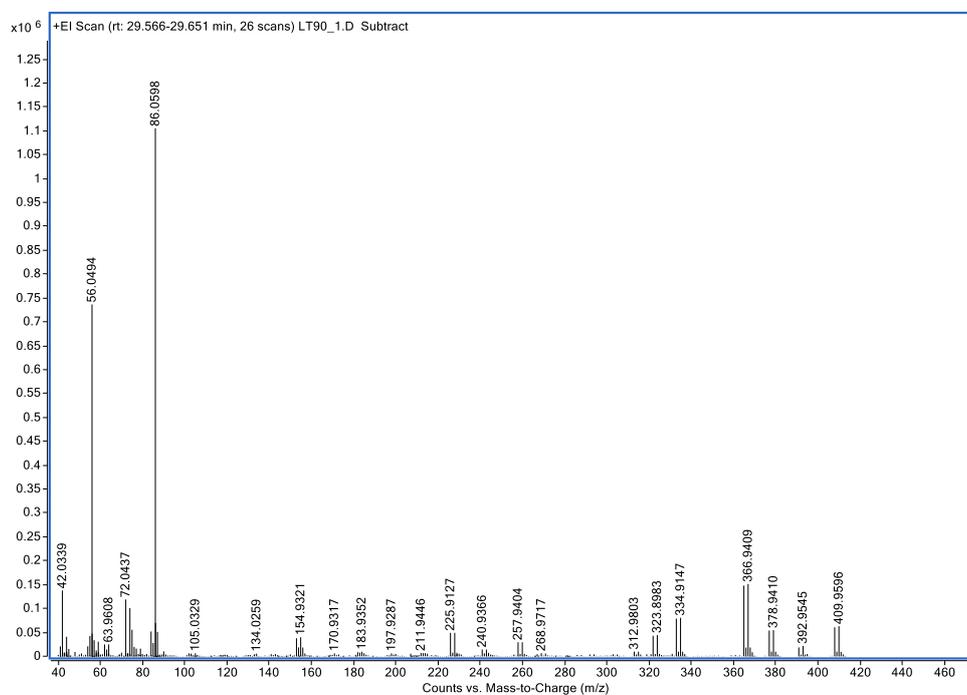
Observed mass	Formula & Ion Species	Calculated mass	Diff (ppm)	Loss Formula	Loss Mass	Ion Type
395.9802	[C12 H15 Br N2 O6 S]+	395.9809	1.72			Molecular Ion
393.9818	[C12 H15 Br N2 O6 S]+	393.9829	2.61			Molecular Ion
380.9575	[C11 H12 Br N2 O6 S]+	380.9574	-0.35	CH3	15	Fragment Ion
378.9595	[C11 H12 Br N2 O6 S]+	378.9594	-0.24	CH3	15	Fragment Ion
364.9618	[C11 H12 Br N2 O5 S]+	364.9625	1.93	CH3O	31	Fragment Ion
362.9637	[C11 H12 Br N2 O5 S]+	362.9645	2.11	CH3O	31	Fragment Ion
321.9010	[C8 H5 Br N O6 S]+	321.9015	1.54	C4H10N	72.1	Fragment Ion
320.8994	[C8 H4 Br N2 O5 S]+	320.8998	1.25	C4H11O	75.1	Fragment Ion
318.9015	[C8 H4 Br N2 O5 S]+	318.9019	1.29	C4H11O	75.1	Fragment Ion
259.9370	[C8 H5 Br N O4]+	259.9377	2.47	C4H10NO2S	136	Fragment Ion
257.9390	[C8 H5 Br N O4]+	257.9396	2.39	C4H10NO2S	136	Fragment Ion

6c –



Observed mass	Formula & Ion Species	Calculated mass	Diff (ppm)	Loss Formula	Loss Mass	Ion Type
407.9803	[C13 H15 Br N2 O6 S]+	407.9809	1.53			Molecular Ion
405.9822	[C13 H15 Br N2 O6 S]+	405.9829	1.76			Molecular Ion
404.9750	[C13 H14 Br N2 O6 S]+	404.9750	0.22	H	1	Fragment Ion
390.9777	[C13 H14 Br N2 O5 S]+	390.9781	1.08	HO	17	Fragment Ion
388.9796	[C13 H14 Br N2 O5 S]+	388.9801	1.49	HO	17	Fragment Ion
364.9430	[C10 H10 Br N2 O6 S]+	364.9437	1.92	C3H5	41	Fragment Ion
343.0103	[C13 H14 Br N2 O4]+	343.0112	2.64	HO2S	65	Fragment Ion
341.0126	[C13 H14 Br N2 O4]+	341.0131	1.73	HO2S	65	Fragment Ion
323.8988	[C8 H5 Br N O6 S]+	323.8995	2.28	C5H10N	84.1	Fragment Ion
321.9009	[C8 H5 Br N O6 S]+	321.9015	2.16	C5H10N	84.1	Fragment Ion
298.9606	[C11 H10 Br N O2 S]+	298.9610	1.45	C2H5NO4	107	Fragment Ion
259.9370	[C8 H5 Br N O4]+	259.9377	2.8	C5H10NO2S	148	Fragment Ion
257.9394	[C8 H5 Br N O4]+	257.9396	0.95	C5H10NO2S	148	Fragment Ion

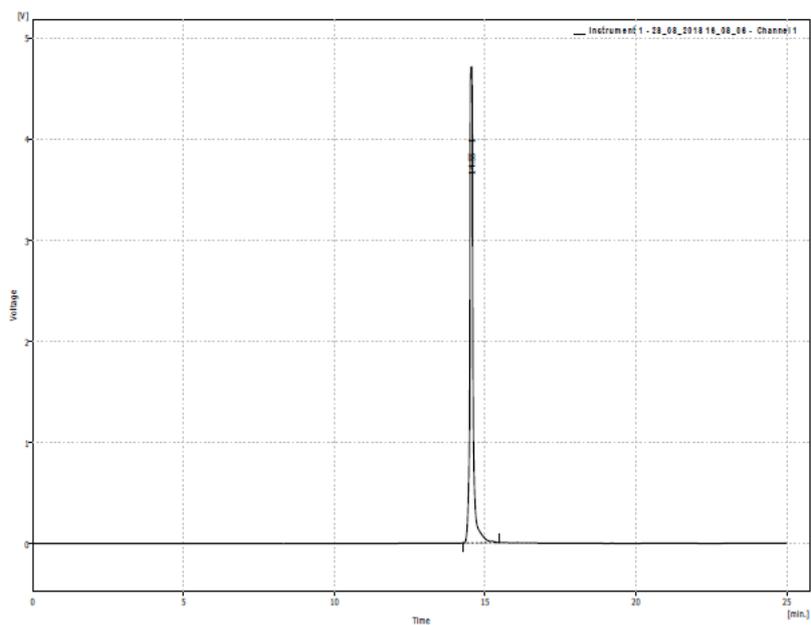
6d –



Observed mass	Formula & Ion Species	Calculated mass	Diff (ppm)	Loss Formula	Loss Mass	Ion Type
409.9596	[C12 H13 Br N2 O7 S]+	409.9602	1.45			Molecular Ion
407.9612	[C12 H13 Br N2 O7 S]+	407.9621	2.36			Molecular Ion
392.9545	[C12 H12 Br N2 O6 S]+	392.9574	7.39	HO	17	Fragment Ion
390.9583	[C12 H12 Br N2 O6 S]+	390.9594	2.72	HO	17	Fragment Ion
378.9410	[C11 H10 Br N2 O6 S]+	378.9417	1.95	CH3O	31	Fragment Ion
376.9426	[C11 H10 Br N2 O6 S]+	376.9437	2.92	CH3O	31	Fragment Ion
366.9409	[C10 H10 Br N2 O6 S]+	366.9417	2.35	C2H3O	43	Fragment Ion
364.9429	[C10 H10 Br N2 O6 S]+	364.9437	2.24	C2H3O	43	Fragment Ion
334.9147	[C9 H6 Br N2 O5 S]+	334.9155	2.42	C3H7O2	75	Fragment Ion
332.9179	[C9 H6 Br N2 O5 S]+	332.9175	-1.19	C3H7O2	75	Fragment Ion
323.8983	[C8 H5 Br N O6 S]+	323.8995	3.7	C4H8NO	86.1	Fragment Ion
321.9005	[C8 H5 Br N O6 S]+	321.9015	3.2	C4H8NO	86.1	Fragment Ion
259.9368	[C8 H5 Br N O4]+	259.9377	3.47	C4H8NO3S	150	Fragment Ion
257.9404	[C8 H5 Br N O4]+	257.9396	-2.92	C4H8NO3S	150	Fragment Ion

4. HPLC data

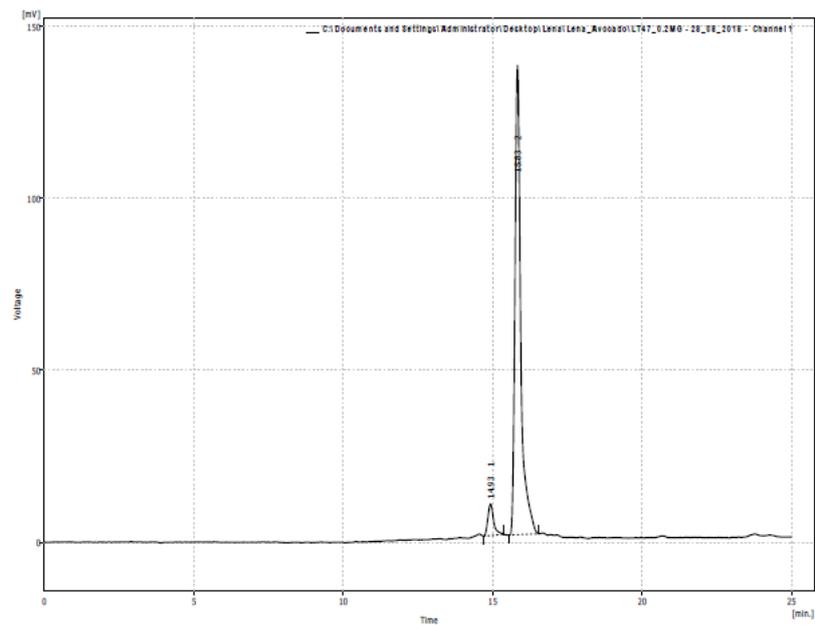
3 –



Result Table (Uncal - Instrument 1 - 28_08_2018 16_08_06 - Channel 1)

	Reten. Time [min]	Area [mV.s]	Height [mV]	Area [%]	Height [%]	W05 [min]	Compound Name
1	14.550	35193.895	4705.444	100.0	100.0	0.10	
	Total	35193.895	4705.444	100.0	100.0		

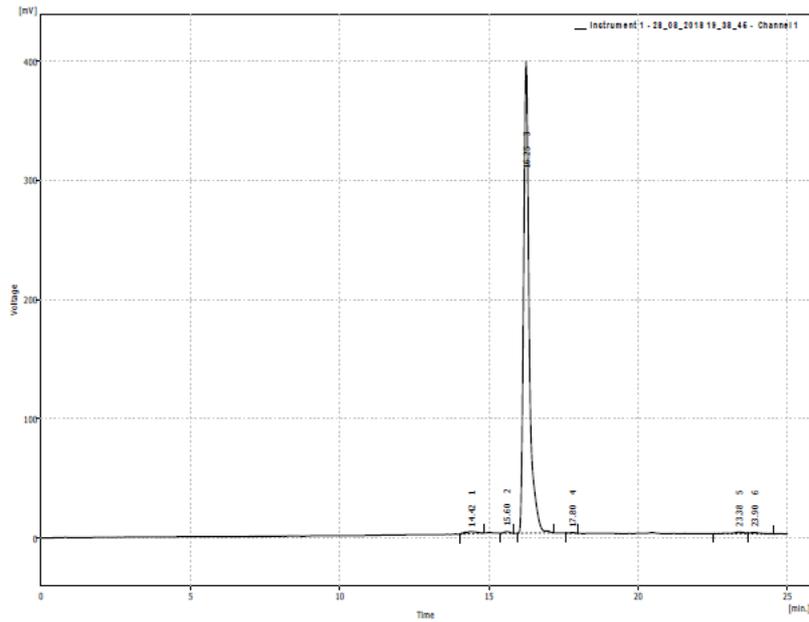
6a –



Result Table (Uncal - C:\Documents and Settings\Administrator\Desktop\Lena\Lena_Avocado\LT47_0.2MG - 28_08_2018 - Channel 1)

	Reten. Time [min]	Area [mV.s]	Height [mV]	Area [%]	Height [%]	W05 [min]	Compound Name
1	14.933	123.146	9.225	6.2	6.3	0.20	
2	15.833	1856.263	136.513	93.8	93.7	0.20	
	Total	1979.409	145.738	100.0	100.0		

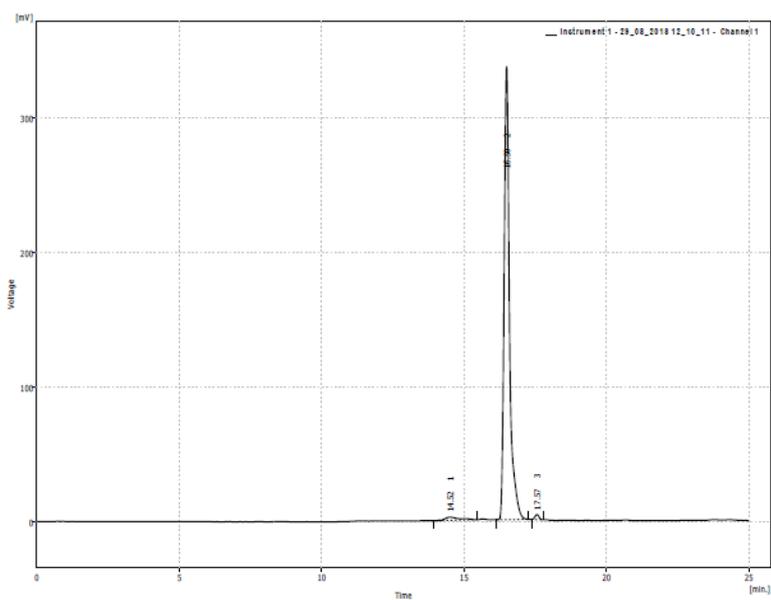
6b -



Result Table (Uncal - Instrument 1 - 28_08_2018 19_38_45 - Channel 1)

	Reten. Time [min]	Area [mV.s]	Height [mV]	Area [%]	Height [%]	W05 [min]	Compound Name
1	14.417	43.402	1.583	0.8	0.4	0.43	
2	15.600	15.658	1.410	0.3	0.4	0.20	
3	16.250	5170.480	395.250	97.6	98.5	0.20	
4	17.800	5.701	0.431	0.1	0.1	0.23	
5	23.383	38.671	1.419	0.7	0.4	0.43	
6	23.900	26.215	0.977	0.5	0.2	0.45	
	Total	5300.127	401.070	100.0	100.0		

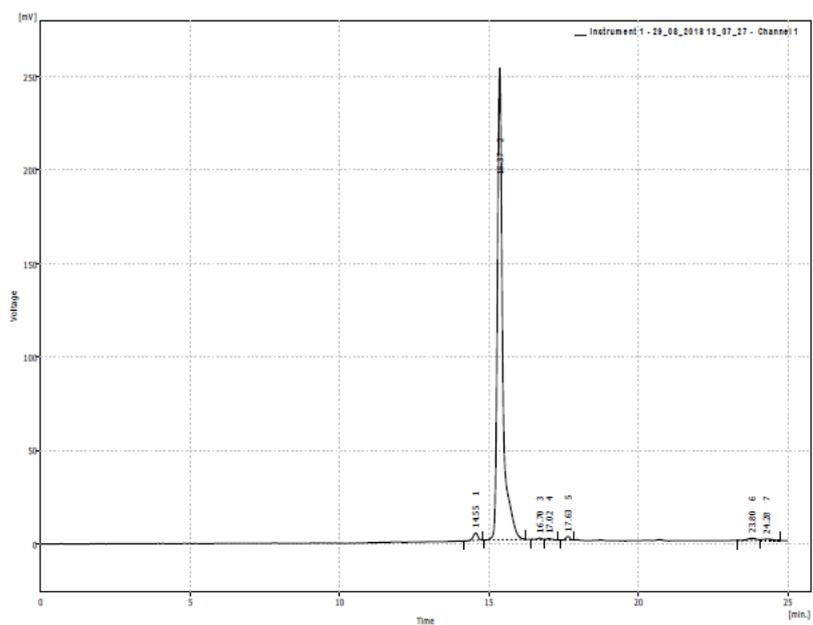
6c –



Result Table (Uncal - Instrument 1 - 29_08_2018 12_10_11 - Channel 1)

	Reten. Time [min]	Area [mV.s]	Height [mV]	Area [%]	Height [%]	W05 [min]	Compound Name
1	14.517	80.374	2.317	1.8	0.7	0.52	
2	16.500	4401.855	336.605	97.4	98.2	0.20	
3	17.567	37.328	3.719	0.8	1.1	0.18	
	Total	4519.557	342.641	100.0	100.0		

6d –



Result Table (Uncal - Instrument 1 - 29_08_2018 13_07_27 - Channel 1)

	Reten. Time [min]	Area [mV.s]	Height [mV]	Area [%]	Height [%]	W05 [min]	Compound Name
1	14.550	42.625	3.918	1.3	1.5	0.18	
2	15.367	3132.579	252.262	96.2	96.4	0.18	
3	16.700	9.840	0.933	0.3	0.4	0.18	
4	17.017	8.445	0.649	0.3	0.2	0.22	
5	17.633	17.177	1.893	0.5	0.7	0.15	
6	23.800	27.090	1.183	0.8	0.5	0.40	
7	24.283	18.666	0.781	0.6	0.3	0.43	
	Total	3256.422	261.619	100.0	100.0		