Electronic Supplementary Information:

Racemic and diastereoselective construction of indole alkaloids under solvent- and catalyst-free microwave assisted Pictet-Spengler condensation

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1. General information

^{1}H NMR and ^{13}C NMR were recorded at room temperature on a Bruker™ DPX 300 at 300 and 100 MHz, respectively. Chemical shifts are in parts per million (ppm). The assignments were made using one dimensional (1D) ^{1}H and ^{13}C spectra or two-dimensional (2D) HSQC and COSY spectra. Mass spectra were recorded with a LCMS-MS triple-quadrupole system (Varian 1200ws). HPLC analysis were performed using a C18 TSK-GEL Super ODS 2 µm particle size column, dimensions 50 * 4.6 mm with a gradient starting from 100% H_2O / 0.1% formic acid and reaching 20% H_2O /80% CH_3CN / 0.08% formic acid within 10 min at a flow rate of 1 mL/min Melting points were determined on a Büchi B-540 apparatus and are uncorrected. Reactions were performed using a Discover™ microwave from CEM™. All commercial reagents and solvents were used without further purification. Specific rotations were measured on a Jasco™ DIP-370 polarimeter using a 10 cm cell.

Crystal data were collected with a Bruker™ Smart Apex-II CCD diffractometer using graphite monochromated MoKα radiation (λ = 0.71073 Å) at 298 K. Cell parameters were retrieved using APEX2[1] software and refined with SAINT[2] on all observed reflections. Data reduction was performed with the SAINT software and corrected for Lorentz and polarization effects. Absorption corrections were applied with the program SADABS[3]. The structure was solved by charge flipping methods using SUPERFLIP[4] program and refined by full-matrix least-squares methods on F using CRYSTALS software[5]. All non-hydrogen atomic positions were located in difference Fourier maps and refined anisotropically. The hydrogen atoms were placed in their geometrically generated positions. Colorless crystals were isolated in rectangular shape at room temperature.

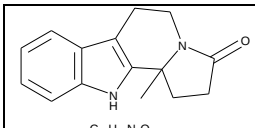
[1] *APEX2 V2008.2-0*. Bruker AXS Inc., Madison, Wisconsin, USA. (**2008**)
[2] *SAINT V7.34A*. Bruker AXS Inc., Madison, Wisconsin, USA. (**2008**)
[3] SADABS V2004/1 - Bruker Nonius area detector scaling and absorption correction. Bruker AXS Inc., Madison, Wisconsin, USA. (**2004**)
[4] Palatinus, L. & van der Lee, A. (**2008**). *J. Appl. Cryst.* **41**, 975.
[5] Betteridge, P.W., Carruthers, J.R., Cooper, R.I., Prout, K. & Watkin, D.J. (**2003**). J. Appl. Cryst. **36**, 1487.

2. General Procedure for Pictet-Spengler using solvent-free microwave conditions.

The tryptamine derivative (0.5 mmol, 1eq.) and the ketoacid (0.5 mmol, 1 eq.) were mixed in a capped 10-mL microwave-vessel. The mixture was heated at 180 °C for 2 min (average effective ramp time =1 min). The power was set at 100 W and the pressure was set at 15 bar (average effective pressure = 3 bar). After completion of the reaction, the crude product was dissolved in DCM/MeOH : 90/10 (10 mL). The organic layer was washed with $NaHCO_3$ sat. (5mL), and dried over $MgSO_4$. Solvent was removed under reduced pressure. In some cases, the product was purified by simple precipitation in MeOH. If required flash chromatography (95/5: EtOAc/MeOH) was used for purification. In all cases, the resulting products were isolated in total purity, as determined by LC-MS and afforded analytically pure products in excellent yields as a white solid. In general, the reaction is very clean.

3. Characterization of compounds.

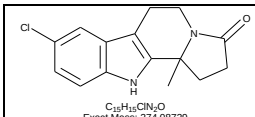
(11b-Methyl-1,2,5,6,11,11b-hexahydro-indolizino[8,7-*b*]indol-3-one (6a):
Synthesized from levulinic acid and tryptamine



$C_{15}H_{16}N_2O$
Exact Mass: 240,12626
Mol. Wt.: 240,30034

Yield (109 mg, 91%); off-white solid; mp= 260–262 °C; Purity: 100% ; ^{1}H NMR (300 MHz, DMSO) δ 11.22 (br s, 1H, NH), 7.36 (d, *J* = 7.8 Hz, 1H), 7.31 (d, *J* = 7.8 Hz, 1H), 7.06 (dd, *J* = 7.2, 1.2 Hz, 1H) , 6.95 (dd, *J* = 7.2, 1.2 Hz, 1H), 4.19 (dd, *J* = 13.2, 5.4 Hz, 1H), 3.04 (dt, *J* = 19.8, 4.8 Hz, 1H), 2.73-2.53 (m, 3H), 2.33-2.18 (m, 2H), 2.04 (t, *J* = 9.9 Hz, 1H), 1.54 (s, 3H); ^{13}C NMR (75 MHz, DMSO) δ 172.38 (Cq), 139.44 (Cq), 136.40 (Cq), 126.70 (Cq), 121.40, 118.99, 118.40, 111.63, 105.00 (Cq), 59.39 (Cq), 34.73, 33.09, 30.55, 25.39, 21.37; rt(LCMS) = 2.40 min; HRMS-ESI (m/z): $[M+H]^+$ calcd 241.13354; found 241.13292 (Δ = 2.8 ppm).

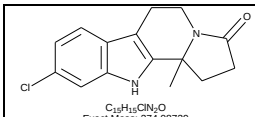
8-Chloro-11b-methyl-1,2,5,6,11,11b-hexahydro-indolizino[8,7-*b*]indol-3-one (6b):
Synthesized from levulinic acid and 5-chloro tryptamine



$C_{15}H_{15}ClN_2O$
Exact Mass: 274,08729
Mol. Wt.: 274,7454

Yield (130 mg, 95%); off-white solid; mp= 227-229 °C; Purity: 100%; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.95 (br s, 1H, NH), 7.43 (d, *J* = 1.8 Hz, 1H), 7.25 (t, *J* = 8.4 Hz, 1H), 7.11(dd, *J* = 8.4, 1.8 Hz, 1H), 4.49 (dt, *J* = 12.6, 2.1 Hz, 1H), 3.16-3.06 (m, 1H), 2.81-2.63 (m, 3H), 2.52-2.43 (m, 1H), 2.37-2.29 (m, 1H), 2.25-2.18 (m, 1H), 1.62 (s, 3H); ^{13}C NMR (300 MHz, $CDCl_3$) δ 173.07 (Cq), 139.44 (Cq),134.67 (Cq), 127.91 (Cq), 125.43 (Cq), 122.34, 118.17, 112.17, 106.46 (Cq), 59.75 (Cq), 35.06, 32.81, 30.62, 25.47, 21.22; rt(LCMS) = 2.70 min; HRMS-ESI (m/z): $[M+H]^+$ calcd 275.09457; found 275.09389 (Δ = 2.5 ppm).

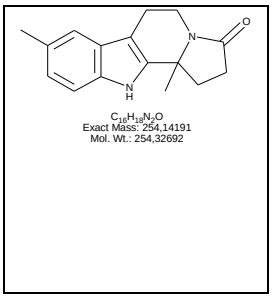
9-Chloro-11b-methyl-1,2,5,6,11,11b-hexahydro-indolizino[8,7-*b*]indol-3-one (6c):
Synthesized from levulinic acid and 4-chloro tryptamine



$C_{15}H_{15}ClN_2O$
Exact Mass: 274,08729
Mol. Wt.: 274,7454

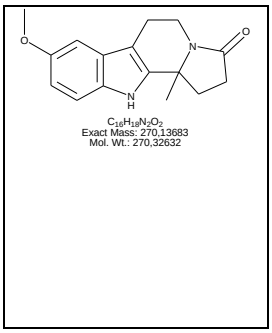
Yield (127 mg, 93%); white crystals; mp= 220-222 °C; Purity: 100%; ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.66 (br s, 1H, NH), 7.36 (d, *J* = 4.5 Hz, 1H), 7.31 (s, 1H), 7.07 (d, *J* = 8.4 Hz, 1H), 4.49 (dd, *J* = 12.3, 3.9 Hz, 1H), 3.20-3.07 (m,1H), 2.87-2.64 (m,3H), 2.51-2.31 (m, 2H), 2.25-2.15 (m, 1H), 1.63 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 172,71 (Cq), 138.20 (Cq), 136.17 (Cq), 126.89 (Cq), 124.72, 119.49, 118.71, 110.64, 105.64 (Cq), 59.37 (Cq), 34.53, 32.11, 30.30, 24.66, 20.62; rt(LCMS) = 2.70 min; HRMS-ESI (m/z): $[M+H]^+$ calcd 275.09457; found 275.09370 (Δ = 2.4 ppm).

8,11b-Dimethyl-1,2,5,6,11,11b-hexahydro-indolizino[8,7-*b*]indol-3-one (6d):
Synthesized from levulinic acid and 5-methyl tryptamine



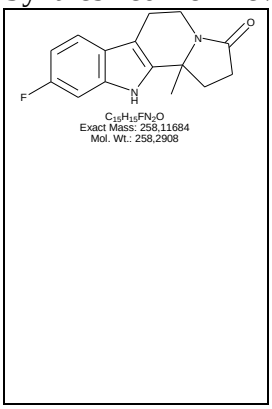
Yield (118 mg, 93%); off-white solid; mp= 203-205 °C; Purity: 100% ; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.58 (br s, 1H, NH), 7.25 (t, *J* = 8.1 Hz, 2H), 7.24 (d, *J* = 8.1 Hz, 1H), 4.48(dd, *J* = 12.6, 3.9 Hz, 1H), 3.18-3.05 (m,1H), 2.86-2.66 (m, 3H), 2.55-2.48 (m, 1H), 2.46 (s, 3H), 2.35-2.13(m, 2H), 1.61 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 172.73 (Cq), 137.68 (Cq), 134.21 (Cq), 128.73 (Cq), 126.64 (Cq), 123.31, 117.96, 110.47, 105.84 (Cq), 59.46 (Cq), 34.84, 32.56, 30.51, 25.10, 21.20, 20.98; rt(LCMS) = 2.63 min; HRMS-ESI (m/z): $[M+H]^+$ calcd 255.14919; found 255.14869 (Δ = 1.9 ppm).

8-Methoxy-11b-methyl-1,2,5,6,11,11b-hexahydro-indolizino[8,7-*b*]indol-3-one (6e):
Synthesized from levulinic acid and 5-metoxy tryptamine



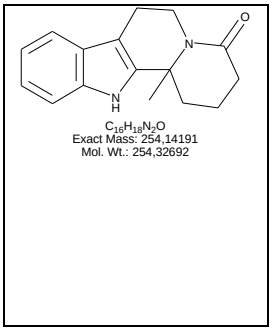
Yield (130 mg, 94%); off-white solid; mp= 199-201 °C; Purity: 100%; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.81 (br s, 1H, NH), 7.24 (d, *J* = 9 Hz, 1H), 6.93 (d, *J* = 2.4 Hz, 1H), 6.85 (dd, *J* = 9, 2.4 Hz, 1H), 4.48 (dd, *J* = 12.6, 4.2 Hz, 1H), 3.86 (s, 3H), 3.15-3.03 (m, 1H), 2.86-2.75(m, 2H), 2.71-2.62(m, 1H), 2.52-2.43(m, 1H), 2.32-2.23(m, 2H), 1.60 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 167.96 (Cq), 163.35 (Cq), 135.23 (Cq), 133.20 (Cq), 132.38 (Cq), 128.99, 128.44, 128.19, 127.60, 122.79 (Cq), 64.22, 58.25(Cq), 47.92, 45.77, 29.47, 22.36; rt(LCMS) = 2.75 min; HRMS-ESI (m/z): $[M+H]^+$ calcd 271.13683; found 271.13619 (Δ = 2.8 ppm).

9-Fluoro-11b-methyl-1,2,5,6,11,11b-hexahydro-indolizino[8,7-*b*]indol-3-one (6f):
Synthesized from levulinic acid and 4-fluoro tryptamine



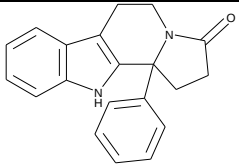
Yield (120 mg, 93%); off-white solid; mp= 196-198 °C; Purity: 100%; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.96 (br s, 1H, NH), 7.37 (dd, *J* = 8.7, 5.1 Hz, 1H), 7.02 (dd, *J* = 9.6, 2.4 Hz, 1H), 6.87 (ddd, *J* = 9.6, 5.1, 2.4 Hz, 1H), 4.46 (dd, *J* = 12.3, 3.9 Hz, 1H),3.17-3.03 (m, 1H), 2.84-2.78 (m, 2H), 2.77-2.67 (m, 1H), 2.52-2.44 (m, 1H), 2.33-2.32 (m, 1H), 2.30-2.22 (m, 1H), 1.62 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 172.89 (Cq), 159.80 (d, *J* = 235.5 Hz, 1Cq), 136.27 (d, *J* = 12.2 Hz, 1Cq), 135.99 (d, *J* = 3.8 Hz, 1Cq), 123.16 (Cq), 118.96 (d, *J* = 9.8 Hz, 1C), 108.05 (d, *J* = 24 Hz, 1C), 106.36 (Cq), 97.48 (d, *J* = 25.5 Hz, 1C), 59.56 (Cq), 34.88, 32.62, 30.63, 25.21, 21.06; rt(LCMS) = 2.53 min; HRMS-ESI (m/z): $[M+H]^+$ calcd 259.12412; found 259.12335 (Δ = 2.8 ppm).

12b-Methyl-2,3,6,7,12,12b-hexahydro-1*H*-indolo[2,3-*a*]quinolizin-4-one (7):
Synthesized from 4-acetylbutyric acid and tryptamine



Yield (116 mg, 92%); off-white solid; mp= 257 -259 °C; Purity: 100%; ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.91 (br s, 1H, NH), 7.57 (d, *J* = 7.8 Hz, 1H), 7.43 (d, *J* = 7.8 Hz, 1H,), 7.25 (td, *J* = 7.8, 1.2 Hz, 1H) , 7.15 (td, *J* = 7.8, 1.2 Hz, 1H), 5.22 (dd, *J* = 12.3, 3.6 Hz, 1H), 3.13 (dt, *J* = 19.5, 4.8 Hz, 1H), 2.97-2.80 (m, 2H), 2.79-270 (m, 1H), 2.69-2.43 (m, 2H), 1.99-1.83 (m, 3H), 1.76 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 169.88 (Cq), 139.03 (Cq), 136.53 (Cq), 126.63 (Cq), 121.78, 119.37, 118.32, 111.35, 107.10 (Cq), 57.26 (Cq), 36.86, 35.31, 32.28, 25.85, 21.48, 16.76; rt(LCMS) = 2.46 min; HRMS-ESI (m/z): $[M+H]^+$ calcd 255.14919; found 255.14857 (Δ = 2.4 ppm).

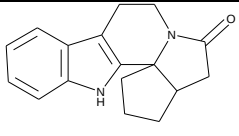
11b-Phenyl-1,2,5,6,11,11b-hexahydro-indolizino[8,7-*b*]indol-3-one (8):
Synthesized from 3-benzoylproponic acid and tryptamine



$C_{20}H_{18}N_2O$
Exact Mass: 302,14191
Mol. Wt.: 302,36972

Yield (136 mg, 90%); off-white crystals; mp= 262-264 °C; Purity: 100%; ^{1}H NMR (300 MHz, DMSO) δ 11.43 (br s, 1H, NH), 7.42-7.28 (m, 7H), 7.12 (td, *J* = 7.2, 1.2 Hz, 1H), 6.99 (td, *J* = 7.2, 1.2 Hz, 1H), 4.26-4.17 (m, 1H), 2.85-2.61(m, 4H), 2.52 (dd, *J* = 10.2, 1.8 Hz, 1H), 2.49 (dd, *J* = 10.2, 1.8 Hz, 1H), 2.41-2.32 (m, 1H); ^{13}C NMR (75MHz, DMSO) δ 173.60 (Cq), 144.36 (Cq), 136.65 (Cq), 136.44 (Cq), 129.05, 128.00, 126.51 (Cq), 126.32, 121.90, 119.25, 118.59, 111.80, 107.23 (Cq), 65.30 (Cq), 35.41, 34.10, 30.71, 20.77; rt(LCMS) = 2.77 min; HRMS-ESI (m/z): $[M+H]^+$ calcd 303.14919; found 303.14837 (Δ = 2.7 ppm).

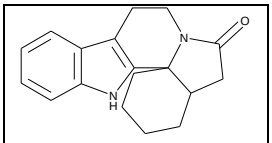
2,3,3a,4,8,13-hexahydro-7*H*-cyclopenta[1,8a]indolizino[8,7-*b*]indol-5(1*H*)-one (9):
Synthesized from 2-oxocyclopentanacetic acid (rac) and tryptamine



$C_{17}H_{18}N_2O$
Exact Mass: 266,14191
Mol. Wt.: 266,33762

Yield (128 mg, 96%); off-white solid; mp= 237-239 °C; Purity: 100%; ^{1}H NMR (300 MHz, DMSO) δ11.00 (br s, 1H, NH), 7.33 (t, *J* = 7.8 Hz, 2H), 7.06 (td, *J* = 7.2, 1.2 Hz, 1H), 6.96 (td, *J* = 7.2, 1.2 Hz, 1H), 4.26-4.19 (m, 1H), 3.09-2.99 (m, 1H), 2.86-2.78 (m, 1H), 2.66-2.60 (m, 3H), 2.24-2.06 (m,3H), 1.84-1.75 (m, 2H), 1.67-1.57 (m, 2H); ^{13}C NMR (75 MHz, DMSO) δ 173.79 (Cq), 138.03 (Cq), 136.74 (Cq), 126.74 (Cq), 121.49, 119.03, 118.18, 111.61, 106.65 (Cq), 70.80 (Cq), 41.14, 39.17, 38.63, 36.52, 34.80, 24.68, 20.92 ; rt(LCMS) = 2.60 min; HRMS-ESI (m/z): $[M+H]^+$ calcd 267.14919; found 267.14834 (Δ = 3.2 ppm).

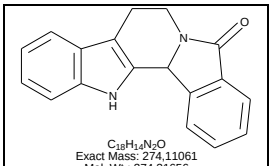
1,2,3,4,4a,5,9,14-octahydro-6*H*,*8H*-pyrido[3,4-*b*:2,1-i'] diindol-6-one (10):
Synthesized from 2-oxocyclohexanacetic acid (rac) and tryptamine



$C_{18}H_{20}N_2O$
Exact Mass: 280,15756
Mol. Wt.: 280,3642

Yield (133 mg, 95%); off-white solid; mp= 256-258 °C; Purity: 100%; ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.22 (br s, 1H, NH) , 7.54 (d, *J* = 7.8 Hz, 1H), 7.45 (d, *J* = 7.8 Hz, 1H), 7.27-7.15 (m, 2H), 4.52 (dd, *J* = 12.9, 6.0 Hz, 1H), 3.19 (dt, *J* =18.6, 6.0 Hz, 1H), 3.01-2.81 (m, 2H), 2.59-2.43 (m, 3H), 2.28-2.24 (m, 1H), 2.16-2.05 (m, 1H), 1.88-1.59 (m, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 173.52 (Cq), 138.13 (Cq), 136.25 (Cq), 126.57 (Cq), 122.00, 119.67, 118.38, 111.34, 106.73 (Cq), 60.72 (Cq), 37.95, 35.88, 34.94, 34.23, 25.98, 21.69, 21.16, 20.55; rt(LCMS) = 2.73 min; HRMS-ESI (m/z): $[M+H]^+$ calcd 281.16433; found 281.16433 (Δ = 1.8 ppm).

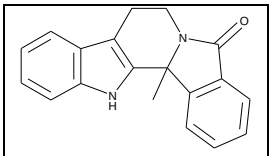
5,6,11b,12-Tetrahydro-6a,12-diaza-indeno[1,2-*a*]fluoren-7-one (11):
Synthesized from 2-formylbenzoic acid and tryptamine



$C_{18}H_{14}N_2O$
Exact Mass: 274,11061
Mol. Wt.: 274,31656

Yield (130 mg, 95%); off-white solid; mp= 261-263 °C; Purity: 100%; ^{1}H NMR (300 MHz, DMSO) δ 11.37 (br s, 1H, NH), 8.31 (dd, *J* = 7.8, 0.6 Hz, 1H), 7.77-7.68 (m, 2H), 7.54 (t, *J* = 7.5 Hz, 1H), 7.41 (d, *J* = 8.7 Hz, 2H), 7.12 (td, *J* = 7.5, 1.2 Hz, 1H), 6.99 (td, *J* = 7.5, 1.2 Hz, 1H), 6.04 (s, 1H), 4.60 (dd, *J* = 13.2, 5.4 Hz, 1H), 3.45-3.31(m, 1H), 2.86-2.69 (m, 2H); ^{13}C NMR (75MHz, DMSO) δ 167.64 (Cq), 144.12 (Cq), 136.92 (Cq), 132.34, 132.17 (Cq), 131.36 (Cq), 129.09, 126.63 (Cq), 124.25, 123.61, 122.01, 119.35, 118.62, 111.75, 107.63 (Cq), 57.12, 38.18, 21.87; rt(LCMS) = 2.70 min; HRMS-ESI (m/z): $[M+H]^+$ calcd 275.11789; found 275.11681 (Δ = 1.1 ppm).

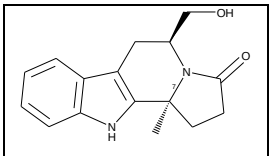
11b-Methyl-5,6,11b,12-tetrahydro-6a,12-diaza-indeno[1,2-*a*]fluoren-7-one (12):
Synthesized from 2-acetylbenzoic acid and tryptamine



$C_{19}H_{16}N_2O$
Exact Mass: 288,12626
Mol. Wt.: 288,34314

Yield (139 mg, 97%); off-white solid; mp= 253-255 °C; Purity: 100%; ^{1}H NMR (300 MHz, DMSO) δ 11.37 (br s, 1H, NH), 8.33(d, *J* = 7.8 Hz, 1H), 7.72 (t, *J* = 7.8 Hz, 2H), 7.51 (t, *J* = 7.8 Hz, 1H), 7.38 (d, *J* = 7.8 Hz, 2H), 7.09 (t, *J* = 7.8 Hz, 1H), 6.97 (t, *J* = 7.8 Hz, 1H), 4.53 (dd, *J* = 13.2, 5.1 Hz, 1H), 3.44-3.34 (m, 1H), 2.82-2.63 (m, 2H), 1.85 (s, 3H); ^{13}C NMR (75 MHz, DMSO) δ 167.68 (Cq), 149.80 (Cq), 136.65 (Cq), 135.63 (Cq), 132.68, 130.73 (Cq), 129.06, 126.45 (Cq), 123.64, 123.24, 122.07, 119.36, 118.79, 111.68, 106.81 (Cq), 62.49 (Cq), 35.90, 26.35, 21.93; rt(LCMS) = 2.77 min; HRMS-ESI (m/z): $[M+H]^+$ calcd 289.13354; found 289.13246 (Δ = 1.1 ppm).

(5S,11bS)-5-Hydroxymethyl-11b-methyl-1,2,5,6,11,11b-hexahydro-indolizino[8,7-*b*]indol-3-one (13):
Synthesized from levulinic acid and L-tryptophanol

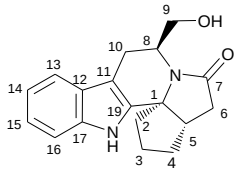


$C_{16}H_{18}N_2O_2$
Exact Mass: 270,13683
Mol. Wt.: 270,32632

Yield (124 mg, 92%); off-white solid; mp= 224-226 °C; $[\alpha]_D$ = -1.8 ° (*c* 0.6, CH_2Cl_2); Purity: 100%; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.81 (br s, 1H, NH), 7.48 (d, *J* = 7.5 Hz, 1H), 7.31 (d, *J* = 7.8 Hz, 1H), 7.19 (dd, *J* = 7.8, 1.5 Hz, 1H), 7.16 (dd, *J* = 7.8, 1.5 Hz, 1H), 4.28-4.14 (m, 1H), 3.70 (br s, 1H, OH), 3.06-2.89 (m, 1H), 2.83-2.61 (m, 2H), 2.54-2.36 (m, 2H), 2.32-2.10 (m, 3H), 1.66 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 174.86 (Cq), 137.35 (Cq), 136.40 (Cq), 126.53 (Cq), 122.21, 119.70, 118.46, 111.17, 106.81 (Cq), 62.84, 62.36 (Cq), 55.51, 32.69, 31.39, 25.36, 24.29; rt(LCMS) = 2.23 min; HRMS-ESI (m/z): $[M+H]^+$ calcd 271.14410; found 271.14380 (Δ = 1.1 ppm).

(3aS,7S,13bS)-7-(Hydroxymethyl)-2,3,3a,4,7,8-hexahydro-1*H*-cyclopenta[1,8a]indolizino[8,7-b]indol-5(13*H*)-one (14):

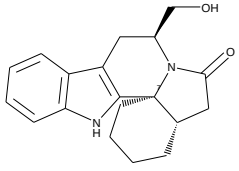
Synthesized from 2-oxocyclopentanacetic acid (rac) and L-tryptophanol



Yield (140 mg, 95%); white crystals; mp= 144-146 °C; $[\alpha]_D$ = -87 ° (*c* 0.5, CH_2Cl_2); Purity 100 %; δ_H (300 MHz, $CDCl_3$) 11.01 (br s, 1H, NH), 7.37 (d, *J* = 7.8 Hz, 1H, $C_{(16)}H$), 7.31 (d, *J* = 7.8 Hz, 1H, $C_{(13)}H$), 7.06(dd, *J* = 7.2, 3 Hz, 1H, $C_{(15)}H$), 6.97 (dd, *J* = 7.2, 1.2 Hz, 1H, $C_{(14)}H$), 5.05 (dd, *J* = 7.5, 5.1 Hz, 1H, $C_{(9)}H$), 4.14-3.99 (m, 2H, $C_{(9)}H$, $C_{(10)}H$), 3.55-3.47 (m, 1H, $C_{(8)}H$), 3.35 (br s, 1H, OH), 2.89-2.68(m, 3H, $C_{(5)}H$, $C_{(6)}H$, $C_{(10)}H$), 2.57 (dd, *J* = 18, 10.8 Hz, 1H, $C_{(2)}H$), 2.27-2.07 (m, 3H, $C_{(2)}H$, $C_{(6)}H$, $C_{(3)}H$), 1.88-1.58 (m, 3H, $C_{(3)}H$, $C_{(4)}H$); δ_C (50 MHz, $CDCl_3$) 24.0 ($C_{(3)}$), 24.9 ($C_{(4)}$), 34.8 ($C_{(2)}$), 38.9 ($C_{(6)}$), 39.5 ($C_{(10)}$), 41.3 ($C_{(5)}$), 56.6 ($C_{(8)}$), 62.2 ($C_{(9)}$), 73.9 ($C_{(1)}$), 107.8 ($C_{(11)}$), 111.6 ($C_{(13)}$), 118.1 ($C_{(16)}$), 119.1 ($C_{(14)}$), 121.5 ($C_{(15)}$), 126.7 ($C_{(12)}$), 136.8 ($C_{(19)}$), 138.1 ($C_{(17)}$), 176.0 ($C_{(7)}$); rt(LCMS) = 2.37 min; HRMS-ESI (m/z): $[M+H]^+$ calcd 297.15975; found 297.15880 (Δ = 3.2 ppm).

(4aS,8S,14bS)-8-(Hydroxymethyl)-1,2,3,4,4a,5,8,9-octahydropyrido[3,4-*b*:2,1-i']diindol-6(14*H*)-one (15):

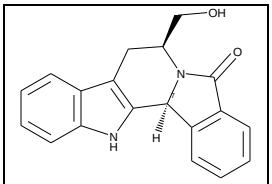
Synthesized from 2-oxocyclohexanacetic acid (rac) and L-tryptophanol



Yield (147 mg, 95%); off-white solid; mp= 233-235 °C; $[\alpha]_D$ = -105 ° (*c* 0.6, CH_2Cl_2); Purity: 100%; ^{1}H NMR (300 MHz, DMSO) δ 10.91 (br s, 1H, NH), 7.35 (t, *J* = 7.5 Hz, 2H), 7.05 (dt, *J* = 7.5, 0.9 Hz, 1H), 6.96 (t, *J* = 7.5 Hz, 1H), 4.97 (t, *J* = 6 Hz, 1H), 4.08-3.99 (m, 1H), 3.96 (br s, 1H, OH), 3.62-3.53 (m, 1H), 2.86-2.66 (m, 2H), 2.59-2.48 (m, 1H), 2.10 (d, *J* = 6.6 Hz, 2H), 2.01-1.87 (m, 3H), 1.64-1.45 (m, 5H); ^{13}C NMR (75 MHz, DMSO) δ 178.03 (Cq), 139.32 (Cq), 136.49 (Cq), 126.74 (Cq), 121.46, 119.10, 118.21, 111.82, 107.29 (Cq), 64.17, 62.61 (Cq), 54.34, 37.70, 36.46, 33.69, 27.65, 23.47, 22.40, 21.25; rt(LCMS) = 2.63 min; HRMS-ESI (m/z): $[M+H]^+$ calcd 311.17540; found 311.17476 (Δ = 2.1 ppm).

(6S,11bS)-6-Hydroxymethyl-5,6,11b,12-tetrahydro-6a,12-diaza-indeno[1,2-*a*]fluoren-7-one (16):

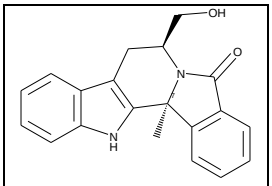
Synthesized from 2-formylbenzoic acid and L-tryptophanol



Yield (145 mg, 96%); white crystals; mp= 276-279 °C; $[\alpha]_D$ = -67 ° (*c* 0.6, CH_2Cl_2); Purity: 100%; ^{1}H NMR (300 MHz, DMSO) δ 11.28 (br s, 1H, NH), 8.28 (d, *J* = 7.5 Hz, 1H), 7.71 (t, *J* = 7.5 Hz, 2H), 7.53(t, *J* = 7.5 Hz, 1H), 7.40 (dd, *J* = 12.6, 7.8 Hz, 2H), 7.09(t, *J* = 7.8Hz, 1H), 7.53(t, *J* = 7.2 Hz, 1H), 6.10 (s, 1H), 5.18(t, *J* = 6.6 Hz, 1H), 4.35-4.28 (m, 1H), 4.27 (br s, 1H, OH), 3.91-3.82 (m, 1H), 2.97-2.76 (m, 2H); ^{13}C NMR (75 MHz, DMSO) δ 168.27 (Cq), 143.84 (Cq), 137.04 (Cq), 132.67 (Cq), 132.51,131.89 (Cq),129.16 (Cq), 126.58, 124.08, 123.53, 122.00, 119.42, 118.60, 111.80, 108.56 (Cq), 61.93, 59.83, 58.89, 25.30; rt(LCMS) = 2.77 min; HRMS-ESI (m/z): $[M+H]^+$ calcd 305.12845; found 305.12731 (Δ = 1.1 ppm).

(6S,11bS)-6-Hydroxymethyl-11b-methyl-5,6,11b,12-tetrahydro-6a,12-diaza-indeno[1,2-*a*]fluoren-7-one (17):

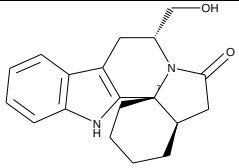
Synthesized from 2-acetylbenzoic acid and L-tryptophanol



Yield (149 mg, 94%); white crystals; mp= 250-252 °C; $[\alpha]_D$ = -83 ° (*c* 0.5, CH_2Cl_2); Purity: 100%; ^{1}H NMR (300 MHz, DMSO) δ 11.33 (br s, 1H, NH), 8.32 (d, *J* = 7.5 Hz, 1H), 7.71(d, *J* = 7.5 Hz, 2H), 7.50 (t, *J* = 7.2 Hz, 1H), 7.40 (t, *J* = 7.2 Hz, 2H),7.09 (t, *J* = 7.2 Hz, 1H), 6.98 (t, *J* = 7.2 Hz, 1H), 5.23 (t, *J* = 6.6 Hz, 1H), 4.43-4.31 (m, 1H), 4.29 (br s, 1H, OH), 3.92-3.82 (m, 1H), 3.01-2.72 (m, 2H), 1.89 (s, 3H); ^{13}C NMR (75 MHz, DMSO) δ 168.83 (Cq), 149.61 (Cq), 136.80 (Cq), 136.17(Cq), 132.88, 131.07 (Cq), 129.12, 126.41 (Cq), 123.56, 123.18, 122.08, 119.44, 118.79, 111.72, 107.82 (Cq), 64.96, 62.34 (Cq), 55.87, 50.97, 25.29; rt(LCMS) = 2.72 min; HRMS-ESI (m/z): $[M+H]^+$ calcd 319.14410; found 319.14296 (Δ = 1.1 ppm).

(4aR,8R,14bR)-8-(Hydroxymethyl)-1,2,3,4,4a,5,8,9-octahydropyrido[3,4-*b*:2,1-i']diindol-6(14*H*)-one (18):

Synthesized from 2-oxocyclohexanacetic acid (rac) and D-tryptophanol

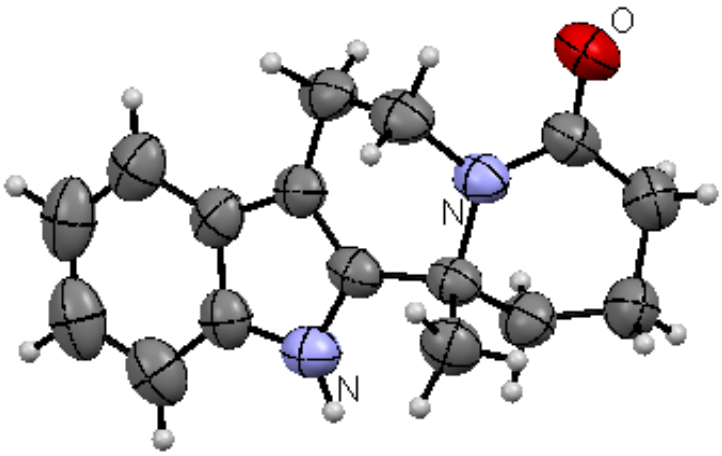


Yield (144 mg, 93%); off-white solid; mp= 247-249 °C; $[\alpha]_D$ = +107 ° (*c* 0.6, CH_2Cl_2); Purity: 100%; ^{1}H NMR (300 MHz, DMSO) δ 10.91 (br s, 1H, NH), 7.36 (t, *J* = 7.5 Hz, 2H),7.06 (t, *J* = 7.5 Hz, 1H), 6.96 (t, *J* = 7.5 Hz, 1H), 4.99 (t, *J* = 5.7 Hz, 1H), 4.12-3.99 (m, 1H), 3.96 (br s, 1H, OH), 3.63-3.51 (m, 1H), 2.87-2.65 (m, 2H), 2.58-2.47 (m, 1H), 2.11 (d, *J* = 6.3 Hz, 2H), 1.83-1.76 (m, 3H), 1.66-1.38 (m, 5H);^{13}C NMR (75 MHz, DMSO) δ 178.00 (Cq), 139.30 (Cq), 136.52 (Cq), 126.75 (Cq), 121.47, 119.11, 118.22, 111.83, 107.29 (Cq), 64.17, 62.62 (Cq), 54.36, 37.68, 36.48, 33.69, 27.62, 23.48, 22.38, 21.26; rt(LCMS) = 2.66 min; HRMS-ESI (m/z): $[M+H]^+$ calcd 311.17540; found 311.17476 (Δ = 2.1 ppm).

4. X-ray diffraction data for 7 and 14 and CCDC codes.

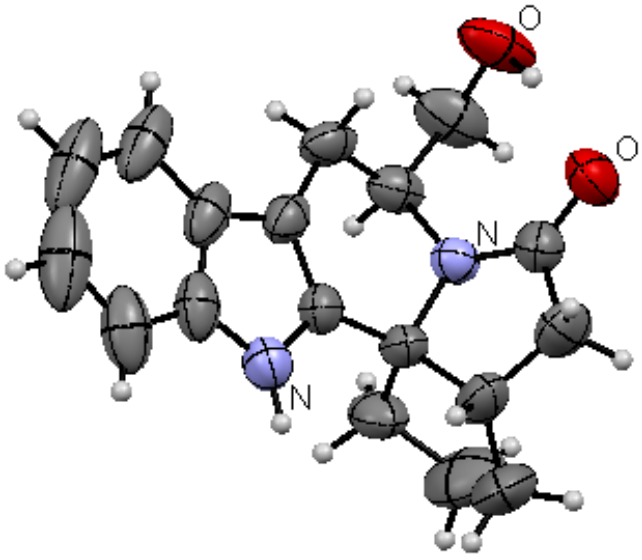
12b-Methyl-2,3,6,7,12,12b-hexahydro-1*H*-indolo[2,3-*a*]quinolizin-4-one (7):

CCDC 856036
Unit cell parameters: a 8.715(4) b 11.090(4) c 13.771(7) beta 90.303(6)
space group P21/c



(1R,5S,11bR)-5-Hydroxymethyl-1,11b-cyclohexyl-1,2,5,6,11,11b-hexahydro-indolizino[8,7-*b*]indol-3-one (14):

CCDC 749287
Unit cell parameters:
a 8.4078(8) b 8.3744(8) c 11.4399(10) beta 98.698(4)space group P21



Basic crystal data for the product 7

CCDC 856036 contains the supplementary crystallographic data for the product **7**. These data can be obtained free of charge from The Cambridge Crystallographic Data Center via www.ccdc.cam.ac.uk/data_request/cif.

Datablock: 1

Bond precision: C-C = 0.0041 A Wavelength=0.71073

Cell: a=8.715(4) b=11.090(4) c=13.771(7)
alpha=90 beta=90.303(6) gamma=90

Temperature: 293 K

	Calculated	Reported
Volume	1330.9(10)	1330.9(10)
Space group	P 21/c	P 21/c
Hall group	-P 2ybc	?
Moiety formula	C16 H18 N2 O	C16 H18 N2 O1
Sum formula	C16 H18 N2 O	C16 H18 N2 O1
Mr	254.32	254.33
Dx,g cm-3	1.269	1.269
Z	4	4
Mu (mm-1)	0.080	0.080
F000	544.0	544.0
F000'	544.20	
h,k,lmax	11,14,18	11,14,18
Nref	3315	3310
Tmin,Tmax	0.976,0.990	0.900,0.990
Tmin'	0.953	

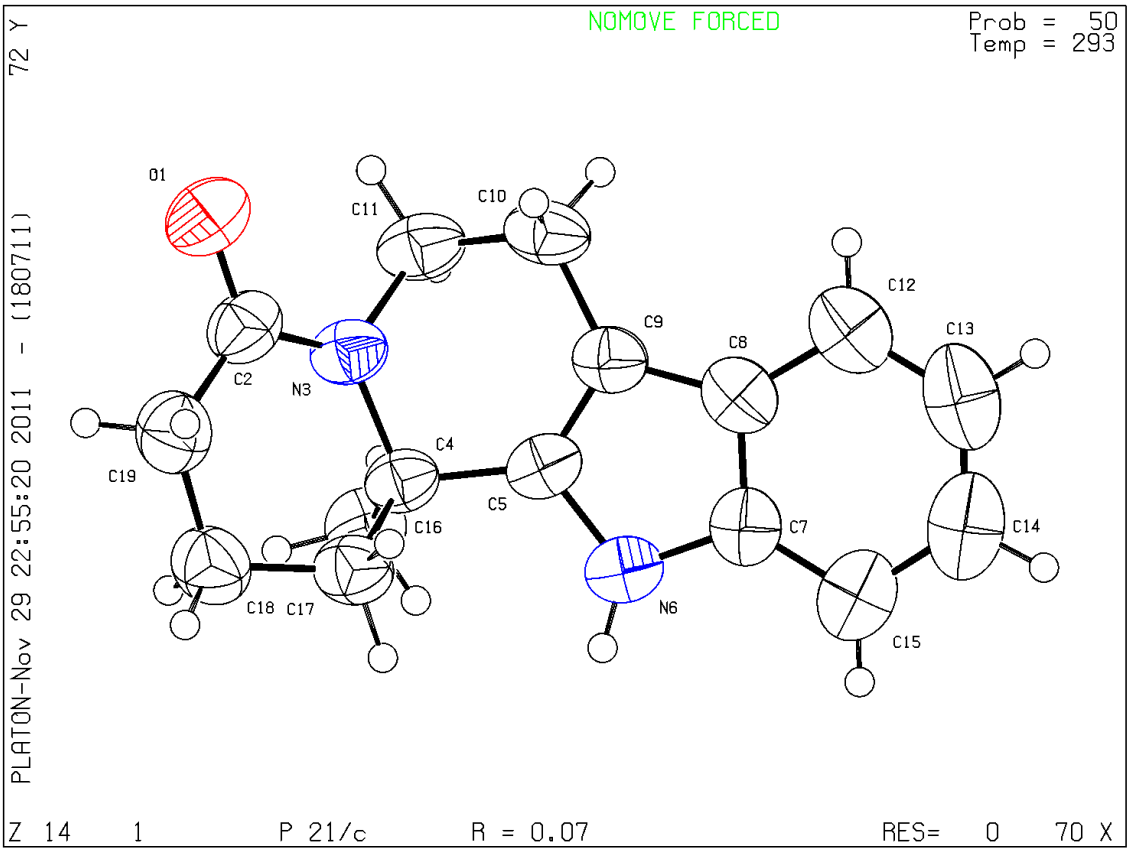
Correction method= MULTI-SCAN

Data completeness= 0.998 Theta(max)= 28.296

R(reflections)= 0.0718(2128) wR2(reflections)= wR= 0.0602(1281)

S = 1.051 Npar= 173

The following ALERTS were generated. Each ALERT has the format
test-name_ALERT_alert-type_alert-level.
Click on the hyperlinks for more details of the test.


NOMOVE FORCED
Prob = 50
Temp = 293
72 Y
PLATON-Nov 29 22:55:20 2011 - (180711)
O1
C11
C10
C12
C9
C8
C13
C2
N3
C4
C5
C19
C16
C7
C14
C18
C17
N6
C15
Z 14 1
P 21/c
R = 0.07
RES= 0 70 X

Basic crystal data for the product 14

CCDC 749287 contains the supplementary crystallographic data for the product **14**. These data can be obtained free of charge from The Cambridge Crystallographic Data Center via www.ccdc.cam.ac.uk/data_request/cif.

Datablock: 1

Bond precision: C-C = 0.0053 A Wavelength=0.71073

Cell: a=8.4078(8) b=8.3744(8) c=11.4399(10)
alpha=90 beta=98.698(4) gamma=90

Temperature: 293 K

	Calculated	Reported
Volume	796.22(13)	796.22(13)
Space group	P 21	P 21
Hall group	P 2yb	P 2yb
Moiety formula	C18 H20 N2 O2	C18 H20 N2 O2
Sum formula	C18 H20 N2 O2	C18 H20 N2 O2
Mr	296.36	296.37
Dx,g cm-3	1.236	1.236
Z	2	2
Mu (mm-1)	0.081	0.081
F000	316.0	316.0
F000'	316.13	
h,k,lmax	10,10,14	10,10,14
Nref	1769[3303]	1767
Tmin,Tmax	0.999,0.999	0.940,0.990
Tmin'	0.998	

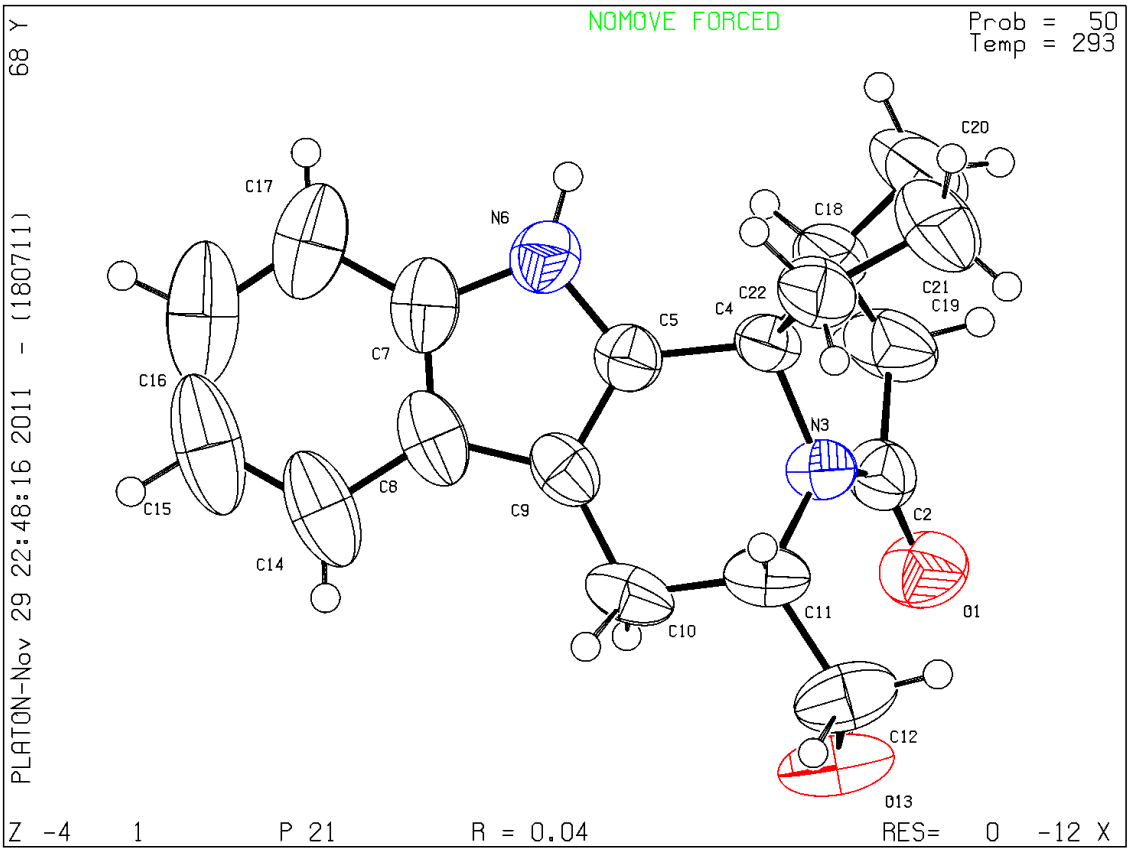
Correction method= MULTI-SCAN

Data completeness= 1.00/0.53 Theta(max)= 26.463

R(reflections)= 0.0398(1463) wR2(reflections)= wR= 0.0441(1411)

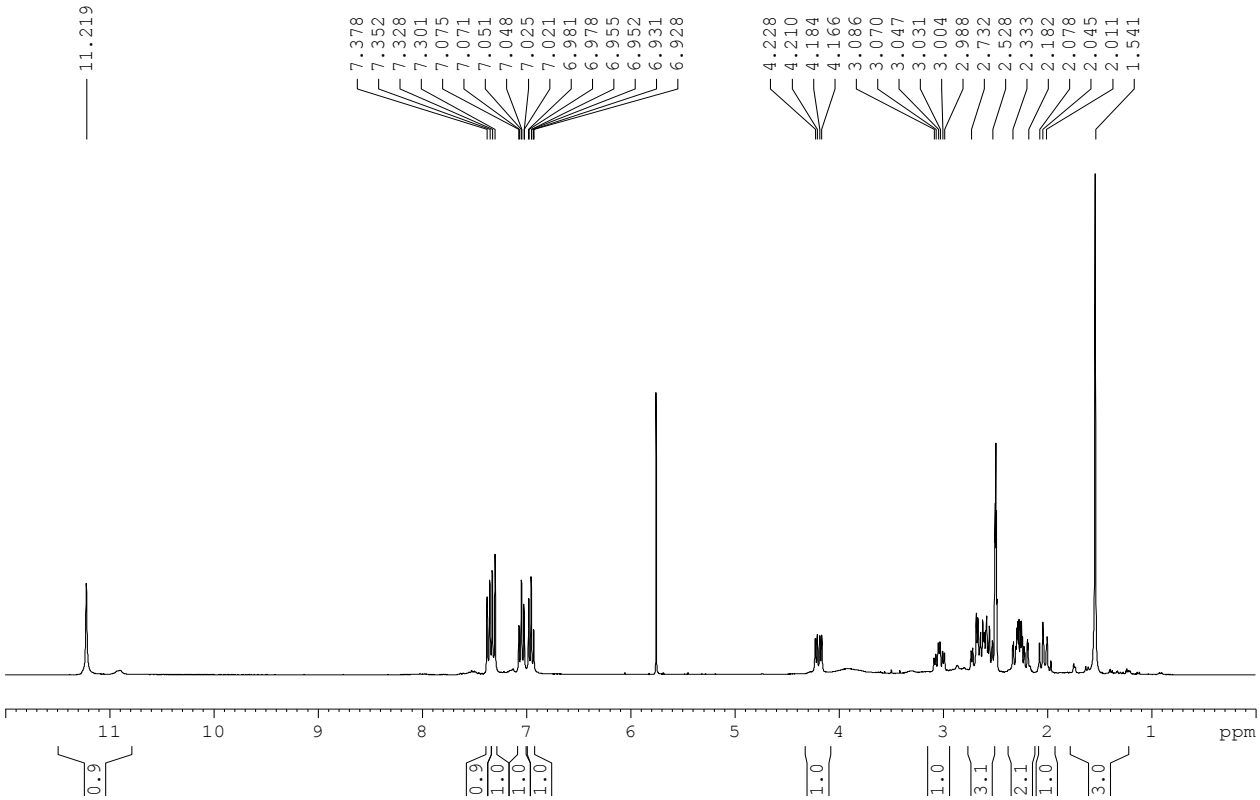
S = 1.152 Npar= 199

The following ALERTS were generated. Each ALERT has the format
test-name_ALERT_alert-type_alert-level.
Click on the hyperlinks for more details of the test.

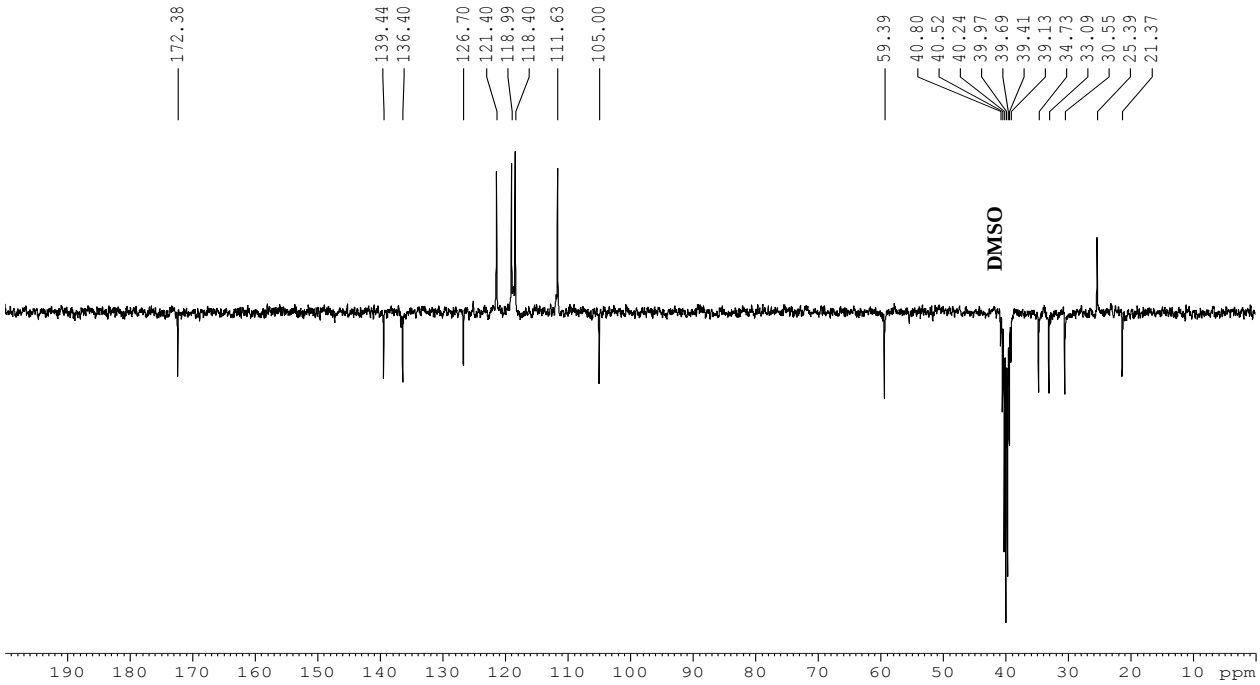

NOMOVE FORCED
Prob = 50
Temp = 293
68 Y
PLATON-Nov 29 22:48:16 2011 - (180711)
C17
N6
C20
C18
C21
C19
C22
C4
C5
C7
C16
N3
C8
C15
C9
C2
C14
O1
C10
C11
C12
O13
Z -4 1 P 21 R = 0.04 RES= 0 -12 X

5. NMR Spectra

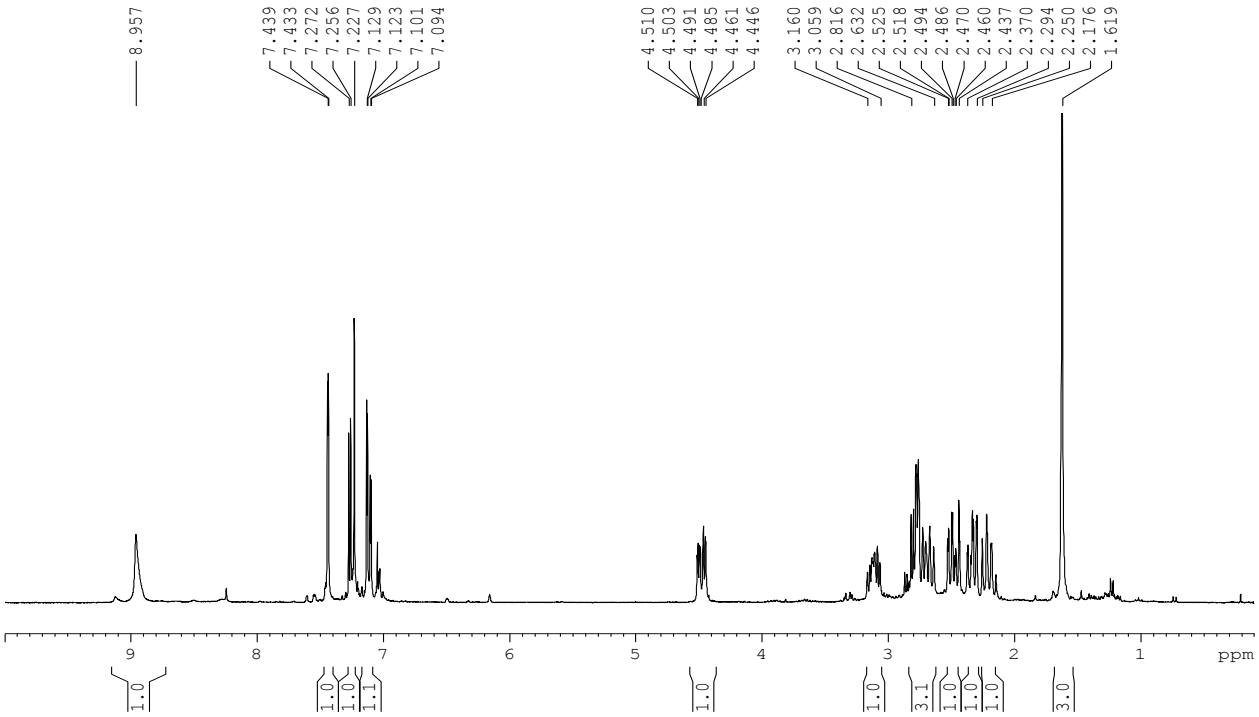
(6a): ^{1}H NMR (300 MHz, DMSO)



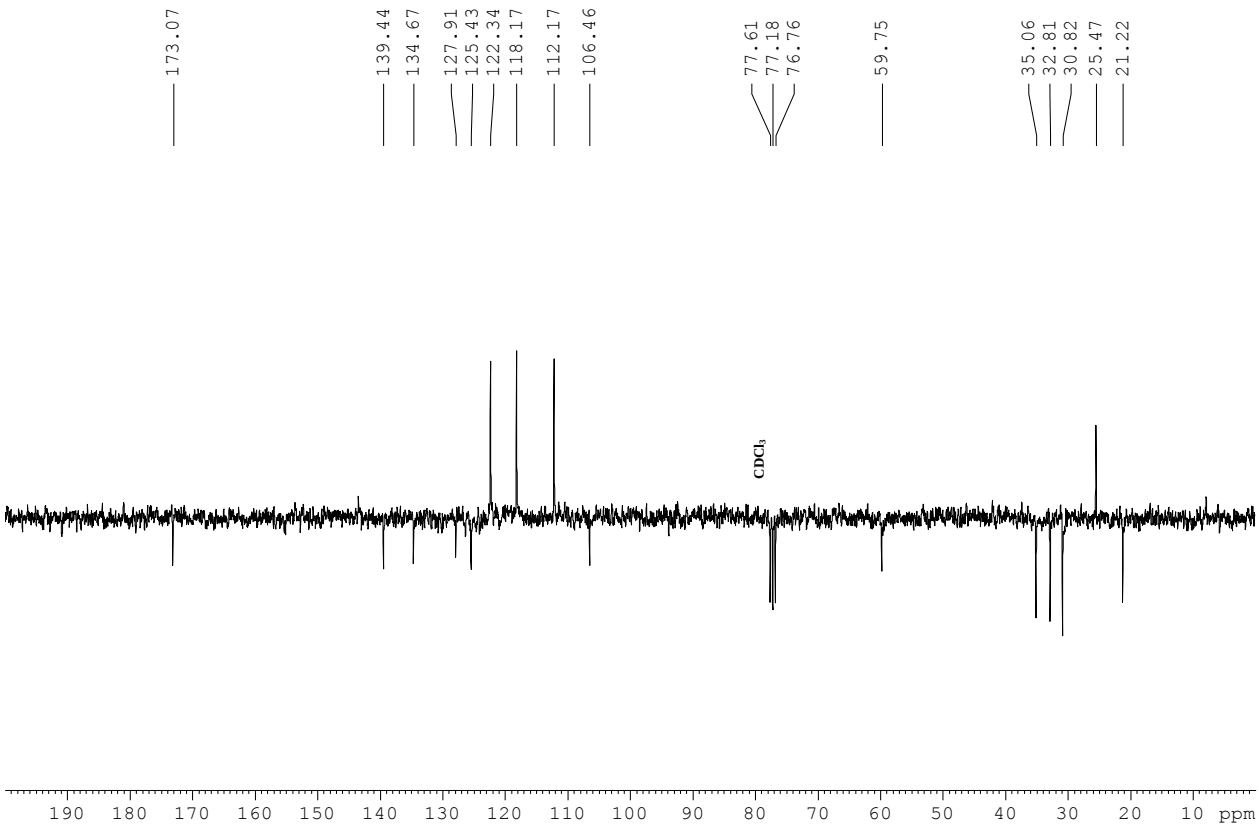
(6a): ^{13}C NMR (75 MHz, DMSO)



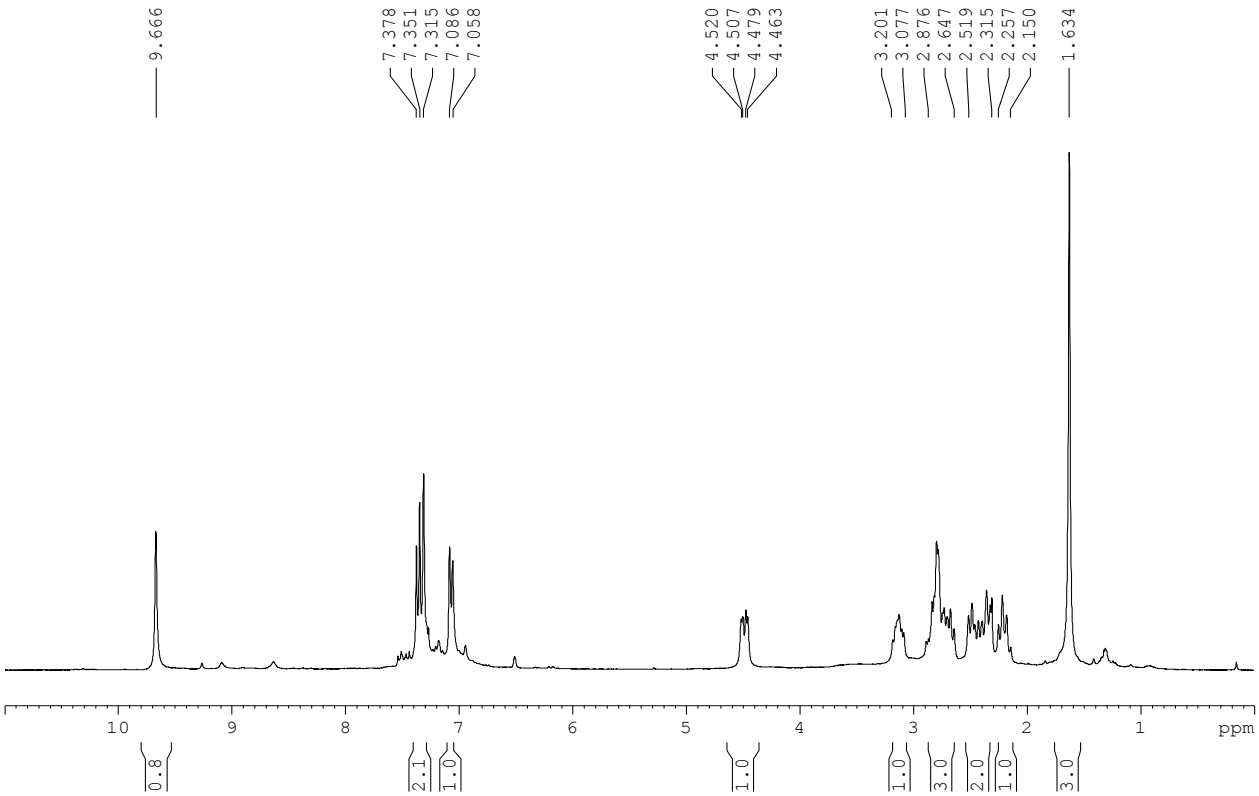
(6b): ^{1}H NMR (300 MHz, $CDCl_3$)



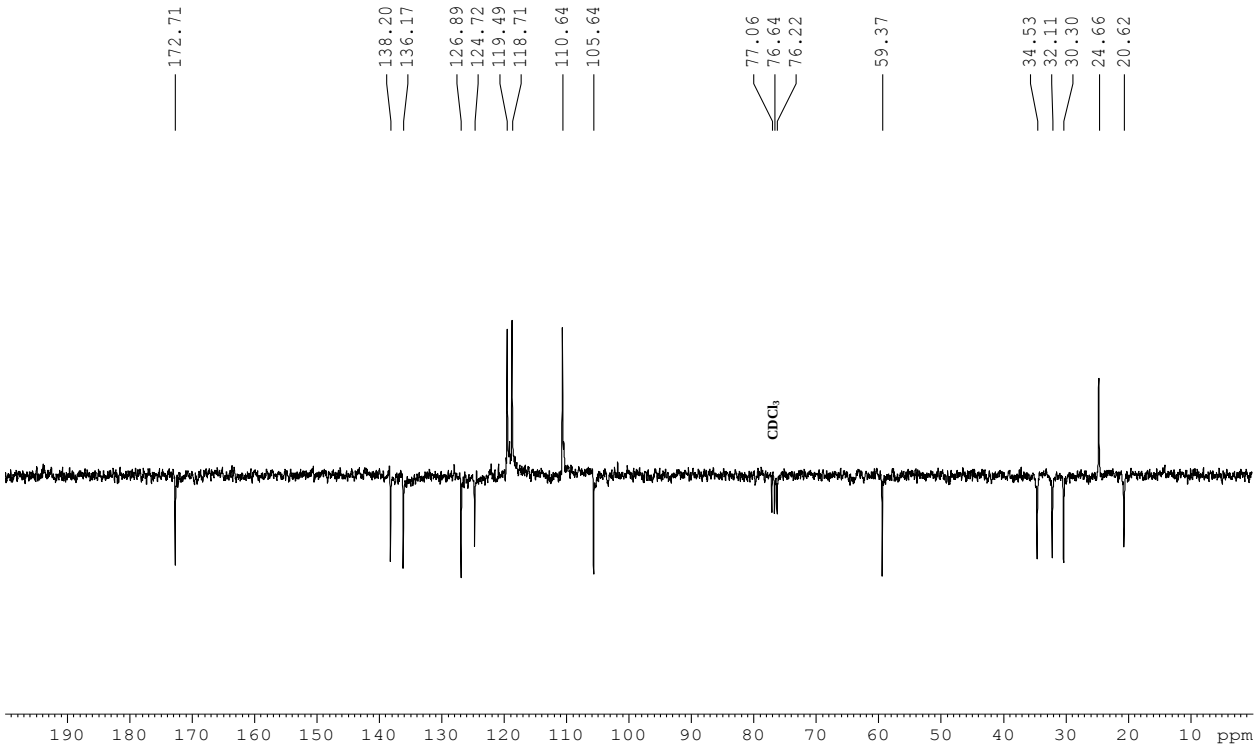
(6b): ^{13}C NMR (75 MHz, $CDCl_3$)



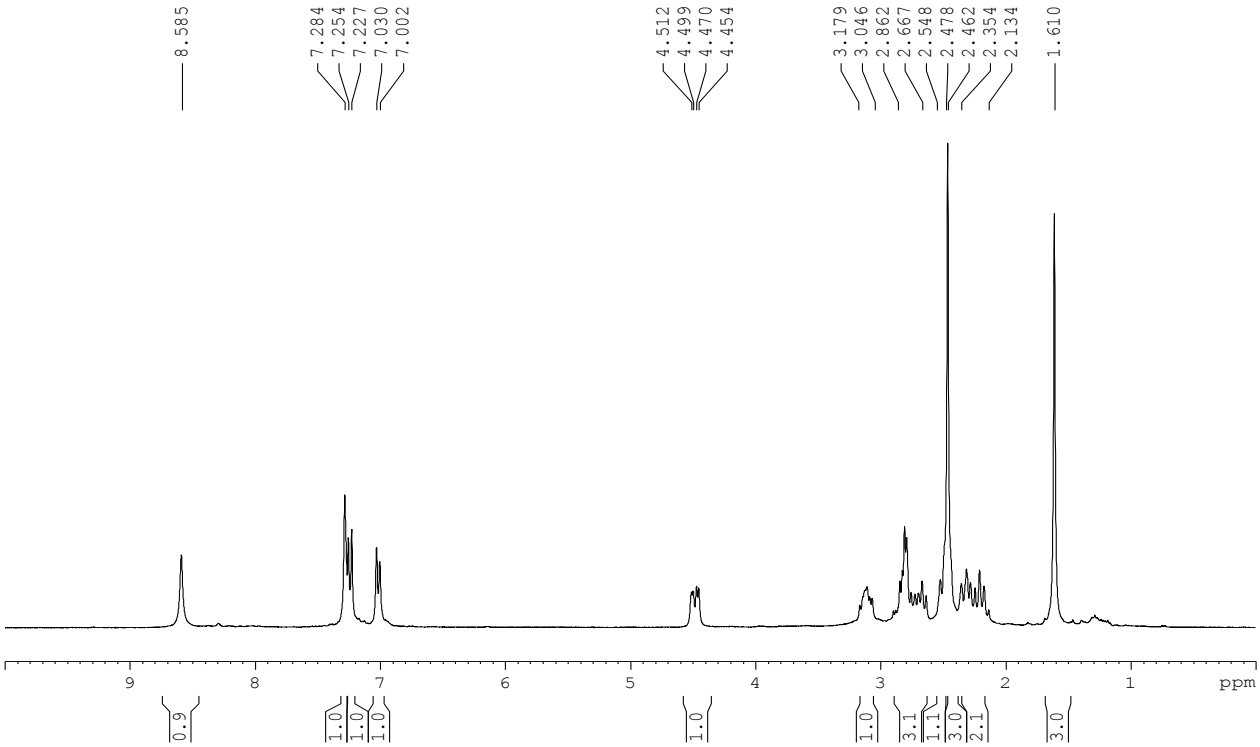
(6c): ^{1}H NMR (300 MHz, $CDCl_3$)



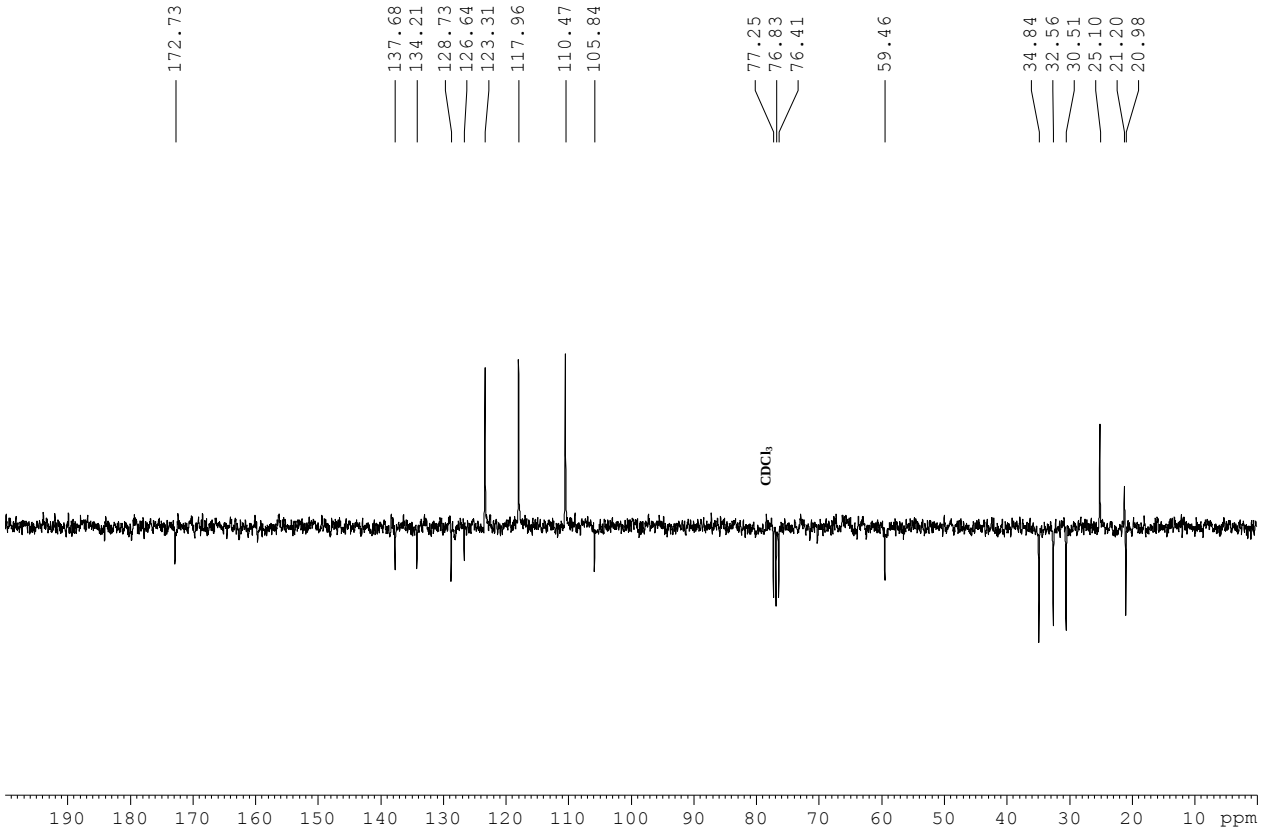
(6c): ^{13}C NMR (75 MHz, $CDCl_3$)



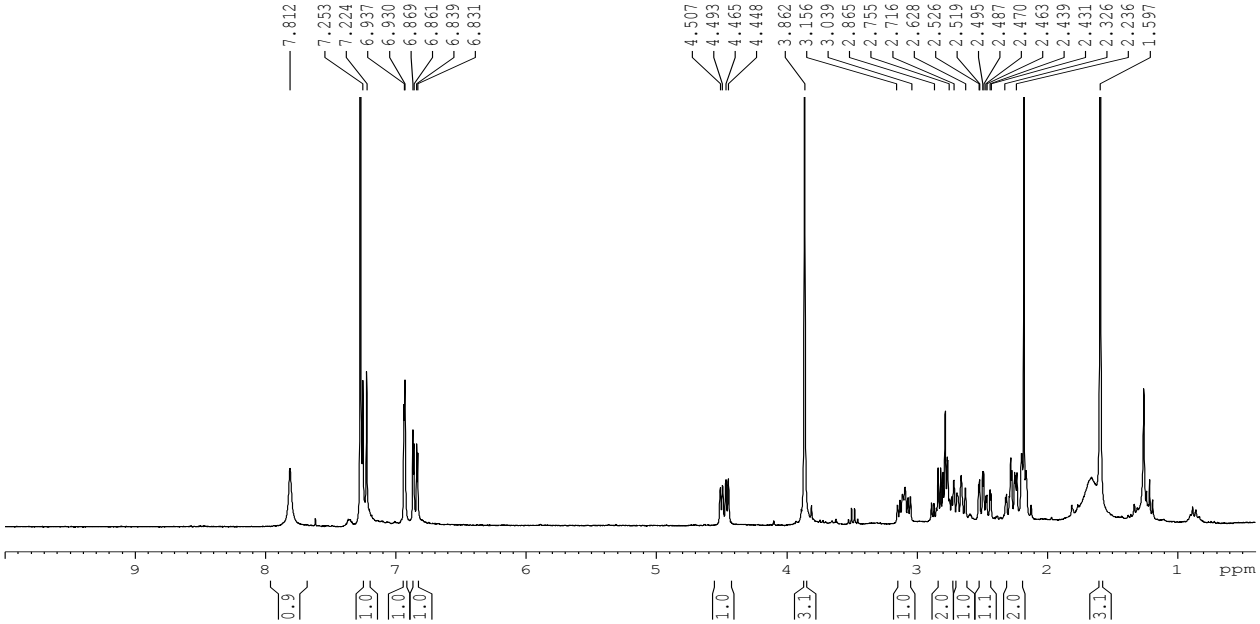
(6d): ^{1}H NMR (300 MHz, $CDCl_3$)



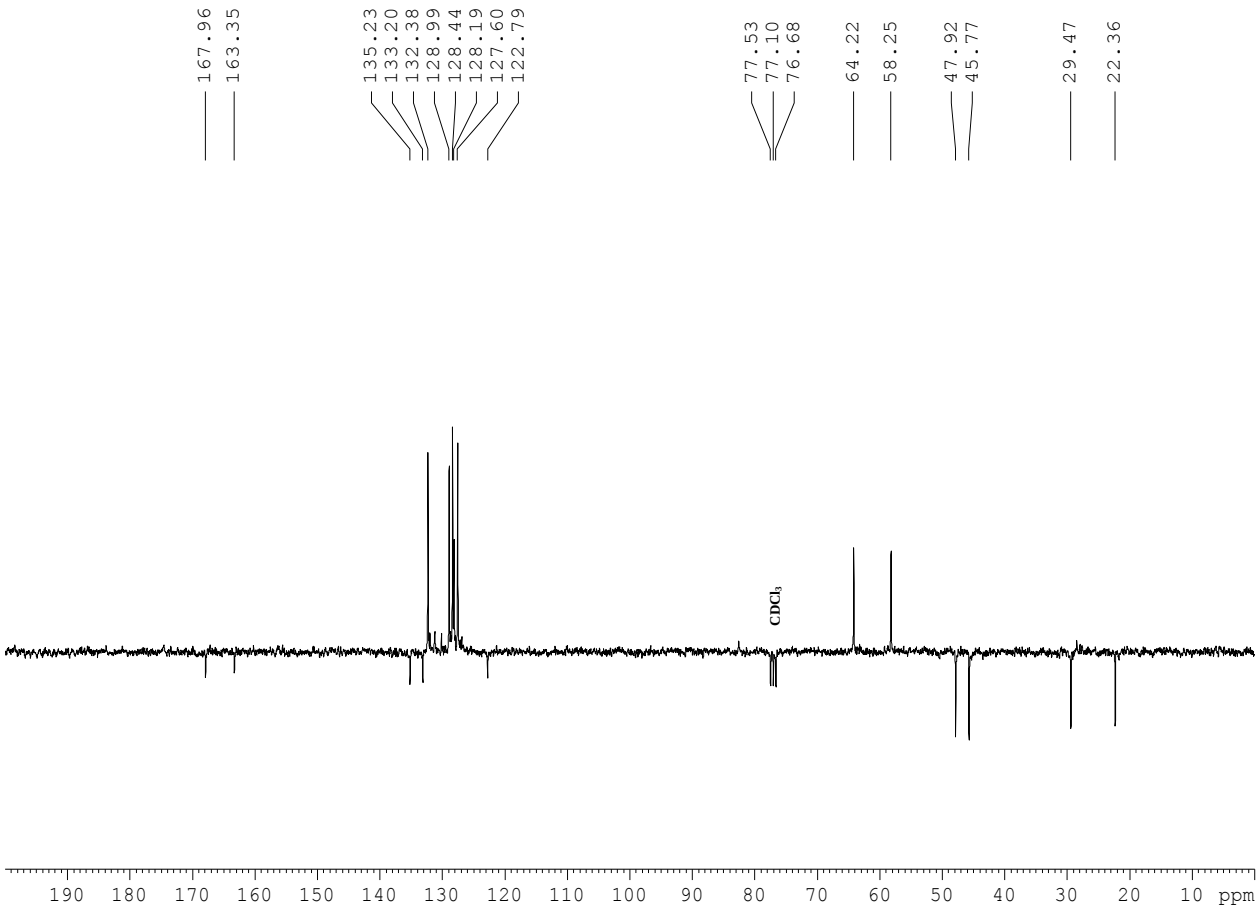
(6d): ^{13}C NMR (75 MHz, $CDCl_3$)



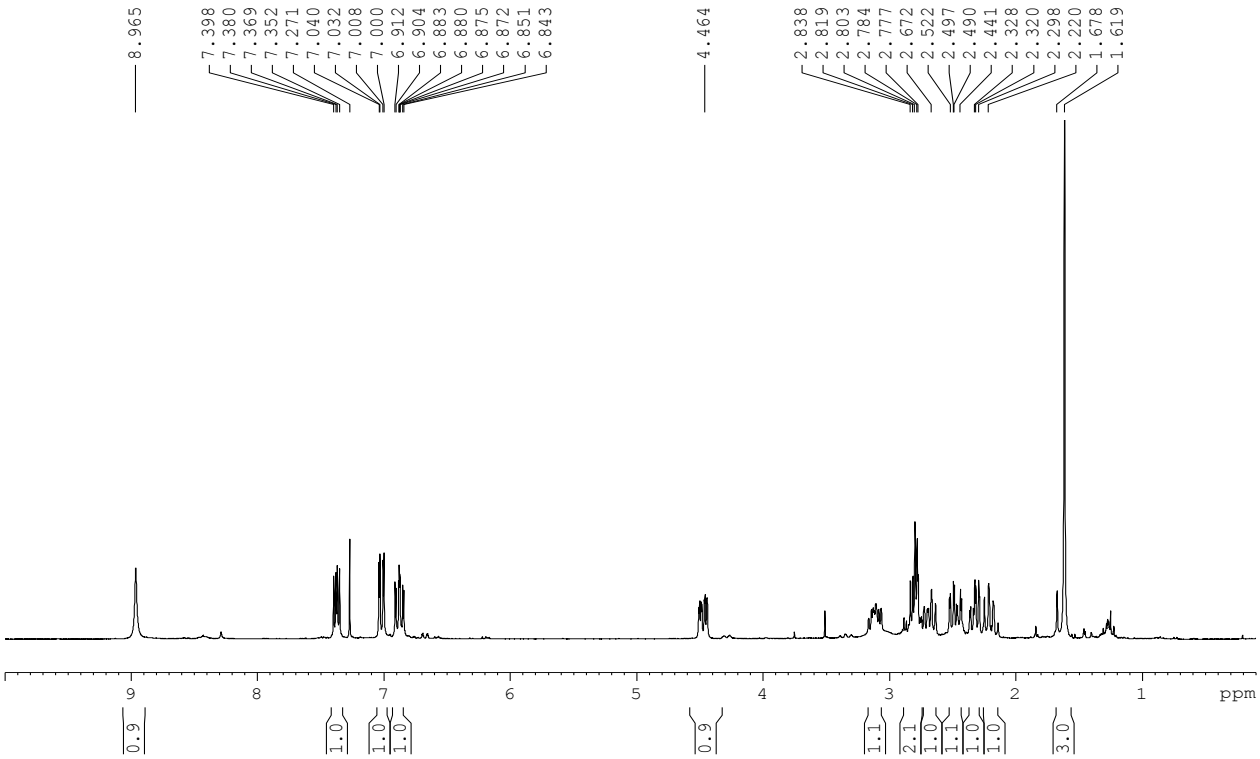
(6e): ^{1}H NMR (300 MHz, $CDCl_3$)



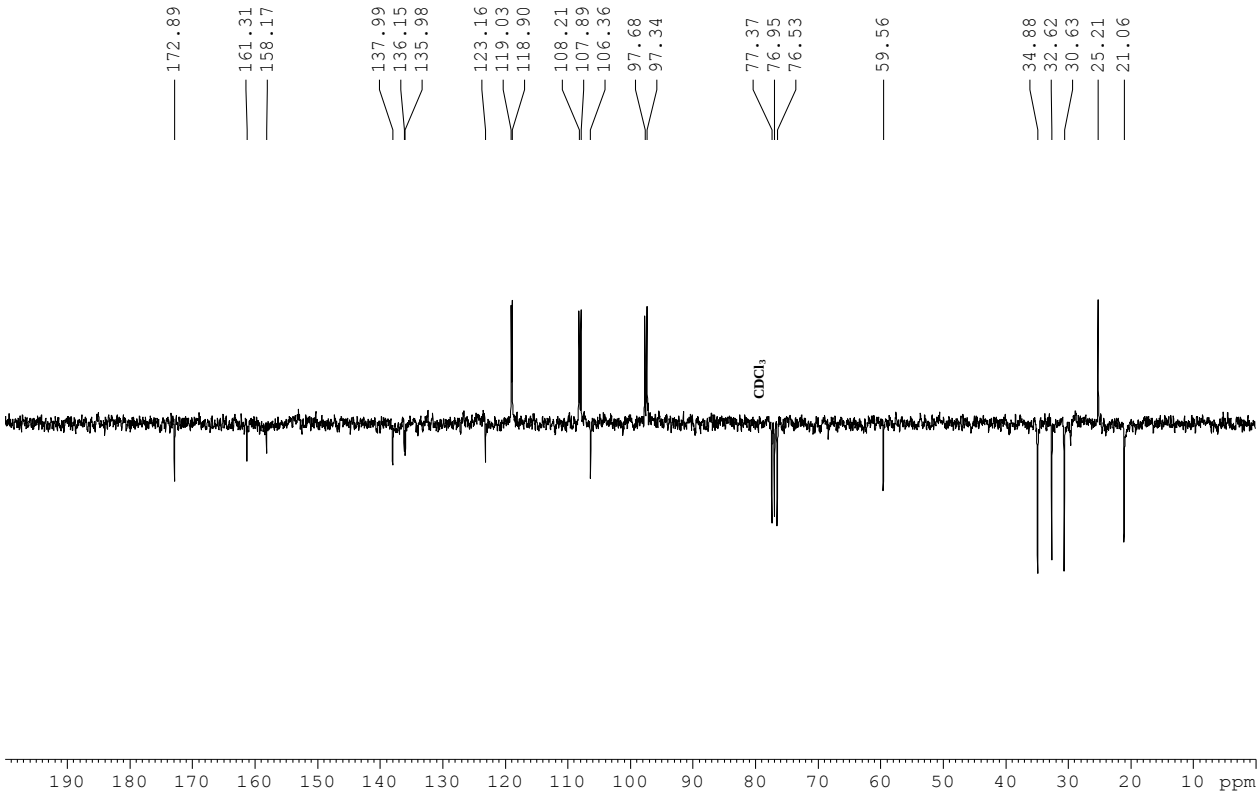
(6e): ^{13}C NMR (75 MHz, $CDCl_3$)



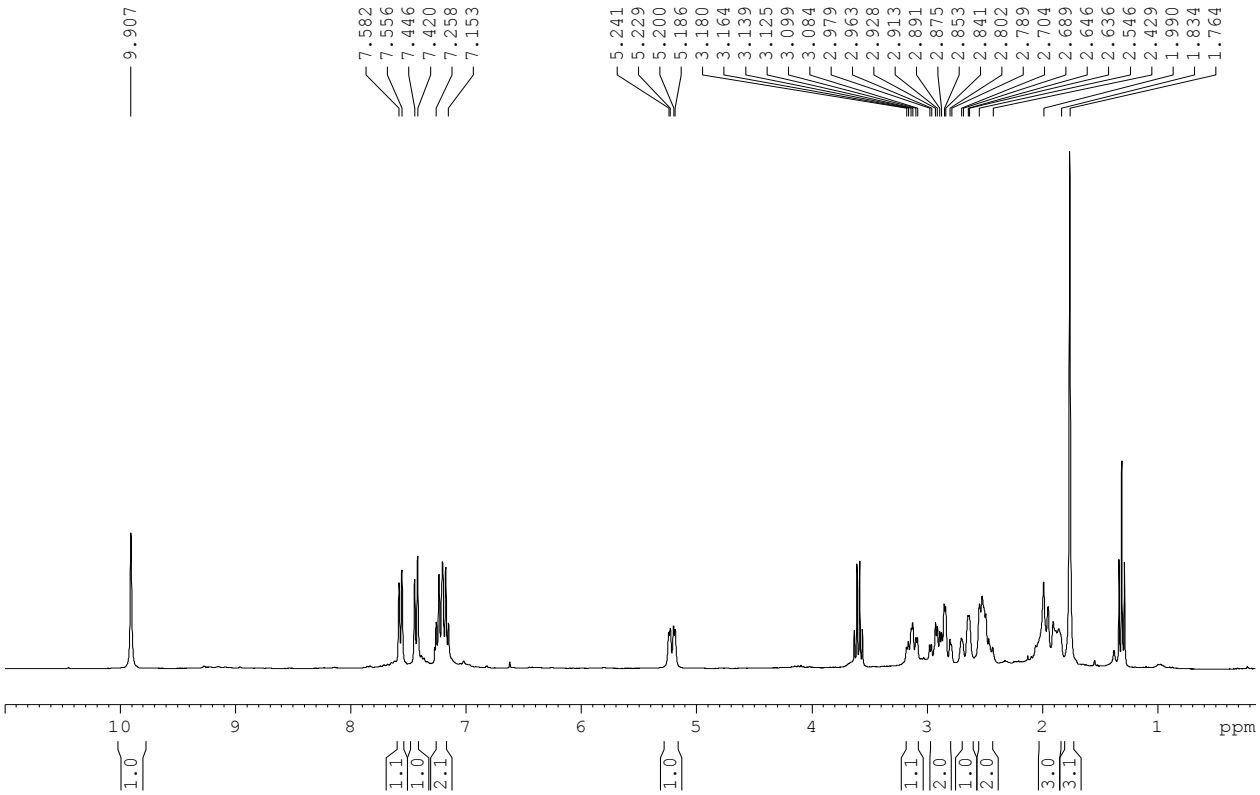
(6f): ^{1}H NMR (300 MHz, $CDCl_3$)



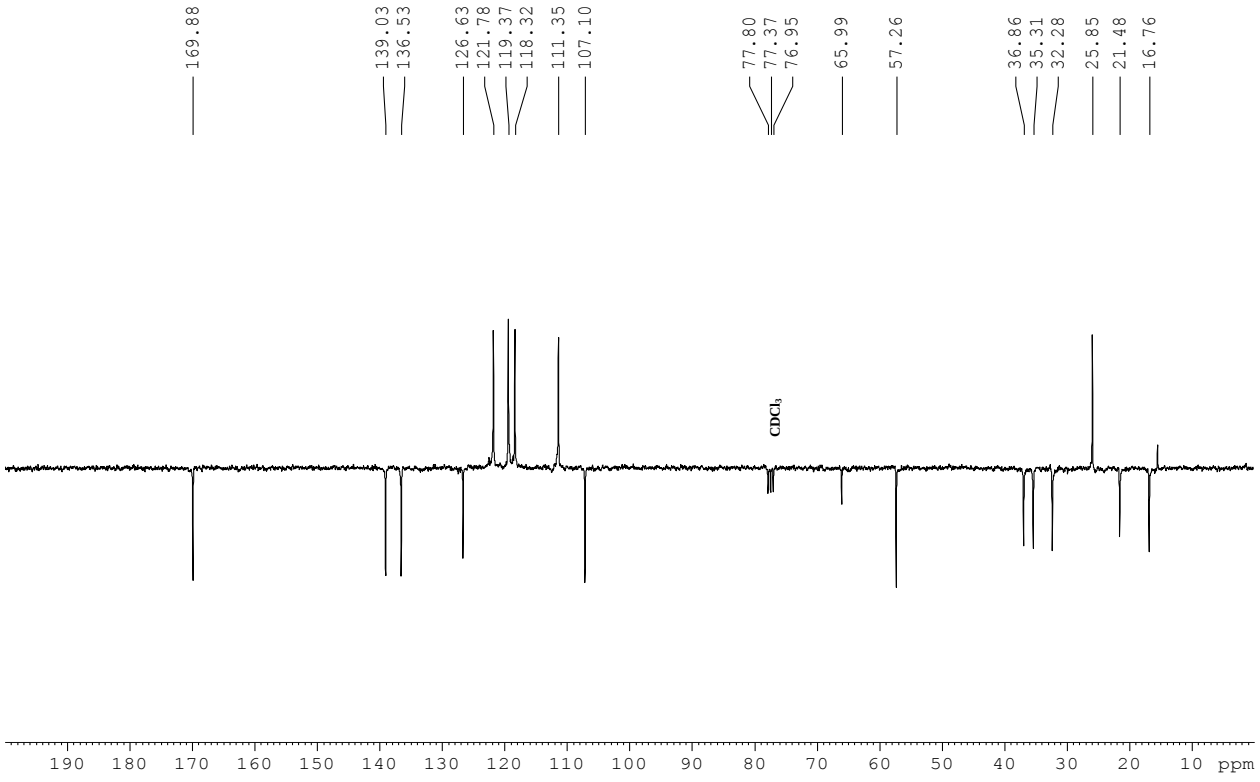
(6f): ^{13}C NMR (75 MHz, $CDCl_3$)



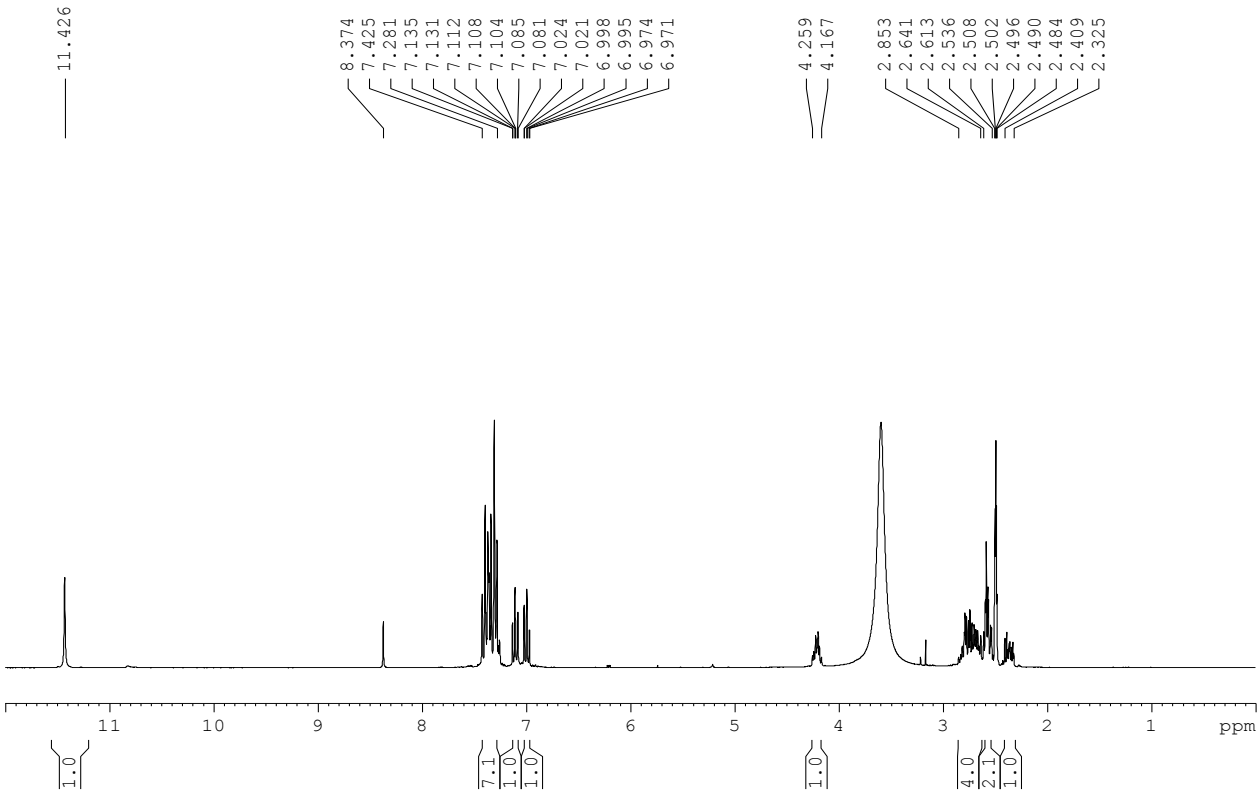
(7): ^{1}H NMR (300 MHz, $CDCl_3$)



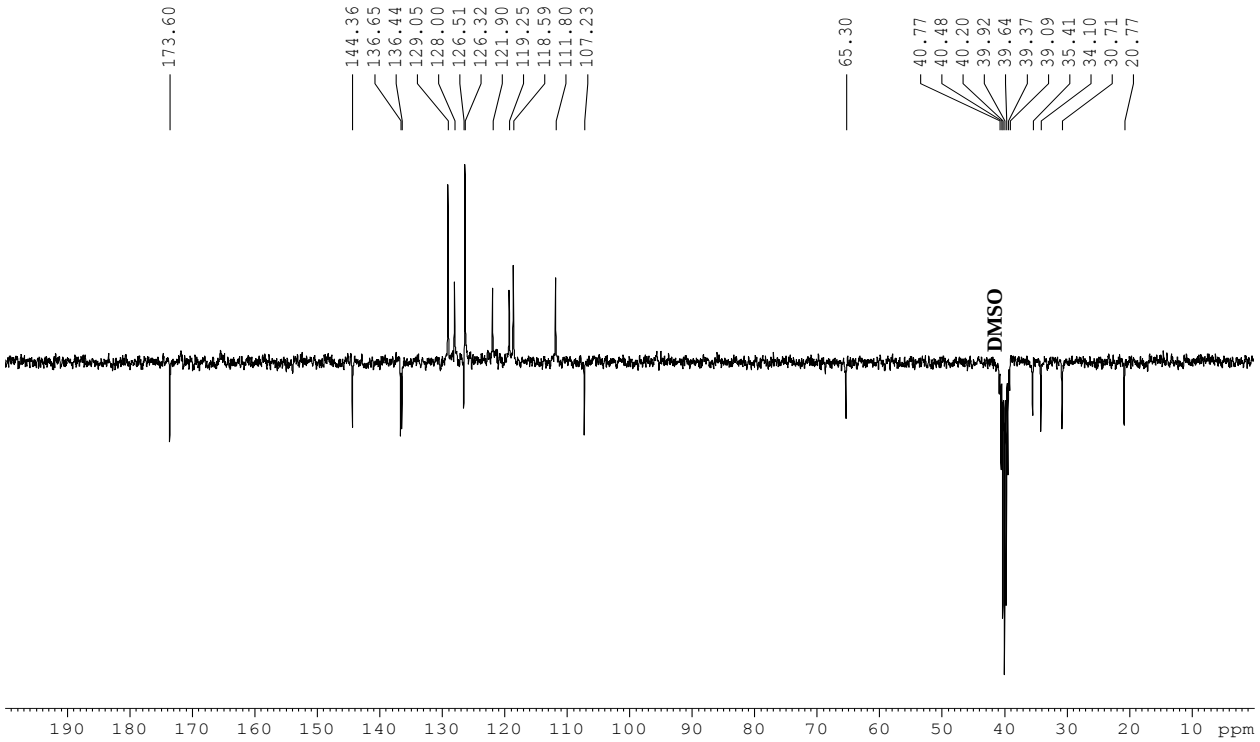
(7): ^{13}C NMR (75 MHz, $CDCl_3$)



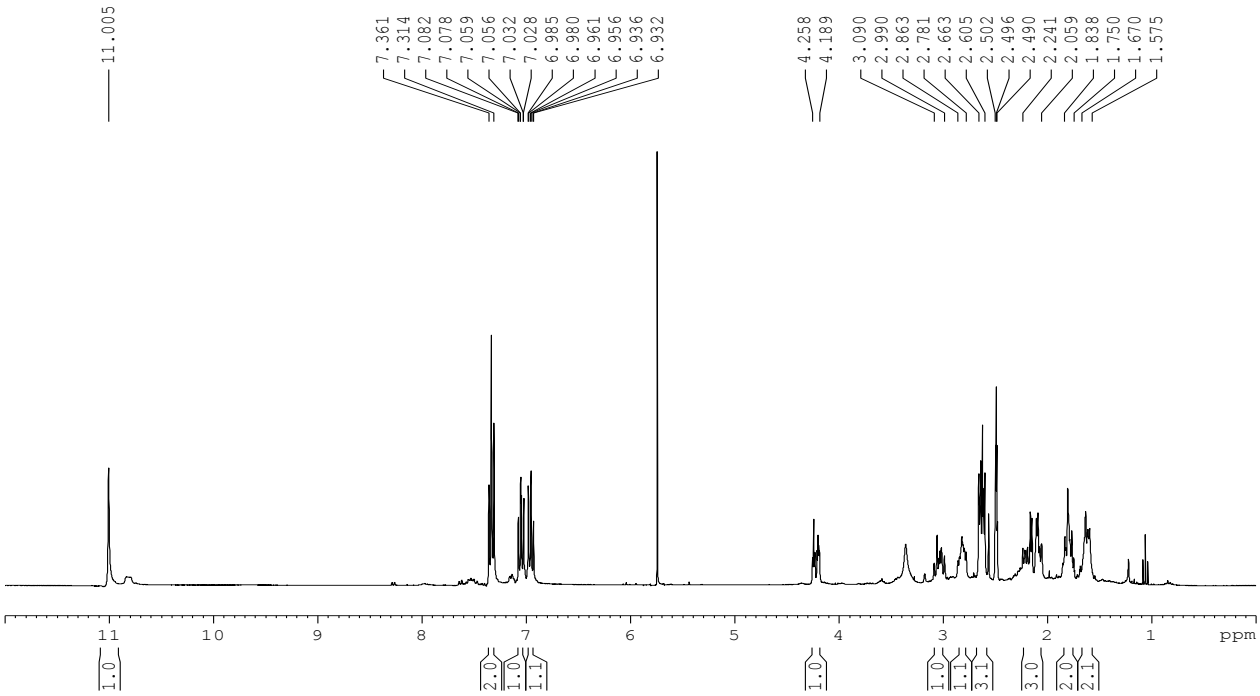
(8): ^{1}H NMR (300 MHz, DMSO)



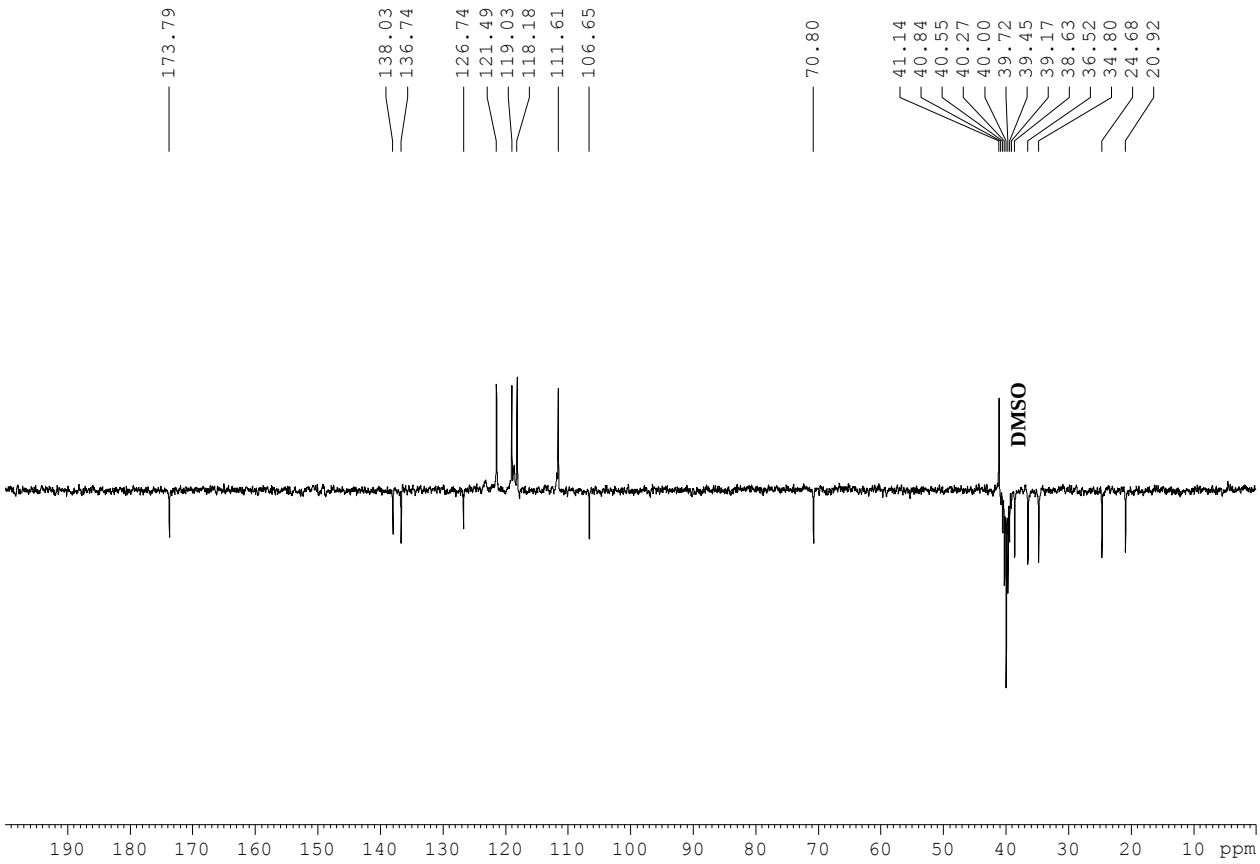
(8): ^{13}C NMR (75 MHz, DMSO)



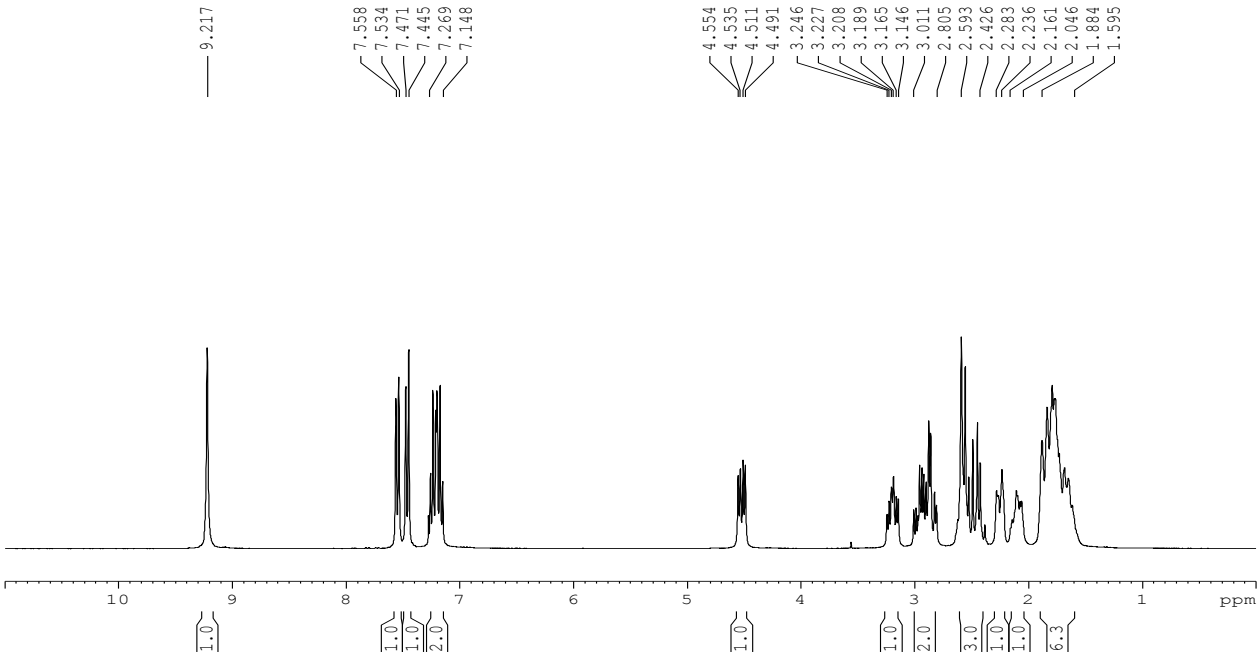
(9): ^{1}H NMR (300 MHz, DMSO)



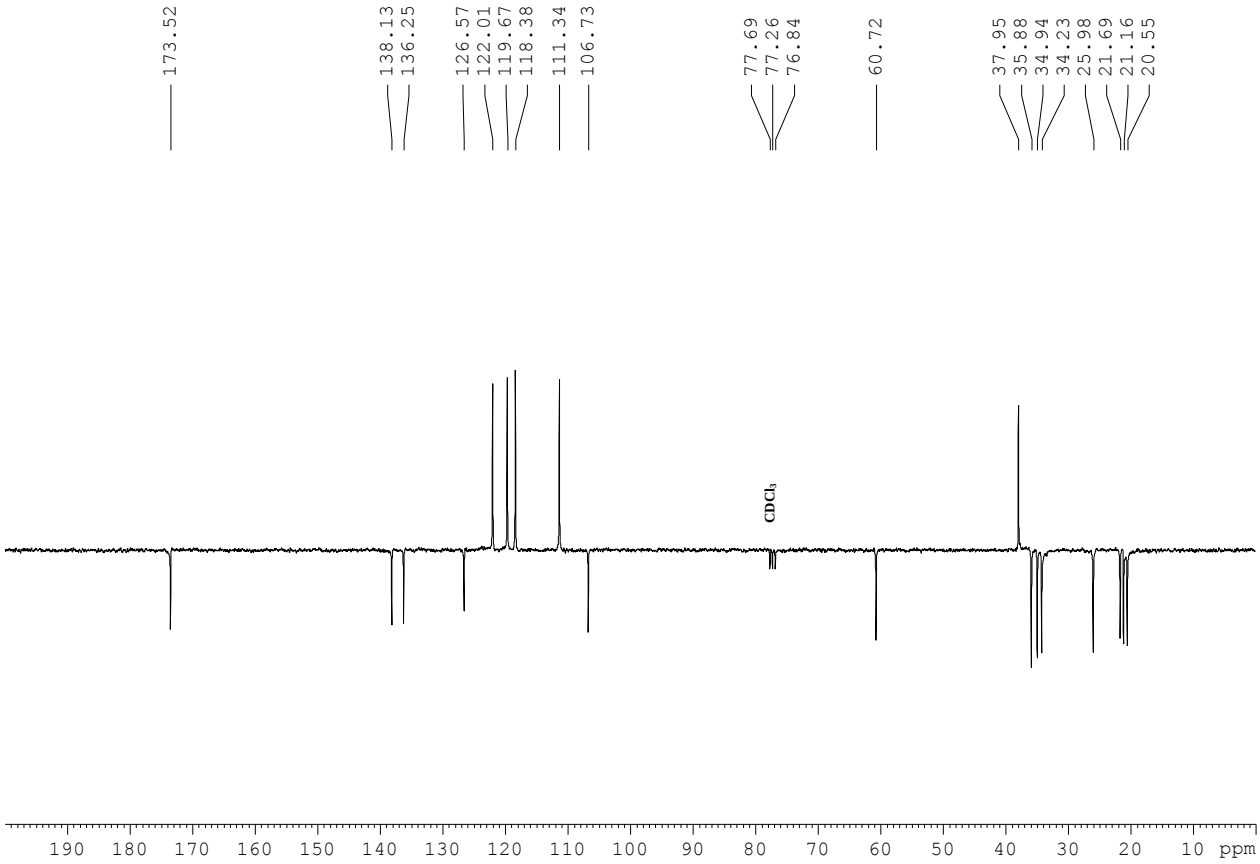
(9): ^{13}C NMR (75 MHz, DMSO)



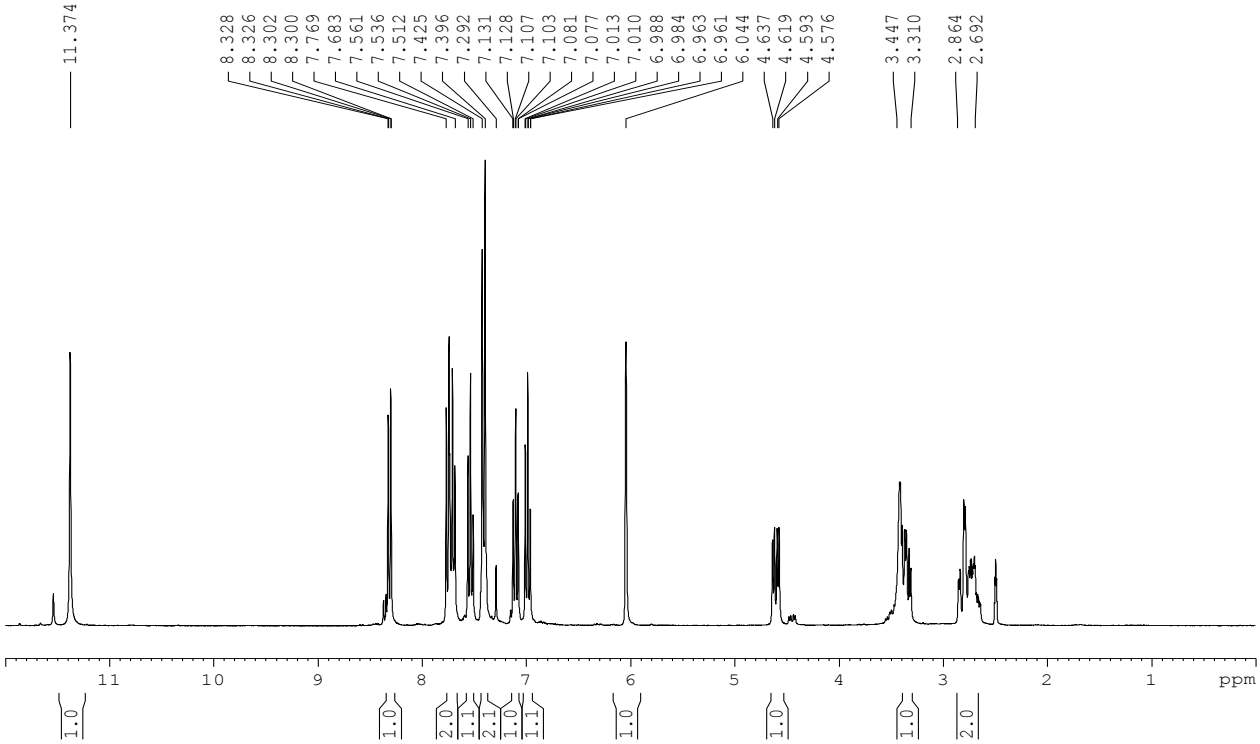
(10): ^{1}H NMR (300 MHz, $CDCl_3$)



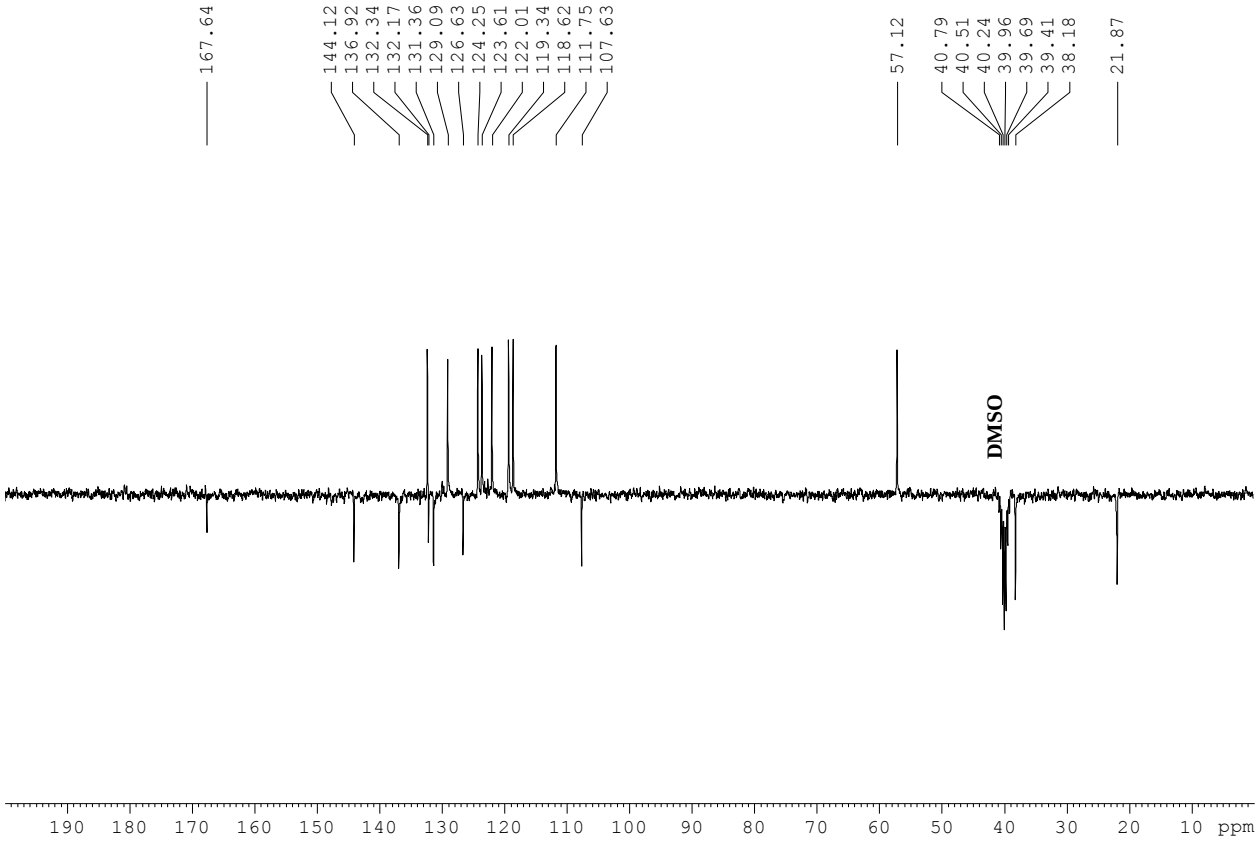
(10): ^{13}C NMR (75 MHz, $CDCl_3$)



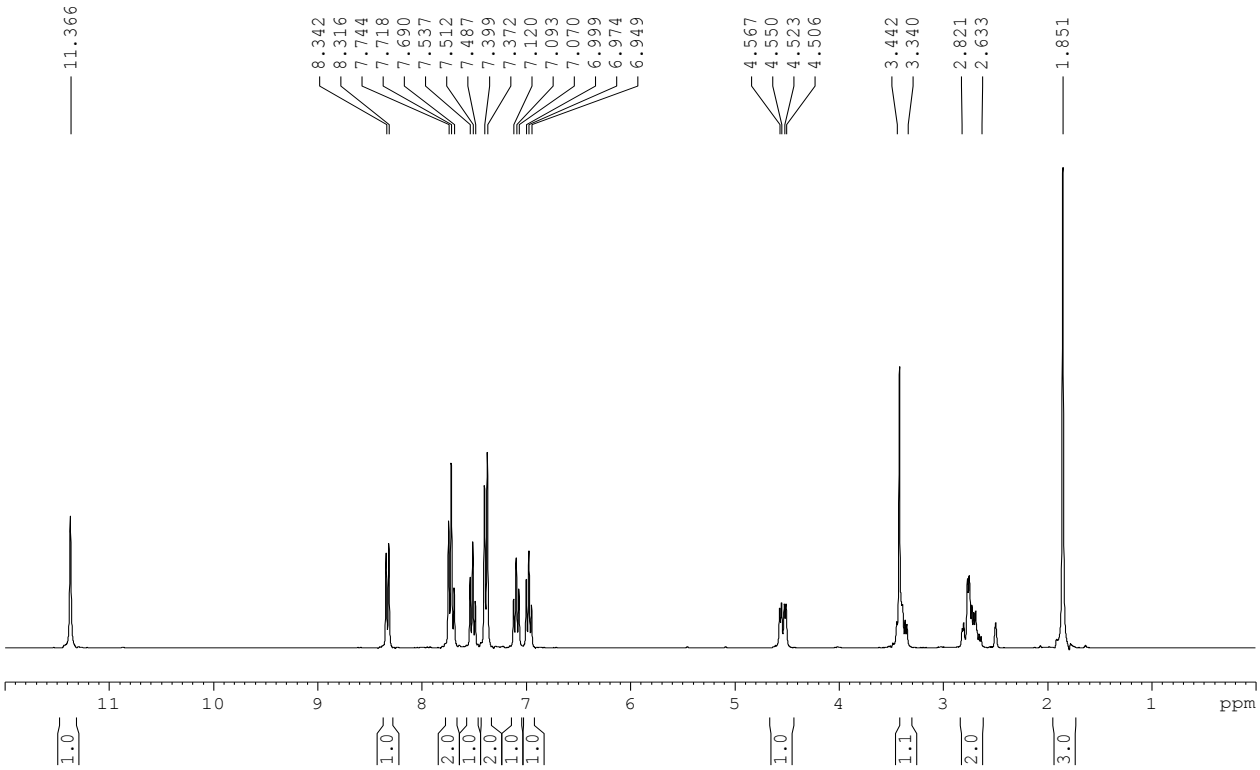
(11): ^{1}H NMR (300 MHz, DMSO)



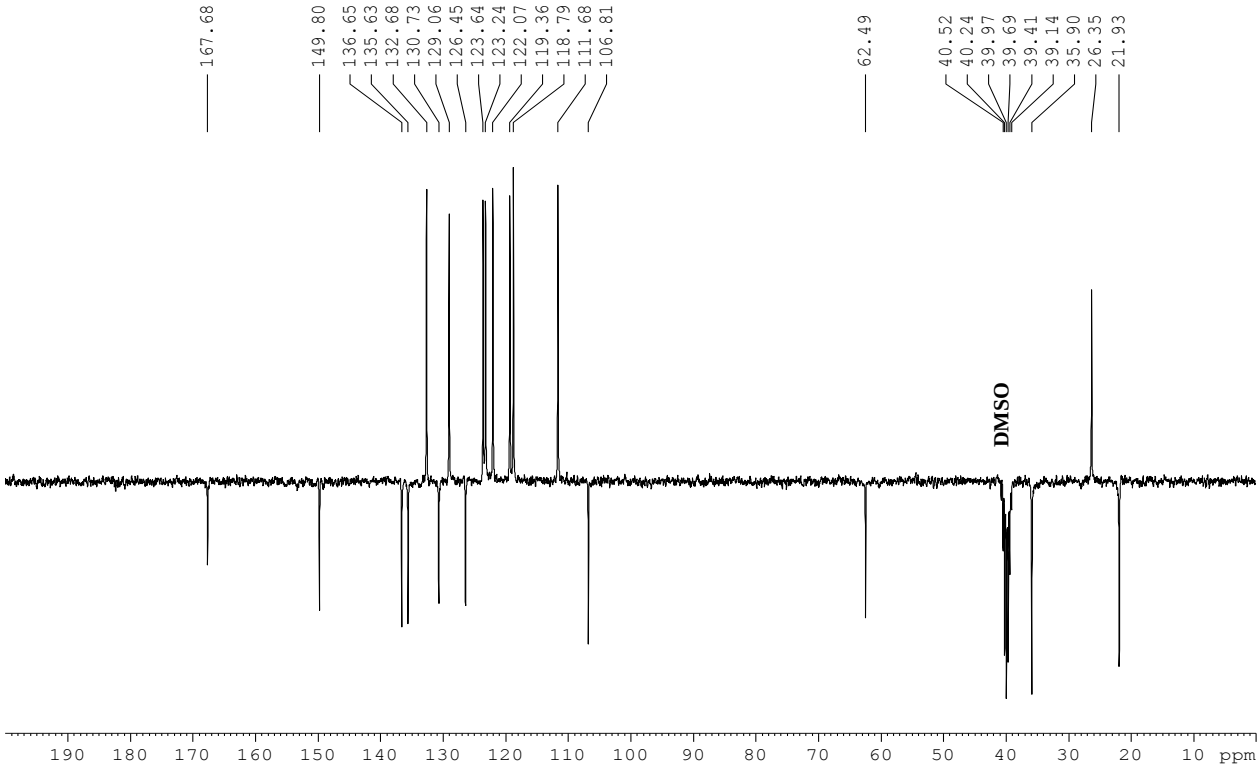
(11): ^{13}C NMR (75 MHz, DMSO)



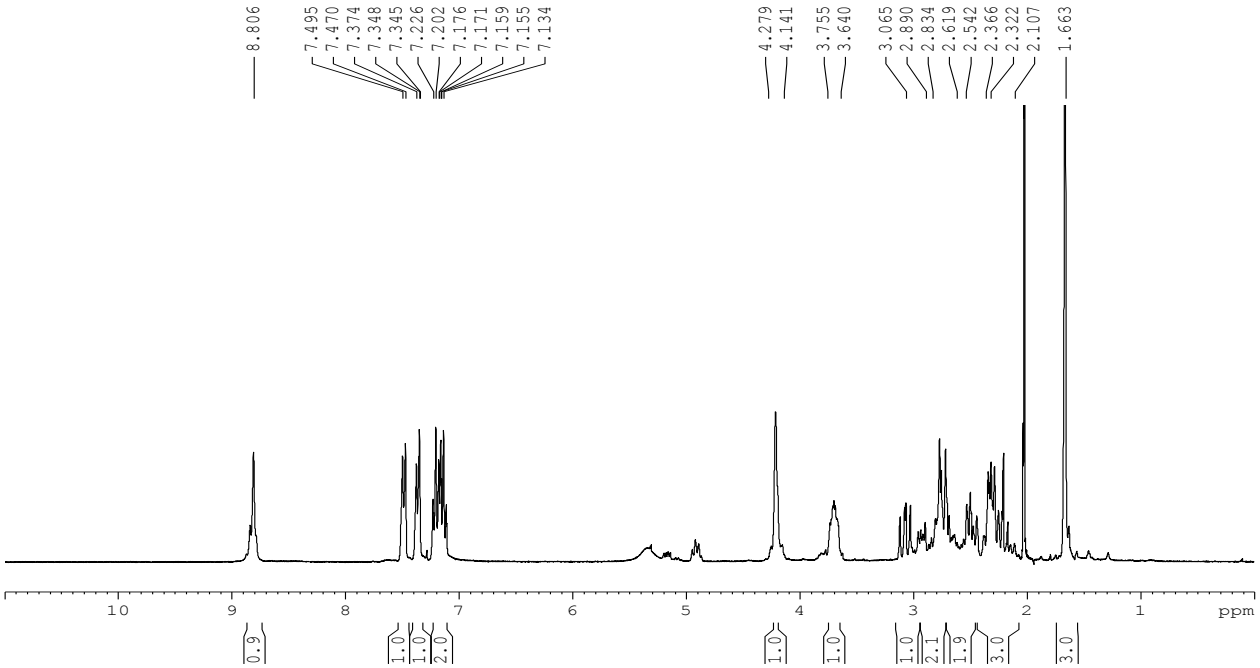
(12): ^{1}H NMR (300 MHz, DMSO)



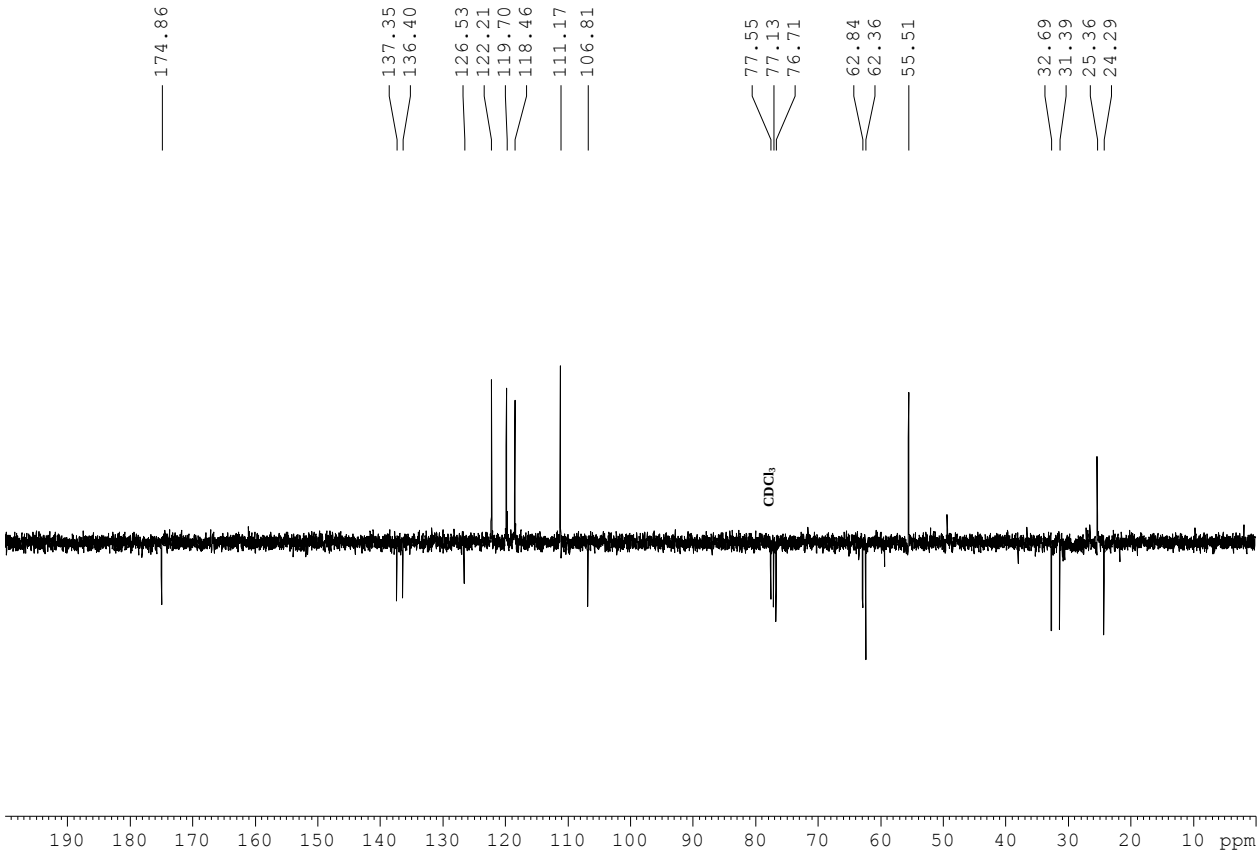
(12): ^{13}C NMR (75 MHz, DMSO)



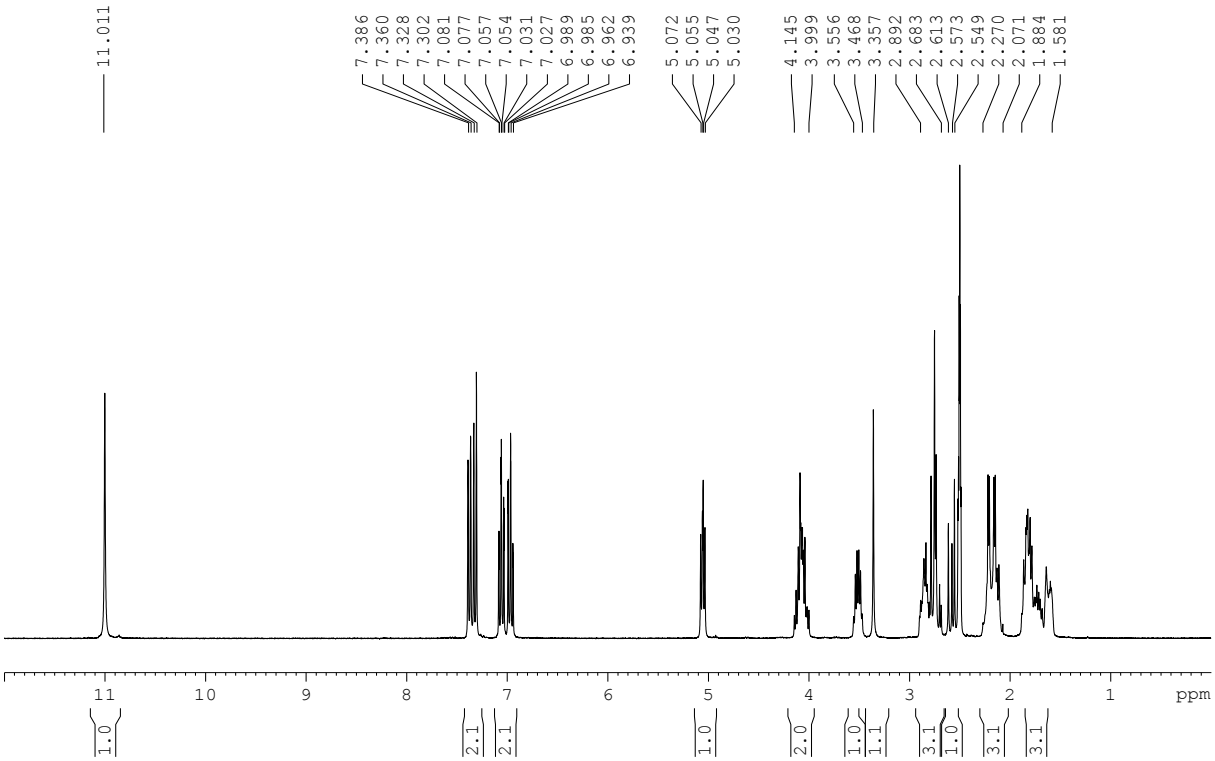
(13): ^{1}H NMR (300 MHz, $CDCl_3$)



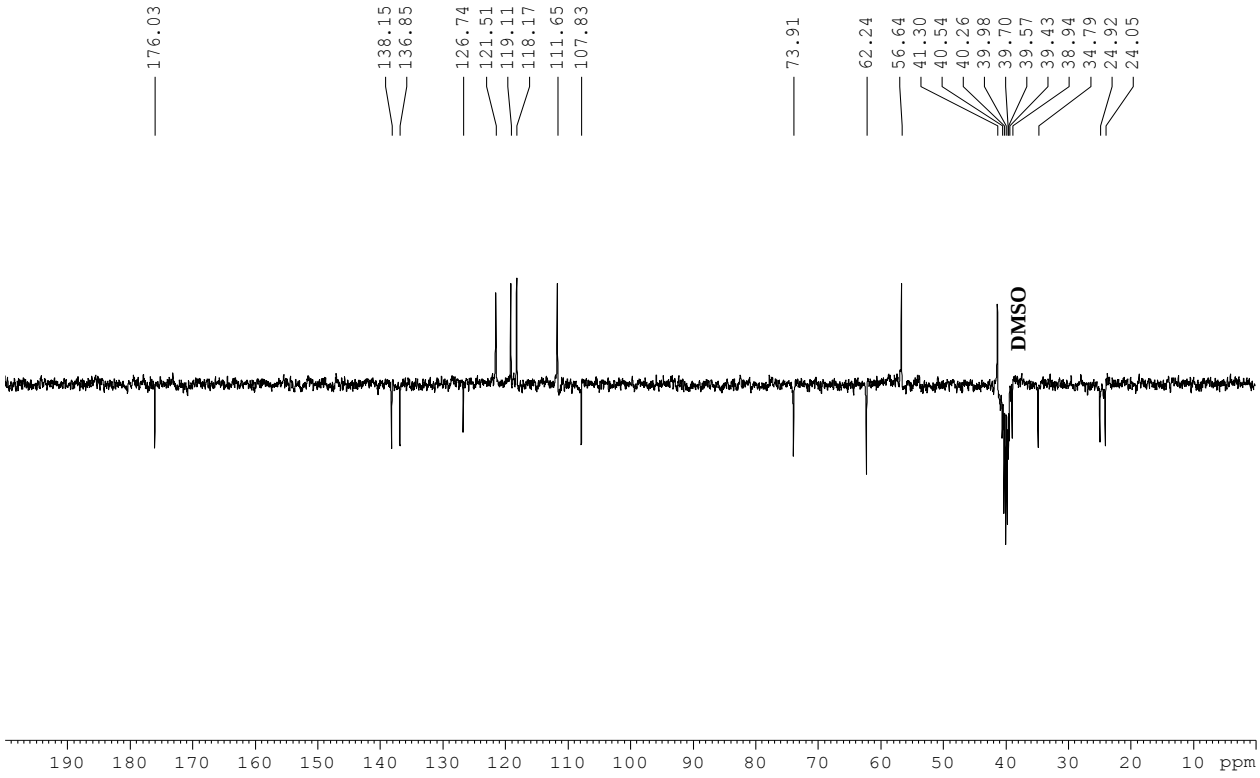
(13): ^{13}C NMR (75 MHz, $CDCl_3$)



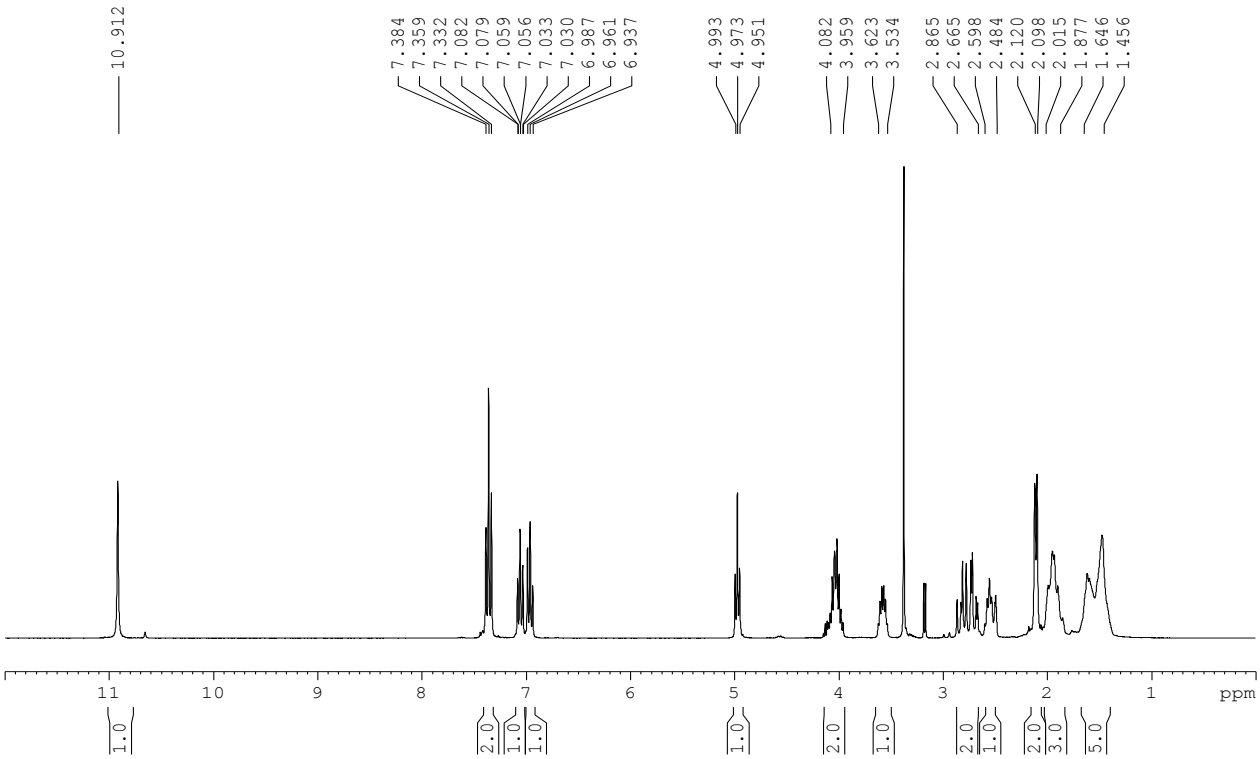
(14): ^{1}H NMR (300MHz, DMSO)



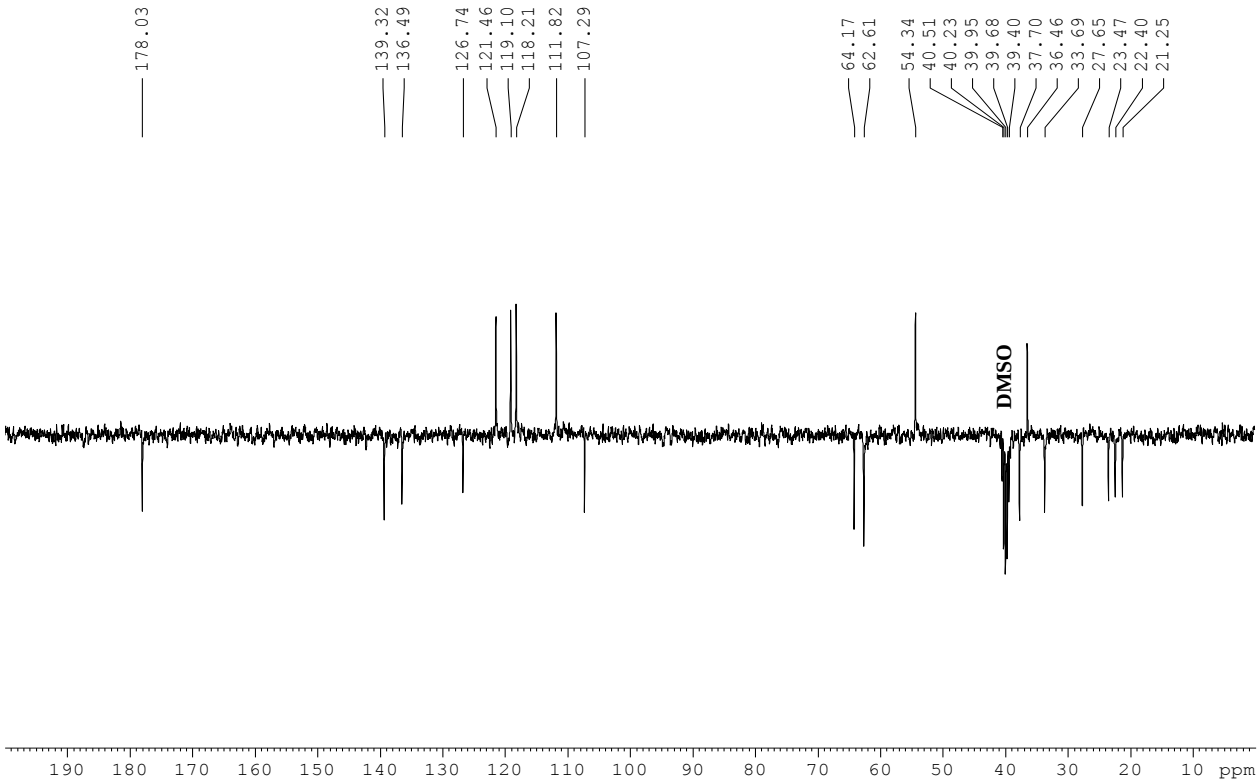
(14): ^{13}C NMR (75 MHz, DMSO)



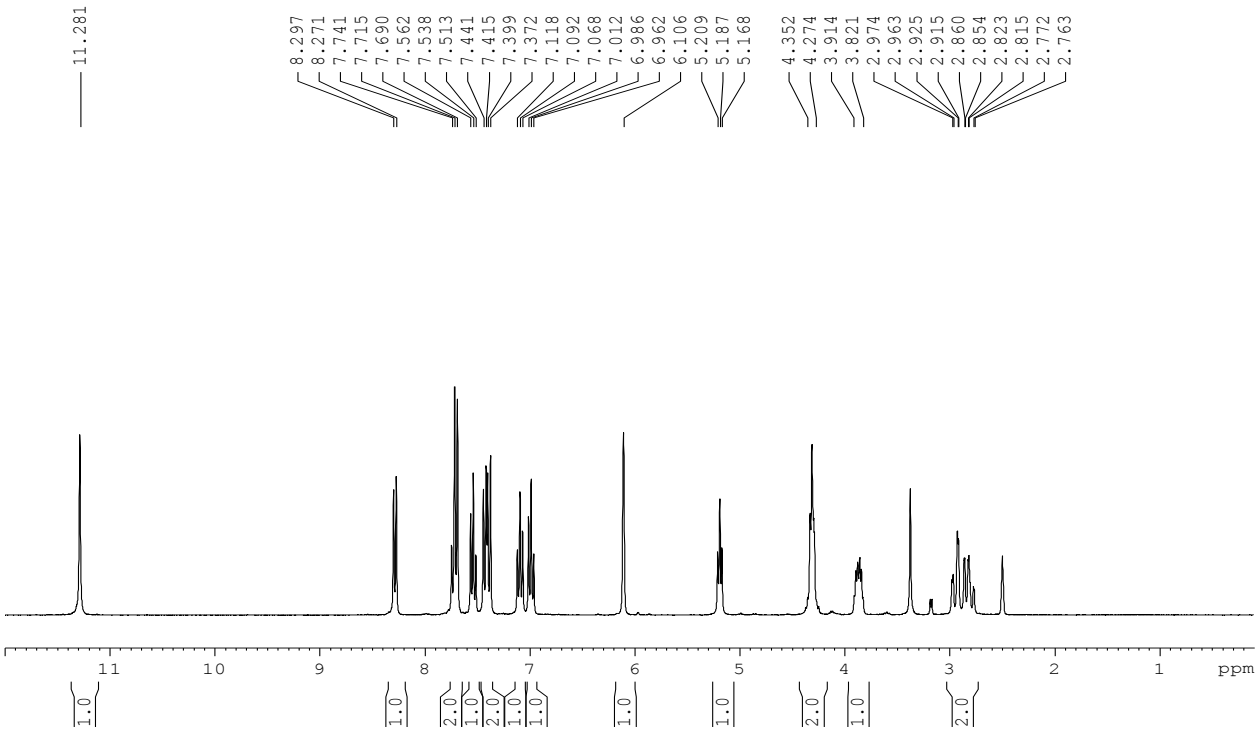
(15): ^{1}H NMR (300 MHz, DMSO)



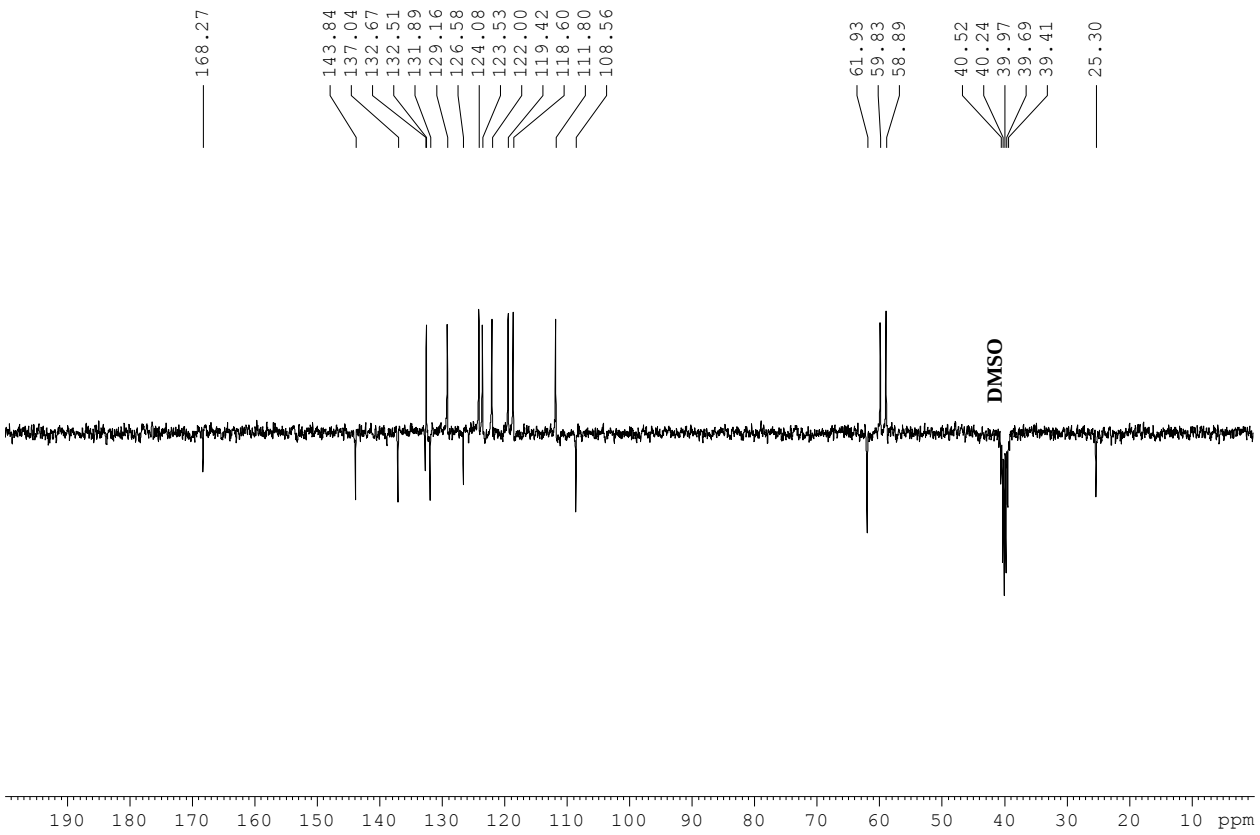
(15): ^{13}C NMR (75 MHz, DMSO)



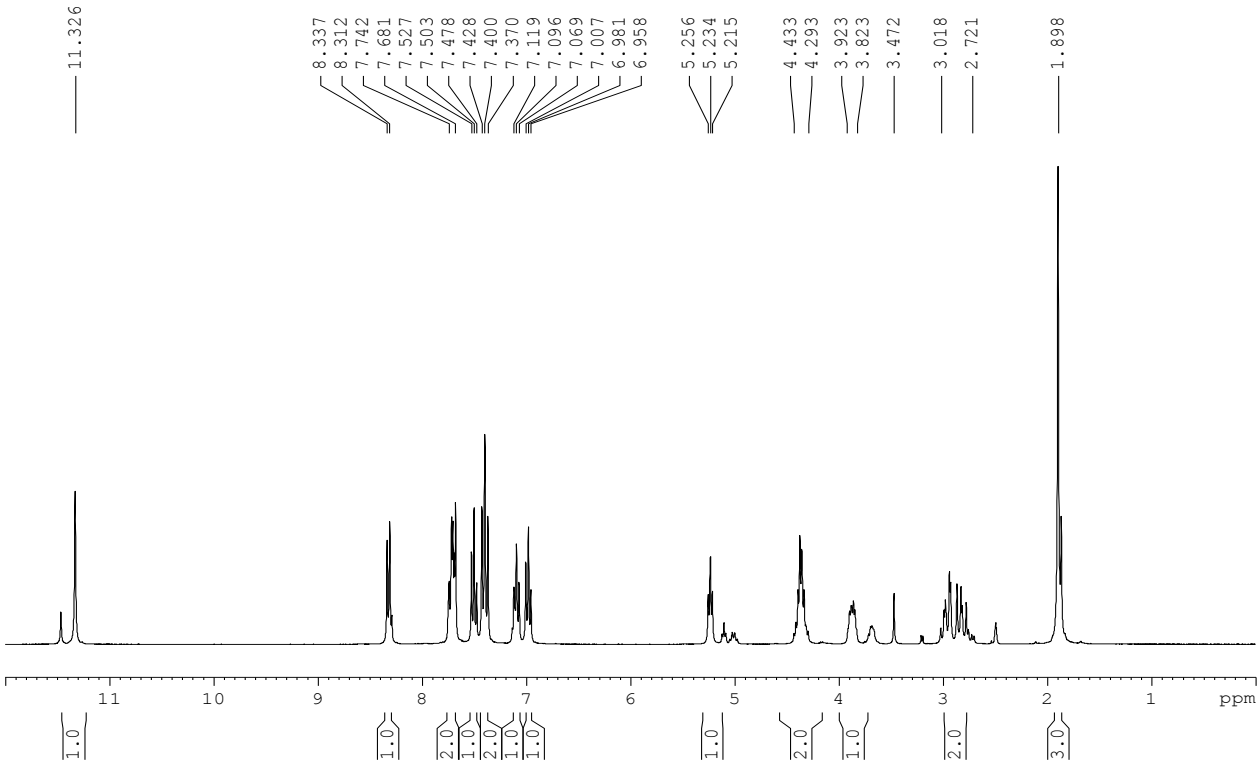
(16): ^{1}H NMR (300 MHz, DMSO)



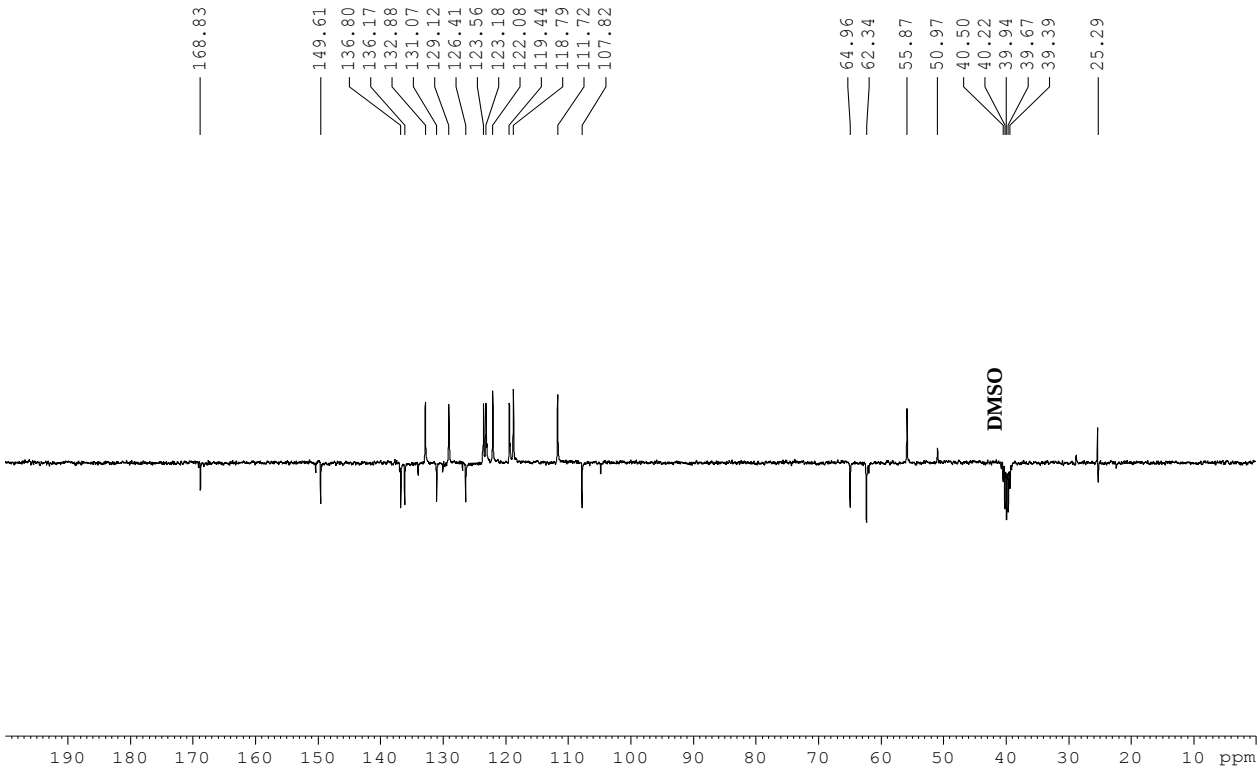
(16): ^{13}C NMR (75 MHz, DMSO)



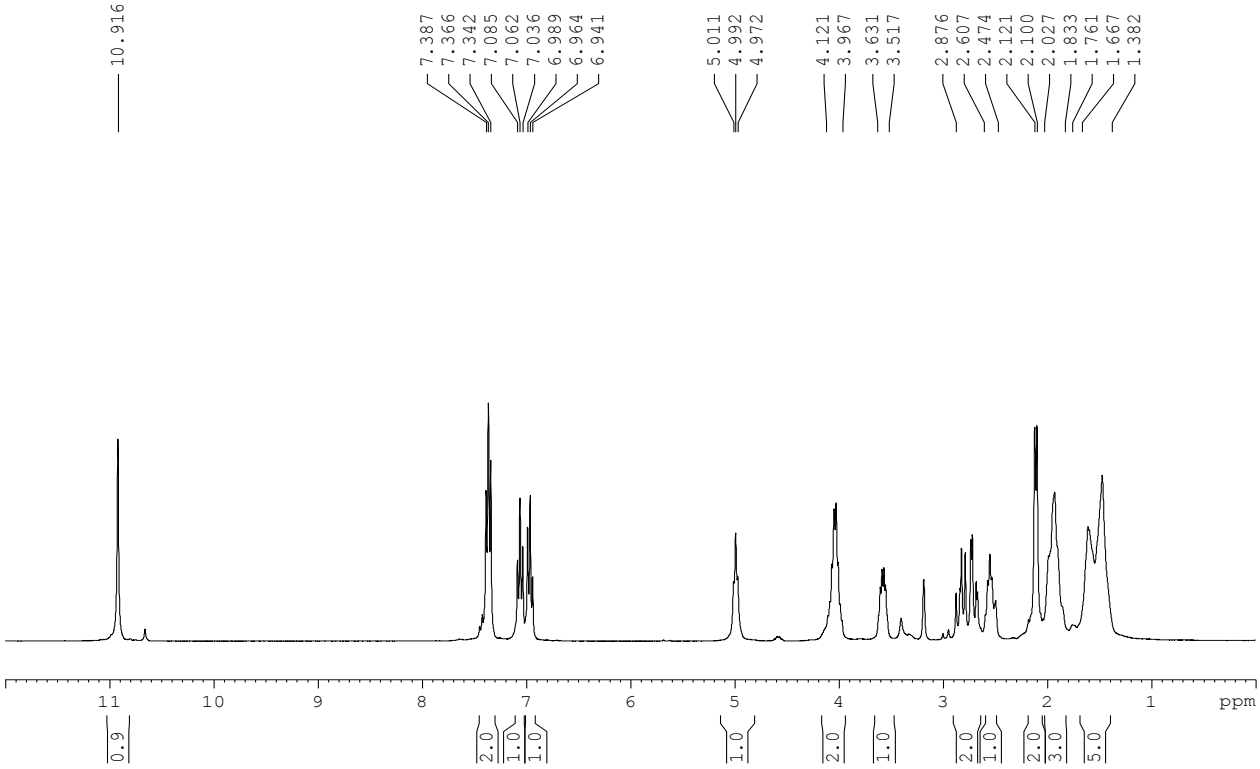
(17): ^{1}H NMR (300 MHz, DMSO)



(17): ^{13}C NMR (75 MHz, DMSO)



(18): ^{1}H NMR (300 MHz, DMSO)



(18): ^{13}C NMR (75 MHz, DMSO)