Supporting Information for

2,14-Dithiacalix[4]arene and its homooxa analogues: Synthesis and dynamic NMR study of conformational behaviour

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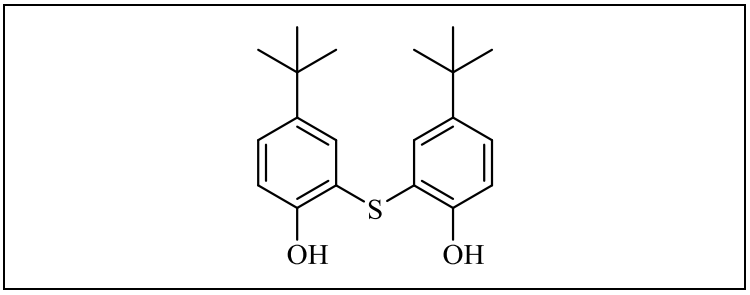
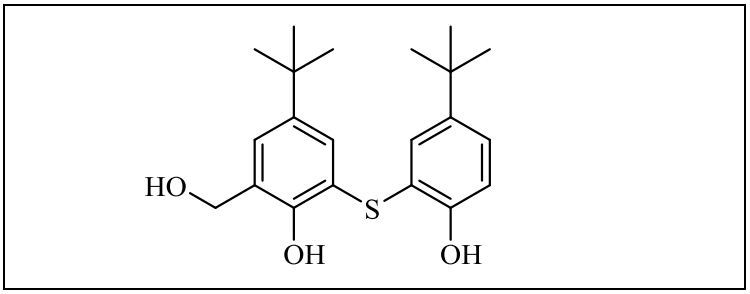
List of synthesized compounds

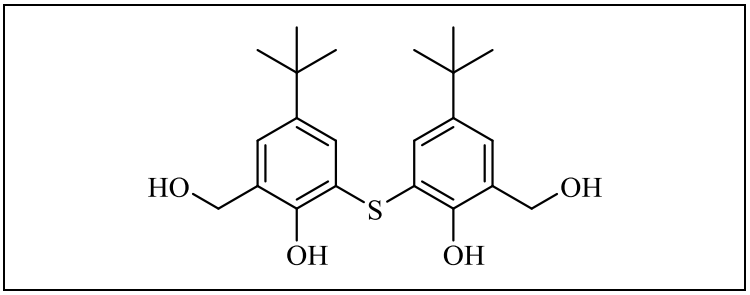
2: 4,4'-di-*tert*-butyl-2,2'-sulfandiyl diphenol



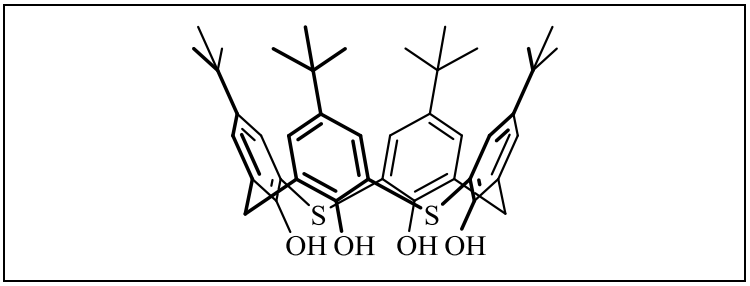
3: 4-*tert*-butyl-2-(5-*tert*-butyl-2-hydroxyphenylsulfanyl)-6-(hydroxymethyl) phenol



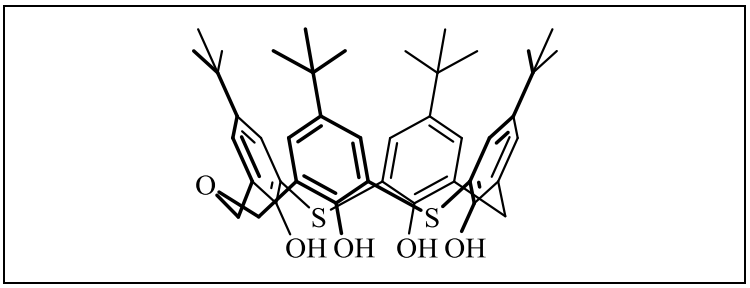
4: 4,4'-di-*tert*-butyl-2,2'-bis(hydroxymethyl)-6,6'-sulfandiyl diphenol



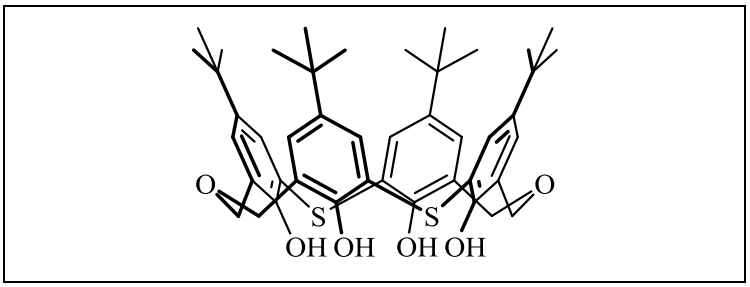
5: 5,11,17,23-tetra-*tert*-butyl-25,26,27,28-tetrahydroxy-2,14-dithiacalix[4]arene



6: 5,13,19,25-tetra-*tert*-butyl-27,28,29,30-tetrahydroxy-8,9-dihomo-9-oxa-2,16-dithiacalix[4]arene



7: 5,13,19,27-tetra-*tert*-butyl-29,30,31,32-tetrahydroxy-8,9,22,23-tetrahomo-9,23-dioxa-2,16-dithiacalix[4]arene



Experimental procedures

General Experimental Procedures

All chemicals were purchased from commercial sources and used without further purification. Solvents were dried and distilled using conventional methods. NMR spectra were performed on Varian Gemini 300 (^{1}H: 300 MHz, ^{13}C: 75 MHz) and on Bruker Advance III^{TM} DRX 500 (^{1}H: 500 MHz, ^{13}C: 125 MHz) spectrometers. Deuterated solvents used are indicated in each case. Chemical shifts (δ) are expressed in ppm and are referred to the residual peak of the solvent or TMS as an internal standard; coupling constants (J) are in Hz. The mass analyses were performed using ESI technique on Q–TOF (Micromass) spectrometer. Elemental analyses were done on Perkin–Elmer 240 or Mitsubishi TOX–100 instruments. The IR spectra were measured on an FT–IR Nicolet 740 or Bruker IFS66 spectrometers equipped with a heatable Golden Gate Diamante ATR–Unit (SPECAC) in KBr. Melting points were measured on Heiztisch-Mikroskop Polytherm (Wagner & Munz). The courses of the reactions were monitored by TLC using TLC aluminum sheets with Silica gel 60 F_{254} (Merck). The column chromatography was performed using Silica gel 60 (Merck).

Synthesis of 2:

Sulfur dichloride (4.90 g, 47.55 mmol) was added to a solution of *p-tert*-butylphenol (**1**, 50 g, 332.85 mmol) in dry dichloromethane (300 mL) over 20 minutes at 0 °C and then the reaction mixture was stirred for 1 hour at the same temperature. After that the pH was adjusted by saturated aqueous solution of sodium hydrogen carbonate to the neutral and resulting mixture was extracted with dichloromethane. The mixture was concentrated and unreacted **1** was removed by steam distillation. Then the dichloromethane was added, the organic layer was separated, washed three times with water and dried over anhydrous magnesium sulfate. Solvent was removed under reduced pressure and the residual mass was crystallized from hexane to give a first crop of **2**. The residual part was purified by column chromatography (Silica gel, eluent: dichloromethane/hexane = 1/5) and was crystallized from hexane to give another crop of **2**. In total was obtained **2** as colorless crystals in yield 91 % (14.36 g), m. p. 99 – 101 °C. ^{1}H NMR ($CDCl_3$, 300 MHz, 298 K) − δ (ppm) = 1.24 (s, 18H, ^{t}Bu**H**), 6.08 (br s, 2H, Ar-O**H**), 6.89 (d, 2H, J = 8.5 Hz, Ar**H**), 7.26 (dd, 2H, J_1 = 8.5 Hz, J_2 = 2.3 Hz, Ar**H**), 7.33 (d, 2H, J = 2.3 Hz, Ar**H**). MS (APCI): m/z for $C_{20}H_{26}O_2S_1$ − calcd: 330.17, found: 329.16 [M − H^+].

Synthesis of 3:

Aqueous solution of sodium hydroxide (2 %, 0.12 g, 3.03 mmol) was added to a mixture of **2** (1 g, 3.03 mmol) and aqueous solution of formaldehyde (37 %, 0.09 g, 3.03 mmol) under the nitrogen atmosphere. Then the reaction mixture was stirred for 2 hours at 50 °C. After cooling down to room temperature the reaction mixture was acidified to pH = 6 with 1 M HCl to give a white precipitate. Then the chloroform was added, precipitate was dissolved, the organic layer was separated, washed three times with water and dried over anhydrous magnesium sulfate. Solvent was removed under reduced pressure and the residual was purified by column chromatography (Silica gel, eluent: ethyl acetate/hexane = 1/5) and triturated with hexane to give **3** as white powder in yield 64 % (0.70 g), m. p. 146 − 148 °C. ^{1}H NMR ($CDCl_3$, 300 MHz, 298 K) − δ (ppm) = 1.19 (s, 9H, ^{t}Bu**H**), 1.27 (s, 9H, ^{t}Bu**H**), 2.43 (t, 1H, J = 5.7 Hz, CH_2-O**H**), 4.86 (d, 2H, J = 5.6 Hz, C**H$_2$**), 6.69 (s, 1H, Ar-O**H**), 6.93 (d, 1H, J = 8.5 Hz, Ar**H**), 7.00 (d, 1H, J = 2.3 Hz, Ar**H**), 7.12 (d, 1H, J = 2.3 Hz, Ar**H**), 7.32 (dd, 1H, J_1 = 8.5 Hz, J_2 = 2.3 Hz, Ar**H**), 7.51 (d, 1H, J = 2.3 Hz, Ar**H**), 7.81 (s, 1H, Ar-O**H**). MS (APCI): m/z for $C_{20}H_{26}O_2S_1$ − calcd: 360.18, found: 359.17 [M − H^+].

Synthesis of 4:

Aqueous solution of potassium hydroxide (25 %, 1.02 g, 18.15 mmol) was added to a mixture of **2** (3 g, 9.08 mmol) and aqueous solution of formaldehyde (37 %, 5.45 g, 181.54 mmol) under the nitrogen atmosphere. Then the reaction mixture was stirred for 20 hours at 50 °C. After cooling down to room temperature the water was added (200 mL) and the mixture was acidified to pH = 6 with 1 M HCl at 0 °C to give a white precipitate. After filtration and drying was obtained **4** as white powder in yield 97 % (3.44 g), m. p. 91 − 93 °C. ^{1}H NMR ($CDCl_3$, 300 MHz, 298 K) − δ (ppm) = 1.23 (s, 18H, ^{t}Bu**H**), 4.80 (s, 2H, C**H$_2$**), 7.12 (d, 2H, J = 2.3 Hz, Ar**H**), 7.34 (d, 2H, J = 2.3 Hz, Ar**H**), 7.84 (s, 2H, Ar-O**H**). MS (APCI): m/z for $C_{22}H_{30}O_4S_1$ − calcd: 390.19, found: 389.18 [M − H^+].

Synthesis of 5:

A mixture of **2** (0.43 g, 1.30 mmol) and **4** (0.51 g, 1.30 mmol) in dry chloroform (100 mL) was slowly added to a mixture of TsOH (0.50 g, 2.60 mmol) in dry chloroform (250 mL) over 4 hours at reflux. Then the reaction mixture was stirred for 1 hour at the same temperature. The solvent was removed under reduced pressure and the residual was triturated with methanol to give white precipitate. After filtration and drying was obtained **5** as white powder in yield 58 % (0.52 g), m. p. > 300 °C. IR (KBr): 3277 cm^{-1}. ^{1}H NMR ($CDCl_3$, 300 MHz, 298 K) − δ (ppm) = 1.23 (s, 36H, ^{t}Bu**H**), 7.22 (d, 4H, J = 2.3 Hz, Ar**H**), 7.50 (d, 4H, J = 2.3 Hz, Ar**H**), 9.94 (s, 4H, Ar-O**H**). ^{13}C NMR ($CDCl_3$, 75 MHz, 298 K) − δ (ppm) = 31.6, 33.4, 34.3, 121.5, 127.4, 129.7, 133.0, 144.8, 151.2. MS (ESI): m/z for $C_{42}H_{52}O_4S_2$ − calcd: 684.33, found: 707.32 [M + Na^+].

Synthesis of 6:

A mixture of **3** (0.15 g, 0.42 mmol), **4** (0.16 g, 0.42 mmol) and TsOH (0.08 g, 0.42 mmol) in dry chloroform (120 mL) was stirred for 5 days at 30 °C. Then the solvent was removed under reduced pressure and the residual was purified by column chromatography (Silica gel, eluent: chloroform/hexane = 1/15) and triturated with methanol to give white precipitate. After filtration and drying was obtained **6** as white powder in yield 27 % (0.08 g), m. p. > 300 °C. IR (KBr): 3354 cm^{-1}. ^{1}H NMR ($CDCl_3$, 300 MHz, 298 K) − δ (ppm) = 1.23 (s, 18H, ^{t}Bu**H**), 1.26 (s, 18H, ^{t}Bu**H**), 3.92 (br s, 2H, C**H$_2$**), 4.61 (s, 4H, C**H$_2$**), 7.08 (d, 2H, J = 2.3 Hz, Ar**H**), 7.28 (d, 2H, J = 2.3 Hz, Ar**H**), 7.47 (d, 2H, J = 2.3 Hz, Ar**H**), 7.70 (d, 2H, J = 2.3 Hz, Ar**H**), 8.69 (s, 2H, Ar-O**H**), 9.18 (s, 2H, Ar-O**H**). ^{13}C NMR ($CDCl_3$, 75 MHz, 298 K) − δ (ppm) = 31.3, 31.4, 32.8, 34.1, 71.5, 120.2, 121.0, 121.9, 126.8, 128.3, 129.1, 132.7, 133.8, 143.0, 144.5, 151.1, 154.5. MS (ESI): m/z for $C_{43}H_{54}O_5S_2$ − calcd: 714.34, found: 737.33 [M + Na^+].

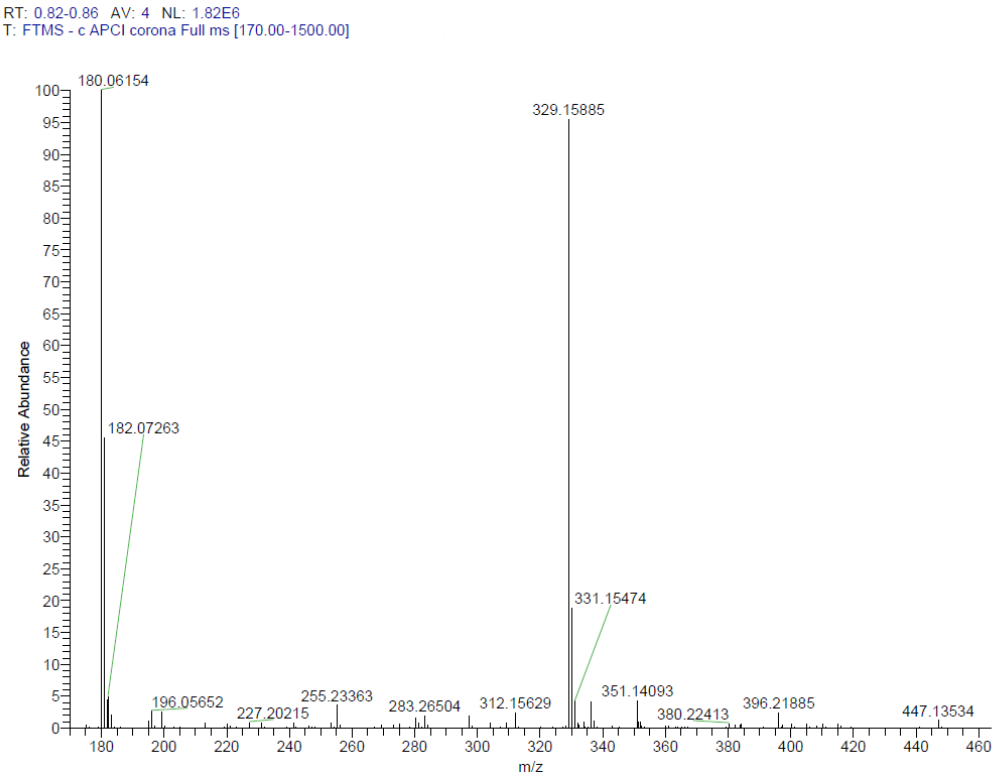
Synthesis of 7:

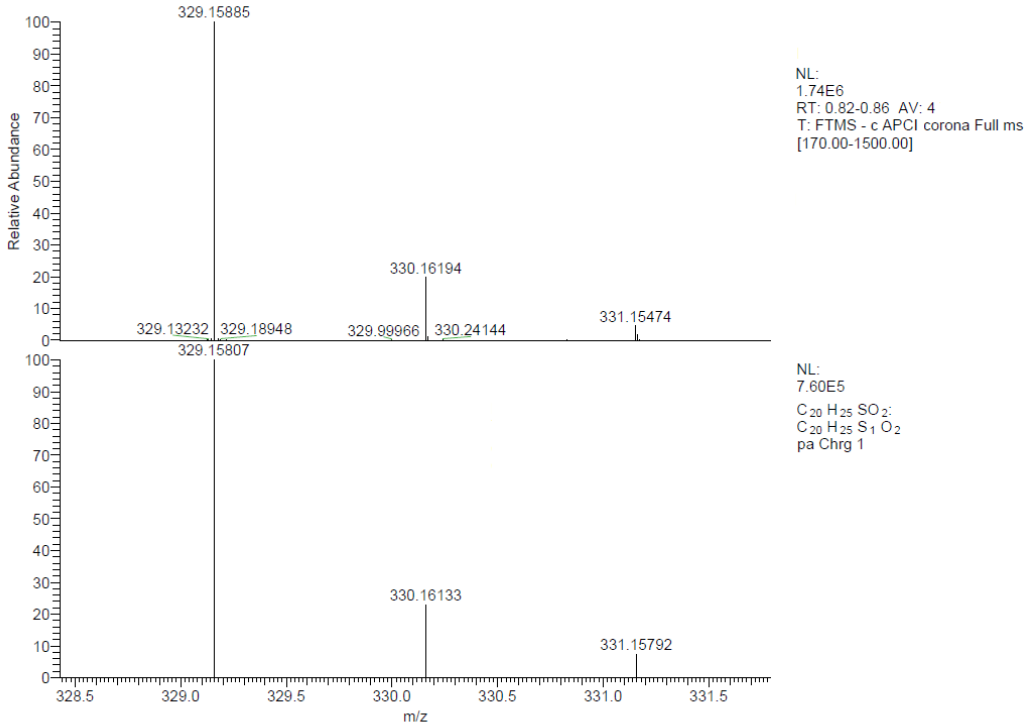
A mixture of **4** (1 g, 2.56 mmol) and TsOH (0.06 g, catalytic amount) in dry chloroform (80 mL) was stirred for 7 days at 35 °C. Then the solvent was removed under reduced pressure and the residual was triturated with methanol to give white precipitate. After filtration and drying was obtained **7** as white powder in yield 34 % (0.32 g), m. p. > 300 °C. IR (KBr): 3357 cm^{-1}. ^{1}H NMR ($CDCl_3$, 300 MHz, 298 K) − δ (ppm) = 1.27 (s, 36H, ^{t}Bu**H**), 4.64 (s, 8H, C$\mathbf{H_2}$), 7.11 (d, 4H, J = 2.3 Hz, Ar**H**), 7.65 (d, 4H, J = 2.3 Hz, Ar**H**), 8.68 (br s, 4H, Ar-O**H**). ^{13}C NMR ($CDCl_3$, 75 MHz, 298 K) − δ (ppm) = 31.6, 34.3, 72.4, 121.0, 122.5, 128.3, 133.7, 143.2, 154.4. MS (ESI): m/z for $C_{44}H_{56}O_6S_2$ − calcd: 744.35, found: 767.34 [$M + Na^+$].

Spectra of compounds

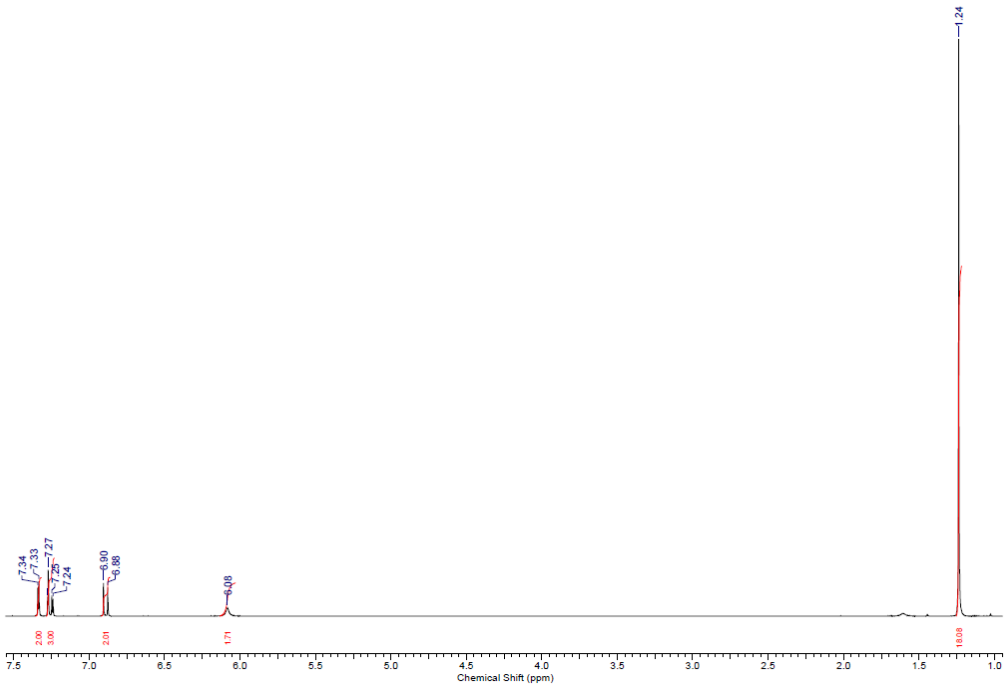
Compound 2:

MS:





^{1}H NMR ($CDCl_3$, 300 MHz, 298 K):



Compound 3:

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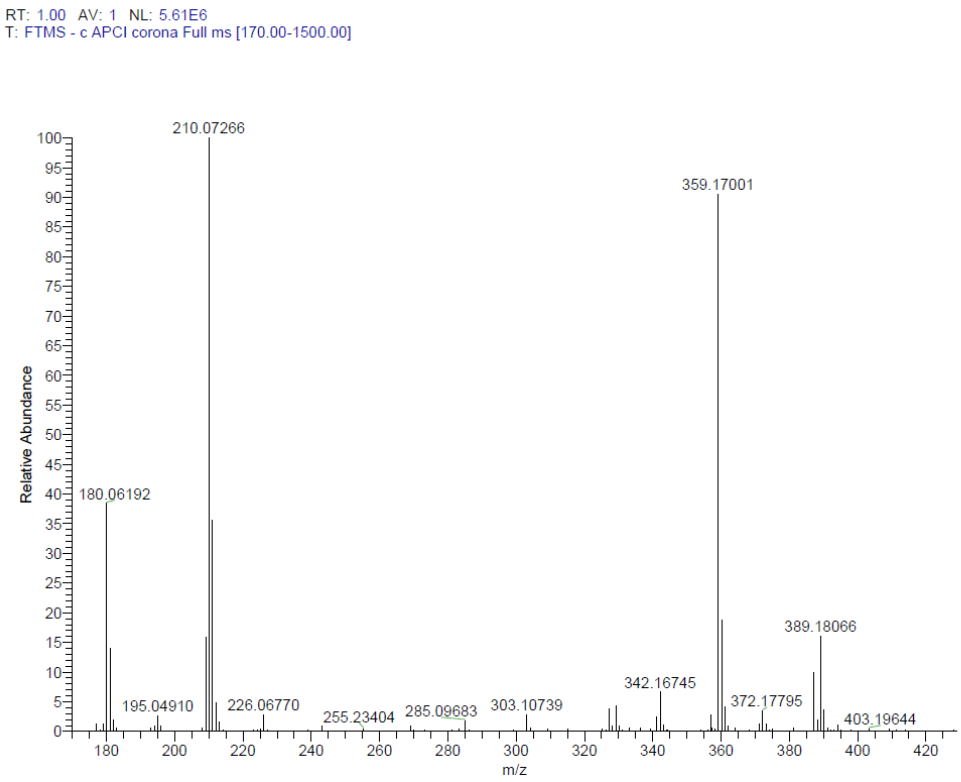
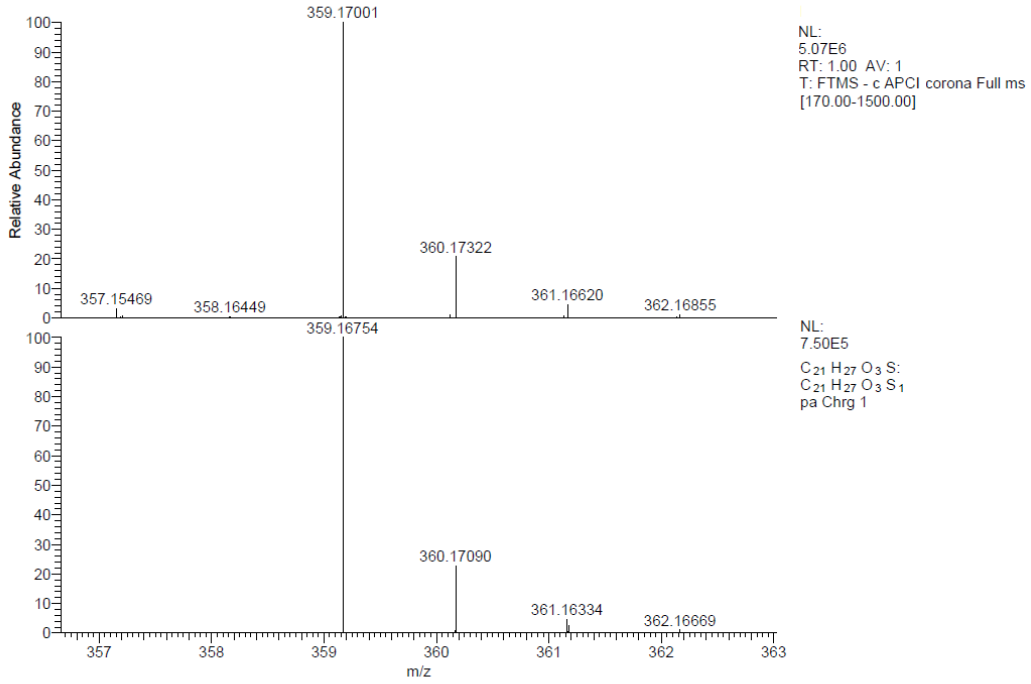
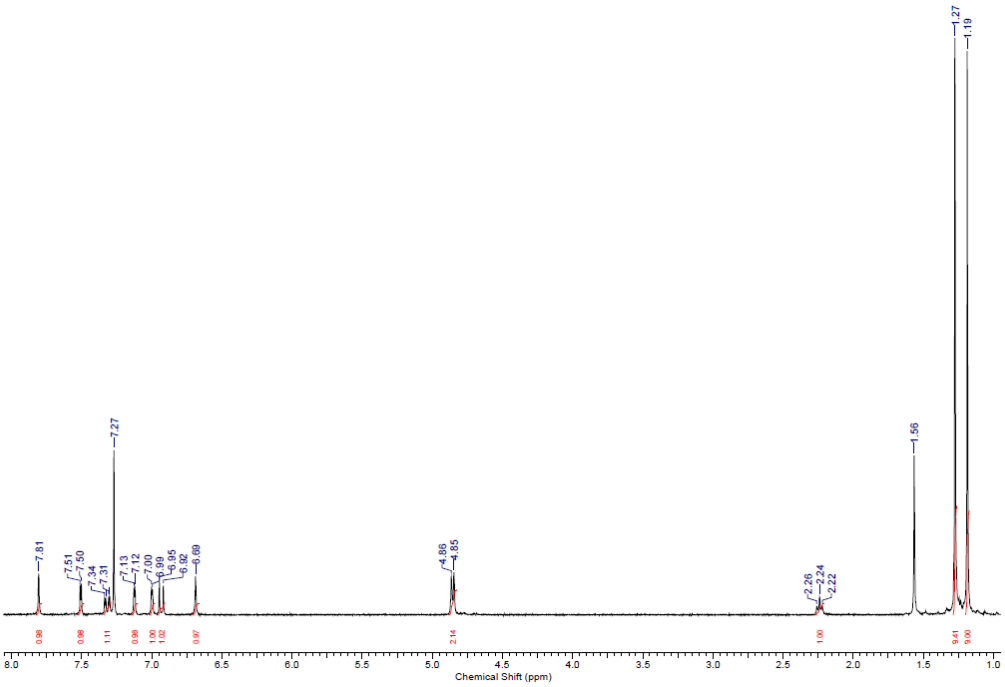




^{1}H NMR ($CDCl_3$, 300 MHz, 298 K):



Compound 4:

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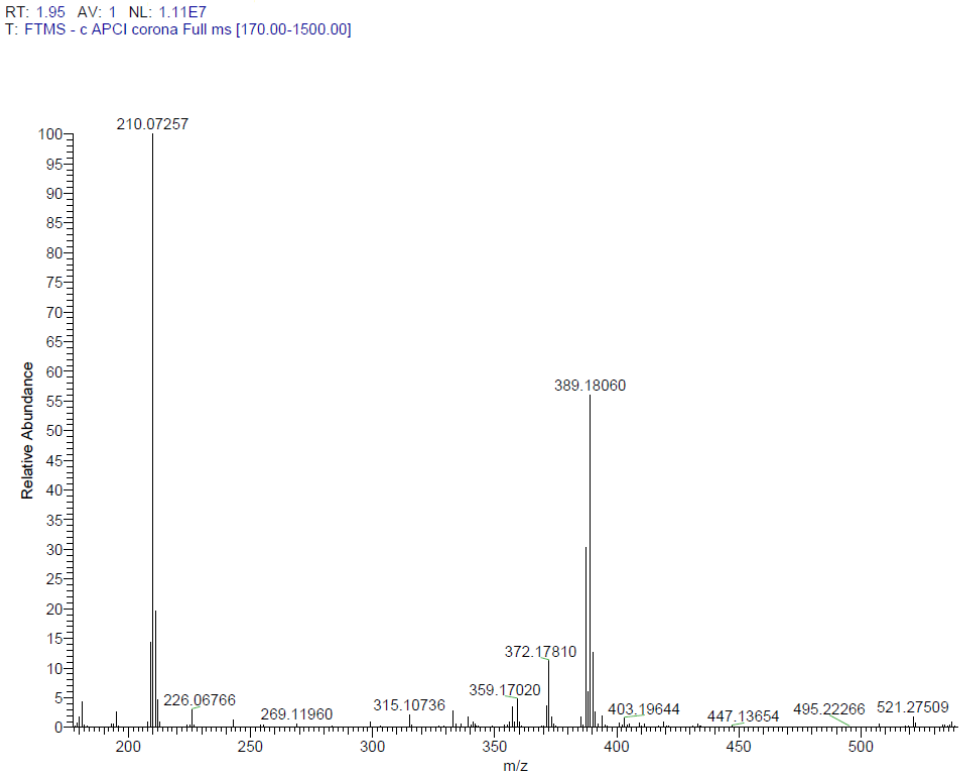
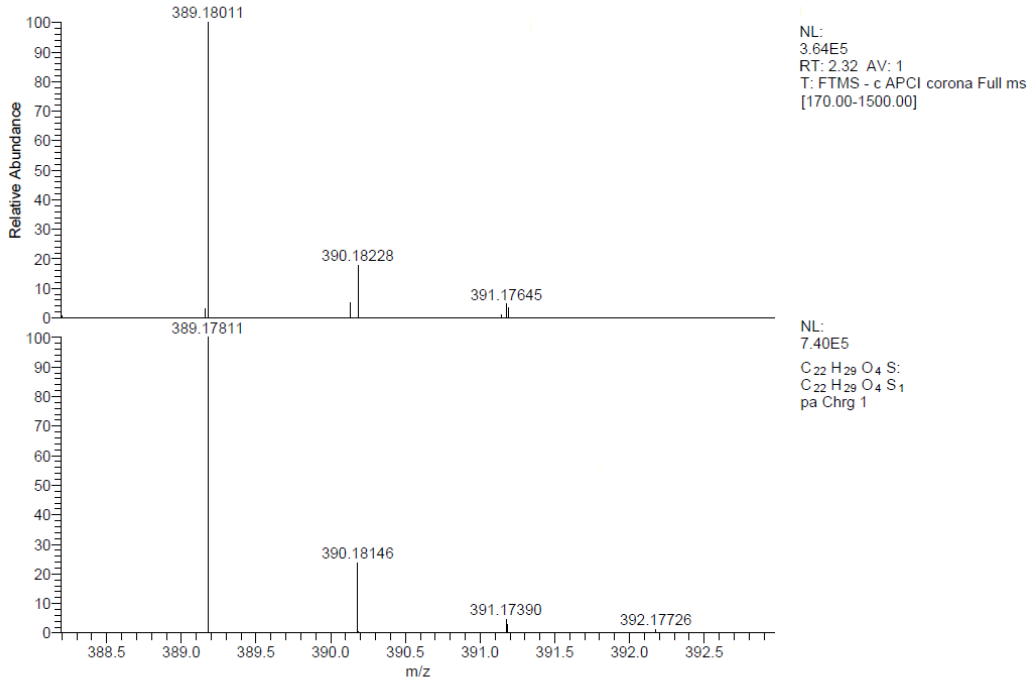
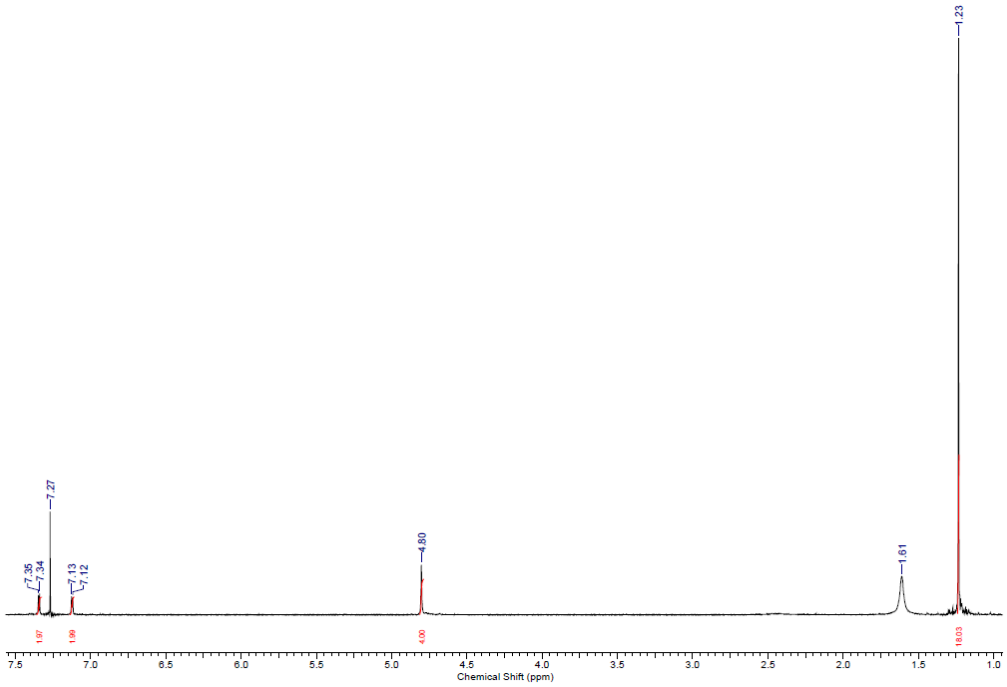




^{1}H NMR ($CDCl_3$, 300 MHz, 298 K):



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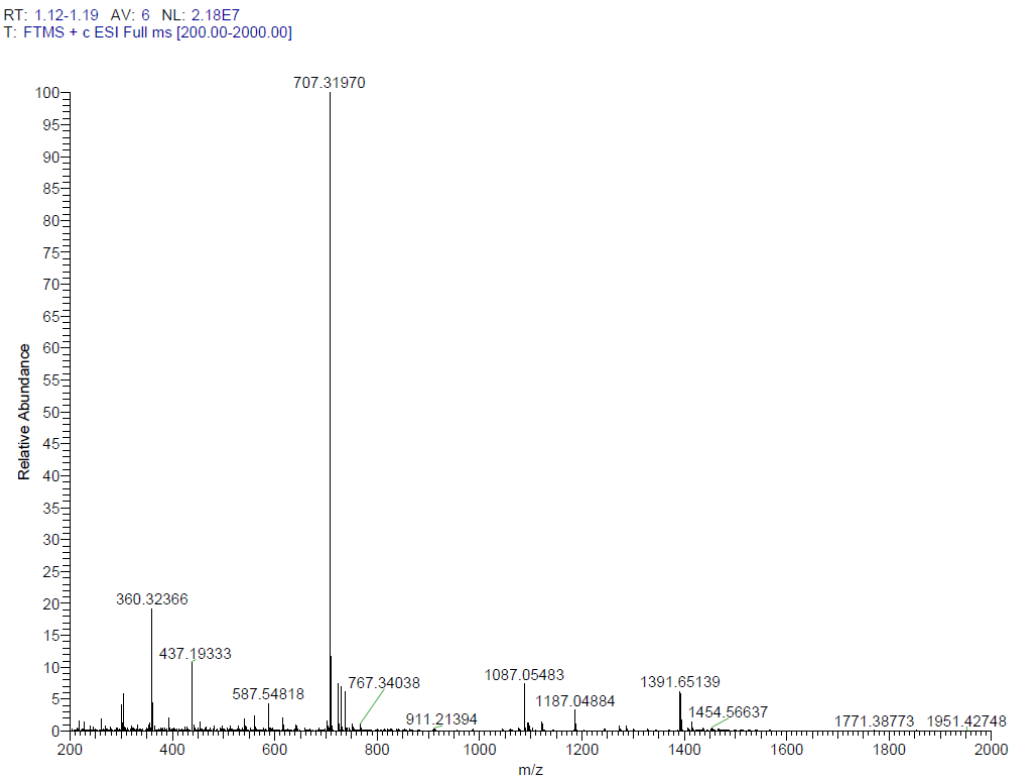

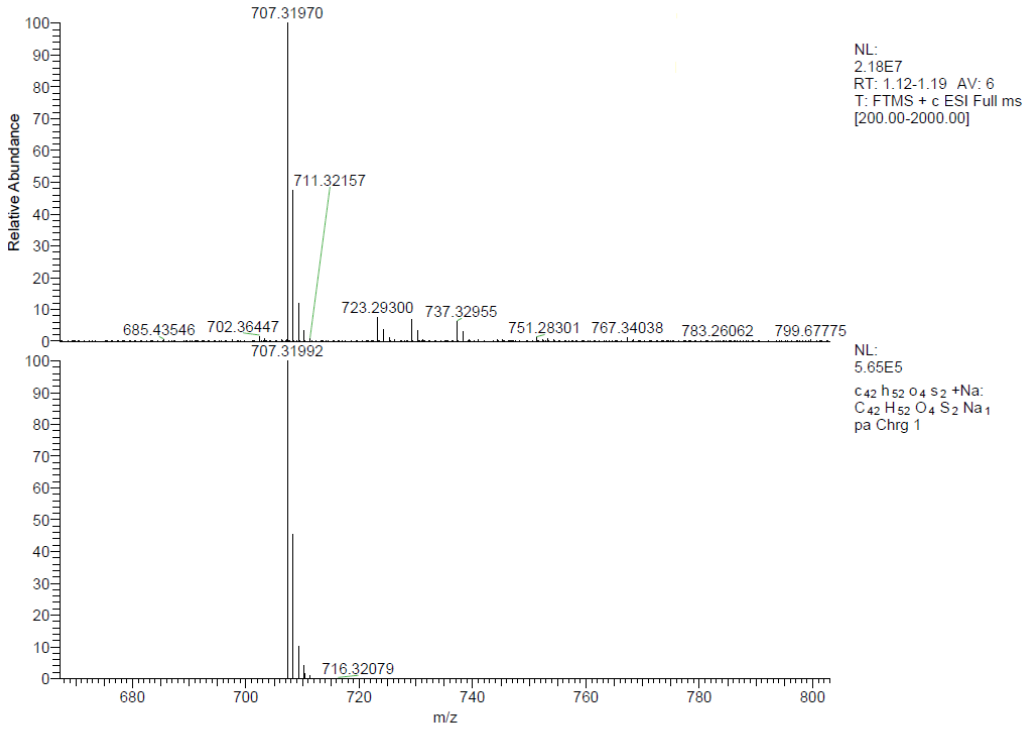

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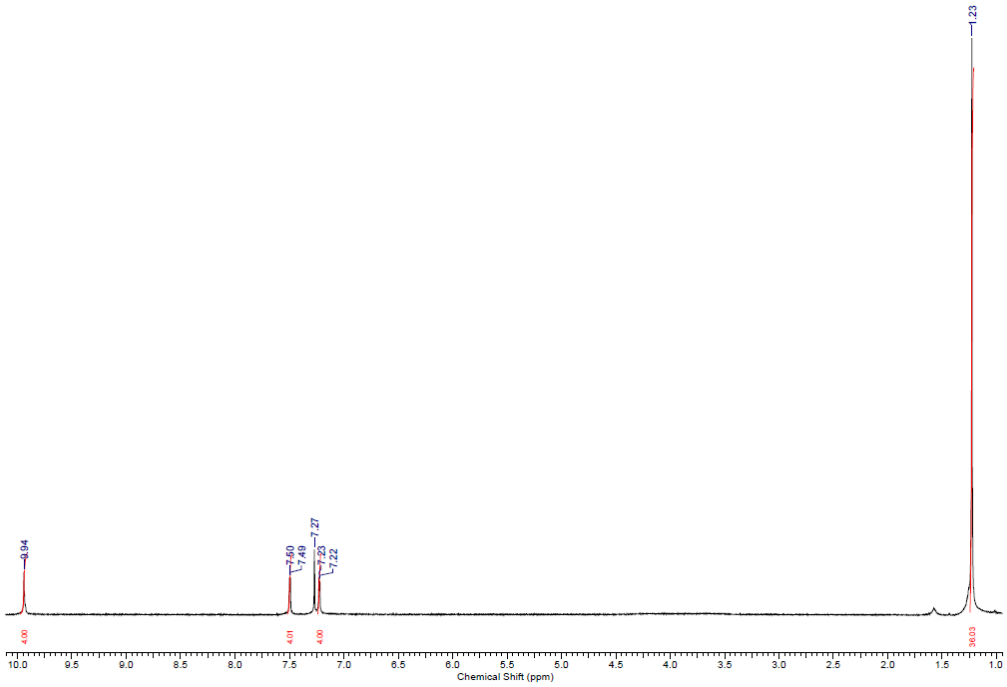
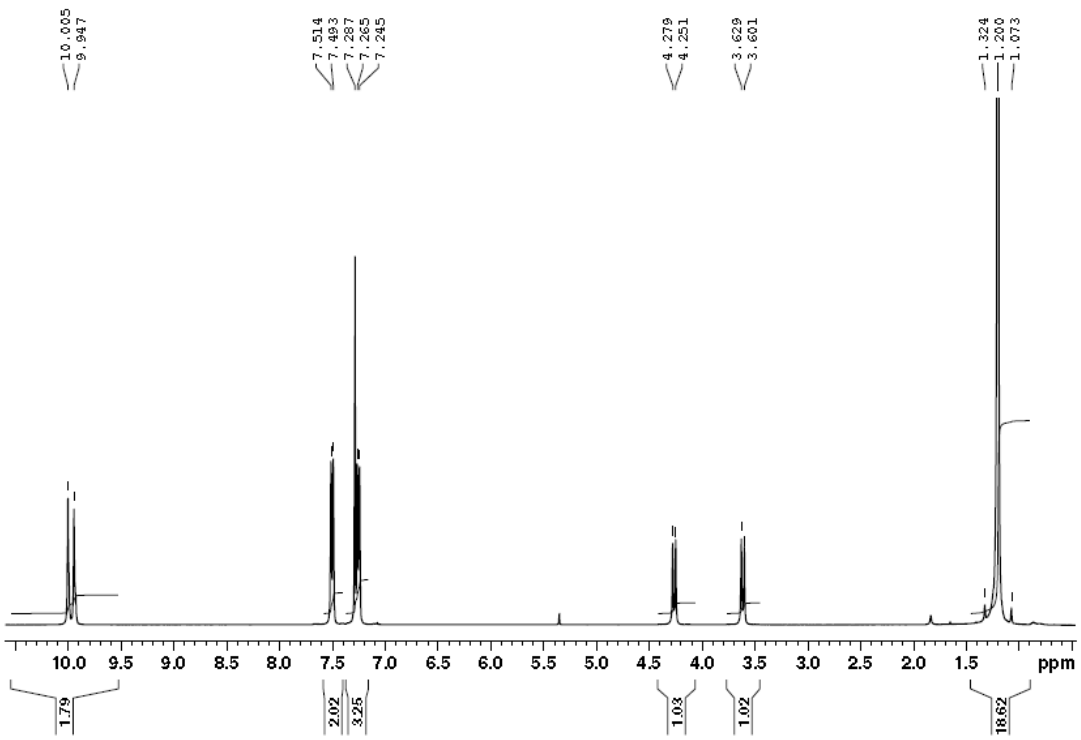
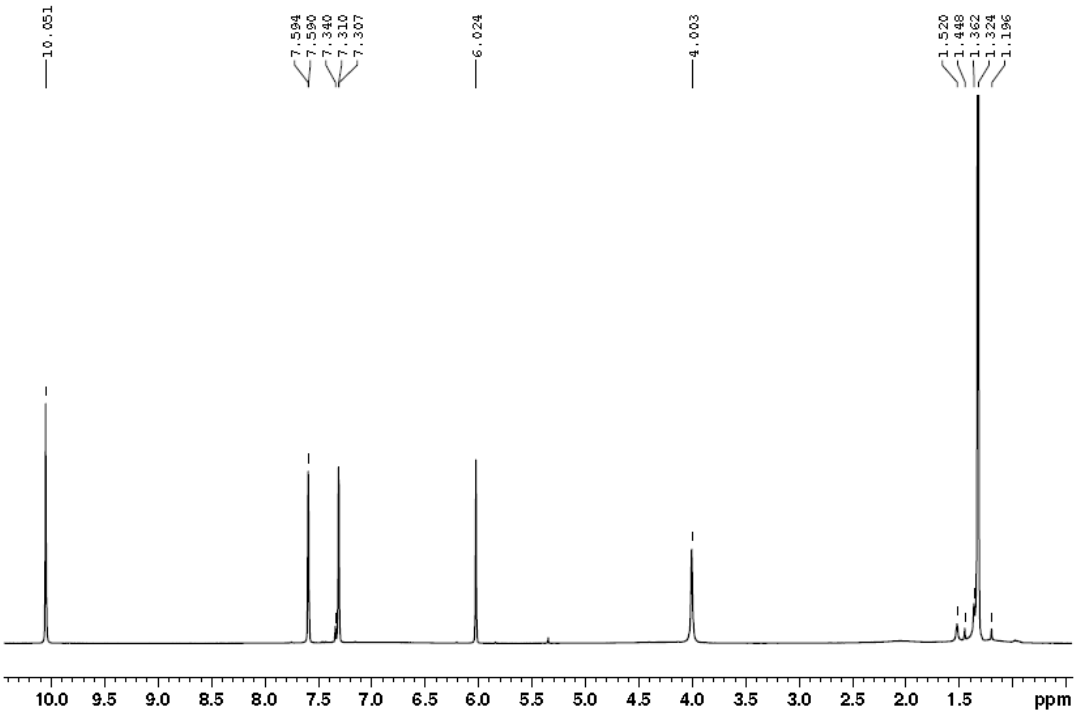


^{1}H NMR ($CDCl_3$, 500 MHz, 213 K):



^{1}H NMR ($C_2D_2Cl_4$, 500 MHz, 363 K):



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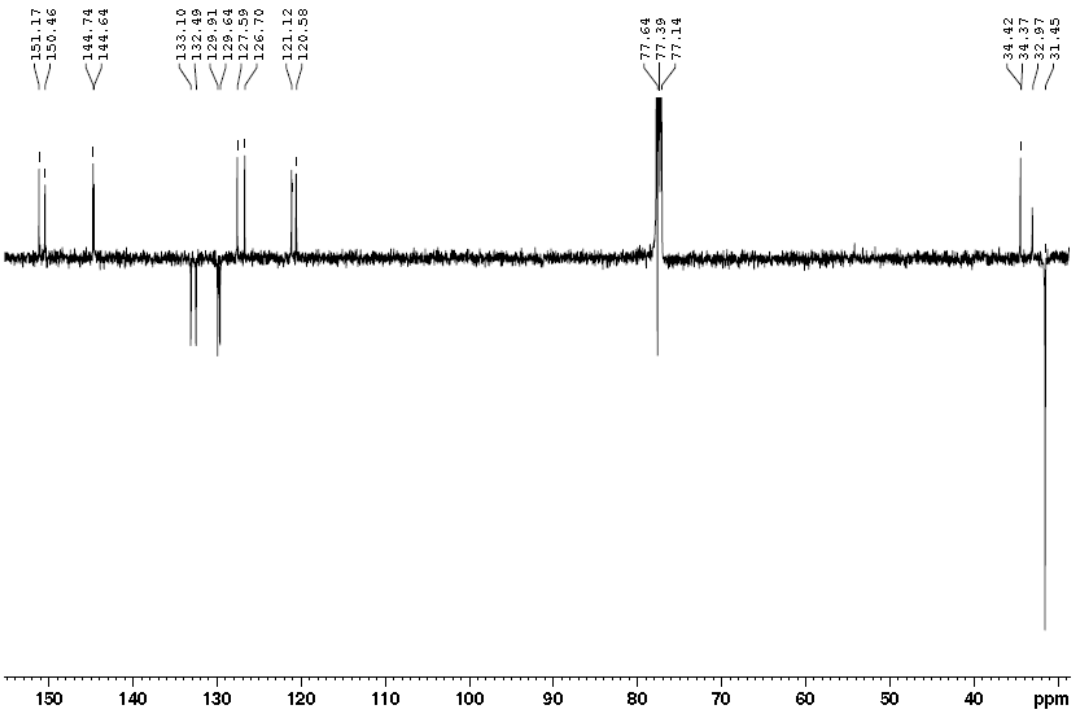
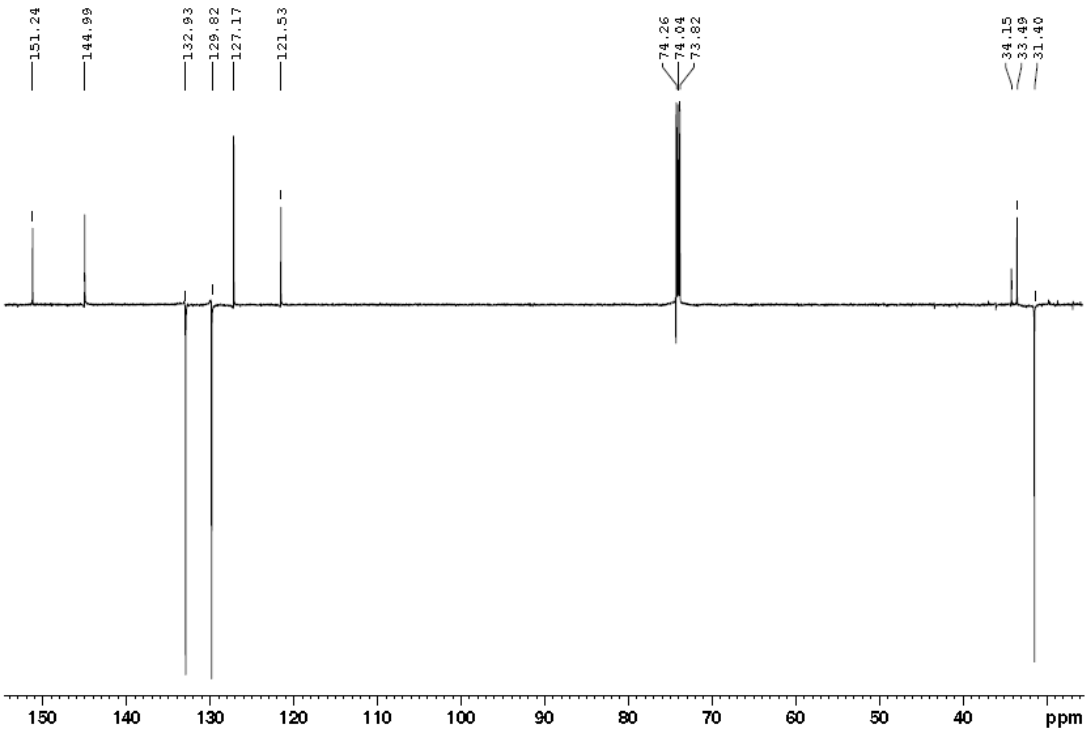
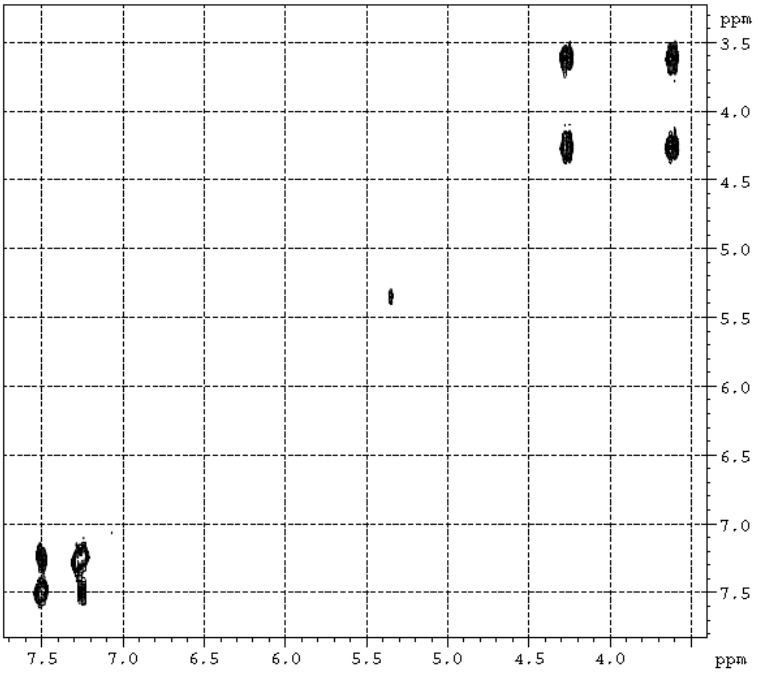


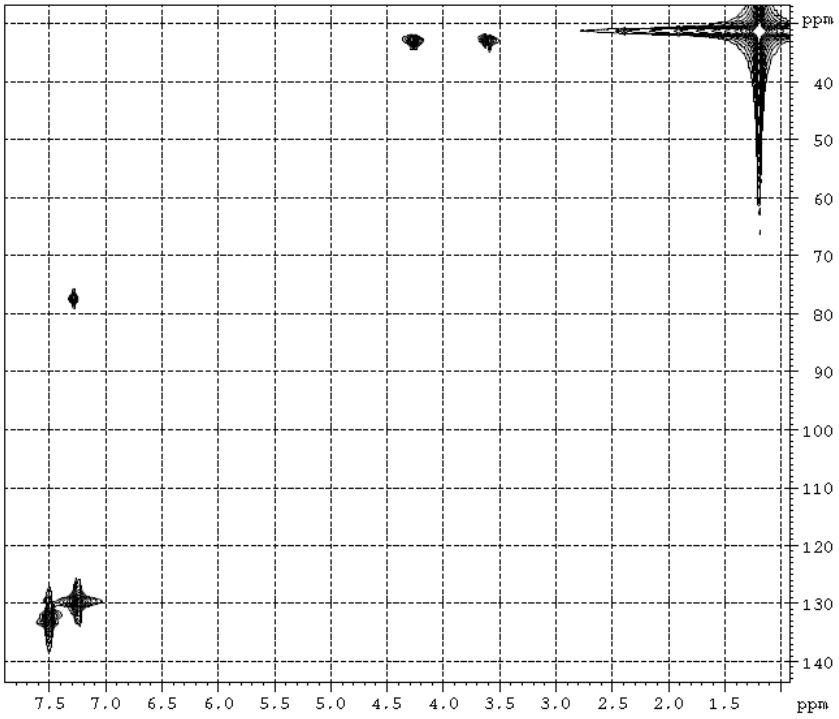
^{13}C NMR ($C_2D_2Cl_4$, 500 MHz, 363 K):



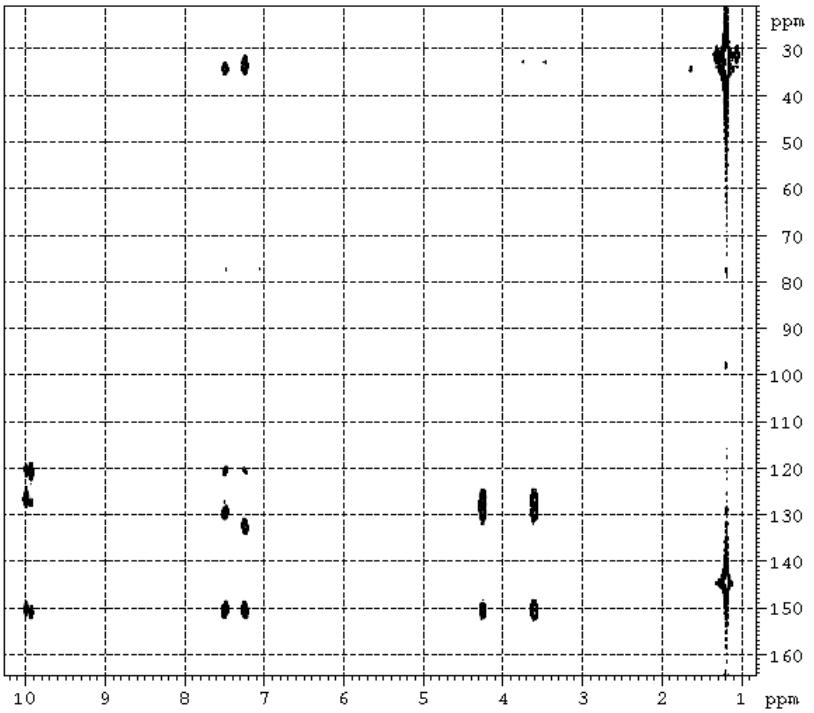
Partial COSY ($CDCl_3$, 500 MHz, 213 K):



HMQC ($CDCl_3$, 500 MHz, 213 K):

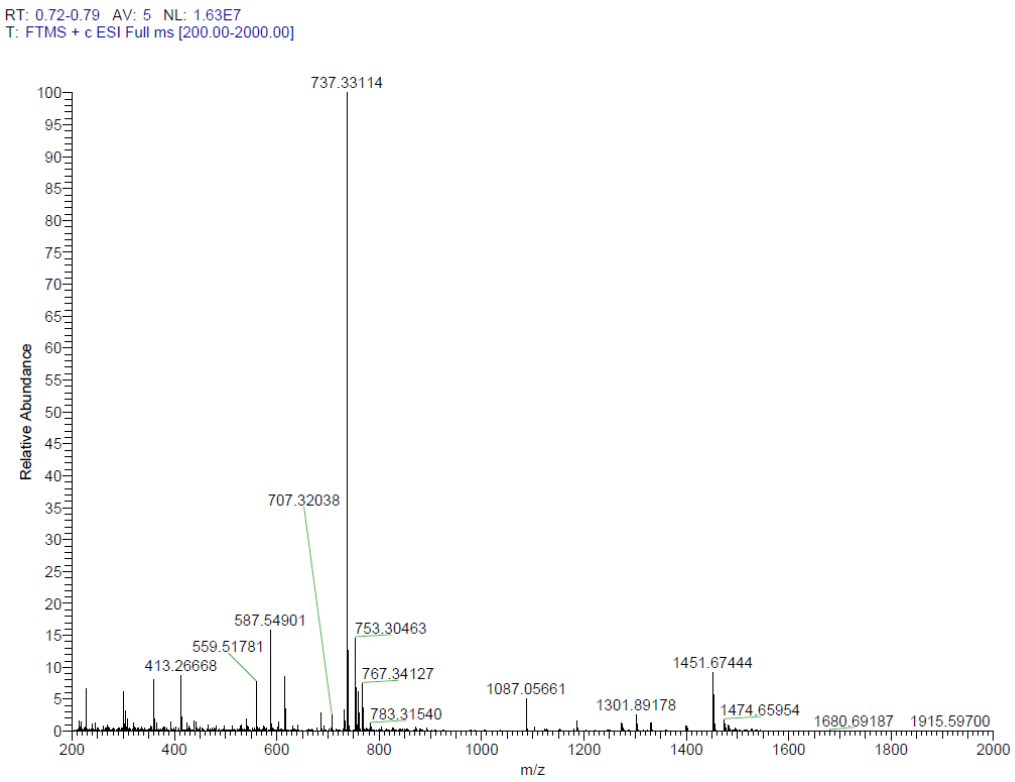


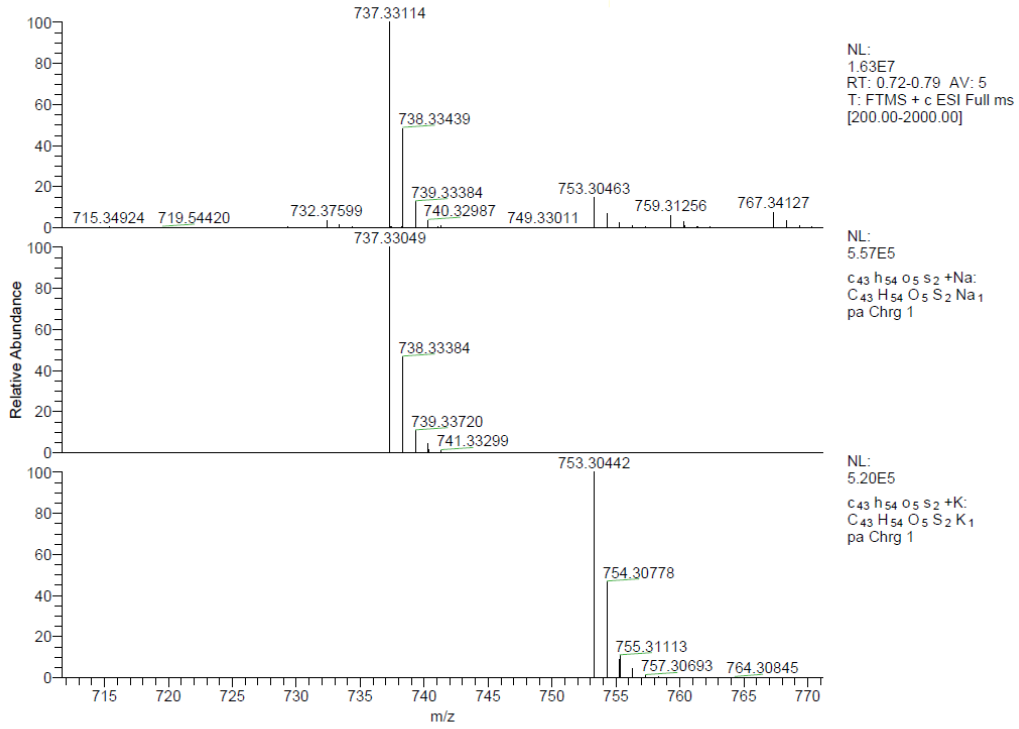
HMBC ($CDCl_3$, 500 MHz, 213 K):



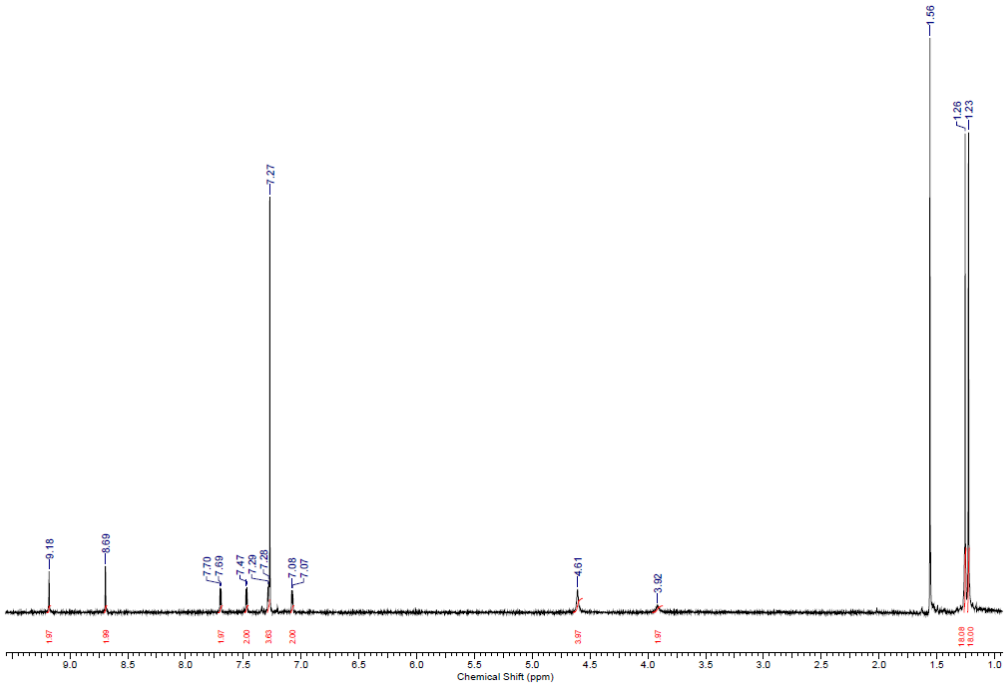
Compound 6:

MS:

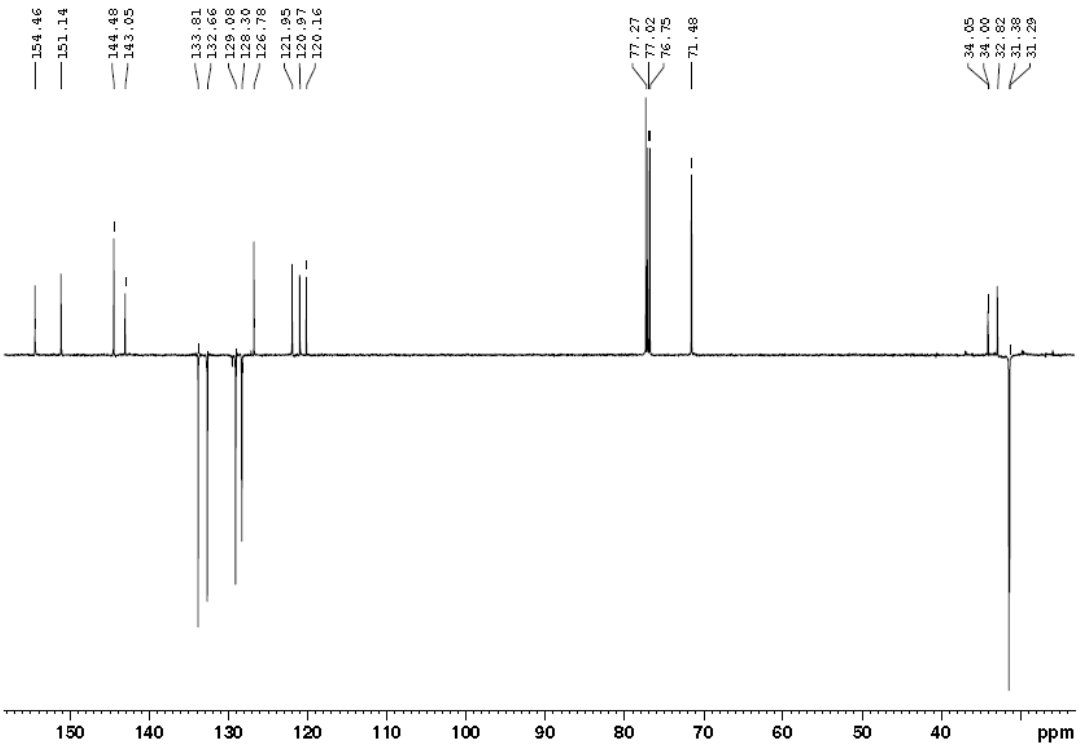




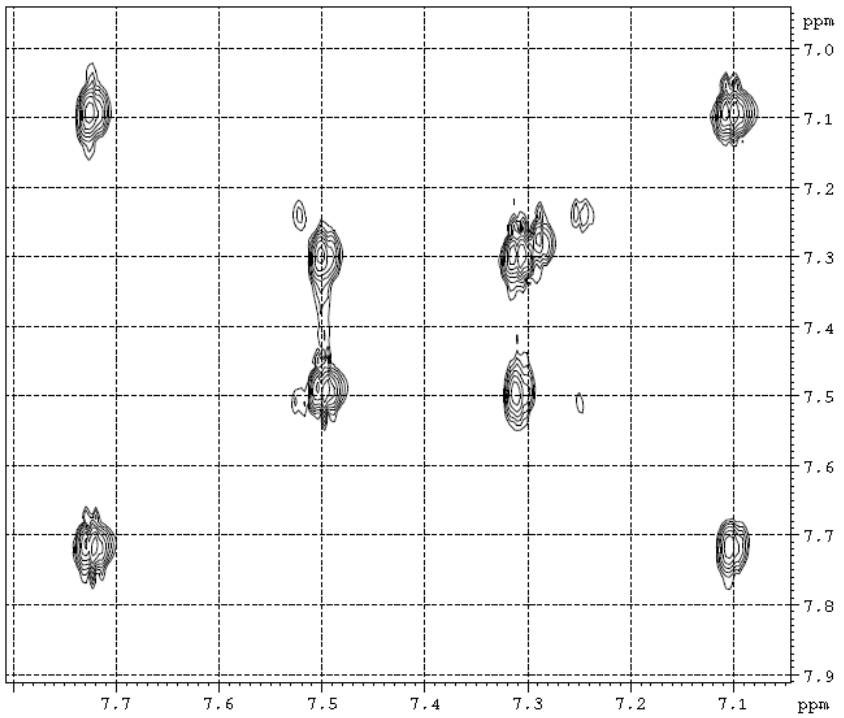
^{1}H NMR ($CDCl_3$, 300 MHz, 298 K):



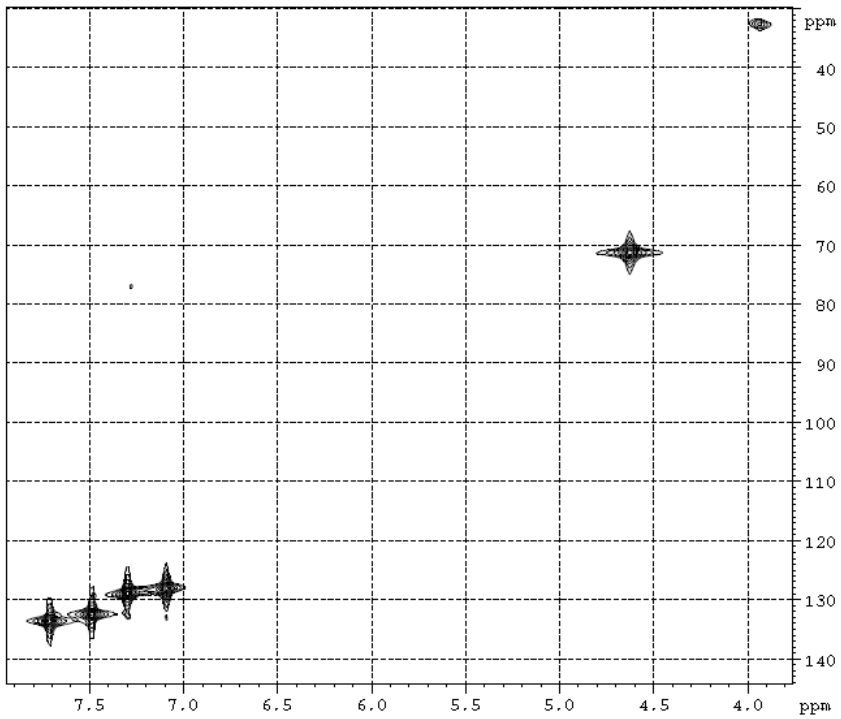
^{13}C NMR ($CDCl_3$, 500 MHz, 298 K):



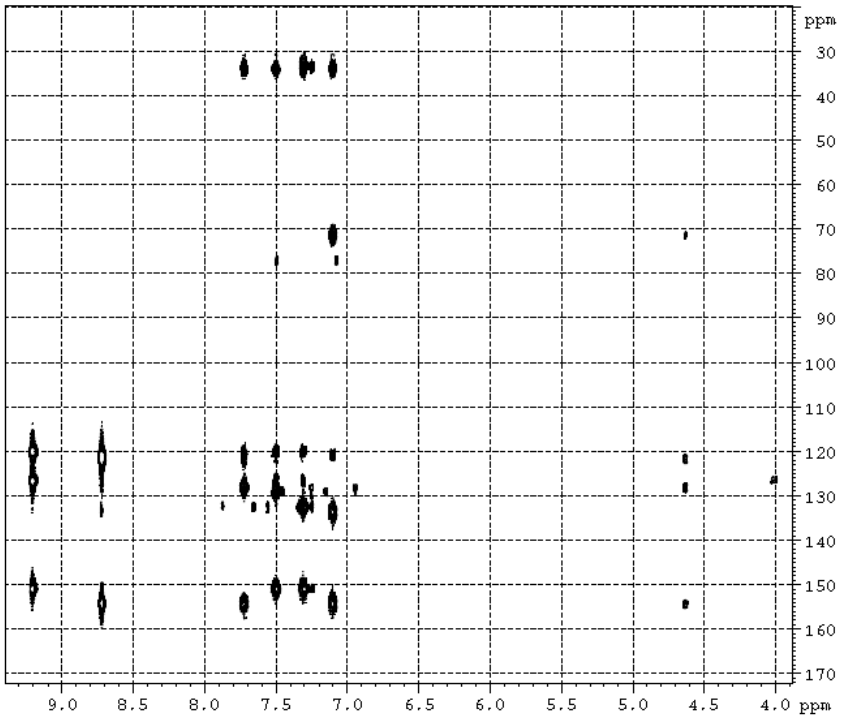
Partial COSY ($CDCl_3$, 500 MHz, 298 K):

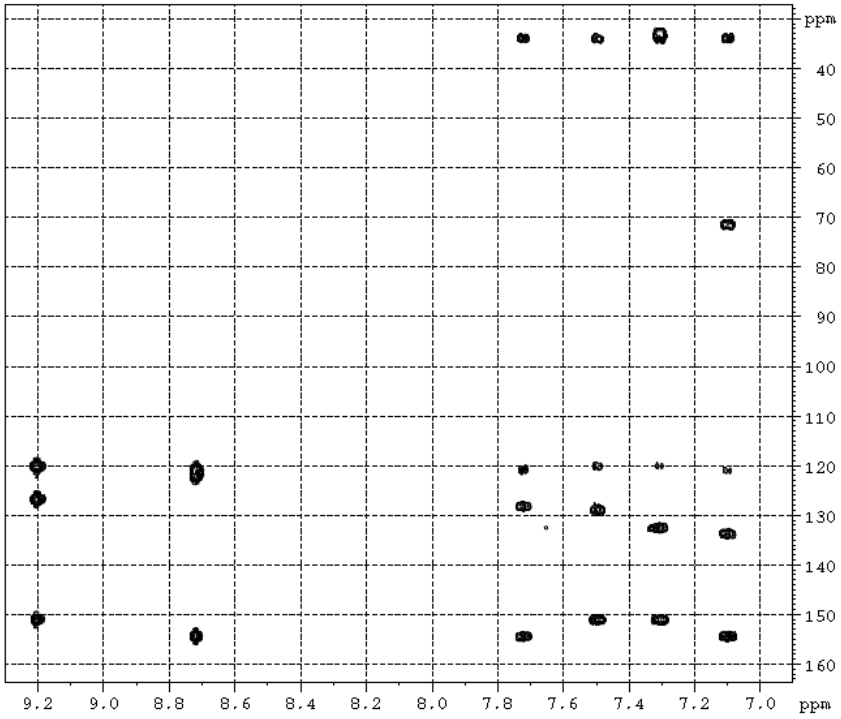


Partial HMQC ($CDCl_3$, 500 MHz, 298 K):



Partial HMBC ($CDCl_3$, 500 MHz, 213 K):





Compound 7:

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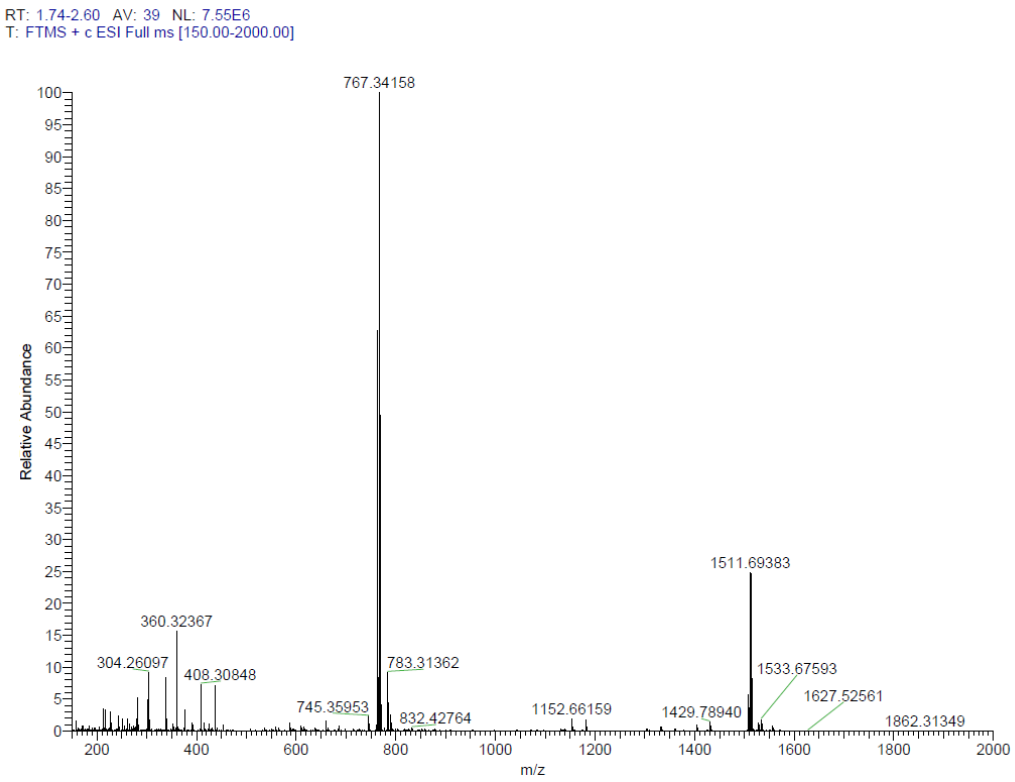
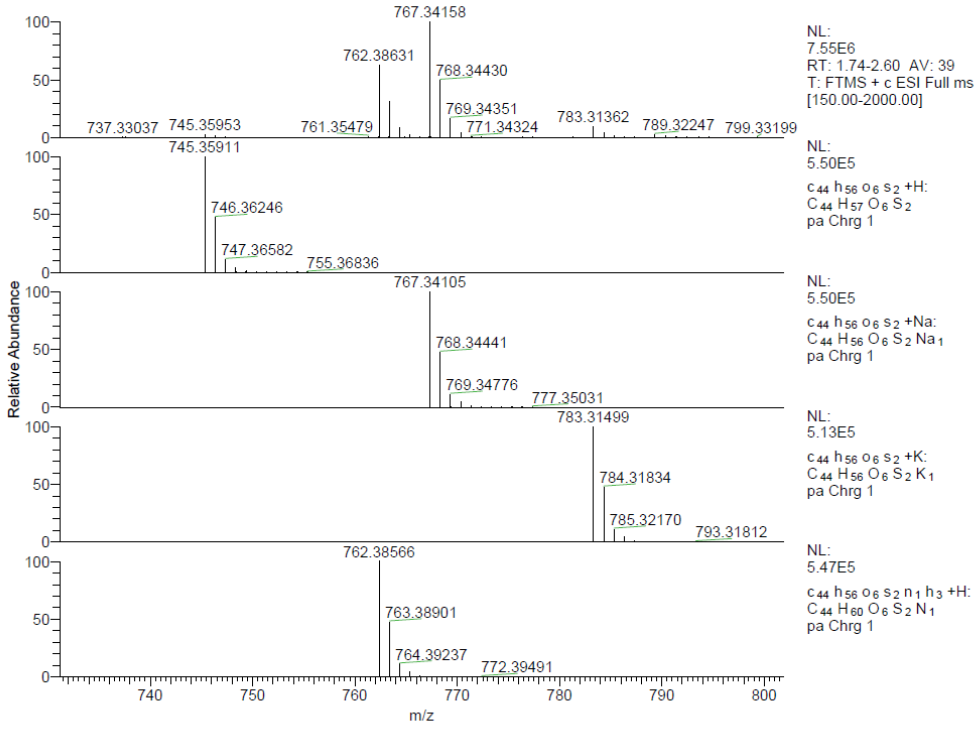
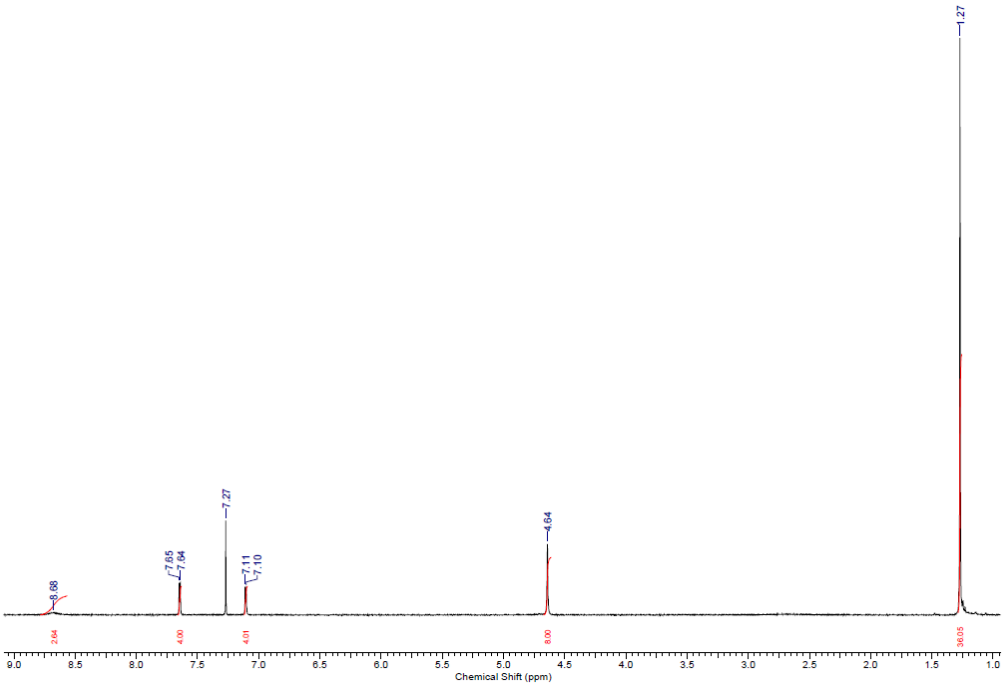
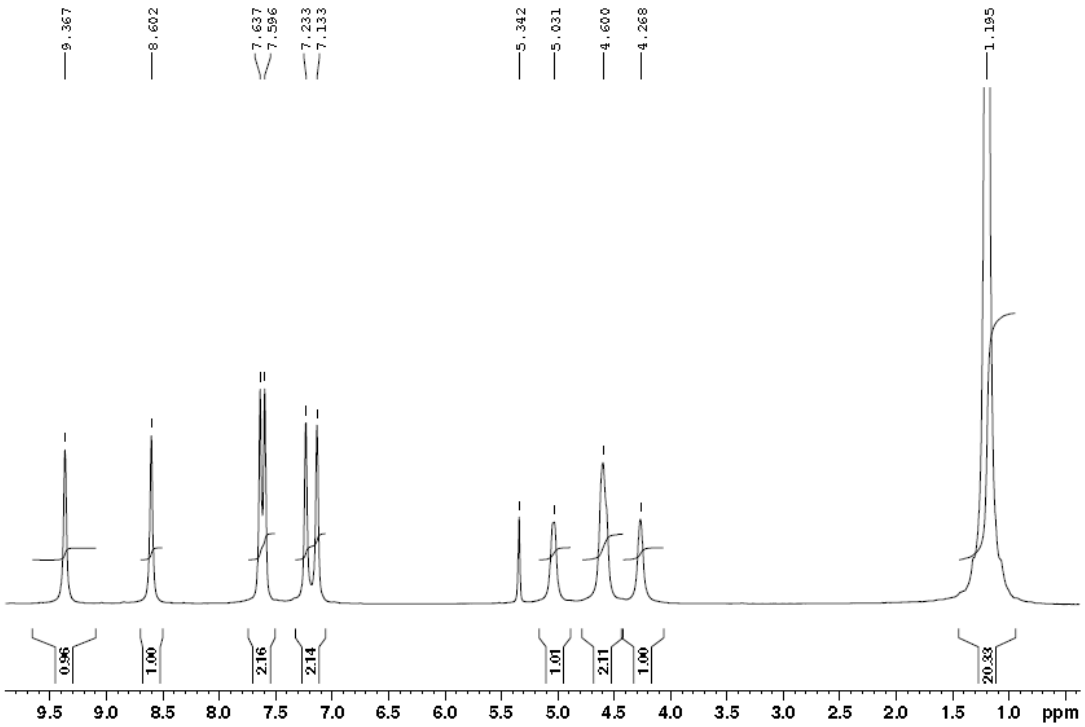




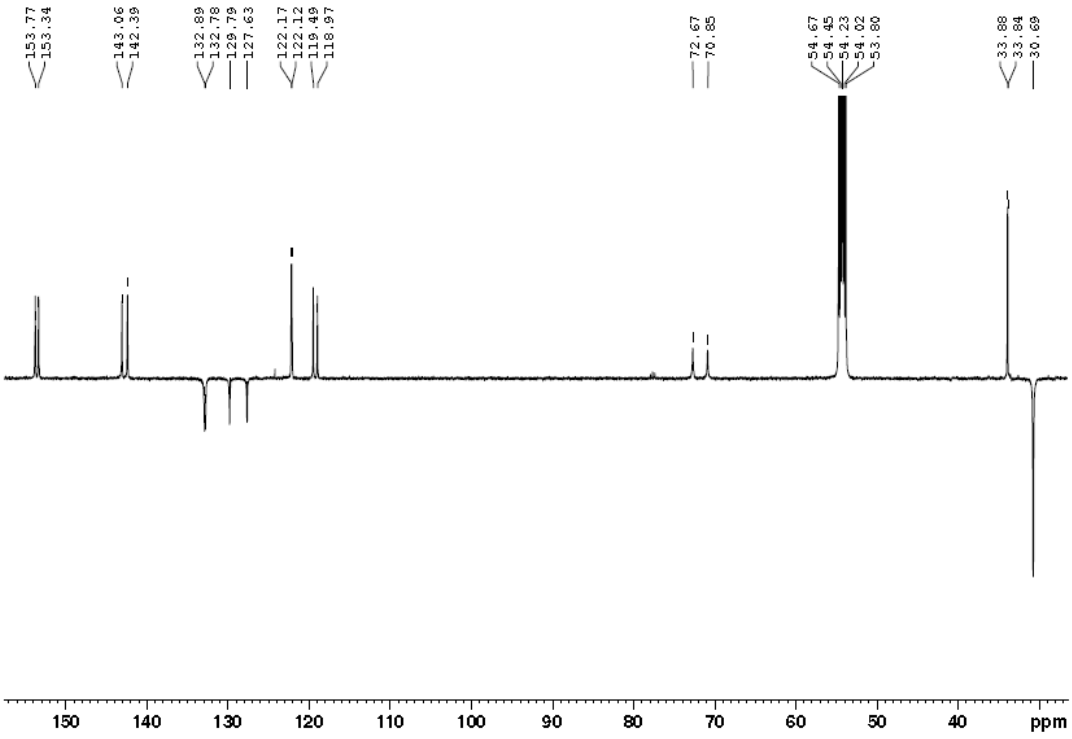
^{1}H NMR ($CDCl_3$, 300 MHz, 298 K):



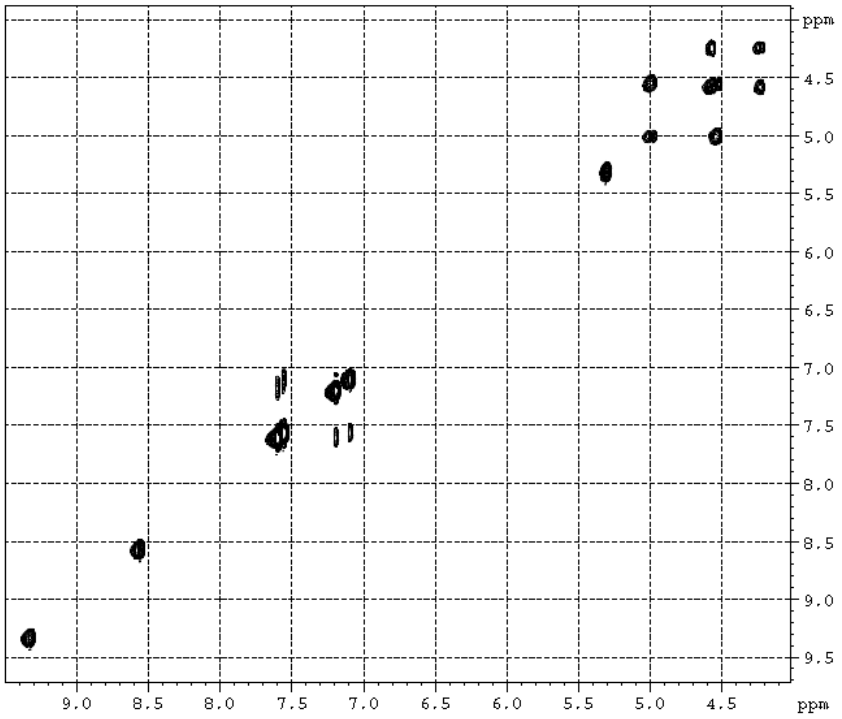
^{1}H NMR (CD_2Cl_2, 500 MHz, 163 K):



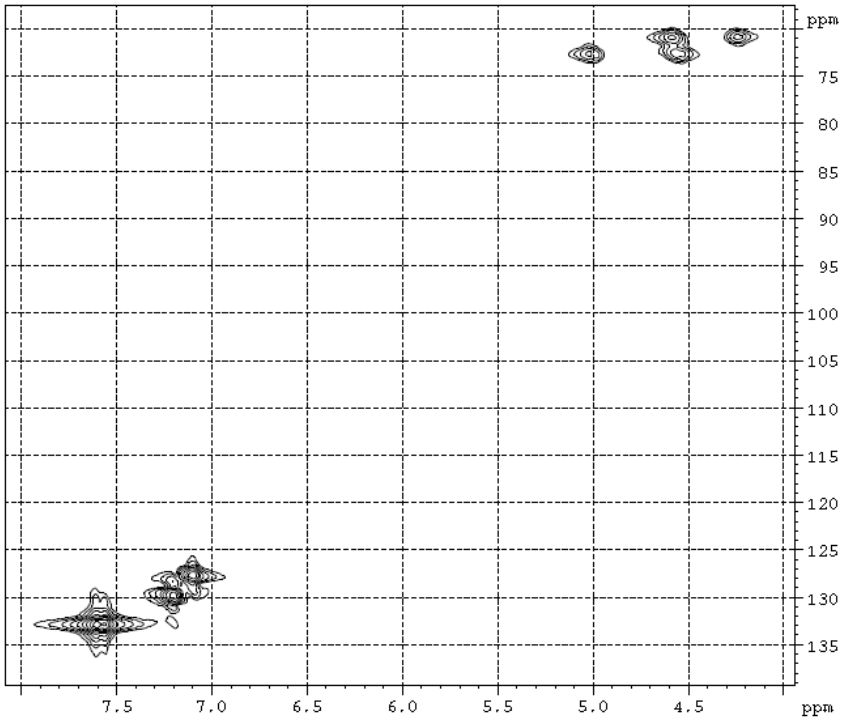
^{13}C NMR (CD_2Cl_2, 500 MHz, 163 K):



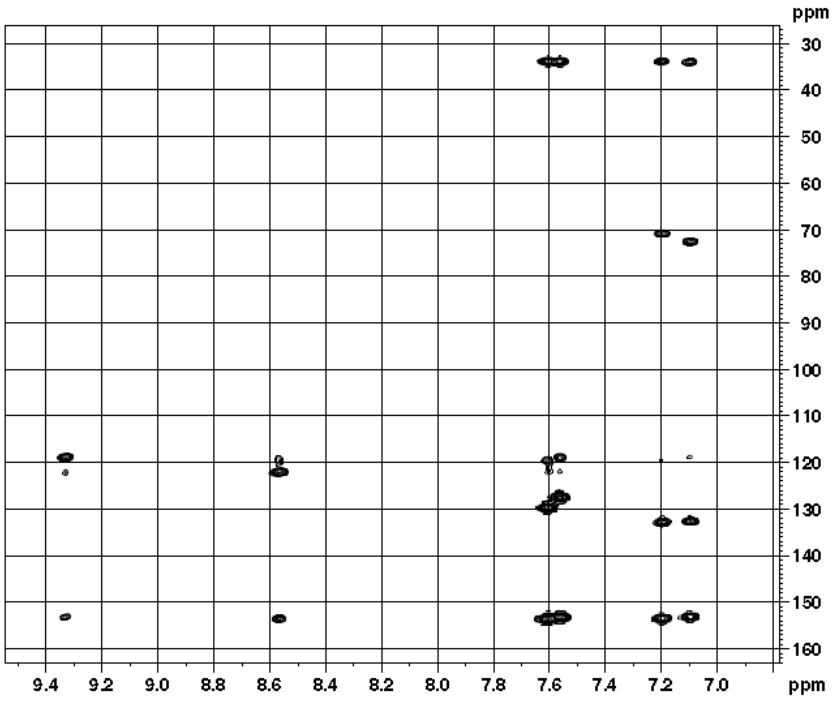
Partial COSY (CD_2Cl_2, 500 MHz, 163 K):



Partial HMQC (CD_2Cl_2, 500 MHz, 163 K):



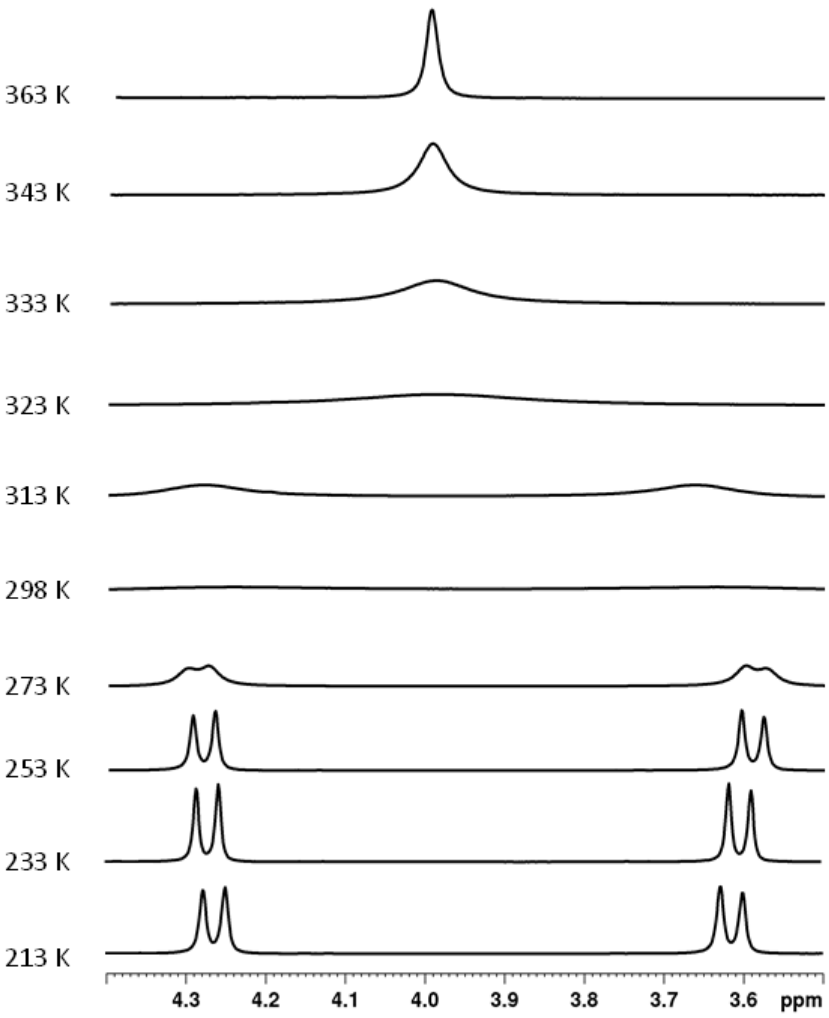
Partial HMBC (CD_2Cl_2, 500 MHz, 163 K):



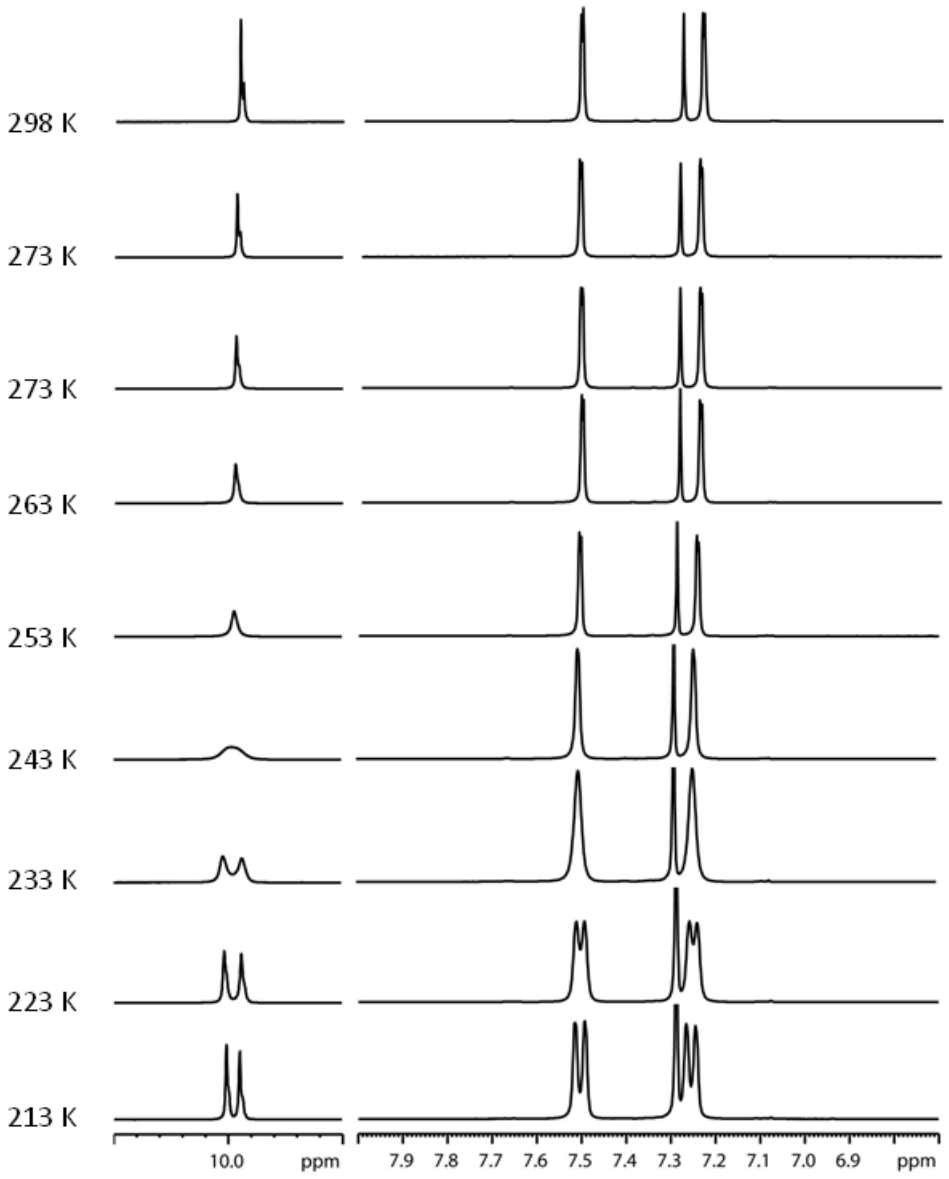
Dynamic NMR measurements

Compound 5:

Partial ^{1}H NMR (213 – 298 K in $CDCl_3$ and 313 – 363K in $C_2D_2Cl_4$, 500 MHz):

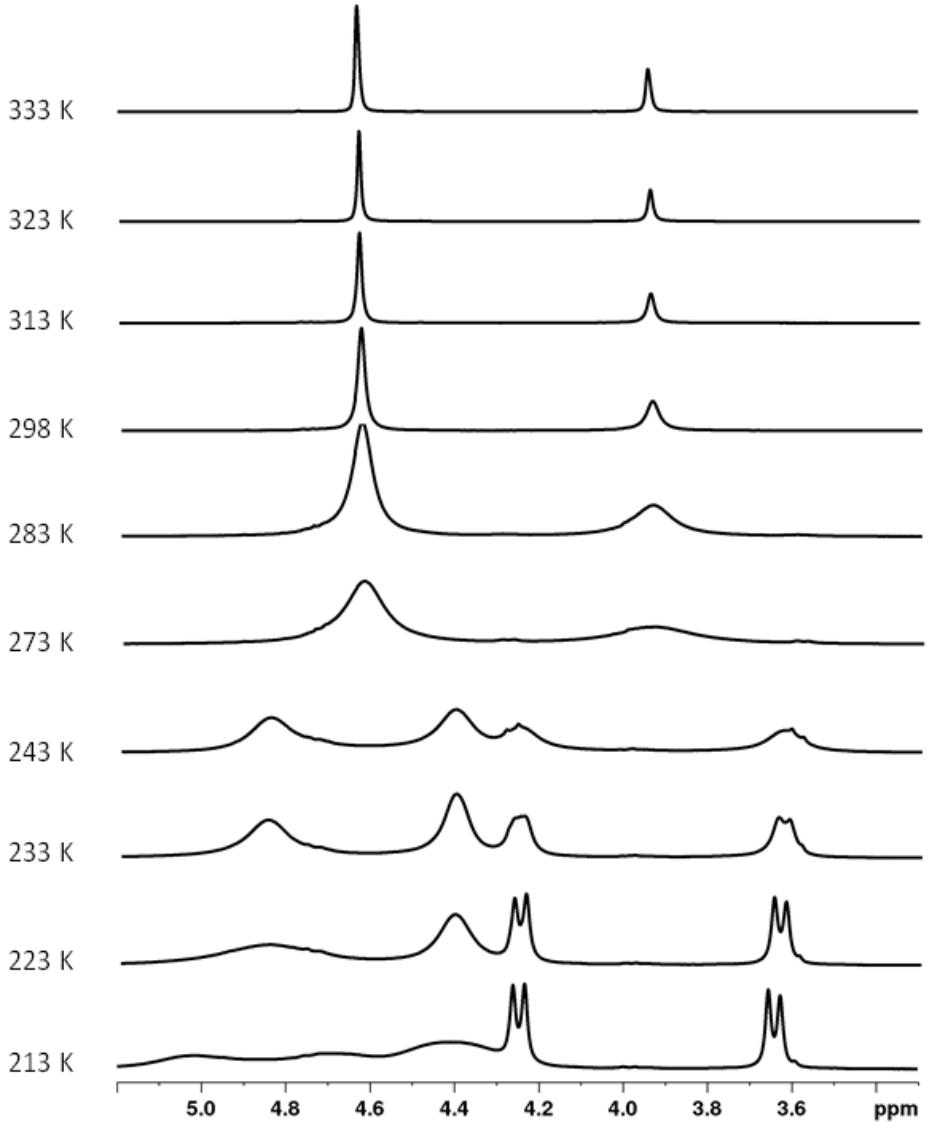


Partial ^{1}H NMR (213 – 298 K, $CDCl_3$, 500 MHz):

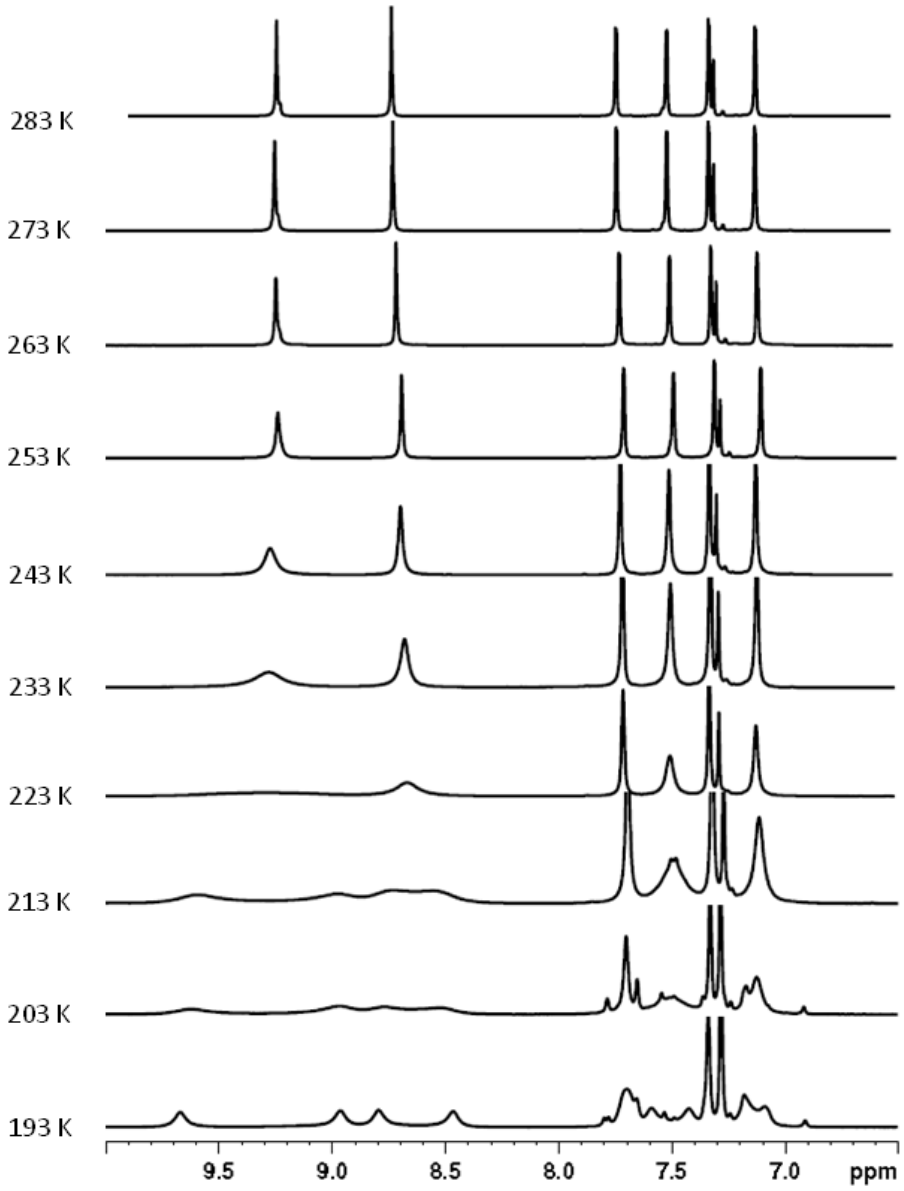


Compound 6:

Partial ^{1}H NMR (213 – 333 K, $CDCl_3$, 500 MHz):

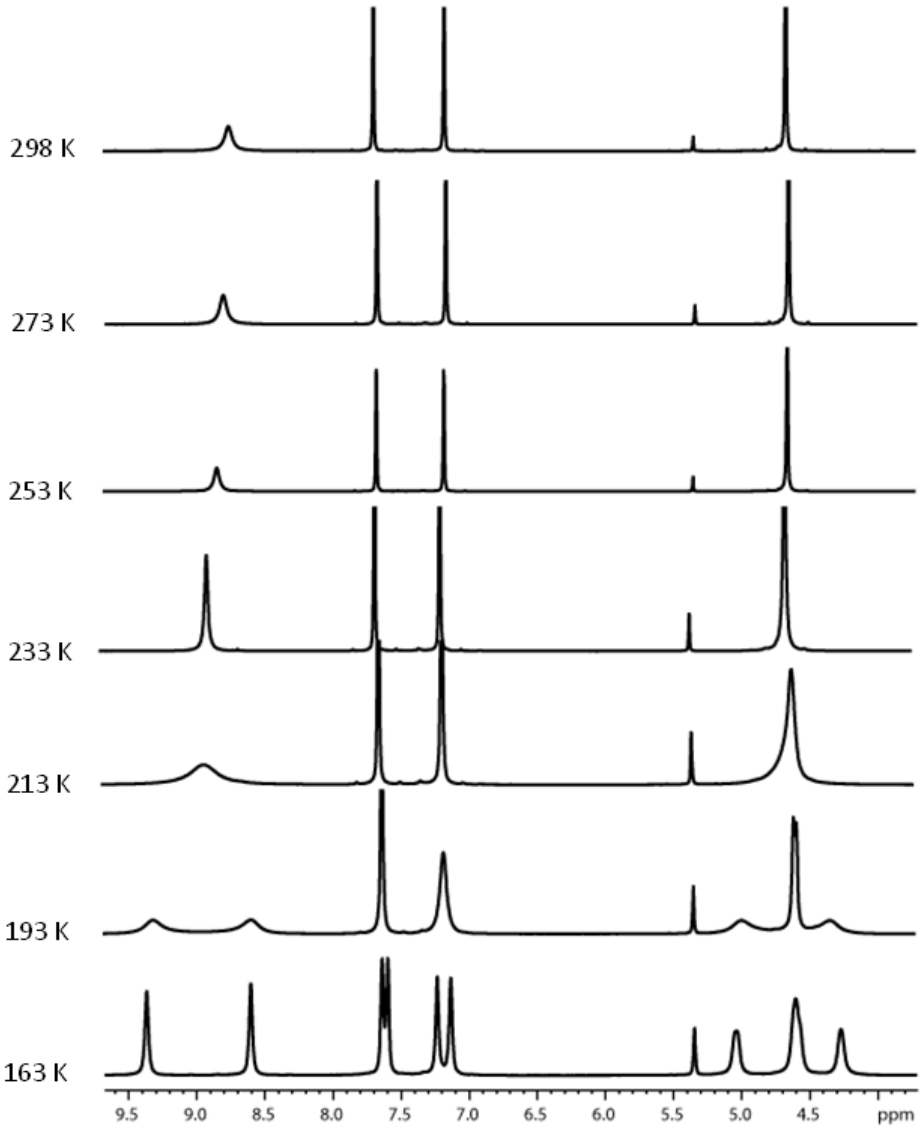


Partial ^{1}H NMR (193 – 283 K, $CDCl_3$, 500 MHz):



Compound 7:

Partial ^{1}H NMR (163 – 298 K, CD_2Cl_2, 500 MHz):



Crystallographic results

Compound 6:

M = 715.03 g·mol^{-1}, monoclinic system, space group $P2_1/a$, a = 13.3707 (2) Å, b = 18.8446 (3) Å, c = 16.9728 (3) Å, β = 107.5447 (16)°, Z = 4, V = 4077.62 (11) Å^3, Dc = 1.165 g·cm^{-3}, μ(Cu-Kα) = 1.51 mm^{-1}, crystal dimensions of 0.27 × 0.18 × 0.12 mm. Data were collected at 180 (2) K on a Xcalibur Onyx CCD diffractometer with graphite monochromated Cu-Kα radiation. The structure was solved by direct methods [1] using the CRYSTALS suite of programs [2, 3] and anisotropically refined by full matrix least squares on F squared value to final R = 0.048 and R_w = 0.098 using 8206 independent reflections (Θ_{max} = 75.9°), 535 parameters and 108 restrains. The positions of disordered functional groups were found from the electron density maps and then placed in appropriate positions. All distances between neighboring atoms and angles were fixed. Site occupancies were refined resulting in full occupation for each disordered group. The structure was deposited into Cambridge Structural Database under number CCDC 1032388.

Compound 7:

M = 745.06 g·mol^{-1}, triclinic system, space group P-1, a = 9.2441 (3) Å, b = 9.4374 (3) Å, c = 11.5116 (4) Å, α = 81.533 (3)°, β = 81.481 (3)°, γ = 87.419 (3)°, Z = 1, V = 982.10 (6) Å^3, Dc = 1.260 g·cm^{-3}, μ(Cu-Kα) = 1.60 mm^{-1}, crystal dimensions of 0.26 × 0.19 × 0.15 mm. Data were collected at 180 (2) K on a Xcalbur Onyx CCD diffractometer with graphite monochromated Cu-Kα radiation. The structure was solved by direct methods [1] using the CRYSTALS suite of programs [2, 3] and anisotropically refined by full matrix least squares on F squared value to final R = 0.039 and R_w = 0.089 using 3937 independent reflections (Θ_{max} = 76.0°), 271 parameters and 36 restrains. The positions of disordered functional groups were found from the electron density maps and then placed in appropriate positions. All distances between neighboring atoms and angles were fixed. Site occupancies were refined resulting in full occupation for each disordered group. The structure was deposited into Cambridge Structural Database under number CCDC 1032387.

Literature

[1] A. Altomare, G. Cascarano, C. Giacovazzo, A. Guagliardi, M. C. Burla, G. Polidori, M. Camalli, Ch. Kabuto, *J. Appl. Cryst.*, **1994**, 27, 435.

[2] P. W. Betteridge, J. R. Carruthers, R. I. Cooper, K. Prout, D. J. Watkin, *J. Appl. Cryst.*, **2003**, 36, 1487.

[3] J. Rohlicek, M. Husak, *J. Appl. Cryst.*, **2007**, 40, 600.