Multifarenes: new modular macrocycles

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Supporting Information

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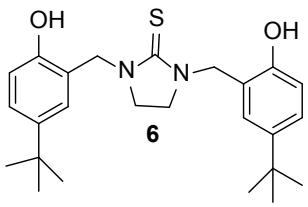
1. General Information

Unless stated otherwise, all chemicals and solvents were purchased from commercial sources and used without further purification. Reactions were carried out using oven dried glassware. Flash chromatography was carried out on Merck Kieselgel 60 (230-400 mesh) as the stationary phase under a positive pressure using LR grade solvents; the procedure includes removal of solvents under reduced pressure. TLC was performed on pre-coated Merck Kieselgel silica gel plates (60 F_{254}, Merck, Germany) monitored by UV light and Iodine. Melting points were measured on a Stuart SMP11 apparatus and are reported uncorrected. Optical rotation was measured on AA-10 polarimeter (Optical Activity Ltd., UK), and is reported as follows: $[\alpha]_D^T$ (c: g/100 mL, solvent). NMR spectra were recorded on Bruker DPX200, AV300, AVIII400, and Bruker AVIII500 instruments. Chemical shifts are reported in parts per million (ppm) from high to low frequency and referenced to the residual solvent resonance. Coupling constants (J) are reported in hertz (Hz). 2D-NMR methods include COSY, HSQC and HMBC. High resolution ESI mass spectrometry was performed with a Water Micromass LCT Premier instrument. HPLC-MS was performed on a Waters LCQ Fleet instrument.

2.1 Syntheses of linear compounds 6, 7 and 8.

2.1.1 Compound 6

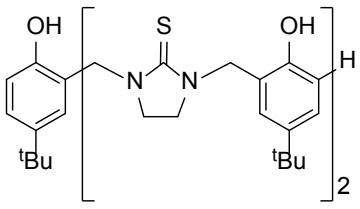


6

A solution of 2-imidazolidenthione, **5** (2 g, 19.6 mmol), 4-tert-butylphenol, **4** (11.8 g, 78.6 mmol), paraformaldehyde (1.6 g, 58.8 mmol) and *p*-toluenesulfonic acid monohydrate (PTSA, 0.75g, 3.9 mmol) in toluene (250 mL) was stirred at 70˚C for 2d. After cooling to room temperature, all volatiles were removed under reduce pressure and the residue was purified over a silica gel column (ethyl acetate/hexane, 1:3), affording compound **6** (7.19 g, 86% yield) as a white solid. M.P. 169-171 ˚C. ^{1}H NMR [400 MHz, $CDCl_3$] δ1.24 (s, 9H, $(CH_3)_3C$-), 3.52 (s, 4H, NCH_2CH_2N), 4.71 (s, 4H, $ArCH_2N$), 6.83 (d, *J*=8.0 Hz, 2H, Ar*H*), 7.03 (s, 2H, Ar*H*), 7.21 (dd, *J*=7.2 Hz, 2H, Ar*H*), 7.31 (bs, 2H, 2 × O*H*). ^{13}C NMR [100 MHz, $CDCl_3$] δ 31.6 ($(CH_3)_3C$-), 34.0 ($(CH_3)_3C$-), 45.7 ($N(CH_2)_2N$), 48.8 ($ArCH_2N$), 117.2 (*C*HArOH), 119.7 (*C*ArOH), 127.2 (^{t}Bu-C*C*HCHCOH(Ar)), 128.0 (^{t}Bu-C*C*HCCOH(Ar)), 142.8 (^{t}Bu-*C*(Ar)), 153.2 (*C*(Ar)-OH), 179.2 (*C*=S). HR-MS: m/z calcd. for $C_{25}H_{33}N_2O_2S$ $[M-H]^-$ 425.2263; found 425.2271.

2.1.2 Compounds 7 and 8

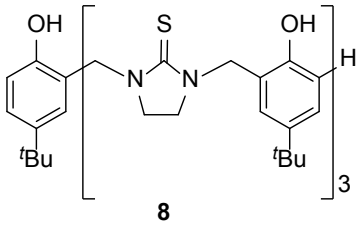
A solution of **5** (1.0 g, 9.8 mmol), **4** (2.2 g, 14.8 mmol), paraformaldehyde (1.18 g, 39.2 mmol) and PTSA (0.62 g, 3.3 mmol) in toluene (250 mL) was stirred at 70˚C for 4d. After cooling to room temperature all volatiles were removed under reduced pressure, the residue was dissolved in dichloromethane (30 mL), washed with sat. aq. sodium bicarbonate and purified over a silica gel column (ethyl acetate/hexane 1:3), affording compound **6** (1.16 g, 28% yield), compound **7** (0.82 g, 24% yield), and compound **8** (0.79 g, 10% yield) as white solids.



7

Compound 7: M.P. 150-152 ˚C. ^{1}H NMR[400 MHz, $CDCl_3$] δ1.24 (s, 9H, $(CH_3)_3C$-), 1.27 (s, 18H,), 3.49-3.60 (m, 8H, NCH_2CH_2N), 4.73-4.76 (m, 8H, $ArCH_2N$), 6.81 (d, *J*=8.8 Hz, 2H, Ar(C*H*COH), 7.07 (s, 2H, Ar*H*), 7.21 (d, *J*=8.8, 2H, Ar*H*), 7.71 (s, 2H, 2 × O*H*), 7.91 (s, 1H, O*H*). ^{13}C NMR [100 MHz, $CDCl_3$] δ 31.5 ($(CH_3)_3C$-), 31.6 ($(CH_3)_3C$-), 33.9 ($(CH_3)_3C$-), 45.6 ($N(CH_2)_2N$), 46.2 ($N(CH_2)_2N$), 47.5 ($ArCH_2N$), 48.8 ($ArCH_2N$), 116.9, 119.9, 121.8, 127.0, 128.1, 128.6, 142.5 (^{t}Bu-*C*(Ar)), 142.8

(^{t}Bu-*C*(Ar)), 151.5 (*C*(Ar)-OH), 153.3 (*C*(Ar)-OH), 179.6 (*C*=S). HR-MS: m/z calcd. for $C_{40}H_{53}N_4O_3S_2$ $[M-H]^-$701.3559; found 701.3589.



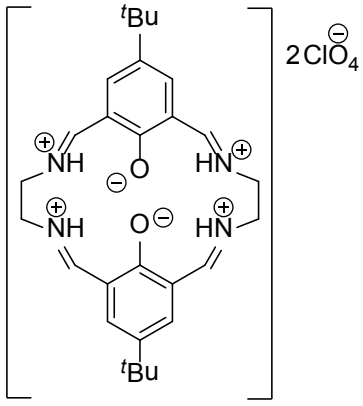
8

Compound **8**: M.P. 131-133 ˚C. ^{1}H NMR [400 MHz, $CDCl_3$] δ1.46 (s, 18 H, $(CH_3)_3C$-), 1.49 (s, 27 H), 3.70-3.80 (m, 12, NCH_2CH_2N), 4.97 (s, 12 H, $ArCH_2N$), 7.04 (d, J = 8.0 Hz, 2 H, Ar*H*), 7.40-7.52 (m, 10 H, Ar*H*), 7.94 (s, 1 H, O*H*), 8.24 (s, 1 H, O*H*). ^{13}C NMR [100 MHz, $CDCl_3$] δ 31.6 ($(CH_3)_3C$-), 31.7 ($(CH_3)_3C$-), 34.1 ($(CH_3)_3C$-), 45.7 ($N(CH_2)_2N$), 46.3 ($N(CH_2)_2N$), 47.4, 47.9 ($ArCH_2N$), 49.1 ($ArCH_2N$), 117.1, 119.9, 121.8, 122.2, 127.2, 128.1, 128.6, 142.6 (^{t}Bu-*C*(Ar)), 142.7 (^{t}Bu-*C*(Ar)), 151.7 (*C*(Ar)-OH), 153.5 (*C*(Ar)-OH), 179.9 (*C*=S). HR-MS: m/z calcd. for $C_{55}H_{75}N_6O_4S_3$ $[M-H]^-$ 979.5012; found 979.4979.

2.2 Synthesis of Multifarene [2,2] (1)

Multifarene-[2,2], **1**, was synthesized in three steps starting from 2,6-diformyl-4-tert-butylphenol **9** and 1,2-ethylenediamine.

2.2.1 Synthesis of 10

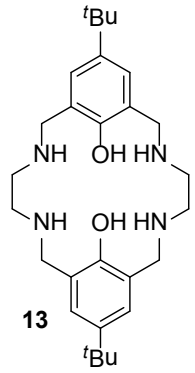


10

To a boiling solution of **9** (0.412 g, 2 mmol), $NaClO_4$ (1.0 g, 8 mmol) and acetic acid (0.25 mL, 4 mmol) in methanol (39 mL) a solution of 1,2-ethylenediamine(0.2 mL, 2 mmol) in methanol (20 mL) was added drop-wise over a period of 2h. The reaction was refluxed for another 30 min, cooled to room temperature and the solvent was reduced to half volume under reduced pressure. The solution was allowed to stand for 24h and the precipitate was filtered and washed with methanol and diethyl ether, affording **10** as a yellow orange solid.[1] The filtrate was evaporated to dryness and the remaining residue was suspended in methanol, filtered and washed with hot methanol affording a second crop of pure product in combined 70-75% yield. ^{1}H NMR [400MHz, CD_3CN] δ 1.31 (s, 18 H, $(CH_3)_3C$-), 4.09 (s, 8 H, NCH_2CH_2N), 7.99 (s, 4 H, Ar*H*), 8.66 (s. 4 H, C*H*=N), 14.51 (bs, 4 H, N*H*). ^{13}C NMR [100MHz, CD_3CN] δ 31.2 ($(CH_3)_3C$-), 34.7 ($(CH_3)_3C$-),

51.7 (N(CH_2)$_2$N), 118.2 (Ar*C*CH=N), 138.9 (CH*C*(Ar)), 143.7 (^{t}Bu-*C*(Ar)), 171.0 (Ar*C*-O$^-$), 177.6 (Imine *C*H).

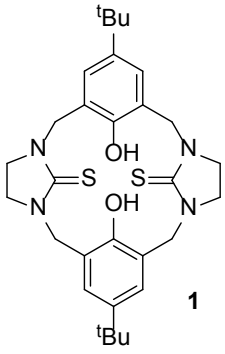
2.2.2 Synthesis of cyclic tetra-amine13



13

To a stirred suspension of **10** (1.32g, 2 mmol) in methanol (10 mL) at 0˚C was slowly added sodium borohydride (0.46g, 12 mmol). The yellow suspension turned to a clear solution as the reaction proceeded. The reaction was stirred for 1h and quenched with water, extracted with dichloromethane (3×15 mL), washed with water, brine and dried over anhydrous sodium sulfate. The combined organic layers were concentrated to give crude **13** (90-95% yield), which was subjected to the next step without further purification. ^{1}H NMR [400 MHz, $CDCl_3$] δ 1.25 (s, 18 H, (CH_3)$_3$C-), 2.86 (s, 8 H, NCH_2CH_2N), 3.84 (s, 8 H, ArCH_2N), 7.00 (s, 4 H, Ar*H*).^{13}C NMR [100 MHz, $CDCl_3$] δ 31.7 ((*C*H$_3$)$_3$C-), 34.0 ((CH$_3$)$_3$*C*-), 48.9 (N(*C*H$_2$)$_2$N), 52.8 (Ar*C*H$_2$N), 124.2 (CH$_2$*C*(Ar)), 125.5 (*C*H(Ar)), 141.4 (^{t}Bu-*C*(Ar)), 154.3 (*C*(Ar)-OH). HR-MS: m/z calcd. for $C_{28}H_{45}N_4O_2$ $(M+H)^+$ 469.3543; found 469.3561.

2.2.3 Synthesis of Multifarene[2,2] (1)



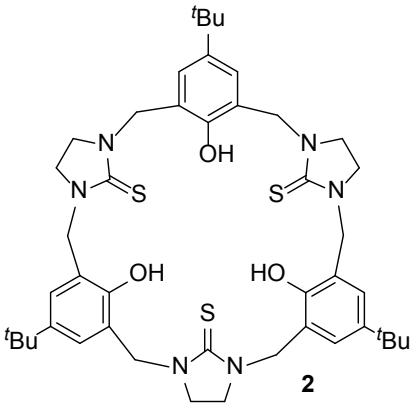
1

To a solution of **13** (1 mmol) in anhydrous THF (10 mL) was added dropwise a solution of 1,1′-thiocarbonyldiimidazole (2.2mmol) in anhydrous THF (5 mL) and the mixture was stirred at room temperature for 3h. The volatiles were removed under reduced pressure and the residue was dissolved in a minimum amount of dichloromethane and diluted with an excess of diethyl ether in order to precipitate out the product. The resulting suspension was stirred for 5 minutes, filtered and washed thoroughly with diethyl ether. The creamy white solid was dried under vacuum to afford pure MF[2.2], **1**, in 65-70% yield. M.P. 245 ˚C (dec). ^{1}H NMR [400 MHz, $CDCl_3$] δ1.25 (s, 18H, (CH_3)$_3$C-), 2.66-2.70 (m, 4H, CH_aH$_b$CH_aH$_b$N), 3.25-3.30(m, 4H, NCH$_a$$H_bCH_a$$H_b$N), 3.76 (d, 4H, J = 14.2 Hz, ArCH_aH$_b$N), 6.08 (d, 4H, J = 14.2 Hz, ArCH_aH$_b$N), 7.03 (s, 4H, Ar*H*), 7.06 (s, 2H, 2 × O*H*). ^{13}C NMR [100 MHz, $CDCl_3$] δ 31.7 ((*C*H$_3$)$_3$C-), 33.9 ((CH$_3$)$_3$*C*-), 44.1 (N(*C*H$_2$)$_2$N), 49.4 (Ar*C*H$_2$N), 121.4

(CH_2C(Ar)), 128.5 (CH(Ar)), 141.6 (^{t}Bu-C(Ar)), 152.6 (C(Ar)-OH), 180.9 (C=S). HR-MS: m/z calcd. for $C_{30}H_{41}N_4O_2S_2$ $(M+H)^+$ 553.2671; found 553.2689.

2.3 Synthesis of Multifarene[3,3], 2.

2.3.1 Procedure A: A mixture of compound **7** (0.303 g, 0.43 mmol), **5** (0.044 g, 0.43 mmol), paraformaldehyde (0.065 g, 2.16 mmol) and PTSA (0.041 g, 0.22 mmol) in toluene (10 mL) was heated to 60˚C for 48h. The mixture was cooled to room temperature and the volatiles were removed under reduced pressure. The crude solid product was dissolved in hot aqueous solution of NaOH (60 mL, 1M), and the suspension was filtered to remove insoluble impurities. The filtrate was neutralized to pH 7 by the addition of aq. HCl, and the resultant precipitate was filtered, washed with water, methanol and dried under vacuum affording MF[3,3], **2** (62% yield) as an off-white solid. M.P. 225 ˚C (dec). ^{1}H NMR [400 MHz, $CDCl_3$] δ 1.23 (s, 27H, $(CH_3)_3$C-), 3.51 (s, 12H, NCH_2CH_2N), 4.78 (bs, 12H, $PhCH_2N$), 7.31 (s, 6 H,Ar*H*), 7.79 (s, 3H, 3 × O*H*). ^{13}C NMR [100 MHz, $CDCl_3$] δ 31.5 ($(CH_3)_3$C-), 34.0 ($(CH_3)_3C$-), 46.6 ($N(CH_2)_2N$), 47.8 ($ArCH_2N$), 122.4 (CH_2C(Ar)), 129.5 (CH(Ar)), 142.6 (^{t}Bu-C(Ar)), 151.6 (C(Ar)-OH), 180.9 (C=S). HR-MS: m/z calcd. for $C_{45}H_{61}N_6O_3S_3$ $(M+H)^+$ 829.3960; found 829.3967.

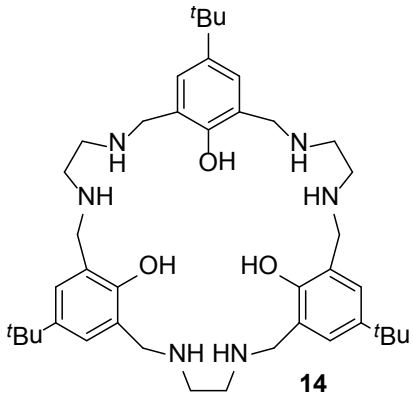


2.3.2 Procedure B: Similarly to the synthesis of **1**, MF[3.3] was also prepared in three steps starting from 2,6-diformyl-4-tert-butylphenol **9** and 1,2-diaminoethane.

2.3.2.1 Synthesis of 14

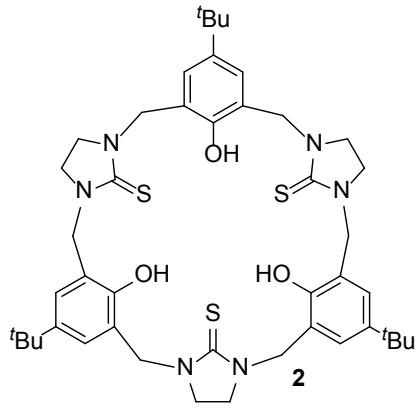
To a vigorously stirred solution of **9** (0.62g, 3 mmol) in MeCN (120 mL) was slowly added a solution of 1,2-diaminoethane (0.18g, 3 mmol) in methanol (80 mL) at -10˚C. The mixture was kept at that temperature for 5h and filtered, affording polyimine **11** (85-90% yield) as a yellow solid, which was used directly in the next step.

Reduction of **11** was performed in the same manner as described for **10**. $NaBH_4$ (1.75g, 18 eq) in methanol (50 mL) at



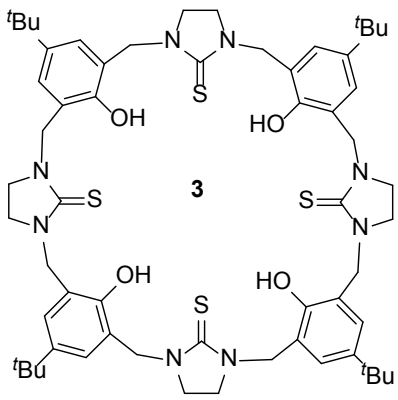
0˚C, affording hexamine **14** (90-95%), which was subjected to the next reaction without further purification. ^{1}H NMR [400 MHz, $CDCl_3$] δ 1.26 (s, 27H, $(CH_3)_3C$-), 2.76 (s, 12 H, NCH_2CH_2N), 3.82 (S, 12H, CH_2N), 6.96 (s, 6H, Ar*H*). ^{13}C NMR [100 MHz, $CDCl_3$] δ 31.6 ($(CH_3)_3C$-), 33.9 ($(CH_3)_3C$-), 47.9 ($N(CH_2)_2N$), 51.2 ($ArCH_2N$), 123.9 (CH_2C(Ar)), 125.2 (*C*H(Ar)), 141.1 (^{t}Bu-*C*(Ar)), 154.2 (*C*(Ar)-OH).

2.3.2.2 Synthesis of Multifarene[3,3], 2.



MF[3,3], **2**, was prepared using the same conditions employed for the synthesis of MF[2,2], **1** (procedure **2.2.3**). A solution of **14** (1.41g, 2 mmol) in THF (30 mL) was reacted with 3.3 eq. of 1,1′-thiocarbonyldiimidazole (1.17g, 6.6 mmol). The resulting crude product was dissolved in ethyl acetate and filtered to remove suspended solid impurities. The solvent was removed under reduced pressure and the residue was recrystallized from ethyl acetate/hexane to give **2** in 50% yield.

2.4. Synthesis of Multifarene[4.4], 3.



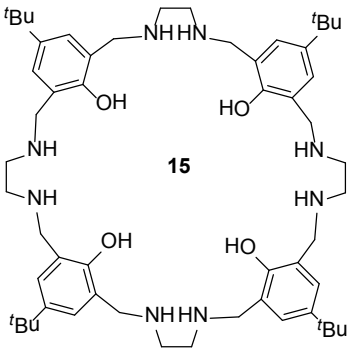
2.4.1 Procedure A (one-pot synthesis). A solution of **4** (5 g, 0.033 mol), **5** (10.2 g, 0.1 mol), paraformaldehyde (10 g, 0.34 mol) and PTSA (3.17 g, 0.017 mol) in toluene (500 mL) was heated to 55˚C for 6d and then cooled to room temperature. The solvent was removed under reduced pressure, the solid residue was dissolved in hot 1M aqueous solution of NaOH (500 mL), and all insoluble impurities were removed by filtration.The filtrate was neutralized by HCl to pH 7 and the precipitate was filtered and washed with water, methanol and dried under vacuum to give MF[4,4], **3** in 67% yield in the form of a white solid. M.P. 216-220 ˚C (dec). ^{1}H NMR [500MHz, $CDCl_3$] δ 1.27 (s, 36H, $(CH_3)_3C$-), 3.58 (s, 16H, NCH_2CH_2N), 4.79 (s, 16H, $PhCH_2N$), 7.27 (s, 8H, Ar*H*), 8.26 (bs, 4H, 4 × O*H*). ^{13}C NMR [125 MHz, CD_2Cl_2] δ 31.2 ($(CH_3)_3C$-), 33.7 ($(CH_3)_3C$-), 46.1 ($N(CH_2)_2N$), 47.5 ($ArCH_2N$), 122.0 (CH_2C(Ar)), 127.7 (*C*H(Ar)), 142.2 (^{t}Bu-*C*(Ar)), 151.5

(*C*(Ar)-OH), 180.6 (*C*=S). HR-MS: m/z calcd. for $C_{60}H_{80}N_8O_4S_4$ $[M+Na]^+$1127.5083; found 1127.5076.

2.4.2 Procedure B (2 steps). A suspension of **8** (0.239 g, 0.24 mmol), **5** (0.0253 g, 0.24 mmol) paraformaldehyde (0.037 g, 1.22 mmol) and PTSA (0.023 g, 0.12 mmol) in toluene (10 mL) was heated to 60˚C for 48h and then cooled to room temperature. The solvent was removed under reduced pressure, the residue was dissolved in hot 1M aqueous solution of NaOH (100 mL) and all insoluble impurities were removed by filtration.The filtrate was neutralized to pH 7 by the addition of HCl, and the precipitate was filtered and washed with water, methanol and dried under vacuum affording MF[4,4], **3** (180 mg, 72% yield) as a white solid.

2.4.3 Procedure C (3 steps)

2.4.3.1 Synthesis of 15



Compound **9** (0.618 g, 3.0 mmol) was mixed with $Mg(OAc)_2{\cdot}4H_2O$ (0.321 g, 1.5 mmol) and $Mg(NO_3)_2{\cdot}6H_2O$ (0.384 g, 1.5mmol) in methanol (300 mL) and heated to reflux for 15 min. A solution of 1,2-diaminoethane (0.180 g, 3.0mmol) in methanol (12 mL) was slowly added over a period of 4h and the mixture was refluxed for another 4h. The resultant orange-yellow complex **12** with magnesium(II) was precipitated and filtered, washed with methanol and chloroform and dried in air. This product (50% yield) was taken to the next step without further purification.

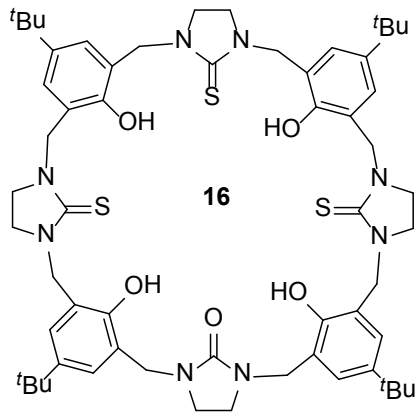
A suspension of crude **12** (0.35 g, 0.37 mmol) in methanol (5.0 mL) was cooled to 15˚C. Solid $NaBH_4$ (0.14 g, 10 eq) was added in small portions over a period of 1h, the mixture was stirred for 1h and the resultant colorless solution was filtered to remove any suspended material. The filtrate was diluted with water (5.0 mL), acidified to pH 2 with HCl (4 M) and mixed with an aq. solution (5.0 mL) of the disodium salt of ethylenediaminetetraacetate (Na_2H_2EDTA, 0.1 g) and aqueous ammonia. The solution was extracted with chloroform (3×20 mL), the combined organic layer was washed with water and dried over Na_2SO_4 to afford **15** (0.31g, 90%). ^{1}H NMR [400 MHz, $CDCl_3$] δ 1.21 (s, 36H, $(CH_3)_3C$-), 1.99 (s, 8H, N*H*CH_2CH_2N*H*), 2.72 (s, 16H, NHCH_2CH_2NH), 3.78 (S, 16H, CH_2NH), 6.93 (s, 8H, Ar*H*). ^{13}C NMR [100 MHz, $CDCl_3$] δ

31.6 ((*C*H$_3$)$_3$C-), 33.9 ((CH$_3$)$_3$*C*-), 48.1 (N(*C*H$_2$)$_2$N), 51.4 (Ar*C*H$_2$N), 123.8 (CH$_2$*C*(Ar)), 125.2 (*C*H(Ar)), 141.1 (^{t}Bu-*C*(Ar)), 154.3 (*C*(Ar)-OH).

2.4.3.2 Synthesis of Multifarene[4.4], 3.

By following the procedure of **2.2.3** crude **15** was subjected to reaction with 4.4 eq of TCDI to furnish **3** (0.18g, 50% yield).

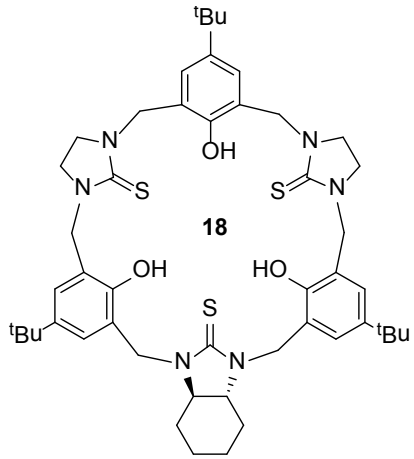
2.5. Synthesis of hetero-Multifarene[4, 3$_S$, 1$_O$], 16.



Compound **8** (0.832g, 0.85mmol), paraformaldehyde (0.128g, 4.25 mmol), PTSA (0.081g, 0.42 mmol) and imidazolidinone (0.073 g, 0.85 mmol) were mixed in toluene (25 mL). The reaction mixture was heated to 60˚C for 48h and then cooled to room temperature.The solvent was removed under reduced pressure, the residue was dissolved in hot 1M aqueous solution of NaOH (50 mL), and the obtained suspension was filtered to remove solid impurities. The filtrate was neutralized to pH 7 by conc. aq. HCl and the precipitate was filtered, washed with water and methanol and dried under vacuum, to afford **16** (0.52 g, 56% yield) in the form of an off-white solid. M.P. 186-188 ˚C. ^{1}H NMR [500 MHz, $CDCl_3$,] δ 1.25-1.27 (broad s, 36H, (C*H*$_3$)$_3$C-), 3.40 (s, 4H, NC*H*$_2$C*H*$_2$NCO), 3.55 (s, 12H, NC*H*$_2$C*H*$_2$NCS), 4.27 (s, 4H, ArC*H*$_2$N(C=O)), 4.77 (s, 12H, ArC*H*$_2$N(C=S)), 7.05 (s, 3H, Ar*H*), 7.14-7.37 (m, 8H, Ar*H*), 8.27 (s, 4H, 4 × O*H*). ^{13}C NMR [125 MHz, CD_3Cl, via HMBC experiment] δ 31.6 ((*C*H$_3$)$_3$C-), 34.0 ((CH$_3$)$_3$*C*-), 43.4 (N(*C*H$_2$)$_2$NO), 46.2 (N(*C*H$_2$)$_2$NS), 47.2 (Ar*C*H$_2$N), 128.5 (*C*H(Ar)), 142.4 (^{t}Bu-*C*(Ar)), 151.9 (*C*(Ar)-OH), 162.8 (*C*=O), 180.8 (*C*=S). HR-MS: m/z calcd. for $C_{60}H_{81}N_8O_5$ $[M+H]^+$1089.5492; found 1089.5448.

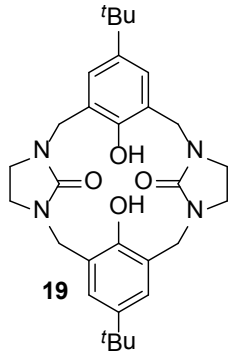
2.6. Synthesis of chiral hetero-Multifarene[3,2,1], 18. *(R,R)-trans*-4,5-tetramethyleneimidazolidine-2-thione, **17**,[4] (10 mg, 0.064 mmol), compound **7** (45 mg, 0.064 mmol), paraformaldehyde (4 mg, 0.133 mmol) and PTSA (7 mg, 0.037 mmol) were heated in toluene (5 mL)at70˚Cfor 3d. The mixture was cooled to room temperature and the solvent was removed under reduced pressure. The residue was dissolved in dichloromethane (5 mL) and washed with saturated aq. sodium bicarbonate (5 mL).The solvent was removed again to give **18** (46.4 mg, 82% yield). M.P. 216-220 ˚C. $[\alpha]_D^{22}$ = +30.0 (*c*: 0.4, chloroform). ^{1}H-NMR [500

MHz, $CDCl_3$]: δ1.21-1.31 (m, 4H,), 1.23 (s, 18H, 2 × (CH_3)$_3$C-), 1.26 (s, 9H, (CH_3)$_3$C-), 1.59 (s, 2H), 1.81 (s, 2H), 2.88-2.96 (broad m, 2H), 3.55 (s, 8H, NCH_2CH_2N), 4.78 (m, 8H, ArCH_2N), 4.88 (m, 2H, NC*H*C*H*N), 7.16-7.28 (m, 6H, Ar*H*), 8.29 (3H, broad s, 3 × O*H*).^{13}C-NMR [125MHz, CDCl3] δ 21.4 (CH_2CH_2-cyclohexyl) , 24.2 (CHCH_2-cyclohexyl), 31.4 ((CH_3)$_3$C-), 33.8 ((CH_3)$_3$*C*-), 46.1 (N(CH_2)$_2$N), 47.5 (ArCH_2N), 122.0 (CH_2C(Ar)), 125.2, 127.9, 128.2 (*C*H(Ar)), 129.0, 137.8, 142.0 (cyclohexyl-^{t}Bu-*C*(Ar)), 142.3 (^{t}Bu-*C*(Ar)), 151.3 (*C*(Ar)-OH), 151.6 (*C*(Ar)-OH), 180.2 (cyclohexyl-*C*=S), 180.4 (*C*=S). HR-MS: m/z calcd. for $C_{49}H_{67}N_6O_3S_3$ $[M+H]^+$883.4437; found 883.4465.



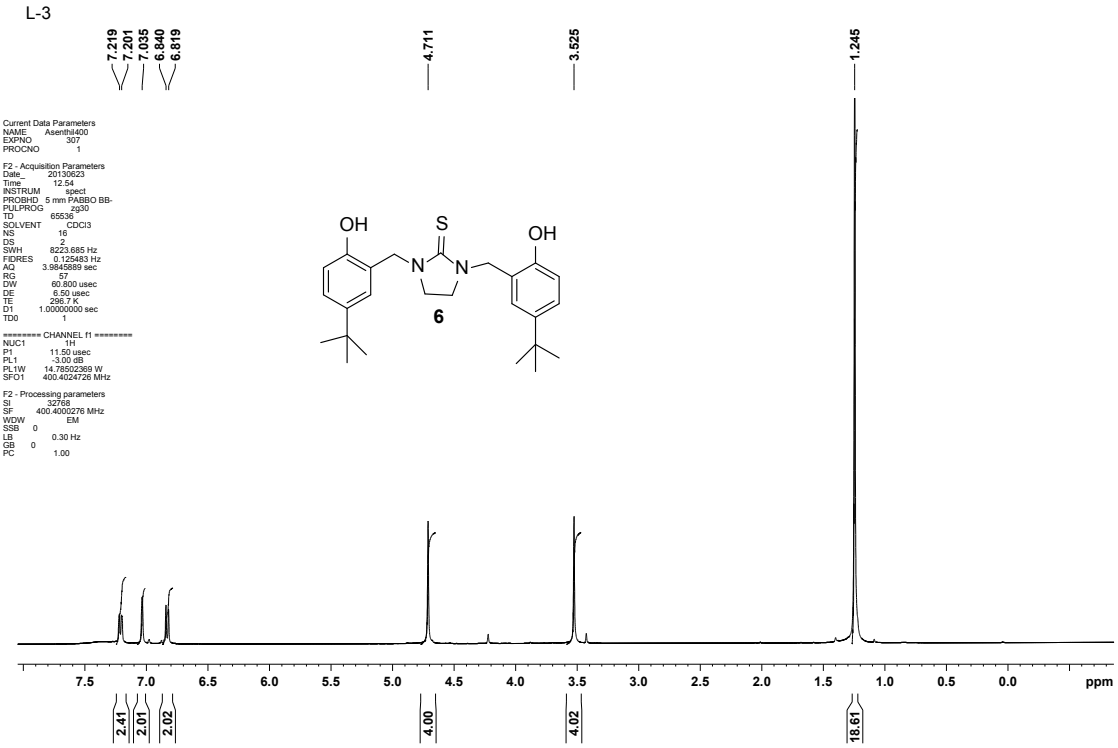
2.7. Synthesis of Multifarene[2,2$_O$], 19.

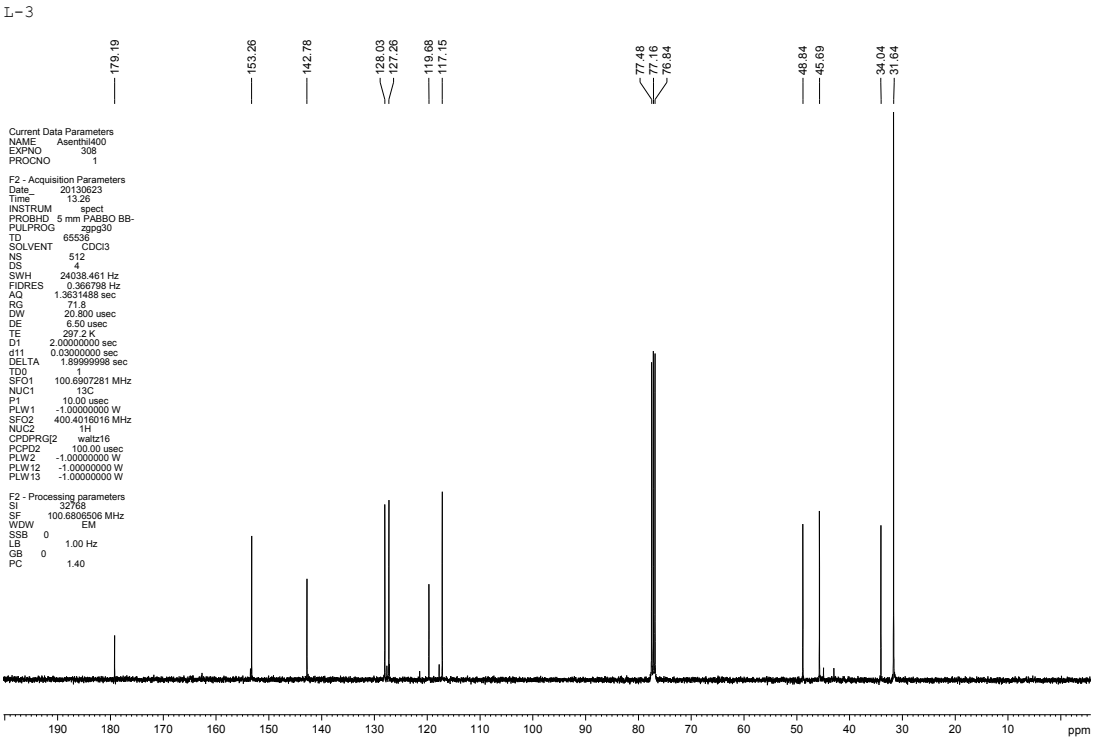
A solution of 1,1′-carbonyldiimidazole (45 mg, 0.28mmol) in dry THF (1 mL) was added drop-wise to a solution of **13** (40.0 mg, 0.085mmol) in dry THF (1mL) under nitrogen and the mixture was stirred at RT for 2.5h. The solvent was removed under reduced pressure, and the residue was dried overnight under high vacuum. Chromatography on a preparative silica gel plate with ethyl acetate/hexane (1:1) afforded **19** (R_f=0.4, 22mg, 49% yield). M.P. 228-234 ˚C (dec). ^{1}H NMR [500 MHz, $CDCl_3$, at –33˚C] *δ* 1.20 (s, 18H, (CH_3)$_3$C-), 2.88 (s, 4H), 3.26 (s, 4H, (N(CH_2)$_2$N), 3.47 (d, *J* = 7Hz, 4H, ArCH_aH$_b$N), 5.23 (d, *J* = 7Hz, 4H, ArCH$_a$$H_b$N), 6.94 (s, 4H, Ar*H*), 8.67 (s, 2H, 2 × O*H*). ^{13}C NMR [125MHz, $CDCl_3$] *δ* 31.9 ((CH_3)$_3$C-), 34.1 ((CH_3)$_3$*C*-), 45.0 (N(CH_2)$_2$N), 46.1 (ArCH_2N), 122.8 (CH_2C(Ar)), 128.5 (*C*H(Ar)), 140.7 (^{t}Bu-*C*(Ar)), 152.8 (*C*(Ar)-OH), 161.2 (*C*=O). HR-MS: m/z calcd. for $C_{30}H_{41}N_4O_4$ $[M+H]^+$521.3128; found 521.3127.



3. NMR and Mass spectra

Compound 6





Elemental Composition Report **Page 1**

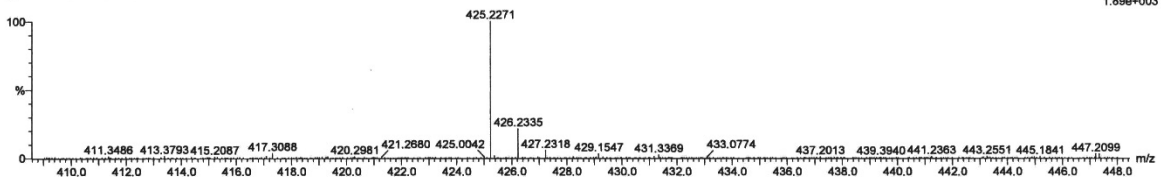
Single Mass Analysis
Tolerance = 50.0 mDa / DBE: min = -1.5, max = 50.0
Element prediction: Off
Number of isotope peaks used for i-FIT = 3

Monoisotopic Mass, Even Electron Ions
35 formula(e) evaluated with 11 results within limits (up to 4 best isotopic matches for each mass)
Elements Used:
C: 22-27 H: 30-40 N: 0-3 O: 0-3 S: 0-3

24-Feb-2009
K_1160n 56 (1.049) Cm (55:56-39)

GP73-3-f2

Keinan
TOF MS ES-
1.89e+003



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Maximum:		50.0	10.0	50.0						
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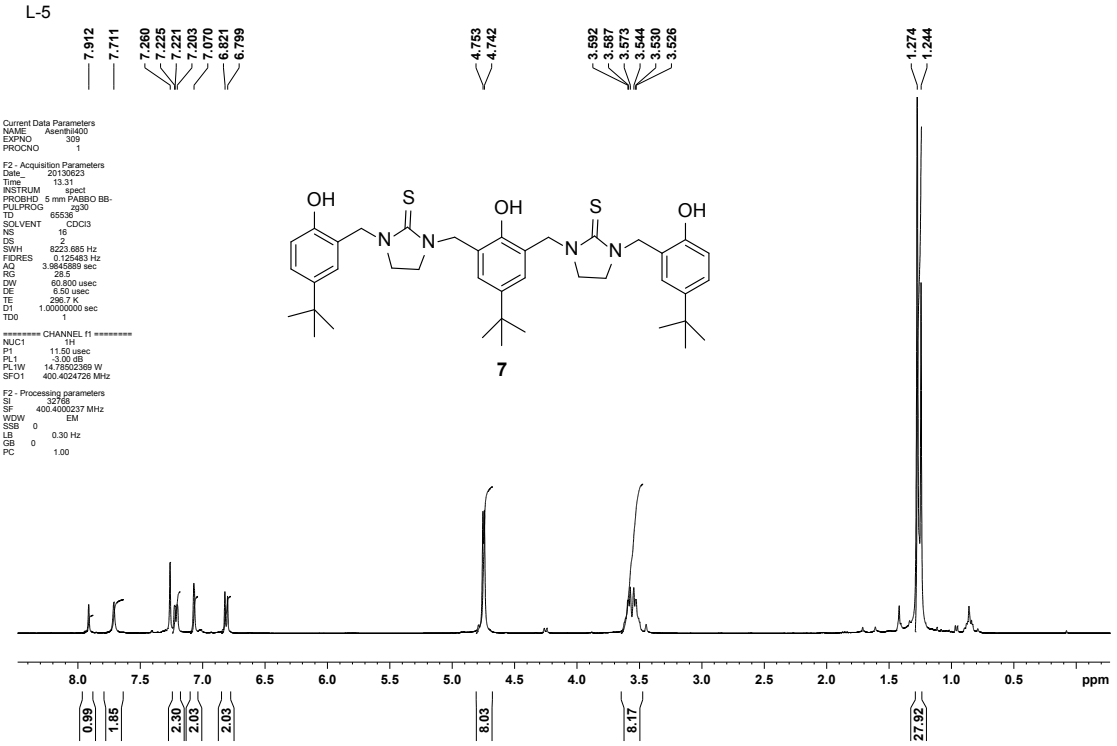
	425.2150	12.1	28.5	10.5	46.7	C26	H33	O3	S	
	425.2514	-24.3	-57.1	9.5	67.3	C27	H37	O2	S	
	425.2296	-2.5	-5.9	5.5	74.9	C22	H37	N2	O2	S2

Compound 7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7.260
7.225
7.221
7.203
7.070
6.821
6.799
4.753
4.742
3.592
3.587
3.573
3.544
3.530
3.526
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1.244
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PROCNO 1
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Time 13.31
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PULPROG zg30
TD 65536
SOLVENT CDCl3
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DS 2
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FIDRES 0.125483 Hz
AQ 3.9845889 sec
RG 28.5
DW 60.800 usec
DE 6.50 usec
TE 296.7 K
D1 1.00000000 sec
TD0 1
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PL1 -3.00 dB
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SFO1 400.4024726 MHz
F2 - Processing parameters
SI 32768
SF 400.4000237 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00
OH
S
N
N
OH
S
N
N
OH
7
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
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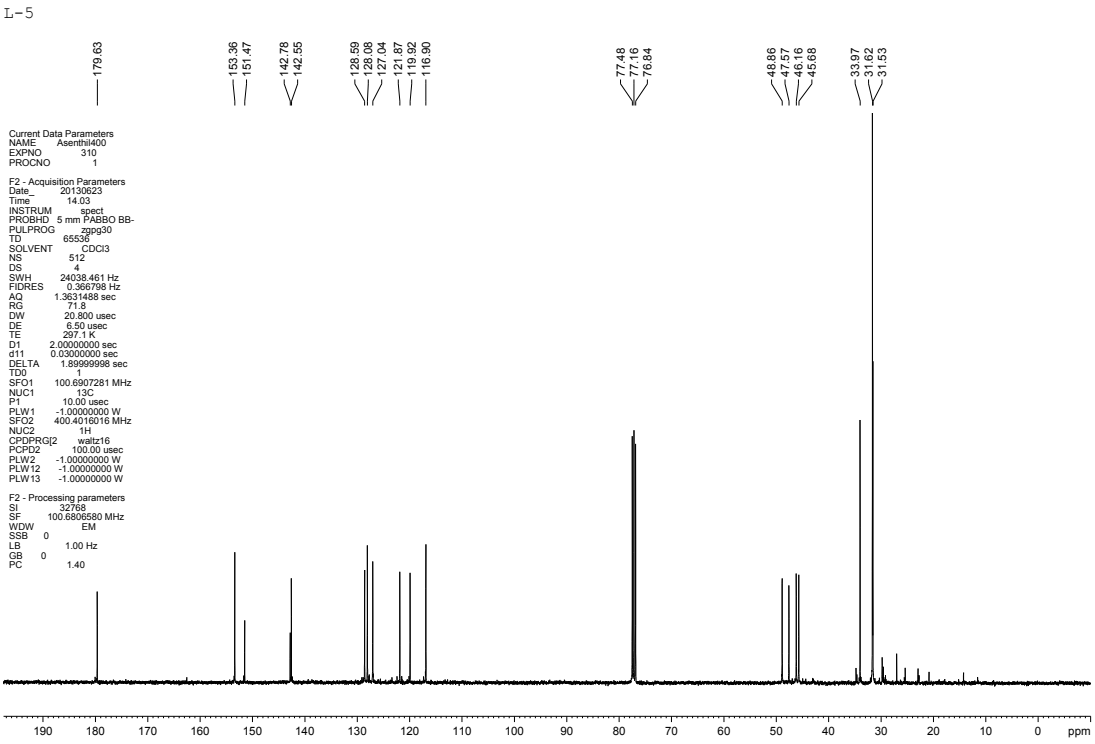
2.30
2.03
2.03
8.03
8.17
27.92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153.36
151.47
142.78
142.55
128.59
128.08
127.04
121.87
119.92
116.90
77.48
77.16
76.84
48.86
47.57
46.16
45.68
33.97
31.62
31.53
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EXPNO 310
PROCNO 1
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Time 14.03
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SOLVENT CDCl3
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FIDRES 0.366798 Hz
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RG 71.8
DW 20.800 usec
DE 6.50 usec
TE 297.1 K
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d11 0.03000000 sec
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P1 10.00 usec
PLW1 -1.00000000 W
SFO2 400.4016016 MHz
NUC2 1H
CPDPRG[2 waltz16
PCPD2 100.00 usec
PLW2 -1.00000000 W
PLW12 -1.00000000 W
PLW13 -1.00000000 W
F2 - Processing parameters
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SF 100.6806580 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 1.40
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180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm

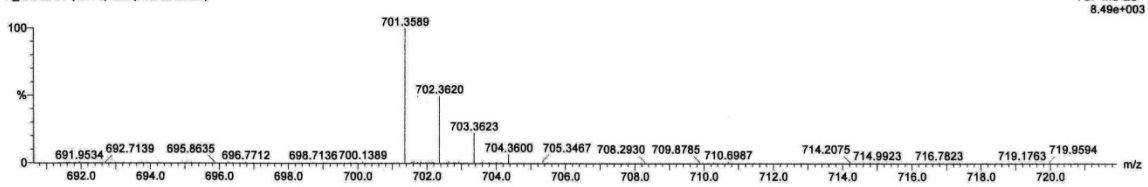
Elemental Composition Report **Page 1**

Single Mass Analysis
Tolerance = 50.0 mDa / DBE: min = -1.5, max = 50.0
Element prediction: Off
Number of isotope peaks used for i-FIT = 3

Monoisotopic Mass, Even Electron Ions
67 formula(e) evaluated with 19 results within limits (up to 4 best isotopic matches for each mass)
Elements Used:
C: 35-45 H: 50-60 N: 1-5 O: 1-5 S: 0-3
06-Apr-2009
K_1250n 81 (0.818) Cm (79:105-20:29)

GP76-b3

Keinan
TOF MS ES-
8.49e+003



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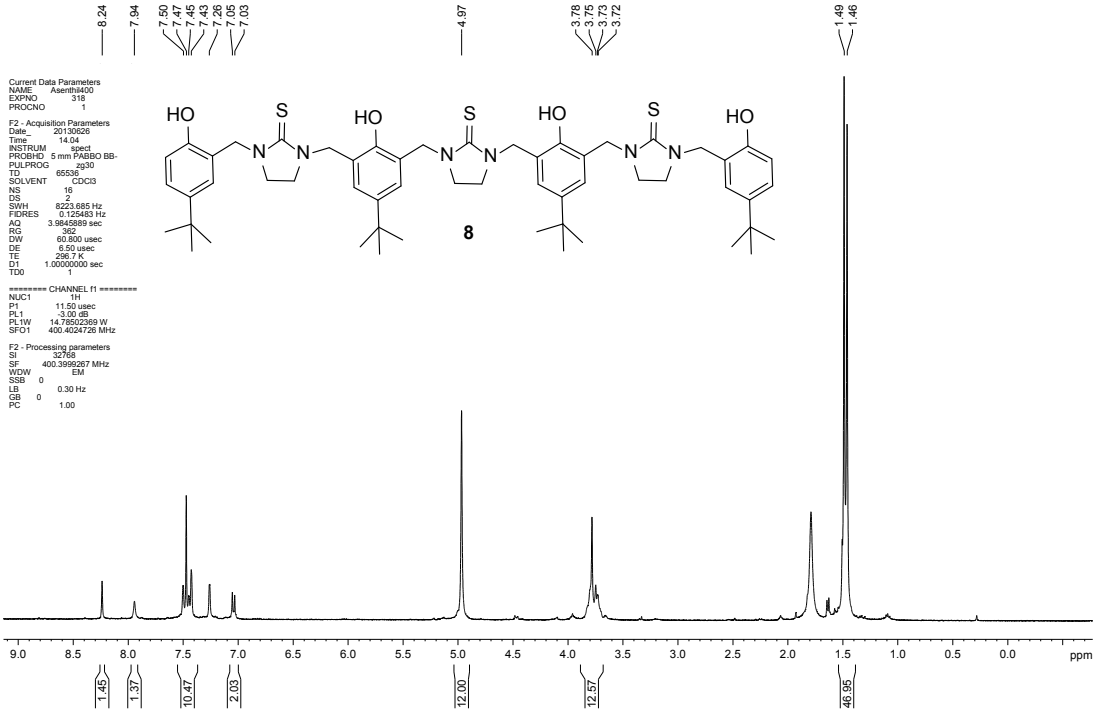
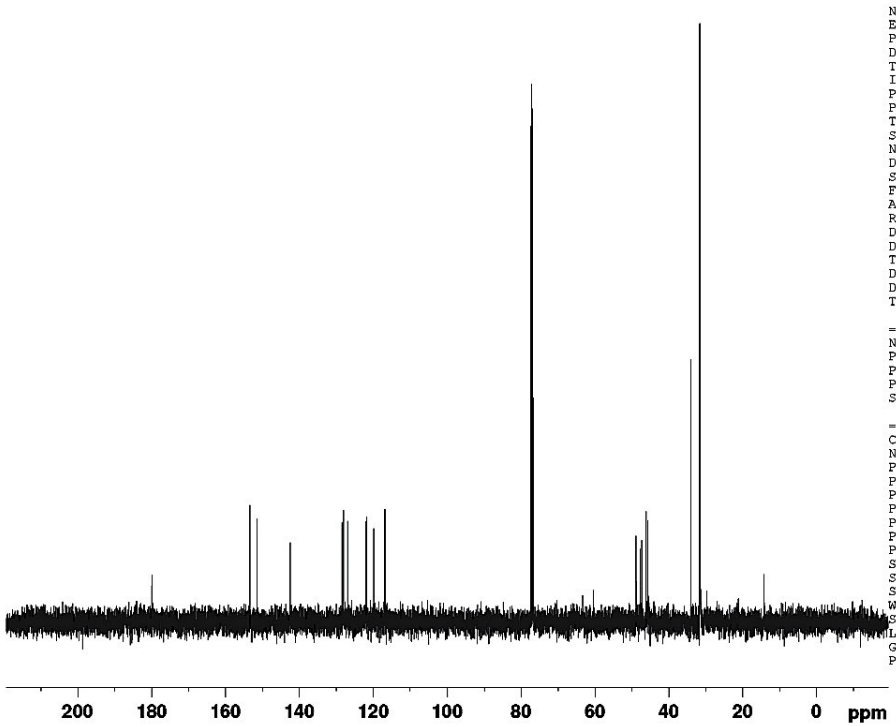
	701.3599	-1.0	-1.4	20.5	6.9	C45 H53 N2 O S2
	701.3447	14.2	20.2	16.5	18.4	C41 H53 N2 O4 S2
	701.3593	-0.4	-0.6	11.5	19.0	C37 H57 N4 O3 S3

Compound 8

Linear-7





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PULPROG	zgpg30
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SOLVENT	CDCl3
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DS	2
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FIDRES	0.366798 Hz
AQ	1.3631988 sec
RG	1030
DW	20.800 usec
DE	6.50 usec
TE	295.6 K
D1	2.00000000 sec
D11	0.03000000 sec
TD0	1
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NUC1	13C
P1	10.00 usec
PL1	-1.00 dB
PL1W	46.16925430 W
SFO1	100.6907281 MHz
======== CHANNEL f2 ========	
CPDPRG2	waltz16
NUC2	1H
PCPD2	100.00 usec
PL2	-3.00 dB
PL12	15.79 dB
PL13	15.79 dB
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PL12W	0.19535387 W
PL13W	0.19535387 W
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SI	32768
SF	100.6806600 MHz
WDW	EM
SSB	0
LB	1.00 Hz
GB	0
PC	1.40

Elemental Composition Report **Page 1**

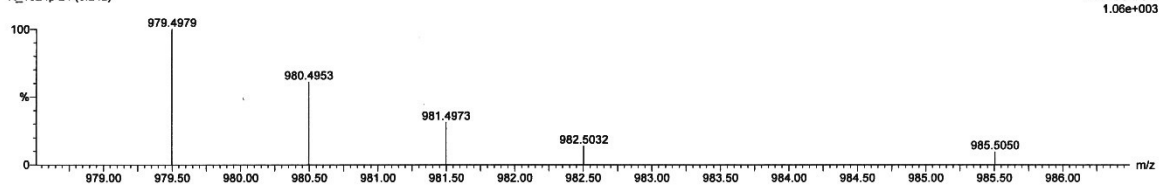
Single Mass Analysis
Tolerance = 50.0 mDa / DBE: min = -1.5, max = 50.0
Element prediction: Off
Number of isotope peaks used for i-FIT = 3

Monoisotopic Mass, Even Electron Ions
212 formula(e) evaluated with 28 results within limits (up to 4 best isotopic matches for each mass)
Elements Used:
C: 54-60 H: 72-80 N: 3-10 O: 0-10 S: 0-5

16-Jul-2009
K_1624p 24 (0.242)

GP100-Frk7

Keinan
TOF MS ES+
1.06e+003



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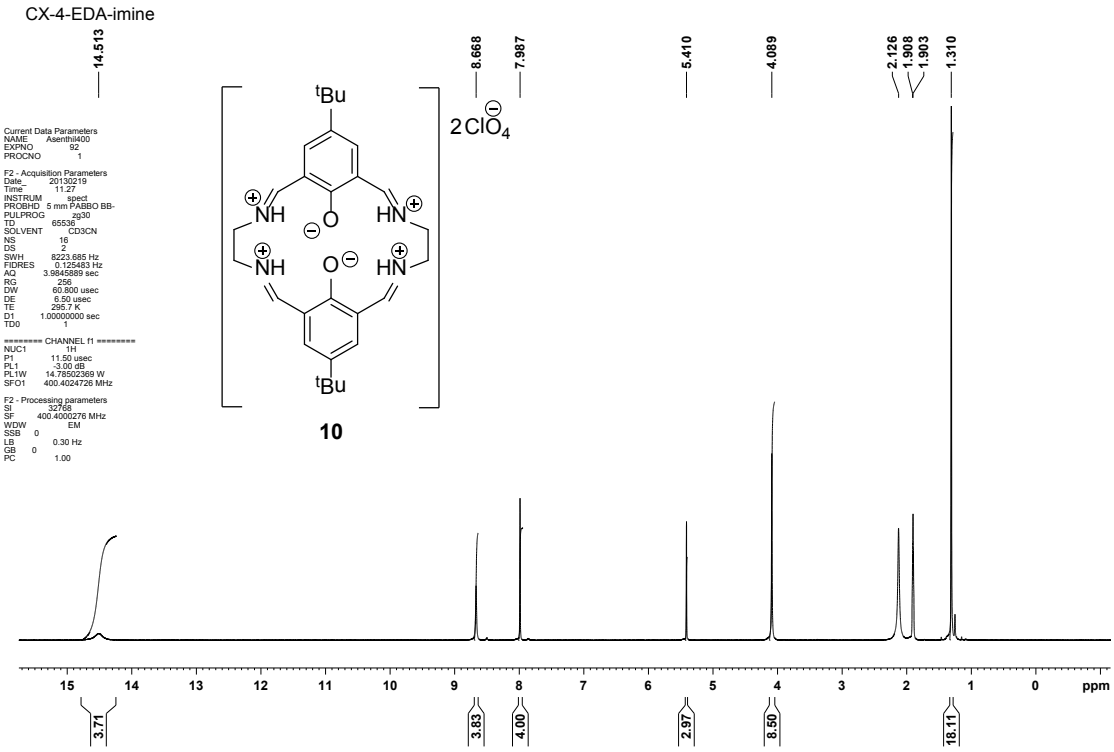
	979.5012	-3.3	-3.4	21.5	4.0	C55 H75 N6 O4 S3
	979.4900	7.9	8.1	21.5	4.7	C56 H75 N4 O5 S3
	979.5190	-21.1	-21.5	21.5	4.8	C55 H75 N6 O6 S2

Compound 10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1.903
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3.83
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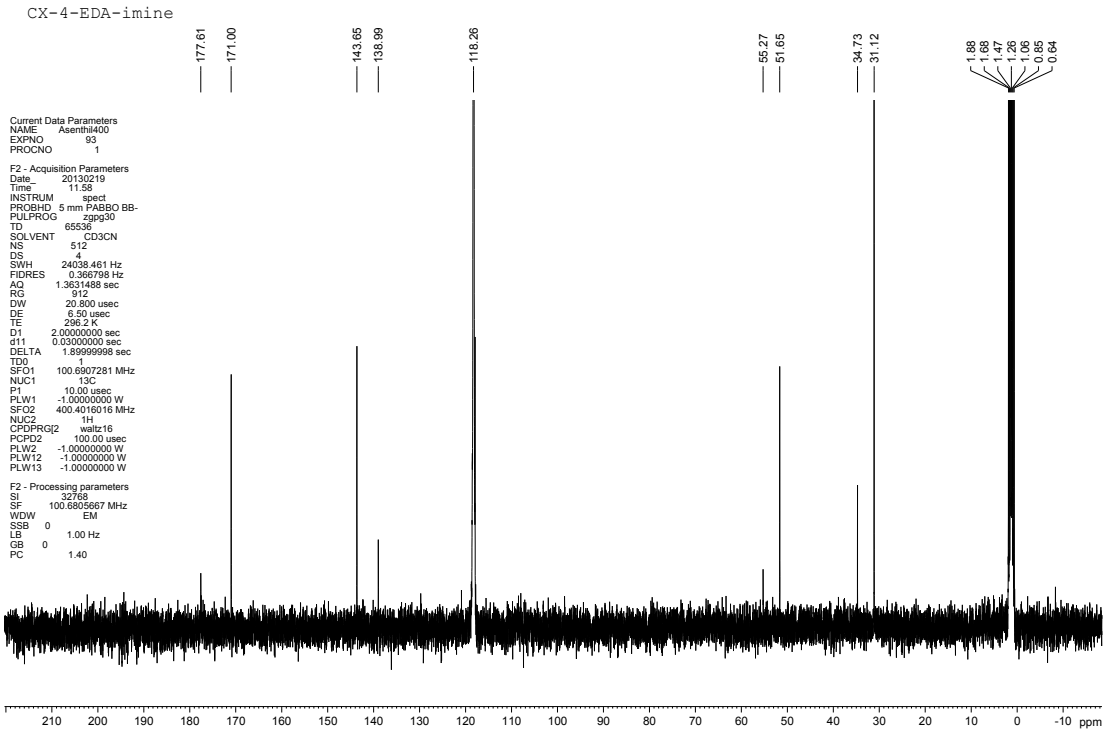
18.11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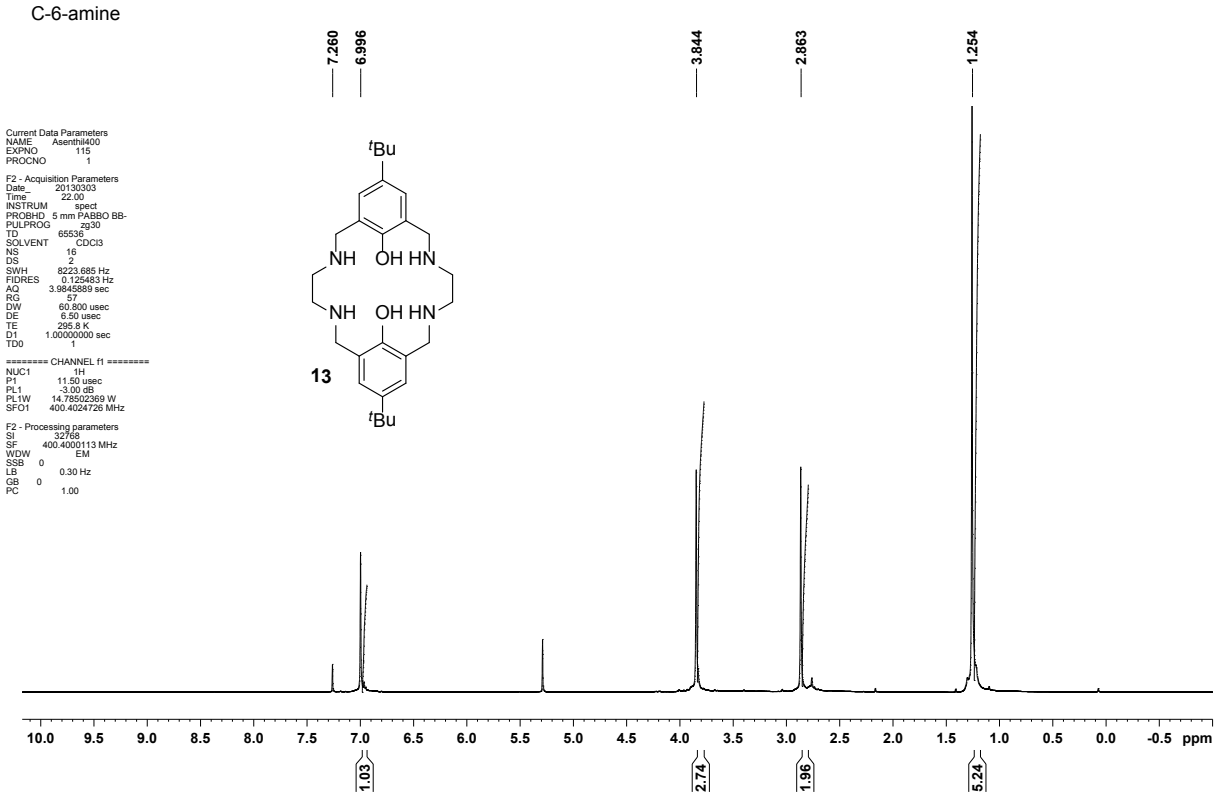
ppm

Compound 13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PROCNO 1
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RG 57
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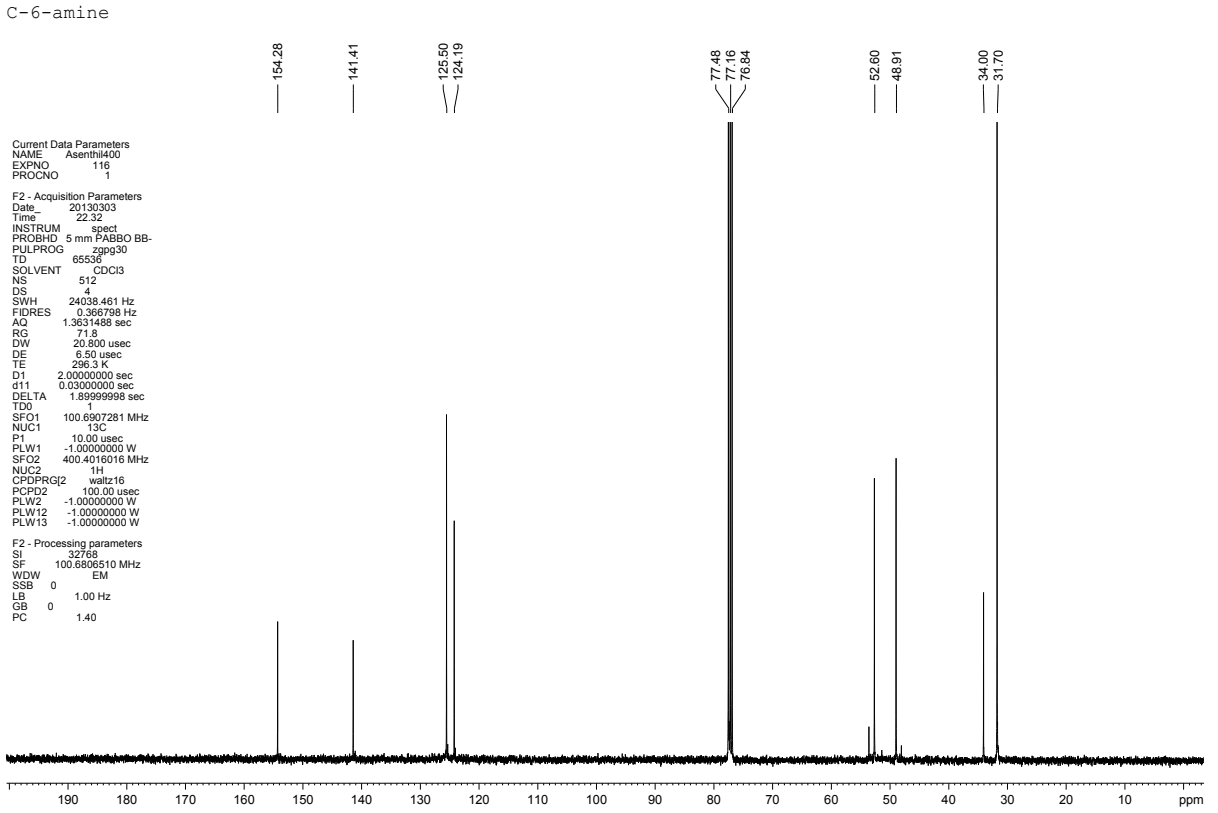
DE 6.50 usec
TE 295.8 K
D1 1.00000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 1H
P1 11.50 usec
PL1 -3.00 dB
PL1W 14.78502369 W
SFO1 400.4024726 MHz
F2 - Processing parameters
SI 32768
SF 400.4000113 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00
tBu
NH OH HN
NH OH HN
13
tBu
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 ppm
1.03
2.74
1.96
5.24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48.91
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Current Data Parameters
NAME Asenthil400
EXPNO 116
PROCNO 1
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Time 22.32
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PULPROG zgpg30
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NS 512
DS 4
SWH 24038.461 Hz
FIDRES 0.366798 Hz
AQ 1.3631488 sec
RG 71.8
DW 20.800 usec
DE 6.50 usec
TE 296.3 K
D1 2.00000000 sec
d11 0.03000000 sec
DELTA 1.89999998 sec
TD0 1
SFO1 100.6907281 MHz
NUC1 13C
P1 10.00 usec
PLW1 -1.00000000 W
SFO2 400.4016016 MHz
NUC2 1H
CPDPRG[2 waltz16
PCPD2 100.00 usec
PLW2 -1.00000000 W
PLW12 -1.00000000 W
PLW13 -1.00000000 W
F2 - Processing parameters
SI 32768
SF 100.6806510 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 1.40
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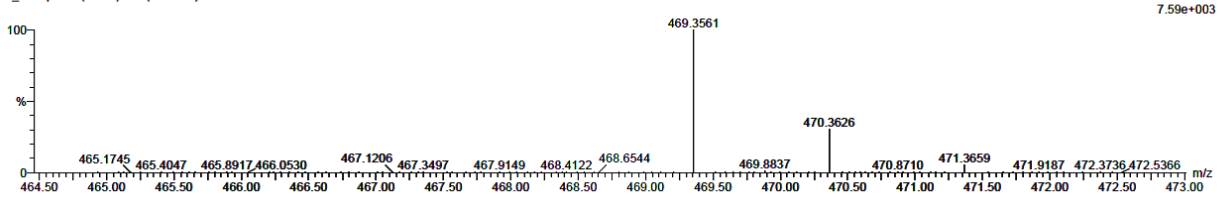
Single Mass Analysis
Tolerance = 20.0 mDa / DBE: min = -1.5, max = 50.0
Element prediction: Off
Number of isotope peaks used for i-FIT = 3

Monoisotopic Mass, Even Electron Ions
9 formula(e) evaluated with 2 results within limits (all results (up to 1000) for each mass)
Elements Used:
C: 20-30 H: 40-50 N: 0-4 O: 0-3

25-Feb-2013
K_5279p 290 (2.505) Cm (288:292)

tBu-N4

Keinan
TOF MS ES+
7.59e+003



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Maximum:		20.0	10.0	50.0		
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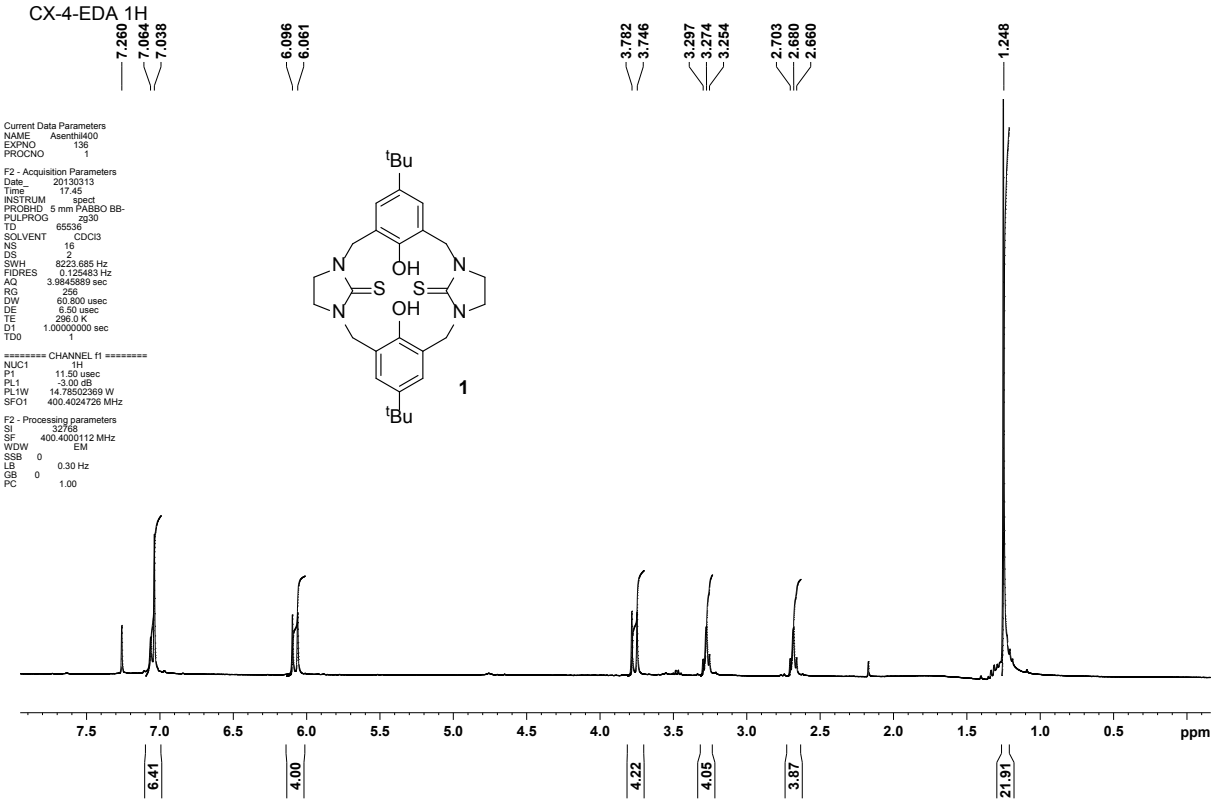
Compound 1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2.660
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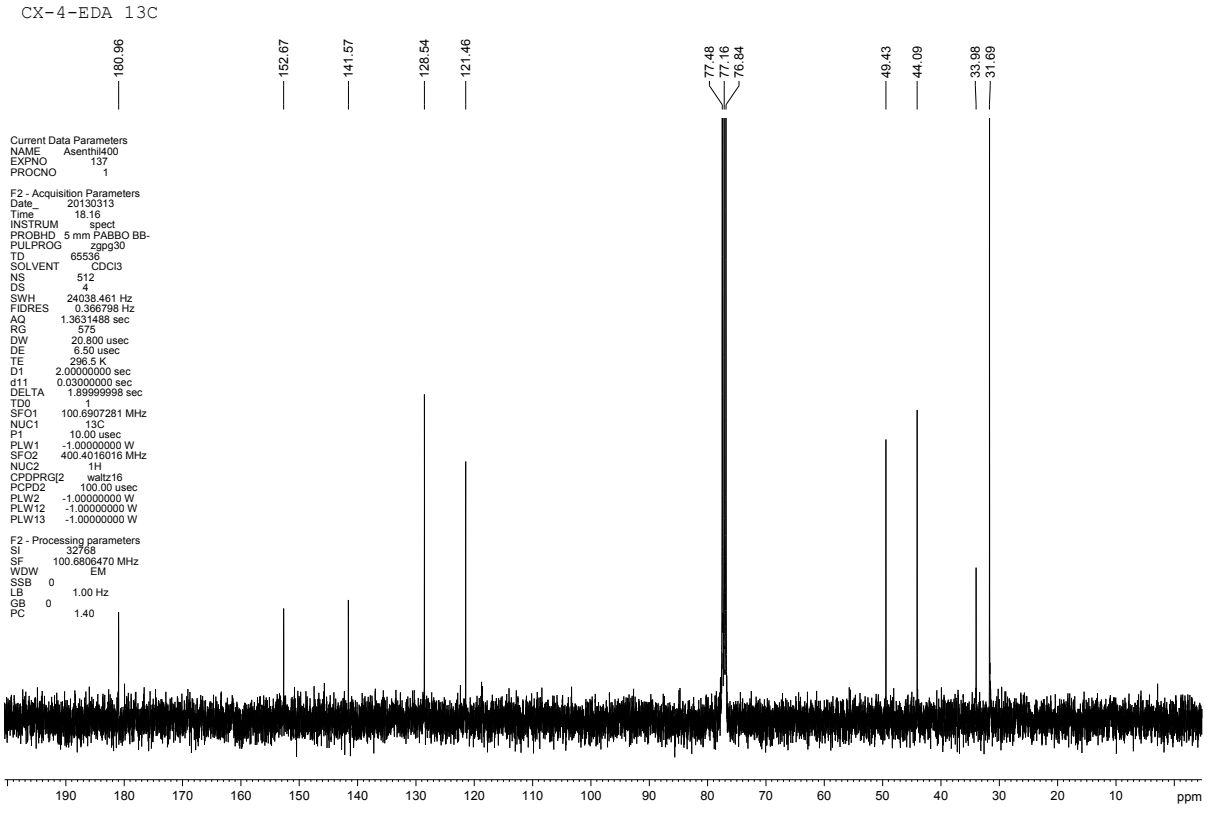
tBu
OH
N
S
OH
tBu
1
ppm
6.41
4.00
4.22
4.05
3.87
21.91


CX-4-EDA 13C
180.96
152.67
141.57
128.54
121.46
77.48
77.16
76.84
49.43
44.09
33.98
31.69
ppm

Elemental Composition Report **Page 1**

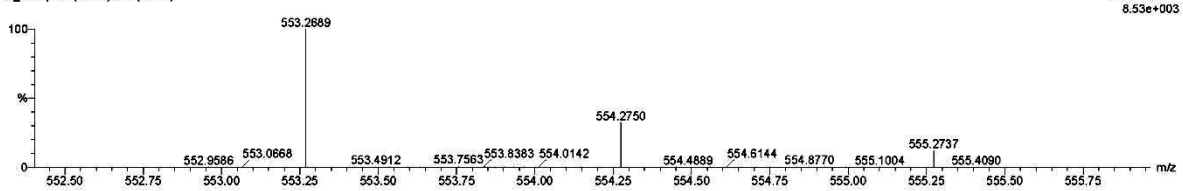
Single Mass Analysis
Tolerance = 20.0 mDa / DBE: min = -1.5, max = 50.0
Element prediction: Off
Number of isotope peaks used for i-FIT = 3

Monoisotopic Mass, Even Electron Ions
23 formula(e) evaluated with 5 results within limits (all results (up to 1000) for each mass)
Elements Used:
C: 25-35 H: 35-45 N: 3-4 O: 0-5 S: 1-2

18-Mar-2013
K_5362p 95 (0.819) Cm (95:98)

C4

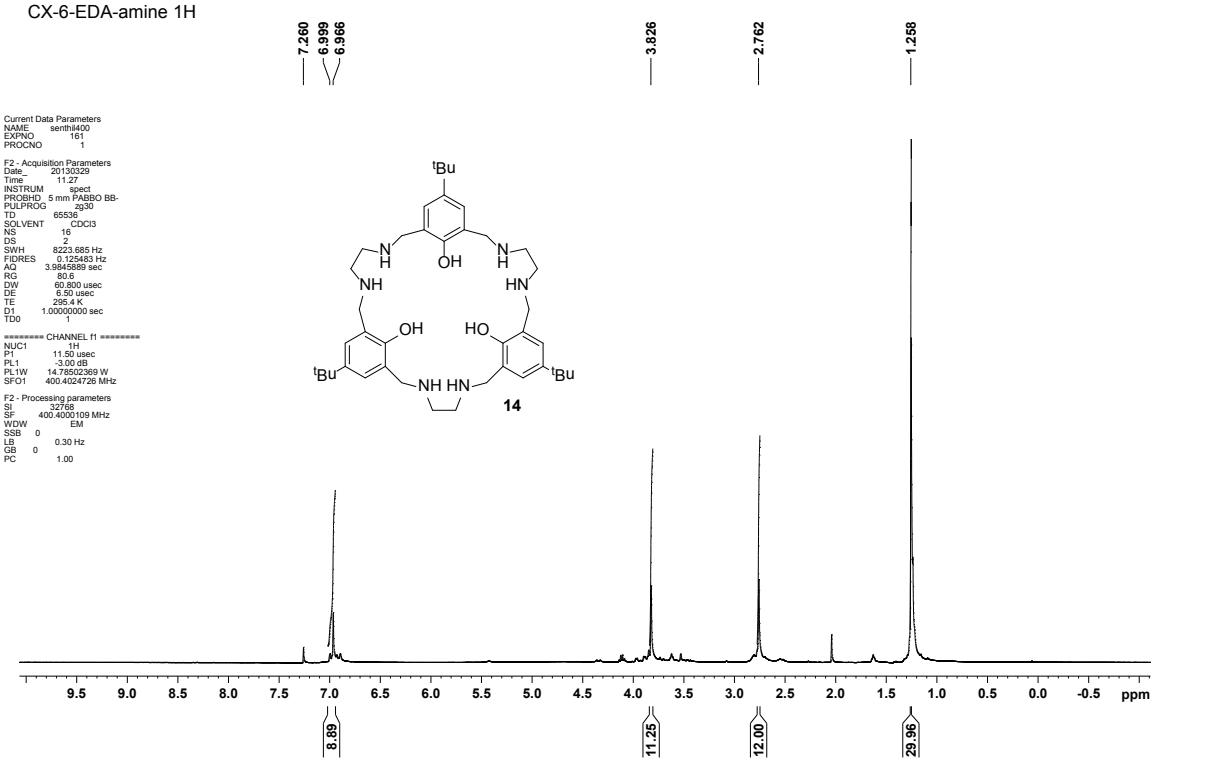
Keinan
TOF MS ES+
8.53e+003

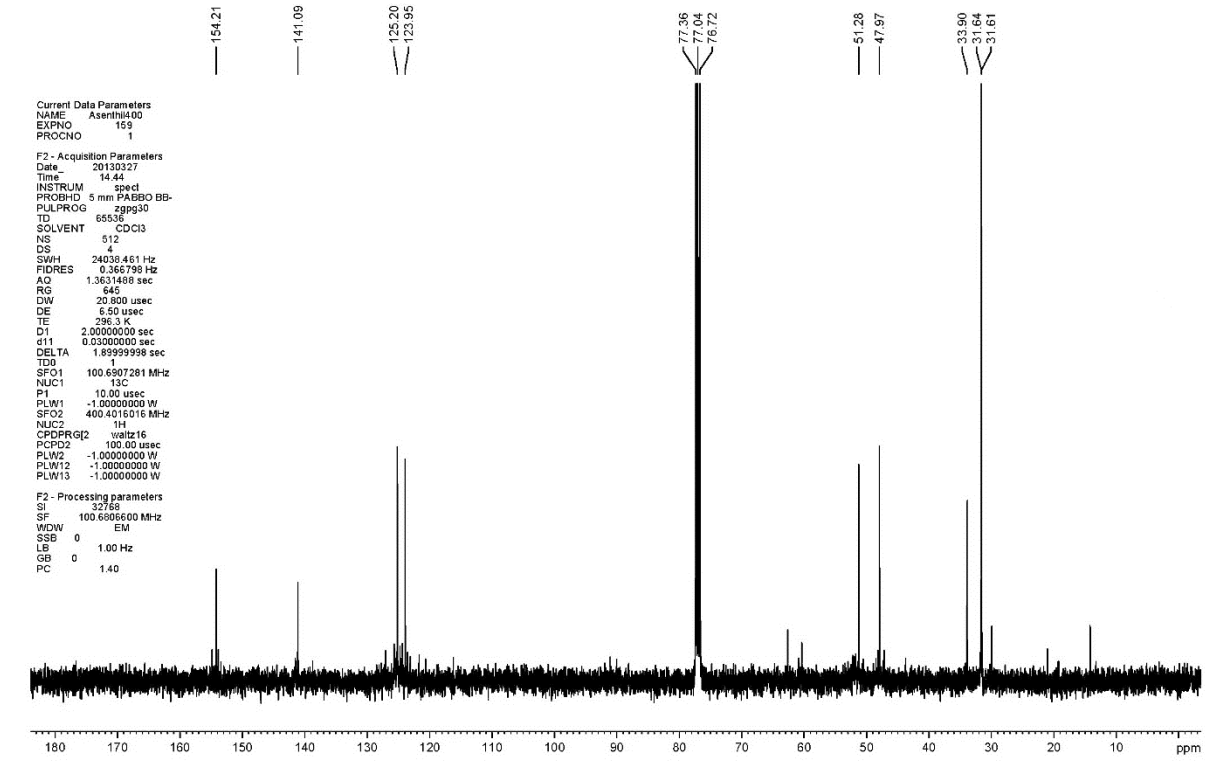


Minimum:				-1.5						
Maximum:		20.0	10.0	50.0						
Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Formula				
553.2689	553.2671	1.8	3.3	12.5	61.7	C30	H41	N4	O2	S2
	553.2637	5.2	9.4	17.5	52.5	C33	H37	N4	O2	S
	553.2849	-16.0	-28.9	12.5	42.6	C30	H41	N4	O4	S
	553.2518	17.1	30.9	8.5	69.7	C26	H41	N4	O5	S2
	553.2882	-19.3	-34.9	7.5	72.6	C27	H45	N4	O4	S2

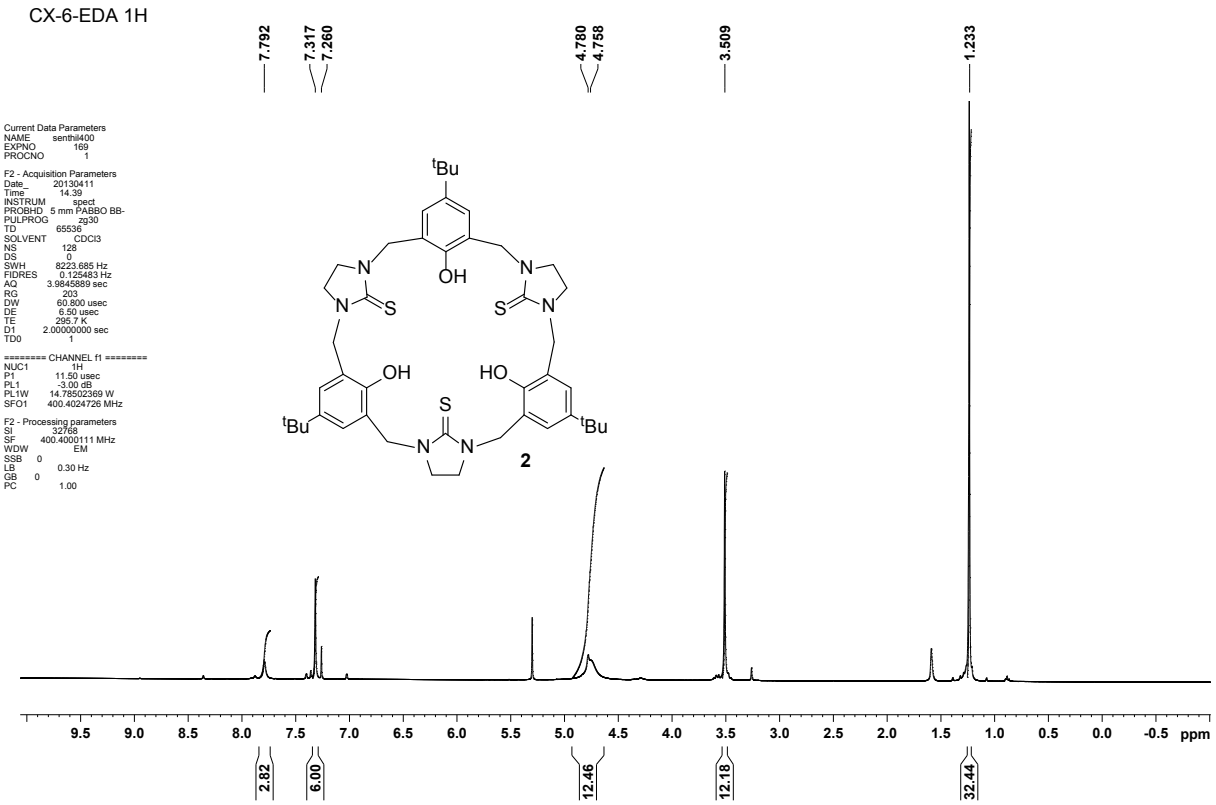
Compound 14

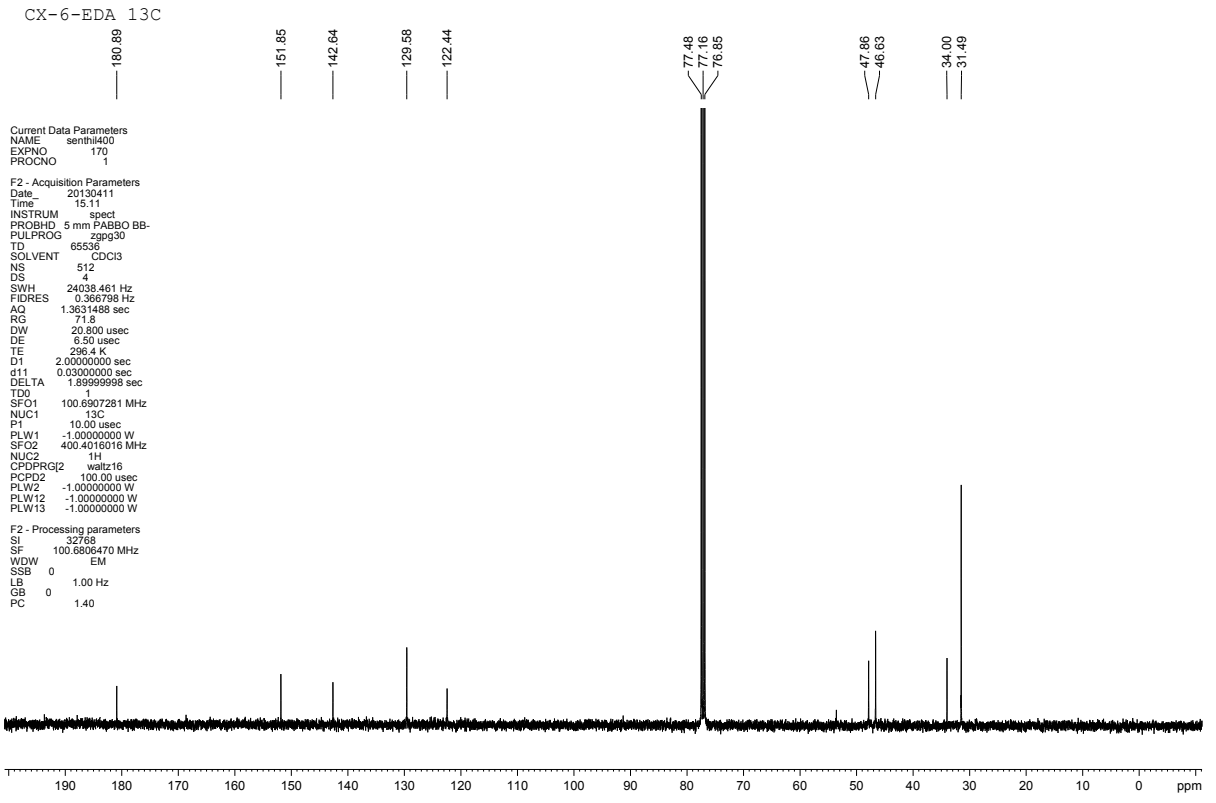
CX-6-EDA-amine 1H





Compound 2


CX-6-EDA 1H
7.792
7.317
7.260
4.780
4.758
3.509
1.233
Current Data Parameters
NAME senthil400
EXPNO 169
PROCNO 1
F2 - Acquisition Parameters
Date_ 20130411
Time 14.39
INSTRUM spect
PROBHD 5 mm PABBO BB-
PULPROG zg30
TD 65536
SOLVENT CDCl3
NS 128
DS 0
SWH 8223.685 Hz
FIDRES 0.125483 Hz
AQ 3.9845889 sec
RG 203
DW 60.800 usec
DE 6.50 usec
TE 295.7 K
D1 2.00000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 1H
P1 11.50 usec
PL1 -3.00 dB
PL1W 14.78502369 W
SFO1 400.4024726 MHz
F2 - Processing parameters
SI 32768
SF 400.4000111 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00
tBu
OH
N
S
HO
2
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 ppm
2.82
6.00
12.46
12.18
32.44


CX-6-EDA 13C
180.89
151.85
142.64
129.58
122.44
77.48
77.16
76.85
47.86
46.63
34.00
31.49
Current Data Parameters
NAME senthil400
EXPNO 170
PROCNO 1
F2 - Acquisition Parameters
Date_ 20130411
Time 15.11
INSTRUM spect
PROBHD 5 mm PABBO BB-
PULPROG zgpg30
TD 65536
SOLVENT CDCl3
NS 512
DS 4
SWH 24038.461 Hz
FIDRES 0.366798 Hz
AQ 1.3631488 sec
RG 71.8
DW 20.800 usec
DE 6.50 usec
TE 296.4 K
D1 2.00000000 sec
d11 0.03000000 sec
DELTA 1.89999998 sec
TD0 1
SFO1 100.6907281 MHz
NUC1 13C
P1 10.00 usec
PLW1 -1.00000000 W
SFO2 400.4016016 MHz
NUC2 1H
CPDPRG[2 waltz16
PCPD2 100.00 usec
PLW2 -1.00000000 W
PLW12 -1.00000000 W
PLW13 -1.00000000 W
F2 - Processing parameters
SI 32768
SF 100.6806470 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 1.40
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm

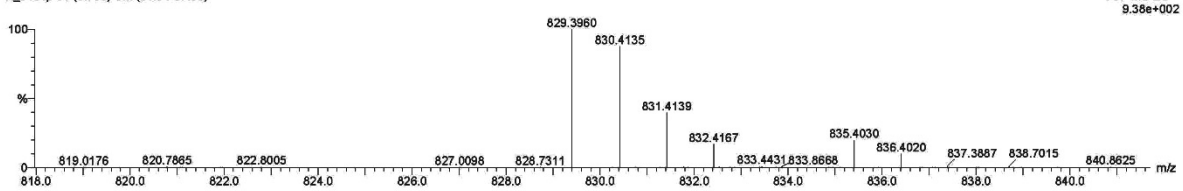
Elemental Composition Report **Page 1**

Single Mass Analysis
Tolerance = 20.0 mDa / DBE: min = -1.5, max = 50.0
Element prediction: Off
Number of isotope peaks used for i-FIT = 3

Monoisotopic Mass, Even Electron Ions
59 formula(e) evaluated with 8 results within limits (all results (up to 1000) for each mass)
Elements Used:
C: 40-50 H: 55-65 N: 5-7 O: 0-5 S: 0-4

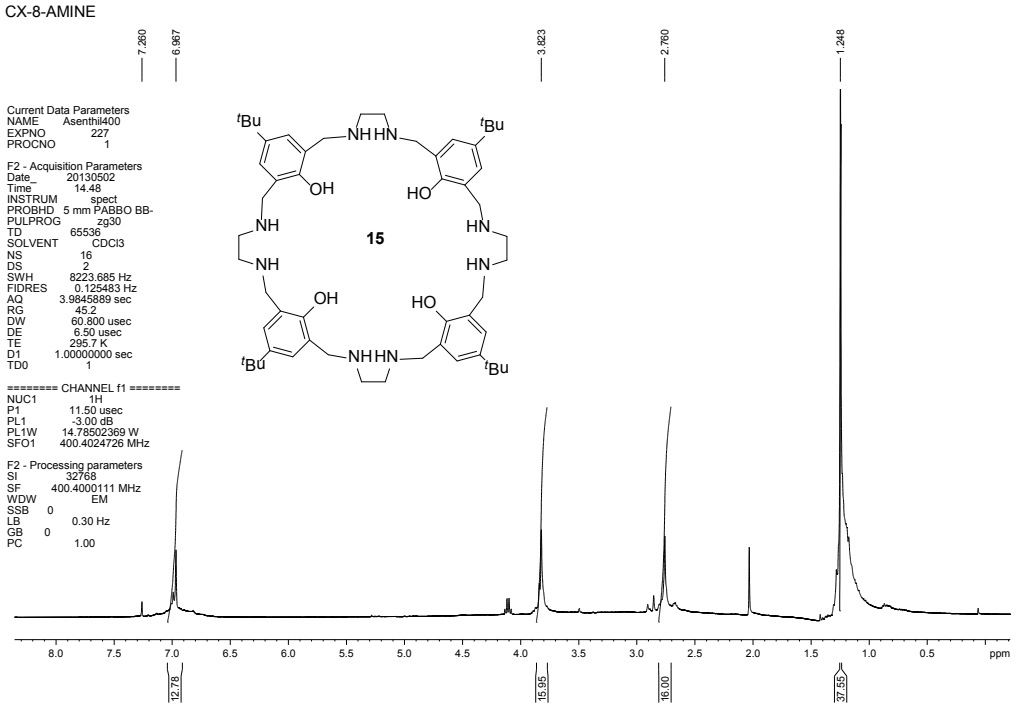
15-Apr-2013
K_5431p 91 (0.786) Cm (91:94-37:56)

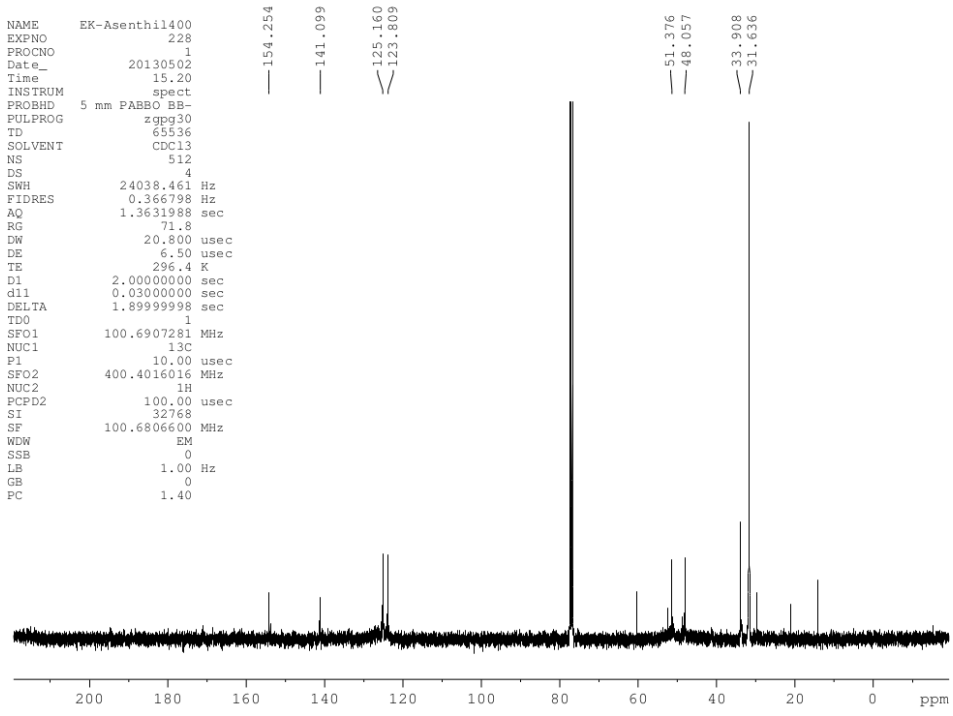
Keinan
TOF MS ES+
9.38e+002



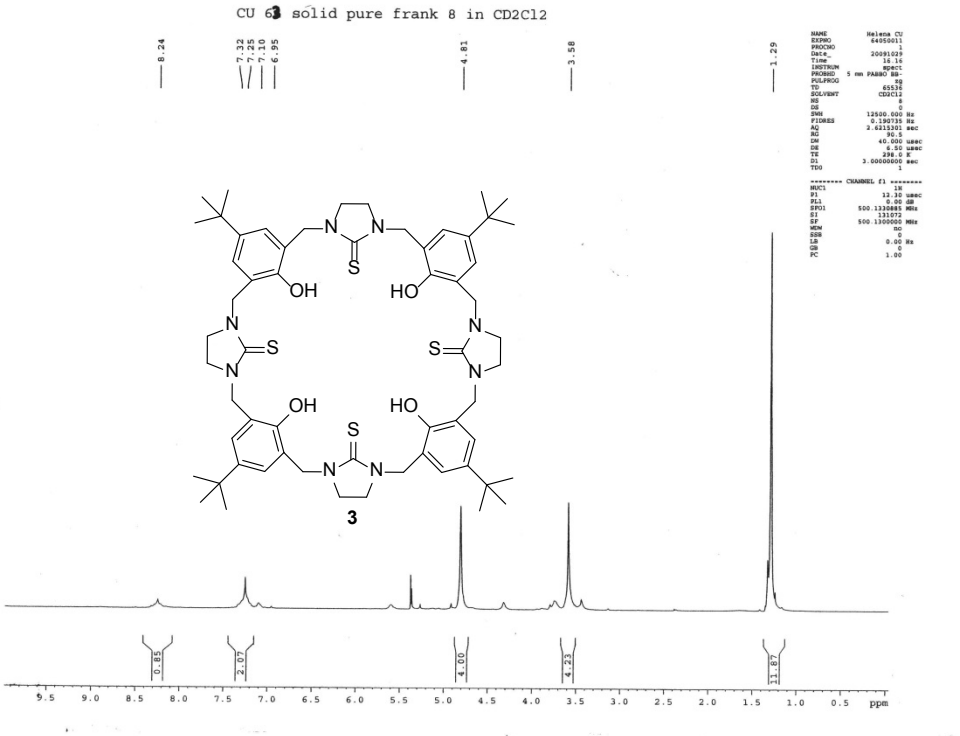
Minimum:				-1.5							
Maximum:		20.0	10.0	50.0							
Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Formula					
829.3960	829.3967	-0.7	-0.8	18.5	45.0	C45	H61	N6	O3	S3	
	829.3934	2.6	3.1	23.5	45.0	C48	H57	N6	O3	S2	
	829.4001	-4.1	-4.9	13.5	49.1	C42	H65	N6	O3	S4	
	829.4111	-15.1	-18.2	23.5	60.0	C48	H57	N6	O5	S	
	829.4120	-16.0	-19.3	22.5	31.8	C49	H61	N6	S3		
	829.3790	17.0	20.5	18.5	44.5	C45	H61	N6	O	S4	
	829.4145	-18.5	-22.3	18.5	56.8	C45	H61	N6	O5	S2	
	829.4154	-19.4	-23.4	17.5	36.7	C46	H65	N6	S4		

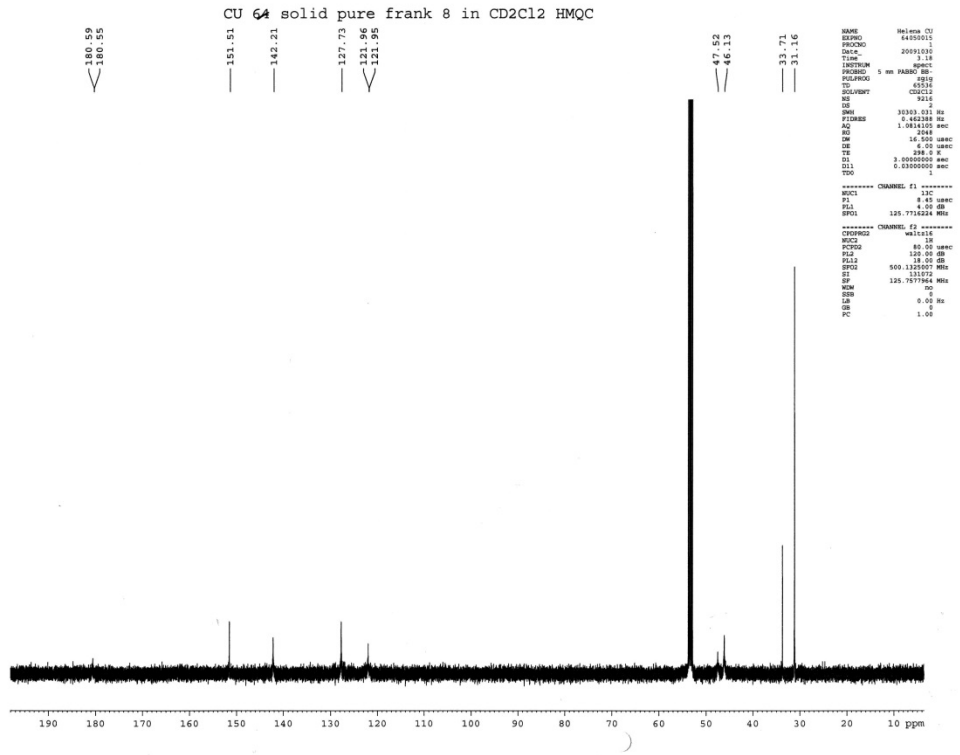
Compound 15


CX-8-AMINE
7.280
6.967
3.823
2.760
1.248
Current Data Parameters
NAME Asenthil400
EXPNO 227
PROCNO 1
F2 - Acquisition Parameters
Date_ 20130502
Time 14.48
INSTRUM spect
PROBHD 5 mm PABBO BB-
PULPROG zg30
TD 65536
SOLVENT CDCl3
NS 16
DS 2
SWH 8223.685 Hz
FIDRES 0.125483 Hz
AQ 3.9845889 sec
RG 45.2
DW 60.800 usec
DE 6.50 usec
TE 295.7 K
D1 1.00000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 1H
P1 11.50 usec
PL1 -3.00 dB
PL1W 14.78502369 W
SFO1 400.4024726 MHz
F2 - Processing parameters
SI 32768
SF 400.4000111 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00
tBu
NH HN
OH
HO
NH
HN
15
ppm
12.78
15.95
16.00
37.65


NAME EK-Asenthil400
EXPNO 228
PROCNO 1
Date_ 20130502
Time 15.20
INSTRUM spect
PROBHD 5 mm PABBO BB-
PULPROG zgpg30
TD 65536
SOLVENT CDCl3
NS 512
DS 4
SWH 24038.461 Hz
FIDRES 0.366798 Hz
AQ 1.3631988 sec
RG 71.8
DW 20.800 usec
DE 6.50 usec
TE 296.4 K
D1 2.00000000 sec
d11 0.03000000 sec
DELTA 1.89999998 sec
TD0 1
SFO1 100.6907281 MHz
NUC1 13C
P1 10.00 usec
SFO2 400.4016016 MHz
NUC2 1H
PCPD2 100.00 usec
SI 32768
SF 100.6806600 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 1.40
154.254
141.099
125.160
123.809
51.376
48.057
33.908
31.636
ppm

Compound 3


CU 63 solid pure frank 8 in CD2Cl2
8.24
7.32
7.25
7.10
6.95
4.81
3.58
1.29
OH
HO
S
N
3
0.85
2.07
4.00
4.23
11.87
ppm


CU 64 solid pure frank 8 in CD2Cl2 HMQC
180.59
180.55
151.51
142.21
127.73
121.96
121.95
47.52
46.13
33.71
31.16
ppm

Elemental Composition Report

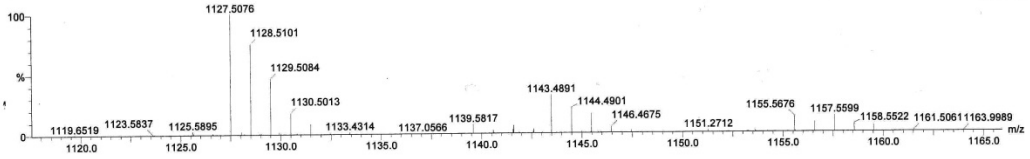
Single Mass Analysis
Tolerance = 20.0 mDa / DBE: min = -1.5, max = 50.0
Element prediction: Off
Number of isotope peaks used for i-FIT = 3

Monoisotopic Mass, Even Electron Ions
15 formula(e) evaluated with 7 results within limits (all results (up to 1000) for each mass)
Elements Used:
C: 59-61 H: 79-83 N: 5-10 O: 2-5 Na: 0-1 S: 3-5

14-Sep-2009
K_1740p 33 (0.333) Cm (31:36-(37:40+21:24))

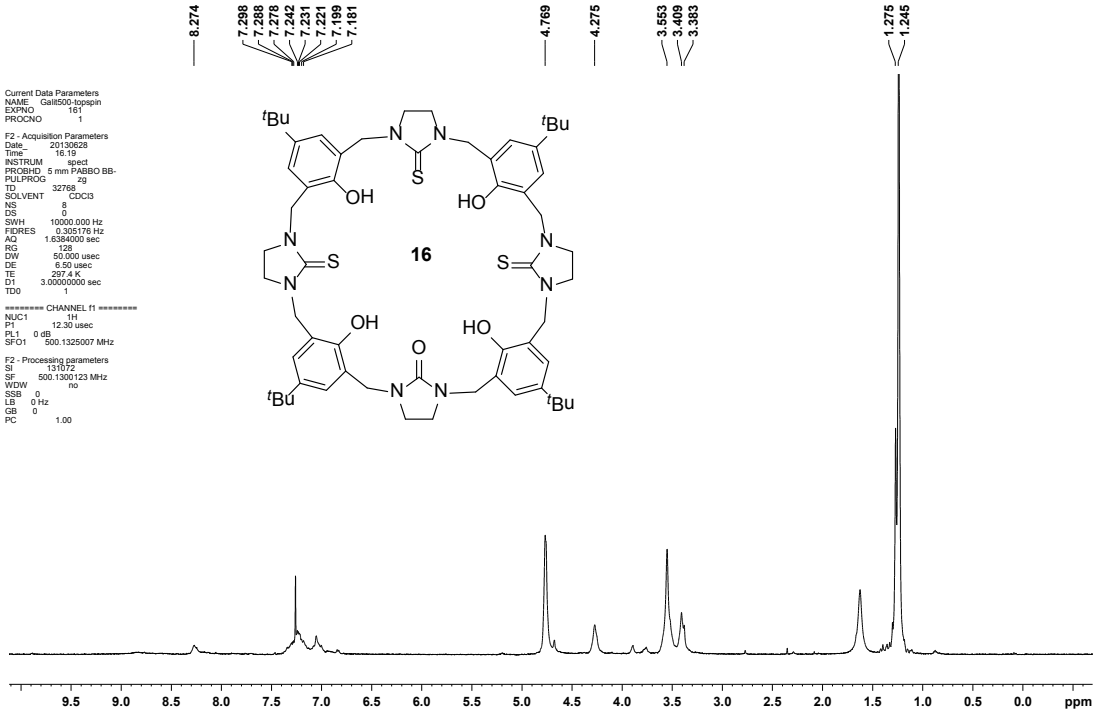
HC-CU-39pure

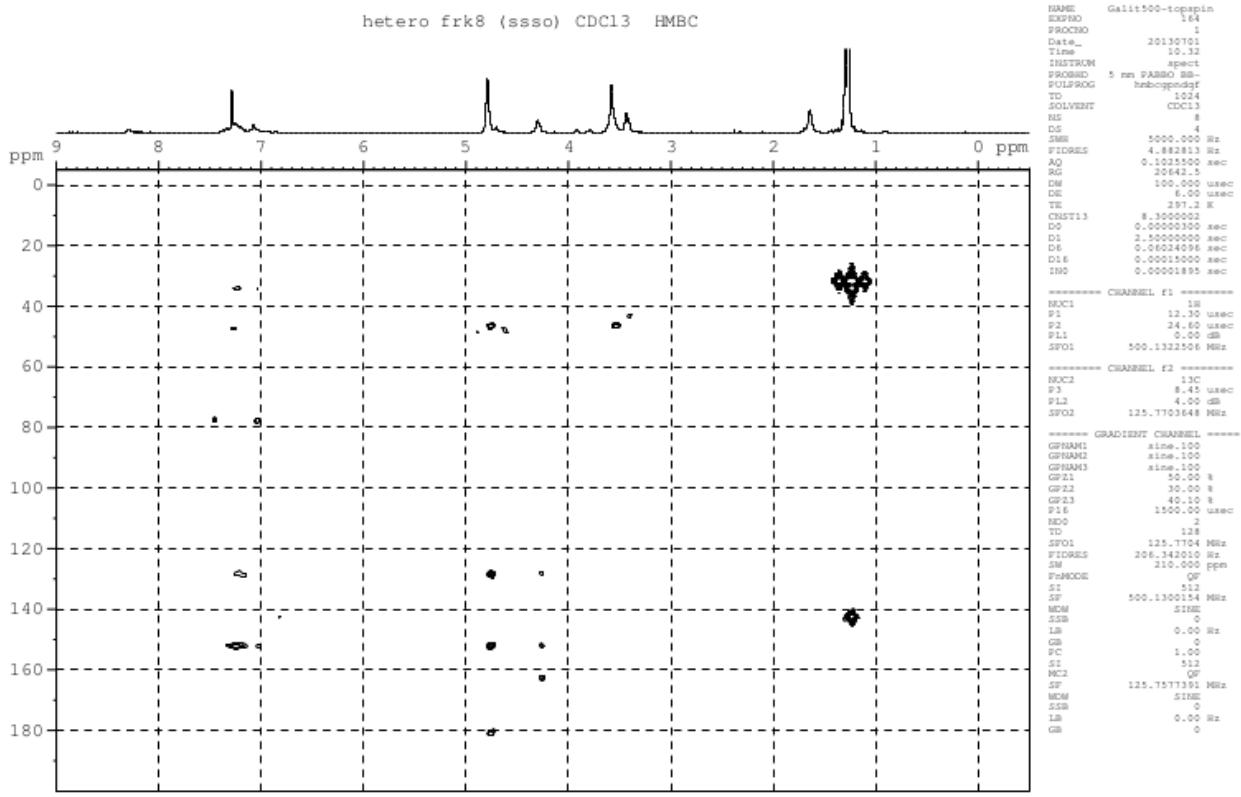
Keinan
TOF MS ES+
9.98e+003



Minimum:				-1.5		
Maximum:		20.0	10.0	50.0		
Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Formula
1127.5076	1127.5083	-0.7	-0.6	24.5	0.6	C60 H80 N8 O4 Na S4
	1127.5029	4.7	4.2	22.5	16.2	C60 H83 N6 O5 S5
	1127.5141	-6.5	-5.8	22.5	15.1	C59 H83 N8 O4 S5
	1127.4971	10.5	9.3	24.5	5.0	C61 H80 N6 O5 Na S4
	1127.5195	-11.9	-10.6	24.5	8.6	C59 H80 N10 O3 Na S4
	1127.5219	-14.3	-12.7	27.5	10.8	C61 H79 N10 O3 S4
	1127.4906	17.0	15.1	24.5	26.2	C60 H80 N8 O2 Na S5

Compound 16


8.274
7.298
7.288
7.278
7.242
7.231
7.221
7.199
7.181
4.769
4.275
3.553
3.409
3.383
1.275
1.245
Current Data Parameters
NAME Galit500-topspin
EXPNO 161
PROCNO 1
F2 - Acquisition Parameters
Date_ 20130628
Time 16.19
INSTRUM spect
PROBHD 5 mm PABBO BB-
PULPROG zg
TD 32768
SOLVENT CDCl3
NS 8
DS 0
SWH 10000.000 Hz
FIDRES 0.305176 Hz
AQ 1.6384000 sec
RG 128
DW 50.000 usec
DE 6.50 usec
TE 297.4 K
D1 3.00000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 1H
P1 12.30 usec
PL1 0 dB
SFO1 500.1325007 MHz
F2 - Processing parameters
SI 131072
SF 500.1300123 MHz
WDW no
SSB 0
LB 0 Hz
GB 0
PC 1.00
tBu
OH
HO
N
S
O
16
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 ppm


hetero frk8 (ssso) CDCl3 HMBC
ppm
9 8 7 6 5 4 3 2 1 0 ppm
0
20
40
60
80
100
120
140
160
180
NAME Galit500-topspin
EXPNO 164
PROCNO 1
Date_ 20130701
Time 10.32
INSTRUM spect
PROBHD 5 mm PABBO BB-
PULPROG hmbcgpndqf
TD 1024
SOLVENT CDCl3
NS 8
DS 4
SWH 5000.000 Hz
FIDRES 4.882813 Hz
AQ 0.1025500 sec
RG 20642.5
DW 100.000 usec
DE 6.00 usec
TE 297.2 K
CNST13 8.3000002
D0 0.00000300 sec
D1 2.50000000 sec
D6 0.06024096 sec
D16 0.00015000 sec
IN0 0.00001895 sec
======== CHANNEL f1 ========
NUC1 1H
P1 12.30 usec
P2 24.60 usec
PL1 0.00 dB
SFO1 500.1322506 MHz
======== CHANNEL f2 ========
NUC2 13C
P3 8.45 usec
PL2 4.00 dB
SFO2 125.7703648 MHz
====== GRADIENT CHANNEL =====
GPNAM1 sine.100
GPNAM2 sine.100
GPNAM3 sine.100
GPZ1 50.00 %
GPZ2 30.00 %
GPZ3 40.10 %
P16 1500.00 usec
ND0 2
TD 128
SFO1 125.7704 MHz
FIDRES 206.342010 Hz
SW 210.000 ppm
FnMODE QF
SI 512
SF 500.1300154 MHz
WDW SINE
SSB 0
LB 0.00 Hz
GB 0
PC 1.00
SI 512
MC2 QF
SF 125.7577391 MHz
WDW SINE
SSB 0
LB 0.00 Hz
GB 0

Elemental Composition Report

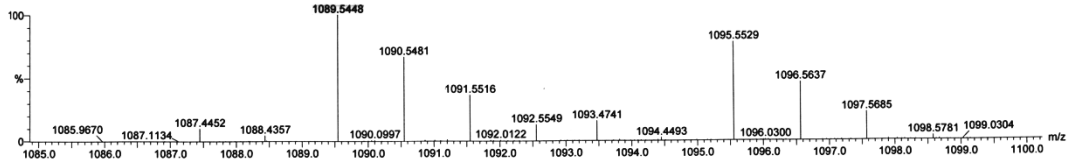
Single Mass Analysis
Tolerance = 20.0 mDa / DBE: min = -1.5, max = 50.0
Element prediction: Off
Number of isotope peaks used for i-FIT = 3

Monoisotopic Mass, Even Electron Ions
35 formula(e) evaluated with 5 results within limits (all results (up to 1000) for each mass)
Elements Used:
C: 60-65 H: 80-85 N: 7-9 O: 0-7 S: 0-5

19-Aug-2009
K_1707p 26 (0.263) Cm (24:29-14)

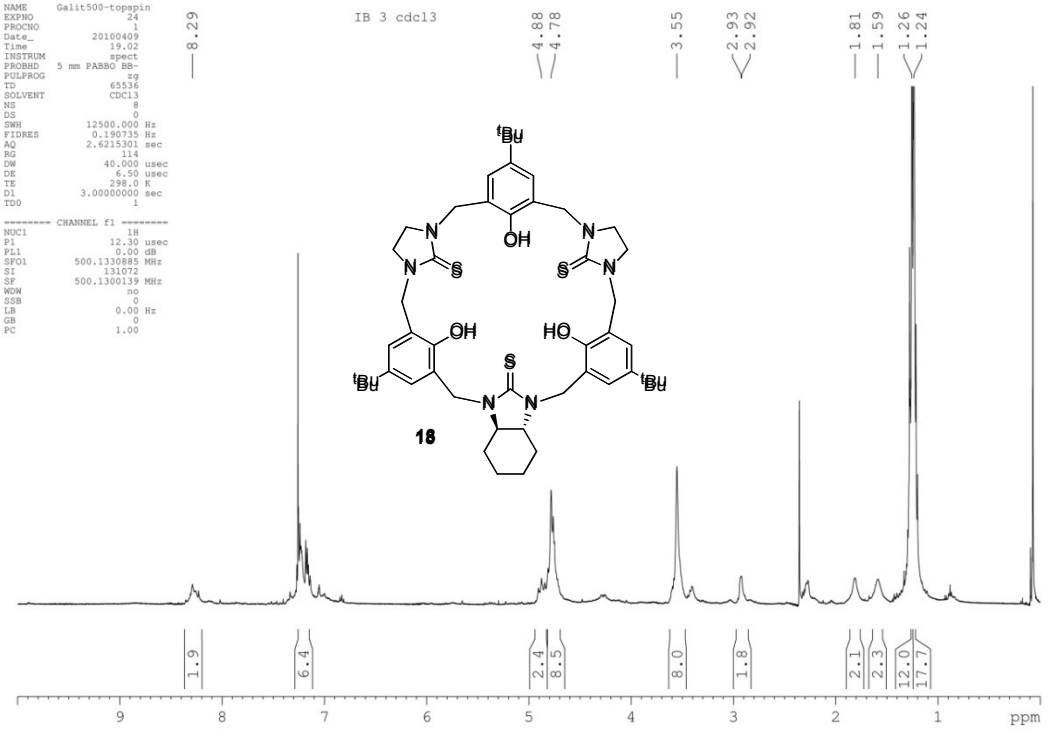
HC-CU-40pure

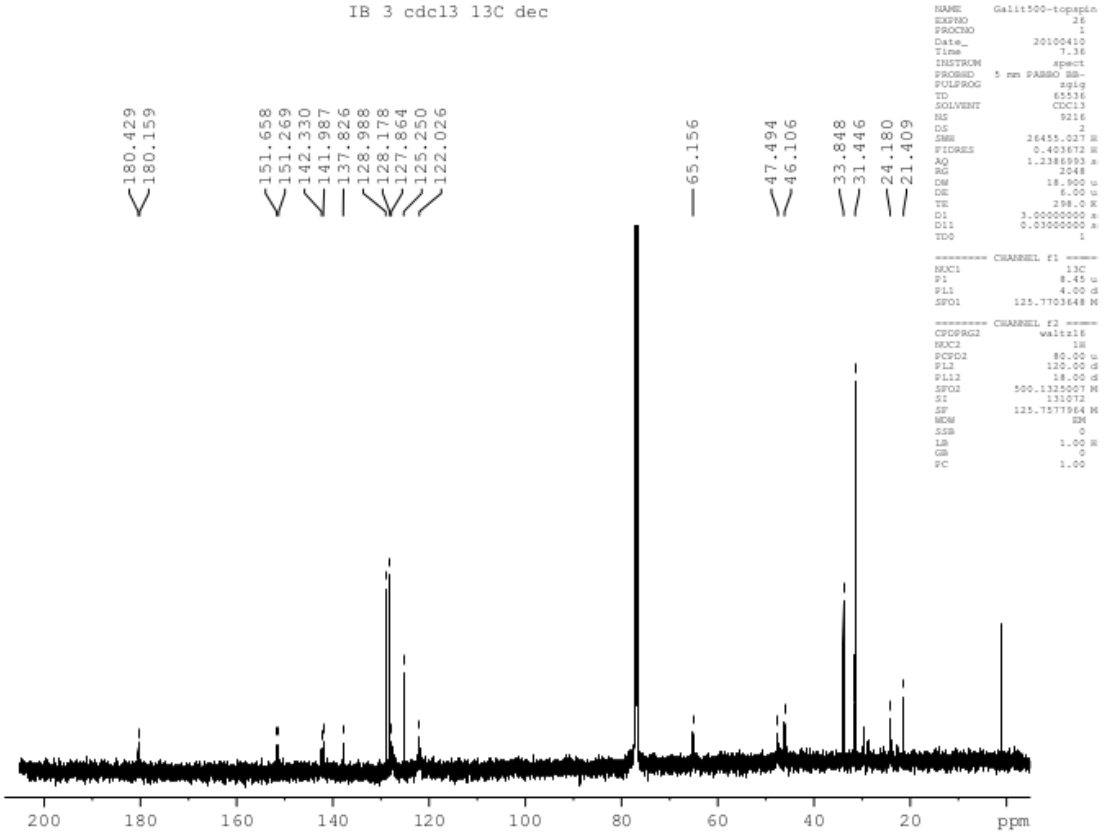
Keinan
TOF MS ES+
3.97e+003



Minimum:				-1.5						
Maximum:		20.0	10.0	50.0						
Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Formula				
1089.5448	1089.5467	-1.9	-1.7	28.5	49.8	C64	H81	N8	S4	
	1089.5492	**-4.4**	**-4.0**	**24.5**	**11.4**	**C60**	**H81**	**N8**	**O5**	**S3**
	1089.5501	-5.3	-4.9	23.5	65.7	C61	H85	N8	S5	
	1089.5315	13.3	12.2	24.5	33.5	C60	H81	N8	O3	S4
	1089.5645	-19.7	-18.1	28.5	33.6	C64	H81	N8	O2	S3

Compound 18


IB 3 cdcl3
8.29
4.88
4.78
3.55
2.93
2.92
1.81
1.59
1.26
1.24
1.9
6.4
2.4
8.5
8.0
1.8
2.1
2.3
12.0
17.7
ppm
18


IB 3 cdcl3 13C dec
180.429
180.159
151.658
151.269
142.330
141.987
137.826
128.988
128.178
127.864
125.250
122.026
65.156
47.494
46.106
33.848
31.446
24.180
21.409
ppm

Elemental Composition Report **Page 1**

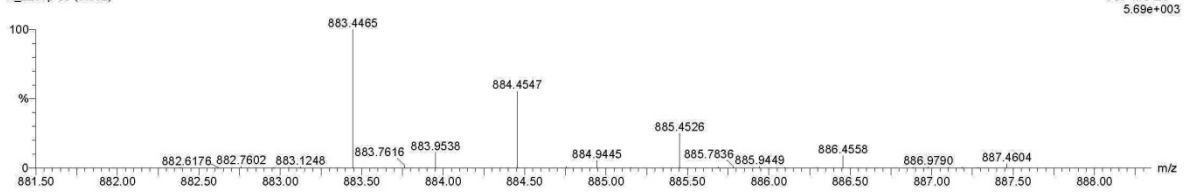
Single Mass Analysis
Tolerance = 20.0 mDa / DBE: min = -1.5, max = 50.0
Element prediction: Off
Number of isotope peaks used for i-FIT = 3

Monoisotopic Mass, Even Electron Ions
26 formula(e) evaluated with 2 results within limits (all results (up to 1000) for each mass)
Elements Used:
C: 48-50 H: 60-68 N: 4-7 O: 0-4 S: 0-4

08-Apr-2010
K_2267p 35 (0.302)

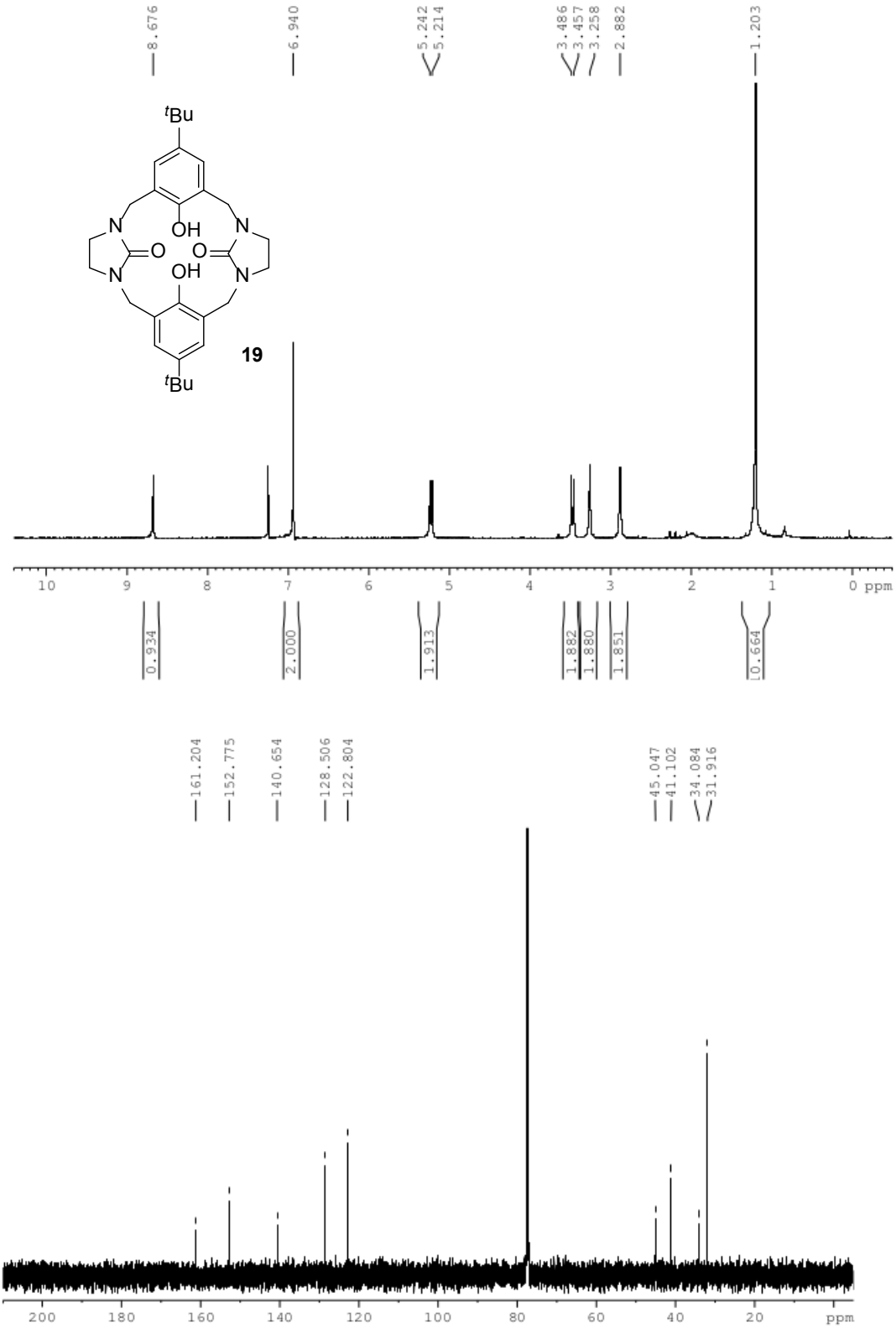
IB3

Keinan
TOF MS ES+
5.69e+003



Minimum:				-1.5		
Maximum:		20.0	10.0	50.0		
Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Formula
883.4465	883.4437	2.8	3.2	19.5	40.4	C49 H67 N6 O3 S3
	883.4324	14.1	16.0	19.5	54.2	C50 H67 N4 O4 S3

Compound 19 (NMR spectra recorded at -33ºC)



Elemental Composition Report **Page 1**

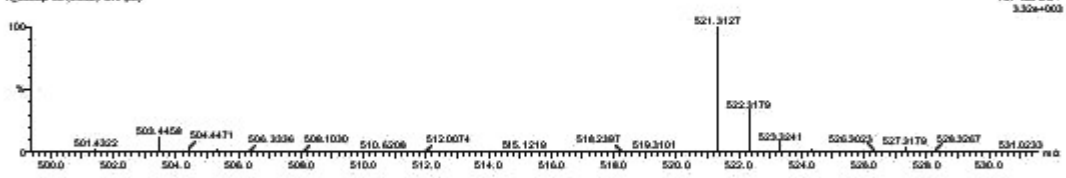
Single Mass Analysis
Tolerance = 20.0 mDa / DBE: min = -1.5, max = 50.0
Element prediction: Off
Number of isotope peaks used for i-FIT = 3

Monoisotopic Mass, Even Electron Ions
29 formula(e) evaluated with 4 results within limits (all results (up to 1000) for each mass)
Elements Used:
C: 25-32 H: 39-50 N: 0-5 O: 0-7

05-Jun-2013
K_565#p 65 (0.562) Cm (65)

GP-193-2-64

Kaiser
TOF MS ES+
3.32e+003



Min Limits:				-1.5					
Max Limits:		20.0	10.0	50.0					
Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Formula			
521.3127	521.3129	-0.1	-0.2	12.5	3.3	C30	H41	N4	O4
	521.3227	-10.0	-19.2	7.5	6.0	C28	H45	N2	O7
	521.3015	11.2	21.5	12.5	10.0	C31	H41	N2	O5
	521.2875	15.2	29.2	8.5	17.5	C26	H41	N4	O7

4. Single crystal X-ray data

The following CCDC numbers contain the supplementary crystallographic data for this paper.

Compound **1**: CCDC 952891

Compound **2**: CCDC 952890

Compound **3**: CCDC 952889

These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif

Crystal data and structure refinement for 1

Empirical formula	C30.25 H38.50 Cl0.50 N4 O0.50 O2 S2
Formula weight	580.00
Temperature	293(2) K
Wavelength	0.71073 A
Crystal system, space group	Monoclinic, C 2/c
Unit cell dimensions	a = 27.239(6) Aalpha = 90 deg.
	b = 14.560(3) Abeta = 120.20(3)deg.
	c = 19.951(4) Agamma = 90 deg.
Volume	6839(2) A^3
Z, Calculated density	8, 1.127 Mg/m^3
Absorption coefficient	0.226 mm^-1
F(000)	2468
Crystal size	0.56 x 0.44 x 0.35 mm
Theta range for data collection	1.75 to 25.05 deg.
Limiting indices	-32<=h<=32, -16<=k<=17, -23<=l<=23
Reflections collected/unique	11571 / 6051 [R(int) = 0.0243]
Completeness to theta	25.0599.7 %
Absorption correction None	
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	6051 / 1 / 367
Goodness-of-fit on F^2	1.073
Final R indices [I>2sigma(I)]	R1 = 0.0842, wR2 = 0.2504
R indices (all data)	R1 = 0.1092, wR2 = 0.2704
Extinction coefficient	0.0013(6)
Largest diff. peak and hole	0.817 and -0.331 e.A^-3

Crystal data and structure refinement for 2

Empirical formula	C49 H70 N6 O4 S3
Formula weight	903.29
Temperature	293(2) K
Wavelength	0.71073 A
Crystal system, space group	Hexagonal, P 31
Unit cell dimensions	a = 12.741(1)Aalpha = 90 deg.
	b = 12.741(1)Abeta = 90 deg.
	c = 27.303(3)Agamma = 120 deg.
Volume	3838.4(6) A^3
Z, Calculated density	3, 1.172 Mg/m^3
Absorption coefficient	0.192 mm^-1
F(000)	1458
Crystal size	0.73 x 0.58 x 0.46 mm
Theta range for data collection	1.85 to 25.68 deg.
Limiting indices	-13<=h<=15, -14<=k<=15, -33<=l<=33
Reflections collected/unique	37973 / 9738 [R(int) = 0.0366]
Completeness to theta	25.68100.0 %
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	0.915 and 0.875
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	9738 / 6 / 559
Goodness-of-fit on F^2	1.047
Final R indices [I>2sigma(I)]	R1 = 0.0673, wR2 = 0.1920
R indices (all data)	R1 = 0.0914, wR2 = 0.2091
Absolute structure parameter	-0.12(9)
Largest diff. peak and hole	0.485 and -0.296 e.A^-3

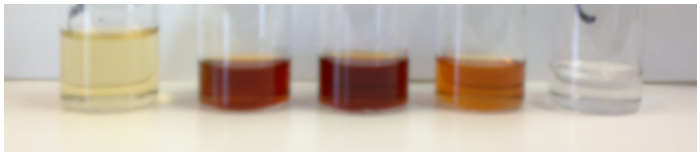
Table 1. Crystal data and structure refinement for 3

Empirical formula	C66 H94 N8 O6 S4
Formula weight	1223.73
Temperature	293(2) K
Wavelength	0.71073 A
Crystal system, space group	Monoclinic,Cc
Unit cell dimensions	a = 21.716(4) Aalpha = 90 deg. b = 12.428(2) Abeta = 111.59(3) deg. c = 27.774(6) Agamma = 90 deg.
Volume	6970(2) A^3
Z, Calculated density	4,1.166 Mg/m^3
Absorption coefficient	0.189 mm^-1
F(000)	2632
Crystal size	0.32 x 0.18 x 0.05 mm
Theta range for data collection	1.93 to 25.00 deg.
Limiting indices	0<=h<=25, 0<=k<=14, -32<=l<=30
Reflections collected/unique	20236 / 6007 [R(int) = 0.0980]
Completeness to theta	25.0097.8 %
Absorption correction	None
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	6007 / 17 / 724
Goodness-of-fit on F^2	0.882
Final R indices [I>2sigma(I)]	R1 = 0.0912, wR2 = 0.2294
R indices (all data)	R1 = 0.2215, wR2 = 0.2876
Absolute structure parameter	0.0(3)
Largest diff. peak and hole	0.881 and -0.299 e.A^-3

5. Metal Binding Studies – $Pd(OAc)_2$ complexation with 1

5.1 General information

In all cases the solvent used was chloroform and all samples were prepared immediately before use. The solution of $Pd(OAc)_2$ has a pale yellow color, and that of **1** is colorless. Upon addition of either of these to the other, an immediate color change occurs to orange/brown, presumably of the complexes formed.

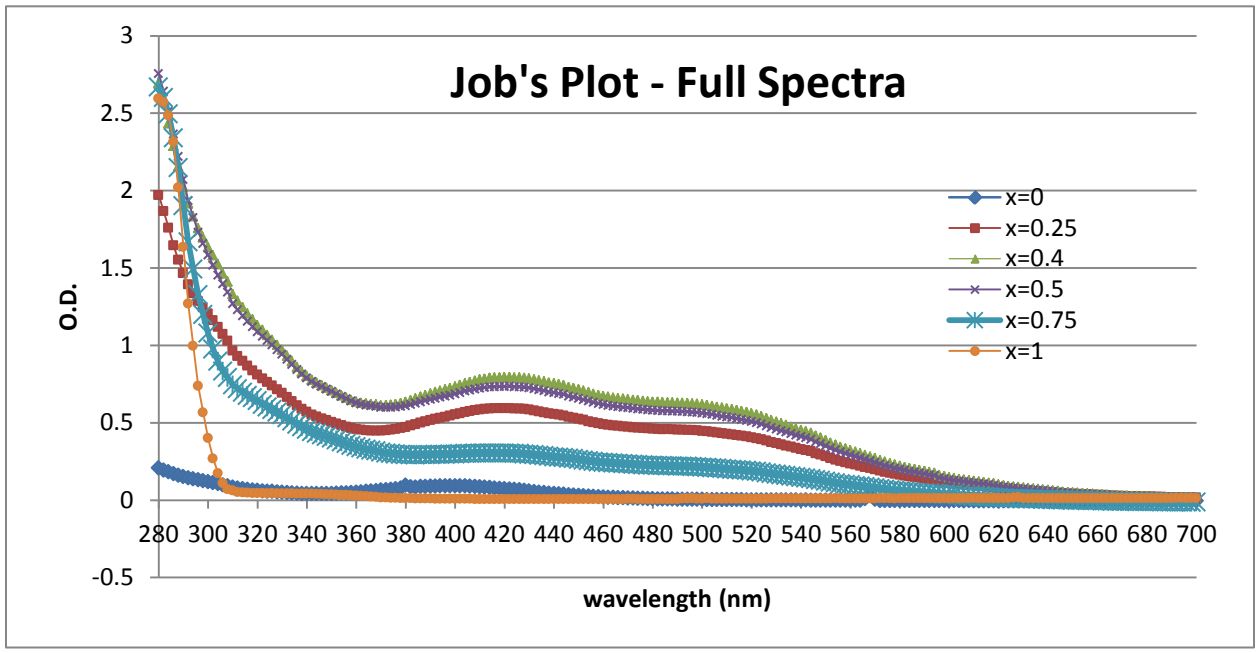


*Photograph of various solutions in the complexation study. Left – $Pd(OAc)_2$ only. Right – **1** only (transparent). Middle – various mixtures of both components, leading to color changes according to the ratios of the two components.*

In all series studied by UV-Vis absorption the OD ranges were kept between to 0.1 to 0.9 OD to comply with Beer Lambert linearity. The wavelength found suitable for tracking the complexes' formation was 420nm.

5.2 Complex Stoichiometry

A Job's Plot method[5] was undertaken to determine complex stoichiometry. A ratio of 3:2 between Pd and **1** respectively is afforded. Several different series were prepared from fresh batches and with different sums of component concentrations (for each series this sum was kept constant) in order to verify this finding. All series examined provide the maxima at this ratio. An example is brought below for one of these series, in which the total concentrations (sum of both components) was 4.20E-4 M. The molar fraction, χ, is marked for **1**.

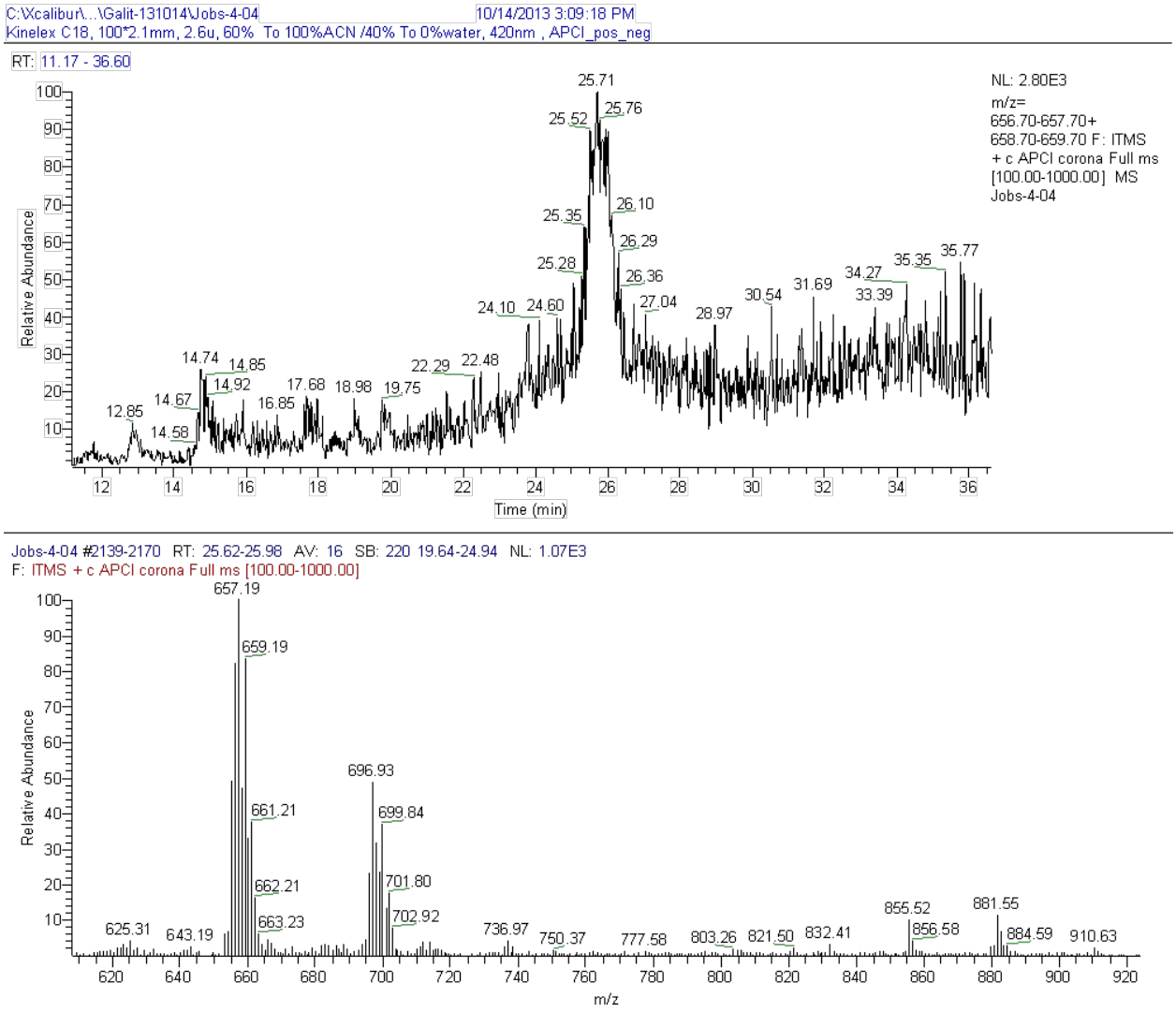


5.3 Complex Studies by HPLC-MS

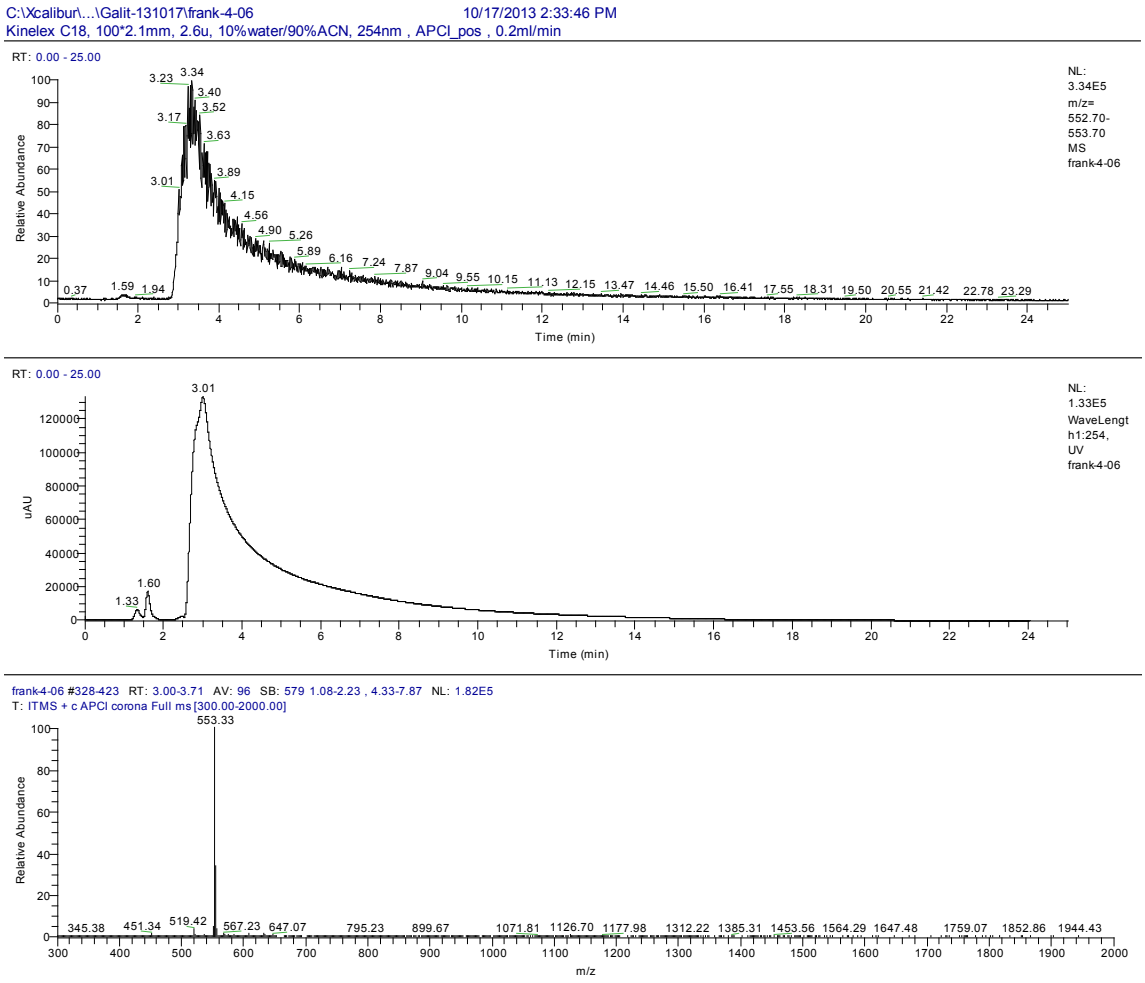
In order to elucidate the uncommon stoichiometry found in section 5.2, and to verify the existence of Pd·1 complexes, HPLC-MS studies were carried out. Solutions from the studies in section 5.2 were injected into a reverse phase column (Kinetex XB-C18, 2.6u, 100x2.1mm, S/N569808-41, Phenomenex) at a flow of 0.2 ml/min with water-acetonitrile (1:9) eluent.

Detection was by UV absorbance at 254nm, and MS. MS analysis of the resulting peaks (positive polarity, APCI source - voltage 6.0 kV, current 5.0 uA, capillary voltage 48 V) provides both complexes of 1:1 stoichiometry (m/z 657, 697 with ACN ligand) and of 1:2 stoichiometry (**1**:Pd respectively, m/z 881). Further, addition of $Pd(OAc)_2$ into a solution of **1** that has previously been injected, provides not only the expected decrease in the peak corresponding to **1**, but also a series of several different new peaks, providing evidence that several different complexes (of differing stoichiometries) form in the solution.

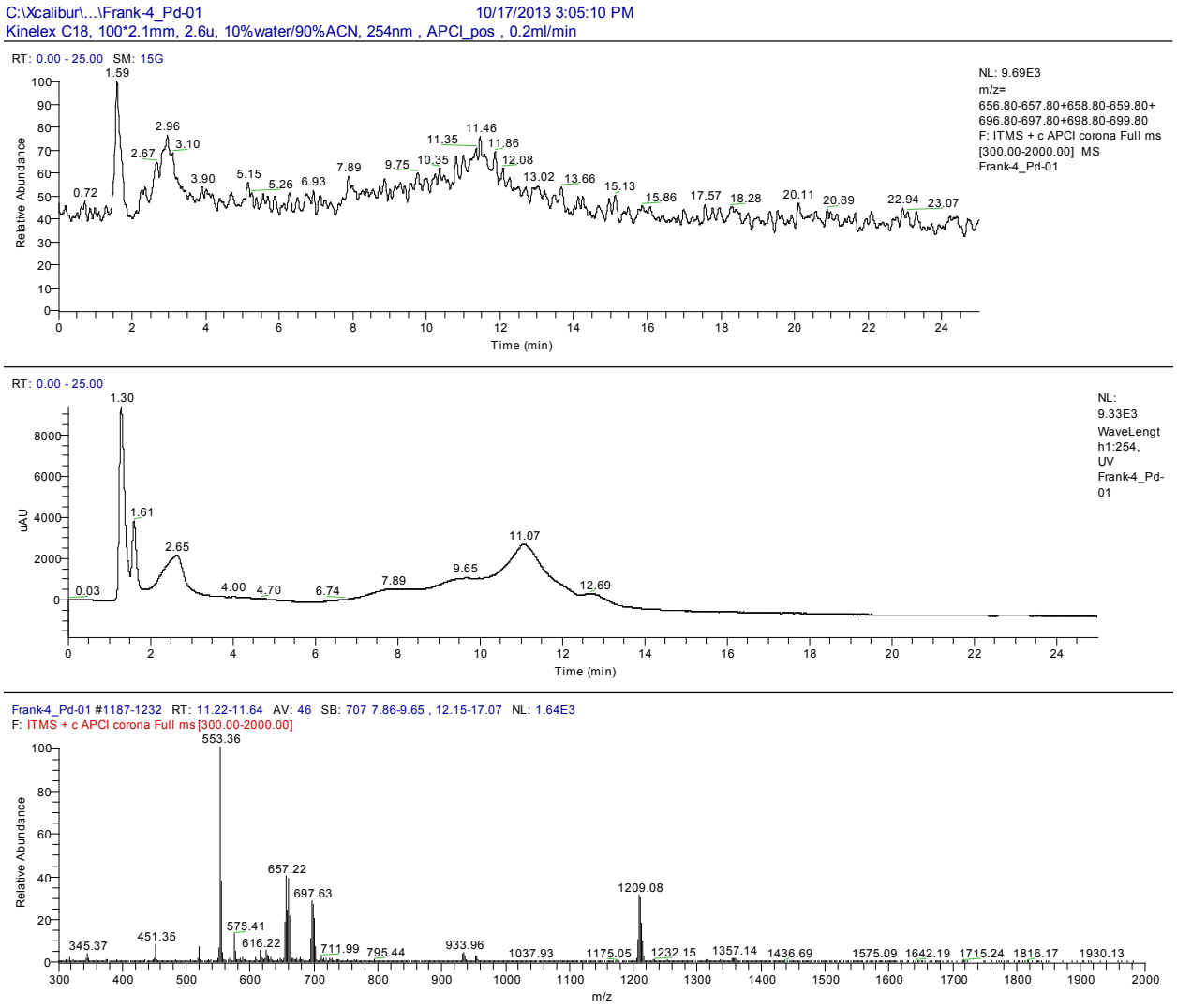
Spectra from complexation solutions:



Spectra for **1** prior to Pd salt addition:



Spectra after $Pd(OAc)_2$ addition (bottom spectra is for one of the new HPLC peaks, at RT 11.2 min, corresponding to RT 11.07 at the UV-Vis detector):



5.4 Determination of Average Binding Constant

Three titrations of $Pd(OAc)_2$ by **1** were performed in chloroform solutions and examined by UV-Vis absorption (focusing on the 420nm maxima formed). Across a titration series the concentration of $Pd(OAc)_2$ was kept constant at 1.50E-4 M and the concentrations of **1** varied from 0 to 3.00E-4 M, in which range saturation was observed (begins before 1.50E-4 M). All series were prepared from fresh stock solutions prepared separately for each titration, and absorption measurements were performed within 5 minutes of sample preparation.

For each titration the complex concentration was calculated and then derived, with the slope (derivative) serving for calculation of the binding constant. The slope obtained for the complex concentration (by increasing concentration of **1**) equals 1.49, which not only corresponds well to the studies in section 5.1, but also enables derivation of this average complex stoichiometry independently. It was normalized to 1 to provide the binding constant at this ratio (3:2).

The binding constant calculation was based on the first points of titration, and derived from slope according to:

$$K = \frac{C\prime}{(1-C\prime)} \cdot \frac{1}{P_0^{\beta}}$$

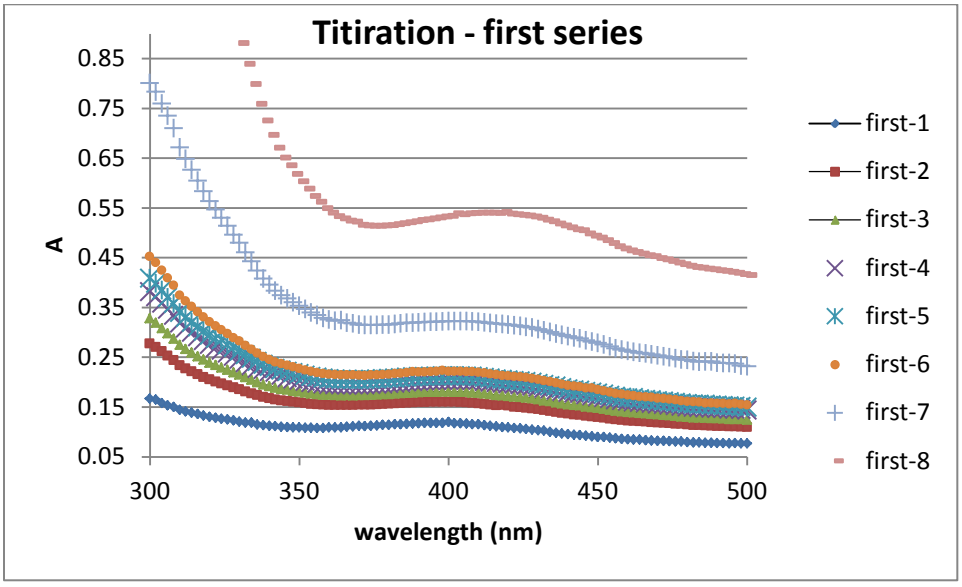
Where C' is the slope of the complex concentration, P_0 is the initial concentration of $PdCl_2$ in the solution, and β is the stoichiometric ratio, set to 1.5.

The concentration of the complex (as a function of **1**) was derived from the absorbance measurements, according to:

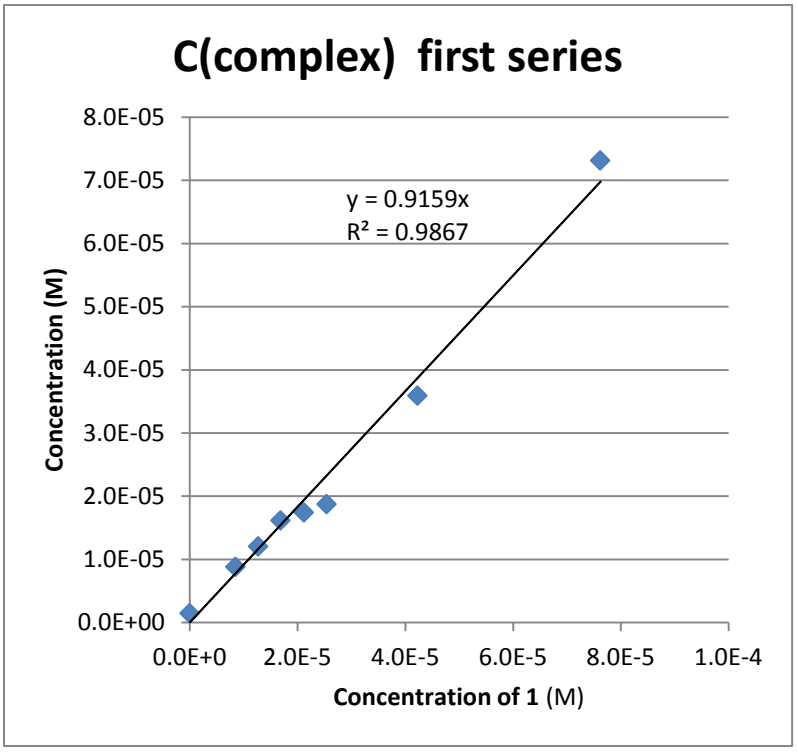
$$C = \frac{P_0}{\beta} \cdot \frac{A - A0}{A\infty - A0}$$

A_0 represents the absorbance from the Pd salt alone and was obtained separately by a calibration series. It was set to 0.10 for the titration concentration of 1.50E-4 M. "$A_{infinity}$" (absorbance at saturation, presumably from the complex alone, an approximation based on solutions with a 5-fold excess of **1** over Pd) was set to 0.70. A is the absorbance measured for the solution at titration.

First Series:



C(**1**) M	A at 420	C(complex) M (calculated)
0	0.1089	1.48E-06
8.47E-06	0.1528	8.80E-06
1.27E-05	0.1723	1.21E-05
1.69E-05	0.1969	1.62E-05
2.12E-05	0.2046	1.74E-05
2.54E-05	0.2125	1.88E-05
4.23E-05	0.3153	3.59E-05
7.62E-05	0.5386	7.31E-05

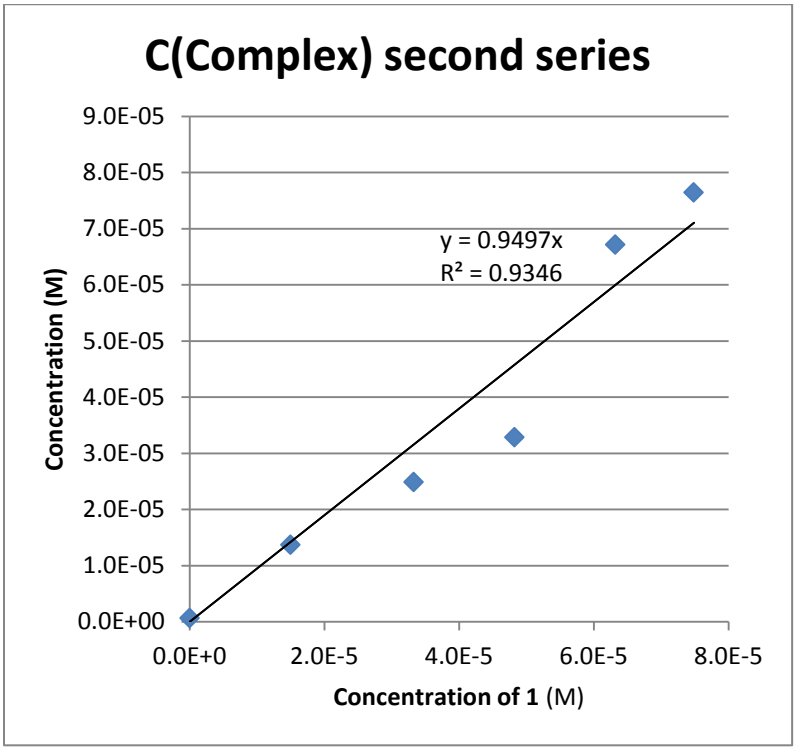


Slope: 0.915

Binding constant: 5.86E+06

Second Series:

C(**1**) M	A at 420	C(complex) M (calculated)
0	0.1040	5.40E-06
1.5E-05	0.1823	1.78E-05
3.33E-05	0.2494	2.85E-05
4.82E-05	0.2971	3.60E-05
6.32E-05	0.5031	6.87E-05
7.49E-05	0.5588	7.76E-05

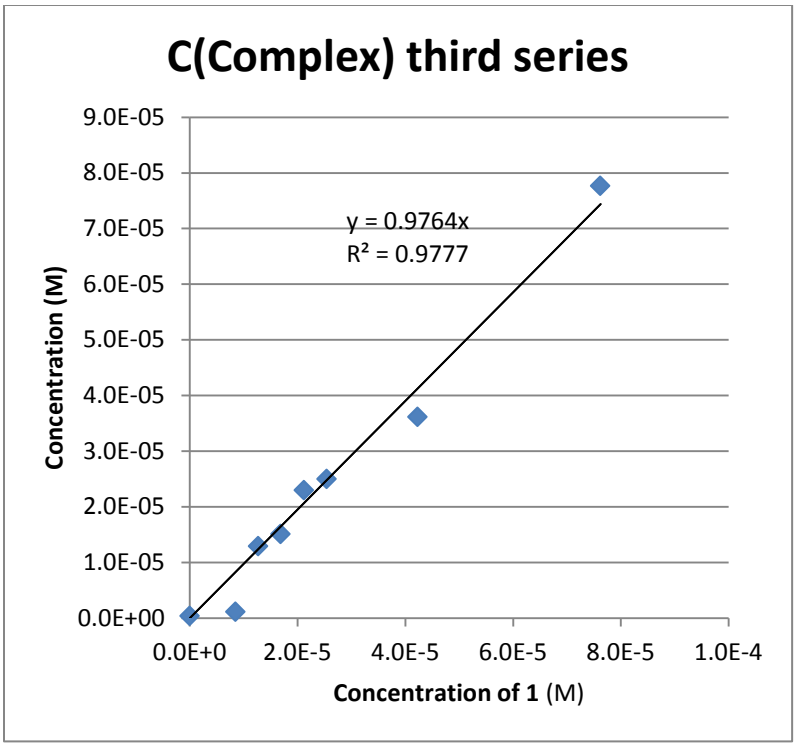


Slope: 0.949

Binding constant: 1.01E+07

Third Series:

C(**1**) M	A at 420	C(complex) M (calculated)
0	0.1022	3.67E-07
8.47E-06	0.1068	1.13E-06
1.27E-05	0.1773	1.29E-05
1.69E-05	0.1906	1.51E-05
2.12E-05	0.2378	2.30E-05
2.54E-05	0.2497	2.50E-05
4.23E-05	0.3166	3.61E-05
7.62E-05	0.5658	7.76E-05



Slope: 0.976

Binding constant: 2.21E+07

Binding Constant average ± standard deviation = $(1.27 \pm 0.84) \cdot 10^7$

6. Metal Binding Studies – $HgCl_2$ complexation with 1

6.1 Determination of stoichiometry

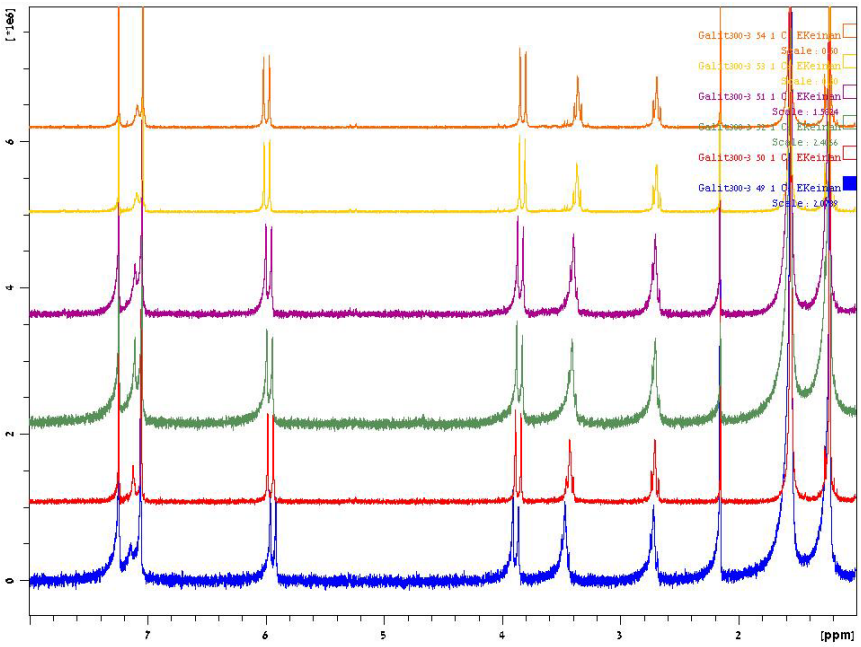
A Job's method[5] was followed, with the sum of the concentration of the **1** and $HgCl_2$ being constant (6mM) with the ratios changing as shown in the table below. The downfield doublet of the methylene protons was used as the measured variable ($CDCl_3$ peak set as 7.260 ppm). A maximum was achieved at a 50:50 stoichiometry (molar fraction, χ, =0.5).

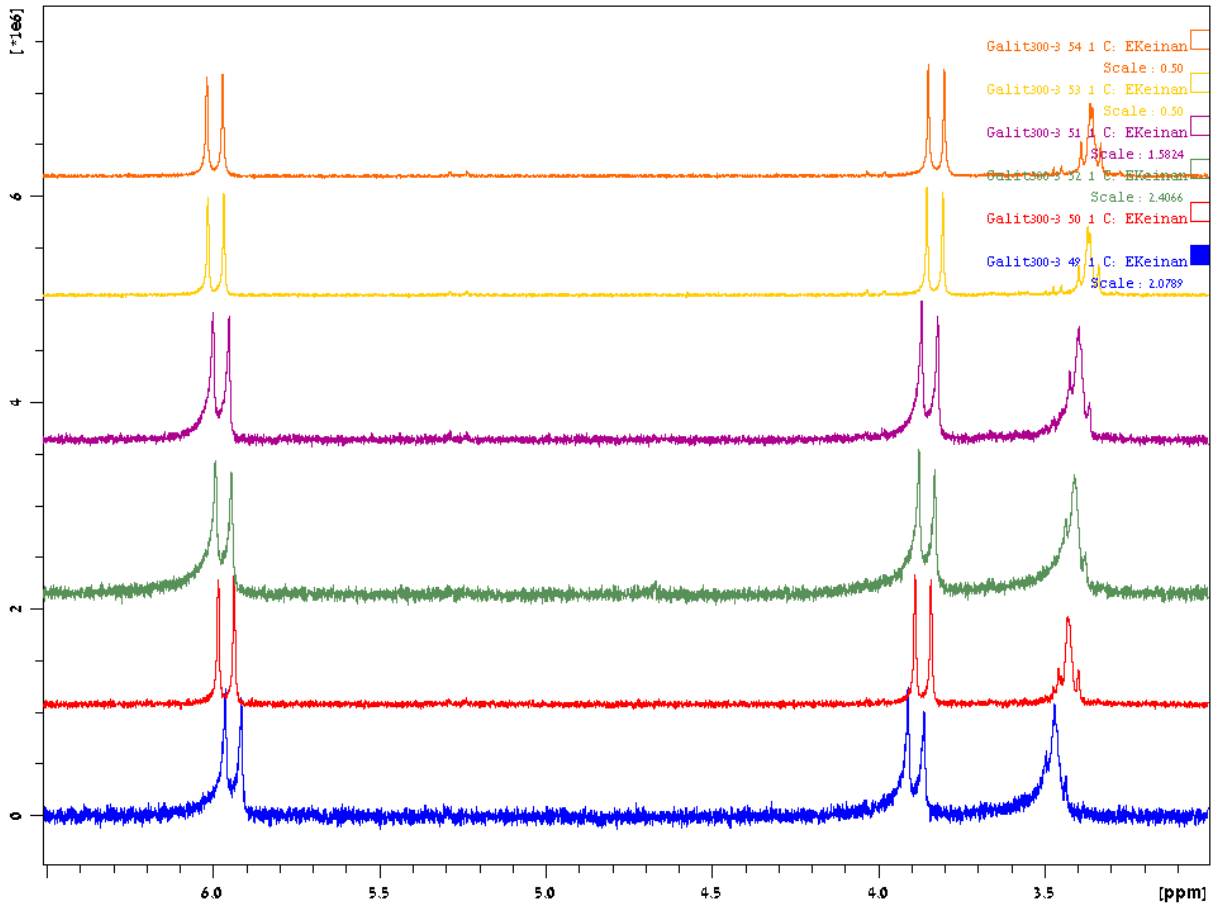
1:$HgCl_2$	**1**(mM)	$HgCl_2$ (mM)	δ (ppm)	Δδ (ppm)	[**1**]x Δδ
100:0	6	0	6.09		
60:40	3.6	2.4	5.9086	0.1814	0.65304
50:50	**3**	**3**	**5.83335**	**0.25665**	**0.76995**
40:60	2.4	3.6	5.8131	0.2769	0.66456
30:70	1.8	4.2	5.7716	0.3184	0.57312

6.2 Determination of binding constant

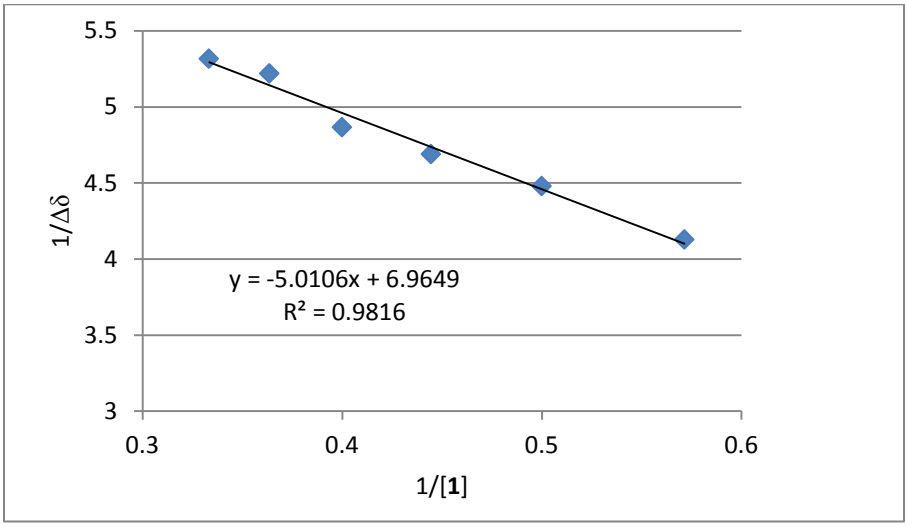
For each series fresh stock solutions of **1** (20mM) and $HgCl_2$ (3mM) in $CDCl_3$ were prepared and sonicated for 2 min prior to use. In each of the following series the concentration of $HgCl_2$ was held constant at 2.5mM while changing the concentration of **1**. The solutions were kept at 22˚C overnight and then analyzed using a Bruker Avance (AV) 300 NMR spectrometer. The Ka value was derived from the Benessi-Hildebrandt treatment[6] with the downfield doublet of the methylene protons being used as the measured variable ($CDCl_3$ peak set as 7.260 ppm).

First series:





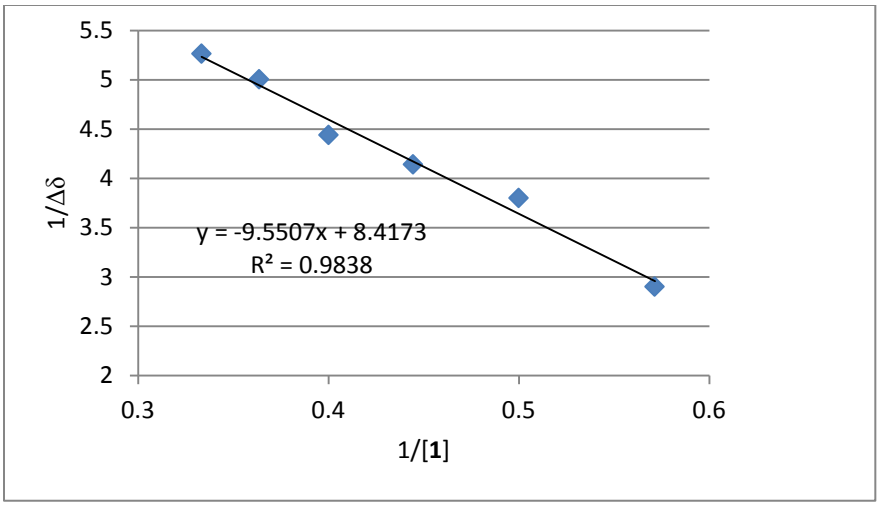
1(mM)	δ (ppm)	1/[**1**]	Δδ (ppm)	1/Δδ
1 only	6.2			
1.75	5.95775	0.57142	0.24225	4.127967
2	5.9767	0.5	0.2233	4.47828
2.25	5.98675	0.444444	0.21325	4.689332
2.5	5.9945	0.4	0.2055	4.86618
2.75	6.0084	0.363636	0.1916	5.219207
3	6.0119	0.333333	0.1881	5.316321



$$\text{Ka} = \frac{6.964}{5.010} * 1{,}000\,\frac{mM}{M} = 1389 M^{-1}$$

Second series:

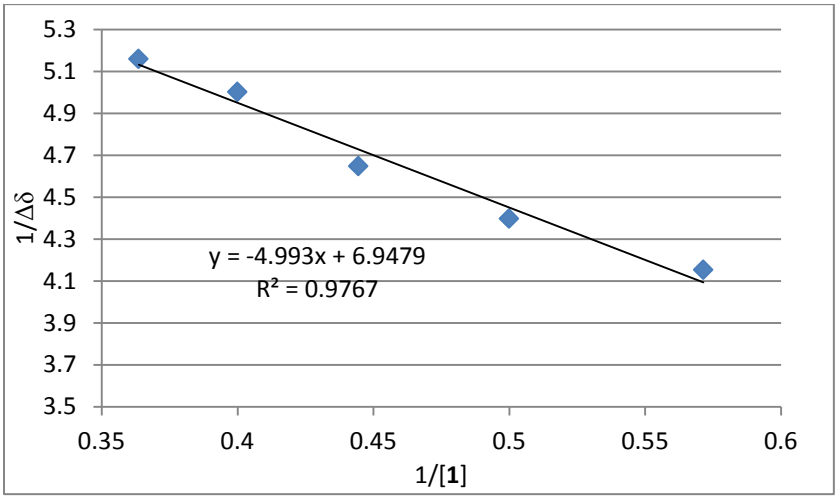
1(mM)	δ (ppm)	1/[**1**]	Δδ (ppm)	1/Δδ
Only **1**	6.2			
1.75	5.85525	0.571429	0.34475	2.900653
2	5.93685	0.5	0.26315	3.800114
2.25	5.9585	0.444444	0.2415	4.140787
2.5	5.9747	0.4	0.2253	4.438526
2.75	6.0002	0.363636	0.1998	5.005005
3	6.01005	0.333333	0.18995	5.264543



$Ka = \frac{8.417}{9.550} * 1{,}000 \frac{mM}{M} = 881 M^{-1}$

Third Series:

1(mM)	δ (ppm)	1/[**1**]	Δδ (ppm)	1/Δδ
1 only	6.0837			
1.75	5.8429	0.571429	0.2408	4.152824
2	5.8563	0.5	0.2274	4.397537
2.25	5.86855	0.444444	0.21515	4.64792
2.5	5.88375	0.4	0.19995	5.00125
2.75	5.88985	0.363636	0.19385	5.158628

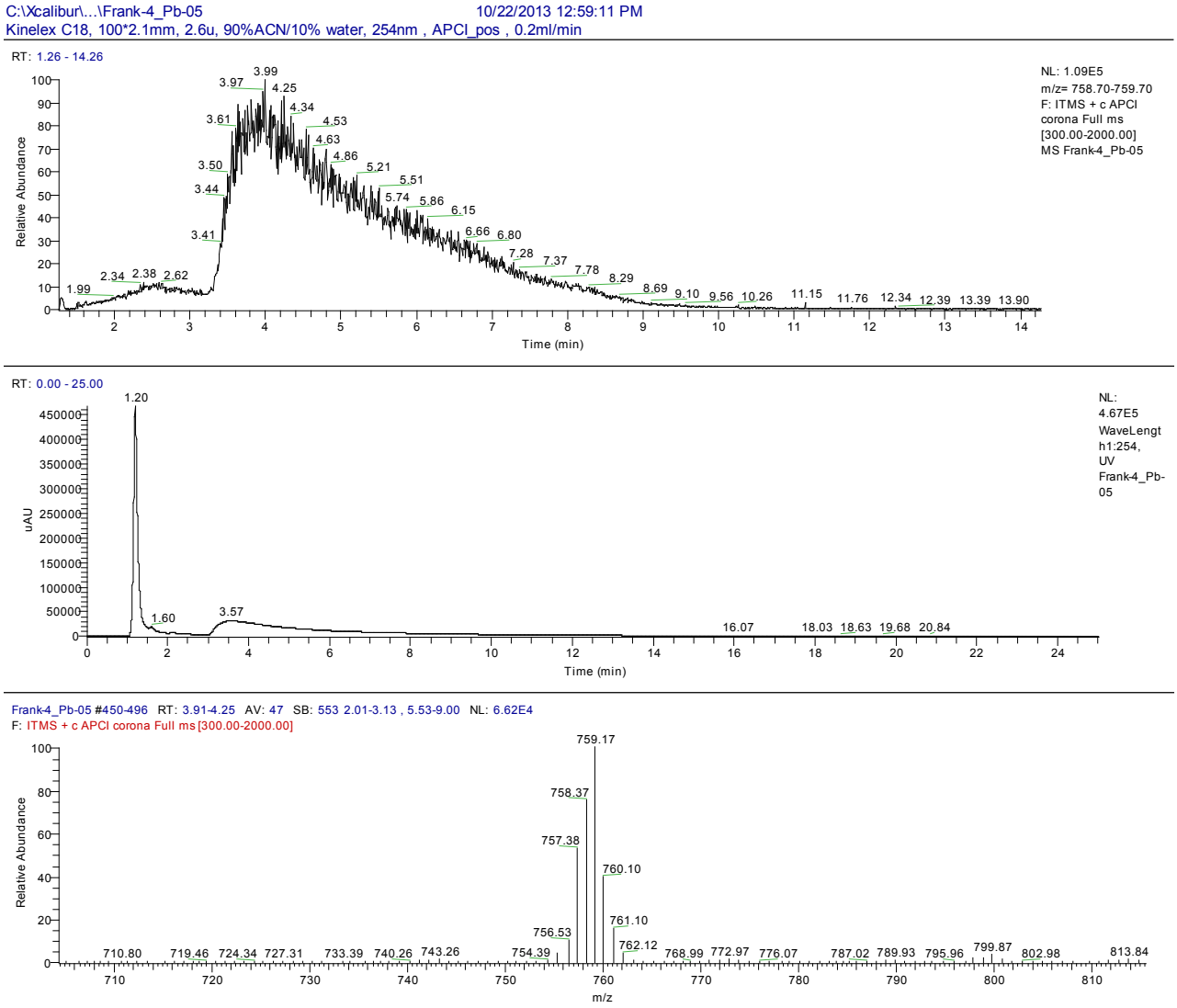


$Ka = \frac{6.947}{4.993} * 1{,}000 \frac{mM}{M} = 1{,}391 M^{-1}$

Average binding constant: $(1.2 \pm 0.3) \cdot 10^3$

7. Metal binding Studies – $Pb(NO_3)_2$ complexation with 1

Similarly to the studies described in section 5.3, HPLC-MS studies provide evidence of complexation of **1** to Pb salt (a predominant 1:1 complex stoichiometry):



8. References

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[6] a) H. A. Benessi, J. H. Hildebrand, *J. Am. Chem. Soc.,* 1949, **71,** 2703-2707. b) L. Fielding, *Tetrahedron*, 2000, **56**, 6151-6170.