Electronic Supplementary Material (ESI) for Organic Chemistry Frontiers.

Binding of ion pairs in a thiourea-functionalized self-folding cavitand.

Agustí Lledó,* and Anna Soler

Institut de Química Computacional i Catàlisi (IQCC), and Departament de Química, Universitat de Girona
Maria Aurèlia Campmany 69, 17003, SPAIN. e-mail: agusti.lledo@udg.edu

Electronic Supplementary Information

I. General Considerations.

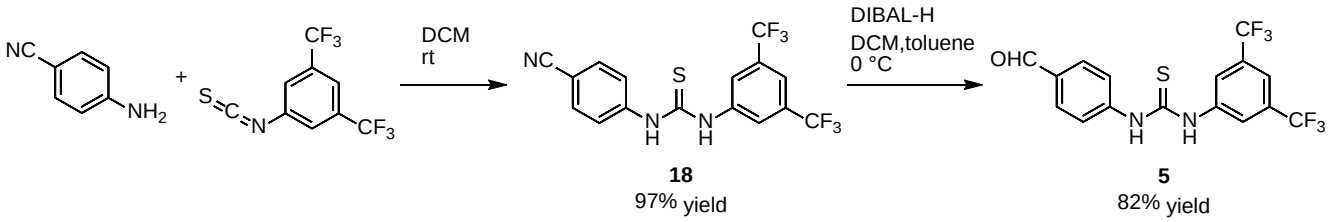
Unless otherwise noted, materials were obtained from commercial suppliers and used without further purification. THF was degassed and dried under nitrogen by passing it through solvent purification columns (MBraun, SPS-800). Reaction progress during the preparation of all compounds was monitored using thin layer chromatography on Macherey-Nagel Xtra SIL G/UV254 silica gel plates. Flash column chromatography was performed on silica gel 60 (40-63 μm). IR spectra were recorded on a Agilent Cary 630 FT-IR spectrometer equipped with an ATR sampling accessory. ^{1}H and ^{13}C NMR spectra were recorded at 298 K unless otherwise stated, at 400 MHz and 100 MHz respectively. A Bruker Ultrashield AVANCE III 400 spectrometer equipped with a 5 mm BBI probe and a Bruker ASCEND 400 spectrometer equipped with a 5 mm BBFO probe were used. The NMR data are reported as follows: chemical shift (δ) in ppm from internal tetramethylsilane (TMS), multiplicity (br = broad, s = singlet, d= doublet, t = triplet, q = quartet, m = multiplet), coupling constants (Hz), integration (^{1}H) and assignment. Mass spectrometry analyses were recorded on a Bruker Esquire 6000 ion trap mass spectrometer or a Bruker micrOTOF-Q II mass spectrometer (high resolution), both equipped with electrospray ion sources. Elemental analyses were performed on Perkin Elmer EA2400 series II analyzer.

Ethyl-footed hexaamide-dinitro cavitand **3a**[1] was prepared by a procedure adapted from the C_{11}-footed version.[2] Ammonium guests **8**-**16** were prepared by treating a solution of the corresponding amine in dry diethyl ether at 0 °C with equimolar amounts of AcOH, HCl (2.0M solution in Et_2O) or H_2SO_4. The precipitated solids were triturated in a ultrasonic bath, filtered, washed with dry diethyl ether and thoroughly dried under high vacuum yielding white powders.

II. Synthesis of **1**.

Hexaamide-dinitro cavitand **4a**[10] (306 mg, 0.216 mmol) was dissolved in 4 mL of toluene and 12 mL of ethyl acetate in a 100 mL 2-necked flask equipped with a reflux condenser. The system was purged with nitrogen and then a pipette tip of a Ra-Ni suspension in 12 mL of methanol was added (the commercial aqueous suspension of Ra-Ni was previously decanted and rinsed with 2 small fractions of methanol). Next, 4 mL (4.0 mmol) of 1.0M hydrazine solution in THF were added, and the mixture was heated in bath at 100 °C with vigorous stirring for 1 h, after which the initial orange solution had faded to almost colorless (pale brown). The volatiles were removed under reduced pressure and the crude diamino cavitand **4b** was further dried under high vacuum for 30 min (off-white resinous solid). At this point **5** (93 mg, 0.238 mmol, 1.10 eq.) was added, the flask flushed with nitrogen and 10 mL of anhydrous dimethylformamide were added. The resulting solution was stirred at room temperature for 1 h at which time it was sparged with air with an immersed long needle, applying vacuum shortly a few times. Then $FeCl_3.6H_2O$ (3.2 mg, 0.012 mmol, 0.055 eq.) was added and the mixture rapidly turned orange. The solution was stirred overnight at room temperature in the sealed flask, and then evaporated under reduced pressure. The crude product was dissolved in 60 mL of dichloromethane, washed twice with water and once with brine, dried with Na_2SO_4, filtered, and concentrated under reduced pressure. The product was purified by sequential flash column chromatography on SiO_2, first employing $CHCl_3$/AcOEt (9:1 to 6:4) and then $CHCl_3$/MeOH (100:0, 99.5:0.5. 99:1, 98:2), to obtain **1** as a pale beige solid (220 mg, 59% yield). M.p. > 312 °C (decomp.). ^{1}H NMR (400 MHz, acetone-d_6) δ 11.76 (1H, NH), 9.98 (1H, NH), 9.94 (1H, NH), 9.88 (1H, NH), 9.72 (1H, NH), 9.66 (1H, NH), 9.13 (1H, NH), 8.91 (1H, NH), 8.68 (1H, NH), 8.30 (m, 2H, CH), 8.08 (s, 1H, CH), 8.03 (s, 1H, CH), 8.01 (s, 2H, CH), 7.94 (s, 1H, CH), 7.93 (s, 1H, CH), 7.89–7.80 (m, 7H, CH), 7.75 (m, 2H, CH), 7.72 (m, 2H, CH), 7.47 (m, 2H, CH), 7.44 (s, 2H, CH), 5.62 (t, J = 8.5 Hz, 2H, CH), 5.71 (t, *J* =8.3 Hz, 1H, CH), 5.65 (t, *J* = 8.4 Hz, 1H, CH), 2.74–2.20 (m, 20H, CH_2), 1.36–0.92 (m, 30H, CH_3) ppm. ^{13}C NMR (101 MHz, acetone-d_6) δ 181.4 (CS), 175.7 (CO), 175.0 (CO), 174.8 (CO), 174.2 (CO), 173.7 (CO), 173.5 (CO), 158.9 (Cq), 157.7 (Cq), 157.0 (Cq), 156.0 (Cq), 155.8 (Cq), 155.7 (Cq), 155.5 (Cq), 153.7 (Cq), 151.4 (Cq), 151.0 (Cq), 150.8 (Cq), 150.4 (Cq), 150.0 (Cq), 149.6 (Cq), 142.7 (Cq), 142.0 (Cq), 141.0 (Cq), 136.9 (Cq), 136.10 (Cq), 135.8 (Cq), 133.7 (Cq), 132.8 (Cq), 131.9 (q, J_F = 33 Hz, Cq), 130.1 (Cq), 128.4 (CH), 127.3 (CH), 126.1 (CH), 125.9 (CH), 125.5 (CH), 125.4 (CH), 125.1 (CH), 124.5 (CH), 124.4 (q, J_F = 272 Hz, CF_3), 122.5 (CH), 122.1 (CH), 121.5 (CH), 118.6 (CH), 118.4 (CH), 117.9 (CH), 117.4 (CH), 117.0 (CH), 114.0 (CH), 106.9 (CH), 36.7 (CH), 36.6 (CH), 32.6 (CH_2), 32.5 (CH_2), 31.6 (CH_2), 27.3 (CH_2), 26.8 (CH_2), 26.2 (CH_2), 25.8 (CH_2), 25.5 (CH_2), 14.3 (CH_3), 13.0 (CH_3), 12.9 (CH_3), 11.2 (CH_3), 10.6 (CH_3), 10.0 (CH_3) ppm. ^{19}F NMR (377 MHz, acetone-d_6) δ -63.44 ppm. IR ν 3230, 2961, 1656, 1596, 1479, 1273 cm^{-1}. HRMS (ESI+) m/z calcd. for $C_{94}H_{87}F_6N_{10}O_{14}S^+$ ([M+H]$^+$): 1726.6054; found: 1726.6038.

III. Synthesis of **5**.

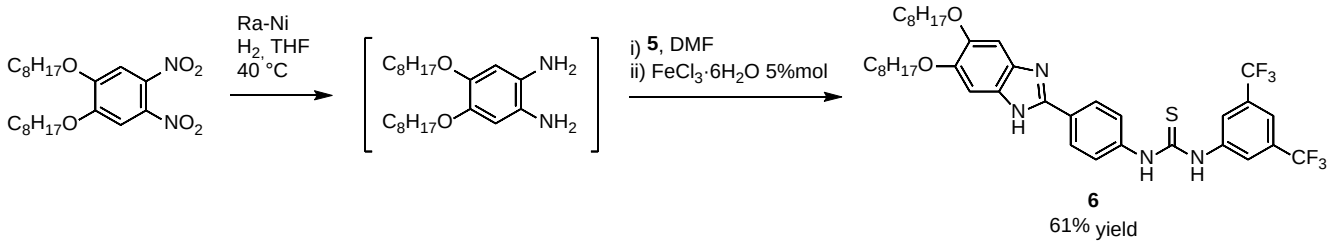


Scheme S1

1-(3,5-bis(trifluoromethyl)phenyl)-3-(4-cyanophenyl)thiourea, 18. To a solution of 4-aminobenzonitrile (324 mg, 2.74 mmol) in THF (5 mL), 3,5-bis(trifluoromethyl)phenyl isothiocyanate (0.500 mL, 2.74 mmol) was added dropwise and the solution stirred overnight at room temperature. After this time a white precipitate had formed and the mixture was concentrated under reduced pressure. The resulting solids were triturated in 10 mL of refluxing dichloromethane, filtered when cold and further dried under high vacuum, to obtain 1.03 g (97%) of the title compound as a fine, pale yellow powder. M.p. 197 °C. ^{1}H NMR (400 MHz, acetone-d_6) δ 9.82 (bs, 1H, NH), 9.75 (bs, 1H, NH), 8.29 (m, 2H, CH), 7.85 (m, 1H, CH), 7.81 (s, 1H, CH), 7.77 (m, 1H, CH) ppm. ^{13}C NMR (101 MHz, acetone-d_6) δ 181.3 (CS), 144.1 (Cq), 142.3 (Cq), 133.8 (CH), 132.1 (q, J_F = 33 Hz, Cq), 125.1 (m, CH), 124.5 (CH), 124.3 (q, J_F = 272 Hz, CF_3), 119.3 (CN), 118.9 (m, CH), 108.8 (Cq) ppm. ^{19}F NMR (377 MHz, acetone-d_6) δ -63.51 ppm. IR ν 3365, 3255, 2229, 1644, 1582, 1545, 1470, 1117 cm^{-1}. MS (ESI+) *m/z* 390 ([M+H]$^+$). EA calc.: C 49.36; H 2.33; F 29.28; N 10.79; S 8.23. Found: C 49.28; H 2.30; N 10.65 (dif. 37.76, calc. 37.52).

1-(3,5-bis(trifluoromethyl)phenyl)-3-(4-formylphenyl)thiourea, 5. 1-(3,5-Bis(trifluoromethyl)phenyl)-3-(4-cyanophenyl)thiourea (**18**, 942 mg, 2.42 mmol) was weighed in a 2-neck, 100 mL round bottom flask which was then purged with nitrogen. Anhydrous dichloromethane (24 mL) was then added and the resulting solution cooled to 0 °C in an ice bath. DIBAL-H (9.7 mL of a 1.0 M solution in toluene, 9.7 mmol) was then added dropwise via syringe over 10 minutes. The mixture was stirred at 0 °C for further 2 h and then quenched by slow addition of methanol (2 mL). After stirring at 0 °C for 5 min., 25 mL of 10% HCl solution and dichloromethane were added and the biphasic mixture stirred at room temperature for 15 min. A minimal amount of ethyl acetate was added to dissolve some suspended solids and the phases were separated. The aqueous phase was washed three times with dichloromethane and the combined organic layers were dried with Na_2SO_4, filtered and concentrated under reduced pressure. The crude product was dissolved in a 1:1 hexane/ethyl acetate and filtered through a short plug of SiO_2. Upon evaporation of the solvent under reduced pressure a solid was obtained, which was triturated in refluxing dichloromethane and filtered once cold. Upon drying under high vacuum 568 mg of **5** are obtained as a fine pale yellow powder. From the mother liquor of the trituration, an additional 211 mg of spectroscopically pure compound were obtained after column chromatography (SiO_2, hexane/acetone 8:2), for a total of 779 mg (82% yield). M.p. 192 °C. ^{1}H NMR (400 MHz, acetone-d_6) δ 9.99 (s, 1H, CHO), 9.84 (bs, 1H, NH), 9.75 (bs, 1H, NH), 8.32 (s, 2H, CH), 7.94 (m, 2H, CH), 7.86 (m, 2H, CH), 7.81 (s, 1H, CH) ppm. ^{13}C NMR (101 MHz, acetone-d_6) δ 191.6 (CO), 181.3 (CS), 145.1 (Cq), 142.4 (Cq), 134.3 (Cq), 132.1 (q, J = 33 Hz, Cq), 131.2 (CH), 125.0 (m, CH), 124.3 (q, J = 272 Hz, CF_3), 124.0 (CH), 118.7 (m, CH) ppm. ^{19}F NMR (377 MHz, acetone-d_6) δ -63.51 ppm. IR ν 3352, 3245, 1668, 1586, 1540, 1471, 1378, 1251, 1117 cm^{-1}. MS (ESI+) *m/z* 393 ([M+H]$^+$). EA calc.: C 48.98; H 2.57; F 29.06; N 7.14; S 8.17. Found: C 49.02; H 2.45; N 7.10 (dif. 41.43, calc. 41.31).

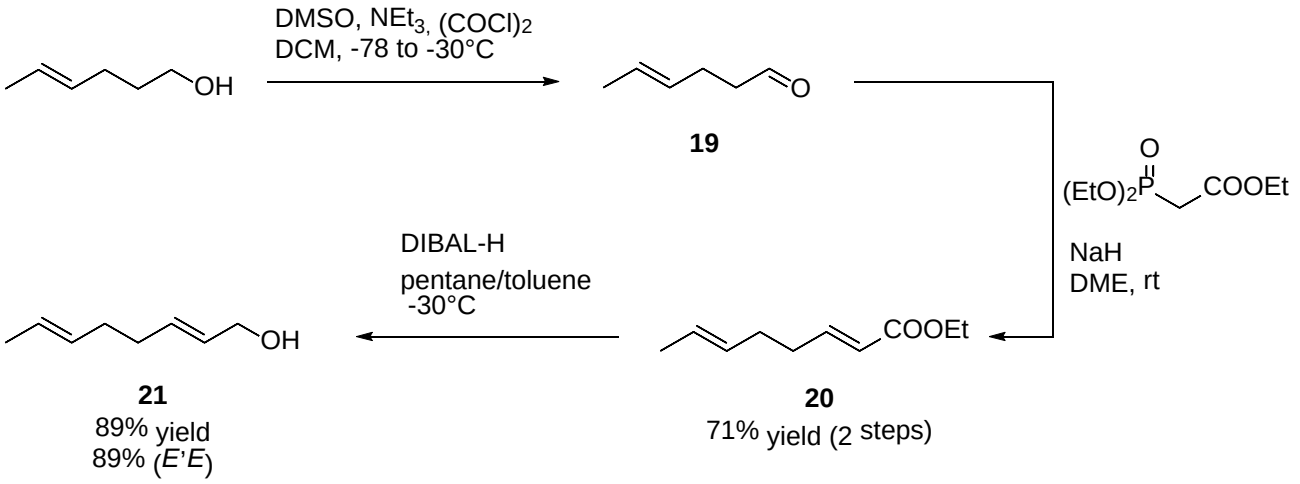
IV. Synthesis of model compound **6**.



Scheme S2

1,2-dinitro-4,5-bis(octyloxy)benzene[3] (232 mg, 0.545 mmol) was weighed in a 100 mL low pressure glass vessel (Ace Glass). A pipette tip of Raney-Nickel was added by suspending it in THF (2x3mL fractions used for a total volume of 6 mL, Ra-Ni was previously washed twice with THF). The flask was capped with a PTFE Swagelok adapter equipped with a low pressure manometer and a ball valve. The flask was purged with hydrogen and then the pressure set to 1 bar. The flask was immersed in an oil bath at 40 °C and the suspension was vigorously stirred. As the reaction progressed a drop in the hydrogen pressure was observed. The solution went from yellow to deep orange and 2.5 h the solution became mostly colorless, indication total reduction of the nitro groups (TLC monitoring can be done using CH_2Cl_2 as eluent). At this point the flask was let to cool down and then purged with nitrogen. The adapter was replaced with a septum and the solution was decanted from the Ra-Ni stuck to the stirring magnet and transferred by syringe to a 50 mL round bottom flask purged with nitrogen. The pressure vessel was rinsed with two additional portions of anhydrous DMF. Next, a solution of aldehyde **5** (214 mg, 0.545 mmol, 1.0 eq.) in 4 mL of anhydrous DMF was added dropwise (the flask rinsed with 2x1 mL portions of DMF), and the resulting mixture was stirred at room temperature for 2 h. At this point the flask was purged with air from the atmosphere and $FeCl_3.6H_2O$ was added (7.0 mg, 0.0259 mmol, 0.0475 eq.). The mixture turned dark green quickly and was stirred for 1 further hour in the sealed flask. After this time most of the DMF was removed under reduced pressure (T < 35 °C). The resulting oil was dissolved in an AcOEt/CH_2Cl_2 3:1 mixture which was washed 4 times with water (containing a little bit of NaCl). Finally the organic layer was washed with brine, dried with Na_2SO_4, filtered and concentrated under reduced pressure. The resulting dark green residue was subjected to careful column chromatography using silica gel and CH_2Cl_2/MeOH mixtures as eluent (0%, 0.5%, 0.75%, 1%, 2% in MeOH). The title compound was isolated as an ochre solid (246 mg, 61% yield). M.p. 86 °C (decomp.). ^{1}H NMR (400 MHz, acetone-d_6) δ 9.69 (s, 1H, NH), 9.66 (bs, 1H, NH), 8.36 (s, 2H, CH), 8.13 (d, J = 8.6 Hz, 2H, CH), 7.78 (s, 1H, CH), 7.68 (d, J = 8.6 Hz, 2H, CH), 7.13 (s, 2H, CH), 4.03 (t, J = 6.4 Hz, 4H, CH_2), 1.81 (m, 4H, CH_2), 1.55 (m, 4H, CH_2), 1.46 – 1.23 (m, 16H, CH_2), 0.89 (t, J = 6.7 Hz, 6H, CH_3) ppm. ^{13}C NMR (101 MHz, acetone-d_6) δ 181.2 (CS), 150.5 (Cq), 148.3 (Cq), 142.8 (Cq), 140.1 (Cq), 131.89 (q, J_F = 33 Hz, Cq), 128.9 (Cq), 127.5 (CH), 125.2 (CH), 124.8 (CH), 124.4 (q, J_F = 272 Hz, CF_3), 118.3 (CH), 101.2 (CH), 70.4 (CH_2), 32.6 (CH_2), 30.3 (CH_2), 30.2 (CH_2, overlap D_3CCOCD_3), 30.1 (CH_2), 27.0 (CH_2), 23.4 (CH_2), 14.4 (CH_3) ppm. ^{19}F NMR (377 MHz, acetone-d_6) δ -63.50 ppm. IR ν 3225, 2920, 2851, 1539, 1452, 1378, 1273, 1170, 1129 cm^{-1}. HRMS (ESI+) m/z calcd. for $C_{38}H_{46}F_6N_4O_2S^+$ ([M+H]$^+$): 737.3318; found: 737.3325.

V. Preparation of non-commercial allylic alcohols.



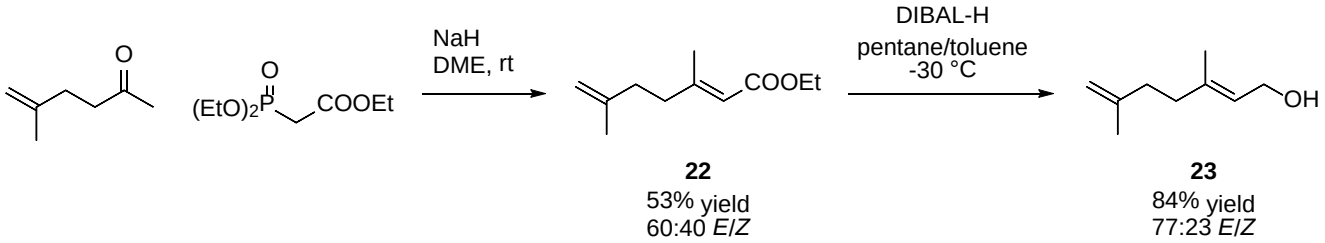
Scheme S3

(*E*)-4-Hexenal (19) was prepared by Swern oxidation of (*E*)-4-hexen-1-ol (2.35 mL, 20.0 mmol, Sigma-Aldrich, ≥85% *E*) following a reported procedure.[4] After work-up, the organic layer containing the crude aldehyde was concentrated under reduced pressure (200 mbar) at 0 °C, and the resulting oil was used immediately in the next step.

Ethyl (2*E*,6*E*)-octa-2,6-dienoate (20).[5] Sodium hydride (880 mg, 60% w/w, 22.0 mmol) was weighed in a dry 250 mL round bottom flask which was capped with rubber septa and flushed with nitrogen. Anhydrous dimethoxyethane (40 mL) was then added. To the resulting suspension, triethyl phosphonacetate (4.17 mL, 21.0 mmol) is added dropwise, providing an outlet for H_2 evolution. After stirring at room temperature for 30 min., a solution of the crude (*E*)-4-hexenal in ca 80 mL dichloromethane was added dropwise via cannula. The resulting orange solution was stirred at room temperature overnight. The reaction was quenched with saturated NH_4Cl aq. solution. The mixture was extracted 3 times with dichloromethane and the combined organic layers then washed with brine, dried with Na_2SO_4 and concentrated under reduced pressure. The crude product was subjected to flash column chromatography (SiO_2, hexane/ethyl acetate 1:0 to 98:2) to obtain 2.39 g of a colorless oil (71% yield, 2 steps, 82% *E*, *E* by ^{13}C NMR). ^1H NMR (400 MHz, $CDCl_3$) δ 6.95 (dt, *J* = 15.7, 6.8 Hz, 1H, CH), 5.82 (dt, *J* = 15.7, 1.6 Hz, 1H, CH), 5.54 – 5.34 (m, 2H, CH), 4.18 (q, *J* = 7.1 Hz, 2H, CH_2), 2.25 (m, 2H, CH_2), 2.14 (m, 2H, CH_2), 1.65 (m, 3H, CH_3), 1.29 (t, *J* = 7.1 Hz, 3H, CH_3) ppm. ^{13}C NMR (101 MHz, $CDCl_3$) δ 166.8 (CO), 148.8 (CH), 129.8 (CH), 126.2 (CH), 121.6 (CH), 60.3 (CH_2), 32.4 (CH_2), 31.1 (CH_2), 18.0 (CH_3), 14.4 (CH_3) ppm.

(2*E*,6*E*)-Octa-2,6-dien-1-ol (21).[6] Ethyl (2*E*,6*E*)-octa-2,6-dienoate (2.37 g, 14.1 mmol) was weighed in a 2-neck, 250 mL round bottom flask equipped with an addition funnel and rubber septa. The system was purged with nitrogen and 30 mL of pentane were added. The mixture was cooled at -30 °C in a dewar and then DIBAL-H (42 mL, 1.0M solution in toluene, 42.0 mmol) was added dropwise through the addition funnel over 10 min. The mixture was stirred for 2 additional hours during which time the temperature of the cooling bath had risen to -10 °C and no starting material was observed upon TLC monitoring. The mixture was quenched by careful addition of methanol (4.5 mL) at 0 °C and stirred for 30 min., and then treated with 400 mL of iced 5% aq. HCl and 200 mL of diethyl ether. The biphasic mixture was stirred for further 15 min. and the phases were then separated. The aqueous layer was further extracted with two portions of Et_2O and the combined organic layers

were then dried (Na_2SO_4), filtered and concentrated under reduced pressure. The residue was distilled on a Kugelrohr apparatus (1 – 1.5 mmHg, oven temperature 90 °C) to furnish 1.58 g (89% yield, 89% *E*, *E* by ^{1}H NMR) of a clear transparent oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.80 – 5.58 (m, 2H, CH), 5.52 – 5.34 (m, 2H, CH), 4.09 (d, *J* = 4.9 Hz, 2H, CH_2), 2.22 – 2.01 (m, 4H, CH_2), 1.65 (d, *J* = 4.1 Hz, 3H, CH_3), 1.43 (bs, 1H, OH) ppm. ^{13}C NMR (101 MHz, $CDCl_3$) δ 132.8 (CH), 130.6 (CH), 129.3 (CH), 125.4 (CH), 63.8 (CH_2), 32.4 (CH_2), 32.3 (CH_2), 18.0 (CH_3) ppm.



Scheme S4

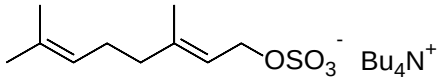
Ethyl (*E*)-3,6-dimethylhepta-2,6-dienoate (22).[7] Sodium hydride (1.70 g, 60% w/w, 42.5 mmol) was weighed in a dry 500 mL round bottom flask which was capped with rubber septa and flushed with nitrogen. Anhydrous dimethoxyethane (80 mL) was then added. To the resulting suspension, triethyl phosphonacetate (8.0 mL, 40.3 mmol) was added dropwise, providing an outlet for H_2 evolution. After stirring at room temperature for 45 min., 5-methylhex-5-en-2-one (5.0 mL, 38.6 mmol) was added dropwise. The resulting mixture was stirred at room temperature overnight, and then at 50 °C for 3 h. The reaction was quenched with saturated NH_4Cl aq. solution. The mixture was extracted 3 times with dichloromethane and the combined organic layers then washed with brine, dried with Na_2SO_4 and concentrated under reduced pressure. The residue was distilled under reduced pressure (0.8 mmHg, bp 57-58 °C) to yield 3.72 g (53% yield) of a clear transparent oil (*E*/*Z* ratio 6:4 by ^{1}H NMR). ^{1}H NMR (400 MHz, $CDCl_3$): δ 5.67 (m, 1H, CH), 4.74 (m, 0.8H *E*, CH_2), 4.72 (m, 0.4H *Z*, CH_2), 4.69 (m, 0.8H *E*, CH_2), 4.15 (q, *J* = 7.1 Hz, 2H, CH_2), 2.76 (m, 0.4H *Z*, CH_2), 2.27 (m, 1.6H *E*, CH_2), 2.23 – 2.13 (m, 2H, CH_2), 2.17 (d, *J* = 1.4 Hz, 2.4H *E*, CH_3, overlap with prev. res.), 1.89 (d, *J* = 1.4 Hz, 0.6H *Z*, CH_3,), 1.77 (m, 0.6H *Z*, CH_3), 1.73 (m, 2.4H *E*, CH_3), 1.28 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 167.0 (CO *E*), 166.4 (CO *Z*), 160.0 (Cq *Z*), 159.6 (Cq *E*), 145.5 (Cq *Z*), 144.7 (Cq *E*), 116.5 (CH *Z*), 115.8 (CH *E*), 110.7 (CH *E*), 110.3 (CH *Z*), 59.61 (CH_2 *E*), 59.59 (CH_2 *Z*), 39.2 (CH_2 *E*), 36.2 (CH_2 *Z*), 35.7 (CH_2 *E*), 32.0 (CH_2 *Z*), 25.3 (CH_3 *Z*), 22.5 (CH_3 *E*), 22.4 (CH_3 *Z*), 18.9 (CH_3 *E*), 14.4 (CH_3) ppm.

(*E*)-3,6-Dimethylhepta-2,6-dien-1-ol (23).[8] Ethyl 3,6-dimethylhepta-2,6-dienoate (3.66 g, 20.1 mmol) was weighed in a 2-neck, 250 mL round bottom flask equipped with an addition funnel and rubber septa. The system was purged with nitrogen and 40 mL of pentane were added. The mixture was cooled at -30 °C in a dewar and then DIBAL-H (60 mL, 1.0M solution in toluene, 60.0 mmol) was added dropwise through the addition funnel over 0.5 h. The mixture was stirred for 3 additional hours during which time the temperature of the cooling bath had risen to 10 °C and no starting material was observed upon TLC monitoring. The mixture was quenched by careful addition of methanol (5 mL) at 0 °C and stirred for 30 min., and then treated with 500 mL of iced 5% aq. HCl and 200 mL of diethyl ether. The biphasic mixture was stirred for further 15 min. and the phases were then separated. The aqueous layer was extracted with two additional portions of Et_2O and the combined organic layers were then dried (Na_2SO_4), filtered and concentrated under reduced pressure. The residue was distilled under high vacuum (0.8 – 0.9 mmHg, bp 60 – 62 °C) to furnish 2.37 g (84% yield) of a clear transparent oil (*E*/*Z* ratio 77:23 by ^{1}H NMR). ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.43 (m, 1H, CH), 4.76 – 4.64 (m, 2H,

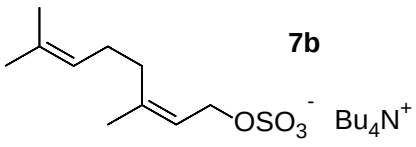
CH_2), 4.15 (d, *J* = 6.9 Hz, 1.54H *E*, CH_2), 4.11 (d, *J* = 7.1 Hz, 0.46H *Z*, CH_2), 2.15 (m, 4H, CH_2), 1.76 (m, 0.69H *Z*, CH_3), 1.75 (m, 0.69H *Z*, CH_3), 1.73 (m, 2.31H *E*, CH_3), 1.69 (m, 2.31H *E*, CH_3), 1.23 (s, 1H, OH) ppm. ^{13}C NMR (101 MHz, $CDCl_3$) δ 145.7 (Cq *Z*), 145.6 (Cq *E*), 139.9 (Cq *Z*), 139.6 (Cq *E*), 124.6 (CH *Z*), 123.6 (CH *E*), 110.4 (CH_2 *Z*), 110.1 (CH_2 *E*), 59.4 (CH_2 *E*), 59.1 (CH_2 *Z*), 37.8 (CH_2 *E*), 36.5 (CH_2 *Z*), 36.2 (CH_2 *E*), 30.5 (CH_2 *Z*), 23.5 (CH_2 *Z*), 22.6 (CH_2 *Z*), 22.5 (CH_2 *E*), 16.3 (CH_2 *E*) ppm.

VI. Synthesis of tetrabutylammonium sulphate guests **7a-h**.

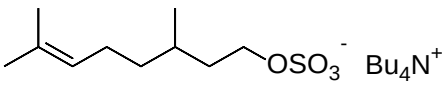
General procedure: SO_3·Pyr (627 mg, 3.94 mmol) is weighed in a dry 50 mL flask and slurried under nitrogen with 1 mL of dry THF. A solution of the alcohol (3.94 mmol) in 1 mL of dry THF is then added and the mixture stirred for 2 h at room temperature. After this time tetrabutylammonium bromide (1.27 g, 3.94 mmol) is added together with chloroform and water and the mixture is stirred for 10 min. The layers are separated and the organic phase is extracted 3 times with water and then dried with Na_2SO_4 and filtered. The solvent is evaporated under reduced pressure and the resulting thick, clear, transparent oil is further dried under high vacuum. The resulting material is analytically pure in most instances. If unreacted alcohol remains, this can be removed by extraction with n-heptane: the oil is shaken and/or sonicated with *n*-heptane and then let sit in the fridge overnight. The *n*-heptane layer is decanted and the residual solvent is removed under vacuum. Addition of pentane and evaporation facilitates complete removal of the solvents. All reactions were carried out on a scale of 3 – 4 mmol (starting alcohol).

Tetrabutylammonium (*E*)-3,7-dimethylocta-2,6-dien-1-yl sulphate (tetrabutylammonium geranyl sulphate), 7a, 

7a
Yield 70%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.42 (tq, *J* = 6.7, 1.3 Hz, 1H, CH), 5.09 (m, 1H, CH), 4.58 (d, *J* = 6.8 Hz, 2H, CH_2), 3.29 (m, 8H, CH_2), 2.07 (m, 2H, CH_2), 1.99 (m, 2H, CH_2), 1.70 – 1.60 (m, 14H, CH_2+CH_3+CH_3), 1.59 (s, 3H, CH_3), 1.44 (tq, *J* = 7.4, 7.4 Hz, 8H, CH_2), 1.00 (t, *J* = 7.3 Hz, 12H, CH_3) ppm. ^{13}C NMR (101 MHz, $CDCl_3$) δ 139.4 (Cq), 131.6 (Cq), 124.1 (CH), 120.4 (CH), 64.1 (CH_2), 58.7 (CH_2), 39.6 (CH_2), 26.5 (CH_2), 25.7 (CH_3), 24.0 (CH_2), 19.8 (CH_2), 17.7 (CH_3), 16.5 (CH_3), 13.7 (CH_3) ppm. IR ν 2959, 2872, 1668, 1459, 1216 cm^{-1}. HRMS (ESI-) m/z calcd. for $C_{10}H_{17}O_4S^-$: 233.0842; found: 233.0844. MS (ESI+) *m/z* 242 ($C_{16}H_{36}N^+$).

Tetrabutylammonium (*Z*)-3,7-dimethylocta-2,6-dien-1-yl sulphate (tetrabutylammonium neryl sulphate), 7b. 

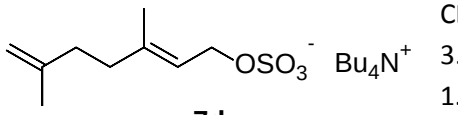
7b
Yield 98%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.41 (m, 1H, CH), 5.0.7 (m, 1H, CH), 4.56 (d, *J* = 6.9 Hz, 2H, CH_2), 3.28 (m, 8H, CH_2), 2.00 – 2.13 (m, 4H, CH_2), 1.71 (m, 3H, CH_3), 1.69 – 1.59 (m, 11H, CH_2+CH_3), 1.58 (s, 3H, CH_3), 1.44 (tq, J = 7.4, 7.4 Hz, 8H, CH_2), 1.00 (t, *J* = 7.3 Hz, 12H, CH_3) ppm. ^{13}C NMR (101 MHz, $CDCl_3$) δ 139.4 (Cq), 131.8 (Cq), 124.0 (CH), 121.6 (CH), 63.8 (CH2), 58.6 (CH2), 32.3 (CH2), 26.8 (CH2), 25.7 (CH3), 24.0 (CH2), 19.7 (CH2), 17.7 (CH3), 13.7 (CH3) ppm. IR ν 2959, 2872, 1668, 1459, 1216 cm^{-1}. HRMS (ESI-) m/z calcd. for $C_{10}H_{17}O_4S^-$: 233.0842; found: 233.0839. MS (ESI+) *m/z* 242 ($C_{16}H_{36}N^+$).

Tetrabutylammonium 3,7-dimethylocta-6-en-1-yl sulphate (tetrabutylammonium citronellyl sulphate), 7c. 

7c
Yield 93%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.08 (m, 1H, CH), 4.06 (m, 2H, CH_2), 3.28 (m, 8H, CH_2), 1.95 (m, 2H, CH_2), 1.79 – 1.55 (m, 14H, CH_2+CH_3+CH_2+CH), 1.58 (s, 3H, CH_3), 1.45 (m, 9H, 2xCH_2), 1.34 (m, 1H, CH_2), 1.16 (m, 1H, CH_2), 1.01 (t, *J* = 7.3, 12H, CH_3), 0.89 (d, *J* = 6.6, 3H,

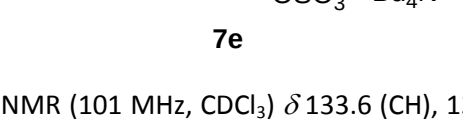
CH_3) ppm. ^{13}C NMR (101 MHz, $CDCl_3$) δ 131.0 (Cq), 125.0 (CH), 65.7 (CH_2), 58.8 (CH_2), 37.4 (CH_2), 36.7 (CH_2), 29.6 (CH), 25.8 (CH_3), 25.6 (CH_2), 24.1 (CH_2), 19.8 (CH_2), 19.5 (CH_3), 17.7 (CH_3), 13.8 (CH_3) ppm. IR ν 2959, 2872, 1459, 1217 cm^{-1}. HRMS (ESI-) m/z calcd. for $C_{10}H_{19}O_4S^-$: 235.0999; found: 235.0987. MS (ESI+) *m/z* 242 ($C_{16}H_{36}N^+$).

Tetrabutylammonium (*E*)-3,6-dimethylhepta-2,6-dien-1-yl sulphate, 7d. Quantitative yield. ^1H NMR (400 MHz, $CDCl_3$) δ 5.42 (m, 1H, CH), 4.67 (m, 2H, CH_2), 4.57 (d, *J* = 6.8 Hz, 2H, CH2), 3.28 (m, 8H, CH_2), 2.25 – 1.99 (m, 4H, 2xCH_2), 1.72 (m, 3H, CH_3), 1.70 – 1.57 (m, 11H, CH_2+CH_3), 1.44 (tq, J = 7.4, 7.4 Hz, 9H), 1.00 (t, *J* = 7.3 Hz, 12H, CH_3). ^{13}C NMR (101 MHz, $CDCl_3$) δ 145.8 (Cq), 145.7 (Cq min.), 139.3 (Cq. min.), 139.2 (Cq), 121.6 (CH min.), 120.6 (CH), 109.9 (CH_2 min.), 109.8 (CH_2), 64.1 (CH_2), 63.8 (CH_2 min.), 58.7 (CH_2), 37.9 (CH_2), 36.3 (CH_2 min.), 36.1 (CH_2), 30.6 (CH_2 min.), 24.0 (CH_2), 23.5 (CH_3 min.), 22.5 (CH_3), 19.8 (CH_2), 16.5 (CH_3), 13.7 (CH_3) ppm (min=minor isomer). IR ν 2959, 2873, 1647, 1459, 1216 cm^{-1}. HRMS (ESI-) m/z calcd. for $C_9H_{15}O_4S^-$: 219.0686; found: 219.0697. MS (ESI+) *m/z* 242 ($C_{16}H_{36}N^+$).



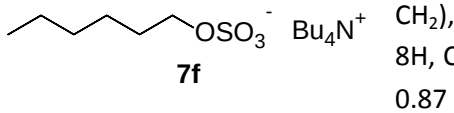
7d

Tetrabutylammonium (2*E*,6*E*)-octa-2,6-dien-1-yl sulphate, 7e. Quantitative yield. ^1H NMR (400 MHz, $CDCl_3$) δ 5.83 – 5.55 (m, 2H, 2xCH), 5.42 (m, 2H, 2xCH), 4.47 (d, *J* = 5.9 Hz, 2H, CH_2), 3.28 (m, 8H, CH_2), 2.19 – 1.95 (m, 4H, 2xCH_2), 1.76 – 1.53 (m, 11H, CH_2+CH_3), 1.44 (tq, *J* = 7.3, 7.3 Hz, 8H), 1.00 (t, *J* = 7.3 Hz, 12H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$) δ 133.6 (CH), 130.7 (CH), 126.3 (CH), 125.2 (CH), 68.0 (CH_2), 58.8 (CH_2), 32.5 (CH_2), 32.2 (CH_2), 24.1 (CH_2), 19.8 (CH_2), 18.0 (CH_3), 13.8 (CH_3). IR ν 2960, 2873, 1459, 1216 cm^{-1}. HRMS (ESI-) m/z calcd. for $C_8H_{13}O_4S^-$: 205.0529; found: 205.0532. MS (ESI+) m/z 242 ($C_{16}H_{36}N^+$).



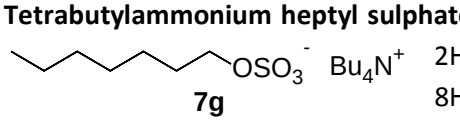
7e

Tetrabutylammonium hexyl sulphate, 7f. Quantitative yield. ^1H NMR (400 MHz, $CDCl_3$) δ 4.01 (t, *J* = 6.9 Hz, 2H, CH_2), 3.29 (m, 8H, CH_2), 1.74 – 1.57 (m, 10H, 2xCH_2), 1.45 (tq, *J* = 7.4, 7.4 Hz, 8H, CH_2), 1.37 (m, 2H, CH_2), 1.28 (m, 4H, 2xCH_2), 1.01 (t, *J* = 7.3 Hz, 12H, CH_3), 0.87 (t, *J* = 7.0 Hz, 3H, CH_3) ppm. ^{13}C NMR (101 MHz, $CDCl_3$) δ 67.0 (CH_2), 58.4 (CH_2), 31.4 (CH_2), 29.4 (CH_2), 25.4 (CH_2), 23.7 (CH_2), 22.4 (CH_2), 19.5 (CH_2), 13.8 (CH_3), 13.4 (CH_3) ppm. IR ν 2957, 2872, 1464, 1218 cm^{-1}. HRMS (ESI-) m/z calcd. for $C_6H_{13}O_4S^-$: 181.0529; found: 181.0529. MS (ESI+) m/z 242 ($C_{16}H_{36}N^+$).



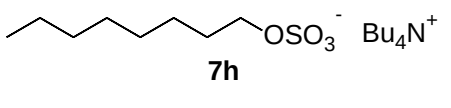
7f

Tetrabutylammonium heptyl sulphate, 7g. Quantitative yield. ^1H NMR (400 MHz, $CDCl_3$) δ 3.99 (t, *J* = 6.9 Hz, 2H, CH_2), 3.27 (m, 8H, CH_2), 1.63 (m, 10H, 2xCH_2), 1.43 (tq, *J* = 7.4, 7.4 Hz, 8H, CH_2), 1.37 – 1.19 (m, 8H, 4xCH_2), 0.99 (t, *J* = 7.3 Hz, 12H, CH_3), 0.85 (t, *J* = 7.0 Hz, 3H, CH_3) ppm. ^{13}C NMR (101 MHz, $CDCl_3$) δ 67.3 (CH_2), 58.7 (CH_2), 31.9 (CH_2), 29.8 (CH_2), 29.2 (CH_2), 26.0 (CH_2), 24.1 (CH_2), 22.7 (CH_2), 19.8 (CH_2), 14.2 (CH_3), 13.8 (CH_3) ppm. IR ν 2958, 2872, 1463, 1218 cm^{-1}. HRMS (ESI-) m/z calcd. for $C_7H_{15}O_4S^-$: 195.0686; found: 195.0685. MS (ESI+) m/z 242 ($C_{16}H_{36}N^+$).



7g

Tetrabutylammonium octyl sulphate, 7h. Quantitative yield. ^1H NMR (400 MHz, $CDCl_3$) δ 4.01 (t, *J* = 6.9 Hz, 2H, CH), 3.29 (m, 8H, CH_2), 1.65 (m, 10H, 2xCH_2), 1.45 (tq, *J* = 7.3, 7.3 Hz, 8H, CH_2), 1.37 (m, 2H, CH_2), 1.32 – 1.19 (m, 8H, 4x CH_2), 1.01 (t, *J* = 7.3 Hz, 12H, CH_3), 0.86 (t, *J* = 7.0 Hz, 3H, CH_3) ppm. ^{13}C NMR (101 MHz, $CDCl_3$) δ



7h

67.3 (CH_2), 58.7 (CH_2), 31.9 (CH_2), 29.8 (CH_2), 29.5 (CH_2), 29.3 (CH_2), 26.0 (CH_2), 24.0 (CH_2), 22.7 (CH_2), 19.8 (CH_2), 14.2 (CH_3), 13.7 (CH_3) ppm. IR ν 2927, 2872, 1462, 1219 cm^{-1}. HRMS (ESI-) m/z calcd. for $C_8H_{17}O_4S^-$: 209.0842; found: 209.0839. MS (ESI+) m/z 242 ($C_{16}H_{36}N^+$).

VII. Molecular model of a complex of **1** with geranyl sulphate.

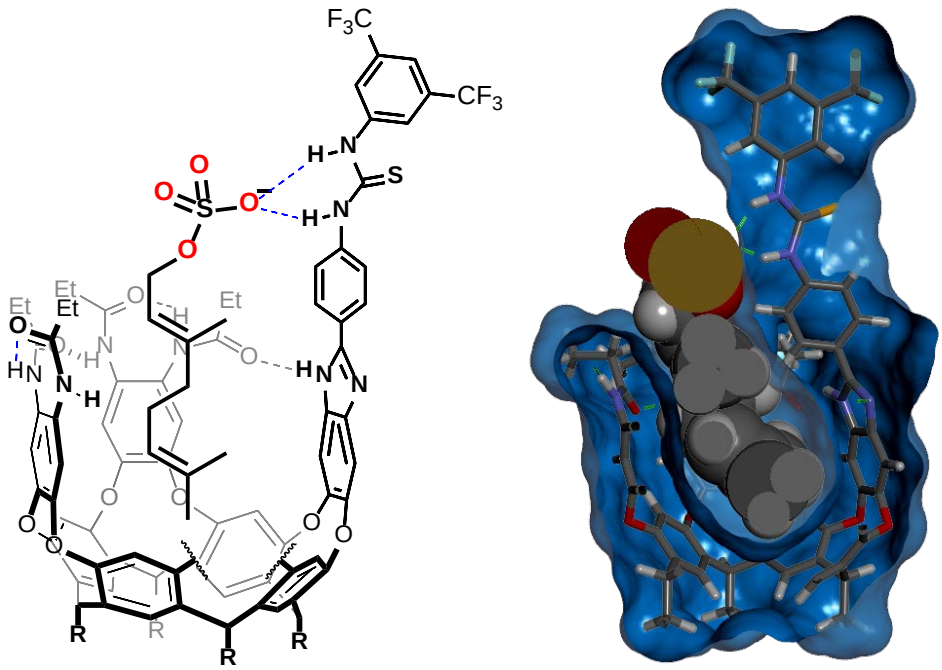


Figure S1 Scheme and molecular model for the geranylsulphate⊂**1** complex (some parts removed for clarity. The geometry of the complex was optimized in the gas phase at the PM6 level of theory with Gaussian 09W.[9] Methyl instead of ethyl groups were used on the resorcinarene base. A sliced view of the complex is shown with a solvent accessible surface on the cavitand and the guest in CPK representation (i.e. with a Van de Waals surface).

VIII. ^{1}H NMR evidence for thiourea-alkyl sulphate interactions.

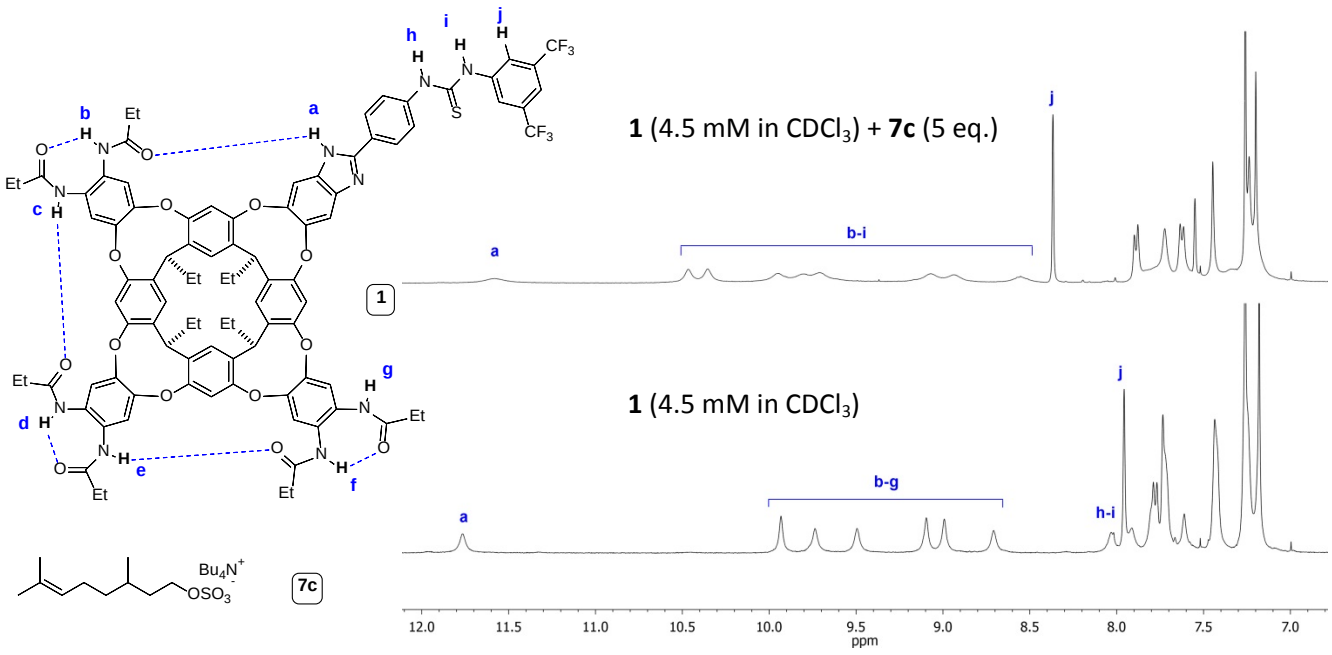


Figure S2 Downfield region of the ^{1}H NMR (400 MHz) showing the downfield shift of the amide's and thiourea's NH's upon addition of excess tetrabutylammonium citronellyl sulphate (**7c**).

IX. ^{19}F NMR titration data for **1** and **6**.

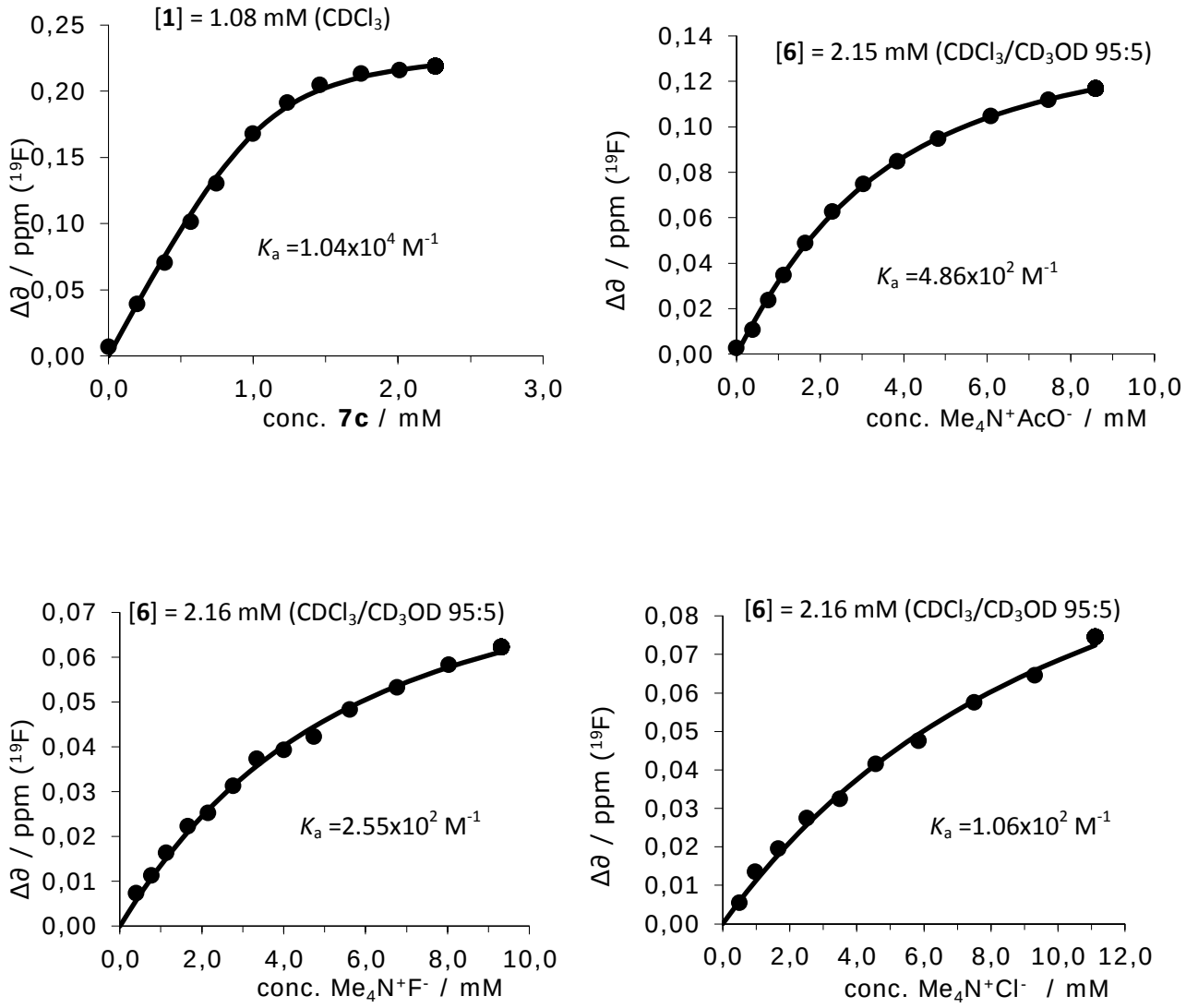


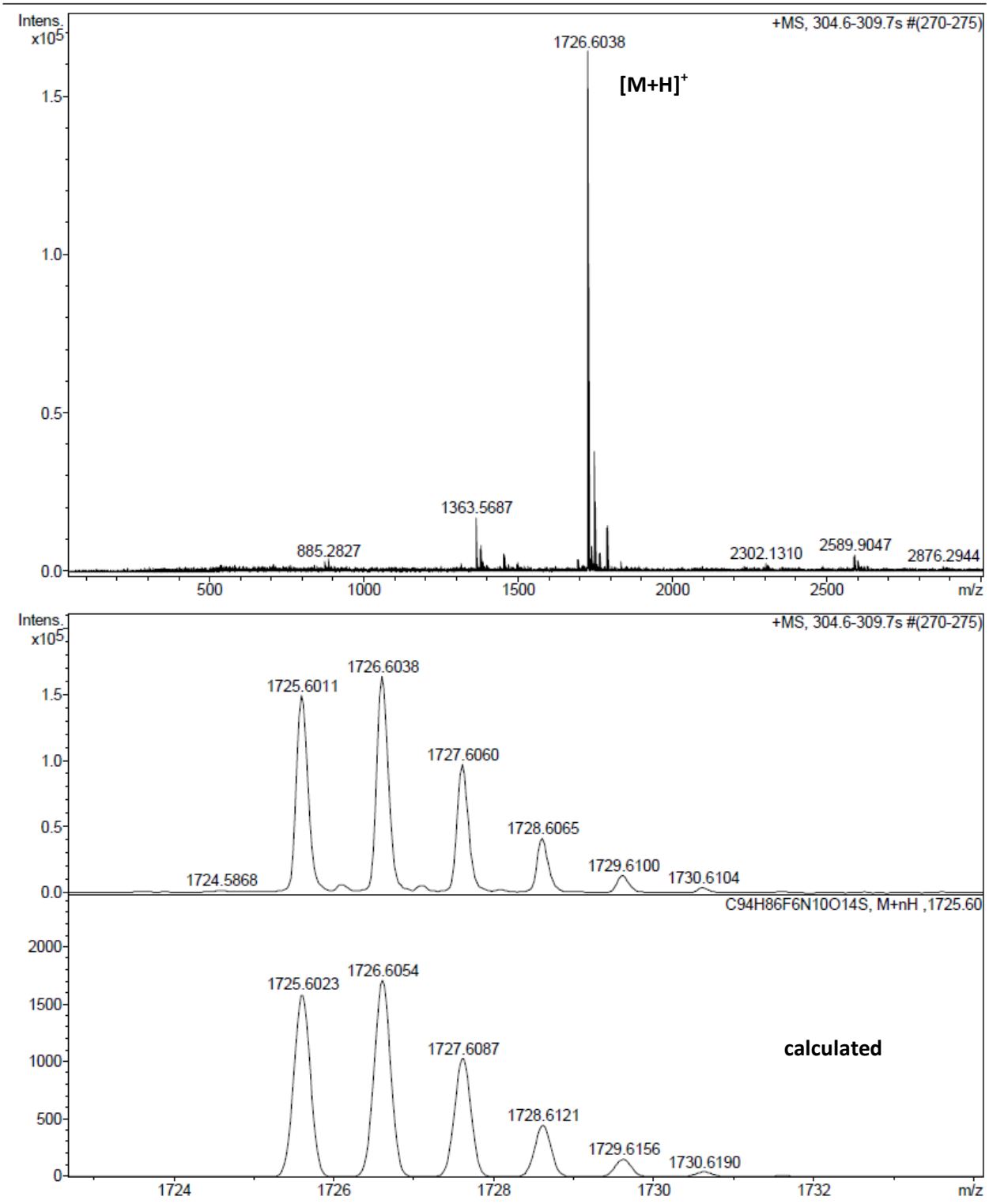
Figure S3 NMR titration data for various guests in **1** and **6** at 300 K, showing the change in the chemical shift of the ^{19}F signal as a function of guest concentration. The line shown is the best fit to a 1:1 binding isotherm obtained with a purpose written software in Microsoft Excel.

References

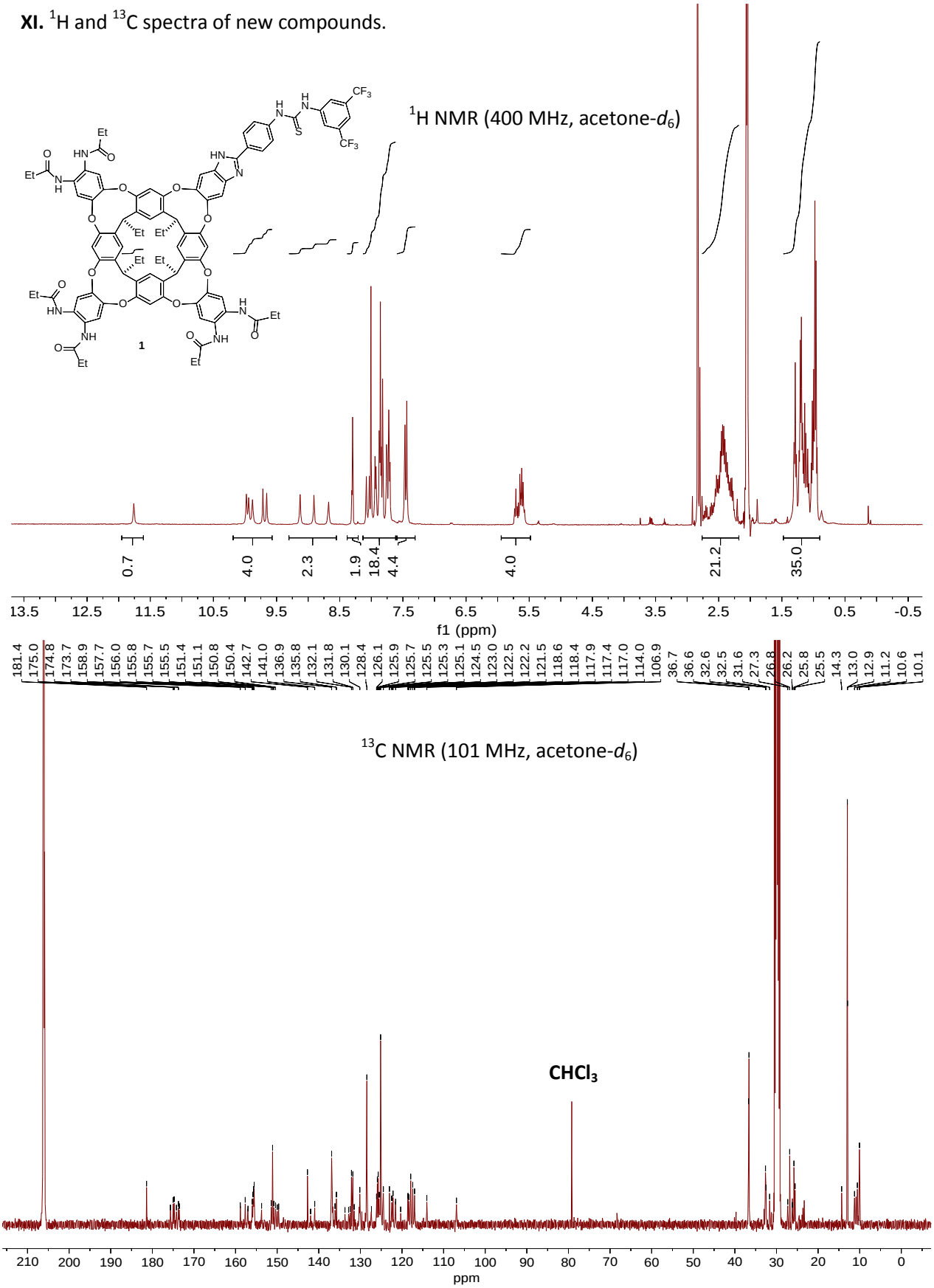
1 P. Amrhein, A. Shivanyuk, D. W. Johnson and J. Rebek, Jr., *J. Am. Chem. Soc.*, 2002, **124**, 10349-10358.
2 T. Iwasawa, P. Wash, C. Gibson and J. Rebek Jr, *Tetrahedron*, 2007, **63**, 6506-6511.
3 Y. Li, Y. Chen, X. Liu, Z. Wang, X. Yang, Y. Tu and X. Zhu, *Macromolecules*, 2011, **44**, 6370-6381.
4 J. D. Aebi, D. T. Deyo, C. Q. Sun, D. Guillaume, B. Dunlap and D. H. Rich, *J. Med. Chem.*, 1990, **33**, 999-1009.
5 R. J. Lundgren and B. N. Thomas, *Chem. Commun.*, 2016, **52**, 958-961.
6 G. Stork and M. Marx, *J. Am. Chem. Soc.*, 1969, **91**, 2371-2373.
7 B. B. Snider, E. Ron and B. W. Burbaum, *J. Org. Chem.*, 1987, **52**, 5413-5419.
8 Z. Li, H. Jung, M. Park, M. S. Lah and S. Koo, *Adv. Synth. Catal.*, 2011, **353**, 1913-1917.

[9] Gaussian 09, Revision A.02, M. J. Frisch, G. W. Trucks, H. B. Schlegel, G. E. Scuseria, M. A. Robb, J. R. Cheeseman, G. Scalmani, V. Barone, B. Mennucci, G. A. Petersson, H. Nakatsuji, M. Caricato, X. Li, H. P. Hratchian, A. F. Izmaylov, J. Bloino, G. Zheng, J. L. Sonnenberg, M. Hada, M. Ehara, K. Toyota, R. Fukuda, J. Hasegawa, M. Ishida, T. Nakajima, Y. Honda, O. Kitao, H. Nakai, T. Vreven, J. A. Montgomery, Jr., J. E. Peralta, F. Ogliaro, M. Bearpark, J. J. Heyd, E. Brothers, K. N. Kudin, V. N. Staroverov, R. Kobayashi, J. Normand, K. Raghavachari, A. Rendell, J. C. Burant, S. S. Iyengar, J. Tomasi, M. Cossi, N. Rega, J. M. Millam, M. Klene, J. E. Knox, J. B. Cross, V. Bakken, C. Adamo, J. Jaramillo, R. Gomperts, R. E. Stratmann, O. Yazyev, A. J. Austin, R. Cammi, C. Pomelli, J. W. Ochterski, R. L. Martin, K. Morokuma, V. G. Zakrzewski, G. A. Voth, P. Salvador, J. J. Dannenberg, S. Dapprich, A. D. Daniels, O. Farkas, J. B. Foresman, J. V. Ortiz, J. Cioslowski, and D. J. Fox, Gaussian, Inc., Wallingford CT, 2009.

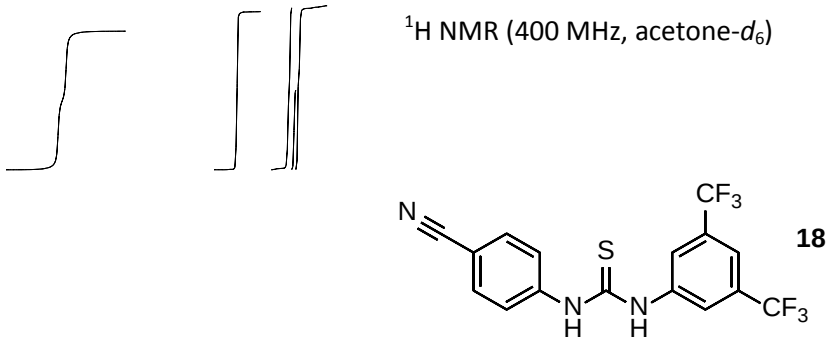
X. HRMS spectrum of **1** (ESI+ QTOF).



XI. ^{1}H and ^{13}C spectra of new compounds.



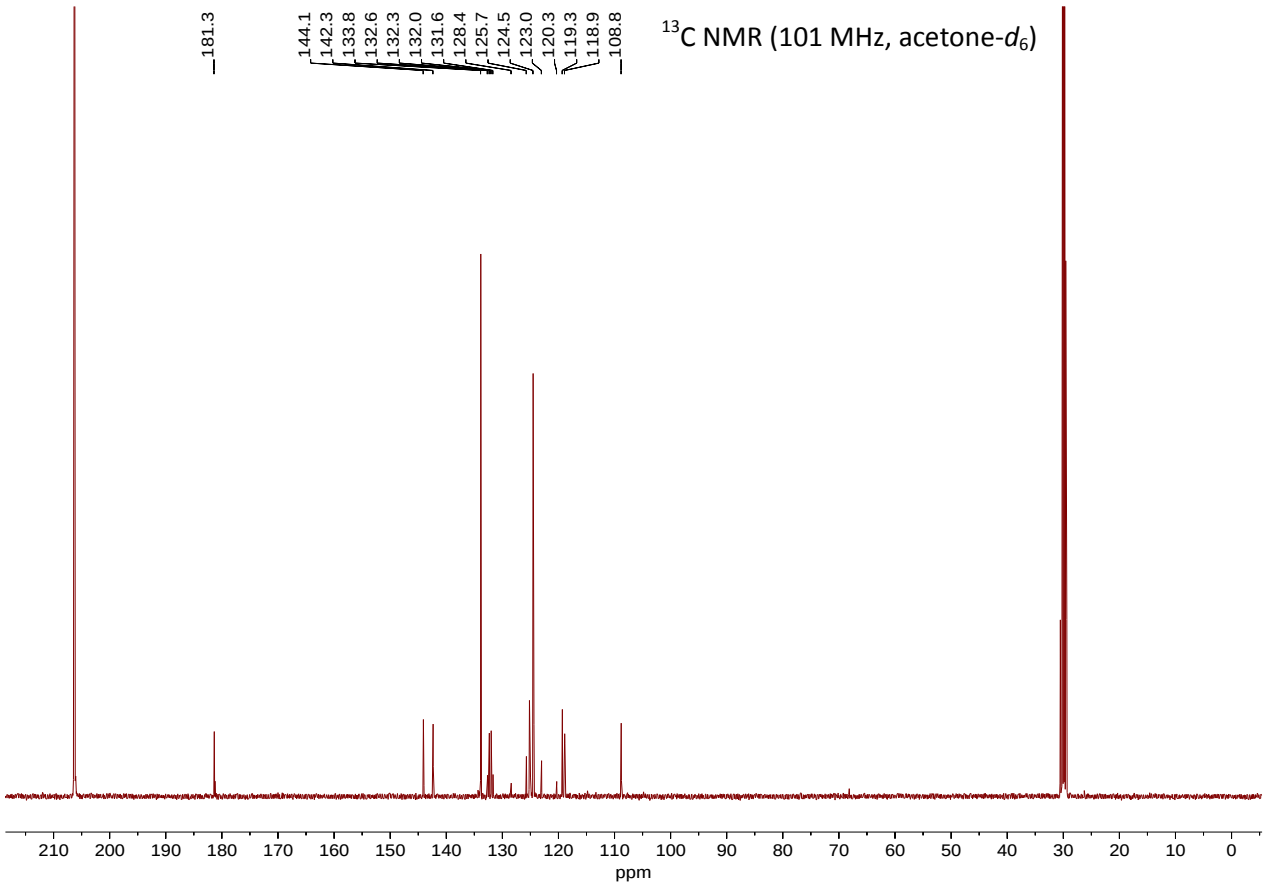
^{1}H NMR (400 MHz, acetone-d_6)



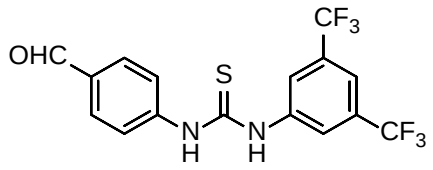
18

^{13}C NMR (101 MHz, acetone-d_6)

181.3
144.1
142.3
133.8
132.6
132.3
132.0
131.6
128.4
125.7
124.5
123.0
120.3
119.3
118.9
108.8

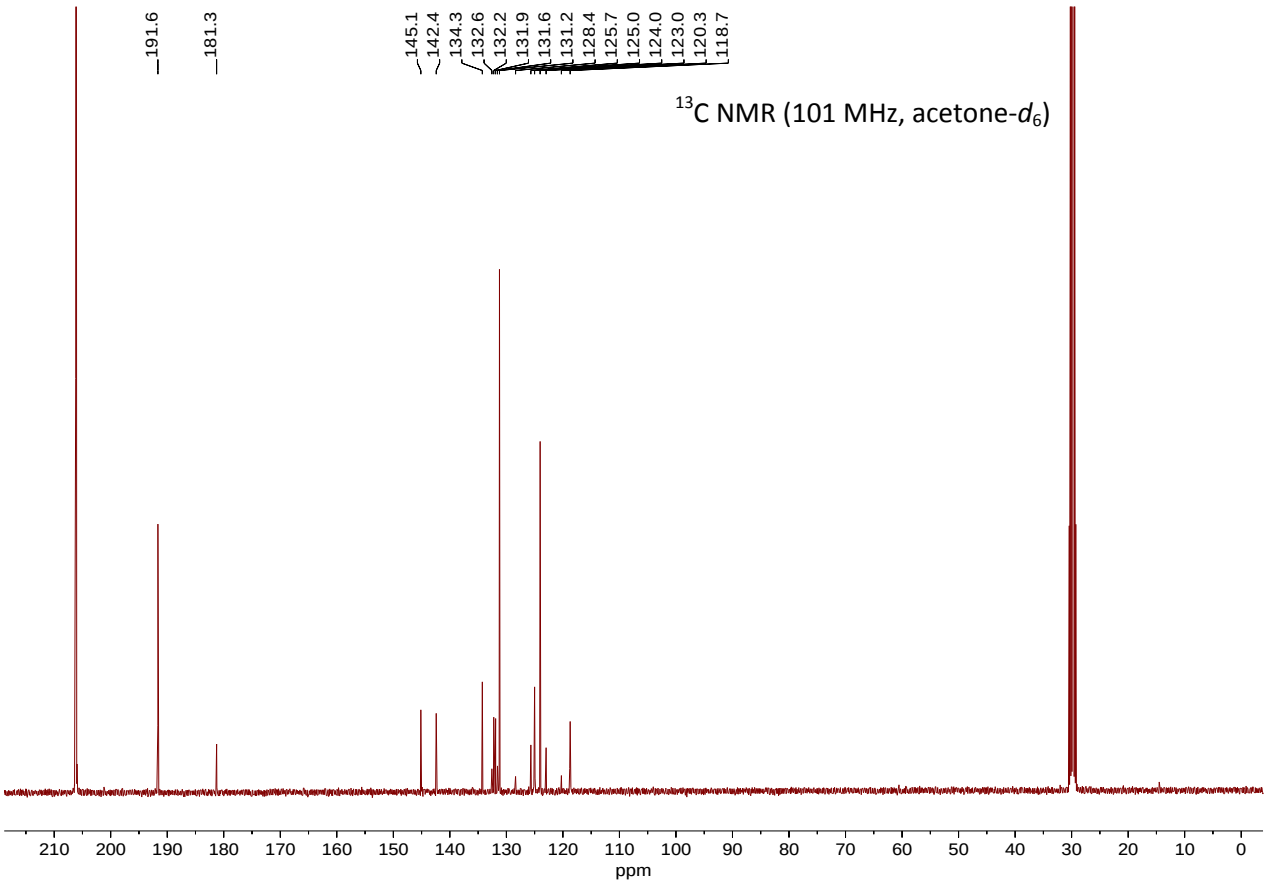


^{1}H NMR (400 MHz, acetone-d_6)



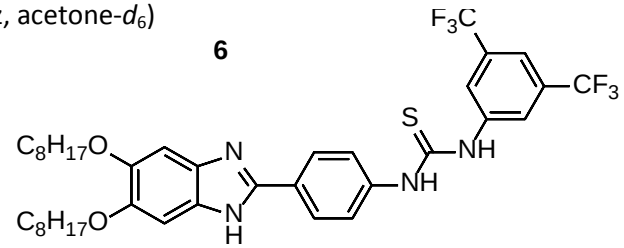
5

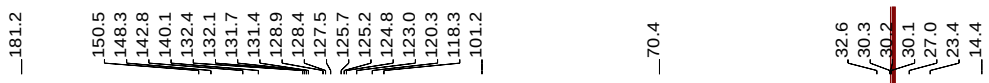
^{13}C NMR (101 MHz, acetone-d_6)



^{1}H NMR (400 MHz, acetone-d_6)

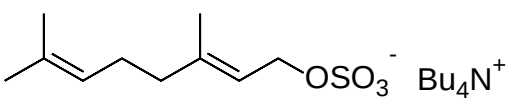
6





^{13}C NMR (101 MHz, acetone-d_6)

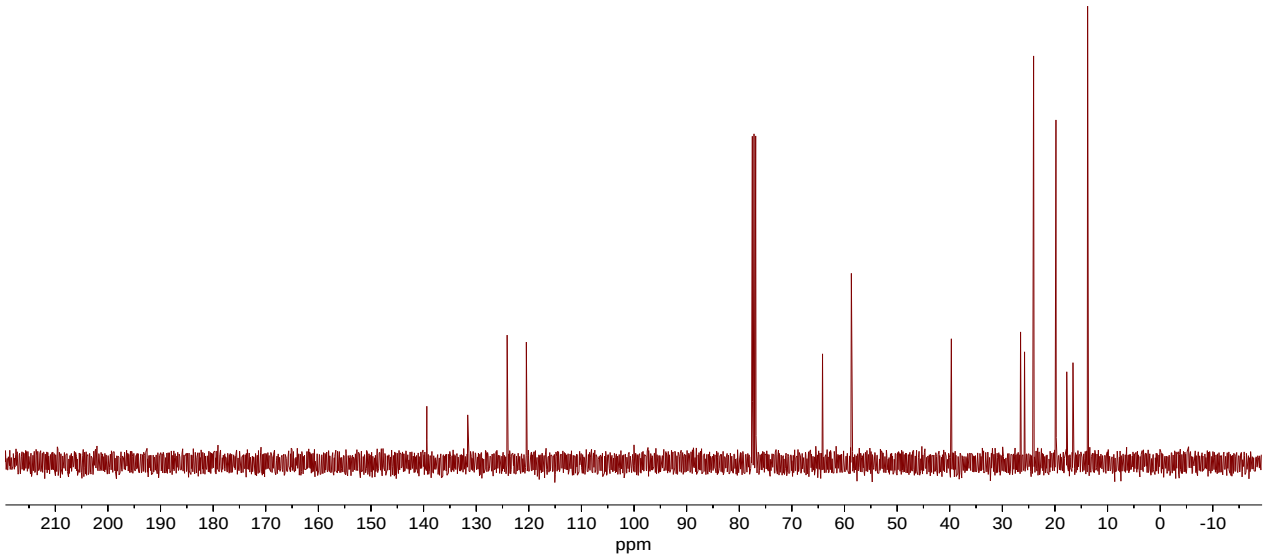
^{1}H NMR (400 MHz, $CDCl_3$)



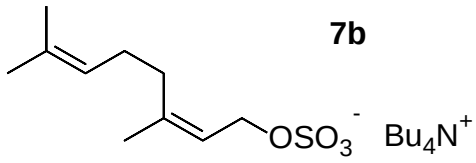
7a

^{13}C NMR (101 MHz, $CDCl_3$)

139.4
131.6
124.1
120.4
64.1
58.7
39.6
26.5
25.7
24.0
19.8
17.7
16.5
13.7

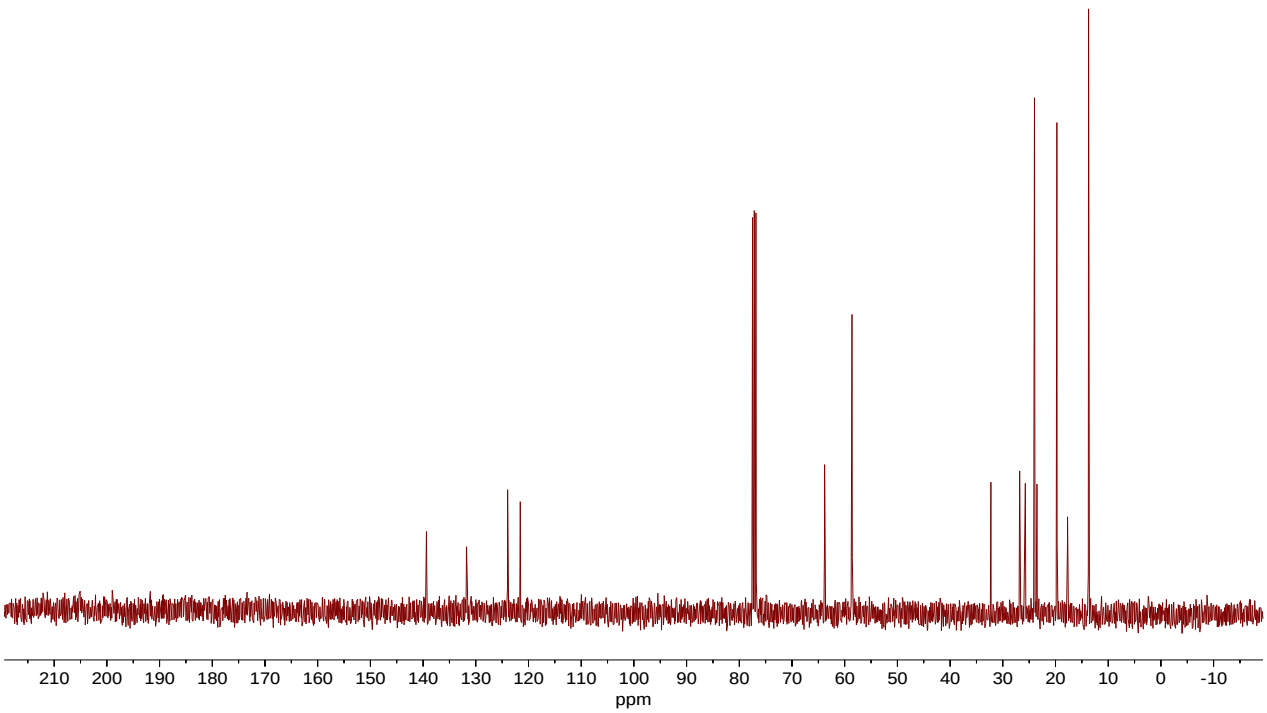


^{1}H NMR (400 MHz, $CDCl_3$)

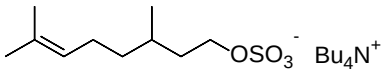


^{13}C NMR (101 MHz, $CDCl_3$)

139.4
131.8
124.0
121.6
63.8
58.6
32.3
26.8
25.7
24.0
19.7
17.7
13.7

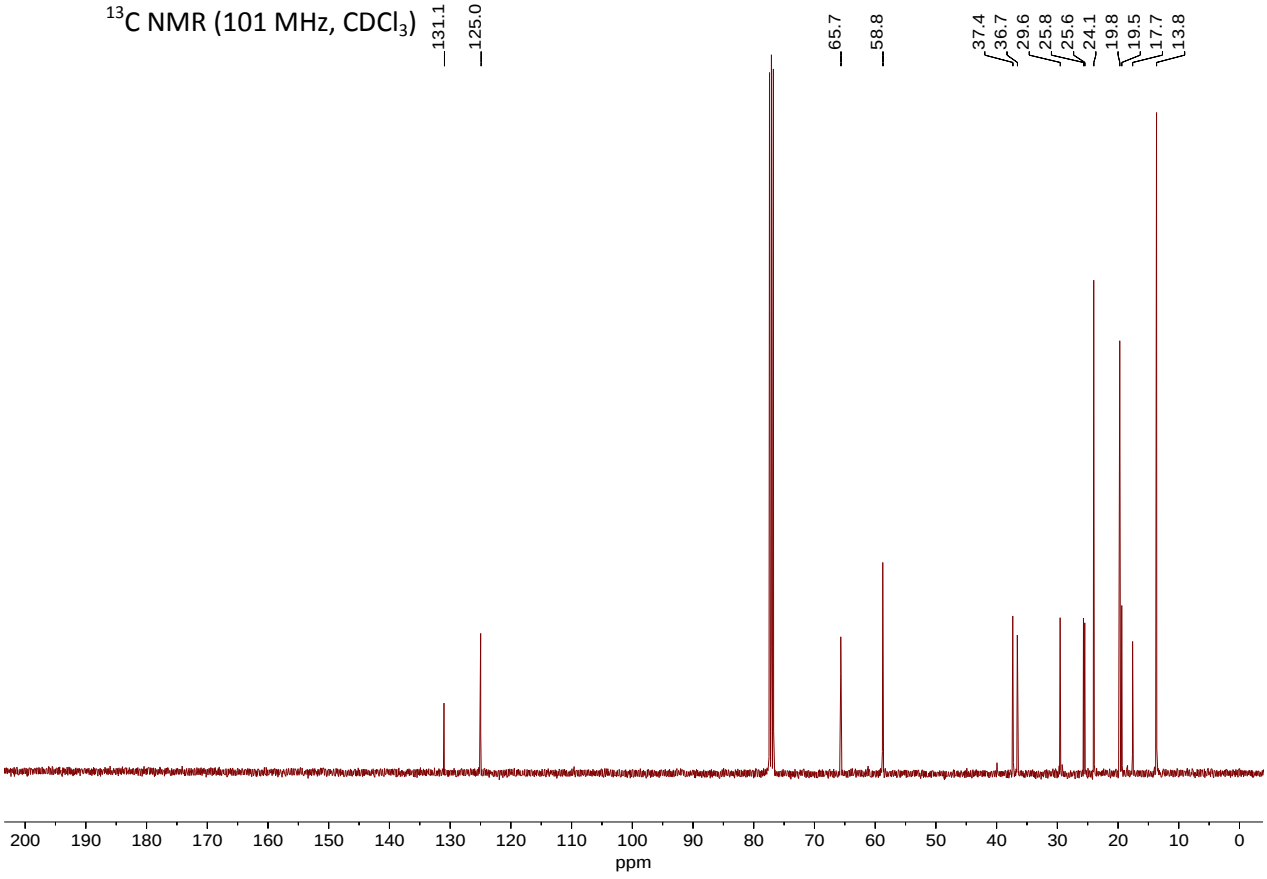


^{1}H NMR (400 MHz, $CDCl_3$)

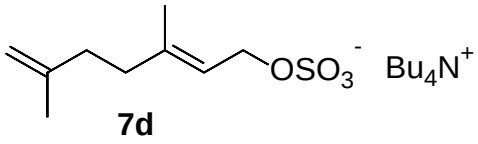


7c

^{13}C NMR (101 MHz, $CDCl_3$)



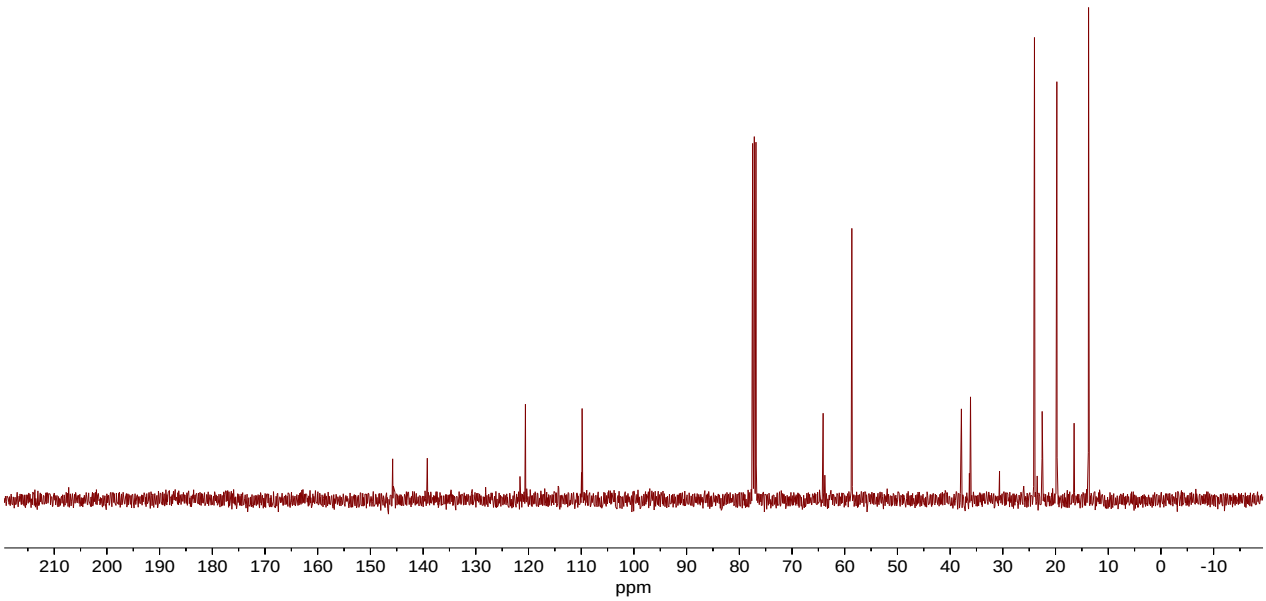
^{1}H NMR (400 MHz, $CDCl_3$)



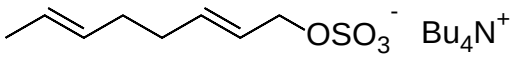
7d

^{13}C NMR (101 MHz, $CDCl_3$)

145.8 145.7 139.3 139.2 121.6 120.6 109.9 109.8 64.1 63.8 58.7 37.9 36.3 36.1 30.6 24.0 23.5 22.5 19.8 16.5 13.7



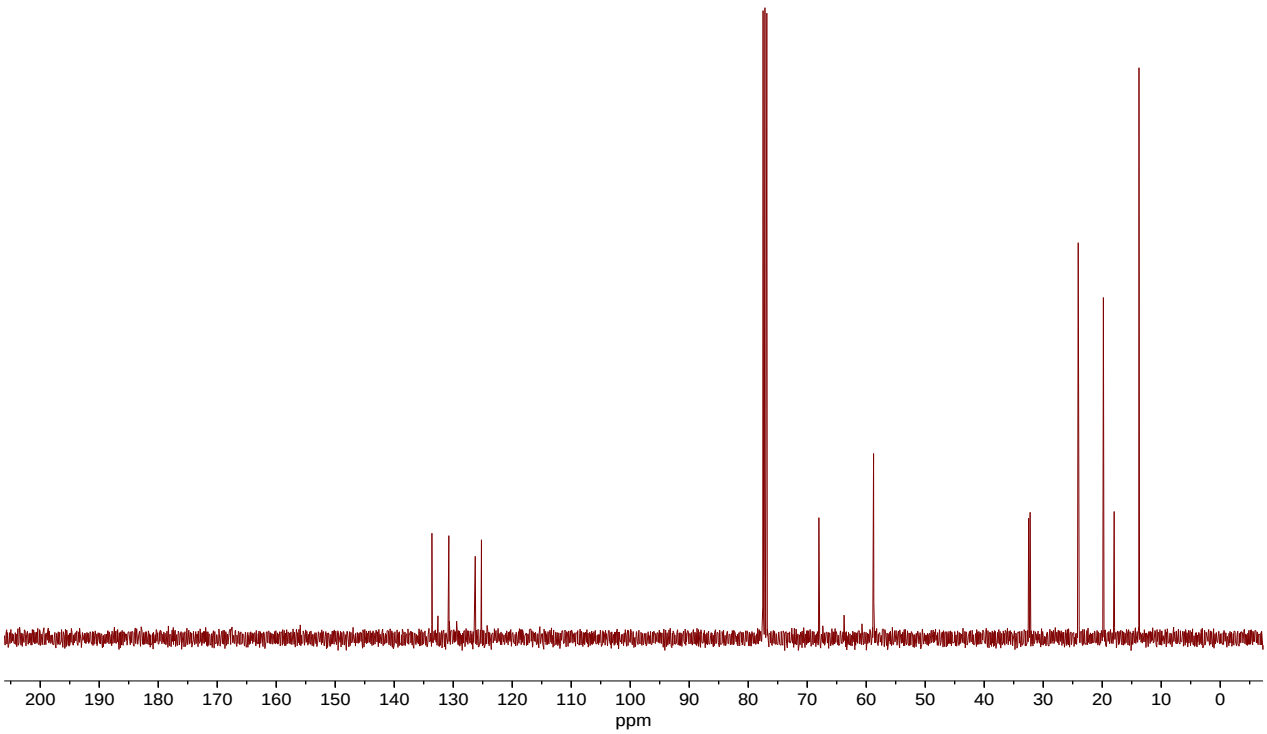
^{1}H NMR (400 MHz, $CDCl_3$)



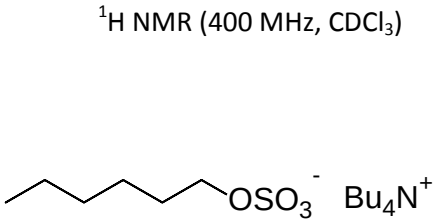
7e

^{13}C NMR (101 MHz, $CDCl_3$)

133.6
130.7
126.3
125.2
68.0
58.8
32.5
32.2
24.1
19.8
18.0
13.8

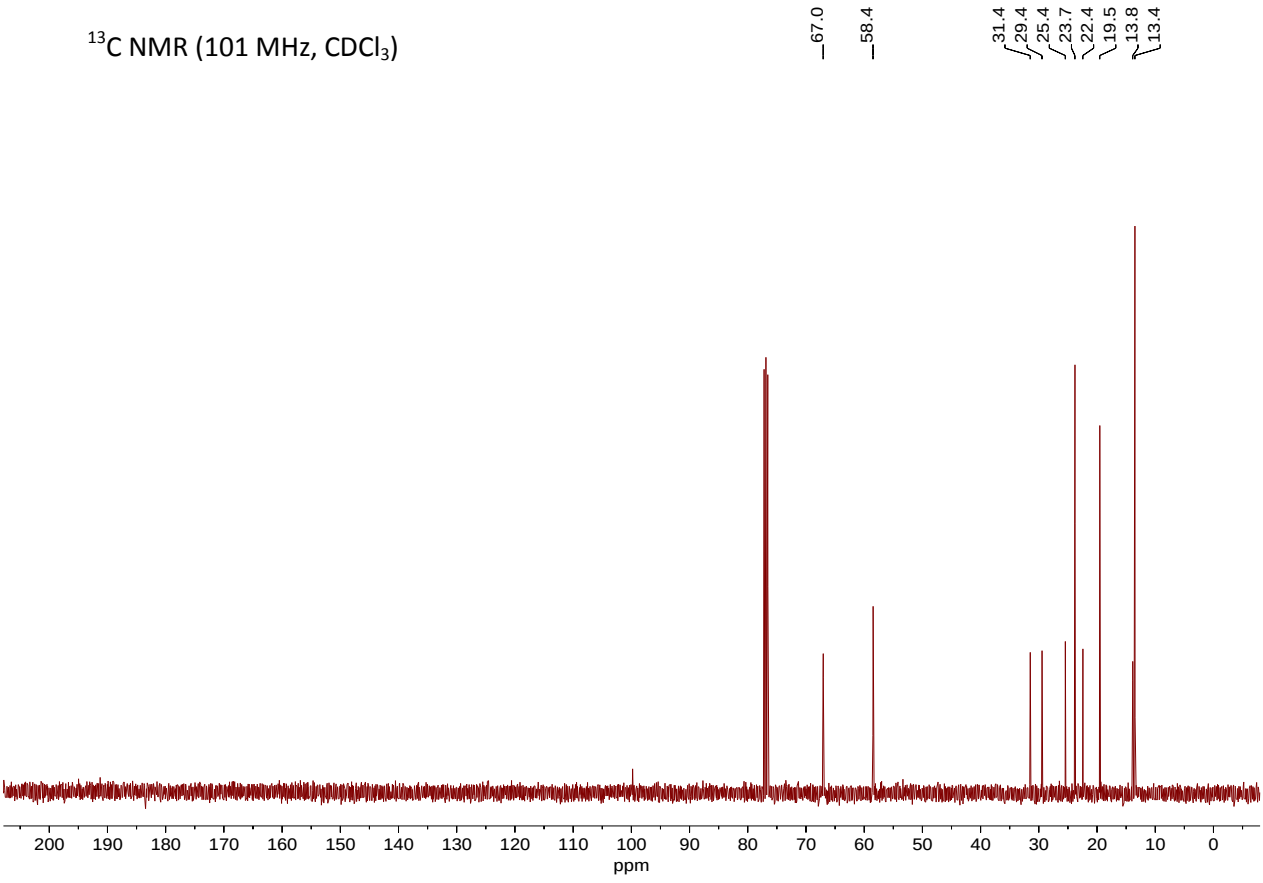


^{1}H NMR (400 MHz, $CDCl_3$)

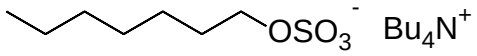


7f

^{13}C NMR (101 MHz, $CDCl_3$)

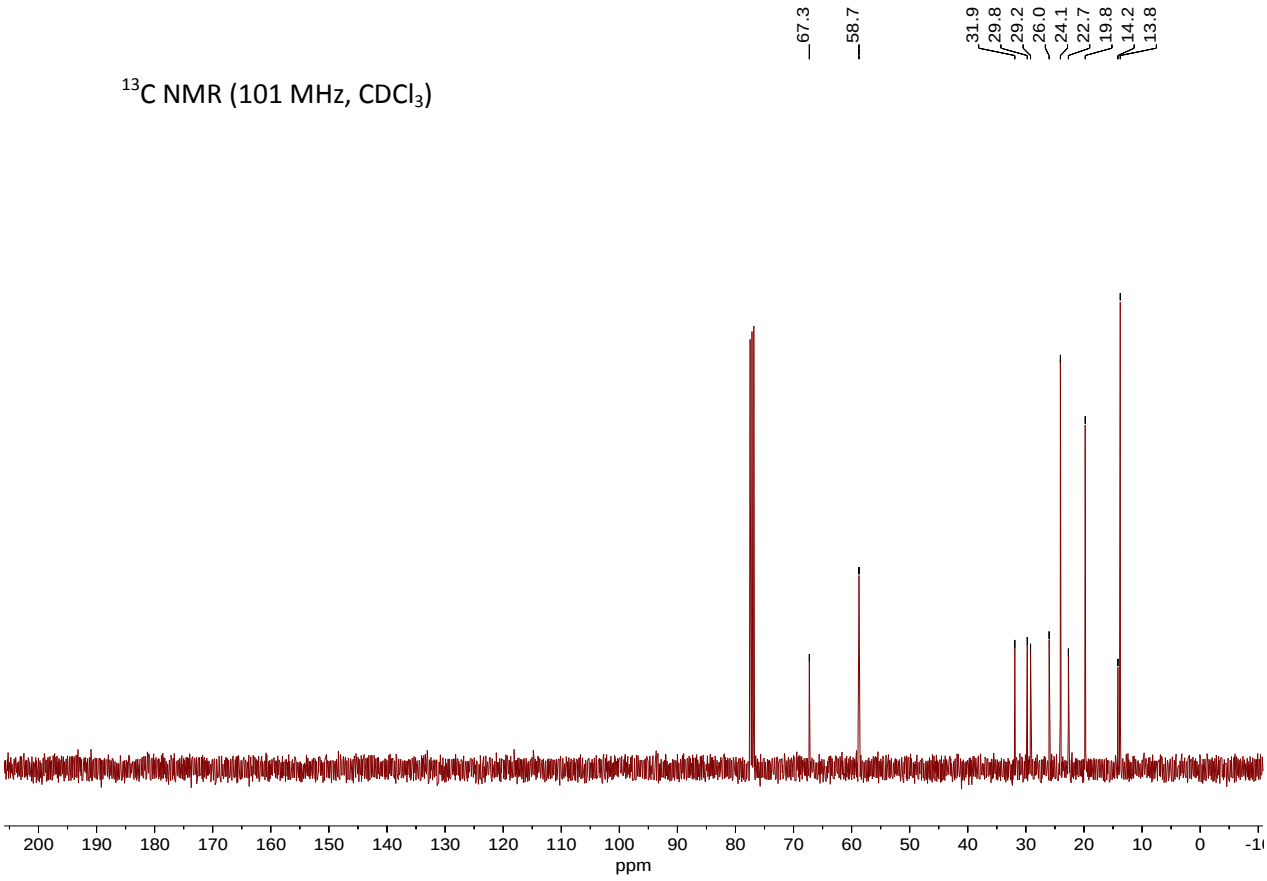


^{1}H NMR (400 MHz, $CDCl_3$)

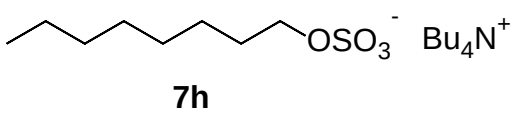


7g

^{13}C NMR (101 MHz, $CDCl_3$)



^{1}H NMR (400 MHz, $CDCl_3$)



7h

^{13}C NMR (101 MHz, $CDCl_3$)