Allosteric release of cucurbit[6]uril from a rotaxane using a molecular signal

Supporting Information

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1 Material, methods and instruments

All solvents, reagents, starting compounds and macrocyclic compounds were of analytical grade, purchased from commercial sources and used without further purification if not stated otherwise. Diethyl ether, toluene, benzene and 1,4-dioxane were dried over sodium and freshly distilled before use. Tetrahydrofuran was pre-dried over potassium hydroxide and freshly distilled from sodium chips before use. Dichloromethane was distilled over phosphorus pentoxide. Methanol was dried over activated 3 Å molecular sieve overnight and subsequently distilled from sodium methoxide.

Melting points were measured on a Kofler block.

Elemental analyses (C, H and N) were performed using a Thermo Fisher Scientific Flash EA 1112.

Gas chromatography–quadrupole mass spectrometry (GC-EI-MS) was performed on Shimadzu QP2010 with EQUITY1 column (30 m × 0.32 mm × 1.0 µm). Temperature program: 100 °C / 7 min; 25 $°C \cdot min^{-1}$; 250 °C / 17 min. Helium was used as a carrier gas at a constant linear velocity 52.4 $cm \cdot s^{-1}$; ion source 200 °C, 70 eV.

NMR spectra were recorded using a Jeol JNM-ECZ400R/S3 spectrometer operating at frequencies of 399.78 MHz (^{1}H) and 100.53 MHz (^{13}C). ^{1}H- and ^{13}C-NMR chemical shifts were referenced to the signal of the solvent [^{1}H: δ(residual DMSO-d_5) = 2.50 ppm, δ(residual HDO) = 4.70 ppm, δ(residual $CHCl_3$) = 7.27 ppm; ^{13}C: δ(DMSO-d_6) = 39.52 ppm, δ($CDCl_3$) = 77.23 ppm]. The signal multiplicity is indicated by ‘s‘ for singlet, ‘d‘ for doublet, ‘t‘ for triplet, ‘q‘ for quartet, ‘sep‘ for septet, ‘dt‘ for doublet of triplets, ‘tt‘ for triplet of triplets and ‘m‘ for multiplet. All measurements were carried out at 30 °C (30 °C), unless stated otherwise.

IR spectra were collected on FT-IR spectrometer Alpha (Bruker Optics GmbH Ettlingen, Germany) with a KBr pellets technique.

Electrospray mass spectra (ESI-MS) were recorded using an amaZon X ion-trap mass spectrometer (Bruker Daltonics, Bremen, Germany) equipped with an electrospray ionisation source. All the experiments were conducted in the positive-ion polarity mode. The instrumental conditions used to measure the single diammonium salts (**5a**–**5e**) and rotaxanes (**6a**–**6e**) were different; therefore, they are described separately. Diammonium salts: Individual samples (with concentrations of 0.5 $\mu g \cdot cm^{-3}$) were infused into the ESI source in methanol:water (1:1, *v*:*v*) solutions using a syringe pump with a constant flow rate of 3 $\mu l \cdot min^{-1}$. The other instrumental conditions were as follows: an electrospray voltage of −4.2 kV, a capillary exit voltage of 140 V, a drying gas temperature of 220 °C, a drying gas flow rate of 6.0 $dm^{3} \cdot min^{-1}$, and a nebulizer pressure of 55.16 kPa. Rotaxanes: An aqueous solution of the rotaxane (6.25 µM) was infused into the ESI source at a constant flow rate of 3 $\mu l \cdot min^{-1}$. The other instrumental conditions were as follows: an electrospray voltage of −4.0 kV, a capillary exit voltage of 140 V, a drying gas temperature of 300 °C, a drying gas flow rate of 6.0 $dm^{3} \cdot min^{-1}$, and a nebulizer pressure of 206.84 kPa. Nitrogen was used as both the nebulizing and drying gas for all of the experiments. Tandem mass spectra were collected using CID with He as the collision gas after the isolation of the required ions.

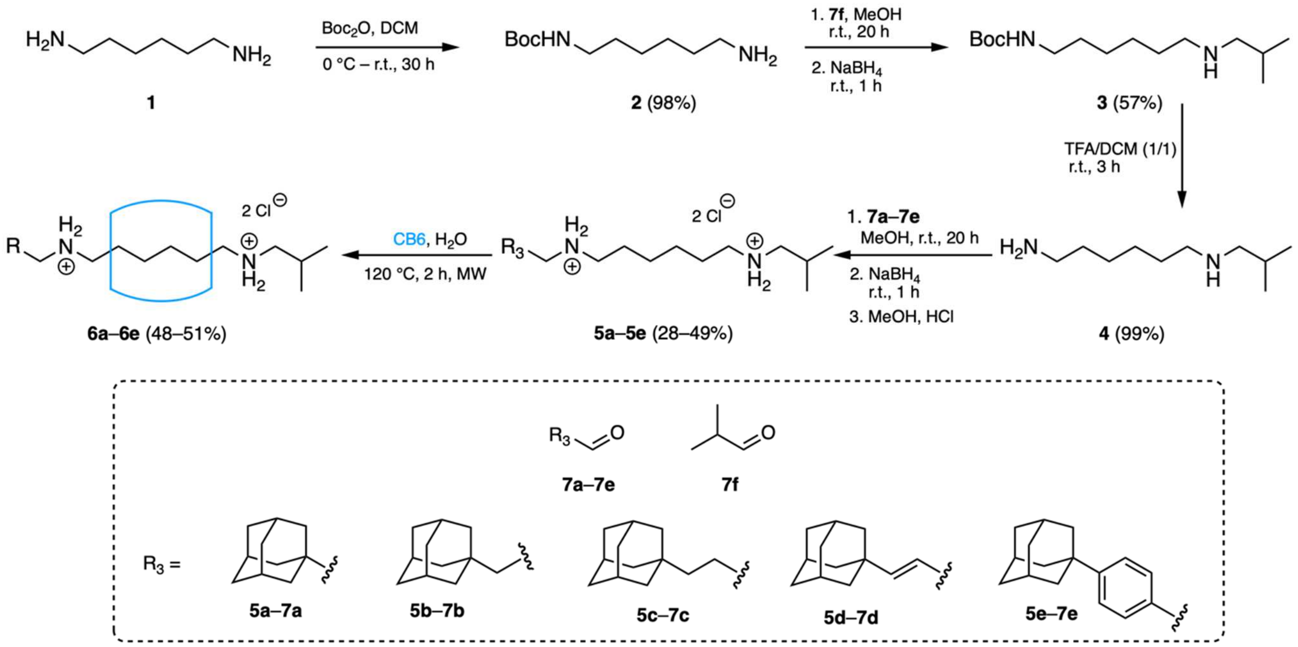
High-resolution mass spectra (HRMS) were recorded using a quadrupole time-of-flight mass spectrometer (6530 Q-TOF, Agilent Technologies, Santa Clara, USA) equipped with an electrospray ionisation source. All the experiments were conducted in the positive-ion polarity mode. The mass spectrometer operated under following parameters: a capillary voltage of −4.0 kV, a nebulizer pressure of 275.79 kPa, a drying gas flow rate of 8.0 $L \cdot min^{-1}$, and a drying gas temperature of 300 °C. Mass spectra were acquired over the *m/z* 100–1500 range at a scan rate of 3 $scan \cdot s^{-1}$. Accurate mass measurements were obtained via a calibrating solution involving the use of internal reference masses (purine ($C_5H_4N_4$) at *m/z* 121.050873, and HP-0921 [hexakis-(1*H*,1*H*,3*H*-tetrafluoropentoxy)-phosphazene] ($C_{18}H_{18}O_6N_3P_3F_{24}$) at *m/z* 922.009798). Data were recorded and processed in MassHunter software v.B.05.01 (Agilent Technologies).

Isothermal titration calorimetry (ITC) measurements were carried out using a VP–ITC MicroCal instrument in 50 mM NaCl at 30 °C and were used for the determination of association constants and thermodynamical parameters for the complexations of guests (IBA, HMDA, SP) with CB6 or CB7. The concentrations of the host in the cell and the guest in the microsyringe were approximately 0.05 and 0.5 mM respectively. The raw experimental data were analysed with the MicroCal ORIGIN software. The heats of dilution were considered for each guest compound. A theoretical titration curve was fitted to the experimental data using the 'One Set of Sites' model. Association constants higher than 10^7 M^{-1} were determined by the competitive titration method, where cyclopentanone (K=9.76 × 10^4 M^{-1}) was used as a competitor.

The single crystal X-ray data were collected at −153 °C using mirror-monochromated Cu-Kα (λ = 1.54184 Å) radiation on a Rigaku XtaLAB Synergy-R diffractometer with a HyPix-Arc 100 detector. All structures were solved by intrinsic phasing (SHELXT)[1] and refined by full-matrix least squares on F^2 using Olex2,[2] utilising the SHELXL module.[3] Anisotropic displacement parameters were assigned to non-H atoms and isotropic displacement parameters for all H atoms were constrained to multiples of the equivalent displacement parameters of their parent atoms with $U_{iso}(H) = 1.2\ U_{eq}(CH)$ or $1.5\ U_{eq}(NH, CH_2, CH_3, OH)$ of their respective parent atoms.

Kinetic measurements: The reproducibility of the k values for all four rotaxanes was tested at the highest temperature and found to be within a ±5% range. The activation parameters $\Delta H^{\ddagger}$, $\Delta S^{\ddagger}$ and $\Delta G^{\ddagger}$ were determined from a single set of k values measured at five different temperatures, demonstrating satisfactory linearity. The half-life values for rotaxanes **6b**–**6d** were extrapolated from Eyring plots, while the half-life value for rotaxane **6a** was determined in triplicate.

2 Synthetic procedure towards rotaxanes 6a–6e



Scheme S1 Synthetic pathway towards **6a–6e**.

tert-Butyl 6-aminohexylcarbamate (2)

The title compound **2** was prepared according to a slightly modified, previously published, procedure.[4] Using a syringe pump, a solution of di-*tert*-butyl dicarbonate (2.2 g, 10 mmol) in dry dichloromethane (25 cm^3) was added dropwise to an ice-cool solution of 1,6-hexanediamine (**1**, 5.8 g, 50 mmol) in dry dichloromethane (150 cm^3) over a 5.5 h period under an argon atmosphere. The reaction mixture was stirred for additional 24 h at room temperature. The cloudy white mixture was diluted with distilled water until a clarification was observed. Subsequently, the organic phase was separated, washed with water (4 × 50 cm^3), dried over Na_2SO_4 and evaporated to dryness under vacuum to yield the title compound **2** (2.1 g, 98%) as a colourless oil. The obtained product was used in the next reaction without further purification. ^{1}H NMR (400 MHz, $CDCl_3$, 30 °C) δ[ppm] = 1.32–1.34 (m, 4H), 1.44–1.54 (m, 13H), 2.68 (t, J = 6.8 Hz, 2H), 3.11 (q, J = 6.4 Hz, 2H), 4.50 (br, 1H). The collected data are in agreement with those previously published.[4]

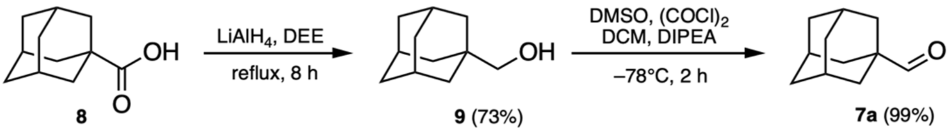
tert-Butyl 6-(isobutylamino)hexylcarbamate (3)

The title compound **3** was prepared according to a slightly modified, previously published, procedure.[13a] Boc-protected amine derivative **2** (1.1 g, 5 mmol) and isobutyraldehyde (**7f**, 541 mg, 0.69 cm^3, 7.5 mmol) were dissolved in dry methanol (11 cm^3). The resulting solution was stirred for 20 h at room temperature under an argon atmosphere. Sodium borohydride (570 mg, 15 mmol) was then added portion-wise into the reaction mixture, which was stirred for an additional 30 min until the disappearance of the imine proton signal from ^{1}H NMR spectroscopy. The mixture was diluted with diethyl ether (70 cm^3) and then washed with 10% sodium hydroxide solution (40 cm^3), distilled water (3 × 40 cm^3) and brine (40 cm^3). The organic phase was dried over Na_2SO_4 and evaporated to dryness under vacuum to afford a light yellow oil, which was purified by column chromatography (silica gel, CH_3OH/Et_3N, 100/1, v/v, ninhydrin alcoholic solution was used for staining the TLC plates) to afford compound **3** (0.78 g, 57%) as a yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$, 30 °C) δ [ppm] = 0.89 (d, J = 6.4 Hz, 6H), 1.30–1.34 (m, 4H), 1.43–1.50 (m, 13H), 1.73 (sep, J = 6.8 Hz, 1H), 2.39 (d, J = 6.8 Hz, 2H), 2.56 (t, J = 7.2 Hz, 2H), 3.09 (q, J = 6.4 Hz, 2H).

***N*-(isobutyl)hexane-1,6-diamine (4)**

The title compound **4** was prepared according to a slightly modified, previously published, procedure.[13a] Boc-protected amine **3** (0.52 g, 2 mmol) was dissolved in a mixture of trifluoroacetic acid (5 cm^3) and dichloromethane (5 cm^3). The resulting solution was stirred for 3 h at room temperature and concentrated under stream of nitrogen. The obtained residue was diluted with ethyl acetate (50 cm^3) and washed with 10% sodium hydroxide solution (50 cm^3). The aqueous layer was extracted with ethyl acetate (3 × 20 cm^3) and the combined organic layers were washed with brine (50 cm^3), dried over Na_2SO_4 and evaporated to dryness under vacuum to yield compound **4** (0.34 g, 99%) as a yellow oil. ^{1}H NMR (400 MHz, DMSO-d_6, 30 °C) δ [ppm] = 0.83 (d, J = 6.4 Hz, 6H), 1.24–1.38 (m, 8H), 1.61 (sep, J = 6.8 Hz, 1H), 2.27 (d, J = 6.4 Hz, 2H), 2.44 (t, J = 7.2 Hz, 2H), 2.47–2.50 (m, 2H). ^{13}C NMR (101 MHz, DMSO-d_6, 30 °C) δ [ppm] = 21.24, 26.93, 27.34, 28.47, 30.20, 33.26, 41.88, 50.15, 58.22.

Synthetic procedure towards aldehyde 7a



Scheme S2 Synthetic route towards **7a**.

1-Adamantylmethanol (9)

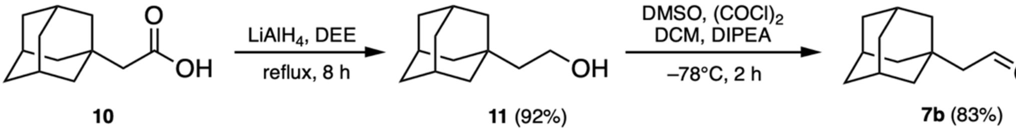
A 500 cm^3 three-necked round-bottom flask, filled with argon and containing dry diethyl ether (100 cm^3), was cooled to 0 °C in an ice bath. $LiAlH_4$ (6.0 g, 158 mmol) was added portion-wise over 30 min and the resulting suspension was stirred for 10 min. 1-Adamantanecarboxylic acid (**8**, 10.0 g, 55.5 mmol) was added during the next 30 min and the reaction mixture was stirred for 3 h at room temperature.

Subsequently, the mixture was heated to reflux for 8 h. After that, the reaction mixture was cooled again to 0 °C and portions of distilled water (7.5 cm^3), 15% sodium hydroxide solution (7.5 cm^3) and distilled water (22.5 cm^3) were consecutively added to the mixture. The resulting colourless suspension was filtered off using a Büchner funnel and thoroughly washed with diethyl ether. The filtrate was washed with 1.16 M K_2CO_3 (4 × 20 cm^3), dried over Na_2SO_4 and the solvent was removed under vacuum to afford a white crystalline powder. The powder was redissolved in diethyl ether and was crystallized from hexane at –30°C. The colourless crystals were filtrated off and dried under vacuum to afford **9** (6.8 g, 73%). Mp 115–118 °C. GC-EI-MS (t_R = 11.6 min): 41(8), 67(10), 77(6), 79(20), 81(5), 91(6), 93(18), 107(11), 135(100), 136(11), 166(M$^+$, 4) *m/z* (%).

1-Adamantanecarbaldehyde (7a)

A 50 cm^3 round-bottom reaction flask was annealed under vacuum using a heat gun for 1 h and filled with argon. The flask was charged with dry dichloromethane (5 cm^3) and dimethyl sulfoxide (0.64 cm^3, 9 mmol) and cooled in an acetone bath with liquid N_2 to –80 °C. Oxalyl chloride (0.75 cm^3, 10 mmol) was added dropwise and the reaction mixture was stirred under argon atmosphere for 15 minutes. A solution of compound **9** (500 mg, 3.0 mmol) in dry dichloromethane (5 cm^3) was then added dropwise. After 1 h, *N*-ethyl-*N*-isopropylpropan-2-amine (3.4 cm^3, 20 mmol) was added dropwise and after another 30 minutes, the reaction mixture was allowed to warm to room temperature. The reaction progress was monitored by GC-MS. After complete consumption of the starting compound, the reaction mixture was washed with 10% $NaHCO_3$ (2 × 20 cm^3) and distilled water (4 × 20 cm^3). The organic layer was dried over anhydrous Na_2SO_4 and evaporated under vacuum to obtain the desired compound **7a** as an orange oil in the yield 487 mg (99%). The purity of this material was sufficient for the next step. GC-EI-MS (t_R = 11.1 min): 41(10), 67(10), 77(7), 79(21), 81(6), 91(6), 93(20), 107(10), 135(100), 136(11), 164(M$^+$, 4) *m/z*(%).

Synthetic procedure towards aldehyde 7b



Scheme S3 Synthetic route towards **7b**.

2-(1-Adamantyl)ethan-1-ol (11)

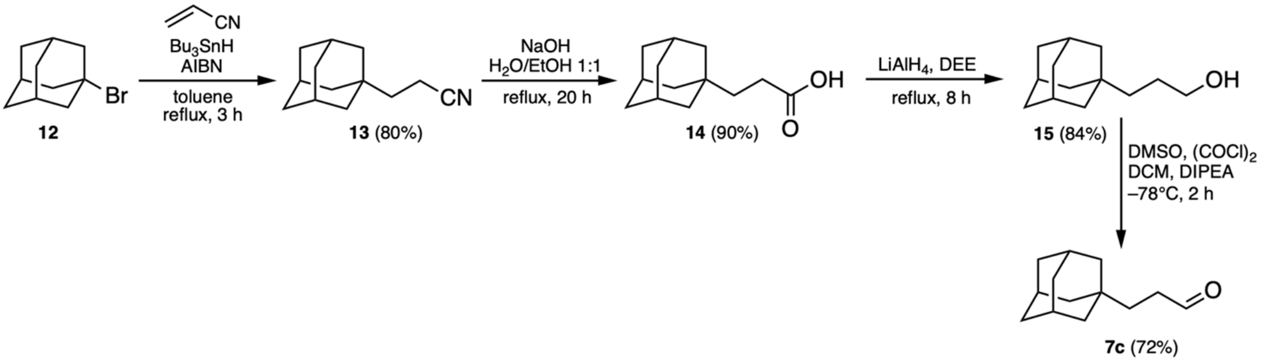
The title compound **11** was prepared analogously to compound **9**, using 1-adamantaneacetic acid (**10**, 10 g, 51.5 mmol) to obtain 8.5 g (92%) of colourless crystals. Mp 73–75 °C. GC-EI-MS (t_R = 12.4 min):

41(7), 67(8), 77(6), 79(16), 91(7), 93(16), 105(5), 107(9), 135(100), 136(11), 152(13) *m/z*(%). The collected data are in agreement with those previously published.[5]

2-(1-Adamantyl)-1-acetaldehyde (7b)

The title compound **7b** was prepared analogously to compound **7a**, using alcohol **11** (271 mg, 1.5 mmol) as a starting material. The aldehyde **7b** (223 mg, 83%) was obtained as a brown oil. The product was used in the next step without further purification. ^{1}H NMR (400 MHz, $CDCl_3$, 30 °C) δ [ppm] = 1.64–1.75 (m, 12H), 1.99 (s, 3H), 2.12 (d, J = 3.2 Hz, 2H), 9.87 (t, J = 3.3 Hz, 1H). The collected data are in agreement with those previously published.[6]

Synthetic procedure towards aldehyde 7c



Scheme S4 Synthetic route towards **7c**.

3-(1-Adamantyl)propanenitrile (13)

A 100 cm^3 reaction flask was annealed under vacuum using heat gun for 30 min and filled with argon. 1-Bromoadamantane (**12**, 2.2 g, 10 mmol) was added into the flask and dissolved in dry toluene (20 cm^3). Acrylonitrile (2.7 cm^3, 42 mmol), tributyltin hydride (7.5 cm^3, 28 mmol) and few drops of 0.2 M solution of azobisisobutyronitrile in toluene were added and the reaction mixture was heated to reflux for 3 h. Subsequently, the mixture was cooled to room temperature, diluted with ethyl acetate (20 cm^3), washed with 0.5 M NH_3 solution (3 × 30 cm^3), distilled water (30 cm^3) and brine (30 cm^3) and dried over anhydrous Na_2SO_4. After removing the solvent, the oily residue was purified by column chromatography (silica gel, petroleum ether/ethyl acetate, 30/1, v/v) to afford **13** (1.5 g, 80%) as a colourless crystalline powder. Mp 48–49 °C. ^{1}H NMR (400 MHz, $CDCl_3$, 30 °C) δ [ppm] = 1.46–1.50 (m, 8H), 1.72 (dd, J = 12.4, 28.8 Hz, 6H), 1.99 (s, 3H), 2.27 (t, J = 7.6 Hz, 2H). GC-EI-MS (t_R = 13.2 min): 41(10), 67(8), 77(7), 79(17), 91(10), 93(17), 107(9), 135(100), 136(11), 189(M^+, 2) *m/z*(%). The collected data are in agreement with those previously published.[7]

3-(1-Adamantyl)propanoic acid (14)

In a 50 cm^3 reaction flask, the nitrile **13** (1.5 g, 8 mmol) was dissolved in a mixture of ethanol (16 cm^3) and distilled water (16 cm^3) and sodium hydroxide (2 g, 50 mmol) was added. The reaction mixture was heated to reflux for 20 h, cooled to room temperature and concentrated under vacuum. The residue was acidified with concentrated HCl. Precipitate was filtered off using Büchner funnel and dried under vacuum to yield the acid **14** (1.5 g, 90%) as a colourless solid. Mp 139–140 °C. ^{1}H NMR (400 MHz, DMSO-d_6, 30 °C) δ[ppm] = 1.29 (t, J = 8.8 Hz, 2H), 1.41 (s, 6H), 1.61 (dd, J = 12.0, 18.4 Hz, 6H), 1.91 (s, 3H), 2.12 (t, J = 8.0 Hz, 2H), 11.9 (br, 1H). The collected data are in agreement with those previously published.[8]

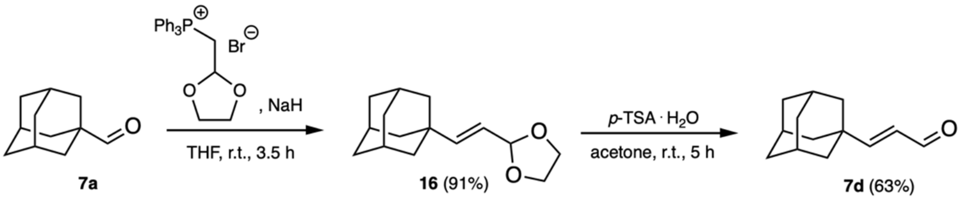
3-(1-Adamantyl)propan-1-ol (15)

The title compound was prepared analogously to compound **9**, using acid **14** (1.5 g, 7.2 mmol) as a starting material. The compound **15** (1.2 g, 84%) was obtained as colourless crystals. Mp 55–56 °C (59 °C). ^{1}H NMR (400 MHz, DMSO-d_6, 30 °C) δ[ppm] = 0.96–1.99 (m, 2H), 1.27–1.35 (m, 2H), 1.39 (s, 6H), 1.59 (dd, J = 12.0, 18.8 Hz, 6H), 1.87 (s, 3H), 3.30 (q, J = 6.8 Hz, 2H), 4.26 (t, J = 5.2 Hz, 1H). GC-EI-MS (t_R = 13.1 min): 41(11), 55(5), 67(8), 77(6), 79(20), 81(5), 91(11), 93(18), 107(10), 135(100), 136(11), 194(M$^+$, 2) m/z (%). The collected data are in agreement with those previously published.[9]

3-(1-Adamantane)propan-1-al (7c)

The title compound was prepared analogously to compound **7a**, using alcohol **15** (583 mg, 3 mmol) as a starting material. The compound **7c** (416 mg, 72%) was obtained as brown oil. The product was used in the next step without further purification. ^{1}H NMR (400 MHz, CDCl$_3$, 30 °C) δ[ppm] = 1.40 (t, J = 8.0 Hz, 2H), 1.46 (s, 6H), 1.66 (dd, J = 12.0, 24.8 Hz, 6H), 1.96 (s, 3H), 2.38 (t, J = 8.0 Hz, 2H), 9.76–9.77 (m, 1H). GC-EI-MS (t_R = 12.7 min): 41(15), 53(5), 55(7), 67(11), 77(10), 79(27), 81(7), 91(14), 92(5), 93(24), 107(13), 135(100), 136(11), 174(15) m/z(%).

Synthetic procedure towards aldehyde 7d



Scheme S5 Synthetic route towards **7d**.

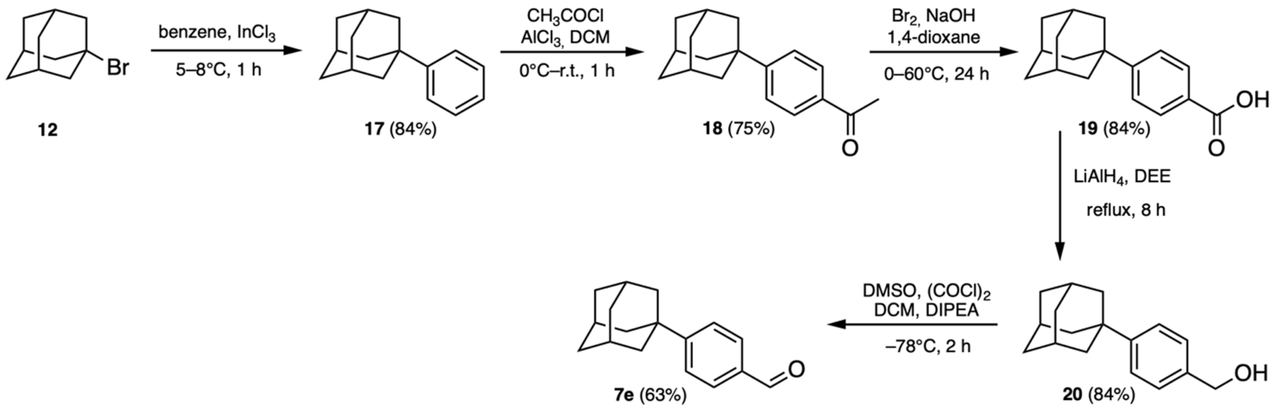
2-(2-(1-Adamantyl)ethenyl)-1,3-dioxolane (16)

In a 50 cm^3 reaction flask, (1,3-dioxolane-2-ylmethyl)-triphenylphosphonium bromide (1.7 g, 4 mmol) was dissolved in dry THF (10 cm^3) under an argon atmosphere. Sodium hydride (190 mg, 8 mmol) was added into the mixture over a period of 10 min and the reaction mixture was vigorously stirred at room temperature for 40 min. Subsequently, a solution of compound **7a** (490 mg, 3 mmol) in a dry tetrahydrofuran (5 cm^3) was slowly added dropwise. The light-coloured mixture became dark brown and was stirred at room temperature for 2.5 h. Reaction progress was monitored by GC-MS. Finally, the mixture was diluted with distilled water (10 cm^3) and extracted with dichloromethane (3 × 15 cm^3). Collected organic phases were dried over anhydrous Na_2SO_4 and evaporated under vacuum. The residue was washed several times with ice-cold pentane to remove the residual triphenylphosphine oxide. The solvent was evaporated under vacuum to afford the crude dioxolane **16** (640 mg, 91%) as a brown oil, which was used in the next step without further purification. ^{1}H NMR (400 MHz, DMSO-*d$_6$*, 30 °C) δ [ppm] = 1.64–1.79 (m, 12H), 1.92 (s, 3H), 3.75–3.79 (m, 2H), 3.85–3.89 (m, 2H), 5.10–5.15 (m, 1H), 5.34 (d, J = 12.8 Hz, 1H), 5.64 (d, J = 7.6 Hz, 1H). GC-EI-MS (t_R = 14.4 min): 41(7), 55(7), 73(14), 77(5), 79(9), 91(8), 93(6), 99(100), 135(6) *m/z*(%).

3-(1-Adamantyl)prop-2-enal (7d)

The crude dioxolane **16** (640 mg, 2.7 mmol) was dissolved in acetone (24 cm^3) and *p*-toluenesulfonic acid monohydrate (616 mg, 3.2 mmol) was added in one portion. The reaction mixture was stirred at room temperature for 5 h and the reaction progress was monitored by GC-MS. Saturated solution of $NaHCO_3$ (10 cm^3) was added and mixture was extracted with toluene (3 × 25 cm^3). The collected organic portions were washed with brine, dried over anhydrous Na_2SO_4 and evaporated under vacuum. The resulting brown oil was purified by column chromatography (silica gel, petroleum ether/ethyl acetate, 1/1, v/v) to afford compound **7d** (325 mg, 63%) as an orange oil. ^{1}H NMR (400 MHz, DMSO-*d$_6$*, 30 °C) δ [ppm] = 1.63–1.73 (m, 12H), 1.99 (br, 3H), 5.91 (dd, J = 8.0, 16.0 Hz, 1H), 6.82 (d, J = 16.0 Hz, 1H), 9.47 (d, J = 7.6 Hz, 1H). GC-EI-MS (t_R = 13.0 min): 40(7), 41(65), 43(8), 51(11), 52(6), 53(24), 55(31), 57(11), 65(24), 66(13), 67(38), 68(7), 69(9), 70(7), 77(51), 78(19), 79(83), 80(26), 81(30), 82(5), 83(8), 91(82), 92(42), 93(63), 94(25), 95(27), 96(13), 97(15), 103(9), 104(8), 105(49), 106(22), 107(21), 108(10), 109(8), 110(10), 111(19), 115(10), 117(16), 118(7), 119(29), 120(17), 121(11), 129(11), 130(5), 131(14), 133(54), 134(19), 135(12), 147(24), 148(8), 161(10), 162(8), 175(17), 190(M^+, 100), 191(15) *m/z*(%). The collected data are in agreement with those previously published.[10]

Synthetic procedure towards aldehyde 7e



Scheme S6 Synthetic route towards **7e**.

1-Phenyladamantane (17)

To a 50 cm^3 reaction flask, charged with argon and indium chloride (0.21 g, 0.93 mmol), dry benzene (25 cm^3) was added and the mixture was cooled to 5–8 °C in an ice bath. 1-Bromoadamantane (**12**, 2.0 g, 9.3 mmol) was added in one portion and the reaction mixture was stirred at 5–8 °C for 1 h. Reaction progress was monitored by GC-MS. The reaction mixture was diluted with 10% $NaHCO_3$ solution (20 cm^3) and the water phase was extracted with ethyl acetate (3 × 20 cm^3). The collected organic portions were washed with distilled water (2 × 30 cm^3) and brine (30 cm^3), dried over anhydrous Na_2SO_4 and evaporated under vacuum to yield the titled compound **17** (1.7 g, 84%) as a colourless crystalline powder. Mp 80–83 °C. ^{1}H NMR (400 MHz, $CDCl_3$, 30 °C) δ[ppm] = 1.75–1.82 (m, 6H), 1.93–1.94 (m, 6H), 2.11 (br, 3H), 7.16–7.20 (m, 1H), 7.30–7.39 (m, 4H). GC-EI-MS (t_R = 12.5 min): 41(14), 51(5), 67(5), 77(20), 78(7), 79(18), 91(33), 93(8), 94(30), 115(15), 118(5), 128(12), 129(10), 141(9), 142(7), 143(5), 153(6), 154(10), 155(100), 156(21), 169(12), 212(M^+, 54), 213(10) *m/z*(%). The collected data are in agreement with those previously published.[11]

1-(4-(1-Adamantyl)phenyl)ethan-1-one (18)

In a 100 cm^3 reaction flask, compound **17** (283 mg, 1.33 mmol) was dissolved in dry dichloromethane (50 cm^3) under argon atmosphere and the resulting solution was cooled to 0 °C in an ice bath. Then, aluminium chloride (530 mg, 3.99 mmol) was added in few portions followed by acetyl chloride (261 mg, 3.33 mmol). The reaction mixture was stirred at room temperature for 1 h, cooled to 0 °C, cautiously quenched with distilled water (250 cm^3) and diluted with dichloromethane (250 cm^3). The organic phase was washed with 1 M HCl (2 × 250 cm^3) and dried over anhydrous Na_2SO_4. The solvent was removed under vacuum and the crude product was purified by column chromatography (silica gel, petroleum ether/chloroform, 1/5, v/v) to afford compound **18** (253 mg, 75%) as a colourless crystalline powder. Mp 93–96 °C. ^{1}H NMR (400 MHz, $CDCl_3$, 30 °C) δ[ppm] = 1.75–1.83 (m, 6H), 1.93–1.94 (m, 6H), 2.12 (br, 3H), 2.59 (s, 3H), 7.45 (d, J = 8.4 Hz, 2H), 7.91 (d, J = 8.4 Hz, 2H). GC-EI-MS (t_R = 15.1 min): 41(10), 43(79), 77(9), 79(13), 91(12), 93(6), 94(5), 105(5), 115(9), 128(7), 239(100), 240(18), 254(M$^+$, 25), 255(5) *m/z*(%). The collected data are in agreement with those previously published.[12]

4-(1-Adamantyl)benzoic acid (19)

To a 25 cm^3 reaction flask, 6 M sodium hydroxide solution (10 cm^3) was added and the system was cooled to 0 °C using an ice bath. Bromine (0.52 cm^3, 10 mmol) was added dropwise to the solution. Subsequently, a solution of compound **18** (500 mg, 1.97 mmol) in 1,4-dioxane (7 cm^3) was added dropwise to the resulted sodium hypobromite solution during 2.5 h. After 1 h, the reaction mixture was allowed to warm to room temperature and stirred for additional 1 h. The temperature was elevated to 60 °C and the two-phase mixture was vigorously stirred for 24 h and monitored by TLC. After completing, the mixture was cooled to room temperature and $Na_2S_2O_3$ (225 mg, 1.42 mmol) was added. The resulting solution was washed with chloroform (3 × 25 cm^3) and acidified with concentrated HCl. The product was extracted with diethyl ether (6 × 20 cm^3), dried over anhydrous Na_2SO_4 and evaporated to dryness under vacuum to yield the titled acid **19** (424 mg, 84%) as a colourless solid. Mp 251–271 °C. ^{1}H NMR (400 MHz, DMSO-*d$_6$*, 30 °C) δ[ppm] = 1.73 (s, 6H), 1.87 (s, 6H), 2.05 (br, 3H), 7.47 (d, J = 8.4 Hz, 2H), 7.87 (d, J = 8.4 Hz, 2H), 12.68 (br, 1H). The collected data are in agreement with those previously published.[13]

4-(1-Adamantylphenyl)methanol (20)

The title compound was prepared analogously to compound **9**, using acid **19** (240 g, 0.94 mmol) as a starting material. The compound **20** (190 mg, 84%) was obtained as a colourless solid. Mp 96–100 °C. ^{1}H NMR (400 MHz, DMSO-*d$_6$*, 30 °C) δ[ppm] = 1.72 (s, 6H), 1.84 (s, 6H), 2.03 (br, 3H), 4.42 (d, J = 6.0 Hz, 2H), 5.00 (t, J = 5.6 Hz, 1H), 7.22 (d, J = 8.4 Hz, 2H), 7.28 (d, J = 8.4 Hz, 2H). ^{13}C NMR (101 MHz, DMSO-*d$_6$*, 30 °C) δ[ppm] = 28.30, 35.48, 36.18, 42.67, 62.72, 124.23, 126.32, 139.51, 149.24. GC-EI-MS (t_R = 17.6 min): 41(15), 53(5), 55(7), 65(7), 67(9), 77(23), 78(5), 79(28), 91(31), 92(6), 93(17), 94(32), 107(9), 115(17), 117(6), 118(5), 121(6), 128(15), 129(13), 132(8), 133(6), 135(75), 136(10), 141(10, 148(11), 153(8), 154(8), 155(100), 156(14), 167(7), 169(19), 183(12), 185(27), 198(6), 226(10), 240(24), 241(6), 242(M$^+$, 60), 243(12) *m/z*(%). The collected data are in agreement with those previously published.[14]

4-(1-Adamantyl)benzaldehyde (7e)

The title compound was prepared analogously to compound **7a**, using alcohol **20** (172 mg, 0.71 mmol) as a starting material. After purification by column chromatography (silica gel, petroleum ether/ethyl acetate, 10/1, v/v), the compound **7e** (107 mg, 63%) was obtained as a colourless solid. Mp 97–100 °C. ^{1}H NMR (400 MHz, $CDCl_3$, 30 °C) δ [ppm] = 1.75–1.84 (m, 6H), 1.94 (s, 6H), 2.13 (br, 3H), 7.53 (d, J = 8.0 Hz, 2H), 7.83 (d, J = 8.4 Hz, 2H), 9.98 (s, 1H). ^{13}C NMR (101 MHz, $CDCl_3$, 30 °C) δ [ppm] = 28.80, 36.65, 36.97, 42.89, 125.61, 129.72, 134.16, 158.51, 192.05. The collected data are in agreement with those previously published.[12]

N-(1-adamantylmethyl)-*N'*-isopropylhexane-1,6-diamine dihydrochloride (5a)

The title compound **5a** was prepared according to a slightly modified, previously published procedure.[13a] Amine **4** (115 mg, 0.67 mmol) and aldehyde **7a** (166 mg, 1.01 mmol) were dissolved in dry methanol (4 cm^3) in a reaction flask and the resulting solution was kept at room temperature for 20 h under argon atmosphere. Sodium borohydride (76 mg, 2 mmol) was added portion-wise into the mixture, which was stirred for an additional 30 min until the disappearance of the imine proton signal in the ^{1}H NMR spectrum. The mixture was diluted with diethyl ether (40 cm^3) and then washed with 10% sodium hydroxide solution (20 cm^3), distilled water (3 × 20 cm^3) and brine (20 cm^3). The organic phase was dried over anhydrous Na_2SO_4 and concentrated. The oily residue was dissolved in dry methanol (5 cm^3) and freshly generated hydrogen chloride was bubbled through the mixture for 1 h. The resulting solution was concentrated to half its volume using a stream of nitrogen and dry diethyl ether was added. The resulted precipitate was filtered off and dried under vacuum to obtain the ligand **5a** (130 mg, 49%) as a colourless solid. Mp 245–249 °C. ^{1}H NMR (400 MHz, DMSO-d_6, 30 °C) δ [ppm] = 0.94 (d, J = 6.4 Hz, 6H), 1.30 (br, 4H), 1.58–1.68 (m, 16H), 1.95 (s, 3H), 2.00 (sep, J = 6.8 Hz, 1H), 2.56–2.59 (m, 2H), 2.67–2.72 (m, 2H), 2.80–2.88 (m, 4H), 8.51 (br, 2H), 8.81 (br, 2H). ^{13}C NMR (101 MHz, DMSO-d_6, 30 °C) δ [ppm] = 20.11, 24.37, 24.83, 25.22, 25.49, 27.33, 31.82, 35.95, 39.08, 47.11, 48.14, 53.77, 58.16. ^{1}H NMR (400 MHz, D_2O, 30 °C) δ [ppm] = 0.92 (d, J = 6.8 Hz, 6H), 1.30–1.38 (m, 4H), 1.52 (s, 6H), 1.57–1.70 (m, 10H), 1.89–1.99 (m, 4H), 2.68 (s, 2H), 2.82 (d, J = 7.2 Hz, 2H), 2.94–2.99 (m, 4H). ^{13}C NMR (101 MHz, D_2O, 30 °C) δ [ppm] = 19.20, 24.87, 25.26, 25.42, 25.42, 25.64, 27.73, 31.77, 35.97, 39.22, 47.98, 48.74, 54.72, 59.31. IR (KBr): 3425 (br), 2909 (vs), 2850 (s), 2772 (s), 2433 (w), 1591 (w), 1453 (m), 1372 (w), 1021 (w), 735 (w) cm^{-1}. ESI-MS (pos.) m/z (%): 321.2 $[M+H^+]^+$ (100), 173.1 $[M+2{\cdot}H^+-AdCH_2^+]^+$ (12), 161.0 $[M+2{\cdot}H^+]^{2+}$ (50), 149.0 $[AdCH_2^+]^+$ (9). HRMS (ESI) m/z calcd for $C_{21}H_{40}N_2+H^+$: 321.3264 $[M+H^+]^+$; found: 321.3211.

N-(2-(1-adamantyl)ethyl)-*N'*-isobutylhexane-1,6-diamine dihydrochloride (5b)

The title compound was prepared analogously to ligand **5a**, using aldehyde **7b** (260 mg, 1.5 mmol) as a starting compound. The ligand **5b** (150 mg, 37%) was obtained as a colourless solid. Mp 272–278 °C. ^{1}H NMR (400 MHz, DMSO-d_6, 30 °C) δ [ppm] = 0.91 (d, J = 6.4 Hz, 6H), 1.29 (br, 4H), 1.35–1.39 (m, 2H), 1.43 (s, 6H), 1.55–1.66 (m, 10H), 1.92 (br, 3H), 1.95 (sep, J = 6.8 Hz, 1H), 2.68 (m, 2H), 2.82 (m, 6H), 8.60 (br, 4H). ^{13}C NMR (101 MHz, DMSO-*d*$_6$, 30 °C) δ [ppm] = 20.64, 25.48, 25.81, 25.87, 26.00, 26.02, 28.33, 31.86, 36.93, 39.48, 42.04, 42.78, 47.07, 47.68, 54.46. ^{1}H NMR (400 MHz, D_2O, 30 °C) δ [ppm] = 0.92 (d, *J* = 7.2 Hz, 6H), 1.33–1.38 (m, 6H), 1.45 (s, 6H), 1.55–1.67 (m, 10H), 1.87–1.99 (m, 4H), 2.82 (d, *J* = 7.2 Hz, 2H), 2.94–3.01 (m, 6H). ^{13}C NMR (101 MHz, D_2O, 30 °C) δ [ppm] = 19.20, 25.23, 25.39, 25.42, 25.44, 25.64, 28.35, 31.23, 36.48, 39.55, 41.55, 43.27, 47.36, 47.99, 54.71. IR (KBr): 3440 (br), 2908 (vs), 2848 (m), 2789 (m), 2437 (w), 1785 (w), 1759 (m), 1599 (w), 1451 (m), 1225 (m), 1178 (w), 1035 (w), 998 (m), 700 (m) cm^{-1}. ESI-MS (pos.) *m/z* (%): 335.3 $[M+H^+]^+$ (100), 168.0 $[M+2\cdot H^+]^{2+}$ (28). HRMS (ESI) *m/z* calcd for $C_{22}H_{42}N_2+H^+$: 335.3421 $[M+H^+]^+$; found: 335.3440.

***N*-(3-(1-adamantyl)propyl)-*N'*-isobutylhexane-1,6-diamine dihydrochloride (5c)**

The title compound was prepared analogously to ligand **5a**, using aldehyde **7c** (530 mg, 2.8 mmol) as a starting compound. The ligand **7c** (222 mg, 29%) was obtained as a colourless solid. Mp 276–281 °C. ^{1}H NMR (400 MHz, DMSO-*d*$_6$, 30 °C) δ [ppm] = 0.94 (d, *J* = 6.4 Hz, 6H), 1.02–1.06 (m, 2H), 1.31 (br, 4H), 1.44 (s, 6H), 1.52–1.69 (m, 12H), 1.92 (br, 3H), 1.98 (sep, *J* = 6.8 Hz, 1H), 2.68–2.73 (m, 2H), 2.75–2.87 (m, 6H), 8.63 (br, 2H), 8.72 (br, 2H). ^{13}C NMR (101 MHz, DMSO-*d*$_6$, 30 °C) δ [ppm] = 18.89, 20.04, 24.88, 25.16, 25.26, 25.39, 25.44, 27.94, 31.61, 36.54, 40.49, 41.69, 46.43, 47.13, 47.52, 53.80. ^{1}H NMR (400 MHz, D_2O, 30 °C) δ [ppm] = 0.92 (d, *J* = 7.2 Hz, 6H), 1.01–1.05 (m, 2H), 1.33–1.36 (m, 4H), 1.41 (s, 6H), 1.54–1.66 (m, 12H), 1.85 (br, 3H), 1.94 (sep, *J* = 7.2 Hz, 1H), 2.82 (d, *J* = 7.2 Hz, 2H), 2.90–2.99 (m, 6H). ^{13}C NMR (101 MHz, D_2O, 30 °C) δ [ppm] = 19.19, 25.24, 25.37, 25.41, 25.64, 28.52, 31.52, 36.74, 40.48, 41.79, 47.29, 47.98, 48.53, 54.72. IR (KBr): 3432 (br), 2956 (s), 2928 (s), 2906 (s), 2847 (m), 2787 (m), 2418 (w), 1451 (m) cm^{-1}. ESI-MS (pos.) *m/z* (%): 349.3 $[M+H^+]^+$ (100), 175.0 $[M+2\cdot H^+]^{2+}$ (30). HRMS (ESI) *m/z* calcd for $C_{23}H_{44}N_2+H^+$: 349.3577 $[M+H^+]^+$; found: 349.3595.

***N*-((*E*)-3-(1-adamantyl)prop-2-en-1-yl)-*N'*-isobutylhexane-1,6-diamine dihydrochloride (5d)**

The title compound was prepared analogously to ligand **5a**, using aldehyde **7d** (190 mg, 1.0 mmol) as a starting compound. The ligand **5d** (95 mg, 35%) was obtained as a colourless solid. Mp 253–259 °C. ^{1}H NMR (400 MHz, DMSO-*d*$_6$, 30 °C) δ [ppm] = 0.94 (d, *J* = 6.4 Hz, 6H), 1.31 (br, 4H), 1.55 (s, 6H), 1.60–1.71 (m, 10H), 1.96 (br, 3H), 2.00 (sep, *J* = 6.8 Hz, 1H), 2.67–2.71 (m, 2H), 2.74–2.86 (m, 4H), 3.44–3.48 (m, 2H), 5.40 (dt, *J* = 6.8, 7.2 Hz, 1H), 5.73 (d, *J* = 15.6 Hz, 1H), 8.78 (br, 2H), 8.99 (br, 2H). ^{13}C NMR (101 MHz, DMSO-*d*$_6$, 30 °C) δ [ppm] = 20.69, 25.41, 25.63, 25.82, 26.00, 26.06, 28.19, 35.27, 36.74, 41.86, 45.96, 47.70, 48.84, 54.38, 116.20, 149.72. ^{1}H NMR (400 MHz, D_2O, 30 °C) δ [ppm] = 0.92 (d, *J* = 6.8 Hz, 6H), 1.23–1.38 (m, 4H), 1.54 (s, 6H), 1.57–1.69 (m, 10H), 1.91–1.99 (m, 4H), 2.82 (d, *J* = 6.8 Hz, 2H), 2.92–2.99 (m, 4H), 3.54 (d, *J* = 7.2 Hz, 2H), 5.32 (dt, *J* = 7.2, 8.4 Hz, 1H), 5.82 (d, *J* = 16 Hz, 1H). ^{13}C NMR (101 MHz, D_2O, 30 °C) δ [ppm] = 19.20, 25.24, 25.27, 25.39, 25.41, 25.64, 28.12, 34.91, 36.31, 41.31, 46.01, 47.98, 49.20, 54.72, 113.87, 152.95. IR (KBr): 3428 (br), 2956 (s), 2930 (s), 2906 (vs), 2848 (s), 2793 (s), 2438 (m), 1594 (w), 1450 (m), 1414 (w), 978 (w), 789 (w) cm^{-1}. ESI-MS (pos.) *m/z* (%): 347.3 $[M+H^+]^+$ (100), 175.0 $[AdCHCHCH_2^+]^+$ (14), 174.0 $[M+2\cdot H^+]^{2+}$ (4). HRMS (ESI) *m/z* calcd for $C_{23}H_{42}N_2+H^+$: 347.3421 $[M+H^+]^+$; found: 347.3441.

N-(4-(1-adamantyl)benzyl)-*N'*-isobutylhexane-1,6-diamine dihydrochloride (5e)

The title compound was prepared analogously to ligand **5a**, using aldehyde **7e** (107 mg, 0.45 mmol) as a starting compound. The ligand **5e** (40 mg, 28%) was obtained as a colourless solid. Mp 266–271 °C. ^{1}H NMR (400 MHz, DMSO-d_6, 30 °C) δ[ppm] = 0.94 (d, J = 6.8 Hz, 6H), 1.31 (br, 4H), 1.65 (br, 4H), 1.73 (s, 6H), 1.85 (s, 6H), 2.00 (sep, J = 6.8 Hz, 1H), 2.05 (br, 3H), 2.67–2.71 (m, 2H), 2.81–2.85 (m, 4H), 4.03–4.06 (m, 2H), 7.39 (d, J = 8.0 Hz, 2H), 7.50 (d, J = 8.4 Hz, 2H), 8.81 (br, 2H), 9.31 (br, 2H). ^{13}C NMR (101 MHz, DMSO-d_6, 30 °C) δ[ppm] = 20.10, 24.80, 24.96, 25.21, 25.43, 24.46, 28.20, 35.68, 36.06, 42.44, 46.20, 47.09, 49.53, 53.76, 124.85, 129.15, 129.82, 151.51. ^{1}H NMR (400 MHz, D_2O, 30 °C) δ[ppm] = 0.92 (d, J = 6.8 Hz, 6H), 1.31–1.33 (m, 4H), 1.59–1.75 (m, 10H), 1.84 (s, 6H), 1.93 (sep, J = 6.8 Hz, 1H), 2.01 (br, 3H), 2.81 (d, J = 7.2 Hz, 2H), 2.96 (q, J = 7.6 Hz, 4H), 4.14 (s, 2H), 7.38 (d, J = 8.0 Hz, 2H), 7.49 (d, J = 8.4 Hz, 2H). ^{13}C NMR (101 MHz, D_2O, 30 °C) δ[ppm] = 19.19, 25.21, 25.29, 25.36, 25.45, 25.63, 28.73, 36.08, 36.24, 42.70, 46.75, 47.96, 50.57, 54.71, 125.86, 128.05, 129.98, 153.77. IR (KBr): 3423 (br), 2929 (s), 2905 (vs), 2848 (s), 2791 (m), 2428 (m), 1588 (w), 1518 (w), 1448 (m), 1018 (w), 840 (w), 801 (w), 547 (w) cm^{-1}. ESI-MS (pos.) *m/z* (%): 397.3 $[M+H^+]^+$ (100), 225.0 $[AdPhCH_2^+]^+$ (29). HRMS (ESI) *m/z* calcd for $C_{27}H_{44}N_2+H^+$: 397.3577 $[M+H^+]^+$; found: 397.3558.

Rotaxane 6a

The title compound **6a** was prepared according to a slightly modified, previously published, procedure.[13a] Ligand **5a** (20.0 mg, 50.8 μmol) and CB6 (50.6 mg, 50.8 μmol) were mixed together in H_2O (6 cm^3) and the resulted milky-like colloidal dispersion was heated at 120 °C for 2 h using a microwave reactor. The colourless solution was lyophilised to obtain a colourless solid (65 mg) which was purified by column chromatography (silica gel, $H_2O/CH_3CN/HCOOH$, 5/2/1, v/v/v) to afford rotaxane **6a** (36 mg, 51%) as a colourless solid. Mp > 360 °C. ^{1}H NMR (400 MHz, D_2O, 30 °C) δ[ppm] = 0.41–0.45 (m, 4H), 0.63–0.77 (m, 4H), 1.11 (d, J = 6.8 Hz, 6H), 1.65–1.76 (m, 12H), 2.00 (br, 3H), 2.15 (sep, J = 6.8 Hz, 1H), 2.79–2.85 (m, 4H), 2.94 (t, J = 7.2 Hz, 2H), 3.00 (d, J = 7.2 Hz, 2H), 4.29 (d, J = 16.0 Hz, 12H), 5.54 (s, 12H), 5.72 (dd, J = 5.2, 10.4 Hz, 12H). ^{13}C NMR (101 MHz, D_2O, 30 °C) δ[ppm] = 19.44, 25.94, 25.97, 26.03, 26.51, 26.73, 27.87, 32.01, 36.14, 39.09, 48.56, 49.16, 51.57, 56.23, 61.13, 70.47, 156.34. IR (KBr): 3435 (br), 3168 (br), 2992 (w), 2915 (m), 2850 (w), 1738 (vs), 1632 (s), 1593 (m), 1473 (s), 1418 (m), 1377 (m), 1325 (m), 1295 (m), 1256 (m), 1235 (m), 1189 (m), 965 (m), 818 (m), 800 (s), 795 (w), 673 (w) cm^{-1}. ESI-MS (pos.) *m/z* (%): 659.3 $[M^{2+}]^{2+}$ (100). HRMS (ESI) *m/z* calcd for $C_{57}H_{76}N_{26}O_{12}+2\cdot H^+$: 659.3141 $[M+2\cdot H^+]^{2+}$; found: 659.3195.

Rotaxane 6b

The title compound was prepared analogously to rotaxane **6a**, using a ligand **5b** (20.0 mg, 49.1 μmol) as a starting compound. The rotaxane **6b** (35 mg, 51%) was obtained as a colourless solid. Mp > 360 °C. ^{1}H NMR (400 MHz, D_2O, 30 °C) δ[ppm] = 0.42–0.44 (m, 4H), 0.59–0.75 (m, 4H), 1.11 (d, J = 6.4 Hz, 6H), 1.55–1.69 (m, 14H), 1.91 (br, 3H), 2.12 (sep, J = 6.8 Hz, 1H), 2.84 (t, J = 7.6 Hz, 2H), 2.93 (t, J = 6.8 Hz, 2H), 2.99 (d, J = 6.8 Hz, 2H), 3.15–3.20 (m, 2H), 4.27 (d, J = 15.6 Hz, 12H), 5.53 (s, 12H), 5.69

(dd, *J* = 1.2, 14.0 Hz, 12H). ^{13}C NMR (101 MHz, D_2O, 30 °C) δ[ppm] = 19.42, 25.95, 26.02, 26.06, 26.34, 26.48, 28.45, 31.34, 36.52, 40.09, 41.68, 44.55, 48.06, 48.39, 51.61, 56.26, 70.49, 156.34. IR (KBr): 3435 (br), 3163 (br), 2906 (m), 2848 (w), 2659 (w), 1740 (s), 1632 (vs), 1473 (s), 1418 (m), 1377 (m), 1326 (m), 1234 (m), 1189 (m), 966 (m), 800 (s), 759 (m), 672 (m), 629 (m) cm^{-1}. ESI-MS (pos.) *m/z* (%): 666.3 $[M^{2+}]^{2+}$ (100). HRMS (ESI) *m/z* calcd for $C_{58}H_{78}N_{26}O_{12}+2\cdot H^+$: 666.3219 $[M+2\cdot H^+]^{2+}$; found: 666.3277.

Rotaxane 6c

The title compound was prepared analogously to rotaxane **6a**, using a ligand **5c** (20.0 mg, 47.4 μmol) as a starting compound. The rotaxane **6c** (34 mg, 50%) was obtained as a colourless solid. Mp > 360 °C. ^{1}H NMR (400 MHz, D_2O, 30 °C) δ[ppm] = 0.43–0.45 (m, 4H), 0.62–0.77 (m, 4H), 1.12 (d, *J* = 6.8 Hz, 6H), 1.22–1.26 (m, 2H), 1.49 (s, 6H), 1.63 (dd, *J* = 11.6, 20.0 Hz, 6H), 1.77–1.85 (m, 2H), 1.89 (br, 3H), 2.14 (sep, *J* = 6.8 Hz, 1H), 2.86 (t, *J* = 7.2 Hz, 2H), 2.93 (t, *J* = 6.8 Hz, 2H), 3.01 (d, *J* = 6.8 Hz, 2H), 3.10 (t, *J* = 7.6, 2H), 4.27 (d, *J* = 14.0 Hz, 12H), 5.53 (s, 12H), 5.69 (dd, *J* = 2.0, 13.2 Hz, 12H). ^{13}C NMR (101 MHz, D_2O, 30 °C) δ[ppm] = 19.43, 19.84, 25.91, 26.05, 26.39, 26.51, 28.60, 31.68, 36.80, 40.64, 41.93, 48.23, 48.47, 50.03, 51.61, 56.33, 70.48, 156.29, 156.43. IR (KBr): 3435 (br), 3166 (br), 2905 (m), 2847 (m), 2659 (w), 1738 (s), 1632 (vs), 1474 (s), 1418 (m), 1377 (m), 1326 (m), 1235 (m), 1189 (m), 966 (m), 800 (s), 759 (m), 672 (m), 629 (w) cm^{-1}. ESI-MS (pos.) *m/z* (%): 673.3 $[M^{2+}]^{2+}$ (100). HRMS (ESI) *m/z* calcd for $C_{59}H_{80}N_{26}O_{12}+2\cdot H^+$: 673.3297 $[M+2\cdot H^+]^{2+}$; found: 673.3373.

Rotaxane 6d

The title compound was prepared analogously to rotaxane **6a**, using a ligand **5d** (20.0 mg, 47.7 μmol) as a starting compound. The rotaxane **6d** (32 mg, 48%) was obtained as a colourless solid. Mp > 360 °C. ^{1}H NMR (400 MHz, D_2O, 30 °C) δ[ppm] = 0.37–0.44 (m, 4H), 0.57–0.65 (m, 2H), 0.78–0.85 (m, 2H), 1.11 (d, *J* = 6.8 Hz, 6H), 1.59–1.69 (m, 12H), 1.90 (s, 3H), 2.11 (sep, *J* = 6.8 Hz, 1H), 2.77 (t, *J* = 8.4 Hz, 2H), 2.94–3.00 (m, 4H), 3.67 (d, *J* = 6.8 Hz, 2H), 4.27 (dd, *J* = 4.4, 11.2 Hz, 12H), 5.52 (s, 12H), 5.58 (t, *J* = 6.8 Hz, 1H), 5.70 (dd, *J* = 4.4, 11.2 Hz, 12H), 5.95 (d, *J* = 15.6 Hz, 1H). ^{13}C NMR (101 MHz, D_2O, 30 °C) δ[ppm] = 19.43, 25.82, 26.13, 26.36, 26.55, 26.64, 28.20, 34.90, 36.39, 41.40, 47.72, 48.30, 50.62, 51.58, 51.63, 56.31, 70.47, 115.00, 151.20, 156.20, 156.47. IR (KBr): 3436 (br), 3161 (br), 2905 (m), 2847 (w), 2659 (w), 1739 (s), 1632 (vs), 1473 (s), 1418 (m), 1377 (m), 1326 (m), 1296 (w), 1235 (m), 1189 (m), 1146 (m), 966 (m), 818 (m), 800 (s), 759 (m), 672 (w), 629 (w) cm^{-1}. ESI-MS (pos.) *m/z* (%): 672.3 $[M^{2+}]^{2+}$ (100). HRMS (ESI) *m/z* calcd for $C_{59}H_{78}N_{26}O_{12}+2\cdot H^+$: 672.3219 $[M+2\cdot H^+]^{2+}$; found: 672.3275.

Rotaxane 6e

The title compound was prepared analogously to rotaxane **6a**, using a ligand **5e** (10.0 mg, 21.3 μmol) as a starting compound. The rotaxane **6e** (15 mg, 50%) was obtained as a colourless solid. Mp > 360 °C. ^{1}H NMR (400 MHz, D_2O, 30 °C) δ[ppm] = 0.38–0.47 (m, 4H), 0.63–0.71 (m, 2H), 0.79–0.87 (m, 2H), 1.10 (d, *J* = 6.8

Hz, 6H), 1.72 (q, *J* = 12.4, 8.8 Hz, 6H), 1.87 (s, 6H), 2.02 (s, 3H), 2.12 (sep, *J* = 6.8 Hz, 1H), 2.80 (t, *J* = 8.0 Hz, 2H), 2.99 (d, *J* = 7.2 Hz, 2H), 3.04 (t, *J* = 7.2 Hz, 2H), 4.24–4.29 (m, 14H), 5.52 (s, 12H), 5.68 (dd, *J* = 6.4, 9.2 Hz, 12H), 7.51 (d, *J* = 8.4 Hz, 2H), 7.61 (d, *J* = 8.4 Hz, 2H). ^{13}C NMR (101 MHz, D_2O, 30 °C) δ [ppm] = 19.43, 25.90, 26.11, 26.38, 26.64, 26.77, 28.76, 36.08, 36.27, 42.72, 48.37, 48.47, 51.59, 52.02, 56.21, 70.47, 125.79, 129.08, 129.78, 153.43, 156.25, 156.42. IR (KBr): 3422 (br), 3158 (br), 2905 (m), 2847 (w), 2361 (w), 2343 (w), 1736 (s), 1632 (vs), 1598 (m), 1474 (s), 1418 (m), 1377 (m), 1325 (m), 1234 (m), 1189 (m), 965 (m), 818 (m), 800 (s), 759 (m), 671 (w) cm^{-1}. ESI-MS (pos.) *m/z* (%): 697.3 [M^{2+}]$^{2+}$ (100). HRMS (ESI) *m/z* calcd for $C_{63}H_{80}N_{26}O_{12}+2\cdot H^+$: 697.3297 [$M+2\cdot H^+$]$^{2+}$; found: 697.3318.

3 NMR characterisation spectra of ligands 5a–5e and rotaxanes 6a–6e

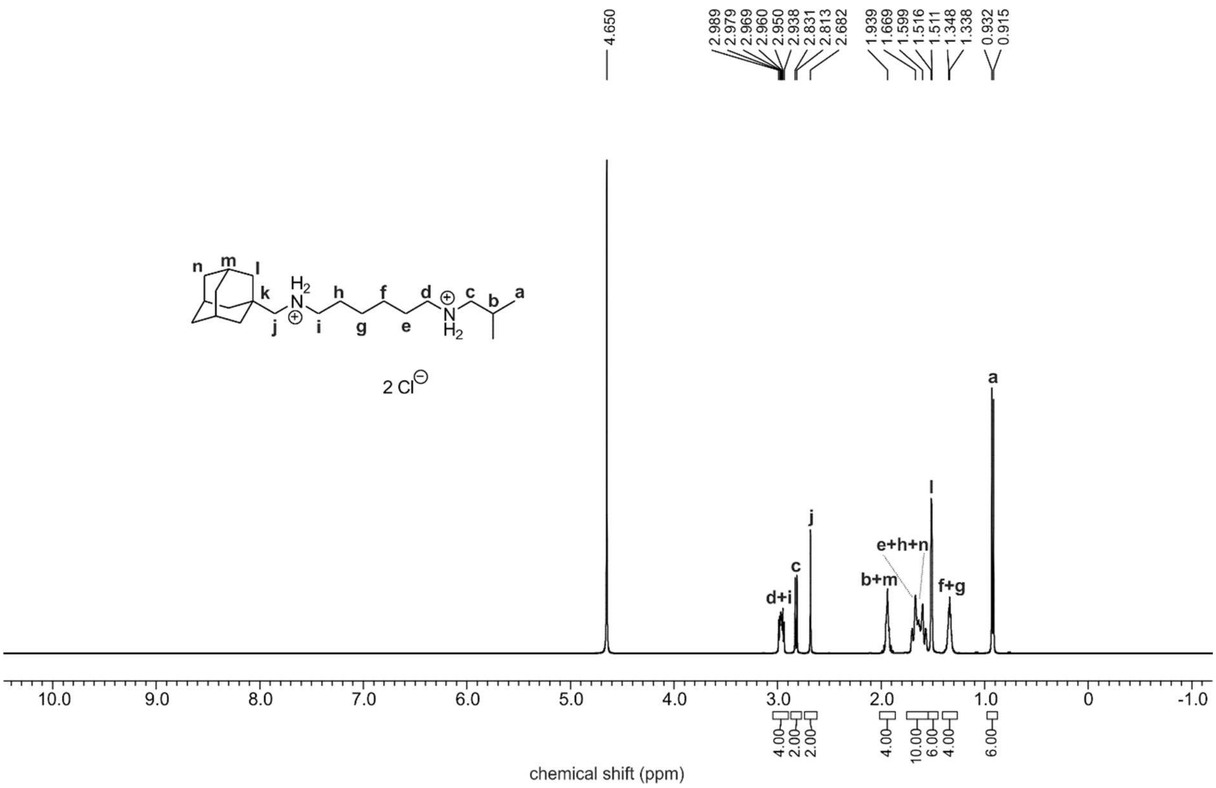


Figure S1 ^{1}H NMR (D_2O, 30 °C, 400 MHz) spectrum of **5a**.

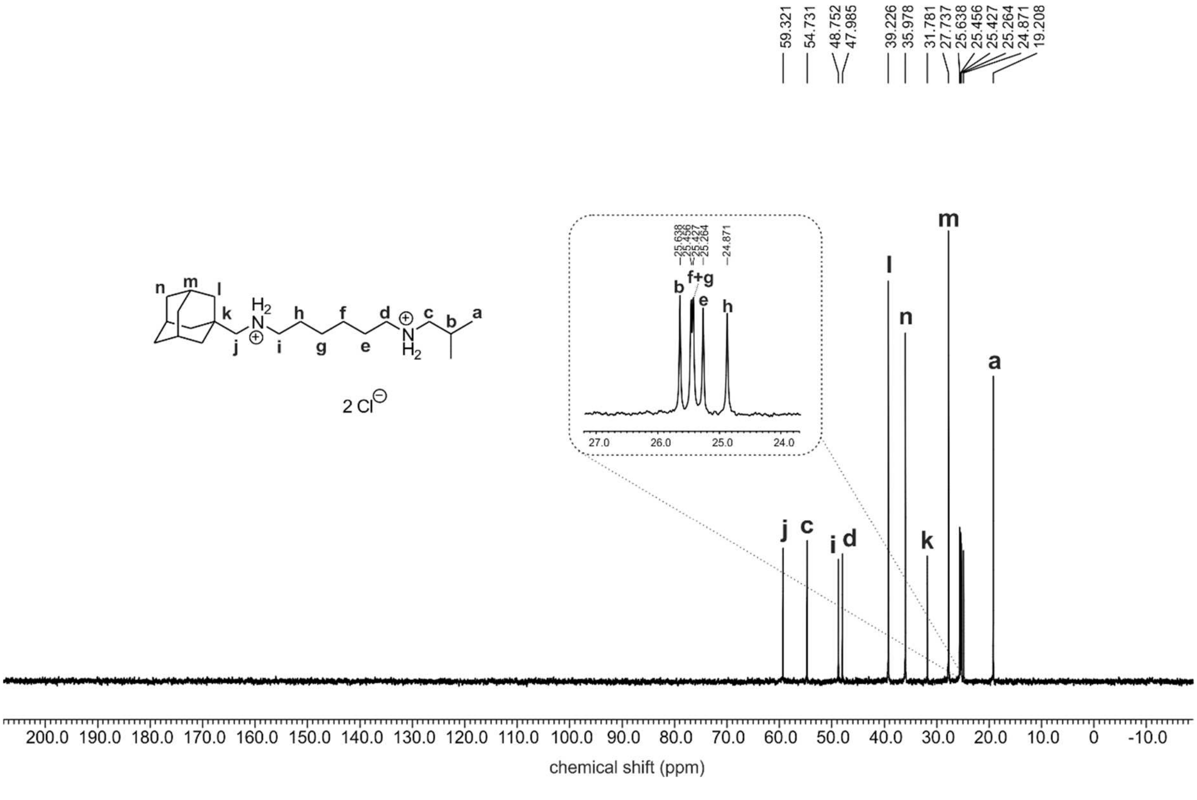


Figure S2 ^{13}C NMR (D_2O, 30 °C, 101 MHz) spectrum of **5a**.

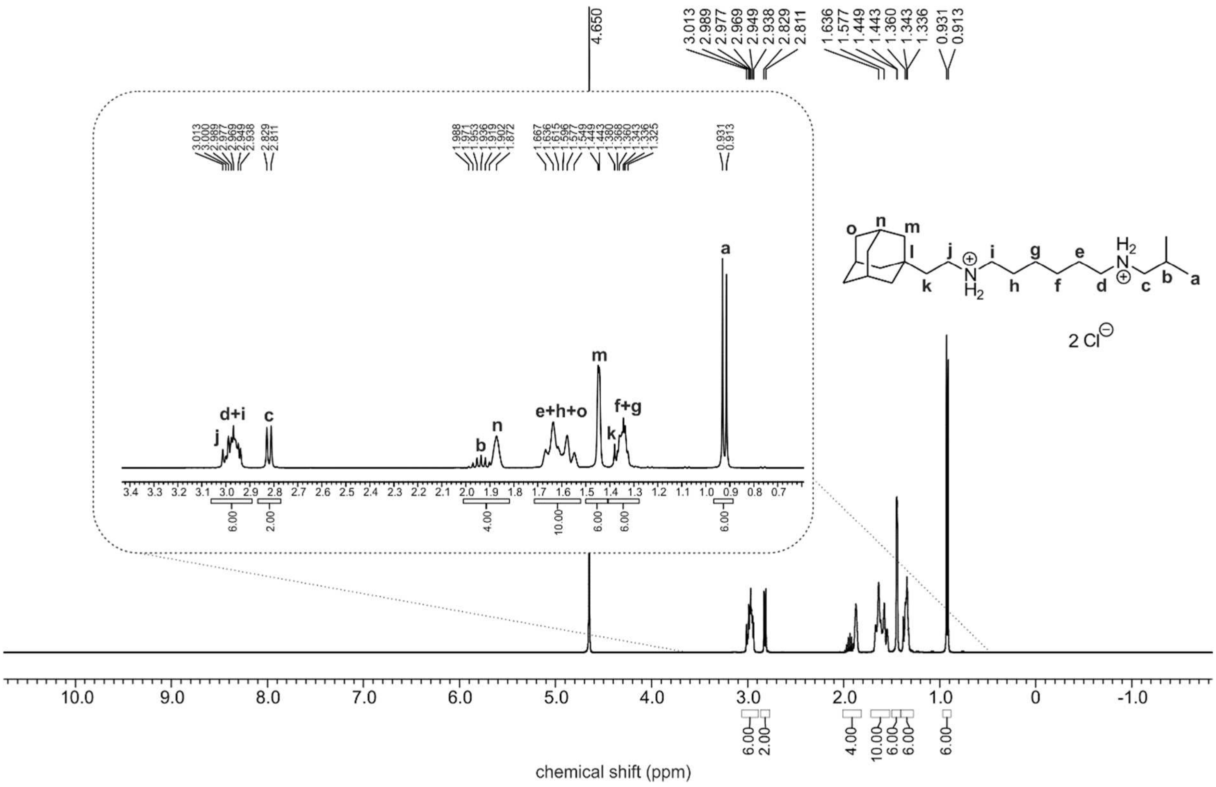


Figure S3 ^{1}H NMR (D_2O, 30 °C, 400 MHz) spectrum of **5b**.

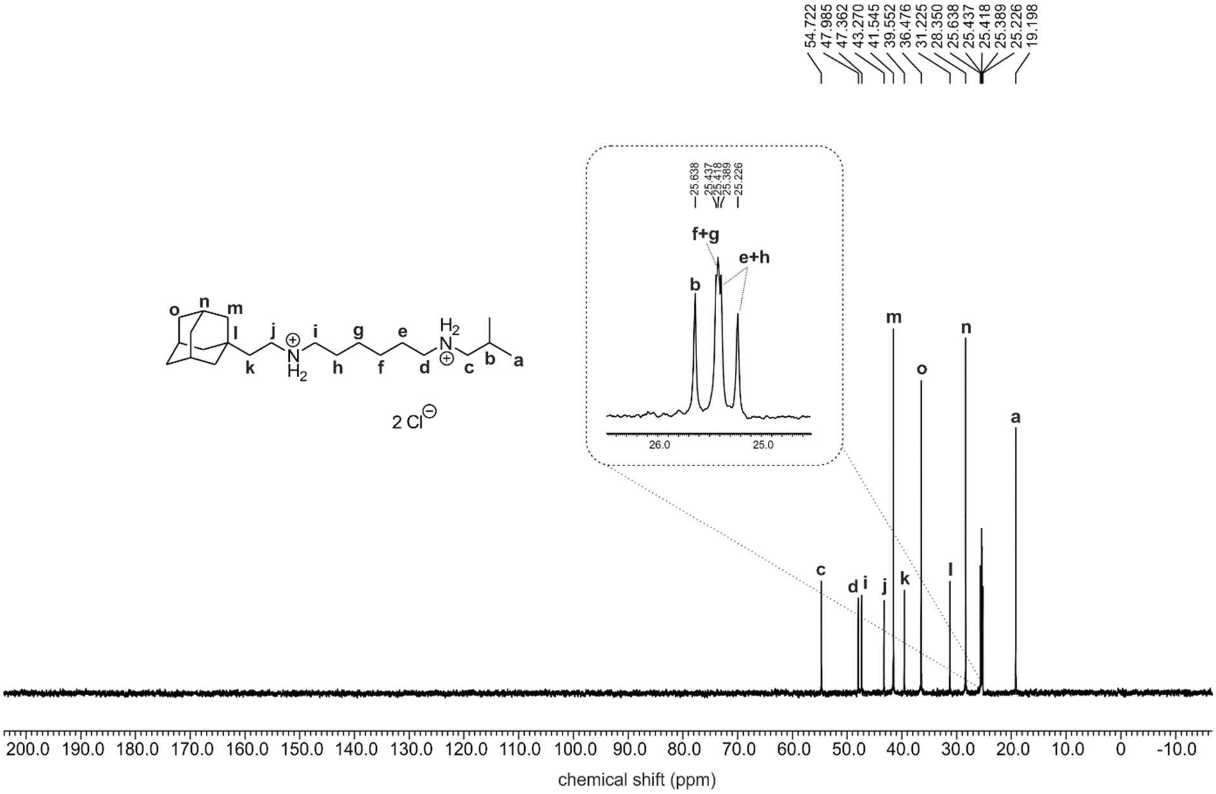


Figure S4 ^{13}C NMR (D_2O, 30 °C, 101 MHz) spectrum of **5b**.

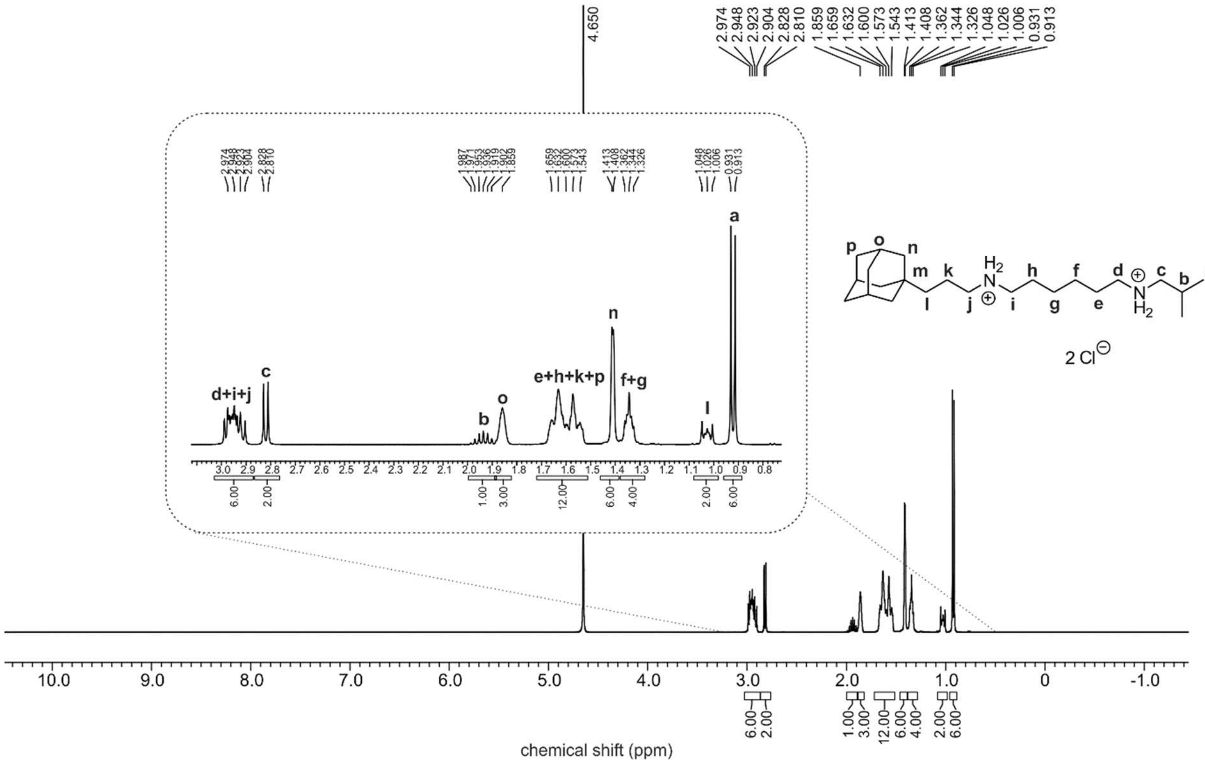


Figure S5 ^{1}H NMR (D_2O, 30 °C, 400 MHz) spectrum of **5c.**

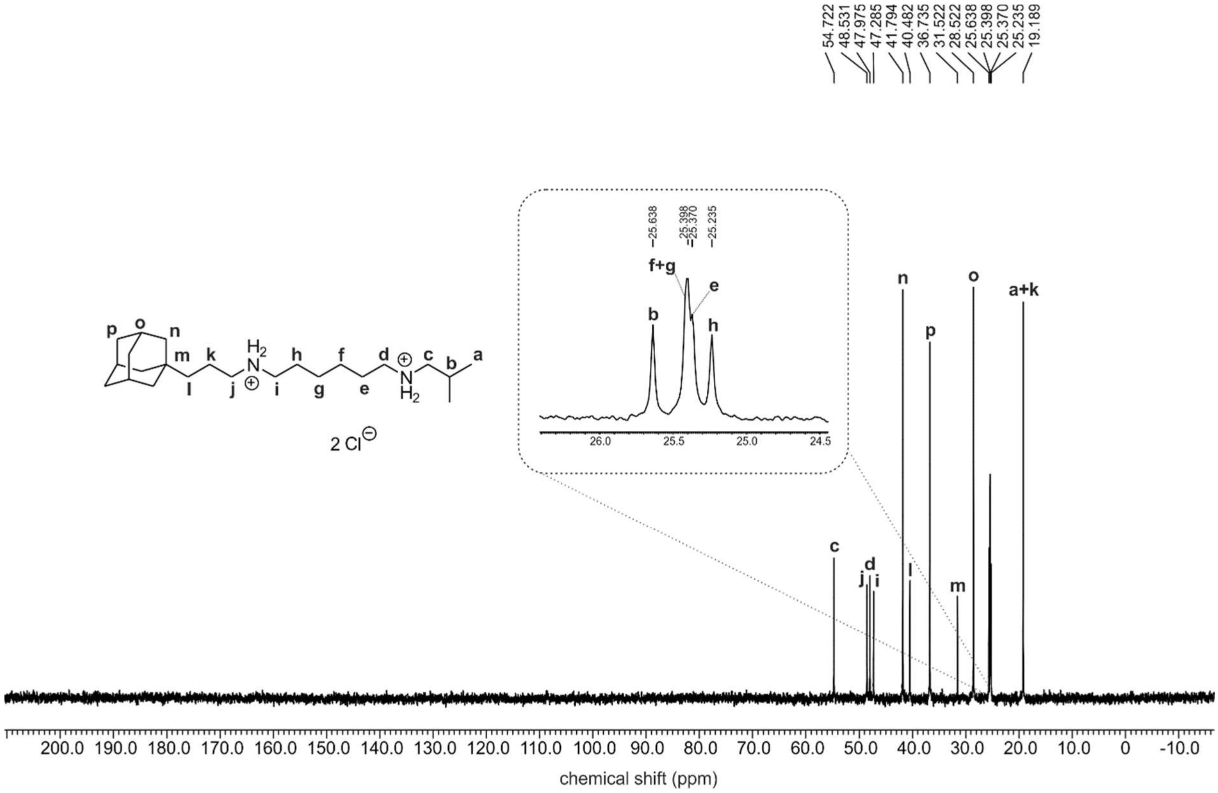


Figure S6 ^{13}C NMR (D_2O, 30 °C, 101 MHz) spectrum of **5c.**

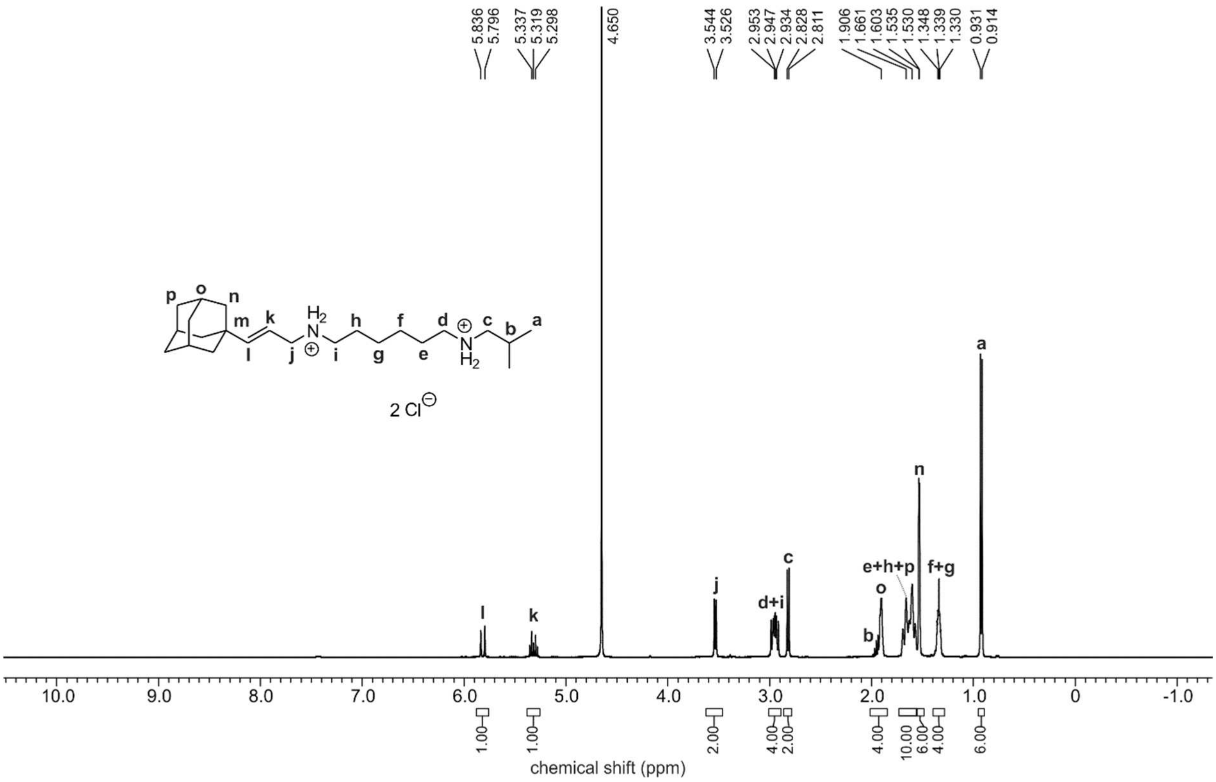


Figure S7 ^{1}H NMR (D_2O, 30 °C, 400 MHz) spectrum of **5d.**

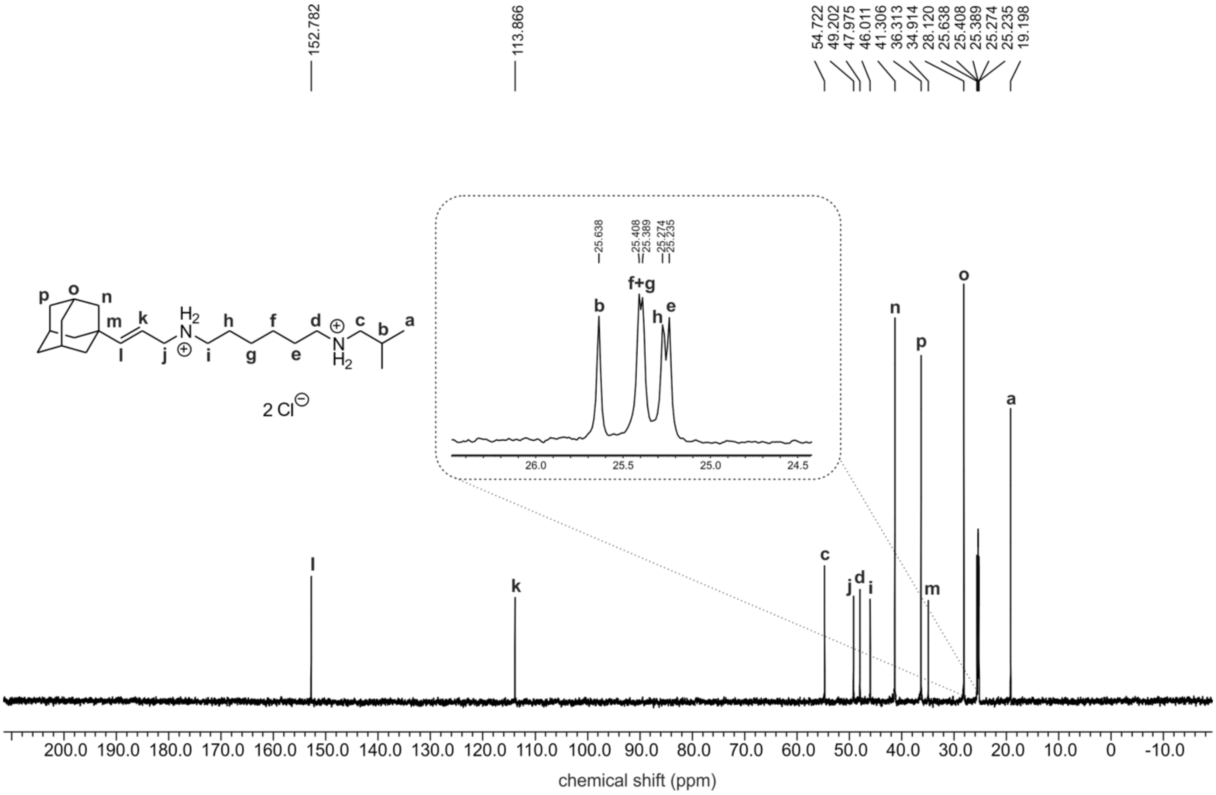


Figure S8 ^{13}C NMR (D_2O, 30 °C, 101 MHz) spectrum of **5d.**

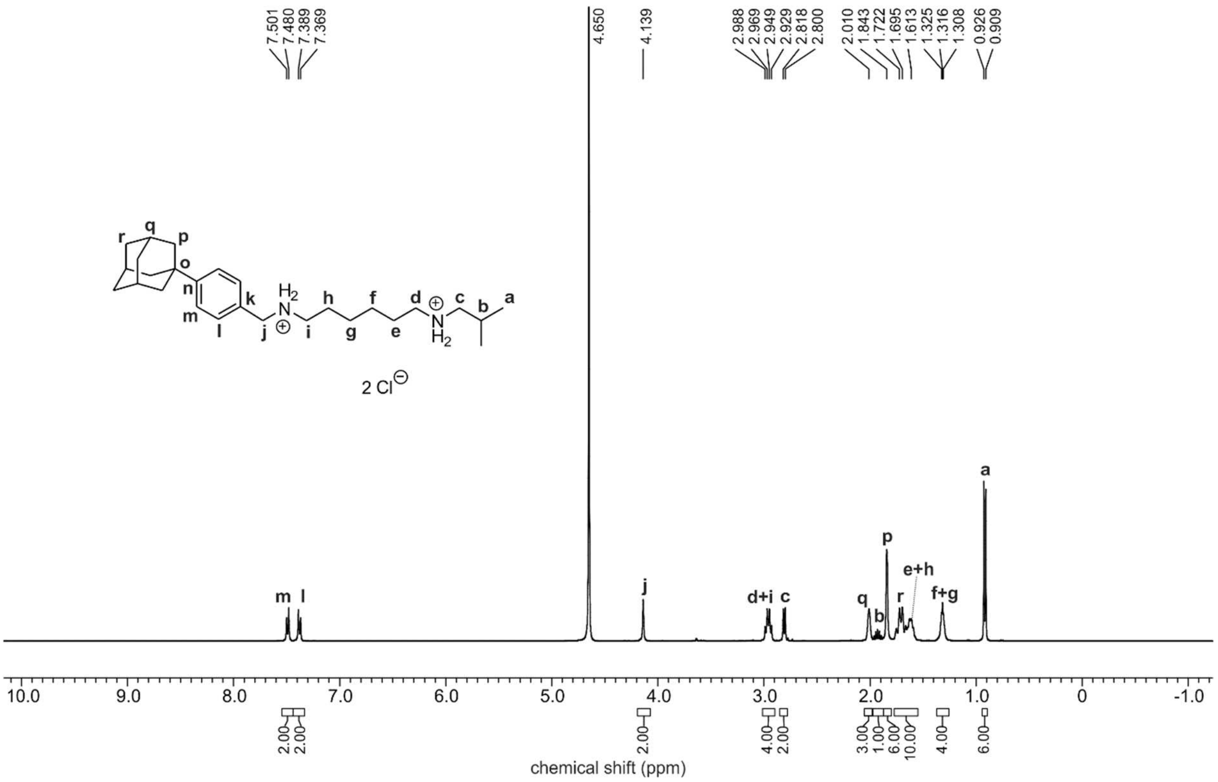


Figure S9 ^{1}H NMR (D_2O, 30 °C, 400 MHz) spectrum of **5e**.

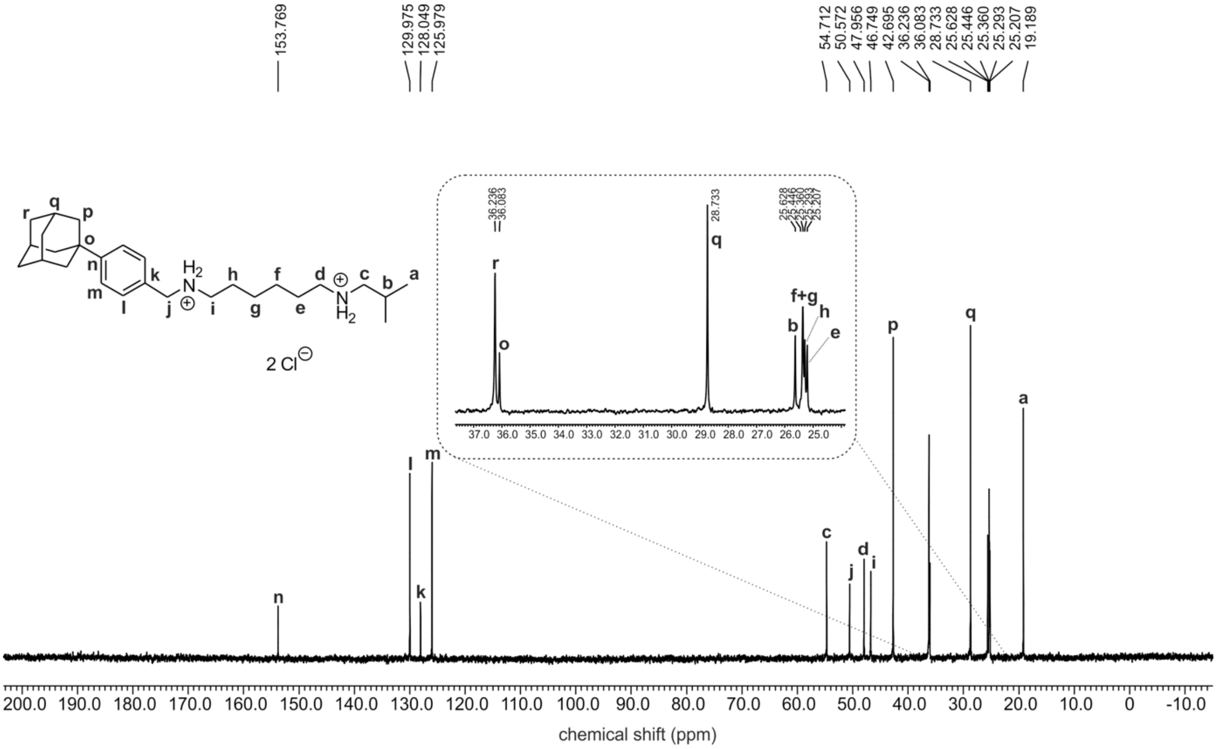


Figure S10 ^{13}C NMR (D_2O, 30 °C, 101 MHz) spectrum of **5e**.

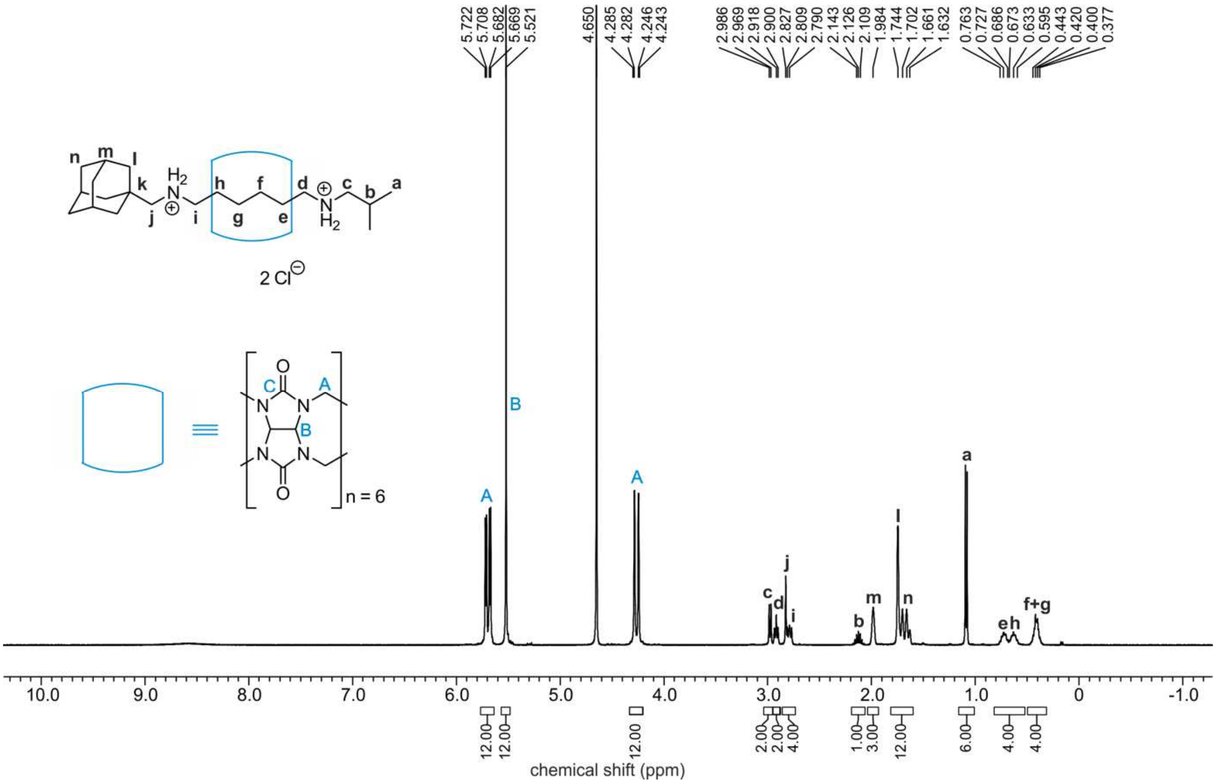


Figure S11 ^{1}H NMR (D_2O, 30 °C, 400 MHz) spectrum of **6a.**

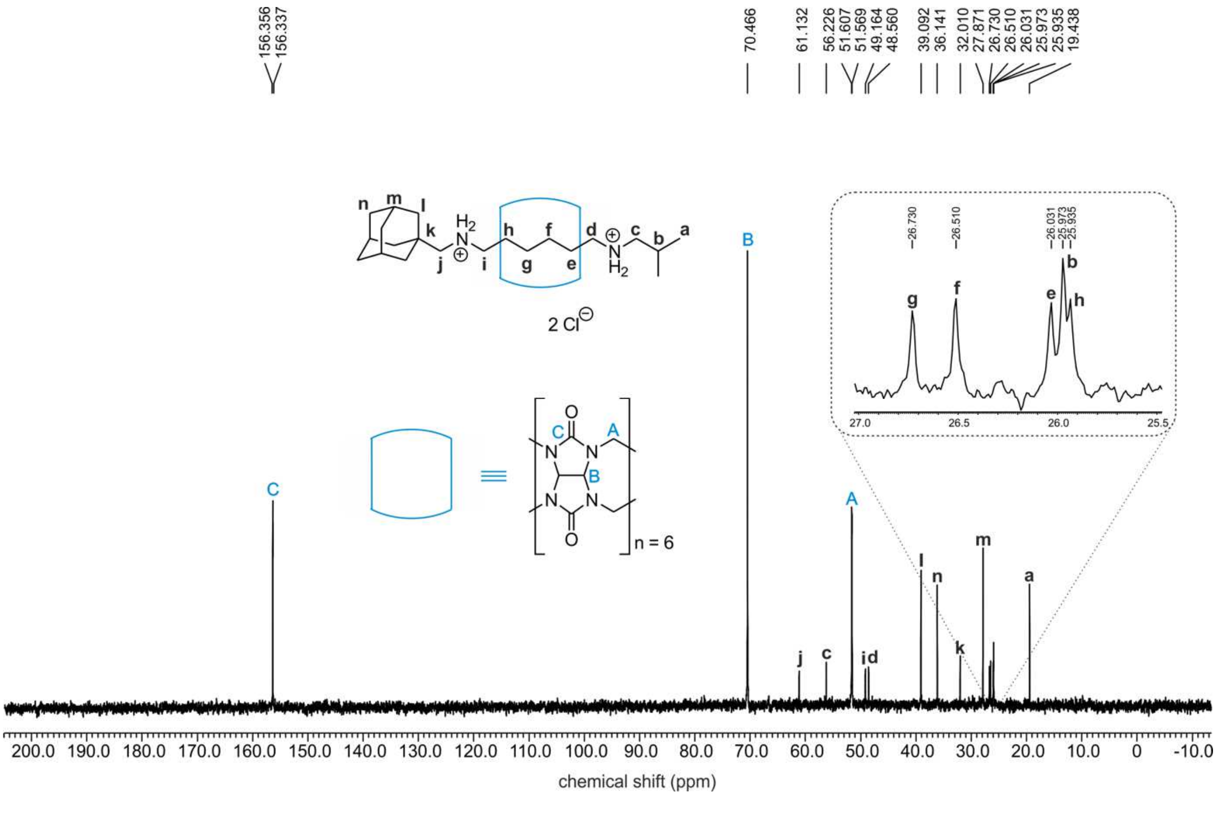


Figure S12 ^{13}C NMR (D_2O, 30 °C, 101 MHz) spectrum of **6a.**

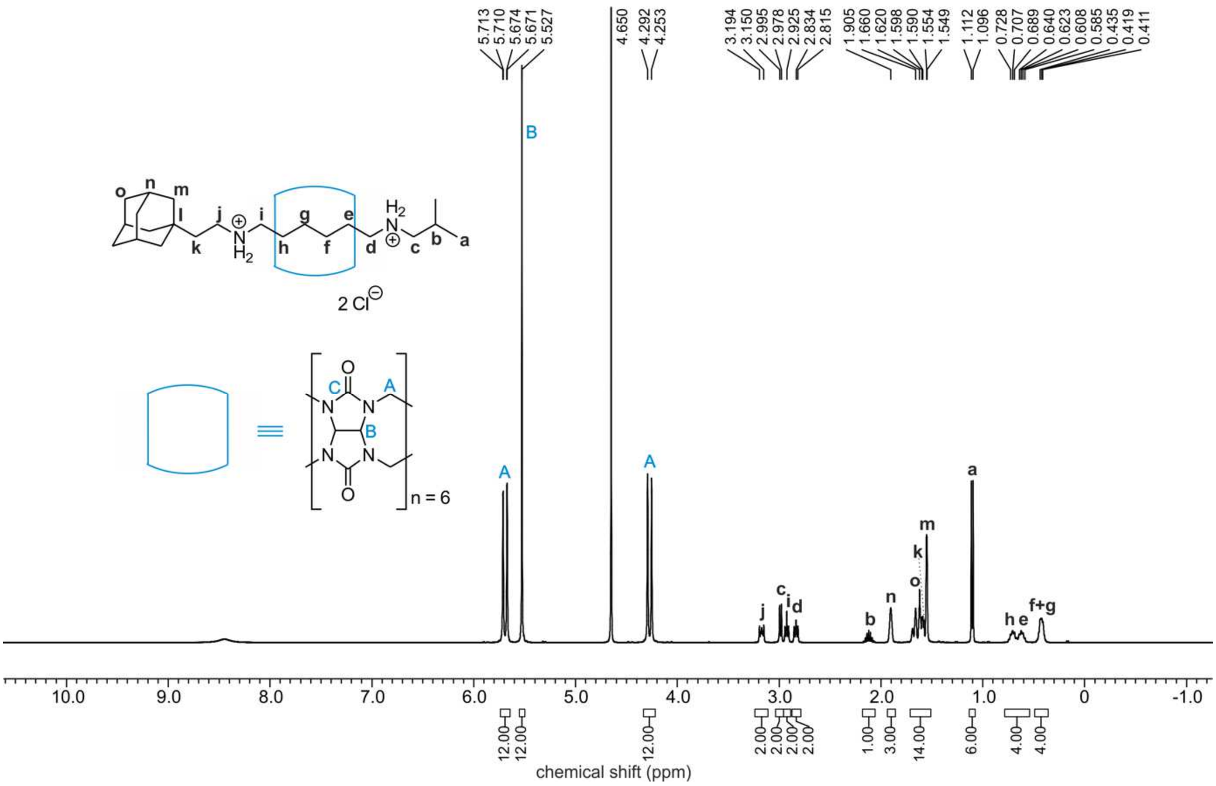


Figure S13 ^{1}H NMR (D_2O, 30 °C, 400 MHz) spectrum of **6b.**

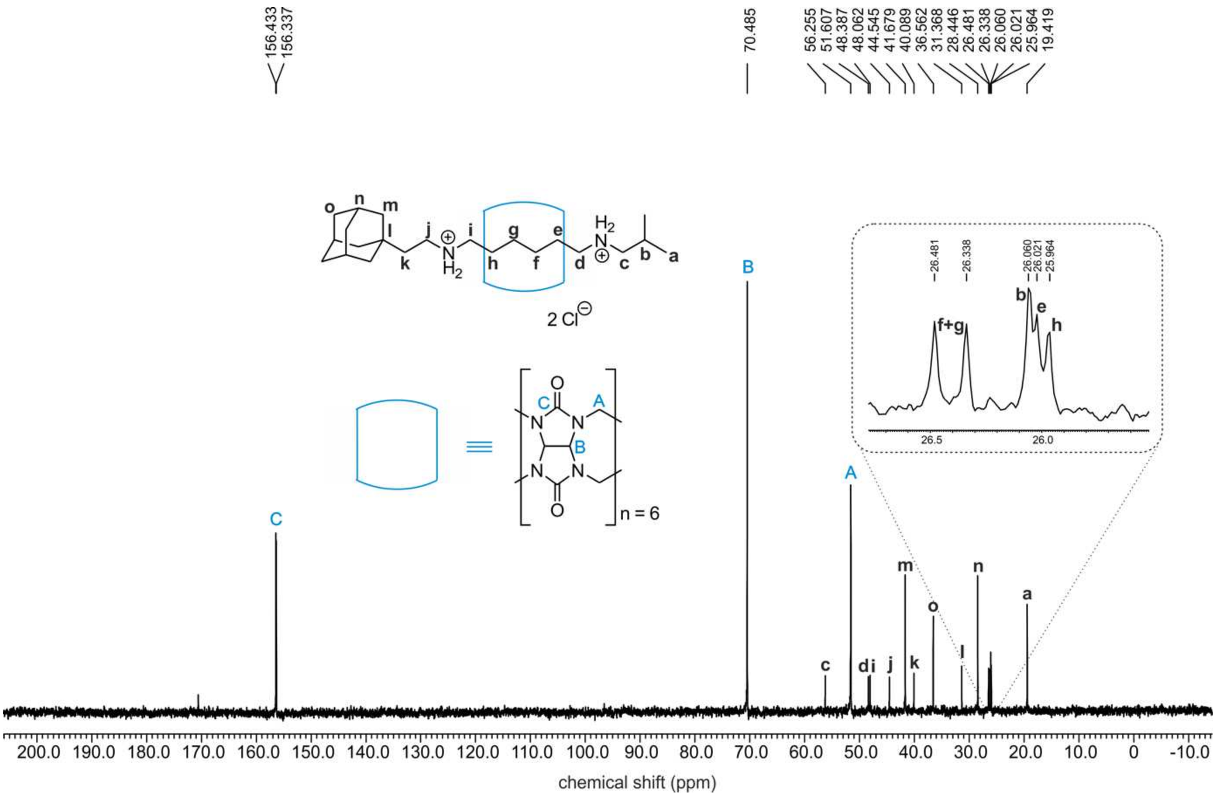


Figure S14 ^{13}C NMR (D_2O, 30 °C, 101 MHz) spectrum of **6b.**

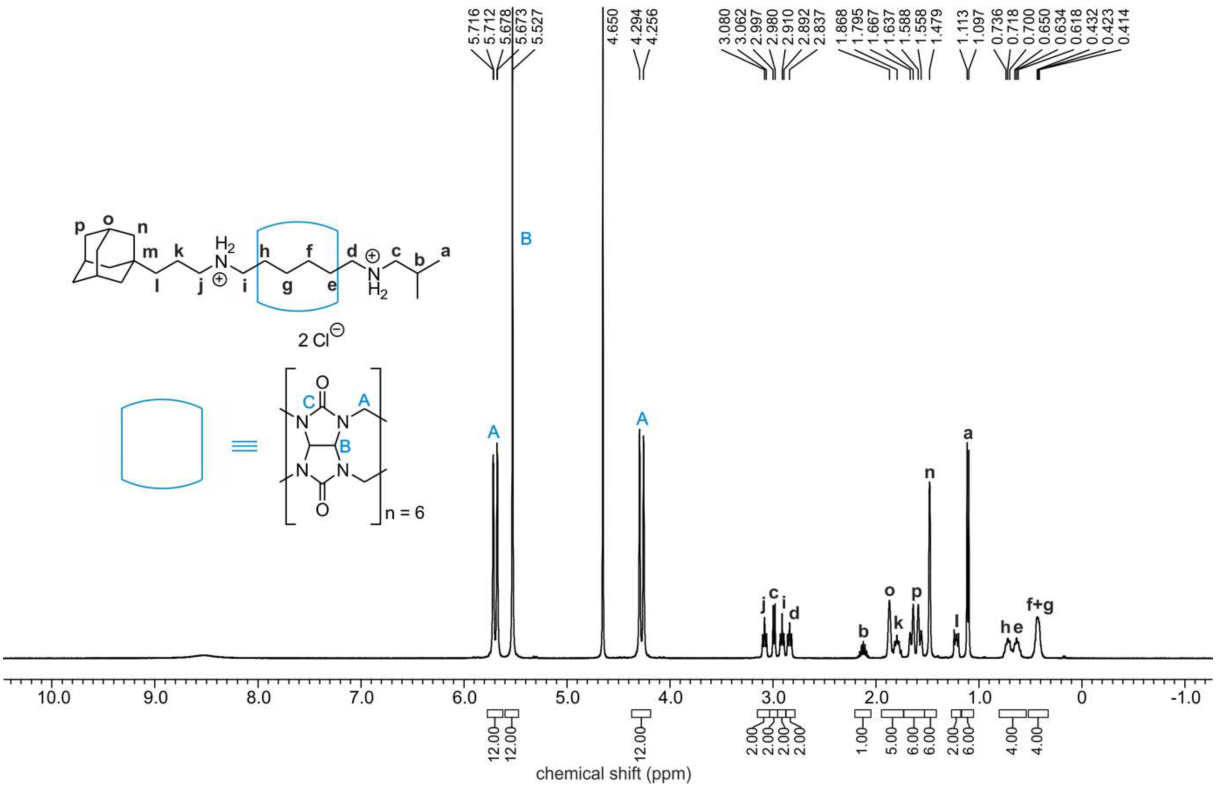


Figure S15 ^{1}H NMR (D_2O, 30 °C, 400 MHz) spectrum of **6c.**

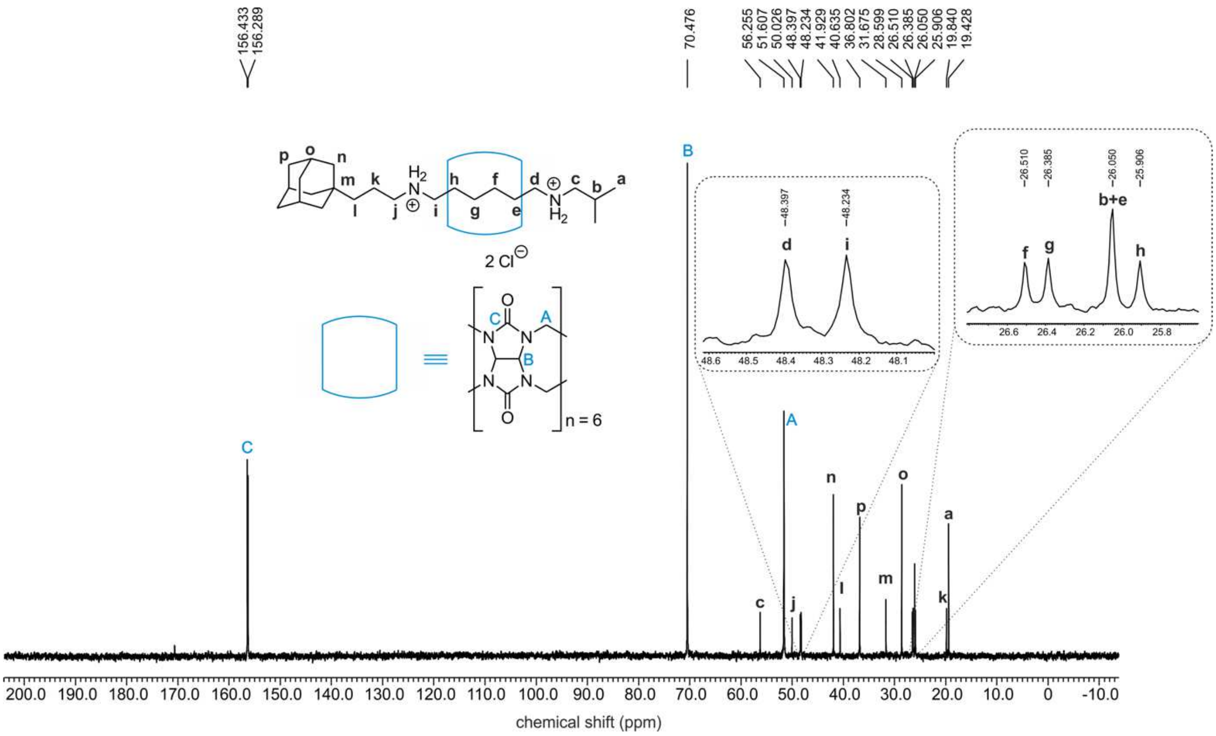


Figure S16 ^{13}C NMR (D_2O, 30 °C, 101 MHz) spectrum of **6c.**

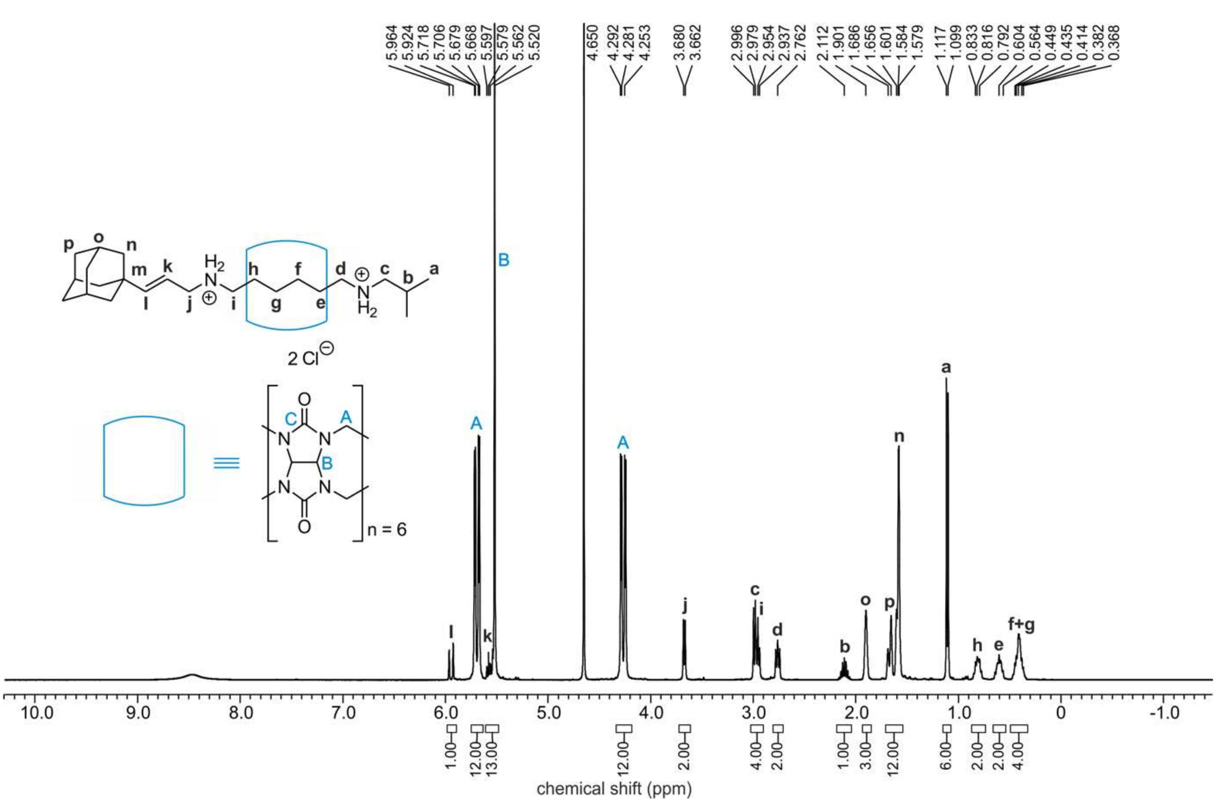


Figure S17 ^{1}H NMR (D_2O, 30 °C, 400 MHz) spectrum of **6d.**

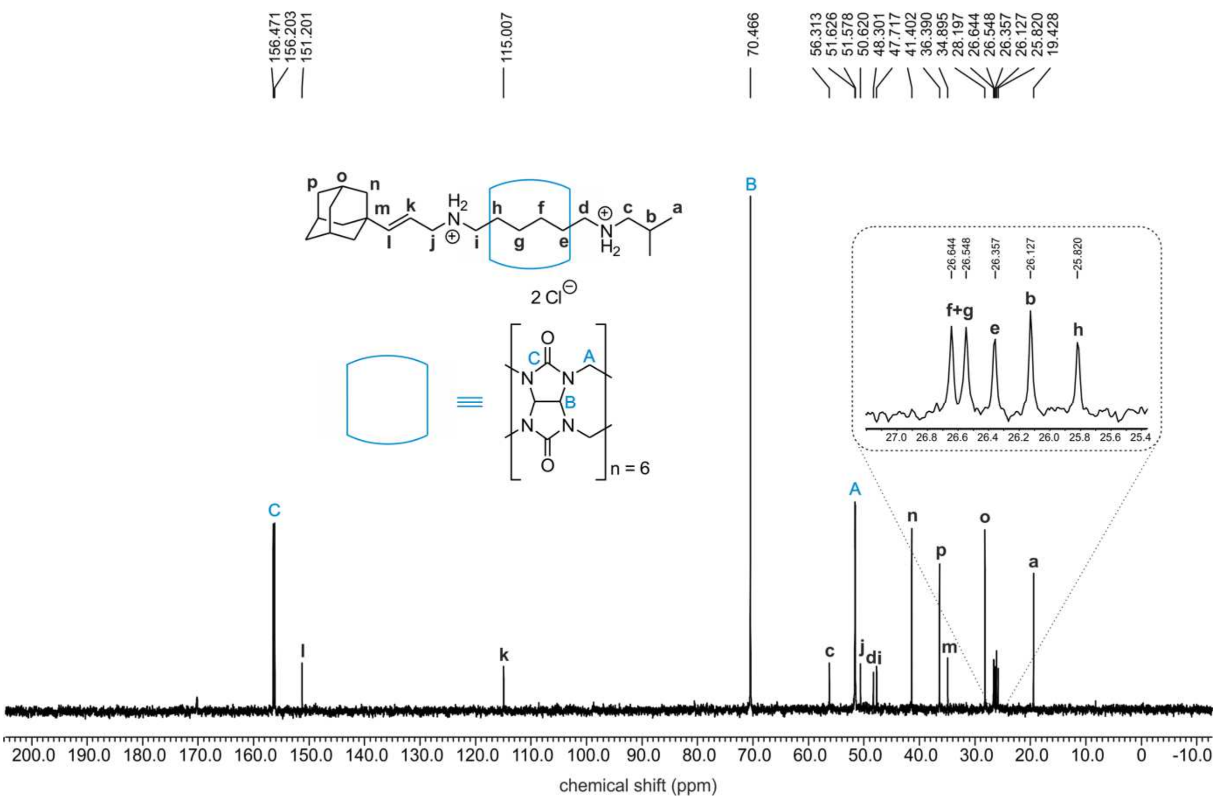


Figure S18 ^{13}C NMR (D_2O, 30 °C, 101 MHz) spectrum of **6d.**

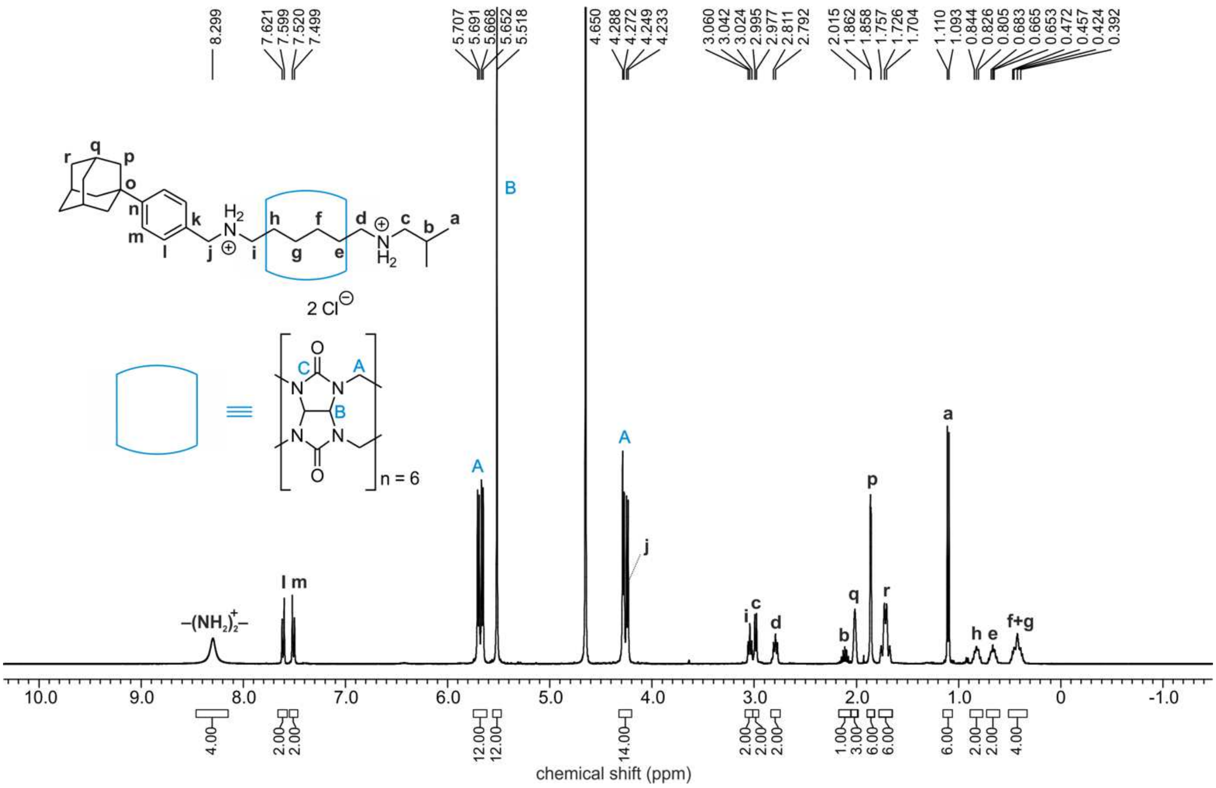


Figure S19 ^{1}H NMR (D_2O, 30 °C, 400 MHz) spectrum of **6e.**

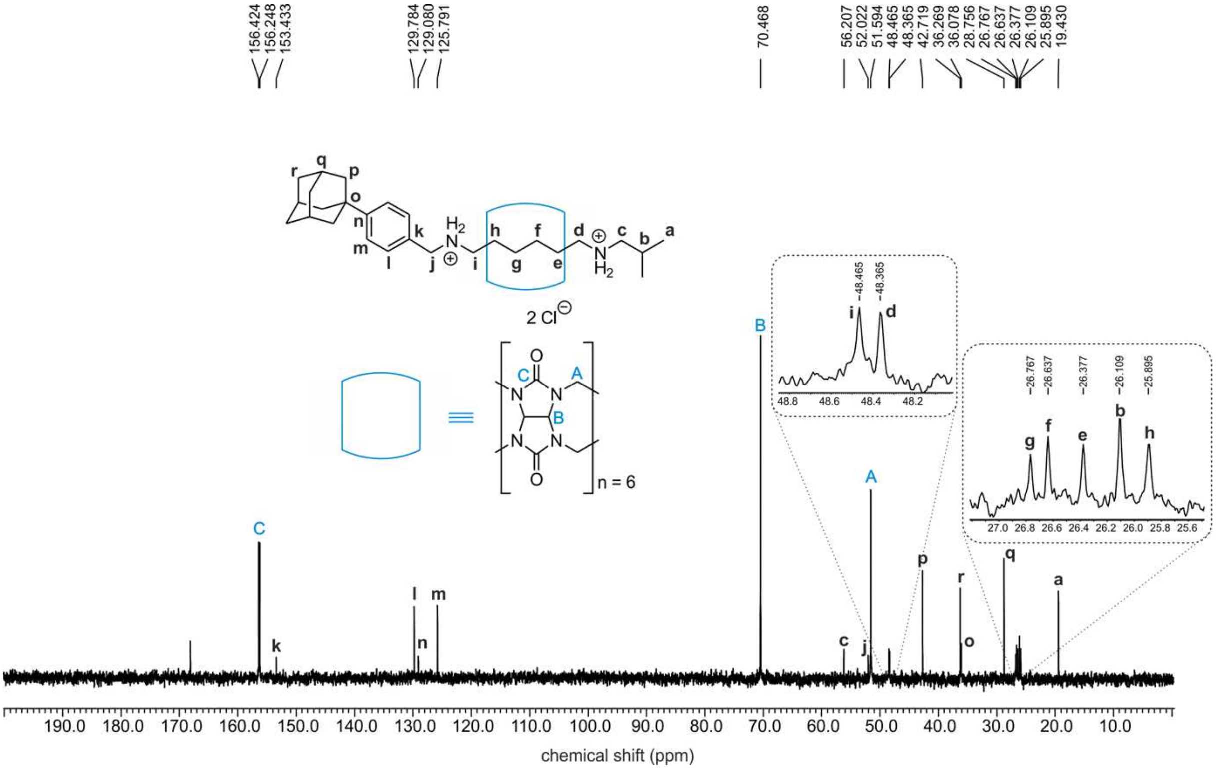


Figure S20 ^{13}C NMR (D_2O, 30 °C, 101 MHz) spectrum of **6e.**

4 ESI-MS characterisation spectra of ligands 5a–5e and rotaxanes 6a–6e

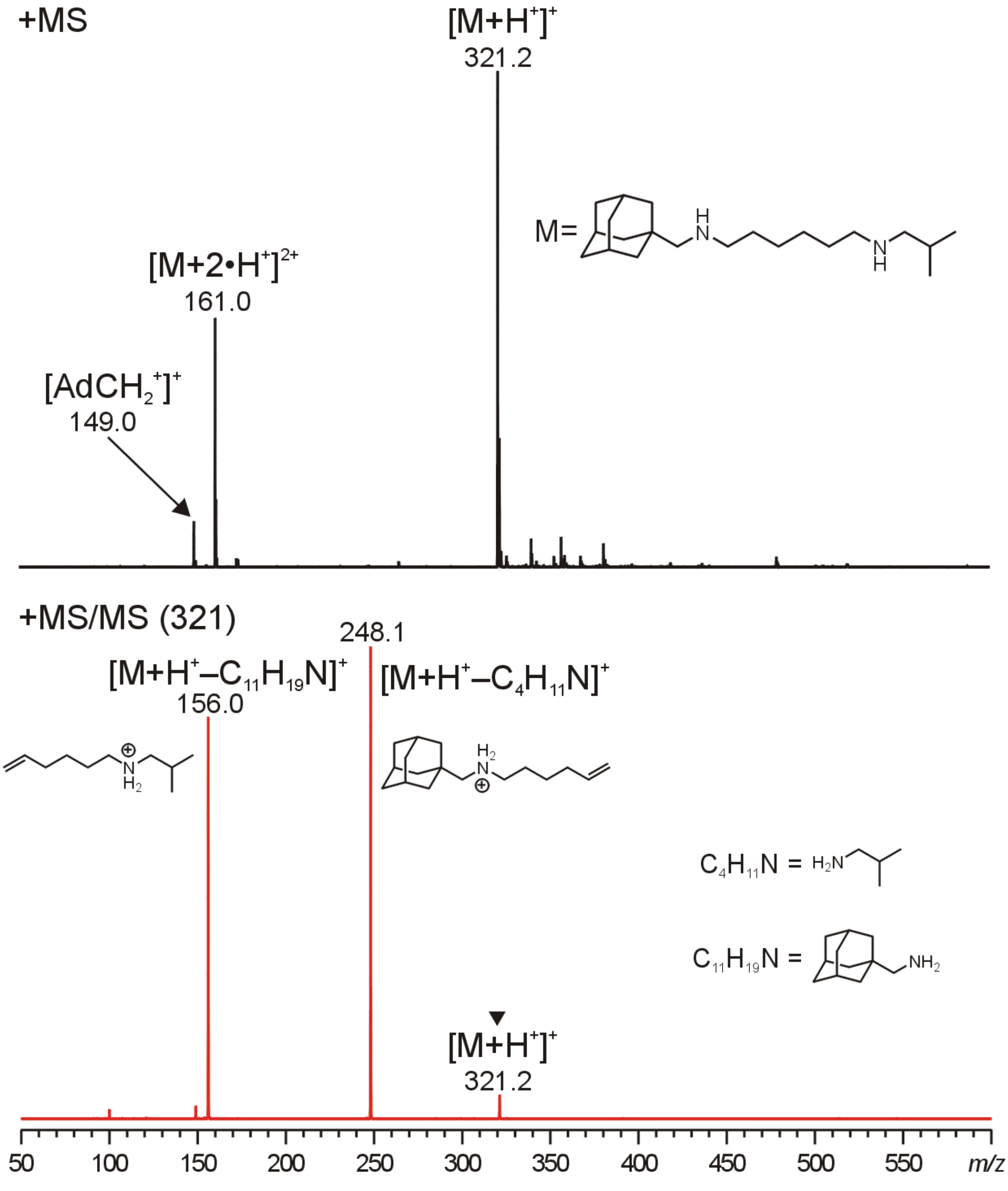


Figure S21 The positive-ion first-order ESI-MS (black line) and MS/MS (red line) of a MeOH:H_2O (1:1, v:v) solution of compound **5a**. The assignments for observed signals are shown in the brackets. The fragmented ion in MS/MS spectra is marked with a downward-facing triangle.

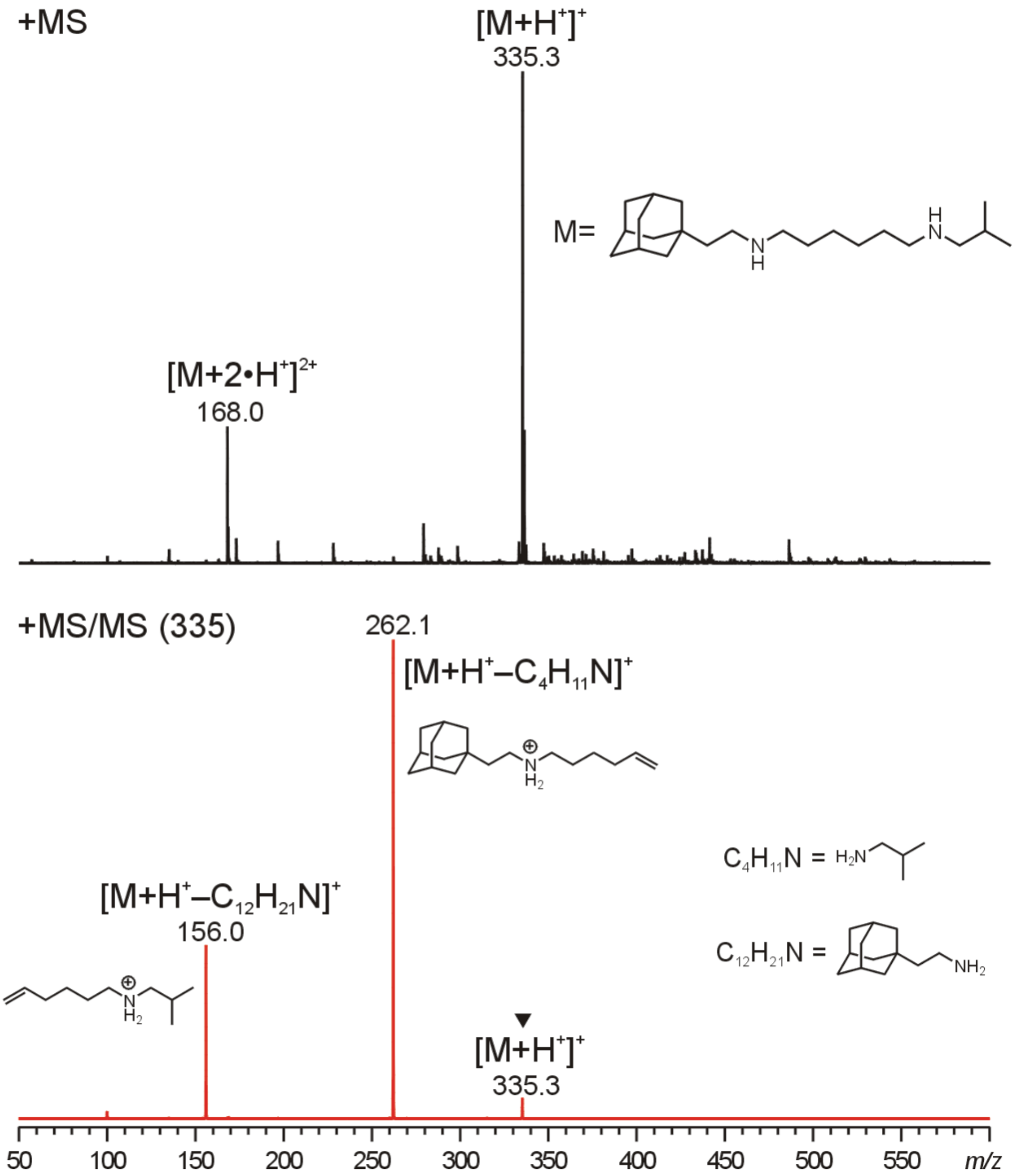


Figure S22 The positive-ion first-order ESI-MS (black line) and MS/MS (red line) of a MeOH:H_2O (1:1, v:v) solution of compound **5b.** The assignments for observed signals are shown in the brackets. The fragmented ion in MS/MS spectra is marked with a downward-facing triangle.

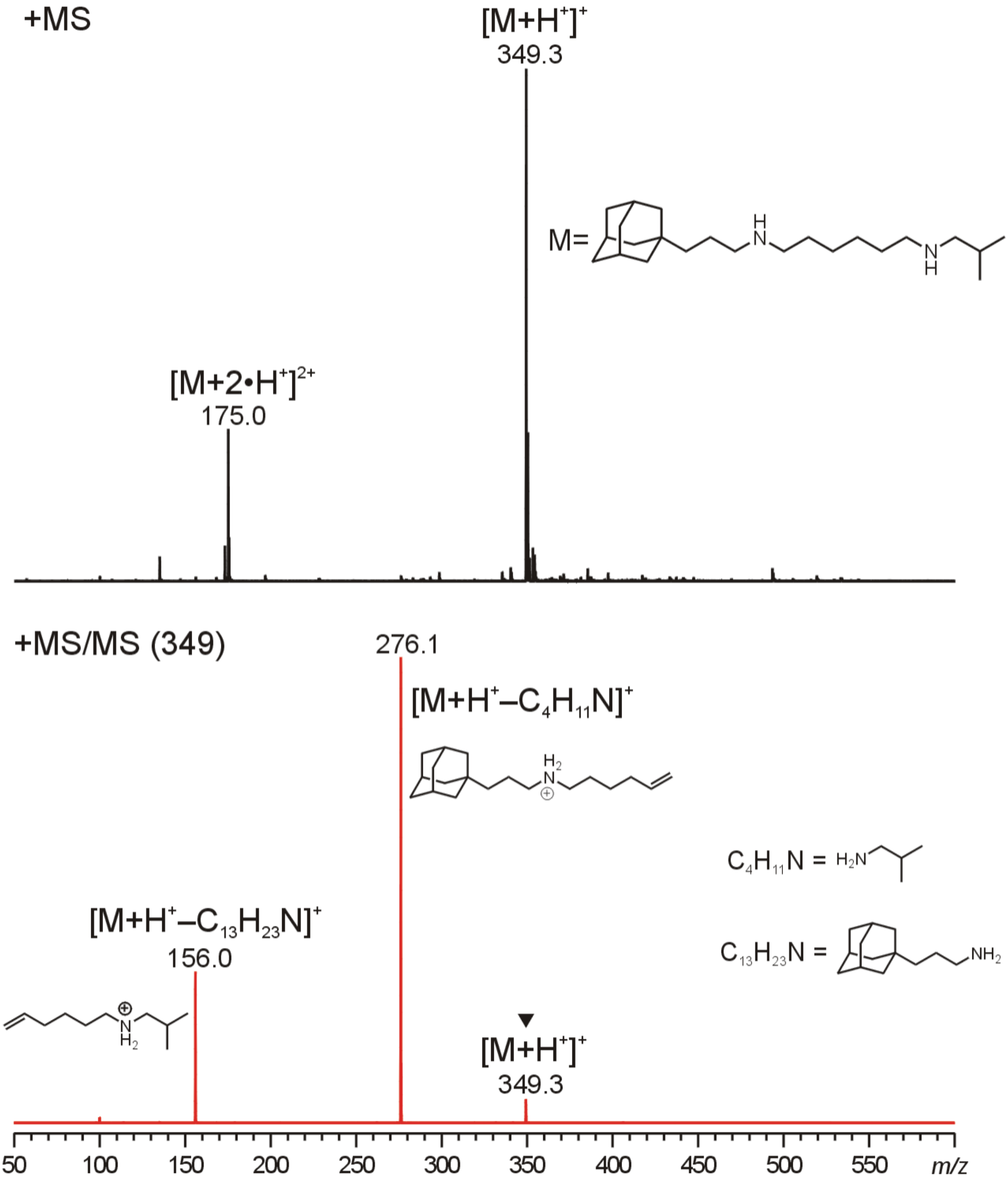


Figure S23 The positive-ion first-order ESI-MS (black line) and MS/MS (red line) of a MeOH:H_2O (1:1, v:v) solution of compound **5c**. The assignments for observed signals are shown in the brackets. The fragmented ion in MS/MS spectra is marked with a downward-facing triangle.

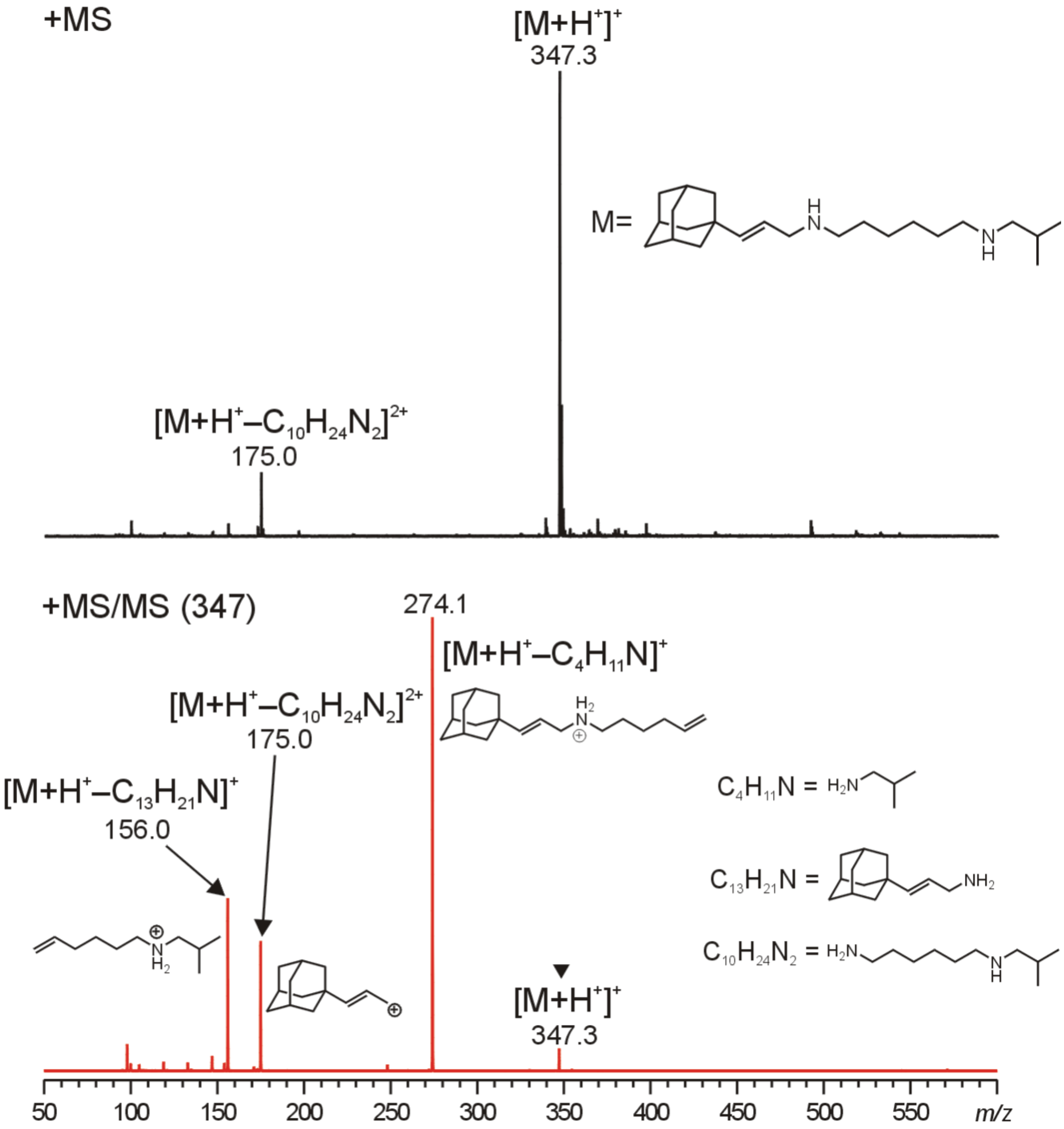


Figure S24 The positive-ion first-order ESI-MS (black line) and MS/MS (red line) of a MeOH:H_2O (1:1, v:v) solution of compound **5d**. The assignments for observed signals are shown in the brackets. The fragmented ion in MS/MS spectra is marked with a downward-facing triangle.

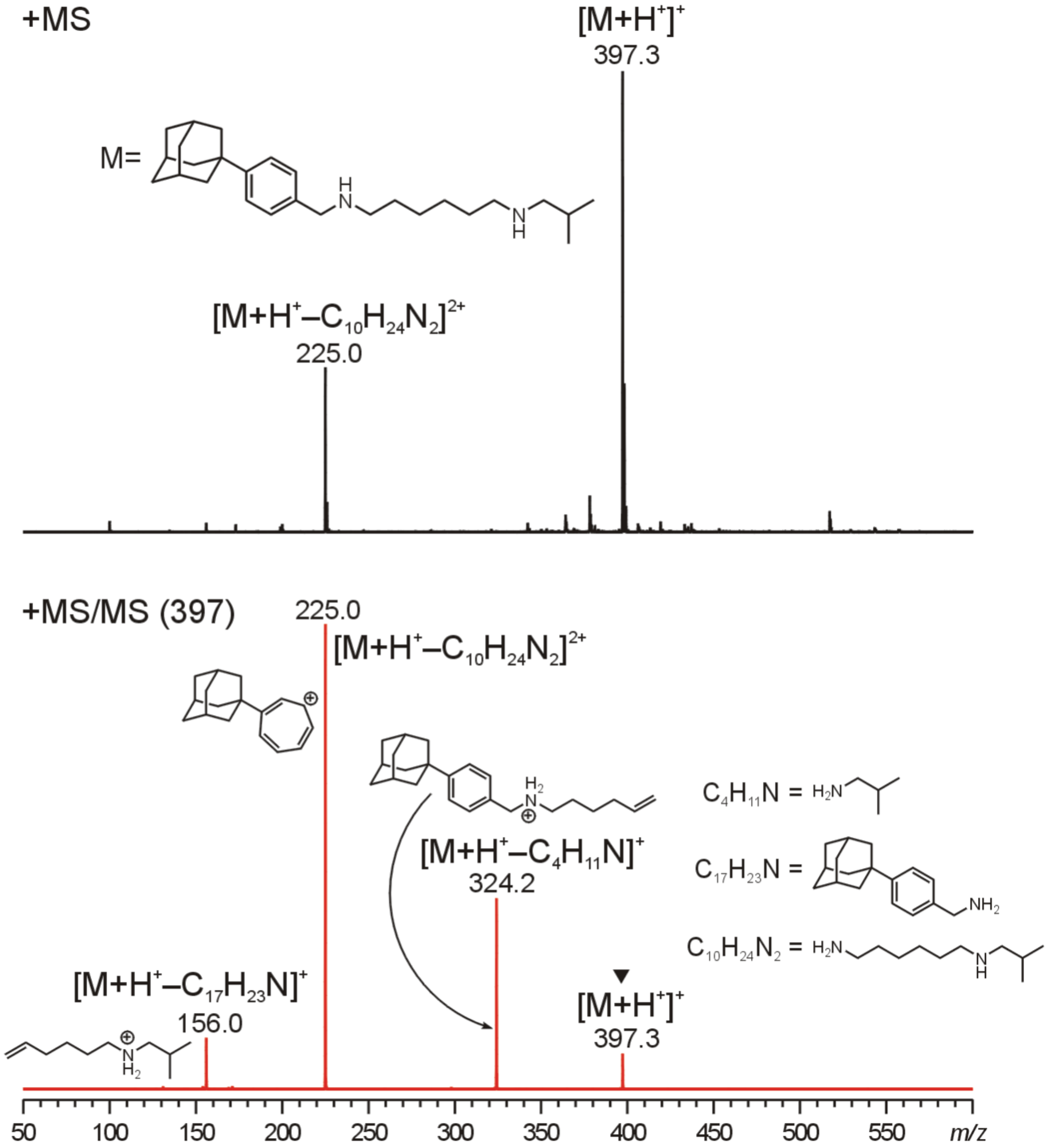


Figure S25 The positive-ion first-order ESI-MS (black line) and MS/MS (red line) of a MeOH:H_2O (1:1, v:v) solution of compound **5e**. The assignments for observed signals are shown in the brackets. The fragmented ion in MS/MS spectra is marked with a downward-facing triangle.

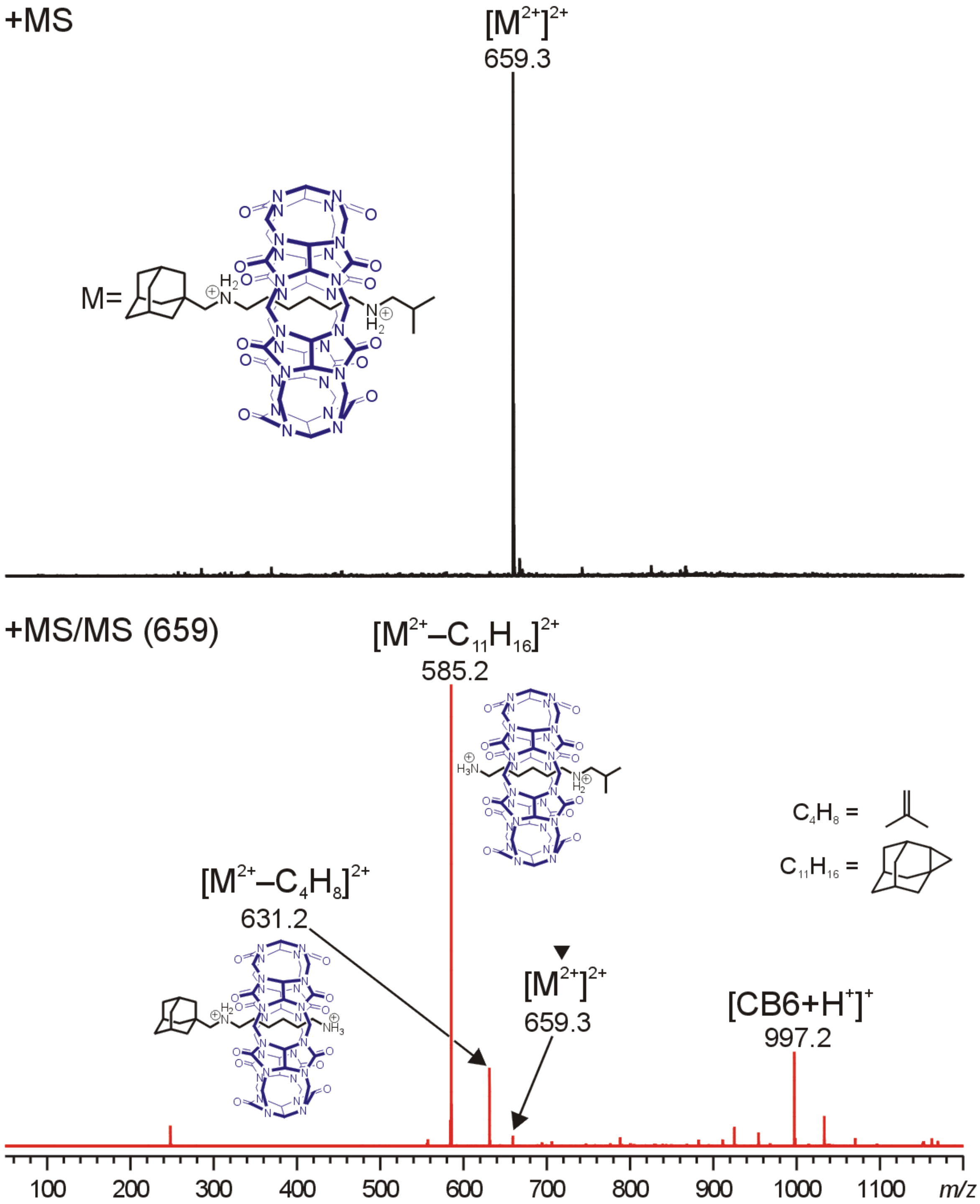


Figure S26 The positive-ion first-order ESI-MS (black line) and MS/MS (red line) of an aqueous solution of compound **6a**. The assignments for observed signals are shown in the brackets. The fragmented ion in MS/MS spectra is marked with a downward-facing triangle.

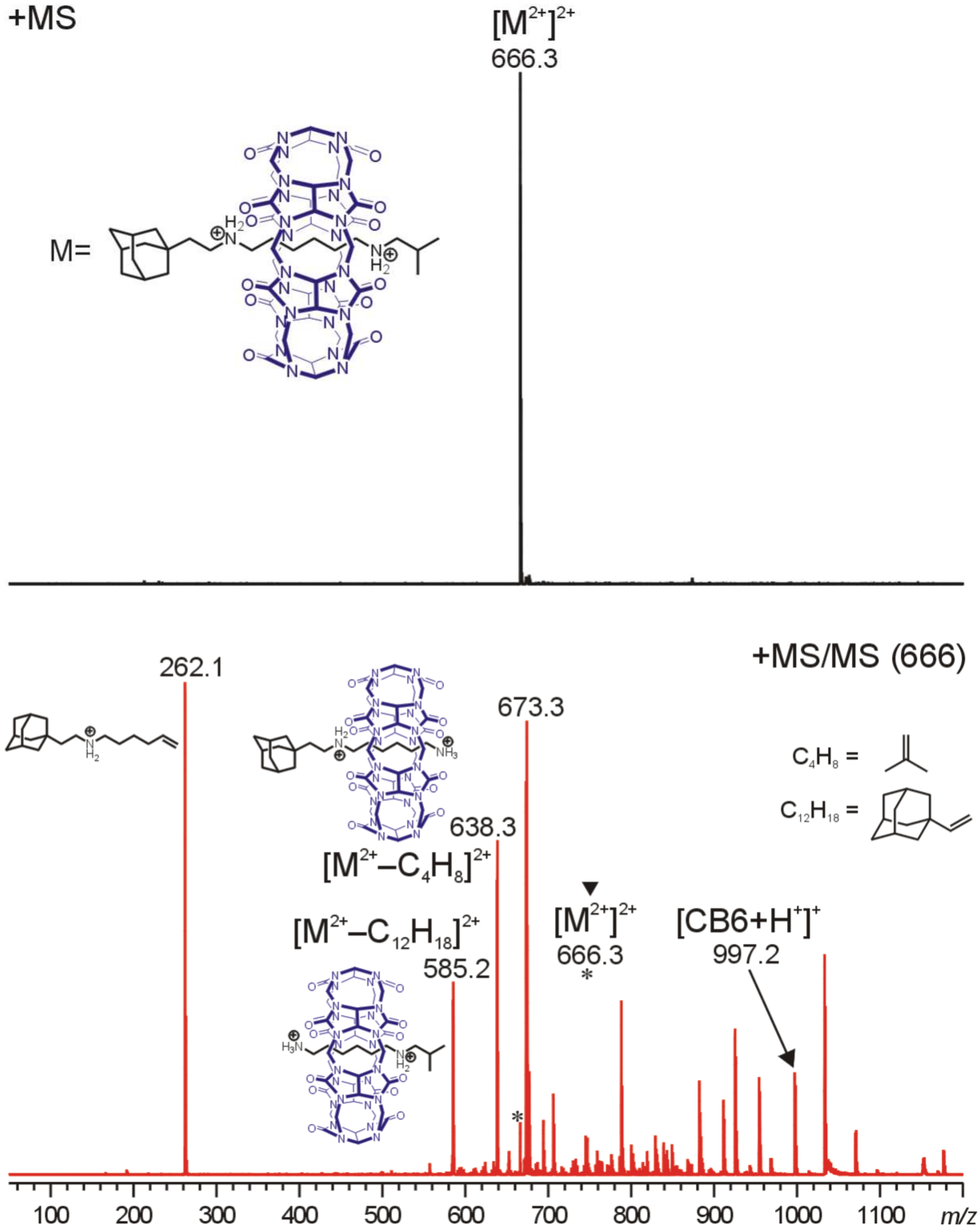


Figure S27 The positive-ion first-order ESI-MS (black line) and MS/MS (red line) of an aqueous solution of compound **6b.** The assignments for observed signals are shown in the brackets**.** The fragmented ion in MS/MS spectra is marked with a downward-facing triangle.

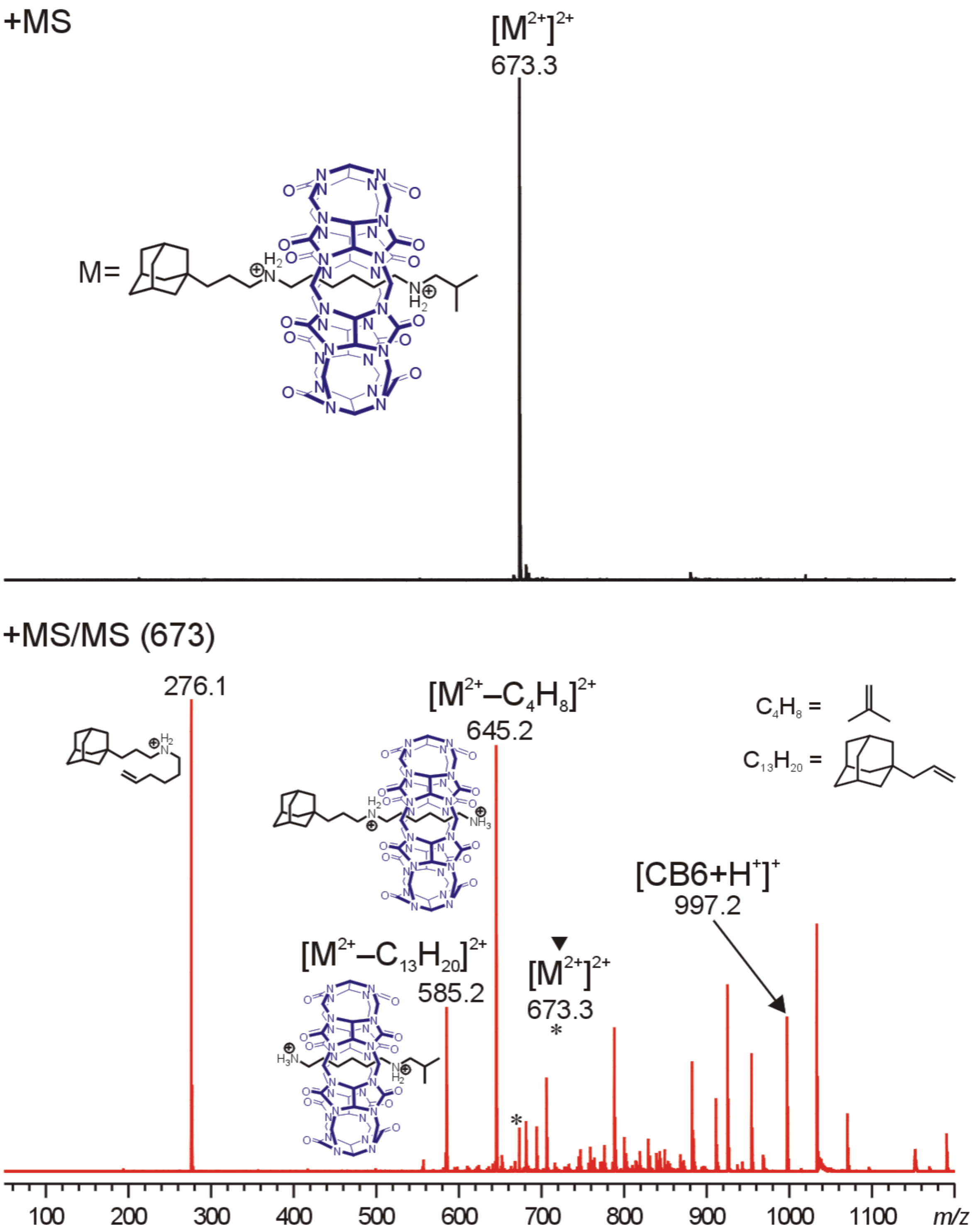


Figure S28 The positive-ion first-order ESI-MS (black line) and MS/MS (red line) of an aqueous solution of compound **6c**. The assignments for observed signals are shown in the brackets. The fragmented ion in MS/MS spectra is marked with a downward-facing triangle.

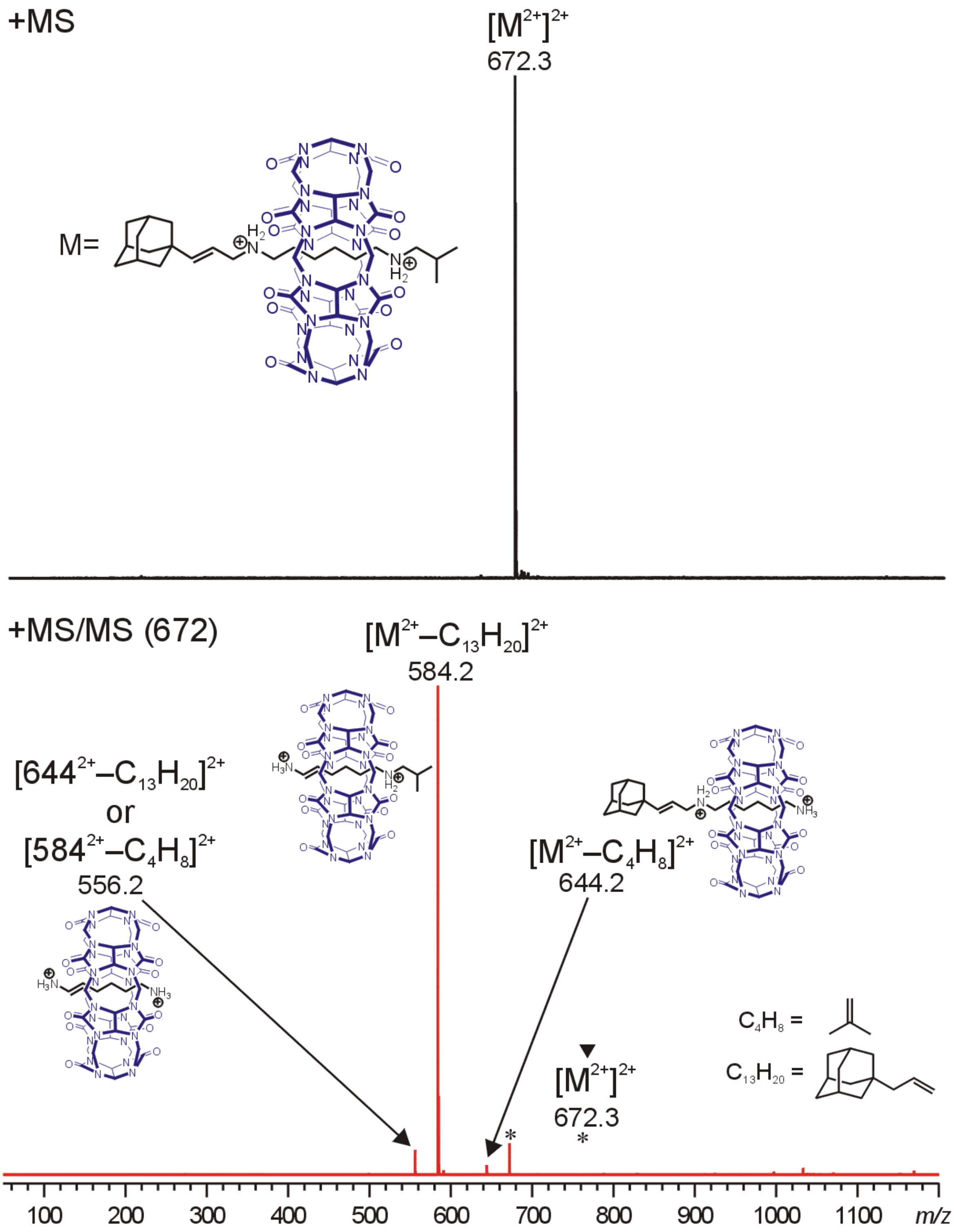


Figure S29 The positive-ion first-order ESI-MS (black line) and MS/MS (red line) of an aqueous solution of compound **6d.** The assignments for observed signals are shown in the brackets. The fragmented ion in MS/MS spectra is marked with a downward-facing triangle.

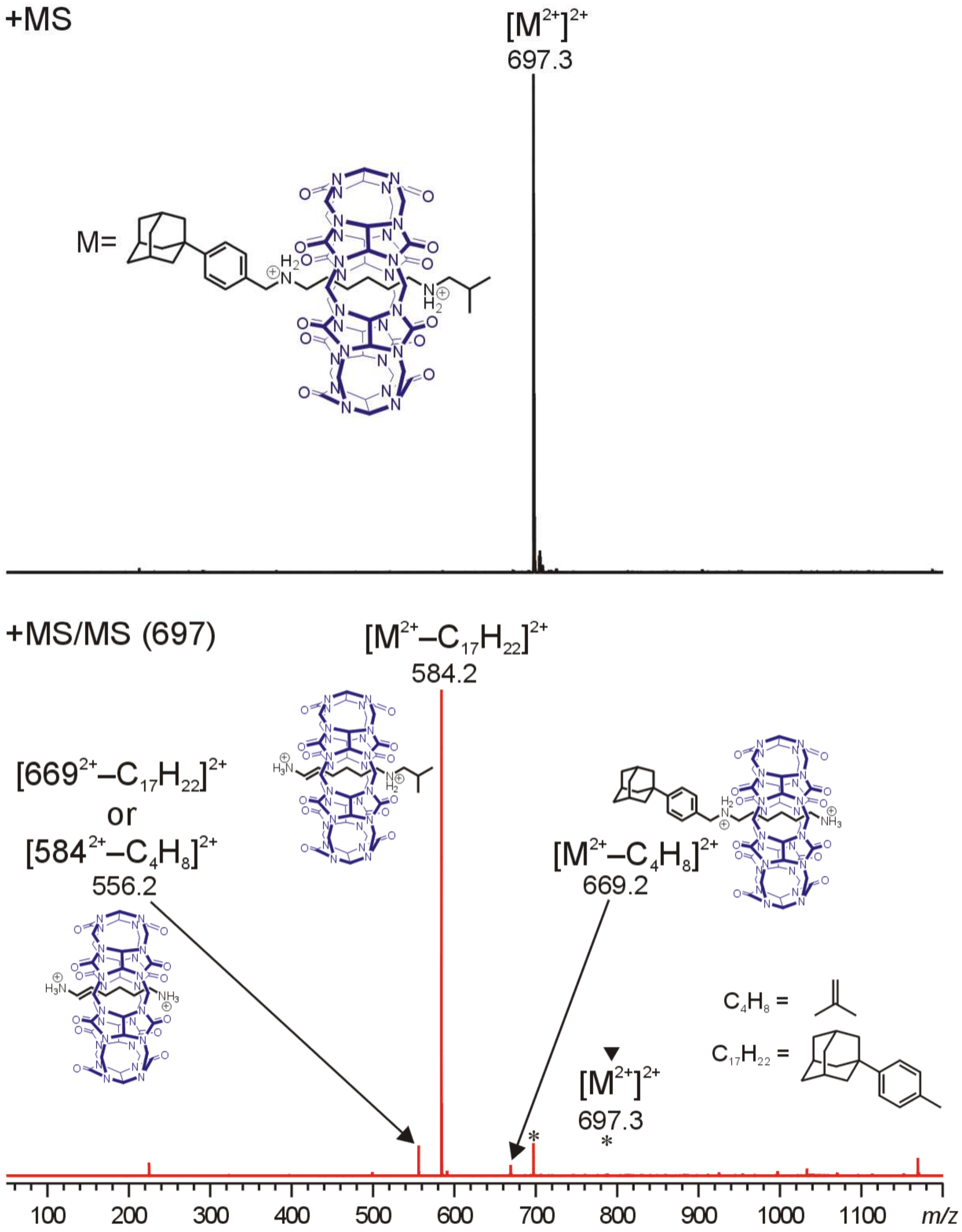


Figure S30 The positive-ion first-order ESI-MS (black line) and MS/MS (red line) of an aqueous solution of compound **6e.** The assignments for observed signals are shown in the brackets**.** The fragmented ion in MS/MS spectra is marked with a downward-facing triangle.

5 Thermodynamic parameters

5.1 NMR spectra of competitive binding experiments

Association constants for complexes **5**@CB6^{IB}, **5**@CB7^{Ad} and **6**@CB7^{Ad} were determined using competitive ^{1}H NMR method and are summarized in Table S1.

The concentrations of the solutions in 50 mM NaCl in D_2O or in D_2O were determined by ^{1}H NMR spectroscopy using maleic acid as an internal standard. Unless stated otherwise, equimolar amounts of ligands, competitors and CB6/CB7 were mixed. The samples were equilibrated over 72 h for complexes with **5** and over 10 days for complexes with **6** at room temperature. Subsequently, ^{1}H NMR spectra were recorded, and the key signals corresponding to the free/complexed ligand and free/complexed competitor were identified. Integral intensities of these signals along with the known total concentrations of **5**/**6** and competitor, provided the association constants according to the formula given below. Figures S21–S34 represent the competitive experiments, where the key signals are color-coded for clarity. The signals associated with complexed states are marked with an asterisk (*). It should be noted that signal corresponding to the free state of competitor (in case of **5**@CB6) is not well-separated in the spectrum because it overlaps with the signal of the free **5**. However, the ratio of the free and complexed **5** can be calculated using different well-separated signals of free and complexed **5**. Thus, the integral intensity values for free competitor were calculated by subtracting the integral value for the free **5** from the intensity of the mixed signal of the free **5** and free competitor.

$$K = \frac{[\mathbf{L}/\mathbf{R}@\text{CB6/CB7}]\cdot[\text{C}]_{\text{free}}}{[\text{C}@\text{CB6/CB7}]\cdot[\mathbf{L}/\mathbf{R}]_{\text{free}}}\cdot K(\text{C})$$

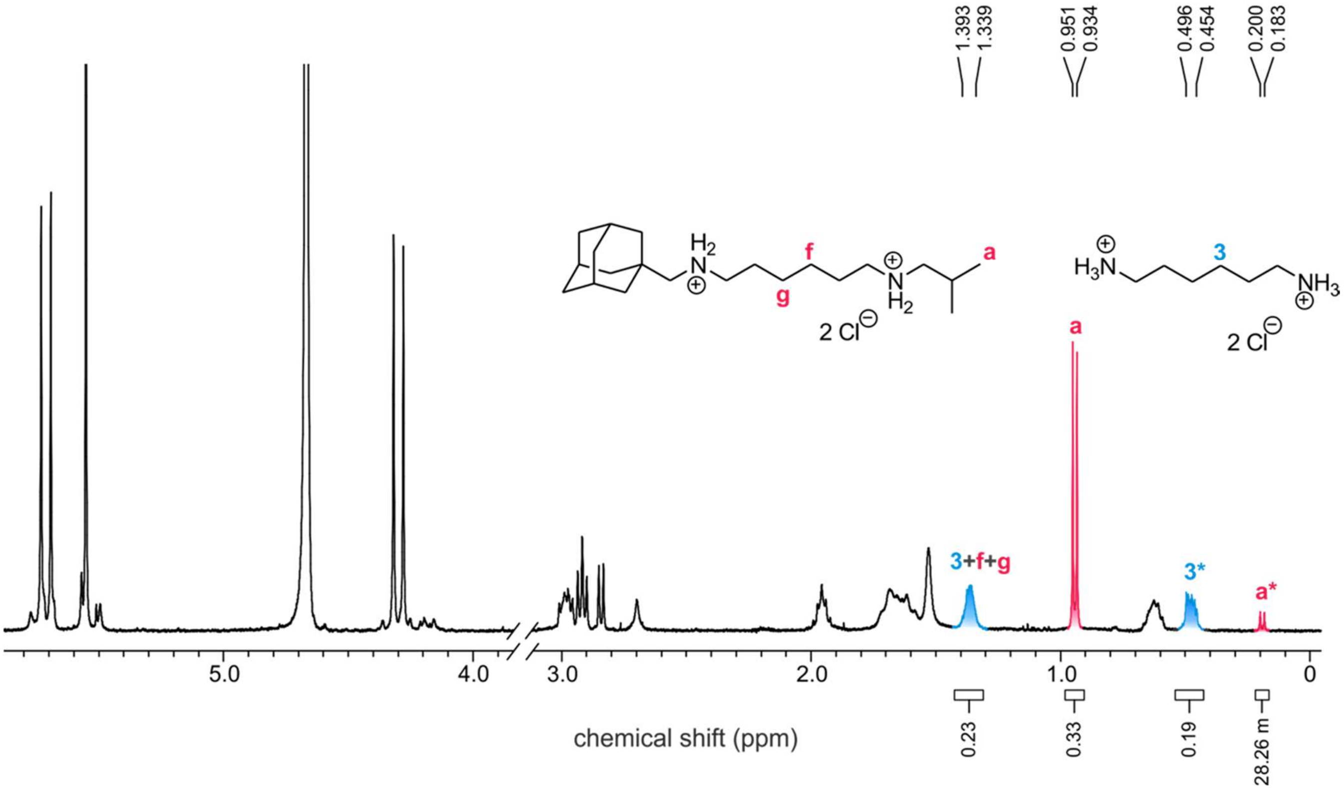


Figure S31 ^{1}H NMR (50 mM NaCl in D_2O, 30 °C, 400 MHz) spectrum used for association constant determination of **5a**@CB6^{IB} (c_{5a}=0.7 mM, competitor: 1,6-hexamethylenediammonium dichloride).

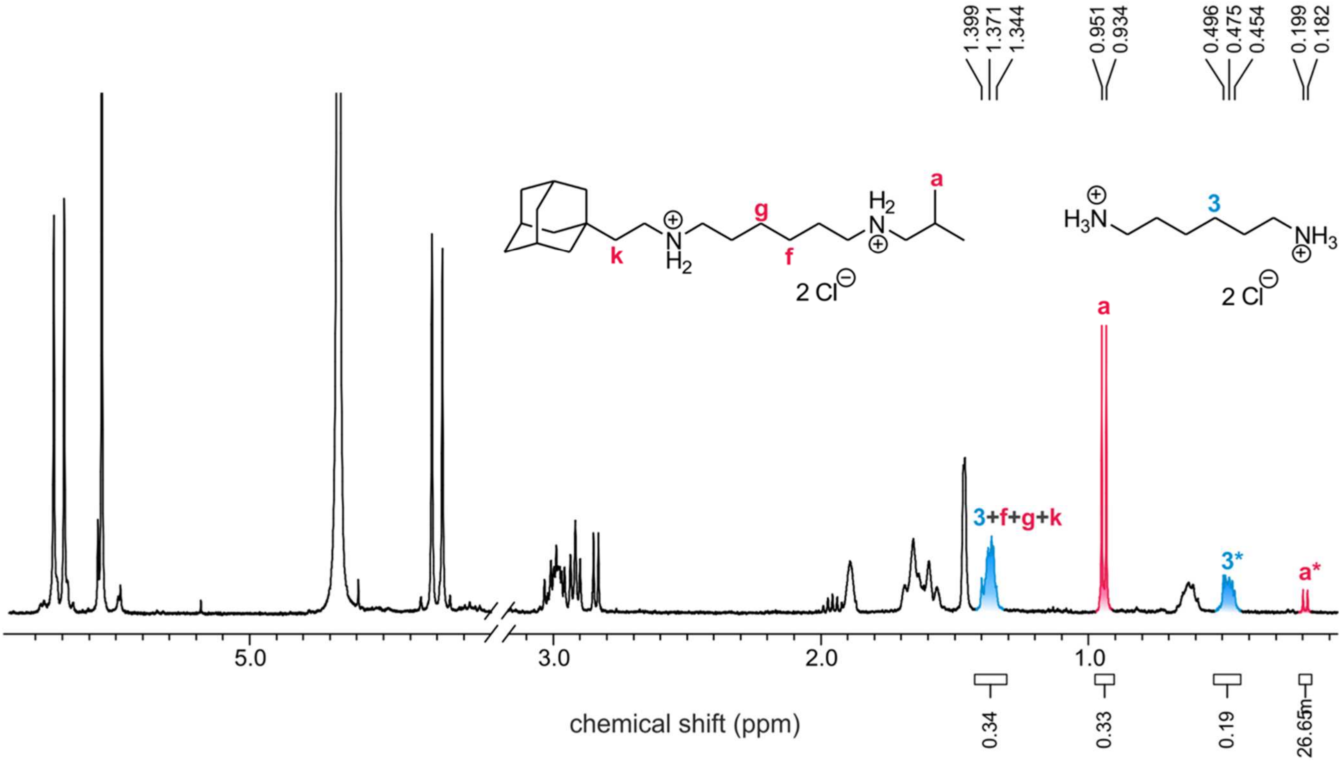


Figure S32 ^{1}H NMR (50 mM NaCl in D_2O, 30 °C, 400 MHz) spectrum used for association constant determination of **5b**@CB6^{IB} (c_{5b}=0.7 mM, competitor: 1,6-hexamethylenediammonium dichloride).

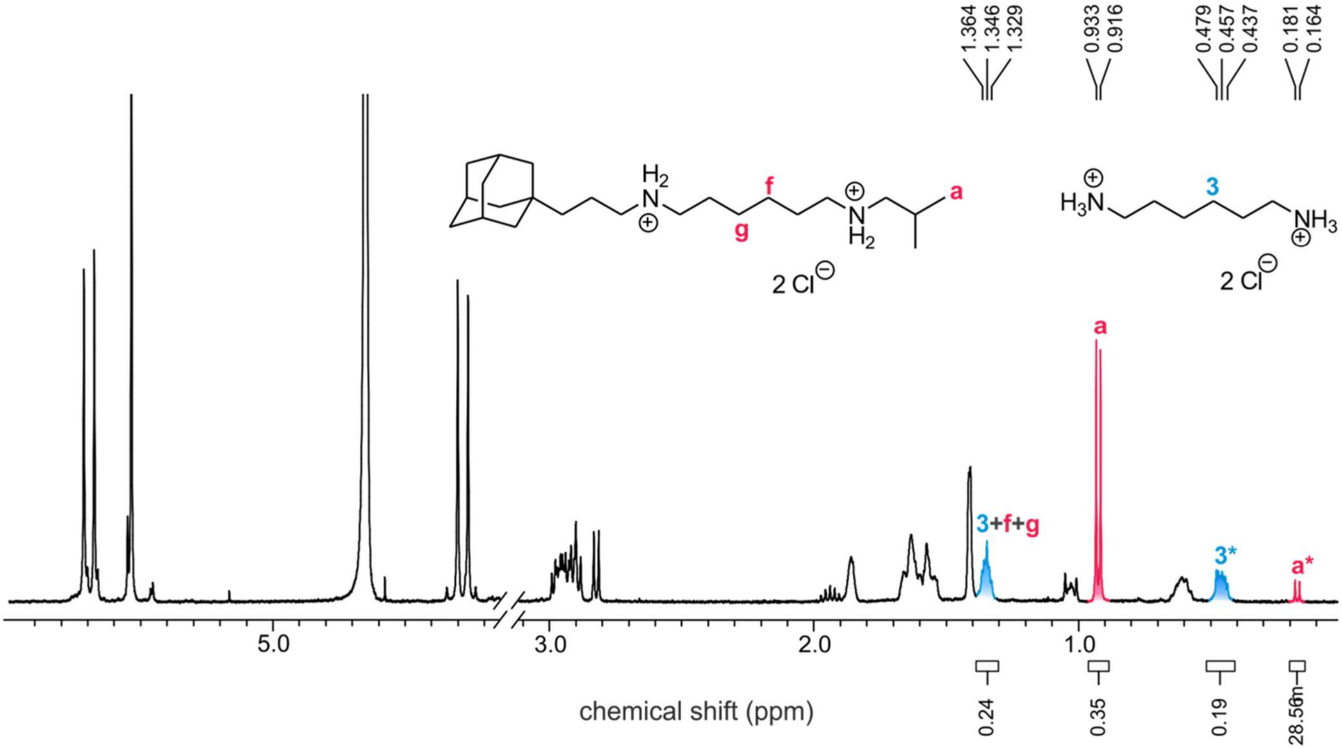


Figure S33 ^{1}H NMR (50 mM NaCl in D_2O, 30 °C, 400 MHz) spectrum used for association constant determination of **5c**@CB6^{IB} (c_{5c}=0.7 mM, competitor: 1,6-hexamethylenediammonium dichloride).

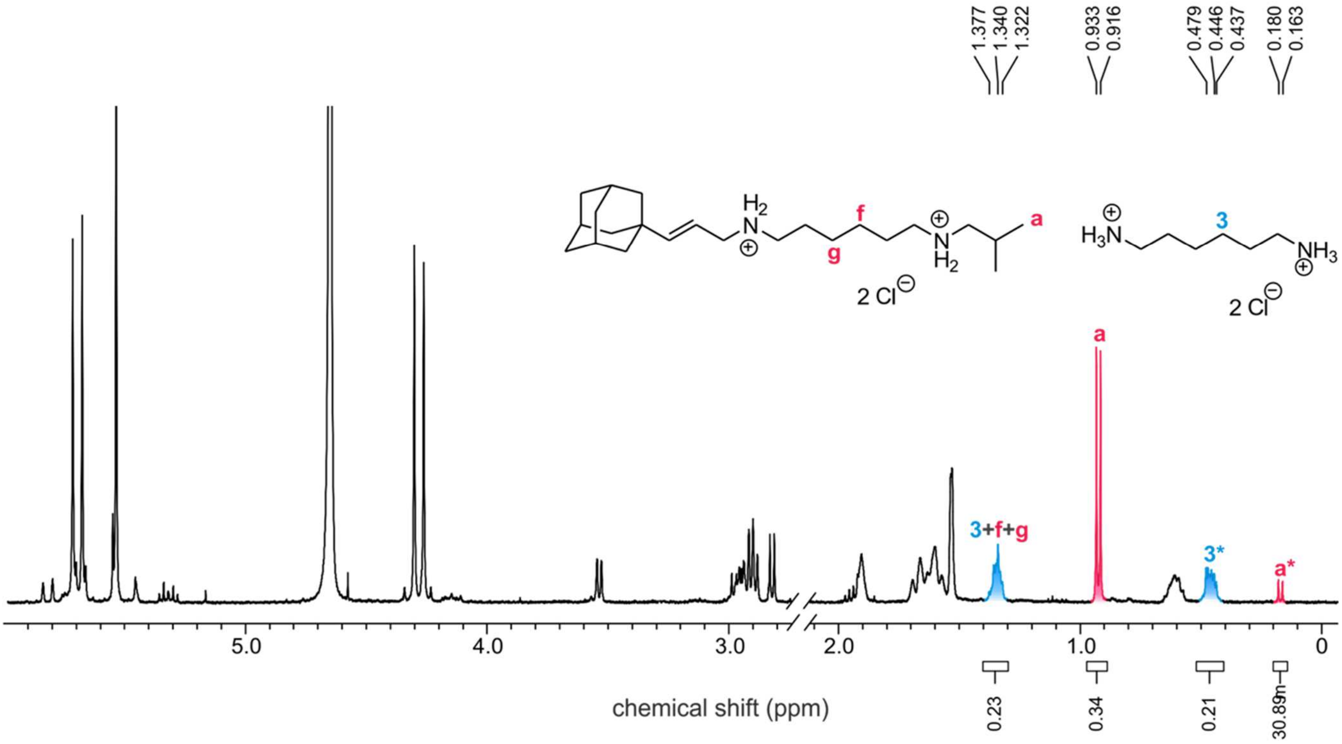


Figure S34 ^{1}H NMR (50 mM NaCl in D_2O, 30 °C, 400 MHz) spectrum used for association constant determination of **5d**@CB6^{IB} (c_{5d}=0.7 mM, competitor: 1,6-hexamethylenediammonium dichloride).

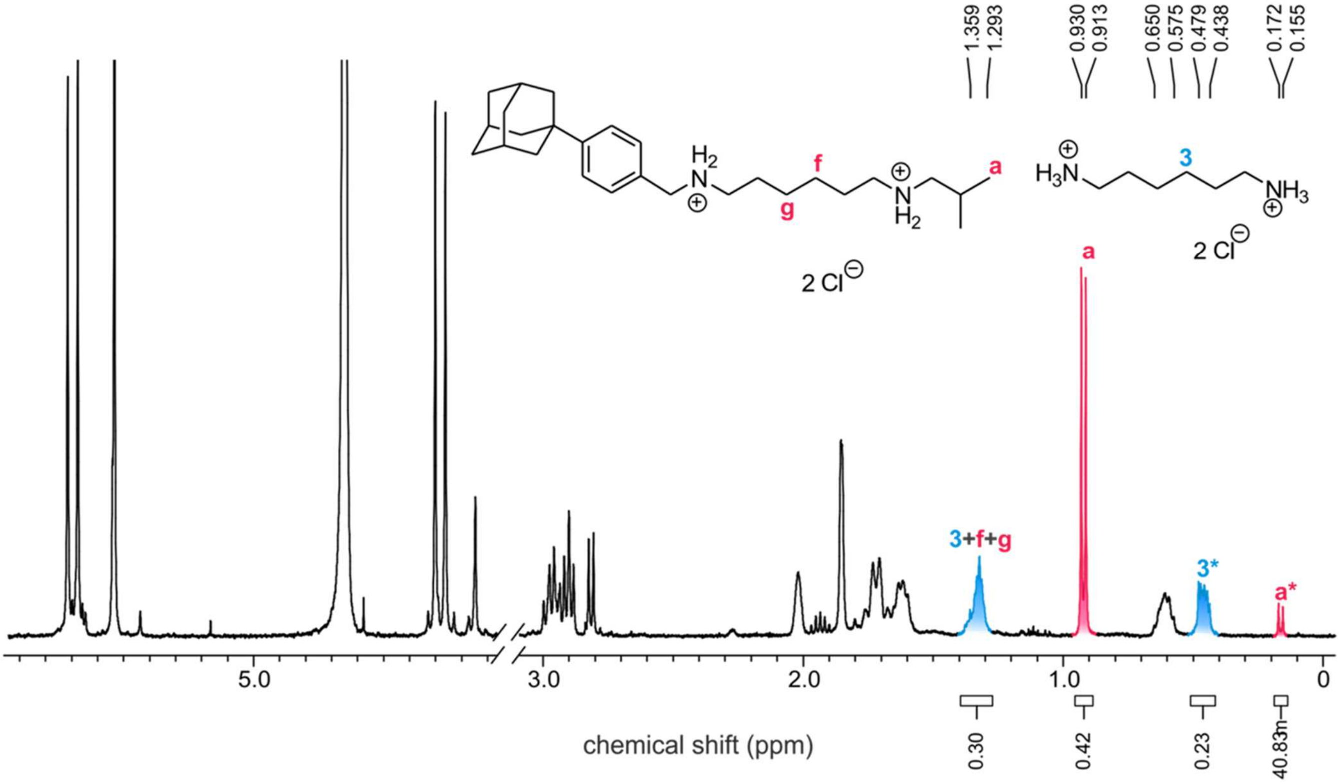


Figure S35 ^{1}H NMR (50 mM NaCl in D_2O, 30 °C, 400 MHz) spectrum used for association constant determination of **5e**@CB6^{IB} (c_{5e}=0.7 mM, competitor: 1,6-hexamethylenediammonium dichloride).

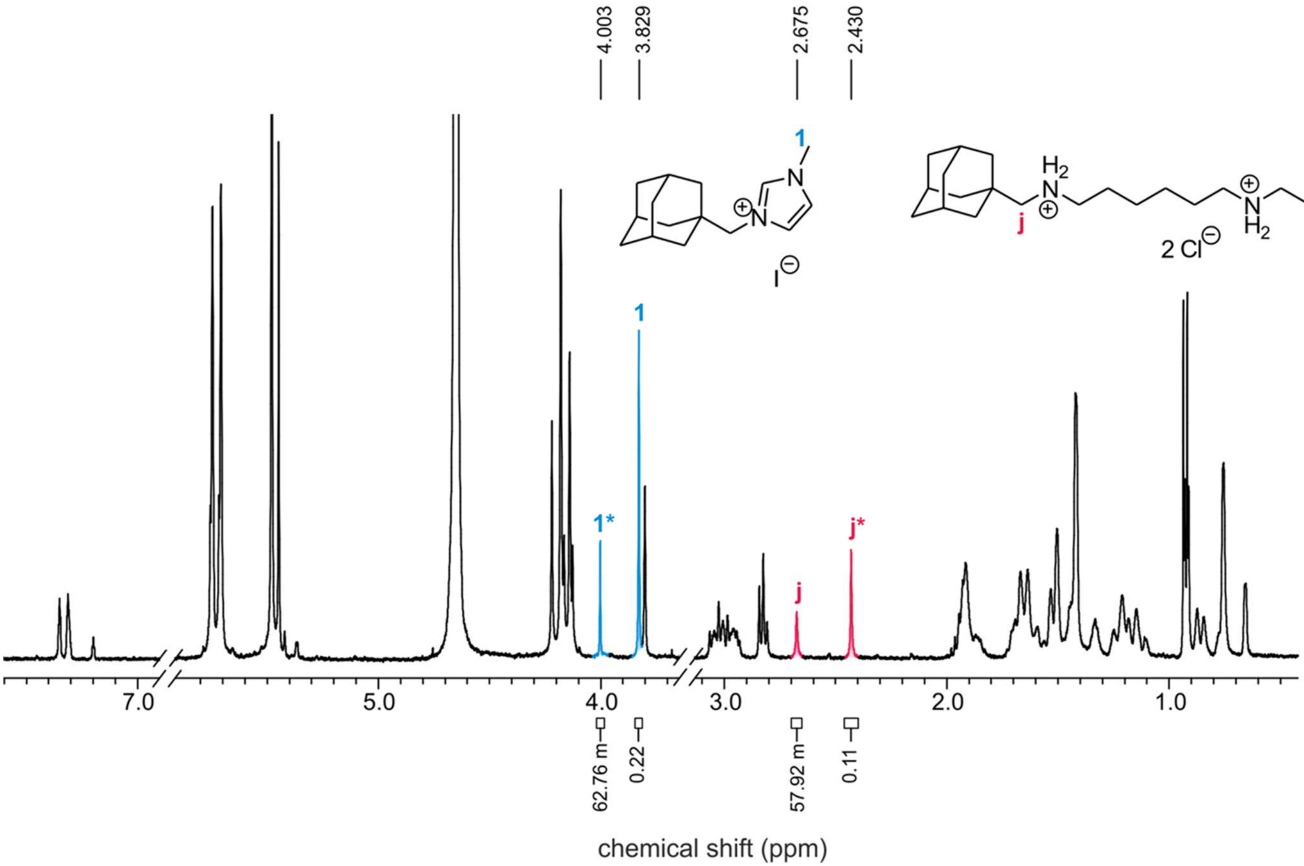


Figure S36 ^{1}H NMR (D_2O, 30 °C, 400 MHz) spectrum used for association constant determination of **5a**@CB7^{Ad} (c_{5a}=0.6 mM, competitor: 1-(1-adamantylmethyl)-3-methylimidazolium iodide).

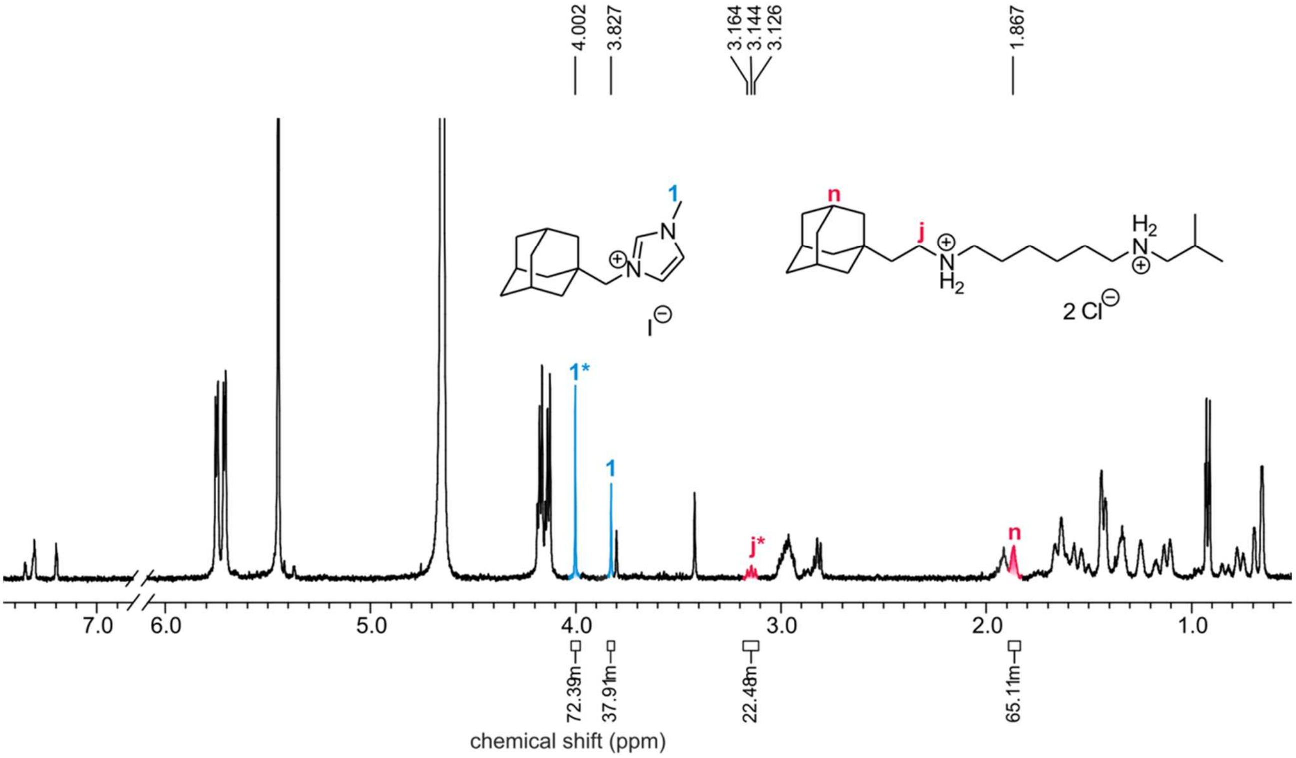


Figure S37 ^{1}H NMR (D_2O, 30 °C, 400 MHz) spectrum used for association constant determination of **5b**@CB7^{Ad} (c_{5b}=0.6 mM, competitor: 1-(1-adamantylmethyl)-3-methylimidazolium iodide).

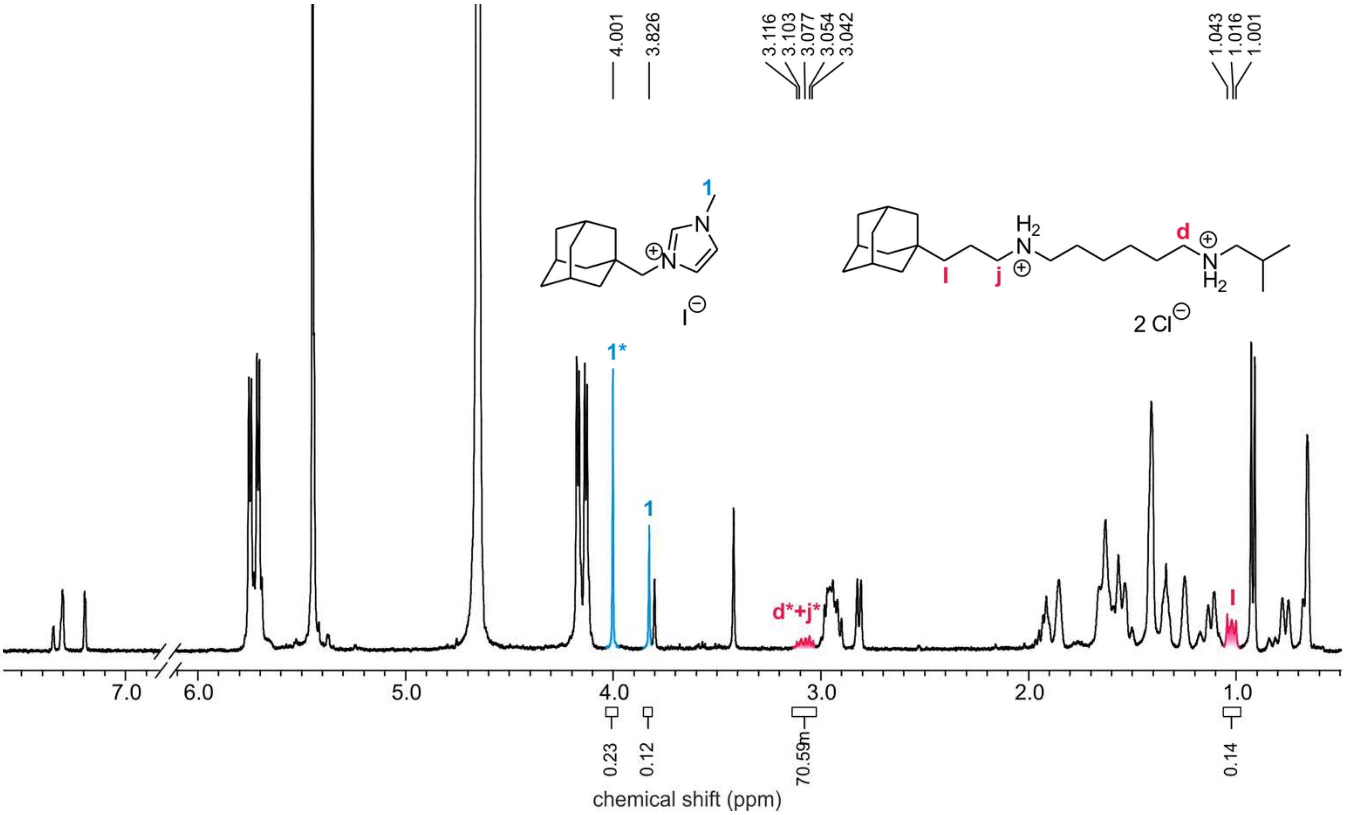


Figure S38 ^{1}H NMR (D_2O, 30 °C, 400 MHz) spectrum used for association constant determination of **5c**@CB7^{Ad} (c_{5c}=0.6 mM, competitor: 1-(1-adamantylmethyl)-3-methylimidazolium iodide).

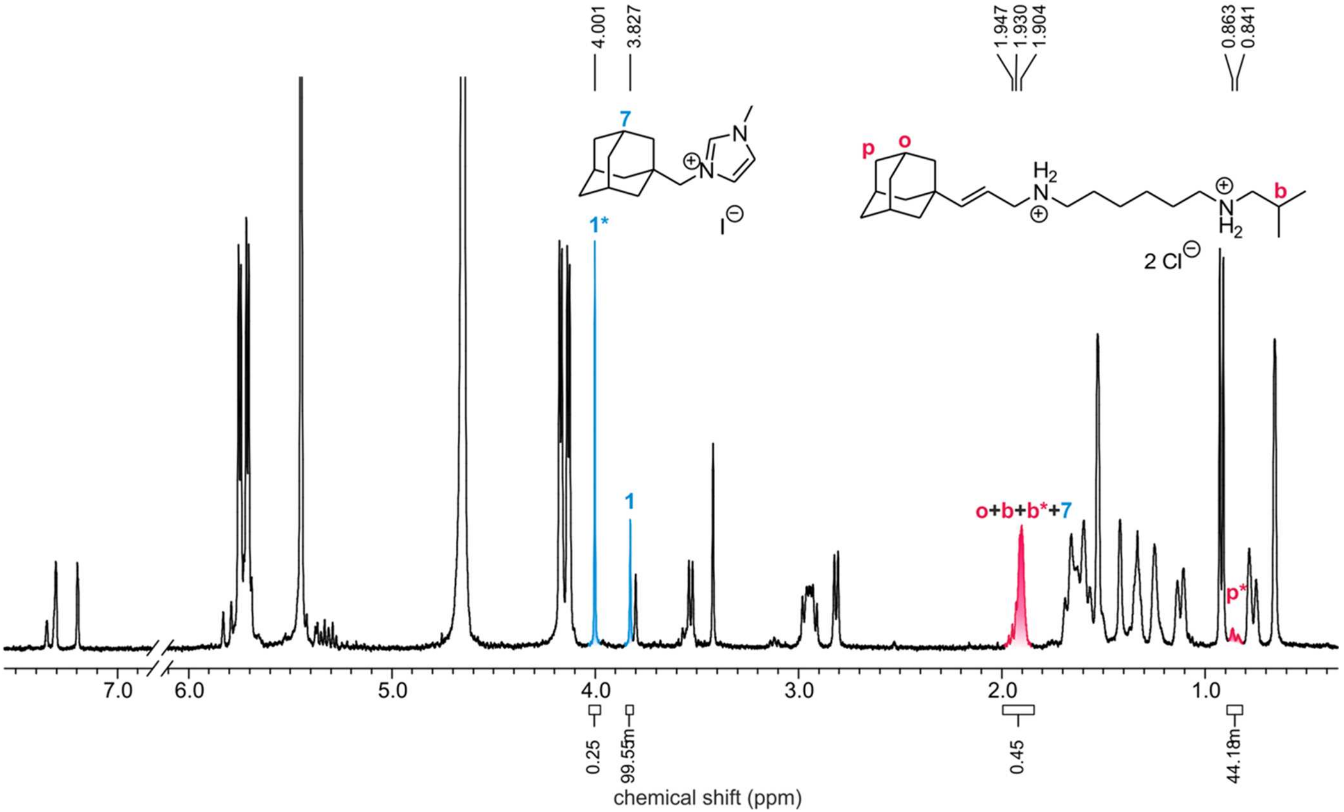


Figure S39 ^{1}H NMR (D_2O, 30 °C, 400 MHz) spectrum used for association constant determination of **5d**@CB7^{Ad} (c_{5d}=0.6 mM, competitor: 1-(1-adamantylmethyl)-3-methylimidazolium iodide).

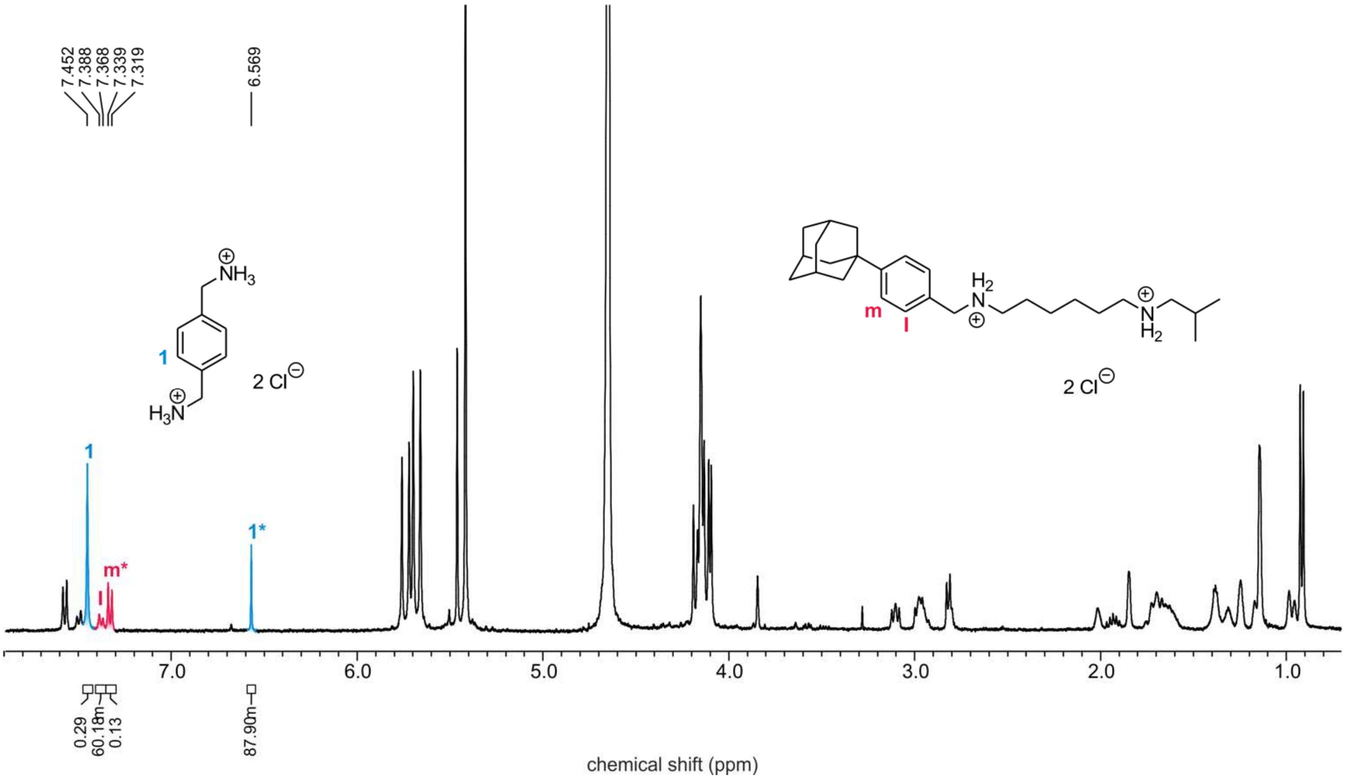


Figure S40 ^{1}H NMR (D_2O, 30 °C, 400 MHz) spectrum used for association constant determination of **5e**@CB7^{Ad} (c_{5e}=0.6 mM, competitor: *p*-xylylenediammonium chloride).

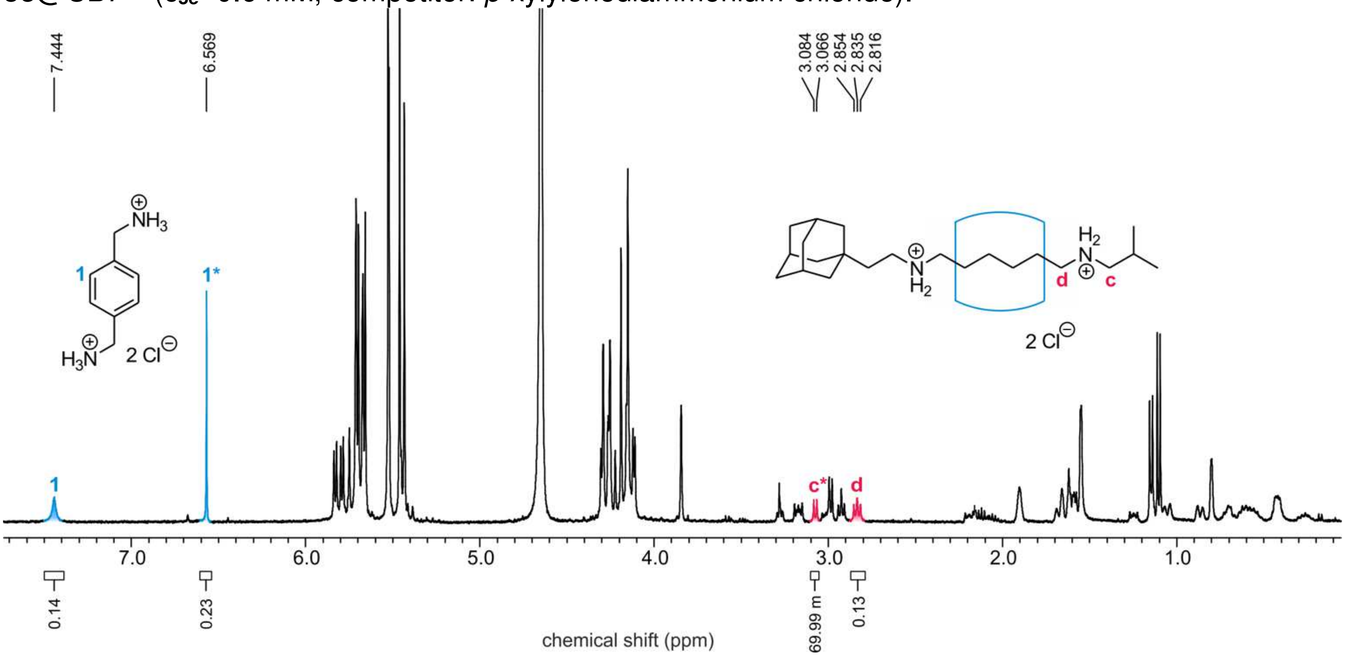


Figure S41 ^{1}H NMR (D_2O, 30 °C, 400 MHz) spectrum used for association constant determination of **6b**@CB7 (c_{6b}=0.6 mM, competitor: *p*-xylylenediammonium chloride).

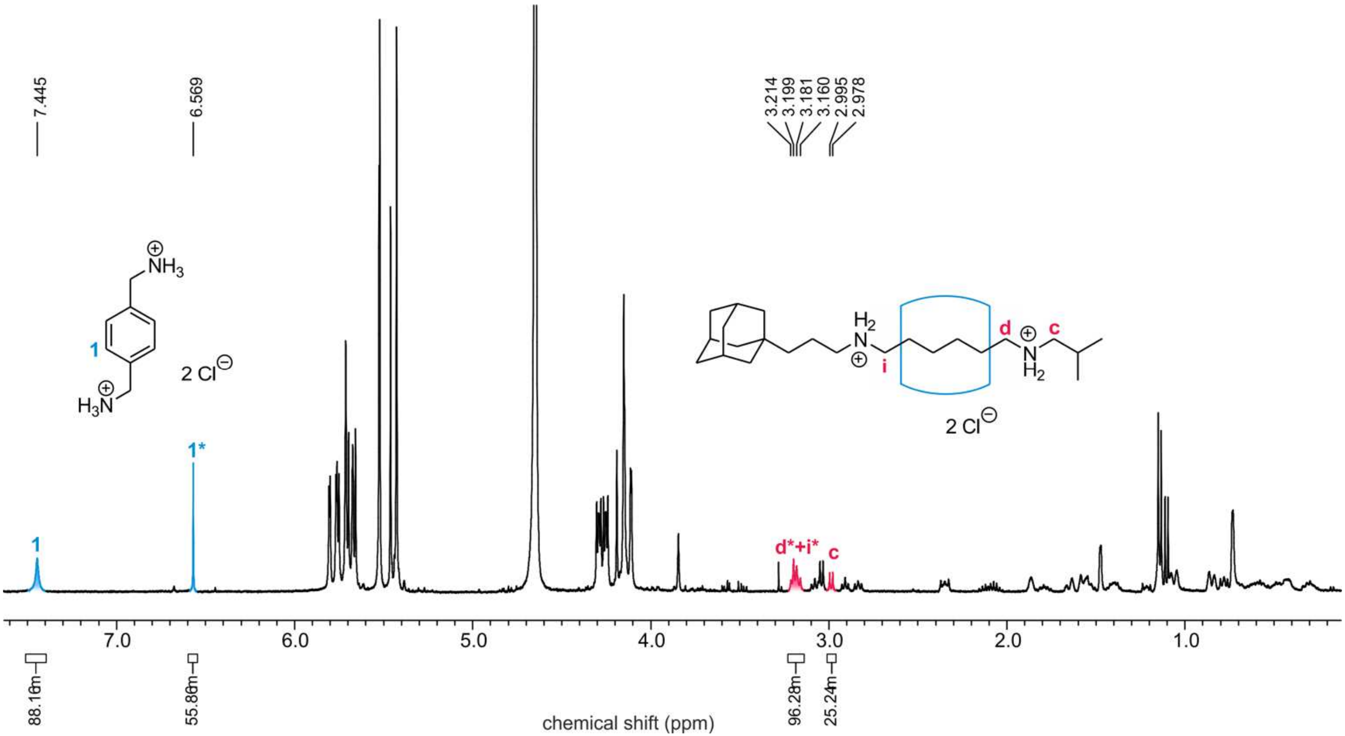


Figure S42 ^{1}H NMR (D_2O, 30 °C, 400 MHz) spectrum used for association constant determination of **6c**@CB7^{Ad} ($c_{\mathbf{6c}}$=0.6 mM, competitor: *p*-xylylenediammonium chloride).

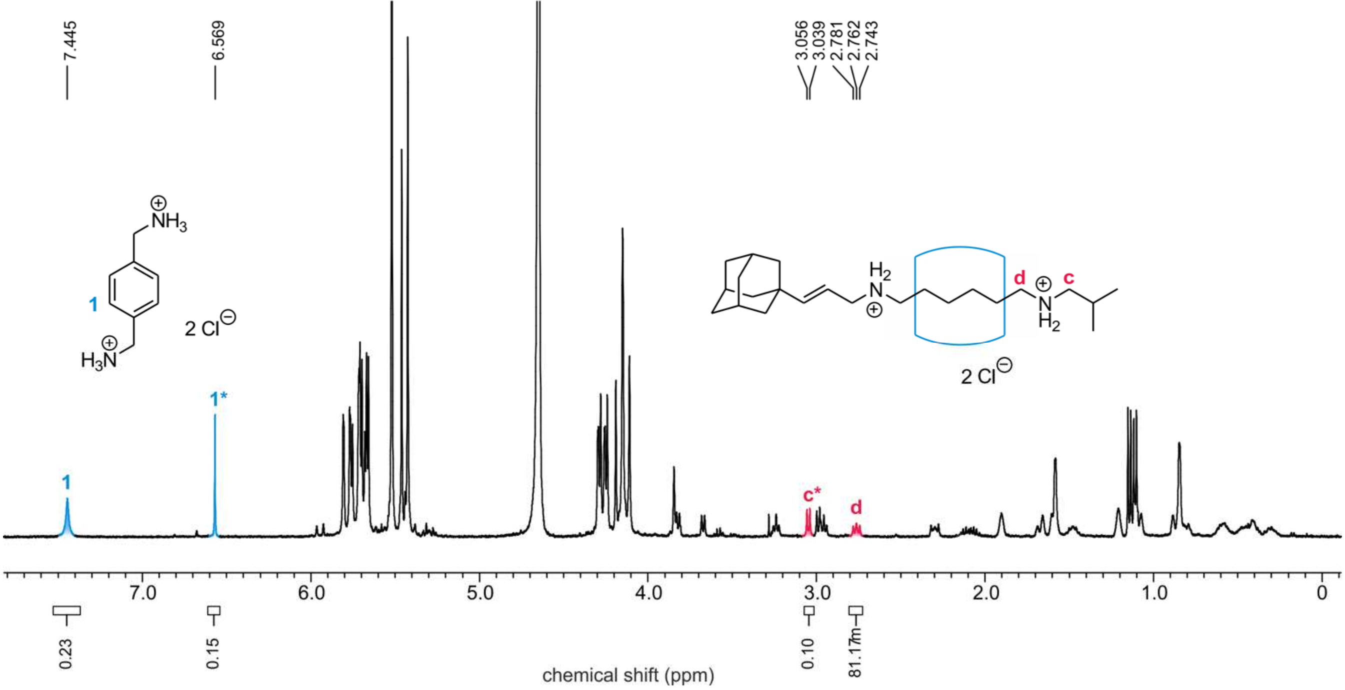


Figure S43 ^{1}H NMR (D_2O, 30 °C, 400 MHz) spectrum used for association constant determination of **6d**@CB7^{Ad} ($c_{\mathbf{6d}}$=0.6 mM, competitor: *p*-xylylenediammonium chloride).

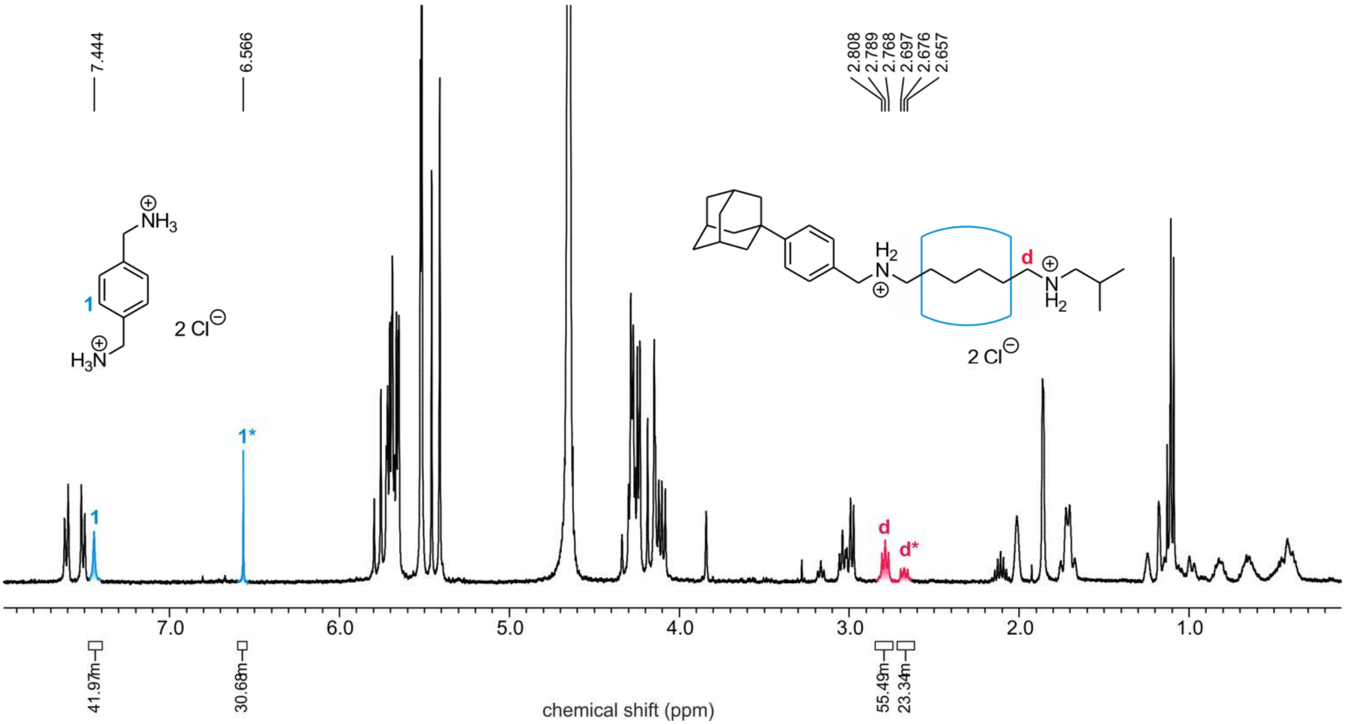


Figure S44 ^1H NMR (D_2O, 30 °C, 400 MHz) spectrum used for association constant determination of **6e**@CB7^{Ad} ($c_{\mathbf{6e}}$=0.8 mM, competitor (0.4 mM): *p*-xylylenediammonium chloride).

5.2 Isothermal titration calorimetry data

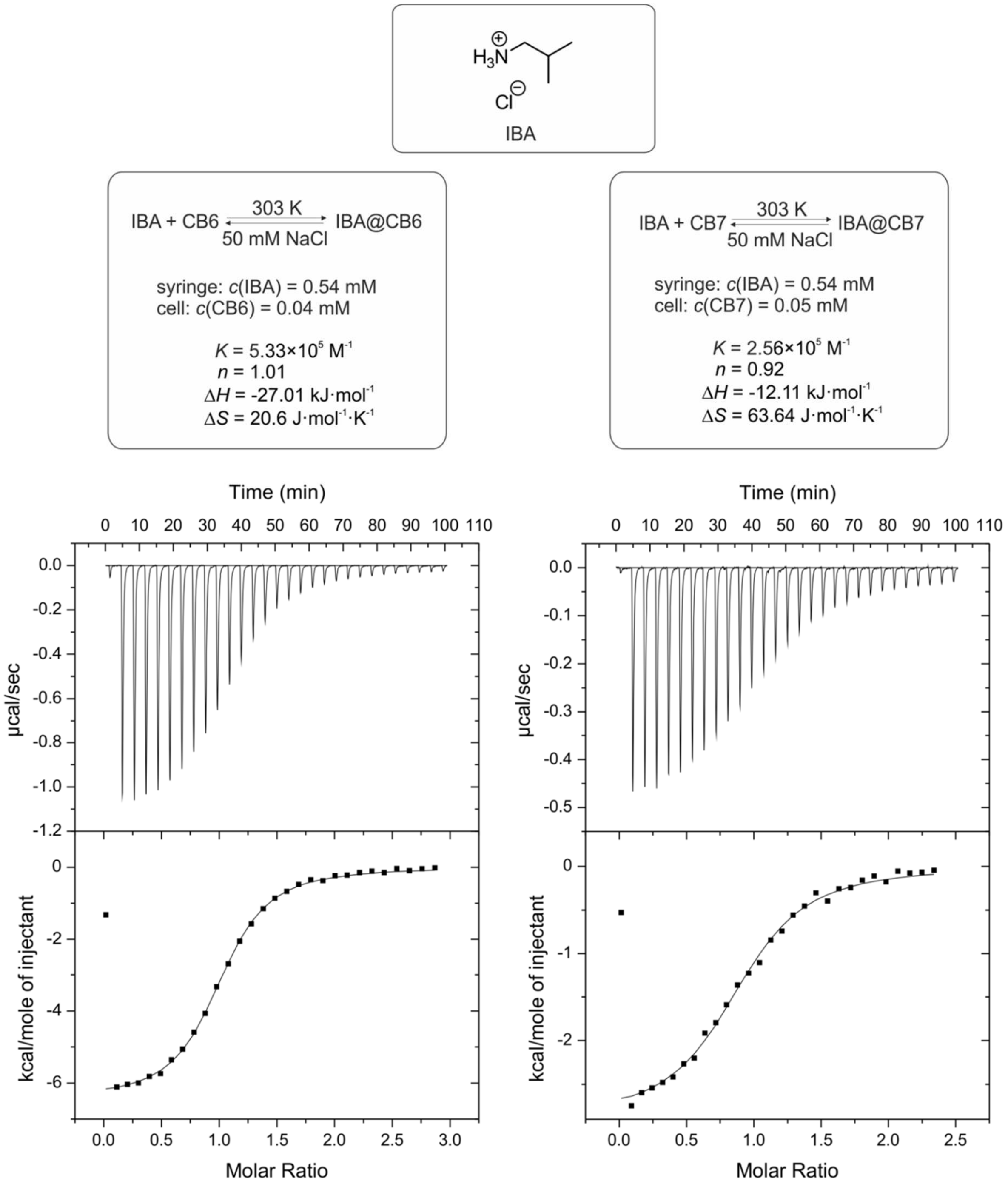
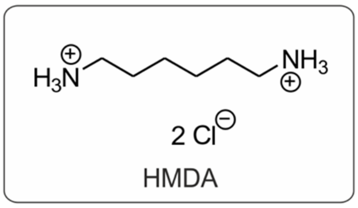


Figure S45 ITC data for the guest isobutylamine hydrochloride (IBA) and CB6 (left) and CB7 (right).



$$\text{HMDA} + \text{CB7} \underset{\text{50 mM NaCl}}{\overset{\text{303 K}}{\rightleftarrows}} \text{HMDA@CB7}$$

syringe: c(HMDA) = 0.5 mM
cell: c(CB7) = 0.05 mM
c(cyclopentanone) = 0.7 mM

$K = 2.17\times10^{7}\ \mathrm{M^{-1}}$
$n = 1.01$
$\Delta H = -13.31\ \mathrm{kJ\cdot mol^{-1}}$
$\Delta S = 96.42\ \mathrm{J\cdot mol^{-1}\cdot K^{-1}}$

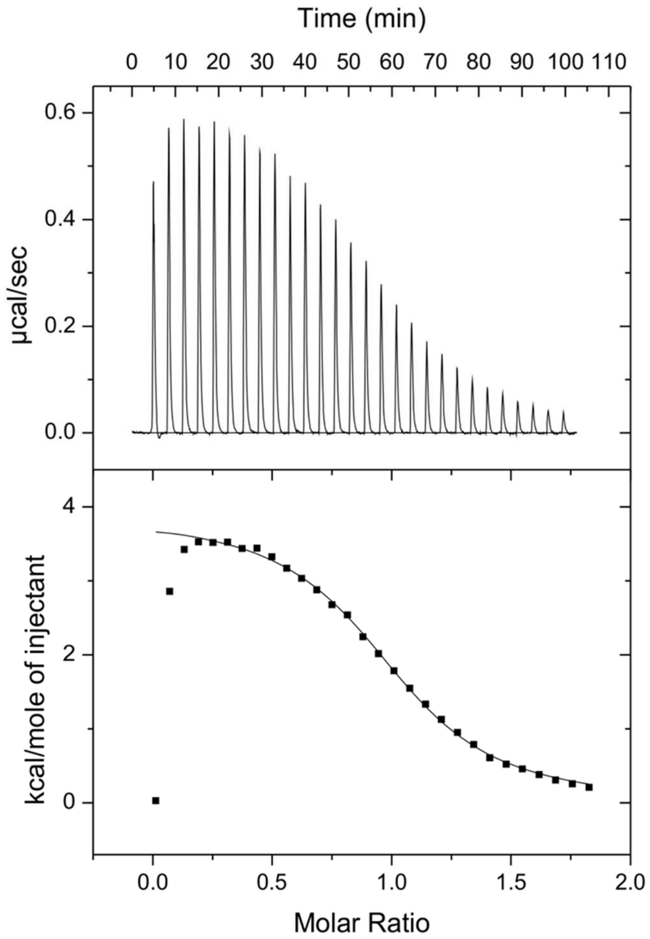
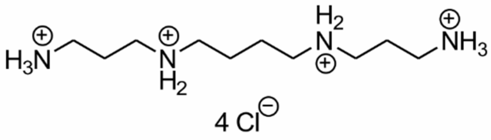


Figure S46 ITC data for the guest 1,6-hexamethylenediammonium dichloride (HMDA) and CB7.



SP

$$\text{SP} + \text{CB7} \underset{\text{50 mM NaCl}}{\overset{\text{303 K}}{\rightleftharpoons}} \text{SP@CB7}$$

syringe: $c(\text{SP}) = 0.53$ mM
cell: $c(\text{CB7}) = 0.05$ mM

$K = 9.92\times10^{5}\ \text{M}^{-1}$
$n = 0.92$
$\Delta H = -9.8\ \text{kJ}\cdot\text{mol}^{-1}$
$\Delta S = 82.48\ \text{J}\cdot\text{mol}^{-1}\cdot\text{K}^{-1}$

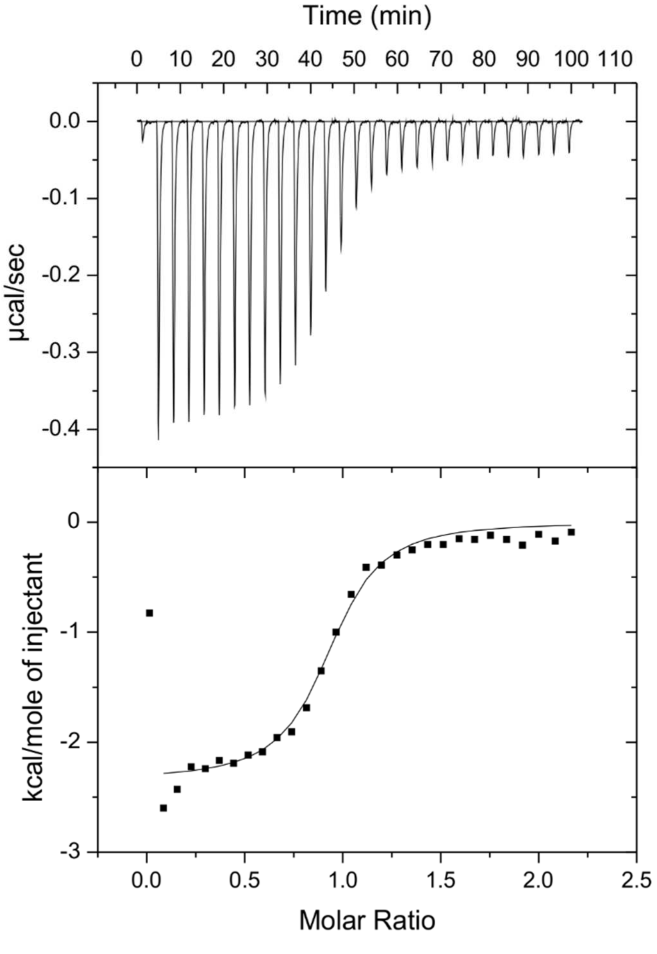


Figure S47 ITC data for the guest spermine tetrahydrochloride (SP) and CB7.

Table S1. Association constants determined by ^{1}H NMR or ITC.

Guest	CB6	CB7
6a	nb	na
6b	nb	$(7.5\pm1.0)\times10^{9}$[d]
6c	nb	$(5.7\pm0.6)\times10^{10}$[d]
6d	nb	$(4.0\pm0.4)\times10^{10}$[d]
6e	nb	$(1.04\pm0.02)\times10^{10}$[d]
5a	$(2.5\pm0.1)\times10^{6}$[a]	$(2.1\pm0.4)\times10^{13}$[e]
5b	$(2.3\pm0.2)\times10^{6}$[a]	$(9.7\pm0.2)\times10^{11}$[e]
5c	$(2.5\pm0.3)\times10^{6}$[a]	$(3.4\pm0.6)\times10^{11}$[e]
5d	$(2.4\pm0.1)\times10^{6}$[a]	$(1.44\pm0.05)\times10^{11}$[e]
5e	$(2.7\pm0.1)\times10^{6}$[a]	$(1.81\pm0.15)\times10^{11}$[d]
isobutylamine·HCl (IBA)	5.3×10^{5}[b]	2.6×10^{5}[b]
hexamethylene diamine·2HCl (HMDA)	2.9×10^{8}[c][25b]	2.2×10^{7}[f]
spermine·4HCl (SP)	3.3×10^{9}[c][25b]	9.9×10^{5}[b]

[a]Determined by NMR, 50 mM NaCl in D_2O, 30 °C, HMDA (K=2.9×10^{8}) as competitor. [b]Determined by ITC, 50 mM NaCl in H_2O, 30 °C. [c]Determined by ITC, 50 mM NaCl in H_2O, 25 °C. [d]Determined by NMR, D_2O, 30 °C, *p*-xylylenediamine·2HCl (K=2.16×10^{10}) as competitor. [e]Determined by NMR, D_2O, 30 °C, 1-(1-adamantylmethyl)-3-methylimidazolium bromide (K=3.68×10^{12}) as competitor. [f]Determined by ITC, 50 mM NaCl in H_2O, 30 °C, cyclopentanone (K=9.76×10^{4}) as competitor. nb= no binding. na=not applicable.

6 Kinetic data

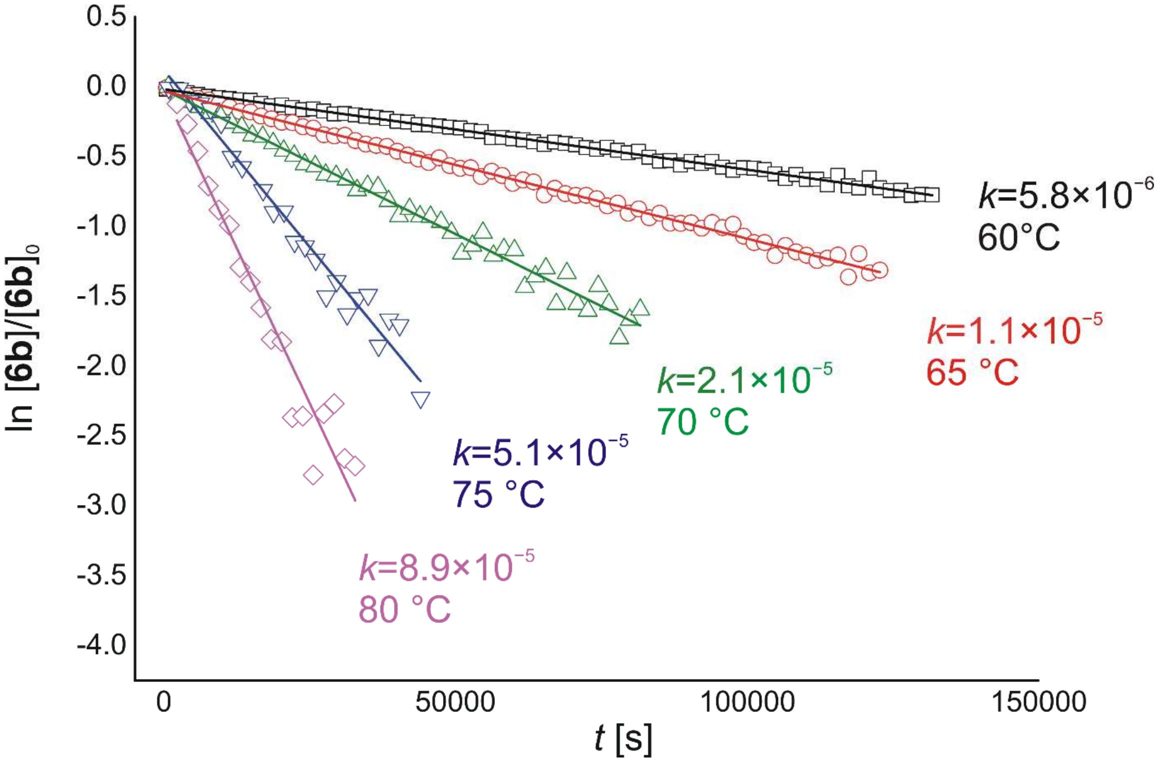


Figure S48 The first-order linearisation plot for **6b**@CB7.

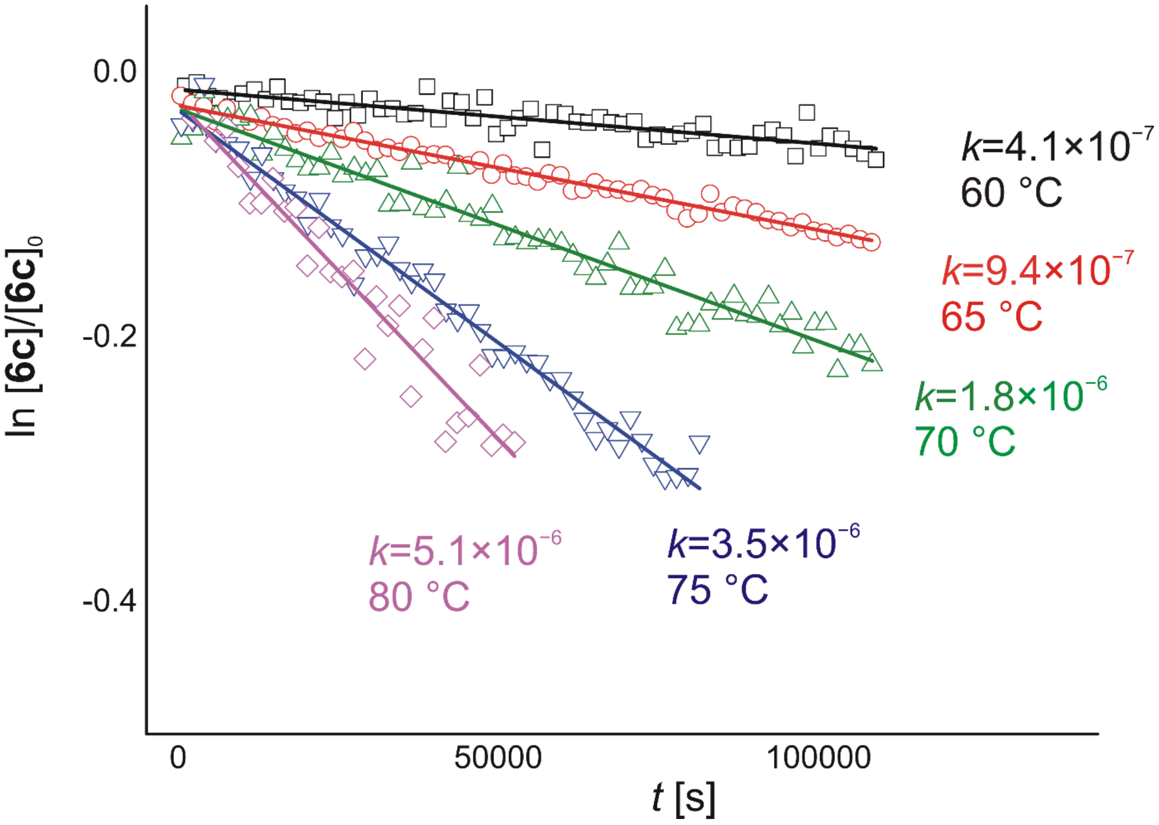


Figure S49 The first-order linearisation plot for **6c**@CB7.

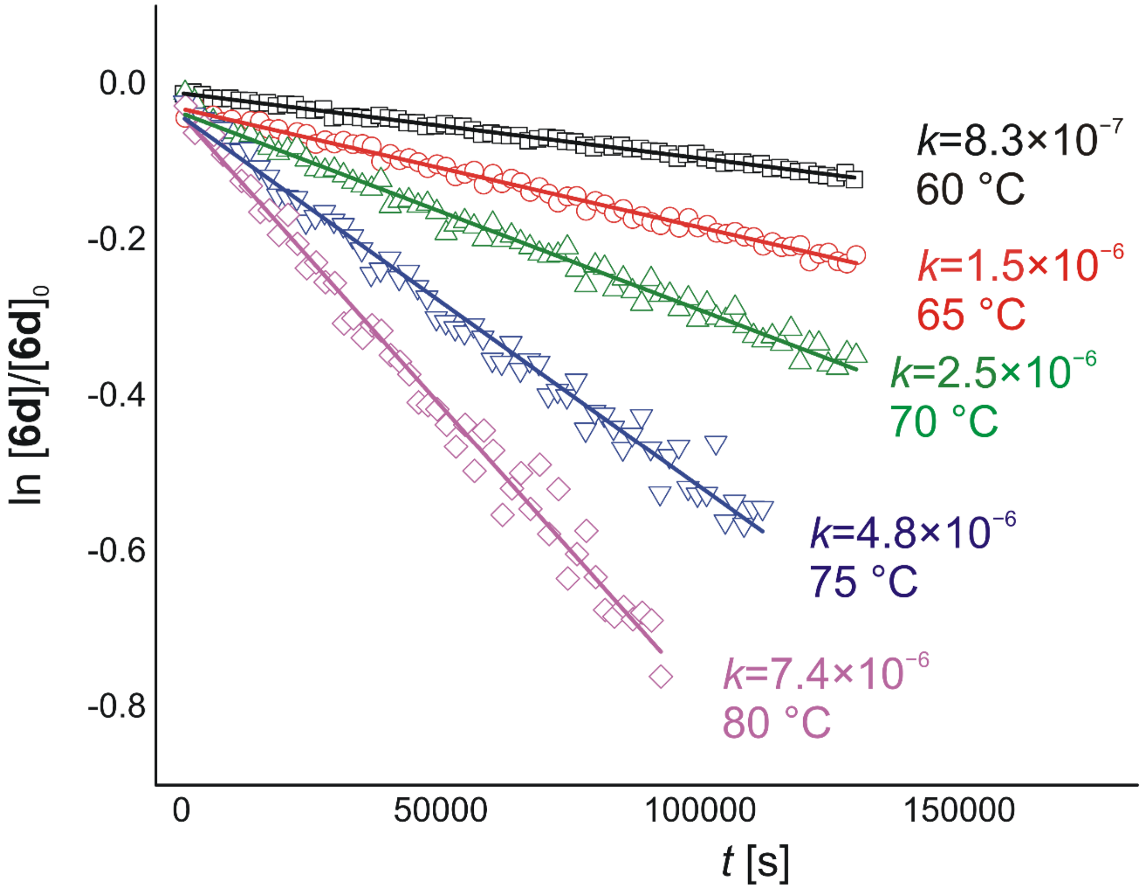
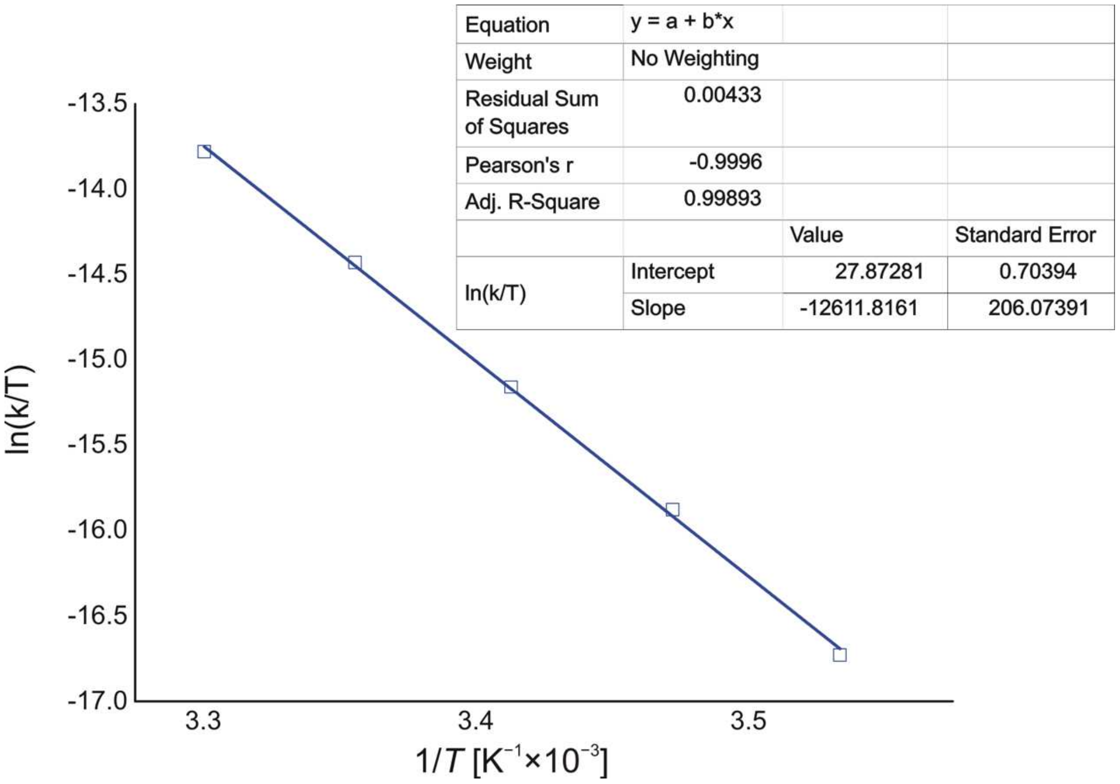
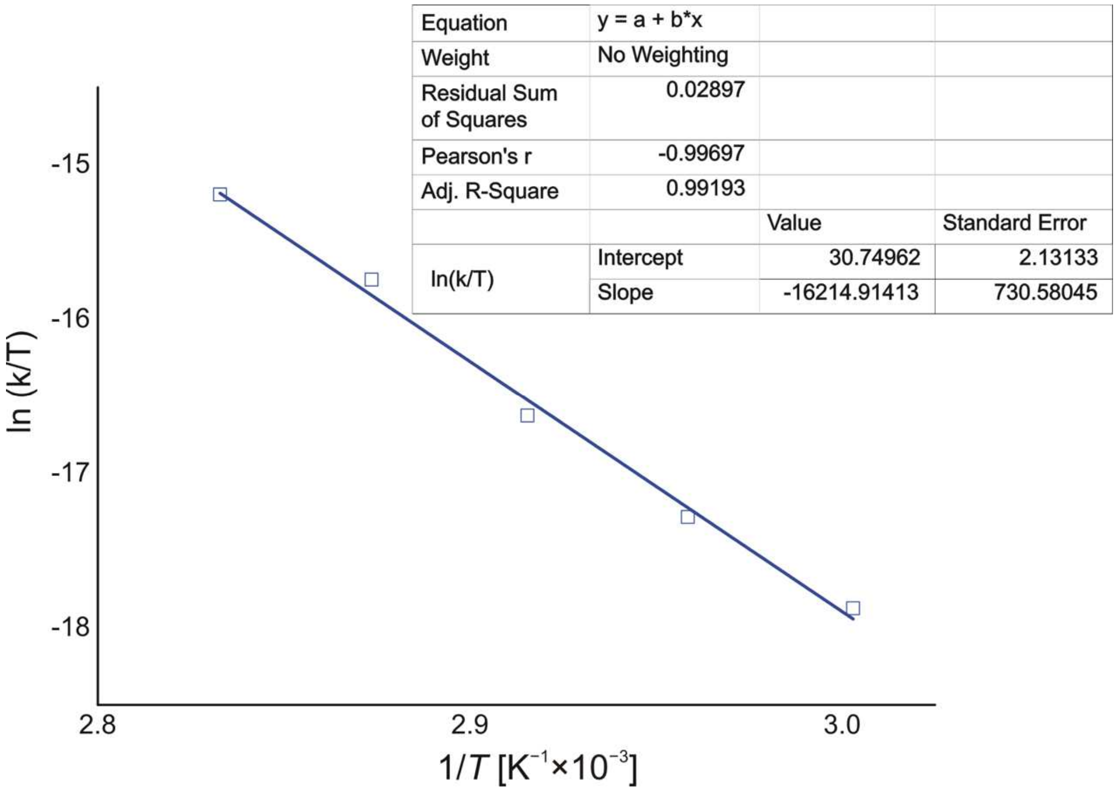


Figure S50 The first-order linearisation plot for **6d**@CB7.



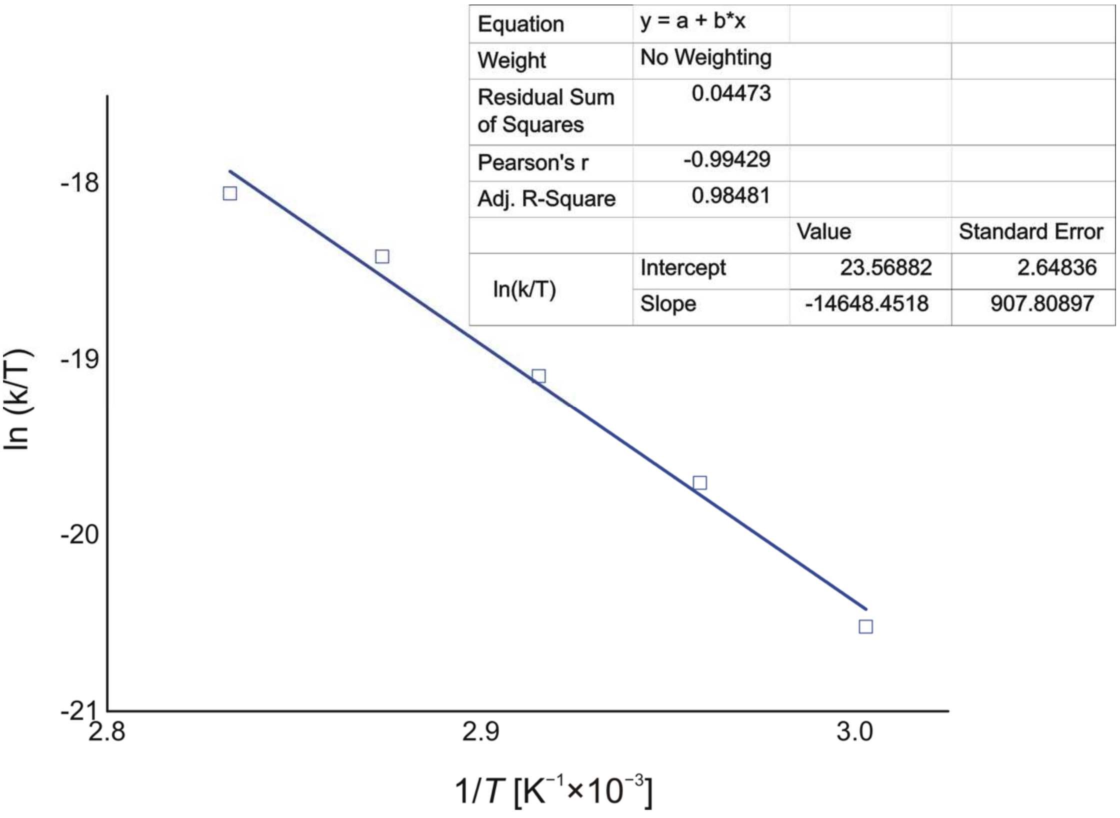
Equation	y = a + b*x		
Weight	No Weighting		
Residual Sum of Squares	0.00433		
Pearson's r	-0.9996		
Adj. R-Square	0.99893		
		Value	Standard Error
ln(k/T)	Intercept	27.87281	0.70394
	Slope	-12611.8161	206.07391

Figure S51 Eyring plot describing the decomposition of **6a**.



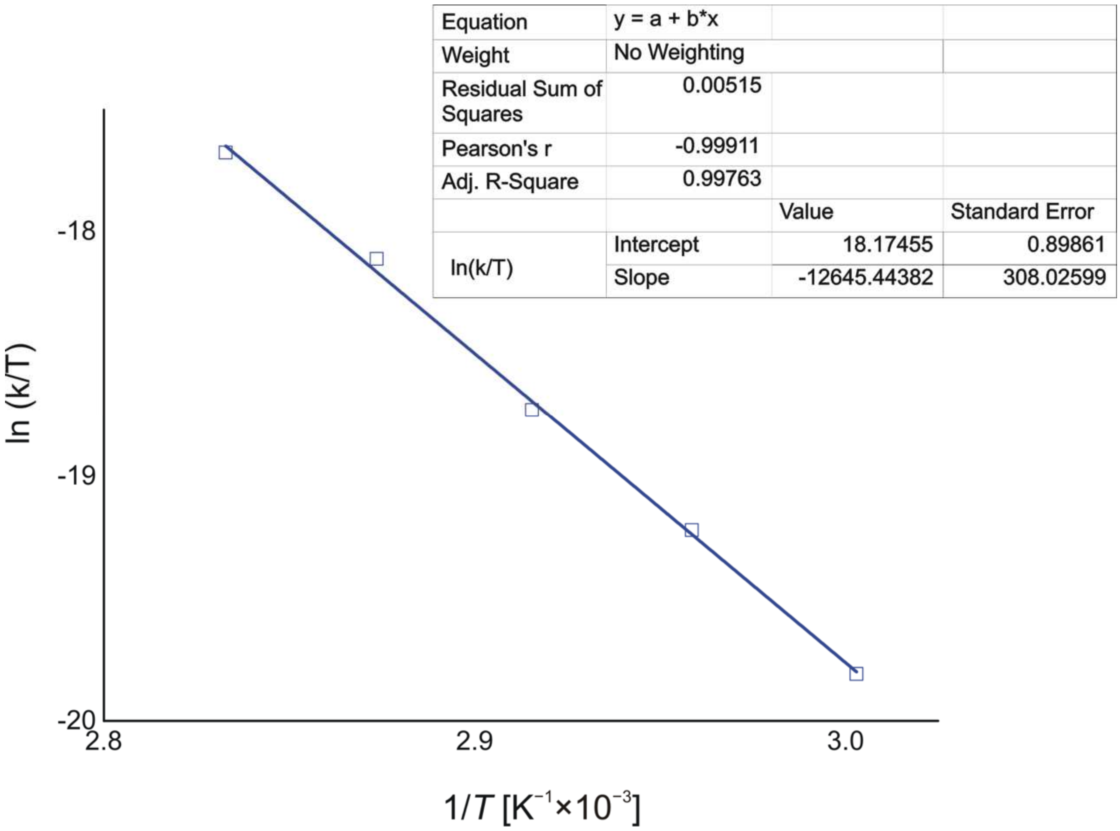
Equation	y = a + b*x		
Weight	No Weighting		
Residual Sum of Squares	0.02897		
Pearson's r	-0.99697		
Adj. R-Square	0.99193		
		Value	Standard Error
ln(k/T)	Intercept	30.74962	2.13133
	Slope	-16214.91413	730.58045

Figure S52 Eyring plot describing the decomposition of **6b.**



Equation	y = a + b*x		
Weight	No Weighting		
Residual Sum of Squares	0.04473		
Pearson's r	-0.99429		
Adj. R-Square	0.98481		
		Value	Standard Error
ln(k/T)	Intercept	23.56882	2.64836
	Slope	-14648.4518	907.80897

Figure S53 Eyring plot describing the decomposition of **6c**.



Equation	y = a + b*x		
Weight	No Weighting		
Residual Sum of Squares	0.00515		
Pearson's r	-0.99911		
Adj. R-Square	0.99763		
		Value	Standard Error
ln(k/T)	Intercept	18.17455	0.89861
	Slope	-12645.44382	308.02599

Figure S54 Eyring plot describing the decomposition of **6d**.

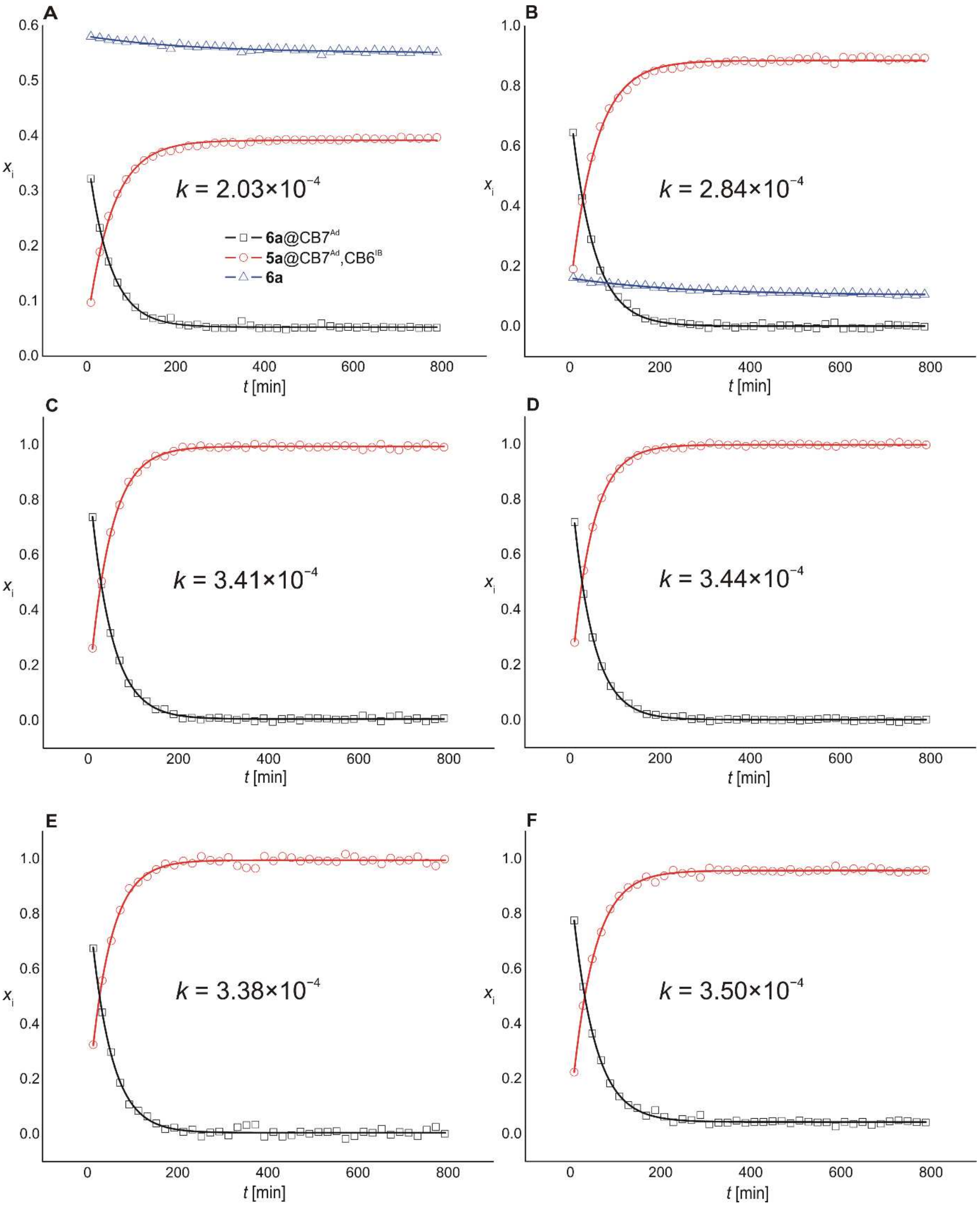
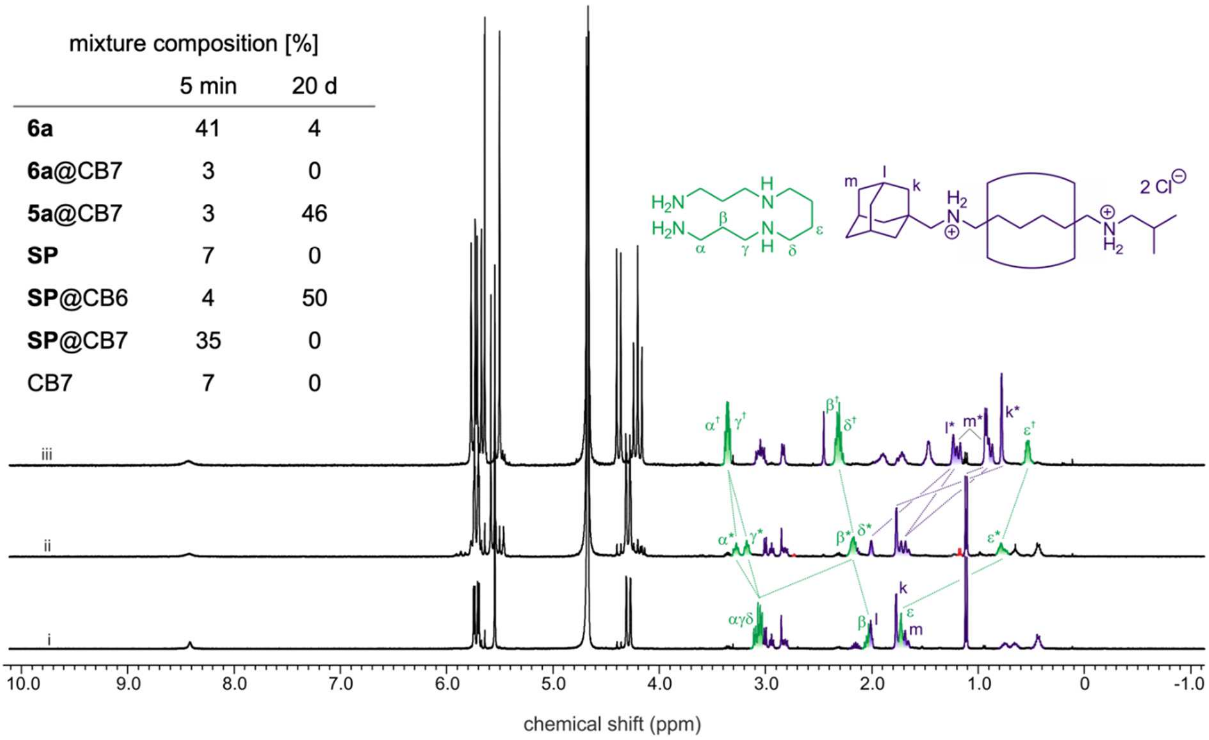


Figure S55 The kinetic curves (integration of spectra from ^{1}H NMR kinetics analysis recorded in D_2O at 30 °C) for decomposition of **6a**@CB7 complexes for various concentrations of CB7: (**A**) $c_{\mathbf{6a}}$=0.833 mM, c_{CB7}=0.415 mM; (**B**) $c_{\mathbf{6a}}$=0.833 mM, c_{CB7}=0.835 mM; (**C**) $c_{\mathbf{6a}}$=0.833 mM, c_{CB7}=1.250 mM; (**D**) $c_{\mathbf{6a}}$=0.833 mM, c_{CB7}=1.665 mM; (**E**) $c_{\mathbf{6a}}$=0.850 mM, c_{CB7}=2.550; (**F**) $c_{\mathbf{6a}}$=0.850 mM, c_{CB7}=4.250. The k values are given in s^{-1} with SD<5%.

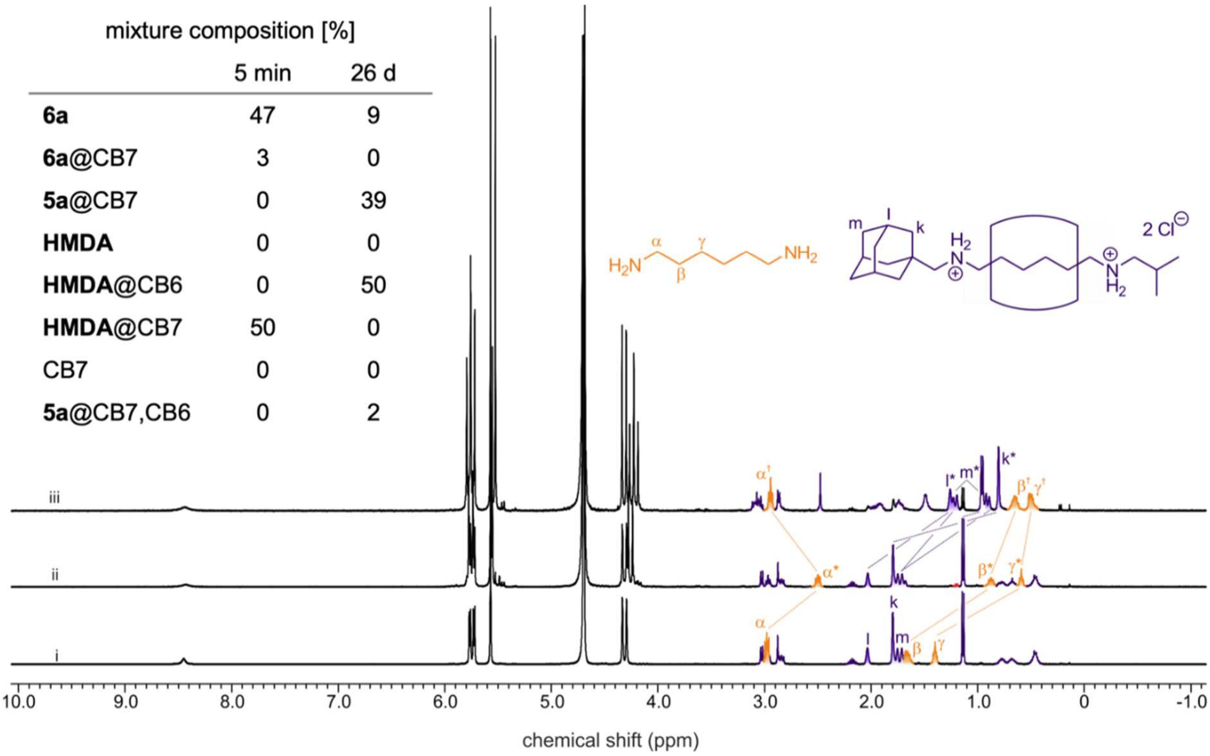
7 Released CB6 complexed with other guests



mixture composition [%]

	5 min	20 d
6a	41	4
6a@CB7	3	0
5a@CB7	3	46
SP	7	0
SP@CB6	4	50
SP@CB7	35	0
CB7	7	0

Figure S56 Portions of ^{1}H NMR spectra (D_2O, 30 °C, 400 MHz). i) **6a** (0.68 mM) + SP (1 equiv.); ii) **6a** + SP + CB7 (1 equiv.) in *t* = 5 min; iii) the same sample as previous in 20 days. The signals of the component complexed with CB6 and CB7 are labelled with † and *, respectively.



mixture composition [%]

	5 min	26 d
6a	47	9
6a@CB7	3	0
5a@CB7	0	39
HMDA	0	0
HMDA@CB6	0	50
HMDA@CB7	50	0
CB7	0	0
5a@CB7,CB6	0	2

Figure S57 Portions of ^{1}H NMR spectra (D_2O, 30 °C, 400 MHz). i) **6a** (0.68 mM) + HMDA (1 equiv.); ii) **6a** + HMDA + CB7 (1 equiv.) in *t* = 5 min; iii) the same sample as previous in 26 days. The signals of the component complexed with CB6 and CB7 are labelled with † and *, respectively.

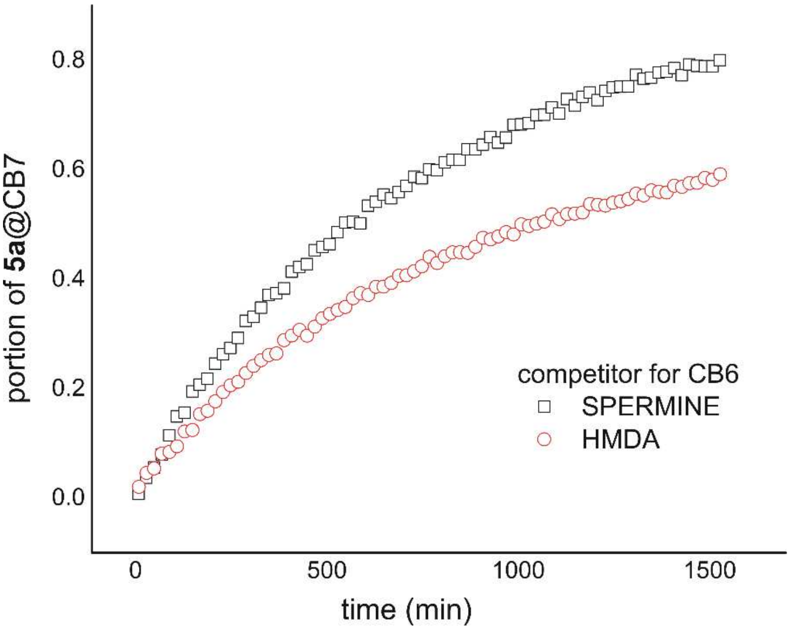


Figure S58 Portion of **5a**@CB7 followed by ^{1}H NMR spectroscopy for spermine and hexamethylene-1,6-diamine (HMDA) as competitors for CB6.

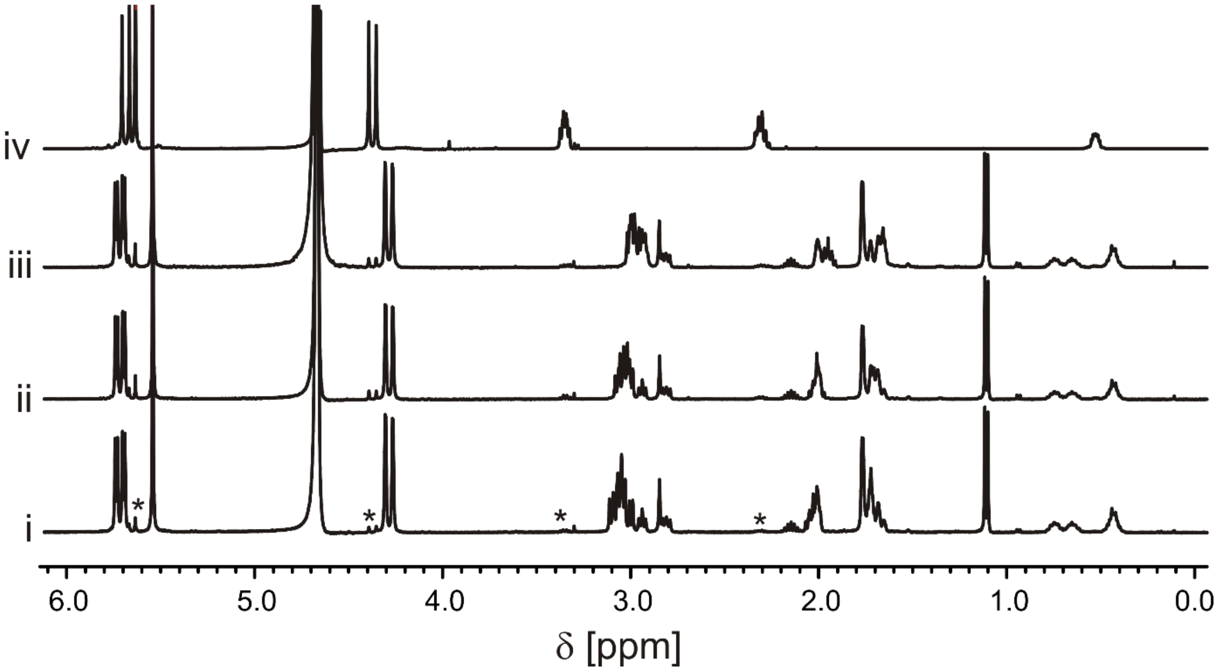


Figure S59 Portions of ^{1}H NMR spectra (D_2O, 30 °C, 400 MHz) of a mixture **6a** (0.68 mM) + SP (1 equiv.) immediately after mixing i), in 30 days ii), and in 320 days iii). The sample was stored at 30 °C. iv) ^{1}H NMR spectrum of a mixture of SP (1.0 mM) + CB6 (1 equiv.). A small amount of free CB6 and **5a**@CB6^{IB} from the used **6a** sample provided the SP@CB6 complex indicated by asterisks.

8 Computational details

Conformer screening of the corresponding guest and spermine was carried out using default iMTD-GC sampling of Grimme's CREST[15] tool (version 2.12) and xTB software[16] (version 6.6.1) at the GFN2-xTB[17] level of theory, incorporating an implicit solvation model (ALPB) for water.[18] Vibration frequencies were calculated for the lowest-lying structures (within 6 kcal·mol^{-1}) to identify the most stable conformer.

For the conformer screening of host–guest complexes involving guests with CB6 and/or CB7, a sequence of Minimum Hopping (metaopt) was employed. The initial structure was generated by manual placing the macrocycle into the respective binding site and optimizing it at the GFN Force Field level of theory (GFN-FF).[19] This structure underwent Minimum Hopping (save=2000; k_{push}=0.1 Eh; α=1.2 Bohr^{-1}) with an implicit water solvation model (ALPB) at the GFN-FF level of theory. The resulting trajectory was sorted using the CREGEN function of CREST with an energetic window of 20 kcal·mol^{-1}. Conformers from the sorted ensemble were reoptimised at the GFN2 level of theory, and the lowest-lying structure was subjected to another round of Minimum Hopping at the GFN2 level of theory (save=1000; k_{push}=0.05 Eh; α=1.0 Bohr^{-1}). After sorting with CREGEN, the ensemble within 6 kcal·mol^{-1} was reoptimised at the GFN2 level of theory with a tighter energy convergence threshold (10^{-7} Eh). Vibration frequencies were calculated to ensure a local minimum and identify the lowest-lying structure based on Total Free Energy.

To determine the average distance between the centre of the adamantane cage and the adjacent nitrogen atom in the guest molecules, biased molecular dynamics (meta-dynamics)[20] were employed at the GFN2 level of theory with an implicit water solvation model (ALPB). The total length of the molecular dynamics simulation was 2 ns, utilizing the root mean square deviation (RMSD) of all atoms as the collective variable. The hydrogen mass was set to 4 u, and covalent bonds were maintained using the SHAKE algorithm. The simulation parameters included a temperature of 25 °C, a time step of 4 fs, k_{push} of 0.02 Eh, and α of 1.2 Bohr^{-1}. The trajectory data were analysed using the TRAVIS[21],[22] software (Version: Jul 29 2022), and the average distance was estimated using the radial distribution function (rdf).

9 Single-crystal X-ray diffraction data

Preparation of rotaxanes hexafluorophosphate salts

The hexafluorophosphate salts of **6a**–**6d** were prepared quantitatively by the addition of a 0.5 M aqueous solution of ammonium hexafluorophosphate to the rotaxanes hydrochloride salts dissolved in a minimum volume of distilled water. The white precipitate was collected by suction filtration, washed with distilled water, and dried under vacuum.

Methods for growing of single crystals

Single crystal of **6a** was grown in acetonitrile solution (2 mg/cm^3) by toluene (5 cm^3) vapour diffusion at –20 °C over several days. Single crystal of **6b** was grown in acetonitrile/water (1/1, 2 mg/cm^3) solution by evaporation at room temperature over several days. Single crystal of **6c** was grown in acetonitrile solution (2 mg/cm^3) by diethyl ether (5 cm^3) vapour diffusion at room temperature over several days. Single crystal of **6d** was grown in acetonitrile solution (2 mg/cm^3) by diethyl ether (5 cm^3) vapour diffusion at room temperature over several days.

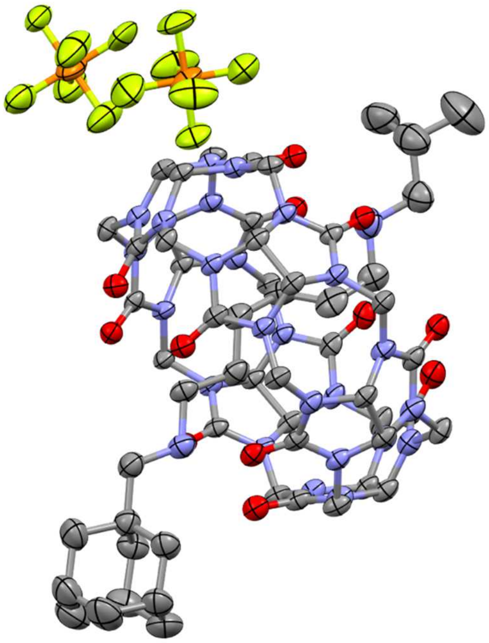


Figure S60 The X-ray crystal structure of **6a** (thermal ellipsoids at 50% probability; minor disorder, H-atoms and solvents are omitted for clarity).

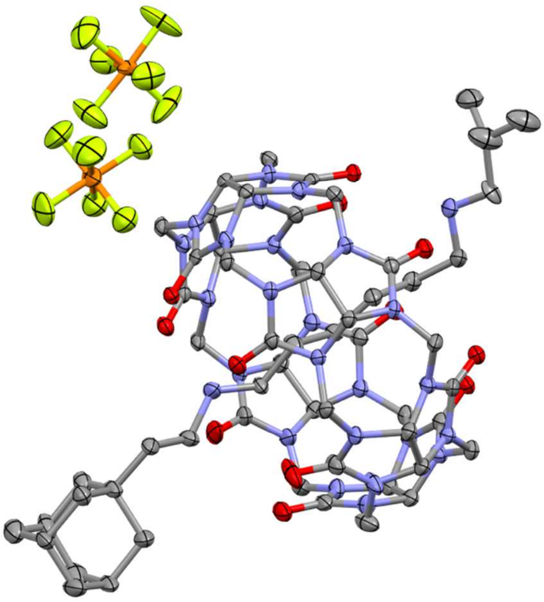


Figure S61 The X-ray crystal structure of **6b** (thermal ellipsoids at 50% probability; minor disorder, H-atoms and solvents are omitted for clarity).

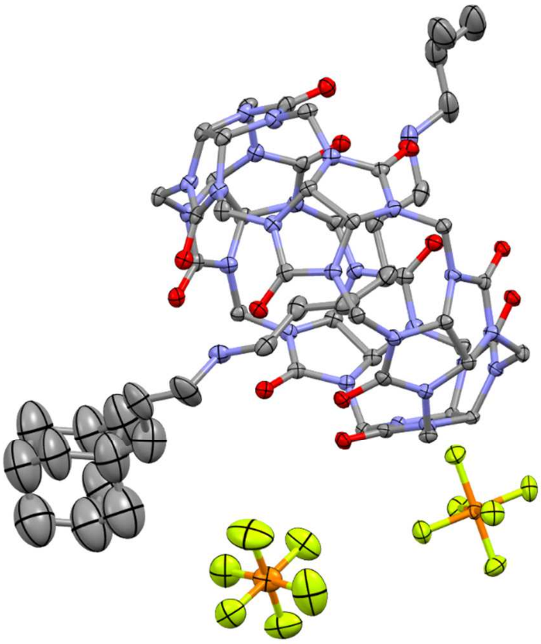


Figure S62 The X-ray crystal structure of **6c** (thermal ellipsoids at 30% probability; H-atoms and solvents are omitted for clarity).

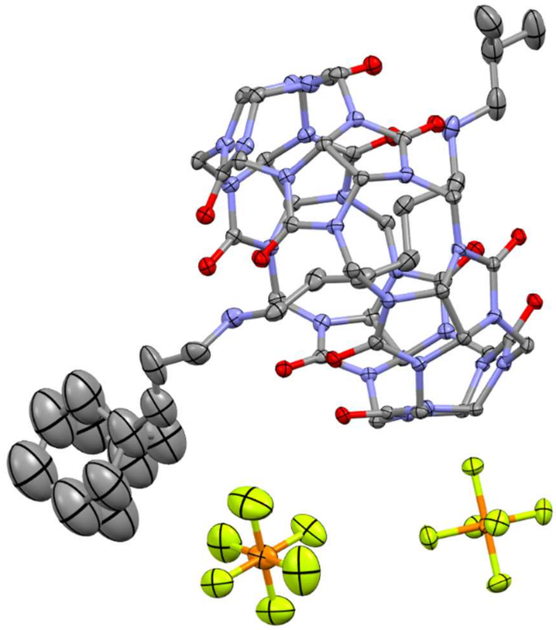


Figure S63 The X-ray crystal structure of **6d** (thermal ellipsoids at 30% probability; H-atoms and solvents are omitted for clarity).

Table S2 Crystallographic data for **6a–6d**.

Compound	**6a**	**6b**	**6c**	**6d**
CCDC deposition number	2312915	2312916	2312917	2312918
Empirical formula*	$C_{119}H_{167}F_{12}N_{29}O_{12}P_2$	$C_{58}H_{91.5}F_{12}N_{26}O_{17.75}P_2$	$C_{67}H_{99}F_{12}N_{29}O_{14}P_2$	$C_{67}H_{98}F_{12}N_{29}O_{14.5}P_2$
Moiety*	$C_{21}H_{42}N_2$, $C_{36}H_{36}N_{24}O_{12}$, 2(F_6P), 3(C_2H_3N), 7(C_7H_8)	$C_{22}H_{44}N_2$, $C_{36}H_{36}N_{24}O_{12}$, 2(F_6P), 5.75(H_2O)	$C_{23}H_{46}N_2$, $C_{36}H_{36}N_{24}O_{12}$, 2(F_6P), 3(C_2H_3N), 0.5($C_4H_{10}O$), 1.5(H_2O)	$C_{23}H_{44}N_2$, $C_{36}H_{36}N_{24}O_{12}$, 2(F_6P), 3(C_2H_3N), 0.5($C_4H_{10}O$), 2(H_2O)
Formula weight (g·mol^{-1})*	2485.71	1727.01	1824.61	1831.61
Colour; shape	Colourless; plate	Colourless; block	Colourless; block	Colourless; block
Crystal size	0.239 × 0.121 × 0.065	0.163 × 0.086 × 0.051	0.144 × 0.092 × 0.084	0.166 × 0.095 × 0.087
Measured temperature (K)	120.0 (1)	120.0 (1)	120.0 (1)	120.0 (1)
Crystal system	Monoclinic	Orthorhombic	Cubic	Cubic
Space group	$P2_1/n$	$Ama2$	$Pa\bar{3}$	$Pa\bar{3}$
Unit cell dimensions (Å, °)	a = 16.05160(10)	a = 17.47878(10)	a = 36.76500(10)	a = 36.79372(9)
	b = 25.7006(2)	b = 27.72924(12)	b = 36.76500(10)	b = 36.79372(9)
	c = 27.3571(2)	c = 15.22975(7)	c = 36.76500(10)	c = 36.79372(9)
	α = 90	α = 90	α = 90	α = 90
	β = 91.6470(10)	β = 90	β = 90	β = 90
	γ = 90	γ = 90	γ = 90	γ = 90
Volume (Å^3)	11281.12(14)	7381.45(6)	49694.0(4)	49810.5(4)
Z	4	4	24	24
D_x (g·cm^{-3})*	1.463	1.554	1.463	1.465
μ (mm^{-1})*	1.177	1.566	1.405	1.409
F(000)*	5272	3606	22896	22968
θ Range (°)	2.359 to 74.504	3.187 to 74.502	2.081 to 74.408	2.080 to 74.491
Completeness to θ (%)	0.999	0.998	0.992	0.998
h	$-20 \le h \le 19$	$-21 \le h \le 21$	$-44 \le h \le 42$	$-43 \le h \le 40$
k	$-32 \le k \le 30$	$-34 \le k \le 29$	$-43 \le k \le 37$	$-44 \le k \le 45$
l	$-33 \le l \le 34$	$-19 \le l \le 19$	$-46 \le l \le 43$	$-37 \le l \le 45$
Reflections collected	187105	74539	284279	226496
Reflections unique	23051 [R(int) = 0.0301]	7788 [R(int) = 0.0249]	16806 [R(int) = 0.0725]	16955 [R(int) = 0.0855]
Unique reflections with $I \ge 2\sigma(I)$	20122	7679	14899	14778
Number of parameters	1172	689	1072	1045
Number of restraints	128	38	278	289
Goodness-of-fit on F^2	1.068	1.04	1.803	1.775
Final R indices [$I \ge 2\sigma(I)$]	R_1 = 0.0800 wR_2 = 0.2415	R_1 = 0.0383 wR_2 = 0.1092	R_1 = 0.1130 wR_2 = 0.3818	R_1 = 0.1167 wR_2 = 0.3824
R indices (all data)	R_1 = 0.0861 wR_2 = 0.2465	R_1 = 0.0387 wR_2 = 0.1096	R_1 = 0.1189 wR_2 = 0.3864	R_1 = 0.1234 wR_2 = 0.3887
Residual highest peak and deepest hole (e·Å^{-3})	0.874 and −0.512	0.655 and −0.324	1.150 and −0.811	1.373 and −1.121

* *The Empirical Formula, Moiety, Formula Weight, D_x, μ, and F(000) for complexes **6a**, **6c**, and **6d** have been modified to include the estimated unit cell contents (https://journals.iucr.org/c/services/cif/reqdata.html) including the solvates which were accounted for using Squeeze within Platon;[23] all other values reflect the crystallographic outputs resulting from the use of Platon Squeeze to account for the omitted solvates.*

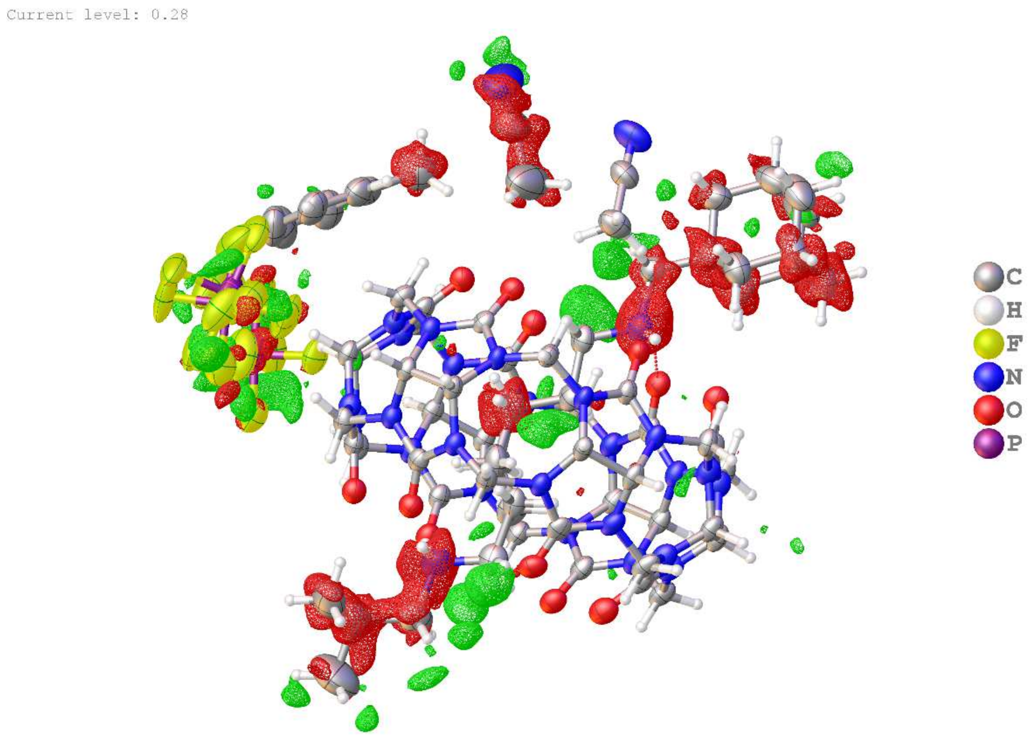


Figure S64 The electron difference map of crystal structure **6a** (thermal ellipsoids at 50% probability), showing the regions of residual electron density that could not be fully resolved in the final structure.

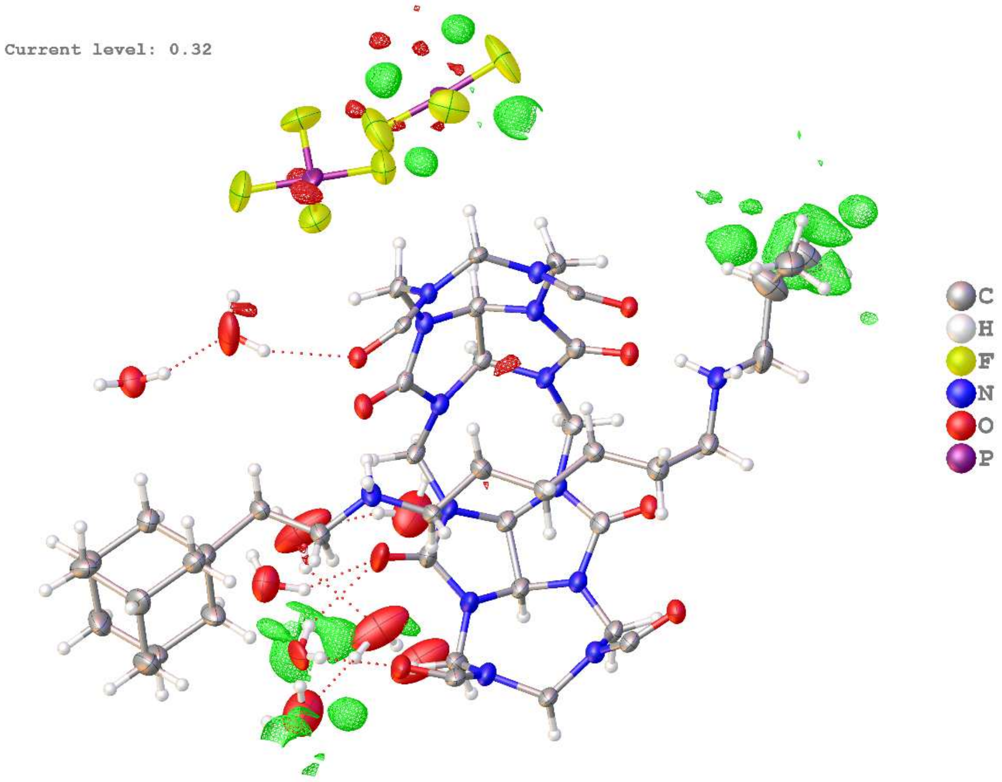


Figure S65 The electron difference map of crystal structure **6b** (thermal ellipsoids at 50% probability), showing the regions of residual electron density that could not be fully resolved in the final structure.

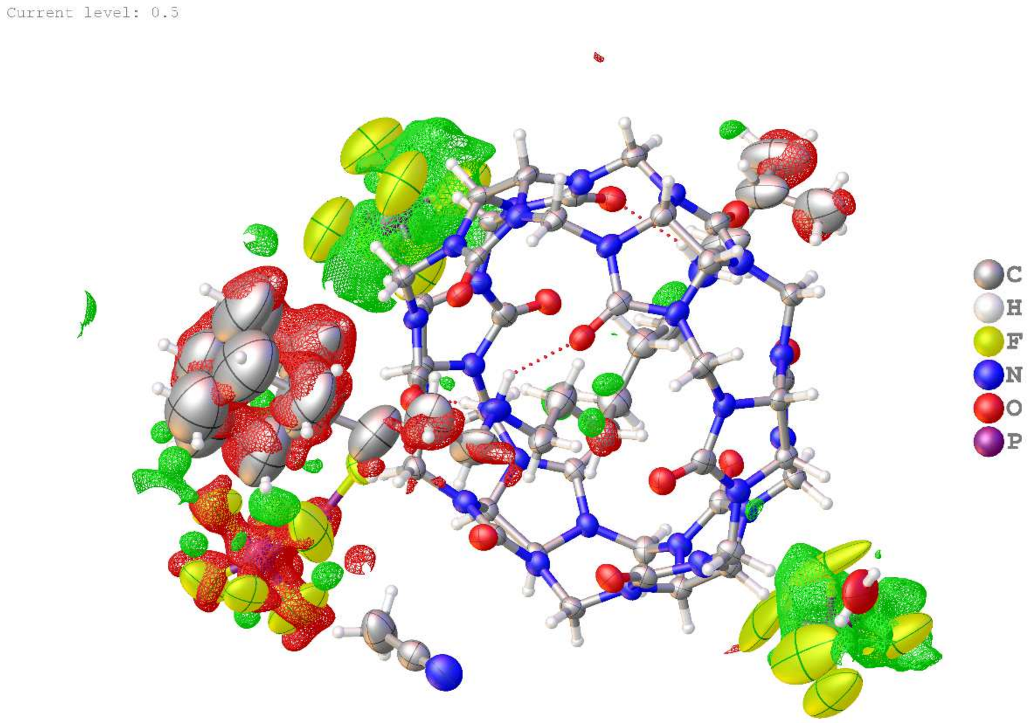


Figure S66 The electron difference map of crystal structure **6c** (thermal ellipsoids at 50% probability), showing the regions of residual electron density that could not be fully resolved in the final structure.

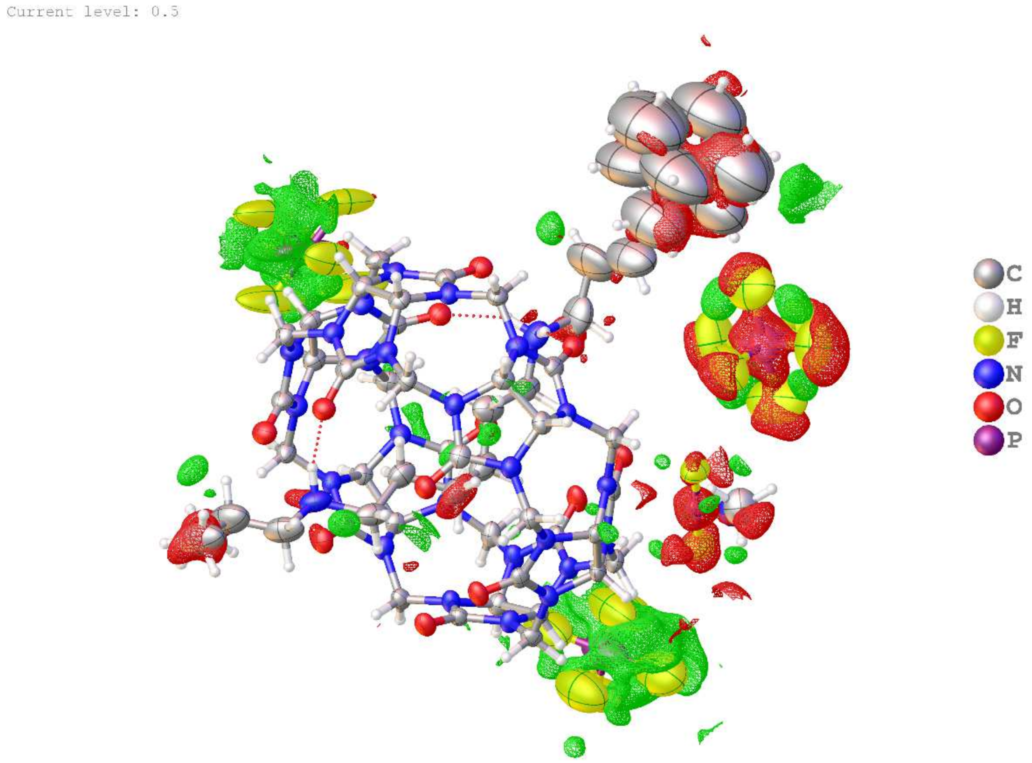


Figure S67 The electron difference map of crystal structure **6d** (thermal ellipsoids at 50% probability), showing the regions of residual electron density that could not be fully resolved in the final structure.

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