

Cucurbit[6]uril–Cucurbit[7]uril Heterodimer Promotes Controlled Self-assembly of Supramolecular Networks and Supramolecular Micelles by Self-sorting of Amphiphilic Guests

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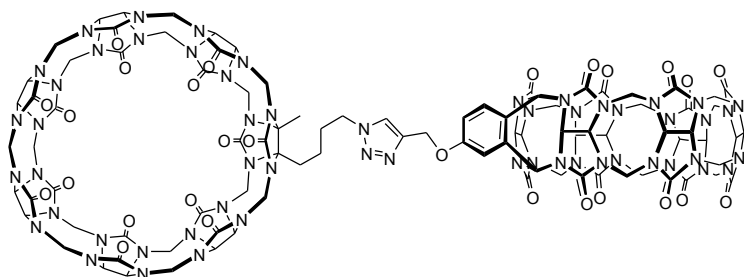
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Supporting Information

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General Experimental Details. Starting materials were purchased from commercial suppliers were used without further purification. Compounds **2**,^[1] **3**,^[2] **S1** and **S2**^[3] were prepared according to the literature procedures. Melting points were measured on a Meltemp apparatus in open capillary tubes and are uncorrected. IR spectra were recorded on a JASCO FT/IR 4100 spectrometer and are reported in cm^{-1} . NMR spectra were measured on spectrometers operating at 400, 500, or 600 MHz for ^1H and 100, 125, and 150 MHz for ^{13}C NMR spectra. Diffusion-ordered spectroscopy (DOSY) was done on a spectrometer operating at 600 MHz. Routine mass spectrometry was performed using a JEOL AccuTOF electrospray instrument (ESI). Scanning electron microscopy (SEM) was done on Hitachi SU-70 Analytical UHR. Transmission electron microscopy (TEM) was done on JEOL JEM 2100.

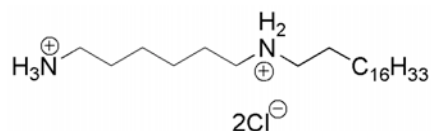
Synthetic Procedures and Characterization Data.



Compound 1. A mixture of azide-CB[7] (**2**, 180 mg, 0.14 mmol) and propargyloxy-CB[6] (**3**, 160 mg, 0.14 mmol), Pericas' catalyst (10 mg, 0.017 mmol), and bisethylimidazolium bromide (133

mg, 0.28 mmol) were dissolved in H_2O (10 mL). The mixture was stirred at $80\text{ }^\circ\text{C}$ for 4-5 days. The reaction solution was poured into MeOH (40 mL) which resulted in a white precipitate. The mixture was centrifuged at 7200 rpm for 5 min. The supernatant was decanted and the precipitate was washed with MeOH (40 mL \times 3) and centrifuged at 7200 rpm for 5 min. The precipitate was dried under high vacuum to give crude complex **1** bisethylimidazolium salt as white powder (283 mg). The crude compound was directly used in the next step. A mixture of crude compound (283 mg) and NH_4PF_6 (68 mg, 0.42 mmol) were dissolved in CH_2Cl_2 (60 mL). The mixture was stirred and refluxed for 3 days. The mixture was centrifuged at 7200 rpm for 5 min. The supernatant was decanted and the precipitate was dried under high vacuum to give crude **1** without bisethylimidazolium salt as white powder (300 mg, 69%). The crude solid was dissolved in a solution of 88% formic acid/1.0 M HCl (1:1, v:v) (5 mL). The solution containing the crude solid was loaded onto a column (3 cm diameter) containing 25 cm Dowex 50WX2 ion-

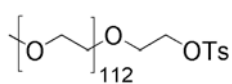
exchange resin pretreated with 88% formic acid/1.0 M HCl (1:1, v:v). The column was eluted with a gradient solvent system (88% formic acid/1.0-6.0 M HCl (1:1, v:v)). The fraction purity was assessed by ^1H NMR using *p*-xylylenediamine (PXDA) as a probe. The appropriate fractions were combined and solvent was removed by rotary evaporation and dried under high vacuum. The yellow solid was then washed with MeOH (40 mL) and centrifuged at 7200 rpm for 5 min. The supernatant was decanted and the precipitate was dried under high vacuum to give compound **1** as a white powder (58 mg, 0.024 mmol, 17.3%). M.p. > 300 °C. IR (KBr, cm^{-1}): 3002w, 2930w, 2332w, 1731s, 1475s, 1420m, 1377m, 1322m, 1295m, 1235s, 1193s, 968m. ^1H NMR (600 MHz, D_2O , 3 equiv. PXDA): 8.16 (s, 1H), 7.62 (d, $J = 8.6$, 1H), 7.48 (s, unbound PXDA), 7.48 (d, $J = 2.4$, 1H), 7.28 (dd, $J = 2.4$ and 8.6, 1H), 6.85 (s, 1H), 6.82 (s, 1H), 6.56 (s, 4H), 6.52 (s, 4H), 5.89 (d, $J = 15.9$, 2H), 5.75-5.40 (m, 38H), 5.33 (s, 2H), 5.28 (d, $J = 9.1$, 2H), 5.21 (d, $J = 9.1$, 2H), 5.15 (d, $J = 9.8$, 2H), 4.99 (d, $J = 9.8$, 2H), 4.56 (d, $J = 15.9$, 2H), 4.49 (t, $J = 6.2$, 2H), 4.41 (s, 2H), 4.39 (s, 2H), 4.30-4.10 (m, 18H), 4.18 (s, unbound **17**), 4.01 (d, $J = 15.1$, 4H), 3.86 (s, 4H), 2.30-2.20 (m, 2H), 2.05-1.95 (m, 2H), 1.67 (s, 3H), 1.05-0.95 (m, 2H). ^{13}C NMR (125 MHz, D_2O , 22 °C, dioxane as internal reference, 3 equiv. *p*-xylylenediammonium ion): 160.0, 157.0, 156.6, 156.6, 156.5, 156.5, 156.4, 156.4, 156.0, 155.7, 155.7, 133.6, 133.6, 132.9, 132.6, 131.3, 129.6, 127.9, 125.7, 123.9, 123.8, 117.0, 116.9, 80.4, 78.6, 71.6, 71.5, 71.4, 71.3, 71.2, 71.2, 71.0, 70.7, 70.0, 69.8, 65.6, 64.4, 64.0, 61.5, 53.2, 52.9, 52.6, 52.5, 52.3, 51.4, 50.9, 50.0, 49.2, 48.8, 42.7, 42.4, 41.6, 28.6, 27.2, 19.0, 14.6 (only 56 of the 74 resonances expected were observed). HR-MS: m/z 891.3204 ($[\mathbf{1}\cdot\text{PXDA}_2]^{3+}$, calcd. for $[\text{C}_{92}\text{H}_{90}\text{N}_{55}\text{O}_{27}\cdot(\text{C}_8\text{H}_{14}\text{N}_2)]^{3+}$, 891.3233).



Compound 4b. 1-Bromooctadecane (3.30 g, 10 mmol) and 1,6-hexanediamine (11.6 g, 100 mmol) were dissolved into acetonitrile (100 mL) and heated at 35 °C for 12 h under

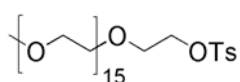
magnetic stirring. After cooling to room temperature and evaporating solvent, the crude product was stirred in water (100 mL) for 10 min. Then the product was filtered and washed with water to give a white solid. The white solid was dissolved in acetone (100 mL) and then aqueous HCl solution (3 M, 20 mL) was added to give a precipitate which was filtered and dried to give compound **4b** as a white solid (4.2 g, 95%). M. p. 268–272 °C. IR (KBr, cm^{-1}): 2951s, 2918s, 2844s, 2787s, 2562m, 2448m, 2020w, 1042w, 785w, 725w. ^1H NMR (400 MHz, D_2O , RT):

2.95–3.01 (m, 6H), 1.60–1.70 (m, 6H), 1.20–1.42 (m, 34H), 0.84 (t, $J = 6.8$ Hz, 3H). ^{13}C NMR (125 MHz, D_2O , RT, dioxane as internal reference): 47.0, 43.4, 39.0, 31.2, 29.2, 29.0, 28.9, 28.7, 28.4, 26.0, 25.9, 25.1, 24.9, 24.9, 24.7, 21.9, 13.2. HR-MS: m/z 369.4185 ($[\mathbf{4} - 2\text{Cl} - \text{H}]^+$), calcd. for $[\text{C}_{24}\text{H}_{53}\text{N}_2]^+$, 369.4203).



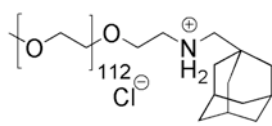
Compound S1. Poly(ethylene glycol) methyl ether ($M_n = 5000$, 10.0 g, 2 mmol) and *p*-toluenesulfonyl chloride (3.8 g, 20 mmol) were dissolved in

dichloromethane (100 mL) under nitrogen atmosphere and cooled in an ice-water bath. Then triethylamine (3.0 mL, 21.5 mmol) was added dropwise. The resulting solution was stirred for 24 h. After that, the reaction mixture was washed with aqueous HCl solution (1 M, 100 mL \times 2) and water (100 mL \times 2). The organic layer was dried over anhydrous Na_2SO_4 and the solvent was removed to give a crude product. The crude product was dissolved in dichloromethane (25 mL) and poured into Et_2O (250 mL) to give compound **S1** as a white solid (6.2 g, 60%). The spectroscopic data matches that reported in the literature.³



Compound S2. Poly(ethylene glycol) methyl ether ($M_n = 750$, 1.5 g, 2 mmol) and *p*-toluenesulfonyl chloride (3.8 g, 20 mmol) were dissolved in

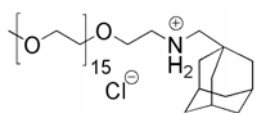
dichloromethane (10 mL) under nitrogen atmosphere and cooled in an ice-bath. Then triethylamine (3.0 mL, 21.5 mmol) was added and the reaction mixture was stirred for 24 h. After that, the reaction mixture was washed with aqueous HCl solution (1 M, 100 mL \times 2) and water (100 mL \times 2). The organic layer was dried over anhydrous Na_2SO_4 and the solvent was removed by rotary evaporation to give a crude product. The crude product was dissolved in water (25 mL) and washed with Et_2O (20 mL \times 3). The aqueous phase was collected, dried over anhydrous Na_2SO_4 and concentrated to give compound **S2** as a colorless liquid (1.2 g, 68%). The spectroscopic data matches that reported in the literature.



Compound 5b. Compound **S1** (1.03 g, 0.2 mmol) and 1-adamantanemethylamine (0.13 g, 0.8 mmol) were dissolved in DMF (10 mL). Triethylamine (0.22 mL, 1.6 mmol) was added and the reaction

mixture was stirred at 70 °C for 12 h. Then the reaction mixture was poured into Et_2O (80 mL) to give a white precipitate which was collected and purified by flash column chromatography (SiO_2 ,

CHCl₃:CH₃OH:NH₃•H₂O = 10:1:0.1) to give the free base which was dissolved in water, treated with conc. HCl and concentrated to give compound **5** as a white solid (0.48 g, 46%). M.p. 54–56 °C. IR (KBr, cm⁻¹): 2915m, 2883w, 2740w, 2687w, 1149m, 1103s, 1056w, 960w, 842w. ¹H NMR (400 MHz, D₂O, 22 °C): 3.88 (t, *J* = 3.4 Hz, 4H), 3.58–3.85 (m, 596H), 3.52 (t, *J* = 3.4 Hz, 4H), 3.38 (s, 4H), 3.28 (t, *J* = 4.9 Hz, 2H), 2.80 (s, 2H), 2.01 (s, 3H), 1.73–1.77 (m, 3H), 1.59–1.67 (m, 9H). ¹³C NMR (125 MHz, CDCl₃, RT): 72.7, 72.1, 70.7, 70.5, 61.9, 59.2, 40.2, 36.5, 28.1.



Compound 5c. Compound **S2** (0.52 g, 0.80 mmol) and 1-adamantanemethylamine (0.53 g, 3.2 mmol) were first dissolved in DMF (4 mL). Triethylamine (0.90 mL, 6.4 mmol) was added and the reaction

mixture was stirred at 70 °C for 12 h. Then the reaction mixture was poured into dichloromethane (30 mL) and washed with 1 M aqueous HCl solution (30 mL × 2) and water (30 mL × 2). The organic layer was collected, dried over anhydrous Na₂SO₄ and purified by flash column chromatography (SiO₂, CHCl₃:CH₃OH:NH₃•H₂O = 10:1:0.1) to give the free base which was dissolved in water, treated with conc. HCl and concentrated to give to give compound **6** as a colorless liquid (0.32 g, 58%). ¹H NMR (400 MHz, D₂O, 22 °C): 3.50–3.86 (m, 58H), 3.36 (s, 3H), 2.93 (t, *J* = 5.0 Hz, 2H), 2.46 (s, 2H), 1.96 (s, 3H), 1.70–1.74 (m, 3H), 1.61–1.65 (m, 3H), 1.50–1.58 (m, 6H). ¹³C NMR (125 MHz, D₂O, RT, dioxane as internal reference): 70.6, 69.1, 68.9, 60.0, 57.6, 48.1, 39.3, 35.9, 31.9, 27.5.

References:

1. B. Vinciguerra, L. Cao, J. R. Cannon, P. Y. Zavalij, C. Fenselau and L. Isaacs, *J. Am. Chem. Soc.* 2012, **134**, 13133–13140.
2. L. Cao, L. Isaacs, *Org. Lett.* 2012, **14**, 3072–3075.
3. C. Hua, S.-M. Peng, C.-M. Dong, *Macromolecules* 2008, **41**, 6686–6695.

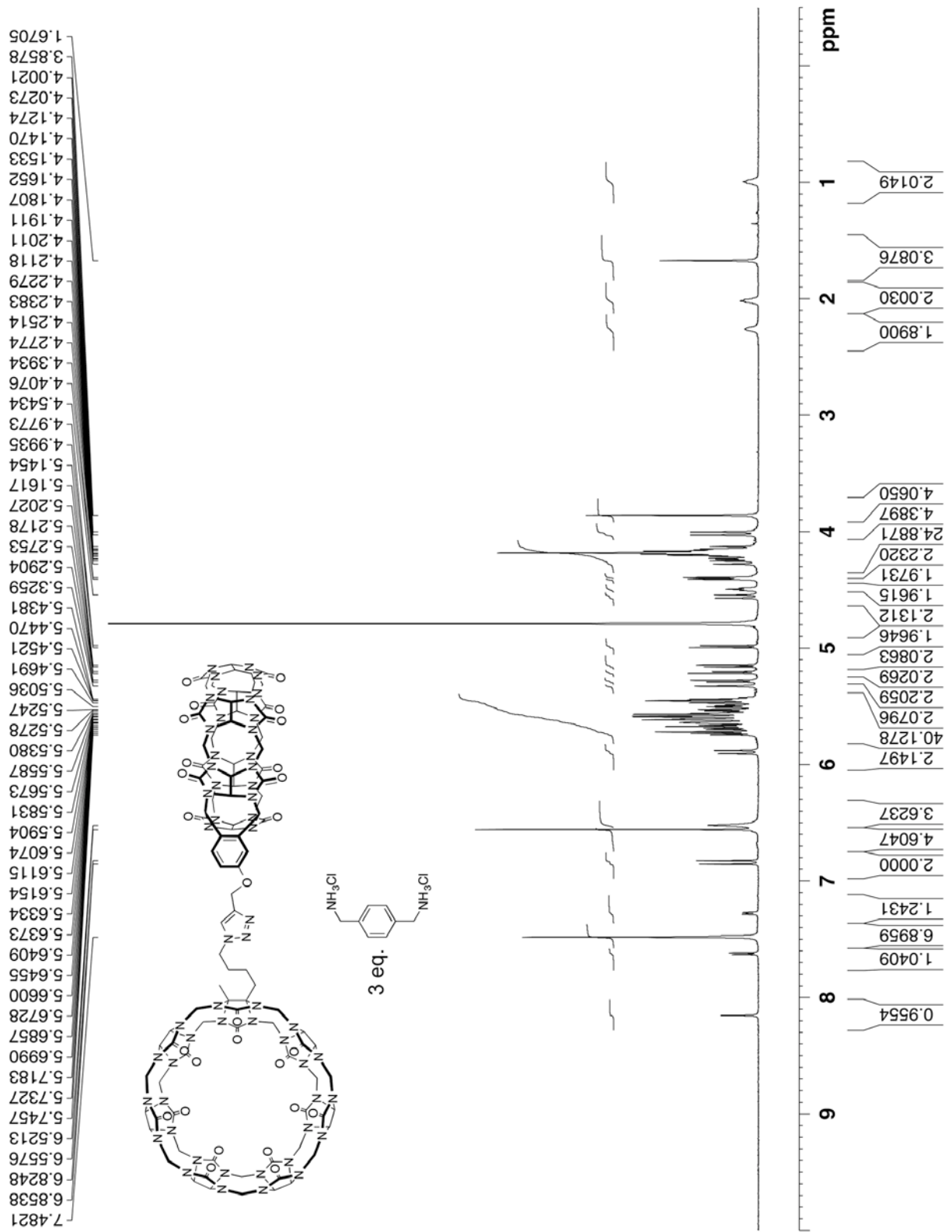


Figure S1. ¹H NMR spectrum recorded (600 MHz, D₂O, RT) for a mixture of **1** and excess PXDA.

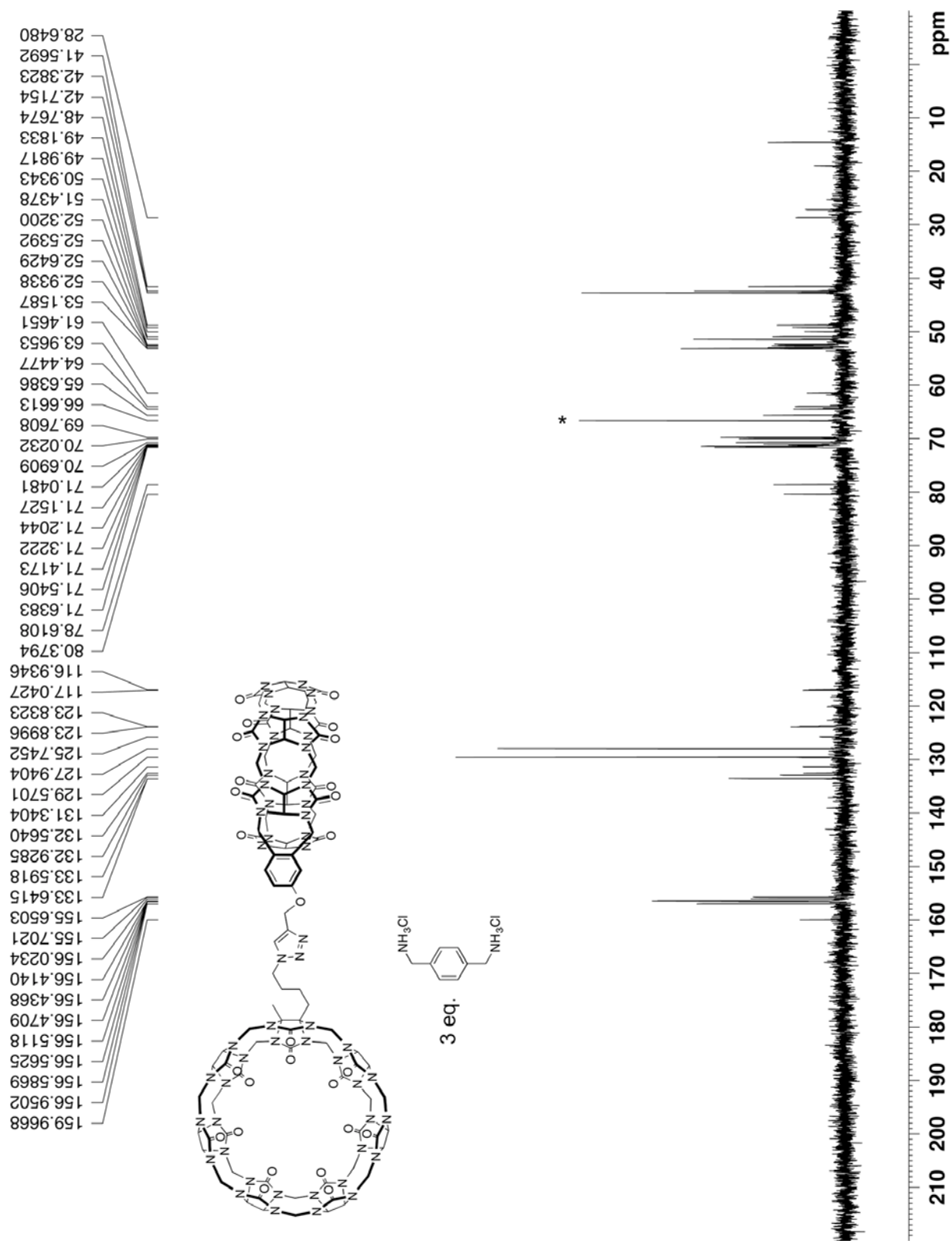


Figure S2. ^{13}C NMR spectrum recorded (125 MHz, D_2O , RT) for a mixture of **1** and excess PXDA. Internal reference = dioxane (*)

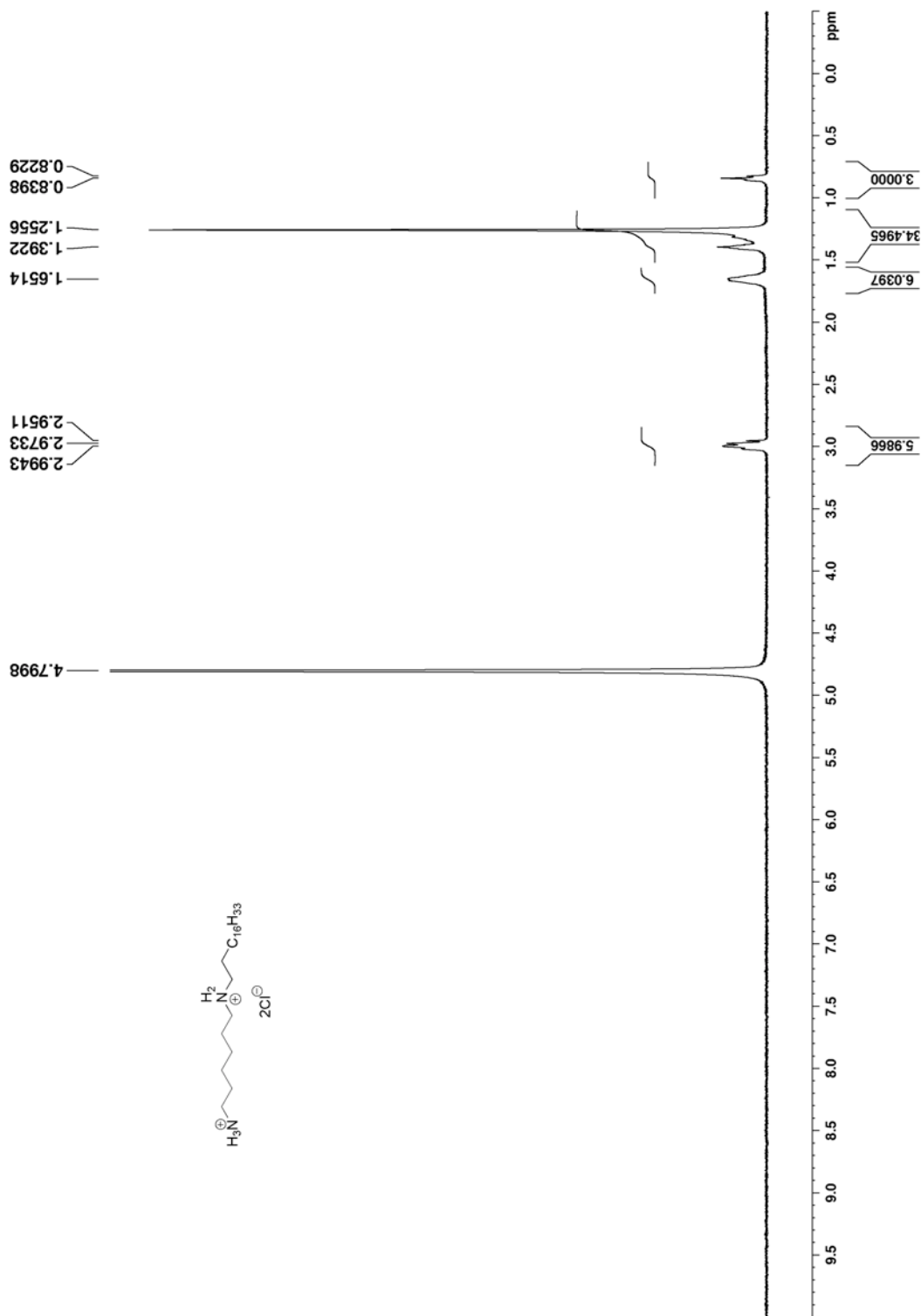


Figure S3. ^1H NMR spectrum recorded (400 MHz, D_2O , 22°C) for **4b**.

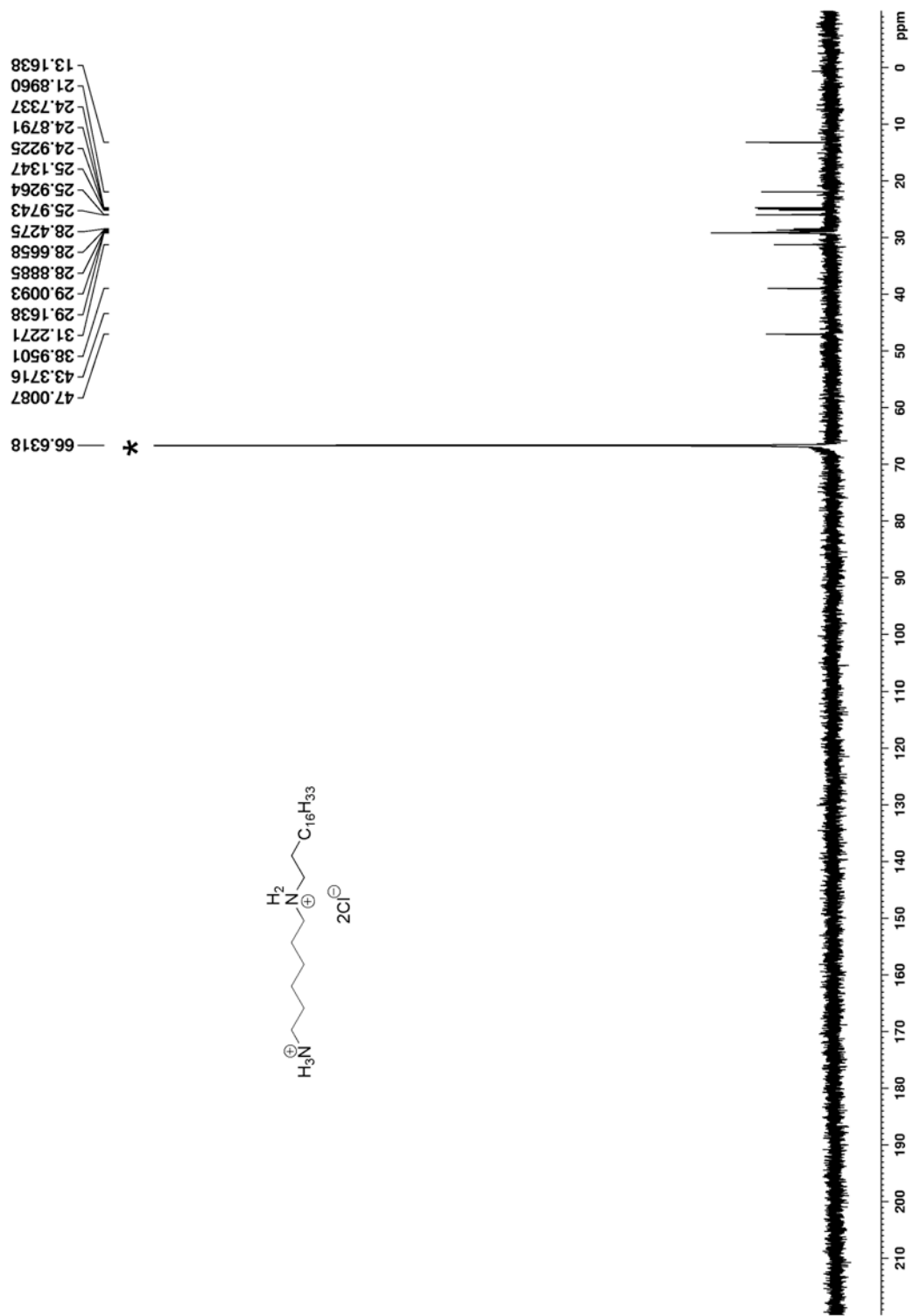


Figure S4. ^{13}C NMR spectrum recorded (125 MHz, D_2O , RT) for **4b**. Internal reference = dioxane (*).

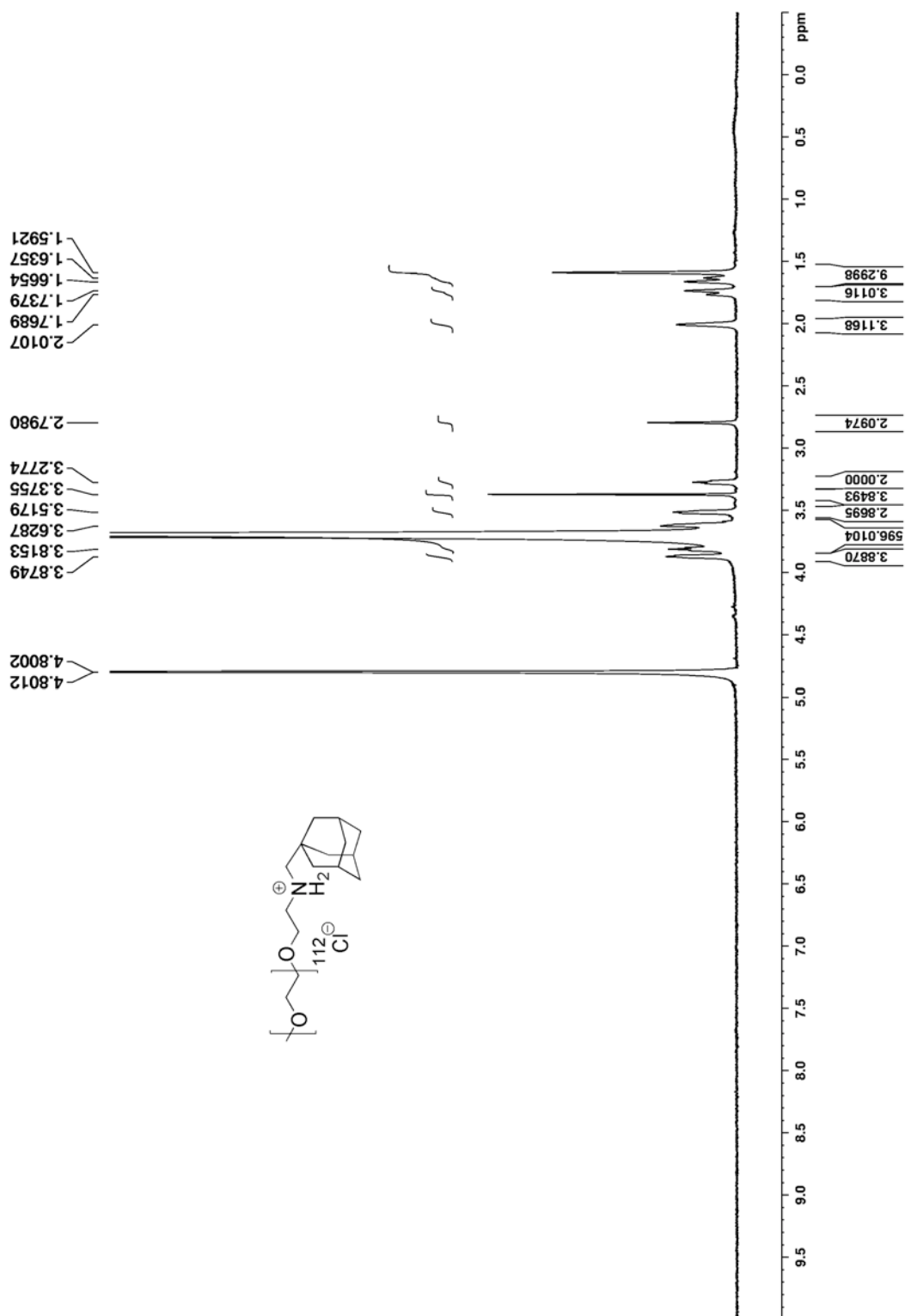


Figure S5. ^1H NMR spectrum recorded (400 MHz, D_2O , RT) for **5b**.

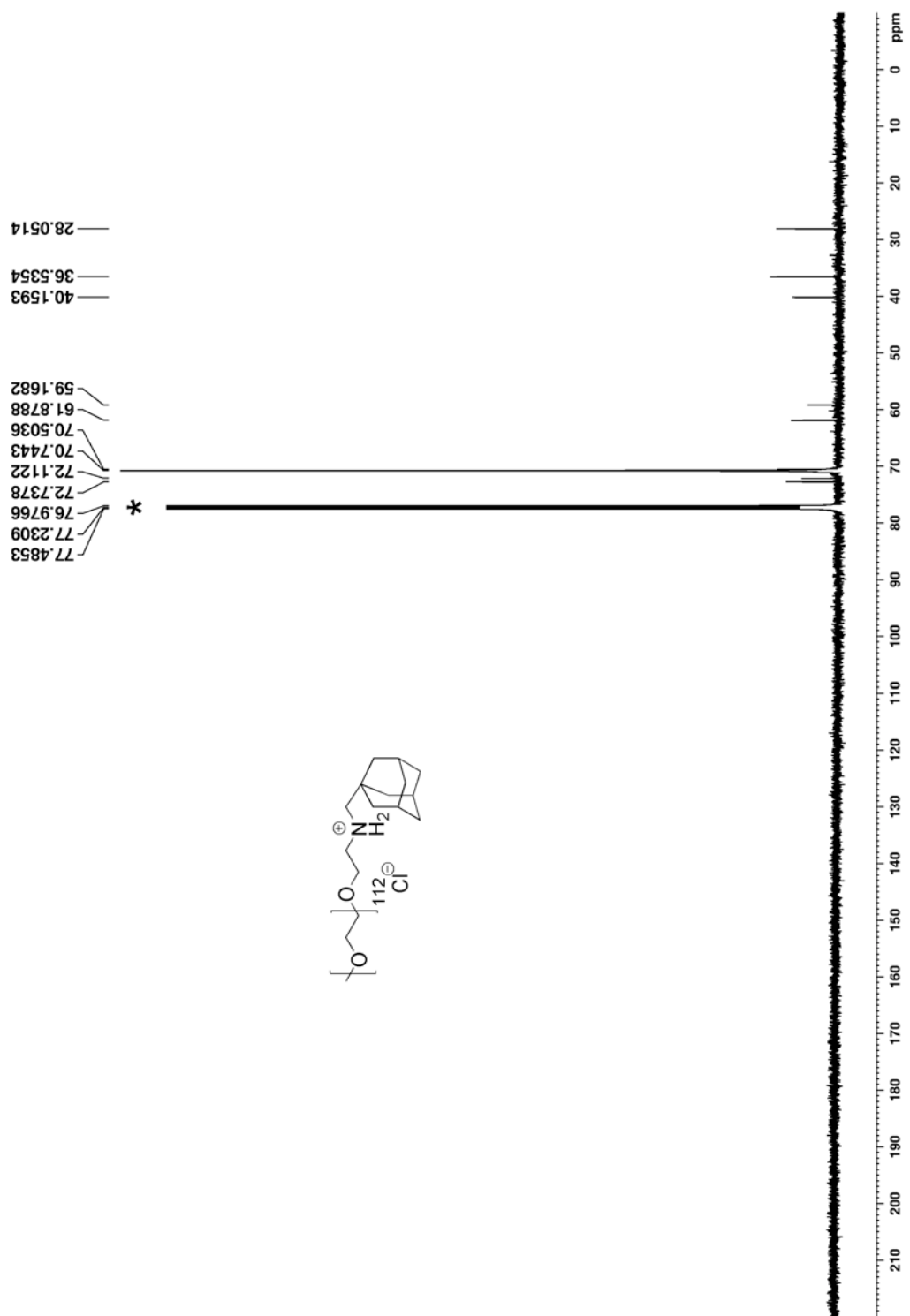


Figure S6. ¹³C NMR spectrum recorded (125 MHz, CDCl₃, RT) for **5b**. Ref. = chloroform (*)

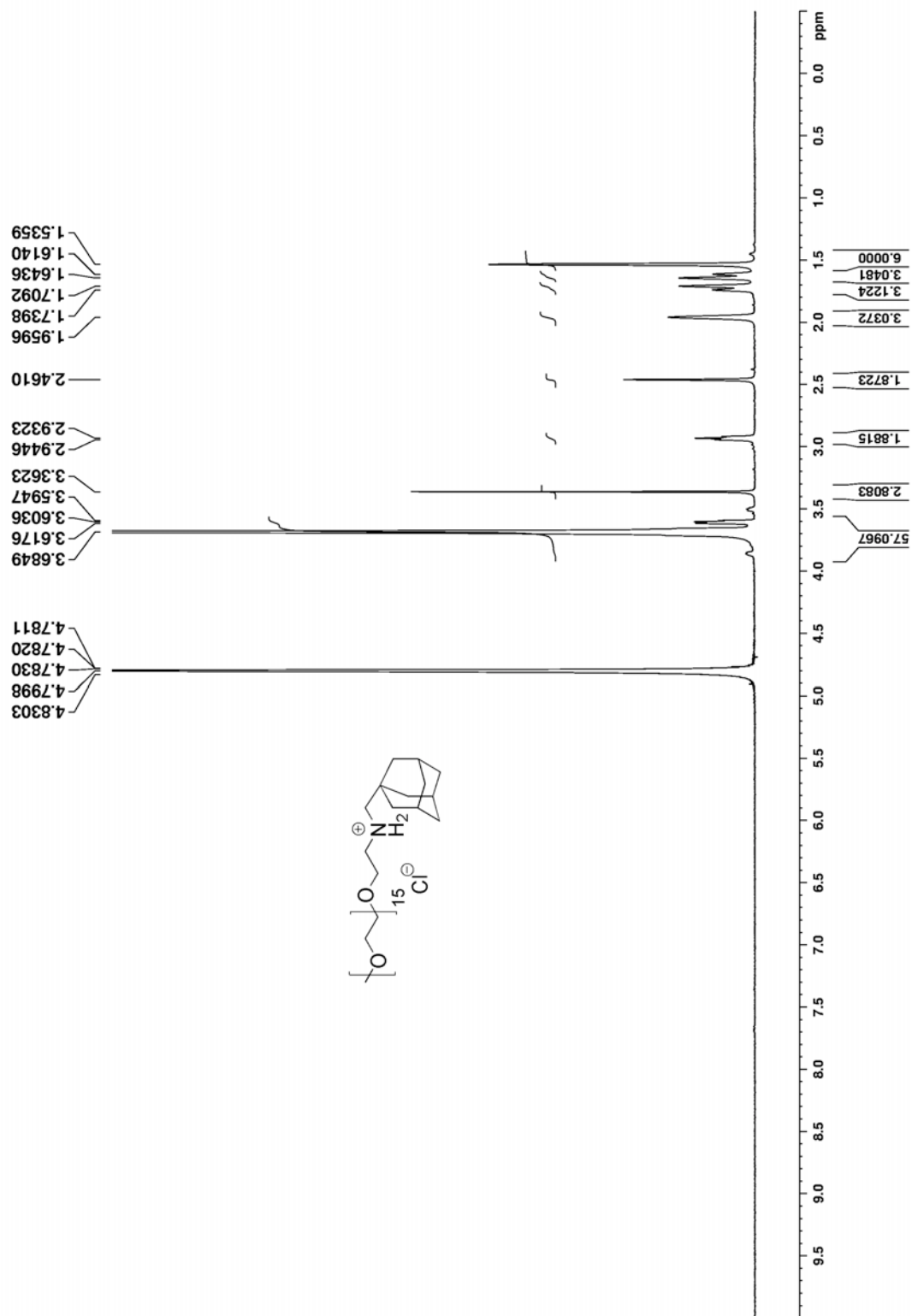


Figure S7. ¹H NMR spectrum recorded (400 MHz, D₂O, RT) for 5c.

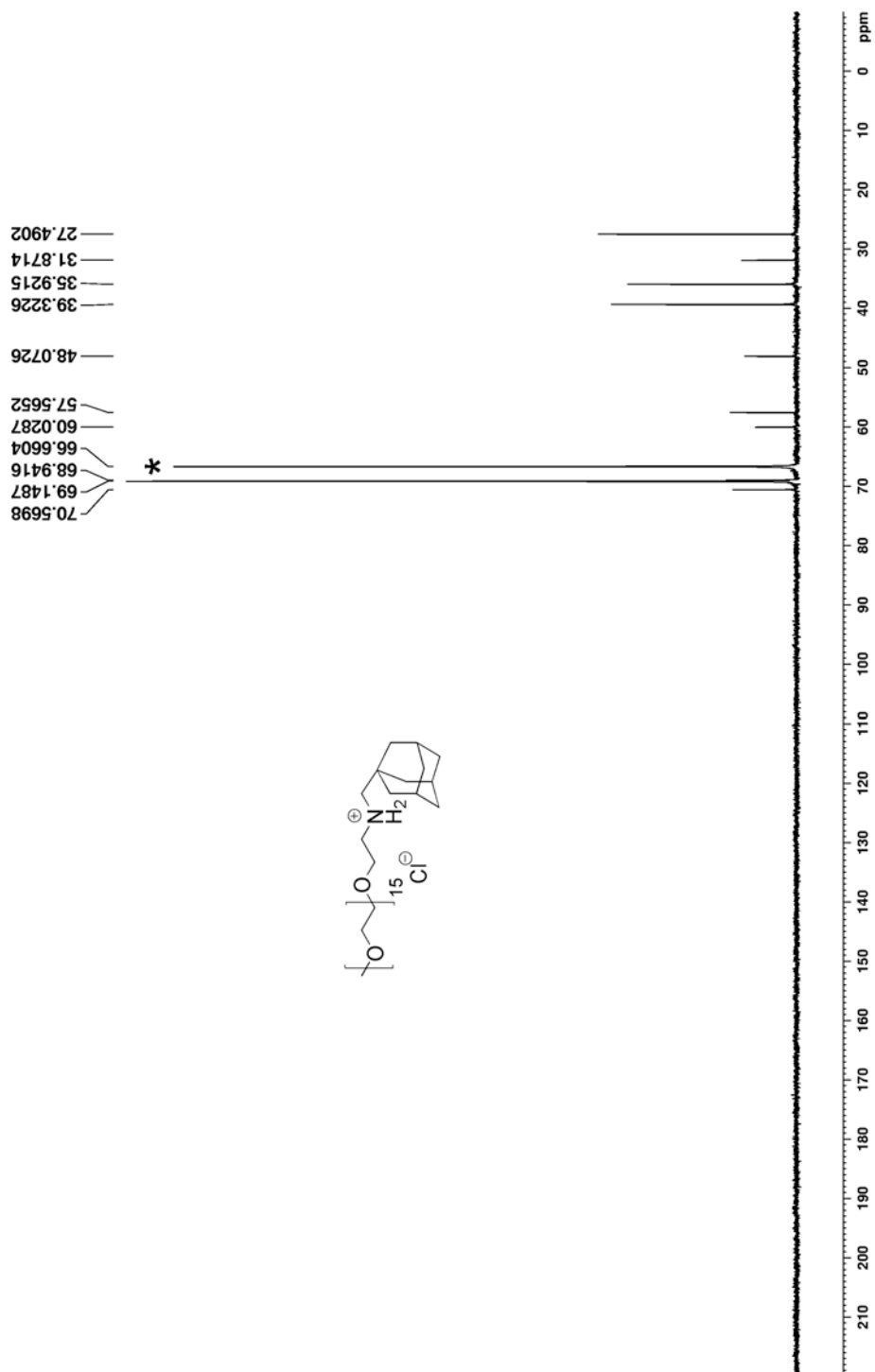


Figure S8. ^{13}C NMR spectrum recorded (125 MHz, D_2O , RT) for **5c**. Internal ref = dioxane (*).

Binding Study by ^1H NMR.

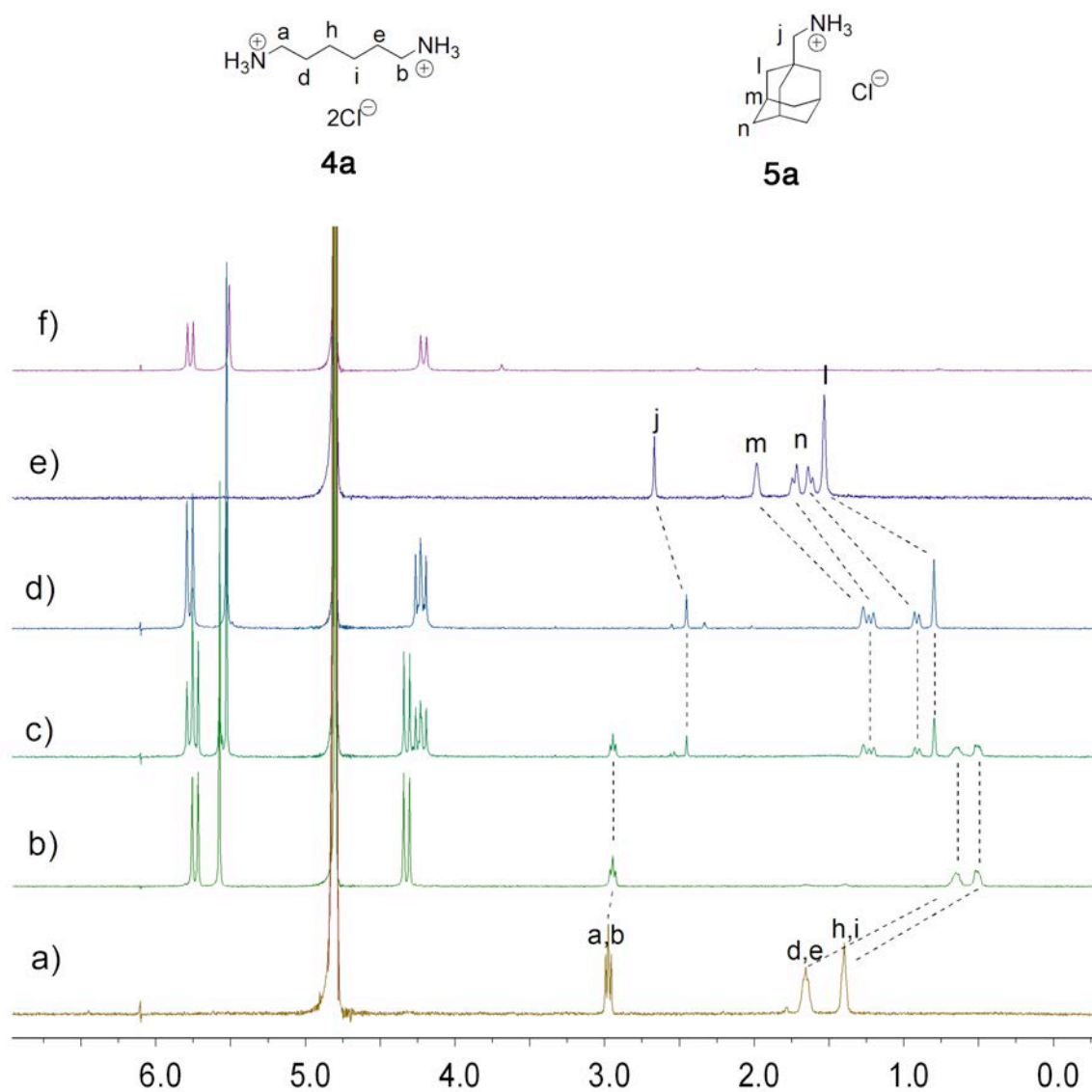


Figure S9. Partial ^1H NMR (400 MHz, D_2O , RT) of a) CB[6]; b) hexanediammonium **4a**; c) 1.0 mM CB[6] and hexanediammonium **4a**; d) 1.0 mM CB[6], CB[7], hexanediammonium **4a** and adamantylammonium **5a**; e) 1.0 mM CB[7] and adamantylammonium **5a**; f) adamantylammonium **5a** and g) CB[7].

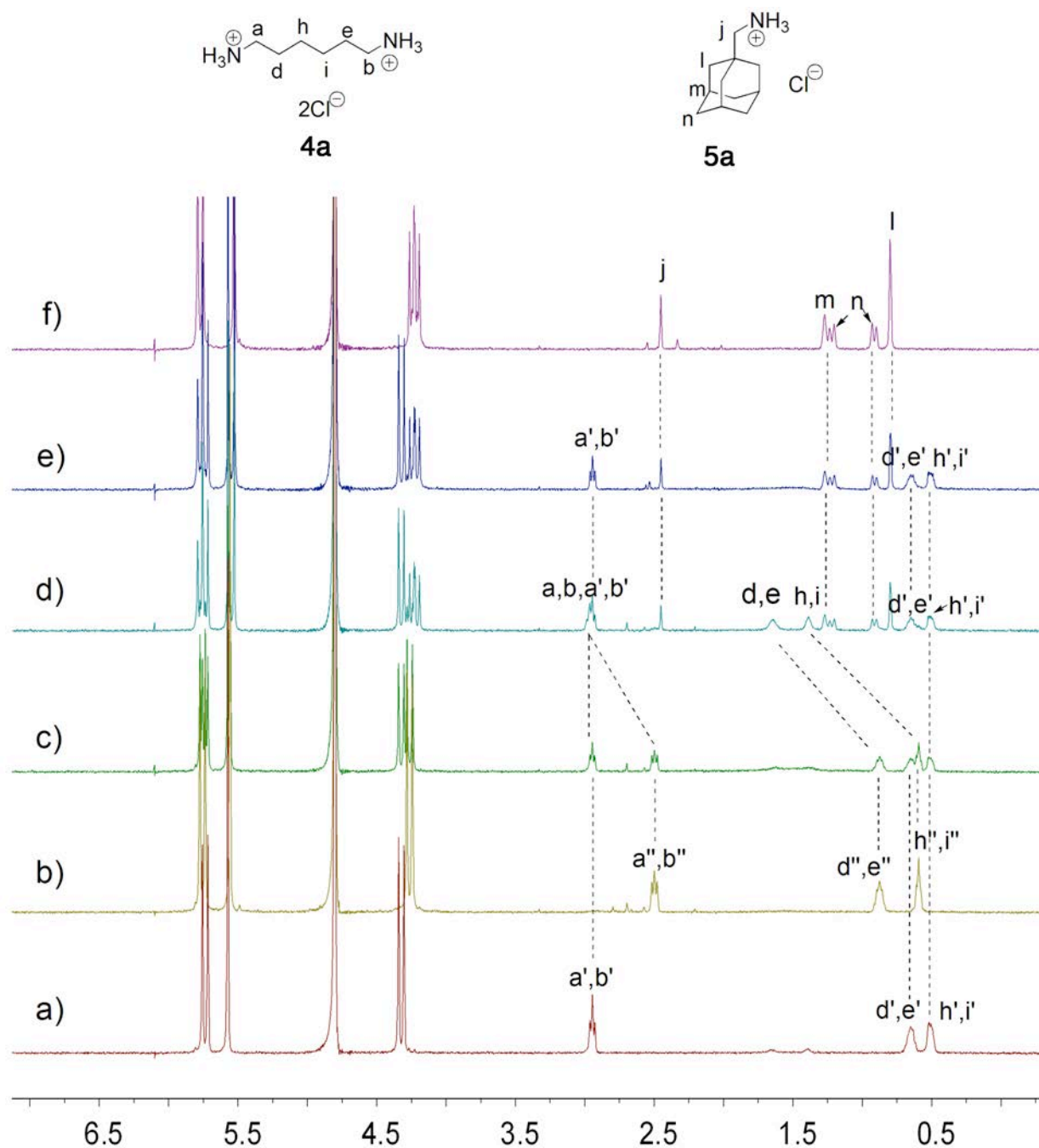


Figure S10. Partial ^1H NMR (400 MHz, D_2O , RT) of a) 1.0 mM CB[6] and hexanediammonium **4a**; b) 1.0 mM CB[7] and hexanediammonium **4a**; c) 1.0 mM CB[6], CB[7] and 2.0 mM hexanediammonium **4a**; d) 1.0 mM CB[6], CB[7], 2.0 mM hexanediammonium **4a** and 1.0 mM adamantanemethylammonium **5a**; e) 1.0 mM CB[6], CB[7], hexanediammonium **4a** and adamantanemethylammonium **5a**; f) 1.0 mM CB[7] and adamantanemethylammonium **5a**. Here “'” and “''” denote protons binding with CB[6] and CB[7], respectively.

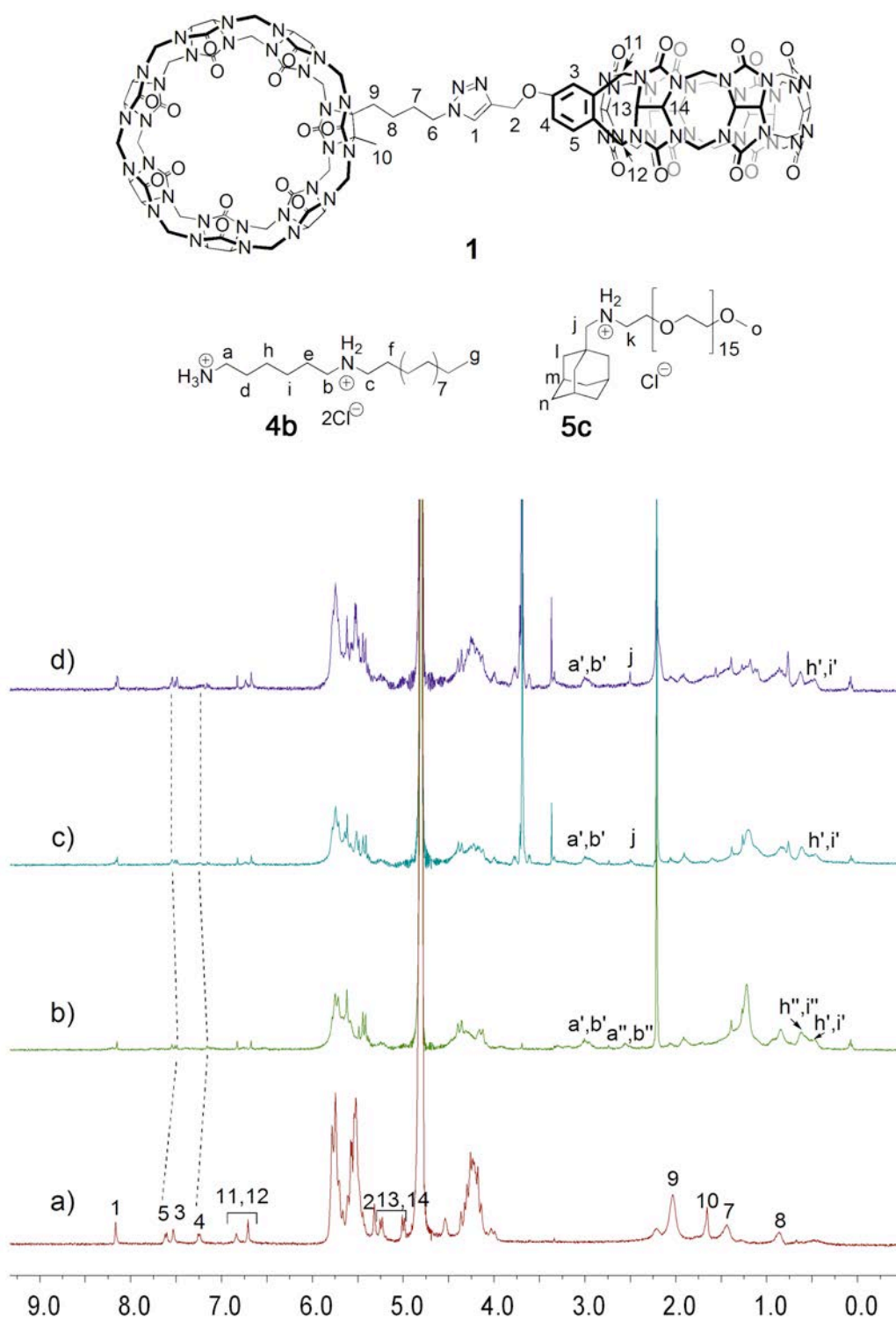


Figure S11. Partial ^1H NMR spectra (400 MHz, D_2O , 22 °C): a) CB[6]/CB[7] heterodimer **1**; b) 0.5 mM **1** and 1.0 mM **4b**; c) 0.5 mM **1**, 1.0 mM **4b** and 0.5 mM **5c**; d) 0.5 mM **1**, **4b** and **5c**. Here “i'” and “i''” denote protons binding with CB[6] and CB[7] moieties, respectively.

Microscopy Images.

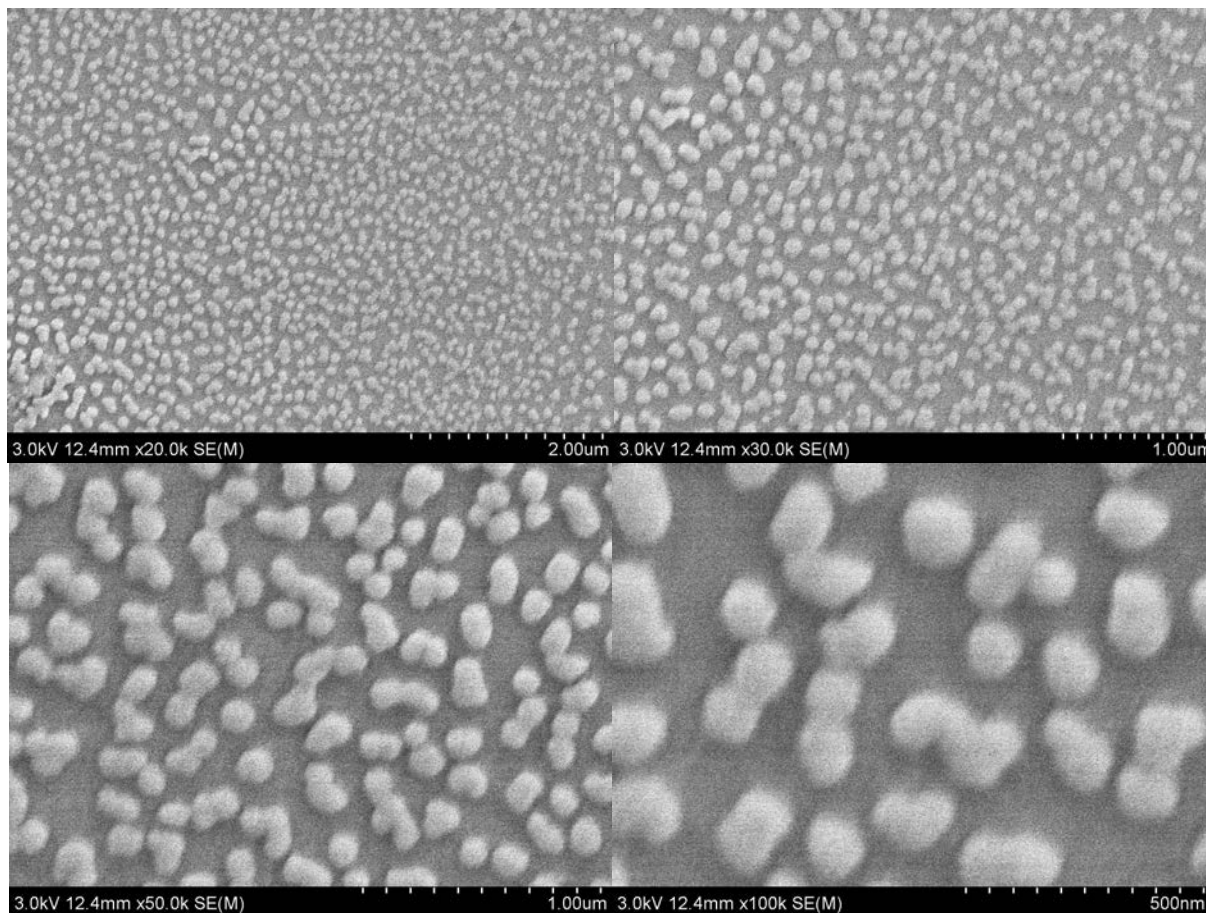


Figure S12. Scanning electron microscopy (SEM) images of 0.01 mM heterodimer **1**, hexanediamine derivative **4b** and adamantanemethylamine derivative **5b**.

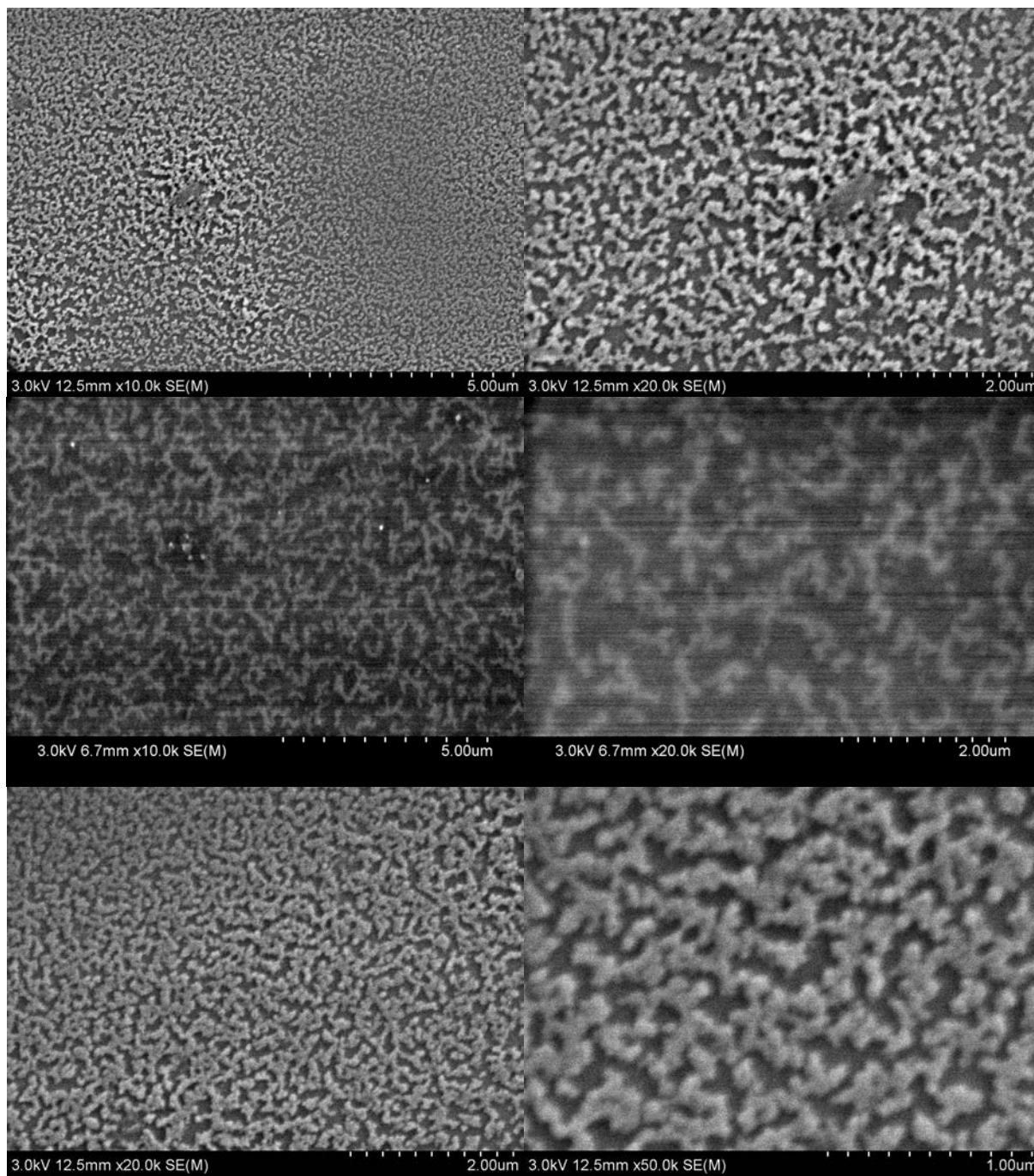


Figure S13. SEM images of 0.01 mM heterodimer **1** and 0.02 mM hexanediammonium **4b**.

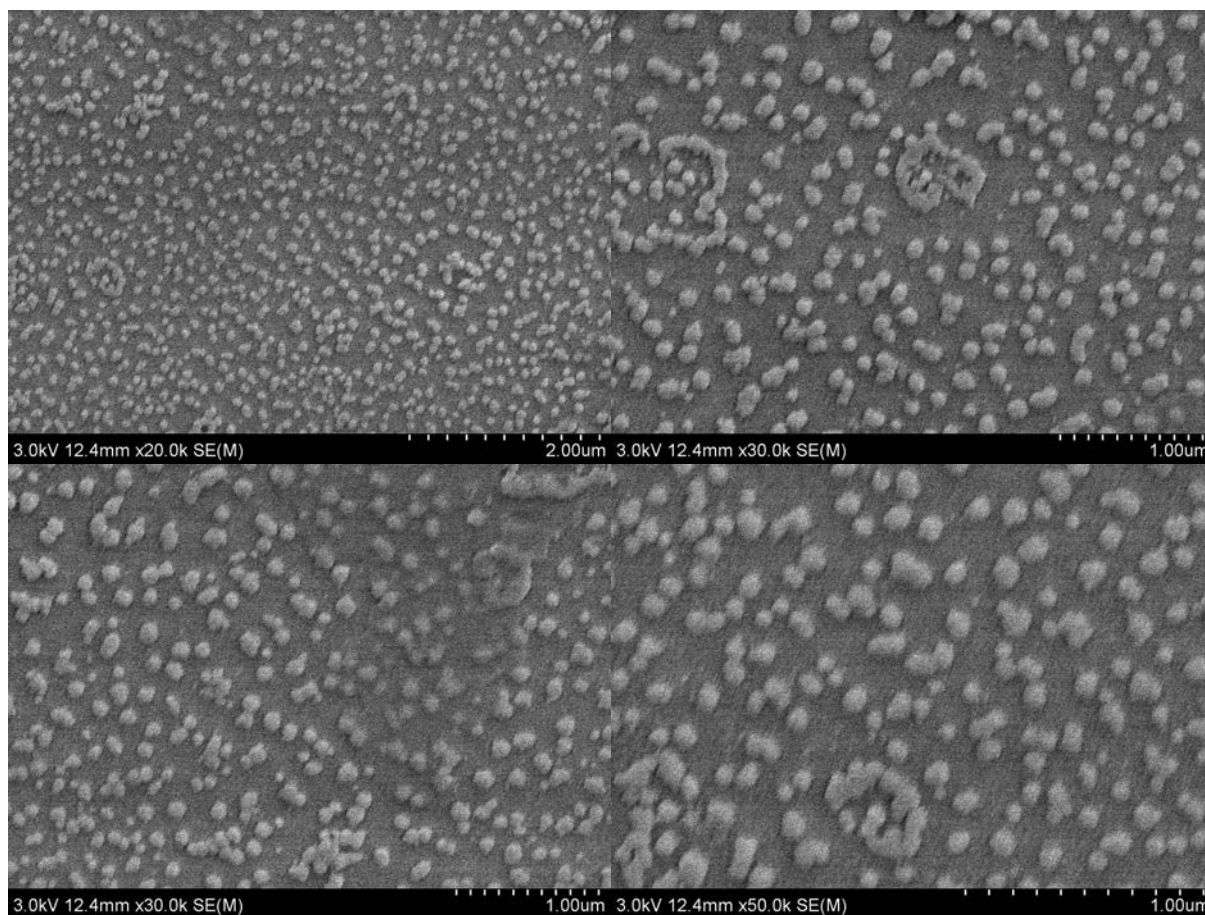


Figure S14. SEM images of 0.01 mM heterodimer **1**, 0.02 mM hexanediammonium derivative **4b** and 0.01 mM adamantanemethylammonium derivative **5b**.

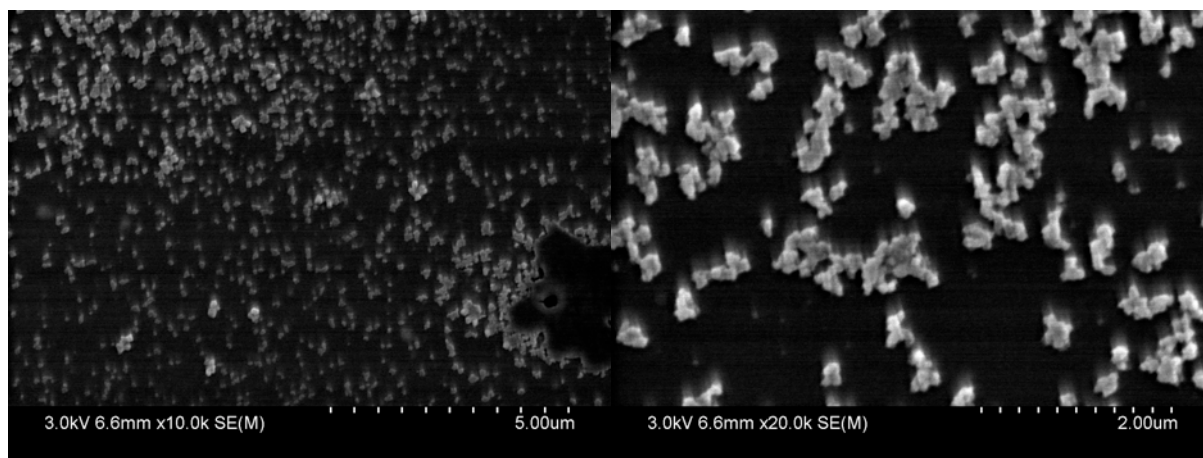


Figure S15. SEM images of 0.01 mM heterodimer **1**, hexanediammonium derivative **4b** and adamantanemethylammonium derivative **5c**.

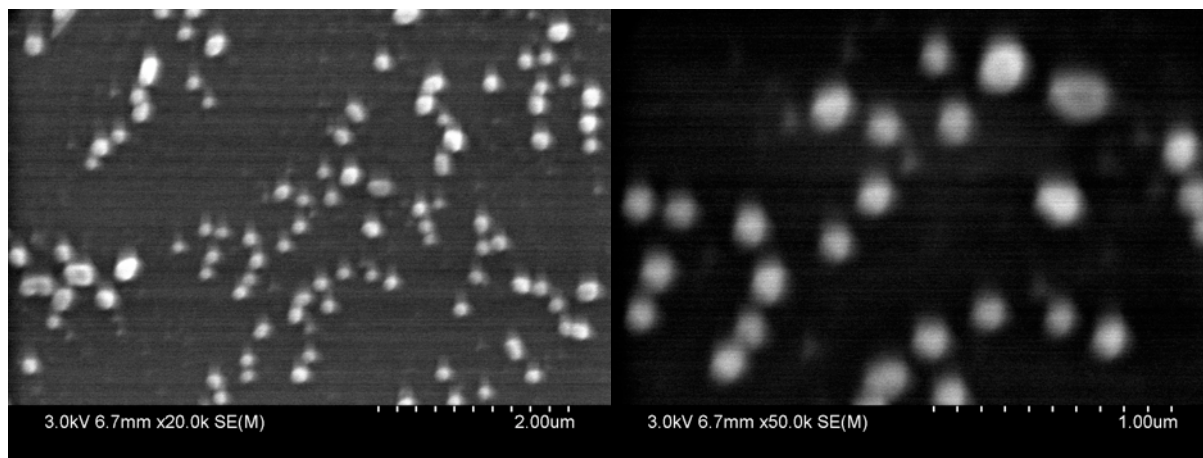


Figure S16. SEM images of 0.01 mM heterodimer **1**, 0.02 mM hexanediammonium derivative **4b** and 0.01 mM adamantanemethylammonium derivative **5c**.

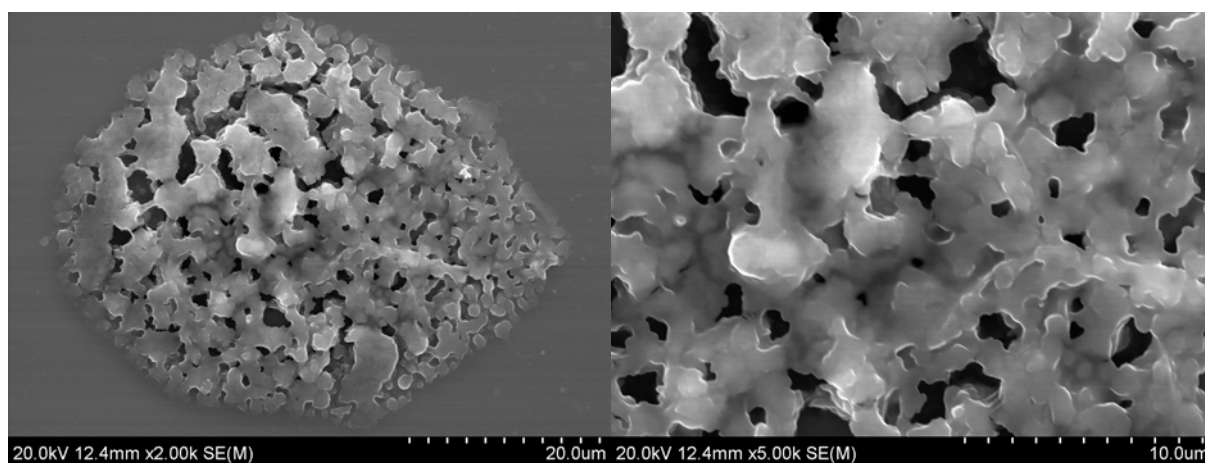


Figure S17. SEM images of 0.01 mM heterodimer **1** and adamantanemethylammonium **5b**.

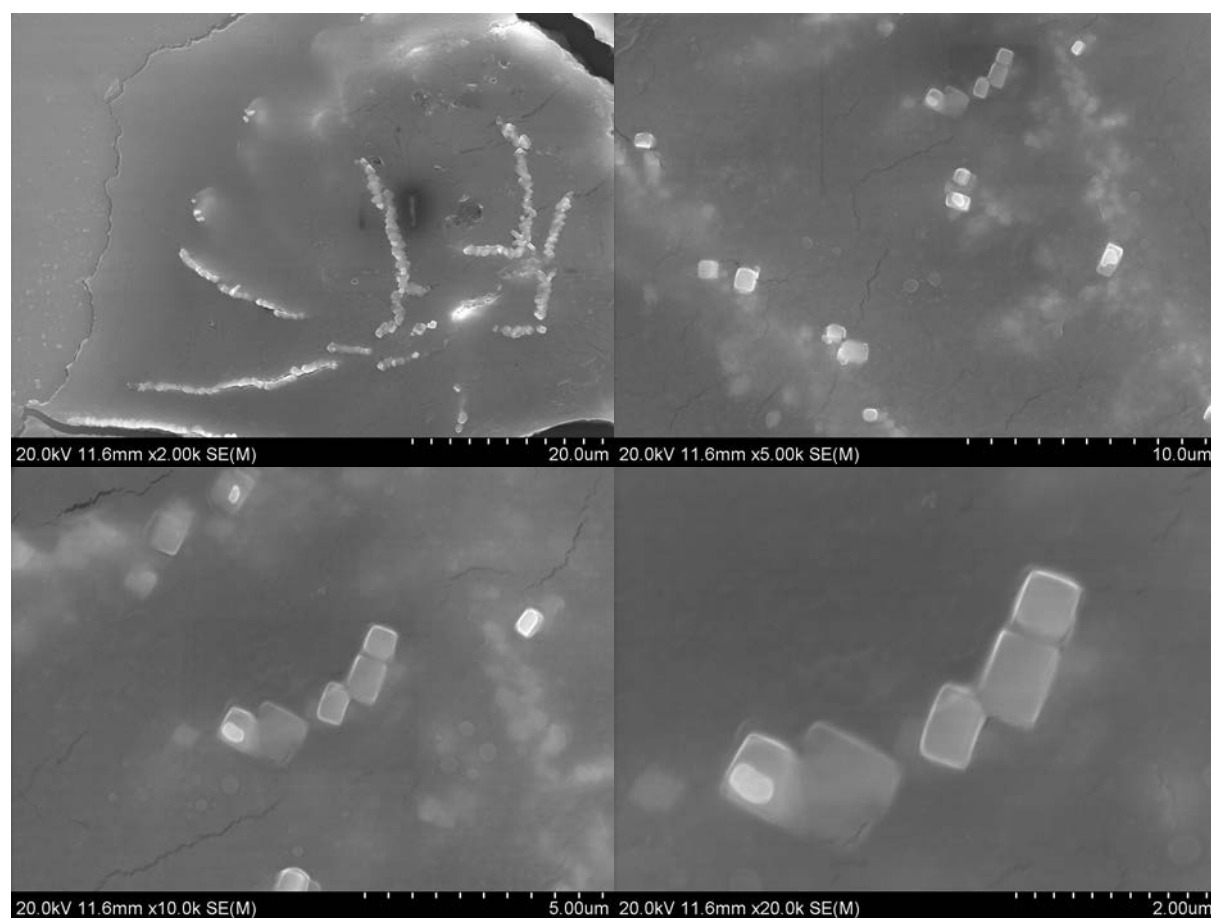


Figure S18. SEM images of 0.01 mM heterodimer **1** and 0.02 mM hexanediammonium **4a**.

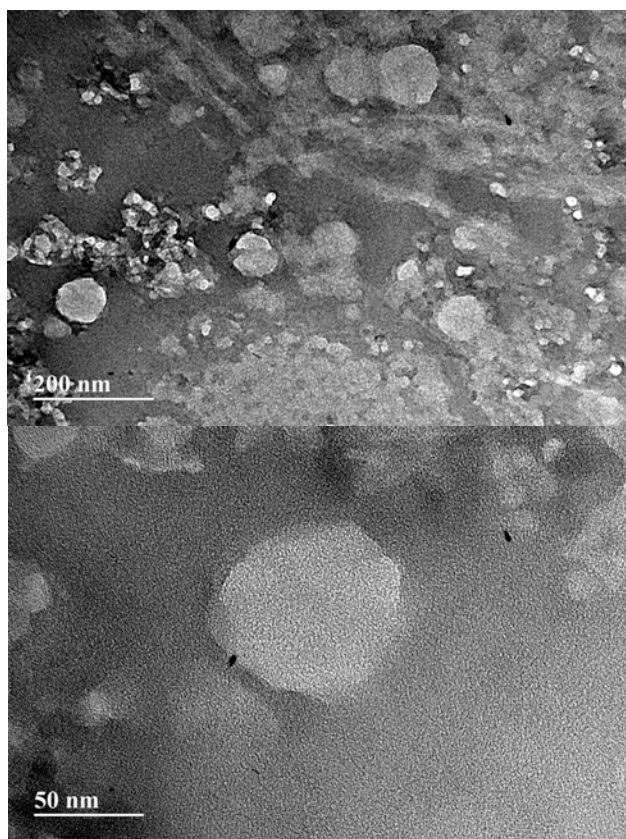


Figure S19. Transmission electron microscope (TEM) images of 0.01 mM heterodimer **1**, hexanediammonium derivative **4b** and adamantanemethylammonium derivative **5b**.

DOSY Data.

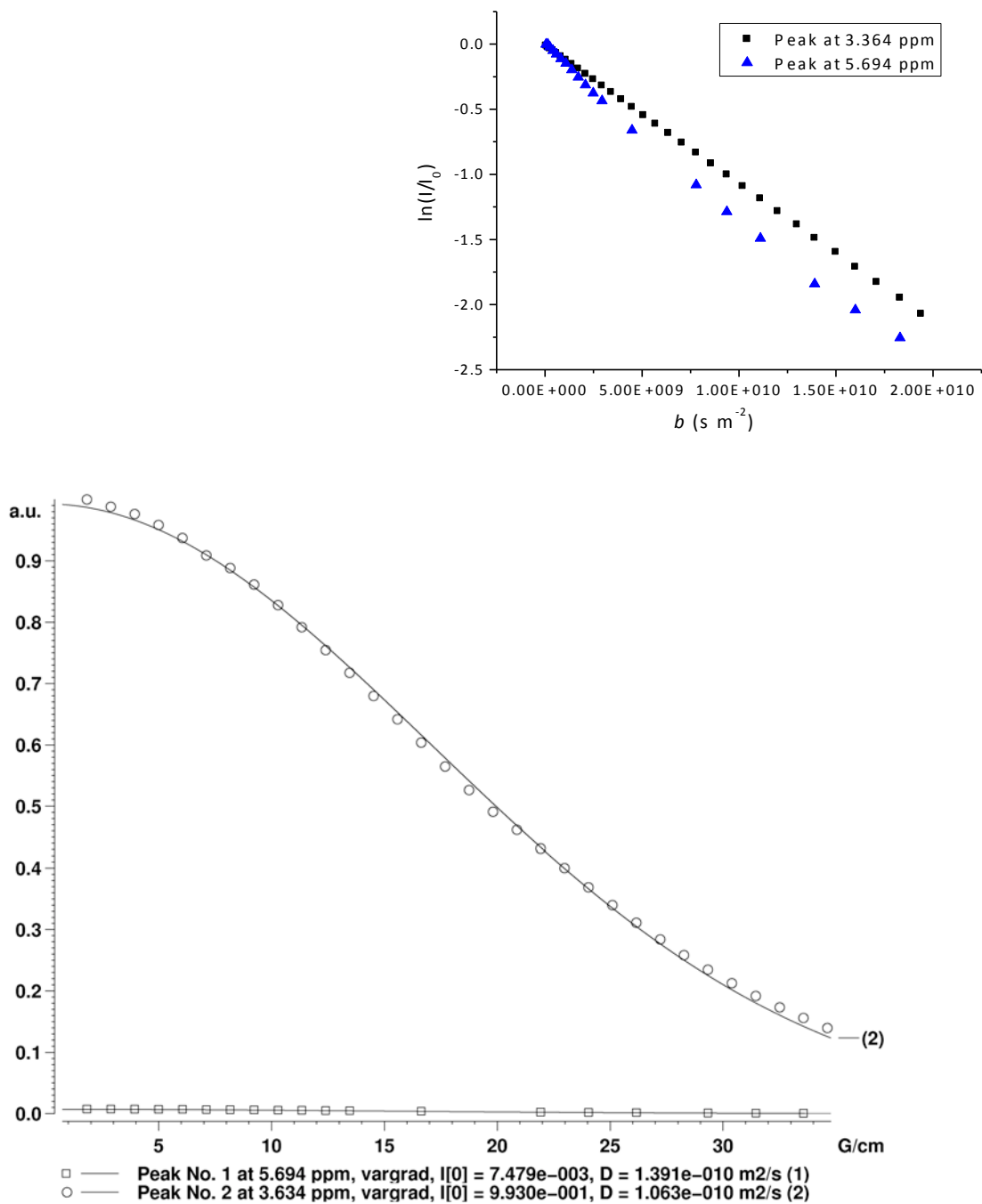


Figure S20. Plots of the change in intensity of the indicated NMR resonances in the DOSY spectra as a function of magnetic field gradient recorded (600 MHz, D₂O, 298 K) for 0.5 mM heterodimer **1**, hexanediammonium derivative **4b** and adamantanemethylammonium derivative **5b**. Top inset: linearized form.

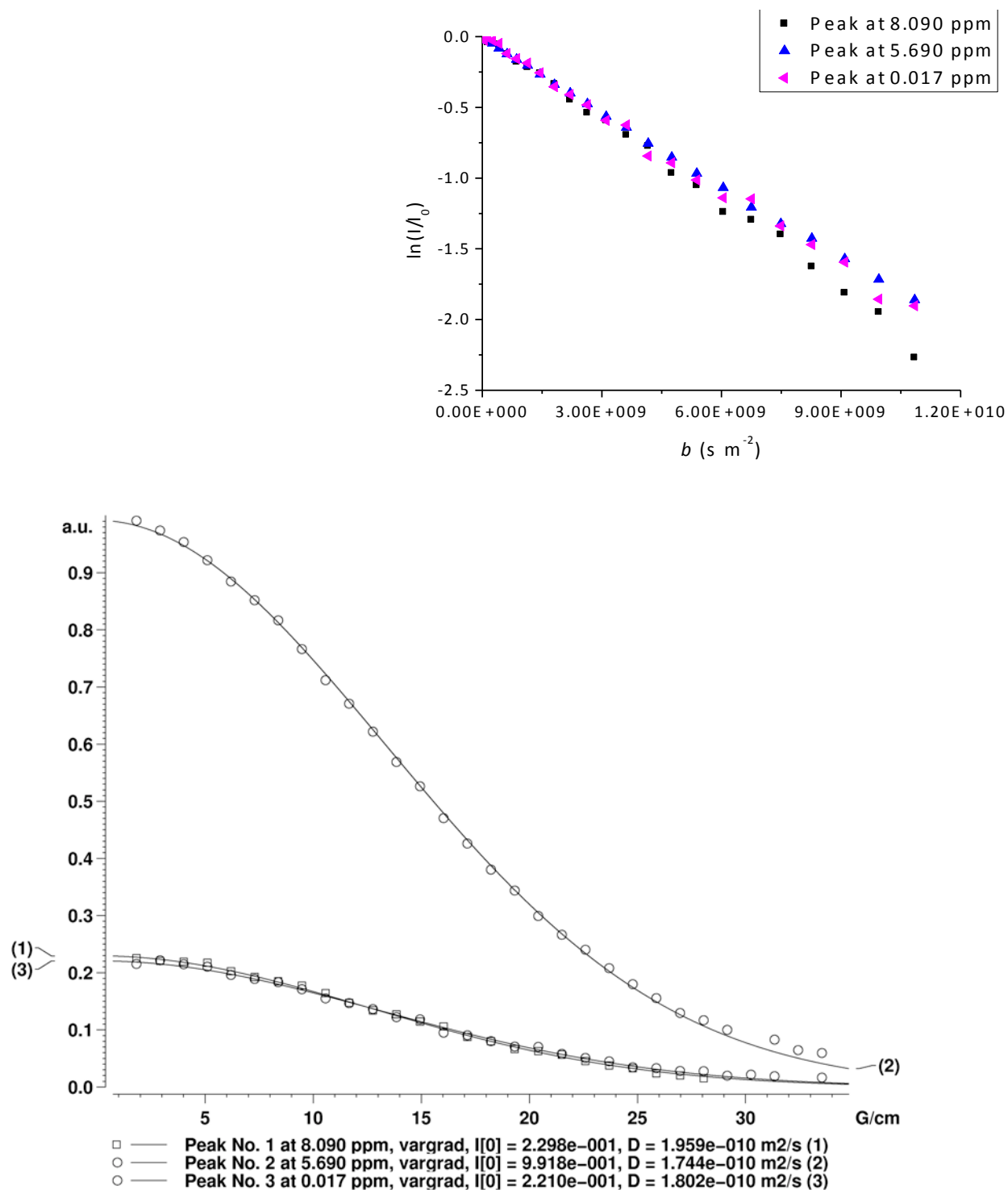


Figure S21. Plots of the change in intensity of the indicated NMR resonances in the DOSY spectra as a function of magnetic field gradient recorded (600 MHz, D_2O , 298 K) for 0.5 mM heterodimer **1**, and 1.0 mM hexanediammonium derivative **4b**. Top inset: linearized form.

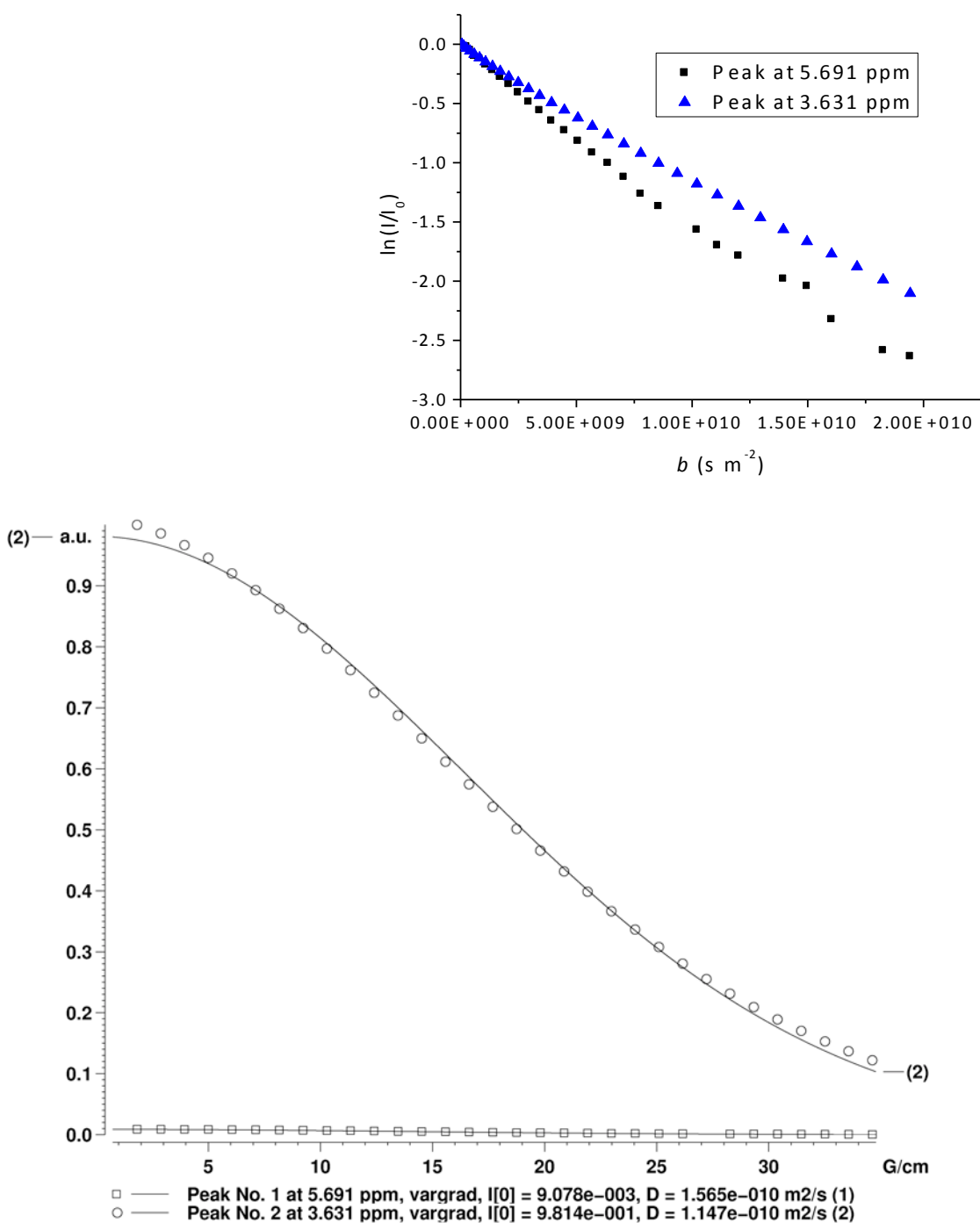


Figure S22. Plots of the change in intensity of the indicated NMR resonances in the DOSY spectra as a function of magnetic field gradient recorded (600 MHz, D_2O , 298 K) for 0.5 mM heterodimer **1**, 1.0 mM hexanediammonium derivative **4b** and 0.5 mM adamantanemethylammonium derivative **5b**. Top inset: linearized form.

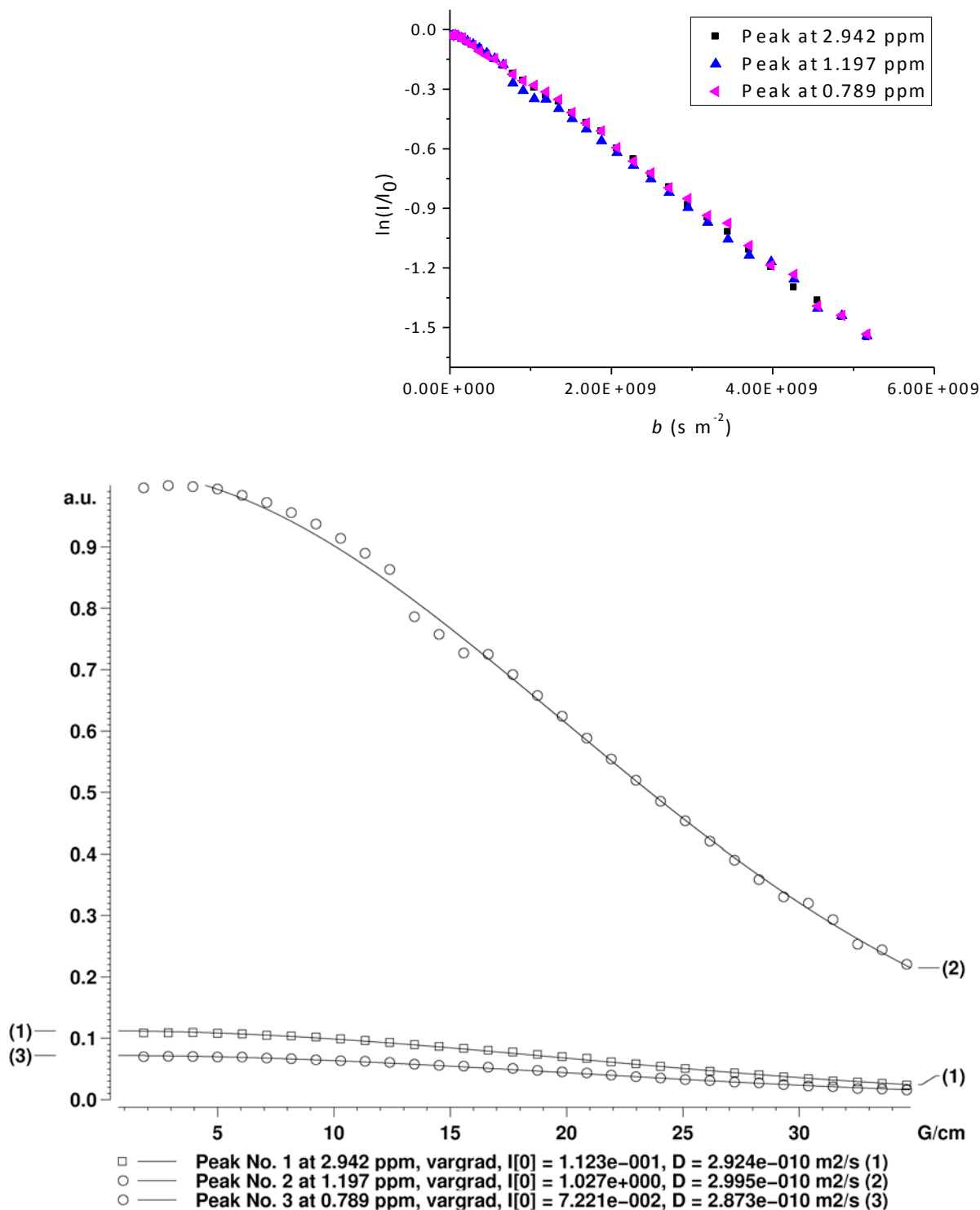


Figure S23. Plots of the change in intensity of the indicated NMR resonances in the DOSY spectra as a function of magnetic field gradient recorded (600 MHz, D₂O, 298 K) for 1.0 mM hexanediamine derivative **4b**. Top inset: linearized form.

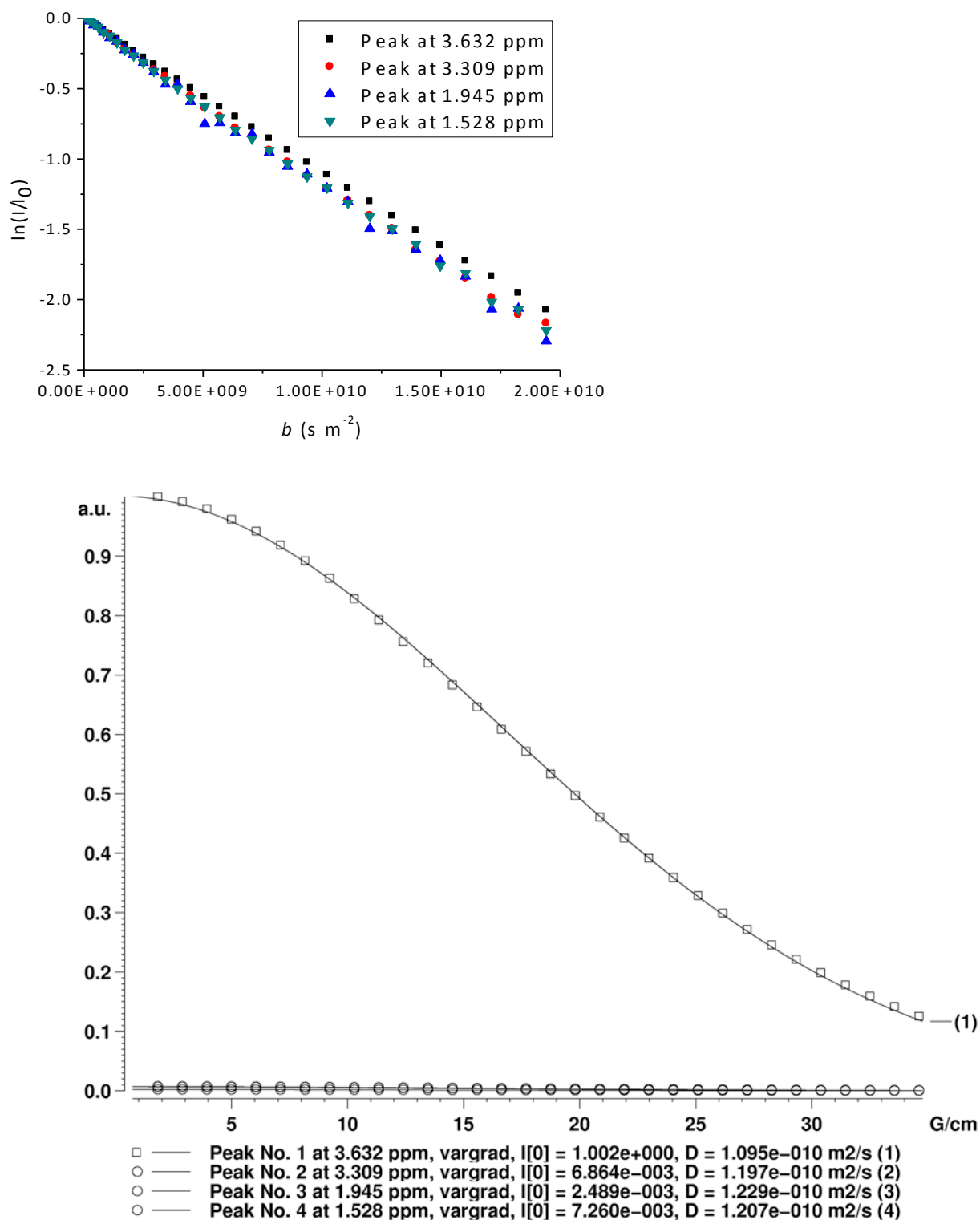


Figure S24. Plots of the change in intensity of the indicated NMR resonances in the DOSY spectra as a function of magnetic field gradient recorded (600 MHz, D_2O , 298 K) for 0.5 mM adamatanemethylamine derivative **5b**. Top inset: linearized form.

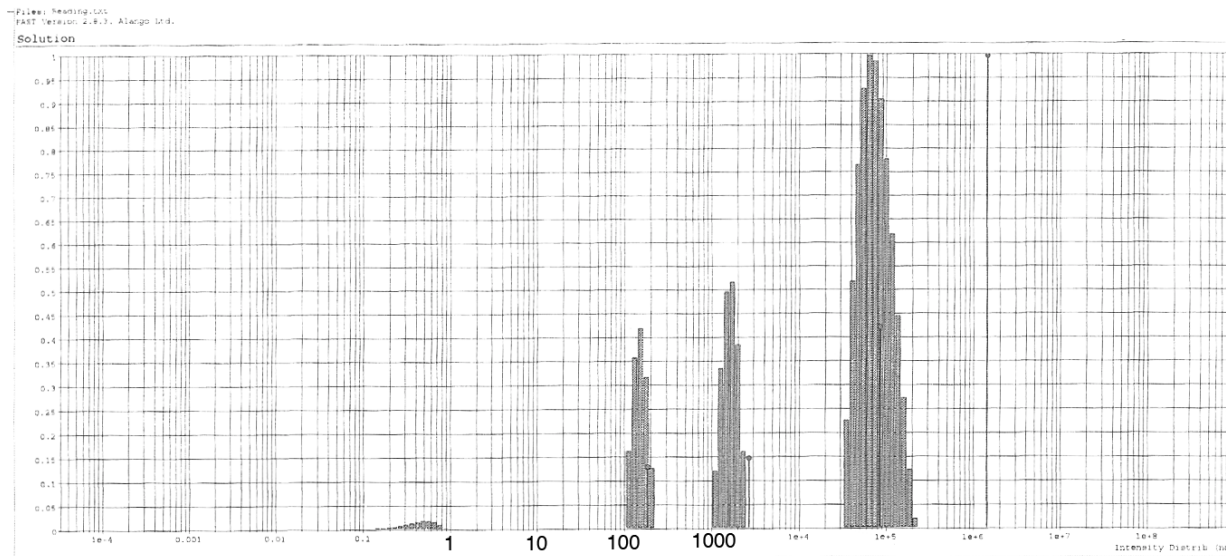


Fig. S25 Dynamic light scattering (DLS) data for 0.5 mM heterodimer **1**, hexanediamine derivative **4b** and adamantanemethylamine derivative **5b**.

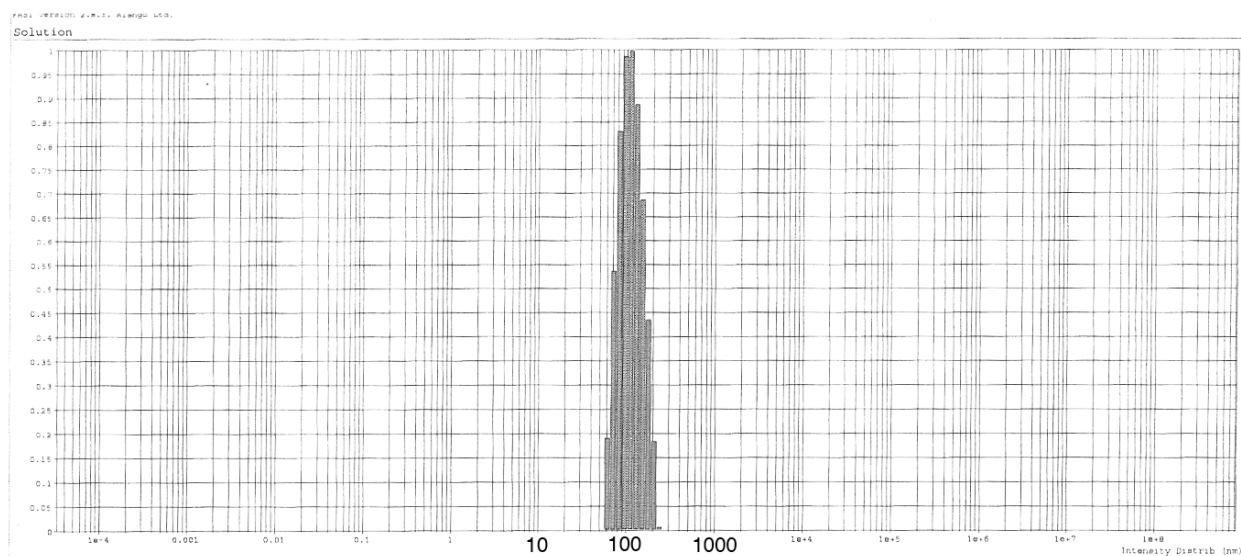


Fig. S26 Dynamic light scattering (DLS) data for 0.5 mM heterodimer **1** and 1.0 mM hexanediamine derivative **4b**.

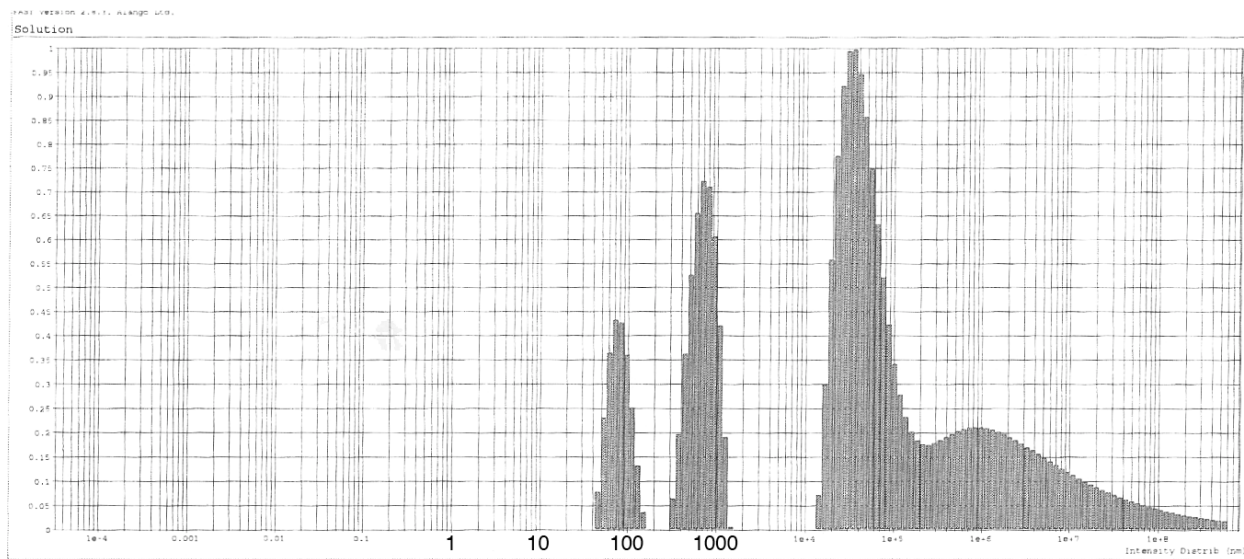


Fig. S27 Dynamic light scattering (DLS) data for 0.5 mM heterodimer **1** and 1.0 mM hexanediamine derivative **4b** and 0.5 mM adamantanemethylamine derivative **5b**.