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Size discrimination in intramolecular complexation of modified α-cyclodextrins:† a preparative and nuclear magnetic resonance study‡

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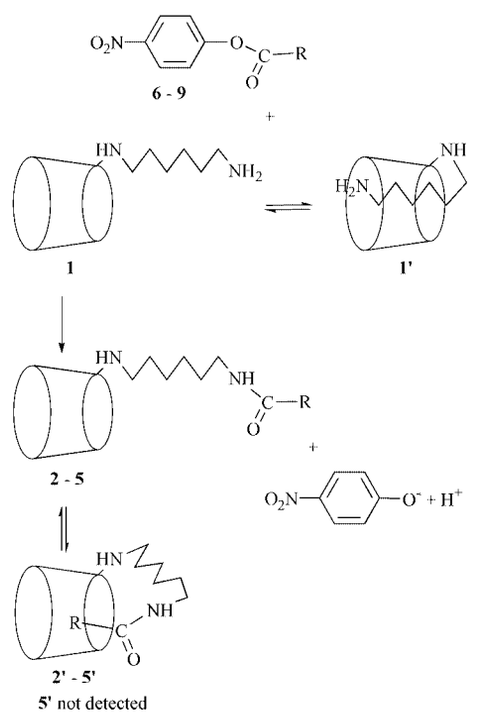
Acylation of the primary amine group of 6^A-(6-aminohexylamino)-6^A-deoxy-α-cyclodextrin **1** by 4-nitrophenyl trinorbornane-2-acetate **6**, 1-methoxycarbonyl-8-(4-nitrophenoxycarbonyl)cubane **7**, 1-methoxycarbonyl-2,3-dimethyl-8-(4-nitrophenoxycarbonyl)cubane **8**, and 1-(4-nitrophenoxycarbonyl)adamantane **9**, respectively, gives 6^A-deoxy-[6-(trinorbornan-2-ylacetylamino)hexylamino]-α-cyclodextrin **2**, 6^A-[6-(8-carboxycuban-1-ylcarbonylamino)hexylamino]-6^A-deoxy-α-cyclodextrin **3**, 6^A-[6-(8-carboxy-2,3-dimethylcuban-l-ylcarbonylamino)hexylamino]-6^A-deoxy-α-cyclodextrin **4**, and 6^A-[6-(adamantan-1-ylcarbonylamino)hexylamino]-6^A-deoxy-α-cyclodextrin **5**, in good yields together with 4-nitrophenolate. In basic D_2O, the substituents of **1**–**4** complex intramolecularly within the α-cyclodextrin annulus, whereas that of **5** does not due to its larger size, as shown by ^{1}H ROESY NMR spectroscopy. This facilitates a mechanistic comparison with the formation of βCD analogues of **2**–**5**.

Introduction

α-Cyclodextrin (αCD), βCD and γCD are composed of six, seven and eight α-1,4 linked glucopyranose residues, respectively, are doughnut shaped, and possess annuli with hydrophobic interiors. In water, they and their modified forms act as hosts in a wide range of inter- and intramolecular host–guest complexes where many of the guests contain aromatic groups which, because of their hydrophobic nature, are usually positioned in the CD annulus in the host–guest complex.[1–3] However, because of their planarity, aromatic guests only occupy a portion of the truncated cone-shaped volume of CD annuli, and most other guests studied do likewise. In reactions where the guest undergoes elaboration after formation of an intermolecular host–guest complex, as in the formation of rotaxanes and catenanes,[4–6] it is desirable that this complex should be as stable as possible. It is anticipated that the closer the fit of the guest to the CD annulus, the greater will be the stability of the host–guest complex, as is supported by the increasingly high stabilities observed for αCD and βCD host–guest complexes as the annular fit of guests derived from bridged cycloalkanes improves.

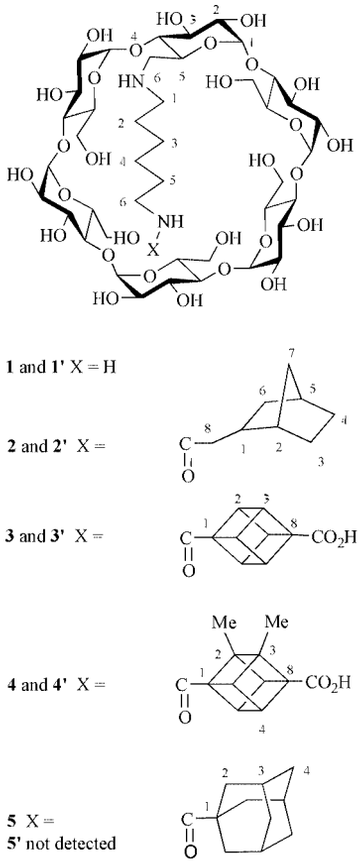
We are particularly interested in guests containing the cubyl entity[7,8] as it is both hydrophobic and appears to closely fit the annulus of αCD which we have used to form rotaxanes and related mechanically restrained species.[6,9] However, poor water solubility of simple cubyl and dimethylcubyl derivatives hampersstudiesoftheirintermolecularcomplexation.Fortunately, both are solubilised when tethered to αCD at C(6), as in structures **3** and **4**, through substitution at the primary amine of **1** as shown in Scheme 1. By comparison with an intermolecular complex, the amidohexylamino tether confers an entropic advantage on the intramolecular complex, and is of sufficient length to allow intramolecular complexation if the sizes of the cubyl, dimethylcubyl, trinorbornylmethyl, and adamantyl entities and the αCD annulus are compatible (Scheme 1). The latter two entities were added to the study because they are smaller and larger than the cubyl and dimethylcubyl entities, respectively, and thereby provide an opportunity to experimentally calibrate the size of the αCD annulus through a ^{1}H ROESY NMR spectroscopic study of NOE interactions



Scheme 1

† α-Cyclodextrin = cyclomaltohexaose.
‡ Electronic supplementary information (ESI) available: ROESY spectra of **4′**, **5**, **1′**, **3** and **1**. See http://www.rsc.org/suppdata/p1/b1/b107324a/

between protons inside the αCD annulus and those of the substituents of **2**–**5**. This also facilitates a mechanistic comparison with analogous βCD systems.[7,8]



Results and discussion

Acylation of the primary amine group of 6^A-(6-aminohexylamino)-6^A-deoxy-α-cyclodextrin, **1** (Scheme 1), by 4-nitrophenyl trinorbornane-2-acetate **6**, 1-methoxycarbonyl-8-(4-nitrophenoxycarbonyl)cubane **7**, 1-methoxycarbonyl-2,3-dimethyl-8-(4-nitrophenoxycarbonyl)cubane **8**, and 1-(4-nitrophenoxycarbonyl)adamantane **9**, respectively, produces 6^A-[6-(trinorbornan-2-ylacetylamino)hexylamino]-6^A-deoxy- α-cyclodextrin **2**, 6^A-deoxy-6^A-[6-(8-carboxycuban-1-ylcarbonylamino)hexylamino]-α-cyclodextrin **3**, 6^A-deoxy-6^A-[6-(8-carboxy-2,3-dimethylcuban-1-ylcarbonylamino)hexylamino]-α-cyclodextrin **4**, and 6^A-[6-(adamantan-1-ylcarbonylamino)hexylamino]-6^A-deoxy-α-cyclodextrin, **5**, in good yield. It was found that the methyl ester groups of esters of **3**/**3′** and **4**/**4′** initially produced were partially hydrolysed in water during the work-up procedures. To avoid mixed products this hydrolysis was taken to completion by heating the esters of **3**/**3′** and **4**/**4′** in water and in water made slightly basic with triethylamine, respectively, at 80 °C for 24 h.

In D_2O at pD ≥ 12 where no protonation of the substituent amino group occurs, substituents of **1**–**4** complex within the αCD annulus to form **1′**–**4′** (Scheme 1), whereas that of **5** does not due to its larger size, as is discussed below. The ^{1}H ROESY NMR spectrum of **1**/**1′** shows strong cross-peaks arising from NOE interactions between the hexyl protons and the αCD H3 and H5 protons consistent with the hexyl entity entering the αCD annulus. (The 599.957 MHz ^{1}H NMR ROESY spectra of **1**/**1′**, **3**/**3′**, **4**/**4′**, and **5** appear in the Supplementary Data.) Also observed are cross-peaks arising from interactions between the H1–H6 protons of the hexyl entity and from interactions among the αCD H1, H2, H3, H5 and H6 protons, as is also the case in the other spectra discussed below. The analogous spectrum of **2**/**2′** shows strong cross-peaks between the trinorbornylmethyl protons and the αCD H3 and H5 protons (Fig. 1). Some of the resonances overlap with those of hexyl H2–H5 and it is possible that some of the cross peaks observed in Fig. 1 may arise from dipolar interactions between hexyl H2–H5 and αCD H3 and H5. No cross-peaks between the hexyl protons and the αCD H3 and H5 protons of **3**/**3′** and **4**/**4′** are observed, consistent with the cubyl and dimethycubyl entities complexing more strongly than the hexyl entity in the αCD annulus. The small chemical-shift difference between the resonances of the cubyl protons and those of the H3 and H5 of **3**/**3′** does not allow cross-peaks between them to be unequivocally identified; however, strong cross peaks between the methyl protons and the H3 and H5 protons of **4**/**4′** are clearly seen. No cross-peaks between the adamantyl entity and the H3 and H5 protons of **5** are observed. Neither are cross-peaks between the hexyl protons and the H3 and H5 protons observed, consistent with the adamantyl entity being too big to enter the αCD annulus and with the hexyl entity being too short to enter the αCD annulus while tethering the adamantyl entity. (Intramolecular complexation of aromatic substituents of modified βCDs is well established, particularly in the case of those incorporating the dansyl entity.[10]) The spectra were obtained at pD ≥ 12 under which circumstances some deprotonation may have occurred as the pK_as of OH(2) and OH(3) are 12.33 for native αCD.[3]

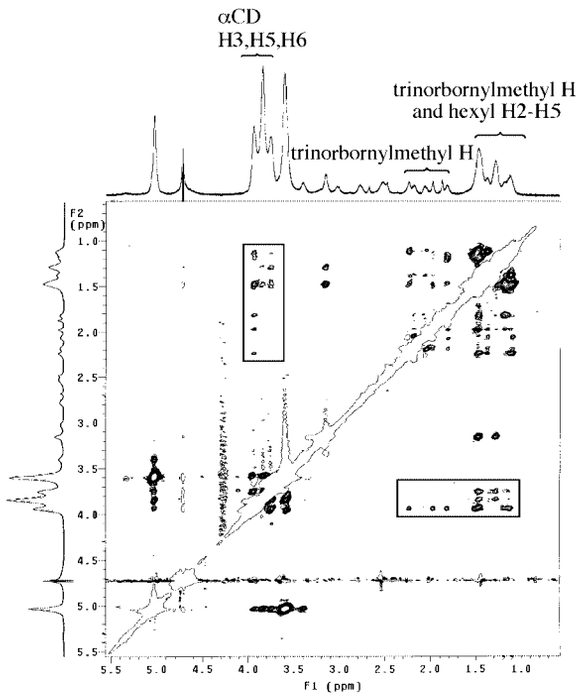


Fig. 1 ^{1}H (599.957 MHz) NMR ROESY spectrum of **2′** in D_2O at pH ≥12. The rectangles enclose the cross-peaks arising from NOE interactions between the trinorbornylmethyl protons and the αCD H3, H5 and H6 protons.

These complexations are similar to those observed for the βCD analogues of **2**–**4** where intramolecular complexation of the trinorbornylmethyl, cubyl and dimethylcubyl entities also occurred.[7,8] However, the βCD analogue of **5** showed strong cross-peaks arising from NOE interactions between the adamantyl protons and the H3 and H5 protons of βCD in its ^{1}H ROESY NMR spectrum, whereas such cross-peaks are not observed for **5**. This is consistent with the primary end of the βCD annulus being sufficiently wide to allow entry of the adamantyl entity, whereas that of αCD is not as a consequence of its smaller diameter resulting from one less glucopyranose unit composing the αCD macrocycle.

These observations resolve a mechanistic quandary associated with the formation of the βCD analogues of **2**–**5**, where in each case intramolecular complexation occurred to form βCD

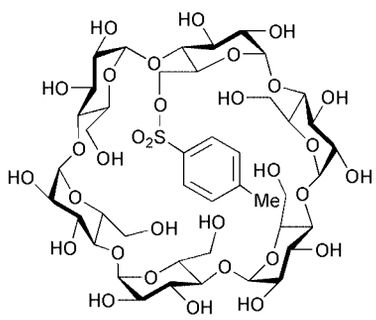
analogues of **2′**–**5′**. Two mechanistic possibilities arise. In the first, intramolecular complexation occurs after attachment of the trinorbornylmethyl, cubyl, dimethylcubyl and adamantyl (only for βCD) entities to the tether as shown in Scheme 1. In the second, the intramolecularly complexed aminohexylamine substituent of **1** makes a nucleophilic attack on the carbonyl carbon of the 4-nitrophenyl ester precursors of the trinorbornylmethyl, cubyl, dimethylcubyl and adamantyl entities through the wide end of either the αCD or βCD annulus to form a molecular knot.§ This is indistinguishable from the intramolecular complex formed through the first mechanism, unless the substituents are too large to pass through the narrow end of the annulus. This was tested in the βCD system by competing the intramolecular formation of **2′**–**5′** against the intermolecular complexation of adamantane-1-carboxylate by **2**–**5**.[7,8] Adamantane-1-carboxylate displaced the tethered trinorbornylmethyl, cubyl and dimethycubyl entities from the βCD annulus. However, the tethered adamantyl entity was not displaced from the βCD annulus, consistent with the tethered adamantyl entity either being too large to pass through the narrow end of the annulus, or possessing an entropic advantage in competing with adamantane-1-carboxylate for occupancy of the annulus.[7] The new αCD data showing the formation of **2′**–**4′**, but not **5′**, is inconsistent with the intramolecularly complexed aminohexylamine substituent of **1** making a nucleophilic attack on the carbonyl carbon of the 4-nitrophenyl ester precursors to form a molecular knot. The inability of adamantane-1-carboxylate to displace the adamantyl entity from the annulus of **5′** in the βCD system is attributable to the entropic advantage gained by being tethered.

Experimental

General

^{1}H (300.145 MHz) and ^{13}C{^{1}H} (75.47 MHz) NMR spectra were recorded using a Varian Gemini 300 NMR spectrometer. ^{1}H (599.957 MHz) 2D-ROESY NMR spectra were recorded on a Varian Inova 600 spectrometer using a standard sequence with a mixing time of 0.3 s.[10] Modified αCD derivatives were dissolved in 0.1 mol dm^{-3} NaOH in D_2O to give concentrations of approximately 0.06 mol dm^{-3} and pH 12. MALDI-TOF mass spectrometry was carried out at the Research School of Chemistry at the Australian National University, Canberra, ACT. ESI mass spectrometric studies were made in positive-ion mode with a Finnigan MAT-ion trap LC-Q mass spectrometer fitted with an electrospray ionisation source. Accurate mass spectrometry was carried out at the University of Tasmania, Hobart. Samples were dissolved in water for injection. Elemental analyses were performed by the Microanalytical Service of the Chemistry Department, University of Otago, Dunedin, New Zealand. As modified αCDs have water molecules associated with them, they were characterised by adding whole numbers of water molecules to the molecular formula to give the best fit to the microanalytical data. Thin layer chromatography (TLC) was carried out on Kieselgel 60 F254 (Merck) on aluminium-backed sheets. Plates were developed with 7 : 7 : 5 : 4 v/v ethyl acetate–propan-2-ol–ammonium hydroxide–water. αCDs were visualised by drying the plate then dipping it into a 1% sulfuric acid in ethanol solution and heating it with a heat gun. To visualise αCDs bearing amino groups, plates were dried then dipped into a 0.5% ninhydrin in ethanol solution and heated with a heat-gun, prior to being dipped in the acid solution. The value R_c represents the R_f of a modified αCD relative to the R_f of the parent cyclodextrin.

All reagents used were obtained from Aldrich and were not further purified before use, unless otherwise stated. α-CD (Nihon Shokuhin Kako Co.) was dried by heating at 100 °C under vacuum for 18 h. Pyridine and 1-methylpyrrolidin-2-one (NMP) were dried by distillation from calcium hydride. *N,N′*-Dimethylformamide (DMF) was dried over 4 Å molecular sieves. The 4-nitrophenol esters **6**–**9**, were prepared by reaction of the corresponding carboxylic acids with 4-nitrophenol in the presence of dicyclohexylcarbodiimide.[7] 6^A-*O*-(4-Methylphenylsulfonyl)-α-cyclodextrin **10** was prepared by a literature method.[11]



10

6^A-(6-Aminohexylamino)-6^A-deoxy-α-cyclodextrin 1

A solution of **10** (0.495 g, 0.44 mmol) and 1,6-diaminohexane (0.201 g, 1.73 mmol) in dry NMP (2 cm^3) was stirred in a lightly stoppered flask at 70 °C for 18 h. Ethanol (50 cm^3) was added and the pale orange precipitate was collected by vacuum filtration and washed successively with ethanol (50 cm^3) then diethyl ether (30 cm^3). The solid was dissolved in water (5 cm^3) and loaded onto a BioRex 70 (H^+-form) cation-exchange column (4.5 cm × 4.5 cm). αCD and **10** were washed off the column with water and **1** was eluted with 1 mol dm^{-3} aq. ammonia. Water was removed under reduced pressure and the residue was dissolved in water (10 cm^3) and concentrated under vacuum to remove ammonia. This process was repeated three times. The product **1** was obtained as an off-white powder after freeze-drying (0.213 g, 44%), R_c = 0.60 [Found: C, 43.83; H, 7.14; N, 2.33. Calc. for **1**·4H_2O ($C_{42}H_{82}N_2O_{33}$): C, 44.13; H, 7.23; N, 2.45%]; δ_H(D_2O–NaOH, pH 12) 5.04 (s, 6H, H1), 3.82–3.97 (m, 22H, H3, H5, H6), 3.58–3.66 (m, 11H, H2, H4), 3.45 (t, J = 9.0 Hz, 1H, H4^A), 3.05 (d, J = 12.0 Hz, 1 H, 6^A), 2.75–2.91 (m, 3H, H6$^{A\prime}$, hexyl H6), 2.50–2.61 (m, 2H, hexyl H1), 1.44–1.67 (m, 4H, hexyl H2, hexyl H5), 1.31–1.44 (m, 4H, hexyl H3, H4); δ_C(D_2O–NaOH, pH 12) 104.15, 103.98 (C1), 84.47 (C4^A), 83.99, 83.84 (C4), 75.98, 74.75, 74.37 (C2, C3, C5), 73.30 (C5^A), 63.02 (C6), 52.29, 51.77 (C6^A, hexyl C6), 42.68, (hexyl C1), 31.27, 29.19, 28.95, 28.77 (hexyl C2–C5); MALDI-TOF mass spectrum m/z 1072 (M + H^+).

General procedure for synthesis of the modified αCDs 2–5

Typically, a DMF (3 cm^3) solution of **1** (≈0.190 mmol) and the appropriate 4-nitrophenyl ester (≈0.230 mmol) was stirred at room temperature for 12 h. The reaction mixture was then added dropwise to cold acetone (50 cm^3) and the precipitate which formed was collected by suction filtration and washed successively with acetone (30 cm^3) and 1 : 1 acetone–diethyl ether (30 cm^3). The precipitate was dissolved in water (3 cm^3) and acidified to pH 1, then washed with dichloromethane (35 cm^3). Dichloromethane (from the partially emulsified aqueous

§ It should be noted that despite the absence of the hydrophobic driving force for complexation in DMF in which the preparation of **2**–**5** and of their βCD analogues was carried out, the dipole–dipole, instantaneous dipole and related secondary bonding forces driving intramolecular complexation remain. This results in substantial intramolecular complexation of the 6-aminohexylamino substituent in the CD annulus. This is shown by the ^{1}H NMR ROESY spectrum of 6^A-(6-aminohexylamino)-6^A-deoxy-β-cyclodextrin in [$^2H_7$]DMF where strong cross-peaks between hexyl H2–H5 and βCD H3 and H5 exist consistent with substantial intramolecular complexation as seen in Fig. S5 of the Supplementary Data.)

phase) was removed under reduced pressure and the solution was loaded onto an AG-4X4 (free-base-form)-anion-exchange column (4.5 cm × 4.5 cm). The modified αCD was eluted with water (100 cm^3). Water was removed under reduced pressure to leave a pale yellow solid, which was dissolved in water (3 cm^3) and loaded onto a BioRex 70 (NH_4^+-form) cation-exchange column (4.5 cm × 4.5 cm). Elution with water (≈200 cm^3) removed the modified αCD. Fractions containing the modified αCD were combined and water was removed under vacuum. The residue was freeze-dried to yield the modified αCD as a white solid.

6^A-Deoxy-[6-(trinorbornan-2-ylacetylamino)hexylamino]-α-cyclodextrin 2. A DMF (3 cm^3) solution of **1** (0.205 g, 0.191 mmol) and 1-(4-nitrophenyloxycarbonylmethyl)trinorborane **6** (0.0547 g, 0.199 mmol) was stirred at room temperature for 12 h and **2** was obtained as a white solid after purification (0.051 g, 22%), R_c = 1.2 [Found: C, 44.12; H, 7.00; N, 2.29. Calc. for **2**·9H_2O ($C_{50}H_{102}N_2O_{39}$): C, 44.13; H, 7.59; N, 2.07%]; δ_H(D_2O–NaOH, pH 12) 4.88–4.93 (m, 6H, H1), 3.73–3.93 (m, 22H, H3, H5, H6), 3.21–3.62 (m, 12H, H2, H4), 3.10 (t, J = 6.6 Hz, 1H, hexyl H6), 3.94 (d, J = 6.0 Hz, 1H, $H6^A$), 2.29–3.82 (m, 4H, hexyl H1, $H6^{A\prime}$, trinorbornylmethyl H), 1.83–2.20 (m, 4H, trinorbornylmethyl H), 1.71–1.78 (m, 1H, hexyl H6), 1.01–1.63 (m, 16H, hexyl H2–hexyl H5, trinorbornylmethyl H); δ_C(D_2O–NaOH, pH 12) 178.79 (C=O), 105.04 (C1), 87.04 ($C4^A$), 84.39 (C4), 76.86, 76.75, 75.29, 74.86 (C2, C3, C5), 72.92 ($C5^A$), 63.27 (C6), 52.20, 51.23 (hexyl C1, $C6^A$), 45.44, 43.36, 41.90, 39.65, 39.27, 37.45 (trinorbornylmethyl C), 33.58, 32.21, 30.95, 28.72, 28.57 (hexyl C). Accurate mass spectrum m/z 1207.528. Calc. 1207.534 (M + H^+).

6^A-[6-(8-Carboxycuban-1-ylcarbonylamino)hexylamino]-6^A-deoxy-α-cyclodextrin 3. A DMF (3 cm^3) solution of **1** (0.208 g, 0.194 mmol) and 1-(4-nitrophenoxycarbonyl)-8-(methoxycarbonyl)cubane **7** (0.083 g, 0.253 mmol) was stirred at room temperature for 12 h. Analysis by TLC of the residue after the general purification treatment revealed two spots of high R_f (R_c = 1.8, 1.9). After stirring of the residue in water (20 cm^3) at 80 °C for 24 h, analysis by TLC revealed a single spot of high R_f (R_c = 1.5). Water was removed under reduced pressure and the residue was freeze-dried to yield **3** as a white solid (0.041 g, 17%) [Found: C, 44.05; H, 6.52; N, 1.88. Calc. for **3**·9H_2O ($C_{52}H_{98}N_2O_{41}$): C, 44.36; H, 7.02; N, 1.99%]; δ_H(D_2O) 5.01–5.09 (m, 6H, H1), 4.08–4.10 (m, 3H, cubyl H), 4.03–4.07 (m, 3H, cubyl H), 3.67–3.99 (m, 22H, H3, H5, H6), 3.54–3.65 (m, 11H, H2, H4), 3.47–3.52 (m, 2H, $H4^A$, $H6^A$), 3.28–3.31 (m, 1H, $H6^{A\prime}$), 3.18 (t, J = 5.8 Hz, 2H, hexyl H6), 2.99–3.04 (m, 2H, hexyl H1), 1.46–1.69 (m, 4H, hexyl H2, hexyl H5), 1.29–1.36 (m, 4H, hexyl H3, hexyl H4); δ_C(D_2O) 181.96 (C=O), 175.49 (C=O), 102.34, 101.67, 101.31 (C1), 83.35 ($C4^A$), 81.76, 81.51, 81.45, 81.38 (C4), 73.65, 73.60, 73.53, 73.36, 73.31, 72.84, 72.55, 72.39, 72.34, 72.23 (C2, C3, C5), 68.17 ($C5^A$), 61.05, 60.75 (C6), 59.14, 57.86 ($C6^A$, hexyl C6), 48.56, 48.40, 47.17, 47.03, 46.63, 46.58, 46.41, 39.16 (cubyl C); 39.16 (hexyl C1), 28.44, 25.68, 25.64, 25.50 (hexyl C2, hexyl C3, hexyl C4, hexyl C5). ESMS spectrum m/z 1245.5 (M + H^+).

6^A-[6-(8-Carboxy-2,3-dimethylcuban-1-ylcarbonylamino)-hexylamino]-6^A-deoxy-α-cyclodextrin 4. A DMF (3 cm^3) solution of **1** (0.223 g, 0.208 mmol) and 2,3-dimethyl-1-(4-nitrophenoxycarbonyl)-8-(methoxycarbonyl)cubane **8** (0.080 g, 0.224 mmol) was stirred at room temperature for 12 h. After the general purification procedure, the product was stirred in water (20 cm^3) with 1 drop of triethylamine (24 h). Analysis by TLC revealed one product (R_c = 1.0). The product was obtained as a white powder after freeze-drying (0.049 g, 19%) [Found: C, 45.46; H, 7.04; N, 1.89. Calc. for **4**·9H_2O ($C_{54}H_{102}N_2O_{41}$); C, 45.19; H, 7.16; N, 1.95%]; δ_H(D_2O) 5.02–5.08 (m, 6H, H1), 4.04 (t, J = 10.7 Hz, 1H, $H5^A$), 3.68–3.98 (m, 27H, H3, H5, H6, cubyl H), 3.47–3.65 (m, 13H, H2, H4, $H6^A$), 3.25–3.31 (m, 1H, $H6^{A\prime}$), 3.18 (t, J = 6.6 Hz, 2H, hexyl H6), 2.95–3.05 (m, 2H, hexyl H1), 1.62–1.68 (m, 2H, hexyl H2), 1.46–1.50 (m, 2H, hexyl H5), 1.29–1.36 (m, 4H, hexyl H3, hexyl H4), 1.34 (s, 3H, Me), 1.44 (s, 3H, Me); δ_C(D_2O) 183.40 (C=O), 176.89 (C=O), 104.15, 103.79 (C1), 85.87 ($C4^A$), 85.86, 84.22, 83.98, 83.93, 83.66 (C4), 76.13, 76.08, 76.01, 75.84, 75.80, 75.33, 75.02, 74.87, 74.71, 74.37, 74.16 (C2, C3, C5), 70.78 ($C5^A$), 63.52, 63.24 (C6), 60.97, 59.75 ($C6^A$, hexyl C6), 58.78, 58.03, 51.07, 50.95, 50.48, 49.51, 46.80, 45.67 (cubyl C), 41.54 (hexyl C1), 31.16, 28.22, 28.16 (hexyl C2, hexyl C3, hexyl C4, hexyl C5). Accurate mass spectrum m/z 1273.507. Calc. 1273.508 (M + H^+).

6^A-[6-(1-Adamantylcarbonylamino)hexylamino]-6^A-deoxy-α-cyclodextrin 5. A DMF (3 cm^3) solution of **1** (0.193 g, 0.180 mmol) and 1-(4-nitrophenoxycarbonyl)adamantane **9** (0.0694 g, 0.230 mmol) was stirred at room temperature for 12 h. After purification, **5** was collected as a white solid (0.0840 g, 38%), R_c = 1.7 [Found: C, 47.64; H, 6.92; N, 2.14. Calc. for **5**·6H_2O ($C_{53}H_{100}N_2O_{36}$): C, 47.46; H, 7.41; N, 2.09%]; δ_H(D_2O–NaOH, pH 12) 4.98 (s, 6H, H1 + solvent), 3.76–3.92 (m, 22H, H3, H5, H6), 3.39–3.49 (m, 11H, H2, H4), 3.23 (t, J = 8.7 Hz, 1H, $H4^A$), 3.13 (t, J = 5.8 Hz, 2H, hexyl H6), 3.01 (d, J = 11.6 Hz, 1H, $H6^A$), 2.61–2.69 (m, 1H, $H6^{A\prime}$), 2.47–2.52 (m, 2H, hexyl H1), 1.62–2.00 (m, 15H, adamantyl H), 1.41–1.49 (m, 4H, hexyl H2, hexyl H5), 1.25–1.31 (m, 4H, hexyl H3, hexyl H4). δ_C(D_2O–NaOH, pH 12) 184.22 (C=O), 105.13, 104.94, 104.78, 104.69 (C1), 87.13 ($C4^A$), 84.38, 84.27 (C4), 76.89, 75.34, 74.97, 74.85 (C2, C3, C5), 73.11 ($C5^A$), 63.36 (C6), 52.51, 51.35 ($C6^A$, hexyl C6), 43.28, 41.85 (hexyl C), 41.34, 38.69 (adamantyl C), 31.06, (hexyl C), 30.51 (adamantyl C), 28.83, 28.49 (hexyl C). MALDI-TOF mass spectrum m/z 1234.4 (M + H^+).

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