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Original Research Article

Polyethylene Glycol as String for the Simultaneous Complexation of α-Cyclodextrin and Cucurbit[6]uril

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Abstract

α-Cyclodextrin and cucurbit[6]uril are macrocyclic ligands with nearly identical molecular properties. Both ligands possess nonpolar cavities with similar dimensions. They are able to include nonpolar molecules within their cavities. The main difference between both ligands is their solubility in water. An acceptable solubility for cucurbit[6]uril is only given in the presence of acids or salts. Due to the similarity of both ligands, the formation of mixed polyrotaxanes seems to be possible. The synthesis of statistically threaded α-cyclodextrin and cucurbit[6]uril on polyethylene glycol 2000 is verified using elemental analysis, ^{1}H-NMR spectroscopy and differential scanning calorimetry. Under the experimental conditions used the number of threaded α-cyclodextrin molecules is higher compared with cucurbit[6]uril. However it is shown that the formation of mixed complexes is possible.

Introduction

α-Cyclodextrin and cucurbit[6]uril are known since a long time. Cyclodextrins are naturally formed substances while cucurbit[6]uril is a fully synthetic molecule. The cyclodextrins were observed in 1891 during an enzymatic degradation process from starch [1]. Ten years later they were characterized as polysaccharides and they were named "Schardinger-Dextrine" [2]. α-Cyclodextrin is a cyclic polysaccharide which is made up of six D-glucose monomer units which are linked covalently at the 1 and 4 carbon atoms. These D-glucose units form a hydrophobic cavity in which a large number of substances, especially organic substances, can be complexed. The first detailed discussion about the formation of inclusion compounds with cyclodextrins was published in 1954 by Cramer [3].

The synthesis of cucurbit[6]uril and the formation of complexes with e.g. dyes has been published in 1905 [4]. Cucurbit[6]uril is a condensation product from urea, glyoxal and formaldehyde. In 1981, the structure of cucurbit[6]uril was enlightened by crystal structure [5]. Like α-cyclodextrin also cucurbit[6]uril possesses a hydrophobic cavity in which organic substances can be complexed. The first complex formations between amines and cucurbit[6]uril was described in 1983 [6]. In the meantime, further derivatives of cucurbit[6]uril are known [7–11]. The chemical structure of α-cyclodextrin and cucurbit[6]uril is shown in Figure 1 and their molecular properties are given in Table 1.

The molecular and cavity dimensions of both macrocyclic ligands are very similar. The main differences between these two ligands are their solubilities in water and their possibilities to form complexes with cations. A good solubility for cucurbit[6]uril is only achieved in acidic solutions or in the presence of e.g. alkaline or alkaline earth ions [16, 17].

Harada *et al.* [18, 19] synthesized the first complexes between α-cyclodextrin and polyethylene glycols (PEG). They reported that no complex formation occurred until the minimum molecular weight of PEG has reached 200 [20]. The complex formation becomes almost quantitative at a molecular weight for PEG above 1000. Depending on the chain length of PEG, a large number of α-cyclodextrin molecules are threaded on the PEG chains. Because of the hydroxyl groups at the bottom and top of the α-cyclodextrin molecule, it is possible to connect the threaded cyclodextrins using e.g. epichlorohydrin. After dethreading of the PEG chain, tubular polymers of α-cyclodextrin remain [21].

The behavior of α-cyclodextrin and cucurbit[6]uril is nearly identical in case of complexing organic substances, due to the similar sizes of the hydrophobic cavities of both ligands. Taking advantage of the different solubilities of the ligands, the synthesis of complexes with α-cyclodextrin and cucurbit[6]uril threaded on PEG2000 in which both macrocyclic ligands are

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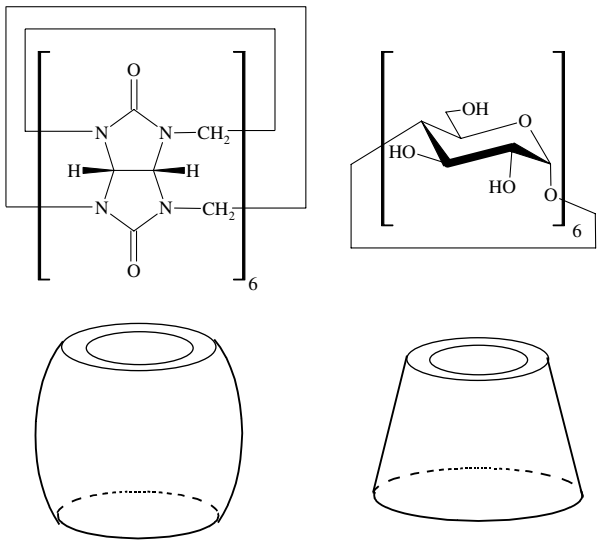

Figure 1. Chemical structures of cucurbit[6]uril (left) and α-cyclodextrin (right).

Table 1. Some properties of cucurbit[6]uril and α-cyclodextrin

Properties	Cucurbit[6]uril	α-Cyclodextrin
Number of monomer units	6	6
Molecular weight	997	972
Solubility in water [g/l] at 25 °C	0.02[a]	145[b]
Cavity diameter [pm]	550[c]	470–530[a]
Height of molecule [pm]	600[d]	790[a]
Water content [mol]	3–11[e]	6.0–7.5[b]

[a]Ref. [12]. [b]Ref. [13]. [c]Ref. [14]. [d]Ref. [K. Kim, personal communication]. [e]Ref. [15].

distributed statistically on the polymer chain is possible. A schematical structure of a mixed complex of PEG with α-cyclodextrin and cucurbit[6]uril is shown in Figure 2. We report the simultaneous formation of PEG complexes with α-cyclodextrin and cucurbit[6]uril in solution.

Experimental

Cucurbit[6]uril (Cuc[6]) is synthesized and characterized as described in the literature [22]. α-Cyclodextrin (α-CD) is a commercial product of the highest purity available (WACKER Chemie, Burghausen). Polyethylene glycol 2000 (PEG 2000, Fluka) is a commercial product and used without further purification. As solvents water (Membra Pur Millipore) and hydrochloric acid (32 vol%, Fluka) are used. The solubility of α-cyclodextrin in solutions containing different concentrations of hydrochloric acid (8 vol% and 16 vol%) is determined gravimetrically. α-Cyclodextrin, cucurbit[6]uril and the synthesized complexes are analyzed by elemental analysis (EA 3000, Hekatech), ^{1}H-NMR spectroscopy (WM Avance DRX 500, 500 MHz, Bruker) and differential scanning calorimetry (DSC 2910 with Thermal Analyst 2000, TA Instruments). Solvents for the ^{1}H-NMR spectroscopy are D_2O (Merck, >99.75%) and CF_3COOD (Aldrich, >99.5%). As internal standard 3-(Trimethylsily)propionic-2,2,3,3-d_4 acid sodium salt (TMSPA, Aldrich >98%) is used.

Analysis of the macrocyclic ligands used and PEG2000

Cucurbit[6]uril ($C_{36}H_{36}N_{24}O_{12}\cdot 4.80H_2O$). *Calc*. C, 39.91; H, 4.24; N, 31.03; O, 24.81; C/N, **1.29**. *Exp*. C, 39.94; H, 4.73; N, 31.34; C/N, **1.27**.

^{1}H-NMR (CF_3COOD, 500 MHz): [$(AX)_6\delta_A$ 4.36 (d, 12 H, J = 16.0 Hz, CH_2), δ_X 5.99 (d, 12 H, J = 15.8 Hz, CH_2)], δ 5.64 (s, 12 H, CH).

α-Cyclodextrin ($C_{36}H_{60}O_{30}\cdot 5.66H_2O$). *Calc*. C, 40.22; H, 6.69; O, 53.09. *Exp*. C, 40.14; H, 6.55.

^{1}H-NMR (D_2O, 500 MHz): δ 3.28–3.38 (m b, 12 H), δ 3.52–3.69 (m b, 18 H), δ 3.69–3.76 (m b, 6 H), δ 4.75–4.82 (b, 6 H).

^{1}H-NMR (CF_3COOD, 500 MHz): δ 3.73–3.82 (m b), δ 3.89–3.95 (m b, 6 H), δ 4.15–4.26 (m b, 6 H), δ 4.30–4.38 (m b, 6 H), δ 4.55–4.71 (m b, 6 H), δ 4.83–4.97 (m b, 6 H), δ 5.09–5.18 (m b, 6 H).

PEG2000. ^{1}H-NMR (CF_3COOD, 500 MHz): δ 3.85 (s).

DSC measurements of PEG2000, α-cyclodextrin and cucurbit[6]uril are shown in Figure 3.

Preparation of the PEG2000 complexes with α-CD and cuc[6]

Synthesis of the PEG2000 complex with α-cyclodextrin

α-CD (1.5 g) is dissolved in 10 ml of water under stirring until complete dissolution. Solid PEG2000 (100 mg) is

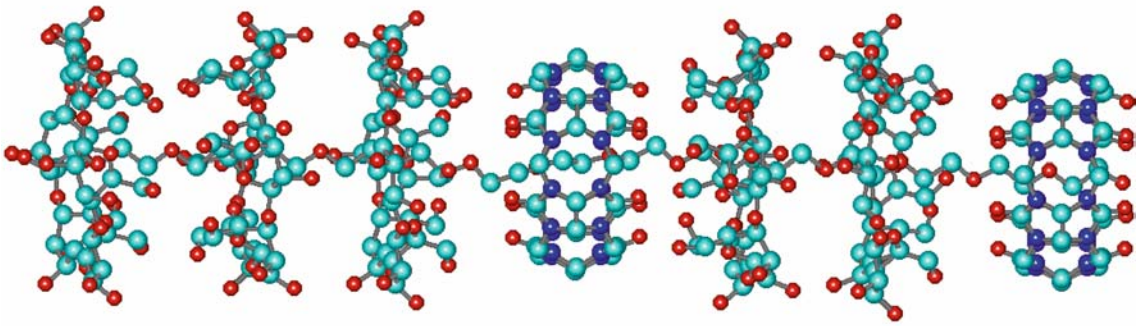

Figure 2. Schematical structure of a mixed complex of PEG with α-cyclodextrin and cucurbit[6]uril.

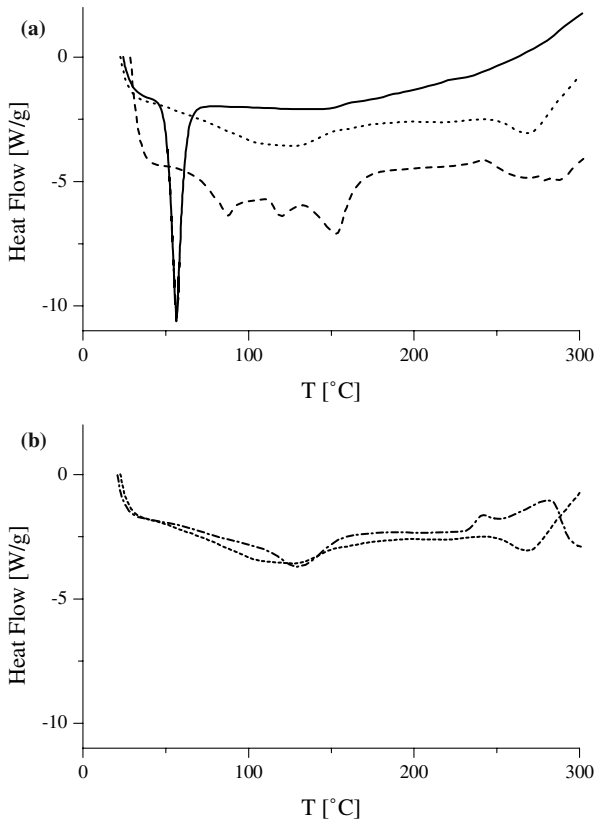

Figure 3. Differential scanning calorimetry measurements of (a) PEG2000 (———), α-cyclodextrin (– – –) and cucurbit[6]uril (- - - - - - -). (b) PEG2000·$(\alpha\text{-CD})_{15}$·$(H_2O)_{45}$(–·–·–) and PEG2000·$(\alpha\text{-CD})_{12.38}$·$(Cuc[6])_{2.62}$ (– – – – –).

added to the stirred solution. Within few minutes, a white precipitate is formed. The solution is stirred one additional hour at room temperature and then the solution is diluted by the addition of 10 ml of water. The solid product is filtered and washed with 20 ml water and 20 ml acetone. The solid product is dried in vaccum.

Precipitate: 831 mg. PEG_1· $(\alpha\text{-CD})_{15}$· $(H_2O)_{45}$ *Calc*. C, 43.48; H, 6.79; O, 49.73. *Exp*. C, 43.52; H, 6.74; O, 49.74.

^{1}H-NMR (500 MHz, CF_3COOD): δ 2.88–2.33 (m, 3 H), δ 3.70–3.82 (m, 6 H, α-CD), δ 3.82–3.89 (s b, 12 H, 3 PEO), δ 3.90–3.96 (m b, 6 H, α-CD), δ 4.14–4.28 (m b, 6 H, α-CD), δ 4.29–4.41 (m b, 6 H, α-CD), δ 4.56–4.71 (m b, 6 H, α-CD), δ 4.81–5.01 (m b, 6 H, α-CD), δ 5.07–5.24 (m b, 6 H, α-CD).

The synthesis of the PEG2000 complex with α-CD is repeated in aqueous HCl (8 or 16 vol%). Due to the higher solubility of α-CD in the aqueous acid (215 g/l in 8 vol% and 615 g/l in 16 vol% HCl) 2.15 or 6.15 g are dissolved in 10 ml of aqueous HCl (8 vol% or 16 vol%). The further procedure is described above.

Synthesis in HCl (8 vol%), precipitate: 1150 mg. PEG_1·$(\alpha\text{-CD})_{15}$·$(H_2O)_{50}$·$(HCl)_{10}$ *Calc*. C, 42.48; H, 6.70; O, 48.94. *Exp*. C, 42.54; H, 6.56; O, 49.02.

Synthesis in HCl (16 vol%), precipitate: 355 mg. PEG_1·$(\alpha\text{-CD})_{15}$·$(H_2O)_{50}$·$(HCl)_{40}$ *Calc*. C, 40.14; H, 6.49; O, 46.25. *Exp*. C, 40.15; H, 6.20; O, 46.53.

The ^{1}H-NMR spectra are identical with the product obtained from pure water. A DSC measurement of the solid PEG·$(\alpha\text{-CD})_{15}$·$(H_2O)_{45}$ complex is shown in Figure 3.

To obtain the number of α-CD molecules threaded on PEG2000 the solid complex is dissolved in D_2O and in CF_3COOD and ^{1}H-NMR measurements are recorded. From the integration of all proton signals, the number of moles of α-CD are calculated in respect of 1 mol PEG2000. The number of moles of α-CD vary between 18 in D_2O and 15 in CF_3COOD. This is an accordance with the results from the elemental analysis.

Synthesis of mixed PEG2000 complexes with α-CD and Cuc[6] in 8 vol% HCl (Procedure A)

Solid cuc[6] (10–70 mg) is added in 10 mg steps to saturated solutions of α-CD (2.15 g) dissolved in 10 ml aqueous HCl (8 vol%). The further procedure follows the description given for the synthesis of pure α-CD complexes with PEG2000.

Characterization of the solid products

Due to the results obtained from the elemental analysis of the pure α-CD complexes with PEG2000 neither water nor HCl present in the solid complexes has been taken into account in case of the mixed complexes. Only the ratio of C/N reflects the amount of Cuc[6] threaded simultaneously together with α-CD. At high values of C/N one can assume that the number of moles of α-CD threaded on one chain of PEG2000 remains unaffected due to the very low number of Cuc[6] present on the chain. At higher amount of Cuc[6] one can assume due to the similar molecular dimensions that the total number of threaded molecules *n* on one chain is more or less constant ($n = 15$). Using calculated values of C/N at different ratios of α-CD to Cuc[6], the number of moles of threaded Cuc[6] can be obtained. A double logarithmic plot of the calculated ratio C/N as a function of the number of moles of Cuc[6] threaded together with α-CD gives a straight line, see Figure 4. Thus the number of moles of threaded Cuc[6] can be calculated using this correlation.

Product A1: (Amount of Cuc[6] present in solution: 10 mg): Precipitate: 917 mg. PEG_1·$(\alpha\text{-CD})_{14.984}$·$(Cuc[6])_{0.016}$. *Calc*. C, 45.04; H, 6.40; N, 0.03; O, 48.52; C/N, **1336**. *Exp*. C, 39.87; H, 6.21; N, 0.03; C/N, **1329**.

Product A2: (Amount of Cuc[6] present in solution: 20 mg). Precipitate: 833 mg. PEG_1·$(\alpha\text{-CD})_{14,973}$·$(Cuc[6])_{0.027}$. *Calc*. C, 45.04; H, 6.40; N, 0.06; O, 48.50; C/N, **792**. *Exp*. C, 39.82; H, 6.24; N, 0.05; C/N, **796**.

Product A3: (Amount of Cuc[6] present in solution: 30 mg): Precipitate: 767 mg. PEG_1·$(\alpha\text{-CD})_{14.984}$·$(Cuc[6])_{0.016}$. *Calc*. C, 45.04; H, 6.40; N, 0.03; O, 48.52; C/N, **1336**. *Exp*. C, 39.86; H, 6.34; N, 0.03; C/N, **1329**.

Product A4: (Amount of Cuc[6] present in solution: 40 mg): Precipitate: 790 mg. PEG_1·$(\alpha\text{-CD})_{14.958}$·$(Cuc[6])_{0.042}$. *Calc*. C, 45.04; H, 6.39; N, 0.09; O, 48.47; C/N, **509**. *Exp*. C, 40.14; H, 6.28; N, 0.08; C/N, **502**.

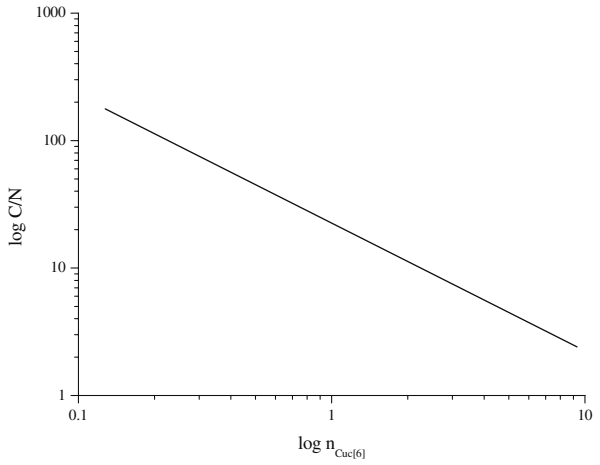

Figure 4. Double logarithmic plot of the calculated ratio C/N as a function of the number of moles of cuc[6] threaded together with α-CD.

Product A5: (Amount of Cuc[6] present in solution: 50 mg): Precipitate: 927 mg. $PEG_1{\cdot}(\alpha\text{-CD})_{14.937}{\cdot}(Cuc[6])_{0.063}$. *Calc*. C, 45.04; H, 6.39; N, 0.13; O, 48.44; C/N, **339**. *Exp*. C, 40.72; H, 6.27; N, 0.12; C/N, **339**.

Product A6: (Amount of Cuc[6] present in solution: 60 mg): Precipitate: 979 mg. $PEG_1{\cdot}(\alpha\text{-CD})_{14.921}{\cdot}(Cuc[6])_{0.079}$. *Calc*. C, 45.04; H, 6.39; N, 0.17; O, 48.41; C/N, **271**. *Exp*. C, 40.44; H, 6.25; N, 0.15; C/N, **270**.

Product A7: (Amount of Cuc[6] present in solution: 70 mg): Precipitate: 883 mg. $PEG_1{\cdot}(\alpha\text{-CD})_{14.896}{\cdot}(Cuc[6])_{0.104}$. *Calc*. C, 45.04; H, 6.38; N, 0.22; O, 48.36; C/N, **206**. *Exp*. C, 41.23; H, 6.20; N, 0.20; C/N, **206**.

Synthesis of mixed PEG2000 complexes with α-CD and Cuc[6] in 16 vol% HCl (Procedure B)

To saturated solutions of α-CD (6.15 g) dissolved in 16% HCl (10 ml) an increasing amount of solid Cuc[6] (10–190 mg) is given. To these solutions, 100 mg solid PEG2000 is added under stirring. Within a few minutes, a white precipitate is formed. After 1 h stirring at room temperature, the precipitate is diluted by adding 10 ml HCl (16%), the product is filtered and washed with 20 ml water and 10–20 ml acetone.

DSC measurements show no significant differences between the synthesized products.

Product B1: (Amount of Cuc[6] present in solution: 10 mg): Precipitate: 1064 mg. $PEG_1{\cdot}(\alpha\text{-CD})_{14.984}{\cdot}(Cuc[6])_{0.016}$. *Calc*. C, 45.04; H, 6.40; N, 0.03; O, 48.52; C/N, **1336**. *Exp*. C, 39.86; H, 6.22; N, 0.03; C/N, **1329**.

Product B2: (Amount of Cuc[6] present in solution: 20 mg): Precipitate: 327 mg. $PEG_1{\cdot}(\alpha\text{-CD})_{14.935}{\cdot}(Cuc[6])_{0.065}$. *Calc*. C, 45.04; H, 6.39; N, 0.14; O, 48.43; C/N, **329**. *Exp*. C, 39.52; H, 6.11; N, 0.12; C/N, **329**.

Product B3: (Amount of Cuc[6] present in solution: 30 mg): Precipitate: 460 mg. $PEG_1{\cdot}(\alpha\text{-CD})_{14.930}{\cdot}(Cuc[6])_{0.070}$. *Calc*. C, 45.04; H, 6.39; N, 0.15; O, 48.42; C/N, **304**. *Exp*. C, 39.84; H, 6.20; N, 0.13; C/N, **307**.

Product B4: (Amount of Cuc[6] present in solution: 40 mg): Precipitate: 105 mg. $PEG_1{\cdot}(\alpha\text{-CD})_{14.923}{\cdot}(Cuc[6])_{0.077}$. *Calc*. C, 45.04; H, 6.39; N, 0.16; O, 48.41; C/N, **278**. *Exp*. C, 38.94; H, 6.18; N, 0.14; C/N, **278**.

Product B5: (Amount of Cuc[6] present in solution: 50 mg): Precipitate: 140 mg. $PEG_1{\cdot}(\alpha\text{-CD})_{14.865}{\cdot}(Cuc[6])_{0.135}$. *Calc*. C, 45.04; H, 6.38; N, 0.28; O, 48.30; C/N, **158**. *Exp*. C, 39.47; H, 6.14; N, 0.25; C/N, **158**.

Product B6: (Amount of Cuc[6] present in solution: 60 mg): Precipitate: 235 mg. $PEG_1{\cdot}(\alpha\text{-CD})_{14.839}{\cdot}(Cuc[6])_{0.161}$. *Calc*. C, 45.03; H, 6.38; N, 0.34; O, 48.25; C/N, **133**. *Exp*. C, 39.98; H, 6.13; N, 0.30; C/N, **133**.

Product B7: (Amount of Cuc[6] present in solution: 70 mg): Precipitate: 104 mg. $PEG_1{\cdot}(\alpha\text{-CD})_{14.819}{\cdot}(Cuc[6])_{0.181}$. *Calc*. C, 45.03; H, 6.37; N, 0.38; O, 48.21; C/N, **118**. *Exp*. C, 41.39; H, 6.14; N, 0.35; C/N, **118**.

Product B10: (Amount of Cuc[6] present in solution: 100 mg): Precipitate: 184 mg. $PEG_1{\cdot}(\alpha\text{-CD})_{14.772}{\cdot}(Cuc[6])_{0.228}$. *Calc*. C, 45.03; H, 6.36; N, 0.48; O, 48.13; C/N, **94**. *Exp*. C, 41.44; H, 6.16; N, 0.44; C/N, **94**.

Product B13: (Amount of Cuc[6] present in solution: 130 mg): Precipitate: 114 mg. $PEG_1{\cdot}(\alpha\text{-CD})_{14.666}{\cdot}(Cuc[6])_{0.334}$. *Calc*. C, 45.02; H, 6.35; N, 0.70; O, 47.93; C/N, **64**. *Exp*. C, 41.51; H, 6.16; N, 0.65; C/N, **64**.

Product B16: (Amount of Cuc[6] present in solution: 160 mg): Precipitate: 84 mg. $PEG_1{\cdot}(\alpha\text{-CD})_{14.545}{\cdot}(Cuc[6])_{0.455}$. *Calc*. C, 45.01; H, 6.33; N, 0.96; O, 47.70; C/N, **47**. *Exp*. C, 41.03; H, 6.14; N, 0.87; C/N, **47**.

Product B19: (Amount of Cuc[6] present in solution: 190 mg): Precipitate: 152 mg. $PEG_1{\cdot}(\alpha\text{-CD})_{14.452}{\cdot}(Cuc[6])_{0.548}$. *Calc*. C, 45.01; H, 6.31; N, 1.16; O, 47.52; C/N, **39**. *Exp*. C, 41.19; H, 6.09; N, 1.06; C/N, **39**.

Synthesis of mixed PEG2000 complexes with α-CD and Cuc[6] in 16 vol% HCl followed by a dilution with water (Procedure C)

To saturated solutions of α-CD (6.15 g) dissolved in 16% HCl (10 ml), solutions with increasing amount of cucurbit[6]uril (200, 300, 400 mg dissolved in 10 ml 16% HCl) are added under stirring. After the addition of 100 mg solid PEG2000, no precipitate is formed even after 16 h. After the dilution of these solutions with 20 ml water, a white precipitate forms. The rate of precipitation depends on the amount of cucurbit[6]uril present in solution. The mixture is stirred for an additional hour. The precipitate is filtered and washed with 2–3 ml HCl (8%), 20 ml water and 10–20 ml acetone. ^{1}H-NMR spectra of these products are shown in Figure 5.

Product C200: (Amount of Cuc[6] present in solution: 200 mg): Precipitate: 220 mg. $PEG_1{\cdot}(\alpha\text{-CD})_{13.83}{\cdot}(Cuc[6])_{1.17}$. *Calc*. C, 44.97; H, 6.21; N, 2.47; O, 46.35; C/N, **18.23**. *Exp*. C, 39.56; H, 5.98; N, 2.17; C/N, **18.27**. ^{1}H-NMR (500 MHz, CF_3COOD): δ 2.88–2.33 (m, 3 H), δ 3.69–3.83 (m, 6 H, α-CD), δ 3.83–3.89 (s b, 10 H, 3 PEO), δ 3.91–3.98 (m b, 6 H, α-CD), δ 4.16–4.27 (m b, 6 H, α-CD), 4.30–4.47 (m b, 6 H, α-CD), δ 4.56–4.71 (m b, 6 H, α-CD), δ 4.80–4.97 (m b, 6 H, α-CD), δ 5.10–5.23 (m b, 6 H, α-CD).

Product C300: (Amount of Cuc[6] present in solution: 300 mg): Precipitate: 1322 mg. $PEG_1{\cdot}(\alpha\text{-CD})_{13.13}{\cdot}$

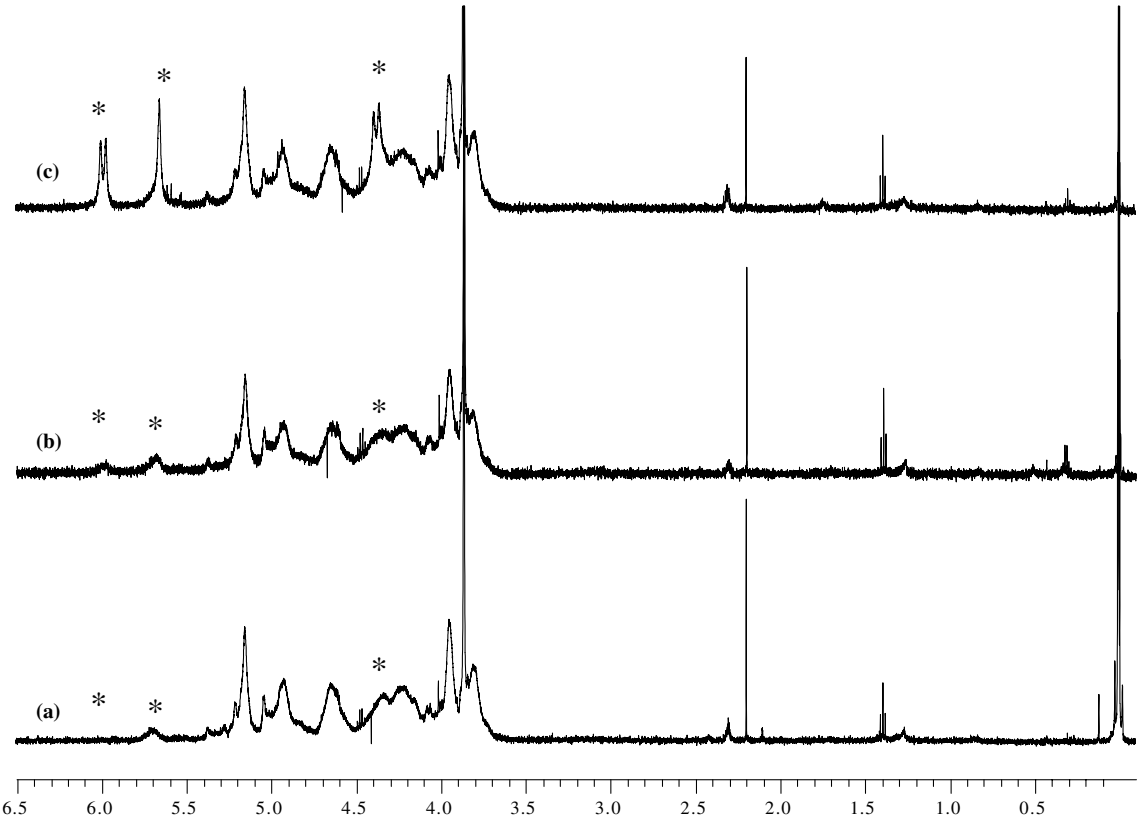

Figure 5. ^{1}H-NMR spectra of PEG2000 complexes with simultanously threaded α-CD and cuc[6] in CF_3 COOD with TMSPA as internal standard. (a) $PEG_1{\cdot}(\alpha\text{-CD})_{13.83}{\cdot}(Cuc[6])_{1.17}$, (b) $PEG_1{\cdot}(\alpha\text{-CD})_{13.13}{\cdot}(Cuc[6])_{1.87}$ and (c) $PEG_1{\cdot}(\alpha\text{-CD})_{12.38}{\cdot}(Cuc[6])_{2.62}$. The signals typical for cucurbit[6] are marked with an asterisk.

$(Cuc[6])_{1.87}$. *Calc*. C, 44.92; H, 6.10; N, 3.94; O, 45.04; C/N, **11.40**. *Exp*. C, 41.11; H, 6.61; N, 3.60; C/N, **11.42**. ^{1}H-NMR (500 MHz, CF_3COOD): δ 3.73–3.84 (m, 6 H, α-CD), δ 3.85–3.89 (s b, 12 H, 3 PEO), δ 3.92–3.99 (m b, 6 H, α-CD), δ 4.12–4.28 (m b, 6 H, α-CD), δ 4.30–4.45 (m b, 6 H, α-CD.Cuc[6]), δ 4.54–4.73 (m b, 6 H, α-CD), δ 4.88–5.05 (m b, 6 H, α-CD), δ 5.10–5.25 (m b, 6 H, α-CD), δ 5.62–5.76 (m b, Cuc[6]), δ 5.94–6.03 (m b, Cuc[6]).

Product C400: (Amount of Cuc[6] present in solution: 400 mg): Precipitate: 1568 mg. $PEG_1{\cdot}(\alpha\text{-CD})_{12.38}{\cdot}(Cuc[6])_{2.62}$. *Calc*. C, 44.87; H, 5.98; N, 5.52; O, 43.63; C/N, **8.13**. *Exp*. C, 37.93; H, 5.54; N, 4.67; C/N, **8.12**. ^{1}H-NMR (500 MHz, CF_3COOD): δ 3.72–3.83 (m, 6 H, α-CD), δ 3.85–3.88 (s b, 12 H, 3 PEO), δ 3.92–3.97 (m b, 6 H, α-CD), δ 4.15–4.26 (m b, 6 H, α-CD), δ 4.30–4.44 (m b, 6 H, α-CD, 3 H, Cuc[6]), δ 4.58–4.72 (m b, 6 H, α-CD), δ 4.89–5.05 (m b, 6 H, α-CD), δ 5.11–5.20 (m b, 6 H, α-CD), δ 5.66–5.79 (m b, 3 H, Cuc[6]), 5.95–6.03 (m b, 3 H, Cuc[6]).

A DSC measurement of the solid $PEG_1{\cdot}(\alpha\text{-CD})_{12.38}{\cdot}(Cuc[6])_{2.62}$ complex is shown in Figure 3.

Results and discussion

Cucurbit[6]uril and α-cyclodextrin are molecules which behave relative similar in solution. Both ligands form inclusion complexes with various organic molecules. Surprising no attempt has been published up to now concerning the synthesis of polyrotaxanes formed by both ligands. A suitable chain to thread α-CD and cuc[6] seems to be a PEG. The threading of α-CD on PEGs is well known [18–21, 23, 24]. For comparison, a complex between α-cyclodextrin and PEG2000 has been synthesized. The number of moles of threaded α-CD is calculated using the integrals of the ^{1}H-NMR spectra. On one PEG2000 chain between 15 and 18 molecules of α-CD are complexed depending on the solvent used for the dissolution of the solid complexes. These results are not identical with those reported by Harada [20]. They observed that 22 α-CD molecules are fixed on one PEG2000 molecule. The use of different solvents for recording the NMR spectra might be responsible.

Due to the rather low solubility of Cuc[6] in water a simultaneous threading with α-CD is only possible in acidic solution. Thus, the threading of α-CD is studied first in acidic solution. The characterization of the solid complexes by elemental analysis causes some problems due to the presence of water and hydrochloric acid molecules. However NMR measurements confirm the formation of the complexes of PEG2000 with α-CD in acidic solution. From these measurements the number of threaded α-CD molecules on the chain of PEG2000 is calculated to be in the range of 15–18 depending on the solvent used. From the elemental analysis of the complex obtained in pure water, the threading of 15 molecules of α-CD is confirmed. All further calculations

regarding the number of moles of the threaded cuc[6] are done under the assumptions that not more than 15 guest molecules are threaded on one PEG2000 chain.

In 8 vol% HCl, only very small amounts of cuc[6] are threaded on the PEG chain. The experimentally observed number of moles of Cuc[6] indicate that mainly α-CD is threaded. Only very few molecules of cucurbit[6]uril are present, e.g. a molecular content of Cuc[6] of 0.01 means that one molecule of Cuc[6] is threaded on one hundred chains of PEG2000. In this solvent, only minor amounts of Cuc[6] are threaded simultaneously with α-CD. In 16 vol% HCl, the number of threaded Cuc[6] molecules increase significantly. The solubility of Cuc[6] strongly depends on the concentration of hydrochloric acid [12]. Thus, with increasing acid concentration the amount of dissolved Cuc[6] increases. In this way, the molar ratio of dissolved α-CD to Cuc[6] is changed and from a statistical point of view the probability to thread Cuc[6] is increased.

If the threading process proceeds identical for both macrocyclic ligands the concentration of both ligands in solution and threaded on the PEG2000 chain should be identical. The nitrogen content calculated from the molar ratio of both ligands in solution should be identical with the experimental nitrogen content in the solid complex. This is shown in Figure 6. Surprisingly the amount of nitrogen for the mixed complexes synthesized in 8 vol% HCl is much lower than expected. The mixed complexes obtained from 16 vol% HCl possess the expected nitrogen content. Obviously the higher acid concentration favors the threading process of Cuc[6] compared with α-CD. ^{1}H-NMR spectroscopic measurements are made using the PEG complexes with the highest amounts of threaded Cuc[6]. These spectra are shown in Figure 5. Depending on the amount of Cuc[6] used for synthesis [(I) 200 mg, (II) 300 mg, (II) 400 mg] additional peaks appear in the ^{1}H-NMR spectra. One of these peaks is a doublet at 4.37 ppm, which is overlapped by α-cyclodextrin signals. Another peak is a singlet at 5.65 ppm and a doublet at 5.99 ppm. These three peaks and the chemical shifts are typical for the presence of Cuc[6] in the solvent used. These peaks are marked with an asterix in Figure 5. The observed broadening of the signals is caused by the kinetic of the threading and dethreading of the macrocyclic ligands on the PEG. The singlet at 3.86 ppm can be assigned to PEG. From the ^{1}H-NMR spectra of the complex with the highest amount of Cuc[6] (product C400) the molar ratio between α-CD and Cuc[6] can be calculated. One gets a value of 4.7. This value is absolute identical with the value obtained from the elemental analysis.

A further qualitative proof of the formation of mixed complexes between PEG2000 and α-CD and Cuc[6] is obtained from the DSC measurements. The heat flow measured in case of the solid complexes of PEG·α-CD and PEG·α-CD·Cuc[6] is not identical. It is well recognized that in all formed complexes, the melting peak of the pure PEG2000 does not exist although PEG2000 is present in the solid samples, which is verified by

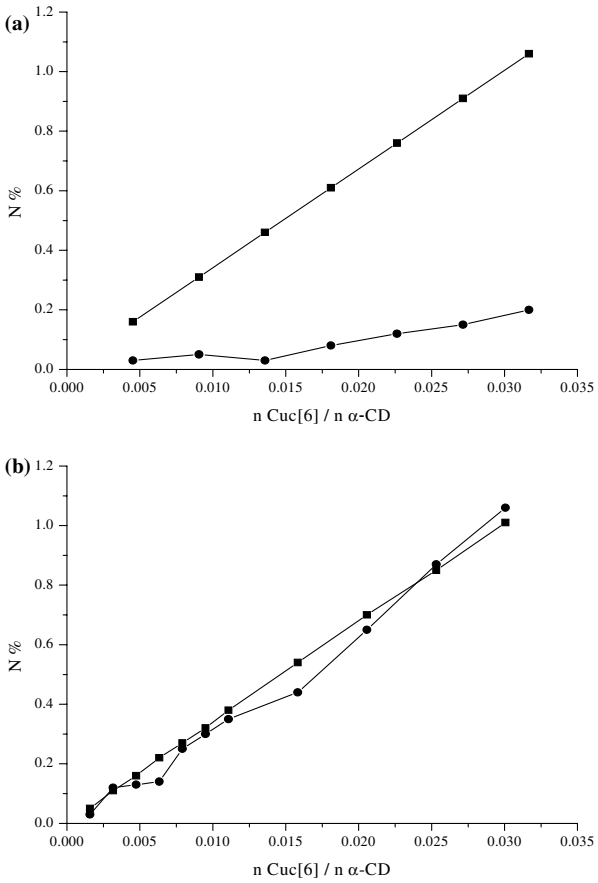

Figure 6. Nitrogen content calculated using the molar ratio Cuc[6] over α-CD in solution (■) and the experimental nitrogen content found in the solid complexes (●) synthesized in 8 vol% HCl (a) and in 16 vol% HCl (b).

^{1}H-NMR measurements (see Figure 5). Due to the inclusion of PEG into the cavities of both ligands the thermal behavior of PEG2000 is changed. The complex formation prevents any interactions between the chains of PEG.

Conclusions

The formation of mixed PEG complexes with α-CD and cuc[6] is possible. The amount of threaded Cuc[6] depends on the solvent composition used during the synthesis. Further experiments are necessary to increase the number of moles of Cuc[6] threaded simultaneously with α-CD. The formation of mixed complexes with Cuc[6], α-CD and PEGs enables the synthesis of comparable polyrotaxanes. These results will be reported separately.

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