Upper-rim alternately tethered α-cyclodextrin molecular receptors: synthesis, metal complexation and interfacial behavior

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Three novel α-cyclodextrin tripods bearing three ureido-bipyridyl tethers symmetrically distributed on their upper rim in the A,C,E positions and alternated with hydroxyl, acetyl or lauryl moieties were prepared by the tandem Staudinger–Aza–Wittig *alias* "phosphine imide" strategy. The functionalisations on the cyclodextrin upper rim allowed a fine-tuning of the metal complexation and amphiphilic properties.

Introduction

Currently, metallocyclodextrins (metallo-CyDs) are viewed as interesting coordination compounds in which one or several modified CyDs act as ligands and/or as "distributors" of spatially preorganised substituents. In the past decade the metallocyclodextrins have been shown to be a valuable source of original supramolecular devices exhibiting a wide range of interesting properties;[1–8] formation of metal and host–guest complexes showed to be particularly interesting in this respect to obtain mimes of metalloenzymes,[9,10] new catalysts,[11] and photomolecular devices.[12,13] Furthermore, metallo-CyDs are viewed as efficient and selective coordination molecules in which the rigid truncated cone of the CyD acts as an organizing platform distributing spatially preorganised bidendated heterocyclic ligands able to form selective metal complexes.[14] In a precedent work we demonstrated that a $6^A,6^C,6^E$–α-CyD was highly selective in the complexation of "hard" and "soft" cations (HSAB classification).[15] Moreover, the fluorescence A–ET–E light conversion process in the corresponding lanthanide complexes were improved in the tripods, compared to fully substituted derivatives.[16,17] In this work, we present an original synthesis of a family of new symmetrically tri-functionalised α-CyDs derivatives, as well as their metal complexation and air-water interface properties.

Results and discussion

Synthesis of the alternately tethered α-cyclodextrins

In continuation of our work on $6^A,6^C,6^E$–triazido-6^A, $6^C,6^E$-trideoxy-$6^B,6^D,6^F$-tri-*O*-methyl-hexakis(2,3-di-*O*-methyl)-cyclomaltohexaose[2] preparation, here we describe the synthesis of new sets of α-CyD tripods. The first set consists of $6^A,6^C,6^E$-triazido-$6^A,6^C,6^E$-trideoxy-$6^B,6^D,6^F$-tri-*O*-acetyl-hexakis-(2,3-di-*O*-acetyl)cyclomaltohexaose **1**, its deacetylated derivative **2** and the $6^A,6^C,6^E$-triazido-$6^A,6^C,6^E$-trideoxy-$6^B,6^D,6^F$-tri-*O*-lauroyl-hexakiscyclomaltohexaose-cyclomaltohexaose **3**; the second set consists of bipyridyl derivatives, the $6^A,6^C,6^E$-(5-methyleneureido-5′-methyl-2,2′-bipyridine)-$6^A,6^C,6^E$-trideoxy-$6^B,6^D,6^F$-tri-*O*-acetyl-hexakis(2,3-di-*O*-acetyl)cyclomaltohexaose **4**, its deacetylated derivative **5** and the alternately upper-rim substituted $6^A,6^C,6^E$-(5-methyleneureido-5′-methyl-2,2′-bipyridine)-$6^A,6^C,6^E$-trideoxy-$6^B,6^D,6^F$-tri-*O*-lauroyl-hexakiscyclomaltohexaose **6** (Scheme 1). Functionalisation by the bipyridyl tethers were conducted using the tandem Staudinger–Aza–Wittig *alias* "phosphine imide" reaction[16,17] The esterification with lauryl chloride was achieved using a method described in the literature.[18] Compounds **1–6** were characterised by IR, UV-Vis, ^{1}H, ^{13}C NMR and elemental analysis. The spectroscopic data are in agreement with the assigned structures (see Experimental section). As expected, the IR spectra of **4–6** exhibited characteristic frequencies of the carbonyl functions: urea ν_{CO-NH} at 1654 cm^{-1}; ester ν_{CO-O} at 1750 cm^{-1} (acetates) and aromatic double bonds of bipyridyl groups $\nu_{C=C}$ at around 1550 cm^{-1}. In the case of the podand **6** the carbonyl ester frequencies are split and shifted to 1735 and 1715 cm^{-1} from their natural position near 1750 cm^{-1} indicating that the ester carbonyls are very likely engaged in strong C=O···H–N–CO hydrogen bonds with vicinal urea nitrogen protons; the splitting shows that the lauryl chains are in different environment, which suggests a probable inclusion of one lauryl chain inside the CyD cavity.[19] In the corresponding lanthanide complexes, the urea and ester group frequencies are shifted and collapse into a single large absorption band centered at 1635 cm^{-1} indicating an efficient coordination of both carbonyls with the lanthanide cation. The ^{13}C NMR spectra of **4–6** in solution (DMSO) indicate that the ligands have a C_2 symmetry. The signals corresponding to the NH–CO–NH carbonyl carbons at δ 165.2–159.0, to the *CO*–O carbonyl carbons at δ 167.9–162.2 and the sharp signals corresponding to the bipyridyl carbons at δ 159 to 120 were detected.

Metal ion complexation

The electronic spectra of the free podands **4**, **5** and **6** recorded in MeOH show one, two and three absorption maxima in the UV

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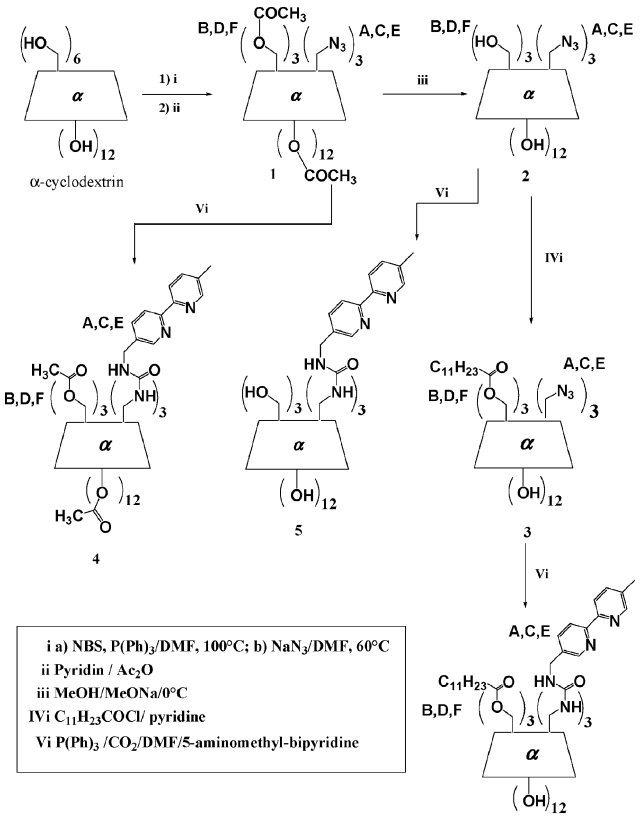

Scheme 1

region, respectively. Indeed, the non-acetylated tripod **5** exhibits one maximum at λ_{max} = 290 nm (38 000 mol^{-1} dm^3 cm^{-1}), the acetylated tripod **4** exhibits two maxima at λ_{max} = 245 (92 000 mol^{-1} dm^3 cm^{-1}) and 289 nm (112 000 mol^{-1} dm^3 cm^{-1}) and the lauryl tripod **6** exhibits two maxima at 273 (69 000 mol^{-1} dm^3 cm^{-1}) and 293 nm (73 000 mol^{-1} dm^3 cm^{-1}) as well as a shoulder at 319 nm (43 000 mol^{-1} dm^3 cm^{-1}). These absorptions correspond to the π–π* and n–π* transitions of bipyridyls, and to the urea and carboxylate carbonyl double bonds. The extinction value calculated from the molecular extinction coefficient in **5** is around 12 700 mol^{-1} dm^3 cm^{-1} per bipyridine unit; the latter value is situated in the range found in the literature.[15] All the coefficients were enhanced in the tripods **4** and **6** after esterification with acetyl or lauryl moieties.

As illustrated in Fig. 1, the tripods **4**, **5** and **6** represent a new family of three heterotritopic molecular receptors having two metal coordination sites: one formed by the bipyridyl units and the second by ureas and/or carboxylates, the third site is formed by the CyD torus cavity, which is well known to form host–guest complexes by inclusion of small organic hydrophobic molecules.

The titrations of **4**, **5** and **6** with the $EuCl_3 \cdot 6H_2O$, $TbCl_3 \cdot 6H_2O$ (“hard” HSAB) lanthanide cations and $CuCl_2$, $CoCl_2$ (“borderline” transition cations) were monitored by UV-Vis spectroscopy. As expected based on the previous experiments performed with the tripod $6^A,6^C,6^E$-(5-methylene-ureido-5′-methyl-2,2′-bipyridine)-$6^A,6^C,6^E$-trideoxy-$6^B,6^D,6^F$-tri-*O*-methyl-hexakis(2,3-di-*O*-methyl)cyclomaltohexaose,[15] the titration

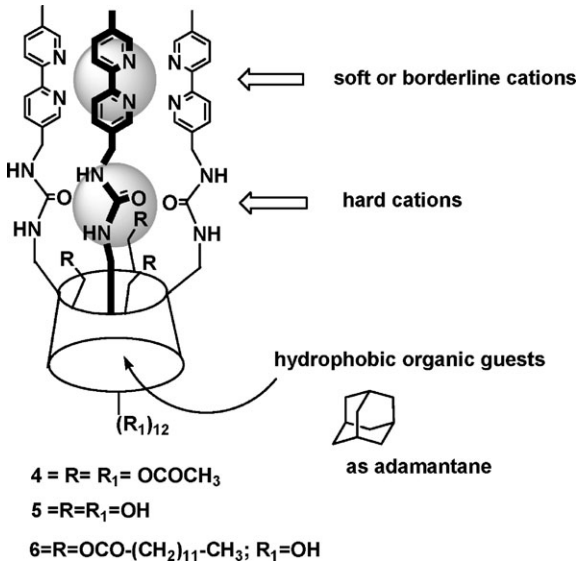

Fig. 1 Schematic representation of the α-CyD tripods and their complexation sites.

(Fig. 2) and the ligand speciation curves (Fig. 3) showed formation of mononuclear podandates of [1 : 1] stoichiometry with podand **5** and Eu^{III}, Co^{II} and Cu^{II}.

The complexation constants log(β_{11}) have been determined[20] and were 6.0 ± 0.4, 6.2 ± 0.8 and 6.6 ± 0.5, for Eu^{III}, Co^{II} and Cu^{II}, respectively. It should be assumed that the Eu^{III} cation in **5** is localised and coordinated at the urea functions (“hard” HSAB lanthanide cation interaction), with a constant value of 6.0 ± 0.4, slightly higher than Tb^{III}. Looking at Co^{II} and Cu^{II} borderline cations they are coordinated in a different site (to the nitrogens of the three bipyridyl units). Observed constants for the analogous permethylated tripod[15] were 6.4 for Cu^{II} and 6.7 for Fe^{II}, while in the present case, constants are of the same order, 6.2 for Co^{II} and 6.6 for Cu^{II} and were found always greater than those of lanthanides at the urea sites. Nevertheless, in the case of the non-acetylated podands **5** and **6**, an unexpected formation of dinuclear [2 : 1] Tb^{III} complexes was observed, as determined by the presence of a second isosbestic point in the titration curve (Fig. 4, inset). As demonstrated with similar podands,[14,15] the absence of the red shift during the complexation of Tb^{III} indicated that the bipyridyl units were not involved in this secondary complexation step. Consequently, it was deduced that one of the two Tb^{III} cations

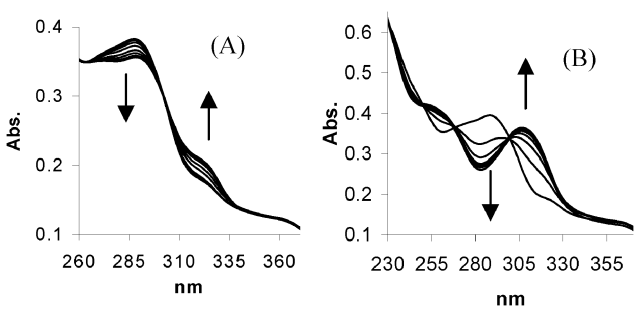

Fig. 2 Spectrophotometric titration of ligand **5** ($c = 1.0 \times 10^{-5}$ mol L^{-1}) in MeOH: (A) with $EuCl_3 \cdot 6H_2O$, (B) with $CoCl_2 \cdot 6H_2O$.

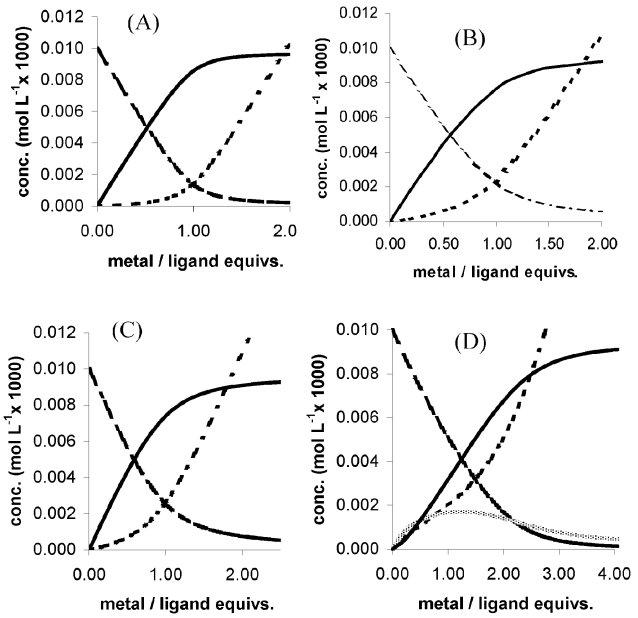

Fig. 3 Ligand speciation curves for (A) Cu^{II}, (B) Co^{II}, (C) Eu^{III}, (D) Tb^{III} with podand **5**. Free metal (dashed line), complexes (solid line), [1 : 1] Tb^{III} complex (light grey line), free ligand (dashed–doted line).

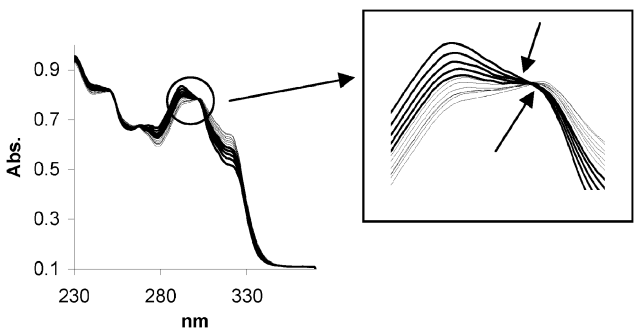

Fig. 4 Spectrophotometric titration of tripod **6** ($c = 1.0 \times 10^{-5}$ mol L^{-1}) with $TbCl_3{\cdot}6H_2O$. For the inset the arrows indicate the isosbestic points.

was complexed by the ureas, and the second by the free secondary hydroxyl groups of the CyD lower rim acting like a chelating crown. Taking into account the weaker solvation energy of the lanthanide cations with MeOH compared to H_2O, one can assume a possible complexation of the cation with the CyD secondary hydroxyls at the lower rim. The determined complexation constants $\log(\beta_{11})$ and $\log(\beta_{12})$ were 5.2 ± 0.2 and 11.2 ± 0.5 for the Tb^{III} mononuclear and dinuclear complexes of the tripod **5** and 5.0 ± 0.2 and 9.7 ± 0.7 for the Tb^{III} mononuclear and dinuclear complexes of the tripod **6**. For each tripod, the first value corresponds to the Tb^{III} cation coordinated by ureas; these values are consistent with the data obtained previously with the permethylated tripod.[15]

The second value corresponds to the Tb^{III} cation coordination at the secondary hydroxyls of the CyD core.[21] The unexpected preference for Tb^{III} compared to Eu^{III} complexation by the α-CyD lower-rim free hydroxyls of podands **5** and **6** pushed us to investigate the effective Tb^{III} cation location. The titration

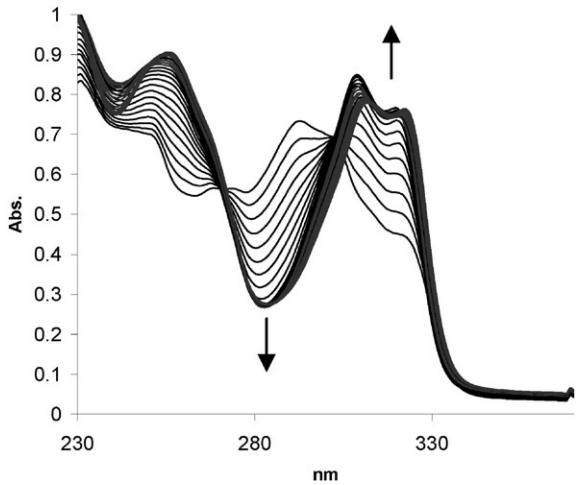

Fig. 5 Spectrophotometric titration of tripod **6** ($c = 1.0 \times 10^{-5}$ mol L^{-1}) with $CuCl_2$ in MeOH.

of **6** with Tb^{III} was conducted on the [1 : 1] stoichiometric [adamantane-**6**-CyD] host–guest complex instead of the free ligand, because the adamantane-CyD complex is highly stable in solution.[22] In these conditions, complexation of the Tb^{III} cation at the α-CyD secondary hydroxyls becomes impossible as illustrated in Fig. 5. As expected, the titration curve indicates that only the mononuclear Tb^{III} complex was formed with ureas; the complexation constant $\log(\beta_{11}) = 5.5 \pm 0.5$ was of the same order as those measured with the free tripods **5** and **6**. This result confirms the preference of the unsubstituted α-CyD lower rim for Tb^{III} complexation. A supplementary evidence of this preference was obtained with the formation of the Eu^{III} or Tb^{III} mononuclear complexes at the urea site with the peracetylated tripod **4**, having all its secondary hydroxyls acetylated.

On the other hand, these results were supported by study of the corresponding homotrinuclear [L : M_3] complexes by addition of Co^{II} or Cu^{II} to the tripod **6**. Formation of these complexes was evidenced by the appearance of three isosbestic points at 303, 314, 321 nm (Fig. 5), together with red shifts of the 294 and 320 nm absorption bands to 309 and 323 nm due to the coordination of Cu^{II} by the bipyridyl moieties and other functional groups.

It is important to note that this complexation has never been observed before in this series of molecules and could not be achieved either with β- or γ-CyDs,[23] or with the lower-rim permethylated-α-CyDs analogous podand derivatives.

As observed above with Tb^{III}, the titration with Cu^{II} performed on the [1 : 1] stoichiometric [adamantane-**6**-CyD] host–guest complex instead of the free ligand, did not give the [L : M_3] but the dinuclear [L : M_2] complex. This result confirms that Cu^{II} was initially complexed at the three sites, namely urea/esters, bipyridines and secondary hydroxyls in the α-CyD tripod **6**.

Fluorescence spectroscopy

The luminescence excitation of [**4**–**6**⊂Eu^{III}]Cl_3 and [**4**–**6**⊂Tb^{III}]Cl_3 [1 : 1] complexes in methanol, from 316 to 320 nm results in a standard emission of the Eu^{III} and Tb^{III} by

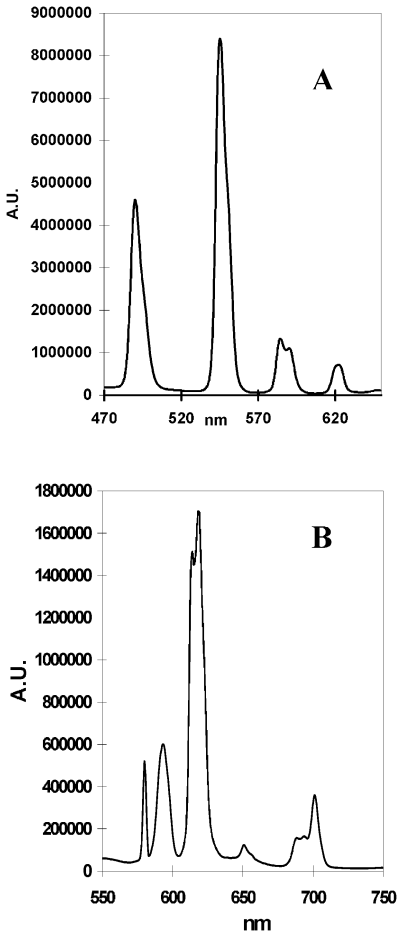

Fig. 6 Fluorescence emission spectra of peracetylated [**4** : Tb^{3+}] (A) and [**4** : Eu^{3+}] (B) complexes in MeOH at 20 °C, $c = 1.05 \times 10^{-5}$ mol L^{-1}; $\lambda_{ex} = 320.4$ nm.

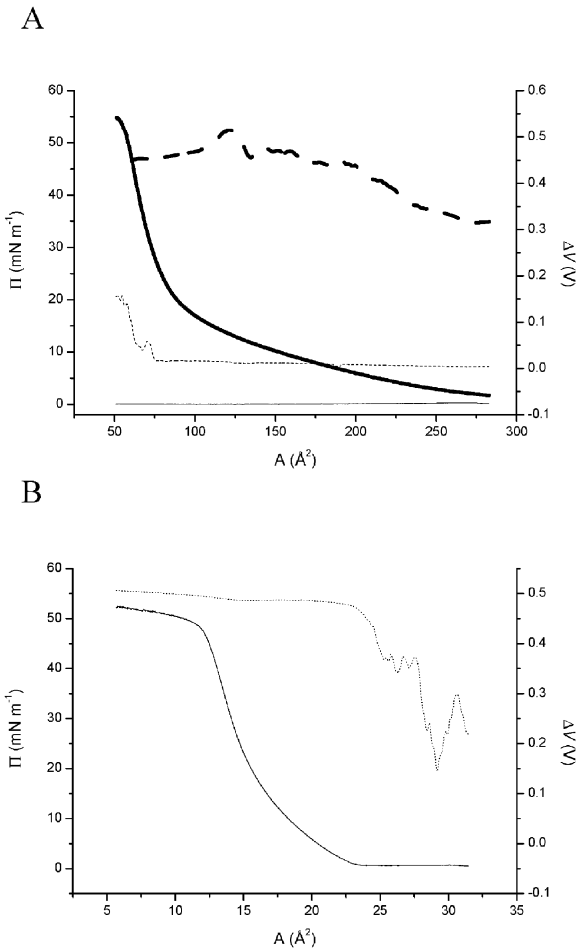

Fig. 7 Compression isotherms of the tripod **6**: *Π–A* and Δ*V–A* (solid and dashed lines, respectively) isotherms obtained on pure water (thin lines) and on 5 M NaCl solution (thick lines). The isotherms were obtained with 100 μL (A) and 900 μL (B) of a chloroform solution of the podand **6** (conc. 1.02 mg mL^{-1}) spread at the air/aqueous solution interface.

an absorption–energy transfer–emission light conversion process (antennae effect; A–TE–E), with the transitions corresponding to $5D_0$–$7F_j$ (Eu^{III}), and $5D_4$–$7F_j$ (Tb^{III}) (Fig. 6). The lifetimes $\tau_{(300\ K)}$ recorded in the time-resolved mode from the measurement of the decreasing emission intensity at 615 (europium) and 544 nm (terbium) were $\tau_{(300\ K)} = 0.82$, 0.58, 0.80 ms for the [**4–6**⊂Eu^{III}]Cl_3 and $\tau_{(300\ K)} = 0.82$, 0.58, 0.66 ms for the [**4–6**⊂Tb^{III}]Cl_3 complexes, respectively. The quantum yields of the peracetylated [**4**⊂Tb^{III}]Cl_3 and [**4**⊂Eu^{III}]Cl_3 complexes were calculated using the relation of Haas and Stein[24] and gave, respectively, $\Phi_f = 0.18 \pm 30\%$ and $0.02 \pm 30\%$. These values are situated within the range expected for such structures and strengthen the results obtained before in the case of the permethylated tripod analogue[15] and for the URFT β-CyDs Eu^{III} and Tb^{III} podandates.[14]

It can be noticed that these values are also in accordance with the NH and OH groups vibronic deactivation power which is more efficient in the case of europium compared to terbium. This effect is particularly obvious in the case of the fully deacetylated podandate **5**, which displays accordingly the lowest lifetimes.

Interfacial behavior

The utility of the new derivatives for elaborating new materials was evaluated using the Langmuir film technique. To this end, Langmuir films of the podand **6** were formed at the air/aqueous interface. It has to be mentioned that the tripod **6** is amphiphilic due to the presence of three hydrophobic lauryl chains at the CyD upper rim. On the other hand, this molecule is analogous to a hexapod ureido-bipyridyl α-CyD derivative, which we studied before.[14] Comparing the tripod **6** and the previously studied hexapod was expected to yield valuable information on the relation between the molecule structure and the properties of the films. Both surface pressure–area (*Π–A*) and surface potential–area (Δ*V–A*) isotherms (Fig. 7) indicate formation of aggregates in the films spread on the pure water surface with the podand **6** (Fig. 7B). We propose that this effect is due to the inclusion of lauryl chains into the CyD cavity, leading to formation of complexes; the latter was also observed in the bulk using IR spectroscopy.

Importantly, the compression isotherms of the films spread on the 5 M NaCl subphase (Fig. 7A, thick lines) indicate formation of true monomolecular films. Indeed, the values of the molecular areas measured at the collapse of the film correspond to the projection of this molecule on the water

plane.[25] By comparing the results obtained with the two subphases (Fig. 7), the number of molecules of the podand **6** per aggregate in the film spread on pure water is estimated to be five.

The film formed on the 5 M NaCl subphase collapses at A_{coll} = 57.2 Å^2 and Π_{coll} = 51.9 mN m^{-1}. The compressibility modulus[25] calculated for the most compact state of the film is Cs^{-1} = 145.4 mN m^{-1}. It can be noticed that the ureido-bipyridyl α-CyD hexapod formed less rigid (Cs^{-1} = 41.7 mN m^{-1}) and less stable films (Π_{coll} = 29.4 mN m^{-1}) compared to the podand **6**.[26] The higher rigidity of the film formed with the podand **6** may be due to the strong C=O···H–N–CO hydrogen bonds, as observed with IR. On the other hand, the higher rigidity of this film may be linked to the presence of lauryl moieties, making it more hydrophobic compared to the hexapod. The molecular dipole moment determined from the ΔV–A isotherms at the most compact state of the film is 0.164 and 0.683 D for pure water and NaCl subphase, respectively. These results indicate a more upright orientation of the molecules in the latter case. The overall properties of the film formed with the podand **6** indicate its higher suitability for depositing high density, homogeneous supramolecular films[27–30] on solid surfaces compared to the hexapod derivative. The results obtained previously with the hexapod indicate that NaCl present in the subphase would not modify the optical properties of the transferred film.[25] On the basis of the results obtained, a new tripod bearing longer hydrocarbon chains will be synthesized with the aim to decrease its water solubility.

Conclusions

This work reports a four or five steps original synthesis of three novel α-cyclodextrin tripods bearing three ureido-bipyridyl tethers symmetrically distributed in the A, C and E positions on the cyclodextrin upper rim, or alternated with lauryl ester moieties grafted in the B, D and F positions. The complexation properties towards Eu^{III}, Tb^{III} cations and Cu^{II}, Co^{II} cations were examined in solution. We can conclude that formation of mononuclear to trinuclear complexes is strongly dependant on the chemical functions present at the upper rim of the α-cyclodextrin. An unexpected behaviour of tripods **5** and **6** was observed with Tb^{III}. Indeed, these lower rim non-acetylated derivatives showed coordination of the lanthanide cation at the secondary free hydroxyls of the CyD core analogues to that observed with the tripod **6** in the case of the trinuclear Cu^{II} complex. Efficient absorption–energy transfer–emission light conversion processes (antennae effect; A–TE–E) were observed with the Eu^{III} and Tb^{III} lanthanide complexes. These effects indicate that the long lifetime complexes could be interesting as potent fluorescent tracers. However, the acquired fluorescence properties are situated within the range obtained before for the upper-rim fully tethered β-CyDs lanthanide podandates. Taken together, the results obtained in this work let us think that the new α-CyD derivative with adjusted chelating and amphiphilic properties can be useful for elaborating new nanosurfaces with specific physical and chemical properties for applications as actuators or sensors.

Experimental

General

Structures of all compounds were assigned by ^{1}H and ^{13}C NMR spectra recorded on a Bruker DRX-400 spectrometer. FTIR spectra were recorded on a Bruker Vector 22 apparatus. UV/Vis spectra were done on a Safas Uvmc^2 at 20 °C, the ionic strength of the solutions was not controlled.

Stability constants were determined by UV-Vis titrations at 20 °C, of the ligands (c = 1.0 × 10^{-5} mol L^{-1}) in MeOH by addition of metal ion 5 μL aliquots in water (from 0.2 to 3 equiv.). Metal complexation and speciation equilibria among the free metal ion (M), free ligand (L) and their complexes were solved using the SPECFIT® program (using the iterative Newton–Raphson method). The equilibria are defined in terms of overall stability constants for the general case: $\beta_{ml} = [M_mL_l]/[M]^m[L]^l$ where M = a free metal ion, L = a free ligand and the stoichiometric indices m, l can take any integral value to define the state of complexation of a particular species (for the mathematical treatment see ref. 20).

Luminescence experiments were performed on a Spex Fluorolog II photon counting spectrofluorimeter equipped with a 450 W xenon continuous-wave and a 150 W pulsed xenon irradiation sources. Lifetimes have been obtained from measurement of the decreasing emission intensity at 615 nm (europium) and 544 nm (terbium) and calculated using the relation $I(t) = I_0\exp(-t/\tau)$ (correlation coefficient $r \geq 0.999$; estimated error 10%). Quantum yields were calculated using the relation: $\Phi_{[c]} = \Phi_{ref.}(OD_{[c]}S_{ref}n^2_{[c]}/OD_{ref}S_{[c]}n^2_{ref})$ in which $\Phi_{[c]}$ and $\Phi_{ref.}$ are the quantum yields of the sample (unknown) and reference, $OD_{[c]}$ and OD_{ref} are the optical density of the sample and reference, S_{ref} and $S_{[c]}$ are the integrated intensity of the reference and sample signals, $n_{[c]}$ and n_{ref} are the refractive index of the sample and reference.[24] with an experimental uncertainty of *ca.* 30%. Standards were: $\Phi_{Eu\ aq}^{3+}$ = 0.006 (618 nm); $\Phi_{Tb\ aq}^{3+}$ = 0.08 (542 nm); λ_{exc} wavelengths of europium and terbium standards are 395 and 265 nm, respectively.

The surface pressure (Π) and electric surface potential (ΔV) measurements were carried out with a KSV 5000 Langmuir balance (KSV Instruments Ltd., Helsinki, Finland). A Teflon® trough (15 cm × 58 cm × 1 cm) with two hydrophilic Delrin barriers (symmetric compression) was used in compression isotherm experiments. The system was equipped with an electrobalance and a platinum Wilhelmy plate (perimeter 3.94 cm) as a surface pressure sensor. Surface potential was measured using a KSV Spot 1 with a vibrating plate electrode and a steel counter electrode immersed in the subphase. The apparatus was closed in a Plexiglas box, and temperature was kept constant at 20 °C. The monolayers were spread from calibrated solutions of the podand **6** (concentration 1.02 mg mL^{-1}) in chloroform by the use of a microsyringe (Hamilton Co., USA). After the equilibration time of 20 min, the films were compressed at the rate of 2.5 mm min^{-1} barrier^{-1} by two symmetrically moving barriers. A PC computer and KSV software were used to control the experiments. Each compression isotherm was performed at least three times. The standard error was ±0.5 Å^2 with mean

molecular area, ±0.2 mN m^{-1} with surface pressure and ±5 mV with surface potential measurements.

All new compounds gave satisfactory spectroscopic data. DMF was dried over $CaSO_4$, filtered off and flushed with argon to eliminate dimethylamine.

Syntheses

$6^A,6^C,6^E$-Triazido-$6^A,6^C,6^E$-trideoxy-$6^B,6^D,6^F$-tri-*O*-acetyl-hexakis(2,3-di-*O*-acetyl)cyclomaltohexaose 1. This was prepared by a previously published procedure.[31]

$6^A,6^C,6^E$-Triazido-$6^A,6^C,6^E$-trideoxycyclomaltohexaose 2. A 1 M NaOMe (11.92 mmol, 40 equiv.) solution in MeOH (12 mL) was added dropwise to a MeOH solution (40 mL) of **1** (0.3 mmol, 0.5 g) at 0 °C. The mixture was stirred 1 h at this temperature, then 1 h more at rt. The reaction mixture was neutralised by addition to a batch of ion-exchange resin Amberlyst IRN77 until pH = 6. After filtration and evaporation, distilled water (20 mL) was added to the residue which was lyophilised. A white snow-like powder 96% (0.298 g, 0.28 mmol) was obtained (Found: C, 36.43; H, 5.95 N, 10.07. $C_{36}H_{57}N_9O_{27}\cdot 7H_2O$ requires: C, 36.81; H, 6.05; N, 10.73%); FTIR (KBr): ν/cm^{-1} = 2103 (N_3); ^{1}H NMR (400 MHz, D_2O, 25 °C): δ 5.14 (m, 6H, H1), 3.96 (m, 6H, H3), 3.96–3.80 (m, 18H, H6a, H5), 3.72–3.66 (m, 18H, H6b, H2), 3.54 (m, 6H, H4). ^{13}C NMR (100 MHz, D_2O, 25 °C): δ 102.1 (C1), 81.5 (C4), 74.0 (C2), 72.3 (C3), 72.1 (C6), 60.9 (C5).

$6^A,6^C,6^E$-Triazido-$6^A,6^C,6^E$-trideoxy-$6^B,6^D,6^F$-tri-*O*-lauroyl-hexakiscyclomaltohexaose-cyclomaltohexaose 3. Lauroyl chloride (0.1 mL, 0.433 mmol, 5 equiv.) was added to a solution of **2** (0.200 g, 0.190 mmol) in anhydrous pyridine (50 mL) at rt. under argon. The resulting mixture was stirred 20 h more and evaporated to dryness. The residue was treated with toluene (3 × 30 mL) then with (3 × 100 mL) of methanol. The crude material was purified by flash chromatography on silica gel (MeOH–CH_2Cl_2 1 : 1). An ivory, soap-like powder 47% (0.143 g, 0.090 mmol) was obtained (Found: C, 51.97; H, 6.31; N, 7.45. $C_{71}H_{121}N_9O_{30}\cdot 3H_2O$ requires: C, 52.15; H, 6.38; N, 7.71%); ^{1}H NMR (400 MHz, D_6-DMSO, 25 °C): δ 12.00 (s, 12H, OH); 5.93–5.30 (m, 6H, H1 CyD), 4.03–2.97 (m, 36H, H5, H3, H6 CyD), 1.48 (t, 6H, J = 6.55 Hz, CH_2–COO-lauryl), 1.25 (m, 54H, CH_2-lauryl), 0.86 (t, 9H, J = 5.32 Hz, CH_3 lauryl). ^{13}C NMR (400 MHz, D_6-DMSO, 25 °C): δ 158.6 (CO ester), 82.9 (C1, CyD), 72.1 (C4, CyD), 65.7 (C6a, CyD), 62.5 (C2-C3, CyD), 58.6 (C5-CyD), 54.7 (C6b, CyD), 31.9, 27.0, 26.5, 22.3 (CH_2 lauryl), 16.4 (CH_3 lauryl).

$6^A,6^C,6^E$-(5-Methyleneureido-5′-methyl-2,2′-bipyridine)-$6^A,6^C,6^E$-trideoxy-$6^B,6^D,6^F$-tri-*O*-acetyl-hexakis(2,3-di-*O*-acetyl)-cyclomaltohexaose 4. Triphenylphosphane (4.190 g, 15.98 mmol, 70 equiv.) were added to a solution of **1** (0.383 g, 0.228 mmol) in anh. DMF (25 mL). The reaction mixture was stirred 30 min. under argon, then an anhydrous CO_2 gas stream was bubbled for 30 min through the solution and mono-aminomethyl-5-methyl-5′-2,2′-bipyridine (0.150 g, 0.753 mmol, 3.3 equiv.) was added to the mixture. After 24 h the mixture was evaporated to dryness and then MeOH (2 mL) was added to the residue. The resulting solution was treated by ether and allowed to precipitate. The crude product was extracted by a Soxhlet (ether) during 24 h to eliminate triphenylphosphane residue. The resulting white powder 46% (0.239 g, 0.105 mmol) was dried over KOH *in vacuo* (Found: C, 55.31; H, 5.50; N, 7.12. $C_{105}H_{126}N_{12}O_{45}$ requires: C, 55.39; H, 5.53; N, 7.39%); UV/Vis (MeOH) λ_{max}/nm (ε/mol^{-1} dm^3 cm^{-1}): 245 (92 000), 289 (112 000); FTIR (KBr): ν = 3020 cm^{-1} (C–H arom.), 2925–2880 cm^{-1} (CH_2, CH_3 alkyl), 1750 cm^{-1} (C═O ester), 1684 cm^{-1} (C═O urea). ^{1}H NMR (400 MHz, D_6-DMSO, 25 °C): δ 8.55 (s, 3H, H6′), 8.51 (s, 3H, H6), 8.30 (d, 3H, J 7.8 Hz, H3′), 8.26 (d, 3H, J 7.8 Hz, H3), 7.78 (d, 3H, J 7.8 Hz, H4′), 7.74 (d, 3H, J 7.8 Hz, H4), 7.25 (t, 3H, NH), 6.71 (t, 3H, NH), 5.55–4.95 (m, 6H, H1 CyD), 4.80–3.59 (m, 36H, H2, H3, H5 CyD), 4.31 (m, 6H, CH_2–bipy), 2.36 (s, 9H, CH_3–bipy), 2.01 (m, 35H, CH_3–C═O). ^{13}C NMR (100 MHz, D_6-DMSO, 25 °C): δ 167.9 (*C*═O urea), 165.2 (*C*═O ester), 159.5 (C6 bipy), 158.7 (C6′ bipy), 153.7 (C4, bipy), 148.5 (C4′ bipy), 136.9, 136.6, 136.3 (C5, C5′, C3, C3′ bipy), 120.1 (*C*H_2-bipy), 99.1 (C1 CyD), 81.8 (C4, CyD), 70.6 (C6a, CyD), 61.2 (C2, C3, CyD), 57.3 (C6b, CyD), 18.3 (*C*H_3–C═O), 18.1 (*C*H_3, bipy).

$6^A,6^C,6^E$-(5-Methyleneureido-5′-methyl-2,2′-bipyridine)-$6^A,6^C,6^E$-trideoxycyclomaltohexaose 5. Triphenylphosphane (4 g, 15.16 mmol, 70 equiv.), were added to a solution of **2** (0.5 g, 0.477 mmol) in anhydrous DMF (100 mL). The reaction mixture was stirred for 30 min under argon, then an anhydrous CO_2 gas stream was bubbled for 30 min through the solution and monoaminomethyl-5-methyl-5′-2,2′-bipyridine (0.150 g, 0.758 mmol, 3.5 equiv.) was added to the mixture. After 72 h the reaction mixture was evaporated to dryness then MeOH (2 mL) was added to the residue. The resulting solution was treated by ether for precipitation. The crude product was extracted by a Soxhlet (ether) during 24 h to eliminate traces of triphenylphosphane. The resulting white powder 38% (0.298 g, 0.180 mmol) was dried over KOH *in vacuo* (Found: C, 49.98; H, 6.01; N, 9.31. $C_{75}H_{96}N_{12}O_{30}\cdot 6H_2O$ requires: C, 51.35; H, 6.16; N, 9.58); UV/Vis (MeOH) λ_{max}/nm (ε/mol^{-1} dm^3 cm^{-1}) = 290 (38 000); FTIR (KBr): ν = 1653 cm^{-1}, (C═O urea). ^{1}H NMR (400 MHz, D_6-DMSO, 25 °C): δ 8.56 (s, 3H, H6′ bipy), 8.51 (s, 3H, H6 bipy), 8.30 (d, 3H, J = 8.06 Hz, H3′ bipy), 8.26 (d, 3H, J = 8.06 Hz, H3), 7.24 (d, 3H, J = 7.30 Hz, H4′), 7.17 (d, 3H, J = 7.30 Hz, H4), 5.73 (s, 6H, H1 CyD), 4.81 (s, 6H, CH_2–bipy), 4.04–2.90 (m, 36H, H2, H3, H5, H6 CyD), 1.10 (t, 9H, J = 7.05 Hz, CH_3–bipy).

$6^A,6^C,6^E$-(5-Methyleneureido-5′-methyl-2,2′-bipyridine)-$6^A,6^C,6^E$-trideoxy-$6^B,6^D,6^F$-tri-*O*-lauroyl-hexakiscyclomaltohexaose 6. Triphenylphosphane (3.98 g, 15.2 mmol, 40 equiv.), were added to a solution of **3** (0.608 g, 0.381 mmol) in anhydrous DMF (50 mL). The reaction mixture was stirred for 30 min under argon, then an anhydrous CO_2 gas stream was bubbled for 30 min through the solution and mono-aminomethyl-5-methyl-5′-(2,2′-bipyridine) (0.303 g, 1.52 mmol, 4 equiv.) was added to the mixture. After 24 h the mixture was evaporated to dryness then CH_2Cl_2 (5 mL) was added to the residue. The resulting solution was treated with hexane and the precipitate was then filtered. The crude product was purified

by flash chromatography (Silica gel, eluent: MeOH–CH_2Cl_2 1 : 2). The resulting white powder 24% (0.198 g, 0.090 mmol) was dried over KOH *in vacuo* (Found: C, 60.67; H, 7.61; N, 7.19. $C_{112}H_{163}N_{12}O_{33}\cdot 3H_2O$ requires: C, 60.97; H, 7.66; N, 7.62%); UV/Vis (MeOH) λ_{max}/nm (ε/mol^{-1} dm^3 cm^{-1}) = 273 (69 300), 293 (73 100), 319 (43 000); FTIR (KBr): ν/cm^{-1} = 1735, 1715 (C=O ester), 1654 (C=O urea). ^{1}H NMR (400 MHz, D_6-DMSO, 25 °C): δ 8.55 (s, 3H, H6′ bipy), 8.28 (s, 3H, H6 bipy), 8.27 (d, 3H, J = 8.04 Hz, H3′ bipy), 8.14 (d, 3H, J = 8.04 Hz, H3 bipy), 7.24 (d, 3H, J = 7.04 Hz, H4′ bipy), 7.17 (d, 3H, J = 7.04 Hz, H′ bipy), 6.85 (s, 3H, NH), 5.43–5.27 (m, 6H, H1, CyD), 4.31 (m, 6H, CH_2-bipy), 3.98–2.64 (m, 36H, H2, H3, H5, H6 CyD), 2.30 (s, 9H, CH_3 bipy), 2.08 (d, poorly resolved, CH_2–CO lauryl), 1.09 (t, 9H, J = 7.04, CH_3 lauryl). ^{13}C NMR (100 MHz, D_6-DMSO, 25 °C): δ 162.2 (*C*=O urea), 159.0 (*C*=O ester), 158.5 (C6, C6′ bipy), 155.3 (C4 bipy), 153.3 (C4′), 137.7 (C5 bipy), 137.6 (C5′bipy), 136.9 (C3, C3′ bipy), 120.6 (*C*H_2–bipy), 82.0 (C1, CyD), 71.2 (C4, CyD), 64.8 (C6a, CyD), 61.6 (C2, C3 CyD), 57.7 (C6b), 31.0, 26.1, 25.6, 21.4 (*C*H_2 lauryl), 15.5 (*C*H_3 lauryl).

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