J Incl Phenom Macrocycl Chem (2009) 63:267–272
DOI 10.1007/s10847-008-9516-3

ORIGINAL ARTICLE

Formation of an α-cyclodextrin/16-mercaptohexadecanoic acid complex and its deposition on gold surfaces

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Received: 25 July 2008 / Accepted: 24 October 2008 / Published online: 11 November 2008

Abstract Using ^{1}H NMR, XRD and XPS techniques we show new findings concerning the nature of the complex formed between 16-mercaptohexadecanoic acid (MHA) and α-cyclodextrin. Stabilization was achieved by dipole-induced dipole interactions between the carboxyl groups of the MHA with the hydroxyls on the cavity rim of the α-cyclodextrin. Deposition of the complex onto a gold substrate with subsequent ethanol washing showed retention of the thiol moiety and removal of cyclodextrin.

Keywords 16-mercaptohexadecanoic acid · α-cyclodextrin · ^{1}H NMR · XRD · XPS

Introduction

The spacing of alkanethiols on gold surfaces is of interest in developing interfacial modifiers and in the fabrication of switchable devices. An interesting means of achieving such spacing involves the use of cyclodextrin inclusion complexes. However, the exact nature of the host/guest complexes formed is unclear. Self-assembled monolayers (SAMs) of alkanethiols, $X(CH_2)_nSH$, where X = functional head group, have attracted much interest as potential modifiers of interfacial properties, such as wettability. The performance of these SAM layers can also be directly influenced by local conformation, dispersion, packing arrangement and density [1–3].

Critical in the selection and use of SAMs as interfacial modifiers is the functional head group, for example amine, methyl and carboxyl groups. Studies by Lahann et al. [2] of conformational transitions of these surface-confined molecules has focused on dynamically controllable [4] and "switchable" surfaces whereby changes in wettability are said to occur in response to reversible electrical potential triggers (+80 or −300 mV vs SCE). The authors suggested that this caused the methylene chains of 16-mercaptohexadecanoic acid (MHA) low density SAMs, attached to gold via a thiolate bond, to change from and all-*trans* (straight molecule) to a partially gauche orientated (bent molecule) conformation [2]. For this bending to occur a SAM requires adequate spatial freedom. Molecular dynamic simulations have predicted that this spacing should be approximately one alkanethiol/0.65 nm^2 [2].

To acquire this degree of spacing of the SAM layer Liu et al. [5] have proposed the use of cyclodextrins. Cyclodextrins are cyclic oligomers of six (α-CD), seven (β-CD) and eight (γ-CD) glucose units with two hydrophilic rims and a hydrophobic cavity in which an alkanethiol (guest molecule) can potentially reside (see Fig. 1a, b for α-cyclodextrin). The larger hydrophilic rim is occupied by secondary –OH groups, linked to C2 and C3, while the narrower rim has the primary hydroxyl groups in position 6 of the glucose ring. The whole structure is cone shaped (see Fig. 1b). Cyclodextrins are particularly useful for the spacing of molecules on surfaces because of their particular spatial dimensions; ca. 1.57 nm^2, 1.84 nm^2 and 2.65 nm^2 for α-CD, β-CD and γ-CD respectively [5].

Host/guest complex stability may be favored at a binding site on the guest by (a) high electron density, (b) high polarizability and (c) low polarity. Electron density and

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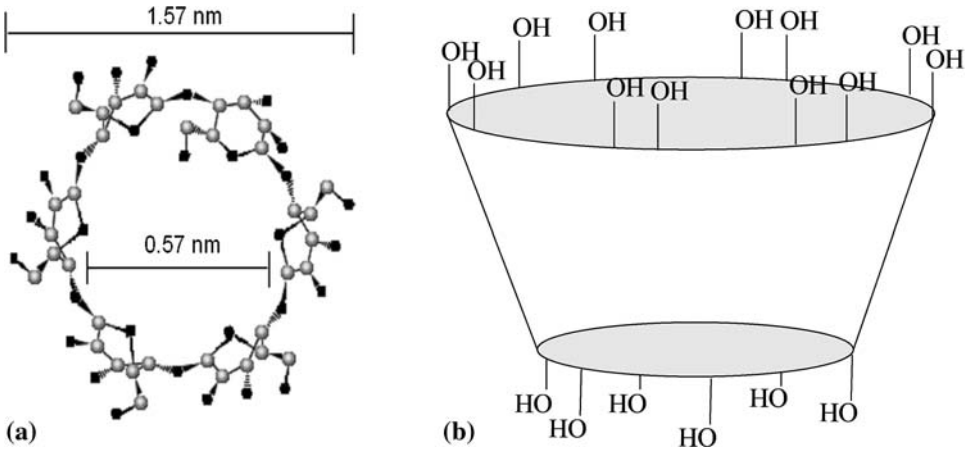

Fig. 1 Depicts the α-cyclodextrin hydrate (α-CD)/MHA inclusion complex

polarizability imply that induction and dispersion forces may be significant contributors to complex stability. The latter polarity implies that the hydrophobic interaction may be a major contributor. Three current theories on the origins of cyclodextrin-guest binding energy are: the relief on cyclodextrin strain energy [6], release of high-energy cyclodextrin cavity water [7] and London dispersion forces [7, 8].

It is known that γ-cyclodextrin readily includes short chain carboxylic acids [9]. However, for this work the spatial dimensions afforded by the α-cyclodextrin appeared most appropriate and an attempt was made to produce an α-cyclodextrin/MHA complex as a means for producing low density SAMs. Using this combination of host/guest it was envisaged that the polymethylene hydrophobic tail of the MHA guest would be sufficiently hydrophobic to overcome the potential barrier of MHA inserting itself into the cyclodextrin hydrophobic cavity.

To this end we describe the synthesis of an α-CD/16-mercaptohexadecanoic acid (MHA) complex, and characterize it using solution ^{1}H NMR, XRD and XPS. The results show that no inclusion complex was formed and that in fact the stability of the complex was maintained through the dipole-induced dipole interactions of the carboxylic acid group on the MHA with the H2 and H3 hydroxyls on the outer rim of the α-cyclodextrin.

Experimental

Materials

16-mercaptohexadecanoic acid (MHA, 99%), α-cyclodextrin hexahydrate (α-CD) and Multisolvent® grade absolute ethanol were purchased from Sigma. MilliQ water (18 MΩ) was used for all experiments.

Formation of α-cyclodextrin/16-mercaptohexadecanoic acid complex

16-mercaptohexadecanoic acid (MHA, 20 mg) was added to an aqueous solution of α-cyclodextrin hexahydrate (α-CD, 270 mg) in 100 mL Milli Q water. A molar ratio of 1:4 was used to give an excess of α-CD [5]. It is important to note that the formation of inclusion complexes does not involve covalent interactions and that the driving force for complex formation is often of a solvophobic nature and for which a liquid matrix is required [10]. After light sonication for 5 min the solution was kept in an oil bath (40 ± 0.1 °C) with constant stirring for 48 h. The mixture became gradually turbid over time indicating the formation of a crystalline complex between the MHA and α-CD. The solution was then cooled and filtered through Whatman microfilter paper (0.45 μm). The residue retained on the filter (white solid) was further characterized using ^{1}H NMR, XRD and XPS techniques. Total yield was 80 mg.

Self-assembly of α-cyclodextrin/16-mercaptohexadecanoic acid complex onto gold (111) slides

Gold slides were prepared by firstly thermally depositing a 20 nm thick film of titanium onto a cleaned glass microscope slide, with the subsequent deposition of a 350 nm thick layer of Au. After deposition the slides were cleaned in piranha solution (70:30 vol/vol H_2SO_4:H_2O_2) for 15 min at 40 °C. They were then washed with MilliQ water. Gold slides were then placed into a solution containing α-cyclodextrin/16-mercaptohexadecanoic acid complex (0.35 mM in MilliQ water) and at 4 °C for 16 h. The slides were then rinsed in ethanol to remove the CD from the MHA and dried in under a flow of argon.

Scanning electron microscopy (SEM)

Scanning electron micrographs of the α-CD/MHA complex that had crystallized out of solution onto a gold slide were obtained using a Leo 440 Scanning Electron Microscope (SEM).

^{1}H nuclear magnetic resonance (NMR) spectroscopy

^{1}H NMR is the most widely used technique to obtain information about inclusion modes and geometries and is able to confirm whether the MHA had been hydrophobically bound internally within the α-CD cavity or externally as a complex [11]. High-resolution ^{1}H NMR spectra were acquired on the α-CD/MHA complex in D_2O (0.35 mM) using a Varian Unity 400 FT-NMR instrument operating at 400 MHz at 298 K.

X-ray diffractometry (XRD)

Powder X-ray diffraction (XRD) patterns were recorded with a Philips PW1700 series powder diffractometer. All diffractograms were acquired under ambient conditions employing Co Kα radiation ($\lambda = 1.78896$ Å) with 40 kV voltage, 35 mA current, and a scan speed of 3° min^{-1}.

X-ray photoelectron spectroscopy (XPS)

X-ray photoelectron spectra measurements carried out on the following samples: (a) a gold slide, (b) α-CD/MHA complex (4.4 mg in 10 mL MilliQ water) deposited on a gold slide at 4 °C for 16 h, and (c) sample prepared as in (b) but washed with ethanol for 5 min, soaked in ethanol for 25 min then washed with MilliQ water. XPS analyses were performed on a Kratos Axis Ultra DLD spectrometer that focussed monochromatic Al-Kα X-rays onto each sample. A survey spectrum over a binding energy range of 0–1486.6 eV with an analyzer pass energy of 160 eV was used. Narrow scans were conducted at 10 eV. All carbon peaks were referenced to aliphatic hydrocarbon at 285 eV.

Results and discussion

Figure 2 shows a scanning electron micrograph image of an example of α-cyclodextrin/16-mercatohexadecanoic acid complex crystallites that were deposited from solution onto a gold slide over a period of 16 h. This crystallite remained after washing the slide many times with MilliQ water. It is expected that any other crystallites of pure cyclodextrin were removed. The structure appears to be a series of layered or flat channeled assemblages. It is within these layers or channels that the guest molecules normally would reside [12–14].

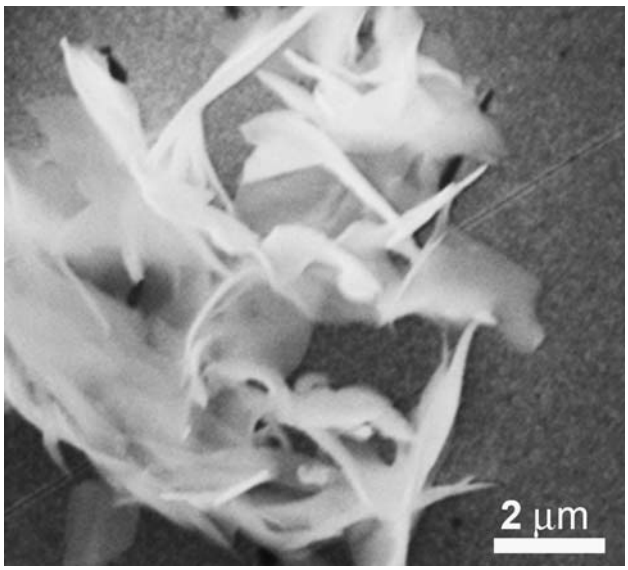

Fig. 2 Scanning electron micrograph of α-CD/MHA inclusion complex as deposited on gold after being washed and soaked in ethanol

NMR spectra have been found to give valuable information on the structural characterization for supramolecular host-guest complexes [10]. The cavity of the α-CD has a diameter of 0.57 nm (Fig. 1a) and so should accommodate the hydrocarbon chain of MHA, which has an approximate diameter of 0.3 nm. In fact the ^{1}H NMR, in this case, indicated different complex formation. Figure 3 shows the upfield region of the high resolution ^{1}H NMR spectra for (a) α-CD and the (b) α-CD/MHA complex. The spectra show differences in the signals at δ0.8–2.8 in which new peaks

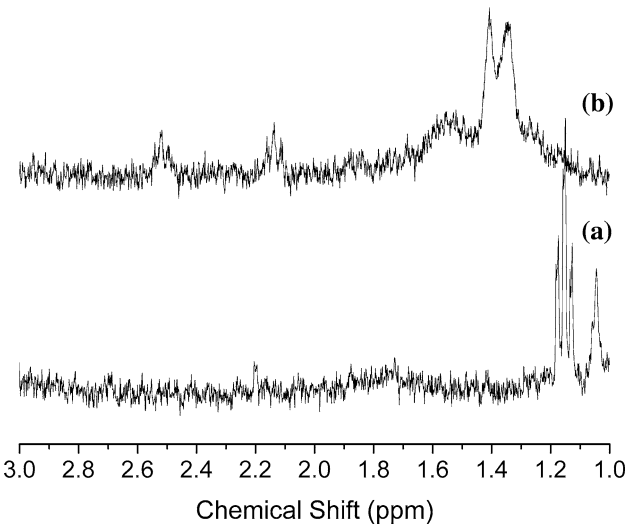

Fig. 3 Partial upfield ^{1}H NMR spectrum (400 MHz) of (**a**) α-cyclodextrin hydrate (α-CD); and (**b**) α-cyclodextrin hydrate (α-CD)/MHA inclusion complex in D_2O (0.35 mM) at 298 K

appear after the formation of an α-CD/MHA complex. Specifically, the new peaks at δ2.55 and 2.15 arise from –CH_2–S groups [15] implying that the MHA has its surface active –SH groups in two different environments on the outside of the CD cavities. Polymethylene groups of the MHA hydrophobic backbone are observed at δ1.35, 1.4 and 1.54.

To look more closely for evidence of the contribution of hydrophobic interactions in the formation of the complex, an analysis of the proton shifts in the region δ3.5–5.0 is required. Figure 4 shows the more downfield region of the NMR spectra between δ3.4–4.2. Typically, complexes with aliphatic guest molecules lacking strong shielding tensors show only small shielding effects on both the host and the guest [13]. In addition, host protons outside of the cavity show the smallest effects.

Table 1 shows the effect on the chemical shifts (ppm) of α-CD/MHA complex formation and in particular, the deshielding of the H-2 and H-4 external protons of values around +0.020 ppm. Figure 4 also indicates that the H-6 protons on the CH_2OH side chain have been slightly affected. The OH-6 group is on a flexible arm and it is these groups which are displayed on the narrower rim of the structure (Fig. 1b). Alpha cyclodextrins can, in their native state, form hydrogen-bonding networks between the secondary hydroxyls (OH-3 and OH-2), at the wider rim.

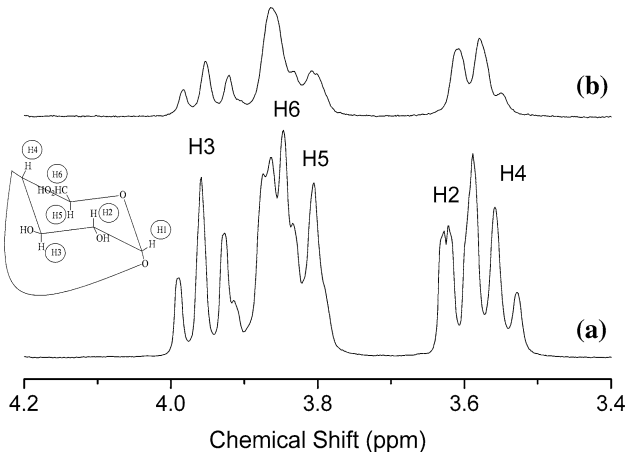

Fig. 4 Partial downfield ^{1}H NMR spectrum (400 MHz) of (**a**) α-cyclodextrin hydrate (α-CD); and (**b**) α-cyclodextrin hydrate (α-CD)/MHA inclusion complex in D_2O (0.35 mM) at 298 K

Table 1 ^{1}H NMR chemical shifts (ppm) at 400 MHz and 273 K for α-CD and the α-CD/MHA complex

	H-1	H-2	H-3	H-4	H-5	H-6
α-CD	5.026	3.589	3.960	3.559	3.806	3.848
α-CD/MHA	5.025	3.609	3.954	3.580	3.809	3.856
Δ shift	–	(+.020)	(−.006)	(+.021)	(+.003)	(+.008)

This is because in their "empty" state, that is without a guest, the structure is strained and this strain can be relieved by the formation of hydrogen bonds between OH-3 (donor) and OH-2 (acceptor) groups of adjacent glucose units in α-cyclodextrin [16]. This leads to a belt of hydrogen bonds that form a very rigid structure. Protons involved in this type of hydrogen-bonded structure are far more deshielded than "free protons", giving rise to a resonance displacement of about 1 ppm [17]. The observed downfield shifts for the H-2 and H-4 external protons are much smaller than this, +0.020 and +0.021 ppm, respectively and are more indicative of the proximity of an electronegative area, namely the carboxyl group on the guest MHA. This effect has been previously observed for nonanal and ethyl dodecanoate [11]. Both strain energy and high-energy water theories suggest that it does not matter how the guest penetrates the cavity as long as it relieves the ring strain or displaces the high energy cavity water. From these results it is hard to rationalise that the guest is included into the cavity and we propose that it is London dispersion forces that contribute to the overall binding energy for such polar substrates. In this case the guest forms dipole-induced dipole interactions, and is strongly orientated to the cyclodextrin.

Proton shielding differences amounts to little shifting in the anomeric H-1 (δ5.03) positions of the α-CD and complex, not shown in Fig. 4.

Figure 5 shows the XRD patterns of α-CD (bottom), MHA (middle) and the α-CD/MHA complex (top). In general, the type of guest molecule and experimental conditions of formation determine the packing type which can be described as cage, layered or channel/columnar structures [18]. The spectra of the pure α-CD hexahydrate shows many reflections but there are eight salient peaks

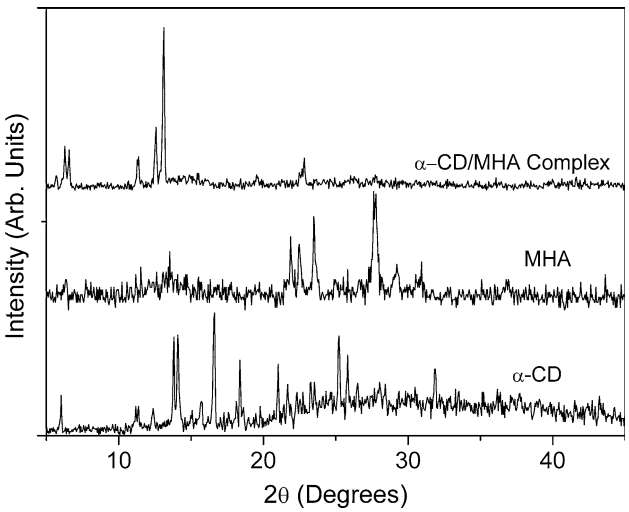

Fig. 5 Figure 3 shows the XRD patterns of α-CD (bottom), MHA (Middle) and the α-CD/MHA IC (top)

Table 2 XPS data of carbon and oxygen for gold, α-CD/MHA and abs ethanol washed α-CD/MHA

Sample	C 1s(%)			O 2p(%)	
	285.0 eV	286.0 eV	289.1 eV	532.3 eV	534.0 eV
Gold slide	79.0	17.5	3.5	86.4	13.6
α-CD/MHA	85.9	9.9	4.1	54.6	45.4
Abs ethanol washed α-CD/MHA	83.1	11.7	5.2	88.7	11.3

associated with this crystal structure occurring at $2\theta = 6.1^\circ$, 12.4°, 13.8°, 14.1°, 16.6°, 18.4°, 21.0°, 25.2°. Pure MHA show four salient peaks at $2\theta = 21.9^\circ$, 22.5°, 23.5°, 27.8°. There are fewer reflections in the α-CD/MHA complex (top) with salient peaks centred at $2\theta = 6.3^\circ$, 6.6°, 11.3°, 12.6°, 13.1°, 22.7°. For an α-CD inclusion complex which has a columnar structure the (110) plane is at $2\theta = 13.1^\circ$, and for the (300) plane $2\theta = 22.7^\circ$ [18]. From the results we may conclude that the structure formed here is of the columnar type, how the complex structure is specifically aligned is unclear.

It could be argued that there is no interaction between the MHA and the CD at all. If indeed there is an interaction this can readily be released by washing the complex with ethanol to remove the cyclodextrin and thus break up the complex. We deposited the complex onto a gold coated glass slide over a period of 16 h. This allowed sufficient time for the MHA to form a thiolate bond with the gold. XPS analysis was then performed both and before after washing the complex with ethanol. XPS analysis on a wide scan of the gold sulphur bond showed the presence of S 2p, present as a weak peak with a maximum at 163.1 eV of S $2p^{3/2}$, in both the before and after washed α-CD/MHA complex deposited on gold. This Au–S binding energy is very different from that expected for disulphides (163.7 eV S $p^{3/2}$ and 164.9 eV S $p^{1/2}$) [19]. The results indicate that after washing the Au–S bond remains intact.

However, to establish whether the complex had been destabilized a narrow scan of the carbon and oxygen binding energies was performed. Different C 1s peaks were clearly present in the spectra. These are tabulated in Table 2 (C-alkyl 285.0 eV; C–O 286.0 eV and O–C–O or COOH 289.1 eV) and the composition of the deposited layers is reflected by the integration of the carbon and oxygen peaks. Table 2 indicates that any major difference between specific carbon types before and after ethanol washing is inconclusive. This may be due to residue alcohol from the washing process. The oxygen peaks assigned are: C–O 532.3 eV and C–O–C or COOH 534.0 eV. The XPS data in Table 2 clearly demonstrates that the C–O–C signal from the cyclodextrin is decreased following the ethanol wash, i.e., cyclodextrin was removed.

Conclusions

From these results we propose that the complex does not involve inclusion of MHA into the hydrophobic cyclodextrin cavity but binding of the guest MHA to the outer rim of the cyclodextrin through London dispersions forces. Overall this results in a columnar-type assembly, perhaps with interdigitation of the MHA polymethylene groups. These structures have been shown to deposit onto gold surfaces and facile removal of the cyclodextrin with ethanol leaves attached thiols. Outer attachment of thiols to cyclodextrins, of fixed diameter, may be of use in self-assembling ordered monolayers onto gold surfaces.

Acknowledgements This work was funded by the New Zealand Foundation of Research, Science and Technology (Contract No's: C08X0410 and IRL0402).

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