Langmuir–Schäfer films of a new calix[4]pyrrole-based macrocycle exhibiting induced chirality upon binding with chiral alcohol vapours

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A new calix[4]pyrrole-based macrocycle, *meso*-tetra(methyloctyl)calix[4]pyrrole (MTP), has been synthesized and fully characterized. Thin films of MTP have been transferred onto hydrophobized quartz and silicon oxide sheets by using the Langmuir–Schäfer (LS) method (horizontal lifting). Scanning force microscopy (SFM) investigation showed that the LS films are almost homogeneous and are consistent with the X-type configuration with the hydrophobic tails of MTP disposed almost perpendicularly with respect to the substrate. Induced circular dichroism (ICD) measurements have been performed in the presence of chiral alcohol vapours, such as (−)-(*R*)-2-butanol, (−)-(*R*)-2-pentanol and (−)-(*R*)-2-hexanol. The results showed that although not chiral by themselves the MTP molecules within the film exhibit chirality induced by binding with the chiral guests. The appearance of ICD signals is accounted for by the close proximity of the alcohol molecules to the pyrrole moieties of MTP. The reversibility of the binding event, coupled with the differentiated response observed towards the alcohols investigated, makes the LS films promising active layers for the chemical recognition of short-chain polar neutral molecules.

Introduction

Molecular recognition of neutral small species such as short-chain alcohols and simple monoamides represents nowadays an exciting challenge in the crowded arena of supramolecular chemistry. The binding of such molecules is actually fairly difficult since they dispose of only a few sites for hydrogen bonding and small tails for possibly either hydrophobic or π–π interactions.[1] Thanks to the outstanding work carried out since the mid-1990s from Sessler and co-workers, calix[4]pyrroles are currently one of the most intriguing class of receptors in the chemical recognition of small anionic and neutral polar species.[2,3] It has been highlighted that both sensitivity and selectivity exhibited by these macrocycles towards a wide range of guests is mainly governed by the harmonic synergism between their chemical and conformational properties. Indeed, while the (N–H) groups of the pyrrole moieties may act as receptors through H-bond interactions, the tetrahedral carbon bridges linking together the pyrrole units assure an adequate conformational flexibility during the binding event.[2,3] However, while the excellent recognition capability of these receptors in solution is widely documented and is currently the object of investigation by a number of research groups worldwide, the sensing properties of calix[4]pyrrole-based thin films are almost unexplored. Deposition of these derivatives under such a form can be, in fact, an appropriate strategy to make active coatings addressed to the chemical recognition of small molecules in gas phases. In this regard we have recently shown that films of *meso*-octaethylcalix[4]pyrrole, prepared by the Langmuir–Blodgett (LB) technique, constitute an interesting class of compounds for application in the optical recognition of alcohol vapours.[4] These films exhibited a non-conventional LB aspect with the general appearance of nanofeatured surfaces consisting of nanometric ellipsoidal bumps.[5] Nevertheless, we demonstrated that such porous structures were able to discriminate different small alcohol molecules and that the performance observed was strictly related to the films' structural properties.[6] The encouraging outcome of these results stimulated the idea to appropriately tailor the structure of the *meso*-octaethylcalix[4]pyrrole through the introduction of longer hydrophobic tails. Such substitutents should, in principle, improve the stability and the homogeneity of the films, presumed to be connected to their sensing ability.

In this paper we report the synthesis of a novel calix[4]pyrrole derivative, *meso*-tetra(methyloctyl)calix[4]pyrrole (MTP, Fig. 1), and its deposition as thin films on solid surfaces by the Langmuir–Schäfer (LS) method (horizontal lifting). Scanning force microscopy (SFM) was employed to investigate the film structure at the molecular level. Induced circular dichroism (ICD) measurements were carried out in the presence of saturated vapours of chiral alcohols such as (−)-(*R*)-2-butanol, (−)-(*R*)-2-pentanol and (−)-(*R*)-2-hexanol with the aim to ascertain the potential sensing capability of these films.

Experimental

Synthesis and characterization of MTP

MTP was synthesized according to the method reported as a modification of the so-called "acetone-pyrrole" synthesis.[7] Pyrrole (1 ml, 0.0145 mol), 2-decanone (2.75 ml, 0.0145) and methanesulfonic acid (catalytic amount) were stirred under

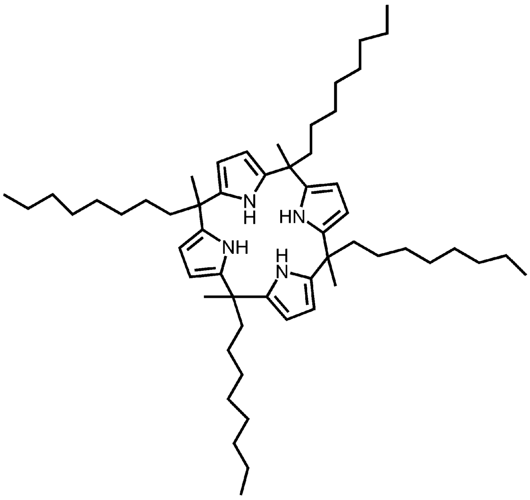

Fig. 1 Molecular structure of MTP.

nitrogen for 12 h at room temperature. The reaction mixture was cooled in the freezer until precipitation of a white crystalline solid. This solid was filtered off, washed several times with a small quantity of ethanol and dried under vacuum (30% yield). MTP was fully characterized by ^{1}H NMR and ESI mass spectrometry.

^{1}H NMR ($CDCl_3$): $\delta = 6.98$ (br m, 4H, pyrrole NH), 5.89 (d, $^4J_{H-H} = 2{,}6$ Hz, 8H, pyrrole β-H), 0.87 [m, 12H, $-(CH_2)_7CH_3$], 1.42 [s, 12H, $-(CH_2)_7CH_3$], 1.21 (br m, chain), 1.05 (br m, chain). MS (ESI-MS): $[M - H]^-$ 820.30 (100%); 821.30 (63.5%); 822.30 (19.8%); 823.30 (4.8%).

NMR experiments carried out in $[D_6]$DMSO confirmed unequivocally that condensation occurred exclusively at the α position of the pyrrole rings.[8]

NMR experiments were performed on a Varian Unity Inova spectrometer at 470.30 MHz. Absorption and induced circular dichroism spectra were recorded with Beckman 650 DU spectrophotometer and a Jasco 7-715 dichrograph, respectively.

Film preparation and characterization

Langmuir–Schäfer (LS) films of MTP were deposited by a KSV 5000 System 3 Langmuir–Blodgett (LB) apparatus (850 cm^2). During the experiments, after each run, the trough was carefully washed with chloroform, acetone, ethanol and water. Ultrapure water (Millipore Milli-Q, 18.2 MΩ cm) was used as subphase. The temperature of the subphase was regulated at 20 °C by a Haake GH-D8 apparatus. MTP was dissolved in $CHCl_3$ at a concentration of 2.6×10^{-4} M. Two hundred microliters of this solution was randomly spread by a gas-tight syringe onto the water subphase. After solvent evaporation, the floating film at the air–water interface was compressed continuously at a speed of 10 mm min^{-1}. The surface pressure was simultaneously monitored by a Wilhelmy balance while obtaining an isotherm of the sample. The surface layer was transferred onto the substrate by horizontal Langmuir–Schäfer (LS) deposition at a surface pressure of 25 mN m^{-1}. Deposition was carried out on clean quartz or silicon oxide slides (30×40 mm^2). Prior to the transfer both substrates were hydrophobized by exposition for 24 h to a saturated atmosphere of 1,1,1,3,3,3-hexamethyldisilazane. The substrates hydrophobized with this procedure will be henceforth named as quartz* and SiO_2*, respectively.

Scanning force microscopy (SFM) was carried out in air by using a Multimode/Nanoscope IIIa equipped with an extender electronics module (Digital Instruments) in tapping mode. Commercially available tapping etched silicon probes (Digital Instruments) with a pyramidal shape tip, having a nominal curvature of 10 nm and a nominal internal angle of 35°, were used. During the analysis, the cantilever, about 125 μm long, with a nominal spring constant of 20–100 N m^{-1}, oscillated at its resonance frequency of about 300 kHz. For each scan, 512×512 points were recorded and the scan rate was maintained below 1 Hz.

Results and discussion

MTP forms stable monolayers at the air–water interface. Fig. 2 reports the surface pressure *vs.* area isotherm ($T = 20$ °C) of a monolayer of MTP molecules spread at the air–water interface. The curve shows four distinct regions that indicate different packing conditions of the floating molecules. In the first region, ranging from roughly 190 to 160 Å^2, the surface pressure is practically unaffected by the barrier movement. This is consistent with a state where molecules are largely dispersed on the subphase in a gas-like phase. The pressure starts to increase steeply at about 160 Å^2 and the curve maintains almost the same slope up to a molecular area of about 100 Å^2. The behavior observed in this region is in agreement with a picture in which the MTP molecules are in an almost packed phase. By extrapolating to zero pressure this last part of the curve, a limiting area of 141 Å^2 is obtained. Such a large value is accounted for by the presence of the four hydrophobic tails in the MTP molecule.

The MTP molecules are supposed to be with their polar terminations (the four N–H groups) in contact with the water subphase and the four C8 chains pointing outwards from the contact with the aqueous subphase. Such a molecular arrangement is well corroborated by the SFM analysis reported below. Above a surface pressure of 30 mN m^{-1} (correspondingly to an area per molecule smaller than 100 Å^2) the slope of the curve decreases and the pressure monotonically increases upon compression. Probably the floating layer progressively loses its previous rigidity since the MTP molecules begin to superimpose on each other, thus disrupting the ordered packed arrangement.

MTP films prepared at the air–water interface have been transferred at 25 mN m^{-1} on a SiO_2* substrate by the LS method and their morphological structure has been investigated by SFM. Fig. 3(a) shows a top view SFM image obtained on a film of 4 MTP layers on a SiO_2* substrate. The film structure resembles that of conventional Langmuir–Blodgett films, showing an almost flat surface with randomly dispersed worm-like and hole-like defects ranging from tens to hundreds of nanometers in diameter. The root mean square roughness (RMS) of these films was of about 0.8 nm.

In order to inspect the nanoscale layer-by-layer structure of the LS film, an image showing a large hole-like defect has been obtained and is shown in Fig. 3(b). The section analysis,

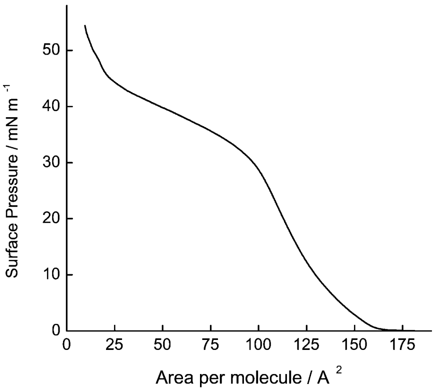

Fig. 2 Isotherm of the Langmuir film of MTP at the air–water interface at 20 °C.

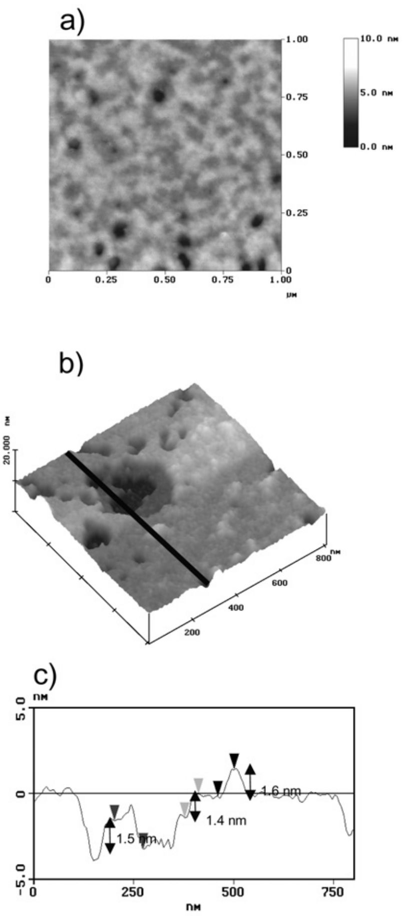

Fig. 3 SFM investigation of MTP multilayers on SiO_2* substrates: (a) 2D tapping mode image; (b) 3D view of a peculiar defective region; (c) section analysis along the line marked in (b).

performed along the line marked in Fig. 3(b), is reported in Fig. 3(c). This section shows steps 1.5 ± 0.1 nm high, a value corresponding to the length of an almost fully stretched MTP molecule. By considering the LS procedure (horizontal lifting), this fact suggests that the molecules should be disposed in the film as pictorially sketched in Fig. 4,that is, in an X-type configuration and quite perpendicular with respect to the substrate.

The above findings point out that the tailoring of calix[4]-pyrrole with longer hydrophobic tails, combined with the LS technique, considerably improves the structural organization of the films with respect to that observed in LB films of untailored calix[4]pyrrole molecules. As outlined earlier, these latter films exhibited a disordered structure characterized by an ensemble of almost ellipsoidal aggregates.[5] Moreover, a remarkable influence of the substituent's chain length was also observed on the floating layer stability at the air–water interface. For example, the MTP Langmuir isotherm does not exhibit a dependence on the concentration of the spreading solutions, typical of the previous calix[4]pyrrole with eight ethyl substituents at *meso* positions and also of molecules with a high tendency to form aggregates, nor significant hysteresis upon compression-relaxation cycles between 0 and 25 mN m^{-1}. Lastly, the floating film sustained a surface pressure of 25 mN m^{-1} for 12 h without any area loss.

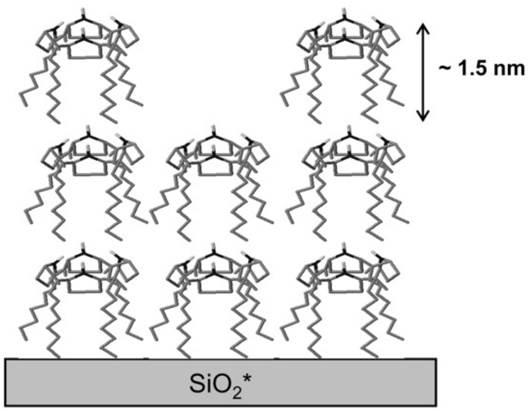

Fig. 4 Pictorial view of the MTP molecular arrangement in the film.

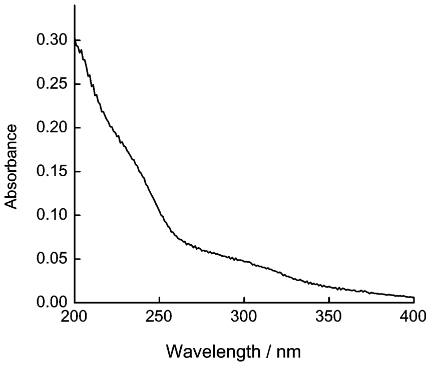

Fig. 5 UV absorption spectrum of a typical MTP LS film (30 layers) on quartz*.

All these experimental evidences suggest that the so-called hydrophile-lipophile balance (HLB)[9] was improved in the new calix derivative, thus bestowing adequate amphiphilic character to MTP as far as film stability and transfer are concerned.

Fig. 5 shows the UV spectrum of the LS film containing 30 layers of MTP. The absorption in the 260–400 nm region, typical of the calix[4]pyrrole units, is red-shifted in comparison to that observed in CH_2Cl_2–methanol solution. This finding is further consistent with the high head-to-tail organization of the MTP chromophores in the LS film.[10,11]

In order to ascertain the potential of LS films of MTP in the recognition of alcohol vapours, we fixed the quartz slide in a 1 cm spectrophotometric cell and carried out ICD experiments, both in the absence and in the presence of saturated vapours of three different chiral alcohols, (−)-(*R*)-2-butanol, (−)-(*R*)-2-pentanol and (−)-(*R*)-2-hexanol. The LS film of MTP did not show any significant ICD signal by itself, in accordance with the absence of chiral centres in its molecular structure. On the other hand, differentiated responses were observed upon alcohol addition. Interestingly, saturation of the sample with either (−)-(*R*)-2-butanol or (−)-(*R*)-2-pentanol gave rise to significant ICD spectra (Fig. 6), which appears to be a result of the binding of the chiral guests with the achiral

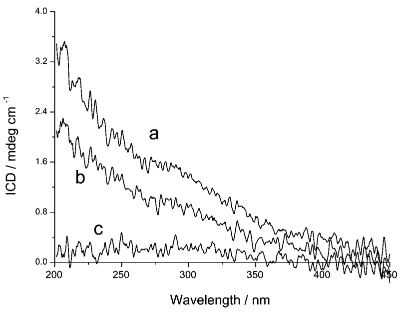

Fig. 6 ICD spectra of typical MTP LS films (30 layers) on quartz* obtained in the presence of saturated vapours of (a) (−)-(*R*)-2-butanol, (b) (−)-(*R*)-2-pentanol and (c) (−)-(*R*)-2-hexanol.

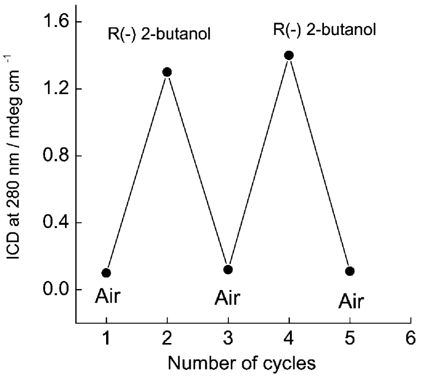

Fig. 7 Intensity of the ICD signal of a typical MTP LS film (30 layers) on quartz* after 3 cycles of air–(−)-(*R*)-2-butanol saturation.

receptor. In contrast, no ICD was observed upon saturation with (−)-(*R*)-2-hexanol. It is noteworthy that although the ICD bands observed are quite broad, both the shape and spectral position correspond fairly well to those of the absorption UV spectrum (see Fig. 5 for comparison), thus ruling out the existence of exciton splitting phenomena.

The presence of the ICD bands affords some hints on the binding mode of the alcohol molecules with the LS layers. ICD signals are in general strictly dependent on the host-guest distance. Therefore, their appearance in the typical absorption region of the pyrrole chromophores provides a strong indication that the alcohol molecules may be localized very close to the pyrrole moieties. In this respect, a binding mode mainly governed by an H-bond interaction involving the pyrrole unit of the MTP layers with the alcoholic OH group appears highly probable.[1–3] The absence of ICD signal in the case of (−)-(*R*)-2-hexanol rules out, of course, a close proximity of this substrate with the pyrrole centre of MTP and may be tentatively related to the higher sterical hindrance of this guest. However, localization of such a guest in more hydrophobic regions far from the pyrrole center cannot, at the moment, be completely excluded.

In Fig. 7 the intensity of the ICD signal monitored at 280 nm is reported after 3 cycles of saturation of the MTP LS sample with either air or (−)-(*R*)-2-butanol. The almost full recovery of the ICD signal clearly highlights the reversibility of the binding event. A similar trend was also observed for (−)-(*R*)-2-pentanol.

In conclusion, we have shown that the tailoring of the calix[4]pyrrole with longer hydrophobic tails, together with application of the LS technique, gives rise to structurally ordered thin films. ICD measurements have provided direct evidence for differentiated and reversible binding between the MTP films and alcohol vapours. Such binding, mainly involving the participation of the pyrrole units of the MTP, makes the above films very promising for the chemical recognition of polar neutral molecules.

In light of these results we are currently investigating the molecular recognition capability of these LS layers towards a variety of alcohol vapours by using very sensitive transduction tools such as surface plasmon resonance and quartz crystal microbalance. The results of these studies will be reported in due course.

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