A novel ditopic zinc-salophen macrocycle: a potential two-stationed wheel for [2]-pseudorotaxanes†‡

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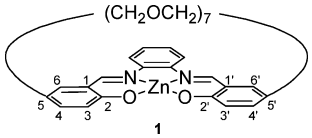
Crown ether macrocycle **1** including a zinc-salophen unit is obtained *via* a *de novo* synthetic design to give a potential pH-driven two-stationed wheel component of [2]-pseudorotaxane systems.

Introduction

Considerable efforts in supramolecular chemistry and nanoscience have been devoted lately to the construction of dynamic molecular assemblies whose movements can be controlled by external stimuli.[1] A number of studies in this field have been focused on supramolecular systems that can be switched between two stable states in the prospect for applications as memory units for information storage of a single bit in binary code.[2]

Pseudorotaxanes formed by a crown ether and a dialkylammonium cation belong to such systems, since the write–erase process consists of a reversible threading–dethreading motion achieved by pH changes[1a,3] that can easily be detected by optical methods.[4] As a matter of fact, their practical application as nanoscale devices is limited by the fact that one of the two states corresponds to the disassembled components. To overcome this problem, many [2]-rotaxanes have been developed in which the disassembling process is prevented by the presence of bulky groups at the ends of the axle. In this way, the deprotonation of the ammonium group does not lead to dissociation, but it promotes the shuttling of the wheel to another station positioned on the axle itself.[5] A quite different approach is the one adopted by Sauvage and coworkers who prepared an electrochemically driven [2]-rotaxane system based on the Cu(II)–Cu(I) couple, in which the molecular axis contains a 2,2′-bipyridine motif and the wheel a 1,10-phenanthroline and a trispyridine unit. Depending on its oxidation state, copper translocates between the two stations of the wheel, to coordinate the bidentate chelate or the tridentate fragment.[6]



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Here we report on the newly synthesised zinc-salophen complex **1** that represents a potential two stationed wheel for the construction of dynamic systems in which the movement of the axle is promoted by pH-changes rather than by electrochemical stimuli. Actually, compound **1** is a ditopic receptor, since it can bind a secondary ammonium ion by means of the crown ether oxygens (Fig. 1) and the corresponding deprotonated species thanks to the ability of zinc-salophen compounds to form 1 : 1 complexes with amines.[7] The peculiarity of the 5,5′ junction of the polyoxyethylene chain implies that one of the axial binding sites of zinc is oriented inside the cavity pointing toward the chain. Such a feature qualifies **1** as a candidate to act as a wheel in the formation of [2]-pseudorotaxanes feasible of a pH promoted translocation of a dialkylammonium axle between two stations. The status of the system can be easily monitored thanks to the presence of the zinc-salophen moiety that acts as a luminescent sensor.

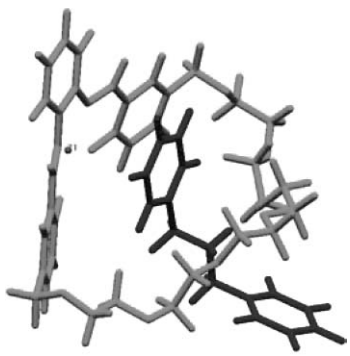

Fig. 1 Calculated structure of the complex between **1** and a dibenzylammonium cation.

Salophens are tetradentate ligands that bind strongly to metal dications to form neutral complexes widely used as receptors, catalysts, and carriers.[8] These complexes are usually square planar and one or two coordination sites are available on the central metal for axial complexation of additional ligands. As far as we know, in all macrocyclic metal salophen compounds reported in the literature, the polyether chain connects either positions 3 and 3′ of the side rings[9] or two positions of the central ring,[10] and in both cases lies more or less on the same plane as the salophen ligand. The consequence of this is that any species bound to the polyether chain remains far from the axial coordination site of the metal centre. Conversely, a chain connecting positions 5 and 5′ of the side rings has to pass above one of the faces of the planar salophen moiety so that one axial coordination site of the metal centre points toward the inside of the cavity. The appropriate chain length was chosen on the basis of a computational study aimed at establishing the right size to form a pseudorotaxane complex with the dibenzylammonium cation.

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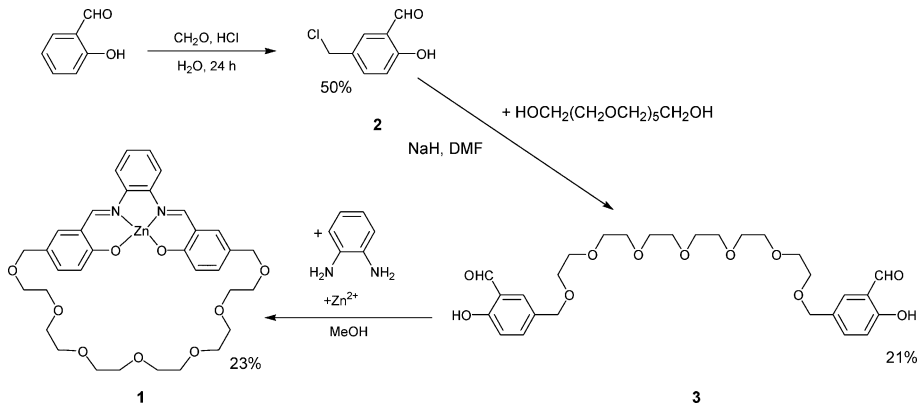
† Electronic supplementary information (ESI) available: Spectrophotometric titrations, computational details and coordinates of calculated structures. See DOI: 10.1039/b613705a

‡ The HTML version of this article has been enhanced with colour images.



Scheme 1 Synthetic route to compound **1**.

Results and discussion

Compound **1** was synthesised in three steps (Scheme 1) in reasonable yield, from easily available starting materials. Introduction of the methylene group between the aromatic rings and the first oxygen atoms of the chain was essential to avoid slow oxidation of the final product.

Unambiguous evidence for the formation of a strong complex between **1** and a dibenzylammonium cation is provided by ^{1}H NMR spectra in $CDCl_3$ (Fig. 2). In the spectrum of the free macrocycle, the imine and benzyl protons appear as multiplets (signals a and b of spectrum (i) in Fig. 2) which suggests the coexistence of at least three slowly equilibrating species, possibly corresponding to aqua complexes involving variable numbers of water molecules. Upon addition of dibenzylammonium methanesulfonate (spectrum (ii) in Fig. 2) signals a and b turn into sharp singlets. Consistent with the spectra of similar systems available in the literature,[9d,11] the resonances of the CH_2N^+ and the NH_2^+ protons of dibenzylammonium (signals B and C) are shifted downfield and upfield, respectively, as a consequence of the formation of N–H $\cdots$ O hydrogen bonds.

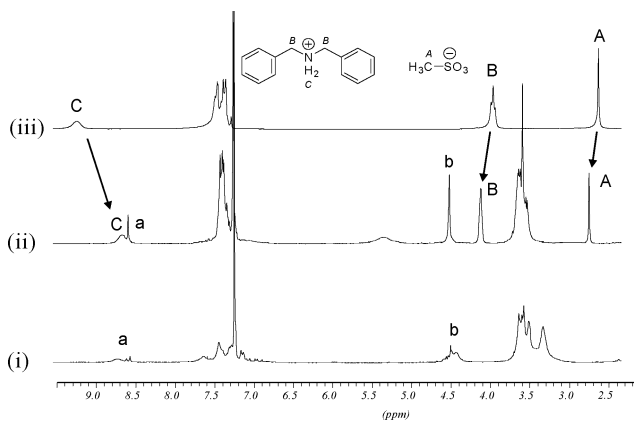


Fig. 2 ^{1}H NMR spectra of (i) **1**, (ii) **1**–dibenzylammonium methanesulfonate, and (iii) dibenzylammonium methanesulfonate at 300 MHz in $CDCl_3$ at 298 K. Resonances a and b correspond to the imine and benzyl protons in **1**, respectively.

The formation of the complex is also confirmed by small but detectable changes in both UV–Vis and fluorescence spectra of **1** upon addition of dibenzylammonium methanesulfonate, Fig. 3. UV–Vis titration experiments showed that association is virtually quantitative ($K > 10^6$ M^{-1}). Even larger spectral changes are detected upon formation of the complex with neutral dibenzylamine.

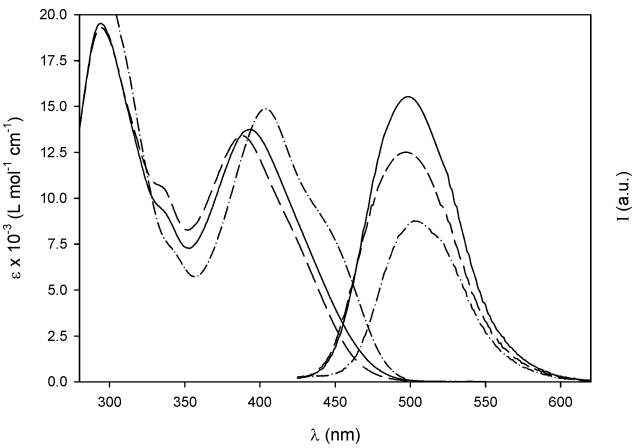


Fig. 3 Absorption and emission spectra (λ_{ex} = 350 nm) at room temperature in an air equilibrated $CHCl_3$ solution of **1** (full lines), **1**–dibenzylammonium complex (dashed lines), and **1**–dibenzylammine complex (dash–dotted lines). Concentrations are 5.4 $\times$ 10^{-5} M.

To verify the reversibility of the axle motion between the two stations of the wheel, we used the classical protocol consisting of successive additions of stoichiometric amounts of base and acid.[1a] Since the association constant between **1** and dibenzylamine (K = 90 M^{-1}, $CHCl_3$, 25 °C) measured by UV–Vis titration is too small to guarantee a high association degree, the less hindered dipropylamine (K = 4500 M^{-1}) was chosen to play the role of the axle.[12] The expectation is that after deprotonation, the neutral secondary amine does not remain free in solution, but is complexed by the metal centre either inside or outside the cavity (Fig. 4). A molecular mechanics calculation carried out utilising the force field MM3 indicates that in the gas phase, inner complexation is favoured by 14.5 kcal mol^{-1} mainly due to intra complex hydrogen bonding between the amino group of dipropylamine and one of the oxygen atoms of **1** (Fig. 5). The molecular motions were followed by ^{1}H NMR spectroscopy on a 0.05 M solution of both components, a concentration at which the

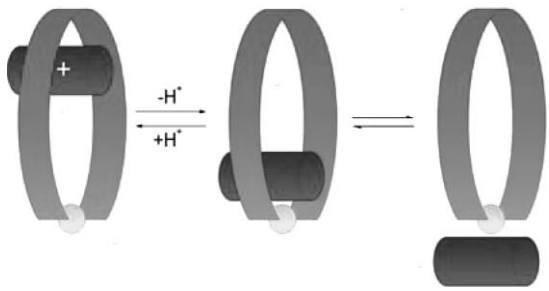


Fig. 4 Schematic representation of the pH-driven motion of the dynamic molecular system formed by compound **1** and a secondary ammonium salt.

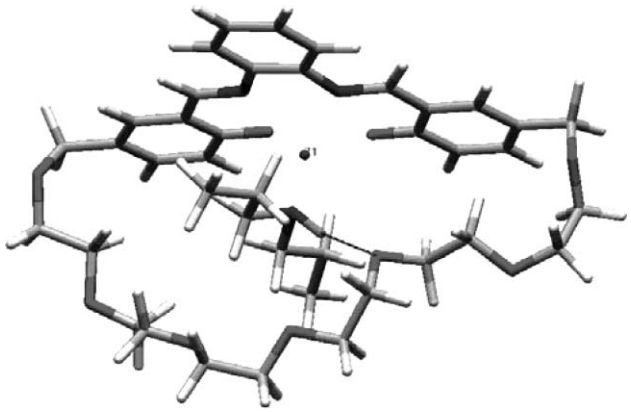


Fig. 5 Calculated structure of the complex between **1** and dipropylamine showing the intra complex hydrogen bond between the amino group of dipropylamine and one of the oxygen atoms of **1**.

association degree is calculated to be 93.5%. Association with **1** shifts downfield the resonances of all the amine protons (spectra (i) and (ii) in Fig. 6). Addition of 1 mol equiv. of acid to the **1**–amine complex (full arrows) converts this complex into the pseudorotaxane (compare spectra (iii) and (v)). The subsequent deprotonation of the dipropylammonium cation with use of 1 mol equiv. of Hünig base (dotted arrows) causes the amine to move back to the metal centre (compare spectra (ii) and (iv)).

Experimental

Methods

^{1}H NMR spectra were recorded with either a Bruker AC 200 or a Bruker AC 300 spectrometer. UV–Vis spectra were recorded with a Perkin Elmer Lambda 18 spectrophotometer. Luminescence spectra were recorded with a Shimadzu RF-5001PC spectrofluorimeter.

Materials

Solvents and chemicals were purchased from Aldrich and were used as received. Hexaethylene glycol was prepared according to a literature procedure.[13]

5-Chloromethyl-2-hydroxybenzaldehyde (2). According to an already described procedure,[14] salicylaldehyde (5.0 mL, 0.047 mol), formaldehyde 37 wt. % in H_2O (3.6 mL), and

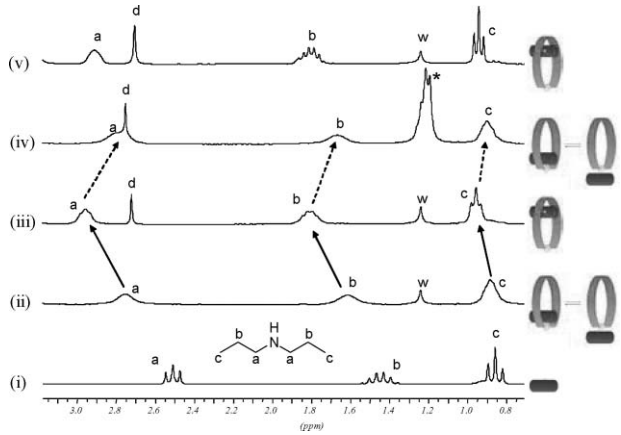


Fig. 6 ^{1}H NMR spectra at 300 MHz in chloroform at 25 °C: (i) dipropylamine, (ii) **1**–dipropylamine complex, (iii) after addition of 1 mol equiv. of methanesulfonic acid, (iv) after addition of 1 mol equiv. of Hünig base, (v) **1**–dipropylammonium complex. The signals labeled with w represent water, the signal labelled with an asterisk belongs to the protonated Hünig base, and the signal labelled with d represents the methyl group of the methanesulfonate anion.

concentrated hydrochloric acid (48 mL) were mixed and stirred overnight. The solid that separated from the reaction mixture was filtered, dissolved in diethyl ether, and dried over sodium sulfate. Recrystallization from *n*-hexane afforded **2** in 50% yield. ^{1}H NMR (200 MHz, $CDCl_3$, 25 °C) δ 11.05 (s, 1H); 9.89 (s, 1H); 7.57–7.52 (m, 2H); 7.01–6.97 (d, 1H, $J = 8.46$ Hz); 4.58 (s, 2H).

5-[(2-{2-[2-(2-{2-[2-({3-formyl-4-hydroxybenzyl}oxy) ethoxy] ethoxy} ethoxy) ethoxy]ethoxy}ethoxy)methyl]-2-hydroxybenzaldehyde (3). Sodium hydride 60% dispersion in mineral oil (1.07 g, 26.8 mmol) was placed under an argon atmosphere in a dry flask, washed three times with *n*-hexane, and suspended in anhydrous DMF (4 mL). The flask was then cooled with an ice bath and a solution of hexaethylene glycol (1.06 g, 3.75 mmol) in anhydrous DMF (4 mL) was slowly added. After the evolution of hydrogen had ceased, **2** (1.30 g, 7.61 mmol) was slowly added. The resulting yellow solution was stirred overnight at room temperature and then poured over ice. After the ice had dissolved, the resulting water solution was neutralized with 0.1 M hydrochloric acid and extracted with two 25 mL portions of dichloromethane. The organic layers were collected, washed with brine, and dried over anhydrous sodium sulfate. Chromatographic purification of the crude product (silica gel, 10% acetone in diethyl ether) afforded the desired product as a colourless oil in 21% yield. ^{1}H NMR (200 MHz, $CDCl_3$, 25 °C) δ 10.98 (s, 2H); 9.88 (s, 2H); 7.55–7.47 (m, 4H); 6.98–6.93 (d, 2H, $J = 8.51$ Hz); 4.51 (s, 4H), 3.64 (m, 24H). ^{13}C NMR (50 MHz, $CDCl_3$) $\delta = 197.4$, 160.3, 138.3, 131.2, 130.0, 127.7, 115.3, 73.0, 71.3, 70.2 ppm.

Compound 1. A solution of **3** (0.102 g, 0.185 mmol) in 2.5 mL of dichloromethane and a solution of 1,2-diaminobenzene (0.020 g, 0.184 mmol) in 2.5 mL of a 1 : 1 dichloromethane–methanol mixture were added separately and simultaneously by a syringe pump over 4 h to a solution of zinc acetate dihydrate (0.046 g, 0.209 mmol) in 100 mL of refluxing methanol. The mixture was refluxed for an additional 30 minutes and then sodium carbonate (0.046 g, 0.434 mmol) was added. After cooling, the reaction mixture was filtered, slowly concentrated under reduced

pressure at room temperature to a volume of about 5 mL, and kept overnight at −18 °C. Under these conditions, the product precipitated as a yellow solid that was separated from the mother liquor by filtration (0.029 g, yield 23%). Elemental analysis: calcd (%) for $C_{34}H_{40}N_2O_9Zn{\cdot}3H_2O$: C, 55.27; H, 6.23; N, 3.79; found: C, 55.46; H, 6.01; N, 3.77. ^{1}H NMR (200 MHz, acetone-d_6, 25 °C) δ 8.77 (bs, 2H); 7.88–6.75 (bm, 10H); 4.34 (bs, 4H); 3.76 (s, 2H); 3.60–3.09 (m, 22H). ^{13}C NMR (50 MHz, $CDCl_3$) δ = 164.3, 158.9, 148.5, 136.1, 135.0, 129.7, 127.8, 122.9, 119.0, 116.8, 73.0, 71.3, 70.2 ppm. MS-ESI-TOF for $C_{34}H_{40}N_2O_9Zn\ Na^+$ calcd: 707.2; found: 707.3.

Computational details

Geometries of all the stationary structures were fully optimised using the force field MM3 as implemented in Macromodel version 6.0. Additional parameters have been introduced for zinc, imine nitrogens, phenoxide oxygens, and imine hydrogens and are reported in the ESI.† Partial atomic charges were computed using the electrostatic potential (ESP) from the wavefunction obtained by an AM1 calculation in SPARTAN version 5.0.1. A +2 charge was used for the zinc cation. These parameters gave good agreement with X-ray structures of known complexes between zinc-salophen compounds and amines.[7]

Conclusions

In summary, we have synthesised and fully characterised the new crown ether macrocycle **1** containing a zinc-salophen unit. The novel design of this host, based on the 5,5′ junction of the polyoxyethylene chain, allows for the first time the isolation of a metallomacrocycle in which the zinc orients one of its two axial binding sites towards the inside of the cavity of the macrocycle to face the crown ether chain. This compound behaves as a wheel in the formation of [2]-pseudorotaxanes with secondary ammonium ions. We found that the alternate addition of base and acid controls guest shuttling between the two different binding sites of the macrocycle. The future development of stoppering methodologies compatible with the metal salophen moiety will lead to rotaxanes in which the motion of the axle between the two stations will be a "pure" intra-wheel translocation.

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