Sn(IV) Porphyrins as NMR Shift Reagents and Supramolecular Protecting Groups: Preparation of a Carboxylate–Catenane Porphyrin Complex
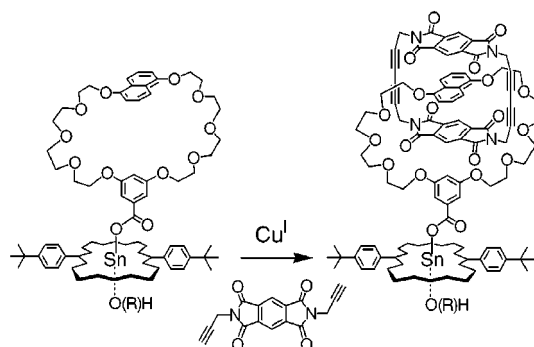
Yin Tong, Darren G. Hamilton, Jean-Christophe Meillon, and Jeremy K. M. Sanders*

University Chemical Laboratory, Lensfield Road, Cambridge, CB2 1EW, U.K.

jkms@cam.ac.uk

ABSTRACT

Coordination of a carboxylic acid diaryl crown ether to a Sn(IV) porphyrin promotes its ability to act as a template for the formation of a [2]catenane: in the absence of the porphyrin the acid–crown yields only a tiny amount of the interlocked derivative. Once isolated the free acid–[2]catenane presents extremely broad resonances in its 500 MHz ^{1}H NMR spectrum, but complexation to a Sn(IV) porphyrin results in dramatic resolution via a combination of dynamic and dispersive effects.

In this Letter we describe a supramolecular system that exploits two of the previously reported properties of tin(IV) porphyrins: (i) their ability to coordinate, and therefore potentially protect, carboxylic acid groups[1,2] and (ii) the dispersive influence of the porphyrin ring current.[3] Since the complexation process is effectively instantaneous and de-complexation can be achieved by controlled addition of a more strongly coordinating acid, or by the addition of an

excess of an alcohol, the tin porphyrin unit can be regarded as a mild protecting group. A practical demonstration of these potential applications awaited the demands of a suitable supramolecular system, such as the preparation of [2]catenane **1**.

We have recently reported the synthesis of methyl ester [2]catenane **2**.[4] This molecule may be prepared in around 30% yield by oxidative coupling of 2 equiv of acetylenic diimide **3** in the presence of methyl ester crown **5**.[4,5] However, attempts to cleave the methyl ester functionality

(1) Arnold, D. P.; Morrison, E. A.; Hanna, J. V. *Polyhedron* **1990**, *9*, 1331–1336.

(2) Smith, G.; Arnold, D. P.; Kennard, C. H. L.; Mak, T. C. W. *Polyhedron* **1991**, *10*, 509–516.

(3) Hawley, J. C.; Bampos, N.; Abraham, R. J.; Sanders, J. K. M. *Chem. Commun.* **1998**, 661–662.

(4) Zhang, Q.; Hamilton, D. G.; Feeder, N.; Teat, S. J.; Goodman, J. M.; Sanders, J. K. M. *New J. Chem,* **1999**, *23*, 897–903.

(5) Menzer, S.; White, A. J. P.; Williams, D. J.; Belohradsky, M.; Shipway, A. N.; Stoddart, J. F. *Macromolecules* **1998**, *31*, 295–307.

of **2** were unsuccessful: treatment with alkali-metal hydroxides in THF/water mixtures led to destruction of the interlocked molecule, indicated by the disappearance of the characteristic orange color of the [2]catenane arising from the donor−acceptor interactions between the constituent electron-rich aromatic diether and electron-deficient diimide components.[6]


1 R = H
2 R = Me

4 R = H
5 R = Me

R = CH₂CH₂CO₂Me

R = CH$_2$CH$_2$CO$_2$Me

6
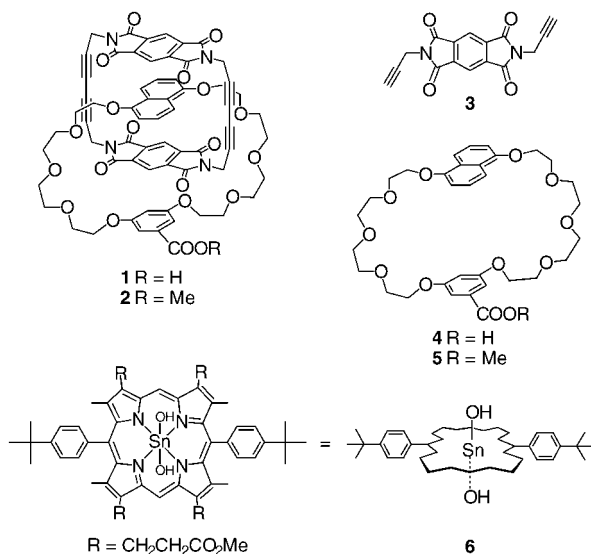
While it is likely that a method for hydrolysis could be found,[7] these interlocked molecules are relatively precious materials and we preferred to consider direct ways in which to introduce the carboxylate function. However, mixed solutions of acid−crown **4**[8] and acetylenic diimide **3** do not exhibit strong charge-transfer coloration. Subsequent addition of Cu(I)Cl, to effect the coupling process, does allow isolation of [2]catenane **1**, but in an unreliable and unsatisfactory yield of around 3%. By contrast, mixed solutions of **3** and ester−crown **5** are strongly colored and coupling gives [2]catenane **2** in reasonable yield. The yields for the two cases directly implicate the carboxylate functionality of **4**, and we therefore decided to use a Sn(IV) porphyrin derivative as a protecting group for the acid.

The 400 MHz ¹H NMR spectrum of a 2:1 molar ratio of crown **4** and porphyrin **6** in CDCl₃,[9] assigned with the aid of a 500 MHz COSY spectrum, revealed for the phenyl aromatic protons of the crown shifts of a magnitude expected from the shielding effect of the porphyrin: the shifts are very similar to those of the corresponding protons of benzoic acid upon its coordination to Sn(IV) porphyrins and indicate that the phenyl ring is essentially perpendicular to the porphyrin

plane.[3] Predictably smaller shifts of the aromatic protons of the more distant naphthalene unit of the crown are also observed.

Diimide **3** is virtually insoluble in chloroform, necessitating the use of DMF as the solvent for the catenane-forming reactions (Scheme 1).[10] Coupling was effected by the action
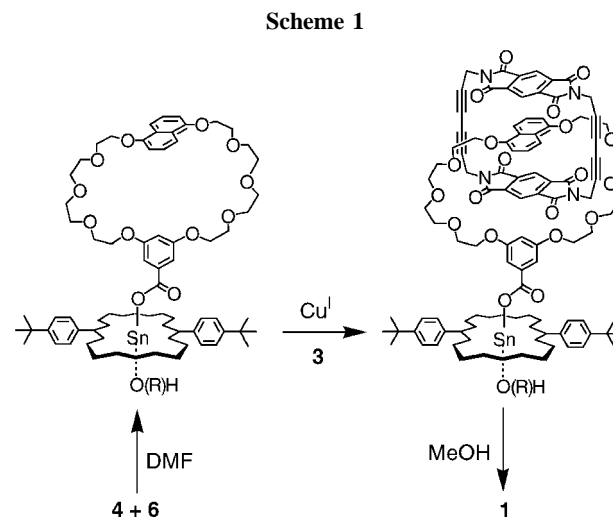
of Cu(I) as previously reported for the preparation of related systems.[6] Subsequent carboxylate decomplexation was achieved by stirring the crude reaction mixture with an excess of methanol. Isolation and purification of the organic material gave [2]catenane **1** as an orange solid in 17−20% yield.

The catenane proved sufficiently soluble in CDCl₃ to allow its 500 MHz ¹H NMR spectrum to be recorded. All the

(6) Hamilton, D. G.; Davies, J. E.; Prodi, L.; Sanders, J. K. M. *Chem. Eur. J.* **1998**, *4*, 608−620.

(7) We suspect that the diimide macrocycle is susceptible to nucleophilic cleavage at sites adjacent to imide nitrogen since only the carboxylic acid crown **4** can be isolated from the attempted hydrolyses. A reagent that specifically attacks the methyl carbon of the ester group, for example a thiolate anion, may avoid this problem and effect the desired cleavage.

(8) We prepared acid−crown **4** by alkaline hydrolysis of **5** (10% aqueous KOH in THF) at reflux for 16 h. **4** was obtained as a white solid in 95% yield after acidification (HCl) and extraction (CHCl₃) and had identical spectroscopic properties to those reported in ref 5.

(9) 3,5-Dimethoxybenzoic acid has a pK_a of 3.97 (*Dictionary of Organic Compounds*; Chapman and Hall: London, 1996), so that of acid−crown **4** would be expected to be very similar. At this acid strength full complexation is reported to take several minutes so carboxylic acid/porphyrin mixtures were stirred for 30 min to ensure full complex formation before spectra were recorded. The complexes typically contained a little excess porphyrin, which increased the complexity of the porphyrin areas of the ¹H NMR spectra. However, the complexed carboxylates were insensitive to the presence, or absence, of a bound group on the other porphyrin face, thus simplifying assignment of their resonances. In contrast, the porphyrin spectrum is sensitive to the number of axial substituents. In particular monosubstituted complexes lose the plane of the porphyrin system as a symmetry element and as a consequence those regions of the spectrum containing porphyrin resonances greatly increase in complexity if a significant amount of such a species is present. The number and relative amounts of the complex species can be most conveniently followed by examination of the meso region of the spectrum (10−11 ppm) and by examining the first methylene group of the propionate side chains of the porphyrin (≈ 4.5 ppm). The protons of the latter are diastereotopic in monosubstituted complexes where the two faces of the porphyrin are inequivalent.

(10) Catenane-forming reactions were conducted in dry DMF under an atmosphere of dry air at 5 mM crown concentration. A 4:2:1 molar ratio of acetylenic diimide **3**, acid−crown **4**, and Sn(IV) porphyrin **6** was stirred and heated in dry DMF until complete dissolution was observed. Once the solution had cooled to ambient temperature, it was treated with anhydrous CuCl (≈ 100 equiv) and CuCl₂ (≈ 20 equiv) and stirred for 48 h. The crude mixture was subsequently poured into MeOH (80 mL) and stirred for 30 min, and the solvent was removed. Partitioning between H₂O and CHCl₃ gave an orange organic layer from which [2]catenane **1** could be obtained by column chromatography (SiO₂; MeOH/CHCl₃, 10:90) followed by preparative TLC (SiO₂; MeOH/CHCl₃, 93:7). The protocol for reactions conducted in the absence of porphyrins was identical in all respects save for the omission of the Sn(IV) porphyrin.

signals appeared in positions familiar from the study of related systems but were too broad to give structurally useful information. Preliminary confirmation of the preparation of **1** was obtained by electrospray mass spectrometry which revealed a molecular ion at m/z 1228, $[M + NH_4]^+$, in the positive ion spectrum. Significantly, an ion at m/z 1209 was obtained in the negative ion mode, corresponding to the carboxylate anion of the catenane.

Full ^{1}H NMR characterization of **1** required recomplexation of the catenane to Sn(IV) porphyrin **6** (approximately 0.5 equiv), whereupon the dynamic processes responsible for the extreme broadening of the spectrum of free **1** were altered such that beautifully resolved spectra were obtained at 500 and 800 MHz. As with methyl ester [2]catenane **2**, only one resonance for the pyromellitimide protons is observed, indicating fast exchange of the two diimide subunits on the chemical shift time scale. The aromatic region is also strikingly similar to that of **2**, although the naphthalene diether and pyromellitimide protons are shifted 0.1−0.2 ppm further upfield in the porphyrin-complexed catenane, presumably, as noted in the precursor crown−porphyrin complex, due to a long-range shielding effect of the porphyrin ring current. Numerous NOE connectivities could be observed in the catenane−porphyrin complex, between elements of the catenane itself and between the catenane and the attached porphyrin.

From the previously reported characterization of methyl ester crown **5**, and its derivative [2]catenane **2**, we can construct a cycle to examine the effects on the chemical shift of various probe protons of either molecular interlocking or porphyrin complexation (Figure 1).

While a very large number of shift comparisons can be made, we focused attention on those protons attached to the carboxylate-appended group of the crown. These are the protons most likely to reveal any interesting features since they become sandwiched between the porphyrin and catenane structures on complex formation and are located on that part of the crown structure that we have shown to dramatically alter the efficiency of molecular interlocking. Figure 1 depicts in schematic form the crown **5**, catenane **2**, and porphyrin complexes among which we can draw comparisons.

The chemical shift differences for the labeled protons H_a and H_b are given as bold numbers, for molecular interlocking (left to right) and porphyrin complexation (top to bottom). We find that shifts of H_b are consistent for a given process: roughly the same shift is observed on interlocking whether the template is methyl ester crown **5** or the porphyrin−crown complex; the porphyrin complexation process induces approximately the same shift whether the crown is free or interlocked. In contrast, H_a is quite sensitive to both of these processes. An increase in chemical shift difference of around 0.7 ppm is observed for interlocking depending on the presence of the porphyrin; a similar difference is noted on complexation of the crown macrocycle to the porphyrin depending on whether the crown is interlocked in a catenane structure. For H_b the sum of the separate effects, interlocking and complexation, is close (−3.70 ppm) to that experimentally observed in the catenane−porphyrin complex (−3.77
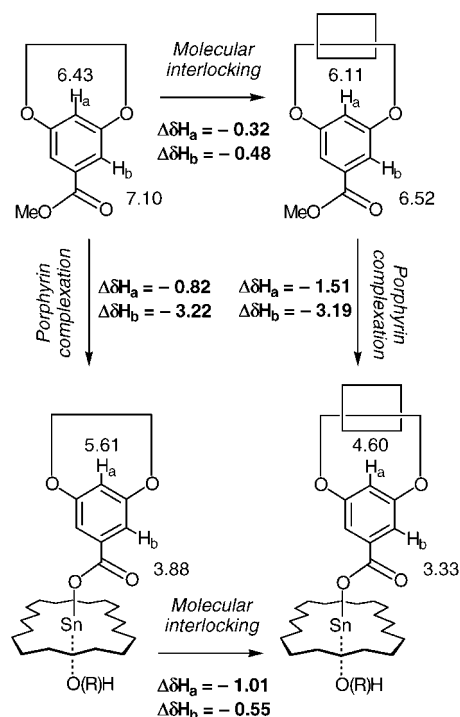

Figure 1. Schematic complexation and derivative cycle for analysis of chemical shifts. Positions (in ppm) for protons H_a and H_b are labeled; relative shifts ($\Delta\delta$) are given as bold numbers.

ppm); the observed shift of H_a (−1.83 ppm) is significantly greater than that predicted by the cycle in Figure 1 (−1.14 ppm).

Overinterpretation of these figures would be misplaced, but the fact that H_b remains relatively insensitive to local environmental changes while H_a responds certainly suggests a closer proximity to the remainder of the catenane structure for the latter. The perpendicular orientation of the carboxylate-appended phenyl ring with respect to the porphyrin plane, as depicted in the porphyrin−crown complex in Figure 1, is consistent with earlier work and the observed chemical shifts. Such a conformation places H_a in a position where it will be sensitive to the interlocking process since a neighboring diimide π-system will sit directly above this point. The relationship between these two sites will also change markedly if the orientation of the phenyl ring is altered, as will occur on porphyrin complexation.

A possible explanation for the difference in the isolated yields of **1** in the two cases (i.e., with and without porphyrin complexation), and one that does not place a primary emphasis on much discussed donor−acceptor interactions,[11] is that the porphyrin coordination process alters the conformation of the complexed crown in a manner that favors molecular inclusion. Perhaps the conformation of porphyrin-complexed **4** is similar to that of methyl ester crown **5** since

(11) Houk, K. N.; Menzer, S.; Newton, S. P.; Raymo, F. M.; Stoddart, J. F.; Williams, D. J. *J. Am. Chem. Soc.* **1999**, *121*, 1479−1487.

the yields on interlocking are of a similar order.[12] Unfortunately, no direct evidence for a conformational difference between acid−crown **4** and ester−crown **5** could be obtained from NMR spectra since in both CDCl$_3$ and d_7-DMF the crowns exhibit virtually identical chemical shifts for all their aromatic protons.

In our description of the Sn(IV) porphyrin as a protecting group, we do not seek to imply "traditional" protection in the sense in which the term is used in synthetic organic chemistry. Rather, the addition of a temporary prosthetic group that alters conformation, or disables a particular form of noncovalent interaction, can be regarded as an example of supramolecular protection. We have previously described how the complexation of cobalt carbonyl clusters to the acetylene links of a host molecule inhibits molecular inclusion.[13] Leigh and co-workers have recently reported the reversible modulation of the templating hydrogen-bonding interactions that direct the assembly of a class of amide-linked catenanes.[14] The development of these methods of supramolecular protection is an inevitable and necessary stage in establishing the supramolecular tools that are likely to prove necessary in the assembly of increasingly complex molecular systems.

(12) No concentration dependence for the ^{1}H NMR resonances of **4** was found in the range 1.5−30 mM in CDCl$_3$. It is therefore improbable, especially in a competitive hydrogen-bonding solvent such as DMF, that a conformational constraint imposed by carboxylic acid dimer formation is responsible for the poor yield of **1** obtained from the free crown.

(13) Hamilton, D. G.; Sanders, J. K. M. *Chem. Commun.* **1998**, 1749−1750.

(14) Kidd, T. J.; Leigh, D. A.; Wilson, A. J. *J. Am. Chem. Soc.* **1999**, *121*, 1599−1600.