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Synthesis of macrocyclic chromotropic acid-based sulfonamides; their complexation properties and an unexpected photochemical reaction

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ABSTRACT

Chromotropic acid (CTA), a dihydroxynaphthalenedisulfonic acid is a reagent that is widely used for dyestuff manufacture, as a chromogen-forming reagent for the analysis of formaldehyde and as an intermediate for azo derivatives used as analytical reagents. The synthesis of two new CTA-based macrocyclic tetra-sulfonamides **7** and **7a** and their corresponding bis-sulfonamides **10** and **10a** and their complexation properties toward tetra-*n*-butylammonium halides were studied. The X-ray structure of **10a** was determined and it provided key evidence for an unexpected photochemical reaction that the tetra-sulfonamides underwent.

We have been interested in the chemistry of chromotropic acid **1** (4,5-dihydroxy-2,7-naphthalenedisulphonic acid, or 'CTA') for some time now.[1] CTA has been used as a key reagent for the syntheses of various azo derivatives, which can be used not only in the dye industry, but also in a variety of analytical chemistry applications.[2] Eegriwe[3] first described its use in 1937 as a formaldehyde-specific reagent but it was only more recently in 1989 that the mechanism of the chromogen-forming reaction was deciphered.[1] In the same year, Poh et al. showed that the reaction of **2**, the disodium salt of CTA, with formaldehyde in an aqueous solution, in the absence of concentrated sulfuric acid produced a water-soluble cyclic tetramer which he called 'cyclotetrachromotropylene' (**3**) (Scheme 1).[4] This compound which can be considered to be a calixarene analogue, could not, however, be crystallized and was mainly characterized by its mass spectrum. Nevertheless, Poh's group published several papers[5] which revealed that **3** showed typical host-guest properties with various guest species.

We were therefore interested in investigating the potential host–guest properties of macrocyclic CTA-based sulfonamides which could be formed using the diamino compounds, Jeffamines® EDR-148 and EDR-176.[6] The products formed from these diamino compounds with isophthaloyl dichloride were previously studied for their complexation properties with Groups 1 and 2 halides and also with tetrabutylammonium halides (TBAX, where X = Cl, Br, I).[7] As further impetus for our work, Lan et al.[8] had reported the synthesis (Scheme 2) of macrocyclic tetrasulfonamides **4** based upon 3,6-dihydroxy-2,7-naphthalene disulfonic acid, a regioisomer of CTA, via the corresponding 3,6-dimethoxy-disulfonyldichloride (**5**). These authors reported that their compounds were used as good hosts for small solvent molecules such as DMF. Bocheńska et al.[9] reported some other macrocyclic sulfonamides however which were ion-selective ionophores for K^+, Rb^+, and Cs^+.

In this Letter we report the synthesis of four new CTA-based macrocyclic sulfonamides which were conducted in order to evaluate their potential host–guest properties. Some of these properties were evaluated in complexation studies with Groups 1 and 2, and tetrabutylammonium (TBA) halides. As well, the single-crystal X-ray structure of one of these compounds was determined and is reported. During the course of these studies, an unexpected photochemical reaction was observed which is also described herein.

The original macrocyclic sulfonamides which were targeted as shown in Scheme 3, were **6** and **6a** in which the naphthalene rings bear free hydroxyl groups, as in CTA itself. The reaction of the disulfonyldichloride of CTA with 1,8-diamino-3,6-dioxaoctane (**9**, 'Jeffamine® EDR-148')[6] or with 1,10-diamino-4,7-dioxadecane (**9a**, 'Jeffamine® EDR-176') was envisioned as a potential route to **6** and **6a**, respectively. Paruch et al.[10] in 2000 showed that an efficient way to functionalize CTA to its disulfonyldichloride **8**, was to first convert it, via its sodium salt **2**, to the corresponding ditosylate which could then form **8** in good yields. Therefore, this approach was taken by us and after considerable experimentation, conditions were found from which the syntheses of the tosylated macrocycles **7** and **7a** were achieved.

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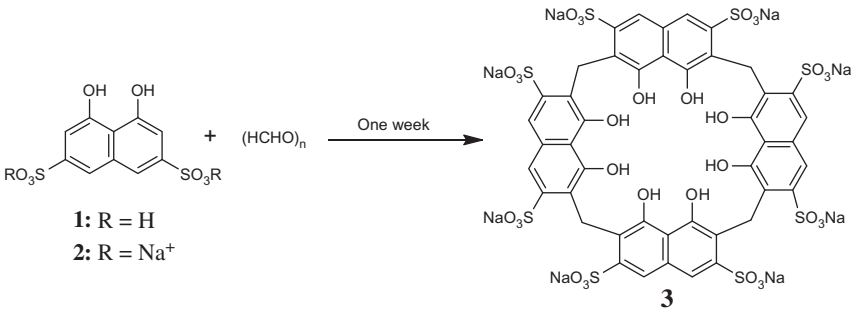
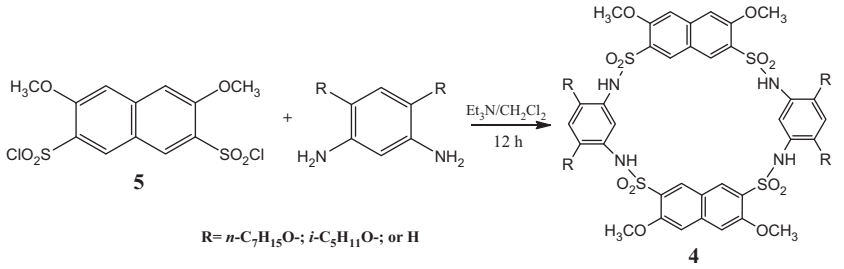


Scheme 1. Poh's synthesis of cyclotetrachromotropylene (**3**).[4]

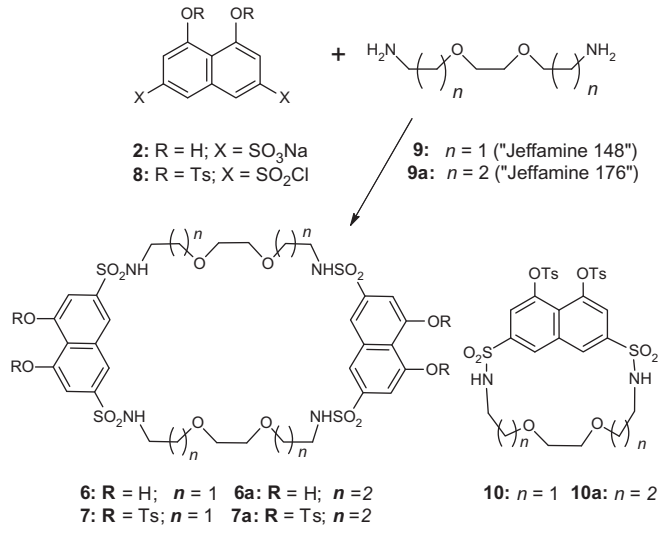


Scheme 2. Lan's synthesis of macrocyclic tetrasulfonamides.[8]

In our initial experiments reacting **8** with **9** with triethylamine, in acetonitrile under high dilution conditions, at either 0 °C or −78 °C afforded only the [1+1] product **10** in 65% yield. However, when dichloromethane was used instead as the solvent, at −100 °C, the desired [2+2] product **7** was formed in 47% yields in a mixture with **10** which was formed in 16% yields. Similarly, reaction of **8** with **9a** in acetonitrile only afforded the corresponding [1+1] product **10a**, in 76% yields. Using dichloromethane instead as the solvent at −100 °C however, formed the desired [2+2] product **7a** in 45% yields in a mixture together with **10a** in 13% yields.

Although Paruch et al.[10] reported being able to de-tosylate their CTA-derived product, all attempts to de-tosylate our compounds only afforded intractable products which could not be characterized. Therefore since it was not possible to produce the free hydroxy group-containing sulfonamides **6** or **6a**, host–guest complexation studies were conducted on all four of the tosylated products instead.

Each of the macrocyles **7**, **7a**, **10,** and **10a** were tested using ^{1}H NMR titration experiments with Groups 1 and 2 chlorides. An analogous study with isophthaloyl macrocyclic amides was previously reported by us.[7] In all cases, in contrast to the findings with the macrocyclic amides, no chemically-induced shifts (CIS) could be observed when solutions of the CTA macrocycles in a 9:1 $CDCl_3$; DMSO-d_6 solvent mixture were saturated with the metal salts. TBAX halides were also tested with each of macrocyles **7**, **7a**, **10,** and **10a**, again, in analogous experiments to those conducted with the isophthaloyl macrocyclic amides[7] described above. In these tests, in $CDCl_3$ solutions, no ^{1}H NMR CIS were observed with **10** or **10a**.



Scheme 3. Synthetic routes to macrocyclic CTA-based bis- and tetra-sulfonamides.

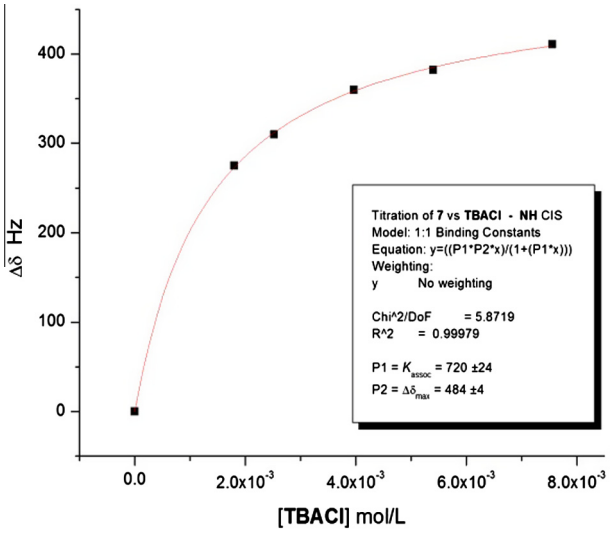


Figure 1. 1:1 Binding plots for the titration of **7** (0.62×10^{-3} M in $CDCl_3$) with TBACl using ^{1}H NMR (300 MHz) CIS for the N–H protons).