

## Spectacular Rate Enhancement in the Self-Assembly of a [2]Catenane

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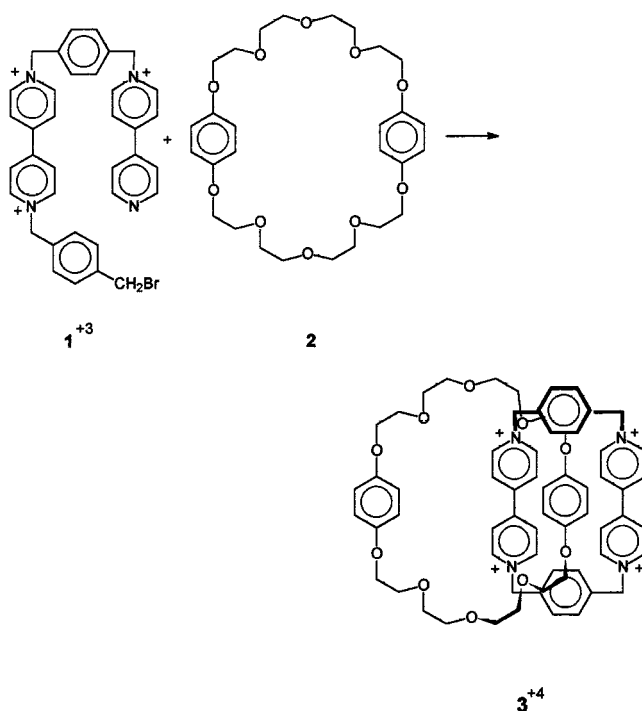
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The efficient preparation of catenanes, which has eluded chemists until recently, has enormously benefited from template-directed approaches.<sup>1</sup> One of the most fruitful of these requires that one ring be threaded by the precursor of the second ring and that this assembly be held together as the second ring is formed. In other words, one macrocycle must act as a template for the formation of the second macrocycle. Despite the numerous examples of template-directed syntheses of catenanes that can be found in the literature, no kinetic study of template effects in catenane formation has been reported to date, apart from a study by Stoddart and co-workers in which the *relative* template abilities of two different crown ethers in the formation of [2]catenanes have been assessed by competitive experiments.<sup>2</sup>

Here, we wish to report on the quantitative evaluation of template effect exerted by bis(*p*-phenylene)[34]crown-10 (**2**) in the ring-closure reaction of the trication **1**<sup>3+</sup> to yield the [2]catenane **3**<sup>4+</sup> (eq 1).

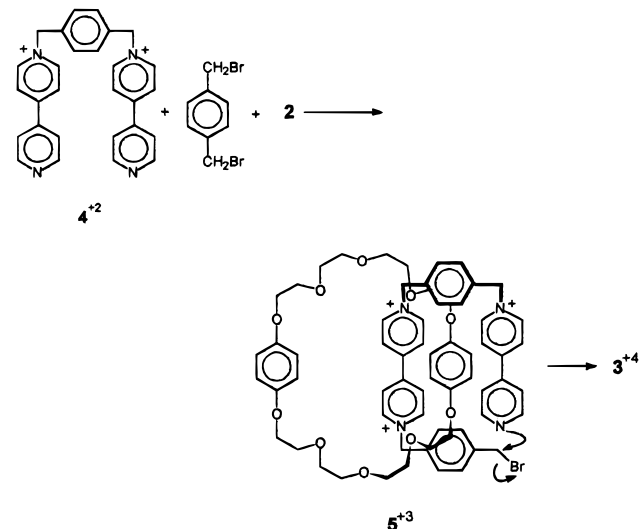
The catenane **3**<sup>4+</sup> was the first catenane synthesized by Stoddart and co-workers in an extraordinary 70% yield from *p*-bis(bromomethyl)benzene and the dication **4**<sup>2+</sup> in the presence of ca. 3 equiv of the macrocyclic polyether **2** in acetonitrile (Scheme 1).<sup>3</sup>

According to the mechanism proposed by Stoddart, one of the dication's free nitrogen atoms quaternizes upon treatment with the dihalide to afford the tricationic intermediate **1**<sup>3+</sup>, which can thread its way through the macrocyclic polyether's cavity to form a pseudorotaxane **5**<sup>3+</sup> (also termed a precatenane) that is stabilized by  $\pi$ - $\pi$  stacking interactions. This species is ideally predisposed to form the



[2]catenane **3**<sup>4+</sup> via nucleophilic attack of the residual free nitrogen atom on the remaining benzylic halide site. Thus, the reaction occurs in two steps, and only the second one would benefit from template effect.<sup>4</sup> This prompted us to carry out a detailed kinetic study of the reaction reported in eq 1.

Scheme 1



In a previous work,<sup>5</sup> we obtained by <sup>1</sup>H NMR in CD<sub>3</sub>CN at 62 °C the first-order rate constant ( $k_0 = 8.3 \times 10^{-7} \text{ s}^{-1}$ ) for the cyclization of the trication **1**<sup>3+</sup>, in the absence of any added template, to yield cyclobis(paraquat-*p*-phenylene) (**6**<sup>4+</sup>) (eq 2).

In the present investigation, the kinetics of formation of the catenane has been studied by UV-vis spectroscopy in acetonitrile at 62 °C, by following, at  $\lambda$  470 nm, the

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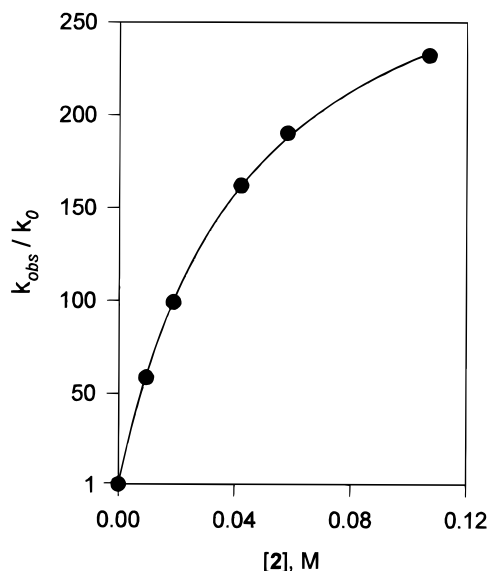
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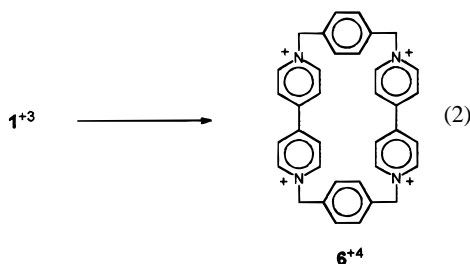
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**Figure 1.** Rate enhancements produced by the template **2** on the ring closure of the trication  $1^{3+}$ . The points are experimental, and the curve is calculated (see text).

appearance of its charge-transfer band. To avoid polymerization reactions, the concentration of the substrate  $1^{3+}$  has been kept as low as possible ( $\sim 7 \times 10^{-4}$  M). First-order rate constants ( $k_{obs}$ ) have been obtained in the presence of variable excess amounts of the polyether template **2**, up to its solubility limit ( $\sim 0.1$  M).<sup>6</sup> The ratios  $k_{obs}/k_0$ , plotted in Figure 1 against the concentration of **2**, provide a measure of the rate enhancements produced by the presence of the template.



The data in Figure 1 show that the ring closure of the trication  $1^{3+}$  is strongly accelerated by the presence of the template **2**, up to 232 times at  $[2] \sim 0.1$  M. However, before commenting upon this spectacular rate increase, it is useful to go deep into the analysis of kinetic data.

The following kinetic scheme (Scheme 2) can be envisaged for the reaction of the trication  $1^{3+}$  in the presence of the template **2**.

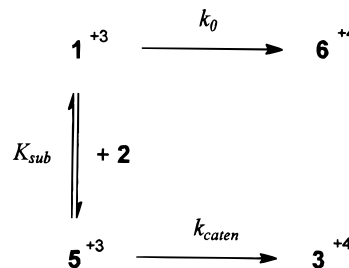
Assuming that the equilibrium for the formation of the precatenane  $5^{3+}$  is fast with respect to the ring-closure reactions, the following equation can be easily obtained

$$\frac{k_{obs}}{k_0} = \frac{1 + K_{T\#}[2]}{1 + K_{sub}[2]} \quad (3)$$

where  $K_{sub}$  is the equilibrium constant for the "threading"

(6) In a typical run, a 2.5 mL solution of **2** at the appropriate concentration (see below) was thermostated in the cell compartment of the spectrophotometer and then added with 100  $\mu$ L of a 0.0193 M solution of  $1 \cdot 3PF_6$ . The recorded increase of absorbance at 470 nm showed in all of the cases a clean first-order behavior. Relative kinetic constants ( $k_{obs}/k_0$ ) at the various guest concentrations (corrected for the volume increase at 62  $^{\circ}$ C and given in parentheses in M) were as follows: 58.4 ( $9.50 \times 10^{-3}$ ), 99.0 ( $1.88 \times 10^{-2}$ ), 161.8 ( $4.20 \times 10^{-2}$ ), 190.2 ( $5.80 \times 10^{-2}$ ), 232.0 ( $1.07 \times 10^{-1}$ ).

### Scheme 2



reaction leading to the precatenane  $5^{3+}$  and  $K_{T\#}$  ( $= k_{caten}K_{sub}/k_0$ ) is the association constant of the template **2** with the cyclic transition state.<sup>7</sup> Catalysis will be observed when the template binds the transition state more strongly than the reactants.<sup>8</sup>

Nonlinear least-squares fit to eq 3 of the  $k_{obs}/k_0$  ratios provided the following values for the association constants:  $K_{T\#} = 7550 \pm 140 \text{ M}^{-1}$  and  $K_{sub} = 23 \pm 1 \text{ M}^{-1}$ . The curve in Figure 1, calculated by inserting these values in eq 3, shows a clear tendency to saturation. The saturation value, which is given by the ratio  $k_{caten}/k_0 = K_{T\#}/K_{sub}$ , is the maximum theoretical rate enhancement that would be attained when the substrate is completely bound to the template. This value indicates that the complexed form of  $1^{3+}$  is ca. 330 times more reactive than the free one. This is one of the highest template effects in cyclizations recorded up to now, competing with the record value of ca. 360 relative to the formation of benzo[18]crown-6, template-directed by strontium ion in methanol at the same temperature.<sup>9</sup> Such a spectacular rate enhancement is due to the fact that the association of the acyclic trication  $1^{3+}$  with the template **2** is rather weak, whereas the cyclic transition state shows a much greater ligand affinity toward it. This is mainly due to the preorganization of the cyclic transition state and, secondarily, to the development of a further positive charge on the initially neutral nitrogen atom.

In a previous work, we studied the template effect exerted by  $p\text{-C}_6\text{H}_4(\text{OCH}_2\text{CH}_2\text{OCH}_2\text{CH}_2\text{OH})_2$  (**7**) on the reaction reported in eq 2 obtaining the following values for the association constants:  $K_{T\#} = 144 \text{ M}^{-1}$  and  $K_{sub} = 1.9 \text{ M}^{-1}$ .<sup>5</sup> The greater associations shown by the cyclic template **2** with respect to the acyclic template **7** can be mainly attributed to the operation of two factors. These are (i) the greater  $\pi$  surface of template **2**, which should provide stronger stabilizing  $\pi$ - $\pi$  stacking interactions with the pyridinium rings of both the substrate and the transition state,<sup>10</sup> and (ii) the preorganization of the cyclic template, which is lacking in the acyclic template. It was suggested that the oxygen atoms of the polyetheral chains significantly contribute to the binding by  $[\text{C}-\text{H}\cdots\text{O}]$  hydrogen bonds with the  $\alpha$ -protons of the pyridinium rings.<sup>10</sup> These interactions, which involve a reduction of the rotational entropy of the polyetheral chains, should be more favorable with the preorganized cyclic template **2**.

In conclusion, it is our belief that a quantitative evaluation of template effects, as that here reported, should prove useful both to an understanding of self-assembling processes and to the rational design of new self-assembling systems.

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