Synthesis and physical properties of novel guanidine containing molecular clips. Strong host-guest binding and formation of a lyotropic liquid crystalline phase

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New guanidine containing molecular clips are described which show a high affinity (Kₐ = 25 000 dm³ mol⁻¹) for aromatic guest molecules; they aggregate to form scrolls when suspended in 1 mol dm⁻³ HCl.

The synthesis of neutral molecules by synthetic receptors is a topic of great current interest in supramolecular chemistry. Initially attempts to replace the urea oxygen atoms of 1 by sulfur or nitrogen atoms by thiation using P₂S₅ or similar reagents, and by alkylation at oxygen (the first required step for replacement with nitrogen) were unsuccessful. It was possible however to synthesize clip 2 from thiourea and benzil in 60% overall yield via a route analogous to that published for clip 1. Only one of the thiourea groups of 2 was alkylated using one of the powerful alkyllating reagents methyl triflate (MeOSO₂CF₃) or triethylammonium tetrafluoroborate (Et₃OBF₄). Compound 3 was prepared by treating 2 with methyl triflate, followed by reaction with water and a base. A similar monoalkylation of 2 and subsequent reaction with ammonia or a primary amine provided compounds 4. Using similar procedures clips 5 can be synthesized from 3 in 60–90% yield depending on the substituent R (Scheme 1). Full experimental details will be reported in a forthcoming paper.

It was possible to obtain crystals of 4b suitable for X-ray analysis by the slow diffusion of hexane into a chloroform solution of this compound. Refinement of the data to an R value of 0.114 resulted in the structure shown in Fig. 1, which proves that changing the binding sites does not alter the overall shape of the clip molecules.

The unit cell contains four molecules of 4b and two molecules of chloroform. The former are present as two pairs (A and B) having slightly different conformations. The most important difference is the twist in the skeleton, as expressed by the Ph-C–Ph torsion angle, which is 24.0° in compound A and 14.0° in compound B. In the crystal structure of compound 1 this angle is 22.0°. The centres of the cavity walls are at a distance of 6.84 Å in compound A and 6.94 Å in compound B (6.67 Å in compound 1).

The binding properties of hosts 2–5 for the reference guest resorcinol were evaluated by ¹H NMR titrations in chloroform using the H₂ and H₄,resorcinol hydrogens as a probe. The results are presented in Table 1. The association constant of the

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Table 1 Association constants of complexes between various clips and resorcinol

<table>
<thead>
<tr>
<th>Clip</th>
<th>Kₐ/dm³ mol⁻¹</th>
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<tbody>
<tr>
<td>1</td>
<td>2600</td>
</tr>
<tr>
<td>2</td>
<td>50</td>
</tr>
<tr>
<td>3</td>
<td>750</td>
</tr>
<tr>
<td>4a</td>
<td>4500</td>
</tr>
<tr>
<td>5a</td>
<td>25000</td>
</tr>
</tbody>
</table>

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*a In chloroform, T = 25 °C. † Estimated errors: 20% for 1 and 2, 10% for 3 and 4a, and 50% for 5a. ‡ Value taken from ref. 2c.

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![Fig. 1 X-ray structure showing two views of conformation A of compound 4b. Hydrogen atoms have been omitted for clarity.](image-url)
complex between 5a and resorcinol was very high ($K_a = 25,000 \text{ dm}^3\text{ mol}^{-1}$).§ This is a 10-fold increase compared with the value of $K_a = 2600 \text{ dm}^3\text{ mol}^{-1}$ found for the complex of 1 with resorcinol. The guanidine function of 5a probably deprotonates the resorcinol to give an ion pair. As expected clip 2 had a low association constant, $K_a = 50 \text{ dm}^3\text{ mol}^{-1}$, and the $K_a$ value for clip 3 was found to lie in between the values of clip 1 and 2. $K_a = 750 \text{ dm}^3\text{ mol}^{-1}$. The relatively high association constant measured for clip 4a indicates that the guanidine group more than compensates for the loss of binding energy which results from the replacement of urea by the thiourea group.

The aggregation behaviour of compounds 4d and 5d was then studied. A sample of these clip molecules was suspended in aqueous $1 \text{ mol dm}^{-3} \text{ HCl}$ and electron micrographs were taken by the negative staining/platinum shadowing technique. Both compounds were found to give multi-bilayer sheets which roll up to form scrolls [Fig. 2(a)]. This result is remarkable given the unusual structure of the amphiphilic clip molecules. Electron diffraction experiments proved that the observed structures were aggregates and not crystals (clip 4c, which forms crystals when treated in the same manner, was used as a reference sample). A sample of clip 4d was prepared in the same way as for electron microscopy and then evaporated to dryness to determine the bilayer thickness. The resulting powder was analysed by X-ray powder diffraction. The data revealed a repetitive distance of 40 Å. This result can be explained reasonably if it is assumed that the aliphatic tails of 4d have an intercalated structure. The clips are probably packed as shown in Fig. 2(b) since the positively charged nitrogen centres will since the positively charged nitrogen centres will

Fig. 2 (a) Electron micrograph of a dispersion of 4d (0.2 mass%) in 1 mol dm$^{-3}$ HCl, (left) negative staining, (right) platinum shadowing; (b) Proposed arrangement of the clip molecules in a multi-bilayer of 4d

Footnotes

† Selected spectroscopic data for 2: $^1\text{H NMR}$ (CDCl$_3$, 400 MHz, 25 °C) δ 7.06 (m, 6 H), 6.97 (m, 4 H), 6.72 (s, 4 H), 6.12 (d, 4 H, $^3\text{J} = 15.7 \text{ Hz}$), 4.11 (d, 4 H, $^3\text{J} = 15.7 \text{ Hz}$), 3.82 (s, 12 H); FABMS $m/z = 689$ (M$^+\text{, 100%}$).

‡ Crystal data for 4b: $\text{C}_7\text{H}_7\text{N}_2\text{O}_2\text{S}_2\text{Cl}_3$, $M = 1414.96$, crystal size = 0.31 × 0.16 × 0.11 mm, space group $P1$, triclinic, $a = 13.5402(8)$, $b = 14.6630(6)$, $c = 18.8913(16)$ Å, $\alpha = 83.953(8)$, $\beta = 87.081(8)$, $\gamma = 77.54(10)$°; Cell volume = 3444.56 Å$^3$; $z = 2$; $D_{c} = 1.364$ g cm$^{-3}$; radiation Mo-K$\alpha$, 0.71073 Å; 208 K; preliminary $R = 0.090$ for $F > 6\sigma$. Full details will be reported elsewhere.§

References


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