Octaamide Hemicarcerands

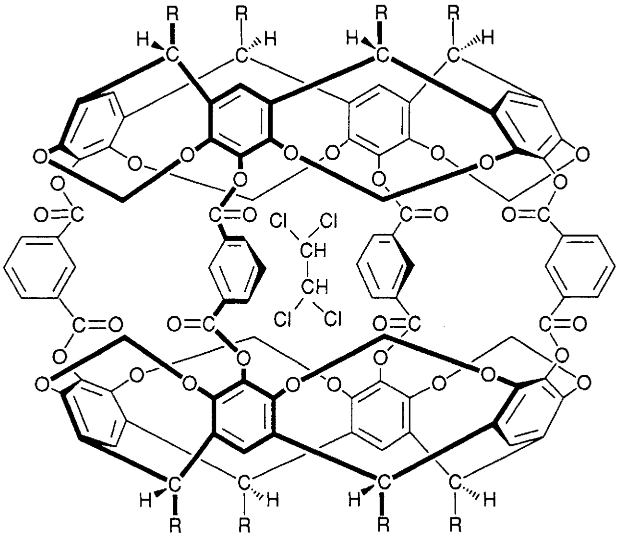
Heung-Jin Choi, Dirk Bühring, Mimi L. C. Quan, Carolyn B. Knobler and Donald J. Cram*

Department of Chemistry and Biochemistry, University of California at Los Angeles, California 90024, USA

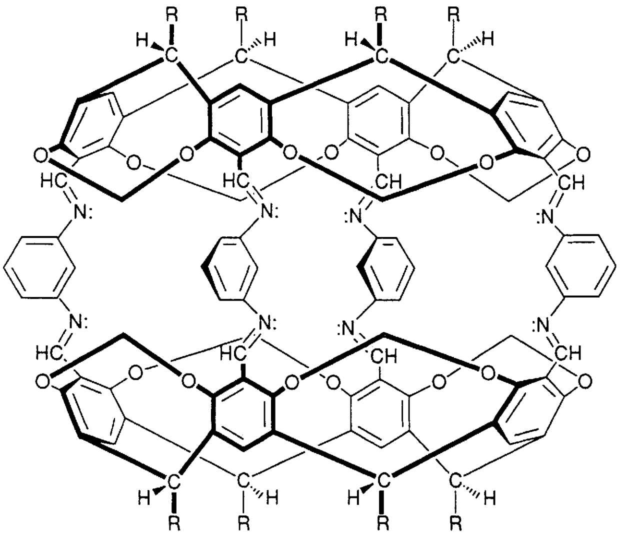
The syntheses, characterization (including a crystal structure determination), and limited constrictive binding properties of two octaamide hemicarcerands are reported, as well as a fourfold rearrangement of an acid–acetal to a phenol–lactone–acetal, the crystal structure of which has been determined.

We previously reported the synthesis and constrictive binding properties of hydrolytically unstable hemicarcerands **1**[1] and **2**[2] with portals and enforced interiors large enough to admit and expel neutral guests at high temperatures, but which were stable at ambient temperature. We now report the syntheses and characterization of the hydrolytically more stable systems, **3** and **4**, derived from **5**–**10**, and the interesting rearrangement of the tetracarboxylic acid related to **8** to give **11**.

The syntheses of **3** and **4** were accomplished by the reaction sequences **5**[3] → **8**† → **9**† → **3**†, and **6**[3] → **10**† → **4**,† respectively. Standard reactions were used and normal yields were observed for all steps except the shell closures (7% for each) **9** → **3** and **10** → **4**. These involved adding over a period of 12 h concurrently, tetraacid chloride and 1,3-phenylenediamine to tetrahydrofuran solutions of triethylamine at 55 °C under high dilution conditions. The elemental analyses of **4** indicated the presence of 1 mol of CH_2Cl_2, probably present as guest, whereas **3** was free of guest. The ^1H and ^{13}C NMR spectra of both hemicarcerands in $CDCl_3$ showed in effect they possessed C_{4d} symmetry as a result of rapid conformational equilibrations and solvent entering and departing the cavity rapidly on the NMR timescale at 25 °C, as expected from Carey–Pauling–Koltun model examination.

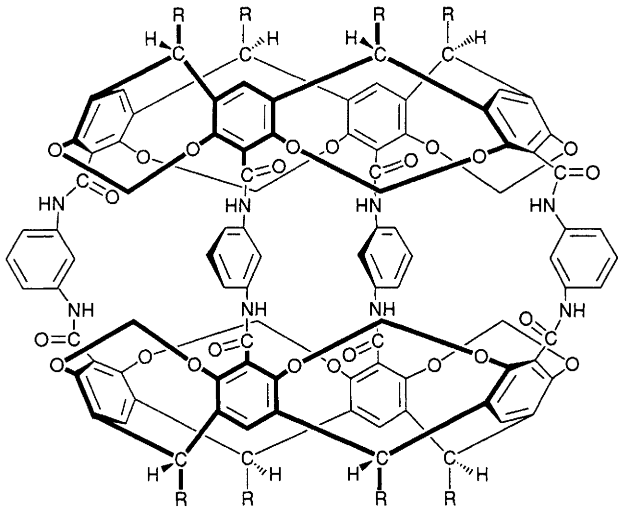


1; R = CH_2CH_2Ph



2; R = CH_2CH_2Ph

The base-catalysed hydrolysis of ester **7** gave a salt solution, acidification of which caused a fourfold, acid-catalysed rearrangement of the tetracarboxylic acid to produce the phenolic lactone acetal **11** (18%) whose crystal structure demonstrated its constitution.‡ Examination of scale molecular models of the tetracarboxylic acid indicated that the carboxy groups are well located to act as neighbouring groups in participating in exchanging four eight-membered for four six-membered rings to give **11** (see A → B).



3; R = CH_2CH_2Ph
4; R = $(CH_2)_4Me$

---

† These new compounds all gave C, H and N (when present) within 0.30% of theory, M^+ m/z signals of substantial intensity, and ^1H and ^{13}C NMR spectra consistent with their structures.

‡ *Crystal data* for: **3** (crystallised from $PhNO_2$) triclinic, space group $P\bar{1}$, $a = 15.358(1)$, $b = 16.029(1)$, $c = 21.009(2)$ Å; $\alpha = 93.435(3)$, $\beta = 105.838(3)$, $\gamma = 92.280(3)°$, $V = 4958$ Å^3, $Z = 1$; 11 642 reflections; 3206 with $I > 3\alpha(I)$, $2\theta_{max} = 100°$, Cu-Kα radiation, $T = 25$ °C. Final $R = 0.11$.

11 (crystallised from CH_2Cl_2–EtOH) monoclinic, space group $P2_1/a$, $a = 17.034(5)$, $b = 16.714(4)$, $c = 21.543(5)$ Å; $\beta = 117.378(6)°$, $V = 5446$ Å^3, $Z = 4$; 5602 reflections; 1808 with $I > 2\sigma(I)$, $2\theta_{max} = 100°$, Cu-Kα radiation, $T = 25$ °C. Final $R = 0.14$.

Atomic coordinates, bond lengths and angles, and thermal parameters for both structures have been deposited at the Cambridge Crystallographic Data Centre. See Notice to Authors, Issue No. 1.

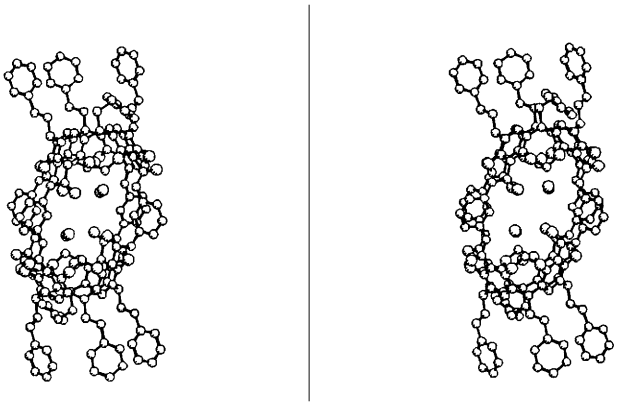
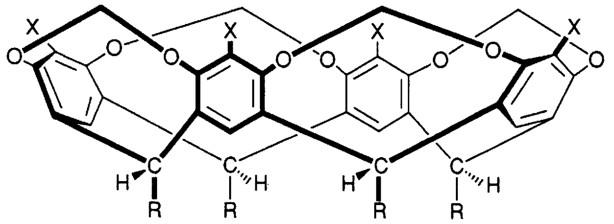
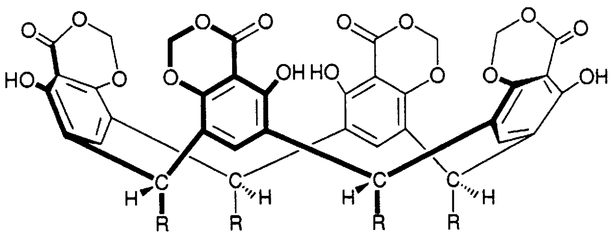


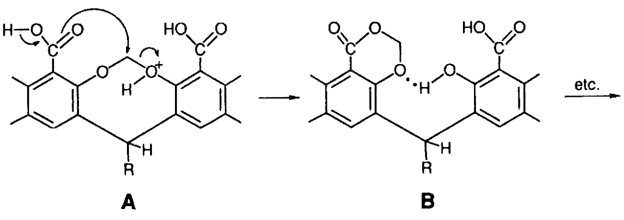
Fig. 1 Stereoview of **3**



5; X = Br, R = CH_2CH_2Ph
6; X = Br, R = $(CH_2)_4Me$
7; X = CO_2Me, R = CH_2CH_2Ph
8; X = CO_2Li, R = CH_2CH_2Ph
9; X = COCl, R = CH_2CH_2Ph
10; X = COCl, R = $(CH_2)_4Me$



11; R = CH_2CH_2Ph



The crystal structure (R = 0.11) of **3**·$7H_2O$·$10PhNO_2$ possesses a number of interesting features. The seven H_2O molecules occupy the cavity. Each of four nitrogen atoms are within 3.0 Å of one of the oxygens of H_2O. The four inward-pointing carbonyl oxygens of the host are within 2.8–3.0 Å of the H_2O-oxygen atoms. Although not located, the hydrogen atoms of these H_2O molecules undoubtedly form a network of host-to-guest and guest-to-guest hydrogen bonds. The host is centrosymmetric, but lacks a C_4 axis due to displacement of the northern and southern hemispheres by about 1.9 Å, as is evident in the stereoview, **3**·$7H_2O$ (Fig. 1).

A stereoview of the four $CONHC_6H_4NHCO$ units of **3** that bridge the two polar caps is shown in Fig. 3. Each of the eight amide groups is anti-planar, and not far from being coplanar with the central attached benzenes. Each bridge contains one inward- and one outward-pointing carbonyl arranged in such a way as to place the inward-pointing carbonyl oxygens distant from one another. The distance from the carbonyl oxygen in the northern hemisphere at about 11 o'clock to the opposite carbonyl oxygen in the southern hemisphere at about 5 o'clock is 6.80 Å. The four carbonyl oxygens of the southern hemisphere and the four of the northern are each within 0.04 Å of being coplanar, the distance between the least-square planes being 4.2 Å. Each hemispheric set of four nitrogen atoms is also nearly coplanar to within 0.04 Å, the two nitrogen planes being 4.8 Å apart.[‡]

Crystals of tetralactone **11** gave a structure refined to R = 0.14. The hydrogen atoms were not located, but intramolecular C=O···HOC oxygen-to-oxygen distances lie between 2.5 and 2.6 Å, suggesting hydrogen bonding (see stereoview in Fig. 2).[‡]

Host **3** showed high structural recognition in complexation. When potential guests were high-boiling liquids, they served as solvent for solutions of host that were heated to 120–170 °C for 24–72 h in attempts to produce complexes. When potential guests were solids, **3** and large excesses of guest dissolved in tripiperidylphosphoramide were heated to 120–160 °C. The solutions were cooled and the host, complex, or mixture were precipitated by addition of large amounts of hexane. The precipitate was washed with hexane and methanol, dried, and its 500 MHz ^1H NMR taken in $CDCl_3$. Evidence of complexation were the changes of the eight inward-turned protons of the host's OCH_2O groups from their normal δ 4.83 (doublet, J 7.4 Hz) position, or the usual large upfield shift of the guest protons.[1–4] Thirteen potential guests were examined: aspirin, adamantane, 1,4-diisopropylbenzene, azulene, bromobenzene, 3-bromotoluene, 4-methylanisole, tetrachloroethane, 1,4-dibromobenzene, menthol, *N,N'*-tetramethylterephthalic diamide and 1,4-diacetoxybenzene. Only **3**·1,4-diacetoxybenzene was isolated as a stable complex, whose Me protons were moved upfield from their normal δ 2.3 signals (in a 500 MHz spectrum) to δ −1.0 when incarcerated. Although most of the other potential guests probably reversibly formed complexes, they were unstable to the conditions of isolation. We speculate

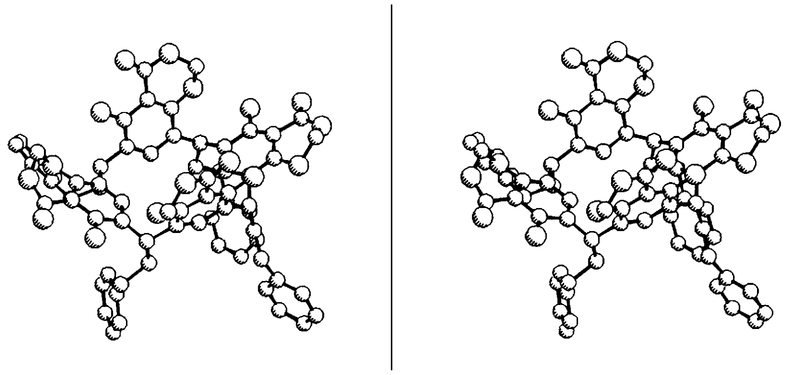


Fig. 2 Stereoview of **11**

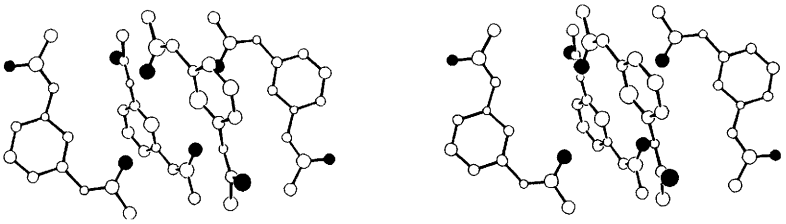


Fig 3 Stereoview of the four, $CONHC_6H_4NHCO$ units that bridge the two polar caps (● = carbonyl oxygen)

that 1,4-diacetoxybenzene uniquely combines intrinsic and constrictive binding[4] to **3** to provide a slow enough decomplexation rate to allow manipulation of the complex at room temperature.[4]

The authors thank the National Science Foundation and the US Public Health Service for Research Grants.

Received, 26th August 1992; Com. 2/04609A

References

1 M. L. Quan, C. B. Knobler and D. J. Cram. *J. Chem. Soc., Chem. Commun.*, 1991, 660.

2 M. L. C. Quan and D. J. Cram, *J. Am. Chem. Soc.*, 1991, **113**, 2754.

3 J. A. Bryant, M. T. Blanda, M. Vincenti and D. J. Cram, *J. Am. Chem. Soc.* 1991, **113**, 2167.

4 D. J. Cram, *Nature*, 1992, **356**, 29.