Novel Concave Building Block for the Synthesis of Organic Hosts

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Natural hosts frequently contain a cavity or cleft whose inner concave surface matches the convex surface of a guest. Recently, synthetic hosts that mimic this feature (cavatands)a have been designed. If new and more elaborate host-guest systems are to be developed, versatile and readily accessible building blocks must be available. Here, we describe a novel building block, 2, that meets these requirements. Compound 2 contains two fused 2-imidazolidinone rings, which are flanked by two ortho-xylene units. Its overall shape is concave and its convex side is shielded by two phenyl substituents. The use of 2 in the synthesis of three new cavatands is demonstrated.

Diphenylglycoluril (1a) was treated with paraformaldehyde and NaNH in Me2SO to yield the tetrakisoxyethyl)uracil derivative 1b (85%). Refluxing 1b in benzene with 4 equiv of p-toluene sulfonic acid gave 2a in 35% yield. Similarly, treatment of 1b with an excess of hydroquinone or 1,4-dimethoxybenzene gave 2b (75%) and 2c (50%), respectively. Molecular models indicate that the ortho-xylene units of 2 can have upward (u) or downward (d) orientations, leading to three possible conformers: uu, ud, or dd. Molecular mechanics calculations reveal that conformer uu has the lowest energy. For compound 2b an X-ray structure determination was performed. This structure determination (3) confirms the uu conformation of 2 in the solid state.

The 1H NMR spectrum of fully acetylated 2b in CD2Cl2 and in Me2SO-d6 displays one pair of well-defined doublets for the CH2 protons at δ 5.05 and 3.85 (J = 16 Hz). The position and splitting pattern of the doublets did not change over a temperature range as large as −95 to 150 °C. This led us to believe that either one conformer (uu or dd) is present or that all three conformers interconvert rapidly. To solve this question we synthesized compound 2d. The (CH3OH)2 bridges of this compound do not allow for any other conformation than uu. As the 1H NMR spectra of 2d and its nonbridged analogue 2e show identical pairs of doublets for the CH3N protons (±0.05 ppm), we conclude that compounds 2b also adopt the uu conformation in solution.

Basket-shaped cavatand 4 was prepared (75%) by treating 2b with 2 equiv of 1,11-dichloro-3,6,9-trioxaoctadecane and K2CO3 in Me2SO. The oxygen atoms of the urea units and the oxyethylene bridges form two receptor sites at the far ends of the molecule. These receptor sites bind alkanol metal ions with affinities peaking for K+. 2' Cavatand 4 forms strong 1:1 complexes with protonated diamines e.g., [H2N(CH2)3NH]2+. In these complexes the guest is wedged in between the α-xylene rings as is concluded from the observed upfield shifts (up to 1.5 ppm) of the guest CH2 protons in the 1H NMR spectrum.

Reflexing 1b and hydroquinone (molar ratio 1:1) in 1,2-dichloroethane in the presence of 4 equiv of p-toluene sulfonic acid produced cavatand 5 (3%), yield not optimized. This compound 5 structure determination (3) confirms the uu conformation of 2 in the solid state.

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(4) (a) Rebek, J., 4m. disclosures.


(7) Crystal data for 2b: IR (KBr) 3350, 2910, 1715, 1475, 1450 cm−1; 'H NMR (CDCl3) δ 7.09 (s, 10 H, Ar H), 6.92 (s, 4 H, Ar H), 5.05 and 3.85 (2 d, J = 16 Hz), 2.34 (s, 12 H, CH2), FAB MS (triethyl citrate), m/z 731 (M + H)+. Compound 4: IR (KBr) 2910, 1715, 1475, 1450, 1130, 1070 cm−1; 1H NMR (CDCl3) δ 7.09 (s, 10 H, Ar H), 6.92 (s, 4 H, Ar H), 5.05 and 3.85 (2 d, J = 16 Hz), 2.34 (s, 12 H, CH2), FAB MS (trityl citrate), m/z 879 (M + H)+. Compound 5: FAB MS (glyceraldehyde, H2O), m/z 905 (M + H)+. Fully acetylated 4: IR (KBr) 3605 and 3555 (bound H2O), 3940, 1760, 1730, 1470, 1465, 1430 cm−1; 1H NMR (CD2Cl2) δ 7.13 (s, 20 H, Ar H), 4.93 and 3.82 (2 d, J = 16 Hz, CH2), 1.15 (9H, J = 2.54 (s, 2 H, CH2CO), FAB MS (trityl citrate), m/z 1073 (M + H)+. Compound 6: UV–vis (Me2SO) 413 nm (ε 223); 'H NMR (Me2SO-d6) δ 8.45 (4 H, NCHN), 7.65 and 7.10 (2 m, 26 H, Ar H), 6.60 (s, 4 H, Ar H), 5.40 (d, 4 H, NCH2Ar, J = 16 Hz), 4.40 (m, 8 H, NCH2Ar and OCH2CH2), FAB MS (glyceraldehyde, H2O), m/z 1522 M+, 1487 (M−Cl)+, 1452 (M−2Cl)+, 1418 (M − 3Cl)+, 1316 (M − RCH2Cl) + H)+; conductivity measurements (Me2SO, 10−3 M): 11 electrolyte, δ 34 Ω cm2 mol−1. All compounds gave C, H, and N analyses within 0.3% of theory.

(9) Binding free energies of picrate salt guests of 4 at 25 °C in CDCl3 (−ΔG°/kcal mol−1 for 1:1 complex): Li+, 8.45; Na+, 8.95; K+, 11.45; Rb+, 10.50; Cs+, 9.25; NH4+, 9.50; [H2N(CH2)3NH]2+, 15.0; [H2N(CH2)3NH]3+, 16.0.
contains two diphenylglycoluril and two hydroquinone rings linked through eight methylene bridges. The void in 5 (2.5 × 2.0 Å) is not large enough to hold an organic guest. However, higher homologues of 5, e.g., those containing additional diphenylglycoluril and hydroquinone rings, do have large enough voids.10

Starting from 2, hosts that a metal center next to a cavity are readily accessible. As an example, we prepared 6 by reacting 2(a) with: excess of Tos(OCH2CH2)2Cl and base in Me2SO, excess of benzimidazole (Bz) and NaH in DMF, and 1 equiv of RhCl3 in Me2SO (overall yield 70%). Compound 6 has two trans-coordinated Cl ligands, one being inside the cavity, the other outside. The binding and catalytic properties of hosts 4–6 are currently being investigated and will be published in forthcoming papers.

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Observation of a Nonconcerted Double Proton Transfer in the Solid State by 15N CPMAS NMR

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We present here for the first time NMR spectroscopic evidence of a nonconcerted double proton transfer. The double proton motion studied occurs along slightly asymmetric double-minimum potentials in solid TTAA4 according to Scheme I. For H-chelates of the malonaldehyde type like TTAA, it has been very difficult to establish the double-minimum character of the proton potential using different spectroscopic techniques3 including NMR.4 Goedken et al.5 have performed an X-ray crystallographic analysis of solid TTAA, have postulated the "diagonal" tautomerism 1—2 shown in Scheme I, and have further suggested that the degeneracy of this process is lifted due to a rhombic distortion of the cavity.

Since solid-state proton transfers between nitrogen atoms are most directly probed by 15N CPMAS NMR,6,7 we have performed such experiments on 95% 15N-enriched TTAA.8 Figure 1 shows some of the 15N CPMAS spectra obtained with an apparatus described previously.9 We observe four lines, a–d, of equal intensity. Between 100 and 80 K, the lowest temperature where experiments were performed, no spectral changes occur, indicating that the chemical shifts are temperature independent within experimental error. Taking into account 15N solution NMR data,10 we assign the overlapping lines a and d to NH atoms and the two resolved lines b and c to two inequivalent =N— atoms in solid TTAA. As the temperature is increased, lines d and c move toward each other without coalescing, as do lines a and b. The low-field shift of line a from 96 to 288 K matches the high-field shift of line b over the same temperature range. The same is true for lines d and c. Since the intrinsic chemical shifts are temperature independent, these changes can only be explained by fast proton transfer from atom a to b and from atom d to c. In other words, the position of line n depends on the average proton density such that

\[ \delta_{mn} = \delta_m - \delta_n \]

Figure 1. 15N CPMAS NMR spectra of 95% 15N-enriched TTAA at 6.082 MHz as a function of temperature: 10-Hz line broadening, 1K–4K zero filling, 25-Hz cross-polarization time, 6000-Hz sweep width, 1.5-s repetition time, 9–us 1H–7/2 pulses, quadrature detection, 1000 scans on the average; reference, external 15NH4NO3.

Scheme I

(10) In addition to 5 a compound is isolated which contains three diphenylglycoluril and three hydroquinone rings, linked through 12 methylene bridges (symmetry D16). The cavity of this compound has a diameter of ~5 Å. Sijbesma, R. P.; Smeets, J. W. H.; Nolte, R. J. M., unpublished results.