Pergamon

Tetrahedron 59 (2003) 7067–7070

TETRAHEDRON

Anion dependent molecular recognition of cations

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Received 1 March 2003; revised 5 June 2003; accepted 10 June 2003

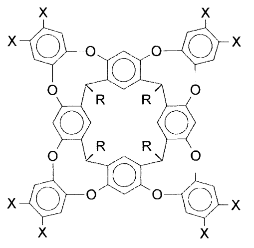
Abstract—In DMF-d_7 tetrabenzimidazole cavitands **2** exist as monomeric species and vase-like conformers. Several possible arrangements of the four benzimidazole NHs are indicated by ^{1}H NMR spectroscopy. The cavitands form 1:1 inclusion complexes with tetraethyl ammonium and phosphonium cations only when strong hydrogen bonding anions like chloride or acetate are present. These complexes are stable on the NMR time scale at 295 K feature a C_{2V}-symmetrical arrangement of benzimidazole functions. The stability of the C_{2V}-symmetrical tetramethylammonium acetate complex is independent of the temperature. In contrast, tetramethylammonium and phosphonium chloride complexes exist at 233 K as several isomers. This complicated behavior is, in part, attributed to the hydrogen bonding interactions between the anions and the NH groups of benzimidazole functions.

1. Introduction

Cavitands are open ended, unimolecular hosts that more or less surround various guests in the crystalline state and in solution.[1] A cyclic array of hydrogen bonds on the rim of cavitand **1** stabilizes the vase-like conformation and results in high kinetic stability of its inclusion complexes in solution. Exchange rates of neutral guests[2] in and out of the cavity are slow on the NMR timescale at ambient temperatures. Alkylammonium ions offer cation-π interactions to the aromatic rings of the host and these complexes are even more stable.[3] The tetrabenzimidazoles **2** cannot form a cyclic seam of intramolecular hydrogen bonds, but solvents with the appropriate donors and acceptors can fill in the gaps and stabilize the vase. In wet $CDCl_3$ water molecules played this role and kinetically stable complexes with tetramethyl-phosphonium ion were obtained.[4] Anions can also participate and we report here their effects on complexation of ammonium salts by **2** in DMF-d_7.

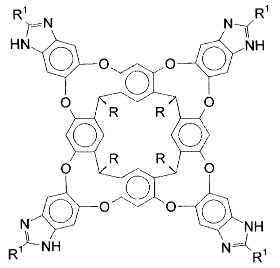
2. Structure

Compounds **2** are easily prepared by condensation of the corresponding octaamine[4] with an excess of the appropriate orthoester. The ^{1}H NMR spectrum of benzimidazole **2b** in the mixture of DMF-d_7 and methanol-d_4 (8:2) indicates the C_{4V}-symmetrical vase conformation of the cavitand. This spectrum contains one triplet for the methine protons of the bridges centered at 5.8 ppm, two singlets for the protons of the resorcinol rings and one singlet for the aromatic protons of the cavitand walls. One singlet corresponds to the methyl protons of the imidazole rings while no NH resonance was detected due to the fast exchange with methanol co-solvent.



1

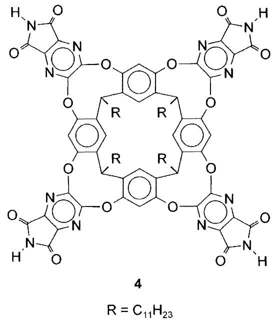
$R = C_{11}H_{23}$
$X = NHC(O)C_7H_{15}$



2

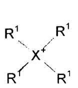
$R = C_{11}H_{23}$

$R^1 = H$ **2a**
$R^1 = CH_3$ **2b**



4

$R = C_{11}H_{23}$



X = N, R^1 = Me **3a⁺**
X = P, N = Me **3b⁺**

3⁺

In DMF-d_7 alone at 295 K, the ^{1}H NMR spectrum of **2** contains a complicate set of signals for the aromatic protons,

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Keywords: supramolecular chemistry; cavitands; inclusion of cations; anion effects.

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0040–4020/$ - see front matter © 2003 Elsevier Ltd. All rights reserved.
doi:10.1016/S0040-4020(03)00917-7

while the NH protons emerge as four, partly overlapping and broadened resonances between 11.7 and 12.6 ppm (Fig. 1(a)). The protons of the methine bridges emerge as two overlapping resonances at 5.9 ppm indicating the vase conformation, but lacking high symmetry. In contrast, the ^{1}H NMR spectrum of cavitand tetraimide **4** measured at 303 K contains one sharp and one broad signal for the protons of the resorcinol ring and one triplet for the methine protons of the bridges at 4.0 ppm. At 243 K four singlets are observed for the aromatic protons of **4** indicating a C_{2V}-symmetrical kite conformation.[5] This results from interconversion of two kite conformers of **4** that is fast on the NMR time scale at 303 K but becomes slow at lower temperatures. In short, a polar rim alone is not enough to enforce a vase conformation and binding properties in DMF.

The ^{1}H NMR spectrum of 1:1 mixture of **2a** and **2b** contains no signals for heteroaggregates. Accordingly, the cavitands are monomeric structures, even though a dimeric capsular structure appears possible. In DMSO-d_6, the NH protons emerged as three sharp singlets and one broadened resonance between 12.0 and 13.5 ppm. The complicated patterns observed are due to the tautomerism available to the benzimidazoles in the relative arrangements of their NH protons. Four such arrangements are possible; they feature C_4-, C_{2V}-, C_s- and C_1-symmetry (Fig. 2). The broadening and overlap of the signals at 295 K do not allow an unambiguous assignment to particular isomers. Protonation of **2b** with excess HCl removes the tautomerism and the ^{1}H NMR spectrum of **2b**·4HCl in DMF-d_7 contains only one singlet for the NH protons at 14.5 ppm and the sharp signals indicate the C_{4V}-symmetrical pattern for the cavitand.

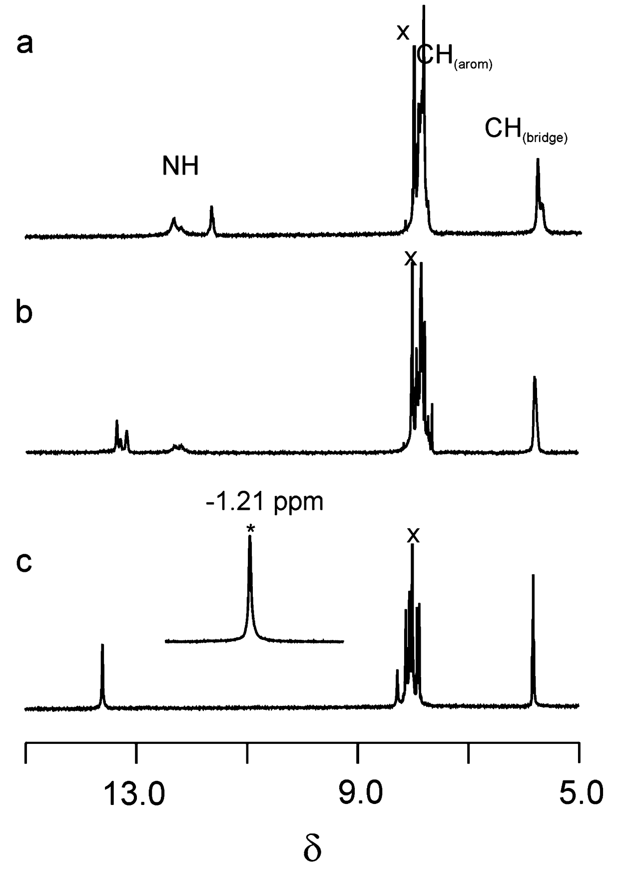

Figure 1. The ^{1}H NMR spectra in DMF-d_7 (600 MHz, 295 K): (a) **2b**; (b) **2b**+Bu$_4$N$^+$Cl$^-$; (c) **2b**+**33a**$^+$Cl$^-$ at 295 K. Signals of the encapsulated cation are marked by an asterisk; ×—residual signal of DMF.

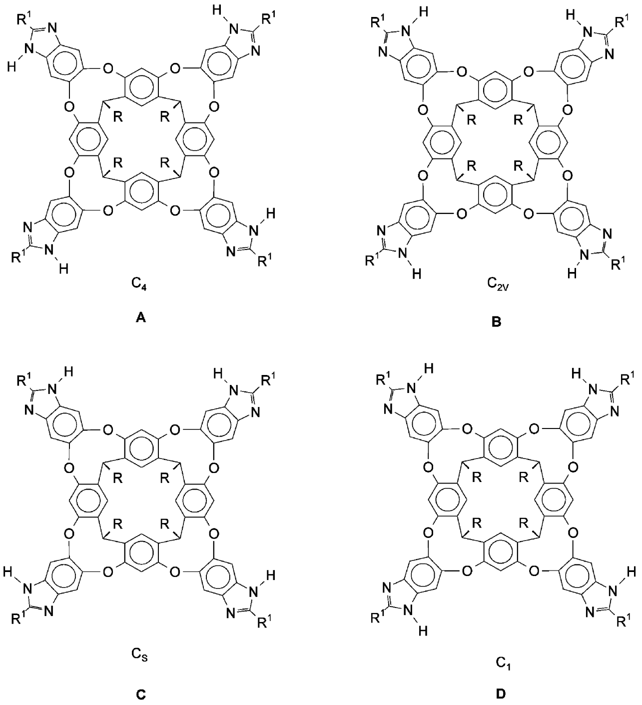

Figure 2. Four possible isomers of cavitands **2**.

Modeling indicates that no intermolecular hydrogen bonds are possible at the upper rim of cavitands **2**,[4] instead, the benzimidazole NH groups must be hydrogen bonded to DMF or DMSO solvent molecules. The addition of tetrabutylammonium chloride to the solution of **2b** in DMF-d_7 influences the NH resonances considerably. The bulky cation is not a guest; but chloride is involved. Five signals (Fig. 1(b)) are observed at 295 K that are shifted downfield, indicating hydrogen bonding interactions between the NH hydrogens and chloride anion. No such changes are detected under the same conditions on addition of the non-hydrogen bonding salt Bu$_4$N$^+$ BF$_4$.

3. Complexation

The ^{1}H NMR spectra of **2** in DMF measured between 303 and 223 K, did not contain signals for encapsulated solvent. The addition of tetramethylammonium chloride or acetate resulted in drastic changes in the spectrum. The spectrum of the chloride complex at 295 K is sharp and contains one triplet for the methine proton of the bridges at 5.8 ppm and one singlet for the NH protons while the protons of the aromatic rings emerge as two singlets each (Fig. 1(c)).[6] This pattern corresponds to the C_{2V}-symmetrical structure B (Fig. 2). In the up-field window of the ^{1}H NMR spectrum a broadened singlet emerges at −1.2 ppm that corresponds to the methyl protons of the cation, held in the cavity of **2b**. The induced up-field shift ($\Delta\delta = -4.7$ ppm) manifests close proximity of the methyl groups to the shielding regions of

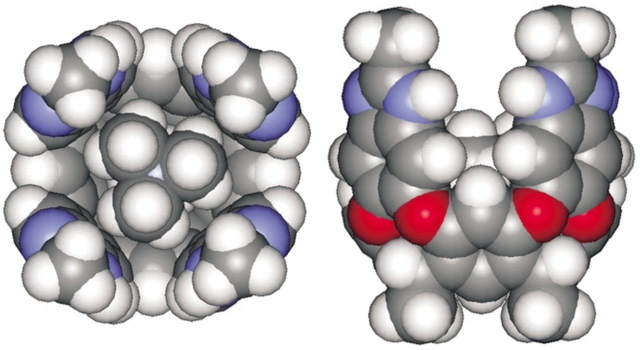

Figure 3. Optimized structure of **2b**·**3a**$^+$ (C_{2V}-symmetry) in space filling presentation: left-top view, right-side view.

the cavitand aryl rings (Fig. 3). The exchange of the guest in and out of the cavitand is slow on the NMR time scale and integration of the spectrum revealed the 1:1 stoichiometry for the complex. A similar spectrum was observed for the complex with **3a**$^+$AcO$^-$. No significant change was detected for the chemical shift of the acetate anion suggesting that only the cation is inside the cavity. The 1:1 complexes are also kinetically stable on ^{13}C NMR time scale; the resonance of the included methyl carbons is shifted up-field by 4.3 ppm. The aromatic region of the ^{13}C NMR spectrum of **2b**·**3a**$^+$Cl$^-$ and **2b**·**3a**$^+$AcO$^-$ contains 15 and 14 (due to overlap) signals, respectively, and confirms the C_{2V} symmetrical structure B (Fig. 2). Cavitands **2** also form 1:1 inclusion complexes with tetramethylphosphonium chloride **3b**$^+$Cl$^-$. The protons of the included cation emerge as broadened singlet at −2.1 ppm ($\Delta\delta$=−4.6 ppm) while the ^{13}P-resonance shifts up-field by 8.3 ppm.

The inclusion of cations **3**$^+$ in DMF-d_7 depends strongly on the hydrogen bonding abilities of the anion of the salt added. The ^{1}H NMR signals for the NH protons of **2b** appeared at 15.0 and 13.6 ppm in the case of the complexes with **3a**$^+$AcO$^-$ and **3a**$^+$Cl$^-$, respectively. Strong down field induced shifts for the NH protons indicate hydrogen bonding interaction between the anion(s) and the benzimidazole fragments of **2b**.[7] The addition of Bu_4N^+ Cl$^-$ to the solution of **3a**$^+$AcO$^-$ did not change the shift of the NH resonance indicating much higher stability of the acetate complex. No complexation was observed using **3a**$^+$BF$_4^-$ or **3b**$^+$Br$^-$.

The effect of temperature on the spectrum of **2b**·**3a**$^+$Cl$^-$ was examined. At 223 K two singlets in a 1:1 ratio were observed for the protons of the encapsulated cation. Additional sets of signals emerged also for the aromatic C–H and NH protons of the cavitand. The ratio between the singlets of the encapsulated cation depended on the temperature and at 253 K it was approximately 1:2. In the case of the tetramethylphosphonium complex **2b**·**3b**$^+$Cl$^-$ the ^{1}H NMR spectrum at 233 K contained three overlapping doublets between −2.25 and −2.45 ppm corresponding to the included cation and a complicated pattern for the protons of **2b**. The ^{31}P NMR spectrum revealed three different environments for the encapsulated tetramethyl phosphonium cation. The ^{1}H NMR spectrum of **2b**·**3a**$^+$AcO$^-$ does not depend on temperature indicating a remarkable stability of C_{2V}-symmetrical structure of **2b**.

The different arrangements of the benzimidazole NH groups (Fig. 2) can give rise to three complexes that could be conformationally stabilized by anion bonding; only the C_4-isomer cannot chelate an anion. The relative stabilities of these complexes are far from predictable, but only the C_{2V}-isomer can chelate two anions.

The addition of 5% of methanol-d_4 to the solution of **2b**·**3a**$^+$AcO$^-$ or **2b**·**3a**$^+$Cl$^-$ in DMF-d_7 gives rise to a new set of signals for the cavitand protons. The new set, corresponding to the C_{4V}-symmetrical vase conformation increases upon further addition of methanol-d_4 at the expense of the original complex. In the presence of 20% methanol no inclusion complex remains. Apparently, solvation of the anions with methanol is preferred to hydrogen bonding to the benzimidazoles, and solvation of the cavitand with methanol is preferred to the cation. The cation is also likely better solvated in methanol.

In conclusion, readily available cavitand tetrabenzimidazoles **2** are capable of inclusion of tetramethyl ammonium and phosphonium cations in DMF. In spite of the solvent's high polarity, the complexes of cavitands **2** are kinetically stable on the NMR time scale at ambient temperatures. Slow exchange of protons between the nitrogens of the benzimidazole fragments results in isomeric cavitands, and the equilibrium between these isomers depends strongly on the temperature. At 223 K the C_{2V}-symmetrical arrangement appears to be the most stable in the presence of acetate, while the presence of chloride several isomeric complexes with comparable stability are formed. Both the cation guest in the cavity and anion bound to the rim contribute to the high kinetic stability of the complexes.

Acknowledgements

We are grateful to the Skaggs Foundation and the National Institute of Health (GM 27932) for financial support. J. C. F. thanks DAAD (German Academic Exchange Service) for a postdoctoral stipend and A. S. is a Skaggs Postdoctoral Fellow.

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