Structural Studies of Self-Folding Cavitands

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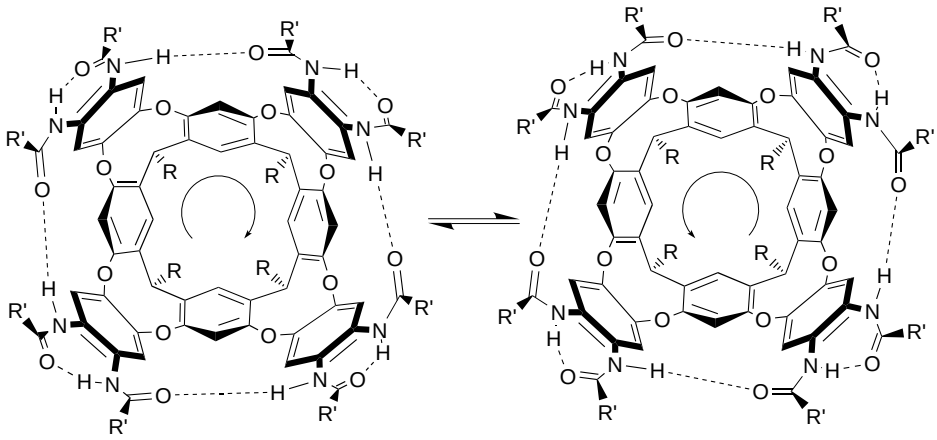
Dedicated to Professor *Albert Eschenmoser* on the occasion of his 75th birthday

Resorcinarene-based cavitands **1a**–**c** fold into a deep open-ended cavity by means of intramolecular hydrogen bonds in both apolar solutions and the solid state. The X-ray crystal-structure analysis of cavitand **1a** features a seam of secondary amide C=O···H–N interactions that bridge adjacent rings and are held in place by intra-annular hydrogen bonds. This results in a cavity of 9.2×7.0 Å dimensions. The arrangement of the amides in **1a**–**1c** is cycloenantiomeric, with clock- and counterclockwise orientation of the head-to-tail amide sequence. Interconversion rates of the two enantiomers are controlled by solvent polarity: the rate is slow on the NMR time-scale in aromatic solvents and $CDCl_3$, but fast in (D_6)acetone. The ^{1}H- and ^{13}C-NMR-spectral analysis is in agreement with the crystallographic data. Chiral cavitand **1b** with eight HN–C(O)–C*HMeEt ((+)-(*S*)) groups on its upper rim exists as two cyclodiastereoisomers (in a *ca.* 3:1 ratio) in apolar solution. A 'library' of 512 diastereoisomeric cavitands **1c** is obtained as a mixture by using the corresponding racemic acid chloride.

1. Introduction. – Cavitands are open-ended synthetic structures capable of binding smaller, complementary organic compounds and ions [1]. Self-folding cavitands are synthetic hosts such as **1**, in which intramolecular H-bonding and solvent effects control the molecule's conformational dynamics [2]. A particularly intriguing aspect of these hosts has been the unusual kinetic stability of their host-guest complexes, the 'caviplexes'; exchange rates are slow on the NMR time-scale (600 MHz, ambient temperatures), even though the binding affinities are quite modest (1–3 kcal/mol). Spectroscopic studies and molecular modeling point to a seam of intramolecular H-bonds formed by the secondary amide groups at the upper rim of the structure as a cause of this behavior (*Fig. 1*).

We proposed that these H-bonds indirectly slow the exchange rates of guests into and out of the vase, to a degree that allows us to observe separate signals for free and bound guest in the NMR spectra. The spectra clarify the orientation of the guests inside the cavity [2][3] and reveal the stereochemical subtleties of caviplex formation [3]. The hosts have been further elaborated to self-complementary cavitands [4] and much larger, nanoscale semi-capsular structures [5]. Here, we report on the structural underpinnings of the binding and spectroscopic behavior of cavitands **1a**–**1c** both in the solid state and in solution. The single-crystal X-ray structure of **1a** confirms the seam of H-bonds proposed earlier in solution and provides a detailed picture of the internal



1a R = $(CH_2)_{10}CH_3$, R' = $(CH_2)_6CH_3$
1b R = $(CH_2)_{10}CH_3$, R' = $C^*H(CH_3)C_2H_5$
1c R = $(CH_2)_{10}CH_3$, R' = $CH(CH_3)C_2H_5$

Fig. 1. *Two cycloenantiomeric forms of cavitand* **1**

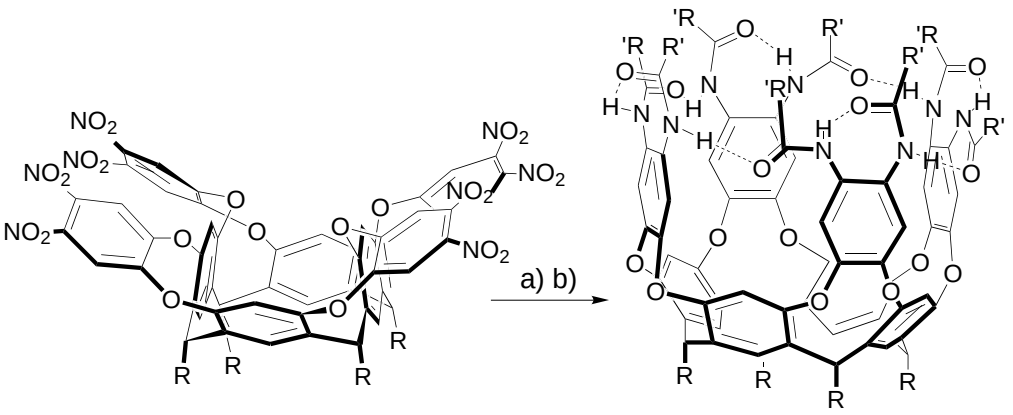
cavity's size and shape. In addition, we describe the first chiral self-folding cavitand **1b**. It provides evidence for cycloenantiomerism and cyclodiastereoisomerism at the supramolecular level. The results show promise for the use of cooperative, cyclic arrays of H-bonds for stereoselective recognition [6–10].

2. Results and Discussion. – 2.1. *Synthesis.* Octanitro cavitand **2** [2] was reduced (H_2, *Raney*-Ni, toluene, 45°) and subsequently acylated with appropriate acyl chlorides under *Schotten-Baumann* conditions in AcOEt/H_2O in the presence of K_2CO_3 to afford octaamides **1a**–**1c** as pale-yellow solids in 25–55% yields (*Scheme*).

2.2. *X-Ray Crystal-Structure Analysis.* Diffraction-quality crystals of cavitand **1a** were obtained from acetone and were stable without the mother liquor. In the crystalline state, the resorcinarene skeleton of **1a** has an almost perfect cone conformation (*Fig. 2*). Four bridging aromatic rings form the walls of the extended cavity of 9.2×7.0 Å dimensions, in which one acetone molecule is entrapped. Four longer intramolecular but interannular C=O···HN H-bonds bridge the neighboring aromatic walls (*Table*); four shorter, intra-annular H-bonds fix the orientations of the two amide groups on a given 1,2-phenylenediamine unit. The geometries of the intra-annular H-bonds are far from ideal and probably represent a default conformation: the alternative, nearly coplanar arrangement of two amide groups is destabilized by unfavorable dipole-dipole interactions.

Overall, the eight amide groups provide a head-to-tail seam of H-bonds along the upper rim of the structure **1a**. The cyclic array of H-bonds is reminiscent of those seen in naturally occurring receptors such as cyclodextrins [6] or ionophores such as valinomycin [7]. In these, the cyclic array is thought to impart additional strength to the H-bonds through cooperative effects. Cooperativity is also implicated in the H-bonds

Scheme



2 R = $(CH_2)_{10}CH_3$ **1a–1c**

a) *Raney*-Ni, H_2, toluene, 45°, 12 h; >90%. b) RC(O)Cl (*ca.* 10 equiv.), K_2CO_3, AcOEt/H_2O 1:1, r.t., 2 h; 25–55%.

Table. *Geometry of the H-Bonds of* **1a**·*Acetone* [Å, °]

D–H···A	*d*(D···A)	<(DHA)
N(1)–H(1)···O(16)	2.906(6)	157.8
N(2)–H(2)···O(9)	2.747(5)	141.5
N(3)–H(3)···O(10)	2.871(4)	163.5
N(4)–H(4)···O(11)	2.762(4)	139.3
N(5)–H(5)···O(12)	2.812(4)	154.6
N(6)–H(6)···O(13)	2.793(4)	139.3
N(7)–H(7)···O(14)	3.052(4)	159.3
N(8)–H(8)···O(15)	2.702(5)	146.0

that cause dimerization of the vancomycin antibiotics [8], the stabilization of the spectacular synthetic array of six resorcinarenes discovered by *MacGillivray* and *Atwood* [9], and even the monomeric calixarenes [10]. Cooperativity has a precise thermodynamic definition, but its evaluation or determination is rarely possible as it is an all-or-nothing event in the cases mentioned above.

The seam of the secondary amide groups makes possible two cycloenantiomers [11], with clockwise and counterclockwise orientation of the HN–CO bonds. The crystal of **1a**·acetone is indeed a racemate. Two molecules of **1a** form a centrosymmetric dimer *via* two dipole-dipole (charge-transfer) interactions between the O-(O(13) and O(13a)) and the C-atoms (C(58) and C(58b)) of the C=O groups (*Fig. 3*,*a*). The distance C(58)–O(13a) is 3.25 Å, while the distance O(14)–N(7) (3.052(4) Å) is considerably longer than a normal H-bond (*Table*). This is apparently a crystal-packing effect, reflecting a compromise between intra- and intermolecular interactions.

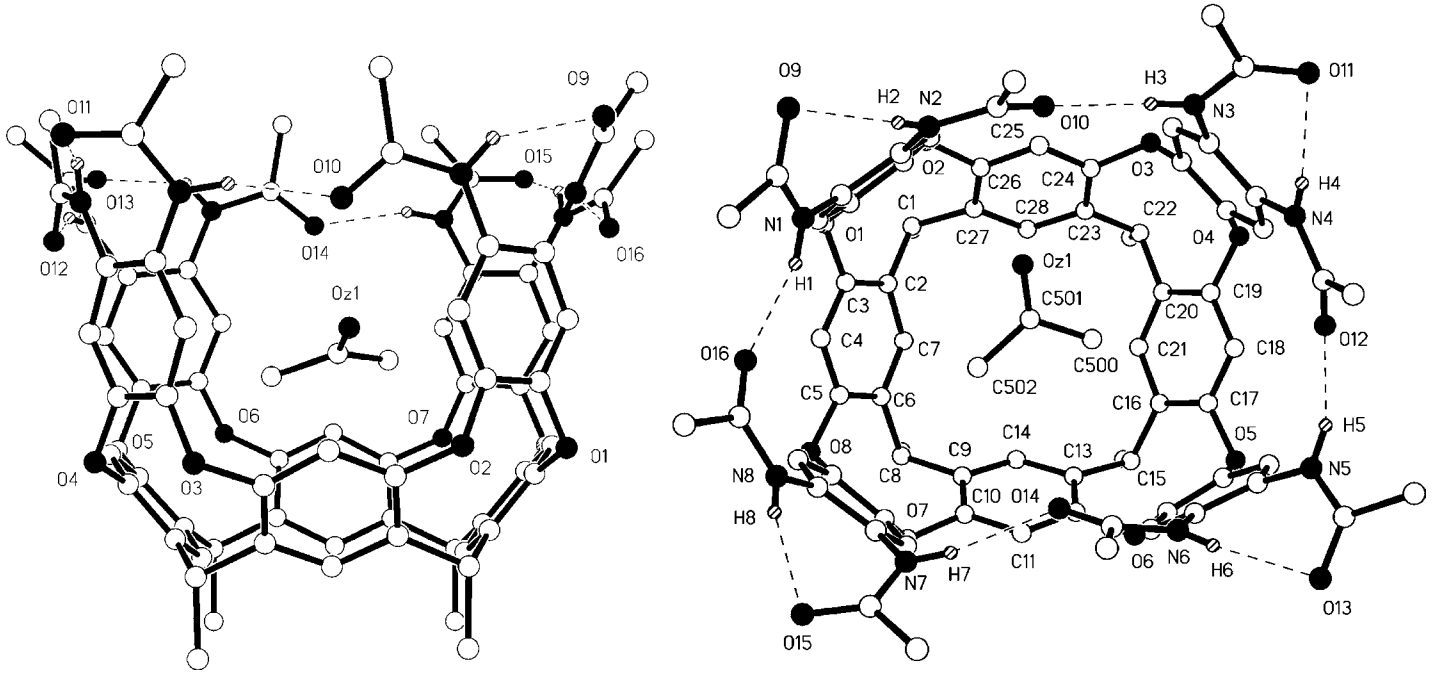


Fig. 2. *Single-crystal X-ray structure of caviplex* **1a** · *acetone: side and top views.* Only one cycloenantiomer is shown. CH H-Atoms and long aliphatic chains are omitted for clarity. N- and O-atoms are darkened, and H-bonds are shown in dotted lines.

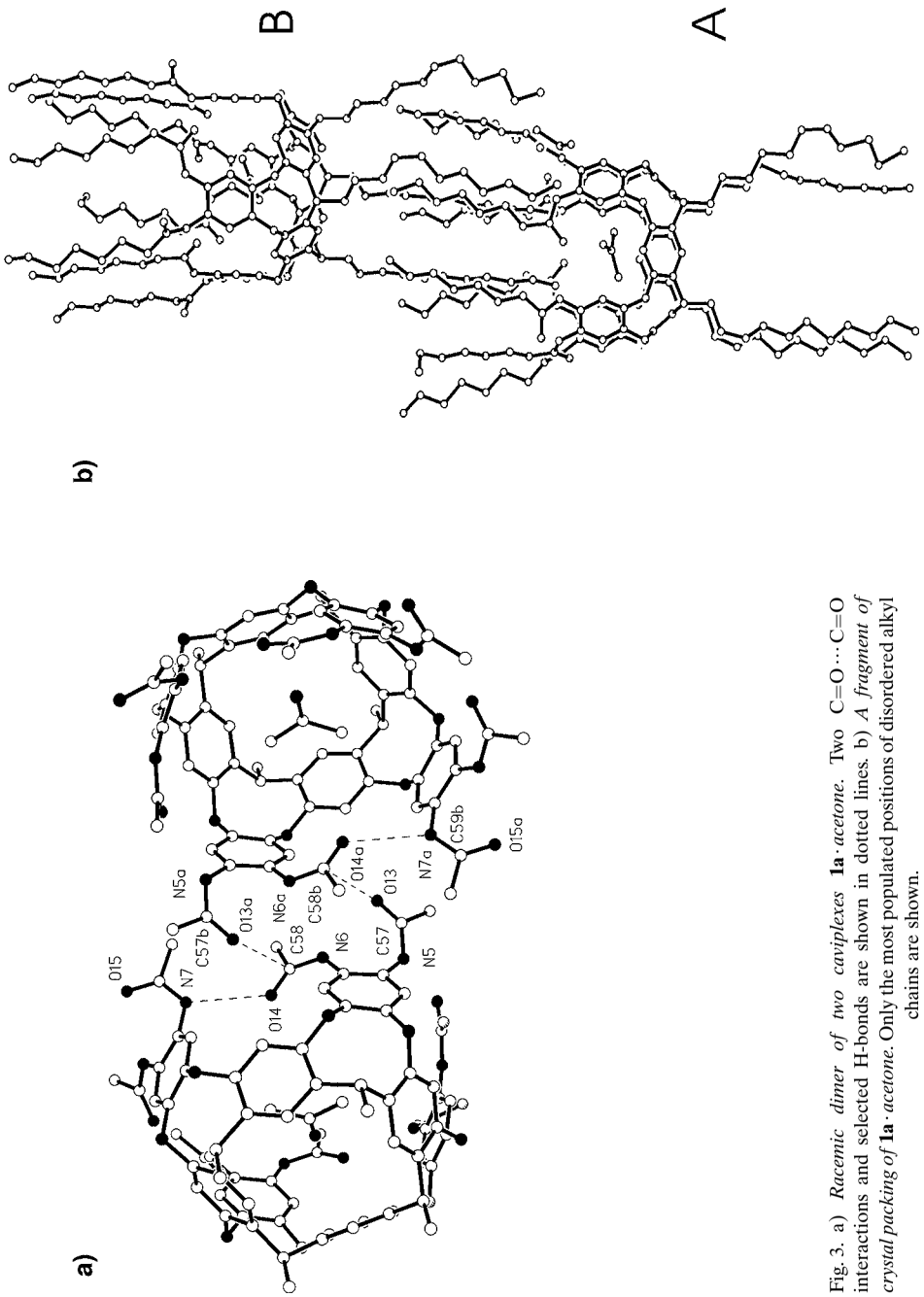


Fig. 3. a) *Racemic dimer of two caviplexes* **1a**·*acetone*. Two C=O···C=O interactions and selected H-bonds are shown in dotted lines. b) *A fragment of crystal packing of* **1a**·*acetone*. Only the most populated positions of disordered alkyl chains are shown.

The packing of **1a** · acetone in the crystal is presented in *Fig. 3,b*. All eight heptyl chains of the amide groups are oriented in more or less the same direction and create a rather deep, hydrophobic channel. The two undecyl chains of molecule B are partly included in the channel of molecule A (*Fig. 3,b*). In this way, the vase-shaped cavity is closed at its wider rim. Both heptyl and undecyl chains of **1a** are strongly disordered, this factor being responsible for the rather high *R* values.

The encapsulated acetone molecule occupies a position deep in the cavity of **1a**. Its molecular plane is above that defined by the O-atoms of the resorcinarene skeleton (O(1)–O(8)), and the two planes intersect at an angle of 24.6° (*Fig. 2*). The shortest distance between the center of gravity (O(1)–O(8)) to the acetone (C(500)) molecule is 1.86 Å. The distance between C(500) of the guest and the center of the resorcinol ring C(16)–C(21) (3.43 Å) is in accord with a CH-π interaction, but no close intermolecular contacts were found for the C(502)-atom of the guest.

The interannular H-bonds of **1a** are anomalous when compared to simpler compounds with 1,2-phenylenediamine fragments. Intramolecular H-bonding between the two amide moieties is conceivable, yet IR and ^{1}H-NMR experiments with the number of such diamides in apolar solvents suggest that the H-bonds are intermolecular instead [2][12]. The single-crystal X-ray analysis of **3** revealed only intermolecular C=O···H–N H-bonds (*Fig. 4*). In addition, two close C=O···C=O contacts are evident between neighboring molecules **3**, similar to those found in the dimer of **1a** (*Fig. 3,a*). These results suggest that the preorganization provided by the interannular H-bonds is responsible for the existence of the intraannular ones in **1a**.

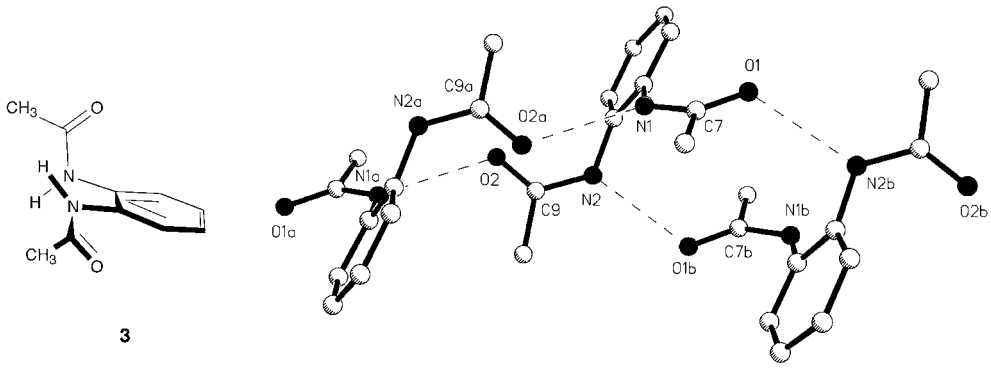


Fig. 4. *Single-crystal X-ray structure of model diamide* **3**. O(2)···N(1a) 2.879(2) Å, O(1)···N(2b) 2.894(2) Å, O(2)···C(9a) 3.043(2) Å, O(1)···C(7b) = 3.386(2) Å. H-atoms are omitted for clarity.

2.3. *^{1}H-NMR Spectroscopy.* The structure of **1a** · acetone caviplex agrees with the C_4-symmetric structure deduced from NMR studies in apolar aromatic solvents and $CDCl_3$. In particular, the ^{1}H-NMR spectrum in $CDCl_3$ includes two downfield amide NH *singlets*, two *singlets* for the aromatic CH protons of the phenylene walls, one set of the *singlets* for the resorcinarene skeleton, and the characteristic methine-CH *triplet* at *ca.* 5.5 ppm (*Fig. 5,a*). In contrast, the ^{1}H-NMR spectrum of **1a** in the more polar (D_6)acetone corresponds to the C_{4v}-symmetric structure (*Fig. 5,c*): only one set of signals is seen for all groups of protons. In a mixture of (D_6)acetone/$CDCl_3$ 1:2, the ^{1}H-NMR signals for the amide NH and the CH protons of the phenylene walls are

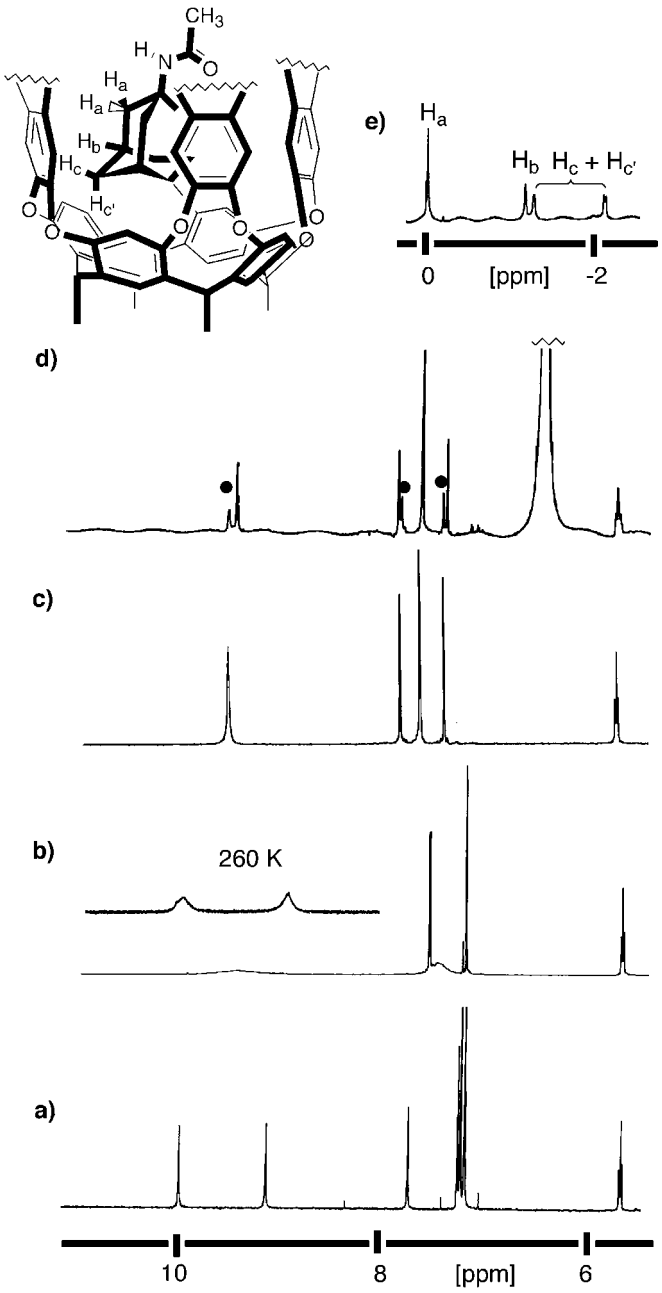


Fig. 5. *Portion of the* ^{1}*H-NMR spectra* (600 MHz) *of:* a) *cavitand* **1a** *in* $CDCl_3$ *at 295 K*; b) **1a** *in* (D_6)*acetone/*$CDCl_3$ *1:2 at 295 K*; c) **1a** *in* (D_6)*acetone at 315 K*; d) *caviplex* **1a**·N-*(1-adamantyl)acetamide in* (D_6)*acetone at 295 K* (residual signals of guest-free **1a** are marked as '·'); e) *upfield window of* d *showing the encapsulated adamantyl fragment*. The signal for the methine CH *triplet* is at 5.5 ppm, characteristic of a vase conformation. The association constants are low ($K_{ass} \leqslant 10\,M^{-1}$), and a large excess ($\geqslant$ 100 equiv.) of the guest is needed to observe the complexes at concentrations convenient for NMR spectroscopy.

significantly broadened (*Fig. 5,b*). Upon lowering the temperature, the broad amide NH signal clearly separates ($T_c \approx 285$ K) into two *singlets*, giving the $\Delta G^{\neq}$ value of 12.5 ± 0.5 kcal $\times$ mol^{-1} ($k \approx 1.1 \times 10^3$ s^{-1}).

The spectrum at 260 K features the C_4-symmetry and is quite similar to that measured in pure $CDCl_3$ at 295 K (*Fig. 5,a*). This is the result of slow interconversion of the cycloenantiomers within the vase-shaped conformation of **1a**. It is unlikely that the two C_{2v}-symmetric kite-like conformations are involved in this process, since the resonance for the methine *triplet* – a telltale sign of vase *vs.* kite conformations [13] – remains at a constant chemical shift.

The considerable decrease of $\Delta G^{\neq}$ in (D_6)acetone compared to (D_8)toluene or 1,4-(D_{10})xylene ($\Delta G^{\neq} \approx 17.5$ kcal $\times$ mol^{-1}, $T_c \approx 360$ K) [2] suggests better solvation of the more polar transition state aided by the H-bond-accepting properties of the acetone. The entire array of H-bonds must be disrupted during the cycloracemization process. Even in a polar medium, the time-averaged cyclic array of H-bonds preserves a vase-shaped conformation of cavitand **1** when a good guest is resident. The exchange rates of guests in (D_6)acetone solution, for example *N*-(1-adamantyl)acetamide, are slow on the NMR timescale (at 295 K; *Fig. 5,d* and *e*). In the absence of a good guest, collapse to the kite and thence to the velcraplex can be expected.

Further details about the cyclic H-bonding arrays were obtained from the NMR analysis of the chiral cavitand **1b** with eight HN–C(O)–C*HMeEt ((+)-(*S*)) groups on its upper rim. In (D_6)acetone, the spectrum showed the spectroscopic earmarks of the C_4-conformation (*Fig. 6,c*); two NH resonances appeared in the downfield part of the spectrum (*Fig. 6,c*). More interestingly, two C_4-symmetrical structures were seen in the spectra of **1b** in the less polar solvents $CDCl_3$ and (D_6)benzene; two sets of signals for all groups of protons were observed in a ratio of *ca.* 3:1 at 295 K.

Accordingly, chiral molecule **1b** exists as two cyclodiastereoisomers in solutions where the interconversion between two cycloenantiomeric seams is slow on the NMR time-scale. The reason for the preference of one diastereoisomer over the other is not obvious but is likely to be a steric effect, since the arrays are quite crowded. This phenomenon has its counterpart in the behavior of calixarene tetraureas bearing asymmetric side chains [14].

2.4. *^{13}C-NMR Spectroscopy.* Analysis of ^{13}C-NMR spectra of self-folding cavitands fully agrees with that detailed above (*Fig. 7*). In short, **1a** possesses a C_{4v} symmetry in (D_6)acetone and a C_4 symmetry in $CDCl_3$. One amide C=O *singlet* is observed at 173 ppm in (D_6)acetone and two amide C=O *singlets* are seen at 174 and 172 ppm in $CDCl_3$. The spectrum of chiral cavitand **1b** in (D_6)acetone is C_4-symmetrical, with the signals of two amide C=O groups at 176 and 177 ppm.

3. Conclusions. – There is an agreement of structures predicted from NMR studies in solution with those observed by X-ray crystallography in the solid state for self-folding cavitands. But what can be said about the breathing motions of the cavitand, the dynamics of guest exchange? These motions include the cycloracemization of the H-bonding seam, and the vase-to-kite interconversion. Numerous intermediates are possible – even likely – but they have yet to be observed. Visualizing how things get in and out of cavities is a process akin to photographing moving targets. Even for the limited motions available to these caviplexes, the sequence of events remains poorly

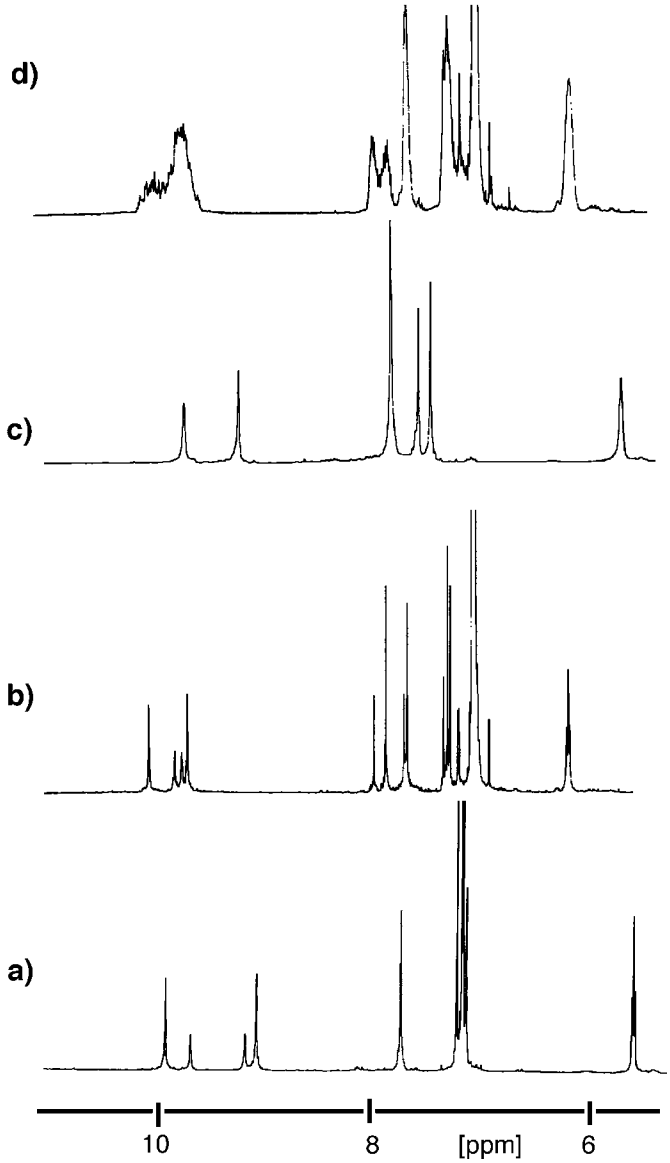


Fig. 6. *Portion of the ^{1}H-NMR spectra* (600 MHz, 295 K) *of* a) *cavitand* **1b** *in $CDCl_3$ at 295 K*; b) **1b** *in (D_6)benzene*; c) **1b** *in (D_6)acetone*; d) **1c** *in (D_6)benzene*

understood. For the present, the sequence of events proposed earlier for guest exchange in apolar aromatic solvents and $CDCl_3$ still holds [2]: the seam of H-bonds is ruptured as the inversion of the nine-membered rings takes place on the way to the kite conformation. This exposes the resident guest to solutes or solvents that can physically displace the guest in a supramolecular version of a substitution reaction.

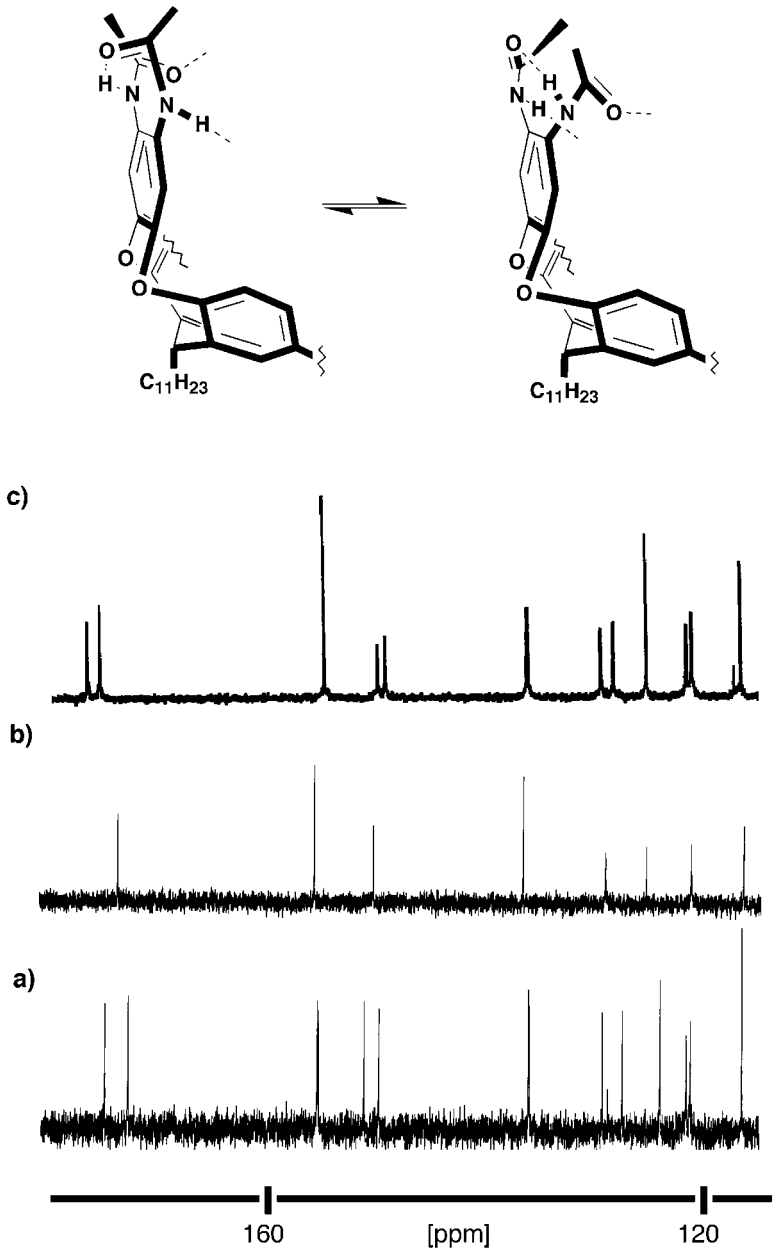


Fig. 7. *Portion of the ^{13}C-NMR spectra* (151 MHz, 295 K) *of* a) *cavitand* **1a** *in* $CDCl_3$; b) **1a** *in* (D_6)*acetone*; c) **1b** *in* (D_6)*acetone*

The rate of guest exchange is slowed by unravelling the array of H-bonds, without which – as in the original *Cram* and *Dalcanale* molecules [15] – guest exchange is very rapid in solution.

4. Outlook. – Chiral cavities provide, of course, the greatest opportunities for enantioselective guest recognition, and we are pursuing that goal. At the same time, these cavitands offer an unusual type of molecular diversity. For example, use of the *racemic* acid chloride Cl–C(O)–CHMeEt in the final step of the synthesis produces a 'library' of 512 (!) diastereoisomeric octaamide cavitands **1c**, all at once: the eight stereocenters give 2^8 compounds, and this number is doubled by the two cyclo-enantiomeric arrangements possible. Not surprisingly, the corresponding ^{1}H-NMR spectra in $CDCl_3$ (*Fig. 6,d*), (D_6)benzene, and even (D_6)acetone look broad, but all the signals are in their right places. The use of eight different acid chlorides gives a library of > 30 million self-folding cavities. Can these be made, and made useful? We will report on this in the sequel.

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Experimental Part

General. All experiments with moisture- or air-sensitive compounds were performed in anh. solvents under a dry N_2 or Ar atmosphere. Silica-gel chromatography: with silica gel *60* (*EM Science or Bodman*, 230–400 mesh). M.p.: *Thomas-Hoover* cap. melting-point apparatus; uncorrected. FT-IR Spectra: *Perkin Elmer Paragon 1000 PC* FT-IR spectrometer. ^{1}H- (600 MHz) and ^{13}C-NMR (151 MHz) spectra: *Bruker DRX-600* spectrometers; the chemical shifts (δ; in ppm) were measured relative to residual non-deuterated solvent resonances. Electrospray-ionization (ESI) MS: in MeOH on a *Perkin Elmer API 100 Sciex* single quadrupole mass spectrometer; matrix-assisted laser-desorption/ionization mass spectrometry (MALDI-MS) experiments were performed on a *IonSpec HiResMALDI* Fourier-transform mass spectrometer (with DHB as a matrix). For compounds **1b** and **1c**, with significantly high molecular weight ($\cdot$ 2000), lower resolution was achieved; for details on high-resolution (HR) mass spectrometry, see [16].

General Procedure for the Preparation of Octaamides **1a**–**1c.** (+)-(*S*)-α-Methylbutyric acid (1.1 ml, 10 mmol) was dissolved in benzene (10 ml) and added to a cooled (0°) soln. of oxalyl chloride (0.82 ml, 10 mmol) in benzene (10 ml). The mixture was stirred overnight at r.t., and the solvent was evaporated under reduced pressure [17]. The resulting acid chloride was directly submitted for the next step without further purification.

A mixture of octanitro compound **2** [2] (390 mg, 0.22 mmol) and cat. amounts of *Raney*-Ni (prewashed with EtOH (2×5 ml) and toluene (2×5 ml)) was dissolved in toluene (60 ml) and EtOH (5 ml), and stirred at 45° under H_2 atmosphere overnight. After cooling, the mixture was filtered through *Celite*, and the solvent was evaporated. The residue was dissolved in a mixture of AcOEt (10 ml) and H_2O (10 ml), and K_2CO_3 (276 mg, 2 mmol) and the corresponding acid chloride were then added. The mixture was vigorously stirred for 2 h. The phases were separated, and the H_2O phase was extracted with AcOEt (3×20 ml). The combined org. phases were dried ($MgSO_4$) and evaporated. Pure octaamides **1a**–**1c** were obtained as pale-yellow solids by CC (hexane/AcOEt, 5:1).

*2,3,9,10,16,17,23,24-Octakis(octanoylamido)-29,31,33,35-tetraundecyl-27,37:28,36-dimetheno-29*H,*31*H,*33*H,*35*H-*dibenzo[*b,b′*]bis[1,7]benzodioxonino[3,2-*j*:*3′,2′*-j′]benzo[1,2-*e*:*5,4-*e′]-bis[1,3]-benzodioxonin* (**1a**) [2]. ^{1}H-NMR ((D_6)acetone): 9.48 (*s*, 8 NH); 7.84 (*s*, 4 arom. H); 7.69 (*s*, 8 arom. H); 7.44 (*s*, 4 arom. H), 5.86 (*t*, $J = 8.2$, 4 CH); 2.6–2.4, 2.0–1.8, 1.6–1.4 (6*m*, 176 H, CH_2), 1.00 (*t*, $J = 7.2$, 4 Me), 0.95 (*t*, $J = 7.2$, 8 Me). ^{13}C-NMR (315 K, (D_6)acetone): 172.9 (C=O); 155.2; 149.9; 136.4; 129.0; 125.3; 121.2; 116.5 (arom. C); 37.8; 33.9; 32.4; 32.1; 32.0; 30–28 (multiple signals); 26.4; 22.8; 22.75; 13.77; 13.75 (alkyl C). ^{13}C-NMR ($CDCl_3$): 174.3; 172.2 (C=O); 155.0; 154.9; 150.8; 149.5; 135.94; 135.88; 129.2; 127.4; 124.0; 121.6; 121.2; 116.6 (arom. C); 39.6; 36.7; 33.7; 32.8; 32.4; 32.2; 32.1; 31–29 (multiple signals); 29.6; 29.5; 28.5; 27.3; 26.2; 23.1; 23.0; 14.5; 14.4 (alkyl C).

*2,3,9,10,16,17,23,24-Octakis[(+)-(S-)-2-methylbutanamido]-29,31,33,35-tetraundecyl-27,37:28,36-dimetheno-29*H,*31*H,*33*H,*35*H-*dibenzo[*b,b′*]bis[1,7]benzodioxonino[3,2-*j*:*3′,2′*-j′]benzo[1,2-*e*:*5,4-*e′]bis[1,3]benzodioxonin* (**1b**). Yield 26%. Pale-yellow solid. M.p. 173–176°. IR (KBr): 3142, 2920, 2672, 2248, 2062, 1815, 1788, 1643, 1467, 1375, 1115, 1093, 970, 970, 899, 723, 644. ^{1}H-NMR ((D_6)acetone): 9.74 (*s*, 4 NH); 9.25 (*s*, 4 NH); 7.89, 7.88 (2*s*, 8 arom. H); 7.66 (*s*, 4 arom. H); 7.55 (*s*, 4 arom. H); 5.83 (br. *t*, $J = 7.0$, 4 CH(methine)); 2.6 (*m*, 4 CHCO);

2.5–2.4 (2*m*, 4 CHCO, 4 CH_2); 1.8–1.7, 1.6–1.4, 1.4–1.1 (6*m*, 98 H, CH_2, 8 MeCH_2CH, 4 *Me*CH); 1.20 (*d*, *J* = 6.8, 4 *Me*CH); 1.02 (*t*, *J* = 7.3, 4 *Me*CH_2CH); 0.88 (2*t*, *J* = 7.3, 7.2, 8 Me). ^{13}C-NMR ((D$_6$)acetone): 177.1; 175.9 (C=O); 155.1; 150.2; 149.5; 136.4; 136.2; 129.5; 128.3; 125.3; 121.6; 121.1; 116.5 (arom. C); 45–11 (*m*, alkyl C). ESI-MS: 2192.5 ($[M-H]^-$), 2214 ($[M+Na]^+$). HR-MALDI-FT-MS can not be obtained due to the significantly high molecular weight (· 2000); for details, see [16].

*2,3,9,10,16,17,23,24-Octakis(2-methylbutanamido)-29,31,33,35-tetraundecyl-27,37:28,36-dimetheno-29*H,*31*H,-*33*H,*35*H-*dibenzo[*b,b′*]bis[1,7]benzodioxonino[3,2-*j*:*3′,2′-*j′*]benzo[1,2-*e*:*5,4-e′*]bis[1,3]benzodioxonin* (racemate, **1c**). Yellow solid. M.p. 165–170°. IR (KBr): 3148, 2919, 2249, 1818, 1790, 1642, 1465, 1379, 1092, 964, 906, 729, 658. ^{1}H-NMR ((D$_6$)acetone): 9.64 (*m*, 8 NH); 7.90 (*m*, 8 arom. H); 7.75 (*m*, 4 arom. H); 7.54 (*m*, 4 arom. H); 5.83 (*m*, 4 CH(methine)); 1.7–0.8 (*m*, CHCO, 164 H, CH_2, MeCH_2CH, *Me*CH, *Me*CH_2CH, Me, 164 H). ESI-MS: 2192 ($[M-H]^-$), 2228 ($[M+Cl]^-$), 2194 ($[M+H]^+$), 2216 ($[M+Na]^+$). HR-MALDI-FT-MS can not be obtained due to the significantly high molecular weight (· 2000); for details, see [16].

X-Ray Crystallography. Crystallographic data measurements at 170 K by a *Kappa CCD*, MoK_α radiation (graphite monochromator, $\lambda = 0.7107$ Å). The data was processed with *Denzo-SMN v0.93.0* [18]. Structures were solved by direct methods [19] and refined with full-matrix *vs.* F^2 (block refinement for **1a**·acetone) analysis [20]. **1a**·*acetone:* $C_{163}H_{246}O_{17}N_8$ (M_r 2589.7), crystal size $0.5 \times 0.3 \times 0.2$ mm^3, monoclinic, *P*21/*c*, a = 23.1013(4) Å, b = 16.0947(4) Å, c = 42.0376(9) Å, β = 101.789(4)°, Z = 4, V = 15300.2(6) Å^3, ρ_{calc} = 1.252 g/cm^3, $2\Theta_{max}$ = 50.06°, μ = 0.08 mm^{-1}, 1848 parameters, R = 0.0991 (for 15062 refl. $I > 2\sigma(I)$), $wR(F^2)$ = 0.2476 for all 25732 unique reflections (R_{int} = 0.055), S = 1.043, $\Delta\rho$ (min, max) = −0.35, −0.56 e/Å^3. The H-atoms were calculated to their idealized positions with isotropic temp. factors and refined as riding atoms. No H-atoms were located at C-atoms of strongly disordered parts of the aliphatic chains. Compound **3** (recrystallized from AcOEt/MeCN): $C_{10}H_{10}O_2N_2$ (M_r 192.2), crystal size $0.8 \times 0.5 \times 0.3$ mm^3, monoclinic, *C*2/*c*, a = 14.490(1) Å, b = 9.246(1) Å, c = 15.928(1) Å, β = 113.051(1)°, Z = 8, V = 1963.57(9) Å^3, ρ_{calc} = 1.30 g/cm^3, $2\Theta_{max}$ = 60.98°, μ = 0.092 mm^{-1}, 153 parameters, R = 0.062 (for 2109 refl. $I > 2\sigma(I)$), $wR(F^2)$ = 0.143 for all 2902 unique reflections, S = 1.055, $\Delta\rho$ (min, max) = −0.37, −0.28 e/Å^3.

The H-atoms of the aromatic ring and NH groups were located from the electron-density map. The H-atoms of the Me groups were calculated to their idealized positions with isotropic temp. factors and refined as riding atoms.

Crystallographic data of structures described in this publication (excluding structure factors) have been deposited with the *Cambridge Crystallographic Data Centre* as supplementary publication No. CCDC 138600 and CCDC 138601. Copies of the data can be obtained free of charge on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK (fax: (+44) 1223-336-033; e-mail: deposit@ccdc.cam.ac.uk).

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