PAPER

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Diaminotriazine substituted 1,3-alternate calix[4]arenes

Olaf G. Barton, Marc Schmidtmann, Achim Müller and Jochen Mattay*

Department of Chemistry, University of Bielefeld, Universitätsstr. 25, 33615 Bielefeld, Germany. E-mail: mattay@uni-bielefeld.de; Fax: +49 521 106 6417; Tel: +49 521 106 2072

Received (in Durham, UK) 7th June 2004, Accepted 17th September 2004
First published as an Advance Article on the web 18th October 2004

The synthesis and crystal structures of two calix[4]arenes adopting the 1,3-alternate conformation substituted at the *wide rim* with diaminotriazine moieties are described. The crystal structure of the disubstituted calixarene **8** is governed by the diaminotriazine moieties which form infinite bands through hydrogen bonding. Around the diaminotriazine bands the calix[4]arene backbones are placed. In contrast hydrogen bonding between the diaminotriazine moieties of the tetrasubstituted calixarene **9** favour face to face complexes resulting in infinite strands. Hydrogen bonds in both compounds **8** and **9** are broken by polar solvents as the ^{1}H NMR spectra in DMSO-d_6 indicates.

Introduction

An effective strategy in crystal engineering make use of a concept called molecular tectonics.[1] In this concept the word tecton from the Greek word for builder is given to the associating molecules which dominate the building of the crystal. A tecton can be considered to consist of multiple peripheral sticky sites that direct molecular association linked to a core that holds the sticky sites in a suitable orientation. Recently the diaminotriazine group was extensively used as the sticky sites for a number of tectons to construct porous hydrogen-bonded networks.[2] Furthermore it was used to build up a two-dimensional (2D) crystal lattice of oligo-(*p*-phenylenevinylines) on a graphite surface.[3] We describe two new tectons also exploiting the directional effect of diaminotriazine groups as sticky sites. They are grafted to the wide rim of a calix[4]arene in the 1,3-alternate conformation which serves as the core of the tectons. Calix[4]arenes in the cone conformation with diaminotriazine groups are already known.[4] They show intramolecular hydrogen bonding as well as formation of gels by addition of suitable complex partners. However, no crystals could be obtained. Remarkably, by replacing the diaminotriazine group for the similar melamine molecular synthon in combination with complex partners crystal structures of discrete hydrogen-bonded assemblies (Reinhoudt's rosettes) were possible.[5]

Synthesis

The synthesis of tectons **8** and **9** are presented in Scheme 1. In the case of the tetra substituted calix[4]arene **9** the 1,3-alternate conformation was fixed first. According to a literature procedure alkylation at the phenolic groups of the parent calix[4]arene **1** lead to compound **2**.[6] In the next step the functionality at the wide rim was introduced. Iodination with AgTFA/I$_2$ following a procedure[7] used with calix[4]arenes in the cone conformation gave the new compound **4** in a yield of 89%. An X-ray structure corroborates its 1,3-alternate conformation (Table 1). A common method to prepare diametrical disubstituted calix[4]arenes was applied to construct tecton **8**. After selective 1,3-alkylation of the narrow rim[8] the dialkoxy derivative was selectively brominated on the free two phenols to yield compound **3**.[9] The remaining phenolic groups of **3** were then also alkylated and simultaneously the conformation fixed in the 1,3-alternate state to give compound **5**.[9] The halogenated calix[4]arenes **4** and **5** were then converted to the new di- and tetra cyano calix[4]arenes **6** and **7** under Rosenmund–von Braun conditions in yields of 35% and 83%, respectively. In both cases the successful substitution is supported by crystal structure determination (Table 1†). Finally a base-catalysed condensation with cyanoguanidine gave the diaminotriazine substituted calix[4]arenes **8** and **9** in a yield of 20% and 66% after crystallization, respectively.

Discussion

Both tectons **8** and **9** show good solubility in DMSO, pyridine or THF–water mixtures. However, in pure ethanol they are insoluble which suggests that the solvent should be polar as well as a good hydrogen bond acceptor. Tecton **9** is insoluble in apolar solvents whereas the solubility of tecton **8** is low. Therefore it was possible to get a ^{1}H NMR spectrum of **8** in CDCl$_3$. Only broad signals were observed at room temperature indicating the formation of complexes with dynamic properties. Temperature dependent ^{1}H NMR spectra were recorded in nonpolar 1,1,2,2-tetrachlorethane-d_4 (Fig. 1). The spectrum at room temperature is very similar to that in CDCl$_3$. Even at a high temperature of 80 °C the ^{1}H NMR spectrum showed broadened signals which became sharpened at 120 °C. This behaviour of **8** in nonpolar solvents resembles supramolecular polymers and can be explained by hydrogen bonding between the diaminotriazine moieties. In polar competitive solvents it is expected that aggregation by hydrogen bonding is prevented. Indeed the ^{1}H NMR spectra of **8** and **9** recorded in DMSO-d_6 show signals for monomeric species with significant sharp signals for the amino protons (Fig. 2).

Crystals of tecton **8** suitable for X-ray structure determination were obtained by crystallization from a chloroform–methanol mixture (Table 1). No solvent molecules are included and the asymmetric unit contains only one molecule (Fig. 3). The alignment of the tectons is determined by the diaminotriazine moieties forming infinite bands (Fig. 4). Every second diaminotriazine moiety uses both of its amino groups for hydrogen bonding each with one neighbouring unit. For the other half of diaminotriazine moieties only one amino group is involved binding two neighbours each with one hydrogen

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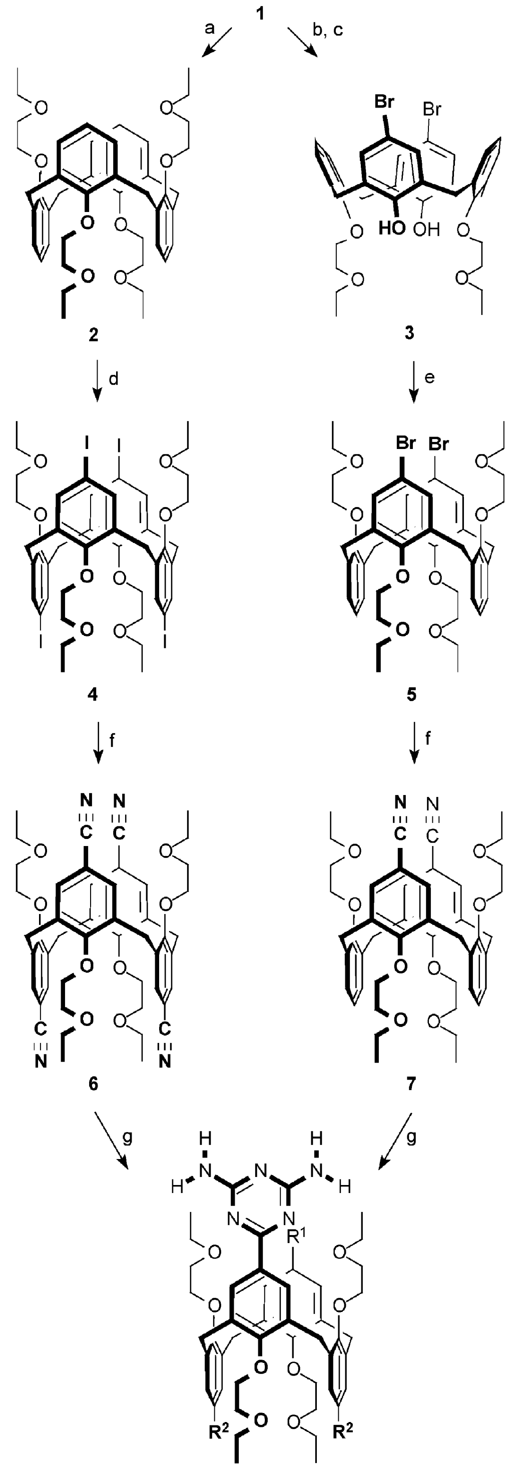
† CCDC reference numbers 246171–246175. See http://www.rsc.org/suppdata/nj/b4/b408592b/ for crystallographic data in .cif or other electronic format.

DOI: 10.1039/b408592b



8 R^1 = diaminotriazine, R^2 = H
9 $R^1 = R^2$ = diaminotriazine

Scheme 1 Synthesis of tectons **8 and 9**. Reagents and conditions: (a) 2-ethoxyethyltosylate, K_2CO_3, MeCN, reflux, 36%, (b) 2-ethoxyethylbromide, BaO, $Ba(OH)_2$, DMF, rt, 36%, (c) Br_2, $CHCl_3$, 87%, (d) AgTFA, I_2, $CHCl_3$, 89%, (e) 2-ethoxyethylbromide, Cs_2CO_3, acetone, 84%, (f) CuCN, NMP, reflux, 35% for **6**, 83% for **7**, (g) cyanguanidine, KOH, 1-pentanol, reflux, 23% for **8**, 66% for **9**.

atom. In summary, every diaminotriazine moiety is linked to two others by two hydrogen bonds. The calixarene backbones are placed around the bands (Fig. 5). Every tecton is associated with four other thereby forming a three-dimensional (3D) network.

Crystals of tecton **9** suitable for X-ray structure determination were obtained by crystallization from a 1,4-dioxane–ethanol mixture (Table 1). The asymmetric unit contains one molecule **9** as well as three 1,4-dioxane and two ethanol molecules. One region of electron density in the dimension of a solvent molecule could not be solved and diminished the quality of the structure determination slightly. The tectons are connected to each other in a face to face manner (Fig. 6). The two sides of each tecton differ to a small extent in conformation, *e.g.* the distance between the *para* nitrogen atoms of the triazine ring is 7.7 Å on side A and 8.6 Å on side B. Sides with the same conformation face each other (A to A and B to B). The connection is made up of two hydrogen bonds between opposing diaminotriazine moieties. The distances for nitrogen atoms of the H-donor and acceptor groups are 2.92 Å, 2.98 Å, 3.04 Å and 3.08 Å. These values are smaller than twice the nitrogen van der Waals radii of 3.10 Å and therefore clearly indicate H-bonding.[10] Overall every tecton is linked to each of its two neighbours by a total of four hydrogen bonds. This results in infinite strands with solvent molecules around.

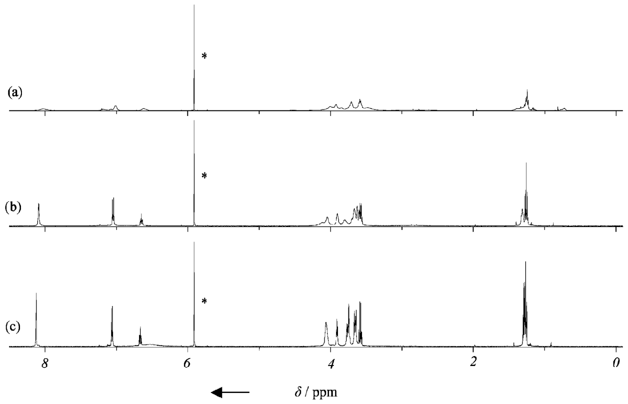


Fig. 1 Temperature dependent ^1H NMR spectra of **8** in 1,1,2,2-tetrachlorethane-d_4 at (a) 20 °C, (b) 80 °C, (c) 120 °C; residual solvent signals are marked with an asterisk.

Experimental

Melting points are uncorrected. Elemental analyses were performed with a Perkin Elmer 240. ^1H NMR and ^{13}C NMR spectra were recorded on a Bruker DRX 500 spectrometer using residual solvent protons as internal standard at room temperature. MALDI-TOF mass spectra were obtained with a PerSeptive Biosystems Voyager-DE spectrometer using 2,5-dihydroxybenzoic acid as matrix, a Bruker Esquire 3000 was used to record ESI mass spectra and the exact mass was measured on a Bruker APEX III (FT-ICR). Compounds **1–3** and **5** were prepared according to literature methods.[6,8,9,11] All other materials and substrates were commercially available and used without further purification.

5,11,17,23-Tetraiodo-25,26,27,28-tetra(ethoxyethoxy)-calix[4]arene (4)

A suspension of silver trifluoroacetate (3.00 g, 13.6 mmol) and **2** (1.94 g, 2.72 mmol) $CHCl_3$ (100 ml) was refluxed for 15 min. After cooling to room temperature iodine (3.45 g, 13.6 mmol) was added in portions until the deep purple colour was permanent. During the addition, AgI precipitated from the solution as a yellow powder. The reaction mixture was refluxed another 15 min, cooled to room temperature and filtered over celite. The filtrate was washed with 10% sodium sulfite (20 ml), water (3 times 20 ml), brine (20 ml) and dried over $MgSO_4$. Recrystallisation from $CHCl_3$–MeOH gave a colourless solid (2.93 g, 2.41 mmol, 89%), mp 237 °C (Found: C, 43.23; H, 4.08. $C_{44}H_{52}I_4O_8$ requires C, 43.44; H, 4.31%); δ_H(500 MHz, $CDCl_3$) 7.49 (8 H, s), 3.85–3.84 (8 H, m), 3.78–3.77 (8 H, m), 3.77 (8 H, q, J 7.0), 3.41 (8 H, s), 1.37 (12 H, t, J 7.0); δ_C(125

Table 1 Crystal data and collection parameters for **4** and **6–9**

	4	**6**	**7**	**8**	**9**
Empirical formula	$C_{44}H_{52}I_4O_8$	$C_{48}H_{52}N_4O_8$	$C_{46}H_{54}N_2O_8$	$C_{50}H_{62}N_{10}O_8$	$C_{72}H_{104}N_{20}O_{16}$
Formula weight/g mol^{-1}	1216.46	812.94	762.91	931.10	1505.75
T/K	183(2)	183(2)	183(2)	183(2)	183(2)
Crystal system	Monoclinic	Monoclinic	Monoclinic	Orthorombic	Triclinic
Space group	$P2(1)/c$	$P2(1)/c$	$P2(1)/c$	$P2(1)2(1)2(1)$	$P\bar{1}$
a/Å	19.7097(7)	18.0389(9)	24.3057(9)	14.3264(6)	14.2874(6)
b/Å	20.1100(7)	13.1731(6)	17.3007(6)	16.9472(7)	14.6477(6)
c/Å	25.8943(9)	19.2678(9)	22.9460(9)	20.0115(9)	20.2360(8)
α/°	90	90	90	90	84.7460(10)
β/°	111.2190(10)	100.5250(10)	115.7390(10)	90	81.8940(10)
γ/°	90	90	90	90	72.1310(10)
U/Å^3	9567.7(6)	4501.5(4)	8691.6(6)	4858.6(4)	3985.1(3)
Z	8	4	8	4	2
ρ/g cm^{-1}	1.689	1.200	1.166	1.273	1.255
$\mu(\mathrm{Mo}_{K\alpha})$/mm^{-1}	2.652	0.082	0.079	0.088	0.091
Meas. reflect.	54904	25700	43673	28484	40431
Indep. reflect.	20579	9693	15298	10482	16975
R_{int}	0.0201	0.0167	0.0270	0.0244	0.0244
R_1 $[I > 2\sigma(I)]$	0.0223	0.0491	0.0460	0.0409	0.0681
wR_2 $[I > 2\sigma(I)]$	0.0529	0.1298	0.1069	0.1030	0.1774

MHz, $CDCl_3$) 155.46, 139.14, 134.99, 85.97, 72.15, 69.84, 66.88, 33.55, 15.42. m/z (ESI, $CHCl_3$–MeOH–$NaBF_4$) 1234.1 (M + NH_4^+), 1239.1 (M + Na^+).

5,11,17,23-Tetracyano-25,26,27,28-tetra(ethoxyethoxy)-calix[4]arene (6)

A mixture of **4** (3.23 g, 2.66 mmol) and CuCN (1.66 g, 18.6 mmol) in *N*-methyl-2-pyrrolidinone (100 ml) was refluxed 4 h. The temperature was adjusted to 100 °C and a solution of $FeCl_3$ trihydrate (6.46 g, 23.9 mmol) in 2 N HCl (200 ml) was added. After stirring for 1 h the mixture was filtrated over celite. The filtrate was extracted with dichloromethane (300 ml) and the organic layer was washed with 5% sodium sulfite (200 ml), water (2 times 200 ml), brine (200 ml) and dried over $MgSO_4$. The product was crystallized from ethyl acetate–*n*-hexane to give a colourless solid (0.75 g, 0.92 mmol, 35%), mp 246–247 °C (Found: C, 70.92; H, 6.25; N, 6.87. $C_{48}H_{52}N_4O_8$ requires C, 70.92; H, 6.45; N, 6.89%); δ_H(500 MHz, $CDCl_3$) 7.49 (8 H, s), 3.94–3.93 (8 H, m), 3.81–3.79 (8 H, m), 3.75 (8 H, q, *J* 7.0), 3.56 (8 H, s), 1.36 (12 H, t, *J* 7.0); δ_C(125 MHz, $CDCl_3$) 158.89, 134.38, 133.90, 118.46, 106.08, 73.16, 69.30, 67.01, 33.08, 15.18. m/z (MALDI-TOF) 813 (M + H^+).

5,17-Dicyano-25,26,27,28-tetra(ethoxyethoxy)-calix[4]arene (7)

A mixture of **5** (1.73 g, 2.38 mmol) and CuCN (853 mg, 9.52 mmol) in *N*-methyl-2-pyrrolidinone (50 ml) was refluxed 4 h. The temperature was adjusted to 100 °C and a solution of $FeCl_3$ trihydrate (2.53 g, 9.52 mmol) in 2 N HCl (100 ml) was added. After stirring for 1 h the mixture was filtrated over celite. The filtrate was extracted with dichloromethane (200 ml) and the organic layer was washed with 5% sodium sulfite (200 ml), water (2 times 200 ml), brine (100 ml) and dried over $MgSO_4$. The product was crystallized from ethyl acetate–*n*-hexane to give a colourless solid (1.51 g, 1.98 mmol, 83%), mp 116 °C (Found: C, 72.37; H, 7.06; N, 3.65. $C_{46}H_{54}N_2O_8$ requires C, 72.42; H, 7.13; N, 3.67%); δ_H(500 MHz, $CDCl_3$) 7.52 (4 H, s), 7.06 (4 H, d, *J* 7.6), 6.62 (2 H, t, *J* 7.6), 3.93–3.91 (4 H, m), 3.89–3.87 (4 H, m), 3.79–3.77 (4 H, m), 3.76 (4 H, q, *J* 6.9), 3.73–3.72 (4 H, m), 3.62 (4 H, q, *J* 7.0), 3.60 (4 H, s), 1.38 (6 H, t, *J* 7.0), 1.29 (6 H, t, *J* 7.0); δ_C(125 MHz, $CDCl_3$) 159.25, 155.12, 134.51, 133.95, 132.27, 130.21, 121.92, 118.95, 105.04, 72.39, 72.28, 69.63, 69.43, 66.81, 66.44, 33.61, 15.12, 15.06. m/z (MALDI-TOF) 763 (M + H^+), 785 (M + Na^+), 801 (M + K^+).

5,17-Bis(2,6-diamino-1,3,5-triazine-4-yl)-25,26,27,28-tetra(ethoxyethoxy)-calix[4]arene (8)

A mixture of **7** (1.21 g, 1.59 mmol), cyanoguanidine (2.67 g, 31.8 mmol) and KOH (446 mg, 7.95 mmol) in 1-pentanol (40 ml) was refluxed for 1 d. After cooling to room temperature the precipitate was filtered off and rinsed with water. The residue was stirred in water (200 ml) at 100 °C for 3 h, whereupon the suspension was filtered while still hot. The residue was rinsed

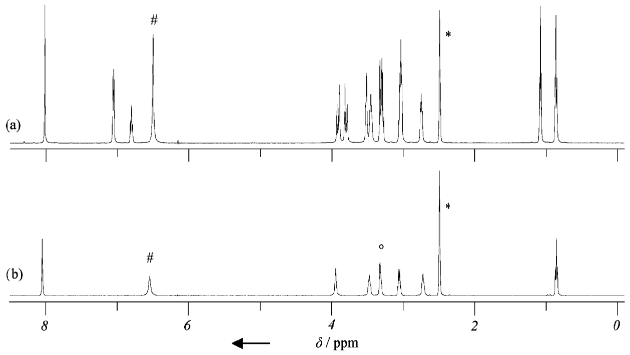


Fig. 2 ^1H NMR spectra in DMSO-d_6 of (a) **8** and (b) **9** at 20 °C, # indicates the amine protons, residual solvent signals are marked with an asterisk and residual water signal with a circle.

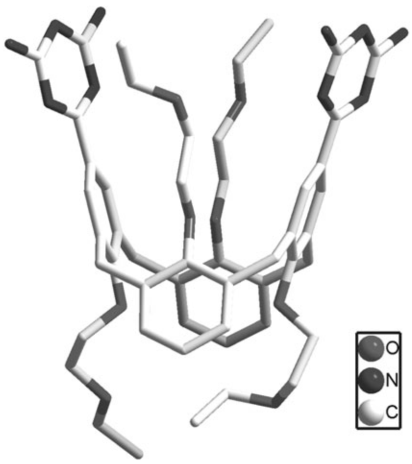


Fig. 3 Crystal structure of **8**, hydrogen atoms are omitted for clarity.

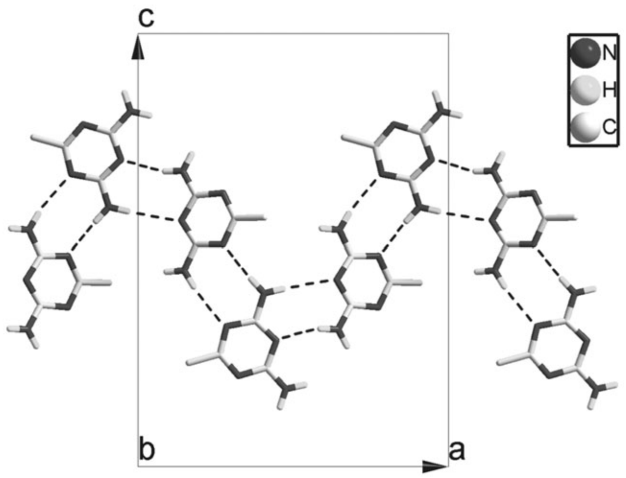


Fig. 4 Part of the crystal structure of **8** showing a band of diaminotriazine moieties, view along the *b* axis.

thoroughly with hot water, dried over P_2O_5 (Sicapent) and crystallized from $CHCl_3$–MeOH to give a colourless solid (300 mg, 0.322 mmol, 20%), mp 298–299 °C (Found: C, 64.22; H, 6.70; N, 14.86. $C_{50}H_{62}N_{10}O_8$ requires C, 64.50; H, 6.71; N, 15.04%); δ_H(500 MHz, DMSO-d_6) 8.01 (4 H, s), 7.06 (4 H, d, *J* 7.5), 6.80 (2 H, t, *J* 7.5), 3.91 (4 H, d, *J* 16.0), 3.80 (4 H, d, *J* 16.0), 3.51 (4 H, t, *J* 5.5), 3.45 (4 H, t, *J* 7.0), 3.29 (4 H, q, *J* 6.9), 3.06–3.02 (8 H, m), 2.74 (4 H, t, *J* 7.2), 1.08 (6 H, t, *J* 6.9), 0.86 (6 H, t, *J* 6.9). *m*/*z* (ESI, $CHCl_3$–MeOH) 931.8 (M + H^+), 953.7 (M + Na^+), 969.6 (M + K^+).

5,11,17,23-Tetrakis(2,6-diamino-1,3,5-triazine-4-yl)-25,26,27,28-tetra(ethoxyethoxy)-calix[4]arene (9)

A mixture of **6** (750 mg, 0.922 mmol), cyanoguanidine (3.10 g, 36.9 mmol) and KOH (425 mg, 9.22 mmol) in 1-pentanol (40 ml) was refluxed for 2 d. After cooling to room temperature the precipitate was filtered off and rinsed with water. The residue was stirred in water (200 ml) at 100 °C for 3 h, whereupon the suspension was filtered while still hot. The residue was rinsed thoroughly with hot water, dried over P_2O_5 (Sicapent) and recrystallized from 1,4-dioxane–EtOH to give a colourless solid (700 mg, 0.609 mmol, 66%), decomposition >375 °C. δ_H(500 MHz, DMSO-d_6) 8.04 (8 H, s), 6.54 (16 H, s), 3.95 (8 H, s), 3.47 (8 H, t, *J* 6.6), 3.05 (8 H, q, *J* 6.9), 2.72 (8 H, t, *J* 6.8), 0.85 (12 H, t, *J* 6.9); δ_C(125 MHz, DMSO-d_6) 169.86, 167.18, 158.65, 133.05, 130.86, 128.69, 67.57, 67.32, 65.47, 37.65, 14.81. *m*/*z* (ESI exact mass, MeOH–H_2O–2% formic acid) 575.28375 (M + 2 H^+), 383.85875 (M + 3 H^+).

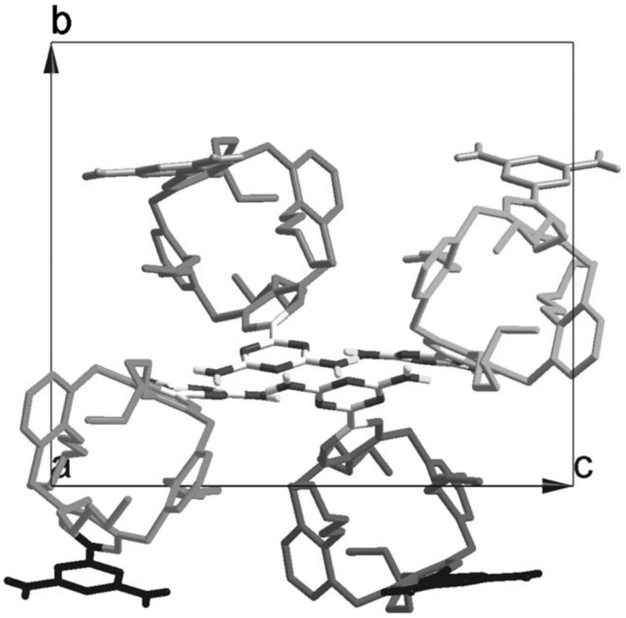


Fig. 5 Crystal structure of **8** displaying the arrangement of calixarene backbones around a diaminotriazine band, view along the *a* axis.

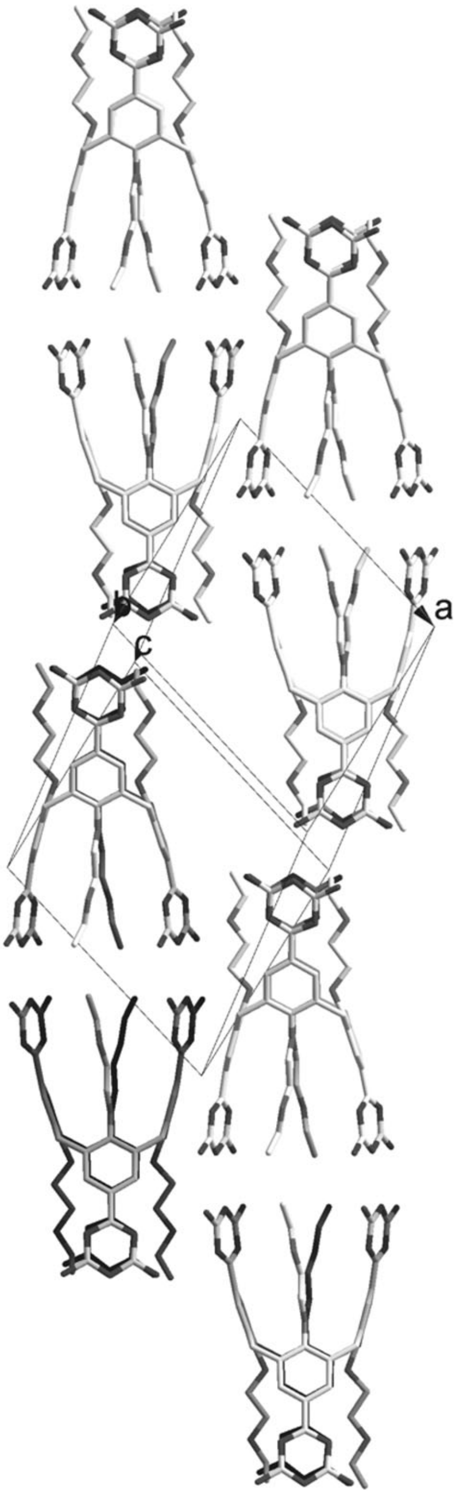


Fig. 6 Crystal structure of **9**, hydrogen atoms and solvent molecules are omitted for clarity, the elemental cell is indicated.

Acknowledgements

Financial support by the Deutsche Forschungsgemeinschaft and the University of Bielefeld is gratefully acknowledged.

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