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Preferred dimerization of tetra-tolyl- and tetra-tosylurea derivatives of flexible and rigidified calix[4]arenes†

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The dimerization of tetratolyl- and tetratosyl-urea derivatives **1** and **2**, derived from a tetrapentoxy calix[4]arene in the *cone* conformation and of the corresponding tetra-urea derivatives **3** and **4**, in which the *cone* conformation is rigidified by the two crown-3 tethers, have been studied. All six possible equimolar mixtures were examined by ^{1}H NMR using $CDCl_3$ and CD_2Cl_2 as solvents. While no heterodimers are found for the combinations **1/3** and **2/4** in either solvent, all remaining combinations lead to the (exclusive) formation of heterodimers in CD_2Cl_2. In $CDCl_3$ heterodimers are only observed for the combinations of **3** with **2** or **4**. These results are discussed in terms of entropic and enthalpic contributions and compared with MD-simulations in a box of chloroform solvent molecules.

Introduction

It is now well established that tetraurea derivatives of calix[4]arenes form dimeric capsules in apolar, aprotic solvents. In chloroform or benzene these are held together by a seam of hydrogen bonds between the urea functions attached to the wider rim.[1] The inclusion of a suitable guest, often the solvent, is a necessary condition for this dimerization. The dimeric structure, initially proposed on the basis of ^{1}H NMR spectra,[2] has been confirmed subsequently by several X-ray structures,[3] and for cationic guests by mass spectroscopy.[4]

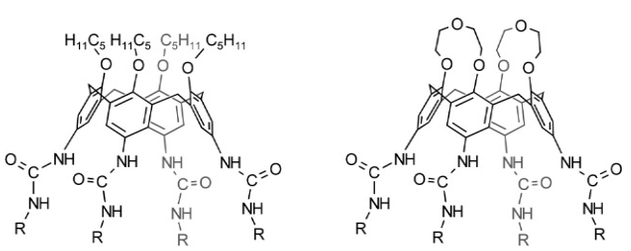

Chart 1 Tetraurea derivatives of calix[4]arene.

If two tetraurea derivatives of type **1** (Chart 1), where R may be alkyl or aryl are mixed in a suitable solvent the two possible homodimers and the heterodimer are usually formed in a (more or less) statistical ratio of 1 : 2 : 1. This formation of heterodimers could be considered as a strong and unambiguous proof of the dimerization.[5] Unexpected, and still not understood in detail, was the observation, that a mixture of the tolyl urea **1** with the tetra tosyl urea **2** contained only the heterodimer **1**·G·**2**, if **1** and **2** are present in stoichiometric amounts, accompanied inevitably by the respective homodimer, if one of the tetraureas is present in excess.[6] This exclusive formation of heterodimers was successfully used to control the structure of larger assemblies.[7]

We recently showed that the rigidification of the calix[4]arene skeleton by two short crown ether bridges in tetraureas of type **3** led to remarkable changes of their properties. There is, for instance, a strong increase of the thermodynamic stability of dimers **3**·**3** which tolerate larger amounts of DMSO than the analogous dimers **1**·**1**.[8] The kinetic stability expressed by the rate of guest exchange[9] is higher as well. Rather unexpected was the observation that **1** and **3** obviously do not form heterodimers. A mixture of both tetraureas in $CDCl_3$ contains only the two homo-dimers **1**·**1** and **3**·**3**.

To get a better understanding of the factors which control the homo- or hetero-dimerization of such tetraurea calix[4]arenes we studied the dimers formed in binary mixtures of tetraureas **1**–**3** including the hitherto unknown rigid tetra-tosylurea **4**.

Results and discussion

The NMR spectra shown in Fig. 1 clearly show that the two homodimers are present in the mixture of **1** with the corresponding tetra tolyl urea **3**, derived from the rigidified calix[4]arene. This result can be tentatively explained on an entropic basis, since the internal mobility of a dimer/capsule formed with **3**

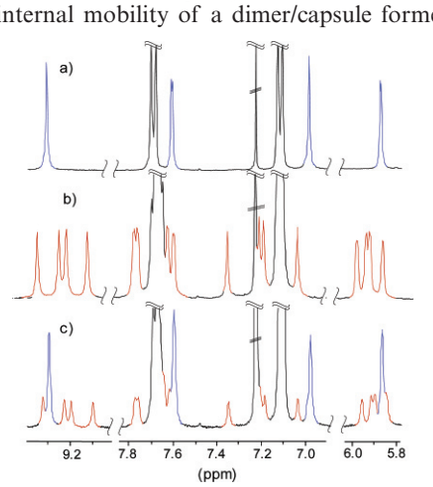

Fig. 1 Sections of the ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C) spectra of: a) homodimer **1**·**1**; b) homodimer **3**·**3**; c) mixture of **1** and **3** resulting in two homodimers.

† Electronic supplementary information (ESI) available: Molecular dynamics simulations and free energy analyses. See http://www.rsc.org/suppdata/ob/b4/b410462e/

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Table 1 Dimerization experiments between tetraurea calix[4]arenes **1**–**4**

		$CDCl_3$		CD_2Cl_2	
Entry	Mixture	Equilibrium state picture	Determining factor	Equilibrium state picture	Determining factor
I	**1** (Tol, F) + **3** (Tol, R)	**−**	*S*	**(−)**	*S*
II	**2** (Tos, F) + **4** (Tos, R)	**−**	*S*	**−**	*S*
III	**1** (Tol, F) + **2** (Tos, F)	**+**	*H*	**+**	*H*
IV	**3** (Tol, R) + **4** (Tos, R)	**−**	*H*	**+**	*H*
V	**1** (Tol, F) + **4** (Tos, R)	**+**	$H > S$	**+**	$H > S$
VI	**3** (Tol, R) + **2** (Tos, F)	**−**	$H < S$	**+**	$H > S$

+ indicates the exclusive formation of the heterodimer; **−** means that only the two homodimers are present; **(−)** stands for an irregular assembly; the factor which disfavors the formation of heterodimers is designated by *S* (entropic factor); the factor which favors the formation of heterodimers is designated by *H* (enthalpic factor).

(homo- or heterodimer) is much more restricted than that of a homodimer of **1**. Thus, the formation of heterodimers **1**·G·**3** would be entropically less advantageous than the exclusive formation of homodimers **1**·G·**1** and **3**·G·**3**.

This observation raises the question, which of the two tendencies would be more pronounced, the formation of heterodimers between tolyl and tosyl ureas, or the absence of heterodimers in a mixture of a flexible and rigid tetra urea? In other words, with the compounds discussed so far, are heterodimers formed exclusively in a mixture of **2** and **3** or not? To obtain a complete answer on this question, which might be important for the selective construction of supramolecular assemblies *via* reversible bonds, we included also the tetra-tosyl urea **4**, derived from the rigidified calix[4]arene.

As expected, all four tetraureas form homodimers in $CDCl_3$ solutions containing only a single calixarene as evidenced by clear ^{1}H NMR spectra with sharp signals. Surprisingly however, both tetratosyl ureas **2** and **4** form homodimers also in CD_2Cl_2, where the spectrum of **1** shows only broad and uninterpretable bands. Broadening of signals is also observed for **3** in CD_2Cl_2 but the chemical shifts are in accordance with those of the homodimer **3**·**3** in $CDCl_3$ (Fig. 2).

To study the formation of heterodimers the single calixarenes were dissolved either in $CDCl_3$ or in CD_2Cl_2 (at c = 3.08 mM), equimolar amounts of the two solutions (containing the respective homodimers) were mixed, and spectra were recorded immediately, after 3 h, 20 h‡ and one week. In those cases, where heterodimers with the rigid calixarenes **3** and **4** were formed, this formation was slow. After 3 h usually about 50% conversion was observed. The reaction was complete in all cases after 20 h (see Fig. 3), and no further changes were noticed in the spectra after one week.

Table 1 summarizes the results obtained for all combinations of **1** to **4** and both solvents after equilibrium was reached. They can be rationalized by considering two factors.

a) The combination of a flexible with a rigid calixarene disfavors the formation of heterodimers. For entries I) and II) this is the only factor and heterodimers are not observed for tolyl as well as tosyl ureas in both solvents.

b) The combination of tolyl with tosyl ureas favors the exclusive formation of heterodimers. This is the only factor in entries III) and IV) and it is working for rigid as well as flexible calixarenes in CD_2Cl_2. The situation is less clear for $CDCl_3$ where the heterodimer is formed for flexible ureas but **not** for the rigid ones. Thus we have the interesting situation (entry IV), that the dimerization can be «switched» between hetero (CD_2Cl_2) and homo ($CDCl_3$) by the solvent, or (perhaps better) by the guest, since most probably the/a solvent molecule is included as guest.

In entries V) and VI) both effects are present. And in CD_2Cl_2 the situation is clear, the tendency of tosyl/tolyl residues to induce the formation of heterodimers is dominant for both combinations. In $CDCl_3$ however, in agreement with entry IV) the «tosyl/tolyl» effect is less pronounced than the «flexible/rigid» effect, and heterodimers are not formed in entry VI). This may be due to **3**, the compound present in both entries IV) and VI).

Although this is not yet a detailed explanation, it is a self-consistent, general picture. In accordance to all observations the mixing of **1**·G·**2** and **3**·G·**4** heterodimers together does not lead to any changes in the spectra during 3 days.

Stereochemistry

Dimers of the tetraureas **3** and **4** are interesting also for their stereochemistry. The single calix[4]arene has C_{2v} symmetry, like a calix[4]arene consisting of two different phenolic units in alternating sequence (ABAB). However, the symmetry planes intersect opposite methylene bridges and not opposite phenolic units. A homodimer **3**·**3** or **4**·**4** thus has D_2-symmetry, which is reduced to C_2 by the directionality of the hydrogen bonded belt. Thus, with or without directionality, they form only ***one*** pair of enantiomers, since the chirality is caused by the combination of the two calixarenes and not by this directionality.

‡ The rate of the dimerization depends on the amount of water in the solvents.

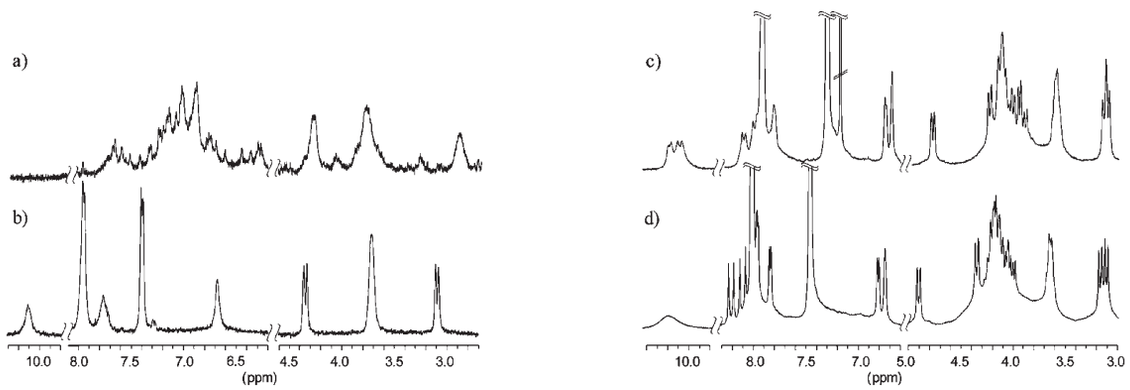

Fig. 2 Selected ^{1}H NMR spectra (400 MHz, 25 °C) of tetraureas: a) irregular aggregates of **1** in CD_2Cl_2; b) homodimer **2**·**2** in CD_2Cl_2; c) homodimer **4**·**4** in $CDCl_3$ d) homodimer **4**·**4** in CD_2Cl_2.

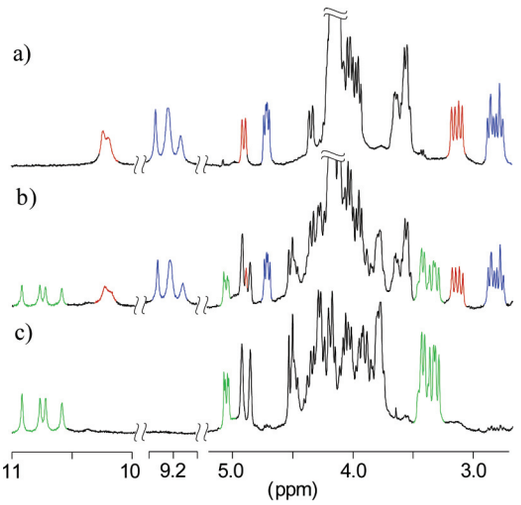

Fig. 3 Formation of heterodimers of **3** and **4** in CD_2Cl_2. ^1H NMR spectra (400 MHz, 25 °C) were recorded a) immediately after mixing; b) 3 h after mixing; c) 20 h after mixing. The NH and calixarene aromatic signals of dimers **3**·**3**, **4**·**4** and **3**·**4** are represented by the blue, red and green colours, respectively.

The situation is different for heterodimers, which are C_{4v} (**1**·**2**) or C_{2v}-symmetric (**1**·**4**, **2**·**3**) and become chiral (C_4 and C_2-symmetric, respectively) by the directionality of the hydrogen bonded belt. Both factors are present in heterodimers **3**·**4** which are C_2-symmetric already by the combination of the two calixarenes. The directionality of the H-bonded belt is added now as an independent element of chirality (this is the case only in heterodimers) and *two* diastereomeric pairs of enantiomers (C_2-symmetry) are expected, as demonstrated schematically in Fig. 4. Indeed, these are observed in the ^1H NMR spectra.

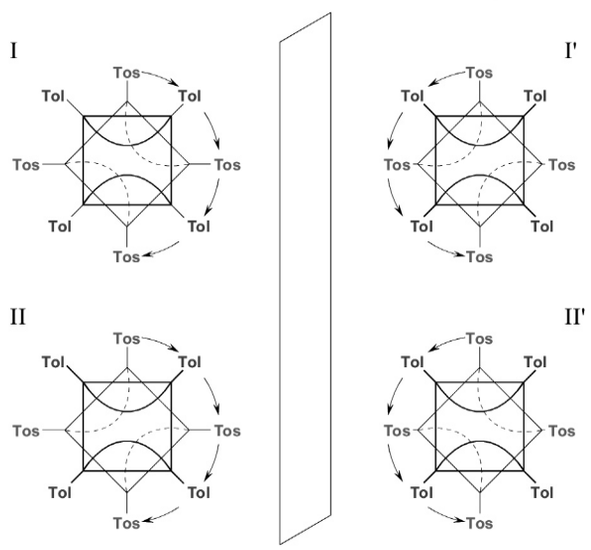

Fig. 4 Schematic representation of the possible stereoisomers of heterodimers **3**·**4**. The directionality of the hydrogen bonded belt is indicated by arrows. Without directionality I and II′ are identical as well as II and I′.

Molecular dynamics simulations

The tendency to form heterodimers between tolyl and tosylureas is entirely predominant in methylene chloride, as shown by entries III–VI (Table 1), and is the most important factor in chloroform for entries III and V. To get a better understanding of this phenomenon we started molecular dynamics simulations for all combinations of tetraureas **1** to **4**, since numerous attempts to obtain diffraction quality single crystals from such a heterodimer failed (so far).

Simulations were carried out in a chloroform box using the AMBER 7[10] software package. The starting geometry of a capsule was obtained from the known crystal structures, placing one chloroform molecule as guest in the interior, and replacing the ether groups (Y) and the urea groups (R) appropriately. To save computation time Y = Et was used for **1** and **2**. After equilibration[11] MD simulations were performed for 8 ns and snapshots were collected every 2 ps.

Table 2 Mean free energy and entropic term calculated for all possible dimeric capsules

Dimer	$G_{total}{}^a \pm \sigma^b$/kcal mol^{-1}	$-TS$/kcal mol^{-1}
1·**1**	−114.4 ± 2.1	−212.7
2·**2**	−71.1 ± 2.3	−235.6
3·**3**	−35.8 ± 2.0	−205.0
4·**4**	−7.8 ± 2.3	−244.6
1·**3**	−76.0 ± 1.9	−208.7
2·**4**	−30.5 ± 2.3	−248.6
1·**2**	−94.2 ± 2.2	−233.3
3·**4**	−13.5 ± 2.2	−225.6
1·**4**	−53.5 ± 2.3	−229.8
2·**3**	−52.7 ± 2.0	−229.8

[a] Average free energies from 4000 structures. [b] σ = standard errors of the mean energies.

Unfortunately significant differences could not be found for the averaged geometrical parameters between the ten dimers (four homodimers and six heterodimers). For example the pole to pole distances (between the centers of the planes of the methylene bridge carbons) vary between 9.15 and 9.44 Å and the volume of the capsule between 207 and 220 Å^3. The N···O distances for hydrogen bonds for the amino functions attached to the calixarene ranged from 2.25 to 2.36 Å and those for amino functions attached to the urea residues R from 2.07 to 2.14 Å. Significant differences are also not found for the time averaged number of hydrogen bonds formed by the two types of NH-groups. Occasionally NH···O=S hydrogen bonds were observed in homo- and heterodimers containing the tosylureas **2** and **4**.

Energetic parameters (ΔG, ΔS) for the dimerization are collected in Tables 2 and 3. They were calculated by post-processing of the MD trajectories using the MM-PBSA method[12] on the basis of all 4000 snapshots. As seen from the third column of Table 3, where a negative ΔG_{total} means, that the heterodimer is favored over the two homodimers, these values are in agreement with the experimental results in Table 1, with the single exception of entry I. However, keeping in mind that the standard errors of the mean free energy ΣG_{total} is in the range of 1.9–2.3 kcal mol^{-1} one has to state that these differences in $\Delta G_{total,}$ ranging between −2.2 and 3.0 kcal mol^{-1}, are not really significant.

Thus, we have to conclude that the equilibrium between the two homodimers and the respective heterodimer, *e.g.* **1**·**1** + **2**·**2** ⇌ 2 **1**·**2** is too delicate to be modelled by MD simulations. Larger geometric factors of a dimeric capsule, such as the general difference between hydrogen bonds formed by the inner and outer NH-groups are correctly reported by the MD simulations (in agreement with NMR- and X-ray data). However the energetic differences between various dimers are obviously too small and cannot be sufficiently explained by the simulations. Although this is disappointing with respect to our initial ambitions, we believe that this result nevertheless should be reported.

Conclusions

Wide rim tetratolyl (**1, 3**) and tetratosyl (**2, 4**) ureas with a more flexible calix[4]arene tetrapentylether (**1, 2**) or a rigidified biscrown-3 ether derivative (**3, 4**) as basic skeleton form homodimers in apolar solvents such as $CDCl_3$. For mixtures of two tetraureas there is the additional possibility to form heterodimers. Very subtle enthalpic and entropic contributions involving also the solvent (and guest) are obviously responsible for the exclusive formation of either homo- or heterodimers in stoichiometric (1 : 1) mixtures. This may be concluded from the observation that for two pairs (**3**–**2** and **3**–**4**) the self-assembly

Table 3 Formation of homo- and heterodimers; energies in kcal mol^{-1}

Entry	Mixture	Homodimer ΣG_{total}[a]	Heterodimer ΣG_{total}[b]	ΔG_{total}[c]	$-T\Delta S$
I	**1**·**3**	−150.3	−152.0	−1.7	0.4
II	**2**·**4**	−63.3	−61.1	2.2	1.0
III	**1**·**2**	−185.5	−188.5	−3.0	−0.6
IV	**3**·**4**	−28.0	−27.0	1.0	−1.9
V	**1**·**4**	−106.7	−107.0	−0.3	−2.0
VI	**3**·**2**	−106.9	−105.4	1.5	−1.3

[a] Calculated as sum of G_{total} of the two homodimers. [b] Two times G_{total} of the heterodimer. [c] Column 4 − column 3.

switches from hetero- to homodimers when going from CD_2Cl_2 to $CDCl_3$. Obviously these subtle effects are also the reasons why no significant conclusions can be drawn from MD-simulations.

Experimental

All solvents were of analytical quality (p. a.) and were used without additional purification. The melting points were uncorrected. All solvents for NMR were purchased from Deutero GmbH. ^{1}H NMR were recorded on a Bruker Avance DRX 400 or a Bruker AC200 instrument at 400 or 200 MHz. ^{13}C NMR spectra were recorded on a Bruker Avance DRX 400 at 100 MHz. The solvent signals were used for calibration of NMR spectra. Starting tetraamino tetrapentoxy **5**[13] and tetraamino biscrown **6**[14] calix[4]arenes were synthesized in accordance with the published procedures.

5,11,17,23-Tetratosylurea-25,26,27,28-tetrapentoxycalix[4]-arene 2

The tetraamine **5** (0.50 g, 0.65 mmol) was dissolved in CH_2Cl_2 (10 ml) and tosyl isocyanate (0.77 g (0.60 ml), 3.92 mmol) was added to the solution. The reaction mixture was stirred overnight at room temperature and then MeOH (20 ml) was added. The precipitate was filtered, washed with MeOH (3 × 10 ml) and dried, yielding a white powder (0.65 g, 77%); mp 216 °C; δ_H (400 MHz; DMSO-d_6) 10.17 (4H, s, N*H*), 8.42 (4H, s, N*H*), 7.79 (8H, d, *J* 7.8, ArH_{Tos}), 7.42 (8H, d, *J* 7.8, ArH_{Tos}), 6.60 (8H, s, Ar*H*), 4.20 (4H, d, *J* 12.5, ArCH_2Ar), 3.71 (8H, t, *J* 7.0, OCH_2), 3.01 (4H, d, *J* 12.5, ArCH_2Ar), 2.40 (12H, s, CH_{3Tos}), 1.80 (8H, br s, CH_2), 1.31 (16H, br s, CH_2), 0.87 (12H, t, *J* 6.4, CH_3); δ_H (400 MHz, CD_2Cl_2) 10.11 (4H, s, N*H*), 7.95 (12H, m, Ar*H*, ArH_{Tos}), 7.76 (4H, s, N*H*), 7.39 (8H, d, *J* 7.8, ArH_{Tos}), 6.67 (4H, s, Ar*H*), 4.34 (4H, d, *J* 11.7, ArCH_2Ar), 3.71 (8H, br s, OCH_2), 4.34 (4H, d, *J* 11.7, ArCH_2Ar), 2.41 (12H, s, CH_{3Tos}), 1.90 (8H, br s, CH_2), 1.32–1.20 (16H, m, CH_2), 0.87 (12H, t, *J* 6.8, CH_3); *m*/*z* (ESI) 1575.7 (M$^+$Na, 100%).

5,11,17,23-Tetratosylurea-25,26-27,28-biscrown-3-calix[4]-arene 4

Tetraamine **6** (0.34 g, 0.54 mmol) was dissolved in a mixture of THF–$CHCl_3$ = 1 : 1 (50 ml) and tosyl isocyanate (1.28 g (0.99 ml), 6.53 mmol) was added to the solution. The reaction mixture was stirred overnight at room temperature. The solvent was removed at reduced pressure and Et_2O (30 ml) was added. The crude product was filtered, washed with Et_2O (3 × 15 ml), MeOH (5 ml), precipitated from a $CHCl_3$–MeOH mixture and dried yielding a light yellow powder (0.35 g, 46%); mp > 206 °C decomp.; δ_H (200 MHz; DMSO-d_6) 10.47 (4H, br s, N*H*), 8.44 (4H, s, N*H*), 7.82 (8H, d, *J* 7.80, ArH_{Tos}), 7.41 (8H, d, *J* 7.80, ArH_{Tos}), 6.90 (8H, s, Ar*H*), 4.80 (2H, d, *J* 12.2, ArCH_2Ar), 4.31–4.12 (14H, m, ArCH_2Ar, OCH_2), 3.61–3.35 (4H, m, OCH_2), 3.15–3.12 (2H, d, *J* 12.2, ArCH_2Ar), 2.39 (12H, s, CH_3); δ_H (400 MHz, CD_2Cl_2) 10.20 (4H, br s, N*H*), 8.24 (1H, s, N*H*), 8.19 (1H, s, N*H*), 8.13 (1H, s, N*H*), 8.07 (1H, s, N*H*), 8.02 (4H, d, *J* 8.2, ArH_{Tos}), 8.01 (4H, d, *J* 8.2, ArH_{Tos}), 7.97 (1H, d, *J* 2.4, Ar*H*), 7.95 (1H, d, *J* 2.4, Ar*H*), 7.85 (1H, d, *J* 2.4, Ar*H*), 7.83 (1H, d, *J* 2.4, Ar*H*), 7.46 (8H, d, *J* 8.2, ArH_{Tos}), 6.82 (1H, d, *J* 2.4, Ar*H*), 6.80 (1H, d, *J* 2.4, Ar*H*), 6.75 (1H, d, *J* 2.4, Ar*H*), 6.74 (1H, d, *J* 2.4, Ar*H*), 4.92 (2H, d, *J* 11.6, ArCH_2Ar), 4.36 (2H, d, *J* 11.6, ArCH_2Ar), 4.23–3.98 (12H, m, OCH_2), 3.67–3.63 (4H, m, OCH_2), 3.17 (2H, d, *J* 11.6, ArCH_2Ar), 3.12 (2H, d, *J* 11.6, ArCH_2Ar), 2.48 (6H, s, CH_3), 2.47 (6H, s, CH_3); *m*/*z* (ESI) 1435.5 (M$^+$Na, 100%).

Self-assembly studies

In a typical experiment tetraurea calix[4]arenes **1** (5.55 mg, 4.32 μmol) and **2** (6.68 mg, 4.32 μmol) were mixed together, dichlormethane-d_2 (0.7 mL) was added and the solution formed (sometimes with the help of an ultrasonic bath) was transferred in an NMR tube and ^{1}H NMR spectra were recorded. Heterodimers **1**·**4**, **2**·**3** and **3**·**4** were prepared analogously. ^{1}H NMR spectra of the heterodimers are given below.

1·**2** δ_H (400 MHz, CD_2Cl_2) N***H***: 10.81 (4H, s), 8.04 (4H, s), 7.96 (4H, s), 6.91 (4H, br s); Ar$\boldsymbol{H}_{\mathbf{Tos}}$: 8.14 (8H, d, *J* 8.2), 7.48 (8H, d, *J* 8.2); Ar$\boldsymbol{H}_{\mathbf{Tol}}$: 7.60 (8H, d, *J* 7.7), 6.87 (8H, d, *J* 7.7); Ar$\boldsymbol{H}_{\mathbf{cal}}$: 7.88 (4H, s), 7.01 (4H, s), 6.96 (4H, s), 4.86 (4H, s); **ArC*H*$_2$Ar**: 4.58 (4H, d, *J* 11.7), next 4H are overlapped with multiplet at 4.00–3.89, 3.33 (4H, d, *J* 11.7), 2.59 (4H, d, *J* 11.7); **OC*H*$_2$**: 4.00–3.89 (12H (from them 4H belong to **ArC*H*$_2$Ar**), m), 3.60–3.45 (8H, m); **C*H*$_{3\mathbf{Tos}}$**: 2.50 (12H, s); **C*H*$_{3\mathbf{Tol}}$**: 2.08 (12H, s); **C*H*$_2$**: 1.83–1.72 (8H, m), 1.60–1.19 (40H, m); **C*H*$_{3\mathbf{alk}}$**: 0.99 (12H, t, *J* 7.2), 0.90 (12H, t, *J* 7.2).

1·**2** δ_H (400 MHz, $CDCl_3$) N***H***: 10.52 (4H, s), 8.04 (4H, s), 8.02 (4H, s), 7.62 (4H, s); Ar$\boldsymbol{H}_{\mathbf{Tos}}$: 8.14 (8H, d, *J* 8.2), 7.48 (8H, d, *J* 8.2); Ar$\boldsymbol{H}_{\mathbf{Tol}}$: 7.57 (8H, d, *J* 8.3), 6.79 (8H, d, *J* 8.3); Ar$\boldsymbol{H}_{\mathbf{cal}}$: 7.86 (4H, d, *J* 2.3), 7.04 (4H, d, *J* 2.3), 6.87 (4H, d, *J* 2.3), (4H, d, *J* 2.3); **ArC*H*$_2$Ar**: 4.54 (4H, d, *J* 11.7), 3.91 (4H, d, *J* 11.7), 3.37 (4H, d, *J* 11.7), 2.52 (4H, d, *J* 11.7); **OC*H*$_2$**: 3.95–3.84 (8H, m), 3.53–3.40 (8H, m); **C*H*$_{3\mathbf{Tos}}$**: 2.48 (12H, s); **C*H*$_{3\mathbf{Tol}}$**: 2.05 (12H, s); **C*H*$_2$**: 1.72–1.68 (8H, m), 1.45–1.12 (40H, m); **C*H*$_{3\mathbf{alk}}$**: 0.97 (12H, t, *J* 7.0), 0.88 (12H, t, *J* 7.0).

1·**4** δ_H (400 MHz, CD_2Cl_2) N***H***: 10.91 (2H, br s), 10.68 (2H, br s), 8.09 (4H, s), 7.99 (2H, s), 7.96 (2H, s), 7.09 (2H, br s), 6.95–6.90 (2H, br s); Ar$\boldsymbol{H}_{\mathbf{Tos}}$: 8.14 (8H, d, *J* 8.3), 7.48 (8H, d, *J* 8.3); Ar$\boldsymbol{H}_{\mathbf{Tol}}$: 7.64 (4H, d, *J* 8.3), 7.61 (4H, d, *J* 8.3), 6.93 (4H, d, *J* 8.3), 6.90 (4H, d, *J* 8.3); Ar$\boldsymbol{H}_{\mathbf{cal}}$: 7.91 (2H, d, *J* 1.9), 7.88 (2H, d, *J* 1.9), 7.16 (2H, s), 7.02 (2H, d, *J* 1.9), 6.99 (4H, s), 4.96 (2H, s), 4.93 (2H, d, *J* 1.9); **ArC*H*$_2$Ar**: 4.60 (2H, d, *J* 11.7), 4.59 (2H, d, *J* 11.7), 4.51 (2H, d, *J* 11.7), next 2H are overlapped with multiplet at 4.12–3.82, 3.35 (2H, d, *J* 11.7), 3.34 (2H, d, *J* 11.7), 2.64 (2H, d, *J* 11.7), 2.57 (2H, d, *J* 11.7); **OCH$_2$**: 4.12–3.82 (22H (from them 2H belong to **ArC*H*$_2$Ar**), m), 3.48–3.40 (4H, m); **C*H*$_{3\mathbf{Tos}}$**: 2.51 (12H, s); **CH$_{3\mathbf{Tol}}$**: 2.12 (12H, s); **CH$_2$**: 1.51–1.40 (24H, m); **CH$_{3\mathbf{alk}}$**: 1.02–0.98 (12H, m).

1·**4** δ_H (400 MHz, $CDCl_3$) N***H***: 10.54 (2H, s), 10.29 (2H, s), 8.08 (2H, s), 8.06 (2H, s), 8.05 (2H, s), 8.00 (2H, s), 7.84 (2H, s), 7.76 (2H, s); Ar$\boldsymbol{H}_{\mathbf{Tos}}$: 8.13 (8H, d, *J* 8.3), 7.41 (8H, d, *J* 8.3); Ar$\boldsymbol{H}_{\mathbf{Tol}}$: 7.59 (4H, d, *J* 8.3), 7.56 (4H, d, *J* 8.3), 6.83 (4H, d, *J* 8.3), 6.81 (4H, d, *J* 8.3); Ar$\boldsymbol{H}_{\mathbf{cal}}$: 7.86 (4H, s), 7.04 (4H, s), 7.00 (2H, s), 6.90 (2H, s), 5.04 (2H, s), 4.92 (2H, s); **ArC*H*$_2$Ar**: 4.55 (2H, d, *J* 11.7), 4.54 (2H, d, *J* 11.7), 4.42 (2H, d, *J* 11.7), next 2H are overlapped with multiplet at 4.12–3.78, 3.37 (2H, d, *J* 11.7), 3.36 (2H, d, *J* 11.7), 2.57 (2H, d, *J* 11.7), 2.52 (2H, d, *J* 11.7); **OC*H*$_2$**: 4.12–3.78 (22H (from them 2H belong to **ArC*H*$_2$Ar**), m), 3.48–3.42 (4H, m); **C*H*$_{3\mathbf{Tos}}$**: 2.46 (12H, s); **C*H*$_{3\mathbf{Tol}}$**: 2.06 (12H, s); **C*H*$_2$**: 1.50–1.36 (24H, m); **C*H*$_{3\mathbf{alk}}$**: 1.01–0.96 (12H, m).

2·3 δ_H (400 MHz, CD_2Cl_2) **N*H***: 10.86 (2H, s), 10.73 (2H, s), 8.12 (4H, s), 8.04 (2H, s), 8.03 (2H, s), 7.10–6.95 (2H, br s), 6.81 (2H, br s); **Ar*H*$_{Tos}$**: 8.14 (8H, d, *J* 7.7), 7.48 (8H, d, *J* 7.7); **Ar*H*$_{Tol}$**: 7.61 (8H, br s), 7.87 (4H, d, *J* 8.0), 6.85 (4H, d, *J* 8.0); **Ar*H*$_{cal}$**: 7.97 (2H, d, *J* 1.9), 7.92 (2H, d, *J* 1.9), 7.10 (2H, d, *J* 1.9), 7.03 (2H, d, *J* 1.9), 6.96 (4H, s), 4.88 (2H, s), 4.79 (2H, s); **ArC*H*$_2$Ar**: 5.05 (2H, d, *J* 11.6), 4.53 (2H, d, *J* 11.6), 3.98 (2H, d, *J* 11.1), 3.95 (2H, d, *J* 11.1), 3.34 (2H, d, *J* 11.6), 3.31 (2H, d, *J* 11.6), 2.59 (2H, d, *J* 11.1), 2.52 (2H, d, *J* 11.1); **OC*H*$_2$**: 4.40–4.17 (12H, m), 3.82–3.75 (4H, m), 3.56–3.46 (8H, m); **C*H*$_{3Tos}$**: 2.50 (12H, s); **C*H*$_{3Tol}$**: 2.09 (6H, s), 2.07 (6H, s); **C*H*$_2$**: 1.79–1.74 (8H, m), 1.34–1.23 (16H, m); **C*H*$_{3alk}$**: 1.89 (6H, t, *J* 9.7), 0.90 (6H, t, *J* 9.7).

3·4 δ_H (400 MHz, CD_2Cl_2) **N*H***: 10.93 (1H, s), 10.78 (1H, s), 10.73 (1H, s), 10.60 (1H, s), next 4H are overlapped with doublet at 8.16, 8.11 (2H, s), 8.07 (2H, s), 7.23 (1H, s), 7.22 (1H, s), 7.07 (1H, s), 7.04 (1H, br s); **Ar*H*$_{Tos}$**: 8.16 (12H (from them 4H belong to **N*H***), d, *J* 8.3), 7.50 (4H, d, *J* 8.3), 7.49 (4H, d, *J* 8.3); **Ar*H*$_{Tol}$**: 7.67–7.61 (8H, m), 6.93 (4H, d, *J* 8.3), 6.90 (4H, d, *J* 8.3); **Ar*H*$_{cal}$**: 8.02 (1H, d, *J* 2.4), 7.99 (1H, d, *J* 2.4), 7.95 (1H, d, *J* 2.4), 7.92 (1H, d, *J* 2.4), 7.18 (1H, s), 7.17 (1H, s), 7.12 (1H, d, *J* 2.4), 7.11 (1H, d, *J* 2.4), 7.05 (1H, d, *J* 2.4), 7.02 (1H, d, *J* 2.4), 7.01 (1H, s), 6.99 (1H, s), 4.95 (2H, s), 4.88 (2H, s); **ArC*H*$_2$Ar**: 5.09 (1H, d, *J* 11.7), 5.07 (1H, d, *J* 11.7), 4.55 (2H, d, *J* 11.7), next 4H are overlapped with multiplet at 4.49–3.78, 3.37 (2H, d, *J* 11.7), 3.43 (2H, d, *J* 11.7), 2.76–2.52 (4H, m); **OC*H*$_2$**: 4.49–3.78 (32H (from them 4H belong to **ArC*H*$_2$Ar**), m), 3.49–3.41 (4H, m); **C*H*$_{3Tos}$**: 2.52 (12H, s); **C*H*$_{3Tol}$**: 2.12 (12H, s).

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