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Folding and dimerization of resorcarene tetrasulfonates†

Alexander Shivanyuk‡

Department of Chemistry, University of Jyväskylä, P.O. Box 35, FIN-40351, Jyväskylä, Finland

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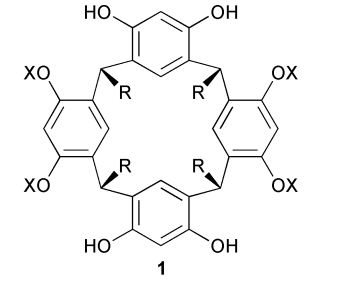
In the solid state and in $CDCl_3$ resorcarene tetramesitylsulfonates fold by intramolecular S=O···H–O hydrogen bonds and dimerise *via* intermolecular O–H···OH hydrogen bonding.

Intramolecular folding and intermolecular association of several sub-units are key properties of biologically important macromolecules.[1] A few synthetic compounds also exhibit these features. For instance, the bowl shaped crown conformers of resorcarene octols[2] formed by intramolecular hydrogen bonds lead to hydrogen bonded dimeric and hexameric aggregates.[3] A seam of intramolecular hydrogen bonds in the calix[4]arene tetraurea derivatives was shown to change considerably the stability and binding properties of self-assembled dimeric capsules.[4] The dimer of an artificial β-sheet[5] is also an example of self-assembly involving both intra- and inter-molecular hydrogen bonds.

Novel hydrogen bonded self-assembly of tetramesityl sulfonates **1a, b**[6] is reported here which is a combination of folding and dimerization.



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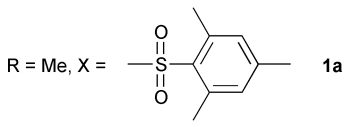
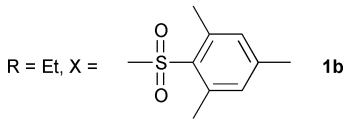


1a



1b

In the crystalline state§ the molecule of **1a** adopts a strongly pinched and twisted boat conformation with almost parallel unsubstituted resorcinol rings (Fig. 1). Two of mesitylsulfonyl fragments oriented clock- or counter-clockwise form short intramolecular S=O···H–O hydrogen bonds to the neighboring hydroxy groups making the whole conformation inherently chiral. The asymmetric unit contains two crystallographically independent molecules (A and B) which are different mainly in the arrangement of one *non*-hydrogen bonded mesitylsulfonyl residue (Fig. 1).

Two molecules of **1a** form a cross-shaped dimer linked by four intermolecular O–H···OH hydrogen bonds (Fig. 2). Short intra- and inter-molecular contacts between hydroxy and *ortho*-methyl groups of the mesityl residues (O···C 3.2–3.4 Å) clearly indicate the C–H···O interactions which may additionally stabilize the assembly. The unsubstituted resorcinol rings of

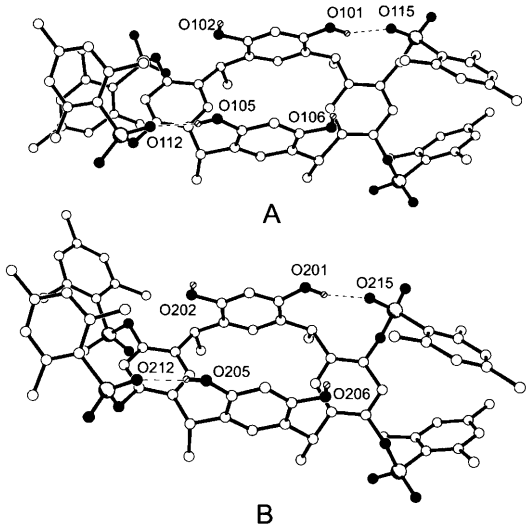


Fig. 1 Two crystallographically independent molecules of **1a**. C–H-hydrogen atoms are omitted for clarity. Hydrogen bonds are shown in dotted lines. O···O distances (Å) and O–H···O angles for intramolecular hydrogen bonds (°): O101···O115 2.590(5) (148.3), O105···O112 2.611(5) (148.1), O201···O215 2.510(5) (148.1), O205-O212 2.513(4) (145.3).

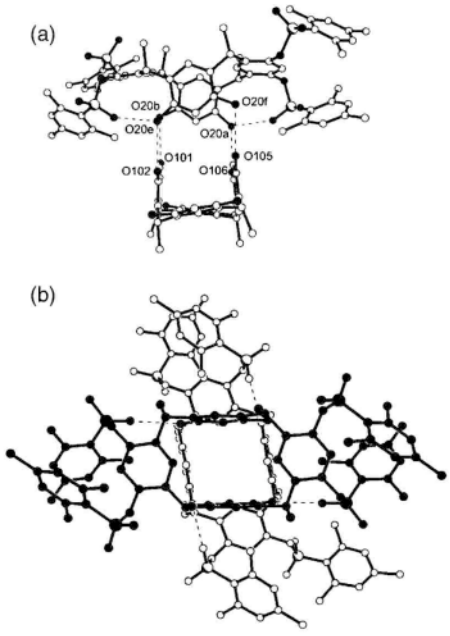


Fig. 2 Hydrogen bonded dimer of **1a**. (a) Side view. Mesitylsulfonyl groups of one molecule are omitted for clarity. (b) Top view. Molecule A is darkened. Selected intermolecular distances (Å): O101···O20B 2.808, O102···O20E 2.836, O105···O20F 2.829, O106···O20A 2.774.

† Dedicated to Volker Böhmer on the occasion of his 60th Birthday.

‡ Current address: The Skaggs Institute for Chemical Biology, The Scripps Research Institute, MB-26, 10550 North Torrey Pines Rd., La Jolla, CA 92037, USA. E-mail: shivan@scripps.edu

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molecule A are nearly perpendicular both to diacylated and unsubstituted resorcinol rings of molecule B. Such a geometry leaves no space for the encapsulation of guest species within the dimer so that the solvent molecules are included in voids of the crystal.

In the dimer the molecules of **1a** have an opposite orientation of hydrogen bonded mesitylsulfonyl groups obviously owing to the requirements of complementarity. A simple consideration reveals that the molecules of **1a** having the same sense of inherent chirality cannot form the dimer.

The ^{1}H NMR spectrum of **1a**, **b** measured in $CDCl_3$ at 303 K contains four singlets for the protons of resorcinol rings, one singlet for the protons of hydroxy groups (δ 7.0) and one set of signals for other protons in accordance with C_{2v}-symmetric structure. 2D NOESY (t_m = 300 ms) and long range COSY ($CDCl_3$, 500 MHz) techniques showed that the molecules of **1** exist in the boat conformation with *parallel* unsubstituted resorcinol rings.[7] At 223 K a double set of ^{1}H NMR signals corresponds to the protons of the methyne bridges [Fig. 3(a), (b)], hydroxy groups and the aromatic protons of the mesitylene residues while the protons of the resorcinol rings emerge again as four singlets. This pattern can be ascribed to the slow exchange between two enantiomeric C_2-symmetric conformations having clock- or counter-clockwise orientation of two hydrogen bonded mesitylsulfonyl groups similar to that found in the solid state (Fig. 1). The signals of methyne bridges undergo a clear coalescence at 247 K corresponding to ΔG^* of 11.7 kcal mol^{-1}. The mixing of **1a** and **1b** in 1 : 1 molar ratio results in additional set of ^{1}H NMR signals for both resorcarenes [Fig. 3(c)]. This can be explained only by the formation of hetero-associate **1a** · **1b** which co-exists with **1a** · **1a** and **1b** · **1b** in a statistical 2 : 1 : 1 ratio. This is in accordance with the MALDI-TOF mass spectra of **1a** and **1b** which showed the peaks of both the monomer and the dimer.

The ^{1}H NMR spectrum of **1a** measured at 223 K in a 1 : 1 mixture of **1a**, **b** in CD_3OD–$CDCl_3$ (1 : 1) exhibits a sharp C_{2v}-symmetric pattern which presumably corresponds to the monomer. Furthermore, in less competing mixtures of $CDCl_3$ and acetonitrile-d_3 both C_{2v}- and C_2-symmetrical pattern are observed simultaneously, in a ratio proportional to the polarity of the medium. Since no signals of the monomer were observed at 223 K in $CDCl_3$ the dimerization constant should be $> 10^5$ M^{-1}.

The NOESY (t_m = 300 ms) spectrum of **1a** in $CDCl_3$ at 223 K reveals close proximity of the protons in 5-positions of diacylated resorcinol rings to the protons in 2-positions of unsubstituted resorcinol rings as found in the solid state dimer [Fig. 2(a)]. The singlet of hydroxy groups at δ 7.5 shows intense cross-peaks to the signal of the protons in 2-positions of unsubstituted resorcinol rings and to the OH resonance at δ 7.0. This is in accordance with the geometry of *intermolecular* O–H···O–H hydrogen bonding in the solid state dimer (Figs. 1 and 2). On the other hand, the correlation between *one* signal of the methyne bridges (δ 4.5) and the OH resonance at δ 7.0 is in keeping with the *intramolecular* S=O···H–O hydrogen bonds (Fig. 1).

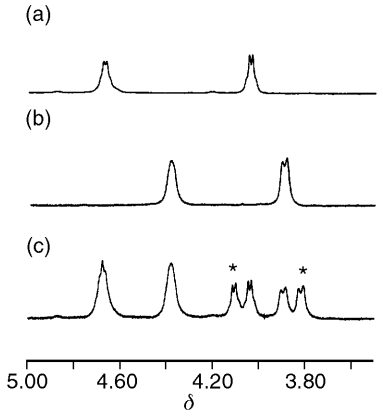

Fig. 3 The ^{1}H NMR signals of the methyne protons of the bridges at 223 K ([**1a**] = [**1b**] = 10 mM, 500 MHz, $CDCl_3$): (a) **1a**, (b) **1b**, (c) **1a** + **1b**. Signals of the heterodimer are indicated by an asterisk.

The above results strongly suggest the structural similarity of $\mathbf{1a}_2$ in $CDCl_3$ and in the solid state. The fact that only one C_2-symmetrical pattern is observed in the NMR spectra of $\mathbf{1a}_2$, $\mathbf{1b}_2$ and **1a**·**1b** reflects, most probably, the regioselective formation of one dimer—a feature predicted from the crystal structure of $\mathbf{1a}_2$.

In conclusion, the dimerization described above provides a novel structural motif for molecular self-assembly which is based on the interplay of intra- and inter-molecular hydrogen bonds. Obviously, the aggregation of resorcarene tetramesityl sulfonates characterized by cation and anion binding sites, hydrogen bonding, photochemically and/or electrochemically active groups could give novel polyfunctional molecular assemblies. Such systems are being investigated and will be reported in due course.

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Notes and references

§ *Crystal data*: the data was recorded with a Kappa CCD diffractometer using graphite monochromatised Mo-Kα radiation [λ(Mo-Kα) = 0.71073 Å]. The data was processed with Denzo-SMN v0.93.0 (Z. Otwinowski and W. Minor, *Processing of X-Ray Diffraction Data Collected in Oscillation Mode; Methods Enzymol*, 1997, **276**, 307). The structures were solved by direct methods (G. M. Sheldrick, SHELXS-97, *Acta Crystallogr., Sect. A.* 1990, **46**, 467) and refinements, based on F^2, were made by full-matrix least-squares techniques (G. M. Sheldrick, SHELXL-97: A program for crystal structure refinement, University of Göttingen, Germany, 1997).

$\mathbf{1a}_2$·4EtOH·2H_2O: crystal size 0.5 × 0.3 × 0.2 mm, monoclinic, space group *Pn*, a = 18.1461(3), b = 14.8718(1), c = 23.3306(4) Å, β = 92.654(1)°, V = 6289.3(2) Å^3, Z = 2, D_c = 1.403 g cm^{-3}, μ = 0.228 mm^{-1}, $F(000)$ = 2797, 1760 parameters, $R1$ = 0.0696, $wR2$ = 0.1746 [for 20725 reflections with $I > 2\sigma(I)$], $R1$ = 0.0968, $wR2$ = 0.1980 (for 26601 unique reflections), S = 1.077, $\Delta\rho$ = −0.43/0.72 e Å^{-3}.

CCDC reference number 163620. See http://www.rsc.org/suppdata/cc/b1/b104076f/ for crystallographic data in CIF or other electronic format.

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