

# Sulfone-calixarenes: a new class of molecular building block

Gilles Mislin,<sup>a</sup> Ernest Graf,<sup>a</sup> Mir Wais Hosseini,<sup>\*a†</sup> André De Cian<sup>b</sup> and Jean Fischer<sup>b</sup>

<sup>a</sup> Laboratoire de Chimie de Coordination Organique, Université Louis Pasteur, (UMR 7513 CNRS), F-67000 Strasbourg, France

<sup>b</sup> Laboratoire de Cristallographie et Chimie Structurale, Université Louis Pasteur, (UMR 7513 CNRS), F-67000 Strasbourg, France

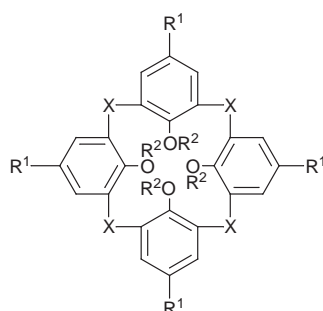
The synthesis of a new calix[4]arene derivative based on the linkage of the phenolic rings by four sulfone groups was achieved and its 1,3-alternate conformation in the crystalline phase, resulting from both inter- and intra-molecular H-bonding, was established by crystallography.

Over the past two decades, the calixarene framework has been the most used macrocyclic structure.<sup>1,2</sup> The increasing interest in these compounds seems to be due to their versatility. Indeed, a variety of calixarene based molecules displaying a wide range of properties ranging from molecular receptors and enzyme mimics as well as extractants to liquid crystals and conducting polymers have been reported. In our own hands, calix[4]arene derivatives have been used either for the design of hollow molecular modules<sup>3,4</sup> and their assembly into inclusion molecular networks in the crystalline phase,<sup>5</sup> or as backbones for the design of exo-ligands.<sup>6–8</sup>

In dealing with calix[4]arene **1**, its structural and functional tunings at various positions have been extensively studied. Whereas partial or complete substitution of the *p-tert*-butyl moieties by a variety of groups leads to the modification of the upper rim, the functionalisation of the hydroxyl moieties affords modified calixarenes at the lower rim. On the other hand, examples of partial<sup>7</sup> or complete<sup>8,9</sup> replacement of the OH by SH groups have been also reported. However, dealing with the linkage of the aromatic rings, only recently few examples of substitution of CH<sub>2</sub> groups by Me<sub>2</sub>Si<sup>10</sup> or S<sup>11,12</sup> have been reported. An example of tetrathiacalix[4]arene based on four thiophene moieties has been also published.<sup>13</sup>

Here we report the first synthesis as well the solid state structural analysis of a new class of calix[4]arene analogues based on the linking of four phenolic rings by sulfone groups. These compounds may be of interest for the design of new receptors and backbones.

The synthetic strategy for the preparation of the tetrasulfone **6** was based on the complete oxidation of the thiacalix **3** (Scheme 1). The latter was obtained following the reported



- 1 X = CH<sub>2</sub>, R<sup>1</sup> = Bu<sup>t</sup>, R<sup>2</sup> = H
- 2 X = S, R<sup>1</sup> = R<sup>2</sup> = H
- 3 X = S, R<sup>1</sup> = Bu<sup>t</sup>, R<sup>2</sup> = H
- 4 X = S, R<sup>1</sup> = Bu<sup>t</sup>, R<sup>2</sup> = Me
- 5 X = SO<sub>2</sub>, R<sup>1</sup> = Bu<sup>t</sup>, R<sup>2</sup> = Me
- 6 X = SO<sub>2</sub>, R<sup>1</sup> = Bu<sup>t</sup>, R<sup>2</sup> = H

Scheme 1

procedure.<sup>11a</sup> In a first attempt, all four OH moieties of **3** were protected as methoxy groups prior to the oxidation of the sulfide linkages to sulfones. The treatment of **3** under reflux with MeI in the presence of NaH in dry THF–DMF (1 : 9) for two days afforded, after recrystallisation from CHCl<sub>3</sub>–MeOH, the desired compound **4** in 73% yield. The complete oxidation of **4** to the tetrasulfone **5** was first attempted by refluxing the compound **4** in a 30% H<sub>2</sub>O<sub>2</sub>–glacial AcOH mixture for eight days. Probably owing to the low solubility of **4**, the reaction isolated yield was only *ca.* 10%. The latter was increased to 88% when performing the oxidation with *m*-chloroperbenzoic acid in CHCl<sub>3</sub> at room temp. for 4 days. The pure compound **5** was isolated by recrystallisation from CH<sub>2</sub>Cl<sub>2</sub>–MeOH. Since the removal of the protecting groups by treatment with a large excess of BBr<sub>3</sub> in CH<sub>2</sub>Cl<sub>2</sub> afforded the final compound **6** in only *ca.* 30% yield, the direct oxidation of the tetrasulfide **3** was carried out in 59% yield using 30% H<sub>2</sub>O<sub>2</sub>–glacial AcOH. The pure compound **6** was obtained after crystallisation from THF–hexane.

In solution, for all compounds **4–6**, both the <sup>1</sup>H and <sup>13</sup>C NMR spectra were extremely simple and in agreement with the proposed structure. In marked contrast with calix **1** derivatives for which both the <sup>1</sup>H and <sup>13</sup>C NMR signals corresponding to the methylene groups are usually used for conformational assignment in solution, due to the absence of such NMR probes for the thia- and sulfone-calix[4]arenes **2–6** their conformation could not be established unambiguously. For both compounds **4** and **5**, no changes in the proton spectra could be detected between –85 and 125 °C. However, bidimensional (<sup>1</sup>H,<sup>1</sup>H) ROESY experiments at room temp. showed correlations between the methoxy groups and both the CH<sub>3</sub> and CH aromatic proton indicating thus a rapid conformational interconversion. For the final compound **6** the dramatic changes observed upon cooling from 25 to –100 °C indicated temperature dependent conformational dynamics.

In the solid state, all compounds **4–6** were studied by X-ray diffraction methods on monocrystals. Suitable monocrystals<sup>‡</sup> were obtained by slow diffusion of MeOH into a CH<sub>2</sub>Cl<sub>2</sub> solution of either compound **4** or **5**, or by slow evaporation of a chlorobenzene solution of the compound **6**. In marked contrast with the tetramethoxy derivative of **1** which was shown to adopt a partial cone conformation,<sup>14</sup> and with the tetrathiacalix[4]-

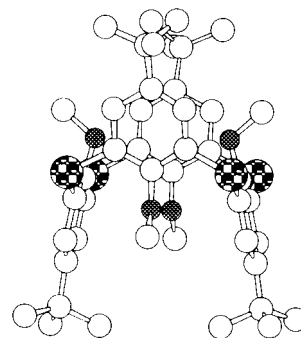
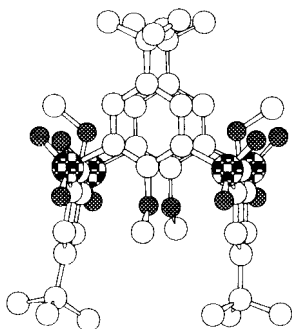
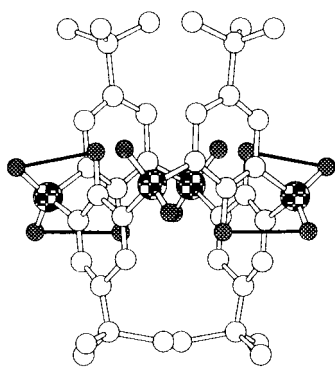


Fig. 1 X-Ray structure of the tetrasulfide **4** demonstrating the adopted 1,3-alternate conformation in the crystalline phase; for clarity H atoms are not presented



**Fig. 2** X-Ray structure of the tetrasulfone **5** demonstrating the adopted 1,3-alternate conformation in the crystalline phase; for clarity H atoms are not presented

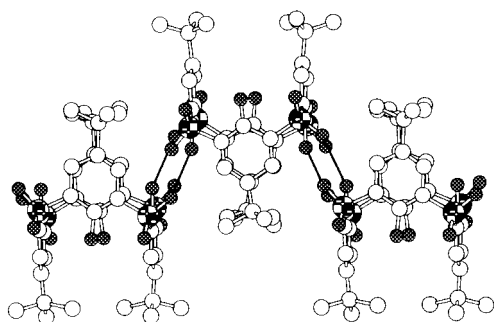


**Fig. 3** X-Ray structure of the tetrasulfone **6** demonstrating the adopted 1,3-alternate conformation in the crystalline phase. The bold lines represent the intramolecular H-bonding pattern; for clarity H atoms are not presented.

arene **2** and the parent compound **3** which were present in cone conformation,<sup>12</sup> the thia analogue **4** was found to be in the 1,3-alternate conformation (Fig. 1).

For the two sulfone derivatives **5** (Fig. 2) and **6** (Fig. 3), again the conformation was found to be 1,3-alternate with oxygen atoms of the sulfones pointing outward. The average SO bond distance was *ca.* 1.43 and 1.44 Å for **5** and **6**, respectively. The average CS bond distance was *ca.* 1.77 Å for both cases. The average distance between two adjacent sulfur atoms was *ca.* 5.52 Å.

Based on the observed average O...O distance between two adjacent oxygen atoms of *ca.* 2.70, 2.85 and 2.64 Å for **1**, **2** and **3** respectively, as previously proposed in the case of **1**,<sup>1</sup> for both compounds **2**<sup>12</sup> and **3**<sup>12</sup> the cone conformation was, at least partially stabilised, by an array of intramolecular H-bonds. Interestingly, the 1,3-alternate conformation for compound **6** may be also rationalised in terms of H-bonding between the OH and SO<sub>2</sub> groups (Fig. 3). Indeed, O...OS distances varying from 2.81 to 3.02 Å were observed. Furthermore, compound **6** was found to form a 3-D network through intermolecular H-bonding



**Fig. 4** A portion of the X-ray structure of the 3-D network formed between consecutive compounds **6**. The 3-D network is obtained by intermolecular H-bonding between OH and SO groups; for clarity H atoms are not presented.

between the OH and SO<sub>2</sub> groups belonging to adjacent units with an average O...OS distance of *ca.* 2.87 Å (Fig. 4).

In conclusion, the synthesis of new calix[4]arene derivatives based on sulfone linkages between the phenolic rings was achieved. All compounds were shown to adopt the 1,3-alternate conformation in the solid state. In the case of *p*-*tert*-butyl-tetrasulfonecalix[4]arene **6**, due to inter- and intra-molecular H-bonds, a 3-D network was observed in the solid state. The use of sulfonecalix derivatives for the design of receptors and building blocks is under current investigation.

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## Notes and References

† E-mail: hosseini@chimie.u-strasbg.fr

‡ *Crystallographic data:* **4** (colorless, 173 K): C<sub>44</sub>H<sub>56</sub>O<sub>4</sub>S<sub>4</sub>·CH<sub>2</sub>Cl<sub>2</sub>, *M* = 862.12, orthorhombic, *a* = 15.210(1), *b* = 12.747(1), *c* = 12.220(1) Å, *U* = 2369.2(5) Å<sup>3</sup>, space group *P*2<sub>1</sub>2<sub>1</sub>2<sub>1</sub>, *Z* = 2, *D*<sub>c</sub> = 1.21 g cm<sup>-3</sup>, Nonius CCD, Mo-Kα, μ/mm<sup>-1</sup> = 0.343, 1523 data with *I* > 3σ(*I*), *R* = 0.047, *R*<sub>w</sub> = 0.054.

**5** (colorless, 294 K): C<sub>44</sub>H<sub>56</sub>O<sub>12</sub>S<sub>4</sub>, *M* = 905.19, monoclinic, *a* = 10.9822(5), *b* = 18.567(2), *c* = 11.8055(6) Å, β = 101.941(4), *U* = 2355.1(5) Å<sup>3</sup>, space group *P*12<sub>1</sub>1, *Z* = 2, *D*<sub>c</sub> = 1.28 g cm<sup>-3</sup>, MACH3 Nonius, Mo-Kα, μ/mm<sup>-1</sup> = 0.248, 3435 data with *I* > 3σ(*I*), *R* = 0.037, *R*<sub>w</sub> = 0.047.

**6** (colorless, 173 K): C<sub>40</sub>H<sub>48</sub>O<sub>12</sub>S<sub>4</sub>, *M* = 849.08, tetragonal, *a* = 15.992(1), *b* = 15.992(1), *c* = 17.712(1) Å, *U* = 4529.7(8) Å<sup>3</sup>, space group *I*4<sub>1</sub>, *Z* = 4, *D*<sub>c</sub> = 1.24 g cm<sup>-3</sup>, Nonius CCD, Mo-Kα, μ/mm<sup>-1</sup> = 0.254, 1615 data with *I* > 3σ(*I*), *R* = 0.055, *R*<sub>w</sub> = 0.082. CCDC 182/856.

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