



Selective oxidation of thiacalix[4]arene (*cone*) to all corresponding sulfoxides



Jiří Mikšátko^a, Václav Eigner^b, Hana Dvořáková^c, Pavel Lhoták^{a,*}

^a Department of Organic Chemistry, University of Chemistry and Technology Prague (UCTP), Technická 5, 166 28 Prague 6, Czech Republic

^b Department of Solid State Chemistry, UCTP, Technická 5, 166 28 Prague 6, Czech Republic

^c Laboratory of NMR Spectroscopy, UCTP, Technická 5, 166 28 Prague 6, Czech Republic

ARTICLE INFO

Article history:

Received 17 June 2016

Revised 30 June 2016

Accepted 7 July 2016

Available online 9 July 2016

Keywords:

Thiacalixarene

Oxidation

Sulfoxide

Pinched cone

Conformation

ABSTRACT

An upper rim unsubstituted thiacalix[4]arene immobilised in the *cone* conformation was regioselectively oxidized to give all possible sulfoxide isomers using NaBO₃·4H₂O as the oxidizing reagent. Single crystal X-ray analysis undoubtedly assigned the stereochemistry of the sulfoxide group with the oxygen atom pointing toward the upper rim of the thiacalix[4]arene. As revealed by dynamic ¹H NMR, the presence of the sulfoxide groups has dramatic consequences on the conformational behavior of the thiacalix[4]arenes. Namely, that the number of sulfoxide groups is inversely proportional to the ΔG barrier of the *pinched cone*–*pinched cone* equilibrium as determined by ΔG values 45.4 kJ/mol for monosulfoxide **5** and ΔG <32 kJ/mol for tetrasulfoxide **9**.

© 2016 Elsevier Ltd. All rights reserved.

Introduction

Thiacalix[4]arene **1** emerged¹ as a novel member of the calix[*n*]arene² family two decades ago, and since then, this molecule has attracted considerable attention as a potential candidate for use as a novel building block and molecular scaffold. As recently reviewed,³ the introduction of sulfur atoms (instead of CH₂ groups) has a dramatic consequence on the complexation ability, amended conformational behavior and even substantially different chemistry compared with that of the classical (methylene-bridged) calixarenes. Consequently, some reactions which are virtually unknown and/or impossible in the chemistry of calix[4]arene have been reported for thiacalix[4]arenes, such as regio- and stereoselective S-alkylation to form sulfonium salts,⁴ or chemoselective S-oxidation to provide various sulfoxides or sulfones (Fig. 1).⁵

Thus, the extensive oxidation of parent thiacalixarene **1** (H₂O₂/TFA or NaBO₃/CHCl₃–AcOH) provides the corresponding tetrasulfone derivative **3** whereas an equivalent amount of oxidizing agent (NaBO₃) gives tetrasulfoxide **2**.⁶ While the oxidation of all bridging sulfur atoms in lower rim-unsubstituted or substituted⁷ thiacalix[4]arenes is well documented, regioselective partial oxidation of the individual bridges is still rare in the literature. In fact, only two compounds, thiacalix[4]arene fixed in the *cone* conformation

by four benzyl^{7b,8} or ethyl acetate⁹ groups, both possessing the *tert*-butyl groups on the upper rim, have been reported so far for selective partial oxidation. As the chemical and/or conformational behavior of thiacalixarene systems could be dramatically dependent on the upper rim substitution we postulated that the upper rim-unsubstituted thiacalix[4]arenes could also be selectively oxidized. In this Letter we report the regioselective oxidation of tetrapropoxythiacalix[4]arene **4**, immobilized in the *cone* conformation, leading to the formation of all possible sulfinyl derivatives. Based on dynamic NMR studies, these products show an interesting relationship between the number of sulfinyl groups and the conformational behavior of the macrocycles.

Results and discussion

Starting tetrapropoxythiacalixarene **4** (*cone*) was oxidized using various oxidizing agents. Thus, treatment with PCC provided monosulfinyl derivative **5** in acceptable yields, on the other hand, the same reagent used in excess (up to 40 equiv) always yielded a mixture of mono- and di-sulfinyl compounds **5–7** in various ratios. Similar reactivity was observed for 35% aqueous H₂O₂ in AcOH, again leading only to the less oxidized derivatives. The application of 100% HNO₃ in AcOH (successfully used for oxidation of the tetraester⁹) or NO₂⁺BF₄ gave very complex reaction mixtures where the oxidized products were always accompanied by unwanted nitration by-products. Finally, NaBO₃·4H₂O was selected

* Corresponding author. Tel.: +420 220445055; fax: +420 220444288.

E-mail address: lhotakp@vscht.cz (P. Lhoták).

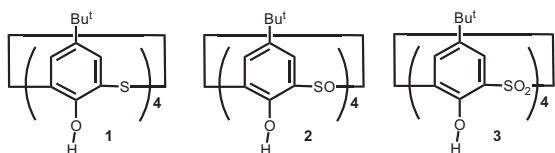


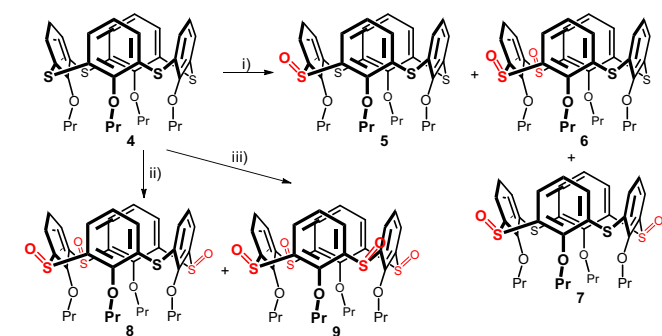
Figure 1. Structures of thiocalix[4]arene **1** and the corresponding sulfinyl and sulfonyl analogues **2** and **3**.

as the best choice which gave the corresponding sulfinyl calixarenes **5–9** depending on the stoichiometry (Scheme 1) without any signs of overoxidation to the sulfones. Heating of **4** in $\text{CHCl}_3/\text{AcOH}$ (60°C , 4 h) with 1.5 equiv of $\text{NaBO}_3 \cdot 4\text{H}_2\text{O}$ led to a mixture of mono- and di-oxidized products from which compounds **5**, **6**, and **7** were isolated¹⁰ using column chromatography on silica gel in 34%, 22%, and 16% yields, respectively. Similarly, application of 3 equiv of the oxidizing agent led to a mixture of tri- and tetrasulfinyl derivatives **8** and **9** in 44% and 14% yields, respectively.¹¹ Tetrasulfinyl derivative **9** was selectively produced in very high yield (88%)¹² using 4.0 equiv of $\text{NaBO}_3 \cdot 4\text{H}_2\text{O}$.

Theoretically, the oxygen atom of the sulfinyl group could come from either the upper rim or from the lower rim directions (Fig. 2). Under such circumstances, monosulfoxide **5** should possess two different orientations leading to two stereoisomers **5A** and **5B**. Similarly, distal disulfoxide **7** could form up to three stereoisomers **7A**, **7B**, and **7C**. These theoretical considerations were in stark contrast to the results of the oxidation reactions, where all regioisomers **5–9** were clearly isolated as single stereoisomers. This indicated that the oxidation of **4** follows the same trend as described in the literature^{7b,9} for upper rim-substituted *cone* thiocalix[4]arenes—the oxygen comes from the upper rim direction, probably to minimize stereo-electronic repulsion with the lower rim substituents, thus leading exclusively to stereoisomers of type **A** (Fig. 2).

The structures of the products were determined using a combination of HRMS ESI and NMR spectroscopy. The splitting pattern and multiplicity of the signals corresponded with proposed structures **5–9**. Thus, one type of propyl group in the ^1H NMR spectrum (1.03 (t), 1.85 (m) and 4.20 (t) ppm) together with one type of aromatic unit (7.23 (d), 7.15 (d), and 6.89 (t) ppm) and 9 signals in ^{13}C spectrum reflected the expected C_{2v} symmetry of distal isomer **7**. Similarly, the extremely simple ^1H and ^{13}C NMR spectra of **9**, possessing 5 and 7 signals, respectively, suggested the highest possible C_{4v} symmetry of this compound.

The stereochemistry on the sulfur atom was unequivocally assigned using single crystal X-ray analysis. Monosulfinyl derivative **5** crystallized in the monoclinic system, space group $\text{P}2_1/n$.¹³



Scheme 1. Reagents and conditions: (i) $\text{NaBO}_3 \cdot 4\text{H}_2\text{O}$ (1.5 equiv), $\text{CHCl}_3/\text{AcOH}$, 60°C , 4 h (34% **5**, 22% **6**, 18% **7**); (ii) $\text{NaBO}_3 \cdot 4\text{H}_2\text{O}$ (3 equiv), $\text{CHCl}_3/\text{AcOH}$, 60°C , overnight (44% **8**, 14% **9**); (iii) $\text{NaBO}_3 \cdot 4\text{H}_2\text{O}$ (4 equiv), $\text{CHCl}_3/\text{AcOH}$, 60°C , overnight (88% **9**).

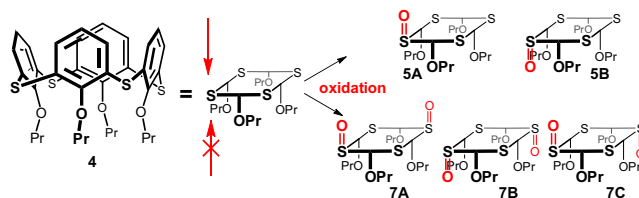


Figure 2. Stereoselectivity of the oxidation of thiocalix[4]arene **4**.

As shown in Figure 3a and b, the calixarene adopted a highly pronounced *pinched cone* conformation with two aromatic rings pointing outside the cavity (the corresponding interplanar angles Φ between the main plane of the macrocycle defined by the four S bridging atoms and the phenolic subunits were 135.22° and 145.16°). The other two phenolic rings were distinctly oriented into the cavity ($\Phi = 65.88^\circ$ and 80.09°). The oxygen atom of the sulfinyl group was clearly pointing toward the upper rim (Fig. 3a), thus confirming the proposed stereochemistry. All of the above mentioned structural features (monoclinic system, space group $\text{P}2_1/n$, $\Phi = 137.58^\circ$, 146.35° , 81.66° and 87.55°) including the stereochemistry was found also in tetrasulfinyl **9** (Fig. 3c and d).¹⁴

It is well known^{2,3} that the ^1H NMR spectra of calix[4]arenes or thiocalix[4]arenes, seemingly possessing the C_{4v} symmetry, are in fact time averaged signals of two other structures with lower C_{2v} symmetry, called *pinched cone* conformations, that are in rapid equilibrium under common conditions (Scheme 2). As a consequence, the ^1H NMR spectrum (300 MHz, CDCl_3) of starting compound **4** consisted of very broad signals¹⁵ at room temperature as the equilibrium is close to the coalescence temperature. Interestingly, the oxidation of the sulfur bridges led to a reasonable change in the *pinched cone–pinched cone* interconversion. While compound **5** still exhibited a distinctly broadened spectrum, particularly in the aromatic region, the introduction of additional sulfinyl groups (e.g., **7–9**) led to normally resolved sharp spectra.

To further the study we examined a possible relationship between the level of oxidation (number of sulfoxide groups) and the activation free energies (ΔG^\ddagger) of the corresponding *pinched cone–pinched cone* interconversion using dynamic NMR techniques. Temperature dependent ^1H NMR measurements in the temperature range of 148 K (resp. 173 K, 183 K)–298 K in CD_2Cl_2

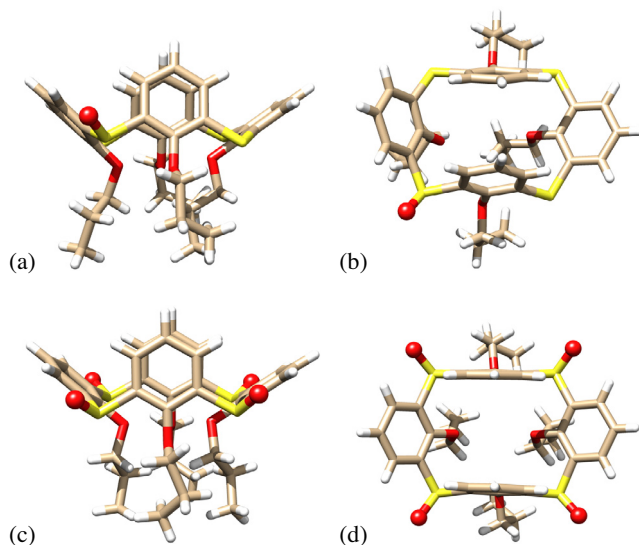


Figure 3. Single crystal X-ray structures of: (a) compound **5** side view, (b) compound **5** top view, (c) compound **9** side view, (d) compound **9** top view.

Download English Version:

<https://daneshyari.com/en/article/5260516>

Download Persian Version:

<https://daneshyari.com/article/5260516>

[Daneshyari.com](https://daneshyari.com)