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The first approach to a new family of macrocycles: synthesis and characterization of thiacalix[2]thianthrenes

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The Letter is dedicated to the memory of Dr. J. M. Létoffé and Dr. B. Bonnetot

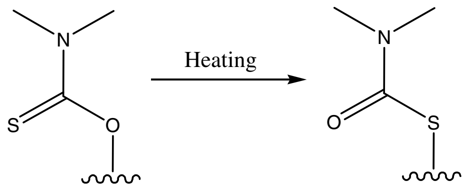
Abstract—New thianthrene based macrocycles with basket shaped structures were prepared by thermal treatment of tetrakis-(N,N'-dimethylthiocarbamoyl)-tetra-*tert*-butyl-thiacalix[4]arene. Their structural characterization as well as the study of the formation mechanisms are presented in this article. The influence of the conformation of the starting thiacalixarene on the reaction is also discussed.

1. Introduction

The field of calixarene chemistry has been strongly developed through the last decade for a wide range of applications, for example, extraction processes, material science or biomedical developments.[1] We have been interested in the chemistry of their homologue thiacalixarene for use in optical materials or coordination chemistry due to very unique properties and highly coordinating ability of these macrocycles.[2–7] On the other hand, thianthrene derivatives were mentioned to be very interesting candidates for a wide variety of applications in pharmacology,[8] material chemistry (conducting and luminescent polymers,[9,10] liquid crystals[11]), synthesis of dyes,[12] polymers or lubricants,[13] photopolymerization initiator (catalysis).[14] Introduction of thianthrene cores in macrocycles can thus appear as an interesting alternative to improve the overall properties of the molecular platform and its derivatives. We describe in this Letter the first synthesis of a new macrocycle, that we have called the thiacalix[2]thianthrene referring to both thiacalixarene and thianthrene cores, which are combined in the same molecular unit.

With the aim to understand the chemistry of thiacalixarenes, we have been studying in detail the thermal rearrangement of *O*-thiocarbamoyl derivative into the *S*-thiocarbamoyl species used as an intermediate to the formation of mercaptothiacalixarenes, where the OH groups are replaced by SH groups following the Newman–Kwart method (Scheme 1).[15,16] This method has been used for the preparation of SH substituted calixarenes and thiacalixarenes.[17,18]

Slight differences were noticed by the authors between the two rearrangements, depending on whether the macrocycle is a calixarene or a thiacalixarene, in particular concerning the temperature, which is necessary for the reaction. We have thus decided to conduct thermal investigations on the mechanisms using DSC and TGA techniques. The DSC experiments performed on the *O*-thiocarbamoyl derivative (Fig. 1) showed three signals, at 270 °C, 330 °C and 390 °C. According to



Scheme 1. Newman–Kwart method for converting phenols to thiophenols.

Keywords: Thianthrene; Macrocycle; Thiacalixarene; Newman–Kwart rearrangement.

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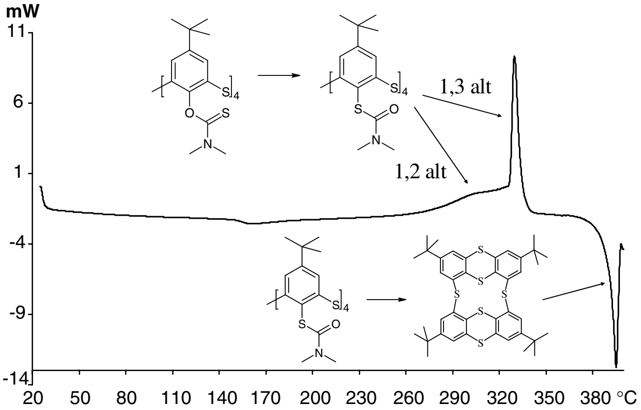


Figure 1. DSC experiment on the *O*-thiocarbamoyl derivative used as starting material.

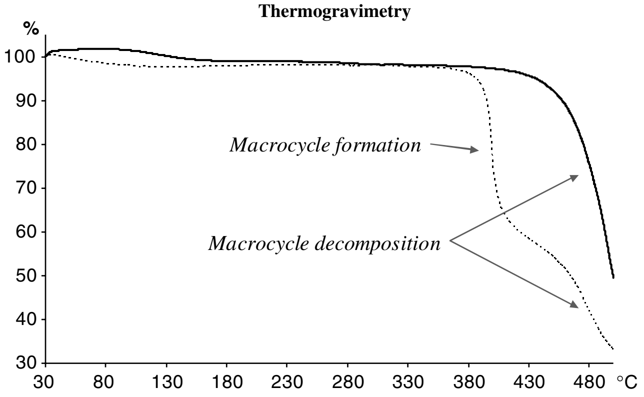


Figure 3. TGA analysis on both the starting thiacalixarene (**2a**) (dashed line) and the thiacalixthianthrene (**4a**) (continuous line).

the temperatures given in the literature, the first two exothermic peaks could be attributed to the rearrangement reactions. Since the starting material presents a mixture of conformers, 1,2- and 1,3-alternate, we assume, that the peaks at 270 °C and 330 °C can be assigned to the rearrangement of the two mentioned conformers, respectively. This was confirmed by a second experiment, performed with a mixture of the two conformers with inverted ratio, with a majority of 1,2-alternate (Fig. 2). A third DSC experiment was performed on the pure isolated *S*-carbamoyl derivative, which indicated no rearrangement peak. The thermogram showed only the last peak at 380 °C, as expected. TGA analysis was performed in the temperature range 30°C–500 °C under the same experimental conditions as the DSC (Fig. 3). No changes were observed up to 380 °C, since the rearrangement does not lead to weight loss. However, at 380 °C, exactly the same temperature as of the process observed by DSC, a weight loss of approximately 40% occurred. A second reaction was then observed at 430 °C leading to over 70% weight loss, probably due to the decomposition of the compound. Based on these observations, the reaction was realized in glassware in a large scale at 380 °C and the crude product was extracted with chloroform and purified to obtain single crystals of the first tetra *tert*-butylthiacalix[2]thianthrene derivative (**1**).

The Newman–Kwart rearrangement was initially used for the preparation of aromatic thiols, but formation of cyclization by-products was also observed.[19,20] It was found later that the reaction conditions could be optimized in order to produce the derivatives issued from cyclization as principal products. This reaction has found some applications in synthesis (Scheme 2).[21–26] However, applications were limited only to the formation of 5-membered rings—thiophene systems.

The optimized synthesis was achieved starting from tetra-*tert*-butylthiacalix[4]arene (**1a**) (Scheme 3) or its de-*tert*-butylated analogue (**1b**).[27,28] The *O*-thiocarbamoyl derivatives (**2**) were prepared according to the literature method.[29] The *S*-thiocarbamoyl derivative (**3**) could be prepared practically in quantitative yield upon heating compound (**2**) up to 290 °C for 2 h under vacuum. When heating up to higher temperature (410 °C) for approximately 5 min, the intended thianthrene derivative (**4**) was obtained. Longer heating times led to the formation of more insoluble polymers with lower yields.

The temperature to obtain the cyclization products (**4**) is higher than the temperature reported for synthesis of thiophenes ($\sim$300 °C). This is, to our opinion, due to the bonding strain, imposed on this relatively rigid molecule, or by more difficult formation of the six membered ring, or finally a combination of the two factors. This

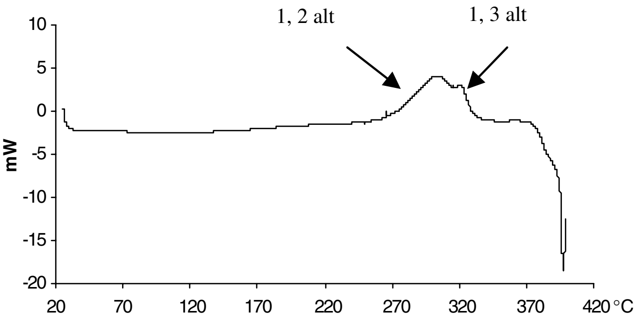
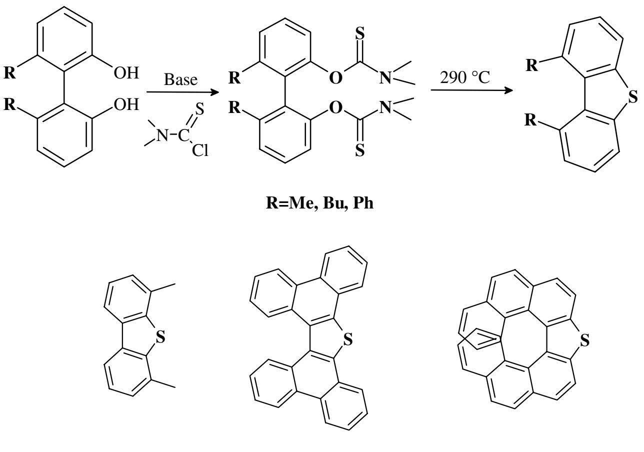
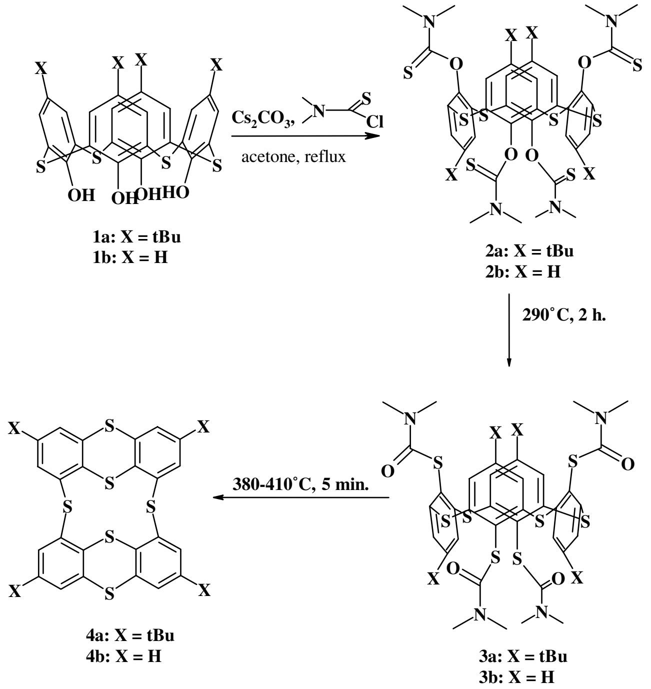


Figure 2. DSC experiment on a mixture of the two conformers with a high ratio of 1,2-alternate and some residual 1,3-alternate conformer.



Scheme 2. Synthesis of dibenzothiophene derivatives by Newman–Kwart reaction and examples of derivatives prepared using this method.



Scheme 3. Synthesis of thianthrene based macrocycle by Newman–Kwart method.

synthesis also represents, to the best of our knowledge, the first example for the formation of six membered ring by the Newman–Kwart rearrangement, as well as a new approach to the synthesis of thianthrenes.

The new macrocycle (**4a**) consists of two moieties of thianthrene, which are connected by two sulfur bridges and possesses concave cavity, resembling to somewhat flattened cone conformation of the calixarenes (Figs. 4 and 5). The structure is strongly stabilized and rigidified compared to the calixarene species. Thiacalix[2]thianthrene can be also considered to be a derivative of tetrabenzo-12-crown-4-thioether with two additional sulfur bridges, considerably decreasing the symmetry of this molecule. The molecule possesses three non-equivalent sulfur bridges, suggesting the possibility of selective oxidation to sulfoxides and sulfones or even radicals stabilized through charge delocalization over the thianthrene units, as well as three non-equivalent positions at the benzene rings, offering many possibilities of substitution. The macrocycle was characterized by NMR spectrometry, elemental analysis, mass spectrometry and the solid-state structure was determined using single crystal X-ray diffraction.[30] The structure of the macrocycle (**4a**) is blocked in the cone conformation by two external sulfur bridges (Figs. 4–6). All the sulfur bridges stand on the same side of the macrocycle core, pointing outside the cavity.

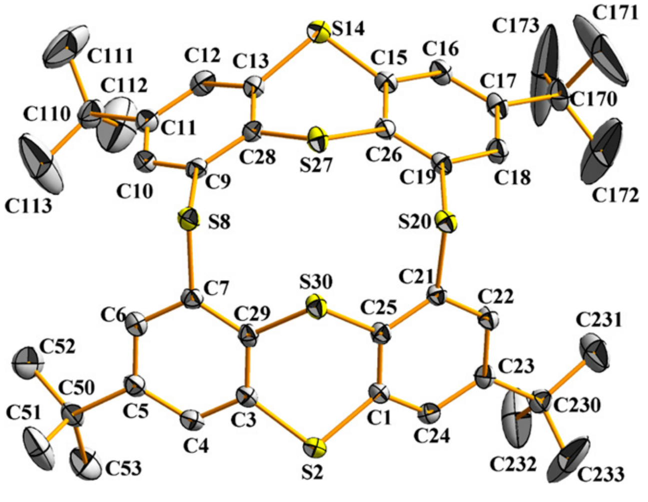


Figure 4. X-ray structure of (**4a**).

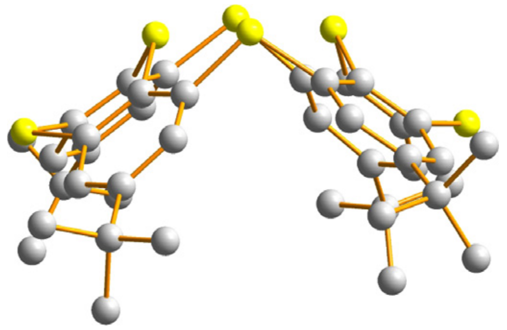


Figure 5. Side view for the structure of compound (**4a**).

The overall structure of (**4a**) can be considered as a rigid semi-spherical entity. The macrocycle (**4a**) was reproducibly synthesized from tetra-*tert*-butylthiacalix[4]arene in overall yield around 33%. Functionalization of such macrocycle would open a wide range of opportunities to chemists and materials scientists for the applications in coordination chemistry, optics, medicine and so on. We have also prepared compound (**4b**), which should be a suitable starting material for the preparation of substituted thiacalixthianthrenes. The de-*tert*-butylation was achieved either prior to the thermal Newman–Kwart reaction or after the formation of the thianthrene product (Scheme 4).

The structure of compound (**4b**) was also solved using single crystal X-ray diffraction.[30] The conformation and the core of the macrocycle is very similar to the cone conformation found in compound (**4a**) (Figs. 7 and 8).

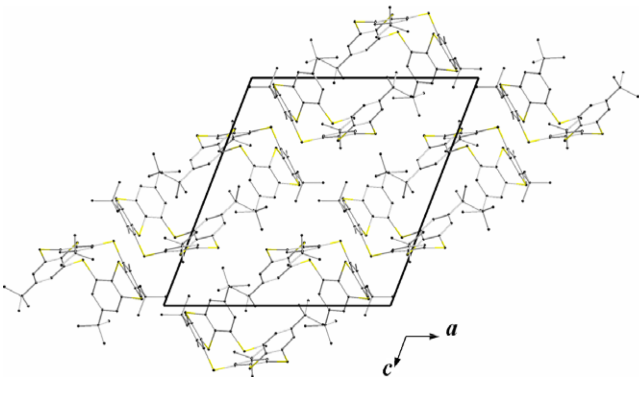
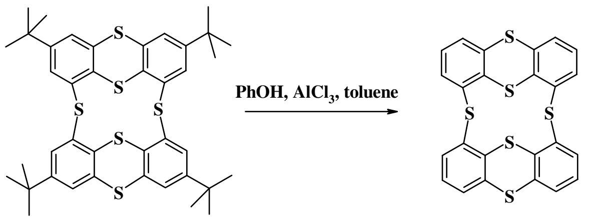


Figure 6. Packing view for the structure of (**4a**).



Scheme 4. Alternative synthesis of compound (**4b**).

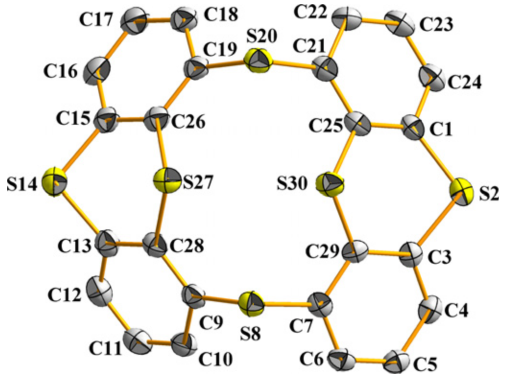


Figure 7. X-ray structure of (**4b**).

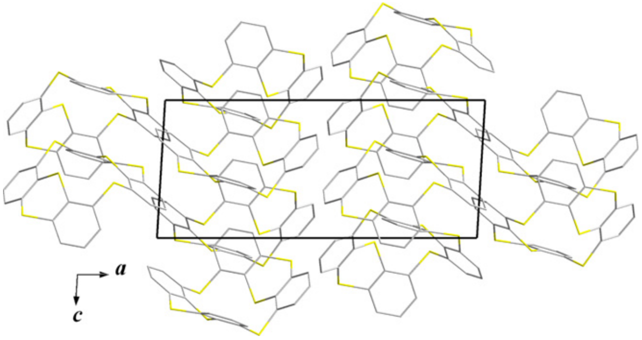


Figure 8. Packing view for the structure of (**4b**).

The main differences arise when looking at the packing of the two macrocycles. In compound (**4a**), the macrocycles lay face to face, thus forming an arrangement of 'dimeric' units (Fig. 6). On the other hand, in compound (**4b**), the molecules pack along the *c* axis of the unit-cell giving rise to one-dimensional chains (Fig. 8). These chains are then organized head to tail in respect to each other. The difference in the packing of the two compounds lead to a much higher packing index for compound (**4a**) (63.4%) than for compound (**4b**) (72.2%).[31]

In conclusion, thiacalixarenes have attracted attention of scientists because of their wide range of applications in particular to material and molecular material science. On the other side thianthrenes were shown to be promising candidates in molecular chemistry and material sciences, biology, pharmacology, for the production of dyes, polymers, photoactive molecules, catalysts, lubricants etc. We believe that the combination of those properties of thianthrene with macrocyclic, cone shaped structure and good thermal stability can be fruitful in supramolecular and material chemistry, for example, for the design of molecules with non-linear optical properties, electrochromic or luminescent molecules, as well as switchable receptors in molecular recognition etc. Research on the chemical modifications of sulfur bridges and aromatic rings of this new macrocycle, structural aspects and electronic properties as well as investigation on electrochemical and complexation properties are underway in our laboratory and will be the scope of the next articles.

2. Synthesis

Starting materials (**1a**), (**1b**), (**2a**) were synthesized according to the literature method.[27–29]

2.1. Synthesis of the *O*-carbamate derived thiacalixarene (2b)

To a dispersion of 2 g (4.03 mmol) of thiacalixarene (**1b**) in acetone, 2.98 g (24.16 mmol) of $(CH_3)_2NCSCl$ were added, followed by 7.84 g (24.16 mmol) of Cs_2CO_3. The reaction mixture was stirred at 50 °C for two days, then acetone was evaporated. The residue was dissolved in 50 mL of 1 M HCl and 50 mL of dichloromethane. The organic layer was separated and the water phase was extracted three times with chloroform. The organic phase was dried over $MgSO_4$, filtered and concentrated by evaporation under reduced pressure. The compound was precipitated by slow addition of methanol to the solution. After filtration, 0.5 g (15%) of the pure product was isolated.

^1H NMR ($CDCl_3$, TMS, 300 MHz) in ppm: 7.46 (8 H, d, $J = 8.0$ Hz, Ar-H), 6.99 (4H, t, $J = 8.0$ Hz, Ar-H), 3.4 (12H, s, N–CH_3), 2.39 (12H, s, N–CH_3).

2.2. Synthesis of the tetra-*tert*-butylthiacalix[2]thianthrene (4a)

Five grams of the starting material (**2a**) were placed into a Schlenk tube and heated up to 410 °C under air for approx. 3 min (until all the starting material was converted into dark boiling liquid). Then it was allowed to cool down to room temperature and the resulting black mass was dissolved in 60 mL of chloroform. The solution was filtered, concentrated under vacuum and precipitated with methanol. The precipitate was washed abundantly first with acetone and then with diethyl ether. The crude product was finally purified by filtration through silica gel column using a mixture of chloroform and cyclohexane 1:1 as eluent. 1.2 g (36%) of product in a form of white powder was obtained.

^1H NMR ($CDCl_3$, 300 MHz): 7.73 (4H, d, $J = 1.8$ Hz, Ar-H), 7.46 (4H, d, $J = 1.8$ Hz, Ar-H), 1.26 (36H, s, tBu). Elemental analysis, element % found (% calculated): C, 64.91 (64.37); H, 6.84 (6.41); S, 24.02 (24.54). MS (ESI): calculated: 716.17, found: 717.2 (MH^+).

2.3. Synthesis of the thiacalix[2]thianthrene (4b)

Method A: 150 mg (0.2788 mmol) of starting material (**4a**) were suspended in 30 mL of toluene, 0.3 g (3.067 mmol) of phenol and cautiously 1.3 g (10.0 mmol) of $AlCl_3$ were added upon vigorous stirring. The mixture was then refluxed for 48 h. The black solution was let to cool down to room temperature and then it was poured cautiously in 200 mL of water. After stirring for 2 h, the organic layer was separated. Approximately three quarters of the toluene were distilled off and methanol was added. After stirring for 1 h, the suspension was filtered. The residue was washed with methanol and acetone. The product was obtained as a beige powder (40 mg, 40% yield).

Method B: 100 mg of compound (**3b**) was introduced in a crucible, which was placed in a tubular furnace. Then it was heated under argon in the following way: heating up to 310 °C for 120 min, dwell at 380 °C for 20 h. 38 mg of dark solid was obtained. It was purified through column chromatography using chloroform and petroleum ether mixture 3:7 to afford 26 mg (44%) of product.

^{1}H NMR ($CDCl_3$, TMS, 300 MHz) in ppm: 7.65 (4H, dd, $J = 7.8$ Hz, $J = 1.5$ Hz, Ar-H), 7.49 (4H, dd, $J = 7.8$ Hz, $J = 1.5$ Hz, Ar-H), 7.19 (4H, t, $J = 7.8$ Hz, Ar-H). MS (ESI): calculated: 491.92, found: 493.0 (MH$^+$).

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Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.tetlet.2007.06.006.

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