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Synthesis and Structural Characterization of an S-linked Calix[3]azine

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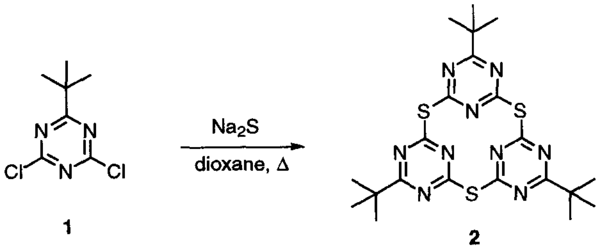
Abstract: An S-linked, heterocyclic calix[3]arene analogue **2** is prepared by condensation of a dichloro-1,3,5-triazine with sulfide ion. X-ray structural analysis shows that **2** is approximately disk shaped in the solid state, while molecular modelling indicates a high degree of conformational mobility.

The enormous interest in the host-guest properties of calixarenes has stimulated efforts to synthesize analogous structures with aromatic constituents other than benzene and/or linking atoms other than carbon. For example, calix[n]furans, -pyrroles, -thiophenes, and -indoles have been described,[1-4] as well as calixarene homologs linked by N, O, or S atoms.[5,6] We now report the preparation and crystal structure determination of a molecule in which three 1,3,5-triazine rings are bridged by sulfur; a calix[3]triazine **2**. 'Calixazines' with their electron deficient cavities are of potential interest as electronic complements to the π-basic calixarenes, and might include electron rich species where the calixarenes themselves tend to interact more effectively with electron deficient ones. The synthetic approach to molecules such as these is also fundamentally different from that of phenol-formaldehyde condensation chemistry.

It is for the above reasons we were most interested to encounter some early work containing speculation that cyclic S-linked 1,3,5-triazine oligomers were being observed during polymerization reactions between chlorotriazines and triazinethiones.[7] Unfortunately, the products were only characterised by microanalysis and eubullioscopic mass determinations. We therefore set out to reproduce some of this chemistry and look for evidence of macrocyclic species with the benefit of modern analytical techniques.

Reaction of 2,4-dichloro-6-phenyl-1,3,5-triazine with Na_2S as described[7b] gave a mixture of oligomeric materials of uncertain composition whose isolation was hampered by poor solubility. We therefore quickly abandoned the original work in favour of incorporating a calixarene-analogous tertiary butyl group into the system. The revised synthesis (Scheme 1) provided a cyclic trimer **2** in 90% yield,[8] with no evidence of a tetramer or any other higher oligomer being found.[9]



Scheme 1

Single crystals of **2** could be grown from diethyl ether solution and X-ray analysis[10] revealed the structure shown in Figure 1. The molecule is surprisingly flat, with the triazine rings inclined +3.4, +16.3 and -32.1° to the plane of the three sulfur atoms. The three nitrogen atoms are within each other's van der Waals radii, the N···N distances being between 2.73 and 2.79 Å, and each triazine ring participates in π-stacking interactions with neighboring molecules. Although no cavity is defined, modelling[11] shows that only 4.0 kJ mol^{-1} separate the minimum energy structure (a partial cone), and the cone conformer.

Easily accessible molecules such as **2** and related heteroatom-linked calix[n]azines, with conformational behavior similar to the calixarenes but their own unique functionality/reactivity, should prove worthwhile targets for future investigation.

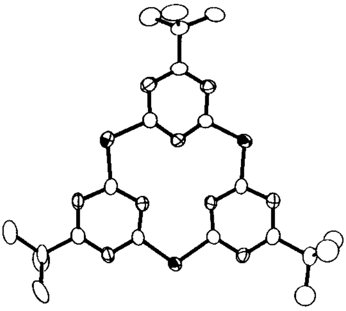


Figure 1

References and Notes

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8. Compound **2**: To a solution of 2,4-dichloro-6-*tert*-butyl-1,3,5-triazine (**1**) (5.36 g, 26.0 mmol) in refluxing dioxane (600 ml) was added dropwise over a 90 min period a solution of sodium sulfide nonahydrate (6.00 g, 25.0 mmol) in water (17 ml). After the addition was complete, the mixture was heated at reflux for an additional 48 h. The solvent was evaporated and the crude product was chromatographed on silica gel (5:1 petroleum ether - ether) to give the trimer **2** (3.91 g, 90 %) as colorless, fibrous crystals, m.p. 200-205 °C; δ_H (400 MHz, $CDCl_3$) 1.36 (s); δ_C (100 MHz, $CDCl_3$) 28.5, 39.6, 176.5, 185.1; *m/z* (EI) 501 (M^+, 30%), 486 (100).
9. This is in contrast to the original work (ref. 7), where the existence of both a cyclic trimer and tetramer is implied.
10. Crystal data: $C_{21}H_{27}N_9S_3$, M = 501.70, monoclinic, a = 12.925(6), b = 21.505(5), c = 10.404(4) Å, ß = 111.83(3)°, V = 2647.0(9) Å^3, space group $P2_1/c$, $Z = 4$, D_x = 1.259 g cm^{-3}, colorless lath 0.59 x 0.19 x 0.09 mm, μ(Mo-K_α) = 0.307 mm^{-1}. A total of 4865 data ($2\theta_{max}$ = 50°) were collected at 297 K using graphite-monochromated Mo-K_α *X*-radiation (λ = 0.71073 A). Merging gave 4522 unique data [merging $R = 0.126$], of which 2586 had $F \geq 4\sigma(F)$ and all 4522 were retained in subsequent calculations. The structure was solved by direct methods (*SHELXS*-86) and refined (*SHELXL*-93) on F^2 with all non-H atoms anisotropic; hydrogen atoms were introduced at geometrically-calculated positions and thereafter allowed to ride on their parent C atoms with $U_{iso}(H) = 1.5U_{eq}(C)$. Disorder in one *tert*-butyl group was identified and modelled, with alternative, equally-populated orientations for its methyl groups. The weighting scheme $w^{-1} = [\sigma^2(F_o^2) + (0.023P)^2 + 11.10P]$, $P = {}^1/_3[MAX(F_o^2,0) + 2F_c^2]$, gave satisfactory agreement analyses. Final R_1 [$F \geq 4\sigma(F)$] = 0.106, wR_2 [all data] = 0.230, $S[F^2]$ = 1.23 for 296 refined parameters. The somewhat high value for R_1 is attributed to residual disorder but the final Δ*F* synthesis showed no features more significant than ±0.34 *e*Å^{-3}.
11. Monte-Carlo simulation in MACROMODEL, version 4.0 (Mohamadi, F.; Richards, N. G. J.; Guida, W. C.; Liskamp, R.; Lipton, M.; Caufield, C.; Chang, G.; Hendrickson, T.; Still, W. C. *J. Comp. Chem.*, **1990**, *11*, 440) with the MM3 force field.

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