On the selective deprotection of cyanoethyl-protected tetrathiafulvalene thiolates

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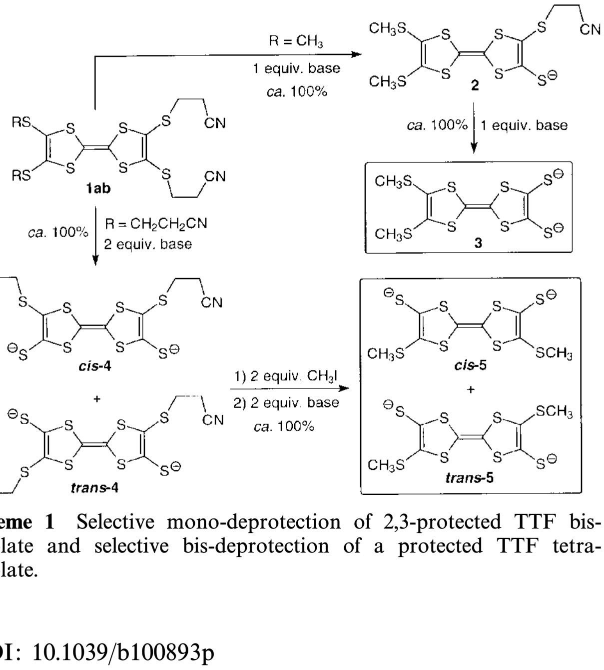
The selective deprotection protocol of cyanoethyl-protected tetrathiafulvalene thiolates is explained by DFT calculations on isomeric dithiolates; the minimum energy conformation of the 2,3-dithiolate (**3**) is non-planar and lies 34.6 kcal mol^{-1} higher in energy than that of the 2,6-dithiolate (*trans*-**5**).

The development of a number of synthetic strategies has allowed the ready incorporation of the π-donor tetrathiafulvalene (TTF) into macrocyclic[1] as well as oligomeric and dendritic systems.[2] One major breakthrough in synthetic TTF chemistry occurred with the discovery of cyanoethyl as a protecting group for TTF thiolates by Becher and coworkers.[3] Stepwise deprotection/realkylation protocols were developed and exploited for the incorporation of TTF into many different molecular structures, of which some have found interesting uses in supramolecular chemistry.[4]

Thus, treating 2,3-bis(2-cyanoethylthio)-6,7-bis(methylthio)-tetrathiafulvalene (**1a**, R = CH_3) with one equivalent of base results in elimination of one cyanoethyl protecting group generating the monothiolate **2**, which is converted into the bisthiolate **3** upon treatment with another equivalent of base (Scheme 1). The same ability to discriminate between neighbouring cyanoethyl groups was observed in the formation of an isomeric mixture of *cis*-**4** and *trans*-**4** (*ca.* 1 : 1), from deprotection of tetrakis(2-cyanoethylthio)tetrathiafulvalene (**1b**, R = CH_2CH_2CN), when adding only two equivalents of base. This strategy was employed successfully for the construction of ribbon-like macrocycles.[1,5] Subsequent alkylation with methyl iodide followed by deprotection of the two remaining thiolates affords *cis*-**5** and *trans*-**5**. In order to explain the observed selectivities on a firm basis, we decided to carry out calculations for the three dithiolate isomers **3**, *cis*-**5** and *trans*-**5**.



Scheme 1 Selective mono-deprotection of 2,3-protected TTF bisthiolate and selective bis-deprotection of a protected TTF tetrathiolate.

Calculations

Density functional theory (DFT) and Hartree–Fock (HF) calculations were performed with the GAUSSIAN 98 program package at the B3LYP/6-311++G(2d,p)//HF/6-31+G(d) level of theory.[6] It is essential to include diffuse functions in the basis set for anions and sulfur-containing molecules, and we have therefore used the 6-31+G(d) basis set for geometry optimisation, earlier employed by Gronert[7] in a computational study on dianions.[8] In order to confirm that the obtained stationary point of each isomer corresponded to a minimum on the potential energy surface, a vibrational analysis was carried out which showed no negative frequencies. Subsequently, a single point energy calculation was performed at a much higher theoretical level (containing more polarisation functions in the basis set together with diffuse functions on both heavy and hydrogen atoms), B3LYP/6-311++G(2d,p), and corrected for zero-point motion [employing the HF/6-31+G(d) frequencies]. Since we are comparing relative energies of similar isomers (**3**, *cis*-**5** and *trans*-**5**), any systematic errors in our computational method are likely to cancel out.

Results and discussion

The calculated results are collected in Table 1. It is evident that the energies of *cis*-**5** and *trans*-**5** are almost identical whereas the energy of the 2,3-dithiolate **3** is considerably higher, by 34.6 kcal mol^{-1} relative to *trans*-**5**; that is, reducing the distance from 9.9/9.3 Å (*trans*-**5**/*cis*-**5**) to 3.7 Å (**3**) between the two negatively charged sulfurs on the TTF core results in a significant increase in the energy. Hence, the calculated energies clarify the experimental selectivities: 2,7- (*cis*) and 2,6-(*trans*) dithiolates are preferentially formed from **1** (R = CH_2CH_2CN) rather than the 2,3-dithiolate, but no discrimination exists between the *cis* and *trans* isomers.

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Table 1 Total energies, zero-point kinetic energies (ZKEs), relative energies corrected for zero-point motion, together with the thiolate–thiolate distances (r) and the purely electrostatic (ES) relative energies between two charges in a vacuum separated by a distance r. Computational level: B3LYP/6-311++G(2d,p)//HF/6-31+G(d)

	trans-**5**	*cis*-**5**	**3**
Energy/hartrees	−3494.3203	−3494.3201	−3494.2651
ZKE/hartrees	0.1298	0.1298	0.1297
Relative energy/kcal mol^{-1}	0	0.13	34.6
$r(S^{-}\cdots S^{-})$/Å	9.9	9.3	3.7
Relative ES energy/kcal mol^{-1}	0	2.16	56.2

From the obtained sulfur–sulfur distances (r), the purely electrostatic relative energies were calculated, assuming the negative charges to be localised on the two sulfur centers with a vacuum in-between (Table 1). Comparison of the actual energy differences, which are lower than the purely electrostatic ones, reveals a significant delocalisation of the negative charges within the molecules.

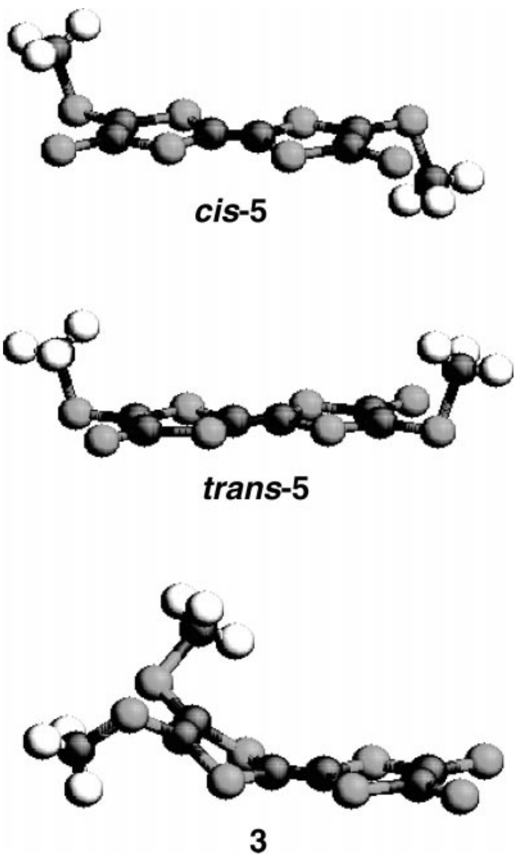

Fig. 1 Optimised structures (HF/6-31+G(d)).

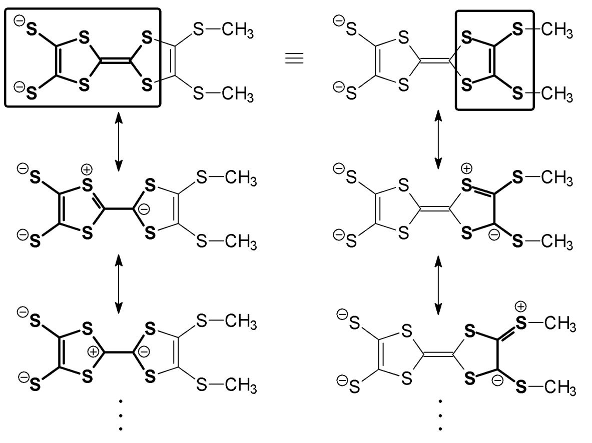

Fig. 2 Some of the possible resonance formulae within the two planes of **3**.

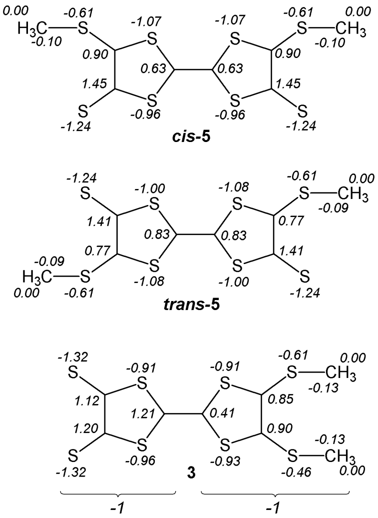

Fig. 3 Mulliken charge analysis of the three isomers.

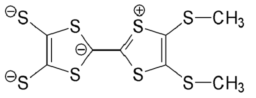

Fig. 4 Unfavorable direction of charge delocalisation in **3**.

Now we consider in more detail the differences between the three isomers with respect to their conformations and charge distributions. In contrast to the optimised structures of *cis*-**5** and *trans*-**5**, the TTF core of **3** is not completely planar. Actually, the 1,4-dithiole ring containing the two SCH_3 substituents is bent with an angle of 28° to the rest of the core (Fig. 1). This non-planarity may at first sight seem surprising but can be understood by considering the resonance forms of **3** (Fig. 2). In order to spread out the two negative charges, electron delocalisation from the thiolate-bearing dithiole ring to the SCH_3-bearing dithiole ring is likely to occur. Indeed, a Mulliken charge analysis shows that each dithiole ring does in fact contain a total charge of −1 in all three isomers (Fig. 3). Charge delocalisation along the central fulvene bond in the direction from the SCH_3-bearing dithiole ring of **3** to the thiolate-bearing dithiole ring is very unfavourable on account of the two negative charges already present in this part of the molecule (Fig. 4). In the absence of π-delocalisation within the whole SCH_3-bearing dithiole ring, the $(H_3CS)C{=}C(SCH_3)$ unit is no longer restricted to the plane of the central fulvene bond. Consequently, a non-planar conformation is adopted.

In conclusion, the stepwise deprotection protocol for cyanoethyl-protected TTF thiolates can be explained by the unfavorable Coulomb repulsion between negatively charged thiolate groups on the same dithiole ring which forces, by charge delocalisation, the other dithiole ring to adopt a non-planar conformation.

Acknowledgements

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