Caesium Tetrathiafulvalene-thiolates: Key Synthetic Intermediates

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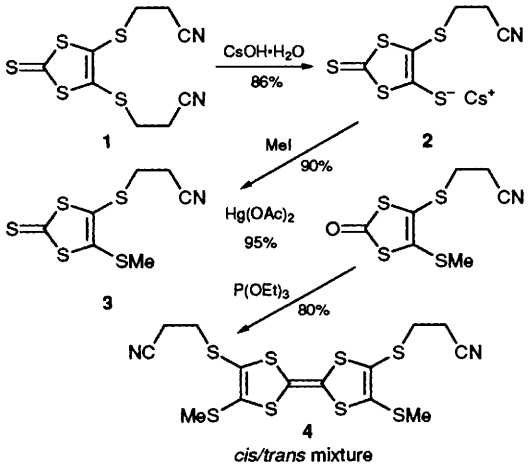
Treatment of cyanoethylated tetrathiafulvalene-thiolates or cyanoethylated 1,3-dithiole-2-thione-4,5-dithiolate with one equiv. of caesium hydroxide hydrate selectively and in high yield produces the corresponding monocaesium salts, which can subsequently be alkylated.

The development of synthetic methodologies for the synthesis of functionalised tetrathiafulvalenes[1] has largely been stimulated by the search for new tetrathiafulvalene-based organic metals.[2] Furthermore, there has recently been a steadily increasing interest in incorporating the tetrathiafulvalene into macrocyclic and supramolecular compounds,[3] but the lack of an easily functionalisable tetrathiafulvalene derivative has severely restricted the speed of progress in this area.

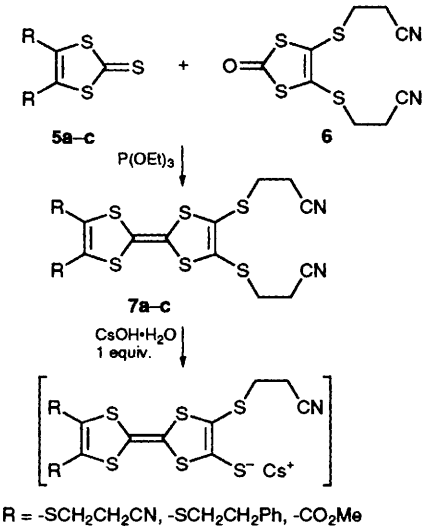
Structurally modified tetrathiafulvalenes have been synthesised employing two different synthetic strategies: (i) coupling of the corresponding 1,3-dithiole derivatives (1,3-dithiole-2-thiones or 1,3-dithiolium salts) to form the central double bond in the last step;[1] or (ii) lithiation of a pre-formed tetrathiafulvalene, followed by reaction with an electrophile.[4] The 1,3-dithiole route is easier to carry out on a synthetically useful scale, but it involves more steps than the lithiation route, and a number of substituents are incompatible with the coupling reagents. The lithiation route, on the other hand, offers a one-step synthesis of a highly functionalised tetrathiafulvalene, but is of limited preparative use due to the high price of TTF.

A third synthetic route, which combines the advantages of the two traditional routes, offers itself as the optimal way of incorporating tetrathiafulvalenes into larger assemblies: deprotection of a preformed tetrathiafulvalene-thiolate protected with the 2-cyanoethyl group. We have previously demonstrated[5] that 2,3,6,7-tetrakis(2′-cyanoethylthio)tetrathiafulvalene, which is easily prepared in a few steps, can be deprotected under mild conditions, and realkylated with a variety of alkylating agents.

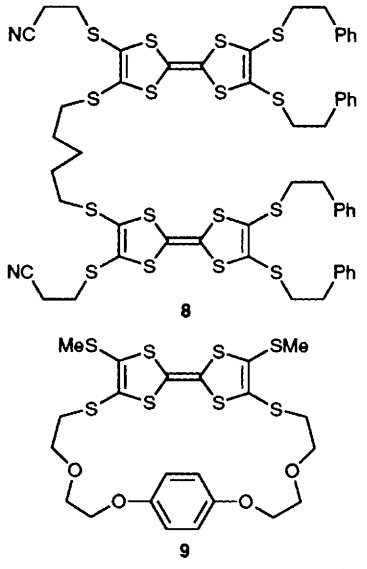
One thing remains, however: the ability to synthesize disubstituted tetrathiafulvalenes in a selective fashion. Most building blocks for macrocyclic compounds—such as hydroquinone, the bipyridines and the ethylene glycols—are divalent by nature[6] (that is, they have two reactive 'handles'), while tetrathiafulvalene is tetravalent. This challenge has now been met as follows.



Scheme 1 Synthesis of a bisprotected TTF-dithiolate



Scheme 2 Synthesis of asymmetric bisprotected TTF-dithiolates



Scheme 3 Macromolecules prepared from the synthons described; compound **9** is obtained from the mixture of *cis/trans* isomers by chromatography

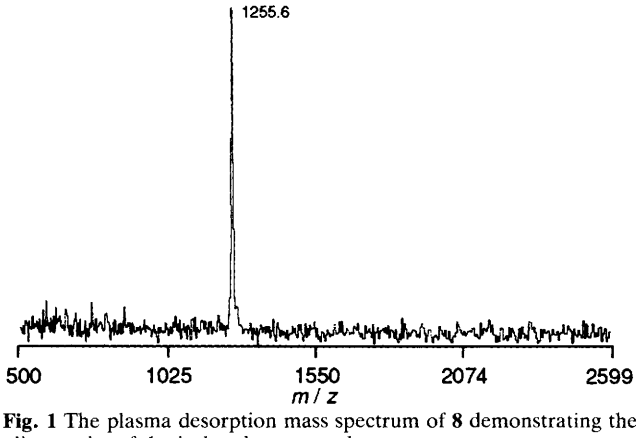


Fig. 1 The plasma desorption mass spectrum of **8** demonstrating the oligo-purity of the isolated compound

Treatment of a chloroform solution of 4,5-bis(2′-cyanoethylthio)-1,3-dithiole-2-thione **1** with one equiv. of caesium hydroxide hydrate in methanol selectively generates the monocaesium salt **2**, which precipitates from the reaction mixture in near quantitative yield.[7] This compound is considerably more stable than the corresponding dicaesium salt,[8]‡—it can be stored for several months, and provides a useful precursor to asymmetrically substituted 1,3-dithiole-2-thiones. The monocaesium salt is easily alkylated in acetone solution, *e.g.* with methyl iodide to give **3**, which after *trans*-chalcogenation and coupling in neat triethyl phosphite afforded tetrathiafulvalene **4** as a mixture of isomers (Scheme 1).

This strategy could be further extended to diprotected TTFs, in which the two thiolate functions were situated on the same dithiole ring of the TTF moiety. These asymmetric TTFs were synthesised by standard procedures, by cross-coupling of the bis-protected 1,3-dithiole-2-one **6** with 1,3-dithiole-2-thiones **5a–c** (Scheme 2).

Using **4** or **7** as starting materials, it is now possible to assemble macrocyclic or multi-tetrathiafulvalene systems by a specific route, as opposed to the previously employed statistical methods. Thus, deprotection of **4** or **7** using one or two equivs. of caesium hydroxide, followed by realkylation with various bisalkylating agents provides easy access to such relatively complex molecules as **8** and **9**, providing a convincing demonstration of the synthetic utility of the caesium tetrathiafulvalene-thiolate salts.§

As we have demonstrated in this communication, we have developed a set of potentially very versatile building blocks for the incorporation of tetrathiafulvalenes into macrocyclic and supramolecular assemblies.

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Footnotes

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‡ Of the lithium, sodium, potassium and caesium salts of 1,3-dithiol-2-thione-4,5-thiolate, only the caesium salt can be manipulated in air, although the sodium and potassium salts can be isolated using Schlenck techniques. The tetrabutylammonium salt is also quite air-stable, and consequently the van der Waals radius of the countercation seems to be the determining factor, rather than electronegativity considerations. It is, however, advantageous to use caesium as the cation, because alkylations of the caesium salts proceed very cleanly, and because it enables the exploitation of the controversial *caesium effect* in macrocyclic synthesis.

§ All new compounds were characterised using NMR (^{1}H and ^{13}C), MS, IR, CV and elemental analysis (satisfactory results obtained). CV: counter and working electrode, platinum; reference electrode, Ag/AgCl; supporting electrolyte, tetrabutylammonium hexafluorophosphate. Measurements carried out at room temp. with scan speed 100 mV s^{-1}. *Selected data* for **2**: ^{1}H NMR in CD_3OD (*vs.* $SiMe_4$): δ 3.22 (2H, t, J = 6.9 Hz), 2.93 (2H, t, J = 6.9 Hz); ^{13}C NMR: 215.1, 168.6, 120.3, 115.8, 31.9, 19.3; mp 138–141 °C. For **9′** (*trans* stereoisomer): ^{1}H NMR in $CDCl_3$ (*vs.* $SiMe_4$): δ 6.84 (4H, s), 4.15–4.07 (4H, m), 3.87–3.77 (8H, m), 3.08–3.00 (2H, m), 2.94–2.86 (2H, m), 2.39 (6H, s). CV (MeCN): $E^1_{\frac{1}{2}}$ = 0.46 V, $E^2_{\frac{1}{2}}$ = 0.74 V, $E^3_{\frac{1}{2}}$ = 1.01 V; mp 99–101 °C.

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