A novel route towards formylated 1,3-dithiole-2-thiones *via* an unprecedented allylic 1,4-diol rearrangement†

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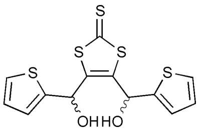
In the presence of perchloric acid, an unusual 1,4-aryl shift is observed for two electron-rich 4,5-bis[hydroxy(aryl)methyl]-1,3-dithiole-2-thiones; the X-ray crystal structure of compound 8 confirms the structural identity of the rearrangement product.

The chemistry of the 1,3-dithiole-2-thione heterocycle and its derivatives has been studied extensively,[1] mainly because these compounds are efficient precursors to tetrathiafulvalenes (TTFs), which are famous components in conducting materials.[2] Innovative steps towards the functionalisation of 1,3-dithiole-2-thiones and TTFs continue to attract attention and the formyl group has been one of the most commonly used functional groups for the preparation of TTFs with simple or complex architecture.[3]

Some of our recent work has involved the synthesis of triaryl systems annelated to the 1,3-dithiole-2-thione heterocycle.[4] During these investigations, we discovered that one of our key intermediates, 4,5-bis[hydroxy(thien-2-yl)methyl]-1,3-dithiole-2-thione **1**, rearranges under acidic conditions to give a variety of products (*e.g* **2**), depending on the choice of solvent and acid.[5] *En route* to a series of dihydrofuran derivatives, we have discovered that electron-rich benzyl analogues undergo a different type of rearrangement to **1**, involving an unexpected 1,4-aryl shift and the concomitant formation of an aldehyde functionality. Herein, we discuss the likely mechanism involved in the reaction sequence and comment on substituent effects.



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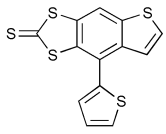

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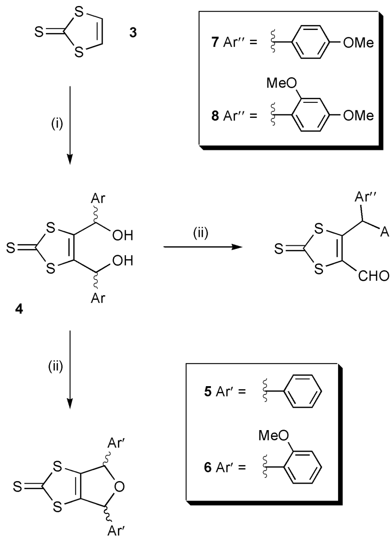
Using a four-step procedure,[4a] 1,3-dithiole-2-thione **3** can be lithiated by LDA and reacted with aryl carbaldehydes to afford bisalcohol products. Thus, compounds **4** (Ar = phenyl, 2-methoxyphenyl, 4-methoxyphenyl, 2,4-dimethoxyphenyl and 3,5-dimethoxyphenyl) were prepared in 75–90% yield, according to Scheme 1.‡ The diols slowly decomposed under ambient conditions; treatment of 3-6 drops of perchloric acid to solutions of **4** in DCM increased the rate of decomposition of the starting material and in all cases the diol was consumed within 24 h. Dihydrofurans **5** and **6** (87 and 23%, respectively)[6] were isolated from the corresponding diols as mixtures of stereoisomers, whereas the 4-methoxyphenyl and 2,4-dimethoxyphenyl diols gave the rearrangement products **7** and **8** in 44 and 83% yields, respectively. The rearrangement products from **4** were all obtained as the major product (by TLC), however, the diol obtained from the reaction of 3,5-dimethoxybenzaldehyde gave an intractable series of reaction products on addition with $HClO_4$.



Scheme 1 *Reagents and conditions*: (i) LDA (1 eq.), ArCHO (1 eq.), then repeat, −78 °C, THF; (ii) $HClO_4$, CH_2Cl_2, rt.

Crystals of compounds **6**† and **8**§ were grown from DCM–petroleum ether.

The X-ray crystal structure of compound **8**§ (Fig. 1) provides irrevocable proof for the structure of the rearrangement product. There are considerably less weak interactions in **8** when compared to **6**, allowing more flexible conformations of the dimethoxyphenyl substituents and forming a supramolecular assembly of one-dimensional chains (C(13)···2O(5) = 3.394 Å).

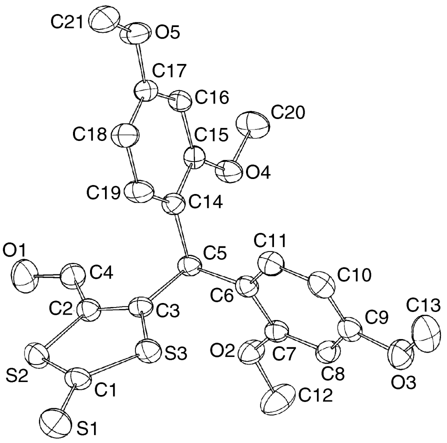


Fig. 1 Molecular structure of compound **8**.

The Pinacol rearrangement of 1,2-diols, affording aldehydes or ketones, is one of the classic transformations in organic chemistry. The reaction involves the acid-mediated 1,2-shift of an alkyl or aryl group as part of a concerted mechanism. Despite the similarity in structure of the reaction products **7** and **8**, one

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† Electronic supplementary information (ESI) available: molecular structure of compound **6**. See http://www.rsc.org/suppdata/cc/b0/b009550h/

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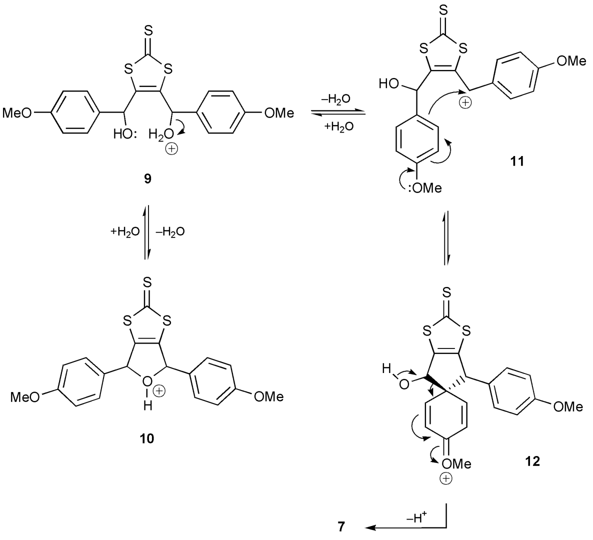
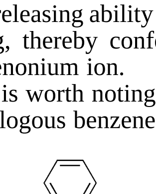


Scheme 2

cannot assume that the mechanism is Pinacol-type. The proposed mechanism for the decomposition of **4** in the presence of perchloric acid is depicted in Scheme 2, using **7** as the example. Protonation of the diol **4** (Ar = 4-methoxyphenyl) gives intermediate **9** which, upon loss of water, generates the dihydrofuran derivative **10** or the free cation **11**. In the case of compounds **5** and **6**, the dihydrofuran species predominates and there is no further transformation. However, for compounds **7** and **8**, the *p*-methoxy group assists in the formation and stabilisation of a phenonium intermediate **12**. The loss of a proton from this species results in **7** *via* an overall step-wise migration of the aryl unit and the formation of a formyl group.

The involvement of a phenonium intermediate in aryl shifts has been seen previously.[7] Theoretical studies have shown that there is significant stabilisation of the phenonium ion through back-bonding from the ethylene unit of spirocyclopropylbenzenium species.[8] However, we propose a spirocyclopentylbenzenium intermediate **12** in Scheme 2, which can only be stabilised by the methoxy unit. The position of the electron releasing groups is important and it is obvious that complications arise in the case of the 3,5-dimethoxy species, since neither the dihydrofuran or 1,4-shift products are observed. In this case, the formation of a spirocyclic intermediate is not possible. It is also unusual that the sole product from the 2-methoxyphenyl species is the dihydrofuran derivative **6**, particularly since the electron donating substituent effect should be identical to that of the 4-methoxy derivative, which gives the rearrangement product **7**. One possible explanation for this can be derived from the X-ray crystal structure of compound **6**.† The intramolecular close contacts between O(2)··S(2) and O(3)··S(3) arise from a π–d orbital interaction, which decreases the electron releasing ability of the methoxy groups towards the benzene ring, thereby conferring a weaker stabilising effect upon the phenonium ion.

Finally, it is worth noting that we have carried out a similar study on analogous benzene derivatives (**13**). In each case, the addition of perchloric acid resulted in a complex mixture of products, which could not be easily separated. None of the isolated fractions proved to be the dihydrofuran or rearrangement products such as compounds **5**–**8** (by MS and ^{1}H NMR). The function of the 1,3-dithiole heterocycle in stabilising the allylic cation (shown in structure **14**) is, therefore, an important process in the formation of compounds **5**–**8**. To check the generality of this stabilisation effect in diols such as **4**, we also substituted the 1,3-dithiole-2-thione ring with thiophene, *via* the lithiation (*n*-BuLi) of 2,3-dibromothiophene and subsequent reaction with 2,4-dimethoxybenzaldehyde. The resulting diol decomposed to the corresponding dihydrofuran (by MS and ^{1}H NMR) on standing, whilst the addition of perchloric acid did not yield the 1,4-rearrangement product. Clearly, there is further scope to investigate the versatility of structure **14** by replacing the 1,3-dithiole-2-thione unit with alternative electron-rich moieties and this will be the focus of future work.



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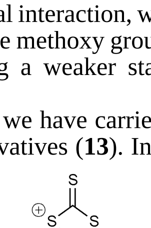

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In conclusion, we have reported the first example of a 1,4-aryl shift in an allylic 1,4-diol system. This reaction is important for understanding the stabilising effects of substituents upon the allylic cation and, independently, the phenonium intermediate, as well as providing an alternative strategy towards the functionalisation of benzylated 1,3-dithiole-2-thione and TTF derivatives.

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Notes and references

‡ Satisfactory spectroscopic data was obtained for all new compounds.

§ *Crystal Data for* **8**: $C_{21}H_{20}O_5S_3$, M_r = 448.55, Monoclinic space group $P2_1/n$, a = 12.732(3), b = 13.131(3), c = 13.040(3) Å, β = 96.88(3), U = 2164.3(7) Å^3, Z = 4, D_c = 1.377 g cm^{-3}, μ = 0.372 mm^{-1}, $F(000)$ = 936, crystal size 0.3 × 0.25 × 0.1 mm, 4938 unique data produced from 16442 measured reflections (R_{int} = 0.0533). 266 parameters refined to R_1 = 0.0493 and wR_2 = 0.1220 [$I > 2\sigma(I)$] (R_1 = 0.1006 and wR_2 = 0.1432 for all data), with residual electron densities of 0.226 and −0.337eÅ^{-3}.

All data were collected at 150 K, on a Nonius KappaCCD area detector diffractometer,[9] equipped with a Nonius FR591 rotating anode (λ Mo-Kα = 0.71073 Å). A correction was applied to account for absorption effects by means of comparing equivalent reflections, using the program SORTAV.[10] A solution was obtained *via* direct methods and refined[11] by full-matrix least-squares on F^2, with hydrogens included in idealised positions.

CCDC 154927 and 154928. See http://www.rsc.org/suppdata/cc/b0/b009550h/ for crystallographic files in .cif format.

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