Tetrathiafulvalene as a Catalyst for Radical–Polar Crossover Reactions

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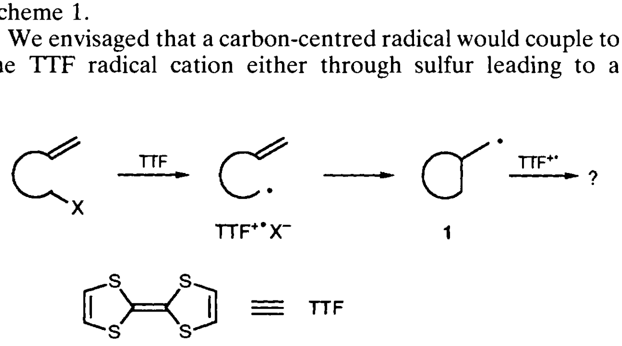
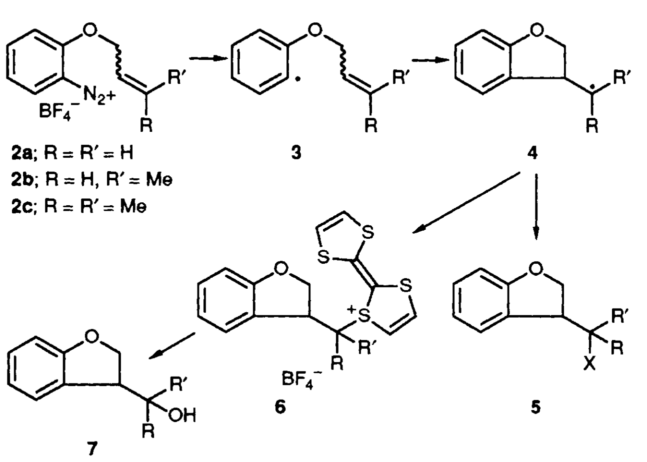
Tetrathiafulvalene behaves as a catalyst in mediating reaction cycles which feature electron transfer reactions, radical cyclisations and nucleophilic displacements.

Among the most interesting current developments in chemistry are the reactions featuring (*a*) samarium diiodide[1] and (*b*) the manganese(III) acetate–copper(II) acetate[2] system. These reagents permit multi-step reactions to proceed *via* radical intermediates, but with polar *i.e.* non-radical termination steps. This allows the extremely useful combination of the reactivities of radicals and of polar species. In this paper a novel link is proposed between polar and radical chemistry using tetrathiafulvalene (TTF). This and related compounds have been extensively used in generating new types of semiconductors[3] but have been little exploited in synthesis. TTF is an excellent electron donor which we anticipated could be utilised in a reaction sequence such as that shown in Scheme 1.

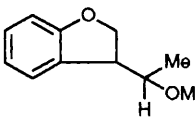
We envisaged that a carbon-centred radical would couple to the TTF radical cation either through sulfur leading to a synthetically useful sulfonium salt, or through carbon to give a novel route to functionalised TTF. No information is available on the rate constant for coupling of carbon radicals with TTF radical cation, but it was hoped that the coupling would be sufficiently slow to permit a cyclisation of the initially formed radical to **1** before coupling.



Scheme 1



Scheme 2



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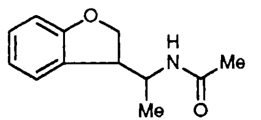

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It is known that aryldiazonium salts **2a** and **2b** react with copper(I) halides, copper(I) cyanide, thiophenate ion and iodide ion to give products **5a** and **5b** (X = halide, CN, SPh) resulting from radical cyclisation (Scheme 2).[4] We now report that the salts **2b** and **2c** react with TTF in acetone to give the corresponding alcohols **7b** and **7c**. Reactions were conducted at a concentration of 0.1 mol dm^{-3} in diazonium salt. As the dihydrobenzofuran can only arise by radical cyclisation we conclude that the reaction proceeds *via* electron transfer, dediazonisation and free radical cyclisation to give intermediate **4**. The formation of alcohol **7** must arise from intermediate **6**, the product of trapping the TTF radical cation on sulfur. The intermediacy of **6** has been demonstrated by the isolation of **6b**, as a yellow, crystalline solid, from the reaction of **2b** and TTF. That **6b** is a discrete compound which involves a σ-bond between the methyl-bearing carbon and one of the TTF sulfur atoms is evident from the ^1H NMR spectrum. Thus four doublets are seen for the methyl group in **6b**, which is consistent with the presence of four diastereoisomers (1 : 1 : 1 : 1) and results from the three asymmetric centres, two on carbon and one on the cationic sulfur. This compound has been analysed by high resolution mass spectrometry [*m*/*z* (FAB): **6b** found M^+ 351.0015; $C_{16}H_{15}OS_4$ requires *M*, 351.0016]. Moreover **6b** is smoothly converted into **7b** as a mixture of diastereoisomers on treatment with moist acetone. That the oxygen in **7** comes from moisture in acetone, and not from acetone itself followed by hydrolysis *in situ*, has been investigated by performing the reaction with **2b** in acetone doped with 10%-labelled $H_2{}^{18}O$. The ^{18}O-labelled alcohol **7b** was isolated [*m*/*z* (EI^+): **7b** found M^+ 164.0819 (36.32%); $C_{10}H_{12}{}^{16}O_2$ requires *M*, 164.0837. (^{18}O-labelled **7b**) found M^+ 166.0894 (2.45%); $C_{10}H_{12}{}^{16}O^{18}O$ requires *M* 166.088]. Although $H_2{}^{18}O$ exchanges with acetone,[5] the speed of the reaction with TTF (the reaction is terminated within 2 min) and the extent of incorporation indicate that the labelled oxygen in the product derives from water.

Nucleophiles other than water can also displace TTF from **6**. Thus when **2b** was treated in methanol, the methyl ether **8** was isolated (34%) and similarly the amide **9** was obtained in 57%

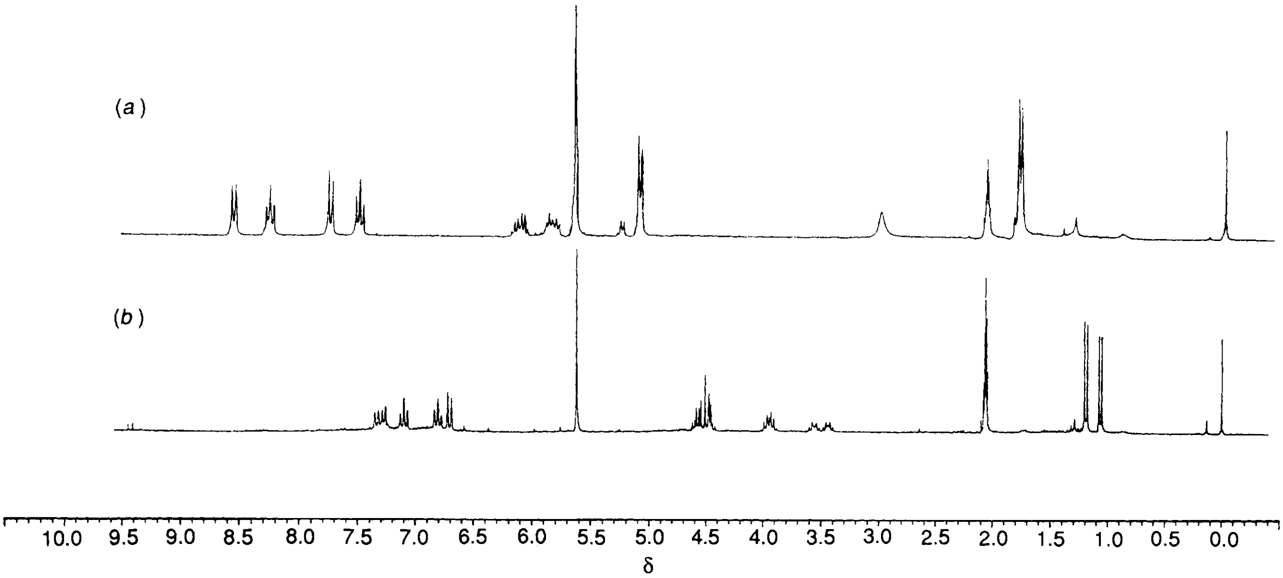

Fig. 1 NMR spectra of (*a*) compound **2b** in [$^2H_6$]acetone with dichloromethane added as an internal calibrant, and (*b*) the same sample after addition of TTF; the spectrum shows clean conversion into **7b**

yield upon reaction in acetonitrile at room temperature. These results show that the particular advantage of TTF over other electron transfer agents for example, iodide, lies in the extreme ease of displacement.

TTF is regenerated in our reaction scheme and it follows that it should be capable of acting catalytically. The NMR spectra shown in Fig. 1 demonstrate the clean conversion of **2b** into **7b** in the presence of 0.2 equiv. of TTF. The reaction was conducted in [$^2H_6$]acetone in an NMR tube using dichloromethane as an integration calibrant. Comparison of the integrals of the methylene protons of dichloromethane to those of the methylene protons in **2b** and **7b** show that there is a quantitative yield in this reaction. Moreover, **7b** was isolated in 72% yield from this reaction. Clearly TTF is acting as a catalyst.

In summary, TTF opens a new catalytic link between polar and free radical processes which potentially has extensive application in synthesis.

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