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Review

Perfluoroalkylation initiated with sodium dithionite and related reagent systems

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Abstract

Perfluoroalkylations promoted by sodium dithionite and related reagent systems have been reported for the following groups of compounds, viz. (i) conjugated dienes, (ii) enol ethers, and (iii) aromatic and heteroaromatic compounds. The results of some chemical conversions of the reaction products for the synthesis of useful synthetic intermediates have also been presented. A comparison between the dithionite initiated reaction and other related systems was made and discussed.

Introduction

Sulfinatodehalogenation is an interesting reaction in that a perfluoroalkyl halide is converted directly into the corresponding perfluoroalkanesulfinate without going through an organometallic intermediate [1]. Among the various perfluoroalkyl halides, the iodide is more reactive than the bromide, and the chloride is inactive [2]. However, a terminal CCl_3 group will react to give the corresponding sulfinate $-CCl_2SO_2^-$ [3], thus:

$$R_FX \longrightarrow R_FSO_2^- \ (X=I,\ Br)$$

$$RCCl_3 \longrightarrow RCCl_2SO_2^- \ (R=R_F,\ F,\ Cl)$$

Several reagent systems have been developed for these conversions, i.e. (a) sulfite plus an oxidant [1, 4, 5], (b) sodium dithionite [6] and (c) hydroxymethane sulfinate [7] and thiourea dioxide [8], and the active species were shown to be anion radicals $SO_3^{\bullet -}$, $1SO_2^{\bullet -}$ and the sulfoxylate ion HSO_2^-, respectively. The reactions were shown to be free radical in nature and electron-transfer processes were involved, e.g.

$$SO_3^{2-} \text{ (or } (HSO_3^-) \xrightarrow{-e} SO_3^{\bullet -} \text{ (or } SO_3^{\bullet -} + H^+)$$

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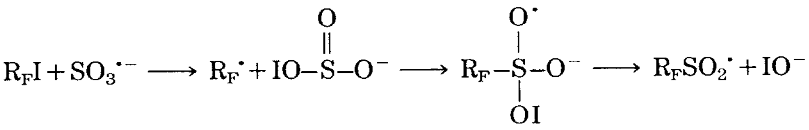


$$R_FI + SO_3^{\cdot -} \longrightarrow R_F^{\cdot} + IO{-}\overset{\overset{O}{\|}}{S}{-}O^- \longrightarrow R_F{-}\underset{\underset{OI}{|}}{\overset{\overset{O^{\cdot}}{|}}{S}}{-}O^- \longrightarrow R_FSO_2^{\cdot} + IO^-$$

$$R_FSO_2^{\cdot} + SO_3^{2-} \longrightarrow R_FSO_2^- + SO_3^{\cdot -}$$

$$S_2O_4^{2-} \rightleftharpoons 2SO_2^{\cdot -}$$

$$R_FI + SO_2^{\cdot -} \longrightarrow R_F^{\cdot} + SO_2 + I^-$$

$$R_F^{\cdot} + SO_2^{\cdot -} \longrightarrow R_FSO_2^-$$

$$\text{or } R_F^{\cdot} + S_2O_4^{2-} \longrightarrow R_FSO_2^- + SO_2^{\cdot -}$$

$$HOCH_2SO_2^- \longrightarrow HCHO + HSO_2^-$$

$$(H_2N)_2CSO_2 \xrightarrow{OH^-} (H_2N)_2CO + HSO_2^-$$

$$R_FI + HSO_2^- \longrightarrow R_F^{\cdot} + I^- + HSO_2^{\cdot}$$

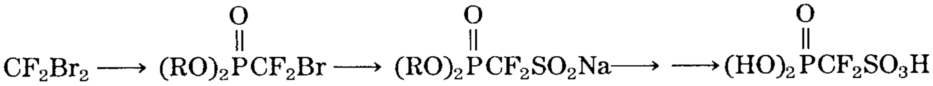
$$HSO_2^{\cdot} \xrightarrow{OH^-} SO_2^{\cdot -}$$

For these reasons, these reagent systems have also been utilized to initiate the addition of R_FI to olefinic and acetylenic compounds [5, 8a, 9–12] such as:

$$R_FI + CH_2{=}CHR \longrightarrow R_FCH_2CHIR$$

$$R_FI + HC{\equiv}CR' \longrightarrow R_FCH{=}CIR'\ (E/Z)$$

These findings have aroused some interest in other laboratories: for example, Burton, Shreeve and their coworkers have used the reaction to synthesize perfluoromethanesulfonic phosphonic acid [13].



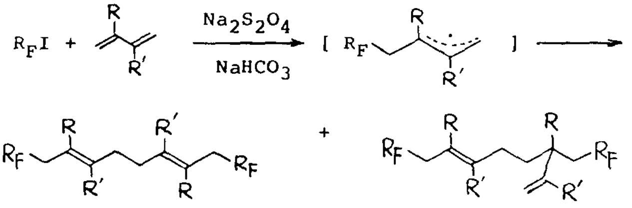
$$CF_2Br_2 \longrightarrow (RO)_2\overset{\overset{O}{\|}}{P}CF_2Br \longrightarrow (RO)_2\overset{\overset{O}{\|}}{P}CF_2SO_2Na \longrightarrow \longrightarrow (HO)_2\overset{\overset{O}{\|}}{P}CF_2SO_3H$$

Tordeux, Langlois and Wakselman have prepared trifluoromethanesulfinate from CF_3Br using $Na_2S_2O_4$ in the presence of Na_2HPO_4 [14] and performed the perfluoroalkylation of aniline [15]. Saveant *et al.* studied the electrochemical generation of $SO_2^{\cdot -}$ and the mechanism of the reaction [16]. Rong and Keese made use of ultrasound in promoting the addition of R_FI to olefins and acetylenes initiated with dithionite [17].

The present review presents some new results from our laboratory on the perfluoroalkylation of several groups of new substrates using these and related reagent systems and their application in the syntheses of perfluoroalkylated organic molecules.

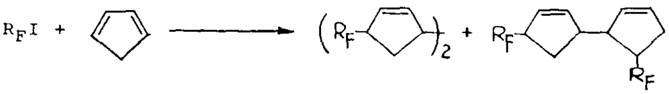
1. Reactions involving conjugated dienes [18]

This reaction gave a dimeric adduct, apparently through the coupling of the intermediary allylic radical, viz.

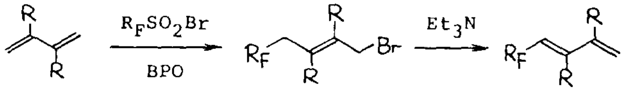


R=R'=H, Me; R=Me, R'=H R=R'=H

Only the symmetrical adduct was formed in the case of 2,3-dimethyl butadiene. Cyclopentadiene gave a mixture of two dimeric adducts.

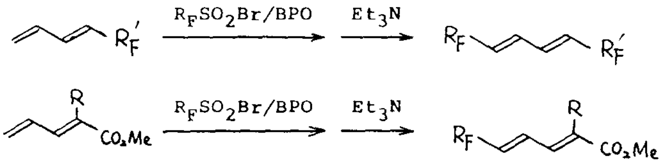


R_F radicals generated from R_FSO_2Na plus Mn^{III} gave the same results. However, the reaction of conjugated dienes with R_FSO_2Br gave the expected monomeric adduct, viz.



R = H, Me; BPO = benzoyl peroxide

The 1:1 adducts were readily converted to perfluoroalkyl-substituted 1,3-dienes in good yield. The latter and related compounds can be further perfluoroalkylated [19], thus:

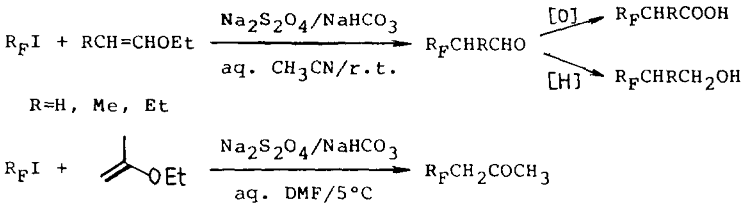


R=H, Me

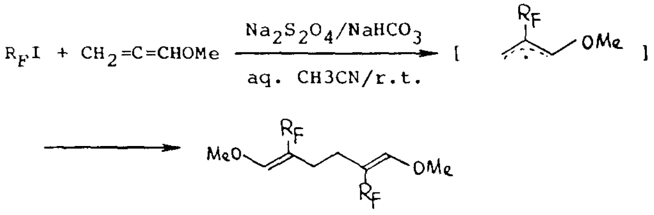
Hence, these reactions provide convenient methods for the synthesis of perfluoroalkyl-substituted conjugated dienic compounds. Different results, i.e. dimerization in the former case and a 1:1 adduct in the latter, may be due to differences in relative bond strengths, e.g. a $CF_2{-}I$ bond being stronger than a $CF_2{-}SO_2Br$ bond.

2. Reactions with enol ethers

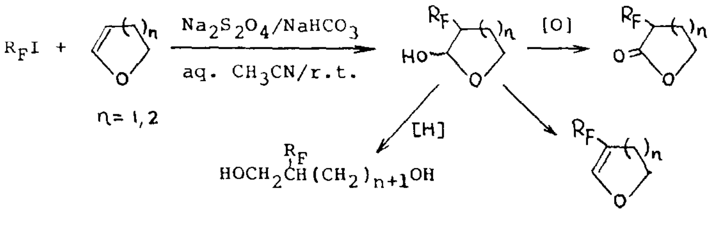
(a) Simple enol ethers were readily converted into perfluoroalkyl-substituted aldhehydes or ketones in high yield; the former products were in turn transformed to the corresponding alcohols and acids in the usual way [20], thus:



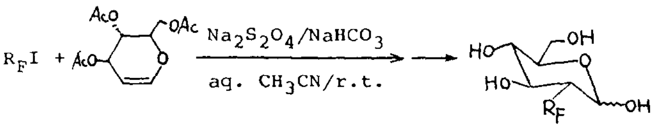
(b) However, an alkoxy-substituted allenic compound, i.e. formally an enol ether of a vinyl carbonyl compound, gave a dimeric product resulting from an initial attack of the R_F radical on the central carbon of the allene, followed by dimerization of the intermediary allylic radical [21], thus:



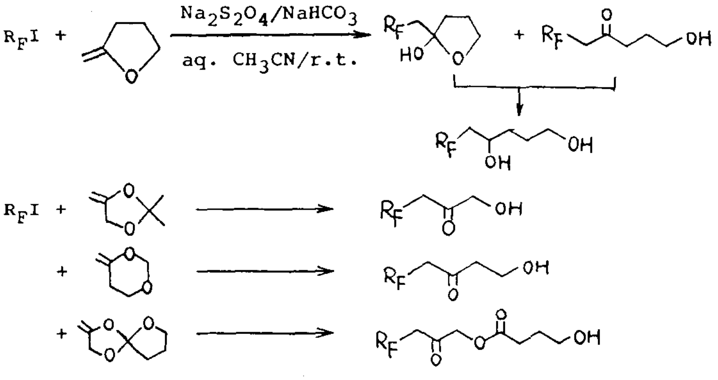
(c) Cyclic enol ethers gave the normal adducts, which were then converted into R_F-substituted diols, R_F-substituted enol ethers or lactones [22], thus:



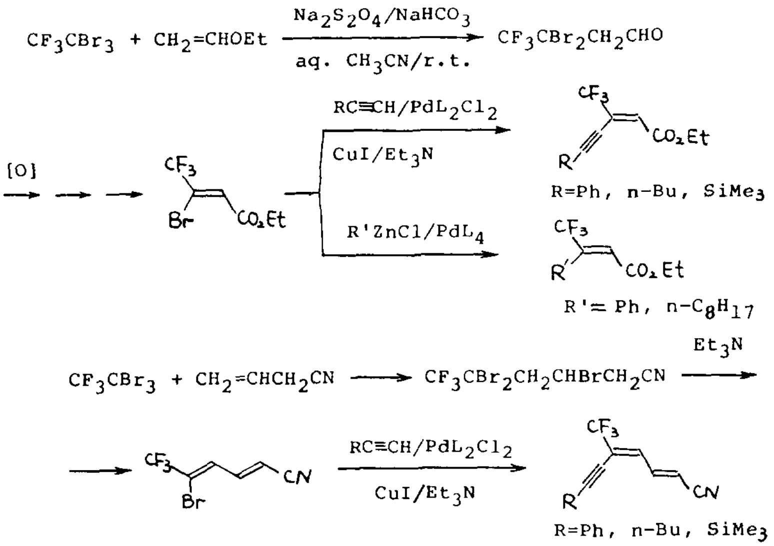
A 2-R_F-2-deoxy-D-glucose has also been synthesized [23].



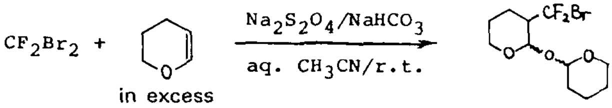
(d) α-Methylene cyclic ethers and spiro ethers reacted smoothly to give hydroxyketone and related compounds [24], thus:



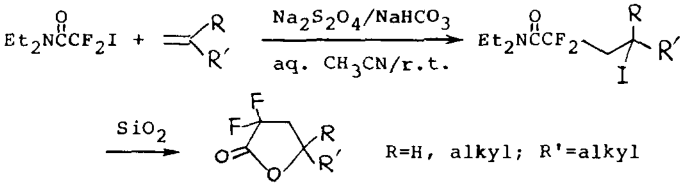
CF_3-substituted compounds were synthesized using 1,1,1-tribromo-2,2,2-trifluoroethane [21, 25], thus:



A peculiar reaction occurred when CF_2Br_2 was allowed to react with excess 3,4-dihydro-2*H*-pyran [21]. However, an analogous reaction did not take place with 2,3-dihydrofuran.



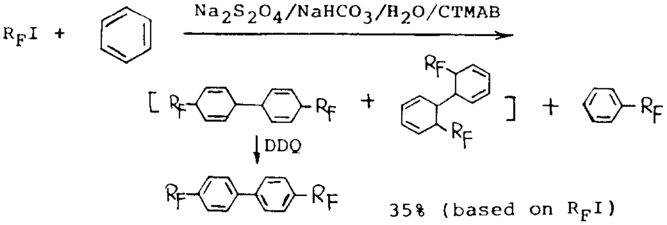
A related reaction was used to prepare α,α-difluoro-γ-lactones [26].



3. Reactions with aromatic and heteroaromatic compounds

(i) Aromatic compounds

Electron-rich aromatic compounds such as aniline were perfluoroalkylated readily, but phenol gave only very low yields [14]. We have found that phenolate generated *in situ* can be perfluoroalkylated in good yield (40–80%) at the *o*,*p*-positions [27]. Benzene itself is not reactive enough under normal conditions; however, $Na_2S_2O_4$ in combination with a cationic phase-transfer catalyst such as cetyltrimethylammonium bromide (CTMAB) was able to convert benzene into perfluoroalkyl benzene and a mixture of dimeric products, the latter being dehydrogenated with dichlorodicyanobenzoquinone (DDQ) to give bis-perfluoroalkyl biphenyls [28], thus:

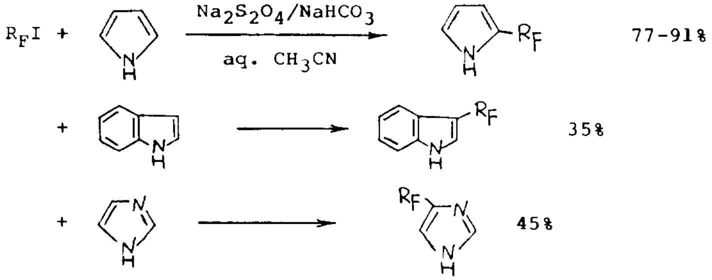


The structures of the dimeric adducts were deduced from the spectral data for the mixture. Preliminary results indicated that the mixed *o*,*p*-adduct was not formed. The *p*,*p*′-disubstituted biphenyl crystallized readily whereas the *o*,*o*′-analogs did not.

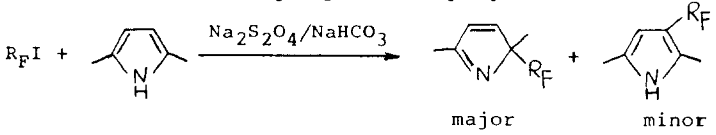
Through the use of the R_FSO_2Br/BPO system, benzene and toluene as well as bromobenzene can be perfluoroalkylated. In the last two cases, a mixture of *o*,*p*-substituted products was formed with *p*-substitution dominating [29].

(ii) Heteroaromatic compounds

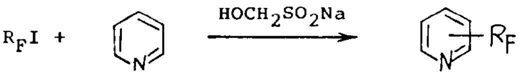
We have undertaken some work on these compounds, for example [30]:



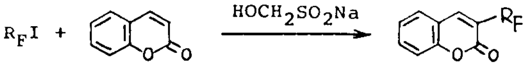
It is interesting that 2,5-dimethylpyrrole reacted to give 2-R_F-2*H*-pyrrole derivatives as the major products [31].



$Na_2S_2O_4$ was not capable of initiating the perfluoroalkylation of pyridine in good yield, but the reaction of pyridine with R_FI and $HOCH_2SO_2Na$ gave a mixture of α, β and γ-perfluoroalkylpyridine [32]:



In the case of coumarin, the same reagent system gave 3-perfluoroalkyl coumarin in good yield [33], thus



The $Na_2S_2O_4$/CTMAB system gave a somewhat lower yield. A similar conversion was reported very recently using $(R_FCOO)_2$ as the perfluoroalkylating agent [34].

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