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PREPARATION AND FLUORINATION OF ARYLTRIFLUOROMETHYLSULPHONES

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SUMMARY

A series of chloro- and nitrophenyl trifluoromethyl sulphides and sulphones have been synthesised from the corresponding aryl halides [1]. The fluorination of these compounds by tetra-n-butyl ammonium fluoride and potassium fluoride has been investigated. Our results show that generally they are more susceptible to fluorodenitration than fluorodechlorination.

INTRODUCTION

The growing demand for selectively fluorinated aromatic molecules with applications in the pharmaceutic, agricultural, chemical, electronic, and advanced materials industries make research on methods of selective fluorination more important [2]. Many molecules of interest now include combinations of fluorine containing substituents of which F, CF_3, CF_3S and CF_3SO_2 are among the most interesting due to their desirable effects on molecular stability, activity and solubility. As part of our research programme on new selective organofluorination methodology we have recently reported the synthesis and use of $CuSCF_3$ for the synthesis of aryl trifluoromethylsulphides from haloaromatics. As an extension of that research we now describe our results from a study of the following synthetic sequence:

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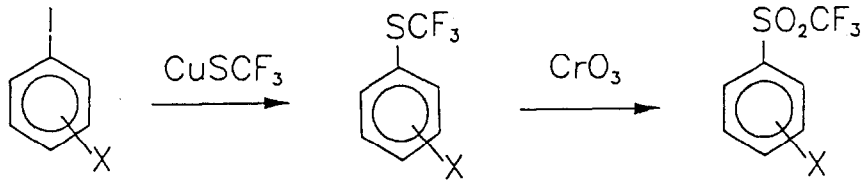
$$XArY \longrightarrow XArSCF_3 \longrightarrow XArSO_2CF_3 \longrightarrow FArSO_2CF_3$$

This sequence allows us to study routes to aromatic molecules containing a combination of F and CF_3SO_2 substituents and to study the activating effects of CF_3SO_2 on groups labile to nucleophilic fluorine transfer.

RESULTS AND DISCUSSION

The following sequence was used for the synthesis of a range of chloro- and nitrophenyl trifluoromethylsulphones:



The first step of the reaction was carried out using an excess of $CuSCF_3$ in either DMF or DMAc. Although all but one of the trifluorothiomethylations gave quantitative conversions by g.c. the actual isolated yields were only moderate (Table 1). Low recovered yields from copper(1)-dipolar aprotic solvent reaction systems such as this are not uncommon and while we attempted to improve on this by the use of the recently reported supported $CuSCF_3$[3], the results were inconsistent and we decided to focus on the former system for the purpose of this research. The second oxidation step in the reaction was carried out at 100°C using conditions similar to those reported by **Yagupolskii et al. [1] giving in most cases moderate to good isolated yields (Table 1).**

TABLE 1

Synthesis of Aryltrifluoromethyl Sulphides and Sulphones

Substrate	Yield of Sulphide	Yield of Sulphone
$2\text{-}IC_6H_4NO_2$	48%	17%
$4\text{-}IC_6H_4NO_2$	54%	64%
$2\text{-}IC_6H_4Cl$	55%	40%
$4\text{-}ClC_6H_4SCF_3$	-	75%

The next step in the research was to study the reactions of the sulphones with F^- so as to produce the corresponding fluorosulphones. Reactions were carried out using two different sources of F^-:

(i) $KF/Ph_4PBr/DMSO/130^oC$ [4]

(ii) Tetra-n-butylammonium fluoride (TBAF)/THF/20^oC [5]

The results are summarised in Table 2. Generally while (ii) had the advantage of employing milder conditions, the product mixtures were complicated by the presence of phenols, presumably resulting from the presence of hydrogen bond activated water from the highly hygroscopic TBAF. The nitrosulphones proved to be more reactive towards F^- (fluorodenitration) than the chlorosulphones (halex). The initial fluorination step for the former was very fast so that the reaction could be stopped at the point of quantitative fluorination. Longer reaction times resulted in the build up of phenols and ethers resulting either from the ingress of atmospheric moisture or back attack of the NO_2^- ion [6]. Thus, in the case of the reaction of 4-nitrophenyltrifluoromethylsulphone under conditions (i), there is a rapid build up of the fluorodenitration product reaching 89% conversion after only 15 minutes. After one hour, this is reduced to 51% with the phenol and the ether building up in concentration. This trend continues with time. Interestingly competitive fluorodetrifluoromethyl sulphonylation (to give 4-fluoronitrobenzene) is only a

relatively minor process (10%). In comparison, reaction of the 4-chlorosulphone under conditions (i) gives a steady build up of the fluorosulphone product over a much longer period of time reaching 80% after 19 hours before declining as a result of phenol and ether formation. No competitive fluorination to give the 4-chlorofluorobenzene is observed, presumably due to the weaker activating effect of the chloro substituent compared to the nitro group.

TABLE 2

Fluorination of Aryltrifluoromethyl Sulphones

Substrate	Conditions	Time/h	Products(g.c. yields)
$2\text{-}NO_2C_6H_4SO_2CF_3$	(i)	0.25	$2\text{-}FC_6H_4SO_2CF_3$ (100%)
$4\text{-}NO_2C_6H_4SO_2CF_3$	(i)	0.25	$4\text{-}FC_6H_4SO_2CF_3$ (89%)
$4\text{-}NO_2C_6H_4SO_2CF_3$	(i)	1	$4\text{-}FC_6H_4SO_2CF_3$ (51%) $4\text{-}FC_6H_4NO_2$ (10%) $4\text{-}HOC_6H_4SO_2CF_3$ (17%) $(4\text{-}F_3CSO_2C_6H_4)_2O$ (22%)
$2\text{-}ClC_6H_4SO_2CF_3$	(i)	19	$2\text{-}ClC_6H_4SO_2CF_3$ (20%) $2\text{-}FC_6H_4SO_2CF_3$ (74%) $2\text{-}HOC_6H_4SO_2CF_3$ (6%)
$4\text{-}ClC_6H_4SO_2CF_3$	(i)	19	$4\text{-}ClC_6H_4SO_2CF_3$ (6%) $4\text{-}FC_6H_4SO_2CF_3$ (80%) $4\text{-}HOC_6H_4SO_2CF_3$ (9%) $(4\text{-}F_3CSO_2C_6H_4)_2O$ (5%)
$2\text{-}NO_2C_6H_4SO_2CF_3$	(ii)	1	$2\text{-}FC_6H_4SO_2CF_3$ (43%) $2\text{-}HOC_6H_4SO_2CF_3$ (19%) $2\text{-}HOC_6H_4NO_2$ (38%)
$4\text{-}NO_2C_6H_4SO_2CF_3$	(ii)	1	$4\text{-}FC_6H_4SO_2CF_3$ (67%) $4\text{-}HOC_6H_4SO_2CF_3$ (33%)
$2\text{-}ClC_6H_4SO_2CF_3$	(ii)	2	$2\text{-}FC_6H_4SO_2CF_3$ (13%) $2\text{-}ClC_6H_4SO_2CF_3$ (60%) $2\text{-}HOC_6H_4SO_2CF_3$ (27%)
$4\text{-}ClC_6H_4SO_2CF_3$	(ii)	2	$4\text{-}FC_6H_4SO_2CF_3$ (18%) $4\text{-}ClC_6H_4SO_2CF_3$ (44%) $4\text{-}HOC_6H_4SO_2CF_3$ (38%)

EXPERIMENTAL

Synthesis of the Aryltrifluoromethyl Sulphides and Sulphones

4-Chlorophenyltrifluoromethylsulphide was purchased from Lancaster Synthesis. All the other aryltrifluoromethyl sulphides and sulphones were synthesised from the corresponding iodoaromatics via the method of Yagupolskii [1].

2-Nitrophenyltrifluoromethylsulphone [384-37-2]
^{19}F NMR: -74.37ppm.
MS: M^+ 255: 186(100), 50(27), 76(22), 64(21), 95(14), 39(10), 255(4).

4-Nitrophenyltrifluoromethylsulphone [432-87-1]
^{19}F NMR: -78.47ppm.
MS: M^+ 255: 186(100), 122(48), 76(34), 50(22), 92(20), 32(10), 64(8), 255(3).

2-Chlorophenyltrifluoromethylsulphone [382-70-7]
^{19}F NMR: -78.9ppm.
MS: M^+ 244: 111(100), 175(82), 75(65), 113(35), 177(28), 50(27), 244(20), 69(18).

4-Chlorophenyltrifluoromethylsulphone [383-11-9]
^{19}F NMR: -79.17ppm.
MS: M^+ 244: 111(100), 175(86), 75(33), 113(35), 177(30), 32(18), 50(15), 244(12).

Fluorination of the Aryltrifluoromethylsulphones

The fluorination reactions were carried as follows:

(i) Fluorination by KF

Potassium fluoride (1 mmole) which had been dried at 300°C and tetraphenylphosphonium bromide (0.25 mmole) dried at 60°C under vacuum was stirred with the substrate (0.5 mmole) in dry DMSO (10 ml) at 130°C.

(ii) Fluorination by TBAF

Tetra-n-butylammonium fluoride (2.5 mmole) which had been

dried at 50°C under vacuum for 24 hours was stirred with the substrate (0.5 mmole) in dry THF (10 ml) at 20°C.

The reactions were monitored by g.c. and the products were identified by ^{19}F nmr and mass spectrometry. ^{19}F nmr spectra were recorded in $CDCl_3$ at 75.26MHz on a Bruker WP80SY spectrometer. Chemical shifts are given relative to $CFCl_3$. Mass spectra were recorded on a Kratos MS-3074 mass spectrometer.

2-Fluorophenyltrifluoromethylsulphone

^{19}F NMR: CF_3 -79.21ppm, F -104.70ppm.

MS: M^+ 228: 159(100), 95(86), 75(40), 69(24), 50(15), 228(10).

4-Fluorophenyltrifluoromethylsulphone

^{19}F NMR: CF_3 -79.33ppm, F -98.71ppm.

MS: M^+ 228: 95(100), 159(76), 75(20), 50(5), 228(4).

2-Hydroxyphenyltrifluoromethylsulphone

^{19}F NMR: -79.96ppm.

MS: M^+ 226: 65(100), 157(68), 93(55), 39(46), 109(43), 226(30), 53(12), 75(5).

4-Hydroxyphenyltrifluoromethylsulphone

^{19}F NMR: -79.74ppm.

MS: M^+ 226: 157(100), 65(70), 93(68), 39(34), 109(43), 226(30), 53(7), 79(4).

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