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Reactions of caesium fluoroxysulphate with organic molecules Part 25 [1]. Reactions with ethers

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Abstract

The reactions of caesium fluoroxysulphate in MeCN suspension at room temperature with di-benzyl, di-alkyl or benzyl-alkyl ethers resulted in oxidative cleavage of the ethers forming pairs of corresponding aldehydes and alcohols, which could be further transformed into acid fluorides under the reaction conditions used. Di-benzyl ether was thus transformed to a mixture of benzyl alcohol, benzaldehyde and benzoyl fluoride as the main products and benzyl benzoate as the a minor one, while di-n-hexyl ether resulted in a mixture of n-hexanol, hexanal, hexanoyl fluoride and hexyl hexanoate. The reaction of benzyl hexyl ether resulted in a mixture of benzaldehyde, benzoyl fluoride and hexanol as the main, and benzyl alcohol, hexanal, hexanoyl fluoride and hexyl benzoate as the minor products. A reaction mechanism including radical intermediates was proposed. © 1997 Elsevier Science S.A.

Keywords: Caesium fluoroxysulphate; Oxidative cleavage of ethers

1. Introduction

Caesium fluoroxysulphate, $CsSO_4F$, (CFS) is the most stable and easily handled among the group of fluoroxy compounds which, in spite of their high reactivity and moderate stability, are often used in organic synthesis as reagents for selective fluorofunctionalisation or other transformations of organic molecules [1]. The reactions of CFS with organic molecules have been extensively studied during the last decade, leading to a recognition of the strong effect of the structure of the organic molecule and the reaction conditions on the course of reaction [1,2]. Since the fluoroxysulphate ion is one of the most potent oxidants used in organic chemistry [3], the presence of oxidisable functional groups or heteroatoms in the organic molecule can cause competition between fluorination and oxidation during CFS mediated reactions. This fact can significantly influence the selectivity of reaction, and therefore it is important to know which heteroatoms, functional groups or building blocks can undesirably interfere with the course of reaction.

It is well known that ethers can be oxidised even by weaker oxidants than CFS. Normally, esters are the products of these reactions if less powerful oxidants are used. When strong oxidants are involved, oxidative cleavage of the carbon–oxygen bond often takes place resulting in the formation of carbonyl derivatives and alcohols as final products [4]. On the other hand, aryl ethers or enol ethers are also known to be excellent precursors for the selective introduction of a fluorine atom into an aromatic ring [5] or α-to a keto group [6] using CFS and other fluoroxy or 'electrophilic' fluorinating reagents, while very limited information is available on the reactions of alkyl ethers with these reagents. In order to learn more about the role of this functional group in the organic chemistry of CFS, we now report a study of its reactions with alkyl and benzyl ethers.

2. Results and discussion

In a typical experiment, described in detail in Section 3, we treated dibenzyl ether (**1a**) with an equimolar amount of CFS in acetonitrile suspension for 1 h at room temperature. We established that 71% of the starting material was consumed and four products: benzyl alcohol (**2a**), benzaldehyde (**3a**), benzoyl fluoride (**4a**) and benzyl benzoate (**5a**) were formed as a result of the reaction, following the relative distribution shown in Scheme 1. Under the same reaction conditions, less than half of the molar amount of di-n-hexyl ether

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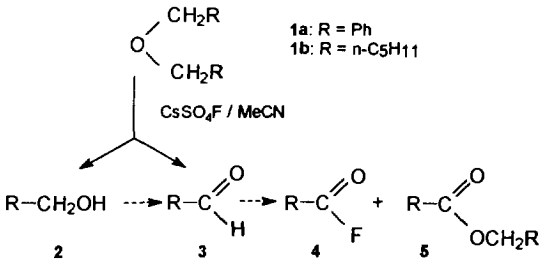


Solvent	Conv.(%) of 1	Product distribution [a] (%) 2	3	4	5
1a MeCN	71	28	47	12	13
MeCN/1 mmol $PhNO_2$	36	29	54	2	15
1b MeCN	47	32	28	21	19

[a] Standard reaction conditions: 1 mmol of substrate, 2 ml of solvent, inert atmosphere, T=22°C, 1 h; conversion determined from GLC using anisole as internal standard; relative product distribution determined by GLC.

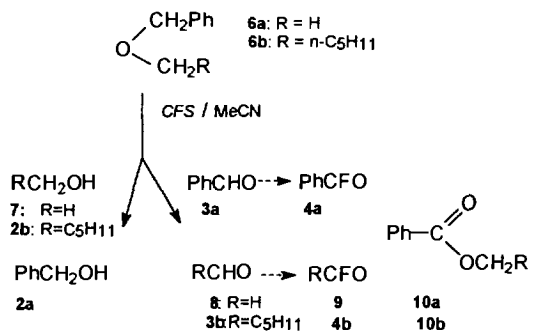
Scheme 1.

(**1b**) was consumed, but the same type of products were formed: n-hexanol (**2b**), n-hexanal (**3b**), n-hexanoyl fluoride (**4b**) and n-hexyl–n-hexanoate (**5b**). It is evident from the data in Scheme 1 that di-benzyl ether is more reactive towards CFS than di-alkyl ether, and that in both cases oxidative cleavage of the ether bond is the main process. The results of the reactions can be compared to those obtained by other strong oxidants, especially by the peroxydisulphate anion [7], Fenton's reagent [8], nitric [9] or nitrous acid [10], UF_6 [11] and $HOF \cdot CH_3CN$ [12]. The only notable difference is the formation of acid fluoride **4**, which is not surprising knowing that CFS readily converts primary alcohols and aldehydes to acid fluorides [13,14]. The difference in relative distributions of the products can also be explained as the consequence of the rate of these transformations which are different for benzyl and alkyl derivatives. The rate of transformation of aldehydes to acid fluorides is higher in the alkyl than in the benzyl series [14], while for the transformation of primary alcohols to acid fluorides the opposite holds [15]. Therefore, in the case of oxidation of **1a**, benzaldehyde is the main and benzoyl fluoride the minor product, while in the case of **1b**, a relatively greater amount of aldehyde **3b** was further transformed in acid fluoride **4b**.

Furthermore we established that the presence of nitrobenzene, known as an effective radical scavenger, considerably suppressed the reaction of di-benzyl ether with CFS. An equimolar amount of nitrobenzene halved the conversion of the starting material under the standard reaction conditions, and, as expected [14,15], reduced the relative amount of benzoyl fluoride considerably.

Benzyl methyl ether (**6a**) has often been used as a probe for mechanistic elucidation of the oxidation of ethers [7–10]. Under the same reaction conditions as used for the symmetric ethers **1**, 65% of **6a** was consumed and a mixture of benzaldehyde, benzoyl fluoride and methylbenzoate (**10**) (Scheme 2), accompanied with trace amount of benzyl alcohol, was detected in the crude reaction mixture using GC–MS analysis. Oxidative cleavage was again found to be the predominant process, but since the expected products methanol, formaldehyde or formyl fluoride are too volatile or unstable for accurate detection with the method used, the regioselectivity of the process as well as its degree could not be well established. In order to avoid this, we chose benzyl hexyl ether (**6b**) as a test compound and found that 64% of the starting material was consumed and transformed to a mixture of pairs of benzyl and hexyl alcohols (**2a**, **2b**), aldehydes (**3a**, **3b**) and acid fluorides (**4a**, **4b**), and hexyl benzoate (**10b**). It is evident from the relative distribution of the products, shown in Scheme 2, that ordinary oxidation to the ester derivative is the minor process, while oxidative cleavage displays considerable selectivity and formation of the benzyl carbonyl/alkyl alcohol pair of products predominates considerably over the formation of the benzyl alcohol/alkyl carbonyl pair.

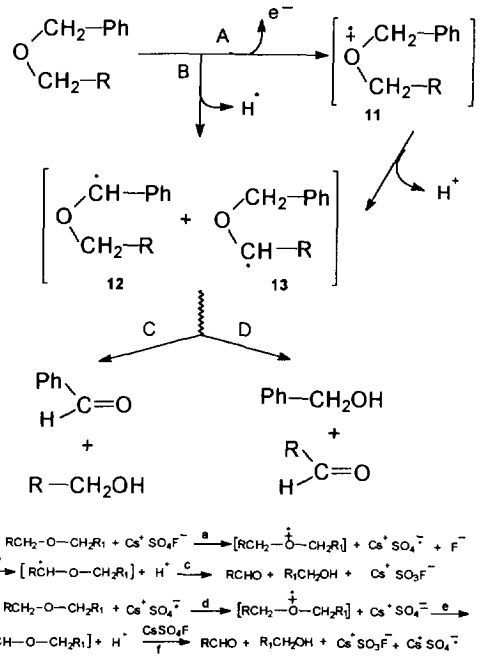
On the basis of the results presented and by analogy with the reactions of ethers with other oxidants, especially the peroxydisulphate anion [7,8], we propose the mechanism shown in Scheme 3 as a feasible reaction pathway for the reaction of dialkyl ethers with caesium fluoroxysulphate. As a strong oxidant CFS is a species carrying a powerful electron demand which can induce the electron transfer process (A), resulting in the formation of a cation radical intermediate **11**, which, followed by proton loss, transforms into radical intermediates **12** or **13**. The process is mediated by SO_4F^- (A1a), or by $SO_4^{\cdot-}$ (A2d) as was generally accepted in the case of the oxidation of ethers by peroxydisulphate [7,8]. Since the fluoroxysulphate moiety is an even stronger oxidant than peroxydisulphate and the ionisation potentials of dialkyl ethers are around 9 eV, path A is a very probable process, but direct hydrogen abstraction (B) as the second possibility leading to radical intermediates could not be neglected. Nev-



	Conv. (%)	Relative product distribution [a] (%) 2a	7; 2b	3a	4a	8; 3b	9; 4b	10
6a	65	1	[b]	51	18	[b]	[b]	30
6b	64	8	24	32	15	5	3	12

[a] Standard reaction conditions: 1 mmol of substrate, 2 ml of solvent, inert atmosphere, T=22°C, 1 h; conversion determined from GLC using anisole as internal standard; relative product distribution determined by GLC. [b] Too volatile for detection.

Scheme 2.



Scheme 3.

ertheless, the hydrogen atom is removed from one of the α-carbon atoms depending on the stability of the intermediate, and therefore when benzyl alkyl ethers are involved, the formation of radical **12** should be favoured, since in this case the electron deficiency could be stabilised over the benzene ring. The next step of the reaction, oxidative cleavage as well formation of the ester, demand the introduction of an additional oxygen atom into the intermediates. The most probable source would be sulphate species (A1c or A2f), as already proved in the case of the oxidation of sulphur or phosphorus containing organic molecules with CFS [16]. Cleavage results in the formation of benzaldehyde and alkyl alcohol by following path C or through path D to benzyl alcohol and alkyl aldehyde. According to the results shown in Scheme 2, path C was found to be preferred, as well as formation of the radical intermediate **12**, since the ester product isolated was hexyl benzoate and no benzyl hexanoate could be detected in the reaction mixture.

A definitive picture of the mechanism of the reactions of CFS with ethers cannot be given, but considering the pronounced effect of the radical inhibitor on the reaction and the product distribution analysis, we consider that the intermediates **12** and **13** play an important role in these reactions, and conclude that the benzyl or alkyl ether functional block could be an undesirable reaction centre when treating organic molecules with caesium fluoroxysulphate.

3. Experimental section

^{1}H- and ^{19}F-NMR spectra were recorded at 60 and 56.4 MHz, respectively. Ethers were from commercial sources or prepared following known procedures [17] were purified before use. CFS was prepared and handled according to the literature [18].

3.1. Reactions of ethers with $CsSO_4F$: general procedure

A solution of 1 mmol of ether in 2 ml of freshly distilled and dry MeCN was degassed with argon. Then 250 mg (1 mmol) of CFS was introduced and the reaction suspension was stirred under Ar at 22°C for 1 h. After dilution with 40 ml of CH_2Cl_2 the insoluble residue was filtered off, the filtrate washed with saturated aqueous $NaHCO_3$ (30 ml) and water (30 ml), dried (Na_2SO_4), and evaporated to 1 ml under reduced pressure. The crude reaction mixtures were analysed by GLC and ^{1}H- and ^{19}F-NMR spectroscopy. Conversion of the starting material was determined from the GL chromatogram of the crude reaction mixture using anisole as internal standard, while the product distribution and identification was determined using GC–MS analysis on an HP-5890 II chromatograph with an HP-5971 MS detector (HP-5, 25 m×0.2 mm×0.11 mm; T=80 °C (1 min)–10 °C min^{-1}–250 °C (5 min)). The relative distributions of products, presented in Schemes 1 and 2, are the average of three experiments.

3.2. The effect of radical inhibitor on the transformation of alcohols

In a degassed solution of 1 mmol of di-benzyl ether in 2 ml of MeCN, 1 mmol of $PhNO_2$ and 1 mmol of CFS were introduced and the reaction suspension stirred at 22 °C under argon for 1 h. The crude reaction mixture was isolated and analysed as described above, and the effect on the transformation presented in Scheme 1.

Acknowledgements

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References

[1] S. Rozen, Chem. Rev. 96 (1996) 1717.
[2] (a) L. German, S. Zemskov, Eds., New Fluorinating Agents in Organic Syntheses, Springer–Verlag, Berlin, 1989. (b) M. Zupan, S. Stavber, The Role of Reagent Structure in the Mild Introduction of a Fluorine Atom into Organic Molecules in Trends in Organic Chemistry, Vol. V, Council of Scientific Information, Trivandrum, India, 1995, pp. 11–36.
[3] W.V. Steele, P.A.G. O'Hare, E.H. Appelman, Inorg. Chem. 20 (1981) 1022.
[4] M. Hudlický, Oxidations in Organic Chemistry, ACS Monograph 186, ACS, Washington, DC, 1990.
[5] S. Stavber, M. Zupan, J. Org. Chem. 50 (1985) 3609.
[6] S. Rozen, Tetrahedron 41 (1985) 1111.
[7] C. Walling, G.M. El-Taliawi, K. Amarnath, J. Am. Chem. Soc. 106 (1984) 7537.

[8] M.E. Snook, G.A. Hamilton, J. Am. Chem. Soc. 96 (1974) 860.
[9] Y. Ogata, Y. Sawaki, J. Am. Chem. Soc. 88 (1966) 5832.
[10] R.B. Moodie, S.N. Richards, J. Chem. Soc. Perkin Trans. 1 (1986) 1833.
[11] P.J. Vergamini, J. Chem. Soc. Chem. Commun. (1979) 54.
[12] S. Rozen, S. Dayan, Y. Bareket, J. Org. Chem. 60 (1995) 6267.
[13] S. Stavber, Z. Planinšek, M. Zupan, Tetrahedron Lett. 30 (1989) 6095.
[14] S. Stavber, Z. Planinšek, M. Zupan, J. Org. Chem. 57 (1992) 5334.
[15] S. Stavber, I. Košir, M. Zupan, J. Org. Chem. submitted.
[16] S. Stavber, M. Zupan, Tetrahedron 48 (1992) 5875.
[17] Vogel's Textbook of Practical Organic Chemistry, Fifth Ed., Longman, London, 1989.
[18] E.H. Appelman, Inorg. Synthesis 24 (1986) 22.