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Room Temperature Reactions of XeF_2 with Phenyl Substituted Alcohols

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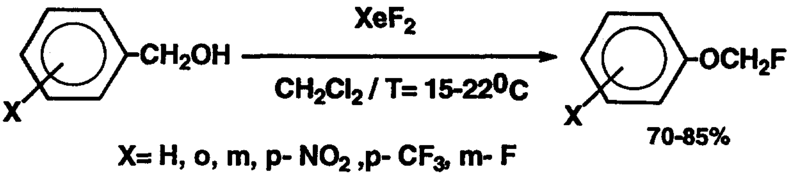
Abstract: Benzyl alkohol and its analogues with a non-activated benzene ring are transformed to fluoromethoxy derivatives by reaction with XeF_2. The same reaction with diphenyl methanol gives di diphenylmethylether, while 2-phenyl-2-propanol transforms to 2,4-diphenyl-4-methyl-1-pentene.

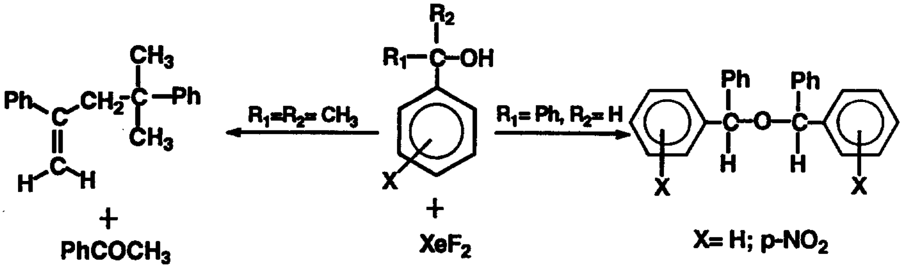
Selective introduction of a fluorine atom into organic molecule under mild reaction conditions is still only a partly solved problem. Several promising results have been obtained recently using reagents of N-F class, R-O-F class, $CsSO_4F$ and XeF_2. Xenon difluoride is one of the most easy handling and safe fluorinating agents, though, its reactions with organic molecules strongly depend on the structure of the organic molecule and the reaction conditions[1]. Recently XeF_2 has been used for the introduction of a fluorine atom into some bioactive compounds[2].

The reactivity of XeF_2 in the presence of various alcohols and water has been studied in recent years[3]. Valuable results from these reactions could only be obtained in the presence of appropriate alkenes where the proposed alkoxyxenon fluoride intermedaites are trapped and the fluoroalkoxy adducts formed. The catalyst used (BF_3 or HF) has a critical role on the regioselectivity of the reaction[3]. In order to obtain more basic information on the reactions of XeF_2 with hydroxyalkyl functional blocks, which are often present in bioactive molecules, we studied the reactions of XeF_2 with phenyl substituted alkohols.

In a typical experiment we dissolved 1 mmol of XeF_2 in a solution of 1 mmol of benzyl alkohol in 2 ml of CH_2Cl_2. The solution was, without stirring, kept at a temperature of 30-35°C until continuous gas evolution from the reaction mixture was confirmed, then cooled to room temperature. In the case of too vigorous a reaction, the mixture was cooled to not less than 15°C and stirred for half to one hour, then diluted with 20 ml of CH_2Cl_2, washed with a 10% aqueous solution of $NaHCO_3$ and water, dried and evaporated under reduced pressure. After GLC, ^1H and ^{19}F nmr analysis, 70% of fluoromethoxybenzene was determined in the crude reaction mixture, the rest being starting material and some benzaldehyde. The substituents on the benzene ring have a considerable influence on the



course of the reaction. Ring deactivating substituents (o-, m- or p-NO_2, p-CF_3, m-F) improved the selectivity of the reaction and the yields of fluoromethoxy derivatives formed rose to 75-85%. The reaction with methyl substituted benzyl alcohol under the above mentioned reaction conditions was vigorous and not more than the 20% of the fluoromethoxy derivative could be obtained from a considerably tarred and complex reaction mixture. No valuable and reproducible results could be obtained if the ring was derivatised with strong electron donating groups (-OH, -OR, -NHR). Further, we examined the effect of additional substituents on the benzylic position, and a completely different course of reaction was established when one or both benzylic protons in the benzyl alcohol molecule were replaced with phenyl or methyl substituents. In the case of diphenyl methanol or its para-nitro analogue, the only product from the reaction with XeF_2 was di-diphenylmethyl ether or its nitro derivative and a few percent of benzaldehyde. On the other hand, 2-phenyl-2-propanol readily reacted with XeF_2 and after very intensive gas release during the reaction, 2,4-diphenyl-4-methyl-1-pentene and acetophenone in a 2:1 relative ratio were isolated from the reaction mixture.



The crucial role of small structural variations in the organic molecule on the course of reactions with XeF_2 was demonstrated in the present and previous work[3]. Examination of the above reported unusual reaction with some other hydroxyalkyl model molecules with measurements of kinetic parameters are in progress.

References

1. Eds. German,L.; Zemkov,S. "New Fluorinating Agents in Organic Synthesis", Springer-Verlag: Berlin **1989**; Zupan,M. "Xenon Halide Halogenations" in the Chemistry of Functional Groups" Supplement D: "The Chemistry of Halides, Pseudo-Halides and Azides" Part 1 and 2, eds. Patai,S.; Rappoport,Z. Wiley: Chichester, **1983**; Wilkinson,A.J. *Chem.Rew.* **1992**, *92*, 505.
2. Filler,R.; Kobayashi,Y. "Biomedicinal Aspects of Fluorine Chemistry", Elsevier: Amsterdam **1982**; Mann,J. *Chem.Soc.Rew.* **1987**, *16*, 381; Robins,J.M.; Wnuk,F.S.; Mullah,B.K.; Dalley,N.K. *J.Org.Chem.* **1991**, *56*, 6878; *J.Org.Chem.* **1992**, *57*, 2357; Garrett,S.G.; Emge,J.T.; Lee,C.S.; Fischer,M.; Dyehouse,K.; McIver,M.J. *J.Org.Chem.* **1991**, *56*, 4823; Geilen,C.C.; Loch,N.; Reutter,W.; Seppelt,K. *Tetrahedron Lett.***1992**,*33*,2435.
3. Shellhamer,F.D.; Curtis,M.C.; Dunham,H.R.; Hollingsworth,R.D.; Ragains,L.M.; Richardson,E.R.; Heasley,L.V.; Shackelford,A.S.; Heasley,E.G. *J.Org.Chem.* **1985**, *50*, 2751; Shellhamer,F.D.; Carter,L.S.; Dunham,H.R.; Spitsbergen,P.M.; Heasley,L.V.; Chapman,D.R.; Druelinger,L.M. *J.Chem.Soc. Perkin Trans. II*, **1989**, 159; Shellhamer,F.D.; Carter,L.D.; Chiaco,C.M.; Harris,E.T.; Henderson,D.R.; Low,S.C.W.; Metcalf,T.B.; Willis,C.M.; Heasley,L.V.; Chapman,D.R. *J.Chem.Soc. Perkin Trans. II* **1991**, 401.

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