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Direct Epoxidation of Unprotected Olefinic Carboxylic Acids Using HOF-CH3CN

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Abstract: The reaction of HOF•CH3CN complex, made directly by passing fluorine through aqueous acetonitrile, with double bond containing unprotected carboxylic acids and alcohols results in fast and almost quantitative epoxidation.

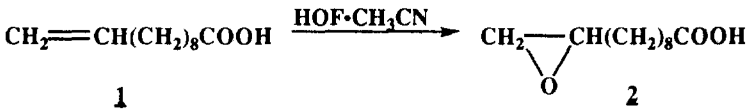
In recent years the HOF•CH_3CN complex has proved to be probably the best oxygen transfer agent. It is able to oxidize tertiary unactivated CH bonds[1], amines and amino acids[2], sulfur compounds[3], alcohols[4], aromatic rings[5], ethers[6] and more. Its uniqueness is based on its oxygen, which being bonded to fluorine - the only atom with higher electronegativity, becomes a strongly electrophilic species. Its reactions have been shown to be of ionic nature and are usually complete in a few minutes at temperatures ranging from 0 °C to 25 °C. We used this reagent also for direct epoxidation of olefins[7] including those that are extremely difficult to epoxidize by other methods.[8] These last reactions, and the known difficulties of direct epoxidation of unprotected acids[9], prompted us to investigate the possibilities of direct, fast and efficient epoxidation of this type of compound.

HOF•CH_3CN is easily prepared in a matter of minutes in a glass reactor by bubbling about 10% F_2 in N_2 through an aqueous acetonitrile solution (10% H_2O in CH_3CN) at 0 °C. Concentrations of 0.25 to 0.5 molar are readily achieved and are monitored by any iodometric titration method. No isolation, purification or other manipulation of the reagent is required. There is still a large body of prominent chemists who retain mythical, unjustified fears of working with fluorine, but the truth is that this is no more complicated than working with any other corrosive gas such as chlorine, especially as premixed mixtures of 10% F_2 in N_2 are now commercially available.

When we added a cold (0 °C) chloroform solution of Δ^{10}-undecanoic acid (1) to a twofold excess of HOF•CH_3CN solution, the reactant was completely consumed in a matter of 3 minutes, and the only organic product found was identified as 10,11-epoxyundecanoic acid (2) obtained in 90% yield.[10] For comparison the reaction of 1 with MCPBA required up to 48 hours to produce the epoxide in 75% yield.[11] The epoxidation of oleic acid (3) has been studied in detail in connection with the use of epoxidized unsaturated vegetable oils as plasticizers and stabilizers for PVC and other plastics. Thus the use of peracetic acid[12] and more recently oxygen in the presence of Co^{+3}/PhCHO catalyst[13] have been thoroughly examined. The yields ranged from very low to up to 65% achieved after many reaction hours. Applying HOF•CH_3CN on 3 at room temperature resulted in the formation of the epoxide 4 in 90% yield and in about 10 minutes .

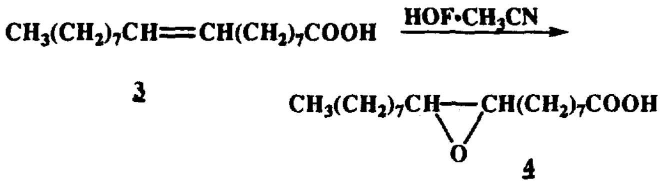
Linoleic acid 5 with its two double bonds had been bis-epoxidized in the past by reacting it with a variety of peracids, achieving yields of 35% after many hours. Application of a twofold excess of HOF•CH_3CN (4 mole oxidant per mole of 5) formed the diepoxide 6 in a clean reaction (90% yield) in 3 minutes. Similar results were obtained with an unsaturated alcohol citronellol (7), proving that a free hydroxyl group is not an obstacle to the reaction and the double bond reacts considerably faster than does hydroxyl.[4] The only product formed proved to be the not previously described citronellol epoxide (8), oil; 90% yield; ^1H NMR: 3.68 ppm (2H, m, CH_2OH), 3.38 (2H, m, CH_2O epoxide); ^{13}C NMR: 73.27 ppm (C-Me epoxide), 62.88 (CH_2 epoxide), 60.52 (CH_2OH); MS (chem. ionization) m/e: 173 $(M + 1)^+$, 155 $(M - OH)^+$.

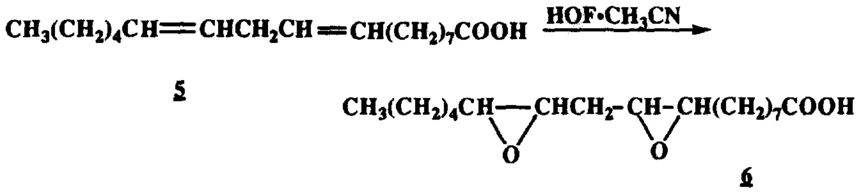
Aromatic rings, another potentially oxidizable moiety[5], also do not interfere with the reaction, even when the double bond is relatively electron depleted. Trans-cinnamic acid (9) was reacted with the acetonitrile complex of hypofluorous acid to give the sensitive epoxide 10[14] in higher than 90% yield.

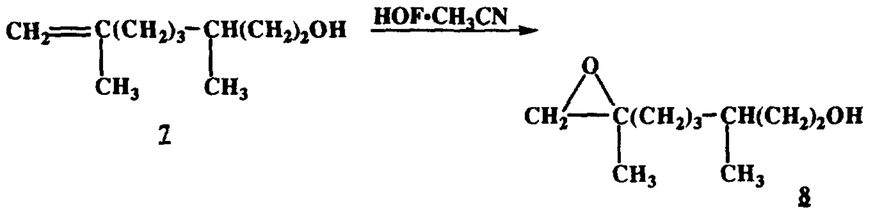


$$\mathrm{CH_2{=}CH(CH_2)_8COOH} \xrightarrow{\mathrm{HOF\cdot CH_3CN}} \underset{\mathrm{O}}{\mathrm{CH_2{-}CH}}\mathrm{(CH_2)_8COOH}$$

1 2







In conclusion it seems that HOF•CH3CN has a very high affinity towards double bonds. An advantage over alternative methods is that it does not react with the free carboxylic or free hydroxyl groups to make peroxides, which can decompose radically resulting in low yields.[14] The ease of the reaction, the mild conditions and nearly quantitative yields are remarkable and offer a new, practical synthesis of epoxy-acids and alcohols.

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9. See for example: Sattler, A.; Haufe, G *Liebigs Ann. Chem.* **1994,** 921. The authors of this paper were unable to epoxidize free acids en route to the synthesis of fluorolactones. They first esterified them and afterwards hydrolyzed them back to the corresponding epoxy acids.
10. Upon completion of the reaction it was poured into bicarbonate solution, most of the acetonitrile evaporated and the aqueous residue slightly acidified. The reaction mixture was then extracted three times with chloroform, washed with water, dried under $MgSO_4$ and the solvent evaporated. The epoxides were the only materials found, but the yield was not considered quantitative since the mass balance was about 90%. With the exception of 8 all epoxides are known in the literature and referenced accordingly. All physical properties are in excellent agreement with the ones published.
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