

Trifluoroacetylation of Alcohols: a Newly Detected Reaction of $\text{CF}_3\text{CO}_3\text{H}$

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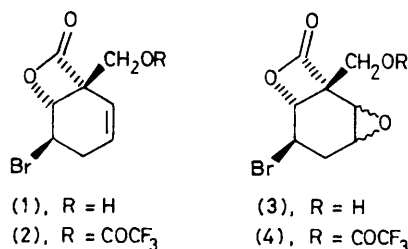
Summary Alcohols form trifluoroacetates in the presence of $\text{CF}_3\text{CO}_3\text{H}$.

THE epoxidation of unsaturated compounds which are resistant to the usual oxidizing agents (*m*- $\text{ClC}_6\text{H}_4\text{CO}_3\text{H}$, PhCO_3H , MeCO_3H) has customarily been accomplished with peroxytrifluoroacetic acid.¹ We had occasion² to prepare (3) from the very hindered olefinic alcohol (1) using $\text{CF}_3\text{CO}_3\text{H}$ and now disclose what is apparently the first report that hydroxy groups are concomitantly trifluoroacetylated by this reagent.

The peroxyacid was prepared from trifluoroacetic anhydride (5 equiv.) and 90% H_2O_2 (7 equiv.) in CH_2Cl_2 containing an excess of anhydrous Na_2HPO_4 to neutralize trifluoroacetic acid. After stirring the heterogeneous suspension for 3 h at room temperature, its i.r. spectrum indicated the absence of the anhydride. Addition of (1) (1 equiv.) to the oxidant followed by workup with aqueous NaHCO_3 after 4 h afforded the stereoisomeric epoxytrifluoroacetates in 83% yield. In a control experiment, (2) was not formed from (1) and trifluoroacetic acid in the presence of Na_2HPO_4 .

The facility of this unexpected Fischer esterification can be attributed both to the strongly electrophilic nature of the carbonyl group of the peroxyacid and to the readiness with which hydroperoxide may be ejected from a tetrahedral intermediate. In accordance with this mechanism, strong proton donors such as trifluoroacetic acid itself catalyse the reaction. To illustrate its scope, the following alcohols were transformed into their trifluoroacetates in the yields noted: cyclohexylmethanol (55%), 3 β -cholestanol (60%),

and 2-phenylpropan-2-ol (10–15% + recovered starting material).



A recent compendium³ lists numerous unsaturated compounds (including alcohols) which have been epoxidized with $\text{CF}_3\text{CO}_3\text{H}$. However, no mention is made of this side-reaction, probably because crude products in many instances were inadvertently hydrolysed during purification. The esters (4), for instance, suffered rapid cleavage to their corresponding alcohols (3) upon column chromatography on silica gel. Although this adventitious trifluoroacetylation does not detract from the generally accepted utility of $\text{CF}_3\text{CO}_3\text{H}$, it may have significant mechanistic repercussions as a competing secondary process in anchimerically assisted epoxidations^{4†} and in the oxidation of other nucleophilic functional groups such as amines^{1,5} and oximes.⁶

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† For instance, epoxidation of the ester (2) is dramatically slower than that of (1).

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