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SYNTHESIS OF ESTERS *via* ALKYL TERT.-BUTYL ETHERS

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Activation of hydroxyl groups for the purpose of involving them in nucleophilic substitution reactions is an important and timely problem. Nevertheless no general approach to the activation of hydroxyl in reactions of this type, e.g. esterification exists. We have recently demonstrated that alkyl tert.-butyl ethers are readily subjected to glycosylation, a typical nucleophilic substitution reaction, giving rise to alkyl glycosides (I).

Further investigations of the reactivity of alkyl tert.-butyl ethers revealed them to be transformed smoothly and in high yields to esters when reacted with carboxylic acids. This reaction may be of considerable preparative value.

$$\text{R-O-tert.-}C_4H_9 \quad + \quad R'\text{-}CO_2 \longrightarrow R'\text{-}CO_2R \quad + \quad CH_2{=}C(CH_3)_2 \quad + H_2O$$

The esterification reaction proceeds in the presence of catalytic amounts of various proton donating agents, e.g. H_2SO_4 or $CH_3C_6H_4SO_3H$. The yields of esters formed in this new reaction are generally good to excellent: n.-butyl acetate, 94%; benzyl acetate, 94%; sec.-butyl acetate, 80%; iso-propyl acetate, 82%; benzyl butyrate, 87%; benzyl benzoate, 53%.

The properties of all the esters obtained are very close to literature data. The homogeneity of all the compounds synthesized was also proved by comparison of their retention times upon GLC with those of authentic specimens.

The interaction of n.-butyl-tert.-butyl ether with acetic acid in the presence of acidic catalysts was subjected to a more detailed study. Heating of the reactants without solvent under reflux or on a steam bath leads to completion of the reaction within 2-5 minutes, accompanied by a quantitative evolution of isobutylene. More prolonged heating is unwarranted since it results in hydrolysis of the ester formed with a concomitant lowering of the yield.

It is worthy of emphasis that esterification of carboxylic acids of greater acidic strength than those mentioned above does not require the addition of any mineral acid as catalyst. Thus heating under reflux of n.-butyl tert.-butyl ether with pyruvic or trifluoroacetic acid for 1 - 1.5 hours resulted in the formation of n.-butyl pyruvate and n.-butyl trifluoroacetate in 86% and 85% yield respectively.

Monitoring the interaction of tert.-butyl ethers with carboxylic acids by means of GLC revealed the reaction mixture to consist exclusively of the excess carboxylic acid and the ester. It does not contain any of the alcohol that might be derived from alkyl tert.-butyl ether by acid hydrolysis.

The mechanism of esterification of carboxylic acids by means of tert.-butyl ethers may be tentatively explained as protonation of the carboxylic acid with subsequent nucleophilic attack of the ether oxygen atom on the positively charged carboxyl carbon atom. The intermediate formed undergoes facile splitting off the relatively stable tert.-butyl cation and a molecule of water giving rise to ester.

Standard procedure: Alkyl tert.-butyl ether (0.1 mole) is mixed with carboxylic acid (0.12-0.15 mole) and 0.02-0.05 ml of sulfuric acid (or 0.05 - 0.1 g of p-toluenesulfonic acid) and heated either under reflux or on the steam bath for several minutes until the evolution of isobutylene ceased. The reaction mixture is then cooled, diluted with 50-100 ml of diethyl ether, washed with aqueous sodium hydrogen carbonate and water and dried over sodium sulfate or magnesium sulfate. After removal of diethyl ether the residue is subjected to distillation to give the corresponding ester.

Reference

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