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# THE ESTERIFICATION OF CARBOXYLIC ACIDS USING A BORON TRIFLUORIDE-ETHERATE-ALCOHOL REAGENT

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The boron trifluoride-alcohol procedure is used routinely to esterify stable acids prior to glpc analysis (1). However, boron-trifluoride-alcohol is not generally considered as a useful reagent in the synthetic preparation of esters from carboxylic acids; the literature gives no examples of such an application of the boron trifluoride-alcohol reagent since the 1930's, when a few simple carboxylic acids were esterified by this method (2,3).

In connection with our work with the Birch reductions of benzene (4) and other aromatics (5), we have prepared various esters of unusual carboxylic acids which required special treatment. We have found that the boron trifluoride-alcohol procedure was unique in that it was both thorough and mild. Furthermore, we found that a successful esterifying reagent could be prepared easily by simply mixing boron trifluoride-etherate, instead of boron trifluoride gas, in the alcohol. We now use this simple procedure routinely for all of our esterifications.

The thoroughness of this procedure is illustrated by the esterification of p,p'-biphenyldicarboxylic acid. This acid was inert to the diazomethane reaction (6) and to proton-catalyzed reaction conditions (7), but gave a 40% yield of the corresponding dimethyl ester (8,9) when refluxed in 10% boron trifluoride-etherate in methanol for three days.

The mildness of the procedure is exemplified by the esterification of 1,4-dihydrobenzoic acid (4). 1,4-Dihydrobenzoic acid (which can be isomerized to conjugated isomers and which is oxidized by atmospheric oxygen to benzoic acid) is converted cleanly to the ester by this method. Thus were formed the methyl, ethyl, and isopropyl esters (distilled yields of 75, 81, and 78%, respectively) (10). Expectedly, the tert-butyl ester was not formed (3); the starting material was recovered unchanged. An analogous procedure with a larger alcohol, cyclohexyl alcohol, did not go to completion; starting material was recovered along with 30% conversion to the ester.

A sample procedure follows. A solution of 4.11 g of 1,4-dihydrobenzoic acid, 4.9 ml of boron trifluoride-etherate, and 50 ml of anhydrous ethanol was stirred and refluxed (11) for 20 hours. After cooling, 150 ml of water was added, and the resulting mixture was extracted with three 100-ml portions of ether. The combined ethereal phases were washed with saturated sodium chloride solution, dried with anhydrous magnesium sulfate, concentrated under reduced pressure, and distilled to yield 5.04 g (81%), bp 54-56° (0.3 mm).

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(9) All esters described herein had a satisfactory elemental analysis for carbon and hydrogen.

(10) All these esters exhibited an identical nmr pattern to that for the parent acid (4) with the additional signals of the alkyl group. No trace of isomeric conjugated esters could be found.

(11) For the dihydrobenzoic acid esterifications, the reaction was done under a blanket of nitrogen.