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CINNAMYL AS A PROTECTING GROUP.
A MILD METHOD FOR THE CLEAVAGE OF CINNAMYL ESTERS.

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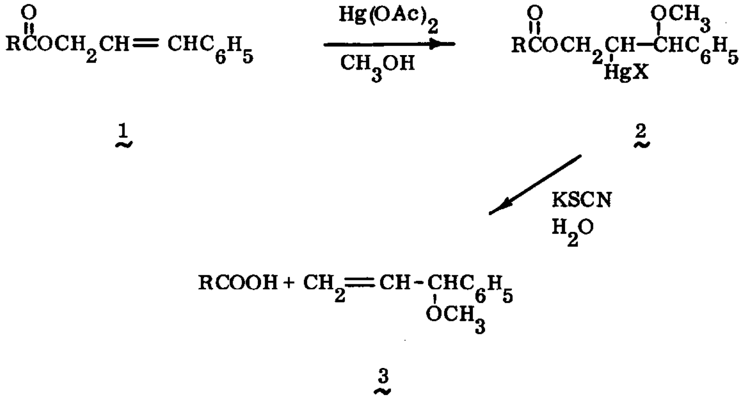
This note describes a mild procedure for the cleavage of esters of cinnamyl alcohol under nearly neutral conditions. Since cinnamyl esters are readily prepared from commercially available cinnamyl alcohol and activated carboxylic acid derivatives, are comparably stable to methyl esters toward acids and bases, and absorb in the ultraviolet (facilitating analytical determination and chromatographic analysis) the use of the cinnamyl group as an alternative to other protection techniques would seem to merit careful consideration.

The method devised for cleavage of cinnamyl alcohol involves the mercuration-demercuration sequence outlined in the following chart. The cinnamyl ester (1)[1] is treated in methanol solution with 1.15 equiv of mercuric acetate and 0.1 equiv of nitric acid[2] at 23° for 2-4 hr, the time usually required for consumption of all of the starting ester. The reaction mixture is quenched by stirring with 1.15 equiv of solid[3] sodium or potassium bicarbonate and after evaporation of methanol under reduced pressure demercuration is effected by stirring vigorously with a mixture of cyclohexane and excess (8-12 equiv) of aqueous potassium thiocyanate[4] until both layers of the two-phase system are clear and free of suspended matter (12-16 hr, 23°). Thin layer chromatographic (tlc) analysis of the cyclohexane layer shows the presence of only the methyl ether 3. The carboxylic acid is then obtained from the aqueous phase by (1) extraction with hydrocarbon solvent to remove the last traces of neutral organic material, (2) acidification with aq. hydrochloric acid, (3) extraction with ether, (4) drying (over $MgSO_4$) and evaporation (*in vacuo*) of the ethereal extract. By this procedure the following acids were obtained cleanly from the corresponding cinnamyl esters in yields of 90%: (1) cyclohexane carboxylic acid, (2) benzoic acid, (3) *p*-methoxybenzoic acid and (4) phenylacetic acid.



The intermediate organomercurial may also be isolated by treatment of an ethereal solution of the acetoxy mercurial 3, X = OAc, (obtained directly from the mercuration by evaporation of methanol) with

1.5 equiv of aqueous potassium chloride. The reaction affords solid chloromercury derivatives (**3**, X = Cl) in $>$ 95% yield, and from these the free carboxylic acids can be obtained by the procedure outlined above.

The essentially neutral deprotection procedure described herein is one of the mildest of available methods for ester cleavage. The cinnamyl protecting group ought to be applicable not only to carboxylic acids but also to alcohols (cinnamyloxycarbonyl esters) and amines (cinnamyloxycarbonyl amides).[5]

References and Notes

1. The cinnamyl esters used in this study were obtained from cinnamyl alcohol and the corresponding acid chlorides. All reaction products were analyzed and characterized spectroscopically and by comparison with authentic samples.
2. The mercuration reaction was found to be accelerated by small amounts of acid; see (a) R. L. Clarke and F. W. Gubitz, U.S. Patent 2,921,068 [*C.A.*, **54**, 8867 (1960)] and (b) Houben-Weyl, *Methoden der Organischen Chemie*, 4th ed., XIII/2b, Thieme, Stuttgart, 1974, p. 134.
3. The use of aqueous bicarbonate was found to lead to inferior results.
4. Four molar equiv of potassium thiocyanate are theoretically required per equiv of organomercurial to form the soluble complex $K_2Hg(SCN)_4$ (*cf.* ref 2b, p. 208).
5. This study was assisted financially by a grant from the National Science Foundation.