AN IMPROVED METHOD FOR PREPARING PHENOXYACETIC ACIDS-1-^{14}C

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SUMMARY

High radiopurity substituted phenoxyacetic acids-1-^{14}C were synthesized by the hydrolysis of their ethyl esters which were prepared from ethyl bromoacetate-1-^{14}C and the appropriate sodium phenolate.

Key words: Phenoxyacetic acids-1-^{14}C, ethyl phenoxyacetate-1-^{14}C. Improved synthesis.

INTRODUCTION

Research to distinguish characteristics of plant translocation from structural modifications of pesticides requires the use of extremely pure phenoxyacetic acids=1-^{14}C. Published methods of the acid synthesis (1)(2) result in a yield of several difficult-to-separate radioactive by-products, in addition to the labelled phenoxyacetic acid. Adapting a procedure used by Fields, *et al.* (3), I found that substituted phenoxyacetic acids-1-^{14}C prepared by hydrolysis of ethyl ester intermediates formed in good yield with high radiopurity. These esters were prepared from the reaction of ethyl bromoacetate-1-^{14}C and the appropriate sodium phenolate. The final product was purified by preparative thin-layer chromatography. The method was applied to the synthesis of 4-chloro- and 4-fluorophenoxyacetic acids=

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1-^{14}C and also to a similar synthesis of ethyl 3'-methyl-4'-nitrophenoxyacetate=1-^{14}C. Overall yields of purified and labelled phenoxyacetic acids from bromoacetic acid-1-^{14}C were in the order of 50 to 70%. This method may be used for synthesis of other substituted phenoxyacetic acids-1-^{14}C.

EXPERIMENTAL

Ethyl Bromoacetate. A solution of bromoacetic acid-1-^{14}C (0.64 mg, 4.6 μmole, 250 μCi purchased from New England Nuclear), 0.1 ml oxalyl chloride, and 10 ml dry benzene was allowed to stand in a calcium chloride-protected flask overnight at room temperature. Approximately 1 ml of the solution was evaporated by using a dry nitrogen stream. Absolute ethanol (0.5 ml) was added, and the resulting mixture heated under reflux for 30 minutes. The mixture was then concentrated to about 0.25 ml with a nitrogen stream, and the resulting ethyl bromoacetate solution used in the next step.

p-Chlorophenoxyacetic Acid-1-^{14}C. To the ethyl bromoacetate was added a solution of 36 mg (230 μMole) solium *p*-chlorophenolate in 7.5 ml dimethyl sulfoxide. This solution was heated at 50-60°C for 9 to 10 hours in an oil bath. The reaction mixture was diluted with 15 ml water and extracted 4 times with 5 ml methylene chloride. The methylene chloride extract was dried over anhydrous magnesium sulfate, filtered, and evaporated to dryness. The residue was hydrolyzed in 2 ml water and 0.1 g sodium hydroxide heated under reflux for 15 minutes. The resulting solution was acidified with 12N hydrochloric acid and extracted with 3 x 5 ml methylene chloride. Drying and evaporation gave a residue of *p*-chloro=phenoxyacetic acid-1-^{14}C and another radioactive compound of unknown structure. The phenoxyacetic acid was separated by using preparative thin-layer chromatography on kieselguhr-silica gel G (3:2) plates with a solvent mixture of hexane, ethyl acetate, and formic acid (20:5:0.1).

Authenticity of the *p*·chlorophenoxyacetic acid-1-^{14}C was determined by co-chromatography with unlabelled *p*·chlorophenoxyacetic acid placed on a thin-layer chromatographic plate and using several solvent systems (eq. solvent system mentioned above; benzene:dioxane:acetic acid, 45:10:2; chloroform:hexane:acetic acid, 66:33:1). Coincidental spots were detected by methyl yellow spray (in ethanol) or 0.5% silver nitrate spray (in water) and exposure to a low pressure mercury UV lamp and autoradiogram. The overall yield of *p*·chlorophenoxyacetic acid-1-^{14}C was 68% (170 µCi from 250 µCi bromoacetic acid).

That this method may be of general use is suggested by the preparation of two other phenoxyacetic acids or esters. *P*·fluorophenoxyacetic acid to yield 134 µCi was prepared from 250 µCi of bromoacetic acid and sodium *p*-fluorophenolate. Detection of *p*-fluorophenoxyacetic acid was made with bromcresol green (4). In a similar preparation, 135 µCi of chloroacetic acid-1-^{14}C and sodium 4-nitro-3= cresolate gave 133 µCi of ethyl 4'-nitro-3'-methyl phenoxyacetate-1-^{14}C (not hydrolyzed).

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