SMALL-SCALE PREPARATION OF $^{14}C_2$-PENTAERYTHRITOL

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SUMMARY

$^{14}C_2$-Pentaerythritol (^{14}C-PE) at approximately 8 mCi/mmole was prepared in 76% yield on a 3-mmole scale via a base-catalyzed condensation of acetaldehyde-$^{14}C_2$ with 1.5% aqueous CH_2O.

Key Words: $^{14}C_2$-Pentaerythritol, $^{14}C_2$-Acetaldehyde

INTRODUCTION

The need for ^{14}C-labeled pentaerythritol as a key labeled intermediate for the preparation of various flame retardants for environmental and/or related studies prompted our investigation aimed at defining an efficient small-scale radiochemical synthesis for this compound. The preparation of unlabeled pentaerythritol and its inorganic and organic esters on a molar scale via the reaction of acetaldehyde with formaldehyde has been extensively described in the literature [1]. Although procedures concerning the preparation of ^{14}C-PE are available [2,3], the smallest scale indicated was 25 mmoles with a reported yield of 42% [3]. Further, both procedures report the formation of significant amounts of by-products, such as di- and tripentaerythritol, which were removed by the conversion of the reaction products to the corresponding acetate esters followed by fractional distillation, alcoholysis, and recrystallization of the pure ^{14}C-PE from water.

We now report a simple and efficient (75% yield) method for the preparation of ^{14}C-PE on a 3-mmole scale via a base-catalyzed condensation of acetaldehyde-$^{14}C_2$ and CH_2O in a molar ratio of formaldehyde:acetaldehyde-$^{14}C_2$:calcium hydroxide of 5:1:0.5. The overall reaction is outlined below. This procedure is a modification of the method reported by Trevoy and Myers [3] for the preparation of ^{14}C-PE. As expected, it was found that using a dilute aqueous solution of

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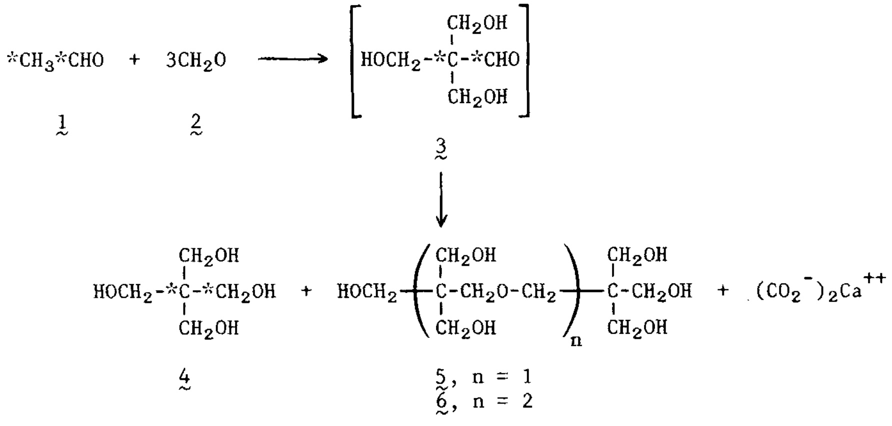

formaldehyde, approximately 1.5% in water, provided for an excellent conversion of acetaldehyde-$^{14}C_2$ to ^{14}C-PE of 85% purity which required only simple isolation procedures to give the desired final product in 76% yield with a chemical and radiochemical purity of $\geq$ 98%. That is, under the reaction conditions employed, very little of the undesired polypentaerythritol side products, such as 5 and 6 were obtained [4]. Higher concentrations of CH_2O in water such as 10, 20, and 30% gave increasing amounts (30 to 60%) of the unwanted 5 and 6, as shown by GLC analysis of the corresponding acetate esters.

EXPERIMENTAL

Radioactivity was determined in a Packard Model 2425 liquid scintillation counter using Liquifluor (New England Nuclear) as the counting medium. The radiochemical purity was determined by autoradiography (on Eastman Kodak SB-5 X-ray film) and radiochromatogram scanning (Packard Model 7201 Radiochromatogram Scanner) of the TLC plates (precoated fluorescent silica gel, 5 x 20 cm, Brinkmann 60F-254). The chemical purity of $^{14}C_2$-PE was established by GLC of the corresponding acetate ester [5] using a Varian 2400 gas chromatograph equipped with ionization detector and temperature programming. Column length: 6 ft; diameter: 1/8 in.; solid support: Chromosorb W, 30-60 mesh; liquid phase: SE-30, 15% weight concentration; temperature programmed at 5°/min (180° to 320°); detector temperature: 325°; injector temperature: 350°; helium flow: 120 ml/min.

Acetaldehyde-$^{14}C_2$

Acetaldehyde-$^{14}C_2$ was prepared as a ∿ 0.15 molar solution in water via the addition of water to acetylene-$^{14}C_2$ in the presence of $HgSO_4$ [6]. Thus, a solution of 2 g of mercuric sulfate in 40 ml of water was suspended in 3.3 ml of concentrated H_2SO_4 contained in a 250-ml round bottom flask equipped with a stopcock adapter for a vacuum manifold and a stirring bar. This suspension was then attached to the vacuum manifold, frozen with liquid nitrogen, and evacuated to 0.1 mm Hg. Acetylene-$^{14}C_2$ (78 mCi, 10 mmoles) was then condensed in the reaction flask, and the resulting reaction mixture was allowed to warm to room temperature. The reaction mixture was then treated at 105° for 25 min, followed by removal of the unreacted acetylene-$^{14}C_2$ (0.2 mmole) by vacuum distillation. The aqueous solution of acetaldehyde-$^{14}C_2$ was subsequently collected by heating the flask at 100° under pulling vacuum, and the product was condensed in a trap cooled with liquid nitrogen. A total of 44 mCi (5.6 mmoles, 38 ml of aqueous solution) of acetaldehyde-$^{14}C_2$ was collected.

Pentaerythritol-$^{14}C_2$

A solution of acetaldehyde-$^{14}C_2$ (3.1 mmoles, 24 mCi) in 21 ml of water was added with stirring at 0° to a suspension of calcium hydroxide (111 mg, 1.5 mmoles) in water (14.4 ml) and 40% aqueous formaldehyde solution (1.92 ml, 15 mmoles). The mixture was stirred in a 100-ml stoppered flask, first at 0° for 0.5 hr, then at room temperature for 1 day. The suspension was neutralized to pH ∿ 6.5 with 5% sulfuric acid, and the $CaSO_4$ precipitate was removed by filtration. Next, 60 ml of methanol was added to the filtrate, which was evaporated to dryness *in vacuo* at 40°. (It should be noted that higher temperatures and stronger acidity, such as 60° and pH < 5, lead to a significant amount of decomposition of the crude pentaerythritol-$^{14}C_2$.) A total of 394 mg (2.9 mmoles, 22.6 mCi) of crude ^{14}C-PE of 85% radiochemical purity, as established by TLC radiochromatogram scanning [silica gel, solvent system IsoProH:conc. $NH_4OH:CHCl_3$ (6:2:2), $R_f = 0.5$], was obtained. Trituration of this material with 1 ml of hot methanol gave, after cooling to 0°, 320 mg, 18.4 mCi, 76% yield, of ^{14}C-PE with a radiochemical purity of ≧ 98% established by TLC radiochromatogram scanning and a chemical purity of ≧ 98% established by GLC of the corresponding acetate ester.

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