NOTE

TRITIUM LABELLING OF POLYOLS

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SUMMARY

Mannitol, galactitol and myo-inositol were labelled by a solid state isotope exchange with gaseous tritium. The labelled polyols were prepared with specific activities in the range 740-4440 TBq/mol (20-120 kCi/mol) after purification by HPLC.

Key words: Tritium labelling, polyols, solid state exchange reaction

INTRODUCTION

The synthesis of tritium-labelled open-chain polyols is usually achieved by the reduction of corresponding aldoses, aldolactones or ketoses with tritiated reducing agents ($NaBT_4$, $LiAlT_4$) or by exchange with gaseous tritium in the presence of a catalyst [1,2]. Other methods for labelling polyols are also known which include isotope exchange with tritiated water [3] or exposure to a tritium gas atmosphere (Wilzbach method and its modifications) [1,4]. The comparatively low specific activities of the labelled compounds so obtained is often a practical limitation for some of these methods. In addition, in many cases (during ketoses reduction, for example) epimeric pairs are formed which require separation.

In the present study we have used the method of solid state isotope exchange (SSIE) for preparation of tritium-labelled polyols. Over several years this method has been used in our laboratories for tritium incorporation into compounds of different classes [5-8]. In the present examples chosen of tritium-labelled mannitol, galactitol and myo-inositol the possibility has been demonstrated of effectively using the SSIE method for the label to be incorporated into both open-chain and cyclic polyols.

MATERIALS AND METHODS

The reaction mixtures were prepared as previously described [9]: the polyol (1 mg) was dissolved in 0.5 ml of distilled water and 50 mg of a catalyst was added. The mixture was rotary evaporated to dryness. The dry residue

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was placed in an atomosphere of gaseous tritium (50 kPa) and heated at 115°-130°C for 1-2 h. After cooling to room temperature the reaction cell was evacuated and the catalyst with labelled polyol was placed on a glass filter. The reaction products were dissolved on the filter by portions of hot water (3 x 4ml). The resulting solution was taken to dryness using a rotary evaporator at 40°C. Labile tritium was removed by repeated (triple) evaporation to dryness of the aqueous solutions.

Purifications and measurement of the specific activity of the polyols were performed by HPLC [10]. A TSK-Gel NH_2-60 column (4.6 x 250 mm) at 20°C and a mixture of acetonitrile with water (70 : 30 v/v) as eluent were used. The chromatography process was performed on the LKB equipment with a refractive index detector. Concentration of the polyol in the solution investigated was measured by a comparison of areas under the peaks of the analyzed compound and a reference standard. Radioactivity was measured by liquid beta scintillation counting.

RESULTS

Different palladium catalysts have been tested to catalyse isotope exchange between gaseous tritium and polyol on the catalyst surface. A catalyst with 10% palladium on calcium carbonate is found to be best. Optimum temperature of the process is 115°-130°C, and duration of 1-2 h. Any decrease of the temperature or time period leads to lowering of the specific activity of labelled compounds. Increase of the temperature results in a lower yield and after 1-2 h at 150°C the compounds degrade completely.

The conditions for chromatographic purification were determined by the solubility of the polyols in the mobile phase. The elution volume of carbohydrates on the amino phases depends upon the acetonitrile content of the eluent and the separation power of the column is sharply increased with high acetonitrile concentrations (up to 70-90% of acetonitrile). However, decrease of the water content of the eluent leads to essential lowering of the polyols solubility and restricts this procedure for preparative purposes.

The specific activity of the tritiated mannitol and galactitol obtained was 740-2220 TBq/mol (20-60 kCi/mol), and that of the myo-inositol was 740-4440 TBq/mol (20-120 kCi/mol). The chemical yield was in the range 40-50% for the purified labelled products.

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