

NOTES

SYNTHESIS OF $[1-^{14}\text{C}]n\text{-HEPTANE}$

SUMMARY

Synthesis of n-heptane labelled with carbon-14 in the 1-position is described. The procedure involves five steps starting with reaction of $[^{14}\text{C}]$ carbon dioxide with n-hexyl magnesium bromide and finishing with reduction of $[1-^{14}\text{C}]n\text{-heptyl bromide}$. The purity of the final product was more than 97% and the overall yield was 36%.

Key words; Carbon-14, $[1-^{14}\text{C}]n\text{-heptane}$, Synthesis

INTRODUCTION

Dinonylnaphthalenesulphonic acid (HD) in n-heptane has been used extensively as a liquid cation-exchanger (1). On agitation with an aqueous solution the sulphonic acid imbibes water and forms micelles. From radiochemical measurements it has been shown that on equilibration with an aqueous phase consisting of 0.50 or 1.00 M perchloric acid the hydrous micelles are all of one kind and have the composition $(\text{HD})_{7.54}\text{H}_2\text{O}$ (2). In order to obtain further information on the structures of the micelles various methods have been employed (3), and one of these required the use of labelled n-heptane. The present report outlines the procedure used by us to prepare $[1-^{14}\text{C}]n\text{-heptane}$ with quite good yield. Other routes were tried but were found to be less convenient.

SYNTHESIS

The reaction sequence used to prepare $[1-^{14}\text{C}]n$ -heptane is shown in Fig.1. *N*-hexyl magnesium bromide is prepared by the Grignard method from 1-bromohexane. This is reacted with $[^{14}\text{C}]\text{CO}_2$ to give $\text{C}_6\text{H}_{13}^{14}\text{CO}_2\text{MgBr}$, which in turn on treatment with hydrochloric acid yields $[1-^{14}\text{C}]$ heptanoic acid. The organic acid is reduced to $[1-^{14}\text{C}]n$ -heptyl alcohol, which is brominated to produce $[1-^{14}\text{C}]$ bromoheptane. Finally the labelled alkyl bromide is reduced with lithium aluminium hydride and lithium hydride to give $[1-^{14}\text{C}]n$ -heptane.

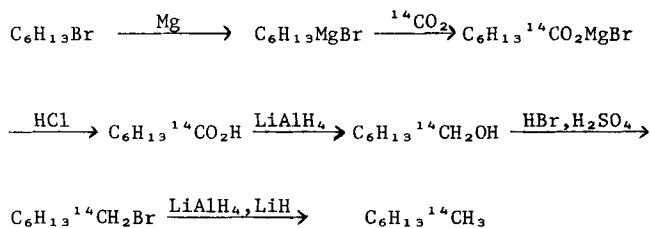


Fig.1 Pathway to the synthesis of $[1-^{14}\text{C}]n$ -heptane.

The preparation of medium chain length fatty acids and alcohols, and their conversion into the bromides is well documented in the literature (4), and hence preparative details as far as 1-bromo $[1-^{14}\text{C}]$ heptane are not given here. The reaction of the bromo-compound to yield $[1-^{14}\text{C}]n$ -heptane (5) is less well covered in publications on radiosynthesis, and details of this stage will be described.

EXPERIMENTAL

Preparation of $[1-^{14}\text{C}]n$ -heptane from 1-bromo $[1-^{14}\text{C}]$ heptane. About 0.5g of lithium aluminium hydride, 1.5 g of lithium hydride, and 50 cm³

of tetrahydrofuran (THF) are placed in a three-neck round bottom flask. One opening of the flask is stoppered, a dropping funnel is fitted in the second, and a reflux condenser in the third. The mixture is stirred and gently refluxed. $[1\text{-}^{14}\text{C}]n\text{-heptyl}$ bromide is added dropwise from the funnel over a period of 30 min. and refluxing is continued for several hours. After cooling to 10°C , 30 cm^3 of a mixture of 18 cm^3 THF and 12 cm^3 water are added and the temperature is not permitted to rise above 25°C . When there is little further effervescence, the contents of the flask are added to 75 cm^3 of cold 2.5M sulphuric acid. The organic layer is separated, and the aqueous phase is washed repeatedly with portions of THF and the washings added to the labelled hydrocarbon. The $[^{14}\text{C}]$ heptane is washed with water, purified by micro-distillation (b.p. 98.4°C), and dried over potassium carbonate in a refrigerator.

The yield of $[1\text{-}^{14}\text{C}]n\text{-heptane}$ obtained in this step was 90 percent. IR and PMR spectra corresponded with standard spectra. A GLC measurement showed that the purity of the compound was not less than 97%.

Measurements of radioactivity were performed with a Tracerlab 535 BL Liquid Scintillation System. Aliquots of sample (0.02 cm^3) were dissolved in 15 cm^3 of scintillation solvent consisting of 5 g of PPO and 280 mg of POPOP per dm^3 of toluene. The counting efficiency (65 - 68%) was determined by the external standard gross count method (6) using various quench standards of $[^{14}\text{C}]n\text{-hexadecane}$ in toluene (The Radiochemical Centre, Amersham).

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