

SYNTHESIS OF CARBON-14 DISULFIDE AND N,N'-DICYCLOHEXYLCARBO-¹⁴C-DIIMIDE

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SUMMARY

Methyl-¹⁴C iodide of high specific activity was converted to carbon-14 disulfide in quantitative yield by reaction with phosphorus pentasulfide at 300-325°C. Following literature procedures, N,N'-dicyclohexylcarbo-¹⁴C-diimide was prepared in 54% yield from the carbon-14 disulfide.

Key Words: Carbon-14 Disulfide, N,N'-Dicyclohexylcarbo-¹⁴C-diimide, N,N'-Dicyclohexylthio-¹⁴C-urea.

INTRODUCTION

N,N'-Dicyclohexylcarbo-¹⁴C-diimide (3, DCC-¹⁴C) of high specific activity was desired for use in a study of proton permeability of Escherichia coli membrane vesicles⁽¹⁾. Neither DCC-¹⁴C, nor its precursor carbon-14 disulfide, has been reported, but sulfur-labeled carbon disulfide has been prepared by isotopic exchange of elemental sulfur⁽²⁾ or sulfide ion⁽³⁾ with carbon disulfide, by reaction of elemental sulfur with elemental carbon⁽⁴⁾, and by reaction of phosphorus pentasulfide with carbon tetrachloride⁽⁵⁾. In addition, elemental sulfur reacts with hydrocarbons at high temperatures to yield carbon disulfide⁽⁶⁾.

In all of these reactions, carbon bearing either hydrogen or halogen reacted with either sulfur or phosphorus pentasulfide to afford carbon disulfide. Therefore, Methyl-¹⁴C iodide⁽⁷⁾, the most

Following known procedures^(8,9) as outlined above, the carbon disulfide was converted to DCC (5) in 66% overall yield based on methyl iodide. Using the same procedures, DCC-¹⁴C was prepared in 54% yield with a specific activity of 46 mCi/mmmole from methyl-¹⁴C iodide of the same specific activity.

EXPERIMENTAL

Melting points are uncorrected. Radioactivity was measured by liquid scintillation using a Packard Tricarb Model 2010 spectrometer.

Carbon-14 disulphide (2) - Methyl-¹⁴C iodide (1, 173 mg, 1.2 mmole), prepared⁽⁷⁾ from methanol-¹⁴C of specific activity 46 mCi/mmmole, was vacuum-transferred into trap A (Figure 1) and stopcocks 2 and 3 were closed. U-tube B, half filled with a mixture of phosphorus pentasulfide and dry sea sand (1:9 w/w), was attached to trap A, purged with dry nitrogen at 10 ml/min (stopcock 1 open), and heated in an oven to 300-325°C. Trap C was attached and cooled in liquid nitrogen. Stopcocks 2 and 3 were opened and trap A was allowed to warm slowly to room temperature, allowing the nitrogen stream to carry the dilute methyl-¹⁴C iodide vapor slowly into the reactor (B). The nitrogen flow was continued for 10-15 min after no more radioactivity was detected in trap A (total reaction time about 1 hr), then the nitrogen flow was stopped and trap C was closed off by means of the stopcocks. The material collected in trap C was vacuum-transferred into a 100 ml flask, degassed at -195°C, and warmed to -75°C to vaporize the hydrogen sulfide, which was then removed by vacuum transfer (a few seconds only, or until radioactive material starts to transfer). The residual carbon-14 disulphide was transferred at about -30°C into a tared 10 ml flask, leaving behind iodine and some less volatile impurities. The purified product, containing a trace of iodine and some hydrogen sulfide, weighed 97 mg (104% yield based on 1).

Cyclohexylammonium N-cyclohexyldithiocarb-¹⁴C-amate (3) (8) - The carbon-14 disulfide (2) was vacuum-transferred into a frozen, degassed solution of cyclohexylamine (250 mg, 2.5 mmoles) and sodium hydroxide (2 mg) in ethanol (1 ml). The mixture was allowed to react at room temperature for 1 hr and all volatile material was transferred out under vacuum, leaving the non-volatile salt 3 (316.5 mg, 1.15 mmole, 95.6% yield based on 1).

N,N'-Dicyclohexylthiourea-¹⁴C (4) (8) - The residual salt 3 was refluxed under nitrogen for 2 hrs with 2 ml of ethanol, then all volatile material was transferred out under high vacuum, leaving a residue of crude 4 (230 mg, 0.95 mmole, 79% yield based on 1). [In a model experiment, unlabelled crude 4 was recrystallized from 1 ml of ethanol with 77% recovery. The recrystallized material had mp 178.5-179.5° and gave no mp depression on admixture with an authentic sample. Thin layer chromatography (EM precoated Silica Gel 60 F254 plates, developed in chloroform-ethyl acetate, 9:1 v/v, and viewed by short-wave ultraviolet light) of the mother liquor showed it was almost pure 4 also].

N,N'-Dicyclohexylcarbo-¹⁴C-diimide (5) (9) - Dry silver oxide (200 mg) and acetone (2 ml, dried by passage through a column of activity I alumina) were added to the crude thiourea 4 and the mixture was stirred and refluxed gently for 18 hrs. Solids were removed by filtration and the solvent was removed by vacuum transfer, leaving a residue which was distilled in a short-path still at 80°C/0.01 mm to afford 5 (135 mg, 0.65 mmole, 54% yield based on 1), mp 34-36°C (lit. mp 34-35°C⁽¹⁰⁾), specific activity 222 μ Ci/mg (46 mCi/mmmole). [In a corresponding model experiment 240 mg of unlabelled 4 gave 170 mg of 5 (83% yield)].

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