SYNTHESIS OF PENTACHLORONITROBENZENE-$^{14}C_6$[1]

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SUMMARY

Pentachloronitrobenzene-$^{14}C_6$ was synthesized in 81.7% yield by exhaustive chlorination of nitrobenzene-$^{14}C_6$. Hexachlorobenzene-$^{14}C_6$ was produced in 11% yield as a by-product of the reaction.

Key Words: Pentachloronitrobenzene, Hexachlorobenzene, PCNB, Terrachlor, Synthesis, Carbon-14

INTRODUCTION

Pentachloronitrobenzene (PCNB, Terrachlor) is a broad spectrum fungicide in wide-spread use in agriculture in the United States. Although the metabolism of this fungicide has been studied (1-4), these studies were made without the benefit of radioactive PCNB and dealt primarily with the metabolism of PCNB in mammals. Published literature on the metabolism of PCNB in higher plants is incomplete and there appears to be some disagreement as to whether PCNB is

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translocated from the roots to the foliar tissue (3, 5). Definitive studies on the uptake, translocation, and metabolism of PCNB in higher plants required the use of ^{14}C-labeled PCNB. Based on the availability of radioactive starting materials, it seemed most appropriate to attempt the synthesis by exhaustive chlorination of nitrobenzene-$^{14}C_6$ in chlorosulfonic acid with iodine as the catalyst.

EXPERIMENTAL

Nitrobenzene-$^{14}C_6$ (Mallinckrodt), 25.3 mg (0.205 mmole, specific activity 4.87 mCi/mmole) 36 µl (0.352 mmole) non-labeled nitrobenzene, 1.5 ml chlorosulfonic acid, and 0.10 ml of 5% iodine in chlorosulfonic acid were added to a flask fitted with a chlorine inlet tube, magnetic stirrer, Dry Ice/acetone-filled Dewar condenser, and an external oil bath. The reaction was initiated by admitting chlorine into the flask until a reflux rate of about 10 drops per minute was obtained; thereafter chlorine was admitted at 8-hr intervals in sufficient quantity to maintain a steady reflux. The reaction temperature was held at 25° for the first 3 days, and at 50° for the next 2 days. The mixture was then cooled, diluted with 25 ml of carbon tetrachloride, transferred to a separatory funnel with three 25-ml rinses, and extracted with 100 ml of cold aqueous 5% sodium bisulfite. After extraction, the carbon tetrachloride solution was washed with ice-water, dried over sodium sulfate, filtered, concentrated to 4 ml on a rotary evaporator at 20° and diluted to 10 ml with benzene. The concentrate (0.947 mCi) was streaked onto fourteen 20- X 20-cm X 500-µ silica gel HF_{254} thin-layer plates and one 5- X 20-cm X 500-µ thin-layer plate. The solvent was evaporated from the streaked zones without the use of heat or forced air as the use of either resulted in a substantial loss of product. The thin-layer plates were then developed in hexane-acetic acid (90:10) and air-dried without the assistance of forced air or heat. Two radioactive zones at R_f 0.50 and R_f 0.90 were detected by examination of the chromatograms under UV light and by scanning the 5- X 20-cm X 500-µ

chromatogram on a Model 7201 Packard Radiochromatogram Scanner. The radioactive zones of gel were collected separately, placed in small chromatography columns and eluted with 40 ml of methylene chloride. The product from the zone at R_f 0.50 (Product A) was recovered in 0.815 mCi yield and the product from the zone at R_f 0.90 (Product B) in 0.109 mCi yield. An additional 0.018 mCi was detected on the silica gel remaining on the thin-layer plates.

Radioactivity was quantitated by liquid scintillation counting techniques with either a standard toluene cocktail or a cabosil/toluene cocktail. Counting efficiency was determined by automatic external standardization.

Thin-layer chromatography with cyclohexane-acetic acid (95:5), hexane-chloroform (90:10), and hexane-acetic acid (95:5) indicated that A was radiochemically homogeneous PCNB-^{14}C. The absence of chemical contaminants was indicated by examination of the chromatograms under UV light. Product A was also shown to be chemically and radiochemically homogeneous PCNB-^{14}C by gas chromatography on 1.83-m X 4-mm ID glass column of 3% OV-1 on 60/80 mesh Gas Chrom Q, with helium carrier gas (60 ml/min), a linear temperature program (from 130° to 220° at 5°/min), a 10:1 stream splitter and a flame-ionization detector. Product A eluted as a single peak at 161°; it was detected by the flame-ionization detector and by liquid scintillation counting of products trapped from the effluent gas. The standard PCNB, hexachlorobenzene, and pentachlorobenzene, were eluted at 161°, 157°, and 144°, respectively.

Product A was confirmed as PCNB-^{14}C by comparison of its IR and mass spectra with those of standard PCNB. The specific activity of the PCNB-^{14}C — determined by UV absorption at 300 nm, and gas chromatography under isothermal conditions at 160° — was 1.76 ± 0.01 mCi/mmole. The yield of PCNB-^{14}C was 81.7%.

When analyzed by the previously described chromatographic methods, B was characterized as radiochemically homogeneous hexachlorobenzene-$^{14}C_6$

which was contaminated with two non-radioactive components. Final confirmation of the structure of the radioactive component was achieved by gas chromatographic/mass spectral comparison with authentic hexachlrobenzene. The specific activity of the hexachlorobenzene-$^{14}C_6$, determined by gas chromatography under isothermal conditions at 145°, was 1.81 ± 0.05 mCi/mmol. The yield of hexachlorobenzene-$^{14}C_6$ was 11.0%.

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