Syntheses of Isotopically Labeled 2,4-Dichlorophenoxyacetic Acid (2,4-D) and Derivatives

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The great interest in and wide use of 2,4-dichlorophenoxyacetic acid (2,4-D) in recent years has prompted us to investigate the synthesis of this compound and some of its derivatives incorporating radioactive isotopes.

One synthesis employs radioactive I^{131} and leads to 2,4-dichloro-5-iodophenoxyacetic acid-I^{131} through the sequence of the reactions shown in Fig. 1.

The 5-amino compound was prepared as indicated (*3*), diazotized and treated with radioactive sodium iodide, diluted with inactive material, thus yielding iodine-labeled 2,4-D. The butyl ester was obtained from the free acid through the acid chloride prepared by means of thionyl chloride (*3*). In this manner we have synthesized 75 mg of the free acid, 80 mg of its morpholine salt, and 92 mg of its butyl ester, showing specific activities of 28, 23, and 24 μc/mg, respectively.

We have also developed a method leading to 2,4-dichlorophenoxyacetic acid-1-C-14 by means of the sequence in Fig. 2.

Potassium acetate-1-C-14 prepared in the conventional manner (*1*) is chlorinated in nitrobenzene, using a modification of Ostwald's synthesis (*2*). Alkaline condensation of the chloroacetic acid, which is never isolated as such, with 2,4-dichlorophenol then leads to the desired product. In this manner, 0.68 g of C^{14} labeled 2,4-D was obtained, and showed a specific activity of 1.0 μc/mg. Complete details of the work will be published elsewhere.

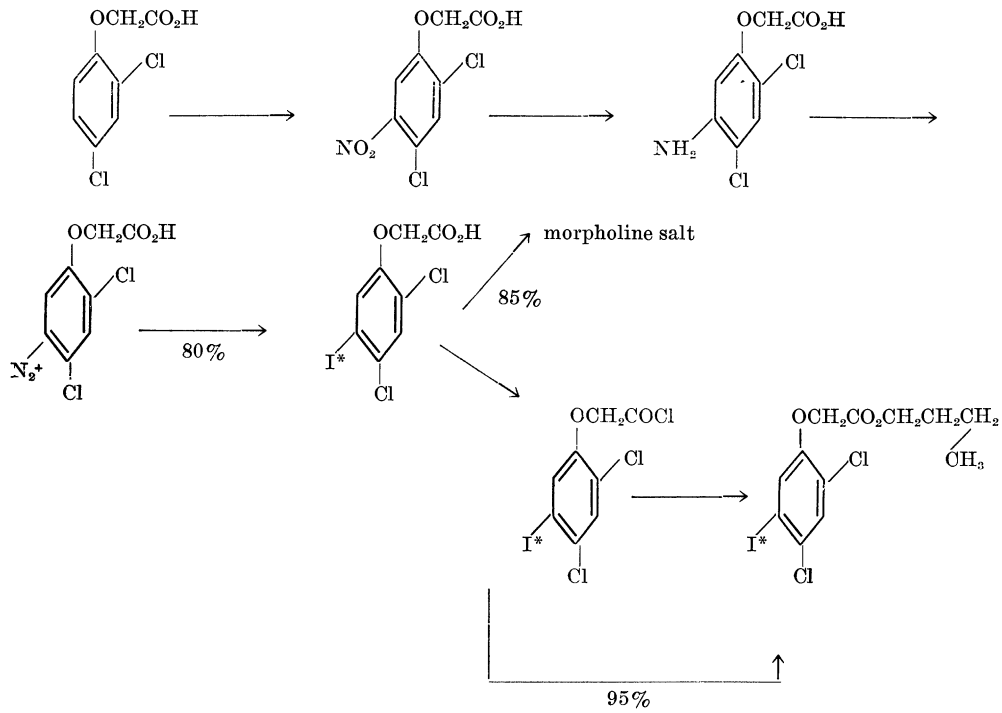

FIG. 1.

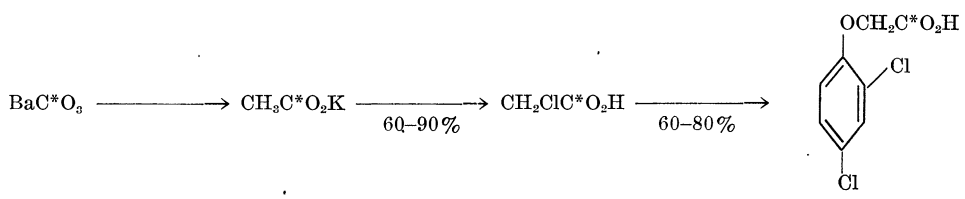

FIG. 2.

References

1. CALVIN, M. *et al.* *Isotopic carbon.* New York: John Wiley, 1949, p. 178.
2. OSTWALD, R. *J. biol. Chem.*, 1948, **173**, 207.
3. WOLFE, W. C. *et al.* *J. org. Chem.*, 1949, **14**, 900.