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PREPARATION OF RADIOACTIVE IODOTRIPHENYLETHYLENE

D. C. Morrison

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PREPARATION OF RADIOACTIVE IODOTHRIPHENYLETHYLENE (1).

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By D. C. Morrison

Crocker Laboratory, University of California,
Berkeley, California

It was desired to prepare the iodine analogue of the biologically active bromotriphenylethylene, containing radioiodine as tracer, for work on synthetic estrogens. This radioactive iodotriphenylethylene was used for uptake studies in human and animal tumors. The iodotriphenylethylene was prepared by a modification of the method of Koelsch (2). The method was adapted

(2). Koelsch, J. Am. Chem. Soc. 54 2045 (1932).

to a smaller scale with some variations and radioiodine (I^{131}) was employed. An attempt to obtain the compound by iodination of triphenylethylene using iodine chloride in glacial acetic acid failed.

EXPERIMENTAL

Experimental work was done behind lead and Lucite shields in a hood

Preparation of radioiodine.- (This method was suggested by Dr. Earl Hoerger). The sodium iodide carrier (0.3 g.) was dissolved in water in a

separatory funnel and the desired amount of I^{131} (as sodium iodide, Oak Ridge isotope) activity added. An equal volume of benzene was added and then 0.4 g. of sodium nitrite in concentrated aqueous solution. The mixture was treated dropwise with shaking with 6N nitric acid until an excess was present. The contents were agitated vigorously behind a lead shield. If the aqueous phase (after separation of layers) was still colored by an additional drop of acid, more of the latter was added until the aqueous layer remained colorless. After standing twenty minutes, the layers were separated carefully and the organic layer washed once by extraction with water. The benzene solution of radioiodine could then be added to the Grignard reagent, with or without previous drying over sodium sulfate.

The radioiodine was also generated in some runs by the reaction of active iodide with potassium iodate and dilute sulfuric acid, but the above method was preferable. Any excess of either iodide or iodate seemed to cause retention of activity in the aqueous layer. This was probably caused, in the case of excess iodate, by an exchange reaction.

Preparation of Iodotriphenylethylene.- One gram of magnesium was reacted in a nitrogen atmosphere with 0.3 ml. of ethyl bromide in 25 ml. of ether. After the reaction was well under way, one gram of bromotriphenylethylene (MP 114) was added in a few portions during 10-15 minutes. No iodine was used as a primer as Koelsch recommends (2). This mixture was refluxed for 2.5 hours. After cooling, the gray solution (yellow if air has been admitted) was treated with I^{131} solution. Solid inactive iodine was then added until its color was permanent. It was thought best to use an insufficient amount of carrier iodine for the reaction, and then to destroy the remaining Grignard reagent with inactive iodine in order to utilize as much activity as possible. The mixture

was now hydrolyzed by a mixture of ice and 1N hydrochloric acid.

The ether-benzene layer was washed with bisulfite solution and with water and was then evaporated. The residue in ether-petroleum ether solution was decolorized with Nuchar and the solvents removed. The crystalline residue was extracted with four small portions of cold petroleum ether by grinding under this solvent. This removes a small amount of oil. The iodo compound could be used as such or recrystallized from boiling petroleum ether or from alcohol. One recrystallization from the former gave a product with MP 125.5-127. Koelsch gives 126-127. A similar run using inactive iodine gave a product yield of 68.8% based on the bromo compound. A specific activity of 23 μc/mg. was obtained.

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