A Simple Method for General Labelling of Organic Molecules by Gaseous Tritium

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Summary A new method for general labelling of organic compounds by catalytic exchange with gaseous tritium combines the advantages of the catalytic exchange with tritiated water and the gas exposure technique.

GENERAL labelling of organic molecules by tritium is performed usually by one of two principal methods:

(a) an exchange procedure by tritium gas exposure (Wilzbach method)[1] or by modifications of this method.[2] (b) An exchange procedure with tritiated solutions in the presence of a catalyst (Group VIII transition metal) which has previously been activated.[3] This method is very effective, especially for aromatic compounds, where the most active catalyst used was platinum oxide pre-reduced to platinum black.[4]

However, gaseous tritium, which is handled in a simple vacuum line, is far easier to manipulate than tritiated water. In addition, its toxicity is lower by two orders of magnitude than that of tritium oxide.

A simple procedure of labelling with gaseous tritium, that does not involve long exposure time, as in the Wilzbach method, is suggested. Tritium oxide is produced in the reaction vessel that already contains the compound to be labelled. The same catalyst serves both to produce tritium oxide and to activate the exchange between hydrogen and tritium in the organic molecule.

The unlabelled compound (50—100 mg) is dissolved in a minimum volume of the appropriate solvent (dioxan, methanol, or water) and a small, weighed, quantity of platinum oxide is added. The vessel, containing the mixture is then connected to the vacuum line. A measured volume of gaseous tritium, enough to reduce all the platinum oxide, is transfered into the reaction vessel and the mixture is stirred. The reduction of the platinum oxide is rapidly achieved (1—2 h). The formation of tritium oxide may be followed by observing the change in the gas pressure in the vessel. The reaction is performed with 1—20 Curies of gaseous tritium (0·017—0·34 mmole) at ambient temperature.

The tritium oxide is produced with very high specific activity and the exchange between the tritium atoms in the oxide and the hydrogen atoms of the compound is catalysed by the platinum black just formed.† The optimum time for completion of the reaction varies from one compound to another. In the case of the compounds labelled in this laboratory, the time required was 4—24 h.

After the exchange reaction, the solvent, the excess of tritium oxide, and all the volatile impurities are distilled into a cold trap and removed. The handling of highly active volatile compounds is therefore avoided.

This procedure is effective with many types of compounds such as those involving double bonds or aromatic compounds. The following compounds were labelled by this procedure: geraniol, gibberellic acid, linalool, naphthalene, oxytetracycline, phenylalanine, phenylhydrazine, and poly(ethylene glycol), with specific activities from 50 to 500 mCi/mmole.

After separation of the volatile compounds, chromatographic analysis of the crude product showed very few (one to three) active impurities. These were easily removed by preparative chromatographic techniques.

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† The possibility of a competitive catalytic reduction[5] of some compounds suggests the need to limit the reaction time.

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