A Radioactive Local Anæsthetic

THE method of production of the local anæsthetic, dibromo procaine, described below, is of wide application, permitting the rapid formation of a saturated solution of radioactive hydrobromic acid from a small mass of active bromide. The hydrobromic acid serves as a basis for many brominations.

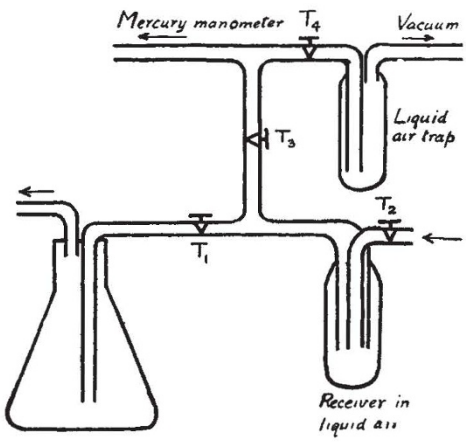
A solution of active bromide is converted to silver bromide by addition of excess silver nitrate. The precipitated silver bromide is dried, and reduced in a silica tube furnace at 800° C. by a stream of dry hydrogen. The furnace outflow, consisting of hydrogen and hydrobromic acid gas, is led through a receiver standing in liquid air and containing the calculated volume of distilled water. A manometer at the hydrogen inlet gives warning by showing a rise of pressure should the receiver become 'iced up'; this should not occur if the bore of the receiver tube is adequate for the mass of silver bromide to be reduced.

The hydrogen escaping from the receiver is led through a solution of silver nitrate (left of diagram), thence out to the air. Clouding of this solution indicates that hydrobromic acid is being carried through, and the rate of hydrogen flow is appropriately adjusted. Forty-five minutes is more than adequate for total reduction of 0·5 gm. silver bromide.

The furnace is disconnected, taps T_1 and T_2 closed, T_3 and T_4 opened and the receiver exhausted with a suitable pump. Tap T_4 is now closed and the receiver, connected only with the manometer in the vacuum circuit, is removed from the liquid air and its base slowly immersed in water at room temperature; the ice melts before the hydrobromic acid higher in the trap. The acid then resumes the gaseous state and dissolves in the water. Should the manometer show a significant rise of pressure above atmospheric, it is only necessary to re-immerse the flask in liquid air for a moment and recommence. In about five minutes, the fuming radioactive hydrobromic acid is ready for use.

Bromination is achieved according to the method of Morel and Leulier[1], who, in 1929, produced a dibromo procaine and investigated it pharmacologically and chemically, ascribing to it the formula $C_{13}H_{18}Br_2N_2O_2HBr$.

The calculated quantity of procaine is added to the hydrobromic acid in the receiver and about 0·5 c.c. of 100-volume hydrogen peroxide introduced. There is a brisk reaction and rapid precipitation of dibromo procaine. If the reaction becomes too violent, further peroxide is added to slow it down. The time taken for this reaction may vary from minutes to hours, depending on the concentration of reagents and, since the half-life of Br^{82} is only 34 hours, the need for a concentrated acid is obvious. In my series of experiments, the dibromo procaine was recrystallized. The conversion of potassium bromide to dibromo procaine can be completed comfortably in one and a half hours. An account of my radio-autographic studies will be given later.



Discussion. The method described has advantages over the simpler techniques for bromide–acid conversion. It is almost quantitative and commends itself when a bromide of small mass and low activity is to be dealt with. It involves no intermediate stages with loss of active substance. Radioactive bromine is usually provided as a simple bromide, so the method has a wide field of application; it is also satisfactory with highly active bromide, in that the system is a closed one and in no stage is a radioactive gas, with its attendant hazards, liberated in the laboratory.

Morel *et al.* have produced several brominated natural alkaloids, and have studied their properties, thus paving the way for experiments with the active bromine isotope.

As yet the synthesis of a complex molecule incorporating one or more radioactive C^{14} atoms presents considerable difficulty and involves losses of C^{14}, in spite of the most careful technique, while many compounds of great pharmacological interest cannot yet be synthesized; it is to bridge this gap that some simple method of labelling is required, and a halogen seems to be the 'label' of greatest general utility at present.

I wish to thank the staff of the Liverpool and Cambridge cyclotrons, and also Prof. A. D. Macdonald, for facilities in his laboratory.

FRANK HOWARTH

Department of Pharmacology,
Victoria University of Manchester.

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[1] Morel, A., Leulier, A., and Denoyel, P., *Bull. Soc. Chim.*, **45**, 435, 457 (1929).

"Plant Geography"

BOOK reviews are of value not only to readers but also to writers, and I am therefore sorry that Sir Edward Salisbury did not, in his notice of my book "The Geography of the Flowering Plants" in *Nature* of May 8, give us his views on any of the more profound modern problems of phytogeography with which it tries to deal.

With regard to the point which he particularly stresses, namely, the question of the value of specialized dispersal mechanisms, I remain unrepentant and see no reason to modify my belief that a broad acquaintance with the Angiosperms and their distribution allows of no other conclusion than that which the reviewer criticizes.

It is also only proper to point out that the incomplete sentence which Sir Edward quotes from my book in the second paragraph of his notice is not, as the context might imply, from the chapter on the dispersal of plants but from an earlier chapter, and from the very pages of it in which the "critical consideration" he desires is, in fact, given at some length.

RONALD GOOD

University College, Hull.