Fast and Efficient Radiobromination Technique for the Preparation of Carrier-free Labelled Compounds

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Summary A novel and rapid method for the preparation of a variety of compounds labelled with carrier-free radiobromine is described

RADIOHALOGENATED compounds have become widely used in medical and biochemical research and in diagnostic medical procedures, and interest in their use is growing with the increasing availability of the radionuclides ^{77}Br and ^{123}I [1] While a variety of reports have appeared on methods by which these radiohalogens can be incorporated into molecules, most of the techniques appear to have limitations For example the chloramine-T labelling method has been applied to a number of small molecules,[2] although it can give poor radiochemical yields if the halogen is carrier-free and cannot be used with target molecules which are susceptible to oxidation or other reaction with chloramine-T Enzymatic labelling[3,4] has been used for labelling both macromolecules and small molecules,[2] although enzymatic brominations, using chloroperoxidase, must be carried out at a low pH, which can lead to the damage of target proteins and renders the technique unsuitable for use with acid-sensitive target molecules Excitation labelling[5,6] has received some attention and, although carrier-free material can sometimes be produced, specificity of labelling and radiochemical yields can be poor

We report here a novel method of radiohalogenation which appears to work rapidly and efficiently for carrier-free radiobromine, works under very mild chemical conditions,

and leaves the labelled product in a mixture from which it can be isolated readily.

A slow stream of air is drawn through two 25 ml flasks so that the air bubbles through the liquid in each flask. Into the first flask (the generator) is placed 1 ml of an aqueous solution of the carrier-free radiohalide ion (in our case $Na^{77}Br$) and *ca.* 1 ml of 0·1 M $KMnO_4$ solution. The second flask (the reactor) contains *ca.* 2 ml of a solution of the target compound in water or phosphate buffer (for example, uracil 0·5 g l^{-1} in pH 7·4 buffer). On adding to the first flask *ca.* 100 μl of conc. HCl the activity is found to pass from the generator to the reactor, over a period of a few minutes (dependent on the airflow rate, typically *ca.* 30 ml min^{-1}). After allowing reaction to occur within the reactor for a further 5 min a 1 ml sample of the solution may be separated by reverse-phase h.p.l.c. and the carrier-free labelled product collected in the usual manner.[2,7] (We add a small amount of sodium metabisulphite solution to most reaction mixtures before h.p.l.c. separation. This is done to protect the h.p.l.c. column and has no effect on the reaction in the reactor, except to terminate it.)

Using *ca.* 40 kBq of ^{77}Br per reaction we find that the efficiency of activity transfer from generator to reactor flasks is >90%. For uracil, the example above, the radiochemical yield (from the radiochromatographic separation record) is >90% of [5-^{77}Br]uracil. This efficiency appears to be maintained if small amounts of carrier are used. We have also used the technique for labelling tyrosine, deoxyuridine, tyramine, cytosine, human serum albumin, and fibrinogen. While we have not yet optimised the conditions to achieve maximum radiochemical yields in these systems, the radiochemical yields obtained in our initial experiments with a number of these target compounds are shown in the Table. Full details and optimised radiochemical yields will be published in a future paper.

TABLE. Radiochemical yields following radiobrominations with carrier-free ^{77}Br

Target material	Amount used (approx.) /mg	Radiochemical yield /% (±3%)
Uracil	1·0	92
Tyrosine	0·1	69
Tyramine	1·0	81
2′-deoxyuridine	1·0	42
Bovine fibrinogen	0·1	71

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