

Short Research Article

Radiolabelled compounds production programme in India[†]

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Received 30 June 2006; Revised 21 February 2007; Accepted 2 March 2007

Abstract: The paper highlights our experience of more than four decades of research gained and expertise attained in the production of various radiolabelled compounds. An active programme for the production of various classes of compounds labelled with radioisotopes like ^{14}C , ^3H , ^{35}S , ^{32}P , ^{33}P and ^{125}I by well-standardized procedures is going on in the country. Recent trends show an increasing demand for the custom-synthesis of various labelled compounds, especially those labelled with ^{14}C . Copyright © 2007 John Wiley & Sons, Ltd.

Keywords: labelled compounds; synthesis; ^{14}C ; tritium

Introduction

In India, the commercial production of radiolabelled compounds started in 1959 at BARC, in a centralized laboratory facility. Through R&D efforts, methods for the production of more than 200 compounds labelled with carbon-14 and tritium (^3H) were developed, procedures standardized and products made available indigenously to researchers by 1975.^{1,2} Within another decade, the number of radiolabelled compounds synthesized increased to 300 and the number of users increased to 1300, spread over 150 institutions in India. ^{35}S -labelled amino acids and $^{32}\text{P}/^{33}\text{P}$ -labelled nucleotides were added to the list of products at a later stage.³ The important classes of compounds produced include uniformly and/or specifically labelled nucleotides, amino acids, fatty acids, carbohydrates, purines, pyrimidines, steroids, hormones, nucleosides, fertilizers, agrochemicals and other miscellaneous intermediate compounds such as urea, thiourea, potassium thiocyanate, sodium bicarbonate, etc.. Since 1989, the responsibility of production and supply of radiolabelled compounds was transferred to Board of Radiation & Isotope Technology (BRIT), a Unit of Department of Atomic Energy. BRIT has, amongst others, an exclusive laboratory for the production of

^{32}P - and ^{33}P -labelled nucleotides for Life Science applications. Scientists in BRIT are also regularly producing ^{125}I -labelled peptides and proteins for RIA application using procedures standardized in-house. Various compounds labelled with $^{99\text{m}}\text{Tc}$, ^{32}P , ^{153}Sm and ^{131}I are produced as radiopharmaceuticals for medical applications.

In addition to the regular ^{14}C , ^3H , ^{35}S and ^{32}P products, custom synthesis of ^{14}C - and ^3H -labelled compounds are taken up which have specific application and use in drug discovery, cell biology and Life Science research. Microwave-assisted synthesis is the current R&D effort for the production of labelled compounds in BRIT. All the labelled compounds synthesized are subjected to stringent quality control tests before release shipment. We are deeply committed to supply the highest quality products.

Results and discussion

The basic approach to the labelled compound production programme has been built up on the solid foundation of ensuring optimum yields in millimolar and sub-millimolar scales of operation, sound quality control measures and time-tested storage conditions to minimize, if not avoid, radiochemical and radiolytic decomposition. Tremendous R&D efforts have also been put in for the development of new synthetic routes and for the improvement of existing procedures in preparing, processing, purifying, storing and controlling quality of various labelled compounds.

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[†]Proceedings of the Ninth International Symposium on the Synthesis and Applications of Isotopically Labelled Compounds, Edinburgh, 16–20 July 2006.

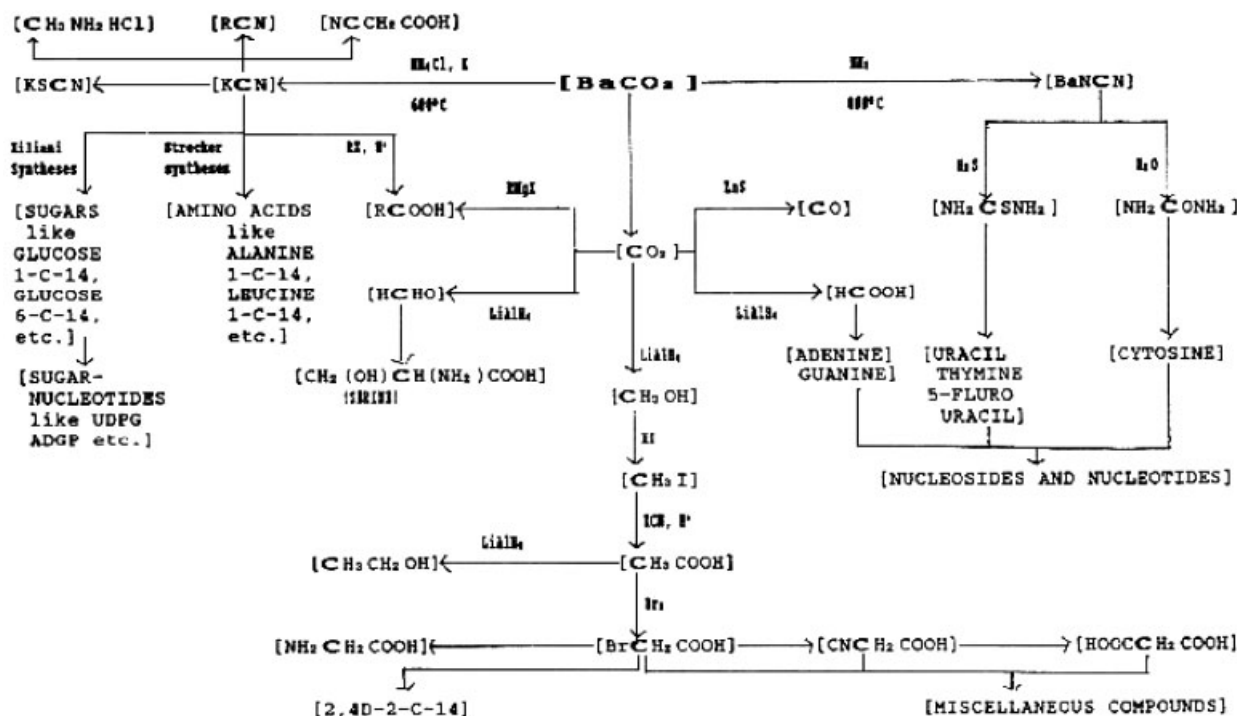


Figure 1 Reaction schemes for the chemical synthesis of ^{14}C -labelled compounds starting from $\text{Ba}^{14}\text{CO}_3$.

Chemical and biological methods of synthesis were followed for the production of various classes of ^{14}C -labelled compounds. The radioactive starting material used for the production of all these ^{14}C -labelled compounds is barium carbonate- ^{14}C . The reaction schemes for the preparation of some important classes of ^{14}C -labelled compounds by chemical method are depicted in Figure 1. Uniformly ^{14}C -labelled sugars and amino acids are prepared by biosynthetic procedures. A few other important ^{14}C -labelled compounds prepared are thiocyanate, fatty acids, coenzyme-A, chloramphenicol, lauryl sulphate, etc.^{4,5} Compounds custom-synthesized in the recent past include diuron, dimethyl isosorbide, pyriothobac sodium, fothiozate, etc. A few other compounds could not be listed here on account of the confidentiality agreement entered into by us with the users of those products. Extension of microwave-assisted preparation of many of the labelled compounds has helped us in saving time and in reducing the waste generation on account of low consumption of solvents.⁶

Tritium-labelled compounds are prepared by any of the well-standardized procedures like tritium-gas exchange method, catalytic reduction using tritium gas, etc. Important classes of compounds in this category include nucleosides and their derivatives, nucleotides, amino acids, purines, pyrimidines, fatty acids, etc. Tritiated water is another compound routinely prepared and supplied.

The most important ^{35}S -labelled compounds regularly prepared are ^{35}S -labelled amino acids, namely, L- ^{35}S -

methionine and L- ^{35}S -cysteine. These products having high specific activity of the order of 1000 Ci/mmol are prepared by the biosynthetic method. Very high-quality ^{32}P -labelled nucleotides are regularly prepared by well-standardized enzymatic methods. Labelled fertilizers prepared are used by agricultural research organizations as radiotracers for uptake studies of plant nutrients like P, S, Ca, etc. under varying agro climatic conditions. The products under this category include ^{32}P single superphosphate, ^{32}P triple superphosphate and 26 other various combinations.

Conclusion

We are actively engaged in the production and supply of a variety of compounds labelled with isotopes such as ^{14}C , ^3H , ^{35}S , ^{32}P , ^{33}P and ^{125}I . Well-established procedures are followed for the synthesis and quality control of these products. We have the capability, expertise and experience in undertaking the radiosynthetic/radiolabelling work leading to the preparation and supply of a large number of radioisotopically labelled compounds.

Acknowledgements

We are grateful to the pioneers of radioisotopes and radioisotopically labelled compounds production programme in the country. We sincerely thank Dr A. K. Kohli, Chief Executive, BRIT for all the encouragement

and support. Thanks are also due to all colleagues in the laboratory for their co-operation.

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