Vol.2 No.4 NUCLEAR SCIENCE AND TECHNIQUES Nov. 1991

SYNTHESIS OF (2–^{3}H) BROMOACETAMIDE

Wang Guoping (王国平), Zhou Meiying (周美英) and Zhao Xialing (赵夏令)

(Institute of Nuclear Research, Academia Sinica, Shanghai 201800, China)

(Received November 1989)

ABSTRACT

(2– ^{3}H) bromoacetamide, a radiotracer of oncomelanicide for various biological studies, has been synthesized by multiple organic reactions from ^{3}H– sodium acetate. The radiochemical purity checked by radio– HPLC was 95% and the specific activity was 11.3GBq/mmol (305mCi/mmol). Moreover, ^{3}H– NMR spectrum indicated that all tritium atoms were labelled on the position 2.

Keywords: Bromoacetamide Tritium labelled

Ⅰ. INTRODUCTION

Bromoacetamide was used as a new oncomelanicide with higher efficiency (over 90% per day) at low concentration (ppb) in water and lower toxity to the other aquatic. A radiolabelled compounds was required for various biological studies, including mechanism, toxicology and other biological examinations. In this paper (2– ^{3}H) bromoacetamide was first synthesized.

(2– ^{3}H) acetic acid was prepared from ^{3}H– sodium acetate by acetyl group isotopic exchange[1]. Ethyl (2– ^{3}H) bromoacetate was obtained by bromination and esterification[1]. Finally, the ester was amidated in ammonia solution. total chemical and radiochemical yield of (2– ^{3}H) bromoacetamide were 17% and 11% respectively.

A manifold vacuum system was used[1] for handling micro volatile radiochemicals.

Ⅱ. EXPERIMENTAL

1. Synthesis

1) (2– ^{3}H) acetic acid 59.2 GBq of anhydrous (2– ^{3}H) sodium acetate (ca. 0.16 mmol) was mixed with 0.15 ml of acetic acid and 0.03ml of acetic anhydride in a tube. The reaction mixture was refluxed at 100 to 110°C for 2 h. (2– ^{3}H) acetic acid obtained was used for the next step.

2) (2– ^{3}H) bromoacetic acid (2– ^{3}H) Acetic acid was vacuum transferred from the tube to the other tube containing 0.1ml bromine, the mixture was refluxed at 100 to 110°C for 2 h. The excess bromine was evaporated and frozen into another tube cooled with liquid nitrogen at 3.99 Pa. The crude (2– ^{3}H) bromoacetic acid obtained was a pink scale crystal.

3) Ethyl (2- ^{3}H) bromoacetate 0.3ml ethanol, 3.0ml benzene and 0.05ml sulfuric acid were added into a glass tube containing (2- ^{3}H) bromoacetic acid, mixed completely. The reactant was refluxed at 75 to 80°C for 1h. Then it was neutralized to pH7 with sodium bicarbonate. The supernatant was transferred into other glass tube. Finally, it was connected with the manifold vacuum system, the ethyl (2- ^{3}H) bromoacetate was obtained after the benzene and other volatiles were evaporated.

4) (2- ^{3}H) bromoacetamide 0.4ml of 25- 28% ammonia solution was mixed with the ethyl (2- ^{3}H) bromoacetate in a glass tube. The reactant was stirred in a bath of dry ice- alcohol at - 10 to - 20°C for 1.7h. The excess ammonia solution was removed under vacuum of 2.66Pa. The product (2- ^{3}H) bromoacetamide was white powder.

2. Analysis

The radiochemical and chemical purities obtained were 95% and 85% respectively. A Dupont ODs column in radio- HPLC with 0.05mol/l phosphate buffer/Methanol (9/1 V/V) as eluent at 0.8 ml/min was used. The distribution tritium was determined by ^{3}H-NMR, and the spectrum has indicated that all tritium atoms were incorporated at the position 2.

III. DISCUSSION

1. (2- ^{3}H) bromoacetamide is unstable, it would debrominated and deamidated in solution at the temperature over - 10°C. So it is difficult to purify the product in micro- quantity using the method of distillation and recrystallization as usual. In the experiment, the product obtained had 85% of chemical purity, but the impurity was mainly composed of some involatile inorganic salts which would not influence the radiochemical purity and the bioactivity.

2. In the reaction of bromination, about 1/3 tritium atoms labelled on methyl group of acetic acid were substituted by bromine atoms. This is the reason that the radiochemical yield was lower than the chemical yield, and the specific activity of tritiated bromoacetamide was lower than that of the starting tritiated sodium acetate.

ACKNOWLEDGEMENT

We wish to thank Ms. Zheng Dongzhu and Mr. Hu Gengseng for providing ^{3}H- NMR spectra data and (2- ^{3}H) sodium acetate.

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