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PREPARATION OF SODIUM 2-MERCAPTO-[^{14}C]ETHANESULFONATE

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SUMMARY

Starting from [1-^{14}C]ethanol 1,2-dibrom-[^{14}C]-ethane was prepared by an usual method through [^{14}C]-ethylene. Sodium sulfite was alkylated by 1,2-dibrom--[^{14}C]ethane and the formed sodium 2-brom-[^{14}C]ethane sulfonate was transferred without isolation to a labelled 2-[(aminoiminomethyl)thio]-[^{14}C]ethanesulfonic acid. After purification by crystallization of the acid 2-mercapto-[^{14}C]ethanesulfonic acid was prepared through guanidinium salt. After the neutralization of 2-mercapto-[^{14}C]ethanesulfonic acid by sodium hydroxide the corresponding sodium salt with specific activity 0.083 μCi/mmol (0.31 MBq/mmol) was prepared.

Key words: ^{14}C MESNA, sodium 2-mercapto-[^{14}C]ethanesulfonate

INTRODUCTION

For studying kinetics and distribution of the sodium 2-mercaptoethanesulfonate (MESNA) in the organism of a laboratory animal (sewer rat) after peroral administration sodium

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2-mercapto-[^{14}C]ethanesulfonate was synthetized starting from [^{14}C]ethanol. Radioactive ethanol was transferred by a modified method (1) by means of catalytic dehydration into ethylene and the latter was immediately collected into the solution of bromine in carbon tetrachloride. Formed 1,2-dibromo-[^{14}C]-ethane diluted by inactive dibromoethane was then transferred according to described modified methods (2,3) first to labelled sodium 2-bromo-[^{14}C]ethanesulfonate and this to the 2-[(amino-iminomethyl)-thio]-[^{14}C] ethanesulfonic acid without isolation. The salt was purified regardless the chemical yield by crystallization to a pure product. The crystalline compound was treated by concentrated ammonia and gave the solution of guanidinium 2-mercapto-[^{14}C]ethanesulfonate, from which 2-mercapto-[^{14}C]-ethanesulfonic acid was obtained by means of an acidic ion exchanger without isolation. By neutralization of this acid solution to pH 6.6 by diluted sodium hydroxide and after distillation of water sodium 2-mercapto-[^{14}C]ethanesulfonate was prepared.

EXPERIMENTAL

Purity and identity of the intermediates and final product were controlled and compared with unlabelled appropriate substances (prepared by above mentioned method) by means of thin layer chromatography on Silica Gel G according to Stahl. The content of SH groups of the final product was controlled by iodometric titration. The starting [1-^{14}C]ethanol used in this work was commercial product (Amersham lab., Buckinghamshire, England).

1,2-Dibrom-[^{14}C]ethane. 30 mg of [1-^{14}C]ethanol (activity 5.5 mCi, 200 MBq) and 3 ml of inactive ethanol were put into a 10 ml vessel with glass wool and while heated this mixture was evaporated into a pyrolytic reactor during 2 hours. The bath

temperature under the distillation vessel was gradually increased to 120°C, 2 ml of inactive ethanol being added from a dropping funnel controlled by a magnetic valve. The pyrolitic reactor was a 60 ml tube with electrical heated cover, filled with aluminium oxide (Condea SB, BDR) activated in argon stream at 450°C for 3 hours. Pyrolitic dehydration of ethanol was carried out at 350°C. The formed gas containing [^{14}C]ethylene was inserted to the bottom of two receivers containing the solution of 4.5 ml of bromine in 25 ml carbon tetrachloride in the first and 0.5 ml of bromine in 20 ml of the same solvent in the second receiver. After the end of the reaction a slow argon stream was blown into the apparatus for about 10 minutes. The contents of both receivers, almost colourless, were distilled on a 30 cm column (inner tube diameter 14 mm, gap 0.8 mm). During distillation the distilled product was washed down three times with 1.5 ml of inactive 1,2-dibromethane. The final yield of the distillate containing 1,2-dibrom-[^{14}C]ethane was 15.66 g, activity 2.12 mCi (78.3 MBq).

2-[(Aminoiminomethyl)thio]-[^{14}C]ethanesulfonic acid. To the solution of 6.4 g of sodium hydroxide in 65 ml of distilled water 5 g of sulphur dioxide from the pressure gas vessel and then 100 ml of ethanol were added. After adding 50 g of 1,2-dibromo-[^{14}C]ethane with activity 2.12 mCi (78.3 MBq) the reaction mixture was stirred and heated for 4 hours under the reflux (bath temperature 120°C), the original suspension was homogenized to a pure solution. The latter was then distilled under lower pressure to dryness. 15 ml of water and 5.5 g of thiourea were added to this prepared solution of raw sodium 2-bromo-[^{14}C]ethanesulfonate and this reaction mixture was boiled for further 3 hours. The next day the formed crystals were three times recrystallized from 15 ml of water. 5.5 g of 2-[(aminoiminomethyl)thio]-[^{14}C]ethanesulfonic acid melted

at 269°C (dec.) were isolated, activity 232 uCi (8.6 MBq). The prepared acid was of the same Rf (0.70) on the thin layer chromatography as the unlabelled product and no thiourea (Rf=0.85) was present (eluting system methanol-chloroform 9:1, detection by I_2).

Sodium 2-mercapto-[^{14}C]ethanesulfonate. The mixture of 5.5 g of the 2-[(aminoiminomethyl)thio]-[^{14}C]ethanesulfonic acid with 15 ml of concentrated ammonia was heated to 50°C in argon atmosphere. An exothermic reaction (with ammonia development) started and then stopped after 10 minutes. The reaction mixture was heated for 2 hours and concentrated in a rotary evaporator to the half volume at 40°C. The gained solution was poured in a chromatography column with 50 ml acid ion exchanger Ostion KS and washed with distilled water under argon. The eluate was neutralized by 4% solution of sodium hydroxide to pH 6.6 in the argon atmosphere, concentrated to 10 ml at reduced pressure and diluted by 200 ml of ethanol. The formed fine crystals were filtered off and dried under reduced pressure. 2.6 g of the sodium 2-mercapto-[^{14}C]-ethanesulfonate (53% chemical yield) with 89% of SH groups were isolated, activity 131.5 μCi (4.86 MBq), specific activity 0.083 μCi/mmol (0.31 MBq/mmol). The prepared product was of the same Rf (0.82) as the unlabelled one at the TLC analysis (eluting system methanol-chloroform 4:3 and 3 drops of acetic acid, detection by heating after spraying with 10% solution of sulfuric acid with 1% of ceric sulfate).

RESULTS

The behaviour of labelled sodium 2-mercaptoethansulfonate (known also as "MESNA") in the organism of the laboratory rat after i.v. administration has been described (4). MESNA is considerably quickly oxidized in blood to sodium 2,2-dithio-

-bis-ethanesulfonate (DIMESNA) ($t_{1/2}$= 16.5 min) (4). Lately MESNA has been used mainly for eliminating urotoxic effects of the metabolite (acrolein) of cytostatics of cyclophosphamide type.

The results of the experiments after peroral application of labelled MESNA at observing the incorporation and excretion of this substance and DIMESNA in sewer rat organism are described elsewhere (5).

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