

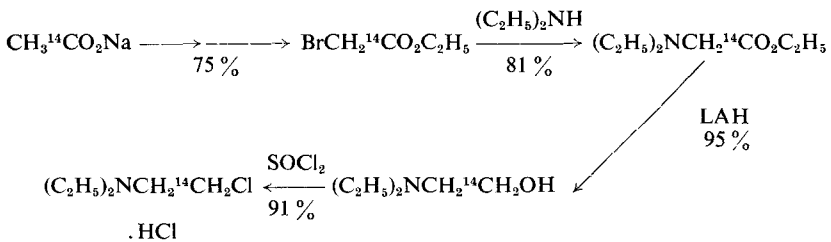
SHORT COMMUNICATIONS**Synthesis of diethylaminoethanol-1-¹⁴C** *

A convenient synthesis of the pharmacological intermediates, diethylaminoethanol-1-¹⁴C and diethylaminoethyl-1-¹⁴C chloride, was developed using barium carbonate-¹⁴C as the starting material. Sodium acetate-1-¹⁴C was converted to diethylaminoethanol-1-¹⁴C on a 5-30 millimolar scale in 50 % yields.

A number of pharmacological active compounds use the diethylaminoethyl moiety as an integral part of their activity or as a physiological modifier of adsorption, solubility or partitioning of the active structure. We found it necessary to prepare diethylaminoethanol-1-¹⁴C for tagging compounds where carbon-14 insertion in other parts of the molecule was difficult or where the fate of the diethylaminoethyl moiety was desired for double isotope studies.

The chemical route used by DAUBEN and GEE⁽¹⁾ for preparing choline-β-¹⁴C using dimethylaminoethanol-1-¹⁴C as an intermediate appeared to be the most direct method, although reported yields were 16 % from sodium acetate-1-¹⁴C. By modified procedures we have obtained 50-58 % yields of diethylaminoethanol-1-¹⁴C and correspondingly excellent yields of diethylaminoethyl-1-¹⁴C chloride for use in tagging biologically active compounds.

The ethyl bromoacetate-1-¹⁴C, prepared by a combination of standard radiochemical procedures, was converted in excellent yields into diethylaminoethanol-1-¹⁴C by successive reaction with diethylamine and lithium aluminum hydride (LAH) :



Ethyl bromoacetate-1-¹⁴C. — 15 millimoles (43 mC) of sodium acetate-1-¹⁴C was converted to acetyl-1-¹⁴C chloride in 94 % yields by the method of COX and TURNER⁽²⁾ employing phthaloyl chloride.

* Received 5 July 1965.

The acetyl-1-¹⁴C chloride was diluted with carrier to 28.0 millimoles (1.43mC/mM) and converted to bromoacetyl-1-¹⁴C bromide by the method of OSTWALD and co-workers⁽³⁾ and to ethyl bromoacetate-1-¹⁴C in 86 % yield by esterification and distillation of the product⁽⁴⁾. Yields from a number of cold and hot runs have been 70-80 % from sodium acetate-1-¹⁴C.

Ethyl diethylaminoacetate-1-¹⁴C. — The ethyl bromoacetate-1-¹⁴C (22.4 mM) was dissolved in 40 ml of benzene and the solution was cooled to 5° C. An excess of diethylamine (8.0 ml) was added dropwise to the cool solution, and the reaction mixture was stirred for seventeen hours at room temperature. The diethylamine hydrobromide was filtered and washed with ether. The filtrate was concentrated *in vacuo* and the residual crude ethyl diethylaminoacetate-1-¹⁴C was distilled at 56° C/6.5 mmHg. The product weighed 2.98 g (81 % yield) and was 97 % pure by vapor phase chromatography.

Diethylaminoethanol-1-¹⁴C. — A solution of 2.98 g (18.2 mM) of ethyl diethylaminoacetate-1-¹⁴C in 20 ml of ether was added to a solution of 1.19 g (30mM) of lithium aluminum hydride in 80 ml of ether at such a rate as to maintain reflux. The reaction mixture was stirred under reflux for eighteen hours and cooled to 0-5° C. The mixture was then hydrolyzed by adding in succession 1.0 ml of water, 1.0 ml of 10 % sodium hydroxide and finally 1.0 ml of water. The mixture was stirred until the insoluble aluminum salts were granular in appearance and then filtered. The ether was removed *in vacuo* and the residual diethylaminoethanol-1-¹⁴C weighed 2.08 g (95 % yield) and was 98 % pure by vapor phase chromatography. The specific activity of the diethylaminoethanol-1-¹⁴C was 1.23 mC/mM.

A previous hot synthesis using one-third of the molar excess of lithium aluminum hydride as used in this synthesis gave 10 % of the unreacted ester in the product. The over-all chemical yield of diethylaminoethanol-1-¹⁴C was 58 % from sodium acetate-1-¹⁴C, and the radiochemical yield was 50 %.

Diethylaminoethyl-1-¹⁴C chloride hydrochloride. — The 2.08 g of diethylaminoethanol-1-¹⁴C was converted to diethylaminoethyl-1-¹⁴C chloride hydrochloride by the method of BRESLOW and his co-workers⁽⁵⁾. The crude tan solid was recrystallized from ethanol and ether, and 2.76 g (91 %) of diethylaminoethyl-1-¹⁴C chloride hydrochloride melting at 204-6° C was obtained. The material was converted to the free base as needed for further syntheses.

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