NOTES

Iodoform-*d* and Methylene-d_2 Iodide

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Although both of the title compounds have been reported,[1-3] a need for a more economical and convenient route to methylene-d_2 iodide has led to the development of the procedure here reported, based upon known chemistry of unlabelled compounds[4-6].

About 0.1 g of anhydrous aluminium chloride was added to a dry mixture of 25 ml (37.5 g, 0.311 mole) of chloroform-*d* and 75 ml (145 g, 0.929 mole) of iodoethane at 55 °C. The mixture turned violet and a gas was evolved. After 24 h, during which further additions of aluminium chloride were sometimes necessary to keep the gas evolution going, the unreacted starting materials and iodine were removed with a water aspirator. The product iodoform-*d* was then sublimed at 70 °C (1 mm) to give 87.9 g (72 %) of yellow plates, mp 117-119 °C; darkening above 112 °C. The isotopic purity of the product reflected that of the chloroform-*d* employed. Mass spectroscopic analysis of one sample indicated over 99 % CDI_3.

To a mechanically stirred solution of 33.65 g (0.624 mole) of sodium methoxide in 100 g (5.00 moles) of 99.8 % deuterium oxide was added 41.07 g (0.104 mole) of iodoform-*d* followed by 14.64 g (0.113 mole) of commercial sodium *meta*-arsenite. The mixture was maintained at 65 °C for 7 h and then allowed to cool and settle overnight. The water layer was decanted and replaced with fresh water, which was also decanted; and the process was repeated until no solid sodium arsenate remained. The yellow organic layer was then dried (Na_2SO_4) and distilled to yield 18.61 g (66 %) of light straw liquid at 84-85 °C (32 mm). The product was stored over iron wire in a blackened bottle. A mass spectroscopic analysis indicated 97 % CD_2I_2 and 3 % $CHDI_2$.

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Synthesis of 1-Methyl-4-(5-^{14}C-3-methyl-5-isoxazolyl) pyridinium Chloride

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1-Methyl-4-(3-methyl-5-isoxazolyl)pyridinium chloride (**1**) has been found to display interesting hypoglycemic activity in laboratory animals, and is currently undergoing extensive evaluation as a potential antidiabetic drug. To facilitate the study of the bodily distribution and metabolism of **1**, a radiolabelled sample was required.

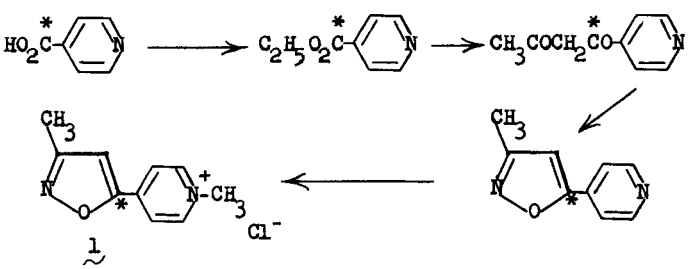

FIG. 1. Synthesis of 1-Methyl-4-(5-^{14}C-3-methyl-5-isoxazolyl)pyridinium Chloride (**1**).

The previously developed synthesis[2] of **1** was modified to permit efficient small-scale preparation. Commercially available labelled starting materials include ^{14}C-methyl chloride, 2-^{14}C-acetone, and α-^{14}C-isonicotinic acid, thus permitting a choice of three different sites of radioactivity in **1**. For metabolic studies, it is desirable to utilize compounds with the radio-label centrally located in the molecular skeleton to preclude loss of radioactivity at an early stage of the process. α-^{14}C-Isonicotinic acid, which leads to **1** labelled at the 5-isoxazolyl carbon (Fig. 1), was therefore chosen as the starting material. From 13.7 mCi of α-^{14}C-isonicotinic acid was obtained 4.0 mCi of labelled **1**.

Ethyl α-^{14}C-Isonicotinate.

The method of Gilman and Broadbent [3] was employed. A stream of dry hydrogen chloride was bubbled through a stirred refluxing suspension of