preparation of Carbon-14 labelled mecarbam  $(0, 0-DI - [1-^{14}C] - ETHYL$ s-[n-ethoxycarbonyl-n-methylcarbamoylmethyl] phosphorothiolothionate)

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#### SUMMARY

 $O, O-Di-[1^{-14}C]$ -ethyl S-[N-ethoxycarbonyl-N-methylcarbamoylmethyl] phosphorothiolothionate has been prepared with a specific activity of 1.97 mCi mmol<sup>-1</sup>. The procedure involved the interaction of  $[1^{-14}C]$ -ethanol with phosphorus pentasulphide in benzene, followed by conversion of the so-formed diethyl dithiophosphoric acid to its potassium salt and reaction of this with ethyl N-chloroacetyl-Nmethylcarbamate in acetone. G.l.c. analysis of the final product in benzene solution showed the purity to be not less than 97 %.

### INTRODUCTION

Mecarbam is an example of an organophosphorus carbamate having insecticidal and acaricidal properties. <sup>(1,2)</sup> It is used for the protection of olives, citrus fruits, and rice, and for the control of a number of root larvae. The compound was required with carbon-14 labelling of the phosphorus-bonded ethoxy groups, for use in a programme of metabolic studies. Its preparation from  $[1-^{14}c]$ -ethanol is described below. U362-4803/80/0317-0341\$01.00 @1980 by John Wiley & Sons, Ltd.

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#### DISCUSSION

A general method for the preparation of 0,0-dialkyl S-(N-alkoxycarbonylcarbamoylmethyl) phosphorothiolothionates has been described.  $^{(3)}$  For the preparation of mecarbam (<u>1</u>), the route starting from ethanol, phosphorus pentasulphide, and the appropriate carbamate (2) is shown (Scheme I). We have

$$4 \text{EtOH} + P_2 S_5 \longrightarrow 2 (\text{EtO})_2 P S_2 H + H_2 S$$

$$(\text{EtO})_2 P S_2 H + \text{KOH} \longrightarrow (\text{EtO})_2 P S_2 K$$

$$(\text{EtO})_2 P S_2 K + \text{ClCH}_2 \text{CON} (\text{Me}) \text{CO}_2 \text{Et} \longrightarrow (\text{EtO})_2 P S_2 \text{CON} (\text{Me}) \text{CO}_2 \text{Et} + \text{KCl}$$

$$(\underline{2})$$
  $(\underline{1})$ 

## Scheme I

now found that this route is capable of being used successfully on a semimicro scale to give a product of high purity if exactly equivalent amounts of pure reagents are used at each stage.  $\left[1-\frac{14}{C}\right]$ -Ethanol was first allowed to react with the calculated amount of phosphorus pentasulphide,  $^{
m (4)}$  to yield carbon-14 labelled 0,0-diethyl dithiophosphoric acid. The potassium salt of this was then obtained by treatment with powdered potassium hydroxide.<sup>(3)</sup> We found that the solid product formed in this way could be extracted with acetone (leaving traces of insoluble impurities) to give a solution which did not require further purification before use in the subsequent step. Although isolation and recrystallization of the potassium salt can be carried out at this stage if desired, a number of trial experiments with unlabelled materials showed that this process did not lead to the formation of a final product of higher purity than could be obtained by direct use of the initial acetone extract. After condensation of the potassium salt with ethyl N-chloroacetyl-N-methylcarbamate (2), the acetone was removed to leave a product (subsequently taken up in benzene) of not less than 97% purity by g.l.c. (5) and with a specific activity of  $1.97 \text{ mCi mmol}^{-1}$ .

#### EXPERIMENTAL

 $[1-^{14}C]$ -Ethanol was supplied by The Radiochemical Centre, Amersham, U.K., and ethyl N-chloroacetyl-N-methylcarbamate<sup>(6)</sup> by Cheminova AS, Lemvig, Denmark. Analag solvents were used, benzene and ether being dried over sodium. Phosphorus pentasulphide was BDH Laboratory Reagent grade (not less than 98 %).

<u>Preparation of 0,0-di-[1-<sup>14</sup>c]-ethyl dithiophosphoric acid</u>.- The ampoule of  $[1-^{14}c]$ -ethanol (2.5 mCi, 577 µCi mg<sup>-1</sup>) was opened at -78 °C and absolute ethanol was added to give a total of 109.5 mg (2.38 mmol). The labelled alcohol was transferred with benzene (2.5 cm<sup>3</sup>) to a 5 cm<sup>3</sup> round-bottomed flask fitted with a reflux condenser, and phosphorus pentasulphide (132 mg, 0.595 mmol) was added. With gentle agitation, the mixture was heated in an oil bath (3 h at 85 °C followed by 5 h at 88 ~ 90 °C)until evolution of H<sub>2</sub>S ceased and a clear solution remained.

Preparation of an acetone solution of the potassium salt. - Powdered 85 % potassium hydroxide (823 mg, 1.25 mmol) was thoroughly mixed with the benzene solution of labelled diethyl dithiophosphoric acid. The white solid which was formed was filtered off, washed with benzene, and ether, and dried. It was then extracted with acetone (lo cm<sup>3</sup>) to leave a small insoluble residue (24.6 mg) and to give a solution containing the required potassium salt (229 mg).

Formation of  $[{}^{14}C]$ -labelled mecarbam. - Recrystallized ethyl N-chloroacetyl-N-methylcarbamate<sup>(6)</sup> (183.5 mg, 1.02 mmol) was added to the acetone solution of potassium di- $[1-{}^{14}C]$ -ethyl dithiophosphate (229 mg, 1.02 mmol) and the mixture was heated under gentle reflux (2 h).<sup>(3)</sup> Potassium chloride was removed by filtration and the solution was evaporated under reduced pressure to leave an almost colourless oily residue of mecarbam (340 mg, 1.03 mmol). The product was taken up in benzene (50 cm<sup>3</sup>) to give a solution which was shown by g.l.c.<sup>(5)</sup> to contain 0.64 % w/v of mecarbam (320 mg, overall yield 81.7 %) (purity  $\langle 97\%$ ). The specific activity was 1.97 mCi mmol<sup>-1</sup> (Calc. 2.10 mCi mmol<sup>-1</sup> based on the activity of the ethanol used). 343

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