NOTES

SYNTHESIS OF $|1,2\text{-}^{14}C_2|$OXALACETIC ACID

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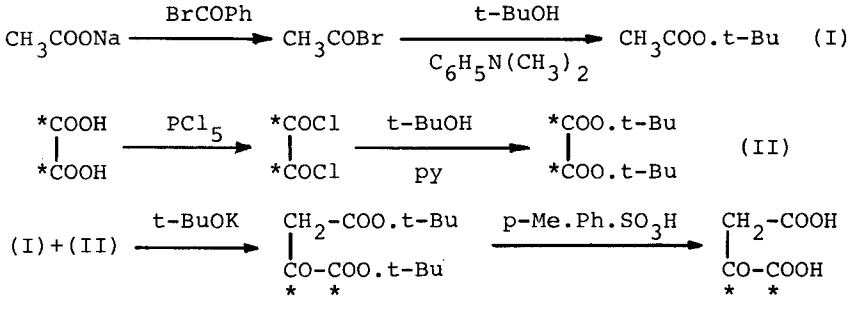
In connection with our work on the biosynthesis of bufadienolides[1] labelled oxalacetic acid was required for biosynthetic experiments. Oxalacetic acid labelled at C-4 has been previously prepared[2,3] but as far as we know there is no reported synthesis of this acid labelled at C-1 and C-2. Accordingly, we now report a synthetic approach to the title compound based on a known method for obtaining β-keto esters[4]. The procedure (Scheme 1) consisted in the condensation of t-butyl esters of acetic and oxalic acids, followed by the hydrolysis of the di-t-butyl oxalacetate thus obtained.

Scheme 1



EXPERIMENTAL

Melting points are uncorrected. NMR spectra were recorded at 60 MHz. Radioactivity was measured by liquid scintillation counting.

Di-t-butyl $|^{14}C_2|$oxalate. It was prepared following the reported method[5] for the unlabelled compound. Anhydrous $|^{14}C_2|$oxalic acid (35 mg; 0.85 mCi) was diluted with unlabelled anhydrous oxalic acid (930 mg) and treated with phosphorus pentachloride (10 g). The solid mixture was shaked at room tempera ture until it liquified (2 days) and then for 1 additional day. From the mixture, oxalyl dichloride was distilled and collected at 60-90°C; lit.[5] b.p. 62°C. The $|^{14}C_2|$oxalyl dichloride was added to a solution of t-butyl alcohol (9.5 ml), pyridine (4.8 ml) in ether (9.0 ml). The reaction mixture was refluxed under nitrogen for 3 h. The cooled solution was filtered, the

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filtrate was acidified with 2% sulphuric acid solution and extracted with ether (3 x 10 ml). The organic layer was washed with saturated sodium hydrogen carbonate solution (2 x 2.5 ml), and with water (2 x 3 ml) and dried over anhydrous potassium carbonate. Evaporation of the solvent afforded a white crystalline solid (803 mg, 37%) of m.p. 70-71°C; lit.[5] m.p. 70.5-71°C. It was recrystallized from petroleum ether until constant specific activity of 0.18 mCi/mmol; NMR ($CDCl_3$-TMS): δ 1.27 (s).

Di-t-butyl $|1,2-^{14}C_2|$oxalacetate. A mixture of di-t-butyl $|^{14}C_2|$oxalate (800 mg) and t-butyl acetate (462 mg) was added to a solution of potassium (150 mg) in t-butyl alcohol (5 ml), and the reaction mixture was refluxed for 3 h. The cooled mixture was washed with ether (10 ml), acidified with 2% sulphuric acid solution and extracted with ether (3 x 10 ml). The dried organic extract was evaporated to yellow needles (676 mg, 70%) of m.p. 90-91°C; lit.[2] m.p. 90-91°C. Specific activity: 0.17 mCi/mmol.

$|1,2-^{14}C_2|$Oxalacetic acid. A solution of 670 mg of the previous compound in anhydrous benzene (3.5 ml) was treated with p-toluensulphonic acid (10 mg) and the mixture was refluxed until no more evolution of isobutene (almost 1 h). A yellow precipitate (280 mg, 80%) of oxalacetic acid (actually hydroxyfumaric acid) of m.p. 182-183°C was obtained on cooling; lit.[2] m.p. 183-184°C. The product was recrystallized from ether-petroleum ether to a white crystalline solid (271 mg) of m.p. 161-163°C (hydroxymaleic acid) and constant specific activity of 0.17 mCi/mmol.

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