Optically Active Mevaldic Acids

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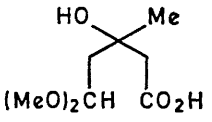
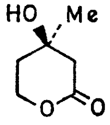
Summary Racemic 3-hydroxy-3-methyl-5,5-dimethoxypentanoic acid was resolved into its antipodes by means of fractionation of the quinine salts, and the (*R*)- and (*S*)-mevaldic acids recovered therefrom were related to mevalonolactone.

IN connection with studies on the mechanism of action of 3-hydroxy-3-methylglutaryl CoA (HMG CoA) reductase from yeast (mevalonate/NADP/oxidoreductase [acylating CoA] E.C. 1.1.1.34) we needed the optically active forms of mevaldic acid, the preparation and characterisation of which will be described in the sequel.



(I)



(II)

The barium salt of 3-hydroxy-3-methyl-5,5-dimethoxypentanoic acid[1] (I) gave upon reaction with an equimolecular amount of quinine sulphate a diastereomeric mixture of the 1 : 1 quinine salts, which were fractionated by repeated crystallisations from ethyl acetate–hexane. After four crystallisations (total yield 50%) the quinine salt (m.p. 148°) was decomposed and the dimethylacetal hydrolysed with Dowex 50. Reduction with $NaBH_4$[1] gave (−)-(*R*)-mevalonolactone (II) ($[\alpha]^{20}_{D}$ − 10·0°, chloroform).[2] The (*R*)-mevalonolactone was further characterised as the crystalline tertiary acetate.†

(3*S*)-Mevaldic acid was recovered from the first mother-liquor of the quinine salt and transformed to the tertiary acetate of (3*S*)-mevalonolactone which, after two recrystallisations, gave the optically pure compound in 24% yield.

Our procedure for the preparation of optically active mevalonolactone offers several advantages over the methods previously reported.[3] Specifically, it provides a simple means for obtaining both (3*R*)- and (3*S*)-mevalonolactones labelled with hydrogen isotopes at C-5.

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