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# MEVALONOLACTONE ACETATE (3-ACETOXY-3-METHYLVALEROLACTONE)

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The crystalline acetate of 3RS-mevalonolactone was first prepared in 1958.* More recently, Dr. J. Rétey of Eidg. Technische Hochschule, Zürich, was seeking a derivative of chiral mevalonic acid with favourable crystallising power and optical rotation for determination of the chirality of mevalonic acid produced from mevaldic acid and some of its derivatives by 3-hydroxy-3-methylglutaryl-coenzyme-A-reductase. The author therefore prepared the acetate of synthetic (1) 3R-mevalonolactone; happily this proved to be much less soluble in ether than the racemate and Blattman and Rétey (2) were able to prepare optically pure 3S-mevalonolactone acetate from 3S-mevalonolactone of 72% optical purity after only two recrystallisations from ether. The difference in solubility between the chiral and racemic forms of mevalonolactone acetate also provided Blattmann and Rétey with an elegant means of determining the chirality of their enzymically produced mevalonates. Carrier 3RS-mevalonolactone was used to assist the isolation of micromolar quantities of $^3$H-labelled mevalonate; after acetylation the products were co-crystallised with authentic (3R)- and (3S)-mevalonolactone acetates; after two crystallisations the specific radioactivity of the (3R)-acetate was unchanged while that of the (3S)-acetate was reduced to zero. The lactone acetate thus has a usefulness not shared by the few other known crystalline derivatives.

## Experimental

(3RS)-Mevalonolactone acetate. Mevalonolactone (785 mg), isopropenyl acetate (1.5 ml) and p-toluene sulphonic acid (5 mg) were heated to 95 - 100° for 30 minutes while the liberated acetone distilled off. Sodium acetate (5-10 mg) was added and excess isopropenyl acetate was removed in a water-pump vacuum; the product (938 mg) distilled at 84°/0.02 mm. Recrystallisation from ether-light petroleum (b.p. 60-80°) gave 578 mg colourless prisms m.p. 49-50°. (Found: C,55.5; H, 6.9%. $C_8H_{12}O_4$ requires C,55.8; H,7.0%).

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*The compound is mentioned in "Natural Products derived from Mevalonic Acid", p. 13 (1970), (Goodwin, T.W., Ed.) Academic Press Inc., London and New York.

(3R)-Mevalonolactone acetate prepared similarly from synthetic (3R)-mevalonolactone(1) and recrystallised from dry ether at 0° formed large chunky prisms m.p. 39-41°. (Found: C,55.4; H,6.8% $C_8H_{12}O_4$ requires C,55.8; H,7.0%). ORD (22°): $[\alpha]_D$ - 48.0 ± 0.4°, $[\alpha]_{322}$ - 225° (c = 1% in EtOH); $[\alpha]_{238}$ - 1090° (trough), $[\alpha]_{219}$ ± 0° (c = 0.1% in EtOH). For comparison the values for (R)-mevalonolactone at the same concentrations and temperature are $[\alpha]_D$ - 23.2 ± 0.4°, $[\alpha]_{322}$ -98°; $[\alpha]_{241}$ - 774° (trough), $[\alpha]_{228}$ ± 0°. The diphenylmethyl amide of (S)-mevalonic acid gave a plain ORD curve with values (at 20°): $[\alpha]_D$ + 2.45 ± 0.05% (C = 1.5% in EtOH); $[\alpha]_{322}$ + 14°, $[\alpha]_{238}$ + 94° (C = 0.27% in EtOH). Blattman and Rétey (2) record $[\alpha]_D$ - 51° (c = 0.386 in EtOH) for the (R)-acetate and $[\alpha]_D$ + 51° (c = 0.382 in EtOH) for the (S)-acetate.

Treatment of mevalonolactone acetate with equimolar quantities of bases led to extensive elimination of acetic acid with formation of the αβ unsaturated lactone.

The author thanks Dr. G. Ryback for the ORD measurements which were carried out on a Bellingham and Stanley Polarmatic 62 spectropolarimeter.

## References

1. R. H. Cornforth, J. W. Cornforth and G. Popják, Tetrahedron, 1962, 18, 1351.

2. P. Blattmann and J. Rétey, Z. physiol. Chem., 1971, 352, 369.