

Synthesis of Racemic Loliolide

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LOLIOLIDE, isolated from *Lolium perenne*¹ and *Digitalis purpurea*,² was assigned the structure (I) by Hodges and Porte,¹ and also independently by Wada.² This is an interesting monoterpene with the trimethylcyclohexane ring A of the higher terpenoids. We now report a synthesis of racemic loliolide which corroborates the proposed structure.

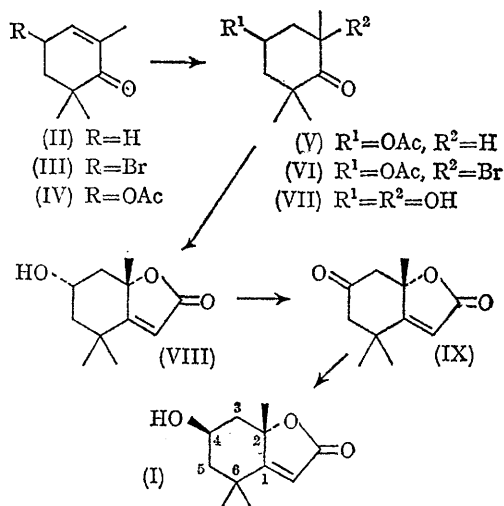
2-Bromo-2,6,6-trimethylcyclohexanone³ was dehydrobrominated with lithium bromide and

lithium carbonate in dimethylformamide to give the $\alpha\beta$ -unsaturated ketone (II). Allylic bromination of (II) with *N*-bromosuccinimide gave the bromo-ketone (III), which was heated with silver acetate in benzene to give the acetoxy-ketone (IV). Catalytic hydrogenation of (IV) over 5% palladium-charcoal in ethanol and bromination of the resulting saturated ketone (V) afforded the acetoxy-bromo-ketone (VI). The latter was transformed by

treatment with sodium methoxide in methanol, followed by hydrolysis with aqueous methanol containing a few drops of dilute sulphuric acid, into the dihydroxy-ketone (VII). Condensation of (VII) with lithium ethoxyacetylde⁴ in anhydrous ether at -30° and subsequent treatment of the crude triol with dilute sulphuric acid in tetrahydrofuran yielded the hydroxy-butenolide (VIII), ν_{\max} 1745, 1633 cm^{-1} , the epimer of (I) at C-4. N.m.r. spectrum of (VIII) showed a peak at τ 5.85 as a triplet of triplets ($J = 11.8$ and 3.7 c./sec.) due to an axial proton at C-4.

Oxidation of (VIII) with Jones reagent gave the keto-butenolide (IX), m.p. $69-70^{\circ}$, ν_{\max} 1755, 1724, 1635 cm^{-1} . Reduction of (IX) with sodium borohydride in methanol yielded racemic loliolide (I), m.p. $138-139^{\circ}$, which was identical with natural loliolide in infrared and ultraviolet spectra, and retention time in gas-liquid chromatography.

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⁴ J. F. Arens, *Adv. Org. Chem.*, 1960, **2**, 203.