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THE STEREOSELECTIVE TOTAL SYNTHESIS OF RACEMIC γ-EUDESMOL

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Certain projects currently underway in our laboratory called for a supply of pure γ-eudesmol.[1] A recent report by Pinder and Williams[2] suggests that this material as found in nature cannot be easily purified. These workers synthesized a pure sample of the naturally occurring (+)-form of γ-eudesmol starting from (+)-α-cyperone.[3] In view of the scarcitv of this latter substance, we decided to investigate potential routes to the racemic form of γ-eudesmol (8).† From these investigations an efficient total synthesis of racemic γ-eudesmol (9) has evolved whose essential features are outlined below.

The known ketone 1[4] was converted by treatment with sodium hydride in diethyl carbonate to the corresponding β-keto ester 2 [bp 118° (bath temp.) at 0.05 mm]. Selective reduction (KBH_4)

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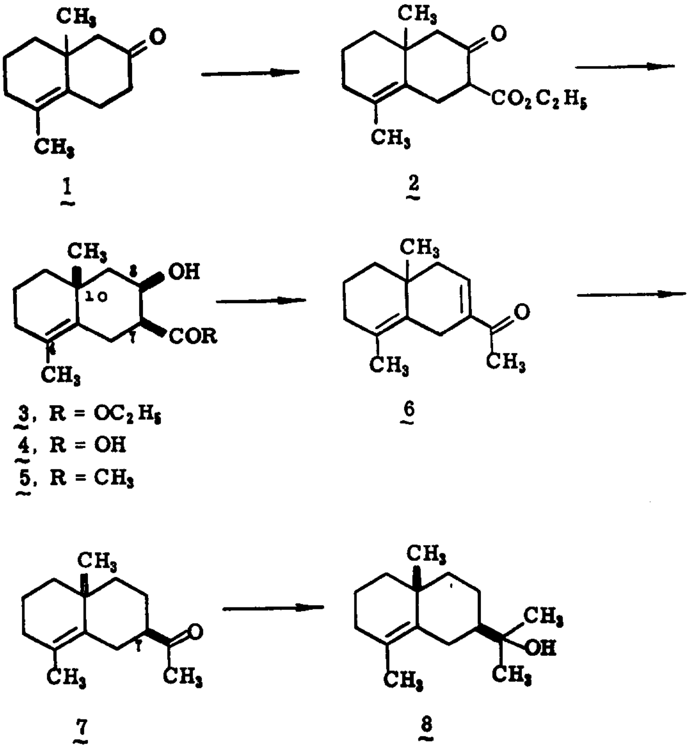
† All formulas represent racemic substances even though only one enantiomer is depicted.



afforded hydroxy ester 3 [$\lambda_{\max}^{\text{film}}$ 2.85 (OH), 5.78 (CO), 8.35, 9.10, 9.60, and 10.50 μ] which, in turn, yielded hydroxy acid 4 [mp 140-142°, $\lambda_{\max}^{\text{KBr}}$ 2.90 (OH), 3.0-4.0 (COOH), 5.85 (CO), 8.20, 8.50, 8.70, 10.50, and 11.25 μ; $\delta_{\text{TMS}}^{\text{CDCl}_3}$ 7.05 (OH; 2H), 4.43 (H-8, $W_{1/2}$ = 7Hz), 1.67 (C-4 CH_3), and 1.26 ppm (C-10 CH_3); 60% yield based on ketone 1] when saponified with ethanolic potassium hydroxide. The nmr spectrum of this acid supports the assigned C-8 stereochemistry;[4] the orientation depicted for C-7 follows from stability considerations.

The crude hydroxy ketone 5 [λ_{max}^{film} 2.94 (OH), 5.83 (CO), 8.48, and 9.51 μ] which resulted from addition of ethereal methyllithium to hydroxy acid 4, smoothly dehydrated in refluxing aqueous ethanolic potassium hydroxide giving unsaturated ketone 6 [bp 95° (bath temp.) at 0.05 mm; λ_{max}^{film} 6.00 (CO), 8.00, 9.32, 10.47, 11.20, and 12.48 μ; $\delta_{TMS}^{CCl_4}$ 6.78 (H-8), 2.20 (CH_3CO), 1.62 (C-4 CH_3), and 0.96 ppm (C-10 CH_3); λ_{max}^{EtOH} 232 mμ (ε 10,000)]. Catalytic hydrogenation over 5% palladium-on-carbon in ethanolic potassium hydroxide[5] afforded the dihydro derivative 7 [bp 110° (bath temp.) at 0.05 mm; $\delta_{TMS}^{CCl_4}$ 2.06 (CH_3CO), 1.61 (C-4 CH_3), and 1.04 ppm (C-10 CH_3)]. The gas chromatogram[6] of this material revealed about 8% of a second component, presumably the C-7 epimer, which could be completely removed by preparative gas chromatography. Equilibration in refluxing methanolic sodium carbonate afforded a 10:1 mixture of epimeric ketones, predominantly 7. Racemic γ-eudesmol (8) [bp 100° (bath temp.) at 0.04 mm; λ_{max}^{film} 2.95 (OH), 8.30, 8.66, 8.78, 10.72, 10.93, 11.80, 12.20, and 12.98 μ; $\delta_{TMS}^{CCl_4}$ 1.58 (C-4 CH_3), 1.13 (isopropyl CH_3's), and 1.01 ppm (C-10 CH_3)[1]; 40% based on hydroxy acid 4] was secured *via* addition of ethereal methyllithium to ketone 7. The infrared spectrum and gas chromatographic retention time were identical with those of the natural (+)-isomer.

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6. A 10% DC-550 Silicone oil on 60-80 Chromosorb W column was used.