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# SYNTHESIS OF TWO STEREO-ISOMERS OF DEHYDROABIETIC ACID

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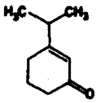
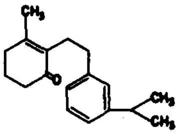
THE condensation product from 3-keto-4-methylpentenyl chloride and ethyl acetoacetate was hydrolysed with a mixture of acetic and sulphuric acid, leading to the formation of m-isopropylcyclohexenone (I, red 2:4-dinitrophenylhydrazone, m.p. 155°. Found: C, 56.3; H, 5.7; N, 17.6. $C_{15}H_{18}O_4N_4$ requires C. 56.6; H, 5.7: N. 17.6). The ketone (I) was condensed with ethyl bromoacetate to afford a doubly unsaturated ester (b.p. 128°/0.6 mm; Found: C, 75.1; H, 9.3. $C_{13}H_{20}O_2$ requires C, 75.0; H, 9.6). This was dehydrogenated with sulphur (b.p. 105-110°/ 4 mm; Found: C, 75.5; H, 8.6. $C_{13}H_{18}O_2$ requires C, 75.7; H, 8.7). The ester so obtained, was reduced with lithium-aluminium-



I



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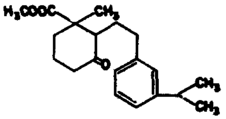
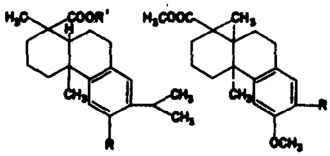


III



IV R = H; R' = H

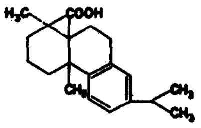
V R = —$COCH_3$; R' = —$CH_3$

VI R = —$OCH_3$; R' = —$CH_3$

VII R = H

VIII R = —$COCH_3$

IX R = —$C(CH_3)_2OH$



X

hydride to afford m-isopropylphenethyl alcohol[1] (b.p. 95-100°/ 4 mm; Found: C, 79.9; H, 9.7. $C_{13}H_{16}O$ requires C, 80.4; H, 9.8). The condensation product from the corresponding bromide with Hagemann's ester in the presence of potassium-t-butoxide afforded on alkaline hydrolysis the unsaturated ketone[2] (II) in a good yield. This was boiled with an ethanolic solution of potassium cyanide[3] and the crude condensation product was subjected to alkaline hydrolysis. The acidic product so obtained, was esterified with an excess of diazomethane to afford the keto-ester (III) (b.p. 195°/0.4 mm; Found: C, 75.5; H, 8.7. $C_{20}H_{28}O_3$ requires C, 75.9; H, 8.9; yellow 2:4-dinitrophenylhydrazone, m.p. 151°; Found: C, 62.8; H, 6.3; N, 11.7. $C_{26}H_{32}O_6N_4$ requires C, 62.9; H, 6.4; N, 11.3). The keto-ester (III) was condensed with methylmagnesium-iodide and the crude carbinol was dehydrated by boiling with oxalic acid in toluene. The product was found to be a mixture of the corresponding unsaturated ester and the related γ-lactone (5.677). The unsaturated ester was cyclised with polyphosphoric acid[4] and the neutral and acidic products were separated. The acidic material was again separated into two definite individuals (I) m.p. 202° (Found: C, 80.1; H, 9.4. $C_{20}H_{28}O_2$ requires C, 80.0; H, 9.4; Methyl ester, m.p. 98°; found: C, 79.7; H, 9.5. $C_{21}H_{30}O_2$ requires C, 80.2; H, 9.6) and (ii) m.p. 155° (Found: C, 80.3; H, 9.7. $C_{20}H_{30}O_2$ requires C, 80.0; H, 9.4; methyl ester, m.p. 62°; Found: C, 80.5; H, 9.4. $C_{21}H_{30}O_2$ requires C, 80.2; H, 9.6). The

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[1] R.D. Hawarth and R.L. Barker, J. Chem. Soc. 1299 (1939).

[2] G. Stork and A. Burgstahler, J. Amer. Chem. Soc. **73**, 3544 (1951).

[3] U.R. Ghatak, D.K. Datta and S.C. Ray, J. Amer. Chem. Soc. **82**, 1728 (1960).

[4] F.E. King, T.J. King and J.G. Topliss, Chem. & Ind. 113 (1956).

ester melting at 98° afforded a mono-keto ester[5] on oxidation with chromic acid (orange-red 2:4-dinitrophenylhydrazone, m.p. 200°; Found: C, 64.1; H, 6.2; N, 10.8. $C_{27}H_{32}O_6N_4$ requires C, 64.3; H, 6.3; N, 11.1). From the rate of hydrolysis and formation of the mono-keto ester mentioned above, the acid melting at 202[2] is represented by the stereoformula (IV).

The above methyl ester m.p. 98° was allowed to react with acetylchloride in the presence of aluminium chloride to afford the ketone (V), m.p. 141° ($\lambda^{alc}_{max}$ 257 mμ; log ε 3.9; Found: C, 77.4; H, 8.8. $C_{23}H_{32}O_3$ requires C, 77.5; H, 9.0. orange 2:4-dinitrophenylhydrazone, m.p. 214°, Found: C, 64.8; H, 6.8. $C_{29}H_{36}O_6N_4$ requires C, 64.9; H, 6.7). The keto ester (V) was allowed to react with excess of perbenzoic acid[6] in chloroform and the crude product thus obtained, on alkaline hydrolysis and subsequent treatment with excess of diazomethane afforded (VI) m.p. 130-131° (Found: C, 76.4; H, 9.6. $C_{22}H_{32}O_2$ requires C, 76.6; H, 9.4). With a view to preparing an authentic sample of (VI), methyl o-methylpodocarpate[7] was condensed with acetyl chloride in the presence of aluminium chloride. The ketone (VIII, m.p. 124°; Found: C, 73.4; H, 8.3. $C_{21}H_{28}O_4$ requires C, 73.2; H, 8.1. Orange 2:4-dinitrophenylhydrazone, m.p. 265°; Found: C, 61.9; H, 6.3; $C_{27}H_{32}O_7N_4$ requires C, 61.8; H, 6.1) was treated with methylmagnesium-iodide to afford the carbinol (IX), m.p. 148° (Found: C, 73.5; H, 8.9. $C_{22}H_{32}O_4$ requires C, 73.3; H, 8.9). This was dehydrated by heating with glacial acetic acid and the unsaturated compound, on catalytic hydrogenation afforded an ester, m.p. 130-131° alone or mixed with (VI).

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[5] E. Wenkert and B.G. Jackson, J. Amer. Chem. Soc. **80**, 211 (1958).

[6] E. Wenkert and B.G. Jackson, J. Amer. Chem. Soc. **80**, 217 (1958).

[7] B.K. Bhattacharyya, J. Indian Chem. Soc. 22, 165 (1945).

The acid melting at 155° is most probably represented by the stereoformula (X) as belonging to the cis-series. This followed from detailed studies with the four stereo-isomers[3] of the desisopropyl acid, although the cis-locking could not be definitely established through the formation of di-keto-ester.[5]

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