Synthesis of *trans*-4,4a-Dimethyl-2-decalone; Establishment of Configuration by Optical Rotatory Dispersion

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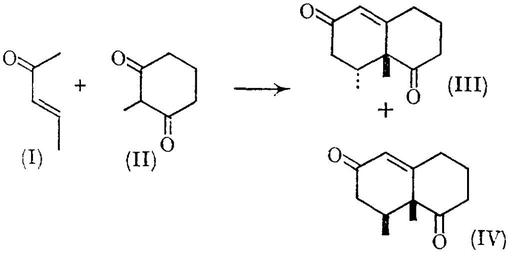
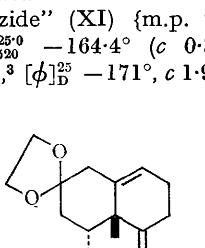
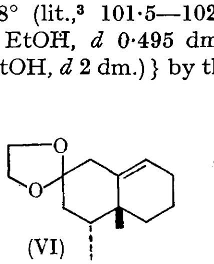
THE recent report[1] on the stereoselectivity in the synthesis of *cis*- and *trans*-4,4a-dimethyl-2-octalone derivatives has prompted us to report our observations concerning the Robinson annelation reaction of 2-methylcyclohexane-1,3-dione (II) with pent-3-en-2-one (I) in refluxing benzene–ethanol (1 : 1) containing potassium hydroxide and pyrrolidine. Under these conditions the major product was the *trans*-diketone (III) (71%)† [m.p. 81·5—83°; λ_{max} (KBr) 1705, 1670, and 1620 cm.$^{-1}$; δ ($CDCl_3$) 5·75 (s, vinyl H), 1·40 (s, Me), and 0·80 (d, *J* 7 c./sec., Me)]. A minor product, presumably the *cis*-diketone (IV), was also formed [(III) : (IV) 6 : 1] along with very small amounts (< 1%) of two other products. The stereochemistry of (III) was established as described below.

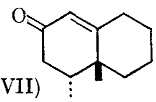


Treatment of (III) with ethylene glycol and toluene-*p*-sulphonic acid in refluxing benzene led to selective acetalization of the $\alpha\beta$-unsaturated carbonyl group to give the acetal (V) [53%; λ_{max} (KBr) 1707 and 1666 cm.$^{-1}$]. Wolff–Kishner reduction of (V) gave acetal (VI) [84%; λ_{max} (film) 1100 cm.$^{-1}$] as a yellow oil which was hydrolysed in 5% hydrochloric acid in aqueous dioxan to the $\alpha\beta$-unsaturated ketone (VII) [94%; m.p. 34—35°; b.p. 76—78°/0·5 mm.; λ_{max} (KBr) 1670 and 1616 cm.$^{-1}$; δ ($CDCl_3$) 1·01, (d,3H, *J* 6·5 c./sec.), 1·29, (s, 3H), and 5·75 (d, 1H, *J* 1·5 c./sec.)]. Reduction (Li–NH_3) of (VII) in tetrahydrofuran gave the ketone (VIII) [79%; b.p. 60—63°/0·7 mm.; λ_{max} (film) 1710 cm.$^{-1}$; δ ($CDCl_3$) 0·91 (d, *J* 7 c./sec., Me), and 1·15 (s, Me)].

Partial resolution of (VIII) was accomplished by fractional crystallization of the diastereoisomeric "(−)-menthydrazones" (IX) and (X) formed by reaction of racemic (VIII) with "(−)-menthydrazide" (XI) {m.p. 96—98° (lit.,[3] 101·5—102); $[\phi]^{25\cdot0}_{520}$ −164·4° (*c* 0·3922, EtOH, *d* 0·495 dm.) (lit.,[3] $[\phi]^{25}_{D}$ −171°, *c* 1·961, EtOH, *d* 2 dm.)} by the method of Woodward, *et al.*[2] Acid hydrolysis [10% H_2SO_4 in water–ethanol (1 : 1)] of (IX) [m.p. 197—199°, $[\phi]^{25\cdot0}_{520}$ −45·5° (*c* 0·236, EtOH, *d* 0·525 dm)] gave optically active (VIII) [81%; r.d. (*c* 0·36, *d* 0·1 dm., MeOH) $[\phi]_{450}$ −125°; $[\phi]_{307}$ −1800°; $[\phi]_{268}$ +2450°; $[\phi]_{240}$ +2275°]. Addition of a trace of concentrated hydrochloric acid to the solution gave: $[\phi]_{450}$ −100°; $[\phi]_{307}$ −963°; $[\phi]_{268}$ +875; $[\phi]_{240}$ +625°. The relative stereochemistry of the methyl groups as well as the absolute configuration shown for (VIII) was established by comparison of its r.d. curve with


(V)


(VI)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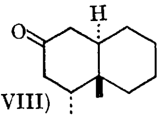
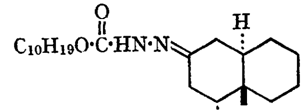
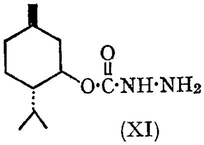
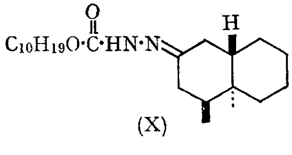

(VIII)



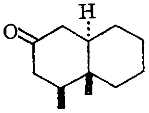
(IX)



(XI)



(X)



(XII)

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† Yields based on 2-methylcyclohexane-1,3-dione used and determined by v.p.c. analysis of the crude product mixture on a 6 ft. × ⅛ in. glass column of 3% OV-17 on 100/120 mesh Gas-Chrom Q at 145° and He flow rate of 95 ml./min.

that of the ketone (XII) of known absolute configuration,[3] r.d. (*c* 0·305, MeOH, *d* 0·1 dm.) $[\phi]_{450}$ $-148°$; $[\phi]_{305·5}$ $-1800°$; $[\phi]_{266·5}$ $+1889°$; $[\phi]_{225}$ $+1015°$. Addition of a trace of concentrated hydrochloric acid to the solution gave: $[\phi]_{450}$ 0°; $[\phi]_{305·5}$ $-177°$; $[\phi]_{266·5}$ $+118°$; $[\phi]_{225}$ $+30°$. The sign ($a = -42·4$) of the Cotton effect of (VIII) is as predicted by the octant rule since the axial methyl group at C-4 falls into the upper right-hand (negative) octant. In the ketone (XII) ($a = -36·8$) the C-4 methyl group is equatorial and ring B lies in the upper right-hand octant. The relatively small reduction (57%) in amplitude of the Cotton effect of (VIII) as compared with that observed for (XII) (92%) upon the addition of a trace of acid further establishes the *trans*-diaxial relationship of the C-4 and C-4a methyl groups in (VIII).‡ Acetal formation would introduce new 1,3 diaxial interactions into (VIII) but not into (XII) and therefore acetal formation is inhibited in the former case. These results firmly establish the *trans*-relationship suggested by Coates and Shaw[1] for the two methyl groups in octalone (III).

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‡ Although the 57% reduction observed for (VIII) is larger than the approximately 10% reduction reported for 2-keto-steroids (C. Djerassi, L. A. Mitscher, and B. J. Mitscher, *J. Amer. Chem. Soc.*, 1959, **81**, 947) the 92% reduction for (XII) is likewise larger, under the particular conditions employed here, than the previously reported (ref. 3) 72%.

[1] R. M. Coates and J. E. Shaw, *Chem. Comm.*, 1968, 47.
[2] R. B. Woodward, T. P. Kohman, and G. C. Harris, *J. Amer. Chem. Soc.*, 1941, **63**, 120.
[3] L. H. Zalkow, F. K. Markley, and C. Djerassi, *J. Amer. Chem. Soc.*, 1960, **82**, 6354.