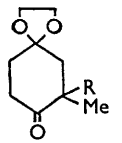
574. *Synthetical Studies of Terpenoids. Part V.*[1] *A New Synthesis of* (±)-6β-*Acetoxy*-5,5,9β-*trimethyl*-trans-2-*decalone.*

By SARAN ADHAR NARANG and PHANINDRA CHANDRA DUTTA.

A new synthesis of the compound named in the title begins with preparation of the ketone (II) and its condensation with 2-chloroethyl ethyl ketone.

As the first stage in a new synthesis of 6-hydroxy-5,5,9β-trimethyl-*trans*-2-decalone, ethyl 5,5-ethylenedioxy-2-oxocyclohexanecarboxylate, obtained by cyclisation of diethyl γγ-ethylenedioxypimelate,[2] was methylated *in situ* in very good yield. Alkaline hydrolysis of the product (I) yielded the keto-ketal (II), which on removal of the ethylenedioxy-group[3] gave 2-methylcyclohexane-1,4-dione.[2] With 2-chloroethyl ethyl ketone in the presence of sodamide[4] the ketal (II) yielded a viscous liquid, whence cyclisation with methanolic alkali afforded the αβ-unsaturated keto-ketal (III), the yield depending on the purity of the chloro-ketone. The structure of compound (III) was proved by its spectral properties [$\lambda_{\text{max.}}$ 247 mμ (log ε 4·15), $\nu_{\text{max.}}$ 1660 cm.$^{-1}$] and by conversion into the solid diketone (IV), the latter being reduced and dehydrogenated by selenium to 1-methylnaphthalene. Methylation[5] of compound (III) gave an oil from which a solid was isolated. " Over-methylation "[6] led at first to poor yields but finally conditions were found affording 40% of the trimethyl ketone (VI).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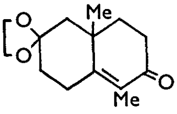
(II) R = H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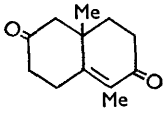
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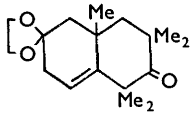
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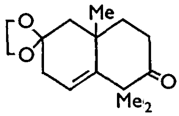
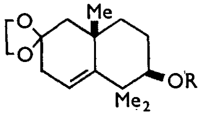
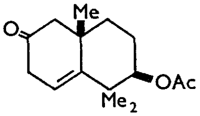
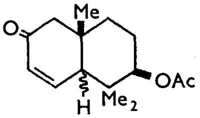

(VI)


(VII) R = H
(VIII) R = Ac


(IXa)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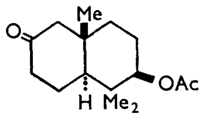
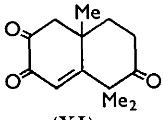
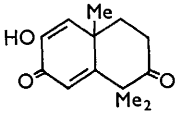

(X)


(XI)


(XII)

The trimethyl ketone (VI) was reduced with sodium and ethanol with a view of obtaining the 3β-alcohol (VII). The product gave an oily acetate (VIII), which was difficult to hydrogenate and was therefore hydrolysed to the acetoxy-ketone (IX). The absorption [$\lambda_{\text{max.}}$ 229 mμ (log ε 3·45)] of this ketone indicated partial migration[7,8] of the double bond into conjugation with the carbonyl group. The compound, however, formed only one (red) 2,4-dinitrophenylhydrazone, evidently owing to the electron-withdrawing effect of the dinitrophenylhydrazono-moiety.[8] The ketone (IX) was only slowly hydrogenated in presence of palladium–charcoal in ethanol; extensive chromatography afforded a solid

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[1] Part IV, Mukherjee and Dutta, *J.*, 1960, 67.
[2] Lukeš, Poos, and Sarett, *J. Amer. Chem. Soc.*, 1952, **74**, 1401.
[3] Segre, Viterbo, and Parisi, *J. Amer. Chem. Soc.*, 1957, **79**, 3503.
[4] Chakrabarti, Dutt, and Dutta, *J.*, 1956, 4978.
[5] Conia, *Bull. Soc. chim. France*, 1954, 690, 943.
[6] Sondheimer and Elad, *J. Amer. Chem. Soc.*, 1957, **79**, 5542.
[7] Halsall, Rodewald, and Willis, *J.*, 1959, 2798.
[8] Soffer and Jevnik, *J. Amer. Chem. Soc.*, 1955, **77**, 1003.

ketone, m. p. 147—148°, $\nu_{max.}$ 1710 (CO), 1380 and 1360 cm.$^{-1}$ (*gem*-Me_2), in a very poor yield giving a yellow 2,4-dinitrophenylhydrazone, m. p. 238—239°. Analyses of the solid ketone and of its derivative corresponded to formula (X) but its properties differed from those of an authentic sample and also from those of the isomeric *cis*-decalone [7] (m. p. 111°) and the corresponding decalin-3-ones [1] (m. p.s 111—112° and 113°). Because of considerable aerial oxidation of the unsaturated ketones, particularly the unsaturated diketone (see below), and the poor and variable yield, no definite structure could be assigned to this ketone. Finally, the unsaturated acetoxy-ketone (IX) was hydrogenated in acetic acid over Adams platinum catalyst and the crude product was reoxidised, affording the acetoxy-*trans*-decalone (X), whose identity has been established by a mixed-melting-point determination (by courtesy of Dr. T. G. Halsall).

Removing the ethylenedioxy-group from the keto-ketal (VI) yielded an oil, $\lambda_{max.}$ 247 mμ (log ε 3·5), which when kept in cold light petroleum furnished a small quantity of a solid, m. p. 62—63°, that had no absorption in the region 240—250 mμ. In contact with air this in turn changed to a paste which, however, was sparingly soluble in light petroleum; crystallisation then afforded a crystalline triketone (XI), m. p. 157°, $\lambda_{max.}$ 215, 249, and 228 mμ (log ε 3·8, 4·0, and 4·32) in presence of alkali, $\nu_{max.}$ 3448 (OH), 1724 and 1645 cm.$^{-1}$, evidently formed by aerial oxidation of the unsaturated diketone. In confirmation, the triketone was obtained when air was passed through an alkaline solution of the pure diketone. The triketone (XII) developed a reddish-violet ferric chloride colour in alcoholic solution and this coupled with infrared absorption shows that the enolic form (XII) is present in appreciable amount.[9]

EXPERIMENTAL

Ultraviolet light absorption data refer to EtOH solutions. Light petroleum refers to the fraction with b. p. 40—60°. Alumina used for chromatography was prepared as described by Gaspert *et al.*[10]

Diethyl γγ-Ethylenedioxypimelate.—β-Furylacrylic acid (160 g.) afforded diethyl γ-oxopimelate (250 g.), b. p. 160—164°/6 mm. (yellow 2,4-dinitrophenylhydrazone, m. p. 81—82°; lit.,[11] 82—83°). This gave diethyl γγ-ethylenedioxypimelate (200 g.), b. p. 140—145°/0·5 mm., along with a higher-boiling fraction (70 g.) that furnished diethyl γ-oxopimelate (35 g.) when refluxed with alcohol (350 c.c.) and concentrated sulphuric acid (15 c.c.) for 6 hr.

Ethyl 5,5-Ethylenedioxy-1-methyl-2-oxocyclohexanecarboxylate (I).—To sodium ethoxide [from sodium dust (24·5 g.) and alcohol (64 c.c.) under benzene (200 c.c.)], a solution of diethyl γγ-ethylenedioxypimelate (200 g.) in benzene (550 c.c.) was added. The mixture was refluxed for 3 hr. During the last 2 hr. benzene (500 c.c.) was gradually distilled off, and at the same time benzene (500 c.c.) was added slowly to the refluxing solution. The mixture was then cooled below 0° and methyl iodide (150 c.c.) was added slowly. The mixture was left overnight at room temperature, then refluxed for 2 hr. and decomposed with 5% sodium carbonate solution (400 c.c.). The dark-brown layer was taken up, and the aqueous layer extracted twice, with benzene. The combined benzene layers were washed once with water and evaporated. Distillation of the residue gave the *ester* (I) (120 g.), b. p. 148—150°/5 mm., cubes (from light petroleum), m. p. 72° (Found: C, 59·5; H, 7·3. $C_{12}H_{18}O_5$ requires C, 59·5; H, 7·5%).

4,4-*Ethylenedioxy*-2-*methylcyclohexanone* (II).—The ester (I) (120 g.) was refluxed with 10% aqueous potassium hydroxide (720 c.c.) for 16 hr., then saturated with sodium chloride and extracted with ether. The extract was washed with water, dried (Na_2SO_4), and evaporated. The residue was distilled, to afford 4,4-*ethylenedioxy*-2-*methylcyclohexanone* (70 g.), b. p. 98—100°/4 mm. (Found: C, 63·5; H, 8·55. $C_9H_{14}O_3$ requires C, 63·5; H, 8·3%).

The product (2 g.) was refluxed in dry acetone (20 c.c.) containing toluene-*p*-sulphonic acid (75 mg.) for 3 hr. The solvent was removed *in vacuo* at <40° and the residue was washed in ether with 5% sodium hydrogen carbonate solution, recovered, and crystallised from light petroleum, affording methylcyclohexane-1,4-dione, m. p. 47° (lit., 47—48°).

[9] Henecka, *Chem. Ber.*, 1948, **81**, 190; Baran, *J. Amer. Chem. Soc.*, 1958, **80**, 1687.

[10] Gaspert, Halsall, and Willis, *J.*, 1958, 624.

[11] Gardner, Rand, and Haynes, *J. Amer. Chem. Soc.*, 1956, **78**, 3425.

*6,6-Ethylenedioxy-*1,10β-*dimethyl-*$\Delta^{1(9)}$*-octal-*2*-one* (III).—To freshly prepared sodamide (16·5 g.) under ether (750 c.c.) the ketone (II) (60 g.) was slowly added. After 2 hours' refluxing with constant stirring, the volume of ether was reduced to half and the residue cooled below 0°. Freshly distilled 2-chloroethyl ethyl ketone (55 g.), b. p. 85—86°/35 mm., was added dropwise with vigorous stirring, and refluxing was continued for a further 2 hr. The mixture was then further concentrated, kept overnight, and decomposed with ice-cold 5% sodium carbonate solution. The ethereal layer was separated, the aqueous layer extracted twice with ether, and the combined extracts were washed with water and dried (Na_2SO_4). On distillation, unchanged ketone (II) (10 g.) was recovered. The residue was refluxed with potassium hydroxide (50 g.) in methanol (950 c.c.) for 6 hr. under nitrogen. Methanol (600 c.c.) was distilled off, and the residue cooled to room temperature and diluted with water. The mixture was then saturated with sodium chloride and extracted with ether thrice. The ethereal solutions were washed with water, dried (Na_2SO_4), and evaporated. Distillation gave the *octalone* (III) (30 g.), b. p. 140—142°/0·3 mm., cubes (from light petroleum), m. p. 61—62° (Found: C, 71·2; H, 8·3. $C_{14}H_{20}O_3$ requires C, 71·2; H, 8·5%). This readily afforded a *semicarbazone* as needles (from methanol), m. p. 208—209° (Found: C, 61·1; H, 7·7. $C_{15}H_{23}O_3N_3$ requires C, 61·4; H, 7·9%).

1,10β-*Dimethyl-*$\Delta^{1(10)}$*-octalin-*2,6*-dione* (IV).—The foregoing ketone (III) (1 g.) in dry acetone (20 c.c.) and toluene-*p*-sulphonic acid (75 mg.) were refluxed for 3 hr. The *diketone* (IV) crystallised in needles (750 mg.), m. p. 103—104°, from light petroleum (Found: C, 74·9; H, 8·6. $C_{12}H_{16}O_2$ requires C, 75·0; H, 8·4%).

This diketone (600 mg.) was treated in ethanol with sodium borohydride (400 mg.), kept overnight, diluted with water, and decomposed with concentrated hydrochloric acid. The aqueous solution was saturated with sodium chloride and extracted with ether. The gum left on removal of the solvent was heated with selenium (1·5 g.) in a sealed tube at 300—325° for 50 hr. The purified hydrocarbon was converted into a picrate, which on crystallisation from ethanol melted at 139—140° (lit., 140—141°), alone or mixed with authentic 1-methylnaphthalene.

*6,6-Ethylenedioxy-*1,1,3,3,10β-*pentamethyl-*Δ^{8}*-octal-*2*-one* (V) (?).—To an ice-cold solution of potassium 1,1-dimethylpropyl oxide (prepared from potassium, 2·7 g.) in benzene (150 c.c.) the ketone (III) (5 g.) was added dropwise with occasional shaking. The mixture was kept at 50—60° for an hr., cooled in ice, treated with methyl iodide (5 c.c.) dropwise, and refluxed for 2 hr. It was then poured into ice-cold 5% sodium carbonate solution. The organic layer was washed with water and dried (Na_2SO_4). It furnished an oil (4 g.), b. p. 150—152°/0·5 mm. On cooling, part of it solidified (1 g.) and this on repeated crystallisation from dilute methanol gave what was probably the *pentamethyl ketone* as needles, m. p. 82—83° (Found: C, 73·4; H, 9·35. $C_{17}H_{26}O_3$ requires C, 73·3; H, 9·4%).

*6,6-Ethylenedioxy-*1,1,10β-*trimethyl-*Δ^{8}*-*2*-octalone* (VI).—The ketone (III) (18 g.) in t-butyl alcohol (200 c.c.) was treated with potassium t-butyl oxide (prepared from potassium, 5 g.) in the same solvent (250 c.c.) and stirred at room temperature for 2 hr. under nitrogen. Methyl iodide (24 c.c.) was added and stirring continued overnight. The mixture afforded an oil (19 g.) which was passed in light petroleum (40 c.c.) through alumina (600 g.). Elution was first with the same solvent, which removed an oil (9 g.) in four fractions (40 c.c. each). Elution next carried out with benzene–light petroleum (1 : 1) and finally with benzene gave the unchanged ketone (III), m. p. 61—62°, in the later fractions. The first four fractions were combined and rechromatographed, affording the *octalone* (VI) (7 g.), b. p. 138°/0·5 mm. (Found: C, 72·0; H, 8·8. $C_{15}H_{22}O_3$ requires C, 72·0; H, 8·9%), $\nu_{max.}$ 1710 (CO), 1380 and 1364 cm.$^{-1}$ (*gem*-Me_2).

*6,6-Ethylenedioxy-*1,1,10β-*trimethyl-*Δ^{8}*-octalin-*6β*-ol* (VII).—Sodium (5·6 g.) was added to dry ethanol (70 c.c.) containing the ketone (VI) (10 g.). After the vigorous reaction, the mixture was heated to dissolve the remaining sodium. The excess of ethanol was then steam-distilled. The *alcohol* (8 g.), extracted with ether, had b. p. 148—150°/0·3 mm. (Found: C, 71·4; H, 9·45. $C_{15}H_{24}O_3$ requires C, 71·4; H, 9·6%), $\nu_{max.}$ 3630 (OH) and 1380 and 1360 cm.$^{-1}$ (*gem*-Me_2).

6β*-Acetoxy-*5,5,9β*-trimethyl-*Δ^{4}*-*2*-octalone* (IXa) *and its* Δ^{3}*-Isomer* (IXb).—The alcohol (VII) (8 g.) was dissolved in pyridine (24 c.c.) and cooled below 0°. A mixture of acetyl chloride (12 c.c.) and acetic anhydride (16 c.c.) was added slowly. Ether (80 c.c.) was added and the mixture kept overnight at room temperature. 6β*-Acetoxy-*2,2*-ethylenedioxy-*5,5,9β*-trimethyl-*Δ^{4}*-octalin* (8·5 g.) distilled at 140—142°/0·2 mm. (Found: C, 69·45; H, 9·0. $C_{17}H_{26}O_4$ requires C, 69·4; H, 8·9%). This was refluxed in acetone (80 c.c.) for 3 hr. with toluene-*p*-sulphonic acid (300 mg.). The oily product (7 g.) was chromatographed in light petroleum (10 c.c.) on alumina

(200 g.). Elution with light petroleum–benzene (1 : 1) failed to afford a solid product. The oil collected by chromatography gave a mixture of the ketones (IXa and b) (5·5 g.), b. p. 135—137°/0·2 mm. A 2,4-*dinitrophenylhydrazone* formed red needles, m. p. 257—258° from chloroform–light petroleum (Found: C, 58·8; H, 6·2. $C_{21}H_{26}O_6N_4$ requires C, 58·6; H, 6·1%).

6β-*Acetoxy*-5,5,9β-*trimethyl*-trans-2-*decalone* (X).—The mixture obtained as in the preceding paragraph (2 g.) in acetic acid (30 c.c.) in presence of Adams platinum catalyst (300 mg.) (previously saturated with hydrogen) rapidly absorbed 2 mols. of hydrogen. Working up in the usual way gave an oil (1·8 g.) which was oxidised in acetone (8 c.c.) by slow addition of chromic oxide (1·2 g.) in concentrated sulphuric acid (1 c.c.) and water (3 c.c.). The mixture was kept for 0·5 hr. at room temperature, then diluted with water and extracted thrice with ether. The crude oil (1·6 g.) obtained from this extract was chromatographed in light petroleum (4 c.c.) on alumina (60 g.). Elution with light petroleum (10 × 20 c.c.) afforded a gum (0·4 g.). A further quantity of gum (0·7 g.) was eluted by 4 : 1 benzene–light petroleum. Finally elution with benzene (10 × 20 c.c. each) removed a solid which on repeated crystallisation from light petroleum afforded 6β-acetoxy-5,5,9β-trimethyl-*trans*-2-decalone (150 mg.), m. p. 113° alone or mixed with an authentic sample (Found: C, 71·7; H, 9·7. Calc. for $C_{15}H_{24}O_3$: C, 71·4; H, 9·6%) [2,4-*dinitrophenylhydrazone*, yellow plates (from ethyl acetate–methanol), m. p. 235° (Found: C, 57·9; H, 6·8. $C_{21}H_{28}O_6N_4$ requires C, 58·3; H, 6·5%)].

5,5,9β-*Trimethyl*-Δ^4-*octalin*-2,3,6-*trione* (XI) *and its Enolic Form* (XII).—(*a*) The oil obtained on removal of the ethylenedioxy-group from the ketone (VI) (2 g.) distilled at 135—138°/0·4 mm., and afforded cubes, m. p. 62—63°, from ether–light petroleum. This could not be analysed because of its instability. It yielded the *trione* (XI) as plates, m. p. 157—158°, from light petroleum (b. p. 80—100°) (Found: C, 70·9; H, 7·2. $C_{13}H_{16}O_3$ requires C, 70·9; H, 7·3%). The mother-liquor, left in contact with air for 7 days, slowly solidified and a further quantity of the same solid was obtained.

(*b*) Air, purified by passage through potassium hydroxide solution, was passed through a solution of the oil (1 g.) used in experiment (*a*) dissolved in 10% alcoholic potassium hydroxide (5 c.c.), for 5 hr. A green colour developed and changed to brown. The product, isolated as usual, distilled at 120—125°/0·3 mm., afforded the triketone, m. p. and mixed m. p. 157—158°.

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