Section B

Synthesis of a tetrathyldocalin-derivative.

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THEORETICAL

With the elucidation of the essential features, both structural and stereo-chemical, present in naturally occurring di- and tri-terpenoid bodies, synthetic studies in this field have also assumed major importance in recent years. The most outstanding contribution is perhaps the synthesis of pentacyclo-squalane (I) by Corey et al. (J. Am. Chem. Soc., 1957, 72, 3925) and Eschenmoser et al. (Helv. Chim. Acta, 1957, 40, 1960).

The salient feature of the synthetic studies, successfully employed in the case of triterpenoid bodies is coupling of two components with a view to obtaining the desired carbon-skeleton. This approach has proved to be very fruitful instead of building up the rings step by step, and evidently the latter one will be an extremely laborious process and also involving complicated stereochemistry. For this type of synthetic approaches in this field, the following bicyclic
The stereochemistry of these isomeric ketones containing as it does, three asymmetric centres, should have trans ring-junction with the angular methyl group axial and the acetoxy-group equatorial in nature. The ketone (II) has recently been synthesised by Kalvoda and Loeffel (Helv. Chim. Acta, 1957, 40, 2240); Sondheimer and Elad (J. Amer. Chem. Soc., 1957, 79, 5544) and Halsall et al. (J. Chem. Soc., 1958, 624). All the four possible stereochemical racemates are by now known and one of its forms on introduction of a methyl group α to the carbonyl function, has been found to be identical with a tetramethyl-hydroxy-decalone isolated from β-amyrin. The synthesis of ketone (III) has recently been announced in a short communication (Halsall et al., Proc. Chem. Soc., 1958, 231).

The present investigation details a synthesis of the hydroxy-ketone (IV) in two out of its four stereochemically possible forms with a view to synthesising some of the important intermediates having a functional group in ring B.
and to extending the synthesis to the naturally occurring triterpenoid bodies. With that end in view attempts have been made to extend synthetic studies to the di-keto-ester (XXI) which could easily be correlated to Drimoniol (V; Brooks and Overton, Proc. Chem. Soc., 1957, 322) and the keto-unsaturated ester (VI; Ruzicka et al., Helv. Chim. Acta, 1949, 32, 1075). The stereochemistry of both the ketones (XII, XIV) are now on a well-founded basis. The sequence of synthetic studies has been carried out with sufficient control of stereochemistry at each step in order to make the synthesis stereospecific as far as possible and it may be schematically represented below:

(V)

(VI)

(VII)

(VIII)

(IX)
The starting material for these studies is dimethyl-octalone (VII); (a) Gunstone and Heggie, J. Chem. Soc., 1952, 1437; (b) Chakravarty, Dutt and Dutta, J. Chem. Soc., 1953, 4973. After a series of experiments, methylation of this ketone to (VIII) in presence of potassium tert.-amylate (Conia, Bull. Soc., Chim., France, 1954, 690, 943) was carried in 92% yield.

The synthesis of this ketone has recently been described (Yanagita et al., J. Org. Chem., 1953, 22, 2441) and they have isolated a series of by-products during methylation and the desired product was isolated in a poor yield. The synthetic material described here is evidently purer as shown by the melting point of the solid derivatives. The trimethyl-ketone (VIII) is reduced with sodium-ethanol with a view to obtaining the 3-hydroxyl group in (IX) in the desired equatorial position. This was acetylated to afford (X). On allylic oxidation with tert.-butyl chromate (Heusler and Wettstein, Helv. Chim. Acta, 1952, 25, 284) or better with sodium dichromate in acetic acid (Corey and Urspring, J. Amer. Chem. Soc., 1956, 78, 123), (X) afforded the unsaturated ketone (XI) in a very good yield.

With a view to introducing the desired chain having a functional group at C₃ and which could eventually be utilized for the coupling of the two bicyclic units, it was desired to build up a dieneone system and for that purpose (XI) was brominated (Abe et al., J. Amer. Chem. Soc., 1956, 78, 1422) and (XII) was isolated in a highly crystalline state. Attempts at dehydrohalogenation failed and it was ultimately found that the major product arose from reductive dehalogenation leading to the
original acetoxy-ketones (XI) (N.L. Wordier et al., J. Amer. Chem. Soc., 1957, 79, 4476). Another attempt to develop the dieneone system was also made through oxidation with selenium dioxide (Ringold et al., J. Org. Chem., 1966, 31, 230; Masait et al., J. Org. Chem., 1993, 58, 690). The product so obtained was phenolic in nature as it gave a pink colour with ferric chloride solution and no well-defined ketonic derivative could be obtained. The double bond in (XI) was catalytically reduced in presence of palladium-charcoal catalyst in glacial acetic acid to afford a mixture of the acetoxy-ketones (XIII and XIV) in an approximate ratio (1:4). The preponderance of the trans-form (XIV) is evident for obvious steric reasons controlling catalytic reduction because of the presence of 1,3-diaxial substituents (Woodward et al., J. Chem. Soc., 1957, 1131; Stork and Schulembry, J. Amer. Chem. Soc., 1956, 78, 260). It appears that catalytic reduction of the hydroxy-ketone (XI,a) slightly alters the proportion of the isomers, more in favour of the desired trans-isomer (cf. Halsall et al., Proc. Chem. Soc., loc. cit.). The separation of the mixture in pure constituents would require extensive chromatography and indeed (XIII) could only be obtained pure by that process. To determine the ring-junction of the major constituent (XIV), it was subjected to Huang-Minlon reduction to remove the carbonyl group and the alcohol (XVI) so obtained, was oxidised with chromic acid in acetone (Bowers et al., J. Chem. Soc., 1953, 2548) to afford the ketone (XVII). It was characterised by an orange 2,4-dinitrophenylhydrazone.
which showed no depression in melting point when mixed with an authentic sample (Gasper, Halsall and Willis, J. Chem. Soc., loc. cit.), kindly carried out by Dr. Halsall. This establishes definitely the trans-junction in the ketone (XIV). To establish definitely the point that the isomers (XIII) and (XIV) differ in ring-junction, both the ketones (XIII) and (XIV) was separately hydrolysed to the corresponding hydroxy-ketones and these were oxidised in their turn to the corresponding diketones (XV) and (XVIII). Their non-identity has been further established through their mixed melting point determination. This establishes the cis-junction of the ring in (XIII). Stereochemistry of the acetoxy-group in both the ketones is most probably equatorial, arising as it does, through chemical reduction of the carbonyl group followed by acetylation and the ratio of cis- and trans- isomers on catalytic reduction of the unsaturated ketone (XI) also supports this statement (Kalvoda and Loeffel, loc. cit.; Halsall et al, Proc. Chem. Soc., loc. cit.). Stereochemistry of the ketone (XIV) being placed on a firm basis, attempts were next made to introduce a methyl group α - to the carbonyl function with a view to extending further the synthetic scheme. Methylation of the ketone (XIV) was first attempted through the oxalyl derivative according to Sondheim or al, (loc. cit.). The oxalyl derivative was obtained in an excellent yield and it gave a deep-violet colouration with ferric chloride in ethanolic solution.
On methylation with methyl iodide in presence of freshly ignited potassium carbonate, it afforded a neutral compound. This on alkaline hydrolysis afforded a product which on acetylation was found to be identical with the starting material (XIV). Apparently methylation has failed to proceed and regeneration of the ketone can be explained from the following considerations. Because of the presence of trans-junction of the rings in (XIV), the oxalyl derivative will enolise preferably to afford (XIVa) (Taylor, Chem. & Ind., 1954, 250). This structure will be favoured because of the well-known tendency of the cyclohexanone ring to accommodate the double bond in an endocyclic form (Brown et al., J. Amer. Chem. Soc., 1954, 76, 497; Turner et al., ibid, 1958, 80, 1424). Apparently the neutral material obtained on methylation will correspond to the structure (XIVb) from which the regeneration of the ketone (XIV) during working-up of the product, could be better explained.

\[
\text{XIV a, } R = \text{H} \quad [\text{XIV b, } R = \text{-CH}_3]
\]
Attempt was next made to methylate the ketone (XIV) through formylation, acetylation and catalytic reduction (Kolff et al., loc. cit.). The whole series of reactions have been carried out in situ. To ensure the stereochemistry of the newly introduced methyl group, it was treated with alkali for epimerization to the more favourable equatorial form leading to the formation of the tetramethyl compound (XIX) in a highly crystalline state on acetylation. In one operation, the tetra-methyl compound crystallised out directly after catalytic reduction and no epimerisation with alkali and subsequent acetylation were necessary. The tetra-methyl acetoxy-ketone (XIX) was smoothly brominated with bromine in acetic acid and dehydrobromination was carried out by heating with collidine (F. Futaki, J. Org. Chem., 1963, 22, 451).

It may be of interest to note here that the following bromo-ketone on dehydrohalogenation with boiling collidine leads to a mixture of the corresponding unsaturated ketones (Djerassi et al., J. Amer. Chem. Soc., 1958, 80, 3936).

The unsaturated ketone, obtained in these studies, has been assigned the structure (XX), because it forms a single red 2,4-dinitrophenylhydrazone in an almost quantitative
Assignment of this structure (XX) in preference to an alternative one involving the ring functionality may be based on the results of a detailed study towards the addition of potassium cyanide to a closely related system described in the following section of this dissertation. The unsaturated ketone (XX) was allowed to react with potassium cyanide and the addition product was subsequently hydrolysed with alkali. On oxidation of the secondary hydroxyl group (Bowers, loc. cit.) in the acidic material to a ketonic acid and final esterification of the acidic material with diazomethane, a few milligrams of a highly crystalline material, melting at 143-149°, were obtained on purification through a column of alumina as long, fibrous needles. It did not however analyse well for the expected compound (XXI) although it exhibited two distinct bands (5.73 μ and 5.83 μ) in the infra-red. The investigation is in progress to isolate more of the material and to determine its structure.
EXPERIMENTAL

1:1:10-Trimethyl-2-keto-δ-octalin (VIII)

To an ice-cold solution of potassium-tert.-anlylate (potassium, 6 g.) in benzene (450 c.c.) was dropwise added the ketone (VII, 20.4 g.) with occasional shaking. The reaction mixture gradually assumed a dirty-grey colour and was kept at 50-60° for one hour. It was next cooled in ice and methyl iodide (23 c.c.) was added dropwise and refluxed for 2 hours. The dark colour gradually faded away and at the end, the reaction mixture was almost milk-white. It was poured in ice-cold water (ca. 400 c.c.) containing a small amount of hydrochloric acid (7 c.c.). The organic layer was separated, washed successively with 5% sodium bisulphite solution, water and dried over sodium sulphate. On removal of the solvent, the residue on distillation furnished 20.4 g. (92.7%) of the desired ketone with a fruity odour, b.p. 105-107°/2 mm. The yellow 2:4-dinitrophenylhydrazone was crystallised from ethyl alcohol, m.p. 163° (Lit. 159-160°).

Anal. Calcd. for C_{19}H_{34}O_{4}N_{4}: C, 61.3; H, 6.4; N, 15.0.

Found: C, 61.0; H, 6.3; N, 14.5.

1:1:10-Trimethyl-2-hydroxy-δ-octalin (IX)

A warm solution of the ketone (20 g.) in absolutely dried ethanol (240 c.c.) was added quickly to sodium (17.4 g.).
After 35 minutes, it was heated at 140-145° (bath-temperature) till whole of sodium dissolved. On cooling to room-temperature, the product was diluted with water (ca 2000 c.c.), saturated with sodium chloride and extracted with ether. The ethereal extract was washed with water and dried over sodium sulphate. The solvent being removed, the residue on distillation furnished 12.3 g. (90.5\%) of a colourless viscous liquid with a sweet odour, b.p. 113-115°/2 mm., $n_D^{29.5}$ 1.5110. It afforded no 2,4-dinitrophenylhydrazone.

Anal. Calcd. for $C_{15}H_{22}O$: C, 80.3; H, 11.4.  
Found: C, 79.9; H, 11.2.

1:1:10-Trimethyl-2-acetoxy-4\(\beta\)-octalin (X).

To a thoroughly cooled solution of the hydroxy-octalin (13.58 g.) in pyridine (27.35 g.) was slowly added a mixture of acetic anhydride (23.31 g.) and acetyl chloride (10.99 g.). This was followed by the addition of ether (25 c.c.) and kept overnight at room-temperature. It was then poured on ice containing concentrated hydrochloric acid (35 c.c.) and ether. The organic layer was separated and the aqueous layer was twice extracted with ether. The combined ethereal extract was washed successively with water, 2\% sodium bicarbonate solution and dried over sodium sulphate. On removal of the solvent, the residue afforded 14.7 g. (89\%), b.p. 122-123°/3-4 mm. $n_D^{39.5}$ 1.4997.

Anal. Calcd. for $C_{15}H_{24}O_2$: C, 76.3; H, 10.2.  
Found : C, 76.4; H, 10.3.
11110-Trimethyl-2-acetoxy-7-keto-1,8-octalin (XI).

(a) Oxidation with tert.-butyl chromate: To a solution of the acetoxy-octalin (14.5 g.) in carbon tetrachloride (150 c.c.) was added at room-temperature and with vigorous stirring, a mixture of tert.-butyl chromate (216 c.c.), acetic acid (67 c.c.) and acetic anhydride (27 c.c.) and the solution was kept overnight. It was next stirred at 80° for 3-4 hours and finally cooled to room-temperature. The reaction mixture first assumed a deep-red colour which turned green on heating. A solution of oxalic acid (45 g.) in water (450 c.c.) was added with ico-cooling in the course of 30 minutes. After 15 minutes, solid oxalic acid (31.5 g.) was added and stirred vigorously for 2 hours whereby the mixture slowly attained room-temperature. The pale-yellow carbon tetrachloride layer was then separated and the aqueous layer was extracted with carbon tetrachloride. The combined organic layer was washed with water, 5% sodium bicarbonate solution, finally with water, dried and the solvent removed. The residue on distillation furnished 9.7 g. (63.15%) of an orange-yellow viscous liquid having a sweet smell, b.p. 150-175°/4 mm. A solution of potassium hydroxide (15 g.) in methanol (150 c.c.) was added to the viscous liquid (9.7 g.) and the mixture was kept overnight at room-temperature. Next, it was refluxed for one and a half hours and neutralised with (12 N) hydrochloric acid. Methyl alcohol was removed almost completely over a boiling water-bath under suction. The residue was diluted with water and finally extracted with ether after saturating the solution with
sodium chloride. On removal of the solvent, the residue on distillation furnished 6.3 g. (43.03%) of a viscous liquid with a yellowish tinge, b.p. 165-170°/4 mm., $n_D^{27.5}$ 1.5255.

**Anal. Calcd. for $C_{13}H_{20}O_2$:** C, 75.0; H, 9.6.
**Found:** C, 74.8; H, 9.9.

The deep-red 2,4-dinitrophenylhydrazone crystallised from ethyl acetate in short needles, m.p. 210°.

**Anal. Calcd. for $C_{19}H_{24}O_4N_4$:** C, 58.7; H, 6.2; N, 14.4.
**Found:** C, 58.4; H, 6.0; N, 14.1.

The hydroxy-ketone (5.3 g.) was acetylated with pyridine (3.4 c.c.), acetic anhydride (8.1 c.c.), acetyl chloride (7 c.c.) and ether (15 c.c.) as described before. The product on distillation, afforded 4.3 g. (77.34%), b.p. 173-175°/4 mm., $n_D^{27.5}$ 1.5053. λ alc. max. 240 m/μ (log ħ 4.05).

**Anal. Calcd. for $C_{15}H_{22}O_3$:** C, 72.0; H, 3.8.
**Found:** C, 72.1; H, 3.8.

The deep-red 2,4-dinitrophenylhydrazone crystallised from ethyl acetate in flakes, m.p. 243°.

**Anal. Calcd. for $C_{21}H_{26}O_6N_4$:** C, 58.6; H, 6.0; N, 13.0.
**Found:** C, 58.3; H, 5.8; N, 12.7.
(b) Oxidation with sodium dichromate in acetic acid

A solution of the acetox-octalin (23.6 g.) and sodium dichromate (60 g.) in glacial acetic acid (900 c.c.) was kept overnight at room temperature and then heated at 95-100° for 2 hours with vigorous stirring. Ethanol (30 c.c.) was added to the hot solution to decompose the excess of dichromate and the resulting green solution was diluted with hot water (2650 c.c.). The cold solution was extracted with ether. The ethereal extract was washed thoroughly with 5% sodium carbonate solution, and dried over sodium sulphate and the solvent removed. The residue, on distillation furnished 19.5 g. (78%) of the ketonic product, b.p. 190°/0.1 mm.; \( \lambda_{\text{max}} \) 240m/\( \mu \) (log \( E \) 4.05); n\( D^2 \) 1.5053. It afforded an identical 2:4-dinitrophenylhydrazone, m.p. 243°, alone or mixed with the derivative described before.

1:1:10-Trimethyl-2-acetoxy-7-keto-decalin (XIII, XIV).

The unsaturated ketone (33.5 g.) dissolved in glacial acetic acid (45 c.c.) was shaken in an atmosphere of hydrogen over palladium-charcoal catalyst (1 g., 10%). At the end of 24 hours, the calculated amount of hydrogen had been absorbed and further uptake stopped. The catalyst was filtered off and the solution was diluted with water and extracted with ether. The ethereal extract was thoroughly washed with 5% cold sodium carbonate solution, water and dried over sodium sulphate. The solvent being removed the residue on distillation, furnished
32.6 g. (88.67%) of a sweet-smelling colourless liquid, b.p. 150-155°/5 mm. The distillate (b.p. 150-155°/5 mm.), on trituration in the cold with petroleum-ether (40-60°) afforded needle-shaped crystals 10.4 g. (31.8%). From the filtrate further lots of crystals (2 g.) separated on long standing in the cold. The operation was repeated and the yield of the solid in third and fourth operations was 1.6 g. and 0.8 g. respectively. The solid collected from first three batches melted at 110-111°, which on subsequent crystallisations rose to 113-114° (XIV).

Anal. Calcd. for C_{15}H_{24}O_3: C, 71.4; H, 9.5.
Found: C, 71.1; H, 9.3.

It formed quantitatively a 2,4-dinitrophenylhydrazone, m.p. 220°, which recrystallised from ethanol-ethyl acetate (3:1) in yellow glistening flakes, m.p. 220-221°.

Anal. Calcd. for C_{21}H_{28}O_6N_4: C, 53.3; H, 6.5.
Found: C, 53.1; H, 6.3.

The fourth batch of crystals (m.p. 93-94°) even on repeated crystallisation, showed an anomalous melting point. This (200 mg.) was chromatographed on neutralised alumina (30 g.) and the column eluted with petroleum-ether (40-60°); fractions 1-15; 30 c.c. each; fractions 16-43; 100 c.c. each. Fractions 12-23 gave prismatic crystals (120 mg.), m.p. and mixed m.p. 111-112° (XIII) which on further crystallisation
from petroleum-ether (40-60°) showed no change in melting point.

Anal. Calcd. for C_{18}H_{24}O_3: C, 71.4; H, 9.5.
Found: C, 71.4; H, 9.4.

The 2,4-dinitrophenylhydrazone crystallised from ethanol in yellow glistening flakes, m.p. 172-173°.

Anal. Calcd. for C_{21}H_{22}O_6N_4: C, 58.3; H, 6.5.
Found: C, 58.5; H, 5.5.

The mixed melting point of (XIII and XIV) was 88° and that of 2,4-dinitrophenylhydrazones 167-168°.

**1,1,10-Trimethyl-trans-decalin-2-ol (XVII).**

The acetoxy-ketone (756 mg, XIV, m.p. 112-114°) in redistilled diethylene glycol (6.3 c.c.) was heated under reflux with hydrazine hydrate (0.45 c.c., 100%) and potassium hydroxide (405 mg.) for one hour. The excess of water was then removed by distillation until the reaction temperature reached 185-190°; refluxing was continued for one hour more.

On dilution with water and acidification with (6 N) hydrochloric acid, the ethereal extract afforded a sweet-smelling colourless viscous liquid (431 mg.), b.p. 130°/4 mm.

Anal. Calcd. for C_{18}H_{24}O: C, 79.6; H, 12.2.
Found: C, 79.5; H, 12.1.
1:1:10-Trimethyl-trans-decalin-2-one (XVII).

The decalol (431 mg.) in acetone (10 c.c.) was treated with (8 N) chromic acid (1.5 c.c.) till orange colour persisted and was kept at room-temperature for 30 minutes. After dilution with water and saturating with sodium chloride, it was extracted with ether which, in its turn, was thoroughly washed with water, dried over sodium sulphate and the solvent removed. Finally it afforded a liquid (300 mg.). The 2:4-dinitrophenyl-hydrazone separated from ethanol in orange needles, m.p. 185.5-186.5°, which melted at 186-187° on admixture with an authentic sample.

1:1:10-Trimethyl-trans-decalin-2,7-dione (XVIII).

The acetoxy-ketone (500 mg., XIV, m.p. 113-114°) was added to potassium hydroxide (1 g.) in ethanol (10 c.c.) and the whole refluxed for 2 hours. Concentrated hydrochloric acid was then added dropwise to the cold solution till colourless and ethanol was distilled off under reduced pressure. On evaporation of the ethereal extract, it furnished an yellowish viscous liquid (400 mg.). This was dissolved in acetone (15 c.c.) and treated with (8 N) chromic acid (1 c.c.) as above. Finally it afforded a solid (380 mg.), m.p. 118°, which recrystallised from petroleum-ether (40-60°) in shining needles, m.p. 121-122°.

Anal. Calcd. for C_{15}H_{20}O_{2}: C, 75.0; H, 9.6.

Found: C, 74.8; H, 9.6.
She acetoxy-ketone (180 mg., XIII, m.p. 111-112°) was hydrolysed and the crude semi-solid residue (146 mg.) was oxidised as before. On working up in the usual way the gummy residue afforded a solid (122 mg.) on trituration with petroleum-ether (40-60°) in the cold. On chromatographic purification of the crude solid over neutralised alumina (7 g.) traces of an oil was obtained on elution with petroleum-ether (40-60°) and a semi-solid mass (90 mg.) was eluted with ether. On crystallisation from petroleum-ether (40-60°) it afforded the isomeric cis-diketone, m.p. 87-88°. The mixed melting points with trans-dione (XVIII, m.p. 121-122°) was 77-79°.

Anal. Calcd. for C_{13}H_{20}O_2: C, 75.0; H, 9.6.
Found: C, 74.8; H, 9.7.

1:1:10-Trimethyl-cis-decalin-2,7-dione (XV).

The acetoxy-ketone (180 mg., XIII, m.p. 111-112°) was hydrolysed and the crude semi-solid residue (146 mg.) was oxidised as before. On working up in the usual way the gummy residue afforded a solid (122 mg.) on trituration with petroleum-ether (40-60°) in the cold. On chromatographic purification of the crude solid over neutralised alumina (7 g.) traces of an oil was obtained on elution with petroleum-ether (40-60°) and a semi-solid mass (90 mg.) was eluted with ether. On crystallisation from petroleum-ether (40-60°) it afforded the isomeric cis-diketone, m.p. 87-88°. The mixed melting points with trans-dione (XVIII, m.p. 121-122°) was 77-79°.

To a solution of the ketone (XI, 2.9 g.) in dry ether (100 c.c.), immersed in ice-bath, was added a solution of bromine (1.5 g.) in glacial acetic acid (10 c.c.). After the addition was completed, it was occasionally shaken at room-temperature when the colour of bromine suddenly disappeared and was kept for an hour more. The solution was then poured in ice-cold water and extracted with ether. The ethereal layer was washed with water, 5% sodium bicarbonate solution, followed by water and finally dried over sodium sulphate. The solvent being
removed, the residue was dried in vacuum and chilled when it solidified. This was washed with petroleum-ether (40-60°) and crystallised from methanol whereupon white long needle-shaped crystals (2.3 g.) was obtained, m.p. 146-147°, $\lambda_{\text{max}}$ 240 nm (log $\varepsilon$ 4.1).

Anal. Calcd. for C$_{18}$H$_{21}$O$_3$Br : C, 54.7; H, 6.4; Br, 24.3.

Found : C, 54.4; H, 6.4; Br, 24.1.

Attempted dehydrobromination of the bromo-octalone (XII).

A solution of the bromo-octalone (1.3 g.) in collidine (10 c.c.) was placed in an oil-bath at 170° under nitrogen atmosphere and kept there for an hour. It was cooled and poured in ice-water containing concentrated hydrochloric acid (20 c.c.) when a deep-brown coloured oil separated. It was extracted with ether and the ethereal extract was washed with water, dried and the solvent removed. The residue on distillation furnished an yellowish viscous liquid (0.7 g.), b.p. 150-155°/0.6 mm. $\lambda_{\text{max}}$ 233 nm (log $\varepsilon$ 4.1).

Anal. (a) Calcd. for C$_{15}$H$_{20}$O$_3$ (dione) : C, 72.6; H, 3.8.

(b) Calcd. for C$_{15}$H$_{22}$O$_3$ (monoacnone) : C, 72.0; H, 3.8.

Found : C, 72.0; H, 3.8.

The deep-red needle-shaped 2:4-dinitrophenylhydrazone was crystallised from ethyl acetate, m.p. 243°. It melted at 246° when mixed with the corresponding derivative (m.p. 248°) of 1:1:10-trimethyl-2-acetoxy-7-keto- $\Delta^5$-octalin.
Attempt was also made to prepare the dienone by dehydrogenation of the octalone (XI, 8.75 g., 0.035 mole) with selenium dioxide (10 g.), benzene (300 c.c.) and water (5 c.c.). After 64 hours' reflux it was worked up and finally on distillation it gave a product (6 g.), b.p. 140-152°/0.2 mm., which showed deep pink colour with ferric chloride and also gave an ill-defined brick-red 2,4-dinitrophenylhydrazone which could not be crystallised and further characterised.


To an agitated suspension in dry thiophene-free benzene (85 c.c.) of freshly prepared sodium methoxide (2.975 g.), dried in high vacuum, ethyl formate (12.8 c.c.) was added under nitrogen and with exclusion of moisture. After ca 30 minutes trimethylacetoxv-ketone (900 mg.) in absolute benzene (42.5 c.c.) was added dropwise under cooling. The reaction mixture was then agitated for 20 hours at room-temperature and subsequently poured in ice-water. Benzene portion was further extracted with ice-cold 5% sodium carbonate solution and combined aqueous portions were slowly acidified with cold dilute hydrochloric acid (14). The acidic solution saturated with sodium chloride, was extracted thrice with ether. The ethereal layer was washed with water (saturated with brine) and dried over sodium sulphate.
In the usual way the solvent was removed and the acidic product (800 mg.) could be isolated. The viscous brown oil gave a deep violet colour with ethanolic ferric chloride and it was acetylated without any subsequent purification. With acetic anhydride (33.2 c.c.) and pyridine (12.8 c.c.), the solution was allowed to stand at 20° for 18 hours. After dilution of the reaction mixture with cold water, it was taken up in ether and the organic layer was thoroughly washed with 5% sodium bicarbonate solution till faintly alkaline, with water and finally dried over sodium sulphate. After removing the solvent a neutral oil (2.08 g.), giving no colouration with ferric chloride, could be isolated. This crystallized out on standing. It was however directly taken in glacial acetic acid (40 c.c.) and hydrogenated with 10% palladium-charcoal catalyst (750 mg.). In 40 minutes 2 moles of hydrogen were taken up and then the reaction came to a stop. The catalyst was filtered off and the solution was diluted with water. The ethereal extract was thoroughly washed with 2% cold sodium carbonate solution, water and dried over sodium sulphate. After removal of the solvent the brown oily residue (800 mg.) did not solidify even on keeping in cold for sometime. It was added to 10% ethanolic potassium hydroxide solution, potassium hydroxide (1 g.) in ethanol (10 c.c.), and the solution was refluxed for 2 hours when the colour became yellow. To the cold solution, (12 N) hydrochloric acid (5 c.c.) was slowly added and it became colourless. It was then poured into water (100 c.c.) and extracted with ether. The organic
layer was washed with water and dried (sodium sulphate). On removal of the solvent, the residue crystallised in short needles. The crude solid hydroxy-ketone was acetylated by dissolving in pyridine and adding slowly a mixture of acetic anhydride (1.5 c.c.) and acetyl chloride (0.7 c.c.) in the cold. Dry ether (10 c.c.) was then added and kept overnight at room temperature. Next it was poured in ice containing (12 N) hydrochloric acid (4 c.c.) and ether. The organic layer was separated and the aqueous layer was twice extracted with ether. The combined ethereal extract was washed with water, cold 2% sodium bicarbonate solution and dried over sodium sulphate. Ether being removed the residue (750 mg.) solidified and it was taken in petroleum-ether (20 c.c., 40-60°) and chromatographed through a column of neutral aluminium oxide (11 g.). The column was eluted with petroleum-ether (40-60°) yielding tetramethyl-acetoxy-ketone (670 mg.), m.p. 87-89°, in eleven fractions (100 c.c. each fraction). After two recrystallisations from petroleum-ether (40-60°), the long shining needle-shaped crystals were obtained melting at 89-90°. The mixed melting point (m.p. 73-80°) was depressed on admixture with the trimethyl-trans-acetoxy-ketone (113-113.5°).

Anal. Calcd. for C₁₆H₂₆O₃ : C, 72.2; H, 9.3.
Found : C, 72.1; H, 9.3.
The yellow 2,4-dinitrophenylhydrazone was crystallised from ethyl acetate in flakes, m.p. 245-246°C.

Anal. Calcd. for C₂₂H₃₀O₆N₄: C, 53.2; H, 6.7; N, 12.5.
Found: C, 53.2; H, 6.6; N, 12.6.

Attempt was also made to methylate the trimethyl-trans-acetoxy-decalone (XIV) through the oxalyl derivative. An orange-coloured ethoxy-oxalyl derivative (53.6%) was isolated in the usual way as an oil, which also gave scarlet-red colouration with alcoholic ferric chloride. The acidic product (6.45 g.) was then dissolved in dry acetone (60 c.c.) and refluxed with methyl iodide (20 c.c.) over freshly ignited potassium carbonate (5 g.) for 17 hours under nitrogen. On working up in the usual way, a neutral product (6.1 g.) could be isolated which gave no colouration with alcoholic ferric chloride. Hydrolysis of the neutral substance was carried out by refluxing with 10% ethanolic potassium hydroxide solution (from potassium hydroxide, 6.7 g.) for 7 hours. On working up in the usual way the residue on repeated crystallisation from petroleum-ether (40-60°C) afforded a white needle-shaped crystalline solid, m.p. 113-114°C. There was no depression in the melting point (113-114°C) on admixture with the original trimethyl-acetoxy-decalone (XIV, 113-113.5°C).
To a cooled and stirred solution of the tetramethyl-
trans-decalone (XIX, 850 mg.) in glacial acetic acid (5.5 c.c.)
there was added a solution of dry bromine (0.176 c.c.) in
acetic acid (2.31 c.c.). After a first few drops of the bromine
solution had been decolourised, the residual bromine was added
dropwise during 7 minutes. Stirring was continued for 3 hours.
The slightly coloured solution thus obtained was poured into
ice-cold water. The viscous oil which separated out was
extracted with ether. The ethereal extract was successively
washed with water, 5% sodium bicarbonate solution and again
with water, dried over sodium sulphate and the solvent removed.
The crude viscous residue (1.15 g.) was taken in collidine
(10 c.c.) and the flask containing the mixture was immersed in
an oil-bath at 180° and kept for 30 minutes at that temperature
in nitrogen atmosphere whereupon collidine hydrobromide precipi-
tated out. It was cooled and poured in ice-cold water (ca 150 c.c.)
containing concentrated hydrochloric acid (30 c.c.). A deep-brown
oily liquid was extracted thoroughly with ether which, in turn,
was washed with water, dried and the solvent removed. The crude
gummy residue (650 mg.) afforded almost quantitatively a red
2:4-dinitrophenylhydrazone, m.p. 262-264°. It was recrystallised
from ethyl acetate-ethanol (1:2), m.p. 265-266°. \( \text{CHCl}_3 \)
max. 376 m\( \mu \) (log e 4.38).

Anal. Calcd. for \( \text{C}_{22}\text{H}_{30}\text{O}_4\text{N}_2 \): C, 59.5; H, 6.3.
Found: C, 59.0; H, 6.2.