213. *Synthetical Studies of Terpenoids. Part VIII.*[1] *Synthesis of an Isomer of (±)-Cyclocolorenone.**

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The bicyclic ketone (XII) has been prepared and used to synthesise a tricyclic compound (XVII) having the gross structure of cyclocolorenone. The oily tricyclic product is a stereoisomeric mixture, partly separable into small needles, but the stereochemistry of this solid could not be established definitely.

The essential oil of *Pseudowintra colorata*, a shrub endemic to New Zealand, contains a tricyclic sesquiterpenoid ketone, cyclocolorenone, for which the structure (I) has recently been proposed.[2] The compound has been described as an oil ($\lambda_{max.}$ 264 mμ; log ε 4·17) which affords a scarlet 2,4-dinitrophenylhydrazone, m. p. 217—218°, $\lambda_{max.}$ (in $CHCl_3$) 404 mμ (log ε 4·5), but the stereochemistry of cyclocolorenone was not considered. We have synthesised a compound having the gross structure of cyclocolorenone and with $\lambda_{max.}$ 262 mμ (log ε 4·1). Recently [3] epicyclocolorenone has been synthesised by using *O*-acetylisophotosantonic acid lactone [4] as a relay, and thereby it has been possible to define all the asymmetric centres in cyclocolorenone and its epi-compound; these findings were further confirmed by nuclear magnetic resonance studies.

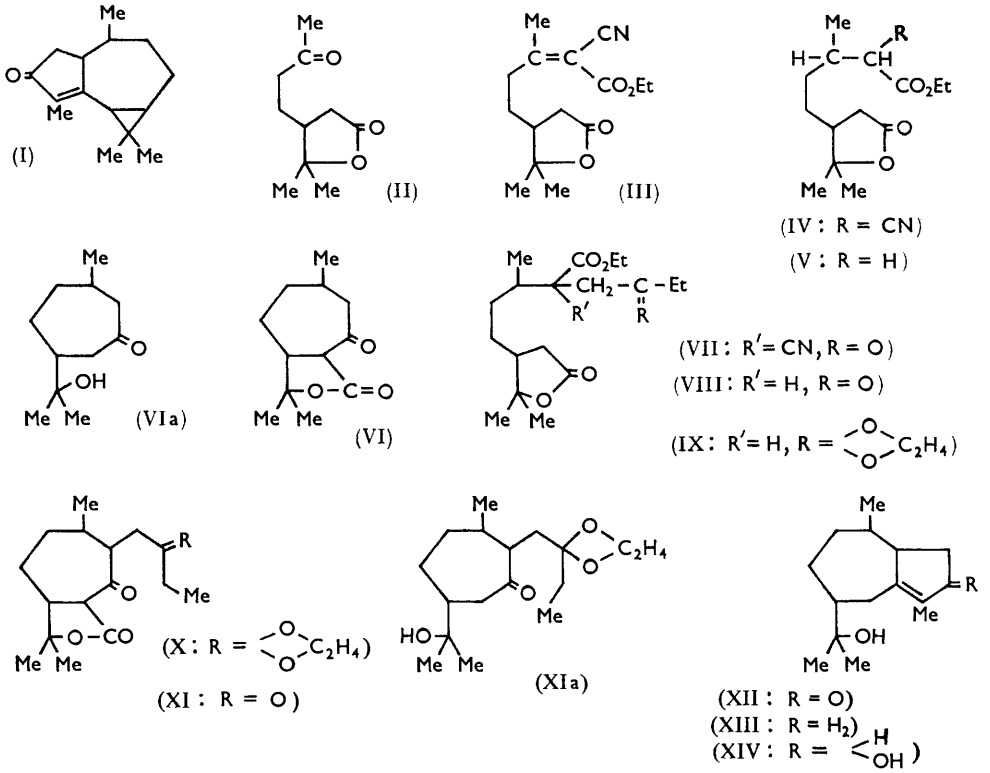
(±)-α-Terpineol was oxidised with potassium permanganate followed by chromic acid, leading to the homoterpenyl methyl ketone (II) in 40% yield; the previously reported [5] yield was poor (*ca.* 1%). Condensation with ethyl cyanoacetate [6] afforded the lactone (III) which was obtained in two crystalline polymorphs; this was reduced in presence of palladium–charcoal to the saturated compound (IV), which was subjected to hydrolysis and decarboxylation by heating with a mixture of hydrochloric acid and acetic acid. The crude acidic product was directly esterified to afford β-(4-ethoxycarbonyl-3-methylbutyl)-γ-methyl-γ-valerolactone (V). With a view to studying conditions of cyclisation of the ester-lactone (V), it was subjected to ring-closure in the presence of potassium t-butoxide in boiling xylene according to the high-dilution technique,[7] leading to the lactone (VI), whose structure was confirmed by its hydrolysis to the hydroxy-ketone (VIa); the infrared spectrum of the latter exhibits the characteristic OH (3600 $cm.^{-1}$) and CO (1703 $cm.^{-1}$) bands. Initial attempts to condense bromomethyl ethyl ketone with compound (IV) under different conditions failed, but the desired condensation proceeded smoothly in the presence of potassium t-butoxide, with the formation of compound (VII).

Owing to the difficulty in isolating this product by distillation, the crude mass was subjected to hydrolysis and decarboxylation by heating with hydrochloric acid and acetic acid. The crude acidic material left after the removal of low-boiling products was

* Presented at the Second International Symposium on the Chemistry of Natural Products, Prague, 1962.

[1] Part VII, Kundu and Dutta, *J.*, 1962, 533.
[2] Corbett and Speden, *J.*, 1958, 3710.
[3] Büchi and Loewenthal, *Proc. Chem. Soc.*, 1962, 280.
[4] Barton, de Mayo, and Shafig, *J.*, 1957, 929; Arigoni, Bossohard, Bruderer, Büchi, Jeger, and Krebaum, *Helv. Chim. Acta*, 1957, **40**, 1732.
[5] Wallach, *Annalen*, 1893, **275**, 151; **277**, 110; *Ber.*, 1895, **28**, 1775; Tiemann, *ibid.*, p. 1778.
[6] Cope, Hofmann, Wyekoff, and Hardenberg, *J. Amer. Chem. Soc.*, 1941, **63**, 3452.
[7] Leonard and Schimelfenig, jun., *J. Org. Chem.*, 1958, **23**, 1708; Mahajan and Dutta, *J.*, 1960, 62.

esterified to afford the lactone (VIII). The corresponding ethylenedioxy-lactone (IX) was then subjected to ring-closure with potassium t-butoxide, as before, to give the cyclised product (X) in good yield; it was converted into the cycloheptanone (XIa) in excellent yield on mild alkaline hydrolysis. This compound shows an infrared absorption band at 1135 cm.$^{-1}$, characteristic of the ketal function, in addition to bands due to hydroxyl and carbonyl groups. The ethylenedioxy-group in the lactone (X) was removed by treating it with toluene-*p*-sulphonic acid in acetone, to give compound (XI), but this could not be isolated in a pure state, probably owing to contamination with a furan derivative, generally formed in the presence of mineral acids.[8] Hence the crude product was directly used for the next step. After a series of experiments, optimum conditions were worked out for the ring-closure in the presence of dilute potassium hydroxide solution, and the desired neutral material (XII) was obtained. This readily afforded a red 2,4-dinitrophenylhydrazone, had the expected ultraviolet absorption at 242 mμ (log ε 4·1), and strong bands at 1710 (αβ-unsaturated cyclopentenone) and 3610 cm.$^{-1}$ (t-OH), with no absorption characteristic of a γ-lactone. When the ethylenedioxy-group in compound (X) was removed in the presence of hydrochloric acid, and the crude product was subjected to ring-closure under alkaline conditions as mentioned before, impure compound (XII) was obtained. It had $\lambda_{max.}$ 242 mμ (log ε 3·88), $\nu_{max.}$ 1703 (αβ-unsaturated cyclopentenone),



3610 (t-OH), and a weak band at 1735 cm.$^{-1}$, characteristic of a cyclopentanone derivative and possibly arising from the partial migration of the double bond. In the bicyclic ketone (XII), the quaternary angular hydrogen atom was originally considered to be β or axial [9a] because of its ease of epimerisation. These views have been modified recently,[9b]

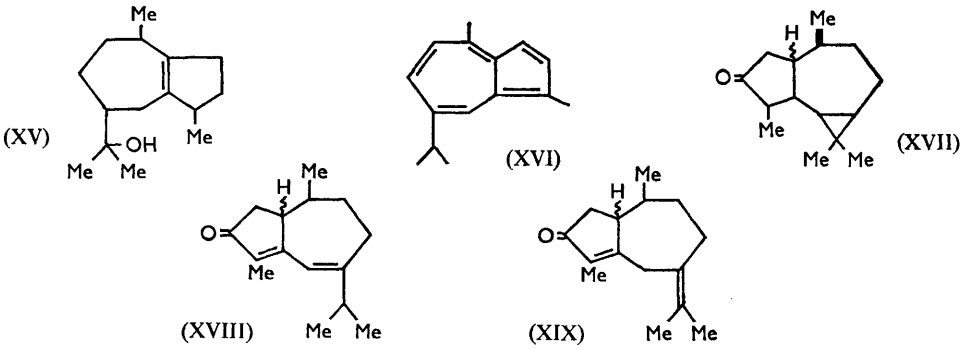
[8] Wild and Close, *J. Amer. Chem. Soc.*, 1946, **68**, 83; Baumgarten, Creger, and Villars, *J. Amer. Chem. Soc.*, 1958, **80**, 6609; Mahajan and Dutta, *loc. cit.*

[9] (*a*) Djerassi, Osiecki, and Herz, *J. Org. Chem.*, 1957, **22**, 1361; (*b*) Asher and Sim, *Proc. Chem. Soc.*, 1962, 111.

and the ease of epimerisation appears now to be dependent on the stereochemistry[3] of the 4-methyl group. The steric disposition of the substituted isopropyl group may be taken as a reference point, as it arises from (±)-terpineol. Incidentally, this also defines the other asymmetric centre, which involves the cyclopropane ring in cyclocolorenone. The stereochemistry of the 4-methyl is still uncertain because catalytic reduction proceeded in a non-stereospecific way, leading to the formation of two diastereoisomers of (III). This is supported by gas chromatographic analysis of the ketone (VIa), which contains two isomers in the ratio 50 : 47. Gas chromatography of the ketone (XIa) indicates that it is a complex mixture, and it was not well separated on the column.

The bicyclic ketone (XII) may be regarded as a potential intermediate in synthetic studies of a few important bicyclic and tricyclic sesquiterpenoids, *e.g.*, guaiol, the stereochemistry of which has been elucidated by Minato.[10] In the present studies an attempt was also made to synthesise guaiol (XV) or its isomer. Huang-Minlon reduction of (XII) afforded, in poor yield, a bluish liquid having the expected boiling point, along with a tarry mass. The liquid was separated chromatographically into guaizulene (XVI), identified through its trinitrobenzene complex,[11] and a colourless liquid which was an inseparable mixture. Reduction of the carbonyl group through the formation of the thioketal, and subsequent treatment with Raney nickel,[12] was also unsuccessful. Next, it was thought desirable to synthesise a bond isomer (XIII) of guaiol having the double bond at the position shown. For this purpose the ketone (XII) was reduced with sodium borohydride to the diol (XIV), and the allylic hydroxyl group was removed by treatment with lithium-ammonia in tetrahydrofuran and t-butyl alcohol,[13] to give the decene derivative (XIII). This product was dehydrogenated with sulphur, affording *s*-guaiazulene (XVI). Evidently the product (XIII) is a mixture of different isomers of guaiol (XV), both structural and stereochemical, the former arising from the undefined position of the double bond.

With the ultimate aim of achieving the synthesis of cyclocolorenone, the bicyclic intermediate (XII) has been utilised successfully according to the well-established method developed for the syntheses of eucarvone[14] and maaliol.[15] This involved the treatment of (XII) with hydrogen bromide in acetic acid, yielding the bromide, which was subjected to dehydrobromination with methanolic potassium hydroxide solution. The crude

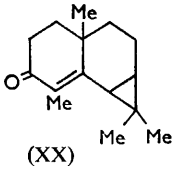


product showed three distinct absorptions, $\lambda_{max.}$ 243, 264, and 296 mμ (log ε 3·9, 3·8, and 4), suggesting the presence of three different chromophoric systems. It was subjected to extensive chromatographic separation, and four colourless oily fractions were isolated along with a dark blue azulenic fraction; the last was eluted first and finally rejected. Compound (XII) was identified as the fourth fraction. Another fraction, evidently (XIX),

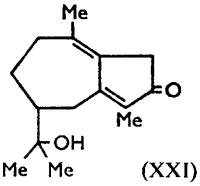
[10] Minato, *Tetrahedron*, 1962, **18**, 365.
[11] Pfau and Plattner, *Helv. Chim. Acta*, 1936, **19**, 871.
[12] Hartman, *J. Org. Chem.*, 1957, **22**, 466.
[13] Dryden, jun., Webber, Burtner, and Cella, *J. Org. Chem.*, 1961, **27**, 3244.
[14] Van Tamelen, McNary, and Lornitzo, *J. Amer. Chem. Soc.*, 1957, **79**, 1231.
[15] Bates, Büchi, Matsuura, and Shaffer, *J. Amer. Chem. Soc.*, 1960, **82**, 2327.

showed $\lambda_{max.}$ 243 mμ and formed a red 2,4-dinitrophenylhydrazone, $\lambda_{max.}$ (in $CHCl_3$) 395 mμ (log ε 4·5); this indicated the presence of the αβ-unsaturated carbonyl system, and the absence of absorption at 890 $cm.^{-1}$ further suggested the presence of an isolated and non-methylenic double bond, the latter arising from dehydrobromination through the action of alkali on the tertiary bromide. This structure was confirmed by its conversion into compound (XVIII) by treatment with toluene-*p*-sulphonic acid in boiling benzene, and by the ready formation of the doubly conjugated ketone (XVIII) from the ketone (XII) under identical conditions. The ketone (XVIII) showed one absorption peak, at 296 mμ, and it furnished a dark red 2,4-dinitrophenylhydrazone, $\lambda_{max.}$ (in $CHCl_3$) 408 mμ (log ε 4·53). This derivative was identical (melting point and infrared) with the 2,4-dinitrophenylhydrazone, available in almost quantitative yield, from the third fraction of chromatogram mentioned above. The second fraction, isolated in a comparatively poor yield, showed $\lambda_{max.}$ 261—262 mμ, and afforded a red 2,4-dinitrophenylhydrazone, $\lambda_{max.}$ (in $CHCl_3$) 4·2 mμ (log ε 4·5). This oily product solidified partially when kept at low temperature and the solid was very soluble in the common organic solvents. On slow evaporative crystallisation of a solution of the substance from light petroleum, a small quantity of needles, m. p. 71—72°, were obtained; they afforded an almost quantitative yield of the last-mentioned 2,4-dinitrophenylhydrazone, and the parent ketone is evidently (XVII). The mixed melting points of the 2,4-dinitrophenylhydrazone from this synthetic product with those of the derivatives from natural cyclocolorenone and from epicyclocolorenone were both depressed. The infrared spectra of these three 2,4-dinitrophenylhydrazones differed in the fingerprint region, indicating their stereochemical differences. It appears that a different stereoisomer of cyclocolorenone is being dealt with and a *cis*-relationship of the 4-methyl and the cyclopropane ring (*e.g.*, XVII) appears probable in this compound through a process of elimination of the isomers described by Büchi.[3] The stereochemistry of the angular hydrogen atom is, however, undefined in this synthetic compound as depicted in (XVII). Through the action of *N*-bromosuccinimide on cyclocolorenone, Corbett and Speden[2] obtained a small quantity of a dienone ($\lambda_{max.}$ 296 mμ), which afforded a dark-red 2,4-dinitrophenylhydrazone which showed no depression in mixed melting point with the derivative from compound (XVIII); their infrared spectra are superimposable. Thus, the dienone obtained by Corbett and Speden[2] is evidently (XVIII); their identity is due to the disappearance of asymmetry connected with the cyclopropane ring of cyclocolorenone with respect to the other two asymmetric centres in structure (I). The steric relation of the angular hydrogen and 4-methyl in the dienone is not known.

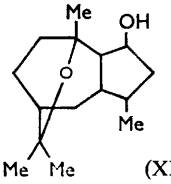
The spectral properties of the second chromatographic fraction are of immediate interest. The bathochromic shift[15] of 20 mμ as compared to compound (XII) clearly indicated that the cyclopropane ring was conjugated with the αβ-unsaturated ketone group. The absorption peak compares with the value [$\lambda_{max.}$ (in EtOH) 264 mμ] observed for compound (XX), a closely related tricyclic intermediate utilised by Büchi for the synthesis of maaliol, and that [$\lambda_{max.}$(in EtOH) 268 mμ] for 22-dihydroisosuprasterone-II.[16] The effect of the cyclopropane ring was also discernible in the ultraviolet spectra of the 2,4-dinitrophenylhydrazones.



(XX)



(XXI)



(XXII)

Some preliminary studies have been carried out with a view to controlling the stereochemistry at C-4 by the introduction of a double bond and subsequent reduction, and also

[16] Dauben, Bell, Hutton, Laws, Rheiner, jun., and Urscheler, *J. Amer. Chem. Soc.*, 1958, **80**, 4116.

for building up the ring system present in kessyl alcohol (XXII). The ketone (XII) was treated with *N*-bromosuccinimide in the presence of anhydrous potassium carbonate.[17] The crude bromo-product was treated under reflux with dimethylformamide containing a small quantity of calcium carbonate,[18] and the dienone (XXI) so obtained has been characterised through its 2,4-dinitrophenylhydrazone.

The other 2,4-dinitrophenylhydrazone isolated from the above reaction mixture was found to be identical with that from the ketone (XVIII). The desired tetrahydropyran ring may be capable of formation from compound (XXI) under alkaline conditions, as has been observed in the case of geigerin.[19] This, however, will depend on the stereochemistry of the substituted isopropyl group in the ketone (XII),[15] and some of these aspects are under investigation.

Experimental

Ultraviolet spectra were measured for ethanol solutions. Light petroleum had b. p. 40—60°. All the compounds herein containing asymmetric carbon atoms are the racemic forms.

Homoterpenyl Methyl Ketone (II).—Thoroughly cooled α-terpineol (50 g.) was oxidised with potassium permanganate (75 g.) in water (2000 c.c.). The filtrate was evaporated to a thick brown syrup (*ca.* 175 g.) and oxidised with chromic oxide (70 g.) in concentrated sulphuric acid (90 c.c.) and water (100 c.c.), with cooling. Next day the mixture was diluted with water and extracted thrice with chloroform, to afford the keto-lactone (II) (24 g.), b. p. 150—152°/0·5 mm.,which solidified; it formed spear-like crystals (from ethyl acetate–light petroleum), m. p. 63° (lit.,[3] 62—63°).

β-(4-*Cyano*-4-*ethoxycarbonyl*-3-*methylbut*-3-*enyl*)-γ-*methyl*-γ-*valerolactone* (III).—The keto-lactone (II) (100 g.), ethyl cyanoacetate (70 g.), acetic acid (14 c.c.), ammonium acetate (14 g.), and benzene (120 c.c.) were heated under reflux in a water-separator for 8 hr. The cooled mixture was washed with water, the low boiling products were removed, and the residue was distilled, to afford the *lactone* (III) (140 g.), b. p. 205—207°/0·4 mm. On crystallisation from ethyl acetate–light petroleum it furnished two polymorphic solids, m. p.s 92—93 and 108—109° (Found: C, 64·4; H, 7·6. $C_{15}H_{21}NO_4$ requires C, 64·5; H, 7·6%).

β-(4-*Cyano*-4-*ethoxycarbonyl*-3-*methylbutyl*)-γ-*methyl*-γ-*valerolactone* (IV).—The unsaturated cyano-compound (III) (40 g.), suspended in ethanol (50 c.c.), was hydrogenated in the presence of 10% palladium–charcoal (300 mg.). The suspended solid gradually dissolved to give a clear solution. The *lactone* (IV) (38 g.), b. p. 200—202°/0·4 mm., was a viscous liquid (Found: C, 63·8; H, 8·2. $C_{15}H_{23}NO_4$ requires C, 64·05; H, 8·25%).

β-(4-*Ethoxycarbonyl*-3-*methylbutyl*)-γ-*methyl*-γ-*valerolactone* (V).—The saturated cyano-compound (IV) (20 g.) was refluxed for 20 hr. with concentrated hydrochloric acid (80 c.c.) and acetic acid (20 c.c.). After removal of low-boiling products under reduced pressure, the dried residue was esterified with ethanol (100 c.c.) and concentrated sulphuric acid (10 c.c.), to afford the *lactone* (V) (14 g.), b. p. 165—170°/0·4 mm., as a pale yellow liquid (Found: C, 65·3; H, 9·2. $C_{14}H_{24}O_4$ requires C, 65·6; H, 9·4%).

7-(1-*Hydroxy*-1-*methylethyl*)-4-*methyl*-2-*oxocycloheptanecarboxylic Acid Lactone* (VI).—Potassium (2·5 g.) was dissolved in t-butyl alcohol and excess of the solvent distilled off. Dry xylene (300 c.c.) was introduced, and a portion of the solvent was distilled off to remove the last traces of the alcohol. A high-dilution apparatus was fitted to the reaction flask and β-(4-ethoxycarbonyl-3-methylbutyl)-γ-methyl-γ-valerolactone (V) (12 g.) in xylene (60 c.c.) was added dropwise. The cyclisation period was reduced to 3 hr., instead of the several days mentioned by previous workers. The critical factors were slow and gradual addition of the ester-lactone, continuous removal of the alcohol formed during the reaction, efficient stirring, and an atmosphere of dry pure nitrogen. At the end of the reaction, the brown mixture was cooled to room temperature and acidified with acetic acid. The xylene layer was separated and washed with water, and the solvent removed under reduced pressure. The brown residue

[17] Barton and Pinhey, *Proc. Chem. Soc.*, 1960, 279; experimental details through personal communication from Professor D. H. R. Barton.
[18] Knox, Zderic, Ruelas, Djerassi, and Ringold, *J. Amer. Chem. Soc.*, 1960, **82**, 1230.
[19] Barton and Levisalles, *J.*, 1958, 4518.

was distilled to afford the *lactone* (VI) (7 g.), b. p. 130—135°/0·4 mm. It gave a purple ferric reaction. The product solidified on keeping, to yield shining thick needles (from ethyl acetate–light petroleum), m. p. 93°; $\nu_{max.}$ 1585 cm.$^{-1}$ (CO·CH·CO) (Found: C, 68·9; H, 8·7. $C_{12}H_{18}O_3$ requires C, 68·5; H, 8·65%).

6-(1-*Hydroxy*-1-*methylethyl*)-3-*methylcycloheptanone* (VIa).—The lactone (VI) (3 g.) was heated under reflux with 2·5% aqueous potassium hydroxide (50 c.c.) for 8 hr. The mixture was diluted with water, saturated with sodium chloride, and extracted with ether. The extract was washed with water, and dried (Na_2SO_4), and the solvent was removed. The residue was distilled, to afford the *product* (VIa) (1·7 g.), b. p. 127°/9 mm. (Found: C, 71·9; H, 10·9. $C_{11}H_{20}O_2$ requires C, 71·7; H, 10·8%). The 2,4-*dinitrophenylhydrazone*, on repeated crystallisation from ethyl acetate–light petroleum formed needles, m. p. 124° (Found: C, 56·3; H, 6·4. $C_{17}H_{24}N_4O_5$ requires C, 56·0; H, 6·6%).

β-(4-*Ethoxycarbonyl*-3-*methyl*-6-*oxo*-*octyl*)-γ-*methyl*-γ-*valerolactone* (VIII).—Potassium (8·5 g.) was dissolved in t-butyl alcohol, and the latter was distilled off until a solid appeared. This was cooled to room temperature and the valerolactone (IV) (50 g.) was added in one portion with shaking. The orange mixture was left at room temperature for 4 hr., with occasional shaking. Bromomethyl ethyl ketone (60 g.) was next added; the resulting turbid mixture was heated under reflux for 12 hr., cooled to room temperature, acidified with dilute hydrochloric acid, and extracted with ether. The ethereal layer was washed thrice with water and dried (Na_2SO_4). After removal of the solvent, the dark brown product decomposed when distillation in a high vacuum was attempted. The crude residue (*ca.* 60 g.) was then heated under reflux for 20 hr. with concentrated hydrochloric acid (400 c.c.) and acetic acid (80 c.c.), and, after removal of the low-boiling products under reduced pressure, the dried residue was esterified with ethanol (600 c.c.) and concentrated sulphuric acid (30 c.c.), to afford the *lactone* (VIII) (35 g.), b. p. 210—215°/0·5 mm: (Found: C, 66·0; H, 9·1. $C_{18}H_{30}O_5$ requires C, 66·25; H, 9·25%), along with a forerun (8 g.), b. p. 160—170°/0·5 mm.

β-(4-*Ethoxycarbonyl*-6,6-*ethylenedioxy*-3-*methyloctyl*)-γ-*methyl*-γ-*valerolactone* (IX).—The ketolactone (VIII) (35 g.), freshly distilled ethylene glycol (15 c.c.), dry benzene (250 c.c.), and toluene-*p*-sulphonic acid (200 mg.) were heated under reflux for 25 hr., the water formed during the reaction being removed occasionally. The cooled mixture was washed with 5% sodium carbonate solution and water, the solvent was removed, and the residue on distillation afforded the lactone (IX) (20 g.), b. p. 220—230°/0·5 mm., as a viscous yellow liquid (Found: C, 65·15; H, 9·1. $C_{20}H_{34}O_6$ requires C, 64·85; H, 9·25%), along with a forerun (6 g.), b. p. 210°/0·5 mm.

3-(2,2-*Ethylenedioxybutyl*)-7-(1-*hydroxy*-1-*methylethyl*)-4-*methyl*-2-*oxocycloheptanecarboxylic Acid Lactone* (X).—The valerolactone (IX) (20 g.), in xylene (75 c.c.), was cyclised with potassium t-butoxide [from potassium (2·7 g.) in boiling xylene (350 c.c.)], as described before. The brown mass was cooled to room temperature and acidified with ice-cold dilute acetic acid. The xylene layer was separated and washed with cold water until neutral. The solvent was removed under reduced pressure and the thick brown residue was distilled, to afford the *lactone* (X) (11 g.), b. p. 185—190°/0·5 mm., as a viscous yellow liquid. It gave an intense purple colour with ethanolic ferric chloride solution (Found: C, 66·4; H, 8·3. $C_{18}H_{28}O_5$ requires C, 66·65; H, 8·6%).

2-(2,2-*Ethylenedioxybutyl*)-6-(1-*hydroxy*-1-*methylethyl*)-3-*methylcycloheptanone* (XIa).—The lactone (X) (4 g.) was heated under reflux with 2·5% aqueous potassium hydroxide (100 c.c.) for 8 hr. The mixture was cooled, diluted with water, saturated with sodium chloride, and extracted repeatedly with ether. The extract was washed with water, dried (Na_2SO_4), and the solvent was removed. The residue afforded the *product* (XIa) (2·8 g.), b. p. 176—180°/0·4 mm., as a viscous liquid (Found: C, 68·5; H, 10·6. $C_{17}H_{30}O_4$ requires C, 68·4; H, 10·0%).

5-(1-*Hydroxy*-1-*methylethyl*)-2,8-*dimethylbicyclo*[5,3,0]*dec*-7(8)-*en*-9-*one* (XII).—(*a*) A solution of the product (XIa) (10 g.) in dry acetone (100 c.c.) containing toluene-*p*-sulphonic acid (250 mg.) was heated under reflux for 3 hr. The solvent was removed under reduced pressure, keeping the bath-temperature below 40°. The oily residue was dissolved in ether and the ethereal solution washed once with 10% sodium hydrogen carbonate solution and with water. The solvent was evaporated and the residue (*ca.* 7 g.) treated with water (400 c.c.) (previously boiled to remove the dissolved air) in an atmosphere of purified nitrogen. A solution of potassium hydroxide (6 g.) in boiled water (200 c.c.) was added during 10 min. to the refluxing suspension. After 2 hours' heating under reflux, a solution of potassium hydroxide (14 g.) in boiled water (200 c.c.) was added slowly to raise the concentration of alkali to 2·5%, and the

mixture was heated for a further 9 hr. The pale yellow suspension was cooled in a nitrogen atmosphere and thoroughly extracted with ether after saturation of the solution with sodium chloride. After washing the ethereal layer with water, drying (Na_2SO_4), and removing the solvent, the residue was distilled, to afford the *product* (XII) (3 g.) b. p. 140—142°/0·4 mm. (Found: C, 76·5; H, 10·05. $C_{15}H_{24}O_2$ requires C, 76·2; H, 10·25%). It readily gave a 2,4-*dinitrophenylhydrazone*, fine needles (from ethyl acetate–methanol), m. p. 176—177° (Found: C, 60·6; H, 6·9; N, 13·4. $C_{21}H_{28}N_4O_5$ requires C, 60·5; H, 6·8; N, 13·45%).

(*b*) The lactonic keto-ketal (5 g.) was dissolved in methanol (20 c.c.), and concentrated hydrochloric acid (0·5 c.c.) in water (2 c.c.) was added dropwise. The solution was heated under reflux for 10 min. and left at room temperature overnight. It was diluted with water, and extracted with ether after saturation of the aqueous layer with sodium chloride. The ethereal layer was washed with water and dried (Na_2SO_4). On removal of the solvent, the crude residue (3·5 g.) afforded, after treatment with alkali as above, the bicyclic product (XII) (1 g.), b. p. 140—142°/0·4 mm. The 2,4-*dinitrophenylhydrazone*, on repeated crystallisation from ethyl acetate–methanol, had m. p. 176—177° alone or mixed with the sample described in (*a*).

5-(1-*Hydroxy*-1-*methylethyl*)-2,8-*dimethylbicyclo*[5,3,0]-*dec*-7(8)-*en*-9-*ol* (XIV).—The bicyclic ketone (XII) (1 g.) was dissolved in ethanol (5 c.c.), sodium borohydride (300 mg.) was slowly added, and the mixture was kept overnight. It was diluted with water and decomposed with a drop of concentrated hydrochloric acid. Saturation with sodium chloride, extraction with ether, washing of the ethereal layer with water, drying (Na_2SO_4), removal of the ether, and distillation afforded the *product* (XIV) (750 mg.), b. p. 145—147°/0·4 mm. (Found: C, 75·5; H, 10·7. $C_{15}H_{26}O_2$ requires C, 75·6; H, 10·9%).

5-(1-*Hydroxy*-1-*methylethyl*)-2,8-*dimethylbicyclo*[5,3,0]*dec*-7(8)-*ene* (XIII) *and/or its Bond Isomer*.—Lithium (500 mg.) was dissolved in liquid ammonia (30 c.c.). About half of a mixture of tetrahydrofuran (10 c.c.) and t-butyl alcohol (10 c.c.) was added, followed by a solution of the diol (XIV) (750 mg.) in the remaining portion of the solvent mixture. After 30 min. the lithium had been consumed. Methanol (2 c.c.) was added cautiously, and the ammonia was allowed to evaporate. The residual sludge was decomposed with water (10 c.c.) and extracted thoroughly with ether. The organic layer was separated, washed with water, and dried (Na_2SO_4). After removal of the solvent, the residue, on distillation, afforded the *product* (XIII) (200 mg.), b. p. 100—105°/0·5 mm. This was dissolved in light petroleum–benzene and chromatographed on a column of neutral alumina (10 g.), development being with a mixture of light petroleum and benzene. The desired alcohol (100 mg.) was obtained when the column was eluted with benzene–ether (1 : 1) (Found: C, 80·9; H, 11·6. $C_{15}H_{26}O$ requires C, 81·0; H, 11·8%).

s-*Guaiazulene* (XVI).—The alcohol (XIII) (50 mg.) was dehydrogenated by heating with sulphur (25 mg.) at 220—225° for 4 hr. The mixture was thoroughly extracted with light petroleum and chromatographed on neutral alumina (10 g.). The intense blue fractions were collected. On evaporation of the solvent, a blue residue (10 mg.) remained. This was converted into the trinitrobenzene complex, which, after crystallisation from ethanol, had m. p. and mixed m. p. 149—150°. It was dried at room temperature over calcium chloride in a desiccator for 4 days (Found: C, 61·4; H, 5·0. $C_{21}H_{21}N_3O_6$ requires C, 61·3; H, 5·1%).

3,3,7,11-*Tetramethyltricyclo*[6,3,0,$0^{2,4}$]*undec*-11-*en*-10-*one* (*Cyclocolorenone Isomer*) (XVII).—A solution of dry hydrogen bromide (12 g.) in acetic acid (32 c.c.) was added slowly, with stirring, to an ice-cooled solution of the ketone (XII) (5 g.) in glacial acetic acid (10 c.c.). After being kept at room temperature overnight, the brown mixture was poured into ice–water and extracted with ether. The ethereal layer was washed with cold sodium hydrogen carbonate solution and water, dried (Na_2SO_4), and concentrated (to 10 c.c.) under reduced pressure below room temperature. The concentrated solution containing the crude bromide was heated under reflux with potassium hydroxide (15 g.), dissolved in magnesium-dried methanol (150 c.c.) for 1 hr. under a nitrogen atmosphere. After removal of the solvent, the mixture was poured into ice–water and extracted with ether. The ethereal layer was washed with water, and dried, and the solvent was evaporated, leaving a residue (*ca.* 4 g.).

This crude oily mass was dissolved in the minimum quantity of light petroleum and chromatographed on neutral alumina (100 g.; Woelm grade I). Elution with light petroleum afforded a dark blue liquid fraction. Further elution with light petroleum (10 × 10 c.c.) afforded an oily mass which by repeated chromatography on alumina (20 g. each time), afforded a colourless oil (XIX) (500 mg.), $\lambda_{max.}$ 243 mμ (log ε 4·1), b. p. 125—130°/0·4 mm. (Found:

C, 82·5; H, 10·0. $C_{15}H_{22}O$ requires C, 82·6; H, 10·05%). It readily gave a 2,4-*dinitrophenylhydrazone*, m. p. 186—187° (from methanol) (Found: C, 63·4; H, 6·4. $C_{21}H_{26}N_4O_4$ requires C, 63·3; H, 6·6%).

A further quantity of an oily material (*ca.* 500 mg.), $\lambda_{max.}$ 261—262 mμ, was eluted by increasing the proportion of benzene in benzene–light petroleum until pure benzene was used. This was chromatographed twice more, and afforded a fraction which partially solidified after cooling for a week. It was highly soluble in the common organic solvents, and attempts to crystallise it at low temperature failed. The solid was collected and dissolved in light petroleum, and the solvent was evaporated slowly at room temperature. Small shining needles, m. p. 71—72°, were deposited at the mouth of the conical flask, and these were collected and redissolved in the same solvent. On repeating the process, the crystalline solid again had m. p. 71—72° (*ca.* 3 mg.). This afforded a scarlet 2,4-*dinitrophenylhydrazone*, m. p. 152—153°, which, crystallised once from ethyl acetate–methanol, had m. p. 156—157° alone or mixed with the product described below. The major liquid fraction (*ca.* 50 mg.) was distilled at 127—129°/0·4 mm.; $\lambda_{max.}$ 262 mμ, (log ε 4·1) (Found: C, 82·4; H, 10·0. $C_{15}H_{22}O$ requires C, 82·6; H, 10·05%). It afforded a scarlet 2,4-*dinitrophenylhydrazone*, m. p. 140—142° (crude) which, after 5 crystallisations from ethyl acetate–methanol, had m. p. 156—157° (Found: C, 63·3; H, 6·6. $C_{21}H_{26}N_4O_4$ requires C, 63·3; H, 6·6%). The liquid product darkened in air but the crystals were stable.

Finally, elution of the column was carried out with benzene–ether (1 : 1) (20 × 20 c.c.). On removal of the solvent, the oily mass (*ca.* 1·5 g.) was further chromatographed on alumina (40 g.), and the pure fractions, *A* and *B* were isolated by elution with benzene–ether (1 : 3) and ether, respectively.

Fraction *A* contained compound (XVIII) (0·7 g.), b. p. 128—130°/0·4 mm., $\lambda_{max.}$ 296 mμ (log ε 4·35) (Found: C, 82·5; H, 10·1. $C_{15}H_{22}O$ requires C, 82·6; H, 10·05%). It afforded a dark red 2,4-*dinitrophenylhydrazone*, m. p. 217—218° (from ethyl acetate) (Found: C, 63·3; H, 6·6. $C_{21}H_{26}N_4O_4$ requires C, 63·3; H, 6·6%).

Fraction *B* contained compound (XII) (0·3 g.), b. p. 145—149°/0·4 mm., had $\lambda_{max.}$ 242 mμ (log ε 4·0). It formed a red 2,4-dinitrophenylhydrazone, m. p. and mixed m. p. 176—177°.

5-*Isopropyl*-2,8-*dimethylbicyclo*[5,3,0]-*deca*-5,7(8)-*dien*-9-*one* (XVIII).—(*a*) The bicyclic keto-alcohol (XII) (100 mg.) was heated under reflux with toluene-*p*-sulphonic acid (10 mg.) in benzene (10 c.c.) for 30 min. The dark mixture was decomposed with water, and the benzene layer was washed with 5% sodium carbonate solution and water. Removal of the solvent and distillation of residue, afforded the product (XVIII), b. p. 125—127°(bath)/0·4 mm. $\lambda_{max.}$ 296 mμ (log ε 4·3). It readily gave a dark red 2,4-dinitrophenylhydrazone, m. p. and mixed m. p. 217—218°.

(*b*) The bicyclic ketone (XIX) (50 mg.) was heated under reflux with toluene-*p*-sulphonic acid (10 mg.) in benzene (10 c.c.) for 30 min., and the dark mixture was worked up as above. After removal of the solvent, the residue, on distillation, afforded the product (XVIII) (*ca.* 20 mg.), b. p. 125—127°/0·4 mm., $\lambda_{max.}$ 296 mμ (log ε 4·3). It afforded the same 2,4-dinitrophenylhydrazone, m. p. 217—218°, as the above sample.

5-(1-*Hydroxy*-1-*methylethyl*)-2,8-*dimethylbicyclo*[5,3,0]*deca*-1(2),7(8)-*dien*-9-*one* (XXI).—The keto-alcohol (XII) (1·5 g.), *N*-bromosuccinimide (1 g.), and anhydrous potassium carbonate (0·4 g.) were heated under reflux for 20 min. in pure dry carbon tetrachloride (20 c.c.). The green mixture was filtered at room temperature, the filtrate was washed with water and dried, and the solvent was removed. The residue (*ca.* 1·5 g.) was heated under reflux for 1 hr. with freshly distilled dimethylformamide (20 c.c.) containing a suspension of calcium carbonate (1 g.), in an atmosphere of nitrogen. The mixture was diluted with cold water and extracted with ether. The ethereal layer was washed thoroughly with water, and dried. The residue, on distillation, afforded an oily product (0·9 g.), $\lambda_{max.}$ 298 mμ (log ε 3·9), b. p. 130—132°/0·4 mm. It readily afforded two deep red 2,4-*dinitrophenylhydrazones*, m. p. 167—168° (from methanol–ethyl acetate) (Found: C, 60·6; H, 6·5. $C_{21}H_{26}N_4O_5$ requires C, 60·8; H, 6·3%), and m. p. 217—218°, which showed no depression when mixed with the sample described above.

We thank Professor D. H. R. Barton, F.R.S., for very helpful discussions and for comparison of infrared spectra of 2,4-dinitrophenylhydrazones, and Dr. Sukhdev for a sample of the trinitrobenzene complex of guaiazulene. The kind help of Dr. Corbett in providing us with samples of three 2,4-dinitrophenylhydrazones, and for release of valuable information before publication, is gratefully acknowledged as this has helped us in assigning a tentative stereochemistry to our

product. One of us (S. A. N.) thanks the Council of Scientific and Industrial Research, Government of India, for financial assistance. Microanalyses were carried out by Mrs. Chhabi Dutta, and ultraviolet absorption measurements by Mr. A. Ghosal, and we acknowledge their assistance with thanks. Gas chromatography was carried out at Johns Hopkins University. Part of this investigation was assisted by financial support from the Chemical Society Research Fund. We also thank Dr. R. C. Banerjee for the preparation of compounds (VIa) and (XIa).

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