Bridged Ring Systems. Part XV.† Structure of Neoclovene [1] (2,6,8,8-Tetramethyltricyclo[5,2,2,$0^{1,6}$]undec-2-ene)

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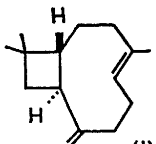
The structural elucidation of neoclovene (4), a new rearrangement product of caryophyllene, shows it to be 2,6,8,8-tetramethyltricyclo[5,2,2,$0^{1,6}$]undec-2-ene with the stereochemistry shown.

On treatment with concentrated sulphuric acid in ether, the sesquiterpene caryophyllene (1) is converted into a mixture of products[2] in which the hydrocarbon clovene (2) and the tertiary alcohol caryolan-1-ol (3) predominate. When the total synthesis of (±)-clovene was nearing completion in the Glasgow laboratories,[3] it became imperative to obtain a pure sample of the naturally derived hydrocarbon for comparison purposes. However, careful g.l.c. analysis of the hydrocarbon fraction obtained from rearrangement of caryophyllene indicated no less than 13 discernible peaks, two of which, in the ratio of 3 : 2, constituted about 90% of this mixture. The lower-boiling fractions obtained from spinning-band distillation[4] of this mixture were shown by comparative g.l.c. and i.r. spectroscopy to be clovene, the major constituent of the mixture. This sample was 98% pure and final purification was achieved by regeneration of the hydrocarbon from the isomeric dibromides as described by Lutz and Reid.[5] The higher-boiling hydrocarbon, a hitherto undetected isomer now designated neoclovene (4), was obtained in only 90% purity by this distillation procedure, but preparative g.l.c. with a 10% Ucon Polar stationary phase provided acceptable quantities of neoclovene, n_D^{20} 1·5088, $[\alpha]_D^{20}$ −72·0°, which was at least 99·5% pure by analytical g.l.c. criteria. Treatment of either clovene or caryolan-1-ol with concentrated sulphuric acid in ether gave no neoclovene.



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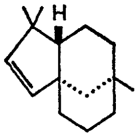

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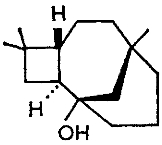

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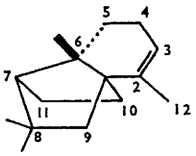

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The deduction of the structure of neoclovene proceeded as follows; for clarity the results will be illustrated in terms of the finally derived structure. The mass spectrum and elemental analysis of neoclovene (4) indicated a molecular formula of $C_{15}H_{24}$ and it was shown to be tricyclic by catalytic hydrogenation to a fully saturated dihydro-derivative containing one secondary and three tertiary methyl groups. The i.r. spectrum showed maxima at 3023 and 1657 cm.$^{-1}$ and a multitude of peaks in the 950—700 cm.$^{-1}$ region which did not permit an unambiguous assignment to the double-bond substitution pattern. This was adduced from the ^{1}H n.m.r. spectrum which clearly indicated one vinylic proton as a broad multiplet at τ 4·19, in addition to three tertiary methyl groups as singlets at τ 8·80 (3H) and 8·99 (6H) and a doublet at τ 8·41 (J 1·5 Hz) suggesting a vinylic methyl group. The fact that neoclovene possessed *four* methyl groups was interesting since this implied a novel carbon skeleton hitherto not encountered in caryophyllene rearrangement products.

Neoclovene was smoothly converted into a crystalline secondary–tertiary diol by treatment with osmium tetroxide in pyridine and subsequent mild oxidation yielded a ketol the carbonyl absorption at 1718 cm.$^{-1}$ of which was indicative of a six-membered ring. Confirmation of this fact was obtained by hydroboration of neoclovene to a separable mixture of two crystalline alcohols which, on oxidation and base-catalysed epimerisation, both gave the same ketone ν(C=O) 1712 cm.$^{-1}$. The ^{1}H n.m.r. spectrum of the diol clearly indicated four tertiary methyl groups at τ 8·75 (6H), 8·91 (3H), and 8·93 (3H), in addition to a multiplet (1H) at τ 6·3. Sodium metaperiodate cleavage of the diol gave an unstable keto-aldehyde (5) the ^{1}H n.m.r. spectrum of which showed a sharp singlet at τ 7·98 (3H) confirming the original contention that neoclovene had a methyl group on a trisubstituted double-bond. Furthermore, the aldehydic proton at τ 0·2 was split into a triplet (J 2·5 Hz) thus revealing the presence of a neighbouring methylene group. The keto-aldehyde (5) on oxidation gave the corresponding crystalline keto-acid (6; R = H). This keto-acid could very conveniently be isolated from chromium trioxide–acetic acid oxidation of the crude hydrocarbon mixture from rearranged caryophyllene. The work-up procedure effected anhydride formation of the clovenic acid present and mild base extraction and subsequent acidification separated the crude keto-acid which was purified by column chromatography of the

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† Part XIV, W. D. K. Macrossan, J. Martin, W. Parker, and A. B. Penrose, *J. Chem. Soc.* (*C*), 1968, 2323.

[1] For a preliminary account see W. Parker, R. A. Raphael, and J. S. Roberts, *Tetrahedron Letters*, 1965, 2313.

[2] For leading references, see A. Nickon, *Perfumery Essent. Oil Record*, 1954, **45**, 149 and D. H. R. Barton and P. de Mayo, *Quart. Rev.*, 1957, **11**, 189.

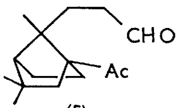
[3] P. Doyle, I. R. Maclean, R. D. H. Murray, W. Parker, and R. A. Raphael, *J. Chem. Soc.*, 1965, 1344.

[4] A. Eschenmoser and H. Günthard, *Helv. Chim. Acta*, 1951, **34**, 2338.

[5] A. W. Lutz and E. B. Reid, *J. Chem. Soc.*, 1954, 2265.

corresponding methyl ester (6; R = Me). This method furnished sufficient keto-acid (6; R = H) to permit the completion of the degradation sequence and made prolonged preparative g.l.c. separation of clovene and neoclovene unnecessary.

To obtain more information about the environment of the double bond in neoclovene, the keto-ester (6; R = Me) was subjected to a Baeyer–Villiger oxidation with trifluoroperacetic acid.[6] The ^{1}H n.m.r. spectrum of the resultant acetoxy-methyl ester (7; R^1 = Me; R^2 = OAc) showed that the acetoxy-group was tertiary since there was no resonance in the τ 5—6 region attributable to a proton on carbon bearing such a group. In addition, none of the three tertiary methyl groups at τ 8·81 (3H), 8·87 (3H), and 8·93 (3H) showed any appreciable downfield shift to be expected if one or two of them were substituted on the carbon bearing the acetoxy-function. Hence the partial structure (8) could be derived for neoclovene. Further verification of an unsaturated six-membered ring in neoclovene was obtained from base hydrolysis of (7; R^1 = Me; R^2 = OAc) to give the corresponding hydroxy-acid (7; R^1 = H; R^2 = OH) which when subsequently heated produced the crystalline δ-lactone (9), ν(C=O) 1745 cm.$^{-1}$.



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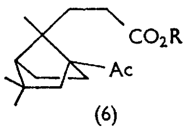

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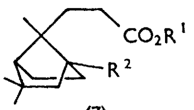

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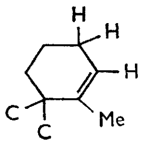

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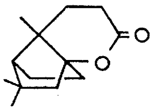

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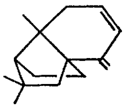
A possible method of opening the cyclohexene ring of neoclovene involved transformation to the corresponding homoannular diene followed by photolysis to the ring-opened conjugated triene.[7] However, treatment of neoclovene with *N*-bromosuccinimide followed by collidine dehydrobromination gave predominantly the heteroannular diene (10). Allylic oxidation of neoclovene with selenium dioxide in acetic acid–acetic anhydride produced an unsaturated acetate which was hydrolysed to a crystalline unsaturated alcohol (11). Unfortunately, oxidation had occurred on the allylic methyl group [8] as ascertained from the resonances at τ 6·09 (2H) and 4·63 (1H, unresolved multiplet) in the ^{1}H n.m.r. spectrum. Dehydration of this alcohol with toluene-*p*-sulphonic acid in acetone gave predominantly one diene the spectral properties of which were identical with the heteroannular diene isolated above. Oxidation of the alcohol with manganese dioxide produced the corresponding αβ-unsaturated aldehyde (12) the ^{1}H n.m.r. spectrum of which exhibited a singlet aldehydic proton at τ 0·66 and a triplet vinylic proton at τ 3·54 (*J* 4 Hz). Significantly, the two allylic protons at τ 7·5 were split into at least a six-line multiplet implying neighbouring protons in addition to the vinylic proton.



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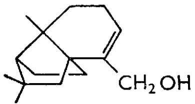

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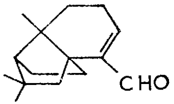

(12)

An alternative degradation mode was therefore adopted; the acetoxy-methyl ester (7; R^1 = Me; R^2 = OAc) was converted into the corresponding hydroxy-ester (7; R^1 = Me; R^2 = OH) by standard procedures and then treated with an excess of phenylmagnesium bromide in a Barbier–Wieland degradation. The resultant crude diol was dehydrated with acetic acid–acetic anhydride under reflux and purification of the product by chromatography gave a diphenylene-acetate (13) which could not be induced to crystallise. The ^{1}H n.m.r. spectrum of (13) permitted an extension of the partial structure of neoclovene to (14) since the vinylic proton signal at τ 3·89 was clearly resolved into a triplet (*J* 8 Hz) demonstrating the juxtaposition of a methylene group. This diphenylene-acetate (13) was then treated with a catalytic amount of ruthenium dioxide and an excess sodium metaperiodate in aqueous acetone [9] * to give in high yield the desired acetoxy-acid (15; R^1 = H; R^2 = OAc) which was hydrolysed with methanolic sodium hydroxide and then esterified with diazomethane to give the *nor*-hydroxy-ester (15; R^1 = Me; R^2 = OH). A second Barbier–Wieland sequence performed on (15; R^1 = Me; R^2 = OH) gave a crystalline nor-diphenylene-acetate (16) the ^{1}H n.m.r. spectrum of which revealed the vinylic proton as a sharp singlet at τ 3·62 indicative of a neighbouring *quaternary* centre. In addition, one of the tertiary methyl groups had moved downfield in the conversion of the diphenylene-acetate (13) (lowest field methyl signal at τ 8·78) into the *nor*-diphenylene-acetate (16) (lowest field methyl signal at τ 8·65) suggesting that one of the substituents at this quaternary centre was probably a methyl group.

The ruthenium dioxide–sodium metaperiodate oxidation of (16) gave the corresponding bis-nor-hydroxy-acid (17; R = CO_2H) which was then converted into the corresponding methyl ester (17; R = CO_2Me). [It is noteworthy that isolation with dilute sodium hydroxide of the acidic product from oxidation of (13) gave the nor-acetoxy-acid (15; R^1 = H; R^2 = OAc) in contrast with the nor-diphenylene-acetate (16) where the bis-nor-hydroxy-acid (17; R = CO_2H) was isolated. In the

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* It is noteworthy that only ruthenium dioxide prepared by controlled dehydration of ruthenium hydroxide will react with sodium metaperiodate, whereas the form of the dioxide prepared by oxidation of ruthenium metal sponge is inert.

[6] W. D. Emmons and G. B. Lucas, *J. Amer. Chem. Soc.*, 1955, **77**, 2287.

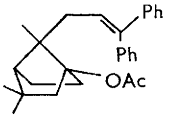
[7] W. G. Dauben and R. M. Coates, *J. Amer. Chem. Soc.*, 1964, **86**, 2490.

[8] A. Guillemonat, *Ann. Chim.* (*France*), 1939, **11**, 143.

[9] R. Pappo and A. Becker, *Bull. Res. Council Israel*, 1956, **5***A*, 300; G. Stork, A. Meisel, and J. E. Davies, *J. Amer. Chem. Soc.*, 1963, **85**, 3419.

latter instance, a carboxylate anion participation in the hydrolysis of the acetoxyl-group to afford a readily hydrolysed mixed anhydride is probably involved.] In the series of hydroxy-methyl esters (7; $R^1 = Me$; $R^2 = OH$), (15; $R^1 = Me$; $R^2 = OH$) and (17; $R = CO_2Me$) a downfield shift of one of the tertiary methyl groups to τ 8·64 was observed in the ^{1}H n.m.r. spectra of (17; $R = CO_2Me$), the lowest value in (7; $R^1 = Me$; $R^2 = OH$) and (15; $R^1 = Me$; $R^2 = OH$) being τ 8·88 and 8·83 respectively. Hence the partial structure of neoclovene could now be expanded to (18).

The problem at this stage was to devise a means of breaching the remaining bicyclic system. In view of the established 1,3-relationship of the two remaining functionalities, it was decided to utilise a retro-Prins reaction of the type employed by Corey in the synthesis of caryophyllene.[10] Accordingly, the bis-nor-hydroxy-ester (17; $R = CO_2Me$) was converted into the crystalline primary–tertiary diol (17; $R = CH_2{\cdot}OH$) by lithium aluminium hydride reduction. The ^{1}H n.m.r. and i.r. spectra of this diol exhibited some interesting features. In addition to the three tertiary methyl signals at τ 8·66 (3H), 8·81 (3H), and 8·93 (3H), the ^{1}H n.m.r. spectrum showed an ill-resolved doublet (1H) at τ 5·95 (*J* 11 Hz) and a very broad resonance (1H) at τ 6·3 ($w_{\frac{1}{2}}$ 20 Hz). When a little D_2O was added to the deuteriochloroform solution of the diol a substantial change in the spectrum was produced. The disappearance of the signal at τ 7·4 (2H) was accompanied by an alteration of the broad resonance at τ 6·3 into a sharp doublet centred at τ 6·36 (*J* 11·5 Hz) and the doublet at τ 5·95 (*J* 11·5 Hz) also became more well-defined. The same effect was observed when a drop of 6N-hydrochloric acid was added to the deuteriochloroform solution. At present, no satisfactory explanation can be offered to explain this phenomenon, but it would appear to be a consequence of the rate of proton exchange in the intramolecular hydrogen bonded species, which may, in turn, induce chemical shift and/or coupling differences. The i.r. spectrum of the diol in moderately concentrated solution in carbon tetrachloride showed four maxima at 3640, 3614, 3553, and 3400 cm.$^{-1}$; dilution caused the disappearance of the last maximum whereas the band at 3553 cm.$^{-1}$ due to intramolecular hydrogen bonding did not vary appreciably. The $\Delta\nu$ value of 87 cm.$^{-1}$ is characteristic of 1,3-diols.[11]



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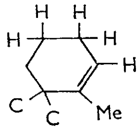

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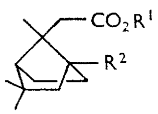

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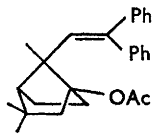

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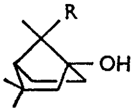

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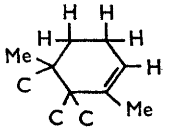
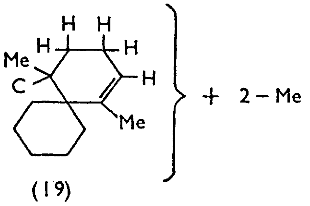


(18)

The diol (17; $R = CH_2{\cdot}OH$) was converted into the primary mono-tosylate (17; $R = CH_2OTs$) in the usual manner and treatment of this derivative with methylsulphinylcarbanion (dimsyl sodium)[12] gave, in 80% yield, an unsaturated ketone, $C_{11}H_{18}O$, the i.r. spectrum of which showed maxima at 1720 and 897 cm.$^{-1}$ indicative of a six-membered ketone and an *exo*-methylene group respectively. The u.v. spectrum showed no absorption characteristic of an $\alpha\beta$-unsaturated ketone. The ^{1}H n.m.r. spectrum exhibited signals at τ 5·04 ($w_{\frac{1}{2}}$ 4 Hz) and 5·23 ($w_{\frac{1}{2}}$ 3 Hz) (2H, $C{=}CH_2$), 8·19 (3H, *J* 1 Hz, $CH_3{-}C{=}CH_2$), 8·98 (3H), and 9·18 (3H). In this isopropenyldimethylcyclohexanone the appearance of two methyl singlets rigorously defines the presence of a *gem*-dimethyl group both in this compound and neoclovene. Catalytic hydrogenation afforded the corresponding saturated ketone ν(C=O) 1718 cm.$^{-1}$, τ 8·94 (3H), 9·14 (3H), and 8·99 (3H, *J* 7 Hz), and 9·16 (3H, *J* 7 Hz).

The partial structure for neoclovene could now be extended to (19) and since this structure contains 16 carbon atoms, two of them must be common. The final clarification of the neoclovene structure hinged on the determination of the constitution of the above isopropyldimethylcyclohexanone. Structures with a *gem*-dimethyl group α to the carbonyl function were deemed unlikely for the saturated degradation ketone in view of the ^{1}H n.m.r. spectrum which integrated for *four* protons over the region τ 7·7—8·0. This was corroborated by the corresponding i.r. spectrum which showed two significant bands at 1429 and 1419 cm.$^{-1}$ attributable to two different sets of methylene protons α to a ketone.[13] The mass spectrum of the saturated ketone showed intense peaks at *m*/*e* 83, 69, and 55 which were shown by high-resolution measurements to consist mainly of



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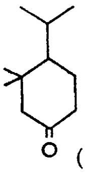

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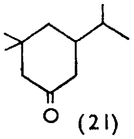

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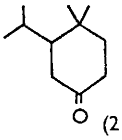

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[10] E. J. Corey, R. B. Mitra, and H. Uda, *J. Amer. Chem. Soc.*, 1964, **86**, 485.

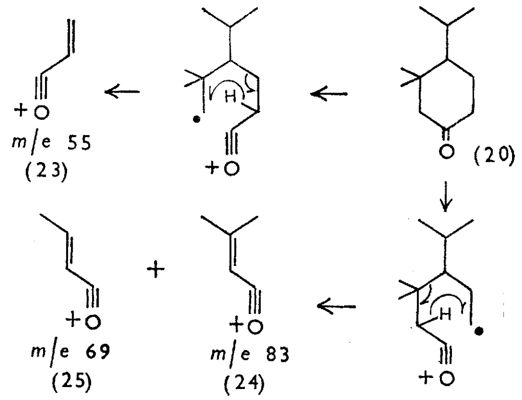
[11] P. von R. Schleyer, *J. Amer. Chem. Soc.*, 1961, **83**, 1368.

[12] E. J. Corey and M. Chaykovsky, *J. Amer. Chem. Soc.*, 1962, **84**, 866.

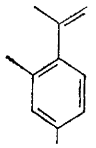
[13] R. N. Jones, A. R. H. Cole, and B. Nolin, *J. Amer. Chem. Soc.*, 1952, **74**, 5662; C. S. Barnes, D. H. R. Barton, A. R. H. Cole, J. S. Fawcett, and B. R. Thomas, *J. Chem. Soc.*, 1953, 573.

oxygen-containing fragments. By analogy[14] with the spectra of other substituted cyclohexanones, the formulae (23)—(25) could be assigned to these ions and they are readily derived from (20) as shown, whereas the virtual absence of fragments expected from (21) and (22) suggested that they were unlikely structures for the ketone.

Djerassi[15] and Fétizon[16] have elegantly demonstrated that acetal and thioacetal groupings direct fragmentation in the mass-spectrometer in a highly predictable manner. Hence the mass spectrum of the acetal of the saturated ketone should provide an unequivocal decision between the three possible structures (20)—(22). In the event, the acetal showed two predominant peaks at m/e 127 and 99, a result compatible only with structure (20) for the ketone obtained from degradation of neoclovene. This in turn, establishes the gross structure of neoclovene as (4).



A confirmatory synthesis of (20) was then accomplished starting with a Friedel–Crafts acylation of *m*-methylanisole with acetic anhydride and aluminium chloride to give mainly 2-methyl-4-methoxyacetophenone[17] which, on subsequent treatment with methylmagnesium iodide and dehydration, gave 6-isopropenyl-3-methoxy-1-methylbenzene (26). This compound on hydrogenation, Birch reduction, and acid hydrolysis afforded a good yield of 4-isopropyl-3-methylcyclohex-2-enone (27) contaminated with a separable small amount of 6-isopropyl-3-methylcyclohex-2-enone arising from the isomeric 2-methoxy-4-methylacetophenone formed in the Friedel–Crafts step. The conjugate addition of methylmagnesium iodide to (27) was accomplished in 20% yield in the presence of cupric acetate.[18] Careful preparative t.l.c. then gave the pure racemic saturated ketone (20) identical in all respects with the degradation ketone (i.r. and mass spectra and analytical g.l.c. on six different stationary phases).



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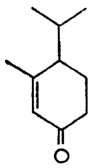
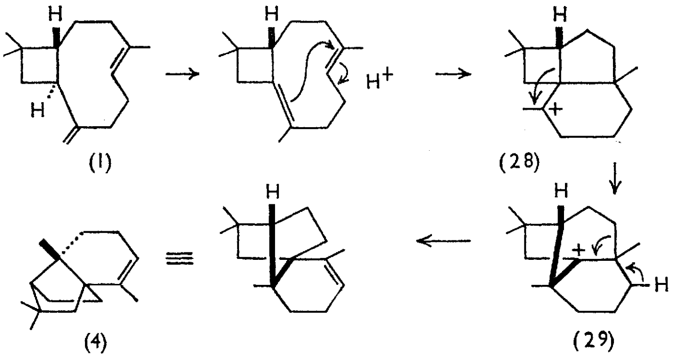


(27)

It was now possible to rationalise the acid-catalysed rearrangement of caryophyllene into neoclovene in terms of the mechanistic scheme depicted in the Scheme below. A model of the homoannular diene produced by the initial isomerisation of the exocyclic double-bond shows that in a certain conformation there is a maximum overlap of the π-electrons of the two double-bonds which would permit an acid-catalysed cyclisation to the tricyclic cation (28). A Wagner–Meerwein rearrangement of this cation produces the bridge-head[19] cation (29). A final Wagner–Meerwein rearrangement and subsequent proton-loss then generates the neoclovene structure with the stereochemistry depicted. This scheme has been given a firmer basis by a synthesis of neoclovene based on these steps.[20]



SCHEME

With the absolute stereochemistry of caryophyllene known,[21] it was possible to predict the sign of the Cotton effect of the ketone degradation product (20) by an application of the octant rule[22] and it was gratifying to learn that our prediction of a positive Cotton effect was fully substantiated by the o.r.d. curve.

The remaining obstacle to the establishment of the full stereochemical structure of neoclovene lay in the assignment of the relative configuration of the tertiary methyl group at C-6 with respect to the *gem*-dimethyl group at C-8. The proposed mechanism predicts that they will be *syn* and this relationship was confirmed in the following

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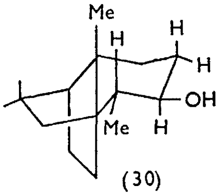
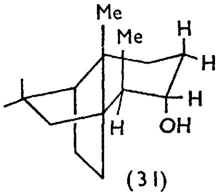
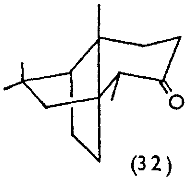
manner. As mentioned above, hydroboration of neoclovene gave two crystalline epimeric alcohols in the approximate ratio of 3 : 2 which were separated by preparative t.l.c. The ^{1}H n.m.r. spectrum of the predominant alcohol (m.p. 71—72°) exhibited a six-line multiplet (1H) at τ 6·44 ($w_{\frac{1}{2}}$ 15 Hz) which was attributed to the methine proton at C-3 corresponding to an A_2BX system. The spectrum of the other alcohol, m.p. 143—144°, showed an ill-resolved multiplet (1H) ($w_{\frac{1}{2}}$ 5 Hz) at τ 6·12. In view of the known *cis*-addition during hydroboration, a comparison of the chemical shifts and multiplicities of the carbinyl proton signal of these two alcohols indicated that this proton in the lower-melting alcohol was *axial* and coupled with one equatorial and two axial protons *i.e.* (30). Conversely, this proton in the higher-melting alcohol is *equatorial* and is coupled with one axial and two equatorial protons *i.e.* (31). Jones oxidation of each alcohol gave the corresponding ketones (32) and (33) respectively; ketone (33) was readily epimerised to (32) by treatment with methanolic sodium hydroxide. This finding corroborated the stereochemical assignments of the two alcohols in terms of which the secondary methyl group in (31) would necessarily be axial and therefore the derived ketone (33) would be expected to undergo rapid epimerisation.



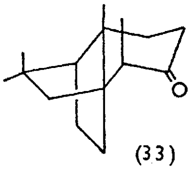
(30)



(31)



(32)



(33)

The o.r.d. curve of the ketone (32) showed a marked negative Cotton effect which is in harmony with that predicted from application of the octant rule, taking into account the known absolute configuration of caryophyllene and the suggested mechanism for its conversion into neoclovene. On the other hand, were this ketone to possess a stereostructure in which the C-6 methyl group was *anti* to the C-8 *gem*-dimethyl group then the Cotton curve would be expected to show a strong positive effect. Hence the absolute stereochemistry of neoclovene is as shown in formula (4).

EXPERIMENTAL

All m.p.'s were recorded on a Kofler block and are corrected; boiling points are uncorrected. The alumina used for routine chromatography (Spence type H) was acid-washed and activated according to Brockmann and Schodder's method. Thin (0·25 mm.) and thick (1·0 mm.) layer chromatoplates were prepared from Kieselgel (Merck). Analytical chromatograms were run on the Pye Argon Chromatograph on columns 4 ft. × $\frac{1}{8}$ in., and on the Aerograph 'Autoprep' A-700 model for preparative separations. Light petroleum refers to the fraction of b.p. 40—60°, unless otherwise stated. All organic extracts were dried with anhydrous magnesium sulphate.

U.v. spectra, measured on an Unicam S.P. 800 instrument, refer to ethanol solutions. Routine i.r. spectra were measured on a Perkin-Elmer 'Infracord' or Unicam S.P. 200 model, and for high-resolution spectra on a Unicam S.P. 100 double-beam i.r. spectrophotometer equipped with an S.P. 130 sodium chloride prism-grating double monochromator operated under vacuum. Mass spectra were measured on an A.E.I. M.S. 9 spectrometer. ^{1}H n.m.r. spectra were determined on a Perkin-Elmer 60 Mc./sec. instrument, equipped with an integrator. The samples were run in carbon tetrachloride or deuteriochloroform solutions with tetramethylsilane as an internal reference.

Purification of Caryophyllene (1).—Commercial caryophyllene, in light petroleum, was washed several times with dilute aqueous sodium hydroxide and then shaken with saturated aqueous silver nitrate; the organic extract was dried. The extract was concentrated under reduced pressure and absorbed on alumina (Grade I—II). Elution with light petroleum, removal of the solvent, and distillation afforded pure caryophyllene, n_D^{20} 1·4986; b.p. 75—76°/0·14 mm.; $\nu_{max.}$ (liq. film) 3070, 1670, 1635, 890, 825, and 815 cm.$^{-1}$.

R_T on a 20% tris-cyanoethoxypropane (TCEP) column (flow rate 62 ml./min.; temperature 75°), 17 min.; on a 25% Apiezon L (APL) column (flow rate 72 ml./min.; temperature 175°), 14 min.

Acid-catalysed Rearrangement of Caryophyllene.—Concentrated sulphuric acid (36 g.) was added dropwise to anhydrous ether (68 ml.) at 0°. Pure caryophyllene (120 g.) was then added dropwise to this solution at such a rate that the temperature did not rise above 10°. The solution was stirred for 20 hr., and then basified with aqueous sodium hydroxide solution; it was then exhaustively steam distilled. The steam distillate was saturated with brine and thoroughly extracted with ether; the organic extract was dried and subsequent removal of the solvent under reduced pressure yielded an oily solid (88 g.). This material, adsorbed on alumina (Grade H) (2·4 kg.), was eluted with light petroleum to give the crude hydrocarbon rearrangement products (40 g.).

Analytical g.l.c. on the following columns showed two predominant peaks, which represented 90% of the hydrocarbon mixture with clovene having the shorter R_T: 25% APL (flow rate 82 ml./min. temperature 175°), R_T 12·4 and 19·5 min.; 20% TCEP (flow rate 62 ml./min., temperature 75°), R_T 8·2 and 17·3 min.

Preparative G.l.c. Separation of Neoclovene (4).—The Aerograph 'Autoprep' A-700 was adjusted for automatic injection and collection after the conditions for the best separation had been determined manually; these were 20 ft. × $\frac{3}{8}$ in. 10% Ucon Polar column on Chromasorb 60—80 W; helium flow rate 163 ml./min.; injector temperature 197°; detector temp. 186°; collector temp. 158°; column temp. 162°; sample size 100 μl of neat mixture; R_T clovene, 15·5 min., R_T neoclovene, 24 min.

Each sample of neoclovene was checked for purity on an analytical column and the purest samples (*ca.* 99% pure) were combined and distilled (3·9 g.), b.p. 52°/0·03 mm.;

n_D^{20} 1·5088; $[\alpha]_D^{20}$ −72·0° (*c*, 1·78 in $CHCl_3$); $\nu_{max.}$ (liq. film) 3023, 1657, 1383, 1376, 1362, 838, 812, 788, and 771 cm.$^{-1}$; τ 4·91br (1H), 8·41 (3H, *J* 1—2 Hz), 8·80 (3H) and 8·99 (6H). [Found: C, 88·35; H, 11·75%; *M* (mass spectrum), 204. $C_{15}H_{24}$ requires C, 88·15; H, 11·85%; *M*, 204].

Neoclovane (2,6,8,8-*Tetramethyltricyclo*[5,2,2,$0^{1,6}$]*undecane*).—Neoclovene (204 mg.) in ethyl acetate (20 ml.) was hydrogenated in the presence of palladium–charcoal (10%) (50 mg.). At the end of 2 hr., the uptake of hydrogen was 21·5 ml. (*i.e.* 96% of the theoretical). The ethyl acetate solution was filtered through glass paper and the solvent was removed to yield an oil which was distilled to give pure *neoclovane*, b.p. 50°/0·04 mm.; n_D^{20} 1·4973; $\nu_{max.}$ (liq. film) 1382, 1376, 1372, and 1362 cm.$^{-1}$; τ 8·81 (3H), 8·95 (6H) and 9·26 (3H), (d, *J* 6·5 Hz) [Found: C, 87·05; H, 12·6%; *M* (mass spectrum) 206. $C_{15}H_{26}$ requires C, 87·3; H, 12·7%; *M*, 206].

Neoclovan-2,3-*diol* (2,6,8,8-*Tetramethyltricyclo*[5,2,2,$0^{1,6}$]-*undecan*-2,3-*diol*).—Neoclovene (368 mg.), osmium tetroxide (600 mg.), and pyridine (0·36 ml.) were mixed in anhydrous ether (15 ml.) and left overnight at room temperature. A small sample of the osmate–pyridine complex was isolated and crystallised from methylene chloride–ether (1 : 2) as brownish-green needles, m.p. 177—178° (decomp.). Hydrogen sulphide gas was bubbled through the bulk of the osmate complex in ether for ½ hr. The ethereal solution was filtered through glass paper, washed successively with 3N-hydrochloric acid, saturated aqueous sodium hydrogen carbonate solution, and dried. Removal of the solvent yielded a viscous oil which solidified on trituration with light petroleum. Recrystallisation from light petroleum afforded needles of the *diol*, m.p. 90·5—91°; $[\alpha]_D^{22}$ −43·2° (*c*, 1·6 in $CHCl_3$); $\nu_{max.}$ (CCl_4) 3637, 3580, 1384, 1368, 1103, 1072, 1050, and 1028 cm.$^{-1}$; τ 6·30br (1H), 8·75 (6H), 8·91 (3H), and 8·98 (3H) (Found: C, 75·7; H, 10·75. $C_{15}H_{26}O_2$ requires C, 75·6; H, 11·0%).

The *monobrosylate* of the diol was prepared with *p*-bromobenzenesulphonyl chloride in pyridine. The crude product was freed from starting diol by chromatography on silica and crystallised from light petroleum as needles, m.p. 100·5—101·5°; $\nu_{max.}$ (CCl_4) 3610, 1579, 1186, 943, 869, and 750 cm.$^{-1}$ (Found: C, 55·45; H, 6·35. $C_{21}H_{29}BrO_4S$ requires C, 55·15; H, 6·4%).

2-*Hydroxy*-3-*oxoneoclovane* (2-*Hydroxy*-2,6,8,8-*tetramethyltricyclo*[5,2,2,$0^{1,6}$]-*undecan*-3-*one*.—The above diol (50 mg.) was dissolved in acetone (5 ml.) and cooled at 0°. Jones reagent was added dropwise with shaking until a permanent orange colour was obtained. Water (20 ml.) was immediately added and the solution was extracted with light petroleum. The extract was dried and concentrated under reduced pressure; and it was then absorbed on silica (2 gm.). Elution with light petroleum–ether (17 : 3) yielded the pure ketol (29 mg.), $\nu_{max.}$ (CCl_4) 3600, 3480, 1718, and 1100 cm.$^{-1}$.

Hydroboration of Neoclovene.—Redistilled boron trifluoride (1·8 gm.) was added to neoclovene (426 mg.) in anhydrous ether (20 ml.) at 0° under dry nitrogen. A suspension of lithium aluminium hydride (400 mg.) in anhydrous ether (40 ml.) was slowly added with stirring. After 3·5 hr. at room temperature acetone (AnalaR) (2 ml.) was added to destroy the excess of hydride, followed by 3N-sodium hydroxide (2 ml.) and 30% hydrogen peroxide (2 ml.). The solution was stirred for a further 1 hr. and then extracted with ether. The ethereal extract was washed with brine and aqueous ferrous sulphate and then dried. Removal of the solvent under reduced pressure yielded a viscous oil (481 mg.).

T.l.c. [light petroleum–ethyl acetate (17 : 3)] indicated two spots, corresponding to the two epimeric alcohols (30) and (31); R_F (31) = 0·43; R_F (30) = 0·25.

G.l.c. analysis on a 10% 20 M Carbowax column (temp. 175°; flow rate 50 ml./min.) indicated R_T (31) 19·2 min. and R_T (30) 17·5 min. [ratio of (31) : (30), 43 : 57].

The two alcohols were separated by preparative t.l.c. employing the same solvent as above. Alcohol (31) had m.p. 143—144°; $\nu_{max.}$ (CCl_4) 3620, 1122, and 1010 cm.$^{-1}$; τ 6·12 (1H) ($w_{\frac{1}{2}}$ 5 Hz), 8·81 (3H), 8·82 (3H), 8·96 (3H) and 9·09 (3H) (d, *J* 7·5 Hz) (Found: C, 80·8; H, 11·65. $C_{15}H_{26}O$ requires C, 81·0; H, 11·8%). Alcohol (30) had m.p. 71—72°; $\nu_{max.}$ (CCl_4) 3620, 1143, 1120, and 1020 cm.$^{-1}$; τ 6·44 (1H) (six-line multiplet, $w_{\frac{1}{2}}$ 15 Hz, X part of an A_2BX system), 8·83 (3H), 8·87 (3H), 9·00 (3H), and 9·10 (3H), (d, *J* 6 Hz) (Found: C, 80·85; H, 11·75. $C_{15}H_{26}O$ requires C, 81·0; H, 11·8%).

Ketone (32) [2(eq.),6,8,8-*Tetramethyltricyclo*[5,2,2,$0^{1,6}$]-*undecan*-3-*one*].—The alcohol (30) (25 mg.) was dissolved in acetone (5 ml.) and cooled to 0°. Jones reagent was added dropwise with stirring until a permanent orange colour was obtained. Water (10 ml.) was added and the solution was extracted with light petroleum. The organic extract was dried and the solvent was removed under reduced pressure to yield an oil (21 mg.) which was purified by microdistillation (block temperature 135°/0·2 mm.); $\nu_{max.}$ (CCl_4) 1712, 1422, 1385, 1380, 1369, and 1364 cm.$^{-1}$; o.r.d. (*c* 1·04 in MeOH): $[\Phi]_{400}$ −460°, $[\Phi]_{307}$ −3140°, $[\Phi]_{269}$ +1880°, and $[\Phi]_{222}$ −1250°. [Found: C, 81·4; H, 10·6; *M* (mass spectrum), 220. $C_{15}H_{24}O$ requires C, 81·75; H, 11·0%; *M*, 220]. T.l.c. [light petroleum–ethyl acetate (9 : 1)] indicated one spot, R_F 0·46. G.l.c. analysis on a 10% 20 M Carbowax column (temp. 150° flow rate 33 ml./min.) showed one homogeneous peak, R_T 28·7 min.

Ketone (33) [2(ax.),6,8,8-*Tetramethyltricyclo*[5,2,2,$0^{1,6}$]-*undecan*-3-*one*].—A small sample of this ketone was prepared by Jones oxidation of the alcohol (31) as described above for ketone (32), $\nu_{max.}$ (CCl_4) 1714, 1420, 1386, 1378, 1367, and 1361 cm.$^{-1}$; o.r.d. (*c*, 3·17 in MeOH): $[\Phi]_{500}$ −155°, $[\Phi]_{400}$ −230°, $[\Phi]_{310}$ −655°, $[\Phi]_{287}$ −555°, and $[\Phi]_{223}$ −2440° [Found: C, 81·45; H, 10·75; *M* (mass spectrum), 220. $C_{15}H_{24}O$ requires C, 81·75; H, 11·0%; *M*, 220]. T.l.c. [light petroleum–ethyl acetate (9 : 1)] indicated one spot, R_F 0·42. G.l.c. analysis on a 10% 20 M Carbowax column (temp. 150°; flow rate 33 ml./min.) showed one homogeneous peak R_T 30·3 min.

A small sample of each ketone (*ca.* 10 mg.) was separately heated under reflux in methanol containing sodium hydroxide (25 mg.). The methanol was removed under reduced pressure and the residue was extracted with ether. Both t.l.c. and g.l.c. under identical conditions (see above) identified both products as ketone (32).

12-*Acetoxyneoclovene*(2-*Acetoxymethyl*-6,8,8-*trimethyltricyclo*[5,2,2,$0^{1,6}$]*undec*-2-*ene*).—Neoclovene (214 mg.) was heated under reflux with a suspension of selenium dioxide (132 mg.) in glacial acetic acid (2·5 ml.) and acetic anhydride (2·5 ml.) for 2 hr. The solution was cooled and diluted with light petroleum (50 ml.); it was then filtered into a saturated brine solution. The light petroleum extract was thoroughly washed with saturated aqueous sodium hydrogen carbonate solution, and then dried; the solvent was removed to leave a dark-red oil. Filtration through an alumina–silver column (1 : 1) removed some of the colloidal selenium. Adsorption on silica (10 gm.) and elution with light petroleum–ether (19 : 1) yielded the pure acetate (174 mg.) as an oil, ν(C=O) (liq. film) 1740 cm.$^{-1}$.

12-*Hydroxyneoclovene* (11) (2-*Hydroxymethyl*-6,8,8-*trimethyltricyclo*[5,2,2,0^{1,6}]*undec-2-ene*).—The above acetate (174 mg.) was heated under reflux in methanol (10 ml.) with sodium hydroxide (200 mg.) for 2·5 hr. The methanol was removed under reduced pressure and brine was added to the residue; the mixture was then extracted with ether. The extract was dried and the solvent was removed under reduced pressure to yield the crystalline alcohol (143 mg.), which was purified by sublimation, m.p. 90·5—91·5°; $\nu_{max.}$ (CCl_4) 3605, 1055, and 1000 cm.$^{-1}$; τ 4·63br (1H), 6·09 (2H), 8·80 (3H), 8·96 (3H), and 9·01 (3H).

12-*Oxoneoclovene* (12) (2-*Formyl*-6,8,8-*trimethyltricyclo*-[5,2,2,0^{1,6}]*undec-2-ene*). The above alcohol (35 mg.) dissolved in chloroform (10 ml.) was shaken for 22 hr. with neutral manganese dioxide (600 mg.). The solution was filtered through Celite and solvent was removed from the filtrate to yield an oil; this was freed from starting alcohol by elution from silica (1 g.) with light petroleum–ether (19 : 1) (26 mg.), $\nu_{max.}$ (CCl_4) 2800, 2710, 1692, and 1620 cm.$^{-1}$; τ 0·66 (1H), 3·54 (1H), (t, 4 Hz), 8·79 (3H), 8·90 (3H) and 9·00 (3H); $\lambda_{max.}$ 237 mμ (ε 12,000). The corresponding 2,4-dinitrophenylhydrazone crystallised from methanol–chloroform (5 : 1) as fine needles, m.p. 260·5—261·5°.

Allylic Bromination of Neoclovene.—Neoclovene (210 mg.) was heated under reflux with *N*-bromosuccinimide (188 mg.) in dry carbon tetrachloride (10 ml.) containing a catalytic amount of dibenzoyl peroxide (5 mg.) for 2 hr. The precipitate of succinimide was filtered off and the carbon tetrachloride filtrate was evaporated under reduced pressure. Collidine (5 ml.) was added to the residual oil which was warmed on a steam-bath for 15 min. The solution was diluted with light petroleum and washed with 6N-hydrochloric acid and aqueous sodium hydrogen carbonate solution. The organic extract was dried and the solvent was removed to yield an oil (150 mg.); $\nu_{max.}$ (liq. film) 1640, 1600, 890, 780, 750, 730, and 695 cm.$^{-1}$; $\lambda_{max.}$ 232 and *ca.* 260sh mμ. The ^{1}H n.m.r. spectrum showed numerous peaks in the τ 4—5 region and a distinct doublet at τ 5·2 and 5·34.

G.l.c. analysis on a 25% APL column (temp. 175°; flow rate 80 ml./min.) indicated two peaks R_T, 10·8 and 15·6 min. respectively in an approximate ratio of 1 : 15.

Dehydration of 12-*Hydroxyneoclovene*.—The alcohol (10 mg.) was heated under reflux in acetone (5 ml.) with toluene-*p*-sulphonic acid (10 mg.) for 12 hr. The acetone solution was diluted with water and thoroughly extracted with light petroleum. The organic extract was washed successively with brine and aqueous sodium hydrogen carbonate solution and then dried. Removal of the solvent yielded an oil (9 mg.); $\nu_{max.}$ (liq. film) 1635, 1600, 890, 785, and 735 cm.$^{-1}$; $\lambda_{max.}$ 232 mμ. The ^{1}H n.m.r. spectrum showed a multiplet in the τ 4·0—4·4 region and a doublet at τ 5·2 and 5·34.

Keto-aldehyde (5) [1-*Acetyl*-3,3,7-*trimethyl*-7-(3-*oxopropyl*)*bicyclo*[2,2,1]*heptane*].—Neoclovan-2,3-diol (140 mg.) in AnalaR methanol (10 ml.) was added to a stirred solution of sodium metaperiodate (1 g.) in water (9 ml.) at room temperature; more methanol (2 ml.) was then added until the solution was homogeneous. After 2·5 hr., the aqueous methanolic solution was thoroughly extracted with ether, and the organic extract was washed with saturated brine and dried. Removal of the solvent under reduced pressure yielded an oil (150 mg.) which was purified by preparative t.l.c. [solvent system: light petroleum–ethyl acetate (7 : 3)], and micro-distillation afforded the *keto-aldehyde* (5) as a clear, mobile oil (block temperature 120°/0·18 mm.); $[\alpha]_D^{20}$ −51·2° (*c*, 1·5 in $CHCl_3$); $\nu_{max.}$ (CCl_4) 2805, 2708, 1729, 1702, 1692, 1384, 1378, and 1352 cm.$^{-1}$; τ 0·20 (1H, t, *J* 2·5 Hz), 7·98 (3H), 8·75 (3H), 8·84 (3H) and 8·96 (3H) (Found: C, 75·45; H, 10·0. $C_{15}H_{24}O_2$ requires C, 76·25; H, 10·25%).

The keto-aldehyde was unstable, undergoing aerial oxidation to the corresponding keto-acid. This would explain the relatively poor analysis.

Keto-acid (6; R=H)(1-*Acetyl*-7-(2-*carboxyethyl*)-3,3,7-*trimethylbicyclo*[2,2,1]*heptane*).—The keto-aldehyde (5) (50 mg.) in acetone (3 ml.) was treated with Jones reagent. Work up afforded the crystalline *keto-acid* (52 mg.). Recrystallisation from light petroleum gave an analytical sample of the keto-acid as needles, m.p. 97·5—98·5°; $[\alpha]_D^{20}$ −52·5° (*c*, 1·96 in $CHCl_3$); $\nu_{max.}$ (CCl_4) 3535, 1756, 1707, 1695sh, 1384, 1370, and 1352 cm.$^{-1}$; τ −1·81 (1H), 7·97 (3H), 8·72 (3H), 8·81 (3H), and 8·93 (3H) [Found: C, 71·05; H, 9·4%; *M* (mass spectrum), 252. $C_{15}H_{24}O_3$ requires C, 71·4; H, 9·6%; *M*, 252].

Keto-acid (6; R=H) *from Oxidation of Crude Clovene*.—To crude clovene (50 gm.) in AnalaR acetic acid (804 ml.) was added chromium trioxide (70 gm.) in AnalaR acetic acid (402 ml.) and water (40 ml.) dropwise with cooling, such that the temperature did not rise above 30°. This mixture was set aside at room temperature for 82 hr., after which time the acetic acid was removed under reduced pressure on a steam-bath. Water was added to the dark-green residue and the aqueous solution was thoroughly extracted with light petroleum (b.p. 60—80°). The organic extract was washed with 4N-sodium hydroxide solution to remove the acidic material. The alkaline extract was acidified with concentrated hydrochloric acid and thoroughly extracted with light petroleum (b.p. 60—80°). The organic extract was dried and the solvent removed under reduced pressure to yield a viscous oil, which was treated with ethereal diazomethane.

The crude keto-ester (13·1 g.) was adsorbed on silica (250 g.) and elution with light petroleum–ether (7 : 3) afforded fairly pure keto-ester (7·4 g.). The keto-ester (7·4 g.) was heated under reflux for 3 hr. in methanol (130 ml.) containing sodium hydroxide (9 gm.). The methanol was removed under reduced pressure and the residue was dissolved in water, which was then extracted with ether. The aqueous alkaline solution was acidified with hydrochloric acid and thoroughly extracted with ether. The ethereal extract was dried and the solvent was removed to yield a viscous oil (6 g.), which crystallised on trituration with light petroleum. Recrystallisation from light petroleum afforded the pure keto-acid (6; R = H), m.p. 98—99°, which was undepressed on admixture with a sample of (6; R = H) previously prepared from pure neoclovene.

The corresponding keto-ester (6; R = Me) was obtained by treating the pure keto-acid with ethereal diazomethane. Micro-distillation afforded a pure sample of the *keto-ester* as an oil (block temp. 130°/0·2 mm.), $[\alpha]_D^{20}$ −48·2° (*c*, 2·0 in $CHCl_3$); τ 6·39 (3H), 8·01 (3H), 8·76 (3H), 8·84 (3H), and 8·96 (3H) [Found: C, 71·85; H, 9·85%; *M* (mass spectrum), 266. $C_{16}H_{26}O_3$ requires C, 72·15; H, 9·85%; *M*, 266].

G.l.c. analysis of the keto-esters derived from the two keto-acids (*vide supra*) showed one homogeneous peak on a 10% 20 M Carbowax column (temp. 175°; flow rate 63 ml./min.), R_T 27 min.

Acetoxy-ester (7; $R^1 = Me$, $R^2 = Ac$) (1-*Acetoxy*-3,3,7-*trimethyl*-7-(2-*methoxycarbonylethyl*)*bicyclo*[2,2,1]*heptane*).—A solution of trifluoroperacetic acid was prepared[6] by dropwise addition of trifluoroacetic anhydride (6·35 ml.) to a stirred suspension of 99% hydrogen peroxide (1·05 ml.) in dry methylene chloride (7 ml.) at 0°. This solution was stored at 0° for 4 hr.

To a dry methylene chloride (9 ml.) solution of the pure keto-ester (6; R = Me) (323 mg.), containing dry, finely ground disodium hydrogen phosphate (1 g.) was added the solution of trifluoroperacetic acid (9 ml.) dropwise with stirring. The solution was set aside at room temperature for 21 hr. The inorganic salts were dissolved in water and the solution was extracted with methylene chloride; the extract was washed with 10% aqueous sodium hydrogen carbonate and then dried. The solvent was removed under reduced pressure to yield an oil (344 mg.).

Elution from silica (15 gm.) with light petroleum–ether (9 : 1) and micro-distillation (block temp. 132°/0·15 mm.) afforded a pure sample of the *acetoxy-ester* (251 mg.) (73%); $\nu_{max.}$ (CCl_4) 1741, 1434, 1384, 1379, 1365, and 1243 cm.$^{-1}$; τ 6·36 (3H), 8·05 (3H), 8·81 (3H), 8·87 (3H), and 8·93 (3H) (Found: C, 67·05; H, 9·1. $C_{16}H_{26}O_4$ requires C, 67·05; H, 9·3%).

δ-*Lactone* (9) *from* (2-*Carboxyethyl*)-1-*hydroxy*-3,3,7-*trimethyl*-7-*bicyclo*[2,2,1]*heptane*.—The pure acetoxy-ester (7; $R^1 = Me$; $R^2 = OAc$) (251 mg.) in methanol (15 ml.) containing sodium hydroxide (400 mg.) was heated under reflux for 2·5 hr. The methanol was removed under reduced pressure and the residue was dissolved in water. The aqueous alkaline solution was extracted with ether and then acidified. The aqueous acidic solution was extracted with ether and the extract was dried; careful removal of the solvent yielded the crystalline *hydroxy-acid* (7; $R^1 = H$, $R^2 = OH$).

The hydroxy-acid (34 mg.) was heated in a sublimation tube for 2 hr. at atmospheric pressure. The δ-lactone was then sublimed under reduced pressure and crystallised from light petroleum, m.p. 80·5—81·5°. The lactone resublimed, for analysis, as needles, m.p. 60—60·5°. This lower-melting compound was identical (i.r. spectrum and t.l.c.) with the higher melting δ-lactone; $\nu_{max.}$ (CCl_4) 1745, 1386, and 1365 cm.$^{-1}$; τ 8·73 (6H) and 8·89 (3H) (Found: C, 75·1; H, 9·4. $C_{13}H_{20}O_2$ requires C, 74·95; H, 9·7%).

Treatment of the hydroxy-acid (7; $R^1 = H$; $R^2 = OH$) with ethereal diazomethane and elution from silica with light petroleum–ether (7 : 3) afforded the pure *hydroxy-ester* as a low-melting solid which crystallised from light petroleum as needles, m.p. 46—47°; $\nu_{max.}$ (CCl_4) 3613, 1741, 1434, 1383, and 1378 cm.$^{-1}$; τ 6·35 (3H), 8·88 (6H) and 9·00 (3H) (Found: C, 69·7; H, 10·2. $C_{14}H_{24}O_3$ requires C, 69·95; H, 10·05%).

Diphenylene-acetate (13) (1-*Acetoxy*-3,3,7-*trimethyl*-7-(3,3-*diphenylallyl*)*bicyclo*[2,2,1]*heptane*).—A solution of the pure hydroxy-ester (7; $R^1 = Me$; $R^2 = OH$) (650 mg.) in dry ether (15 ml.) was added dropwise to a solution of an excess of phenylmagnesium bromide, prepared from magnesium (600 mg.) and redistilled bromobenzene (4 gm.). The reaction mixture was heated under reflux for 2 hr. and then the Grignard complex was decomposed with saturated aqueous ammonium chloride (50 ml.). The resultant mixture was thoroughly extracted with ether and brine; the organic extract was dried and the solvent was removed to yield a crystalline solid, which was not purified.

The crude hydroxy-diphenylcarbinol was heated under reflux in acetic anhydride (20 ml.) and acetic acid (10 ml.) for 3 hr. The acetic anhydride and acetic acid were removed under reduced pressure and the residue was diluted with brine. The aqueous solution was extracted with ether and the organic extract was washed with aqueous hydrogen carbonate; the extract was then dried and the solvent was removed to yield a viscous oil (1·32 g.).

The crude diphenylene-acetate was freed from impurities (*e.g.* biphenyl) by elution from silica (40 g.) with light petroleum–ether (24 : 1) (880 mg.) (83%). Neither trituration with various organic solvents nor sublimation induced the diphenylene-acetate to crystallise; $\nu_{max.}$ (CCl_4) 1742, 1599, 1576, 1494, 1464, 1443, 1365, 1243, 1074, and 700 cm.$^{-1}$; $\nu_{max.}$ (liq. film) 760 cm.$^{-1}$; τ 2·84 (10H), 3·89 (1H, t, J 7·5 Hz), 8·14 (3H), 8·78 (3H), 8·83 (3H), and 8·98 (3H); $\lambda_{max.}$ 252 mμ (ϵ, 18,500).

Hydroxy-ester (15; $R^1 = Me$; $R^2 = OH$)(1-*Hydroxy*-3,3,7-*trimethyl*-7-*methoxycarbonylmethylbicyclo*[2,2,1]*heptane*).—The diphenylene-acetate (13) (1 g.) in AnalaR acetone (50 ml.) was added to sodium metaperiodate (1 g.) in distilled water (20 ml.). To this stirred solution was added ruthenium tetroxide (250 mg.) in a minimum volume of acetone. Immediately the ruthenium tetroxide had been added, a black precipitate of ruthenium dioxide was formed, whereupon more sodium metaperiodate (1·5 g.) was added. A further quantity (4·5 g.) of sodium metaperiodate was added during the next 24 hr.; finally, isopropyl alcohol (10 ml.) was added to destroy the excess of ruthenium tetroxide. The solution was filtered through glass paper and the precipitate was washed with acetone and ether. The filtrate was concentrated under reduced pressure and constant ether-extracted for 70 hours to yield a viscous oil. The oil was dissolved in ether and the ethereal solution was washed with 2N-sodium hydroxide solution. The aqueous alkaline extract was acidified and thoroughly extracted with brine and ether. The ethereal solution was dried and removal of the solvent yielded a viscous oil (701 mg.).

This crude product was heated under reflux for 3 hr. in methanol (45 ml.) containing sodium hydroxide (1·2 g.). The methanol was removed under reduced pressure and the residue was dissolved in water and extracted with ether. The aqueous alkaline extract was acidified with 6N-hydrochloric acid and thoroughly extracted with ether. The ethereal extract was dried and the solvent was removed to yield the crude hydroxy-acid, which was esterified with ethereal diazomethane.

The crude ester was adsorbed on silica (30 g.) and elution with light petroleum–ether (13 : 7) gave the pure *hydroxy-ester* (15; $R^1 = Me$; $R^2 = OH$) as a mobile oil (400 mg.) (70%); $\nu_{max.}$ (CCl_4) 3618, 3470, 1740, and 1719 cm.$^{-1}$; τ 6·35 (3H), 7·58 (2H, CH_2CO_2Me), 8·83 (6H), and 8·98 (3H) (Found: C, 68·75; H, 9·7. $C_{13}H_{22}O_3$ requires C, 69·0; H, 9·8%).

Nor-diphenylene-acetate (16) [1-*Acetoxy*-3,3,7-*trimethyl*-7-(2,2-*diphenylvinyl*)*bicyclo*[2,2,1]*heptane*].—A solution of the pure hydroxy ester (15; $R^1 = Me$; $R^2 = OH$) (400 mg.) in anhydrous ether (15 ml.) was added to a stirred ethereal solution of an excess of phenylmagnesium bromide [prepared from magnesium (400 mg.) and redistilled bromobenzene (2·6 gm.)]. The reaction mixture was heated under reflux for 4 hr. and then the Grignard complex was decomposed with saturated aqueous ammonium chloride (50 ml.). The resultant mixture was thoroughly extracted with ether and the ethereal extract was dried; solvent was removed to yield an oil.

The crude hydroxy-nor-diphenylcarbinol was heated under reflux in acetic anhydride (14 ml.) and acetic acid (7 ml.) for 3·5 hr. Most of the acetic anhydride and acetic acid was removed under reduced pressure and the residue was diluted with brine. The aqueous solution was extracted with ether and the organic extract was washed with aqueous sodium hydrogen carbonate solution; the extract was then dried and the solvent was removed to yield an oily solid (600 mg.).

The crude product was adsorbed on silica (30 g.) and elution with light petroleum–ether (97 : 3) afforded the pure crystalline-*nor-diphenylene-acetate* (16). Recrystallisation from ether gave an analytical sample, m.p. 182—182·5°; $\nu_{max.}$ (CCl_4) 1741, 1599, 1573, 1495, 1460, 1442, 1364, 1244, 1072, and 695 cm.$^{-1}$; τ 2·76 (10H), 3·62 (1H), 7·94 (3H), 8·65 (3H), 9·06 (3H), and 9·13 (3H); $\lambda_{max.}$ 251 mμ (ε 17,400) (Found: C, 83·1; H, 8·25. $C_{26}H_{30}O_2$ requires C, 83·40; H, 8·05%).

Bis-nor-hydroxy-ester (17; R = CO_2Me) (7-*Methoxycarbonyl*-3,3,7-*trimethylbicyclo*[2,2,1]*heptan*-1-*ol*).—The nor-diphenylene-acetate (16) (994 mg.) in AnalaR acetone (100 ml.) was added to a stirred 5% aqueous solution of sodium metaperiodate (25 ml.) containing ruthenium dioxide (300 mg.). The reaction mixture was stirred for 24 hr. with the further addition of solid sodium metaperiodate (3 g.). Isopropyl alcohol (3 ml.) was added to destroy the excess of ruthenium tetroxide. The work-up procedure described for the diphenylene acetate (13) was then carried out to yield a viscous oil (697 mg.).

The crude bis-nor-hydroxy-acid was then esterified with ethereal diazomethane and elution from silica (20 g.) with light petroleum–ether (4 : 1) gave the pure *bis-nor-hydroxy-ester* (17; R = CO_2Me) as an oil (500 mg.) (88%); $\nu_{max.}$ (liq. film) 3550 and 1720 cm.$^{-1}$; τ 6·31 (3H), 8·64 (3H), 8·83 (3H), and 9·00 (3H) (Found: C, 66·85; H, 9·45. $C_{12}H_{20}O_3$ requires C, 67·9; H, 9·5%).

Primary–Tertiary Diol (17; R = $CH_2\cdot OH$) (7-*Hydroxymethyl*-3,3,7-*trimethylbicyclo*[2,2,1]*heptan*-1-*ol*.—The pure bis-nor-hydroxy-ester (17; R = CO_2Me) (500 mg.) in anhydrous ether (30 ml.) was slowly added to a stirred suspension of lithium aluminium hydride (2·6 g.) in anhydrous ether (70 ml.), under dry nitrogen. The solution was heated under reflux for 4 hr. after which the excess of hydride was destroyed by careful addition of a saturated solution of ammonium sulphate (50 ml.). The mixture was thoroughly extracted with ether and the ethereal extract was dried; the solvent was removed under reduced pressure to yield a crystalline solid (447 mg.). Recrystallisation from light petroleum (b.p. 60—80°) afforded a pure sample of the *diol*, m.p. 108—108·5°; $\nu_{max.}$ (CCl_4) 3640, 3614, 3553, 3400, 1385, 1379, 1364, 1088, 1023, and 1010 cm.$^{-1}$; τ ($CDCl_3$–D_2O) 5·95 and 6·36 (2H, AB quartet, J 11·5 Hz), 8·66 (3H), 8·81 (3H), and 8·98 (3H) (Found: C, 71·5; H, 10·8. $C_{11}H_{20}O_2$ requires C, 71·7; H, 10·95%).

The diol was converted into the primary mono-tosylate as follows. To the diol (360 mg.) in dry pyridine (2·4 ml.) was added toluene-*p*-sulphonyl chloride (600 mg.) and a few drops of ether. The solution was warmed briefly and was then set at room temperature for 22 hr. Brine was added to the solution which was then extracted with ether. The ethereal extract was washed successively with N-hydrochloric acid and aqueous sodium hydrogen carbonate solution; it was then dried and the solvent was removed under reduced pressure to yield a viscous oil (650 mg.).

The hydroxy-tosylate failed to crystallise even after preparative t.l.c. purification, $\nu_{max.}$ (liq. film) 3550, 1600, 1180, 1100, 970, 870, and 820 cm.$^{-1}$.

4-*Isopropenyl*-3,3-*dimethyl-cyclohexanone*.—A mineral oil suspension of sodium hydride (320 mg.) was washed three times with dry light petroleum under dry, oxygen-free nitrogen. Dry, redistilled dimethyl sulphoxide (9·2 ml.) was then added with a syringe to the amorphous sodium hydride under dry, oxygen-free nitrogen. The solution was stirred at 66—67° for 45 min. (until the evolution of hydrogen was complete). The solution of dimsyl sodium was cooled to room temperature and the hydroxy-tosylate (17; R = CH_2OTs) (640 mg.) in dry dimethyl sulphoxide (12 ml.) was then added with a syringe; the solution was then stirred at room temperature for 2·5 hr. With external cooling, brine (15 ml.) was added dropwise and the mixture was diluted with additional brine (100 ml.). The aqueous solution was extracted with light petroleum–ether (1 : 2) and the organic layer was washed with brine (50 ml.); it was then dried and the solvent was carefully removed under reduced pressure to yield a sweet-smelling, volatile oil (271 mg.). Elution from silica (10 g.) with light petroleum–ether (9 : 1) afforded the pure *unsaturated ketone* (250 mg.) (78%); $\nu_{max.}$ (CCl_4) 3080, 1720, 1640, 1420, 1386, 1375, 1367, and 897 cm.$^{-1}$; τ 5·04 (1H) ($w_{\frac{1}{2}}$ 4 Hz), 5·23 (1H, $w_{\frac{1}{2}}$ 3 Hz), 8·19 (3H, d, J *ca.* 1 Hz), 8·98 (3H), and 9·10 (3H). [M (mass spectrum), 166. $C_{11}H_{18}O$ requires M, 166]. G.l.c. analysis on a 10% 20 M Carbowax column (temperature 125°; flow rate 60 ml./min.) indicated one peak, R_T 6·77 min.

4-*Isopropyl*-3,3-*dimethyl-cyclohexanone* (20).—4-Isopropenyl-3,3-dimethyl-cyclohexanone (230 mg.) in AnalaR ethyl acetate (25 ml.) was hydrogenated in the presence of palladium–charcoal (10%) (270 mg.). At the end of 8 hr., an aliquot was removed and analysed by g.l.c., which indicated that the hydrogenation had gone to completion. The bulk of the hydrogenation product was filtered through glass paper and the solvent was carefully removed under reduced pressure to yield a sweet-smelling, volatile oil. A pure sample of the *ketone* was obtained by microdistillation (block temp. 85°/0·8 mm.) as an oil (217 mg.), m.p. *ca.* 5°; $[\alpha]_D^{20}$ + 29·3° (*c*, 2·0 in $CHCl_3$); $\nu_{max.}$ (CCl_4) 1718, 1429, 1419, 1386, and 1368 cm.$^{-1}$; τ 7·7—8·0 (4H), 8·94 (3H), 8·99 (3H, d, J 7 Hz), 9·14 (3H), and 9·16 (3H, d, J 7 Hz); o.r.d. (*c*, 2·85 in MeOH): $[\Phi]_{500}$ +65°, $[\Phi]_{400}$ +110°, $[\Phi]_{305}$ +930°, $[\Phi]_{265}$ −725°, and $[\Phi]_{234}$ −225°; [M (mass spectrum), 168·1509 ± 3 p.p.m. $C_{11}H_{20}O$ requires 168·1514].

G.l.c. analysis on a 10% 20 M Carbowax column (temp. 125°; flow rate 45 ml./min.) indicated one homogeneous peak, R_T 7·12 min.

The corresponding 2,4-*dinitrophenylhydrazone* crystallised from methanol as prisms, m.p. 131—132° (Found: C, 58·9; H, 6·7; N, 16·4. $C_{17}H_{24}N_4O_4$ requires C, 58·6; H, 6·95; N, 16·1%).

Acetal of 4-*Isopropyl*-3,3-*dimethyl-cyclohexanone*.—The ketone (58) (64 mg.) in anhydrous benzene (14 ml.) containing redistilled ethylene glycol (71 mg.) and toluene-*p*-sulphonic acid (7 mg.) was heated under reflux in a micro-Dean and Stark apparatus for 20 hr. The benzene solution was washed with half-saturated sodium hydrogen carbonate solution and the solvent was carefully removed under reduced pressure to yield a viscous oil (70 mg.).

The acetal was freed from starting ketone by preparative t.l.c. Microdistillation afforded a pure sample of the *acetal* as a viscous oil (block temp. 100°/0·2 mm.); $\nu_{max.}$ (liq. film) 1390, 1370, 1172, 1152, 1100, 1048, and 1025 cm.$^{-1}$

[*M* (mass spectrum), 212. $C_{13}H_{24}O_2$ requires *M*, 212). The detailed mass spectrum of the acetal was as follows, *m*/*e* (% abundance): 39 (6·4), 40 (2·0), 41 (26·2), 42 (7·9), 43 (9·9), 45 (2·0), 53 (4·4), 55 (21·0), 56 (4·9), 57 (2·5), 67 (4·9), 69 (11·1), 77 (2·0), 79 (2·2), 81 (3·0), 83 (8·9), 84 (3·0), 86 (24·7), 87 (4·9), 99 (100·0), 100 (6·4), 113 (8·6), 127 (56·8), 128 (4·7), 155 (11·6), 167 (9·9), 168 (4·9), 197 (9·9), 212 (9·9), 213 (1·4).

4-Methoxy-2-methyl-acetophenone.—This compound was prepared from *m*-methylanisole in good yield (80%) according to the procedure of Noller and Adams[17] as a pale yellow oil, b.p. 182—186°/12 mm.; $\nu_{max.}$ (liq. film) 2840, 1675, 1610, 1570, 1510, and 1260 cm.$^{-1}$; τ 2·32 (1H, d, *J* 9·6 Hz), 3·31 (2H, m, 6·24 (3H, OCH_3), 7·51 (3H, ArCH_3), and 7·59 (3H, CH_3–C=O).

*2-(4-Methoxy-*o*-tolyl)isopropyl Alcohol*.—4-Methoxy-2-methyl-acetophenone (32·8 g.) in anhydrous ether (100 ml.) was slowly added with stirring to methylmagnesium iodide (48·3 g.). The solution was heated under reflux for 2·5 hr. and the Grignard complex was decomposed with saturated ammonium chloride solution. The mixture was extracted with ether and the organic extract was dried; the solvent was removed to give a quantitative yield of the liquid alcohol which was not further purified.

2-Isopropenyl-5-methoxytoluene (26).—The above alcohol (36 gm.) was heated under reflux in acetic anhydride (200 ml.) for 4 hr. The acetic anhydride was removed under reduced pressure and the residual oil was taken up in ether. The ethereal solution was thoroughly washed with saturated sodium carbonate solution, dried, and the solvent removed to yield an oil which was distilled, b.p. 66—68°/1 mm. (23·1 g.); n_D^{20} 1·5264; $\nu_{max.}$ (liq. film) 3075, 2850, 1640, 1610, 1575, 1510, 1240, 900, and 820 cm.$^{-1}$; τ 3·03 (1H, d, *J* 9·5 Hz), 3·35—3·43 (2H, m), 4·85br (1H), 5·19br (1H), 6·31 (3H, OCH_3), 7·73 (3H, ArCH_3), and 8·00 (3H, barely resolved quartet, *J ca.* 2 Hz, CH_3–C=CH_2).

2-Isopropyl-5-methoxytoluene.—The above olefin (12·16 gm.) in AnalaR ethyl acetate (355 ml.) was hydrogenated in the presence of palladium–charcoal (10%) (2·45 g.). After 3 min. the theoretical uptake of hydrogen was complete (1660 ml.). The ethyl acetate solution was filtered through glass paper and the solvent was removed under reduced pressure. Distillation gave a pure sample as an oil, b.p. 55—56°/0·6 mm.; n_D^{20} 1·5090; $\nu_{max.}$ (liq. film) 1615, 1580, 1510, 1255, and 820 cm.$^{-1}$; τ 2·87 (1H, d, *J* 9·5 Hz), 3·28 (2H, m), 6·43 (3H, OCH_3), 6·98 (1H, septet, *J* 7 Hz), 7·76 (3H, ArCH_3), and 8·83 (6H, d, *J* 7 Hz).

4-Isopropyl-3-methyl-cyclohex-2-enone (27).—The above methyl ether (2·36 gm.) in anhydrous ether (15 ml.) was added to liquid ammonia (300 ml.). With vigorous stirring, under oxygen-free, dry nitrogen, small pieces of lithium (4·4 g.) were then added during 15 min. to the solution; the mixture was stirred for a further 2 hr. Isopropyl alcohol was then added until the lithium bronze was destroyed. The reaction flask was warmed on a water-bath (70°) to remove most of the ammonia and then ice was slowly added to the stirred solution until all the lithium isopropoxide was dissolved. The reaction mixture was extracted with light petroleum, the organic layer washed with half-saturated brine, dried, and the solvent removed to yield a pale yellow oil (2·26 g.) (95%); $\nu_{max.}$ (liq. film) 2850, 1695, 1665, 1210, and 800 cm.$^{-1}$.

This dihydro-derivative in AnalaR methanol (110 ml.) was warmed to 60° and 3N-hydrochloric acid (75 ml.) was added to the stirred solution. The solution was stirred at this temperature for 30 min. and then poured into half-saturated brine (200 ml.). The aqueous methanol solution was extracted with light petroleum and the organic extract was washed successively with half-saturated brine (100 ml.) and saturated sodium hydrogen carbonate solution (200 ml.); the solution was dried and the solvent was removed under reduced pressure to yield an oil (1·72 g.) (87%).

T.l.c. examination revealed the presence of one predominant spot, R_F 0·21 and a minor component, R_F 0·36 [solvent system: light petroleum–ethyl acetate (17 : 3)].

The less-polar, minor component was eluted from silica (70 g.) with light petroleum–ether (17 : 3) and was shown by t.l.c., g.l.c., and i.r. spectrum to be identical with an authentic sample of 6-isopropyl-3-methylcyclohex-2-enone. The major component was eluted with the same solvent system (4 : 1) and distilled to yield a pure sample of 4-isopropyl-3-methylcyclohex-2-eneone, b.p. 62—63°/0·4 mm.; $\nu_{max.}$ (liq. film) 3020, 1675, 1620, 1420, and 870 cm.$^{-1}$; τ 4·23 (1H, q, *J* 1·5 Hz), 8·07 (3H, d, *J* 1·5 Hz), 8·96 (3H, d, *J* 6·5 Hz), and 9·18 (3H, d, *J* 6·5 Hz); $\lambda_{max.}$ 238 mμ (ε 15,570).

G.l.c. analysis on a 10% 20 M Carbowax column (temp. 100°; flow rate 60 ml./min.) indicated one peak, R_T 33·3 min. and a small impurity (*ca.* 5%) of 6-isopropyl-3-methylcyclohex-2-enone, R_T 19 min.

*Racemic 4-Isopropyl-*3,3*-dimethyl-cyclohexanone* (20).—To a stirred solution of methylmagnesium iodide at 0° [prepared from magnesium (640 mg.) and redistilled methyl iodide (3·87 g.)] was added, dropwise, the unsaturated ketone (304 mg.) and cupric acetate monohydrate (88 mg.) in dry tetrahydrofuran (21 ml.) under an atmosphere of oxygen-free, dry nitrogen. The resultant suspension was stirred for a further 3 hr. at 0° and then at room temperature overnight. With external cooling, saturated ammonium chloride (50 ml.) was added to the stirred solution. The aqueous mixture was extracted with light petroleum–ether (1 : 1) and the organic layer was washed with half-saturated brine (200 ml.); it was then dried and the solvent was carefully removed to yield an oil (350 mg.).

The pure racemic ketone (67 mg.) (20%) was obtained as an oil by preparative t.l.c. and microdistillation.

I.r. and mass spectra indicated that the synthetic, racemic ketone was identical to the ketonic degradation product.

G.l.c. analysis of a 1 : 1 mixture of the two ketones showed one symmetrical peak on the following columns (all at 100°):

Column	Flow rate (ml./min.)	Retention time (min.)
20% TCEP	50	35·5
10% 20M Carbowax	53	14·2
5% QF 1	42	19·1
5% APL	48	13·3
5% B34 dinonyl phthalate	57	37·8

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