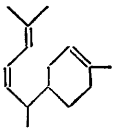
180. *The Structure of γ-Curcumene.*

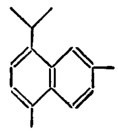
By R. D. Batt and S. N. Slater.

The structure of (+)-γ-curcumene, the main sesquiterpene component of the essential oil of *Libocedrus bidwillii*, Hook, has been investigated. Of the possible formulæ considered, (III) is regarded as the most satisfactory representation.

The essential oil of *Libocedrus bidwillii*, Hook, a coniferous tree endemic to New Zealand, has been examined by Goudie (*J. Soc. Chem. Ind.*, 1923, **42**, 350T) and by Birrell (*ibid.*, 1932, **51**, 398T). Goudie made a preliminary study of a dextrorotatory sesquiterpene fraction which was more fully examined by Birrell. Recently, a precise fractionation of this oil has been completed (Batt and Hassall, to be published elsewhere), and this communication deals with an investigation into the structure of the purified main sesquiterpene component, to which the name (+)-*γ-curcumene* is assigned.

The analysis of the sesquiterpene confirms the molecular formula $C_{15}H_{24}$. In conformity with the findings of Goudie (*loc. cit.*) but contrary to those of Birrell (*loc. cit.*), no crystalline nitrosite, nitrosate, nitrosochloride, or hydrochloride could be prepared. Prolonged hydrogenation (335 hours) of the sesquiterpene in acetic acid using Adams's platinum oxide catalyst gave a product whose analytical figures suggested that uptake of hydrogen corresponding to nearly two double bonds had taken place; perbenzoic acid titration of this hydrosesquiterpene indicated a slight residual unsaturation. A determination of the unsaturation of the sesquiterpene itself with perbenzoic acid gave figures corresponding to an uptake of two atoms of oxygen. On the basis of the degradation of the sesquiterpene to a monocyclic compound of known structure, however, we conclude that the sesquiterpene is monocyclic and must therefore contain three double bonds. One of these might be resistant to hydrogenation and attack by perbenzoic acid, but an alternative explanation is provided below. Two double bonds appear to be conjugated, as reaction occurs with maleic anhydride, although the product decomposes on attempted distillation and has not yet been isolated in a pure state. Sodium and alcohol reduction yields mainly resinous materials. The molecular refraction of (+)-γ-curcumene (68·1) also shows an exaltation over that calculated for a monocyclic sesquiterpene (67·8) which, although small, is considered significant and not due to contamination with other sesquiterpenes. The absorption spectrum in *cyclo*hexane (Fig. 1) shows an absorption maximum at 2670 A. ($\varepsilon_{max.}$ 3500) which, on the basis of the findings of Booker, Evans, and Gillam (*J.*, 1940, 1453) on the absorption spectra of monocyclic dienes of the type of α-phellandrene and α-terpinene, would indicate that the two conjugated double bonds are present in the ring system. Such dienes are characterised by abnormally low $\varepsilon_{max.}$ values as compared with the acyclic and semicyclic dienes.


(I.)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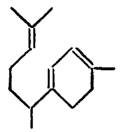
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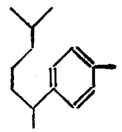

(IV.)

Birrell (*loc. cit.*) showed that on dehydrogenation his specimen of (+)-γ-curcumene yielded cadalene, and this has been confirmed. Dehydrogenation with sulphur at 270° yielded cadalene, identified as the picrate, which may be compared with the formation of cadalene (II) from zingiberene (I) under similar conditions (Ruzicka, Meyer, and Mingazzini, *Helv. Chim. Acta,* 1922, **5**, 345). Zingiberene, however, is conjugated in the side chain and it might be expected that a *cyclo*hexadiene would tend to form a derivative of benzene. It was found, in fact, that selenium dehydrogenation of (+)-γ-curcumene at 280° gave an isomeric hydrocarbon, $C_{15}H_{24}$. If the structure (III) be accepted for γ-curcumene, then such an isomerisation could arise by an intramolecular disproportionation (cf. Linstead, Michaelis, and Thomas, *J.*, 1940, 1139) and would be expected to yield 6-*p*-tolyl-2-methylheptane (IV). This compound was obtained by Ruzicka and van Veen (*Annalen,* 1929, **468**, 143) in an impure form by dehydrogenation of hexahydrozingiberene with palladised charcoal, and subsequently synthesised. The physical properties of our hydrocarbon, however, differ from those recorded by Ruzicka *et al.* for their specimen of (IV) and the relationship of the two substances is not yet clear. This aspect of the problem is being further investigated. The possibility of our dehydrogenation product being α-curcumene (see below) is excluded since it does not form a nitrosate.

FIG. 1.

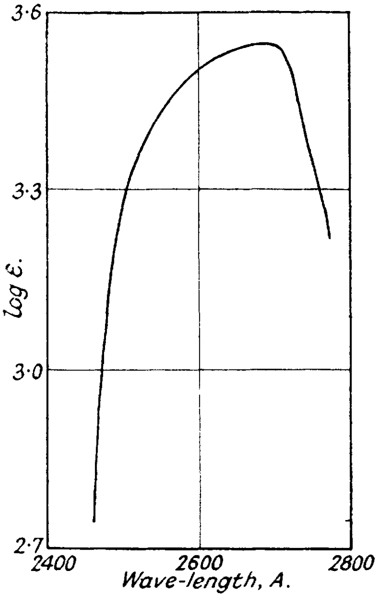
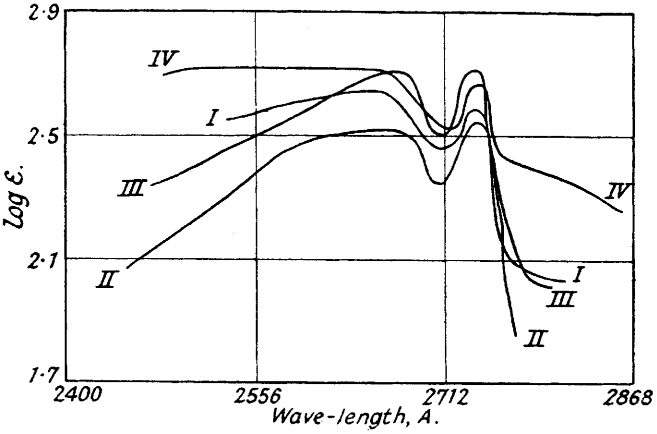


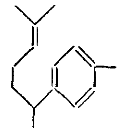
FIG. 2.



I. C_{12} *acid.*
II. *Ester of* C_{12} *acid.*
III. *γ-*p*-Tolyl-*n*-valeric acid.*
IV. *Neutral ozonolysis product.*

Oxidative degradation of (+)-γ-curcumene gave valuable information. Birrell (*loc. cit.*) had identified acetone as an ozonolysis product, but no trace of formic acid or formaldehyde was observed. The formation of acetone has been confirmed, and except in one case where a slightly impure specimen of the sesquiterpene was ozonised, no formaldehyde was detected, indicating that the side chain must terminate substantially in the *iso*propylidene arrangement. From larger-scale ozonolysis, in addition to acetone and acetone peroxide, it was possible to isolate a neutral liquid product and a dextrorotatory acid, analysed as the *methyl* ester, $C_{13}H_{18}O_2$, and characterised as the p-*phenylphenacyl* ester, m. p. 74°, and the S-*benzylthiuronium* salt, m. p. 139—139·5°. The acid on further degradation with alkaline permanganate gave terephthalic acid, characterised as the dimethyl ester. Presumably the aromatic ring of terephthalic acid is present in the C_{12} acid and its (C_{13}) ester, and the ultra-violet absorption spectra of both the crude acid and the pure ester (Fig. 2) show the typical resolved absorption for a compound containing a benzene nucleus (Webb, *J. Org. Chem.*, 1939, **4**, 389; Jones, *Chem. Reviews*, 1943, **32**, 1). (—)-γ-*p*-Tolyl-*n*-valeric acid (VI) was isolated by Carter, Copp, Rao, Simonsen, and Subramaniam (*J.*, 1939, 1504) as an ozonolysis product of (—)-α-curcumene (V), its *p*-phenylphenacyl ester melting at 73—74°. The C_{12} acid is therefore formulated as the dextro-form of (VI).

A specimen of racemic γ-*p*-tolyl-*n*-valeric acid (VI) was prepared; the p-*phenylphenacyl* ester melts at 69—69·5° and, mixed with the *p*-phenylphenacyl ester (m. p. 74°) of the ozonolysis acid, at 70—70·5°. Its absorption spectrum (Fig. 2) is closely similar to that of the dextrorotatory ozonolysis acid and its methyl ester.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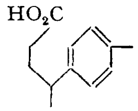
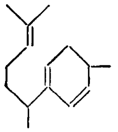


(VI.)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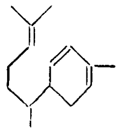

(VIII.)

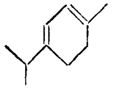
It is difficult to avoid the conclusion that the action of ozone upon the sesquiterpene has resulted in the conversion of a *cyclo*hexadiene structure into the aromatic state in addition to its normal action upon the double bond of the side chain. It is known that such dehydrogenations may be effected in polynuclear systems with, for example, selenium dioxide (Robinson and Slater, *J.*, 1941, 376), and α-terpinene on oxidation with chromyl chloride gives derivatives of benzene (Henderson and Cameron, *J.*, 1909, **95**, 969), but we are not aware of any case where ozone has been found to bring about this change. It may be significant that the percentage of ozone in the stream of gases from the ozoniser was low.

The neutral product from ozonolysis could not be distilled without decomposition. An impure 2 : 4-dinitrophenylhydrazone was prepared, m. p. 85—86°, and oxidation with either neutral permanganate or silver oxide gave (+)-γ-*p*-tolyl-*n*-valeric acid. The absorption spectrum of the neutral product showed the same absorption band as that given by the ozonolysis acid and its methyl ester. The neutral product is probably substantially (+)-γ-*p*-tolyl-*n*-valeraldehyde, the enantiomorph of which (m. p. of dinitrophenylhydrazone, 94—95°) was obtained by Simonsen *et al.* (*loc. cit.*) as one of the products of ozonolysis of (—)-α-curcumene.

From the above results the sesquiterpene may be formulated as (III), (VII), or (VIII). Baeyer has shown (*Ber.*, 1894, **27**, 815) that α-terpinene (IX) may be distinguished from other closely related terpenes by its characteristic rapid reaction with Beckmann's chromic acid reagent, accompanied by the formation of brown resinous flakes. This reaction is also given by (+)-γ-curcumene and in the absence of other evidence this points to (III) as the most likely structure.

The obviously close relationship between the sesquiterpene under examination and the α- and β-curcumenes (V and X, respectively) suggests the name γ-curcumene. α-Curcumene is not strictly a sesquiterpene, and it would be preferable to rename it *ar.*-curcumene, following the method adopted in the analogous tumerone series (Rupe *et al.*, *Helv. Chim. Acta*, 1934, **17**, 372; 1936, **19**, 569), where both the sesquiterpene (ketone), tumerone, and its aromatic counterpart, *ar.*-tumerone, are also known. It is interesting to note that the α- and β-curcumenes of *C. aromatica* are accompanied by about 1—2% of a conjugated hydrocarbon (Simonsen *et al.*, *loc. cit.*).

In connection with the conversion of (+)-γ-curcumene into aromatic products on ozonolysis, it may be significant that Simonsen *et al.* (*loc. cit.*) isolated from the ozonolysis of (—)-β-curcumene, regenerated from its hydrochloride, small amounts of the degradation products of (—)-α-curcumene. It is stated that the (—)-β-curcumene was not pure, but the characteristic nitrosate of (—)-α-curcumene could not be prepared from it, and hence if α-curcumene were present it must have been in small amount only. An alternative explanation is that the removal of hydrogen chloride from (—)-β-curcumene trihydrochloride forms, in addition to the main product, (—)-β-curcumene (X), smaller amounts of (—)-γ-curcumene which on ozonolysis would give the degradation products of (—)-α-curcumene.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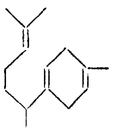
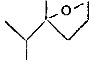

(X.)


(XI.)

The ready passage of the conjugated *cyclo*hexadiene system into the aromatic state may also account for the anomalous hydrogenation results obtained with (+)-γ-curcumene. It is known, for example, that piperitone (Read, Watters, Robertson, and Hughesdon, *J.*, 1929, 2068) and carvone (Linstead *et al.*, *loc. cit.*) undergo partial disproportionation to the corresponding phenols on hydrogenation at room temperature, the uptake of hydrogen, at first rapid, becoming very slow in the final stages owing to the comparative resistance of the aromatic material to hydrogenation. Finally, it may be noted that Elson, Gibson, and Simonsen (*J.*, 1929, 2732) have shown that the action of perbenzoic acid upon α-terpinene (IX) results in 1 : 4-addition with the formation of 1 : 4-oxido-Δ^2-*p*-menthene (XI), and it might therefore be expected that a structure such as (III) would show similar behaviour and absorb two, rather than three atoms of oxygen when treated with perbenzoic acid.

EXPERIMENTAL.

(+)-γ-*Curcumene*.—The main portion of the sesquiterpene fraction of *L. bidwillii*, distilled through a Lecky and Ewell column of 39 plates, had the following constants: b. p. 94°/3 mm., $d_{4^\circ}^{20^\circ}$ 0·8810, $n_D^{25^\circ}$ 1·4975, $[\alpha]_D$ +31·78° (Found: C, 88·3; H, 11·7. $C_{15}H_{24}$ requires C, 88·2; H, 11·8%). No crystalline derivatives were obtained in attempted preparations of the nitrosochloride, nitrosite, nitrosate, and hydrochloride. The absorption spectrum in spectroscopically pure *cyclo*hexane solution, successively diluted, showed an absorption maximum at 2670 A. and an extinction coefficient of 3500. With maleic anhydride an unstable adduct was obtained which decomposed on attempted distillation. Reduction with sodium in hot alcoholic solution gave mainly a resinous solid.

When a chloroform solution of perbenzoic acid was added to (+)-γ-*curcumene* (0·308 g.), and the mixture kept at 0° until the iodine titre was constant, the oxygen absorption corresponded to 6·24 milliequiv. (Calc. for two double bonds: 6·04).

Hydrogenation of (+)-γ-*Curcumene*.—(*a*) A solution of (+)-γ-curcumene (4 g.) in glacial acetic acid (40 c.c.) was shaken for 335 hours with freshly-prepared Adams's catalyst (0·12 g.) under a pressure of 2 atm. of hydrogen, with periodic reactivation of the catalyst. The redistilled product (3·4 g.) had the following constants: b. p. 106°/2 mm., $n_D^{25^\circ}$ 1·4736, $d_{20^\circ}^{20^\circ}$ 0·8551, $[\alpha]_D$ +11·1° (Found: C, 87·2; H, 13·3. $C_{15}H_{26}$ requires C, 87·4; H, 12·6. $C_{15}H_{28}$ requires C, 86·5; H, 13·5%). Perbenzoic acid titration indicated the presence of slight residual unsaturation (0·060 milliequiv. of oxygen absorbed. Calc. for one double bond, approx. 0·511). Molecular refraction (*M*, 208), 68·5 (Calc. for a dihydromonocyclic sesquiterpene, 68·33; for a tetrahydromonocyclic sesquiterpene, 68·8).

(*b*) A solution of (+)-γ-curcumene (4·6 g.) in absolute alcohol was shaken with hydrogen in the presence of palladised strontium carbonate. The reduction was stopped when the calculated volume of hydrogen for the saturation of one double bond had been absorbed. Distillation of the product gave two fractions, b. p. 90—92°/1·5 mm. (2·54 g. of a colourless mobile liquid) and 134°/1 mm. (0·8 g. of a very viscous yellow oil, $n_D^{25^\circ}$ 1·4915). The lower-boiling fraction had the following constants: $n_D^{25^\circ}$ 1·4856, $d_{20^\circ}^{20^\circ}$ 0·8735, $[\alpha]_D$ +18·6°, $[R_L]_D$ 67·95.

Dehydrogenation of (+)-γ-*Curcumene*.—(*a*) A mixture of (+)-γ-curcumene (7 g.) and finely powdered selenium (7 g.) was heated to 250° and the temperature then gradually raised to 280° and held there for 50 hours. Extraction of the mixture with ether and distillation of the product yielded a blue liquid (4·6 g.), b. p. 130°/6 mm., which was treated by Sherndal's method (*J. Amer. Chem. Soc.*, 1915, **37**, 167) for the isolation of azulene, but only a small quantity of a dark green oil, which did not give a picrate, was obtained. The oil remaining from the azulene extraction was redistilled over sodium. The distillate, b. p. 130°/6 mm., n_D^{25} 1·4932, $d_{20^\circ}^{16^\circ}$ 0·875, was a colourless mobile oil from which no picrate was obtained (Found: C, 88·2; H, 11·7. Calc. for $C_{15}H_{24}$: C, 88·2; H, 11·8%).

(*b*) A mixture of (+)-γ-curcumene (5·0 g.) and flowers of sulphur (2·5 g.) was heated at 270° for 6 hours. The liquid obtained from the ether extraction was distilled, and the distillate (2·4 g.) separated by distillation over sodium into two fractions, b. p. 138—141°/9 mm. and 150—170°/9 mm. On treatment of the higher-boiling fraction with the calculated quantity of picric acid dissolved in the minimum amount of hot alcohol, heating on the water-bath for 15 minutes, and then cooling, an intensely red solution was obtained which deposited long orange needles; m. p., after repeated crystallisations from alcohol, 114°. No mixed m. p. depression was observed with an authentic specimen of cadalene picrate (yield, 0·1 g. from 0·2 g. of distillate). Under similar conditions the lower-boiling fraction gave only picric acid.

Ozonolysis of (+)-γ-*Curcumene*.—(*a*) Pure (+)-γ-curcumene (10 g.) was ozonised in pure carbon tetrachloride until a portion of the solution no longer decolorised a solution of bromine in carbon tetrachloride. The solid ozonide was filtered off, and the filtrate evaporated under reduced pressure. The residue was combined with the solid ozonide, and after standing overnight with water (20 c.c.) was heated under reflux on a water-bath for one hour. The low-boiling material was distilled, yielding a distillate (A), a solid (B) which crystallised in the condenser, and a residue (C). (A) formed a 2 : 4-dinitrophenylhydrazone, m. p. 124—125° alone and mixed with an authentic specimen of acetone 2 : 4-dinitrophenylhydrazone, but no positive tests were obtained for formic acid or formaldehyde. (B), recrystallised from ether, had m. p. 131—133° and sublimed readily, even at room temperature, and no smell of formaldehyde was noticed on heating; combustion was difficult owing to the readiness with which the compound exploded (Found: C, 41·1; H, 6·67. Calc. for CH_2O: C, 40·0; H, 6·6%). (C) was extracted repeatedly with ether, and the combined ether extracts shaken out with 2N-sodium carbonate solution. The residual ethereal layer gave a pale yellow, pleasant-smelling liquid (D, 3·5 g.) which suffered extensive decomposition on attempted distillation. The acid (E, 2 g.) obtained from the sodium carbonate extract was esterified with diazomethane and distilled (with considerable decomposition) to yield a pale yellow liquid (1 g.), b. p. 105—110°/2 mm. In none of a series of small-scale ozonolyses of the pure material was the formation of formaldehyde observed.

(*b*) A larger sample (17·1 g.) of a slightly less pure specimen was ozonised as described above, and in this case by passing the gases from the reaction vessel through water and changing the water several times it was possible to detect the liberation first of acetone (formation of 2 : 4-dinitrophenylhydrazone) and then of formaldehyde (formation of a 2 : 4-dinitrophenylhydrazone, m. p. 165—166°, undepressed by mixing with an authentic specimen). The neutral fraction (D, above) of the decomposed ozonide amounted to 5·6 g. It furnished a red tarry product with alcoholic 2 : 4-dinitrophenylhydrazine which on repeated extraction with hot alcohol gave a solid. Repeated recrystallisation gave a small amount of material, m. p. 85—86°. Attempts to prepare a crystalline semicarbazone were unsuccessful. The absorption curve of the impure neutral material, dissolved in rectified spirits and successively diluted, had absorption maxima at 2600 A. (approx.) and 2735 A.; $\varepsilon_{\text{max.}}$ values are not significant owing to the impure state of the material.

The acid fraction (E, above), amounting to 7·7 g., had $[\alpha]_D$ +19·2°, and on esterification with diazomethane and distillation (twice) the *methyl* ester of (+)-γ-*p*-tolyl-*n*-valeric acid was obtained, b. p. 106°/2—3 mm. (Found : C, 75·2; H, 9·75. $C_{13}H_{18}O_2$ requires C, 75·7; H, 8·74%). The acid was characterised as the S-*benzylthiuronium* salt, m. p. (from alcohol) 139—139·5° (Found : N, 7·7. $C_{20}H_{26}O_2N_2S$ requires N, 7·8%), and the p-*phenylphenacyl* ester, m. p. 74° (from methanol) (Found : C, 80·4; H, 7·31. $C_{26}H_{26}O_3$ requires C, 80·8; H, 6·7%). The absorption spectrum of the acid was determined in absolute alcohol; absorption maxima occurred at 2735 and at 2665 A. with $\varepsilon_{\text{max.}}$ values of 398 and 426, respectively. The absorption spectrum of the purified methyl ester was determined in alcoholic solution; absorption maxima occurred at 2735 and 2670 A. with $\varepsilon_{\text{max.}}$ values of 355 and 330, respectively.

Oxidation of the Neutral Fraction (*D*) [(+)-γ-p-*Tolyl*-n-*valeraldehyde* ?].—A solution of the neutral fraction (D, 4·0 g.) in acetone (120 c.c.) and water (20 c.c.) was heated under reflux, and finely powdered potassium permanganate (21 g.) was gradually added until there was no further decolorisation. The product was filtered, the acetone removed, and the residue extracted with ether. By shaking out the ethereal solution with aqueous sodium carbonate solution (+)-γ-*p*-tolyl-*n*-valeric acid (1·5 g.) was obtained and characterised as the *p*-phenylphenacyl ester, m. p. and mixed m. p. 73—74°.

Oxidation of (+)-γ-p-*Tolyl*-n-*valeric Acid* (*E*).—The acid fraction of the ozonolysis product (3 g.) in aqueous sodium carbonate was treated under reflux with a 4% aqueous solution of potassium permanganate, the reaction being complete after the addition of 18 g. of permanganate. The product was decolorised with sulphur dioxide, boiled with concentrated sodium hydroxide solution, filtered through sintered glass, and acidified. The white solid (0·5 g.) which separated was centrifuged off and dried. It had no definite m. p. but started to sublime at 280°. The methyl ester melted at 139—140° and showed no depression with authentic methyl terephthalate.

Racemic γ-p-*Tolyl*-n-*valeric Acid*.—γ-*p*-Tolylpentenoic acid (Rupe and Steinbach, *Ber.*, 1911, **44**, 584; 0·75 g.) in absolute alcohol (35 c.c.) was hydrogenated in the presence of palladised strontium carbonate (0·5 g.), the reaction proceeding rapidly. After removal of the catalyst the solution was made alkaline, the alcohol distilled off, and the product acidified and extracted with ether. The acid was obtained as a clear viscous liquid (0·72 g.) which crystallised after standing for some weeks; m. p. 30—31° (Rupe and Steinbach give m. p. 32°). The p-*phenylphenacyl* ester melted at 69—69·5° (Found : C, 80·7; H, 6·7. $C_{26}H_{26}O_3$ requires C, 80·8; H, 6·7%). A mixture with the *p*-phenylphenacyl ester of (+)-γ-*p*-tolyl-*n*-valeric acid melted at 70—70·5°.

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