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SYNTHESIS OF D- AND L-*ISO*IRIDOMYRMECIN AND RELATED COMPOUNDS

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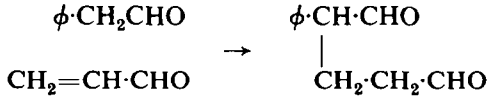
Abstract—Starting from D-citronellal of natural origin, D-iridodial and D-*iso*iridomyrmecin were synthesised.* The latter furnished, on oxidation, a *nepetalinic acid*, which was the enantiomorph of a degradation product of nepetalactone. A mixture of the two specimens afforded a *racemate* of higher melting point.

L-Citronellal, obtained (Boake, Roberts & Co.) by a series of chemical transformations from pinene was similarly converted into L-iridodial and L-*iso*iridomyrmecin. The latter was identical with the natural product from *Iridomyrmex nitidus*.

INSPECTION of the structure (I) of iridomyrmecin[1,2] and related compounds[3,4] isolated from different species of ants of the genus *Iridomyrmex* suggested a biogenesis by disproportionation of the dialdehyde (II), which, known as iridodial, has been isolated from *I. conifer* and *I. detectus* and actually converted into *iso*iridomyrmecin, epimeric with (I) at the asterisked C-atom. It is accordingly probable that iridodial is the biological precursor both of (I) and its epimer.

Going back a stage further in the analysis it was evident that iridodial could be regarded as a cyclised oxo-citronellal ($=CMe_2 \rightarrow =CMeCHO$), the ring-formation being of a normal Michael reaction type as exemplified by the addition of phenylacetaldehyde to acrolein:—



The oxidation itself was thought a plausible process in view of the activation of terminal methyl by the neighbouring double bond.

The syntheses now described represent the realisation of this biogenetic scheme in the laboratory.

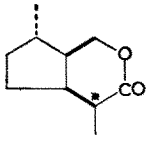
The structure (I)† proposed for iridomyrmecin,[2] and later for its epimer *iso*-iridomyrmecin[4,5] appears to be firmly established except that the configuration at the asterisked C-atom has not yet been defined.

* U.K. Patent Application No. 18220/57.

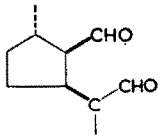
† The recently revised steric formulae[4,5] are used for this and related compounds.

[1] M. Pavan, *Chim. e Industr.* **37**, 625 (1955).
[2] R. Fusco, R. Trave and A. Vercellone, *Chim. e Industr.* **37**, 251, 958 (1955).
[3] G. W. K. Cavill, D. L. Ford and H. D. Locksley, *Chem. & Ind.* 465 (1956); *Austr. J. Chem.* **9**, 288 (1956).
[4] G. W. K. Cavill and H. D. Locksley, *Austr. J. Chem.* **10**, 352 (1957).
[5] S. M. McElvain and E. J. Eisenbraun, *J. Org. Chem.* **22**, 976 (1957).

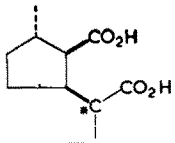
The iridolactones* have been oxidised to two epimeric nepetalinic acids[6,8] (III) and thus are related to nepetalactone (IV), a constituent of catnip oil.[6–9] In order to realise the above scheme of synthesis we started from the more readily accessible



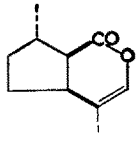
I



II

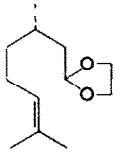


III

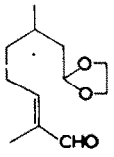


IV

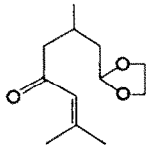
D-citronellal. Its ethylene acetal (V)† was oxidised by means of selenium dioxide in ethanol to the $\alpha\beta$-unsaturated aldehyde (VI). There was no evidence of the formation of the isomeric ketone (VII). A similar oxidation could not be effected with citronellal diethyl acetal, the starting material being recovered virtually quantitatively. After isolation of the product (VI) by means of the bisulphite addition compound its infra-red spectrum showed the characteristic stretching frequency of an aldehydic C—H bond at 3·70 μ and had bands at 5·92 and 6·10 μ for a conjugated carbonyl group and double bond, respectively. Further evidence for the constitution of (VI) was provided by almost quantitative oxidation with alkaline silver oxide to the corresponding acid (VIII).



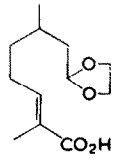
V†



VI

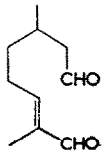


VII

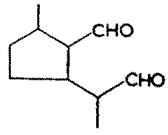


VIII

It was anticipated that acid hydrolysis of the aldehydo-acetal (VI) would yield the aliphatic dialdehyde (IX), but examination of various conditions soon revealed that, in addition, the alicyclic dialdehyde (X) was formed in acid media. Thus carefully controlled hydrolysis of the aldehydo-acetal (VI) with 50 per cent aqueous acetic acid in an inert atmosphere consistently produced the two isomeric dialdehydes



IX



X

(IX) and (X) in approximately equal quantities; the products were readily separated by fractional distillation and their infra-red spectra were in agreement with the structures assigned to them. The two dialdehydes readily polymerised and also formed acidic material in contact with air. Hence they tended to give low carbon values on analysis.

* The term iridolactones is used to cover both iridomyrmecin and *iso*iridomyrmecin.

† Formulae (V), (VI), (IX) and (X) are used for both D- and L-isomers.

[6] S. M. McElvain and E. J. Eisenbraun, *J. Amer. Chem. Soc.* **77**, 1955 (1955).

[7] E. J. Eisenbraun and S. M. McElvain, *J. Amer. Chem. Soc.* **77**, 3383 (1955).

[8] R. B. Bates, E. J. Eisenbraun and S. M. McElvain, *J. Amer. Chem. Soc.* **80**, 3420 (1958).

[9] S. M. McElvain, R. D. Bright and P. R. Johnson, *J. Amer. Chem. Soc.* **63**, 1558 (1941); J. Meinwald, *Ibid.* **76**, 4571 (1954).

The compounds (IX) and (X) were characterised as the bis-2:4-dinitrophenylhydrazones and bis-semicarbazones; the derivatives of the cyclic dialdehyde (X) had the same melting points as those reported for the corresponding derivatives of natural iridodial[3] and were undepressed on admixture with authentic samples, kindly provided by Dr. G. W. K. Cavill.

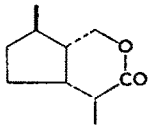
Attempts to increase the yield of the cyclic dial (X) at the expense of the aliphatic isomer (IX) by prolonging the treatment with aqueous acetic acid remained unsuccessful. We found, however, that cyclisation of the dialdehyde (IX) could be achieved by refluxing this substance with acetone containing some dilute hydrochloric acid; thus iridodial (X) was obtained in up to 50 per cent yield, but the remainder of the material polymerized under these conditions.

Contrary to expectations the aliphatic dialdehyde (IX) failed to cyclise in the presence of mild basic reagents (e.g. piperidine).[10] Treatment with sodium methoxide in methanol and subsequent acidification produced a neutral, sweetly smelling liquid which analysed for the empirical formula $C_{10}H_{16}O_2$ and had a band in the carbonyl region at 5·76 μ, indicating that the substance was a δ-lactone.

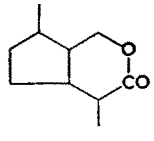
A portion of this material was oxidised with alkaline permanganate and the resulting mixture of acids was separated by means of their barium salts. The soluble salts furnished a di-basic acid, m.p. 142–143° $[\alpha]_D^{28}$ −16° which analysed for the empirical formula $C_{10}H_{16}O_4$ and formed a bis-*p*-bromphenacyl ester, m.p. 139°. We suspected this to be a nepetalinic acid but it did not correspond to any of the known nepetalinic acids and has not yet been further investigated. The di-basic acid regenerated from the insoluble barium salt had m.p. 87·5–88·5°, $[\alpha]_D^{27}$ −40°, which indicated that it was the enantiomorph of the nepetalinic acid m.p. 85°, $[\alpha]_D$ +30·2° [6] derived from nepetalactone and also known to arise from the oxidation of *iso*iridomyrmecin.[3,4] An equimolar mixture of the two optical isomers (a sample of the (+)-acid was kindly provided by Professor S. M. McElvain) melted, after crystallisation from ether–light petroleum, at 126·5–127·5° and had no measurable rotation, thus confirming the stereochemical relationship of the two acids. It should be noted that the configurational relationship of nepetalactone to L-citronellal follows by way of L-pulegone and its degradation to (+)-α-methylglutaric acid.[7] Hence it is clear that the iridodial and *iso*iridomyrmecin obtained from D-citronellal are in the same D- series and are enantiomorphs of the natural products.

Treatment of the dialdehyde (X) with warm aqueous alkali and lactonisation of the resulting δ-hydroxy acid by means of mineral acid gave a crystalline compound, m.p. 58·5–59°, $[\alpha]_D^{26}$ +56°, which formed a hydrazide, m.p. 118–119° and therefore must be D-*iso*iridomyrmecin (XI). Naturally occurring *iso*iridomyrmecin is reported to have m.p. 58–59°, $[\alpha]_D$ −62°, and its hydrazide to melt at 118°.[3]

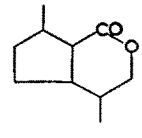
The production of nepetalinic acids by oxidation of our synthetic lactonic mixture demonstrated that it contained substances possessing either or both of the bicyclic



XI



XII



XIII

[10] H. Meerwein, *J. pr.* **97**, 225 (1918); *Ber.* **53**, 1829 (1920).

δ-lactone structures (XII) and (XIII). Standard techniques failed to separate the mixture; eventually a quantity (20 per cent of the total weight) of crystalline lactone was isolated by a procedure known to separate *iso*iridomyrmecin from its stereoisomers.[4] The beautifully crystalline substance was in every respect identical with the specimen of D-*iso*iridomyrmecin previously prepared from D-iridodial.

We examined several alleged sources of L-citronellol but were unable to acquire a supply of this substance or of L-citronellal which was adequately optically homogeneous. We are all the more greatly indebted to Mr. E. E. Boake for the provision of a quantity of L-citronellal, kindly prepared for us in the Research Laboratories of Messrs. A. Boake, Roberts & Co. Ltd. With this material the synthesis was repeated in the correct stereochemical series and gave as the end product L-*iso*iridomyrmecin, which was identical with the lactone isolated from *Iridomyrmex nitidus*.

It must be emphasised that the L-citronellal put at our disposal was a partially synthetic material; the infra-red spectrum showed that it was a mixture of approximately 40 per cent α- and 60 per cent β-citronellal, while the D-citronellal used by us existed exclusively in the β-form.

The α-form of L-citronellal, however, was apparently eliminated when reaction of the aldehyde with ethylene glycol produced the cyclic acetal (V) in unexpectedly low yield (34 per cent),* together with a large amount of polymer; the acetal showed no absorption at 11·25 μ (terminal methylene group) in its infra-red spectrum.

Thereafter the synthesis proceeded essentially along the lines worked out in detail in the D-series. Owing to the limited amount of laevo-rotatory material available, fractional distillation did not completely free the alicyclic dialdehyde (X) from the higher boiling aliphatic isomer (IX), but the latter was obtained in pure form and characterised as the bis-2:4-ninitrophenylhydrazone. Both dialdehydes were converted by the previously described methods into the same crystalline lactone, which was obtained in the form of very long, colourless prisms, m.p. 57·5–58°, undepressed on admixture with authentic *iso*iridomyrmecin (kindly supplied by Dr. G. W. K. Cavill), $[\alpha]_D^{28}$ −56°. A mixture prepared by dissolving equimolar amounts of D- and L-*iso*iridomyrmecin crystallised very slowly after most of the solvent had been removed, and melted at 32–34°, $[\alpha]_D \pm 0°$.

In order to obtain a sample of pure L-iridodial (X) a small quantity of a mixture of both isomeric dialdehydes (IX) and (X) was treated with a solution of dilute hydrochloric acid in acetone under the conditions known to effect the ring closure (IX → X) Distillation provided as the lowest boiling fraction a liquid whose infra-red absorption spectrum was consistent with the structure (X). This substance formed a bis-2:4-dinitrophenylhydrazone, m.p. 228° (decomp.) which was identical with the corresponding derivative of natural iridodial (undepressed mixed melting point).

Cavill *et al.*[4] found the infra-red absorption due to the carbonyl group of iridomyrmecin at 5·74 μ and that of *iso*iridomyrmecin at 5·69 μ (both spectra in carbon tetrachloride). The infra-red absorption spectra of Nujol mulls of our synthetic L-*iso*iridomyrmecin (Fig. 1) and its enantiomorph were identical, each showing a carbonyl band at 5·76 μ. An authentic specimen of iridomyrmecin (for which we are greatly indebted to Professor M. Pavan) (Fig. 2) showed the carbonyl frequency also at 5·76 μ.

* Recently Messrs. A. Boake, Roberts and Co. Ltd. sent us a sample of L-citronellal containing less than 20% of the α-form; this material gave a much improved yield of cyclic acetal (45%).

Bio-assays* demonstrated that there is no difference in the insecticidal activity of natural iridomyrmecin and the two epimeric synthetic iridolactones, within the limits of the experimental method.

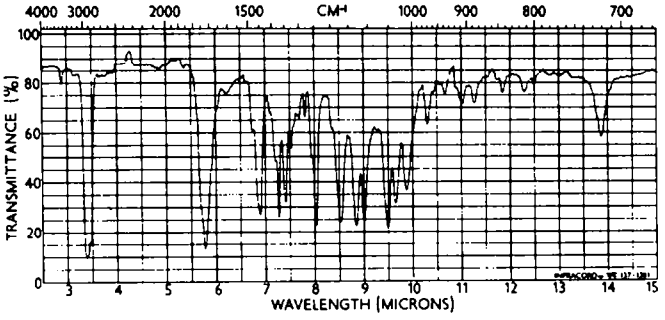


FIG. 1. L-*iso*Iridomyrmecin.

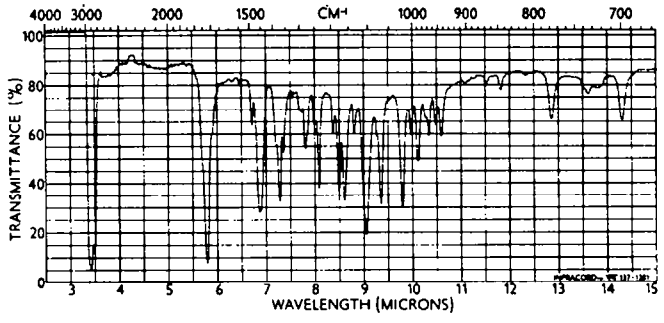


FIG. 2. Iridomyrmecin.

EXPERIMENTAL

Unless otherwise indicated, light petroleum means the fraction of b.p. 40–60°. Extracts were normally dried over anhydrous magnesium sulphate. Infra-red spectra of solids were determined for Nujol mulls.

D(+)-2:6-*Dimethyl*-8:8-*ethylenedioxyoct*-2-*ene* (V)

A mixture of D-citronellal $[\alpha]_D^{22}$ +11·6° (214 g), ethylene glycol (100 cc), benzene (600 cc) and toluene-*p*-sulphonic acid (approx. 100 mg) was refluxed for 12 hr under a Dean–Stark water separator. The solution was diluted with ether, washed with aqueous sodium hydrogen carbonate and water, dried and evaporated. Fractionation of the residue yielded the *cyclic acetal* of D-citronellal as a colourless liquid (190 g), b.p. 125–130°/18 mm, $[\alpha]_D^{22}$ +3·02° (homog.) (Found: C, 73·1; H, 11·1. $C_{12}H_{22}O_2$ requires: C, 72·8; H, 11·1%).

D(+)-2:6-*Dimethyl*-8:8-*ethylenedioxyoct*-2-*en*-1-*al* (VI)

Freshly sublimed selenium dioxide (34 g), dissolved in ethanol (200 cc), was added over a period of 2 hr to a vigorously stirred solution of the above acetal (60 g) in ethanol (100 cc), warmed at 50°. The bath temperature was slowly raised to 95–100° and the mixture stirred and refluxed for 24 hr. When cold it was filtered, the solvent removed *in vacuo* and the residue dissolved in ether, washed with aqueous sodium hydrogen carbonate, dried and fractionally distilled. The fraction b.p. 114–116°/0·2 mm (32·6 g) was stirred for 6 hr with a solution of sodium sulphite heptahydrate (157 g) and sodium

* We are grateful to Shell Research Limited for tests carried out at Woodstock Agricultural Research Centre.

hydrogen carbonate (90 g) in water (900 cc), and undissolved oil extracted with ether. The ice cold aqueous solution was basified with 10 per cent aqueous sodium hydroxide solution (ca. 450 cc) and repeatedly extracted with ether. After the washed and dried extract was freed from the solvent the *aldehyde* (VI) (23·85 g) was obtained as a colourless oil which was sufficiently pure for use in the next stage. A sample distilled at b.p. 100–106°/0·1 mm and had $[\alpha]_D^{17}$ +5·95° (homog.) (Found: C, 67·5; H, 9·7. $C_{12}H_{20}O_3$ requires: C, 67·9; H, 9·4%). The infra-red spectrum had bands at 3·70 (aldehydic C—H), 5·92 (conjugated C=O) and 6·10 μ (conjugated C=C).

D-2:6-*Dimethyl*-8:8-*ethylenedioxyoct*-2-*enoic acid* (VIII)

A solution of sodium hydroxide (1·24 g) in water (50 cc) was added dropwise at room temperature to a well-stirred mixture consisting of the above aldehyde (1·5 g) in ethanol (23 cc) and silver nitrate (1·24 g) in water (13 cc). After stirring for 3 hr the reaction mixture was filtered and the filtrate concentrated *in vacuo*, and any neutral material extracted with ether. Acidification of the aqueous alkaline solution with dilute sulphuric acid precipitated the *acid* (VIII; 1·59 g) as a pale yellow, thick oil which was evaporatively distilled at 200–205°/0·1 mm (bath temperature) (Found: C, 62·8; H, 8·9. $C_{12}H_{20}O_4$ requires: C, 63·1; H, 8·8%).

Hydrolysis of D-2:6-*dimethyl*-8:8-*ethylenedioxyoct*-2-*en*-1-*al*

The cyclic acetal (VI; 27 g) was refluxed with 50 per cent aqueous acetic acid (270 cc) under nitrogen for 2 hr (oil bath), cooled rapidly and poured into brine. The mixture was extracted with ether and the extract repeatedly washed with water, dilute sodium hydrogen carbonate solution and more water, dried and evaporated. The residue was fractionally distilled to yield as the first main fraction *D*-α-(2-*formyl*-3-*methylcyclopentyl*)-*propional* (X) as a pale yellow liquid (7·55 g), b.p. 78–82°/0·4 mm (Found: C, 70·9; H, 9·3. $C_{10}H_{16}O_2$ requires: C, 71·4; H. 9·5%). The infra-red spectrum had bands at 3·70 (aldehydic C—H) and 5·82 μ (C=O). As the second main fraction D-2:6-*dimethyloct*-2-*en*-1:8-*dial* (IX) distilled as a colourless liquid, (7·2 g), b.p. 90–93°/0·5 mm. (Found: C, 71·3; H, 9·8. $C_{10}H_{16}O_2$ requires: C, 71·4; H, 9·5%). The infra-red spectrum had absorption bands at 3·70 (aldehydic C—H), 5·80 (C=O), 5·92 (conjugated C=O) and 6·10 μ (conjugated C=C). D-2:6-*Dimethyloct*-2-*en*-1:8-*dial bis*-2:4-*dinitrophenylhydrazone* was prepared with Brady's reagent and separated from chloroform-ethanol as a brick-red, crystalline powder, m.p. 211–212° (decomp.) (Found: C, 50·1; H, 4·4; N, 21·4. $C_{22}H_{24}O_8N_8$ requires: C, 50·0; H, 4·5; N, 21·2%). The *bis-semicarbazone* of the aliphatic dial (IX) crystallised from ethanol as colourless prisms, m.p. 219° (decomp.) (Found: C, 50·9; H, 7·9; N, 30·1. $C_{12}H_{22}O_2N_6$ requires: C, 51·1; H, 7·8; N, 29·8%).

The *bis*-2:4-*dinitrophenylhydrazone* of the alicyclic dialdehyde (X) crystallised from ethyl acetate–ethanol as orange prisms, m.p. 227° (Found: C, 49·9; H, 4·7; N, 21·2. $C_{22}H_{24}O_8N_8$ requires: C, 50·0; H, 4·5; N, 21·2%). The *bis-semicarbazone* of the dialdehyde (X) formed colourless needles in methanol, m.p. 197–198° (decomp.) (Found: C, 51·0; H, 7·7; N, 30·1. $C_{12}H_{22}O_2N_6$ requires: C, 51·1; H, 7·8; N, 29·8%).

Cyclisation of D-2:6-*dimethyloct*-2-*en*-1:8-*dial* (IX)

The aliphatic dialdehyde (IX) (7·0 g) was refluxed for 1 hour with acetone (100 cc) and 10 per cent hydrochloric acid (2 cc) under nitrogen. The mixture was concentrated on the water bath, diluted with ether and poured into brine. After washing the ethereal layer with aqueous sodium hydrogen carbonate and water, it was dried and evaporated. Fractionation furnished D-α-(2-formyl-3-methyl-*cyclo*pentyl)-propional (X) as a pale yellow liquid (3·5 g), b.p. 74–76°/0·1 mm which was identical with the previously prepared specimen.

D(+)-iso*Iridomyrmecin* (XI)

(a) *From the alicyclic dialdehyde* (X). D-α-(2-Formyl-3-methyl*cyclo*pentyl)-propional (7·1 g) was warmed for 1 hr with N-sodium hydroxide solution (100 cc) under nitrogen. Undissolved material was extracted with ether, the aqueous layer cooled in ice and cautiously acidified with 5 N-hydrochloric acid (20 cc). The colourless precipitate was collected, briefly washed with ice-cold ether, suspended in ether and shaken with 5 N-hydrochloric acid. The organic layer was washed with aqueous sodium hydrogen carbonate and water, dried and evaporated. The residue partly solidified at room temp; repeated crystallisations from light petroleum yielded D-iso*iridomyrmecin* as elongated prisms (1·03 g).

m.p. 58·5–59°, $[\alpha]_D^{26}+56°$ (*c*, 1·41 in CCl_4) (Found: C, 71·8; H, 9·8. $C_{10}H_{16}O_2$ requires: C, 71·4; H, 9·5%). The infra-red absorption spectrum showed the carbonyl frequency at 5·76 μ.

(b) *From the aliphatic dialdehyde* (IX) *by Michael condensation.* Anhydrous methanol (50 cc) was added at room temp to D-2:6-dimethyloct-2-en-1:8-dial (11 g) under nitrogen, followed by 10 per cent methanolic sodium methoxide (5 cc). After 16 hr at room temp the brownish solution was refluxed for 8 hr and finally left to cool over night. The solution was then chilled in an ice bath, acidified with dilute hydrochloric acid, poured into brine and thoroughly extracted with ether. The acidic organic extract was kept for 3–5 hr (to complete lactonisation), freed from acidic matter by means of aqueous sodium hydrogen carbonate, washed and dried. Evaporation of the solvent left a brown, mobile liquid (10·3 g) which had a pungent, sweet odour and gave on distillation as the main fraction a colourless liquid (4·85 g), b.p. 87–90°/0·2 mm, $[\alpha]_D^{23}-39°$ (*c*, 1·048 in CCl_4) (Found: C, 71·4; H, 9·5. $C_{10}H_{16}O_2$ requires: C, 71·4; H, 9·5%). The infra-red spectrum showed a band in the carbonyl region at 5·76 μ. This material could not be induced to crystallise and was evidently a mixture of bicyclic δ-lactones.

A portion of this mixture (1·9 g) was dissolved in warm 2 N-potassium hydroxide solution (26 cc), chilled in ice and 50 per cent aqueous acetic acid (21 cc) was added dropwise with swirling (cf. ref. 4). The colourless precipitate was lactonised as described in section (a) and the resulting solid recrystallised twice from light petroleum to yield the lactone (XI), m.p. 58–59°, which was identical with the previously prepared specimen. The *hydrazide* crystallised from benzene and had m.p. 118–119° (Found: C, 59·8; H, 10·2; N, 13·8. $C_{10}H_{20}O_2N_2$ requires: C, 60·0; H, 10·0; N, 14·0%).

Oxidation of the mixture of lactones obtained from the Michael reaction

Potassium permanganate (5·2 g) was added in small portions during 2½ hr to a stirred solution of the oil, b.p. 87–90°/0·2 mm (3·4 g) in 5 per cent sodium hydroxide solution (40 cc), the temp being kept below 10°. After standing at room temp overnight, the reaction mixture was filtered, undissolved material extracted with ether and the aqueous layer treated with a concentrated solution of barium hydroxide in water. The acid liberated from the crystalline salt was recrystallised twice from light petroleum and was a D(−)-*nepetalinic acid* m.p. 87·5–88·5°, $[\alpha]_D^{27}-40°$ (*c*, 1·44 in $CHCl_3$) (Found: C, 60·3; H, 8·0. $C_{10}H_{16}O_4$ requires: C, 60·0; H, 8·0%). A specimen of its enantiomorph, kindly provided by Professor S. M. McElvain, had m.p. 84–85°, $[\alpha]_D^{28}+30·2°$ (*c*, 2·45 in $CHCl_3$). An equimolar mixture of the two enantiomorphous acids was crystallised from ether-light petroleum to give a *racemic nepetalinic acid*, m.p. 126·5–127·5°, $[\alpha]_D \pm 0°$. (Found: C, 60·2; H, 8·1. $C_{10}H_{16}O_4$ requires: C, 60·0; H, 8·0%).

The filtrate and washings from the above crystalline barium salt were treated with hydrochloric acid and the acidic material collected in ether. The crystalline residue (0·50 g) was recrystallised three times from ether–light petroleum, to give a *dicarboxylic acid*, m.p. 142–143°, $[\alpha]_D^{28}-16°$ (*c*, 1·00 in $CHCl_3$) which analysed correctly for a nepetalinic acid. (Found: C, 60·2; H, 8·0. $C_{10}H_{16}O_4$ requires: C, 60·0; H, 8·0%). Its *bis*-p-*bromophenacyl ester* crystallised from ethanol as needles, m.p. 138·5–139·5° (Found: C, 52·5; H, 4·3; Br, 27·1. $C_{26}H_{26}O_6Br_2$ requires: C, 52·6; H, 4·4; Br, 26·9%).

L(−)-2:6-*Dimethyl*-8:8-*ethylenedioxyoct*-2-*ene* (V)

A mixture of L-citronellal, $[\alpha]_D^{28}-10·5°$ (47·8 g), ethylene glycol (22 cc), benzene (200 cc) and toluene-*p*-sulphonic acid (approximately 30 mg) was reacted as described for the preparation of the corresponding enantiomorph. Fractionation yielded the *cyclic acetal* as a colourless liquid (20·7 g), b.p. 120–125°/18 mm, $[\alpha]_D^{26}-3·9°$ (Found: 72·9; H, 11·0. $C_{12}H_{22}O_2$ requires: C, 72·8; H, 11·1%).

L(−)-2:6-*Dimethyl*-8:8-*ethylenedioxyoct*-2-*en*-1-*al* (VI)

The above acetal (20 g), dissolved in ethanol (35 cc), was oxidised with a solution of selenium dioxide (11·4 g) in ethanol (70 cc), and the fraction, b.p. 108–114°/0·25 mm (12·5 g) stirred for 6 hr with a solution of sodium heptahydrate (47 g) and sodium hydrogen carbonate (27 g) in water (270 cc), followed by treatment with dilute sodium hydroxide solution (125 cc); the conditions were those employed for the preparation of the corresponding optical isomer. The *aldehyde* was thus obtained as a colourless oil (10 g), b.p. 88–90°/0·1 mm, $[\alpha]_D^{27}-5·45°$ (Found: C, 67·6; H, 9·7. $C_{12}H_{20}O_3$ requires: C, 67·9; H, 9·4%).

Hydrolysis of L(−)-2:6-*dimethyl*-8:8-*ethylenedioxyoct*-2-*en*-1-*al*

A solution of the above compound (10 g) in aqueous acetic acid (100 cc of 50%) was refluxed (oil bath) under nitrogen for 2 hr and worked up as previously described in the D-series. Fractionation of the reaction mixture gave: (a) a pale yellow liquid, b.p. 70–72°/0·15 mm (2·35 g), whose infra-red spectrum showed that it consisted chiefly of L-α-(2-formyl-3-methyl*cyclo*pentyl)-propional (X), having absorption bands of appropriate intensity at 3·70 and 5·82 μ, but weak bands at 5·92 and 6·10 μ indicated that some of the aliphatic dialdehyde (IX) contaminated this fraction; (b) a colourless liquid (2·1 g), b.p. 78–82°/0·15 mm, whose infra-red spectrum was in agreement with the structure of pure L-2:6-*dimethyloct*-2-*en*-1:8-*dial* (IX) with bands at 3·70, 5·80, 5·92 and 6·10 μ (Found: C, 70·8; H, 9·6. $C_{10}H_{16}O_2$ requires: C, 71·4; H, 9·5%); the *bis*-2:4-*dinitrophenylhydrazone* crystallised from chloroform–ethanol as brick-red needles, m.p. 211–212° (decomp.) (Found: C, 49·9; H, 4·6; N, 20·2. $C_{22}H_{24}O_8N_8$ requires: C, 50·0; H, 4·5; N, 21·2%).

L-α-(2-*Formyl*-3-*methylcyclopentyl*)-*propional bis*-2:4-*dinitrophenylhydrazone*

L-2:6-Dimethyloct-2-en-1:8-dial (0·4 g), which was contaminated with some of the cyclic dialdehyde (X), was refluxed for 1 hr with acetone (35 cc) and 10 per cent hydrochloric acid (1 cc) under nitrogen. Most of the solvent was then evaporated in an inert atmosphere, the residue dissolved in ether, washed and dried. Evaporative distillation gave an almost colourless oil (0·19 g) which distilled at 85–90°/0·1 mm (bath temperature); the infra-red spectrum showed that this was L-α-(2-formyl-3-methyl*cyclo*pentyl)-propional (X) (bands at 3·10 and 5·82 μ). The entire material was converted into the *bis*-2:4-*dinitrophenylhydrazone*, which formed orange prisms in ethyl acetate–ethanol, m.p. 228° (decomp.), undepressed on admixture with authentic iridodial bis-2:4-dinitrophenylhydrazone (Found: C, 50·3; H, 4·3; N, 21·1. $C_{22}H_{24}O_8N_8$ requires: C, 50·0; H, 4·5; N, 21·2%).

L(−)-Iso*iridomyrmecin* (XI)

(a) *From the fraction containing the alicyclic dialdehyde* (X). The above fraction, b.p. 70–72°/0·15 mm (2·22 g) was warmed with 2 N-potassium hydroxide solution (30 cc) for 1 hr under nitrogen Undissolved material was extracted with ether, the aqueous solution cooled in ice and acidified with 8 N-acetic acid (25 cc). The colourless precipitate was treated in the manner described for the corresponding experiment in the D-series. The lactone thus obtained (273 mg) crystallised from light petroleum as elongated colourless prisms, m.p. 57·5–58°, $[\alpha]_D^{26}$ −56° (*c*, 1·09 in CCl_4); the melting point was undepressed on admixture with genuine *iso*iridomyrmecin (kindly supplied by Dr. G. W. K. Cavill), which showed that our material was L-iso*iridomyrmecin* (Found: C, 71·7; H, 9·2. $C_{10}H_{16}O_2$ requires: C, 71·4; H, 9·5%). The infra-red spectrum was identical with that of its enantiomorph.

(b) *From* L-2:6-*dimethyloct*-2-*en*-1:8-*dial* (IX) *by Michael condensation.* A solution of the aliphatic dialdehyde (IX; 1·69 g) in anhydrous methanol (8 cc) was treated with 10 per cent methanolic sodium methoxide (1 cc) and worked up under the conditions described for the corresponding experiment in the D-series. The resulting lactone was identical with L(−)-*iso*-iridomyrmecin.

An equimolar mixture of D- and L-*iso*iridomyrmecin failed to crystallise from light petroleum, but after slow evaporation of the solvent long thread-like crystals were obtained, m.p. 32–34°, which had no measurable rotation.