THE CHEMISTRY OF ANTS

V. STRUCTURE AND REACTIONS OF DOLICHODIAL

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Summary

Dolichodial, isolated from *Dolichoderus acanthoclinea Clarki* (Wheeler), is shown to be α-(2-formyl-3-methylcyclopentyl)acraldehyde (I). The conversion of dolichodial into iridodial (II), and independently, into isoiridomyrmecin (X), establishes further relationships in the cyclopentanoid monoterpenes.

I. INTRODUCTION

The isolation of dolichodial and related compounds from various *Dolichoderus* and *Iridomyrmex* species of ants has been reported in Part IV of this series (Cavill and Hinterberger 1960). The determination of structure, and some reactions of dolichodial are now described.

Dolichodial, used in the present studies, has been extracted from *Dolichoderus acanthoclinea Clarki* (Wheeler). It is an almost colourless, strongly lachrymatory liquid, b.p. 96 °C/2 mm, $[\alpha]_D^{22\cdot5}$ −26°, and has been characterized by the formation of two derivatives, B and C, on treatment with 2,4-dinitrophenylhydrazine. Each of these products has been formulated as $C_{22}H_{22}N_8O_8$, whence the parent compound, $C_{10}H_{14}O_2$, has two carbonyl functions. Derivative B, m.p. 177 °C, has been converted into derivative C, m.p. 242 °C, on treatment with mineral acid (cf. Cavill and Hinterberger 1960).

II. ULTRAVIOLET AND INFRARED ABSORPTION DATA

Dolichodial has an absorption in the ultraviolet region at 223 mμ (ε 6950 in water), indicating the presence of an α- or a β-monosubstituted, αβ-unsaturated, aldehyde group. Comparably, crotonaldehyde has a band at 223 mμ (water). The infrared spectrum of dolichodial shows a strong band at 1725 cm^{-1}, and a medium band at 2720 cm^{-1}, attributable to the carbonyl group of an aliphatic aldehyde (cf. Bellamy 1958). Further, a strong band at 1690–1700 cm^{-1} and a medium band at 1633 cm^{-1} are characteristic of the carbonyl group, and the carbon–carbon double bond, of an αβ-unsaturated aldehyde. Rasmussen (1948) reports absorptions at 1695 and 1639 cm^{-1} for α-methylacraldehyde. Thus dolichodial may contain an isolated aldehyde group, and an αβ-unsaturated aldehyde group.

Dolichodial is a highly reactive compound which darkens rapidly on standing, and this deterioration is accompanied by the appearance of a band at 1757 cm^{-1} in the infrared spectrum. This process is to be examined in more detail.

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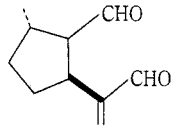
Typical carbonyl reagents do not appear to form simple derivatives with dolichodial. For example, the bis-derivatives with 2,4-dinitrophenylhydrazine, B and C, show an absorption ~360 mμ characteristic of a saturated 2,4-dinitrophenylhydrazone, but no absorption is shown ~380 mμ, which is characteristic of an αβ-unsaturated derivative. Attempts to prepare a disemicarbazone and a dithiosemicarbazone have been unsuccessful.

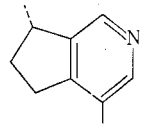
These difficulties emphasize a need for deactivation of the double bond, prior to the formation of carbonyl derivatives. Now, thiolacetic acid adds to the double bond of αβ-unsaturated aldehydes yielding the β-thiolacetate (Brown, Jones, and Pinder 1951). Dolichodial reacts with thiolacetic acid, giving a yellow oil with an absorption at 233 mμ (ε 5180), characteristic of the thiolacetate (cf. Cunneen 1947). Dolichodial thiolacetate is then characterized as a normal bis-2,4-dinitrophenylhydrazone, $C_{24}H_{26}N_8O_9S$.

III. Structure and Configuration of Dolichodial

Hydrogenation of dolichodial, in the presence of a palladium/barium sulphate catalyst, results in an uptake of one molar proportion of hydrogen, and the absorption at 223 mμ is reduced in intensity to 15% of that of the control. The reaction mixture gives an immediate precipitate with 2,4-dinitrophenylhydrazine, whence chromatography on alumina yields two products: a red derivative, m.p. 217 °C, and the major component, a yellow derivative, m.p. 228 °C. This compound does not depress the m.p. of an authentic specimen of iridodial bis-2,4-dinitrophenylhydrazone.



(I)



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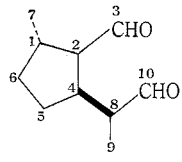
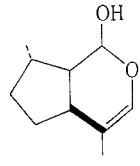


(II)



(III)

The conversion of dolichodial into iridodial (II) establishes the cyclopentanoid monoterpene skeleton, and as dolichodial has an absorption in the ultraviolet region at 223 mμ, it is assigned the monosubstituted acraldehyde structure (I). Dolichodial would have the same configuration as iridodial at the stable C_1 and C_4 centres.

On reaction with hydrochloric acid in acetic acid, each of the bis-2,4-dinitrophenylhydrazones, m.p. 217 and 228 °C, is converted into 1′,5-dimethyl-3,4-cyclopentenopyridine (IV), isolated as its picrate, m.p. and mixed m.p. 146 °C, with an authentic specimen (Cavill and Ford 1960). This transformation

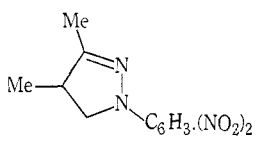
establishes that the newly isolated bis-derivative, m.p. 217 °C, is a stereoisomer of the known derivative, m.p. 228 °C, and differs in configuration at C_2 and/or C_8.

Ozonolysis of dolichodial, then decomposition of the ozonide with zinc dust in aqueous acetic acid, gives formaldehyde, isolated as the 2,4-dinitrophenylhydrazone. The remaining fragment/s have not been characterized satisfactorily, however, the isolation of formaldehyde, in 30% yield, confirms the α-acraldehyde structure (I), initially proposed on the basis of its light absorption data.

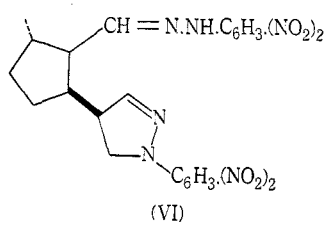
The infrared spectrum of dolichodial supports a 1,5-dialdehyde formulation (I), and in contrast to iridodial, there is little tendency for lactol tautomerism (cf. II⇌III). Indirectly, this observation would confirm the lactol structure (III) for iridodial, which requires enolization at C_8. This lactol (type III) was previously suggested as the tautomeric form of iridodial on conformational grounds (cf. Cavill and Ford 1960).

IV. Structure of Derivatives B and C

The bis-derivatives B and C, which have no absorption ~380 mμ for an αβ-unsaturated 2,4-dinitrophenylhydrazone, may be assigned pyrazoline structures on the basis of the acraldehyde structure (I) for dolichodial. The high intensity absorption ~360 mμ, shown by each of these derivatives, results from the 2,4-dinitrophenylhydrazone and the 2,4-dinitrophenylpyrazoline chromophores. Comparably, the pyrazoline (V) obtained from isopropenyl methyl ketone has an absorption at 360·5 mμ (Kawahara 1957). Thus derivative B is assigned structure (VI). It gives a green colour on treatment with bromine in chloroform, and this reaction is characteristic of pyrazolines (cf. Raiford and Peterson 1937). Derivative C, which is only slightly soluble in chloroform, gives a black crystalline solid. In contrast, no colour reaction has been observed for iridodial bis-2,4-dinitrophenylhydrazone.



(V)



(VI)

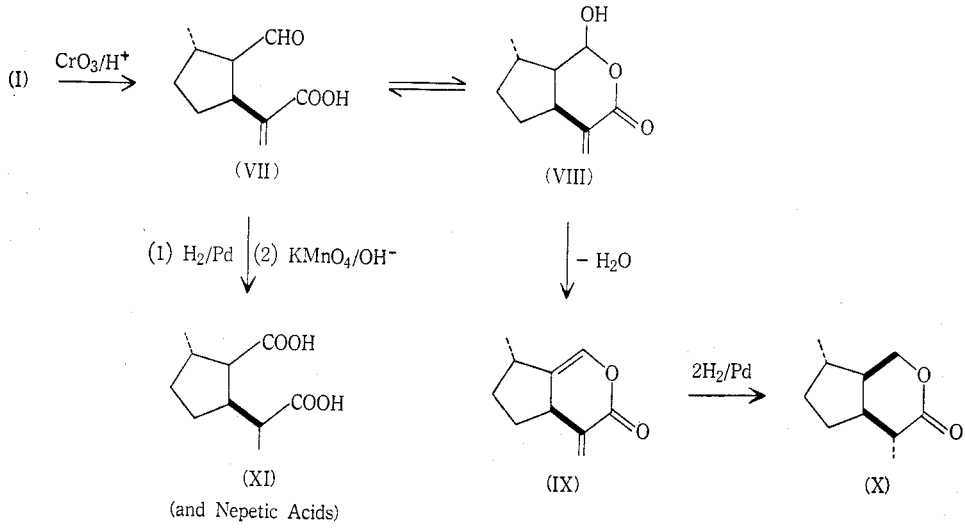
As derivative B is converted into derivative C, by the action of hydrochloric acid, and as each of these compounds has similar light absorption properties, it is possible that they are stereoisomers. Alternatively, the more complex infrared absorption spectrum of derivative C may indicate that it is a dimeric product, derived from B. Unfortunately, the highly insoluble nature of derivative C has prevented further investigation.

V. Oxidation, and Subsequent Transformations of Dolichodial

A mild oxidation of dolichodial with chromic acid/sulphuric acid in acetone (cf. Bowers *et al.* 1953) gives a yellow acidic oil, which has an absorption at 221 mμ (ε 20,400 in water), characteristic of an αβ-unsaturated acid. This product is

characterized as an orange 2,4-dinitrophenylhydrazone, $C_{16}H_{18}N_4O_6$, $\lambda_{max.}$ 370 mμ, which is soluble in sodium hydrogen carbonate solution. Thus the parent aldehydo-acid, $C_{10}H_{14}O_3$, is assigned structure (VII). A neutral fraction remained from the oxidation.

The aldehydo-acid (VII) readily absorbs 1·1M proportions of hydrogen, in the presence of a palladium catalyst, and the resultant aldehydo-dihydroacid/s then give a mixture of dicarboxylic acids, on oxidation with alkaline potassium permanganate solution. Paper chromatography indicates that this mixture contains the nepetalinic and nepetic acids. Esterification with diazomethane, followed by a microdistillation, and then saponification of a major fraction, yields a mixture of nepetalinic acids. These acids could not be resolved.



The neutral fraction, isolated during the original chromic acid oxidation of dolichodial, does not give a derivative with 2,4-dinitrophenylhydrazine. In the presence of a palladium catalyst, it absorbs 2·1M proportions of hydrogen, yielding isoiridomyrmecin, identical with an authentic specimen from *I. nitidus* (Cavill and Locksley 1957).

These oxidation and reduction sequences, which result in the conversion of dolichodial into isoiridomyrmecin (X), and separately, into the nepetalinic acids (XI), establish new relationships in the cyclopentanoid monoterpenes. Moreover, they support the assignment of structure (VII) to the aldehydo-acid, which is the primary oxidation product of dolichodial, whence the neutral product may be assigned structure (IX), resulting from a dehydration of the lactol form (VIII) of the aldehydo-acid.

VI. Experimental

Melting points are uncorrected. Light petroleum has b.p. 40–60 °C. Alumina refers to aluminium oxide, "Peter Spence, grade H." Solvent extracts were dried over anhydrous magnesium sulphate. Microanalyses are by Dr. E. Challen of this University. and by Dr. K. W. Zimmerman and assistants, C.S.I.R.O. and University of Melbourne Microanalytical Laboratory. Infrared spectra are by Mr. I. Reece of this University.

(*a*) *Isolation of Dolichodial.*—Dolichodial has been obtained from the light petroleum extract of *Dolichoderus acanthoclinea clarki* as previously reported (Part IV loc. cit.). It is an almost colourless, lachrymatory liquid, b.p. 96 °C/2 mm, n_D^{23} 1·4792, $[\alpha]_D^{22\cdot5}$ —26° (*c*, 4·36 in benzene).

(*b*) *Spectroscopic Data.*—(i) The crude extract has an ultraviolet absorption at 223 mμ (in water). Freshly distilled dolichodial has an absorption at 223 mμ (ε 6950 in water), and comparably, acraldehyde has $\lambda_{max.}$ 212 mμ, and crotonaldehyde has $\lambda_{max.}$ 223 mμ.

(ii) Freshly distilled dolichodial has the following infrared absorptions (liquid capillary)*: 3400w, 3092w, 2930s, 2860s, 2720m, 1725s, 1690s, 1633m, 1460m, 1392sh, 1375m, 1332sh, 1305m, 1247m, 1228m, **1172m**, 1140w, **1135w**, 1113m, 1078m, 1042m, 1014w, 1008w, 952m cm^{-1}. In carbon tetrachloride: 3365w, 2930s, 2860m, 2820m, 2730m, 1757sh, 1725s, 1700s cm^{-1}.

A specimen of dolichodial, kept at 2 °C, for 4 weeks, has bands (liquid capillary): 3470w, 2930s, 2860s, 2727m, 1745s, 1730sh, 1700s, 1640m, 1464m, 1380m, 1357w, 1330w, 1305m, 1285w, 1250m, 1173m, 1160m, 1132m, 1110m, 1054m, 1036m, 1016w, 988m, 950m, 812w, 723w cm^{-1}. In carbon tetrachloride: 2920s, 2860m, 2730m, 1757s, 1725m, 1700m cm^{-1}.

(*c*) *Biscarbonyl Derivatives.*—(i) The preparation of derivative B, m.p. 177 °C, $\lambda_{max.}$ 362 mμ (ε 38,000 in ethanol) and of derivative C, m.p. 242 °C, $\lambda_{max.}$ 358 mμ (ε 46,000 in chloroform), has been described previously (Part IV loc. cit.).

(ii) Attempts at the preparation of a disemicarbazone gave a colourless gum. The attempted preparation of the dithiosemicarbazone yielded a white amorphous solid, with absorptions at 275 mμ (ε 27,400), and at 300 mμ (ε 13,100), characteristic of an isolated, and an αβ-unsaturated, thiosemicarbazone (cf. Gillam and Stern 1957). The product could not be purified, and each attempt at recrystallization from ethanol resulted in a reduction in the intensity of the band at 300 mμ.

(*d*) *Reaction of Dolichodial with Thiolacetic Acid.*—Dolichodial (300 mg) was treated with thiolacetic acid (0·35 ml) at room temperature (18 hr), then the acid in excess was removed by distillation (at 40 °C/2 mm), and the residual oil extracted with ether. This extract was washed with saturated sodium hydrogen carbonate solution, water, and dried. Evaporation of the solvent gave the *thiolacetate*, as a viscous liquid (450 mg), $\lambda_{max.}$ 233 mμ (ε 5180 in ethanol).

The crude thiolester (300 mg) gave a liquid derivative, on treatment with 2,4-dinitrophenylhydrazine sulphate solution, which was extracted into chloroform, and purified by chromatography on alumina. *Dolichodial thiolacetate bis-2,4-dinitrophenylhydrazone* was finally isolated as yellow needles (30 mg), m.p. 93 °C, from benzene (Found: C, 48·1; H, 4·6; N, 17·9; S, 4·8%. Calc. for $C_{24}H_{26}N_8O_9S$: C, 47·7; H, 4·3; N, 18·6; S, 5·3%).

Treatment of crotonaldehyde, as described above, gave a yellow thiolacetate, $\lambda_{max.}$ 232 mμ (ε 6050), which was converted into the 2,4-dinitrophenylhydrazone, m.p. 93 °C. Brown, Jones, and Pinder (1951) report m.p. 95 °C.

(*e*) *Hydrogenation.*—Freshly distilled dolichodial (245 mg) in ethanol (7 ml) was hydrogenated in the presence of a palladium catalyst (100 mg, from 5% palladium oxide on barium sulphate) at r.t.p, and 38 ml of hydrogen (1·1M proportion) was consumed (30 min). Removal of the catalyst, and evaporation of the solvent, gave a pale yellow oil (250 mg), $\lambda_{max.}$ 223 mμ (ε 1080; that is, 15% of the intensity of the control).

An alcoholic solution of the reduction product (240 mg), on treatment with 2,4-dinitrophenylhydrazine reagent, gave an orange precipitate (562 mg), which was purified by chromatography on alumina. Derivative B (5 mg), m.p. and mixed m.p. 177 °C, and derivative C (15 mg), m.p. and mixed m.p. 242 °C, were eluted with benzene, then a red *compound* (39 mg), m.p. 217 °C, and a yellow compound (94 mg), m.p. 228 °C, were obtained. The latter product does not depress the m.p. of iridodial bis-2,4-dinitrophenylhydrazone (Found: C, 49·9; H, 4·5; N, 20·9%. Calc. for $C_{22}H_{24}N_8O_8$: C, 50·0; H, 4·6; N, 21·2%).

Each of the derivatives, m.p. 217 and 228 °C, was converted into 1′,5-dimethyl-3,4-cyclopentenopyridine, $\lambda_{max.}$ 262 and 269 mμ, and the base isolated as the picrate, m.p. and mixed m.p. 146 °C, with an authentic specimen (Found: C, 50·9; H, 4·0; N, 14·5%. Calc. for $C_{16}H_{16}N_4O_7$: C, 51·1; H, 4·3; N, 14·9%).

* Bands are characterized as s, strong; m, medium; w, weak; sh, shoulder.

(*f*) *Ozonolysis.*—A mixture of ozone and oxygen was passed through a solution of dolichodial (430 mg) in dry ethyl acetate (30 ml), at —30 °C (15 min). The reaction mixture was slowly added (1 hr) to a cooled, well-stirred, suspension of zinc powder (2 g) in acetic acid (50 ml ; 50%). Evaporation of the solvent (at 40 °C/40 mm), then removal of the excess of zinc, gave a pale yellow solution, which was treated with an excess of 2,4-dinitrophenylhydrazine reagent. The gummy red product (775 mg) was purified by chromatography on alumina, the major constituent, formaldehyde 2,4-dinitrophenylhydrazone (151 mg), m.p. and mixed m.p. 165 °C, being eluted with light petroleum (Found : C, 40·3 ; H, 3·0 ; N, 26·4%. Calc. for $C_7H_6N_4O_4$: C, 40·0 ; H, 2·9 ; N, 26·7%).

Benzene eluted derivative B (10 mg), m.p. and mixed m.p. 177 °C, then benzene/chloroform (1/1) eluted derivative C (16 mg), m.p. and mixed m.p. 242 °C. The residual products, from the chloroform eluate, were rechromatographed giving a dark red compound (5 mg), m.p. 212 °C, as hexagonal plates from benzene. A second product (7 mg), m.p. 81 °C, was obtained as yellow needles from light petroleum/benzene. These products have not been identified.

(*g*) *Chromic Acid Oxidation, and Subsequent Reactions.*—(i) A solution of dolichodial (540 mg) in acetone (10 ml) was treated with chromic acid (2·5 ml of a standard solution, prepared by the method of Djerassi, Engle, and Bowers (1956)). The reaction mixture, after standing at room temperature (3 hr), was diluted with water, and then extracted with ether. An acidic product was extracted from the ethereal layer with sodium hydrogen carbonate solution (4 × 10 ml), and a neutral fraction (188 mg) remained, which had a positive reaction with 2,4-dinitrophenylhydrazine. This fraction was reoxidized with chromic acid (6 hr), and then worked up as described above. The neutral fraction, which now remained (100 mg, 18%), does not give a positive test for carbonyl compounds.

The combined sodium hydrogen carbonate extracts gave a yellow acidic oil (296 mg, 50%), which could not be crystallized. It has an absorption at 221 mμ (ε 20,400 in water). This acidic mixture, on treatment with 2,4-dinitrophenylhydrazine, gave an orange product, in 65% yield, which was purified via its sodium salt. This *2,4-dinitrophenylhydrazone* of the aldehydo-acid (VII) was finally isolated as orange needles, m.p. 196–197 °C, $\lambda_{max.}$ 370 mμ, from benzene (Found : C, 52·7 ; H, 5·0%. Calc. for $C_{16}H_{18}N_4O_6$: C, 53·0 ; H, 5·0%).

(ii) The aldehydo-acid mixture (210 mg) in ethanol (10 ml) was hydrogenated, as described above, 28 ml (1·1M proportion) of hydrogen being taken up (10 min). Removal of the catalyst, and evaporation of the solvent, gave a pale yellow acidic gum (210 mg), which showed no absorption between 215–260 mμ. Attempts at crystallization of these acid/s were unsuccessful, in addition, they did not give a solid derivative with 2,4-dinitrophenylhydrazine.

(iii) The aldehydo–dihydro–acid mixture (200 mg), from (ii), was oxidized with potassium permanganate (160 mg), in aqueous sodium hydroxide solution (5 ml ; 5%) at room temperature (18 hr). After working up the reaction mixture in the normal manner, an acidic oil (180 mg) was obtained, which on paper chromatography, employing an ethanol–ammonia–water (85 : 5 : 15) system, showed the presence of at least two nepetalinic acids, R_F values 0·63 and 0·62, and one nepetic acid, R_F 0·49. Reference compounds, run in the same chromatogram, were the *cis,trans*-nepetalinic acid, m.p. 82 °C, which has an R_F value 0·62, and the *cis,trans*-nepetic acid, which has R_F 0·49 (see Cavill and Ford 1960).

This acid mixture (100 mg) was esterified with diazomethane, and the major fraction, a colourless ester (30 mg), b.p. 90–100 °C/2 mm, separated by a microdistillation. Saponification of this ester fraction gave a colourless acidic oil (16 mg) (Found : equiv. wt, 100·0. Calc. for $C_{10}H_{16}O_4$: equiv. wt, 100·0).

(iv) The neutral product (60 mg), formed during the initial chromic acid oxidation of dolichodial, in (i), on hydrogenation, as above, consumed 20 ml (2·1M proportions) of hydrogen (15 min). A colourless oil (40 mg) was obtained, which on sublimation yielded isoiridomyrmecin, finally isolated as colourless needles, m.p. 56 °C, from light petroleum. The m.p. was undepressed on admixture with an authentic specimen from *I. nitidus* (Cavill and Locksley 1957).

VII. Acknowledgment

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VIII. References

BELLAMY, L. J. (1958).—" Infrared Spectra of Complex Molecules." 2nd Ed. (Methuen & Co.: London.)

BOWERS, A., HALSALL, T. G., JONES, E. R. H., and LEMIN, A. J. (1953).—*J. Chem. Soc.* **1953**: 2548.

BROWN, R., JONES, W. E., and PINDER, A. R. (1951).—*J. Chem. Soc.* **1951**: 2123.

CAVILL, G. W. K., and FORD, D. L. (1960).—*Aust. J. Chem.* **13**: 296.

CAVILL, G. W. K., and HINTERBERGER, Hertha (1960).—*Aust. J. Chem.* **13**: 514.

CAVILL, G. W. K., and LOCKSLEY, H. D. (1957).—*Aust. J. Chem.* **10**: 352.

CUNNEEN, J. I. (1947).—*J. Chem. Soc.* **1947**: 134.

DJERASSI, C., ENGLE, R. R., and BOWERS, A. (1956).—*J. Org. Chem.* **21**: 1547.

GILLAM, A. E., and STERN, E. S. (1957).—" An Introduction to Electronic Absorption Spectroscopy." 2nd Ed. (Edward Arnold Ltd.: London.)

KAWAHARA, F. K. (1957).—*J. Amer. Chem. Soc.* **79**: 1448.

RAIFORD, R. C., and PETERSON, W. J. (1937).—*J. Org. Chem.* **1**: 544.

RASMUSSEN, R. S. (1948).—*Fortschr. Chem. Org. Naturst.* **5**: 331.