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THE CONVERSION OF D-ISOIRIDOMYRMECIN INTO D-IRIDOMYRMECIN

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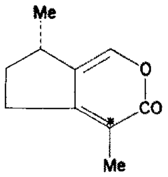
THE two iridolactones iridomyrmecin and isoiridomyrmecin are represented by the structure (I), the position α to the lactone carbonyl being epimerizable, but the configuration at this asymmetric centre (marked by an asterisk) has not yet been assigned. Previous work[1,2] indicates, however, that the configuration corresponding to isoiridomyrmecin appears to be the more stable of the two, since 83 per cent conversion into this epimer has been obtained by treatment of iridomyrmecin with alcoholic alkali.



I

A polarimetric examination[2] of the epimerization of isoiridomyrmecin with sodium ethoxide in absolute ethanol revealed a complex reaction and led to the conclusion that the equilibration gave a 14 per cent conversion into iridomyrmecin, which complements the 83 per cent conversion of iridomyrmecin $[\alpha]_D^{20}$ + 210° into isoiridomyrmecin $[\alpha]_D^{24}$ - 59°. From this equilibrated mixture only isoiridomyrmecin was isolated. Thus the epimerization of isoiridomyrmecin into iridomyrmecin and isolation of the latter from the reaction mixture had still to be accomplished and the present report described a method by which this was achieved.

The synthesis of D- and L-isoiridomyrmecin from D- and L-citronellal respectively has been described.[3] The latter was shown to be identical with the natural product isolated from the ant *Iridomyrmex nitidus*. D-Isoiridomyrmecin, however, is much more readily available, since D-citronellal is a commercial product and accordingly was used in preference to the L-isomer.

D-Isoiridomyrmecin $[\alpha]_D^{28}$ + 60° was refluxed for 48 hr with quinoline. The liquid reaction product had $[\alpha]_D^{27}$ - 41° which represents a 37.5 per cent conversion into iridomyrmecin. The equilibrated mixture was separated at a low temperature by crystallization from light petroleum into two portions of approximately equal weight: (i) a material which was crystalline at

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[1] R. Fusco, R. Trave and A. Vercellone, *Chim. e Industr.* **37**, 251 (1955).

[2] G. W. K. Cavill and H. D. Locksley, *Aust. J. Chem.* **10**, 352 (1957).

[3] K. J. Clark, G. I. Fray, R. H. Jaeger and Sir Robert Robinson, *Angew. Chem.* **70**, 704 (1958); *Tetrahedron* **6**, 217 (1959).

-15° but was liquid at toom temperature $[\alpha]_D^{27}$ -23°; (ii) a liquid recovered from the mother liquor, $[\alpha]_D^{27}$ -65°. This specific rotation corresponds to 46 per cent iridomyrmecin being present in this fraction. A solution of the material in light petroleum was chromatographed on neutral alumina; arbitrary fractions were collected and the rotation of each eluate was determined. It was found that although no clear-cut separation of the two epimers could be effected in this way, light petroleum eluated material containing a high proportion of iridomyrmecin. By repeating the chromatography with the fractions having the highest negative rotation, pure D-iridomyrmecin, m.p. 61-62°, $[\alpha]_D^{29}$ -207° was eventually obtained. The infra-red spectrum of this material was

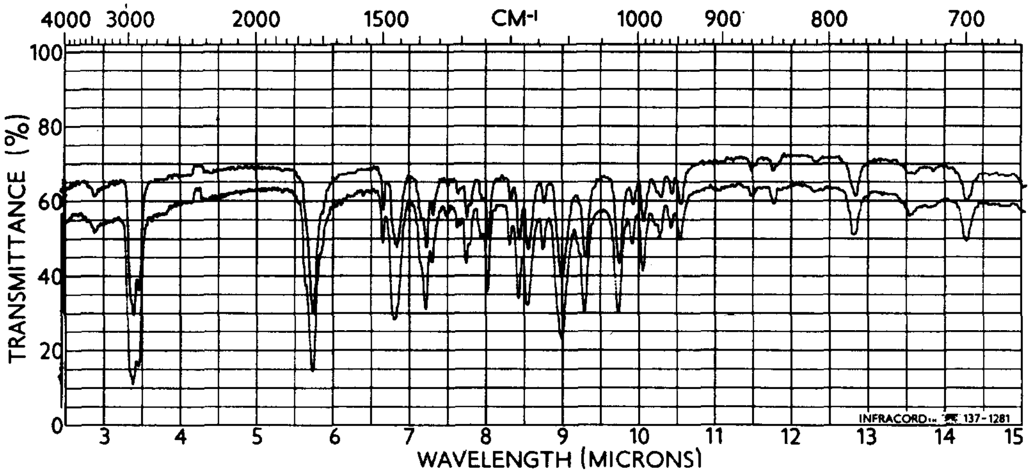

FIG. 1. Top: D-Iridomyrmecin (synthetic)

Bottom: L-Iridomyrmecin (natural).

indistinguishable from that of its enantiomorph, the natural product L-iridomyrmecin, m.p. 61-62°, $[\alpha]_D^{20}$ + 210° [1] (cf. Fig. 1).

With the completion of this work it has now been demonstrated that the three terpenoid compounds isolated from various Iridomyrmex ants, i.e. iridomyrmecin, isoiridomyrmecin and iridodial, can be synthesized from citronellal.

A racemic mixture prepared by crystallizing equal weights of D- and L-iridomyrmecin from light petroleum had m.p. 59.5° and no measurable rotation.

Experimental

Infra-red spectra of D- and L-iridomyrmecin were determined in Nujol mulls. Light petroleum without specification means the fraction of b.p. 40-60°. Ethereal extracts were dried over anhydrous magnesium sulphate. Rotations were determined at c, 1.0 in CCl_4.

Epimerization of D-isoiridomyrmecin. D-Isoiridomyrmecin $[\alpha]_D^{28}$ + 60° (1.42 g) was refluxed with quinoline (70 cc) for 48 hr in an atmosphere of nitrogen. The reaction mixture was poured into hydrochloric acid internally cooled with crushed ice. The product was collected in ether, the ethereal layer washed successively with water, aqueous sodium hydrogen carbonate and water. The dried extract was freed from solvent and the residue evaporatively distilled at 80-90°/0.4 mm (bath temperature). The colourless oil (1.39 g), $[\alpha]_D^{27}$ -41° solidified at -15°; a little light petroleum was added and the material allowed to dissolve almost completely at room temperature. When only a few crystals remained undissolved the mixture was again chilled at -15° which caused crystallization of part of the product. The supernatant solution was removed with a pipette, and the solvent evaporated. The crystalline material (695 mg) melted at room temperature and had $[\alpha]_D^{27}$ -23°. The residue recovered from the mother liquor was a liquid (696 mg), $[\alpha]_D^{27}$ -65°.

A solution of the latter material in a little light petroleum was adsorbed on neutral alumina (75 g); the same solvent eluted some impure material (15 mg), followed by crystalline material (77 mg), $[\alpha]_D^{28}$ -192°; light petroleum (b.p. 60-80°) eluted more crystalline material (68 mg), $[\alpha]_D^{28}$ -152°; a 4:1 mixture of light petroleum (b.p. 60-80°) - benzene eluted a yellow oil (206 mg), $[\alpha]_D^{28}$ -96°; the material eluted with benzene was a crystalline solid (55 mg), $[\alpha]_D^{28}$ + 12°. The crystalline portions possessing the highest negative rotations were united and re-chromatographed to yield D-iridomyrmecin (76 mg) which crystallized from light petroleum (b.p. 30-40°) as beautiful elongated colourless prisms, m.p. 61-62°, $[\alpha]_D^{29}$ -207° (Found: C, 71.7; H, 9.7. $C_{10}H_{16}O_2$ requires C, 71.4; H, 9.5%). The infra-red spectrum of this compound was absolutely indentical with that of natural L-iridomyrmecin (kindly provided by Professor M. Pavan), m.p. 61.5 - 62.5° $[\alpha]_D^{20}$ + 210° (cf. Fig. 1).

D,L-Iridomyrmecin. A sample prepared by crystallizing a mixture of equal weights of D- and L-iridomyrmecin from light petroleum had m.p. 59.5° and no measurable rotation. This accords with the results of Korte *et al.*[4] who ascribe the m.p. 59° to synthetic DL-iridomyrmecin.

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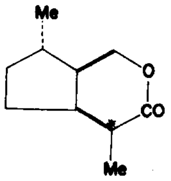
[4] F. Korte, J. Falbe and A. Zschocke, Tetrahedron 6, 201 (1959).

ERRATUM

R. H. Jaeger and Sir Robert Robinson, The conversion of D-isoiridomyrmecin into D-iridomyrmecin, Tetrahedron Letters No. 15, 14-18 (1959).

An unfortunate error occurred in the publication of formula I on p. 14 of the above article. The correct formula is reproduced below.



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