950. *The Relation between Dextro- and* iso*Dextro-pimaric Acid.*

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Dextro- and *iso*dextro-pimaric acid have been shown to be epimeric at positions 7 and 13.*

THE structures of dextro- and *iso*dextro-pimaric acid have been well established,[2,3] together with the stereochemistry at positions 1, 11, and 12 which is identical with that of abietic acid [2] as in (I). Neither the relative nor the absolute configurations at positions 7 and 13 in these acids have been defined unequivocally although this is a problem not only of chemical but also of possible biogenetic significance (cf. Wenkert [4]).

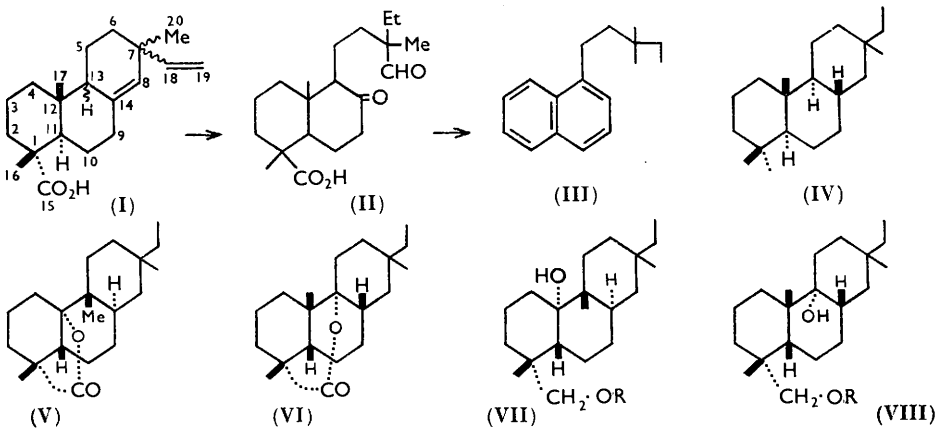
Harris and Sanderson [2] converted dihydrodextropimaric acid into the keto-aldehyde (II), by ozonolysis, and thence by reduction and dehydrogenation into the hydrocarbon (III) which was also obtained from dihydro*iso*dextropimaric acid by the same reactions. These results were construed as proof that dextro- and *iso*dextro-pimaric acid are epimeric

* Some of this work have been the subject of a preliminary communication.[1]

[1] Green, Harris, and Whalley, *Chem. and Ind.*, 1958, 1084.
[2] Harris and Sanderson, *J. Amer. Chem. Soc.*, 1948, **70**, 2081.
[3] Simonsen and Barton, " The Terpenes," Cambridge Univ. Press, London, 1952, Vol. III, p. 447.
[4] Wenkert, *Chem. and Ind.*, 1955, 284.

at position 7, but are equally compatible with the view that the two precursors of (III) are epimeric at position 13,[4] or as we indicate below, at both these positions.*

Dihydro*iso*dextropimaric acid (infrared absorption at 825 cm.$^{-1}$; >C=CH–) is converted by concentrated sulphuric acid into a mixture of a γ-lactone (infrared absorption at 1773 cm.$^{-1}$) and a δ-lactone (infrared absorption at 1724 cm.$^{-1}$) which are formulated as 12α-hydroxy-13β-methyl-12-nor-11β-7-*allo*pimaran-15-oic lactone (V) and 13-hydroxy-11β-7-*allo*pimaran-15-oic lactone (VI) respectively, by analogy with the corresponding products derived from dihydrodextropimaric acid.[6]



Collateral evidence in support of structures (V) and (VI) and hence for the analogous, similarly derived γ- and δ-lactones of dihydrodextropimaric acid [6] is provided by the reduction of the δ-lactone (VI) with lithium aluminium hydride to 11β-7-*allo*pimarane-13 : 15-diol (VIII; R = H) which, in accordance with this formula, furnishes a monoacetate (VIII; R = Ac) which has infrared absorption (in Nujol) at 3534 (OH) and 1724 cm.$^{-1}$ (acetate). The γ-lactone (V) similarly furnishes the diol (VII; R = H) which in turn yields a monoacetate (VII; R = Ac) with infrared absorption (in Nujol) at 3436 (OH) and 1721 cm.$^{-1}$ (acetate).

The formation of these two lactones which differ from the corresponding γ- and δ-lactones derived from dihydrodextropimaric acid, under similar conditions during which the stereochemistry at all centres except $C_{(1)}$ and $C_{(7)}$ may be disturbed, indicates that dextro- and *iso*dextro-pimaric acid are epimeric at least at position 7,† and that pimara- and 7-*allo*pimara-8(14) : 18-dienes occur naturally [7-*allo*pimara-9(14) : 18-dien-15-oic acid [7,9] belongs to the same $C_{(7)}$-series], and thus the hypothesis [4] that only pimara-8(14) : 18-dienes having quasi-axial vinyl groups occur naturally is untenable.

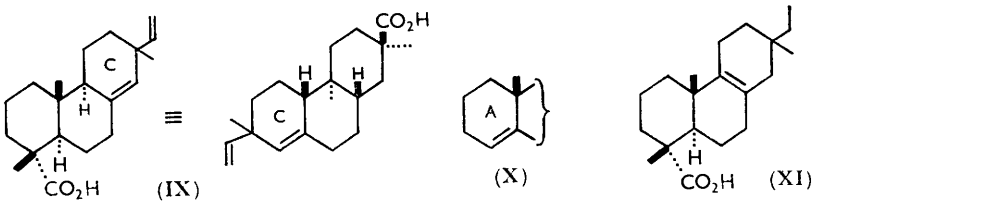
The well-established stability of dextropimaric acid to mineral acids [10] indicates that the 12-methyl group and the 13-hydrogen atom are *trans* to one another as in (IX). This conclusion has been substantiated by molecular-rotational data.[5] In addition, if dextropimaric acid is correctly represented by (IX) ring C of this acid must be analogous to ring A

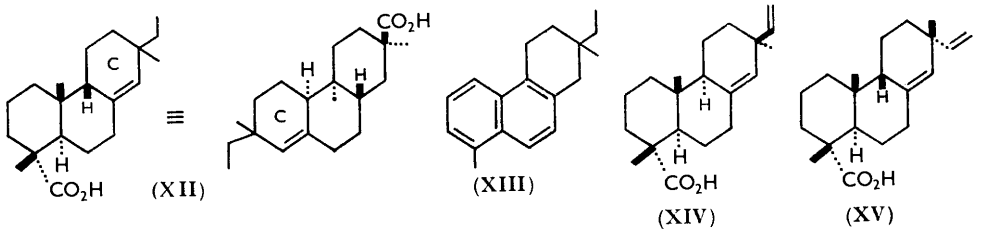
* For nomenclature Klyne's suggestions [5] have been modified and the name pimarane is now allocated to the hydrocarbon (IV) which has the same configuration at position 7 as dextropimaric acid, whilst the hydrocarbon (IV), having the epimeric configuration at position 7, *i.e.*, as in *iso*dextropimaric acid, is called 7-*allo*pimarane. We are indebted to the Editor for helpful comment on these proposals.

† Preliminary communications by Edwards and Howe,[7] and by Wenkert and Chamberlin [8] published during the preparation of this manuscript confirm our conclusion.

[5] Klyne, *J.*, 1953, 3072.
[6] Le Van Thoi and Ourgaud, *Bull. Soc. chim. France*, 1956, 202.
[7] Edwards and Howe, *Chem. and Ind.*, 1958, 629.
[8] Wenkert and Chamberlin, *J. Amer. Chem. Soc.*, 1958, **80**, 2912.
[9] Ukita, Tsumita, and Utsugi, *Pharm. Bull.* (*Japan*), 1955, **3**, 441.
[10] Ref. 4, p. 448 and references therein.

of cholest-4-ene (X) (cf. Klyne [5] and Djerassi *et al.*[11]) which has a positive Δ(C:C) value, *viz.*, (+240°) − (+91°) = +149°. Dihydrodextropimaric acid has a small but positive Δ(C:C) value = (+60°) − (+55°) = +5°, confirming the structure (IX).





When treated with dilute hydrochloric acid under conditions of much less severity than those which do not isomerise dextropimaric acid,[12] dihydro*iso*dextropimaric acid readily yields 7-*allo*pimar-13(14)-en-15-oic acid (XI), which is devoid of infrared absorption at 825 cm.$^{-1}$ (absence of >C=CH−), may be formed more readily by use of toluene-*p*-sulphonic acid in benzene, and is lactonised to the γ-lactone (V). Similarly, *iso*dextropimaric acid furnishes 7-*allo*pimara-13(14) : 18-dien-15-oic acid which is hydrogenated to (XI). The ease of transformation of dihydro*iso*dextropimaric acid to 7-*allo*pimar-13(14)-en-15-oic acid (XI) indicates that dextro- and *iso*dextro-pimaric acid are epimeric at position 13, and thus in *iso*dextropimaric acid the 12-methyl group and the 13-hydrogen atom are *cis* to one another as in (XII). The molecular-rotational evidence supports this thesis.

The contribution of $C_{(7)}$ to the molecular rotation is negligible, as is apparent from, *inter alia*, (*a*) the close similarity of the $[M]_D$ values for dextropimar-13(14)-en-15-oic acid (+224°) and *iso*dextropimar-13(14)-en-15-oic acid (+234°), (*b*) the very similar $[M]_D$ values for tetrahydrodextropimaric acid (+55°) and for tetrahydro*iso*dextropimaric acid (+73°), (*c*) the almost identical $\Delta[M]_D$ values, *viz.*, (+234°) − (−43°) = 277°, and (+221°) − (−52°) = 273°, for the conversion of dextropimar-13(14)-en-15-oic acid and *iso*dextropimar-13(14)-en-15-oic acid into the respective γ-lactones (V), and (*d*) the $\Delta[M]_D$ values, *viz.*, (+234°) − (−121°) = +355°, and (+221°) − (−137°) = + 358°, for conversion of the same pair of acids into the corresponding δ-lactones (VI).

Thus, when considering the molecular-rotational data for dextro- and *iso*dextropimaric acid it may be regarded as established that the contribution of $C_{(7)}$ is negligible and since the stereochemistry at positions 1, 11, and 12 is identical any significant variation from the expected values may be attributed to stereochemical differences at position 13. Thus $\Delta[M]_D$ for the conversion of dihydro*iso*dextropimaric acid into the γ-lactone (V) = (−16°) − (−43°) = +27°, and into the δ-lactone (VI) $\Delta[M]_D$ = (−16°) − (−122°) = +106°, whilst the figures for the conversion of dihydrodextropimaric acid into the γ-lactone (V) are (+60°) − (−52°) = +112° and into the δ-lactone (VI) are (+60°) − (−137°) = +197°. These results strongly indicate that the configurations at position 13 in dihydrodextro- and in dihydro*iso*dextro-pimaric acid are not identical, *i.e.*, the acids are epimeric. Additional evidence for this view is afforded by the fact that if dihydro*iso*dextropimaric

[11] Djerassi, Riniker, and Riniker, *J. Amer. Chem. Soc.*, 1956, **78**, 6362.
[12] Vesterberg, *Ber.*, 1886, **19**, 2167.

acid is correctly represented by (XII) then the surroundings of the double bond in ring C are enantiomeric to those in ring A of cholest-4-ene (X) (cf. Klyne [5]) which has $\Delta(C{:}C) = +149°$. Using tetrahydro*iso*dextropimaric acid [7] as the saturated reference compound we have $\Delta(C{:}C)$ in dihydro*iso*dextropimaric acid $= (-16°) - (+73°) = -89°$, a result which substantiates the stereochemistry (XII) for dihydro*iso*dextropimaric acid and hence for *iso*dextropimaric acid.

From surface-tension measurements Bruun [13] concluded that dextro- and *iso*dextropimaric acid are epimeric at position 7 and that the vinyl residues are probably quasi-axial and quasi-equatorial respectively. Although these results were calculated on the basis of the *trans-anti-trans* arrangement of rings A, B, and C in *iso*dextropimaric acid models indicate that his conclusions would probably not be invalidated by its formulation as (XII). Consequently dextro- and *iso*dextro-pimaric acid may be provisionally allocated the absolute configurations (XIV) and (XV) respectively.

By partial dehydrogenation of dextro- and *iso*dextro-pimaric acid Harris and Sanderson [2] obtained the hydrocarbon (XIII) in small quantity and claimed that the products from the two sources were identical. The hydrocarbons had zero rotation and thus racemisation at position 7 was assumed to have occurred during dehydrogenation. Racemisation of a quaternary centre such as this under these conditions cannot be accepted and in view of the foregoing considerations it is most probable that the hydrocarbons (XIII) derived from dextro- and *iso*dextro-pimaric acid are *not* identical but are enantiomeric and have very small molecular rotations.

Experimental

*Lactonisation of Dihydro*iso*dextropimaric Acid.*—A solution of dihydro*iso*dextropimaric acid (0·5 g.), $[\alpha]_D^{18}$ −5°, in concentrated sulphuric acid (5 ml.) was kept at room temperature for 15 min., then poured on ice. After isolation with ether, the extract was washed with 2N-sodium hydroxide and with water, dried, and evaporated to an oil (0·4 g.), $\nu_{max.}$ 1724 and 1773 cm.$^{-1}$. Purification from methanol gave 12α-*hydroxy*-13β-*methyl*-12-*nor*-11β-7-allo-*pimaran*-15-*oic lactone* in prisms (200 mg.), m. p. 108°, $[\alpha]_D$ −14° (Found: C, 78·9; H, 10·6. $C_{20}H_{32}O_2$ requires C, 78·9; H, 10·6%). Harris and Sanderson [2] record m. p. 109—110° for an uncharacterised lactone which is probably identical with our preparation, derived from dihydro-*iso*dextropimaric acid.

Reduction of this lactone (0·04 g.) in boiling ether (25 ml.) containing lithium aluminium hydride (0·1 g.) during 10 hr. furnished 13β-methyl-12-nor-11β-7-*allo*pimarane-12α : 15-diol which formed prisms (0·02 g.), m. p. 184°, from ethyl acetate. Prepared by the action of acetic anhydride–pyridine at room temperature during 10 hr., 15-*acetoxy*-13β-*methyl*-12-*nor*-11β-7-allo*pimaran*-12α-*ol* separated from aqueous methanol in prisms, m. p. 84° (Found: C, 74·8; H, 10·7. $C_{22}H_{38}O_3$ requires C, 75·4; H, 10·9%).

The mother-liquors from the purification of the γ-lactone (V) contained a δ-lactone which was more readily obtained when a solution of dihydro*iso*dextropimaric acid (500 mg.) in concentrated sulphuric acid (10 ml.) was kept at room temperature during 24 hr. Isolated in the usual manner and purified from aqueous methanol or light petroleum (b. p. 40—60°) at 0°, 13-*hydroxy*-11β-7-allo*pimaran*-15-*oic lactone* formed prisms (300 mg.), m. p. 62°, $[\alpha_D^{18}]$ −37°, readily soluble in organic solvents (Found: C, 78·5; H, 10·6. $C_{20}H_{32}O_2$ requires C, 78·9; H, 10·6%).

Reduction of this lactone (0·14 g.) in boiling ether (25 ml.) containing lithium aluminium hydride (0·2 g.) during 16 hr. furnished 11β-7-allo*pimarane*-13 : 15-*diol* which separated from ethyl acetate in needles (0·08 g.), m. p. 142° (Found: C, 77·7; H, 11·7. $C_{20}H_{36}O_2$ requires C, 77·9; H, 11·8%). Formed by the action of acetic anhydride–pyridine at room temperature during 24 hr., 11β-15-*acetoxy*-7-allo*pimaran*-13-*ol* separated from aqueous methanol in prisms, m. p. 83° (Found: C, 74·6; H, 10·7. $C_{22}H_{38}O_3$ requires C, 75·4; H, 10·9%).

7-allo*Pimar*-13(14)-*en*-15-*oic Acid.*—(*a*) A solution of *iso*dextropimaric acid (0·5 g.) in benzene (20 ml.) containing toluene-*p*-sulphonic acid (25 mg.) was refluxed for 1 hr., cooled, washed with water, dried, and evaporated, to furnish 7-allo*pimar*-13(14) : 18-*dien*-15-*oic acid* which separated from aqueous methanol in needles, or from aqueous acetic acid in prisms (0·5 g.), m. p. 118°, $[\alpha]_D^{19}$ +58° (Found: C, 79·0; H, 10·6. $C_{20}H_{30}O_2$ requires C, 79·4; H, 10·0%).

[13] Bruun, *Acta Acad. Aboensis, Math. Phys.*, 1954, **19**, (3), 7.

Hydrogenation of 7-*allo*pimara-13(14) : 18-dien-15-oic acid (0·4 g.) in methanol (50 ml.) containing platinic oxide (0·05 g.) was complete in 20 min., and 7-allo*pimar*-13(14)-*en*-15-*oic acid* separated from aqueous methanol in prisms (0·4 g.), m. p. 110°, $[\alpha]_D^{20}$ +60° (Found: C, 79·2; H, 11·0. $C_{20}H_{32}O_2$ requires C, 78·9; H, 10·6%). Lactonisation of this acid (200 mg.) with sulphuric acid as previously described gave the γ-lactone (100 mg.), m. p. and mixed m. p. 108°, having the requisite infrared spectrum. A mixed m. p. with dihydro*iso*dextropimaric acid was *ca.* 102°.

(*b*) Isomerisation of dihydro*iso*dextropimaric acid (0·5 g.) with toluene-*p*-sulphonic acid (50 mg.) in boiling benzene (50 ml.) during 1 hr. furnished 7-*allo*pimar-13(14)-en-15-oic acid in prisms (0·5 g.) [m. p. and mixed m. p. with the preparation (*a*); infrared spectrum].

(*c*) Dihydro*iso*dextropimaric acid (0·2 g.) in alcohol (50 ml.) containing 10N-hydrochloric acid (1 ml.) was refluxed for 3 hr., then diluted with water, and the sticky precipitate was repeatedly crystallised from aqueous methanol, to furnish 7-*allo*pimar-13(14)-en-15-oic acid (50 mg.), identical with the compound prepared by methods (*a*) and (*b*).

The authors are grateful to Dr. R. V. Lawrence, U.S. Department of Agriculture, Olustee, Florida, for a gift of *iso*dextropimaric acid, to Dr. Le Van Thoi (formerly of Paris, now of the University of Saigon) for specimens of the γ- and the δ-lactone derived from dihydrodextropimaric acid, and to Professor E. Wenkert for informing us of his results in this field before their publication.

Rotations refer to ethanol solutions and the infrared absorption spectra to CCl_4 solutions (Perkin-Elmer Model 21 spectrophotometer).

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