CCCCXXXII.—*Dehydrogeranic Acid.*

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IT was observed by one of us (A. R. P.) (*Perf. & Ess. Oil Rec.*, 1925, Jan.; 1927, Aug.) that the oil present in the wood of *Callitropsis araucarioides* contained the geranyl ester of an acid, $C_{10}H_{14}O_2$,

m. p. 183—184°. A quantity of the oil having become available, the acid has been further examined. The melting point of the acid has been raised to 185—186°, but the formula originally assigned to it has been confirmed. The acid, which is optically inactive, decolorises immediately potassium permanganate and reacts with bromine in chloroform solution, the bromo-acid formed being, however, unstable. On catalytic hydrogenation in the presence of palladised charcoal, it absorbs three molecules of hydrogen, yielding a liquid acid, which has been identified as *dl*-tetrahydrogeranic acid by the comparison of its crystalline amide and p-*toluidide* with authentic specimens of these substances. The validity of identification by mixed melting points in this series is supported by the satisfactory depressions obtained on admixture with the corresponding derivatives of *n*-decoic acid, which was synthesised, since their melting points are almost identical with those found in the tetrahydrogeranic acid series. There can thus be no doubt that the acid, m. p. 185—186°, has the same carbon structure as geranic acid and, since it contains an additional ethylenic linkage, we propose to designate it *dehydrogeranic acid.*

Excluding stereoisomerides, there are seven theoretically possible formulæ for this acid, but unfortunately it has not proved possible by direct chemical evidence to decide definitely between these. Owing to the sparing solubility of the acid in organic solvents the ozonolysis could only be carried out in dilute alkaline solution. Under these conditions much resinification occurs and only acetic and oxalic acids could be identified amongst the degradation products. On oxidation in alkaline solution with cold aqueous potassium permanganate, formic, acetic, and oxalic acids and acetone were obtained; ketonic acids could not be isolated, nor could malonic acid, but hydroxy-acids appeared to survive the oxidation. Of these products, oxalic acid has manifestly no diagnostic value and acetic acid must be derived by the decomposition or further oxidation of a primarily formed ketonic acid, such as pyruvic, acetoacetic, or oxaloacetic acid. It does not appear to be permissible to draw any conclusions from the absence of malonic acid, inasmuch as only approximately 60% of the theoretical quantity of potassium permanganate was reduced and it is possible that the stable hydroxy-acids might have yielded malonic acid on complete degradation. Further, the acetone may have been derived from a terminal *iso*propylidene group, $Me_2C\colon$, or alternatively by the decomposition of acetoacetic or acetonedicarboxylic acid. On the other hand, the production of formic acid necessarily implies the presence of either a β- or a ζ-methylene group. The former alternative appears to us to be unlikely, for although a methylene group in this position is not unknown amongst naturally occurring compounds (compare myrcene), yet in dehydrogeranic acid it would necessarily involve the structure $CH_2{:}\dot{C}{\cdot}CH_2{\cdot}CO_2H$. Since isolation of the acid requires prolonged treatment with alkali (see p. 3139), we regard it as unlikely that this structure would not have isomerised to $Me{\cdot}\dot{C}{:}CH{\cdot}CO_2H$. If the formulæ containing a β-methylene group be excluded, the number of possibilities is reduced to four :

(I.) $Me_2C{:}CH{\cdot}CH{:}CH{\cdot}CMe{:}CH{\cdot}CO_2H$
(II.) $CH_2{:}CMe{\cdot}CH_2{\cdot}CH{:}CH{\cdot}CMe{:}CH{\cdot}CO_2H$
(III.) $CH_2{:}CMe{\cdot}CH{:}CH{\cdot}CH{:}CMe{\cdot}CH_2{\cdot}CO_2H$
(IV.) $CH_2{:}CMe{\cdot}CH{:}CH{\cdot}CH_2{\cdot}CMe{:}CH{\cdot}CO_2H$

The production of formic acid would then necessitate the existence of a terminal *iso*propenyl group, thus excluding (I), but a further difficulty is encountered here. As a rule the acyclic terpenes and their derivatives occur in nature as a mixture containing the *iso*propenyl and *iso*propylidene groups in varying proportions and this particular form of isomerism appears to have little effect on the apparent homogeneity even of crystalline derivatives (compare citronellal semicarbazone; Harries, *Annalen*, 1915, **410**, 1; Comberg, *ibid.*, p. 40). It is thus not even certain that dehydrogeranic acid, although apparently homogeneous, is really one chemical individual.

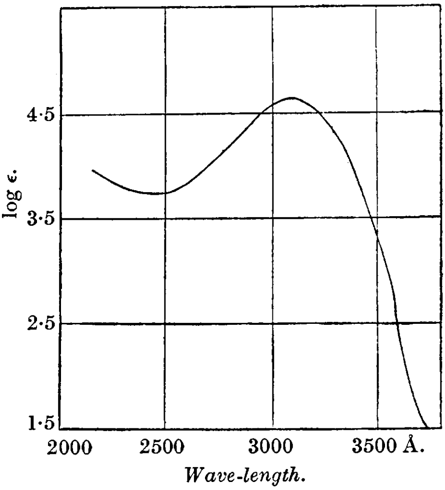
Of the formulæ given above, (III) appears to be the least probable, since it does not contain an αβ-ethylenic linkage, and we regard (I) and (II) as the most probable, since they allow the possible *iso*propenyl–*iso*propylidene isomerism to take place unhampered by conjugation with the rest of the molecule. We desire, however, to emphasise the fact that we have not been able to establish definitely the position of the ethylenic linkages (beyond the presence to some extent at any rate of a methylene group) and in view of the absence of evidence as to the general behaviour of such highly conjugated, but probably mobile, systems, the formula must necessarily be speculative. It will be observed that only two, (I) and (III), of the formulæ given above contain all three ethylene linkages conjugated and accordingly attempts were made to condense the acid with maleic anhydride. These were, however, unsuccessful (see p. 3140). Whilst a positive result might have yielded valuable information, nevertheless, in view of the widely varying conditions governing this condensation, we do not feel justified in drawing any deductions from our failure.

Indirect evidence that dehydrogeranic acid is most probably represented by (I) was furnished by a study of its absorption spectrum in alcoholic solution, which was kindly determined for us by Dr.

R. A. Morton and Mr. A. Gouveia at the University of Liverpool and is shown in Fig. 1. The acid exhibits a broad absorption band over the region 2500—3500 Å. with a maximum near 3110 Å. The curve exhibits no fine structure and the molecular extinction coefficient at the maximum is of the order 35,500. Whilst this number is by no means unusually high for organic compounds in general, it is very much greater than that shown by saturated aliphatic acids, and both the extinction coefficient and the location of the band in the near ultra-violet region are consistent with the high unsaturation of the acid. We are much indebted to Professor R. Kuhn for undertaking a comparison of the absorption spectrum of dehydrogeranic acid with that of his closely related synthetic acid, $\Delta^{\alpha\gamma\epsilon}$-octatrienoic acid (Kuhn and Hoffer, *Ber.*, 1930, **63**, 2170). The details of the absorption spectra of the latter and related acids will be published elsewhere, but he informs us that whilst the absorption band of octatrienoic acid lies at 295 μμ as compared with 310 μμ, the close and general resemblance of the absorption spectra would appear to leave no doubt that dehydrogeranic acid is correctly represented by (I). The slightly lower absorption and shift of the band is due to the presence of the branched chain, which is known to have a depressent effect.

FIG. 1.

Absorption spectrum of dehydrogeranic acid in alcohol.



Professor E. A. Owen and Mr. L. Pickup are investigating the *X*-ray structure of dehydrogeranic acid. The full details of this will be published later, but they have kindly furnished us with the following note.

" A preliminary *X*-ray investigation shows that the crystal probably belongs to the monoclinic prismatic class. Rotation photographs of single crystals taken about the principal axes give the following dimensions for the unit cell: $a = 14{\cdot}5$, $b = 19{\cdot}5$ and $c = 5{\cdot}7$ with $\beta \doteqdot 137°$.

" Direct experiment gave a value of 1·10 g. per c.c. for the density of the crystal. This when substituted in the formula $abc \,.\, \rho \,.\, \sin \beta =$

1·663 *Mn*, where *M* is the molecular weight, yields for *n* the value 4·01, so that there are four molecules to the unit cell.

" The crystal shows well developed (010) faces and a marked cleavage parallel to the (001) planes."

With the possible exception of plantagenic acid, $C_9H_{12}O_2$ (Emmanuel and Papavasiliou, *Arch. Pharm.*, 1920, **258**, 142), the constitution of which is unknown, dehydrogeranic acid appears to be the most unsaturated acid, containing as few as ten carbon atoms, which has been found to occur in nature. Citronellic acid has been isolated from camphor oil (Rochussen, *J. pr. Chem.*, 1922, **105**, 120), but the occurrence of geranic acid has not so far been observed. The existence of dehydrogeranic acid seems to us to be of peculiar interest. Although it may arise by the oxidation and dehydrogenation of geraniol, with which it is associated in the oil, it may result also by the oxidation of the aldehyde $Me_2C{:}CH{\cdot}CH{:}CH{\cdot}CMe{:}CH{\cdot}CHO$, which is regarded by Kremers (*J. Biol. Chem.*, 1922, **50**, 31) and others as a precursor of citral. Alternatively it may be considered to be a breakdown product of substances of the squalene, phytol, or carotene type. With this possible connection in view and also because the acid gave colour reactions characteristic of poly-ene compounds in general (compare Kuhn and Hoffer, *loc. cit.*), tests for vitamin-*A* activity were carried out by Dr. F. L. Pyman and Mr. W. A. Broom, to whom we are greatly indebted, at the Research Laboratories, Messrs. Boots Pure Drug Co., Ltd., Nottingham, by the method of Drummond and Morton (*Biochem. J.*, 1929, **23**, 786). These indicated that " it has less than a twentieth of the activity of carotin and quite possibly no activity at all."

According to the observations of Kuhn and Hoffer (*loc. cit.*) colour occurs only in poly-ene acids when they contain at least four conjugated ethylenic linkages. Dehydrogeranic acid, as originally obtained by the hydrolysis of the ester in alcoholic solution, had a definite pale yellow colour, which could not be removed by any of the ordinary methods of purification. A later sample, prepared by hydrolysis with aqueous alkali, was, however, colourless. The yellow and the colourless variety had the same m. p. and were both analytically pure and the yellow acid was recovered colourless from an attempted condensation with maleic anhydride (see p. 3140). Both forms decompose on keeping (by oxidation, since the acid is stable in the absence of oxygen) with deepening or development of the yellow colour and the colourless form becomes yellow when kept in alcoholic potassium hydroxide solution; this induced colour can be readily removed from the originally colourless acid and the deep yellow acid can be obtained pale yellow but not colourless. We consider, therefore, the colour of the original yellow acid to be due to some impurity introduced in minute amount from another component of the essential oil by the use of alcoholic potassium hydroxide as the hydrolytic agent. These results emphasise the care that is necessary before the decision is made that these unstable acids are really yellow.

EXPERIMENTAL.

The oil obtained in a yield of 6·7% by the distillation in steam of the wood of *Callitropsis araucarioides* from New Caledonia had the following constants: $d_{15^\circ}^{15^\circ}$ 0·9606—0·9684, $n_D^{20^\circ}$ 1·5131—1·5181, $[\alpha]_D$ + 6·9°, ester value 64·5—92·5, after acetylation 171·5—207·3. Eudesmol, m. p. 79—80°, $[\alpha]_D^{20^\circ}$ + 37·8°, constituted 50—70% of the oil, which contained also a sesquiterpene (possibly eudesmene), phenols (*ca.* 1%), and geranyl dehydrogeranate. By distillation this ester was concentrated into a fraction, b. p. 115—125°/3 mm., but it could not be obtained pure and the crude oil was therefore used for the preparation of dehydrogeranic acid.

Dehydrogeranic Acid.—The crude oil (100 c.c.; ester value 92·5), heated under reflux with an excess of 0·5*N*-aqueous potassium hydroxide solution for 24 hours, yielded dehydrogeranic acid (6·5 g.), which, after crystallisation successively from methyl alcohol and ethyl acetate, was quite colourless. When the crude oil was kept for 24 hours at room temperature in 0·5*N*-alcoholic potassium hydroxide solution dehydrogeranic acid was obtained in the same yield, but it had a pronounced yellow colour, which could not be removed by repeated crystallisation (charcoal), nor by purification through its salts. *Dehydrogeranic acid* crystallised from ethyl acetate in highly iridescent, slender prisms, which sintered at 183° and decomposed at 185—186°. Both the colourless and the yellow acid were analysed (Found: C, 72·1, 72·1; H, 8·3, 8·5; *M*, 167·7. $C_{10}H_{14}O_2$ requires C, 72·3; H, 8·4%; *M*, 166). The acid is readily soluble in hot benzene, acetic acid, and methyl alcohol, but only sparingly so in these solvents in the cold. It is insoluble in cold water and it is optically inactive in 0·03% aqueous sodium hydroxide. In chloroform solution bromine is readily absorbed, but hydrogen bromide is at the same time evolved; in alkaline solution it immediately decolorises potassium permanganate. When the acid is kept in a sample tube it becomes sticky and yellow (or deeper yellow in the case of the yellow acid). A pure colourless specimen kept for 3 months had m. p. 182—183° after sintering at 178°; a portion of this sample became colourless after recrystallisation from ethyl acetate (charcoal); another portion was dissolved in ethyl-alcoholic potassium hydroxide, and the solution, which rapidly became somewhat deep yellow, was kept for 18 hours, but the colour did not deepen appreciably; the acid recovered from the solution after crystallisation from methyl alcohol was pale yellow, but became colourless on recrystallisation from ethyl acetate (charcoal). Dehydrogeranic acid gives with concentrated sulphuric acid a yellow colour, becoming on warming orange and then reddish-brown, the acid finally carbonising. It is colourless in formic acid even on boiling. On warming with a large excess of antimony chloride in chloroform, the solution becomes successively yellow, greenish-yellow, reddish-brown and light wine-red. These colour changes are given by both the colourless and the yellow acid.

The *p*-toluidide is a gum; the methyl ester, prepared from the silver salt, was obtained crystalline, but rapidly liquefied when drained on porous porcelain; two attempts to repeat this preparation gave only oils.

In an attempt to condense the acid with maleic anhydride, a mixture of the acid (1 g., yellow form) and the anhydride (0·6 g.) was dissolved under reflux in dry xylene (20 c.c.), cooled somewhat, and then heated on the water-bath for 4·5 hours. A large amount of dehydrogeranic acid separated on cooling; a small portion recrystallised from ethyl acetate was now quite colourless and had the correct m. p. The mixture was then boiled for 4 hours; on cooling, very little material separated. The solution contained a trace of a neutral substance, non-volatile in steam, and less than 0·2 g. of acidic material, from which *ca.* 0·05 g. of pure dehydrogeranic acid was recovered. Most of the acid apparently underwent decomposition.

Reduction of Dehydrogeranic Acid.—Dehydrogeranic acid (1·077 g.) was dissolved in sodium hydroxide solution (4%; 9 c.c.), and very dilute hydrochloric acid added until the precipitate formed just did not redissolve. The solution was made up to 50 c.c., palladised norite (10%; 1 g.) added, and the whole shaken in hydrogen, of which 434 c.c. were absorbed in 115 minutes (calc. for 3 mols., 436 c.c.). The filtered solution was concentrated, acidified, and extracted twice with ether. The dried ethereal solution left on evaporation a colourless oil, which was converted by thionyl chloride into the acid chloride and thence in the usual manner into the amide and *p*-toluidide. The former crystallised from aqueous acetone in very pale yellow plates, m. p. 101—102°, but it was not analytically pure; mixed with *n*-decoamide (prepared by the malonic ester synthesis from *n*-octyl iodide), m. p. 97—98°, it melted indefinitely at about 88°; mixed with the amide of *dl*-tetrahydrogeranic acid (see below), at 101—102°. The p-*toluidide* (Found: C, 77·8; H, 10·2; N, 5·5. $C_{17}H_{27}ON$ requires C, 78·2; H, 10·3; N, 5·4%) crystallised from light petroleum (b. p. 60—80°) and had m. p.

81—82°, alone and mixed with the *p*-toluidide of *dl*-tetrahydrogeranic acid; in admixture with the *p*-toluidide of *n*-decoic acid (m. p. 78°) it melted indefinitely at 69—72°.

dl-*Tetrahydrogeranic Acid.*—The preparation of this acid from geraniol (of which a pure and almost optically inactive specimen was available) was first attempted through tetrahydrogeraniol. Hydrogenation in acetic acid solution with a palladised norite catalyst gave much βη-dimethyloctane with less tetrahydro- and dihydro-geraniol (compare Willstätter and Mayer, *Ber.*, 1908, **41**, 1475; Ishizaka, *ibid.*, 1914, **47**, 2453). The same products resulted when alcohol (75%) was used as the solvent (compare Sabetay and Bléger, *Bull. Soc. chim.*, 1928, **43**, 839; Longuinov and Margoliss, *ibid.*, 1929, **45**, 156). The oxidation of tetrahydrogeraniol with chromic acid was also found not to proceed smoothly (compare Wallach and Behnke, *Annalen*, 1912, **389**, 198; von Braun and Kaiser, *Ber.*, 1923, **56**, 2268) and an alternative route was sought.

Geraniol was converted into citral (Semmler, *Ber.*, 1890, **23**, 2966) and thence into geranionitrile (Tiemann and Semmler, *Ber.*, 1899, **26**, 2716). The nitrile, which was very slowly attacked by aqueous baryta, was hydrolysed with aqueous-alcoholic potassium hydroxide solution. The yield of distilled geranic acid was low (1·2 g. from 6·3 g. of nitrile) and much tar was formed (compare Tiemann and Semmler, *loc. cit.*, who nevertheless recommend this method).

Geranic acid (1·3 g.) in water (100 c.c.) and sufficient sodium hydroxide to give a clear solution, after the addition of palladised norite (10%; 1 g.), absorbed hydrogen (350 c.c.; calc. for 2 mols., 360 c.c.) in about 12 hours (compare Paal, Germ. Pat., 298,193). The filtered solution was extracted with ether to remove a trace of turbidity and the *dl*-tetrahydrogeranic acid was isolated in the usual manner. It was converted without distillation into the *p*-toluidide, which, after two crystallisations from light petroleum, had m. p. 81°, and into the amide, which crystallised from aqueous acetone and had m. p. 101—102°. Wallach (*Annalen*, 1897, **296**, 28) records m. p. 108—109° for this amide, but his acid was probably optically active, since it was prepared from *d*-menthone.

Oxidation of Dehydrogeranic Acid.—To a mechanically stirred, alkaline solution of dehydrogeranic acid (5 g.), potassium permanganate (1000 c.c.; 2·5%) was gradually added, carbon dioxide being passed through the solution, which was maintained below 5°. Oxidation was rapid and after 2 hours the colour was permanent. After remaining over-night, the solution was filtered and distilled in steam. The distillate gave the iodoform reaction in the cold, and the nitroprusside and sodium hydroxide–acetic acid test for acetone, and on addition of *p*-bromophenylhydrazine in dilute acetic acid a precipitate of acetone-*p*-bromophenylhydrazone was obtained, which crystallised from light petroleum in plates, m. p. 91—93°, both alone and after admixture with an authentic specimen. Evaporation on the water-bath of the original solution from the steam distillation caused darkening and an odour of burnt sugar (due to hydroxy-acids). The solid residue was extracted with alcohol; the filtered solution gave on evaporation a dark oily residue entirely soluble in alcohol. It was dissolved in water, acidified with dilute sulphuric acid, filtered from a brown amorphous precipitate, saturated with ammonium sulphate, and filtered from a further quantity of an amorphous solid; an almost colourless solution was then obtained. Extraction with ether (10 times) gave a pale yellow oil smelling strongly of acetic acid and giving ethyl acetate on esterification. Attempts to crystallise it or to prepare a crystalline copper salt failed. The oil was distilled in steam and the distillate was shaken with mercuric oxide, filtered, and boiled; a white precipitate changing to black metallic mercury and white crystals of mercurous acetate resulted. A very small residue, insoluble in water, remained in the distillation flask.

The salt residue insoluble in alcohol was dissolved in water, acidified with dilute sulphuric acid, and repeatedly extracted with ether, and the ethereal extract dried over calcium chloride. After filtration the calcium chloride was dissolved in water, made alkaline with a drop of ammonia, and the trace of ether present removed in a current of air. The calcium oxalate was collected and identified by decolorisation of an acidified solution of potassium permanganate and by its precipitation from its solution in dilute hydrochloric acid on the addition of sodium acetate. Evaporation of the ethereal solution gave a brown oil, which did not give the acetic anhydride–acetic acid reaction for malonic acid. Attempts to crystallise the oil were not successful.

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