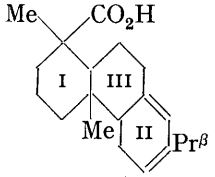
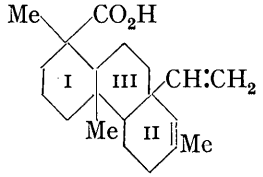
49. *Studies in the Resin Acid Series. Part I. The Synthesis of Vocke's Unsaturated Acid,* $C_{10}H_{14}O_4$.

By H. N. Rydon.

Although the dehydrogenation of abietic acid (I) and dextropimaric acid (II) to retene and pimanthrene respectively and the synthesis of these hydrocarbons (for references, see Fieser, " Chemistry of Natural Products related to Phenanthrene," 1936) have conclusively established the basic structure of these resin acids, the method is incapable of affording definite evidence as to the position of those groups that are eliminated during dehydrogenation.

Direct synthetic evidence for the position of the carboxyl group and the methyl group in ring I is therefore lacking. The most suitable derivatives for the synthetic attack of this problem are the acids, $C_{11}H_{16}O_6$ and $C_{12}H_{18}O_6$, obtained by various workers by the oxida-


(I.)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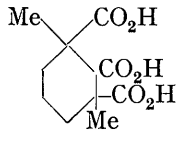
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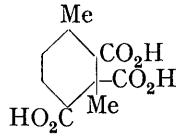
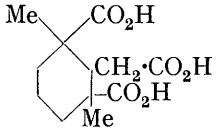

(III*a*.)

tion of abietic acid (Ruzicka, Meyer, and Pfeiffer, *Helv. Chim. Acta*, 1925, **8**, 637; Levy, *Ber.*, 1929, **62**, 2497; Ruzicka, Goldberg, Huyser, and Seidel, *Helv. Chim. Acta*, 1931, **14**, 545) and of dextropimaric acid (Ruzicka, de Graaff, Goldberg, and Frank, *Helv. Chim. Acta*, 1932, **15**, 915). Vocke (*Annalen*, 1932, **497**, 247) obtained from the C_{11} acid an unsaturated acid, $C_{10}H_{14}O_4$, and an isomeric lactonic acid; these he considered to have the structures (V) and (VI) respectively, leading to (III) and (IV) for the C_{11} and the C_{12} acid and finally to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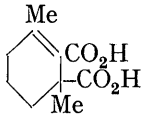
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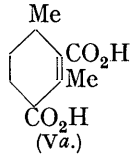
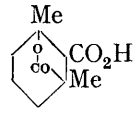
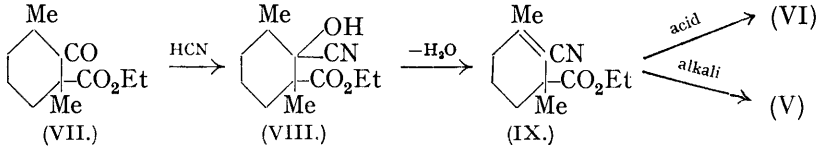

(V*a*.)


(VI.)

(I) and (II) for the parent resin acids, in so far as the arrangement of groups in ring I is concerned. The alternative structure (V*a*) for the unsaturated acid, leading to (III*a*) for the C_{11} acid, was not, however, completely excluded by the experimental evidence. Only synthesis could afford a final solution of the problem.

The acids (V) and (VI) have now been synthesised by the reactions


(VII.) (VIII.) (IX.)

and found to be identical with Vocke's two compounds. Only one of the possible stereoisomeric cyanohydrins (VIII) appears to be produced from the keto-ester (VII) by the action of hydrogen cyanide; this has the remarkably high m. p. of 75° and may be distilled in steam without decomposition.

It is therefore to be concluded that the C_{11} acid has the structure (III), the alternative structure (III*a*) being ruled out by the synthetic evidence. This affords the first direct synthetic evidence for the orientation of the substituents in ring I of abietic and dextropimaric acids. Final proof of this point rests with the synthesis of the C_{11} and the C_{12} acid; experiments with this end in view are in hand.

Experimental.

(All analyses are micro-analyses by Dr. G. Weiler, Oxford.)

Ethyl 2 : 6-dimethyl*cyclo*hexanone-2-carboxylate (VII), b. p. 92—94°/2·5 mm., was prepared in 78% yield by the methylation of the sodio-derivative of ethyl 2-methyl*cyclo*hexanone-6-carboxylate (Ruzicka, Koolhaas, and Wind, *Helv. Chim. Acta*, 1931, **14**, 1163) in petroleum solution (b. p. 60—80°). This procedure (private communication from Dr. A. F. Millidge) is an improvement on that employing sodium ethoxide in alcohol.

Cyanohydrin (VIII).—A mixture of 25 g. of the keto-ester (VII) and 5 g. (30% excess) of hydrogen cyanide (Wade and Panting, J., 1898, **73**, 256) was cooled in ice, and a few drops of diethylamine added; a vigorous reaction took place. After standing overnight, the solid product was triturated with light petroleum (b. p. 40—60°) and collected. Crystallisation of the crude cyanohydrin (18·5 g.; 65%), m. p. 74°, from petroleum (b. p. 60—80°) afforded *ethyl 2-hydroxy-2-cyano-1 : 3-dimethyl*cyclo*hexane-1-carboxylate* (VIII) in massive aggregates of transparent

prisms, m. p. 75° (Found: C, 64·3; H, 8·6. $C_{12}H_{19}O_3N$ requires C, 64·0; H, 8·4%). The product was stable to keeping, but could not be distilled in a vacuum without serious decomposition.

Dehydration. The excess of hydrogen cyanide was removed in a vacuum from the crude cyanohydrin obtained from 50 g. of the keto-ester and 10 g. of hydrogen cyanide. The product was mixed with 40 g. (2 mols.) of pyridine and cooled in ice while 66 g. (2·2 mols.) of thionyl chloride were added dropwise with shaking during 25 minutes. The dark product was heated under reflux on the water-bath for an hour, poured on ice, and acidified. After filtration the liquid was extracted with ether, and the extract washed twice with 5% sodium hydroxide solution and with water. After drying, distillation afforded 34 g. of the unsaturated cyano-ester (IX), b. p. 116—120°/1·5 mm.; redistillation yielded 31 g. (60%) of a product, b. p. 112°/1 mm., which still contained some unchanged cyanohydrin (Found: C, 66·6; H, 8·4. Calc. for $C_{12}H_{17}O_2N$: C, 69·6; H, 8·2%. Calc. for $C_{12}H_{19}O_3N$: C, 64·0; H, 8·4%).

Acid hydrolysis. 10 G. of the unsaturated cyano-ester (IX) were refluxed for 5 days with 50 c.c. of concentrated hydrochloric acid. The product was poured into an excess of 10% sodium bicarbonate solution, ether extraction then affording some 4 g. of ketone derived from undehydrated cyanohydrin. The residual solution was acidified and thoroughly extracted with ether. Evaporation of the dried extract left 6·25 g. (60%) of an oil, which readily solidified in a vacuum desiccator. The product was drained on a porous tile and crystallised once from petroleum (b. p. 60—80°) and twice from benzene. 2-Carboxy-1:3-dimethyl-1:3-*cyclo*hexanolide (VI) (1·54 g.) so obtained formed feathery rosettes of prismatic needles, m. p. 145° (Found: C, 60·6; H, 7·2. Calc. for $C_{10}H_{14}O_4$: C, 60·6; H, 7·1%). Vocke (*loc. cit.*) gives m. p. 146°.

Alkaline hydrolysis. 12 G. of the unsaturated cyano-ester (IX) were refluxed for 5 days with 22 g. of potassium hydroxide in 175 c.c. of water. The product was cooled and extracted with ether to remove neutral by-products. The acidified solution was again extracted with ether; evaporation of the dried extract left 7·5 g. (70%) of a gum. This was refluxed for 3 hours with 10 g. of concentrated sulphuric acid in 200 c.c. of methyl alcohol. The greater part of the methyl alcohol was removed under reduced pressure, and the residue poured into water and extracted with ether. The extract was washed repeatedly with 10% sodium carbonate solution, dried, and evaporated; the residue, on standing, deposited 0·85 g. of a saturated nitrogenous solid, crystallisation of which from dilute methyl alcohol yielded 2-*cyano*-1:3-*dimethyl*-1:3-cyclo*hexanolide* in transparent plates, m. p. 168—169° (Found: C, 67·4, 67·1; H, 7·5, 7·5. $C_{10}H_{13}O_2N$ requires C, 67·0; H, 7·3%), which dissolved in warm dilute sodium hydroxide solution and were reprecipitated on acidification.

Acidification of the sodium carbonate washings, followed by extraction with ether and evaporation of the dried extract, yelded 1·7 g. of a product which rapidly solidified in a vacuum desiccator. After draining on a porous tile, two crystallisations from petroleum (b. p. 100—120°) yielded 0·5 g. of methyl hydrogen 1:3-dimethyl-Δ^2-*cyclo*hexane-1:2-dicarboxylate in rosettes of prismatic needles, m. p. 129—130° (Found: C, 62·3; H, 8·0. Calc. for $C_{11}H_{16}O_4$: C, 62·3; H, 7·6%). Vocke (*loc. cit.*) gives m. p. 132°.

Evaporation of the mother-liquors from the crystallisations yielded 0·75 g. of crude ester, which was refluxed for 4 hours with 1 g. of potassium hydroxide in 5 c.c. of ethyl alcohol. The alcohol was removed, and neutral material extracted with ether. The residual solution was acidified and again extracted with ether. Evaporation of the dried extract yielded a gum, which was thrice crystallised from acetic acid; in this way 0·11 g. of 1:3-dimethyl-Δ^2-*cyclo*hexene-1:2-dicarboxylic acid (V) was obtained in transparent prisms, m. p. 185° (decomp.) (Found: C, 60·9; H, 7·5. Calc. for $C_{10}H_{14}O_4$: C, 60·6; H, 7·1%). The same product was also obtained by direct hydrolysis of the crude monomethyl ester. A specimen of the unsaturated acid, $C_{10}H_{14}O_4$, prepared from abietic acid by Dr. Vocke had m. p. 181—183° (decomp.), and 183—185° (decomp.) when mixed with the synthetic acid.

Attempted Acid Hydrolysis of the Cyanohydrin (VIII).—The crude product from 25 g. of the keto-ester and 5 g. of hydrogen cyanide was refluxed for 72 hours with 150 c.c. of concentrated hydrochloric acid. Steam-distillation afforded a small amount of ketone together with a large amount of unchanged cyanohydrin, m. p. and mixed m. p. 73—75°. The residual solution deposited 3·5 g. of a neutral nitrogenous product, m. p. 255°, unchanged on crystallisation from dilute ethyl alcohol; this was not further investigated.

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