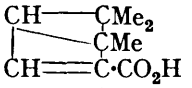
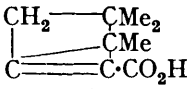
165. α- *and* β-*Camphylic Acids.*

By J. R. Lewis and J. L. Simonsen.

The products of the fusion of sulphocamphylic acid with alkaline hydroxides, examined first by Kachler (*Annalen*, 1872, **169**, 183) and Damsky (*Ber.*, 1887, **20**, 2957), formed the subject of a detailed investigation by Perkin, jun. (J., 1898, **73**, 829; 1903, **83**, 835). The main product of the fusion in the presence of reducing agents, such as are furnished by an iron pot, consists of *iso*lauronolic acid; if, however, the fusion is carried out in a nickel dish, the isomeric acids, α- and β-camphylic acids, $C_9H_{12}O_2$, are obtained. From a study of their reactions Perkin suggested that they were dicyclic unsaturated acids represented respectively by (I) and (II).


(I.)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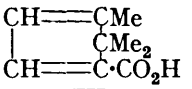
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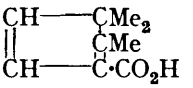
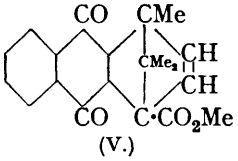

(IV.)

On stereochemical grounds it is obvious that the formula (II) suggested for β-camphylic acid is improbable, and a renewed study of these acids has shown α-camphylic acid to be 2 : 2 : 3-trimethyl-$\Delta^{3:5}$-*cyclo*pentadiene-1-carboxylic acid (dehydro-α-campholytic acid) (III) and β-camphylic acid to be 2 : 3 : 3-trimethyl-$\Delta^{1:4}$-*cyclo*pentadiene-1-carboxylic acid (dehydro*iso*lauronolic acid) (IV).

Before proceeding to discuss the evidence upon which the structure now advanced for these acids is based, we may refer briefly to their separation. We can confirm fully Perkin's statement that this is extremely laborious, more especially since the composition of the mixture varies considerably in different experiments. We find the relative proportion of the two acids formed to be dependent largely upon the pressure at which the product from the fusion is distilled. At the ordinary pressure or at pressures from 200—300 mm., α-camphylic acid predominates; the percentage of β-camphylic acid increases as lower pressures are used. In the latter case Perkin's method of separation by fractional steam distillation from the ammonium salts fails. If, however, an ethereal solution of the acids is fractionally extracted with ammonium carbonate solution, β-camphylic acid is preferentially removed and the residue can then be purified by Perkin's method. α-Camphylic acid is readily obtained pure by crystallisation from dilute acetic acid, but, in agreement with Perkin, we find that pure β-camphylic acid can only be prepared by digestion of *iso*bromodihydro-β-camphylic acid with water.

Although on titration with percamphoric acid α-camphylic acid shows only the presence of one ethylenic linkage, two molecules of hydrogen are absorbed on catalytic hydrogenation with the formation of dihydro-α-campholytic acid, characterised by the preparation of the *p-phenylphenacyl* ester, m. p. 93°, identical with the same derivative obtained from the authentic *cyclo*pentane acid. On oxidation with ozone, α-camphylic acid yields methyl *iso*propyl ketone and oxalic acid, products which would result from the oxidation of an acid having the structure (III). Confirmation of the presence of a conjugated system of ethylenic linkages in the acid was obtained by the condensation of its methyl ester with α-naphthaquinone, the crystalline additive *compound* (V), m. p. 106°, being obtained.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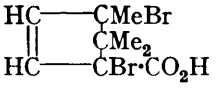
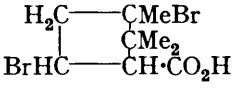
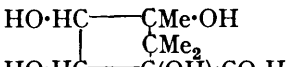

(VI.)

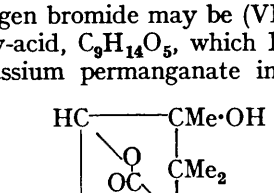

(VII.)

The structure now assigned to α-camphylic acid is not incompatible with the reactions of the acid as described by Perkin. It accounts for its reduction by sodium amalgam to α-campholytic acid, only the αβ-ethylenic linkage being reduced. With bromine the acid yields a dibromide, probably represented by (VI) (1 : 4-addition), and the dihydrobromide

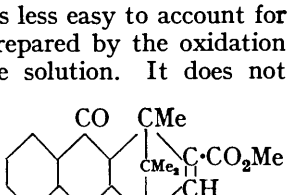
obtained by the action of hydrogen bromide may be (VII). It is less easy to account for the formation of the trihydroxy-acid, $C_9H_{14}O_5$, which Perkin prepared by the oxidation of α-camphylic acid with potassium permanganate in alkaline solution. It does not



(VIII.)



(IX.)



(X.)

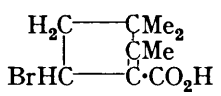
appear to us improbable that this substance was actually the lactone of the tetrahydroxy-acid (VIII), which would be the primary oxidation product of an acid (III). If the lactone be represented by (IX), it would account also for the fact that it only yields a monoacetyl derivative on acetylation, since two of the hydroxy-groups are tertiary.

In the light of the structure now assigned to α-camphylic acid it is of interest to note that it can be prepared also by the digestion of ethyl dibromodihydro*iso*lauronolate with diethylaniline. Since *iso*lauronolic acid is isomerised to α-campholytic acid by hydrobromic acid (Walker and Cormack, J., 1900, **77**, 378), it appears to us probable that the dibromo-ester used by Perkin was in reality ethyl dibromodihydro-α-campholate.

Proof of the structure of β-camphylic acid was obtained in a similar manner. Titration with percamphoric acid showed the presence of two ethylenic linkages and on catalytic hydrogenation a tetrahydro-acid was obtained, which was characterised by the preparation of the p-*phenylphenacyl* ester, m. p. 68—69°, and the amide, m. p. 160—161°. These were identical with derivatives prepared from authentic dihydro*iso*lauronolic acid. Oxidation with ozone gave methyl *iso*propyl ketone and oxalic acid, and with α-naphthaquinone the additive *compound* (X), m. p. 135°, was obtained from methyl β-camphylate, thus confirming the conjugation of the ethylenic linkages.

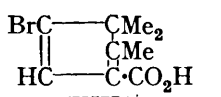
*iso*Bromodihydro-β-camphylic acid, which is prepared readily by the action of hydrogen bromide on crude β-camphylic acid, gives on ozonolysis an unstable bromo-acid, which after treatment with alkali is oxidised by sodium hypobromite to bromoform and *as*-dimethylsuccinic acid. This suggests that the cyclic acid is 5-bromo-2 : 3 : 3-trimethyl-Δ^1-*cyclo*pentene-1-carboxylic acid (XI).

Like α-camphylic acid, the β-acid gives on bromination a dibromide. We have not prepared this substance, but, since hydrogen bromide attacks the Δ^4-linkage, we suggest that it is represented by (XII) and that bromo-γ-camphylic acid obtained from it by digestion with diethylaniline or acetic acid is (XIII) or (XIV).

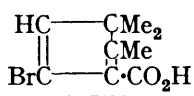


(XI.)

(XII.)



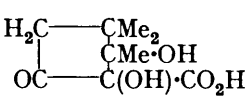
(XIII.)

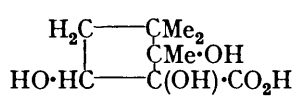


(XIV.)

It is more difficult on the basis of (IV) to account for the formation of the hydroxyketo-acid, $C_9H_{14}O_5$, obtained by Perkin by the oxidation of β-camphylic acid with potassium permanganate. This acid was assumed to be (XV), since it gave on further oxidation with chromic acid acetone and *as*-dimethylsuccinic acid. It is possible that hydration and oxidation occur simultaneously; (XVI) would then be the primary product. It is somewhat remarkable, in any case, that an acid having the structure (XV), which is that of a substituted acetoacetic acid, should be sufficiently stable to permit of its isolation.

(XV.)





(XVI.)

In view of the mobility of the ring system these experiments cannot be regarded as a contribution to the debated problem of the constitution of sulphocamphylic acid, and experiments on this are in progress.

Experimental.

α-Camphylic Acid.—In chloroform solution the acid reacted very slowly with percamphoric acid. After about 1 week, titration showed absorption of oxygen corresponding to one ethylenic linkage, and no change took place on further keeping.

Dihydro-α-campholytic Acid.—α-Camphylic acid was reduced in alkaline solution with hydrogen and a palladium-norit catalyst, complete reduction requiring approximately 24 hours. Acidification of the filtered solution, followed by extraction with ether, gave the dihydro-acid as an oil, which crystallised to a low-melting solid. This liquefied under water and was extremely readily soluble in the ordinary organic solvents. The p-*phenylphenacyl* ester crystallised from methyl alcohol in leaflets, m. p. 93° (Found: C, 79·0; H, 7·4. $C_{23}H_{26}O_3$ requires C, 78·9; H, 7·4%).

Oxidation of α-Camphylic Acid.—The acid (1 g.), dissolved in a mixture of carbon tetrachloride and ethyl acetate, was oxidised with ozone at 0°; no formaldehyde was detected in the issuing gases. After removal of the solvents under diminished pressure, the ozonide was decomposed in water (10 c.c.) on the water-bath. The solution, which contained a little resin in suspension, was distilled, the distillate having a strong odour of methyl *iso*propyl ketone. The *phenylsemicarbazone* crystallised from dilute methyl alcohol in needles, m. p. 101—102° (Found: N, 19·4. $C_{12}H_{17}ON_3$ requires N, 19·2%), unaltered on admixture with an authentic specimen (Found: N, 19·0%). The 2 : 4-dinitrophenylhydrazone crystallised from alcohol in yellow needles, m. p. and mixed m. p. 119—120° (Found: N, 21·3. Calc.: N, 21·1%). The residue in the distilling flask gave on evaporation oxalic acid, m. p. 100—101°.

Condensation of Methyl α-Camphylate and α-Naphthaquinone.—The methyl ester (0·35 g.), prepared by the action of diazomethane on the acid, and α-naphthaquinone (0·4 g.) in methyl alcohol (5 c.c.) were heated on the water-bath for 6 hours. Evaporation of the solvent left a brown solid which contained unchanged α-naphthaquinone. This was removed in steam and the gum which remained in the distilling flask was collected and crystallised from ligroin (b. p. 60—80°) (charcoal). The addition *product* separated in rosettes of needles, m. p. 106° (Found: C, 73·8; H, 6·4. $C_{20}H_{20}O_4$ requires C, 74·1; H, 6·2%).

β-Camphylic Acid.—The acid used in the experiments described below was purified through *iso*bromodihydro-β-camphylic acid. Preliminary experiments with an acid of the correct m. p. which had not been purified in this manner showed it to contain impurities leading to the formation of anomalous degradation products.

Interaction of β-camphylic acid with percamphoric acid in chloroform solution was rapid; addition of oxygen corresponding to one ethylenic linkage had occurred after 3 hours, and the reaction was complete in about 40 hours. A similar difference in the reactivity of the two ethylenic linkages was observed on hydrogenation in alkaline solution with a palladium-norit catalyst: 1 mol. of hydrogen was absorbed in 3 minutes, but complete reduction required 24 hours. The acid, dihydro*iso*lauronolic acid, so obtained, which was an oil, gave a p-*phenylphenacyl* ester crystallising from ligroin (b. p. 40—60°) in prisms, m. p. 68—69° (Found: C, 79·3; H, 7·4. $C_{23}H_{26}O_3$ requires C, 78·9; H, 7·4%). The amide prepared from the acid chloride had m. p. 160—161°.

Oxidation of β-Camphylic Acid.—The acid (1 g.) was ozonised in carbon tetrachloride solution at 0°, and the ozonide decomposed with water in the usual manner. Distillation of the aqueous solution gave methyl *iso*propyl ketone (2 : 4-dinitrophenylhydrazone, m. p. and mixed m. p. 119—120°) (Found: N, 21·5. Calc.: N, 21·1%). The aqueous residue from the steam distillation gave on evaporation oxalic acid, m. p. 99—100°.

Condensation of Methyl β-Camphylate and α-Naphthaquinone.—This condensation was carried out under conditions similar to those used in the case of the ester from the α-acid, the yield being quantitative. The addition *product*, recrystallised from ligroin (b. p. 40—60°) (charcoal) and finally from *cyclo*hexane, was obtained in rosettes of needles, m. p. 135° (Found: C, 73·9; H, 6·3. $C_{20}H_{20}O_4$ requires C, 74·1; H, 6·2%).

Oxidation of iso*Bromodihydro-β-camphylic Acid.*—The acid (1 g.) was ozonised in ethyl acetate solution at 0°; after removal of the solvent the product was decomposed by hot water. Evaporation of the water in a vacuum left an oil, which partly crystallised, decomposition with evolution of hydrogen bromide gradually occurring. The oil was dissolved in sodium hydroxide solution (10%) and heated on the water-bath for 1 hour, and the cooled solution treated with an excess of sodium hypobromite at 0°; bromoform then separated. This was removed, the excess of hypobromite destroyed by sulphur dioxide, and the solution acidified and extracted with ether. Evaporation of the solvent gave an oil (0·6 g.) which crystallised when stirred with

hydrochloric acid. The acid, m. p. 130°, was purified through its sparingly soluble calcium salt; the recovered acid, after recrystallisation from water, had m. p. 139—140°, both alone and in admixture with *as*-dimethylsuccinic acid.

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