264. *Terpene Compounds. Part II. Experiments on the Synthesis of Homoapofenchocamphoric Acid.*

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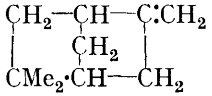
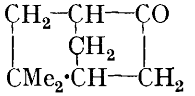
The Wagner rearrangement of fenchyl and *iso*fenchyl alcohols leads to the formation of β-fenchene to which structure (I) has been assigned (Bertram and Helle, *J. pr. Chem.*, 1900, **61**, 353; Wallach and Neumann, *Annalen*, 1901, **315**, 281; Komppa and Roschier, *Ann. Acad. Sci. Fennicae*, 1915, *A*, vii, **14**, 1; Quist, *Annalen*, 1919, **417**, 278; also Semmler, "Die Ätherischen Öle," III, 548), since on oxidation it furnishes β-fenchocamphorone (II) (Wallach, *Annalen*, 1898, **302**, 384) and apofenchocamphoric acid (cf. Short, J., 1927, 961).

(I.)





(II.)

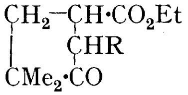
Furthermore, Komppa and Roschier (*Ann. Acad. Sci. Fennicae*, 1917, *A*, x, **15**, 1) have effected a partial synthesis of β-fenchene from β-fenchocamphorone, a substance, which has not, however, been prepared synthetically. We attempted this synthesis, and although we were unsuccessful, the results obtained are now recorded.

Ethyl αα-dimethylglutarate, prepared from *iso*laurolonic acid by known methods, was condensed with ethyl oxalate in the presence of potassium ethoxide, and the resulting product on distillation under reduced pressure yielded *ethyl γ-methylbutane-ααγ-tricarboxylate* (III). This readily furnished a sodio-derivative with alcoholic sodium ethoxide, and the product on digestion with ethyl bromoacetate gave a good yield of *ethyl β-methylpentane-βδδε-tetracarboxylate* (IV). The latter on hydrolysis and elimination of carbon dioxide formed *β-methylpentane-βδε-tricarboxylic acid* (as V) (m. p. 185—187°), from which the corresponding *ethyl* ester (V) was readily obtained by the alcohol-vapour method.

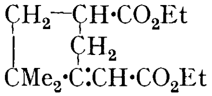
(III.) $CO_2Et{\cdot}CMe_2{\cdot}CH_2{\cdot}CH(CO_2Et)_2$ $CO_2Et{\cdot}CMe_2{\cdot}CH_2{\cdot}C(CO_2Et)_2{\cdot}CH_2{\cdot}CO_2Et$ (IV.)

$CO_2Et{\cdot}CMe_2{\cdot}CH_2{\cdot}CH(CO_2Et){\cdot}CH_2{\cdot}CO_2Et$ (V.)

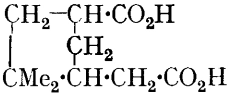
The cyclisation of (V) by means of sodium proceeded normally, with the formation of *ethyl* 2 : 2-*dimethyl*cyclo*pentan*-1-*one*-4 : 5-*dicarboxylate* (VI; $R = CO_2Et$). This was hydrolysed by 8% sulphuric acid to 2 : 2-*dimethyl*cyclo*pentan*-1-*one*-4-*carboxylic acid.* The corresponding *ethyl* ester (VI; $R = H$), on treatment with ethyl bromoacetate and zinc, gave a product (hydroxy-ester) which could not be obtained pure and was converted into a mixture of unsaturated esters (VII, and an isomeride) by means of phosphoryl chloride in dry benzene.



(VI.)



(VII.)



(VIII.)

This mixture was reduced with hydrogen and platinum oxide to give the fully saturated ester (as VIII), which on hydrolysis with alcoholic potash gave homoapofenchocamphoric acid (VIII) in a crystalline state (m. p. 246°), but sufficient has not yet been obtained to study its conversion into β-fenchocamphorone (II).

Experimental

Ethyl αα-Dimethylglutarate.—The preparation of *iso*laurolonic acid (Lees and Perkin, J., 1901, **79**, 341; cf. also Blanc, *Compt. rend.*, 1896, **123**, 749; **124**, 468; *Bull. Soc. chim.*, 1896, **15**, 1191) presented some difficulty until it was discovered that, contrary to the observation of previous workers, the success of the operation depended largely on the temperature during the initial stage of the reaction. Camphoric anhydride (100 g.), dissolved in chloroform (400 c.c.), was gradually mixed with anhydrous aluminium chloride (100 g.), the temperature being kept between 22° and 25° during the process. The product was worked up and the *iso*laurolonic acid purified according to Lees and Perkin (*loc. cit.*); yield 64·5 g., m. p. 134°. This acid (200 g.) was oxidised with nitric acid (Perkin, J., 1902, **81**, 251), and the residue (132 g.) of crude αα-dimethylglutaric acid, which completely solidified in an evacuated desiccator, was directly esterified by absolute alcohol and concentrated sulphuric acid. The ester (86—98 g.) had b. p. 110—115°/9 mm. (Blaise, *Bull. Soc. chim.*, 1896, **21**, 626, gives b. p. 235—236°/atm.), $d_{4^\circ}^{31\cdot6^\circ}$ 0·9849, $n_{\mathrm{D}}^{31\cdot6^\circ}$ 1·4249, $[R_L]_{\mathrm{D}}$ 56·06 (Calc., 56·3) (Found: C, 59·9; H, 9·2. Calc.: C, 61·1; H, 9·2%).

Ethyl γ-Methylbutane-ααγ-tricarboxylate (III).—To granulated potassium (5·6 g.) covered with anhydrous ether (100 c.c.), absolute alcohol (6·5 g.) diluted with anhydrous ether (10 c.c.) was added during ½ hour, the ether not being allowed to boil too vigorously. On standing, the liquid became filled with a flocculent precipitate of potassium ethoxide. Ethyl oxalate (21 g.) was now added, the clear yellow solution cooled in ice, and treated drop-wise with ethyl αα-dimethylglutarate (81 g.) dissolved in a little ether. The mixture, which became dark brown, was kept at room temperature for 24 hrs.; it was then mixed with ice and dilute hydrochloric acid, and the dark red oil which separated was extracted with ether, dried, and freed from solvent. The residue, which gave a violet coloration with alcoholic ferric chloride, was repeatedly fractionated under reduced pressure, 26 g. of a colourless oil being obtained; b. p. 145—148°/10 mm., $d_{4^\circ}^{29^\circ}$ 1·0334, $n_{\mathrm{D}}^{29^\circ}$ 1·4328, $[R_L]_{\mathrm{D}}$ 72·3 (Calc., 71·8) (Found: C, 58·4; H, 8·4. $C_{14}H_{24}O_6$ requires C, 58·3; H, 8·3%).

Ethyl β-Methylpentane-βδδε-tetracarboxylate (IV).—Sodium (2·03 g.) dissolved in absolute alcohol (45 c.c.), was mixed with the above ester (26 g.) and ethyl bromoacetate (10·1 c.c.), and the whole heated on a water-bath for 2 hrs. The product was cooled, diluted with a large volume of water, extracted with ether, the extract washed, dried, and evaporated. The required *ester* formed a colourless, somewhat viscous liquid (25 g.), b. p. 175—176°/9 mm., $d_{4^\circ}^{30\cdot8^\circ}$ 1·0750, $n_{\mathrm{D}}^{30\cdot8^\circ}$ 1·4433, $[R_L]_{\mathrm{D}}$ 92·24 (Calc., 91·94) (Found: C, 58·2; H, 8·1. $C_{18}H_{30}O_8$ requires C, 57·8; H, 8·0%).

β-Methylpentane-βδε-tricarboxylic Acid (as V).—The foregoing tetracarboxylic ester (50 g.) was boiled under reflux with water (150 c.c.) and concentrated hydrochloric acid (150 c.c.) until a clear solution resulted (24 hrs.). On evaporation of the solution under reduced pressure, the crude *acid* (22·5 g.) separated as crystals. Recrystallised from dilute hydrochloric acid, it had m. p. 185—187° [Found: C, 49·2; H, 6·4; equiv., by titration, 72·6. $C_9H_{14}O_6$ (tribasic) requires C, 49·5; H, 6·4%; equiv., 72·6]. The *ethyl* ester (V) was obtained in an almost quantitative yield when the acid (40 g.) mixed with absolute alcohol (150 c.c.) and concentrated sulphuric acid (10 c.c.) was heated for 6 hours at 110° in a current of alcohol vapour. Purified in the usual way, it had b. p. 159°/8 mm., $d_{4^\circ}^{29^\circ}$ 1·0351, $n_{\mathrm{D}}^{29^\circ}$ 1·4376, $[R_L]_{\mathrm{D}}$ 76·45 (Calc., 76·43) (Found: C, 59·8; H,8·5. $C_{15}H_{26}O_6$ requires C, 59·6; H, 8·6%).

*Ethyl 2:2-Dimethyl*cyclo*pentan-1-one-4:5-dicarboxylate* (VI; $R = CO_2Et$).—"Molecular" sodium (3·1 g.) was mixed with dry benzene (40 c.c.), the foregoing ethyl ester (20·13 g.) added, and the whole heated on a water-bath for 3 hrs. The resulting brown sodio-compound was decomposed with ice and excess of dilute hydrochloric acid. The benzene layer was separated, well washed with sodium carbonate solution and water, dried, evaporated, and the residual oil fractionated under diminished pressure, almost the whole (12 g.) distilling at 147—149°/9 mm., $d_{4^\circ}^{28\cdot7^\circ}$ 1·0661, $n_{\mathrm{D}}^{28\cdot7^\circ}$ 1·4510, $[R_L]_{\mathrm{D}}$ 64·6 (Calc., 63·4) (Found: C, 60·7; H, 7·9. $C_{13}H_{20}O_5$ requires C, 60·9; H, 7·8%). *Ethyl 2:2-dimethyl*cyclo*pentan-1-one-4:5-dicarboxylate* possesses an agreeable odour and gives in alcoholic solution a violet coloration with ferric chloride.

*2:2-Dimethyl*cyclo*pentan-1-one-4-carboxylic Acid* (as VI; $R = H$).—The preceding keto-ester (31 g.) was digested on the sand-bath with 10 times its volume of 8% sulphuric acid until solution was complete (3 hrs.). The clear liquid was neutralised with sodium carbonate, evaporated on the water-bath until free from alcohol, and acidified. The *acid*, which separated as an oil, quickly solidified (14 g.), and recrystallisation (charcoal) from benzene–petroleum (b. p. 60—80°) afforded clusters of colourless prisms, m. p. 93° (Found: C, 61·0; H, 7·6. $C_8H_{12}O_3$ requires C, 61·5; H, 7·7%). The acid is sparingly soluble in water and almost insoluble in petroleum. The *ethyl* ester (VI; $R = H$), prepared in the usual way, formed a colourless liquid, b. p. 113°/9 mm., $d_{4^\circ}^{27\cdot5^\circ}$ 1·0176; $n_{\mathrm{D}}^{27\cdot5^\circ}$ 1·4454, $[R_L]_{\mathrm{D}}$ 48·2 (Calc., 47·9) (Found: C, 65·3; H, 8·8. $C_{10}H_{16}O_3$ requires C, 65·2; H, 8·7%).

Ethyl Dehydrohomoapofenchocamphorate (VII or isomeride).—The above keto-ester (14 g.), ethyl bromoacetate (13 g.), and 6 g. of zinc were heated in 100 c.c. of dry benzene, with the addition of a crystal of iodine, until the exothermic reaction began. Reaction was finally completed by heating on a steam-bath for 1 hr., the product decomposed with ice-cold dilute sulphuric acid, and the neutral portion isolated in the usual way. Fractional distillation of this gave unchanged keto-ester (4 g.), b.p. 90—115°/5 mm., and the expected condensation product

(8 g.), b. p. 115—155°/5 mm., which, however, was not analytically pure, probably containing hydroxy-ester. The mixture was therefore converted into the unsaturated ester as follows. A solution of the crude ester (20 g.) in dry benzene (45 c.c.) was refluxed for 5 hrs. with phosphorus oxychloride (7 g.), cooled, poured into water, and the benzene layer separated, washed with sodium carbonate solution, dried (sodium sulphate), and the solvent removed. The unsaturated *ester* was isolated as a transparent, mobile liquid, b. p. 126—127°/4 mm., $d_{4^\circ}^{23\cdot5^\circ}$ 1·0246, $n_{\mathrm{D}}^{23\cdot5^\circ}$ 1·45292, $[R_L]_{\mathrm{D}}$ 67·1 (Calc., 67·4) (Found : C, 66·1; H, 8·8. $C_{14}H_{22}O_4$ requires C, 66·1; H, 8·6%).

Homoapofenchocamphoric Acid (VIII).—10 G. of unsaturated ester (above) were dissolved in 60 c.c. of ether and shaken with 5 g. of platinum oxide in an atmosphere of hydrogen, the calculated quantity of hydrogen being absorbed in 2 hrs. The catalyst was filtered off, ether evaporated, and the residual colourless oil, consisting of the saturated ester, directly hydrolysed with alcoholic potash (KOH, 15 g.; methyl alcohol, 100 c.c.; water, 10 c.c.). After removal of excess of alcohol by repeated addition of water and evaporation, the residue was diluted with water, filtered, and the clear cold solution acidified with an excess of hydrochloric acid, saturated with ammonium sulphate, and extracted several times with ether. The syrupy *acid*, isolated in the usual way, partly solidified in an evacuated desiccator. The crystals were freed from the adhering gum by spreading on a porous plate, and were obtained in minute colourless prisms, m. p. 246°, after several crystallisations (charcoal) from dilute acetone (Found : 60·3; H, 7·9. $C_{10}H_{16}O_4$ requires C, 60·0, H, 8·0%). Like homocamphoric acid (cf. Lapworth, J., 1900, **77**, 1062), it readily crystallised from nitrobenzene, in which it is freely soluble on warming. Its solution in sodium carbonate does not decolorise potassium permanganate even on prolonged standing. The porous plate on extraction with ether afforded a gummy acid, the investigation of which is not yet complete.

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