40. *The Carbonyl Constituents of Eucalyptus Oils. Part IV. The Constitution of Phellandral.* d-, l-, *and* dl-β-iso*Propyladipic Acids.*

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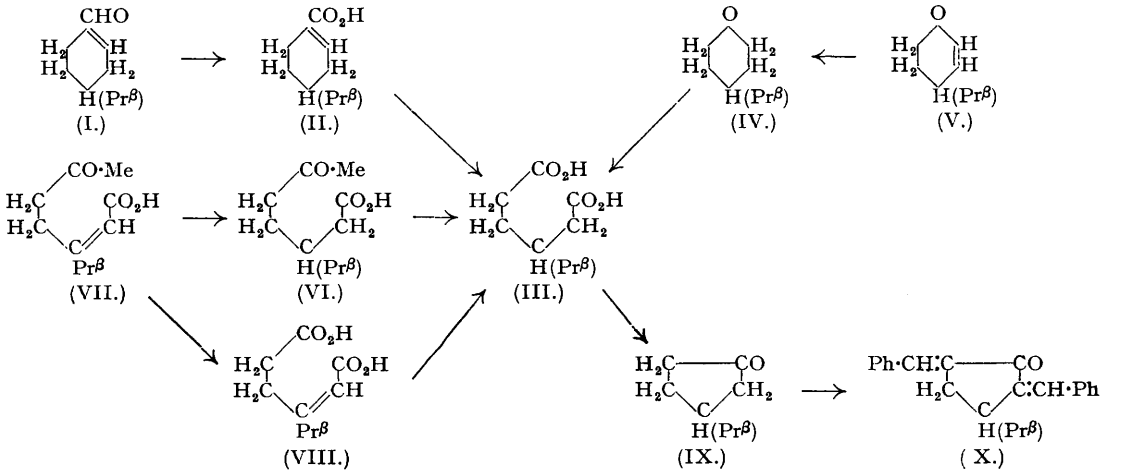
The constitution of phellandral is verified by its oxidation to β-*iso*propyladipic acid. *d*- and *l*-Phellandral respectively yield *d*- and *l*-β-*iso*propyladipic acids, which, however, show no rotation although they yield a series of optically active derivatives. The *d*- and *l*-acids differ markedly in crystalline form and m. p. from *dl*-β-*iso*propyladipic acid, and the properties of corresponding derivatives are also distinct.

In a previous paper (Cooke, Macbeth, and Swanson, *J.*, 1940, 808) the 1 : 4 positions of the substituents in phellandral were confirmed by the conversion of the aldehyde into hexahydrocuminic acid, and the position of the ethylene linkage was indicated by the synthesis of *dl*-phellandric acid from α-bromohexahydrocuminic acid. Further support for the constitution has been sought in the oxidation of *l*-phellandral (I) through *l*-phellandric acid (II) to *l*-β-*iso*propyladipic acid (III). Analytical data indicated that the acid obtained was an *iso*propyladipic acid, but it showed no optical rotation when examined in acetone solutions of varying concentrations. It had, however, a different crystalline form and a considerably lower m. p. than *dl*-β-*iso*propyladipic acid prepared by the oxidation of dihydrocryptone (IV) obtained by the catalytic hydrogenation of cryptone (V) (Cahn, Penfold, and Simonsen, *J.*, 1931, 1366; Berry, Macbeth, and Swanson, *J.*, 1937, 986).



The identity and characteristics of *dl*-β-*iso*propyladipic acid were confirmed by its preparation by the catalytic hydrogenation of β-thujadicarboxylic acid (VIII) which was obtained from β-thujaketonic acid (VII) on oxidation with hypobromite; more satisfactory yields, however, were obtained by reduction of (VII) to δ-acetyl-β-*iso*propyl-*n*-valeric acid (VI) and oxidation of the latter.

dl-β-*iso*Propyladipic acid was further characterised by the preparation of its p-*chloro*- and p-*bromo-phenacyl esters*, and it was also converted into 3-*iso*propyl*cyclo*pentan-1-one (IX) and its dibenzylidene derivative (X) (cf. Wallach and Challenger, *Annalen*, 1911, **388**, 60).

Further examination showed that the acid obtained on the oxidation of *l*-phellandral was l-β-iso*propyladipic acid*, and that the absence of rotation, which at first caused some difficulty, was fortuitous. Braun and Werner (*Ber.*, 1929, **62**, 1050) prepared *dl*-β-*iso*propyladipic acid by the controlled oxidation with permanganate of *p-iso*propyl*cyclo*hexanol, and resolved the inactive acid into its *d*- and *l*-forms. No rotations were recorded for the free acids, and only remarkably low rotations were found in the case of the sodium salts and other derivatives. The m. ps. of all three acids were substantially lower than those we have found, and this causes some doubt concerning the purity of the acids (cf. Blanc, *Bull. Soc. chim.*, 1908, **3**, 294). *l*-β-*iso*Propyladipic acid was characterised by its p-*chloro*- and p-*bromo-phenacyl esters* both of which were optically active. It was also converted into *l*-3-*iso*propyl*cyclo*pentan-1-one which had a considerable *lævo*-rotation and gave an optically active *semicarbazone*. The ketone was further characterised by its 2 : 4-*dinitrophenylhydrazone* and by its *dibenzylidene derivative*, both of which have higher m. ps. than the corresponding derivatives of the *dl*-ketone.

The oxidation of a sample of *d*-phellandral (Berry, Macbeth, and Swanson, *J.*, 1937, 1448) in a similar way yielded *d*-β-*iso*propyladipic acid which gave an optically active *d*-3-*iso*propyl*cyclo*pentan-1-one. The *d*-ketone was characterised by its *semicarbazone*, 2 : 4-*dinitrophenylhydrazone*, and *dibenzylidene derivative*.

To complete the proof a sample of synthetic *dl*-phellandric acid was oxidised to *dl*-β-*iso*propyladipic acid identical with authentic samples obtained from dihydrocryptone and β-thujaketonic acid.

Experimental.

dl-β-iso*Propyladipic Acid.*—(a) *From β-thujaketonic acid.* The ketonic acid (10 g.) on oxidation by means of sodium hypobromite gave crude β-thujadicarboxylic acid (4·5 g.) which on recrystallisation from ether–ligroin had m. p. 115—116° (cf. Birch and Earl, *J. Proc. Roy. Soc. N.S.W.*, 1938, **72**, 55). β-Thujadicarboxylic acid (2·3 g.) in alcohol (40 c.c., 90%) containing palladised charcoal (0·5 g.) was hydrogenated at the laboratory temperatures; the reaction was slow and, during 3 days, the absorption of hydrogen (320 c.c.) was complete. After filtration and removal of solvent, a slowly crystallising oil (2·3 g.) remained; this, after distillation under high vacuum and crystallisation from ether–ligroin, gave *dl-iso*propyladipic acid, m. p. 81°, not depressed on admixture with a sample of the acid (m. p. 82—83°) obtained by the oxidation of dihydrocryptone (Found: C, 57·2; H, 8·5. Calc. for $C_9H_{16}O_4$: C, 57·4; H, 8·6%).

(b) *From δ-acetyl-β-isopropyl-n-valeric acid.* β-Thujaketonic acid (2 g.) was hydrogenated at laboratory temperature in methanol containing palladised charcoal, complete absorption of hydrogen (275 c.c. at 25°/765 mm.) occurring within 30 mins. The resulting acid, a colourless oil (2 g.), was dissolved in sodium hydroxide (10 c.c., 5%) and added to bromine (2·8 c.c.) in sodium hydroxide (100 c.c., 6%) at 0°. After an hour in ice-water, the solution was extracted with ether, treated with a little sodium bisulphite solution and, after acidification, was exhaustively extracted with ether. An oil (1·8 g.), which subsequently crystallised, was obtained on removal of the solvent. On recrystallisation from water containing HCl it had m. p. 81—82°, not depressed on admixture with the above samples.

(c) *From* dl-*β-phellandric acid.* The acid (10 g.) dissolved in acetone (200 g.) at 0° was oxidised, whilst continuously stirred and kept at < 10°, by the gradual addition of finely powdered potassium permanganate. After the addition of the major part of the permanganate (25 g., 4 atoms oxygen) some water was added and further quantities of permanganate (4 g.) until the solution retained the pink colour for more than 30 mins. Excess permanganate was removed by addition of a little bisulphite, and the oxide sludge separated and well washed with hot water. After concentration of the combined filtrate and washings under reduced pressure, acidification of the concentrate, extraction with ether and removal of the solvent a clear oil (9 g.) was obtained which subsequently solidified. Distillation in high vacuum and recrystallisation from dilute hydrochloric acid gave *dl-β-iso*propyladipic acid, m. p. 82°, which was not depressed on admixture with the samples above (Found: C, 57·3; H, 8·4%).

p-*Bromophenacyl Ester of* dl-β-iso*Propyladipic Acid.*—This was prepared by the usual procedure. The resulting oil partly solidified; after it had remained on porous porcelain it was crystallised from alcohol giving the *ester*, m. p. 83° (Found: C, 51·5; H, 4·5; Br, 27·5. $C_{25}H_{26}O_6Br_2$ requires C, 51·5; H, 4·5; Br, 27·45%). The p-*chlorophenacyl ester* of *dl-β-iso*propyladipic acid was similarly prepared and had m. p. 65–67° (Found: C, 60·75; H, 5·2; Cl, 14·3. $C_{25}H_{26}O_6Cl_2$ requires C, 60·8; H, 5·3; Cl, 14·4%).

dl-3-iso*Propyl*cyclo*pentan*-1-*one.*—*dl-β-iso*Propyladipic acid (4·8 g.) was heated with barium hydroxide (0·5 g.) up to 110° in an air-bath during 40 mins. and the temperature then gradually raised to 200° during 30 mins. On raising the temperature to 250°, oil and water began to distil and the temperature was maintained at 250—260°. The collected oil (3·6 c.c.) was dissolved in 60% alcohol and the semicarbazone prepared by the addition of semicarbazide hydrochloride and potassium acetate. The semicarbazone (3·3 g.), after recrystallisation from alcohol, had m. p. 191—192°, and was optically inactive (Found: C, 59·1; H, 9·25. Calc. for $C_9H_{17}ON_3$: C, 59·0; H, 9·35%). The purified semicarbazone was steam-distilled in the presence of dilute sulphuric acid (50 c.c., 10%) and the distillate extracted with ether. After drying and removal of the solvent, the ketone remained as a colourless oil which had b. p. 184°/762 mm., $n_D^{18°}$ 1·4439, and was optically inactive. dl-3-iso*Propyl*cyclo*pentan*-1-*one*-2 : 4-*dinitrophenylhydrazone*, prepared in the usual way and recrystallised from alcohol, separated as yellow needles having m. p. 133—134° (Found: C, 54·9; H, 5·85. $C_{14}H_{18}O_4N_4$ requires C, 54·9; H, 5·9%). The dibenzylidene derivative was prepared by the addition of freshly distilled benzaldehyde (0·5 g.) to a solution of the ketone (0·0025 mol.) in a few c.c. of alcohol. The yellowish crystals were washed with a little alcohol and had m. p. 138° (Found: C, 87·2; H, 7·3. Calc. for $C_{22}H_{22}O$: C, 87·4; H, 7·3%) (cf. Wallach and Challenger, *loc. cit.*).

Oxidation of l-*Phellandral.* l-β-iso*Propyladipic Acid.*—*l*-Phellandral (20 g.) having $[\alpha]_D$ — 133·4° was dissolved in acetone (400 c.c.) cooled in ice and stirred mechanically during the gradual addition of finely powdered potassium permanganate at such a rate that the temperature did not rise above 10°. After the addition of some 40 g. of oxidant, ice-water was added to the reaction mixture and further permanganate (20 g.) added until the mixture had a permanent pink coloration. Filtration and thorough washing of the sludge with hot water followed by concentration of the combined filtrate and washings gave a separation of a little cuminic acid, m. p. 115°, on acidification. (In all phellandral oxidations some separation of cuminic acid was observed. This appears to be formed by oxidation of phellandral itself and not from traces of cuminal which might supposedly be present, since it has also been isolated in oxidation of phellandric acid.) Exhaustive extraction of the acidified concentrate with ether gave finally a syrupy oil (18·8 g.) which solidified to a waxy solid. Trituration with a little warm ligroin (60—90°) and suction-filtration gave a crystalline residue which when recrystallised from water yielded *l-β-iso*propyladipic acid, m. p. 73—73·5°. The m. p. could not be raised by further crystallisation; the m. p. was lowered on admixture with authentic samples of the *dl*-acid. Solutions of various concentration of the acid in acetone were optically inactive. The crystalline form was markedly different from that of the *dl*-acid (Found: C, 57·5; H, 8·55. Calc. for $C_9H_{16}O_4$: C, 57·4; H, 8·55%). The p-*chlorophenacyl ester* of *l-β-iso*propyladipic acid, prepared in the usual way, had m. p. 48—49°. It had $[\alpha]_D^{22°}$ — 9·43° in methanol (*c*, 0·9544) (Found: C, 60·65; H, 5·4; Cl, 14·25. $C_{25}H_{26}O_6Cl_2$ requires C, 60·8; H, 5·3; Cl, 14·4%). The p-*bromophenacyl ester* had m. p. 63—64° and $[\alpha]_D^{25}$ — 7·41° in alcohol (*c*, 1·8896) (Found: C, 51·6; H, 4·6; Br, 27·4. $C_{25}H_{26}O_6Br_2$ requires C, 51·4; H, 4·5; Br, 27·45%).

l-3-iso*Propyl*cyclo*pentan*-1-*one.* *l-β-iso*Propyladipic acid (5·6 g.) and barium hydroxide (0·5 g.) when distilled as described for the *dl*-acid yielded a pale yellow-green oil (4 c.c.) which, after purification through the semicarbazone, gave the pure *l*-ketone, b. p. 183°/761 mm., $n_D^{18°}$ 1·4443 and $[\alpha]_D^{20°}$ —191·3° in alcohol (*c*, 5·1172). The *semicarbazone* of the *l*-ketone had m. p. 191—192° and $[\alpha]_D^{20°}$ —76·4° in acetone (*c*, 0·2722) (Found: C, 59·2; H, 9·45; N, 22·95. $C_9H_{17}ON_3$ requires C, 59·0; H, 9·35; N, 22·95%). The 2 : 4-*dinitrophenylhydrazone* had m. p. 137° (Found: C, 54·9; H, 5·85. $C_{14}H_{18}O_4N_4$ requires C, 54·85; H, 5·9%). The *dibenzylidene derivative* of the *l*-ketone had m. p. 149—150° (Found: C, 87·3; H, 7·3. $C_{22}H_{22}O$ requires C, 87·4; H, 7·35%).

Oxidation of d-*Phellandric Acid.* d-β-iso*Propyladipic Acid.*—*d*-Phellandric acid (3·3 g.) in acetone (80 c.c.) was oxidised as described above. The product was an oil (3·4 g.) which did not crystallise. It was treated with hot water and filtered from a small amount of insoluble oil and cuminic acid (0·24 g.). The concentrated filtrate was exhaustively extracted with ether and, after removal of the solvent, the solidified residue was left on porous porcelain. The product was recrystallised from dilute hydrochloric acid and *d-β-iso*propyladipic acid (0·9 g.) obtained. It had m. p. 72—73° and its crystalline form was similar to that of the *l*-acid (Found: C, 57·3; H, 8·4. Calc.: C, 57·4; H, 8·6%).

d-3-iso*Propyl*cyclo*pentan*-1-*one.*—*d-β-iso*Propyladipic acid (0·8 g.) when distilled with barium hydroxide (0·2 g.) gave the crude ketone (0·45 g.) which when purified through the semicarbazone gave the pure *d*-ketone as a colourless oil having the characteristic odour and b. p. 183°/760 mm., $n_D^{17°}$ 1·4438, and $[\alpha]_D^{17°}$ + 190° in alcohol (*c*, 1·0052). The *semicarbazone* of the *d*-ketone, prepared in the usual way, had m. p. 191° (Found: C, 59·05; 9·35. $C_9H_{17}ON_3$ requires C,

59·0; H, 9·35%). The 2 : 4-*dinitrophenylhydrazone*, pale yellow needles, had m. p. 136° (Found: C, 55·0, H, 6·0. $C_{14}H_{18}O_4N_4$ requires C, 54·85; H, 5·9%). The *dibenzylidene derivative* had m. p. 149—150° (Found: C, 87·2; H, 7·3. $C_{22}H_{22}O$ requires C, 87·4; H, 7·35%).

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