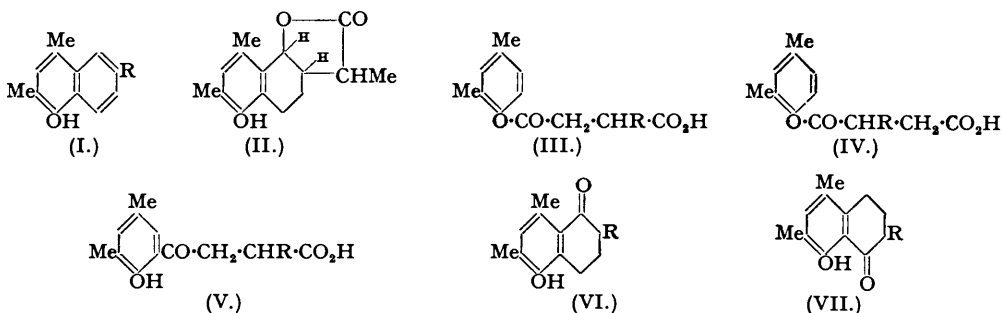


208. The Constitution of ψ -Santonin. Part VIII. Synthesis of
6-Ethyl-2:4-dimethyl-1-naphthol.

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6-Ethyl-2:4-dimethyl-1-naphthol (I; R = Et) and 2:4:6-trimethyl-1-naphthol (I; R = Me) have been synthesised. The former is identical with the product of dehydrogenation of desmotropo- ψ -santonin (Cocker *et al.*, *J.*, 1950, 1781).

COCKER *et al.* (*loc. cit.*) dehydrogenated desmotropo- ψ -santonin with palladised charcoal and obtained a product which they concluded was 6-ethyl-2:4-dimethyl-1-naphthol (I; R = Et). Synthesis of this compound has shown the conclusion to be correct and there is now little doubt that (II) adequately represents the desmotropo-compound (cf. previous papers in this series).



Condensation of succinic anhydride and its derivatives with methyl *m*-4-xylyl ether in presence of aluminium chloride takes place predominantly *meta* to the methoxy-group. Alkylsuccinic anhydrides yield largely α -alkyl- β -(5-hydroxy-2:4-dimethylbenzoyl)propionic acids, the corresponding β -alkyl compounds being produced in negligible yield (cf. Cocker, Lipman, and Whyte, *J.*, 1950, 1519; Cocker *et al.*, *loc. cit.*; Cocker, Fateen, and Lipman, preceding

paper). Thus, workable yields of the tetralones of type (VI; R = alkyl) cannot be obtained by this means. However, rearrangement of the alkylsuccinic esters of *m*-4-xyleneol (cf. Cocker, *J.*, 1946, 36) could possibly yield keto-acids of type (V; R = alkyl) which would form the starting points for the synthesis of the tetralones mentioned and, hence, of 6-alkyl-2:4-dimethyl-1-naphthols.

In model experiments, *m*-4-xyleneol was esterified with succinic anhydride and the ester (III or IV; R = H) was rearranged with aluminium chloride to β -(2-hydroxy-3:5-dimethylbenzoyl)propionic acid. Attempts to oxidise this acid to the corresponding benzoic acid failed, but there can be little doubt as to its structure in view of the fact that (a) it differs from β -(5-hydroxy-2:4-dimethylbenzoyl)propionic acid obtained by demethylation of its methyl ether (Cocker and Lipman, *J.*, 1947, 533; Cocker, Lipman, and Whyte, *loc. cit.*), and (b) the corresponding butyric acid readily cyclised to 5:6:7:8-tetrahydro-5-keto-2:4-dimethyl-1-naphthol (VI; R = H) which differs from the tetralone (VII; R = H) obtained by the workers mentioned, but (c) it yields the same tetralin as was obtained by these workers.

m-4-Xyleneol, esterified with ethylsuccinic anhydride, gave a mixture of esters (III and IV; R = Et) from which a pure ester was isolated. Its exact nature is being investigated. The ester was rearranged with aluminium chloride, and a pure keto-acid was obtained. Attempts to oxidise this acid failed, but (a) it differed from α -ethyl- β -(5-hydroxy-2:4-dimethylbenzoyl)propionic acid (Cocker *et al.*, *loc. cit.*), and (b) it could not be methylated. The latter experience is reminiscent of our attempts to methylate the "hindered" hydroxyl group of 2-hydroxy-3:5-dimethylbenzoic acid, whilst the isomer 5-hydroxy-2:4-dimethylbenzoic acid can be readily methylated. There seems to be no doubt, therefore, that *ortho*-migration takes place in the Fries reaction. The keto-acid, first reduced to the butyric acid, gave a tetralone, different from (VII; R = Et), which did not yield a semicarbazone and must, therefore, possess a hindered carbonyl group (cf. Cagniant and Buu-Hoi, *Bull. Soc. chim.*, 1942, 9, 841; Cocker *et al.*, *loc. cit.*). In view of this evidence, the keto-acid must be represented as (V; R = Et) and the tetralone as (VI; R = Et). Reduction of the tetralone and dehydrogenation of the product yielded 6-ethyl-2:4-dimethyl-1-naphthol (I), which along with its picrate and trinitrobenzene adduct was identical with the "natural" naphthol of Cocker *et al.* (*loc. cit.*) and its corresponding derivatives, and differed from 7-ethyl-2:4-dimethyl-1-naphthol (Cocker *et al.*, *loc. cit.*).

Two pure esters, m. p.s 112—113° and 65°, respectively, were isolated from the reaction between *m*-4-xyleneol and methylsuccinic anhydride. The former ester was rearranged and yielded the keto-acid (V; R = Me), which gave the hydroxy-tetralone (VI; R = Me). This gave no semicarbazone and differed from the isomer (VII; R = Me) described by Cocker, Fateen, and Lipman (preceding paper). 2:4:6-Trimethyl-1-naphthol was obtained from the tetralone by conventional methods and characterised as its picrate and trinitrobenzene adduct.

The second ester, m. p. 65°, was also rearranged to a keto-acid, but this was obtained in such small yields that little could be done to establish its constitution. It is possibly β -(2-hydroxy-3:5-dimethylbenzoyl)- β -methylpropionic acid.

The melting points of the isomeric hydroxy-tetralones (types VI and VII) are interesting and provide further evidence for the structures of the tetralones (type VI) obtained through the keto-acids produced in the Fries rearrangement. In the tetralones of type (VI), intramolecular hydrogen bonding between hydroxyl and keto-groups is impossible, but those of type (VII) should be chelated. The table makes this point clear.

| | Type (VI). | Type (VII). |
|--------------|----------------|---------------------------|
| R = H | M. p. 180—181° | M. p. 61.5° ¹ |
| R = Me | M. p. 147—148° | M. p. 56—57° ² |
| R = Et | M. p. 105—106° | M. p. 28° ³ |

¹ Cocker, Lipman, and Whyte, *loc. cit.* ² Cocker, Fateen, and Lipman, *loc. cit.* ³ Cocker *et al.*, *loc. cit.*

EXPERIMENTAL.

m-4-Xylyl Hydrogen Succinate.—*m*-4-Xyleneol (5 g.), when heated with succinic anhydride (5 g.) at 130° for 3 hours and then rapidly chilled, yielded a solid. This was extracted with aqueous sodium carbonate, and the extract washed with ether and acidified. The required ester (8 g.) was collected and dried. It crystallised from benzene-light petroleum as colourless rods (6.8 g.), m. p. 78° (Found: C, 64.7; H, 6.7. C₁₃H₁₄O₄ requires C, 64.9; H, 6.3%).

β -(2-Hydroxy-3:5-dimethylbenzoyl)propionic Acid.—A solution of the above ester (2 g.) in nitrobenzene (30 c.c.) was heated to 140°, and aluminium chloride (8 g.) in nitrobenzene (100 c.c.) was added. The mixture was heated for 0.5 hour, cooled, and decomposed with ice and hydrochloric acid. The product was purified by dissolution in aqueous sodium carbonate, filtration, acidification, and finally

crystallisation from dilute alcohol, from which the *keto-acid* (0.3 g.) separated as shining needles, m. p. 147—148° (Found : C, 64.9; H, 6.5. $C_{12}H_{14}O_4$ requires C, 64.9; H, 6.3%).

γ -(2-Hydroxy-3 : 5-dimethylphenyl)butyric Acid.—The *keto-acid* (1.1 g.), reduced with amalgamated zinc, yielded the required *acid* (0.3 g.) which separated from light petroleum as hair-like needles, m. p. 82° (Found : C, 69.2; H, 7.7. $C_{12}H_{16}O_3$ requires C, 69.2; H, 7.7%).

5 : 6 : 7 : 8-Tetrahydro-5-keto-2 : 4-dimethyl-1-naphthol (0.2 g.) was obtained from the preceding acid (0.3 g.) on treatment with concentrated sulphuric acid (1.5 g.). It crystallised from benzene-light petroleum as needles, m. p. 180—181° (Found : C, 75.7; H, 7.5. $C_{12}H_{14}O_2$ requires C, 75.8; H, 7.4%). Its *semicarbazone* crystallised from dilute alcohol as needles, m. p. 226—227° (Found : C, 63.9; H, 6.9. $C_{13}H_{17}O_2N_3$ requires C, 63.2; H, 6.9%).

β -(5-Hydroxy-2 : 4-dimethylbenzoyl)propionic acid obtained from its methyl ether (Cocker and Lipman, *J.*, 1947, 533; Cocker, Lipman, and Whyte, *J.*, 1950, 1519) consisted of plates, m. p. 139° (Found : C, 64.5; H, 6.8. $C_{12}H_{14}O_4$ requires C, 64.9; H, 6.3%).

2 : 4 : 6-Trimethyl-1-naphthol (I; R = Me).—*m*-4-Xylyl esters of methylsuccinic acid. A mixture of the xylene (5 g.) and methylsuccinic anhydride (5 g.) was heated at 140° for 4 hours. After chilling, extraction with sodium carbonate solution, and reprecipitation, a solid (7.5 g.; m. p. 85—105°) was obtained. Crystallisation from benzene-light petroleum yielded two esters, A (2.6 g.; m. p. 112—113°) (Found : C, 66.1; H, 6.8. $C_{13}H_{16}O_4$ requires C, 66.1; H, 6.8%), and B (0.45 g.; m. p. 65°) (Found : C, 65.2; H, 6.6%).

Fries rearrangement of ester A. The ester (2 g.) was stirred and heated with aluminium chloride (6 g.) for 40 minutes at 140°, and was then decomposed in the usual way. The dark solution was extracted with ether from which a sticky solid (1.4 g.) was obtained. It was crystallised from benzene (charcoal) and obtained (0.9 g.) as needles, m. p. 122°. This was considered to be β -(2-hydroxy-3 : 5-dimethylbenzoyl)- α -methylpropionic acid (Found : C, 65.9; H, 6.8. $C_{13}H_{16}O_4$ requires C, 66.1; H, 6.8%).

5 : 6 : 7 : 8-Tetrahydro-5-keto-2 : 4 : 6-trimethyl-1-naphthol (0.2 g.) was obtained by reduction of the above *keto-acid* with amalgamated zinc, and cyclisation of the resultant liquid butyric acid (0.6 g.) with 98% sulphuric acid. It crystallised from benzene-light petroleum as needles, m. p. 148—149° (Found : C, 76.2; H, 7.7. $C_{13}H_{16}O_2$ requires C, 76.4; H, 7.8%). It did not form a semicarbazone.

5 : 6 : 7 : 8-Tetrahydro-2 : 4 : 6-trimethyl-1-naphthol, prepared by reduction of the hydroxytetralone (0.6 g.) with amalgamated zinc, crystallised from light petroleum as needles (0.5 g.), m. p. 91° (Found : C, 81.9; H, 9.7. $C_{13}H_{18}O$ requires C, 82.1; H, 9.5%).

2 : 4 : 6-Trimethyl-1-naphthol (I; R = Me). The above hydroxy-tetralin (0.4 g.) was heated with selenium (1.2 g.) for 2.5 hours at 340°. The product (0.15 g.) separated from light petroleum (b. p. 40—60°) as needles, m. p. 123° (Found : C, 83.6; H, 7.6. $C_{13}H_{16}O$ requires C, 83.9; H, 7.5%). Light absorption: Max., 2410, 3030 (3180), and 3330 Å.; log ϵ = 4.59, 3.66 (3.53), and 3.41 respectively. Its *picrate* crystallised from benzene as scarlet needles, m. p. 162° (Found : C, 55.3; H, 4.4. $C_{19}H_{17}O_8N_3$ requires C, 54.9; H, 4.1%). Its *trinitrobenzene* adduct crystallised from benzene as orange needles, m. p. 170° (Found : C, 56.9; H, 4.6. $C_{19}H_{17}O_7N_3$ requires C, 57.2; H, 4.3%).

Fries rearrangement of ester (B). The ester (1.7 g.) was treated as (A) and yielded a heavy oil which solidified and was crystallised several times from benzene-light petroleum from which the *keto-acid* separated as plates, m. p. 133° (Found : C, 65.3; H, 6.6. $C_{13}H_{16}O_4$ requires C, 66.1; H, 6.8%).

6-Ethyl-2 : 4-dimethyl-1-naphthol (I; R = Et).—*m*-4-Xylyl esters of ethylsuccinic acid. Ethylsuccinic acid was prepared by Wren and Haller's method (*J.*, 1937, 230). A mixture of xylene (10 g.) and ethylsuccinic anhydride (12 g.), heated at 140°, yielded a solid (4.3 g.), m. p. 55—72°. This was repeatedly crystallised from benzene-light petroleum, thus affording shining prisms of a pure ester (1.4 g.), m. p. 84—85° (Found : C, 67.9; H, 7.3. $C_{14}H_{18}O_4$ requires C, 67.2; H, 7.2%).

α -Ethyl- β -(2-hydroxy-3 : 5-dimethylbenzoyl)propionic acid. The ester (3.5 g.) in nitrobenzene (50 c.c.) was heated to 140°, and aluminium chloride (16 g.) in nitrobenzene (40 c.c.) was added during 15 minutes. The product (0.3 g.; m. p. 103—113°) was crystallised from benzene from which the required *keto-acid* (0.2 g.) was deposited as plates, m. p. 140—141° (Found : C, 67.8; H, 7.2. $C_{14}H_{18}O_4$ requires C, 67.2; H, 7.2%).

α -Ethyl- γ -(2-hydroxy-3 : 5-dimethylphenyl)butyric acid obtained from the preceding compound failed to crystallise.

6-Ethyl-5 : 6 : 7 : 8-tetrahydro-5-keto-2 : 4-dimethyl-1-naphthol (0.45 g.) obtained from the liquid butyric acid (0.7 g.) separated from light petroleum (b. p. 60—80°) as needles, m. p. 105—106° (Found : C, 76.9; H, 8.1. $C_{14}H_{18}O_3$ requires C, 77.1; H, 8.3%). It failed to yield a semicarbazone.

6-Ethyl-5 : 6 : 7 : 8-tetrahydro-2 : 4-dimethyl-1-naphthol (0.2 g.), obtained by reduction of the preceding compound (0.4 g.) with amalgamated zinc, was purified by sublimation and gave m. p. 61—65°. It was directly heated with selenium (0.6 g.) for 2.5 hours at 340°. The product, extracted with methanol, was first sublimed in a vacuum and then crystallised from light petroleum (b. p. 40—60°) as needles, m. p. 110—111°. Its *picrate* had m. p. 142° and its *trinitrobenzene* adduct m. p. 150°. Both derivatives and the naphthol itself were identical (mixed m. p.) with the naphthol and its corresponding derivatives obtained from desmotropo- ψ -santonin by Cocker *et al.* (*J.*, 1950, 1781).

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