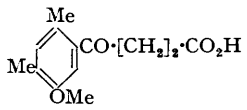
315. *The Constitution of ψ-Santonin. A Correction to Part III.*

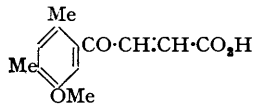
By Wesley Cocker, Cyril Lipman, and D. R. A. Whyte.

The products of condensation of *m*-4-xylyl methyl ether with succinic and maleic anhydrides are respectively β-(5-methoxy-2 : 4-dimethylbenzoyl)-propionic acid (*A*) and -acrylic acid (*B*), and not β-(2-methoxy-3 : 5-dimethylbenzoyl)-propionic (*C*) and -acrylic acids (*D*) as stated by Cocker and Lipman (*J.*, 1947, 533).

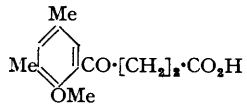
In an earlier communication, Cocker and Lipman (*loc. cit.*) assumed that succinic and maleic anhydrides condense with *m*-4-xylyl methyl ether in the *ortho*-position to the methoxy-group. It has now been shown by oxidation of the products to 5-methoxy-2 : 4-dimethylbenzoic acid (cf. Cocker *et al.*, in the press) that condensation takes place predominantly at the *meta*-position to the methoxy-group, thus confirming the work of von Auwers and Mauss (*Ber.*, 1928, **61**, 1495) (previously overlooked by Cocker and Lipman) who showed that reaction of acyl chlorides with *m*-4-xylyl methyl ether gave mainly 5-methoxy-2 : 4-dimethylphenyl ketones. This development involves the re-orientation of a number of compounds, described by Cocker and Lipman, which were derived from the initial condensation products, β-(5-methoxy-2 : 4-dimethylbenzoyl)-propionic (*A*) and -acrylic acids (*B*) respectively.



(*A*.)

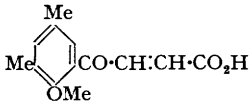


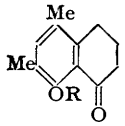
(*B*.)



(*C*.)

(*D*.)





(*E*.)

Reduction of (*A*) affords γ-(5-methoxy-2 : 4-dimethyl)phenylbutyric acid * which on cyclisation with concentrated sulphuric acid at 65° yields almost pure 1-keto-8-methoxy-5 : 7-dimethyl-1 : 2 : 3 : 4-tetrahydronaphthalene (*E*; R = Me), whilst 80% sulphuric acid on the water-bath affords a mixture in which the hydroxy-compound (*E*; R = H) predominates. The subsequent stages in the production of 2 : 4-dimethyl-1-naphthol (Cornforth, Cornforth, and Robinson, *J.*, 1943, 168; Clemo and Cocker, *J.*, 1946, 30; Cocker and Lipman, *loc. cit.*) are unaffected by the new orientation.

* This acid, stated to have m. p. 92°, has been obtained in another modification, m. p. 120°. Both, however, yield the same hydroxy-butyric acid, m. p. 116—117°, on demethylation (Cocker and Lipman, *loc. cit.*).

Cocker and Lipman (*loc. cit.*) described the tetralone, m. p. 61·5°, obtained by the use of 80% sulphuric acid as 1-keto-5-methoxy-6 : 8-dimethyl-1 : 2 : 3 : 4-tetrahydronaphthalene. Later work has shown that the tetralone was in fact a hydroxy-compound now known to be (*E*; R = H). Its methyl ether (*E*; R = Me) melts at 41—42°. There seems to have been some confusion at this point in the earlier work since the semicarbazone, glyoxylate, and bromotetralone described were correctly formulated as methoxy-compounds. The piperonylidene derivative was undoubtedly a hydroxy-compound and the analytical figures given in the earlier paper are in good agreement with this view. We have been unable to obtain the hydroxytetralone, m. p. 145°, previously described.

Cocker and Lipman's tetralone gave a violet ferric chloride colour, but was insoluble in sodium hydroxide solution, and a methoxyl determination performed by other workers gave a value in good agreement with that expected for the methoxy-tetralone. At the time, it was concluded that enolisation was responsible for the ferric chloride reaction, whereas we now know that the colour was associated with the phenolic group. The insolubility of the tetralone in aqueous sodium hydroxide is a result of steric hindrance; thus, for example, 2 : 4-dimethyl-6-*tert.*-butylphenol is sparingly soluble in all but the strongest alkali. The liquid tetralone used in the preparation of derivatives was actually a mixture of hydroxy- and methoxy-compounds and not a mixture of keto and enol forms.

We have now prepared the semicarbazone of the hydroxy-tetralone (*E*; R = H) and the piperonylidene derivative of its methyl ether (*E*; R = Me). 5-Hydroxy-6 : 8-dimethyl-1 : 2 : 3 : 4-tetrahydronaphthalene was obtained from both the tetralones (*E*; R = H or Me) and was readily dehydrogenated to 2 : 4-dimethyl-1-naphthol.

In addition to the compounds mentioned above, the various products described by Cocker and Lipman (*loc. cit.*), who denoted them by the numbers in parenthesis, have to be re-orientated as follows :

Route A.—2-Bromo-1-keto-8-methoxy-5 : 7-dimethyl-1 : 2 : 3 : 4-tetrahydronaphthalene (VIII).

Route B.—Ethyl 1-keto-8-methoxy-5 : 7-dimethyl-1 : 2 : 3 : 4-tetrahydronaphthalene-2-glyoxylate (XI) and -carboxylate (XII).

Route C.—Ethyl α-chloro-β-(5-methoxy-2 : 4-dimethylbenzoyl)propionate (XIV). Ethyl α-(5-methoxy-2 : 4-dimethylbenzoyl)butane-βγγ-tricarboxylate (XV). α-(5-Methoxy-2 : 4-dimethylbenzoyl)butane-βγ-dicarboxylic acid (XVI). α-(β-5-Methoxy-2 : 4-dimethylphenylethyl)-α′-methylsuccinic acid (XVII). Lactone of 1-keto-8-methoxy-5 : 7-dimethyl-1 : 2 : 3 : 4-tetrahydronaphthalene-2-α-propionic acid (III; R = Me).

Re-orientation of the methoxy-dimethylacetophenone, m. p. 76°, described by Cocker and Lipman (*loc. cit.*), leads to 5-methoxy-2 : 4-dimethylacetophenone. The melting point of this ketone is given by von Auwers and Mauss (*loc. cit.*) as 50—51°, and a specimen recently prepared in these laboratories had m. p. 52°; consequently the constitution of this ketone, m. p. 76°, is still uncertain. It is possible that the difference in melting point is due to dimorphism.

Experimental.

1-*Keto*-8-*methoxy*-5 : 7-*dimethyl*-1 : 2 : 3 : 4-*tetrahydronaphthalene* (*E*; R = Me).—γ-(5-Methoxy-2 : 4-dimethylphenyl)butyric acid was heated with 5 times its weight of concentrated sulphuric acid at 65—70° for 10 minutes. The product was poured on ice, collected with ether, and washed with aqueous sodium hydroxide, and the solvent removed, leaving the *methoxy-tetralone* as an oil (20%) which solidified and crystallised from light petroleum (b. p. 40—60°) as needles, m. p. 41—42° (Found : C, 76·5; H, 7·8; OMe, 14·7. $C_{13}H_{16}O_2$ requires C, 76·5; H, 7·8; OMe, 15·2%). Its *piperonylidene* derivative crystallised from alcohol as pale yellow needles, m. p. 112—113° (Found : C, 75·1; H, 5·8. $C_{21}H_{20}O_4$ requires C, 75·0; H, 5·9%).

The *semicarbazone* of the hydroxy-tetralone (*E*; R = H) crystallised from dilute alcohol as needles, m. p. 273—275° (Found : C, 63·5; H, 6·9. $C_{13}H_{17}O_2N_3$ requires C, 63·2; H, 6·9%).

5-*Hydroxy*-6 : 8-*dimethyl*-1 : 2 : 3 : 4-*tetrahydronaphthalene*.—Obtained by the demethylation of its methyl ether, this *hydroxy*-compound crystallised from light petroleum (b. p. 40—60°) as needles, m. p. 76—76·5° (Found : C, 82·25; H, 8·9. $C_{12}H_{16}O$ requires C, 81·8; H, 9·1%).

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