CCCXXXVII.—*Unsaponifiable Matter from the Oils of Elasmobranch Fish. Part VIII. The Structure of the Naphthalene Hydrocarbon derived from Squalene.*

By Isidor Morris Heilbron and Donald Graham Wilkinson.

It was shown in Part III of this series (Harvey, Heilbron, and Kamm, J., 1926, 3136) that, whereas squalene suffers complete decomposition when heated with sulphur, tetra*cyclo*squalene yields on similar treatment a naphthalene hydrocarbon, $C_{13}H_{14}$. Almost simultaneously with the appearance of this paper, Ruzicka, Steiger, and Schinz (*Helv. Chim. Acta*, 1926, **9**, 962) published the results of an investigation into the nature of Manila copal and described the isolation of a hydrocarbon of the same empirical formula as ours and having similar physical constants.

By oxidation of the hydrocarbon with potassium ferricyanide these authors obtained an acid, m. p. 310°, which gave the analytical figures of a naphthalenedicarboxylic acid and hence concluded that the hydrocarbon itself was a methylethylnaphthalene.

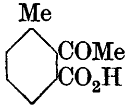
Prior to the appearance of the above paper, we had carried out a similar oxidation of the squalene hydrocarbon and obtained an acid, m. p. 270—272°, which also corresponded to a naphthalenedicarboxylic acid. It thus appeared as though the two hydrocarbons were isomeric rather than identical, but this view was shown to be untenable when mixed melting-point determinations with the two hydrocarbons and with their picrates and styphnates, rendered possible by an interchange of specimens, established their identity beyond doubt. The discrepancy was ultimately cleared up in a private communication from Professor Ruzicka stating that, by more energetic oxidation of the $C_{13}H_{14}$ hydrocarbon with potassium ferricyanide, he had obtained an acid giving a pure methyl ester, m. p. 89°, corresponding to a naphthalenetricarboxylic acid. Meanwhile we also had prepared this ester and arrived at analytical values in excellent agreement with the formula $C_{10}H_5(CO_2Me)_3$. It is thus apparent that the oxidation with potassium ferricyanide takes place in stages and that what we first took to be a pure substance was actually a mixture containing, besides the naphthalenetricarboxylic acid, partly oxidised methyl- and dimethyl-carboxylic acids. The hydrocarbon is therefore not a methylethylnaphthalene but a trimethylnaphthalene.

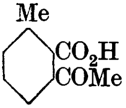
In order to gain further insight into the position of the methyl groups and establish the constitution of the hydrocarbon, resort was made to other methods of oxidation. For this purpose a large quantity of material had to be accumulated and selenium was substituted for sulphur as the dehydrogenating agent (compare Diels, Gädke, and Kording, *Annalen*, 1927, **459**, 1), whereby a much improved yield was obtained.

Trial experiments showed that chromic acid was a suitable oxidising agent. The conditions employed were similar to those used by Weissgerber and Kruber in their oxidation of various dimethylnaphthalenes (*Ber.*, 1919, **52**, 346) and resulted in the formation of both neutral and acid products, the latter largely predominating.

Acid products. The crude acids were isolated as a thick oil, from which, after treatment with benzene, a single solid *acid* separated. Analysis of the purified substance, m. p. 126°, gave the formula $C_{10}H_{10}O_3$, and the formation of a *semicarbazone* showed the presence of a carbonyl group. Further mild oxidation with sodium hypobromite yielded 3-methylphthalic acid, from which it follows (*a*) that the acid itself must be represented by either formula (I) or (II), (*b*) that, of the three methyl groups in the original hydrocarbon, two must occupy positions 1 : 5 or 1 : 8 in the naphthalene nucleus, and (*c*) that in all probability the methyl group eliminated during the oxidation occupies a β-position in the molecule.

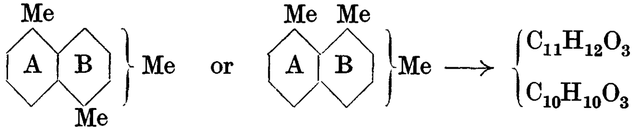
(I.)





(II.)

The residual oil, after removal of the above acid, was esterified with methyl alcohol, and the product fractionally distilled. Two solid *esters*, m. p.'s 78—79° and 71—72°, were obtained, both differing from the methyl ester (m. p. 47—48°) of the keto-acid already described. Analysis of the higher-melting compound gave an empirical formula $C_{12}H_{14}O_3$ corresponding with an *acid* having the structure $C_6H_2Me_2(COMe)\cdot CO_2H$. It is thus evident that the chromic acid oxidation leads to scission of the hydrocarbon in both rings A and B.



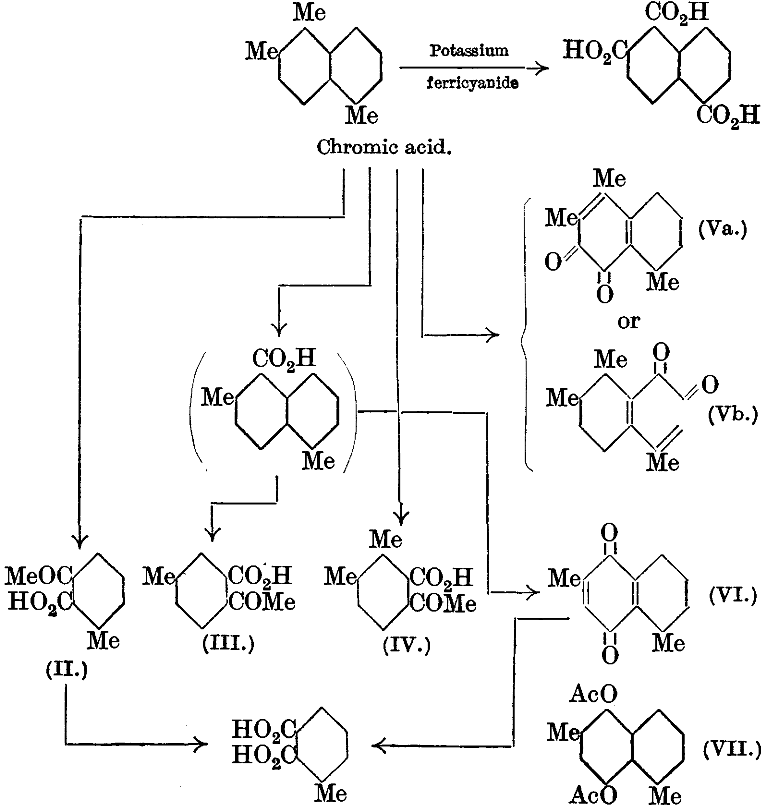
The lower-melting ester was found on analysis to be derived from an *acid* isomeric with (I) or (II); as will be shown later, it must have the constitution (III), its formation being due to elimination of one of the α-methyl radicals.

Neutral products. These vary according to the conditions of oxidation. After incomplete oxidation, whereby unchanged hydrocarbon was recovered, the only definite neutral product isolated was a small amount of a non-volatile, red, crystalline substance, $C_{13}H_{12}O_2$, undoubtedly a *trimethyl-β-naphthaquinone*.

With more prolonged oxidation two further substances, both volatile in steam, resulted. Of these, the higher-melting, of formula $C_{12}H_{10}O_2$, was obtained as a yellow crystalline solid, m. p. 94°. Its identity with 1 : 6-dimethyl-α-naphthaquinone, for which Weissgerber and Kruber (*loc. cit.*) give m. p. 95°, was shown by direct comparison with an authentic specimen kindly supplied by Professor Kruber, to whom we desire to express our thanks. In addition the *phenylhydrazones* of both substances were prepared and found to have the same melting point and to give no depression in admixture. The elucidation of the structure of this substance proves that, of the two β-methyl groups present in the parent hydrocarbon, one has been eliminated during the oxidation. Further, the third methyl group is now definitely established as occupying a β-position in the naphthalene nucleus. It follows, therefore, *that the hydrocarbon can be only* 1 : 2 : 5- or 1 : 3 : 8-*trimethylnaphthalene*, a result in agreement with the evidence derived from the study of the ketonic acids already discussed. The formation of the acid (III) is obviously connected with the ready elimination of the α-methyl group in the disubstituted benzene ring and suggests that of the two possible constitutions for the hydrocarbon the 1 : 2 : 5-formulation is the more probable.

The lower-melting solid accompanying the 1 : 6-dimethyl-α-naphthaquinone and separable from it by fractional crystallisation was obtained in colourless crystals, m. p. 70—71°, giving analytical data agreeing with an empirical formula $C_{16}H_{16}O_4$. Although the quantity of this material in our hands did not permit of a detailed examination, the compound is probably 5 : 8-*diacetoxy*-1 : 6-*dimethylnaphthalene* (VII), its formation being reminiscent of the production of 1 : 2 : 4-triacetoxynaphthalene by the action of acetic anhydride and concentrated sulphuric acid or zinc chloride on α-naphthaquinone (Thiele and Winter, *Annalen*, 1900, **311**, 345).

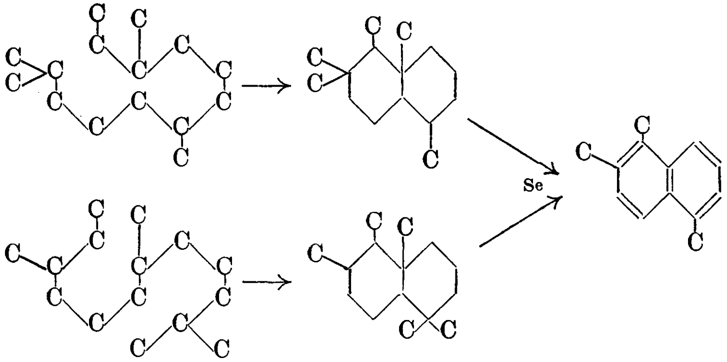
In order finally to decide between the two possible structures resort has been made to direct synthesis. As shown on p. 2542, we



have carried out the synthesis of 1 : 3 : 8-trimethylnaphthalene : this hydrocarbon (m. p. 48°) is not identical with the one under review, which consequently must be the 1 : 2 : 5-isomeride. Complete confirmation of this has been supplied by Professor Ruzicka, who has now synthesised this compound (unpublished result) and to whom we are indebted for specimens of its picrate and styphnate, neither of which shows any depression in melting point when mixed with the similar derivative from the " squalene " hydrocarbon.

The scheme on p. 2549 indicates in outline the course of the oxidation.

The formation of this new naphthalene hydrocarbon is a matter of considerable interest. It has already been shown (Harvey, Heilbron, and Kamm, *loc. cit.*) that the fragment of the tetra*cyclo*squalene molecule yielding the hydrocarbon is essentially a sesquiterpene. Hitherto, only two naphthalene homologues, cadalene and eudalene (Ruzicka, Meyer, and Mingazzini, *Helv. Chim. Acta*, 1922, **5**, 345), have been isolated from the products of dehydrogenation of the known sesquiterpenes. There is, however, no difficulty in theoretically formulating the formation of the 1 : 2 : 5-trimethylnaphthalene from a sesquiterpene of the farnesene type in the manner outlined below, whereby two methyl groups must be ejected on passage from the hydroaromatic to the true aromatic condition.



EXPERIMENTAL.

*Preparation of the Naphthalene Hydrocarbon from Tetra*cyclo*squalene.*—Tetra*cyclo*squalene was prepared as described by Harvey, Heilbron, and Kamm (*loc. cit.*). The crude product was dehydrogenated in 200 g. portions with selenium (150 g.) in distillation flasks (500 c.c.) fitted with long air-condensers, and heated to 300° in baths composed of molten potassium and sodium nitrates. Throughout the dehydrogenation there was a steady evolution of hydrogen selenide and alkyl selenides, which were absorbed in concentrated caustic soda solution. After 50 hours' heating, the oil was decanted from unchanged selenium and distilled over sodium at 15 mm. pressure until the temperature reached 250°. The distillate (300 g. from 1000 g. of tetra*cyclo*squalene), which consisted of a complex mixture containing cymene, partly dehydrogenated sesquiterpenes, and the naphthalene hydrocarbon, was roughly fractionated and the fraction of b. p. 130—200°/15 mm. was treated with a warm concentrated alcoholic solution of picric acid. The hydrocarbon was obtained from the purified picrate as described in Part III. In this manner 2000 g. of tetra*cyclo*squalene were dehydrogenated, yielding 80 g. of hydrocarbon.

Oxidation with Potassium Ferricyanide.—The hydrocarbon (4 g.) was well shaken at 60° for 70 hours with a solution of potassium ferricyanide (470 g.) and potassium hydroxide (82 g.) in water (1180 c.c.). During the oxidation a further quantity of potassium ferricyanide (185 g.) and potassium hydroxide (50 g.) was added. The liquid was thoroughly extracted with ether, whereby a considerable amount (2·5 g.) of hydrocarbon was recovered. The solution was then rendered acid and extracted twenty times with ether. The solid *acid* obtained after removal of solvent was crystallised from methyl alcohol and finally sublimed in a vacuum. It formed colourless feathery needles, m. p. 270—272° [Found: (micro) C, 66·4; H, 3·8. $C_{12}H_8O_4$ requires C, 66·7; H, 3·7%. $C_{13}H_8O_6$ requires C, 60·0; H, 3·1%]. The *methyl* ester, prepared by heating the acid with methyl alcohol and sulphuric acid, formed colourless crystals, m. p. 89° [Found: (micro) C, 63·6; H, 4·8. $C_{14}H_{12}O_4$ requires C, 68·9; H, 4·9%. $C_{16}H_{14}O_6$ requires C, 63·6; H, 4·6%].

Oxidation with Chromic Acid.—A solution of chromic acid (100 g.) in 80% acetic acid (200 c.c.) was added gradually from a tap funnel during 3 hours to a well-stirred solution of the hydrocarbon (20 g.) in 80% acetic acid (200 c.c.) heated to 60°. The liquid was maintained at this temperature for a further 2 hours and was then poured into water (1500 c.c.) and thoroughly extracted with ether. The ethereal solution was first washed with concentrated sodium bicarbonate solution, the removal of the greater part of the acetic acid thus being effected. The acidic products of oxidation were then separated by shaking with sodium hydroxide solution. The alkaline liquid was acidified and the acids were extracted with ether. On evaporation of the dried solution a thick brown oil (8 g.) was obtained. The ethereal extract, after removal of the acidic products, was dried and yielded the neutral substances as a reddish-brown oil (3 g.).

Neutral substances. 1 : 2 : 5-*Trimethyl*-β-*naphthaquinone* (Va or b) was only isolated in appreciable amount when the quantity of chromic acid was reduced by 30% and the oxidation was not allowed to proceed for longer than 2 hours. The neutral oil (6 g.), which was deep red, was diluted with methyl alcohol (5 c.c.) and left in the ice-chest for several days; the quinone then crystallised in orange-red needles (0·1 g.). It was separated from the oil and recrystallised from methyl alcohol, in which it was sparingly soluble. The residual oil still contained unchanged hydrocarbon, which was recovered by means of its picrate. 1:2:5-Trimethyl-β-naphthaquinone crystallises in red needles having no definite melting point but decomposing between 130° and 135°. The compound is unstable and gradually decomposes on standing; it gives an intense violet colour with concentrated sulphuric acid [Found : (micro) C, 77·7; H, 6·1. $C_{13}H_{12}O_2$ requires C, 78·0; H, 6·0%].

1 : 6-*Dimethyl-α-naphthaquinone* (VI). The neutral oil, which partly crystallised on standing, was steam-distilled, whereby a yellow solid was carried over. On crystallisation from methyl alcohol 1 : 6-dimethyl-α-naphthaquinone separated first, and after further recrystallisation from the same solvent was obtained in bright yellow needles, m. p. 94° [Found : (micro) C, 77·3, 77·4; H, 5·3, 5·3. Calc. for $C_{12}H_{10}O_2$: C, 77·4; H, 5·4%]. The *phenylhydrazone* crystallised from glacial acetic acid in bright red needles, m. p. 225°, which gave no depression in melting point in admixture with the phenylhydrazone, m. p. 226°, prepared from authentic 1 : 6-dimethyl-α-naphthaquinone [Found : (micro) C, 77·8; H, 5·6; N, 9·8. $C_{18}H_{16}ON_2$ requires C, 78·3; H, 5·8; N, 10·1%].

5 : 8-*Diacetoxy*-1 : 6-*dimethylnaphthalene* (VII). The methyl-alcoholic filtrate obtained after removal of the above quinone was concentrated; colourless crystals separated on cooling and were recrystallised from methyl alcohol. The pure compound formed large prisms, m. p. 70—71° [Found : (micro) C, 70·6, 70·4; H, 6·0, 6·1. $C_{16}H_{16}O_4$ requires C, 70·6; H, 5·9%].

Acidic products. 3-*Methylacetophenone*-2-*carboxylic acid* (II). The thick oily acid portion obtained from the oxidation was diluted with benzene and the solid material which separated after some time was filtered off (10 g. from 80 g. of hydrocarbon). On repeated crystallisation from benzene 3-*methylacetophenone*-2-*carboxylic acid* was obtained in small colourless needles (4 g.), m. p. 126° (Found : C, 67·7, 67·4; H, 5·5, 5·6; equiv., 180. $C_{10}H_{10}O_3$ requires C, 67·4; H, 5·6%; equiv., 178). The *semicarbazone*, prepared in the usual manner, crystallised from alcohol in small needles, m. p. 177° (decomp.) [Found : (micro) C, 56·2; H, 5·2; N, 18·4. $C_{11}H_{13}O_3N_3$ requires C, 56·1; H, 5·5; N, 17·9%].

Methyl 3-*methylacetophenone*-2-*carboxylate* was prepared by refluxing the dry silver salt with methyl iodide in dry ether. It was obtained as an oil which solidified on standing and separated from benzene–light petroleum in large crystals, m. p. 47—48° [Found: (micro) C, 69·0, 68·7; H, 6·6, 6·5. $C_{11}H_{12}O_3$ requires C, 68·7; H, 6·2%]. The *semicarbazone* crystallised from alcohol in colourless needles, m. p. 215° (decomp.) [Found: (micro) C, 57·7; H, 5·9. $C_{12}H_{15}O_3N_3$ requires C, 57·8; H, 6·0%].

Oxidation of 3-*methylacetophenone*-2-*carboxylic acid to* 3-*methylphthalic acid.* A dilute solution of sodium hypobromite was added gradually to a well-cooled solution of 3-methylacetophenone-2-carboxylic acid (0·9 g.) in aqueous sodium hydroxide (20 c.c. of 5%) until a faint yellow colour persisted. After 12 hours, sulphur dioxide was passed in to remove the excess of sodium hypobromite and the bromoform was extracted with ether. 3-Methylphthalic acid, obtained by extracting the acidified solution with ether, separated from ethyl acetate in colourless crystals, m. p. 157—160° (depending on the rate of heating). Jürgens (*Ber.*, 1907, **40**, 4413) gives m. p. 154° and Weissgerber and Kruber (*loc. cit.*) give m. p. 157° [Found: (micro) C, 60·3; H, 4·6. Calc. for $C_9H_8O_4$: C, 60·0; H, 4·4%]. That the acid was actually the 3- and not the isomeric 4-methylphthalic acid was proved by its oxidation with potassium permanganate to hemimellitic acid.

Attempts to obtain any further single acid directly from the residual oil from which the 3-methylacetophenone-2-carboxylic acid had been isolated were unsuccessful. The oil (20 g.) was therefore esterified by refluxing it with methyl alcohol and sulphuric acid and the esterified material (13 g.) was fractionated from a Willstätter flask at 5 mm. pressure, yielding the following fractions: (1) 4 g., wholly crystallised, b. p. up to 125°, m. p. 45—48°; (2) 3 g., partly crystallised, b. p. 125—135°, m. p. 55—65°; (3) 2 g., partly crystallised, b. p. 145—155°, m. p. 64—73°; (4) 1 g., liquid, b. p. above 145° (the m. p.'s are those of the separated crystals).

Methyl 4-*methylacetophenone*-2-*carboxylate* was isolated in long needles, m. p. 71—72°, from fraction 1, by repeated crystallisation from light petroleum–benzene. The yield of pure substance was small (0·5 g.), the solid obviously being a complex mixture [Found: (micro) C, 69·0; H, 6·2. $C_{11}H_{12}O_3$ requires C, 68·7; H, 6·2%]. Hydrolysis of the ester yielded 4-methylacetophenone-2-carboxylic acid (III), which crystallised from benzene in needles, m. p. 125—126°, and readily gave a semicarbazone, m. p. 182° (decomp.).

3 : 4-*Dimethylacetophenone*-2-*carboxylic acid* (IV). The *methyl* ester of this acid (1 g.) was obtained by repeated crystallisation from light petroleum–benzene of the total solid (3 g.) from fractions 2 and 3. It separated in rosettes of needles, m. p. 78—79° [Found: (micro) C, 69·5; H, 6·7. $C_{12}H_{14}O_3$ requires C, 69·9; H, 6·8%].

3 : 4-*Dimethylacetophenone-2-carboxylic acid,* obtained by hydrolysis of the ester, crystallised from benzene–light petroleum in needles, m. p. 105° [Found: (micro) C, 68·7; H, 6·3. $C_{11}H_{12}O_3$ requires C, 68·7; H, 6·2%]. The acid formed a very sparingly soluble semicarbazone, m. p. 217° (decomp.).

In conclusion we gratefully acknowledge the assistance given us in this work by Dr. J. Harvey, who carried through the oxidation of the naphthalene hydrocarbon with potassium ferricyanide. Further, we desire to express our thanks to Professor L. Ruzicka for his friendly co-operation and also to make acknowledgment of our indebtedness to the Department of Scientific and Industrial Research for a grant to one of us (D. G. W.).

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