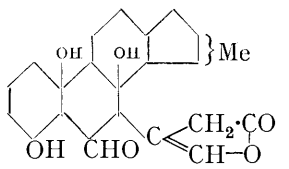
96. *Syntheses of Polycyclic Compounds related to the Sterols. Part III. 9-Methyl- and 3′ : 9-Dimethyl-*cyclo*pentenophenanthrene.*

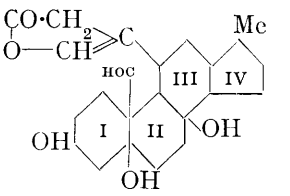
By D. J. C. Gamble and G. A. R. Kon.

In a discussion of the constitution of strophanthidin it was suggested by one of us (Kon, *Chem. and Ind.*, 1934, **53**, 593, 956) that the structure (I) provisionally adopted by Jacobs and his collaborators (compare Jacobs and Elderfield, *J. Biol. Chem.*, 1933, **102**, 237; 1934, **107**, 143; Elderfield and Rothen, *ibid.*, 1934, **106**, 71) must be abandoned in favour of a formula such as (II) or (III); these two structures have the same arrangement of substituents in rings I and II but differ in the position of the lactone side-chain and the accompanying tertiary hydroxyl group. The principal reason for the suggested change was that the hydrocarbon (IV) has been obtained by the dehydrogenation both of strophanthidin (Jacobs and Elderfield, *J. Biol. Chem.*, 1934, **107**, 143; Jacobs and Fleck, *ibid.*, 1932, **97**, 57) and of uzarigenin (Tschesche and Knick, *Z. physiol. Chem.*, 1933, **222**, 58).

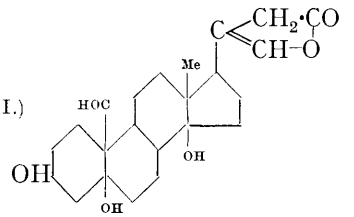
(I.)



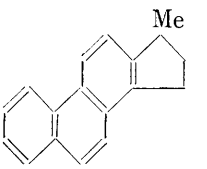
(II.)



(III.)

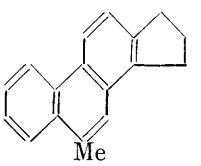


(IV.)

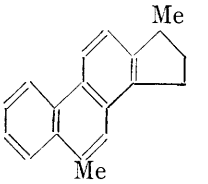


Now it has been proved that uzarigenin has the same carbon skeleton as periplogenin (Tschesche, *Z. physiol. Chem.*, 1933, **222**, 50), which differs from strophanthidin in that the aldehydo-group of the latter is replaced by methyl (Jacobs, Elderfield, Grave, and Wignall, *J. Biol. Chem.*, 1931, **91**, 617); the dehydrogenation of uzarigenin, if the latter had a skeleton such as (I), should therefore lead to a hydrocarbon with a methyl group in the position 9, namely, (V) or (VI):

(V.)



(VI.)



Although the identity of the hydrocarbon (IV) has been definitely established (Harper, Kon, and F. Ruzicka, J., 1934, 124; Hillemann, *Ber.*, 1935, **68**, 102), its purification is difficult and its identification somewhat uncertain because the melting points of the hydrocarbon and its derivatives are not always depressed by the admixture of closely related compounds. For this reason the compounds (V) and (VI) have been synthesised by the method of Harper, Kon, and Ruzicka (*loc. cit.*). Both are different from (IV), for definite depressions of melting point are observed with mixtures of the hydrocarbons and also of corresponding derivatives. It can therefore be inferred that the skeleton (I) cannot express the structure of strophanthidin and related cardiac aglucones.

The above conclusion had already become probable as a result of the observations of Bernal and Crowfoot (*Chem. and Ind.*, 1934, **53**, 953), which rule out formulæ (I) and (II)

(compare Kon., *ibid.*, p. 956), whilst the correctness of formula (III) was established by Tschesche (*Z. physiol. Chem.*, 1934, **229**, 219) when the present investigation was nearly complete. The formula (III) has also been adopted by Jacobs and Elderfield (private communication from Prof. W. A. Jacobs).

Experimental.

α-(4-*Methyl*-1-*naphthyl*)*ethyl Alcohol*.—28 G. of ethylene oxide in absolute ether were added to an ice-cold solution of a Grignard reagent prepared from 111·5 g. of 1-bromo-4-methylnaphthalene (Meyer and Sieglitz, *Ber.*, 1922, **55**, 1835) and 13 g. of magnesium activated with iodine. The mixture was allowed to reach room temperature and the ether was then distilled off. By the common procedure, 60—65 g. of the *alcohol* were obtained, b. p. 135°/0·5 mm.; it solidified and crystallised from ether–ligroin in lustrous rhombic plates, m. p. 60° (Found: C, 83·7; H, 7·6. $C_{13}H_{14}O$ requires C, 83·8; H, 7·6%). The *picrate* formed orange needles, m. p. 107° (Found: C, 55·0; H, 4·3. $C_{19}H_{17}O_8N_3$ requires C, 54·9; H, 4·1%).

The orientation of the bromide employed in the above preparation was checked by its conversion, through the Grignard reagent, into 4-methyl-1-naphthoic acid, m. p. 175—176° (Meyer and Sieglitz, *loc. cit.*), and oxidation of the latter with alkaline permanganate to naphthalene-1 : 4-dicarboxylic acid.

α-(4-*Methyl*-1-*naphthyl*)*ethyl Bromide*.—20 G. of the pure alcohol were heated in a pressure bottle with 100 g. of hydrobromic acid in acetic acid (33% w./v.) for 14 hours at 100°. The *bromide* (23 g.) had b. p. 142°/0·5 mm., solidified at once on cooling, and formed needles, m. p. 45—46°, from ether–ligroin (Found: Br, 32·3. $C_{13}H_{13}Br$ requires Br, 32·1%). The picrate, long orange needles, m. p. 72—73°, was unstable.

1 : 9-*Dimethyl*-1 : 2-cyclo*pentano*-1 : 2 : 3 : 4-*tetrahydrophenanthrene*.—50 G. of 2-methyl*cyclo*pentanone were added to a cooled Grignard reagent prepared from the above bromide (93 g.) and 10 g. of activated magnesium, the mixture being then warmed for ½ hour, decomposed with ice and acetic acid, and worked up in the usual way. The desired carbinol (14 g.) distilled at 170—195°/0·2 mm. as a colourless viscous oil with a blue fluorescence; it was accompanied by a fraction, b. p. about 230°/0·4 mm., doubtless αδ-*di*-(4-*methyl*-1-*naphthyl*)*butane*, which formed needles, m. p. 126—127°, from benzene (Found: C, 91·9; H, 7·8. $C_{26}H_{26}$ requires C, 92·3; H, 7·7%), and gave a dipicrate, m. p. 174—175°, and a bis-*s*.-trinitrobenzene compound, m. p. 192—193°. The crude carbinol was dehydrated by heating with 20 g. of phosphoric oxide at 140° for 40 minutes under reduced pressure. The *hydrocarbon* was isolated by addition of ice and extraction with ether, purified by two distillations over sodium, and obtained (7·5 g.) as a colourless viscous oil with a blue fluorescence, b. p. 160°/0·5 mm. (Found: C, 91·3; H, 8·6. $C_{19}H_{22}$ requires C, 91·1; H, 8·9%). A definite picrate was not obtained.

9-*Methyl*-1 : 2-cyclo*pentenophenanthrene* (V).—7·5 G. of the above hydrocarbon were heated with 12 g. of selenium for 20 hours at 290—300° (bath temperature). The product, isolated in good yield, was distilled over sodium; after the first few drops of unchanged material had been collected, the distillate solidified and was recrystallised from methyl alcohol, forming long needles, m. p. 109—110°; it was unaltered in m. p. after regeneration from the pure picrate (Found: C, 92·8; H, 7·0. $C_{18}H_{16}$ requires C, 93·1; H, 6·9%). The *picrate* formed orange-red needles, m. p. 153—154°, stable in boiling alcohol (Found: C, 62·2; H, 4·1. $C_{24}H_{19}O_7N_3$ requires C, 62·5; H, 4·2%). The *s*.-trinitrobenzene *compound* formed long yellow needles, m. p. 170—171° (Found: C, 64·5; H, 4·2. $C_{24}H_{19}O_6N_3$ requires C, 64·7; H, 4·3%). The trinitrotoluene *compound* formed pale yellow needles rather soluble in alcohol, m. p. 135—136° (Found: C, 65·2; H, 4·5. $C_{25}H_{21}O_6N_3$ requires C, 65·3; H, 4·6%). The *styphnate* was sufficiently stable to be recrystallised from alcohol and forms yellow needles, m. p. 190—191° (decomp.) (Found: C, 60·3; H, 3·9. $C_{24}H_{19}O_8N_3$ requires C, 60·4; H, 4·0%). The hydrocarbon is more soluble in alcohol than the 3′-methyl isomeride; its derivatives are less soluble and particularly easy to purify.

2 : 5-*Dimethyl*-1-β-(4-*methyl*-1-*naphthyl*)*ethyl*cyclo*pentan*-1-*ol*.—The carbinol was prepared exactly as described above, by using 2 : 5-dimethyl- in place of 2-methyl-*cyclo*pentanone. The yield was appreciably improved (23 g. from 60 g. of bromide) by using an excess of magnesium and of ketone, and by distilling off the ether at the end of the operation; the *carbinol* boiled at 185—190°/0·5 mm. (Found: C, 85·8; H, 9·0. $C_{20}H_{26}O$ requires C, 85·1; H, 9·3%). The somewhat high percentage of carbon suggests the presence of some αδ-di-(4-methyl-1-naphthyl)butane. The picrate of the carbinol could not be obtained pure.

1 : 9 : 3′-*Trimethyl*-1 : 2-cyclo*pentano*-1 : 2 : 3 : 4-*tetrahydrophenanthrene*.—The dehydration

of the above carbinol gave the *hydrocarbon* in good yield, b. p. 170°/0·6 mm. after redistillation over sodium (Found : C, 90·9; H, 8·9. $C_{20}H_{24}$ requires C, 90·8; H, 9·2%).

9 : 3′-*Dimethyl*-1 : 2-cyclo*pentenophenanthrene* (VI).—16 G. of the above hydrocarbon gave 13 g. of the new *hydrocarbon* on dehydrogenation; this was at first obtained as an oil and was converted into the *picrate*, which crystallised from alcohol–benzene in orange needles, m. p. 134—135° (Found : C, 63·5; H, 4·6. $C_{25}H_{21}O_7N_3$ requires C, 63·1; H, 4·5%). The hydrocarbon regenerated from it formed colourless needles from methyl alcohol, m. p. 80° (Found : C, 92·3; H, 7·3. $C_{19}H_{18}$ requires C, 92·6; H, 7·4%). The *s*.-trinitrobenzene *compound* formed long yellow needles, m. p. 149—150° (Found : C, 65·2; H, 4·6. $C_{25}H_{21}O_6N_3$ requires C, 65·3; H, 4·6%), the trinitrotoluene *compound* pale yellow needles, m. p. 113—114° (Found : C, 65·9; H, 4·9. $C_{26}H_{23}O_6N_3$ requires C, 65·9; H, 4·9%), and the *styphnate* orange needles, m. p. 159—160°, which tended to decompose somewhat on recrystallisation from alcohol (Found : C, 61·3; H, 4·2. $C_{25}H_{21}O_8N_3$ requires C, 61·1; H, 4·3%).

Styphnate of 3′-*Methyl*cyclo*pentenophenanthrene*.—This derivative, although it cannot be recrystallised, appears to be suitable for the identification of the hydrocarbon owing to its sharp melting point, 135—136°; a specimen prepared from molecular proportions of the components in alcoholic solution formed fine yellow needles (Found : C, 60·0; H, 4·1. $C_{24}H_{19}O_8N_3$ requires C, 60·4; H, 4·0%). The specimen for analysis was prepared from the hydrocarbon obtained by the method of Harper, Kon, and Ruzicka; another specimen, with identical properties, was prepared from the hydrocarbon synthesised by Bergmann and Hillemann's method (*Ber.*, 1933, **66**, 1302). The styphnate of *cyclo*pentenophenanthrene, which was prepared for comparison, melted sharply at 154° and did not depress the m. p. of the foregoing compound; it was not obtained sufficiently pure for analysis.

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