119. *Syntheses of Polycyclic Compounds related to the Sterols. Part VI.*

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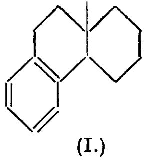
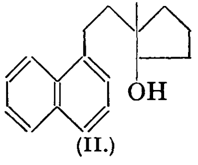
In Part I (J., 1933, 1081) it was stated that the direct cyclodehydration of 2-methyl-2-β-phenylethyl*cyclo*hexanol gave 11-methyloctahydrophenanthrene (I), in which the angular methyl group occupies a position corresponding to C_{13} of the sterols. Further work shows that the dehydration of carbinols of this type is accompanied by a retropinacolic change and the hydrocarbon produced is the 12-methyl compound, with the methyl group in a position corresponding to C_{10} of the sterols. The above carbinol, the isomeric 2-methyl-1-β-phenylethyl*cyclo*hexanol, and the corresponding phenylethyl- and naphthylethyl-*cyclo*pentanols have been dehydrated to the unsaturated hydrocarbons by the xanthate method, which does not cause rearrangement; those hydrocarbons in which the methyl and the arylethyl group are on adjacent carbon atoms can be cyclised by the action of aluminium chloride, whereas the isomeric 1-methyl-1-arylethyl compounds are not cyclised. Compounds of the latter type can be cyclised by means of phosphoric oxide, but the change is accompanied by a rearrangement and hydrocarbons with an angular methyl group in a position corresponding to C_{13} of the sterols cannot be obtained by this process.

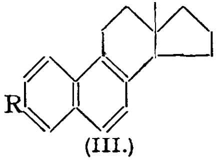
In Part I one of us (Kon, J., 1933, 1081) described the preparation of the hydrocarbon (I) by the cyclodehydration of 2-methyl-2-β-phenylethyl*cyclo*hexanol, and an analogous hydrocarbon has since been obtained in these laboratories by Dr. F. C. J. Ruzicka from the corresponding *cyclo*pentanol.



(I.)



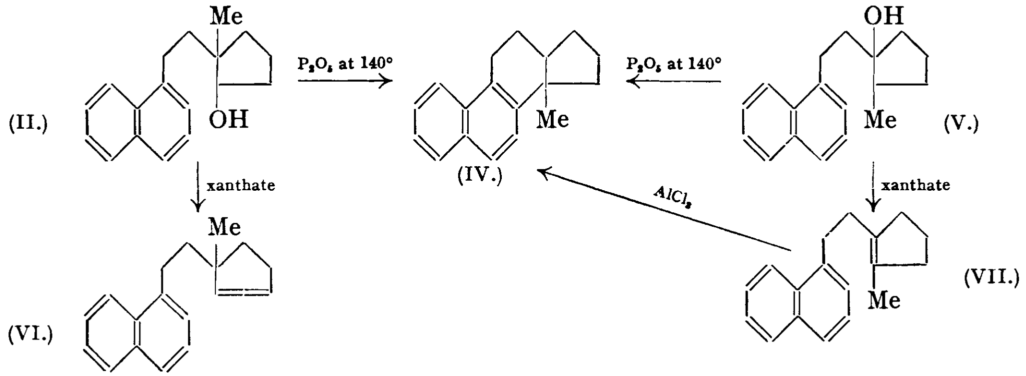
(II.)



(III.)

It was hoped to employ the same method for the preparation of the tetracyclic compound (III, R = H), which was to serve as a model for the synthesis of deoxoequilenin methyl ether (III, R = OMe) or a stereoisomeride of it.

An initial difficulty arose in the preparation of the carbinol (II) from the corresponding ketone, because the reduction of the latter with sodium in moist ether gave an *alcohol* $C_{18}H_{24}O$, containing two atoms of hydrogen more than was expected. This underwent cyclodehydration, giving a *hydrocarbon* $C_{18}H_{22}$ possessing the expected skeleton, since it was smoothly dehydrogenated to *cyclo*pentenophenanthrene, but it is clear that the production of dihydronaphthalene derivatives in the reduction of naphthylethyl*cyclo*pentanones, already noted in Part I (*loc. cit.*), renders this method valueless for the synthesis of deoxoequilenin methyl ether. Trial experiments on the reduction of 2-β-naphthylethyl*cyclo*pentanone showed that Ponndorf's method could not be applied, but the desired result was ultimately achieved by using hydrogen in the presence of Adams's catalyst. The *carbinol* (II) gave on dehydration with phosphoric oxide a hydrocarbon, which was characterised by its crystalline addition *compound* with *s*-trinitrobenzene; this proved to be identical with that prepared from the cyclisation product of the isomeric carbinol (V), which must have the structure (IV) (Harper, Kon, and Ruzicka, J., **1934**, 124).



It is clear that in the dehydration of one of these carbinols a retropinacolic change must have taken place. Such a change would, indeed, be expected in a carbinol of the structure (II), in which there is a quaternary carbon atom next to the carbon atom carrying the hydroxyl, even though there is a methylene group on the other side of it, which allows dehydration without rearrangement. It has been possible to show that it is the carbinol (II) and not (V) which undergoes this abnormal reaction. Both carbinols were dehydrated to the corresponding cyclo*pentenes*, (VI) and (VII) respectively, by the xanthic ester method of Tschugaev as modified by Whitmore and Simpson (*J. Amer. Chem. Soc.*, **1933**, **58**, 3809); the two hydrocarbons were quite distinct and were characterised by their addition products with *s*-trinitrobenzene. The compound (VII) was cyclised to the hydrocarbon (IV) by means of aluminium chloride (compare Cook and Hewett, J., **1933**, 1098), but the isomeride (VI) could not be cyclised by any of the reagents tried and we have thus been unable to prepare the hydrocarbon (III, R = H).

The simpler hydrocarbons of the types (VI) and (VII) with a phenyl residue in place of naphthyl were similarly prepared from the isomeric *cyclo*pentanols and were found to behave in the same way. The structures of the hydrocarbons, which differ appreciably in their physical constants, have been confirmed by oxidation: the compound of the type (VII), which is most readily prepared by distilling 2-methyl-1-β-phenylethyl*cyclo*pentanol with a trace of iodine, gives a diketone on treatment with permanganate, and is easily cyclised by means of aluminium chloride to the tricyclic compound analogous to (IV), which has already been prepared by direct cyclodehydration of the parent carbinol. The isomeric hydrocarbon of type (VI) is oxidised to an acidic product by the action of permanganate; in place of the expected glutaric acid a ketonic *acid* is obtained, characterised by the formation of a *semicarbazone*. As this acid does not react with *o*-phenylenediamine or give a colour with ferric chloride, it must be inferred that it is a γ-keto-acid formed by the oxidation of the methylene group next to the phenyl group, of the formula $Ph{\cdot}CO{\cdot}CH_2{\cdot}CMe(CO_2H){\cdot}CH_2{\cdot}CH_2{\cdot}CO_2H$, the formation of which fully confirms the structure assigned to the parent hydrocarbon (the oxidation of phenylated side-chains in the manner assumed above is well known). All attempts to cyclise the hydrocarbon to a saturated isomeride were unsuccessful, except with the aid of phosphoric oxide; the properties of the compound formed in the latter case left little doubt that it was formed as the result of a rearrangement and was identical with the product of direct cyclodehydration of *either* isomeric carbinol. Precisely similar observations were made with the analogous *cyclo*hexane derivatives; two isomeric *cyclo*hexenes were prepared, their structures confirmed by oxidation, and cyclisation attempted. Only the compound analogous to (VII) could be converted into the hydrophenanthrene with aluminium chloride and it can be inferred that the compound previously described as (I) has in reality the alternative structure with the angular methyl group in position 12, not 11, a conclusion well supported by a comparison of the physical properties of the supposed 11-methyl compound with those of its isomeride (Kon, *loc. cit.*); it is unfortunately impossible to obtain a more conclusive proof of their identity, as the hydrocarbons are liquid and do not form solid derivatives.

EXPERIMENTAL.

2-β-1′-*Naphthylethyl*cyclo*pentanone*.—This ketone was prepared as described by Kon (*loc. cit.*), but it was found that the yield is greatly influenced by the temperature at which the pyrolysis of the naphthylethyladipic acid is carried out; the highest yield (50%) is obtained at 360° and diminishes rapidly below and above this temperature with the formation of α-methylnaphthalene at the expense of the ketone. A 50% yield of the latter is, however, invariably obtained if the acid is first heated with twice its weight of acetic anhydride for 2 hours, the reagent then distilled off, and the residue slowly pyrolysed.

2-β-1′-*Naphthylethyl*cyclo*pentanol*.—5·6 G. of the ketone in 50 c.c. of ethyl alcohol were shaken in an atmosphere of hydrogen with 0·5 g. of Adams's catalyst for 7 hours; absorption then ceased. When the filtered solution was treated with semicarbazide acetate, no semicarbazone was obtained; the *alcohol* was recovered by addition of water and extraction with ether and purified in the usual way, 5 g. of a pale yellow, viscous oil being obtained, b. p. 168—174°/0·4 mm. (Found: C, 84·4; H, 8·2. $C_{17}H_{20}O$ requires C, 84·9; H, 8·4%). The 3 : 5-dinitrobenzoate formed small needles, m. p. 194—195°.

The alcohol readily undergoes cyclisation with phosphoric oxide at 140° and the resulting hydrocarbon, b. p. 108—110°/0·4 mm., gives a good yield of 1 : 2-*cyclo*pentenophenanthrene on dehydrogenation with selenium.

2-*Methyl*-2-β-1′-*naphthylethyl*cyclo*pentanone*.—The preceding ketone (22 g.) was methylated in the presence of sodamide by the method of Haller and Cornubert (*Bull. Soc. chim.*, 1931, **41**, 367) as described by Kon (*loc. cit.*), the product distilled, and the appropriate fraction converted into the *semicarbazone*. This was fractionally crystallised from alcohol and 6·5 g. of product, m. p. 209°, were obtained (Found: C, 73·8; H, 7·6. $C_{19}H_{23}ON_3$ requires C, 73·7; H, 7·5%). The *ketone* regenerated from it by means of hydrochloric acid had b. p. 182°/0·2 mm. (Found: C, 85·6; H, 7·9. $C_{18}H_{20}O$ requires C, 85·7; H, 7·9%).

Reduction. (1) The ketone (10·5 g.) was reduced with sodium in moist ether (compare Bardhan and Sen-Gupta, J., 1932, 2520) and gave 8·5 g. of an *alcohol*, b. p. 194°/1 mm., together with a little unchanged ketone, which was recovered as the semicarbazone. The alcohol was the dihydro-derivative of the expected compound (Found: C, 83·9; H, 9·1. $C_{18}H_{24}O$ requires C, 84·3; H, 9·5%); it formed a 3 : 5-dinitrobenzoate, m. p. 170°, and gave on cyclisation with phosphoric oxide at 140° a *hydrocarbon*, b. p. 159—170°/0·2 mm. (Found: C, 90·6; H, 9·3. $C_{18}H_{22}$ requires C, 90·7; H, 9·3%), which gave 1 : 2-*cyclo*pentenophenanthrene on dehydrogenation with selenium.

(2) The ketone was catalytically reduced as described above, giving a quantitative yield of 2-*methyl*-2-β-1′-*naphthylethyl*cyclo*pentanol* (II), b. p. 214—220°/1 mm.; this solidified to a greasy mass, m. p. 69—71°, which could not be recrystallised (Found: C, 85·3; H, 9·0. $C_{18}H_{22}O$ requires C, 85·0; H, 8·7%), and formed a 3 : 5-dinitrobenzoate, m. p. 186°.

Cyclodehydration. 2·5 G. of the carbinol (II) were heated with 5 g. of phosphoric oxide for 1 hour at 140°. The hydrocarbon (IV) (1·7 g.), isolated after addition of ice and extraction with ether, was a colourless oil with a blue fluorescence, b. p. 208—212°/3 mm., which did not decolorise bromine in chloroform (Found: C, 91·5; H, 8·6. Calc. for $C_{18}H_{20}$: C, 91·5; H, 8·5%). It formed an unstable orange-yellow picrate, m. p. 71—72°, and the s-*trinitrobenzene* complex crystallised from alcohol in fine needles, m. p. 103—103·5°, not depressed by the compound, m. p. 104°, described below (Found: C, 63·7; H, 5·3. $C_{18}H_{20},C_6H_3O_6N_3$ requires C, 64·1; H, 5·2%). The hydrocarbon was dehydrogenated by heating with half its weight of selenium for 22 hours at 310° and gave 1 : 2-*cyclo*pentenophenanthrene.

2-*Methyl*-2-β-1′-*naphthylethyl*-Δ^5-cyclo*pentene* (VI).—4·5 G. of the carbinol (II) in 50 c.c. of ether were added to 1 g. of potassium hydroxide, 50 c.c. of carbon tetrachloride, and 30 c.c. of ether; the mixture was mechanically stirred for an hour, and 1·1 c.c. of carbon disulphide then added. After a further 8 hours' stirring, 1·2 c.c. of methyl iodide were added, and the mixture heated under reflux overnight. After removal of the potassium iodide the filtrate was distilled, finally in a high vacuum; 3·7 g. of the unsaturated *hydrocarbon* (VI), b. p. 168—172°/0·5 mm., were then collected (Found: C, 91·4; H, 8·5. $C_{18}H_{20}$ requires C, 91·5; H, 8·5%). The *s*-trinitrobenzene complex crystallised from alcohol in pale yellow needles, m. p. 102·5—103°; it was more soluble and paler in colour than that of the cyclic isomeride (IV), but did not depress its m. p.

2-*Methyl*-1-β-1′-*naphthylethyl*-Δ^1-cyclo*pentene* (VII).—2-Methyl-1-β-1′-naphthylethyl*cyclo*pentanol (Harper, Kon, and Ruzicka, *loc. cit.*) was very readily dehydrated; distillation with a trace of iodine gave an excellent yield of the unsaturated *hydrocarbon* (VII), b. p. 132—140°/0·2 mm., which, like its isomeride (VI), decolorised bromine in chloroform (Found: C, 91·4; H, 8·5. $C_{18}H_{20}$ requires C, 91·5; H, 8·5%). The s-*trinitrobenzene* complex formed pale yellow needles, m. p. 85°, from alcohol (Found: C, 64·2; H, 5·0. $C_{18}H_{20},C_6H_3O_6N_3$ requires C, 64·1; H, 5·2%).

Cyclisation. 2 G. of the hydrocarbon (VII) in 20 c.c. of carbon disulphide were treated at 0° with 2·7 g. of powdered aluminium chloride in several portions, then kept overnight at 0°. After addition of ice and hydrochloric acid, the hydrocarbon (IV) was extracted with ether, 1 g., b. p. 160—165°/0·5 mm., being obtained as a colourless oil saturated to bromine. The *s*-trinitrobenzene complex formed deep yellow needles, m. p. 104°, from alcohol (Found: C, 63·7; H, 5·3. Calc.: C, 64·1; H, 5·2%). The hydrocarbon regenerated from the complex was still a viscous oil, $d_{4°}^{19·4°}$ 1·0692, n_D 1·6176. It is most readily obtained by the direct cyclodehydration of the carbinol (V).

2-*Methyl*-2-β-*phenylethyl*cyclo*pentanone*.—54 G. of 2-β-phenylethyl*cyclo*pentanone (Kon, *loc. cit.*) were methylated with sodamide and methyl iodide by the method used for the corresponding *cyclo*hexanone (*loc. cit.*), 40 g. of a fraction, b. p. 135—140°/1 mm., being obtained; this was converted into the *semicarbazone*, which, repeatedly crystallised from methyl alcohol, in which it was appreciably more soluble than the semicarbazone of the parent compound, formed small prisms, m. p. 191—192° (Found: C, 69·5; H, 8·5. $C_{15}H_{21}ON_3$ requires C, 69·3; H, 8·2%). The *ketone* regenerated from it had b. p. 136—137°/1 mm., $d_{4°}^{16·3°}$ 1·0064, n_D 1·52480, $[R_L]_D$ 61·53 (Found: C, 82·9; H, 9·2. $C_{14}H_{18}O$ requires C, 83·1; H, 9·0%).

2-*Methyl*-2-β-*phenylethyl*cyclo*pentanol*.—Reduction of the ketone with sodium in moist ether gave an almost quantitative yield of the *alcohol*, b. p. 161°/3 mm. (Found: C, 82·3; H, 9·8. $C_{14}H_{20}O$ requires C, 82·2; H, 9·9%).

*Cyclodehydration.** Treatment of the alcohol (16 g.) with phosphoric oxide as described on p. 674 gave 12 g. of a hydrocarbon, b. p. 134°/13 mm. This was shaken in petroleum solution with successive small quantities of sulphuric acid until the latter was no longer coloured. The hydrocarbon thus freed from a small amount of unsaturated material had b. p. 125—126°/11 mm., $d_{4°}^{16·0°}$ 0·99575, n_D 1·5480, $[R_L]_D$ 59·37, properties very close to those recorded for 1-methyl-1 : 2-*cyclo*pentano-1 : 2 : 3 : 4-tetrahydronaphthalene (Kon, *loc. cit.*).

2-*Methyl*-2-β-*phenylethyl*-Δ^5-cyclo*pentene*.—In this and subsequent preparations Tschugaev's original method was adopted, as Whitmore and Simpson's procedure gave a poor yield of unsaturated hydrocarbon. 10 G. of the alcohol were boiled overnight with 2 g. of potassium in 70 c.c. of benzene, 5 c.c. of carbon disulphide added with 50 c.c. of ether, and the mixture boiled for 8 hours, then again overnight after addition of 5 c.c. of methyl iodide. The cooled solution was filtered, the solvent distilled, and the residue slowly distilled under reduced pressure. The crude distillate was shaken in ethereal solution with 20% aqueous potassium hydroxide, then with a saturated solution of mercuric chloride until no further precipitation of mercury salts took place. After drying, and distillation of the solvent, the residue was distilled and finally redistilled over sodium, 7 g. of the *hydrocarbon*, b. p. 142°/23 mm., being obtained,

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* For this and the two preceding preparations we are indebted to Dr. F. C. J. Ruzicka.

$d_{4°}^{16·3°}$ 0·93055, n_D 1·52148, $[R_L]_D$ 60·30 (Found : C, 90·5; H, 9·5. $C_{14}H_{18}$ requires C, 90·3; H, 9·7%).

Oxidation. 2 G. of the above hydrocarbon were shaken overnight with the theoretical amount of 3% potassium permanganate solution; as the colour of the reagent had disappeared, a further amount was added, and the shaking continued until the colour persisted. The excess of reagent was destroyed with sulphur dioxide, and the product extracted with ether and shaken with alkali. No neutral products had been formed; acidification of the alkaline extract gave, on evaporation of the solution, an *acid* which crystallised from water in needles, m. p. 184° (Found : C, 63·6; H, 6·1. $C_{14}H_{16}O_5$ requires C, 63·6; H, 6·1%). This formed a *semicarbazone*, m. p. 183° (Found : C, 56·2; H, 5·9. $C_{15}H_{19}O_5N_3$ requires C, 56·1; H, 6·0%).

2-*Methyl*-1-β-*phenylethyl*cyclo*pentanol*.—A Grignard reagent prepared from 45 g. of β-phenylethyl bromide in 500 c.c. of ether was gradually treated with 24 g. of 2-methyl*cyclo*pentanone in the cold, and the mixture then warmed for ½ hour; 16 g. of the carbinol, b. p. 154—156°/20 mm., were ultimately obtained.

2-*Methyl*-1-β-*phenylethyl*-Δ¹-cyclo*pentene*.—This compound has already been obtained by the accidental dehydration of 1-methyl-2-β-phenylethyl*cyclo*pentanol (Kon, *loc. cit.*). A specimen prepared from the above carbinol by distillation with a trace of iodine had b. p. 143—144°/22 mm., $d_{4°}^{18·5°}$ 0·93644, n_D 1·52523, $[R_L]_D$ 60·93 (Found : C, 89·7; H, 9·6. Calc. for $C_{14}H_{18}$: C, 90·3; H, 9·7%). A specimen obtained by the xanthate method had $d_{4°}^{20·3°}$ 0·93747, n_D 1·52391.

Oxidation. The hydrocarbon was oxidised as described above ; no acidic material was produced. When the neutral portion was treated with semicarbazide acetate, a *disemicarbazone*, needles, m. p. 191—192°, from alcohol, was formed (Found : C, 58·0; H, 7·4. $C_{16}H_{24}O_2N_6$ requires C, 58·0; H, 7·3%).

Cyclisation. 2 G. of the hydrocarbon were cyclised as described on p. 675, giving 1·2 g. of the cyclic hydrocarbon, b. p. 140—141°/19 mm., $d_{4°}^{18·5°}$ 0·99141, n_D 1·54468, $[R_L]_D$ 59·18. A hydrocarbon of very similar properties was also obtained by the action of phosphoric oxide at 140° on the *cyclo*pentene, and by direct cyclodehydration (Kon, *loc. cit.*).

2-*Methyl*-2-β-*phenylethyl*-Δ⁶-cyclo*hexene*.—10 G. of 2-methyl-2-β-phenylethyl*cyclo*hexanol (Kon, *loc. cit.*) gave, on dehydration by the method given on p. 675, 5·6 g. of the *hydrocarbon*, b. p. 152—153°/20 mm., $d_{4°}^{17·6°}$ 0·93492, n_D 1·52695, $[R_L]_D$ 65·81 (Found : C, 89·8; H, 10·0. $C_{15}H_{20}$ requires C, 89·9; H, 10·1%). On oxidation this compound gave no neutral products; the acidic product has not yet been obtained crystalline and is still under investigation.

2-*Methyl*-1-β-*phenylethyl*cyclo*hexanol*.—This *alcohol* was prepared from 2-methyl*cyclo*hexanone and β-phenylethylmagnesium bromide as described above, the yield of the fraction, b. p. 168—175°/17 mm., being 21 g. from 30 g. of the bromide; the alcohol is always contaminated by αδ-diphenylbutane, which accounts for the high percentage of carbon found on analysis (Found : C, 85·3, 85·3; H, 9·7, 9·5. $C_{15}H_{22}O$ requires C, 82·7; H, 9·9%).

2-*Methyl*-1-β-*phenylethyl*-Δ¹-cyclo*hexene*.—Dehydration of the above alcohol with a trace of iodine gave the unsaturated *hydrocarbon*, b. p. 153—154°/14 mm., $d_{4°}^{19·4°}$ 0·95142, n_D 1·53617, $[R_L]_D$ 65·61 (Found : C, 90·2; H, 10·1. $C_{15}H_{20}$ requires C, 89·9; H, 10·1%). Dehydration by the xanthate method gave a very similar product (6 g. from 10 g. of the carbinol), b. p. 161—163°/23 mm., $d_{4°}^{19·4°}$ 0·95644, n_D 1·53804.

Oxidation. After treatment with potassium permanganate as described above no acidic products were isolated; when the neutral product was treated with semicarbazide acetate, a *disemicarbazone*, m. p. 175°, was obtained; the figures obtained on analysis suggest that this still contained some compound richer in carbon, such as the semicarbazone of an unsaturated ketone formed by loss of water from the 1 : 5-diketone originally formed (Found : C, 60·2, 60·1; H, 7·4, 7·3. $C_{17}H_{26}O_2N_6$ requires C, 58·9; H, 7·6%).

Cyclisation. Treatment of the *cyclo*hexene (3 g.) with aluminium chloride as described on p. 675 gave 2·1 g. of the saturated hydrocarbon, b. p. 162—163°/18 mm., $d_{4°}^{17·8°}$ 1·0053, n_D 1·55403, in good agreement with the constants given in Part I (*loc. cit.*) for 12-methyl-1 : 2 : 3 : 4 : 9 : 10 : 11 : 12-octahydrophenanthrene.

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