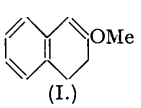
145. *The Preparation of β-Tetralone from β-Naphthol and some Analogous Transformations.*

By JOHN W. CORNFORTH, (MRS.) RITA H. CORNFORTH, and SIR ROBERT ROBINSON.

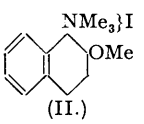
It was already known that the enol methyl ether of β-tetralone may readily be hydrolysed and two examples of the reduction of substituted 2-methoxynaphthalene to dihydro-derivatives are on record. The processes have not, however, hitherto been combined.

We find that 2-methoxynaphthalene may be reduced by sodium and alcohol and that the product on hydrolysis with dilute hydrochloric acid furnishes β-tetralone. It is hard to oxidise β-tetralol in satisfactory yield to the ketone, which becomes readily accessible by the new method for the first time. Substituted 2-methoxynaphthalenes may be similarly converted into β-tetralone derivatives, an interesting application being the conversion of equilenin into a keto-alcohol.

VON BRAUN (*Ber.*, 1930, **63**, 3052) showed that 2-methoxy-3 : 4-dihydronaphthalene (I), obtained by pyrolysis of the quaternary iodide (II), could be hydrolysed to β-tetralone by means of cold dilute hydrochloric acid. This method of preparation of (I) is laborious and expensive. On the other hand, Windaus and Dappe (*Ber.*,



(I.)



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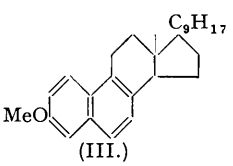

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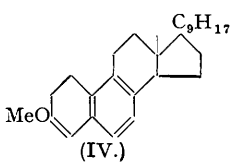
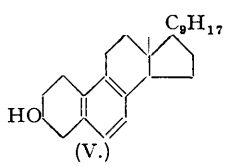


(IV.)

1937, **70**, 76) reduced *O*-methyldehydro*neo*ergosterol (III) to the dihydro-derivative (IV) by means of sodium and propyl alcohol, but did not hydrolyse the substance to a ketone.



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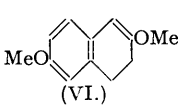

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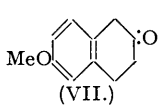

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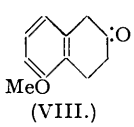


(VIII.)

The constitution (IV) was based on the absorption spectrum of the substance and on its conversion into (V) by catalytic hydrogenation in ether–acetic acid solution.

Similarly Robinson and Weygand (J., 1941, 386) reduced 2 : 6-dimethoxynaphthalene to a dihydro-derivative by means of sodium and *iso*amyl alcohol but did not hydrolyse the product (VI) to 6-methoxytetralone (VII). The latter stage has now been carried out and the ketone proved to be identical with a specimen synthesised by the method of Crowley and Robinson (J., 1938, 2001).

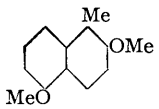
In the case of 2-methoxynaphthalene, sodium and methyl alcohol do not effect reduction and the yield of tetralone when propyl alcohol was used was inferior. The best results were obtained with sodium and ethyl alcohol, the yield of ketone obtained on hydrolysis of the product being 56%, and this can probably be improved.

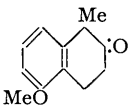
Analogously, 2-methoxy-1-methylnaphthalene afforded 1-*methyl*-β-*tetralone* in 10% yield. Here reduction also occurred in the unsubstituted nucleus and 2-methoxy-1-methyl-5 : 6 : 7 : 8-tetrahydronaphthalene was isolated from the products of the reaction.

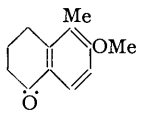
Reduction, followed by hydrolysis, of 1 : 6-dimethoxynaphthalene furnished 5-*methoxy*-2-*tetralone* (VIII) in good yield. On the other hand, the reduction and later hydrolysis of 2 : 5-*dimethoxy*-1-*methylnaphthalene* (IX) (1 : 6-dimethoxy-5-methylnaphthalene) gave the β-tetralone (X) and a small quantity of the α-tetralone (XI). The methylation of β-tetralone by means of methyl iodide and sodium *iso*propoxide in *iso*propyl-alcoholic solution (cf. Suter and Weston, *J. Amer. Chem. Soc.*, 1942, **64**, 533) afforded 1-methyl-β-tetralone, but when (VIII) was treated in this way the product was a dimethyl derivative, probably 5-*methoxy*-1 : 1-*dimethyl*-β-*tetralone*.

When equilenin methyl ether is reduced by means of sodium and alcohol, and the product hydrolysed, the

keto-alcohol (XII) is produced. This observation opens up many possibilities of synthesis of potentially androgenic substances and the physiological properties of (XII) will be examined.


(IX.)


(X.)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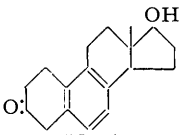
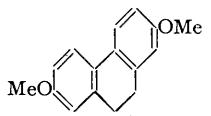

(XII.)


(XIII.)

Reduction of 2 : 7-dimethoxyphenanthrene gave only the 9 : 10-dihydro-derivative (XIII) (Cornforth and Robinson, preceding paper). Hence the reaction is general only for true 2-methoxynaphthalenes.

β-Tetralone is characterised by the blue coloration produced when it is treated with alcoholic sodium hydroxide in the presence of air. This reaction is given by all the β-tetralones (including XII) that we have examined, but not by those bearing substituents in the 1-position. Tetralone-blue is changed by acid to an orange-coloured substance, and it is noteworthy that both the blue and the orange colour are extractable by benzene. The reversible change is effected by ammonia and carbon dioxide and hence occurs at about p_H 7.

Experimental.

β-Tetralone.—Sodium (20 g.) was added during 10 minutes to a solution of 2-methoxynaphthalene (16 g.) in commercial " absolute " alcohol (200 c.c.) heated under reflux (bath at 115°). Heating was continued until all the metal disappeared; the cooled solution was then diluted with water (200 c.c.), and concentrated hydrochloric acid (200 c.c.) added as rapidly as possible (otherwise " tetralone-blue " is formed). The mixture was heated on the steam-bath for 15 minutes with occasional shaking, then cooled and shaken with ether. The oil from the washed extract was shaken with concentrated sodium bisulphite solution (70 c.c.). The crystals that soon separated were collected after ½ hour, washed well with ether, and decomposed either by warming with 10% hydrochloric acid or by sodium carbonate solution in the cold. The ketone was isolated by means of ether and distilled as an almost colourless oil, b. p. 130—131°/11 mm. (yield, 8·2 g. or 56%). The ketone was characterised as the phenylhydrazone

1-*Methyl-β-tetralone.*—2-Methoxy-1-methylnaphthalene (17 g.) was reduced as above with sodium (20 g.) and alcohol (200 c.c.). The oil isolated after hydrolysis with acid was treated with semicarbazide hydrochloride (5 g.) and sodium acetate (7·5 g.) in aqueous alcohol (50 c.c.), and the mixture kept overnight. The solid was collected, washed with alcohol, water, and again alcohol, and dried (2 g., 10%). A portion recrystallised from alcohol gave 1-*methyl-β-tetralone semicarbazone* in fine colourless needles, m. p. 200—202° (decomp.) (Found: N, 19·4. $C_{12}H_{15}ON_3$ requires N, 19·4%). Another portion was hydrolysed by warming with 10% hydrochloric acid; the ketone was isolated by means of ether and distilled. 1-*Methyl-β-tetralone* is a colourless oil, b. p. 137—138°/18 mm. (Found: C, 82·7; H, 7·7. $C_{11}H_{12}O$ requires C, 82·5; H, 7·5%).

In another experiment the oil after hydrolysis was distilled under diminished pressure. The distillate deposited crystals, which were recrystallised from alcohol. The substance had m. p. 51°, alone or mixed with authentic 2-methoxy-1-methyl-5 : 6 : 7 : 8-tetrahydronaphthalene kindly supplied by Dr. R. Martin (new substance, private communication).

5-*Methoxy-β-tetralone* (VIII).—1 : 6-Dimethoxynaphthalene (10·5 g.) was reduced with sodium (11 g.) and alcohol (120 c.c.), the product hydrolysed, and the ketone isolated as the bisulphite compound. This was best decomposed by solution in water and addition of sodium carbonate solution. The *ketone* was isolated by means of ether and distilled as a colourless, viscid oil, b. p. 120—122°/0·4 mm. (6·2 g.; 63%) (Found: C, 74·6; H, 7·1. $C_{11}H_{12}O_2$ requires C, 75·0; H, 6·8%). With alcoholic alkali a fine purple coloration was developed, more slowly than with β-tetralone.

6-*Methoxy-β-tetralone.*—A mixture of the dihydro-derivative of 2 : 6-dimethoxynaphthalene (2 g.) (Robinson and Weygand, *loc. cit.*), alcohol (20 c.c.), and hydrochloric acid (5 c.c. of 10%) was heated on the steam-bath for 10 minutes, water (50 c.c.) added, and the cooled mixture stirred until the oil crystallised. The solid, drained free from oil, crystallised from light petroleum (b. p. 40—60°) in colourless needles, m. p. 36·5°. This material (1 g.) was mixed with 0·5 g. of 6-methoxy-β-tetralone (Crowley and Robinson, *loc. cit.*) which was not quite pure; the whole on crystallisation gave needles, m. p. 36°

2 : 5-*Dimethoxy-1-methylnaphthalene.*—6-Methoxy-5-methyl-α-tetralone (30 g.) was heated with sulphur (3·75 g.; 75% of the theoretical amount) at 220—225° for 1½ hours. The phenolic product was separated and methylated with methyl sulphate and sodium hydroxide; the neutral product was again dehydrogenated, and the phenols separated and methylated as before. The combined methylated products were distilled, b. p. 190—191°/16 mm. (21 g.). The distillate crystallised immediately; a portion, recrystallised from alcohol, formed fine hexagonal plates, m. p. 85° (Found: C, 77·2; H, 6·9. $C_{13}H_{14}O_2$ requires C, 77·2; H, 6·9%).

5-*Methoxy-1-methyl-β-tetralone* (X).—2 : 5-Dimethoxy-1-methylnaphthalene (10 g.) was reduced with sodium (10 g.) and alcohol (100 c.c.). The oil isolated after hydrolysis with acid was treated with semicarbazide acetate, and the solid collected, washed with water and alcohol, and dried (4 g.). A portion after two crystallisations from alcohol gave 5-*methoxy-1-methyl-β-tetralone semicarbazone* in small, four-sided prisms, m. p. 188—190° (Found: C, 63·2; H, 7·3; N, 16·9. $C_{13}H_{17}O_2N_3$ requires C, 63·2; H, 6·8; N, 17·0%). This semicarbazone, the main product, is not identical with the semicarbazone of 6-methoxy-5-methyl-α-tetralone (XI). (The latter ketone is an intermediate in another investigation in progress in this laboratory.) Hence it follows that it must be a derivative of the expected β-tetralone.

The *crude* semicarbazone (3 g.) was hydrolysed by heating for a short time with 10% hydrochloric acid (20 c.c.), and the product (2 g.) isolated by distillation at 0·2 mm. (bath at 130—140°). A portion of the distillate was converted into the 2 : 4-dinitrophenylhydrazone, which was crystallised from acetic acid. A few deep red crystals were the first to separate, and these were collected before the main crop could be deposited. The red material after another crystallisation from acetic acid formed leaflets with a metallic glance, m. p. 249—250°, undepressed by the 2 : 4-dinitrophenylhydrazone of 6-methoxy-5-methyl-α-tetralone (XI).

C-*Methylation of β-Tetralone.*—Sodium (1·26 g.) was dissolved in dry *iso*propyl alcohol (40 c.c.). Air was displaced from the apparatus by nitrogen, and β-tetralone (8 g.) added. The solution was then cooled in ice during the gradual addition of methyl iodide (10·9 g.) in *iso*propyl alcohol (25 c.c.), and the reaction finally completed by refluxing on the steam-bath for 2 hours. After dilution and acidification out of contact with the atmosphere, the oily product was isolated by means of ether and shaken with saturated aqueous sodium bisulphite (50 c.c.). After ½ hour the bisulphite compound was collected and washed with ether. The ethereal filtrate was washed with water, dried, and evaporated, and the residue distilled as a colourless oil, b. p. 137—138°/18 mm. (5·2 g.); 1·5 g. of β-tetralone were recovered from the bisulphite

compound. The alcoholic alkali test revealed the presence of only a trace of unchanged β-tetralone, and the identity and homogeneous nature of the product were shown by preparation of the semicarbazone, which after a single crystallisation had m. p. 200—202°, undepressed by the semicarbazone of 1-methyl-β-tetralone previously described.

5-Methoxy-1 : 1-dimethyl-β-tetralone.—The methylation of 5-methoxy-β-tetralone (6 g.) was carried out as described for β-tetralone. The product (2·5 g.) had b. p. 105—110°/0·2 mm. It partly crystallised and was recrystallised from light petroleum, forming colourless rhombic plates, m. p. 77—79° (1·2 g.). Another crystallisation from methyl alcohol raised the m. p. to 83—85° (Found : C, 76·1; H, 7·4. $C_{13}H_{16}O_2$ requires C, 76·5; H, 7·8%).

The *semicarbazone* crystallised from alcohol in colourless rods, m. p. 192—194° (Found : N, 16·1. $C_{14}H_{19}O_2N_3$ requires N, 16·1%).

The 2 : 4-*dinitrophenylhydrazone* crystallised from alcohol in orange-yellow needles, m. p. 184° (Found : N, 14·8. $C_{19}H_{20}O_5N_4$ requires N, 14·6%).

Reduction of Equilenin Methyl Ether.—Equilenin (2 g.) was methylated with sodium hydroxide and methyl sulphate, and the precipitated ether washed and dried at 100°. It was dissolved in alcohol (100 c.c.) and reduced with sodium (10 g.). The reaction mixture was worked up as described for β-tetralone, and a bisulphite compound obtained, which was dissolved in water and decomposed by sodium carbonate. The product was taken up in ether, and the dried extract evaporated; the residue (0·8 g.) crystallised at once. It was sublimed at 160—170°/0·3 mm. and crystallised from benzene. The product (XII) formed rhombic platelets, m. p. 152—153° (Found : C, 79·8; H, 8·3. $C_{18}H_{22}O_2$ requires C, 80·0; H, 8·1%). $[\alpha]_D^{22°}$ +33·6° (*c*, 3·3 in ethanol). With alcoholic alkali the substance gave a green fluorescence, which vanished slowly as a deep purple colour developed.

Reduction of 2 : 7-Dimethoxyphenanthrene.—2 : 7-Dimethoxyphenanthrene (5 g.) was reduced with sodium (25 g.) and alcohol (300 c.c.), the large amounts being rendered necessary by its sparing solubility. The solution was hydrolysed in the usual way. The resulting oil partly crystallised on keeping. The crystals were recrystallised from benzene, forming rhombic prisms, m. p. 108—109°, undepressed by 2 : 7-dimethoxy-9 : 10-dihydrophenanthrene. The non-crystalline fraction gave ketonic reactions, but no pure substance could be isolated.

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DYSON PERRINS LABORATORY, OXFORD UNIVERSITY. [*Received, August 4th*, 1942.]