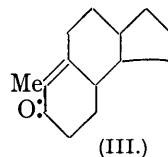
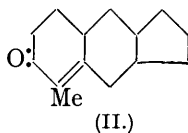
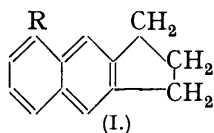


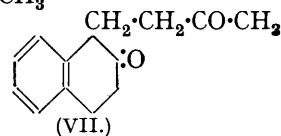
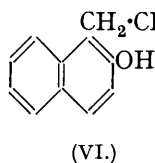
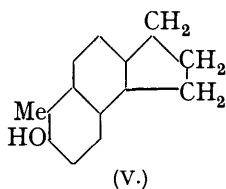
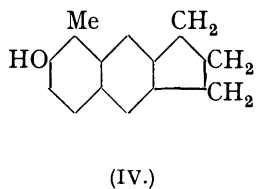
105. Experiments on the Synthesis of Substances related to the Sterols.
Part XXXIX. (A) Some Derivatives of Hydrindene. (B) Reduction
of 1- γ -Ketobutyl-2-naphthol.

By F. J. McQUILLIN and SIR ROBERT ROBINSON.

A. 5 : 6-Benzhydrindene (I, R = H) and 3'-methyl-5 : 6-benzhydrindene (I, R = Me) have been synthesised as further reference compounds in order to facilitate the determination of the constitution of the ketone, $C_{15}H_{22}O$, described in Part XX (J., 1938, 1097) as well as that of its lower homologue (II or III) mentioned below.



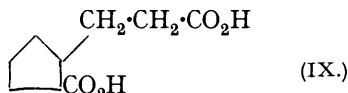
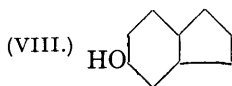
Unfortunately, as already recorded (present authors, *loc. cit.*), the dehydrogenation of $C_{15}H_{22}O$ (methyl in the angle) proved very difficult and that of the new ketone, $C_{14}H_{20}O$, gave a phenol $C_{14}H_{14}O$. This might be (IV) or (V) and as the work reported by Bateman and Robinson (Part XXXIII, this vol., p. 398) opens up a route to (V), it is in this direction that the investigation will be continued.



B. The preparation of 1- γ -ketobutyl-2-naphthol (VI) (Miller and Robinson, J., 1935, 1535) has been improved. It has been reduced to a *sec.*-alcohol and also to hydroaromatic benzchroman derivatives, but the objective (VII) has not been reached. A further development of this subject will, it is hoped, soon be submitted to the Society.

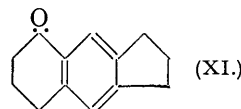
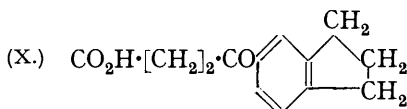
A. It is known that 9-methyl-3-decalone (Part XIV, J., 1937, 53) condenses with the methiodide of δ -diethylaminobutan- β -one to a hydroanthracene derivative, but it is not safe to assume that the lower ring-homologous 5-keto-8-methylhydrindane (Part XX) will behave in a similar fashion and give the linear 5 : 6-benzhydrindene derivative. Indeed Cook and Linstead (J., 1934, 946) showed that *cis*-5-hydroxyhydrindane (VIII)

furnished the acid (IX) on oxidation, and this points to reactivity of the corresponding ketone in position 4 rather than in 6.

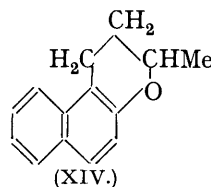
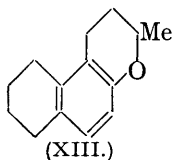
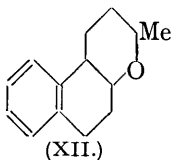


Accordingly *cis*-5-ketohydrindane was condensed with α -diethylaminopentan- γ -one methiodide in the presence of sodamide, and the resulting *ketone* (II or III) treated with selenium. No hydrocarbon product could be isolated, but the phenol, $\text{C}_{14}\text{H}_{14}\text{O}$, which was obtained is a characteristic substance, and its synthesis will be attempted. Reduction of the ketone $\text{C}_{14}\text{H}_{20}\text{O}$ by Clemmensen's method and subsequent dehydrogenation gave a few mg. of a substance, m. p. 38—42°, which may be 3'-methyl-4 : 5-benzhydrindene, m. p. 44° (Part XX, *loc. cit.*), but this important point could not be established before the work was interrupted.

Meanwhile we had prepared one of the hydrocarbons (I, R = Me) which might have resulted from the dehydrogenation of the ketone $\text{C}_{14}\text{H}_{20}\text{O}$. Condensation of hydrindene and succinic anhydride in the presence of aluminium chloride gave γ -keto- γ -5-hydrindylbutyric acid (X), which was oxidised to hydrindene-5-carboxylic acid in good yield. On reduction of (X) by Clemmensen's method, γ -5-hydrindylbutyric acid was obtained and this was cyclodehydrated to (XI). The hydrocarbons (I, R = H and R = Me) were then obtained by Wolff-Kishner reduction and the action of methylmagnesium iodide, respectively, followed by dehydrogenation of the products. The structure assumed for (XI) is based on numerous analogies indicating the preference for 5 : 6-disubstitution of hydrindene and it is confirmed by the fact that the properties of our 5 : 6-benzhydrindene (I, R = H) differ from those reported for 4 : 5-benzhydrindene (Mayer and Sieglitz, *Ber.*, 1922, 55, 1855; Cook and Hewett, *J.*, 1933, 1098).



B. 1- γ -Ketobutyl-2-naphthol (VI) is more readily obtained by the condensation of β -naphthol with methyl β -chloroethyl ketone than with methyl vinyl ketone, in alcoholic sodium ethoxide solution. It was hydrogenated in acetic acid solution in the presence of Adams's catalyst to a *methyltetrahydrobenzchroman* (XII or XIII). This substance was resistant to oxidation but could be dehydrogenated to 2-methyl-5 : 6-benzchroman (XIV).



The *alcohol* corresponding to (VI) could be obtained by an application of the Pondorff method and on full catalytic reduction afforded a poor yield of *methyldecahydrobenzchroman*. A further study of this substance will be described in Part XL of this series.

EXPERIMENTAL.

γ -Keto- γ -5-hydrindylbutyric Acid (X).—Hydrindene (29 g.) was added to a cooled mixture of nitrobenzene (230 c.c.) and aluminium chloride (66 g.), and succinic anhydride (32 g.) gradually introduced with agitation. After 4 days the red mixture was decomposed, and nitrobenzene removed by steam-distillation. The product crystallised on cooling and was purified by extraction with benzene (Soxhlet). Large, elongated prisms (20 g.) were obtained, m. p. 123°, after recrystallisation from benzene-light petroleum (b. p. 60—80°) (Found : C, 71.3; H, 6.5. $\text{C}_{13}\text{H}_{14}\text{O}_3$ requires C, 71.5; H, 6.4%). Oxidation by means of alkaline sodium

hypochlorite afforded hydrindene-5-carboxylic acid, m. p. 184° alone or mixed with an authentic specimen.

The *keto-acid* (14 g.) was refluxed for 24 hours with concentrated hydrochloric acid (150 c.c.), amalgamated zinc (56 g.), and a layer of toluene. The last was separated, dried, and evaporated. The oily residue of γ -5-hydrindylbutyric acid crystallised, but was distilled, b. p. 169—171°/0.8 mm. (8.7 g.), m. p. 48° (Found: C, 76.6; H, 7.6. $C_{13}H_{16}O_2$ requires C, 76.5; H, 7.8%).

8-Keto-5 : 6 : 7 : 8-tetrahydro-2 : 3-cyclopentenonaphthalene (XI).—A mixture of γ -5-hydrindylbutyric acid (6.7 g.), concentrated sulphuric acid (21 c.c.), and water (7 c.c.) was heated on the steam-bath for 1 hour. After addition of ice the product (4.5 g.) was isolated by means of ether; it had b. p. 128—130°/0.2 mm., n_D^{18} 1.5870 (Found: C, 83.8; H, 7.5. $C_{13}H_{14}O$ requires C, 83.8; H, 7.5%). The pale yellow oil crystallised on keeping. The *semicarbazone* formed prisms, m. p. 245°, from pyridine (Found: C, 69.3; H, 7.0. $C_{14}H_{17}ON_3$ requires C, 69.2; H, 7.0%).

5 : 6-Benzhydrindene (I, R = H).—The above semicarbazone (1.4 g.) was intimately mixed with potassium hydroxide (2.5 g.) and carefully heated (20 mm.). The oil (1.0 g.) that distilled was heated with palladised charcoal (0.2 g., according to Ruzicka) for 4 hours at 300°. Extraction of the residue afforded a solid (0.6 g.) that crystallised from methyl alcohol in rosettes of long prisms, m. p. 94° (Found: C, 92.7; H, 7.2. $C_{13}H_{12}$ requires C, 92.8; H, 7.2%). The *picrate* crystallised from alcohol in golden needles, m. p. 118° (Found: N, 10.7. $C_{13}H_{12}, C_6H_3O_7N_3$ requires N, 10.7%).

3'-Methyl-5 : 6-benzhydrindene (I, R = Me).—A solution of ketotetrahydrocyclopentenonaphthalene (4 g.) in ether (70 c.c.) was added to one of methylmagnesium iodide (magnesium, 1.2 g.; methyl iodide, 7 g.) in ether (50 c.c.) with shaking. After 12 hours the mixture was refluxed for 3 hours, and the product (3.5 g.) isolated as a yellow oil, b. p. 159—162°/15 mm. This material (2.4 g.) was dehydrogenated as above and yielded a colourless liquid (1.8 g.), b. p. 170—172°/20 mm., n_D^{18} 1.6029 (Found: C, 92.3; H, 7.8. $C_{14}H_{14}$ requires C, 92.3; H, 7.7%). The *picrate* crystallised from methyl alcohol in orange-coloured needles, m. p. 109—110° (Found: N, 10.3. $C_{20}H_{17}O_7N_3$ requires N, 10.2%).

6-Keto-5-methyl-7 : 8-dihydro-1 : 2 (or 2 : 3)-cyclopentenonaphthalene (III or II).—5-Hydroxyhydrindene (17.8 g.) (Cook and Linstead, *loc. cit.*) was hydrogenated, with the help of Adams's catalyst in acetic acid solution at room temperature, to 5-hydroxyhydrindane (12.3 g.), b. p. 118°/20 mm., n_D^{18} 1.4987 (C. and L., b. p. 113°/15 mm., n_D^{18} 1.4931). Oxidation with chromic acid gave 10.2 g. of the ketone, b. p. 102—104°/15 mm., n_D^{18} 1.4868 (C. and L., b. p. 96.5°/11 mm., n_D^{18} 1.4848). Hydrindan-5-one (10.2 g.) in ether (100 c.c.) was added to powdered sodamide (5.7 g.) under ether (150 c.c.), and the whole refluxed with stirring for 2 hours. After 12 hours, ϵ -diethylaminopentan- γ -one methiodide (21.9 g.) in pyridine (100 c.c.) was added during 3 hours with vigorous stirring. After 12 hours the mixture was refluxed for 2 hours. The pyridine was removed by washing with acid, and the *ketone* distilled, b. p. 153—155°/1.6 mm. (5 g.); redistilled, b. p. 142—144°/0.2 mm., n_D^{18} 1.5428 (Found: C, 82.3; H, 9.7. $C_{14}H_{20}O$ requires C, 82.4; H, 9.8%).

The 2 : 4-dinitrophenylhydrazone crystallised from ethyl acetate-alcohol in deep red prisms with a metallic reflex, m. p. 174—175° (Found: C, 62.4; H, 6.2. $C_{20}H_{24}O_4N_4$ requires C, 62.5; H, 6.2%).

Dehydrogenation. (i) The ketone (1.6 g.) was heated with selenium (4 g., gradually added) for 14 hours at 330°. The product (0.5 g., m. p. 142—145°) was extracted with ether. A benzene solution was filtered through activated alumina, and the solid recovered and crystallised from benzene-light petroleum (b. p. 60—80°), forming colourless leaflets, m. p. 162—163° (Found: C, 85.1; H, 7.4. $C_{14}H_{14}O$ requires C, 84.8; H, 7.1%). The *substance* was readily soluble in aqueous sodium hydroxide but gave no ferric reaction in alcoholic solution. On addition of picric acid to an alcoholic solution a red coloration was produced, but the *picrate* could not be isolated.

(ii) The ketone (1.7 g.) was hydrogenated in alcoholic solution in the presence of a palladium catalyst (180 c.c. of hydrogen absorbed). The product was isolated, submitted to Clemmensen's reduction process (under toluene), again isolated, and dehydrogenated with palladised charcoal at 300—320°. A very small quantity of crystals, m. p. 38—42°, was obtained by trituration of the residue from the last ethereal extraction with alcohol. The mother-liquors afforded no solid *picrate*.

1- γ -Ketobutyl-2-naphthol (VI).—Methyl β -chloroethyl ketone (53 g.) was added dropwise with good shaking to a solution of β -naphthol (72 g.) in alcoholic potassium ethoxide (39 g. of potassium in 300 c.c.) cooled in a freezing mixture. After keeping at 0° for 3 days, the solvent

was removed under diminished pressure, and an aqueous solution of the residue saturated with carbon dioxide. The solid was collected, washed, dried, and crystallised from aqueous alcohol (63 g., m. p. 88—89°). The orange-red solution in concentrated sulphuric acid exhibited a green fluorescence. The *semicarbazone* crystallised from methyl alcohol in pale yellow prisms, m. p. 179—180° (Found: C, 66.1; H, 6.2. $C_{15}H_{17}O_2N_3$ requires C, 66.4; H, 6.3%). The *oxime* formed hard prisms, m. p. 168—169°, from aqueous methyl alcohol (Found: C, 73.4; H, 6.5. $C_{14}H_{15}ON$ requires C, 73.4; H, 6.5%). The *acetate* was obtained by the action of acetic anhydride on a solution of the naphthol in aqueous sodium hydroxide; it had b. p. 174—176°/0.2 mm. (Found: C, 75.0; H, 6.4. $C_{16}H_{16}O_3$ requires C, 75.0; H, 6.2%).

Hydrogenation. (i) Ketobutyl-naphthol (5 g.) in acetic acid (70 c.c.) at 70° was stirred in hydrogen at atmospheric pressure along with Adams's catalyst (0.15 g.). After 48 hours, 1480 c.c. of hydrogen had been absorbed (2H₂ requires 1550 c.c.). The product (4.1 g.) crystallised from methyl alcohol in prisms, m. p. 69°, b. p. 117—122°/0.3 mm. (Found: C, 83.2; H, 8.6. $C_{14}H_{18}O$ requires C, 83.2; H, 8.9%).

(ii) A similar result was obtained when the hydrogenation was conducted at 20° until 1H₂ had been absorbed and the reduction then completed at 70°. The hydrogenation did not proceed at 30° in alcoholic or ethyl acetate solution.

(iii) Hydrogenation of the acetate or oxime, substantially as in (i), also afforded the substance $C_{14}H_{18}O$, m. p. 68—69°.

The substance $C_{14}H_{18}O$ was unchanged by treatment with chromic acid in acetic acid solution or with potassium permanganate in hot aqueous alkaline or acetone solution. It was unchanged by boiling with acetic acid saturated with hydrogen bromide. It is therefore undoubtedly a cyclic ether (XII or XIII). Dehydrogenation with palladised charcoal under the usual conditions gave 2-methyl-5:6-benzchroman (XIV), which formed pearly plates, m. p. 90—91°, from ethyl alcohol (Found: C, 84.8; H, 6.9. $C_{14}H_{14}O$ requires C, 84.8; H, 7.1%).

1- γ -Hydroxybutyl-2-naphthol.—From a mixture of ketobutyl-naphthol (35 g.), isopropyl alcohol (300 c.c.), and aluminium isopropoxide (30 g.), the alcohol was slowly distilled through a column, with additions of isopropyl alcohol to maintain the original volume; the process occupied 24 hours (bath at 120—125°). Removal of the solvent and acidification gave a solid which, crystallised from methyl alcohol, had m. p. 135—136° (yield, 24.3 g.) (Found: C, 77.8; H, 7.3. $C_{14}H_{16}O_2$ requires C, 77.8; H, 7.4%).

Hydrogenation. A solution of the naphtholic alcohol (5 g.) in acetic acid (50 c.c.) at 60°, along with Adams's catalyst (0.2 g.), was stirred with hydrogen; a little more than 5H₂ was absorbed. Distillation of the product gave (i) 0.5 g., b. p. 111—122°/0.5 mm., n_D^{19} 1.5042; (ii) 0.4 g., b. p. 123—126°/0.5 mm., n_D^{19} 1.5044 (Found: C, 80.0; H, 11.2. $C_{14}H_{24}O$ requires C, 80.7; H, 11.5%), possessing an α -naphthol-like odour; (iii) a small amount, b. p. 135—160°/0.5 mm., n_D^{19} 1.5144.

Ethyl 3-Keto-4-methyl- Δ^4 :¹⁰-octalin-9-carboxylate.— α -Diethylaminopentan- γ -one (28.7 g.) in alcohol (50 c.c.) was added to a solution of ethyl cyclohexanone-2-carboxylate (17 g.) in alcoholic sodium ethoxide (4.7 g. of sodium in 150 c.c.). After 24 hours the mixture was refluxed for 2 hours. The solvent was removed under diminished pressure, dilute hydrochloric acid added, and the product collected by means of ether. Distillation afforded some recovered keto-ester and then 9.7 g., b. p. 172—175°/14 mm.; redistilled, b. p. 135—136°/0.2 mm., $n_D^{16.5}$ 1.5141 (Found: C, 71.6; H, 8.5. $C_{14}H_{20}O_3$ requires C, 71.2; H, 8.5%).

The *semicarbazone* crystallised from alcohol in small prisms, m. p. 166—167° (Found: C, 61.2; H, 8.1. $C_{15}H_{23}O_3N_3$ requires C, 61.4; H, 7.8%).

This *ester* could not be converted into an oxide by treatment with aqueous methyl-alcoholic potassium hydroxide and hydrogen peroxide.

Ethyl 2- γ -Ketobutylcyclohexanone-2-carboxylate.—An alcoholic solution of sodium ethoxide (0.2 g. of sodium in 3 c.c.) was added to a mixture of ethyl cyclohexanone-2-carboxylate (25.5 g.), pyridine (50 c.c.), and δ -diethylaminobutan- β -one (21.5 g.); after 4 days a further equal quantity of alcoholic sodium ethoxide was introduced. After 7 days longer, dilute hydrochloric acid in excess was added, and the product isolated by means of ether. On distillation, 16 g., b. p. 180—184°/15 mm., n_D^{16} 1.4880, were obtained; redistilled, b. p. 176—180°/12 mm., n_D^{19} 1.4868 (Found: C, 66.1; H, 8.4. $C_{13}H_{20}O_4$ requires C, 65.0; H, 8.3%). It is hard to obtain these diketones free from the products of their cyclodehydration ($C_{13}H_{18}O_3$ requires C, 70.3; H, 8.1%).

An attempt to form a pinacol from this diketone by reduction with magnesium and a trace of iodine in ether-benzene gave as sole product, as the result of cyclodehydration, ethyl 4-keto- Δ^5 :¹⁰-octalin-9-carboxylate (cf. du Feu, McQuillin, and Robinson, J., 1937, 53). The substance

so formed had b. p. 174—175°/15 mm., n_D^{18} 1.5018, and gave a semicarbazone, m. p. 194—195° (Found : C, 60.4; H, 7.5. Calc. for $C_{14}H_{21}O_3N_3$: C, 60.2; H, 7.5%). Direct comparison established the identity with an authentic specimen.

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