

327. *Hydroaromatic Steroid Hormones. Part III.\* Some Angular-methylated Intermediates.*

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An attempt to introduce an angular methyl group into the 4-methylanilino-methylene derivative of 1 : 2 : 3 : 4 : 5 : 6-hexahydro-3-keto-10-methoxy-chrysene (IV) gave 1 : 2-dihydro-3 : 10-dimethoxy-4-*N*-methylanilinomethyl-chrysene (VI), but the direct methylation of 1 : 2 : 3 : 4 : 5 : 8-hexahydro-1-keto-6-methoxynaphthalene (IX) produced 1 : 2 : 3 : 4 : 8 : 9-hexahydro-1-keto-6-methoxy-9-methylnaphthalene (XI), an important intermediate in steroid synthesis. Further reactions led to the 1-hydroxy-6-keto-9-methyl compound. Similar angular methylation of 4 : 7-dihydro-5-methoxyindan-1-one was achieved.

THE reduction of aromatic systems by alkali metals and alcohols in liquid ammonia, which has been used so far in this series in attempts to synthesise biologically active analogues of steroid hormones, leads readily to the 19-nor-steroid hormones, 19-nortestosterone † and 19-norprogesterone, which have high hormone activity (Birch, *J.*, 1950, 367; Birch and Smith, Part II \*; Miramontes, Rosenkranz, and Djerassi, *J. Amer. Chem. Soc.*, 1951, 73, 3540). However, the method cannot lead directly, by the reduction of aromatic rings, to compounds containing angular methyl groups, and some exploratory work has been carried out on the introduction of these groups into compounds accessible by means of the reduction reactions.

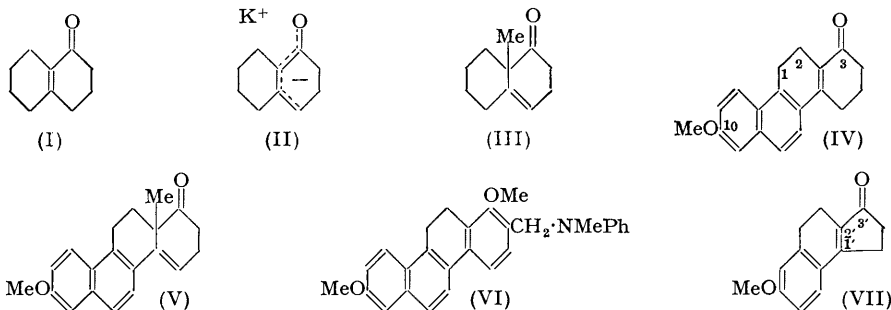
Preliminary work on an indirect route for the introduction of the C<sub>(10)</sub>-Me into the 19-nortestosterone indicates that, although probably feasible, it is not likely to be of practical importance (Birch, *Chem. and Ind.*, 1951, 616). Accordingly, methods for the direct introduction of a methyl group into octahydroketonaphthalene derivatives of type (I) are now being explored, on the basis of theoretical ideas on the conversion of  $\alpha\beta$ - into  $\beta\gamma$ -unsaturated ketones which have already been outlined (Birch, *J.*, 1950, 1551) and have been successfully exploited in the conversion of cholest-4-en-3-one into cholest-5-en-3-one (Birch, *J.*, 1950 2523). Briefly, if compounds of type (I) can be converted into salts containing mesomeric anions of type (II), then the action of methyl iodide on these salts may be expected to lead chiefly to compounds of type (III). It is probable that the requisite salts may in some cases be directly produced by the action of the correct enolising agent; in other cases indirect routes may be necessary, *e.g.*, through enol esters (cf. *loc. cit.*). This aspect is being examined.

Preparation of the chrysene ketone (IV) was reported in Part II of this series, and its conversion into (V) would constitute a synthesis of ( $\pm$ )-D-homoequilenin, because hydrogenation of the double bond has been shown to give the correct *trans*-linkage of the C-D rings (Burnop, Elliott, and Linstead, *J.*, 1940, 727; Bachmann and Holmes, *J. Amer. Chem.*

\* Part II, *J.*, 1951, 1882.

† Formerly called 10-nortestosterone. For the present nomenclature see *J.*, 1951, 3526.

*Soc.*, 1941, **63**, 2592) : direct angular methylation of 1-ketodecalin derivatives, on the other hand, leads predominantly to the unwanted *cis*-isomer (e.g., Birch and Robinson, *J.*, 1944, 501). In order to prevent enolisation in its direction, the 4-methylene group was protected as the *N*-methylanilinomethylene derivative (Birch and Robinson, *J.*, 1944,



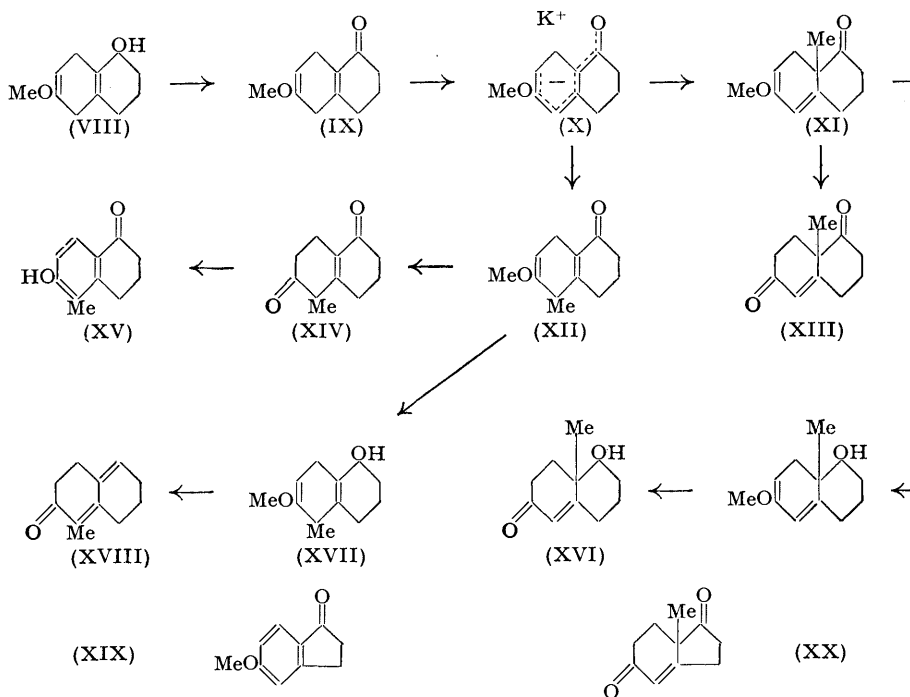
510). This with potassium *tert*-butoxide and methyl iodide gave a colourless base which did not lose its nitrogen on acidic or alkaline hydrolysis and appeared to be (VI), formed by bond-migration and methylation. Now, with a five-membered D-ring such aromatisation is impossible. Accordingly, (VII) was synthesised by the general method of Johnson, Johnson, and Petersen (*J. Amer. Chem. Soc.*, 1945, **67**, 1360). Its methylanilinomethylene derivative gave after the methylation procedure and hydrolysis only impure starting material in poor yield. Introduction of the methyl group by this procedure is therefore not easy, although it should be possible in the right experimental conditions. Since this work was completed, Woodward, Sondheimer, Taub, Heusler, and McLamore (*J. Amer. Chem. Soc.*, 1951, **73**, 2403) have reported a closely analogous reaction in which a carbon atom becomes quaternary, a similarly protected  $\alpha\beta$ -unsaturated ketone being caused to condense with acrylonitrile.

Attention was then turned to what, on theoretical grounds, was considered to be a particularly favourable case: the direct methylation of 1:2:3:4:5:8-hexahydro-1-keto-6-methoxynaphthalene (IX). This was expected to form a salt readily because it can give rise to a fully conjugated anion of the type (X) by loss of a proton from the dihydroanisole ring, a process known to be easy with potassium amide in liquid ammonia (cf. Birch, *Quart. Reviews*, 1950, **4**, 69). According to the results obtained by Birch (*J.*, 1950, 1551) such a salt should react with methyl iodide to give the methoxy-ketone (XI) with a smaller likelihood of the formation of its isomer (XII). In fact, the chief product obtained after methylation and acid hydrolysis was identified as the diketone (XIII) by a mixed melting point determination and infra-red and ultra-violet spectra. A specimen of the authentic substance was kindly provided by Dr. R. H. Jaeger. A small amount of the phenol (XV) was also identified in the product, and was evidently formed by oxidation of the unstable ketone (XIV) derived from (XII). That (XII) was formed in some 10–15% yield in the methylation was further indicated by the reduction results below.

As a practical preparation of the diketone (XIII) the method is unlikely to rival that from 2-methylcyclohexane-1:3-dione (unpublished work in various laboratories; cf. also Wendler, Slates, and Tishler, *J. Amer. Chem. Soc.*, 1951, **73**, 3816), but the enol ether (XI) is likely to be very useful. The structure of this is confirmed by its ultra-violet absorption maximum at 274  $m\mu$  ( $\epsilon$  5200) with an inflexion at 241  $m\mu$  ( $\epsilon$  4450). It contains a grouping readily convertible by acid hydrolysis into that found in the A-B rings of physiologically active hormones such as testosterone, progesterone, and cortisone; for the potential carbonyl group in the steroid 3-position is protected as the enol ether against anionoid reagents, while the other carbonyl group is in the right position to facilitate the addition of rings C and D. Furthermore, (XI) is a potential starting material for rings C-D of D-homosteroids and ring-opened analogues. Its reduction with lithium aluminium hydride followed by acid hydrolysis produced the keto-alcohol (XVI) and, as by-product, the dienone (XVIII) formed from (XII) (present as impurity) by reduction to (XVII) and dehydration

during acid hydrolysis (cf. Birch, *J. Proc. Roy. Soc., N.S.W.*, 1950, **83**, 245). The steric configuration of the hydroxyl group has not been ascertained. It may be  $\beta$  by analogy with the reduction of 17-ketosteroids, but Heusser, Wahba, and Herzig (Abs. 120th Meeting Amer. Chem. Soc., 1951, 9L) have shown that 17 $\alpha$ -keto-D-homo-steroids do not necessarily obey the rule of  $\alpha$ -attack of a reagent.

The preparation of (IX) was based on the 6:8-reduction, already described (Birch, *loc. cit.*), of the readily available 1:2:3:4-tetrahydro-1-keto-6-methoxynaphthalene (Stork, *J. Amer. Chem. Soc.*, 1947, **69**, 576) to (VIII) by means of sodium and ethanol in liquid ammonia. The yield has been raised to 55%, and it is clear from unpublished work that prior reduction of the carbonyl group with a milder reagent would further improve this yield by largely eliminating the reductive removal of methoxyl, which is a side-reaction. The principal loss is due to hydrogenolysis of the hydroxyl group, and it may be noted that in absence of the "p"-methoxyl group hydrogenolysis is complete. An Oppenauer-type oxidation of the alcohol (VIII) gave the crystalline ketone (IX), the structure of which is in accord with the ultra-violet absorption maximum at 238  $\mu$ . The reduced benzene ring was unaffected by this structure-specific oxidation process, despite the extreme sensitivity of (VIII) and (IX) to the usual oxidising agents and to air. In order to avoid the reduction and re-oxidation of the carbonyl group attempts were made to protect this as the acetal, following the successful reduction of the ring in anisaldehyde when this method of protection is used. However, all efforts to prepare cyclic or acyclic acetals by standard methods failed.



As a further application of the general angular-methylation procedure, 5-methoxyindan-1-one (XIX) was converted by the same stages into the diketone (XX) in rather poor yield. Extensions of the process are being investigated.

#### EXPERIMENTAL

1:2:3:4:5:6-Hexahydro-3-keto-10-methoxy-4-N-methylanilinomethylenechrysenes.—Ethyl formate (3.75 c.c.) in benzene (3.75 c.c.) was added under nitrogen to dry sodium methoxide (from the metal, 0.54 g.) and, after 15 minutes, 1:2:3:4:5:6-hexahydro-3-keto-10-methoxychrysenes (1.06 g.) in benzene (15 c.c.) was added. The mixture was shaken occasionally and

left overnight. After the addition of water (5 c.c.) and a little ice, the sparingly soluble yellow sodium salt was filtered off and washed with benzene, followed by a little alcohol and ether. Acetic acid (10 c.c.) and water (90 c.c.) liberated the formyl compound as a buff-coloured solid (1.0 g.) which gave a deep purple colour with ferric chloride. The crude substance (1.0 g.), benzene (50 c.c.), and methylaniline (0.5 g.) were refluxed in the presence of anhydrous sodium sulphate for 30 minutes and then filtered. Evaporation of the solvent under reduced pressure left a brownish resin which was repeatedly extracted with boiling light petroleum (b. p. 40—60°) containing 5% of benzene. Concentration of the extract to *ca.* 30 c.c. gave a crystalline solid which was recrystallised from tetrahydrofuran-ethanol (1 : 1), to give 1 : 2 : 3 : 4 : 5 : 6-hexahydro-3-keto-10-methoxy-4-N-methylanilinomethylenechrysene (0.75 g.) as yellow needles, m. p. 183° (Found : C, 81.9; H, 6.0; N, 3.8.  $C_{27}H_{35}O_2N$  requires C, 82.0; H, 6.3; N, 3.5%).

1 : 2-Dihydro-3 : 10-dimethoxy-4-N-methylanilinomethylchrysene.—The above compound (0.75 g.) in tetrahydrofuran (20 c.c.) was added to a solution of potassium (0.7 g.) in *tert.*-butanol (20 c.c.) under nitrogen. The mixture was refluxed for 5 minutes and methyl iodide added to the boiling solution to discharge the brown colour. Water (30 c.c.) was added. The oily precipitate rapidly crystallised to aggregates of needles. The product was purified by passage in benzene through alumina (50 g.). Crystallisation from benzene-methanol (1 : 1) gave 1 : 2-dihydro-3 : 10-dimethoxy-4-N-methylanilinomethylchrysene (0.52 g.) as long white needles, m. p. 144—145° (Found : C, 81.8; H, 6.7; N, 3.5.  $C_{28}H_{27}O_2N$  requires C, 82.2; H, 6.6; N, 3.4%). The compound was soluble in concentrated hydrochloric acid and was recovered unchanged after 3 hours in a boiling mixture of ethanol (14 c.c.), water (3 c.c.), and sulphuric acid (1 c.c.). Attempted methylation of the unprotected hexahydroketo-methoxychrysene under the same conditions resulted in recovery of most of the starting material.

3 : 4-Dihydro-3'-keto-6-methoxycyclopenteno(1' : 2'-1 : 2)naphthalene.—1 : 2 : 3 : 4-Tetrahydro-1-keto-6-methoxynaphthalene (17.6 g.) and methyl succinate (21.9 g.) were added (in nitrogen) to a chilled solution of potassium (4.3 g.) in *tert.*-butanol (80 c.c.), and the light orange suspension was heated under reflux for 90 minutes. On cooling, the mixture was acidified and the solvents were removed under reduced pressure, to give an oily residue which was taken up in ether and washed with water. The washings were re-extracted with ether. The combined ethereal extracts were extracted thoroughly with saturated sodium hydrogen carbonate solution, and the extract was acidified. The pink oil was taken up in ether, washed with water, dried, and evaporated, to leave a golden-brown viscous oil which failed to crystallise. This product (6 g.) in acetic anhydride (60 c.c.) was added to fused zinc chloride (0.6 g.) in acetic acid (30 c.c.), and the whole refluxed under nitrogen for 3 hours. Excess of anhydride was decomposed by cautious addition of water (60 c.c.), concentrated hydrochloric acid (24 c.c.) was added, and refluxing continued until the evolution of carbon dioxide had ceased (3 hours). The solvents were removed under reduced pressure and the dark residue was heated on the steam-bath for 40 minutes with aqueous potassium hydroxide (5%). The residual oil was taken up in ether-ethyl acetate (1 : 1), and the solvent evaporated under reduced pressure. The residue was repeatedly extracted with boiling light petroleum (b. p. 40—60°), and the crystalline compound obtained by concentration of the extracts purified by passage in benzene-light petroleum (b. p. 60—80°) (2 : 1) through alumina (20 g.). Crystallisation from benzene-light petroleum (b. p. 60—80°) (1 : 1) gave 3 : 4-dihydro-3'-keto-6-methoxycyclopenteno(1' : 2'-1 : 2)naphthalene as pale yellow needles (1.1 g.), m. p. 96—97° (Found : C, 78.8; H, 6.2.  $C_{14}H_{14}O_2$  requires C, 78.5; H, 6.5%). It had bands in the ultra-violet at 329 ( $\epsilon = 23,960$  and 238  $m\mu$   $\epsilon = 12,270$ ), in accord with the assigned structure. The 2 : 4-dinitrophenylhydrazone separated from ethyl acetate as dark purple-red needles, m. p. 275°. Unchanged methoxytetralone (14 g.) was recovered, and the total amount of product obtained was 2.5 g. or 57% based on the methoxytetralone consumed. Oxidation with hot aqueous permanganate gave as the only recognisable product succinic acid, m. p. 184°.

3 : 4-Dihydro-3'-keto-6-methoxy-4'-N-methylanilinomethylenecyclopenteno(1' : 2'-1 : 2)naphthalene.—Ethyl formate (7.5 c.c.) in benzene (7.5 c.c.) was added under nitrogen to pure dry sodium methoxide (from the metal, 1.02 g.) and, after 15 minutes, the above ketone (1.5 g.) in benzene (10 c.c.) was added. The deep yellow mixture was shaken occasionally during 1 hour and then left for 18 hours and worked up as for the formyl compound above, to give a yellow solid (1.4 g.) producing an intense purple colour with ferric chloride. A solution of this in benzene with methylaniline (1.5 g.) was refluxed for 1 hour under nitrogen in the presence of anhydrous sodium sulphate. Worked up as above, the methylanilinomethylene compound (1.0 g.) crystallised from ethyl acetate as orange-yellow needles, m. p. 139—140° (Found : N, 4.2.  $C_{22}H_{21}O_2N$  requires N, 4.2%). The compound (0.3 g.) in *tert.*-butanol (15 c.c.) was added to a solution of potassium

(0.38 g.) in *tert.*-butanol (10 c.c.) under nitrogen and the mixture refluxed for 5 minutes (with development of a dark brown colour). Methyl iodide (3 g.) was added, the colour being rapidly discharged. Water (20 c.c.) was added, the product taken up in ethyl acetate, and the solvent removed under reduced pressure. A dark red oil was obtained which failed to crystallise and which was hydrolysed by 2 hours' refluxing under nitrogen with sulphuric acid (4 c.c.), water (20 c.c.), and alcohol (15 c.c.), followed by 1 hour's refluxing with sodium hydroxide solution (5%). The dark red neutral oil obtained gave a dark purple 2 : 4-dinitrophenylhydrazone, m. p. 273°, identical with that obtained from the initial ketone; no other pure compound could be isolated.

1 : 2 : 3 : 4-Tetrahydro-1-keto-6-methoxynaphthalene.—Slight modifications of this preparation (Stork, *J. Amer. Chem. Soc.*, 1947, **69**, 576) have been made which somewhat increase the ease of working-up. The oxidation was carried out on tetrahydromethoxynaphthalene (54 g.) as described; the acetic acid solution was then evaporated under reduced pressure to a dark green tar. This became granulated on trituration with ether (total, 1 l.) and was finely ground in a mortar with ethyl acetate (total, 1 l.). The combined extracts were distilled, the product, b. p. 165—170°/18 mm., being collected. It was passed in benzene through a short column of alumina. On concentration of the solvent the colourless tetrahydroketomethoxynaphthalene (36 g.) crystallised; it had m. p. 78°.

1 : 2 : 3 : 4 : 5 : 8-Hexahydro-1-hydroxy-6-methoxynaphthalene.—Sodium (20 g.) in small pieces was added with stirring to a solution of the methoxytetralone (17.6 g.) in ammonia (500 c.c.) and ethanol (200 c.c.). On completion of the reaction, water (500 c.c.) was added, and the mixture extracted with ether. The extract was washed with water, dried ( $K_2CO_3$ ), and evaporated at room temperature under nitrogen. The oil obtained crystallised overnight in the refrigerator after addition of a little light petroleum (b. p. 40—60°). The 1 : 2 : 3 : 4 : 5 : 8-hexahydro-1-hydroxy-6-methoxynaphthalene (10 g.) was obtained as prisms, m. p. 76—77° after recrystallisation in the refrigerator from light petroleum (b. p. 40—60°) containing a little ether.

1 : 2 : 3 : 4 : 5 : 8-Hexahydro-1-keto-6-methoxynaphthalene.—A solution of the compound above (8 g.) in toluene (35 c.c.) and acetone (20 c.c.) containing aluminium isopropoxide (1.5 g.) was refluxed under nitrogen for 4.5 hours. The solution was then decomposed with water (15 c.c.), the aqueous solution extracted with ether (200 c.c.), and the solvent evaporated under reduced pressure in nitrogen. The resulting oil could be distilled almost quantitatively at 130°/1 mm., but could also be crystallised directly in the refrigerator under nitrogen after addition of light petroleum (b. p. 40—60°; 20 c.c.). 1 : 2 : 3 : 4 : 5 : 8-Hexahydro-1-keto-6-methoxynaphthalene was obtained as long colourless needles (6 g.), m. p. 46—48° (Found : C, 73.6; H, 8.2.  $C_{11}H_{14}O_2$  requires C, 74.15; H, 7.9%). The ultra-violet absorption maximum was at 238  $m\mu$  ( $\epsilon = 9320$ ) in accord with the assigned structure. 1 : 2 : 3 : 4 : 5 : 6 : 7 : 8-Octahydro-1 : 6-diketonnaphthalene dioxime was obtained by the action of aqueous hydroxylamine hydrochloride at 70°, followed by the addition of sodium acetate, and, crystallised from aqueous ethanol, had m. p. 185° (decomp.) (Found : C, 62.3; H, 7.6; N, 14.3.  $C_{10}H_{14}O_4N_2$  requires C, 61.9; H, 7.2; N, 14.4%). Use of a higher proportion (*ca.* 5 g.) of aluminium isopropoxide gave a product, b. p. 130°/1.5 mm., which did not crystallise but gave the same dioxime; it probably contained some of the fully conjugated compound.

1 : 2 : 3 : 4 : 8 : 9-Hexahydro-1-keto-6-methoxy-9-methylnaphthalene.—The above hexahydroketomethoxynaphthalene (6.0 g.) in ether (30 c.c.) was added to a solution of potassium amide (from the metal, 1.5 g.) in liquid ammonia (100 c.c.) with development of a deep yellow-brown colour. After 4 minutes, methyl iodide (15 g.) was added cautiously, the colour being discharged in a rapid reaction. Water (150 c.c.) was then added; the oil obtained by ether-extraction was then distilled (5.7 g.) (b. p. 115°/0.4 mm.). The reactions below show that it was chiefly 1 : 2 : 3 : 4 : 8 : 9-hexahydro-1-keto-6-methoxy-9-methylnaphthalene (Found : C, 75.1; H, 8.6.  $C_{12}H_{16}O_2$  requires C, 75.0; H, 8.3%). The assigned structure was supported by the absorption max. at 274  $m\mu$  ( $\epsilon = 5200$ ), inflexion at 241  $m\mu$  ( $\epsilon = 4450$ ).

1 : 2 : 3 : 4 : 6 : 7 : 8 : 9-Octahydro-1 : 6-diketo-9-methylnaphthalene.—The above enol ether (2.5 g.) and 0.5N-hydrochloric acid (10 c.c.) were heated on the steam-bath with shaking for 10 minutes under nitrogen. The product was extracted with ether (4 × 50 c.c.), then dried ( $Na_2SO_4$ ), and the solvent removed under reduced pressure. The resulting oil could be distilled (b. p. 106—108°/10<sup>-3</sup> mm.) (Found : C, 73.6; H, 8.2. Calc. for  $C_{11}H_{14}O_2$  : C, 74.1; H, 7.9%) and had  $\lambda_{max}$ . 243—244 ( $\epsilon = 10,390$ ) and 342  $m\mu$  ( $\epsilon = 490$ ) and  $\lambda_{min}$ . 327  $m\mu$  ( $\epsilon = 460$ ). Wendler *et al.* (*loc. cit.*) give  $\lambda_{max}$ . 244  $m\mu$  ( $\epsilon = 12,335$ ) for pure 1 : 2 : 3 : 4 : 6 : 7 : 8 : 9-octahydro-1 : 6-diketo-9-methylnaphthalene. The distilled product crystallised, but it was not necessary to distil it. The crude product was extracted with boiling light petroleum (b. p. 40—60°) until

only a small amount of a yellowish gum (A) was left, and on concentration of the extract and addition of pure ether (6 c.c.) the diketone crystallised as massive prisms on storage in the refrigerator. The mother-liquor was concentrated and added to (A) and the whole passed in ether (3 c.c.) through neutral alumina (40 g.); ether-light petroleum (b. p. 40—60°) (1 : 1) was used as eluent. The first fractions contained more of the crystallisable diketone, and the later fractions a small amount of 1 : 2 : 3 : 4-tetrahydro-6-hydroxy-1-keto-5-methylnaphthalene, crystallising as cream-coloured prisms (from aqueous acetone), m. p. 198—200° undepressed by an authentic specimen. The combined diketone fractions were recrystallised from ether-light petroleum (b. p. 40—60°) (2 : 1), to give the massive prisms of 1 : 2 : 3 : 4 : 6 : 7 : 8 : 9-octahydro-1 : 6-diketo-9-methylnaphthalene (0.95 g.), m. p. 49°, undepressed by an authentic specimen. The infra-red spectrum of the molten substance was also identical with that of the authentic material, having bands at the following wave-lengths ( $\mu$ ) (s = strong; m = medium; w = weak; s-b = side-band): 3.43s 5.84s, 5.99s, 6.17m, 6.84s-b, 6.90s, 7.05s, 7.27s, 7.42s, 7.55s, 7.88s, 8.08s, 8.47s, 8.66s, 9.30m, 9.75s-b, 9.85s, 10.1w, 10.42m, 10.64s, 11.38s, 11.67s, 12.05s, and 12.93m. The band at 5.84  $\mu$  doubtless is due to the saturated C-C-CO group, and that at 5.99 $\mu$  to the  $\alpha\beta$ -unsaturated carbonyl group. The bis-2 : 4-dinitrophenylhydrazone separated from tetrahydrofuran as a brick-red microcrystalline powder, m. p. 247—248° undepressed by an authentic specimen (Found: C, 51.8; H, 4.3; N, 20.8. Calc. for  $C_{22}H_{22}O_8N_8$ : C, 51.3; H, 4.1; N, 20.8%). The dioxime was prepared by refluxing the diketone with hydroxylamine acetate in aqueous methanol for 1.5 hours, and crystallised from ethyl acetate-light petroleum (b. p. 40—60°) as colourless needles, m. p. 204°.

1 : 2 : 3 : 4 : 6 : 7 : 8 : 9-Octahydro-1-hydroxy-6-keto-9-methylnaphthalene.—The above hexahydroketo-methoxymethylnaphthalene (3 g.) in ether (10 c.c.) was reduced in the usual manner with lithium aluminium hydride (1 g.) in ether (20 c.c.). The crude reduction product was heated on the steam-bath for 10 minutes with 0.5N-hydrochloric acid (5 c.c.), then extracted with ether (3  $\times$  20 c.c.), and evaporated. The product was taken up in ether (5 c.c.), water (5 drops) added, and the solution left in the refrigerator overnight. The 1 : 2 : 3 : 4 : 6 : 7 : 8 : 9-octahydro-1-hydroxy-6-keto-9-methylnaphthalene monohydrate (800 mg.) crystallised in elongated colourless prisms, m. p. 59—60° (Found: C, 66.8; H, 9.0.  $C_{11}H_{18}O_3$  requires C, 66.7; H, 9.1%). The structure was supported by the absorption max. at 240  $m\mu$  ( $\epsilon = 14,700$ ). When dried in a vacuum the crystals liquefied and the anhydrous substance could not be induced to crystallise. The combined mother-liquors were passed through a column of alumina (30 g.) in ether-light petroleum (b. p. 40—60°) (1 : 2), to give an oil (A) (350 mg.), and further elution gave the above keto-alcohol (60 mg.). The oil (A) was treated with Brady's reagent, and the product crystallised from tetrahydrofuran-ethanol, to give 2 : 3 : 4 : 6 : 7 : 8-hexahydro-2-keto-1-methylnaphthalene 2 : 4-dinitrophenylhydrazone as dark purple flat prisms, m. p. 192° (Found: C, 59.55; H, 5.1.  $C_{17}H_{18}O_4N_4$  requires C, 59.6; H, 5.3%). The constitution was supported by the absorption max. at 404  $m\mu$ , ( $\epsilon = 62,400$ ) (cf. Braude and Jones, *J.*, 1945, 502).

5 : 6 : 7 : 8-Tetrahydro-8-methylindane-1 : 5-dione (XX).— $\beta$ -m-Methoxyphenylpropionic acid (10 g.) was added to a solution of phosphoric anhydride (25 g.) in phosphoric acid (*d* 1.5; 25 c.c.) at 130°, and the mixture stirred at that temperature for 15 minutes and then cooled. Water (100 c.c.) was added, and the solid taken up in ethyl acetate and washed with 0.5N-sodium hydroxide, dried, and evaporated under reduced pressure. 5-Methoxyindan-1-one crystallised from ethyl acetate as cream-coloured needles (5.8 g.), m. p. 108°.

This product (3 g.) was reduced with sodium (4.6 g.) after addition in ethanol (70 c.c.) to ammonia (150 c.c.). The 4 : 7-dihydro-1-hydroxy-5-methoxyindane could be distilled under nitrogen (b. p. 120°/1 mm.), but was best purified by chromatography in ether-light petroleum (b. p. 40—60°) (1 : 1) on alkaline alumina (30 g.). After neglect of a small oily first fraction, the bulk of the product crystallised in the refrigerator from light petroleum (b. p. 40—60°) as colourless elongated prisms (1.7 g.), m. p. 50° (Found: C, 72.2; H, 8.6.  $C_{10}H_{14}O_2$  requires C, 72.3; H, 8.4%). Treatment with Brady's reagent gave the deep red 2 : 4 : 5 : 6-tetrahydro-6-ketoindene 2 : 4-dinitrophenylhydrazone, m. p. 178° (Found: C, 57.4; H, 4.45; N, 17.6.  $C_{15}H_{14}O_4N_4$  requires C, 57.3; H, 4.45; N, 17.8%). The constitution of this was supported by its absorption max. at 397  $m\mu$  ( $\epsilon = 32,900$ ) and min. at 332  $m\mu$  ( $\epsilon = 7180$ ) in chloroform.

The dihydrohydroxymethoxyindane (3.7 g.) in toluene (35 c.c.) was oxidised under nitrogen with aluminium isopropoxide (0.9 g.) and acetone (20 c.c.) in the same manner as the naphthalene derivative above. The product, obtained after addition of water, ether-extraction, and evaporation of the solvent under reduced pressure in nitrogen, could be distilled (b. p. 106°/0.01 mm.), but was best crystallised in the refrigerator under nitrogen after addition of a little light petroleum (b. p. 40—60°). 4 : 7-Dihydro-5-methoxyindan-1-one (2.7 g.) formed colour-

less needles, m. p. 82—83° (Found: C, 73.5; H, 7.4.  $C_{10}H_{12}O_2$  requires C, 73.2; H, 7.3%). It was very unstable in air. Hot aqueous hydroxylamine hydrochloride, followed by sodium acetate, gave 5 : 6 : 7 : 8-tetrahydroindane-1 : 5-dione dioxime, m. p. 190° (decomp.) (Found: C, 60.3; H, 6.6.  $C_9H_{12}O_2N_2$  requires C, 60.0; H, 6.7%).

The dihydroketomethoxyhydrindene (2.7 g.) in ether (10 c.c.) was added to potassium amide (from the metal, 0.75 g.) in ammonia (100 c.c.), followed by methyl iodide to discharge the deep yellow colour. The product (2.9 g.) was worked up as for the naphthalene compound above. The crude substance (1.2 g.) was hydrolysed by 0.5N-hydrochloric acid (1 c.c.) on the steam-bath for 5 minutes. The product was taken up in ether, washed with sodium hydrogen carbonate solution, and dried, and the solvent was evaporated. Extraction with boiling light petroleum (b. p. 40—60°) ( $3 \times 10$  c.c.) and evaporation, followed by chromatography in ether-light petroleum (b. p. 40—60°) (2 : 1) on neutral alumina (20 g.), gave a preliminary oily fraction, followed by a crystalline solid and finally a yellow gum (A). 5 : 6 : 7 : 8-Tetrahydro-8-methylindane-1 : 5-dione recrystallised from light petroleum (b. p. 40—60°) as colourless prisms (70 mg.), m. p. 71—72° (Found: C, 73.5; H, 7.2. Calc. for  $C_{10}H_{12}O_2$ : C, 73.2; H, 7.3%). The ultra-violet absorption showed max. at 236 ( $\epsilon = 10,200$ ) and 290  $m\mu$  ( $\epsilon = 375$ ) and a min. at 278  $m\mu$  ( $\epsilon = 330$ ) in ethanol; Wieland and Miescher (*loc. cit.*) gave m. p. 71—72° and  $\lambda_{max}$ , 235  $m\mu$  ( $\epsilon = 12,000$ ). The residue from the petroleum extractions was added to (A), and the whole dissolved in ether. Fractional extraction with sodium hydroxide solution removed two compounds (as bright yellow solutions) with m. p. 180° and 240° (decomp.) respectively. These are evidently phenolic ketones, and were not further investigated.

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