174. A Convenient Synthesis of Cholanthrene.

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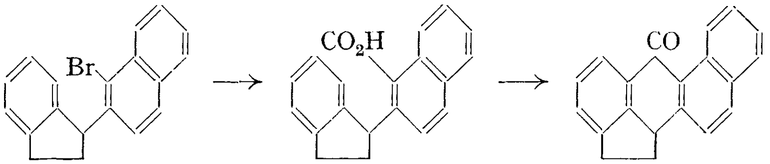
The two synthetic methods by which cholanthrene has been obtained (this vol., pp. 667, 767) provide complete proof of the structure of the product, but they are very tedious and not well adapted to the preparation of a supply of material for biological investigation. The method now described is more suitable for this purpose.

Evidence was obtained by Salkind (*Ber.*, 1934, **67**, 1031) that the β-bromine atom of 1 : 2-dibromonaphthalene is the more reactive towards magnesium. It thus seemed possible that the monomagnesio-compound would react with α-hydrindone to give, after dehydration and reduction, the bromo-compound (I). In order to enhance the reactivity of the β-halogen atom we employed 1-bromo-2-iodonaphthalene, and we also used Grignard's device (*Compt. rend.*, 1934, **198**, 625) of adding a molecule of ethylmagnesium bromide to facilitate the formation of the Grignard compound. Unfortunately, the product of interaction of the resulting magnesio-derivative with α-hydrindone was a bromine-free compound, probably a cyclic oxide, which gave analytical figures in agreement with $C_{19}H_{14}O$.

As an alternative route to the desired bromo-compound (I) we studied the bromination of 1-β-naphthylhydrindene. It was anticipated that bromination of the naphthalene nucleus would take place at the required position, and there was also a likelihood of substitution in the hydrindene system. This proved to be the case. A resinous mixture of bromo-compounds was obtained, from which compounds brominated in the five-membered ring were removed by the procedure described in the experimental section. The product was then combined with magnesium, and the resulting Grignard solution treated with carbon dioxide. This gave a resinous mixture of acids, 40% of which was isolated as a crystalline compound which proved to be β-1-*hydrindyl-α-naphthoic acid* (II). Dehydration with ice-cold sulphuric acid led to an anthrone-like product (III), which was reduced in the crude state with zinc dust and alkali, cholanthrene being formed in good yield.



(I.) (II.) (III.)

Experimental.

1-β-*Naphthylhydrindene.*—This was obtained by hydrogenation (palladium-black) of the indene resulting from interaction of α-hydrindone and β-naphthylmagnesium bromide. The yield of the indene was 57%. The same two compounds were obtained by v.Braun, Manz, and Reinsch (*Annalen*, 1929, **468**, 298), who stated that they used α-naphthyl bromide, but it is clear from the text of their paper that they really used the β-compound. Our indene had m. p. 87° and the hydrindene 52—53° (Found: C, 93·1; H, 6·6. Calc.: C, 93·4; H, 6·6%). The above authors give 88° and 47°, respectively, for the m. p.'s of these two compounds.

β-1-*Hydrindyl-α-naphthoic Acid* (II).—Bromine (3·7 c.c.), diluted with carbon disulphide (30 c.c.), was added to a solution of the naphthylhydrindene (18·7 g.) in carbon disulphide (30 c.c.), a little aluminium chloride having been introduced as a halogen carrier. The mixture was kept in the dark at room temperature for 7 hours. After removal of the solvent, the resulting yellow oil was boiled with anhydrous pyridine (50 c.c.) for an hour. The dark-coloured solution was treated with excess of dilute acid and extracted with benzene, and the extract twice agitated with 80% sulphuric acid. Distillation of the product gave an orange viscous liquid (17 g.), b. p. 180—195°/0·2 mm. This product was mixed with magnesium turnings (2·4 g.) and anhydrous ether (50 c.c.), ethyl bromide (3·8 c.c.) in ether (20 c.c.) being then added to promote interaction with magnesium. After an hour's boiling, the whole was cooled in ice, and treated for 6 hours with a slow stream of dry carbon dioxide. After decomposition with dilute hydrochloric acid, the acidic products were isolated by extraction with dilute alkali. The reprecipitated resinous acids (10 g.) were shaken with hydrogen and palladium-black to reduce a small amount of unsaturated material which was present. The product slowly crystallised, and after trituration with acetic acid yielded white crystals (4·2 g.), m. p. 151—154°. β-1-*Hydrindyl-α-naphthoic acid* (II) crystallised from benzene in colourless lustrous prisms, which dried to a powder, m. p. 155—156° (Found: C, 83·2; H, 5·6. $C_{20}H_{16}O_2$ requires C, 83·3; H, 5·6%).

Cholanthrene.—The finely powdered acid (II) (1 g.) was dissolved in ice-cold concentrated sulphuric acid (5 c.c.), and the solution kept at 0° for 2 hours. The yellow precipitate obtained by pouring it on ice was insoluble in sodium carbonate solution, and with boiling sodium hydroxide gave the typical orange-yellow colour with a green fluorescence characteristic of an anthranol. The compound was undoubtedly the anthrone (III) or its enolic tautomeride, but isolation in the pure state was not attempted. Reduction was effected by boiling 3*N*-sodium hydroxide (100 c.c.) and zinc dust (3 g.) in 4 hours. The suspended solid was then collected, and digested with hydrochloric acid to remove the excess of zinc. The residue was collected, and sublimed at 210—215°/0·2 mm. The pale yellow sublimate (0·8 g.) was recrystallised from benzene–alcohol, yielding pure cholanthrene, m. p. 168·5—170° (picrate, m. p. 167—168°).

Cholanthrene (0·3 g.) was oxidised with sodium dichromate in boiling acetic acid, and the acidic product extracted and recrystallised from xylene and then acetic acid. 1 : 2-*Benzanthraquinonyl*-5-*acetic acid* formed yellow leaflets which decomposed at 245—265° (Found: C, 74·9; H, 3·9. $C_{20}H_{12}O_4$ requires C, 75·9; H, 3·8%). Decarboxylation of this acid gave 5-methyl-1 : 2-benzanthraquinone (compare this vol., p. 670).

Condensation of 1-*Bromo*-2-*naphthylmagnesium Iodide with α-Hydrindone.*—1-Bromo-2-iodonaphthalene (Meldola, J., 1885, **47**, 523) (2·7 g.) and magnesium turnings (0·2 g.) were added to a Grignard solution prepared from ethyl bromide (0·6 c.c.), magnesium (0·2 g.), and ether (20 c.c.). After boiling for 3 hours, the cooled solution was treated with α-hydrindone (2·2 g.) in ether (10 c.c.). The product was isolated in the usual way, and distilled. The fraction, b. p. 210°/0·1 mm., formed an orange gum which crystallised from ligroin. Recrystallisation from alcohol gave slender yellow needles, m. p. 142—143° (Found: C, 88·3; H, 5·8. $C_{19}H_{14}O$ requires C, 88·4; H, 5·4%).

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