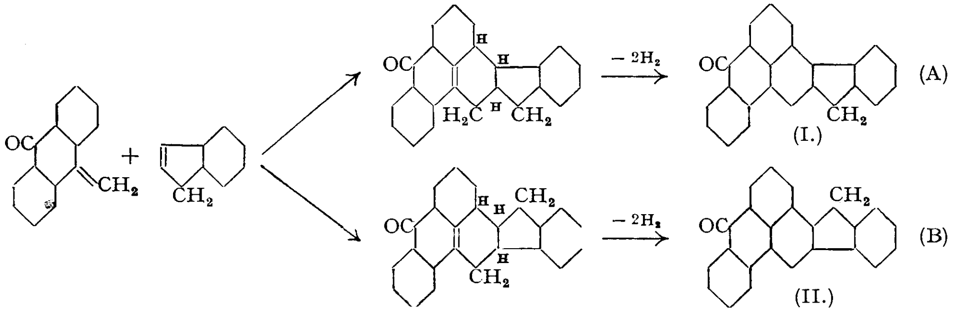
130. *Indeno-2″ : 3″ : 2′ : 1′-benzanthrone.*

By G. Swain and A. R. Todd.

Indeno-2″ : 3″ : 2′ : 1′-benzanthrone and a *dihydroindeno-2″ : 3″ : 2′ : 1′-benzanthrone* have been prepared by the reaction of indene with methyleneanthrone in nitrobenzene solution. Oxidation of both products gave *1″-ketoindeno-2″ : 3″ : 2′ : 1′-benzanthrone,* the structure of which has been determined by an alternative synthesis from ethyl cinnamate and methyleneanthrone.

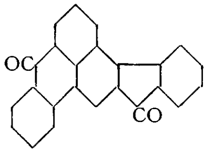
The marked tumour-inhibitory properties of 1 : 2 : 5 : 6-dibenzfluorene (Haddow and Robinson, *Proc. Roy. Soc.*, 1939, *B*, **127**, 277) lends interest to the preparation and examination in this sense of other readily accessible complex fluorene derivatives. Concurrently with the work on this hydrocarbon (Swain and Todd, J., 1941, 674) we synthesised for this purpose *indeno-2″ : 3″ : 2′ : 1′-benzanthrone* (I).

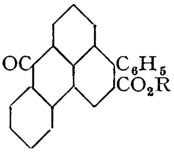
The synthesis of benzanthrone derivatives by the Diels–Alder reaction with methyleneanthrone, or methylene-substituted methyleneanthrones, as the diene component has been demonstrated by Clar (*Ber.*, 1936, **69**, 1686; D.R.-P. 619,246; cf. also I. G. Farbenindustrie A.-G., D.R.-P., 591,496, 597,325), using maleic anhydride, cinnamic acid, benzoquinone and similar compounds as active olefin components. Alder and Rickert (*Ber.*, 1938, **71**, 379) found that indene undergoes 1 : 4 addition to 2 : 3-dimethylbutadiene and *cyclo*pentadiene. It thus appeared that indene might condense with methyleneanthrone to an indenobenzanthrone according to scheme (A) or (B). If the reaction proceeded according to (B), the product (II) on oxidation would yield 1″-ketoindeno-3″ : 2″ : 2′ : 1′-benzanthrone, a probable by-product in the preparation of dibenzpyrenequinone from 1 : 5-dibenzoylnaphthalene (I. G. Farbenindustrie A.-G., D.R.-P. 426,710, 1923; *Chem. Zentr.*, 1936, II, 653). On general grounds, however, scheme (A) seemed the more likely mode of reaction and, in fact, this has been confirmed experimentally.



Methyleneanthrone and indene, heated together in nitrobenzene solution, gave a mixture of indeno-2″ : 3″ : 2′ : 1′-benzanthrone (I) and a *dihydroindeno-2″ : 3″ : 2′ : 1′-benzanthrone* in yields of 15% and 31% respectively. In benzene or xylene solution, only the dihydro-compound was obtained but in lower yield; by heating with nitrobenzene, it was dehydrogenated in part to indeno-2″ : 3″ : 2′ : 1′-benzanthrone. That the product obtained in larger quantity was a dihydro- and not a tetrahydro-indenobenzanthrone was proved by dehydrogenation with palladised charcoal, only one mol. of hydrogen being obtained; the location of the two extra hydrogen atoms in the dihydro-compound remains uncertain.

(III.)





(IV.)

Both indeno-2″ : 3″ : 2′ : 1′-benzanthrone and its dihydro-derivative have been converted into *1″-keto-indeno-2″ : 3″ : 2′ : 1′-benzanthrone* (III) in almost quantitative yield by oxidation with selenious acid, although separation of the ketone from selenium proved rather troublesome. The fact that no vat could be obtained from either the indenobenzanthrone or the ketoindenobenzanthrone was an indication that diene synthesis had occurred in the manner illustrated in (A). The ketoindenobenzanthrone would then possess an odd number of carbon atoms in the chain linking the two carbonyl groups, whereas if it had the structure related to (II) it would possess an even number of carbon atoms and should therefore vat. The constitution, however, was firmly established by independent synthesis from methyleneanthrone and ethyl cinnamate. Heated together in nitrobenzene solution, these compounds yielded two esters, both of which gave on hydrolysis *1′-phenylbenzanthrone-2′-carboxylic acid* (IV; R = H). Although interconversion was not achieved, it would seem probable that they represent dimorphs of *ethyl 1′-phenylbenzanthrone-2′-carboxylate* (IV; R = Et), formed by dehydrogenation of the initial adduct by the nitrobenzene employed as solvent. The structure of the parent acid was proved by decarboxylation to 1′-phenylbenzanthrone, which, as Clar (*loc. cit.*) has shown, results directly from the reaction between cinnamic acid and methyleneanthrone in nitrobenzene. Ring closure of 1′-phenylbenzanthrone-2′-carboxylic acid to 1″-ketoindeno-2″ : 3″ : 2′ : 1′-benzanthrone, identical with the specimen previously prepared, was readily effected by sulphuric acid.

In the above experiments the formation of a dihydroindenobenzanthrone as sole product when the diene synthesis was carried out in xylene or benzene was surprising even if the initially formed tetrahydro-derivative might be expected to be rather unstable; no exactly analogous case has come to our notice. It is, of course, known that nitrobenzene used as a solvent in diene synthesis can effect dehydrogenation of newly formed six-membered rings, giving dihydrobenzene (Weizmann, E. Bergmann, and Berlin, *J. Amer. Chem. Soc.*, 1938, **60**, 1331) or fully aromatic nuclei (Clar, *Ber.*, 1936, **69**, 1686; F. Bergmann, *J. Amer. Chem. Soc.*, 1942, **64**, 176). According to F. Bergmann (*loc. cit.*) this action of nitrobenzene can only occur in cases where the initial adduct is capable of double ortho-enolisation as in the adducts with quinones or maleic anhydride. While this mechanism may apply to adducts formed with such reagents, and while this enolisation tendency may predispose them to dehydrogenation, it is obvious from the work here described and from that of Clar (*loc. cit.*) that such conditions are not necessary and that the determining factor in other cases may be simply the tendency towards formation of a stable ring system.

In animal experiments carried out by Dr. A. Haddow at the Royal Cancer Hospital, details of which will be published elsewhere, both indeno-2″ : 3″: 2′ : 1′-benzanthrone and 1″-ketoindeno-2″ : 3″ : 2′ : 1′-benzanthrone showed tumour-inhibitory properties of a moderate order.

EXPERIMENTAL.

Condensation of Methyleneanthrone and Indene.—(a) *In nitrobenzene.* Methyleneanthrone (30 g.), indene (20 g.), and nitrobenzene (75 c.c.) were refluxed for 1½ hours. The solution, on cooling, deposited an orange-yellow crystalline solid (27 g.), which was separated and washed with benzene. The product (27 g.) was refluxed with benzene (750 c.c.) for 1 hour and filtered hot from a yellow solid (A). The filtrate deposited orange needles (10·7 g.), m. p. 207—212°, contaminated with a little of (A). Recrystallisation from benzene yielded *indeno-2″ : 3″ : 2′ : 1′-benzanthrone* (4·4 g.) in orange needles, m. p. 218—219° (Found : C, 90·8; H, 4·65. $C_{24}H_{14}O$ requires C, 90·6; H, 4·4%).

The solid (A) was again extracted with boiling benzene (300 c.c.) for 1 hour, and the undissolved solid recrystallised from xylene. *Dihydroindeno-2″ : 3″ : 2′ : 1′-benzanthrone* separated in yellow prismatic plates (11·0 g.), m. p. 252—253° (Found : C, 90·5; H, 5·2. $C_{24}H_{16}O$ requires C, 90·0; H, 5·0%). Further quantities of pure indeno-2″ : 3″ : 2′ : 1′-benzanthrone (2·6 g.) and its dihydro-derivative (4·0 g.) were obtained from the mother-liquors, and addition of benzene to the nitrobenzene mother-liquors caused slow separation of a little more crude indeno-2″ : 3″ : 2′ : 1′-benzanthrone (3 g. approx.).

(b) *In xylene.* Methyleneanthrone (5 g.), indene (3·5 g.), and xylene (25 c.c.) were refluxed for 2½ hours. The solution rapidly became orange-coloured and a yellow crystalline solid commenced to separate. After cooling, the solid (2·3 g.) was collected, washed with xylene, and recrystallised from the same solvent, dihydroindeno-2″ : 3″ : 2′ : 1′-benzanthrone separating in pale yellow, prismatic plates, m. p. 252—253°, undepressed by the specimen obtained in (a).

(c) *In benzene.* Methyleneanthrone (5 g.), indene (3·5 g.), and benzene (100 c.c.) were refluxed for 18 hours. On cooling, dihydroindeno-2″ : 3″ : 2′ : 1′-benzanthrone (2·0 g.) separated, m. p. 252—253° after crystallisation from xylene, undepressed by specimens from (a) or (b).

Dehydrogenation of Dihydroindeno-2″ : 3″ : 2′ : 1′-benzanthrone.—(a) *By nitrobenzene.* The substance (1·0 g.), refluxed for 4 hours with nitrobenzene (10 c.c.), yielded an orange crystalline solid (0·7 g.) on cooling. This was extracted with boiling benzene (*ca.* 25 c.c.), and the sparingly soluble unchanged dihydro-compound removed; the filtrate, after cooling, was decanted from the first deposited dihydro-compound and, on standing, gave orange needles (0·15 g.).

Recrystallisation from benzene yielded indeno-2″ : 3″ : 2′ : 1′-benzanthrone (0·1 g.), m. p. 217—219°, undepressed by that previously obtained.

(b) *By palladised charcoal.* The compound (0·41 g.), m. p. 252—253°, was heated at 270° in an inert atmosphere with palladium–charcoal (0·2 g.), the temperature being raised to 310° as the gas evolution ceased. The volume of hydrogen collected was 24·5 c.c. at N.T.P. (calc. for dihydro-compound, 28·7 c.c.). The product was again indeno-2″ : 3″ : 2′ : 1′-benzanthrone.

1″-*Ketoindeno*-2″ : 3″ : 2′ : 1′-*benzanthrone*.—Dihydroindeno-2″ : 3″ : 2′ : 1′-benzanthrone (4 g.), selenium dioxide (8 g.), and water (8 cc.) were heated together in a sealed tube for 4½ hours at 230°. The resultant red-brown crystalline solid (5·2 g.) was washed with water, dried in the steam oven, and extracted (Soxhlet) with xylene. The solid was still contaminated with selenium, most of which was removed by sublimation at 150—180°/*ca.* 0·0001 mm. The ketone sublimed readily at about 280° and was recrystallised from nitrobenzene. 1″-*Ketoindeno*-2″ : 3″ : 2′: 1′-*benzanthrone* (3·0 g.) separated in red needles, m. p. 336—338° (Found : C, 86·4; H, 4·0. $C_{24}H_{12}O_2$ requires C, 86·7; H, 3·6%).

1″-Ketoindeno-2″ : 3″ : 2′ : 1′-benzanthrone was also obtained from indeno-2″ : 3″ : 2′ : 1′-benzanthrone by an exactly similar oxidation; it is, therefore, unnecessary to separate the mixture obtained from the reaction between indene and methyleneanthrone if the ketone is desired as the final product.

Condensation of Ethyl Cinnamate and Methyleneanthrone.—Methyleneanthrone (5 g.), ethyl cinnamate (5·0 g.), and nitrobenzene (10 c.c.) were refluxed for 1½ hours, and alcohol (50 c.c.) added to the cooled, dark brown solution. After 12 hours the crystalline solid (3·0 g.) was removed, and alcohol (50 c.c.) added to the filtrate; more solid slowly separated (1·5 g.). The combined solids were fractionally crystallised from ethyl acetate. *Ethyl* 1′-*phenylbenzanthrone*-2′-*carboxylate* separated in golden yellow prismatic plates (2·0 g.), m. p. 155—156° (Found : C, 82·6; H, 4·8. $C_{26}H_{18}O_3$ requires C, 82·5; H, 4·8%), accompanied by a smaller amount of a second *ester* crystallising in clusters of very small, yellow needles, m. p. 190—210° (Found : C, 81·9; H, 4·5. $C_{26}H_{18}O_3$ requires C, 82·5; H, 4·8%).

1′-*Phenylbenzanthrone*-2′-*carboxylic Acid.*—A solution of ethyl 1′-phenylbenzanthrone-2′-carboxylate (1·0 g.) in alcohol (50 c.c.) was refluxed with alcoholic potash (4 g. of potassium hydroxide, 4 c.c. of water, 20 c.c. of alcohol) for 1½ hours; water (100 c.c.) was then added to give a clear orange solution. The yellow flocculent precipitate (0·95 g.) obtained by acidification with hydrochloric acid was collected, washed with water, and crystallised from acetic acid, 1′-*phenylbenzanthrone*-2′-*carboxylic acid* separating as a felted mass of yellow needles, m. p. 284—286° (Found : C, 82·3; H, 4·0. $C_{24}H_{14}O_3$ requires C, 82·3; H, 4·0%). Hydrolysis of the ester, m. p. 190—210°, by the above method gave the same 1′-phenylbenzanthrone-2′-carboxylic acid.

1′-*Phenylbenzanthrone.*—The acid (0·5 g.), m. p. 284—286°, was refluxed for 1 hour with quinoline (5 c.c.) and copper bronze (50 mg.), methyl alcohol added, and the yellow needles (0·35 g., m. p. 182—184°) collected, washed with a little methyl alcohol, and recrystallised from ethyl acetate. 1′-Phenylbenzanthrone separated in yellow needles, m. p. 182—183° (Found: C, 90·2; H, 4·5. Calc. for $C_{23}H_{14}O$: C, 90·2; H, 4·6%), undepressed by a specimen, m. p. 185—186°, prepared from cinnamic acid and methyleneanthrone according to the method of Clar (*loc. cit.*).

Ring-closure of 1′-*Phenylbenzanthrone*-2′-*carboxylic Acid.*—The acid (0·4 g.) was heated on the steam-bath for 30 mins. with sulphuric acid (4·5 c.c., *d* 1·84, diluted with 0·5 c.c. of water). The colour changed from cherry-red to greenish-violet. Ice was added, and the red precipitate collected, washed with water, and dried (0·3 g.). Crystallisation from nitrobenzene yielded red needles of 1″-ketoindeno-2″ : 3″ : 2′ : 1′-benzanthrone, m. p. 336—338°, undepressed by a specimen prepared by oxidation of indeno-2″ : 3″ : 2′ : 1′-benzanthrone.

The authors thank I.C.I. (Dyestuffs) Ltd. for their support of this investigation.

UNIVERSITY OF MANCHESTER.

[*Received, July 9th,* 1942.]