

**379. *Synthesis of 10-Methyl-3:4-benzopyrene and  
8:10-Dimethyl-3:4-benzopyrene.***

By A. D. CAMPBELL.

10-Methyl- and 8:10-dimethyl-3:4-benzopyrene have been synthesised from 1:2:3:11*b*-tetrahydro-3-oxomesobenzanthrene by an alternative route to that of Adelfang and Daub.<sup>1</sup> The properties of the two hydrocarbons are in agreement with those previously reported.

THE method used by Cameron, Cook, and Schoental<sup>2</sup> for the synthesis of 8-methyl-3:4-benzopyrene has been extended to the preparation of 8:10-dimethyl-3:4-benzopyrene (III; R = Me) to study the effect of methyl substitution on the carcinogenic activity of 3:4-benzopyrene. The biological properties of 8:10-dimethyl-3:4-benzopyrene are of interest in connection with the view that carcinogenic action of polycyclic hydrocarbons is associated with metabolic oxidation at specific molecular centres. During the course of this investigation Adelfang and Daub<sup>1</sup> reported the synthesis of this hydrocarbon starting also from 1:2:3:11*b*-tetrahydro-3-oxomesobenzanthrene but using an alternative route.

$\beta$ -Ethoxycarbonyl- $\beta$ -(1:2:3:11*b*-tetrahydromesobenzanthr-3-ylidene)propionic acid<sup>3</sup> (I; R = Et) and the corresponding dibasic acid (I; R = H) undergo cyclisation to ethyl 1:2:8:9:10:11-hexahydro-8-oxo-3:4-benzopyrene-10-carboxylate (II; R = Et) and the corresponding keto-acid (II; R = H) respectively on treatment with anhydrous hydrogen fluoride. The ultraviolet absorption spectra (which resemble that of anthracene) show that cyclisation is accompanied by migration of the double bond. Reduction of the keto-ester (II; R = Et) with lithium aluminium hydride afforded a dihydric alcohol which, without purification, was dehydrated and dehydrogenated in the presence of palladium black to 10-methyl-3:4-benzopyrene (III; R = H). A suggestion<sup>4</sup> that the

<sup>1</sup> Adelfang and Daub, *J. Amer. Chem. Soc.*, 1955, **77**, 3297.

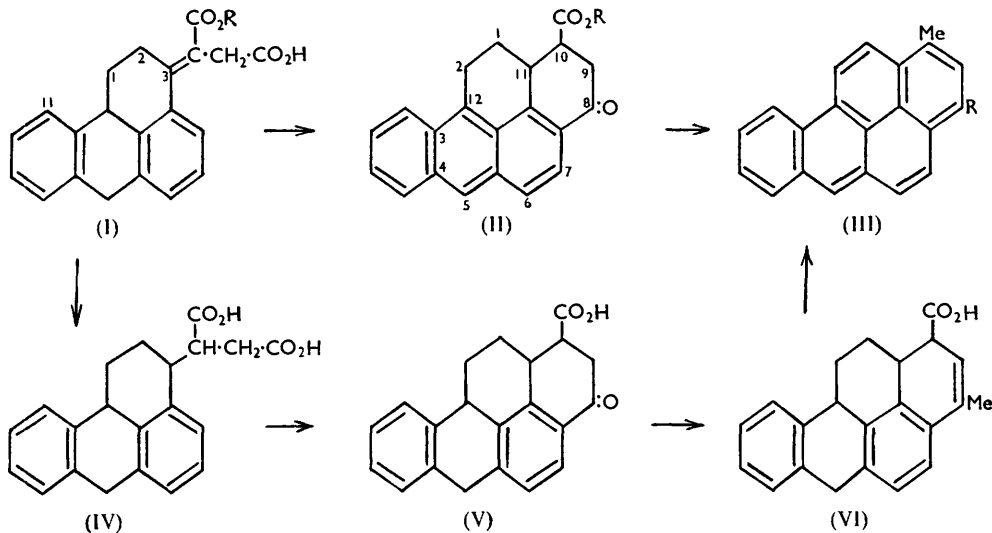
<sup>2</sup> Cameron, Cook, and Schoental, *J.*, 1952, 257.

<sup>3</sup> Cook, Ludwiczak, and Schoental, *J.*, 1950, 1112.

<sup>4</sup> Radt in Elsevier's "Encyclopaedia of Organic Chemistry" Elsevier Publ. Co., Amsterdam, 1951, Vol. XIV, p. 693s.

9(?) -methyl-3 : 4-benzopyrene of Bergmann and Blum-Bergmann<sup>5</sup> was the 10-methyl derivative is supported by a comparison of the properties of the two hydrocarbons. The keto-acid (II; R = H) does not react readily with a methyl Grignard reagent, thus necessitating an alternative route to obtain methyl substitution in the 8-position.

Of the several methods investigated for the hydrogenation of the acid (I; R = H) reduction of the sodium salt with hydrogen in the presence of Raney nickel was the most successful, affording the succinic acid (IV) whose insoluble sodium salt facilitated isolation.



An isomeric form of this acid, giving a water-soluble sodium salt, is obtained in low yield by use of sodium in pentyl alcohol but, because of the difficulties associated with the separation of the dibasic acids produced, the products obtained by this and other methods of reduction were not fully investigated. Cyclisation of the succinic acid (IV) with anhydrous hydrogen fluoride afforded 1 : 2 : 5 : 8 : 9 : 10 : 11 : 12-octahydro-8-oxo-3 : 4-benzopyrene-10-carboxylic acid (V) which with methylmagnesium iodide readily gave the hexahydro-acid (VI). Treatment of the derived methyl ester with lithium aluminium hydride gave an alcohol which was dehydrated and dehydrogenated in the presence of palladium black to 8 : 10-dimethyl-3 : 4-benzopyrene (III; R = Me). The ultraviolet spectra of 8-methyl- and 8 : 10-dimethyl-3 : 4-benzopyrene were almost identical with those previously reported.<sup>1</sup>

#### EXPERIMENTAL

*Ethyl 1 : 2 : 8 : 9 : 10 : 11-Hexahydro-8-oxo-3 : 4-benzopyrene-10-carboxylate* (II; R = Et).— $\beta$ -Ethoxycarbonyl- $\beta$ -(1 : 2 : 3 : 11b-tetrahydromesobenzanthr-3-ylidene)propionic acid (1.0 g.) was treated with anhydrous hydrogen fluoride (30 g.). After 18 hr. the remaining hydrogen fluoride was allowed to evaporate, ice was added, and the product was taken up in benzene, dried, and purified by chromatography on alumina. The main yellow band which was eluted with benzene afforded the *keto-ester* as yellow plates (0.4 g.), m. p. 189–190° after recrystallisation from ethyl acetate (Found: C, 79.9; H, 6.1.  $C_{23}H_{20}O_3$  requires C, 80.2; H, 5.8%). Light absorption: Max. at 244, 267, 286, 330, 347, 365, and 417 m $\mu$  (log  $\epsilon$  4.0, 4.72, 4.64, 3.52, 3.72, 3.70, and 3.66 respectively) in EtOH. Hydrolysis by 6 hours' refluxing with aqueous potassium hydroxide gave the *keto-acid* which crystallised as golden plates, m. p. 295–296°, from ethyl acetate (Found: C, 79.5; H, 5.5.  $C_{21}H_{16}O_3$  requires C, 79.7; H, 5.1%).

*10-Methyl-3 : 4-benzopyrene* (III; R = H).—The above *keto-ester* (0.4 g.) was extracted with refluxing ether into a solution of lithium aluminium hydride (1.2 g.) in anhydrous ether

<sup>5</sup> E. Bergmann and O. Blum-Bergmann, *J. Amer. Chem. Soc.*, 1936, **58**, 1678; E. Bergmann and F. Bergmann, *ibid.*, 1938, **60**, 1805.

(200 c.c.) during 5 hr. The resulting solution was refluxed for a further 4 hr., then poured into ice and dilute sulphuric acid, and the ether extract was evaporated. The remaining white solid was filtered off, dried, and heated with palladium black (0.1 g.), slowly at first, to 350° at 0.1 mm. The sublimate was chromatographed in benzene-hexane on alumina, to give the hydrocarbon (0.13 g.) as yellow needles, m. p. 176—177° after recrystallisation from hexane (Found : C, 94.8; H, 5.4. Calc. for  $C_{21}H_{14}$  : C, 94.7; H, 5.3%). This gave a picrate as brown plates, m. p. 176—177° (from benzene-ethanol) (Found : C, 65.3; H, 3.5; N, 8.6. Calc. for  $C_{27}H_{17}O_7N_3$  : C, 65.5; H, 3.5; N, 8.5%), and a trinitrobenzene derivative as bright red needles, m. p. 210—211° (from ethanol) (Found : C, 67.5, 67.7; H, 3.5, 3.5.  $C_{27}H_{17}O_6N_3$  requires C, 67.6; H, 3.6%). Adelfang and Daub<sup>1</sup> give hydrocarbon, m. p. 177—178°, and picrate, m. p. 179.5—180.5°.

1 : 2 : 8 : 9 : 10 : 11-Hexahydro-8-oxo-3 : 4-benzopyrene-10-carboxylic Acid (II; R = H).—1 : 2 : 3 : 11b-Tetrahydromesobenzanthr-3-ylidenesuccinic acid (5.0 g), m. p. 223—224° (Found : C, 75.2; H, 5.6. Calc. for  $C_{21}H_{18}O_4$  : C, 75.4; H, 5.4%) (Cook, Ludwiczak, and Schoental<sup>3</sup> give m. p. 208—209°), was treated with anhydrous hydrogen fluoride (approx. 100 g.) for 12 hr. The product was taken up in alkali (charcoal), reprecipitated, and recrystallised from ethyl acetate as golden plates, m. p. 295—296°. It gave a methyl ester as yellow needles, m. p. 187—188° (from ethyl acetate) (Found : C, 79.7; H, 5.6.  $C_{22}H_{18}O_3$  requires C, 80.0; H, 5.5%).

1 : 2 : 10 : 11-Tetrahydro-8-methyl-3 : 4-benzopyrene-10-carboxylic Acid.—The above keto-acid (1.2 g.) was extracted during 6 hr. into a reagent prepared from magnesium turnings (0.6 g.), methyl iodide (3.8 g.), and ether (75 c.c.). After refluxing for 4 hr. the product was poured into ice and dilute sulphuric acid, the ether was evaporated, and the solid acid was filtered off, taken up in alkali, reprecipitated, and recrystallised from ethyl acetate as yellow needles, m. p. 255—256° (Found : C, 83.9; H, 5.6.  $C_{22}H_{18}O_2$  requires C, 84.1; H, 5.8%).

1 : 2 : 3 : 11b-Tetrahydromesobenzanthr-3-ylsuccinic Acid (IV).—(a)  $\beta$ -Ethoxycarbonyl- $\beta$ -(1 : 2 : 3 : 11b-tetrahydromesobenzanthr-3-ylidene)propionic acid (I; R = H) (5 g.) was heated with 2N-sodium hydroxide (150 c.c.) for 2 hr. After cooling, Raney nickel (from 5.0 g. of alloy) was added and the sodium salt was hydrogenated at atmospheric pressure for 6 hr. An insoluble sodium salt separated. The sodium salt was filtered off and acidified; the dibasic acid, recrystallised from ethyl acetate containing a small amount of ethanol, had m. p. 248—249° (bath preheated to 245°) (yield 1.8 g.) (Found : C, 74.8; H, 6.2.  $C_{21}H_{20}O_4$  requires C, 75.0; H, 6.0%).

(b) The unsaturated acid (I; R = H) (4 g.) in refluxing pentyl alcohol (300 c.c.) was reduced by the addition of sodium (12 g.) during 5 hr. The product was worked up in the usual way, to give an isomeric 1 : 2 : 3 : 11b-tetrahydromesobenzanthr-3-ylsuccinic acid (0.7 g.) (sodium salt, soluble in water), m. p. 230—231° (from ethyl acetate) (Found : C, 74.5; H, 6.4%).

1 : 2 : 5 : 8 : 9 : 10 : 11 : 12-Octahydro-8-oxo-3 : 4-benzopyrene-10-carboxylic Acid (V).—(a) The above dibasic acid (insoluble sodium salt) (2.1 g.) was treated with anhydrous hydrogen fluoride (ca. 50 g.). After 5 hr. the product was worked up in the usual way, to give the keto-acid (1.3 g.) as pale yellow needles, m. p. 269—270° (from ethyl acetate) (Found : C, 78.9; H, 5.4.  $C_{21}H_{18}O_3$  requires C, 79.2; H, 5.7%). Light absorption : Max. at 212 and 266 m $\mu$  (log  $\epsilon$  4.60 and 4.28 respectively) in EtOH. It gave a methyl ester as pale yellow needles, m. p. 234—235° (from methanol) (Found : C, 79.1; H, 6.4.  $C_{22}H_{20}O_3$  requires C, 79.5; H, 6.1%). (b) The isomeric dibasic acid (soluble sodium salt), when similarly treated, afforded a keto-acid which crystallised as pale lime-green needles, m. p. 243—244°, from ethyl acetate (Found : C, 79.2; H, 5.4%).

1 : 2 : 5 : 10 : 11 : 12-Hexahydro-8-methyl-3 : 4-benzopyrene-10-carboxylic Acid.—The above keto-acid (m. p. 269—270°) (2.8 g.) was extracted during 6 hr. into a refluxing solution prepared from magnesium (0.8 g.) and methyl iodide (4.6 g.) in ether (300 c.c.) and refluxed for a further 2 hr. The resulting solution was worked up in the usual manner, to give the unsaturated acid (1.7 g.) as colourless needles, m. p. 230° (from ethyl acetate) (Found : C, 84.1; H, 5.8.  $C_{22}H_{18}O_2$  requires C, 84.1; H, 5.8%). It gave a methyl ester as pale yellow needles, m. p. 163—164° (from methanol) (Found : C, 84.0; H, 5.9.  $C_{23}H_{20}O_2$  requires C, 84.1; H, 6.1%).

8 : 10-Dimethyl-3 : 4-benzopyrene (III; R = Me).—The methyl ester of the above acid (0.8 g.) was reduced with lithium aluminium hydride and the alcohol was dehydrated and dehydrogenated as in the preparation of 10-methyl-3 : 4-benzopyrene above. The hydrocarbon was purified by chromatography in benzene on alumina and recrystallised from benzene-hexane as yellow plates, m. p. 235—236° (0.1 g.) (Found : C, 94.5; H, 5.6. Calc. for  $C_{22}H_{16}$  : C, 94.3; H, 5.7%). It gave a derivative with trinitrobenzene as bright red needles, m. p. 202—203° (from benzene-ethanol) (Found : C, 67.9; H, 3.6.  $C_{28}H_{19}O_6N_3$  requires C, 68.2; H, 3.9%).

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