844. *Friedel–Crafts Succinoylation of Anthracene. Synthesis of 1′- and 4′-Hydroxy-1 : 2-benzanthracene.*

By (Miss) R. Schoental.

Condensation of anthracene with succinic anhydride in the presence of aluminium chloride in cold methylene chloride yielded a mixture from which β-1-anthroylpropionic acid, m. p. 184—185°, and β-9-anthroylpropionic acid, m. p. 177°, have been isolated. The structure of the former acid has been proved by its conversion into the known 4′-hydroxy-1 : 2-benzanthracene; the latter acid was oxidised to anthraquinone and reduced to the known β-(9 : 10-dihydro-9-anthroyl)propionic acid. The product, m. p. 125°, believed to be β-1-anthroylpropionic acid (Bergmann and Weizmann, *J.*, 1938, 1243), was obviously a mixture.

β-2-Anthroylpropionic acid, which is a minor constituent of the mixture of products under the above conditions, has been converted into 1′-hydroxy-1 : 2-benzanthracene, the methyl ether of which was required for biological testing.

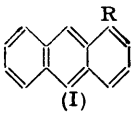
A disuccinoylation product of anthracene has also been isolated in small yield.

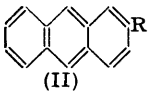
Anthracene has been subjected to Friedel–Crafts condensations with succinic anhydride in nitrobenzene by several groups of workers (for references, see Berliner, *Org. Reactions*, 1949, **5**, 234) * but the course of the reaction has not been completely elucidated. Of the three theoretically possible monosubstitution products (I), (II), (III), only (II) has been consistently obtained. Berliner (*loc. cit.*), using benzene as solvent, recorded, without details, the isolation of β-(9 : 10-dihydro-9-anthroyl)propionic acid and Bergmann and Weizmann (*loc. cit.*) reported the isolation besides (II) of a second keto-acid, m. p. 125°, which they believed to be (I) but this structure is now shown to be incorrect.

From the published results it is evident that, equimolecular proportions of reactants being used, most of anthracene is recovered unchanged, and only about 20% could be accounted for in the form of (II). It seems therefore probable that condensation of anthracene with more than one molecule of succinic anhydride takes place. The isolation

* The product of condensation of anthracene with maleic anhydride in the presence of aluminium chloride (Oddy, *J. Amer. Chem. Soc.*, 1923, **45**, 2156) is recorded in this Review (p. 286) as a 9-substitution product, but it is obviously the well-known maleic anhydride adduct (Diels and Alder, *Annalen*, 1931, **486**, 191), as shown by its m. p. and that of the methyl ester.

of all the acidic components of a reaction product which may contain, besides the three isomeric monopropionic acids, some at least of the 15 possible di-isomers presents obvious difficulties: hence, the intractable mixtures which have often been encountered.


(I)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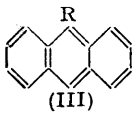

(III)

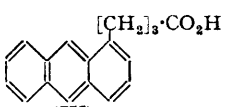
[R = $CO{\cdot}CH_2{\cdot}CH_2{\cdot}CO_2H$.]

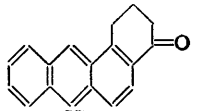
Since methylene chloride proved advantageous as solvent in some Friedel–Crafts reactions, favouring α-substitution (Baddeley, *J.*, 1949, S 99), its use for this case has been studied. Although none of the reactants is readily soluble in methylene chloride, a homogeneous solution is rapidly formed even when a small volume of the cold solvent is used. The product is thereafter slowly deposited. As a low-boiling solvent, methylene chloride presents another obvious advantage over nitrobenzene, the removal of which by prolonged steam-distillation may have deleterious effects on sensitive keto-acids.

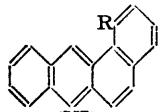
When 1—2 mols. of aluminium chloride were used, about half the anthracene remained unchanged; but use of 2 mols. each of succinic anhydride and aluminium chloride resulted in an almost complete transformation of anthracene into acidic products. However, the isolation of individual acids in this case was more difficult than from a product obtained under equimolecular conditions, and only the latter is here described.

Leaching of the mixture of acids with ethyl acetate left a small insoluble residue of disuccinoylation product, m. p. *ca.* 235° (decomp.), characterised by its methyl ester; the positions of substitution were not established. It formed an easily soluble sodium salt, whereas the acid (II), which is similar in appearance and m. p., forms a rather insoluble sodium salt. Acids (I) and (III) also form well-crystallised sodium salts, but only in the presence of excess of sodium ions. The monopropionic acids were separated by chromatography on silica from the other acidic products, which were strongly adsorbed. Acid (II) is less easily eluted than (I) and (III). Acid (I), the main product of the reaction, was readily obtained pure by crystallisation from ethyl acetate; acid (III), more soluble, remained in the mother-liquor, from which it was recovered on further concentration and was purified through its sodium salt and repeated crystallisation from benzene. Its structure was proved by oxidation to anthraquinone and by reduction to β-(9 : 10-dihydro-9-anthroyl)propionic acid.

Acid (I) was reduced to the corresponding butyric acid (IV), and the latter cyclised by the stannic chloride method (Fieser and Novello, *J. Amer. Chem. Soc.*, 1940, **62**, 1855) to 1′ : 2′ : 3′ : 4′-tetrahydro-4′-keto-1 : 2-benzanthracene (V), which yielded on dehydrogenation the known 4′-hydroxy-1 : 2-benzanthracene (Sempronj, *Gazzetta*, 1939, **69**, 448). This proves the structure of acid (I).


(IV)


(V)


(VI)

Similar dehydrogenation of 1′ : 2′ : 3′ : 4′-tetrahydro-1′-keto-1 : 2-benzanthracene (Cook and Robinson, *J.*, 1938, 505) yielded 1′-hydroxy-1 : 2-benzanthracene (VI; R = OH), the methyl ether of which was required for biological testing.

Experimental

Friedel–Crafts Succinoylation of Anthracene in Methylene Chloride and Separation of the Keto-acids.—Anthracene (71·4 g.) and succinic anhydride (40 g.) were ground finely together, suspended in methylene chloride (350 c.c.), and treated in an ice-bath with finely powdered, anhydrous aluminium chloride (55 g.) with constant shaking. The colourless suspension became dark red on the addition of aluminium chloride and after less than an hour the mixture formed a homogeneous dark red solution. It was then left at 0—4° overnight, and a sticky

precipitate was formed. Crushed ice, dilute hydrochloric acid, and ethyl acetate were then added, to decompose this complex. The orange-coloured suspension was freed from solvents on a water-bath, and the solid collected, washed free from aluminium salts, and leached with dilute potassium carbonate solution. The remaining unchanged anthracene was filtered off (about 30 g.). The acids obtained by acidification of the carbonate solution were collected, washed, dried, and leached with a small quantity of ethyl acetate. The insoluble residue (about 1·0 g.) was dissolved in dilute sodium carbonate solution and filtered, and the acid obtained on acidification of the filtrate was crystallised from " Cellosolve " (2-ethoxyethanol). This *acid*, a disuccinoylation product of anthracene, formed golden-yellow needles, m. p. *ca.* 235° (decomp.) (Found: C, 69·85; H, 5·1. $C_{22}H_{18}O_6$ requires C, 69·8; H, 4·8%). Its *dimethyl* ester, prepared in methanol by the action of ethereal diazomethane, crystallised from benzene in yellow, silky needles, m. p. 138—139·5° (Found: C, 71·0; H, 5·7. $C_{24}H_{22}O_6$ requires C, 70·9; H, 5·5%).

The ethyl acetate solution was freed from solvents *in vacuo*, and the residue dissolved in benzene and chromatographed on silica gel (200—300 mesh). The forerun, containing coloured, neutral, high-melting products, was discarded. The column on being washed with benzene developed a bright yellow zone (below a strongly adsorbed brown one) which was eluted with chloroform, and the extract concentrated *in vacuo*. The solid which slowly crystallised out was filtered off (see below); the mother-liquor was concentrated further, and the solid filtered off, dissolved in 10% sodium carbonate, treated with an approximately equal volume of saturated sodium chloride solution, and left in the cold; the sodium salt crystallised; it was collected and the recovered acid crystallised several times from benzene. β-9-*Anthroylpropionic acid* (III) formed small, yellowish prisms, m. p. (with some softening) 177° (Found: C, 78·0; H, 5·3. $C_{18}H_{14}O_3$ requires C, 77·7; H, 5·1%). Oxidation of this acid with chromic acid in glacial acetic acid yielded anthraquinone, and reduction for 16 hours by Martin's modification of Clemmensen's method (*J. Amer. Chem. Soc.*, 1936, **58**, 1438) gave the known β-(9 : 10-dihydro-9-anthroyl)propionic acid as colourless, lustrous scales (from benzene) or needles (from benzene–light petroleum), m. p. 163—163·5° (Found: C, 77·1; H, 5·9. Calc. for $C_{18}H_{16}O_3$: C, 77·1; H, 5·75%) (Cook, Robinson, and Roe, *J.*, 1939, 266, give m. p. 160—161°).

The solid obtained on concentration of the chloroform eluate from the yellow zone of the silica column was purified through its sodium salt and crystallised from ethyl acetate. β-1-*Anthroylpropionic acid* (I) formed golden-yellow, lustrous scales, m. p. 184—185° (Found: C, 77·5; H, 5·3. $C_{18}H_{14}O_3$ requires C, 77·7; H, 5·1%). Its *methyl* ester, obtained by use of ethereal diazomethane, formed yellow, transparent, heavy prisms, m. p. 65·5—66·5° (Found: C, 77·8; H, 5·6; OMe, 10·2. $C_{19}H_{16}O_3$ requires C, 78·0; H, 5·5; OMe, 10·6%). The acid recovered from the methyl ester had the same m. p., 184—185°.

Development of the dark zone of the silica column with chloroform yielded a small amount of the known β-2-anthroylpropionic acid (II), m. p. 223°.

γ-1-*Anthrylbutyric acid* (IV).—The keto-acid (I) (7·0 g.) was reduced by Martin's method (*loc. cit.*) for 28 hours. The reduced *acid* (IV) formed colourless needles (from benzene–light petroleum), m. p. 148—149° (Found: C, 81·8; H, 6·2. $C_{18}H_{16}O_2$ requires C, 81·8; H, 6·1%).

1′ : 2′ : 3′ : 4′-*Tetrahydro*-4′-*keto*-1 : 2-*benzanthracene* (V).—The foregoing acid (1·3 g.) in thiophen-free benzene (dried over sodium) (5 c.c.) was treated in an ice-bath with phosphorus pentachloride (1·2 g.) in benzene (5 c.c.), left for 2·5 hours at 0°, then treated with stannic chloride (2 c.c.) in benzene (2 c.c.). A deep violet precipitate separated immediately. After about 30 minutes in the ice-bath and a further 10 minutes at room temperature the complex was decomposed with ice and dilute hydrochloric acid. The product was extracted into benzene and purified by chromatography on alumina. 1′ : 2′ : 3′ : 4′-*Tetrahydro*-4′-*keto*-1 : 2-*benzanthracene* crystallised from methanol in almost colourless prismatic needles (0·80 g.), m. p. 196—197° (Found: C, 88·1; H, 5·7. $C_{18}H_{14}O$ requires C, 87·8; H, 5·7%). It formed an orange *picrate*, m. p. 163° (Found: N, 8·0. $C_{18}H_{14}O,C_6H_3O_7N_3$ requires N, 8·8%).

4′-*Hydroxy*-1 : 2-*benzanthracene*.—A solution of the foregoing ketone (160 mg.) in 1-methylnaphthalene (5 c.c.) was boiled under reflux in a nitrogen atmosphere with palladium black (30 mg.) for 16 hours. The product crystallised from benzene in colourless needles, m. p. 225° (decomp.), not depressed when mixed with a specimen prepared according to Sempronj (*loc. cit.*), and gave a methyl ether, m. p. 163°, not depressed by admixture with an authentic specimen.

1′-*Hydroxy*-1 : 2-*benzanthracene* (VI; R = OH).—1′ : 2′ : 3′ : 4′-Tetrahydro-1′-keto-1 : 2-benzanthracene, m. p. 114°, prepared from (II) according to Cook and Robinson (*J.*, 1938, 505), was dehydrogenated by boiling it (0·6 g.) in 1-methylnaphthalene (4 c.c.) in a nitrogen atmosphere with palladium black (60 mg.) for 18 hours. Crystallised from benzene–light petroleum, the *phenol* formed silky, yellowish needles, m. p. 168—170° (Found: C, 88·8; H, 4·5.

$C_{18}H_{12}O$ requires C, 88·5; H, 4·9%). Its *methyl ether*, prepared by the action of methyl sulphate and alkali and purified by chromatography on alumina from benzene–light petroleum, crystallised from methanol in colourless thin needles, m. p. 131—132° (Found: C, 88·0; H, 5·5; OMe, 11·5. $C_{19}H_{14}O$ requires C, 88·3; H, 5·5; OMe, 12·0%), and gave a s-*trinitrobenzene* complex in the form of salmon-orange needles (from benzene), m. p. 188—189° (Found: N, 9·2. $C_{25}H_{17}O_7N_3$ requires N, 8·9%).

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