CHAPTER I

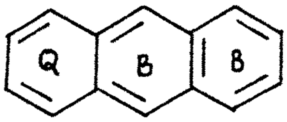
General Introduction

Pattern of addition and substitution in anthracene and hydroxyanthracenes.

The linear tricyclic hydrocarbon, anthracene, found in coal tar, is an important dye intermediate. In the form of its derivatives such as polyhydroxyanthraquinones it is widely distributed in the insect world in the form of kermesic, carmanic and laccaic acids and also in the vegetable kingdom in the form of colouring matters such as alizarin, purpurin, chrysophanic acid, ~~and~~ emodin etc. (cf. Naturally occurring quinones, by Thomson, Butterworths Scientific Publications, London, 1957).

Anthracene differs in certain very important respects from benzene and naphthalene particularly as regards the ease with which it undergoes oxidation to anthraquinone and its readiness to form stable addition compounds with several reagents such as hydrogen, halogen etc. The points of attack in all these reactions are the 9 and 10 positions called the meso positions.

No formulation of anthracene is possible in which all three rings have the normal bond arrangement of an isolated benzene ring. Structure (I) at least contains only one *o*-quinonoid ring, whereas the alternate structure (II) has two and hence on the basis of the Fries rule (I) would be more stable. Chemical evidence indicates that the diquinonoid form (II) does not participate in the reactions of derivatives of the hydrocarbon.



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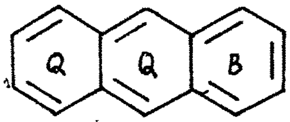
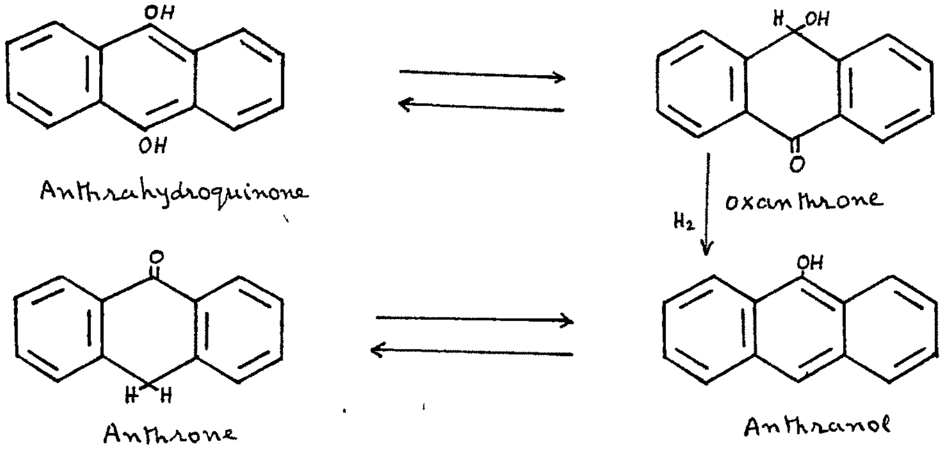


II

A few reactions on anthracene and 1- and 2-hydroxyanthracene (1- and 2-anthrol) may now be described. These will indicate the pattern of addition and substitution in anthracene and the changes in this pattern with the introduction of a hydroxy group in the terminal ring. Further, these reactions illustrate the diversity of products obtained with changes in the reagents or reaction conditions.

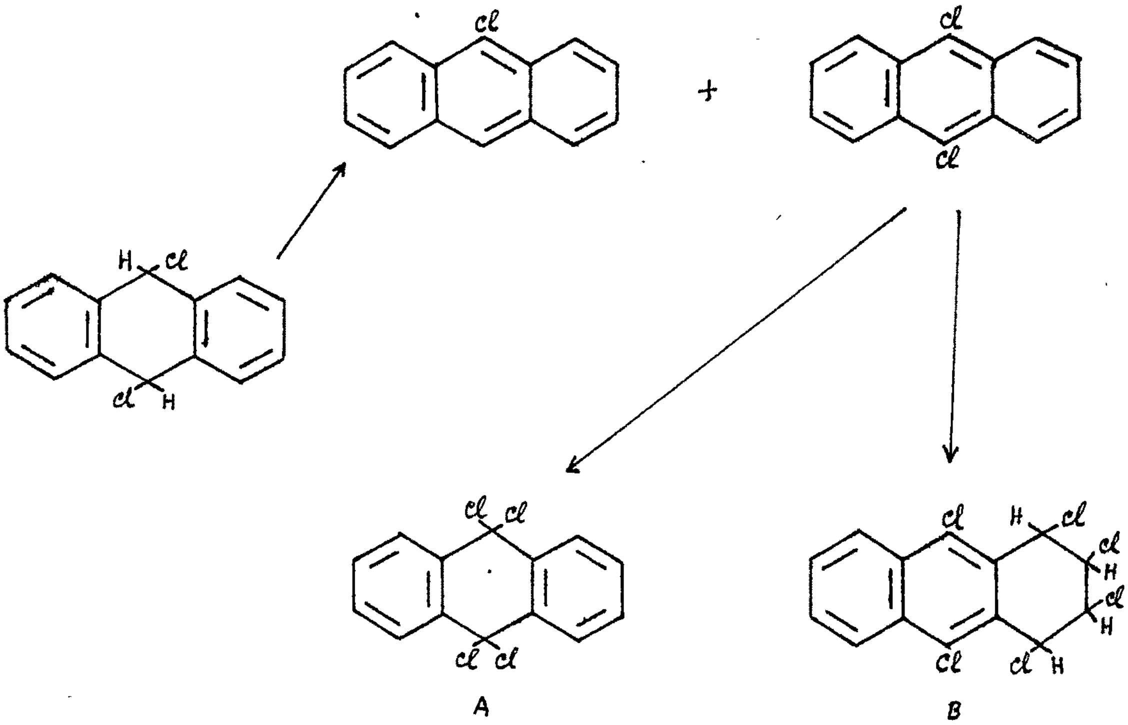
Reactions of Anthracene.

Oxidation : Chromic acid in boiling acetic acid oxidises both the meso-carbon atoms with the ultimate formation of anthraquinone. Similar result is obtained when potassium dichromate or sodium dichromate in sulphuric acid (Graebe and Liebermann, Ann.Suppl., 1870, 7, 257 ; Beisler and Jones, J. Am. Chem. Soc., 1922, 44, 2296 ; Majer and Mareuk, Z. Physik. Ch., 1932, A 159, 181), or hydrogen peroxide in acetic acid (Henderson and Boyd., J. Chem. Soc., 1910, 97, 1659 ; Charrier and Cripps, Gazz., 1927, 57, 741) or aqueous solutions of sodium chlorate or sodium hypochlorite in presence of traces of osmium tetroxide (Hofmann, Ber., 1912, 45, 3329 ; Hofmann and Ritter, Ber., 1914, 47, 2233) are used. However, on oxidation with lead tetracetate, manganese dioxide, cerium acetate or vanadium pentoxide in acetic acid solution, acetates of anthranol and oxanthrone are formed (Meyer, Ann., 1911, 379, 73). Halogens in moist solvents also act as oxidising agents giving oxanthrone or 9-halogenoanthrones (Meyer et al., loc.cit., p. 166 ; ibid., 1913, 396, 166 ; Price and Weaver, J. Am. Chem. Soc., 1939, 61, 3360.).



Hydrogenation : Anthracene is hydrogenated much more easily than benzene or naphthalene. The initial product is 9,10-dihydroanthracene, when a copper chromite catalyst is employed (Mosettig et al., J. Am. Chem. Soc., 1935, 57, 2371 ; 1945, 67, 2255) or anthracene is reduced by sodium amalgam in boiling alcohol, sodium in amyl alcohol, hydriodic acid and phosphorus at 160-170° (Graebe and Liebermann, loc.cit. ; Bamberger and Lodter, Ber., 1887, 20, 3073 ; Lucas, Ber., 1888, 21, 2510) or by calcium in alcohol (Marschalk and Nicolajewsky, Ber., 1910, 43, 1700). Continued hydrogenation, using nickel catalysts (Schroeter, Ber., 1924, 57, 2003), affords first 1,2,3,4-tetrahydroanthracene and then 1,2,3,4,5,6,7,8-octahydroanthracene (Cameron et al., J. Chem. Soc., 1945, 286). A decahydroanthracene and three perhydroanthracenes, $C_{14}H_{24}$, have also been obtained (Schroeter, loc.cit. ; Fries and Schilling, Ber., 1932, 65, 1494 ; Durand and Marvel, J. Am. Chem. Soc., 1936, 56, 1594).

Halogenation : Anthracene readily undergoes addition reactions with halogens. Both substitution and addition occurs with fluorine, the product being perfluoranthracene, $C_{14}F_{24}$ (Cady et al., Ind. Eng. Chem., 1947, 39, 290). With one mole of bromine in carbon disulphide cooled in a freezing mixture, it forms the dibromide, 9:10-dibromo-9:10-dihydroanthracene. This compound decomposes even at room temperature and especially on warming, giving hydrobromic acid, 9-bromoanthracene, anthracene and 9:10-dibromoanthracene (Barnett et al., J. Chem. Soc., 1924, 125, 1084 ; Rec. Trav. Chim., 1924, 43, 530). The latter then undergoes addition with the formation of either 9:9:10:10-tetrabromo-9:10-dihydroanthracene or 1:2:3:4:9:10-hexabromo-1:2:3:4-tetrahydroanthracene which may be obtained in stereoisomeric forms (Meyer and Zahn, Ann., 1913, 396, 166). Anthracene reacts similarly with chlorine. Low temperatures in chloroform or carbon tetrachloride favour the formation of (A) and high temperatures and benzene that of (B) (G.P. 283,106; 284,790). With excess of bromine in carbon disulphide without cooling 9:10-dibromoanthracene is obtained (Graebe and Liebermann, loc. cit.).

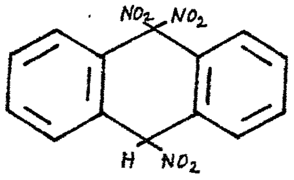


With bromine in moist dioxane, 9-bromoanthrone and anthraquinone are formed, but in dry dioxane if atmospheric moisture is excluded, 9:10-dibromoanthracene is obtained (Price and Weaver, loc.cit.).

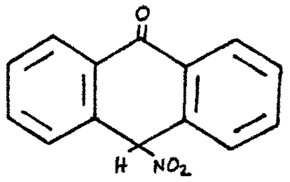
The substitution of halogen takes place initially on the meso-positions, then in the 2- and 6-positions and finally in the other positions such as 1- and 5. Similar results are obtained whether halogen is used alone or in presence of a carrier or whether a halogenating agent like sulphuryl chloride is used in nitrobenzene (Diel, Ber., 1878, 11, 173 ; Kaufler and Imhoff, ibid., 1904, 37, 4708 ; G.P. 292,356).

Nitration : When warmed with dilute nitric acid, anthracene is more readily oxidised than nitrated, the reaction products are anthraquinone and nitroanthraquinones

(Laurent, Ann. Chim., 1835, (ii), 60, 220 ; Laurent, ibid., 1837, 66, 136 ; Graebe and Liebermann, 1870 loc.cit., Schmid. J. pr. Chem., 1874, (ii), 9, 241 ; Fichter and Pluss, Helv., 1932, 15, 236). When anthracene is treated with concentrated nitric acid oxidation occurs with the formation of anthraquinone. On adding anthracene to a mixture of one part of fuming nitric acid (d. 1.5) and two parts of nitrobenzene, avoiding rise of temperature, 9:10-dinitroanthracene is obtained together with anthraquinone (Perkin, J. Chem. Soc., 1891, 59, 634 ; Meisenheimer et al., Ann., 1904, 33, 133). 9-Nitro- and small amounts of 9:10-dinitroanthracene are formed by nitration in acetic acid with diacetyl orthonitric acid at 20° ; when excess of nitric acid (d. 1.4) diluted with acetic acid is used at 30-35° small amounts of 9:10-dinitroanthracene, 9:9:10-trinitro-9:10-dihydroanthracene and 10-nitroanthrone are formed, together with some anthraquinone (Meisenheimer, 1904, loc.cit.).

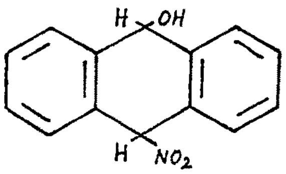


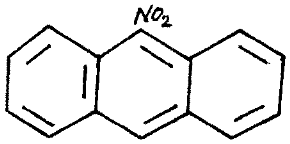
9,9,10-tri-nitro-9,10-dihydroanthracene



10-nitro-anthrone

On addition of one mole of nitric acid (d. 1.4) to one mole of anthracene in acetic acid below 30°, the acetate of 10-nitro-9:10-dihydroanthranol is obtained from which, on treatment with alkali, 9-nitroanthracene can easily be obtained (Dimroth, Ber., 1901, 34, 219 ; Meisenheimer, 1904, loc.cit. ; Barnett et al., J. Chem. Soc., 1923, 123, 1994) ; if, however, the solution is refluxed 10:10'-bianthronyl is obtained (Dimroth, 1901, loc.cit. ; Barnett and Matthews, J. Chem. Soc., 1923, 123, 380).


10-nitro-9,10-dihydro-anthranol

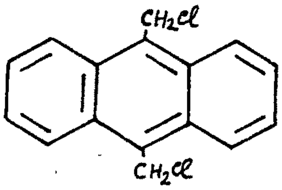

9-nitro-anthracene

with two moles of nitric acid first at 7 - 8°, then at 50-55° Turski obtained dinitrotetrahydrobianthranol (Roczniki Chemji., 1927, 7, 457). On treating anthracene in chloroform at 0° with excess of nitric acid (d. 1.4), the nitrate of 10-nitro-9:10-dihydroanthranol is formed (Meisenheimer, 1904, loc.cit.). By nitrating anthracene with the theoretical amount of pyridinium nitrate in pyridine, 9-nitroanthracene is formed together with small amounts of 10-nitroanthrone and anthraquinone (Battegay and Brant, Bull. Soc. Chem., Fr., 1922, (iv), 31, 910). By passing nitrous fumes into an anthracene suspension in acetic acid or chloroform, 9:10-dinitro-9:10-dihydroanthracene is formed which with warm aqueous sodium hydroxide or cold pyridine and alcohol, readily gives 9-nitroanthracene (Liebermann and Lindemann, Ber., 1880, 13, 1584 ; Meisenheimer, 1904, loc.cit. ; Barnett, J. Chem. Soc., 1925, 127, 2040).

Sulphonation : When anthracene is sulphonated in acetic acid with oleum (Battegay and Brandt, Bull. Soc. Chim., Fr., 1923, (iv), 33, 1667) or with chlorsulphonic acid (Bayer, G.P. 251,695) a mixture of anthracene 1- and 2-sulphonic acids is produced. When it is sulphonated with pyridinium anhydrosulphate in basic or neutral solution, anthracene-1-sulphonic acid is almost exclusively formed (Battegay, 1923, loc.cit.). By sulphonating anthracene with sulphuric acid on the water bath, Liebermann (Ber., 1879, 12, 182) obtained two disulphonic acids, judged to be the 1:5- and 1:8-acids. At higher temperatures (150°) anthracene 2:6- and 2:7-disulphonic acids are formed (Birkenheim and Snamenskaya, J. Gen. Chem., U.S.S.R., 1934, 4, 31). With sulphur dichloride at room temperature anthracene gives anthracene-9-dithiochloride $C_{14}H_9S_2Cl$ (Friedlander and Simon, Ber., 1922, 55, 3969), but on heating with sulphur dichloride in benzene, 9:10-dichloroanthracene is obtained (Lippmann and Pollak, Ber., 1901, 34, 2767).

Alkylation and acylation : Direct acylation, alkylation and aralkylation, also occurs on the meso-carbon atoms. It condenses with benzoyl chloride in nitrobenzene without catalyst to give 9-benzoylanthracene (Nenitzescu et al., Ann., 1931, 491, 210). In presence of aluminium chloride, in addition to this compound, 1- and 2-benzoylanthracenes and 9:10-dibenzoylanthracenes are formed in small yield (Perrier, Ber., 1900, 33, 816 ; Lippmann and Keppich, Ber., 1900, 33, 3086 ; Cook, J. Chem. Soc., 1926, 1677). Acetyl chloride readily affords 9-acetylanthracene (Org. Synth., 30, 1). By the interaction of anthracene with aluminium chloride, two moles of hydrocyanic acid and dry hydrochloric acid in chlorobenzene at 70° anthracene-9-aldehyde is obtained (Hinkel et al., J. Chem. Soc., 1936, 339). It can also be obtained by treating the hydrocarbon with methyl-formanilide and phosphorus oxychloride in o-dichlorobenzene (Fieser et al., Org.Synth., 1940, 20, 11). In presence of aluminium chloride cyanogen bromide gives the 9-cyanoanthracene (Karrer and Zeller, Helv., 1919, 2, 482). By heating anthracene with phosgene at 180-200° or preferably with oxalyl chloride at 160°, the chloride of 9-anthroic acid (anthracene-9-carboxylic acid) is obtained (Graebe and Liebermann, Ber., 1869, 2, 678 ; Liebermann et al., Ber., 1911, 44, 208 ; 1912, 45, 1213) ; at higher temperatures, this chloride is converted into the chloride of 10-chloro-9-anthroic acid and (on long heating) into 9:10-dichloroanthracene (Behla, Ber., 1885, 18, 3169). With oxalyl chloride in presence of aluminium chloride in carbon disulphide, 1:9-oxalylanthracene and 9-anthroic acid chloride are formed (Liebermann, 1911, loc.cit.). With malonyl chloride in presence of aluminium chloride, 1:9-malonylanthracene (Kardos, Ber., 1913, 46, 2086), and with dimethyl- and diethyl-malonyl chloride 2:3 (or 1:2)- dimethyl- or diethyl-malonyl-anthracenes are the products obtained (Freund and Fleischer, Ann., 1910, 373, 291 ; 1913, 399, 182). With succinic anhydride in nitrobenzene β-(2-anthroyl-) propionic acid is formed in small amount (Fieser and Peters, J. Am. Chem. Soc., 1932, 54, 4347). It gives o-(9-anthroyl-)benzoic acid with phthalic anhydride and aluminium chloride in benzene(Heller and Schulke, Ber., 1908, 41, 3627, 3634 ; Heller, Ber., 1912, 45, 665, 669).

Chloromethylation occurs on the meso-atoms giving 9:10-bis(chloromethyl)-anthracene (Miller et al., J.Am.Chem. Soc., 1955, 77, 2845).

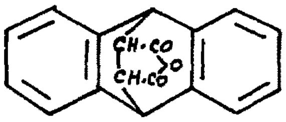


Diels-Alder diene reaction : When anthracene and maleic anhydride are heated together in xylene, addition occurs across the meso-positions with the formation of cis-9:10-dihydroanthracene-9:10-endo succinic anhydride (i) (Diels and Alder, Ann., 1931, 486, 191 ; Clar, Ber., 1931, 64, 1676, 2194 ; Bechmann and Kloetzel, J.Am.Chem.Soc., 1938, 60, 481). Fumaric acid reacts more slowly giving the corresponding trans-acid (Bechmann and Scott, ibid., 1948, 70, 1458).

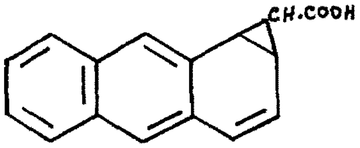
Action of ethyl diazoacetate and Osmium tetroxide :

The reagents employed in the above reactions react with the most reactive centres in the anthracene molecule, there are two reagents, however, which undergo addition to the most reactive bonds, namely, esters of diazoacetic acid, which add across the 1:2-bond giving 1:2-dihydroanthr-1:2-yelneacetic acid (ii) (Badger et al., J.Chem.Soc., 1951, 3456). Osmium tetroxide reacts with the 1:2-bond and the

3:4-bond giving 1:2:3:4-tetrahydroxy-1:2:3:4-tetrahydro-anthracene (Cook and Schoental, J.Chem.Soc., 1948, 170 ; Nature, 1948, <u>161</u>, 237).



(i)



(ii)

<u>Reactions of 1- and 2-anthrol</u> :

<u>Oxidation</u> : 1-Anthrol is easily oxidised in air. When a solution of 1-anthrol in alkali is left exposed to air for sometime, a bluish black product begins to separate. (Schmidt and Trust, Ber., 1904, <u>37</u>, 70). 1-Acetoxyanthracene is oxidised by chromic acid in hot acetic acid solution to 1-acetoxyanthraquinone (Dienel, Ber., 1905, <u>38</u>, 2862).

2-Anthrol is oxidised by ferric chloride to 3,3'-dihydroxy-10,10'-bianthronyl and the hydroxydianthrylene oxide (Ioffe, J.Gen.Ch. U.S.S.R., 1935, <u>5</u>, 1210 ; Efross, ibid., 1939, <u>7</u>, 1272, 2712). 2-Acetoxyanthracene is oxidised by chromic acid in hot acetic acid solution to 2-acetoxy-anthraquinone (Liebermann and Horiann, Ber., 1879, <u>12</u>, 589 ; Liebermann, Ann., 1882, <u>212</u>, 1, 26, 49, 100).

<u>Reduction</u> : When 1-anthrol is treated with sodium in alcohol, it is reduced to 9,10-dihydro-1-anthrol (Braun and Bayer, Ann., 1929, <u>472</u>, 90). It is reduced by one mole of hydrogen when heated in decalin below 200° in an autoclave

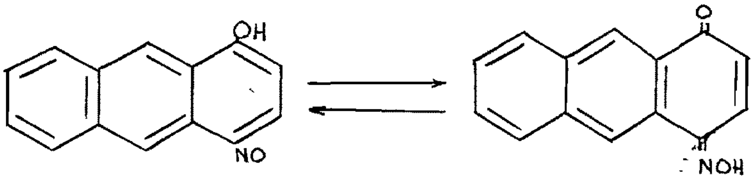
in presence of nickel salts, to a mixture of products, 9,10-dihydro-1-anthrol, 1-keto-1,2,3,4-tetrahydroanthracene and a substance of very high molecular weight. On complete hydrogenation, octahydroanthracene is obtained (Braun and Bayer, Ber., 1926, 59, 914 ; Braun and Bayer, 1929, loc.cit.).

2-Anthrol on reduction with sodium and alcohol, gives 9,10-dihydro-2-anthrol and 9,10-dihydroanthracene (Bambeger and Hoffmann, Ber., 1893, 26, 3068). When it is reduced with one mole of hydrogen, in decalin above 200° in an autoclave in presence of nickel salt, 9,10-dihydro-2-anthrol is obtained together with small amounts of 1,2,3,4-tetrahydro-2-anthrol and a trace of 2-keto-1,2,3,4-tetrahydroanthracene ; on further hydrogenation, octahydro-2-anthrol and octahydroanthracene are obtained (Braun and Bayer, 1929, loc.cit.). 2-Anthrol, hydrogenated (7 hours) in alcohol over copper chromite at 200°/122 atmos., gives an easily separable mixture of 9,10-dihydro-2-anthrol and 1,2,3,4-tetrahydro-2-anthrol (Cook et al., J.Chem.Soc., 1950, 911).

Halogenation : 1-Anthrol is found to ~~absorb~~ react with two moles of bromine, one in the 9,10-positions and the other in the ortho position to the hydroxyl group (Oda et al., Sci. Papers Inst. Phys.Chem.Research (Tokyo), 1938, 34, 596).

2-Acetoxyanthracene in polychlorobenzene solution treated with chlorine in acetic acid at 5-7° over one hour and stirred two hours at room temperature gives a mixture of 9,10-dichloro- and 9-chloro-2-acetoxyanthracene which on hydrolysis gives 9,10-dichloro-2-anthrol and 9-chloro-2-anthrol respectively (Fedorov, Izvest. Akad. Nauk. S.S.S.R., Otdel. Khim. Nauk., 1951, 582). 2-Anthrol with bromine in cold acetic acid undergoes both oxidation and bromination to give 2-hydroxy-1,1'-bianthranyl-9,2'-oxide, 1,10-dibromo-2-hydroxyanthracene and 1,9-dibromo-2-hydroxyanthracene isolated only as the acetyl derivative. ~~Whereas~~ 2-Acetoxyanthracene with bromine in cold glacial acetic acid gives the 9-bromo-2-anthrol (Ioffe et al., J.Gen.Chem., U.S.S.R., 1939, 9, 1128).

Nitrosation : 1-Anthrol on boiling in aqueous alcohol with sodium nitrite in presence of zinc chloride gives the zinc salt of 2-nitroso-1-anthrol and 4-nitroso-1-anthrol (Dienel, Ber., 1906, 39, 926). This nitroso-compound is tautomeric and may be regarded as the monoxime of 1,4-anthraquinone.



2-Anthrol on treatment with sodium nitrite under similar conditions, gives 1-nitroso-2-anthrol (Legodzinski, Ber., 1894, 27, 1438 ; Ann., 1905, 342, 59).

Miscellaneous reactions : 2-Amino-1-anthrol hydrochloride is obtained by the reduction of 2-nitroso-1-anthrol or its salts by stannous chloride and hydrochloric acid (Dienel, loc.cit.).

On heating 2-anthrol for six hours ~~to~~ at 125-130° in a sealed tube with excess ammonium sulphite and 28% ammonium hydroxide, 2-anthramine is obtained (Fedorov, 1951, loc.cit.). On heating with sodium sulphite for ten hours at 130-140° it gives 2-anthrol-9-sulphonic acid, isolated as the sodium salt (Fedorov, loc.cit.).

1-Anthrol on treatment with benzenediazonium chloride in alcohol, gives 4-benzeneazo-1-anthrol (Sircer, J.Chem.Soc., 1916, 109, 757). Under similar conditions, 2-anthrol gives 1-benzeneazo-2-anthrol (Nils Ospenson, Acta Chem. Scand., 1951, 5, 491).

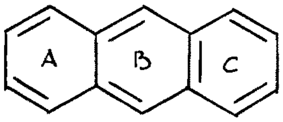
By passing dry hydrogen chloride into the alcoholic solution of 1-anthrol, 1-anthryl ethyl ether is obtained in more than 70% yield (Lampe, Ber., 1909, 42, 1413) and almost quantitative yield of 2-anthryl ethyl ether is obtained from 2-anthrol when treated as above or with ethyl iodide in alkaline solution.

1-Anthrol reacts with phthalic anhydride and boric acid at 100° to give o-(1-hydroxy-2-anthroyl)-benzoic acid (Schaarschmidt, Ber., 1916, 49, 381).

1-Anthrol as well as 2-anthrol condense~~s~~ with isatin α-anil in acetic anhydride to give the corresponding anthracene indole indigo (Bezdzik and Friedlander, Monatsh, 1909, 30, 871).

Some work has been done on the substitution in dihydroxyanthracenes with a view to find out whether the bonds in anthracene derivatives are rigid or labile.

To test the conclusion that (I) is the preferred structure for anthracene, which was derived from purely theoretical considerations, Fries studied bromination of 2,6-dihydroxyanthracene (Fries, Walter and Schilling, Ann., 1935, 516, 248). If the bond structure of this compound is (II), the bromine atoms would be directed to the two enolic ortho positions, 1 and 5, while the alternate structure (III) would lead to 3,5-substitution. It was found that bromination occurs at the 1- and 5-positions, as predicted for a substance of the structure (II).



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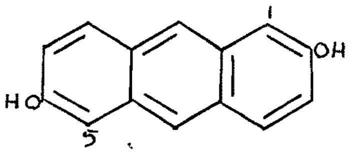

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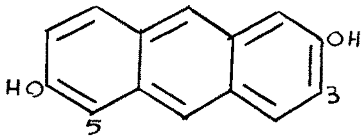

III

In an attempt to substantiate the views of Fries by providing more conclusive evidence, Fieser and Lothrop (J.Am.Chem.Soc., 1936, 58, 749) subjected 1,5-dimethyl- and 1,5-diallyl-derivatives of 2,6-dihydroxyanthracene to further reactions. These substances were investigated for their ability to couple with diazotized amines. The structure (II) for such a compound would permit of no reaction, since both of the normal ortho positions are blocked by alkyl groups, but if the substance can exist to any appreciable extent in the form with the bond structure (III) coupling should occur at the available ortho position C_3, for this is connected to the hydroxylated carbon atom by an enolic double bond. There was in no case any indication of a reaction and consequently it is concluded that the substances exist entirely in the forms corresponding to (II) and that tautomerization is negligible. According to modern concepts, there is resonance in these molecules, with the predominant contribution by the structure (II) suggested by Fries and Fieser.

PRESENT WORK

Various phenols and naphthols have been subjected to numerous reactions but the 1- and 2-anthrols, probably because they are not readily accessible, have not been studied so extensively. It was therefore of interest to synthesise the aldehydes, ketones and carboxylic acids from 1- and 2-anthrol and establish their structures. This work has been described in chapter II.

In chapter III the synthesis of various anthra α- and γ-pyrones from 1- and 2-anthrol or their derivatives such as 1-hydroxy-2-acetyl- or 2-hydroxy-1-acetyl-anthracene and 1-formyl-2-hydroxyanthracene by the application of suitable reactions such as Pechmann reaction, Simonis reaction, Kostanecki-Robinson acylation, Kostanecki Chalkone reaction, Perkin's reaction and Knoevenagel reaction, has been described.

In chapter IV the synthesis of anthra furan derivatives from 1-hydroxy-2-acetylanthracene and 1-formyl-2-hydroxy- and 1-acetyl-2-hydroxy-anthracene is described.

Having synthesised the anthracene derivatives it was thought of interest to see if these could be oxidised under controlled conditions to the corresponding anthraquinone derivatives which were hitherto unknown. The oxidation of the anthracene derivatives described in the earlier chapters to the anthraquinone derivatives and further synthetical work on some of these anthraquinone derivatives such as 1-hydroxy-2-acetyl- and 2-hydroxy-1-acetyl-anthraquinone forms the subject matter of chapter V.