runs. It has been found that the solvent affects the course of the reaction; ethyl 1-ethyl-2,5-pyrrolidinedicarboxylate is produced in these solvents. It is therefore concluded that 1,1-diethyl-2,5-dicarbethoxypyrrolidinium bromide cannot be an intermediate in the cleavage.

The 1,4-biradical theory of Criegee offers a satisfactory explanation of the facts.

The reaction of dimethylamine and ethyl α,α'-dibromoadipate carried out without a solvent gives a 35% yield of ethyl 1-methyl-2,5-pyrrolidinedicarboxylate with no evidence of any cleavage.

URBANA, ILLINOIS RECEIVED MAY 2, 1938

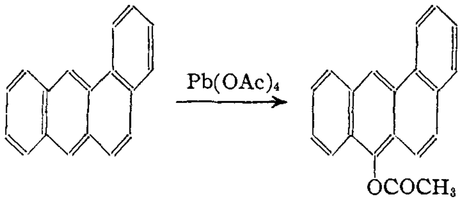
[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF HARVARD UNIVERSITY]

Substitution Reactions and Meso Derivatives of 1,2-Benzanthracene

BY LOUIS F. FIESER AND E. B. HERSHBERG[1]

Among various miscellaneous observations reported in this paper is a study of the action of lead tetraacetate on 1,2-benzanthracene and two related carcinogenic hydrocarbons. The idea of investigating the action of this oxidizing agent on polynuclear aromatic hydrocarbons was suggested by an observation of K. H. Meyer[2] which heretofore has attracted little attention. Schulze[3] at an early date had investigated the action of lead dioxide on anthracene in acetic acid solution, but it remained for Meyer to interpret the reaction correctly and to show that with two moles of oxidizing agent the chief product is hydroxyanthrone acetate. Using one mole of lead dioxide, Meyer obtained anthranyl acetate in 40–50% yield and noted that this was the first instance of the direct oxidation of a hydrocarbon to a phenol derivative. It occurred to us that this method of hydroxylation might have preparative value, that it might afford a useful method of probing for centers of reactivity in polynuclear compounds, and that the reaction would form an interesting model for a possible hydroxylation of carcinogenic hydrocarbons introduced into the animal organism.

In trial experiments lead tetraacetate was found to act as well as lead dioxide and it is a generally superior reagent. The reaction of one mole of lead tetraacetate with 1,2-benzanthracene in glacial acetic acid is complete after short heating on the steam-bath, and the purified reaction product, isolated in 52% yield, was found to be identical with synthetic 1,2-benzanthranyl-10-acetate[4] (II). The chief point of attack in the oxidation therefore is at the less hindered meso position 10.



I II

Little previous work has been done on the orientation of 1,2-benzanthracene in monosubstitutions. Cook and Hewett[5] found that the chief product of the Friedel and Crafts reaction with acetyl chloride at a low temperature is a meso ketone, but a distinction between the 9- and 10-positions was not made. With oxalyl chloride, Dansi[6] obtained besides a diketone a small amount of an acidic substance regarded as 1,2-benzanthracene-10-carboxylic acid. Barnett and Matthews[7] prepared a mononitro compound which they regarded as a 9- or 10-derivative, but they did not investigate the structure. We prepared a sample of the nitro compound by their method and reduced it to the amine. The same amine was obtained in good yield from 1,2-benz-10-anthranol[4] by the Bucherer reaction, from which it is evident that the nitration product prepared by Barnett and Matthews is 10-nitro-1,2-benzanthracene. The nitration of the hydrocarbon thus follows the same course as the oxidation with lead tetraacetate. Since 10-substituted derivatives of 1,2-benzanthracene are of particular interest in connection with the problem of carcinogenesis, it is significant that such compounds are available by the route of direct substitution reac-

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[1] Research Fellow on funds from the National Cancer Institute and the Ely Lilly Company.

[2] K. H. Meyer, *Ann.*, **379**, 73 (1911).

[3] Schulze, *Ber.*, **18**, 3036 (1885).

[4] Fieser and Hershberg, THIS JOURNAL, **59**, 1028 (1937).

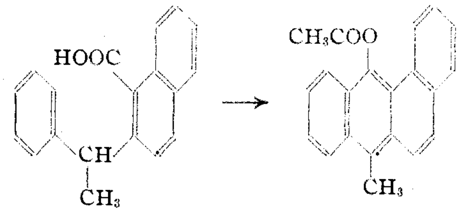
[5] Cook and Hewett, *J. Chem. Soc.*, 1408 (1933).

[6] Dansi, *Gazz. chim ital.*, **67**, 85 (1937).

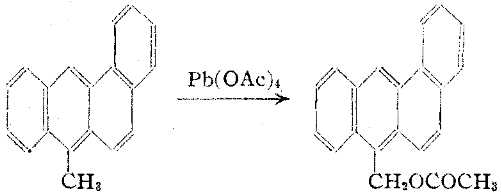
[7] Barnett and Matthews, *Chem. News*, **130**, 339 (1925).

tions.[8] Two additional 10-derivatives described in the Experimental Part are 3,10-dimethoxy-1,2-benzanthracene, prepared by methylation of the MgBr-salt of the corresponding 10-hydroxy compound, and a glycol dibenzoate resulting from the action of the silver benzoate–iodine compound[9] on 10-allyl-1,2-benzanthracene.

Lead tetraacetate reacts somewhat less smoothly with 10-methyl-1,2-benzanthracene than with the parent hydrocarbon, but a crystalline reaction product (m. p. 151°) was isolated in a pure condition if in rather low yield. The substance has the composition of a monoacetoxy compound, and it seemed possible that oxidation had occurred in the available meso position 9. The hitherto unknown 9-acetoxy-10-methyl-1,2-benzanthracene (IV) was therefore synthesized for comparison by the acetylative cyclization[4] of the previously described[10] acid III with zinc chloride catalyst in acetic acid–anhydride, but the synthetic acetate (m. p. 154°) gave a marked depression when mixed with the product of oxidation. We next prepared the 3-acetoxy derivative of 10-methyl-1,2-benzanthracene, since a sample of the hydroxy compound was available from earlier work,[4] but this acetate melted much higher (215°) than the compound in question. The substance was finally identified as 10-acetoxymethyl-1,2-benzanthracene (VI) by direct comparison with a sample of this substance kindly provided by Professor J. von Braun, who in unpublished work has prepared the acetoxy compound by a method leaving no doubt as to the structure. The oxidation of an alkyl side chain is not without parallel, for Dimroth and Schweizer[11] obtained benzyl acetate in about 12% yield on refluxing toluene with lead tetraacetate for four hours, and Criegee[12] found that tetralin is converted by the reagent into the 1-acetoxy derivative (one hour). The oxidation of the hydrocarbon V is complete after fifteen minutes, but whether or not this indicates a special reactivity of the 10-methyl group cannot be determined until more data are available. At all events it is very surprising that the methyl group is attacked in preference to oxidation at the free meso position. In comparison with the meso reactivity of anthracene, and that manifested at the 10-position in 1,2-benzanthracene, the 9-position of the hydrocarbon in question appears to be definitely inert. We are inclined to attribute this effect to steric hindrance, and it may be noted that the 9-position of 1,2-benzanthracene corresponds to position 4 in the phenanthrenoid system present in the molecule and that there are definite indications of hindrance at this position in phenanthrene.[13] While 4-substitution is not unknown,[14] it is extremely rare.



III IV



V VI

In 1,2,5,6-dibenzanthracene both meso positions should be subject to any blocking effect which may be exerted by an angular ring and, in line with the expectations from the behavior of 10-methyl-1,2-benzanthracene, it was found that the tetracyclic hydrocarbon is more resistant to attack by lead tetraacetate than 1,2-benzanthracene. From the reaction of the pure, colorless hydrocarbon with one mole of reagent we invariably recovered some unchanged material, and no homogeneous reaction product was isolated. In the course of the experiments it was observed that the yellow chrysogen (1,2,6,7-dibenzanthracene[15,16]) present in crude 1,2,5,6-dibenzanthracene is oxidized more readily than this hydrocarbon by lead tetraacetate and converted into more soluble products. This suggested a method for the purification of the widely used carcinogenic hydrocarbon which has been found very convenient and efficient. The yellow material

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(8) Dr. J. L. Hartwell of this Laboratory has prepared 1,2-benzanthracene-10-aldehyde, m. p. 147.3–148°, corr., by direct substitution.

(9) Prévost, *Compt. rend.*, **196**, 1129 (1933); **197**, 1661 (1933); Hershberg, *Helv. Chim. Acta*, **17**, 351 (1934).

(10) Fieser and Newman, THIS JOURNAL, **58**, 2376 (1936).

(11) Dimroth and Schweizer, *Ber.*, **56**, 1375 (1923).

(12) Criegee, *Ann.*, **481**, 263 (1930).

(13) Fieser, "The Chemistry of Natural Products Related to Phenanthrene," 2d ed., Reinhold Publishing Corp., New York, N. Y., 1937, pp. 13–14.

(14) Bachmann and Kloetzel, THIS JOURNAL, **59**, 2207 (1937).

(15) Cook, *et al.*, *Proc. Roy. Soc.* (London), **B111**, 469 (1932).

(16) Winterstein and Schön, *Z. physiol. Chem.*, **230**, 146 (1934).

is refluxed for a short time in benzene–acetic acid with about 0.1 mole of lead tetraacetate, and after concentrating and cooling the solution there is obtained very satisfactory, colorless 1,2,5,6-dibenzanthracene in over 80% yield. In our experience this method is considerably more rapid and sparing of material than preferential sulfonation of the chrysogen,[17] reaction with maleic anhydride,[15,18] or chromatographic adsorption.[16]

The lead tetraacetate reaction offers promise of providing information of value concerning the reactivity of various types of polynuclear aromatic hydrocarbons, with or without side chains and alicyclic rings, and the investigation of the reaction is being extended. The conversion of 3,4-benzpyrene and methylcholanthrene into monoacetoxy derivatives, m. p. 208.5–209°, corr., and m. p. 179.5–180.5°, corr., will be described at a later date.

In connection with the acetylative cyclization of the acid III, mentioned above, to an enol acetate (IV), the present paper reports a few additional observations concerning the application of this method[4] of ring closure. The most novel result is the cyclization of γ-(3-acenaphthyl)-butyric acid[19] by the catalytic method to 1-keto-1,2,3,4-tetrahydro-8,9-acephenanthrene[18] in 78% yield. Reference is also made below to a dimolecular product previously obtained[4] from 1,2-benz-10-anthranol.

Experimental Part[20]

Oxidation of 1,2-Benzanthracene.—A solution of 0.5 g. of colorless 1,2-benzanthracene and 1.5 g. of lead tetraacetate in 20 cc. of glacial acetic acid (distilled from permanganate) was warmed on the steam-bath for fifteen minutes and diluted with water to the point of saturation. On cooling there was obtained 0.43 g. (69%) of crude **1,2-benz-10-anthranyl acetate**, m. p. 130–140°, which yielded 0.33 g. (52%) of pure material, m. p. 160–163°, on crystallization from benzene–ligroin. This did not depress the melting point of the previously described sample.[4]

10-Acetoxymethyl-1,2-benzanthracene (VI).—The reaction was conducted as above at the steam-bath temperature, using 1.2 g. of 10-methyl-1,2-benzanthracene in 50 cc. of glacial acetic acid and 2.2 g. of lead tetraacetate in 50 cc. of this solvent. After fifteen minutes the solution was cooled well and diluted with two volumes of ice water. The precipitated material was collected and washed in the cold (otherwise it becomes gummy), dried in vacuum at 50°, and taken into ether–petroleum ether. An amorphous solid was obtained after concentrating the solution, and on three crystallizations from methanol the product formed pale greenish-yellow needles, m. p. 150.5–151.5°; yield, 0.25 g. (17%).

Anal. Calcd. for $C_{21}H_{16}O_2$: C, 83.98; H, 5.37. Found: C, 83.95; H, 5.53.

The substance did not depress the melting point of a sample of 10-acetoxymethyl-1,2-benzanthracene (of nearly identical m. p.) obtained from Professor J. von Braun.

Cyclization Experiments.—Following the exact procedure described[4] for the cyclization of 2-(α-naphthylmethyl)-benzoic acid, *o*-benzylbenzoic acid gave satisfactory **anthranyl-10-acetate** in 73% yield. It was not found easy to obtain material of constant melting point either from this source or from a sample prepared from anthrone; the best material melted at 134.5–135.5°. With 2-(4′-methyl-1′-naphthylmethyl)-benzoic acid[21] (5 g.), the amount of acetic anhydride was cut in half and the time of heating extended to one and one-half hours; the yield of **3-methoxy-10-acetoxy-1,2-benzanthracene,**[21] m. p. 193–194°, was 4.15 g. (86%). Two further crystallizations from glacial acetic acid gave colorless needles, m. p. 194–194.5°. Using the standard procedure,[4] γ-(3-acenaphthyl)-butyric acid[19] was converted in 78% yield into **1-keto-1′,2′,3′,4′-tetrahydro-8,9-acephenanthrene,**[19] m. p. 143–145°, and 2-(α-methylbenzyl)-1-naphthoic acid[10] (III) afforded **9-acetoxy-10-methyl-1,2-benzanthracene** (see below), m. p. 152.5–153.5°, in 95% yield.

9-Acetoxy-10-methyl-1,2-benzanthracene (IV).—Recrystallization of the cyclization product just mentioned from methanol gave small, colorless prisms, m. p. 153.5–154°. When mixed with 10-acetoxymethyl-1,2-benzanthracene the m. p. was depressed to 130–133°.

Anal. Calcd. for $C_{21}H_{16}O_2$: C, 83.98; H, 5.37. Found: C, 83.77; H, 5.33.

3-Acetoxy-10-methyl-1,2-benzanthracene.—The free hydroxy compound[4] was refluxed with acetic anhydride and fused sodium acetate and the product crystallized from methanol. It formed pale yellow prisms, m. p. 214–215°.

Anal. Calcd. for $C_{21}H_{16}O_2$: C, 83.98; H, 5.37. Found: C, 83.55; H, 5.49.

3,10-Dimethoxy-1,2-benzanthracene.—A mixture of 2.5 g. of 3-acetoxy-10-methyl-1,2-benzanthracene in 50 cc. of benzene and the Grignard reagent from 4.3 g. of *n*-butyl bromide in ether was refluxed for one hour, treated with 12 g. of dimethyl sulfate in 50 cc. of benzene, and refluxed for three hours. After hydrolysis with dilute acid a benzene solution of the product was passed through a tower of alumina to remove any hydroxy compound escaping methylation and the filtrate was evaporated. The residual material was very soluble in methanol or petroleum ether (b. p. 20–40°) and from the latter solvent it separated as transparent yellow cubes, m. p. 84–87°; yield, 1.2 g. (53%). This appeared to be a metastable form of the compound, for on being rubbed it changed to an opaque solid considerably less soluble than before. On recrystallization from ligroin (b. p. 60–70°) there was obtained 0.95 g. of light yellow, diamond-shaped prisms, m. p. 145–146.5°. Two more crystallizations from this solvent and one from methanol brought the melting point to 146–146.5°.

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(17) Cook, *J. Chem. Soc.*, 487 (1931).

(18) Cook, *ibid.*, 3273 (1931).

(19) Fieser and Peters, THIS JOURNAL, **54**, 4373 (1932).

(20) All melting points are corrected. Analyses by Mrs. G. M. Wellwood, Mrs. Verna R. Keevil, and the Arlington Laboratories.

(21) Fieser and Dietz, THIS JOURNAL, **51**, 3141 (1929).

Anal. Calcd. for $C_{20}H_{16}O_2$: C, 83.31; H, 5.60. Found: C, 83.08; H, 5.80.

9-Methoxy-10-methyl-1,2-benzanthracene.—This was prepared from the acetoxy compound IV (0.85 g.) by cleavage with the Grignard reagent from *n*-butyl bromide (1.95 g.) and methylation (8 cc. of dimethyl sulfate, several hours), as above, except that at the end of the reaction the mixture was treated with alkali and stirred for two hours and then acidified. From the benzene solution there was obtained material which after one crystallization from methanol melted at 143–144°; yield, 0.46 g. (60%). The substance formed thin, pale greenish-yellow, square plates and recrystallization did not alter the melting point.

Anal. Calcd. for $C_{20}H_{16}O$: C, 88.20; H, 5.92. Found: C, 88.11; H, 6.00.

Purification of Yellow 1,2,5,6-Dibenzanthracene.—A warm solution of 0.6 g. of lead tetraacetate in 150 cc. of glacial acetic acid was added in small portions to a solution of 3 g. of bright yellow commercial hydrocarbon in 150 cc. of benzene. The addition must be made slowly to prevent precipitation of the hydrocarbon. After refluxing for one-half hour, the solution was concentrated in the course of one hour to a volume of about 100 cc. and allowed to cool. There was obtained 2.5 g. (83%) of 1,2,5,6-dibenzanthracene in the form of colorless leaflets melting at 265–266° and having a blue fluorescence in ultraviolet light. In other experiments in this Laboratory with larger amounts of a new lot of crude hydrocarbon the recovery has been somewhat lower. On comparing samples of hydrocarbon purified and recrystallized in various ways, the best material was found to melt at 266–266.5°.

10-Amino-1,2-benzanthracene. (a) **From the Nitro Compound.**—The hydrocarbon (4.6 g.) was nitrated at room temperature according to Barnett and Matthews[7] and the crude product (2 g.) crystallized twice from alcohol (100 cc. per g.). There was obtained 1.38 g. (25%) of **10-nitro-1,2-benzanthracene**, m. p. 164–165°.

Hydrogenation of the nitro compound (1.26 g.) in ethyl acetate (75 cc.) was conducted in the presence of Adams catalyst (25 mg.), and the filtered solution was concentrated and treated with ligroin. The solid which separated afforded on recrystallization from ether–ligroin 0.6 g. (54%) of the amine in the form of yellow leaflets, m. p. 174–175°. This did not depress the melting point of the analytical sample described in the next section.

(b) **From the Hydroxy Compound.**—A mixture of 0.5 g. of 1,2-benz-10-anthranol, 5 cc. of concentrated ammonia solution, 2.5 g. of sodium bisulfite in 5 cc. of water, and 2 cc. of dioxane was heated in a sealed tube at 150° for fifty hours. After dilution with water the precipitated solid was dried in vacuum and crystallized from ether–ligroin, giving in all 0.37 g. (74%) of product melting in the range 163–168°. Three more crystallizations gave material melting constantly at 174.5–175.5°. Depending on the relative proportions of ether and ligroin, the amine separated as yellow leaflets or as long yellow needles.

Anal. Calcd. for $C_{18}H_{13}N$: N, 5.76. Found: N, 6.00.

3-(1,2-Benz-10-anthryl)-1,2-propylene Glycol Dibenzoate.—A mixture of 0.93 g. of 10-allyl-1,2-benzanthracene, 1.59 g. of silver benzoate, and 0.88 g. of iodine in 25 cc. of dry benzene was refluxed for fifteen hours on the steam-bath, the solution was filtered, concentrated, and treated with ligroin. This gave 1.5 g. (85%) of satisfactory material, m. p. 148–151°. Two further crystallizations from benzene gave clusters of fluffy, colorless needles, m. p. 152.5–153.5°.

Anal. Calcd. for $C_{35}H_{26}O_4$: C, 82.33; H, 5.13. Found: C, 82.44; H, 5.03.

?-Chloro-1,2-benz-10-anthrone(ol?).—A suspension of 1 g. of powdered 1,2-benz-10-anthranol in 10 cc. of dry ether was treated with 0.6 cc. of *t*-butyl hypochlorite and shaken for about ten minutes, when the orange solid had been converted into a yellow microcrystalline product. Collected and washed with ether, in which it is practically insoluble, the material weighed 0.87 g. (76%) and melted at about 125–130° with decomposition. After three crystallizations from ethyl acetate it melted constantly at 197–198°, dec., when inserted in a bath at 193° and heated rapidly. The substance contains chlorine and forms colorless, highly refractive prisms. It becomes yellow on storage or on being heated.

Anal. Calcd. for $C_{18}H_{18}OCl$: C, 77.58; H, 3.98. Found: C, 77.37; H, 3.94.

Dimolecular Product from 1,2-Benz-10-anthranol.[22]—The above chloro compound was converted on attempted crystallization from methanol into a sparingly soluble chlorine-free product. The same substance was obtained on shaking a suspension of 0.5 g. of 1,2-benz-10-anthranol in 20 cc. of methanol with 0.3 cc. of *t*-butyl hypochlorite for fifteen minutes and boiling the mixture for five minutes. The sparingly soluble material which precipitated (0.25 g.) on crystallization from acetic acid and from toluene formed fine, colorless needles, m. p. 261–263°, dec.

Anal. Calcd. for $C_{36}H_{24}O_2$: C, 88.49; H, 4.94. Found: C, 88.23; H, 4.73.

The substance gave no depression when mixed with the "condensation product" (m. p. 265–267°, dec.) previously described. The present method of preparation suggests that the substance is an oxidation product, and the composition, particularly as indicated by the earlier analyses, appears to be approximately that of a dianthrone (calcd. for $C_{36}H_{22}O_2$: C, 88.86; H, 4.56).

Summary

1,2-Benzanthracene reacts with lead tetraacetate to give the 10-acetoxy derivative, while with 10-methyl-1,2-benzanthracene the reagent attacks the methyl group and the product is 10-acetoxymethyl-1,2-benzanthracene. A very simple and effective method of removing the yellow impurity accompanying 1,2,5,6-dibenzanthrene prepared by the Elbs reaction consists in preferential oxidation with lead tetraacetate.

Various miscellaneous *meso*-substituted derivatives of 1,2-benzanthracene are described in this paper, and it is shown that nitration of the hydrocarbon gives the 10-nitro compound.

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CAMBRIDGE, MASSACHUSETTS

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[22] Ref. 4, pp. 1034–1035.