[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY OF ACTON TECHNICAL COLLEGE]

Abnormal Substitution Reactions of Anthracene and Phenanthrene

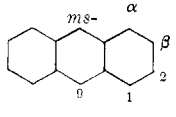
P. H. GORE

Received July 16, 1956

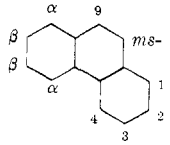
A reinterpretation has been attempted of the abnormal sulfonation and Friedel-Crafts acylation reactions of anthracene and phenanthrene. In each system it is believed that rapid initial substitution occurs at the hydrocarbon's most reactive position. This may be followed, provided solubility relationships are favorable, and because steric circumstances are apt, by a slower removal of the substituent and slow essentially irreversible substitution at the less reactive positions of the hydrocarbon.

In spite of the continued interest which is being shown in the reactivity of polycyclic aromatic systems, no satisfactory general explanation seems to have been advanced for those substitution reactions which proceed abnormally. These generally comprise sulfonation and Friedel-Crafts acylation processes. The hitherto neglected importance of reversibility in acylation reactions generally has recently been emphasized.[1] It is the purpose of this communication to reassess the evidence concerning the reversibility of the sulfonation reactions in the anthracene and phenanthrene fields, to supply further evidence of reversibility in acylation reactions, and to examine the factors governing reversibility in these systems.

Anthracene (I). The *meso* position is the most reactive in anthracene being preferentially substituted in most reactions excepting Friedel-Crafts and sulfonation reactions. Thus, sulfonation usually gives the 1- and 2-sulfonic acids only, as initial products. This result has been described as anomalous,[2,3] and the abnormal orientation ascribed to steric hindrance to the approach of the SO_3H^+ reagent.[cf. 4] An alternative explanation was envisaged by Clar,[5, cf. 6] *viz.* that primary attack occurs in the *meso* positions, and is followed by a wandering of the $-SO_3H$ group to the outer positions. The observed desulfonation of anthracene-9-sulfonic acid by means of dilute mineral acid[7] has now been confirmed, providing evidence favoring Clar's hypothesis. The reported formation, as intermediates in this reaction, of anthranol and sulfur dioxide[7] could not be confirmed, and a direct reversal of sulfonation is therefore preferred as a mechanism. The sodium salt of the related dianthryl-9-sulfonic acid could similarly be split to dianthryl and sulfuric acid without a trace of sulfur dioxide being formed, as claimed earlier.[7]



I



II

Sulfonation at the *meso*-position of anthracene may therefore be regarded as rapidly reversible, a consequence no doubt of the high reactivity at the *meso*-position, and of the steric instability of the bulky sulfonic acid group at this hindered position (see below). The α-positions may likewise be considered to be reversibly substituted, though more slowly, since anthracene-1,8-disulfonic acid is slowly desulfonated to anthracene by 75% sulfuric acid.[8] An actual isomerization of anthracene-1-sulfonic acid to the 2-sulfonic acid by the action of hot sulfuric acid has not been observed, further sulfonation intervening.[9] No comparable evidence of mobility appears to exist for the 2-anthryl position, which may be assumed to be stable. The ease of desulfonation seems therefore to decrease in the expected order of reactivity of these positions to electrophilic reagents (here H^+).

Recently, Gold and Long[10] have determined the rate of isotopic interchange at the 9-anthryl-position using deuterium-labeled anthracene and concentrated sulfuric acid. It was found that some loss of anthracene resulted through sulfonation, which was, however, slower than the isotope exchange. In view of the probably very rapid reversible sulfonation at the 9-anthryl-position, the observed exchange might in part be due to such a process, and unlikely to be wholly due to the mechanism put forward.

Certain uncatalyzed Friedel-Crafts type reactions cause substitutions in the 9- position of anthracene exclusively,[11,12] thus proceeding normally;

(1) Gore, *Chem. Revs.*, **55**, 229 (1955).
(2) deBruyn, *Ann. chim. Paris*, xi, **20**, 551 (1945).
(3) Braude and Fawcett, *J. Chem. Soc.*, 800 (1950).
(4) Badger, *The Structures and Reactions of the Aromatic Compounds*, University Press, Cambridge, 1954, p. 305.
(5) Clar, *Aromatische Kohlenwasserstoffe*, Springer Verlag, 1952, p. 177.
(6) Fukui, Yonezawa, and Shingu, *J. Chem. Phys.*, **20**, 722 (1952).
(7) Minaev and Fedorov, *J. Russ. Phys. Chem. Soc.*, **61**, 143 (1929).
(8) Berkenheim and Snamenskaya, *Zhur. Obshchei Khim.*, **4**, 31 (1934).
(9) Battegay and Brandt, *Bull. soc. chim. France*, 4, **33**, 1667 (1923).
(10) Gold and Long, *J. Am. Chem. Soc.*, **75**, 4543 (1953).
(11) Nenitzescu, Isacescu, and Ionescu, *Ann.*, **491**, 210 (1931).
(12) Liebermann and Zsuffa, *Ber. deut. chem. Ges.*, **44**, 202 (1911).

catalyzed acylations, however, have been regarded as abnormal. *Meso*-substitution is effected under quite mild experimental conditions, and usually with carbon bisulfide or other solvent, from which the reaction complex invariably precipitates, thus preventing subsequent reaction.[1] Moreover, abnormal products are obtained by use of solvents of good solvent power, such as nitrobenzene, which allows subsequent rearrangement to take place in solution of the *meso*- product first formed. For example, 9-anthryl methyl ketone, obtainable under mild conditions, can be converted into mixtures of 1- and 2-anthryl methyl ketones[2,13–16] under the more strenuous conditions approximating those for the preparation of the latter ketones. The migration hypothesis was first advanced by Linstead,[15] and indeed was very attractive. However, such observed migrations may alternatively be considered to have no parallel in the actual acylation process, particularly in nitrobenzene solution, where a solvated reaction complex is undoubtedly formed, which may not find spatial accommodataion in the sterically hindered *meso*- position and would thus enter the outer rings.[1] In one particular benzoylation experiment quoted in the literature,[17] the acyl group could enter the *meso*-position (giving a 79% yield) under specially mild conditions: at −10° and reaction time 5 min., supporting the migration hypothesis for substitution in the outer positions.

This has now been established unequivocally for acetylation in the case of benzene as solvent. A reaction, which is usually prolonged for 20 hr. to give 1- and 2-anthryl methyl ketones only, when interrupted after 3 hr. is found to give only 9-anthryl methyl ketone.

In such a system it is most unlikely that a reagent of large steric requirements is involved in the initial substitution stage.[18] In the system undergoing rearrangement it would appear that the over-all rate of substitution at the outer positions, very probably by a reagent of large steric requirements, is faster than the attack at the *meso*-positions by a reagent of small size, presumably the free acyl cation. One of the causes of the rapid rearrangement is therefore probably this duality of mechanism. It should be noted that of the two outer positions of anthracene the 1- position is the one substituted to a greater extent in nitrobenzene solution, which is in contrast to the case of naphthalene, in which the 2-position is favored.

In support of the concept of a deacylation-reacylation process is the smooth conversion of 9-anthryl methyl ketone to 9-anthryl phenyl ketone[14] under conditions identical with the preparation of the latter compound,[19] and the ready removal of the acyl substituent by boiling of 9-anthryl methyl ketone,[20] 9-anthryl phenyl ketone[19] or indeed 9-anthraldehyde (see Experimental) with a solution of sulfuric acid in glacial acetic acid. The deacylations with orthophosphoric acid of certain *o*-alkyl substituted acetophenones,[21–24] with nitric acid of acetylated pyrroles,[25] and with trichloroacetic acid of 3-acetyl guiaazulene,[26] appear to be analogous. The deacylation process clearly involves an electrophilic attack by H^+ with probable formation of the usual σ-complex transition state.

Summarizing then, the initial accumulation of the 9-isomer in anthracene acylations is due to its faster formation and low solubility of the ketone complex. The ultimate formation of the 1- and 2-isomers is the result of slow deacylation of the 9-isomer and the greater thermodynamic stability of the 1- and 2- isomers.

Phenanthrene (II). Studies of the reactivity of this hydrocarbon have led to conflicting results. In general the 9- position is the one most readily attacked, followed by the 1- position, *e.g.* nitration.[27] Both the Friedel-Crafts acylation and sulfonation reactions show the usual "abnormal" features. Werner[28, *cf.* 29] first noted that a low temperature of sulfonation favors formation of the 9-sulfonic acid, *i.e.* the normal product. At 120–130° this acid was reported to be formed only in traces, and at 170–180° not at all. At the higher temperatures phenanthrene 2- and 3-sulfonic acids predominate. Fieser[30] next showed that a reaction with sulfuric acid at 60° gave mainly phenanthrene 2- and 3-sulfonic acid, with less of the 9- and 1-acids, while at 120° increased yields of the 2- and 3-acids but no 1- and 9-acids were obtained. Fieser investigated the possibility of reversible sulfonation by heating the 9-, 2-, and 3-sulfonic acids separately with sulfuric acid. This failed to reveal any rearrangement, because of further sulfonation. It must be stressed, however, that in Fieser's[31] elucidation

(13) British Patent **289,585** (J. Y. Johnson to I. G. Farbenindustrie, A. G.).
(14) Batten, *D.I.C. Thesis, London*, 1933.
(15) Linstead, *Ann. Repts. on Progr. Chem. Chem. Soc. London*, **35**, 254 (1937).
(16) French Patent **633,071** (I. G. Farbenindustrie, A.G.).
(17) Krollpfeifer and Schutz, *Ber. deut. chem. Ges.*, **56**, 2360 (1923).
(18) Gore, *Chemistry & Industry*, **1954**, 1385.
(19) Cook, *J. Chem. Soc.*, 1282 (1926).
(20) Krollpfeifer, *Ber. deut. chem. Ges.*, **56**, 2363 (1923).
(21) Klages and Lickroth, *Ber. deut. chem. Ges.*, **32**, 1562 (1899).
(22) Arnold & Rondesvedt, *J. Am. Chem. Soc.*, **68**, 2177 (1946).
(23) Schubert and Latourette, *J. Am. Chem. Soc.*, **74**, 1829 (1952).
(24) Baddeley, *J. Chem. Soc.*, 232 (1944).
(25) Fischer and Zerweck, *Ber. deut. chem. Ges.*, **55**, 1949 (1922).
(26) Galloway, Reid, and Stafford, *Chemistry & Industry*, **1954**, 724.
(27) Dewar and Warford, *Chemistry & Industry*, **1956**, 98.
(28) Werner, Frey, Kunz, Lowenstein, Rekner, and Wack, *Ann.*, **321**, 248 (1902).
(29) Sandqvist, *Ann.*, **392**, 76 (1912).
(30) Feiser, *J. Am. Chem. Soc.*, **51**, 2460 (1929).
(31) Feiser, *J. Am. Chem. Soc.*, **51**, 2471 (1929).

of the structures of his disulfonic acids it was assumed that no rearrangement occurred either prior to or subsequent to further sulfonation. Ioffe later showed in a careful study of this reaction that the 9-sulfonic acid was formed even at higher temperatures, contrary to previous reports,[28] but quickly rearranged to other monosulfonic acids, the yield falling off to zero within a half to one hour. The 3-isomer was also shown to rearrange slowly to the 2-isomer. It appears to follow then[33] that in the sulfonation of this hydrocarbon there is competition between the formation and hydrolytic fission of sulfonic acids, proceeding at different rates for the different isomers, leading initially to appreciable amounts of the *meso*- and α-isomers and ultimately to an accumulation of the β-isomers, which are most stable to hydrolysis. The β-sulfonation of phenanthrene should therefore no longer be regarded as due to steric hindrance to attack at the α- positions.[34]

In most acylation reactions the 2- and 3-positions are favored, even in carbon bisulfide suspensions, though better over-all yields have been obtained in the presence of nitrobenzene.[1] *Meso*-substitution has been reported in a number of cases[35-37] using carbon bisulfide, a low yield being obtained in each case. An early acetylation of phenanthrene[35] was claimed to afford mainly the *meso*-isomer, but this claim was disproved some years later.[38] Since the reaction conditions cited were sufficiently mild, and as carbon bisulfide was being used as solvent, it was suggested[39] that the *meso*-isomer should here predominate, being first formed and precipitated from the solution as its aluminum chloride complex. This has recently been confirmed by Bavin and Dewar,[36] who showed that the *meso*-isomer is the main product, but that the β- isomers are formed likewise.

A report of *meso*-benzoylation of phenanthrene[35] in carbon bisulfide was not confirmed by later workers,[40,41] a 9% yield of 1-phenanthryl phenyl ketone being isolated instead, this being facilitated by the low solubility of its aluminum chloride complex. In the present work, by a modification of the experimental procedure, the yield of this ketone could be raised to 19%. The 1-position of phenanthrene is therefore of appreciable reactivity, and may be substituted under mild reaction conditions.*cf.* [36] Benzoylation in nitrobenzene solution[40,41] gives mainly the 3-isomer with lesser amounts of the 1- and 2-phenanthryl phenyl ketones. The general similarity between the acylation and the sulfonation of phenanthrene is emphasized by evidence, here presented, that 3-phenanthryl methyl ketone is slowly converted to the 2-isomer under Friedel-Crafts acetylating conditions. Treatment in nitrobenzene solution of phenanthrene with 1.4 equivalents of acetyl chloride and 2.2 equivalents of aluminum chloride gives mixtures of 2- and 3-phenanthryl methyl ketones, which may be separated quantitatively. After 6 hr. at 25°, the reaction mixture affords a 16% yield of 2- and a 62% yield of 3-phenanthryl methyl ketone (confirming values of 15% and 65%, respectively, previously reported[38]). On allowing the reaction to proceed at 25° for 17 hr., the yields are, respectively, 26% and 50%, indicating that during 11 hr. some 20% of the 3- ketone is converted to the more stable 2-ketone.

Strong circumstantial evidence therefore exists for some reversibility of acylation reactions with phenanthrene, the *meso*- and the 1-positions being initially formed but of lower stability than the 2- and 3-isomers which ultimately accumulate. However, treatment of 9-phenanthryl methyl ketone under Friedel-Crafts conditions with aluminum chloride or bromide[41] has failed to show any of the expected isomerization. This may perhaps be due to the absence of added hydrogen halide, without which reversible acylation cannot proceed.[1] Also, the sulfuric acid/acetic acid reagent is unable to deacylate either 9-phenanthraldehyde or 1-phenanthryl phenyl ketone; this is perhaps not unexpected since acyl groups must be displaced out of coplanarity much more in the *meso* anthyl series than in either position of the phenanthrene molecule,[42] the former therefore being the more easily replaceable.

In conclusion, it is of interest to consider briefly in what way the Friedel-Crafts acylation and sulfonation reactions are unusual and lead to the formation of abnormal isomers in the polycyclic aromatic series. The most reactive positions in anthracene and phenanthrene are the most central ones, which happen at the same time to be the sterically less accessible positions. When a substituent has entered the *meso*- position, it will cause interference to, and will therefore be twisted out of plane by, the *peri*- hydrogen atom(s). This is the position in particular where the entering group is a bulky solvated sulfonic acid group of an aluminum chloride-complexed acyl group. This out-of-plane distortion will cause an appreciable lowering of resonance stabilization, to below that possible at the unhindered positions, and proton catalyzed rearrangement will therefore proceed.

(32) Ioffe, *Zhur. Obshchei Khim.*, **3**, 448 (1933).
(33) Ioffe, *Org. Chem. Ind. U.S.S.R.*, **7**, 374 (1940).
(34) Feiser and Feiser, *Organic Chemistry*, D. C. Heath and Company, Boston, 1950, p. 805.
(35) Willgerodt and Albert, *J. prakt. Chem.*, 2, **84**, 383 (1911).
(36) Bavin and Dewar, *J. Chem. Soc.*, 166 (1956).
(37) Clar, *Ber. deut. chem. Ges.*, **62**, 350 (1929).
(38) Mosettig and de Kamp, *J. Am. Chem. Soc.*, **52**, 3704 (1930).
(39) Gore, personal communication to Dewar (1954).
(40) Bachmann, *J. Am. Chem. Soc.*, **57**, 555 (1935).
(41) Bachmann and Boatner, *J. Am. Chem. Soc.*, **58**, 2097 (1936).
(42) Jones, *J. Am. Chem. Soc.*, **67**, 2127 (1945).

EXPERIMENTAL

Acetylation of anthracene. (*a*) A mixture of 300 g. of benzene, 54 g. of anthracene and 72 g. of acetyl chloride was stirred at 0°, and 120 g. of powdered aluminum chloride was added in portions, the temperature being maintained at 5–10°. Stirring was continued for a further 2.50 hr. The red complex which had precipitated was collected on a sinter-funnel, washed with dry benzene, and hydrolyzed by adding to a stirred mixture of ice and 5 *N* hydrochloric acid. The benzene extract was washed with water, dried over sodium sulfate, filtered through a short column of alumina, and the filtrate evaporated. The residue was finally heated at 1 mm. and 100°, in order to remove acetophenone, and yielded 36 g. of 9-anthryl methyl ketone, m.p. 76°, on crystallization from benzene.

(*b*) As for (*a*). Stirring was continued for 1 hr., after addition of the aluminum chloride, at 5–10°, and then for 20 hr. at 20°. The product was isolated as in (*a*). The chromatographed mixture was crystallized from benzene, to give 4.2 g. of 2-anthryl methyl ketone, m.p. 185–186°; the mother liquors were evaporated and the residue crystallized from ethyl acetate, giving 22 g. of 1-anthryl methyl ketone, m.p. 105–106°.

Deformylation of 9-anthraldehyde. A solution of 1 g. of 9-anthraldehyde in 18 ml. of glacial acetic acid was treated with 2 ml. of concentrated sulfuric acid, and the mixture refluxed for 80 min., when an aliquot no longer gave a positive test with 2,4-dinitrophenylhydrazine solution, and then diluted with water. The precipitate (0.7 g.) on recrystallization from dilute acetic acid afforded 0.4 g. of anthracene, m.p. and mixed m.p. 210–212°, which on oxidation with chromic acid in glacial acetic acid gave anthraquinone, m.p. and mixed m.p. 282°–283°.

Sodium anthracene 9-sulfonate. Prepared and purified according to the method of Minaev and Fedorov.[7] Treatment of the salt with 3 *N* hydrochloric acid immediately produced, in the cold, some sulfur dioxide. Subsequent boiling produced no further amounts of the gas. The reported formation of anthracene was confirmed, but anthranol could not be detected.

Sodium 9,9'-dianthryl-10-sulfonate was prepared by the method of Minaev and Fedorov.[7] One gram of the salt was boiled for 3.5 hr. with 25 ml. of 4 *N* hydrochloric acid and 20 ml. of acetic acid. The reaction mixture on dilution with water gave 0.7 g. of dianthryl, m.p. 311–312°, after recrystallization from acetic acid.

1-Phenanthryl phenyl ketone. A mixture of 114 ml. of benzoyl chloride and 150 g. of aluminum chloride was heated until a clear solution resulted. The mixture was cooled, 850 ml. of carbon bisulfide was added, and the complex dissolved by stirring. One hundred seventy-five grams of phenanthrene was added to this solution during 20 min. Evolution of hydrogen chloride, at first rapid, ceased after a further 20 min., when the mixture was cooled to 0°. The precipitated complex was collected and decomposed by adding to a mixture of ice and 10 *N* hydrochloric acid. The residual carbon bisulfide was allowed to evaporate, and 38 g. of 1-phenanthryl phenyl ketone, m.p. 141–142°, was collected by filtration. A further crop of 2.4 g. of the ketone was obtained by extracting the above filtrate with chloroform, washing the extract with water, concentrating to 120 ml., adding 50 ml. of ether and setting aside at 0°. The pure ketone, obtained by recrystallization from acetone, had a melting point of 148–149.5° (literature m.p. 148–149°[40,41]).

Acetylation of phenanthrene. Using the method of Mosettig and de Kamp,[38] the reaction mixture being kept at 25°, (*a*) after 6 hr. a 16% yield of 2-phenanthryl methyl ketone, m.p. 142.5–143.5°, and a 62% yield of 3-phenanthryl methyl ketone, m.p. 72.5–73.5°, were obtained by careful fractional crystallization; (*b*) after 17 hr. the yields were 26% and 50%, respectively.

Attempted deacylations. (*a*) *1-Phenanthryl phenyl ketone.* A solution of 1 g. of the ketone in 50 ml. of glacial acetic acid, containing 5 ml. of concentrated sulfuric acid, was refluxed for 4.5 hr., and then poured into water. The product (0.98 g.) was the unchanged ketone, m.p. and mixed m.p. 144–145°.

(*b*) *9-Phenanthraldehyde.* One gram of the aldehyde was treated as in (*a*) for 3.5 hr. The product (0.9 g.) proved to be unchanged aldehyde, m.p. 94°, pure (m.p. and mixed m.p. 100°) after one recrystallization.

LONDON, ENGLAND

[CONTRIBUTION FROM AVERY LABORATORY, UNIVERSITY OF NEBRASKA]

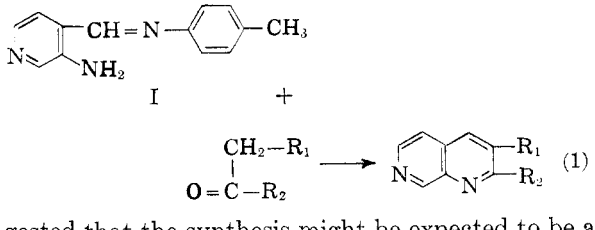
Naphthyridines. II. Synthesis of 1,7-Naphthyridines by Borsche Synthesis[1,2]

HENRY E. BAUMGARTEN AND KENNETH C. COOK

Received July 13, 1956

The preparation of six new 1,7-naphthyridines (II–VII) by condensation of the appropriate carbonyl compound with N-(3-amino-4-picolylidene)-*p*-toluidine is described.

In an earlier communication[2] the synthesis of two 1,7-naphthyridines using the Borsche[3] modification of the Friedlander synthesis was reported. The preparative sequence employed consisted of the synthesis of N-(3-amino-4-picolylidene)-*p*-toluidine (I) and the condensation of I with an appropriate carbonyl compound (Equation 1). It was suggested that the synthesis might be expected to be a general one for the preparation of 1,7-naphthyri-



(1)

(1) This work was supported in part by grant G-1090 of the National Science Foundation.

(2) Paper I, Baumgarten and Krieger, *J. Am. Chem. Soc.*, **77**, 2438 (1955).

(3) Borsche, Doeller, and Wagner-Roemich, *Ber.*, **76**, 1099 (1943); Borsche and Barthenhier, *Ann.*, **548**, 50 (1941); Borsche, Wagner-Roemich, and Barthenhier, *Ann.*, **550**, 165 (1942); Borsche and Ried, *Ann.*, **554**, 269 (1943).