[CONTRIBUTION FROM THE COBB CHEMICAL LABORATORY, UNIVERSITY OF VIRGINIA]

# STUDIES IN THE PHENANTHRENE SERIES. XIX. NAPHTHOQUINOLINES SYNTHESIZED FROM AMINOPHENANTHRENES*,[1]

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The considerations that led us to undertake the synthesis of compounds derived from condensed ring systems consisting of a phenanthrene nucleus and a pyridine ring, have been stated in the first communication on naphthoquinolines.[1] In this paper we shall set forth the structural proof of the previously described naphthoquinoline prepared from 3-aminophenanthrene, and the synthesis and the structural proof of the naphthoquinolines and their derivatives that were prepared from 2-aminophenanthrene and 2-amino-9,10-dihydrophenanthrene.

We obtained our starting materials, the various aminophenanthrenes by the Beckmann rearrangement of the oximes of the corresponding acetylphenanthrenes. This rather simple and very convenient method for large-scale preparation of aminophenanthrenes has been employed recently and independently by Adelson and Bogert,[2] Bachmann and Boatner,[3] Fieser and Price,[4] and in our laboratory.[1] These authors used phosphorus pentachloride in ether or benzene, while we employed as rearranging agent hydrogen chloride in a mixture of glacial acetic acid and acetic anhydride. Furthermore we used only sterically homogeneous oximes. Although 2-amino-9,10-dihydrophenanthrene may be prepared analogously,[5] we found a quicker and more convenient way to this amine through the corresponding nitro compound which, itself, was obtained in a yield of 65 per cent. by nitration of 9,10-dihydrophenanthrene.[6]

In the Skraup quinoline synthesis, applied to 3-aminophenanthrene

* The work reported in this paper is part of a unification of effort by a number of agencies having responsibility for the solution of the problem of drug addiction. The organizations taking part are: The Rockefeller Foundation, the National Research Council, the U. S. Public Health Service, the U. S. Bureau of Narcotics, the University of Virginia, and the University of Michigan.

[1] First paper on naphthoquinolines, MOSETTIG AND KRUEGER, *J. Am. Chem. Soc.*, **58**, 1311 (1936).

[2] ADELSON AND BOGERT, *ibid.*, **58**, 653 (1936).

[3] BACHMANN AND BOATNER, *ibid.*, **58**, 857, 2097 (1936).

[4] FIESER AND PRICE, *ibid.*, **58**, 1838 (1936).

[5] BURGER AND MOSETTIG, *ibid.*, **59**, 1302 (1937).

[6] See following communication (XX).

(I), naphtho[1,2-*f*]quinoline (II) was produced in a yield of 45 per cent.[1],† Careful examination, in several experiments, of the reaction mixture indicated that no isomeric naphthoquinoline had been formed. Ring closure had taken place only in one position, namely in position 4.

The reduction of this naphthoquinoline was studied under a variety of experimental conditions. Electrolytic reduction, reduction with tin and hydrochloric acid, and with sodium and alcohol did not give satisfactory results. The substance was either incompletely reduced, or partly resinous products that could neither be separated nor characterized appeared. When platinum oxide was used as catalyst and glacial acetic acid as solvent in the hydrogenation, the base (II) absorbed hydrogen exceedingly slowly, in contrast to its isomers IX and XXII. The reaction mixture contained at least two hydrogenation products, a tetrahydro derivative (III) and an octahydro derivative (IV). The pure tetrahydro compound, under the same conditions, was much more quickly hydrogenated than the naphthoquinoline itself. When the hydrogenation of the naphthoquinoline was allowed to go to completion, only the octahydro derivative could be isolated. The tetrahydro compound is most readily prepared by high-pressure hydrogenation at 140° using Adkins' chromite catalyst.[7] When the temperature was raised to 170°, the yield dropped to 45 per cent.; however, no octahydro derivative could be isolated in such an experiment. The latter compound was rather conveniently obtained by hydrogenation of the tetrahydro compound, using platinum oxide as catalyst. 4-Methyl-1,2,3,4-tetrahydronaphtho[1,2-*f*]quinoline (VI) was prepared by thermal decomposition of the methiodide (V) which itself was obtained by complete methylation of 1,2,3,4-tetrahydronaphtho[1,2-*f*] quinoline (III).

The methiodide (V), when boiled in aqueous solution with sodium amalgam (Emde degradation), gave an ether-soluble oily reaction product which was not homogeneous. A partial separation was effected by slow vacuum distillation. The oily base in the distillate was converted to the hydrochloride, which was further purified by crystallization. Of the three theoretically possible fissions in the degradation,[8] apparently the one be-

† The orientation, numbering and names of the heterocyclic compounds included in this paper have been recommended to us by Dr. Capell through the kindness of Dr. Crane. *Cf.* PATTERSON, *J. Am. Chem. Soc.*, **50**, 3074 (1928).

[7] The wide usefulness of this catalyst, particularly in selective hydrogenation, has been repeatedly demonstrated by Adkins and his co-workers. See the monograph "Reactions of Hydrogen with Organic Compounds over Copper-Chromium Oxide and Nickel Catalysts" by HOMER ADKINS, The University of Wisconsin Press, **1937**.

[8] (*a*) *Cf.* EMDE AND KULL, "Degradation of Quaternary Ammonium Compounds with Sodium Amalgam, a Review," *Arch. Pharm.*, **272**, 469 (1934). (*b*) See also MOSETTIG AND ROBINSON, *J. Am. Chem. Soc.*, **57**, 902 (1935).

tween the nitrogen atom and the adjacent benzene nucleus predominated. Analyses of the degradation product and its salts for carbon and hydrogen do not indicate clearly whether or not, simultaneously with ring opening, reduction of the 9,10-double bond of phenanthrene (7,8 of the naphthoquinoline derivative) had taken place. The degradation product was different in every respect from 2-[3-(dimethylamino)-*n*-propyl] phenanthrene and also from 2-[3-(dimethylamino)-*n*-propyl]-9,10-dihydrophenanthrene. To the degradation product, therefore, must be assigned the formula of a 4-[3-(dimethylamino)-*n*-propyl] phenanthrene (VII), or the less probable formula of a 4-[3-(dimethylamino)-*n*-propyl]-9,10-dihydrophenanthrene. Ring closure in the Skraup synthesis had taken place in position 4, yielding naphtho[1,2-*f*]quinoline (II). Although 4-acetylphenanthrene, which might serve as starting material in the synthesis of the propylamino derivative (VII), is known through the work of Fieser,[9] the synthesis of VII was not attempted on account of the difficult and long route to this ketone.

The remote possibility that the degradation product might be a 3-dimethylamino-4-*n*-propylphenanthrene (or 3-dimethylamino-2-*n*-propylphenanthrene or a corresponding 9,10-dihydro derivative) can be excluded through the known facts that such compounds form methiodides only with difficulty[10] and that, in our experience, salts of phenanthrene derivatives carrying the dimethylamino group directly on the nucleus hydrolyze strongly. In contrast to such behavior, the degradation product forms the methiodide readily, and its hydrochloride does not hydrolyze. It is, of course, not impossible that such compounds carrying the dimethylamino group directly on the nucleus, and also the tertiary base VI, are present in the residue from the first vacuum distillation of the crude degradation products.

The structure of the tetrahydro compound (III) seems to be sufficiently supported by the empirical rule that in the hydrogenation of quinolines by various means, the pyridine portion is attacked first, further, by the formation of an *N*-methyl derivative (VI) and by the course of the degradation. More difficult is the assignment of a structural formula to the octahydro compound. Neglecting the possibility of a shift of hydrogen atoms during the hydrogenation from the tetrahydro compound to the octahydro compound, formulas IV-*a* and IV-*b* have to be considered first, since they appear to be the only theoretically possible formulas that do not contain isolated double bonds. Without experimental evidence, we prefer formula IV-*a* to formula IV-*b*.

[9] FIESER, FIESER, AND HERSHBERG, *J. Am. Chem. Soc.*, **58**, 2322 (1936).
[10] VON BRAUM AND AUST, *Ber.*, **49**, 501 (1916).

Somewhat similar compounds were obtained by Bamberger and co-workers[11] in the sodium-amyl alcohol reduction of "β-naphthoquinolines" or their tetrahydro derivatives to the corresponding octahydro compounds. (A "β-naphthoquinoline" which is, in the nomenclature used in this paper, a benzo[*f*]quinoline, may be visualized by omitting from formula II the terminal benzene nucleus.) The relatively strong basicity of octahydronaphtho[1,2-*f*] quinoline would speak, on the basis of Bamberger's experiments for formula IV-*b*, this being the analog of the "ac. octahydro-β-naphthoquinoline." The stronger basicity, however, of IV in comparison with III does not necessarily imply that the benzene nucleus C in III had been hydrogenated. Any higher degree of hydrogenation, irrespective of the location of the additional hydrogens, may increase the basicity. Furthermore the fact that in Bamberger's experiments the "ac. octahydro-β-naphthoquinolines" are formed only in minimal yields, the "ar. octahydro-β-naphthoquinolines" being the main products, and finally the difference between Bamberger's reducing agents and ours apparently do not permit drawing analogies from this author's experiments as a support in the decision between formulas IV-*a* and IV-*b* for octahydronaphtho[1,2-*f*]quinoline.

The hydrochloride of the octahydro compound does not hydrolyze, in contrast to the hydrochloride of the tetrahydro compound and of the naphthoquinoline itself. Under the conditions imposed in the Emde degradation of the tetrahydro derivative, the methiodide of the *N*-methyl-octahydro compound was hardly attacked. By prolonged boiling with sodium amalgam, chiefly ether-insoluble products were obtained. The thermal decomposition of the methiodide does not result in the formation of an *N*-methyl derivative, but rather in a deep-seated decomposition.

In the Skraup synthesis applied to 2-aminophenanthrene (VIII) a homogeneous naphthoquinoline was obtained in a yield of 80–90 per cent., to which the structure of a naphtho[2,1-*f*]quinoline (IX) must be assigned on the basis of the following evidence. A tetrahydro compound (X) was readily obtained by catalytic hydrogenation, using platinum oxide as catalyst. The same compound was obtained by high pressure hydrogenation at 140°, using chromite catalyst. By employing a higher temperature, a homogeneous hydro derivative could be isolated from the reaction mixture, to which we assigned the structure of a hexahydronaphthoquinoline (XI).

The Emde degradation of the 1-methyl-1,2,3,4-tetrahydronaphtho-[2,1-*f*]quinoline methiodide (XIII) was carried out as in the 1,2-*f* series. The carbon-hydrogen analyses of the final, carefully purified degradation product do not decide the question whether or not simultaneous hydrogenation of the 9,10 double bond (of the phenanthrene nucleus) has taken place. The degradation product (XVII) is obviously different from 1-[3-(dimethylamino)-*n*-propyl]-9,10-dihydrophenanthrene (XVIII) obtained by degradation of the methiodide (XV) of 1-methyl-1,2,3,4,5,6-hexahydronaphtho[2,1-*f*]quinoline (XVI). Furthermore it is different from

[11] BAMBERGER AND MÜLLER, *ibid.*, **24**, 2648 (1891). BAMBERGER AND STRASSER, *ibid.*, **24**, 2662 (1891).

synthetic 3-[3-(dimethylamino)-*n*-propyl]phenanthrene (XXX) and from 3-[3-(dimethylamino)-*n*-propyl]9,10-dihydrophenanthrene (XXIX), which was obtained in the degradation of the methiodide (XXVII) of 8-methyl-5,6,8,9,10,11-hexahydronaphtho[1,2-*g*]quinoline, as was shown by comparison of the respective hydrochlorides and picrates. Degradation product XVII must therefore be a 1-[3-(dimethylamino)-*n*-propyl]phenanthrene. Ring closure in the Skraup synthesis with 2-aminophenanthrene had taken place in position 1. We did not attempt the preparation of XVII from 1-acetylphenanthrene that has been synthesized recently by Bachmann and Boatner[3] through a long and difficult series of reactions. A final structural proof of IX is found in the fact that IX is not identical with naphtho[1,2-*g*]quinoline (XXII), which was obtained by dehydrogenation of 5,6-dihydronaphtho[1,2-*g*]quinoline (XXI).

To the tetrahydronaphthoquinoline compound in this series, formula X must be assigned on the basis of the results of catalytic hydrogenation, and the course of degradation. For the more highly hydrogenated derivative, which appears to be, from its carbon-hydrogen analyses, a hexahydro derivative, we assume as most likely the structure of a 1,2,3,4,5,6-hexahydro compound (XI). As next most probable might be considered the structure of a 1,2,3,4,11,12-hexahydro compound (XII). If this were correct, the Emde degradation of the methiodide of the 1-methyl derivative of XII should lead to a 1-[3-(dimethylamino)-*n*-propyl]-3,4-dihydrophenanthrene (XIX) which, very likely, would be further hydrogenated to a tetrahydrophenanthrene derivative during degradation. This did not take place. It is worthy of mention that the methiodide (XV), when boiled in aqueous solution, partially decomposed into the *N*-methyl derivative (XVI) and methyl iodide.

By application of Skraup's method to 2-amino-9,10-dihydrophenanthrene (XX) a dihydronaphthoquinoline (XXI) was obtained in a yield of 50 per cent. The hydrogenation of this compound, using platinum oxide catalyst proceeds moderately rapidly, yielding the hexahydronaphthoquinoline (XXIV). In the high-pressure hydrogenation this hexahydro derivative is formed in surprisingly low yields, not exceeding 40 per cent. It was converted to the methiodide (XXVII) of 8-methyl-5,6,8,9,10,11-hexahydronaphtho[1,2-*g*]quinoline which in the Emde degradation yielded 3-[3-(dimethylamino)-*n*-propyl]-9,10-dihydrophenanthrene (XXIX). This amine could be dehydrogenated (in one experiment only) to 3-[3-(dimethylamino)-*n*-propyl]phenanthrene (XXX).

By palladium dehydrogenation of the dihydronaphthoquinoline (XXI) a naphthoquinoline (XXII) was obtained in an average yield of 50 per cent., which was different in every respect from the naphthoquinoline (IX) prepared from 2-aminophenanthrene. In hydrogenation under atmospheric pressure, using platinum oxide catalyst, it absorbs two moles

of hydrogen, decidedly faster than its isomers II and IX, to produce the tetrahydro derivative (XXV).

It is suggestive that this difference in speed of hydrogen absorption is based on the structural difference of II and IX on the one hand, and XXII on the other hand. In II and IX, the original phenanthrene structure, in respect to the location of the double bonds, has not been changed, both structural formulas containing a naphthalene and quinoline nucleus in which the double bonds are symmetrically arranged. This is not the case in naphtho[1,2-*g*]quinoline, which may be depicted as XXII or XXIII. In formula XXII the double bonds are arranged as in the analogous isocyclic 1,2-benzanthracene formula advanced by Fieser and Lothrop.[12]

The methiodide (XXVIII) of 8-methyl-8,9,10,11-tetrahydronaphtho[1,2-*g*]quinoline, obtained by complete methylation of XXV gave, in the Emde degradation, a product XXX that proved to be identical with synthetic 3-[3-(dimethylamino)-*n*-propyl]phenanthrene. This constitutes a direct structural proof of naphtho[1,2-*g*]quinoline (XXII) and its dihydro derivative (XXI), and consequently an indirect proof of the structure of naphtho[2,1-*f*]quinoline (IX).

3-[3-(Dimethylamino)-*n*-propyl]phenanthrene and 2-[3-(dimethylamino)-*n*-propy]-9,10-dihydrophenanthrene were synthesized as follows:

$$RCOCH_3 \xrightarrow{CH_2O,NH(CH_3)_2} RCOCH_2CH_2N(CH_3)_2 \xrightarrow{Pt,H_2} RCHOHCH_2CH_2N(CH_3)_2 \xrightarrow{PCl_5}$$

$$RCHClCH_2CH_2N(CH_3)_2 \xrightarrow{Pd,H_2} RCH_2CH_2CH_2N(CH_3)_2$$

R = $C_{14}H_9-$ or $C_{14}H_{11}-$

Assuming a symmetrical arrangement of double bonds in naphthalene and analogously in quinoline, Marckwald[13] formulated the rule that a condensation of a pyridine nucleus to a benzene nucleus takes place only when the two condensing carbon atoms are connected by a double bond. Apparently this rule has been upheld with rare exceptions[14] up to the present. If one adopts, furthermore, a phenanthrene structure with fixed double bonds, as postulated by Fieser and Young[15] it is to be expected that in the Skraup synthesis, starting from 2-aminophenanthrene, ring closure will take place in position 1, and starting from 3-aminophenanthrene, in position 4, since positions 2 and 1 and positions 3 and 4 are connected by double bonds.

On the other hand there exists apparently and quite consistently a

[12] FIESER AND LOTHROP, *J. Am. Chem. Soc.*, **58**, 749 (1936). See also FIESER AND HERSHBERG, *ibid.*, **59**, 2502 (1937).

[13] MARCKWALD, *Ann.*, **274**, 331 (1893). Compare LELLMANN AND SCHMIDT, *Ber.*, **20**, 3154 (1887); FIESER AND LOTHROP, *J. Am. Chem. Soc.*, **57**, 1459 (1935); FIESER, in GILMAN, "Organic Chemistry," Wiley, New York, **1938**, Vol. I, 89.

[14] FRIES, WALTER, AND SCHILLING, *Ann.*, **516**, 248 (1935).

[15] FIESER AND YOUNG, *J. Am. Chem. Soc.*, **53**, 4120 (1931).

parallelism between the fusion of the isocyclic carbon ring and the heterocyclic nitrogen-containing ring to a benzene nucleus. Thus, in the Skraup synthesis on 2-aminonaphthalene,[16] as well as in the ring closure of γ-(2-naphthyl)-*n*-butyric acid,[17] the angular tricyclic ring systems are formed. Like the pyridine ring, the isocyclic carbon ring needs, or at least prefers, the double bond for the condensation.[18] In the dehydration of γ-(2-phenanthryl)-*n*-butyric acid and β-(2-phenanthryl)propionic acid ring closure, forming the six- and five-membered rings, takes place exclusively, or to a very large extent, in position 1,[19] as in the application of the Skraup synthesis to 2-aminophenanthrene. Surprisingly, however, all ring closures of side-chains located in position 3 and involving the attachment of a *six*-membered carbon atom ring take place exclusively, or to a very large extent, in position 2. From γ-(3-phenanthryl)-*n*-butyric acid[19a] and γ-(3-phenanthryl)-α-methyl-*n*-butyric acid[20] only 1,2-benzanthracene derivatives were obtained. Equally, by hydrogenation and subsequent cyclization of methyl-(3-phenanthryl)itaconic acid[21] cyclization takes place with the formation of a 1,2-benzanthracene derivative. In this instance, however, a very small amount of the isomeric 3,4-benzophenanthrene derivative was isolated. We expected, therefore, that the ring closure of the pyridine nucleus, in the Skraup synthesis applied to 3-aminophenanthrene, also would extend to position 2. This, however, was not the case, as we have shown in this investigation. It is of interest that β-(3-phenanthryl)propionic acid[19b] and β-(3-phenanthryl)-*n*-butyric acid[22] cyclize principally at position 4, forming the cyclopenteno ring along the double bond. We believe that the difference, in respect to cyclization, of the three-carbon side chains —C—C—C— and the side chain —N—C—C—C— on the one hand, and the four-carbon side chain —C—C—C—C— on the other hand must be attributed to steric influences.[23] It has been shown by Burger and Mosettig[5] that, in the 9,10-

[16] SKRAUP AND COBENZL, *Monatsh.*, **4**, 436 (1883); *J. Chem. Soc. Abstracts*, **44**, 1010 (1883).

[17] SCHROETER, MÜLLER, AND HUANG, *Ber.*, **62**, 645 (1929); HAWORTH, *J. Chem. Soc.*, **1932**, 1125.

[18] See the ring closure of α-(2-naphthyl)-o-amino-cinnamic acid in the Pschorr phenanthrene synthesis [COOK, *J. Chem. Soc.*, **1931**, 2524] and the low yield in the ring closure of γ-(8-methyl-2-naphthyl)-n-butyric acid to 1-keto-5-methyl-1,2,3,4-tetrahydroanthracene where a phenanthrene ring closure is sterically inhibited [HAWORTH AND SHELDRICK, *J. Chem. Soc.*, **1934**, 1950.]

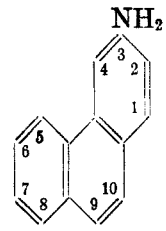
[19] (*a*) HAWORTH AND MAVIN, *J. Chem. Soc.*, **1933**, 1012. (*b*) BACHMANN AND KLOETZEL, *J. Am. Chem. Soc.*, **59**, 2207 (1937). (*c*) BERGMANN AND HILLEMANN *Ber.*, **66**, 1302 (1933).

[20] COOK AND HASLEWOOD, *J. Chem. Soc.*, **1934**, 428.

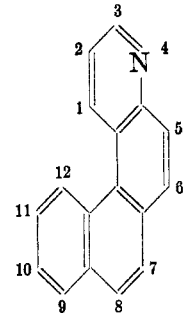
[21] COOK AND ROBINSON, *ibid.*, **1938**, 505.

[22] HILLEMANN, *Ber.*, **69**, 2610 (1936).

[23] Compare BERGMANN AND BLUM-BERGMANN, *J. Am. Chem. Soc.*, **59**, 1574 (1937).



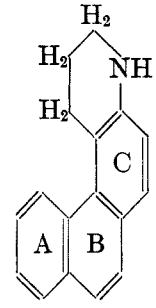
I



II, Naphtho[21,2-*f*]quinoline

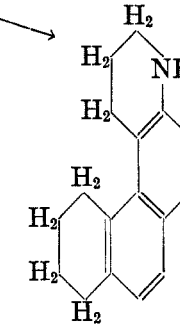
Chromite or $PtO_2$

$PtO_2$



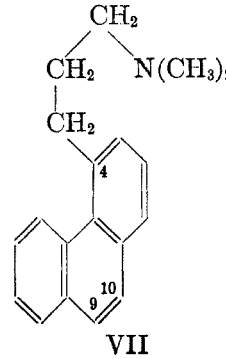
III

$PtO_2$

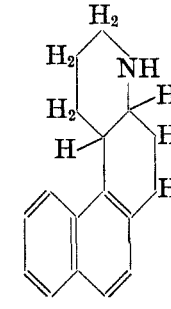


IV*a*

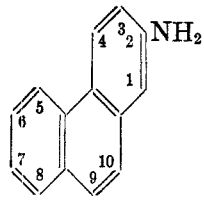
V, Methiodide of *N*-methyl derivative ⇌ VI, *N*-Methyl derivative of III



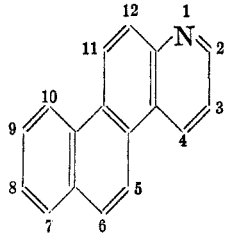
VII



IV*b*



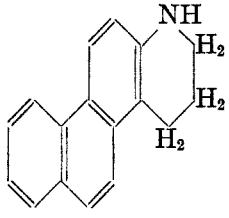
VIII



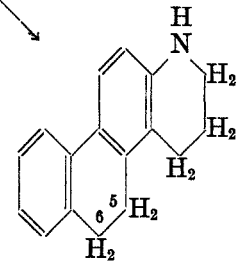
IX, Naphtho[2,1-*f*]quinoline

Chromite or $PtO_2$

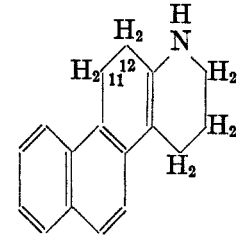
Chromite



X



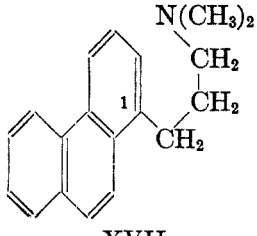
XI



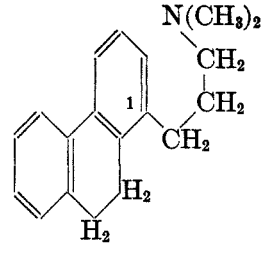
XII

XIII, Methiodide ⇌ XIV, *N*-Methyl derivative of *N*-methyl derivative of X

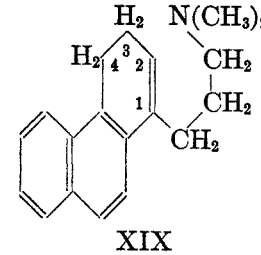
XV, Methiodide ⇌ XVI, *N*-Methyl derivative of *N*-methyl derivative of XI



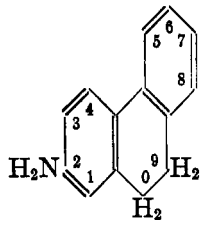
XVII



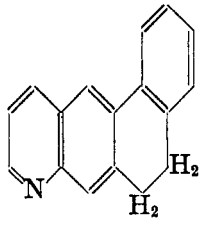
XVIII



XIX

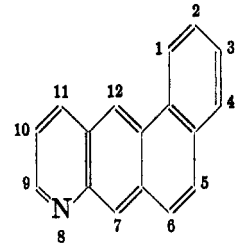


XX

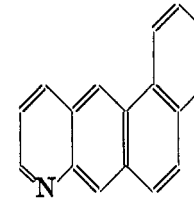


XXI

Pd



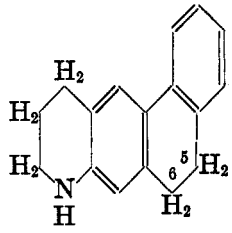
XXII, Naphtho[1,2-*g*]-quinoline



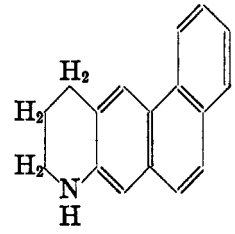
XXIII

Chromite or $PtO_2$

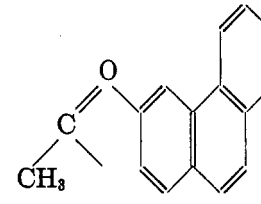
$PtO_2$



XXIV



XXV



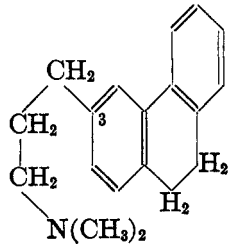
XXVI

XXVII, Methiodide of *N*-methyl derivative of XXIV

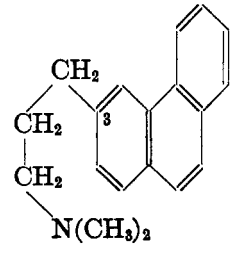
XXVIII, Methiodide of *N*-methyl derivative of XXV

4 steps

Pd



XXIX



XXX

dihydrophenanthrene series, three- and four-carbon side-chains attached to position 2, when forming five- and six-membered rings, will be directed entirely or chiefly to position 3. In striking analogy to this fact, in the quinoline synthesis applied to 2-amino-9,10-dihydrophenanthrene, ring closure takes place entirely in position 3. Furthermore, such analogy can be adduced in the tetrahydronaphthalene series. In application of the Skraup synthesis to *ar.*-tetrahydro-2-naphthyl amine, ring closure takes place in position 1 (30 per cent.), as well as in position 3 (60 per cent.).[24] Ring closure of the analogous γ-[7-(1,2,3,4-tetrahydro)naphthyl]-*n*-butyric acid, similarly takes place in positions 6 and 8, the anthracene and phenanthrene derivatives being formed in about equal amounts.[25] This discussion is not intended to be a support to any of the structural formulas that have been proposed for di- or polycyclic ring systems, but rather, points out the striking regularities and analogies in the attachments of rings to such systems which are satisfactorily expressed by the customary formulas with alternating single and double bonds.

4-Methyl-1,2,3,4-tetrahydronaphtho[1,2-*f*]quinoline (VI) and 1-methyl-1,2,3,4-tetrahydronaphtho[2,1-*f*]quinoline (XIV) were investigated pharmacologically by Dr. N. B. Eddy at the University of Michigan. VI showed only a slight analgesic action (200 mg. per kg.) in the cat, while XIV shows no analgesic action at all at this dosage. Both substances cause slight depression in doses of 200 mg.[26]

On account of the structural analogy of naphtho[1,2-*f*]quinoline (II), naphtho[2,1-*f*]quinoline (IX), and naphtho[1,2-*g*]quinoline (XXII) to 3,4-benzophenanthrene, chrysene, and 1,2-benzanthracene respectively, Dr. Carl Voegtlin of the National Institute of Health suggested the investigation of the naphthoquinolines II, IX, XXI, and XXII for carcinogenic activity.[27] The result of the tests will be reported elsewhere.

## EXPERIMENTAL

### *Preparation of 2- and 3-Aminophenanthrene*

A sterically nearly homogeneous oxime of 3-acetylphenanthrene, melting at 142–144° (the pure *trans* form melts at 144–145°) was conveniently prepared by the method employed by Bachmann and Boatner.[3] The yield was quantitative.

The preparation of a sterically homogeneous oxime of 2-acetylphenanthrene has been described previously.[1]

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[24] VON BRAUN AND GRUBER, *Ber.*, **55**, 1711 (1922).

[25] SCHROETER, *ibid.*, **57**, 2003, 2017 (1924); KROLLPFEIFFER AND SCHÄFER, *ibid.*, **56**, 628 (1923).

[26] EDDY, unpublished results.

[27] Some ring-nitrogen-containing analogs of polycyclic hydrocarbons, as dibenzacridines, are known to show some carcinogenic activity. See COOK, *Ber.*, **A69**, 38 (1936).

*3-Aminophenanthrene.*—Fifty grams of the pure 3-oxime was dissolved in a mixture of 240 cc. of glacial acetic acid and 100 cc. of acetic anhydride. Dry hydrogen chloride was passed through the reaction mixture, with occasional shaking, for twelve hours. After the mixture stood for twelve hours longer a thick paste-like crystalline mass of 3-acetylaminophenanthrene (m. p. 195–200°) had separated. The acetylamino compound was hydrolyzed, according to Werner and Kunz,[28] by boiling it with a mixture of 400 cc. of glacial acetic acid and 400 cc. of 20% aqueous hydrochloric acid, until the amine hydrochloride precipitated. The hydrochloride, after being triturated with acetone, gave a practically pure amine (m. p. 86–87°). The yield calculated on oxime was 70%.

Obviously the acetyl derivative of the oxime was an intermediate in the rearrangement. This compound precipitated almost immediately when hydrogen chloride was passed into the reaction mixture. It was isolated in a preliminary experiment, and crystallized from alcohol in needle-like prisms; m. p. 140–142°.

*Anal.* Calc'd for $C_{18}H_{15}NO_2$: C, 77.94; H, 5.46.
Found: C, 77.81; H, 5.60.

*2-Aminophenanthrene.*—Fifty-three grams of the pure 2-oxime was suspended in a mixture of 200 cc. of glacial acetic acid and 150 cc. of acetic anhydride. Dry hydrogen chloride was passed through the mixture for six hours, and the thick paste was then transferred to several Lintner pressure bottles and heated at 100° for three hours. The 2-acetylaminophenanthrene melted at 220–224°. It was hydrolyzed like the corresponding 3-isomer. The yield of amine (m. p. 85–86°) was 86% (based on oxime).

When the rearrangement mixture was filtered before heating, a compound of m. p. 144–146° was obtained. This substance could be hydrolyzed in the presence of acid to 2-acetylphenanthrene, and is, most likely, the acetyl derivative of the oxime.

### *Naphtho[1,2-f] quinoline Series*

The preparation of naphtho[1,2-*f*] quinoline (II) has been described by us in a previous communication.[1] It was named there "naphthoquinoline." We simplified somewhat the former preparative procedure. The mixture of the reactants was heated in an oil bath for an hour at 135–150°, and then kept at a gentle boil on a hot plate for three hours. The boric acid may be omitted.

### *Hydrogenations*

*Naphtho[1,2-f]quinoline (II) to octahydronaphtho[1,2-f]quinoline (IV).*—To this previously described experiment may be added: the octahydro compound can be conveniently purified by distillation in an oil-pump vacuum. The product is so strongly basic that when carbon dioxide is passed into a suspension of the base in water, the base goes partly into solution and may be reprecipitated with alkali. The aqueous alcoholic solution of the base turns litmus paper blue. The hydrochloride is sparingly soluble in water and does not hydrolyze.

In the hydrogenation from II to IV, 5 g. of base and 60 cc. of glacial acetic acid and 0.5 g. of platinum oxide were employed; the hydrogen absorption (2600 cc., calc'd for 4 moles, 2230 cc.) came to a standstill in two days. The yield of IV was approximately the same as in the previous experiment. Hydrogenation of base or hydrochloride, using platinum oxide catalyst, could not be effected in alcoholic solution.

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[28] WERNER AND KUNZ, *Ann.*, **321**, 314 (1902).

*Tetrahydronaphtho[1,2-f]quinoline (III) to octahydronaphtho[1,2-f]quinoline (IV).*—Five grams of III of m. p. 74–76°, dissolved in 62 cc. of glacial acetic acid, absorbed 1300 cc. of hydrogen (calc'd for 2 moles, 1150 cc.) in fifteen hours (0.5 g. of platinum oxide). The yield of hydrochloride of the octahydro compound (IV) was 3.2 g.

*N*-Methyltetrahydronaphtho[1,2-*f*]quinoline (VI) of m. p. 77–78.5° absorbs approximately 2 moles of hydrogen under similar conditions. It was, however, impossible to isolate any well-defined compound from the reaction mixture.

*Naphtho[1,2-f]quinoline (II) to tetrahydronaphtho[1,2-f]quinoline (III).*—In an experiment employing 9 g. of II, 0.46 g. of platinum oxide, and 125 cc. of glacial acetic acid, the hydrogen absorption was interrupted when, after sixty hours, 2600 cc. of hydrogen had been taken up (calc'd for 2 moles, 2000 cc.). Sodium chloride was added to the filtered solution of the reaction mixture, whereby a hydrochloride of m. p. 225–250° precipitated. This salt yielded 2.4 g. of the rather unstable tetrahydro derivative of m. p. 74–75°. (The hydrochloride crystallized from alcohol in white leaflets of m. p. 255–260°.) The mother liquor from the crude hydrochloride was neutralized with sodium carbonate and extracted with ether. Three and one-tenth grams of an oil was obtained from the ether. No individual substances could be isolated from this oily material. Furthermore there was formed a crystalline precipitate, insoluble in the aqueous or ethereal layer, which was obviously a carbonate of the octahydro compound. By treating this precipitate with 10% potassium hydroxide and extracting the mixture with ether, 1.4 g. of octahydronaphtho[1,2-*f*]quinoline (IV), melting at 109–110°, was obtained.

The most convenient method of preparing the tetrahydro compound (III) has been described in the previous paper.[1] It may be added that by employing a higher temperature (170°) the yield of tetrahydro compound drops to about 40%. No other hydrogenated derivative could be isolated.

### *Degradations*

*Methiodide (V) and methochloride of 4-methyl-1,2,3,4-tetrahydronaphtho[1,2-f]-quinoline (VI).*—To an ice-cold mixture of 11 g. of 1,2,3,4-tetrahydronaphtho-[1,2-*f*]quinoline, 40 cc. of acetone, and 10 cc. of methyl iodide was added 6 g. of sodium hydroxide in 10 cc. of water. The mixture was allowed to stand at room temperature for nine hours with occasional shaking. Five cubic centimeters of methyl iodide was added, and after twenty hours the precipitate was separated by filtration and boiled with a little water in order to remove inorganic material. The crude methiodide was recrystallized from alcohol; colorless slabs, m. p. 185–187° (decomp.); yield, 15.2 g.

*Anal.* Calc'd for $C_{19}H_{20}IN$: I, 32.61. Found: I, 32.19.

This methiodide may be obtained quantitatively by allowing VI and methyl iodide to react in acetone solution for several hours at room temperature. The precipitation is completed by addition of ether.

The methochloride of VI was obtained nearly quantitatively by heating the methiodide in aqueous suspension, with stirring, with freshly precipitated silver chloride. The silver halides were filtered off and the filtrate was evaporated to dryness in a vacuum. The substance crystallized from alcohol in long needles or little cubes of m. p. 174–176° (decomp.).

*Anal.* Calc'd for $C_{19}H_{20}ClN$: Cl, 11.91. Found: Cl, 12.24.

*4-Methyl-1,2,3,4-tetrahydronaphtho[1,2-f]quinoline (VI).*—Fifteen grams of methiodide (V) was slowly heated in a water-pump vacuum using a luminous flame. The distillate was redistilled in an oil-pump vacuum. The C-H analyses of this

product of m. p. 75–77.5° (yield 90%) were consistently too high (0.5–1%). Recrystallization from ether yielded clusters of flat rods of m. p. 77–78.5° (corr.).

*Anal.* Calc'd for $C_{18}H_{17}N$: C, 87.40; H, 6.93; N, 5.67.
Found: C, 87.59; H, 7.32; N, 5.88.

The hydrochloride was prepared by adding alcoholic hydrochloric acid to an acetone solution of the base. It crystallizes from alcohol-ether in colorless tablets, m. p. 215–217° (decomp.).

*Anal.* Calc'd for $C_{18}H_{18}ClN$: C, 76.16; H, 6.40.
Found: C, 76.08; H, 6.51.

*Methiodide of 4-methyl-1,2,3,4,9,10,11,12-octahydronaphtho[1,2-f]quinoline.*—To a solution of 2.0 g. of base (IV) in 10 cc. of acetone was added 1.5 g. of sodium hydroxide and 5 cc. of methyl iodide. The reaction mixture was allowed to stand for two hours. The precipitate was collected by filtration and washed well with water. The methiodide crystallized from water in white needles, m. p. 275–280 (decomp.), yield 75%.

*Anal.* Calc'd for $C_{19}H_{24}IN$: I, 32.28. Found: I, 31.89.

*Emde degradation of the methochloride and methiodide of 4-methyl-1,2,3,4-tetrahydronaphtho[1,2-f]quinoline (VI) to 4-[3-(dimethylamino)-n-propyl]phenanthrene (VII).*—To a solution of 2.2 g. of methochloride in 20 cc. of water was added 25 g. of 4% sodium amalgam. The mixture was boiled for fifteen minutes, although an oil precipitated immediately at the beginning of boiling. The oil was extracted with ether, the ether solution was filtered and dried with sodium sulfate. The residue remaining after removal of the ether was distilled in an oil-pump vacuum at 120° until about three-fourths of the material has passed over. From this distilled oil 0.6 g. of hydrochloride of m. p. 115–122° was obtained. It was recrystallized from 3 cc. of absolute alcohol, and melted, air-dried, at 123–125° with softening at 115°.

*Anal.* Calc'd for $C_{19}H_{22}ClN + C_2H_5OH$: C, 72.90; H, 8.16.
Found: C, 73.26; H, 7.51.

The hydrochloride was dried fifteen minutes in a water-pump vacuum over phosphorus pentoxide at room temperature, when it melted at 125–127°.

*Anal.* Calc'd for $C_{19}H_{22}ClN + C_2H_5OH$: C, 72.90; H, 8.16.
Found: C, 72.71; H, 7.80.

The hydrochloride was dried for two hours over calcium chloride at 103°; m. p. 157–159°.

*Anal.* Calc'd for $C_{19}H_{22}ClN$: C, 76.09; H, 7.40.
Calc'd for $C_{19}H_{24}ClN$: C, 75.58; H, 8.02.
Found: C, 75.42, 75.14; H, 7.19, 7.38.

The hydrochloride was dried for two hours in an oil-pump vacuum at 160°, at which temperature it begins to sublime; m. p. 157–159°. (The sublimed portion melts at the same temperature.)

*Anal.* Calc'd for $C_{19}H_{22}ClN$: C, 76.09; H, 7.40.
Calc'd for $C_{19}H_{24}ClN$: C, 75.58; H, 8.02.
Found: C, 75.48; H, 7.49.

The oily free base was liberated from the hydrochloride with ammonia and distilled in an oil-pump vacuum.

*Anal.* Calc'd for $C_{19}H_{21}N$: C, 86.63, H, 8.04.
Calc'd for $C_{19}H_{23}N$: C, 85.97; H, 8.74.
Found: C, 85.91, 85.59; H, 8.54, 8.70.

Six and five-tenths grams of methiodide was degraded with 3% sodium amalgam. By treatment of the reaction mixture as described above, 1.4 g. of a hydrochloride,

melting at 115–120° was obtained. It was recrystallized from absolute alcohol and dried in an oil-pump vacuum at 125°; m. p. 159–160°; yield, 0.8 g.

*Anal.* Calc'd for $C_{19}H_{22}ClN$: C, 76.09; H, 7.40.
Found: C, 75.96, 76.03; H, 7.74, 7.78.

The oily base was obtained as described above.

*Anal.* Calc'd for $C_{19}H_{21}N$: C, 86.63; H, 8.04.
Found: C, 86.53, 86.41; H, 7.52, 7.72.

*Methiodide of 4-[3-(dimethylamino)-n-propyl]phenanthrene.*—This compound precipitated almost immediately when the oily amine VII and methyl iodide were combined in acetone—ether solution. It crystallized from alcohol in white slabs of melting point 208–208.5° (corr.).

*Anal.* Calc'd for $C_{20}H_{24}IN$: C, 59.24; H, 5.97.
Found: C, 58.84; H, 5.79.

### *Naphtho[2,1-f]quinoline Series*

*Preparation of naphtho[2,1-f]quinoline (IX).*—Thirty grams of 2-aminophenanthrene, 30 cc. of dry nitrobenzene, 60 g. of dry glycerine, and 6 g. of ferrous sulfate were well mixed in an Erlenmeyer flask. Twenty-nine cc. of C.P. sulfuric acid was added with thorough stirring, whereby considerable heat was evolved. The mixture was heated in an oil bath for one hour at about 145°, and was then transferred to a hot plate and gently boiled for two and one-half hours. The reaction mixture was steam-distilled, diluted with water, heated, and filtered. Addition of saturated sodium chloride solution to the filtrate caused precipitation of yellow crystals, which were suspended in hot water and treated with 10% ammonia with thorough stirring, whereupon the free base separated as a grayish precipitate. It was purified by sublimation in an oil-pump vacuum at 180° and by crystallization from toluene; colorless leaflets of m. p. 226–227° (corr.), yield 80–90%.

*Anal.* Calc'd for $C_{17}H_{11}N$: C, 89.04; H, 4.84; N, 6.11.
Found: C, 88.79; H, 4.82; N, 6.10.

The hydrochloride crystallized from alcohol, in which it is sparingly soluble, in tiny bright yellow needles of m. p. 296–300° (evac. tube).

*Anal.* Calc'd for $C_{17}H_{12}ClN$: Cl, 13.35. Found: Cl, 13.24.

### *Hydrogenations*

*Naphtho[2,1-f]quinoline (IX) to tetrahydronaphtho[2,1-f]quinoline (X).*—A solution of 2.7 g. of IX in 75 cc. of glacial acetic acid absorbed 680 cc. of hydrogen (calc'd for 2 moles, 600 cc.) in seven and one-half hours, in the presence of 0.15 g. of platinum oxide catalyst. To the yellow reaction solution was added a concentrated sodium chloride solution, whereby a hydrochloride was precipitated. The free base was liberated by sodium carbonate and extracted with ether. The ether solution yielded 2.3 g. of white prisms of m. p. 153–155°. The base crystallized from chloroform or ethyl acetate in pale yellow tablets, m. p. 157–159° (corr.).

*Anal.* Calc'd for $C_{17}H_{15}N$: C, 87.51; H, 6.49; N, 6.01.
Found: C, 87.60; H, 6.24; N, 6.06.

The hydrochloride crystallizes from alcohol, in which it is sparingly soluble, in white blades of m. p. 310–313° (decomp.).

*Anal.* Calc'd for $C_{17}H_{16}ClN$: Cl, 13.15. Found: Cl, 13.00.

Twenty grams of the naphthoquinoline (IX), 2 g. of chromite catalyst (37 KAF) and 50 cc. of absolute alcohol were heated to 130° during one hour and kept for two hours at 136° at a hydrogen pressure of 162 atm. The filtrate from the reaction mix-

ture gave 1.2 g. of base of m. p. 149–153°. The precipitate consisting of catalyst and crystalline reaction product was treated with acetone. The acetone solution yielded 19 g. of base, melting at 149–153°. This practically pure compound gave no melting-point depression with the tetrahydro base obtained in the previous hydrogenation experiment.

*Naphtho[2,1-f]quinoline (IX) to hexahydronaphtho[2,1-f]quinoline (XI).*—Ten grams of the naphthoquinoline, 1 g. of chromite catalyst and 30 cc. of absolute alcohol were heated during two hours to 230° under a hydrogen pressure of 217 atm. From the crystalline material and from the original mother liquor were obtained a fraction of 2.6 g., melting at 110–115°, and a fraction of 1.2 g., melting at 105–111° respectively. By recrystallization from ethyl acetate a hexahydronaphthoquinoline was obtained in large white prisms that melted at 115–116° (corr.).

*Anal.* Calc'd for $C_{17}H_{17}N$: C, 86.76; H, 7.29; N, 5.96.
Found: C, 86.81, 86.56; H, 7.56, 7.37; N, 6.13.

The hydrochloride crystallized from alcohol in white leaflets of m. p. 274–285° (corr., evac. tube).

*Anal.* Calc'd for $C_{17}H_{18}ClN$: C, 75.11; H, 6.67.
Found: C, 75.11; H, 6.92.

When the high-pressure hydrogenation using chromite catalyst was carried out at 172° a mixture containing the hexahydro base and the tetrahydro base, the latter predominating, was obtained.

An impure hexahydro base (probably containing some tetrahydro compound) was obtained by hydrogenating the tetrahydro compound in glacial acetic acid, employing platinum oxide catalyst. It is noteworthy that this hydrogenation proceeds exceedingly slowly. Five grams absorb 1160 cc. of hydrogen (calc'd for 1 mole, 620 cc.) in 85 hours, giving 2.7 g. of crystalline material of m. p. 104–105°.

### *Degradations*

*Methiodide (XIII) of 1-methyl-1,2,3,4-tetrahydronaphtho[2,1-f]quinoline (XIV).*—(*a*) A mixture of 5 g. of X, 25 cc. of acetone, 8 cc. of methyl iodide, and 3 g. of sodium hydroxide was allowed to react for two hours and shaken occasionally. After the addition of 2 cc. of methyl iodide the mixture was allowed to stand for two days. Six and seven-tenths grams of crude methiodide was obtained. It crystallized from water in white lozenges of melting point 204–205° (decomp.).

*Anal.* Calc'd for $C_{19}H_{20}IN$: I, 32.61. Found: I, 32.28.

(*b*) This methiodide is also obtained quantitatively by combining methyl iodide and the base XIV in acetone solution and allowing the reaction mixture to stand for one day.

The corresponding methochloride of m. p. 188–190° was prepared by treating the methiodide with silver chloride as described in the 1,2-*f* series.

*1-Methyl-1,2,3,4-tetrahydronaphtho[2,1-f]quinoline (XIV).*—Six grams of the methiodide gave, on heating in a vacuum and redistillation of the first distillate, 3.2 g. of a base melting at 164–166°. By repeated recrystallization from ethyl acetate the *N*-methyltetrahydro base was obtained in the form of large flat tablets of melting point 170–171° (corr.).

*Anal.* Calc'd for $C_{18}H_{17}N$: C, 87.40; H, 6.93; N, 5.67.
Found: C, 87.44; H, 6.95; N, 5.89.

The hydrochloride was prepared like the corresponding compound in the 1,2-*f* series, m. p. 240–260° (decomp.).

*Anal.* Calc'd for $C_{18}H_{18}ClN$: C, 76.16; H, 6.40.
Found: C, 76.07; H, 6.49.

*Methiodide (XV) of 1-methyl-1,2,3,4,5,6-hexahydronaphtho[2,1-f]quinoline (XVI).*—(*a*) This methiodide was prepared from (XI) in the usual manner (0.7 g. of XI, 2 cc. of methyl iodide, 0.1 g. of sodium hydroxide, 5 cc. of acetone). When the precipitate was boiled with water, it was observed that the salt decomposed partly, whereby the tertiary base XVI was formed. This was separated by filtration, and the methiodide XV (0.5 g.) was precipitated from the filtrate by potassium iodide. It crystallized from alcohol in flat rods, m. p. 189–192° (decomp.).

*Anal.* Calc'd for $C_{19}H_{22}IN$: C, 58.29; H, 5.69.
Found: C, 58.03; H, 5.47.

(*b*) This methiodide was also readily formed when methyl iodide was added to the acetone solution of the *N*-methylhexahydro base (XVI) (from the decomposition of the methiodide); m. p. 193–195°.

The 1-methyl-1,2,3,4,5,6-hexahydronaphtho[2,1-*f*]quinoline (XVI), obtained by boiling the methiodide (XV) with water, was purified by recrystallization from absolute alcohol and sublimation in an oil-pump vacuum at 120°; m. p. 129–131°. The methiodide had been thoroughly washed with ether in order to eliminate the possibility of the presence of the tertiary base XVI before decomposition.

*Anal.* Calc'd for $C_{18}H_{19}N$: C, 86.69; H, 7.68.
Found: C, 86.45; H, 7.65.

*Emde degradation of the methiodide and methochloride of 1-methyl-1,2,3,4-tetrahydronaphtho[2,1-f]quinoline (XIV) to 1-[3-(dimethylamino)-n-propyl]phenanthrene (XVII).*—Five and six-tenths grams of the methochloride of XIV was boiled in 200 cc. of water with 100 g. of 5% sodium amalgam for fifteen minutes. The oily basic reaction product was extracted with ether, distilled in an oil-pump vacuum and converted into a hydrochloride of m. p. 195–200°. This hydrochloride appeared to be unstable, turning gray and brown on standing. The base liberated from it was redistilled in an oil-pump vacuum.

*Anal.* Calc'd for $C_{19}H_{21}N$: C, 86.63; H, 8.04.
Calc'd for $C_{19}H_{23}N$: C, 85.97; H, 8.74.
Found: C, 85.84; H, 8.47.

Further distillation of the crude Emde degradation products yielded 0.2 g. of the *N*-methyltetrahydro base (XIV), identified by mixture melting point.

In another degradation, carried out in the same manner, but with 3% sodium amalgam, 0.2 g. of methochloride gave 0.1 g. of a hydrochloride melting at 200–202°. It was converted with sodium picrate solution to the picrate, which crystallized from alcohol in clusters of short needles, m. p. 164.5–166.5° (corr.).

*Anal.* Calc'd for $C_{25}H_{26}N_4O_7$: C, 60.70; H, 5.30.
Calc'd for $C_{25}H_{24}N_4O_7$: C, 60.95; H, 4.91.
Found: C, 60.68; H, 4.81.

In mixture with the picrate of 1-[3-(dimethylamino)-*n*-propyl]-9,10-dihydrophenanthrene (XVIII), of m. p. 144–145°, it softens at 135° and melts at 139–143°.

Another degradation was carried out using the methiodide instead of the methochloride. The degradation product was purified by fractional liberation of the base with insufficient amounts of ammonia and by crystallization of the hydrochloried from alcohol-ether. The salt was obtained in clumps of white rectangular plates of m. p. 210–213° (slight softening at 198°). When recrystalized from alcohol-acetone-ether, it precipitated in form of fine white needles of m. p. 206–207°. The

mixture melting point of this hydrochloride with the hydrochloride of the degradation product (XVIII) (m. p. 207–209°) from the methiodide (XV) of 1-methyl-1,2,3,4,5,6-hexahydronaphtho[2,1-*f*]quinoline (XVI) was at 205–206°. They are, however, not identical (see Table I).

*Emde degradation of the methiodide (XV) of 1-methyl-1,2,3,4,5,6-hexahydronaphtho[2,1-f]quinoline (XVI) to 1-[3-(dimethylamino)-*n*-propyl]-9,10-dihydrophenanthrene (XVIII).*—A solution of 0.4 g. of XV in 20 cc. of water was boiled for twenty minutes with 3% sodium amalgam. The hydrochloride (0.1 g.) of the purified degradation product was recrystallized from alcohol and ether, and melted at 207–209° (uncorr.).

*Anal.* Calc'd for $C_{19}H_{24}ClN$: C, 75.57; H, 8.02.
Found: C, 75.33; H, 7.90.

The hydrochloride was converted with sodium picrate solution to the picrate, which crystallized from alcohol in pale yellow prisms, m. p. 145.5–146.5° (corr.).

*Anal.* Calc'd for $C_{25}H_{26}N_4O_7$: C, 60.70; H, 5.30.
Found: C, 60.73; H, 5.08.

TABLE I

MELTING POINTS OF HYDROCHLORIDES AND PICRATES

| | M. P. OF HYDROCHLORIDE, °C | M. P. OF PICRATE (CORR.), °C |
|---|---|---|
| XVII | 206–207 (210–213) | 164.5–166.5 |
| XVIII | 207–209 | 145.5–146.5 |
| XXX | 160.5–162 (corr.) | 150.5–151.5 |
| XXIX | 150–151 (corr.) | 101.5–103 |

In Table I the non-identity of the degradation products XVII and XVIII and of each of them with synthetic 3-[3-(dimethylamino)-*n*-propyl]phenanthrene (XXX) and 3-[3-(dimethylamino)-*n*-propyl]-9,10-dihydrophenanthrene (XXIX) is illustrated by the melting points of the respective hydrochlorides and picrates.

*Naphtho[1,2-g]quinoline Series*

*Preparation of 5,6-dihydronaphtho[1,2-g]quinoline (XXI).*—To a mixture of 30 g. of 2-amino-9,10-dihydrophenanthrene, 30 cc. of nitrobenzene, 6 g. of ferrous sulfate, and 60 g. of glycerine was added 29 cc. of C.P. sulfuric acid. The mixture was heated at 150–160° for five hours in a metal bath. The black product was poured into 1500 cc. of water and extracted with ether. The naphthoquinoline hydrochloride precipitated from the aqueous solution in the form of hair-like yellow crystals when saturated sodium chloride solution was added. The free base was liberated with ammonia, extracted with ether and distilled in an oil-pump vacuum at 150°. It crystallized from ethyl acetate in large white prisms, m. p. 72–74° (corr.), yield 50%.

*Anal.* Calc'd for $C_{17}H_{13}N$: C, 88.27; H, 5.67.
Found: C, 87.89; H, 5.85.

The hydrochloride crystallized from alcohol as a yellow powder, m. p. 258–262° (corr., evac. tube).

*Anal.* Calc'd for $C_{17}H_{14}ClN$: Cl, 13.26. Found: Cl, 12.83.

*Hydrogenations*

*5,6-Dihydronaphtho[1,2-g]quinoline (XXI) to 5,6,8,9,10,11-hexahydronaphtho-[1,2-g]quinoline (XXIV).*—Five grams of XXI in 62 cc. of glacial acetic acid with 0.5 g. of platinum oxide catalyst absorbed 1400 cc. of hydrogen (calc'd for 2 moles, 1150 cc.) within six hours. The base was liberated with sodium carbonate solution, extracted with ether, and distilled at 150° in an oil-pump vacuum. The oily, pale yellow base was converted into the hydrochloride (4.6 g.) which was recrystallized from alcohol and reconverted to the base which, eventually, became crystalline. It was obtained by recrystallization from ethyl acetate as colorless prisms, m. p. 72–73° (corr.) (the mixture melting point with XXI was 65°).

*Anal.* Calc'd for $C_{17}H_{17}N$: C, 86.76; H, 7.29; N, 5.96.
Found: C, 86.95; H, 7.44; N, 5.72.

The hydrochloride crystallized from alcohol in minute white needles, m. p. 240–244° (evac. tube).

*Anal.* Calc'd for $C_{17}H_{18}ClN$: C, 75.11; H, 6.68.
Found: C, 74.75; H, 7.01.

Ten grams of XXI, 30 cc. of absolute alcohol and 1 g. of chromite catalyst were heated during three hours to 150°, during an hour and a half to 170° and finally to 197° for half an hour under a hydrogen pressure of 183 atm. By readings on the pressure gauge, the temperature at which hydrogenation took place could not be determined. As far as could be judged by plotting pressure against temperature for both heating and cooling of the bomb, the hydrogenation appeared to have taken place between 150–160°. The reaction product yielded 7 g. of a hydrochloride of m. p. 215–217°, from which finally 4.2 g. of hexahydro base (XXIV) of m. p. 70–73° was obtained.

*Methiodide (XXVII) of 8-methyl-5,6,8,9,10,11-hexahydronaphtho[1,2-g]quinoline.*—Four and two-tenths grams of XXIV in 30 cc. of acetone, 5 cc. of methyl iodide, and 1 g. of potassium hydroxide in 2 cc. of water were allowed to react for two days. The heavy precipitate that formed did not give a clear solution when boiled with water. Potassium iodide was added, and the dry precipitate (consisting of methiodide and *N*-methylhexahydro base ?) was suspended in ether containing methyl iodide. Finally the methiodide was recrystallized from alcohol; large, slightly yellow needles, m. p. 196–200° (decomp.), yield 65%.

*Anal.* Calc'd for $C_{19}H_{22}IN$: N, 3.58. Found: N, 3.67.

*Emde degradation of XXVII to 8-[3-(dimethylamino)-n-propyl]-9,10-dihydrophenanthrene (XXIX).*—An aqueous solution of 6.3 g. of XXVII was boiled for one hour with 3% sodium amalgam. The oily reaction product gave, after distillation in an oil-pump vacuum at 130°, 3.2 g. of a hydrochloride melting at 138–142°. The base was liberated again, distilled, and reconverted to the hydrochloride, which crystallized from alcohol in white needles of melting point 150–151° (corr.).

*Anal.* Calc'd for $C_{19}H_{24}ClN$: C, 75.57; H, 8.02; Cl, 11.76.
Found: C, 75.68; H, 8.07; Cl, 12.13.

The picrate crystallized from alcohol in pale yellow prisms of m. p. 101.5–103° (corr.).

*Anal.* Calc'd for $C_{25}H_{26}N_4O_7$: C, 60.70; H, 5.30.
Found: C, 60.32; H, 5.15.

In only one of several dehydrogenation experiments was the transformation of XXIX to XXX accomplished. A mixture of 1.2 g. of base XXIX and 50 mg. of

palladium black[29] was heated in a nitrogen atmosphere at 190–200° for thirty minutes. Only a small amount of hydrochloride, approximately 10 mg., insoluble in acetone and melting at 155–157° could be isolated from the reaction mixture. The mixture melting point with 3-[3-(dimethylamino)-*n*-propylphenanthrene of m. p. 157–159° was at 156–158°. The hydrochloride from the dehydrogenation experiment was converted to the picrate which melted after four recrystallizations from alcohol at 147–148.5°.

*Preparation of naphtho[1,2-g]quinoline (XXII) by dehydrogenation of 5,6-dihydronaphtho[1,2-g]quinoline (XXI).*—Two grams of XXI and 0.1 g. of palladium black were placed in a wide test-tube and heated gradually in a nitrogen atmosphere. The evolution of hydrogen began at about 300°. The temperature was raised to 350–360° and maintained there for two hours. The contents of the tube were subjected to distillation in an oil-pump vacuum at 170°, yielding a distillate (1.6 g.) that melted at 135–149°. The naphthoquinoline crystallized from benzene or ethyl acetate in fine white needles of m. p. 159–160° (corr.), yield 50%.

*Anal.* Calc'd for $C_{17}H_{11}N$: C, 89.04; H, 4.84.
Found: C, 88.99; H, 5.21.

The hydrochloride crystallized from alcohol in yellow needles, m. p. 280–295° (evac. tube).

*Anal.* Calc'd for $C_{17}H_{12}ClN$: C, 76.82; H, 4.55.
Found: C, 76.74; H, 5.03.

In a series of twelve experiments, no more than 3 g. of substance was dehydrogenated in one run. Increase of the amount of catalyst increases the yield to some extent. (Two and seven-tenths grams of dihydro compound, 0.5 g. of palladium, and 25 minutes of heating yielded 1.8 g. of a naphthoquinoline, melting at 154–156°.)

*Hydrogenation of naphtho[1,2-g]quinoline (XXII) to 8,9,10,11-tetrahydronaphtho[1,2-g]quinoline (XXV).*—Two and six-tenths grams of XXII with 0.2 g. of platinum oxide in glacial acetic acid absorbed in one hour and twenty minutes 680 cc. of hydrogen (calc'd for 2 moles, 590 cc.). The hydrochloride was precipitated with saturated sodium chloride solution and the base obtained from the hydrochloride (ammonia and ether) was distilled in an oil-pump vacuum at 180°. The pale yellow oil could not be induced to crystallize.

*Anal.* Calc'd for $C_{17}H_{15}N$: C, 87.51; H, 6.49.
Found: C, 87.23; H, 6.67.

*Methiodide of 8-methyl-8,9,10,11-tetrahydronaphtho[1,2-g]quinoline (XXVIII).*—A mixture of 0.9 g. (not distilled) of tetrahydro base (XXV), 10 cc. of acetone, 3 cc. of methyl iodide, and 1 g. of potassium hydroxide was allowed to stand for two days. The precipitate was filtered out, and 2 cc. of methyl iodide and 1 g. of potassium hydroxide were added to the mother liquor. The total yield of methiodide, recrystallized from water, was 0.8 g. It melted after recrystallization from alcohol at 200–203° (white needles). The distilled base yielded a slightly purer methiodide melting at 203–205° (decomp.).

*Anal.* Calc'd for $C_{19}H_{20}IN$: C, 58.60; H, 5.18.
Found: C, 58.53; H, 5.38.

*Emde degradation of XXVIII to 3-[3-(dimethylamino)-n-propyl]phenanthrene (XXX).*—An aqueous solution of 0.7 g. of XXVIII was boiled with 5% sodium amalgam for one hour following the usual procedure. A hydrochloride (0.08 g.) of m. p. 156–157° was obtained by treating the crude hydrochloride with acetone and

[29] WILLSTÄTTER AND WALDSCHMIDT-LEITZ, *Ber.*, **54**, 123 (1921).

ethyl acetate. By extremely slow crystallization from alcohol this hydrochloride was obtained in small white needles melting at 160–160.5° (corr.).

*Anal.* Calc'd for $C_{19}H_{22}ClN$: C, 76.09; H, 7.43.
Found: C, 75.48; H, 7.71.

The mixture melting point with the hydrochloride of XXIX was 143–147°.

The following derivatives were obtained from various degradation experiments in which XXX was obtained in essentially the same manner:

The picrate crystallized from alcohol in clusters of pale yellow needles of m. p. 150.5-151.5° (corr.).

The methiodide of XXX precipitated immediately when an acetone-ether solution of XXX was mixed with methyl iodide. It crystallized from alcohol in white prisms of m. p. 173–174°.

The perchlorate of XXX precipitated in white glistening leaflets, melting point 84.5–89° (corr.), when ethereal perchloric acid was added to an ethereal solution of XXX.

TABLE II

MELTING POINTS OF DERIVATIVES OF 3-[3-(DIMETHYLAMINO)-*n*-PROPYL] PHENANTHRENE

| DERIVATIVE | BY SYNTHESIS, °C | BY DEGRADATION, °C | MIXTURE, °C |
|---|---|---|---|
| Base | Oily | Oily | |
| Hydrochloride | 160.5–162 | 160–160.5 | 160–161 |
| Picrate | 150–150.5 | 150.5–151.5 | 150–150.5 |
| Methiodide | 164–165 | 174–175 | 164–165 |
| Perchlorate | 86–89 | 84.5–89 | 85–89 |

In Table II are listed melting points and mixture melting points of the corresponding derivatives of XXX obtained by degradation and by synthesis. All melting points are corrected. No explanation of the difference in melting points of the methiodide can be offered.

*Synthesis of Dimethylamino-*n*-propyl-phenanthrenes*

The hydrochloride of 3-[3-(dimethylamino)-1-hydroxy-*n*-propyl]phenanthrene is hygroscopic and apparently undergoes changes in the presence of free hydrochloric acid (either by loss of water or by chlorination). It can be obtained by evaporation to dryness of the alcoholic solution resulting from the catalytic hydrogenation of the corresponding amino ketone hydrochloride.[30]

*3-[3-(Dimethylamino)-1-chloro-*n*-propyl]phenanthrene hydrochloride.*—Seven-tenths of a gram of amino alcohol hydrochloride was added to a suspension of 1 g. of phosphorus pentachloride in 10 cc. of chloroform. After half an hour the excess of phosphorus pentachloride was destroyed with alcohol, and ether was added to precipitate the salt. The air-dried product melted at 150–155°, solidified and finally melted at 238–240°.

*Anal.* Calc'd for $C_{19}H_{21}Cl_2N$: C, 68.24; H, 6.34.
Found: C, 68.13; H, 6.91.

[30] VAN DE KAMP AND MOSETTIG, *J. Am. Chem. Soc.*, **58**, 1568 (1936).

*3-[3-(Dimethylamino)-n-propyl]phenanthrene.*—A suspension of 0.4 g. of palladous hydroxide-calcium carbonate catalyst[31] (palladium content 1%) and 1.2 g. of the hydrochloride of the chloro compound were shaken in a hydrogen atmosphere. Absorption was complete in thirty minutes. The catalyst was filtered off, the solvent was evaporated, and the residue was treated with ammonia, extracted with ether, and distilled in an oil-pump vacuum at 140°. The oily base (ca. 0.75 g.) was converted to the hydrochloride, which crystallized from alcohol—ethyl acetate in small white prisms of m. p. 160.5–162° (corr.).

*Anal.* Calc'd for $C_{19}H_{22}ClN$: C, 76.09; H, 7.40; Cl, 11.83.
Found: C, 75.73; H, 7.34, Cl, 11.81.

The picrate crystallized from alcohol in pale orange needles of m. p. 149.5–151° (corr.).

*Anal.* Calc'd for $C_{25}H_{24}N_4O_7$: C, 60.95; H, 4.91.
Found: C, 61.03; H, 5.06.

The methiodide crystallized from alcohol in small white prisms of m. p. 163–164°.

*Anal.* Calc'd for $C_{20}H_{24}IN$: C, 59.24; H, 5.97.
Found: C, 59.52; H, 6.06.

The perchlorate was prepared exactly as described for this derivative of the degradation product XXX, and melted at 86–89° (corr.).

The preparation of 2-[3-(dimethylamino)-*n*-propyl]phenanthrene hydrochloride of m. p. 222–227° has been described in the previous communication.[1] The base of this hydrochloride is apparently little attacked when boiled in aqueous alcoholic solution with 5% sodium amalgam for four hours. The hydrochloride prepared from the reaction mixture melted at 210–213°. Boiling the base for four hours with sodium and alcohol yielded finally a mixture of hydrochlorides melting at 170–180° from which no individual compound could be isolated.

*2-[3-(Dimethylamino)-1-oxo-propyl]-9,10-dihydrophenanthrene.*—Seven grams of 2-acetyl-9,10-dihydrophenanthrene, 1.9 g. of trioxymethylene, 6.3 g. of dimethylamine hydrochloride, and 26 cc. of isoamyl alcohol were boiled under reflux for twelve minutes. The reaction mixture was poured into water, and the base was liberated from the aqueous solution with ammonia, extracted with ether, and recrystallized from ligroin; m. p. 69–70°, yield 5.0 g. It crystallized from ethyl acetate in white prisms of melting point 70–71° (corr.).

*Anal.* Calc'd for $C_{19}H_{21}NO$: C, 81.67; H, 7.58.
Found: C, 81.79; H, 7.73.

The hydrochloride crystallized from acetone-alcohol in long flat rods, m. p. 162–163° (corr.).

*Anal.* Calc'd for $C_{19}H_{22}ClNO$: Cl, 11.23. Found: Cl, 11.67.

*2-[3-(Dimethylamino)-1-hydroxy-n-propyl]-9,10-dihydrophenanthrene.*—The amino alcohol was prepared by reducing 4.7 g. of the amino ketone hydrochloride in 100 cc. of 60% alcohol, using 0.2 g. of platinum oxide catalyst. It melted, after recrystallization from ether-petroleum ether, at 72–74° (corr.), yield 80%.

*Anal.* Calc'd for $C_{19}H_{23}NO$: C, 81.08; H, 8.24.
Found: C, 80.69; H, 8.29.

The hydrochloride crystallized from alcohol-ether in small white needles of m. p. 159–161° (corr.).

*Anal.* Calc'd for $C_{19}H_{24}ClNO$: Cl, 11.16. Found: Cl, 11.43.

*2-[3-(Dimethylamino)-1-chloro-n-propyl]-9,10-dihydrophenanthrene hydrochloride.*—The chloro compound was obtained by chlorinating the amino alcohol hydrochloride

[31] Busch and Schulz, *Ber.*, **62**, 1460 (1929).

in chloroform with phosphorus pentachloride. The hydrochloride was recrystallized from alcohol and dried over calcium chloride in the desiccator. It melted around 160°, solidified, and remelted at 214–216° (decomp.).

*Anal.* Calc'd for $C_{19}H_{23}Cl_2N$: C, 67.83; H, 6.89.
Found: C, 67.53; H, 7.09.

*2-[3-(Dimethylamino)-n-propyl]-9,10-dihydrophenanthrene hydrochloride.*—The elimination of the chlorine was effected by catalytic hydrogenation employing palladous hydroxide—calcium carbonate catalyst. The propyl amino compound was obtained in a yield of 75%. The hydrochloride melted at 204–206° (corr.).

*Anal.* Calc'd for $C_{19}H_{24}ClN$: C, 75.57; H, 8.02; Cl, 11.76.
Found: C, 75.29; H, 8.05; Cl, 11.59.

## SUMMARY

By application of the Skraup method to 3-aminophenanthrene, 2-aminophenanthrene, and 2-amino-9,10-dihydrophenanthrene, naphthoquinolines were obtained in satisfactory yields.

Various hydro derivatives of the naphthoquinolines were obtained by catalytic hydrogenation using platinum oxide catalyst under normal conditions and chromite catalyst at elevated temperature and hydrogen pressure.

The constitutional proof of the naphthoquinolines was established by degradation of the respective *N*-methyltetrahydronaphthoquinolines to dimethylamino-*n*-propylphenanthrenes, which were compared with the corresponding phenanthrene derivatives of known structure.

3-[3-(Dimethylamino)-*n*-propyl]phenanthrene and 2-[3-(dimethylamino)-*n*-propyl]-9,10-dihydrophenanthrene were synthesized from 3-acetylphenanthrene and 2-acetyl-9,10-dihydrophenanthrene respectively.