sium carbonate, it was distilled under 14 mm. pressure. Three fractions were collected, (a) 15 cc. distilling at 36–40°, (b) 38 cc. distilling at 72.5–75°, (c) 10 cc. distilling at 80–91°. The first of these fractions reacted violently with sodium and was considered to be methyl cellosolve containing some water. The second and third fractions evolved little or no hydrogen when treated with sodium. Two more distillations of the combined second and third fractions gave a colorless liquid which had a b. p. of 73–74.5° at 16 mm.; yield, 37.5 g. (46.5%).

Anal. Calcd. for $C_8H_{19}NO_2$: neut. equiv., 161.2. Found: neut. equiv., 160.5.

Attempts to make a satisfactory solid derivative were not very successful. When the amino ether was treated with a saturated benzene solution of picric acid and the mixture evaporated, a very viscous oil was obtained. When placed on a watch glass, it solidified to a sticky solid which melted at approximately 73°. Attempted crystallization from alcohol–water (1:1) failed to improve the poor crystalline properties.

When dry hydrogen chloride was passed into an absolute ether solution of the amino ether, diethylammonium chloride was obtained. When ethyl iodide was heated with the amino ether to form a quaternary ammonium salt, the odor of formaldehyde was noticeable, indicating decomposition, and the only product obtained appeared to be impure tetraethylammonium iodide.

However, when 1 g. of ethyl iodide and 1 g. of the amino ether were dissolved in 10 cc. of absolute ether and the solution allowed to stand overnight, a few long white needles appeared, which melted at 49.5°. Since diethylamine and ethyl iodide react under the same conditions to give a solid melting at 164°, it is reasonable to assume that the low melting compound is the quaternary ammonium salt, triethyl-β-ethoxyethoxymethylammonium iodide. This procedure was considered unsuitable for purposes of qualitative organic analysis and no further work was done with it.

Summary

Solid derivatives of three cellosolves and two carbitols have been described in the form of (a) azo compounds obtained by diazotization of *p*-aminobenzoates of the cellosolves and carbitols, and coupling with dimethylaniline, (b) picrates and hydrochlorides of β-4-morpholinoethyl ethers of cellosolves and carbitols.

A method suitable for the qualitative identification of the cellosolves and carbitols has been described.

Limitations and difficulties involved in other possible methods of identification have been outlined.

BOSTON, MASS. RECEIVED APRIL 12, 1940

[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF HARVARD UNIVERSITY]

20-Methyl-4-azacholanthrene

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

On considering in broad perspective the biological actions of the various organic compounds of established carcinogenic activity, it is rather striking to note that the hydrocarbons usually produce tumors at the site of application while the majority of nitrogen-containing carcinogens tend to exert an effect at a remote site. Action at a distance is characteristic of the azo dyes of the type of *o*-aminoazotoluene,[2] of 3,4,5,6-dibenzcarbazole,[3] and of commercial β-naphthylamine,[4] if not of styryl 430.[5] There is such a vast structural difference between an azo dye and a cholanthrene, for example, and perhaps even between a dibenzcarbazole and a dibenzanthracene, that one would hesitate without further evidence to associate the difference in biological action with the difference in composition. The perhaps purely circumstantial indications, however, are so suggestive as to invite further investigation of the matter, and it seemed to us that the most satisfactory evidence would be that derived from a study of nitrogen heterocycles closely analogous in structure to the particularly potent carcinogenic hydrocarbons.

Pyridine isologs of various inactive or weakly active polynuclear hydrocarbons have already been investigated by others. Sempronj and Morelli[6] found the compound I to have weak carcinogenic activity in rats, with the particular property of acting upon kidney tissues. Joseph[7] administered the same compound to mice and obtained no tumors, but the observations were extended over a much shorter period. The substance had been synthesized by Graebe[8] and

(1) Research Fellow on grants from the National Cancer Institute and the Eli Lilly Company.

(2) Sasaki and Yoshida, see Shear, *Am. J. Cancer*, **29**, 267 (1937).

(3) Boyland and Brues, *Proc. Roy. Soc.* (London), **B122**, 429 (1937).

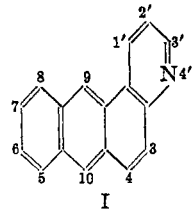
(4) Hueper, Wiley, Wolfe, Ranta, Leming and Blood, *J. Ind. Hyg. Toxicol.*, **20**, 46 (1938).

(5) Browning, Gulbransen and Niven, *J. Path. Bact.*, **42**, 155 (1936).

(6) Sempronj and Morelli, *Am. J. Cancer*, **35**, 534 (1939).

(7) Joseph, *Proc. Soc. Exptl. Biol. Med.*, **41**, 334 (1939).

(8) Graebe, *Ann.*, **201**, 344 (1880).

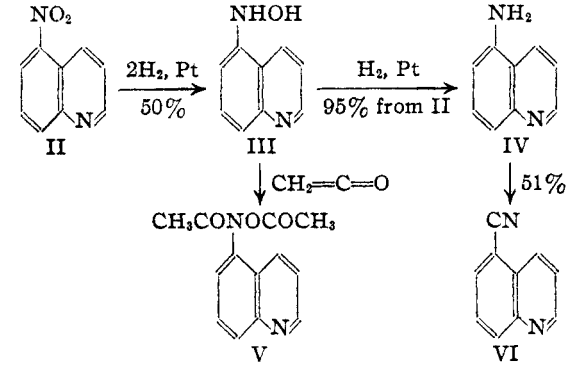


I

called β-anthraquinoline. For convenience in correlating heterocycles of this type with the hydrocarbons which they resemble, we shall use the system wherein I is designated 4′-aza-1,2-benzanthracene. Mosettig and Krueger[9] have synthesized 1,2-benz-5-aza-anthracene, 1-azachrysene, and 3,4-benz-8-azaphenanthrene, and the last-mentioned isomer has been tested for carcinogenicity by Joseph[7] with negative results. A compound isologous with the potent 3,4-benzpyrene was prepared many years ago by Jahoda[10] (pyrenolin) and more recently by Vollmann, *et al.*[11] [3(N)-4-pyridinopyrene]. A sample of this substance, which we designate 1′-aza-3,4-benzpyrene, has been obtained through the courtesy of Dr. G. Kränzlein and is in process of being tested.

In the present work we undertook the synthesis of azacholanthrenes by application of the Elbs reaction to suitable quinolyl hydrindyl ketones. The 5- and 8-amino derivatives of quinoline have been obtained from the nitro compounds by various methods of reduction. The use of stannous chloride[12] or tin and hydrochloric acid[13] is stated[14] to give either impure or partially chlorinated products, and it appears more satisfactory to employ iron and calcium chloride[15] or iron and acetic acid[14] (yields of about 61%). Winterbottom[16] obtained the amines in 69–75% yield by hydrogenation of the nitro compounds in alcohol in the presence of Raney nickel and reported no unusual phenomena in connection with the reactions.

On investigating the hydrogenation of 5-nitroquinoline in the presence of Adams catalyst we encountered an intermediate product characterized by its sensitivity to hot alcohol and by being less soluble than the nitro compound or the amine. The substance dissolves better and is more stable in ethyl acetate, but when this solvent was employed alone and in a purified condition the hydrogenation proceeded only very slowly. A small amount of alcohol, however, has a marked promoter action, and by using a combination of ethyl acetate and alcohol the reaction could be conducted smoothly to the stage of absorption of two moles of hydrogen and the purified intermediate isolated in 50% yield. The composition and properties of the compound indicate that it has the structure of 5-hydroxylaminoquinoline (III). It has strong reducing properties, is convertible to the amine, and on treatment with



benzoyl chloride in pyridine or with ketene it affords a dibenzoate and a diacetate (V), respectively. 8-Hydroxylaminoquinoline was similarly isolated in 62% yield by the partial hydrogenation of the nitro compound. With a knowledge of the properties of the intermediates, conditions could be selected permitting hydrogenation of both nitro compounds to the amines in excellent yields.

As far as we are aware this is the first instance of the conversion of nitro compounds to hydroxylamines by hydrogenation. Possibly the present examples of the reaction constitute a somewhat special case associated with the presence of a basic hetero atom, for under conditions normally employed in conducting hydrogenations the separation of the sparingly soluble intermediate is a striking phenomenon presenting a marked contrast to the results noted with ordinary nitro compounds. The sparing solubility may indeed be due to a complex or inner salt structure involving the basic ring nitrogen atom. The present observations are being extended by an investigation of the partial hydrogenation of various heterocyclic nitro compounds and of combinations of carbocyclic nitro compounds with bases.

In a trial of one possible route to ketones of the type required for pyrolysis we attempted to convert 5-bromoquinoline into the Grignard reagent

(9) Mosettig and Krueger, THIS JOURNAL, **60**, 2962 (1938); *J. Org. Chem.*, **3**, 317 (1938).
(10) Jahoda, *Monatsh.*, **8**, 442 (1887).
(11) Vollmann, Becker, Corell and Streeck, *Ann.*, **531**, 1 (1937).
(12) Meigen, *J. prakt. Chem.*, **77**, 472 (1908).
(13) Kaufmann, *Ber.*, **50**, 1628 (1917).
(14) Dikshoorn, *Rec. trav. chim.*, **48**, 147 (1929).
(15) Seka, *Monatsh.*, **45**, 287 (1924).
(16) Winterbottom, THIS JOURNAL, **62**, 160 (1940).

and condense this with *o*-tolunitrile, but as the result was unpromising we turned to the use of the cyanoquinolines. 5-Cyanoquinoline, previously obtained from the sulfonate,[17] was prepared satisfactorily from the amine by the Sandmeyer reaction. This method failed in the case of the 8-isomer, but the compound was obtained readily by the action of cuprous cyanide in pyridine on 8-chloroquinoline, prepared by the known Skraup synthesis.

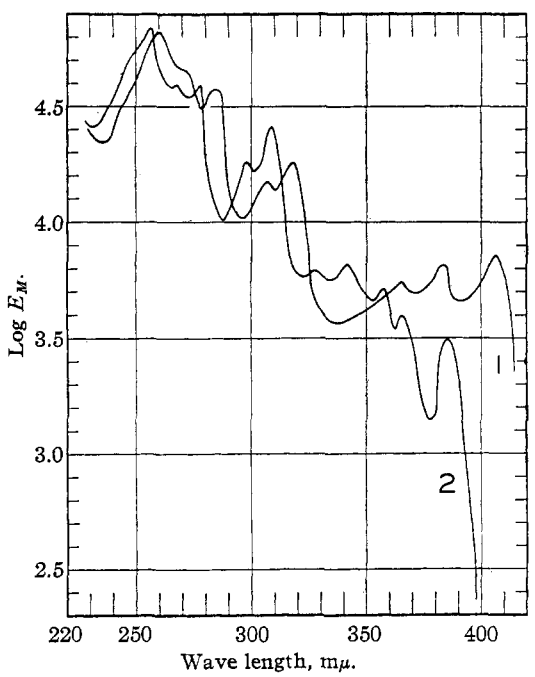
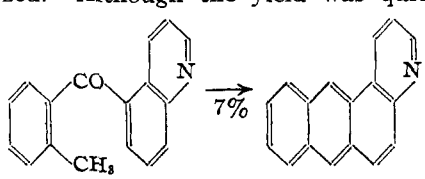


Fig. 1.—Curve 1, 20-methyl-4-azacholanthrene in alcohol; principal maxima (log E_M values in parentheses): 260 (4.82), 284 (4.57), 318 (4.26), 384 (3.82), 406 (3.86). Curve 2, 4′-aza-1,2-benzanthracene in alcohol, maxima: 256 (4.84), 278 (4.59), 309 (4.41), 342 (3.82), 385 (3.49).

As a convenient means of determining whether the Elbs synthesis is applicable to the purpose at hand, *o*-tolylmagnesium bromide was condensed with 5-cyanoquinoline and the ketone VII was pyrolyzed. Although the yield was quite low,

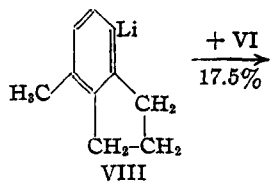


VII I

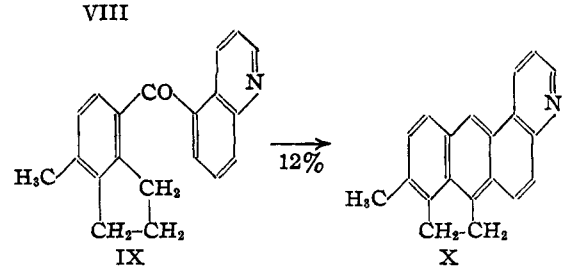
the product corresponded in properties with Graebe's[8] "β-anthraquinoline," I, prepared from β-anthramine by the Skraup synthesis. The

(17) Bedall and O. Fischer, *Ber.*, **14**, 2570 (1881); Lellmann and Reusch, *ibid.*, **21**, 397 (1888).

lithium derivative (VIII) prepared from 4-chloro-7-methylhydrindene was then condensed with 5-cyanoquinoline; considerable tar was formed, but the ketone IX was isolated in a crystalline condition. On pyrolysis of the ketone at 440° there was obtained in low yield a crystalline yellow



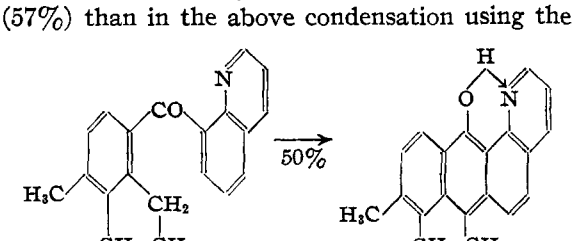
VIII



IX X

compound, m. p. 184–185°, having the composition of the expected 20-methyl-4-azacholanthrene (X). A clear indication that the substance has this structure is provided by spectrographic determinations made by Dr. R. N. Jones and recorded in Fig. 1. The spectrum of the new compound (Curve 1) closely resembles that found for the 4′-aza-1,2-benzanthracene (I) of Graebe (Curve 2), with a shift to longer wave lengths consistent with the presence of three alkyl substituents. The absorption curves for the heterocyclic compounds as determined in alcoholic solution bear little resemblance to those of the corresponding hydrocarbons. It is also of interest that the spectrum is altered to a marked extent, at least with compound I, on conducting the determination in 50% aqueous alcoholic–hydrochloric acid solution. This matter is being investigated further by Dr. Jones.

The isomeric 8-quinolyl 7-methyl-4-hydrindyl ketone (XI) was prepared from 8-cyanoquinoline and the Grignard reagent from 4-bromo-7-methylhydrindene. The yield was decidedly better (57%) than in the above condensation using the



XI XII (?)

lithium derivative. On pyrolysis the ketone gave in good yield and as the sole product isolated an oxygen-containing product having the composition of the anthrone or anthranol. The formation of such a substance would involve a dehydrogenation, and indeed the best yield was obtained by conducting the pyrolysis in the presence of palladium charcoal. The compound does not have the properties normally associated with either an anthrone or an anthranol, for it was recovered unchanged after treatment with Grignard reagent, attempted reduction with zinc and ammonia, and treatment with acetic anhydride and pyridine. A benzanthrone derivative might be produced from XI as the result of a rearrangement,[18] but the substance does not show the characteristic behavior of benzanthrones in the reductive acetylation reaction.[19] Possibly the anthranol structure is stabilized by chelation or salt formation between the hydroxyl group and the ring nitrogen atom, as in XII. Such a stabilization would account for the retention of the oxygen during the pyrolysis and for the high yield (50%), which far surpasses that obtained in those few instances where the Elbs reaction has been observed to lead in part to anthrones.[20] The spectrum of the substance does not resemble that of the 4-aza compound X, but since the spectrum characteristic of the 1,2-benzanthracenes is vastly altered by the introduction of a hetero atom it is quite possible that the position of this atom is also an important determining factor. While the base I and its ion have markedly different spectra, the oxygen-containing substance is about the same, spectrographically, in an acidic as in a neutral medium. This is perhaps a further indication that the nitrogen atom is bound in an ionic or near-ionic combination.

Experimental Part[21]

5- and 8-Nitroquinoline.—Synthetic quinoline was nitrated essentially as described in the literature.[12,14] The sulfate prepared by adding 65 cc. of concentrated sulfuric acid to 150 g. of quinoline in an evaporating dish was broken up when cool and placed in a 1.5-liter flask equipped with a tantalum stirrer, a dropping funnel and thermometer. The flask was cooled in ice to keep the temperature below 40° during the addition of 400 g. of 65% oleum; after the solid had dissolved 110 g. of fuming nitric acid was dropped in in the course of one hour at 15–20°, and after four hours at this temperature the clear yellow solution was poured onto ice. The crude nitration product precipitated by neutralization with ammonia was dissolved by heating in 1 liter of nitric acid, sp. gr. 1.12, and the 5-nitroquinoline nitrate which crystallized on cooling was dissolved in 500–600 cc. of hot water, the solution was clarified with Darco and treated with 100 cc. of concentrated nitric acid. The pale yellow nitrate which crystallized was dissolved in 1 liter of hot water, and on neutralization with ammonia 71 g. (35%) of satisfactory **5-nitroquinoline** separated, m. p. 70–71°. The **8-nitroquinoline** was precipitated with ammonia from the first nitrate mother liquor and amounted to 87 g., m. p. 77–87°. Recrystallization from alcohol gave material melting at 88–89°.

Hydrogenation of the Nitroquinolines.—The intermediate reduction products are less soluble than the nitro compounds or the amines; they are sensitive substances and may undergo some decomposition in the course of a hydrogenation involving a rapid temperature rise. Hydrogenation occurs rapidly in an alcoholic medium, but alcohol promotes decomposition, particularly with the highly sensitive 8-hydroxylamino compound, and the solvent power is not great. Ethyl acetate dissolves the nitro and hydroxylamino derivatives better and the intermediates are much more stable in this solvent, but hydrogenation proceeds only at a slow rate in pure ethyl acetate. The reaction is markedly promoted by the addition of as little as 8% of alcohol, and a combination of the two solvents is the most satisfactory medium found for this type of hydrogenation. Hydrogenation proceeds only very slowly when ether is employed and there seems to be no advantage in using ether in conjunction with the other two solvents, as in one of the experiments listed below.

5-Hydroxylaminoquinoline.—A solution of 3.48 g. of 5-nitroquinoline in 50 cc. of ethyl acetate and 50 cc. of absolute alcohol was shaken with hydrogen in the presence of 100 mg. of Adams catalyst until 2 moles of hydrogen had been absorbed. The clear yellow solution was treated with Darco to coagulate the catalyst and the filtrate was evaporated to dryness in vacuum keeping the temperature below 25°. The solid was dissolved in the minimum amount of methanol at room temperature, benzene was added and the solution was concentrated until crystallization began. The crystallizate of hydroxylamino compound amounted to 1.74 g. (50%), m. p. 155–160°, dec. The decomposition temperature, which varies considerably with the rate of heating, remained the same after four recrystallizations from ether–hexane and benzene–methanol. The substance is very sensitive to heating in solutions containing ethanol but is more stable in mixed solvents in which methanol is one component. The purified material consisted of light yellow, flat needles.

Anal. Calcd. for $C_9H_8ON_2$: C, 67.48; H, 5.04. Found: C, 67.69; H, 4.91.

The substance reduces Tollens reagent and forms a silver salt when treated with alcoholic silver nitrate.

For preparation of the **dibenzoyl derivative,** 0.2 g. of the substance was dissolved in 3–4 cc. of pyridine and a few drops of benzoyl chloride were added, keeping the temperature below 25°. The solution became nearly black and

(18) Fieser and Desreux, THIS JOURNAL, **60**, 2255 (1938).

(19) Fieser and Hershberg, *ibid.*, **61**, 1565 (1939).

(20) Morgan and Coulson, *J. Chem. Soc.*, 2551 (1929); Fieser and Peters, THIS JOURNAL, **54**, 3742 (1932).

(21) All melting points are corrected. Microanalyses by Lyon Southworth.

after twenty-four hours thick white prisms had separated admixed with black tar. The crystals were separated, and after clarification of an ethereal solution with Norit the substance crystallized from ether–hexane in the form of fine white needles, m. p. 162.8–163.3°.

Anal. Calcd. for $C_{28}H_{16}O_3N_2$: C, 74.97; H, 4.38; N, 7.61. Found: C, 75.19; H, 4.48; N, 7.47.

The **diacetyl derivative** was obtained by adding excess ketene to a suspension of 0.5 g. of the hydroxylamino compound in 15 cc. of anhydrous acetone. After standing at room temperature for one-half hour the solution was concentrated, hexane was added, and on distillation of most of the remaining acetone a tar began to separate. The liquor was decanted, diluted with ether and clarified with Norit, and after concentration a further quantity of tar was removed. After repeating the process the solution eventually afforded a crystallizate which separated from ether–hexane in the form of colorless prisms, m. p. 115.5–116°.

Anal. Calcd. for $C_{13}H_{12}O_3N_2$: C, 63.90; H, 4.96. Found: C, 64.19; H, 4.87.

8-Hydroxylaminoquinoline.—A solution of 1.74 g. of the nitro compound in 10 cc. of ethyl acetate was treated with 20 mg. of Adams catalyst, hydrogenated as above (slow), and the solution was diluted with hexane without removing the catalyst, giving 1.0 g. (62%) of precipitated product, m. p. 99–100°, dec. This was recrystallized by dissolving it in ether, clarifying the solution with Darco, concentrating the filtrate and adding hexane until crystals began to separate. The substance formed straw-colored, flat needles (0.73 g.), m. p. 101–102°, dec.; it has reducing properties as noted for the 5-isomer and is more sensitive than this substance, the purified solid turning brown in a few days.

Anal. Calcd. for $C_9H_8ON_2$: C, 67.49; H, 5.04; N, 17.49. Found: C, 67.42; H, 5.33; N, 17.13.

The substance formed a picrate from absolute alcohol which separated as orange-yellow needles, melting with decomposition at about 120–125°, but the complex decomposed on attempted recrystallization and the nitrogen content was about 1% low. A trinitrobenzene derivative apparently forms in alcoholic or ethereal solution but is even more readily dissociated.

5-Aminoquinoline.—A suspension of 34.8 g. of 5-nitroquinoline in 200 cc. of absolute alcohol was hydrogenated in the presence of 0.4 g. of Adams catalyst, the reaction proceeding to completion, with marked temperature rise, in about two hours. To prevent the intermediate hydroxylamino compound from plugging the gas inlet tube this was equipped with a widened opening provided with a series of baffles and holes. The solution of the amine was clarified with charcoal, the solvent was removed in vacuum, and the residue distilled, giving 27.5 g. (95%) of product, b. p. 180–181° at 7 mm., m. p. 100–107°. Crystallization from ether gave a total of 23.5 g. (82%) of amine, m. p. 108–110°.

8-Aminoquinoline.—A suspension of 34.8 g. of 8-nitroquinoline and 0.25 g. of Adams catalyst in 150 cc. of ethyl acetate, 25 cc. of absolute alcohol and 25 cc. of ether absorbed three moles of hydrogen in one and one-half hours. On recovery of the product as above there was obtained 27.6 g. (96%) of distillate, b. p. 140.5–141.5° at 7 mm., m. p. 62.5–63.5°. On recrystallization from ether–hexane the amine melted at 64–65°.

5- and 8-Cyanoquinoline

5-Cyanoquinoline[17] was prepared by the Sandmeyer reaction from 10 g. of the amine, diazotized at 0° in 70 cc. of concentrated hydrochloric acid and 140 cc. of water with 6 g. of sodium nitrite in 30 cc. of water. The solution was neutralized with excess sodium carbonate (about 30 g.) and poured into a solution of 12.6 g. of cuprous cyanide and 13 g. of potassium cyanide in 100 cc. of water, previously titrated with hydrochloric acid until only a faint precipitate of cuprous cyanide persisted. The reaction product was removed from the tarry mixture by steam distillation. The distillate, amounting to about 4 liters, was saturated with sodium chloride and the cyanide collected by extraction with ether and distilled. There was obtained 5.44 g. (51%) of pure product, b. p. 145–147° at 7–8 mm., m. p. 87–88°.

8-Cyanoquinoline.—As attempts to prepare this isomer by the Sandmeyer reaction resulted only in the formation of intractable tars, the route through the chloride was investigated. 8-Chloroquinoline was obtained by the Skraup synthesis following the directions of Fourneau, Tréfouel and Wancolle,[22] the yield of material b. p. 137–140° at 7 mm., being lower (33%) than reported.

A mixture of 5 g. of 8-chloroquinoline, 3.3 g. of cuprous cyanide, 10 cc. of pyridine and 3–4 drops of acetonitrile was heated in a sealed tube at 200° for eighteen hours. The deep brown solution was shaken with aqueous ammonia, benzene and ether and the organic layer was washed and dried and the product distilled at 2 mm. The pale yellow distillate quickly solidified and on crystallization from ether–hexane afforded 3.2 g. (67%) of satisfactory material, m. p. 82–83.5°. Lellmann and Reusch,[17] who prepared the compound from the sulfate, found the m. p. 84°.

Preparation and Pyrolysis of the Ketones

5-Quinolyl *o*-Tolyl Ketone (VII).—The addition of a solution of 2.8 g. of 5-cyanoquinoline in 50 cc. of benzene to the Grignard reagent from 4.6 g. of *o*-bromotoluene in ether gave an immediate reddish-brown precipitate which slowly changed to deep red on refluxing overnight. Dilute hydrochloric acid was added in excess and after refluxing for two hours to hydrolyze the ketimine the mixture was made alkaline and extracted with benzene, the precipitated magnesium hydroxide being readily separated by centrifugation. Distillation of the dark residue from the benzene extract at 2 mm. (b. p. 190–200°) and crystallization from ether–petroleum ether gave 1.5 g. (33%) of ketone, m. p. 90–91°. On recrystallization from the same solvent the substance formed colorless, diamond-shaped prisms, m. p. 91.7–92.2°.

Anal. Calcd. for $C_{17}H_{13}ON$: N, 5.67. Found: N, 5.98.

An attempt to synthesize the ketone from 5-bromoquinoline and *o*-tolunitrile was unsuccessful. The bromide (b. p. 137–140° at 8 mm.), prepared from the amine in 49% yield according to Dikshoorn,[14] was added with one equiva-

(22) Fourneau, Tréfouel and Wancolle, *Bull. soc. chim.*, [4] **47**, 738 (1930).

lent of ethyl bromide in ether to two equivalents of magnesium in ether and the resulting tarry mixture refluxed with *o*-tolunitrile for two days, but no ketone could be isolated.

4'-Aza-1,2-benzanthracene (β-Anthraquinoline, I).—Pyrolysis of 0.4 g. of the above ketone with 0.1 g. of zinc dust at 420–425° for one hour followed by vacuum distillation gave a yellow distillate. On passing a benzene solution of the material through a column of alumina the product was adsorbed in an intermediate zone showing blue fluorescence in ultraviolet light. After removing an upper yellow layer the column was eluted with benzene–alcohol and the material collected by evaporating the filtrate was crystallized from hexane, giving 25 mg. (7%) of yellowish crystal aggregates, m. p. 167–168°. On recrystallization the substance melted at 168.5–169.5° (Graebe,[8] m. p. 170°).

5-Quinolyl 7-Methyl-4-hydrindyl Ketone (IX).—A solution of 4 g. of 5-cyanoquinoline in 25 cc. of benzene was added to the lithium derivative from 6.5 g. of 4-chloro-7-methylhydrindene in ether and after refluxing for eight hours dilute hydrochloric acid was added, the organic solvent was evaporated, and the solution heated for fifteen hours on the steam-bath. On making the solution alkaline a dark tar separated, and this was extracted with benzene. Distillation at 2 mm. gave an oil boiling at 240–250° which solidified on scratching. Two crystallizations from ether gave 1.3 g. (17.5%) of material, m. p. 133.5–135°, and two further crystallizations from ether–hexane raised the m. p. to 135–135.5°. The ketone formed glistening, colorless blades.

Anal. Calcd. for $C_{20}H_{17}ON$: C, 83.57; H, 5.96. Found: C, 83.59; H, 6.05.

20-Methyl-4-azacholanthrene (X).—Pyrolysis of 0.86 g. of the ketone IX for three to four minutes at 440° and distillation of the residue at 2 mm. gave a solid distillate which when dissolved in benzene and passed through a column of alumina and Super-Cel was adsorbed in a fluorescent light yellow zone. After elution with benzene and removal of the solvent the residual oil was crystallized from hexane, giving 95 mg. (12%) of pale yellow leaflets, m. p. 181–183°. Two recrystallizations from ether–hexane raised the m. p. to 184–185°. When treated with dilute hydrochloric acid the solid turns orange-red, and on boiling the solid becomes yellow and some material dissolves to give a yellow solution.

Anal. Calcd. for $C_{20}H_{15}N$: C, 89.20; H, 5.61. Found: C, 89.03; H, 5.47.

Picrate.—With picric acid in benzene the substance gives an amorphous precipitate which is insoluble in benzene, alcohol, acetone or ether and only slightly soluble in dioxane or glacial acetic acid. From glacial acetic acid it formed golden brown needles, m. p. 288–290°, dec.

Anal. Calcd. for $C_{20}H_{15}N \cdot C_6H_3O_7N_3$: N, 11.24. Found: N, 11.02.

The **trinitrobenzene derivative** crystallized from benzene–ligroin in fine red needles, m. p. 175–176°.

Anal. Calcd. for $C_{20}H_{15}N \cdot C_6H_3O_6N_3$: N, 11.62. Found: N, 11.90.

8-Quinonyl 7-Methyl-4-hydrindyl Ketone (XI).—A solution of 4 g. of 8-cyanoquinoline in 50 cc. of benzene was added to the ethereal Grignard solution from 6.5 g. of 4-bromo-7-methylhydrindene and after refluxing for forty-eight hours the tarry reaction mixture was worked up as above. Distillation of the extracted product at 2 mm. gave 4.7 g. of yellow-brown, viscous distillate, b. p. 240–245°, which crystallized when treated with ether. Recrystallization from ether gave 4.25 g. (57%) of ketone in two crops, m. p. 133–135°. After a further crystallization the substance formed colorless prisms, m. p. 135–135.6°.

Anal. Calcd. for $C_{20}H_{17}ON$: C, 83.57; H, 5.96. Found: C, 83.80; H, 5.76.

Pyrolysis of Ketone XI.—In the most satisfactory experiment 1.0 g. of the ketone was heated with 20 mg. of 30% palladium charcoal at 400–410° for ten minutes. Distillation of the product at 2 mm. and crystallization from benzene–ligroin gave 0.51 g. (50%) of golden brown needles. When heated slowly in a capillary the substance (possibly XII) melted at 182–182.5°; when immersed in a bath at 170° it melted at 175.5–176.5°, solidified, and remelted at 182–182.5°.

Anal. Calcd. for $C_{20}H_{15}ON$: C, 84.19; H, 5.30. Found: C, 83.98; H, 5.07.

On attempted reduction by prolonged boiling with zinc dust and ammonia, the starting material was recovered unchanged. No reaction was observed on treatment with acetic anhydride and pyridine, with acetic anhydride, zinc dust and sodium acetate, or with methylmagnesium bromide.

Summary

The Elbs reaction was shown applicable to the synthesis of pyridine isologs of 1,2-benzanthracene and cholanthrene by its use in the preparation of the known 4'-aza-1,2-benzanthracene (β-anthraquinoline, I). The reaction was then used successfully for the synthesis of 20-methyl-4-azacholanthrene (X). The compound is being tested to see if it produces tumors at the site of application, like the corresponding hydrocarbon, or resembles certain of the azo dyes and other nitrogen-containing carcinogens in acting at a remote site. In an attempt to synthesize the isomeric 1-aza derivative the pyrolysis afforded in 50% yield an unreactive substance which most likely is the chelated anthranol XII.

It has been found that 5- and 8-nitroquinoline can be converted smoothly by partial catalytic hydrogenation into the corresponding hydroxylamine derivatives, which separate as sparingly soluble intermediates, possibly of salt-like structure. A study of the behavior of other nitro compounds is now in progress.

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