TABLE I

EMPIRICAL CONSTANTS, MOLAR REFRACTIONS, MOLAR POLARIZATIONS AND ELECTRIC MOMENTS IN BENZENE SOLUTION AT 25°

Compound	ϵ_1	a	v_1	b	P_2	MR_D	$\mu_{obsd.}$
11-Methyl-11-azabicyclo[5.3.1]hendecan-4-one	2.2730	33.17	1.14478	−0.496	537.6	52.79	4.87
Pseudopelletierine	2.2725	10.65	1.14478	− .443	198.5	43.49	2.75
1-Ethyl-4-piperidone	2.2725	11.90	1.14476	− .158	214.6	36.26	2.95
1-Methylpiperidine	2.2725	0.555	1.14480	− .117	44.68	31.65	0.80

Anal. Calcd. for $C_{17}H_{22}N_4O_8$: C, 49.75; H, 5.41; N, 13.65. Found: C, 49.42; H, 5.38; N, 13.34.

The infrared spectrum of the picrate (mull) exhibited strong maxima at 3225, 3100 and 1637 cm.$^{-1}$ and was transparent in the region 2000–1640 cm.$^{-1}$. The spectrum was similar to that of 1-methyl-1-azacyclodecan-6-one picrate.[17]

Pseudopelletierine.—The ultraviolet spectrum of pseudopelletierine[18] in absolute ether exhibited maxima at 213 mμ, log ϵ 2.99, and 246 mμ, log ϵ 2.93. The infrared spectrum of a 5% solution in carbon tetrachloride exhibited a strong sharp maximum at 1709 cm.$^{-1}$.

The **perchlorate** salt was formed in ether and recrystallized from absolute ethanol as colorless needles, m.p. 256–258°, infrared maxima (Nujol mull) at 3070, 1728 and 1710 cm.$^{-1}$, the latter the more intense of the carbonyl pair.

Anal. Calcd. for $C_9H_{16}ClNO_5$: C, 42.62; H, 6.36; N, 5.52. Found: C, 42.61; H, 6.63; N, 5.33.

The ***p*-toluenesulfonate** salt was made in order to determine whether the double carbonyl peak for the perchlorate would be found in salts with other anions or whether this infrared anomaly might not be a property of the crystal. The *p*-toluenesulfonate was formed in ether and recrystallized from absolute ethanol as colorless plates, m.p. 171–172°. The salt exhibited infrared maxima at 2680, 2560 $(\overset{+}{N}-H)$ and 1733 cm.$^{-1}$ (C═O) in Nujol mull, and at 3440, 2480 $(\overset{+}{N}-H)$ and 1729 cm.$^{-1}$ (C═O) in chloroform (5% solution).

Anal. Calcd. for $C_{16}H_{23}NO_4S$: C, 59.05; H, 7.12; N, 4.30. Found: C, 59.46; H, 7.16; N, 4.29.

Other Materials.—1-Ethyl-4-piperidone[19] and 1-methylpiperidine[20] were prepared in the usual way and purified by fractional distillation. Benzene was purified by fractional crystallization and was dried over sodium.[21]

Apparatus and Method.—The dielectric constants and densities of five solutions, ranging in concentration from 0.0007 to 0.007 in mole fraction solute, were measured in benzene solution at 25°. The apparatus, technique, method of calculation and definition of symbols have been given elsewhere.[21] The constants ϵ_1, a, v_1, b of the Halverstadt–Kumler equation are shown in Table I for each compound along with the derived value of the molar polarization of solute at infinite dilution, P_2. The sum of the electronic and atomic polarizations was taken to be equal to the molecular refraction MR_D calculated from empirical constants. The observed values of the electric moments are shown in Table I; the probable error in each is about ±0.1D.

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[17] N. J. Leonard, M. Ōki and S. Chiavarelli, THIS JOURNAL, **77**, 6234 (1955).

[18] A. C. Cope, H. L. Dryden, Jr., C. G. Overberger and A. A. D'Addieco, *ibid.*, **73**, 3416 (1951).

[19] S. M. McElvain, *ibid.*, **46**, 1721 (1924).

[20] J. von Braun, *Ber.*, **37**, 2915 (1904).

[21] M. T. Rogers, THIS JOURNAL, **77**, 3681 (1955).

URBANA, ILLINOIS
EAST LANSING, MICHIGAN

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, IOWA STATE COLLEGE]

The Chemistry and Synthetic Applications of the Phenanthridinone System

BY HENRY GILMAN AND JOHN EISCH

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In a study of the substitutional chemistry of phenanthridinone it was found that this system could be chlorinated, iodinated and sulfonated readily at the 2-position. A nitro group could be introduced easily into the 4-position only if the 2-position was blocked. However, nitration and bromination of 2-acetaminophenanthridinone may have led to the 1- or 3-substituted derivatives. In addition, the N-methylation of certain electronegatively substituted phenanthridinones was accomplished by heating their potassium salts with methyl iodide in ethanol. The reduced reactivity of the carbonyl group of phenanthridinone was shown in its slow reaction with butyllithium and also by the halogen–metal interconversion reaction possible between the 2-bromo isomer and butyllithium. Although phenanthridine could be hydroxylated by potassium hydroxide to give phenanthridinone, infrared data did not support the representation of this compound as 6-hydroxyphenanthridine.

Although phenanthridine (9-azaphenanthrene) was isolated as early as 1884,[1] the system received little attention until some 50 years later, when 6-arylphenanthridines were shown to be efficacious in fighting bovine trypanosomiasis.[2] Consequently, in recent years a multitude of phenanthridine derivatives have been prepared by the cyclization of 2-acylaminobiphenyls, in order to develop superior trypanocides and to evaluate the general biological activity of this heterocyclic system.[3] Generally, the ring closure of 2-acylaminobiphenyls is successful, but oftentimes the suitably substituted 2-aminobiphenyl is cumbersome to synthesize.

The recently developed cyclization of 2-biphenylyl isocyanate[4] to phenanthridinone (I) affords an excellent preparative method for this amide. Accordingly, the attractive alternative of introduc-

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[1] C. Graebe, *Ber.*, **17**, 1370 (1884).

[2] G. T. Morgan and L. P. Walls, *J. Chem. Soc.*, 389 (1938).

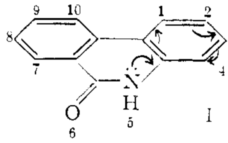
[3] (a) L. P. Walls, *ibid.*, 294 (1945); 1031 (1946); 67 (1947); 3511 (1950); (b) R. S. Theobald and K. Schofield, *Chem. Revs.*, **46**, 171 (1950).

[4] J. M. Butler, THIS JOURNAL, **71**, 2578 (1949).

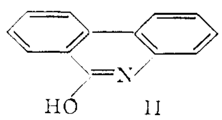
ing substituents into phenanthridinone and converting this system to the corresponding phenanthridine may offer an approach to new chemotherapeutic agents. As there exist several methods for converting phenanthridinones to phenanthridine systems,[5] the present study was proposed to investigate the substitutional chemistry of phenanthridinone.

Up to the present, the N-alkylation,[6] nitration[7] and bromination[8] of this heterocycle have been reported. As long ago as 1893, Graebe and Wander[6] prepared 5-alkylphenanthridinones by heating the solid potassium salt of phenanthridinone with alkyl halides in a sealed tube. The nitration of this amide was first carried out by Moore and Huntress,[7] who isolated two unknown mononitro derivatives. These latter compounds recently were shown to be the 2- and 4-nitro isomers by two independent research groups.[9] Shortly thereafter, Mosby[8] demonstrated that the amide gave an almost quantitative yield of 2-bromophenanthridinone by heating with bromine in glacial acetic acid.

As phenanthridinone (I) is the lactam of 2-aminobiphenyl-2′-carboxylic acid, it may be viewed as a closed model of benzanilide. By empirical analogy it would be expected that the 2-position and, to a lesser extent, the 4-position would be prone to electrophilic substitution. This intuitive approach is supported by the theoretical view that the unshared π-electron pair on the amide nitrogen can enhance the electron density at these same positions.[10]

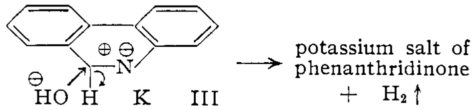


I



II

In regard to the status of the amide linkage there is at least a formal possibility that the tautomeric form (II) (6-hydroxyphenanthridine) may make a contribution. This was suggested by the observation that phenanthridine readily can be converted to phenanthridinone by the Chichibabin hydroxylation reaction, *i.e.*, heating a pyridine base with solid potassium hydroxide.[11] This reaction seems to proceed by a nucleophilic attack of hydroxide ion at C_6 in phenanthridine (a position of low charge density) and expulsion of hydride ion *via* III.



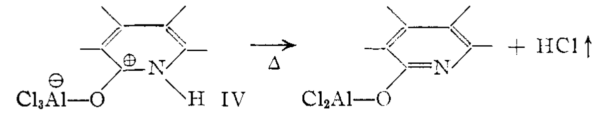
III

However, present investigations of the infrared spectra of phenanthridinone and its derivatives have found sharp N—H bands at 3.1–3.2 μ and intense C=O bands at 6.0 μ. Since there was no discernible absorptions for O—H and C=N, it is felt that the amide tautomer form is an adequate description of the system. The chemical behavior of this heterocycle is in full accord with this conclusion.

On the basis of its similarity to benzanilide, this amide should also be a reactive molecule. Not only can it be quantitatively nitrated[7] and brominated,[8] but it was found that both chlorination and iodination can be performed with facility. Indeed, 2-chlorophenanthridinone could be obtained in 88% yield by simply stirring a slurry of phenanthridinone with chlorine and iron catalyst in acetic acid at moderate temperatures. The use of iodide-iodate in hot acetic acid gave an 88% yield of pure 2-iodophenanthridinone. Likewise, heating the amide with concentrated sulfuric acid was sufficient for quantitative sulfonation.

The major product in these substitution reactions is undoubtedly the 2-isomer. With the chloro- and iodophenanthridinones isolated, this conclusion is supported by their infrared spectra, which are almost superimposable on that of the 2-bromo isomer. Moreover, the N-methylation of the chloro isomer led to a substance with the same melting point as the known 2-chloro-5-methylphenanthridinone.[12] In the case of the sulfonic acid the infrared spectrum showed bands indicative of a 1,2,4-trisubstituted benzene ring. Hence, the location of the sulfonic acid group at the 2-position is presumed.

The ease with which Compound I underwent substitution in the foregoing reactions led to the belief that the system could be acetylated in a Friedel–Crafts reaction. Although hydrogen chloride was evolved copiously when Compound I was heated in tetrachloroethane with acetyl chloride and aluminum chloride, the amide was recovered quantitatively. It appears likely that the amide group reacted with the catalyst to form a complex (IV) which deactivated the system



IV

The introduction of substituents into the 4-position of I is hindered by the superior reactivity of the 2-position. It seems that very reactive electrophilic reagents can attack both positions. In the nitration of I with concentrated nitric acid, the ratio of 2-nitro:4-nitro was found to be 6:1. It is also likely that a low-melting fraction isolated from the chlorination of I was the impure 4-chloro isomer, but the amount was too small to identify. However, once the 2-position was blocked by a substituent, it was possible to introduce a nitro group rather easily into the 4-position. For example, 2-bromo- or 2-chlorophenanthridinone could be nitrated with concentrated nitric acid to give a 60% yield of the 2-halo-4-nitrophenanthridinone. Curiously enough, the attempted preparation of 2-iodo-4-nitrophenanthridinone by the same procedure resulted in the apparent displacement of the iodine atom. The verification of the position of the nitro group is founded upon interesting observations

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(5) L. P. Walls, in R. C. Elderfield, ed., "Heterocyclic Compounds," Vol. IV, John Wiley and Sons, Inc., New York, N. Y., 1950, Chap. 4.

(6) C. Graebe and C. A. Wander, *Ann.*, **276**, 245 (1893).

(7) F. J. Moore and E. H. Huntress, This Journal, **49**, 1324 (1927).

(8) W. L. Mosby, *ibid.*, **76**, 936 (1954).

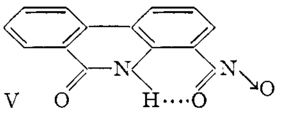
(9) (a) A. G. Caldwell and L. P. Walls, *J. Chem. Soc.*, 2156 (1952); (b) A. J. Nunn, K. Schofield and R. S. Theobald, *ibid.*, 2797 (1952).

(10) C. K. Ingold, "Structure and Mechanism in Organic Chemistry," Cornell University Press, Ithaca, N. Y., 1953, p. 238.

(11) A. E. Chichibabin, *Ber.*, **56**, 1879 (1923).

(12) R. A. Heacock and D. H. Hey, *J. Chem. Soc.*, 4059 (1952).

made with 4-nitrophenanthridinone itself. Since of all the possible nitrophenanthridinones the 4-isomer is the only one having a nitro group situated adjacent to the N-H group, this compound has a favorable structure for intramolecular hydrogen bonding (V)

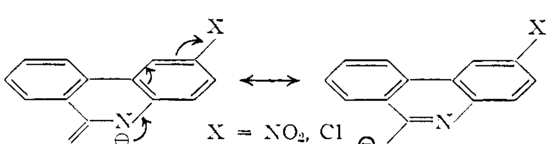


V

The consequences of this intramolecular bonding are a deepening of color (bright yellow), shift of the N-H and NO_2 bands to longer wave lengths and a marked lowering of intermolecular forces. This latter results in an abnormally lower melting point. (The 4-nitro isomer melts 30 degrees lower than I itself.) This collection of properties furnished excellent criteria for the detection of a 4-nitro group in substituted phenanthridinones. Thus the 2-halo-4-nitrophenanthridinones were bright yellow solids melting some 40 degrees lower than the white 2-halophenanthridinones and their infrared spectra exhibited N-H and NO_2 bands shifted to longer wave lengths.

A feasible approach to the synthesis of 1- and 3-substituted phenanthridinones may develop from the reactions of the 2-acetamino derivative. This compound was obtained from the 2-nitro derivative in 80% yield by reduction with zinc in acetic acid. Subsequent nitration and bromination led to presumably either 1- or 3-substituted-2-acetamino derivatives. Of these two positions, the 1-position would seem to be favored because of the greater reactivity of such an "α"-position (*i.e.*, adjacent to an aromatic ring).

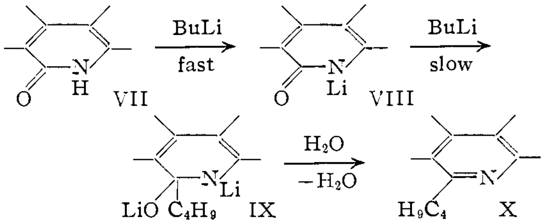
In addition to aromatic substitution of phenanthridinone, some interesting synthetic possibilities of the amide linkage were uncovered. It has been long known that the amide hydrogen is sufficiently acidic to make the amide soluble in alcoholic potassium hydroxide.[6] The heightened acidity of this system can be traced back to the delocalization of the anion's negative charge over the carbonyl group and the aromatic π-cloud. Electronegative substituents such as chloro and nitro should further enhance this effect (VI).



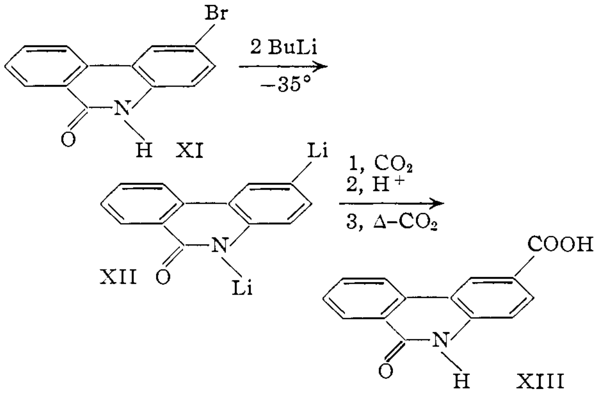
VI

Chemically, this should mean that on the one hand the anion may be methylated readily in ethanol (similar to sodium ethylacetoacetate), and on the other hand the carbonyl group should be deactivated to attack by anions. Both of these assumptions have experimental verification. In the first case, the potassium salts of 2-chloro- and 2-nitrophenanthridinones reacted in ethanol with methyl iodide to give high yields of N-methyl derivatives (compare Graebe's stringent methylation procedure).[6]

Secondly, the carbonyl group was indeed deactivated. Not only could the dissolved amide salt be recovered by acidification without hydrolysis of the amide linkage, but phenanthridinone itself reacted very slowly with two equivalents of butyllithium. Thus 54% of the amide was recovered unchanged after 12 hr.; the other product was 6-butylphenanthridine (VII-X).



This reduced reactivity of the amide linkage in basic medium was used in obtaining a halogen-metal interconversion reaction between 2-bromophenanthridinone and butyllithium at low temperatures. Subsequent carbonation and decarboxylation of the N-carboxy group gave an 82% yield of phenanthridinone-2-carboxylic acid (XI-XIII)



Experimental

The phenanthridinone employed in these studies was supplied by Chas. Hardy and Sons, New York, N. Y., as white needles, m.p. 293°. The melting points herein were obtained upon an electrically heated copper block and are corrected. Spectral data for solid compounds were obtained from samples suspended in Nujol.

Phenanthridinone from Phenanthridine.—The Chichibabin[11] hydroxylation reaction with potassium hydroxide was found to be applicable to phenanthridine. To obtain satisfactory results it was found necessary to fuse the potassium hydroxide beforehand. A mixture of 10.0 g. (0.056 mole) of phenanthridine, 20.5 g. of freshly fused and crushed potassium hydroxide and 5.0 g. of barium oxide was heated in a copper vessel at a bath temperature of 225 ± 5° for 1 hr. The vigorous evolution of hydrogen virtually ceased after the first 30 minutes. The cooled reaction mixture was eluted from the flask with three 60-ml. portions of dilute hydrochloric acid. Upon treating the suspension with sodium hydroxide in excess and filtering, 12.2 g. of tan solid was obtained. Recrystallization from 200 ml. of glacial acetic acid gave 7.3 g. (67%) of white solid, m.p. 290–292°. A sample of white needles was obtained by recrystallization from the same solvent, m.p. 292.5–293.5°. A mixture melting point determination showed it to be phenanthridinone. The infrared spectrum exhibited a N-H band at 3.1 μ and a C=O band at 6.05 μ.

2-Bromophenanthridinone.—The procedure followed to brominate phenanthridinone was essentially that reported by Mosby.[8] On a 0.20-mole run the yield of 2-bromophenanthridinone melting at 323–325° was 91% of the theoretical. Recrystallizations from nitrobenzene gave white microneedles, m.p. 325.5–326.5°, but samples obtained from pyridine melted at 328.5–329°. The infrared spectrum showed prominent bands (in μ) at 3.18 (N—H), 5.95 (C=O), 11.1, 11.3, 11.5, 12.9 and 13.9.

Chlorination of Phenanthridinone.—A mixture of 19.5 g. (0.10 mole) of phenanthridinone, 0.5 g. of iron powder and 400 ml. of glacial acetic acid was treated with a solution of 10 g. (0.14 mole) of chlorine gas in 200 ml. of glacial acetic acid, added to the unheated and stirred suspension over a 1 hr. period. The contents warmed somewhat and the initial orange color became pale yellow. After stirring overnight the mixture was poured into two liters of water. The pale pink solid, upon collection and drying, weighed 23.5 g. and melted over the range 288–305°. After extraction in a Soxhlet apparatus with 300 ml. of absolute ethanol for 9 hr., the residue from the thimble weighed 18.2 g. (80%) and melted from 316–321°. Evaporation of the extracts gave 4.5 g. of solid melting from 245–285°. Upon refluxing this lower melting material with 400 ml. of ethanol, an additional 2.0 g. of residue was obtained, m.p. 319–321°. From the filtrate 0.2 g. of tan powder was obtained, melting over the range 195–205°. Recrystallized from pyridine (Norit), the combined residues (20.2 g., 88%) gave pure 2-chlorophenanthridinone, 16.5 g. (71%), m.p. 327–328°. The infrared spectrum of this chlorophenanthridinone was almost identical with that of 2-bromophenanthridinone.

Anal. Calcd. for $C_{13}H_8ClNO$: Cl, 15.45; N, 6.10. Found: Cl, 15.58; N, 6.10.

Iodination of Phenanthridinone.—In an apparatus similar to that employed in the preceding chlorination procedure, 19.5 g. (0.10 mole) of phenanthridinone, 11.1 g. (0.067 mole) of potassium iodide, 300 ml. of glacial acetic acid and 15 ml. of water were heated between 55 and 60°, while 16.1 g. (0.075 mole) of potassium iodate was added portionwise over 1 hr. The red-colored suspension was then refluxed for 15 hr., after which time most of the iodine color had faded. The mixture was poured into 1.5 l. of water and a little sodium sulfite added to remove the residual iodine. Collection and drying of the solid gave 31.0 g. (96.5%) of fluffy, cream-colored needles, m.p. 321–323°. Recrystallized from 225 ml. of nitrobenzene, the shiny white needles of 2-iodophenanthridinone weighed 28.4 g. (88%) and melted at 323–325°. An analytical sample was obtained from pyridine, m.p. 323.5–325°.

Anal. Calcd. for $C_{13}H_8INO$: I, 39.52; N, 4.36. Found: I, 39.49; N, 4.34.

As in the case of 2-chlorophenanthridinone, the infrared spectrum of this 2-iodophenanthridinone was almost superimposable on that of 2-bromophenanthridinone.

Nitration of Phenanthridinone.—In an adaptation of the original procedure of Moore and Huntress,[7] 19.5 g. (0.10 mole) of stirred phenanthridinone was treated with 244 ml. of concentrated nitric acid during the course of 25 minutes. The resulting golden-yellow solution gradually became orange-red, and after 35 minutes an unstirrable yellow paste formed. After standing overnight the reaction mixture was diluted with water and filtered to give 23.1 g. (96%) of pale yellow solid, melting over the range 360–373°. Extraction with 300 ml. of absolute ethanol left cream-colored 2-nitrophenanthridinone, 19.8 g. (83%), m.p. 378–380°. From glacial acetic acid a white product was obtained, m.p. 382–383°, with blackening.

The ethanolic extracts yielded, upon concentration and cooling, 3.3 g. of the impure 4-nitro isomer, melting from 248–254°. Recrystallizations from glacial acetic acid gave bright yellow needles, m.p. 264–265°.

The infrared spectra of both compounds showed bands at 3.2 μ (N—H), 6.0 μ (C═O) and at 6.6 and 7.5 μ (NO_2). The latter antisymmetric and symmetric nitro bands were shifted to longer wave lengths, especially in the case of the 4-nitro isomer.

Sulfonation of Phenanthridinone.—A mixture of 19.5 g. (0.10 mole) of phenanthridinone and 50 ml. of concentrated sulfuric acid was heated at 150° (oil-bath temperature) for 18 hr. Thereupon the cooled solution was poured onto 400 g. of ice, and the resulting solution treated portionwise with 30 g. of sodium bicarbonate. While heated to boiling, 15 g. of sodium chloride was added, whereupon a cream-colored solid began to separate. Filtration of the cooled mixture gave 34.6 g. of solid. This was digested in 500 ml. of boiling water containing 60 g. of sodium chloride. Collection and drying of the undissolved product gave 29.1 g. (98% based on the sodium salt) of white sodium phenanthridinone-2-sulfonate. The barium salt was prepared and analyzed. The infrared spectrum of the sodium sulfonate exhibited bands at 3.2 μ (N—H), 5.95 μ (C═O) and at 2.8, 8.5 and 9.5 μ (ionic sulfonate). The region from 12 to 16 μ resembled that of 2-bromophenanthridinone's spectrum.

Anal. Calcd. for $C_{26}H_{16}BaN_2O_8S_2$: Ba, 20.02. Found: Ba, 20.07.

A *p*-toluidine salt was prepared by the method of Fieser[13] and recrystallized from water as colorless needles, m.p. 283–284° with darkening.

Attempted Acetylation of Phenanthridinone.—A mixture of 19.5 g. (0.10 mole) of phenanthridinone, 14.2 g. (0.18 mole) of acetyl chloride and 350 ml. of *sym*-tetrachloroethane was treated with anhydrous aluminum chloride (41 g., 0.31 mole) over the course of 20 minutes. Hydrogen chloride was evolved as the reaction slurry became pale yellow. The suspension was stirred for 6 hr. at incipient reflux, during which time more hydrogen chloride was given off and the contents changed to a dark tarry mixture. The mixture then was poured into an ice-concentrated hydrochloric acid mixture, and the suspended tan solid was filtered off. After washing with ether and drying, the collected solid weighed 19.4 g. (99.5% recovery) and melted 290–292°. A mixture melting point determination showed it was phenanthridinone.

2-Acetaminophenanthridinone.—2-Nitrophenanthridinone (20.0 g., 0.083 mole) was stirred for 4 hr. with 40 g. (0.61 g. atom) of zinc dust and 400 ml. of glacial acetic acid. The slurry warmed considerably from the heat of the reaction. To complete acetylation the reaction mixture was heated at incipient reflux for 6 hr. The cooled mixture was poured into water and the solid collected on a filter. The product was extracted with glacial acetic acid in a Soxhlet apparatus. Filtration of the cooled acetic acid gave 17.2 g. (80%) of cream-colored solid, m.p. 358–359.5°. The infrared spectrum displayed bands at 3.1 and 3.2 μ (N−H) and sharp bands at 5.95 and 6.05 μ (C═O).

Anal. Calcd. for $C_{15}H_{12}N_2O_2$: N, 11.01. Found: N, 10.93.

Nitration of 2-Acetaminophenanthridinone.—Two grams (0.0079 mole) of 2-acetaminophenanthridinone in 25 ml. of glacial acetic acid was treated with a solution of 2 ml. of fuming nitric acid in 5 ml. of glacial acetic acid over a 15-minute period. Then 5 ml. of glacial acetic acid was added to fluidize the stiff paste. After standing, the mixture was diluted with water and filtered. The yellow product weighed 2.2 g. and melted over the range 330–340°. Two recrystallizations from glacial acetic acid gave 1.4 g. (59%) of pale yellow, matted needles, m.p. 353.5–354.5° dec.

Anal. Calcd. for $C_{15}H_{11}N_3O_4$: N, 14.13. Found: N, 14.13.

The most prominent bands (in μ) in the infrared spectrum occurred at 3.1 (N—H), 5.98 (C═O), 6.5 (NO_2), 6.58 and 6.7. Because of the absence of an intense yellow color and since the melting point is not much lower than the starting material, it is felt that the nitro group is not at the 4-position (see Discussion). Of the other feasible positions in 2-acetaminophenanthridinone (3- and 1-), the 1-position would seem favored, since its reactivity would be enhanced by being situated next to an aromatic ring.

Bromination of 2-Acetaminophenanthridinone.—Two grams (0.0079 mole) of 2-acetaminophenanthridonone in 25 ml. of glacial acetic acid was treated with 1.8 g. of bromine in 5 ml. of the same solvent and the mixture warmed on the steam-bath for ten minutes. The flocculent tan suspension was poured into water, treated with sodium sulfite and filtered. The cream-colored product melted over the range 235–255°, 1.55 g. Recrystallizations from pyridine gave white, matted needles, m.p. 286–286.5° dec. The infrared spectrum displayed bands at 3.1 and 3.2 μ (N—H), 6.0 and 6.1 μ (C═O), 6.55 and 6.7 μ. The more likely positions of the bromine in 2-acetamino-(*x*-bromo)-phenanthridinone are the 1- and 3-positions.

Anal. Calcd. for $C_{15}H_{11}BrN_2O_2$: Br, 24.12; N, 8.46. Found: Br, 24.09; N, 8.43.

2-Bromo-4-nitrophenanthridinone.—Ten grams (0.037 mole) of stirred 2-bromophenanthridinone was treated with 125 ml. of concentrated nitric acid over a 30-minute period. As an exothermic reaction took place, the suspension turned yellow. After stirring for 2 hr. without heat and 1 hr. with gentle heating, the paste was mixed with water. The pre-

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[13] L. F. Fieser, "Experiments in Organic Chemistry," 2nd ed., D. C. Heath and Co., New York, N. Y., 1941, p. 140.

cipitated product weighed 11.8 g. and melted over the range 245–270°. Two recrystallizations from glacial acetic acid gave 6.8 g. (59%) of yellow needles, m.p. 282–284°. The analytical sample was obtained from pyridine as brilliant yellow needles, m.p. 284–286°.

Anal. Calcd. for $C_{13}H_7BrN_2O_3$: Br, 25.04; N, 8.78. Found: Br, 25.26; N, 8.77.

The infrared spectrum had prominent bands at 3.2 μ (N—H), 6.05 μ (C=O), 6.6 and 7.5 μ (NO_2). The shift in the nitro bands to longer wave lengths pointed to hydrogen bonding of the NO_2 and NH groups. Since this compound melted lower (by 40°) than 2-bromophenanthridinone, the hydrogen bonding seemed to be intramolecular. Hence, the nitro group occupies the 4-position.

2-Chloro-4-nitrophenanthridinone.—One gram (0.0037 mole) of 2-chlorophenanthridinone and 12.5 ml. of concentrated nitric acid were stirred together for ten minutes with gentle heating. The bright yellow suspension was allowed to stand and finally diluted with water. The collected yellow product weighed 1.2 g. and melted over the range 248–270°. Two recrystallizations from 15-ml. portions of pyridine gave 0.75 g. (63%) of bright yellow needles, m.p. 278–281°. The analytical sample melted at 280–281°.

Anal. Calcd. for $C_{13}H_7ClN_2O_3$: Cl, 12.91; N, 10.20. Found: Cl, 12.85; N, 10.15.

The infrared spectrum was quite similar to that of 2-bromo-4-nitrophenanthridinone. Bands were present at 3.2 μ (N—H), 6.01 μ (C=O), 6.58 and 7.45 μ (NO_2). Again the shifts in the nitro bands and the lower melting point (45° less than that of 2-chlorophenanthridinone) indicate the presence of intramolecular hydrogen bonding. Such evidence is in accord with a nitro group situated at the 4-position.

Nitration of 2-Iodophenanthridinone.—When 2-iodophenanthridinone was subjected to nitration in hopes of obtaining 2-iodo-4-nitrophenanthridinone, some displacement of the iodine by the nitro group apparently occurred. Thus when 1.0 g. of 2-iodophenanthridinone was warmed with 12.5 ml. of concentrated nitric acid, the suspended solid soon turned tan in color and the supernatant liquid became reddish-brown. Upon further heating, iodine crystals sublimed in the neck of the reaction vessel (detected with moist starch paper) and nitrous fumes were evolved. Dilution of the cream-colored paste with water and filtration gave 1.15 g. of pale yellow solid, melting range 270–305°. The product was extracted with 30 ml. of hot glacial acetic acid, and the 0.50 g. of cream-colored residue then melted from 386–400°. Several recrystallizations from pyridine raised the melting point to 426–428° dec. This product contained halogen.

2-Chloro-5-methylphenanthridinone.—In a solution of 10 g. of potassium hydroxide in 100 ml. of 95% ethanol was dissolved 5.0 g. (0.022 mole) of 2-chlorophenanthridinone with gentle heating. The solution was allowed to cool somewhat, and then 10 ml. of methyl iodide was added in one portion. After ten minutes the clear, pale yellow solution changed to a thick, white suspension. The cooled mixture was filtered and the solid washed successively with 95% ethanol and with water. Drying gave 4.7 g. (89%) of fluffy, white solid, m.p. 191–192°. Recrystallization from 95% ethanol yielded long, white matted needles, m.p. 192–193°. Heacock and Hey[12] have prepared this compound in poor yield from the suitably substituted N-methylbenzanilide by a Pschorr synthesis. They also reported a melting point of 192°.

5-Methyl-2-nitrophenanthridinone.—2-Nitrophenanthridinone (5.0 g., 0.021 mole) was stirred vigorously with an excess (100 ml.) of ethanolic potassium hydroxide solution. The resulting orange potassium salt was filtered off and washed with ether.

The orange salt was mixed with 10 ml. of methyl iodide in 100 ml. of absolute ethanol, and the suspension was refluxed until the orange suspension became cream-colored (12 hr.). Upon filtration of the reaction mixture, 4.6 g. (87%) of cream-colored product was obtained, melting range 241–247°. Recrystallization from 95% ethanol furnished pale yellow, matted needles, m.p. 248.5–249.5°. The compound also has been prepared by Heacock and Hey[14] (see preceding experiment), and the reported melting point is 249°.

Reaction of Phenanthridinone with Butyllithium.—In order to determine the resistance to nucleophilic attack of the carbonyl group in this cyclic amide, it was treated with butyllithium under stringent conditions. Thus in a 500-ml. flask equipped with a stirrer and reflux condenser and flushed with nitrogen were placed 9.8 g. (0.050 mole) of phenanthridinone and 200 ml. of dry ether. When 0.10 mole of butyllithium[15] in 90 ml. of ether was added during ten minutes, spontaneous reflux took place and an opalescent orange solution was formed. The solution was refluxed under a nitrogen atmosphere for 12 hr. and then hydrolyzed. The ether layer was separated and the suspended solid was filtered off. This colorless solid weighed 5.3 g. (54%) and melted over the range 270–276°. Recrystallization from 50 ml. of glacial acetic acid gave 4.4 g. of recovered phenanthridinone, m.p. 290–292° (mixture melting point).

Distillation of the dried ether extracts left a viscous, orange liquid which was subsequently dissolved in 30 ml. of ethanol and treated with 50 ml. of a saturated ethanolic solution of picric acid. An initial darkening preceded the precipitation of 3.1 g. (13%) of yellow solid, m.p. 191–194°. Recrystallizations from a dioxane–ethanol pair gave stout, yellow needles, m.p. 195.5–197.5°. Admixed with authentic 6-butylphenanthridine picrate,[16] this product melted undepressed.

Reaction of 2-Bromophenanthridinone with Butyllithium.—Since the preceding experiment indicated that the amide carbonyl group was not readily attacked by butyllithium, a halogen–metal interconversion reaction between 2-bromophenanthridinone and butyllithium was considered feasible. A slurry of 27.4 g. (0.10 mole) of 2-bromophenanthridinone in 300 ml. of dry ether was cooled to −35°, and 0.25 mole of butyllithium in 230 ml. of ether was added over a course of ten minutes. The lime-colored suspension was cooled for another ten minutes and then allowed to warm up to 0° over 45 minutes. The resulting dark yellow solution was poured immediately onto a Dry Ice–anhydrous ether mixture. After the carbonated mixture had warmed up to room temperature, the ether was removed and the residual solid extracted with 600 ml. of 5% potassium hydroxide solution. Acidification of the basic extracts yielded 30.9 g. of a white solid melting over 400°. To remove any 5-carboxylic acid, this solid was refluxed for an hour with 500 ml. of glacial acetic acid to give a residue of 19.6 g. (82%) of acid melting at 361–363° dec. Recrystallization of a small sample from a large amount of glacial acetic acid furnished white prisms of the same melting point. This acid was purified by dissolving in base, reprecipitating in acid and then drying at 150°. This product gave a negative test for halogen. The neutral equivalent was run on a sample suspended in warm 50% ethanol. The value agrees well with that of phenanthridinone-2-carboxylic acid. The infrared spectrum exhibited bands at 3.2 μ (N—H) and 6.05 μ (C=O).

Anal. Calcd. for $C_{14}H_9NO_3$: neut. equiv., 239.22. Found: neut. equiv., 238.

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(14) R. A. Heacock and D. H. Hey, *J. Chem. Soc.*, 3 (1953).

(15) H. Gilman, J. A. Beel, C. G. Brannen, M. W. Bullock, G. E. Dunn and L. S. Miller, THIS JOURNAL, **71**, 1499 (1949).

(16) Unpublished studies.