purple end point. A concurrent experiment, carried to completion but without thiocyanate, gave an assay on the diazonium salt, and there was between 98.5 and 99.5% of the calculated acid produced. The assay was applied in calculating the yield of acid (and hence of *p*-cresol). A minor source of error was the perceptible coupling of the diazonium salt with the indicator.

A gas chromatographic analysis for the other products was used. A solution of 1.239 g. of *p*-toluenediazonium bisulfate was dissolved in 150 ml. of potassium thiocyanate solution and cooled, degassed, and decomposed as before. After essentially complete reaction, the mixture was extracted with ether, the ether solution reduced in volume, and a measured amount of methyl benzoate added as an internal standard. A 1-m. column of 5% Carbowax 1500 on Chromosorb P separated all the products and the yield of *p*-tolyl isothiocyanate was calculated from the area of its peak and that of the internal standard. *p*-Tolyl thiocyanate and *p*-cresol were also detected in the chromatogram, but were not measured quantitatively. They were identified by comparison of retention times with those of authentic samples. Tolyl thiocarbamate was not eluted from the column in a reasonable time, and the efficiency of extractions of *p*-cresol was not high, so the areas of the tolyl thiocyanate and the *p*-cresol peaks were not used.

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[CONTRIBUTION NO. 730 FROM THE DEPARTMENT OF CHEMISTRY, FORDHAM UNIVERSITY, NEW YORK, N. Y.]

Heteropolar Ozonization of Aza-Aromatics and Their N-Oxides[1-3]

BY EMIL J. MORICONI AND FRANCIS A. SPANO

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The ozonization of four aza-aromatics [1-methyl- (**12**) and 3-methylisoquinoline (**17**), acridine (**1**), and phenanthridine (**4**)] and five aza-aromatic N-oxides [quinoline-1- (**24**), phenanthridine-5- (**29**), acridine-10- (**32**), isoquinoline-2- (**42**), and 3-methylisoquinoline-2-oxides (**45**)] are reported. Initial electrophilic ozone attack on **1**, **4**, **12**, and **17** led to carbocyclic ring-cleaved carboxylic acids; simultaneous nucleophilic ozone attack at the C-atom adjacent to (**4**), or conjugated with (1), the aza-atom produced cyclic amides. Relative to isoquinoline, the methyl group in **12** and **17** deactivated the aza-aromatic ring to electrophilic ozone attack. Generally, initial nucleophilic ozone attack on aza-aromatic N-oxides led to cyclic hydroxamic acids and cleavage of the C=N aromatic bond (to nitroaldehydes) as primary products. With ozone as an electrophile, further ozonization of the former led to deoxygenated products, cyclic amides. Phthalic acid was also obtained from **42** and **45**. In almost all cases, solvent effects were noted. N→O and C=O absorption frequencies of reactants and products are tabulated.

The low reactivity of the pyridine ring to ozone in the parent compound and its homologs,[4,5] of its N-oxide,[5b] and quinoline and its alkyl derivatives[6,7] is well documented. Although alkyl substituents on the pyridine nucleus effectively enhance its reaction rate with ozone,[4a,8] the rate is still considerably lower than for the corresponding benzene derivative, and the yields of ozonolysis products are little improved over the parent heterocycle. In quinoline and its derivatives, major attack seems to occur initially in the carbocyclic ring, followed by a slower attack at the 3,4-bond of the heterocyclic ring.

What is perhaps surprising is the unusual reactivity of isoquinoline to ozone. Ozonolysis of this aza-aromatic with excess ozone in glacial acetic acid containing trace amounts of water produced 3,4-pyridinedicarboxylic acid, and, after hydrogen peroxide oxidation, phthalic acid in almost equal amounts.[9] From a quantitative measurement of isoquinoline absorption characteristics and of the ammonia formed on hydrolysis of the peroxidic ozonolysis products, Wibaut[6b] has reported that in this heterocyclic ring system, the aza-aromatic moiety reacted one and one-half times more rapidly than the benzenoid nucleus. In all aza-aromatics ozonized, however, it has been generally assumed that only C=C cleavage occurs in both carbocyclic and heterocyclic nuclei[10] and that the ammonia formed resulted from hydrolysis of the primary scission products, the acid amides.

In this paper we report on the ozonization of the aza-aromatics: acridine, phenanthridine, 1-methyl- and 3-methylisoquinoline, their N-oxides, and quinoline-1- and isoquinoline-2-oxide.

Acridine (1) and Phenanthridine (4).—Ozone reacted readily with acridine (**1**) in both methanol and methylene chloride solvents; with two molar ozone equivalents in methanol, followed by alkaline hydrogen peroxide oxidation, **1** gave ring-cleaved 2,3-quinolinedicarboxylic acid (acridinic acid) (**2**) in 73–75% yield and less than 0.1% of the oxygenated 9-acridanone (**3**); in methylene chloride, however, 60–62% of **2** and up to 2.5% of **3** were obtained. In both instances, 2–3% of **1** was also recovered.

Phenanthridine (**4**) did not react with ozone in methanol, and only sluggishly in methylene chloride. In the latter solvent, two molar equivalents ozone absorption followed by alkaline peroxide oxidation produced up

(1) Paper XII in the series entitled "Ozonolysis of Polycyclic Aromatics"; for Paper XI: E. J. Moriconi and L. B. Taranko, *J. Org. Chem.*, **28**, 2526 (1963).

(2) This research was supported predominantly by Grant CA-03325-06 from the U. S. Public Health Service, National Cancer Institute, and in part by the Directorate of Chemical Sciences, Air Force Office of Scientific Research, under Grant AF-AFOSR-62-18.

(3) Presented in part at the Metropolitan Regional Meeting, American Chemical Society, New York, N. Y., Jan., 1962; at the 142nd National Meeting of the American Chemical Society, Org. Div., Atlantic City, N. J., Sept., 1962; and at the XIXth IUPAC Congress, London, July 15, 1963.

(4) (a) F. L. J. Sixma, *Rec. trav. chim.*, **71**, 1124 (1952); (b) J. P. Wibaut and E. C. Kooyman, *ibid.*, **65**, 141 (1946); (c) E. C. Kooyman and J. P. Wibaut, *ibid.*, **66**, 705 (1947).

(5) (a) G. Slomp, Jr., and J. L. Johnson, *J. Am. Chem. Soc.*, **80**, 915 (1958); (b) G. Slomp, Jr., *J. Org. Chem.*, **22**, 1277 (1957).

(6) (a) J. P. Wibaut and H. Boer, *Rec. trav. chim.*, **74**, 241 (1955); (b) H. Boer, F. L. J. Sixma, and J. P. Wibaut, *ibid.*, **70**, 509 (1951); (c) J. P. Wibaut and H. Boer, *Proc. Koninkl. Ned. Akad. Wetenschap.*, **53**, 19 (1950).

(7) W. Shive, E. G. Ballweber, and W. W. Ackerman, *J. Am. Chem. Soc.*, **68**, 2144 (1946).

(8) J. P. Wibaut, *Chimia*, **11**, 298, 321 (1957); J. P. Wibaut, *J. chim. Phys.*, **111**, 143 (1956).

(9) A. F. Lindenstruth and C. A. VanderWerf, *J. Am. Chem. Soc.*, **71**, 3020 (1949). Since ozone oxidizes acetic acid to peracetic acid,[6b] the use of acetic acid as a solvent in ozonization reactions invariably leaves the nature of the actual oxidant in doubt. In this instance, however, Wibaut and co-workers[6b] have reported that the absorption characteristic of isoquinoline in glacial acetic acid at 20° is in principle no different from that in chloroform at −40°. There is no doubt however that further oxidation of the peroxidic ozonolysis products with hydrogen peroxide in acetic acid solvent must be strongly accelerated by the equilibrium presence of peracetic acid. It is unfortunate that no product yields are reported in ref. 6b.

(10) This conclusion is based on a quantitative measurement of ozone uptake and ammonia formed,[4a,6b] and product isolation: 2,2,6-trimethylcyclohexanecarboxamide from 2-(2,2,6-trimethylcyclohexyl)-4,6-dimethylpyridine,[11] methylethylacetamide from 2-(*sec*-butyl)-4,5-dimethylpyridine,[12] and glyoxal, carbon dioxide, and hydrazine from pyrazole.[13] No nitrous or nitric acid was found on ozonolysis of the pyridine nucleus.[4a]

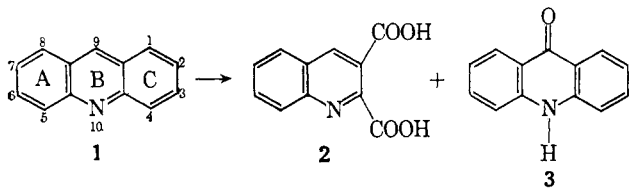
(11) B. Shive, S. M. Roberts, R. I. Mahan, and J. R. Bailey, *J. Am. Chem. Soc.*, **64**, 909 (1942).

(12) H. L. Lochte, W. W. Crouch, and E. D. Thomas, *ibid.*, **64**, 2753 (1942).

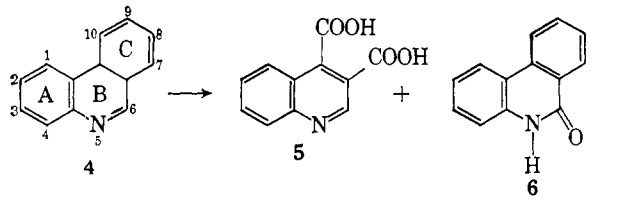
(13) B. P. Jibben and J. P. Wibaut, *Rec. trav. chim.*, **79**, 342 (1960).

to 2% of 3,4-quinolinedicarboxylic acid (**5**) and up to 23% of the cyclic amide 6(5H)-phenanthridinone (**6**) with recovery of some 28% of unreacted **4**.

Formation of **2** and **5** undoubtedly involves conventional electrophilic attack at the 1,2:3,4 bonds of **1** and the 7,8:9,10 bonds of **4** to form primary unstable ozonides; further oxidation with alkaline hydrogen peroxide then leads to the carbocyclic-ring-cleaved products **2** and **5**, respectively. The proximity of the electron-attracting nitrogen atom in **4** must deactivate ring A to electrophilic attack, such that **4** reacts as a quinoline rather than an isoquinoline derivative. The much greater yields of **2** over **5** must reflect the greater conjugation of an angularly-fused ring C in **4** to the quinoline moiety, as compared to the linearly-fused C-ring in **1**.[14]

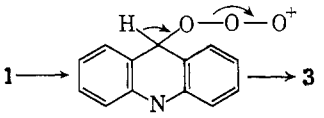


1 **2** **3**



4 **5** **6**

Theoretical calculations which indicate the electron density to be lowest at C-9 in **1**,[16] as well as the experimentally known reactivity of this position toward nucleophilic reagents,[17] suggest a nucleophilic ozone attack at C-9 to the dipolar species **7** which on loss of oxygen and proton shift would lead to the observed **3**.[18] This hypothesis has two experimental supports: (i) a small but



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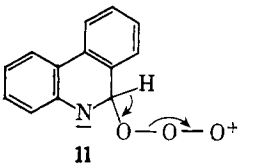
clear-cut higher yield of **3** in solvent methylene chloride over methanol[20]; and (ii) results of ozonolysis of acridine nitrate in methanol. Two molar ozone equivalents convert this salt in aqueous methanol to *only* 21–25% of **2** but the yield of **3** is increased to a maximum of 3%. Thus inductive and resonance effects of the positively charged aza-aromatic ring not only deactivate the flanking carbocyclic rings to electrophilic attack (lower yield of **2**), but also activate C-9 to nucleophilic attack (higher yields of **3**, even in methanol).[21]

Theoretical[25] and experimental[26] evidence also suggest initial nucleophilic ozone attack on **4** *via* some species such as **11**, leading to **6**. The correspondingly



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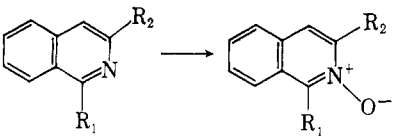
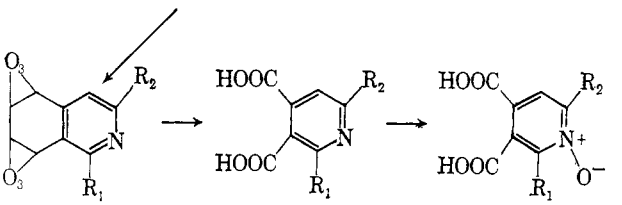
higher yields of **6** compared to **3** indicate a much greater susceptibility of **4** over **1** to nucleophilic attack.

Compounds **1** and **4** are inert to alkaline hydrogen peroxide.

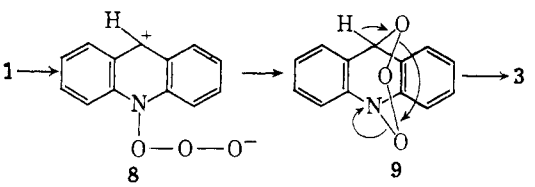
1-Methyl- (12) and 3-Methylisoquinoline (17).—The unusual reactivity of isoquinoline to ozone[9] and the enhanced reactivity of methyl groups at the 1- and 3-positions in the isoquinoline system[28] prompted an examination of the ozonolysis of 1-methyl- (**12**) and 3-methylisoquinoline (**17**).



12, $R_1 = CH_3$, $R_2 = H$ **16**, $R_1 = CH_3$, $R_2 = H$
17, $R_1 = H$, $R_2 = CH_3$ **21**, $R_1 = H$, $R_2 = CH_3$



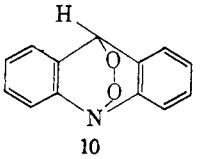
13, $R_1 = CH_3$, $R_2 = H$ **14**, $R_1 = CH_3$, $R_2 = H$ **15**, $R_1 = CH_3$, $R_2 = H$
18, $R_1 = H$, $R_2 = CH_3$ **19**, $R_1 = H$, $R_2 = CH_3$ **20**, $R_1 = H$, $R_2 = CH_3$



8 **9**

(iii) concerted 1,3-dipolar type cycloaddition at C-9 and N-10 to form **9**.[24] Loss of oxygen and protonic shift would then lead to **3**.

(22) K. Lehmstedt and H. Klee [*Ber.*, **69**, 1514 (1936)] have reported the conversion of **1** with the electrophilic oxidant, perbenzoic acid, to the stable transannular peroxide **10**, which on heating reverted to **3**.



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(23) Compound **9** might be compared with the uniquely stable monoozonide of 9,10-dimethylanthracene [R. E. Erickson, P. S. Bailey, and J. C. Davis, Jr., *Tetrahedron*, **18**, 389 (1962)].

(24) R. Huisgen, *Proc. Chem. Soc.*, 357 (1961). The formation of such a neutral intermediate would not require stabilization by polar solvents.

(25) Calculations by H. C. Longuet-Higgins and C. A. Coulson [*J. Chem. Soc.*, 971 (1949)] show C-6 to be the most electron deficient.

(26) The ring system in **4** is very stable to oxidizing agents; it is unaffected by chromic and nitric acids and permanganate. Nucleophilic amination [G. T. Morgan and L. P. Walls, *ibid.*, 2225 (1932)] and hydroxylation reactions [J. Eisch and H. Gilman, *Chem. Rev.*, **57**, 525 (1957)] yield the appropriate 6-substituted products. Peracetic acid, however, does convert **4** to 5-oxide.[27] Thus, alternative mechanisms suggested for the ozonization of 1[21] are also applicable to **4**.

(27) K. Mitsukashi, *J. Pharm. Soc. Japan*, **67**, 74 (1947); *Chem. Abstr.*, **45**, 9544 (1951).

(28) Summarized by W. J. Gensler, "Heterocyclic Compounds," Vol. 4, R. C. Elderfield, Ed., John Wiley and Sons, Inc., New York, N. Y., 1952, pp. 408–452.

(14) One can predict that phenanthridine must have a higher resonance energy than acridine, as does its isostere, phenanthrene (92 kcal./mole) over anthracene (84 kcal./mole).[15]

(15) G. W. Wheland, "Resonance in Organic Chemistry," J. Wiley and Sons, Inc., New York, N. Y., 1955, pp. 98, 132.

(16) H. C. Longuet-Higgins and C. A. Coulson, *Trans. Faraday Soc.*, **43**, 87 (1947).

(17) Summarized in R. M. Acheson, "Acridines," Interscience Publishers, Inc., New York, N. Y., 1956, p. 56.

(18) First suggested by Bailey and co-workers[19] to account for amide formation on ozonization of Schiff bases and C=N bond cleavage on ozonization of nitrones.

(19) A. H. Riebel, R. E. Erickson, C. J. Abshire, and P. S. Bailey, *J. Am. Chem. Soc.*, **82**, 1801 (1960).

(20) Polar methanol should enhance the electrophilicity of ozone by such hydrogen-bonded species as $^-O—O—O^- \cdots HOCH_3$; consequently if initial attack were electrophilic, ozonization in methanol would have increased the yield of **3**. The opposite was observed.

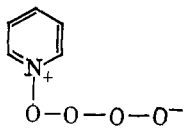
(21) Other less likely alternatives: (i) initial electrophilic attack at the aza atom to yield dipolar ion **8**, followed by intramolecular cyclization to the transannular peroxide **9**[22]; (ii) transannular cyclization of **7** to **9**[23]; and

Ozone did not react with either **12** or **17** in the solvents methanol and methylene chloride. However, ozonolysis over a 10-hr. period of an aqueous acetic acid solution of **12**/**17** precipitated directly the ring-cleaved products 2-methyl-3,4-pyridinedicarboxylic acid (**14**) (19–24% yields) and 2-methyl-4,5-pyridinedicarboxylic acid (**19**) (14–17% yields), respectively. *In situ* peracetic acid oxidation of the acetic acid filtrates produced an additional 23–28% of **14** and **19** as their respective N-oxides **15** and **20**. Unreacted **12** and **17** were also recovered from these same acid filtrates, as their respective N-oxides **16** and **21** in 20–23% yields. We suggest, therefore, that in both instances electrophilic ozone oxidized the carbocyclic rings in **12** and **17** to produce initially soluble, unstable peroxidic ozonolysis products such as **13**/**18**. The presence of peracetic acid in low concentration[9,29] led to further oxidation of these peroxidic ozonolysis products to dicarboxylic acids **14** and **19**, respectively, and these gradually precipitated during the course of the reaction. The addition of hydrogen peroxide to the acetic acid filtrates produced *in situ* excess peracetic acid which not only oxidized the soluble ozonolysis products to dicarboxylic acid-N-oxides **15** and **20**, but also oxidized unreacted **12** and **17** to their respective N-oxides **16** and **21**. Our hypothesis is supported by the fact that direct peracetic acid oxidation of **12** and **17** led to **16** and **21**, respectively, as did **14** and **19** to **15** and **20**, respectively.

Neither heterocyclic ring-cleavage products nor ammonia were found among the reaction products. Clearly observable but unexplained is the fact that the methyl groups deactivated the heterocyclic ring (relative to the parent isoquinoline) to electrophilic ozone attack.

N-Oxides

The only reported instance of the ozonization of an aromatic N-oxide is that of pyridine-1-oxide (**22**).[5b] Ozonization to saturation of **22** in methylene chloride produced a white, crystalline "pyridine oxide–ozone complex" which was unstable. It decomposed rapidly (violently, in one instance) at room temperature, and liberated iodine from potassium iodide in the cold. After outgassing, some 49% of the ozone was found to have reacted, although ultraviolet analysis of the complex disclosed only the quantitative presence of **22**. To account for the enhanced nucleophilicity of ozone in pyridine these same authors later suggested the dipolar



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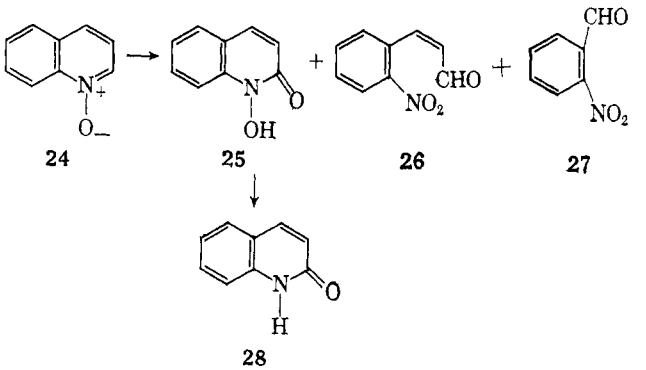
ion **23** as a possible structure of the crystalline complex.[5a]

Quinoline-1- (24), Phenanthridine-5- (29), and Acridine-10-oxides (32).—The N-oxide group has been reported to increase the reactivity of quinoline to both electrophilic and nucleophilic reagents at the 2- and 4-positions.[30] Since current theory considers ozone as both an electrophile and nucleophile, it was of immediate interest to examine the ozonolysis of quinoline-1-oxide (**24**).

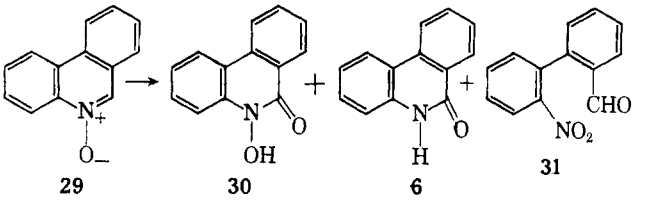
Ozonization of **24** in either methanol or methylene chloride with one molar ozone equivalent, followed by base decomposition of the peroxidic ozonolysis products, afforded 16–17% of the cyclic hydroxamic acid 1-hydroxycarbostyril (**25**); some 40–43% of unreacted **24** was recovered. With two molar ozone equivalents, the yield of **25** increased while small amounts of *o*-nitrocinnamaldehyde (**26**) and *o*-nitrobenzaldehyde (**27**) could also be isolated. The addition of three molar ozone equivalents led only to **27** in 16–17% yields. Since further ozonization of **25** produced only the cyclic amide carbostyril (**28**), the formation of **26** and **27** did not proceed through the intermediacy of **25**.

Similarly the ozonization of phenanthridine-5-oxide (**29**) in methanol, followed by base decomposition of the primary peroxidic ozonolysis products, led to the cyclic hydroxamic acid 5-hydroxy-6(5H)-phenanthridinone (**30**) (56% yield) in addition to the deoxygenated, cyclic amide 6(5H)-phenanthridinone (**6**) and ring-cleaved 2′-nitro-2-biphenylcarboxaldehyde (**31**) in 19–20% and 7–8% yields, respectively.



24 **25** **26** **27** **28**

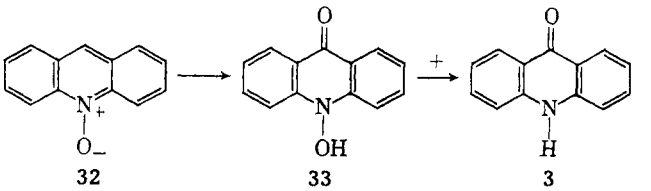
With maximum absorption of ozone (three molar equivalents) only **6** (29–31%) and **31** (11–13%) could be isolated. In solvent methylene chloride, **29** was converted solely to **30** in 59–60% yields with a 16–19% recovery of **29**; maximum yields of **30** (77–80%) were obtained with two molar ozone equivalents.



29 **30** **6** **31**

Although the ozonolysis results in methanol clearly suggest the sequence **29** → **30** → **6** (*cf.* the conversion **24** → **25** → **28**), ozonization of a suspension of **30** in methanol (some reaction was observed in methylene chloride) produced neither **6** nor **31**. It is significant, however, that the formation of products **26**, **27**, and **31** represent the first well defined instance of aromatic C=N bond cleavage by ozone.

Not unexpectedly then, ozonization of acridine-10-oxide (**32**) in methanol produced 10-hydroxy-9-acridanone (**33**) in 45–48% yield, together with 2.0–2.9% of 9-acridanone (**3**). Increasing the ozone absorption to two molar equivalents raised the yields of **33** and **3** to 54–56 and 6–8%, respectively. Maximum yields of **3**



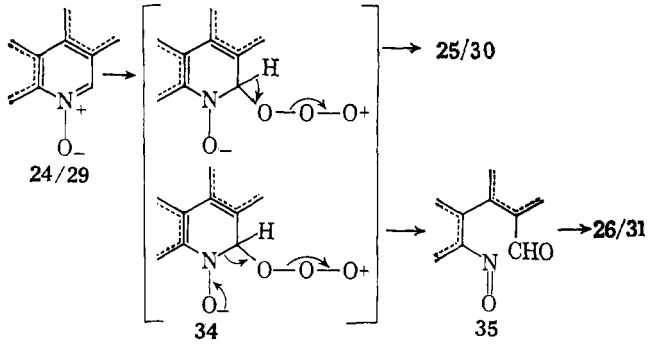
32 **33** **3**

(40%) were obtained with maximum ozone absorption (4.3 molar equivalents); the yield of **33** was correspondingly lowered to 17%. A decisive solvent effect was observed on ozonization in methylene chloride. With one molar ozone equivalent, only 23–29% of **33** was obtained while the yield of **3** rose to 15%. Increasing the

(29) P. S. Bailey, *Chem. Rev.*, **58**, 979 (1958).
(30) R. C. Elderfield, ref. 28, p. 241.

amount of ozone added lowered yields of both products. Since ozonization of **33** in either methanol or methylene chloride produced only **3**, the reaction sequence N-oxide (**32**) → cyclic hydroxamic acid (**33**) → cyclic amide (**3**) is again suggested. Compound **3** suspended in methanol was inert to ozone. Some slight reaction was observed in methylene chloride, but the products were not identified.

Since we could quantitatively convert **29** and **32** to **30** and **33**, respectively, with alkaline hydrogen peroxide (which undoubtedly must involve the strong perhydroxyl nucleophile OOH^-), we envision the ozonization of **24**, **29**, and **32** to **25**, **30**, and **33**, respectively, as occurring by initial nucleophilic ozone attack[18,19] at the carbon adjacent to (**24**, **29**), or conjugated with, **32**, the aza atom. Loss of oxygen and protonic shift in the primary peroxidic species **34** would lead to the observed cyclic hydroxamic acids.[31] Cleavage of the C=N bond from the common peroxidic intermediate **34** would lead

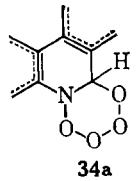


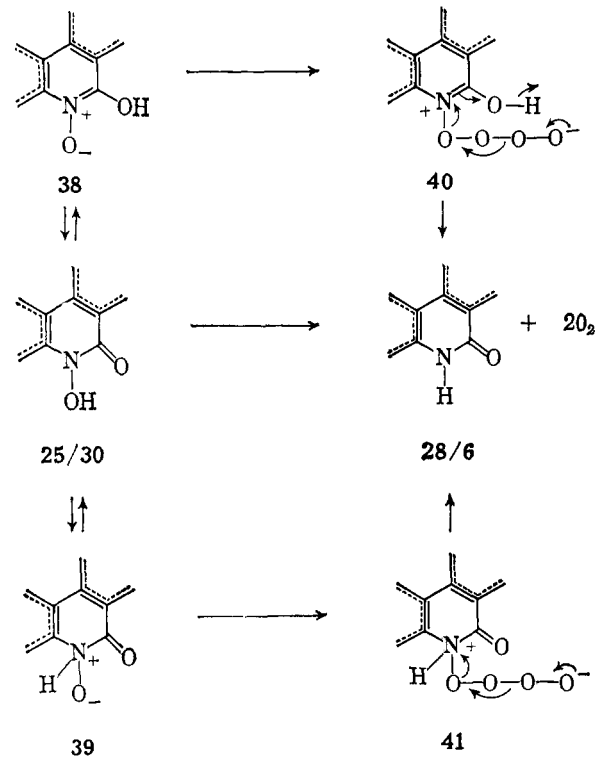
to the nitroso aldehyde **35**, which on further treatment with ozone would be oxidized to the nitroaldehydes **26**/**31**.[18,19] The formation of **27** must involve simple ozonolytic cleavage of the reactive, conjugated double bond in **26**.

We interpret the deoxygenation of **25**, **30**, and **33**, respectively, to cyclic amides **28**, **6**, and **3** in the following manner: **25** and **30** (and by analogy **33**) may exist in three equilibrium tautomeric forms **38** ⇄ **25**/**30** ⇄ **39**.[32]

Tautomers **38** and **39** would be susceptible to electrophilic ozone attack at the anionic oxygen atom to give such dipolar ions at **40** and **41** (*cf.* **23**), which on loss of two molecules of oxygen would lead to the observed carbostyril products. The reduction of **40** to **28**/**6** also requires hydride removal.

Isoquinoline- (42), 3-Methylisoquinoline- (45), and 1-Methylisoquinoline-2-oxides (47).—In the isoquinoline ring system, oxidation *via* electrophilic ozone attack occurs equally in both carbocyclic and heterocyclic rings.[9] Since we have generally observed that (i) methyl groups attached to the heterocyclic moiety in **12** and **17** did not activate it to electrophilic/nucleophilic ozone attack and (ii) the general effect of the N-oxide group in **24**, **29**, and **32** was to enhance nucleophilic ozone attack at the heterocyclic ring, we turned finally to an examination of the combined effect of both



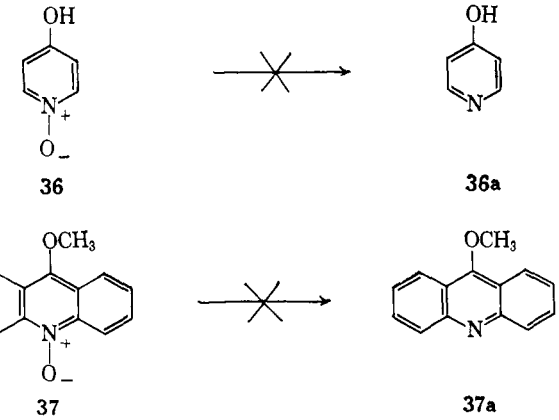


groups on the course of ozonization in the isoquinoline-2-oxide ring system.

Ozonization of **42** and **45** proceeded quite readily in both methanol and methylene chloride solvents. Conversely, **47** in methylene chloride was inert to ozone; in methanol with a large excess of ozone, a sluggish reaction ensued which led to no identifiable products and a 70% recovery of **47**.

In methylene chloride, **42** and **45** with one molar ozone equivalent gave only heterocyclic ring oxidation [2-hydroxyisocarbostyril (**43**) (4–5%) and 2-hydroxy-3-methylisocarbostyril (**46**) (12–15%), respectively] and cleavage product [phthalic acid (**44**), 18–23 and 8–10%, respectively]. The structure of **46** was proved by independent synthesis and reduction to the known 3-methylisocarbostyril.[33]

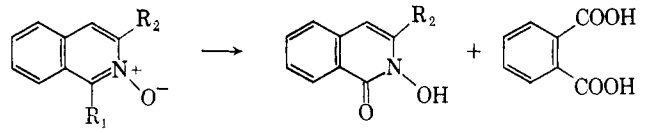
In solvent methanol which favors electrophilic attack,[20] nucleophilic attack at C-1 of the C=N bond of both **42** and **45** decreased to produce a maximum yield of 1% of **43** and **45**, respectively, in addition to **44**.



(31) Other alternatives: (i) intramolecular cyclization of **34** to the six-membered peroxidic species **34a**; (ii) Huisgen's[24] dipolar concerted 1,3-cycloaddition of ozone to **24**/**29** would also lead to **34a**.

(32) These cyclic hydroxamic acids show a strongly bonded C=O group (Table II) and no discernible N-oxide absorption in the infrared. Yet all gave a positive N-oxide test [N. A. Coats and A. R. Katritzky, *J. Org. Chem.*, **24**, 1836 (1959)]. It is perhaps pertinent to note that ozonization of tautomeric 4-hydroxypyridine-1-oxide (**36**) and 9-methoxyacridine-10-oxide (**37**) failed to lead to any deoxygenated products, such as **36a** and **37a**, respectively.

(33) For details of the new synthesis and proof of structure, see E. J. Moriconi, F. J. Creegan, C. K. Donovan, and F. A. Spano, *J. Org. Chem.*, **28**, 2215 (1963).

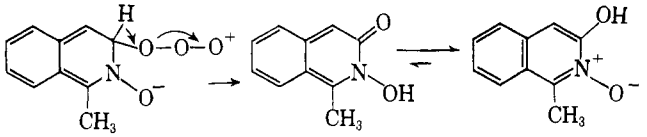


42, $R_1 = R_2 = H$ **43**, $R_2 = H$ **44**
45, $R_1 = H$, $R_2 = CH_3$ **46**, $R_2 = CH_3$
47, $R_1 = CH_3$, $R_2 = H$

Neither **43** nor **46** could be converted to **44** on ozonization in either solvent.[34]

Mechanistically, we consider the ozonization of N-oxides **42** and **45**, respectively, to hydroxyisocarbostyrils **43** and **46**[35] to be similar to that of the conversion of N-oxides **24**, **29**, and **32** to their respective cyclic hydroxamic acids **25**, **30**, and **33**. Compound **44** could evolve from the further electrophilic ozonolysis of such intermediate species as **48** to **49**, which on alkaline peroxide oxidation gave the heterocyclic ring-cleaved **44**.[34]

Their remains now an attempt to explain the inertness of C-1 in **47**. Several possibilities occur to us: (i) the $-CH_3$ group enhances the electron density of the 1-position to the extent that it will no longer undergo nucleophilic substitution by loss of a $-CH_3$ group; (ii) the reactivity of the $-CH_3$ group at the 1-position to oxidants[36] suggests that it would be attacked prior to C-1; and (iii) steric interference by the CH_3 group to ozone attack at position-1; this seems unlikely in view of the ease of reaction between 9,10-dimethylanthracene and ozone.[23] Finally it is of interest to speculate on the ozonization product if reaction had occurred at C-3 in **47**. Our previously suggested mechanism for the formation of **25** and **30** would have predicted the formation of the cyclic hydroxamic acid **50** *via* the following sequence of reactions.



50 **50a**

Further it is not unreasonable to assume that **50** would also exist as the energetically more favorable tautomer 1-methyl-3-hydroxyisoquinoline-2-oxide (**50a**).[37] No **50a** was observed.

Infrared Absorption Studies

Compounds **24**, **29**, **32**, **42**, **45**, and **47** displayed strong sharp bands in the 7.46–7.81 μ region which were not present in the parent aza-aromatic hydrocarbon and are assignable to N→O stretching frequency.[38] Each of these compounds also showed strong bands in the 8.10–9.00 μ region which have been ascribed to new C–H deformations.[39,40] Results are summarized in Table I.

TABLE I

INFRARED SPECTRA OF N-OXIDES IN SATURATED CCl_4 SOLUTION[a]

Compound	N→O stretching, μ	C–H deformation, μ[b]
Quinoline-1-oxide (**24**)	7.62	8.10, 8.76
Isoquinoline-2-oxide (**42**)	7.49	8.42, 8.73
1-Methylisoquinoline-2-oxide (**47**)	7.81[c]	8.15, 8.38, 8.65
3-Methylisoquinoline-2-oxide (**45**)	7.55[c]	8.44
Acridine-10-oxide (**32**)	7.46	9.00
Phenanthridine-5-oxide (**29**)	7.61	8.37

[a] Most of the N-oxides were only slightly soluble in CCl_4; to obtain a sufficiently high concentration for a spectrum, the procedure used was to treat excess N-oxide with boiling CCl_4; the saturated solution was decanted and cooled slowly to room temperature. Crystallization thereupon did not commence for 15–20 min., ample time for a spectrum. [b] Substituted quinoline-1-oxides displayed such bands in the 8.20–9.38 μ region. [c] See ref. 38.

Table II summarizes carbonyl absorption data of the cyclic hydroxamic acids **25**, **30**, **33**, **43**, and **46** and their respective deoxygenated derivatives, the cyclic amides, **28**, **6**, **3**, isocarbostyril, and 3-methylisocarbostyril. The shift in the former to longer wave length undoubtedly reflects the strong intra- (**25**, **30**, **43**, and **46**) or intermolecular (**33**) hydrogen bonding. No free hydroxyl absorption was observed in any of these compounds. Solubility difficulties precluded any precise intramolecular hydrogen bonding studies. All compounds in Table II, however, are under investigation with n.m.r.

TABLE II

COMPARISON OF CARBONYL ABSORPTION BANDS IN CYCLIC HYDROXAMIC ACIDS AND CYCLIC AMIDES

Compound	Carbonyl absorption frequency, μ	
Carbostyril (**28**)	5.95 s[a]	
1-Hydroxycarbostyril (**25**)		6.02 s[a]
Isocarbostyril[41a]	5.98 s[a]	
2-Hydroxyisocarbostyril (**43**)		6.05 s[a]
3-Methylisocarbostyril[33,41b]	5.96 s[a]	
2-Hydroxy-3-methylisocarbostyril (**46**)[33]		6.02 s[a]
9-Acridanone (**3**)	6.08 s[b]	
10-Hydroxy-9-acridanone (**33**)		6.17 s[b]
6(5H)-Phenanthridinone (**6**)	5.97 s[b]	
5-Hydroxy-6(5H)-phenanthridinone (**30**)		6.12 s[b]

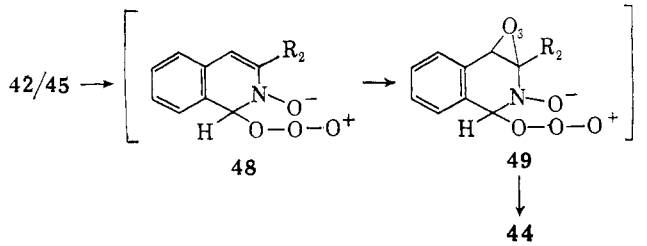
[a] CCl_4 solution spectra. [b] In KBr pellets.

Experimental[42]

General Ozonolyses Procedure.—The ozone was generated from oxygen using the Welsbach T-23 ozonator. The oxygen flow through the ozonator was 0.10 ft.^{3}/min. and the ozone concentration approximately 55 mg. (1.1 mmoles) per liter. Our ozonization procedure is described in a previous publication.[43]

In experiments where pure ozone was used, the ozone–oxygen was passed through a U-tube, 1.5 cm. in diameter and 45 cm. in length, equipped with two ⅌ 14/35 joints at the ends. This tube,

(34) Suggesting that **44** is formed *via* electrophilic C=C bond attack of the primary ozonolysis product (**48**) as in



48 **49** **44**

(35) No electrophilic substitution reactions have ever been reported for the 1-position of isoquinoline.[28] Further, the only position in the isoquinoline molecule active toward nucleophilic substitution (amination, hydroxylation, and reaction with organometallic compounds) is the 1-position. Finally, the π-electron density in the neutral isoquinoline molecule has been calculated to be lowest at the 1-position. Thus we conclude that with **42** and **45**, as with **24**, **29**, and **32**, ozone is acting as a nucleophile in the ultimate formation of cyclic hydroxamic acids.

(36) R. S. Barrows and H. G. Lindwall, *J. Am. Chem. Soc.*, **64**, 2430 (1942).

(37) A. T. Blomquist and E. J. Moriconi, *J. Org. Chem.*, **26**, 3761 (1961).

(38) The N→O stretching frequency in aromatic N-oxides occurs at *ca.* 7.69–8.33 μ.[39] Within this range the frequency is decreased by the presence of electron-donating substituents.

(39) A. R. Katritzky, *Quart. Rev.*, **13**, 372 (1959); K. Nakanishi, "Infrared Absorption Spectroscopy," Holden-Day Inc., San Francisco, Calif., 1962, p. 51.

(40) G. Costa, P. Blasina, and G. Sartori, *Chem. Abstr.*, **50**, 11823 (1956).

(41) (a) M. M. Robison and B. L. Robison, *J. Org. Chem.*, **21**, 1337 (1956); (b) *J. Am. Chem. Soc.*, **80**, 3443 (1958).

(42) All melting points are corrected and all boiling points are uncorrected. The infrared spectra were determined on a Perkin–Elmer, Model 21, infrared recording spectrophotometer fitted with a sodium chloride prism. The ultraviolet spectra were determined on a Cary recording spectrophotometer, Model 15. The microanalyses were performed by Schwarzkopf Microanalytical Laboratory. Solvents methanol and methylene chloride were Fisher certified reagents and were used without further treatment.

(43) E. J. Moriconi, W. F. O'Connor, and F. T. Wallenberger, *J. Am. Chem. Soc.*, **81**, 6466 (1959).

filled with silica gel (14–20 mesh) and enclosed with glass wool plugs at each end, was immersed in a dewar flask at Dry Ice–acetone temperature. Ozone was adsorbed on the silica gel, the residual oxygen was swept out by dry nitrogen (2 l.), and the ozone was desorbed using nitrogen as the carrier gas by slowly raising the U-tube out of the dewar container. The amount of adsorbed ozone was determined by sweeping out the ozone with a stream of dry nitrogen into a 2% potassium iodide solution and titrating with 0.1 *N* sodium thiosulfate.

Preparation of Compounds. N-Oxides.—4-Hydroxypyridine-1-oxide was prepared by treatment of Aldrich 4-nitropyridine-1-oxide with dimethylaniline in acetic anhydride; yellow needles, m.p. 246–247° (from ethanol); lit. m.p. 239–241° dec.,[44] 246–247°.[45] K and K quinoline-1-oxide (**24**) was recrystallized from absolute ethanol as white plates, m.p. 55–60°,[46] lit.[44] m.p. 62°. The Robison and Robison[41] procedure for peracetic acid oxidation of isoquinoline gave isoquinoline-2-oxide dihydrate (**42**) as white needles from ethyl acetate; m.p. 98°,[47] lit.[48] m.p. 98°. 1-Methylisoquinoline-2-oxide (**47**) was prepared by the Robison and Robison method[41] which gave, after recrystallization from ether, a 60% yield of **47**·xH$_2$O, as white needles, m.p. 82–83°.

Anal. Calcd. for $C_{10}H_9NO$[49]: C, 75.44; H, 5.70. Found: C, 75.38; H, 5.86.

The picrate of **47** was obtained in conventional fashion as yellow needles from ethanol; m.p. 172–173°.

Anal. Calcd. for $C_{10}H_9NO \cdot C_6H_3N_3O_7$: C, 49.49; H, 3.12. Found: C, 49.73; H, 3.33.

The Robison and Robison procedure[41] also led to 3-methylisoquinoline-2-oxide (**45**), m.p. 135–140°, lit.[41] m.p. 136–138°, from K and K 3-methylisoquinoline. Acridine-10-oxide (**32**) was prepared *via* the perbenzoic acid oxidation[50] of acridine (Aldrich) as yellow-orange needles, m.p. 169°[47] (from carbon tetrachloride), lit.[50] m.p. 169°. 9-Methoxyacridine-10-oxide (**37**) was prepared in a three-step reaction sequence: 9-acridanone (**3**) → 9-chloroacridine[51] → 9-methoxyacridine[52] → **37**[50]; orange-needles, m.p. 160–161°[47] [from 2:1 benzene–petroleum ether (b.p. 90–100°)], lit.[50] m.p. 158°.

Phenanthridine-5-oxide (**29**) was prepared by the *in situ* peracetic acid[53] oxidation of phenanthridine[27] (Aldrich); beige clusters, m.p. 221–222°[47] (from ethanol), lit. m.p. 205–207°,[27] m.p. 220–222°.[54] The picrate of **29** showed m.p. 195°, lit.[27] m.p. 194°.

When a 5 molar excess of hydrogen peroxide was used, a small amount of 5-hydroxy-6(5H)-phenanthridinone (**30**), m.p. 257–258° (sublimed), lit.[54] m.p. 251–254°, was also obtained.

Cyclic Hydroxamic Acids.—1-Hydroxycarbostyril (**25**) was prepared *via* the peracetic acid oxidation of 2-ethoxyquinoline[55] to the 1-oxide, followed by acid hydrolysis to **25**[56]; white plates (sublimed), m.p. 189–190°, lit.[56] m.p. 189–190°. 2-Hydroxyisocarbostyril (**43**) was prepared in a five-step reaction sequence: 1-indanone → 2-hydroxy-1-indanone[57,58] → *o*-carboxyphenylacetaldehyde[59] → oxime[41b] → **43**; gold needles, m.p. 184–185° (sublimed), lit.[41b] m.p. 184.5–185°.

10-Hydroxy-9-acridanone (**33**) was prepared by the acid permanganate oxidation of acridine-10-oxide (**32**)[52] and, much more conveniently, by the alkaline hydrogen peroxide oxidation of **32**. Thus, a solution of 20 ml. of 10% sodium hydroxide and 20 ml. of 30% hydrogen peroxide was added to 4.0 g. (0.021 mole) of **32** dissolved in 50 ml. of hot methanol, and the whole was refluxed for 1 hr. to yield an orange-red solution. The methanol was evaporated (Rinco) and the hot alkaline solution was acidified with concentrated hydrochloric acid to produce an orange precipitate of crude **33**. The precipitate was collected by centrifugation and recrystallized from ethanol to give 3.5 g. (80%) of **33** as fine yellow-orange needles, m.p. 256–257° dec., lit.[52] m.p. 256° dec. The methyl ether of **33** was obtained as yellow needles, m.p. 145–146° dec. (from 25% ethanol), lit.[60] m.p. 153° dec.

Anal. Calcd. for $C_{14}H_{11}NO_2$: C, 74.65; H, 4.92. Found: C, 74.38; H, 4.89.

5-Hydroxy-6(5H)-phenanthridinone (30).—Similar alkaline hydrogen peroxide oxidation of phenanthridine-5-oxide (**29**) produced **30** in 90% yield as tan plates, m.p. 257–258° (sublimed), lit.[54] m.p. 251–254°. Peracetic acid oxidation of **29** led to a 27% yield of **30** with recovery of some 55% of unreacted **29**. The methylation procedure of Kliegl and Fehrle[60] applied to **30** led in 80% yield to 5-methoxy-6(5H)-phenanthridinone, m.p. 115–116° (from 50% ethanol), as beige plates.

Anal. Calcd. for $C_{14}H_{11}NO_2$: C, 74.65; H, 4.92. Found: C, 74.46; H, 4.77.

Aza-Aromatics

Ozonization of Acridine (1).—A solution of 2.0 g. (11.2 mmoles) in 200 ml. of methanol or 9:1 methylene chloride–methanol or methylene chloride was ozonized with a stream of 22 l. of ozone–oxygen. The pale yellow solution turned to canary-yellow. The reaction mixture was purged with nitrogen for 30 min. The ozonized solution (methanol) or suspension[61] (methylene chloride) was then added to a solution of 20 ml. of 10% sodium hydroxide and 20 ml. of 30% hydrogen peroxide.

In methanol solvent, refluxing for 1 hr. precipitated the sodium salt of 2,3-quinolinedicarboxylic acid (**2**) which was separated by filtration. The filtrate was evaporated to dryness (Rinco) and 50 ml. of water added. The water-insoluble material was collected by filtration and extracted (Soxhlet) with chloroform for 3 hr. The chloroform extract upon evaporation gave unreacted **1**; the insoluble portion gave 9-acridanone[62] (**3**), as tiny yellow needles (ethanol), m.p. 350–355°, lit.[63a] m.p. 350–355°. Acidification with hydrochloric acid of the combined aqueous filtrates and the water solution of the sodium salt of **2** led to **2**; recrystallization from water produced **2** as fine, cream-colored needles. Compound **2** loses CO_2 at 100–120° to give 3-quinolinecarboxylic acid, m.p. 274–275°,[62] lit.[63b] m.p. 275°.

In the solvents methylene chloride and 9:1 methylene chloride–methanol, the peroxide-oxidized solution was heated to distil off the methylene chloride, after which the yellow solution was refluxed for 1 hr. On cooling, the insoluble material was filtered and the residue was extracted with chloroform. The chloroform extract gave unreacted **1**; the chloroform-insoluble material led to **3**; acidification of the aqueous filtrate with hydrochloric acid produced **2**.

Ozonization of Acridine Nitrate.—Two grams (8.3 mmoles) of the nitrate salt of **1**, m.p. 189–190° (lit.[63c] m.p. 189–190°), yellow needles from absolute ethanol, was dissolved in 50 ml. of water and 150 ml. of methanol and ozonized with 20 l. of ozone–oxygen. The reaction mixture was oxidized with alkaline hydrogen peroxide and worked up in the same manner as the ozonization of **1** in methanol.

Ozonization of Phenanthridine (4).—A solution of 2.0 g. (11.2 mmoles) of **4** in 200 ml. of methylene chloride at 0° was treated with a stream of ozone–oxygen. The colorless solution turned to pale yellow after 10 l. of gas had passed through. Approximately 20 l. of ozone–oxygen was required for 1 molar equivalent ozone absorption, and 40 l. for two molar equivalents ozone absorption. After purging with nitrogen for 30 min., the reaction mixture was oxidized with a solution of 20 ml. of 10% sodium hydroxide and 20 ml. of 30% hydrogen peroxide. Removal of the methylene chloride solvent *via* distillation was followed by dilution with 60 ml. of water and cooling. The insoluble material was collected by filtration, dried, and extracted with chloroform. The chloroform-insoluble material was recrystallized from 95% ethanol to yield 6(5H)-phenanthridinone (**6**), m.p. 285° dec.,[62] lit.[64] m.p. 287° dec. The chloroform extract was evaporated to dryness (Rinco) and the residue, recrystallized from 50% ethanol, was unreacted **4**. The alkaline filtrate was acidified with concentrated hydrochloric acid to give a fine yellow precipitate; two recrystallizations from glacial acetic acid led to the acetic acid salt of 3,4-quinolinedicarboxylic acid (**5**) as white needles, m.p. 178–179°. The ultraviolet spectrum: $\lambda_{max}^{95\%\ EtOH}$ 281 (ϵ 5350), 323 (3370) resembled that of quinoline and showed none of the fine line absorption of isoquinoline.

Anal. Calcd. for $C_{11}H_7NO_4 \cdot CH_3CO_2H$: C, 56.32; H, 4.00; N, 5.05; neut. equiv., 92.6. Found: C, 56.58; H, 4.05; N, 5.11; neut. equiv., 93.

Ozonization of 1-Methylisoquinoline (12).—The general procedure of Lindenstruth and VanderWerf[9] was followed. The ozonator was adjusted to deliver 0.5 mmole of ozone per liter of gas.

(44) E. Ochiai, *J. Org. Chem.*, **18**, 534 (1953).
(45) H. J. Hertog and W. P. Combe, *Rec. trav. chim.*, **71**, 745 (1952).
(46) Had correct analysis for dihydrate.
(47) Correct analysis obtained on moisture-free sample.
(48) J. Meisenheimer, *Ber.*, **59**, 1848 (1926).
(49) Just prior to analysis, the sample was dehydrated by vacuum drying (13.90% H_2O).
(50) A. Kliegl and A. Brösamle, *Ber.*, **69**, 197 (1936).
(51) A. Albert and B. Ritchie, *Org. Syn.*, **22**, 5 (1942).
(52) K. Lehmstedt, *Ber.*, **68**, 1455 (1935).
(53) A 2.2:1 molar ratio of hydrogen peroxide:phenanthridine was used.
(54) E. Hayashi and Y. Hotta, *Yakugata Zasshi*, **80**, 834 (1960); *Chem. Abstr.*, **54**, 24597g (1960).
(55) P. Friedlander and H. Ostermaier, *Ber.*, **14**, 1917 (1881).
(56) G. T. Newbold and F. S. Spring, *J. Chem. Soc.*, 1864 (1948).
(57) R. Criegee and K. Klonk, *Ann.*, **564**, 1 (1949).
(58) F. Ishikawa, *J. prakt. Chem.*, **108**, 194 (1924).
(59) S. Schöpf and R. Kühne, *Ber.*, **83**, 390 (1950).
(60) A. Kliegl and A. Fehrle, *ibid.*, **47**, 1629 (1914).
(61) Complete solution was obtained on warming to room temperature. In the several cases where the yellow suspension was quickly filtered to leave a yellow material, it decomposed rapidly and exploded on warming to 75°.
(62) Admixture with an authentic sample produced no m.p. depression, and the infrared spectra were identical; correct C, H, N analyses and, where feasible, neut. equiv., were obtained.
(63) (a) C. Graebe and K. Lagodzinski, *Ann.*, **276**, 35 (1893); (b) C. Graebe and H. Caro, *Ber.*, **13**, 99 (1880); (c) C. Graebe and H. Caro, *Ann.*, **158**, 265 (1871).
(64) P. Wegerhoff, *Ann.*, **252**, 1 (1889).

TABLE III

OZONIZATION OF AZA-AROMATICS

Reactant	Molar equiv. of O_3 (±0.1)	Solvent (temp., °C.)	Cleavage product	Yield, %	Cyclic amide	Yield, %	Unreacted material	Recovery, %
Acridine (**1**)	1.1	Methanol (−78)	**2**[c]	33	..	.....	1	40
	1.9–2.1[a]			73–75	**3**	Trace[d]		2–3
	2.1			72	..	...		5
	3.1			68	..	...		3
	2.1–2.3	9:1 Methylene chloride–methanol (−78)	**2**[c]	73–74	**3**	Trace[d]	1	1–2
	2.2[a,b]			73–75	..	...		3–4
	1.0	Methylene chloride (−78)	**2**[c]	31	..	...	1	40
	2.0–2.1[a]			60–62	**3**	2.0–2.5		2–3
	2.0[b]			60		1.8		5
Acridine nitrate	2.1–2.2[a]	Aq. methanol (−20)	**2**[c]	21–25	**3**	2.8–3.2	1	43–45
Phenanthridine (**4**)	1.0–1.2[a]	Methylene chloride (0)	**5**[c]	1.0	**6**	12–17	**4**	50–54
	1.2			1.2		15		50
	2.0–2.2			2.0–2.1		22–23		28
1-Methylisoquinoline (**12**)	Excess	Acetic acid[e] (23)	**14**	19–24[a]		...	**16**	20–23[a,f]
			15	23–25[a]				
3-Methylisoquinoline (**17**)	Excess	Acetic acid[e] (23)	**19**	14–17[a]		...	**21**	20–25[a,f]
			20	25–28[a]				

[a] Based on at least two runs. [b] Ozone–nitrogen. [c] After alkaline hydrogen peroxide oxidation. [d] Less than 0.1%. In actual experiment, this fraction from a number of runs was accumulated until sufficient amounts were obtained for work-up. [e] To which was added a few drops of water; see Experimental. [f] As the N-oxide.

A solution of 19.0 g. (0.13 mole) of **12** in 1200 ml. of glacial acetic acid (to which a few drops of water were added) was ozonized for a period of 10 hr. During the course of the reaction a fine white suspension appeared (6th hour). After the 10th hour, the white precipitate was collected by filtration and recrystallized from water to give 2-methyl-3,4-pyridinedicarboxylic acid (**14**) as white plates, m.p. 252–256° dec., lit.[65] m.p. 250–255° dec.

Anal. Calcd. for $C_8H_7NO_4$: C, 53.04; H, 3.90; N, 7.73; neut. equiv., 90.6. Found: C, 53.21; H, 3.99; N, 7.44; neut. equiv., 92.

The anhydride of **14** was prepared by heating **14** at 230° (20 mm.) and collecting the sublimed material, m.p. 119–120°, lit.[65] m.p. 92°.

Anal. Calcd. for $C_8H_5NO_3$: C, 58.90; H, 3.09; N, 8.59. Found: C, 58.85; H, 3.31; N, 8.40.

Hydrogen peroxide (30 ml., 30%) was added to the acetic acid filtrate and the mixture refluxed for 4 hr. Evaporation (Rinco) to 50 ml. and cooling gave a white precipitate which was collected by filtration and recrystallized from water to give 2-methyl-3,4-pyridinedicarboxylic acid-1-oxide (**15**) as white needles, m.p. 235–240° dec.

Anal. Calcd. for $C_8H_7NO_5$: C, 48.73; H, 3.52; N, 7.11; neut. equiv., 98.5. Found: C, 48.97; H, 3.72; N, 6.98; neut. equiv., 104.

A positive N-oxide test was obtained by heating 0.1 g. with 2 drops of dimethylaniline and 1 drop of concentrated hydrochloric acid.[32]

The filtrate was evaporated (Rinco) to dryness leaving a yellow sirup which was made alkaline by adding potassium carbonate until a paste was formed. Addition of 150 ml. of chloroform and filtration followed by evaporation to dryness gave 1-methylisoquinoline-2-oxide (**16**) as a yellow solid.[62]

Ozonization of 3-Methylisoquinoline (17).—A procedure identical with that for the ozonization of 1-methylisoquinoline (**12**) was employed. The fine white precipitate was collected by filtration and recrystallized from water to give 2-methyl-4,5-pyridinedicarboxylic acid (**19**) as white needles, m.p. 255–260° dec.

Anal. Calcd. for $C_8H_7NO_4$: C, 53.04; H, 3.90; N, 7.73; neut. equiv., 90.06. Found: C, 52.99; H, 3.85; N, 7.93; neut. equiv., 95.

Attempts to form the acid anhydride derivative (with acetic anhydride or by heating at the melting point) resulted only in the recovery of **19**.

After oxidation (hydrogen peroxide), the acid filtrate was evaporated (Rinco) to 50 ml. and cooled to give a yellow precipitate. Filtration of this material and recrystallization from ethanol gave 2-methyl-4,5-pyridinedicarboxylic acid-1-oxide (**20**), m.p. 205–210° dec., as yellow needles.

Anal. Calcd. for $C_8H_7NO_5$: C, 48.73; H, 3.52; N, 7.11; neut. equiv., 98.5. Found: C, 48.46; H, 3.83; N, 6.95; neut. equiv., 110.

(65) O. Mümm and H. Hünecke, *Ber.*, **51**, 150 (1918).

The acid filtrate was evaporated (Rinco) to dryness, leaving a yellow sirup which was treated with potassium carbonate as previously described. The chloroform extract was evaporated (Rinco) to dryness and the brown residue recrystallized from 1:1 benzene–cyclohexane to give 3-methylisoquinoline-2-oxide (**21**), m.p. 134–135°.[62]

Results of the ozonization of acridine (**1**), acridine nitrate, phenanthridine (**4**), 1-methyl- (**12**), and 3-methylisoquinoline (**17**) are summarized in Table III.

N-Oxides

Ozonization of Quinoline-1-oxide (24). In Methanol.—A yellow solution of 3.0 g. (16.6 mmoles) of **24** dihydrate in 200 ml. of methanol was ozonized at −78° with 1 molar equivalent of ozone. After purging with nitrogen, the solution was treated with 50 ml. of 5% sodium hydroxide solution and the alcohol was removed by azeotropic distillation. The brown alkaline solution was then extracted with 3 × 50 ml. of chloroform which when evaporated to dryness gave a dark brown tar. Treatment of the tar with 50 ml. of a saturated picric acid solution led to the picrate of unreacted **24**, small yellow needles, m.p. 142–143°[62] (from 50% ethanol), lit.[48] m.p. 143°.

Acidification of the alkaline solution to pH 6 produced a brown fluffy precipitate which was collected by filtration and recrystallized from 25% ethanol to give 1-hydroxycarbostyril (**25**) as clumps of tiny beige needles, m.p. 189–190°.[62]

Alkaline peroxide oxidation of the acidic filtrate followed by reacidification led to a black tar which could not be separated or identified either by crystallization or chromatographic techniques. Picrate and phenylhydrazone formation also failed.

With two molar ozone equivalents, the ozonized solution turned brown. The green-tinted chloroform extracts, on evaporation to dryness, yielded (in some cases) fine hairlike yellow needles which were manually separated and determined to be *o*-nitrocinnamaldehyde (**26**), m.p. 126°,[62] lit.[66] m.p. 127–127.5°. Alternatively, the chloroform extract, on reaction with phenylhydrazine in acetic acid, precipitated the phenylhydrazone of *o*-nitrobenzaldehyde (**27**), m.p. 153–154°,[62] as red needles, lit.[67] m.p. 155°.

With three molar ozone equivalents, after the alkaline peroxide oxidation of the acidic filtrate step, acidification produced a fine, cream-colored precipitate (0.15 g., m.p. > 360°) which was not further investigated.

In solvent methylene chloride, color changes and work-up procedures in the ozonization of **24** were essentially the same as that in solvent methanol. Thus the ozonized solution was extracted with 4 × 50 ml. of 1% sodium hydroxide solution which in turn were washed with 2 × 25 ml. of chloroform, and these latter were added to the methylene chloride fraction. Acidification of the alkaline extracts gave **25**, while evaporation of the methylene chloride–chloroform extracts gave unreacted **24** and **27**.

Ozonization of Phenanthridine-5-oxide (29). In Methanol.—A solution of 1.0 g. (5.1 mmoles) in 250 ml. of methanol, at −78°, was treated with a stream of ozone–oxygen. A brown suspension formed almost immediately from the pale yellow solution. A

(66) L. Diehle and A. Einhorn, *ibid.*, **18**, 2335 (1885).

(67) R. Lepetit, *ibid.*, **20**, 1338 (1887).

TABLE IV

OZONIZATION OF AZA-AROMATIC N-OXIDES

Reactant	Molar equiv. of O_3 (±0.1)	Solvent (temp., °C.)	Cyclic hydroxamic acid	Yield, %	Cyclic amide	Yield, %	Cleavage product	Yield, %	% recovery reactant
Quinoline-1-oxide (**24**)	1.0	Methanol (−78)	**25**	17	..	...	..	...	40
	1.1[b]			16	..	...	..	...	42
	2.0[a]			23–25	..	...	**26**; **27**	1; 2–4	11–14
	2.9–3.0[a]			...			**27**	16–17	...
	0.9–1.0	Methylene chloride (0)	**25**	15–17	..	...	..	...	42–43
	1.2[b]			19	..	...	..	...	...
	2.0[a]			22–24	..	...	**27**	1	18–23
	2.9–3.3[a]			...				13–18	...
Phenanthridine-5-oxide (**29**)	1.0–1.1[a]	Methanol (−78)	**30**	56	**6**	19–20	**31**	7–8	...
	1.3[b]			53		22		8	...
	2.0–2.2[a]			12–15		26		10–13	...
	3.0[a]			...		29–31		11–13	...
	1.1	Methylene chloride (−78)	**30**	59	..	...	..	...	19
	1.0[b]			60	..	...	..	...	16
	2.0–2.1[a]			77–80	..	...	..	...	...
	3.1			20	..	...	..	...	...
	4.2			10	..	...	..	...	...
Acridine-10-oxide (**32**)	1.0–1.1[a]	Methanol (−78)	**33**	45–48	**3**	2.0–2.9	..	...	27–30
	1.8–2.1[a]			54–60		8–12	..	...	...
	1.8–2.2[a,b]			60–64		6–15	..	...	...
	3.5			26		30	..	...	...
	4.3			17		40	..	...	...
	1.1[a,b]	Methylene chloride (−78)	**33**	29	**3**	15	..	...	...
	2.1–2.3[a]			17–18		6–13	..	...	...
	4.1			10		5	..	...	...
Isoquinoline-2-oxide (**42**)	1.0–1.2[a]	Methanol (−78)	**43**	1	..	...	**44**	26–31	36–42
	2.0[b]			...	..	...		56	4
	2.1–2.4[a]			...	..	...		65–72[c]	...
	1.0–1.2[a]	Methylene chloride (0)	**43**	3–4	..	...	**44**	18–23	34–42
	1.1[b]			5	..	...		22	36
	2.0–2.4			1.0–1.5	..	...		43–50	...
3-Methylisoquinoline-2-oxide (**45**)	1.0	Methanol (−78)	**46**	1	..	...	**44**	10	38
	1.1[b]			1	..	...		11	33
	2.1							32	3
	1.0–1.1[a]	Methylene chloride (0)	**46**	12–14	..	...	**44**	8–10	32–39
	1.2[b]			15	..	...		10	30
	2.1			1	..	...		31	...

[a] Based on at least two runs. [b] Ozone–nitrogen. [c] 35–38% of which was isolated as monomethyl phthalate.

total of 3.0 molar ozone equivalents was absorbed when 5.0 molar ozone equivalents was bubbled through. The suspension was purged with nitrogen for 30 min. and then warmed to room temperature. After addition of 50 ml. of 5% sodium hydroxide, the methanol was removed by azeotropic distillation, and the alkaline solution was diluted with 150 ml. of water and cooled. The yellow insoluble material which formed was collected by filtration and dissolved in 30 ml. of hot 95% ethanol to which were added a few drops of concentrated hydrochloric acid. After refluxing for 10 min., the alcohol solution was diluted with 90 ml. of water. Cooling gave a pink precipitate which was collected by filtration and washed with three 10-ml. portions of cold 80% ethanol. One recrystallization from 95% ethanol (charcoal) gave 6(5H)-phenanthridinone (**6**), m.p. 284–285°,[62] as white granules.

The aqueous alcohol filtrate was diluted with 200 ml. of water. Refrigeration led to 2-nitro-2′-biphenylcarboxaldehyde (**31**), as pale yellow needles, m.p. 73–74° (from 50% ethanol).

Anal. Calcd. for $C_{13}H_9NO_3$: C, 68.72; H, 3.99; N, 6.17. Found: C, 68.79; H, 4.20; N, 6.08.

The 2,4-dinitrophenylhydrazone of **31** was prepared in conventional manner and obtained as tiny metallic-orange needles, m.p. 232–233° (from 95% ethanol).

Anal. Calcd. for $C_{19}H_{13}N_5O_6$: C, 56.16; H, 3.14; N, 17.24. Found: C, 56.00; H, 3.14; N, 17.44.

The original alkaline filtrate was acidified with concentrated hydrochloric acid to yield a fine white precipitate. Filtration followed by two recrystallizations from acetic acid produced white needles of 5-hydroxy-6(5H)-phenanthridinone (**30**), m.p. 257–258° (sublimed).

Anal. Calcd. for $C_{13}H_9NO_2$: C, 73.97; H, 4.29; N, 6.63. Found: C, 74.12; H, 4.45; N, 6.42.

In solvent methylene chloride, passage of five molar ozone equivalents led to a maximum absorption of 4.2 molar equivalents of ozone. Color changes and work-up procedures were the same as in the ozonization of **29** in methanol. The alkaline-insoluble material was treated with a few drops of hydrochloric acid in alcohol to yield **30**. No **6** or **31** was obtained. Acidification of the alkaline filtrate merely led to additional amounts of **30**.

Ozonization of Acridine-10-oxide (32).—Ozone–oxygen was bubbled through a solution of **32** in 200 ml. of methanol, or methylene chloride, at −78°. Successive color changes during the reaction were: greenish yellow, dark brown, dark red, and finally yellow again. The solution was purged with nitrogen for 30 min. and then added to 50 ml. of 1% sodium hydroxide solution. The methanol was removed by azeotropic distillation and the remainder further diluted with water to 200 ml. Cooling and filtration left a yellow insoluble material which was extracted (Soxhlet) for 3 hr. with chloroform. Evaporation of the chloroform extract led to unreacted **32**. The chloroform-insoluble material was 9-acridanone (**3**), m.p. 350–355°,[62] lit.[63a] m.p. 350–355°. The alkaline filtrate was acidified with hydrochloric acid to give an orange suspension which was collected by centrifugation and recrystallized from ethanol to give 10-hydroxy-9-acridanone (**33**) as yellow-orange needles, m.p. 256° dec.,[62] lit.[52] m.p. 256°.

Ozonization of 4-Hydroxypyridine-1-oxide (36) and 9-Methoxyacridine-10-oxide (37).—Ozonization of **36** in methanol at −78° with 2.3 molar ozone equivalents, and **37** in methanol with 2.0, 3.0, and 4.0 molar ozone equivalents, resulted in reaction in all cases. A wide variety of alkaline and oxidative work-up procedures for both ozonolyses did not produce the sought for deoxygenated products 4-hydroxypyridine (**36a**) and 9-methoxyacridine (**37a**), respectively,[32] and further work on product isolation and identification was abandoned.

Ozonization of Isoquinoline-2-oxide (42). In Methanol.—A pale yellow solution of 3.0 g. (16.6 mmoles) of **42** dihydrate in 200 ml. of methanol at −78° was treated with 16.5 mmoles of ozone with no detectable color change. After flushing with nitrogen, 20 ml. of 10% sodium hydroxide solution was added, and the red-colored alkaline solution extracted with 4 × 50 ml. of chloroform. The chloroform extracts were evaporated to dryness and the residue, recrystallized from ethyl acetate, was unreacted **42**.

The alkaline solution was acidified and extracted with benzene for 24 hr.; evaporation of the benzene extract left <1% of the impure hydroxamic acid **43**. The acid fraction was neutralized and the whole oxidized with 20 ml. of 10% sodium hydroxide and 20 ml. of 30% hydrogen peroxide. After refluxing for 2 hr., the solution was acidified with hydrochloric acid (vapors of NO_2 evolved) and concentrated (Rinco) to 50 ml. On cooling, **44** precipitated, m.p. 195–200°.[62] Continuous ether extraction of the filtrate led to additional amounts of **44**.

When two or more (to a maximum of 2.6) molar ozone equivalents were used, only black tars were obtained on evaporation of the benzene extract. In similar experiments, sodium hydroxide and hydrogen peroxide were added directly to the ozonized methanolic solution. After evaporation of the methanol and refluxing several hours, the solution was acidified and extracted (continuously) with benzene for 24 hr. The benzene extract was evaporated to dryness, and the residue, recrystallized from 1:1 benzene–cyclohexane, gave monomethyl phthalate, m.p. 79–80°,[62] as white plates, lit.[68] m.p. 79°.

In solvent methylene chloride, quantities, ozonization procedure, and nitrogen purging were as in solvent methanol. The ozonized solution was extracted with 5 × 50 ml. of 1% sodium hydroxide; the methylene chloride fraction gave unreacted **42**.

The red alkaline extracts were acidified with concentrated hydrochloric acid to give a yellow, turbid solution which was continually extracted with benzene for 24 hr. Evaporation of the benzene extract left a brown paste which was dissolved in 5% ammonium hydroxide, heated to remove excess ammonia, treated with charcoal, and filtered. Acidification of the filtrate and cooling gave pale yellow needles of 2-hydroxyisocarbostyril (**43**), m.p. 184–185°[62] (sublimed).

The acidic solution, after extraction, was neutralized, and to it was added 20 ml. of 10% sodium hydroxide and 20 ml. of 30% hydrogen peroxide. Refluxing for 2 hr., followed by acidification, concentration to 50 ml. (Rinco), and charcoal treatment, gave **44** on cooling. When **42** was ozonized with 2.4 molar ozone equivalents, the methylene chloride extracts yielded a brown material, m.p. 115–117°, which on oxidation with alkaline hydrogen peroxide ultimately produced a white powder (~1 g.), m.p. > 360°. Both of these products were not further identified.

Ozonization of 3-Methylisoquinoline-2-oxide (45). In Methylene Chloride.—Ozonolysis and alkaline extraction procedures were identical with those used in the ozonization of **42**. The methylene chloride extracts led to unreacted **45**. Acidification of the red alkaline extract with hydrochloric acid produced a brick-red precipitate which was filtered and recrystallized from carbon tetrachloride to give tan needles of 2-hydroxy-3-methylisocarbostyril (**46**), m.p. 172.5–173° (sublimed as white plates), lit. m.p.[33] 172.5–173°.

Anal. Calcd. for $C_{10}H_9NO_2$: C, 68.56; H, 5.18; N, 8.00. Found: C, 68.57; H, 5.21; N, 8.17.

(68) G. Koller and E. Shang, *Monatsh.*, **50**, 48 (1928).

As with **42**, neutralization of the acid filtrate followed by alkaline hydrogen peroxide oxidation and acidification led to **44**, separated both by precipitation and ether extraction.

The benzoate ester of **46** was prepared by treating a solution of 0.2 g. of **46** in 3 ml. of anhydrous pyridine with 0.3 g. of benzoyl chloride. The solution was warmed for a few minutes, then cooled, and added to 25 ml. of cracked ice. The N-benzoate ester was collected by filtration, washed with water, and recrystallized from 50% ethanol (60% yield); m.p. 167–168°,[62] lit.[33] m.p. 167–168°.

With 2.0–2.4 molar equivalents (max. ozone absorption) in methylene chloride, only small amounts (0.1%) of **46** could be isolated.

In solvent methanol, the absorption of one molar ozone equivalent led to **44** and a low yield of **46**. Increasing the amounts of ozone (to a maximum of 2.6 molar equivalents) led only to **44**.

Ozonization of 1-Methylisoquinoline-2-oxide (47).—Compound **47** was insoluble in methylene chloride. A suspension of 3.0 g. (1.90 mmoles) in 200 ml. of methylene chloride was treated with 22 mmoles of ozone. No reaction was observed; some 98% of **45** was recovered and approximately 95% of the ozone passed into the potassium iodide trap. Ozonization of **45** in methanol with 1.7 molar ozone equivalents led to a 70% recovery of unreacted **47**. Work-up procedures similar to those of **42** led to no identifiable products.

Cyclic Hydroxamic Acids

Ozonization of 1-Hydroxycarbostyril (25). In Methanol.—A solution of 644 mg. (4.0 mmoles) of **25** in 100 ml. of methanol at −78° was subjected to a stream of 8 l. of ozone–oxygen. Treatment of the ozonized solution with 50 ml. of 2% sodium hydroxide solution and evaporation of the alcohol left a dark brown solution which was extracted with three 25-ml. portions of chloroform. The chloroform extracts were evaporated to dryness (Rinco) to leave a yellow residue. Recrystallization from 25% ethanol gave 7–10% of carbostyril (**28**), m.p. 198–199°.[62]

The alkaline solution was acidified to recover 8–11% of unreacted **25**. Alkaline peroxide oxidation of the acid filtrate yielded (after reacidification) a fine yellow solid (50 mg.), m.p. > 360°; the infrared spectrum of this material showed no sharp absorption bands. This product was not further investigated.

In methylene chloride, **25** did not yield any **28**. Only 5% of **25** was recovered, in addition to the high-melting yellow solid.

Attempted Ozonization of 2-Hydroxyisocarbostyril (43) and 2-Hydroxy-3-methylisocarbostyril (46).—Using ozonization–base decomposition procedures similar to those for **25**, no deoxygenation or bond cleavage products could be isolated from **43** or **46**. In both cases, alkaline peroxide oxidation of the ozonized isocarbostyrils led to unidentified, high melting, colored (cream, yellow) solids.

Ozonization of 10-Hydroxy-9-acridanone (33).—A suspension of 1.0 g. (4.7 mmoles) of **33** in 220 ml. of methanol or methylene chloride at 20° was ozonized in the usual manner with 1.0 molar ozone equivalent. Conventional nitrogen purge, the addition of 50 ml. of 1% sodium hydroxide, and the azeotropic removal of solvent were as previously described. The red solution was filtered while hot to leave a yellow residue which was washed with 3 × 30 ml. of hot water and then recrystallized from ethanol to give tiny pale yellow needles of 9-acridanone (**3**)[62] in 10% yield. Acidification of the red alkaline solution gave 60–72% of unreacted **33**. Two molar ozone equivalents (ozone–oxygen and ozone–nitrogen) addition to **33** led to 14–18% of **3** and 44–65% recovery of **33**.

[CONTRIBUTION FROM THE SCHOOL OF CHEMISTRY, RUTGERS, THE STATE UNIVERSITY, NEW BRUNSWICK, N. J.]

Reactions of Lewis Acids with Diaroyl Peroxides[1]

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The conversion of benzoyl peroxide to phenyl benzoate by antimony pentachloride has been studied by the oxygen-18 tracer technique. The reaction is shown to involve an initial carboxy-inversion process which gives benzoyl phenyl carbonate. The mixed carbonate is converted to phenyl benzoate and carbon dioxide rapidly by antimony pentachloride. An oxygen-18 tracer study of the formation of 2,4,6-trimethylphenyl *p*-nitrobenzoate (III) from labeled *p,p'*-dinitrobenzoyl peroxide, aluminum chloride, and mesitylene showed that partial equilibration of the label occurs during the transformation. It was found that bimesityl is a product of the reaction. Various mechanistic implications of these results are discussed.

A series of papers appeared, in 1927, in which Reynhart[4] described the reaction of benzoyl peroxide with a number of inorganic acid chlorides. Several reactions were reported, but only two are of concern here. The first involves the reaction of antimony pentachloride

(1) A portion of the material being reported appeared in *J. Am. Chem. Soc.*, **84**, 2455 (1962).

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(4) A. F. A. Reynhart, *Rec. trav. chim.*, **46**, 54, 62, 72 (1927).