Compounds Related to Acridine. I. Condensation of Acridine Derivatives Having Active Methyl Group and Aromatic Nitroso Compounds*

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The basic condensation of the active methylene or the methyl group and the aromatic nitroso compound in general has been known as the Ehrlich-Sachs reaction(1) and has been considered a useful synthetic route to the corresponding ketone or aldehyde. It has been established in recent years that this reaction is accompanied by an oxidative reaction to form the nitrone, besides the anil, as a by-product. It is also known that these two products are difficult to separate.

Recently,(2) we found that the reaction of 7-methyl-4, 5-dihydroindeno [1, 7-bc] acridine (I) with *p*-nitrosodimethylaniline did not take place in the presence of an alkaline catalyst (sodium carbonate, potassium carbonate or piperidine) ; on the other hand, the presence of a catalytic amount of a mineral acid, especially hydrochloric acid, afforded the nitrone compound in a fairly good yield, while only a small amount of the anil compound was formed.

The present investigation was undertaken in order to elucidate the role of hydrochloric acid (HA) as a condensation agent in the reaction of 9-methyl- (II), 2, 9-dimethyl- (III), 4, 9-dimethyl- (IV), 2-chloro-9-methyl- (V), 7-methylbenz [c] - (VI) or 12-methylbenz [a] acridine (VII), which are similar to I in their chemical structures, with several nitroso compounds: nitrosobenzene (VIII), *p*-nitrosodimethyl- (IX), *p*-nitrosodiethylaniline (X) and *p*-nitrosophenol (XI).

These compounds and their reaction products are depicted in Chart 1.

Although the reaction of II with nitroso compounds, especially IX, in the presence of an alkaline catalyst has been investigated by a number of workers, Chardonnens and Heinrich(3) first successfully separated and identified acridine-9-carboxaldehyde anils and *N*-(*p*-substituted phenyl)-α-(9-acridyl) nitrones ; the major product was found to be the anil in most cases.

On the other hand, only a little information has been available regarding the condensation of substituted 9-methylacridines or methylbenzacridines and the nitroso compound. Porai-Koshits and others(4) reported that a

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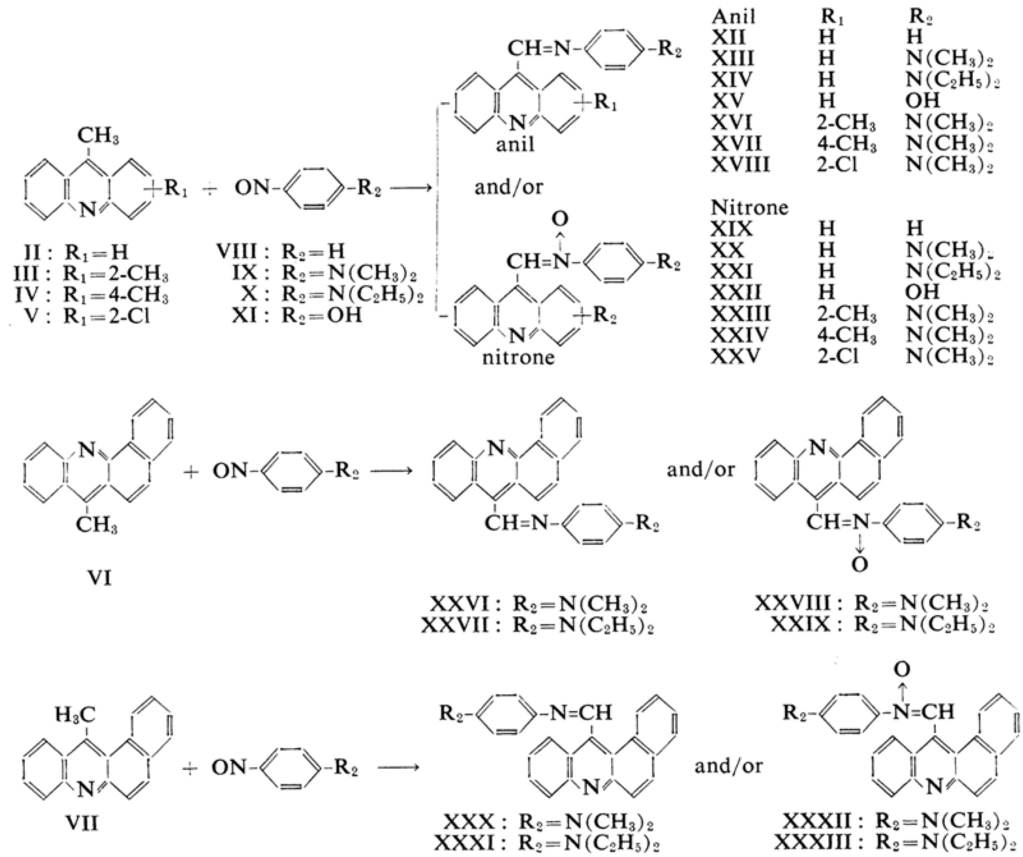
1) P. Ehrlich and F. Sachs, *Ber.*, **32**, 2341 (1899).

2) H. Saikachi, O. Tsuge and M. Tashiro, *J. Pharm. Soc. Japan* (*Yakugaku Zasshi*), **80**, 584 (1960).

3) L. Chardonnens and P. Heinrich, *Helv. Chim. Acta*, 32, 656 (1949).

4) A. E. Porai-Koshits and G. S. Ter-Sarkisyan, *Izvest. Akad. Nauk S. S. S. R., Otdel. Khim. Sci.*, **1951**, 601.



Anil	R_1	R_2
XII	H	H
XIII	H	$N(CH_3)_2$
XIV	H	$N(C_2H_5)_2$
XV	H	OH
XVI	2-CH_3	$N(CH_3)_2$
XVII	4-CH_3	$N(CH_3)_2$
XVIII	2-Cl	$N(CH_3)_2$
Nitrone		
XIX	H	H
XX	H	$N(CH_3)_2$
XXI	H	$N(C_2H_5)_2$
XXII	H	OH
XXIII	2-CH_3	$N(CH_3)_2$
XXIV	4-CH_3	$N(CH_3)_2$
XXV	2-Cl	$N(CH_3)_2$

Chart 1

nitrone compound was formed by the reaction of the dimethylsulfate of VI with IX. It was reported by Mikhailov and Ter-Sarkisyan[5] that the condensation of III and IX with sodium carbonate or the ultraviolet illumination of a mixture of VII and the hydrochloride of IX in methanol gave the corresponding nitrone compounds in a poor yield.

Now, the addition of a small amount of HA in place of an alkaline catalyst to the reaction mixture of the acridine derivatives and nitroso compounds mentioned above in ethanol, revealed interesting results, as had been expected. In addition, this paper will also deal with the infrared spectra of the anil and nitrone compounds.

Results and Discussion

As the optimum conditions for obtaining a nitrone compound by the reaction of I with IX in the presesnce of HA had not been determined, in the reaction of II with IX the effect of reaction conditions on the yield of

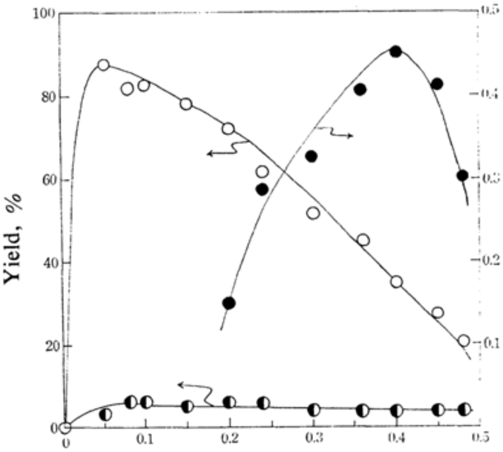


Fig. 1. Effect of hydrochloric acid.

Mixtures of II (1.0 g.) and IX (1.6 g.) in the presence of the specified amounts of HA (d^{27} 1.1748) in ethanol (50 ml.) were refluxed for 2 hr.

-○-○- Nitrone (XX)
-◐-◐- Anil (XIII)
-●-●- Higher melting compound (XXXIV)

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[5] B. M. Mikhailov and G. S. Ter-Sarkisyan, ibid., **1954**, 656.

acridine-9-carboxaldehyde *N*-(*p*-dimethylaminophenyl)anil (XIII) or of *N*-(*p*-dimethylaminophenyl)-α-(9-acridyl)nitrone (XX) was first examined.

Effect of the Amount of Hydrochloric Acid.—The results are given in Fig. 1. In contrast with the condensation in the presence of sodium carbonate, the main product was the nitrone XX, whose yield was greatly affected by the amount of HA. The maximum yield of XX was obtained when the molar ratio of HA to II was about 0.08 (0.03 ml. in Fig. 1) ; its yield rapidly decreased with the increase in the amount of the HA. While the yield of the anil XIII was little affected by the HA, it was very poor.

On the other hand, if the molar ratio of HA to II was over about 0.5 (0.2 ml. in Fig. 1), the higher melting substance (XXXIV)[6] (m. p. over 300°C) began to be formed. When equimolecular amounts of II and of HA were used, the maximum yield of XXXIV was obtained. On the other hand, a large amount of a resinous material came to be formed as the amount of the HA increased.

Effect of the Reaction Time.—The effects of the reaction time on the yields of XIII and XX in the presence of HA or sodium carbonate are shown in Fig. 2. It is clear that HA greatly accelerated the rate of the condensation of II and IX in comparison with sodium carbonate, and that the nitrone XX was formed in a good yield in a short while. In the case of sodium carbonate, more of the anil XIII was obtained than of the nitrone XX, but both yields were very poor, as had been reported by Chardonnens and Heinrich.[3]

Effect of the Amount of *p*-Nitrosodimethylaniline (IX).—The results are given in Table I. The treatment of II with two or three molecular amounts of IX afforded the nitrone XX in an excellent yield. In particular, it is to be emphasized that even when an equimolecular amount of IX was used, XX was formed in a fairly good yield.

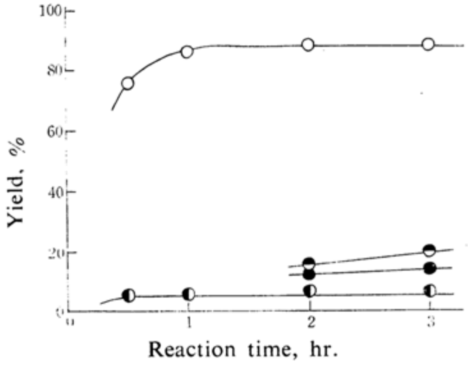


Fig. 2. Effect of the reaction time.

-◐-◐- Anil (XIII) } In the presence of HA
-○-○- Nitrone (XX) }
-◓-◓- Anil (XIII) } In the presence of Na_2CO_3
-●-●- Nitrone (XX) }

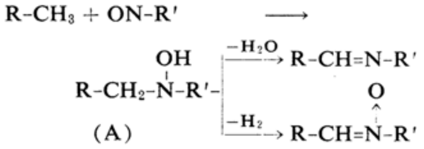
TABLE I. EFFECT OF THF AMOUNT OF IX*

IX**	Product, %	
	Anil (XIII)	Nitrone (XX)
1	4.1	74.8
2	5.0	85.3
3	4.5	90.0

* Mixtures of II (1.0 g.) and the specified amounts of IX in the presence of HA (0.05 ml., d^{27} 1.1748) in ethanol (50 ml.) were refluxed for 3 hr.

** Moles per mole II

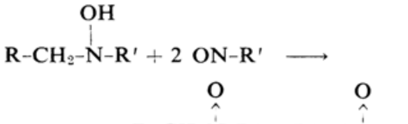
Kröhnke and his co-workers[7,8] have suggested the mechanism for the formation of the anil and nitrone in the presence of an alkaline catalyst depicted in Chart 2:



$$R\text{-}CH_3 + ON\text{-}R' \longrightarrow \underset{(A)}{R\text{-}CH_2\text{-}\overset{OH}{N}\text{-}R'} \begin{cases} \xrightarrow{-H_2O} R\text{-}CH{=}N\text{-}R' \\ \xrightarrow{-H_2} R\text{-}CH{=}\overset{\overset{O}{\uparrow}}{N}\text{-}R' \end{cases}$$

Chart 2

That is, the aldol-type intermediate (A) is formed by the condensation of active methyl and the nitroso compound, and the dehydration of the intermediate (A) chiefly proceeds to give the anil. Simultaneously, the nitrone compound is formed as a by-product by the dehydrogenation. The dehydrogenation is mainly ascribed to the oxidative property of the nitroso compound according to the following scheme:



$$R\text{-}CH_2\text{-}\overset{OH}{N}\text{-}R' + 2\ ON\text{-}R' \longrightarrow R\text{-}CH{=}\overset{\overset{O}{\uparrow}}{N}\text{-}R' + R'\text{-}N{=}\overset{\overset{O}{\uparrow}}{N}\text{-}R'$$

Furthermore, they proposed that the intermediate (A) may be dehydrogenated in a certain degree by air, and that the corresponding phenylhydroxylamine, which is yielded by the reduction of the nitroso compound, is disproportionate to the original nitroso compound and aniline derivative: $2R'\text{-}NO + H_2 \rightarrow 2R'\text{-}NHOH \rightarrow R'\text{-}NO + R'\text{-}NH_2$.

According to this mechanism, at least two moles of the nitroso compound are needed to form one mole of the nitrone compound.

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[6] The structure of XXXIV will be published elsewhere in the near future.

[7] F. Kröhnke, *Ber.*, **71**, 2583 (1938).

[8] F. Kröhnke, H. Leister and I. Vogt, *Chem. Ber.*, **90**, 2792 (1959).

TABLE II. EFFECT OF THE SUBSTITUENT IN NITROSOBENZENES

Nitrosobenzene		Catalyst**	Reaction	Product***			
Kind	Amounts*		time, hr.	Anil	Yield, %	Nitrone	Yield, %
VIII	4	Na_2CO_3	3	XII	—	XIX	53.7
VIII	3	HCl	2	XII	42.9	XIX	+
IX	2	Na_2CO_3	3	XIII	16.9	XX	8.5
IX	2	HCl	2	XIII	4.3	XX	87.2
X	1	Na_2CO_3	6	XIV	53.1	XXI	9.1
X	2	HCl	2	XIV	40.0	XXI	27.3
XI	2	K_2CO_3	3	XV	—	XXII	47.1
XI	2	HCl	3	XV	82.3	XXII	—

* Moles per mole II

** Data with sodium carbonate as a catalyst were quoted from Ref. 3.

*** Yields based on II and a plus-sign, +, means a small amount.

However, the fact that the nitrone XX was obtained in a good yield, even if an equimolecular amount of IX was used, as Table I shows, does not appear to be explained by Kröhnke's mechanism. The mechanism will be considered elsewhere in the near future.

Effect of the Substituent in Aromatic Nitroso Compounds.—Chardonnens and Heinrich[3] also reported that the kind of aromatic nitroso compound affected the relative amounts of the products, the anil and the nitrone. As has been described above, contrary to the case of sodium carbonate, the nitrone XX was chiefly afforded when the mixture of II and IX with a catalytic amount of HA in ethanol was refluxed. Accordingly, it seemed of interest to clarify the variation in the relative amounts of the anil and of the nitrone when the condensations of II and several nitrosobenzenes VIII—XI were carried out in the presence of a catalytic amount of HA in a boiling ethanol solution. The results are summarized in Table II.

Table II shows interesting features regarding the relative amounts of the anil and of the nitrone compound. In the treatment of II and nitrosobenzene (VIII) with sodium carbonate, *N*-phenyl-α-(9-acridyl)nitrone (XIX) was obtained as a major product in place of acridine-9-carboxaldehyde *N*-phenylanil (XII). On the other hand, when HA was used the product ratio of these two compounds was reversed, and the anil XII was formed as the main product.

As has been mentioned above, IX reacted with II in the presence of HA to give the nitrone compound in an excellent yield. The condensation of II and *p*-nitrosodiethylaniline (X) with HA or sodium carbonate afforded acridine-9-carboxaldehyde *N*-(*p*-diethylaminophenyl)anil (XIV) as the major product. In the case of the former, however, *N*-(*p*-diethylaminophenyl)-α-(9-acridyl)nitrone (XXI) was also formed in a fairly large amount.

Drozdov and Yavorskaya[9] have reported that the condensation of II and *p*-nitrosophenol (XI) with sodium carbonate leads to the formation of *N*-(*p*-hydroxyphenyl)-α-(9-acridyl)-nitrone (XXII) (m. p. 230∼231°C) in a 60% yield. We carried out the reaction of II with XI in the presence of HA or potassium carbonate as a condensation agent; acridine-9-carboxaldehyde *N*-(*p*-hydroxyphenyl)anil (XV) (m. p. 275°C) or the nitrone compound (XXII) (m. p. 235°C (decomp.)) was obtained in a 82.3 or a 47.1% yield respectively. The melting point of the anil XV reported by Drozdov and Yavorskaya[9] was 225°C (decomp.), but XV prepared by the condensation of acridine-9-carboxaldehyde and *p*-aminophenol melted at 275°C.

Reaction of Other Acridines with Nitroso Compounds. — We have attempted to clarify the relation between the effect of HA and sodium carbonate on the condensation of other acridines and nitroso compounds. It has been reported that the treatment of 2,9-dimethylacridine (III) with IX in the presence of sodium carbonate in boiling methanol for 5 hr. afforded *N*-(*p*-dimethylaminophenyl)-α-(2-methyl-9-acridyl)nitrone (XXIII) in about a 26% yield.[5] We carried out the reaction of III with IX in the presence of HA or sodium carbonate in boiling ethanol. In the case of HA, 2-methylacridine-9-carboxaldehyde *N*-(*p*-dimethylaminophenyl)anil (XVI) was obtained in a good yield, but XXIII, in only a trace amount. As reported by Mikhailov and Ter-Sarkisyan,[5] in the presence of sodium carbonate only the nitrone XXIII was obtained in a poor yield.

4,9-Dimethyl- (IV) or 2-chloro-9-methylacridine (V), treated with IX in the presence of HA, condensed to afford 4-methylacridine- (XVII) or 2-chloroacridine-9-carboxaldehyde *N*-(*p*-dimethylaminophenyl)anil (XVIII) in a fairly

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[9] N. S. Drozdov and E. V. Yavorskaya, *Zhur. Obshchei Khim.*, **30**, 3421 (1960).

Table III. Condensation of other acridines and nitroso compounds

Acridine	Nitroso* compound	Catalyst	Reaction time, hr.	Product**			
				Anil	Yield, %	Nitrone	Yield, %
III	IX	HCl	3	XVI	77.4	XXIII	+
III	IX	Na_2CO_3	3	XVI	—	XXIII	22.2
IV	IX	HCl	3	XVII	36.6	XXIV	44.9
IV	IX	Na_2CO_3	3	XVII	—	XXIV	15.2
V	IX	HCl	3	XVIII	54.8	XXV	37.7
V	IX	Na_2CO_3	3	XVIII	43.6	XXV	+
VI	IX	HCl	3	XXVI	15.5	XXVIII	14.6
VI	X	HCl	3	XXVII	37.4	XXIX	—
VII	IX	HCl	1	XXX	+	XXXII	82.6
VII	X	HCl	1	XXXI	—	XXXIII	61.5

* Two moles per mole acridine compounds were used.

** Yields based on acridines and a plus-sign, +, means a trace amount.

good yield; the corresponding nitrone, *N*-(*p*-dimethylaminophenyl)-α-(4-methyl-9-acridyl)-(XXIV) or *N*-(*p*-dimethylaminophenyl)-α-(2-chloro-9-acridyl)nitrone (XXV), was also produced. However, the basic condensation of IV or V with IX afforded only the nitrone XXIV or anil XVIII respectively in a low yield.

The methylbenzacridines VI—VII, as well as I, did not react with IX or X in the presence of an alkaline catalyst, but they did react to give the anil and/or nitrone with HA. In the condensation of VI and IX, benz[c]acridine-7-carboxaldehyde *N*-(*p*-dimethylaminophenyl)anil (XXVI) and *N*-(*p*-dimethylaminophenyl)-α-(7-benz[c]acridyl)nitrone (XXVIII) were obtained in almost the same yield, but both yields were poor. However, VI with X reacted to give only the corresponding anil, benz[c]acridine-7-carboxaldehyde *N*-(*p*-diethylaminophenyl)anil (XXVII).

On the other hand, VII with IX or X smoothly reacted to afford the nitrone, *N*-(*p*-dimethylaminophenyl)- (XXXII) or *N*-(*p*-diethylaminophenyl)-α-(12-benz[a]acridyl)nitrone (XXXIII) respectively, in a fairly good yield, although the corresponding anil was not formed. These results are summarized in Table III.

Mikhailov and Ter-Sarkisyan[10] have reported that the order of the reactivity of the methyl component in the reaction with *m*-nitrobenzaldehyde was as follows: II>VI>VII; 4-picoline>4-quinaldine>1-methylbenzo[f]quinoline>4-methylbenzo[h]quinoline.

When the reactivity of the methyl group in VI and VII in the reaction with IX or X is compered, the latter is greater than the former. This seems to be the same as with the relationship of benzoquinoline derivatives mentioned above; it shows that the steric factor alone is not always predominate.

Table IV. Stretching vibrations of C=N and N-O

Compound (XII—XXV)		$\nu_{C=N}$, cm^{-1}		ν_{N-O}, cm^{-1}
R_1	R_2	Anil	Nitrone	(Nitrone)
H	H	1613	1612	1054
H	$N(CH_3)_2$	1621	1606	1048
H	$N(C_2H_5)_2$	1620	1607	1049
H	OH	1616	1613	1047
2-CH_3	$N(CH_3)_2$	1610	1597	1048
4-CH_3	$N(CH_3)_2$	1621	1612	1020
2-Cl	$N(CH_3)_2$	1615	1601	1047
Compound (XXVI—XXIX)				
	R_2			
	$N(CH_3)_2$	1623	1610	1061
	$N(C_2H_5)_2$	1618	—	—
Compound (XXX—XXXIII)				
	$N(CH_3)_2$	1625	1613	1036
	$N(C_2H_5)_2$	—	1608	1042

The structure assignments of all anils and nitrones described above were made on the basis of the infrared spectra as well as of elemental analyses.

Furthermore, all the anils or nitrones were almost quantitatively hydrolyzed to afford the corresponding formyl derivatives, which formed the anils by condensation with anilines.

Infrared Spectra of the Anils and Nitrones.—The infrared spectra of the above-mentioned anils and nitrones were measured in Nujol mull; the characteristic absorption bands for the C=N bond of the Schiff base type and for the *N*-oxide group were thus established. The observed frequencies are summarized in Table IV. The spectra of the anil XIII and nitrone XX as one example are shown in Fig. 3. In general, the C=N stretching frequency in the nitrone compounds was observed at a lower frequency region than that in the anil compounds; this shows that the double-bond

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[10] B. M. Mikhailov and G. S. Ter-Sarkisyan, *Izvest. Akad. Nauk S. S. S. R., Otdel. Khim. Nauk*, **1954**, 846.

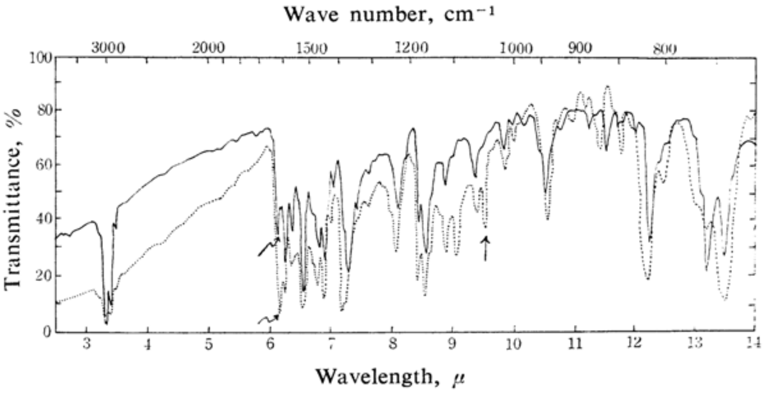

Fig. 3. Infrared spectra of the anil (XIII) and nitrone (XX) in Nujol mull.
—— (XIII), ···· (XX)

character of C=N in the former is smaller than that in the latter, as was expected.

In all nitrone compounds, the moderate absorption band always appeared around 1050 cm^{-1}. The N-O stretching frequency in aliphatic tertiary amine *N*-oxides,[11] aromatic nitroso compounds[12] or pyridine *N*-oxides[13] is assigned to the region of 950, 1380∼1340 or 1200∼1300 cm^{-1} respectively.

Since the N-O bond in the above-mentioned nitrone compounds is considered by mesomerism to have a greater double-bond character than that in aliphatic tertiary amine *N*-oxides and a smaller one than that in aromatic nitroso compounds or pyridine *N*-oxides, it is expected that the N-O band of the present nitrones will appear at a higher frequency region than that of aliphatic *N*-oxides and at a lower region than the aromatics.

Consequently, it seems to be appropriate for the observed band at around 1050 cm^{-1} to be assigned to the N-O streching frequency in the nitrone compounds.

Experimental[14]

Preparation of Methylacridines II—VII.—The reaction conditions in the preparation of 9-methylacridine (II) by the Bernthsen method were examined.[15] It was found that the yield of II became better as the amount of zinc chloride increased and that the following procedure afforded II in a fairly good yield in spite of the relatively short reaction time.

A mixture of diphenylamine (10.0 g.) and glacial acetic acid (10 ml.) in the presence of anhydrous zinc chloride (40.0 g.) was heated to 220°C, while being stirred; the excess acetic acid was thus evaporated, and the mixture was then held at 220∼230°C for 6 hr. The reaction mixture was digested with hot 10% aqueous sulfuric acid and then strongly alkalified with concentrated aqueous ammonia to dissolve zinc chloride. The insoluble residue was extracted with benzene and, after separation, the benzene layer was extracted again with 10% aqueous sulfuric acid. The extract with dilute sulfuric acid was alkalified by the addition of aqueous ammonia, upon which yellow crystals separated out. Filtration gave 10.0 g. (87.5%) of crude II (m. p. 103∼110°C), which on chromatography on alumina and then recrystallization from petroleum benzine afforded pale yellow needles (m.p. 118∼118.5°C) (reported, 117∼118°C[16]). (Found: C, 87.02; H, 5.71; N, 7.60%).

According to this procedure, the following acridines were prepared from the corresponding diarylamine, 2-methyl-, 4-methyl-, 2-chlorodiphenylamine, 1-phenyl- or 2-phenylnaphthylamine; 2, 9-dimethylacridine (III): pale yellow needles (from petroleum benzine), m. p. 89.5∼90°C (reported, 90°C[16]). Yield, 45.5%. (Found: C, 86.62; H, 6.44; N, 6.86 %). 4, 9-Dimethylacridine (IV): pale yellow needles (from petroleum benzine), m. p. 53.5∼54°C. Yield, 51.2%.

Found: C, 86.51; H, 6.03; N, 6.72. Calcd. for $C_{15}H_{13}N$: C, 86.92; H, 6.33; N, 6.76%.

2-Chloro-9-methylacridine (V): pale yellow needles (from petroleum benzine), m. p. 124∼125°C (reported, 124°C[17]). Yield, 71.5%. (Found: C, 73.92; H, 4.50; N, 6.18%). 7-Methylbenz[c]acridine (VI): pale yellow scales (from benzene), m. p. 124∼125°C (reported, 125.5°C[4]). Yield, 68.4%. (Found: C, 88.76; H, 5.09; N, 5.98%). 12-Methylbenz[a]acridine (VII): pale yellow scales (from benzene), m. p. 144∼145°C (reported, 144∼145°C[18]). Yield,

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[11] A. Palm and H. Werbin, *Can. J. Chem.*, 32, 858 (1954).

[12] K. Nakamoto and R. E. Rundle, *J. Am. Chem. Soc.*, 78, 1113 (1956).

[13] H. Shindo, *Chem. Pharm. Bull. Japan*, 7, 791 (1959).

[14] All melting points are uncorrected.

[15] A. Bernthsen, *Ann.*, **224**, 1 (1884). This synthesis of 9-substituted acridines consists of heating a mixture of an aromatic or aliphatic carboxylic acid with diphenylamine and zinc chloride at 200∼270°C for about 20 hr.

[16] H. Jensen and F. Rethwisch, *J. Am. Chem. Soc.*, 50, 1144 (1928).

[17] A. Campbell et al. have reported that they obtained V by the reaction of 2, 9-dichloroacridine with ethyl sodiomalonate (*J. Chem. Soc.*, **1958**, 1145).

[18] A. E. Porai-Koshits and G. S. Ter-Sarkisyan, *Izvest. Akad. Nauk S. S. S. R., Otdel. Khim. Sci.*, **1951**, 771. VI or VII was prepared by the reaction of the corresponding diarylamine with acetic anhydride in a 48.8 or a 26.8% yield respectively.

83.7%. (Found: C, 88.95; H, 5.21; N, 5.80%).

Reaction of 9-Methylacridine (II) with Nitrosobenzene (VIII).—To a solution of II (1.0 g.) and VIII (1.1 g.) dissolved in ethanol (50 ml.), HA (0.03 ml.) was added.[19] The resultant solution was refluxed on a water bath and, after one hour, additional VIII (0.5 g.) was placed into the reaction mixture; it was then refluxed for another hour. A large part of the ethanol was evaporated in vacuo, and the residue was allowed to stand overnight. Filtration gave the anil (XII) (0.52 g.) as yellowish brown crystals; m. p. 158∼160°C. The filtrate was evaporated to dryness, and the residue obtained was dissolved in benzene. The benzene solution was chromatographed on alumina to separate XII (0.18 g.) (m. p. 159∼160°C) and the nitrone (XIX) (m. p. 200°C (decomp.)) in a small amount. The combined anil (XII) was recrystallized from ethanol to give yellow scales; m. p. 161.5°C (reported, 163°C[3]). This compound was identical with the authentic substance which had been prepared by the condensation of acridine-9-carboxaldehyde (XXXV) and aniline. (Found: C, 85.15; H, 5.06; N, 9.88%). The recrystallization of the crude nitrone from ethanol afforded yellow prisms; m. p. 227°C (decomp.) (reported, 220°C (decomp.)). (Found: C, 80.04; H, 4.88; N, 9.45%).

Reaction of II with *p*-Nitrosodimethylaniline (IX).—To a solution of II (1.0 g.) and IX (1.6 g.) in ethanol (50 ml.), HA (0.2 ml.) was added. The refluxing of the reaction mixture resulted in the precipitation of reddish brown crystals in several minutes. After having been refluxed for 2 hr., the mixture was allowed to stand overnight. Filtration gave reddish brown crystals (1.39 g.) which, on washing with hot benzene (5ml.×2), left the nitrone (XX) (1.26 g.) (m. p. 240°C (decomp.)). Recrystallization from a large amount of benzene afforded reddish brown prisms; m. p. 243°C (decomp.) (reported, 243°C (decomp.)[3]). (Found: C, 77.90; H, 5.83; N, 12.31%). The benzene washings were evaporated to give a small amount of the anil (XIII) as red crystals which, on recrystallization from ethanol, afforded red prisms; m. p. 248°C (reported, 248°C[3]). (Found: C, 80.98; H, 5.86; N, 13.01%). The ethanol filtrate after reaction was concentrated in vacuo and then cooled to give 0.15 g. of a higher melting compound (XXXIV); m. p. over 300°C. (Found: C, 79.39, 79.29; H, 4.78, 4.71; N, 7.31, 7.71%).

The results of other reactions under varying conditions are shown in Figs. 1 and 2 and Table I.

Reaction of II with *p*-Nitrosodiethylaniline (X).—A solution of II (1.0 g.), X (1.7 g.) and HA (0.03 ml.) in ethanol (50 ml.) was refluxed for 2 hr. After a large part of the ethanol had been evaporated in vacuo, filtration afforded brown crystals (1.2 g.). The crystals were washed with 15 ml. and then with 5 ml. of hot benzene to leave 0.5 g. of the nitrone XXI, which, on recrystallization from ethanol, gave orange prisms (m. p. 207∼208°C (decomp.)) (reported, 208°C (decomp.)[3]). (Found: 77.94; H, 6.30; N, 11.37%). The benzene washings were evaporated to give the anil XIV (0.4 g.), which, on recrystallization from ethanol, afforded dark violet prisms (m. p. 168∼169°C (reported, 165°C[3])). (Found: C, 81.38; H, 6.66; N, 11.90%).

Reaction of II with *p*-Nitrosophenol (XI).—*With HA.*—A solution of II (1.0 g.), XI (1.3 g.) and HA (0.03 ml.) in ethanol (50 ml.) was refluxed for 3 hr. After the mixture had stood overnight, filtration afforded dark brown crystals (1.21 g.); m. p. 265∼269°C. Recrystallization from chlorobenzene gave brown plates; m. p. 274∼275°C. This compound was proved, by the admixed m. p. and by the infrared spectrum, to be identical with the anil (XV) (m. p. 275°C (reported, 225°C (decomp.)[9])) which was obtained from the condensation of the aldehyde XXXV and *p*-aminophenol.

Found: C, 80.20; H, 4.93; N, 9.24. Calcd. for $C_{20}H_{14}ON_2$: C, 80.52; H, 4.73; N, 9.39%.

With Potassium Carbonate.—The similar reaction of II (0.55 g.) with XI (0.7 g.) in the presence of potassium carbonate (40 mg.) in ethanol (30 ml.) gave 0.42 g. of the nitrone (XXII), which, on recrystallization from chlorobenzene, afforded dark yellowish green scales (m. p. 235°C (decomp.)) (reported, 230∼231°C[9]).

Found: C, 75.99; H, 4.65; N, 9.09. Calcd. for $C_{20}H_{14}O_2N_2$: C, 76.42; H, 4.49; N, 8.91%.

Reaction of 2, 9-Dimethylacridine (III) with IX.—A mixture of III (0.5 g.), IX (0.7 g.) and HA (0.02 ml.) in ethanol (50 ml.) was refluxed for 3 hr. and then allowed to stand overnight. Filtration gave crystals which, on being washed with hot benzene (5 ml.×8), left 30 mg. of red crystals; m. p. 217∼219°C (decomp.). Recrystallization from chlorobenzene afforded red prisms of the nitrone (XXIII) (m. p. 220°C (decomp.)) (reported, 224∼225°C[5]).

Found: C, 77.47; H, 5.70; N, 12.04. Calcd. for $C_{23}H_{21}ON_3$: C, 77.72; H, 5.96; N, 11.82%.

The benzene washings were evaporated in vacuo to give red crystals (0.65 g.), which, on recrystallization from benzene, afforded dark red prisms (m. p. 223°C). This compound was identical with the anil XVI obtained by the condensation of aldehyde XXXVI and *p*-dimethylaminoaniline, as will be mentioned below.

Found: C, 81.48; H, 6.53; N, 12.07. Calcd. for $C_{23}H_{21}N_3$: C, 81.39; H, 6.24; N, 12.38%.

In the presence of concentrated aqueous sodium carbonate (4 drops) in place of HA, the same reaction afforded the nitrone (0.19 g.).

2-Methylacridine-9-carboxaldehyde (XXXVI).—A mixture of XXIII (0.5 g.) in 12% aqueous hydrochloric acid (10 ml.) was heated on a water bath for 30 min. After the mixture had cooled, the precipitated crystals were filtrated and washed with aqueous ammonia. Yield, 0.295 g. (94.8%); m. p. 137∼139°C. Recrystallization from the benzene-petroleum benzine mixture gave the aldehyde (XXXVI) as orange needles; m. p. 145°C (reported, 136∼138°C[5]).

Found: C, 81.50; H, 5.23; N, 6.48. Calcd. for $C_{15}H_{11}ON$: C, 81.43; H, 5.01; N, 6.33%.

A mixture of XXXVI (0.1 g.), *p*-dimethylaminoaniline (0.1 g.) and acetic acid (1 drop) in ethanol

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[19] HA used in this experiment: d^{27} 1.1748.

(10 ml.) was refluxed for 2 hr. After the mixture had cooled, filtration afforded 0.14 g. (90.0%) of the anil XVI as dark red prisms (m. p. 223°C).

Reaction of 4, 9-Dimethylacridine (IV) with IX.—The similar treatment of IV (1.0 g.), IX (1.5 g.) and HA (0.03 ml.) in ethanol (50 ml.) gave benzene-soluble dark red crystals (0.61 g.) (m. p. 188~189°C) and benzene-insoluble orange crystals (0.75 g.) (m. p. 204~205°C (decomp.)). The recrystallization of the former from benzene afforded dark red prisms; m. p. 188~189°C. This compound was proved, by the admixed m. p. and infrared spectrum, to be identical with the anil XVII prepared by the condensation of the corresponding aldehyde XXXVIII and *p*-dimethylaminoaniline, as will be described below.

Found: C, 81.48; H, 6.53; N, 12.07. Calcd. for $C_{23}H_{21}N_3$: C, 81.39; H, 6.24; N, 12.38%.

The latter was recrystallized from chlorobenzene to afford orange plates (m. p. 207~208°C (decomp.)), whose infrared spectrum and elemental analyses showed the nitrone XXIV.

Found: C, 77.73; H, 5.99; N, 11.81. Calcd. for $C_{23}H_{21}ON_3$: C, 77.72; H, 5.96; N, 11.82%.

The reaction of IV (0.5 g.) with IX (0.75 g.) in the presence of concentrated aqueous sodium carbonate (4 drops) in ethanol (25 ml.) afforded 0.13 g. of the nitrone XXIV (m. p. 207~208°C (decomp.)).

4-Methylacridine-9-carboxaldehyde (XXXVIII).—The hydrolysis of 0.5 g. of the mixture of the anil XVII and nitrone XXIV obtained above with 12% aqueous hydrochloric acid (10 ml.) afforded the aldehyde XXXVIII (0.27 g.) (m. p. 112~113°C), which, on recrystallization from petroleum benzine, gave yellow needles (m. p. 114°C).

Found: C, 81.51; H, 5.34; N, 6.55. Calcd. for $C_{15}H_{11}ON$: C, 81.43; H, 5.01; N, 6.33%.

The anil XVII (m. p. 189°C) was quantitatively obtained by a condensation of the aldehyde XXXVIII and *p*-dimethylaminoaniline similar to that in the case of XXXVII.

Reaction of 2-Chloro-9-methylacridine (V) with IX.—A mixture of V (1.0 g.), IX (1.32 g.) and HA (0.03 ml.) in ethanol (50 ml.) was refluxed for 3 hr. After the mixture had stood overnight, the obtained crystals were dissolved in hot chlorobenzene (100 ml.). After they had cooled, filtration gave orange scales (0.62 g.) (m. p. 230°C (decomp.)), which, on recrystallization from chlorobenzene, showed a m. p. of 235°C (decomp.). This compound was confirmed as the nitrone XXV from the infrared spectrum and elemental analyses.

Found: C, 70.25; H, 5.14; N, 11.25. Calcd. for $C_{22}H_{18}ON_3Cl$: C, 70.30; H, 4.83; N, 11.18%.

The filtrate was evaporated in vacuo to give dark red crystals (0.86 g.), which, on recrystallization from chlorobenzene, showed a m. p. of 207~208°C. This compound was identical with the anil XVIII prepared from the corresponding aldehyde XXXIX and *p*-dimethylaminoaniline.

Found: C, 73.35; H, 5.23; N, 11.49. Calcd. for $C_{22}H_{18}N_3Cl$: C, 73.43; H, 5.04; N, 11.68.

The similar reaction of V (0.5 g.) with IX (0.66 g.) in the presence of concentrated aqueous sodium carbonate (4 drops) afforded the anil (0.34 g.) (m. p. 202~204°C), and a small amount of the nitrone.

2-Chloroacridine-9-carboxaldehyde (XXXIX).—The hydrolysis of 0.5 g. of the above mixture of the anil and nitrone with 12% aqueous hydrochloric acid gave 0.31 g. of the aldehyde XXXIX (m. p. 162~163°C), which, on recrystallization from petroleum benzine, afforded yellow needles (m. p. 169°C).

Found: C, 69.72; H, 3.35; N, 5.88. Calcd. for $C_{14}H_8ONCl$: C, 69.58; H, 3.34; N, 5.80%.

The condensation of XXXIX and *p*-dimethylaminoaniline similar to that in the case of XXXVII afforded the anil XVIII (m. p. 209°C) quantitatively.

Reaction of 7-Methylbenz[c]acridine (VI) with Nitroso Compound.—*With IX.*—To a solution of VI (2.0 g.) and IX (2.5 g.) in ethanol (70 ml.), HA (2 drops) was added, and the mixture was refluxed for 3 hr. After the mixture had stood overnight, filtration gave yellowish brown crystals (0.47 g.) (m. p. 220~228°C (decomp.)), which, on recrystallization from benzene, afforded the nitrone XXVIII as orange prisms (m. p. 240°C (decomp.)) (reported, 236~237°C (decomp.)[4]). (Found: C, 79.68; H, 5.40; N, 10.56%). The filtrate was evaporated to give a resinous material, which was then dissolved in benzene. The benzene solution was chromatogaphed on alumina to separate unreacted VI (0.79 g.) and red crystals (0.48 g.) (m. p. 188~197°C). The latter was recrystallized from benzene to give the anil XXVI as red prisms (m. p. 214~215°C).

Found: C, 83.24; H, 5.88; N, 11.24. Calcd. for $C_{26}H_{21}N_3$: C, 83.17; H, 5.64; N, 11.19%.

With X.—The similar treatment of VI (1.0 g.) with X (1.25 g.) in the presence of HA (1 drop) in ethanol (50 ml.) afforded unchanged VI and red crystals (0.61 g.) (m. p. 156~160°C), which, on recrystallization from ethanol, showed a m. p. of 167~168°C and appeared as red prisms. This red compound was proved to be the anil XXVII by its elemental analyses and infrared spectrum.

Found: C, 83.11; H, 6.23; N, 10.36. Calcd. for $C_{28}H_{25}N_3$: C, 83.34; H, 6.22; N, 10.41%.

Reaction of 12-Methylbenz[a]acridine (VII) with a Nitroso Compound.—*With IX.*—A solution of VII (1.0 g.) and IX (1.24 g.) in a mixture of ethanol (50 ml.) and HA (1 drop) was refluxed for 1 hr. After the mixture had cooled, filtration gave yellow needles (1.33 g.) (m. p. 234°C (decomp.)), which, on recrystallization from *o*-dichlorobenzene, showed a m. p. of 235°C (decomp.). This compound was proved to be the nitrone XXXII by its elemental analytical values and infrared spectrum.

Found: C, 79.62; H, 5.70; N, 10.75. Calcd. for $C_{26}H_{21}ON_3$: C, 79.77; H, 5.41; N, 10.73%.

The filtrate was then evaporated, and the residue was dissolved in benzene. The benzene solution was chromatographed on alumina to afford red prisms (m. p. 168~169°C) in a small amount. This compound was proved to be the anil XXX by its elemental analyses and infrared spectrum.

Found: C, 83.09; H, 5.60; N, 11.23. Calcd. for $C_{26}H_{21}N_3$: C, 83.17; H, 5.67; N, 11.19%.

With X.—A mixture of VII (1.0 g.), X (1.25 g.) and HA (1 drop) in ethanol (50 ml.) was heated under reflux for 1 hr. After the reaction mixture had been concentrated in vacuo, filtration afforded yellow crystals (1.12 g.) (m. p. 204~205°C (decomp.)), which, on recrystallization from ethanol, gave yellow needles (m. p. 208~209°C (decomp.)). This compound was the nitrone XXXIII.

Found: C, 79.93; H, 5.89; N, 10.26. Calcd. for $C_{28}H_{25}ON_3$: C, 80.14; H, 6.00; N, 10.02%.

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