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8. Hideyo Shindo : Studies on the Infrared Spectra of Heterocyclic Compounds. VIII.[1] Infrared Spectra of Substituted Pyrazines and their N-Oxides.

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In the previous papers of this series, the infrared spectra of substituted pyridines[2,3] and their N-oxides[1,4,5] were correlated to their structures in many respects, and the characteristics of the ring nitrogen and the N-oxide group in the infrared spectra were established and discussed. It is now of interest to see how these correlations in the pyridine ring system can be extended to the diazine ring system which contains an additional ring nitrogen.

The infrared spectra of pyrazine and pyrimidine have been analysed by Lord, *et al.*,[6] but systematic investigations have not been made on their derivatives. Some simple diazine N-oxides have been studied recently by Koelsch, *et al.*,[7] but detailed discussion has not been given concerning their infrared spectra. The infrared spectra of pyrimidine N-oxide and some methyl derivatives have been studied by Wiley, *et al.*[8]

In the present study, the infrared spectra of pyrazine and its eight monosubstituted derivatives and its ten N-oxide derivatives were determined and were found to be correlated to the structures on the basis of correlations found in pyridine and pyridine N-oxide derivatives. At the same time, comparing with these results, the infrared spectra of pyrimidine N-oxide and its eight derivatives were also examined. Some of the spectra obtained are shown in Fig. 1.

I. N-O Stretching Frequencies

It has been well established[1,4,5] that the N-O stretching frequency in substituted pyridine N-oxides appeared as a strong absorption in the region of 1190 and 1320 cm^{-1}. As can be seen from Fig. 1, all of the pyrazine N-oxides examined showed strong absorption in the range of 1260~1350 cm^{-1} which was absent in the spectrum of the corresponding pyrazine, and these were assigned to their N-O stretching frequencies. The observed frequencies are listed in Table I. Pyrazine mono-N-oxide exhibited its N-O frequency at 1318 cm^{-1} in carbon disulfide, which is 54 cm^{-1} higher than that of pyridine N-oxide, and it is considered that the strongly electronegative effect of the additional ring nitrogen at the *para*-position increases the contribution of the ionic structure (IIa) in the resonance system of pyrazine N-oxide (I~III), and the resultant increase in double-bond character of the N-O bond causes the displacement of its stretching frequency to a higher frequency. Furthermore, the contribution of these resonance structures should be affected by the electronic effect of the ring substituent and actually, as shown in Table I, it was found that the absorption frequency shifted to a higher frequency by the electron-withdrawing substituent such as cyano group, but to a lower frequency by the electron-donating group such as the methyl, in entirely the same way

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1) Part VIII. H. Shindo : This Bulletin, **7**, 791(1959).
2) H. Shindo, N. Ikekawa : *Ibid.*, **4**, 192(1956).
3) H. Shindo : *Ibid.*, **5**, 472(1957).
4) *Idem.* : *Ibid.*, **4**, 460(1956).
5) *Idem.* : *Ibid.*, **6**, 117(1958).
6) R. C. Lord, A. L. Marston, F. A. Miller : Spectrochim. Acta, **9**, 113(1957).
7) C. F. Koelsch, W. H. Gumprecht : J. Org. Chem., **23**, 1603(1958).
8) R. H. Wiely, S. C. Slaymaker : J. Am. Chem. Soc., **79**, 2233(1957).

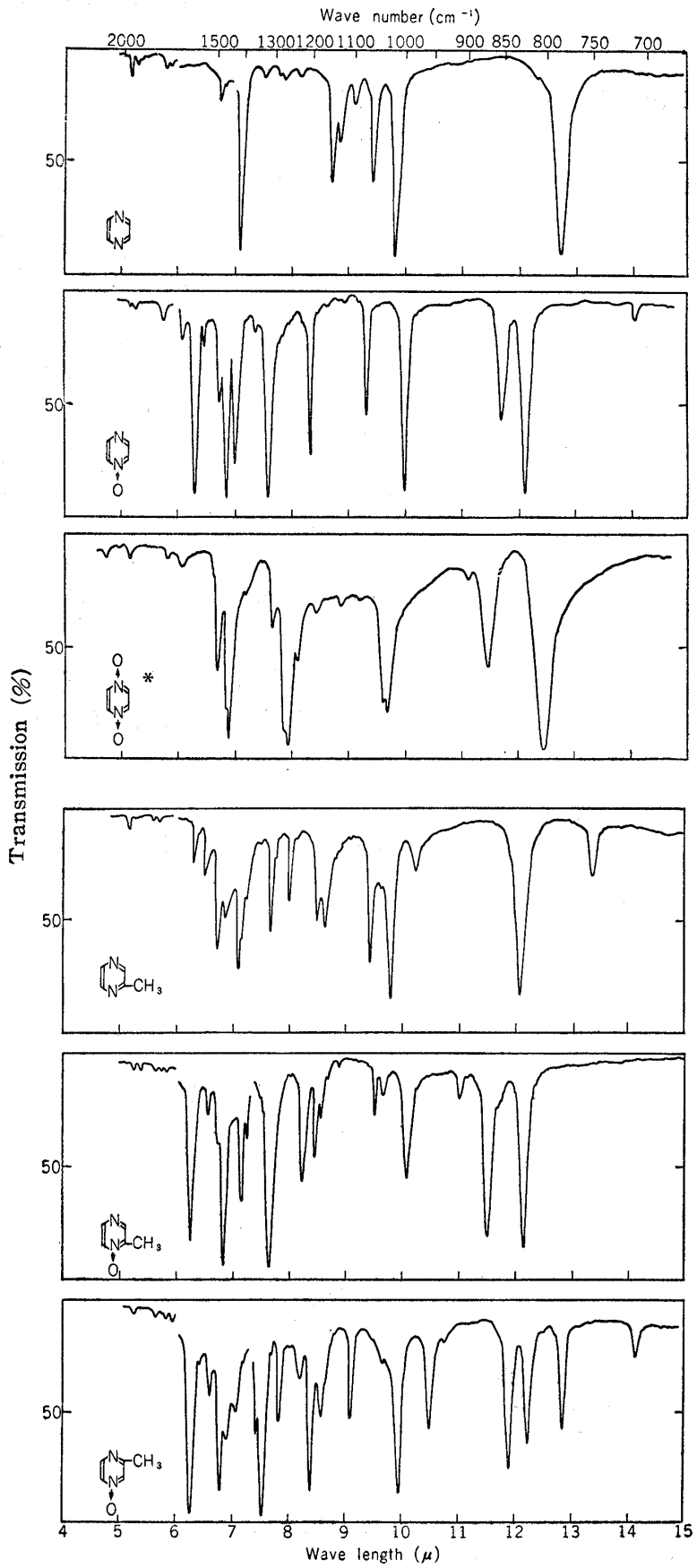


Fig. 1.

Infrared Absorption Spectra of Some Pyrazines and their N-Oxides (1)

(in CS_2 (650~2000 cm^{-1}) and in CCl_4 or $CHCl_3$ (1400~1700 cm^{-1}) solution, * in Nujol mull)

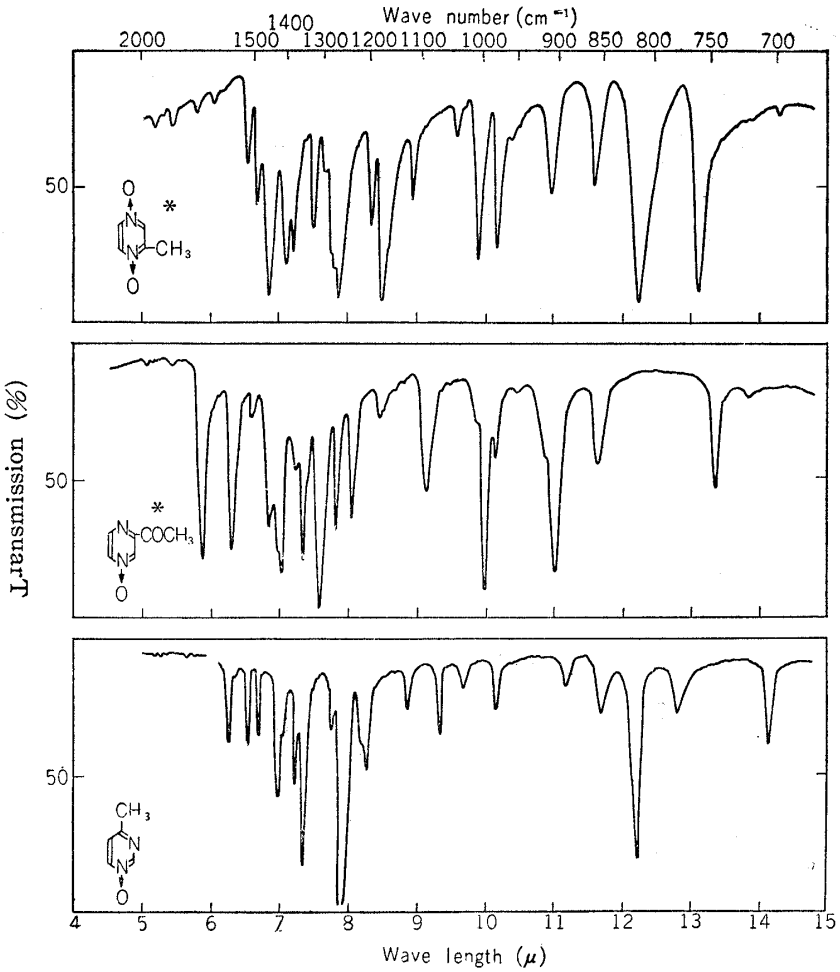
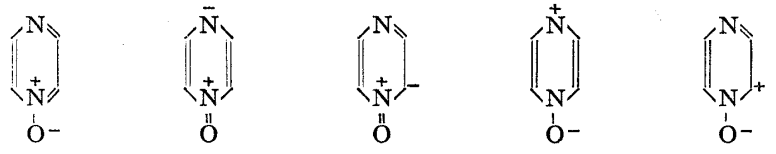


Fig. 1. Infrared Absorption Spectra of Some Pyrazines and their N-oxides (2)

TABLE I. N-O Stretching Frequencies of Substituted Pyrazine N-Oxides

No.	Compound	σ-value[a]	ν_{N-O} (cm^{-1}) in CS_2[b]	ν_{N-O} (cm^{-1}) Solid
1	3-Cyanopyrazine 1-oxide	1.608	1345 vs	1332 s (1306 vs)
2	3-Ethoxycarbonylpyrazine 1-oxide	1.328	1333 vs	1328 vs
3	3-Chloropyrazine 1-oxide	1.303	1334 vs (1316 sh)	1325 s (1334 sh)
4	3-Acetylpyrazine 1-oxide	1.236	1333 vs	1321 vs
5	3-Carboxyaminopyrazine 1-oxide	1.210	c)	1309 s
6	Pyrazine 1-oxide	0.93	1318 vs (1346 sh)	1312 vs
7	3-Methylpyrazine 1-oxide	0.861	1330 vs (1305 sh)	d)
8	2-Methylpyrazine 1-oxide	0.760	1310 vs	1289 vs
9	Pyrazine 1,4-dioxide	0.25	c)	1259 vs
10	Methylpyrazine 1,4-dioxide	{0.08 {0.181	c)	1268 vs 1277 sh

a) Calculated on adding 0.93 and 0.25 for mono- and di-N-oxide, respectively.
b) ca. 0.3% or saturated solution, cell thickness : 1.0 or 5.0 mm.
c) Insoluble in CS_2.
d) Very hygroscopic.



(I) (IIa) (IIb) (IIIa) (IIIb)

as that in substituted pyridine N-oxides.

It has been shown[5] that the N-O stretching frequency of substituted pyridine N-oxides has a linear relation against the σ-values of the substituents. Assuming that the value calculated on adding 0.93, the σ-value of the ring nitrogen toward 4-position of pyridine,[3] to the σ-value[9] of the substituent to be a measure of the electronic effect toward the N-oxide function in substituted pyrazine N-oxides (e.g. for 3-chloropyrazine 1-oxide : 0.373+0.93=1.303), the N-O frequencies of substituted pyrazine N-oxides in carbon disulfide solution were plotted against the σ-values calculated in this way. As shown in Fig. 2-A, it should be clearly noted that all these points gave a reasonable linear plot on the straight line extending from the linear relation in the N-O frequencies of substituted pyridine N-oxides. This result indicates that the electron-withdrawing effect of an additional ring nitrogen gives a constant influence upon the bond character of the N-oxide group entirely additively to the effect of the substituent, and also gives a confirmation on the validity of the value of 0.93 as the σ-value of the ring nitrogen toward 4-position of pyridine.

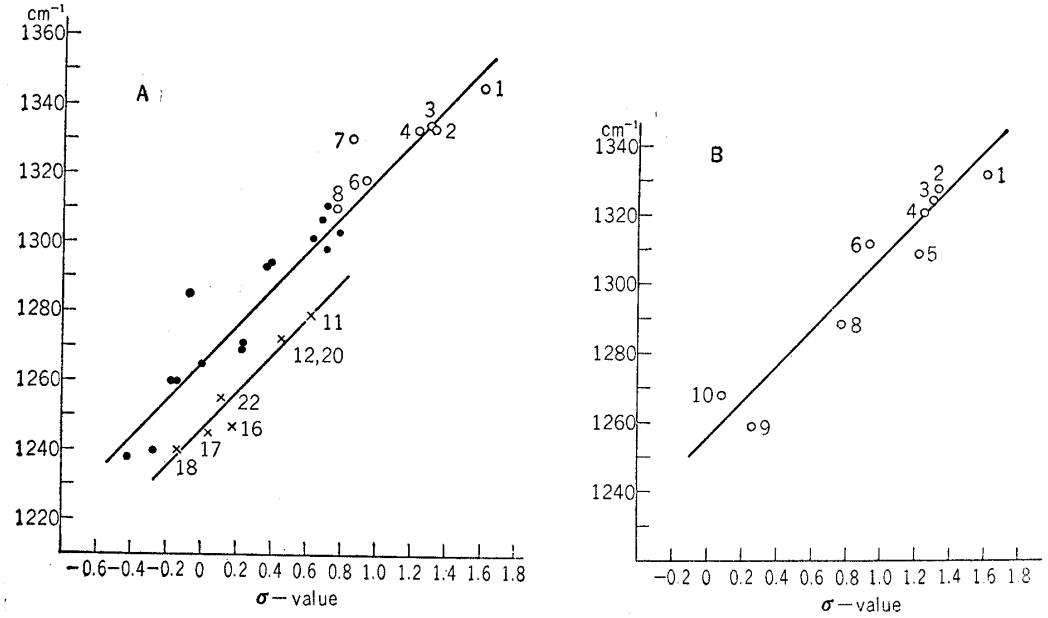


Fig. 2. The Linear Relationship between the N-O Stretching Frequencies and Hammett's Substituent Constant of the Substituent

● Substituted pyridine N-oxides
O Substituted pyrazine N-oxides
× Substituted pyrimidine N-oxides
A Dilute CS_2 solution
B Nujol mull

* Number beside the plot indicates No. of the compound in Tables I and III.

N-Oxidation of methylpyrazine gave two isomeric mono-N-oxides[10] of m.p. 89~91° and 65~67°, showing their N-O frequencies at 1311 and 1330 cm^{-1}, respectively. It was shown in substituted pyridine N-oxides[4,5] that the methyl group at α- and γ-positions causes an appreciable shift of the N-O frequency to a lower frequency, while that at β-position has a characteristic of causing a considerable higher frequency shift. According to these characteristics, the substance of m.p. 65~67°, which absorbs at a higher frequency than that of pyrazine N-oxide, should be 3-methylpyrazine 1-oxide, while the

9) H. H. Jaffe : Chem. Revs., **53**, 191(1953).
10) M. Asai : Yakugaku Zasshi, **79**, 1273 (1959).

substance of m.p. 89~91°, which absorbs at a lower frequency than that of pyrazine N-oxide, should be 2-methylpyrazine 1-oxide. The relationship between these frequencies as well as those in methyl pyridine and pyrimidine N-oxides is shown in Table II. It is clear that the phenomenon of higher frequency shift is entirely specific to the methyl group at β-position with respect to the N-oxide group.

Table II. Characteristic Effect of β-Methyl Group on the N-O Stretching Frequency

Compound	ν_{N-O} (cm^{-1}) in CS_2 or CCl_4	$\Delta\nu$ (cm^{-1})
Pyridine 1-oxide	1265	
4(or 2)-Methylpyridine 1-oxide	1260	− 5
3-Methylpyridine 1-oxide	1285	+20
Pyrimidine 1-oxide	1279	
4(or 2)-Methylpyrimidine 1-oxide	1272	− 7
5-Methylpyrimidine 1-oxide	1300	+21
Pyrazine 1-oxide	1318	
2-Methylpyrazine 1-oxide (m.p. 89~90°)	1311	− 7
3-Methylpyrazine 1-oxide (m.p. 67~69°)	1330	+12

In Fig. 2 the N-O frequency of 2-methyl derivative gave a fairly linear plot against the value calculated by using the σ-value for *p*-methyl group, this being reasonable since[5] α-methyl group had just the same effect on the N-O frequency of pyridine N-oxide as that of γ-methyl group. The N-O frequency of 3-methyl derivative showed a considerable deviation to a higher frequency and this behavior is just the same as that shown by 3-methylpyridine 1-oxide.[5]

In the case of pyridine N-oxides, the N-O frequencies of acetyl and ethoxycarbonyl derivatives showed considerable deviation from the linear relation and this was attributed to the vibrational interaction between the N-O frequency and the band near 1250 cm^{-1} due to the substituent.[5] In the case of pyrazine N-oxides, however, all these carbonyl derivatives gave fairly linear plots and it is assumed that the large shift of the N-O frequency to a higher frequency region resulted in sufficient separation of the two bands and the N-O frequency appeared as an almost pure N-O stretching mode.

In the derivatives with an electron-withdrawing substituent, the N-oxidation is expected to proceed at the nitrogen in β-position with respect to the substituent. This was also supported by the fact that their N-O frequencies gave reasonable linear plots against the σ-values for the *meta*-substituents.

In solid state, the absorption always appeared at a somewhat lower frequency than that in carbon disulfide solution and the observed frequencies (Table I) were found to have a reasonably linear relationship against the σ-values calculated in the same way on adding 0.93, as shown in Fig. 2-B.

Two di-N-oxides examined, which were insoluble in carbon disulfide, showed their N-O frequencies in the solid state at a considerably lower frequency than that of the corresponding mono-N-oxide and this fact indicates that the electron-withdrawing effect of the ring N-oxide group toward *para*-position of the ring is considerably weaker than that of the ring nitrogen. As shown in Fig. 2-B, the N-O frequency of pyrazine 1,4-dioxide gave a fairly linear plot when it was plotted against the value of 0.25, the σ-value of the N-oxide group for 4-position of pyridine.[5] The plot of the N-O frequency of methyl derivative using the value of 0.25 was also reasonable. This result confirms the general validity of the value of 0.25 as the σ-value of the N-oxide group for 4-position of pyridine,[5] because two N-oxide groups in pyrazine 1,4-dioxide are considered to exert their electronic effect in the most normal way upon each other.

From the foregoing results, it may be concluded that the electronic effects of the ring nitrogen, ring N-oxide group, and the ring substituents appear as a constant mag-

nitude of shift in the N-O stretching frequencies of substituted pyrazine N-oxides in entirely the same way and additively as those in substituted pyridines and their N-oxides.

On the other hand, the infrared spectra of pyrimidine N-oxide and its eight derivatives, mainly methyl and alkoxyl derivatives, were also determined. All N-oxide compounds examined showed a strong absorption in the region of 1230 and 1280 cm^{-1}, and these were assigned to their N-O stretching frequencies as listed in Table III. Alkoxyl derivatives usually showed three or four strong absorptions in the region of 1150 and 1400 cm^{-1}, including the absorptions due to alkoxyl group, but only the band around 1245 cm^{-1} which is usually the strongest showed a prominent shift to a lower frequency on adding a trace of methanol.[1)]

Table III. N-O Stretching Frequencies of Substituted Pyrimidine N-Oxides

No.	Compound	σ-value[a)]	ν_{N-O} (cm^{-1}) in CS_2[b)]	ν_{N-O} (cm^{-1}) Solid
11	Pyrimidine 1-oxide	0.62	1279 vs	1256 vs
12	4-Methyl-	0.45	1272 vs (1258 sh)	1244 s (1221 s)
13	4-Phenylthio-6-methyl-		1257 vs	1247 vs
14	4-Phenoxy-6-methyl-		1246 s (1200 vs)	1237 s (1206 s)
15	4-Ethoxy-6-methyl-		1244 vs	1241 vs
16	4-Methoxy-6-methyl-	0.182	1247 vs	1245 vs
17	4-Benzyloxy-6-methyl-	0.034	1245 vs	1242 vs
18	2,6-Dimethyl-4-benzyloxy-	−0.136	1240 vs	1231 vs
19	4-Morpholino-6-methyl-		1236 vs	1225 vs (1203 s)
20	2-Methyl-[c)]	0.45	1272 s	—
21	5-Methyl-[c)]	0.551	1300 s	—
22	2,4,6-Trimethyl-[c)]	0.11	1255 vs	—

a) Calculated on adding 0.62. The σ-value for p-CH_3 was used as that for α-CH_3.
b) ca. 0.3% or saturated solution; cell thickness, 1.0 mm.
c) R.H. Wiley, *et al.*[8)]

Pyrimidine N-oxide exhibited its N-O frequency at 1279 cm^{-1} in carbon disulfide which is 14 cm^{-1} higher than that of pyridine N-oxide, reflecting the electronegative effect of an additional ring nitrogen in *meta*-position. This frequency, however, did not give a linear plot against the value of 0.62, the σ-value of the ring nitrogen toward 3-position of pyridine,[3)] but gave a plot at the frequency about 20 cm^{-1} lower than that expected from the linear relation in substituted pyridine N-oxides.

It can be noted from Table III, however, that the electronic effect of a substituent affects the N-O frequency in entirely the same way as that in substituted pyridine N-oxides. The introduction of a methyl group at α- or γ-position with respect to the N-oxide group caused a shift of 5~8 cm^{-1} to a lower frequency additively; and 4- and 2-methyl, and 2,4,6-trimethyl[8)] derivatives showed a respective shift of 7 and 24 cm^{-1} to a lower frequency than that of pyrimidine N-oxide, and 2,6-dimethyl-4-benzyloxy derivative showed a shift of 5 cm^{-1} to a frequency lower than that of 6-methyl-4-benzyloxy derivative. On the other hand, 5-methylpyrimidine 1-oxide in which the methyl group is at β-position with respect to the N-oxide group showed a shift of 21 cm^{-1} to a higher frequency than that of pyrimidine N-oxide, as already shown in Table II. In 4-substituted 6-methyl derivatives, the N-O frequency shifted to a lower frequency in the following order, the degree of shift depending upon the nature of the 4-substituent: $-S-C_6H_5 >$ $-O-Alkyl > -\overset{\diagup\diagdown}{N}\underset{\diagdown\diagup}{O}$. This order is in accordance with that of increasing electron-donating power of the substituent.

In Fig. 2-A is shown some of these frequencies plotted against the σ-values which were calculated in the same way as that in substituted pyrazine N-oxides using the

value of 0.62 for an additional *meta* ring-nitrogen and the σ-value of *p*-methyl group for an α-methyl group. It should be clearly noted that these points lie close to a straight line which is parallel to that in the N-O frequencies of substituted pyridine N-oxides at about 20 cm^{-1} lower frequency side. This result indicates that the *meta* ring-nitrogen also exerts a constant electronic effect upon the N-O stretching frequency additively to that of the substituent, although this effect is somewhat weaker than that shown in pyridine ring, probably due to interaction with the N-oxide function.

In any way, these correlations permit the approximate position of the N-O stretching frequencies of the substituted diazine N-oxides to be predicted from considerations of the position and electronic effect of the substituents.

II. Ring CH Out-of-plane Bending Frequencies

It was previously shown[2~5] that the ring CH out-of-plane bending frequencies of substituted pyridines and their N-oxides were interpreted by considering the number of adjacent free hydrogen atoms on the ring, in the same way as that in substituted benzene derivatives. This correlation rule seems to hold also for the diazine ring system, and all mono-substituted pyrazines and their N-oxides examined showed an absorption, usually strong, in the region of 800~860 cm^{-1}, corresponding to the two adjacent free hydrogen atoms on the ring, as shown in Table IV. Most of the N-oxide compounds showed an additional absorption of medium strength in the region of 810~870 cm^{-1}, which is considered to be also a characteristic for the N-oxide derivatives.[5,8]

Pyrazine itself exhibited this absorption at an abnormally lower frequency than would be expected, being lower than that of pyrimidine which possesses three adjacent

Table IV. Ring CH Out-of-plane Bending Frequencies of Substituted Pyrazines and their N-Oxides (cm^{-1})

Compound	δ_{CH} (out-of-plane)	$\Delta\nu$[a]	Other prominent bands in 700~900 cm^{-1} region		
Pyrazine	784 vs				
Aminopyrazine*	814 ms				
Methylpyrazine	824 s			746 w	
Chloropyrazine	839 s			762 s	742 w
Acetylpyrazine	846 s			753 m	
Cyanopyrazine	851 s			748 m	
Ethoxycarbonylpyrazine	860 m			734 m	
Pyrazinecarbonamide*	869 s			787 s	
Pyrazinecarboxylic acid*	889 m		822 s	789 m	710 s
Pyrazine 1-oxide	826 s	+42	856 m		
	838 s*		862 m		
Pyrazine 1,4-dioxide*	803 vs		875 m		
2-Methylpyrazine 1-oxide	824 s	0	869 m		
3-Methylpyrazine 1-oxide	819 s	− 5	842 s	779 s	
Methylpyrazine 1,4-dioxide	814 vs		859 m	760 s	
3-Chloropyrazine 1-oxide	835 s	− 4	818 m	738 m	
	854 s*			735 s	
3-Cyanopyrazine 1-oxide	828 m	−23		758 s	
3-Acetylpyrazine 1-oxide	827 m	−19		748 m	
	859 m*			749 m	
3-Ethoxycarbonylpyrazine 1-oxide	832 s	−28	860 m	788 s	
Pyrimidine**	812 m				720 vs
4-Methylpyrimidine	824 s				744 s
Pyrimidine 1-oxide	802 s	−10	843 m		682 s
	820 s*		844 s		685 s
4-Methylpyrimidine 1-oxide	821 s	− 3	853 m		708 m
	843 s*		859 s		717 m

* Nujol mull ** Liquid film, others in CS_2 solution.

a) Frequency differences between the N-oxide and the parent base in the same state.

free hydrogens. Pyrimidine was normal in showing a rather weak band at 812 cm^{-1} and a much stronger band at 720 cm^{-1}, corresponding to the β-substituted pyridine.[3]

The precise positions of these frequencies in substituted pyrazines have a distinct relationship with the nature of a substituent and, as can be seen from Table IV, the frequency shifted to a higher frequency as the electron-withdrawing nature of the substituent increases. According to the view of Kross, *et al.*,[11] this can be explained by the terms of depletion of the ring π-electron density due to electron attraction of the substituent from the ring. However, the fact that the introduction of two strongly electronegative ring nitrogens does not cause any notable displacement of the overall absorption range to a higher frequency as compared to those of the corresponding substitution type in benzenoid compounds cannot be explained on this basis. At any rate, it is of interest to note that this fact permits easy interpretation of the ring CH out-of-plane bending frequencies in N-heteroaromatic compounds.

In the N-oxide compounds, the relationship to the nature of a substituent was not so clear, but a distinct regularity was shown in the direction of the shift of these frequencies from those of the corresponding bases, in the same way as that observed in substituted pyridine N-oxides.[5] It was previously shown that 4-substituted pyridine 1-oxides always showed this absorption at a higher frequency than that of the corresponding pyridine, while 3-substituted derivatives always showed it at a lower frequency. In accordance with this correlation, pyrazine N-oxide showed this absorption at a higher frequency than that of pyrazine and pyrimidine N-oxide at a lower frequency than that of pyrimidine, as shown in Table IV. All mono-substituted pyrazine N-oxides showed a regular shift of this frequency to a lower frequency than those of the corresponding pyrazines and this is considered to be characteristic for this type of substitution, probably corresponding to 3,4-disubstituted pyridine 1-oxides.

It may be concluded that the correlation rules found in ring CH out-of-plane bending frequencies of benzene and pyridine ring systems also hold good for the diazine ring system only by consideration of the type of substitutions.

III. Ring CH In-plane Bending and Ring Vibrations

Aromatic compounds generally show a series of characteristic absorptions in the region of 1000~1600 cm^{-1} due to the ring CH in-plane bending and the ring vibrations, and these absorptions also appear at the comparable positions in N-heteroaromatic compounds.[6,12]

The characteristic pairs of absorptions in the region of 1400~1600 cm^{-1} were also found in substituted pyrazines and their N-oxides as shown in Table V, due to the stretching vibration of ring double bonds. It was shown in substituted pyridines and their N-oxides[2~5] that the relative intensity of the two bands between 1500 and 1600 cm^{-1} had a regular correlation with the position and the nature of a substituent, and the N-oxide compounds showed an entirely reverse behavior in the intensity patterns as compared to those of the corresponding pyridines. A similar phenomenon is also apparent in Table V, and pyrazine and most substituted pyrazines did not show any strong absorption in this region, while all of their mono-N-oxides showed a very strong absorption near 1590 cm^{-1} and a weaker one at the lower frequency side. On the other hand, their di-N-oxides again seems not to show any strong absorption in this region. These behaviors cannot be explained easily, but it is clear that the intensity of these absorptions is closely related to the type of π-electron distribution on the ring as previously discussed.[2~5,13]

11) R. D. Kross, V. A. Fassel, M. Margoshes : J. Am. Chem. Soc., 78, 1332(1956).
12) cf. F. A. Andersen, B. Bak, S. Brodersen, J. R. Andersen : J. Chem. Phys., 23, 1047(1955).

Table V. Ring and Ring CH Vibrations of Mono-substituted Pyrazines and their N-Oxides in the Region of 1000~1600 cm^{-1}

I. Substituted pyrazines

No.	Substituent	near 1580 cm^{-1}	near 1530 cm^{-1}	near 1480 cm^{-1}	near 1400 cm^{-1}	
1	H*			1488 w	1414 vs	
2	CH_3*	1582 w	1529 m	1479 w	1403 s	1299 ms, 1248 m
3	NH_2	1590 s	1535 s	1488 m	1430 s	1318 ms, 1236 m
4	Cl*	1560 vw	1522 m	1462 ms	1387 s	1284 ms
5	CN*			1464 s	1401 vs	1290 m, 1222 m
6	$COCH_3$*	1575 m		1473 w	1370 m	1281 s
7	$COOC_2H_5$*	1575 w		1473 m	1370 m	1277 ms
8	$CONH_2$	1585 s	1530 m	1485 m	1379 vs	

No.	Substituent	near 1170 cm^{-1}	near 1100 cm^{-1}	near 1050 cm^{-1}	near 1020 cm^{-1}
1	H*	1150 ms	1130 m	1063 ms	1018 vs
2	CH_3*	1175 ms	1155 ms	1057 s	1019 s
3	NH_2	1175 ms		1059 m	1005 s
4	Cl*	1175 w	1133 vs	1048 ms	1009 s
5	CN*	1176 m, 1160 ms	1148 ms	1047 ms	1013 s
6	$COCH_3$*	1168 ms	1099 s	1045 ms	1018 s
7	$COOC_2H_5$*	1167 ms		1049 m	1017 s
8	$CONH_2$	1181 s, 1164 s	1087 ms	1054 s	1025 s

II. Substituted pyrazine 1-oxides

No.	Substituent	near 1580 cm^{-1}	near 1530 cm^{-1}	near 1480 cm^{-1}	near 1400 cm^{-1}	
9	H	1597 s	1546 w	1473 vs	1437 s	1212 ms
10	2-CH_3	1600 s	1527 m	1462 vs	1401, 1387 s	1227 ms
11	3-CH_3*	1595 vs	1553 w	1473 s		1276 m
12	3-Cl	1589 s	1546 vw	1504 m	1449, 1412 s	1273 s
13	3-$COCH_3$	1585 s	1514 w		1425 s	1278 m, 1242 m
14	3-$COOC_2H_5$	1599 s	1513 w	1466 s	1370 s	1294 s
15	3-$CONH_2$	1597 s	1513 m		1387 s	1269 s

No.	Substituent	near 1170 cm^{-1}	near 1100 cm^{-1}	near 1050 cm^{-1}	near 1020 cm^{-1}
9	H	1168 w	1076 m		1005 vs
10	2-CH_3	1187 m	1065 m		997 s
11	3-CH_3*	1193 s, 1166 m	1100 m		1007 vs
12	3-Cl	1178 m	1104 s		1001 s
13	3-$COCH_3$	1180 m	1095 m		1003 vs
14	3-$COOC_2H_5$	1183 w			999 vs
15	3-$CONH_2$	1183 m	1085 s		1007 vs

III. Substituted pyrazine 1,4-dioxides

No.	Substituent	near 1580 cm^{-1}	near 1530 cm^{-1}	near 1480 cm^{-1}	near 1400 cm^{-1}	
16	H			1490 ms	1447 vs	1233 m
17	CH_3		1521 m	1488 ms	1451 vs	

No.	Substituent	near 1170 cm^{-1}	near 1100 cm^{-1}	near 1050 cm^{-1}	near 1020 cm^{-1}
16	H	1185 w		1040 sh	1031 s
17	CH_3	1196 m, 1172 vs	1115 m	1041 w	1007 s

vs, very strong; s, strong; ms, medium strong; m, medium; w, weak; vw, very weak.
* in CCl_4 (1400~1700 cm^{-1}) and CS_2 (1000~1400 cm^{-1}) solution, others as Nujol mull.

It was previously shown that a series of weak absorptions in the region of 1000~1200 cm^{-1} shown by substituted pyridines were very characteristic for the type of substitution.[3] Mono-substituted pyrazines showed a very strong band in the region of 1010~1030 cm^{-1} and a considerably strong band in the region of 1040~1060 cm^{-1}, which are considered to be characteristic for this type of derivatives. Their N-oxides always showed a strong band in the region of 1000~1030 cm^{-1}. The band around 1000 cm^{-1} can

13) This point was interpreted more theoretically recently by Katritzky (A. R. Katritzky : J. Chem. Soc., **1958**, 4162).

be assigned to the totally symmetric ring vibration (ν_1 vibration in benzene), and it can be noted that this absorption appears in the narrow range of 990~1040 cm^{-1} through substituted pyridines and their N-oxides, and substituted pyrazines and their N-oxides. Other absorptions shown in Table V are assumed to be mainly due to the ring CH in-plane bending vibrations.

IV. Carbonyl Stretching Frequencies

In the previous papers,[3,5] it was shown that the electronic effect of the ring nitrogen and N-oxide group appeared regularly as a constant frequency shift in the characteristic vibration of a substituent, and the σ-values for the ring nitrogen and the N-oxide group toward each position of pyridine could be deduced. In the pyrazine ring, it is expected that the electronegative effect of an additional ring nitrogen causes further shift in the characteristic frequency of the substituent. As shown in Table VI, the

Table VI. Carbonyl Stretching Frequencies of Substituted Pyrazines and their N-Oxides

Compound	$\nu_{C=O}$ (cm^{-1} in CS_2)	$\Delta\nu$ (cm^{-1})
3-Acetylpyridine	1697	
Acetylpyrazine	1708	+11
3-Acetylpyridine 1-oxide	1706	
3-Acetylpyrazine 1-oxide	1714	+ 8
Ethyl nicotinate	1730	
Ethoxycarbonylpyrazine	1726, 1756 (1741)*	+11
Ethyl nicotinate 1-oxide	1737	
3-Ethoxycarbonylpyrazine 1-oxide	1732, 1764 (1748)*	+11

* mean frequency of the two.

carbonyl stretching frequencies of acetyl and ethoxycarbonyl derivatives showed approximately a constant shift of 8~11 cm^{-1} to a higher frequency than those of the corresponding 3-substituted pyridines and their N-oxides, indicating that the additional ring nitrogen exerts a constant electron-withdrawing effect toward the α-position in an entirely additive way. The carbonyl absorption of the ester group showed splitting into two fine peaks, but their mean frequency showed a reasonable shift which was parallel to that of acetyl carbonyl frequency, as in the case of ethyl picolinate.[3]

The magnitude of these shifts is, however, somewhat smaller than that expected from the large σ-value (1.02) of the ring nitrogen toward α-position of pyridine. When these frequencies were plotted against the σ-values calculated on adding 1.02 in the linear relations between the carbonyl frequencies and the σ-values of the substituents,[3,5] all the plots showed a deviation of about 4~5 cm^{-1} to a lower frequency side, and in order to extend these linear relations to the vibration frequencies in the pyrazine ring system, the value of about 0.65 must be assumed as the σ-value of the ring nitrogen toward α-position of pyrazine ring.

As previously suggested,[3] appearance of double bands in the region attributable to the carbonyl stretching absorption is considered to be a characteristic phenomenon of the ester carbonyl group which is vicinal to an aza-nitrogen, as summarized in Table VII. As the reason for this phenomenon, the following two possibilities can be anticipated; i) the formation of a dimer as (IV) and hence a coupling between the stretching vibrations of the two carbonyl bonds to cause a frequency splitting, thus giving rise to a pair of absorption bands on either side of the unperturbed frequency, and ii) the presence of two rotational isomers like (Va) and (Vb), in which the extent of dipolar interaction between the C=O group and the ring nitrogen differs in the two with a consequential separation of the carbonyl stretching frequencies.

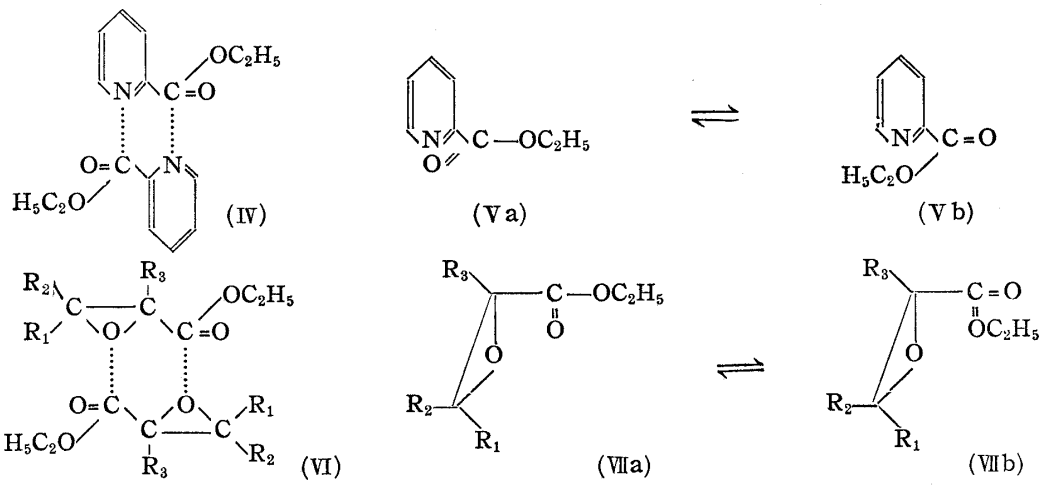
Recently, two analogous explanations have been given and discussed for the splitting phenomenon of the carbonyl stretching absorption in glycidic acid esters. Morris,

Table VII. Splitting of the Carbonyl Stretching Frequency of the Ester Group adjacent to Ring Nitrogen

Compound	$\nu_{C=O}$ (cm^{-1}) in CS_2[a]				$\nu_{C=O}$ (cm^{-1}) in $CHCl_3$[a]	$\nu_{C=O}$ (cm^{-1}) in Nujol
	ν_1	ν_2	$\Delta\nu$	$\varepsilon_{\nu 1}/\varepsilon_{\nu 2}$		
Methyl picolinate	1754 m	1728 s	26	0.39	1729 s	
Ethyl picolinate	1750 m	1722 s	28	0.45	1723 s	1742 ms, 1721 s[b] (0.83)
Isopropyl picolinate	1744 m	1718 s	26	0.48	1720 s	
2-Ethoxycarbonylquinoline	1749 m	1722 s	27	0.35	1721 s	
Ethoxycarbonylpyrazine	1756 ms	1726 s	30	0.52	1725 s, 1737 sh	1737 s
3-Ethoxycarbonylpyrazine 1-oxide[c]	1764 ms	1732 s	32	0.70	1730 s, 1747 sh	1723 s
2-Ethoxycarbonylfuran	1749 s	1722 s	27	1.06	1720 s	1722 s

a) 0.01~0.02*M* solution, cell thickness, 0.1 mm.
b) Liquid film.
c) Saturated solution in CS_2; cell thickness, 1.0 mm.

et al.[14] attributed it to a coupling between two carbonyl frequencies through the formation of a dimer like (VI), while House, *et al.*,[15] more recently attributed it to the existence of two rotational isomers like (VIIa) and (VIIb).



As shown in Table VII, these doublets showed approximetely a constant separation of 26~32 cm^{-1} in carbon disulfide solution and the optical density ratio of the two peaks varied slightly in the range of 0.35~0.70, depending upon the compound, the higher freqency band being always weaker than that of the lower frequency. The relative intensity of the two bands did not show any appreciable change on dilution in the range of 0.2~

Table VIII. Intensity Change of Double Bands in Various Solvents[a]

Compound		CCl_4		Dioxane		MeCN		CCl_4+10% MeOH	
		$\bar{\nu}$	ε[b]	$\bar{\nu}$	ε	$\bar{\nu}$	ε	$\bar{\nu}$	ε
Ethyl picolinate	ν_1	1749	110	1745	167	1740	236		
	ν_2	1721	398	1719	342	1722	276	1723	289
	R[c]		0.28		0.49		0.86		
Ethoxycarbonylpyrazine	ν_1	1755	168	1749	200	1742	240		
	ν_2	1725	392	1723	316	1724	291	1725	295
	R		0.43		0.63		0.82		
Ethyl isonicotinate		1733	457	1728	420	1728	466	1731	395

a) 0.015*M*.; cell thickness, 0.1 mm.
b) Molar extinction coefficient.
c) Extinction ratio, $\varepsilon_{\nu 1}/\varepsilon_{\nu 2}$.

14) H. H. Morris, R. H. Young, Jr. : J. Am. Chem. Soc., **79**, 3408(1957).
15) H. O. House, J. W. Blaker : *Ibid.*, **80**, 6389(1958).

0.0001*M* in carbon tetrachloride and also on elevation of the temperature from 20° to 60°. A considerable change in relative intensity was observed, however, when the spectra were measured in solvents of different polarity, and the optical density ratio increased considerably as the polarity of the solvent increased, as indicated in Table Ⅷ. The doublet appears to become a single peak only in the solvent capable of forming a hydrogen bond, e.g. chloroform and methanol, as well as in the solid state.

These observations on the nature of the double bands support the assumption that the doublet arises from the existence of two rotational isomers. In conformation (Ⅳa), in which the carbonyl oxygen approaches closely to the ring nitrogen in space, it ts expected that the dipolar interaction causes a shift of carbonyl frequency to a higher frequency. Thus the higher frequency band in the doublet should be attributed to the conformation (Ⅳa). The observed increase in intensity of the higher frequency band with the increase of polarity of the solvent indicates that the conformation (Ⅳa), the more polar form, is stabilized in a polar solvent. The considerable increase of optical density ratio in the liquid spectrum of ethyl picolinate is also indicative of this effect. Such effects are in complete agreement with the result obtained from the studies of the infrared spectra of the rotational isomers in α-haloketones and α-haloesters.[16,17] The single peak in chloroform and methanol seems to support the assumption of the formation of a dimer like (Ⅳ), but examination of the molar extinction coefficient of these single peaks revealed that the two bands still remain, the second band being an unresolved shoulder, as shown in Table Ⅷ.

The above assumption, however, cannot give any explanation for the observed behavior in their frequencies. Since the C=O and the ring N dipoles are oriented in opposite direction in the conformation (Ⅳb), the lower frequency band of the doublet, which can be attributed to this conformation from the foregoing considerations, should correspond to an unperturbed frequency. The observed frequencies of these bands, however, are located at a considerably lower frequencies than would be expected from the electronic effect of the ring. For example, 3-ethoxycarbonylpyrazine 1-oxide exhibited the lower frequency band at 5 cm^{-1} lower frequency than that of ethyl nicotinate 1-oxide, in spite of the increase of an electronegative ring nitrogen, and ethyl picolinate exhibited this peak at 2 cm^{-1} lower frequency than that of ethyl benzoate (1724 cm^{-1}). On the other hand, the fact[3] that the mean value of the two frequencies in ethyl picolinate gave a linear plot against the value of 1.02, which was deduced from the carbonyl frequency of 2-acetylpyridine, and that, as indicated in Table Ⅵ, the mean frequencies in pyrazine derivatives showed a fairly reasonable behavior in their shifts, being parallel to those in acetyl carbonyl frequencies, can be explained only by the assumption that the doublet arises from a Fermi type of resonance interaction between two frequencies.

The existence of two analogous rotational isomers in furfural has been proved from its infrared spectrum[18] and the appearance of a doublet in the carbonyl absorption of 2-ethoxycarbonylfuran (Table Ⅶ) can also be attributed to the same cause. Picolinaldehyde, however, showed a single peak at a reasonable position (1716 cm^{-1}) in carbon disulfide, being 8 cm^{-1} higher than that of benzaldehyde, indicating the absence of rotational isomers.

Although the existence of rotational isomers like (Ⅴa) and (Ⅴb) seems to be most

16) L. J. Bellamy, R. L. Williams : J. Chem. Soc., **1957**, 4294.
17) J. Allinger, N. L. Allinger : Tetrahedron, **2**, 64(1958).
18) G. Allen, H. J. Bernstein : Can. J. Chem., **33**, 1055(1955). In this paper, they attributed the lower frequency band (1675 cm^{-1}) to the more polar conformation which corresponds to (Ⅴa) structure of ethyl picolinate, but it is clear that the higher frequency band (1690 cm^{-1}) must be attributed to this conformation.

plausible and evidence for the dimer formation like (IV) cannot be obtained, definite conclusion for the splitting phenomenon cannot be drawn at present. At any rate, it is certain that some vibrational interaction exists between the two carbonyl frequencies and the mean frequency of the two is considered to be an unperturbed frequency.

Experimental

Material—Cyanopyrazine ($b.p_{33}$ 109~110°) and aminopyrazine (m.p. 117~118°) were respectively prepared from pyrazinecarboxamide by dehydration with $POCl_3$ and by Hofmann rearrangement. Chloropyrazine ($b.p_{31}$ 62~63°) was prepared by the action of $POCl_3$ on pyrazine 1-oxide. Acetylpyrazine (m.p. 79~80°. *Anal.* Calcd. for $C_6H_6ON_2$: C, 59.01; H, 4.95; N, 22.94. Found : C, 58.96; H, 4.96; N, 22.86) was prepared by ester condensation of ethoxycarbonylpyrazine (m.p. 52~53°). Other substituted pyrazines used were commercial products. Pyrazine mono- (m.p. 108°) and di- (m.p. 260°) N-oxides were respectively prepared by oxidation of pyrazine with equivalent and excess of perhydrol. 3-Acetylpyrazine 1-oxide (m.p. 184°. *Anal.* Calcd. for $C_6H_6O_2N_2$: C, 52.17; H, 4.38; N, 20.28. Found : C, 52.08; H, 4.31; N, 20.19), 3-ethoxycarbonylpyrazine 1-oxide (m.p. 147°. *Anal.* Calcd. for $C_7H_8O_3N_2$: C, 50.00; H, 4.80; N, 16.66. Found : C, 49.78; H, 5.01; N, 16.83), and 3-carboxyaminopyrazine 1-oxide (m.p. 293°) were prepared from the corresponding pyrazines by oxidation with perhydrol. 3-Cyanopyrazine 1-oxide (m.p. 153°, not so pure) and 3-chloropyrazine 1-oxide (m.p. 96°, not so pure) were prepared from the corresponding pyrazine by oxidation with perhydrol in a very poor yield. The preparation of 2-methylpyrazine 1-oxide (m.p. 89~90°), 3-methylpyrazine 1-oxide (m.p. 67~69°), and methylpyrazine 1,4-dioxide (m.p. 238°(decomp.) have been described elsewhere.[10] Pyrimidine N-oxide and its derivatives were supplied by Dr. H. Yamanaka of the University of Tohoku.

Method—Infrared spectra were measured with a Perkin-Elmer Model 21 double-beam spectrophotometer provided with NaCl prism. Detailed condition of measurements of solution spectra are described in Tables I to VIII. For comparing small frequency shifts in the N-O stretching and carbonyl frequencies, measurements were made carefully under the same conditions for each group of compounds and the chart scale of 20 cm./μ was applied, scanning very slowly. In these cases, accuracy of the frequency is assumed to be within $\pm 1\,cm^{-1}$.

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Summary

The infrared spectra of pyrazine, its eight mono-substituted derivatives, and their ten N-oxide derivatives were analyzed. Their characteristic N-O stretching frequencies (a strong absorption in the region of 1250 and 1350 cm^{-1}) were found to be correlated to the nature of a substituent present and the linear relationship between the N-O frequency and the σ-value of a substituent in substituted pyridine N-oxides could be extended to that in substituted pyrazine N-oxides by applying the σ-value of ring nitrogen (0.93) and the N-oxide group (0.25) toward 4-position of pyridine for mono- and di-N-oxides, respectively. The considerably higher frequency shift of the N-O frequency was shown to be characteristic for the methyl group at β-position with respect to the N-oxide group. Ring and ring CH vibrations were discussed on the basis of the correlations found in the pyridine ring system. The splitting of the carbonyl stretching frequency of ester group adjacent to ring nitrogen was pointed out and discussed. The infrared spectra of pyrimidine N-oxide and its eight derivatives were also examined and discussed in comparison with the above results.

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