IR and NMR Spectroscopic Investigation of 3-Halo-2,6-dimethylpyridine *N*-Oxides and Their 4-Nitro Derivatives

H. BAN-OGANOWSKA and T. TALIK

Department of Organic Chemistry, Academy of Economics, PL-53-345 Wrocław

Received 26 April 1991
Accepted for publication 20 January 1992

IR, ^{1}H NMR and ^{13}C NMR spectra of 3-halo-2,6-dimethylpyridine *N*-oxides and their 4-nitro derivatives were recorded. The influence of electron properties of substituents on changes of wavenumbers of $\nu(N^+—O^-)$ bands and chemical shifts ^{1}H and ^{13}C was analyzed. It was found that the "*ortho*-effect" of 2-methyl group inhibits diamagnetism of halogens.

Pyridine *N*-oxides are an interesting functional class of organic compounds, since the $N^+—O^-$ group exhibits both π-electron-acceptor and π-electron-donor properties [1, 2]. Of these two effects the latter is known as the so-called back donation [3]. It results in the formation of the double bond between N and O. The degree of back donation depends on the substituent(s) in the pyridine ring and can be expressed by the partial π-bond order in the $N^+—O^-$ group. It can be evaluated from various measurable data [3, 4]. For example, the degree of back donation obtained from ^{17}O nuclear quadrupole resonance spectra is equal to 0.247 (25 %) for pyridine *N*-oxide and 0.312 (31 %) for its 4-nitro derivative [4]. Similar calculations based on ^{15}N NMR and IR data show this effect to be more significant, *i.e.* (50 ± 5) and (60 ± 5) %, respectively [3].

In the present work the effects of the substituents and their interaction on the changes of the back donation as well as the chemical shifts in the compounds studied were investigated in an aprotic solvent.

EXPERIMENTAL

All investigated compounds were prepared according to the methods described before [19, 20].

The IR spectra were recorded on a spectrophotometer IR 75 (Specord, Zeiss) as nujol mulls.

The ^{1}H NMR spectra were recorded on a spectrometer BS 589 A (Tesla) (100 MHz) at 303 K in $CDCl_3$. Digital resolution was 0.08 Hz per point. Tetramethylsilane was used as an internal standard.

The ^{13}C NMR spectra (25.14 MHz) were registered under the same conditions as ^{1}H NMR spectra by means of NBD technique using $CDCl_3$ (δ = 77.70) as internal reference. Digital resolution was 1.22 Hz per point (spectral width 7600 Hz, 8 K data points, pulse angle 90°, *i.e.* 13 s and repetition time 2 s).

RESULTS AND DISCUSSION

The IR spectra of 3- and 4-monosubstituted pyridine *N*-oxides as well as 3-substituted 4-nitropyridine *N*-oxides were discussed earlier by *Katritzky* [5, 6] and *Jaffe* [7]. There is given [7] the dependence of wavenumbers of $\nu(N^+—O^-)$ bands on substituent σ_m constants but the points corresponding to the halogens (F, Cl, Br, I) do not follow the correlation line [8].

The $\nu(N^+—O^-)$ values in the IR spectra of 3-halo-2,6-dimethylpyridine *N*-oxides and their 4-nitro derivatives are collected in Table 1. It can be seen that the halogens characterized by $\sigma_m > \sigma_p$, introduced into the position 3 of the ring, cause inductive shortening of $N^+—O^-$ bond in the decreasing order: F, Cl, Br, I (Table 1).

The electron-acceptor substituent ($—NO_2$ group) in the position 4 of investigated *N*-oxides favours the back donation effect of the $N^+—O^-$ group. Additionally, it gives evidence of the molecule polarity lowering because a decrease of dipole moment value from 8.9394×10^{-30} C m to 3.2355×10^{-30} C m is observed in case of 3-fluoro-2,6-dimethylpyridine *N*-oxide and its 4-nitro derivative [9]. However, the influence of 4-nitro group is

Table 1. IR Spectral Data ($\tilde{\nu}$/cm^{-1}) of 3-Halo-2,6-dimethylpyridine *N*-Oxides and Their 4-Nitro Derivatives

3-Halo	$\nu(N^+—O^-)$	3-Halo-4-nitro	$\nu(N^+—O^-)$
F	1259	F	1303
Cl	1235	Cl	1281
Br	1230	Br	1277
I	1218	I	1262

partially reduced due to the presence of two α-methyl groups since wavenumbers of $\nu(N^+—O^-)$ bands are 1295 cm^{-1} for 4-nitro-2,6-dimethylpyridine *N*-oxide and 1310 cm^{-1} for 4-nitropyridine *N*-oxide (when measured in benzene) [10]. This effect is attributed to electron-donor ability of the methyl group as well as to hydrogen bond occurrence between protons of α-methyl groups and oxygen atom of $N^+—O^-$ group [10]. Nevertheless, if $—NO_2$ group is present in the position 4, the strength of this hydrogen bond is extremely low [10] because we have found no absorption band in the region of $\tilde{\nu}$ = 3000—3400 cm^{-1} in the spectra of 3-halo-4-nitro-2,6-dimethylpyridine *N*-oxides. On the contrary, the absorption in this region is present in the IR spectra of 3-halo-2,6-dimethylpyridine *N*-oxides.

The interaction between the substituents in the compounds studied seems to be obvious. The discussion of the differences between the experimental values of dipole moments and those calculated [9] as well as ^1H and ^{13}C NMR data confirm the occurrence of such an effect.

In general, the effect of *N*-oxide functionality, *i.e.* back donation, appears to bring about in ^1H NMR spectra δ = 0.3 increase of magnetic shielding of protons in α- and γ-positions of the ring in comparison to that in pyridine itself [11].

The values of chemical shifts of the aromatic protons and of α-methyl groups protons as well as J_{H_β, H_γ} coupling constants of 3-halo-2,6-dimethylpyridine *N*-oxides and their 4-nitro derivatives are given in Table 2. On the basis of these data a slight decrease of shielding of 2-methyl group protons was possible to be observed in both examined series of *N*-oxides from 3-fluoro to 3-iodo derivatives. Although, if only electronegativity ratios in the group of halogens were taken into account, a reverse consequence should be expected. It should be noted that in coupled systems the bonding energy values for carbon—halogen bonds appear to decrease more rapidly from fluorine down to iodine than the ionization energy values of these bonds. This implies a mesomeric effect lowering in the same direction and effects in protons shielding increase in resonance positions of fluoro derivatives of compounds examined. Steric inhibition of halogen diamagnetism however, is of dominant consequence, especially for atoms as big as bromine or iodine (the "heavy atom effect") if the methyl group in the *ortho* position is present. It provides a sterical hindrance for rotation of electrons in free pairs of halogen atom around the C—Br or C—I bond axis resulting in a lowering of shielding caused by this rotation [12]. For the same reason, shielding of aromatic H-4 protons in 3-halo-2,6-dimethylpyridine *N*-oxides tends to lower in the same direction. Similar regularities also occur in ^1H NMR spectra of 2-halo-3-picoline *N*-oxides [13].

Table 2. ^1H NMR Chemical Shifts (δ) of 3-Halo-2,6-dimethylpyridine *N*-Oxides and Their 4-Nitro Derivatives and Coupling Constants of Protons

Derivative	H-4	H-5	CH_3—C-2	CH_3—C-6	J_{H_β, H_γ}/Hz
3-F-4-NO_2	–	7.93	2.52	2.52	–
3-Cl-4-NO_2	–	7.87	2.68	2.53	–
3-Br-4-NO_2	–	7.80	2.75	2.46	–
3-I-4-NO_2	–	7.77	2.95	2.50	–
3-F	7.12	7.12	2.42	2.42	9.0
3-Cl	7.22	7.18	2.62	2.46	8.3
3-Br	7.35	7.10	2.66	2.42	8.2
3-I	7.56	6.96	2.77	2.43	8.0

On the other hand, shielding of aromatic H-5 proton increases in accordance with halogen electronegativity decrease both in 3-halo-2,6-dimethylpyridine *N*-oxides and their 4-nitro derivatives.

According to the data presented the chemical shift of 6-methyl group protons does not depend on the type of halogen in the position 3 but remains almost constant in a given series of compounds.

Extreme differences in protons shielding of both α-methyl groups occur in the case of 3-iodo derivatives, and the singlets derived from the chemical shift of these protons are extremely distant from each other. Starting from 3-chloro derivatives the singlet of protons in 2-methyl group is gradually shifted upfield and in the case of 3-fluoro derivatives both the singlets of two methyl groups coincide. Analogically, in the case of aromatic H-4 and H-5 protons of 3-fluoro derivative the doublets coincide and they are extremely distant from each other in 3-iodo derivative.

As expected, the nitro group in the position 4 of 3-halo-2,6-dimethylpyridine *N*-oxides brings about a paramagnetic effect both for protons of the two methyl groups and the H-5 proton (Table 2).

Spin-spin coupling constants of H-4 and H-5 protons in 3-halo-2,6-dimethylpyridine *N*-oxides, being read from the spectra, oscillate in the range 8—9 Hz according to the halogen type (see Table 2).

As it is known, the pyridine *N*-oxide shows in ^{13}C NMR spectra a large shielding effect ($\delta \approx 10$) at C-2, C-4, and C-6 and only slight deshielding effect at C-3 and C-5 (δ = 3—4) relative to that observed at the corresponding carbons in pyridine [14—16]. This indicates a high electron density on carbons in α- and γ-positions of pyridine *N*-oxide ring [17] resulting from the back donation effect because the α-carbon atoms in *N*-oxides of saturated quaternary amines are deshielded by δ = 15 compared to those in the parent amine [14]. The reason for carbon atoms deshielding at C-3 and C-5 is a lack of mesomeric interaction of *N*-oxide group with the β-position as well as the electron-acceptor type inductive effect of positively charged nitrogen atom.

Table 3. ^{13}C NMR Chemical Shifts* (δ) of 3-Halo-2,6-dimethylpyridine *N*-Oxides and Their 4-Nitro Derivatives

Derivative	C-2	C-3	C-4	C-5	C-6	CH_3—C-2	CH_3—C-6
3-F	139.79	162.11	112.51	122.29	145.30	10.48	17.65
	(+ 3.59)	(+ 4.51)	(– 1.99)	(– 1.91)	(+ 0.70)		
3-Cl	149.10	130.81	126.03	123.34	149.11	15.70	18.77
	(– 0.4)	(+ 0.11)	(– 2.17)	(+ 0.04)	(+ 0.61)		
3-Br	149.70	119.23	128.79	123.71	148.66	18.17	18.69
	(– 1.60)	(+ 1.73)	(– 2.71)	(+ 0.41)	(+ 0.06)		
3-I	151.50	92.19	134.77	124.38	149.18	22.72	18.54
	(– 7.50)	(+ 1.69)	(– 2.53)	(– 1.02)	(+ 0.48)		
3-F-4-NO_2	145.52	153.90	138.02	118.18	147.09	11.74	18.32
	(+ 7.42)	(+ 0.90)	(+ 6.32)	(– 1.42)	(+ 0.59)		
3-Cl-4-NO_2	151.23	123.79	149.03	119.00	149.11	16.30	18.69
	(– 0.17)	(– 2.31)	(+ 3.63)	(+ 0.30)	(– 1.29)		
3-Br-4-NO_2	151.95	111.53	143.88	118.78	149.03	19.93	18.46
	(– 1.25)	(– 1.37)	(– 4.82)	(0.00)	(– 1.47)		
3-I-4-NO_2	155.29	85.99	148.50	119.08	149.93	24.59	18.91
	(– 5.61)	(+ 0.69)	(– 6.00)	(– 1.00)	(– 0.67)		

* Pyridine *N*-oxide substituent increments were used for the calculations of the chemical shifts. Differences between the observed and calculated chemical shifts are given in parentheses.

The value of those differences caused by *N*-oxidation of pyridine can undergo changes according to the kind and the place of substituents introduced into the pyridine *N*-oxide ring.

Table 3 gives the ^{13}C chemical shifts of 3-halo-2,6-dimethylpyridine *N*-oxides and their 4-nitro derivatives in $CDCl_3$ solutions. The comparison of chemical shifts obtained by addition of the pyridine or benzene substituent increments [18] to the carbon chemical shifts of pyridine *N*-oxide [16] with the experimental ^{13}C NMR spectral data of the compounds studied shows a remarkable agreement for the C-5 and C-6. Bigger differences were found for C-2 when F or I were present in the position 3 and for C-4 of all 3-halo-4-nitro derivatives. The relatively large differences between calculated and observed chemical shifts in this case can be a result of the interaction of halogen and nitro group ("*ortho*-effect"). In some cases the disagreement between the calculated and experimental shifts seems to reflect the strong electronegativity of the halogen or the substituent steric effect.

On the basis of experimental results of ^{13}C chemical shifts shown in Table 3 it can be seen that for both series *N*-oxides halogen influence on carbon "ipso" is paramagnetic in the case of fluoro and chloro derivatives and diamagnetic in the case of bromo and iodo derivatives (the "heavy atom" effect). On the other hand, downfield chemical shifts of carbons C-2 and that of 2-methyl group were observed at a transition from fluoro to iodo derivatives in both the series of examined compounds. This may result, analogically as for protons shielding, either from the fact of mesomeric effect being decreased from fluorine to iodine more rapidly than the inductive effect or, especially for carbon atoms of 2-methyl group, from the fact of diamagnetism of heavier halogen atoms being hindered by a steric hindrance. Inversion is observed of ^{13}C chemical shifts in the spectra since δ for 6-methyl group carbon atoms does not depend on the halogen type and remains practically constant, *i.e.* about 18 [15].

β-Effect of halogens on C-4 in 3-halo-2,6-dimethylpyridine *N*-oxides is diamagnetic for the fluoro derivative and paramagnetic for the rest of the halogen atoms, so it is being changed from fluorine to iodine according to the mesomeric effect lowering.

Chemical shift for C-5, which is only slightly shielded by the methyl group in *para* position, is being shifted due to the halogen γ-effect from fluoro to iodo derivative downfield.

Paramagnetic chemical shifts of C-6 in comparison to theoretical value [15] result from a substantial paramagnetic effect, specific to a methyl group.

Deshielding effect of carbon "ipso" due to a strongly electron-acceptor nitro group is expressed by ^{13}C shift of C-4 to a lower field.

According to expectations the nitro group causes only a slight diamagnetic effect on C-5.

REFERENCES

1. Katritzky, A. R. and Lagowski, J. M., *Chemistry of Heterocyclic N-Oxides.* Academic Press, London, 1971.
2. Ochiai, E., *Aromatic Amine Oxides.* Elsevier, New York, 1967.
3. Paudler, W. W. and Jovanović, M. V., *Heterocycles 19,* 93 (1982).
4. Woyciesjes, P. W., Janes, N., Ganapathy, S., Hiyama, Y., Brown, T. L., and Oldfield, E., *Magn. Reson. Chem. 23,* 315 (1985).

5. Katritzky, A. R. and Gardner, J. N., *J. Chem. Soc. 1958,* 2192.
6. Katritzky, A. R., Beard, J. A. T., and Coats, N. A., *J. Chem. Soc. 1959,* 3680.
7. Jaffe, H. H., *Chem. Rev. 53,* 191 (1953).
8. Rasała, D. and Gawinecki, R., *Bull. Soc. Chim. Fr., 128,* 201 (1991).
9. Ban-Oganowska, H., *Pol. J. Chem. 64,* 87 (1990).
10. Suszko, J. and Szafran, M., *Bull. Acad. Pol. Sci., Ser. Sci. Chim. 10,* 233 (1962).
11. Abramovitch, R. A. and Davis, J. B., *J. Chem. Soc., B 1966,* 1137.
12. Dewar, M. J. S. and Takeuchi, Y., *J. Am. Chem. Soc. 89,* 390 (1967).
13. Puszko, A., Pielichowski, J., and Wilk, W., *Materials of XXII Polish General Seminar on NMR.* Kraków, 1989.
14. Anet, F. A. and Yavari, I., *J. Org. Chem. 41,* 3589 (1976).
15. Cushley, R. J., Naugler, D., and Ortiz, C., *Can. J. Chem. 53,* 3419 (1975).
16. Sojka, S. A., Dinan, F. J., and Kolarczyk, P., *J. Org. Chem. 44,* 307 (1979).
17. Jovanović, M. V., *Spectrochim. Acta, A 41,* 1135 (1985).
18. Kalinowski, H. O., Berger, S., and Braun, S., *Carbon-13 NMR Spectroscopy.* J. Wiley, New York, 1988.
19. Talik, T., Talik, Z., Ban-Oganowska, H., and Puszko, A., *Pr. Nauk. Acad. Economics (Wrocław)* (191), 97 (1982).
20. Ban-Oganowska, H. and Talik, Z., *Rocz. Chem. 48,* 1587 (1974).

Synthesis, Physical Properties, and Spectroscopy of 2,3-Quinoxalinedicarboxamide Complexes

F. DIANZHONG, W. BO, Z. YUKUN, F. WU, and W. JUNNAN

Department of Chemistry, Lanzhou University, 730000 Lanzhou, China

Received 7 October 1991

New complexes of the general formulae $[Ln(Qxda) \cdot Cl_3 \cdot C_2H_6O \cdot H_2O]$ (Ln = La, Pr, Y; Qxda = 2,3-quinoxalinedicarboxamide) and $[Ln_3(Qxda)_2 \cdot 3Cl_3 \cdot 3C_2H_6O \cdot 3H_2O]$ (Ln = Y, La) have been synthesized and characterized by elemental analyses, conductivity measurements, thermal (TG, DTG, DTA) method, and spectral (IR and UV—VIS) studies. All the data are discussed in terms of the nature of bonding and the possible structural types. It has been found that coordination takes place through both oxygen atoms of the amide group and two types of species, mononuclear and linear homopolynuclear, are formed.

Heterocyclic carboxamides are known to possess powerful antitubercular activity [1]. Further, the metal complexes of ligands that have biological activity are more active than the free ligands [2, 3]. In view of this, metal complexes with several ligands of this type, *e.g.* 2-pyrazinecarboxamide [4, 5], 2,3-pyrazinedicarboxamide [5, 6], *N,N,N′,N′*-tetramethyl-2,6-pyridinedicarboxamide [7], and 2-quinoxalinecarboxamide [8] have been studied and different coordination models proposed. However, complexes of 2,3-quinoxalinedicarboxamide with some metals of group IIIb have not been reported so far. The present study describes the synthesis and characterization of some of these complexes.

EXPERIMENTAL

2,3-Quinoxalinedicarboxamide (Qxda) was prepared according to the literature method [9]. Lanthanide(III) chlorides were prepared from their oxides by treatment with hydrochloric acid.

IR spectra were taken on a NIC-5DX spectrophotometer (KBr disks) in the range of $\tilde{\nu}$ = 200—4000 cm^{-1}. UV spectra (in solution) were recorded in the λ = 200—500 nm region using a spectrophotometer 240 (Shimazu, Japan). Molar conductivity measurement were made with a DDS-IIA conductometer with dimethylformamide (DMF) and dimethyl sulfoxide (DMSO) as solvents, separately, at 25 °C. Thermogravimetry (TG) and differential thermal analysis (DTA) were carried out by a TG—DTA meter (Thermoflex) in a nitrogen atmosphere between room temperature and 800 °C.

Lanthanide Complexes

The complexes $[Ln(Qxda) \cdot Cl_3 \cdot C_2H_6O \cdot H_2O]$ were prepared by mixing hydrous lanthanide(III) chloride (1 mmol) in 20 cm^3 of ethanol and Qxda (2 mmol) in 20 cm^3 of dioxane and refluxing the solution for 10 h. The mixture was then concentrated to the appropriate volume. The solid, which