ISSN 1070-3632, Russian Journal of General Chemistry, 2009, Vol. 79, No. 4, pp. 820–825. © Pleiades Publishing, Ltd., 2009.
Original Russian Text © V.P. Andreev, 2009, published in Zhurnal Obshchei Khimii, 2009, Vol. 79, No. 4, pp. 657–662.

Molecular Complexes of the Pyridines and Quinolines *N*-Oxides Styryl Derivatives with the Brønsted–Lowry Acids

V. P. Andreev

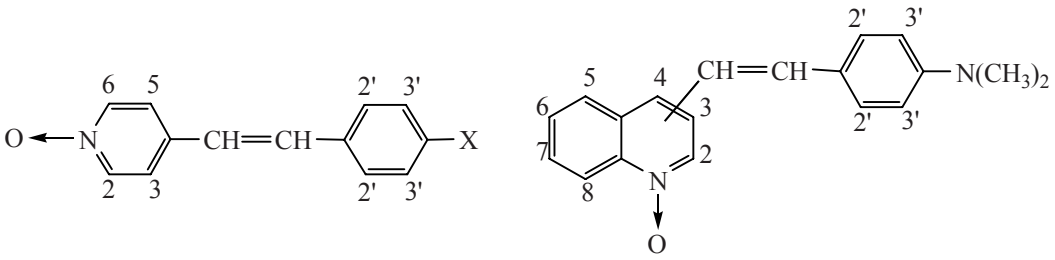
Petrozavodsk State University,
pr. Lenina 33, Petrozavodsk, 185910, Russia
e-mail: andreev@psu.karelia.ru

Received April 11, 2008

Abstract—The processes of the intramolecular charge transfer in the series of the *trans*-isomers of styryl derivatives of pyridines and quinolines *N*-oxides possessing substituents with +*M* effect are investigated. Complex formation of these compounds with Brønsted–Lowry acids is studied by the methods of IR, electronic and ^{1}H NMR spectroscopy. The center of protonation and formation of hydrogen bond with the *N*-oxides dimethylamino derivatives is determined by the nature of the solvent (in water the first protonation occurs at the amino group, in the organic solvents at the group N→O). Composition and structure of molecular complexes depends on the nature of the complex forming compounds and the ratio of reagents.

DOI: 10.1134/S1070363209040239

According to the obtained by us and published data, at the complex formation (in particular, at the protonation) of heteroaromatic *N*-oxides with different types of acceptors, in the majority cases the first donor-acceptor bond is formed with the participation of oxygen atom of group N→O [1, 2]. Moreover, interaction with Brönstedt–Lowry acids leads to formation of the salts of composition *N*-oxide–acid 1:1 or 2:1 [3]. Exception is the *N*-oxide of the *trans*-4- (4-dimetilaminostyryl)pyridine (4-DPyO), which according to [4] is protonated in water initially at the dimethylamino group. At the same time we have shown [5], that the first protonation of 4-DPyO, and also of *trans*-4-(4-dimetilaminostyryl)- and *trans*-2-(4-dimethylaminostyryl)quinoline *N*-oxides (4-DQO and 2-DQO) in chloroform and ethanol occurs at the N→O group and only the second proton is added at $N(CH_3)_2$ group.



X = OCH_3 (4-MeOStPyO), $N(CH_3)_2$ (4-DPyO), 2-DQOI, and 4-DQO.

A priori it is possible to assume two boundary versions of behavior of the dimetilaminostyryl derivatives of a series of pyridine and quinoline *N*-oxides at the complex formation: (a) in the absence and (b) with the presence of essential interaction between the *N*-oxide and the dimethylamino groups. In the first case one should expect the formation of two types of complexes, in which donor centers is solely $N(CH_3)_2$ group or both groups, in accordance with the larger basicity of nitrogen atom, and the secondly (due to the direct polar conjugation of dimethylamino and *N*-oxide groups, the decrease of electron density and,

respectively, of basicity of nitrogen atom) first coordination with the *v*-acceptor should be achieved by the N→O group. However, in this case (according to published data) nature of the solvent, in which the acid-base interaction is accomplished, can decisively influence the type of the formed donor-acceptor bond.

Special attention to these compounds is caused by their high biological activity, since they influence proliferation and induce apoptozis of eritroleykemic cells K 562 [6].

We prepared the pyridine and quinoline *N*-oxides styryl derivatives hydrochlorides by the reaction of the corresponding *N*-oxides with gaseous HCl in chloroform. Their properties, data of electronic and IR spectroscopy are given in Tables 1 and 2. These salts (Table 2) like the corresponding molecular complexes with BF_3 of 1:1 composition [5] in the electron spectra in chloroform show a bathochromic shift relative to the appropriate *N*-oxides [4-MeOStPyO·HCl (+12 nm), 4-DPyO·HCl (+77 nm), 2-DQO·HCl (+78 nm)], especially strong for dimethylaminoderivatives, that indicates the complex formation with the participation of N→O group; in the complexes with BF_3 of composition 1:2 is observed strong hypsochromic shift (–70 nm).

Table 1. Characteristics of pyridine and quinoline *N*-oxides styryl derivatives hydrochlorides

Molecular complex	Color	mp, °C	Yield, %
4-MeOStPyO·HCl	Brilliant yellow	179–180	78
4-DPyO·HCl	Red	199–201	74
4-DPyO·2 HCl	Beige	184–185	53
2-DQO·HCl	Black-violet	198–200	96
2-DQO·2 HCl	Beige	195	90

The data of IR spectroscopy (Table 2) for these compounds (in KBr) also confirm conclusion about formation of *n,v*-complexes (in their spectra disappears or decreases the intensity of absorption band at 1310–1210 cm^{-1}, characteristic of N→O group).

Table 2. Electron and IR spectra of pyridine and quinoline *N*-oxides styryl derivatives and of products of their reaction with HCl[a]

Compound	Acceptor	Solvent	Electron spectra, λ_{max} (nm), log ε	Δλ in $CHCl_3$	IR spectra in KBr		
					N–O	O–B	B–F
4-MeOStPyO	–	Ethanol	356 (4.52)		1250 vs		
		Chloroform	363 (4.81)				
	BF_3	Chloroform	382 (3.40)	+19	1250 m	1152 vs	1092 vs, 950 s
	HCl	Chloroform	375 (3.32)	+12	1256 vs		
4-DPyO	–	Ethanol	420 (4.37)		1260 vs		
		Chloroform	408 (4.31)				
	BF_3	Chloroform	471 (4.15)	+63	–	1136 s	1084 vs, 1044 s, 930 vs
	$2BF_3$	Chloroform	338 (4.13)	–70	–	1120 br.s	1070 br.s
	HCl	Chloroform	485	+77			
2-DQO	–	HCl (conc.)	370, 384 sh		1237 m		
		HCl (conc.)–ethanol, 1:20	518 (4.29)				
		Ethanol	420 (4.41)				
		Chloroform	430 (4.59)				
	BF_3	Chloroform	508 (4.37)	+78	1240 w	1160 s	1070 v.s
	$2BF_3$	Chloroform	359 (4.30), 377 sh,	–71	1240 w	1155 s	1075 s
	HCl	Chloroform	520 (4.30)	+90	1240 vw		

[a] Data for the molecular complexes with BF_3 from [5]; due to very low stability of solutions of hydrochlorides of 1:2 composition their electron spectra are omitted (Δλ of molecular complexes are given relatively to the positions of the absorption maxima of respective *N*-oxides in chloroform).

Table 3. ^{1}H NMR spectra of pyridine and quinoline *N*-oxides styryl derivatives and their molecular complexes with HCl and BF_3 in DMSO

Compound	Acceptor	Chemical shift (δ, ppm), multiplicity							
		H^2	H^6	H^3	H^5	CH=CH	$H^{2'}$	$H^{3'}$	X
4-MeOStPyO	–	8.17 d (2H)		7.45–7.63 H^3, H^5 (2H), and $H^{2'}$ (2H)		7.31 d (1H) 7.03 d (1H)		6.92 d (2H)	3.78 s (3H)
	BF_3	8.57 d (1H)	7.8–8.2 H^6 (1 H) and H^3, H^5 (2H), CH=CH (2H)				7.68 d (2H)	7.04 d (2H)	3.81 s (3H)
	HCl	8.36 d (2H)		7.78 d (2H)		7.50 d (1H) 7.12 d (1H)	7.60 d (2H)	6.96 d (2H)	3.75 s (3H)
4-DPyO	–	8.04 d (2H)		7.48 d (2H)		7.20 d (1H) 6.84 d (1H)	7.39 d (2H)	6.67 d (2H)	3.00 s (6H)
	BF_3	8.22 (2H)		7.66 (2H)		7.39 (1H) 6.98 (1H)	7.50 (2H)	6.78 (2H)	2.94 (6H)
	HCl DMSO	8.41 d (2H)		7.81 d (2H)		7.56 d (1H) 7.11 d (1H)	7.60 d (2H)	6.98 d (2H)	3.00 s (6H)
	HCl methanol	8.75 d (2H)		8.14 d (2H)		7.85 d (1H) 7.49 d (1H)	7.68 d (2H)	7.93 d (2H)	3.32 br.s (6H)
	HCl (D_2O)	8.2–8.5 br (2H)		7.58–7.96 br		~7.35 br (1H) ~7.12 br (1H)	~6.9 (2H)	~7.6 (2H)	3.37 br (6H) 3.14 s (6H)
	2 HCl ($CDCl_3$)	~8.55 (2H)		H^3, H^5 (2H) and $H^{2'}$, $H^{3'}$ (2H) ~8.43 (2H)		~7.44 and ~7.12 (1H) (1H)			

Table 3. (Contd.)

Compound	Acceptor	Chemical shift (δ, ppm), multiplicity										
		H^2	H^3	H^4	H^5	H^6	H^7	H^8	CH = CH	$H^{2'}$	$H^{3'}$	X
2-DQO	–	–	7.84 d (1H)	7.95–8.05 (2H)		7.65 t (1H)	7.77 t (1H)	8.55 d (1H)	7.86 d (1H) 7.72 d (1H)	7.54 d (2H)	6.78 d (2H)	2.96 s (6H)
	BF_3	–	7.84 d (1H)		8.16 d (1H)	7.85–8.00 m H^4, H^6, H^7 (3H)		8.70 d (1H)	7.98 d (1H) 7.69 d (1H)	7.63 d (2H)	6.70 d (2H)	3.09 s 6H
	HCl DMSO	–		7.95–8.05 (2H)		7.62–7.78 H^3, H^6, H^7, and CH=CH (4H)		8.48 d (1H)		7.58 d (2H)	6.79 d (2H)	2.97 s (6H)
	2HCl $CDCl_3$	–	7.8 – 8.1 (4 H)					~8.7 (1H)	7.6–7.8 H^3 and CH=CH (3H)	7.5 (2H)	7.22 (1H) 7.09 (1H)	3.17 (6H)

Finally, the similar regularities in the changes in ^{1}H NMR spectra in aprotic solvents (deuterochloroform and dimethylsulfoxide), occurred at protonation and complex formation with BF_3 of *N*-oxides (Table 3) unambiguously prove that the donor-acceptor bond with hydrogen atom is formed with the participation of the oxygen of *N*-oxide group. This is seen from the downfield shift of the signals of pyridine ring protons in comparison with the signals of the protons of free *N*-oxides. The chemical shifts of the protons of dimethylamino group in this case remain practically unchanged, that would be impossible at protonation of this group.

The fact that in the solid state 2-DQO·HCl and 2-DQO·BF_3 are of black-violet color, and 4-DPyO·HCl and 4-DPyO·BF_3 – of the red color (the initial *N*-

oxides are respectively orange and yellow, and the complexes of the 1:2 composition are colorless), apparently indicates the presence in the crystal lattice of the adducts protonated at the N→O group.

Usually in the case of conjugation with amino group the protonation is achieved with the participation of the unshared electron pair of oxygen (as at the interaction of carbamide with nitric acid [7]). However, in the case of 4-DPyO the styryl fragment must considerably decrease the conjugation, that in principle makes possible (depending on conditions) the process of complex formation with participation of either both, or one of the functional groups. Let us note that in [4] the authors come to the conclusion that in water the first protonation of 4-DPyO occurs at the nitrogen atom of amino group. In connection with that outlined above we continued a study of the processes of protonation of pyridine and quinoline dimethylaminostyryl derivatives.

In Table 4 are listed obtained by us data of electron spectroscopy for the compounds 4-MeOStPyO, 4-DPyO, 4-DQO and 2-DQO in different solvents.

It turned out that the replacement of chloroform (λ = 408 nm) by methanol leads to the bathochromic (Δλ = +6 nm), and by the water to the hypsochromic (–23 nm) shift of the long-wave absorption band of 4-DPyO *N*-oxide. In this case in the first two solvents the optical density of the solutions is proportional to the concentration of 4-DPyO, while with an increase of its concentration in the water appears the second maximum at approximately 340 nm, whose intensity gradually grows and it becomes principal (for 2-DQO and 4-DQO in view of the very poor solubility in the water the last effect cannot be registered). In the aprotic solvent chloroform (incapable of specific interactions) in the spectra of the *N*-oxides styryl derivatives the long-wave shift (Table 4) occurs in the sequence 4-MeOStPyO < 4-DPyO < 2-DQO < 4-DQO.

Table 4. Variations in position of long-wave band in the electron absorption spectra of 4-MeOStPyO, 4-DPyO, 2-DQO and 4-DQO as a dependence on the solvent nature

Solvent	λ_{max}, nm			
	4-MeOStPyO	4-DPyO	2-DQO	4-DQO
Chloroform	363	408	430	442
Methanol	361	414	442	452
Water	350	385	410[a]	420[a]

[a] Due to low solublity of compounds in water the electron spectra were taken from saturated solutions in cells with layer thikness 50 mm.

Alcohols (methanol, ethanol), capable of the formation of hydrogen bonds with the N→O group, enhance the direct polar conjugation, that should lead to ever larger bathochromic shift in comparison with chloroform when the molecule contains $N(CH_3)_2$ group possessing large +*M* effect (stronger than OCH_3 substituent), but they do not change practically the spectrum of 4-MeOStPyO. However, according to published data, in the case of not oxidized styryl derivatives 2-DPy, 4-DPy, 2-DQ and 4-DQ the replacement of the aprotic solvent acetonitrile (Table 5) by methanol leads to the hypsochromic effect. Apparently, direction of the shift of the absorption

Table 5. Position of long-wave absorption band in the electron spectra of pyridine and quinoline styryl derivatives (2-MeOStPy, 2-DPy, 4-DPy, 2-MeOStQ, 2-DQ and 4-DQ) in 96% ethanol, methanol, acetonitrile and solutions of HCl in alcohol

Compound	λ_{max} (nm), log ε				
	ethanol [8]	1 N HCl in ethanol [8]	0.01 N HCl in ethanol [8]	Methanol [9]	acetonitrile [9]
2-MeOStPy	–	–	–	336 (4.40)[a]	320
2-DPy				368 (4.47)[b]	363
4-DPy	–	–	–	375 (4.51)	369
2-MeOStQ	–	–	–	347 (4.44)	355
2-DQ	396 (4.56)	360 (4.50)	490 (4.43)	395 (4.55)	387
4-DQ	404 (4.36)	366 (4.35)	510 (4.13)	402 (4.15)	392

[a] λ = 376 nm in acidified methanol [9]. [b] In acidified methanol λ = 447 nm (4-DPy·HCl), λ = 324 nm (4-DPy·2HCl) [9].

Table 6. Position of long-wave absorption band in the electron spectra of 4-MeOStPyO, 4-DPyO, 2-DQO and 4-DQO in 96% ethanol, sulfuric, and hydrochloric acids

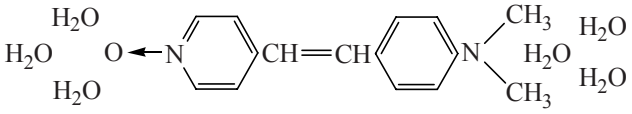
N-Oxide	λ_{max} (nm), log ε					
	H_2SO_4 (conc.)	HCl (conc.)	1 N HCl	0.001 N HCl	ethanol	1 N HCl in ethanol
4-MeOStPyO	368 (4.13)	387 (4.28)	350	350	356 (4.56) 361[a]	– 385[a]
4-DPyO	336 (4.40)	336 (4.53)	330	385	420 (4.37)	–
2-DQO	369 (4.50)	370 (4.50)	353	410	444 (4.55) [8]	365 [8][b] 368[a]
4-DQO	377 (4.27)	380 (4.17)	370	420	448 (4.30) [8]	370 [8] 376[a]

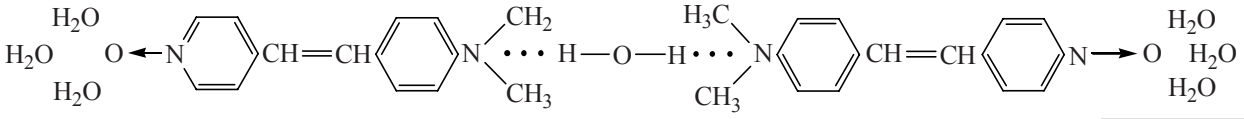
[a] In methanol. [b] In solution of ethanol–HCl (conc.), 20:1 for 2-DQO λ_{max} (nm), log ε: 518 (4.29) [5].

band of dimetilaminostyryl derivatives in the electron spectra to the long-wave region can be used for determining the center of complex formation . In favor of this statement testifies the fact that protonation of 2-(4-dimetilaminostyryl)naphthalene, which has only one basic center [$N(CH_3)_2$], in ethyl acetate causes hypsochromic shift, while protonation of 2-DQ (authors of work [10] report that its first protonation occurs at the nitrogen atom of quinoline ring) induces bathochromic shift.

The short-wave shift in water for all four styryl *N*-oxides is caused possibly by the fact that this solvent possessing the molecules of minimal size and capable of formation of the hydrogen bonds with participation of both hydrogen atoms, can not only solvate OCH_3 and especially $N(CH_3)_2$ group more effectively than alcohol that weaken their conjugation with the group N→O (structure of A type), but also to form addition products of B type, the probability of existence of the latter must grow with an increase in the concentration of *N*-oxide.

However, weakening of the conjugation between the functional groups N→O and $N(CH_3)_2$ in the molecules of 4-DPyO, 2-DQO and 4-DQO in the aqueous phase (compared to chloroform) must lead to leveling of their ΔpK_a values or even to the larger basicity of $N(CH_3)_2$ enhancing during the addition of acid the protonation of just this center. Actually, in the electron spectra of these compounds dissolved in hydrochloric or sulfuric acid is observed even larger short-wave shift (Table 6), caused by the formation of mono- [at the $N(CH_3)_2$ group] or diprotonated (for example, in the conc. HCl) structures.





At dissolving 4-DPyO·HCl (protonated at the oxygen atom of N→O group) in water are formed monoprotonated at the $N(CH_3)_2$ form, as is confirmed by the chemical shift of protonated $N(CH_3)_2$ groups (δ 3.37 ppm, 6H, singlet) in the spectrum PMR of its saturated solution in D_2O (Table 3); whereas for 4-DPyO in $CDCl_3$ and DMSO (dimethyl sulfoxide)-d_6, and also for 4-DPyO·HCl in DMSO-d_6 chemical shift δ 3.00 ppm is registered.

Further we assume a detailed study of the influence solvent nature on the equilibrium processes in the solutions of styryl derivatives and their hydrochlorides.

EXPERIMENTAL

The IR spectra were taken on a Specord M-80 instrument from the KBr tablets, electronic spectra on a SF-2000-02 instrument. The ^1H NMR spectra of

hydrochlorides and complexes with BF_3 were registered at room temperature (internal reference TMS) on Bruker AC 200, WM 400 and DAX 500 instruments. The 4-MeOStPyO *N*-oxides [the *N*-oxide of *trans*-4-(4-methoxystyryl) pyridine], 4-DPyO, 2-DQO and 4-DQO were synthesized by methods [11–13] described earlier. Their hydrochlorides of composition 1:1 and 1:2 were obtained by passing hydrogen chloride through the saturated solutions of *N*-oxides in chloroform. The precipitates formed were washed with chloroform and dried in a vacuum. In view of the fact that the dihydrochlorides 4-DPyO·2HCl and 2-DQO·2HCl are much less stable than monohydrochlorides and they easily loses the second proton even in the presence of as weak base as water (4-DPyO·2HCl in air very rapidly acquires pink nuance), these complexes were obtained by reaction of *N*-oxides with dry gaseous HCl in the the anhydrous $CHCl_3$. The completeness of complex formation was monitored by the method of electron spectroscopy in view of a good resolution of the absorption maxima of *N*-oxides and respective mono- and dihydrochlorides.

The composition of molecular complexes was determined by the titration with aqueous 0.01 N NaOH solutions in the presence of methyl red. The molecular complexes of *N*-oxides with BF_3 were obtained as described in the work [5].

REFERENCES

1. Andreev, V.P. and Ryzhakov, A.V., *Khim. Geterotsikl. Soed*., 1994, no. 8, p. 1087.
2. Ryzhakov, A.V., Andreev, V.P., and Rodina, L.L., *Heterocycles*, 2003, vol. 60, no. 2, p. 419.
3. Andreev, V.P., *Doctorate Sci. (Chem.) Dissertation*, Petrozavodsk, 2007.
4. Korzhenevskaya, N.G. and Rybachenko, V.I., *Zh. Obshch. Khim*., 1999, vol. 69, no. 3, p. 437.
5. Andreev, V.P., Batotsyrenova, E.G., Ryzhakov, A.V., and Rodina, L.L., *Khim. Geterotsicl. Soed*., 1998, no. 8, p. 1093.
6. Volkova, T.O., and Nemova, N.N., *Molekulyarnye mekhanizmy apoptoza leikoznoi kletki* (Molecular Mechanisms of Cell Apoptosis), Moscow: Nauka, 2006.
7. Gur'yanova, E.N., Gol'dshtein, I.P., and Romm, I.P, *Donorno-aktseptornaya svyaz'* (Donor–Acceptor Bonding), Moscow: Khimiya, 1973.
8. Pentimalli, L., *Gazz. Chim. Ital*., 1963, vol. 93, p. 1093.
9. Wang, S. and Ho, T., *J. Photochem. Photobiol., A: Chem*., 2000, vol. 135, p. 119.
10. Wang, S. and Ho, T., *Chem. Phys. Lett*., 1997, vol. 268, p. 434.
11. Brink, C.v.d. M. and de Jager, P.J., *Tydskr. Natuurwet*., 1963, vol. 3. no. 2, p. 74.
12. Titskii, G.D. and Turovskaya, M.K., SSSR Inventor's Sertificate no. 1599366, *Byul. Izobrer*., 1990.
13. Andreev, V.P., Ryzhakov, A.V., and Tekanova, S.G., *Khim. Geterotsicl. Soed*., 1995, no. 4, p. 518.