N-Oxides of polychloropyridines. ^{13}C NMR study

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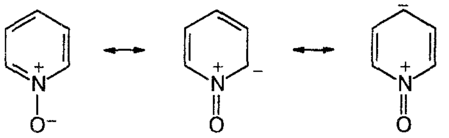
The effect of *N*-oxidation of a series of polychloropyridines on ^{13}C NMR parameters has been studied. It has been established that in *N*-oxides of polychloropyridines an electric field through-space effect of the *N*-oxide group predominates in the shielding of the γ-carbon atom compared to the other carbon atoms. A linear correlation between ^{13}C NMR chemical shifts and total charge densities calculated by the MNDO method for the carbon atoms of *N*-oxides of polychloropyridines has been found.

Key words: ^{13}C NMR, ^{13}C—^{1}H NMR coupling constants, MNDO method, *N*-oxides of polychloropyridines.

The dual, donor-acceptor character of the N→O bond has led to theoretical and experimental studies of *N*-oxides of pyridines.[1—12] According to the data of ^{1}H (Ref. 2) and ^{13}C (Refs. 3—8) NMR spectroscopy, ^{14}N and ^{17}O (Ref. 10) NQR, and quantum chemical calculations by the CNDO (Refs. 3, 5, and 7) and *ab initio* (Ref. 9) methods, the electron structure of pyridine *N*-oxide can be considered as the superposition of resonance forms with predominance of quinoid structures.[1—10]

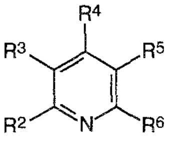


I **Ia** **Ib**

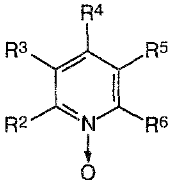
The introduction of electron-donating or electron-accepting substituents into the pyridine ring exerts a considerable effect on the contribution of one or another form to the total resonance hybrid.[10]

However, this description of resonance hybrid **I** is not indisputable. The literature data concerning possible realization of quinoid forms of pyridine *N*-oxide are contradictory. In particular, it has been reported that the values of the C=N [11] and C(2)—C(3)[12] bond lengths are inconsistent with the existence of these forms. However, the *ab initio* calculations of the electron structure of pyridine *N*-oxide indicate a strong conjugation of the *N*-oxide group with the pyridine ring resulting in the *para*-quinoid influence.[8]

In this work, the ^{1}H and ^{13}C NMR parameters of polychloro-substituted pyridines (**1**—**8**) and their *N*-oxides (**1a**—**8a**) are analyzed and compared, and the effect of the *N*-oxide group on the electron density distribution in the pyridine ring is studied.



1—8



1a—8a

1: $R^2 = R^3 = R^5 = R^6 = H$, $R^4 = Cl$
2: $R^2 = R^5 = Cl$, $R^3 = R^4 = R^6 = H$
3: $R^2 = R^6 = Cl$, $R^3 = R^4 = R^5 = H$
4: $R^2 = R^4 = R^6 = H$, $R^3 = R^5 = Cl$
5: $R^2 = R^3 = R^5 = Cl$, $R^4 = R^6 = H$
6: $R^2 = R^3 = R^6 = Cl$, $R^4 = R^5 = H$
7: $R^2 = R^3 = R^5 = R^6 = Cl$, $R^4 = H$
8: $R^2 = R^3 = R^4 = R^5 = R^6 = Cl$

^{1}H NMR signals were assigned on the basis of the literature data[2] and with account of ^{1}H—^{1}H coupling constants. The upfield shift of the H(4) proton (by 0.35—0.5 ppm) is the most noticeable on going from pyridines **1**—**8** to their *N*-oxides **1a**—**8a**. Insignificant shifts of H(2) and H(6) (except those of **5a**) to the higher field and those of H(3) and H(5) to the weak field are also observed (Table 1). The high-field signals of H(3) and H(4) in compound **2a** are easily discernible, because H(4) undergoes the spin-spin interaction with H(6) ($^{4}J_{4,6}$ = 2.2 Hz). The H(4) and H(5) signals in compound **6a** are identified, taking into account the general tendency in changes in the chemical shifts in ^{1}H NMR spectra in this series.

The ^{13}C NMR signals of compounds **1**—**8** and **1a**—**8a** were assigned, taking into account the broaden-

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Table 1. ^{13}C and ^{1}H NMR chemical shifts (δ) of compounds **1—8** and **1a—8a**

Compound	Type of δ	C-2	C-3	C-4	C-5	C-6
1*	δ_C	151.09	124.06	142.87	124.06	151.09
	δ_H	8.60	7.56	—	7.56	8.60
1a	δ_C	139.99	126.30	131.91	126.30	139.99
	δ_H	8.15	7.29	—	7.29	8.15
2	δ_C	149.20	124.94	138.26	130.72	148.21
	δ_H	—	7.29	7.64	—	8.35
2a	δ_C	140.62	126.53	126.02	131.18	139.56
	δ_H	—	7.41	7.18	—	8.32
3	δ_C	150.39	122.76	140.68	122.76	150.39
	δ_H	—	7.29	7.67	7.29	—
3a	δ_C	143.31	124.99	124.41	124.99	143.31
	δ_H	—	7.51	7.20	7.51	—
4	δ_C	146.42	131.90	135.28	131.90	146.42
	δ_H	8.46	—	7.70	—	8.46
4a	δ_C	137.11	132.88	125.59	132.88	137.11
	δ_H	8.07	—	7.20	—	8.07
5	δ_C	147.00	130.56	137.77	130.56	145.67
	δ_H	—	—	7.80	—	8.28
5a	δ_C	140.84	132.30	126.11	129.78	137.78
	δ_H	—	—	7.39	—	8.32
6	δ_C	148.22	129.43	140.64	123.84	148.01
	δ_H	—	—	7.74	7.26	—
6a	δ_C	143.45	130.79	125.20	123.30	141.65
	δ_H	—	—	7.29	7.45	—
7	δ_C	145.91	129.59	140.08	129.59	145.91
	δ_H	—	—	7.89	—	—
7a	δ_C	142.19	129.46	125.48	129.46	142.19
	δ_H	—	—	7.51	—	—
8	δ_C	146.41	129.57	144.61	129.57	146.41
8a	δ_C	142.36	129.50	129.70	129.50	142.36

* See Ref. 13.

Table 2. Values of $^{1}J_{^{13}C-^{1}H}$/Hz of compounds **1—8** and **1a—8a**

Compound	C-2	C-3	C-4	C-5	C-6
1*	182.1	170.5	—	170.5	182.1
1a	190.01	171.1	—	171.1	190.0
2	—	173.7	170.6	—	189.2
2a	—	173.8	177.3	—	193.8
3	—	172.8	167.4	172.8	—
3a	—	173.0	172.5	173.0	—
4	186.2	—	169.5	—	186.2
4a	196.0	—	179.8	—	196.0
5	—	—	173.3	—	190.7
5a	—	—	180.2	—	196.6
6	—	—	168.9	172.9	—
6a	—	—	177.7	178.0	—
7	—	—	174.4	—	—
7a	—	—	180.6	—	—

* See Ref. 13.

ing of the signals of α-carbon atoms, their intensities, and the literature data on chemical shifts of pyridines[13] and their *N*-oxides,[2—8] and on the basis of the analysis of ^{13}C—^{1}H coupling constants of proton-coupled spectra.

The C(2) and C(6) signals are broadened in the ^{13}C NMR spectra of compounds **1a—8a**. The width of the signal of the carbon nucleus directly bonded to the ^{14}N atom depends on the value of coupling constant J_{N-C} and quadrupole relaxation rate of ^{14}N.[4] The narrow lines of α-carbon atoms in the ^{13}C NMR spectra of pyridines are explained by the fact that the J_{N-C} value is close to zero.[14] At the same time, relatively high values of ^{14}N—^{13}C coupling constants are typical of α-carbon atoms of all pyridine derivatives that have no uncoupled electron pairs on the N atom,[4] which likely appears as broadening of the ^{13}C NMR signals of α-C atoms in compounds **1a—8a**. Quadrupole broadening of the lines did not allow us to analyze in detail long-range ^{13}C—^{1}H coupling; therefore, we considered only ^{13}C—^{1}H coupling constants through one bond (Table 2). All compounds **1a—8a** are characterized by an increase in the values of $^{1}J_{C-H}$ coupling constants compared to the corresponding values for pyridines **1—8**. Similar changes in $^{1}J_{C-H}$ were described for various aromatic heterocycles upon their *N*-oxidation or *N*-methylation, when the positive charge appears on the N atom.[4] The change in the $^{1}J_{C-H}$ value in the series $\Delta^{1}J$(C-γ) > $\Delta^{1}J$(C-α) > $\Delta^{1}J$(C-β) is likely caused by different polarities of bonds, which affects the "effective nuclear charge"[15] on C atoms. An increase in $^{1}J_{C-H}$ of pyridine *N*-oxides is also observed, when electronegative substituents, which increase the polarity of bonds involving the atom considered and its effective charge, are introduced to the pyridine ring.[6] In our case, an increase in the number of Cl atoms in the pyridine ring in compounds **1a—8a** results in an increase in the values of $^{1}J_{C-H}$ coupling constants for α- and β-C, unlike for γ-C (see Table 2). Taking into account the inductive character of the electron-accepting effect of substituents,[6,15] one can suppose that in the case of γ-C, unlike the other C atoms, the induction effect of Cl on the effective nuclear charge of the C(4) atom is not predominant.

The comparison of ^{13}C NMR chemical shifts of pyridines **1—8** and the corresponding *N*-oxides **1a—8a** (Table 3) testifies that rather strong α- and γ-effects and weak β-effects are observed in all *N*-oxides. This is consistent with the data for the pyridine—pyridine *N*-oxide pair.[5] The considerable upfield shift of C(4) on going from pyridines **1—8** to their *N*-oxides **1a—8a**, related to an increase in the electron density on this C atom, testifies that the contribution of form **Ib** to resonance hybrid **I** is considerable. The lower values of the changes in chemical shifts of C(3) and C(5) can be explained by the resonance polarization effect,[3] which is due to an increase in the electron density on α- and γ-C resulting in its decrease on β-C. Of the four main

Table 3. Effect of *N*-oxidation on ^{13}C NMR chemical shifts (ppm) of the compounds studied*

Effect	C atom	**1/1a**	**2/2a**	**3/3a**	**4/4a**	**5/5a**	**6/6a**	**7/7a**	**8/8a**
α	C-2	−11.10	−8.58	−7.08	−9.31	−6.16	−4.77	−3.72	−4.05
	C-6	−11.10	−8.65	−7.08	−9.31	−7.89	−6.36	−3.72	−4.05
β	C-3	2.24	1.59	2.23	0.98	1.86	1.36	−0.13	−0.07
	C-5	2.24	0.46	2.23	0.98	−0.78	−0.54	−0.13	−0.07
γ	C-4	−10.96	−12.24	−16.27	−9.69	−11.66	−15.44	−14.60	−14.91

Note. The "minus" sign denotes an upfield shift.
* $\Delta(\delta(C)) = \delta(C_{PyNO}) - \delta(C_{Py})$.

parameters of the electron effect of substituents (*N*-oxide group, in our case) on ^{13}C NMR chemical shifts (the field (σ_F), resonance (σ_R), and induction ($\sigma_{æ}$) effects and the polarization ability (σ_α)[16]), the changes in chemical shifts of C(4) should depend to a great extent on the σ_F and σ_R parameters, while all four factors should affect the chemical shifts of α- and, to a lesser extent, β-C. The *N*-oxide group can also be considered as a polar substituent[16] with weak electron-accepting and strong π-donating effects[6] and a strong through-space field effect.[2] According to the results of the analysis of the ^{14}N and ^{17}O NQR data by the Townes—Dailey method,[10] the main axis of the electric field gradient is directed along the N—O bond in molecules of pyridine *N*-oxide and its 4-substituted derivatives. In our case, when the total electron-accepting character of substituents increases, *i.e.*, on going from **1a** to **8a**, the absolute values of the α- and β-effects decrease, while that of the γ-effect remains relatively unchanged (see Table 3). This can be related to the predominant mechanism of the through-space transfer of the N—O dipole effect[16] in the case of the γ-effect, because an increase in the total electron-accepting character of substituents in the pyridine ring as the number of Cl atoms increases inevitably influences the π-resonance effect. Taking into account that in the majority of cases the σ_F factor depends on the σ_R, $\sigma_{æ}$, and σ_α parameters,[16] one can draw a conclusion that the *para*-effect of the N—O group is a case of the direct influence of σ_F. This can explain the described[6] effect of the considerable change in ^{13}C NMR chemical shifts of γ-C of pyridine *N*-oxide upon the protonation of the N—O group.

Thus, the through-space field effect of the N—O group plays the main role in shielding of γ-C in pyridine *N*-oxides **1a—8a**, while all the other aforementioned electronic factors of the substituent effects are significant for the other C atoms.

The results of the calculations by the MNDO method[17] of the electron density of the compounds studied are presented in Table 4. The electron densities on the C nuclei of the pyridine ring have been calculated by the CNDO method in several works, and a satisfactory linear correlation of ^{13}C NMR chemical shifts with total charges on atoms has been established for various derivatives of pyridine *N*-oxide.[3,5,7] The linear relationship between the electron density on C atoms and their chemical shifts (r = 0.893, n = 30), $\delta_C = 574.06 - 112.99\,q_t$, was also established for compounds **1a—8a**.

Table 4. Results of MNDO calculations of the total charges q_t on C and N atoms of compounds **1—8** and **1a—8a**

Compound	C-2	C-3	C-4	C-5	C-6	N
1	3.9099	4.0306	3.8745	4.0306	3.9099	5.2858
1a	3.9123	4.0024	3.8898	4.0024	3.9123	4.8191
Δ	0.0024	−0.0282	0.0153	−0.0282	0.0024	−0.4667
2	3.7998	4.0252	3.9621	3.9358	3.8931	5.2674
2a	3.8133	3.9997	3.9782	3.9088	3.9007	4.8063
Δ	0.0244	−0.0255	0.0161	−0.0270	0.0076	−0.4611
3	3.8013	4.0249	3.9734	4.0249	3.8013	5.2553
3a	3.8162	3.9994	3.9901	3.9994	3.8162	4.7977
Δ	0.0149	−0.0255	0.0167	−0.0255	0.0149	−0.4576
4	3.8927	3.9355	3.9515	3.9355	3.8927	5.2791
4a	3.8986	3.9087	3.9672	3.9087	3.8986	4.8141
Δ	0.0059	−0.0268	0.0157	−0.0268	0.0059	−0.4650
5	3.7874	3.9230	3.9488	3.9326	3.8880	5.2637
5a	3.8034	3.8977	3.9669	3.9063	3.8980	4.8031
Δ	0.0160	−0.0253	0.0181	−0.0263	0.0100	−0.4606
6	3.7882	3.9226	3.9595	4.0217	3.7963	5.2521
6a	3.8056	3.8976	3.9781	3.9966	3.8135	4.7953
Δ	0.0174	−0.0250	0.0186	−0.0251	0.0172	−0.4568
7	3.7835	3.9206	3.9462	3.9206	3.7835	5.2495
7a	3.8035	3.8952	3.9670	3.8952	3.8035	4.7934
Δ	0.0200	−0.0254	0.0208	−0.0254	0.0200	−0.4561
8	3.7817	3.9105	3.8457	3.9105	3.7817	5.2465
8a	3.8031	3.8851	3.8695	3.8851	3.8031	4.7908
Δ	0.0214	−0.0254	0.0238	−0.0254	0.0214	−0.4557

According to our data, *N*-oxidation results in an increase in the electron density on C(2), C(4), and C(6) and its decrease on C(3) and C(5), which agrees well with the changes in ^{13}C NMR chemical shifts on going from pyridines **1—8** to their *N*-oxides.

Experimental

Compounds **2—6** were obtained by the oxidation of the starting di- and trichloropyridines with 30 % hydrogen peroxide in trifluoroacetic acid.[18—20] Compounds **7** and **8** were synthesized by the oxidation of tetra- and pentachloropyridine with 90—95 % hydrogen peroxide in a mixture of sulfuric and acetic acids.[21]

^1H and ^{13}C NMR spectra of compounds (50—100 mg mL^{-1}) in $CDCl_3$ were recorded on a Bruker AC-200 instrument (200.13 and 50.33 MHz, respectively) at -20 °C (l = 5 mm, $SiMe_4$ as an internal standard). The standard POWGATE and GATEDEC subprograms were used in recording ^{13}C NMR spectra, and the spectrum width was 12000 Hz. $^{13}C—^1H$ coupling constants were measured after increasing the number of data points with the final digital resolution of 0.18 Hz.

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