SUBSTITUENT EFFECT ON RING PROTON CHEMICAL SHIFTS IN PMR SPECTRA OF MONOSUBSTITUTED PYRIDINES

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The relative chemical shifts of ring protons in PMR spectra of 2-, 3-, and 4-monosubstituted pyridines (in DMSO-D_6) are correlated with the F- and R-constants of the substitutents by using a two-parameter approach. Transmission factors characterizing the transfer of inductive and resonance effects in pyridine, pyrimidine, and s-triazine rings are analyzed.

The PMR spectra of monosubstituted pyridines have been used to study the transmission of substituent electronic effects in azaaromatic systems. Correlation of the pyridine ring proton chemical shifts (CS) with substituent electronic effects has been attempted several times [1-12]. Even the first systematic study of PMR spectra for a wide range of substituted pyridines showed a complex quantitative description of the ring proton CS [1]. A rough correlation of CS with Hammett sigma values of substituents in the 2-position was found only for the 5-H proton [4, 5]. The CS for the 4-H proton in a series of 2-substituted pyridines was qualitatively correlated with the substituent σ_m-constants, but significant deviations were observed for cyano-, bromo-, and chloro-derivatives in strong fields [3]. The different transmission of substituent electronic effects through the heterocyclic ring, leading to variation in the ratio of inductive and conjugative components of the Hammett values, is believed to be responsible for the unsuccessful correlations [8]. Regression analysis with two variable parameters σ_I and σ_R^o, separately describing inductive and resonance substituent effects, raises the correlation coefficients to 0.92-0.97 [10]. The quality of the correlations may also be affected by variation in the CS values used in [10] and by the neglect of effects other than electronic.

Refined CS of aromatic protons in PMR of 2- (I), 3- (II), and 4-monosubstituted (III) pyridines (Table 1) were measured in 1 M solutions in DMSO-D_6 [13, 14]. Use of DMSO solvent somewhat expands the CS scale of the aromatic protons [15] and also excludes solvation effects In the present work, regression analysis of the relative CS ($\Delta\delta$) for meta- and para-protons (relative to the substituent) given in Table 1 is carried out using the F- and R-constants [16] for a standard set of substituents as the variable parameters. Moreover, corrections for the magnetic anisotropy of the substituents and the change of aromatic ring anisotropy on introduction into it of substituents are included in the CS of meta-protons ($\Delta\delta'$). The corrections were estimated empirically [15] by comparing the relative CS of meta-protons of benzene in solvents with very different polarities. We demonstrated earlier that use of these corrections is valid in a series of substituted azaaromatic pyrimidines and triazines [17, 18]. Accounting for the corrections raises the correlation coefficients in three of the four pyridine meta-series (Table 2).

The two-parameter correlation of the relative CS of the aromatic protons with the F- and R-constants of the substituents can estimate the contributions to electronic effects of the inductive and conjugative components in the pyridine series. Also, the contributions for related pyridine and benzene series can be correlated by expressing them as transmission factors γ_I and γ_R (Table 2). Weakening of the inductive effect in pyridine compared to benzene is observed only in two series (Eqs. 3 and 8). A similar result was obtained earlier for the 2-H proton in 4- and 5-substituted pyrimidines and 4-H in 2-substituted

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*Deceased.

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TABLE 1. Chemical Shifts for para- and meta-Protons of the Pyridine Ring, ppm, Compounds I-III

Substituent	para-Protons I		meta-Protons I						para-Protons II		meta-Protons II			meta-Protons III		
	$\delta_{5\text{-}H}$	$\Delta\delta_{5\text{-}H}$	$\delta_{4\text{-}H}$	$\Delta\delta_{4\text{-}H}$	$\Delta\delta'_{4\text{-}H}$	$\delta_{6\text{-}H}$	$\Delta\delta_{6\text{-}H}$	$\Delta\delta'_{6\text{-}H}$	$\delta_{6\text{-}H}$	$\Delta\delta_{6\text{-}H}$	$\delta_{5\text{-}H}$	$\Delta\delta_{5\text{-}H}$	$\Delta\delta'_{5\text{-}H}$	$\delta_{2\text{-}H}$	$\Delta\delta_{2\text{-}H}$	$\Delta\delta'_{2\text{-}H}$
$N(CH_3)_2$	6,556	0,839	7,486	0,309	0,259	8,089	0,515	0,465	7,901	0,703	7,165	0,230	0,180	8,125	0,479	0,429
OCH_3	6,977	0,418	7,702	0,093	0,043	8,189	0,415	0,365	8,189	0,415	7,339	0,056	0,006	8,417	0,187	0,137
CH_3	7,174	0,221	7,667	0,128	0,078	8,458	0,146	0,096	8,393	0,211	7,282	0,113	0,063	8,444	0,160	0,110
H	7,395	0,000	7,795	0,000	0,000	8,604	0,000	0,000	8,604	0,000	7,395	0,000	0,000	8,604	0,000	0,000
Cl	7,446	−0,051	7,895	−0,100	−0,270	8,457	0,147	−0,023	8,571	0,033	7,482	−0,087	−0,257	8,599	0,005	−0,165
Br	7,478	−0,083	7,791	0,004	−0,216	8,433	0,171	−0,049	8,596	0,008	7,419	−0,024	−0,244	8,505	0,099	−0,121
$COCH_3$	7,685	−0,290	8,023	−0,228	−0,208	8,756	−0,152	−0,132	8,822	−0,218	7,586	−0,191	−0,171	8,838	−0,234	−0,214
$COOCH_3$	7,690	−0,295	8,041	−0,246	−0,316	8,773	−0,169	−0,239	8,857	−0,253	7,600	−0,205	−0,275	8,838	−0,234	−0,304
CN	7,784	−0,389	8,101	−0,306	−0,406	8,802	−0,198	−0,298	8,897	−0,293	7,660	−0,265	−0,365	8,879	−0,275	−0,375
NO_2	7,954	−0,559	8,309	−0,514	−0,514	8,737	−0,133	−0,133	9,006	−0,402	7,771	−0,376	−0,376	9,008	−0,404	−0,404

TABLE 2. Parameters of Correlation Equation $\Delta\delta(H) = fF + rR + c$

Equation*	Structure	Resonating proton	Parameters of the equation					γ_I	γ_R
			f	r	c	R	s		
			para-Substitution						
1 [15]	XC_6H_5	4-H	−0,54	−0,88	0,012	0,991	0,053	1,00	1,00
2	I	5-H	−0,62	−0,94	0,056	0,996	0,043	1,15	1,07
3	II	6-H	−0,41	−0,81	0,019	0,992	0,048	0,76	0,92
			meta-Substitution						
4 [15]	XC_6H_5	3-H	−0,53	−0,27	−0,030	0,980	0,042	1,00	1,00
5	I	4-H	−0,55	−0,42	0,030	0,962	0,075	—	—
6	I	4-H	−0,69	−0,35	0,011	0,989	0,041	1,30	1,30
7	I	6-H	−0,04	−0,66	0,008	0,969	0,070	—	—
8	I	6-H	−0,18	−0,60	−0,011	0,956	0,082	0,34	2,22
9	II	5-H	−0,44	−0,31	0,021	0,973	0,048	—	—
10	II	5-H	−0,58	−0,25	0,002	0,978	0,046	1,09	0,93
11	III	2-H	−0,39	−0,58	0,025	0,970	0,073	—	—
12	III	2-H	−0,53	−0,52	0,006	0,993	0,035	1,00	1,93

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*Equations 4, 6, 8, 10, and 12 include corrections from [15].

pyrimidines and s-triazines [17-19]. The greatest weakening of the inductive effect is observed for the fragment X—C⋯N⋯C—H, when the resonating proton and X substituent are located in the α-positions of the pyridine ring ($\gamma_I = 0.35$).

The electric dipole and magnetic anisotropy of the azafragment are known to influence the magnetic shielding of protons in the pyridine ring [20, 21]. Calculations show [20] that the electrostatic and anisotropic effects of the azafragment on the α-proton shielding (−0.52 and −0.33 ppm, respectively) significantly surpass those on the β- and γ-positions (−0.19 and −0.01 ppm; −0.14 and 0.03 ppm). The changes in the contributions under the influence of substitutents are important in examining the relative proton CS. These changes are assumed to have smaller values than the total contributions. Since an orbital of the azafragment is orthogonal to the orbitals of the π-system, its population is affected mainly by substituent inductive properties. For example, the kinetic and thermodynamic parameters for reactions at the ring nitrogen atom correlate best with the σ_I and σ_m-constants of the substituents [22, 23]. Hence, the decrease of the paramagnetic influence due to the azafragment electrostatic effect is expected to be maximal for α-substituents with a large −I-effect. Moreover, these substituents have a direct influence on the electron density at the hydrogen atoms, leading to deshielding. The influence of substituents on the magnetic anisotropy of the azafragment is very difficult to estimate. The sharp decrease of the γ_I factor for the 6-H proton in a series of 2-substituted pyridines is probably explained by compensation due to these effects. The transmission factors γ_I through the nitrogen increase for meta-directing substituents in 2- and 4-substituted pyrimidines (0.79 and 0.60) and s-triazines (0.88) [18]. Such a relative growth of transmission factors probably occurs for two reasons. First, the direct field effect of the 2-X substituents on the local diamagnetic shielding of the 6-H proton can strengthen due to the spatial approach of the 2- and 6-positions in pyrimidine and triazine rings. Second, the free electron pairs of the azafragments are less sensitive to the influence of substituents due to a decreased population of the orbitals orthogonal to the π-system [24] and a variation of the electrostatic factor in the pyrimidine and triazine series becomes less noticeable. For other pyridine series, where this azafragment effect is smaller, the transmission factors $\gamma_I \geq 1$.

The transmission factors γ_R, which characterize substituent resonance effects, vary over a wide range (0.93-1.93) for the pyridine meta-series. The 3- and 5-positions in the pyridine ring are frequently likened to those in benzene. The electronic influence of pyridine substituents in the 3-position on the 5-position are similar to meta-substituents in the benzene ring. The value 0.93 for series II agrees with this concept. Transfer of substituent resonance effects increases sharply from the even positions of the pyridine ring, with α-substitution, by 1.3 times; with γ-substitution, by 1.9 times. Such a difference is explained by the more effective conjugation of the γ-substituents than the α-substituents with the heterocyclic π-system. This transfer of resonance effects from the 2-position into the 4-position and vice-versa is not equivalent for the π-system of pyridine and for other azine systems (Az). Summarizing the data for a single structural series in a number of pyridines, pyrimidines, and s-triazines [18], it can be shown that the heteroatoms proportionally change the transfer of resonance effects of the meta-substituents through the aromatic ring:

$$\gamma_{R(\mathrm{Az})} = \prod^{i} \gamma_{R(\mathrm{N}i)}.$$

In this expression, the following $\gamma_{R(Ni)}$ values are valid: for α-substituents relative to the heteroatom $\gamma_{R(2\text{-}N)} = 1.35 \pm 0.05$; for the β-position, $\gamma_{R(3\text{-}N)} = 0.95 \pm 0.05$; for the γ-position, $\gamma_{R(4\text{-}N)} = 2.0 \pm 0.1$. The only exception is for the 6-H—2-X-pyridine series, for which the electrostatic influence of the azafragment on the transfer of substituent effects is substantial.

The difference in transfer of resonance effects through the heterocyclic rings in the forward and reverse directions is observed not only in the meta- but also in the para-series. Thus, γ_R in series I exceeds γ_R in series II, analogous to that which was found earlier for the pyrimidine ring [19].

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SYNTHESIS OF ALKALI AND HEAVY METAL DITHIO- AND THIOCARBAMATES BASED ON N-(β-AMINOETHYL)PIPERAZINE

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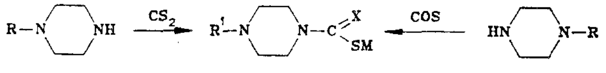
A series of alkali and heavy metal dithio- and thiocarbamates based on N-(β-aminoethyl)piperazine and its derivatives N-(β-piperazinoethyl)imides, N-[(β-2,5-dimethyl-1-pyrrolyl)ethyl]piperazine, and N-(β-salicylideneaminoethyl)-piperazine is prepared. Methods for preparation of dithio- and thiocarbamates based on piperazine are improved. Alkali metal dithio- and thiocarbamates based on piperazines form polymeric complexes with heavy metals.

Reaction of piperazines [1], including N-(β-aminoethyl)piperazine [2], and derivatives with carbon disulfide and carbonyl sulfide to prepare complexing agents and stabilizers for polymers and pesticides generates interest in the production of piperazines.

The reaction of cyclic polyamines and their derivatives with CS_2 and COS has been studied little. The reaction of piperazine Ia with carbon disulfide and NaOH leads to sodium piperazine-N,N'-bisdithiocarboxylate (IIa) [3]. Compound IIa can be prepared by reaction of piperazine Ia with CS_2 in water or alcohol with subsequent neutralization by NaOH. Under these conditions, piperazine Ia and N-(β-aminoethyl)piperazine (Ib) form the corresponding dithiocarbamates IIb-f with yields greater than 80%.



Ia,b IIa, f; IIIa, b

Ia R=H, b $R=(CH_2)_2NH_2$; IIa–c, IIIa $R'=C(=X)SM$, IId–f IIb $R'=(CH_2)_2NH-C(=X)SM$; IIa–f X=S, IIIa,b X=O; IIa,d IIIa,b M=Na, IIb, e M=K, c,f $M=NH_4$

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