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New Basicity/Nucleophilicity Scale on the Basis of Parameters of Formation of Axial *n*,ν-Complexes Derived from Tetraphenylporphyrinatozinc(II) and Base/Nucleophile as Ligand

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Abstract—The stability constants of complexes derived from tetraphenylporphyrinatozinc(II) and various ligands in chloroform at 25°C were proposed as nucleophilicity/basicity parameters of the latter, which reflect the effects of electronic and steric factors. Supernucleophilicity of heteroaromatic *N*-oxides in reactions with electrophiles was interpreted in terms of sp^2–sp^3 rehybridization of the *N*-oxide oxygen atom.

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Although nucleophilicity and basicity of pyridine *N*-oxides were the subject of numerous studies, factors responsible for their much higher reactivity (supernucleophilicity) despite considerably lower basicity, as compared to pyridines, remain so far not clear [1]. Metal porphyrin complexes are very convenient model systems for studying complex formation by electronic absorption, IR, and NMR spectroscopy. From this viewpoint, the formation of *n*,ν-complexes with tetraphenylporphyrinatozinc(II) (Zn-TPP) in aprotic solvents may be selected as model process for studying the effect of electronic and steric factors in molecules of oxygen- and nitrogen-containing compounds (e.g., *N*-oxides) on their reactivity (nucleophilicity and basicity). Tetraphenylporphyrinatozinc(II) is readily accessible and is characterized by fairly simple spectra (due to symmetric structure of the molecule) which change to an appreciable extent upon formation of axial complexes.

Complexation of Zn-TPP with a ligand L (the composition of the complex thus formed depends on the ligand nature and reaction conditions) largely resembles nucleophilic substitution reaction. In both processes, the nucleophile (ligand) may be an anion or neutral molecule possessing at least one unshared electron pair (i.e., Lewis base), and the replaced (departing) group may be both anionic and neutral species.

$$\text{Zn-TPP} \underset{-L}{\overset{L}{\rightleftharpoons}} \text{Zn-TPP}\cdot\text{L} \underset{-L}{\overset{L}{\rightleftharpoons}} \text{Zn-TPP}\cdot 2\text{L} \quad (1)$$

$$\text{RX} \underset{X^-}{\overset{-X^-}{\rightleftharpoons}} \text{R}^+ \underset{-Y^-}{\overset{Y^-}{\rightleftharpoons}} \text{RY} \quad (2)$$

Nucleophilic substitution at an sp^3-hybridized carbon atom can follow both dissociative [S_N1, reaction (2)] and synchronous mechanism [S_N2, reaction (3)].

$$Y^- + RX \rightleftharpoons [Y^{\delta-}\cdots R\cdots X^{\delta-}]^{\neq} \rightleftharpoons YR + X^- \quad (3)$$

In both cases, the reverse process is possible. It should be emphasized that both the coordination entity in Zn-TPP or carbocation with the sp^2-hybridized carbon atom [S_N1 mechanism; the first step in reaction (1) and the second step in (2)] and the activated complex in which the hybrid state of the carbon atom is close to sp^2 [2] [S_N2; the second step in (1) and the first step in (3)] have planar structure. Therefore, these nucleophilic substitution reactions can be regarded as equilibrium processes involving competing interactions of a complexing agent (carbocation, S_N1) with two different ligands or decomposition of a complex containing two different ligands (activated complex, S_N2). On the other hand, the complexation process is similar to substitution (exchange) reaction with 1:1 (Zn-TPP·L) or 1:2 complex (Zn-TPP·2L) where the

nucleophile and departing group may be different or similar. Such analogy may be drawn for other nucleophilic processes, e.g., nucleophilic addition (A_N) to aldehydes and ketones and nucleophilic replacement in carboxylic acids and their derivatives (S_NAcyl), where the carbonyl carbon atom or carbon atom in the carbocation formed by protonation of the oxygen atom in acid medium also have planar configuration (sp^2). From this viewpoint, study on complex formation with Zn-TPP should provide a deeper insight into the effect of solvent and ligand nature on the state of equilibrium (1) and, correspondingly, on the composition, stability, and structure of the complexes thus formed. The latter can be isolated as individual substances and examined by X-ray diffraction. The results can be used to control nucleophilic processes.

Published data [3–6] and our results [7, 8] obtained by calorimetric titration, electronic absorption spectroscopy, and ^{1}H NMR experiments allowed us to presume that rise in the basicity/nucleophilicity of a ligand should be accompanied by increase in the stability of the corresponding 1 : 1 axial complexes with Zn-TPP. Extension of the distance between the zinc atom and macroring plane as a result of complexation should weaken deshielding of the 1-H–8-H protons in the porphyrin macroring (in the ^{1}H NMR spectra) and change electron density distribution and dipole moment; therefore, the electronic absorption spectra should also change. Here, assuming variation of at least electronic (and probably steric) factors for a series of structurally related ligands, the magnitudes of the above changes may be proportional to each other. Then the stability constants K, shifts $\Delta\lambda$ of the absorption maxima in the electronic spectra, and differences $\Delta\delta$ in the chemical shifts in the NMR spectra could be used as parameters characterizing the relative basicity/nucleophilicity of ligands.

In the present article we report on our attempt to apply the above approach to estimate the reactivity of ligands toward Brønsted–Lawry (H^+, basicity) and Lewis acids (nucleophilicity) and propose possible factors responsible for unusually high nucleophilicity of heteroaromatic *N*-oxides.

Tetraphenylporphyrinatozinc(II) was previously proposed [7] as reference for a scale of weak bases. As we showed in [8], shifts of the absorption maxima ($\Delta\lambda$) in the electronic spectra of Zn-TPP in chloroform upon complex formation with pyridine *N*-oxides (Table 1), quinoline *N*-oxides, and acridine *N*-oxides are linearly related to the logarithms of the stability constants of the corresponding complexes, pK_a values of the ligands in water and other solvents, and Hammett constants σ of substituents in the heteroring provided that there are no steric hindrances. Our data indicated that analogous relations are also fulfilled for six pyridine derivatives substituted at position *3* or *4*. Thus, in some cases previously unknown values of K and pK_a in various solvents, as well as substituent constants σ, can be calculated from shifts $\Delta\lambda$ of the absorption maxima of Zn-TPP induced by complex formation with the use of the corresponding correlation equations.

Analysis of the data in Table 1 gave the following correlations:

$$\log K = 0.32\,pK_a + 2.77,\ r = 0.987;$$
$$\log K = -1.10\,\sigma + 3.63,\ r = 0.993;$$
$$\log K = -0.71\,\sigma_{PyO} + 3.03,\ r = 0.988;$$
$$\log K = 0.23\,\Delta\lambda_{II} - 0.11,\ r = 0.992.$$

We also noted [8] that some deviation of the data for 3-methyl-4-nitropyridine *N*-oxide from the linear relations $\log K$—σ and $\Delta\lambda$—σ results from rotation of the nitro group with respect to the pyridine ring, which weakens conjugation between the nitro group and the aromatic system. On the other hand, 2-methyl-4-nitropyridine *N*-oxide, despite the presence of a methyl group in position *2* of the pyridine ring, well fits the above linear relations. This is hardly consistent with generally unusual behavior of reagents having a substituent in the *ortho* position of benzene ring or position *2* of pyridine or quinoline ring due to steric effect on the reaction center. Obviously, the methyl group in 2-methyl-4-nitropyridine *N*-oxide exerts only electronic effect on the reactivity of this compound. From the stability constant K of the Zn-TPP complex with 2-methyl-4-nitropyridine *N*-oxide we calculated the constant σ_{PyO} for methyl group in position *2* for a series of pyridine *N*-oxides using the formula $\log K = -0.71\,\sigma_{PyO} + 3.03$ with a view to elucidate how appropriate would be to use it in the correlations proposed for heteroaromatic *N*-oxides. The calculated substituent constant (–0.35) turned out to be much greater in absolute value than that found for methyl group in position *4* (–0.24) and especially in position *3* of the pyridine ring (–0.139) (Table 1). This means that the size of the 2-substituent is not significant and that its effect on the reactivity of 2-methyl-4-nitropyridine *N*-oxide is very specific: it cannot be rationalized in terms of common inductive effect. The presence of two methyl groups in 2,6-dimethyl-4-nitropyridine *N*-oxide

Table 1. Stability constants of tetraphenylporphyrinatozinc(II) complexes in chloroform at 25°C, shifts of absorption maxima in the electronic spectra of Zn-TPP upon complex formation, substituent constants, and pK_a values of pyridine *N*-oxides $RC_5H_4N\rightarrow O$

R in the ligand	*K*, l/mol	Δλ,[a] nm, Soret band/*II*	pK_a(H_2O) [8, 9]	σ [8, 9]	σ_{PyO} [8, 9]
4-MeO	2860±190	10.0/15.5	2.05	–0.268	–0.603
4-$Me_2NC_6H_4CH$=CH	2110±120	[b]/14.5	1.43 (N→O)	–0.15	–0.31
4-Me	1780±160	9.5/14.5	1.29	–0.17	–0.24
4-$MeOC_6H_4CH$=CH	1050±20	[b]/13.8	1.00	–0.03	–0.10
H	1040±55	8.5/13.5	0.79	0	0
4-Cl	618±18	9.5/12.7	0.36	+0.227	+0.206
4-NO_2	165±22	5.0/10.0	–1.7	+0.778	+1.19
3-Me-4-NO_2	346±17	6.5/11.5	–0.97	+0.778, –0.069	+1.19, –0.139
2-Me-4-NO_2	269±20	3.6/8.2	–0.967	–	+1.19,[c] –0.35
2,6-Me_2-4-NO_2	–	[d]	–0.86	–	–

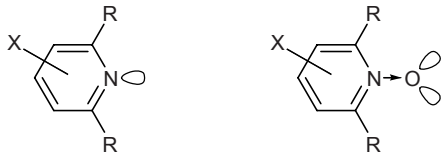
[a] Δλ for bands *I* and *III* are given in [3].
[b] Overlapped by the Soret band of metal porphyrin.
[c] The σ_{PyO} value at position *2* was calculated as described in text.
[d] Bands assignable to molecular complex were not detected.

is likely to increase steric hindrances to complexation with Zn-TPP so strongly than neither Δλ value nor stability constant *K* can be determined (the concentration of the complex is very small).

Pyridines, being much stronger bases than the corresponding *N*-oxides but having spatially less accessible reaction center (nitrogen atom), display a different pattern [5]. As follows from the data in Table 2, the stability constants determined by electronic and fluorescence spectroscopy (they coincided within the experimental error) in toluene for the complexes with Zn-TPP and octaethylporphyrinatozinc(II) (Zn-OEP) decrease in the series 4-methylpyridine > 3-methylpyridine > pyridine >> 2-methylpyridine > 2,6-dimethylpyridine. Thus, unlike pyridine *N*-oxides, introduction of a methyl group into position *2* of the pyridine ring, as might be expected, creates so strong steric hindrances to complex formation that introduction of the second substituent into position *6* produces almost no additional effect. The sharp difference in the substituent effects on the reactivity of pyridines and the corresponding *N*-oxides can be readily interpreted in terms of spatial accessibility of unshared electron pairs occupying sp^2-hybridized orbitals on the nitrogen and oxygen atoms for bonding with ν-acceptors.

Table 2. Stability constants of Zn-TPP and Zn-OEP complexes in toluene at 25°C and pK_a values of the ligands

Ligand	*K*, l/mol		pK_a(H_2O) [5]
	Zn-TPP	Zn-OEP	
2,6-Dimethylpyridine	60	40	6.72
2-Methylpyridine	110	70	6.11
Pyridine	3200	2300	5.29
3-Methylpyridine	4400	2800	5.68
4-Methylpyridine	9200	5000	6.11
Benzonitrile	0.62	0.41	–
Acetonitrile	0.92	0.45	–



Obviously, higher stability constants of the complexes with Zn-TPP as compared to Zn-OEP may be rationalized in terms of weaker +*I* effect (larger residual positive charge on the zinc atom) [10] of four benzene rings {the large torsion angle formed by the benzene rings and porphyrin macroring, 75.15 and 73.14° [11, 12], makes conjugation between these fragments impossible) relative to the effect of eight ethyl groups. The fact that 4-methylpyridine gives stronger complexes with both Zn-TPP and Zn-OEP than does 3-methylpyridine cannot be interpreted in terms of inductive effect which should weaken as the methyl group becomes more distant from the reaction center (nitrogen atom), so that different electronic effects should be taken into account. For example, hyperconjugation [13] is hardly probable for 3-methyl

group in the pyridine ring but it should be efficient for methyl group in position *2*; from this viewpoint, the series of constants σ and σ_{PyO} for methyl group seem to be reasonable.

The values of log*K* for the complexes with Zn-TPP and Zn-OEP in toluene (Table 2) show an excellent correlation with each other ($r = 0.999$); i.e., peripheral substituents in the porphyrin macroring exert only electronic effect on the complexation process. Furthermore, good linear correlations are observed between pK_a values of the ligands and Hammett constants σ, on the one hand, and log*K* of 1:1 complexes of Zn-TPP, Cd-TPP, and Hg-TPP with γ-substituted pyridines in benzene [3, 4] and Zn-TOP complexes with β- and γ-substituted pyridines in methylene chloride [6] (Fig. 1), on the other. Therefore, it is reasonable to presume that the above relations should be applicable to other related metal porphyrins in different solvents.

Decrease in the stability constants of metal porphyrin complexes in the series Zn-TPP > Cd-TPP > Hg-TPP may be attributed to reduction in the efficiency of overlap of frontier orbitals on the pyridine nitrogen atom (in keeping with the Pearson concept [2]) and orbitals of the metal bearing a residual positive charge (Zn^{2+} is a moderately soft, and Cd^{2+} and Hg^{2+} are soft Lewis acids).

Figure 2 shows correlations between the stability constants of Zn-TPP complexes in benzene and carbon tetrachloride, determined by calorimetric titration (Table 3). It is seen that stronger complexes are formed in carbon tetrachloride. In going from benzene to carbon tetrachloride, the stability of the complex with hexamethylenediamine sharply increases, while the complexes with acetone, quinoline, and imidazole are destabilized. The sharp increase of the thermodynamic stability of the Zn-TPP complex with hexamethylenediamine (**XIX**) in going from benzene to carbon tetrachloride is related to change in its composition to 2Zn-TPP·L. This is consistent with the data of [17] and Cambridge Structural Database [11], according to which Zn-TPP forms a 2:1 complex with 1,4-diazabicyclo[2.2.2]octane in chloroform, as well as crystalline 2:1 complexes with propane-1,3-diamine and butane-1,4-diamine. The unusual behavior of acetone, quinoline, and imidazole is likely to be determined by specificity of solvation of ligands **XX**–**XXII** and complexes derived therefrom; this behavior requires additional study.

We can conclude that solvation effects must be taken into account while drawing correlations based on

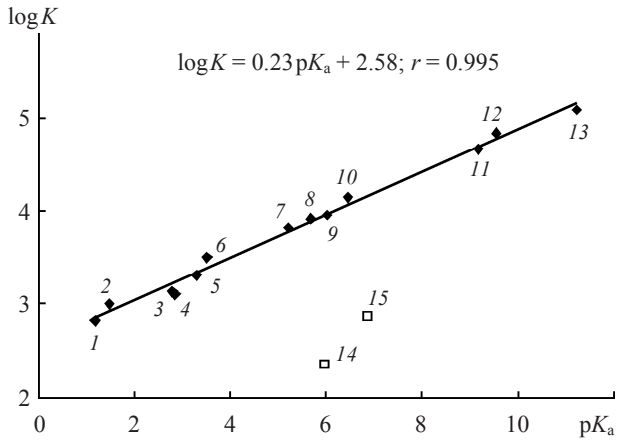


Fig. 1. Correlation of log*K* for Zn-TPP complexes with pyridines in methylene chloride at 25°C with pK_a of the ligands in water according to the data of [6]: (*1*) 3-cyanopyridine, (*2*) 4-cyanopyridine, (*3*) 3-bromopyridine, (*4*) 3-chloropyridine, (*5*) 3-acetylpyridine, (6) 4-acetylpyridine, (*7*) pyridine, (*8*) 3-methylpyridine, (*9*) 4-methylpyridine, (*10*) 3,4-dimethylpyridine, (*11*) 4-aminopyridine, (*12*) 4-dimethylaminopyridine, (*13*) piperidine, (*14*) 2-methylpyridine, and (*15*) 2-aminopyridine.

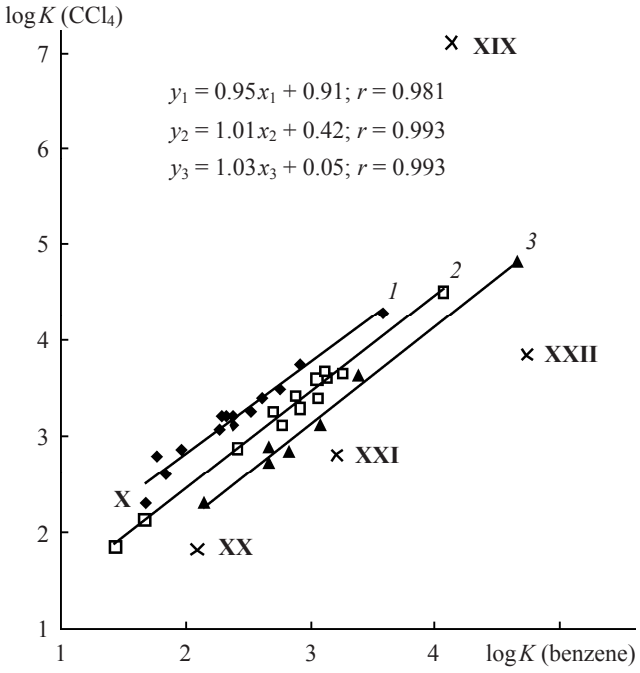


Fig. 2. Plots of log*K* for Zn-TP complexes with various ligands in benzene versus log*K* in carbon tetrachloride at 25°C; ligands: (*1*) $PhCH_2OH$ (**X**), MeOH, EtOH, PrOH, *t*-BuOH, *i*-PrOH, BuOH, *s*-BuOH, $C_5H_{11}OH$, 1,2-dimethoxyethane, DMF, Et_2NH, benzotriazole, pyridine; (*2*) benzylamine, $BuNH_2$, Pr_2NH_2, $(PhCH_2)_3N$, piperidine, 3,5-dimethylpyrazole, *N*-ethylacetamide, HMPA, *N*,*N*-dimethylacetamide, DMSO, $Me_2NCH_2CH_2CN$, MeCN, cyclopentanone; (*3*) $(PhCH_2)_3N$, $PhNH_2$, $PhNEt_2$, morpholine, benzimidazole, THF, 1,4-dioxane; hexamethylenediamine (**XIX**), acetone (**XX**), quinoline (**XXI**), imidazole (**XXII**).

Table 3. Stability constants of Zn-TPP complexes with organic ligands and pK_a values of the latter in water at 25°C

Comp. no.	Ligand	pK_a (H_2O)	logK_1, logK_2 [7]	
			C_6H_6	CCl_4
I	$PhCH_2NH_2$	9.34 [14]	2.70	3.26
II	$BuNH_2$	10.59 [14]	3.26, 2.80	3.66, 3.02
III	Et_2NH	10.98 [14]	2.76, 2.61	3.50, 2.27
IV	Pr_2NH	11.00 [14]	3.05, 2.94	3.60, 2.51
V	$(PhCH_2)_3N$	6.90 [15]	1.43	1.84
VI	Bu_3N	10.89 [14]	2.14	2.30
VII	$PhNH_2$	4.60 [15]	2.68, 2.38	2.88, 2.16
VIII	Piperidine	11.22 [14]	3.13, 3.11	3.61, 2.90
IX	Pyridine[a]	5.21 [15]	3.58	4.30
X	$PhCH_2OH$	–	1.68	2.31
XI	MeOH	–2.2 [13]	1.77	2.78
XII	EtOH	–2.3 [13]	1.96	2.86
XIII	PrOH	–	2.28	3.05
XIV	*t*-BuOH	–3.8 [13]	2.39	3.11
XV	*i*-PrOH	–3.2 [13]	2.37	3.20
XVI	BuOH	–	2.89	3.19
XVII	*s*-BuOH	–	2.52	3.24
XVIII	$C_5H_{11}OH$	–	2.61	3.40

[a] log$K$ = 3.61 in chloroform [16].

any basicity and nucleophilicity parameter and that better correlations are obtained for series of compounds which interact with the medium according to a common mechanism, e.g., for alcohols **X**–**XVIII** (Fig. 2, plot *1*). Here, not only specific interactions involving the hydroxy group (hydrogen bonding with acids and Brønsted bases) but also those related to polarizability of the hydrocarbon fragment are important. For example, benzyl alcohol (Fig. 2, plot *1*) considerably impairs the correlation, for it is better (than other alcohols) solvated by benzene due to dispersion and inductive interactions between the aromatic rings in the substrate and solvent molecules [2].

Figure 2 shows that the stability of Zn-TPP complexes with amines and its solvent-dependent variation are related to the ligand nature. Obviously, the reactivity of amines is largely determined by their structure. If the environment of the nitrogen atom remains unchanged, as in the case of *meta*- and *para*-substituted anilines and pyridines, the electronic effect can be estimated on a quantitative level using the Hammett equation. If variation of the substituent nature affects steric shielding of the reaction center, the extended Taft equation modified for amines [18] is used:

$$\log k = \log K_0 + \rho^* \Sigma\sigma^* + \delta E_N. \quad (4)$$

Here, k is the reaction rate constant, the term $\rho^*\Sigma\sigma^*$ describes the overall inductive effect of all substituents on the nitrogen atom, and δE_N takes into account the steric factor (δE_s in the Taft equation).

We presumed that the complexation of Zn-TPP with ligands should also be described in a similar way. Then the stability constant K (as well as the rate constant) should characterize the nucleophilicity (or basicity pK_a in reaction with H^+) of a ligand. By designating the corresponding constants in both equations as a_1 and a_2, b_1 and b_2, and c_1 and c_2, we obtain Eq. (5) which indicates that the ratio K/k is also determined by electronic and steric factors.

$$\log(K/k) = (a_1 - a_2) + (b_1 - b_2)\Sigma\sigma^* + (c_1 - c_2)E_N = a + b\Sigma\sigma^* + cE_N. \quad (5)$$

Insofar as the same values of $\Sigma\sigma^*$ and E_N are included into equations for the calculation of log$k$ and log$K$, it is obvious that these equations may be converted into two other, each containing only one of the above variables. For this purpose, it is sufficient to multiply the first equation by coefficient b_2, and the second, by b_1, and subtract one from the other. We then arrive at

$$b_2\log K - b_1\log k = (a_1 b_2 - a_2 b_1) - (c_1 b_2 - c_2 b_1)E_N; \quad (6)$$

$$c_2\log K - c_1\log k = (a_1 c_2 - a_2 c_1) - (b_1 c_2 - b_2 c_1)\Sigma\sigma^*. \quad (7)$$

Using Eqs. (6) and (7) we can calculate unknown values of k, K, σ^*, and E_N. Analogous transformations of the Hammett equation (provided that steric factor is not taken into account) lead to the equation

$$\log(K/K_0) = (\rho_1/\rho_2)\log(k/k_0), \quad (8)$$

where ρ_1 and ρ_2 are parameters reflecting, respectively, the sensitivity of the complexation with Zn-TFP and reaction with nucleophiles to substituent in the ligand/nucleophile. Obviously, the ratio ρ_1/ρ_2 reflects the difference in the sensitivities of these processes to electronic effect of substituent in the ligand/nucleophile molecule (or base molecule in log$K$—pK_a correlation).

In fact, in the first approximation the stability constants in benzene and carbon tetrachloride correlate

Table 4. Axial (*n*,ν) complexes of zinc porphyrins and zinc phthalocyanine

Compound no.	Complex	Ligand	CSD refcode[a]	pK_a	Coordination center	r_1,[b] Å	r_2,[c] Å
XXIII	Tetraphenylporphyrinatozinc(II)	2-Phenylethanamine	HAMMIR	9.83 [19]	NH_2	0.356	2.193
XXIV	Tetraphenylporphyrinatozinc(II)	3-Nitroaniline	HAMLAI	2.46 [20]	NH_2	0.249	2.314
XXV	Tetraphenylporphyrinatozinc(II)	Pent-3-en-2-ol	HALXOH	–	OH	0.246	2.267
XXVI	Tetraphenylporphyrinatozinc(II)	4-Chlorophenol	HAMFUW	–	OH	0.122	2.329
XXVII	Tetraphenylporphyrinatozinc(II)	Hexane-2,5-dione	HAMGUX	–	=O	0.221	2.261
XXVIII	Tetraphenylporphyrinatozinc(II)	4-Methylcyclohexanone	HAMHIM	–	=O	0.170	2.306
XXIX	2,3-Dihydrotetraphenylporphyrinatozinc(II)	Pyridine	HPORZN10	5.21 [15]	–N=	0.391	2.171
XXX	2,3,12,13-Tetrahydrotetraphenylporphyrinatozinc(II)	Pyridine	VIXGEO	5.21 [15]	–N=	0.368	2.164
XXXI	2,3,7,8-Tetrahydrotetraphenylporphyrinatozinc(II)	Pyridine	PRPHZN	5.21 [15]	–N=	0.379	2.155
XXXII	Tetraphenylporphyrinatozinc(II)	(*S*)-α-Methylbenzylamine	HALWOG	9.08 [19]	NH_2	0.211	2.256
XXXIII	Tetrakis(4-bromophenyl)porphyrinatozinc(II)	(*R*)-α-Methylbenzylamine	XAMHAU	9.08 [19]	NH_2	0.371	2.227
XXXIV	Tetrakis(4-chlorophenyl)porphyrinatozinc(II)	(*S*)-α-Methylbenzylamine	ZITMIY	9.08 [19]	NH_2	0.378	2.024
XXXV	Tetrakis(4-chlorophenyl)porphyrinatozinc(II)	Benzyl alcohol	ZITMOE	–	OH	0.248	2.188
XXXVI	Tetrakis(4-chlorophenyl)porphyrinatozinc(II)	DMSO	ZITMAQ	–	=O	0.381	2.123
XXXVII	Tetraphenylporphyrinatozinc(II)	DMSO	ATUSOX	–	=O	0.352	2.119
XXXVIII	Tetraphenylporphyrinatozinc(II)	DMF	HEJVUN	–0.19 [21]	N	0.283	2.160
XXXIX	Octaethylporphyrinatozinc(II)	Pyridine	EPOPZN10	5.21 [15]	–N=	0.396	2.200
XL	Phthalocyaninatozinc(II)	Hexylamine	ZNPTCY	10.63 [22]	NH_2	0.610	2.183

[a] Reference to the Cambridge Structural Database.
[b] Distance from the macroring plane to the zinc atom.
[c] Distance from the zinc atom to the coordination center in the ligand.

well with both ligand basicity (Table 3) and electronic effects of substituents. For example, the *K* values of alcohols in benzene and carbon tetrachloride increase in the series **X** → **XVIII**, in keeping with increase in the ligand basicity; this is explained by rise of the positive inductive effect of hydrocarbon groups therein. The unusually high value of log*K* for pentan-1-ol (the butyl and pentyl groups are characterized by almost similar inductive effects), is likely to be related to solvation, as well as to hydrophobic (attractive) interaction with the metal porphyrin complex. However, the relative position in this series of *tert*-butyl alcohol where the oxygen atom is least spatially accessible for complex formation depends on the solvent nature.

Some relations between the structure of axial complexes in the crystalline state and pK_a values of the ligands may be revealed by comparing the X-ray diffraction data. The more basic is the ligand, the longer is the distance r_1 from the macroring plane to the zinc cation and the shorter is the distance r_2 between the

Table 5. Rate constants of the reactions of amines with phenacyl bromides in benzene at 25°C

Amine	$\Sigma\sigma^*$ [18]	E_N [18]	log$k$ [18]
$PhCH_2NH_2$	1.20	–0.38	–3.25
$BuNH_2$	0.85	–0.40	–2.65
Et_2NH	0.29	–1.98	–2.60
$(PhCH_2)_3N$	0.645	–4.15	–6.99
Bu_3N	–0.39	–4.50	–3.84
$PhNH_2$	1.58	–0.98	–5.49
Piperidine	0.31	–0.79	–1.14

latter and the coordination center in the ligand. These variations are observed upon formation of Zn-TPP complexes (Table 4, complexes **XXIII**–**XXVI**).

Partial hydrogenation of the porphyrin ring and introduction of alkyl groups thereinto (complexes **XXIX**–**XXXI**, **XXXIX**) affect the distance r_1 and hence r_2 almost similarly. The presence of halogen atoms in the benzene rings of Zn-TPP considerably extends r_1 (the extension is stronger in the case of chlorine substitution as compared to bromine) and shortens r_2 (in the same order) upon complex formation with strong bases (such as 1-phenylethanamine; complexes **XXXII**–**XXXIV**) but almost does not affect r_1 (while the distance r_2 becomes shorter) upon interaction with weak bases (such as pent-3-en-2-ol and benzyl alcohol; complexes **XXV**, **XXXV**).

In the reaction of phthalocyaninatozinc(II) with hexylamine (complex **XL**), the zinc atom moves from the macroring plane to a distance of 0.610 Å, indicating a higher sensitivity of r_1 to the ligand nature, as compared to Zn-TPP. Obviously, variations in the distances r_1 and r_2 provide valuable information on the relative stability and nucleophilicity of such compounds as ketones, DMSO, and DMF (complexes **XXVII**, **XXVIII**, **XXXVI**–**XXXVIII**). Unfortunately, the available X-ray diffraction data for axial Zn-TPP complexes with ligands belonging to different classes are insufficient to draw more definite correlations between these parameters.

As might be expected, our attempts to obtain general correlations like log$K$—pK_a and log$K$—$\Sigma\sigma^*$ for all amines considered in [7] were unsuccessful, for the substrates strongly differ from each other not only by electron density on the nitrogen atom but also by spatial accessibility of the latter. We can only note similar trends in the variation in both solvents of log$K$, pK_a, and inductive effects of substituents on the nitrogen atom in the couples benzylamine–butylamine, diethylamine–dipropylamine, and tribenzylamine–tributylamine, taking into account that the basicity and nucleophilicity of primary, secondary, and tertiary amines should fit different correlations (provided that steric constants are not involved).

But the use of Eqs. (4)–(7) allowed us to deduce Eqs. (9)–(12) relating log$K$ values in benzene, $\Sigma\sigma^*$, E_N, and log$k$ for the reactions of phenacyl bromide with amines in benzene at 25°C [18] on the basis of the data for seven amines (Tables 3, 5). In this case, the coefficients r characterize correlations between the experimental values of log$K$ [log(K/k)] and those calculated by Eqs. (9)–(12).

$$\log K = 3.75 - 0.55\Sigma\sigma^* + 0.43E_N,\ r = 0.961; \quad (9)$$

$$\log(K/k) = 2.77 + 2.73\Sigma\sigma^* - 0.94E_N,\ r = 0.983; \quad (10)$$

$$\log K = 3.56 + 0.20E_N + 0.16\log k,\ r = 0.957; \quad (11)$$

$$\log K = 3.43 + 0.48\Sigma\sigma^* + 0.31\log k,\ r = 0.951. \quad (12)$$

Equations like (4)–(12) can be applied to both amines and other ligands, taking into account that E_N for amines are numerically equal to E_s in the Taft equation. Moreover, other parameters reflecting electronic effects, e.g., σ_{PyO} for heteroaromatic *N*-oxides, may be used instead of σ^*.

Thus we can conclude that the stability constants K of complexes formed by metal porphyrins (and probably by metal phthalocyanines), determined by calorimetric titration and electronic and fluorescence spectroscopy, are linearly related to K, pK_a, E_N, σ, and $\Delta\lambda$ provided that some constraints are applied. Therefore, we propose to use complex formation with Zn-TPP in chloroform as model process for studying nucleophilicity of ligands. Here, the nucleophilicity parameter depending on the ligand basicity, polarizability of the nucleophilic center and the entire molecule, and electronic and steric factors is the stability constant K of the corresponding 1:1 complex Zn-TPP·L, as well as $\Delta\lambda$ and $\Delta\delta$ (in spectrophotometric or high-resolution NMR measurements).

Chloroform was proposed as solvent due to its much lesser toxicity than that of benzene and carbon tetrachloride [23], better solubility of most polar organic substances in that solvent, and the ability to form weak hydrogen bonds and charge-transfer complexes [24]; therefore, the above nucleophilicity parameter is applicable to processes not involving or involving specific interactions of moderate strength. However,

Table 6. ^{1}H NMR spectra of pyridine *N*-oxides 4-$RC_5H_4N\rightarrow O$ and their molecular complexes with BF_3 in DMSO-d_6

R	Acceptor	Chemical shifts δ, ppm					
		2-H	6-H	3-H	5-H	4-H	R
H	–	8.17 d		7.36 t		7.27 t	–
	BF_3	8.53 d	8.86 d	8.01 t	8.38 t	7.70 t	–
Me	–	8.29 d		7.42 d		–	2.47 s (CH_3)
	BF_3	8.46 d	8.98 d	7.60 d	8.07 d	–	2.59 s (CH_3)
MeO	–	8.01 d		6.97 d		–	3.82 s (OCH_3)
	BF_3	8.68 d		7.45 d		–	4.05 s (OCH_3)
4-$Me_2NC_6H_4CH$=CH	–	8.04 d		7.48		–	3.00 s (NMe_2)
	BF_3	8.22 d		7.66 d		–	2.94 s (NMe_2)

the stability constants can be used as a measure of nucleophilicity only if the corresponding 1 : 1 complexes are axial (i.e., of *n*,ν-type); otherwise, they would be determined by a different set of interactions between species involved in complex formation and would be described by different (probably much more complex) correlation equations.

Formation of 1 : 2 complexes with some ligands (Table 3) could provide additional information on nucleophilicity, and understanding of this information requires some time. Now we can only suppose that the formation of such complexes is determined by the ionization energy (E_i) of the ligand. For example, tetra-*tert*-butylphthalocyaninatozinc(II) forms 1 : 2 complexes with amines whose ionization energy is lower than 8.8 eV at room temperature, whereas analogous complexes with amines with $E_i > 9.2$ eV are formed only at elevated temperature [25].

At present, we are engaged in determining stability constants of Zn-TPP complexes with various *n*-donors in chloroform by calorimetric titration, electronic absorption spectroscopy, and ^{1}H NMR.

We already noted unusual behavior of pyridine *N*-oxides from the viewpoint of nucleophilicity, which was not rationalized so far. It is commonly assumed that the oxygen atom in pyridine *N*-oxides has sp^2 hybridization [9] which does not change during the process. Then the formation of a new bond involving one sp^2-orbital should always lead to an unsymmetrical (with respect to the N–C^4 axis) compound, so that protons in positions *2*, *3*, *5*, and *6* have different chemical shifts in the ^{1}H NMR spectra. However, nonequivalence of these protons in Zn-TPP complexes with pyridine *N*-oxides cannot be detected due to fast ligand exchange, and the positions of signals in the ^{1}H NMR spectrum of the reaction mixture depend on the ratio of the components. Our ^{1}H NMR study on the complexation of Zn-TPP with 4-(4-dimethylaminostyryl)- and 4-(4-methoxystyryl)pyridine *N*-oxides in $CDCl_3$ showed that the formation of axial (*n*,ν) complex is accompanied by upfield shift of signals from 1-H–8-H in the porphyrin ring and 2-H and 6-H in the ligand. This is the result of reduced deshielding effect (dissipation via additional coordination) of the zinc cation on protons in the porphyrin ring due to donor–acceptor bonding with the ligand in the first case and ring current in the macroring, which induces magnetic field directed opposite to the external field in the vicinity of the N→O group.

In continuation of our studies on steric structure of molecular complexes derived from heteroaromatic *N*-oxides we recorded ^{1}H NMR spectra of their complexes with BF_3, where the O–B bond is fairly strong due to relatively high basicity of the ligands ($pK_a \geq 0.8$; Table 6) with a view to elucidate hybridization mode of the oxygen atom therein.

As expected, in the ^{1}H NMR spectra of the complexes formed by BF_3 with pyridine and 4-methylpyridine *N*-oxides, all protons in the pyridine ring have different chemical shifts. However, the 2-H/6-H and 3-H/5-H protons in the complexes derived from more basic 4-methoxy- and 4-(4-dimethylaminostyryl)pyridine *N*-oxides turned out to be equivalent in pairs. We believe that this pattern may be rationalized in terms of different hybridizations of the oxygen atom involved in dative bond with the boron atom. The oxygen atom in the complexes derived from pyridine and 4-methylpyridine *N*-oxides has sp^2 hybridization, while in the complexes formed by 4-methoxy- and 4-(4-dimethylaminostyryl)pyridine *N*-oxides it has sp^3 hybridization.

Obviously, fast (on the ^{1}H NMR time scale) conformational transformations of molecules with a single bond between the pyridine nitrogen atom and sp^3-oxygen atom should lead to averaging of the 2-H/6-H and 3-H/5-H signals {as in the spectrum of 1-dimethylcarbamoyloxy-4-(4-methoxystyryl)pyridinium tetraphenylborate [26]}. On the other hand, we cannot rule out that some complexes formed by heteroaromatic *N*-oxides (e.g., those derived from 2,6-substituted pyridine *N*-oxides) exist as one stable conformer in which the sp^3-hybridized orbital of the oxygen atom, involved in dative bond with boron atom, lies in the plane orthogonal to the pyridine ring and passing through the N and C^4 atoms.

Presumably, the possibility for rehybridization of the oxygen atom under mild conditions and its spatial accessibility are factors responsible for supernucleophilicity of heteroaromatic *N*-oxides. From this viewpoint, the lack of steric hindrances to complex formation between Zn-TPP and 2-methyl-4-nitropyridine *N*-oxide can be readily understood assuming that the new bond is formed with participation of sp^2-orbital which is more distant from the CH_3 group (or even *p*-orbital conjugated with the pyridine ring) with eventual transformation of the oxygen atom into the sp^3 state. On the other hand, the presence of two methyl groups in positions *2* and *6* makes rehybridization of the *N*-oxide oxygen atom even more probable. The formation of a new bond involving sp^3-orbital of the oxygen atom above the pyridine ring plane should eliminate steric strain intrinsic to the initial molecule having sp^2-hybridized oxygen atom.

It should also be noted that just heteroaromatic *N*-oxides are characterized by a unique combination of conjugation between the N→O group and the aromatic ring and the smallest difference in the electronegativities of the neighboring nitrogen and oxygen atoms, which ensures polarization of the semipolar N→O bond in both directions by the action of moderate-strength external field. Therefore, under certain conditions nitro derivatives of heteroaromatic *N*-oxides could give rise to molecular complexes (i.e., could act as nucleophiles and bases) with participation of not only N→O but also NO_2 group and/or π-system of the aromatic ring.

The ^{1}H NMR spectra were recorded at room temperature from solutions in DMSO-d_6 on a Bruker WM-400 instrument (400 MHz) using tetramethylsilane as internal reference. Molecular complexes of heteroaromatic *N*-oxides with BF_3 were synthesized according to the procedures described in [9, 27].

REFERENCES

1. Savelova, V.A., Popov, A.F., Solomoichenko, T.N., Sadovskii, Yu.S., Piskunova, Zh.P., and Lobanova, O.V., *Russ. J. Org. Chem*., 2000, vol. 36, p. 1465.
2. Dneprovskii, A.S. and Temnikova, T.I., *Teoreticheskie osnovy organicheskoi khimii* (Theoretical Foundations of Organic Chemistry), Leningrad: Khimiya, 1991.
3. Kirksey, C.H. and Hambright, P., *Inorg. Chem*., 1970, vol. 9, p. 958.
4. Kirksey, C.H., Hambright, P., and Storm, C.B., *Inorg. Chem*., 1969, vol. 8, p. 2141.
5. Szintay, G. and Horvath, A., *Inorg. Chim. Acta*, 2000, vol. 310, p. 175.
6. Kadish, K.M., Shiue, L.R., Rhodes, R.K., and Bottomley, L.A., *Inorg. Chem*., 1981, vol. 20, p. 1274.
7. Lebedeva, N.Sh., Pavlycheva, N.A., and V'yugin, A.I., *Russ. J. Org. Chem*., 2004, vol. 40, p. 1727.
8. Andreev, V.P., Nizhnik, Ya.P., Bezruchko, D.G., and Morozov, A.K., *Russ. J. Gen. Chem*., 2005, vol. 75, p. 1309.
9. Ochiai, E., *Aromatic Amine Oxides*, Amsterdam: Elsevier, 1967.
10. Lebedeva, N.Sh., Pavlycheva, N.A., V'yugin, A.I., Davydova, O.I., and Yakubov, S.P., *Izv. Ross. Akad. Nauk, Ser. Khim*., 2004, p. 1.
11. Allen, F.H., *Acta Crystallogr., Sect. B*, 2002, vol. 58, p. 380.
12. Byrn, M.P., Curtis, C.J., Hsiou, Y., Khan, S.I., Sawin, P.A., Tendick, S.K., Terzis, A., and Strouse, C.E., *J. Am. Chem. Soc*., 1993, vol. 115, p. 9480.
13. Becker, H., *Einführung in die Elektronentheorie organisch–chemischer Reaktionen*, Berlin: Wissenschaften, 1974, 3rd ed. Translated under the title *Vvedenie v elektronnuyu teoriyu organicheskikh reaktsii*, Moscow: Mir, 1977, pp. 116.
14. Hall, H., *J. Am. Chem. Soc*., 1957, vol. 79, p. 5441.
15. Popov, A.F. and Piskunova, Zh.P., *Problemy fiziko-organicheskoi khimii* (Problems in Physical Organic Chemistry), Kiev: Naukova Dumka, 1978, p. 19.
16. Lebedeva, N.Sh., Mikhailovskii, K.V., and V'yugin, A.I., *Koord. Khim*., 2001, vol. 27, p. 795.
17. Gomila, R.M., Quinonero, D., Frontera, A., Ballester, P., and Deya, P.M., *J. Mol. Struct. (Theochem)*, 2000, vol. 531, p. 381.
18. Litvinenko, L.M., Popov, A.F., and Gel'bina, Zh.P., *Dokl. Akad. Nauk SSSR*, 1972, vol. 203, p. 343.
19. Leffler, E.B., Spencer, H.M., and Burger, A., *J. Am. Chem. Soc*., 1951, vol. 73, p. 2611.
20. Bolton, P.D. and Hall, F.M., *Aust. J. Chem*., 1968, vol. 21, p. 939.

21. Wada, G. and Takenaka, T., *Bull. Chem. Soc. Jpn*., 1971, vol. 44, p. 2877.
22. Hansen, L.D. and Iemer, D.J., *Inorg. Chem*., 1971, vol. 10, p. 1439.
23. Tietze, L.-F. and Eicher, T., *Reactions and Syntheses in the Organic Chemistry Laboratory*, Mill Valley, California: University Science Books, 1989. Translated under the title *Preparativnaya organicheskaya khimiya: reaktsii i sintezy v praktikume organicheskoi khimii i nauchno-issledovatel'skoi laboratorii*, Moscow: Mir, 1999, p. 17.
24. Andrews, L.J. and Keefer, R.M., *Molecular Complexes in Organic Chemistry*, San Francisco: Holden–Day, 1964. Translated under the title *Molekulyarnye kompleksy v organicheskoi khimii*, Moscow: Mir, 1967, p. 69.
25. Mal'kova, E.M., *Cand. Sci. (Chem.) Dissertation*, Ivanovo, 2006.
26. Schroeder, G., Rybachenko, V.I., Chotii, K.Yu., Kovalenko, V.V., Grebenyuk, L.V., Lenska, B., and Eitner, K., *Russ. J. Gen. Chem*., 2003, vol. 73, p. 455.
27. Andreev, V.P., Batotsyrenova, E.G., Ryzhakov, A.V., and Rodina, L.L., *Khim. Geterotsikl. Soedin*., 1998, p. 1093.