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Electronic and Steric Effects of Substituents in Solution and Solvation of Forcedly Distorted Porphyrins

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Abstract — The solubility enhancement effect of *N*-substitution and increasing size of the N-substituent in octaethyl- and tetraphenylporphyrins is strongly dependent of the electronic nature of the β- and *meso*-substituents. It is suggested that *N*-alkyl(aryl) substitution exerts primarily distorting rather than polarizing effect on the porphyrin macroring.

Over the past years more and more evidence has been obtained to show that the profound changes in the physicochemical properties of porphyrins (H_2P), produced by changes in their molecular structure (compounds **I**–**VI**) are explained by the following three reasons: (1) considerable changes in the molecular geometry, rendering the structure either conformationally more rigid (phthalocyanines) or, on the contrary, deformed [*N*-alkyl(aryl)-substituted and dodecasubstituted H_2P (compounds **II**, **IV**–**V** and **VI**, respectively); (2) steric shielding of reaction centers in unsubstituted (N_4H_2) or *N*-substituted [N_3(NR)H] ligands and their metal complexes [MN_4 and (X)$MN_3\cdot$(NR), respectively] as a result of the macrocyclic effect or shielding with substituents and extra ligands; and (3) polarization of usually weakly polarized NH bonds under the influence of functional substitution, convergence of HOMO and LUMO, etc. [1–3].

With changing structure and properties of porphyrins, structural and electronic factors compete with each other [4–6].

Structural changes in the H_2P macroring can be divided into two groups. The first includes changes that affect the chemical affinity of reaction centers. These changes give rise to secondary electronic changes and associated with changing bond lengths and angles in the molecule. Moreover, they affect the overall electron density in the macroring and, consequently, activity of its reaction centers N_4H_2, MN_4, etc. Second-group changes have no effect on the chemical affinity of reaction centers and are associated with shielding or deshielding of the latter, inducing or eliminating the macrocyclic effect or more specifically, its structural component [3].

The interest in distorted H_2P has been generated by the assumption that such a distortion exerts a positive effect on the biological functions of these molecules [7]. In our opinion, this approach mistakenly neglects the role of electronic effects in biological processes. There is an alternative view of biological processes involving H_2P. Thus, Berezin [8] provided a persuasive evidence in favor of the key role electronic effects, including those of peripheral substituents in the chlorophyll molecule, play in photosynthesis.

The aim of the present work was to assess the effect of structural and electronic changes in nonplanar porphyrins **II** and **IV**–**V** distorted by substitution in one of the NH groups [general denotation H(NR)P] [7, 9] on the solvation energy of these molecules. Substitution in endocyclic NH groups in H_2P is one of the most effective ways to distort the planar macroring, even compared with exhaustive (dodeca) substitution of peripheral hydrogen atoms [$H_2(R)_8(X)_4P$], as, for example, in dodecaphenylporphirin **VI**, or with double protonation (H_4P^{2+}) by the tertiary nitrogen atoms =N– [3, 7]. In *N*-substituted molecules **II** and **IV**–**V**, the initially planar macroring (compounds **I**, **III**) loses planarity under the influence of the bulky substituent in the NH group, which also prevents out-of-plane vibrations of the distorted molecule [9]. These findings allow macrocyclic compounds **II**, **IV**, and **V** to be classed with forcedly distorted system.

Features of solvation of distorted porphyrins in organic solvents of various nature have scarcely been studied. In the present work we performed a thermochemical study of planar porphyrins octaethylporphyrin (**I**) and tetraphenylporphyrin (**III**), as well as

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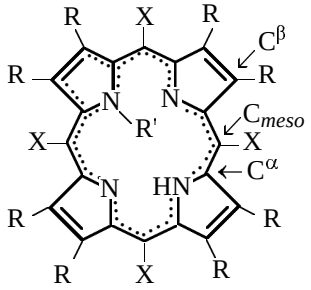


I, R = Et, R' = X = H; **II**, R = Et, R' = Me, X = H; **III**, X = Ph, R = R' = H; **IV**, X = Ph, R = H, R' = Me; **V**, X = R' = Ph, R = H; **VI**, X = R = Ph, R' = H.

of their nonplanar analogs *N*-methyloctaethylporphyrin (**II**), *N*-methyltetraphenylporphyrin (**IV**), and *N*-phenyltetraphenylporphyrin (**V**) in a weakly solvating (C_6H_6, *DN* 0.1, *AN* 8.2) and strongly solvating protic ($CHCl_3$, *DN* 4, *AN* 23.1) and electron-donor (DMF, *DN* 26.6, *AN* 16.0) solvents.

The resulting data show that structural and electronic factors [3, 4] exert a considerable effect of the enthalpy characteristics of solution and solvation of compounds **I**–**V**. In benzene, H_2P molecules are largely universally solvated, whereas in chloroform, in addition, basic centers (=N–) are specifically solvated and in DMF, acidic (NH) [10].

It is known that enthalpy characteristics of solution can be analyzed by solution enthalpies ΔH_{sol}, i.e. directly, or by the enthalpies of transfer ΔH_{tr} (i.e. relative solvation [10] of solute) from a standard solvent (ΔH_{sol}^{st}) to that under investigation (ΔH_{sol}^{inv}).

$$\Delta H_{tr} = \Delta H_{sol}^{inv} - \Delta H_{sol}^{st}.$$

The enthalpy characteristics of solution and relative solvation of compounds **I**–**V** are listed in Table 1. These data allow comparison of the effect of symmetrical peripheral octa-β (compound **I**) and tetra-*meso* (compound **III**) substitution on the solvation characteristics of largely planar H_2P.

Octaethylporphyrin (**I**) and tetraethylporphyrin (**III**), being fairly accessible, are best studied and commonly used as model molecules (classical H_2P [2]). They are taken as standards in studies on macroring distortion or rigidity (aromaticity) enhancement effects [4].

While having largely planar macrorings, compounds **I** and **III** differ considerably in electronic effects. The eight electron-donor β-ethyl groups in **I** are only partly involved in conjugation with the main $C_{12}N_4$ conjugation contour [5] and thus exert a weak effect on molecular geometry. By contrast, the four

Table 1. Standard enthalpies of solution and relative solvation of *N*-substituted porphyrins **I**–**V** in organic solvents (kJ mol^{-1})

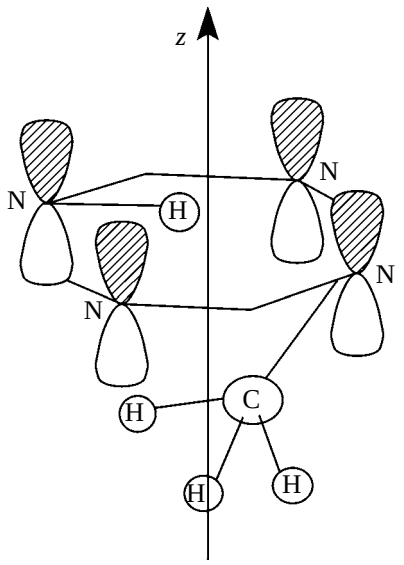
Comp. no	Benzene	Chloroform		DMF	
	ΔH_{sol}	ΔH_{sol}	ΔH_{tr}	ΔH_{sol}	ΔH_{tr}
I	+39.8 ± 3.1	+17.1 ± 3.0	–22.7	+25.7 ± 0.9	–14.1
II	+20.2 ± 0.9	–4.8 ± 0.7	–25.0	+11.7 ± 0.8	–8.5
III[a]	+20.7 ± 0.2	+9.9 ± 0.2	–10.8	+10.9 ± 0.2	–9.8
IV	+17.6 ± 0.7	+1.7 ± 0.2	–15.9	+9.2 ± 0.8	–8.4
V	+11.3 ± 0.5	–3.2 ± 0.5	–14.5	–4.0 ± 1.7	–15.3

[a] Published data [10].

meso-phenyl substituents in **III** are in contact with the main conjugation contour, decreasing the electron density on the macroring and loosening C_{Ph}–C_{meso} and C_{meso}–C^{α} bonds by the *–I* effect. According to X-ray diffraction data [11], compound **I** is a more rigid aromatic molecule than compound **III**. Oscillatory rotatory motions of phenyl groups about C_{Ph}–C_{meso} bonds render molecule **III** slightly more conformationally flexible (markedly nonplanar) [12].

As a result, tetraphenylporphyrin **III** is much easier soluble in benzene than octaethylporphyrin **I**: The enthalpies of solution (ΔH_{sol}) of these two compounds differ from each other by 19.1 kJ mol^{-1} (Table 1). The same situation is observed in going to *N*-derivatives **II** and **IV**–**V**. Endocyclic *N*-substitution in a porphyrin produces a strong distortion of the planar macroring, since the bulky substituent (Me, Ph, etc.) cannot be accommodated in the molecular plane. Introduction of an *N*-substituent into the center of H_2P much loosens the crystal lattice compared with the parent compound, as evidenced by the solubility data for molecules **I**–**V** in benzene [13]. The $\Delta\Delta H_{sol}$ in benzene for the **I**→**II** transition (19.6 kJ mol^{-1}) is larger than for **III**→**IV** (3.1 kJ mol^{-1}). The **I**→**II** transition is accompanied by a much stronger crystal lattice loosening than the transition for the already deformed macroring **III** to macroring **IV**. Apparently, the transition from octaethylporphyrin **I** to *N*-methyloctaethylprophyrin **II** involves a considerable expenditure of energy for distortion of the π system, whereas *N*-methylation of the conformationally more flexible tetraphenylprophyrin **III** has a considerably weaker effect of the energy of the crystal lattice. As the *N*-substituent increases in size, solution of H_2P becomes a more endothermic process (by 6.3 kJ mol^{-1} in going from **IV** to **V**).

On the other hand, the solvation contribution into



Shielding of specific solvation centers in an *N*-substituted porphyrin.

the ΔH^0_{sol} of compound **III** is benzene is appreciably larger than into the ΔH^0_{sol} of compound **I** (Table 1). The reason for this phenomenon is additional solvation of phenyl groups in tetraphenylporphyron derivatives with benzene by the π–π type [13]. Nevertheless, comparison of the ΔH^0_{sol} values of compounds **I**, **III** and their methylated analogs **II**, **IV** in the universally solvating benzene suggests that the slightly increased exothermicity of solution of a macroring distorted by *N*-substitution is more likely to be explained by facilitated solvation of pyrrole fragments of the nonplanar macroring itself than more favorable conditions for solvation of phenyl fragments in tetraphenylporphyrin **III** and *N*-methyltetraphenylporphyrin **IV** (the difference in the ΔH^0_{sol} of octaethylporphyrin **I** and *N*-methyloctaethylporphyrin **II** is larger).

N-Methyl substitution makes the porphyrin molecule more basic, facilitating addition of the first proton. This phenomenon is explained by a number of reasons [14]. They include (1) distortion of macroring planarity, resulting in deshielding of prinicipal endocyclic centers (=N–) (violation of the macrocyclic effect), (2) +*I* effect of the methyl group, which affects the electron density on the N_4 coordination center, (3) lack of the second NH proton required for intramolecular H-bond formation (–NH···N=), and (4) regibridization of the NH nitrogen ($sp^3 \rightarrow p^3$) as a result of *N*-substitution [15]. The regibridized NMe nitrogen acquires a lone electron pair and "amine-like" properties.

By the above reasons, the enthalpies of transfer of *N*-substituted porphyrins into chloroform increase for *N*-methyl derivatives **II** and **IV** and decrease for *N*-phenyl derivative **V**, regardless of the stronger macroring distortion in the latter compound. Phenyl is an electron acceptor that operates to decrease the affinity of tertiary nitrogen atom to proton-donor molecules. No enhanced solvation of compounds **II** and **IV** with chloroform is observed, even though the *N*-substituent effects shielding of specific solvation centers along the axial axis (see figure).

Changes in the acidity of H(N–R)P and in solvation of the NH group in these molecules, too, are explained by a number of reasons. Presumably, distortion facilitates proton abstraction by solvent molecules and, on the other hand, depolarizes the NH bond by decreasing the aromaticity of the conjugated system. Both the +*I* effect of the methyl group and the rehybridization of the NH nitrogen (liberation of the electron pair neighboring to the NH group) increase the electron density on the macroring, depolarize the NH bond, and decreases the acidity of the molecule. It was found that compound **IV** is a weaker acid compared unsubstituted tetraphenylporphyrin **III** (pK_a^{298} in DMSO 22.07 and 21.15, respectievly) [14]. These data suggest that in acidic ionization of molecule **IV** electronic factors still prevail over steric. In this case, no simultaneous increase of acidic and basic properties, like in certain dodecasubstituted porphyrins (as, for instance, in compound **VI** [16]), is observed.

N-Methylation decreases the enthalpy of transfer into the electron-donor DMF, whereas *N*-phenylation increases this value. Apparently, introduction of a methyl substituent into the coordination center N4H2 of molecules **II** and **IV** depolarizes the NH bond, whereas N-phenylation exerts the opposite effect (as, for instance, in compound **V**). According to the electronic absorption spectra (Table 2), the porphyrins studied all form no proton-transfer complexes in electron-donor solvents (DMSO, DMF), like those reported in [17]. Their five-band visible spectral patterns (bands **I**–**IV** and Soret) do not change in these solvents, as was the case with H_2P with a strongly polarized NH bond (dodecasubstituted porphyrins, tetraazaporphyrins) [17, 18]. The solvatochromic effect in going from an inert solvent (benzene, toluene) to electron-donor (DMF), too, is very weak both with planar (**I, III**) and distorted (**II, IV, V**) porphyrins compared with porphyrin **VI** (cf. $\Delta\lambda_I$ values in Table 2). Unfortunately, porphyrins **IV**, **V** were impossible to test for proton-transfer complex formation in more basic media, since they underwent

Table 2. Electronic absorption spectra of porphyrins **I**–**VI** in organic solvents [λ_i, nm (log ε)]

H_2P	Solvent	λ_{Soret}	λ_{IV}	λ_{III}	λ_{II}	λ_{I}	$\Delta\lambda_I$
I	Benzene	395 (5.30)	497 (4.19)	530 (4.07)	567 (3.92) 596 (3.18)	621 (3.81)	–
	DMF	387 (5.31)	495 (4.16)	528 (4.03)	565 (3.86) 592 (3.05)	619 (3.74)	–2
II	Benzene	410 (5.22)	505 (4.25)	534 (3.94)	586 (3.79) 616 (3.32)	642 (3.71)	–
	DMF	401 (5.23)	503 (4.16)	533 (3.94)	583 (3.81) 613 (3.30)	641 (3.56)	–1
III	Benzene	418 (5.58)	514 (4.33)	548 (3.96)	591 (3.81)	647 (3.68)	–
	DMF	416 (5.62)	513 (4.28)	548 (3.91)	590 (3.73)	646 (3.68)	–1
IV	Benzene	433 (5.44)	531 (4.04)	571 (4.19)	615 (3.75)	676 (3.73)	–
	DMF	431 (5.41)	531 (3.98)	572 (4.17)	613 (3.71)	676 (3.70)	0
V	Benzene	443 (5.66)	[a]	592 (4.85)	[a]	705 (4.07)	–
	DMF	443 (5.17)	[a]	593 (4.17)	[a]	703 (3.60)	–2
VI[b]	Toluene	464 (4.96)	555 (3.84)	609 (3.83)	[a]	725 (4.09)	–
	DMF	481 (5.11)	–	–	653 (4.15)	750 (3.97)	+25

[a] Shoulder. [b] Data from [17].

demethylation (dephenylation) in the presence of strong nucleophiles (aliphatic amines) [19]. Thus, in the case of zinc complexes with *N*-substituted compound **III**, the rate of this reaction increases in the order R = C_6H_5 < CH_3 < $CH_2C_6H_5$.

Regardless of the fact that the *N*-alkyl(aryl)-substituted poprhyrins have a distorted macroring, the thermochemistry of solvation of their acid–base centers reveals trends expected from the electronic effects both of the endocyclic and peripheral substituents. Thus, the CH_3 group at the endocyclic nitrogen atom, on the one hand, enhances basic properties of the molecule (enhanced salvation in $CHCl_3$) and, on the other, decreases the degree of polarization of the NH bond, which, even though the molecule is no longer planar and access of solvent molecules to the NH center is facilitated, attenuates solvation in DMSO. Substitution of phenyl for methyl in molecule **IV** renders specific solvation centers even better accessible [9]. However, no further solvation enhancement in chloroform is observed, since the *N*-phenyl substituent exerts an electron-acceptor effect on the prophyrin macroring. The *N*-phenyl substituent may favor protonation of the remaining NH bond, facilitating solvation of the NH center with DMF, whereas the *N*-methyl substituent disfavor solvation of the NH bond compared with compound **III**.

As shown in [10], the electron density on tertiary nitrogen atoms in H_2P strongly affects the solution enthalpies of the latter, whereas NH groups are subject to almost no solvation. Apparently, this trend is characteristic of largely planar porphyrins only and is violated as the distortion degree enhances.

In general, the ΔH^0_{sol} values for N-substituted porphyrins in organic solvents are more endothermic compared with those for another group of strongly nonplanar, dodecasubstituted H_2P. Most of the latter compounds (in particular, dodecaphenylporphyrin **VI**) are dissolved, even in benzene, with heat release [6]. We suggest that the endothermicity of solution of *N*-substituted H_2P is associated with a much weaker polarization of the macroring. Obviously, the effect of *N*-substituion can be considered as purely distorting, whereas with dodecasubstituted H_2P, a combination of distortion and polarization effects takes place [5, 20].

EXPERIMENTAL

The calorimetric experiment was performed using a precision isothermal-shell ampule calorimeter by the procedure described in [21]. The electronic absorption spectra of porphyrins **I**–**V** were measured on a Hitachi U-2000 spectrophotometer.

Porphyrins **I**–**V** were synthesized and purified according to published procedures [5, 9, 22]. The solvents were dried and purified by the procedure described in [23].

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