

## Influence of Nonplanarity and Extended Conjugation on Porphyrin Basicity

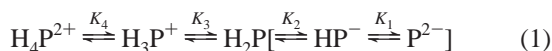
Olga S. Finikova,<sup>†</sup> Andrei V. Cheprakov,<sup>\*,†</sup> Patrick J. Carroll,<sup>‡</sup> Sergio Dalosto,<sup>§</sup> and Sergei A. Vinogradov<sup>\*,§</sup>

Department of Chemistry, Moscow State University, 119899 Moscow, Russia,  
Department of Chemistry, Crystallographic Laboratory, University of Pennsylvania,  
Philadelphia, Pennsylvania 19104, and Department of Biochemistry and Biophysics,  
University of Pennsylvania, Philadelphia, Pennsylvania 19104

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Thermodynamic basicities of several new nonplanar water soluble tetraaryltetracyclohexano- (Ar<sub>4</sub>TCHP) and tetraaryltetrabenzoporphyrins (Ar<sub>4</sub>TBP) have been measured and correlated with their structural parameters. While the degrees of nonplanarity in these porphyrins are similar, Ar<sub>4</sub>TCHPs exhibit significantly higher basicities than Ar<sub>4</sub>TBPs and than planar tetraarylporphyrins. Low basicities of distorted Ar<sub>4</sub>TBPs are believed to be due to extended  $\pi$ -conjugation, which causes delocalization of the core electron density in these porphyrins and reduces negative charges at the protonation site.

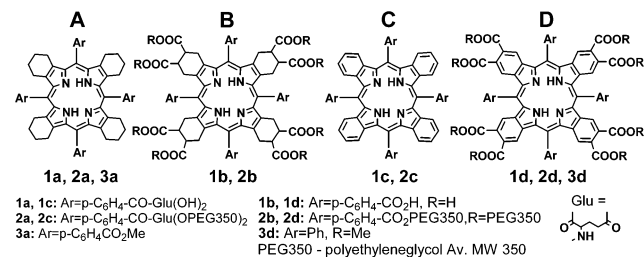
Thermodynamic basicity is a key physicochemical property, which along with electrochemical potentials quantifies the electronic density of porphyrin macrocycles.<sup>1</sup> The basicity provides a measure of proton affinity of core imine nitrogens (eq 1), reflecting the ability of porphyrins to serve as ligands for metal ions.



The values of the constants  $K_3$  and  $K_4$  are known to depend on the electronic effects of macrocycle substituents, on porphyrin planarity,<sup>2</sup> and on the peripheral electrostatic charges surrounding the macrocycle.<sup>3</sup> The interplay of all these factors, however, is complex and not completely understood.

Recently, we developed a useful synthetic route to *meso*-tetraaryltetrabenzoporphyrins (Ar<sub>4</sub>TBPs), bearing multiple peripheral groups.<sup>4</sup> Intrinsic to our method is the intermediate synthesis of precursor *meso*-tetraaryltetracyclohexanoporphyrins (Ar<sub>4</sub>TCHPs),<sup>5</sup> containing exactly the same substituents as Ar<sub>4</sub>TBPs. According to the literature,<sup>6,7</sup> both Ar<sub>4</sub>TBPs and Ar<sub>4</sub>TCHPs are highly nonplanar. Although multiple references point to the fact that nonplanarity enhances the basicity of porphyrins,<sup>2,8</sup> relatively few equilibrium pKs of nonplanar porphyrins have been measured, which is in part due to their poor water solubility.<sup>9</sup> The possibility to assess thermodynamic basicities in the series of water-soluble Ar<sub>4</sub>TCHPs and Ar<sub>4</sub>TBPs, different only by the degree of extended  $\pi$ -conjugation, provided a unique opportunity to sort out purely structural factors (distortion) from the electronic ones ( $\pi$ -conjugation), as they affect the basicity of porphyrin macrocycle.

The porphyrins described in this work are divided into four groups: Ar<sub>4</sub>TCHP (A), Ar<sub>4</sub>TCHP(COOR)<sub>8</sub> (B), Ar<sub>4</sub>TBP (C), and Ar<sub>4</sub>TBP(COOR)<sub>8</sub> (D). Core-substituted com-



pounds of groups B and D were prepared exactly following the reported methods,<sup>4</sup> while the synthesis of core-unsub-

\* Authors to whom correspondence should be addressed. E-mail: vinograd@mail.med.upenn.edu.

<sup>†</sup> Moscow State University.

<sup>‡</sup> Department of Chemistry, Crystallographic Laboratory, University of Pennsylvania.

<sup>§</sup> Department of Biochemistry and Biophysics, University of Pennsylvania.

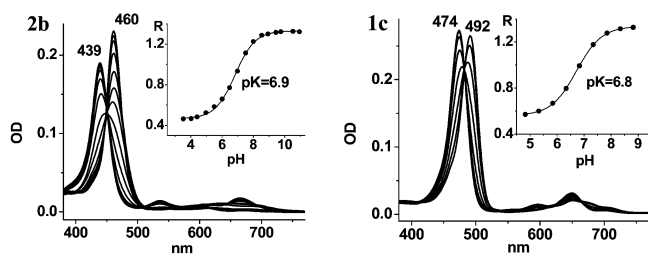
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**Figure 1.** Spectral changes during titrations of porphyrins **2b** and **1c**. The insets show the ratios of intensities and the corresponding fits to the Hasselbach equation.

stituted porphyrins A and C required some modifications. Basicity measurements necessitate the attachment of hydrophilic groups R to the macrocycle. Ar<sub>4</sub>TCHP and especially Ar<sub>4</sub>TBPs, however, appeared to be so hydrophobic that, even when modified with several carboxylic groups, they aggregated in water solutions, making spectroscopic titrations inaccurate. To minimize these limitations, the number of terminal carboxyls on these porphyrins was doubled by attaching glutamic acid fragments (Glu), a strategy shown to be very effective for solubilizing porphyrins,<sup>10</sup> and the peripheral carboxyl groups were esterified with monomethoxy-polyethyleneglycol fragments PEG350 (average MW 350).<sup>10b,11</sup>

The selected absorption spectra of Ar<sub>4</sub>TCHPs and Ar<sub>4</sub>TBPs during pH titrations are shown in Figure 1. Due to strong nonplanar distortions, TCHPs from both groups A and B exhibit significantly red shifted Soret and Q-bands relative to those of tetraphenylporphyrins (TPPs).<sup>8,12</sup> A further shift, induced by extended  $\pi$ -conjugation,<sup>13</sup> is seen in the case of TBPs from groups C and D. The titration curves, derived from rationing the Soret intensities, were fitted to the Hasselbach equation, exhibiting apparent *n* values lower than 1, i.e., 0.5–0.8, in all cases. Since no other spectroscopic transitions were observed, either below or above the protonation range, it is likely that the monoprotonation (*K*<sub>3</sub>) and diprotonation (*K*<sub>4</sub>) constants of the porphyrins are close, and thus the reported apparent p*K*s (or p*K*<sub>1/2</sub><sup>3a</sup>) (Table 1) represent somewhat averaged values.

The data reveal that porphyrins with peripheral carboxylate groups have much higher protonation constants than their

**Table 1.** Apparent p*K*s of Porphyrins A–D

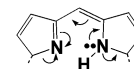
	A	B	C	D
p <i>K</i> <sub>carboxylate</sub>	10.9 ( <b>1a</b> )	10.7 ( <b>1b</b> )	6.8 ( <b>1c</b> )	7.3 ( <b>1d</b> )
p <i>K</i> <sub>PEG ester</sub>	8.5 ( <b>2a</b> )	6.9 ( <b>2b</b> )	4.2 ( <b>2c</b> )	2.4 ( <b>2d</b> )

esterified counterparts. The difference is maximal for the TBPs from group D (close to 5 pH units), in which electronic communication between the substituents and the protonation site is increased due to  $\pi$ -conjugation. In all the other cases, it is likely that the effect is due to the through-space electrostatic shielding of the cations by negative charges on the carboxylates.<sup>3c</sup>

Expectedly, Ar<sub>4</sub>TCHPs (A and B) are protonated at much higher pH than most of the uncharged (at the periphery) planar tetraarylporphyrins. The latter generally exhibit p*K*s of 2–4.<sup>1</sup> Central to this work, however, was the finding that the esterified (uncharged) Ar<sub>4</sub>TCHPs from groups A and B exhibit p*K*s about 4.5 units higher than their Ar<sub>4</sub>TBP counterparts from groups C and D. This difference was especially striking in the case of porphyrins **2a** and **2c**, where substituents are removed at a significant distance and electronically uncoupled from the cores.

With perhaps two exceptions,<sup>14,15</sup> all structurally characterized porphyrin dications are more distorted than the corresponding free bases.<sup>8,16,17</sup> It is useful to divide the total free energy of porphyrin protonation ( $\Delta U_{\text{prot}}$ ) into two terms: *intrinsic* proton affinity ( $\Delta U_{\text{intr}}$ ) and the *structural* term ( $\Delta U_{\text{struct}}$ ), associated with extra deviation of the aromatic macrocycle from planarity upon protonation. The latter balances out the repulsion between protons that are facing each other in dications.

$$\Delta U_{\text{prot}} = \Delta U_{\text{intr}} + \Delta U_{\text{struct}}$$

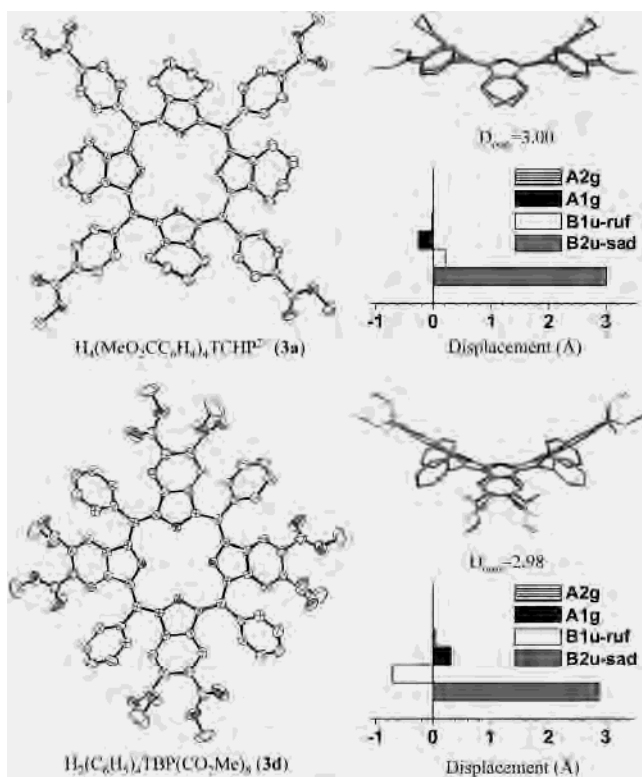


The distortion term  $\Delta U_{\text{struct}}$  is the major penalty ( $\Delta U_{\text{struct}} > 0$ ) to the otherwise energetically favorable attachment of protons to the imine nitrogens. The *intrinsic* basicity of the latter is likely to be very high ( $\Delta U_{\text{intr}} \ll 0$ ) due to the cooperative effect of two sp<sup>3</sup> nitrogens, capable of sharing their lone pairs over the system of conjugated double bonds. In porphyrins with already compromised planarity, such as Ar<sub>4</sub>TCHP, the penalty term ( $\Delta U_{\text{struct}}$ ) due to extra distortion is rather small, making them much stronger bases. Since Ar<sub>4</sub>TBPs exhibit significantly lower p*K*s than the corresponding Ar<sub>4</sub>TCHPs, it was of interest to determine whether such a difference is due to the structural factors.

The X-ray structures<sup>18</sup> of the porphyrin dication of type A, **3a** (parent to the compounds **1a** and **2a**), and of the free-base tetrabenzoporphyrin **3d** (type D)<sup>19</sup> are shown in Figure 2. Two Cl<sup>−</sup> counterions for the dication **3a** and the cocrystallized solvent molecules (<sup>t</sup>BuOMe) are omitted for clarity.

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- (9) Solubilization via incorporation into micelles and subsequent p*K* measurements have been performed, for example, for highly nonplanar dodecaphenylporphyrin.<sup>2c</sup>
- (10) (a) Vinogradov, S. A.; Lo, L. W.; Wilson, D. F. *Chem. Eur. J.* **1999**, *5*, 1338–1347. (b) Rozhkov, V. V.; Wilson, D. F.; Vinogradov, S. A. *Macromolecules* **2002**, *35*, 1991–1993.
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**Figure 2.** X-ray crystallographic structures of porphyrins **3a** (dication) and **3d** (free base). Graphs on the right show the side views of the molecules and the NSD analysis results.<sup>20,21</sup>

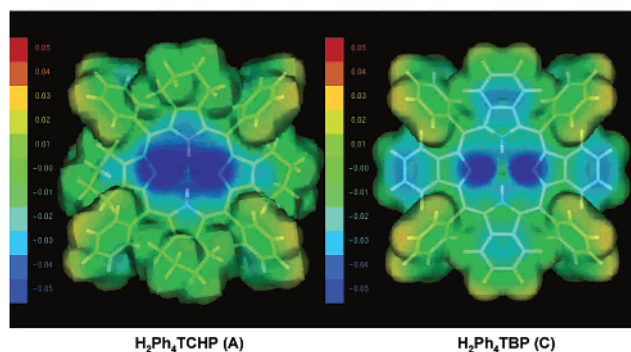
Both porphyrins are severely distorted in a saddle-type manner, which is typical of dodecasubstituted porphyrins as well as of their dications.<sup>8</sup> In both cases ruffling (B1u) and in-plane A1g distortion somewhat contribute to nonplanarity, more so in the case of tetrabenzoporphyrin **3d**. There is presently only one structure of Ar<sub>4</sub>TBP available in the literature, i.e., the ZnPh<sub>4</sub>TBP·THF complex,<sup>7</sup> which also exhibits strong saddle-type distortion with a small contribution of ruffling. As revealed by the normal-mode decomposition (NSD) analysis,<sup>20</sup> the value of the total out-of-plane distortion ( $D_{\text{oop}}$ )<sup>21</sup> in the dication **3a** ( $D_{\text{oop}} = 3.00$ ) is practically the same as in the free-base **3d** ( $D_{\text{oop}} = 2.98$ ).

(18) Crystal data. (a) **3a**: [C<sub>68</sub>H<sub>64</sub>N<sub>4</sub>O<sub>8</sub>]Cl<sub>2</sub>·4CH<sub>3</sub>OC(CH<sub>3</sub>)<sub>3</sub>, dark green prism from CHCl<sub>3</sub>/BuOMe, tetragonal, space group *P42<sub>1</sub>c*,  $a = b = 19.5732(4)$  Å,  $c = 10.8225(2)$  Å,  $V = 4146.21(14)$  Å<sup>3</sup>,  $Z = 2$ ,  $d_{\text{calc}} = 1.192$  g/cm<sup>3</sup>, 3607 reflections (24172 total) with  $F > 4\sigma(F)$ ,  $R1 = 0.0659$ ,  $wR2 = 0.1503$ . (b) **3d** [H<sub>2</sub>Ph<sub>4</sub>TBP(CO<sub>2</sub>Me)<sub>8</sub>]: C<sub>76</sub>H<sub>54</sub>N<sub>4</sub>O<sub>16</sub>, dark green prism from CHCl<sub>3</sub>/BuOMe, tetragonal, space group *P42<sub>1</sub>c*,  $a = b = 20.9448(3)$  Å,  $c = 9.0485(1)$  Å,  $V = 3969.44(9)$  Å<sup>3</sup>,  $Z = 2$ ,  $d_{\text{calc}} = 1.070$  g/cm<sup>3</sup>, 3607 reflections (24172 total) with  $F > 4\sigma(F)$ ,  $R1 = 0.0659$ ,  $wR2 = 0.1503$ ; Cambridge Crystallographic Data Centre depositions 188053 (**3a**) and 188054 (**3d**) contain the supplementary crystallographic data for this paper.

(19) For structural comparisons **3d** is assumed to be a close enough analogue of the core-unsubstituted porphyrins from group C, i.e., the counterparts of Ar<sub>4</sub>TCHPs from group A.

(20) NSD (normal-coordinate Structural Decomposition) analysis was performed using web-based software available at <http://jasheln.unm.edu/>. (a) Jentzen, W.; Song, X.-Z.; Shelnett, J. A. *J. Phys. Chem. B* **1997**, *101*, 1684–1699. (b) Jentzen, W.; Ma, J. G.; Shelnett, J. A. *Biophys. J.* **1998**, *74*, 753–763.

(21) Total out-of-plane distortion  $D_{\text{oop}}$  (Å) is the mean-square of all normal modes contributing to nonplanarity:  $D_{\text{oop}} = |\Delta_{z,\text{sim}}(d_k)| = (\sum_k d_k^2)^{1/2}$ , where  $d_k$  is a coefficient corresponding to the  $k$ -distortion (*sad*, *ruf*, etc). It is convenient to quantify structural distortions in porphyrins **3a** and **3d** using parameter  $D_{\text{oop}}$ , since in both cases the total distortion is dominated by the same mode, i.e., *saddle* distortion.



**Figure 3.** Electrostatic potential (−0.05; 0.05) mapped onto the isosurfaces of electron density (0.002) in H<sub>2</sub>Ph<sub>4</sub>TCHP (group A) and H<sub>2</sub>Ph<sub>4</sub>TBP (group C).

By analogy with other porphyrins, it could be expected that the **3d** dication would be distorted more, while the **3a** free base would be distorted less, compared to the corresponding shown molecules. Although these matching structures are yet to be obtained and analyzed, it seems overall unlikely that small differences in extra distortions of these already deformed macrocycles could result in such large differences in basicities. This leaves the extended  $\pi$ -conjugation the main candidate responsible for lower  $pK_s$  of Ar<sub>4</sub>TBPs.

One possible reason for the influence of  $\pi$ -conjugation is the enhanced delocalization of the nitrogen lone pairs in the TBP free bases, leading to a lesser negative charge at the protonation site than in TCHPs. A simple visualization of the electronic differences between Ar<sub>4</sub>TBPs and Ar<sub>4</sub>TCHP has been obtained by mapping electrostatic potential onto the isosurfaces of electron density in the calculated structures of two model porphyrins (Figure 3).

The single-point calculations were in this case performed at the B3LYP/6–31G(d)//HF/3–21G level. It is clearly seen that the concentration of negative charge (blue) around the nitrogens in H<sub>2</sub>Ph<sub>4</sub>TCHP is much higher than that in H<sub>2</sub>Ph<sub>4</sub>TBP. At the same time, some of the charge in H<sub>2</sub>Ph<sub>4</sub>TBP is shifted into the fused benzo rings, while in H<sub>2</sub>Ph<sub>4</sub>TCHP it is localized mostly in the core.

In summary, the basicity of porphyrins increases with the nonplanarity of the free bases ( $pK_{\text{Ar}_4\text{TCHP}} > pK_{\text{planar porphyrin}}$ ), due to a lesser penalty paid for extra distortion upon protonation. In nonplanar porphyrins, extended  $\pi$ -conjugation decreases  $pK_s$  ( $pK_{\text{Ar}_4\text{TBP}} < pK_{\text{Ar}_4\text{TCHP}}$ ) via delocalization of the core electron density which decreases the *intrinsic* basicity of the macrocycle.

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**Supporting Information Available:** Synthesis and characterization of porphyrins, protocols of spectrophotometric titrations, X-ray analyses (CIF), details of calculations, and NSD analysis. This material is available free of charge via the Internet at <http://pubs.acs.org>.

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