

Evidence for unusually strong intramolecular hydrogen bonding in highly nonplanar porphyrins

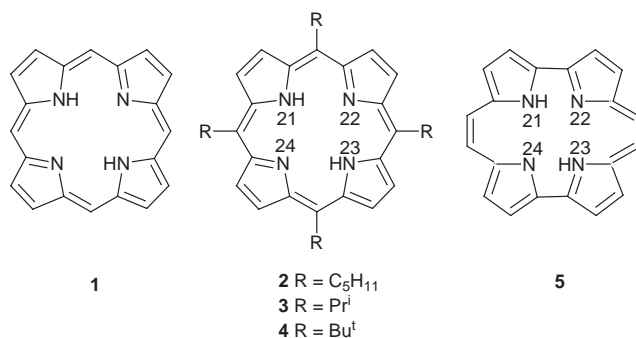
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The ^1H NMR spectra of the 5,10,15,20-tetraalkylporphyrins 2–4 reveal a large downfield shift of the signal for the NH protons and a reduction in the activation energy for NH tautomerism as the alkyl substituents become larger; these unusual changes can be rationalized in terms of greatly enhanced intramolecular hydrogen bonding of the NH protons as the bulkier substituents distort the macrocycle from planarity and contract the porphyrin core.

A novel and highly diagnostic feature of the ^1H NMR spectra of porphyrins 1 is the presence of a signal at very high field (typically $\delta -2$ to -4) arising from the NH protons.^{1,2} Herein, we describe ^1H NMR studies of the tetraalkylporphyrins 2–4 which provide the first example of a porphyrin with an NH signal far downfield of this ‘fingerprint’ region. We then propose a mechanism to explain this novel behavior, as well as the unusually facile tautomerism of the NH protons also observed in this porphyrin, and show that this mechanism is consistent with structural parameters determined using X-ray crystallography.



The investigated 5,10,15,20-tetraalkylporphyrins 2–4 were prepared using published procedures³ and their ^1H NMR spectra were recorded at a frequency of 300 MHz using CDCl₃ as the solvent. The ^1H NMR spectrum of the pentyl substituted porphyrin 2 showed a signal for the NH protons at $\delta -2.64$, which is within the chemical shift range expected for the NH protons in porphyrins.^{1,2} However, the spectrum of porphyrin 3 with more bulky isopropyl substituents showed a significant downfield shift of the NH signal to $\delta -1.80$. In the case of porphyrin 4, which has the even more bulky *tert*-butyl substituents, a very large downfield shift was seen for the NH signal ($\delta +1.58$) and it was far downfield of the range expected for porphyrins.^{1,2}

Large chemical shift changes in the ^1H NMR spectra of porphyrins are usually attributed to differences in the contribution from the porphyrin ring current effect.^{1,2,4} Given the greater nonplanar distortions observed for metal complexes of tetraalkylporphyrins with larger alkyl substituents^{5,6} it is plausible that the downfield shift of the NH signals is the result of a decrease in the porphyrin ring current. However, this approach is unsatisfactory because the ring current decrease determined for some cobalt(III) complexes of 4 is quite small (only about 5%).⁷

Moreover, a change in the ring current would not account for the changes in the activation energies for NH tautomerism also observed in these porphyrins. For example, the activation energy for NH tautomerism in 2 measured using NMR spectroscopy ($\Delta G_{338}^\ddagger = 50 \text{ kJ mol}^{-1}$) was found to be similar to that measured for other nominally planar porphyrins ($\Delta G_{298}^\ddagger = 50 \pm 3 \text{ kJ mol}^{-1}$).⁴ In addition, as with other porphyrins, the activation energy for tautomerism in 2 increased upon replacement of the inner hydrogens with deuteriums ($\Delta G_{283}^\ddagger = 60 \text{ kJ mol}^{-1}$ in 2 vs. $\Delta G_{298}^\ddagger = 57 \pm 2 \text{ kJ mol}^{-1}$ in regular porphyrins).⁴ However, the activation energy for tautomerism in 3 was significantly reduced in both the dihydro ($\Delta G_{183}^\ddagger = 38 \text{ kJ mol}^{-1}$) and dideutero ($\Delta G_{333}^\ddagger = 50 \text{ kJ mol}^{-1}$) forms, and in porphyrin 4 there was no evidence of a dynamic process in either the dihydro or dideutero forms even at the lowest temperatures studied (182 K) indicating an extremely low activation energy.

In order to explain these changes in the NH chemical shifts and activation energies for NH tautomerism, we propose an alternative model in which there is also a substantial increase in intramolecular hydrogen bonding as the substituents become larger. This hydrogen bonding will produce an additional downfield shift for the NH protons, and should also lower the activation energies for tautomerism because intramolecular hydrogen bonding is analogous to the transition state for tautomerism where the hydrogens are co-shared by adjacent nitrogen atoms.^{4,8} Such strong intramolecular hydrogen bonding has not previously been postulated in porphyrins, although this phenomenon has been invoked by Vogel and co-workers⁹ to explain similar NMR behavior in the porphyrin isomer porphycene 5. In porphycene, the unusual ‘oblong’ geometry of the macrocycle appears to provide both short N–N distances (N21–N22 2.83 Å, N21–N24 2.63 Å) and a nearly linear arrangement of a hydrogen bond between N21 and N24. In the case of porphyrins 2–4 it seemed likely that the increased intramolecular hydrogen bonding suggested by the NMR studies might be the result of the bulkier alkyl substituents forcing the porphyrin rings to adopt increasingly ruffled conformations, as seen for metal complexes of related tetraalkylporphyrins.^{5,6} This ruffling distortion would contract the porphyrin core and shorten the distance between adjacent nitrogen atoms, thereby enhancing intramolecular hydrogen bonding.

The crystal structures of porphyrins 2–4 were determined[†] to see if they were consistent with this model. As can be seen in Fig. 1, the porphyrins with larger substituents do show increased ruffling of the macrocycle. This ruffling will maximize core contraction compared to other nonplanar distortion modes¹⁰ and will also keep the nitrogen and hydrogen atoms in the porphyrin plane. Hence, the crystal structures show precisely the kind of nonplanar deformation expected to enhance intramolecular hydrogen bonding and produce the effects observed in the ^1H NMR spectra. Furthermore, the much larger effects seen in the NMR spectra of porphyrin 4 can be related to the significantly greater core contraction seen for this porphyrin (the average distance between the adjacent nitrogen atoms in 4 is only 2.71 Å vs. 2.89 Å in 3 and 2.91 Å in 2). Note

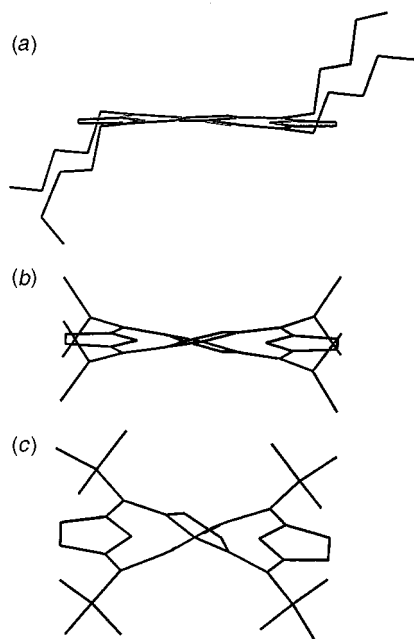


Fig. 1 Side-on views of the crystal structures of porphyrins (a) **2**, (b) **3** and (c) **4**. Hydrogen atoms have been omitted for clarity.

that a more detailed analysis of the pattern of hydrogen bonding within the porphyrin cores was also attempted but did not yield any definitive results. For example, the hydrogens in **4** were localized on an opposing pair of pyrrole rings and tilted towards adjacent nitrogen atoms (NH 21 towards N24 and NH 23 towards N22) possibly suggesting some additional deformation as a result of the severe core contraction. However, a review of other tetraalkylporphyrin crystal structures revealed similar NH tilting even in nominally planar systems.³

The studies reported here show that intramolecular hydrogen bonding in porphyrins can be strongly enhanced by a specific type of nonplanar distortion (ruffling), and also provide another example of the sometimes unexpected ways in which nonplanarity can affect the properties of porphyrins.¹¹ The fact that enhanced intramolecular hydrogen bonding has not previously been noted in other extremely nonplanar porphyrins is probably related to the predominantly saddle conformations¹² adopted by these molecules, where tilting of the pyrrole rings out of the porphyrin plane will disfavor intramolecular hydrogen bonding. Indeed, recent studies of such porphyrins have shown downfield shifts of the NH protons in some solvents due to increased *intermolecular* hydrogen bonding.¹³ Finally, it should be noted that this new information about hydrogen bonding in porphyrins, together with recent studies showing that even large nonplanar distortions result in only modest decreases in the porphyrin ring current effect,⁷ suggests that the practice of using the chemical shift of the NH protons as an indicator of structurally induced changes in the porphyrin ring current may need to be approached with more caution.

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Notes and references

† *Crystal data for 2*: C₄₀H₅₄N₄, crystals were grown *via* slow diffusion of MeOH into a solution of **2** in THF, dimensions 0.20 × 0.38 × 0.55 mm, orthorhombic, space group *P2₁2₁2₁*, *a* = 13.416(2), *b* = 15.734(3), *c* =

16.473(2) Å, *V* = 3477.2(9) Å³, *Z* = 4 (*M* = 590.87). Diffraction data were collected on a Syntex P2₁ diffractometer with a graphite monochromated sealed tube X-ray source [λ (Cu-K α) = 1.54178 Å] at 130(2) K in $\theta/2\theta$ scan mode to $2\theta_{\max}$ = 133.9°. Of 3466 reflections measured (+*h*,+*k*,+*l*), all were independent and 3229 had $I > 2\sigma$ (T_{\max} = 0.77, T_{\min} = 0.91, ρ_{calc} = 1.129 g cm⁻³, μ = 0.497 mm⁻¹). The structure was solved by direct methods and refined (based on *F*² using all independent data) by full-matrix least-squares methods with 398 parameters (Siemens SHELXTL ver. 5.03). All non-hydrogen atoms were refined with anisotropic thermal parameters. Hydrogen atom positions were generated by their idealized geometry and refined using a riding model, except for the hydrogen atoms bonded to the pyrrole nitrogen atoms. In this case, electron density corresponding to a hydrogen atom was present at each pyrrole ring in difference Fourier maps, so each of the nitrogens was assigned a hydrogen at 0.5 occupancy. No absorption correction was applied. The final difference map had a largest peak of 1.45 e Å⁻³ and a largest hole of -0.40 e Å⁻³. Final *R* factors were *R*₁ = 0.0615 (observed data) and *wR*₂ = 0.166 (all data).

For **3**: C₃₂H₃₈N₄, crystal grown *via* slow diffusion of cyclohexane into a solution of **3** in CH₂Cl₂, dimensions 0.24 × 0.24 × 0.14 mm, orthorhombic, space group *Fdd2*, *a* = 20.257(4), *b* = 20.999(4), *c* = 12.373(3) Å, *V* = 5263(2) Å³, *Z* = 8 (*M* = 478.66). Diffraction data were collected on a Syntex P2₁ diffractometer with a graphite monochromated sealed tube X-ray source [λ (Cu-K α) = 1.54178 Å] at 130(2) K in $\theta/2\theta$ scan mode to $2\theta_{\max}$ = 113.0°. Of 996 reflections measured (+*h*,+*k*,+*l*), 920 were independent (*R*_{int} = 0.038), and 817 had $I > 2\sigma$ (T_{\min} = 0.88, T_{\max} = 0.93, ρ_{calc} = 1.203 g cm⁻³, μ = 0.546 mm⁻¹). The structure was solved by direct methods and refined (based on *F*² using all independent data) by full matrix least-squares methods with 168 parameters (SHELXS-86, SHELXL-93). All non-hydrogen atoms were refined with anisotropic thermal parameters. Hydrogen atom positions (except for the core pyrrolic NHs) were generated by their idealized geometry and refined using a riding model. Core hydrogen atoms, located in a difference Fourier map, were found to be localized on one opposing pair of pyrrole nitrogen atoms and were refined freely. An empirical absorption correction was applied using XABS2 (ref. 14). The final difference map had a largest peak of 0.19 e Å⁻³ and a largest hole of -0.22 e Å⁻³. Final *R* factors were *R*₁ = 0.0475 (observed data) and *wR*₂ = 0.1272 (all data). CCDC 182/1265.

Full details of the crystal structure of **4** and related metal complexes of this porphyrin will be presented shortly (ref. 15).

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