

Cis–Trans Isomerism in Porphyrin Isomers

Abhik Ghosh* and Knut Jynge

Department of Chemistry, Institute of Mathematical and Physical Sciences (IMR), University of Tromsø, N-9037 Tromsø, Norway

Received: April 18, 1997[®]

Using local density functional calculations, we have examined whether tetrapyrrolic porphyrin isomers can accommodate *trans* –CH=CH– double bonds within their frameworks and still exist as stable substances. The molecular total energies of the *trans* stereoisomers of free-base [3.0.1.0]- and [3.1.0.0]-porphyrin are only 23.7 and 26.6 kcal/mol above porphine and 7.7 and –12.7 kcal/mol relative to their respective *cis* stereoisomers. Introduction of a *trans* double bond also results in a dramatic stabilization of the [4.0.0.0]-isomer. At least, the *trans* isomers of [3.0.1.0]- and [3.1.0.0]-porphyrin are predicted to be stable, chemically isolable compounds. The energetics results are analyzed in terms of the optimized geometries.

Recent syntheses of porphyrin isomers, with N₄ cores and aromatic tetrapyrrolic frameworks, have opened up a new direction in the chemistry of tetrapyrroles. The new ligands are expected to have intriguing metal-coordinating and optical properties as well as practical applications in areas such as the photodynamic therapy of cancer.¹ Formally, the isomeric porphyrins are related to ordinary porphyrin by different redistributions of the four pyrrole and four methine units. Density functional theoretical (DFT)² calculations have provided a good account of the relative stabilities of the different porphyrin isomers.³ However, no answer is currently available to the intriguing question of whether tetrapyrrolic porphyrin isomers can accommodate *trans* –CH=CH– double bonds within their frameworks and still be sufficiently stable to be isolated.

The choice of a suitable computational method was a crucial issue for this study. Geometry optimizations with *ab initio* Hartree–Fock and semiempirical theories do not yield realistic delocalized structures for porphyrin-type molecules but rather result in “frozen resonance forms” with alternating single and double bonds.⁴ This problem is corrected by simple schemes of electron correlation such as second-order Møller–Plesset perturbation theory or DFT.⁴ For this work, we chose local density functional (LDF) theory as an affordable method that implicitly takes electron correlation into account.⁵ Using C_s symmetry-constrained⁶ geometry optimizations, we explore here the possibility of skeletal *cis*–*trans* isomerism in the [3.0.1.0]-, [3.1.0.0]-, and [4.0.0.0]-isomers of porphyrin. Table 1 presents the LDF/DNP⁵ total energies of “all-*cis*” and “mono-*trans*”⁷ stereoisomers of these porphyrin isomers. Figure 1 presents their optimized geometries as well as that of porphine.

The most striking observation from Table 1 is that the *trans* stereoisomers of [3.0.1.0]- and [3.1.0.0]-porphyrin are surprisingly low-energy species, being only 23.7 and 26.6 kcal/mol above porphine, respectively. These low energies imply that both these *trans* stereoisomers should be stable enough to be chemically synthesized and isolated. *Cis*-[3.0.1.0]-porphyrin is also a relatively low-energy species. In contrast, *cis*-[3.1.0.0]-porphyrin has a high energy, ca. 39 kcal/mol relative to porphine, and Vogel *et al.* have expressed doubt as to whether it can exist as a stable molecule.³ Therefore, it is gratifying to find that *trans*-[3.1.0.0]-porphyrin is dramatically more stable than its *cis* stereoisomer.

TABLE 1: LDF/DNP Total Energies (kcal/mol) of Porphyrin Isomers Relative to Porphine as Zero Level

regioisomer	stereoisomer		energy difference: $E_{trans} - E_{cis}$
	<i>cis</i>	<i>trans</i>	
[3.0.1.0]	16.0 (19.0) ^a	23.7	7.7
[3.1.0.0]	39.3 (38.7) ^a	26.6	–12.7
[4.0.0.0]	69.8 (70.6) ^a	37.2	–32.6

^a These are BLYP/6-31G**//3-21G* values taken from ref 3.

Planar *cis*-[4.0.0.0]-porphyrin, with an energy of ca. 70 kcal/mol above porphine, appears to be a very unstable species that probably cannot be isolated. *trans*-[4.0.0.0]-porphyrin is far more stable, by a margin of ca. 33 kcal/mol. However, it is still about 37 kcal/mol above porphine. The possible synthesis of *trans*-[4.0.0.0]-porphyrin remains an intriguing, if uncertain, goal for porphyrin chemists.

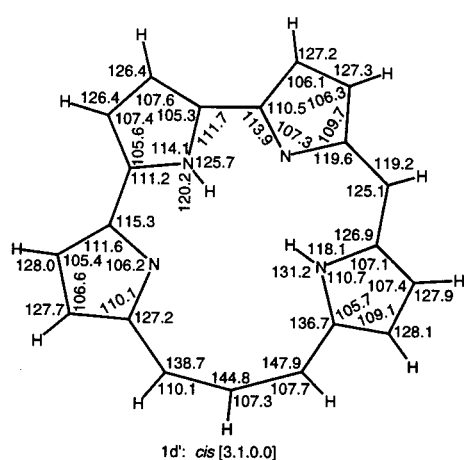
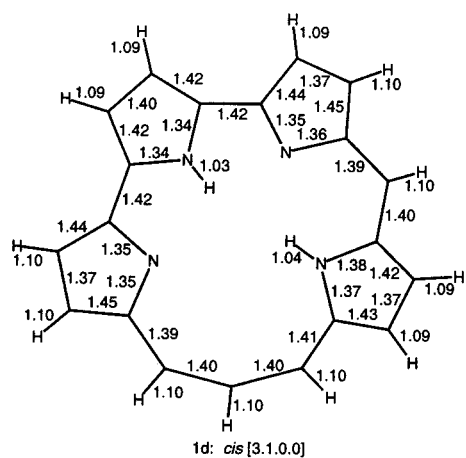
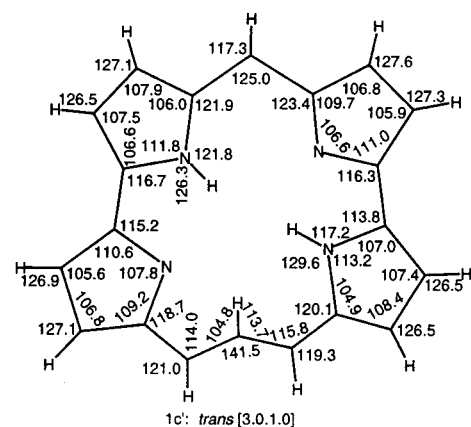
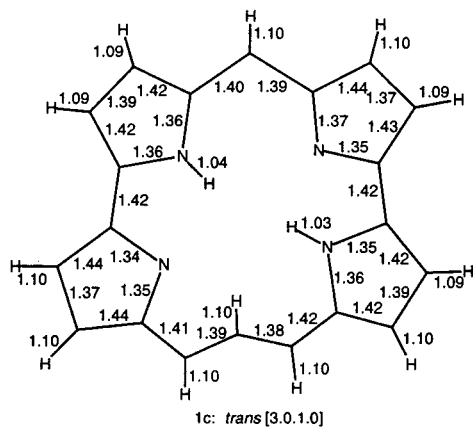
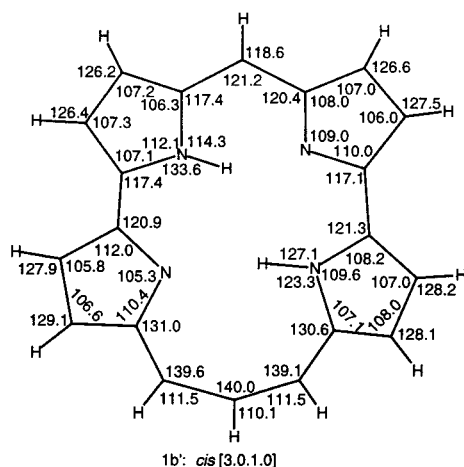
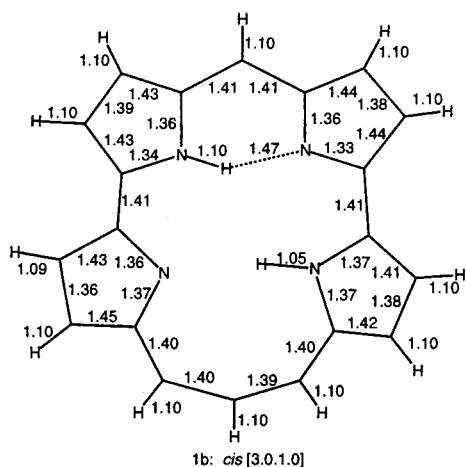
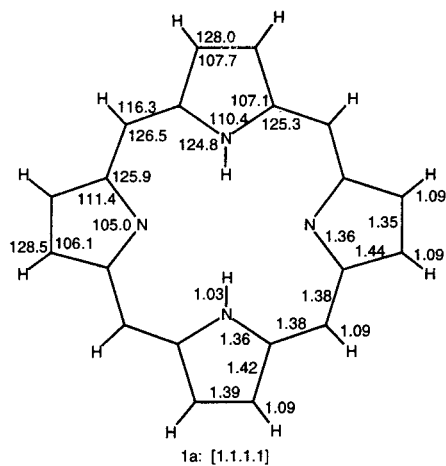
Table 1 shows that for the *cis* stereoisomers the LDF/DNP⁵ total energies are in excellent agreement with previously reported BLYP/6-31G** results.³ In other words, gradient-corrected functionals do not appear to have a significant effect on the energetics computed at the LDF level. This is not surprising in view of the fact that the molecules studied are all isomers and contain the same number of bonds of each type. Accordingly, in this initial study of this subject, we have not employed nonlocal functionals.⁸

The energetics results can be qualitatively correlated with the optimized structures of the molecules, highlights of which are described below. The reader is encouraged to verify the generalizations set forth below by examination of the structural data in Figure 1.

The geometrical features of the pyrrole rings of normal porphine (Figure 1a) are largely conserved in all of its isomers (Figure 1b–g'). Thus, in all the structures studied, the C_α–C_β bonds are long (1.42–1.45 Å) compared to the C_β–C_β (1.36–1.40 Å) and C_α–N (1.33–1.38 Å) bonds and the C_α–N–C_α angles are significantly larger at the protonated nitrogens (110.4–115.7°) than at the unprotonated nitrogens (105.0–109.7°). Like porphine, all the molecules studied have typical aromatic structures with relatively little bond length alternation.

Structural differences among the molecules are most pronounced for bond lengths and bond angles involving the interpyrrole bonds and polymethine linkages. Thus, all in-

[®] Abstract published in *Advance ACS Abstracts*, June 15, 1997.



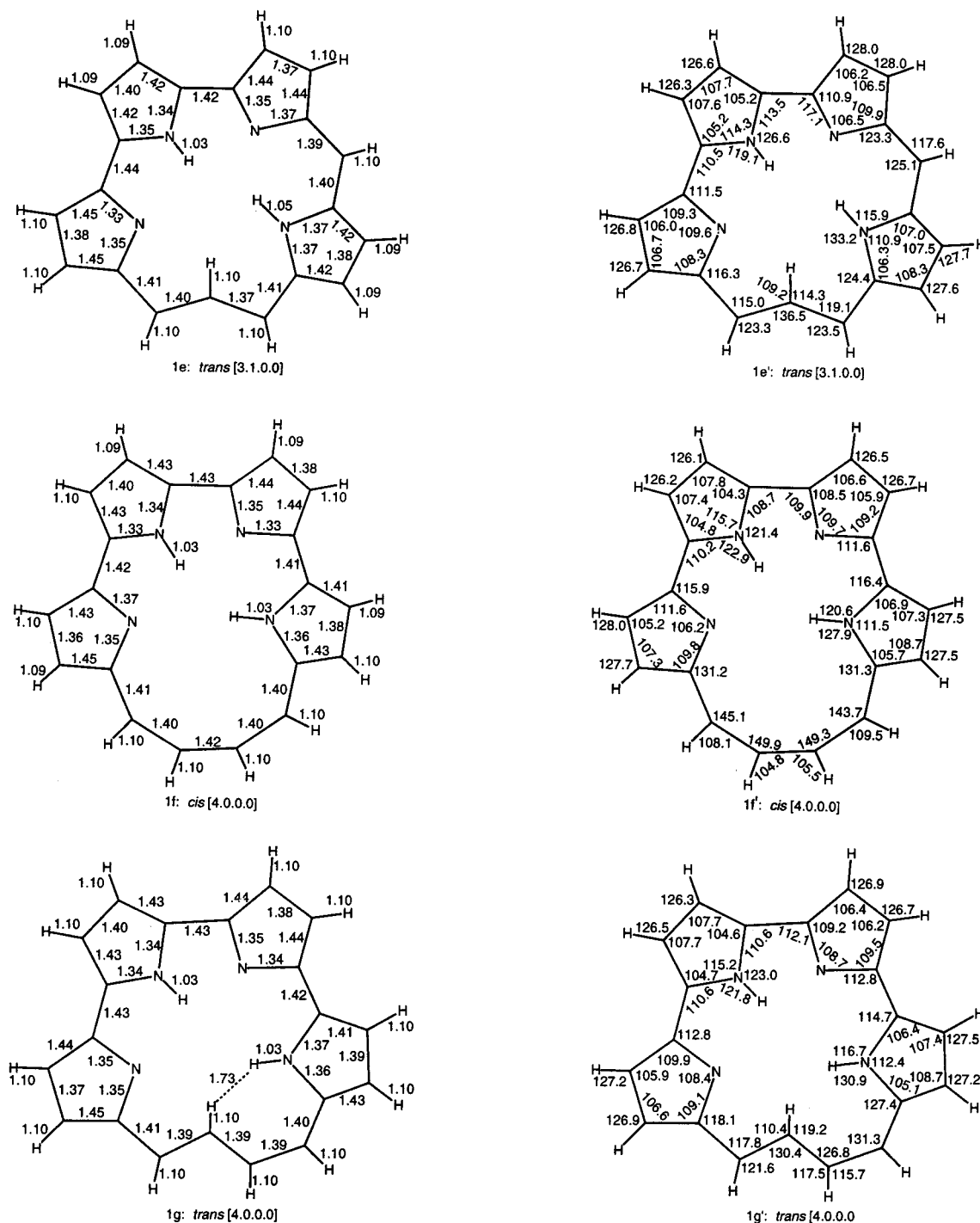


Figure 1. Optimized internuclear distances (Å) and angles (deg) of free-base porphyrin isomers studied. For diagrams b–g, distances and angles are given separately in unprimed and primed diagrams, respectively.

terpyrrole CC bonds in the porphyrin isomers (1.39–1.43 Å) are longer and probably more strained than the C_{α} – C_{meso} bonds in porphine (1.38 Å). Note also the unusually wide and, therefore, strained bond angles subtended at some of the interpyrrole methine units of the porphyrin isomers, especially the all-*cis* stereoisomers (Figure 1b',d',f').

Bond angle strain is clearly the dominant factor contributing to the high energies of all-*cis*-[3.1.0.0]- and all-*cis*-[4.0.0.0]-porphyrin (Figure 1d',f'). Similarly, the relative stability of *trans*-[3.1.0.0]-porphyrin correlates well with the relatively unstrained bond angles in this molecule (Figure 1e'). The reasons for the relatively low energies of both stereoisomers of [3.1.0.0]-porphyrin are somewhat less obvious (Figure 1b–c'), but a careful examination of their structures does reveal

significantly less bond angle strain than what is found for all-*cis*-[3.1.0.0]- and all-*cis*-[4.0.0.0]-porphyrins.

The relatively high energy of *trans*-[4.0.0.0]-porphyrin, which does not have any exceptionally strained bond angles, appears to result from a combination of various factors as opposed to a single dominant cause (Figure 1g,g'). Among its destabilizing geometrical features may be mentioned the relatively long (1.42–1.43 Å) and possibly strained bonds that directly connect the pyrrole rings and a short (1.73 Å) repulsive $\text{CH}\cdots\text{HN}$ contact (note the inequality of the $\text{H}-\text{N}-\text{C}_{\alpha}$ angles at this nitrogen center in Figure 1g').

In addition to strained bonds and angles, hydrogen-bonding patterns play an important role in determining the relative energies of free-base porphyrin isomers. Thus, the low energy

of all-*cis*-[3.0.1.0]-porphyrin undoubtedly owes considerably to the very short (1.47 Å) and strong NH...N hydrogen bond (Figure 1b). Note the extremely long N–H bond (1.10 Å) and the extremely unequal H–N–C_α angles (114.3 and 133.6°). This hydrogen bond lengthens to 1.98 Å in *trans*-[3.0.1.0]-porphyrin (Figure 1c), which certainly accounts for a significant part of the energy difference of ca. 8 kcal/mol between the stereoisomeric [3.0.1.0]-porphyrins.

Overall, we have used DFT to identify and structurally characterize stable porphyrin stereoisomers with *trans* –CH=CH– linkages. These molecules are predicted to be new members of the currently exclusive family of stable porphyrin isomers.

Acknowledgment. This work was supported by the Norwegian Research Council, the VISTA program of Statoil-Norway, and a Senior Fellowship from the San Diego Supercomputer Center.

References and Notes

- (1) This subject has been reviewed: (a) Vogel, E. *Pure Appl. Chem.* **1996**, 68, 1355. (b) Sessler, J. *Angew. Chem.* **1994**, 106, 1410; *Angew. Chem., Int. Ed. Engl.* **1994**, 33, 1348.
- (2) For selected DFT investigations of porphyrins from our laboratory, see, e.g.: (a) Ghosh, A. *J. Phys. Chem.* **1994**, 98, 11004. (b) Ghosh, A. *Angew. Chem., Int. Ed. Engl.* **1995**, 34, 1028; *Angew. Chem.* **1995**, 107, 1117. (c) Ghosh, A. *J. Am. Chem. Soc.* **1995**, 117, 4691. (d) Ghosh, A. *J. Mol. Struct.: THEOCHEM* **1996**, 388, 359. (e) Ghosh, A. *J. Phys. Chem. B* **1997**, 101, 3290.
- (3) Vogel, E.; Bröring, M.; Fink, J.; Rosen, D.; Schmickler, H.; Lex, J.; Chan, K. W. K.; Wu, Y.-D.; Plattner, D.; Houk, K. N. *Angew. Chem.* **1995**, 107, 2705; *Angew. Chem., Int. Ed. Engl.* **1995**, 34, 2511.
- (4) Almlöf, J.; Fischer, T. H.; Gassman, P. G.; Ghosh, A.; Häser, M. *J. Phys. Chem.* **1993**, 97, 10964.
- (5) All calculations were performed with the DMol program system (Molecular Simulations, Inc., San Diego, CA) using previously described methods (Delley, B. *J. Chem. Phys.* **1990**, 92, 508). Numerical basis sets of double- ζ plus polarization (DNP) quality were employed throughout. All calculations were of the spin-restricted type and used the local exchange-correlation potential previously given (von Barth, U.; Hedin, L. *J. Phys. C* **1972**, 5, 1629). An extremely fine mesh was used for numerical integrations of the matrix elements.
- (6) The C_s constraints may be justified as follows. While the isomeric porphyrins studied are probably not rigorously planar, they are not expected to be strongly buckled either. Moreover, relatively soft potential energy surfaces are associated with moderate out-of-plane deformations of porphyrinoids. Thus, our assumption of C_s symmetry, while halving our computational efforts, is unlikely to significantly affect the relative energetics of porphyrin isomers.
- (7) These informal stereochemical descriptors refer only to the –CH=CH– units in these molecules.
- (8) Nonlocal functionals are essential in certain DFT studies of porphyrins such as optimizations of the transition states for NH tautomerism in the free bases (Vangberg, T.; Ghosh, A. *J. Phys. Chem. B* **1997**, 101, 1496). Local functionals severely overestimate the stability of the partially bonded N...H...N moieties in these transition states. However, as long as we are not concerned with transition states, LDF theory has proved both useful and accurate in many studies of free-base tetrapyrroles.²