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ORIGINAL PAPER

A computational study on the stability–aromaticity correlation of triply N-confused porphyrins: CMMSE-09

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Abstract The B3LYP density functional theory methodology in conjunction with the 6-31G(d,p) basis set has been used to characterize triply N-confused *meso*-tetraphenylporphyrins. According to our computations, there is no a direct correlation between stability and aromaticity as already found for non-substituted confused porphyrins. The inclusion of these substituents in the calculations provokes a decrease of the planarity and aromaticity of these macrocycles along with a notable rise of their relative stability with respect to the non-substituted case. Steric repulsions, both among phenyl rings and β atoms in the pyrrolic rings, and among H atoms in the core of the macrocycles, dominate over aromaticity in the establishment of the most stable conformation of each isomer.

Keywords Density functional computations · NICS calculations · Bader analysis · N-confused porphyrins · *Meso* phenyl group effect

1 Introduction

N-confused porphyrins (NCP) are a class of porphyrin isomers, which have one or more of the core nitrogen atoms pointing out of the inner part of the macrocycle (see Scheme 1). Since their discovery in 1994 [1,2], these compounds have been spurring interest owing to their ability to bind a wide variety of cations and anions in their free

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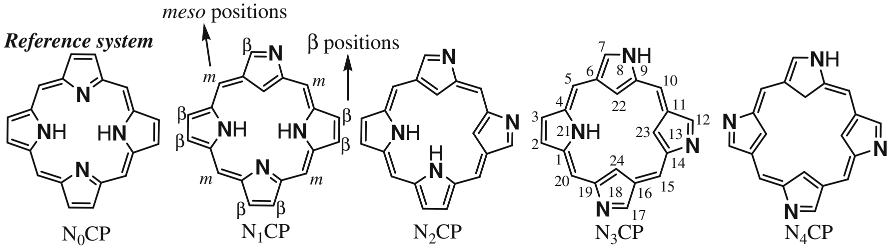


Scheme 1 Structures of normal porphyrin (N_0CP) and some NCP isomers

base and protonated forms, respectively, thus disclosing a rich coordination chemistry and unprecedented reactivity [3–8]. Apart from their coordination abilities, the peripheral nitrogen atom(s) can also serve as hydrogen bonding donor and acceptor, which is important to form multiporphyrin systems [4,5,8]. So far, singly and doubly NCP (N_1CP and N_2CP, respectively) are the two only types of NCP, which have been synthesized [1,2,9–19]. Confused porphyrin derivatives with five and more pyrrole rings have also been reported in the recent literature [5,7,20–23]. Given their relevant practical applications, it seems important to deeply understand the factors affecting their structure and stability.

From the theoretical viewpoint, Furuta and co-workers have performed a thorough analysis of the stability, structure, and aromaticity of the numerous NCP isomers ranging from N_1CP to fully NCP (N_4CP in Scheme 1) [24,25]. No substituents in the *meso* positions of the macrocycles (see Scheme 1) were considered in their calculations though aryl groups are frequently present in the experimentally synthesized NCP. From their results, it has been concluded that, in general, there is not a positive correlation between stability and aromaticity because the steric factor of the inner core atoms of the macrocycle predominates over the aromatic stabilization of NCP in the upper confusion level. However, a positive stability–aromaticity correlation was found in a recent theoretical study on non-confused porphyrin derivatives containing five pyrrole rings, wherein the four *meso* phenyl rings play an important role on the loss of planarity of some of these macrocycles [26]. Could the presence of aryl substituents at the *meso* positions of NCP modify the stability–aromaticity correlation found in their absence?

With the aim of answering this question, we undertook a theoretical investigation on N-confused *meso*-tetraphenylporphyrins (NCTPP). Given the size and the number of this kind of systems, we focussed our attention on the triply NCTPP (N_3CTPP) macrocycles by considering only those systems containing four inner hydrogen atoms denoted as the inner-4H type (see N_3CP in Scheme 1).

2 Computational methodology

All calculations were carried out using the density functional theory with the Jaguar program [27]. Full geometry optimizations and vibrational frequency calculations were performed by using the hybrid functional B3LYP [28–30] along with the

6-31G(d,p) basis set [31]. That functional combines the Becke's three parameter hybrid functional and the gradient-corrected correlation functional of Lee et al. The B3LYP/6-31G(d,p) computational scheme was chosen for comparison purposes with those results obtained for the analogous systems in absence of *meso* phenyl substituents denoted here as N_3CP [25].

A topological analysis of the electron density was performed within the framework of the Atoms in Molecules theory (AIM) [32,33] of Bader using the AIMPAC package [34]. Nucleus-independent chemical shifts (NICS) [35] calculations on the B3LYP/6-31G(d,p) optimized structures were performed by using the GIAO method as implemented in the Gaussian 03 program [36] in order to obtain a quantitative measure of their aromaticity. NICS values were calculated on the projection of the bond critical point of electron density located between the hydrogen atoms of the two opposite inward-pointing CH units on the plane defined by the four *meso* carbon atoms.

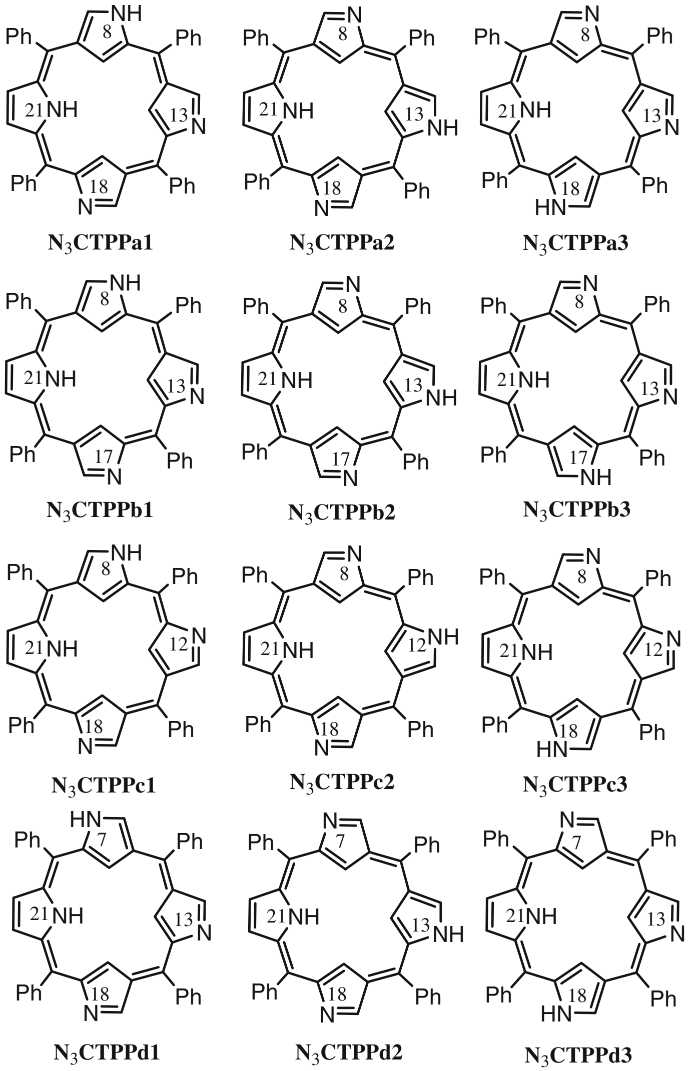
3 Results and discussion

The N_3CTPP isomers investigated in this work are grouped into four types, N_3CTPPa-d in Scheme 2, depending on the relative position of the four nitrogen atoms. According to the atom position numbering shown in Scheme 1 for N_3CP, the type N_3CTPPa presents nitrogen atoms at the positions 8, 13, 18, and 21 of the macrocycle.

For N_3CTPPb and N_3CTPPc, the four nitrogen atoms occupy the positions 8, 13, 17 and 21 and 8, 12, 18, and 21, respectively. Finally, N_3CTPPd, shows the sequence of nitrogen positions 7, 13, 18, and 21. As the N_3CTPP isomers of inner-4H type have three peripheral nitrogen atoms with one of them bearing a hydrogen atom, then, each type contains three isomers (1–3) that differ in the position of the peripheral NH hydrogen atom as displayed in Scheme 2. Figure 1 collects the optimized structures of the twelve N_3CTPP isomers shown in Scheme 2 together with their corresponding absolute and relative energies. The latter ones are referred to the electronic energy of normal *meso*-tetraphenyl porphyrin (N_0CTPP), which is essentially planar as experimentally reported, to compare with those previously obtained for the analogous structures in absence of *meso* phenyl substituents [25].

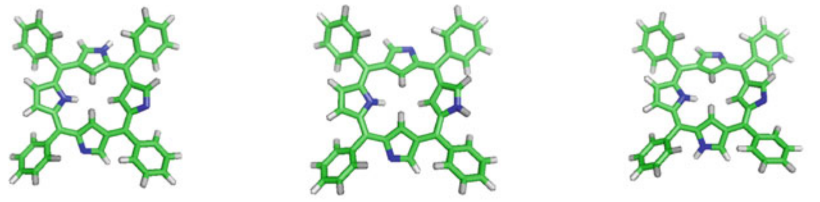
According to our results, all the N_3CTPP isomers are less stable than N_0CTPP as in the non-substituted case, but the presence of the phenyl groups increases their stability in the range 11.3–19.7 kcal/mol when is compared with the analogous N_3CP. The most stable isomer is $N_3CTPPb2$, 35.3 kcal/mol higher in energy than N_0CTPP, while the least stable one is $N_3CTPPc1$, 44.7 kcal/mol above N_0CTPP. In the case of the N_3CP isomers, N_3CPb2 (54.5 kcal/mol) is the most stable macrocycle as well, whereas the least stable one is N_3CPa1 (59.4 kcal/mol). Therefore, the energy difference between the most and the least stable isomers increases from 4.9 kcal/mol in non-substituted N_3CP to 9.4 kcal/mol when the phenyl substituents are present.

To check the correlation between stability and aromaticity in these compounds, we calculated NICS as an aromatic index as described in the Sect. 2. Figure 1 collects the obtained values. The comparison of these results with those obtained for the analogous N_3CP reveals that the presence of phenyl groups clearly reduces the

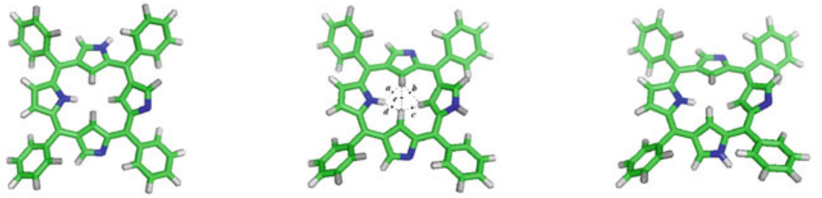


Scheme 2 Schematic view of the twelve N_3CTPP isomers of inner 4H-type. (*Note* that the d series is different from the Furuta's one [25]. The isomers N_3CTPPd1, N_3CTPPd2, and N_3CTPPd3 in this work correspond to N_3CPd3, N_3CPd1, and N_3CPd2 in the Furuta's research, respectively)

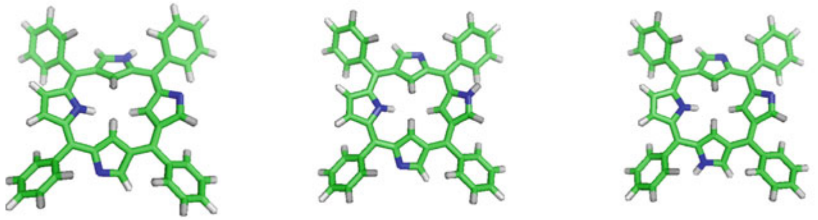
aromaticity of all the species. In effect, NICS values vary from −4.6894 to −1.6184 ppm for N_3CTPP whereas the range from −9.3328 to −3.9419 ppm was found for N_3CP. The isomeric sequences N_3CTPPa1-3, N_3CTPPb1-3, and N_3CTPPd1-3 present a clear reverse correlation since the greater stability of the macrocycle, the lower aromaticity. This behaviour is partly broken in N_3CTPPc1-3 since although the most aromatic isomer of this series (N_3CTPPc1) is the least stable one, the most stable isomer is not the least aromatic one. Therefore, the main trend found is in the line



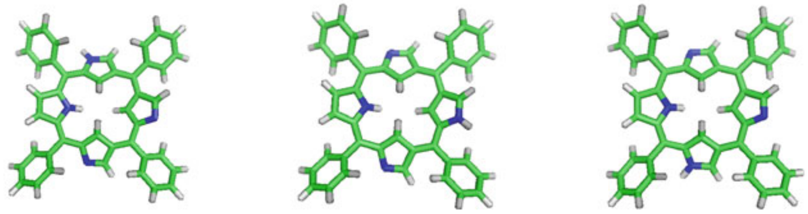
N_3CTPPa1 (-1913.7464118; 40.8) [-4.6894] **N_3 CTPPa2** (-1913.7509672; 38.0) [-3.0626] **N_3CTPPa3** (-1913.7543195; 35.9) [-1.6184]



N_3CTPPb1 (-1913.7481788; 39.7) [-3.3952] **N_3CTPPb2** (-1913.7551638; 35.3) [-2.1067] **N_3CTPPb3** (-1913.7529699; 36.7) [-2.4888]



N_3CTPPc1 (-1913.7402103; 44.7) [-3.8448] **N_3CTPPc2** (-1913.7422930; 43.4) [-2.9737] **N_3CTPPc3** (-1913.7410390; 44.2) [-2.5577]



N_3CTPPd1 (-1913.7488332; 39.3) [-3.5170] **N_3CTPPd2** (-1913.7477663; 40.0) [-3.9129] **N_3CTPPd3** (-1913.7516850; 37.5) [-2.7047]

Fig. 1 Optimizad structures of the N_3CTPP isomers of inner-4H type at the B3LYP/6-31G(d,p) theory level. Absolute (hartree) and relative (kcal/mol) electronic energies and NICS values (ppm) are also given in *parenthesis* and in *square brackets*, respectively. Relative energies of the N_3CTPP isomers are referred to the electronic energy of *meso*-tetraphenylporphyrin (N_0CTPP), which is -1913.8114830 hartree. Bond critical points of electron density located for the isomer N_3CTPPb2 in the inner part of the macrocycle are also given

with that theoretically obtained by Furuta and co-workers on N_3CP wherein no direct correlation between stability and aromaticity was found [25].

The next step in this investigation was to analyze the geometry distortion of all the macrocycles by comparison with the analogous non-substituted ones in order to check its correlation with the aromaticity and, consequently, with the relative energy. It is interesting to note that all the N_3CTPP isomers present a saddle shape as shown in Fig. 1. The four phenyl rings slant towards the upper face of the top and bottom

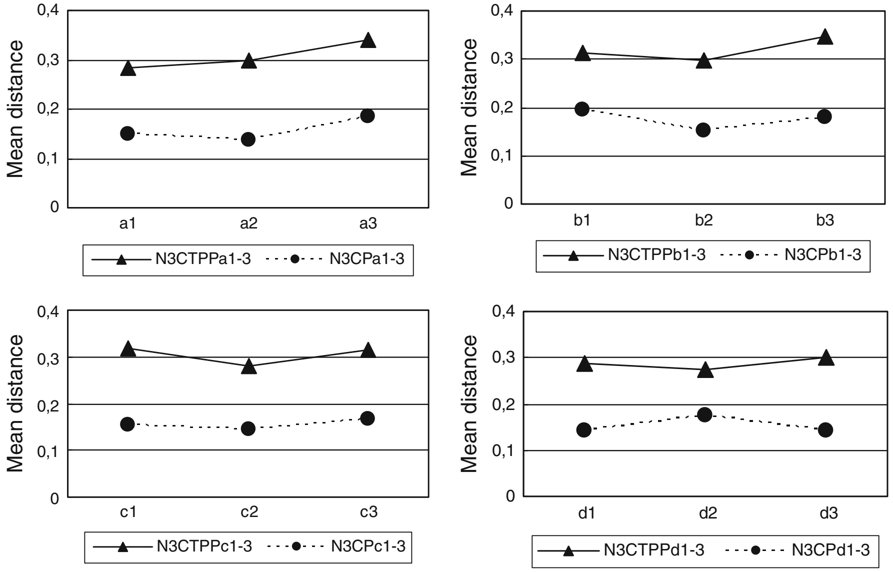


Fig. 2 Mean distance (in Å) of the same 24 heavy atoms of each macrocycle with respect to the plane defined by the *meso* carbon atoms C5, C10, and C20 for the N$_3$CTPP and N$_3$CP isomers

pyrrolyc rings, thus provoking the lowering of the β atoms and the rise of their inner H atoms. As a consequence, the opposite is found for the left and right pyrrolyc rings. Given that the four *meso* carbon atoms are practically in the same plane for all the structures (the corresponding dihedral angles range from −6.7 to +3.2 degrees), we calculated the distance between each of the 24 heavy atoms of the macrocycle and the plane defined by the carbon atoms at the positions 5, 10, and 20. Figure 2 displays the resultant mean distances for the isomeric series N$_3$CTPPa-d and N$_3$CPa-d. The former isomers show mean distances between 0.275 and 0.348 Å, while a range of 0.136–0.195 Å was found for the latter species. Therefore, N$_3$CTPP are more deviated from the reference plane than N$_3$CP, thus explaining their smaller aromaticity due to a poorer π molecular orbital overlapping.

The analysis just performed shows that the presence of the four *meso* phenyl rings renders N$_3$CTPP more stable, less aromatic and more distorted, relative to N$_0$CTPP, than the corresponding non-substituted N$_3$CP porphyrins. Let's try now to get a deeper insight into the role played by phenyl rings in order to produce such effects.

The reason for the macrocycle deformation previously described is the attempt to simultaneously minimize the steric repulsions between each phenyl ring and the β atoms of both pyrrolic rings flanking it (CH, NH, or N). The most important consequence of this deformation to a saddle shape in N$_3$CTPP is the lowering of the steric repulsions among the H atoms in the inner core. To discuss this fact we focus on the most stable isomer both with and without *meso* phenyl rings, N$_3$CTPP-b2 and N$_3$CP-b2, respectively. Table 1 collects the distances between opposite and neighbour H atoms in the core. In the absence of phenyl rings a small deformation of the macrocycle lets the opposite H atoms to be even more distant than in presence of

Table 1 Distances and values of the electron density, ρ, at the bond critical points (BCP) located for the most stable isomers with and without *meso* phenyl rings in the inner part of the macrocycles

	N_3CTPPb2	N_3CPb2
Distances (Å)		
(C22)H–H(C24)	2.232	2.545
(N21)H–H(C23)	2.599	2.770
(N21)H–H(C22)	2.147	1.800
(N21)H–H(C24)	2.128	1.868
(C23)H–H(C22)	2.283	2.061
(C23)H–H(C24)	2.264	1.820
BCP (e/Å^3)		
a	0.0114	0.0174
b	0.0110	0.0120
c	0.0110	0.0166
d	0.0139	0.0213
e	0.0070	–

phenyl rings. However, the four distances between neighbour H atoms are forced to be smaller when there are no *meso* phenyl rings giving rise to important steric repulsions responsible of the greater relative instability of N_3CP. The analysis of the electronic density through the AIM method allows the confirmation of this fact. The network of bond critical points (BCP) in the core is analogous for both porphyrins N_3CTPP-b2 (see Fig. 1) and N_3CP-b2, except for the BCP between the hydrogen atoms of the two opposite inward-pointing CH units, which is absent in N_3CP-b2. However, the smaller value of the electron density in the BCP between neighbour H atoms in N_3CTPP-b2 indicates smaller steric repulsion and, so, greater stability.

In summary, we have theoretically analyzed the effects produced by the four *meso* phenyl rings on the structure and stability of 12 triply confused porphyrins, N_3CTPP. The most important finding is the greater stability of these compounds relative to N_0CTPP in comparison with the relative stability of the unsubstituted triply confused porfirins, N_3CP. Besides, the difference between the most and the least stable isomer amounts to 9.4 kcal/mol for N_3CTPP and to only 4.9 kcal/mol for N_3CP. The most relevant issues simultaneously affecting the relative stability of the studied compounds are aromaticity and steric repulsions, both among phenyl rings and β atoms in the pyrrolic rings, and among H atoms in the core of the macrocycles. The minimization of all these steric repulsions leads to macrocycles saddle shaped much more distorted than in the absence of *meso* phenyl rings. The most distorted isomers are, in most cases, those with the smallest aromaticity and greater stability. Steric repulsions dominate over aromaticity in the establishment of the most stable conformation of each isomer. It seems evident the necessity of including phenyl rings in the theoretical modelling of porphyrin derivatives containing such rings in *meso* positions.

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