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A theoretical study of porphyrin isomers and their core-modified analogues: *cis-trans* isomerism, tautomerism and relative stabilities

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Abstract. Semiempirical (AM1 and PM3) and density functional theory (DFT) calculations were performed on about 50 porphyrin isomers with 25 each of 1,2 (*syn*) and 1,3 (*anti*) tautomeric forms. The corresponding oxa- and thia-core-modified analogues were also computed. The variations of relative energies and stabilities of the core-modified analogues were compared with parent porphyrin **1** and the corresponding oxa- and thia-analogues. The trends in relative energies are not significantly changed while going from parent system to oxa- and thia-core-modified porphyrins in case of both *syn* and *anti* tautomers. Isomers of types [2·2·0·0], [3·0·1·0], [3·1·0·0], and [4·0·0·0] are destabilized due to the absence of methine bridge, which results in angle strain for tetrapyrroles. Isomers having [2·1·1·0], [2·1·0·1], [2·0·2·0] and [2·2·0·0] connectivity, the *Z* isomers, are more stable compared to the corresponding *E* isomers in both *syn* and *anti* forms of parent and core-modified analogues.

Keywords. Porphyrin isomers; core-modified analogues; theoretical studies; tautomerism; oxa-porphyrin; thiaporphyrin.

1. Introduction

Study of porphyrins has developed into a subject of interdisciplinary research due to their importance and relevance in a wide range of areas such as chemistry, biology and medicine.[1–3] These highly coloured tetrapyrrolic macrocyclic pigments[4] play a diverse and critical role in biology, ranging from electron transfer, oxygen transport and storage, and photosynthetic processes to catalytic substrate oxidation.[2,3] Recently there have been a number of reports on the use of modified, expanded and isomeric forms of porphyrins as molecular receptors for various substrates.[5] Other tetrapyrrolic structures, such as chlorins, phthallocyanines, porphyrin-ketones and benzoporphyrins have shown interesting phosphorescence properties.[6]

Theoretical research on porphyrins, like other aspects of porphyrin chemistry, is also driven by considerations of great biological importance of these molecules, their extensive coordination chemistry, and growing number of applications.[1–7] Thus, porphyrin-like molecules, structural variants of tetrapyrrolic macrocycles possessing $(4n + 2)p$ electron delocalization, have been the favourite hunting ground for synthetic chemists in anticipation of their special properties. Therefore, there is a major thrust in designing and synthesizing structural variants of basic tetrapyrrole macro cycles in contemporary research.[5] Research on the synthesis of porphyrin isomers has gained momentum since the discovery of porphycene by Vogel and co-workers and N-confused porphyrin independently by Furuta *et al* and Latos–Grazynski and co-workers.[8] The porphyrin isomers reported to date include, corrphycene, hemiporphycene, and isoporphycene obtained by shuffling the four pyrrolic subunits and the meso-carbon bridge.[5,8–12] Many research groups have recently exploited some of the unique properties exhibited by the N-confused porphyrins because their remarkable ability to act as tetra-coordinate ligands to form transition metal complexes.[4] This led to a flurry of synthetic attempts toward novel porphyrin-like molecules, with structural variants such as ring or bridge extended, reshuffled, inverted, N- and C-fused, contracted and core-modified porphyrins.[5,11–13]

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Wu *et al* carried out density functional calculations using both the BLYP/3-21G and BLYP/6-31G** methods on free-base porphyrins and their possible isomers with an N_4-metal coordination core.[9] Ghosh and Jynge reported BLYP/6-31G** calculations on *cis* and *trans* porphyrin isomers having [3·0·1·0], [3·1·0·0] and [4·0·0·0] connectivity.[10] Core modification in the skeleton by replacing one or two pyrrole nitrogens by other heteroatoms such as O and S alters the electronic structure and results in the formation of modified porphyrins. Introducing other heteroatoms yields new classes of compounds containing novel chelating properties.

The present study is aimed at tetrapyrrolic porphyrin isomers with N_4 cores and their corresponding core-modified structures where the two NH groups are replaced by oxygen and sulphur as heteroatoms. Two types of tautomers, (a) the imino protons on III and I ring (*anti* type), scheme 1; (b) imino protons at II and I ring (*syn* type), scheme 2 are taken into consideration. Thus a total of 150 isomers are considered here. The isomers of the parent porphyrin are divided into eight classes based on the nature of bridging, viz. freebase porphyrin [1·1·1·1], hemiporphycene [2·1·1·0], corrphycene [2·1·0·1], porphycene [2·0·2·0], isoporphycene [3·0·1·0], [2·2·0·0], [3·1·0·0] and [4·0·0·0]. Schemes 1 and 2 depict all the structures considered in the study along with the nomenclature. Except for the freebase **1**, all other classes involving geometrical isomerism *Z* (*cis*) and *E* (*trans*) in both *syn* and *anti* tautomeric forms are studied.

2. Computational methods

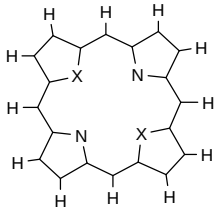
All the structures considered in the study (schemes 1 and 2) were initially taken as planar, and the geometry optimisations and frequency calculations were done to characterize whether they are minima on the potential energy surface or not. AM1 frequency calculations on the planar forms of most isomers indicate that none of them are minima on the potential energy surface. Subsequently, all the non-planar stationary points were found without imposing any symmetry constraints and characterized as minima with all real frequencies. Considering the size and the number of compounds involved in the study, doing full geometry optimisations at higher levels of theory was too expensive. Therefore, we restricted ourselves to single point calculations at B3LYP/6-31G* level on AM1 optimised geometries. All the structures are optimised at the semiempirical AM1[14] and PM3[15] methods. All the calculations in the study are performed using the Gaussian 98 suite of programs.[16] The relative energies of all the isomers are computed considering the parent porphyrin **1** and the corresponding oxa- and thiaanalogues. The distortion energy for each isomer is computed by taking the difference between the planar structure and the corresponding minimum energy structure.

3. Results and discussion

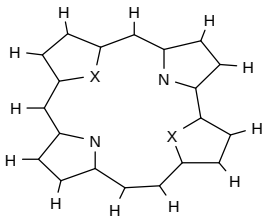
Different types of isomers are arrived at by varying the methine bridges in addition to the parent porphyrin moiety. Considering all the possible geometric isomers, totally 25 structures in each of 1,3 (*anti*) and 1,2 (*syn*) tautomers are considered in the present study, as given in schemes 1 and 2. First we discuss the relative energies and structural preferences in the *anti*-isomers of the parent and its core-modified analogues. This is followed by a discussion on the corresponding *syn* tautomeric forms. Finally, the geometric preference between the *E* and *Z* isomers in both *syn* and *anti* forms is discussed. The relative energies calculated for the porphyrin isomers at AM1, PM3 and B3LYP levels of theory are given in tables 1–6. While the main purpose of the study is to examine the relative energy variations in porphyrin and related isomers, the current study also addresses the applicability of semiempirical methodologies to this type of systems.

3.1 *Anti tautomeric form*

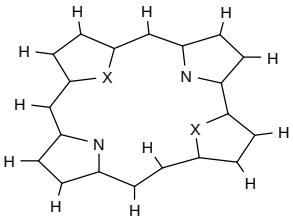
The relative energies and distortion energies of the *anti* tautomers of parent porphyrin and core-modified porphyrin analogues are given in tables 1–3. Among the 25 distinct isomers considered, **3c**-NH, **4e**-NH, and **5f**-NH upon unrestrained geometry optimisation have collapsed to the closely related isomers **3b**-NH, **4d**-NH, and **5d**-NH respectively. Thus, the total number of distinct minimum energy isomers of the porphyrin isomers has reduced to 22. Exactly the same trends were witnessed even for the oxy-modified analogues. However, among the thiaanalogues, the minimum energy structures of **4d**-S and **4e**-S have distinct geometries, while **2c**-S and **2b**-S and isomers **3c**-S and **3b**-S collapse to an identical geometry after optimisation. In this section, we discuss the *anti* tautomeric structures and the results of the parent system are compared of with those of



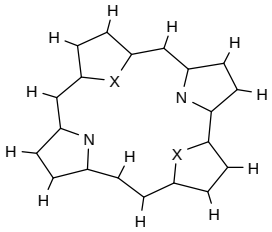
1-X; [1·1·1·1]



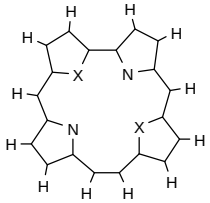
2a-X; [2·1·1·0]



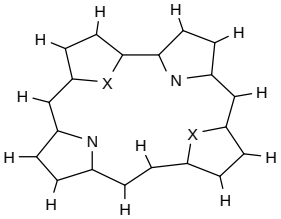
2b-X; [2·1·1·0]



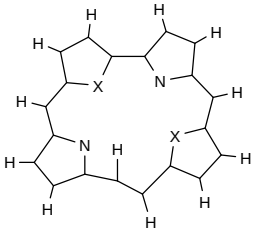
2c-X; [2·1·1·0]



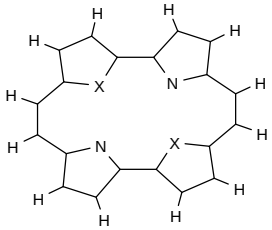
3a-X; [2·1·0·1]



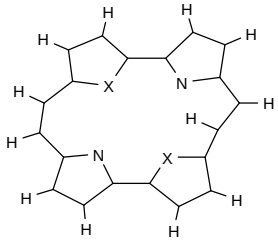
3b-X; [2·1·0·1]



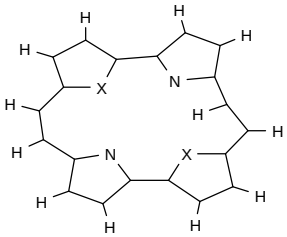
3c-X; **[**2·1·0·1]



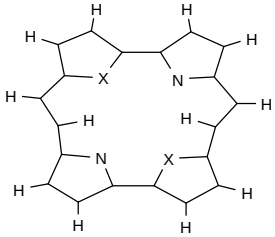
4a-X; [2·0·2·0]



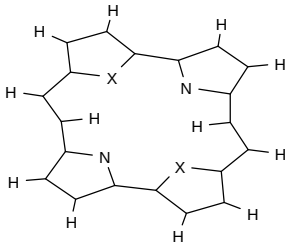
4b-X; [2·0·2·0]



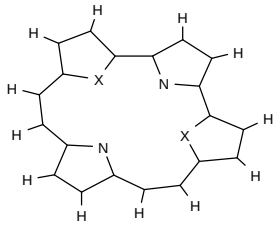
4c-X; [2·0·2·0]



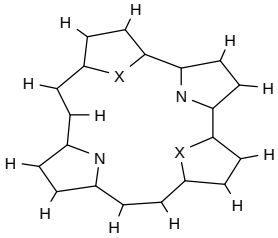
4d-X; [2·0·2·0]



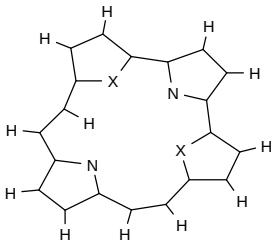
4e-X; [2·0·2·0]



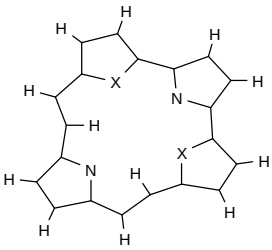
5a-X; [2·2·0·0]



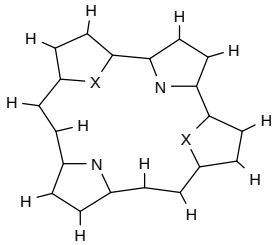
5b-X; [2·2·0·0]



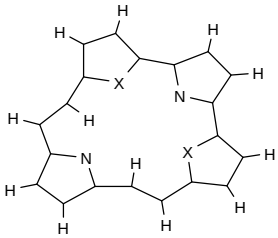
5c-X; [2·2·0·0]



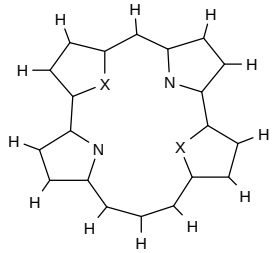
5d-X; [2·2·0·0]



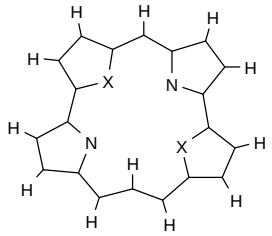
5e-X; [2·2·0·0]



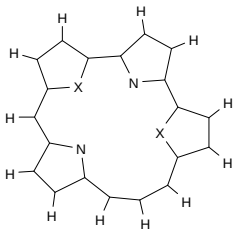
5f-X; [2·2·0·0]



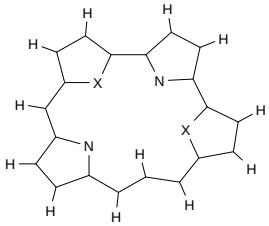
6a-X; [3·0·1·0]



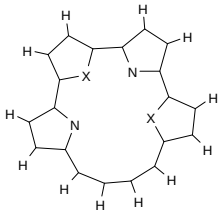
6b-X; [3·0·1·0]



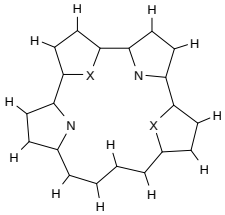
7a-X; [3·1·0·0]



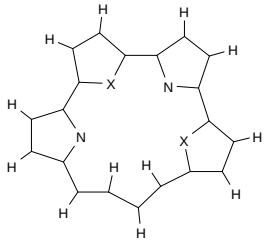
7b-X; [3·1·0·0]



8a-X; [4·0·0·0]

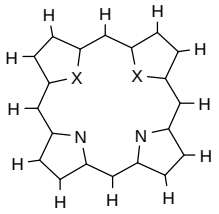


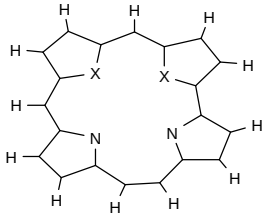
8b-X; [4·0·0·0]

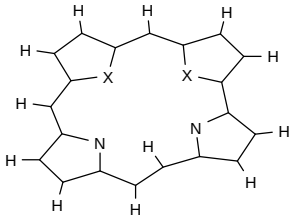


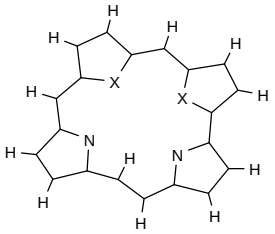
8c-X; [4·0·0·0]

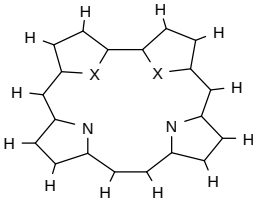
Scheme 1. *Anti* porphyrin ($C_{20}X_2N_2H_{12}$) isomers; here X = NH, O, S. The projections are the AM1 optimised geometry of the parent ($C_{20}N_4H_{14}$) isomers.

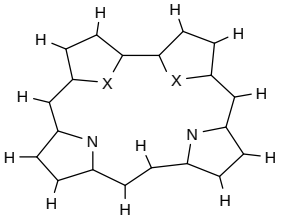

1′-X; [1·1·1·1]

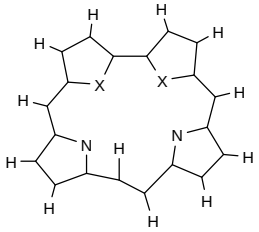

2a′-X; [2·1·1·0]

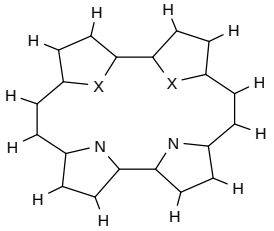

2b′-X; [2·1·1·0]

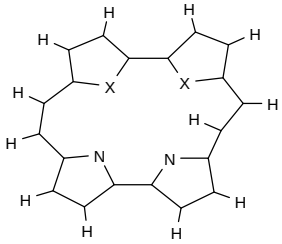

2c′-X; [2·1·1·0]

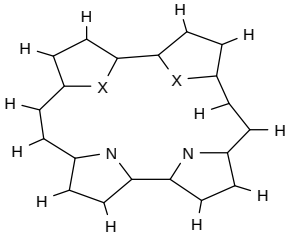

3a′-X; [2·1·0·1]

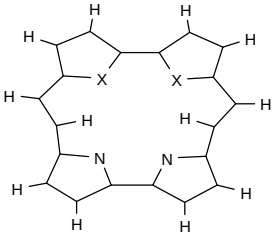

3b′-X; [2·1·0·1]

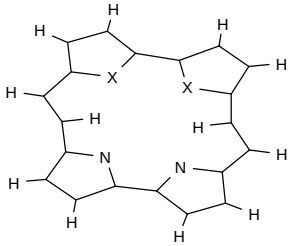

3c′-X; [2·1·0·1]

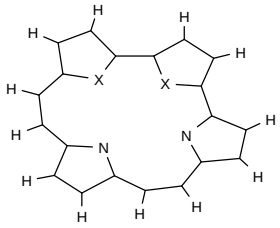

4a′-X; [2·0·2·0]

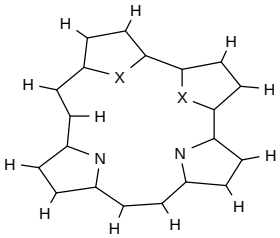

4b′-X; [2·0·2·0]

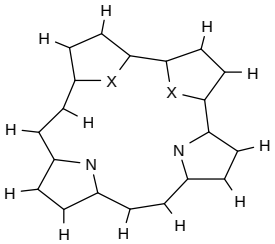

4c′-X; [2·0·2·0]

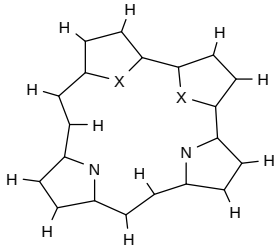

4d′-X; [2·0·2·0]

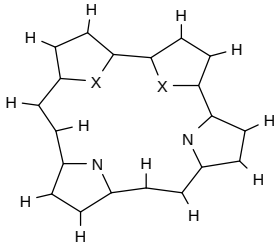

4e′-X; [2·0·2·0]

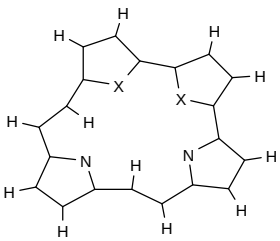

5a′-X; [2·2·0·0]

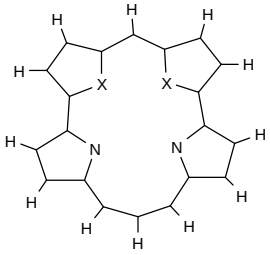

5b′-X; [2·2·0·0]

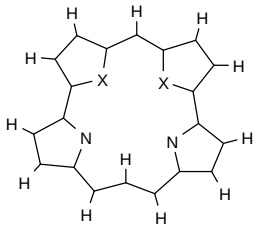

5c′-X; [2·2·0·0]

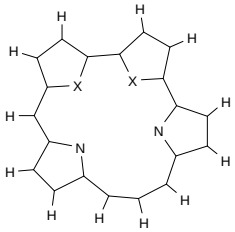

5d′-X; [2·2·0·0]

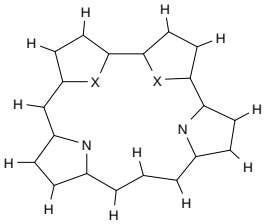

5e′-X; [2·2·0·0]

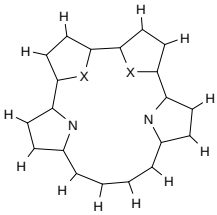

5f′-X; [2·2·0·0]

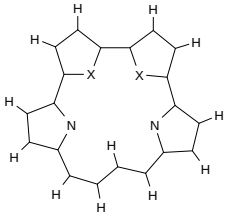

6a′-X; [3·0·1·0]

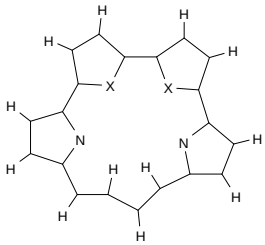

6b′-X; [3·0·1·0]


7a′-X; [3·1·0·0]


7b′-X; [3·1·0·0]


8a′-X; [4·0·0·0]


8b′-X; [4·0·0·0]


8c′-X; [4·0·0·0]

Scheme 2. *Syn* porphyrin ($C_{20}X_2N_2H_{12}$) isomers; here X = NH, O, S. The projections are the AM1 optimised geometry of the parent ($C_{20}N_4H_{14}$) isomers.

Table 1. Total energies, relative energies and distortion energies of *anti* tautomers of porphyrin isomers obtained at semiempirical (AM1, PM3) and DFT (B3LYP/6-31G*//AM1) levels of theory. Total energies are in hartrees, and relative energies and distortion energies (DE) are in kcal mol^{-1}.

	AM1			PM3			B3LYP/6-31G*//AM1		
Structure	HF	Δ*E*	DE	HF	Δ*E*	DE	HF	Δ*E*	DE
1-NH	0·38603	0·0	7·2	0·29627	0·0	7·8	–989·53061	0·0	–5·7
2a-NH	0·39674	6·7	0·1	0·28893	–4·6	0·0	–989·52293	4·8	23·5
2b-NH	0·44034	34·1	45·3	0·33342	23·3	25·6	–989·45347	48·4	7·5
2c-NH	0·44295	35·7	53·5	0·34817	32·6	35·7	–989·44358	54·6	4·1
3a-NH	0·40767	13·6	1·3	0·30264	4·0	0·0	–989·50370	16·9	–6·6
3b-NH	0·43412	30·2	20·1	0·31657	12·7	12·3	–989·46921	38·5	–7·3
4a-NH	0·40785	13·7	0·2	0·29907	1·8	5·5	–989·52051	6·3	–11·3
4b-NH	0·44252	35·4	67·1	0·34120	28·2	44·9	–989·42659	65·3	9·4
4c-NH	0·44167	34·9	73·3	0·34050	27·8	52·7	–989·42973	63·3	15·0
4d-NH	0·49808	70·3	96·5	0·38937	58·4	59·0	–989·37515	97·6	19·4
5a-NH	0·45192	41·4	13·2	0·35148	34·6	5·2	–989·45527	47·3	–11·1
5b-NH	0·47880	58·2	41·4	0·37176	47·3	20·6	–989·40801	76·9	–15·7
5c-NH	0·45986	46·3	74·9	0·35558	37·2	44·9	–989·41503	72·5	10·4
5d-NH	0·50162	72·5	90·9	0·39106	59·5	54·1	–989·37615	96·9	15·3
5e-NH	0·50525	74·8	96·2	0·39618	62·7	62·7	–989·38513	91·3	29·2
6a-NH	0·42558	24·8	6·7	0·31572	12·2	2·4	–989·46654	40·2	–20·4
6b-NH	0·43001	27·6	16·4	0·31609	12·4	7·5	–989·47001	38·0	–11·0
7a-NH	0·45046	40·4	22·6	0·34421	30·1	16·8	–989·42980	63·3	–19·1
7b-NH	0·44744	38·5	24·5	0·33716	25·7	11·6	–989·44848	51·5	–16·3
8a-NH	0·48305	60·9	52·4	0·36428	42·7	40·6	–989·37871	95·3	–14·0
8b-NH	0·47378	55·1	23·1	0·36332	42·1	4·1	–989·40999	75·7	–29·9
8c-NH	0·50567	75·1	84·8	0·39644	62·9	49·8	–989·38282	92·7	16·9

Table 2. Total energies, relative energies and distortion energies of *anti* tautomers of core-modified oxaporphyrin isomers obtained at semiempirical (AM1, PM3) and DFT (B3LYP/6-31G*//AM1) levels of theory. Total energies are in hartrees and relative energies and distortion energies (DE) are in kcal mol^{-1}.

	AM1			PM3			B3LYP/6-31G*//AM1		
Structure	HF	Δ*E*	DE	HF	Δ*E*	DE	HF	Δ*E*	DE
1-O	0·31190	0·0	11·8	0·23261	0·0	13·6	–1029·18965	0·0	–6·5
2a-O	0·32072	5·5	0·1	0·23703	2·8	0·0	–1029·17982	6·2	–2·0
2b-O	0·36026	30·3	26·6	0·26883	22·7	17·2	–1029·12169	42·6	–2·2
2c-O	0·34385	20·0	39·6	0·25947	16·9	29·0	–1029·14049	30·9	12·3
3a-O	0·33046	11·6	1·2	0·24425	7·3	1·6	–1029·14671	27·0	–17·4
3b-O	0·34212	19·0	10·3	0·25472	13·9	5·9	–1029·14620	27·3	–6·9
4a-O	0·32623	9·0	11·8	0·24401	7·2	12·4	–1029·16788	13·7	–12·7
4b-O	0·35604	27·7	49·3	0·26840	22·5	34·5	–1029·11012	49·9	9·6
4c-O	0·34624	21·5	58·7	0·26240	18·7	41·4	–1029·13714	33·0	27·9
4d-O	0·39801	54·0	64·1	0·30650	46·4	40·3	–1029·07557	71·6	15·6
5a-O	0·36801	35·2	9·0	0·27796	28·5	6·5	–1029·11266	48·5	–16·8
5b-O	0·35604	27·7	35·2	0·26840	22·5	24·1	–1029·11012	49·9	–6·4
5c-O	0·36853	35·5	50·9	0·28139	30·6	32·0	–1029·10129	55·4	10·6
5d-O	0·40191	56·4	58·9	0·30959	48·3	37·3	–1029·07537	71·7	12·7
5e-O	0·39478	52·0	73·4	0·30270	44·0	50·3	–1029·08580	65·2	26·6
6a-O	0·33908	17·1	7·4	0·25107	11·6	5·1	–1029·13031	37·2	–17·7
6b-O	0·33868	16·8	6·7	0·24942	10·5	3·3	–1029·15070	24·4	–12·4
7a-O	0·36132	31·0	17·6	0·27307	25·4	13·9	–1029·10600	52·5	–13·0
7b-O	0·35130	24·7	9·7	0·26393	19·6	4·2	–1029·14291	29·3	–8·7
8a-O	0·38060	43·1	46·9	0·28752	34·5	35·3	–1029·08089	68·3	3·9
8b-O	0·36459	33·1	13·7	0·27359	25·7	4·6	–1029·12715	39·2	–11·9
8c-O	0·41187	62·7	56·9	0·31984	54·7	32·9	–1029·06860	76·0	13·0

Table 3. Total energies, relative energies and distortion energies of *anti* tautomers of core-modified thiaporphyrin isomers obtained at semiempirical (AM1, PM3) and DFT (B3LYP/6-31G*//AM1) levels of theory. Total energies are in hartrees and relative energies and distortion energies (DE) are in kcal mol^{-1}.

	AM1			PM3			B3LYP/6-31G*//AM1		
Structure	HF	Δ*E*	DE	HF	Δ*E*	DE	HF	Δ*E*	DE
1-S	0·41422	0·0	10·3	0·36641	0·0	10·4	−1675·14507	0·0	−6·4
2a-S	0·42709	8·1	4·6	0·36904	1·6	0·0	−1675·10476	25·3	−10·0
2b-S	0·46559	32·2	46·0	0·40832	26·3	33·2	−1675·05825	54·5	14·5
3a-S	0·43415	12·5	6·8	0·37784	7·2	9·5	−1675·10541	24·9	−5·6
3b-S	0·45676	26·7	31·0	0·39828	20·0	14·7	−1675·05890	54·1	0·4
4a-S	0·43134	10·7	21·2	0·35245	−8·8	6·1	−1675·09129	33·8	−16·3
4b-S	0·45262	24·1	78·2	0·39172	15·9	68·4	−1675·05468	56·7	35·1
4c-S	0·46528	32·0	75·5	0·41344	29·5	58·5	−1675·05116	58·9	35·3
4d-S	0·50840	59·1	105·8	0·44739	50·8	74·7	−1675·00310	89·1	51·4
4e-S	0·52116	67·1	100·0	0·45961	58·5	64·1	−1674·99658	93·2	49·4
5a-S	0·46274	30·4	19·8	0·40689	25·4	14·6	−1675·07332	45·0	−5·5
5b-S	0·49458	50·4	51·8	0·43359	42·2	33·2	−1675·01080	84·3	5·6
5c-S	0·46943	34·7	88·4	0·41127	28·1	59·8	−1675·03866	66·8	41·1
5d-S	0·51088	60·7	103·2	0·44285	48·0	77·8	−1674·99322	95·3	44·7
5e-S	0·52066	66·8	101·7	0·45988	58·7	73·6	−1675·00793	86·1	57·0
6a-S	0·44878	21·7	17·8	0·39548	18·2	2·0	−1675·07694	42·8	−2·1
6b-S	0·45709	26·9	22·1	0·39627	18·7	14·6	−1675·05514	56·4	−13·9
7a-S	0·47029	35·2	37·6	0·41502	30·5	31·1	−1675·03943	66·3	−1·1
7b-S	0·46773	33·6	35·6	0·41110	28·0	23·4	−1675·05560	56·1	4·5
8a-S	0·49127	48·3	72·0	0·42688	37·9	56·2	−1675·00766	86·2	18·3
8b-S	0·48108	42·0	44·2	0·42186	34·8	29·9	−1675·04447	63·1	6·5
8c-S	0·52320	68·4	96·9	0·46004	58·8	68·9	−1674·98701	99·2	37·5

the oxa- and thia-disubstituted analogues respectively. Unexpectedly, semiempirical AM1 and PM3 methods designate all isomers including the parent porphyrin as non-planar and they are characterized as local minima, highlighting the inadequacy of semiempirical methodology in treating porphyrin-type molecules. Clearly, at higher levels of theory, the parent molecule has planar minima. Thus, we intend to check the energy differences between the planar and minimum energy structures (distortion energy) at B3LYP/6-31G* level also in addition to semiempirical levels to assess the performance of the semiempirical methods. Distortion energy may be taken as a measure of strain energy in the planar form due to steric congestion due to the core hydrogens and the angular strain. As out-of-plane puckering has been observed in expanded porphyrins, we also intend to gauge the performance of semiempirical methodologies in modelling the out-of-plane distortions in this class of compounds. While B3LYP/6-31G* single point calculations on AM1 stationary points show that quite a few structures have positive distortion energies, indicating that the puckered structures are more stable, some of them have negative distortion energies. The negative distortion energy at B3LYP level indicates that the semiempirical methods wrongly estimate that the isomers are puckered. Similar trends are also seen in oxa- and thia-core-modified analogues. Importantly, the magnitude of distortion energy also varies quite significantly at the three levels of theory considered. Thus, the present study clearly exposes the limitations of the semiempirical methodologies in modelling porphyrin-type molecules.

Significant variations in the relative energies and relative energy orderings are observed depending on the level of theory employed. Angle strain and steric repulsion between the inner protons appear to be the principal causative factors for the destabilization of the various isomeric forms. Obviously, direct pyrrolic linkages lead to higher angle strain and cause destabilization. Thus, expectedly, the isomers **8a**-X–**8c**-X are among the least stable isomeric type in parent as well as the core-modified analogues. However, some other isomers, e.g., **4d**-X, **5d**-X and **5e**-X, are also very unstable despite the smaller number of direct

Table 4. Total energies, relative energies and distortion energies of *syn* tautomers of porphyrin isomers obtained at semiempirical (AM1, PM3) and DFT (B3LYP/6-31G*//AM1) levels of theory. Total energies are in hartrees and relative energies and distortion energies (DE) are in kcal mol^{-1}.

	AM1			PM3			B3LYP/6-31G*//AM1		
Structure	HF	Δ*E*	DE	HF	Δ*E*	DE	HF	Δ*E*	DE
1′-NH	0·39719	0·0	7·1	0·30747	0·0	6·7	–989·50293	0·0	–11·8
2a′-NH	0·41630	12·0	10·7	0·32642	11·9	4·9	–989·47144	19·8	–8·8
2b′-NH	0·44377	29·2	55·0	0·39750	25·1	28·7	–989·42245	50·5	–1·6
2c′-NH	0·46334	41·5	27·7	0·35732	31·3	11·9	–989·42025	51·9	–14·3
3a′-NH	0·41025	8·2	4·0	0·31030	1·8	0·2	–989·48421	11·7	–12·2
3b′-NH	0·43853	25·9	19·8	0·32249	9·4	11·4	–989·44810	34·4	–16·9
3c′-NH	0·43750	25·3	20·5	0·32249	9·4	11·4	–989·45199	32·0	–14·4
4a′-NH	0·40374	4·1	0·5	0·29456	–8·1	0·0	–989·51055	–4·8	–8·6
4b′-NH	0·46792	44·4	57·9	0·36116	33·7	40·3	–989·41962	52·3	18·5
4c′-NH	0·46552	42·9	51·6	0·36099	33·6	34·3	–989·41605	54·5	6·4
4d′-NH	0·51160	71·8	96·6	0·40234	59·5	59·6	–989·36018	89·6	34·5
4e′-NH	0·51886	76·3	84·4	0·40537	61·4	54·9	–989·35478	93·0	19·5
5a′-NH	0·43946	26·5	20·3	0·33845	19·4	13·2	–989·42962	46·0	–21·0
5b′-NH	0·47351	47·9	55·0	0·36809	38·0	37·7	–989·39527	67·6	–1·3
5c′-NH	0·46921	45·2	78·8	0·36459	35·8	54·2	–989·40386	62·2	16·0
5d′-NH	0·49811	63·3	90·7	0·38604	49·3	54·6	–989·36116	89·0	12·2
5e′-NH	0·49168	59·3	95·8	0·38194	46·7	63·2	–989·37384	81·0	98·2
5f′-NH	0·49746	62·9	91·1	0·38835	50·7	53·1	–989·37113	82·7	18·4
6a′-NH	0·43148	21·5	7·0	0·32417	10·5	1·8	–989·44685	35·2	–27·6
6b′-NH	0·43564	24·1	19·3	0·32548	11·3	39·4	–989·45055	32·9	–13·8
7a′-NH	0·44954	32·8	25·7	0·34491	23·5	17·1	–989·41439	55·6	–16·6
7b′-NH	0·44968	32·9	28·8	0·34555	23·9	14·0	–989·43074	45·3	–10·3
8a′-NH	0·47213	47·0	68·5	0·36437	35·7	48·5	–989·38603	73·4	–0·5
8b′-NH	0·45405	35·7	37·2	0·34603	24·2	16·3	–989·43330	43·7	–13·2
8c′-NH	0·49286	60·0	88·6	0·38213	46·8	50·9	–989·38187	76·0	18·2

pyrrolic linkages, indicating that the relative stability of the isomers is decided by several intricate factors.

Among the *anti* tautomeric structures of porphyrin isomers the parent isomer **1** was computed to be most stable at AM1 and B3LYP levels. Surprisingly, the PM3 method predicts that the isomer **2a**-NH (hemiporphycene), which has [2·1·1·0] connectivity, and the double bond in the *Z*-form, is predicted to be the most stable. However, in the oxa- and thia-disubstituted analogues, the isomeric form **1** is computed to be most stable in all the three levels of theory. Attempts to locate distinct minimum energy structures for isomers **3b**-NH and **3c**-NH in corrphycene, **4d**-NH and **4e**-NH in porphycene, **5d**-NH and **5f**-NH in [2·2·0·0] were futile, and all the putative structures collapse to other minima energy structures, as depicted in scheme 1. While the corresponding oxa-isomers follow exactly the same trend as the parent aza-isomers, among the thia-isomers, **2b**-S and **2c**-S and isomers **3b**-S and **3c**-S collapse to the same structure. However, in contrast to the parent and oxa-analogues, **4d**-S and **4e**-S have distinct minima on the potential energy surface. Tables 1–3 indicate the quantitative differences among the three theoretical methods in relative stabilities and distortion energies.

Figure 1 depicts the variation of the relative energies in porphyrin, oxaporphyrin and thiaporphyrin isomers. The relative energies and the distortion energies of the *anti* tautomer of oxa- and thia-porphyrin isomers are given in tables 2 and 3. A comparison of tables 2 and 3 with table 1 indicates that the trends in the relative energy orderings of the oxa- and thia-analogues are not drastically altered when compared to the parent porphyrin isomers. Figure 3 depicts the three-dimensional structures for the more distorted isomers in parent, oxa- and thia-porphyrins for the *syn* and *anti* forms.

In oxaporphyrin, isomers [3·0·1·0] and [3·1·0·0], *E* isomers **6b**-O and **7b**-O are more stable than the *Z* form **6a**-O and **7a**-O and are about 13 and 23 kcal/mol more stable than the *Z* isomer respectively. In isomers [4·0·0·0] the relative energies of the isomers

Table 5. Total energies, relative energies and distortion energies of *syn* tautomers of core-modified oxaporphyrin isomers obtained at semiempirical (AM1, PM3) and DFT (B3LYP/6-31G*//AM1) levels of theory. Total energies are in hartrees and relative energies and distortion energies (DE) are in kcal mol^{-1}.

	AM1			PM3		B3LYP/6-31G*//AM1	
Structure	HF	Δ*E*	DE	HF	Δ*E*	HF	Δ*E*
1′-O	0·31476	0·0	10·0	0·23438	0·0	–1029·18455	0·0
2a′-O	0·32344	5·4	0·1	0·24496	6·6	–1029·16976	9·3
2b′-O	0·34475	18·8	58·6	0·26037	16·3	–1029·12910	34·8
2c′-O	0·37861	40·1	25·7	0·28431	31·3	–1029·10425	50·4
3a′-O	0·31588	0·7	0·1	0·23811	2·3	–1029·17111	8·4
3b′-O	0·34918	21·6	20·3	0·25915	15·5	–1029·13659	30·1
4a′-O	0·32121	4·1	1·5	0·23842	2·5	–1029·16336	13·3
4b′-O	0·37202	35·9	43·8	0·28563	32·2	–1029·09795	54·3
4c′-O	0·37207	36·0	27·6	0·28340	30·8	–1029·10547	49·6
4d′-O	0·39958	53·2	74·3	0·30971	47·3	–1029·07183	70·7
4e′-O	0·39990	53·4	48·5	0·30971	47·3	–1029·07598	68·1
5a′-O	0·33674	13·8	7·8	0·25271	11·5	–1029·12745	35·8
5b′-O	0·35544	25·5	14·6	0·27311	24·3	–1029·12248	38·1
5c′-O	0·36084	28·9	23·6	0·28005	28·7	–1029·10378	50·7
5d′-O	0·37858	40·0	68·4	0·29142	35·8	–1029·07771	67·0
5e′-O	0·37498	37·8	79·5	0·28798	33·6	–1029·09790	54·4
5f′-O	0·38038	41·2	67·3	0·29221	36·3	–1029·08407	63·1
6a′-O	0·34199	17·1	8·0	0·25073	10·3	–1029·12539	37·1
6b′-O	0·34019	16·0	8·9	0·24983	9·7	–1029·14239	26·5
7a′-O	0·34608	19·7	17·8	0·25894	15·4	–1029·11375	44·4
7b′-O	0·33668	13·8	2·2	0·25397	12·3	–1029·15153	20·7
8a′-O	0·36099	29·0	30·3	0·27266	24·0	–1029·09714	54·8
8b′-O	0·34832	21·1	5·7	0·25971	15·9	–1029·14142	27·1
8c′-O	0·38123	41·7	70·9	0·29067	35·3	–1029·09475	56·3

range from 68 to 76 kcal/mol respectively. The *EZ* isomer **8b**-O is favoured over the *Z* isomer **8a**-O and the *EE* isomer **8c**-O, which may be due to lower angle strain in the *EZ* form. Isomers [2·2·0·0], [3·0·1·0], [3·1·0·0], and [4·0·0·0] are destabilized by the presence of severe angle strain in the $–(CH)_n–$ linkages like the porphyrin isomers. In the thia-isomer [3·0·1·0], the *Z* isomer **6a**-S is more stable than the *E* isomer **6b**-S by 13 kcal/mol, which is the reverse when compared to the oxa and parent porphyrin isomers, and may be traced to the absence of hydrogen bonding in the case of the thiaporphyrin isomer **6b**-S. In the parent porphyrin and oxaporphyrin, the *E* isomers are stabilized by hydrogen bonding. When the inner proton repulsion is very dominating, the minimum energy structures adopt almost a bowl-like geometry and experience severe angle strain.

3.2 *Syn tautomeric form*

The relative energies and the distortion energies of the *syn* tautomer of porphyrin, oxaporphyrin and thiaporphyrin analogues are given in tables 4, 5 and 6 respectively. Figure 2 depicts the variation of the relative energies with porphyrin isomers, oxaporphyrin and thiaporphyrin isomers.

In this section, we discuss the *syn* tautomeric structure and compare the results of the parent system with that of the oxa- and thia-disubstituted analogues respectively. Like the *anti* tautomeric isomers, here also isomers of types [2·2·0·0], [3·0·1·0], [3·1·0·0], and [4·0·0·0] are destabilized by the presence of severe angle strain owing to the $–(CH)_n–$ linkages. All the 25 isomeric forms considered here are found to be distinct minima on the potential energy surface of the *syn* porphyrin isomers, a feature in slight contrast with the anti-counterparts. However, the twin isomeric forms **3b′**-X and **3c′**-X collapse to an intermediate bowl-like structure for the oxa- and thia-analogues. In isomers [3·0·1·0] and [3·1·0·0], *E* isomers **6b′**-NH and **7b′**-NH are more stable than the corresponding *Z* forms **6a′**-NH and **7b′**-NH respectively. The *EZ* isomer **8b′**-NH is favoured over the *Z* isomer **8a′**-NH and *EE* isomer **8c′**-NH, this

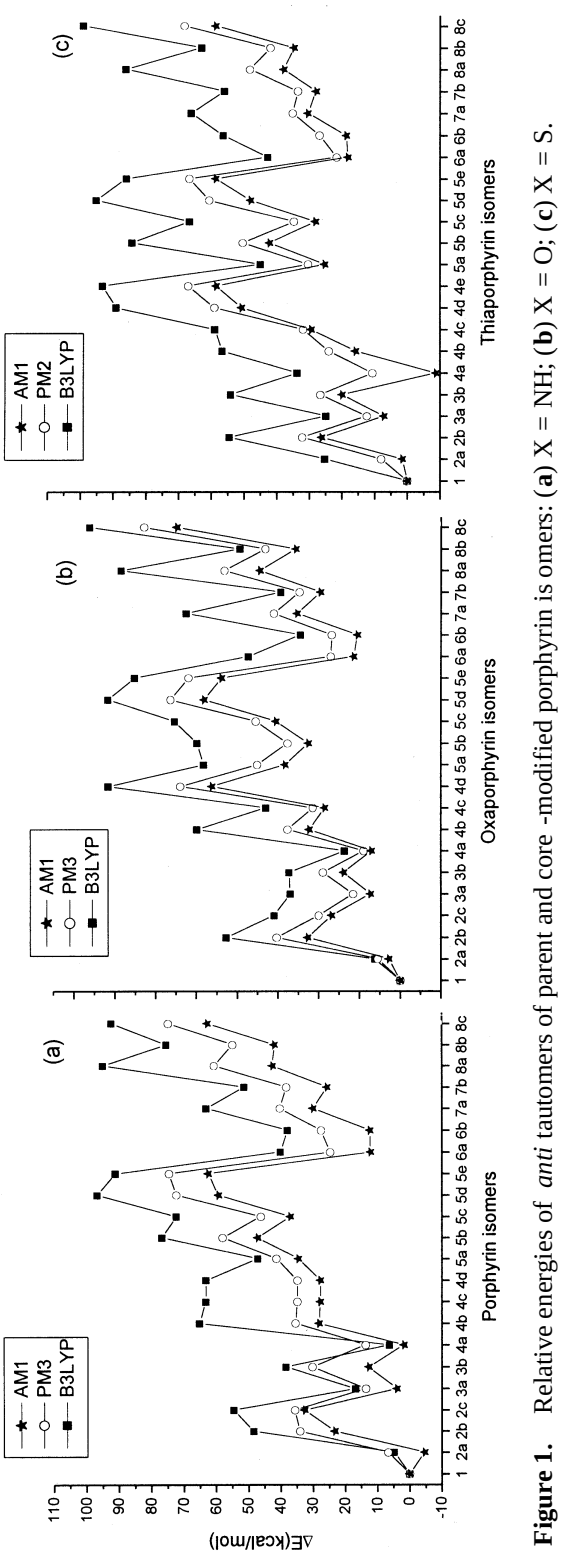


Figure 1. Relative energies of *anti* tautomers of parent and core -modified porphyrin is omers: (**a**) X = NH; (**b**) X = O; (**c**) X = S.

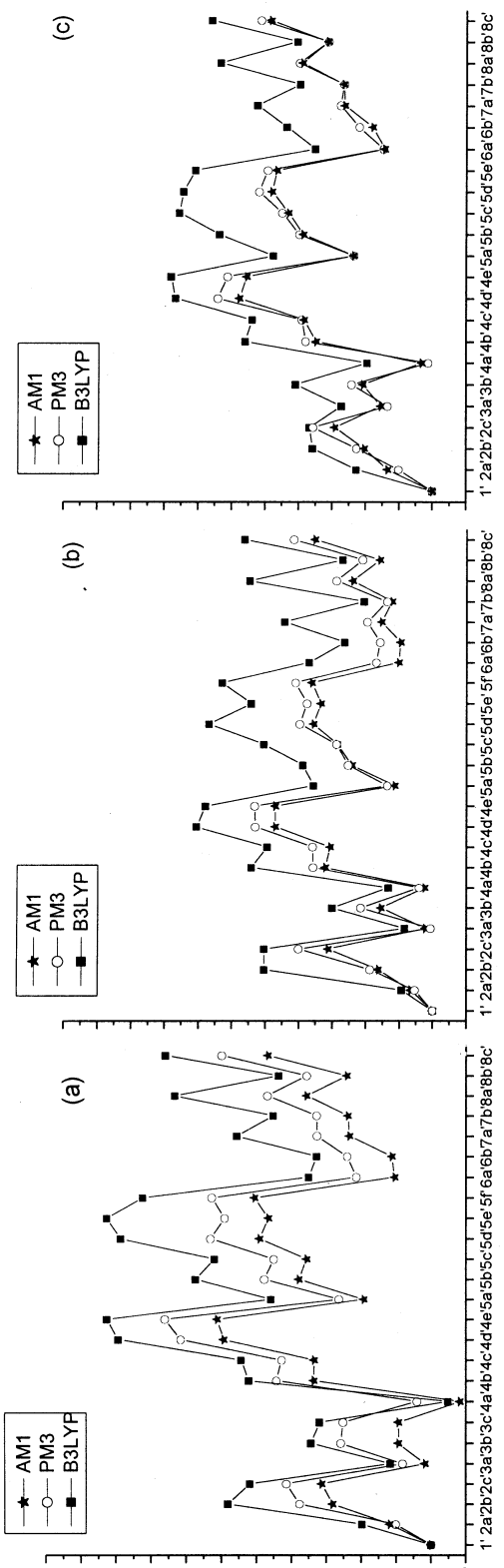


Figure 2. Relative energies of *syn* tautomers of pa rent and core-modified porphyrin i somers: (**a**) X = NH; (**b**) X = O; (**c**) X = S.

Table 6. Total energies, relative energies and distortion energies of *syn* tautomers of core-modified thiaporphyrin isomers obtained at semiempirical (AM1, PM3) and DFT (B3LYP/6-31G*//AM1) levels of theory. Total energies are in hartrees and relative energies and distortion energies (DE) are in kcal mol^{-1}.

	AM1			PM3		B3LYP/6-31G*//AM1	
Structure	HF	Δ*E*	DE	HF	Δ*E*	HF	Δ*E*
1′-S	0·42352	0·0	10·6	0·36831	0·0	–1675·10774	0·0
2a′-S	0·43963	10·1	13·9	0·38971	13·4	–1675·07145	22·8
2b′-S	0·45972	22·7	58·2	0·40076	20·4	–1675·05072	35·8
2c′-S	0·48039	35·7	31·1	0·41482	29·2	–1675·04896	36·9
3a′-S	0·44502	13·5	16·0	0·39291	15·4	–1675·06446	27·2
3b′-S	0·46204	24·2	30·5	0·40147	20·8	–1675·04241	41·0
4a′-S	0·42553	1·3	15·1	0·37349	3·2	–1675·07674	19·5
4b′-S	0·48387	37·9	61·4	0·42381	34·8	–1675·01871	55·9
4c′-S	0·48587	39·1	58·8	0·42953	38·4	–1675·02185	53·9
4d′-S	0·52576	64·2	94·0	0·46029	57·7	–1674·98548	76·7
4e′-S	0·52125	61·3	92·0	0·45683	55·5	–1674·98324	78·1
5a′-S	0·46116	23·6	37·6	0·40599	23·6	–1675·03187	47·6
5b′-S	0·48714	39·9	64·3	0·42999	38·7	–1675·00620	63·7
5c′-S	0·49529	45·0	84·1	0·43704	43·1	–1674·98712	75·7
5d′-S	0·50639	52·0	100·2	0·44495	48·1	–1674·98931	74·5
5e′-S	0·50218	49·4	103·1	0·44253	46·6	–1674·99479	70·9
6a′-S	0·44706	14·8	24·2	0·39122	14·4	–1675·05159	35·2
6b′-S	0·45876	22·1	27·0	0·39707	18·0	–1675·03804	43·7
7a′-S	0·46768	27·7	41·6	0·41038	26·4	–1675·02402	52·5
7b′-S	0·46608	26·7	39·8	0·41092	26·7	–1675·04436	39·8
8a′-S	0·48734	40·0	90·8	0·43066	39·1	–1675·00661	63·5
8b′-S	0·47339	31·3	52·6	0·41837	31·4	–1675·04300	40·6
8c′-S	0·50562	51·5	101·8	0·44561	48·5	–1675·00247	66·1

may be due to the lower angle strain in the *EZ* form **8b′**-NH. The distortion energy trends are also very similar in the *syn*- and *anti*-isomeric forms.

Among the *syn*-isomers, **4a′**-NH (porphycene) was computed to be most stable among all the 25 isomers despite apparently significant angle strain. The intermolecular hydrogen bonding in the core seem to strongly stabilize the isomer **4a′**-NH and importantly it is virtually planar at all levels of theory. However, among the core-modified isomers the normal [1·1·1·1] *anti* isomers was computed to be the most stable for both oxa- and thia-forms. The non-availability of the intramolecular hydrogen bonding may be the reason for such a reversal of relative energy orderings upon core-modification. Thus, hydrogen bonding in the porphyrin core is an extremely important factor in deciding the relative stabilities of the isomers. It is interesting to note that the trends in the relative energy orderings of the oxa- and thia-analogues are not drastically altered when compared to parent porphyrin isomers (figure 2). This indicates that the core-modification is not expected to induce several structural perturbations in this class of compounds.

Figure 2 depicts the relative energy variations of the *syn*-isomeric forms of parent, oxa- and thia-porphyrins. While the trends obtained are similar at the three levels, the quantitative differences are substantial. It is interesting to note that AM1 values are consistently in between PM3 and B3LYP values in all cases. Consistently, the stabilities of the other porphyrin isomers are overestimated at PM3 level compared to B3LYP level. In a majority of the cases AM1 values are much closer to the PM3 values compared to the B3LYP values. Figure 1, which accounts for the relative stabilities for the *anti*-isomers, gives exactly the same trend. Thus, the present analysis clearly exposes the inadequacy of the semi-empirical methodologies when applied to porphyrin type molecules. However, if the *ab initio* or density functional theory based methods are intractable,

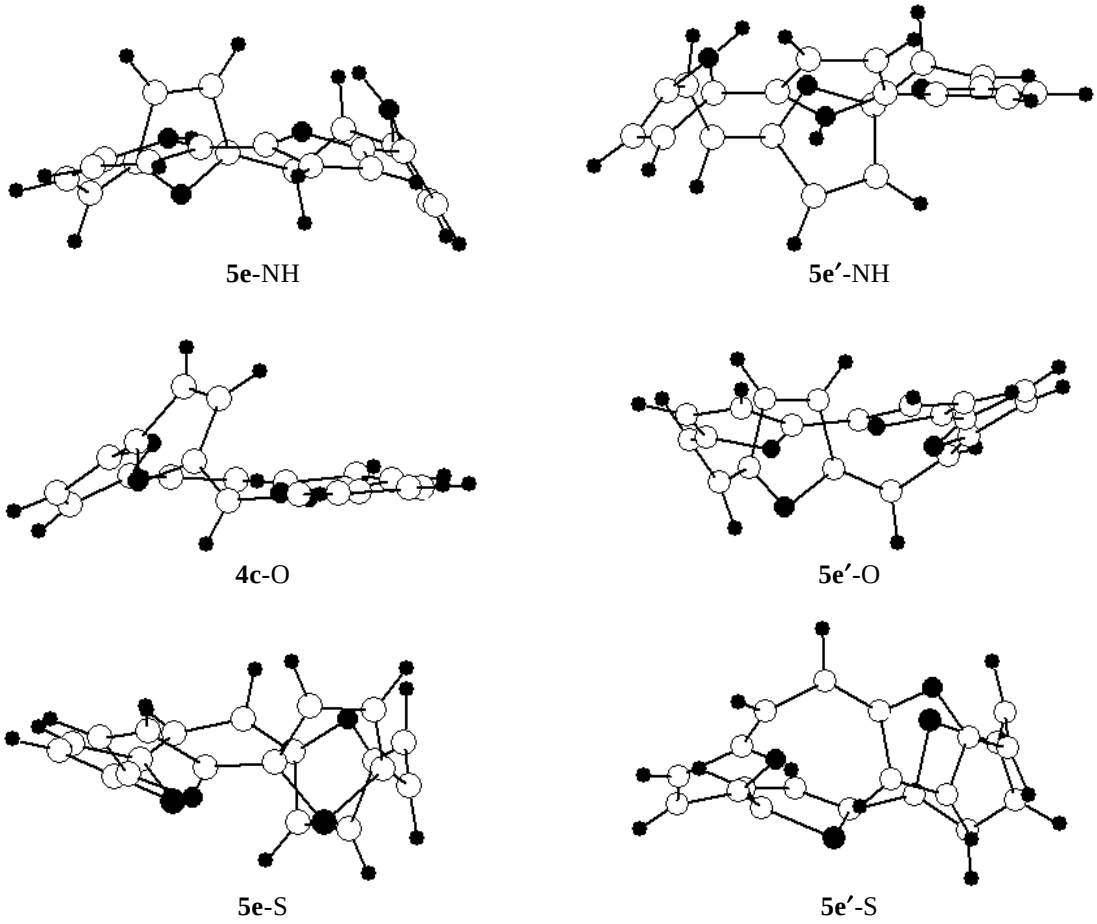


Figure 3. Representative three-dimensional structures for the highly distorted porphyrin and core-modified porphyrin isomers. The open circles and small filled circles are carbon and hydrogen. The larger circles are nitrogen, oxygen and sulphur in the corresponding isomers.

among the semiempirical methods AM1 appears to be a better choice compared to PM3 for modelling the porphyrin type systems.

3.3 *Geometrical isomerism*

Except for the parent [1·1·1·1] form, geometrical isomerism is possible for all the isomeric forms considered for the *syn* and *anti* isomers. The relative stabilities of the geometrical isomers have attracted the attention of theoreticians and experimentalists alike. In hemiporphyrin [2·1·1·0] and corrphycene [2·1·0·1] three isomers are considered in both *syn* and *anti* form (one *Z* form and two *E* forms). In porphycene [2·0·2·0] five isomers are consider (one *Z* form, two *EZ* forms and two *EE* forms) in both tautomeric forms. In both *syn* and *anti* porphyrin isomers, the isomers [2·1·1·0], [2·1·0·1], [2·0·2·0], and [2·2·0·0] have two –(CH)– linkages, the *Z* isomers have lower energy compared to all other isomers in the same series. In isomers [3·0·1·0] and [3·1·0·0], *E* isomers are more stable than *Z* forms in B3LYP level for the *syn* and *anti* parents and oxaporphyrin isomers. Thiaporphyrin isomers [3·0·1·0] prefer the *Z* form over the *E* form in both tautomeric forms. In isomer [4·0·0·0] the *EZ* isomers are favoured over the *Z* and *EE* isomers, this may be due to lower angle strain in the *EZ* form. The distortion energies for the *Z* isomers [2·1·1·0], [2·1·0·1], [2·0·2·0], and [2·2·0·0] having two –(CH)– linkages are substantially smaller compared to the *E* isomers. Thus, the *Z* isomers are expected to have less steric repulsion due to inner protons compared to other geometrical isomers.

In isomers isoporphycene [3·0·1·0] and [3·1·0·0], one *E* form and one *Z* form was considered in both *syn* and *anti* tautomers. In *anti* tautomeric isomers

[2·1·1·0], [2·1·0·1], [2·0·2·0], and [2·2·0·0] having two –(CH)– linkages, prefer *Z* isomers **2a**-X, **3a**-X in case of [2·1·1·0] and [2·1·0·1] and *ZZ* isomers **4a**-X and **5a**-X in case of [2·0·2·0] and [2·2·0·0] where X = NH, O, S respectively. This preference for the *Z*-form seems to be due to the lower steric repulsive interactions involving the inner CH group compared to the corresponding *E* (**2b**-X, **2c**-X, **3b**-X and **3c**-X), *EZ* (**4b**-X, **4c**-X, **5b**-X and **5c**-X) and *EE* isomers (**4d**-X, **4e**-X, **5d**-X, **5e**-X and **5f**-X). In isomers [3·0·1·0], [3·1·0·0], *E* isomers **6b**-NH and **7b**-NH are more stable than *Z* isomers **6a**-NH and **7a**-NH in the B3LYP level. The oxa-core modified isomers seem to be following exactly similar results, and in all cases the trends observed are identical to those in the parent porphyrin isomer. However the *Z* isomer **6a**-S of [3·0·1·0] is more stable than the *E* isomer **6b**-S by 13 kcal/mol. This is due to absence of hydrogen bonding in the case of thiaporphyrin isomers, and it is to be noted that in parent porphyrin and oxaporphyrin isomers, hydrogen bonding stabilizes the *E* isomers. Therefore, the current study on the parent and susbstituted porphyrins exposes the severe limitations of semiempirical methods in quantitatively modelling the relative energies and out-of-plane distortion energies. However, the qualitative trends are reasonable at AM1 level of theory.

Similarly, in *syn* tautomers the isomers [2·1·1·0], [2·1·0·1], [2·0·2·0], [2·2·0·0] having $-(CH)_2-$ linkage, favours *Z* isomers **2a′**-X, **3a′**-X, **4a′**-X and **5a′**-X where X = NH, O, S and this preference may be due to the less steric interactions involving the inner CH group. However, in case of isomers of types [3·1·0·0] and [3·0·1·0], *E* isomer **6b**-NH and **7b**-NH is more stable than *Z* isomer **6a**-NH and **7a**-NH in the B3LYP level. Oxaporphyrin isomers follow similar results. As has been observed for the thia-isomers the lack of hydrogen bonding possibility leads to the stabilization of *Z* isomer **6a′**-S than the *E* isomer **6b′**-S by 8 kcal/mol. Isomer [4·0·0·0] favoured *EZ* isomer **8b**-NH than *Z* isomer **8a**-NH and *EE* isomer **8c**-NH. Similar trend was observed in oxa- and thia-porphyrin isomers having [4·0·0·0] connectivity.

4. Conclusions

The present study reports the results of semiempirical (AM1and PM3) and density functional calculations (B3LYP/6-31G*) on a series of *syn* and *anti* tautomeric forms of porphyrin isomers and their oxa- and thia-analogues. Several factors, such as angle strain, inner proton repulsion, length of the bridge, and the type of geometric isomerism, *E* or *Z*, play vital roles in deciding the relative stability ordering of the porphyrin isomers. The present computational study exposes the limitations of the semiempirical theoretical methodologies when applied to porphyrin-type molecules. Between the two semiempirical methods employed, AM1 performs consistently better than PM3 in reproducing the relative energy values and orderings. The trends in the relative energy orderings for the parent porphyrins are not drastically altered when compared to the oxa- and thia-analogues in both the *syn* and *anti* tauomers.

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