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An ab initio CI study of electronic spectra of substituted free-base porphyrins

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Abstract

Ab initio calculations at the CI (singles) level of theory were carried out for the ground state and the singlet and triplet excited states of substituted free-base porphyrins. The results predict a substantial red-shift in the long-wavelength electronic spectra of compounds due to the push–pull substitution at the π-system of the porphyrin ring or due to the substitution by a nitro-group. The compounds and their derivatives may be good candidates for deep-penetrating photodynamic therapeutic agents. © 2000 Elsevier Science B.V. All rights reserved.

1. Introduction

Photodynamic therapy (PDT) is a quickly developing approach to cancer therapy [1,2]. It involves the use of otherwise harmless dyes that are preferentially retained in tumour tissue and subsequently activated by red light. The induced photo sensitization process is believed to lead to the localized formation of singlet molecular oxygen that rapidly reacts with cell membranes, leading to tumour extinction [3]. The majority of the PDT applications refer to the treatment of skin cancer and other skin diseases. This is due to the fact that most of the photodynamic sensitizers, based on porphyrins and phthalocyanins, absorb light in the region 600–700 nm. At these wavelengths, the light can penetrate tissues only to a depth of a few millimetres, which restricts the use of such photodynamic therapeutic agents to relatively thin malignant tumours.

Therefore, it is of interest to search for longer-wavelength (near infrared) absorbing photodynamically active dyes that could be activated deeper in malignant tissues. The porphyrins have several absorption maxima in their visible spectra that could be shifted appropriately by the insertion of various substituents or by applying other changes in the structure. For instance, it is well known that chlorins, which differ from porphyrins by the partial hydrogenation of one pyrrole ring, exhibit an intense absorption band at longer wavelength (700–780 nm) [4]. The other approaches to induce the red-shift in the long-wavelength spectra of photodynamic dyes involve the insertion of additional double bonds in the ring system [5], the condensation of the benzene or naphthalene moieties with the pyrroles of the ring, and other structural modifications [6].

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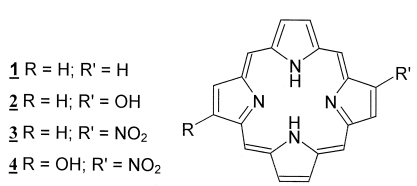
Recently we proposed to investigate the influence of the push–pull substitution at the π-system of the porphyrin on the electronic spectra of compounds. The ZINDO CIS calculations revealed a substantial bathochromic shift in the UV/Vis spectra of porphyrins with electron-donating and electron-accepting substituents at the conjugated positions in the porphyrin ring [7]. This shift was further enhanced by the presence of a polarizable condensed medium (solvatochromic red-shift) [8,9]. The purpose of this Letter is to investigate the effect of the push–pull substitution on the electronic spectra of porphyrins at the level of ab initio configuration interaction (singles) theory. Four compounds, the unsubstituted free-base porphyrin (**1**), 2-hydroxyporphyrin (**2**), 2-nitroporphyrin (**3**) and 2-hydroxy-12-nitroporphyrin (**4**), were studied (see Scheme 1).

The mechanism of the photochemical action by which the photodynamic agents cause the destruction of malignant cells is not completely understood. However, it had been pointed out [10] that singlet oxygen, $^1O_2$, generated by energy transfer from the excited photosensitizer in the triplet state to the oxygen molecule in the triplet ground state is the critical process involved. The luminescence decay of $^1O_2$ at 1270 nm [11,12] indicates that the formation of the singlet oxygen would require the energy supply of at least 0.98 eV. However, in selecting the longest-wavelength maximum for a dye, the energy gap between the respective lowest singlet and triplet excited states has also to be taken into account. The analysis of the triplet state properties and $^1O_2$ generation efficiency of several phthalocyanines and naphthalocyanines has revealed that the triplet state energy of at least 1.13 eV is required for a dye to create $^1O_2$ in solution [11,13]. Whereas it has been found that the silicon(IV)naphthalocyanine with the triplet energy at ~ 0.02 eV below the ^1A_g level of O_2 can still effectively generate the singlet oxygen [14], further reduction of the triplet energy would inactivate the dye [15]. Therefore, in the present work, the excitation energies were calculated for both the singlet–singlet and singlet–triplet transitions of the porphyrins studied.



Scheme 1.

2. Methodology

Because of their extensive size, the geometry of the molecules studied was optimized using the AM1 semiempirical parameterization [16] within the AMPAC program package [17]. A satisfactory agreement has been obtained between the calculated and experimental X-ray diffraction bond lengths and bond angles of porphyrins [7]. The optimized geometry of compounds deviated slightly from the planar structure. Small shifts of atomic coordinates were therefore applied to bring the molecules to a planar C_s symmetry for further ab initio calculations.

The ab initio calculations were carried out using GAUSSIAN 94 program system [18]. The recent extensive ab initio and semiempirical MO calculations [19–26] revealed that the low-lying excited states of free-base porphyrin are described mainly by linear combination of singly excited configurations of porphyrin π-orbitals. Foresman et al. [22] have carried out ab initio CIS calculation on four excited states of free-base porphyrin using basis sets of double-zeta quality and showed that CIS gives the excitation energies with error in order of 1.0 eV but with correct relative ordering. In the present research, we are mainly interested in relative values such as red-shift of absorption bands among the substituted porphyrins. For this purpose, CIS is an appropriate method despite of lacking consideration of the dynamical electron correlation effects.

Two basis sets were used. The first of them is a [2s2p/1s] contracted Gaussian-type set denoted as set A. In set A, only p function is split to double-zeta and the primitive Gaussian-type functions are (9s5p/4s) given by Huzinaga [27,28]. The second set is a valence double-zeta, [3s2p/2s], contracted from (9s5p/4s) primitives [28] using the scheme proposed by Dunning and Hay [29]. This set is denoted in further discussion as set B. In both sets the scale factor 1.2 is applied to the exponents of hydrogen. In the four lowest excited states of porphyrin, the π-orbitals play a central role. For this

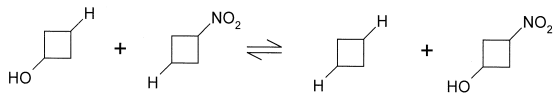
reason, even the smaller basis set A is expected to reproduce qualitatively correct excitation energies.

The configuration interaction calculations were performed at the singles only (CIS) level with the restricted Hartree–Fock (RHF) molecular orbitals. The core molecular orbitals that were composed of carbon, nitrogen, and oxygen 1 s atomic orbitals were kept frozen in the CIS calculations. The RHF ground state configuration does not mix with the singly excited configurations due to Brillouin's theorem and excitation energies were thus obtained using the Davidson diagonalization method and AO integrals that were recomputed at each iteration step. The convergence criteria were 10^{-8} for RHF and 10^{-4} for CIS, respectively.

The semiempirical calculations were carried out on the IBM RISC 6000/3AT workstation at the University of Tartu. The ab initio calculations were performed on the IBM RISC 6000/58H workstation at Chukyo University.

3. Results and discussion

The RHF energies of the compounds in the ground state calculated using two above-described basis sets are given in Table 1. Notably, our results are in good agreement with the results of earlier CIS calculations of the free-base porphyrin [22]. The difference between the two sets of energies is similar for different compounds and increases gradually, as expected, with increase of the size of the molecule. In addition, the substituent effects on the calculated total energy of the porphyrins are remarkably additive. Thus, the reaction energy for an isodesmic reaction (see Scheme 2) where □ denotes the porphin ring, is



Scheme 2.

only ~1.7 kcal/mol in favour of the monosubstituted compounds (1.66 kcal/mol as calculated using basis set A and 1.74 kcal/mol as calculated using basis set B). Consequently, it would be of interest to study if such additivity is valid also for the spectral transition energies.

The CIS-calculated excitation energy of the D_{2h} structure of the unsubstituted porphyrin calculated using the 6-31G set has been reported to have an error of ~0.5 eV for the first Q-band, of ~0.3 eV for the second Q-band, and ~1.5 eV for the two Soret bands [22]. Nevertheless, the relative energy ordering of these four excited states has been predicted correctly. The CIS-calculated singlet–singlet excitation energies together with the oscillator strengths using basis sets A and B are presented in Tables 2 and 3, respectively. The data given in Table 2 evidence that the absolute values of the CIS-calculated and experimental excitation energies are rather different. However, the relative positioning of the transition energies has been calculated correctly. Furthermore, the calculated and experimental oscillator strengths are in a satisfactory agreement with each other.

The first two transitions in the porphyrin spectrum correspond to the Q-bands, and the third and the fourth transition to the B bands (Soret bands). Notably, a small blue-shift is predicted for the most of the electronic transitions of 2-hydroxyporphyrin (**2**), as compared to the unsubstituted compound. The

Table 1
RHF-calculated total energies of the substituted porphyrins

Compound	State	RHF energy basis set A (a.u.)	RHF energy basis set B (a.u.)	Δ (eV)
1	X-1A′	−982.82804928	−982.94230029	3.11
2	X-1A′	−1057.65241159	−1057.77642022	3.37
3	X-1A′	−1186.18993114	−1186.32597022	3.70
4	X-1A′	−1261.01165332	−1261.15731108	3.96

Table 2
CIS-calculated singlet–singlet excitation energies and oscillator strengths for the first four excited states of porphyrins using the basis set A

Compound	State	EE[a] (eV)	λ[b] (nm)	EE[c] (eV)	Shift[d] (eV)	OS[e]	OS[f]
1	1-1A′	2.8767	430.98	2.01	0.00	0.0209	0.02
	2-1A′	3.4993	354.31	2.38	0.00	0.0279	0.07
	3-1A′	4.5887	270.19	3.1	0.00	1.3743	1.15
	4-1A′	4.6023	269.40	3.1	0.00	1.4174	
2	1-1A′	2.8882	429.27		−1.71	0.0285	
	2-1A′	3.5425	349.99		−4.32	0.0318	
	3-1A′	4.5742	271.05		0.86	1.3162	
	4-1A′	4.6375	267.35		−2.05	1.3749	
3	1-1A′	2.7548	450.06		19.08	0.0186	
	2-1A′	3.2448	382.10		27.79	0.0870	
	3-1A′	4.3699	283.72		13.53	1.7224	
	4-1A′	4.4941	275.88		6.48	1.3499	
4	1-1A′	2.7234	455.25		24.27	0.0506	
	2-1A′	3.2512	381.34		27.03	0.0400	
	3-1A′	4.3819	282.95		12.76	1.5950	
	4-1A′	4.4440	278.99		9.59	1.4912	

[a]Calculated excitation energy.
[b]Calculated wavelength of the spectral maximum.
[c]Experimental excitation energy [30].
[d]Calculated spectral shift as compared to the unsubstituted compound (**1**).
[e]Calculated oscillator strength.
[f]Experimental oscillator strength [31].

Table 3
CIS-calculated singlet–singlet excitation energies and oscillator strengths for the first four excited states of porphyrins using the basis set B

Compound	State	EE[a] (eV)	λ[b] (nm)	Shift[c] (eV)	OS[d]
1	1-1A′	2.8636	432.96	0.00	0.0221
	2-1A′	3.4830	355.97	0.00	0.0342
	3-1A′	4.5702	271.28	0.00	1.5048
	4-1A′	4.5985	269.62	0.00	1.5188
2	1-1A′	2.8757	431.15	−1.81	0.0307
	2-1A′	3.5305	351.18	−4.79	0.0376
	3-1A′	4.5647	271.61	0.33	1.4163
	4-1A′	4.6295	267.81	−1.81	1.5083
3	1-1A′	2.7437	451.89	18.93	0.0195
	2-1A′	3.2255	384.38	28.41	0.0928
	3-1A′	4.3421	285.54	14.26	1.7391
	4-1A′	4.4954	275.80	6.18	1.4368
4	1-1A′	2.7092	457.63	24.67	0.0535
	2-1A′	3.2317	383.64	27.67	0.0431
	3-1A′	4.3544	284.73	13.45	1.6507
	4-1A′	4.4428	279.07	9.45	1.5446

[a]Calculated excitation energy.
[b]Calculated wavelength of the spectral maximum.
[c]Calculated spectral shift as compared to the unsubstituted compound (**1**).
[d]Calculated oscillator strength.

Table 4
CIS-calculated singlet–triplet excitation energies (eV, nm) for the first four excited states of porphyrins using the basis set A

Compound	State	EE[a] (eV)	λ[b] (nm)	Shift[c] (eV)
1	1-3A′	1.4028	883.84	0.00
	2-3A′	2.0429	606.89	0.00
	3-3A′	2.1293	582.28	0.00
	4-3A′	2.8207	439.55	0.00
2	1-3A′	1.4162	875.47	−8.37
	2-3A′	2.0405	607.61	0.72
	3-3A′	2.1338	581.04	−1.24
	4-3A′	2.8178	440.00	0.45
3	1-3A′	1.2700	976.25	92.41
	2-3A′	1.9121	648.42	41.53
	3-3A′	2.1246	583.55	1.27
	4-3A′	2.1297	582.17	142.62
4	1-3A′	1.2867	963.57	79.73
	2-3A′	1.9386	639.55	32.66
	3-3A′	2.1317	581.62	−0.66
	4-3A′	2.1407	579.16	139.61

[a]Calculated excitation energy.
[b]Calculated wavelength of the spectral maximum.
[c]Calculated spectral shift as compared to the unsubstituted compound (**1**).

Table 5
CIS-calculated singlet–triplet excitation energies (eV, nm) for the first four excited states of porphyrins using the basis set B

Compound	State	EE[a] (eV)	λ[b] (nm)	Shift[c] (eV)
1	1-3A′	1.4145	876.53	0.00
	2-3A′	2.0542	603.57	0.00
	3-3A′	2.1371	580.15	0.00
	4-3A′	2.8419	436.27	0.00
2	1-3A′	1.4297	867.17	−9.36
	2-3A′	2.0545	603.47	−0.10
	3-3A′	2.1428	578.60	−1.55
	4-3A′	2.8422	436.23	−0.04
3	1-3A′	1.2841	965.49	88.96
	2-3A′	1.9189	646.11	42.54
	3-3A′	2.1292	582.30	2.15
	4-3A′	2.2136	560.11	123.84
4	1-3A′	1.3015	952.59	76.06
	2-3A′	1.9478	636.52	32.95
	3-3A′	2.1380	579.89	−0.26
	4-3A′	2.2251	557.20	120.93

[a]Calculated excitation energy.
[b]Calculated wavelength of the spectral maximum.
[c]Calculated spectral shift as compared to the unsubstituted compound (**1**).

nitrosubstituted compounds **3** and **4** exhibit, however, moderate red-shifts of the spectral transition energies. Gust et al. [32] have observed the red-shift by 21 nm of the Q-bands and by 11 nm of the Soret bands of the 2-nitro-5,10,15,20-tetraphenylporphyrin (TPP-NO_2). Our results demonstrate that the red-shifts for the CIS-calculated transition bands of 4-nitroporphyrin (**3**) compare favorably with these experimental data (19–27 nm for the Q-bands and 6–13 nm for the Soret bands, cf. Tables 3 and 4). Some nonadditivity of the substituent effect is observed in the spectral transition energies, particularly in the case of the long-wavelength Q-bands. At this time, the effect is energetically in favour of the disubstituted compound.

The singlet–triplet transitions of the porphyrins studied by us are characterized by substantially more pronounced substituent effects (cf. Tables 4 and 5). Whereas the transition energies for the hydroxy-substituted compound **4** are still little different from those for the unsubstituted compound, the spectral maxima of nitro-substituted compounds **3** and **4** exhibit large red-shifts except the second Soret band. The large shifts (by 79–91 nm) of the longest-wavelength Q-band are of particular interest as transferring the spectral maxima to the deep infrared region with the much more penetrating IR light while the respective triplet states still stay active as the $^1O_2$ photosensitizers. Notably, the calculated absolute values of the transition energies compare significantly better with the respective experimental energies than those for the singlet–singlet transitions (e.g., CIS-calculated (basis set A) 1.4 eV vs. experimental value 1.58 eV [33].

4. Conclusions

The results of the CIS calculations indicate that the push–pull substituted porphyrins may be good candidates for efficient deep-penetrating photodynamic therapeutic agents. Notably, already the insertion of a single nitro-group at the 2-position of the porphyrin ring leads to a substantial red-shift of the longest-wavelength electronic transition. These transitions may be further shifted due to the presence of a dielectric polarizable medium, e.g. aqueous solution. The respective study using self-consistent reaction field models [34,35] is under way by our groups.

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