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J. Serb. Chem. Soc. 73 (7) 713–726 (2008)
JSCS–3754

Journal of the Serbian Chemical Society

JSCS@tmf.bg.ac.yu • www.shd.org.yu/JSCS
UDC 546.472+547.979.733:543.422.25
Original scientific paper

Studies on Zn(II) monohydroxyphenyl mesoporphyrinic complexes. Synthesis and characterization

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(Received 27 July, revised 29 October 2007)

Abstract: A series of four Zn(II) complexes with asymmetrical porphyrinic ligands were synthesized: [5-(4-hydroxyphenyl)-10,15,20-triphenyl-21*H*,23*H*-porphinato]Zn(II) (Zn(II)TPPOH$_P$), [5-(3-hydroxyphenyl)-10,15,20-triphenyl-21*H*,23*H*-porphinato]Zn(II) (Zn(II)TPPOH$_M$), [5-(2-hydroxyphenyl)-10,15,20-triphenyl-21*H*,23*H*-Zn(II)-porphinato]Zn(II) (Zn(II)TPPOH$_O$) and the well-known (5,10,15,20-tetraphenyl-21*H*,23*H*-porphinato]Zn(II) (Zn(II)TPP) as reference, in a 1:1 mole ratio. In all cases, the free-base porphyrin served as a tetradentate ligand through the four pyrrole nitrogen atoms. The complexes were characterized by elemental analysis, FTIR and UV–Vis spectroscopy, which fully confirmed the structure of the complexes. UV–Vis showed that the spectral absorption of the four complexes was blue-shifted by at least 50 nm compared to that of the free ligands. Also important structural data were obtained from several different NMR experiments (including ^{1}H-NMR, ^{13}C-NMR, DEPT, COSY, HMBC and HMQC). Influences of external substituents on the porphyrin ring were observed.

Keywords: asymmetric porphyrins; Zn(II) porphyrin complexes; sensitizers for photodynamic therapy; molecular absorption coefficients; NMR spectroscopy.

INTRODUCTION

Tetrapyrrolic macrocycles (*i.e.*, porphyrins) play highly diverse and fundamental roles in biological systems.[1,2] They readily combine with metals, coordinating with them in the central cavity.[1,2] One of the more recent and promising applications of metalloporphyrins in medicine is their employment in the detection and cure from tumors, for which they are being intensively investigated as second and third generation photosensitizers for cancer photodynamic therapy (PDT), as efficient sensitizing agents in the photodegradation of malignant tis-

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doi: 10.2298/JSC0807713B

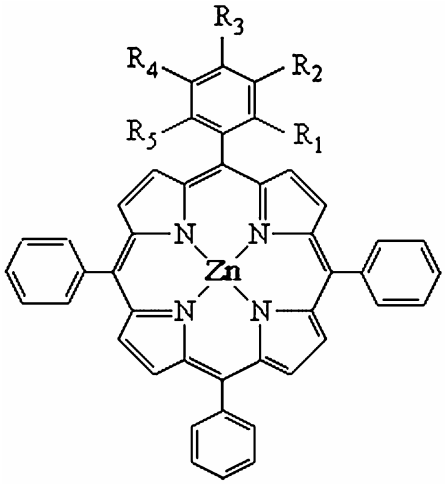
sues.[3–9] PDT is a new, non-surgical, technique for cancer treatment. After administration of a photosensitizer, which is selectively retained by tumor cells, subsequent irradiation with light in the red region of the visible spectrum (within the so-called phototherapeutic window, where light can penetrate living tissues) in the presence of oxygen specifically inactivates neoplastic cells.[3–13]

In spite of some promising studies with other classes of compounds,[14–20] the only PDT photosensitizers already approved for human treatment have a porphyrin-like heterocyclic ring structure, although they absorb only weakly at about 620 nm and are a complex and non-separable mixture of monomers, dimers, and higher oligomers.[21,22]

The increasing need for higher efficiency against tumors continues to determine a great number of synthetic studies directed to the synthesis of single pure porphyrinic compounds with well-established structures and which efficiently absorb light at longer wavelengths[22,23] (in the red region of the absorption spectra, 630–680 nm, in the so-called phototherapeutical window, where the light deeply penetrates body tissues[3–12]), have relevant singlet oxygen quantum yields,[24,25] photostability[26,27] and low toxicity.[28]

In order to achieve the most appropriate locations at the level of the various cellular constituents, photosensitizers further need to possess the most adequate structural characteristics.[29] By modifying the charge density and its distribution at the periphery of the porphyrinic macrocycle, in the meso-position (an H has to be substituted by one −OH functional group), it is possible to control the route of these compounds to the target cells.[26,29–31]

In the present study, a series of new mesoporphyrinic complexes, monohydroxyphenyl Zn(II)-substituted porphyrin complexes, [5-(*x*-hydroxyphenyl)-10,15,20--triphenyl-21*H*,23*H*-porphinato]Zn(II) (*x* = 2, 3 and 4) (Scheme 1), were synthesized and characterized for use in PDT, with a prevalence to the latter mentioned objective.



Scheme 1. Structure of the mono-hydroxy-substituted Zn(II)-porphyrin complexes. For Zn(II)TPP as the reference: $R_{1\text{-}5}$ = H; for Zn(II)TPPOH$_O$: R_1 = OH and $R_{2\text{-}5}$ = H; for Zn(II)TPPOH$_M$: $R_{1,3\text{-}5}$ =H and R_2 = OH; for Zn(II)TPPOH$_P$: $R_{1,2,4,5}$ = H and R_3 = OH.

EXPERIMENTAL

Materials and methods

Commercially available chemicals and solvents were used as received from Aldrich, Merck and Sigma.

The elemental analysis of C, H and N was performed with an automatic Carlo Erba L-1108 analyzer. The metallic ion was determined gravimetrically and volumetrically.

The IR spectra were recorded with a FTIR 400D Nicolet Impact spectrometer. The samples, previously dried at 150 °C for 24 h, were measured as KBr pellets of spectroscopic purity. The spectra were measured in the 4000–500 cm^{-1} spectral range.

The NMR spectra were recorded with a 400 MHz Bruker NMR Spectrometer. ^{1}H-NMR, ^{13}C-NMR, DEPT 90, HMQC, HMBC and COSY spectra were measured.

The molecular absorption spectra were recorded with a Specord M400 Carl Zeiss Jena UV–Vis spectrometer, assisted by an internal computer, within the spectral range of 210–900 nm. All spectra were recorded in a mono-beam system, in order to eliminate the specific absorption of the solvent and the absorption differences caused by the optical pathway. For measurement of UV–Vis absorption both polar (chloroform) and non-polar (benzene) solvents were used.

Synthesis of the Zn(II) complexes

The methods presented in the literature[32,33] for the synthesis of metalloporphyrins, usually result in very low yields, mainly because of the high temperatures and low pH of the environment used during the synthesis. For this reason, the synthesis of the complexes in the present work was instead conducted at moderate temperatures and in the presence of a basic catalyst, 2,6-dimethylpyridine, which determined the removal of a proton from the inner nitrogen atoms inside the porphyrinic macrocycle, thereby enabling the production of the complex. These new experimental conditions considerably reduced the duration of synthesis and increased the yield of the reaction to around 90 %.

Solutions (≈ 10^{-4} M) of each of the four porphyrinic ligands (TPP, $TPPOH_O$, $TPPOH_M$ and $TPPOH_P$)[34] in chloroform were gently heated under stirring until the ligand crystals were completely dissolved. Then, several drops of 2,6-dimethylpyridine were added, together with the appropriate amount of a methanolic solution of $ZnCl_2$ to give a 1:1 stoichiometric ratio. The reaction mixture was refluxed under continuous stirring for 1 h at 55 °C. The presence of the complex in the reaction mixture was monitored during the course of the reaction by thin layer chromatography. After cooling, the reaction mixture was purified by passing it through an alumina chromatographic column. The excess metallic salt was retained by the alumina, while chloroform containing the complex (the deep violet-colored complex was the second band passing through the chromatographic column) was collected. The solutions of the complexes in chloroform were concentrated by simple distillation. The obtained violet crystals were dried at ≈ 100 °C for 12 h.

RESULTS AND DISCUSSION

Elemental analysis

The results of the elemental analysis of the four ligands combinations with Zn(II) are given in Table I.

The experimental values obtained for the percentage elemental analysis of carbon, hydrogen, nitrogen and zinc are in accordance with the theoretical values calculated on the basis of a 1:1 Zn (II):porphyrinic ligand stoichiometry, thus confirming this stoichiometry for all the four synthesized metalloporphyrinic complexes.

TABLE I. Results of elemental analysis

Complex	Content, %							
	C		H		N		Zn	
	Calcd.	Found	Calcd.	Found	Calcd.	Found	Calcd.	Found
Zn(II)TPP	77.86	77.25	4.16	4.50	8.25	8.35	9.64	9.29
Zn(II)TPPOH$_O$	76.06	75.90	4.06	4.12	8.06	8.32	9.42	9.15
Zn(II)TPPOH$_M$	76.06	75.70	4.06	4.19	8.06	8.12	9.42	9.19
Zn(II)TPPOH$_P$	76.06	75.89	4.06	4.21	8.06	8.15	9.42	9.23

IR Spectra

The most relevant results extracted from the IR spectra of the synthesized Zn(II) complexes, together with those for the corresponding free complexes are given in Table II.[34]

The IR spectra of the four Zn-free complexes, *i.e.*, TPP, TPPOH$_O$, TPPOH$_M$, TPPOH$_P$, were previously analyzed.[34] In agreement with the structure of the free complexes, the presence of the characteristic bands of ν_{O-H} (obviously not present for TPP) and ν_{N-H} in the spectral range 3410–3528 cm^{-1} and 3314–3448 cm^{-1} could be identified.[34]

TABLE II. Characteristic IR vibrations of the free-base porphyrins and of the mono-hydroxy-substituted Zn(II) complexes

Characteristic vibration	$\bar{\nu}$ / cm^{-1}							
	TPP[34]	Zn(II)TPP	TPPOH$_O$[34]	Zn(II)-TPPOH$_O$	TPPOH$_M$[34]	Zn(II)-TPPOH$_M$	TPPOH$_P$[34]	Zn(II)-TPPOH$_P$
ν_{O-H}	–	–	3528	3533	3521	3494	3527	3525
ν_{O-H} associated	–	–	3424	3429	3424	3429	3410	3412
ν_{N-H}	3448	–	3448	–	3440	–	3430	–
ν_{N-H} associated	3316	–	3316	–	3316	–	3314	–
$\nu_{C=NH}$	1557	–	1558	–	1558	–	1557	–
ν_{C-O}	–	–	1176	1176	1178	1177	1170	1171

As reported before,[34] two bands corresponding to ν_{N-H} were present: the first one, well individualized in the region 3430–3448 cm^{-1}, can be attributed to ν_{N-H} stretching vibrations; the second one, less intense, in the 3314–3316 cm^{-1} range corresponds to the stretching vibration $\nu_{N-H associated}$. A band attributed to $\nu_{C=NH}$ was also present at 1557–1558 cm^{-1}.

Comparing the IR spectra corresponding to the newly synthesized complex *versus* those for the corresponding free ligand (as can be seen in Table II), the disappearance of three bands from the spectrum of the zinc containing complexes was evidenced. The absence of these bands for Zn(II)TPP and Zn(II)TPPOH$_X$ is very clear evidence for the removal of one proton from the =NH groups (nitrogen atoms in the positions 21 and 23 at the inner part of the porphyrinic ring (Scheme 1),

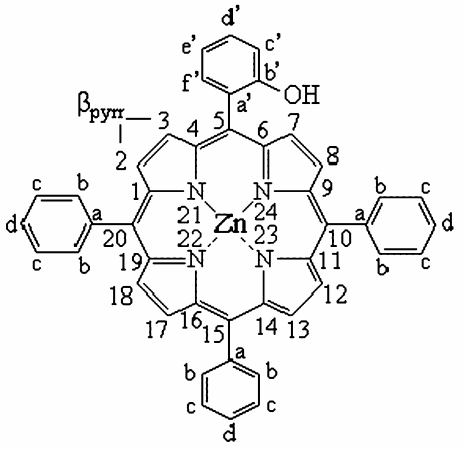
which confirms coordination of the metallic ion to the nitrogen atoms of the porphyrinic macrocycle.

The presence of the −OH functional group in $TPPOH_O$, $TPPOH_M$, $TPPOH_P$[34] and in the corresponding complex combinations with Zn(II) ions was fully confirmed by the IR spectra, in which two bands in the spectral ranges of 3494––3533 cm^{-1} and 3412–3429 cm^{-1} (3521–3528 cm^{-1} and 3410–3424 cm^{-1} for the $TPPOH_X$ free base) corresponding to ν_{O-H} and $\nu_{O-H associated}$ vibrations were identified. For all non-symmetrically substituted compounds (both the free bases[34] and the Zn(II) complexes), a medium intensity band in the 1170–1178 cm^{-1} (1171–1177 cm^{-1} for the metal-containing complexes) spectral range was identified, which was attributed to the ν_{C-O}. The presence of this band in all three Zn(II) complexes further confirms that the −OH functional group was not lost upon metal complexation with the asymmetric porphyrinic macrocycle. Accordingly, neither ν_{O-H} nor ν_{C-O} bands were present for TPP[34] and Zn(II)TPP.

All infrared spectral features described above for the free bases and the Zn(II) complexes fully support and confirm that Zn(II) inclusion onto $TPPOH_O$, $TPPOH_M$, $TPPOH_P$ was fully successful without the destruction of the monohydroxy substitution of the phenyl group of the porphyrinic ligand. The same results were observed before for Cu(II) inclusion on the same ligands.[35] As already stressed, this type of substitution was previously identified as being extremely important for the appropriate location of these types of compounds in biological media.[26,29–31]

NMR experiments

To clearly illustrate the relation between structure and NMR spectra, the *β*-pyrrole *meso*-positions (according to the Fischer rule) in terms of the arrangement of hydroxyl substituents are presented in Scheme 2, in which the ortho-, meta- and para-positions are indicated by b', c' and d', respectively.



Scheme 2. Complete atomic numbering of the $TPPOH_O$ structure for NMR assignment.

The chemical shifts and multiplicities of the ^{1}H-NMR signals for the Zn(II) complexes and other important complementary data provided by the ^{13}C-NMR spectra are presented in Table III.

TABLE III. Chemical shifts and multiplicities of the ^{1}H-NMR and ^{13}C-NMR signals for the Zn(II) complexes

Complex	^{1}H-NMR	^{13}C-NMR
Zn(II)TPP	7.79–7.71 (12H, *m*, *m*-Ph, *p*-Ph) 8.22 (8H, *dd*, *o*-Ph); 8.94 (8H, *s*, β_{pyrr})	121.1 ($C_{5,10,15,20}$); 126.5; 127.4 ($C_{\beta_{pyrr}}$) 132.0; 134.4; 142.8
Zn(II)TPPOH$_O$	7.34 (1H, *t*, c'-Ph); 7.53–7.51 (1H, *m*, e'-Ph); 7.79–7.68 (1H, *m*, d'-Ph); 7.79–7.68 (9H, *m*, c,d-Ph); 7.98 (1H, *d*, f'-Ph); 8.21 (6H, *d*, b-Ph); 8.95–8.89 (8H, *m*, β_{pyrr})	119.3 (C_5); 121.2 ($C_{10,15,20}$); 115.2 ($C_{c'}$); 126.5 (C_c); 127.5 (C_d); 128.8 ($C_{d'}$); 130.0 ($C_{a'}$); 130.8 (C_8); 131.1 ($C_{e'}$); 132.0 ($C_{2,3,\ 8,12,13,17,18}$ β_{pyrr}); 132.7 (C_7); 134.9 (C_b); 142.7 (C_a); 142.8 ($C_{f'}$); 155.5 ($C_{b'}$)
Zn(II)TPPOH$_M$	6.99 (1H, *t*, e'-Ph); 7.43 (1H, *t*, f'-Ph); 7.56 (1H, *m*, d'-Ph); 7.73 (1H, *s*, b'-Ph); 7.75 (9H, *m*, c,d-Ph); 8.19 (6H, *t*, b-Ph); 8.92 (6H, *m*, $H_{2,3,\ 8,12,13,17,18}$ β_{pyrr}); 8.97 (1H, *t*, H_7 β_{pyrr}); 9.02 (1H, *d*, H_3 β_{pyrr})	114.6 ($C_{e'}$); 120.2 ($C_{f'}$); 121.0 (C_5); 121.9 ($C_{10,15,20}$); 126.5 (C_c); 127.4 (C_d); 127.6 ($C_{b'}$); 129.6 ($C_{d'}$); 131.9 ($C_{2,8,12,13,17,18}$ β_{pyrr}); 132.3 (C_7); 134.4 (C_b); 142.8 (C_a); 144.3 ($C_{a'}$); 150.6 ($C_{c'\text{-}OH}$)
Zn(II)TPPOH$_P$	6.99 (1H, *t*, c'-Ph); 7.43 (1H, *t*, b'-Ph); 7.56 (1H, *m*, e'-Ph); 7.73 (1H, *s*, f'-Ph); 7.75 (9H, *m*, c,d-Ph); 8,19 (6H, *t*, b-Ph); 8,92 (6H, *m*, $H_{2,8,12,13,17,18}$ β_{pyrr}); 8.97 (1H, *t*, H_7 β_{pyrr}); 8.97 (1H, *t*, H_7 β_{pyrr}); 9.02 (1H, *d*, H_3 β_{pyrr})	113.5 ($C_{c',e'}$); 120.4 (C_5); 121.0 ($C_{10,15,20}$); 126.5 (C_c); 127.4 (C_d); 131.9 ($C_{2,8,12,13,17,18}$ β_{pyrr}); 132.0 ($C_{3,7}$ β_{pyrr}); 134.4 (C_b); 135.2 ($C_{a'}$); 135.5 ($C_{b',f'}$); 142.7 (C_a); 155.3 ($C_{d'\text{-}OH}$)

The high frequency region of the ^{1}H-NMR spectra ($\delta \approx 9$ ppm) shows the chemical shifts for the pyrrole hydrogen atoms (β_{pyrr}). The observed differences in the signals are due to the vicinity of the substituted phenyl.

Several other experiments, *i.e.*, DEPT 90, HMQC, HMBC and COSY, were also performed. Due to the higher capacity of 2D spectra (which present on same image cross-peaks of ^{1}H-NMR and ^{13}C-NMR for HMQC and HMBC, and proton coupling for COSY), it was possible to identify several carbon atoms and also to elucidate the differences between the influence of the hydroxyl substituent on its surroundings in dependence on whether it was positioned in the *o*-, *m*- or *p*-position, as shown in Figs. 1 to 3.

The HMQC data for Zn(II)TPPOH$_O$ (Fig. 1a, inset) shows the bonding between the pyrrolic protons and the corresponding carbon atoms. The cross-peak revealed the connection between C_7, C_8 and the rest of $C_{\beta_{pyrr}}$ on one side and the H_{pyrr} on the other.

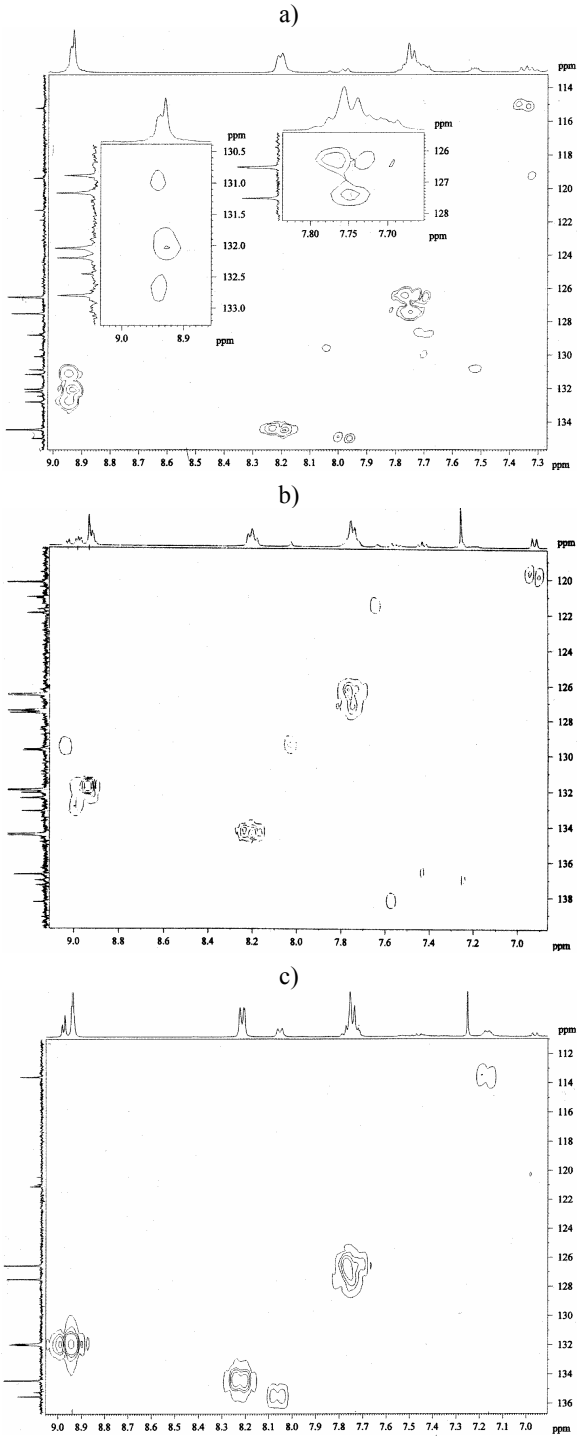


Fig. 1. HMQC spectra for (a) Zn(II)TPPOH$_O$, (b) Zn(II)TPPOH$_M$ and (c) Zn(II)TPPOH$_P$.

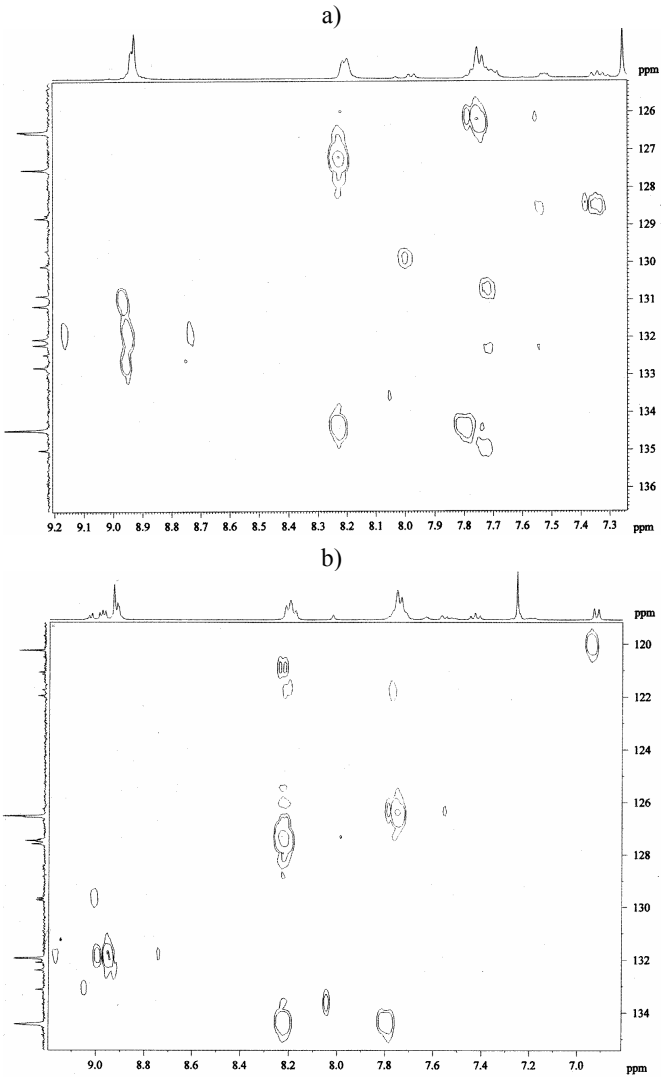


Fig. 2. HMBC spectra for (a) Zn(II)TPPOH$_O$ and (b) Zn(II)TPPOH$_M$.

These kind of data permitted the establishment of the correct interpretation of the C signals and, more important, of the influence of the −OH group on the environment (especially the atoms in the β-pyrrolic positions 2, 3, 7 and 8). The C signal is influenced by the presence of the −OH group, at 132.7, 132.3 and 132.0 ppm for Zn(II)TPPOH$_O$, Zn(II)TPPOH$_M$ and Zn(II)TPPOH$_P$, respectively. Due to the symmetry of the compound, this C type is identical with the C_{3pyrr}. This situation was also confirmed by HMBC (Fig. 2). The presence of the −OH group in the ortho-, meta- and para-positions was also confirmed by the differences in the H–H coupling.

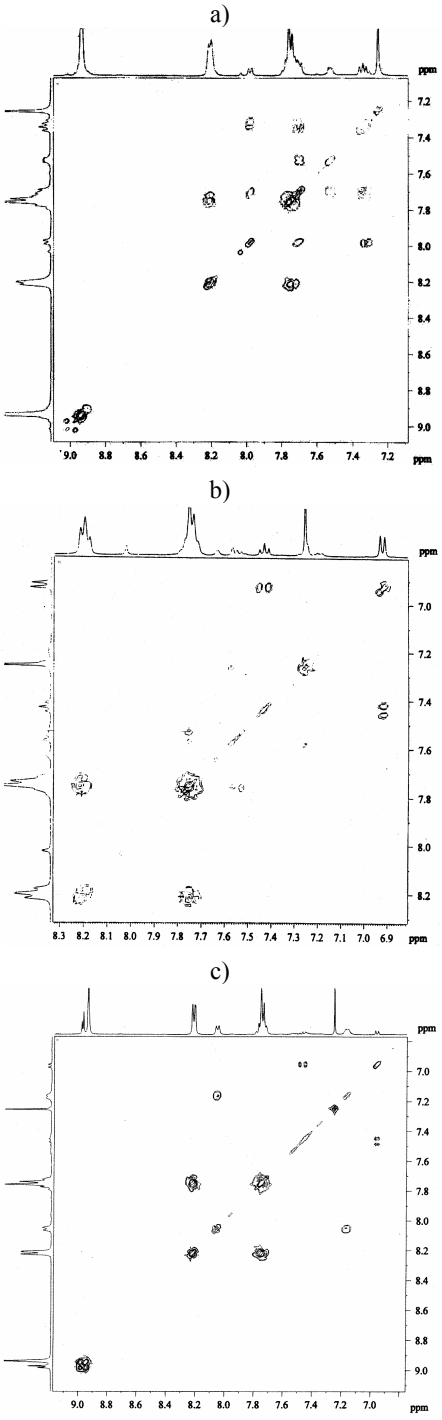


Fig. 3. COSY spectra for:
(a) Zn(II)TPPOH$_O$,
(b) Zn(II)TPPOH$_M$ and
(c) Zn(II)TPPOH$_P$.

Molecular electronic spectra

The molecular electronic absorption spectra are usually used for quantitative determinations of compounds, but in the case of porphyrinic compounds, they were shown to be real "fingerprints".[1,2,12,36–38] Despite the great number of atoms in their structures (typically 40–80 atoms) and of the complex structures adopted by the free base porphyrins and their metal containing complexes, the spectral analysis of their UV–Vis molecular electronic absorption spectra is still an efficient method for the identification of porphyrin. This is explained by the fact that the peripheral substitutions do not significantly disturb the inner π electron ring of the porphyrinic macrocycle, which is responsible for the active electronic transitions in the above-mentioned spectral range.[1,27,39–42]

The molecular electronic absorption spectra of the newly synthesized Zn(II) complexes were measured at room temperature in benzene and chloroform solutions at 20–30 °C, in order to gain evidence for their structures and to determine their molar absorption coefficients at various wavelengths. A series of subsequent dilutions (≈ 10^{-4}–10^{-6} M) were performed in order to obtain absorbance values in the range 0–1.0 and thereby to ensure the maximum accuracy of the determinations. The time required for the complete dissolution of the compounds ranged from several seconds, in the case of chloroform, to several days, for some of the compounds in benzene.

The maxima of the absorption bands and the corresponding molar absorption coefficients of the Zn(II) complexes synthesized in this work are given in Table IV. The four Zn(II) complexes all displayed Soret bands, peaking at 422–424 nm, accompanied by two Q bands peaking in the 548–554 nm and 588–594 nm spectral range.

TABLE IV. UV–Vis spectral characteristics of the mono-hydroxy-substituted Zn(II) complexes

Complex	λ / nm | $\varepsilon \times 10^{-2}$ / m^2 mol^{-1}					
	Solvent					
	Chloroform			Benzene		
	Soret	Q (1,0)	Q (0,0)	Soret	Q (1,0)	Q (0,0)
Zn(II)TPP	422 | 265	552 | 14	594 | 3.9	422 | 253	548 | 14	588 | 2.2
Zn(II)TPPOH$_O$	424 | 252	554 | 12	594 | 3.6	424 | 269	550 | 14	590 | 2.7
Zn(II)TPPOH$_M$	424 | 300	552 | 13	594 | 3.9	424 | 288	550 | 13	588 | 2.4
Zn(II)TPPOH$_P$	424 | 333	554 | 15	594 | 5.1	424 | 277	550 | 15	590 | 3.3

The spectra of the newly synthesized compounds are quite similar to those of symmetrically tetra-substituted compounds, both in shape and in the ratio between the absorption band intensities.

The molar absorption coefficients did not undergo significant changes (see Table IV). The values for the reference compounds were in good agreement with those presented in the literature.[43]

The two Q bands for Zn(II) metalloporphyrins underwent a hypsochromic shift and a partial overlap, as already reported in the literature for other metallo-

porphyrins of the same type[1,12,40] and was also observed for the inclusion of Cu(II) in the same ligands.[35] When using chloroform as the solvent, an absorption band could be observed with a maximum at λ = 552–554 nm, as well as another band at λ = 594 nm, which partially overlaps the first one. In the case of the solutions in benzene, the above-mentioned overlap was slightly more evident, but two absorption bands could still be distinctly identified, displaying absorption maxima, respectively, at λ = 548–550 nm and at λ = 588–590 nm. Similar results were observed for Cu(II) complexes with the same ligands.[35] These results are strikingly different from those of the corresponding free bases,[34] for which four Q bands could clearly be identified. The decrease in the number of Q bands was reported previously for several other metalloporphyrins[1,12,40] and is the consequence of metal inclusion in the free base ligand.[1]

Metal inclusion in the macrocycle increases the symmetry of the latter and conduces its coordination geometry to a higher symmetry class (D_{4h}) than that of the free base porphyrins (D_{2h}). This latter fact yields a simplified Q band spectra which usually collapses from four to only two bands.[1] Therefore, these UV–Vis results present a further strong proof of Zn(II) inclusion on the TPP and $TPPOH_X$ ligands.

As can be seen from Table IV, the spectra of the three Zn(II) non-symmetrical complexes are quite similar to that of Zn(II)TPP, a symmetrically tetra-substituted compound, both in shape and in the ratio between the absorption band intensities. The molar absorption coefficients did not undergo significant changes, apart from the fact that they are mostly slightly higher for the non-symmetrical substituted porphyrinic complexes. Only ε_{Soret}(Zn(II)TPP) = 253×10^2 m^2 mol^{-1} as compared with $\varepsilon_{Soret}(Zn(II)TPPOH_O) = 269\times10^2$ m^2 mol^{-1}, $\varepsilon_{Soret}(Zn(II)TPPOH_M) = 288\times10^2$ m^2 mol^{-1} and $\varepsilon_{Soret}(Zn(II)TPPOH_P) = 277\times10^2$ m^2 mol^{-1} was measured in benzene. The same tendency was observed in chloroform and it was mostly observed both for the Soret and Q bands (see Table IV).

The influence of the solvent on the molar absorption coefficients could be easily observed for the Q bands: the absorption coefficients (ε) were always higher in the case of chloroform. These spectral differences among the spectra of the three mono-hydroxy-substituted Zn(II) porphyrin complexes are explained by the influence of the non-symmetrical substituent *vs.* the inner π-electron ring of the macrocycle (Scheme 1). When the −OH group assumes various positions in the phenyl nucleus (ortho-, meta- or para-), its influence is limited to the π electron of the phenyl. The angles of 70–80° between the phenyl and the tetrapyrrolic macrocycle would practically prevent conjugation. The disturbance of the inner π-electron ring of the macrocycle, which is responsible for the UV–Vis absorption spectra of the porphyrin compounds, is implicitly irrelevant. Regarding the potential inductive effect, it is practically terminated at a distance of 3–5 atoms due to the presence of the oxygen atom towards the electron ring.

The spectra recorded in the above-mentioned solvents (both polar and non-polar) did not provide evidence for the existence of self-association processes in the

investigated concentration range ($c = 10^{-4}$–10^{-6} M). The absence of an isosbestic point in the plot of the absorption spectra of these compounds with increasing concentrations, from 10^{-6} to 10^{-4} M, is strong proof for this.

The spectral absorptions of the Zn(II) complexes can be further compared with those of the free bases (with their Soret band always peaking at 420 nm and their typical four Q bands absorbing at 514–516 nm, 548–550 nm, 590–592 nm and 648–652 nm) for the same solvent, benzene.[34] From the comparison, it can be observed that in practice the Zn(II) complexation did not shift the global absorption features of these compounds into the red region of the spectra. Thus, comparing the data of the Zn(II) complexes with the data previously published for the free bases, the absorption of the latter ones extends up to 670 nm, while those of the metal containing complex had already attained zero by 600–630 nm. A similar result was observed for Cu(II) complexation with the same ligands.[34]

CONCLUSIONS

In this paper, the synthesis of four Zn(II) complexes, one with TPP and the other three with non-symmetrically −OH substituted mesoporphyrinic ligands is presented. A new synthetic method, conducted at moderate temperatures and low pH, was successfully employed, which enabled a reduction of the synthesis time and markedly increased yields of the reaction, to about 90 %. The compounds were synthesized foreseeing their use as PDT sensitizers that could appropriately locate in cellular components. For the latter three Zn(II) complexes, for which the charge density and its distribution at the periphery of porphyrinic macrocycle was modified by the inclusion of an OH group, it is possible to anticipate that their route and localization at the cellular level could be controlled, while keeping most of their relevant photochemical properties intact.

Elemental analysis of the synthesized complexes confirmed Zn(II) inclusion in TPP, as well as in the three non-symmetrically −OH substituted porphyrinic ligands, having a 1:1 stoichiometry for all the four complexes.

The spectral properties of the four Zn(II) complexes were investigated by FTIR, NMR and UV–Vis spectroscopy. FTIR spectra fully confirmed the structure of the herein prepared compounds: Zn(II) coordination to the symmetric and to the non-symmetric ligands was further confirmed; the ionic metal coordination to the porphyrinic ligand does not affect the asymmetric substitution of the ligand. NMR techniques together revealed the complete structure and the influences of the unsymmetrical substituents on the porphyrinic ring. From UV–Vis absorption, it could be observed that although the non-symmetric substitution did not significantly change the absorption properties of the ligands, the Zn(II) complexation unfortunately did not result in the desired improvement of the absorption properties of these porphyrinic compounds towards the red region of the spectra, whereby their absorption would have been shifted into the phototherapeutical window. This result is fully explained by the collapse and overlap of the

four Q bands into only two Q bands, resulting from an increase in the symmetry of the coordination geometry which is experienced by the compounds upon Zn(II) complexation.

И З В О Д

ПРОУЧАВАЊЕ Zn(II) МОНОХИДРОКСИФЕНИЛ-МЕЗОПОРФИРИНСКИХ КОМПЛЕКСА. СИНТЕЗА И КАРАКТЕРИЗАЦИЈА

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Синтетисана је серија од четири Zn(II) комплекса са асиметричним порфиринским прстеновима: [5-(4-хидроксифенил)-10,15,20-трифенил-21*H*,23*H*-порфинато]Zn(II) (Zn(II)TPPOH$_P$), [5-(3-хидроксифенил)-10,15,20-трифенил-21*H*,23*H*-порфинато]Zn(II) (Zn(II)TPPOH$_M$), [5-(2-хидроксифенил)-10,15,20-трифенил-21*H*,23*H*-порфинато]Zn(II) (Zn(II)TPPOH$_O$) и добро познати (5,10,15,20-тетрафенил-21*H*,23*H*-порфинато]Zn(II) (Zn(II)TPP), који је коришћен као референтна супстанца, у 1:1 молском односу. У свим случајевима слободна база порфирин деловала је као тетрадентат преко четири атома азота пирола. Комплекси су окарактерисани елементалном анализом, FTIR и UV–Vis спектроскопијом, чиме су утврђене структуре комплекса. UV–Vis спектри су показали да је спектрална апсорпција четири комплекса померена ка плавом подручју најмање за 50 nm у односу на слободне лиганде. Важни структурни подаци су добијени и из неколико различитих NMR експеримената (^{1}H-NMR, ^{13}C-NMR, DEPT, COSY, HMBC and HMQC). Уочен је и утицај спољних супституената на порфиринском прстену.

(Примљено 27. јула, ревидирано 29. октобра 2007)

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