Polyhedron 98 (2015) 217–223

Contents lists available at ScienceDirect

Polyhedron

journal homepage: www.elsevier.com/locate/poly

Porphyrazine with bulky 2-(1-adamantyl)-5-phenylpyrrol-1-yl periphery tuning its spectral and electrochemical properties

Michal Kryjewski [a], Ewa Tykarska [b], Tomasz Rebis [c], Jolanta Dlugaszewska [d], Magdalena Ratajczak [d], Anna Teubert [e], Jacek Gapiński [f,g], Adam Patkowski [f,g], Jaroslaw Piskorz [a], Grzegorz Milczarek [c], Maria Gdaniec [h], Tomasz Goslinski [b,*], Jadwiga Mielcarek [a]

[a] Department of Inorganic and Analytical Chemistry, Poznan University of Medical Sciences, Grunwaldzka 6, 60-780 Poznan, Poland
[b] Department of Chemical Technology of Drugs, Poznan University of Medical Sciences, Grunwaldzka 6, 60-780 Poznan, Poland
[c] Institute of Chemistry and Technical Electrochemistry, Poznan University of Technology, Piotrowo 3, 60-965 Poznan, Poland
[d] Department of Genetics and Pharmaceutical Microbiology, Poznan University of Medical Sciences, Swiecickiego 4, 60-781 Poznan, Poland
[e] Institute of Bioorganic Chemistry, Polish Academy of Sciences, Noskowskiego 12/14, 61-704 Poznan, Poland
[f] Faculty of Physics, Department of Molecular Biophysics, Adam Mickiewicz University, Umultowska 85, 61-614 Poznan, Poland
[g] NanoBioMedical Centre, Adam Mickiewicz University, Umultowska 85, 61-614 Poznan, Poland
[h] Faculty of Chemistry, Adam Mickiewicz University, Umultowska 89b, 61-614, Poland

ARTICLE INFO

Article history:
Received 3 April 2015
Accepted 25 May 2015
Available online 5 June 2015

Keywords:
Adamantane
Photochemistry
Porphyrazines
Spectroelectrochemistry
Voltammetry

ABSTRACT

The synthesis and physicochemical properties of a novel porphyrazine possessing an alternate system of two peripheral substituents, 2-(1-adamantyl)-5-phenylpyrrol-1-yl and dimethylamino, are presented. Precursor maleonitriles were characterized using X-ray crystallography. Novel porphyrazine was subjected to spectroscopic studies, including the determination of fluorescence quantum yield and singlet oxygen quantum yield. Moreover, its electrochemical and spectroelectrochemical properties were investigated. The antimicrobial photodynamic activities of the novel porphyrazine encapsulated in various liposomal formulations were tested against *Staphylococcus aureus* and *Pseudomonas aeruginosa*.

1. Introduction

Porphyrazines (Pzs) form a class of macrocycles related to porphyrins, phthalocyanines and corroles [1]. Pzs have been tested as potential photosensitizers for photodynamic therapy [2], sensors [3] and building blocks useful in dip-pen nanolithography [4]. Pzs can be modified by the introduction of a metal cation into the core or peripheral substitutions. The most common periphery of Pzs at their β-positions constitute nitrogen and sulfur residues [1,5], including annulated five, six and seven-membered rings. It is noteworthy that numerous examples of aminoporphyrazines possessing annulated diazepine [6], pyrazine [7] (also known as aza-phthalocyanines), 1,2,5-selenodiazole [8], and imidazole [9] rings are known. However, there are limited data on Pzs substituted directly at their β positions with heteroaromatic rings. In the course of our research we reported the synthesis and photochemistry of various Pzs bearing 2,5-dimethylpyrrol-1-yl, 2,5-di(2-thienyl)pyrrol-1-yl and 2,5-diphenylpyrrol-1-yl substituents [10–14]. In the present study, we report the synthesis, spectroscopic, electrochemical, and antimicrobial properties of novel Pz possessing 2-(1-adamantyl)-5-phenylpyrrol-1-yl and dimethylamino groups. We found that bulky 2-(1-adamantyl)-5-phenylpyrrol-1-yl substituents tuned photochemical and electrochemical properties of the investigated macrocycle. Adamantane moiety as a part of various biologically active compounds revealed beneficial features in medicinal chemistry [15,16]. In contrast to phthalocyanine macrocycles, adamantane bearing porphyrazine has not been reported so far. Adamantyl groups have been linked with phthalocyanine macrocycles at their peripheral and non-peripheral sites *via* sulfur [17,18], amino and oxygen groups [19] or even more complex substituents [20,21]. In addition, the photocytotoxicities of phthalocyanines bearing peripheral adamantylethoxy- or axial adamantylmethoxy groups have been tested on human red blood cells [22] and against *Candida albicans* [23], respectively.

* Corresponding author. Tel.: +48 61 854 66 31.
E-mail address: tomasz.goslinski@ump.edu.pl (T. Goslinski).

http://dx.doi.org/10.1016/j.poly.2015.05.033
0277-5387/

2. Experimental

2.1. 2-[2-(1-Adamantyl)-5-phenyl-1H-pyrrol-1-yl]-3-amino-(2Z)-butene-1,4-dinitrile (**6**)

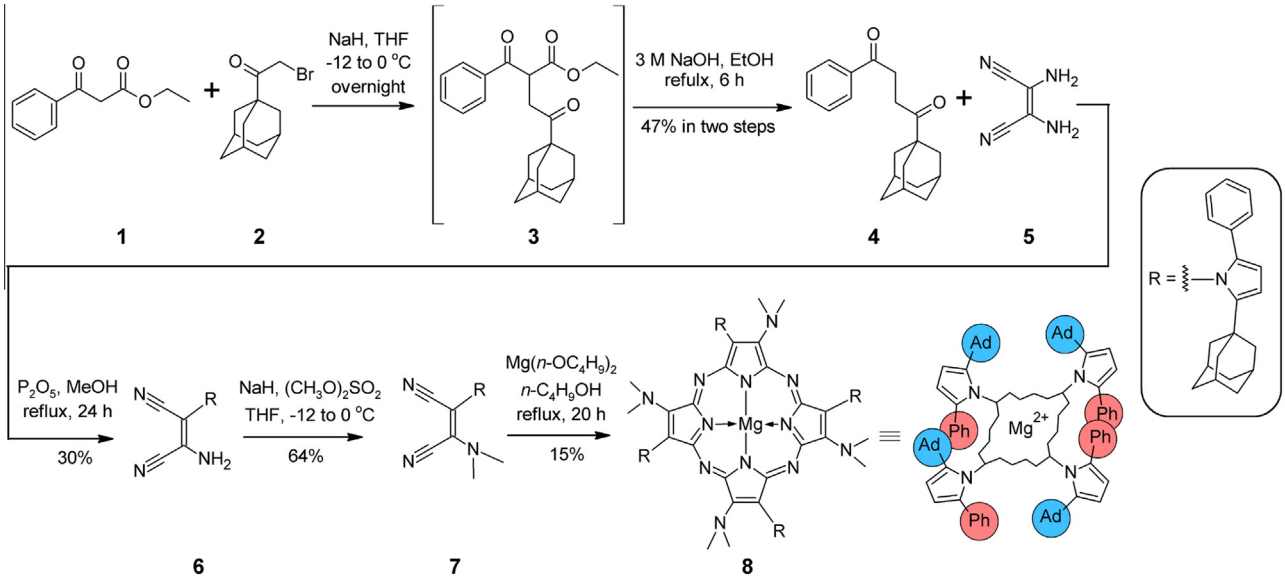
1-(1-Adamantyl)-4-phenylbutane-1,4-dione **4** (1.48 g, 5.0 mmol), diaminomalonitrile **5** (540 mg, 5.0 mmol) and P_2O_5 (190 mg) were stirred in methanol (60 mL) and heated under reflux for 2 h. After that time, an additional amount of P_2O_5 in three portions (800 mg, 7.0 mmol altogether) was added within 2 h and kept under reflux while stirring for the next 20 h. Next the reaction mixture was cooled to room temperature and evaporated to dryness. The dry residue was taken into CH_2Cl_2 and filtered to remove unreacted **5** and side-products. The filtrate containing the crude product in CH_2Cl_2 was concentrated and chromatographed (CH_2Cl_2) to give **6** as yellow, crystalline solid (556 mg, 30% yield). M.p. 190 °C dec.; R_f = 0.43 (CH_2Cl_2); ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.85 (bs, 2H, NH_2), 7.45–7.31 (m, 5H, C_6H_5), 6.24 (d, ^3J = 3.5 Hz, 1H, pyrrole-H), 6.09 (d, ^3J = 3.5 Hz, 1H, pyrrole-H), 2.16–1.94 (m, 6H, adamantane-H), 1.89 (d, ^3J = 11.5 Hz, 3H, adamantane-H), 1.72 (q, ^3J = 12.0 Hz, 6H, adamantane-H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 144.2, 135.8, 132.3, 131.7, 128.2, 128.1, 127.4, 118.3, 112.9, 110.0 107.8, 91.1, 40.9, 36.2, 34.1, 28.0; MS (ES) *m/z* 391 $[M+Na]^+$; *Anal.* Calc. for $C_{24}H_{24}N_4$: C, 78.23; H, 6.57; N, 15.21. Found: C, 78.06; H, 6.62; N, 15.24%. *Crystal data:* $C_{24}H_{24}N_4$, *M* = 368.47, orthorhombic, $P2_12_12_1$, *a* = 8.3432(2) Å, *b* = 11.5355(2) Å, *c* = 20.5641(4) Å, *V* = 1979.15(7) Å^3, *Z* = 4, D_c = 1.237 g·cm^{-1}, μ(Cu Kα) = 0.579 mm^{-1}, *T* = 130 K, 11 267 reflections collected, 3879 independent reflections, R_{int} = 0.016, θ_{max} = 75.94°, R_1(obs.) = 0.028, wR_2(all) = 0.069, 253 refined parameters.

2.2. 2-[2-(1-Adamantyl)-5-phenyl-1H-pyrrol-1-yl]-3-(dimethylamino)-(2Z)-butene-1,4-dinitrile (**7**)

NaH (264 mg, 1.1 mmol, 60% dispersion in mineral oil) was suspended in THF (10 mL) at (−12 °C) and stirred. Next **6** (186 mg, 0.5 mmol) in THF (6 mL) was added dropwise and stirred for additional 30 min. Dimethyl sulfate (0.093 mL, 1.1 mmol) in THF (2 mL) was added dropwise to the reaction mixture for 30 min at (−10 °C) and stirred for 1 h. After that time, the reaction mixture was allowed to warm to room temperature, stirred overnight and poured into ice-water (100 mL). A water layer was extracted with CH_2Cl_2. The organic extracts were dried with $MgSO_4$, concentrated and chromatographed using *n*-hexane:EtOAc 7:1 to give **7** as a yellow solid (151 mg, 75% yield). M.p. 155 °C; R_f = 0.27 (*n*-hexane:EtOAc 7:1, v/v); ^{1}H NMR (400 MHz, pyridine-d_5) δ 7.67 (d, ^3J = 7.0 Hz, 2H, 2',6'-C_6H_5), 7.43 (t, ^3J = 7.5 Hz, 2H, 3',5'-C_6H_5), 7.31 (t, ^3J = 7.5 Hz, 1H, 4'-C_6H_5), 6.38 (d, ^3J = 4.0 Hz, 1H, pyrrole-H), 6.25 (d, ^3J = 4.0 Hz, 1H, pyrrole-H), 2.55 (s, 6H, CH_3), 2.30 (d, ^3J = 11.5 Hz, 3H, adamantane-H), 2.14 (d, ^3J = 11.0 Hz, 3H, adamantane-H), 2.00 (s, 3H, adamantane-H), 1.70 (q, ^3J = 12.5 Hz, 6H, adamantane-H); ^{13}C NMR (100 MHz, pyridine-d_5) δ 147.6, 139.3, 133.6, 132.9, 129.0, 128.9, 128.1, 120.9, 113.3, 109.9, 109.0, 91.9, 42.6, 40.9, 36.7, 35.5, 28.9; MS (ES) *m/z* 397 $[M+H]^+$, 419 $[M+Na]^+$; *Anal.* Calc. for: $C_{26}H_{28}N_4$ C 78.75; H 7.12; N 14.13; Found: C 78.66; H 7.31; N, 13.80; *Crystal data:* $C_{26}H_{28}N_4$, *M* = 396.52, monoclinic, $P2_1/n$, a = 8.9116 (3) Å, b = 12.3745(4) Å, *c* = 19.4130(7) Å, β = 94.599(3)°, V = 2133.9(1) Å^3, Z = 4, D_c = 1.234 g·cm^{-1}, μ(MoK$_\alpha$) = 0.074 mm^{-1}, T = 130 K, 16,460 reflections collected, 3905 independent reflections, R_{int} = 0.033, θ_{max} = 25.35°, R_1(obs.) = 0.038, wR_2(all) = 0.086, 273 refined parameters.

2.3. [2,7,12,17-Tetrakis(2-(1-adamantyl)-5-phenyl-1H-pyrrol-1-yl)-3,8,13,18-tetrakis(dimethylamino)porphyrazinato]magnesium(II) (**8**)

Magnesium turnings (120 mg, 5.0 mmol), a small crystal of I_2, and *n*-butanol (45 mL) were heated under reflux for 6 h. After the reaction mixture was cooled to room temperature, maleonitrile derivative **7** (497 mg, 1.25 mmol) in DMF (2.5 mL) was added and the mixture was heated under reflux for the next 16 h. After being allowed to cool to room temperature, the dark green mixture was filtered through Celite and the solvents were co-evaporated with toluene (2 × 50 mL). Chromatography (CH_2Cl_2) was performed twice to give the main product, porphyrazine (**8**) (75 mg, 15% yield) as a dark blue solid. R_f = 0.16 (CH_2Cl_2); UV–Vis (CH_2Cl_2:CH_3OH 1:1): λ_{max}, nm (log ε) 346 (4.35), 729 (4.26); IR (cm^{-1}) 1581, 1558, 1120, 1063; ^{1}H NMR (400 MHz, pyridine-d_5) δ = 7.80 (d, ^3J = 8 Hz, 5H, –C_6H_5), 7.67 (d, ^3J = 9 Hz, 3H, –C_6H_5), 7.42–7.49 (m, 7H, –C_6H_5), 7.28–7.39 (m, 7H, –C_6H_5), 6.92–6.70 (m, 12H, –C_6H_5), 6.52–6.70 (m, 6H, –C_6H_5), 6.49 (d, ^3J = 4 Hz, 3H, pyrrole-H), 6.38 (d, ^3J = 4 Hz, 1H, pyrrole-H), 6.32 (d, ^3J = 4 Hz, 3H, pyrrole-H), 6.42 (^3J = 4 Hz, 1H, pyrrole-H), 3.03, 3.61, 3.66, 3.70 (m, s, m, s, 24 H, 4 × $N(CH_3)_2$), 2.07–2.41 (m, 24H, adamantane-H), 1.91–1.99 (m, 12H, adamantane-H), 1.63–1.73 (m, 24H,



Scheme 1. Synthesis of porphyrazine **8**.

adamantane-H); ^{13}C NMR (101 MHz, pyridine-d_5) δ = 149.5[h], 146.7, 138.8, 136.7[h], 134.8, 131.3, 130.2, 130.0, 129.6, 129.5, 129.2, 129.2, 129.0, 112.4, 111.5, 109.8, 43.5, 43.5, 38.0, 36.7, 30.1. MS *m*/*z* (MALDI) 1611 $[M+H]^+$.

3. Results and discussion

3.1. Synthesis

The aim of our studies was to obtain new porphyrazine bearing 2-(1-adamantyl)-5-phenylpyrrol-1-yl substituents. Alkylation reaction of ethyl benzoyl acetate (**1**) with 1-adamantyl-bromomethyl ketone (**2**) led to ester **3** (Scheme 1). The crude ester was subjected to hydrolysis and oxidative decarboxylation, following the previously published procedure, leading to the known compound **4** [24]. By adapting the previously published procedure [25], 1-(1-adamantyl)-4-phenyl-butane-1,4-dione (**4**) was used as a substrate in the Paal-Knorr type reaction with diaminomaleonitrile (**5**) in methanol, in the presence of phosphorous pentoxide as both a dehydrating and acidic agent, to give the novel maleonitrile derivative **6**. Product **6** was subjected to methylation reaction to give **7** [26]. Mass spectra, elemental analyses and NMR experiments confirmed the formation of the desired intermediate products (see Supplementary data). Derivative **7** was used in the Linstead macrocyclization [27] reaction using magnesium *n*-butanolate in *n*-butanol, toward a new magnesium porphyrazine **8**, which was obtained in 15% of overall yield. The macrocycle was purified by column chromatography and subsequently analyzed by HPLC. Due to aggregation, typical for some porphyrazine compounds, the HPLC analysis revealed three peaks with virtually the same UV–Vis spectra (see Supplementary data). NMR data of **8** were compared with the results previously obtained for Pzs possessing an alternate [12] and an non-alternate [11] system of dimethylamino and pyrrolyl groups. In the cases above, diagnostic patterns of dimethylamino group signals as one [12] (alternate system) or four [11] of equal intensities singlet signals (non-alternate system) were found. However, for Pz **8**, a more complicated pattern of signals was found. Moreover, in recording the variable-temperature, the NMR spectra did not result in any simplification of the analyzed pattern (see Supplementary data). We propose that it may be due to an arrangement of pyrrolyl substituents, with three adamantane moieties being on one side of the porphyrazine plane, and one on the other side (Scheme 1). Signals of 3′,4′-pyrrolyl protons appearing as four dublets with 3:1:3:1 integration seem to support our observation.

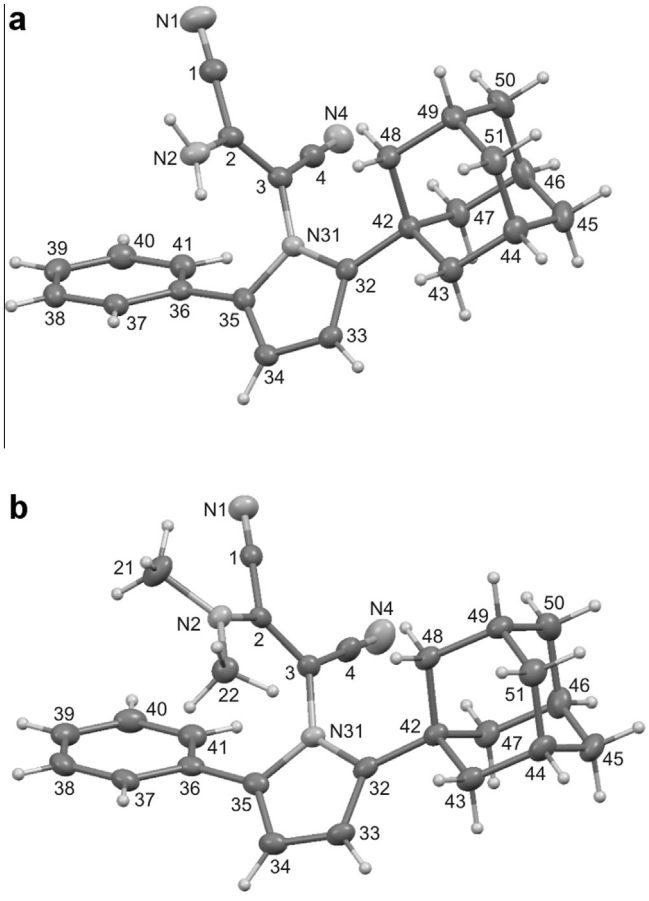


Fig. 1. The molecular structures of (a) **6** and (b) **7** showing the atom labeling scheme. Displacement ellipsoids are drawn at the 50% probability level and H atoms are shown as spheres of arbitrary radii.

3.2. Crystallography

Two maleonitrile derivatives **6** and **7** (Fig. 1) were subjected to crystallization that fortunately resulted in single crystals suitable for X-ray analyses. The maleonitrile units show the expected cis-geometry of the double bond. The exchange of a primary NH_2 amino group present in **6** into a more bulky tertiary $N(CH_3)_2$ group in **7** did not effectively influence the molecular conformation. The amino group N atoms are sp^2 hybridized with the sum of the bond angles around N2 close to 360°. The electron lone pair of N2 is conjugated with the π-system of the maleonitrile moiety resulting in a shortening of the formally single N2–C2 bond (1.339(2) Å in **6** and 1.353(2) Å in **7**). The 2,5-substituted pyrrole ring is strongly twisted relative to the maleonitrile unit attached to the pyrrole N atom due to a steric overcrowding (dihedral angles 77.92(3)° in **6** and 70.43(4)° in **7**). The phenyl ring is also similarly oriented relative to the pyrrole ring with the torsion angle N(31)–C(35)–C(36)–C(37) of −126.8(1)° in **6** and −133.0(1)° in **7**.

In both crystals, molecules are arranged into similarly constructed chiral (001) layers with the adamantyl groups protruding from the layer surface; however, in the crystals of **6** the (001) layers are homochiral, whereas in **7** the layers of the opposite chirality alternate along the *z* axis (Fig. S11, Supplementary data).

3.3. Photochemical studies

Photosensitizing properties of **8** were referred to those previously established for the standard zinc(II) phthalocyanine (ZnPc) [28–30]. 1,3-Diphenylisobenzofuran (DPBF) was used as a chemical quencher of singlet oxygen. Solution of **8** and DPBF was irradiated with light at the wavelength of 729 nm in DMF, corresponding to the maximum of the Q-band. DPBF oxidation was UV–Vis monitored with its absorbance decrease at 417 nm (Fig. 2). A comparison of DPBF oxidation kinetic parameters of **8** and ZnPc allowed the determination of the singlet oxygen generation yield value to be Φ_Δ = 0.17 in DMF.

Fluorescence spectra of Pz **8** were recorded both in DMF and THF. The fluorescence quantum yields were calculated using ZnPc as a reference, according to the method given by Ogunsipe et al. [31]. The quantum yields were found to be Φ_F = 0.031 and 0.039 in DMF and THF, respectively. The Stokes shifts are minor, 240 and 223 cm^{-1} for DMF and THF, respectively, which confirms a small difference in the geometry of the Pz **8** molecule in its singlet, ground S_0 and excited S_1, states.

Photodegradation studies were conducted in DMF as a solvent, changes in the absorption spectra are presented in Fig. 2b. Experiments were performed both in aerobic conditions and with limited access to air in order to find out whether oxygen influences

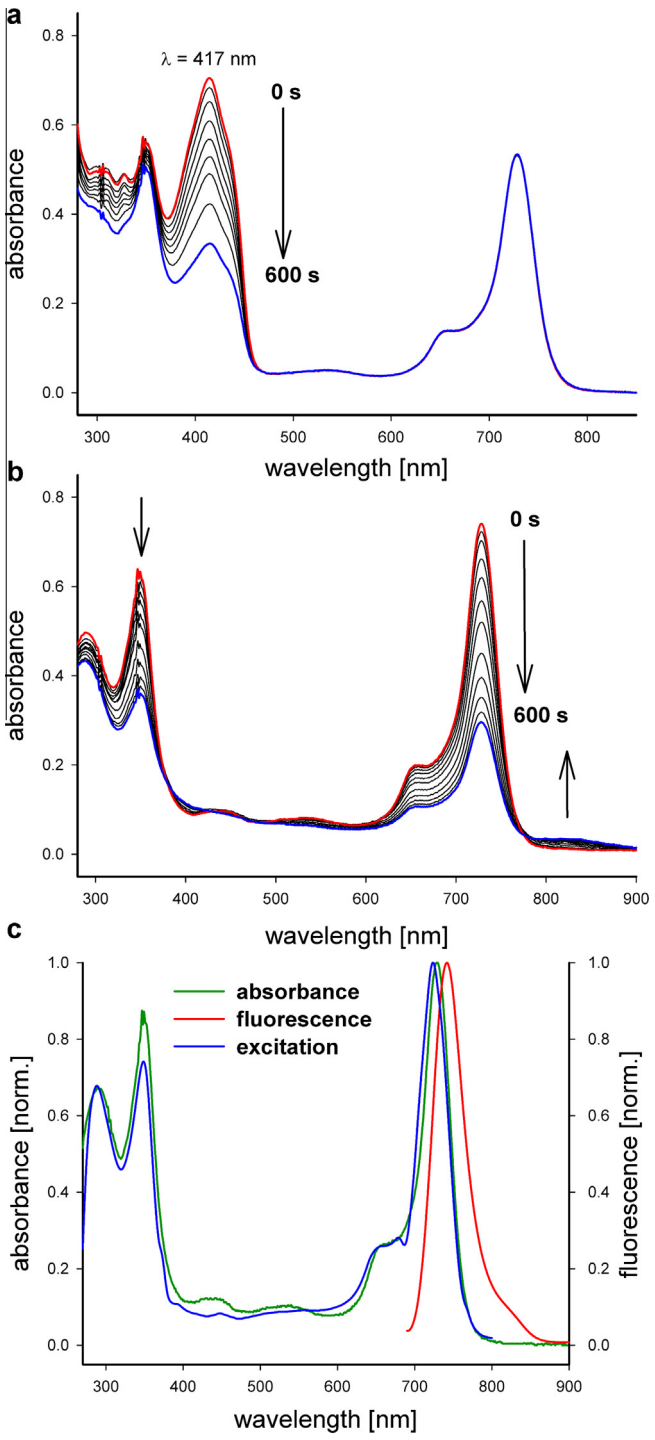


Fig. 2. Changes in the UV–Vis spectra of DPBF and **8** in DMF during irradiation at the Q-band (a), changes in the UV–Vis spectra of **8** in DMF during photodegradation – aerobic conditions (b), absorbance, fluorescence and excitation spectra of **8** in DMF (c).

the decomposition process. Kinetic studies of photobleaching revealed a two-step process, both following first-order kinetics, parameters are presented in Table 1. Deaeration did not significantly impact *k* parameters.

3.4. Electro- and spectroelectrochemical properties

The electrochemical properties of **8** were investigated by using cyclic voltammetry (CV) and differential pulse voltammetry (DPV) and the data is presented in Table 2 and Fig. 3. The obtained results indicate that Pz **8** undergoes two quasi-reversible reduction processes at $E_{1/2} = -1.96$ V (1) and $E_{1/2} = -1.75$ V (2) as well as two reversible oxidations at $E_{1/2} = -0.23$ V (3) and $E_{1/2} = 0.28$ V (4). The number of electrons transferred in all redox transitions, estimated from the peak width in a DPV technique, is equal to one. This is in good agreement with previously reported porphyrinoids, where one electron transfer is typical [32,33].

For the electrochemically inactive metal ion center such as Mg^{2+}, it can be expected that all processes involve ligand – centered oxidations creating π-cation radicals and reductions producing π-anion radicals [7,32,33]. Both reduction couples (Fig. 3a) demonstrate rather poor electrochemical reversibility with small anodic peaks appearing on voltage reversal. However, the scan rate from 25 to 250 mV/s correlates linearly versus $v^{1/2}$ to the peak current, which suggests diffusion controlled processes. Moreover, an increase in the scan rate hardly affects the peak positions (see Supplementary data). Although for the reduction processes the reverse anodic peaks are not-well developed on the CV, the well-defined peaks can be observed on DPV with the current ratio near to unity. The Pz **8** shows two reversible oxidation processes. Anodic to cathodic peak currents (i_a/i_c) are near to unity for the first and second oxidation couple and do not vary significantly when the scan rate is increased. Peak to peak separations recorded for 100 mV/s for the Pz/Pz^+ and Pz^+/Pz^{2+} oxidation process are 66 and 73 mV, respectively, which are close to the theoretical value of ca. 60 mV for perfectly reversible systems. These values remain more or less constant for the whole range of scan rates used during the experiment. No kinetic limitations, suggesting fast charge transfer, were observed. Anodic and cathodic currents of Pz/Pz^+ and Pz^+/Pz^{2+} couples linearly depend on the potential sweep rate square root (see Supplementary data) indicating diffusion controlled reactions. The obtained results indicate that Pz **8** is relatively easy to oxidize with the first couple at −0.23 V versus Fc/Fc^+. This is attributed to the effect of nitrogen containing substituents bonded directly to porphyrazine ring. Dimethylamine groups possess strong electron-donating properties which facilitate the appearance of cation radicals and effectively shifts oxidation potential toward less positive values. Similar values have been noticed for other amino-substituted Pzs [34–36]. However, the Pz **8** is more resistant to reduction in comparison to e.g. sulfur substituted Pzs [32,37–39].

The difference between the first oxidation and the first reduction processes (1.53 V) is assigned as the HOMO–LUMO gap for porphyrazines without an active metal ion in the center, and is in good agreement with the previously reported data [33]. This value is in agreement with the HOMO–LUMO gap [40] (1.70 eV) calculated from UV–Vis λ_{max}, according to equation $E = hc/\lambda$. It seems that Pz **8** which revealed in solution fully reversible, fast electron redox processes with relatively low formal potential, may find applications as electrocatalyst in oxidation processes as well as sensor in materials chemistry.

The monitoring of redox reactions using optical spectroscopy is a powerful approach enabling the examination of macrocycles and coordinated metal ion electronic structures. Thus, in situ spectroelectrochemical measurements were applied to determine anionic and cationic forms of the Pz. Changes in the UV–Vis spectra of Pz **8**

Table 1
Kinetic parameters of photodecomposition of **8**.

Conditions	Stage	
	I 10^2 (k ± Δk) [s^{-1}]	II 10^3 (k ± Δk) [s^{-1}]
Aerobic	0.90 ± 0.06	1.26 ± 0.06
Limited access to air	1.00 ± 0.08	1.20 ± 0.07

Table 2
Voltammetric data of the Pz **8** recorded at 100 mV/s.

	Pz^{-}/Pz^{2-}	Pz/Pz^{-}	Pz^{+}/Pz	Pz^{2+}/Pz^{+}	$\Delta E_{1/2}$
$E_{1/2}$ [V]	−1.96	−1.75	−0.23	0.28	1.52
ΔEP [mV]	–	–	66	73	
ipa/ipc	–	–	0.94	0.82	

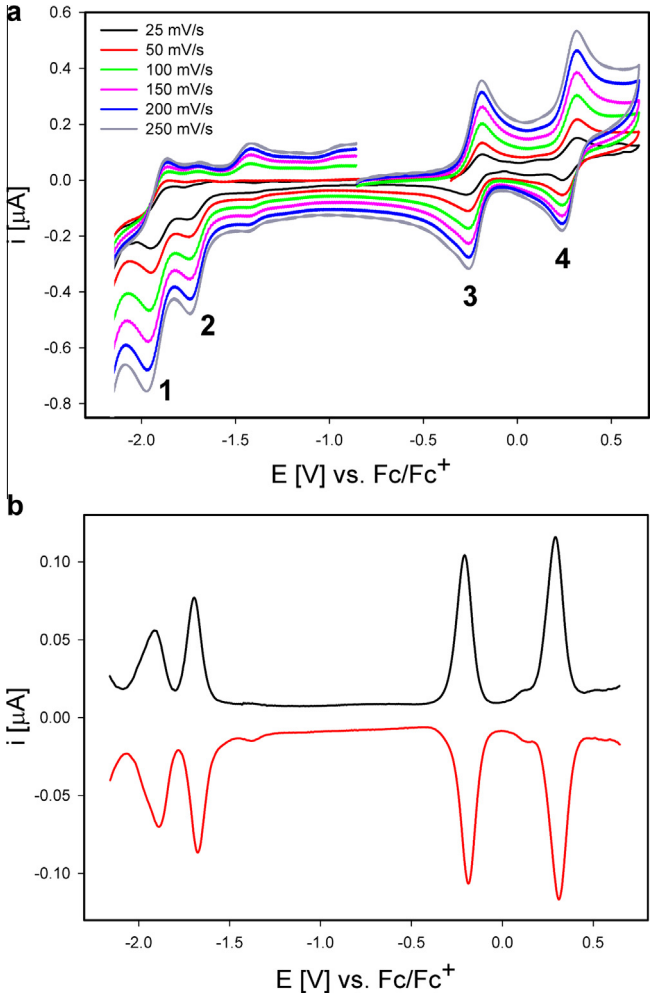


Fig. 3. Cyclic voltammograms of Pz **8** at different scan rate; 1, 2 – reduction processes; 3, 4 – oxidation processes (a), differential pulse voltammograms (DPV) for 8, DPV parameters: modulation amplitude 20 mV, step rate 10 mV/s (b).

(Fig. 4a), recorded during the controlled potential at 0.14 V, indicated a decrease in the Q-band intensity at $\lambda = 728$ nm without shift, which was accompanied by the appearance of a new band at 823 nm. Such a red-shifted band has previously been assigned to the aggregated forms [41]. The spectra recorded at open circuit potential in the function of time showed the progressive increase of absorption in this range with a subsequent decrease after mixing the solution (not shown). At the same time, the decrease of the Soret band intensity at 341 nm accompanied by bathochromic shift to 350 nm was found.

3.5. Liposomes and antimicrobial photocytotoxicity

There is a constant interest in liposomes as a formulation for photosensitizers in photodynamic therapy [42]. Therefore, Pz **8** was encapsulated in liposomes [43,44] consisting of 1-palmitoyl-2-oleoyl-sn-glycero-3-phosphocholine (POPC), L-α-phosphatidyl-

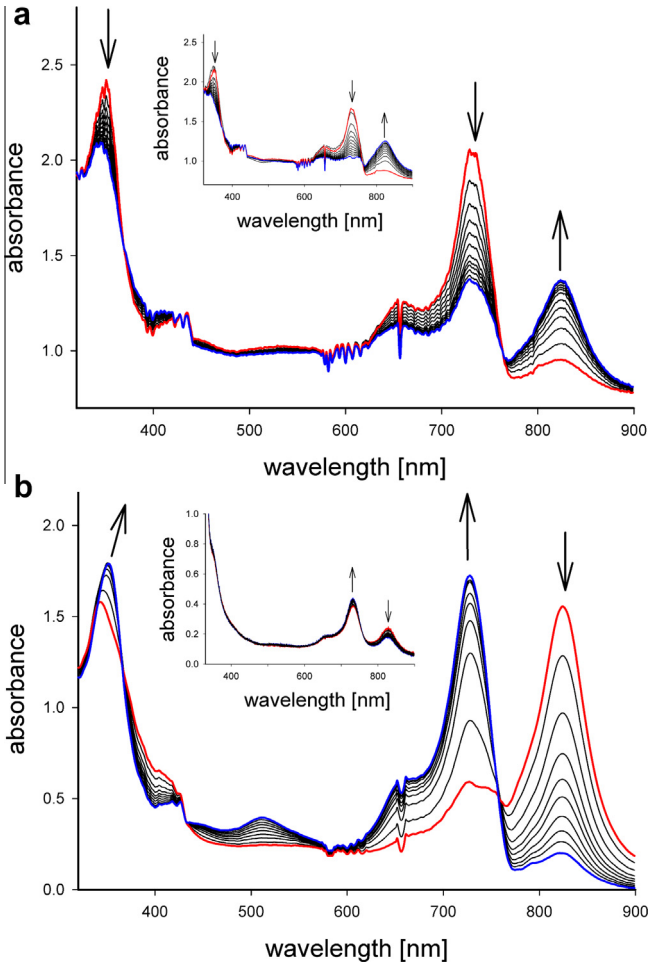


Fig. 4. In situ UV–Vis spectral changes of **8** at constant potential $E_{app} = 0.14$ V, $E_{app} = 0.66$ V (inset) (a); and $E_{app} = -1.79$ V, $E_{app} = -2.1$ V (inset) (b).

DL-glycerol (egg, chicken; PG) 1,2-dioleoyl-3-trimethylammonium-propane (chloride salt, DOTAP) and cholesterol (Chol). Liposomes containing encapsulated Pz **8** were subjected to antibacterial photocytotoxicity study against the standard strains of *Staphylococcus aureus* NCTC 4163 and *Pseudomonas aeruginosa* NCTC 6749 (see Supplementary data). Unfortunately, no significant reduction in the number of bacterial cells was observed in both, the non-irradiated and irradiated samples.

4. Conclusions

Novel porphyrazine **8**, possessing an alternate system of two peripheral substituents, 2-(1-adamantyl)-5-phenylpyrrol-1-yl and dimethylamino was synthesized and fully characterized. Moreover, the precursor maleonitriles were characterized using X-ray crystallography. The macrocycle was found to be moderately active as singlet oxygen generator with Φ_Δ values of 0.17 in DMF. Electrochemical and spectroelectrochemical properties of Pz **8** were studied and revealed that the concerned compound was relatively easy to oxidize with the first couple at −0.23 V versus Fc/Fc^{+}, which may be attributed to the electron-donating properties of nitrogen containing substituents bonded directly to porphyrazine ring. In addition, Pz **8** was encapsulated in various liposomal formulations and subjected to the antimicrobial photocytotoxicity tests against *S. aureus* and *P. aeruginosa*. It seems that novel Pz **8** constitutes an interesting building block for material chemistry and nanotechnology. This study will be continued and presented in due course.

Acknowledgements

The authors acknowledge financial support for the project from the National Science Centre under Grant No. N N404 069440, the European Fund for Regional Development No. UDA-POIG.02.01.00-30-182/09 and National Centre for Research and Development under contract No. PBS1/A9/13/2012. MK is a scholarship holder "Scholarship support for Ph.D. students specializing in majors strategic for Wielkopolska's development", Sub-measure 8.2.2 Human Capital Operational Programme, co-financed by EU under the ESF. MK acknowledges financial support from the National Science Centre for Ph.D. thesis preparation, contract number 2013/08/T/NZ7/00238.

Appendix A. Supplementary data

The following publications refer to the experimental data contained in the Supplementary data [45–47]. CCDC 1003113 for **6** and 1003114 for **7** contain the supplementary crystallographic data for this paper. These data can be obtained free of charge via http://www.ccdc.cam.ac.uk/conts/retrieving.html, or from the Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK; fax: (+44) 1223 336 033; or e-mail: deposit@ccdc.cam.ac.uk. Supplementary data associated with this article can be found, in the online version, at http://dx.doi.org/10.1016/j.poly.2015.05.033. These data include MOL files and InChiKeys of the most important compounds described in this article.

References

[1] S.L.J. Michel, B.M. Hoffman, S.M. Baum, A.G.M. Barrett, Peripherally functionalized porphyrazines: novel metallomacrocycles with broad, untapped potential, in: K.D.K. Ph.D (Ed.), Prog. Inorg. Chem., John Wiley & Sons Inc, 2001: pp. 473–90.
[2] E.R. Trivedi, B.J. Vesper, H. Weitman, B. Ehrenberg, A.G. Barrett, J.A. Radosevich, et al., Chiral bis-acetal porphyrazines as near-infrared optical agents for detection and treatment of cancer, Photochem. Photobiol. 86 (2010) 410.
[3] T. Goslinski, E. Tykarska, M. Kryjewski, T. Osmalek, S. Sobiak, M. Gdaniec, et al., Potential aluminium (III)-and gallium (III)-selective optical sensors based on porphyrazines, Anal. Sci. 27 (2011) 511.
[4] H. Zong, P. Sun, C.A. Mirkin, A.G.M. Barrett, B.M. Hoffman, Varying the electrochemical potential and thickness of porphyrazine SAMs by molecular design, J. Phys. Chem. B 113 (2009) 14892.
[5] M.S. Rodríguez-Morgade, P.A. Stuzhin, The chemistry of porphyrazines: an overview, J. Porphyr. Phthalocyanines 8 (2004) 1129.
[6] J. Piskorz, E. Tykarska, M. Gdaniec, T. Goslinski, J. Mielcarek, Synthesis, spectroscopic and photophysical properties of novel styryldiazepinoporphyrazine, Inorg. Chem. Commun. 20 (2012) 13.
[7] R.Z. Uslu Kobak, E.S. Öztürk, A. Koca, A. Gül, The synthesis and cyclotetramerisation reactions of aryloxy-, arylalkyloxy-substituted pyrazine-2,3-dicarbonitriles and spectroelectrochemical properties of octakis(hexyloxy)-pyrazinoporphyrazine, Dyes Pigm. 86 (2010) 115.
[8] M.P. Donzello, C. Ercolani, P.A. Stuzhin, Novel families of phthalocyanine-like macrocycles—porphyrazines with annulated strongly electron-withdrawing 1,2,5-thia/selenodiazole rings, Coord. Chem. Rev. 250 (2006) 1530.
[9] J.V. Bakboord, M.J. Cook, E. Hamuryudan, Non-uniformly substituted phthalocyanines and related compounds: alkylated tribenzo-imidazolo[4,5]-porphyrazines, J. Porphyr. Phthalocyanines 04 (2000) 510.
[10] T. Goślíński, E. Tykarska, W. Szczołko, T. Osmałek, A. Śmigielska, S. Walorczyk, et al., Synthesis and characterization of periphery-functionalized porphyrazines containing mixed pyrrolyl and pyridylmethylamino groups, J. Porphyr. Phthalocyanines 13 (2009) 223.
[11] T. Goslinski, A.J.P. White, Synthesis, characterization and spectroscopic properties of novel periphery – functionalized unsymmetrical porphyrazines containing mixed dithienylpyrrolyl and dimethylamino groups, Polyhedron 28 (2009) 2579.
[12] W. Szczolko, L. Sobotta, P. Fita, T. Koczorowski, M. Mikus, M. Gdaniec, et al., Synthesis, characteristics and photochemical studies of novel porphyrazines possessing peripheral 2,5-dimethylpyrrol-1-yl and dimethylamino groups, Tetrahedron Lett. 53 (2012) 2040.
[13] L. Sobotta, P. Fita, W. Szczolko, M. Wrotynski, M. Wierzchowski, T. Goslinski, et al., Functional singlet oxygen generators based on porphyrazines with peripheral 2,5-dimethylpyrrol-1-yl and dimethylamino groups, J. Photochem. Photobiol. A 269 (2013) 9.
[14] T. Koczorowski, W. Szczolko, K. Burda, M. Nowak, M. Dawidowska, A. Teubert, et al., Influence of bulky pyrrolyl substituent on the physicochemical properties of porphyrazines, Dyes Pigm. 112 (2015) 138.
[15] J. Liu, D. Obando, V. Liao, T. Lifa, R. Codd, The many faces of the adamantyl group in drug design, Eur. J. Med. Chem. 46 (2011) 1949.
[16] L. Wanka, K. Iqbal, P.R. Schreiner, The lipophilic bullet hits the targets: medicinal chemistry of adamantane derivatives, Chem. Rev. 113 (2013) 3516.
[17] M.C. García Vior, L.E. Dicelio, J. Awruch, Synthesis and properties of phthalocyanine zinc(II) complexes replaced with oxygen and sulfur linked adamantane moieties, Dyes Pigm. 83 (2009) 375.
[18] M. Kryjewski, M. Nowak, P. Kasprzycki, P. Fita, C. Radzewicz, T. Goslinski, et al., Synthesis and photochemical properties of unsymmetrical phthalocyanine bearing two 1-adamantylsulfanyl groups at adjacent peripheral positions, Inorg. Chem. Commun. 27 (2013) 56.
[19] P.W. Causey, I. Dubovyk, C.C. Leznoff, Syntheses and characterization of phthalonitrile and phthalocyanines substituted with adamantane moieties, Can. J. Chem. 84 (2006) 1380.
[20] V. Novakova, J. Roh, P. Gela, J. Kuneš, P. Zimcik, Azaphthalocyanines with fused triazolo rings: formation of sterically stressed constitutional isomers, Chem. Commun. 48 (2012) 4326.
[21] J. Voskuhl, U. Kauscher, M. Gruener, H. Frisch, B. Wibbeling, C.A. Strassert, et al., A soft supramolecular carrier with enhanced singlet oxygen photosensitizing properties, Soft Matter 9 (2013) 2453.
[22] A.L. Ochoa, T.C. Tempesti, M.B. Spesia, M.E. Milanesio, E.N. Durantini, Synthesis and photodynamic properties of adamantylethoxy Zn(II) phthalocyanine derivatives in different media and in human red blood cells, Eur. J. Med. Chem. 50 (2012) 280.
[23] B.-Y. Zheng, T. Lin, H.-H. Yang, J.-D. Huang, Photodynamic inactivation of *Candida albicans* sensitized by a series of novel axially di-substituted silicon (IV) phthalocyanines, Dyes Pigm. 96 (2013) 547.
[24] D.C. Cole, E.S. Manas, J.R. Stock, J.S. Condon, L.D. Jennings, A. Aulabaugh, et al., Acylguanidines as small-molecule β-secretase inhibitors, J. Med. Chem. 49 (2006) 6158.
[25] R.W. Begland, D.R. Hartter, F.N. Jones, D.J. Sam, W.A. Sheppard, O.W. Webster, et al., Hydrogen cyanide chemistry. VIII. New chemistry of diaminomaleonitrile. Heterocyclic synthesis, J. Org. Chem. 39 (1974) 2341.
[26] L.S. Beall, N.S. Mani, A.J.P. White, D.J. Williams, A.G.M. Barrett, B.M. Hoffman, Porphyrazines and norphthalocyanines bearing nitrogen donor pockets: metal sensor properties, J. Org. Chem. 63 (1998) 5806.
[27] R.P. Linstead, M. Whalley, 944. Conjugated macrocycles. Part XXII. Tetrazaporphin and its metallic derivatives, J. Chem. Soc. (1952) 4839.
[28] T. Goślíński, T. Osmałek, J. Mielcarek, Photochemical and spectral characterization of peripherally modified porphyrazines, Polyhedron 28 (2009) 3839.
[29] I. Seotsanyana-Mokhosi, N. Kuznetsova, T. Nyokong, Photochemical studies of tetra-2, 3-pyridinoporphyrazines, J. Photochem. Photobiol. A 140 (2001) 215.
[30] W. Spiller, H. Kliesch, D. Woehrle, S. Hackbarth, B. Roeder, G. Schnurpfeil, Singlet oxygen quantum yields of different photosensitizers in polar solvents and micellar solutions, J. Porphyr. Phthalocyanines 2 (1998) 145.
[31] A. Ogunsipe, D. Maree, T. Nyokong, Solvent effects on the photochemical and fluorescence properties of zinc phthalocyanine derivatives, J. Mol. Struct. 650 (2003) 131.
[32] S. Tuncer, A. Koca, A. Gul, U. Avciata, 1,4-Dithiaheterocycle-fused porphyrazines: Synthesis, characterization, voltammetric and spectroelectrochemical properties, Dyes Pigm. 81 (2009) 144.
[33] H. Nie, A.G.M. Barrett, B.M. Hoffman, Porphyrazinehexamines and dinitroporphyrazines: synthesis, characterization, and complementary electrochemistry, J. Org. Chem. 64 (1999) 6791.
[34] M.J. Fuchter, L.S. Beall, S.M. Baum, A.G. Montalban, E.G. Sakellariou, N.S. Mani, et al., Synthesis of porphyrazine-octaamine, hexamine and diamine derivatives, Tetrahedron 61 (2005) 6115.
[35] S.J. Lange, H. Nie, C.L. Stern, A.G.M. Barrett, B.M. Hoffman, Peripheral palladium(II) and platinum(II) complexes of bis(dimethylamino)porphyrazine, Inorg. Chem. 37 (1998) 6435.
[36] D.M. Eichhorn, S. Yang, W. Jarrell, T.F. Baumann, L.S. Beall, A.J.P. White, et al., [60]Fullerene and TCNQ donor–acceptor crystals of octakis(dimethylamino) porphyrazine, J. Chem. Soc. Chem. Commun. (1995) 1703.
[37] R. Hou, B. Li, K. Zhong, H. Li, L.-Y. Jin, B. Yin, Tetrakis(tetrathiafulvalene-tetrathiacrown ether)porphyrazine triads: synthesis, photophysical, and electrochemical properties, Eur. J. Org. Chem. 2012 (2012) 1138.
[38] A. Koca, E. Gonca, A. Gül, Voltammetric and spectroelectrochemical characterization of porphyrazines: electrochemical metal sensor, J. Electroanal. Chem. 612 (2008) 231.
[39] T. Dubinina, D. Dyumaeva, S. Trashin, M. Sedova, A. Karpo, V. Krasovskii, et al., Synthesis and study of physicochemical properties of new substituted tetrathieno[2,3-b]porphyrazines, Macroheterocycles 5 (2012) 149.
[40] K. Sakamoto, N. Furuya, H. Soga, S. Yoshino, Cyclic voltammetry of non-peripheral thioaryl substituted phthalocyanines, Dyes Pigm. 96 (2013) 430.
[41] M.N. Yaraşir, A. Koca, M. Kandaz, B. Salih, Voltammetry and spectroelectrochemical behavior of a novel octapropylporphyrazinato lead(II) complex, J. Phys. Chem. C 111 (2007) 16558.
[42] P. Skupin-Mrugalska, J. Piskorz, T. Goślíński, J. Mielcarek, K. Konopka, N. Düzgüneş, Current status of liposomal porphyrinoid photosensitizers, Drug Discov. Today 18 (2013) 776.
[43] M. Wierzchowski, L. Sobotta, P. Skupin-Mrugalska, J. Kruk, W. Jusiak, M. Yee, et al., Phthalocyanines functionalized with 2-methyl-5-nitro-1H-

imidazolylethoxy and 1,4,7-trioxanonyl moieties and the effect of metronidazole substitution on photocytotoxicity, J. Inorg. Biochem. 127 (2013) 62.
[44] N. Düzgüneş, Preparation and quantitation of small unilamellar liposomes and large unilamellar reverse-phase evaporation liposomes, Methods Enzymol. 367 (2003) 23.
[45] Agilent Technologies, CrysAlis PRO software, Agilent Technologies, Yarnton, Oxfordshire, England, 2011.
[46] M.C. Burla, R. Caliandro, M. Camalli, B. Carrozzini, G.L. Cascarano, L. De Caro, et al., SIR2004: an improved tool for crystal structure determination and refinement, J. Appl. Crystallogr. 38 (2005) 381.
[47] G.M. Sheldrick, A short history of SHELX, Acta Crystallogr., Sect. A 64 (2008) 112.