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The synthesis, photochemical and photophysical properties of zinc aryloxy- and alkyloxy azaphthalocyanines

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ABSTRACT

Octasubstituted zinc tetrapyrazinoporphyrazines bearing butyloxy, octyloxy, 2,6-diisopropylphenoxy and 4-(hydroxymethyl)phenoxy substituents were synthesized from the corresponding 5,6-disubstituted pyrazine-2,3-dicarbonitriles using $Zn(quinoline)_2Cl_2$ in yields varying from 14 to 44%. The reaction procedure proved to be efficient for the synthesis of both alkyloxy- and aryloxy- substituted zinc tetrapyrazinoporphyrazines and did not require strictly anhydrous conditions. Optimal cyclotetramerization conditions were identified for each derivative, in terms of reaction temperature, as overheating cleaved the ether bond leaving a vacant OH group on the macrocycle. The photochemical and photophysical properties of the synthesized compounds were investigated in pyridine. Singlet oxygen quantum yields (Φ_Δ) ranged from 0.49 to 0.61 and high fluorescence quantum yields (Φ_F) of ~0.30 were observed for non-aggregated compounds.

1. Introduction

Phthalocyanines (Pc) belong to a thoroughly investigated class of dye that enjoys widespread use in a variety of applications [1,2]. Azaphthalocyanines (AzaPc) are aza-analogs of Pc in which some of the carbon atoms in the Pc macrocycle are replaced by nitrogens. Tetrapyrazinoporphyrazines (TPyPz) belonging to the AzaPc subgroup have attracted attention of researchers owing to their promising photosensitizing [3], fluorescent [4], non-linear optical [5] and oxidative [6] properties. The photochemical and photophysical properties of TPyPz are known to be altered significantly by different peripheral substitutions. Whilst the singlet oxygen and fluorescence quantum yields have been investigated for alkylsulfanyl [7], alkylamino [8], aryl [9] or heteroaryl [10] substituted derivatives, this has not been the case for TPyPz with an oxygen linkage between the macrocycle and peripheral substituents. Despite the extensive investigation of aryloxy substituted Pc [11–19], studies of aryloxy as well as alkyloxy TPyPz are rare because of the lack of suitable synthetic procedures. Whilst the synthesis of aryloxy TPyPz was resolved by two research groups only recently [20,21] and the aggregation, crystal structure and UV–vis spectra of the compounds studied in detail [22–24], the photochemical and photophysical properties of the compounds has not attracted attention.

This paper concerns the synthesis of alkyloxy- and aryloxy-substituted zinc TPyPz (ZnTPyPz) and their singlet oxygen production and fluorescence. The peripheral substituents in the investigated compounds were chosen to cover both alkyloxy- and aryloxy- derivatives with the intention of presenting a synthetic procedure that is suitable for both types of substitution.

2. Experimental

All organic solvents were of analytical grade. Anhydrous octanol was stored over magnesium and distilled prior to use. TLC was performed on Merck aluminium sheets coated with silica gel 60 F254. Merck Kieselgel 60 (0.040–0.063 mm) was used for column chromatography. Infrared spectra were measured on an IR-Spectrometer Nicolet Impact 400 (in KBr pellets) or Nicolet 6700 (in ATR mode). ^1H and ^{13}C NMR spectra were recorded on a Varian Mercury – Vx BB 300 (299.95 MHz – ^1H and 75.43 MHz – ^{13}C); reported chemical shifts are relative to Me_4Si. Elemental analysis was carried out using an Automatic Microanalyser EA1110CE (Fisons Instruments S.p.A., Milano, Italy). UV–vis spectra were recorded on a UV-2401PC spectrophotometer (Shimadzu Europa, GmbH, Duisburg, Germany). Fluorescence spectra were obtained using an AMINCO-Bowman Series 2 luminescence spectrometer (SLM-Aminco, Urbana, IL, USA).

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The MALDI-TOF mass spectra were collected on a Voyager-DE STR mass spectrometer (Applied Biosystems, Framingham, MA, USA) calibrated externally with a five-point calibration procedure using Peptide Calibration Mix1 (LaserBio Labs, Sophia-Antipolis, France). A solution of TPyPz in DCM (approximate concentration 1×10^{-5} mol L^{-1}, 1.5×10^{-3} mL) was mixed with *trans*-2-[3-(4-*tert*-butylphenyl)-2-methyl-2-propenylidene]-malononitrile matrix in DCM (0.01 mL, 1 mg/0.5 mL) and spotted on the plate.

2.1. Synthesis

5,6-Dichloropyrazine-2,3-dicarbonitrile (**1**) [25], 5,6-bis(butoxy) pyrazine-2,3-dicarbonitrile (**2**) [26] and Zn(quinoline)$_2$Cl$_2$ (ZnQ_2Cl_2) [27] were prepared according to published procedures.

2.1.1. 5,6-Bis(octyloxy)pyrazine-2,3-dicarbonitrile (**3**)

A solution of triethylamine (895 mg, 8.84 mmol) in anhydrous octanol (6 mL) was stirred for 45 min at room temperature and added dropwise to a suspension of **1** (800 mg, 4 mmol) in anhydrous octanol (25 mL). The suspension dissolved after approximately 15 min and stirring was continued for 60 min at room temperature. Octanol was then removed under reduced pressure and the crude product was purified by column chromatography on silica using toluene/hexane 2:1 as eluent, to provide a yellow oil (785 mg, 51%). ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): $\delta = 0.89$ (t, 6 H, $J = 6.6$ Hz, CH_3), 1.25–1.45 (m, 20 H, CH_2), 1.83 (p, 4 H, $J = 7.0$ Hz, OCH_2CH_2) and 4.45 (t, 4 H, $J = 6.7$ Hz, OCH_2) ppm. ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): δ = 14.06, 22.61, 25.72, 28.16, 29.11 (4 carbons according to rough integration), 31.72, 69.49, 113.49, 122.57 and 151.95 ppm. IR (ATR): ν_{max} = 2953, 2924, 2855, 2236 (CN), 1549, 1495, 1458, 1379, 1344, 1299, 1239, 948 cm^{-1}.

2.1.2. 5,6-Bis(2,6-diisopropylphenoxy)pyrazine-2,3-dicarbonitrile (**4**)

2,6-Diisopropylphenol (446 mg, 2.5 mmol) was stirred for 15 min in an aqueous solution of sodium hydroxide ($c = 1$ mol dm^{-3}, 2.4 mL, 2.4 mmol,). Compound **1** (200 mg, 1 mmol) in THF (15 mL) was added dropwise and the mixture stirred for 30 min at room temperature. The crude product was concentrated to dryness and the brownish-yellow solid washed thoroughly with water (200 mL) and purified using column chromatography on silica with toluene/hexane 1:1, providing a white solid (404 mg, 83%, mp 208.5–209.5 °C (methanol), lit. [22] 253 °C (*n*-hexane)). ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): $\delta = 7.39$–7.24 (m, 6H, aromH), 2.82 (sept, 4 H, $J = 7$ Hz, CH), 1.23 ppm (d, 24H, $J = 7$ Hz, CH_3). ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): $\delta = 23.2$, 28.0, 112.6, 124.2, 124.6, 127.6, 139.8, 146.3, 151.1 ppm. IR (KBr): ν_{max} = 3068, 3032, 2967, 2930, 2871, 2360, 2344, 2237, 1545, 1460, 1441, 1403, 1385, 1357, 1331, 1258, 1233, 1142, 1112, 1089, 1062, 937, 849, 793 and 750 cm^{-1}. Elemental analysis calc. (%) for $C_{30}H_{34}N_4O_2$: C, 74.66, H, 7.10, N, 11.61; found: C, 74.40; H, 7.31; N, 11.99.

2.1.3. 5,6-Bis(4-(hydroxymethyl)phenoxy)pyrazine-2,3-dicarbonitrile (**5**)

Compound **1** (400 mg, 2 mmol) was dissolved in THF (10 mL) and then 4-(hydroxymethyl)phenol (1.24 g, 10.0 mmol) and pyridine (695 mg, 8.8 mmol) were added. After 24 h of stirring at room temperature the solvent was evaporated and the resulting yellow oil was dissolved in chloroform (150 mL) and extracted three times with brine (3 × 100 mL). The organic layer was dried over anhydrous Na_2SO_4. The crude product was purified by column chromatography on silica with ethylacetate/hexane 5:2 and recrystallized from EtOH/H_2O, yielding a white solid (486 mg, 65%, m.p. 150.1–152.5 °C). ^{1}H NMR (300 MHz, $(CD_3)_2CO$, 25 °C): $\delta = 4.33$ (t, 2 H, $J = 5.8$ Hz, OH), 4.69 (d, 4H, $J = 5.8$ Hz, CH_2) 7.31 ppm (d, 4H, $J = 8.6$ Hz, aromH). ^{13}C NMR (75 MHz, $(CD_3)_2CO$, 25 °C): $\delta = 64.0$, 114.3, 121.9, 124.5, 128.9, 142.1, 151.4, 153.3 ppm. IR (ATR): ν_{max} = 3303, 2936, 2873, 2233 (CN), 1729, 1701, 1598, 1544, 1501, 1441, 1400, 1374, 1350, 1237, 1194, 1153, 1105, 1039, 1011, 941, 924, 858, 847 and 809 cm^{-1}. Elemental analysis calc. (%) for $C_{20}H_{14}N_4O_4$: C, 64.17; H, 3.77; N, 14.97; found: C, 62.45; H, 4.25; N, 14.37.

2.1.4. Alternative preparation of 5,6-bis(4-(hydroxymethyl) phenoxy)pyrazine-2,3-dicarbonitrile (**5**)

NaOH (100 mg, 2.5 mmol) was dissolved in water (20 mL) and 4-(hydroxymethyl)phenol (311 mg, 2.5 mmol) was added. The suspension was sonicated and stirred for 20 min at room temperature and ethanol (10 mL) was added to expedite solubilisation. Thereafter, compound **1** (200 mg, 1.0 mmol) in tetrahydrofuran (10 mL) was added dropwise and the ensuing solution was stirred for 10 min at room temperature. Ethanol and tetrahydrofuran were evaporated and the mixture was diluted with water (70 mL) and extracted three times with ethylacetate (3 × 100 mL). The organic layer was dried over anhydrous Na_2SO_4, filtered and evaporated under reduced pressure to dryness. The mixture was purified by column chromatography on silica with chloroform/acetone 10:1. The two important fractions were isolated, one corresponding to **5** ($R_f = 0.15$, white solid, 86 mg, 23%) and the second was 5,6-bis (ethoxy)pyrazine-2,3-dicarbonitrile ($R_f = 0.79$, a pale yellow solid, 89 mg, 41%; m.p. 112.2–113.0 °C, lit.[28] 117–118 °C). ^{1}H NMR (300 MHz, $(CD_3)_2CO$, 25 °C): $\delta = 1.43$ (t, 6 H, $J = 7.1$ Hz, CH_3), 4.54 ppm (q, 4 H, $J = 7.1$ Hz, OCH_2). ^{13}C NMR (75 MHz, $(CD_3)_2CO$, 25 °C): $\delta = 14.15$, 65.82, 114.81, 123.34 and 153.16 ppm.

2.1.5. 2,3,9,10,16,17,23,24-Octakis(butoxy)-1,4,8,11,15,18,22,25-(octaaza)phthalocyanine zinc (II) (**6**)

Precursor **2** (80 mg, 0.29 mmol) and ZnQ_2Cl_2 (115 mg, 0.29 mmol) were mixed in a round bottom flask and heated at 190 °C for 60 min. The crude product was dissolved in chloroform (100 mL), filtered and the solvent removed under reduced pressure. The solid was then washed with water/methanol 1:1 (300 mL), adsorbed on silica and thoroughly washed with methanol (300 mL) on a glass frit. Afterwards, the product was purified by column chromatography on silica using chloroform as eluent to give a blue solid (12 mg, 14%). NMR, IR, UV–vis spectra showed the same characteristics as described in the literature for this compound prepared using different approach [26]. MS (MALDI-TOF) *m*/*z* 1160 $[M]^+$, 1183 $[M + Na]^+$, 1199 $[M + K]^+$, 2321 $[2M]^+$, 2344 $[2M + Na]^+$, 2360 $[2M + K]^+$.

2.1.6. 2,3,9,10,16,17,23,24-Octakis(octyloxy)-1,4,8,11,15,18,22,25-(octaaza)phthalocyanine zinc (II) (**7**)

ZnQ_2Cl_2 (153 mg, 0.39 mmol) was transferred to a round bottom flask, **3** (150 mg, 0.39 mmol) was added and the mixture heated at 190 °C for 60 min. The crude product was dissolved in chloroform (100 mL), filtered and the solvent removed under reduced pressure. The solid was then washed with water/methanol 1:1 (300 mL), adsorbed on silica and thoroughly washed with methanol (300 mL) on a glass frit. The product was purified using column chromatography on silica with chloroform as eluent. The pure product was dissolved in chloroform (1 mL), added dropwise to methanol (50 mL) and the precipitate collected, giving a blue-green solid (31 mg, 20%). ^{1}H NMR (300 MHz, $CDCl_3/C_5D_5N$, 25 °C): $\delta = 0.50$–0.58 (m, 24 H, CH_3), 0.68–1.21 (m, 64 H, CH_2), 1.22–1.45 (m, 16H, CH_2), 1.59–1.91 (m, 16H, CH_2), 4.28–4.85 ppm (m, 16 H, OCH_2). ^{13}C NMR (75 MHz, $CDCl_3/C_5D_5N$, 25 °C): δ = 13.20, 21.79, 25.53, 28.21, 28.54, 28.80, 31.03, 67.49, 139.48, 147.31 and 151.45 ppm. IR (ATR): ν_{max} = 2954, 2921, 2853, 1638, 1541, 1444, 1377, 1303, 1252, 1121, 1062, 960 cm^{-1}. UV/Vis (pyridine): λ_{max} (ε) = 624 (199 700), 599 sh (31 500), 568 (28 400), 369 nm (134 300 dm^3 mol^{-1} cm^{-1}). MS (MALDI-TOF): *m*/*z* 1609 $[M]^+$,

1632 $[M + Na]^+$, 1648 $[M + K]^+$. Elemental analysis calc. (%) for $C_{88}H_{136}N_{16}O_8Zn+4H_2O$: C, 62.78; H, 8.62; N, 13.31; found: C, 62.80; H, 8.90; N, 13.21.

A side product with lower R_f was isolated from column chromatography. MS (MALDI-TOF): *m/z* 1497 $[M - C_8H_{16}]^+$, 1520 $[M - C_8H_{16} + Na]^+$, 1539 $[M - C_8H_{16} + K]^+$, 1385 $[M - 2 \times C_8H_{16}]^+$.

2.1.7. 2,3,9,10,16,17,23,24-Octakis(2,6-diisopropylphenoxy)-1,4,8,11,15,18,22,25-(octaaza)phthalocyanine zinc (II) (**8**)

ZnQ_2Cl_2 (246 mg, 0.6 mmol) and **4** (300 mg, 0.6 mmol) were thoroughly mixed and heated at 260 °C employing a condenser for 90 min. The product was washed thoroughly with methanol/water 1:1 (400 mL) and purified using column chromatography on silica with toluene/chloroform/THF/pyridine 15:15:1:1 as eluent, giving a green solid (85 mg, 27%), m.p. over 400 °C (slow decomp. from 340 °C). ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): $\delta = 7.58$ (t, 8H, $J = 7$ Hz, aromH), 7.45 (d, 16H, $J = 8$ Hz, aromH), 3.32 (sept, 16H, $J = 7$ Hz, CH), 1.30 ppm (d, 96H, $J = 7$ Hz, CH_3). ^{13}C NMR (75 MHz; $CDCl_3$, 25 °C): $\delta = 23.5$, 28.1, 124.4, 126.6, 141.0, 142.4, 147.9, 149.7 and 151.5 ppm. IR (KBr): $\nu_{max} = 3065$, 1965, 2931, 2870, 1541, 1401, 1294, 1249, 1213, 1161, 1145, 1094, 1059 and 929 cm^{-1}. UV/Vis (pyridine): λ_{max} (ε) = 628 (200 200), 571 (27 700), 372 nm (117 600 dm^3 mol^{-1} cm^{-1}). MS (MALDI-TOF): *m/z* 1994 $[M + H]^+$. Elemental analysis calc. (%) for $C_{120}H_{136}N_{16}O_8Zn+5H_2O$: C, 68.50; H, 7.09; N, 10.65; found: C, 68.55; H, 6.13; N, 10.78.

2.1.8. 2,3,9,10,16,17,23,24-Octakis(4-(hydroxymethyl)phenoxy)-1,4,8,11,15,18,22,25-(octaaza)phthalocyanine zinc (II) (**9**)

ZnQ_2Cl_2 (74 mg, 0.18 mmol) and **5** (70 mg, 0.18 mmol) were mixed, transferred to a round bottom flask and heated at 180 °C for 5 min. The crude product was washed thoroughly with methanol/water 1:1 (200 mL) and then with common organic solvents (THF, chloroform, toluene and acetone) (usually 150 mL). The product was dissolved in pyridine (1 mL) and dropped in to chloroform (30 mL). The ensuing precipitate was collected, yielding a blue solid (35 mg, 44%). Solubility of **9** was not sufficient for NMR analysis. IR (ATR): $\nu_{max} = 3335$, 2931, 2864, 1735, 1670, 1655, 1648, 1604, 1578, 1570, 1541, 1528, 1500, 1388, 1382, 1218, 1158, 1106, 1055, 1013, 924, 817 and 745 cm^{-1}. UV/Vis (pyridine): λ_{max} (ε) = 633 (49 100), 579 (12 600), 372 nm (50 000 dm^3 mol^{-1} cm^{-1}). Elemental analysis calc. (%) for $C_{80}H_{56}N_{16}O_{16}Zn + 2H_2O$: C, 60.10; H, 3.78; N, 14.02; found: C, 59.64; H, 3.61; N, 14.43.

2.2. Evaluation of the thermal cyclotetramerization reaction of **4** with ZnQ_2Cl_2

Compound **4** (48 mg, 0.1 mmol) and ZnQ_2Cl_2 (41 mg, 0.1 mmol) were mixed together, transferred to a round bottom flask and heated at different temperatures for various durations. Afterwards the product was washed with methanol/water 1:1 (100 mL), dried and dissolved in chloroform (5.0 mL). The ensuing solution was diluted 500 times and absorption spectrum was measured. Progress of the reaction was monitored at 627 nm (maximum of the Q-band of **8**).

2.3. Singlet oxygen and fluorescence measurements

Singlet oxygen quantum yields were determined according to previously published procedure using decomposition of a chemical trap of singlet oxygen 1,3-diphenylisobenzofuran (DPBF)[29]. Absorption of the dyes in the Q-band region during measurements was ca. 0.1. Zinc phthalocyanine (ZnPc) was used as the reference ($\Phi_\Delta = 0.61$ in pyridine [30]). Fluorescence quantum yields were determined also by comparative method using ZnPc as reference ($\Phi_F = 0.20$ in pyridine [30]). Absorption of the dyes in the Q-band area was approximately 0.05, excitation wavelength 368 nm (for **6**, **7** and **9**) and at 375 nm (for **8**). The ZnPc standard was excited at both wavelengths and corresponding areas under the curve were used for calculations. Excitation spectra were collected by observing emission at 680 nm (**6** and **7**), 690 nm (**8**) or 700 nm (**9**). All measurements were performed three times and the presented data represent mean of these three experiments.

3. Results and discussion

3.1. Synthesis of substituted pyrazine-2,3-dicarbonitriles

The TPyPz macrocycle is built up by cyclotetramerization of appropriately substituted pyrazine-2,3-dicarbonitriles. Alkyloxy- and aryloxy- substituted pyrazine-2,3-dicarbonitriles are easily accessible by nucleophilic substitutions of 5,6-dichloropyrazine-2,3-dicarbonitrile (**1**)[28,31]. Thus, **3** was synthesized in 51% yield from **1** in anhydrous octanol with triethylamine as acceptor of released HCl (Fig. 1). A similar synthesis of **2** was reported to have a yield of 49% [26].

Strictly anhydrous conditions for the preparation of the aryloxy derivatives [20] seem to be unnecessary as the phenolate anion can be produced even in aqueous solution. The published procedure (anhydrous THF, K_2CO_3, reflux, 24 h) was repeated and compound **4** was synthesized with the yield of 60%. However, the reaction gave higher yields (83%) when aqueous NaOH (THF, rt, 5 min) was used to produce phenolate anion. Moreover, it proceeded immediately after mixing the reactants. Changing solvent to DMF (aqueous NaOH, rt, 5 min) led to lower yields (41%) and side products were detected on TLC examination of the mixture.

The above-mentioned procedure (aqueous NaOH, THF) also gave a reasonable yield (48%) for compound **5** bearing both aromatic and aliphatic hydroxyls. Lower yields compared to **4** can be most likely ascribed to side reaction involving attack of **1** by aliphatic hydroxyl as the nucleophile. Similar competition between aliphatic hydroxyl and phenolate anion was observed when ethanol was added into the reaction in order to support solubilization of 4-(hydroxymethyl) phenol. In this case, yield of **5** decreased to 23% and 5,6-bis(ethoxy) pyrazine-2,3-dicarbonitrile was isolated from the reaction as the main product (41%). As a consequence of the aforementioned nucleophilic substitution process we changed the reaction conditions and optimized the yield of **5** using pyridine as the base to 65%. Although the reaction proceeded much slower (24 h), amounts of side products substantially decreased.

3.2. Cyclotetramerization

As previously mentioned the synthesis of alkyloxy- and aryloxy-substituted TPyPz is not an easy task. Carbons at positions 5 and 6 of the pyrazine ring are strongly electron deficient. As a result they are usually attacked by alkoxides used as initiators of cyclotetramerization reaction leading to transetherification [28,32]. This undesirable feature precludes using the common Linstead cyclotetramerization method. Even hindering the reactive centre by bulky aryloxy substituents did not lead to the successful preparation of the target TPyPz [20]. The problem of transetherification can be easily solved for simple aliphatic alkyloxy TPyPz by matching the metal alkoxide initiator with the appropriate alkyloxy side chain of the final product. However, this cannot be used for aryloxy derivatives or TPyPz bearing more complicated alkyloxy substituents.

Recently, Makhseed et al. have developed a method for the cyclisation of various aryloxy TPyPz by heating the corresponding pyrazine-2,3-dicarbonitriles in quinoline [20,23]. This seemed to be an effective method for the synthesis of aryloxy TPyPz derivatives.

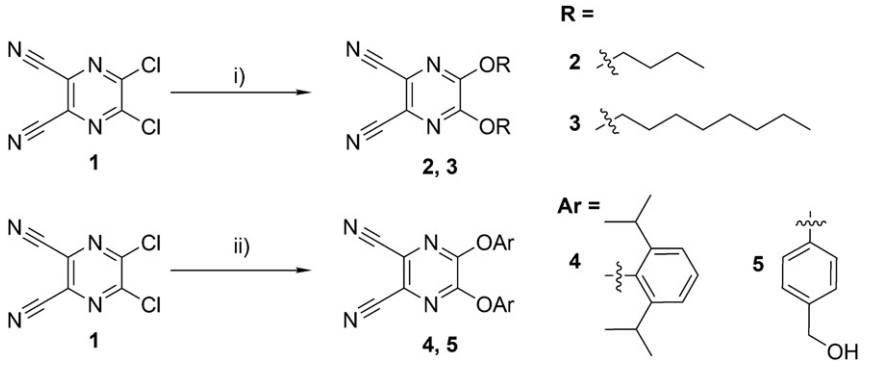

Fig. 1. Synthesis of pyrazine-2,3-dicarbonitriles **2**–**5**. i) TEA, anhydrous R-OH, 75 min, rt (**3**) or 3 h, reflux (**2**), ii) ArOH, aq. NaOH, THF, rt, 5 min (**4**) or pyridine, THF, rt, 24 h (**5**).

Nonetheless, we were not able to repeat their procedure in the beginning. Heating of **4** in freshly distilled quinoline by itself or with anhydrous zinc acetate did not lead to any cyclotetramerization. No absorption in the expected Q-band region in the UV–vis spectrum was detected even after 8 h of heating. A similar failure was also recently described by other authors [32]. Later, the synthesis of **8** was successfully performed by the described procedure [20] in another attempt when the conditions were kept strictly anhydrous and starting materials were carefully dried. The use of alternative solvents for the synthesis was also explored. No formation of **8** was detected in dichlorobenzene. A blue-green product with absorption at expected 628 nm appeared when DMF or pyridine were used as solvent. However, the reaction time was quite long (24–30 h) and a number of side products were detected on TLC examination. In all of the above cases, anhydrous zinc acetate has been added into the reaction in order to obtain zinc complexes and to facilitate cyclotetramerization by using the template effect.

The best results from the alternative methods were obtained employing the route developed by Mørkved et al. with the new efficient cyclisation agent ZnQ_2Cl_2 [21,27]. In this case, compound **4** was heated in a melt with ZnQ_2Cl_2. Different reaction times and temperatures were used and the progress of the reaction was monitored using absorbance of the product **8** in its Q-band region (Fig. 2). The reaction was relatively slow at 220 °C and therefore the temperature was increased to 260 °C or 350 °C. Heating at the latter temperature led to the appearance of significant amounts of side products as detected on TLC examination. Most likely the thermal stability of the whole macrocycle or the peripheral chains (see also below) was exceeded at this high temperature. The decomposition from approx. 340 °C was also observed during melting point determination. This is in accordance with data from thermogravimetric analysis published recently for similar compounds [24]. In that work, extensive decomposition occurred between 350 and 420 °C. That is why a reaction temperature of 260 °C may be considered as optimal for **8**. Similar analyses of reaction conditions were performed also for the other three TPyPz **6**, **7** and **9** (Fig. 3). Care was taken particularly on determination of the optimal reaction temperature. Low temperatures did not allow cyclotetramerization, while decomposition occurred at temperatures above the optimal range. Yields of all the zinc complexes were in the range 14–44%. When compared to the method of Makhseed et al.[20], the yields of the ZnQ_2Cl_2 method were lower but the reaction did not require strictly anhydrous conditions and the reaction times were significantly shorter.

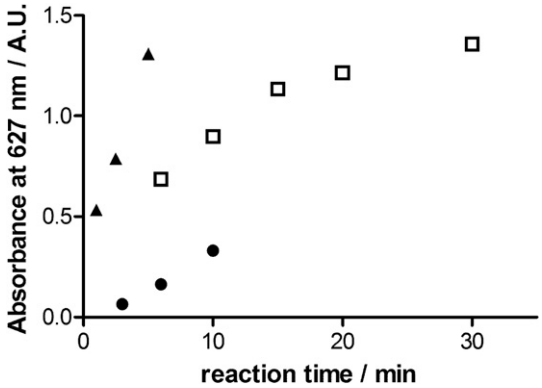

Fig. 2. Progress of cyclotetramerization of **4** in a melt with ZnQ_2Cl_2 observed as increasing absorption of **8** at 627 nm (●) 220 °C, (□) 260 °C, (▲) 350 °C.

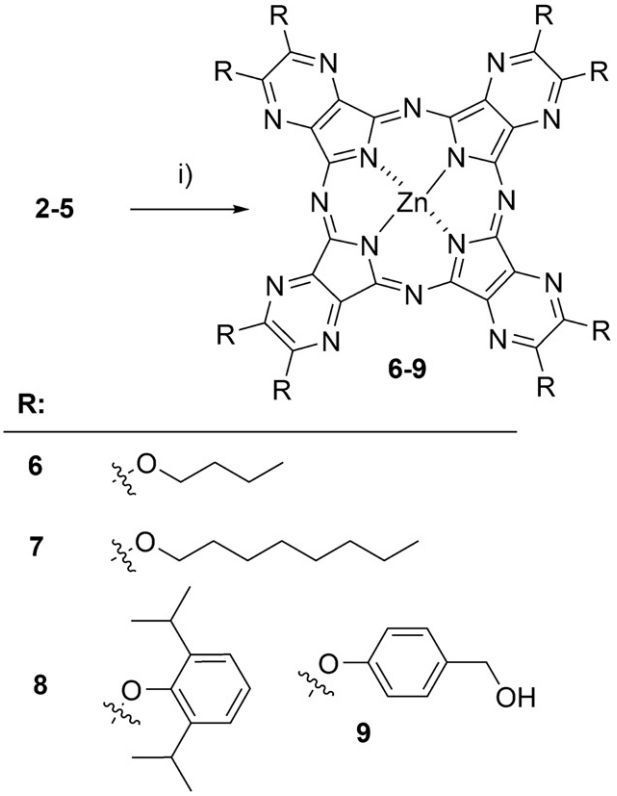

Fig. 3. Synthesis of TPyPz **6**–**9**. i) ZnQ_2Cl_2, 190 °C, 60 min (**6**, **7**), 260 °C, 90 min (**8**), 180 °C, 5 min (**9**).

An effort has also been made to reveal the nature of the decomposition. In the case of **7**, the main side product (lower R_f) was isolated by column chromatography and analyzed by MALDI-TOF mass spectrometry. The mass spectrum of the isolated fraction contained mainly a cluster at m/z 1496.8 and a small cluster at m/z 1384.7 corresponding to stepwise loss of peripheral C_8H_{16} ($\Delta m/z$ 112). Compound **7** had a cluster at m/z 1609.0 $[M]^+$ and it was not detected in this side product. Subsequently, a sample of the side product was reacted with acetylchloride in anhydrous THF in the presence of triethylamine. More components with a higher R_f were detected on TLC suggestive of esterification of the free hydroxyl groups. An assumption from this experiment can be made, that higher temperature of the cyclotetramerization reaction induced thermal cleavage of the ether bond leaving a free OH group on the macrocycle. Therefore, cyclotetramerization in a melt with ZnQ_2Cl_2 can be considered as the effective approach to zinc TPyPz bearing substituents connected through oxygen linkage but care must be taken to establish optimal reaction temperature.

3.3. UV–vis absorption

Compounds **6**–**9** showed a shape of absorption spectra typical for TPyPz and other porphyrazines. A low energy Q-band was found at approx. 630 nm and a high energy B-band was found at 370 nm (see Fig. 4, Table 1). Compounds **6**–**8** were fully monomeric in pyridine, but the broader Q-band of **9** indicated partially aggregated form.

The position of the Q-band is given mostly by the size of the π-conjugated system of macrocyclic core. The connecting heteroatom and the electronic character of the peripheral substituent play a less important but still evident role. Aryloxy- and alkyloxy-substituted Pc usually show small bathochromic shift of the Q-band in the range of 5–10 nm when compared with the unsubstituted derivatives [33]. Contrary to Pc, an oxygen linkage at ZnTPyPz caused hypsochromic shift when compared to the unsubstituted macrocycle (unsubstituted ZnTPyPz absorbs at 636 nm in pyridine [10]). Q-band maxima of **6** and **7** were found at 624 nm in pyridine. On the other hand, the aryls of **8** and **9** extended the conjugated system and red-shifted the absorption spectra when compared to alkyloxy derivatives (628 nm for **8**, 633 nm for **9**). These observations are in accordance with data published recently by Mørkved et al. for pyridin-3-yloxy substituted ZnTPyPz (630 nm in pyridine). [21] The smaller bathochromic shift of **8** can be attributed to a lower degree of the aryl conjugation with the macrocyclic system. The reason is that the bulky isopropyl groups in *ortho* positions on the phenoxy substituent cause rotation of the whole 2,6-diisopropylphenoxy group out of the plane of TPyPz π macrocycle. This fact has been recently confirmed by crystal structure analysis [34].

Table 1
Spectra, photophysical and photochemical properties of studied TPyPz in pyridine.

Compound	Absorbance λ_{max} (nm)/ε ($\times 10^{-5}$ dm^3 mol^{-1} cm^{-1})	Fluorescence λ_{max} (nm)	Φ_Δ	Φ_F
6	624/1.89	631	0.54	0.31
7	624/2.00	631	0.49	0.30
8	628/2.00	637	0.61	0.29
9	633/0.49	639	0.18[a]	0.043[a]

[a] Aggregation.

3.4. Fluorescence and singlet oxygen quantum yields

The singlet oxygen production of **6**–**9** was evaluated quantitatively by determination of singlet oxygen quantum yields (Φ_Δ) in pyridine (Table 1). The decomposition of a chemical trap – 1,3-diphenylisobenzofuran (DPBF) – was used for the measurements. No changes in the absorption spectra were observed during measurements suggesting that photodegradation did not occur. Compounds **6**–**8** showed reasonably high Φ_Δ values in the range 0.49–0.61 suggesting that oxygen substituted ZnTPyPz may find their place in applications based on singlet oxygen production, e.g. as photosensitizers in photodynamic therapy (PDT). The very low Φ_Δ of **9** was most likely caused by aggregation as detected in UV–vis absorption spectra. Aggregated TPyPz usually fail in efficient photosensitization because absorbed energy is released mostly through the heat.

Determined fluorescence quantum yields (Φ_F) followed the observations made for singlet oxygen. High Φ_F values approx. 0.30 were observed for non-aggregated **6**–**8** and several times lower Φ_F was obtained for **9**. High Φ_F values are advantageous in PDT application as well because fluorescence allows simple detection of photosensitizer accumulation in targeted tissue.

Fluorescence emission spectra of **6**–**8** had shape typical for TPyPz and other porphyrazines with only small Stokes shift of approx. 6 nm (Fig. 5, Table 1). Emission maximum of **8** and **9** was red-shifted when compared with **6** and **7** due to conjugation of the aryls with macrocyclic system. The fact that excitation spectra of **6**–**8** superimposed their absorption spectra (Fig. 6a) confirmed exclusive presence of the monomeric form during measurements of fluorescence as well as singlet oxygen generation. On the other hand, the above-mentioned aggregation of **9** was further confirmed by different absorption and excitation spectra (Fig. 6b). Aggregates usually do not fluoresce with the few exceptions of J-dimers [8] and that is why excitation spectrum corresponds to monomeric form only.

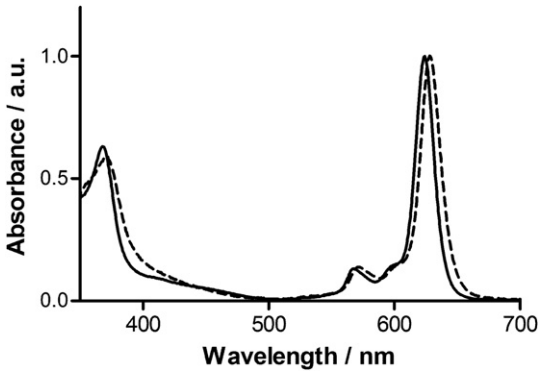

Fig. 4. Normalized absorption spectra of **6** (full line) and **8** (dashed line) in pyridine.

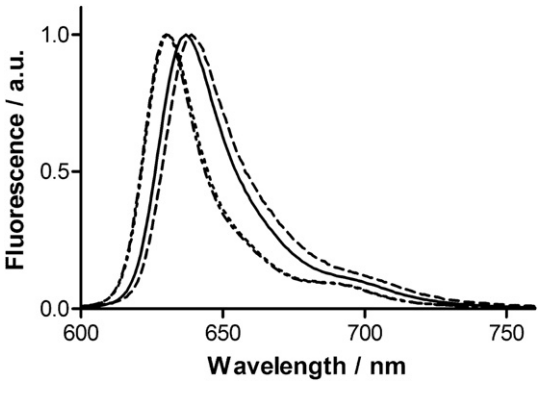

Fig. 5. Normalized emission spectra of **6** (dotted), **7** (dashed-dotted, overlaps with **6**), **8** (full) and **9** (dashed) in pyridine.

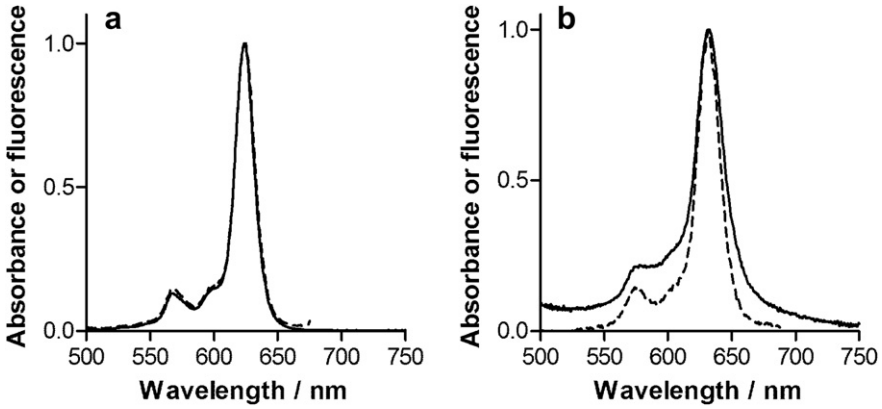

Fig. 6. Normalized absorption (full lines) and excitation (dashed lines) spectra of **6** (a) and **9** (b) in pyridine. Note significant broadening of absorption spectrum of **9** indicating aggregation.

4. Conclusion

The cyclotetramerization of pyrazine-2,3-dicarbonitriles in a melt with $Zn(quinoline)_2Cl_2$ reagent can be used as a suitable method for preparation of aryloxy as well as alkyloxy substituted ZnTPyPz. The procedure does not require strictly anhydrous conditions. The photophysical and photochemical data were obtained and suggested that both aryloxy and alkyloxy ZnTPyPz may be used as photoactive compounds in applications connected with singlet oxygen production. One drawback is the relatively low wavelength of absorption. On the other hand, strong fluorescence in wavelengths optimally suited for human eyes may indicate high potential in photodetection. No significant differences in Φ_F or Φ_Δ values between aryloxy and alkyloxy ZnTPyPz were observed. In absorption spectra, conjugation of the peripheral aryloxy substituents with the macrocyclic system induced small red shift (4–9 nm) compared to the alkyloxy derivatives.

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