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Synthesis, Separation and UV/Vis Spectroscopy of Pyrazino-quinoxalino-porphyrazine Macrocycles

Zbynek Musil,[a] Petr Zimcik,*[a] Miroslav Miletin,[a] Kamil Kopecky,[a] and Juraj Lenco[b]

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Unsymmetrical metal-free and zinc complexes of pyrazino-quinoxalino-porphyrazines (PQP) bearing eight diethylamino groups have been synthesized by statistical tetramerization of 2,3-bis(diethylamino)quinoxaline-6,7-dicarbonitrile and 5,6-bis(diethylamino)pyrazine-2,3-dicarbonitrile in lithium butanolate. For this purpose, a new heteroatom-substituted quinoxaline precursor, 2,3-dichloro-6,7-dicarbonitrile, was prepared and characterized. It is a flexible starting material for new building blocks of quinoxaline-6,7-dicarbonitrile derivatives. All the PQPs (including adjacent and opposite isomers) from the statistical mixture were detected and separated by column chromatography on silica and characterized by MALDI-TOF mass spectrometry, IR, UV/Vis and NMR spectroscopy. The effect of the insertion of benzene rings into the tetrapyrazinoporphyrazine (TPP) system is discussed. Each benzene ring insertion into the TPP system causes a bathochromic shift of 22 nm; the dependence is linear. The final tetra[6,7]quinoxalinoporphyrazines were red-shifted to 744 and 763 nm for the zinc and metal-free derivative, respectively. Splitting of the Q-band was observed for PQPs with lower symmetry.

Introduction

Phthalocyanine (Pc) derivatives and their analogues are a group of compounds that have very stable physical and chemical properties; they absorb strongly in different regions of the electromagnetic spectrum.[1] Symmetrically tetra- and octasubstituted Pc have been intensely investigated with respect to their physical properties and they are used in different areas, such as chemical sensors,[2] liquid crystals,[3] photodynamic therapy (PDT)[4–6] and laser dyes.[7] In some of these applications, absorption at longer wavelengths is very advantageous, for example, in PDT it enables the depth of the therapeutic intervention to be increased. An increase of λ_{max} of Pc can be achieved by peripheral substitution with suitable substituents, the electrons of which will contribute to the conjugation of the π-conjugated system.[8,9] Protonation, unsymmetrical substitution or metal complexation are also known to lead to some bathochromic shift. However, the largest bathochromic shift of the Q-band is usually achievable by linear annelation of the aromatic rings.[10,11] Naphthalocyanines (Nc) are well-known organic dyes and pigments characterized by a significant 80–100 nm red shift of absorption compared with the corresponding Pc.[12,13]

In our previous work we have focused on the investigation of tetrapyrazinoporphyrazines (TPP), aza-analogues of Pc[4,5,8,14] (Figure 1). Their advantage is the relatively simple preparation of synthetic precursors (substituted pyrazine-2,3-dicarbonitriles) and a wide range of available peripheral substitutions not always achievable with Pc. On the other hand, these derivatives suffer from a hypsochromic shift of

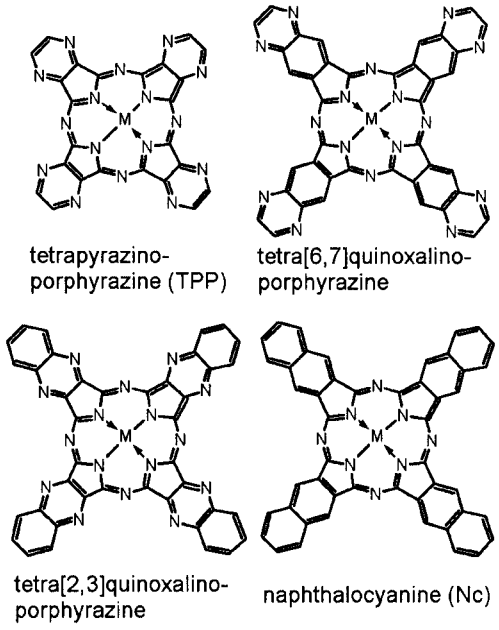


Figure 1. General structures of macrocycles discussed in this work.

[a] Department of Pharmaceutical Chemistry and Drug Control, Faculty of Pharmacy, Charles University,
Heyrovskeho 1203, Hradec Kralove 50005, Czech Republic
Fax: +420-49-5067167
E-Mail: petr.zimcik@faf.cuni.cz
[b] Institute of Molecular Pathology, Faculty of Military Health Sciences, University of Defence,
Hradec Kralove 50005, Czech Republic

the Q-band of around 30–40 nm compared with the parent Pc.[15] This undesirable property can be eliminated by the linear annelation of aromatic rings to the macrocyclic system, thus resulting in tetra[2,3]quinoxalinoporphyrazines or their isomers, tetra[6,7]quinoxalinoporphyrazines (TQP), the aza-analogues of Nc (Figure 1). The tetra[6,7]quinoxalinoporphyrazines are characterized by a stronger red shift of around 40 nm compared with their corresponding isomers, tetra[2,3]quinoxalinoporphyrazines.[11] Tetra[2,3]quinoxalinoporphyrazines have been known for some time,[11,16–18] however, to the best of our knowledge their isomers, which are more suitable from the point of view of the spectral properties, have been investigated in more detail in only one case recently.[19]

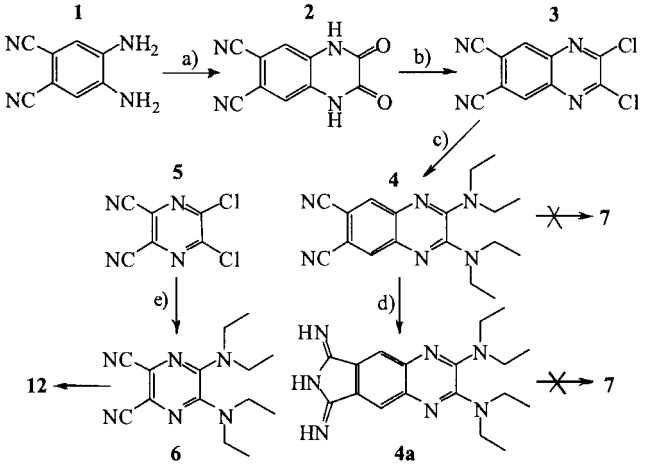
In this work we have focused on porphyrazines containing the [6,7]quinoxalino moiety. They combine good spectral properties, considering the bathochromic shift of the Q-band, and simple synthetic availability with a very wide range of possible peripheral substitutions allowing, in the future, the preparation of compounds with desired properties and behaviour. For this purpose, we synthesized the promising precursor 2,3-dichloroquinoxaline-6,7-dicarbonitrile which undergoes simple nucleophilic substitution and thus is an excellent substrate for the synthesis of various quinoxalinoporphyrazine building blocks. To elucidate the effect of the insertion of benzene rings into the macrocycle system, a series of macrocycles with different numbers of pyrazine and quinoxaline moieties were prepared and their UV/Vis spectral properties investigated. They will be referred to in the text as pyrazinoquinoxalinoporphyrazines (PQP) and, according to the number of each moiety and the central atom, will be abbreviated as $H_2P_{4-x}Q_xP$ and $ZnP_{4-x}Q_xP$, where x = 0–4. For a unified labelling system, this abbreviation will be used throughout the article, that is, also for the members of this series containing only pyrazine (i.e., $H_2P_4Q_0P$ = H_2TPP) or only quinoxaline (i.e. $H_2P_0Q_4P$ = H_2TQP) heterocycles even though we are aware that they are not actually PQPs.

Results and Discussion

Synthesis and Characterization

The synthesis of the starting material 4,5-diaminophthalonitrile (**1**) has been reported in the literature using either 1,2-diamino-4,5-dibromobenzene[19] or 1,2-diamino-4,5-diiodobenzene.[20] As experienced in our laboratory and also reported in the literature, the limiting step in the preparation of **1** is the cyanation of halogenated diaminobenzene. In the case of 1,2-diamino-4,5-diiodobenzene, the yields that we obtained were considerably higher and therefore the synthesis reported by Youngblood[20] was chosen as more suitable. In previous work,[19,21] phthalonitrile **1** was treated directly with different diketones, yielding quinoxaline-5,6-dicarbonitriles in one step. This approach, however, requires the previous complicated synthesis of the desired diketone and some substitutions cannot be achieved by this approach. We therefore opted for an alternative approach.

Our syntheses (Scheme 1) led to preparation of 2,3-dichloroquinoxaline-6,7-dicarbonitrile (**3**), a flexible building block suitable especially for the synthesis of heteroatom-substituted quinoxalinoporphyrazines. The synthesis required two steps: the formation of dioxo derivative **2** and its subsequent chlorination. The preparation of **2** has already been reported[22] using a different, quite complicated synthetic approach. Our method of heating **1** in dimethyl oxalate is simple and gives very good yields of **2**. The formation of two tautomeric forms (lactam and lactim) is possible for compound **2**, but very strong carbonyl bands in the IR spectrum and only one set of ^{13}C and ^{1}H NMR signals show that the equilibrium is shifted exclusively to the lactam form. The next step, chlorination of **2**, proceeded best by refluxing with thionyl chloride and a catalytic amount of DMF in 1,2-dichloroethane. Reactions with thionyl chloride in other solvents (dioxane and THF) as well as chlorination with $POCl_3$ in these solvents (THF, dioxane and 1,2-dichloroethane) were unsuccessful. The chemical properties of **3** are very similar to 5,6-dichloropyrazine-2,3-dicarbonitrile (**5**), which is widely used in the preparation of precursors for TPP.[4,8,23–25] The carbons at positions 2 and 3 are strongly electron-deficient because of the electron-withdrawing ability of the nitrogen atoms in the quinoxaline heterocycle and the peripheral chlorine atoms. This makes them suitable for nucleophilic attack by, for example, amines, thiolates or alkoxides leading to the replacement of one or both chlorine atoms with the desired substituents. Thanks to this variability of peripheral substitution this compound is a very interesting starting material for the preparation of macrocycles with variable properties (e.g., spectral properties, solubility, hydrophilicity and hydrophobicity, the amount of peripheral charges). Moreover, substituted heterocycles containing the pyrazine-2,3-dicar-



Scheme 1. Synthetic strategy. Reagents and conditions: a) EtOH, diethyl oxalate, 140 °C, 8 h; b) 1,2-dichloroethane, $SOCl_2$, DMF, reflux, 3 h; c) diethylamine, THF, room temp., overnight; d) NH_3, butanol, 90 °C, 30 min; e) diethylamine, THF, reflux, 6 h.

bonitrile core have also been investigated for their herbicidal[26,27] and antineoplastic[28,29] activities. Compound **3** is a promising starting material for derivatives of quinoxalinedicarbonitriles, investigated also for their potential in these interesting applications.

The aggregation of planar macrocyclic systems of Pc, Nc or TPP dyes is a well-known problem and it results in poor solubility and consequently problems with purification, isolation and characterization of synthesized products. Introduction of bulky substituents onto the periphery of these macrocycles hinders the stacking of the macrocycle molecules and thus efficiently inhibits aggregation.[12,15] Bulky diethylamino groups were therefore chosen as peripheral substituents for the final PQP to ensure very good monomerization in organic solvents, consequently allowing good isolation of all the synthesized dyes. Thus the reaction of **3** and **5** with diethylamine gave the final precursors for tetramerization, **4** and **6**, respectively. The nucleophilic substitutions proceeded easily for both the pyrazine- and quinoxalinedicarbonitriles, giving high yields of over 70%.

The tetramerization of one precursor gives rise to symmetrical dyes. Because of our good experience[8] (satisfactory yields) in the tetramerization of TPP using butanolate we decided to use lithium butanolate as the cyclization agent. Tetrapyrazinoporphyrazine $H_2P_4Q_0P$ (**12**) was prepared with no further problems from **6** and isolated from the reaction mixture. Preparation of tetraquinoxalinoporphyrazine $H_2P_0Q_4P$ (**7**) proved to be very difficult. The self-condensation of **4** was not successful using various procedures (lithium or magnesium butanolate, DMF or (dimethylamino)ethanol with zinc acetate). Compound **4** was also treated with ammonia to form the diiminoisoindoline analogue **4a** (Scheme 1). Cyclotetramerization of **4a** in dimethylaminoethanol alone or in the presence of zinc acetate gave results similar to all the above-mentioned procedures. The product was always detected in the reaction mixtures through the use of UV/Vis spectroscopy (Q-bands in the expected area) but its amount was insignificant. Surprisingly, the yield of compound **7** was higher in the case of statistical condensation (see below). However, it was isolated as a mixture of two very similar compounds and we did not succeed in the isolation of pure metal-free **7**. NMR spectroscopy indicated the presence of another substance and MALDI-TOF mass spectrometry showed two signals at m/z = 1291 (**7**) and 1281 (impurity) in a ratio of approximately 3:1. Owing to identical R_f values in all tested mobile phases it was impossible to separate these substances even by TLC.

The tetramerization of two different precursors (A and B) in one reaction usually results in a mixture of six different compounds (AAAA, AAAB, ABAB, AABB, BBBA and BBBB) which must be separated using chromatographic procedures. This approach in the synthesis of unsymmetrical Pc and related compounds is sometimes called a statistical condensation.[30] Different selective strategies[30–32] leading to only AAAB (the sub-phthalocyanine approach[33] or the polymer support approach[34]), ABAB[35–37] or AABB[35,38,39] derivatives have also been developed.

Our aim was to isolate all metal-free PQPs arising from the tetramerization of quinoxaline derivative **4** and pyrazine derivative **6**. The synthesis had to be therefore performed by statistical condensation followed by chromatographic separation of the PQP derivatives (**7**–**12**, Figure 2). For simplification, symmetrical **12** was not isolated from the mixture but prepared in a separate reaction (see above). The bulkiness of the diethylamino groups inhibits efficiently the aggregation of all the PQP molecules and therefore they could be separated on a silica gel column by step-gradient chromatography. The compounds were readily soluble in common organic solvents (chloroform, dichloromethane, acetone, tetrahydrofuran and toluene) showing a negligible tendency to aggregate in dilute solution. We succeeded in isolating all the compounds in the reaction mixture; even two isomers (adjacent and opposite) were well separated. Compounds were eluted from the column in the following order: **7**, **8**, **9**, **10**, **11** and **12**. Using toluene/tetrahydrofuran (20:1) as the mobile phase the R_f values were 0.62, 0.60, 0.55, 0.24, 0.10 and 0.02 for compounds **7**, **8**, **9**, **10**, **11** and **12**, respectively. Owing to the different masses of the two precursors, the fractions could be assigned to the correct PQP unequivocally on the basis of MS. Assignment of the adjacent and opposite isomers to two fractions with the same mass was achieved on the basis of their NMR spectra.

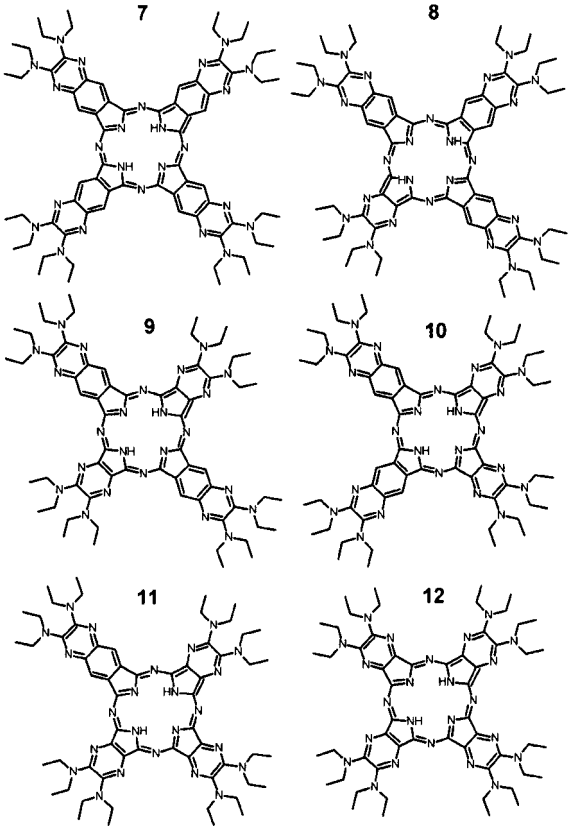


Figure 2. Structures of the PQPs in the reaction mixture.

The diethylamine ^{1}H NMR signals of $H_2P_2Q_2P$ **9** and **10** in $CDCl_3$ were broad and unsplit and therefore they did not allow exact differentiation of the two isomers. The diethylamine ^{13}C NMR signals of $H_2P_2Q_2P$, however, were sharp and allowed the isomers to be distinguished (Figure 3). Owing to different symmetry, the two carbons of the ethyl groups on the periphery gave only two signals each in the case of **9** but four signals each in the case of **10** in the expected areas. Moreover, in the case of **10** we were able to detect all 16 signals of the aromatic carbons. This confirmed unequivocally the assignment of the isomers to each fraction.

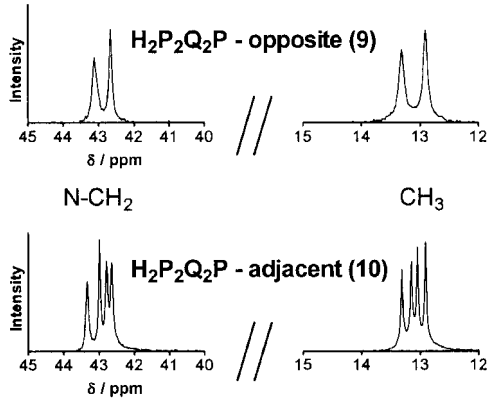


Figure 3. ^{13}C NMR spectra of the peripheral diethylamino groups of **9** (opposite) and **10** (adjacent).

The zinc derivatives were prepared in minimal amounts only to study changes in the UV/Vis spectra. Metal-free PQPs were refluxed for a few minutes in DMF/toluene with zinc acetate to produce zinc PQPs quantitatively, as detected by TLC. The presence of zinc in the centre was confirmed by MS (MALDI-TOF). No signals from the corresponding metal-free PQPs were detected. In the case of $H_2P_0Q_4P$ (**7**), the metal was also introduced into the centre of the impurity (see above). The R_f values of the resulting zinc complexes were different enough to isolate the ZnP_0Q_4P using TLC, allowing this zinc complex to be studied by UV/Vis spectroscopy in a pure form. The identity of the impurity remains unknown, but its porphyrazine character with perhaps a tetraquinoxaline core is implicated because it complexes the metals and its UV/Vis spectrum (not shown) is strongly red-shifted. Also its signal at m/z = 1281 suggests a metal-free system with a tetraquinoxaline core.

UV/Vis Absorption Spectroscopy

The successive insertion of benzene rings into TPP between the porphyrazine system and the pyrazine ring show interesting effects in the UV/Vis spectra of these compounds. It is well known that the position and bandwidth of the Q-bands of Pcs vary with the central metal, the ring system, molecular symmetry, size and number of substituents.[10] The Q-band shifts to the red also because of an expansion of the π-conjugated system by the insertion of benzene rings into the periphery of Pc, thus forming Nc.[13] As shown in Figure 4, a bathochromic shift of the Q-band from 654 to 744 nm for zinc PQPs and from 686 to 763 nm for metal-free PQPs is observed with increasing number of inserted benzene rings. By considering the centre of the split bands as the band position, the Q-band positions of H_2PQP and ZnPQP have a linear relationship, as shown in Figure 5. The slopes of these linear plots show that the insertion of each benzene ring between the pyrazine ring and the porphyrazine macrocycle leads to a bathochromic shift of 22 nm. The two straight lines are parallel. The

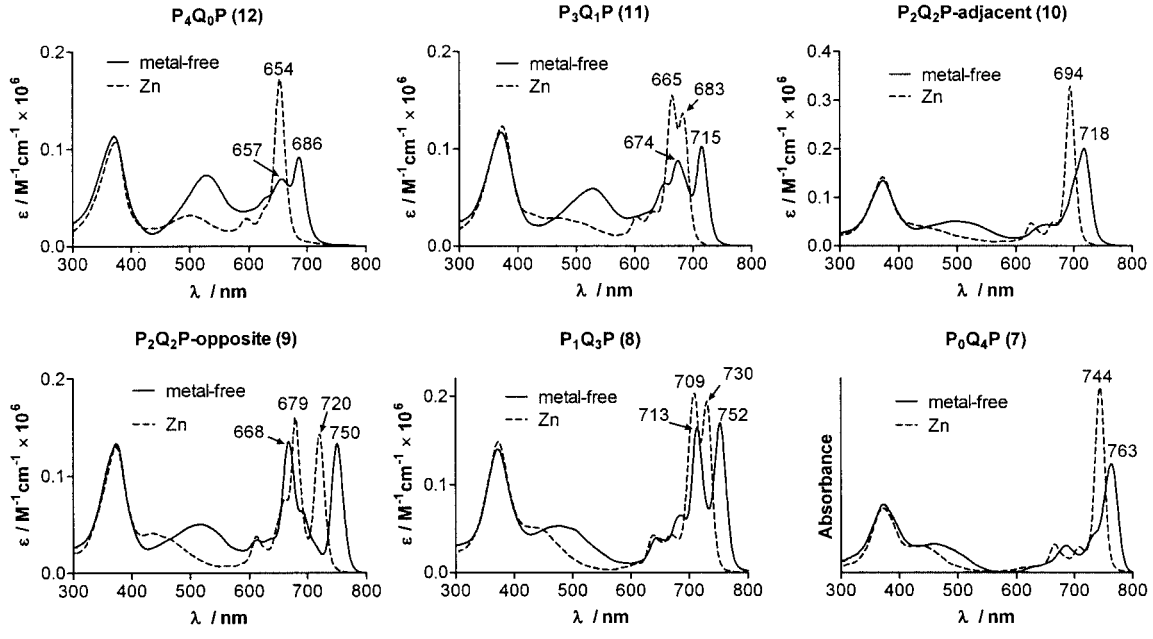


Figure 4. UV/Vis spectra of metal-free PQPs in dichloromethane and zinc PQPs in THF.

metal-free PQPs are red-shifted by 18 nm on average with respect to the corresponding zinc complexes. The conclusion that the Q-band centre shifts linearly with the number of inserted benzene rings in the Pc/Nc series has also been postulated by other authors.[40] The positions of the Q-band centre of all the unsymmetrical PQPs can therefore be nicely predicted by knowing the absorption of the outer macrocycles in the series (in our case TPP and TQP). Concerning the above-mentioned findings, tuning of the absorption maxima of the Q-band is therefore possible by successive insertion of benzene rings into the TPP system. Together with a large variability of peripheral substitutions of the PQP macrocycle, it is an ideal tool for the synthesis of dyes with desired properties.

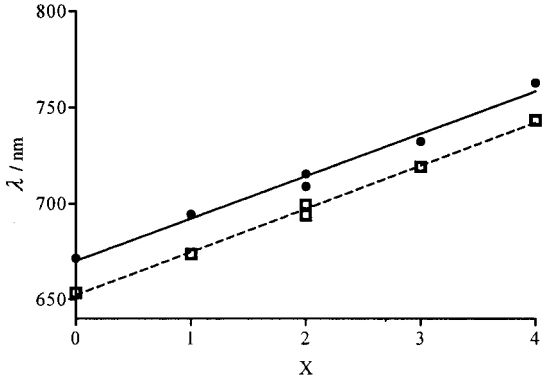


Figure 5. The Q-band absorption centres of $H_2P_{4-x}Q_xP$ (●) and Zn $P_{4-x}Q_xP$ (□), (x = 0–4) vs. x, the number of inserted benzene rings into the macrocycle.

The highly symmetrical (D_{4h}) metal complexes of Pc and related compounds show only a single maximum in the Q-band area. This was observed in the spectra of the two symmetrical complexes ZnP_0Q_4P and ZnP_4Q_0P (Figure 4). In the spectra of metal-free Pcs, the Q-band is usually split into two maxima due to the decreased (D_{2h}) symmetry of the molecule. In the case of $H_2P_4Q_0P$ (**12**) this splitting is clearly observable. However, the spectrum of the enlarged $H_2P_0Q_4P$ (**7**) is not split and exhibits only one main maximum in the Q-band region. Kobayashi et al.[41] investigated the spectral changes of metal-free derivatives of porphyrazines, Pc, Nc and antracocyanines. They found that the splitting of the Q-band of metal-free macrocycles decreases with enlargement of the conjugated system; Q-bands appeared as single bands for H_2Nc and larger systems.[41]

In fact, $H_2P_0Q_4P$ (**7**) is an aza-analogue of Nc so a single band in the Q-band region is expected. However, the impurity in this sample can also influence slightly the shape of the spectrum.

Unsymmetrical macrocycles of C_{2v}-type symmetry show splitting of the Q-band into two bands.[13,40,42] This is the case with the metal-free compounds $H_2P_3Q_1P$ (**11**) and $H_2P_1Q_3P$ (**8**) and the corresponding zinc complexes. All four compounds showed split Q-bands. In the case of metal-free macrocycles, in which the overall symmetry is decreased due to the presence of two central hydrogens, the energy difference ($\Delta\lambda_{max}$) between the two split bands is higher than in the case of the corresponding zinc complexes ($\Delta\lambda_{max}$ = 41 nm for $H_2P_3Q_1P$ compared with 18 nm for ZnP_3Q_1P and 39 nm for $H_2P_1Q_3P$ compared with 21 nm for ZnP_1Q_3P).

The opposite isomer $H_2P_2Q_2P$ (**9**) as well as its zinc complex, which are characterized by D_{2h} symmetry, show a remarkably large splitting of the Q-band. A similar dependence of the splitting of the Q-band of the metal-free PQP and the zinc complex was observed as in the above-mentioned case. The Q-band is split by 82 and 41 nm in the case of the metal-free PQP and its slightly more symmetrical zinc complex, respectively. Unusually, only a single band appeared in the Q-band area for the adjacent isomer $H_2P_2Q_2P$ (**10**) and its metal complex. These compounds are also of lower C_{2v} symmetry and therefore the Q-band is expected to be split. But similar observations,[13,42] as well as theoretical calculations,[10] have shown that this behaviour is typical of adjacent isomers of Pc. This spectral feature is further confirmation of the correct assignment of adjacent and opposite isomers for the two fractions of the same mass.

Conclusions

We have reported herein a synthesis of 2,3-dichloroquinoxaline-6,7-dicarbonitrile, a flexible starting material for building blocks of tetra[6,7]quinoxalinoporphyrazines. It easily undergoes nucleophilic substitution, so can be used for the synthesis of heteroatom-substituted derivatives of quinoxaline-6,7-dicarbonitrile. In this work, the diethylamino-substituted derivative was prepared as an example. A series of PQPs containing different numbers of quinoxalino and pyrazino moieties were then synthesized for the first time by using this building block. Even the adjacent and opposite isomers were separated and unequivocally assigned.

The successive insertion of benzene rings into TPP between the pyrazine and the porphyrazine ring leads to linear bathochromic shifts of the Q-band centre of 22 nm per benzene ring. Thus the absorption wavelength of PQPs can be tuned by increasing the number of quinoxalino moieties in the PQP macrocycle. Owing to the linear dependence of this shift, the position of the Q-band centre can be predicted in the future by knowing the outer members of the series, symmetrical TPP or TQP which are more easily accessible. The shape of the Q-band is strongly dependent on the symmetry of the macrocycle molecule. Splitting of the Q-band was observed for unsymmetrical compounds with D_{2h} and C_{2v} symmetry, whereas derivatives with D_{4h} symmetry exhibited a single band. Two exceptions to this rule were observed: $H_2P_0Q_4P$ with D_{2h} symmetry and adjacent isomer $H_2P_2Q_2P$ with C_{2v} symmetry showed only a single band. Both these exceptions have been observed previously and explained by molecular orbital calculations.[10,41]

Experimental Section

All organic solvents used for synthesis were of analytical grade. All chemicals and solvents were used as received without further

purification except for zinc acetate (Lachema, Czech Republic) which was dried in a drying gun at 78 °C and under a pressure of 13 mbar for 8 h. TLC was performed on silica gel 60 F_{254} (Merck, Darmstadt). Merck Kieselgel 60 (0.040–0.063 mm) was used for column chromatography. Infrared spectra were measured as KBr pellets with a Nicolet Impact 400 IR Spectrometer (USA). ^{1}H and ^{13}C NMR spectra were recorded with a Varian Mercury Vx BB 300 spectrometer (^{1}H: 299.95 MHz; ^{13}C: 75.43 MHz). Chemical shifts are given relative to internal $Si(CH_3)_4$. UV/Vis spectra were recorded with a Shimadzu UV-2401PC spectrophotometer (Shimadzu Europa GmbH, Duisburg, Germany). The slit width of the instrument was set to 0.2 nm. The wavelength accuracy of the instrument at this slit width is ±0.3 nm. MALDI-TOF mass spectra were recorded in positive reflectron mode with a Voyager-DE STR mass spectrometer (Applied Biosystems, Framingham, MA, USA). For each sample, 0.5 μL of the mixture was spotted onto the target plate, air-dried and covered with 0.5 μL of a matrix solution consisting of 10 mg of α-cyano-4-hydroxycinnamic acid in 100 μL ACN containing 0.1% TFA. The instrument was calibrated externally with a five-point calibration using Peptide Calibration Mix1 (LaserBio Labs, Sophia-Antipolis, France). Compounds **1**[20] and **5**[43] were prepared according to previously published methods.

2,3-Dioxo-1,2,3,4-tetrahydroquinoxaline-6,7-dicarbonitrile (2): A suspension of **1** (1.58 g, 10 mmol) in ethanol (10 mL) was refluxed until the heterogeneous mixture turned to a homogeneous solution (app. 10 min). Then diethyl oxalate (50 mL) was added and this mixture was heated at 140 °C for 8 h. The boiling flask was left opened (without condenser) to allow continual removal of ethanol. The mixture was cooled to room temperature and the precipitate filtered and washed with toluene to give **2** (1.6 g, 75%) as a brown solid. M.p. >300 °C. IR (KBr): $\tilde{\nu}_{max}$ = 3192, 3154, 3048, 2237 (CN), 1701, 1608, 1506, 1380 cm^{-1}. ^{1}H NMR (300 MHz, [D$_6$]-DMSO): δ = 12.42 (s, 2 H, NH), 7.51 (s, 2 H, CH) ppm. ^{13}C NMR (75 MHz, [D$_6$]DMSO): δ = 108.1, 116.1, 120.0, 130.2, 155.0 ppm.

2,3-Dichloroquinoxaline-6,7-dicarbonitrile (3): DMF (55 mg, 0.75 mmol) was added dropwise to a slurry of **2** (1.6 g, 7.5 mmol) and thionyl chloride (7.2 g, 60 mmol) in 1,2-dichloroethane (20 mL) and the resulting mixture was refluxed for 3 h. The mixture was cooled to room temperature, concentrated to dryness and extracted with hot THF (3 × 50 mL). The extracts were combined and evaporated to give **3** (1.2 g, 64%) as a yellow solid. M.p. 128 °C (decomp.). IR (KBr): $\tilde{\nu}_{max}$ = 3100, 3069, 3048, 2239 (CN), 1719, 1539, 1387, 1261 cm^{-1}. ^{1}H NMR (300 MHz, [D$_6$]acetone): δ = 8.85 (s, 2 H, arom. CH) ppm. ^{13}C NMR (75 MHz, [D$_6$]acetone): δ = 115.6, 116.5, 136.6, 142.2, 151.0 ppm.

2,3-Bis(diethylamino)quinoxaline-6,7-dicarbonitrile (4): Diethylamine (1.8 g, 24 mmol) was added dropwise to a solution of **3** (1.2 g, 4.8 mmol) in THF (50 mL) and stirred at room temperature overnight. Precipitated diethylamine hydrochloride was filtered off, the solution was evaporated under reduced pressure and the yellow crude product purified by column chromatography on silica with toluene/chloroform (2:1) as eluent to give **4** (1.1 g, 71%) as a yellow solid. M.p. 124–125 °C. UV/Vis ($CHCl_3$): λ_{max} (ε) = 391 (18600), 355 (12300), 300 nm (42200 M^{-1} cm^{-1}). IR (KBr): $\tilde{\nu}_{max}$ = 3012, 2971, 2934, 2868, 2234 (CN), 1526, 1494, 1446, 1384 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.96 (s, 2 H, arom. CH), 3.62 (q, J = 7.0 Hz, 8 H, NCH_2), 1.11 (t, J = 7.1 Hz, 12 H, CH_3) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 12.9, 43.1, 108.7, 116.5, 131.9, 139.4, 148.5 ppm.

6,7-Bis(diethylamino)-1,3-diimino-2*H*-pyrrolo[3,4-*g*]quinoxaline (4a): A rapid stream of ammonia was passed through a stirred mixture of **4** (100 mg, 0.3 mmol) and sodium hydride (1 mg, 0.04 mmol) in butanol (1 mL). The reaction mixture was heated slowly and kept at 90 °C for 30 min. The reaction was monitored by TLC on silica gel with acetone as the eluent. The solvent was removed under reduced pressure, hexane was added to the residue and the yellow solid was filtered off to give **4a** (85 mg, 81%). M.p. 125 °C (slow decomp.). IR (KBr): $\tilde{\nu}_{max}$ = 2969, 2931, 2873, 1648, 1630, 1539, 1448 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.01, (s, 2 H, imino NH), 7.94 (s, 2 H, arom. CH), 3.64 (q, J = 7.0 Hz, 8 H, NCH_2), 1.11 (t, J = 7.1 Hz, 12 H, CH_3) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 12.8, 42.7, 118.8, 129.8, 139.5, 148.3, 166.1 ppm.

5,6-Bis(diethylamino)pyrazine-2,3-dicarbonitrile (6): Diethylamine (1.3 g, 17 mmol) was added dropwise to a solution of **5** (600 mg, 3 mmol) in tetrahydrofuran (100 mL) and refluxed for 6 h. At the end of the reaction the mixture was cooled and precipitated diethylamine hydrochloride was filtered off. The solution was evaporated under reduced pressure and a yellow crude product recrystallized from methanol. Mother liquors from crystallization were combined, evaporated, purified by column chromatography on silica with hexane/ethyl acetate (4:1). The two fractions (from crystallization and chromatography) were combined and finally recrystallized from methanol to give **6** (600 mg, 76%) as yellow plates. M.p. 93–94 °C (lit. 94 °C[44]). IR (KBr): $\tilde{\nu}_{max}$ = 2978, 2935, 2876, 2228 (CN), 1518, 1489, 1347, 1253 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 3.48 (q, J = 7.1 Hz, 8 H, NCH_2), 1.07 (t, J = 7.1 Hz, 12 H, CH_3) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 12.7, 42.8, 115.0, 120.3, 146.1 ppm.

General Procedure for the Synthesis of Unsymmetrical PQP: A solution of **4** (700 mg, 2.2 mmol) and the second precursor **6** (600 mg, 2.2 mmol) was refluxed in dry butanol (15 mL) and metal lithium (196 mg, 28 mmol) was added. The mixture was refluxed for 3 h. The solvent was evaporated under reduced pressure, aq. acetic acid (50% v/v, 30 mL) was added and the mixture was stirred at room temperature for 30 min. The precipitate was filtered, washed thoroughly with water and dried. This mixture of the six different PQPs was separated by column chromatography on silica. The PQPs were obtained as fractions of various colours by using a mobile phase of increasing polarity (reported below as the first column) starting with 20:1 toluene/THF for **7**. Each fraction was then purified on silica once more using either the same or a slightly different mobile phase (reported as the second column).

2,3,11,12,20,21,29,30-Octakis(diethylamino)tetra[6,7]quinoxalinoporphyrazine ($H_2P_0Q_4P$, 7): This compound was synthesized according to the general procedure with the following mobile phases: the first column toluene/THF, 20:1, and the second column with the same mobile phase. Dark solid (4 mg, 0.3%). This compound was obtained with an impurity. UV/Vis (CH_2Cl_2): λ_{max} (ε) = 763 (182000), 685 (48000), 459 (51200), 373 nm (115600 M^{-1} cm^{-1}). IR (KBr): $\tilde{\nu}_{max}$ = 2962, 2919, 2850, 1542, 1481, 1445, 1428 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 4.02–3.72 (m, NCH_2), 1.45–1.00 (m, CH_3), 0.95–0.68 (m) ppm. MALDI-TOF MS: m/z = 1291 [M + H]$^+$, 1281.

Compound 8 ($H_2P_1Q_3P$): This compound was synthesized according to the general procedure with the following mobile phases: the first column toluene/THF, 20:1, and the second column with the same mobile phase. Dark solid (96 mg, 7.0%). UV/Vis (CH_2Cl_2): λ_{max} (ε) = 752 (170000), 713 (165000), 685 (65000), 644 (40000), 477 (53200), 372 nm (140000 M^{-1} cm^{-1}). IR (KBr): $\tilde{\nu}_{max}$ = 2965, 2930, 2869, 1541, 1479, 1445, 1428 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 3.95 (br. s, 32 H, CH_2), 1.49–1.12 (m, 48 H, CH_3) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 13.2, 43.2 ppm. MALDI-TOF MS: m/z (%) = 1241 [M + H]$^+$.

Opposite Isomer 9 ($H_2P_2Q_2P$): This compound was synthesized according to the general procedure with the following mobile phases: the first column toluene/THF, 20:1, and the second column with the same mobile phase. Dark solid (30 mg, 2.3%). UV/Vis (CH_2Cl_2): λ_{max} (ε) = 750 (134500), 690 sh, 668 (136500), 636 sh, 613 (35500), 517 (52000), 373 nm (135000 $M^{-1}cm^{-1}$). IR (KBr): $\tilde{\nu}_{max}$ = 2965, 2930, 2870, 1541, 1477, 1444, 1427 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ = 4.12 (br. s, 16 H, CH_2), 3.84 (br. s, 16 H, CH_2), 1.38 (t, J = 6.8 Hz, 24 H, CH_3), 1.28 (t, J = 6.9 Hz, 24 H, CH_3) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 12.9, 13.3, 42.7, 43.1, 148.3, 150.7 ppm. MALDI-TOF MS: m/z = 1191 $[M + H]^+$.

Adjacent Isomer 10 ($H_2P_2Q_2P$): This compound was synthesized according to the general procedure with the following mobile phases: the first column toluene/THF, 20:1, and the second column with hexane/ethyl acetate, 2:1. Dark solid (105 mg, 8.0%). UV/Vis (CH_2Cl_2): λ_{max} (ε) = 718 (201500), 652 (44600), 495 (51600), 374 nm (135600 $M^{-1}cm^{-1}$). IR (KBr): $\tilde{\nu}_{max}$ = 2966, 2931, 2871, 1640, 1539, 1478, 1445, 1427 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ = 4.05 (br. s, 16 H, CH_2), 3.85 (br. s, 16 H, CH_2), 1.40–1.24 (m, 48 H, CH_3) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 12.9, 13.1, 13.2, 13.3, 42.6, 42.8, 43.0, 43.3, 120.6, 121.2, 134.1, 134.2, 138.8, 139.0, 139.5, 139.7, 143.4, 146.2, 148.1, 148.4, 150.3, 150.4, 152.3, 154.0 ppm. MALDI-TOF MS: m/z = 1191 $[M + H]^+$.

Compound 11 ($H_2P_3Q_1P$): This compound was synthesized according to the general procedure with the following mobile phases: the first column toluene/THF, 20:1, and the second column with hexane/ethyl acetate, 2:1. Dark solid (95 mg, 7.3%). UV/Vis (CH_2Cl_2): λ_{max} (ε) = 715 (103000), 674 (88600), 653 (65000), 529 (60000), 372 nm (118000 $M^{-1}cm^{-1}$). IR (KBr): $\tilde{\nu}_{max}$ = 2966, 2930, 2870, 1641, 1539, 1477, 1445, 1423 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ = 9.83 (s, 2 H, arom. CH), 4.16–3.96 (m, 24 H, CH_2), 3.86 (q, J = 6.9 Hz, 32 H, CH_2), 1.42–1.24 (m, 48 H, CH_3) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 12.9, 13.1, 13.2, 13.3, 42.8, 42.9, 43.3, 120.5, 136.9, 137.5, 138.2, 139.5, 141.3, 141.8, 148.0, 150.2, 150.7, 150.8, 151.9, 159.2 ppm. MALDI-TOF MS: m/z = 1141 $[M + H]^+$.

Compound 12 ($H_2P_4Q_0P$): A solution of **6** (1.08 g, 4 mmol) was refluxed in dry butanol (15 mL) and metal lithium (196 mg, 28 mmol) was added. The mixture was refluxed for 3 h. The solvent was evaporated under reduced pressure, aq. acetic acid (50% v/v, 30 mL) was added and the mixture stirred at room temperature for 30 min. The precipitate was filtered and washed thoroughly with water and methanol. The crude product was then adsorbed on silica (5 g) and washed with methanol on a glass frit until the solution passed through the frit was colourless. The product was dried and purified by column chromatography with hexane/ethyl acetate, 6:1, as eluent. The pure product was dissolved in a minimal amount of dichloromethane and dropped into methanol. The resulting fine suspension was filtered and dried to give a dark purple solid of **12** (270 mg, 25%). UV/Vis (CH_2Cl_2): λ_{max} (ε) = 686 (92800), 657 (70000), 528 (74400), 370 nm (114000 $M^{-1}cm^{-1}$). IR (KBr): $\tilde{\nu}_{max}$ = 2969, 2931, 2872, 1640 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ = 4.05 (q, J = 7.2 Hz, 32 H, CH_2), 1.32 (t, J = 7.2 Hz, 48 H, CH_3) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 150.5, 147.0, 140.2, 42.9, 13.2 ppm. MALDI-TOF MS: m/z = 1091 $[M + H]^+$.

General Procedure for the Preparation of Zinc PQP: A mixture of metal-free PQP (0.02 mmol) and anhydrous zinc acetate (20 mg, 0.1 mmol) was refluxed in a mixture of anhydrous DMF/toluene (1:1) (2 mL) for 15 min. The mixture was cooled, toluene was evaporated and the residue poured into distilled water (20 mL). The fine suspension was filtered, washed with water and air-dried to give a dark green solid. The yield of zinc PQP was quantitative. Only in the case of ZnP_0Q_4P, for which the starting material was impure, was the pure product isolated by TLC for analysis and spectral measurement.

Zinc Complex ZnP_0Q_4P: This compound was isolated by TLC with toluene/THF (20:1, R_f = 0.38) as the mobile phase and by scraping the silica from the TLC plate and washing it with tetrahydrofuran. UV/Vis (THF): λ_{max} = 744, 708, 665, 435, 372 nm. MALDI-TOF MS: m/z = 1353 $[M + H]^+$.

Zinc Complex ZnP_1Q_3P: UV/Vis (THF): λ_{max} (ε) = 730 (193000), 709 (202000), 668 (42300), 638 (42000), 435 sh, 373 nm (147500 $M^{-1}cm^{-1}$). MALDI-TOF MS: m/z = 1303 $[M + H]^+$.

Opposite Isomeric Zinc Complex ZnP_2Q_2P: UV/Vis (THF): λ_{max} (ε) = 720 (142200), 679 (159000), 662 (75400), 613 (37300), 435 (40500), 375 nm (130000 $M^{-1}cm^{-1}$). MALDI-TOF MS: m/z = 1253 $[M + H]^+$.

Adjacent Isomeric Zinc Complex ZnP_2Q_2P: UV/Vis (THF): λ_{max} (ε) = 694 (329000), 664 (48500), 626 (46600), 373 nm (141000 $M^{-1}cm^{-1}$). MALDI-TOF MS: m/z = 1253 $[M + H]^+$.

Zinc Complex ZnP_3Q_1P: UV/Vis (THF): λ_{max} (ε) = 683 (138000), 665 (156000), 633 (34300), 604 (29400), 463 (29200), 374 nm (124200 $M^{-1}cm^{-1}$). MALDI-TOF MS: m/z = 1203 $[M + H]^+$.

Zinc Complex ZnP_4Q_0P: UV/Vis (THF): λ_{max} (ε) = 654 (173000), 595 (29900), 501 (33200), 374 nm (108900 $M^{-1}cm^{-1}$). MALDI-TOF MS: m/z = 1153 $[M + H]^+$.

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