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Pyrazine-Based Porphyrinoids

Pyrazinoporphyrins: Expanding a Pyrrolic Building Block in *meso*-Tetraphenylporphyrin by a Nitrogen Atom

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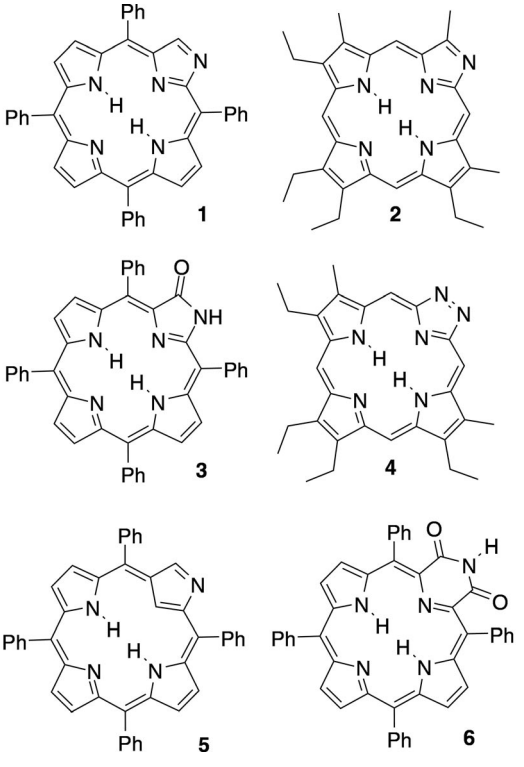
Abstract: Application of a variant of our "porphyrin breaking and mending strategy" to free base and Ni^{II} complexes of *meso*-tetraarylporphyrin – dihydroxylation, oxidative diol cleavage and reaction of the resulting *seco*-chlorin bis(aldehyde) with ammonia – generates pyrazinoporphyrins. Thus, a nitrogen atom was inserted between the two former β-carbon atoms, overall formally replacing a pyrrolic building block by a pyrazine moiety. Treatment of the initially formed pyrazine hemiaminals with alcohols converts them into the corresponding hemiaminal ethers. This stabilizes the chromophores significantly, but the free-base pyrazinoporphyrins still remain sensitive toward (acid-induced) degradation reactions. Free-base pyrazinoporphyrins possess slightly redshifted porphyrin-type UV/Vis spectra, while the spectra of the pyrazinoporphyrin Ni^{II} complexes resemble more those of metallochlorins.

Introduction

The past two decades have seen an enormous increase in the synthesis of porphyrin isomers,[1] porphyrin analogues containing more than four pyrrolic building blocks (the so-called expanded porphyrins),[2] or non-pyrrolic building blocks.[1c,3] Their study has contributed to the fundamental understanding of the key concept of aromaticity, the chemical and photophysical properties of porphyrins and chlorins, and it has provided chromophores with unprecedented properties, particularly with respect to long-wavelength absorption, anion recognition, and metal coordination properties.

Among the porphyrinoids containing non-pyrrolic building blocks are a number in which a β-carbon atom of the parent porphyrin was replaced by a nitrogen atom,[3e] such as imidazoloporphyrins **1**,[4] **2**,[5] and **3**.[4b] Two adjacent β-carbon atoms were replaced in triazoloporphyrin **4**,[6] and related triazole- and thiadiazole-substituted phthalocyanines.[7] *N*-Confused porphyrin **5** is an example of a porphyrin isomer but can also be interpreted as a carbaporphyrin with a β-nitrogen atom.[8] Similarly, pyrazoloporphyrins[9] or pyrazole-containing hexaphyrin analogues[10] are β,β′-dinitrogen carbaporphyrin derivatives. In rare cases, a nitrogen atom was inserted between two β,β′-carbon atoms, as shown in imide-functionalized porphyrin **6**.[11]

Two fundamentally different approaches toward the synthesis of porphyrinoids containing a non-pyrrolic building block are available:[3e] The total synthesis of the macrocycles, as practiced for porphyrinoids **2**, **4**, and **5**, or the stepwise conversion of *meso*-tetraphenylporphyrin, a pathway used to access porphyrinoids **1**, **3**, and **6**.



A key aspect of our ongoing work is the systematic study of the stepwise formal replacement of a pyrrolic building block in porphyrins or chlorins by a non-pyrrolic building block.[3e] Imide **6**, for example, was prepared by a Beckmann rearrangement of a porphyrin dione oxime, itself prepared in three steps from

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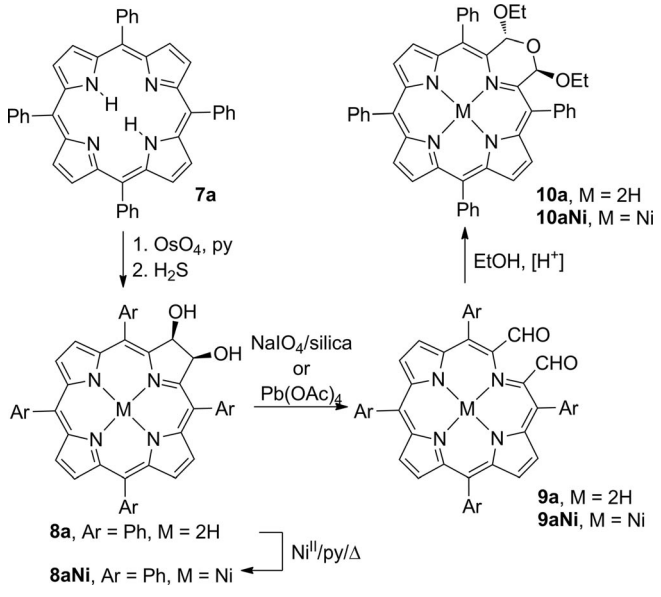
the corresponding porphyrin.[11] This "porphyrin breaking and mending" strategy is further exemplified in Scheme 1, the ring-expansion of *meso*-tetraphenylporphyrin **7a** by an oxygen atom.[12] An OsO_4-mediated dihydroxylation reaction of **7a** generates dihydroxychlorin **8a**.[12a] This diol is oxidatively cleaved, forming *seco*-chlorin bis(aldehyde) **9a**.[13] Treatment with alcohol under acid catalysis led to a ring-closure reaction and subsequent double-acetal formation, generating morpholinochlorins **10a**/**10aNi**.[12] Other nucleophiles eliciting this morpholine-forming ring-closure reaction are known.[12d] The final products are chlorin analogues possessing redshifted optical spectra.[12] Not all nucleophiles provide the expected products, however. For instance, the reaction of *seco*-chlorin bis(aldehyde) with hydrazine did not lead to the expected triazepin derivative. Instead, a porphyrin was formed by an N_2-extrusion reaction.[14]



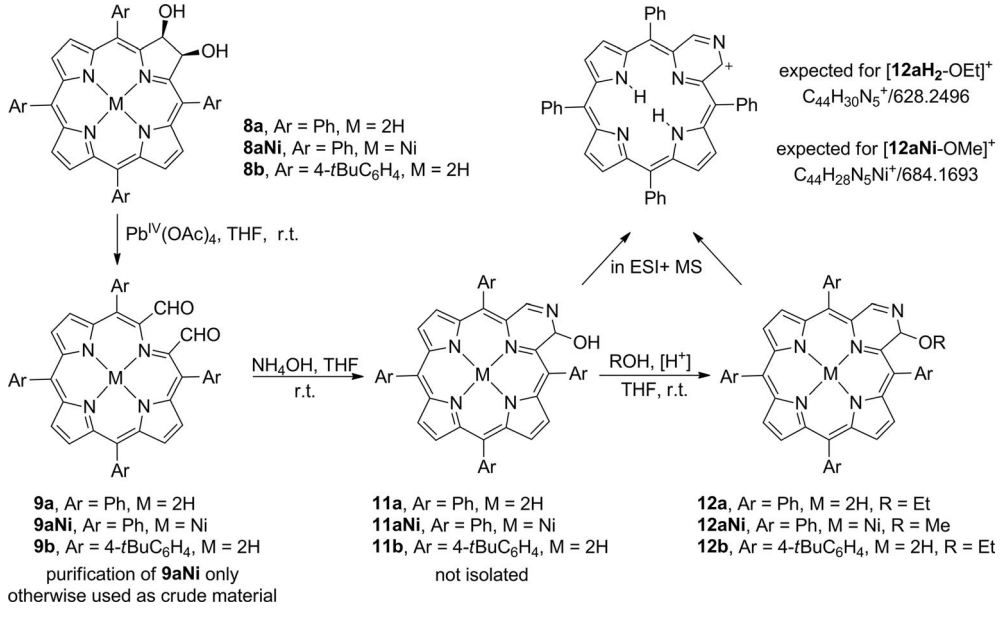
Scheme 1. Ring expansion of tetraphenylporphyrin by an oxygen atom.

In a report on the electrochemical reduction of a number of Ni^{II} complexes of porphyrins and porphyrin analogues, such as **9aNi** and **10aNi**, we included a pyrazinoporphyrin Ni^{II} complex, though we did not report any details of its formation.[15] Moreover, at that time, only the particularly stable Ni^{II} complex **9aNi** was known, and the free-base *seco*-chlorin bis(aldehyde) **9a** had not yet become available. This has changed,[13c] and free-base *seco*-chlorin bis(aldehyde) **9a** demonstrated its versatility in the formation of a number of porphyrinoids containing non-pyrrolic heterocycles.[12b,13c,16] This prompted us to investigate its reaction with ammonia with the goal of preparing the free-base pyrazino derivatives. Free-base chromophores are frequently fluorescent, potentially photosensitizers for singlet oxygen, and they allow the preparation of a wide variety of metal complexes.[17] The nickel complexes are often chemically very stable, but nonfluorescent, possess no photosensitization abilities, and the removal of the Ni^{II} atom from the complexes requires harsh conditions,[17] if it can be accomplished at all without the destruction of the chromophore.[12a] The investigation of the pyrazine-based porphyrinoids is hoped to further unravel the correlation between non-pyrrolic moiety, conformation, conformational flexibility, and optical properties.[11,12,18] Furthermore, the pyrazine nitrogen atom that is part of the chromophore can be potentially utilized for sensing applications, as shown for other pyrrole-modified porphyrins with functionalities at their chromophore.[19] This report presents our findings on the formation and properties of the free base and Ni^{II} complexes of pyrazinoporphyrins.

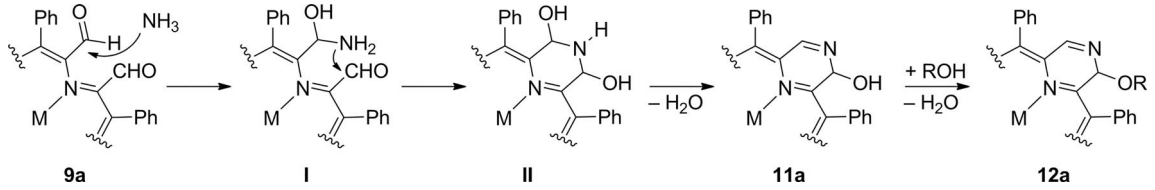
Results and Discussion

Reaction of Secochlorin 9aNi with Ammonia

Reaction of brown-yellow *seco*-chlorin **9aNi**[12a] with aqueous ammonia in THF in homogeneous solution generates immediately a bright green, very polar compound, **11aNi** (R_f < 0.1, alumina/CH_2Cl_2) (Scheme 2). The ESI^+ HR-MS data of the parent



Scheme 2. Formation of pyrazinoporphyrins.



Scheme 3. Mechanism of formation of the pyrazinoporphyrins.

ion ([**11aNi**·H]$^+$) suggested that, relative to the composition of the starting material, an uptake of a nitrogen atom with concomitant loss of 1 equiv. of water had taken place. Prominent in the mass spectrum of **11aNi** was also a fragment ion peak corresponding to the loss of another equivalent of water ([**11aNi** – H_2O]$^+$), suggesting the facile loss of a hydroxy group. This, in turn, is indicative of the presence of a moiety that greatly stabilizes a (carbo)cation.

Treatment of crude **11aNi** with MeOH and catalytic quantities of acid generated compound **12aNi** of much reduced – albeit still significant – polarity (R_f = 0.40, alumina/CH_2Cl_2; R_f = 0.28, silica/2.5 vol.-% MeOH in CH_2Cl_2). The ESI$^+$ HR-MS data of **12aNi** confirmed the replacement of a proton by a methyl group. The major fragmentation was the loss of MeOH, resulting in the formation of the identical cationic species resulting from the loss of water from **11aNi**. These data support the formation of the pyrazinoporphyrin structures **11aNi** and its methoxy derivative **12aNi**.

Based on precedent reactions of *seco*-chlorin bis(aldehydes) with nucleophiles (Scheme 2),[12] the mechanism of the reaction can be deduced in a straightforward manner (Scheme 3): Nucleophilic attack of the amine on one aldehyde group of **9a** forms hemiacetal **I**. Two potential nucleophiles are now available for an intramolecular ring-closure reaction: the alcohol functionality to form a morpholinochlorin or the amine functionality to form a pyrazino derivative. Evidently, the higher nucleophilicity of the amine wins, and the pyrazine intermediate **II** is formed. Loss of water forms the α-hydroxy imine functionality in **11a** with the double bond in conjugation with the porphyrinic chromophore. Note that elimination of 1 equiv. of water is not possible had a morpholinochlorin been formed. The hemiacetal moiety is readily converted into a hemiacetal ether **12a** as well as a stable carbocation under ESI$^+$ MS conditions (Scheme 2).

The NMR spectroscopic data of the pyrazinochlorin **12aNi** (and the free bases **11a**/**12a** described below) suggest that they are formed as racemic mixtures. For a detailed discussion of the NMR spectra and the stereostructures of the pyrazinoporphyrins, see below.

The NMR spectra of **12aNi** also support the methoxy-substituted pyrazinoporphyrin connectivity. The ^{1}H NMR spectrum shows a molecule lacking symmetry; six signals for β-protons can be made out, for example. Three singlets stand out: one at the high-field edge, at δ = 9.12 ppm (1 H), assigned to the imine proton, one at the high-field edge of the aromatic CH protons, at δ = 6.78 ppm (1 H), assigned to the hydrogen atom on the ring sp^3-carbon atom, and a signal at δ = 2.86 ppm (3 H) for the methoxy group. The imine carbon signal (δ = 171.8 ppm) is also very prominent in the ^{13}C NMR spectrum of **12aNi**.

The UV/Vis spectra of **11aNi** and **12aNi** are identical to each other, and typical in overall shape and Q-band position (λ_{max} = 621 nm) for an Ni^{II} chlorin, as illustrated by comparison of the spectrum for the diol chlorin Ni^{II} complex **8aNi** (Figure 1). In contrast, Ni^{II} porphyrin **7aNi** possesses a λ_{max} band at 525 nm. However, the Soret band of pyrazinoporphyrin complex **12aNi** is bathochromically shifted by 22 nm relative to that of diol chlorin nickel **8aNi**. In comparison, the UV/Vis spectrum of the Ni^{II} complex of imide **6** containing two sp^2-hybridized ring atoms in the non-pyrrolic moiety is redshifted as that of an Ni^{II} porphyrin (λ_{Soret} = 439 nm, λ_{max} = 626 nm),[11] whereas morpholinochlorin **10aNi** containing two sp^3-hybridized ring atoms also possesses an Ni^{II} chlorin spectrum (λ_{Soret} = 430 nm, λ_{max} = 640 nm).[12a]

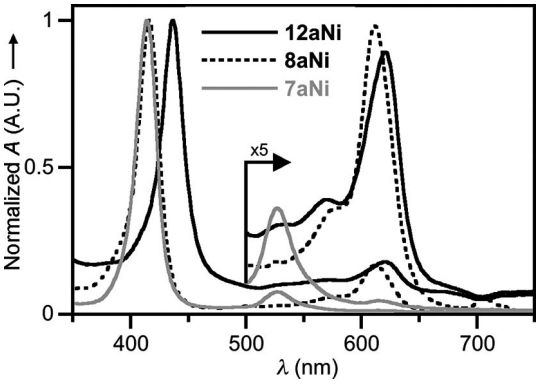


Figure 1. UV/Vis spectra (CH_2Cl_2) of the nickel complexes indicated.

Reaction of Free-Base *seco*-Chlorin 9a with Ammonia

The formation of the free-base pyrazinoporphyrin proceeded in a fashion similar to that described for the Ni^{II} complex. However, free-base *seco*-chlorins **9a** and **9b** were, because of their chemical lability, freshly prepared and immediately used as crude material.[13c] When the *seco*-chlorins were treated under aerobic conditions with a stoichiometric excess of aq. concd. ammonia in pyridine at slightly elevated temperatures (ca. 40–50 °C), the rapid formation of a polar (R_f = 0.5, silica/2.5 vol.-% THF in $CHCl_3$) burgundy-brown product was observed. The reaction was completed, as monitored by TLC, after 20 min, and the products were isolated by preparative plate or column chromatography. The products showed the expected compositions, as per ESI$^+$ HR-MS, and the diagnostic NMR signatures (nonsymmetric molecule; appearance of a diagnostic imine

hydrogen signal at δ = 9.25 ppm; inner NH signals at δ = –1.6 ppm) expected for pyrazinoporphyrin hemiacetals **11a** or **11b**, respectively. While the Ni^{II} complex **12aNi** was stable even under acidic conditions, we noted that the free-base analogues were very sensitive to decomposition, particularly under acidic or oxidative conditions (see also below).

Nonetheless, conversion of hemiacetals **11a** and **11b** into the brown (color on TLC) hemiacetal ethers **12a** and **12b**, respectively, by using EtOH under neutral conditions or acid catalysis (traces of TFA fumes applied by pipette) was possible. These alkylated compounds are more readily isolated and handled than the hydroxylated species primarily because of their relative higher chemical stabilities, but also because of their lower polarities (R_f = 0.51, silica/2 vol.-% THF in $CHCl_3$). We found it nonetheless necessary to neutralize the acidity of the preparative silica gel TLC plates used to purify the free-base chromophores in a chamber over Et_3N for up to 1 week to significantly reduce the decomposition of the pyrazinoporphyrins **12a**/**b** during chromatography.

The out-of-porphyrin-plane configuration of the ethoxy group on the sp^3-hybridized carbon atom is indicated by the diastereotopic splitting of the two methylene signals.[12a–12c] All other spectroscopic findings for the hemiacetal ethers **12a**/**b** are analogous to their corresponding hemiacetals **11a**/**b**.

The UV/Vis spectra of free-base pyrazinoporphyrins **11a** and **12a** are essentially identical (Figure 2; see Supporting Information for a direct comparison of the spectra of **11a** and **12a**). Compared to the spectrum of the parent porphyrin **7a** (λ_{Soret} = 419 nm, λ_{max} = 648 nm), they feature a broadened and redshifted Soret band (at 431 nm), with redshifted Q-bands (λ_{max} = 668 nm). The descending intensity of their Q-bands with increasing wavelengths characterizes them as porphyrin-like chromophores.[20] We therefore named these porphyrinoids pyrazinoporphyrins. Their extinction coefficients are significantly smaller than those of porphyrin **7a**, likely a reflection of their presumed slight nonplanarity. Pyrazinoporphyrin imide **6** also possessed a porphyrin-like optical spectrum.[11] This is in contrast to, for example, the chlorin-like spectra of the morpholinochlorins,[12b] such as **10a**. This dichotomy seen in the UV/Vis spectra within a compound class – the free base is porphyrin-like, and the metal complex is metallochlorin-like – was noted before for the optical properties of the porpholactones, porphyrinoids in which a porphyrin β,β′-bond was replaced by a lactone moiety.[16c] Reflecting the negligible influence of the alkyl substituents on the *meso*-phenyl group, the UV/Vis spectra of all free-base pyrazinoporphyrins **12a** and **12b** are nearly identical (see Supporting Information). Their two-band fluorescence spectra ($\lambda_{emission}$ = 670 and 750 nm, in a 1:0.44 intensity ratio) are also porphyrin-like (see Supporting Information).

All other attempts to modify pyrazinoporphyrins **11a**/**b** and **12a**/**b** failed (such as reduction reactions, oxidations, acid-induced intramolecular ring fusions[12c,12d]) because of their pronounced chemical lability.[21] For instance, protonation of the pyrazinoporphyrins in a UV/Vis cell with traces of TFA generates spectra with a broad λ_{max} band at ca. 940 nm, but this protonation is not reversible. Even immediate neutralization of the acidified solution with NH_4OH or Et_3N does not recover the pyrazinoporphyrin spectra (see Supporting Information). Performance of this acid-induced reaction at a preparative scale allowed the isolation of two major chromophores that could, however, not be characterized. MS suggested the uptake of one and two oxygen atoms, and their UV/Vis spectra were typical for ring-opened, biline-type chromophores, an interpretation also supported by the presence of D_2O-exchangeable protons at the low-field edge of their ^1H NMR spectra (data presented in the Supporting Information).

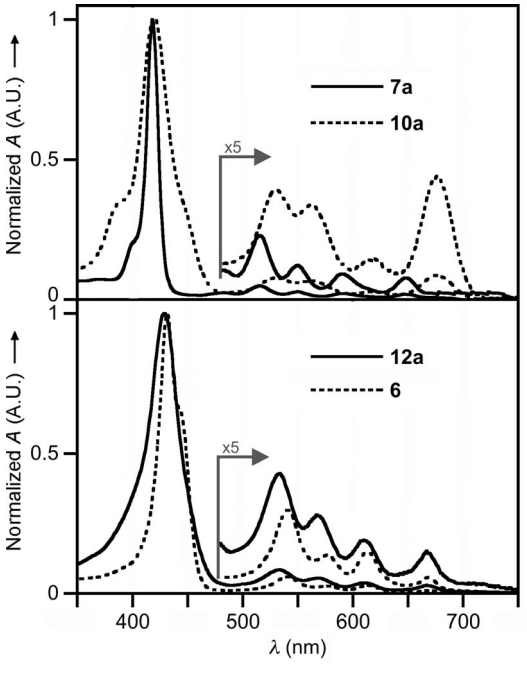


Figure 2. UV/Vis spectra (CH_2Cl_2) of the free-base chromophores indicated.

Stereochemical Considerations

The NMR spectra of the free-base and nickel(II) pyrazinoporphyrins **12a**, **12b**, and **12aNi** indicate the presence of only a single compound. The sp^3-hybridized pyrazine carbon atom is chiral, hence we expect all compounds to be present as racemic mixtures. However, our work on the stereostructure of the related morpholinochlorins suggests that the situation is likely more complex:[12c,12d,22] It is well known that the small ion nickel(II) induces a ruffled conformation in porphyrins.[13b] This ruffling introduces a chiral helimeric axis into the molecule [enantiomers designated (*M*) and (*P*); idealized point group C_2] (Figure 3A). The ruffling is particularly pronounced in the *seco*-chlorin nickel complexes, such as **9aNi** and is largely preserved in the resulting nickel morpholinochlorins, such as **10aNi**,[13b] but is also still present in the free-base morpholinochlorins, such as **10a**.[12d] Nonetheless, the presence of two chiral sp^3-carbon atoms in morpholinochlorins in combination with a chiral axis did not result in the formation of a number of diastereomers. Instead, the ruffling distortion orients the *meso*-phenyl groups adjacent to the morpholine moiety in such a way that sterically one of the two possible isomers [(*R*) or (*S*)] of the flanking sp^3-carbon atoms is fully blocked. Thus, the stereo-

structure of the three chiral elements are tightly coupled, and only a racemic pair is observed.[12d] We suspect a similar process to take place in the pyrazinoporphyrins, though we lack direct (structural) evidence for this hypothesis. The nickel(II) complex **12b** can reasonably be expected to be ruffled, thus exercising the same shielding on the flanking sp^3 center. This would induce the formation of only one stereoisomer at this carbon atom, thus giving rise to the formation of only one racemic pair [such as (*M*-*R*) and (*P*-*S*), but (*M*-*S*), for example, would not be formed] (Figure 3B and C).

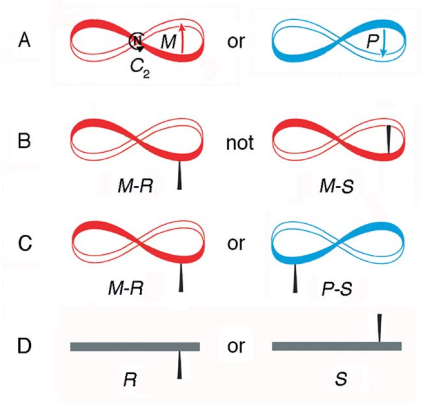


Figure 3. (A) Pictorial representation of the (*M*) and (*P*) helimeric enantiomers of ruffled nickel porphyrinoids, as known for morpholinochlorin nickel complex **10aNi**, and assumed for **12aNi**. (B) Expression of only one of the two possible diasteromers of a given macrocycle helicity if the macrocycle conformation induces the formation of only one of the two possible stereoisomers. (C) Two enantiomers assumed to be present in **11aNi**, **12aNi**. (D) Two enantiomers possible for planar pyrazinoporphyrins, as is possible for the free-base chromophores.

There are two scenarios for the free-base pyrazinoporphyrins: one in which the macrocycle is also ruffled, mirroring the situation of the nickel complex (and of free-base morpholinochlorins),[12d] and one in which the chromophore is planar. As a result of this planarity, the *meso*-phenyl groups are in plane and do not exercise any preference on the sp^3 center. Thus, the racemic mixture arises solely from the two possibilities at sp^3 center (Figure 3D).

Conclusions

The "porphyrin breaking and mending strategy" can be used to expand a pyrrole in *meso*-tetraarylporphyrins by a nitrogen atom to produce a pyrazinoporphyrin. This is only the second example, after imide **6**,[11] in which a pyrrole of a porphyrin was formally replaced by a pyrazine moiety. An independent strategy to accomplish this insertion was demonstrated here, generating a pyrazinoporphyrin with the pyrazine moiety in a lower oxidation state. Nonetheless, because of the presence of one sp^2-hybridized β-carbon atom in the pyrazine moiety, the chromophore of the free-base pyrazinoporphyrins possesses typical, albeit ca. 20 nm red-shifted, porphyrin-type optical spectra. In contrast, the Ni^{II} complexes exhibit metallochlorin-type optical properties. This porphyrin/chlorin dualism was previously also observed for the spectra of the porpholactones.[16c] The otherwise essentially regular UV/Vis spectra are an indication that the conformation of the chromophores are not drastically altered as a result of the modification, but a slight ruffling, particularly for the nickel complexes, can be safely assumed. While the Ni^{II} complex is reasonably stable, the further investigation and potential utility of the free-base chromophores are much hampered by their relatively high chemical instability, particularly in acidic environments.

Experimental Section

Materials and Instrumentation: All solvents and reagents used were reagent grade or better and were used as received. Dihydroxychlorins **4aH$_2$**, **4aNi**, and **4bH$_2$**,[16c,23] and *seco*-chlorin bis(aldehydes) **5aH$_2$**[13c] and **5aNi**[12a] were prepared as described in the literature. The analytical TLC plates used were Silicycle ultra pure silica gel 60 (aluminum backed, 250 μm), and the preparative chromatography plates (500 μm or 1.0 mm silica gel on glass) used were both provided by Scientific Adsorbents Inc., Atlanta, GA. The preparative chromatography plates were stored in a chamber over a bowl of Et_3N for up to 1 week prior to use. ^1H and ^{13}C NMR spectra were recorded with Bruker 300 and 400 MHz instruments in the solvents indicated and are referenced to residual solvent peaks. UV/Vis spectra were recorded with a Cary 50 spectrophotometer, fluorescence spectra with a Cary Eclipse fluorimeter, both Varian, Inc. High- and low-resolution mass spectra were provided by the Mass Spectrometry Facility, Department of Chemistry, University of Connecticut.

[*meso*-Tetraphenylhydroxypyrazinoporphyrinato]Ni^{II} (11aNi): In a 50 mL round-bottom flask equipped with a stir bar, *seco*-porphyrin bis(aldehyde) **9aNi** (150 mg, 0.21 mmol) was dissolved in THF (25 mL), and concd. NH_4OH (0.25 mL) was added. The reaction mixture was stirred for 20 min. When TLC had indicated the complete consumption of the starting material, the reaction mixture was filtered through a short plug of neutral alumina, and the solvents were evaporated to dryness by rotary evaporation. The residue was mainly composed of **11aNi**. R_f < 0.1 (alumina/CH_2Cl_2). ^1H NMR (400 MHz, [D$_6$]DMSO, 25 °C): δ = 9.05 (s, 1 H, C*H*=N$_{pyrazine}$), 8.40 (br. d, $^3J_{H,H}$ = 7 Hz, 1 H, *o*-Ph-H), 8.38 (d, $^3J_{H,H}$ = 4.8 Hz, 1 H, β-H), 8.27–8.35 (m, 3 H, β-H), 8.04 (d, $^3J_{H,H}$ = 4.8 Hz, 1 H, β-H), 7.90–7.75 (br. m, 4 H, *o*-Ph-H), 7.70 (t, $^3J_{H,H}$ = 7 Hz, 1 H, *m*/*p*-Ph-H), 7.65–7.50 (m, 12 H, Ph-H), 7.35 (t, $^3J_{H,H}$ = 7 Hz, 2 H, *m*/*p*-Ph-H), 6.88 (br. d, 1 H, N$_{pyrazine}$-C*H*) ppm. UV/Vis (CH_2Cl_2): λ_{max} (rel. intensity) = 436 (1.0), 520 (sh), 570 (0.06), 621 (0.15) nm. MS (ESI$^+$, 100 % CH_3CN, cone voltage = 30 V): *m*/*z* (%) = 701.9 (80) [M•H]$^+$, 684.1 (100) [M – H_2O]$^+$. HR-MS (ESI$^+$, 100 % CH_3CN, cone voltage = 30 V, TOF): calcd. for $C_{44}H_{30}N_5NiO$ [M•H]$^+$ 702.1798; found 702.1792.

[*meso*-Tetraphenylmethoxypyrazinoporphyrinato]Ni^{II} (12aNi): The entire batch of crude **11aNi** prepared as described above was dissolved in $CHCl_3$ (20 mL), MeOH (0.5 mL), and a drop of concd. aq. HCl was added. The reaction mixture was stirred for 10 min, transferred to a separatory funnel, washed with satd. aq. $NaHCO_3$ and water, the organic phase was isolated, dried with Na_2CO_3, and chromatographed (silica/2.5 vol.-% MeOH in CH_2Cl_2) to provide 85 mg (56 mol-% yield over two steps from **9aNi**) of **12aNi** as a green solid. R_f = 0.40 (alumina/CH_2Cl_2); R_f = 0.28 (silica/2.5 vol.-% MeOH in CH_2Cl_2). ^1H NMR (400 MHz, $CDCl_3$, 25 °C): δ = 9.15 (s, 1 H, C*H*=N$_{pyrazine}$), 8.45 (d, $^3J_{H,H}$ = 7.2 Hz, 1 H, *o*-Ph-H), 8.42 (d, $^3J_{H,H}$ = 4.8 Hz, 1 H, β-H), 8.34–8.34 (m, 2 H, β-H), 8.35 (d, $^3J_{H,H}$ = 4.8 Hz, 1 H, β-H), 8.04 (d, $^3J_{H,H}$ = 4.8 Hz, 1 H, β-H), 7.97 (d, $^3J_{H,H}$ = 4.8 Hz, 1 H, β-H), 7.9 (br. s, 4 H, *o*-Ph-H), 7.74 (t, $^3J_{H,H}$ = 7.2 Hz, 1 H, *m*/*p*-Ph-H), 7.63–7.56 (m, 12 H, Ph-H), 7.34 (t, $^3J_{H,H}$ = 7.2 Hz, 1 H, *m*/*p*-Ph-H), 6.96 (d, $^3J_{H,H}$ = 7.2 Hz, 1 H, *m*/*p*-Ph-H), 6.66 (s, 1 H, N$_{pyrazine}$-C*H*),

2.86 (s, 3 H, OCH_3) ppm. ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): δ = 171.5, 146.4, 143.7, 143.1, 142.1, 139.9, 139.8, 139.6, 137.9, 137.6, 135.5, 134.0, 133.9, 133.85, 133.5, 133.4, 133.2, 131.6, 131.4, 131.3, 130.8, 128.6, 128.4, 128.35, 128.3, 128.2, 127.9, 127.7, 127.6, 124.5, 123.6, 116.0, 114.8, 86.8, 55.9 ppm. UV/Vis (CH_2Cl_2): λ_{max} (log ε) = 436 (5.22), 520 (sh), 570 (4.55), 621 (4.25) nm. MS (ESI$^+$, 100 % CH_3CN, cone voltage = 30 V): *m/z* (%) = 715 (20) [M]$^+$, 684 (100) [M – H_2O]$^+$. HR-MS (ESI$^+$, 100 % CH_3CN, cone voltage = 30 V, TOF): calcd. for $C_{45}H_{31}N_5NiO$ [M$^+$] 715.1882; found 715.2001.

***meso*-Tetraphenylhydroxypyrazinoporphyrin (11a):** Freshly prepared *meso*-tetraphenyl-*seco*-chlorin bis(aldehyde) **9a**[13c] (50 mg, 7.7×10^{-5} mol) was dissolved in THF (ca. 5 mL), followed by concd. NH_4OH (3 mL) and stirred at ambient temperature. The reaction mixture was monitored by TLC. Once the nonpolar, brown spot of *seco*-chlorin **9a** was consumed [R_f = 0.89 (silica/2.5 vol.-% THF in CH_2Cl_2)], the reaction mixture was filtered through a glass frit (M), the filtrate was transferred to a separatory funnel, CH_2Cl_2 (ca. 20 mL) was added, and the solution was washed with distilled water (3 ×). The concentrated organic phase was purified by preparative plate chromatography to provide **11a** in ca. 90 % yield as a film. R_f = 0.14 (silica/2.5 vol.-% THF in CH_2Cl_2). UV/Vis (CH_2Cl_2): λ_{max} (rel. intensity) = 429 (1), 532 (0.17), 568 (0.058), 611 (0.038), 667 (0.003) nm. ^{1}H NMR (400 MHz, [D$_7$]DMF, 25 °C): δ = 9.13 (s, 1 H, C*H*=N$_{pyrazine}$), 8.80 (d, $^3J_{H,H}$ = 5.2 Hz, 1 H, β-H), 8.77 (d, $^3J_{H,H}$ = 5.2 Hz, 1 H, β-H) 8.45–8.65 (m, 6 H, 2 *o*-Ph-H + 4 β-H), 7.75–8.0 (m, 12 H, Ph-H), 7.7 (m, 2 H, Ph-H), 7.55 (br. s, 2 H, Ph-H), 7.23 (d, $^3J_{H,H}$ = 4.0 Hz, 1 H, N$_{pyrazine}$-C*H*), 6.19 (d, $^3J_{H,H}$ = 4.0 Hz, 1 H, O*H*, exchangeable with D_2O), –1.6 (br. s, 2 H, N*H*, exchangeable with D_2O) ppm. ^{13}C NMR (100 MHz, [D$_7$]DMF, 25 °C): δ = 167.9, 154.6, 153.3, 152.2, 142.4, 141.4, 141.3, 141.2, 140.4, 139.5, 138.0, 136.9, 136.8, 136.0, 134.3, 134.1, 134.0, 133.4, 132.8, 128.7, 128.6, 128.5, 128.4, 128.3, 128.2, 127.8, 127.7, 127.6, 127.5, 127.4, 125.4, 123.4, 121.5, 119.4, 119.0, 67.5 ppm. MS (ESI+, 100 % CH_3CN, cone voltage = 5 V): *m/z* (%) = 647 (65) [M•H]$^+$, 628 (100) [M – H_2O]$^+$. HR-MS (ESI+, 100 % CH_3CN, cone voltage = 30 V, TOF): calcd. for $C_{44}H_{32}N_5O^+$ [M•H]$^+$ 646.2601; found 646.2890.

***meso*-Tetraphenylethoxypyrazinoporphyrin (12a):** Prepared in up to 75 % yield (15 mg) from **8a** (20 mg, 3.0×10^{-5} mol) according to the procedure described for **12b** or from crude **11a** in THF (20 mL) and EtOH (1 mL). Fumes of TFA, taken from the headspace of a bottle, were puffed into the flask to catalyze the final step, whereby too much acid reduced the yield on expense of the formation of an unknown green product (see Supporting Information). Purified by preparatory plate TLC (silica/2.5 vol.-% THF in CH_2Cl_2). R_f = 0.40 (silica/3.3 vol.-% THF in CH_2Cl_2). UV/Vis (CH_2Cl_2): λ_{max} (ε) = 429 (4.84), 532 (3.70), 568 (3.55), 611 (3.39), 667 (3.11) nm. ^{1}H NMR (400 MHz, [D$_6$]DMSO, 25 °C): δ = 8.96 (s, 1 H, C*H*=N$_{pyrazine}$), 8.70 (d, $^3J_{H,H}$ = 4 Hz, 1 H, β-H), 8.66 (d, $^3J_{H,H}$ = 4 Hz, 1 H, β-H), 8.5–8.3 (m, 7 H, β-H and *o*-Ph-H), 7.9–7.6 (m, 18 H), 7.46 (br. d, $^3J_{H,H}$ = 4 Hz, 1 H, *o*,*m*-Ph-H), 6.8 (s, 1 H, N$_{pyrazine}$-C*H*), 3.54 (m, 1 H, OCH_AH$_B$CH$_3$) 3.06 (m, 1 H, OCH$_A$$H_BCH_3$), 0.75 (t, $^3J_{H,H}$ = 8 Hz, 3 H, OCH$_2$CH_3), –1.7 (s, 2 H, N*H*) ppm. ^{13}C NMR (100 MHz, [D$_6$]DMSO, 25 °C): δ = 168.9, 154.4, 153.1, 151.9, 148.8, 141.8, 140.9, 140.7, 140.7, 139.8, 139.7, 137.5, 137.1, 136.7, 136.6, 136.1, 134.4, 134.3, 133.8, 132.7, 129.1, 129.0, 128.74, 128.65, 128.5, 128.1, 128.0, 127.69, 127.65, 125.4, 123.5, 121.6, 119.4, 118.8, 83.1, 63.3 ppm. MS (ESI+, 100 % CH_3CN, cone voltage = 30 V): *m/z* = 674 [M•H]$^+$, 628 [M – EtOH]$^+$. HR-MS (ESI+, 100 % CH_3CN, cone voltage = 30 V, TOF): calcd. for $C_{46}H_{36}N_5O$ [M•H]$^+$ 674.2914; found 674.2908.

***meso*-Tetrakis(4-*tert*-butylphenyl)ethoxypyrazinoporphyrin (12b) (from Dihydroxychlorins without Isolation/Purification of the Intermediate *seco*-Chlorin or Hydroxypyrazinoporphyrin):** Diol **8b** (20 mg, 2.3×10^{-5} mol) was dissolved in $CHCl_3$ (5 mL) at room temp. and stirred; Et_3N (50 µL) and $NaIO_4$/silica gel (1.0 g) were added. As the solution changed color from burgundy to brownish-yellow within 20 min, TLC control assured the complete consumption of the diol; more $NaIO_4$/silica was added as needed. After less than 15 min, the reaction had reached completion. The formation of the *seco*-chlorin aldehyde is indicated by its diagnostic UV/Vis spectrum;[13c] R_f = 0.07 (silica/2.5 vol.-% THF in $CHCl_3$). The mixture was filtered by using a glass frit (M) and the filtrate dried by rotary evaporation. The resulting brown-yellow film of **9c** (ca. 20 mg, 2.30×10^{-5} mol) was dissolved in freshly distilled pyridine (ca. 20 mL), the solution was warmed to 40–50 °C, and concd. NH_4OH (2 mL) was added. As the brownish-yellowish solution changed its color to brown-burgundy and was heated to reflux for 30 min, the reaction progress was monitored by TLC and UV/Vis spectroscopy. Upon completion of the reaction, as per TLC, the solution was dried by rotary evaporation, and the crude material was passed through a short column (silica/2.5 vol.-% THF in $CHCl_3$; the solvent was deacidified prior to use by passing it through a column of basic alumina). Crude **11b**: R_f = 0.5 (silica/2.5 vol.-% THF in $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 9.23 (s, 1 H, C*H*=N$_{pyrazine}$), 8.74 (d, $^3J_{H,H}$ = 5 Hz, 1 H, β-H) overlapping with 8.70 (d, $^3J_{H,H}$ = 5 Hz, 1 H, β-H), 8.65–8.55 (m, 2 H, β-H), 8.53–8.30 (m, 4 H, β-H), 7.9–7.7 (m, 8 H, *o*,*m*-Ph-H), 7.62 (d, $^3J_{H,H}$ = 8 Hz, 2 H, *o*,*m*-Ph-H), 7.58–7.40 (m, 6 H, *o*,*m*-Ph-H), 7.3 (br. s, 1 H, N$_{pyrazine}$-C*H*), 2.5 (m, 4 H, C*H*Me$_2$), 1.1 (m, CH_3, 12 H), –1.6 (br. s, 2 H, N*H*) ppm. HR-MS (ESI+, 100 % CH_3CN, cone voltage = 70 V): *m/z* = 870 [MH$^+$], 852 [M – H_2O]$^+$. ^{1}H NMR: see Supporting Information. Crude product **11b** was immediately dissolved in EtOH (ca. 20 mL), shielded from light with aluminum foil, and stirred at ambient temperature. The color of the solution remained brown as a low-polarity product formed. Upon completion as per TLC (after up to 2 h), the solution was concentrated to dryness by rotary evaporation and the residue purified by preparative plate chromatography (silica/1.25 vol.-% THF in $CHCl_3$) to provide **12b** as a purple-brown solid (12 mg, 58 % from diol **8c**). R_f = 0.51 (silica/2.5 vol.-% THF in $CHCl_3$). UV/Vis (CH_2Cl_2): λ_{max} (log ε) = 432 (4.87), 538 (3.74), 573 (3.60), 613 (3.41) 668 (3.12) nm. Fluorescence (CH_2Cl_2, $\lambda_{excitation}$ = 433 nm): λ_{max} = 675 nm. ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 9.2 (s, 1 H, C*H*=N$_{pyrazine}$), 8.74 (br. s, 1 H, β-H), 8.68 (br. s, 1 H, β-H), 8.62–8.55 (m, 2 H, β-H), 8.5–8.4 (m, 4 H, β-H, *o*,*m*-Ph-H), 8.2–8.0 (br. s, 2 H, *o*-Ph-H), 7.9–7.8 (m, 2 H, *o*,*m*-Ph-H), 7.8–7.7 (m, 5 H, *o*,*m*-Ph-H), 7.7–7.6 (m, 1 H, *o*,*m*-Ph-H), 7.6–7.5 (m, 2 H, *o*,*m*-Ph-H), 7.5–7.4 (m, 2 H, *o*,*m*-Ph-H), 7.04 (s, 1 H, N$_{pyrazine}$-C*H*), 3.78 (dq, $^3J_{H,H}$ = 7.2, 9.4 Hz, 1 H), 3.27 (dq, $^3J_{H,H}$ = 7.2, 9.4 Hz, 1 H), 2.62 (m, 4 H, C*H*Me$_2$), 1.2 (m, 12 H, CH_3), 0.93 (m, 6 H), –1.55 (br. s, 2 H, exchangeable with D_2O, N*H*) ppm. ^{13}C NMR (125 MHz, $CDCl_3$, 25 °C): δ = 169.8, 155.0, 153.5, 151.4, 151.0, 150.9, 150.9, 150.8, 148.6, 140.5, 139.4, 138.7, 138.5, 137.4, 138.1, 137.3, 137.3, 137.2, 136.4, 134.4, 134.3, 134.1, 134.1, 133.4, 132.6, 128.4, 128.2, 126.7, 127.6, 124.5, 124.2, 124.1, 124.1, 124.0, 123.5, 121.3, 120.0, 118.6, 83.4, 63.5, 46.2, 35.1, 31.9, 15.6 ppm. IR (neat, ATR): see Supporting Information. HR-MS (ESI+, 100 % CH_3CN, cone voltage = 30 V, TOF): calcd. for $C_{62}H_{68}N_5O$ [M•H]$^+$ 898.5424; found 898.5453.

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