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Pyrrole-Modified Porphyrins Containing Eight-Membered Heterocycles Using a Reversal of the "Breaking and Mending" Strategy

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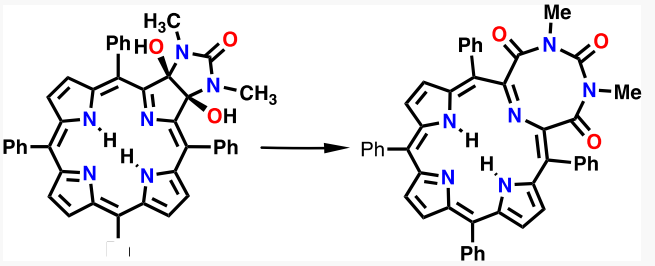
ABSTRACT: The conversion of *meso*-aryl-porphyrins/chlorins to porphyrinoids containing nonpyrrolic heterocycles (so-called pyrrole-modified porphyrins, PMPs) along an approach we dubbed "the breaking and mending of porphyrins" is well known. However, examples are limited to the synthesis of PMPs containing up to six-membered heterocycles; the syntheses of larger rings failed. We report here hitherto unavailable eight-membered chlorin-type PMPs using an inverted "mending and breaking" approach. All examples are based on the addition of *N,N′*-dimethylurea derivatives to a *meso*-phenyl-*β,β′*-dioxoporphyrin, followed by oxidative cleavage of the intermediate diol adduct. We correlate the extremely nonplanar solid-state structures of three crystallographically characterized PMPs containing an eight-membered ring with their solution-state optical properties. The first examples of bis-modified, bacteriochlorin-type PMPs containing either two eight-membered rings or an eight-membered ring and an imidazolone ring are also detailed. Using other *N,N′*-nucleophiles failed to either generate chlorins containing a *β,β′*-dihydroxypyrroline, a prerequisite for the "breaking step," or the cleavage of those substrates that did generate a diol underwent subsequent reactions that thwarted the generation of the desired PMPs. This contribution adds novel PMPs containing eight-membered rings, highlights the effects these derivatizations have on the macrocycle conformation, and how that affects their optical properties.



INTRODUCTION

A wide structural variety of porphyrin analogues containing nonpyrrolic building blocks, the so-called pyrrole-modified porphyrins (PMPs), have become known.[1] Their study has contributed to the understanding of the concept of aromaticity,[2] provided examples for skeletal rearrangements within porphyrinoid macrocycles,[3] furnished macrocycles with chemosensing[4] and small molecule activation properties,[5] presented porphyrinic frameworks for powerful electrochemical hydrogen evolution reaction catalysis,[6] configurational stable and separable enantiomeric helimers,[7] model compounds for naturally occurring prosthetic groups,[8] photosensitizers and luminescent dyes,[9] and identified a number of chromophores with optical properties inaccessible to regular porphyrins or hydroporphyrins.[10]

The majority of PMPs were prepared by total synthesis.[11] In an alternative and complementary approach, we,[1] and others,[11c,e] prepared a variety of PMPs containing one or two nonpyrrolic heterocycles by step-wise conversion of a porphyrin (or chlorin). We dubbed this approach "the breaking and mending of porphyrins."[1] For example, *meso*-tetraphenylporphyrin $\mathbf{1}^{Ph}$ may be dihydroxylated; the diol functionality of the resulting chlorin **2** can then be used as a synthetic handle for oxidative diol cleavage reactions (Scheme 1).[1]

This "breaking" step may result in the formation of a secochlorin bisaldehyde **3** or a secochlorin biscarboxylic acid **4**. These bifunctional intermediates are then reacted in a "mending" step to provide, for example, morpholinochlorin **5** incorporating a six-membered morpholine moiety[7b] or porpholactone **6** containing a five-membered oxazolone moiety,[12] respectively. Our "breaking and mending" approach proved to be versatile for the generation of a variety of four-, five-, and six-membered PMPs.[1]

Porphyrinoids containing seven-membered rings prepared by total synthesis are stable. The best investigated systems are tropiporphyrins, a member of the carbaporphyrin family.[11d] Their phthalocyanine congeners, azepiphthalocyanines, were also reported.[13] In contrast, our attempts to generate seven-membered ring-containing PMPs (such as 1,4,5-triazaazepine

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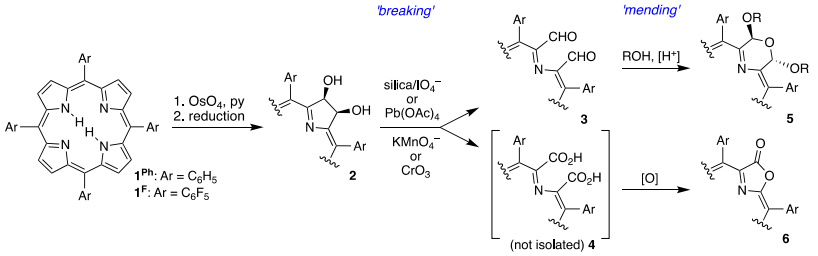
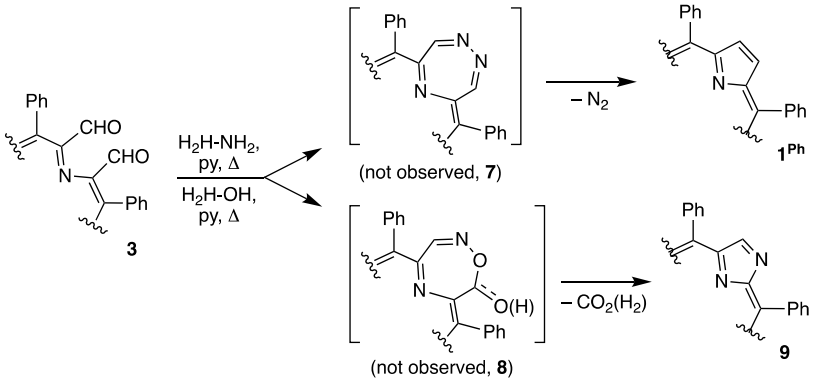
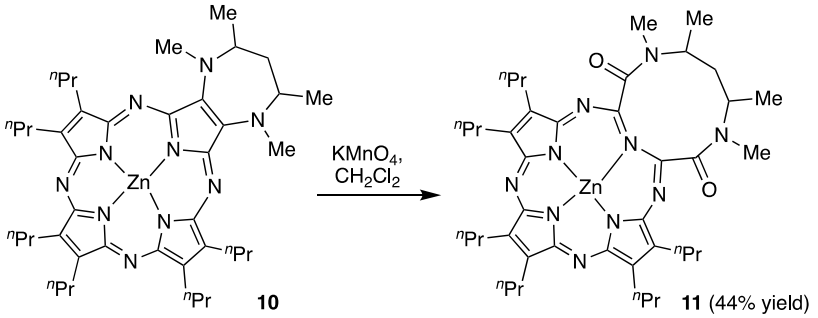
Scheme 1. Examples of the "Breaking and Mending" Methodology of Porphyrin 1 to Generate Pyrrole-Modified Porphyrins (PMPs) 5 and 6



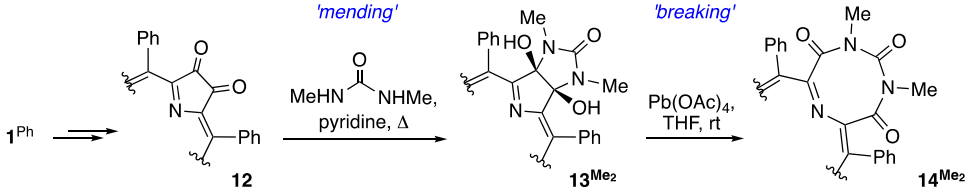
Scheme 2. Examples of "Breaking and Mending" of Porphyrin Reactions that Failed to Provide the Target PMP Containing a Seven-Membered Heterocycles[14]



Scheme 3. Synthesis of a Pyrrole-Modified Porphyrazine Containing a 10-Membered Nonpyrrolic Building Block[15]



Scheme 4. Synthesis of a PMP Containing an Eight-Membered Nonpyrrolic Building Block Using the "Mending and Breaking" Methodology[17]



in 7 or 1,3-diaza-5-oxaazepine in **8**) by cyclization of **3** with hydrazine or hydroxylamine, respectively, failed (Scheme 2).[14]

In all likelihood, PMPs containing a seven-membered heterocycle formed but then rapidly extruded a small molecule (N_2 or CO_2, respectively), regenerating a porphyrinic macrocycle of four five-membered rings.[14] In addition, entirely different pathways not involving a large ring intermediate also became competitive that generated a (substituted) porphyrin.[14a] While these outcomes highlight the large stability of the natural porphyrinic architecture—the driving force for many skeletal rearrangements,[3] they also highlight a limitation of our "breaking and mending" approach toward pyrrole-modified porphyrins containing medium-sized rings.

In 2003, the groups of Barrett and Hoffman provided a simple and elegant example for the generation of a 10-membered heterocycle-containing pyrrole-modified porphyrazine by cleavage of the bridge of a seven-membered ring in **10** that is annulated to a pyrrolic building block (Scheme 3):[15] The β,β'-diamine-substituted double bond was selectively and oxidatively cleaved to provide pyrrole-modified porphyrazine **11**. Precursor diazepine-annulated porphyrazine **10** was prepared by total synthesis.

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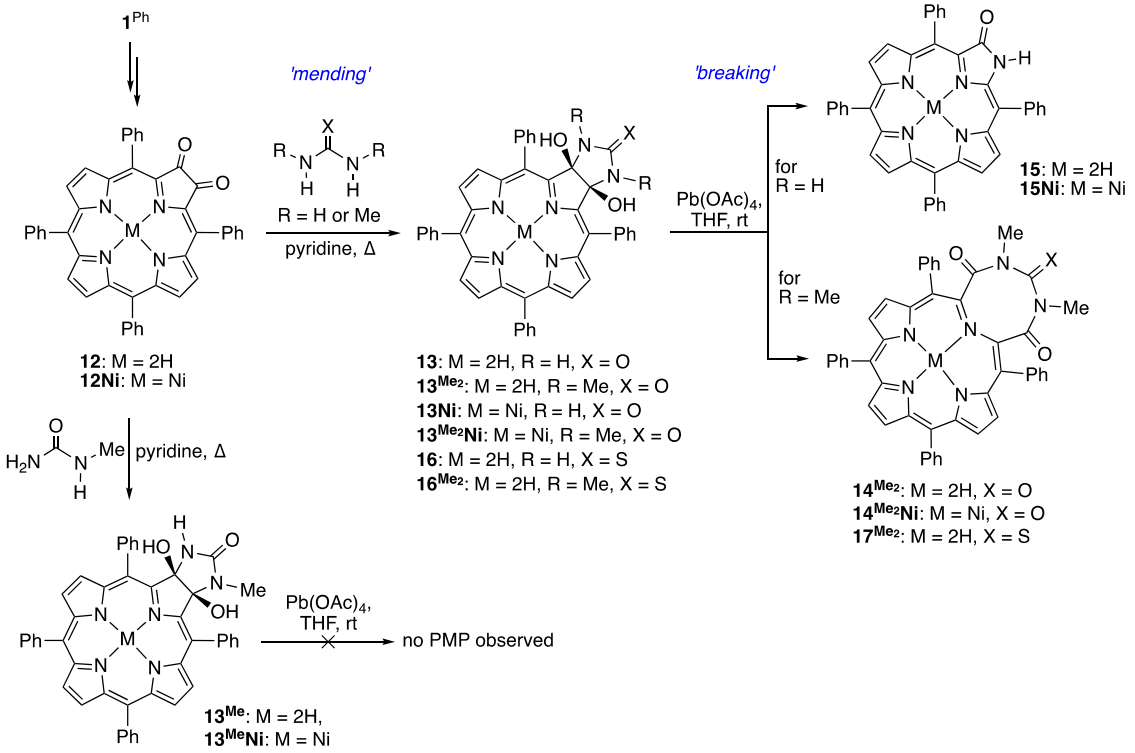
Scheme 5. Formation of Pyrrole-Modified Porphyrins Containing 1,3,6-triazocine-2,4,8-trione Rings



This precedent of cleaving the bridge between two smaller annulated rings to generate a larger ring—a common strategy to generate medium-sized rings outside the realm of porphyrinoid chemistry,[16] inspired our approach toward medium-sized ring PMPs we demonstrated in a preliminary report.[17] Thus, following a reversal of the established "breaking and mending" approach, the formation of a pyrrole-modified porphyrin **14**^{Me2} containing an eight-membered 1,3,6-triazocine-2,4,8-trione heterocycle was possible by oxidative cleavage of the diol functionality in annulated chlorin **13**^{Me2}, the addition product of porphyrin dione **12** with dimethylurea (Scheme 4). However, the diol cleavage of the adduct between dione **12** and urea did not generate the expected eight-membered ring; instead, the product collapsed to provide known porpholactam (Scheme 5).[17] While this reaction is imminently useful for the efficient generation of *meso*-arylporpholactams,[18] it foreshadowed a limitation of the "mending and breaking" methodology.

We present here the full account of our preliminary findings and our attempts to generalize the "mending and breaking" approach toward eight-membered (or larger) ring chlorin-type PMPs, as well as two bis-modified, bacteriochlorin-type PMPs containing one or two eight-membered rings. We thus present a number of examples of hitherto unavailable PMPs for further study that are accessible in few steps from *meso*-tetraphenylporphyrin **1**^{Ph}. We correlate their solid-state structures, as determined by X-ray single-crystal diffractometry, with their solution-state optical properties. As examples presented will highlight also, our "mending and breaking" approach is also imbued with limitations with respect to product scope and a true generalization of the method.

■ RESULTS AND DISCUSSION

Synthesis of Imidazolidinone-Annulated Diol Chlorins. Known *meso*-tetraarylporphyrin β,β'-dione **12** and its nickel complex **12Ni** are accessible from the corresponding porphyrin **1**^{Ph} along a number of complimentary routes.[19] The regular ketone reactivity of these diones was amply demonstrated,[19b] including in reactions generating PMPs.[20] For example, the reaction of dione **12** with diamines generates diimines.[21] We found now that the reaction of **12**/**12Ni** with urea, *N*-methylurea, and *N*,*N*′-dimethylurea generated dihydroxychlorins **13**/**13Ni**, **13**^{Me}/**13**^{Me}**Ni**, and **13**^{Me2}/**13**^{Me2}**Ni**, respectively, bearing imidazolidinone moieties annulated at their β,β'-positions (Scheme 5).

Diagnostics for the formation of the annulated (metallo)-dihydroxychlorin structure are the preservation of the mirror-symmetry of the adducts **13**/**13Ni** and **13**^{Me2}/**13**^{Me2}**Ni**, as seen in their NMR spectra, the pyrroline carbon signals in their ^{13}C NMR spectra (found at δ = 158.1 ppm for **13**), their regular (metallo)chlorin-like spectra when compared to the much broadened spectra for dione **12**/**12Ni**[22] (Figure 1), and their expected compositions (as per high-resolution mass spectrometry (HRMS)). The presence of the urea-type carbonyl functionality in the annulated ring is indicated in their ^{13}C NMR spectra (for **13** at δ = 159.0 and 161.5 ppm for **13**^{Me2}) and IR spectra ($\nu_{C=O}$ at 1716 cm^{-1} for **13** and 1680 cm^{-1} for **13**^{Me2}). ^{1}H NMR spectroscopy also allows a facile distinction between the methylated derivatives **13**^{Me2}/**13**^{Me2}**Ni** (singlets at 2.27/2.14 ppm, 3H) and the nonmethylated derivatives **13**/**13Ni** (singlets at 5.68/5.90 ppm, 1H, exchangeable with D_2O). The methylurea adducts **13**^{Me}/**13**^{Me}**Ni** show essentially the same diagnostic spectroscopic signatures, except that the NMR spectra of these nonaxial symmetric compounds are correspondingly more complex. For further spectroscopic details, see the Supporting Information.

The reaction of urea and thiourea with a β,β'-dione to lead to the formation of the diol adduct is unusual as such additions are usually accompanied by loss of two equivalents of water to afford diimine products.[23] The conformational restrictions

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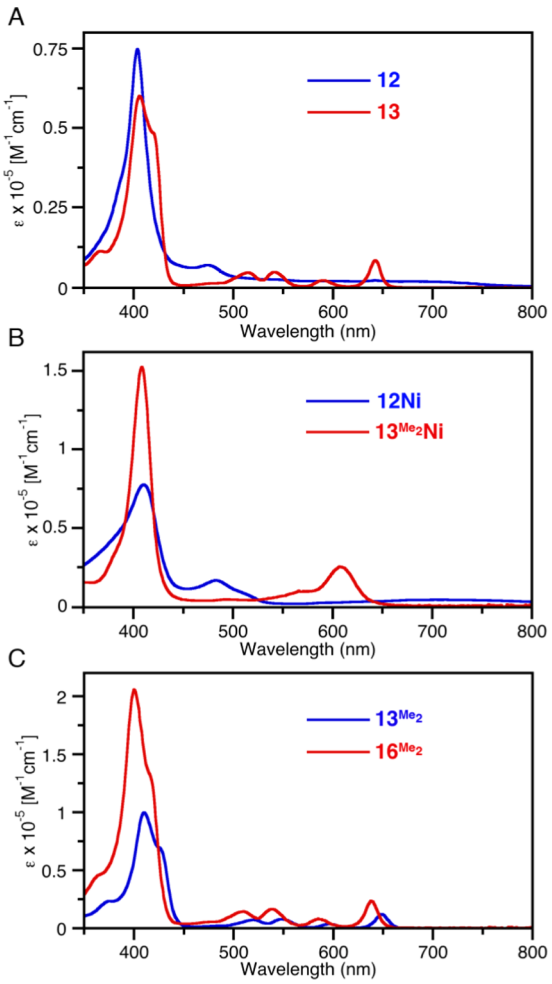

Figure 1. UV−vis spectra (CH_2Cl_2) of the compounds indicated.

imposed by the chlorin framework may prevent the dehydration reaction.

Crystals of annulated chlorin diol $\mathbf{13}^{Me2}$ suitable for single-crystal X-ray analysis could be obtained, confirming its spectroscopically assigned connectivity and its *cis*-diol configuration (Figure 2A−C). The macrocycle conformation of the annulated chlorin shows a considerable ruffling and saddling deformation (Figure 2D,E). In comparison to the parent diol chlorin **2** (as its dimethyl ether derivative),[24] the conformation of $\mathbf{13}^{Me2}$ is significantly more nonplanar, likely as a result of the strain induced by the enforced eclipsed conformation of the two pyrroline−imidazolidinone nitrogen bonds. The deformation of $\mathbf{13}^{Me2}$ removes the spectroscopically determined twofold symmetry of the molecule, suggesting that its conformation is dynamic in solution. A number of comparable chlorins annulated to five-membered heterocycles have been reported before, often made by 1,3-dipolar cycloaddition reactions.[25]

An addition to dione **12** is also possible using thiourea, generating thione chlorin diol adduct **16**. This adduct possesses the expected composition and similar spectroscopic properties as the corresponding oxo-congener **13**, though with a slightly blue-shifted optical spectrum (Figure 1). However, thiourea adduct **16** proved to be chemically much less stable than its oxo-analogue **13**, as evidenced by the facile reversal back to the starting materials during its chromatographic isolation on untreated silica gel or upon standing in solution (CH_2Cl_2, $CHCl_3$). Addition of triethylamine to the eluents suppressed—but did not entirely eliminate—this reversion reaction during chromatography. The corresponding addition reaction using dimethylthiourea generated the comparably more robust dimethylimidazolidinthione chlorin diol adduct $\mathbf{16}^{Me2}$, featuring the expected composition and spectroscopic properties.

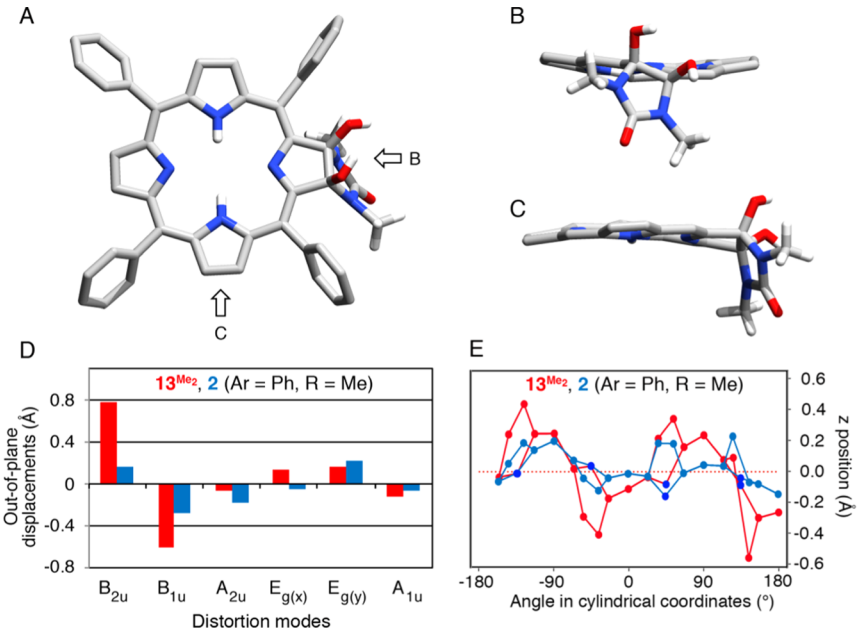

Figure 2. Stick representation of the X-ray single-crystal structures of chlorin diol $\mathbf{13}^{Me2}$. (A) Top view: the arrows indicate the view direction represented in side views (B) and (C). All disorder, all hydrogen atoms bonded to sp^2-carbons, and solvents were removed for clarity. *meso*-Phenyl groups removed for clarity in all side views. (D) NSD analysis[26] of the out-of-plane distortion modes observed in the crystal structures of adducts $\mathbf{13}^{Me2}$ and corresponding chlorin diol **2** (Ar = Ph, R = Me).[24] (E) Overlay of the out-of-plane plots of the macrocycle atomic positions of adducts $\mathbf{13}^{Me2}$ and the corresponding parent chlorin diol **2** (Ar = Ph, R = Me).[24]

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Pyrrole-Modified Porphyrins Containing a 1,3,6-Triazocine-2,4,8-trione Ring. We reasoned that the *vic-cis*-diol moiety in the annulated chlorins **13**/**13Ni** should be susceptible to an oxidative diol cleavage, opening the bridge between the two annulated rings to form an eight-membered ring. Indeed, treatment of these diols using classic diol chlorin cleavage conditions ($Pb(OAc)_4$ in tetrahydrofuran (THF))[27] led to a rapid conversion of the starting materials and the formation of a single main, nonpolar product in acceptable yields. However, the products turned out to be known porpholactams **15**/**15Ni**,[28] respectively. We previously detailed this useful alternate and comparably efficient reaction pathway toward porpholactams.[18] Similarly, thiourea adduct **16** also produced, next to significant amounts of the starting material **12**, porpholactam **15**.

While no intermediates could be observed, we surmise that the target eight-membered ring formed but immediately fragmented (under the expulsion of the formal fragment C_2HNO_2/C_2HNOS). Once again, the expulsion of smaller fragments from the putative target molecule, the medium-size ring derivative, established a stable "tetrapyrrolic" architecture.[14] This reactivity highlights that a major shortcoming of the "breaking and mending" strategy is not principally overcome when using the inverted "mending and breaking" methodology.

To access the desired eight-membered PMPs, we concluded that a blocking of the fragmentation pathways of the putative intermediate (the target PMP) would be required. Alas, we did not know the fragmentation mechanism, but it was simple to test whether the generation of the *N*-alkylated derivatives would block, for example, proton transfer reactions that might be crucial for the fragmentation reactions. This was the drive behind the preparation of the mono- and di-$N_{imidazole}$-methylated chlorin diols $\mathbf{13}^{Me}$/$\mathbf{13}^{Me}$**Ni**, $\mathbf{13}^{Me2}$/$\mathbf{13}^{Me2}$**Ni**, and $\mathbf{16}^{Me2}$.

Our intuition was confirmed: Oxidative cleavage of the $N_{imidazole}$-dimethylated products $\mathbf{13}^{Me2}$, $\mathbf{13}^{Me2}$**Ni**, and $\mathbf{16}^{Me2}$ generated compounds in good yields that possessed compositions of two hydrogen atoms less than the starting material (as per HRMS), suggestive that our target compounds were formed without subsequent fragmentation. On the other hand, the mono-methylated diols $\mathbf{13}^{Me}$/$\mathbf{13}^{Me}$**Ni** degraded upon oxidation, not allowing the identification of any of the dozen compounds formed. This points at the importance of *N*-alkylation of all amide nitrogens in the molecule to prevent fragmentation reactions.

The NMR spectra of the dimethylated oxidation products retained the twofold symmetry of their starting materials with a downfield shift of the inner core protons (δ_{NH} = 1.86 ppm for $\mathbf{14}^{Me2}$; -0.21 ppm for $\mathbf{17}^{Me2}$) when compared to regular porphyrins or chlorins (δ_{NH} typically below -1 ppm), suggestive of a nonplanar chromophore (or a porphyrinoid with a compromised aromatic system), and the presence of two lactam carbon atoms in different environments (δ = 173.1 and 155.5 ppm for $\mathbf{14}^{Me2}$; 171.7 and 155.2 ppm for $\mathbf{14}^{Me2}$**Ni**; 186.9 and 171.8 ppm for $\mathbf{17}^{Me2}$). Thus, all spectroscopic evidence points toward the successful formation of the expanded pyrrole-modified porphyrin $\mathbf{14}^{Me2}$, $\mathbf{14}^{Me2}$**Ni**, and $\mathbf{17}^{Me2}$, respectively.

The optical spectra of the compounds can be characterized as significantly red-shifted chlorin-type optical spectra (Figure 3). The general red shift of the spectra and particularly the observed reduction of the extinction coefficient of their Soret bands suggest the increase in nonplanarity of the chromophore, while their general broadening suggest an increase of conformational flexibility.[29] For a further discussion of the optical spectra, see below. Neither compound was chemically robust enough to be reversibly protonated using trifluoroacetic acid (TFA).

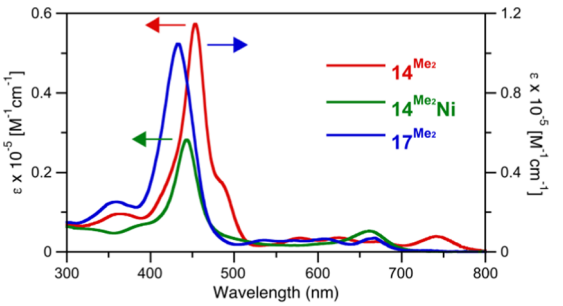

Figure 3. UV−vis absorption spectra (CH_2Cl_2) of the compounds indicated.

A single-crystal X-ray structure analysis of $\mathbf{14}^{Me2}$, $\mathbf{14}^{Me2}$**Ni**, and $\mathbf{17}^{Me2}$ provided the final proof for the unique connectivity of these PMPs (Figure 4A−I). The pyrroline β,β'-bonds of the starting chlorin diols were oxidatively cleaved and both affected β-carbons were converted in the process to lactam carbonyl groups that are incorporated into a 1,3,6-triazocine-2,4,8-trione ring. As designed, this eight-membered ring is the result of a fusion of the three annulated dimethylurea atoms with the five pyrroline atoms.

In $\mathbf{14}^{Me2}$/$\mathbf{14}^{Me2}$**Ni**, the nonpyrrolic moiety assumes a significantly nonplanar conformation with an almost 90° twist along its long axis. This twist translates into the porphyrinic framework, leading to a significantly ruffled conformation. Interestingly, the conformations of both the free base as well as its corresponding nickel complex are qualitative very similar (cf. Figure 4J,L), with the nickel complex quantitatively much less ruffled, whereas in many other cases, the insertion of the small ion Ni(II) into a porphyrinoid causes a significant amplification of an innately ruffled free base or the introduction of a ruffled distortion into a planar free base macrocycle.[30]

The conformation of the thione $\mathbf{17}^{Me2}$ derivative is quantitatively significantly less distorted from planarity than its corresponding oxo-derivative $\mathbf{14}^{Me2}$ and the conformation of the eight-membered ring is qualitatively much different, also.

The greater planarity of the macrocycle of $\mathbf{17}^{Me2}$ compared to that of the oxo-analogue $\mathbf{14}^{Me2}$ is also reflected in the much smaller $C_\beta-C_\alpha-(N)-C_\alpha-C_\beta$ dihedral angle in the eight-membered ring (90.4° in $\mathbf{14}^{Me2}$, 40.9° in $\mathbf{17}^{Me2}$). This angle is important as it was discovered to strongly affect the UV−vis absorption spectrum λ_{max} values of morpholinochlorins,[31] with a larger torsion angle being correlated with a longer λ_{max} in their UV−vis absorption spectra. Indeed, λ_{max} of oxo-derivative $\mathbf{14}^{Me2}$ is 741 nm, whereas that of the thiono-analogue $\mathbf{17}^{Me2}$ is much shorter, with a λ_{max} of 668 nm (Figure 3). This serves as a validation that the influence of the $C_\beta-C_\alpha-(N)-C_\alpha-C_\beta$ dihedral angle on the optical properties of the PMPs is applicable to compounds beyond the morpholinochlorins for which this influence was discovered.[31]

This generalization may also allow a prediction to be made for the (unknown) conformation of pyrrole-modified porphyrazine **11**. As its λ_{max} value is, at 644 nm, surprisingly close to that of a regular porphyrazine,[32] it suggests the presence of a

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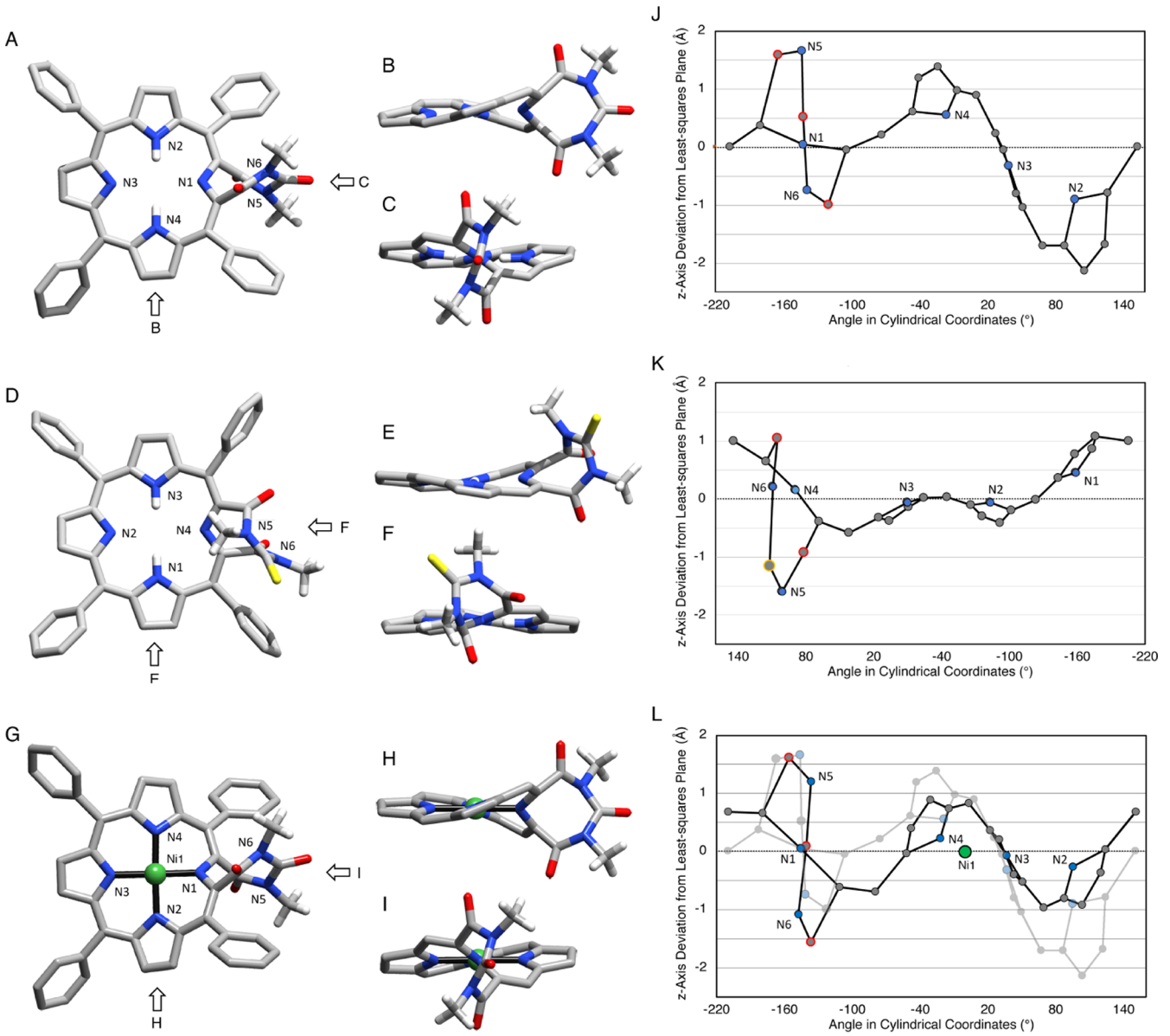

Figure 4. Stick representation of the X-ray single-crystal structures showing top and side views for $\mathbf{14}^{\mathbf{Me2}}$ (A–C) (CCDC # 1479383),[17] $\mathbf{17}^{\mathbf{Me2}}$ (D–F), and $\mathbf{14}^{\mathbf{Me2}}\mathbf{Ni}$ (G–I). The arrows indicate the respective viewing directions. All disorder, all hydrogen atoms bonded to sp^2-carbons, and solvents (where present) are removed for clarity. All *meso*-phenyl substituents also removed in top and side views. Skeletal plots for $\mathbf{14}^{\mathbf{Me2}}$ (J), $\mathbf{17}^{\mathbf{Me2}}$ (K), and $\mathbf{14}^{\mathbf{Me2}}\mathbf{Ni}$ (L). Nickel ion arbitrarily placed at 0° (but with proper z-axis displacement); light gray structure in L is the skeletal plot of $\mathbf{14}^{\mathbf{Me2}}$ (J) for reference. Gray = carbon atoms, gray with red rim = carbonyl carbon atoms, and gray with yellow rim = thiocarbonyl carbon atoms.

very small C_β–C_α–(N)–C_α–C_β dihedral angle in the nonpyrrolic 10-membered ring; since the 10-membered ring is unlikely planar, it might be folded into a figure eight-like conformation, allowing for a smaller C_β–C_α–(N)–C_α–C_β dihedral angle and, by extension, also for more planar macrocycle conformation.

The structurally characterized eight-membered PMPs were crystallized as racemic mixture of two helimers. We were able to show that a number of PMP classes also forming helimeric stereoisomers were conformationally rigid enough to allow their chiral resolution (by chiral HPLC).[7] The study of the conformational flexibility of the triazocinone-based PMPs, including experiments geared toward their chiral resolution, are ongoing and will be reported in due course.

Toward PMPs Containing a Nine-Membered Ring. The preparation of chlorins annulated with six-membered rings to the pyrroline β,β'-bond was also explored (Scheme 6). Cleavage of the annulation site would then give rise to a PMP containing a nine-membered nonpyrrolic building block. For our methodology to succeed, however, we require a diol functionality at the annulation site. Our finding that urea nitrogen atoms add to the dione carbonyl group but do not dehydrate to provide an imine suggested the search for diamides or urea derivatives in which two nucleophilic nitrogen atoms are four atoms apart.

Our first choice, oxamide, yielded no product upon refluxing it with dione **12** in pyridine, even for extended periods. Since the nucleophilic sites in oxamide are trans to each other, not at all favoring the formation of a *syn–vic* adduct, we also tested squaramide (not shown) and di-*N*-methylsquaramide as nucleophiles.[33] In both derivatives, the nucleophilic sites are forced to be cis to each other. Alas, no addition reaction of

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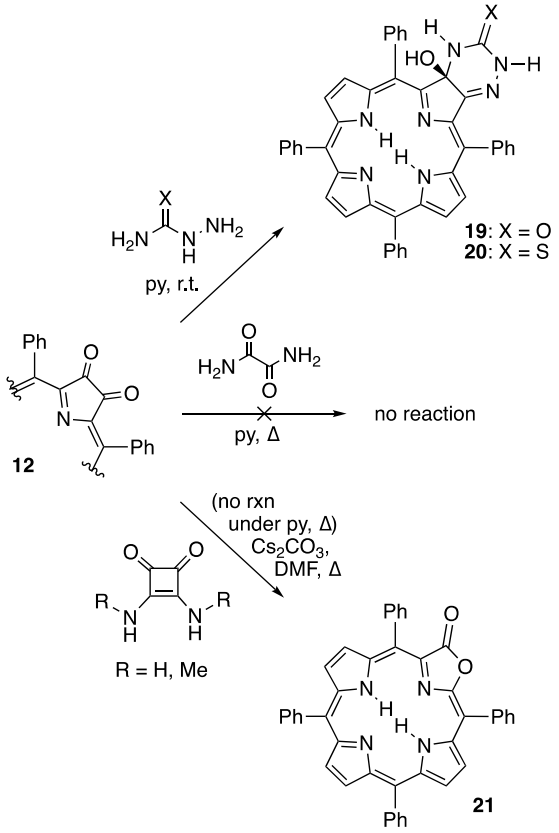
Scheme 6. Reactions Aimed at the Generation of Diol Chlorins Annulated to a Six-Membered Ring



either reagent to **12** could be achieved under a range of conditions tested. If the reaction conditions were too basic or exceedingly long, dione **12** converted to form porpholactone **21**, a known (oxidative) degradation product of *β*,*β*′-dioxoporphyrin **12** under basic conditions.[20a]

We then turned our attention to the hydrazine analogues of urea, semicarbazides and their thio-analogues. Addition of an excess of semicarbazide hydrochloride to dione **12** yielded, within minutes at ambient temperature, a polar red and chemically unstable product with a crude UV−vis spectrum resembling that of a chlorin (not shown) and the composition ($C_{45}H_{34}N_7O_3$ for its $[M + H]^+$, as per HRMS) of the expected adduct diol chlorin. However, it dehydrates readily and forms a stable, less polar, green product **19** (of the composition $C_{45}H_{32}N_7O_2$ for its $[M + H]^+$, as per electrospray ionization $(ESI)^+$ HRMS) upon isolation and purification of the primary product. In product **19**, the chlorin-type characteristics of the UV−vis spectrum of the primary adduct are lost and the spectrum resembles much the spectrum of the starting dione (Figure 5). We interpret this as a clear indication of the position of the dehydration reaction, reestablishing one of the *β*-sp^2-carbon atoms on the chromophore known to severely affect the optical spectra of the chromophore.[22,34] The thiosemicarbazone adduct **20** also possesses the relatively broadened and featureless UV−vis spectrum of its oxo-congener.

The ^{1}H NMR spectrum of the semicarbazide adduct **19** (or the corresponding thiosemicarbazide adduct **20**) showed the presence of a nonsymmetric product with a sharp signal downfield at ∼13 ppm that is exchangeable with D_2O, as well as a pair of exchangeable protons at 4.5 and 5.3 ppm (Figure 6). A ^{1}H−^{1}H NOESY spectrum of the compound revealed that these two protons are close to each other in space, but not neighboring the downfield-shifted exchangeable proton at 13 ppm, suggesting that they are on opposite sides of the annulated six-membered ring. A ^{15}N−^{1}H heteronuclear single quantum coherence (HSQC) experiment confirmed that the peak at 13 ppm corresponds to an N−H proton. An HMBC experiment showed that this proton is correlating with two carbons, further supporting the structure of semicarbazone adduct **19** as the isolated product.

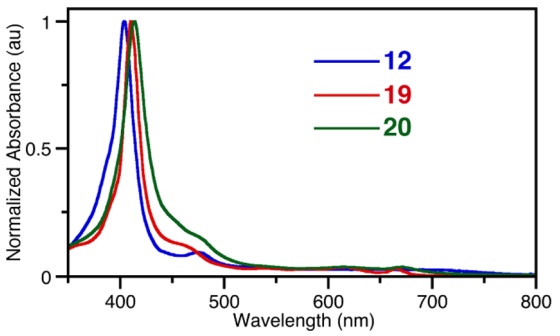


Figure 5. UV−vis spectra (CH_2Cl_2) of the compounds indicated.

Both carbazide adducts **19** and **20** proved to be inert to the $Pb(OAc)_4$-induced (diol) cleavage reaction conditions. We suspect that the greater conformational flexibility within the annulated six-membered ring allows the typical hydrazone formation, thwarting the subsequent oxidative ring expansion of the diol. Attempts to cleave the initially formed product (tentatively assigned to be the diol) in situ also failed. To which degree the utilization of $N_{hydrazine}$-methylated derivatives[35] can prevent the dehydration and any subsequent fragmentation of the diol cleavage product remains to be tested.

Toward PMPs Containing Two Eight-Membered Rings. The conversion of a bacteriochlorin derivative to a bis-modified PMP containing two five- or six-membered heterocycles by performing the same ring-expansion reaction twice concurrently on the same framework is possible, albeit significantly more than "twice as difficult" as the corresponding single pyrrole modification because of the possible formation of regioisomers, stereoisomers, or the chemical instability of the bis-modified systems.[31,36] Doubly modified PMPs containing mixed nonpyrrolic building blocks have also become known; they are generally synthesized in a sequential fashion, as are several bis-modified PMPs that contain the same two nonpyrrolic building blocks.[36a,b,37]

We planned the simultaneous bis-modification of porphyrin $\mathbf{1}^{Ph}$ to incorporate two eight-membered nonpyrrolic rings via the addition of *N*,*N*′-dimethylurea or thiourea to known tetraone **22** and oxidative double cleavage of the resulting bacteriochlorin tetraol. Thus, bis-dihydroxylation of $\mathbf{1}^{Ph}$ generated the well-known bacteriochlorin tetraol;[24] oxidation of the tetraol then delivered known tetraone **22**[38] using a variation of a described transformation (Scheme 7).[39] Reactions of tetraone **22** with stoichiometric excess of *bis*-*N*,*N*′-dimethylurea or thiourea readily generated products. Diagnostics for the formation of the desired adducts **23** and **24** (syn- and anti-isomers; separable for **24** but not for **23**) were their characteristic bacteriochlorin-type UV−vis spectra (Figure 7A) and the high-symmetry ^{1}H and ^{13}C NMR spectra and the expected composition ($C_{50}H_{42}N_8O_6$ and

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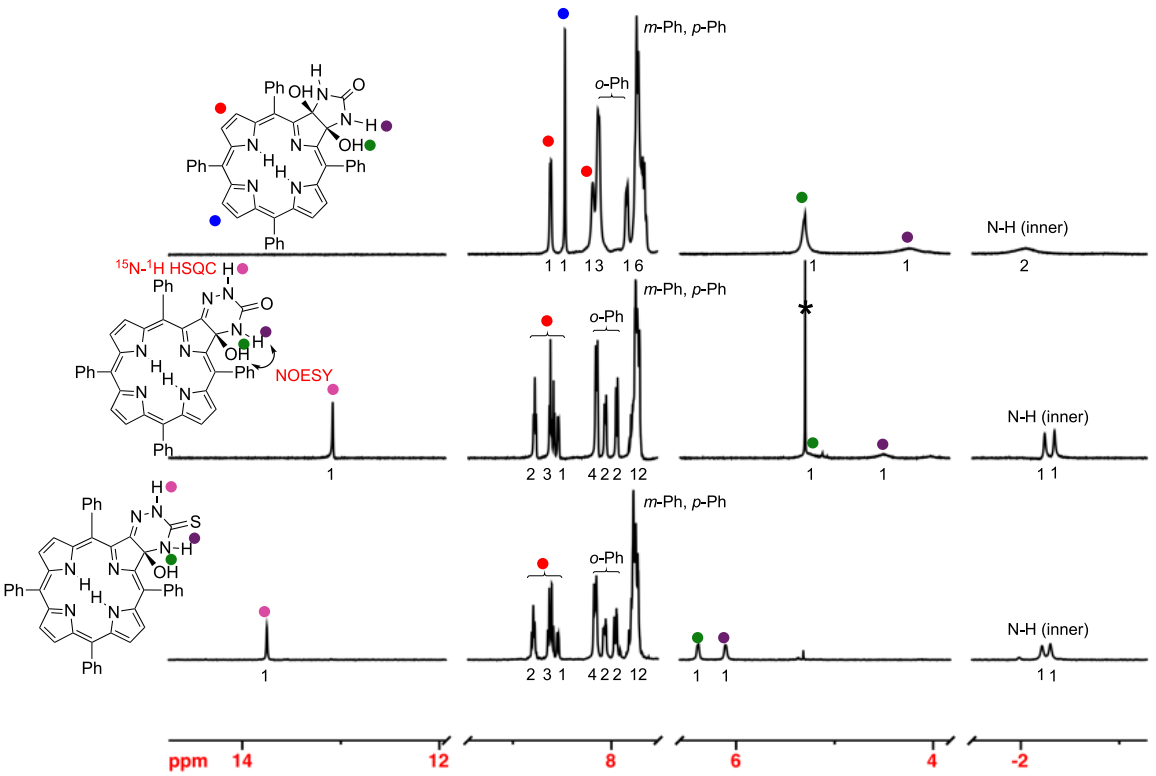
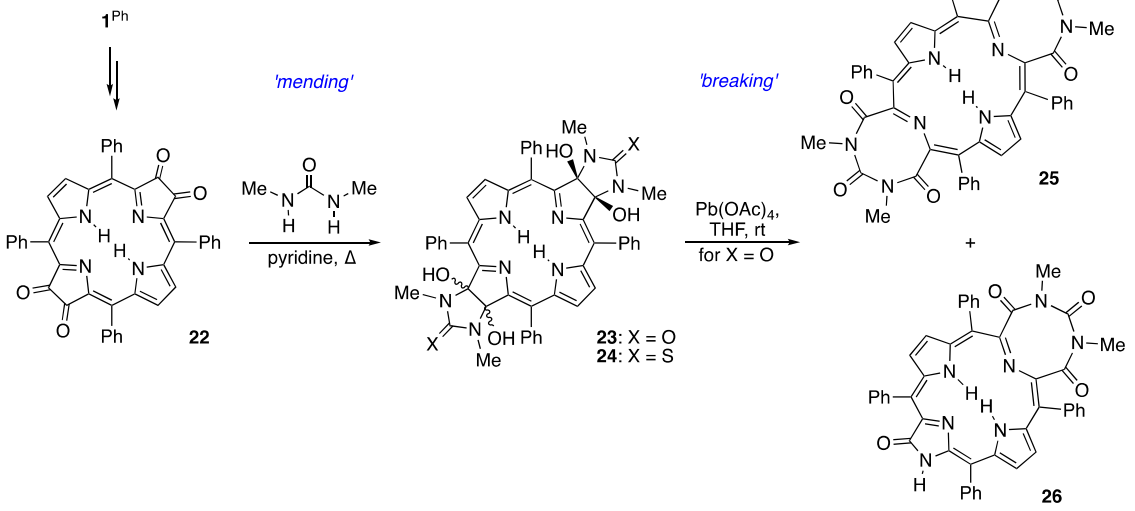


Figure 6. ^{1}H NMR spectra ($CDCl_3$, 25 °C) of the compounds **13** (top), **19** (middle), and **20** (bottom). * residual solvent, CH_2Cl_2.

Scheme 7. Synthesis of Pyrrole-Modified Porphyrins Containing Two 1,3,6-triazocine-2,4,8-trione Rings (25) and One Triazocinetrione Ring and an Imidazolone Moiety (26)



$C_{50}H_{42}N_8O_4S_2$, as per ESI$^+$ HRMS for **23** and **24**, respectively).

The Pb(OAc)$_4$-induced cleavage of tetraol **23** delivered a major product with the expected composition of the bis-expanded PMP product **25** (four hydrogen atoms less than the starting material, i.e., $C_{50}H_{39}N_8O_6$ for $[M + H]^+$, as per ESI$^+$ HRMS). However, chromatographic isolation of this product over silica gel resulted in its decomposition. Pretreatment of the silica with Et_3N, or addition of Et_3N to the eluent, helped to suppress this decomposition enough to allow its isolation and characterization but could not entirely seize it (the compound also slowly decomposes under NMR conditions). Product **25** possesses a much red-shifted, but not typical bacteriochlorin-type, UV–vis spectrum (λ_{max} = 910 nm) (Figure 7B). Diagnostic for the formation of the bis-modified PMP was the preservation of the simplicity of the ^{1}H and ^{13}C NMR spectra of the starting material (see the Supporting Information). The latter feature was also found in the expansion of *meso*-tetraphenyltetrahydroxybacteriochlorins to bis-morpholinobacteriochlorins,[31,36b] but their optical spectra retained bacteriochlorin characteristics.

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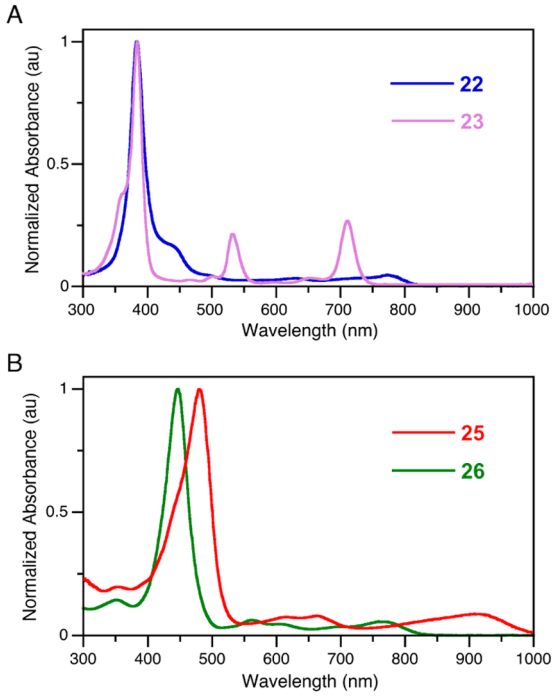

Figure 7. UV−vis spectra (CH_2Cl_2) of the compounds indicated.

The observed high chemical instability of the bis-triazocine expanded PMP is rationalized by the general higher lability of bacteriochlorins toward oxidative processes and the projected high degree of nonplanarity of the chromophore. The latter may also explain the untypical UV−vis spectrum.

In addition to the bis-modified product **25**, we also isolated the most prevalent degradation product formed during its chromatographic isolation. The composition of this product **26** (of $C_{45}H_{31}N_6O_4$ for $[M + H]^+$, as per ESI^+ HRMS) corresponds to a product in which one of the triazocine rings in the bis-expanded precursor **25** collapsed into a five-membered porpholactam ring. The loss of symmetry of this molecule is accordingly reflected in its ^1H and ^{13}C NMR spectra. Diagnostic peaks, like the two inner NH peaks (1H each at 3.03 and 3.12 ppm), two methyl peaks (3H each, at 3.08 and 3.20 ppm), or three lactam carbonyl peaks (at 166.2, 168.8, and 173.7 ppm), can be recognized; the imidazolone lactam NH peak appears to be broadened beyond distinction. The UV−vis spectrum of **26** is similar to the broadened and red-shifted spectrum of the mono-triazocine PMP $\mathbf{14^{Me2}}$ but with an 18 nm red-shifted λ_{max} band (at 759 nm).

The observation of the mixed nonpyrrolic heterocycle PMP **26** is remarkable in multiple ways: First, it highlights that the fragmentation of the *N*-methylated triazocine ring is also possible, even though the results reported above suggested that the *N*-methylated triazocine rings were resistant to fragmentation. Second, the fragmentation also returns the lactam moiety and not, as could have been expected, the *N*-methyl lactam. Thus, we can now only state that the fragmentation of the *N*-methylated expanded derivatives is impeded, but the sterically much more favorable five-membered ring can still form via the expulsion of a fragment, including the cleavage of the *N*-methyl bond. Third, the ESI^+ HRMS spectrum of the bis-modified PMP **26** shows further fragmentations, such as the loss of an $N-CH_3$ fragment, providing hints at possible fragmentation pathways (see the Supporting Information). Finally, the compound also highlights the remarkable electronic influences of the lactam moiety: Its presence induces a significant red shift in **26** compared to the mono-derivatized compound $\mathbf{14^{Me2}}$, even though the parent porpholactams resemble electronically porphyrins very closely. This influence of the β,β'-lactam (and β,β'-lactone) moieties has been described before.[9b,28,37b]

Attempts to oxidatively cleave the bis-thione adduct **24** using $Pb(OAc)_4$ resulted in the reversal back to tetraone **22**. Neither the use of different oxidants (i.e., $NaIO_4$ heterogenized on silica) nor addition of Et_3N to reduce the acidity of the reaction mixture proved successful in preventing this reversion reaction.

CONCLUSIONS

In conclusion, a novel class of ring-expanded pyrrole-modified porphyrins incorporating an eight-membered heterocycle (triazocine) could be accessed using an annulation → oxidative cleavage strategy, i.e., using a reversal of our well-established "breaking and mending strategy." The synthesis and structural characterization of the free base oxo- ($\mathbf{14^{Me2}}$) and thio-analogues ($\mathbf{17^{Me2}}$) and the comparison of their optical properties provided further insight into the validity of a recent proposal that the optical properties of a porphyrinic macrocycle are to a large degree determined by the $C_\beta-C_\alpha-(N)-C_\alpha-C_\beta$ dihedral angle of the modified pyrrole.[31] The nickel complex $\mathbf{14^{Me2}Ni}$ proved to be less conformationally distorted than the free base, in deviation of the common trend upon coordination to nickel(II). The preparation of analogues containing a nine-membered ring along the same methodology proved unsuccessful, however. All attempts were thwarted by our inability to annulate larger than five-membered rings to the pyrrolic β,β'-position while retaining the crucial synthetic diol chlorin handle. Any degree of generalization of the "mending and breaking" method could thusly not be achieved. However, the modification strategy could be applied to the formation of a bacteriochlorin-type PMPs containing two triazocines. The isolation of one of its fragmentation products containing a single triazocine and an imidazolone moiety shed some light on possible fragmentation pathways.

This study contributed to the continued efforts of generating porphyrin analogues that push the limits of conformation, conformational flexibility, and framework heteroatom replacements and makes a range of unique porphyrinoids available for further study.

EXPERIMENTAL SECTION

Materials. All solvents and reagents (Aldrich, Acros) were used as received. *meso*-Tetraphenylporphyrin diones **12** and **12Ni** were prepared as described previously.[19a] Analytical (aluminum backed, silica gel 60, 250 μm thickness) and preparative (20 × 20 cm, glass backed, silica gel 60, 500 μm thickness) thin-layer chromatography (TLC) plates and standard grade, 60 Å, 32−63 μm flash column silica gel were used. All reactions involving the use of heat were carried out using a heating mantle.

Instruments. ^1H NMR and ^{13}C NMR spectra were recorded using Bruker AVANCE III 400 and 500 MHz NMR spectrometers in the solvents indicated. Residual solvent peaks were used to reference the spectra. UV−vis spectra were recorded using a Varian Cary 50 spectrophotometer in the solvents indicated. IR spectra were recorded from neat material on a Bruker α Fourier transform infrared (FT-IR) spectrometer using an attenuated total reflection (ATR) diamond crystal. High-resolution mass spectra were recorded from CH_3CN solutions ($\sim 10^{-6}$ M) using an AB Sciex QStar Elite Quadrupole-TOF mass spectrometer.

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X-Ray Single-Crystal Diffractometry. Details of the data collection and structural parameters for the structure elucidation of **13^{Me2}**, **14^{Me2}Ni**, **17^{Me2}**, descriptions of disorder and hydrogen atom treatment, and software packages used can be found in the Supporting Information.

*meso-Tetraphenyl-imidazolidinone-Annulated Dihydroxychlorin (**13**).* Dione **12** (118.0 mg, 1.83 × 10^{-4} mol) was dissolved in pyridine (25.0 mL) in a round-bottom flask equipped with a magnetic stir bar. Urea (245 mg, 4.08 × 10^{-3} mol, 22 equiv) was added and the mixture was heated to reflux for 30 min under a N_2 atmosphere. Subsequently, the solvent was evaporated in vacuo. The remaining residue was taken up in chloroform and filtered through a glass frit. The filtrate was washed with water (5 × 25 mL) and dried over anhydrous sodium sulfate. The dried residue was separated by column chromatography (silica, CH_2Cl_2-5% MeOH), recovering dione **12** in 8% yield (9 mg), followed by the magenta product **13** in 85% yield (110.5 mg) as a dark solid: R_f (silica-CH_2Cl_2/5% MeOH) = 0.36; ^{1}H NMR (400 MHz, dimethyl sulfoxide (DMSO)-d_6): δ 8.65 (d, ^3J = 4.8 Hz, 1H), 8.40 (s, 1H), 8.19−8.17 (m, 2H), 8.10 (d, ^3J = 6.0 Hz, 2H), 7.93 (d, ^3J = 6.4 Hz, 1H), 7.78−7.73 (m, 6H), 6.97 (s, 1H, exchangeable with D_2O), 5.68 (s, 1H, exchangeable with D_2O), and −2.14 (s, 1H, exchangeable with D_2O) ppm; ^{13}C{^{1}H} NMR (100 MHz, DMSO-d_6): δ 159.0, 158.1, 152.3, 140.9, 140.6, 139.5, 134.9, 134.7, 133.7, 133.6, 132.7, 128.1, 128.0, 127.0, 126.9, 126.8, 125.2, 122.6, 112.4, and 93.1 ppm; UV−vis (CH_2Cl_2) λ_{max} (log ε) 406 (5.41), 512 (4.30), 541 (4.30), 591 (3.96), and 642 (4.53) nm; FT-IR (neat, diamond ATR): $\nu_{C=O}$ = 1715.7 cm^{-1}; HRMS (ESI) m/z: [M + H]$^+$; calcd for $C_{45}H_{33}N_6O_3$ 705.2609; found 705.2607.

*[meso-Tetraphenyl-imidazolidinone-Annulated Dihydroxychlorinato]nickel(II) (**13Ni**).* Prepared from **12Ni** (143 mg, 2.04 × 10^{-4} mol) as described for **13** using urea (234 mg, 3.90 × 10^{-3} mol, 19 equiv). Recovery of 10% of the dione **12Ni** (15 mg) and isolation of the dark blue solid **13Ni** in 75% yield (116 mg): R_f (silica-CH_2Cl_2/5% MeOH) = 0.29; ^{1}H NMR (400 MHz, DMSO-d_6): δ 8.30 (dd, ^3J = 4.8 Hz, 2.8 Hz, 2H), 8.17 (s, 1H), 7.84 (two overlapping d, ^3J = 3.2 Hz, 2H), 7.71−7.68 (m, 5H), 7.60−7.57 (m, 3H), 6.76 (br s, 1H, exchangeable with D_2O), 5.90 (s, 1H, exchangeable with D_2O) ppm; ^{13}C{^{1}H} NMR (100 MHz, DMSO-d_6): δ 158.7, 145.9, 145.6, 140.4, 138.9, 137.5, 137.4, 133.3, 132.6, 132.5, 129.1, 128.2, 127.6, 127.5, 127.4, 123.4, 110.4, 93.8 ppm; UV−vis (CH_2Cl_2) λ_{max} (log ε) 415 (4.26), 575 (sh), 607 (3.49) nm; FT-IR (neat, diamond ATR): $\nu_{C=O}$ = 1716.0 cm^{-1}; HRMS (ESI) m/z: [M − H]$^-$; calcd for $C_{45}H_{29}N_6NiO_3$ 759.1655; found 759.1640.

*meso-Tetraphenyl-N,N′-dimethylimidazolidinone-Annulated Dihydroxychlorin (**13^{Me2}**).* Prepared from 2,3-dioxoporphyrin **12** (30.0 mg, 4.65 × 10^{-5} mol) in pyridine (8.0 mL) as described for **13** but using *N,N′*-dimethylurea (82 mg, 9.31 × 10^{-4} mol, 20 equiv) to afford dihydroxychlorin **13^{Me2}** in 54% yield (18.5 mg) as a dark red solid: R_f (silica-CH_2Cl_2/3% MeOH) = 0.56; ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.58 (d, ^3J = 4.5 Hz, 1H), 8.46 (s, 1H), 8.16 and 8.07 (two overlapping d, ^3J = 6.5 Hz, 5.5 Hz, 5H), 7.77−7.66 (m, 6H), 4.60 (s, 1H, exchangeable with D_2O), 2.27 (s, 3H), and −1.75 (s, 1H, exchangeable with D_2O) ppm; ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): δ 161.5, 154.3, 153.7, 141.6, 139.9, 136.1, 135.6, 134.2, 133.1, 128.9, 128.1, 128.0, 127.9, 127.6, 127.0, 125.4, 123.9, 112.9, 97.3, and 26.9 ppm; UV−vis (CH_2Cl_2) λ_{max} (log ε) 410 (4.99), 520 (3.84), 549 (3.88), 596 (3.53), and 649 (4.08) nm; FT-IR (neat, diamond ATR): $\nu_{C=O}$ = 1680.4 cm^{-1}; HRMS (ESI) m/z: [M + H]$^+$; calcd for $C_{47}H_{37}N_6O_3$ 733.2922; found 733.2941.

*meso-Tetraphenyl-N-methylimidazolidinone-Annulated Dihydroxychlorin (**13^{Me}**).* Prepared from 2,3-dioxoporphyrin **12** (25.0 mg, 3.88 × 10^{-5} mol) in pyridine (10.0 mL) as described for **13** but using *N*-methylurea (57.4 mg, 7.76 × 10^{-4} mol, 20 equiv) to afford dihydroxychlorin **13^{Me}** in 60% yield (16.7 mg) as a dark red solid: R_f (silica-CH_2Cl_2/5% MeOH) = 0.29; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.65 (d, ^3J = 5.2 Hz, 1H), 8.59 (d, ^3J = 4.8 Hz, 1H), 8.48 (s, 2H), 8.29 (d, ^3J = 5.2 Hz, 1H), 8.25 (dd, ^3J = 6.8, ^4J = 1.6 Hz, 2H), 8.17 (d, ^3J = 7.2 Hz, 2H), 8.04-7.95 (m, 5H), 7.81−7.67 (m, 12H), 5.40 (s, 1H, exchangeable with D_2O), 4.60 (s, 1H, exchangeable with D_2O), 4.81 (s, 1H, exchangeable with D_2O), 2.36 (s, 3H), −1.85 (s, 2H, exchangeable with D_2O) ppm; ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 159.6, 156.5, 154.2, 153.2, 141.7, 141.6, 141.5, 141.4, 139.7, 139.6, 136.5, 135.7, 135.6, 135.2, 134.2, 134.1, 134.0, 133.5, 133.4, 132.9, 129.0, 128.9, 128.6, 128.0, 127.9, 127.8, 127.5, 127.3, 127.0, 126.9, 125.5, 125.1, 124.6, 123.4, 113.0, 111.8, 26.3 ppm; UV−vis (CH_2Cl_2) λ_{max} (rel. I) 407 (1.00), 517 (0.08), 545 (0.08), 592 (0.04), 645 (0.13) nm; FT-IR (neat, diamond ATR): $\nu_{C=O}$ = 1710.0 (sh), 1679.0 cm^{-1}; HRMS (ESI) m/z: [M + H]$^+$; calcd for $C_{46}H_{35}N_6O_3$ 719.2765; found 719.2694.

*[meso-Tetraphenyl-N,N′-dimethylimidazolidinone-Annulated Dihydroxychlorinato]nickel(II) (**13^{Me2}Ni**).* Prepared from dioxoporphyrin nickel complex **12Ni** (47.4 mg, 6.76 × 10^{-5} mol) in pyridine (20.0 mL) as described for **13** but using *N,N′*-dimethylurea (119 mg, 1.35 × 10^{-3} mol, 20 equiv) and purified by preparative TLC (silica-CH_2Cl_2/5% MeOH) to afford the dark blue-green solid dihydroxymetallochlorin **13^{Me2}Ni** in 68% yield (36.5 mg): R_f (silica-CH_2Cl_2/5% MeOH) = 0.28; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.29 (d, ^3J = 5.2 Hz, 1H), 8.17 (s, 1H), 8.02 (d, ^3J = 5.2 Hz, 1H), 7.83 (dd, ^3J = 7.2, ^4J = 1.2 Hz, 2H), 7.73−7.70 (m, 2H), 7.63−7.54 (m, 6H), 4.41 (s, 1H, exchangeable with D_2O), and 2.14 (s, 3H) ppm; ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 161.6, 147.2, 142.4, 141.8, 139.7, 138.5, 137.7, 133.5, 133.3, 132.9, 132.8, 129.6, 128.5, 128.1, 128.1, 128.0, 127.3, 125.1, 110.9, 97.4, and 26.6 ppm; UV−vis (CH_2Cl_2) λ_{max} (log ε) 409 (5.16), 562 (sh), and 607 (4.38) nm; FT-IR (neat, diamond ATR): $\nu_{C=O}$ = 1658.0 cm^{-1}; HRMS (ESI) m/z: [M]$^+$; calcd for $C_{47}H_{34}N_6NiO_3$ 788.2046; found 788.2046.

*[meso-Tetraphenyl-N-methylimidazolidinone-Annulated Dihydroxychlorinato]nickel(II) (**13^{Me}Ni**).* Prepared from dioxoporphyrin nickel complex **12Ni** (30.0 mg, 4.28 × 10^{-5} mol) in pyridine (10.0 mL) as described for **13** but using *N*-methylurea (63.3 mg, 8.55 × 10^{-4} mol, 20 equiv) and purified by preparative TLC (silica-CH_2Cl_2/5% MeOH) to afford the dark blue-green solid dihydroxymetallochlorin **13^{Me}Ni** in 62% yield (20.5 mg): R_f (silica-CH_2Cl_2/5% MeOH) = 0.38; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.47 (d, ^3J = 7.2 Hz, 1H), 8.37 (d, ^3J = 4.8 Hz, 1H), 8.34 (d, ^3J = 4.8 Hz, 1H), 8.28 (d, ^3J = 4.8 Hz, 1H), 8.23 (d, ^3J = 4.8 Hz, 1H), 8.17 (d, ^3J = 4.8 Hz, 1H), overlapping peaks (7.87, br s; 7.79, d, ^3J = 4.8 Hz; 7.75, t, ^3J = 8.0 Hz; 7H), 7.65−7.51 (m, 11H), 7.39 (t, ^3J = 7.6 Hz, 1H), 7.00 (d, ^3J = 6.8 Hz, 1H), 5.13 (s, 1H, exchangeable with D_2O), 4.78 (s, 1H, exchangeable with D_2O), 4.41 (s, 1H, exchangeable with D_2O), and 2.25 (s, 3H) ppm; ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 159.8, 147.4, 146.8, 144.7, 142.0, 141.7, 140.2, 139.7, 139.6, 138.8, 138.2, 137.6, 137.2, 134.1, 133.7, 133.0, 132.9, 132.6, 129.8, 129.6, 128.7, 128.6, 128.3, 128.1, 128.0, 127.9, 127.6, 127.4, 127.3, 127.2, 125.6, 124.4, 111.3, 109.9, 97.0, 92.5, and 26.1 ppm; UV−vis (CH_2Cl_2) λ_{max} (rel. I) 417 (1.00), 506 (0.03), 576 (sh), and 613 (0.16) nm; FT-IR (neat, diamond ATR): $\nu_{C=O}$ = 1685.0 cm^{-1}; HRMS (ESI) m/z: [M]$^+$; calcd for $C_{46}H_{32}N_6NiO_3$ 774.1884; found 774.1878.

*meso-Tetraphenyl-2-thioxo-imidazole-Annulated Dihydroxychlorin (**16**).* Prepared from dione **12** (25.0 mg, 3.88 × 10^{-5} mol) in pyridine (10.0 mL) as described for **13** but using thiourea (59 mg, 7.75 × 10^{-4} mol, 20 equiv) and purified by column chromatography (silica-CH_2Cl_2/3% MeOH) to afford the dark red solid **16** in 92% yield (25.6 mg): R_f (silica-CH_2Cl_2/5% MeOH) = 0.25; δ ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.64 (d, ^3J = 4.8 Hz, 1H), 8.49 (s, 1H), 8.21and 8.19 (overlapping dd and d, ^3J = 7.6 Hz, ^4J = 1.6 Hz, 1H; 3J = 4.8 Hz, 1H), 8.10 (d, ^3J = 6.4 Hz, 2H), 7.91 (dd, ^3J = 6.0, ^4J = 2.0 Hz, 1H), 7.76−7.68 (m, 6H), 6.63 (s, 1H, exchangeable with D_2O), and −2.06 (s, 1H, exchangeable with D_2O) ppm; ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): δ 182.2, 155.7, 153.8, 141.7, 141.2, 139.6, 136.1, 134.7, 134.2, 134.0, 133.3, 133.0, 129.0, 128.4, 128.1, 127.9, 127.7, 127.0, 126.9, 125.2, 124.0, 111.6, and 97.7 ppm; UV−vis (CH_2Cl_2) λ_{max} (rel I.) 405 (1.0), 515 (0.07), 545 (0.08), 590 (0.04), and 645 (0.11) nm; FT-IR (neat, diamond ATR) $\nu_{C=S}$ = 1726.0 cm^{-1}; HRMS (ESI) m/z: [M + H]$^+$; calcd for $C_{45}H_{32}N_6O_2S$ 721.2380; found 721.2255. Note: this compound is chemically unstable, reverting back to the dione **12** when isolation and purification is attempted, thwarting the measurement of extinction coefficients.

*meso-Tetraphenyl-N,N′-dimethyl-2-thiono-imidazole-Annulated Dihydroxychlorin (**16^{Me2}**).* Prepared from dione **12** (92.0 mg, 1.43 ×

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10^{-4} mol) in pyridine (32.0 mL) as described for **13** but using *N,N′*-dimethylthiourea (297 mg, 2.85 × 10^{-3} mol, 20 equiv) and purified by column chromatography (silica-CH_2Cl_2/5% MeOH) to afford the dark red solid **16^{Me2}** in 89% yield (95.4 mg): R_f (silica-CH_2Cl_2/5% MeOH) = 0.65; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.60 (d, ^3J = 5.2 Hz, 1H), 8.48 (s, 1H), 8.18 (d, ^3J = 7.2 Hz, 1H), 8.11−8.07 (m, 4H), 7.81−7.66 (m, 6H), 4.62 (s, 1H, exchangeable with D_2O), 2.59 (s, 3H), and −1.74 (s, 1H, exchangeable with D_2O) ppm; $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 185.8, 153.9, 152.7, 141.5, 141.4, 139.6, 136.2, 135.4, 134.3, 133.3, 129.1, 128.3, 128.1, 128.0, 127.6, 127.0, 125.5, 124.2, 112.9, 100.4, and 30.7 ppm; UV−vis (CH_2Cl_2) λ_{max} (log ε) 400 (5.31), 510 (4.16), 539 (4.21), 585, (3.91), and 638 (4.38) nm; FT-IR (neat, diamond ATR): $\nu_{C=S}$ = 1722.0 cm^{-1}; HRMS (ESI) *m/z*: $[M + H]^+$; calcd for $C_{47}H_{37}N_6O_2S$ 749.2699; found 749.2659.

*1,4,6-Triazocine-2,5,7-trione-Based Pyrrole-Modified Porphyrin (**14^{Me2}**).* Dihydroxychlorin-dimethylurea adduct **13^{Me2}** was dissolved in dry THF (5.0 mL) in a round-bottom flask equipped with a magnetic stir bar. $Pb(OAc)_4$ (13.3 mg, 3.00 × 10^{-5} mol) was added and the reaction mixture was stirred at ambient temperature. When the starting material was consumed (reaction progress monitored by UV−vis and TLC), the solvent was evaporated and the residue separated by preparative TLC (silica-CH_2Cl_2/3% MeOH) to afford **14^{Me2}** as a bright green solid in 71% yield (14.1 mg): R_f (silica-CH_2Cl_2/2% MeOH) = 0.66; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.33 (d, ^3J = 4.8 Hz, 1H), 8.25 (br s, 1H), 8.14 (s, 1H), 8.01 (d, ^3J = 4.8 Hz, 1H), 7.96 (br s, 2H), 7.68 (m, 4H), 7.54 (t, ^3J = 7.6 Hz, 1H), 7.41 (br s, 1H), 7.08 (br s, 1H), 3.21 (s, 3H), and 1.86 (s, 1H, exchangeable with D_2O) ppm; $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 173.1, 155.5, 155.1, 147.3, 140.9, 140.2, 140.1, 136.5, 133.6, 129.2, 128.4, 128.3, 128.1, 127.4, 126.3, 125.5, 119.5, and 32.9 ppm; UV−vis (CH_2Cl_2) λ_{max} (log ε) 365 (3.98) 454 (4.76), 578 (3.54), 625 (3.55), 670 (3.40), and 741 (3.59) nm; FT-IR (neat, diamond ATR): $\nu_{C=O}$ = 1709.6, 1614.8 cm^{-1}; HRMS (ESI) *m/z*: $[M + H]^+$; calcd for $C_{47}H_{35}N_6O_3$ 731.2771; found 731.2706.

*[1,3,6-Triazocine-2,4,8-trione-Based Pyrrole-Modified Porphyrinato]nickel(II) (**14^{Me2}Ni**).* Prepared according to the procedure for **14^{Me2}** from **13^{Me2}Ni** (36.5 mg, 4.62 × 10^{-5} mol) in dry THF (12.0 mL) with $Pb(OAc)_4$ (41 mg, 9.25 × 10^{-5} mol, 2 equiv) and purified by column chromatography (silica-CH_2Cl_2) to afford the green solid **14^{Me2}Ni** in 71% yield (26.0 mg): R_f (silica-CH_2Cl_2) = 0.52; ^{1}H NMR (400 MHz; $CDCl_3$): δ 8.23 (d, ^3J = 4.8 Hz, 1H), 8.06 (s, 1H), 7.88 (d, ^3J = 4.8 Hz, 1H), 7.83 (br s, 1H), 7.64−7.60 (br m, 3H), 7.48 (br s, 3H), and 3.21 (s, 3H) ppm; $^{13}C\{^1H\}$ NMR (100 MHz; $CDCl_3$): δ 171.7, 155.2, 148.3, 144.5, 140.6, 138.9, 137.8, 137.2, 134.4, 133.0, 132.9, 131.0, 130.1, 128.4, 127.5, 118.4, and 33.1; UV−vis (CH_2Cl_2) λ_{max} (log ε) 441 (4.45), 661 (3.72) nm; FT-IR (neat, diamond ATR): $\nu_{C=O}$ = 1716.0, 1661.0 cm^{-1}; HRMS (ESI) *m/z*: $[M]^+$; calcd for $C_{47}H_{33}N_6NiO_3$ 786.1889; found 786.1913.

*1,3,6-Triazocine-4,8-dione-2-thione-Based Pyrrole-Modified Porphyrin (**17^{Me2}**).* Prepared according to the procedure for **14^{Me2}**, starting from **16^{Me2}** (26.4 mg, 3.53 × 10^{-5} mol) in dry THF (10.0 mL) with $Pb(OAc)_4$ (49.6 mg, 1.12 × 10^{-4} mol, ∼3 equiv) and purified by preparative TLC (silica-CH_2Cl_2) to recover diketone **12** (2.0 mg, 9% yield) and isolate the product **17^{Me2}** as a dark green solid in 67% yield (17.6 mg): R_f (silica-CH_2Cl_2) = 0.59; ^{1}H NMR (400 MHz, CD_2Cl_2): δ 8.58 (broad s, 1H), 8.51 (d, ^3J = 4.8 Hz, 1H), 8.36 (s, 1H), 8.20 (d, ^3J = 4.8 Hz, 1H), 8.04 (broad s, 2H), 7.76−7.69 (m, 4H), 7.60 (t, ^3J = 7.6 Hz, 1H), 7.35 (broad s, 1H), 6.87 (broad s, 1H), 2.71 (s, 3H), and −0.21 (s, 1H, exchangeable with D_2O) ppm; $^{13}C\{^1H\}$ NMR (125 MHz, CD_2Cl_2): δ 186.9, 171.8, 155.4, 148.3, 140.8, 140.7, 140.0, 137.4, 134.2, 134.1, 133.9, 132.5, 129.3, 128.6, 128.5, 128.3, 127.5, 125.4, 115.2, and 35.6 ppm; UV−vis (CH_2Cl_2) λ_{max} (log ε) 360 (4.4), 432 (5.02), 536 (3.77), 572 (3.75), 607 (3.82), and 668 (3.85) nm; HRMS (ESI) *m/z*: $[M + H]^+$; calcd for $C_{47}H_{35}N_6O_2S$ 747.2537; found 747.2517.

*Semicarbazide Adduct (**19**).* Prepared from **12** in 51% yield (16.5 mg) as a dark green solid on a 4.65 × 10^{-5} mol (30.0 mg) scale using 103.8 mg (9.31 × 10^{-4} mol, 20 equiv) of semicarbazide hydrochloride according to the general procedure for **13**, except at room temperature and purified by column chromatography: R_f (silica-CH_2Cl_2/3% MeOH) = 0.44; ^{1}H NMR (400 MHz, $CDCl_3$): δ 13.08 (s, 1H, exchangeable with D_2O), 8.78 (t, ^3J = 5.2 Hz, 2H), 8.62 (two overlapping doublets, ^3J = 4.9 Hz, 2H), 8.58 (d, ^3J = 4.4 Hz, 1H), 8.54 (dd, ^3J = 4.8 Hz, ^4J = 0.8 Hz 1H), 8.15 (dd, ^3J = 5.6, ^4J = 1.6 Hz, 4H), 8.07−8.05 (m, 2H), 7.96−7.94 (m, 2H), 7.82−7.72 (m, 12H), 5.26 (s, exchangeable with D_2O), 4.47 (s, 1H, exchangeable with D_2O), −2.24 (s, 1H, exchangeable with D_2O), and −2.34 (s, 1H, exchangeable with D_2O) ppm; $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ 187.8, 155.5, 146.7, 142.6, 141.8, 141.6, 141.5, 140.6, 140.4, 139.1, 138.3, 137.8, 137.6, 134.6, 134.4, 134.3, 133.9, 133.6, 132.6, 128.8, 128.2, 128.1, 127.9, 127.7, 127.6, 127.5, 127.4, 127.0, 124.0, 122.1, 115.6, and 112.4 ppm; UV−vis (CH_2Cl_2) λ_{max} (log ε) 410 (5.17), 465 (sh), 613 (sh), and 666, (3.6) nm; FT-IR (neat, diamond ATR) $\nu_{C=O}$ = 1667.1; HRMS (ESI) *m/z*: $[M + H]^+$; calcd for $C_{45}H_{32}N_7O_2$ 702.2617; found 702.2586.

*Thiosemicarbazide Adduct (**20**).* Prepared from **12** in 45% yield (5.0 mg) as a dark green solid on a 1.55 × 10^{-5} mol (10.0 mg) scale using 28.0 mg (3.07 × 10^{-4} mol, ∼20 equiv) of thiosemicarbazide according to the general procedure for **13**, except at room temperature and purified by column chromatography: R_f (silica-CH_2Cl_2) = 0.31; ^{1}H NMR (400 MHz, $CDCl_3$): δ 13.73 (s, 1H, exchangeable with D_2O), 8.77 (t, ^3J = 5.6 Hz, 2H), 8.63−8.57 (m, 3H), 8.52 (dd, ^3J = 5.2 Hz, ^4J = 1.2 Hz, 1H), 8.16−8.13 (m, 4H), 8.05 (dd, ^3J = 8.0, ^4J = 2.0 Hz, 2H), 7.95−7.93 (m, 2H), 7.82−7.71 (m, 12H), 6.37 (s, 1H, exchangeable with D_2O), 6.07 (s, 1H, exchangeable with D_2O), −2.24 (s, 1H, exchangeable with D_2O), and −2.32 (s, 1H, exchangeable with D_2O) ppm; $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 187.5, 181.0, 156.0, 154.7, 146.1, 142.6, 141.7, 141.6, 141.4, 140.5, 140.2, 139.2, 138.3, 137.7, 137.3, 134.7, 134.4, 134.3, 134.0, 133.5, 132.6, 128.9, 128.3, 128.2, 128.1, 128.0, 127.9, 127.7, 127.6, 127.5, 127.1, 124.2, 122.4, 115.7, and 112.4 ppm; UV−vis (CH_2Cl_2) λ_{max} (log ε) 414 (5.07), 480 (sh), 614 (3.59), and 671 (3.59) nm; HRMS (ESI) *m/z*: $[M + H]^+$; calcd for $C_{45}H_{32}N_7OS$ 718.2384; found 718.2347.

meso-Tetraphenyl-bis-(N,N′-dimethylimidazolidinone)-Annulated Tetrahydroxybacteriochlorin 23, Mixture of anti/syn-Isomers. Prepared from tetraone **22** (30.0 mg, 4.45 × 10^{-5} mol) in pyridine (10.0 mL) as described for **13** using *N,N′*-dimethylurea (156.7 mg, 1.78 × 10^{-3} mol, 40 equiv) and purified by column chromatography (silica-CH_2Cl_2/5% MeOH) to afford a (hard to separate) anti/syn-isomer mixture of the pink bacteriochlorin adduct **23** with an approximate ratio of 2:1 in 64% overall yield (24 mg) as a solid: R_f (silica-CH_2Cl_2/5% MeOH) = 0.23; ^{1}H NMR (400 MHz, DMSO-d_6): δ 8.08 (br d, ^3J = 4.4 Hz, $2H^A$), 7.95 (br s, $1H^B$), 7.77 (br s, $2H^A$), 7.74 (d, ^3J = 2.0 Hz, $1H^B$), 7.65 (d, ^3J = 2.0 Hz, $2H^A$, overlaid with br s, $1H^B$), 7.62−7.56 (m, $9H^{A+B}$), 6.89 (s, $2H^A$, exchangeable with D_2O), 6.81 (s, $1H^B$, exchangeable with D_2O), 2.04 (s, $3H^B$), 2.02 (s, $6H^A$), −1.29 (s, $0.5H^A$, exchangeable with D_2O), and −1.45 (s, $1H^B$, exchangeable with D_2O) ppm; $^{13}C\{^1H\}$ NMR (100 MHz, DMSO-d_6): δ 160.6, 160.1, 153.6, 153.5, 140.0, 139.7, 137.4, 136.9, 134.8, 134.3, 127.5, 126.2, 126.0, 125.9, 124.0, 123.3, 116.1, 116.0, 97.7, 96.6, 96.5, 69.8, 26.0, and 25.9 ppm; UV−vis (CH_2Cl_2) λ_{max} (log ε) 384 (5.24), 467 (3.51), 502 (3.76), 534 (4.56), 655 (3.67), and 712 (4.66) nm; FT-IR (neat, diamond ATR): $\nu_{C=O}$ = 1661.0 cm^{-1}; HRMS (ESI) *m/z*: $[M]^+$; calcd for $C_{50}H_{42}N_8O_6$ 850.3222; found 850.3112.

*meso-Tetraphenyl-bis-(N,N′-dimethyl-2-thiono-imidazole)-Annulated Tetrahydroxybacteriochlorin (**24**).* Prepared from tetraone **22** (31.0 mg, 4.59 × 10^{-5} mol) in pyridine (10.0 mL) as described for **13** using *N,N′*-dimethylthiourea (191.4 mg, 1.83 × 10^{-3} mol, 40 equiv) and purified by column chromatography (silica-CH_2Cl_2/5% MeOH) to afford a separable *E/Z*-isomer mixture of bacteriochlorin **30** as a dark red solid in 69% overall yield (28 mg). The isomers were separated on a small scale using preparative TLC plate (silica-CH_2Cl_2/2% MeOH). High-polarity isomer—assigned the *Z*-isomer: R_f (silica-CH_2Cl_2/1% MeOH) = 0.22; ^{1}H NMR (400 MHz, DMSO-d_6): δ 7.92 (broad s, 2H), 7.77 (d, ^3J = 1.6 Hz, 2H), 7.67 (broad s, 2H), 7.60−7.58 (m, 6H), 7.31 (s, 1H, exchangeable with D_2O), 2.39 (s, 3H), and −1.29 (s, 1H, exchangeable with D_2O) ppm; $^{13}C\{^1H\}$ NMR (100 MHz, DMSO-d_6): δ 183.8, 152.3, 139.4, 137.0, 134.1,

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133.3, 127.6, 126.3, 124.2, 116.2, 100.8, 69.8, and 30.0 ppm. Low-polarity isomer—assigned the *E*-isomer: R_f (silica-CH_2Cl_2/1% MeOH) = 0.33; ^{1}H NMR (400 MHz, DMSO-d_6): δ 8.11 (d, ^3J = 6.0 Hz, 2H), 7.82 (broad s, 2H), 7.63−7.60 (m, 8H), 7.39 (s, 2H, exchangeable with D_2O), 2.34 (s, 6H), and −1.40 (s, 1H, exchangeable with D_2O) ppm; $^{13}C\{^1H\}$ NMR (100 MHz, DMSO-d_6): δ 182.9, 152.2, 139.9, 137.7, 135.0, 134.4, 127.6, 126.2, 125.8, 123.2, 116.4, 99.5, 69.8, and 29.9 ppm; UV−vis (CH_2Cl_2) λ_{max} (log ε) 391 (5.27), 475 (3.54), 507 (3.81), 539 (4.57), 652 (3.75), and 711 (4.70) nm; FT-IR (neat, diamond ATR): $\nu_{C=S}$ = 1698.0 cm^{-1}; HRMS (ESI) *m*/*z*: $[M]^+$; calcd for $C_{50}H_{42}N_8O_4S_2$ 882.2765; found 882.2650.

*Oxidative Cleavage of Bacteriochlorin (**23**).* Tetrahydroxybacteriochlorin **23** (25.0 mg, 2.94 × 10^{-5} mol) was dissolved in dry THF (10.0 mL) in a round-bottom flask equipped with a magnetic stir bar. $Pb(OAc)_4$ (57.3 mg, 1.29 × 10^{-4} mol, 4.4 equiv) was added and the reaction mixture was stirred at ambient temperature. Upon consumption of the starting material (reaction progress monitored by UV−vis and TLC), the reaction mixture was filtered through a short-pad of silica and the solvent was evaporated in vacuo using a rotary evaporator. The residue was separated by high-performance preparative TLC (silica-CH_2Cl_2/1% MeOH/Et_3N) to afford bis-modified PMP **25** and the partially collapsed product **26**, both as dark green solids. **25**: R_f (silica-CH_2Cl_2) = 0.25; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.94 (broad s, 2H), 7.60 (d, ^3J = 2.5 Hz, 2H), 7.54 (t, ^3J = 7.0 Hz, 6H), 7.12 (broad s, 2H), 4.30 (s, 1H, exchangeable with D_2O), and 3.15 (s, 6H) ppm; $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ 171.0, 155.1, 146.7, 138.6, 137.7, 128.8, 128.4, 127.7, 127.1, 123.9, and 32.8 ppm; UV−vis (CH_2Cl_2) λ_{max} (rel I.) 352 (0.19), 480 (1.0), 617 (0.06), 663 (0.07), and 910 (0.08) nm; HRMS (ESI) *m*/*z*: $[M + H]^+$; calcd for $C_{50}H_{39}N_8O_6$ 847.2987; found 847.2948. **26**: R_f (silica-CH_2Cl_2) = 0.40; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.16 (dd, ^3J = 5.2 Hz, ^4J = 1.6 Hz, 1H), 7.98 (d, ^3J = 7.2 Hz, 1H), 7.84 (d, ^3J = 6.0 Hz, 2H), two overlapping dd at 7.79 and 7.77 (dd, ^3J = 5.2 Hz, ^4J = 1.6 Hz, 2H), 7.66−7.61 (m, 7H), 7.56−7.52 (m, 4H), 7.41 (t, ^3J = 7.6 Hz, 1H), 7.06 (d, ^3J = 7.6 Hz, 1H), 3.21 (s, 3H), 3.12 (s, 1H, exchangeable with D_2O), 3.08 (s, 3H), and 3.03 (s, 1H, exchangeable with D_2O) ppm; $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 173.7, 168.8, 166.2, 158.5, 156.5, 154.7, 143.6, 142.0, 140.2, 138.1, 136.8, 136.4, 136.3, 135.4, 134.3, 133.2, 132.0, 131.6, 130.5, 129.6, 129.0, 128.9, 128.8, 128.7, 128.5, 128.3, 128.2, 128.1, 127.6, 126.9, 126.3, 125.4, 124.2, 116.8, 106.2, 33.8, 32.1, and 29.9 ppm; UV−vis (CH_2Cl_2) λ_{max} (rel I.) 353 (0.14), 447 (1.0), 560 (0.06), 602 (0.05), 699 (0.04), and 759 (0.06) nm; HRMS (ESI) *m*/*z*: calcd for $C_{46}H_{34}N_7O_4$ ($[M + H]^+$) 748.2667; found 748.2501.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge at https://pubs.acs.org/doi/10.1021/acs.joc.0c02108.

Reproduction of the UV−vis, ^{1}H, and ^{13}C NMR spectra of all novel compounds; experimental details for the crystal structure determinations of **13^{Me2}** (CCDC # 2026025), **14^{Me2}Ni** (CCDC # 2026245), and **17^{Me2}** (CCDC # 2026026), including the.cif files. The cif files can also be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif. (PDF)

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Notes

The authors declare no competing financial interest.

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