Elucidation of the extraordinary 4-membered pyrrole ring-contracted azeteoporphyrinoid as an intermediate in chlorin oxidation†

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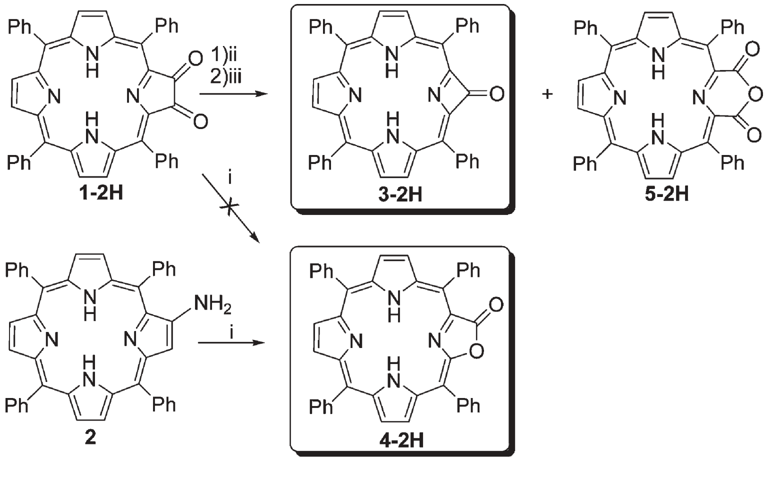
Reaction of 2,3-dioxochlorins with benzeneselenic anhydride (BSA) results in the formation of unusual ring-contracted azetine derivatives that further react with BSA to afford porpholactones.

Porphyrins and chlorins continue to serve as a primary pigment for light harvesting applications such as photomedicine[1–3] and solar materials.[4,5] To this end, synthetic advances have led to the development of unusual porphyrinoids with modulated optical and electronic properties. Specific examples of these include *N*- or *O*-confused carbaporphyrins,[6] β,β′-substituted porphyrins that extend conjugation upon reaction,[7–11] as well as heteroatom containing systems in which a pyrrole subunit is converted to, for example, a morphine (morpholinoporphyrins)[12–15] or oxazolone ring (porpholactones) by oxygen incorporation.[12–16] The diminished conjugation of these compounds can have important electronic influences and have been shown to modulate chemical reactivity such as turnover in the epoxidation of olefins.[17]

In 1984, Crossley *et al.* published in this journal how oxidation methods can lead to a selective modification on the β-pyrrolic position of porphyrins (Scheme 1).[12] Treatment of dione **1-2H** with NaH exposed to air followed by addition of hydrochloric acid resulted in the formation of **3-2H** as a side product in 4% yield and the morpholine derivative **5-2H** in 80% yield. Compound **5-2H** can also be synthesized by reaction of **1-2H** with *m*-chloroperbenzoic acid (MCPBA), however when this procedure is applied to **2**, porpholactone **4-2H** is isolated in 55% yield without evidence of ring-contracted side products. To the best of our knowledge, since this first report, only one proposed structure of an unusual ring-contracted tetrapyrrole such as **3-2H** has been reported,[18] highlighting the scarcity of tools available to contract the macrocycle periphery. The limited reports of ring-contracted species[12,18] implies non-trivial methods are required for their isolation, despite established routes to porpholactones[12–16]

It is well known that BSA is a powerful oxidizing reagent[19] for phenols,[20] hydrocarbons,[21] and 1,2-diarylethanes[22] but its use in porphyrin transformations has not been reported. The fact that the single example of an isolated pyrrole ring-contracted chlorin,[12] and the first[12] and later[13–16] routes to porpholactones proceed under oxidizing conditions, prompted our interest to apply BSA to porphyrin chemistry. In this theme, we demonstrate that pyrrole ring-contracted chlorins participate as intermediates in the oxidation of 2,3-dioxochlorins by BSA *en route* to forming porpholactones. Herein both the unprecedented nickel and copper porpholactones, and pyrrole ring-contracted azetine derivatives are analytically and crystallographically characterized for the first time.

The synthetic strategy employed is illustrated in Scheme 2. Starting materials **1-Ni** and **1-Cu** can be readily prepared by literature procedures.[23,24] Reaction of **1-Cu** in chlorobenzene with BSA under reflux results in the formation of two products; the non-polar green fraction **3-Cu** and a more polar purple fraction **4-Cu**. We also observe that the ratio of chlorin **1-Cu** to BSA plays a major role in reaction time and product formation. As shown in Table 1, BSA consumes all starting material within 5 h if an excess



Scheme 1 (i) MCPBA, (ii) NaH, O_2, CH_2Cl_2, (iii) 3 M aq. HCl.

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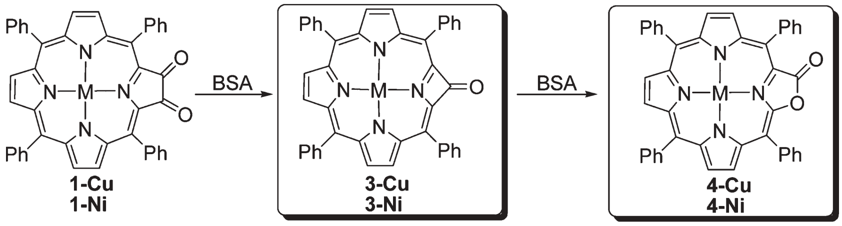
† Electronic supplementary information (ESI) available: Synthesis and characterization of **3-Ni**, **4-Ni**, **3-Cu**, and **4-Cu**. See DOI: 10.1039/b611567e



Scheme 2 Synthetic route to porpholactones *via in-situ* ring-contraction.

of 8-fold is used. When the reaction is carried out in a 1 : 2 ratio of chlorin to BSA, the reaction proceeds very slowly, and after 22 h, 59% of unreacted starting material is recovered. Remarkably, for all starting material to oxidant ratios that allow recovery of unreacted chlorin, the isolated yield of the non-polar green fraction **3-Cu** is consistently low, suggesting that the ring-contracted species may be an intermediate to the porpholactone. At longer reaction times (entry 3, Table 1) complete consumption of starting material is observed, concomitant with a decrease of isolated yield for the azetine intermediate. Based on these observations and earlier reports describing the oxidative formation of porpholactones,[14] we postulated that **3-Cu** is generated in an initial oxidation step and is subsequently converted to the thermodynamic product **4-Cu** by a second oxidation process.

To address this issue **3-Cu** was refluxed in air for 24 h in chlorobenzene. The compound remained unreacted by TLC, indicating that dioxygen does not oxidize the azetine derivative **3-Cu** at an appreciable rate under these conditions. However, addition of 4 equiv of BSA to the refluxing reaction mixture of **3-Cu** generates **4-Cu** within 30 min. The reaction is complete after 16 h, resulting in 59% yield of **4-Cu** following Si-gel column chromatography. Thus BSA is the oxygen atom transfer reagent that generates porpholactone **4-Cu** from **3-Cu**.

Similar reactivity of **1-Ni** with BSA is also observed (entries 5–6, Table 1). Reaction of **1-Ni** with 4 equiv of BSA under reflux for 14 h leads to sluggish conversion to porpholactone **4-Ni** *via* azetine **3-Ni**. An increase in BSA to 6 equiv improves conversion to **4-Ni**, but the same amount of **3-Ni** (19%) is obtained, further supporting the intermediacy of the azetine in the oxidation reaction. These findings suggest that sparse reports of ring-contracted chlorins may be due to their inherent instability to oxidizing conditions.

The molecular structure of **3-Cu** is shown in Fig. 1. The pyrrole ring-contracted derivatives **3-Cu** and **3-Ni** are planar, despite the reduced M–N$_{\text{azetine}}$ bond length (Cu: 1.94 Å; Ni: 1.88 Å). In contrast, the structure of porpholactone **4-Cu** reveals some nonplanarity that may arise from peripheral steric crowding (interactions between the carbonyl and adjacent phenyl group) or crystal packing forces. These molecular structures suggest that the azetine moiety dictates the structure of the macrocycle by forcing a planar conformation. The planarity of these rare molecules may produce an enhanced aptitude for stacking with planar chemical or biological constructs.‡

Table 1 Observed product ratios for reaction of dioxochlorins **1-Cu** and **1-Ni** with BSA

Entry	1-M	BSA	3-M	4-M	Reaction time	1-M recovered
1	**1-Cu**	8 equiv	6%	82%	5 h	traces
2	**1-Cu**	4 equiv	7%	70%	8 h	11%
3	**1-Cu**	4 equiv	traces	75%	18 h	—
4	**1-Cu**	2 equiv	8%	27%	22 h	59%
5	**1-Ni**	6 equiv	19%	35%	9 h	20%
6	**1-Ni**	4 equiv	18%	14%	14 h	65%

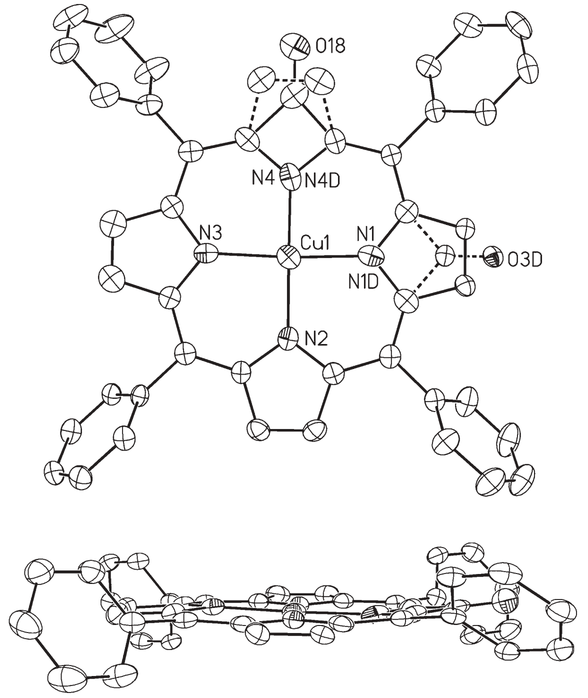


Fig. 1 X-Ray crystal structure of **3-Cu** in which the azetine moiety is disordered with one of the pyrrole rings; top: front view, bottom: side view with disorder removed for clarity. Thermal ellipsoids are illustrated at 50% probability and H-atoms are omitted for clarity.

Notes and references

‡ Crystal data for **3-Cu**: brown crystal, 0.25 × 0.20 × 0.10 mm, $C_{43}H_{26}N_4OCu$, M = 678.22, monoclinic, $P2_1/n$, a = 14.680(2) Å, b = 16.236(2) Å, c = 14.8470(19) Å, β = 119.522(3)°, V = 3079.2(7) Å^3, T = 130(2) K, Z = 4, ρ_{calcd} = 1.463 Mg m^{-3}, μ = 0.754 mm^{-1}, $2\theta_{\max}$ = 51°, Mo Kα (λ = 0.71073). A total of 15876 reflections were measured, of which 5462 (R_{int} = 0.0564) were unique. Final residuals were R = 0.0541 and $wR2$ = 0.1301 (for 3882 observed reflections with $I > 2\sigma(I)$, 455 parameters) and R = 0.0830 and $wR2$ = 0.1488 for all data with GOF 1.021 and largest residual peak 1.144 eÅ^{-3} and hole −0.536 eÅ^{-3}. The azetine ring and one pyrrole ring are disordered (ratio 71 : 29). The remaining electron density is located near the two pyrrole rings that were not disordered suggesting further disorder. However such sites have very low site occupancy and refinement does not converge. CCDC 615719–617062. For crystallographic data in CIF or other electronic format see DOI: 10.1039/b611567e

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