

Indaphyrin, a *meso*-tetraphenylsecochlorin-derived chromophore incorporating *o*-phenyl-to- β -linkages†

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Received (in Corvallis, OR, USA) 26th April 2003, Accepted 21st May 2003

First published as an Advance Article on the web 18th June 2003

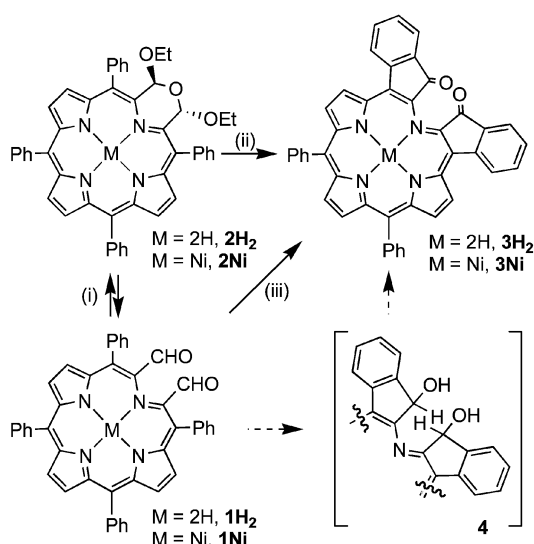
Acid-induced cyclization of *meso*-tetraphenyl-2,3-secochlorin-2,3-dialdehyde produced *meso*-diphenylindaphyrin, a novel secochlorin-based chromophore in which linkages between the *o*-phenyl and the β -position force the *meso*-phenyl groups into co-planarity with the porphyrinic π -system.

One focus in current synthetic porphyrin chemistry is the synthesis of porphyrinic macrocycles with spectroscopic and coordination properties tuned to a variety of applications. One particular aim is the synthesis of chromophores with long wavelengths of absorbance for their use in photomedicine.¹ A number of approaches toward this goal have gained particular prominence: the synthesis of non-planar porphyrinic structures,² the synthesis of porphyrin isomers, expanded porphyrins,³ and porphyrin-like chromophores in which one pyrrolic subunit is (formally) replaced with a non-pyrrolic building block.⁴

We have shown that *meso*-tetraaryl-2,3-dihydroxychlorin can be subjected to diol cleavage, generating secochlorin bisaldehyde derivatives **1**.^{5,6} Nucleophile-induced intramolecular ring-closure of the bisaldehydes generates morpholinochlorins such as **2** (Scheme 1).^{5,7} This ring-closure reaction is acid-catalyzed. When we reacted **1Ni** with EtOH using large amounts of acid or for too long, we noticed the formation of one non-polar, deep green degradation product, **3Ni**, at the expense of the yields of the expected product **2Ni**. The high resolution mass spectrum of **3Ni** indicated its composition to be C₄₄H₂₄N₄NiO₂, *i.e.* formally derived from **1Ni** by loss of four

hydrogens. This composition suggested that EtOH was not involved in the transformation. Indeed, the identical product was obtained as the major product when **1Ni** was reacted with TFA in the absence of an alcohol (80% yield, 5×10^{-5} mol scale).† The UV-vis absorption spectrum of the product **3Ni** is shown in Fig. 1. The two band spectrum (λ_{max} at 447 and 651 nm) resembles that of a bathochromically shifted Ni^{II} chlorin.⁸ The ¹H and ¹³C NMR spectra of this compound are well resolved and indicate a porphyrinic chromophore of two-fold symmetry. However, **3Ni** is unstable and decomposes in solution within 12 hours, providing a red pigment with a spectroscopic signature suggesting a ring-opened oligopyrrolic structure.⁹

Fortunately, free base morpholinochlorin **2H₂** proved to be susceptible to an equivalent acid-induced reaction, producing **3H₂** in 30% isolated yield as a stable, non-polar, deep red chromophore of the composition C₄₄H₂₆N₄O₂.† The ¹H NMR spectrum of **3H₂** is shown in Fig. 2. This spectrum has features generally observed in two-fold symmetric pyrrole-modified porphyrins such as **1** or **2**: two doublets (centered at 8.54 and 9.15 ppm), corresponding to 2H each, with the small coupling constant of 4.9 Hz characteristic of β -protons. Thus, the signals



Scheme 1 Reaction conditions: (i) CHCl₃, EtOH, [H⁺];⁵ (ii) CH₂Cl₂, 10% TFA; (iii) CHCl₃, catalytic amounts of TFA (for **1Ni** only).

† Electronic supplementary information (ESI) available: preparation and spectroscopic data of **3Ni** and **3H₂**, and details of the molecular modelling studies. See <http://www.rsc.org/suppdata/cc/b3/b304647h/>

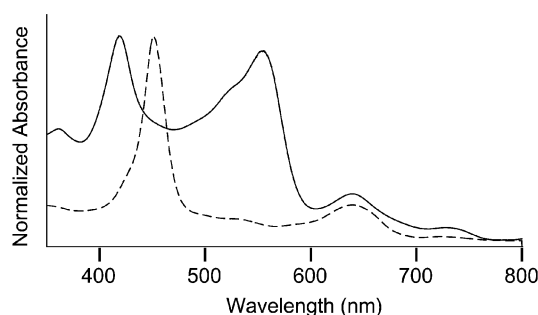


Fig. 1 UV-vis of **3H₂** (—) and of **3Ni** (---) in CHCl₃.

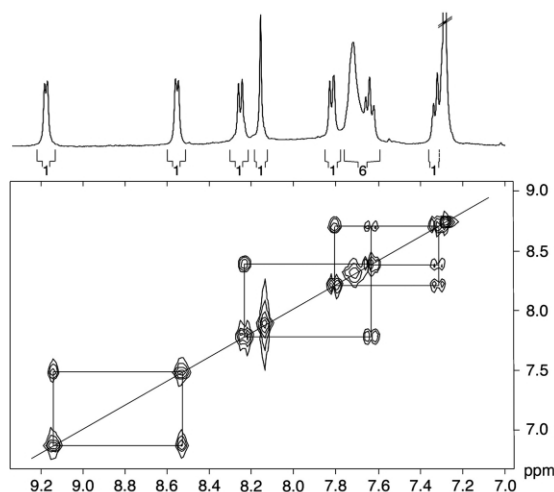


Fig. 2 H,H-COSY Spectrum of **3H₂** (400 MHz, CDCl₃).

are assigned to the β -protons located adjacent to the β,β' -cleavage site. Correspondingly, a singlet (2H, 8.15 ppm) for the β -protons opposite to the site of modification is also present. The phenyl region of the ^1H NMR spectrum is, however, unusual. The signals are split into two distinct sets. One broad peak corresponds to the 10H of two phenyl groups. This unresolved signal is similar to that observed for the phenyl groups in many *meso*-phenylporphyrin derivatives. The second set are four well resolved signals, corresponding to 2H each (two doublet-of-doublets centered at 7.32 and 7.64 ppm, and two doublets centered at 7.81 and 8.24 ppm, all with a coupling constant of 7.7 Hz). The H,H-COSY spectrum of the aromatic region shows the correlation between the four signals, which correspond to a non-symmetrically 1,2-disubstituted phenyl group (Fig. 2).

The ^{13}C NMR spectrum of 3H_2 shows 20 non-equivalent carbons, 19 of which are in the aromatic region, as well as one signal indicative of a carbonyl carbon (189.5 ppm). The presence of a ketone functionality is also evident in its IR spectrum ($\text{C}=\text{O}$ stretch at 1699 cm^{-1}). Based on the spectroscopic evidence, we assigned **3** the structure shown in Scheme 1. A ketone functionality joins the *o*-phenyl position with the α -position of a secochlorin chromophore, thus fusing indanone moieties to a secochlorin backbone. We propose the trivial name indaphyrin for this unprecedented chromophore.

The mechanism of formation of the indaphyrin can be rationalized by an acid-catalyzed intramolecular electrophilic attack of the formyl groups onto the *o*-positions, forming carbinol **4**, which then oxidizes spontaneously to the final product (Scheme 1). The sensitivity of carbinols of this type towards air oxidation was previously shown by Barloy and co-workers.¹⁰ Morpholinochlorin 1H_2 functions as a masked version of the unstable bisaldehyde 2H_2 , liberated under the acidic reaction conditions and reacted *in situ*.⁶

The *o*-phenyl-to- β -connection forms a five-membered exocyclic ring between the phenyl groups and the macrocycle. This forces the phenyl groups into co-planarity with the porphyrinic chromophore. The increased π -conjugation is likely the origin of the unusual UV-vis spectra of **3** (Fig. 1) although β -keto groups on their own have a strong influence on the UV-vis spectra of porphyrins.¹¹

Porphyrinic chromophores with direct pyrrole-to-phenyl linkages are rare,^{10,12,13} and only two free base examples of this type are known.^{10,13} Naphthoporphyrin 5H_2 (Fig. 3), reported by Barloy and co-workers, contains five- and six-membered rings as the results of both a direct and a ketone pyrrole-to-phenyl linkage.¹⁰ The optical spectra of the chromophores 5H_2 and 3H_2 exhibit similarities. In contrast to 5H_2 , however, 3H_2 contains a cleaved β,β' -bond and β -carbons form the ketone link. This structural difference has an important implication. Molecular modelling of 5H_2 suggests that this chromophore is significantly distorted from planarity.¹⁰ The distortion can be attributed to the fused five-membered ring as six-membered rings do not introduce strain, as evidenced by the largely planar structure of, for instance, piconoporphyrin 6H_2 (Fig. 3).¹³ On the other hand, modelling of 3H_2 indicates that a slight twist in the cleaved β,β' -bond largely relieves the strain introduced by the five-membered linkages. As a result, the rest of the

chromophore is largely planar.[†] A similar effect is seen in the X-ray crystal structure of 1H_2 .⁶ The signals for the NH protons in 3H_2 are found at 1.5 ppm. Such a low-field shift for porphyrinic NH protons is associated with non-planar porphyrin derivatives.¹⁴ The apparent conflicts in the spectroscopic properties of 3H_2 (and of 1H_2)⁶ are resolved by assuming a significant conformational flexibility of the secochlorin framework in solution.

The conformation of 3Ni is, analogous to other [secochlorinato]Ni^{II}-derived macrocycles, expected to be significantly non-planar.¹⁵ Molecular modelling suggests that the ruffled conformation observed for 3Ni is more distorted than that observed in the crystal structures of 1Ni or 2Ni (root mean square displacement of the C_{20}N_4 core: 0.56 Å in 3Ni versus 0.465 Å, and 0.468 Å in 1Ni and 2Ni , respectively), introducing additional steric strain.[†] This likely contributes to the unusual instability of 3Ni , and may define the upper limit at which [secochlorinato]Ni^{II}-derivatives can be distorted from planarity without infringing on the stability of the macrocycle.

In conclusion, we have shown the synthesis of a novel class of secochlorin-based chromophores with dramatically bathochromic shifted optical spectra as compared to porphyrins, chlorins or other chromophores incorporating phenyl-to- β -linkages.

This work was supported by the UConn Research Foundation.

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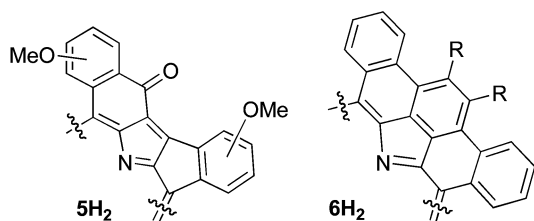


Fig. 3 Known free base porphyrinic structures incorporating *o*-phenyl-to- β -linkages.^{10,13}