ChemComm
www.rsc.org/chemcomm

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

Jason R. McCarthy, Michael A. Hyland and Christian Brückner*
University of Connecticut, Department of Chemistry, Storrs, CT 06269-3060, USA.
E-mail: c.bruckner@uconn.edu; Fax: +860 486-2981; Tel: +860 486-2743

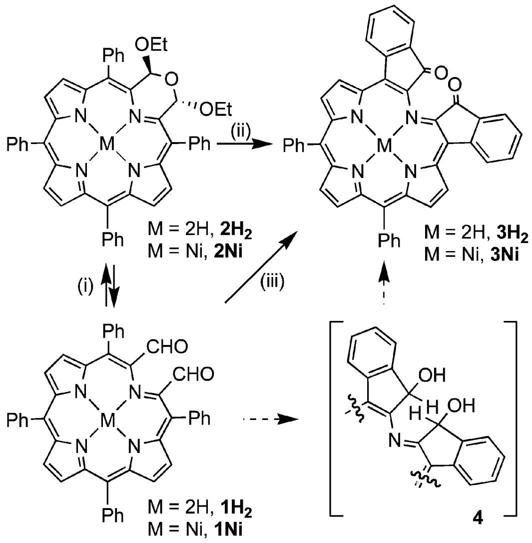
Received (in Corvallis, OR, USA) 26th April 2003, Accepted 21st May 2003
First published as an Advance Article on the web 18th June 2003

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 $C_{44}H_{24}N_4NiO_2$, *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 ^{13}C 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 **2H$_2$** proved to be susceptible to an equivalent acid-induced reaction, producing **3H$_2$** in 30% isolated yield as a stable, non-polar, deep red chromophore of the composition $C_{44}H_{26}N_4O_2$.† The ^1H NMR spectrum of **3H$_2$** 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) $CHCl_3$, EtOH, [H$^+$];[5] (ii) CH_2Cl_2, 10% TFA; (iii) $CHCl_3$, catalytic amounts of TFA (for **1Ni** only).

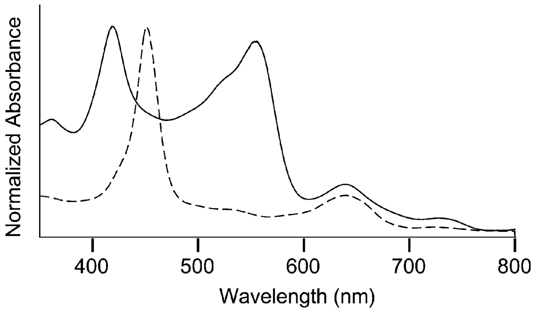


Fig. 1 UV-vis of **3H$_2$** (—) and of **3Ni** (---) in $CHCl_3$.

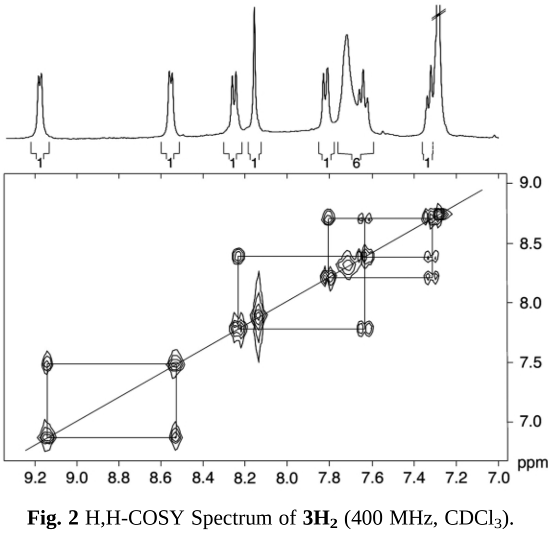


Fig. 2 H,H-COSY Spectrum of **3H$_2$** (400 MHz, $CDCl_3$).

---

† Electronic supplementary information (ESI) available: preparation and spectroscopic data of **3Ni** and **3H$_2$**, and details of the molecular modelling studies. See http://www.rsc.org/suppdata/cc/b3/b304647h/

DOI: 10.1039/b304647h

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 ^{1}H 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 (C=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, picenoporphyrin **$6H_2$** (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.

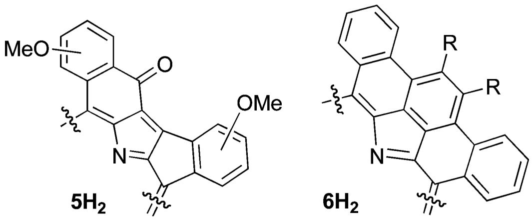


Fig. 3 Known free base porphyrinic structures incorporating *o*-phenyl-to-β-linkages.[10,13]

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.

Notes and references

1 (*a*) R. Bonnett, *Chem. Soc. Rev.*, 1995, 19; (*b*) E. D. Sternberg, D. Dolphin and C. Brückner, *Tetrahedron*, 1998, **54**, 4151.
2 (*a*) M. Ravikanth and T. K. Chandrashekar, *Struct. Bonding (Berlin)*, 1995, **82**, 107; (*b*) J. A. Shelnutt, X.-Z. Song, J.-G. Ma, W. Jentzen and C. J. Medforth, *Chem. Soc. Rev.*, 1998, **27**, 31; (*c*) R. E. Haddad, S. Gazeau, J. Pécaut, J.-C. Marchon, C. J. Medforth and J. A. Shelnutt, *J. Am. Chem. Soc.*, 2003, **125**, 1253.
3 J. L. Sessler and S. Weghorn, *Expanded, Contracted & Isomeric Porphyrins*, Pergamon, New York, 1997.
4 T. D. Lash, Synthesis of Novel Porphyrinoid Chromophores, in *The Porphyrin Handbook*, K. M. Kadish, K. M. Smith and R. Guilard, eds., Academic Press, New York, 2000, **vol. 2**, pp. 1–54.
5 C. Brückner, S. J. Rettig and D. Dolphin, *J. Org. Chem.*, 1998, **63**, 2094.
6 J. R. McCarthy, H. A. Jenkins and C. Brückner, *Org. Lett.*, 2003, **5**, 19.
7 C. J. Campbell, J. F. Rusling and C. Brückner, *J. Am. Chem. Soc.*, 2000, **122**, 6679.
8 UV-Vis of [2,3-dihydroxy-2,3-chlorinato]Ni(II): 416 and 612 nm; UV-vis of **1Ni**, dramatically non-planar chlorin-type chromomophore: 430 and 640 nm, see ref. 5.
9 H. Falk, *The Chemistry of Linear Oligopyrroles and Bile Pigments*, Springer Verlag, Wien, New York, 1989.
10 L. Barloy, D. Dolphin, D. Dupré and T. P. J. Wijesekera, *J. Org. Chem.*, 1994, **59**, 7976.
11 (*a*) C. Brückner, J. R. McCarthy, H. W. Daniell, Z. Pendon, R. Ilagan, T. M. Francis, L. Ren, R. R. Birge and H. A. Frank, *Chem. Phys.*, 2003, in press (*b*) S. D. Starnes, S. Arundundram and C. H. Saunders, *Tetrahedron Lett.*, 2002, **43**, 7785.
12 (*a*) K. Henrick, P. G. Owston, R. Peters and P. A. Tasker, *Inorg. Chim. Acta*, 1980, **45**, L161; (*b*) H. J. Callot, E. Schaeffer, R. Cromer and F. Metz, *Tetrahedron*, 1990, **46**, 5253; (*c*) Y. V. Ishkov and Z. I. Zhilina, *Zh. Org. Khim.*, 1995, **31**, 136; (*d*) M. A. Faustino, M. G. P. M. S. Neves, M. G. H. Vincente, A. M. S. Silva and J. A. S. Cavaleiro, *Tetrahedron Lett.*, 1995, **36**, 5977; (*e*) H. Aihara, L. Jaquinod, D. J. Nurco and K. M. Smith, *Angew. Chem., Int. Ed.*, 2001, **40**, 3439; (*f*) S. Richeter, C. Jeandon, J.-P. Gisselbrecht, R. Ruppert and H. J. Callot, *J. Am. Chem. Soc.*, 2002, **124**, 6168.
13 M. Nath, J. C. Huffmann and J. M. Zaleski, *Chem. Commun.*, 2003, 858.
14 A. Krivokapic, A. R. Cowley and H. L. Anderson, *J. Org. Chem.*, 2003, **68**, 1089.
15 C. Brückner, E. D. Sternberg, J. K. MacAlpine, S. J. Rettig and D. Dolphin, *J. Am. Chem. Soc.*, 1999, **121**, 2609.