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Synthesis of stable free base secochlorins and their corresponding metal complexes from *meso*-tetraarylporphyrin derivatives[†]‡

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Cleavage reactions of 2,3-diamino-*meso*-tetraarylporphyrins and *meso*-tetraarylporphyrins fused to imidazole rings afforded secochlorins including stable free base derivatives.

Secochlorins are chlorin derivatives containing one cleaved β , β' -bond and possessing maximum wavelength absorption bands at around 650 nm. They were first described almost twenty years ago and were initially prepared by the thermolysis of (octadehydrocorrinato)nickel(II) chloride salts.¹ Then, several secochlorins²⁻⁵ and secoporphyrazines⁶ were reported in the literature. Some representative structures of secochlorins (1-Ni, 1-H₂, 2-H₂ and 3-H₂) and secoporphyrazines (4-Ni and 4-H₂) are displayed in Scheme 1. The oxidative pyrrole ring opening of porphyrins and porphyrazines involves activated $\beta_{\beta}\beta'$ -double bonds by the presence of electron-rich substituents. Surprisingly, few examples of free base secochlorins are known in the literature. Secochlorins 2-H₂ and 3-H₂ (Scheme 1) synthesized by Sessler and coworkers are rare examples of stable free base secochlorins.⁴ Indeed, free base secochlorin 1-H₂, which was synthesized by Brückner and coworkers, appeared to be unstable due to its high reactivity.³



Scheme 1 Structures of secochlorins 1-Ni, 1-H₂, 2-H₂ and 3-H₂, and secoporphyrazines 4-Ni and 4-H₂.

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Here, we report some new procedures to obtain secochlorins, including stable free base ones. Hoffman and coworkers showed that amino groups are electron-rich groups activating β , β' -double bonds of porphyrazines and that cleavage reactions afforded secoporphyrazines like **4-Ni** and **4-H**₂. Surprisingly, 2,3-diamino-porphyrins have never been considered as starting material for the synthesis of secochlorins. Recently, Telvekar and Bachhav reported the synthetic utility of hypervalent iodine reagent (diacetoxyiodo)benzene (DIB) for diaminoaryl carbon–carbon cleavage reaction (Scheme 2).⁷ We noticed that 2,3-diamino-porphyrins react in the same way with DIB as observed for diaminoaryl derivatives (Scheme 3).

2,3-Diaminoporphyrin **6-Ni** was easily obtained from the 2-amino-3-nitroporphyrin **5-Ni** through the reduction of the nitro function. Then, two equivalents of DIB were added to a solution of **6-Ni** in CH₂Cl₂. Within a few minutes, the colour of the reaction mixture evolved from brown to green. The compound exhibited a less polar character than the starting reactant, as evidenced by TLC. The major green compound corresponded to the symmetrical 2,3-dicyano-2,3-secochlorin 7-Ni, which could be easily purified by column chromatography on SiO₂ (eluent: CH₂Cl₂). It was obtained in 75% yield after this two-step procedure (reduction and cleavage reactions). No reaction occurred when DIB was added to a solution of

$$\label{eq:holestar} \underbrace{\bigcap_{\mathsf{NH}_2}^{\mathsf{NH}_2} \xrightarrow{\mathsf{DIB 2 eq.}}_{\mathsf{CH}_2\mathsf{Cl}_2\,,\,25^\circ\mathsf{C}}} \quad \underbrace{\bigcap_{\mathsf{CN}}^{\mathsf{CN}}}_{\mathsf{CN}}$$

Scheme 2 Cleavage reaction of 1,2-diaminobenzene with DIB.



Scheme 3 Synthesis of secochlorins 7-Ni and 7-Zn.



Fig. 1 UV-visible spectra of **7-Ni** (dashed), and **7-Zn** (dotted) and **7-H₂** (full) in CH₂Cl₂.

2-amino-3-nitroporphyrin 5-Ni in CH₂Cl₂, showing the importance to have two neighboring electron-rich β -amino groups. The mass peak corresponding to the mono protonated form of 7-Ni was observed by HR-MS ($m/z = 921.4166 [M + H]^+$). The UV-visible spectrum showed the Soret absorption band at $\lambda = 451$ nm and one Q band at $\lambda = 661$ nm (Fig. 1). In the FT-IR spectrum of 7-Ni, the cyano stretching frequencies appeared as a single band at $\nu = 2211 \text{ cm}^{-1}$. ¹H NMR spectroscopy shows the 2-fold symmetry of secochlorin 7-Ni, since signals corresponding to β -hydrogen atoms exhibit the expected splitting pattern: a pair of doublets at $\delta = 7.92$ and 8.35 ppm and one singlet at $\delta = 8.13$ ppm.

Then, we turned our attention to the formation of the corresponding free base secochlorin. The demetallation of 7-Ni by using standard acidic conditions (H₂SO₄ 20% in TFA at 25 °C) failed (a complex mixture of several compounds was obtained). Since Zn^{2+} is easier to remove from the inner core of the macrocycle compared to Ni²⁺, we synthesized 7-Zn and obtained it in 78% yield following the procedure described for the synthesis of 7-Ni (Scheme 3). ¹H NMR and mass spectra are in accordance with the proposed structure for 7-Zn (see ESI[‡]). The electronic absorption spectrum of 7-Zn displayed a Soret band at $\lambda = 443$ nm and an intense Q band at $\lambda = 646$ nm (Fig. 1). In the FT-IR spectrum of 7-Zn, the cyano stretching frequencies appeared as a single band at $\nu = 2208 \text{ cm}^{-1}$. Free base secochlorin **7-H**₂ was then successfully obtained in 95% yield by treating 7-Zn with TFA in CH₂Cl₂ at room temperature (Scheme 4). HR-MS showed a peak at $m/z = 865.4967 ([M + H]^+)$ corresponding to the mono protonated form of 7-H₂. The ¹H NMR signal due to the internal NH of the free base secochlorin was observed at $\delta = -0.38$ ppm. The presence of the cyano groups was confirmed by FT-IR spectroscopy and their stretching frequencies were observed as a single band at $\nu = 2202 \text{ cm}^{-1}$, a lower value



Scheme 4 Synthesis of secochlorin 7-H₂.



Fig. 2 Top (left) and side (right) views of the optimized structure of **7-Ni**. Corresponding views of **7-H**₂ are displayed in Fig. S1 in ESI.‡

compared to complexes 7-Ni and 7-Zn. The UV-visible spectrum of the $7-H_2$ displayed a broadened Soret band centered at 435 nm and Q-bands at 560 nm, 619 nm and 685 nm (Fig. 1).

Molecular modeling was used to gain insight into the possible conformations of those molecules and to help the interpretation of their optical absorption spectra. DFT and TD-DFT methods were applied at the B3LYP/6-31g(d) level to optimise the molecular structure of 7-Ni, 7-Zn and 7-H₂, and simulate their respective optical absorption spectra. All optimised geometries present a ruffled-like conformation induced by the steric interaction between the cyano groups (Fig. 2, left). This is best appreciated from the dihedral angle between the two opposite pyrrole rings along the diagonal direction.⁸ This angle is 23° in 7-H₂, 22° in 7-Zn and 39° in 7-Ni (Fig. 2, right). Thus, while substitution of the internal H with Zn^{2+} has a vanishingly small effect on the conformation of the core, complexation of Ni²⁺ leads to a strongly distorted structure. This is consistent with the smaller size of the nickel ion, combined with the large flexibility of the secochlorin ring allowed by the β , β' -bond cleavage.9 The simulated absorption spectra are chlorin-like and in good agreement with the experimental ones (see ESI[‡], Fig. S2): they predict strong Soret B bands and weak Q bands as expected from the simple Gouterman's four-orbital model.¹⁰

Recently, we were also interested in the synthesis of porphyrins fused to imidazole and imidazolium rings,¹¹ and we showed that free base porphyrins fused to imidazole rings are precursors of secochlorins. We noticed that the free base porphyrin 8-H₂ (R = H) was slowly converted into a green compound both in solution and solid state in the presence of air and light (Scheme 5). Mass spectrometry analysis of this green compound showed that it corresponds to an oxidized species of the free base of imidazole 8-H₂ (m/z = 911.5 compared to $m/z = 879.5 \,[\text{M} + \text{H}^+]$ for 8-H₂). According to ¹H NMR and mass spectra, this oxidized species corresponds to unsymmetrical 2-cyano-3-N-formylamide-2,3-secochlorins $9-H_2$ (R = H, Scheme 5). In the FT-IR spectrum of 9-H₂, a cyano stretching frequency appeared at $\nu = 2203 \text{ cm}^{-1}$, and two carbonyl stretching frequencies appeared at $\nu = 1683$ and 1733 cm⁻¹. The ¹H NMR spectrum of $9-H_2$ confirmed the absence of 2-fold symmetry of the molecule. The broad doublet at $\delta = 9.22$ ppm (J = 9.7 Hz) is the characteristic signal of the N-formyl group CHO.¹² ¹H NMR COSY experiments showed the NOE correlation with the neighboring NH group at $\delta = 8.41$ ppm (see ESI[‡]). ¹³C{¹H} NMR spectroscopy also



Scheme 5 Synthesis of secochlorins 9-H₂ and 11-H₂.



Scheme 6 Possible pathway for the formation of $9-H_2$ and $11-H_2$.

confirmed the presence of two C=O groups at $\delta = 168.1$ and 161.9 ppm. UV-visible spectrum of **9-H**₂ is very similar to that of secochlorin **7-H**₂ with a Soret band at $\lambda = 435$ and Q-bands at $\lambda = 559$, 601 and 684 nm. The same photoxidation reaction carried out with porphyrin **10-H**₂ (R = Me) afforded the corresponding secochlorin **11-H**₂ (R = Me, Scheme 5). As expected for **11-H**₂, the signal due to the CHO group is a broad singlet at $\delta = 9.75$ ppm due to the absence of the neighboring NH group. Absorption bands of **11-H**₂ are slightly hypsochromically shifted compared to secochlorin **9-H**₂: the Soret band is observed at $\lambda = 429$ nm, and three Q-bands are observed at $\lambda = 547$, 597 and 673 nm.

We presume that singlet oxygen $({}^{1}O_{2})$ generated by free base macrocycles under ambient light is the dominant oxidant. Preliminary experiments showed that irradiation of diluted solution of 8-H₂ and 10-H₂ in CH₂Cl₂ during 15 hours with a slide projector (250 W) dramatically increased the yields of secochlorins 9-H₂ (24%) and 11-H₂ (72%). This can also explain why nickel(II) complexes 8-Ni and 10-Ni which are not able to generate ${}^{1}O_{2}$ are not converted into secochlorins (Scheme 5). A possible mechanism to explain the formation of secochlorins $9-H_2$ and $11-H_2$ is the formation of unstable endoperoxide intermediates, which were previously described by Foote and Ryang for imidazole derivatives (Scheme 6).¹³ Interestingly, free base porphyrin 12-H₂ fused to one imidazolium ring is stable and did not undergo cleavage reaction of the β , β' -double bond of the fused pyrrole (Scheme 5): this is consistent with the fact that imidazolium rings are electron-deficient and disfavor the [4+2] cycloaddition of the singlet oxygen.

To summarize, we describe here for the first time some new synthetic pathways to obtain secochlorins, including stable free base derivatives. The interesting aspect of this work is the porphyrin \rightarrow secochlorin transformation with light and oxygen

only (the perfect nontoxic reagents) or hypervalent iodine reagent DIB, which generates iodobenzene and acetic acid as the side compounds (less toxic than osmium and lead complexes). Current investigations are now devoted to the chemical transformations of the cyano groups to obtain more elaborated chromophores.

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