Decapitation of dihydroporphyrazinediol derivatives: synthesis and X-ray structure of a novel seco-porphyrazine

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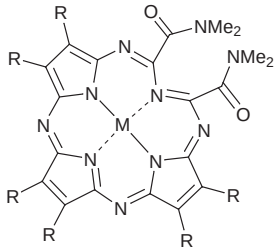
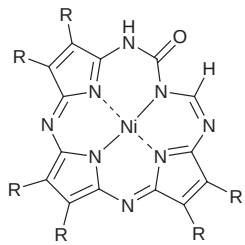
The dihydroporphyrazinediol 8, which was prepared by Linstead macrocyclisation of 2,5-diiminopyrrolidine with 3,4-bis(4-*tert*-butylphenyl)pyrroline-2,5-diimine, followed by TFA demetallation and OsO_4 tetroxide mediated dihydroxylation, underwent reaction with $Ni(OAc)_2$ at 100 °C in the presence of air to give the novel seco-porphyrazine 10, the structure of which was established by an X-ray crystallographic study.

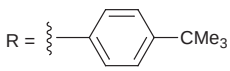
Recently, we described the synthesis of seco-porphyrazines **1a**–**d** by the peripheral oxidations of porphyrazines. Subsequent to our report, several related seco-chlorins have been described, and we have shown that porphyrazine **1d** (M = Zn) sensitises the formation of singlet oxygen with the remarkable overall quantum yield of $\phi_\Delta = 0.54$. In a continuation of our efforts to develop porphyrazines peripherally functionalised for metal bindings and porphyrazines with strong absorptions at wavelengths above 700 nm for biomedical applications, we have prepared porphyrazine *cis*-diols **8** *and* **9** *via* the OsO_4 mediated dihydroxylation of porphyrazines **6** and **7**, respectively. Surprisingly, reaction of diol **8** with $Ni(OAc)_2$ in air at 100 °C did not give any nickel(II) porphyrazinediol **9**. Instead, this procedure gave a mixture of products including a red pigment with much lower polarity than the porphyrazine diols **8** or **9**. Herein, we report the full characterisation of novel compound **10** a new type of seco-porphyrazine ring system generated by the loss of the two β-carbons of a pyrrole.



1a M = 2H, R = -NMe_2
b M = Zn, R = -NMe_2
c M = 2H, R = Pr
d M = Zn, R = Pr



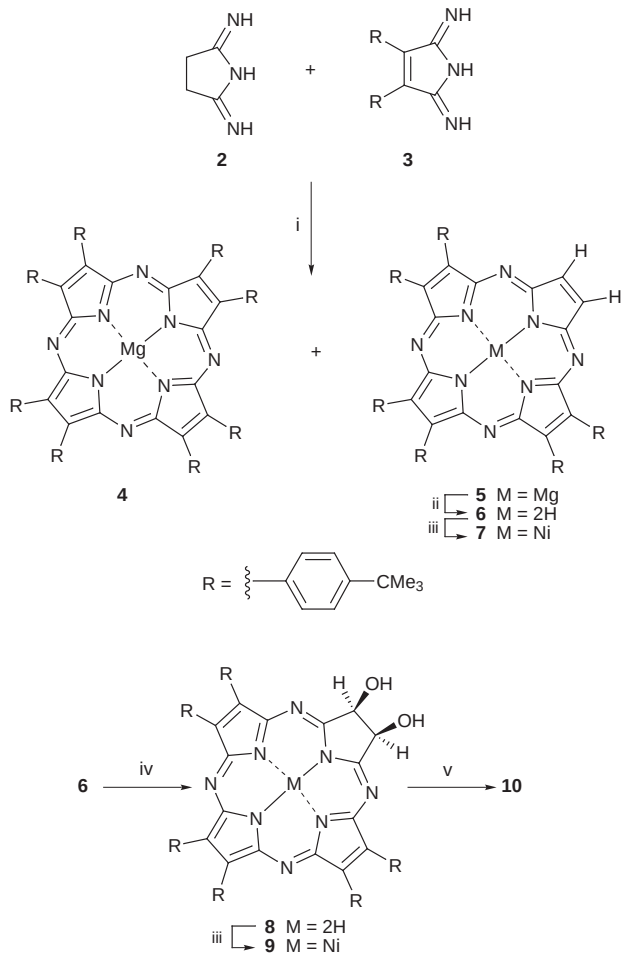
10



2,5-Diiminopyrrolidine **2** was co-macrocyclised with 3,4-bis(4-*tert*-butylphenyl)pyrroline-2,5-diimine **3** using $Mg(OBu)_2$ in BuOH at reflux (Scheme 1). The products contained both the unsymmetrical porphyrazine **5**† and symmetrical porphyrazine **4**, which were separated by chromatography. Demetallation of **5** by treatment with TFA gave the free base porphyrazine **6**. In a typical cyclisation, reaction of **2** with 3.5 equiv. of **3** ultimately led to porphyrazine **6** with an overall yield of 17% following demetallation. Subsequent reaction of **6** with $Ni(OAc)_2$ at 100 °C in PhCl–DMF (3 : 1) under N_2 resulted in the formation of nickel complex **7** (98% yield). Finally, OsO_4 mediated dihydroxylation of **6** and **7** gave dihydroporphyrazinediol **8** (69% yield) and the nickel(II) dihydroporphyrazinediol **9** (65% yield), respectively. Subsequent reflux of a solution of diol **8** with $Ni(OAc)_2$ in $CHCl_3$–MeOH (3 : 1) under nitrogen also gave the nickel diol **9** (90%).

The parent porphyrazine **6** showed a UV-visible absorption spectrum with two well separated Q-bands at λ_{max} 587 and 655 nm; porphyrazine 7 showed a typical metalloporphyrazine absorption spectrum, with a strong Q-band at 615 nm (Fig. 1) whereas the *cis*-diols **8** and **9** displayed different optical spectra from those observed for the related chlorins, 2,3-*vic*-dihydroxy *meso*-tetraphenylchlorins, with strong absorptions at λ_{max} 730 and 702 nm for porphyrazines **8** and **9**, respectively.

Reaction of porphyrazine **8** with 10 equiv. of $Ni(OAc)_2$ at 100 °C in PhCl–DMF (3 : 1) that had been only partially deaerated gave a mixture of products, including a new red pigment, denoted **10**, which was obtained with higher yields when porphyrazinediol **9** was reacted in air under similar conditions (Scheme 1). This pigment,‡ which was less polar



Scheme 1 *Reagents and conditions*: i, $Mg(OBu)_2$, BuOH, reflux; ii, TFA, then NH_4OH (17% from **2**); iii, $Ni(OAc)_2$, MeOH–$CHCl_3$, N_2, reflux (98%); iv, OsO_4, CH_2Cl_2–pyridine, then H_2S (69%); v, $Ni(OAc)_2$, DMF–PhCl, air, 100 °C (40%).

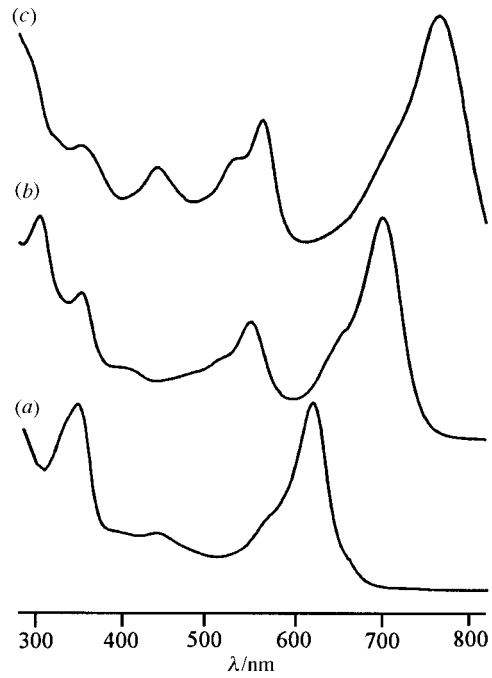


Fig. 1 UV-visible spectra of porphyrazines (*a*) **7** and (*b*) **9**, and (*c*) seco-porphyrazine **10**.

than the diols, was obtained in 40% yield after chromatography (silica, CH_2Cl_2–hexanes 4 : 1). Its UV-visible spectrum (Fig. 1) showed an unusual strong absorption band at λ_{max} 768 nm, which is red shifted by 66 nm compared to that of porphyrazinediol **9**.

Slow diffusion of MeOH into a $CHCl_3$ solution of **10** yielded single crystals suitable for X-ray crystallographic study,§ which (Fig. 2) unequivocally established the structure of the red pigment as seco-porphyrazine **10**. Spectroscopic measurements confirm the tautomeric form shown for **10**. Both ^{1}H and ^{13}C NMR spectra showed that the compound lacks the C_{2v} symmetry of the porphyrazine diols, and FAB$^+$ MS measurement was consistent with the composition of $C_{74}H_{80}N_8NiO$. The IR spectrum displayed a medium intensity band at ν_{max} 3380 cm^{-1} and a strong band at ν_{max} 1674 cm^{-1} which are consistent with the urea-like functionality on the ring of **10**, and ^{1}H NMR analysis showed the expected exchangeable proton signal at δ 9.45.

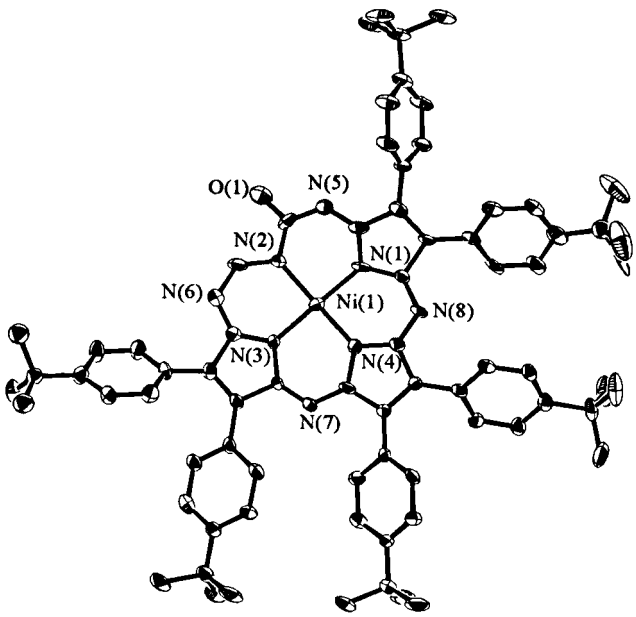


Fig. 2 X-Ray crystal structure of seco-porphyrazine **10**.

Compound **10** represents a novel macrocyclic ring system, which may result from the nickel-mediated air oxidation of the *cis*-diol unit and subsequent double loss of CO_2. Alternatively the mechanism may involve dehydration and subsequent cycloaddition of singlet oxygen, decarboxylation and deformylation. The methodology described above offers the opportunity for synthesis of the same type of heterocycles with other internal metal ions and different peripheral substituents for biomedical applications, and this investigation is in progress.

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Notes and references

† All new compounds were characterised by ^{1}H and ^{13}C NMR, MS, IR and UV-visible spectroscopy, microanalysis and cyclic voltammetry; in all cases the spectroscopic data were consistent with the assigned structures.

‡ *Selected data* for **10**: mp > 320 °C; TLC 0.37 (silica, CH_2Cl_2–hexanes 4 : 1); ν_{max}/cm^{-1} 3380, 2962, 1674, 1598, 1549, 1363, 1266, 1104, 986, 838, 750, 565; $\lambda_{max}(CH_2Cl_2)$/nm (log ε) 352 (4.40), 440 (4.32), 532 (4.33), 562 (4.44), 768 (4.65); δ_H(300 MHz, $CDCl_3$) 10.25 (s, 1H), 9.45 (s, 1H, exch. D_2O), 7.83 (d, *J* 8.4, 2H), 7.79 (d, *J* 8.4, 2H), 7.72 (d, *J* 8.4, 2H), 7.68 (d, *J* 8.7, 2H), 7.65 (d, *J* 8.4, 2H), 7.58 (d, *J* 8.1, 2H), 7.47 (d, *J* 8.4, 2H), 7.40 (d, *J* 8.4, 2H), 7.39 (d, *J* 8.4, 2H), 7.38 (d, *J* 8.7, 2H), 7.34 (d, *J* 8.4, 2H), 7.30 (d, *J* 8.7, 2H), 1.44 (s, 9H), 1.43 (s, 18H), 1.40 (s, 9H), 1.39 (s, 9H), 1.35 (s, 9H); δ_C(100 MHz, $CDCl_3$) 159.1, 153.4, 152.9, 152.8, 152.1, 151.8, 150.7, 150.6, 148.2, 146.5, 144.7, 144.5, 144.0, 143.2, 139.6, 139.5, 137.6, 132.8, 132.7, 132.6, 132.5, 132.0, 131.8, 131.6, 131.0, 130.5, 130.4, 129.6, 128.8, 128.8, 128.0, 126.2, 125.9, 125.8, 125.6, 36.0, 35.8, 35.7, 35.7, 32.68, 32.66, 32.5, 32.5, 32.4; *m/z* (FAB$^+$) 1156 (M$^+$); $E_{1/2}$/V (*vs.* Fc$^+$/Fc) 0.81, 0.45, −1.03 (E_{pc}), −1.07 (E_{pc}) (Calc. for $C_{74}H_{80}N_8NiO$: C, 76.87; H, 6.97; N, 9.69. Found: C, 76.57; H, 6.96; N, 9.67%).

§ *Crystal data* for **10**: $C_{78}N_8OH_{84}NiCl_{12}$, *M* = 1633.70, triclinic, *a* = 14.923(1), *b* = 16.310(1), *c* = 17.626(1) Å, α = 82.070(1), β = 71.520(1), γ = 80.380(1)°, *V* = 3995.0(4) Å^3, *T* = −120 °C, space group $P\bar{1}$ (#2), *Z* = 2, D_c = 1.355 g cm^{-3}, μ(Mo-Kα) = 6.92 cm^{-1}, *F*(000) = 1692.00. Data were collected on a CCD plate area detector with graphite monochromated Mo-Kα radiation. The structure was solved by direct methods and refined by the full-matrix least-squares technique to give *R*1 = 0.10 and *wR*2 = 0.192 for 28117 independent observed reflections among 36794 measured reflections. The structure contains two disordered *tert*-butyl groups on the macrocycle and four disordered $CHCl_3$ solvent molecules. The non-hydrogen atoms on the macrocycle were refined anisotropically except for C25, C45, C47 and C48 on the disordered *tert*-butyl groups; for the solvent, Cl1–C9 were refined anisotropically and C10–C12, isotropically, while the remaining chlorine and carbon atoms were fixed. CCDC 182/1189. Crystal data is available in CIF format from the RSC web site, see: http://www.rsc.org/suppdata/cc/1999/703/

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