# A novel approach to the synthesis of mono- and dipyrroloporphyrins

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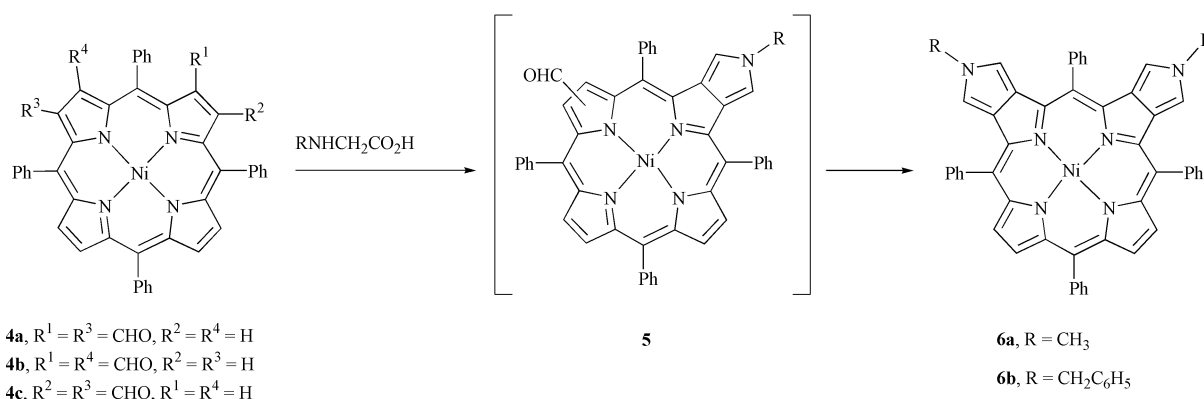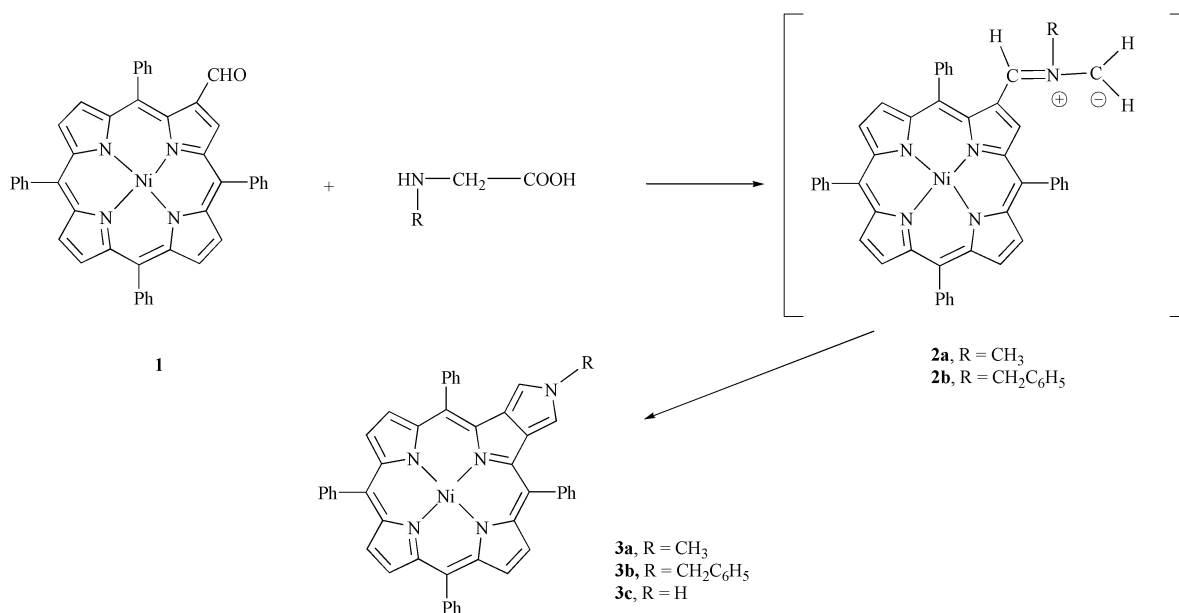*Department of Chemistry, University of Aveiro, 3810-193 Aveiro, Portugal*

**Starting with β-formyl- and β,β′-diformylporphyrins, novel mono- and dipyrroloporphyrins were synthesised via 1,5-electrocyclization of porphyrinic azomethine ylides.**
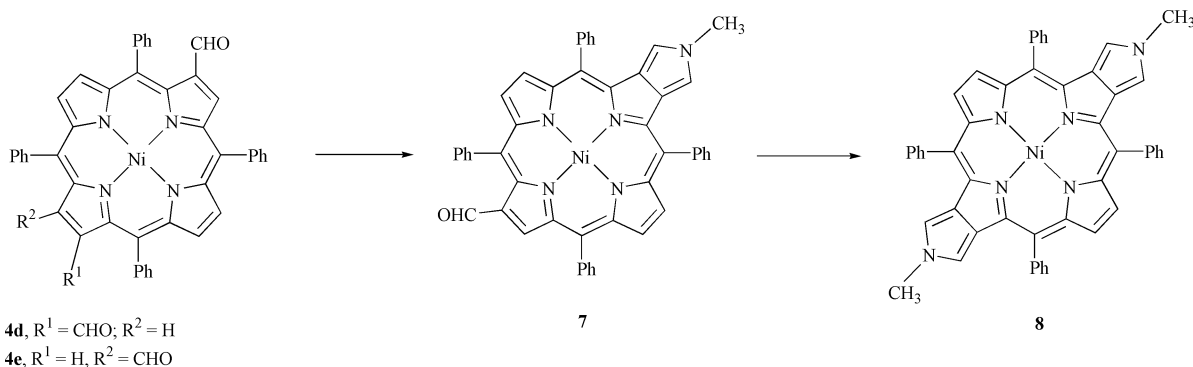
The porphyrin macrocycle is known to display interesting properties. In order to extend or improve those properties, which might be of great significance in the field of medicine or in the production of new electronic materials, carbo- and heterocyclic [b]fused porphyrins are being prepared.[1]

Here we describe a novel approach to the synthesis of pyrrolo[3,4-b]porphyrins **3**, dipyrrolo[3,4-b:3,4-g]porphyrins **6** and dipyrrolo[3,4-b:3,4-l]porphyrins **8** (Schemes 1–3).[2] These syntheses are based on a 1,5-electrocyclic ring closure,[3] followed by autoxidation, of azomethine ylides generated by the reaction of the nickel complexes of β-formylporphyrin derivatives with N-substituted glycines. Previously, we have described the syn-

thesis of the metal-free forms of the hydro analogues of compounds **3a** and **6a** via 1,3-dipolar cycloaddition reactions of azomethine ylides to the peripheral double bonds of the porphyrin macrocycle.[4] Recently Smith *et al.* reported the first synthesis of pyrrolo[3,4-b]porphyrins, based on the Barton–Zard condensation of 2-nitro-5,10,15,20-tetraphenylporphyrin with alkyl isocyanoacetates.[5] By this method, the β-fused pyrroloporphyrins are obtained as alkyl ester derivatives and subsequent hydrolysis and decarboxylation are necessary to afford the 2,5-unsubstituted pyrroloporphyrin **3c**.

The first evidence for the formation of the pyrroloporphyrins via the 1,5-electrocyclization of azomethine ylides **2** was observed during our studies on the 1,3-dipolar cycloaddition reactions of **2a** to several dipolarophiles.[6] We found that with less reactive compounds, together with the expected adducts, a new product was also being formed. Full spectroscopic charac-



**2a**, R = CH₃
**2b**, R = CH₂C₆H₅

**3a**, R = CH₃
**3b**, R = CH₂C₆H₅
**3c**, R = H

**Scheme 1**



**4a**, R¹ = R³ = CHO, R² = R⁴ = H
**4b**, R¹ = R⁴ = CHO, R² = R³ = H
**4c**, R² = R³ = CHO, R¹ = R⁴ = H

**5**

**6a**, R = CH₃

**6b**, R = CH₂C₆H₅

**Scheme 2**

**4d**, R$^1$ = CHO; R$^2$ = H
**4e**, R$^1$ = H, R$^2$ = CHO

**Scheme 3**

terisation of this compound showed that it has the structure **3a**.[7] The structure of this new compound does not incorporate the dipolarophile used. When the reaction of **1** with *N*-methylglycine was carried out in the absence of a dipolarophile, adduct **3a** was obtained in 42% (Scheme 1). Later it was found that better yields (55%) are obtained if potassium carbonate is added to the reaction mixture.[8] When the reaction was carried out with *N*-benzylglycine hydrochloride and potassium carbonate, pyrroloporphyrin **3b**[9] was isolated in 71% yield. Attempts to synthesise compound **3c** by reacting **1** with glycine, under similar conditions, were unsuccessful.

These reactions were also extended to β,β′-diformyl derivatives of *meso*-tetraphenylporphyrin (Schemes 2 and 3). Treatment of each porphyrin derivative **4a–4c**[10] (with the formyl groups in adjacent pyrrole rings) with *N*-methylglycine and potassium carbonate afforded the adduct **6a** in moderate to good yields (40–72%). The highest yield was observed with porphyrin **4b**. When the progress of the reaction of **4b** (and also **4c**) with *N*-methylglycine was monitored by TLC, we observed, in the early stages, the formation of two compounds: the intermediate **5** (confirmed by MS) and the final product **6a**. With porphyrin **4a** two isomeric intermediates **5** were observed. When another similar reaction was carried out with a mixture of the three isomers **4a–c**, avoiding their separation by preparative TLC, compound **6a** was isolated in 43% yield. The structure of this novel dipyrrolo derivative was unambiguously established by spectroscopic data.[11] Similar results were obtained when a mixture of compounds **4a–c** was treated with *N*-benzylglycine hydrochloride and potassium carbonate: the expected adduct **6b** was obtained in 42% yield.

When this type of reaction was carried out with a mixture of compounds **4d** and **4e** (with the formyl groups in opposite pyrrole rings) and *N*-methylglycine (in the absence of potassium carbonate), the only product obtained was, unexpectedly, the monopyrroloporphyrin **7** (13%). However, when the same reaction was carried out in the presence of potassium carbonate the product was the dipyrroloporphyrin **8** (36%). The structures of compounds **7** and **8** were established by considering their spectral data (NMR, MS and UV–Vis).[12] Compound **8**, in contrast to compounds **6a** and **6b**, slowly decomposes in chloroform solutions to yield highly polar products.

Attempts to obtain the metal free mono- and dipyrroloporphyrins by starting from the corresponding demetallated β-formylporphyrins or by demetallation of compounds **3a**, **b** and **6a**, **b** with H$_2$SO$_4$–CHCl$_3$ (1 : 10) were unsuccessful. In both cases only degradation products were obtained.

## Acknowledgements

## Notes and references

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7 The spectroscopic data of product **3a** are identical with those reported in ref. *5b* for the same compound (obtained as a by-product during the decarboxylation of a 2-methoxycarbonylpyrroloporphyrin).

8 Typical procedure: a toluene (5 ml) solution of nickel(II) 2-formyl-5,10,15,20-tetraphenylporphyrin **1** (0.01 mmol), *N*-substituted glycine (0.14 mmol) and potassium carbonate (0.07 mmol) was refluxed for 16 h under a nitrogen atmosphere. New portions of *N*-substituted glycine (0.14 mmol) and potassium carbonate (0.07 mmol) were added to the reaction mixture and reflux was continued for another 8 h. After cooling to room temperature the carbonate was filtered off and washed with dichloromethane. The resulting solution was washed with water and dried (Na$_2$SO$_4$). After concentration, the residue was purified by column chromatography (silica gel) using a mixture of dichloromethane–light petroleum (3 : 7) as eluent.

9 Spectroscopic data for **3b**: $^1$H NMR (300 MHz, CDCl$_3$) δ 5.20 (s, 2 H, C$H_2$C$_6$H$_5$), 6.02 (s, 2 H, H-pyrrole), 7.07–7.10 and 7.36–7.38 (2 m, 5 H, CH$_2$C$_6$$H_5$), 7.67–7.72 (m, 12 H, H$_{meta + para}$-Ph), 7.90–7.93 (m, 4 H, H$_{ortho}$-Ph), 8.01–8.04 (m, 4 H, H$_{ortho}$-Ph), 8.577 (s, 2 H, H-12, 13), 8.578 (d, *J* 4.9, 2 H, H-β), 8.66 (d, *J* 4.9, 2 H, H-β); $^{13}$C NMR (75 MHz, CDCl$_3$) δ 54.1, 112.8, 112.9, 120.2, 126.8, 127.0, 127.5, 127.8, 128.0, 128.7, 128.8, 130.0, 131.0, 132.1, 132.5, 133.4, 137.3, 138.1, 139.6, 140.9, 141.8, 144.3; MS (LSIMS) 800 (M + H)$^+$, 799 M$^+$; MS-HRFAB exact mass *m/z* for C$_{53}$H$_{35}$N$_5$Ni (M$^{+•}$): calculated, 799.2246, found 799.2246.

10 M. A. F. Faustino, T. M. P. C. Silva, A. M. G. Silva, M. G. P. M. S. Neves, A. M. S. Silva, A. C. Tomé and J. A. S. Cavaleiro, XIXth European Colloquium on Heterocyclic Chemistry, p. 96, Aveiro (Portugal), July, 2000; A detailed description of the synthesis, separation and characterisation of the five isomeric diformylporphyrins **4a–4e** is in preparation.

11 Spectroscopic data for **6a**: $^1$H NMR (300 MHz, CDCl$_3$) δ 3.72 (s, 6 H, 2 C$H_3$), 5.80 (d, *J* 1.5, 2 H, H-pyrrole), 5.93 (d, *J* 1.5, 2 H, H-pyrrole), 7.59–7.73 (m, 12 H, H$_{meta + para}$-Ph), 7.79–7.86 (m, 6 H, H$_{ortho}$-Ph), 7.92–7.95 (m, 2 H, H$_{ortho}$-Ph), 8.22 (d, *J* 4.7, 2 H, H-β), 8.33 (d, *J* 4.7, 2 H, H-β); MS (LSIMS) 776 (M$^{+•}$); MS-HRFAB exact mass *m/z* for C$_{50}$H$_{35}$N$_6$Ni (M + H)$^+$: calculated, 777.2277, found 777.2279.

12 Spectroscopic data for **8**: $^1$H NMR (300 MHz, CDCl$_3$) δ 3.76 (s, 6 H, 2 CH$_3$), 5.86 (s, 4 H, H-pyrrole), 7.61–7.70 (m, 12 H, H$_{meta + para}$-Ph), 7.87–7.90 (m, 8 H, H$_{ortho}$-Ph), 8.55 (s, 4 H, H-β); MS-HRFAB exact mass *m/z* for C$_{50}$H$_{35}$N$_6$Ni (M + H)$^+$: calculated, 777.2277, found 777.2291.