New Substituted Tetraphenyl Porphyrins: Synthesis, NMR Characterization and Manganese(III) and Iron(III) Complexes

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Giovanni Bruno,[a] Stefania De Luca,[a] Carla Isernia,[b] Roberto Fattorusso,[b] Filomena Rossi,[a] Carlo Pedone[a] and Giancarlo Morelli*[a]

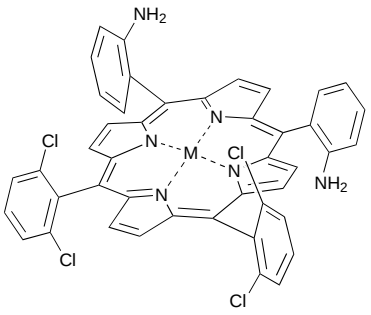
[a]*Centro Universitario di Recerca sui Peptidi Bioattivi, and Centro di Studio di Biocristallografia, CNR, Via Mezzocannone 4, I-80134 Napoli, Italy*
[b]*Dipartimento di Scienze Ambientali, Seconda Università di Napoli, Via Arena 22, I-81100 Caserta, Italy*

Synthetic strategies for new substituted tetraphenylporphyrins and their iron(III) and manganese(III) complexes are reported together with ^{1}H NMR studies on free bases allowing identification of the porphyrin isomers.

Metalloporphyrins, especially those of Fe^{III} and Mn^{III}, have been extensively studied, for oxidative catalytic purposes, as models of haem-containing oxygenases[1] and peroxidases.[2] Owing to the ease of synthesis, the metalloporphyrin catalysts used in biomimetic studies have been of the *meso*-tetraphenylporphyrin type (TPP).[3] Among these, iron(III) tetrakis(*ortho*-dichlorophenyl)porphyrinate, TDCPPFeCl, has been demonstrated as being a very efficient oxidation catalyst, since both electron deficiency and steric bulk are present in molecules with *ortho*-chloro groups.

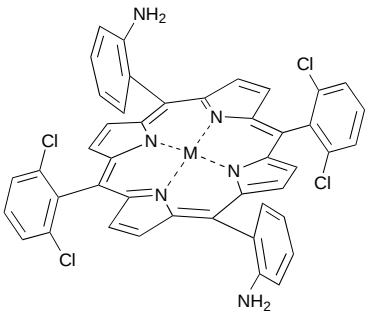
Here we report the synthesis of new iron(III) and manganese(III) tetraphenylporphyrins (shown in Fig. 1) carrying both *ortho*-chloro substituents and reactive NH_2 groups on the phenyl rings. The presence of NH_2 groups gives the opportunity to insert these molecules in supramolecular structures such as peptides. The strategies for porphyrin synthesis and iron(III) and manganese(III) insertion are reported as well as a first Fmoc–amino acid adduct. ^{1}H NMR studies on the free bases allow the identification of the different porphyrin isomers.

We have used the mixed aldehyde condensation method[16] by reacting 2,6-dichlorobenzaldehyde (1 mol equiv.), 2-nitrobenzaldehyde (1 mol equiv.) and pyrrole (2 mol equiv.) when a mixture of 5,10-bis-(2,6-dichlorophenyl)-15,20-bis-(2-nitrophenyl)porphyrin and 5,15-bis-(2,6-dichlorophenyl)-10,20-bis-(2-nitrophenyl)porphyrin was obtained in approximately



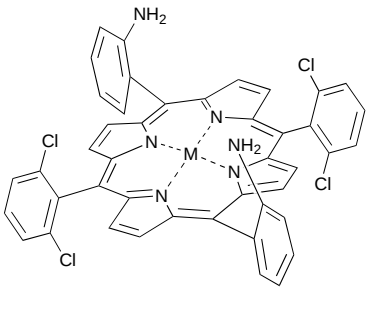
5,10-bis-(2-aminophenyl)-15,20-bis-(2,6-dichlorophenyl)porphyrin (*cis*-αβ)

M = H_2 **1**
M = Mn^{III} **1-Mn^{III}**
M = Fe^{III} **1-Fe^{III}**



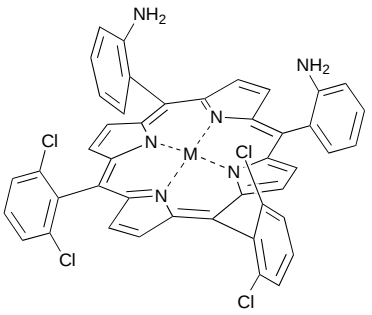
5,15-bis-(2-aminophenyl)-10,20-bis-(2,6-dichlorophenyl)porphyrin (*trans*-αβ)

M = H_2 **2**
M = Mn^{III} **2-Mn^{III}**
M = Fe^{III} **2-Fe^{III}**



5,15-bis-(2-aminophenyl)-10,20-bis-(2,6-dichlorophenyl)porphyrin (*trans*-αα)

M = H_2 **3**
M = Mn^{III} **3-Mn^{III}**
M = Fe^{III} **3-Fe^{III}**



5,10-bis-(2-aminophenyl)-15,20-bis-(2,6-dichlorophenyl)porphyrin (*cis*-αα)

M = H_2 **4**
M = Mn^{III} **4-Mn^{III}**
M = Fe^{III} **4-Fe^{III}**

Fig. 1 Schematic representation of the four isomers of the metal porphyrins under study, with the adopted nomenclature and abbreviation for each isomer

*To receive any correspondence.

equimolar amounts. Moreover, by considering the fact that the presence of *ortho* substituents on the *meso*-phenyl groups prevents the free rotation of the phenyl groups at room temperature,[18] each compound is a mixture of two atropoisomers, $\alpha\alpha$ or $\alpha\beta$, depending on whether the two nitro substituents are present on the same or opposite sides of the porphyrin plane. Subsequent treatment of the porphyrin mixture with tin(II) chloride afforded the corresponding aminophenylporphyrins.

Silica gel chromatography of the mixture enabled separation of the four purified porphyrins (**1**, **2**, **3** and **4** in order of increasing polarity), identified by ^{1}H NMR spectroscopy and by considerations of their polarity as the *cis*-$\alpha\beta$ isomer (**1**), the *trans*-$\alpha\beta$ isomer (**2**), the *trans*-$\alpha\alpha$ isomer (**3**) and the *cis*-$\alpha\alpha$ isomer (**4**).

The NMR identification of the different *cis*–*trans* isomers was based on the β-pyrrole protons. To distinguish between the $\alpha\alpha$ and $\alpha\beta$ atropisomers we examined the signals corresponding to protons H^3 and H^5 of the phenyl rings carrying the chloro substituents. In principle, in the case of the two *trans* isomers different patterns are exhibited by these protons, depending on the atropisomer. In fact, if both the NH_2 groups are on the same side of the porphyrin plane (*trans*-$\alpha\alpha$ isomer) the two H^3 protons that are positioned on the same side as the NH_2 groups are magnetically different from the two H^5 protons positioned on the opposite side; therefore two resonances are expected. In contrast, in the case of the *trans*-$\alpha\beta$ atropisomer the four H^3 and H^5 protons are all magnetically identical and might resonate as a unique doublet.

Metal insertion was easily obtained by reacting the free porphyrin bases with an excess (30–100 fold) of M^{2+} as the acetate salt, according to the usual procedures for metal insertion into porphyrin rings.[21] The reactions were monitored by UV–VIS changes in the Soret and visible regions of the spectrum. None of these new tetraphenylporphyrin metal complexes, or the parent free bases, showed significant atropisomerization at room temperature. Moreover, we also proved the absence of atropisomerization, by TLC analysis, after 3 h of stirring of a solution in DMF at 80 °C. These experimental conditions are suitable for amide bond formation between the NH_2 groups of the porphyrin moiety and the carboxylic groups of protected amino acids. Thus we have obtained the adducts [Fmoc-Glu(OBu^t)]$_2$–(**2-Mn**) and [Fmoc-Asp(OBu^t)]$_2$–(**2-Mn**), in which the C′ carboxylic groups of, respectively, two protected glutamic acid or aspartic acid molecules [N^α-(fluoren-9-ylmethyloxycarbonyl)-γ-(*tert*-butoxycarbonyl)-L-glutamic acid or N^α-(fluoren-9-ylmethyloxycarbonyl)-β-(*tert*-butoxycarbonyl)-L-aspartic acid] are covalently bonded to the amino groups of the *trans*-$\alpha\beta$ isomer of the manganese(III) porphyrinate (**2-Mn**).

Although some covalent peptide–porphyrin compounds have been recently synthesised,[11] they contain natural haem or deuterohaem as the porphyrin moiety. [Fmoc-Glu(OBu^t)]$_2$-(**2-Mn**) and [Fmoc-Asp(OBu^t)]$_2$-(**2-Mn**) are starting blocks for the preparation of peptide–porphyrin compounds based on synthetic TPP derivatives which could be more suitably used for catalytic purposes.

The preparation of the other amino acid–and peptide–metalloporphyrin adducts starting from the metalloporphyrins described here is at present in progress.

Techniques used: ^{1}H NMR, UV–VIS

References: 23

Scheme: 1

Tables: 2

Fig. 2: ^{1}H NMR spectrum of **1** in $CDCl_3$ at 298 K

Fig. 3: Expanded regions of ^{1}H NMR spectra for **1** (*cis* $\alpha\beta$) and **3** (*trans* $\alpha\alpha$) showing β-pyrrole proton resonances in $CDCl_3$ at 298 K

Fig. 4: Expanded regions of the ^{1}H NMR spectra for compounds **2** (*trans* $\alpha\beta$) and **3** (*trans* $\alpha\alpha$) showing H^3, H^5 and H^4 proton resonances in $CDCl_3$ at 298 K

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