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Stepwise Fusion of Porphyrin β,β'-Pyrrolic Positions to Imidazole Rings

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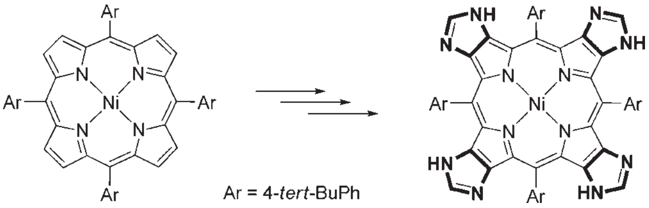
ABSTRACT



A strategy for the stepwise annulation of pyrrolic rings of a porphyrin to imidazole rings is presented. Mono(imidazole), Janus and corner bis(imidazole), T-shaped tris(imidazole), and tetrakis(imidazole) porphyrins have been synthesized and characterized.

Among π-conjugated molecules, porphyrins are of great interest because they are photo- and electroactive molecules which have wide applications in catalysis,[1] medicine,[2] and materials science.[3] The introduction of π conjugated systems fused to the aromatic core of a porphyrin can deeply modify their electronic properties, as illustrated for exocyclic fused rings such as pyridine,[4] quinoxaline,[5] quinoline,[6] isoquinoline,[6a]

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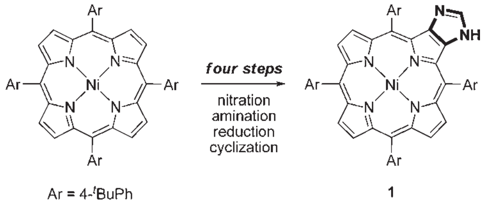
azulene,[7] naphthalene,[8] pyrene,[9] or anthracene.[10] Several porphyrins fused to five-membered *N*-heterocycles such as pyrrole,[11] pyrrazole,[12] triazole,[13] and imidazole[14−17] groups have also been synthesized.

Porphyrins containing imidazole rings fused across β,β'-pyrrolic positions and conjugated to the macrocycle have notably been reported by Crossley and colleagues, who prepared fused porphyrin−imidazole systems by condensation of porphyrin-2,3-diones with an aryl aldehyde in the presence of NH_4OAc.[14] Following this procedure, the compounds obtained have C(2′)-aryl groups, and these molecules were shown to be interesting subunits in donor−acceptor linked dyads[15a] or triads[15b] for the study of photoinduced electron-transfer processes. Following a different synthetic strategy, we synthesized porphyrins fused to an imidazole ring with C(2′)-H. We have shown that the corresponding *N*,*N*′-dialkylimidazolium salts are *N*-heterocyclic carbene (NHC) precursors and that metal complexes such as palladium(II)[16a] or rhodium(I)[16b] complexes can be anchored at the peripheral NHC ligand. These studies led us to develop an efficient synthetic strategy to prepare metalloporphyrins annulated to one exocyclic imidazole ring with a C(2′)-H instead of a C(2′)-aryl group, according to the following four steps:[17] (i) nitration of one β-pyrrolic position, (ii) amination of the adjacent β-pyrrolic position, (iii) reduction of the nitro group to obtain the 2, 3-diaminoporphyrin, and (iv) cyclization, in order to obtain compound **1** which contains one pyrrole annulated to one imidazole ring (Scheme 1). Herein, we show that up to four imidazole rings can be fused to the porphyrin macrocycle by repeating this sequence of reactions. This stepwise ring annelation of each of the four β,β'-pyrrolic positions using successive porphyrin-α-diamines complements that of Crossley and colleagues who elaborated mono-, bis-, tris-, and tetrakis(quinoxalino)porphyrins by their porphyrin-α-dione methodology.[5b,c,18]

Scheme 1. Fusion of Porphyrin β,β'-Pyrrolic Positions to One Imidazole Ring[17]



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The mononitration reaction performed on porphyrin **1** leads to a mixture of three β-pyrrolic functionalized nitroporphyrin isomers **2**−**4** in 92% yield (Scheme 2). The nitration reaction did not occur at the C(2′) of the imidazole ring. Crossley and colleagues studied the nitration of porphyrin-2,3-diones and also obtained a mixture of three β-pyrrolic functionalized nitroporphyrin isomers. They used an elegant metalation/demetalation procedure to separate the three isomers.[19] Here, the β-nitroporphyrin isomers **2**−**4** could not be separated by column chromatography at this stage, and the mixture was thus used as such in the following amination step. The β-pyrrolic carbons next to the β-NO_2 groups were regioselectively aminated with 4-amino-4*H*-1,2,4-triazole under basic conditions. Then, column chromatographic separation on silica gel allowed the separation of isomer **5** (nitro and amino groups on the pyrrole opposed to the one fused to the imidazole ring) with 29% yield from the two other isomers **6** and **7** (nitro and amino groups on the pyrrole next to the one fused to the imidazole ring) obtained as a mixture with 60% yield. The reduction of the nitro group of the porphyrin **5** led to the corresponding diaminoporphyrin, which was not isolated but used directly for the cyclization reaction with $HC(OMe)_3$ under acidic conditions. The Janus bis(imidazole) **8** was thus obtained in 81% yield. The same reduction and cyclization reactions were performed on the mixture of isomers **6** and **7**, leading to the corner bis(imidazole) **9** in 85% yield (Scheme 2). Right mass peaks corresponding to the mono- and diprotonated species were observed for both isomers by ESI-TOF mass spectrometry (m/z = 975.4 $[M + H]^+$ and 488.2 $[M + 2H]^{2+}$, respectively). The signals observed on the ^1H NMR spectra of bis(imidazole) porphyrins **8** and **9** recorded in $CDCl_3$ at room temperature are globally broad due the slow imidazole tautomerism on the ^1H NMR time scale.[20] The ^1H NMR spectrum of Janus bis(imidazole) **8** displayed one singlet at δ = 1.59 ppm corresponding to the *tert*-butyl groups and one broad singlet at δ = 8.82 ppm corresponding to the four Cβ-H. In the ^1H NMR spectrum of the corner bis(imidazole) **9**, the three singlets observed at δ = 1.61, 1.58, and 1.55 ppm corresponding to *tert*-butyl groups

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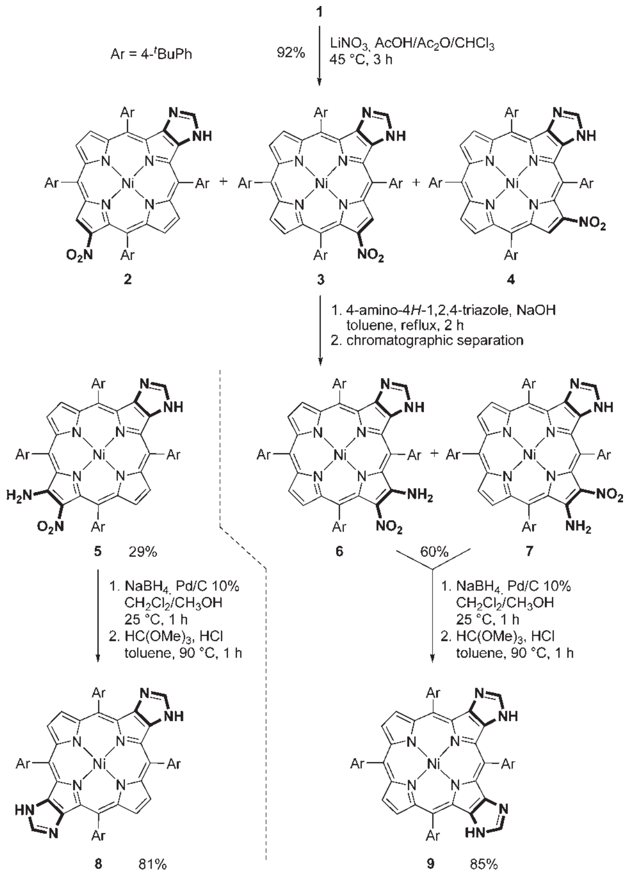
(20) Although bis-, tris-, and tetrakis(imidazole) porphyrin derivatives described here exist as a mixture of tautomers, only one tautomeric structure is represented for each compound in Schemes 2−4 and in the Supporting Information. See also refs 14−17.

are well resolved, whereas the signals corresponding to the pyrrolic protons are not. However, sharper signals were observed after the addition of an excess of trifluoroacetic acid (TFA) to sample **9**: in this case, two signals are observed for the pyrrolic protons (two doublets at δ = 8.97 and 8.92 ppm) due to the lower symmetry of this molecule compared to bis(imidazole) **8**.

Scheme 2. Fusion of Porphyrin β,β'-Pyrrolic Positions to Two Imidazole Rings



In the case of bis(imidazole) **9**, we were able to grow single crystals suitable for X-ray study by adding TFA to the solvent system used for crystallization ($CHCl_3$/*n*-heptane).[21] Single-crystal X-ray analysis unambiguously establishes the structure of bis(imidazole) **9**, showing that two neighboring pyrroles are fused to imidazole rings and that nickel(II) coordination distorts the porphyrin from planarity (Figure 1). The porphyrin macrocycle is saddle-shaped, as shown by the maximum displacement of 0.566 Å for one of the Cβ carbons and the average displacement of 0.283 Å for the core atoms with respect to the porphyrin mean plane (based on a least-squares plane calculated for the 24 core atoms of the porphyrin). The additional imidazole rings and their corresponding fused pyrroles are coplanar. Thus, because of the saddle-shape conformation of the porphyrin, one imidazole ring is above the mean plane of the porphyrin, while the other is underneath. The nickel(II) metal ion is in a slightly distorted square planar geometry: the four Ni−N distances are almost equivalent (1.945(3)−1.960(3) Å), the four N−Ni−N cis-angles are close to 90° (89.67(9)−90.91(9)°), and the two N−Ni−N trans-angles are 172.60(9) and 172.02(10)°. Interestingly, because both imidazole rings are protonated, porphyrins are self-assembled in the solid state thanks to a network of hydrogen bonds between **9-2H^{2+}** dications, trifluoroacetate anions, and TFA molecules (Figure S1, Supporting Information).

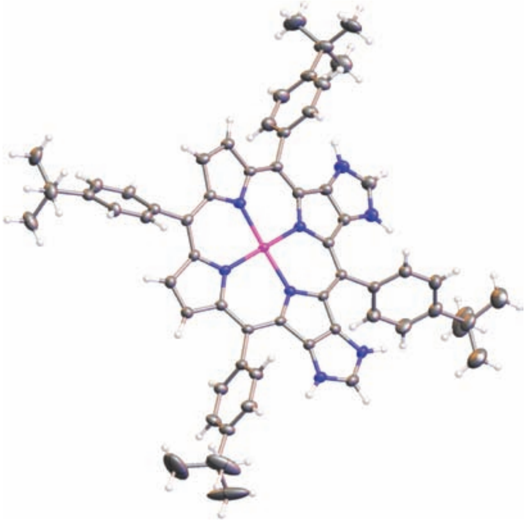


Figure 1. ORTEP view of the X-ray structure of the diprotonated bis(imidazole) **9-2H^{2+}** with displacement ellipsoids drawn at the 50% probability level (CF_3CO_2H and $CF_3CO_2^-$ molecules have been omitted for clarity).[21]

The construction of the third imidazole ring was achieved by performing the same four synthetic steps on the Janus-type bis(imidazole) **8** or on the corner bis(imidazole) **9**. Knowing that the four Cβ-H are equivalent, nitration of Janus-type bis-imidazole **8** with $LiNO_3$ afforded compound **10** as a single compound in 74% yield. Again, the β-pyrrolic carbon next to the β-NO_2 group was regioselectively aminated, and compound **11** was obtained in 83% yield. The reduction of the nitro group of **11** and the cyclization reaction afforded the T-shape tris(imidazole) **16** in 69% yield (Scheme 3). This compound was also obtained starting from corner bis(imidazole) **9**. Nitration of bis(imidazole) **9** afforded an inseparable mixture of nitro isomers **12** and **13** which were subsequently aminated to obtain **14** and **15** as an inseparable mixture. The reduction and cyclization reactions with the mixture of the isomers **14** and **15** afforded the same

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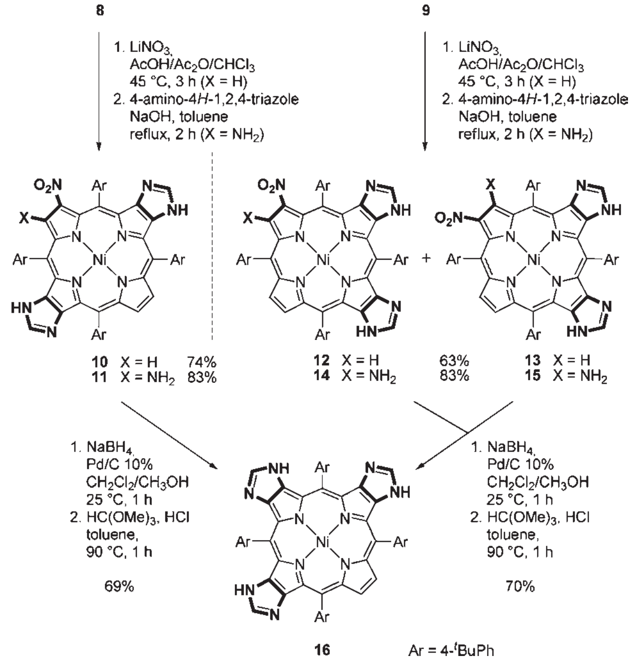
[21] Crystal data for **9-2H^{2+}**: $C_{62}H_{62}N_8Ni\cdot 3(CF_3CO_2H)\cdot 3(CF_3CO_2)$, MW = 1546.01, triclinic, space group *P*-1, a = 12.1781(3) Å, b = 18.0930(4) Å, c = 18.6755(4) Å, α = 94.0274(17)°, β = 108.2505(19)°, γ = 99.0435(17)°, V = 3827.91(15) Å^3, Z = 2, D_{calcd} = 1.365 g cm^{-3}, T = 173 K, λ (Mo Kα) = 0.71073 Å, μ (Mo Kα) = 0.35 mm^{-1}, 17527 reflections collected, 12985 unique reflns $I > 2\sigma(I)$, R_{int} = 0.053, R_F = 0.066 and wR_F = 0.075. See the Supporting Information for experimental details.

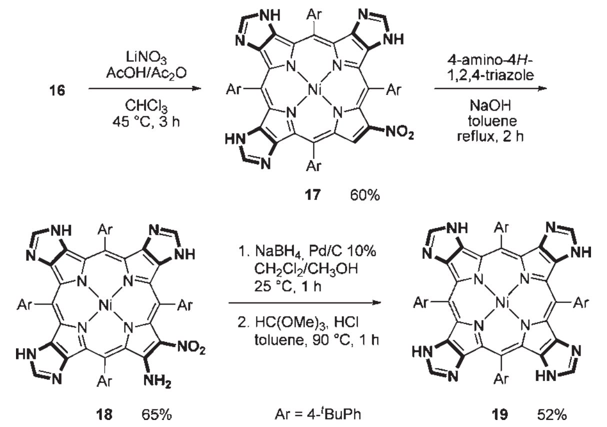
T-shape tris(imidazole) **16** in 70% yield (Scheme 3). As expected, right mass peaks corresponding to the mono-, di- and triprotonated species were observed for **16** by ESI-TOF mass spectrometry (at m/z = 1015.4 $[M + H]^+$, 508.2 $[M + 2H]^{2+}$, and 339.1 $[M + 3H]^{3+}$, respectively). The ^1H NMR spectrum of **16** displayed one singlet at δ = 8.80 ppm corresponding to the two remaining $C\beta$-H.

Scheme 3. Fusion of Porphyrin β,β'-Pyrrolic Positions to Three Imidazole Rings



Further functionalization of these two remaining β-pyrrolic positions of the T-shaped tris(imidazole) **16** was achieved, and compounds **17** and **18** were obtained in 60 and 65% yields, respectively. The cyclization reaction then afforded tetrakis(imidazole) **19** in 52% yield (Scheme 4). The ^1H NMR spectrum of tetrakis(imidazole) **19** is very simple because of its C_4 symmetry. As expected, no signal corresponding to pyrrolic protons was observed. Mono-, di-, and triprotonated species were detected by ESI-TOF mass spectrometry (at m/z = 1055.4 $[M + H]^+$, 528.2 $[M + 2H]^{2+}$, and 352.5 $[M + 3H]^{3+}$, respectively).

Scheme 4. Fusion of Porphyrin β,β'-Pyrrolic Positions to Four Imidazole Rings



In conclusion, a strategy for the stepwise annulation of the pyrrolic rings of a porphyrin to imidazole rings has been presented. Interestingly, all the possible isomers resulting from the fusion of one to four imidazole rings to the porphyrin were obtained by repeating a sequence of four reactions. Using this established synthetic protocol, further complex molecules may then be obtained, such as bis-, tris-, or tetrakis(imidazol-2-ylidene) ligands and their metal complexes, for the formation of 1D-polymeric materials or square grid networks of porphyrins. This research is in progress in our group.

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Supporting Information Available. Detailed experimental procedures, spectroscopic characterizations of all compounds, crystallographic data, and a CIF file for compound **9**. This material is available free of charge via the Internet at http://pubs.acs.org.