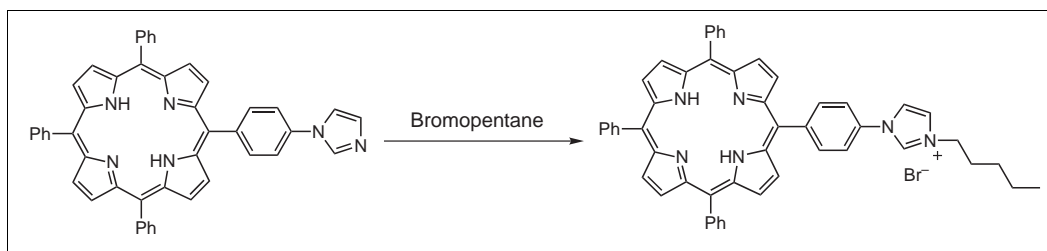# Synthesis of Imidazole and Imidazolium Porphyrins

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A new porphyrin compound, where an imidazole group was attached through the 1-position nitrogen to a phenyl ring located on the porphyrin periphery has been synthesized and characterized. The second nitrogen on the imidazole is available for further chemistry as demonstrated by the attachment of bromopentane forming the imidazolium porphyrin complex. This is the first example of an imidazolium group covalently attached to the porphyrin periphery in which the porphyrin is attached through the nitrogen on the imidazole ring rather than a carbon atom.

Introduction.

Porphyrins with heterocyclic substitutions on the periphery have been utilized to form a variety of arrays and coordination modes to metal centers [1-6]. Specifically, imidazoles covalently attached to porphyrins have been used to form non-covalent arrays through the binding of an imidazole nitrogen to a metal inside of a second porphyrin [7-13].

Our interest was to form imidazole porphyrin complexes in which the porphyrin is attached to the imidazole through a nitrogen rather than a carbon, thus leaving both the second nitrogen and the carbon between the nitrogens available for further chemistry. Herein, we wish to report on the synthesis of a new compound, 5-(4'-(imidazol-1''-yl)-phenyl)-10,15,20-triphenylporphyrin (**1**). Nitrogen substituted imidazoles are well known to react with alkyl halides to form imidazolium moieties. To demonstrate this, we reacted **1** with bromopentane to afford an imidazolium porphyrin complex, 5-(4'-(3''-(pent-1'''-yl)-imidazol-1''-yl)-phenyl)-10,15,20-triphenylporphyrin bromide (**2**), the first example of an imidazolium covalently attached to the porphyrin periphery in which the porphyrin is attached through the nitrogen.

Scheme I
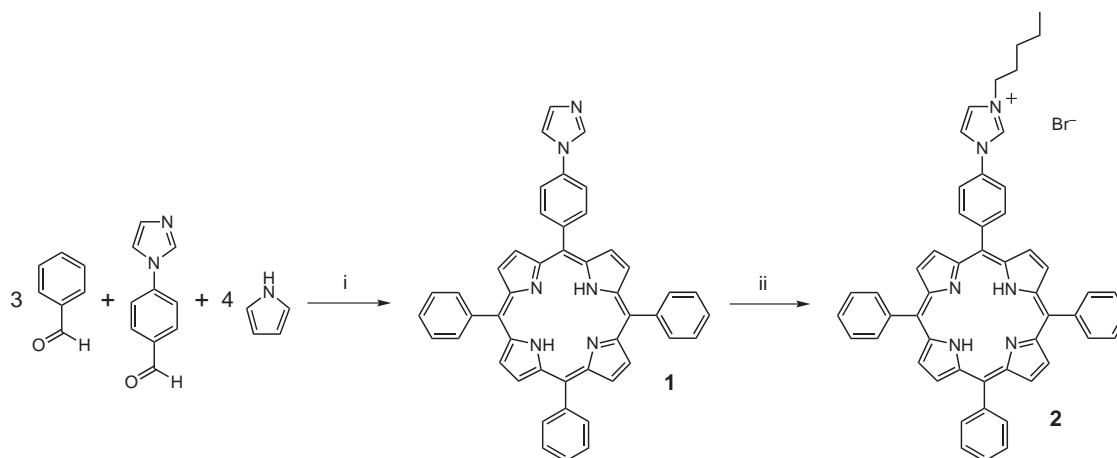
Reagents: (i) refluxing propionic acid; (ii) **1**, bromopentane, THF, 90 °C.
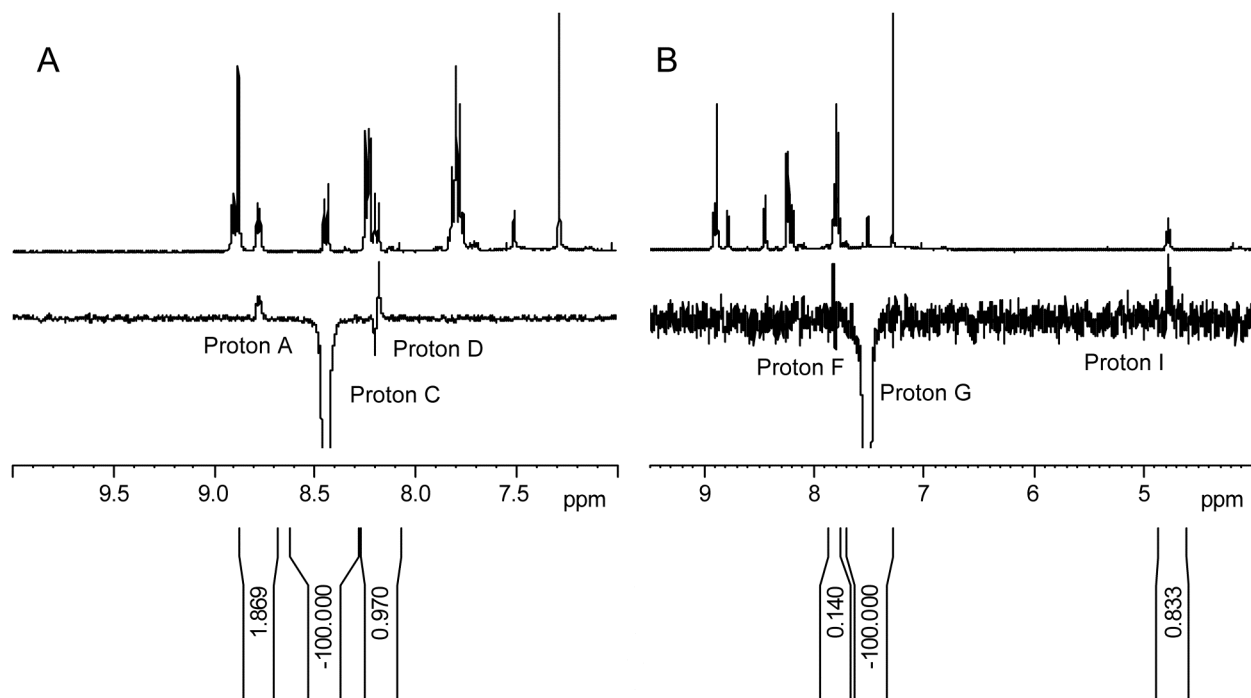
Figure 1. NOESY NMR of **2**: **A** exciting H$_c$ with energy transferred to H$_a$ and H$_d$, and **B** exciting H$_g$ with energy transferred to H$_f$ and H$_i$.

Results and Discussion.

The synthesis of **1** was carried out by using a modified Adler Longo reaction in refluxing propionic acid [14]. Our original route was to utilize a tetraphenylporphyrin (TPP) with a bromine substituted on the phenyl ring and add the imidazole *via* an Ullman coupling reaction, [15,16] but this route proved difficult due to problems isolating the compound from the reaction mixture. Instead, compound **1** was cyclized from pyrrole, benzaldehyde and 4-imidazol-1-yl-benzaldehyde [17] in a 4 to 3 to 1 ratio to yield a statistical mixture of tetra-phenylporphyrin and imidazole substituted porphyrins (Scheme I). Tetraphenylporphyrin was easily separated from the mono-substituted porphyrin product by chroma-tography on silica gel using methylene chloride as the eluant. Compound **1** was then removed from the silica gel with 1% methanol in methylene chloride to give a yield of 31%.

The pentyl substituted imidazolium porphyrin (**2**) was synthesized by the addition of bromopentane to **1** in tetrahydrofuran. The bromopentane was added in an over 50-fold excess and the reaction was refluxed for 2 days under nitrogen. Compound **2** was purified by chroma-tography on alumina using CH$_2$Cl$_2$/MeOH 50:1 to give a yield of 41%. Both compounds contained half an equivalent of methanol in the solid, by elemental analysis.

Scheme II
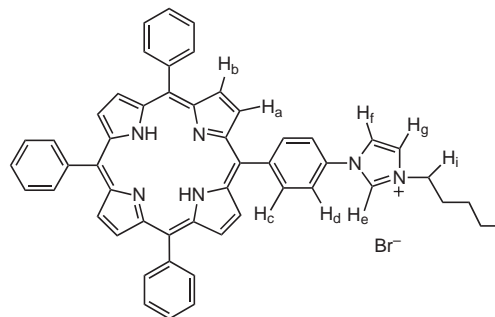
Proton Assignment for **2**

The ^{1}H NMR for **1** shows the aromatic peaks in the normal downfield region and the shift for the two endocyclic protons at about –3 ppm, typical for a porphyrin complex. The β-protons on the porphyrin, adjacent to the imidazole substituted phenyl ring, are shifted slightly upfield from unsubstituted tetraphenylporphyrin while the protons *ortho* to the porphyrin on the imidazole substituted phenyl ring are downfield relative to the unsubstituted phenyl rings. The three imidazole peaks come as broad singlets in the aromatic region.

The pentyl substituted imidazolium porphyrin, **2**, has resonances that span the full range of the ^{1}H NMR window with the proton on the carbon between the two nitrogen atoms on the imidazolium group (H$_e$) at 11.76 ppm and the
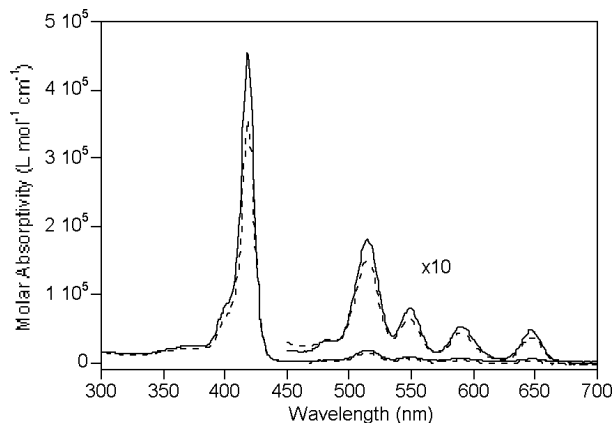
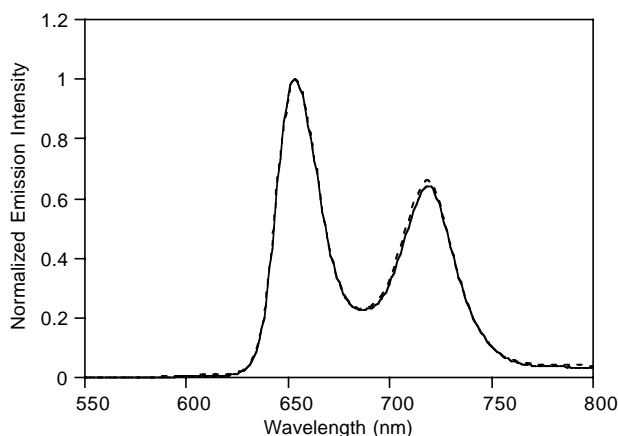Figure 2. Electronic spectrum of **1** (Solid line) and **2** (dashed line).

Figure 3. Normalized emission spectra of **1** (solid line) and **2** (dashed line) in CH_2Cl_2.

Figure 4. Cyclic voltammogram of **1** (solid line) and **2** (dashed line) in CH_2Cl_2, $TBAPF_6$ as supporting electrolyte, 200 mV/sec, Pt working electrode, Ag/AgCl reference electrode.

endocyclic protons at about –3 ppm. The remaining protons were assigned by NOESY NMR (Figure 1) and see Scheme II for assignment of the protons. The pyrrolic protons adjacent to the substituted phenyl ring (H_a) are upfield at 8.78 ppm, and the peak at 8.19 ppm corresponds to the phenyl protons next to the imidazole ring (H_d). The remaining imidazolium protons are at 7.82 (H_f) and 7.51 (H_g) ppm.

The electronic structure of the porphyrin is not greatly perturbed by the incorporation of the imidazole group onto the phenyl ring. The absorption and fluorescence spectra do not show any shifts in the peaks (Table 1 and Figures 2 and 3). The molar absorptivity of the substituted compounds is reduced with increasing substitution but the relative intensity of the two emission bands remains the same. However, the electrochemistry, see Table 1 and Figure 4, shows that **1** and **2** are easier to reduce relative to tetraphenylporphyrin indicating a
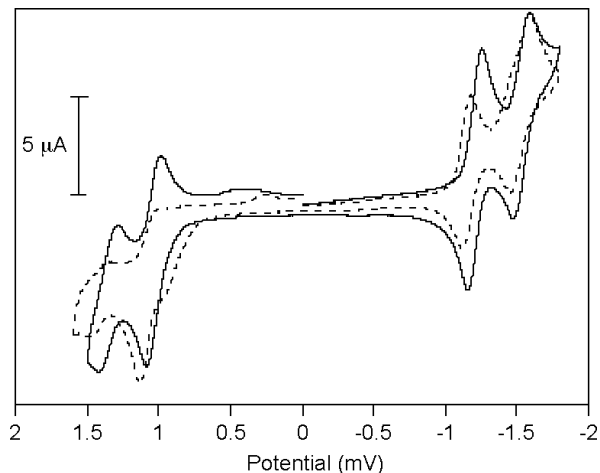
lowering of the lowest unoccupied molecular orbital. In addition, the oxidation waves of **2** become irreversible upon formation of the imidazolium functionality. This is not unexpected since the parent imidazolium group carries a positive charge, and the removal of an electron will most likely induce chemical changes preventing reversibility.

In conclusion, we have synthesized and characterized an imidazole substituted porphyrin and formed the imidazolium salt of the porphyrin. This is the first example demonstrating that the porphyrins can be bound to an imidazolium through the nitrogen. The structure of the imidazolium porphyrin was assigned by NMR and the compounds were electronically characterized. Imidazolium compounds have an acidic proton on the carbon between the nitrogen atoms; and the removal of this hydrogen generates stable *N*-heterocyclic carbene complexes which are known to coordinate to metal centers [18]. We are currently investigating the formation of the *N*-heterocyclic carbene and its ability to bind metals and form arrays.

EXPERIMENTAL

The pnmr spectra were recorded at 400 MHz on a Varian spectrometer. The cnmr spectra were recorded at 100 MHz. All starting materials were commercially available; 4-(imidazol-1-yl)benzaldehyde was prepared according to literature procedures [12]. Pyrrole and benzaldehyde were vacuum transferred immediately prior to use; all other reagents were used without further purification. Elemental analyses were obtained from Robertson Microlit; mass spectral analyses were conducted by the Washington University Center for Biomedical and Bioorganic Mass Spectrometry.

Table 1

Absorption (λ_{abs}) and Emission (λ_{em}) Maxima, Estimated Excited State Energy (E_{00}), and Ground State Redox Potentials (vs Ag/AgCl) of the Complexes in CH_2Cl_2

Compound	λ_{abs}(Soret)/nm ($\epsilon/10^4$ M^{-1}1cm^{-1}) [a]	Soret FWHM/cm^{-1}	λ_{em}/nm [b]	E_{00}/eV [c]	$E_{1/2}$(por)/V [d, e]
1	418 (43.70)	687	653, 719	1.90	1.35, 1.03, −1.21, −1.54
2	418 (34.48)	687	653, 718	1.90	1.50[f], 1.13[f], −1.15, −1.52
TPP	417 (44.2)	631	654, 718	1.89	1.29, 0.96, −1.26, −1.59

[a] In CH_2Cl_2. [b] Excitation at 418 nm. Emission corrected for instrument and detector response. [c] E_{00} estimated as 5% of emission maximum. [d] Potentials reported vs the Ag/AgCl (0.29 V vs NHE) reference electrode in CH_2Cl_2 with 0.1 M ^{n}Bu$_4$NPF$_6$, Scan Rate: 200 mV/s. [e] Assignments: Por$^{2+/+}$, Por$^{+/0}$, Por$^{0/−1}$, Por$^{−1/−2}$. [f] Irreversible, only anodic peak potential given.

5-(4'-(imidazol-1''-yl)-phenyl)-10,15,20-triphenylporphyrin (**1**).

Pyrrole (2.42 mL, 34.9 mmol), benzaldehyde (2.57 mL, 26.1 mmol) and 4-(imidazol-1-yl)-benzaldehyde (1.50 g, 8.71 mmol) were dissolved in freshly distilled propionic acid (150 mL). The solution was brought to reflux and heated for 30 minutes. The solvent volume was reduced to 30 mL by distillation. After cooling the reaction to room temperature, the mixture was poured onto 100 mL of cold water. The propionic acid was carefully neutralized with saturated aqueous K_2CO_3 until basic. The solid was filtered, washed with water and dried. It was then dissolved in CH_2Cl_2 and chromatographed on silica gel (1 in × 8 in) with CH_2Cl_2 as the eluant to remove the tetraphenylporphyrin followed by CH_2Cl_2/MeOH (99:1) to remove **1**. The solvent was removed under vacuum to yield purple crystals, 1.84 g, 31% yield; hrms (fast atom bombardment) m/z 687.2819, ($C_{47}H_{32}N_6$+Li [M + Li$^+$] requires 687.2848); uv-vis (methylene chloride) λ_{max} nm (log ϵ): 418 (5.64), 514 (4.25), 549 (3.90), 590 (3.72), 648 (3.67); pnmr (deuteriochloroform): δ 8.91 (2H, d, J=4.8 Hz, pyrrole C-H), 8.89 (4H, s, pyrrole C-H), 8.85 (2H, d, J=4.7 Hz, pyrrole C-H), 8.31 (2H, d, J=8.3 Hz, o-phenyl C-H), 8.24 (6H, dd, J_1=7.5 Hz, J_2=1.3 Hz, o-phenyl C-H), 8.20 (1H, s, imidazole C-H), 7.77 (11H, m, m-, p-phenyl C-H), 7.57 (1H, s, imidazole C-H), 7.39 (1H, s, imidazole C-H), -2.70 (2H, s, endocyclic C-H); cnmr (deuteriochloroform): δ 142.2, 141.8, 137.2, 136.0, 135.9, 134.8, 131.3, 128.0, 126.9, 120.8, 120.6, 119.7, 118.5, 118.3.

Anal. Calcd for $C_{47}H_{32}N_6 \cdot 1/2CH_3OH$: C, 81.87; H, 4.92; N, 12.06. Found: C, 81.90; H, 4.62; N, 11.70%.

5-(4'-(3''-(pent-1'''-yl)-imidazol-1''-yl)-phenyl)-10,15,20-triphenylporphyrin bromide (**2**).

Under nitrogen, **1** (98.4 mg, 0.144 mmol) and bromopentane (1.00 mL, 8.06 mmol) were dissolved in THF (10 mL) and heated to 90 °C for 2 days. The solvent was removed under vacuum. The solid was dissolved in CH_2Cl_2 and chromatographed on alumina (1.5 in × 4 in). The first fraction, unreacted **1**, was removed with CH_2Cl_2 and the product was eluted with CH_2Cl_2/MeOH (50:1). The solvent was removed under vacuum to yield purple crystals, 48.6 mg, 41% yield; hrms (fast atom bombardment) m/z 751.3566, ($C_{52}H_{43}N_6$ [M$^+$] requires 751.3549); uv-vis (methylene chloride) λ_{max} nm (log ϵ): 418 (5.54), 514 (4.18), 549 (3.80), 589 (3.66), 647 (3.61); pnmr (deuteriochloroform) δ 11.76 (1H, s, imidazole C-H (H$_g$)), 8.90 (2H, d, J=4.8 Hz, pyrrole C-H (H$_b$)), 8.88 (4H, s, pyrrole C-H), 8.78 (2H, d, J=4.8 Hz, pyrrole C-H (H$_a$)), 8.45 (2H, d, J=8.4 Hz, o-phenyl C-H (H$_c$)), 8.24 (6H, dd, J_1=7.6 Hz, J_2=1.6 Hz, o-phenyl C-H), 8.19 (2H, d, J=8.4 Hz, m-phenyl C-

H (H$_d$)), 7.82 (1H, s, imidazole C-H (H$_f$)), 7.79 (9H, m, m- and p-phenyl C-H), 7.51 (1H, s, imidazole C-H (H$_g$)), 4.78 (2H, t, J=7.4 Hz, pentyl C-H (H$_i$)), 2.15 (2H, quintet, J=7.2 Hz, pentyl C-H), 1.52 (4H, broad s, pentyl C-H), 0.99 (3H, t, J=7.0 Hz, pentyl C-H), -2.79 (2H, endocyclic C-H); cnmr (deuteriochloroform) δ 188.7, 145.1, 142.4, 142.3, 136.6, 135.0, 134.5, 128.3, 127.2, 122.5, 121.2, 121.0, 120.4, 120.3, 117.3, 51.2, 30.6, 28.8, 22.6, 14.3.

Anal. Calcd for $C_{52}H_{43}BrN_6 \cdot 1/2CH_3OH$: C, 74.37; H, 5.35; N, 9.91. Found: C, 74.46; H, 5.69; N, 9.96%.

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