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Synthesis of *meso*-tetrakis(imidazol-5-yl)porphyrins

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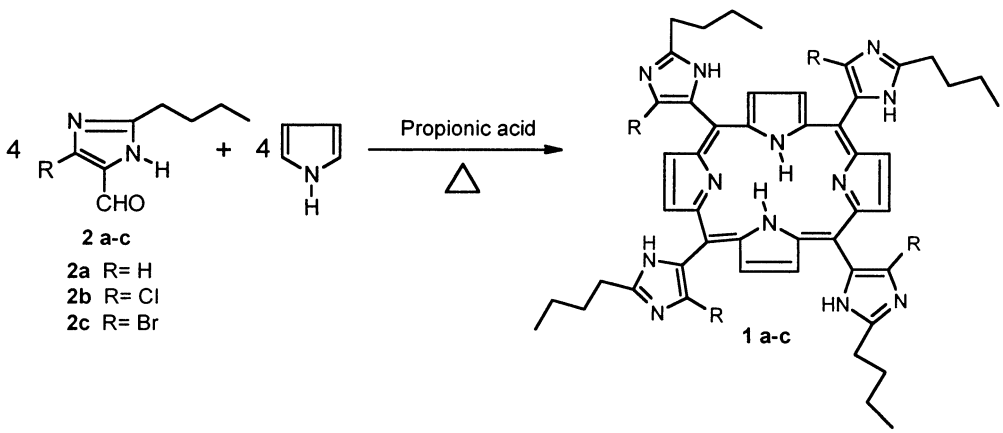
Abstract—*meso*-Tetrakis(imidazol-5-yl)porphyrins (TIP) have been prepared from 2-*n*-butylimidazole-5-carboxaldehyde and pyrrole in refluxing propionic acid. Different substituted imidazole aldehydes with a free NH group are synthesized and treated with pyrrole to afford the corresponding *meso*-tetrakis(2-*n*-butyl-(4-X)-imidazol-5-yl)porphyrins (X = Cl, Br or H).

1. Introduction

meso-Substituted porphyrins are a subgroup of porphyrins with interesting structural properties.[1,2] The substituents on the *meso* positions to date have been phenyl or substituted phenyl groups and very seldom heteroaromatic groups.[3,4] Here we describe porphyrins substituted at the *meso* positions by five-membered aromatic aza-heterocycles, the azoles. Amongst azoles, one of the most interesting substituents is the imidazol-2-yl-group. Recently Milgrom described the *meso*-tetrakis(imidazol-2-yl)porphyrin[5] and its substituted porphyrins.[6] *meso*-Tetrakis(imidazol-2-yl)porphyrin (TIP) shows solid state conductivity. Kobuke and Miyaji have described the *meso*-bis(1-methylimidazol-2-yl)-porphyrin,[7] which on complexation with zinc shows a supramolecular organization forming slipped co-facial dimers.

According to the literature, the synthesis of *meso*-tetrakis(imidazol-2-yl)porphyrins[5,6] (TIP), their imidazol-4-yl isomers[8] and 5,15-bis(imidazol-2-yl)-β-octa alkyl porphyrins[9] have been reported. In the present work, we describe the synthesis of *meso*-tetrakis(2-*n*-butylimidazol-5-yl)porphyrins (TIP) (**1a**–**c**), starting from the corresponding 2-*n*-butylimidazole-5-carboxaldehydes (**2a**–**c**), as new *meso*-azole porphyrins.



Scheme 1.

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2. Results and discussion

The starting materials 2-*n*-butylimidazole-5-carboxaldehyde (**2a–c**) were prepared by a literature method.[10] When 2-*n*-butyl-5-hydroxymethylimidazole was oxidized with ceric ammonium nitrate (CAN), 2-*n*-butylimidazole-5-carboxyaldehyde (**2a**) was obtained. 2-*n*-Butyl-5-hydroxymethylimidazole was halogenated with *N*-chlorosuccinimide or *N*-bromosuccinimide to afford 2-*n*-butyl-4-chloro (or bromo)-5-hydroxymethylimidazole which on oxidation with CAN gave 2-*n*-butyl-4-chloro (or bromo) imidazole-5-carboxaldehyde (**2b** and **2c**), respectively.

These imidazole carboxaldehydes (**2a–c**) were condensed with pyrrole by refluxing in propionic acid to give *meso*-tetrakis(2-*n*-butylimidazol-5-yl)porphyrins (**1a–c**) in 25–26% yield, as shown in Scheme 1.

Porphyrins **1b** and **1c** exhibit the phenomenon of 'atropisomerism' a feature typical of *meso*-(2-substituted aryl)porphyrins.[11] Four distinct bands were observed by TLC for porphyrins **1b** and **1c**. Attempts were made to separate these atropisomers by column chromatography (flash silica gel 230–400 mesh). In the cases of **1b** and **1c**, TLC indicates that after separation each atropisomeric fraction, on standing at ambient temperature, becomes a mixture of all atropisomers. The ^{1}H NMR spectra show complex resonances for the central porphyrin N-H and β-protons for atropisomeric porphyrins **1b** and **1c** and is less complex in the case of non-atropisomeric porphyrin **1a**. The UV–vis spectra of the free base porphyrins were recorded at 2×10^{-5} mol concentration in methanol. In these porphyrins, the B-band is prominent as a single absorption at 432 nm (at 2×10^{-5}) mol and the splitting of the B-band is clearly observed when one drop of HCl is added to the solution at the same concentration.

3. Experimental

UV–vis spectra were recorded on a Shimadzu UV 160 A UV–vis-NIR spectrophotometer, using methanol as solvent. IR spectra were recorded as KBr discs using a Shimadzu 8010 FTIR spectrophotometer. ^{1}H NMR spectra were recorded on a Varian FT 200 MHz instrument using $CDCl_3$ and d_6-DMSO as solvent and TMS as internal reference. FABS mass spectra were recorded on a YG Micromass 7070H (F_1 or CI) auto spectrometer. The C, H, N analysis of the compounds was performed on a Carlo Erba Model EA 1108 CHNS-O elemental analyzer. Porphyrins were purified by flash column chromatography (Aldrich make) using 230–400 mesh silica gel.

3.1. Synthesis of *meso*-tetrakis(2-*n*-butylimidazol-5-yl)porphyrin (1a)

2-*n*-Butylimidazole-5-carboxaldehyde (**2a**, 3.04 g, 0.02 mol) was dissolved in 70 ml of freshly distilled propionic acid and pyrrole (1.34 g, 0.02 mol) was added. The reaction mixture was stirred and refluxed in open air for 1 h. Then half of the propionic acid was distilled off and the remaining mixture was cooled. It was poured into 200 ml of cold water and neutralized carefully with saturated sodium bicarbonate solution. The crude porphyrin was filtered and dried. The crude product was purified by flash chromatography using chloroform:methanol (95:5) as eluent to afford **1a**, as a dark purple solid in 26% yield (1.02 g). Mp >300°C. Anal. calcd for $C_{48}H_{54}N_{12}$: C, 72.18; H, 6.76; N, 21.05. Found C, 72.21; H, 6.77; N, 21.048%; FAB-MS $m/z=799$ (M^++1) requires 798. UV λ_{max} nm (MeOH) (log ξ): 432.5 (5.09), 519 (4.22), 561 (4.08), 591 (3.94), 657.5 (3.86). λ_{max} nm (methanolic HCl) (log ξ): 438.5 (5.096), 461 (5.095), 688.5 (4.61); ^{1}H NMR ($CDCl_3$+d_6-DMSO) δ ppm: 13.12 (s, broad, 4H, imidazole N-H), 9.12 (s, 8H, pyrrole C-H), 7.65 (s, 4H, imidazole C-H), 2.8–2.9 (m, 8H, -CH_2), 2.05 (m, 8H, CH_2-CH_2-CH_3), 1.6 (m, 8H, CH_2-CH_3), 1.05 (m, 12H, *n*-butyl CH_3). IR (KBr) cm^{-1}: 3400–3000 (broad N-H str), 2950, 2830 (w-aliphatic str), 1600, 1560, 1612, 1450 (m, imidazole and C=C, C=N in plane bend), 940 (w, porphyrin macrocylic bend).

3.2. Synthesis of *meso*-tetrakis(2-*n*-butyl-4-chloroimidazol-5-yl)porphyrin (1b)

A mixture of 3.72 g (0.02 mol) of 2-*n*-butyl-4-chloroimidazole-5-carboxaldehyde (**2b**) and 1.34 g (0.02 mol) of freshly distilled pyrrole was dissolved in 70 ml of propionic acid and refluxed for 1 h while stirring. Half the volume of propionic acid was distilled off and remaining mixture was cooled. It was poured into 200 ml of cold water and neutralized with saturated sodium bicarbonate solution. The crude porphyrin was filtered off and subjected to flash column chromatography on silica gel using $CHCl_3$:MeOH (9.5:0.5) as eluent. Four separate purple atropisomeric fractions were eluted, which after concentration gave a dark purple solid **1b** (1.2 g, 25%). Identification and characterization of all four fractions proved that they were the same compound. The first fraction was isolated as a single isomer. Mp: >300°C. Anal. calcd for $C_{48}H_{50}Cl_4N_{12}$: C, 61.53; H, 5.34; N, 17.94. Found C, 61.48; H, 5.44; N, 17.90%. FAB-MS $m/z=937$ (M^++1) requires 936. UV: λ_{max} nm (MeOH)(log ξ): 433 (5.096), 519.5 (3.84), 559 (4.03), 599 (3.62), 657 (3.16). λ_{max} nm (methanolic HCl) (log ξ) 427 (5.096), 454 (4.98), 554 (4.11), 589 (3.65), 666.5 (4.01); ^{1}H NMR ($CDCl_3$+d_6-DMSO): δ ppm: 13.2 (s, 4H, imidazole N-H), 9.12 (s, 8H, pyrrole C-H), 2.8–2.95 (m, 8H, -CH_2), 2.05 (m, 8H, CH_2-CH_2-CH_3), 1.65 (m, 8H, CH_2-CH_3). 1.05 (m, 12H, *n*-butyl-CH_3), −2.6 (s, 2H, porphyrin N-H); IR (KBr) cm^{-1}: 3350 (m, broad, imidazole (H-bonded) N-H str), 2920, 2900, 2850 (m, aliphatic C-H str), 1600, 1510, 1400 (m, imidazole and porphyrin C=C, C=N in plane bend), 940 (w, porphyrin microcyclic bend).

3.3. Synthesis of *meso*-tetrakis(2-*n*-butyl-4-bromoimidazol-5-yl)porphirin (1c)

A mixture of 4.62 g (0.02 mol) of 2-*n*-butyl-4-bromoimidazole-5-carboxaldehyde (**2c**) and 1.34 g (0.02 mol) of freshly distilled pyrrole was dissolved in 70 ml of propionic acid and refluxed for 1 h while stirring. After the usual workup procedure as described above, the black residue was subjected to column chromatography on flash silica gel using $CHCl_3$:MeOH (9.5:0.5) as eluent.

Four separate purple atropisomeric fractions were eluted, and after concentration to gave a dark purple solid **1c** (1.02 g, 18%). Identification and characterization of all four fractions proved that they were the same compound. The first fraction was isolated as a single isomer. Mp: >300°C. Anal. calcd for $C_{48}H_{50}Br_4N_{12}$: C, 51.80; H, 4.50; N, 15.15. Found C, 51.83; H, 4.56; N, 15.12%. FAB-Ms $m/z=1115$ (M^++1) requires 1114. UV: λ_{max} nm (MeOH)(logξ): 431 (5.096), 518 (4.18), 559 (4.02), 593.5 (3.88), 657.5 (3.96); λ_{max} nm (methanolic HCl) (log ξ) 438.5 (5.096), 462 (5.095), 607 (4.137), 589 (3.65), 666 (4.54); ^{1}H NMR ($CDCl_3$+d_6-DMSO): δ ppm: 13.25 (s, broad, 4H, imidazole N-H), 9.1 (s, 8H, pyrrole C-H), 2.85–2.95 (m, 8H, -CH_2), 2.05 (m, 8H, CH_2-CH_2-CH_3), 1.65 (m, 8H, CH_2-CH_3), 1.02 (m, 12H, *n*-butyl-CH_3), −2.62 (S, 2H, porphyrin N-H); IR (KBr) cm^{-1}: 3400 (s, broad, imidazole (H-bonded) N-H str), 2920, 2900, 2830 (m, aliphatic C-H str), 1560, 1510, 1440 (m, imidazole and porphyrin C=C, C=N in plane bend), 945 (w, porphyrin microcyclic bend).

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