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ELECTRON DEFICIENT PORPHYRINS. 1. TETRAKIS(TRIFLUOROMETHYL)PORPHYRIN AND ITS METAL COMPLEXES

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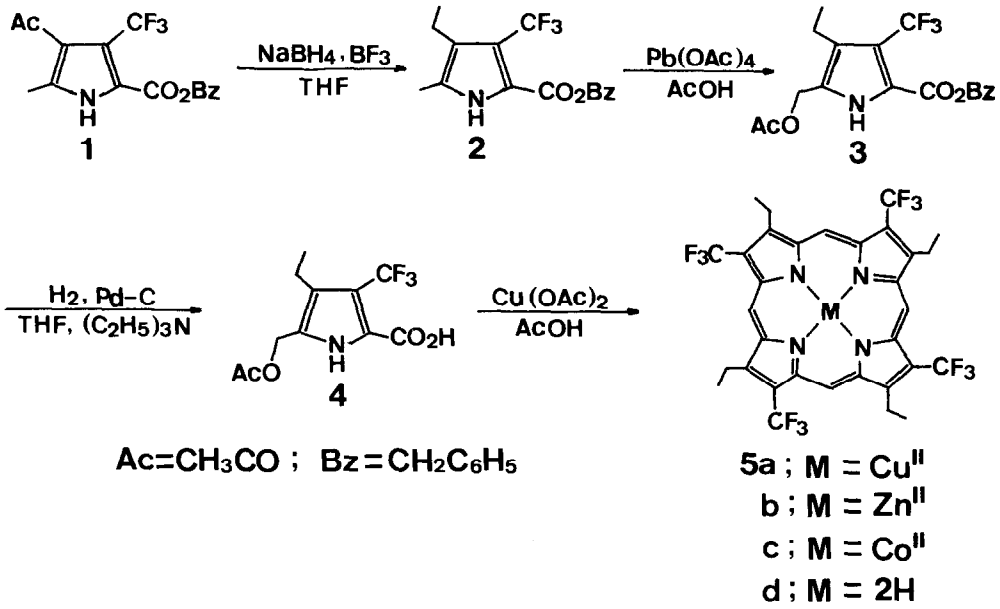
Abstract: 1,3,5,7-Tetrakis(trifluoromethyl)-2,4,6,8-tetraethylporphyrin and its metal (Cu(II), Zn(II), and Co(II)) complexes have been prepared.

The redox property of a porphyrin ligand varies with incorporated metals.[1] The metal redox property in turn can be controlled by the electronic effects of the peripheral substituents of the porphyrin. We are particularly interested in electron-deficient porphyrins having highly electron-withdrawing yet chemically inert peripheral substituents.[2] Trifluoromethyl group meets this criterion.[3] We wish to report here the first preparation of the trifluoromethyl analogue of etioporphyrin and some of its metal complexes.

The modified Knorr condensation route to β-trifluoromethly functionalization of pyrrole has been reported.[4,5] By essentially the same procedure as described for the corresponding ethyl ester,[4] benzyl 4-acetyl-5-methyl-3-trifluoromethylpyrrole-2-carboxylate (1) was prepared by the oximation of benzyl trifluoroacetoacetate with HNO_2 followed by reductive condensation with acetylacetone; yield, 27%.[6] Reduction of (1) (840 mg) with $NaBH_4$ (1.1 g) and BF_3-etherate (11 mL) in dry tetrahydrofuran (30 mL) under nitrogen for 3 h afforded benzyl 4-ethyl-5-methyl-3-trifluoromethylpyrrole-2-carboxylate (2) (754 mg, 94%).[7] Acetoxylation of (2) (1.6 g) with $Pb(OCOCH_3)_4$ (4.5 g) in acetic acid (50 mL) at 60°C for 3 h gave benzyl 5-acetoxymethyl-4-ethyl-3-trifluoromethylpyrrole-2-carboxylate (3) (1.37 g, 72%).[8] Hydrogenolysis of (3) (1.80 g) with 5% palladium carbon (180 mg) in tetrahydrofuran (100 mL) containing triethylamine (6 mL)[9] for 3 h afforded 5-acetoxymethyl-4-ethyl-3-trifluoromethylpyrrole-2-carboxylic acid (4) (1.20 g, 88%).[10] The synthetic route to (4) follows the general method for the preparation of precursor pyrrole of octaethylporphyrin.[11] An important modification was the choice of the benzyl ester functionality. More common ethyl ester proved to be unsatisfactory, since its hydrolysis under basic condition was always accompanied by concomitant hydrolysis of the trifluoromethyl group. The attempt to obtain the porphyrin from (4) by the procedure employed in the preparation of octaethylporphyrin from 2-carboxy-5-hydroxymethylpyrrole derivative[11] was unsuccessful.

We took advantage of the copper template in the condensation-cyclization



of (4). Thus, a mixture of (4) (110 mg) and $Cu(OCOCH_3)_2$ (35 mg) in acetic acid (1.5 mL) was refluxed for 2 h. The precipitates which separated upon addition of acetic acid and water were recrystallized from chloroform-methanol to give the Cu(II) complex of 1,3,5,7-tetrakis(trifluoromethyl)-2,4,6,8-tetraethylporphyrin (5a) (9 mg, 12%): mass spectrum m/e 757 (M^+) and 742 (M^+-15); IR (KBr) 1120 and 1065 cm^{-1} ($\nu(CF_3)$). Zinc acetate was also used as a template, although the yield of the Zn(II) complex (5b) was very poor. A solution of (5a) in fluorosulfonic acid (5 mL) was stirred at room temperature for 5 min. The mixture was poured into ice-water containing methanol. After neutralization with $NaHCO_3$, the mixture was extracted with chloroform. Chromatography on silica gel followed by recrystallization from chloroform-methanol afforded the free base porphyrin (5d) in a nearly quantitative yield: mass spectrum m/e 694 (M^+), 679 (M^+-15), 675 (M^+-19), 625 (M^+-69), and 347 (M^{2+}); IR (KBr) 1120 and 1050 cm^{-1} ($\nu(CF_3)$); ^1H NMR ($CDCl_3$, TMS) δ 10.42 (s, meso-H), 4.29 (q, $C\underline{H}_2CH_3$), 1.94 (t, $CH_2C\underline{H}_3$), and -3.58 (s, NH)[12] in an integration ratio of 2:4:6:1; its ^{19}F NMR showed a single signal at 25.08 ppm downfield of CF_3CO_2H. The free base porphyrin was also obtained by pyrolytic cyclization of (4) in the solid state in very low yield. The electronic spectrum of (5d) was etio-type and each absorption maximum is red-shifted by approximately 10 nm compared with that of octaethylporphyrin free base (Table I). The Co(II) complex (5c) was prepared by refluxing an acetic acid solution of (5d) containing $Co(OCOCH_3)_2$. In Table I are summarized the absorption maxima in the electronic spectra of (5a-d).

In addition to the spectral data, the following observations are indica-

Table I. Absorption Maxima in Electronic Spectra of Porphyrin Derivatives[a]

compound	λ_{max}/nm				
(5d)	407	504	539	579	633
$OEPH_2$[b]	398	497	533	566	619
(5a)	405		532	568	
(5b)	403		533	565	
(5c)	403		526	556	

[a] In dichloromethane. [b] Octaethylporphyrin free base.

tive of the electronic effects of trifluoromethyl substituents. Firstly, compared with octaethylporphyrin free base ($OEPH_2$), (5d) shows a considerably reduced affinity to metal ions. For example, the incorporation of Co^{2+} ion into $OEPH_2$ is effected by refluxing a solution of $OEPH_2$ in chloroform-methanol containing $Co(OCOCH_3)_2$ for 2 h,[13] while under the identical condition most of (5d) remains as free base even after 48 h. Secondly, Cu(II) complex (5a) resists acid demetallation considerably. A super acid (FSO_3H) is required for the complete demetallation; H_2SO_4 gives no satisfactory results, whereas OEPCu(II) can be completely dematallated with H_2SO_4.[14] Thirdly, (5d) shows a considerably reduced proton affinity. In fact, (5d) exists as free base in acetic acid. In a marked contrast, $OEPH_2$ exists as mono-cation in acetic acid. These behaviors of (5a) and (5d) clearly indicate that introduction of the electron-withdrawing trifluoromethyl groups results in a significant reduction in the electron density on pyrrolic nitrogens.

Further work is now under way to elucidate the electron deficiency more quantitatively.

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6. Mp 115.0°C (from methanol); mass spectrum m/e 325 (M^+); IR (KBr) 3300 (ν(NH)), 1690 and 1675 (ν(C=O)), and 1275 and 1120 cm^{-1} (ν(CF_3)); ^1H NMR δ 9.80 (broad s, 1H, NH), 7.36 (s, 5H, $CH_2C_6\underline{H}_5$), 5.35 (s, 2H, $C\underline{H}_2C_6H_5$), 2.44 (s, 3H, $COCH_3$), and 2.33 (s, 3H, CH_3).

7. Mp 106.5°C (from methanol); mass spectrum m/e 311 (M^+); IR (KBr) 3295 (ν(NH)), 1680 (ν(C=O)), and 1275 and 1120 cm^{-1} (ν(CF_3)); ^1H NMR δ 9.56 (broad s, 1H, NH), 7.33 (s, 5H, $CH_2C_6\underline{H}_5$), 5.32 (s, 2H, $C\underline{H}_2C_6H_5$), 2.54 (q, 2H, $C\underline{H}_2CH_3$), 2.19 (s, 3H, CH_3), and 1.13 (t, 3H, $CH_2C\underline{H}_3$).

8. Mp 124.0°C (from dichloromethane-n-hexane); mass spectrum m/e 369 (M^+); IR (KBr) 3295 (ν(NH)), 1720 and 1670 (ν(C=O)), and 1285 and 1120 cm^{-1} (ν(CF_3)); ^1H NMR δ 9.76 (broad s, 1H, NH), 7.41 (s, 5H, $CH_2C_6\underline{H}_5$), 5.37 (s, 2H, $C\underline{H}_2C_6H_5$), 5.08 (s, 2H, CH_2OCO), 2.68 (q, 2H, $C\underline{H}_2CH_3$), 2.11 (s, 3H, CH_3CO), and 1.04 (t, 3H, $CH_2C\underline{H}_3$).

9. Triethylamine is essential for the effective hydrogenolysis.

10. Recrystallized from acetic acid-water; IR (KBr) 3220 (ν(NH)), 1705 (ν(C=O)), and 1265 and 1125 cm^{-1} (ν(CF_3)); ^1H NMR δ 12.10 (broad s, 1H, CO_2H), 5.27 (s, 2H, CH_2OCO), 2.85 (q, 2H, $C\underline{H}_2CH_3$), 2.18 (s, 3H, CH_3CO), and 1.35 (t, 3H, $CH_2C\underline{H}_3$).

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12. ^1H NMR for $OEPH_2$ ($CDCl_3$, TMS) δ 10.18 (meso-H), 4.14 (CH_2), 1.95 (CH_3), and -3.74 (NH).

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