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FERRIC PORPHYRIN ALKYLTHIOLATES: MODEL COMPOUNDS FOR CYTOCHROME P-450

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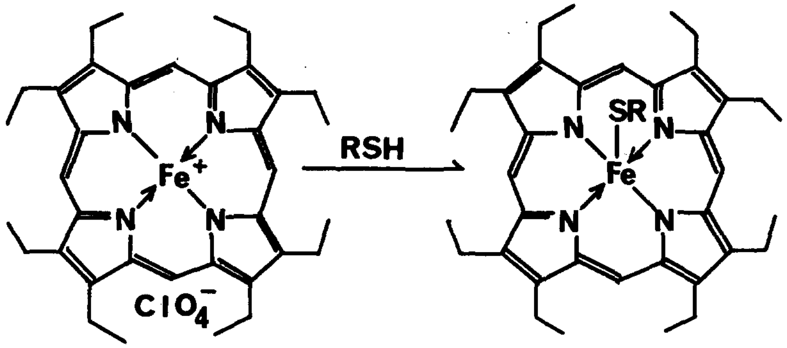
Interaction between sulfur atom and prothetic heme group of heme enzyme such as cytochrome c and cytochrome P-450 has deserved many attention of chemists. In particular, heme enzyme named by cytochrome P-450 is attractive in view of its catalytic action to activate oxygen molecule in hydroxylation at microsome.[1,2] Since it has been suggested that distal thiolate of cystein is plausible axial ligand to heme of the cytochrome P-450, physico-chemical properties of the iron-sulfur bond have been investigated in both heme enzymes and prothetic heme systems.[3-7] Isolation and structural studies on the ferric porphyrin thiolates have been recently reported by two groups.[8-10] The results reported in these works have provided first conclusive evidence of the formation of the Fe-S bond, which has never been established in the previous works. However the aromatic thiolates are only available for the axial ligand to isolate the complexes in stable form. Holm and his coworkers have stated that no ferric porphyrin alkylthiolate could be isolated from the reaction of the ferric octaethylporphyrin μ-oxo dimer $[Fe(OEP)]_2O$ with alkyl thiols.[9] Alkylthiolate seems to be plausible axial ligand, if cystein ligates to heme as a fifth ligand. We briefly report here a facile preparation of the ferric octaethylporphyrin alkylthiolates Fe(OEP)SR.

Treatment of the ferric porphyrin perchlorate $Fe(OEP)ClO_4$[11] with alkylthiols such as $(CH_3)_3CSH$, CH_3SH, and $HSCH_2CH_2CO_2CH_3$ in the presence of sodium hydride afforded the ferric porphyrin alkylthiolates Fe(OEP)·SR (R= $-C(CH_3)_3$ **1**, $-CH_3$ **2**, and $-CH_2CH_2CO_2CH_3$ **3**) in moderate yield (50 ∿ 70 %). Crystallization of crude solid from benzene-hexane solution gave dark violet crystals.



R= $-C(CH_3)_3$ **1**
$-CH_3$ **2**
$-CH_2CH_2CO_2CH_3$ **3**
$-C_6H_5$ **4**

Microanalyses of these complexes show satisfactory agreement with the expected values. The present method can be extended to prepare Fe(OEP)SC_6H_5. As has been reported,[8-10] Fe(OEP)SC_6H_5 and Fe(TPP)SC_6H_5 (TPP = α, β, γ, δ-tetraphenylporphine) are rather stable in solid state. Latter complex decomposes in benzene to generate $(C_6H_5S)_2$ and TPP·Fe(II). The alkylthiolate complexes **1** ∿ **3** are less stable than **4** in organic solvents. Among the alkylthiolate complexes the complex **1** is more stable than **2** and **3**. The latter two complexes even in the solid state decompose gradually at room temperature within two weeks. Addition of pyridine or N-methylimidazole accelerates reduction of the ferric complex to the ferrous complex with generation of disulfide at room temperature. Complexes **1** ∿ **3** react with water to yield μ-oxo dimer. Therefore, it is required to use water-free solvents for the spectroscopic measurements.

$$\mathrm{Fe(III)\cdot OEP\cdot SR} \xrightarrow{\mathrm{L}} \mathrm{FeOEP\cdot L_2} + \mathrm{RSSR}$$

L = pyridine, N-methylimidazole

Figure 1 shows visible spectra of **1** and the corresponding alkoxy ferric

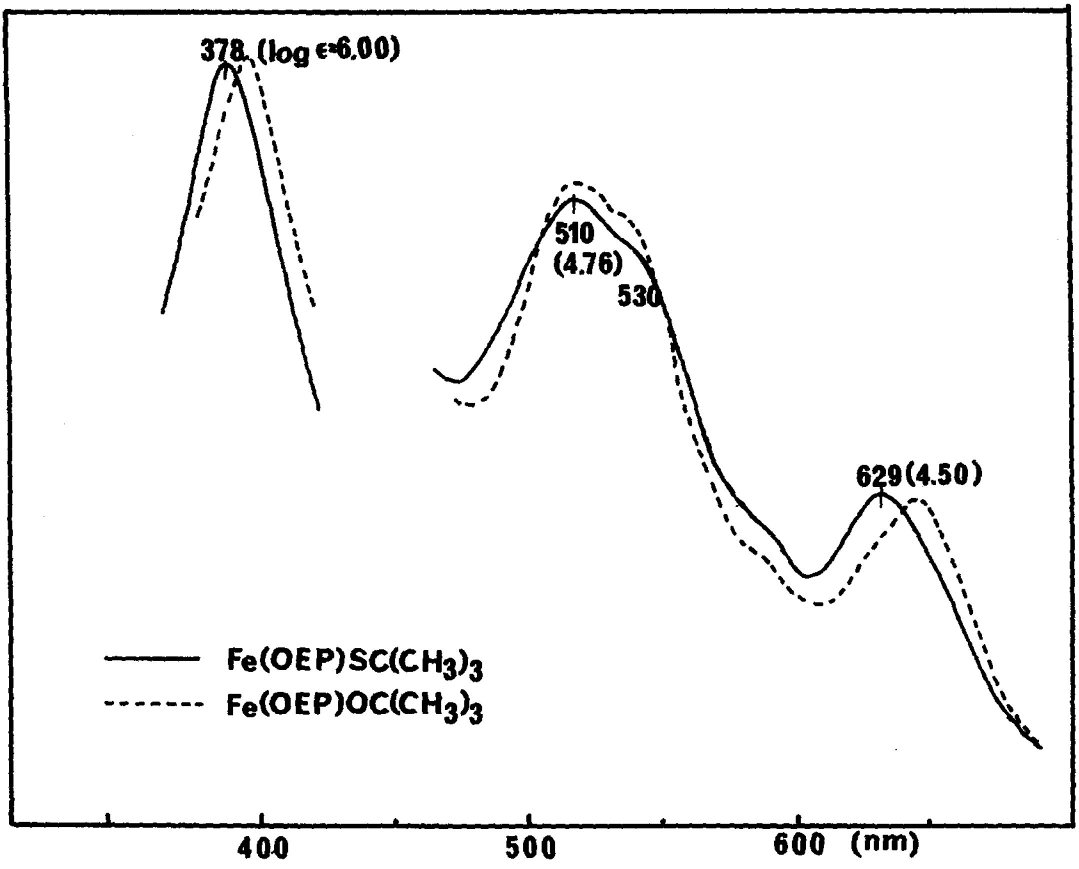


Figure 1

complex in $CHCl_3$, indicating the characteristic absorptions of the high-spin state. The charge transfer absorption appeared at 629 nm is a slightly higher energy transition than that of 4. Magnetic susceptibility of 1 was determined as μ_{eff} = 5.87 BM at 289°K, which is of the high spin state (S = 5/2). The ESR spectrum of 1 in benzene-pyridine at 123°K reveals signals at g_1 = 2.36, g_2 = 2.24, and g_3 = 1.94 for the low-spin state with weak signals at g_1 = 6.34, g_2 = 4.39, and g_3 = 1.99 for the high-spin species. The g-values of the low-spin state are similar to those of the cytochrome P-450 at the low-spin state.[1,2] The present results may provide a facile pathway to prepare the ferric porphyrin alkylthiolates as a model for the cytochrome P-450. Studies on the synthesis of the ferric porphyrin alkylthiolate, their reaction behavior and physico-chemical properties are in progress.

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