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CYCLOPHANE PORPHYRIN - IV

Hisanobu Ogoshi*, Hiroshi Sugimoto, and Zen-ichi Yoshida

Department of Synthetic Chemistry, Kyoto University, Yoshida,

Kyoto, 606, Japan

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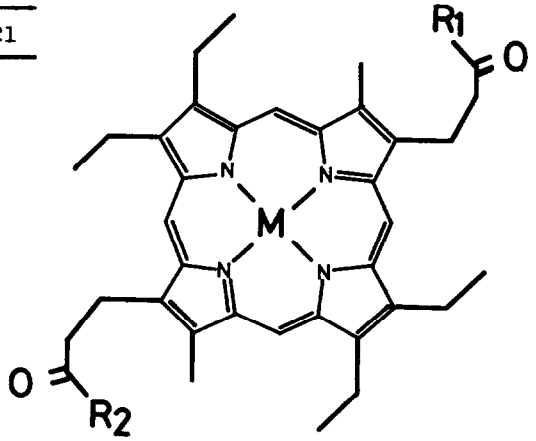
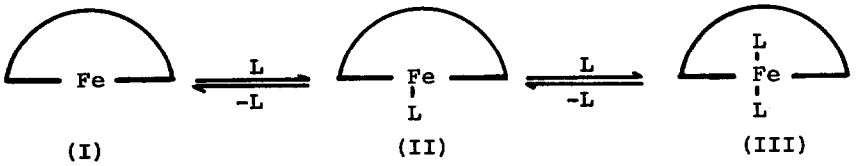
Very recently there have been independently reported the syntheses of the bridged porphyrins[1,2,3] as model ligands for the hemoproteins such as myoglobin and hemoglobin. Main purpose to construct the bridged structure is to prevent the irreversible oxidation of the oxygenated ferrous porphyrin due to dimeric interaction. Hydrophobic pocket in the hemoproteins of the vertebrates plays important role in the reversible oxygenation during the respiratory cycle. Previously, we have reported that the long methylene chain linked across the porphyrin ring gives remarkable effect on axial ligation of the 4-substituted pyridines to the ferric complex of the bridged porphyrin.[1] Here we wish to report the syntheses of cyclophane porphyrins with the various length of the bridge ($-CH_2CH_2CONH(CH_2)_nNHCOCH_2CH_2-$) and the effect of the size of the bridge on the axial ligation of pyridine to their ferrous complexes.

R_1	R_2	M			
		H,H	Zn	Fe^{3+}	Cl
OH	OH	1			
-NH-$(CH_2)_{12}$-NH-			8		
-NH-$(CH_2)_{10}$-NH-		2	9	15	
-NH-$(CH_2)_9$-NH-		3	10	16	
-NH-$(CH_2)_8$-NH-		4	11	17	
-NH-$(CH_2)_7$-NH-		5	12	18	
-NH-$(CH_2)_6$-NH-		6	13	19	
NHC_3H_7	NHC_3H_7	7	14	20	



To a mixture of 1,2,5,6-tetraethyl-3,7-dimethyl-4,8-bis(2-carboxyethyl)-porphin $\underset{\sim}{1}$[4], isobutyl chroloformate and triethylamine in dry tetrahydrofuran was added diamines ($NH_2(CH_2)_nNH_2$, n=6,7,8,9,10). The reaction mixture in high dilution was stirred for 5 hr at room temperature. After the solvent was removed under reduced pressure, the residue was treated with zinc acetate in methanol-pyridine(1:1 vol/vol). The mixture was condensed to a small portion. The thin layer chromatography of the residue on silica gel with CH_2Cl_2-acetone(6:1 vol/vol) gave purple red crystals of the cyclophane porphyrin zinc complexes $\underset{\sim}{9}$,$\underset{\sim}{10}$,$\underset{\sim}{11}$,$\underset{\sim}{12}$ and $\underset{\sim}{13}$ in 20-30% yields. The reference porphyrin $\underset{\sim}{14}$ was also prepared by using n-propylamine according to the similar method as described above. The structure of these complexes were determined by microanalyses, molecular weight measurement and spectral data. For the ^{1}H-nmr spectra of the zinc complexes, it is expected that the methylene groups of the bridge experiences the strong diamagnetic ring current of the porphyrin macrocycle, and the average chemical shift of methylene groups appears at higher magnetic field with decreasing the size of the bridged methylene groups. In fact $\underset{\sim}{13}$ shows signals of the bridged methylenes at τ 11.56(2H), 12.12(4H) and 12.56(2H), respectively. These values are at higher magnetic field by about 2 ppm than those of the zinc complex $\underset{\sim}{8}$[1].

The ferric complexes ($\underset{\sim}{15}$~$\underset{\sim}{20}$) were obtained by the treatment of the zinc complexes with ferrous acetate in glacial acetic acid followed by aeration. The ferrous complexes were generated by reduction of the ferric complexes with $Na_2S_2O_4$ under argon atmosphere. Fig. 1 demonstrates the visible spectra of the ferrous complexes in benzene-pyridine(2:1 vol/vol) at 15°C.



(I) (II) (III)

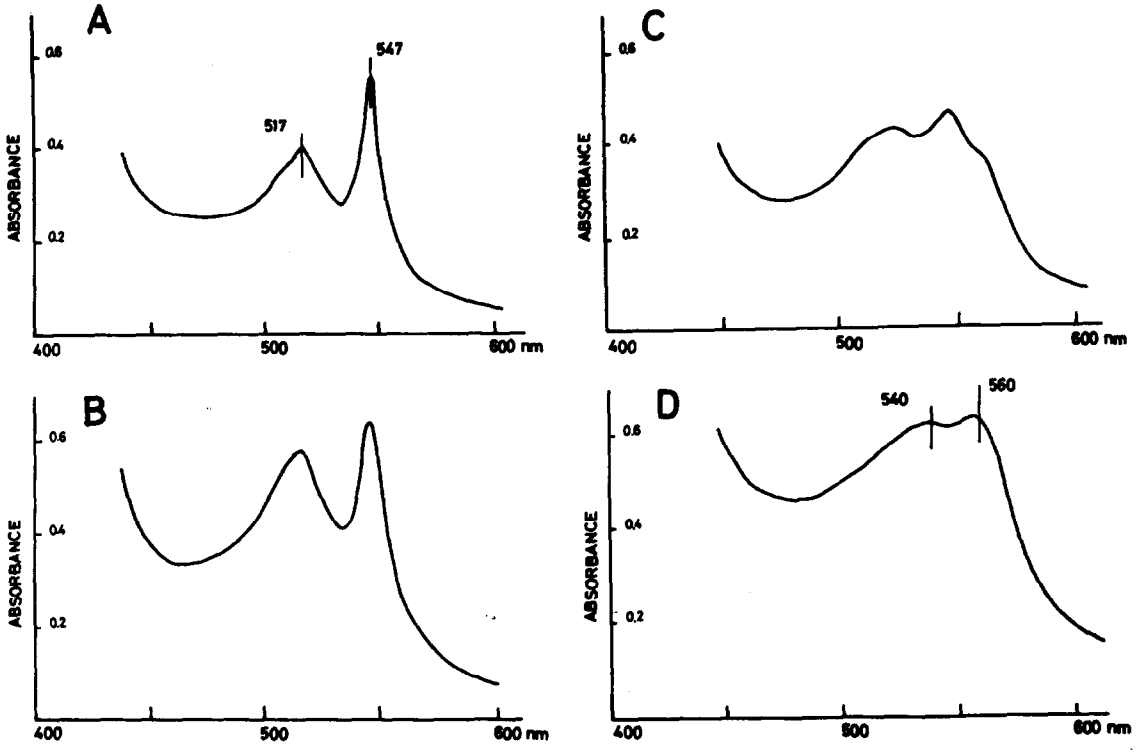


Fig. 1 Visible spectra of ferrous complexes. (A) [ferrous complex of 20] = 2.5×10^{-5} M. (B) [ferrous complex of 15] = 3.6×10^{-5}M. (C) [ferrous complex of 17] = 3.4×10^{-5}M. (D) [ferrous complex of 19] = 3.8×10^{-5}M.

The ferrous complex of 20 and 15 reveal the absorption maxima at 517 and 547 nm which are assignable to the typical spectrum of the pyridine hemechrome (the hexa-coordinated complex (III)). Chemical behavior of the ferrous complex of 15 is almost same as that of the reference complex in the present system. The complex of 15 provides enough space to allow sixth coordination of pyridine molecule to the heme. On the other hand, the ferrous complex of 19 shows absorption maxima at 540 and 560 nm which can be assigned to the deoxyheme (the penta-coordinated complex (II)). This result implies

that the six coordination of pyridine molecule is inhibited due to repulsive interaction between axial ligand and the short bridge of the ferrous complex of 19. Furthermore, in the case of the ferrous complex of 17, the visible spectrum indicates coexistence of complexes (II) and (III). It is evidently shown that the sixth coordination of pyridine molecule to the ferrous complex is markedly dependent on the size of the bridge. Binding of molecular oxygen to the ferrous complexes of 17 and 19 has been examined in benzene-pyridine (2:1 vol/vol) and benzene-N-methylimidazole(2:1 vol/vol) at 15°C. Monitoring the visible spectra showed rapid formation of the ferric μ-oxo dimer (λ_{max} 579 nm). The ferrous complexes of the reference porphyrin 20 and cyclophane porphyrin with a long bridge 15 were found to be stable to oxygen. The present results clearly indicate that the ferrous mono amine complex (II) is readily oxidized to the μ-oxo dimer. Similar trend has been noted in the ferrous complex of the other bridged porphyrin[3]. The ferrous complex of 19 seems to give too small cavity to allow the coordination of molecular oxygen from the bridged face of the porphyrin plane. Less flexibility of the bridge and strong steric constraint in the proximity of the iron(II) atom may be responsible for the oxygen binding to the ferrous complex from the open face to give the μ-oxo dimer.

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