Molecular Structure of Chloro *meso*-Tetra(3,4,5-trimethoxyphenyl)porphyrinato Iron(III) – a Model Compound of Cytochrome P-450 Active Site*

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Abstract

A model compound of cytochrome P-450 active site, FeTTOMPPCl·CH_3OH, has been synthesized. Its crystal and molecular structure have been determined by single crystal X-ray diffraction technique. The crystal is monoclinic, space group *Cm*, with a = 16.3903(32), b = 26.9037(45), c = 14.9382(29) Å, β = 147.783(9), V = 3512.48(1.16) Å^3, Z = 2, D_c = 1.14 g cm^{-3}, μ = 45.1 cm^{-1}, $F(000)$ = 1351.78. The structure was solved by the heavy-atom method and refined by block diagonal and full matrix least-squares procedures to a final R of 0.1087 for the 1157 independent reflections. The molecular formula as determined by elemental analysis and confirmed by the crystal structure is $FeC_{56}H_{52}N_4O_{12}Cl\cdot CH_3OH$. The stereochemistry of the compound and the mechanism of its reaction with O_2 were discussed.

Introduction

In the synthesis of cyto.P-450 model compounds, metal porphyrins, large groups are usually introduced to the vicinity of the porphyrins in order to increase the distance between the two porphyrin groups, and to avoid the formation of the inactive dimer – μ-oxo. Determination of the stereostructures of these porphyrin complexes with large steric effect to find out the shape, size and orientation of the molecular pockets formed with different steric groups is of considerable theoretical and practical interest in the study of the stereomechanism and selectivity of the natural enzymes and the synthetic model compounds [1]. We have so far synthesized and prepared single crystals of TTOMPP, FeTTOMPPCl and FeTPCPPCl·CoLi from a series of porphyrin–metal complexes with different steric groups [2, 3]. This paper reports the molecular and crystal structure of FeTTOMPPCl, (chloro *meso*-tetra(3,4,5-trimethoxyphenyl)porphyrin iron(III).

Experimental

FeTTOMPPCl was recrystallized from a 9:1 chloroform/methanol solution by slow evaporation under room temperature. The crystal used for X-ray diffraction analysis was deep yellow in colour and of approximate dimensions 0.4 × 0.4 × 0.5 mm. A total of 4086 independent reflections, $3° \leqslant 2\theta \leqslant 50°$, were measured with a R3M/E 4-circle diffractometer with Cu Kα radiation and graphite monochromator by θ–2θ scanning. Only 1157 reflections were used in refinement. The crystal was found to be monoclinic, space group *Cm*. Cell dimensions were a = 16.3903(32), b = 26.9037(45), c = 14.9382(29) Å, β = 147.783(9)°, V = 3512.48(1.16) Å^3 and Z = 2. Each molecule of the compound contained a solvent molecule CH_3OH. The molecular formula was $FeC_{56}H_{52}N_4O_{12}Cl\cdot CH_3OH$, with molecular weight M_r = 1096.36, D_c = 1.14 g cm^{-3}, μ = 45.1 cm^{-1} and $F(000)$ = 1351.78.

Determination and Refinement of the Structure

The position of the Fe atom was obtained from Patterson function. Positions of all non-hydrogen atoms were then obtained by Fourier synthesis and were refined by full matrix least-squares using SHELX programmes. Positions of hydrogen atoms were obtained by difference Fourier and geometrical consideration. All non-hydrogen atoms were refined with anisotropic thermal parameters, while hydrogen atoms were refined isotropically. Final values of R = 0.1087 and R_w = 0.0941 were obtained.

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Results and Discussion

Coordinates of non-hydrogen atoms and equivalent isotropic thermal parameters are given in Table 1. Bond lengths and bond angles are given in Tables 2 and 3, respectively. Hydrogen atomic coordinates and thermal parameters are given in Tables 4 and 5. The structure of the molecule is shown in Fig. 1. Each asymmetric unit of the unit cell contains half a molecule of the compound [4]. Fe, Cl, N1 and N3 of the main molecule and C29 and O of the methanol are located on the plane of symmetry. Atoms with a prime are related to those without

TABLE 1. Non-hydrogen atomic coordinates and thermal parameters (Å^2)

Atom	x	y	z	U_{eq}
Fe	0.4192	0.5000	0.4195	0.048(6)
Cl	0.2410(14)	0.5000	0.1494(18)	0.127(10)
N1	0.6310(24)	0.5000	0.5400(26)	0.036(11)
N2	0.4603(21)	0.4252(5)	0.4832(24)	0.042(10)
N3	0.3125(23)	0.5000	0.4377(28)	0.042(11)
O1	1.1302(20)	0.3136(9)	0.9253(25)	0.112(11)
O2	0.9917(16)	0.2611(6)	0.6699(20)	0.077(11)
O3	0.7034(16)	0.2800(6)	0.3561(18)	0.069(10)
O4	0.2394(18)	0.2804(7)	0.6310(19)	0.064(11)
O5	−0.0503(15)	0.2647(5)	0.3217(18)	0.058(10)
O6	−0.1864(17)	0.3161(7)	0.0603(17)	0.061(10)
C1	0.7928(22)	0.4773(7)	0.5858(26)	0.060(11)
C2	0.6968(21)	0.4578(8)	0.5624(26)	0.054(11)
C3	0.6580(18)	0.4102(7)	0.5471(22)	0.038(11)
C4	0.5598(22)	0.3937(8)	0.5209(24)	0.054(11)
C5	0.5235(24)	0.3435(9)	0.5167(25)	0.044(11)
C6	0.4195(25)	0.3435(10)	0.4827(23)	0.043(11)
C7	0.3855(18)	0.3934(6)	0.4687(21)	0.025(10)
C8	0.2796(21)	0.4101(8)	0.4342(25)	0.054(11)
C9	0.2550(19)	0.4607(7)	0.4331(24)	0.043(11)
C10	0.1545(23)	0.4743(8)	0.4126(28)	0.066(11)
C11	0.7405(21)	0.3688(8)	0.5684(23)	0.046(11)
C12	0.8977(21)	0.3626(7)	0.7418(22)	0.042(11)
C13	0.9786(20)	0.3248(8)	0.7733(27)	0.039(11)
C14	0.9061(22)	0.3025(9)	0.6344(25)	0.054(11)
C15	0.7673(23)	0.3085(9)	0.4859(27)	0.066(11)
C16	0.6765(25)	0.3440(9)	0.4473(27)	0.047(11)
C17	1.2157(26)	0.3463(10)	1.0738(27)	0.087(12)
C18	1.1180(23)	0.2738(9)	0.7376(28)	0.069(11)
C19	0.5456(27)	0.2871(11)	0.1824(27)	0.075(12)
C20	0.1909(21)	0.3703(8)	0.4003(23)	0.041(11)
C21	0.2655(23)	0.3458(8)	0.5413(25)	0.039(11)
C22	0.1838(21)	0.3090(8)	0.5133(22)	0.041(11)
C23	0.0299(22)	0.3015(8)	0.3477(23)	0.051(11)
C24	−0.0492(23)	0.3242(9)	0.2145(26)	0.062(11)
C25	0.0430(22)	0.3628(8)	0.2424(25)	0.058(11)
C26	0.3909(27)	0.2837(10)	0.7879(25)	0.080(12)
C27	−0.1701(24)	0.2855(9)	0.2680(28)	0.079(11)
C28	−0.2712(24)	0.3331(10)	−0.0847(26)	0.079(12)
O	−0.2873(27)	0.5000	−0.1468(27)	0.079(12)
C29	−0.1509(36)	0.5000	−0.0768(45)	0.228(15)

TABLE 2. Selected bond lengths and standard deviations

Bond	Bond length (Å)	Bond	Bond length (Å)
Fe–Cl	2.207(20)	Fe–N1	2.172(40)
Fe–N2	2.080(14)	Fe–N3	1.985(53)
Fe–N2′	2.080(14)	N1–C2	1.397(42)
N1–C2′	1.397(42)	N2–C4	1.463(50)
N2–C7	1.354(47)	N3–C9	1.379(46)
N3–C9′	1.379(46)	O1–C13	1.369(21)
O1–C17	1.548(45)	O2–C14	1.494(42)
O2–C18	1.373(50)	O3–C15	1.416(43)
O3–C19	1.450(20)	O4–C22	1.344(41)
O4–C26	1.349(21)	O5–C23	1.411(42)
O5–C27	1.465(51)	O6–C24	1.283(19)
O6–C28	1.318(40)	C1–C2	1.394(61)
C1–C1′	1.219(38)	C2–C3	1.362(33)
C3–C4	1.370(56)	C3–C11	1.563(45)
C4–C5	1.456(39)	C5–C6	1.302(46)
C6–C7	1.400(34)	C7–C8	1.402(54)
C8–C9	1.417(33)	C8–C20	1.507(46)
C9–C10	1.444(63)	C10–C10′	1.383(44)
C11–C12	1.443(19)	C11–C16	1.267(47)
C12–C13	1.400(43)	C13–C14	1.380(46)
C14–C15	1.258(22)	C15–C16	1.419(53)
C20–C21	1.418(46)	C20–C25	1.344(20)
C21–C22	1.413(49)	C22–C23	1.402(20)
C23–C24	1.285(42)	C24–C25	1.571(53)
O–C29	1.461(82)		

TABLE 3. Selected bond angles with standard deviations

Bond angle	Degree	Bond angle	Degree
Cl–Fe–N1	103.3(1.2)	Cl–Fe–N2	104.6(0.7)
N1–Fe–N2	87.1(1.0)	Cl–Fe–N3	107.1(1.0)
N1–Fe–N3	149.6(1.1)	N2–Fe–N3	85.3(1.3)
Cl–Fe–N2′	104.6(0.7)	N1–Fe–N2′	87.1(1.0)
N2–Fe–N2′	150.8(1.5)	N3–Fe–N2′	85.4(1.3)
Fe–N1–C2	124.6(1.7)	Fe–N1–C2′	124.6(1.7)
C2–N1–C2′	108.6(4.4)	Fe–N2–C4	124.2(2.8)
Fe–N2–C7	129.8(2.3)	C4–N2–C7	104.9(1.8)
Fe–N3–C9	129.6(2.3)	Fe–N3–C9′	129.6(2.3)
C9–N3–C9′	100.2(4.4)	C13–O1–C17	115.1(2.9)
C14–O2–C18	117.0(2.0)	C15–O3–C19	120.8(2.7)
C22–O4–C26	116.7(3.0)	C23–O5–C27	112.8(2.0)
C24–O6–C28	134.5(3.3)	C2–C1–C1′	112.1(1.5)
N1–C2–C1	103.5(2.5)	N1–C2–C3	124.6(3.9)
C1–C2–C3	131.6(3.4)	C2–C3–C4	128.6(3.1)
C1–C3–C11	115.9(3.3)	C4–C3–C11	115.5(2.1)
N2–C4–C3	125.3(2.1)	N2–C4–C5	103.9(3.3)
C3–C4–C5	130.8(3.1)	C4–C5–C6	111.7(2.9)
C5–C6–C7	106.4(3.0)	N2–C7–C6	113.0(3.4)
N2–C7–C8	121.8(2.0)	C6–C7–C8	125.1(3.0)
C7–C8–C9	124.4(3.0)	C7–C8–C20	116.0(2.2)
C9–C8–C20	119.6(3.6)	N3–C9–C8	124.1(3.9)
N3–C9–C10	115.1(2.4)	C8–C9–C10	120.6(3.0)
C9–C10–C10′	104.7(1.3)	C3–C11–C12	111.8(2.5)

(continued)

TABLE 3. *(continued)*

Bond angle	Degree	Bond angle	Degree
C3–C11–C16	123.7(1.7)	C12–C11–C16	124.5(3.0)
01–C13–C14	116.4(3.2)	01–C13–C12	126.2(2.5)
02–C14–C13	115.8(1.6)	02–C14–C15	118.4(2.9)
03–C15–C16	120.1(1.6)	03–C15–C14	119.0(3.4)
C8–C20–C25	119.4(2.7)	08–C20–C21	117.2(1.7)
04–C22–C23	116.2(2.8)	04–C22–C21	126.2(1.6)
05–C23–C22	117.0(2.6)	05–C23–C24	115.1(1.8)
06–C24–C25	114.8(3.1)	06–C24–C23	129.7(3.2)

TABLE 4. Hydrogen atomic coordinates ($\times 10^4$) and thermal parameters ($Å^2 \times 10^3$)

Atom	x	y	z	U
H(1)	8516	4574	5997	80
H(5)	5701	3140	5361	80
H(6)	3748	3149	4693	80
H(10)	997	4525	4013	80
H(12)	9439	3830	8299	80
H(16)	5710	3492	3341	80
H(17a)	13200	3354	11754	80
H(17b)	11668	3434	10857	80
H(17c)	12133	3803	10524	80
H(18a)	11622	2444	7528	80
H(18b)	11918	2896	8442	80
H(18c)	10888	2962	6635	80
H(19a)	5213	2650	1114	80
H(19b)	5313	3208	1501	80
H(19c)	4795	2802	1709	80
H(21)	3691	3539	6532	80
H(25)	−49	3806	1497	80
H(26a)	4167	2619	8606	80
H(26b)	4163	3173	8273	80
H(26c)	4472	2741	7878	80
H(27a)	−2195	2591	2543	80
H(27b)	−2441	3026	1632	80
H(27c)	−1248	3083	3517	80
H(28a)	−3714	3186	−1743	80
H(28b)	−2246	3244	−974	80
H(28c)	−2794	3686	−879	80

through mirror. Molecular packing of the unit cell is shown in Fig. 2.

FeTTOMPPCl is a five-coordinated complex of Fe(III). From Fig. 1 it can be seen that the central Fe(III) ion and the Cl ion are on the same side of the plane as the 4 N atoms of the porphyrin ring. Fe(III) is 0.5336 Å and Cl is 2.7404 Å away from the plane. The average of the four Cl–Fe–N angles is 106°. The structure is a square pyramid with the four N atoms as the base and Cl as the top. This is the typical structure of high-spin complexes of Fe. The average Fe–N bond length of 2.079 Å also indicates the high-spin structure of the Fe(III). The average Fe–N bond length of low-spin Fe(III) is only 1.988 Å [5].

TABLE 5. Anisotropic thermal parameters ($Å^2 \times 10^3$)

Atom	U_{11}	U_{22}	U_{33}	U_{23}	U_{13}	U_{12}
Fe	42(2)	37(2)	70(3)	0	48(2)	0
Cl	90(4)	107(5)	140(5)	0	89(4)	0
N1	31(5)	27(5)	47(5)	0	32(4)	0
N2	38(4)	33(5)	63(4)	0(5)	45(3)	0(5)
N3	34(5)	39(6)	69(5)	0	46(4)	0
O1	54(5)	114(6)	105(5)	−17(5)	57(4)	19(5)
O2	73(4)	68(5)	107(5)	3(5)	79(4)	30(4)
O3	69(4)	90(5)	59(4)	−8(4)	56(3)	5(4)
O4	60(5)	62(5)	59(5)	13(4)	49(4)	3(4)
O5	53(4)	48(5)	78(5)	0	56(3)	0
O6	49(4)	94(5)	30(4)	−13(4)	31(3)	−25(4)
C1	41(5)	32(5)	86(5)	−12(5)	50(4)	−3(4)
C2	47(5)	54(6)	81(5)	2(5)	57(4)	2(5)
C3	18(5)	29(5)	40(5)	1(5)	20(4)	5(4)
C4	43(5)	31(5)	55(5)	−9(5)	36(4)	−4(5)
C5	38(5)	21(5)	60(5)	−1(5)	39(4)	3(5)
C6	58(5)	46(6)	36(5)	−4(5)	42(4)	−7(5)
C7	24(4)	17(5)	40(5)	−2(4)	28(4)	−1(4)
C8	39(5)	50(6)	68(5)	5(5)	45(4)	−6(5)
C9	27(4)	37(5)	60(5)	3(5)	37(4)	14(5)
C10	58(5)	57(6)	96(5)	5(5)	67(4)	7(5)
C11	41(5)	53(5)	41(5)	4(5)	34(4)	9(5)
C12	49(5)	37(5)	41(5)	−10(5)	38(4)	2(5)
C13	35(5)	54(5)	44(5)	2(5)	36(4)	15(5)
C14	49(5)	58(6)	51(5)	−8(5)	42(4)	−12(5)
C15	46(5)	55(6)	64(5)	−3(5)	41(4)	−11(5)
C16	46(5)	48(5)	58(5)	3(5)	46(4)	2(5)
C17	71(5)	88(6)	67(5)	−3(5)	53(4)	25(5)
C18	63(5)	73(6)	87(5)	−0(5)	66(4)	19(5)
C19	82(5)	75(6)	52(5)	−15(5)	53(4)	1(5)
C20	48(5)	40(5)	48(5)	−9(5)	43(4)	−6(5)
C21	39(5)	29(5)	45(5)	−0(5)	35(4)	−11(5)
C22	59(5)	53(5)	39(5)	−1(5)	47(4)	7(5)
C23	59(5)	46(5)	34(5)	4(5)	37(4)	−6(5)
C24	47(5)	59(6)	49(5)	−14(5)	35(4)	3(5)
C25	48(5)	42(5)	56(5)	3(5)	39(4)	5(5)
C26	84(5)	62(6)	40(5)	13(5)	43(4)	−1(5)
C27	56(5)	73(6)	82(5)	0(5)	54(4)	−3(5)
C28	52(5)	84(6)	60(5)	18(5)	40(4)	−1(5)
O	100(5)	88(6)	71(5)	0	76(4)	0
C29	111(6)	108(6)	122(6)	0	41(6)	0

Due to the steric interaction of the four trimethoxyphenyl groups on the porphyrin ring, neighbouring benzene rings of the phenyl groups are perpendicular to each other at an average angle of 90.4°. Alternate benzene rings (I and II′ or II and I′) are essentially co-planar at an average twist angle of only 1.5°. The angles between the planes of the porphyrin ring and the four benzene rings, namely I, II, II′, I′, are 104.0, 75.2, 104.8 and 76.0°, respectively, resulting in a propeller shape structure. The C8–C20 bond is 1.507 Å, which is shorter than the usual single C–C bond length of 1.54 Å. The C3–C11 distance has a large standard deviation and may be as short as 1.52 Å. This indicates the conjugation effect between the porphyrin and the benzene rings.

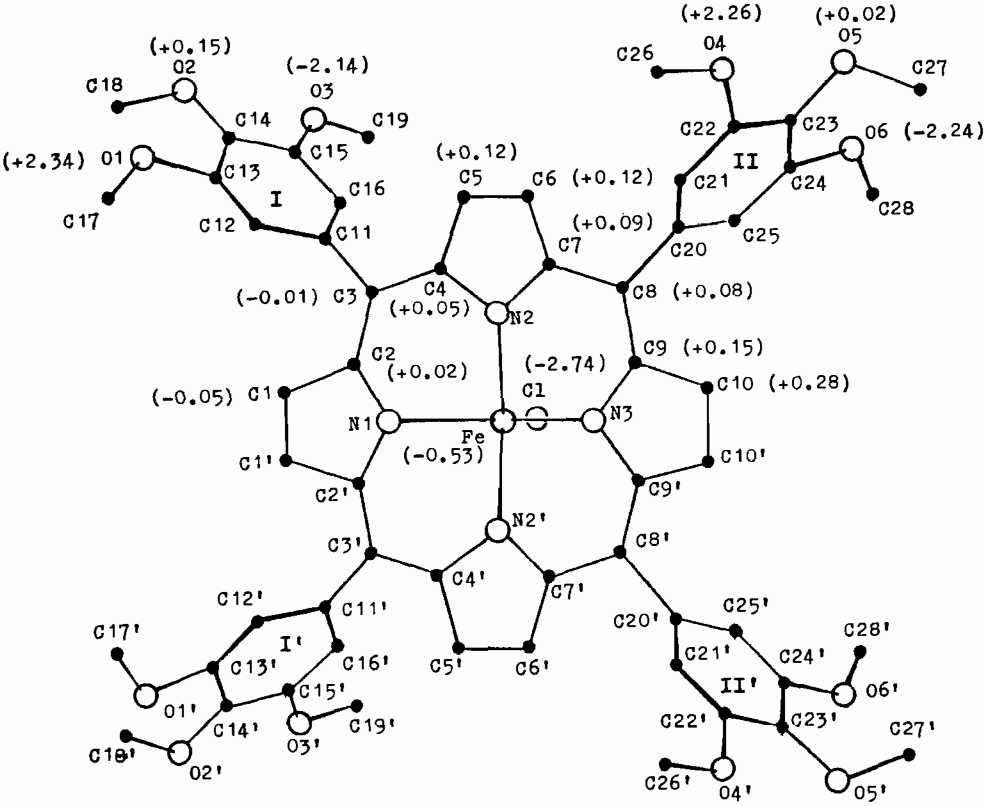

Fig. 1. FeTTOMPPCl molecular stereoconfiguration. Relative distances of some of the atoms from the plane defined by N1–N2–N3–N2 are given in brackets in Å with + and – signs denoting positions above and below the plane respectively.

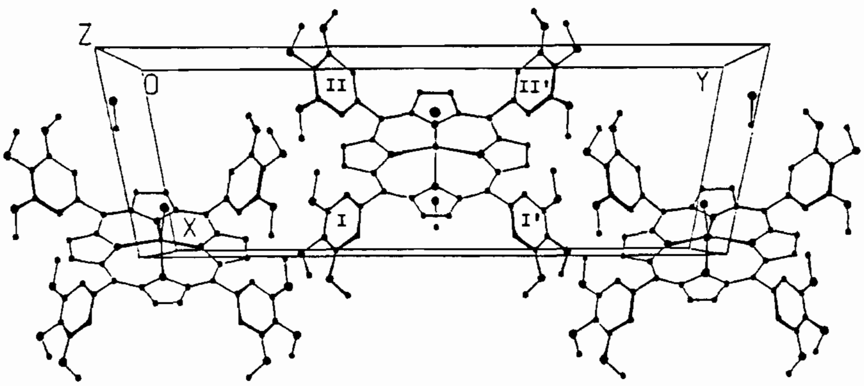

Fig. 2. Molecular packing of FeTTOMPPCl in the cell.

Such a conjugation effect between non-coplanar rings has also been observed in studies of mass spectroscopy [6], IR spectroscopy [7] and kinetics [8].

As a result of the propeller structure of the four trimethoxyphenyl substituent groups on the porphyrin ring, and also the interaction of the methoxy groups, a sterically protected pocket of definite orientation is formed. Figure 1 also shows the distances of the various atoms from the least-squares plane of the four N atoms. It can be noted that the porphyrin ring atoms are essentially on the same plane. The 12 oxygen atoms of the methoxy groups are in three layers. O1–O4–O4 –O1, are on the top layer with an average distance of 2.30 Å from the porphyrin ring. O2–O5–O5 –O2, are on the middle layer which is co-planar with the porphyrin ring. O3–O6–O6 –O3, are on the bottom layer with an average distance of 2.19 Å from the porphyrin ring.

These 12 oxygen atoms define a slant cylindrically shaped pocket which has a depth of 4.49 Å, edge of 11.22 Å, diagonal of 15.8 Å, and which contains the porphyrin ring at the centre, at a depth of 2.25 Å. The Cl atom is outside this pocket. From molecular orbital calculations, it can be shown that the Fe–O bond length of ferryl porphyrins $PFe^{V}=O$ is 1.7 Å, 2.23 Å away from the porphyrin ring [9]. Therefore if FeTTOMPPCl is used as a catalyst, the Fe–O bond will be inside the sterically protected pocket. This intermediate, when reacted with long chain alkanes or alkenes with steric hindrance, will show high steric and shape selectivity. This has been shown by studies of catalytic activities of sterically hindered metal porphyrins [10]. In the crystal, the Fe and Cl atoms are at the same side of the porphyrin plane. This will affect the coordination of O_2 with Fe. However, when in solution, the Cl atom may move away to facilitate the coordination with O_2, resulting in higher catalytic activity.

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