Darriet, J., Soubeyroux, J. L. & Murani, A. P. (1983). *J. Phys. Chem. Solids*, **44**, 269–272.
Drillon, M. (1977). Thesis. Bordeaux Univ.
Koester, L., Rauch, H., Herkens, M. & Schroeder, K. (1981). Kernforschungsanlage Rep., Jülich, p. 1755.
Longo, J. M., Kafalas, J. A. & Arnott, R. J. (1971). *J. Solid State Chem.* **3**, 174–179.
Rietveld, H. M. (1969). *J. Appl. Cryst.* **2**, 65–71.
Shannon, R. D. (1976). *Acta Cryst.* A**32**, 751–767.
Treiber, U., Kemmler-Sack, S. & Ehmann, A. (1982). *Z. Anorg. Allg. Chem.* **487**, 189–198.
Weber, K. (1967). *Acta Cryst.* **23**, 720–725.
Zandbergen, H. W. & IJdo, D. J. W. (1983). *Acta Cryst.* C**39**, 829–832.

Acta Cryst. (1984). C**40**, 922–926

Ferricrocin ($C_{29}H_{44}FeN_9O_{13}.7H_2O$), an Iron(III)-Binding Peptide from *Aspergillus versicolor*

By Charles L. Barnes

Chemistry Department, University of Oklahoma, Norman, OK 73019, *USA*

D. L. Eng-Wilmot

Chemistry Department, Box 2743, *Rollins College, Winter Park, FL* 32789, *USA*

and Dick van der Helm

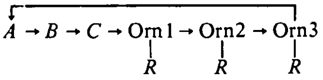
Chemistry Department, University of Oklahoma, Norman, OK 73019, *USA*

(*Received* 21 *July* 1983; *accepted* 29 *November* 1983)

Abstract. $M_r = 908 \cdot 7$, $P2_1$, $a = 11 \cdot 178\,(5)$, $b = 17 \cdot 809\,(11)$, $c = 21 \cdot 805\,(13)$ Å, $\beta = 104 \cdot 14\,(3)^\circ$, $V = 4209 \cdot 2$ Å^3, $Z = 4$, $D_x = 1 \cdot 43$ Mg m^{-3}, Mo $K\bar{\alpha}$, $\lambda = 0 \cdot 71069$ Å, $\mu = 4 \cdot 5$ cm^{-1}, $F(000) = 1924$, $T = 138\,(2)$ K, final $R = 0 \cdot 0991$ for 8973 unique reflections, $R = 0 \cdot 0716$ for 6879 observed data. Ferricrocin was isolated from low-iron cultures of *Aspergillus versicolor,* and purified by silica-gel chromatography. One of the two independent molecules is conformationally very similar to the crystal structure conformations of ferrichrome and ferrichrome A, but the other molecule assumes a somewhat different conformation of the cyclic hexapeptide ring.

Introduction. In response to low iron availability, microorganisms elaborate iron-binding compounds of low molecular mass ($\lesssim$1000 daltons), which are capable of solubilizing ferric iron and making it available to the cell. These compounds have been called siderochromes and siderophores. Emery and Neilands have suggested that the term siderophore be reserved for those compounds proven to transport iron across the cell membrane (Emery, 1980; Neilands, 1981*a,b*).

The ligand of the ferrichrome-type siderophores (hereafter referred to collectively as ferrichromes) are cyclic hexapeptides of the general formula

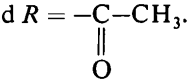


$$A \rightarrow B \rightarrow C \rightarrow \underset{R}{\mathrm{Orn1}} \rightarrow \underset{R}{\mathrm{Orn2}} \rightarrow \underset{R}{\mathrm{Orn3}}$$

where A and B are glycine, alanine or serine residues and C is a glycine residue, and Orn1, 2 and 3 are N^δ-acyl-N^δ-hydroxyornithine residues, with R, the acyl group, derived from one or more of a number of carboxylic acids. Ferrichromes chelate iron with the six oxygens of the hydroxamate moieties of the modified ornithine residues. The dissociation constants of the ferric complexes are of the order of 10^{-30} (Anderegg, L'Eplattenier & Schwarzenbach, 1963).

Ferrichromes have been found to be produced by *Penicillia, Aspergilli, Neurospora* and *Ustilago* species (Neilands, 1981*a*) and by *Fusarium roseum* (Emery, 1980). It is not uncommon that a fungal culture will yield more than one of these siderochromes, though there is species specificity at least in the relative proportions produced.

We report here the crystal structure of ferricrocin, for which $A = C =$ glycine, $B =$ serine, and $R = \underset{\displaystyle \mathrm{O}}{\overset{}{\underset{\|}{-\mathrm{C}}}}-\mathrm{CH}_3$.



Experimental. The iron-free ligand of ferricrocin was produced in low-iron cultures of *Aspergillus versicolor* (wild type). Culture conditions, preparation and extraction of the iron chelate were as described elsewhere (van der Helm, Baker, Eng-Wilmot, Hossain & Loghry, 1980; Garibaldi & Neilands, 1955). Ferricrocin was purified by preparative thin-layer silica-gel chromatography, developing solvent $CHCl_3$: CH_3OH:

0108-2701/84/060922-05$01.50

H_2O (18:6:1, *v*/*v*), followed by silica-gel column chromatography, with eluant $CHCl_3$:$C_6H_5CH_2OH$:CH_3OH (2:1:1, *v*/*v*).

Brick-shaped red crystal from $CHCl_3/CH_3CN$ 0·25 × 0·25 × 0·45 mm, Enraf–Nonius CAD-4 diffractometer with liquid-N_2 low-temperature device, 48 reflections with $10 < \theta < 15°$ used to refine unit-cell parameters; systematic absences $0k0$, $k \neq 2n$; no absorption correction applied; $2\theta_{\max} = 53°$; $0 \leq h \leq 14$, $0 \leq k \leq 22$, $-27 \leq l \leq 27$; 3 standard reflections measured after every 7200 s of X-ray exposure fluctuated <5% during collection, data corrected for this; 8973 unique reflections measured, 6879 observed [$I \geq 2\sigma(I)$]; structure solved by Patterson and Fourier techniques; function minimized during refinement $\sum w(|F_o| - |F_c|)^2$, with $w = 1/\sigma^2(F_o)$; H atoms whose positions could be calculated with confidence were included in the final model, but not refined; non-H atoms, including two water O atoms, refined with anisotropic temperature factors; serine hydroxyl O atom, molecule *A*, was disordered and refined as two sites of equal occupancy; disordered solvent was modelled as four water O atoms of unit occupancy and ten water O atoms of 0·5 occupancy; $R = 0{\cdot}0716$ for 6879 observed data, $R = 0{\cdot}0991$ for all data, $S = 2{\cdot}66$; $(\Delta/\sigma)_{\max} = 25\%$ in final refinement cycle, $(\Delta/\sigma)_{\rm av}$ <10%; final difference synthesis showed $\Delta\rho$ excursions in the area of disordered solvent (e^- max $\lesssim 0{\cdot}7$ Å^{-3}), but was essentially featureless in the vicinity of the siderophore molecules; atomic scattering factors and anomalous-dispersion corrections (Fe) from *International Tables for X-ray Crystallography* (1974); all calculations were performed with *SHELX* (Sheldrick, 1976) and the *NRC* (Ahmed, 1966) suite of programs.

Discussion. A schematic drawing of ferricrocin is shown in Fig. 1. The numbering scheme follows the convention of the IUPAC–IUB Commission on Biochemical Nomenclature (1970) rather than the convention previously used for ferrichrome structures. The absolute configurations of the serine and ornithine residues (all L) were assigned by analogy to those of ferrichrome A (Zalkin, Forrester & Templeton, 1966), ferrichrome (van der Helm, Baker, Eng-Wilmot, Hossain & Loghry, 1980), ferrichrysin (Norrestam, Stensland & Brändén, 1975), and ferrirubin (Barnes, Hossain, Jalal & van der Helm, 1984). Final parameters for the non-H atoms are given in Table 1. Average structure parameters of the peptide bonds and iron chelate rings are given in Table 2.*

The average bond distances and angles about the peptide bonds are compared in Table 2 with values derived from a number of peptide structures in a recent review (Karle, 1981). In three of the four distances compared, the ferricrocin distances are longer, though only the N—C_α distance difference may be statistically significant. This trend may be in part because this structure was determined using low-temperature data, while most of the structures averaged by Karle were room-temperature studies and therefore reflect a greater effect of thermal motion on the calculated bond distances.

The Fe coordination sphere is very similar to those of the other ferrichrome structures. A *Λ-cis* isomer of the octahedral sphere has been observed in all ferrichrome crystal structures, and is believed to be the predominant or only species in solution (Leong & Raymond, 1974; Abu-Dari & Raymond, 1977; Wong, Kappel, Raymond, Matzanke & Winkelmann, 1983). The metal coordination is described by the edge lengths of the coordination sphere and by the ligand bite and twist angle, which are given in Table 2 along with the values from ferrichrome and ferrichrome A. The ligand bite is the ratio of the O–O distances to the Fe–O distances, while the twist angle is the angle of rotation of the O(1ε)–O(2ε)–O(3ε) face of the coordination sphere with respect to the O(1ζ)–O(2ζ)–O(3ζ) face, which would be 60° for an ideal octahedron and 0° for the trigonal prismatic arrangement. Though there is considerable variation in individual bond lengths and angles involving chemically equivalent atoms in the Fe coordination polyhedra of these three structures, perhaps reflecting variations in the distribution of the overall strain of the molecules as well as differences in packing forces, the average values compare very well.

Table 3 lists selected conformational angles. Fig. 2 gives perspective views of the two independent molecules. The conformation of molecule *B* closely resembles the conformations observed in the crystal structures of ferrichrome (van der Helm *et al.*, 1980), ferrichrysin (Norrestam, Stensland & Brändén, 1975) and ferrichrome A (Zalkin, Forrester & Templeton, 1966; van der Helm, Baker, Loghry & Ekstrand, 1981), with a nearly rectangular 18-membered ring formed by

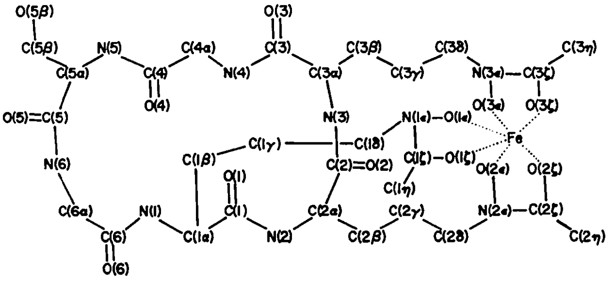


Fig. 1. Schematic drawing of ferricrocin with atom labeling scheme.

---

* Lists of bond distances and angles, hydrogen bonds, anisotropic thermal parameters, H-atom coordinates and structure factors have been deposited with the British Library Lending Division as Supplementary Publication No. SUP 39069 (46 pp.). Copies may be obtained through The Executive Secretary, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

two β turns linking two extended and nearly planar peptide chains. The conformation of molecule *A* deviates from the others primarily by a rotation of the Orn(3)—Gly(4) peptide bond away from co-planarity with the Gly(4)—Ser(5) peptide bond, as seen in the markedly different values for the conformational angles ψ_3 and φ_4 [N(3)—C(3α)—C(3)—N(4) and C(3)—N(4)—C(4α)—C(4)]. In ferrichrome, ferrichrome A and ferrichrysin, these angles are 22, 7, 19 and 165, −164, −166°, respectively. Such a rotation would be hindered when a serine is substituted for Gly(4), as in the case of ferrichrysin and ferrichrome A, by steric interactions between O(3) and the serine side chain. However, there is no reason why ferrichrome, which has a glycine as

Table 1. *Fractional coordinates* $(\times 10^4)$ *and equivalent isotropic temperature factors* $(\text{Å}^2 \times 10^3)$ *for non-hydrogen atoms*

E.s.d.'s are in parentheses.

	x	*y*	*z*	U_{eq}*		*x*	*y*	*z*	U_{eq}*
Molecule *A*					Molecule *B*				
Fe	−236 (2)	3·5 (13)	1257·3 (8)	38·5 (9)	Fe	5160 (2)	1196·4 (12)	8337·4 (7)	31·8 (7)
C(1α)	−1148 (11)	962 (6)	3515 (5)	28 (5)	C(1α)	5769 (11)	1591 (6)	5991 (5)	29 (5)
N(1)	−974 (9)	821 (5)	4190 (4)	28 (5)	N(1)	5631 (9)	1342 (5)	5340 (4)	28 (4)
C(1)	−2329 (11)	572 (6)	3167 (5)	28 (5)	C(1)	7052 (10)	1356 (6)	6381 (5)	27 (5)
O(1)	−3097 (7)	341 (5)	3433 (4)	32 (4)	O(1)	7843 (7)	1087 (5)	6137 (4)	34 (4)
C(1β)	9 (11)	756 (7)	3308 (5)	34 (6)	C(1β)	4700 (11)	1298 (7)	6244 (5)	31 (5)
C(1γ)	399 (11)	−66 (7)	3405 (5)	32 (5)	C(1γ)	4660 (10)	457 (7)	6282 (5)	26 (5)
C(1δ)	1482 (11)	−272 (8)	3156 (5)	37 (6)	C(1δ)	3678 (10)	147 (7)	6607 (5)	32 (6)
N(1ε)	1291 (8)	−94 (7)	2478 (4)	37 (5)	N(1ε)	3777 (8)	518 (6)	7219 (4)	28 (5)
O(1ε)	255 (8)	−450 (5)	2106 (4)	39 (4)	O(1ε)	4913 (7)	429 (5)	7644 (4)	36 (4)
C(1ζ)	1861 (11)	353 (10)	2193 (6)	49 (8)	C(1ζ)	3016 (11)	978 (7)	7385 (5)	31 (6)
O(1ζ)	1463 (9)	449 (8)	1593 (4)	66 (6)	O(1ζ)	3334 (7)	1319 (5)	7921 (3)	33 (4)
C(1η)	2968 (16)	825 (14)	2545 (8)	84 (12)	C(1η)	1747 (10)	1109 (7)	6957 (5)	33 (6)
C(2α)	−3650 (10)	138 (7)	2176 (5)	28 (5)	C(2α)	8518 (11)	1381 (7)	7408 (5)	33 (6)
N(2)	−2529 (8)	507 (5)	2532 (4)	27 (4)	N(2)	7283 (8)	1479 (5)	7004 (4)	25 (4)
C(2)	−3620 (9)	−711 (7)	2310 (4)	24 (5)	C(2)	8828 (11)	544 (7)	7536 (6)	35 (6)
O(2)	−4569 (7)	−1046 (5)	2337 (4)	31 (4)	O(2)	9919 (9)	345 (6)	7731 (7)	69 (7)
C(2β)	−3922 (11)	262 (7)	1464 (5)	30 (6)	C(2β)	8662 (10)	1792 (7)	8036 (5)	32 (6)
C(2γ)	−4097 (13)	1076 (9)	1231 (6)	48 (7)	C(2γ)	8485 (11)	2634 (7)	7989 (5)	36 (6)
C(2δ)	−2945 (13)	1572 (8)	1335 (6)	44 (7)	C(2δ)	7161 (12)	2935 (7)	7803 (6)	39 (6)
N(2ε)	−1938 (10)	1195 (6)	1157 (5)	39 (5)	N(2ε)	6322 (9)	2548 (6)	8100 (4)	34 (5)
O(2ε)	−1238 (7)	738 (5)	1612 (4)	37 (4)	O(2ε)	5858 (7)	1895 (5)	7801 (4)	32 (4)
C(2ζ)	−1670 (12)	1209 (9)	603 (5)	42 (6)	C(2ζ)	6054 (11)	2669 (8)	8650 (5)	39 (6)
O(2ζ)	−756 (9)	784 (6)	535 (4)	51 (5)	O(2ζ)	5366 (8)	2170 (5)	8848 (4)	39 (4)
C(2η)	−2314 (15)	1673 (9)	76 (7)	56 (8)	C(2η)	6436 (13)	3363 (8)	9008 (6)	47 (7)
C(3α)	−2316 (11)	−1842 (7)	2426 (5)	31 (6)	C(3α)	8018 (12)	−738 (7)	7647 (5)	33 (6)
N(3)	−2517 (9)	−1017 (5)	2370 (4)	31 (5)	N(3)	7880 (9)	72 (6)	7472 (4)	32 (5)
C(3)	−1424 (11)	−2004 (7)	3066 (5)	30 (6)	C(3)	7331 (13)	−1235 (8)	7097 (6)	41 (7)
O(3)	−332 (8)	−2106 (6)	3126 (4)	44 (5)	O(3)	7103 (12)	−1901 (6)	7193 (4)	67 (6)
C(3β)	−1787 (11)	−2097 (7)	1869 (6)	35 (6)	C(3β)	7539 (12)	−870 (7)	8238 (5)	36 (6)
C(3γ)	−2719 (11)	−2011 (7)	1241 (6)	35 (6)	C(3γ)	8325 (13)	−475 (8)	8809 (6)	42 (7)
C(3δ)	−2157 (13)	−1970 (8)	680 (6)	44 (7)	C(3δ)	7682 (14)	−358 (10)	9339 (6)	51 (8)
N(3ε)	−1297 (9)	−1343 (7)	738 (4)	38 (5)	N(3ε)	6583 (10)	138 (7)	9128 (4)	41 (5)
O(3ε)	−1624 (7)	−692 (5)	1015 (4)	37 (4)	O(3ε)	6742 (8)	706 (5)	8723 (4)	39 (4)
C(3ζ)	−251 (12)	−1278 (11)	554 (6)	60 (9)	C(3ζ)	5553 (13)	130 (10)	9298 (5)	50 (8)
O(3ζ)	404 (8)	−696 (7)	679 (4)	54 (6)	O(3ζ)	4724 (9)	612 (6)	9062 (4)	47 (5)
C(3η)	134 (14)	−1926 (13)	191 (7)	72 (10)	C(3η)	5351 (18)	−431 (12)	9780 (7)	78 (11)
C(4α)	−1262 (11)	−2131 (6)	4199 (6)	32 (6)	C(4α)	6502 (13)	−1403 (7)	5963 (5)	36 (6)
N(4)	−1954 (9)	−2022 (5)	3547 (4)	29 (5)	N(4)	7101 (10)	−952 (6)	6519 (4)	33 (5)
C(4)	−1058 (11)	−1413 (7)	4589 (5)	29 (5)	C(4)	6312 (10)	−881 (6)	5386 (5)	25 (5)
O(4)	−1472 (7)	−803 (4)	4363 (4)	31 (4)	O(4)	6665 (7)	−227 (4)	5443 (4)	29 (4)
C(5α)	−371 (11)	−918 (7)	5658 (5)	29 (5)	C(5α)	5519 (10)	−711 (6)	4262 (5)	22 (5)
N(5)	−419 (9)	−1511 (5)	5181 (4)	29 (5)	N(5)	5738 (8)	−1173 (5)	4832 (4)	25 (4)
C(5)	65 (10)	−184 (7)	5454 (5)	28 (5)	C(5)	4839 (9)	−11 (6)	4363 (4)	22 (4)
O(5)	1069 (7)	−126 (5)	5306 (4)	34 (4)	O(5)	3923 (7)	−9 (5)	4578 (4)	29 (4)
C(5β)	505 (13)	−1188 (8)	6274 (6)	42 (6)	C(5β)	4706 (11)	−1120 (7)	3690 (5)	27 (5)
O(5β)†	−70 (30)	−1740 (14)	6508 (11)	91 (17)	O(5β)	5384 (8)	−1702 (5)	3469 (4)	36 (4)
O(5β)	535 (18)	−684 (9)	6724 (6)	40 (9)	C(6α)	4654 (13)	1366 (6)	4206 (5)	35 (6)
C(6α)	−372 (11)	1155 (7)	5318 (5)	34 (6)	N(6)	5274 (9)	637 (5)	4169 (4)	25 (4)
N(6)	−680 (8)	402 (5)	5455 (4)	24 (4)	C(6)	4883 (12)	1689 (6)	4868 (5)	32 (6)
C(6)	−648 (11)	1353 (7)	4608 (5)	32 (6)	O(6)	4313 (11)	2270 (5)	4925 (4)	61 (6)
O(6)	−521 (10)	2021 (5)	4459 (4)	46 (5)					
Waters‡									
W(1)	7307 (8)	3842 (5)	4966 (4)	42 (5)	*W*(8)	691 (20)	1323 (14)	9658 (10)	66 (6)
W(2)	7895 (9)	2930 (6)	6088 (5)	62 (6)	*W*(9)	8207 (28)	4253 (18)	301 (14)	99 (9)
W(3)	7009 (11)	2640 (7)	4140 (5)	67 (3)	*W*(10)	8156 (22)	3487 (14)	2295 (11)	68 (6)
W(4)	5842 (14)	4071 (10)	1849 (8)	105 (5)	*W*(11)	1905 (19)	455 (12)	8914 (10)	57 (5)
W(5)	6907 (15)	2399 (10)	2872 (8)	37 (4)	*W*(12)	2216 (28)	1034 (19)	4872 (14)	100 (9)
W(6)	3438 (22)	2580 (14)	864 (11)	70 (6)	*W*(13)	9040 (23)	3064 (15)	1350 (12)	75 (7)
W(7)	4593 (18)	2644 (11)	2130 (9)	50 (5)	*W*(14)	1231 (47)	2170 (33)	1312 (25)	193 (20)

* $U_{eq} = (\frac{1}{6})\pi^2\sum_i\sum_j\beta_{ij}\mathbf{a}_i.\mathbf{a}_j$, waters 2–14 refined isotropically.

† Disordered serine hydroxyl.

‡ *W*(5)–*W*(14), occupancy = 0·5.

residue 4, could not have the conformation of molecule *A*, and indeed the ψ_3 and φ_4 angles for ferrichrome (22 and 165°) are closer to this conformer than are those of ferrichrome A (7, −164°) or ferrichrysin (19, −166°). This observation correlates with data from solution NMR (Llinas, Wilson, Klein & Neilands, 1976), which

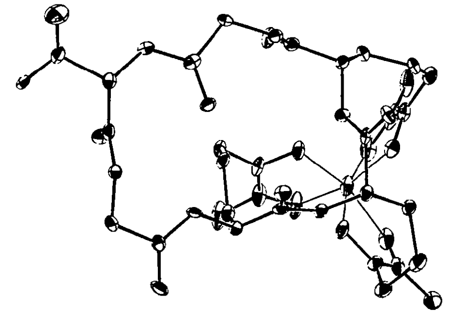
Table 2. *Comparison of structural parameters*

(*a*) Comparison of the average peptide bond parameters for ferricrocin with those given by Karle (1981). The first number in parentheses is the estimated $\sigma = \sum(\Delta)^2/n(n-1)$. The second number in parentheses is the average of the individual e.s.d.'s. Distances are in Å, angles in °.

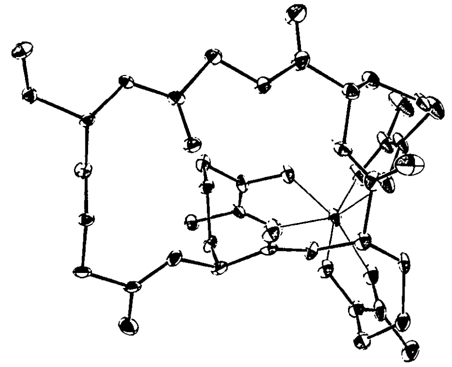
	Ferricrocin	Karle
C(*n*α)–C(*n*)	1·527 (4) (15)	1·522
C(*n*)–O(*n*)	1·233 (3) (14)	1·229
C(*n*)–N(*n* + 1)	1·330 (4) (13)	1·335
N(*n* + 1)–C(*n* + 1α)	1·466 (5) (14)	1·449
C(*n*α)–C(*n*)–O(*n*)	120·9 (6) (9)	120·4
C(*n*α)–C(*n*)–N(*n* + 1)	116·3 (6) (10)	116·6
O(*n*)–C(*n*)–N(*n* + 1)	122·7 (5) (10)	122·9
C(*n*)–N(*n* + 1)–C(*n* + 1α)	121·5 (3) (9)	121·9

(*b*) Comparison of structural parameters of ferrichrome chelate rings. Standard deviations as in (*a*).

	Ferricrocin	Ferrichrome	Ferrichrome A
Fe–O(ε)	1·981 (8) (8)	1·983 (10) (10)	1·980 (6) (4)
Fe–O(ζ)	2·041 (8) (9)	2·034 (6) (10)	2·033 (6) (4)
N–O(ε)	1·384 (4) (13)	1·389 (9) (15)	1·372 (5) (5)
C–O(ζ)	1·289 (8) (16)	1·278 (6) (16)	1·265 (5) (7)
N–C	1·304 (9) (14)	1·305 (9) (19)	1·326 (3) (7)
O(ε)···O(ζ)	2·538 (5) (11)	2·534 (10)	2·527 (7) (7)
Ligand bite	1·26	1·26	1·26
Twist angle	40·4 (8) (6)	42·9 (5)	41·4 (6)
O(ε)–Fe–O(ζ)	78·2 (4) (3)	78·2 (5)	78·0 (1)



Molecule *A*



Molecule *B*

Fig. 2. Perspective views of molecules *A* and *B*. Thermal ellipsoids are drawn at the 30% probability level. Both positions of the disordered serine hydroxyl, O(5β) of molecule *A*, are shown.

Table 3. *Selected conformational angles* (°)

Values for molecule *A* are listed above those for molecule *B*. E.s.d.'s are 0·7–1·4° for endocyclic angles and 0·7–2·1° for exocyclic angles, the largest errors being associated with atoms most distant from the hexapeptide ring.

	Orn *i* = 1	Orn *i* = 2	Orn *i* = 3	Gly *i* = 4	Ser *i* = 5	Gly *i* = 6
Endocyclic angles; φ, ψ, ω						
C(*i* − 1)–N(*i*)–C(*i*α)–C(*i*) φ	−135·6	−69·9	−118·4	102·6	−54·9	83·7
	−153·7	−76·8	−128·1	176·5	−54·8	75·2
N(*i*)–C(*i*α)–C(*i*)–N(*i* + 1) ψ	−167·1	−38·2	81·7	−179·5	125·4	−8·9
	−173·9	−22·8	22·3	−177·7	135·1	3·5
C(*i*α)–C(*i*)–N(*i* + 1)–C(*i* + 1α) ω	−179·9	−172·8	−176·9	−166·5	175·3	−174·9
	−171·2	−172·9	177·0	179·7	176·6	−173·3
Exocyclic angles						
C(*i* − 1)–N(*i*)–C(*i*α)–C(*i*β) χ_0	96·5	166·2	120·4		−176·3	
	80·1	161·0	109·3		−172·8	
N(*i*)–C(*i*α)–C(*i*β)–C(*i*γ) χ_1	60·7	−59·7	−67·0		−71·8/−177·4*	
	63·7	−61·2	−65·9		−73·6	
C(*i*α)–C(*i*β)–C(*i*γ)–C(*i*δ) χ_2	175·8	73·3	158·5			
	173·3	78·9	160·2			
C(*i*β)–C(*i*γ)–C(*i*δ)–N(*i*ε) χ_3	−56·1	46·3	−58·6			
	−50·5	41·3	−62·8			
C(*i*γ)–C(*i*δ)–N(*i*ε)–O(*i*ε) χ_4	−57·8	−84·2	−36·5			
	−59·6	−82·6	−36·4			
C(*i*γ)–C(*i*δ)–N(*i*ε)–C(*i*ζ) χ_5	117·6	91·5	145·6			
	111·8	87·7	147·8			
C(*i*δ)–N(*i*ε)–C(*i*ζ)–C(*i*η) χ_6	0·8	5·3	3·7			
	9·4	12·9	0·8			
O(*i*ε)–N(*i*ε)–C(*i*ζ)–O(*i*ζ) χ_7	−0·2	−0·1	5·9			
	−0·2	−1·2	3·8			

* For serine, this angle is N(5)–C(5α)–C(5β)–O(5β); O(5β) is disordered in molecule *A*.

indicates that substitution of serine or alanine for glycine further limits the already constrained conformational freedom of the metal chelates.

Aside from the above described variation, the overall conformations of molecules *A* and *B* are similar, and closely resemble those of the other ferrichromes, reflecting the limited conformational freedom of these molecules. Though the cyclic hexapeptide ring system presents the possibility for two transannular 4→1 hydrogen bonds, N(1)—H···O(4) and N(4)—H···O(1), in all the ferrichrome crystal structures only the former hydrogen bond is observed. The length of this bond is 3·18 Å in ferrichrome, 2·98 Å in ferrichrome A, 2·988 (10) Å in ferricrocin molecule *A* and 3·018 (10) Å in ferricrocin molecule *B*. Conformational constraints imposed by metal chelation prevent formation of the N(4)—H···O(1) hydrogen bond.

A second intramolecular hydrogen bond, linking the hexapeptide ring with the iron chelation octahedron, is observed in all the ferrichrome crystal structures. This bond, N(2)—H···O(2ε), is 2·81 Å in ferrichrome, 2·77 Å in ferrichrome A, 2·771 (11) Å in ferricrocin molecule *A* and 2·731 (12) Å in ferricrocin molecule *B*.

Fig. 3 is a stereoview of the packing interactions. The ferricrocin molecules pack as *A–B* dimers with an approximate twofold axis relating the independent molecules. The *A–B* dimers are formed by nearly symmetric hydrogen bonds involving donor and recipient atoms of the 18-membered cyclic hexapeptide rings. Adjacent dimers are linked by direct intermolecular hydrogen bonds and by extensive bridging interactions with solvent molecules.

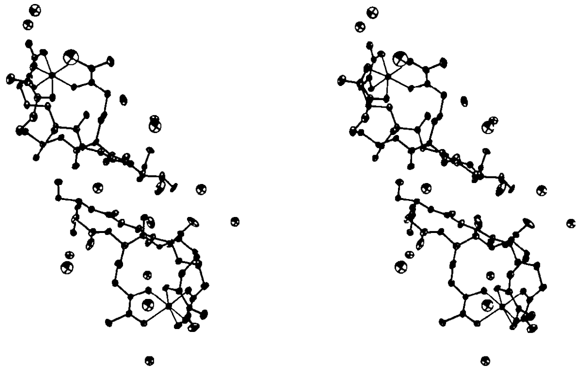


Fig. 3. Stereoview of the packing interactions, showing the hydrogen-bonded *A–B* dimer. Molecule *A* is above molecule *B* in the drawing.

This research was supported by grant GM 21822 from the National Institutes of Health. The authors wish to thank Professor H. Zähner of the University of Tübingen who kindly supplied an authentic sample of ferricrocin for use as a TLC standard. We thank the University of Oklahoma for computing services.

References

Abu-Dari, K. & Raymond, K. N. (1977). *J. Am. Chem. Soc.* **99**, 2003–2005.

Ahmed, F. R. (1966). SFLS program *NRC*-10. National Research Council, Canada.

Anderegg, G., L'Eplattenier, F. & Schwarzenbach, G. (1963). *Helv. Chim. Acta*, **46**, 1400–1408.

Barnes, C. L., Hossain, M. B., Jalal, M. A. F. & van der Helm, D. (1984). In preparation.

Emery, T. (1980). *Biochim. Biophys. Acta*, **629**, 382–390.

Garibaldi, J. A. & Neilands, J. B. (1955). *J. Am. Chem. Soc.* **77**, 2429–2430.

International Tables for X-ray Crystallography (1974). Vol. IV. Birmingham: Kynoch Press.

IUPAC–IUB Commission on Biochemical Nomenclature (1970). *Biochemistry*, **9**, 3471–3479.

Karle, I. L. (1981). *The Peptides*, Vol. 4, edited by E. Gross & J. Meienhofer, p. 1. New York: Academic Press.

Leong, J. & Raymond, K. N. (1974). *J. Am. Chem. Soc.* **96**, 6628–6630.

Llinas, M., Wilson, D. M., Klein, M. P. & Neilands, J. B. (1976). *J. Mol. Biol.* **104**, 853–864.

Neilands, J. B. (1981*a*). *Annu. Rev. Biochem.* **50**, 715–731.

Neilands, J. B. (1981*b*). *Annu. Rev. Nutr.* **1**, 27–46.

Norrestam, R., Stensland, B. & Brändén, C.-I. (1975). *J. Mol. Biol.* **99**, 501–506.

Sheldrick, G. M. (1976). *SHELX*76. Program for crystal structure determination. Univ. of Cambridge, England.

Van der Helm, D., Baker, J. R., Eng-Wilmot, D. L., Hossain, M. B. & Loghry, R. A. (1980). *J. Am. Chem. Soc.* **102**, 4224–4231.

Van der Helm, D., Baker, J. R., Loghry, R. A. & Ekstrand, J. D. (1981). *Acta Cryst.* B**37**, 323–330.

Wong, G. B., Kappel, M. J., Raymond, K. N., Matzanke, B. & Winkelmann, G. (1983). *J. Am. Chem. Soc.* **105**, 810–815.

Zalkin, A., Forrester, J. D. & Templeton, D. H. (1966). *J. Am. Chem. Soc.* **88**, 1810–1814.