Acta Cryst. (1981). B**37**, 323–330

Structures of Alumichrome A and Ferrichrome A at Low Temperature

By Dick van der Helm, J. R. Baker, R. A. Loghry and J. D. Ekstrand

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

(*Received* 2 *June* 1980; *accepted* 11 *September* 1980)

Abstract

The crystal structure of ferrichrome A, the ferric chelate of a natural siderophore, was redetermined, confirming the earlier published structure [Zalkin, Forrester & Templeton (1966). *J. Am. Chem. Soc.* **88**, 1810–1814]. The crystal structure of alumichrome A was determined and shown to be isomorphous with ferrichrome A. Both molecules crystallized in the monoclinic space group $P2_1$, with cell parameters [at 128 (2) K] of a = 10·939 (1), b = 13·190 (1), c = 18·118 (2) Å, β = 99·37 (1)° (ferrichrome A) and a = 10·936 (1), b = 13·146 (2), c = 18·028 (2) Å, β = 99·62 (1)° (alumichrome A). The structures were refined by least-squares methods. The final R values are 0·071 for 6184 reflections (ferrichrome A) and 0·059 for 5503 reflections (alumichrome A). The only significant differences between the two structures are observed in the immediate environments of the metal ions. It also appears that in both compounds the metal ion is not in the center of the distorted octahedral coordination sphere.

Introduction

The availability of Fe to aerobic organisms is limited by the extreme insolubility of ferric hydroxide. This problem has been solved by these organisms through the production of siderophores, specific Fe^{3+} chelating agents, which solubilize ferric iron and transport or facilitate the transport of iron into bacteria and fungi (Neilands, 1973; Emery, 1978). The ferrichromes are one family of siderophores; they are cyclic hexapeptides, the backbones of which contain three adjacent residues of N^{δ}-hydroxy-L-ornithine which are N^{δ}-acylated and form the trivalent iron-ligating hydroxamate groups. Both desferriferrichrome and desferriferrichrome A are produced by *Ustilago sphaerogena* (Neilands, 1952), but only the iron chelate of the first is actively transported into the cell (Emery, 1971). The chemical structures were proven by degradation experiments (Emery & Neilands, 1960, 1961; Rogers, Warren & Neilands, 1963; Rogers & Neilands, 1964), and later confirmed by the complete chemical synthesis of ferrichrome (Keller-Schierlein & Maurer, 1969; Isowa, Ohmori & Kurita, 1974). The molecular structures were also confirmed by the single-crystal X-ray diffraction structure determination of ferrichrome A (Zalkin, Forrester & Templeton, 1966). More recently, the structures of ferrichrysin (Norrestam, Stensland & Brändén, 1975) and ferrichrome (van der Helm, Baker, Eng-Wilmot, Hossain & Loghry, 1980) were determined. Several parts of the ferrichrome A structure reported were disordered, and we hoped to resolve this problem by redetermining the structure at low temperature. The present redetermination, however, shows the same disorder as appeared in the earlier investigation. An extensive study has been made of the solution conformation of aluminum desferriferrichrome (alumichrome), aluminum desferriferrichrome A (alumichrome A), and desferriferrichrome using H, D, ^{13}C, and ^{15}N NMR experiments (Llinás, Klein & Neilands, 1970, 1972, 1973*a*,*b*; Llinás & Klein, 1975; Llinás, Wilson, Klein & Neilands, 1976; Llinás, Horsley & Klein, 1976; Llinás, Wilson & Neilands, 1977; Llinás, Wilson & Klein, 1977; Llinás & Wüthrich, 1978; Llinás & DeMarco, 1980). In the interpretation of these studies, two reasonable assumptions were made: (*a*) the conformations of ferrichrome and ferrichrome A are similar, and (*b*) the conformations of the Al^{III} and Fe^{III} chelates are similar or the same. The first assumption was addressed in an earlier publication (van der Helm *et al.*, 1980), while the second is investigated in the present work.

Experimental

A starter culture of *U. sphaerogena* was obtained from Dr Thomas Emery, Department of Chemistry and Biochemistry, Utah State University, Logan, Utah. The production and preparation of ferrichrome A were performed according to established procedures (Garibaldi & Neilands, 1955). Alumichrome A was a gift from Dr Emery. Single crystals of both compounds were grown by slow evaporation from a

0567-7408/81/020323-08$01.00

CH_3OH/H_2O solution. A colorless, plate-like crystal of alumichrome A with dimensions 0·43 × 0·38 × 0·09 mm was found to be suitable for diffraction experiments, while a dark-red, plate-like crystal of ferrichrome A (0·57 × 0·24 × 0·09 mm) was selected.

Both chelates crystallized in the monoclinic space group $P2_1$ with $Z = 2$. The crystal data are reported in Table 1. The cell parameters were determined from a least-squares fit of the 2θ values of 60 reflections for alumichrome A and 58 for ferrichrome A. These reflections were evenly distributed throughout reciprocal space. All data were taken on a Nonius CAD-4 automatic diffractometer. For the alumichrome A crystal, there were 5503 unique reflections with 2θ between 2 and 150° (Cu $K\bar{\alpha}$). The intensities of these reflections were measured with the θ–2θ scanning technique. The scan angle was calculated with the formula $\theta = (0{\cdot}80 + 0{\cdot}08 \tan\theta)°$. The receiving aperture was at a constant distance of 173 mm from the crystal, and had a fixed height of 6 mm, while the width varied as $(5{\cdot}5 + 0{\cdot}86 \tan\theta)$ mm. The maximum scanning time spent on a reflection was 120 s, with two thirds of the time spent on the peak (P) and the remaining one third divided equally between the high- and low-θ backgrounds (RH and LH). For ferrichrome A, 6184 unique reflections comprising all reflections with $2\theta \leq 56°$ (Mo $K\bar{\alpha}$) were measured, using θ–2θ scans. The angle of the scan varied as $(0{\cdot}60 + 0{\cdot}06 \tan\theta)°$, while the values of the aperture distance and height were the same as reported above. The aperture width was calculated for each reflection as $(5{\cdot}0 + 0{\cdot}86 \tan\theta)$ mm. The maximum scan time was 60 s, divided between P, RH and LH in the same manner as described for alumichrome A. For both compounds, the intensity of a standard reflection was monitored every 25 reflections, and these were used to bring all reflections to a common scale. The crystal orientation was checked every 100 reflections. Reflections were considered indistinguishable from the background if $I < 2\sigma(I)$. This was the case for 99 measurements for alumichrome A and 629 for ferrichrome A. These reflections were assigned intensities of $T^{1/2}$ [$T = P + 4(\mathrm{RH} + \mathrm{LH})$] and included in the refinement calculations. Both data sets were corrected for Lorentz and polarization factors, and for absorption effects ($\mu = 1{\cdot}165$ mm^{-1} for alumichrome A and $\mu = 0{\cdot}400$ mm^{-1} for ferrichrome A). The absorption corrections were calculated with the program of Coppens, Leiserowitz & Rabinovich (1965), employing a Gaussian method and a 6 × 6 × 6 grid. Each structure factor was assigned a weight (van der Helm & Poling, 1976).

The parameters reported by Zalkin, Forrester & Templeton (1966), without those for the solvent molecules and disordered atoms, were used as a starting set for the refinement of both compounds. The remaining atoms were located from subsequent difference Fourier syntheses. It was our hope that the low-temperature data would eliminate the disorder problem; however, this was not the case. The disorder observed in the present structures was of the same type as reported earlier, although the occupations were different.

Table 1. *Crystallographic data*

	Ferrichrome A	Alumichrome A
Molecular formula	$C_{41}H_{58}FeN_9O_{20}\cdot$ 4–5H_2O	$C_{41}H_{58}AlN_9O_{20}\cdot$ 4–5H_2O
Molecular weight	1124·9–1142·9	1096·0–1114·0
Cell dimensions		
at 128 (2) K		
a	10·939 (1) Å	10·936 (1) Å
b	13·190 (1)	13·146 (2)
c	18·118 (2)	18·028 (2)
β	99·37 (1)°	99·62 (1)°
at 298 (1) K		
a	11·023 (1) Å	10·976 (3) Å
b	13·266 (1)	13·266 (3)
c	18·248 (1)	18·162 (8)
β	99·38 (1)°	99·57 (2)°
V	2632·5 Å^3	2607·7 Å^3
ρ_c	1·419–1·442 Mg m^{-3}	1·396–1·419 Mg m^{-3}
ρ_o	1·464 (aq. $ZnCl_2$)	1·404 ($CHCl_3/C_6H_{12}$)
λ(2θ data)	0·7093 Å	1·5405 Å
λ(intensity data)	0·7121	1·5418

The solvent molecules were included in their observed positions and refined. All non-hydrogen atoms were refined anisotropically. Occupancies were estimated from the peak heights in a difference Fourier map and were not refined. All H atoms, except those on methyl groups and those belonging to disordered groups, were also included in the structure factor calculations, but not refined. Anomalous dispersion of the metal atoms was taken into account in the refinement of both structures. The refinement was both by block-diagonal and by two blocks of full-matrix least-squares methods. The results of the two refinement methods showed no significant differences. The results obtained using the latter procedure are presented in this communication (Table 1).* The refinements were terminated when all shifts were less than 50% of the corresponding standard deviations. The final R value ($R = \sum||kF_o| - |F_c||/\sum kF_o$) was 0·071 for all 6184 reflections in ferrichrome A and 0·059 for all reflections of alumichrome A. Scattering factors for Fe^{3+}, C, N and O atoms were taken from *International Tables for X-ray Crystallography* (1962), real and imaginary dispersion corrections for Al (Cu $K\alpha$) and Fe (Mo $K\alpha$) were from *International Tables for*

---

* Lists of structure factors and anisotropic thermal parameters for both compounds have been deposited with the British Library Lending Division as Supplementary Publication No. SUP 35681 (63 pp.). Copies may be obtained through The Executive Secretary, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

X-ray Crystallography (1974) and those for H atoms from Stewart, Davidson & Simpson (1965).

Discussion

The numbering of the residues is shown in Fig. 1. This scheme has been used previously for the ferrichrome-type siderophores. The atom numbering is shown in Fig. 2. Final coordinates, bond distances and bond angles for ferrichrome A and alumichrome A are given in Tables 2, 3 and 4 respectively. The coordinates given are with respect to the same origin as those published by Zalkin, Forrester & Templeton (1966). The present coordinates are for one molecule only, which was not the case in the previously published coordinates. The disorder observed in the two compounds is similar and involves two orientations of the carboxylate group of the *trans-β*-methylglutaconic acid moiety acylated to ornithine (1), two conformations for C(7) and C(9) of ornithine (3), which can be visualized by a rotation around the line C(6)–C(10) of that group, and two orientations of the hydroxyl group of serine (2). Only those dimensions involving the atoms with the highest occupancy are included in Tables 3 and 4. It is interesting to note that all the disordered groups are involved in intermolecular contacts with one another, some of which are shorter than van der Waals contacts. Therefore, a domain structure is indicated, for instance O(51) (Orn 1) with C(92) (Orn 3) 2·80 (2·46) and O(52) (Orn 1) with O(21) (Ser 2) 2·22 (2·14) Å (the alumichrome A distances are in parentheses). The nature of this disorder is thus a characteristic during crystallization, and one would, therefore, not expect to solve this problem with low-temperature data.

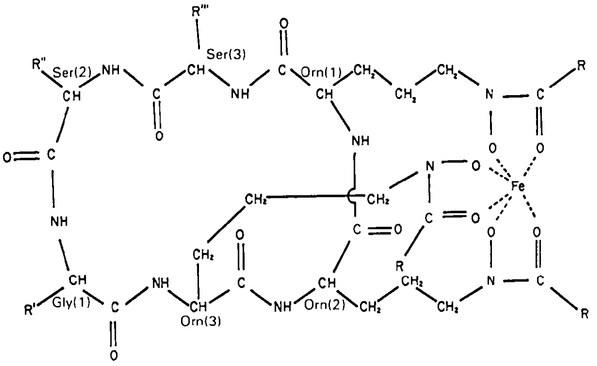

Fig. 1. The numbering of residues in the ferrichromes.

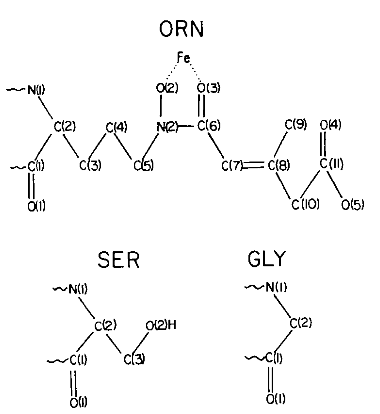

Fig. 2. Atom numbering in ferrichrome A and alumichrome A.

Zalkin, Forrester & Templeton (1966) determined the absolute configuration which indicated that the molecule is derived from L amino acids and that the coordination of the Fe is *Λ-cis*. This configuration has been adopted in the present communication.

Although our standard deviations are two to four times better, all of the conclusions advanced by Zalkin, Forrester & Templeton (1966) are correct, and we will therefore concentrate our discussion on the differences between alumichrome A and ferrichrome A, and on the metal coordination.

From an inspection of the bond distances and angles it can be seen that, with the exception of the metal coordination sphere, alumichrome A and ferrichrome A are closely similar, if not identical. This is also true for the disorder in the molecule and the water molecules of solvation, and can be seen in Fig. 3, which shows a least-squares fit of the two molecules after a 0·5 Å translation of the alumichrome A molecule to the right. The average distance between similar atoms in the two molecules after the least-squares fit of the positional coordinates is 0·08 Å, while for the least-squares fit of ferrichrome and ferrichrome A this value is 0·34 Å (van der Helm *et al.*, 1980). The same conclusion can be drawn from an inspection of the conformational angles (Fig. 4). Differences of up to 7° are observed, while in a comparison of ferrichrome A and ferrichrome, these differences were as large as 18° (van der Helm *et al.*, 1980).

There are several interesting observations to be made about the metal cooordination. Upon inspection of the individual metal–oxygen distances (Table 3), one

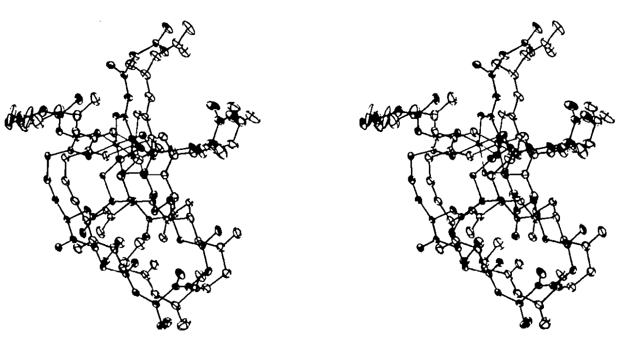

Fig. 3. A stereodrawing (Johnson, 1965) of both ferrichrome A and alumichrome A, with a translation of 0·5 Å to the right for the latter compound, after a least-squares fit to the positional parameters of the two molecules.

Table 2. *Atomic coordinates for ferrichrome A and alumichrome A* ($\times 10^4$)

Standard deviations for the least significant figure are given in parentheses. For each atom, upper values pertain to ferrichrome A and lower values to alumichrome A. $U_{eq} = (1/6\pi^2) \sum_i \sum_j \beta_{ij} \mathbf{a}_i . \mathbf{a}_j$.

	x	y	z	U_{eq} ($\times 10^3$ Å^2)	n†
Fe	434·4 (7)	−9·6 (9)	1265·9 (4)	19·5 (3)	1·0
Al	485·3 (9)	−2·7 (9)	1279·2 (5)	14·7 (4)	
Orn(1)					
C(1)	1872 (6)	−1027 (4)	4562 (3)	30 (3)	1·0
	1945 (3)	−970 (3)	4573 (2)	20 (2)	
C(2)	2563 (5)	−1316 (4)	3921 (3)	27 (2)	1·0
	2614 (3)	−1272 (3)	3924 (2)	19 (2)	
C(3)	3149 (6)	−396 (5)	3611 (3)	29 (2)	1·0
	3224 (3)	−360 (3)	3614 (2)	19 (2)	
C(4)	3955 (6)	−686 (5)	3034 (3)	30 (3)	1·0
	3990 (3)	−661 (3)	3016 (2)	20 (2)	
C(5)	4025 (5)	150 (5)	2460 (3)	30 (2)	1·0
	4025 (3)	159 (3)	2421 (2)	23 (2)	
C(6)	2412 (5)	1306 (4)	1756 (3)	26 (2)	1·0
	2357 (3)	1304 (3)	1742 (2)	23 (2)	
C(7)	3189 (6)	2219 (5)	1908 (3)	33 (3)	1·0
	3122 (4)	2224 (3)	1887 (2)	18 (2)	
C(8)	3120 (6)	3057 (5)	1494 (3)	35 (3)	1·0
	3032 (3)	3059 (3)	1464 (2)	23 (2)	
C(9)	2268 (7)	3223 (6)	767 (4)	50 (4)	1·0
	2160 (4)	3210 (4)	744 (3)	22 (2)	
C(10)	3959 (8)	3964 (6)	1716 (5)	57 (4)	1·0
	3838 (4)	3976 (4)	1685 (3)	35 (2)	
C(11)	5071 (12)	3820 (8)	2263 (6)	81 (6)	1·0
	5032 (7)	3824 (5)	2182 (4)	69 (4)	
N(1)	1744 (4)	−1837 (4)	3301 (2)	26 (2)	1·0
	1795 (3)	−1779 (2)	3308 (2)	18 (1)	
N(2)	2795 (4)	421 (4)	2060 (2)	24 (2)	1·0
	2769 (3)	423 (3)	2041 (2)	18 (1)	
O(1)	2434 (4)	−517 (3)	5094 (2)	34 (2)	1·0
	2506 (3)	−450 (2)	5102 (1)	26 (1)	
O(2)	2021 (3)	−384 (3)	1881 (2)	25 (2)	1·0
	1984 (2)	−390 (2)	1878 (1)	18 (1)	
O(3)	1356 (4)	1323 (3)	1344 (2)	27 (2)	1·0
	1258 (2)	1293 (2)	1341 (1)	18 (1)	
O(41)*	5648 (12)	4411 (10)	2660 (7)	49 (7)	0·4
	5506 (5)	4499 (4)	2612 (3)	35 (3)	0·6
O(42)*	6088 (11)	3913 (11)	2242 (6)	81 (8)	0·6
	5954 (10)	3990 (10)	2222 (6)	53 (6)	0·4
O(51)*	5840 (12)	2978 (13)	2097 (12)	94 (11)	0·4
	5746 (5)	3075 (6)	2023 (6)	82 (5)	0·6
O(52)*	4621 (11)	3993 (8)	2965 (6)	77 (7)	0·6
	4540 (10)	4044 (8)	2965 (5)	45 (5)	0·4
Orn(2)					
C(1)	1765 (5)	−2844 (4)	3209 (2)	22 (2)	1·0
	1765 (3)	−2808 (3)	3233 (2)	15 (1)	
C(2)	1064 (5)	−3261 (4)	2468 (3)	21 (2)	1·0
	1062 (3)	−3220 (3)	2491 (2)	15 (1)	
C(3)	1810 (5)	−3048 (4)	1835 (3)	25 (3)	1·0
	1806 (3)	−3023 (3)	1851 (2)	16 (2)	
C(4)	1307 (6)	−3530 (4)	1083 (3)	27 (3)	1·0
	1269 (4)	−3502 (3)	1092 (2)	19 (2)	
C(5)	143 (5)	−3046 (4)	627 (3)	25 (2)	1·0
	145 (4)	−2966 (3)	643 (2)	18 (2)	
C(6)	672 (5)	−1342 (4)	90 (3)	24 (2)	1·0
	771 (3)	−1265 (3)	149 (2)	18 (2)	
C(7)	847 (6)	−1796 (4)	−631 (3)	28 (2)	1·0
	961 (4)	−1706 (3)	−573 (2)	20 (2)	
C(8)	1213 (6)	−1330 (5)	−1202 (3)	29 (3)	1·0
	1314 (3)	−1222 (3)	−1154 (2)	20 (2)	
C(9)	1740 (7)	−273 (5)	−1214 (3)	39 (3)	1·0
	1787 (4)	−160 (3)	−1167 (2)	24 (2)	
C(10)	1080 (6)	−1901 (5)	−1929 (3)	33 (3)	1·0
	1179 (4)	−1803 (3)	−1893 (2)	25 (2)	
C(11)	−10 (6)	−1612 (5)	−2491 (3)	31 (3)	1·0
	52 (4)	−1528 (3)	−2461 (2)	23 (2)	
N(1)	−200 (4)	−2855 (3)	2317 (2)	20 (2)	1·0
	−194 (3)	−2799 (2)	2336 (2)	15 (1)	
N(2)	260 (4)	−1936 (3)	589 (2)	24 (2)	1·0
	300 (3)	−1858 (2)	625 (2)	17 (1)	
O(1)	2334 (4)	−3417 (3)	3679 (2)	33 (2)	1·0
	2286 (2)	−3368 (2)	3731 (2)	24 (1)	
O(2)	−80 (4)	−1450 (3)	1198 (2)	24 (2)	1·0
	−33 (2)	−1362 (2)	1232 (1)	17 (1)	
O(3)	790 (4)	−402 (3)	237 (2)	26 (2)	1·0
	924 (2)	−318 (2)	327 (1)	18 (1)	
O(4)	−721 (4)	−900 (3)	−2283 (2)	40 (2)	1·0
	−680 (3)	−829 (2)	−2246 (2)	26 (2)	
O(5)	−249 (5)	−2027 (4)	−3104 (2)	49 (2)	1·0
	−171 (3)	−1935 (3)	−3078 (2)	35 (2)	
Orn(3)					
C(1)	−1059 (5)	−3289 (4)	2655 (3)	21 (2)	1·0
	−1083 (3)	−3237 (3)	2653 (2)	15 (1)	
C(2)	−2396 (5)	−2931 (4)	2427 (3)	25 (2)	1·0
	−2417 (3)	−2847 (3)	2417 (2)	16 (1)	
C(3)	−2596 (5)	−1820 (5)	2188 (3)	26 (2)	1·0
	−2567 (3)	−1725 (3)	2179 (2)	20 (2)	
C(4)	−2220 (5)	−1048 (5)	2810 (3)	27 (2)	1·0
	−2163 (3)	−958 (3)	2802 (2)	20 (2)	
C(5)	−2422 (5)	29 (6)	2525 (3)	31 (3)	1·0
	−2299 (3)	133 (3)	2509 (2)	25 (2)	
C(6)	−2010 (6)	570 (5)	1259 (3)	38 (3)	1·0
	−1883 (4)	561 (4)	1231 (3)	35 (2)	
C(71)*	−3270 (8)	1050 (7)	1064 (5)	32 (4)	0·7
	−3112 (5)	1076 (5)	1034 (3)	27 (3)	
C(72)*	−3438 (15)	241 (12)	839 (8)	20 (7)	0·3
	−3208 (10)	252 (10)	746 (7)	19 (5)	
C(8)	−4210 (7)	682 (8)	641 (3)	62 (5)	1·0
	−4098 (4)	728 (5)	640 (2)	41 (3)	
C(91)*	−4189 (12)	−520 (8)	463 (6)	59 (6)	0·7
	−4148 (8)	−505 (6)	462 (4)	45 (4)	
C(92)*	−3846 (22)	2082 (16)	739 (15)	55 (13)	0·3
	−3885 (15)	1988 (15)	971 (14)	63 (11)	
C(10)	−5407 (7)	1019 (8)	346 (4)	60 (4)	1·0
	−5304 (5)	1090 (7)	354 (3)	66 (4)	
C(11)	−5679 (6)	1381 (6)	−451 (4)	44 (4)	1·0
	−5571 (4)	1472 (4)	−443 (2)	35 (2)	
N(1)	−3052 (4)	−3190 (4)	3034 (2)	25 (2)	1·0
	−3080 (3)	−3089 (3)	3031 (2)	18 (1)	
N(2)	−1662 (4)	246 (3)	1950 (2)	26 (2)	1·0
	−1546 (3)	305 (3)	1928 (2)	21 (1)	
O(1)	−811 (4)	−3995 (3)	3098 (2)	29 (2)	1·0
	−871 (2)	−3971 (2)	3085 (1)	21 (1)	
O(2)	−418 (3)	65 (4)	2157 (2)	26 (2)	1·0
	−296 (2)	118 (2)	2141 (1)	19 (1)	
O(3)	−1227 (4)	638 (3)	827 (2)	29 (2)	1·0
	−1061 (2)	571 (2)	798 (2)	25 (1)	
O(4)	−6561 (6)	1902 (5)	−670 (3)	67 (3)	1·0
	6465 (4)	1996 (3)	−654 (2)	49 (2)	
O(5)	−4940 (5)	1061 (5)	−876 (3)	56 (3)	1·0
	−4850 (4)	1116 (3)	−895 (2)	47 (2)	
Gly(1)					
C(1)	−4240 (5)	−3456 (5)	2927 (3)	33 (3)	1·0
	−4279 (3)	−3304 (4)	2920 (2)	26 (2)	
C(2)	−4785 (6)	−3728 (6)	3620 (3)	39 (4)	1·0
	−4832 (4)	−3585 (4)	3617 (2)	30 (2)	
N(1)	−3938 (5)	−3653 (4)	4319 (2)	30 (2)	1·0
	−3973 (3)	−3548 (3)	4316 (2)	22 (2)	
O(1)	−4898 (4)	−3503 (5)	2307 (2)	57 (3)	1·0
	−4941 (3)	−3284 (4)	2297 (2)	51 (2)	

* Disordered atoms.
† Occupancy.

Table 2 (*cont.*)

	x	y	z	U_{eq} ($\times 10^3$ Å^2)	n†
Ser(2)					
C(1)	−3713 (5)	−2748 (5)	4647 (3)	28 (3)	1·0
	−3664 (3)	−2654 (3)	4656 (2)	20 (2)	
C(2)	−2857 (6)	−2783 (5)	5390 (3)	32 (3)	1·0
	−2760 (4)	−2731 (3)	5392 (2)	23 (2)	
C(3)	−3605 (9)	−2613 (8)	6023 (4)	66 (5)	1·0
	−3431 (5)	−2663 (5)	6057 (2)	42 (3)	
O(1)	−4171 (4)	−1953 (4)	4379 (2)	41 (2)	1·0
	−4079 (3)	−1836 (3)	4390 (2)	32 (2)	
O(21)*	−4034 (12)	−1865 (10)	6097 (7)	30 (6)	0·3
	−4031 (4)	−1815 (4)	6123 (3)	31 (2)	
O(22)*	−4561 (8)	−3299 (7)	6062 (5)	67 (5)	0·7
	−4537 (9)	−3225 (9)	6074 (6)	38 (5)	
N(1)	−1893 (5)	−2000 (4)	5425 (2)	33 (2)	1·0
	−1817 (3)	−1945 (3)	5440 (2)	22 (2)	
Ser(3)					
C(1)	−1119 (6)	−1954 (4)	4930 (3)	29 (2)	1·0
	−1048 (3)	−1898 (3)	4937 (2)	25 (2)	
C(2)	−40 (5)	−1211 (5)	5112 (3)	28 (3)	1·0
	43 (3)	−1157 (3)	5123 (2)	23 (2)	
C(3)	−452 (6)	−104 (6)	5154 (3)	38 (3)	1·0
	−373 (4)	−51 (3)	5164 (2)	28 (2)	
O(1)	−1264 (4)	−2479 (3)	4353 (2)	33 (2)	1·0
	−1201 (2)	−2413 (2)	4359 (1)	23 (1)	
O(2)	−1193 (4)	218 (3)	4470 (2)	45 (2)	1·0
	−1088 (3)	276 (3)	4477 (2)	36 (2)	
N(1)	715 (4)	−1354 (4)	4524 (2)	30 (2)	1·0
	794 (3)	−1301 (3)	4540 (2)	21 (1)	
Solvent					
O(1)	−2482 (5)	−394 (3)	−3332 (3)	46 (3)	1·0
	−2449 (3)	−348 (3)	−3310 (2)	36 (2)	1·0
O(2)	328 (4)	945 (5)	3539 (2)	43 (2)	1·0
	415 (3)	1015 (3)	3530 (2)	31 (2)	1·0
O(3)	−2238 (5)	4398 (4)	3399 (2)	45 (2)	1·0
	−2357 (3)	4460 (3)	3379 (2)	29 (2)	1·0
O(4)*	5986 (12)	2219 (13)	3400 (9)	58 (8)	0·3‡
O(5)*	−3026 (12)	1641 (11)	4720 (6)	28 (7)	0·3
	−2846 (11)	1706 (10)	4660 (5)	76 (6)	0·5
O(6)*	−3596 (30)	2228 (28)	4498 (17)	130 (24)	0·3
	−3803 (10)	2318 (10)	4549 (7)	90 (6)	0·5
O(7)*	−4025 (31)	−86 (21)	5043 (17)	135 (20)	0·3
	−4203 (14)	72 (11)	5127 (8)	96 (9)	0·5
O(8)*	−3709 (19)	176 (15)	4495 (17)	78 (13)	0·3
	−3618 (9)	260 (9)	4532 (16)	144 (12)	0·5

* Disordered atoms.
† Occupancy.
‡ Only for alumichrome A.

Table 3. *Bond distances* (Å)

Values for ferrichrome A are on the upper line and for alumichrome A on the lower line in each case.

	Orn(1)	Orn(2)	Orn(3)
M—O(2)	1·967 (4)	1·980 (4)	1·994 (4)
	1·876 (2)	1·872 (3)	1·901 (2)
M—O(3)	2·020 (4)	2·032 (4)	2·048 (4)
	1·896 (3)	1·904 (2)	1·921 (3)
C(1)—O(1)	1·252 (7)	1·229 (6)	1·230 (7)
	1·248 (4)	1·225 (5)	1·237 (4)
C(1)—N(1)(i − 1)	1·328 (8)	1·339 (7)	1·332 (7)
	1·324 (5)	1·359 (5)	1·338 (5)
C(1)—C(2)	1·533 (8)	1·536 (7)	1·528 (8)
	1·532 (5)	1·526 (5)	1·538 (5)
C(2)—N(1)	1·486 (7)	1·466 (7)	1·448 (7)
	1·465 (5)	1·464 (5)	1·456 (6)
C(2)—C(3)	1·522 (9)	1·538 (8)	1·534 (8)
	1·523 (5)	1·541 (5)	1·537 (6)
C(3)—C(4)	1·522 (9)	1·523 (8)	1·525 (8)
	1·524 (5)	1·531 (5)	1·519 (5)
C(4)—C(5)	1·526 (9)	1·539 (8)	1·515 (10)
	1·526 (5)	1·526 (6)	1·527 (6)
C(5)—N(2)	1·465 (7)	1·472 (7)	1·463 (7)
	1·470 (5)	1·467 (5)	1·454 (5)
N(2)—C(6)	1·329 (7)	1·329 (7)	1·319 (7)
	1·324 (5)	1·326 (5)	1·294 (6)
N(2)—O(2)	1·364 (6)	1·379 (5)	1·372 (5)
	1·372 (4)	1·374 (4)	1·379 (4)
C(6)—O(3)	1·269 (7)	1·270 (7)	1·254 (7)
	1·295 (4)	1·290 (5)	1·285 (6)
C(6)—C(7)	1·474 (8)	1·478 (8)	1·506 (11)*
	1·469 (6)	1·471 (5)	1·494 (7)*
C(7)—C(8)	1·331 (9)	1·320 (8)	1·274 (12)*
	1·331 (5)	1·336 (5)	1·273 (7)*
C(8)—C(9)	1·501 (9)	1·510 (9)	1·618 (15)*
	1·490 (6)	1·490 (6)	1·651 (10)*
C(8)—C(10)	1·522 (11)	1·504 (8)	1·404 (11)
	1·507 (6)	1·521 (5)	1·416 (8)
C(10)—C(11)	1·451 (15)	1·486 (9)	1·504 (11)
	1·469 (9)	1·509 (6)	1·504 (7)
C(11)—O(4)	1·126 (18)*	1·313 (8)	1·276 (10)
	1·234 (9)*	1·319 (5)	1·311 (6)
C(11)—O(5)	1·455 (16)*	1·228 (7)	1·198 (11)
	1·318 (10)*	1·222 (5)	1·204 (6)
	Gly(1)	Ser(2)	Ser(3)
C(1)—O(1)	1·233 (7)	1·228 (8)	1·242 (7)
	1·231 (5)	1·233 (5)	1·230 (4)
C(1)—N(1)(i − 1)	1·329 (7)	1·338 (8)	1·331 (8)
	1·323 (5)	1·342 (5)	1·337 (5)
C(1)—C(2)	1·518 (8)	1·510 (8)	1·528 (8)
	1·528 (5)	1·520 (5)	1·533 (5)
C(2)—N(1)	1·446 (7)	1·470 (8)	1·463 (7)
	1·441 (5)	1·452 (6)	1·450 (5)
C(2)—C(3)	–	1·530 (10)	1·534 (10)
	–	1·509 (6)	1·529 (6)
C(3)—O(2)	–	1·393 (14)*	1·430 (7)
	–	1·422 (12)*	1·417 (5)

* Bond distance involving a disordered atom.

observes that both the *M*—O(2) and *M*—O(3) distances for Orn(3) are the longest, while those for Orn(1) are the shortest [with the exception of the *M*—O(2) distances for alumichrome A, where those for Orn(2) and Orn(1) are approximately equal]. These differences are significant and indicate that the metal ion is displaced from the threefold axis of the *Λ-cis* coordination sphere by approximately 0·01 Å. The threefold axis is perpendicular to the view shown in Fig. 5. These are the first structures of metal-coordinated siderophores which are sufficiently accurate for this observation to have been made. Even the original dimensions for ferrichrome A (Zalkin, Forrester & Templeton, 1966) show this same trend. The metal to carbonyl O atom distances are always longer than the metal to nitroso O atom distances, and this causes a second type of asymmetry of the metal coordination. This can also be described by stating that the metal ion is closer to the plane formed by the three O(2) atoms than to that formed by the three O(3) atoms (Fig. 5). This is a general observation, however, for all metal–hydroxamate structures, and is caused by a difference in negative charge on the O(2) and O(3) atoms. Another disturbance from cubic symmetry appears in the O(2)–*M*–O(3) angles, which are significantly smaller than 90°. These angles are internally consistent for alumichrome A and ferrichrome A and can be correlated directly with the ionic radii of the metal ions. Finally, there is a fourth perturbation from cubic symmetry, which is described by the relative orientation of the octahedral faces formed by the three O(2) atoms and the three O(3) atoms. This twist angle, which is 60° for an ideal octahedron and 0° for a trigonal prism, is 41·5° for ferrichrome A and 47·0° for alumichrome A. The last three disturbances from cubic symmetry can be ascribed to the difference in charge on the O(2) and O(3) atoms, the ionic radius in conjunction with the bite of the ligand and the spherical

Table 4. *Bond angles* (°)

Values for ferrichrome A are on the upper line and for alumichrome A on the lower line in each case.

	Orn(1)	Orn(2)	Orn(3)
O(2)*M*O(3)	78·1 (2) 82·7 (1)	78·1 (2) 82·6 (1)	78·0 (2) 81·6 (1)
*M*O(3)C(6)	115·0 (4) 113·9 (2)	114·4 (3) 113·1 (2)	112·4 (4) 112·0 (3)
O(3)C(6)N(2)	117·0 (5) 116·0 (3)	117·8 (5) 117·1 (3)	119·6 (5) 118·6 (4)
O(3)C(6)C(7)	122·5 (5) 123·8 (3)	123·9 (5) 124·7 (3)	121·0 (6)* 122·9 (4)*
N(2)C(6)C(7)	120·5 (5) 120·2 (3)	118·0 (5) 117·9 (3)	118·1 (6)* 116·6 (4)*
C(6)N(2)O(2)	116·3 (4) 115·9 (3)	115·8 (4) 114·8 (3)	115·8 (4) 115·2 (4)
C(6)N(2)C(5)	128·4 (5) 128·6 (3)	131·3 (4) 131·1 (3)	129·0 (5) 129·5 (4)
O(2)N(2)C(5)	114·4 (4) 114·7 (3)	112·8 (4) 114·0 (3)	115·1 (4) 115·2 (3)
N(2)O(2)*M*	113·3 (3) 111·5 (2)	112·6 (3) 111·7 (2)	111·2 (3) 110·3 (2)
N(2)C(5)C(4)	111·7 (5) 111·3 (3)	111·5 (4) 112·6 (3)	111·0 (5) 111·2 (3)
C(5)C(4)C(3)	112·7 (5) 113·3 (3)	117·0 (5) 116·0 (3)	111·6 (5) 111·6 (3)
C(4)C(3)C(2)	112·3 (5) 112·4 (3)	115·6 (5) 115·4 (3)	114·9 (5) 115·2 (3)
C(3)C(2)C(1)	111·7 (5) 111·8 (3)	109·7 (4) 110·2 (3)	117·2 (5) 116·7 (3)
C(3)C(2)N(1)	109·1 (4) 109·3 (3)	113·1 (4) 112·9 (3)	112·0 (4) 112·2 (3)
C(2)C(1)O(1)	118·4 (5) 119·3 (3)	120·7 (4) 122·2 (3)	120·6 (5) 120·2 (3)
C(2)C(1)N(1)(*i* – 1)	117·6 (5) 116·9 (3)	116·6 (4) 116·1 (4)	117·3 (5) 117·5 (3)
O(1)C(1)N(1)(*i* – 1)	124·0 (5) 123·8 (3)	122·7 (5) 121·6 (3)	121·9 (5) 122·1 (3)
C(2)N(1)C(1)(*i* + 1)	122·2 (4) 122·0 (3)	118·1 (4) 118·8 (3)	123·0 (5) 122·6 (4)
C(1)C(2)N(1)	112·1 (4) 112·8 (3)	110·7 (4) 110·6 (3)	107·0 (4) 106·7 (3)
C(6)C(7)C(8)	126·5 (6) 126·3 (4)	127·1 (5) 127·4 (4)	126·8 (8)* 127·9 (5)*
C(7)C(8)C(9)	125·9 (6) 125·8 (4)	127·3 (6) 127·2 (3)	117·2 (8)* 117·3 (5)*
C(7)C(8)C(10)	121·8 (6) 121·6 (4)	117·1 (6) 116·7 (3)	136·0 (8)* 137·1 (5)*
C(9)C(8)C(10)	112·3 (6) 112·6 (4)	115·6 (5) 116·1 (3)	106·1 (7)* 105·1 (5)*
C(8)C(10)C(11)	118·7 (8) 118·3 (5)	115·1 (5) 115·0 (3)	119·5 (7) 118·7 (5)
C(10)C(11)O(4)	133·3 (12)* 121·5 (6)*	115·7 (5) 115·8 (3)	121·5 (8) 120·7 (5)
C(10)C(11)O(5)	102·2 (9)* 117·9 (6)*	122·3 (6) 121·9 (4)	115·4 (7) 115·7 (4)
O(4)C(11)O(5)	119·3 (12)* 118·2 (7)*	122·0 (6) 122·3 (4)	123·0 (8) 123·3 (4)

Table 4 (*cont.*)

	Gly(1)	Ser(2)	Ser(3)
N(1)C(2)C(1)	115·2 (5) 114·9 (4)	110·7 (5) 110·9 (3)	105·5 (5) 105·8 (3)
C(2)C(1)N(1)(*i* – 1)	116·6 (5) 116·5 (4)	114·3 (5) 114·7 (3)	115·9 (5) 115·8 (3)
C(2)C(1)O(1)	119·5 (5) 120·2 (4)	122·2 (5) 122·8 (3)	121·8 (5) 121·7 (3)
O(1)C(1)N(1)(*i* – 1)	123·9 (5) 123·4 (4)	123·6 (5) 122·5 (4)	122·2 (5) 122·5 (3)
C(2)N(1)C(1)(*i* + 1)	119·7 (5) 120·4 (3)	122·3 (5) 120·9 (3)	124·5 (5) 125·0 (3)
N(1)C(2)C(3)	– –	109·4 (6) 110·2 (4)	111·4 (5) 111·6 (3)
C(1)C(2)C(3)	– –	109·5 (6) 111·0 (3)	113·5 (5) 112·8 (3)
C(2)C(3)O(2)	– –	116·1 (8)* 121·0 (6)*	111·7 (5) 111·8 (3)

* Bond angles involving disordered atoms.

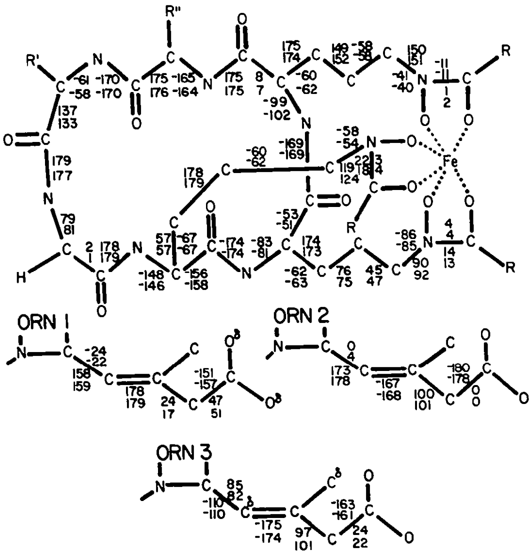

Fig. 4. Conformational angles (°). The values are for ferrichrome A (bottom) and alumichrome A (top). Standard deviations for non-disordered atoms are in the ranges 0·5–1·0° (ferrichrome A) and 0·3–0·6° (alumichrome A). Atoms with superscript δ are disordered.

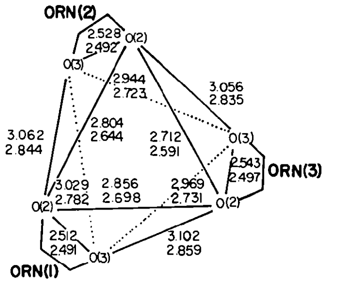

Fig. 5. A schematic drawing of the metal coordination. The distances (Å) on top are for ferrichrome A, while the second line is for alumichrome A (average e.s.d.'s are 0·007 Å and 0·004 Å respectively).

charge density of the Fe^{3+} and Al^{3+} ions, respectively. However, these properties do not explain the perturbation of the threefold-axis symmetry. Llinás & DeMarco (1980) recently used ^{27}Al NMR as a quadrupolar probe in a study of the ferrichrome peptides. Comparing line widths of the Ser(2)-Ser(3) alumichrome homologue, alumichrysin, with aluminum tris(acetylhydroxamate) and taking into account molecular-size effects, they observed a 0·5 kHz discrepancy. This extra contribution to the ligand-field anisotropy, which they ascribed to structural constraints imposed by the peptide conformation or entasis of the chelated state, can probably be directly correlated with the disturbance of threefold symmetry observed in the present results. Additional strain is also observed in the ornithyl side chains [C(8)–C(3)–C(4)–C(5)–N(2)] (van dei Helm *et al.*, 1980). The disturbance of the threefold symmetry may also explain why a rhombic rather than a trigonal field was observed by Mössbauer and ESR studies (Oosterhuis & Spartalian, 1974).

Even though there are significant differences in the individual bond distances for the metal chelation, as described above, the average chelate ring for ferrichrome A and alumichrome A is shown in Fig. 6. It is interesting to note that the difference between the *M*–O(2) and *M*–O(3) distances is larger in ferrichrome A (0·053 Å) than in alumichrome A (0·024 Å), indicating a more even charge distribution over the O(2) and O(3) atoms in alumichrome A, and this is properly correlated with a lengthening of the C(6)–O(3) distances in the latter compound. The *M*–O distances are smaller in alumichrome A, reflecting the decrease in ionic radius of Al^{3+} (0·45 Å) with respect to Fe^{3+} (0·53 Å), and this results directly in an opening of the O(2)–*M*–O(3) angles in alumichrome A. The difference in ionic radii also causes all the O···O distances between different ligand groups in the octahedron to be smaller in alumichrome A than in ferrichrome A (Fig. 5). The only other significant difference is that the bite of the ligand is smaller in alumichrome A. The chelate rings are approximately planar, but the metal ion is significantly out of the plane of the three rings: Orn(1) 0·409 (0·339), Orn(2) 0·250 (0·162), and Orn(3) 0·109 (0·027) Å, with the values for alumichrome A in parentheses.

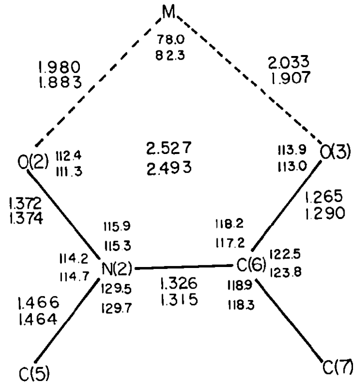

Fig. 6. Average chelate ring. The distances (Å) and angles (°) are for ferrichrome A (top) and alumichrome A (bottom).

The average values of the N(1)–C(2), C(2)–C(1), C(1)–O(1) and C(1)–N(1)(*i* + 1) distances are 1·463 (1·455), 1·526 (1·529), 1·236 (1·234) and 1·333 (1·337) Å, all of which are quite similar to those observed in other linear and cyclic peptides. The details of the conformation of the cyclic peptide in ferrichrome A have been described in comparison with ferrichrome (van der Helm *et al.*, 1980). The peptide conformation in alumichrome A is identical to that in ferrichrome A, and so are the intramolecular hydrogen bonds: N(1)[Orn(3)]···O(1)[Ser(3)] 2·982 (3·016) and N(1)[Orn(2)]···O(2)[Orn(2)] 2·765 (2·771) Å. There are numerous hydrogen bonds involving the water molecules of solvation in addition to three relatively weak intermolecular ones: N(1)-[Ser(2)]···O(5)[Orn(2)](x, y, z + 1) 2·964 (2·962), N(1)[Gly(1)]···O(1)[Orn(1)]($\bar{x}$, $y - \frac{1}{2}$, $1 - z$) 3·052 (3·061) and O(5)[Orn(1)]···O(1)[Gly(1)]($-x - 1, y + \frac{1}{2}, \bar{z}$) 2·632 (2·621) Å.

It is thus apparent, from the present results, that the Al^{III} substitution in ferrichrome A does not change the solid-state conformation, while it is likely that the same holds true for the solution conformation.

This research was supported by Grant No. GM-21822 from the National Institutes of Health. One of the authors (DvdH) expresses his gratitude to Dr T. Emery, Utah State University, for the help and hospitality he received while working in his laboratory and who donated a sample of alumichrome A. We thank the University of Oklahoma for computing services.

References

Coppens, P., Leiserowitz, L. & Rabinovich, D. (1965). *Acta Cryst.* **18**, 1035–1038.

EMERY, T. (1971). *Biochemistry*, **10**, 1483–1488.

EMERY, T. (1978). *Metal Ions in Biological Systems*, Vol. 7, edited by H. SIEGEL, pp. 77–126. New York: Marcel Dekker.

EMERY, T. & NEILANDS, J. B. (1960). *J. Am. Chem. Soc.* **82**, 3658–3662.

EMERY, T. & NEILANDS, J. B. (1961). *J. Am. Chem. Soc.* **83**, 1626–1628.

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

International Tables for X-ray Crystallography (1962). Vol. III, p. 202. Birmingham: Kynoch Press.

International Tables for X-ray Crystallography (1974). Vol. IV, p. 149. Birmingham: Kynoch Press.

ISOWA, Y., OHMORI, M. & KURITA, H. (1974). *Bull. Chem. Soc. Jpn*, **47**, 215–220.

JOHNSON, C. K. (1965). *ORTEP*. Report ORNL-3794. Oak Ridge National Laboratory, Tennessee.

KELLER-SCHIERLEIN, W. & MAURER, B. (1969). *Helv. Chim. Acta*, **52**, 603–610.

LLINÁS, M. & DEMARCO, A. (1980). *J. Am. Chem. Soc.* **102**, 2226–2230.

LLINÁS, M., HORSLEY, W. J. & KLEIN, M. P. (1976). *J. Am. Chem. Soc.* **98**, 7554–7558.

LLINÁS, M. & KLEIN, M. P. (1975). *J. Am. Chem. Soc.* **97**, 4731–4737.

LLINÁS, M., KLEIN, M. P. & NEILANDS, J. B. (1970). *J. Mol. Biol.* **52**, 399–414.

LLINÁS, M., KLEIN, M. P. & NEILANDS, J. B. (1972). *J. Mol. Biol.* **68**, 265–284.

LLINÁS, M., KLEIN, M. P. & NEILANDS, J. B. (1973*a*). *J. Biol. Chem.* **248**, 915–923.

LLINÁS, M., KLEIN, M. P. & NEILANDS, J. B. (1973*b*). *J. Biol. Chem.* **248**, 924–931.

LLINÁS, M., WILSON, D. M. & KLEIN, M. P. (1977). *J. Am. Chem. Soc.* **99**, 6846–6850.

LLINÁS, M., WILSON, D. M., KLEIN, M. P. & NEILANDS, J. B. (1976). *J. Mol. Biol.* **104**, 853–864.

LLINÁS, M., WILSON, D. M. & NEILANDS, J. B. (1977). *J. Am. Chem. Soc.* **99**, 3631–3637.

LLINÁS, M. & WÜTHRICH, K. (1978). *Biochim. Biophys. Acta*, **532**, 29–40.

NEILANDS, J. B. (1952). *J. Am. Chem. Soc.* **74**, 4846–4847.

NEILANDS, J. B. (1973). *Inorganic Biochemistry*, Vol. I, edited by G. L. EICHHORN, pp. 167–202. New York: Elsevier.

NORRESTAM, R., STENSLAND, B. & BRÄNDÉN, C.-I. (1975). *J. Mol. Biol.* **99**, 501–506.

OOSTERHUIS, W. T. & SPARTALIAN, K. (1974). *J. Phys.* (*Paris*) *Colloq.* **35**, 347–350.

ROGERS, S. J. & NEILANDS, J. B. (1964). *Biochemistry*, **3**, 1850–1855.

ROGERS, S. J., WARREN, R. A. J. & NEILANDS, J. B. (1963). *Nature* (*London*), **200**, 167.

STEWART, R. F., DAVIDSON, E. R. & SIMPSON, W. T. (1965). *J. Chem. Phys.* **42**, 3175–3187.

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. & POLING, M. (1976). *J. Am. Chem. Soc.* **98**, 82–86.

ZALKIN, A., FORRESTER, J. D. & TEMPLETON, D. H. (1966). *J. Am. Chem. Soc.* **88**, 1810–1814.

Acta Cryst. (1981). B**37**, 330–339

The Modulated Structure of the Layered Perovskite γ-Bis(n-propylammonium) Tetrachloromanganate(II): Refinement of the Average Structure, the Possible Superspace Group and a Model for the Modulated Structure

BY WULF DEPMEIER

Chimie Appliquée, Science II, 30 *quai Ernest Ansermet, CH Genève* 4, *Switzerland*

(*Received* 16 *June* 1980; *accepted* 16 *September* 1980)

Abstract

Between 344 K and 396 K, $(C_3H_7NH_3)_2MnCl_4$, M_r = 316·98, forms a modulated structure as indicated by satellite reflexions of two different kinds. The average structure, with space group *Abma*, a = 7·39(1), b = 7·25 (2), c = 26·72 (5) Å, V = 1432 (8) Å^3, Z = 4, D_c = 1·47 Mg m^{-3}, $F(000)$ = 652, has been determined with Mo $K\alpha$ radiation at T = 360 (10) K [λ(Mo $K\alpha$) = 0·7107 Å]. Refinement for 553 reflexions converged to R = 0·072 with anisotropic temperature factors. The perovskite-type layer is described with split Mn and Cl atoms. The modulation consists mainly of transverse distortion waves running along a with amplitudes parallel to c. Some weak extra satellites in the $hk0$ reciprocal plane have been interpreted as arising from a small additional longitudinal component of the modulation. The Janner–Janssen–de Wolff (3 + 1)-dimensional superspace-group symbol for the most important satellites is a subgroup of $N^{A\underline{b}ma}_{\bar{1}11}$ and a model of the

0567-7408/81/020330-10$01.00