After 15 h, the sample was worked as usual with the results recorded in Table II.

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Registry No. (*S*)-**1a**, 53318-85-7; (*S*)-**2a**, 53403-10-4; (*R*)-**2b**, 87069-62-3; (*S*)-**3a**, 87040-83-3; (*S*)-**4a**, 87069-63-4; (*R*)-**4b**, 87040-79-7; (*S*)-**5b**, 87040-80-0; (*S*)-**6b**, 87069-66-7; CO, 630-08-0; cyclohexyl isocyanide, 931-53-3.

Crystal and Molecular Structure of the Ferrous Ion Complex of A23187

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Abstract: The 1:2 ferrous ion complex of the ionophorous antibiotic A23187 has been prepared, and its structure has been determined by single-crystal X-ray diffraction techniques. Crystals of the compound formed in the orthorhombic space group $P2_12_12_1$ with unit cell dimensions $a = 24.174$ (11) Å, $b = 17.642$ (12) Å, and $c = 14.947$ (9) Å, and with one molecule of the complex and two disordered molecules of solvent ethanol per asymmetric unit. They are isomorphous with crystals of the corresponding 6-coordinate calcium complex. The structure was refined by blocked-matrix least-squares methods to an R_F of 0.10 based on the 2256 observations with $|F_o| > 3\sigma(|F_o|)$. Coordination to the ferrous ion is approximately octahedral through a carboxyl oxygen, the nitrogen of the benzoxazole ring system, and the carboxyl oxygen of each ligand with the two A23187 moieties being disposed so that the molecule as a whole exhibits pseudo-2-fold symmetry. The Fe–O distances range from 2.01 to 2.19 Å while the Fe–N distances are both 2.22 Å.

The ionophorous antibiotic A23187 (Figure 1) is a monocarboxylic acid which has been shown to transport divalent cations (e.g., Mn^{2+}, Ca^{2+}, Mg^{2+}) across natural and artificial membranes.[2-5] It is unique among ionophores in that its specificity pattern is similar to those of divalent cation pumps in natural membranes.[5] The high selectivity shown by A23187 is a consequence of charge interactions, ion solvation energies, ionic radii, and the small number of ligating atoms available from a single ionophore molecule.[5]

Recent studies have shown that iron is also transported by A23187 across liposomes,[6,7] red blood cells,[6,7] and hepatocytes membranes.[8,9] Hence it is a useful experimental tool for investigating the mechanism of iron transport across biological membranes and may have clinical potential in iron mobilization in diseases associated with iron overload, such as thalassemia.[8,9] A major restriction to the clinical use of A23187, however, is its relatively high toxicity due primarily to its ability to transport calcium ions. Any modification of its structure which resulted in an increase of its affinity for iron relative to that for calcium would therefore increase its potential as an iron mobilizing agent for use in "mixed ligand chelation therapy".[10]

The exact nature of the iron complex with A23187 is not known. The structure of the free acid of A23187 has been determined by chemical methods and by X-ray crystallographic techniques (Figure 1).[11] More recently two different crystal structures of the 1:2 calcium:ionophore complex have been elucidated.[12,13] In both complexes the calcium ion is coordinated to each A23187 molecule through a carboxyl oxygen atom, the nitrogen atom of the benzoxazole ring system, and a carbonyl atom in such a manner that the complexes as a whole exhibit pseudo-2-fold symmetry, the axes passing through the calcium ions. In one structure a water molecule is also bound to the calcium ion, whose coordination number in this case is thus 7.[13,14] To accommodate this extra ligand the geometry surrounding the calcium ion in this complex is considerably different from that in the other nearly octahedral molecule; the calcium–ligand bond lengths, for example, are all 0.2–0.3 Å longer. In both structures the complex molecules are stabilized by head-to-tail hydrogen bonding between the two A23187 molecules.

The work described here was undertaken (1) to determine whether the putative ferrous ion–ionophore complex could be crystallized in stable form, (2) to analyze the chemical nature and detailed structure of the iron complex, and (3) to investigate the feasibility of designing an analogue of A23187 having enhanced specificity for iron transport through biological membranes.

Experimental Section

Single crystals of the iron–A23187 complex were prepared from ethanol under strictly anaerobic conditions. A23187 (5 mg) dissolved in 4 mL of 95% ethanol (pH 4) was warmed to 50 °C, gassed with nitrogen for 5 min, and then mixed with a freshly prepared solution of $FeSO_4$ (equimolar in iron) in 0.1 M ascorbic acid (pH 3.0). After further gassing with nitrogen for 5 min the resulting solution was tightly stoppered and allowed to stand at room temperature. Yellow, elongated

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Table I. Atomic Coordinates and Isotropic Thermal Parameters for the Ferrous Ion Complex of A23187[a]

atom	x/a	y/b	z/c	U, Å²	atom	x/a	y/b	z/c	U, Å²
Fe	−1934 (1)	2064 (2)	2289 (2)	58 (2)	C214	−435 (12)	1130 (16)	−570 (19)	105 (10)
O11	−1854 (6)	2313 (8)	983 (9)	78 (5)	C215	−52 (11)	550 (14)	−136 (18)	88 (9)
O12	−1895 (8)	2825 (10)	−351 (11)	111 (6)	C216	−237 (10)	332 (13)	768 (16)	68 (7)
O13	−3737 (6)	2233 (8)	2127 (10)	70 (4)	C217	68 (10)	−416 (14)	1168 (17)	79 (8)
O14	−3602 (6)	3158 (7)	3750 (9)	63 (4)	C218	−123 (12)	−1132 (17)	637 (20)	117 (11)
O15	−3045 (6)	4234 (7)	3726 (8)	66 (4)	C219	−35 (10)	−456 (15)	2173 (18)	91 (8)
O16	−1989 (5)	3284 (7)	2550 (8)	63 (4)	C220	91 (12)	209 (17)	2676 (22)	119 (10)
O21	−1944 (6)	1912 (8)	3635 (9)	71 (4)	C221	745 (12)	392 (15)	2703 (20)	110 (9)
O22	−1706 (7)	1604 (10)	5007 (12)	109 (6)	C222	−252 (11)	859 (16)	2208 (20)	98 (9)
O23	−1805 (7)	−390 (10)	1899 (11)	92 (5)	C223	−157 (11)	1685 (14)	2605 (18)	95 (9)
O24	−813 (7)	137 (9)	783 (10)	80 (5)	C224	−247 (12)	1690 (16)	3658 (20)	110 (10)
O25	−104 (6)	948 (8)	1279 (10)	65 (4)	C225	−574 (10)	2187 (13)	2159 (16)	72 (7)
O26	−1053 (6)	2101 (9)	2343 (10)	80 (4)	C226	−381 (10)	2668 (12)	1517 (15)	61 (7)
O31	−2900	−1813	2233	429 (26)	C227	81 (11)	2954 (16)	1252 (17)	92 (8)
O41	−5070	−3833	2800	467 (30)	C228	25 (12)	3523 (17)	589 (19)	97 (9)
N11	−2854 (9)	3126 (12)	−1105 (15)	110 (8)	C229	−535 (13)	3488 (18)	402 (20)	115 (10)
N12	−2841 (7)	2170 (10)	2033 (12)	74 (6)	C31	−3300	−2194	2250	429
N13	−1531 (7)	3347 (10)	4234 (12)	70 (6)	C32	−3760	−2014	1733	429
N21	−1773 (9)	188 (13)	5516 (15)	109 (8)	C41	−4980	−3250	2417	467
N22	−1869 (8)	809 (10)	2238 (14)	82 (6)	C42	−4550	−3097	1783	467
N23	−750 (9)	2997 (13)	963 (14)	94 (7)	H11	−2462	3146	−1139	101
C11	−2156 (10)	2600 (13)	333 (16)	69 (7)	H15	−3881	3138	−580	101
C12	−2744 (8)	2634 (11)	442 (13)	50 (6)	H16	−4310	2718	623	101
C13	−3110 (10)	2905 (13)	−325 (14)	71 (6)	H17	−3664	1755	3621	101
C14	−3199 (12)	3336 (15)	−1904 (19)	114 (10)	H18	−3043	1539	3654	101
C15	−3653 (10)	2927 (14)	−126 (15)	76 (7)	H19	−2832	2853	3801	101
C16	−3918 (10)	2707 (13)	592 (16)	76 (8)	H110	−2825	2267	5208	101
C17	−3596 (9)	2454 (11)	1311 (15)	58 (6)	H114	−3076	3394	6032	101
C18	−3009 (9)	2411 (11)	1216 (13)	52 (6)	H115	−2703	3576	5216	101
C19	−3257 (8)	2053 (13)	2553 (13)	62 (6)	H116	−3829	3806	5311	101
C110	−3300 (8)	1920 (11)	3485 (14)	60 (7)	H117	−3384	4436	5235	101
C111	−3174 (9)	2659 (11)	4010 (12)	53 (6)	H118	−4081	4831	4019	101
C112	−3134 (11)	2572 (13)	5049 (15)	75 (7)	H122	−4007	3985	2518	101
C113	−3610 (12)	2170 (18)	5456 (19)	120 (10)	H123	−4262	4789	2594	101
C114	−3057 (11)	3401 (14)	5398 (16)	88 (8)	H124	−3453	4790	1771	101
C115	−3483 (10)	3937 (13)	5055 (17)	88 (8)	H128	−3043	3796	2566	101
C116	−3539 (9)	3926 (12)	4050 (15)	67 (7)	H129	−2303	4995	2801	101
C117	−4051 (11)	4358 (15)	3720 (18)	94 (9)	H133	−1821	5113	4286	101
C118	−4570 (12)	3943 (16)	4000 (19)	115 (10)	H134	−1285	4614	5584	101
C119	−3969 (11)	4470 (16)	2787 (21)	112 (10)	H135	−1159	3289	5455	101
C120	−3449 (11)	4807 (15)	2406 (18)	100 (9)	H136	−1516	2845	4006	101
C121	−3347 (12)	5659 (17)	2640 (20)	131 (11)	H21	−1861	689	5700	101
C122	−2983 (9)	4295 (12)	2786 (15)	77 (7)	H25	−1782	−1171	4687	101
C123	−2392 (9)	4512 (12)	2560 (15)	70 (7)	H26	−1661	−1421	3201	101
C124	−2279 (9)	4586 (13)	1539 (15)	81 (8)	H27	−1803	10	379	101
C125	−2042 (8)	3890 (11)	2997 (13)	57 (6)	H28	−1997	841	507	101
C126	−1763 (9)	3987 (13)	3824 (16)	74 (7)	H29	−1124	1195	785	101
C127	−1698 (9)	4608 (12)	4378 (15)	62 (7)	H210	−1240	1309	−731	101
C128	−1411 (11)	4319 (15)	5092 (17)	90 (8)	H214	−337	1180	−1183	101
C129	−1333 (11)	3598 (16)	5016 (18)	100 (9)	H215	−388	1603	−277	101
C21	−1842 (12)	1386 (17)	4204 (20)	112 (10)	H216	−42	109	−501	101
C22	−1819 (9)	595 (13)	3936 (15)	65 (7)	H217	308	760	−96	101
C23	−1768 (12)	13 (16)	4619 (19)	102 (9)	H218	454	−386	1056	101
C24	−1639 (11)	−416 (15)	6224 (18)	102 (9)	H222	−416	−567	2261	101
C25	−1765 (11)	−763 (16)	4273 (19)	97 (9)	H223	183	−858	2405	101
C26	−1739 (12)	−923 (17)	3406 (22)	119 (10)	H224	−20	151	3282	101
C27	−1829 (10)	−348 (13)	2827 (16)	73 (7)	H228	−633	740	2264	101
C28	−1816 (9)	392 (12)	3059 (14)	55 (6)	H229	207	1855	2475	101
C29	−1837 (12)	325 (16)	1610 (18)	92 (8)	H233	429	2797	1481	101
C210	−1739 (11)	468 (14)	697 (17)	88 (9)	H234	299	3844	339	101
C211	−1180 (11)	738 (14)	460 (17)	81 (8)	H235	−726	3765	−47	101
C212	−1016 (11)	908 (15)	−510 (18)	92 (9)	H236	−1134	2883	977	101
C213	−1216 (11)	219 (16)	−1176 (18)	107 (10)					

[a] Estimated standard deviations in parentheses. All coordinates and esd's × 10^4. Coordinates for hydrogen atoms inferred from geometrical considerations: bond length to hydrogen assumed to be 0.95 Å. The equivalent isotropic thermal parameter for the iron atom was calculated from the anisotropic parameters using the equation $U_{\mathrm{eq}} = 1/3\Sigma_i\Sigma_jU_{ij}a_i{}^*a_j{}^*a_ia_j$.

rhombic prismatic or thick platelike crystals appeared within 24 h. They were stable only under anaerobic conditions. Consequently the single crystal chosen for use in the structure analysis was mounted in a nitrogen atmosphere in a sealed Lindemann glass capillary with small quantities of mother liquor at each end. The crystal's dimensions were 0.35 × 0.23 × 0.16 mm^3. A preliminary X-ray diffraction photographic survey indicated that the crystals are isomorphous with those of one of the forms of the corresponding calcium complex.[12] All subsequent diffraction data were measured by using a Syntex $P2_1$ four-circle diffractometer with graphite-monochromated Mo Kα X-radiation. Unit cell dimensions were determined from a least-squares fit to the 2θ values of 14 reflections. The intensities of 9828 reflections with $0° \leq 2\theta \leq 40°$ from two symmetry-equivalent octants were measured at room temperature in the θ–2θ scanning mode. The scan range was between 1.70 and 1.95°, dependent upon 2θ, while the scan speed varied with increasing intensity from 4.9 to 29.3° m^{-1}. Background was measured at each end of each intensity scan. The crystal orientation was checked periodically during data collection, and the intensities of three standard reflections, monitored

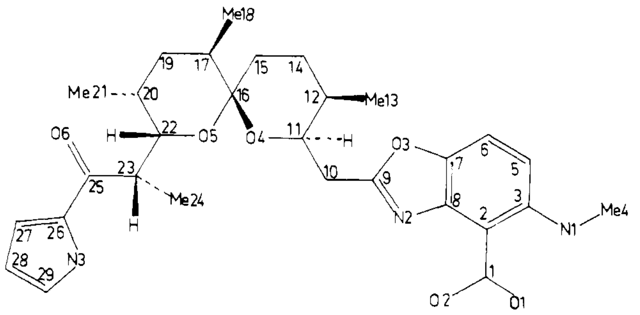

Figure 1. Structural formula of A23187 indicating atom numbering.

every 100 reflections, did not vary systematically during data measurement, the maximum fluctuation being ±2.5%. After the data had been checked for gross systematic errors, Lorentz and polarization factors, but not absorption corrections ($\mu = 3.1$ cm^{-1}), were applied yielding a set of 3357 observations The 2256 of these with $|F(hkl)| \geq 3.0\ \sigma(|F(hkl)|)$ were used in the subsequent analysis.

Crystal Data. Ferrous ion complex of A23187, Fe(A23187)$_2$·2C$_2$H$_5$OH, $C_{58}H_{74}N_6O_{12}Fe.C_4H_{12}O_2$, $M = 1195.245$. Orthorhombic, space group $P2_12_12_1$ (D_2^4, No. 19);[15] $a = 24.174\ (11)$ Å, $b = 17.642\ (12)$ Å, $c = 14.947\ (9)$ Å, $U = 6375\ (6)$ Å^3, $Z = 4$, $D_c = 1.245\ (1)$ g cm^{-3}. Linear absorption coefficient for X-rays [λ(Mo Kα) = 0.71069 Å], $\mu = 3.1$ cm^{-1}. Number of electrons per unit cell, $F(000) = 2552$.

Structure Refinement. Because this crystal structure is isomorphous with that of one of the calcium complexes with A23187, refinement began with use of the atomic coordinates of that structure[12] as a starting model. A Wilson plot had suggested overall scale and temperature factors, and the latter was used as a basis for assigning individual atomic isotropic thermal parameters. After three cycles of isotropic full-matrix least-squares refinement ($R_F = 0.15$[16]) a difference map was plotted. It showed two large regions of diffuse but significant density in which, after some trials, it was possible to postulate the positions of the heavier atoms of two ethanol solvent molecules. Parameters for these atoms, and for the 42 hydrogens whose positions could be inferred from geometrical considerations, were added to the model, and three isotropic blocked-matrix least-squares cycles of refinement were computed. None of the hydrogen parameters was varied. In a further model, the iron atom, the non-coordinated oxygens of the carbonyl groups, the amine nitrogens, and the ten methyl group carbon atoms were assigned anisotropic temperature factors. It was apparent from the behavior of the thermal parameters and from an examination of the structure factors that the major error in the model at this stage lay in the inadequate description of the solvent molecules, which are disordered. All attempts to account for this disorder failed. Consequently least-squares refinement was terminated with a "mixed" thermal parameter model in which only the iron atom was assumed to be anisotropic; this converged at an R_F of 0.10. The maximum parameter shift was 0.03 of its estimated standard deviation. As expected the largest features on a final difference map are broad diffuse electron density excesses in the vicinity of the solvent molecules. No attempt was made to include the methyl hydrogen atoms; their positions were not clearly defined on the final difference map. The absolute configuration of the ferrous ion complex was not determined from the diffraction data; it has been chosen to correspond with that proposed for the free acid.[11]

Atomic scattering factors for the non-hydrogen atoms were computed from numerical Hartree-Fock wave functions[17] and were corrected for anomalous dispersion.[18] The atomic scattering factor of Stewart, Davidson, and Simpson[19] was used for H. Computations were performed with The XRAY System[20] and the least-squares plane program of Ito,[21] as modified locally for the Perkin-Elmer 3240 computer.

Table II. Central Atom Bond Distances in the Iron, 6-Coordinate, and 7-Coordinate Calcium Complexes of A23187 (Å)

coordinating ligand atom	Fe complex	Ca complex (6-coordinate)	Ca complex (7-coordinate)
O(carboxyl)	2.01 (1)	2.01	2.27
	2.03 (1)	1.92	2.28
O(carbonyl)	2.19 (1)	2.10	2.37
	2.13 (2)	2.02	2.38
N(benzoxazole)	2.23 (2)	2.21	2.69
	2.22 (2)	2.22	2.58

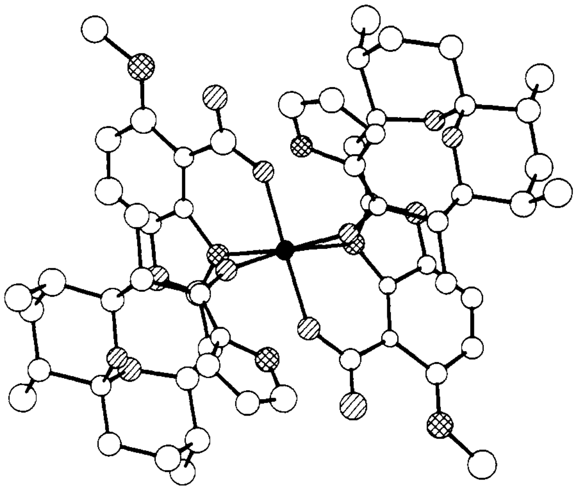

Figure 2. Perspective projection of the ferrous ion complex of A23187 on a plane perpendicular to the pseudo-2-fold molecular axis passing through the 6-coordinated iron atom: filled circle, iron; hatched circles, oxygen; cross-hatched circles, nitrogen; open circles, carbon.

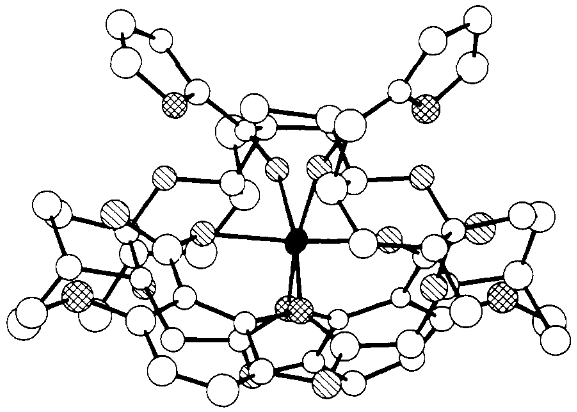

Figure 3. Perspective projection of the ferrous ion complex of A23187 on a plane containing the pseudo-2-fold molecular axis passing through the 6-coordinated iron atom: filled circle, iron; hatched circles, oxygen; cross-hatched circles, nitrogen; open circles, carbon.

Discussion

The final structural parameters are presented in Table I. The number immediately following each atom symbol refers to one or the other A23187 moiety (1 or 2) or to the ethanol molecules (3 or 4). Subsequent numbers are consistent with the A23187 numbering system shown in Figure 1.

Coordination to the ferrous ion is approximately octahedral (Table III) through a carboxyl oxygen, the nitrogen of the ben-

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(15) "International Tables for X-ray Crystallography"; Kynoch Press: Birmingham, England, 1952; Vol. I.

(16) The least-squares function minimized was $\sum\omega(|F_o| - G|F_c|)^2$, where F_o and F_c are the observed and calculated structure factors, G is a variable overall scaling factor, and the weight accorded each observation $\omega = \{\sigma^2(F_o) + 0.0006F_o{}^2\}^{-1}$; $R_F = \sum(G^{-1}|F_o| - |F_c|)/\sum G^{-1}|F_o|$; $R_{\omega F} = \{\sum\omega(G^{-1}|F_o| - |F_c|)^2/\sum\omega(G^{-1}|F_o|)^2\}^{1/2}$; $S = \{\sum\omega(G^{-1}|F_o| - |F_c|)^2/(N_o - N_v)\}^{1/2}$ where N_o and N_v are the number of observations and variables, respectively.

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Table III. Interatomic Distances and Angles for the Ferrous Ion Complex of A23187[a]

Fe-O11	2.01 (1)	Fe-O21	2.03 (1)
-O16	2.19 (1)	-O26	2.13 (2)
-N12	2.23 (2)	-N22	2.22 (2)
O11-C11	1.32 (3)	O21-C21	1.28 (3)
O12-C11	1.27 (3)	O22-C21	1.30 (4)
O13-C17	1.33 (3)	O23-C27	1.39 (3)
-C19	1.36 (2)	-C29	1.33 (3)
O14-C111	1.41 (2)	O24-C211	1.46 (3)
-C116	1.43 (3)	-C216	1.44 (3)
O15-C116	1.40 (3)	O25-C216	1.37 (3)
-C122	1.42 (3)	-C222	1.44 (3)
O16-C125	1.27 (2)	O26-C225	1.20 (3)
N11-C13	1.38 (3)	N21-C23	1.38 (4)
-C14	1.50 (4)	-C24	1.54 (4)
N12-C18	1.36 (3)	N22-C28	1.44 (3)
-C19	1.29 (3)	-C29	1.27 (3)
N13-C126	1.40 (3)	N23-C226	1.35 (3)
-C129	1.34 (3)	-C229	1.31 (4)
C11-C12	1.43 (3)	C21-C22	1.45 (4)
C12-C13	1.53 (3)	C22-C23	1.45 (4)
-C18	1.38 (3)	-C28	1.36 (3)
C13-C15	1.35 (4)	C23-C25	1.46 (4)
C15-C16	1.31 (3)	C25-C26	1.33 (4)
C16-C17	1.40 (3)	C26-C27	1.35 (4)
C17-C18	1.43 (3)	C27-C28	1.35 (3)
C19-C110	1.42 (3)	C29-C210	1.41 (4)
C110-C111	1.55 (3)	C210-C211	1.48 (4)
C111-C112	1.56 (3)	C211-C212	1.53 (4)
C112-C113	1.48 (4)	C212-C213	1.64 (4)
-C114	1.56 (3)	-C214	1.46 (4)
C114-C115	1.49 (3)	C214-C215	1.52 (4)
C115-C116	1.51 (3)	C215-C216	1.47 (4)
C116-C117	1.54 (3)	C216-C217	1.62 (3)
C117-C118	1.51 (4)	C217-C218	1.56 (4)
-C119	1.42 (4)	-C219	1.52 (4)
C119-C120	1.50 (4)	C219-C220	1.43 (4)
C120-C121	1.56 (4)	C220-C221	1.61 (4)
-C122	1.55 (3)	-C222	1.58 (4)
C122-C123	1.52 (3)	C222-C223	1.59 (4)
C123-C124	1.56 (3)	C223-C224	1.59 (4)
-C125	1.53 (3)	-C225	1.50 (4)
C125-C126	1.42 (3)	C225-C226	1.36 (3)
C126-C127	1.38 (3)	C226-C227	1.29 (4)
C127-C128	1.37 (3)	C227-C228	1.42 (4)
C128-C129	1.29 (4)	C228-C229	1.38 (4)
O31-C31	1.18	O41-C41	1.20
C31-C32	1.39	C41-C42	1.43
O11-Fe-O16	87.9 (5)	O16-Fe-O21	87.3 (5)
-O21	173.0 (7)	-O26	91.4 (5)
-O26	86.2 (6)	-N12	83.6 (6)
-N12	84.8 (6)	-N22	171.6 (6)
-N22	100.2 (7)	O21-Fe-O26	88.8 (6)
O26-Fe-N12	169.8 (6)	-N12	99.8 (6)
-N22	87.8 (6)	-N22	84.5 (7)
N12-Fe-N22	98.5 (7)		
Fe-O11-C11	138 (1)	Fe-O21-C21	139 (2)
C17-O13-C19	106 (2)	C27-O23-C29	106 (2)
C111-O14-C116	115 (2)	C211-O24-C216	114 (2)
C116-O15-C122	118 (2)	C216-O25-C222	113 (2)
C13-N11-C14	119 (2)	C23-N21-C24	121 (2)

Fe-N12-C18	118 (1)	Fe-N22-C28	119 (1)
-C19	130 (1)	-C29	134 (2)
C18-N12-C19	111 (2)	C28-N22-C29	106 (2)
C126-N13-C129	105 (2)	C226-N23-C229	114 (2)
O11-C11-O12	116 (2)	O21-C21-O22	117 (2)
-C12	119 (2)	-C22	121 (2)
O12-C11-C12	125 (2)	O22-C21-C22	122 (2)
C11-C12-C13	120 (2)	C21-C22-C23	119 (2)
-C18	123 (2)	-C28	121 (2)
C13-C12-C18	117 (2)	C23-C22-C28	119 (2)
N11-C13-C12	118 (2)	N21-C23-C22	122 (2)
-C15	128 (2)	-C25	124 (3)
C12-C13-C15	114 (2)	C22-C23-C25	114 (2)
C13-C15-C16	130 (2)	C23-C25-C26	123 (3)
C15-C16-C17	117 (2)	C25-C26-C27	117 (3)
O13-C17-C16	131 (2)	O23-C27-C26	126 (2)
-C18	109 (2)	-C28	108 (2)
C16-C17-C18	120 (2)	C26-C27-C28	124 (2)
N12-C18-C12	135 (2)	N22-C28-C22	134 (2)
-C17	103 (2)	-C27	106 (2)
C12-C18-C17	122 (2)	C22-C28-C27	120 (2)
O13-C19-N12	110 (2)	O23-C29-N22	114 (2)
-C110	116 (2)	-C210	118 (2)
N12-C19-C110	133 (2)	N22-C29-C210	127 (3)
C19-C110-C111	110 (2)	C29-C210-C211	116 (2)
O14-C111-C110	104 (2)	O24-C211-C210	104 (2)
-C112	112 (2)	-C212	107 (2)
C110-C111-C112	116 (2)	C210-C211-C212	122 (2)
C111-C112-C113	114 (2)	C211-C212-C213	111 (2)
-C114	104 (2)	-C214	111 (2)
C113-C112-C114	114 (2)	C213-C212-C214	116 (2)
C112-C114-C115	113 (2)	C212-C214-C215	112 (2)
C114-C115-C116	113 (2)	C214-C215-C216	112 (2)
O14-C116-O15	110 (2)	O24-C216-O25	114 (2)
-C115	110 (2)	-C215	112 (2)
-C117	106 (2)	-C217	104 (2)
O15-C116-C115	105 (2)	O25-C216-C215	104 (2)
-C117	113 (2)	-C217	110 (2)
C115-C116-C117	113 (2)	C215-C216-C217	114 (2)
C116-C117-C118	110 (2)	C216-C217-C218	110 (2)
-C119	106 (2)	-C219	109 (2)
C118-C117-C119	117 (2)	C218-C217-C219	115 (2)
C117-C119-C120	123 (2)	C217-C219-C220	117 (2)
C119-C120-C121	115 (2)	C219-C220-C221	113 (2)
-C122	104 (2)	-C222	105 (2)
C121-C120-C122	111 (2)	C221-C220-C222	112 (2)
O15-C122-C120	109 (2)	O25-C222-C220	112 (2)
-C123	110 (2)	-C223	103 (2)
C120-C122-C123	117 (2)	C220-C222-C223	115 (2)
C122-C123-C124	114 (2)	C222-C223-C224	111 (2)
-C125	104 (2)	-C225	106 (2)
C124-C123-C125	112 (2)	C224-C223-C225	110 (2)
O16-C125-C123	116 (2)	O26-C225-C223	118 (2)
-C126	121 (2)	-C226	125 (2)
C123-C125-C126	123 (2)	C223-C225-C226	117 (2)
N13-C126-C125	118 (2)	N23-C226-C225	118 (2)
-C127	109 (2)	-C227	102 (2)
C125-C126-C127	132 (2)	C225-C226-C227	139 (2)
C126-C127-C128	103 (2)	C226-C227-C228	114 (2)
C127-C128-C129	112 (2)	C227-C228-C229	102 (2)
N13-C129-C128	111 (2)	N23-C229-C228	107 (3)
O31-C31-C32	121	O41-C41-C42	128

[a] Estimated standard deviations in the least significant digit are given in parentheses.

zoxazole ring system, and the carbonyl oxygen of each A23187 ligand. The disposition of coordinating atoms is such that the complex molecule as a whole exhibits pseudo-2-fold symmetry (Figures 2 and 3). As in the calcium complexes[12,13] the arrangement is further stabilized by a pair of head-to-tail hydrogen bonds between N(3) of one A23187 ligand and O(1) of the other in the same complex, and by an intraligand hydrogen bond between N(1) and O(2) within each A23187 unit. The Fe–O distances (Table II) are virtually identical within experimental error to the corresponding Ca–O distances in the 6-coordinate calcium complex. However, the calcium ion in the 7-coordinate complex is particularly loosely bound. All the bond distances and angles within the A23187 moieties have their expected values (Table III); the geometries of the two ligand molecules in each complex are closely similar.[22]

The fact that the iron–ionophore crystals are only stable under anaerobic conditions strongly suggests the existence of a ferrous rather than ferric complex. This is in accord with studies on iron transport across liposomal and red cell membranes[6-8] which demonstrated ionophore transport of iron from ferrous complexes only. Hepatocyte iron was mobilized by A23187, demonstrating the presence of an intracellular ferrous iron pool. Hence ferrous

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(22) Supplementary material available; see paragraph at end of paper.

as well as ferric chelators should be considered in iron chelation therapy. A23187 has a number of the structural features required for rapid membrane transport of iron and had potential application in mixed ligand chelation therapy. However, this study has shown the structures of the Fe^{2+} and Ca^{2+} complexes to be closely similar. Hence, attempts to design a ligand analogue of A23187 with enhanced specificity for iron seem unlikely to be successful.

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Supplementary Material Available: Listings of measured structure amplitudes, calculated structure factors, and anisotropic thermal parameters of the iron atom are available (13 pages). Ordering information is given on any current masthead page.

Amorphous Chain Complexes MM'(EDTA)$(H_2O)_4$·$2H_2O$. LAXS Investigation of the Local Structure and Magnetic Behavior

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Abstract: The amorphous MM'(EDTA)$(H_2O)_4$·$2H_2O$ (MM' = NiCo, NiNi) materials comprise infinite chains built up with alternated "hydrated" and "chelated" octahedra bridged by carboxylate groups: ...–M'$(H_2O)_4$–M(EDTA)–M'$(H_2O)_4$–.... Investigation by the LAXS method allows one to precise the following points: (i) the coordination of the EDTA ligand is strictly the same as in the crystalline phase, i.e., hexacoordination toward the M atom and two bridging groups; (ii) the refinement of the MM'M angle of the zigzag infinite chain has been carried out with a precision of 5°; (iii) it was further possible to obtain a partial refinement of the bridging group geometry. The magnetic behavior is discussed in terms of infinite chains of conventional spin assuming a J parameter distribution and a Lande-factor alternation. The results, showing the essential role of the superexchange angle on J values, are in good agreement with structural data.

Extensive studies in the field of polymeric transition-metal complexes have provided valuable information on the correlations between structure and magnetic properties.[1] Thus, in a one-dimensional system with one kind of antiferromagnetically exchange-coupled ions, the temperature dependence of the maximum susceptibility is shown to be related to the strength of the interaction.[2] Such systems have been extensively studied both from the experimental and the theoretical point of view, whatever the dimensionality of this interaction.[3-5]

In contrast, random exchange chains exhibiting some degree of structural disorder have mainly been investigated for their transport properties. The materials reported so far are highly conducting organic charge-transfer salts generally based on the TCNQ molecule as acceptor.[6-11]

A disordered system may be described from structural features even if it is induced by physical phenomena. Two models are currently involved when describing disordered chains: one refers to distinct-sized finite fragments randomly arranged more or less cross-linked, and the other refers to a random distribution of the bond lengths and bond angles between the connected ions. The first case arises when defects are chemically or physically induced, for example, by the introduction of nonmagnetic impurities or by irradiation; the second is better adapted when dealing with flexible chains such as ribbons where interactions only occur within a given ribbon. Obviously, owing to the different frameworks, both arrangements are expected to show well-distinct behaviors from a magnetic point of view.[12]

In this paper, investigation of the correlation of local order and magnetic properties in two amorphous complexes, Ni_2(EDTA)·$6H_2O$ and NiCo(EDTA)·$6H_2O$, is carried out. Both complexes belong to a series formulated as MM'(EDTA)·$6H_2O$ (M and M' are divalent first-row metals). They have been isolated, by appropriate synthesis methods, as crystalline and amorphous varieties.

The magnetic behavior of the crystallized complexes has been previously discussed in terms of well-isolated exchange-coupled chains, in agreement with the structure.[13] It has been specifically emphasized that, for distinct M and M' sublattices, spin alternation results in a ferromagnetic one-dimensional behavior.[14,15]

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