

03.5-17 THE MOLECULAR STRUCTURE OF A NOVEL SIDERO-PHORE, NEOCOPROGEN I, $C_{31}H_{47}N_6O_{12}Fe$

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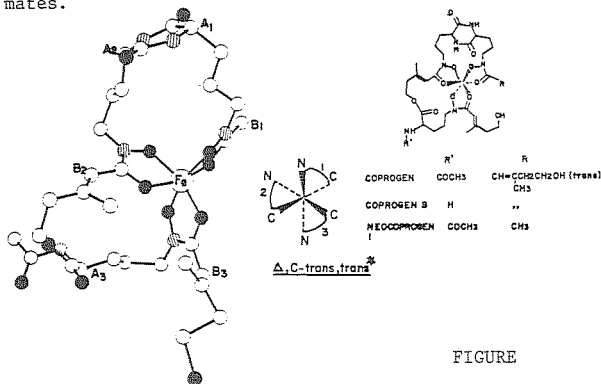
The coprogen family of siderophores (microbial iron chelating agents) are built up of typical units as in other fungal siderophores. Coprogen, like ferrirubin, is built from δ -N-hydroxy ornithine and trans-anhydro mevalonic acid (trans 3-methyl-5-hydroxy-pent-2-enoic acid), but these building stones are arranged in a completely different manner from that in ferrirubin. Two of the amino acids are linked together, head to head, through a diketo-piperazine ring, and the third is linked to the rest of the molecule via an ester linkage. Other members in the coprogen family are coprogen B, rhodotorulic acid and dimerumic acid, but no crystal structure for any of these compounds, either as ligand or complex, have been reported. We report here the isolation and structure determination of a novel member in this family, neocoprogen I.

The compound was isolated from iron-deficient cultures of *Curvularia subulata*, which also produce coprogen, ferricrocin and a few other minor siderophores. It was purified by reversed phase chromatography using C_{18} bonded silica gel as the stationary phase and methanol-water gradient as the mobile phase, and was crystallized from an ethanol solution equilibrated with acetonitrile at 4° C.

Crystal data: orthorhombic, $P2_12_1$, $a=8.683(12)$, $b=28.334(39)$, $c=36.835(40)$ Å, $V=9062.3$ Å³, $Z=2$ ($C_{31}H_{47}N_6O_{12}Fe$) + $10H_2O$ + $1.5C_2H_3N$. Structure from 4798 reflections, $MoK\alpha$, $2\theta_{max}=40^\circ$ at 138K, by direct methods and difference syntheses, final $R=0.125$.

Neocoprogen I differs from coprogen and coprogen B in having dissimilar acyl groups (B_1, B_2, B_3 in Fig.), while the former have three identical acyl groups (B_1, B_2, B_3). The presence of different N-acyl groups in the same siderophore has recently been reported for the first time in the case of the asperchrome series (M.A.F. Jalal et al, *J. Bact.* 1984, in press), and the present structure provides further evidence of the versatility in microbial biosyntheses of these secondary metabolites.

Neocoprogen assumes Δ -trans isomer, and is the first example of a trans-coordination of a ferric trihydroxamate in the solid state, and this is possibly the result of the head-to-head (diketopiperazine ring) condensation of two of the ornithines. The structure of neocoprogen I will be compared with other known ferric trihydroxamates.



FIGURE

*(Leong and Raymond, *J. Am. Chem. Soc.*, 97, 293 (1975).

03.5-18 STRUCTURE AND CONFORMATION OF NITRATES OF AMINO ACIDS: CRYSTAL AND MOLECULAR STRUCTURES OF L-HISTIDINE NITRATE, L-PHENYLALANINE NITRATE AND DL-METHIONINE NITRATE.* T. Srikrishnan, S. Narasinga Rao and R. Parthasarathy, Center for Crystallographic Research Roswell Park Memorial Institute, Buffalo, NY 14263.

Accurate crystal structure determinations of amino acids and peptides play an important role in evaluating the preferred conformations of peptides. Our studies on the nitrates of amino acids began following the work of Rustgi and Box who studied the ESR and ENDOR spectra of several of these amino acid nitrates and found that nitrate ions act as a mediator of radiation damage, scavenging electrons to form free radicals. The crystal structures of L-Histidine Nitrate ($HisNO_3$), L-Phenylalanine nitrate (Pheala NO_3) and DL-Methionine nitrate (Met NO_3) were undertaken to understand from a structural point of view the role of nitrates as an electron scavenger as well as to study the hydrogen bonding patterns of nitrates of amino acids & peptides.

The crystallographic data for the three compounds are given below. L-Histidine Nitrate, $C_6H_{10}N_4O_5$, $a = 5.243(2)$, $b = 7.116(1)$, $c = 25.030(2)$ Å, $V = 933.8$ Å³, $D_{cal} = 1.552$ g/cc, $D_{obs} = 1.56$ g/cc, space group $P2_12_12_1$, $Z = 4$; CAD-4 data 2003 reflections ($792 \geq 3\sigma$); Structure from MULTAN final R-value 0.064 for 792 reflections. L-Phenylalanine Nitrate, $C_{10}H_{13}N_3O_7$, $a = 14.957(3)$, $b = 5.379(1)$, $c = 21.519(1)$ Å, $\beta = 107.78(1)$, $V = 956.1$ Å³, $D_{cal} = 1.580$ g/cc, $D_{obs} = 1.59$ g/cc, space group $P2_1$, $Z = 2$ (two molecules of phenylalanine and one nitrate ion in the asymmetric unit); CAD-4 data 2230 reflections ($1826 \geq 3\sigma$); Structure from MULTAN, final R-value 0.067 for 1826 reflections. DL-Methionine Nitrate, $C_5H_{12}N_2O_5S$, $a = 13.194(4)$, $b = 5.580(1)$, $c = 13.834(5)$ Å, $\beta = 104.49(2)$, $V = 986$ Å³, $D_{cal} = 1.423$ g/cc, $D_{obs} = 1.43$ g/cc, space group, $P2_1/n$, $Z = 2$, CAD-4 data, 2389 reflections ($1666 \geq 3\sigma$); structure from MULTAN final R-value 0.051 for 1666 reflections.

The salient features that emerge from the above structural investigations are: (i) The three N-O bonds are quite unequal in length. The three N-O distances are 1.321, 1.203, 1.187 Å in $HIS NO_3$; 1.264, 1.253, 1.229 Å in $Met NO_3$ and 1.261, 1.235, 1.192 Å in $PheAla NO_3$. There is a correlation between the stretching of the N-O bonds and the number and length of hydrogen bonding. Hence the nitrate group does show some deviations from its classical D_{3h} symmetry since the oxygens attached to the nitrate group are non-equivalently bonded to the nitrogen atom. (ii) In $PheAla NO_3$ we have two molecules of phenylalanine and one nitro group in the asymmetric unit but surprisingly the carboxyl groups have nearly identical geometry. Although the two molecules have similar conformations, there are some essential differences. The torsion angles ψ_1 and ψ_2 are, respectively, -8.1 and 173.2° in molecule A and 1.6 and 179.7° in molecule B. In molecule A, the amino nitrogen is 0.18 Å away from the plane of the carboxyl group whereas in molecule B the amino nitrogen is the plane of the carboxyl group. The deviation of the amino nitrogen atom are -0.62 Å and 0.91 Å in $Met NO_3$ and $HIS NO_3$ respectively. (iii) There are two bifurcated hydrogen bonds involving the amino group. In $PheAla NO_3$, one of the hydrogens of the amino group of molecule A takes part in a bifurcated interaction with one of the oxygens of the nitrogroup and the carboxyl oxygen of the other molecule B. In $MetNO_3$, one of the hydrogen atoms of the amino group takes part in a bifurcated hydrogen bond with two of the oxygens of two symmetry related nitro groups.

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