

CEC for (IV) (Fig. 3) is consistent with octant behavior which has also been observed for (V) (Ruble *et al.*, 1976).

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O.r.d. Studies of β -Amino Ketones. VI. The Crystal Structure and Absolute Configuration of (–)-[(–)-1-Methyl-3-ethyl-3-benzoylpiperidine *R*:*R*-(+)-Bitartrate]

BY J. R. RUBLE

Department of Crystallography, University of Pittsburgh, Pittsburgh, Pennsylvania, 15260 U.S.A.

AND G. HITE* AND J. R. SOARES

Section of Medicinal Chemistry and Pharmacognosy, University of Connecticut, School of Pharmacy, Storrs, Connecticut 06268, U.S.A.

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(–)-[(–)-1-Methyl-3-ethyl-3-benzoylpiperidine *R*:*R*-(+)-bitartrate], $C_{19}H_{27}NO_7$, crystallizes in space group $P2_1$, with unit-cell dimensions $a = 8.612(2)$, $b = 7.074(2)$, $c = 15.510(4)$ Å, $\beta = 98.111(8)^\circ$. There are two formula weights per unit cell giving $D_x = 1.355$ and $D_m(CCl_4-C_6H_6) = 1.353$ g cm $^{-3}$. The structure was solved by direct methods. The positional and thermal parameters were refined by full-matrix procedures, converging at $R = 0.041$. The configuration for the (–)-amine component is *R*. The benzoyl group is axial. The O–C(9)–C(3)–C(2) torsion angle is -1.1° . While other protonated amines in this series exhibit antioctant behavior, the absolute configuration and crystal conformation of the title compound, taken together with the optical rotatory dispersion data, are consistent with octant behavior.

Introduction

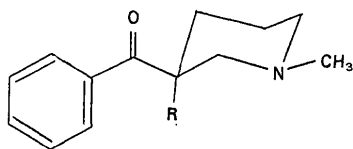
While the optical rotatory dispersion (o.r.d.) curves (Djerassi, 1960) for (–)-(I) in octane and in aqueous acid are of opposite sign, the curves for (–)-(II), which is isoelectronic with (–)-(I), have the same sign in both solvents (Soares, 1971). Other ketones in this series also

exhibit solvent-dependent sign inversion which has been attributed to stabilization of rotameric populations about an equatorial (*e*) acyl-to-ring bond (Smisssman & Hite, 1960; Hite & Soares, 1973; Djerassi, 1960; Djerassi, Fournaguera & Mancera, 1959; Djerassi & Geller, 1958). However, in (+)-(III) methiodide, the conformer with the benzoyl group axial (*a*) appears to be the more stable species (Ruble, Hite & Soares, 1976). In view of the role suggested for the ether oxygen

* To whom inquiries should be addressed.

in stabilizing the benzoyl-*e* conformation of (-)-(I) methiodide (Ruble, Blackmond & Hite, 1976), and since the absolute configuration of (-)-(II) was not known, it was of interest to undertake a crystallographic study of the quarternary and protonated tertiary amine salts of (-)-(II). A report on the former salt will follow.

- (I) R = OCH₃
 (II) R = C₂H₅
 (III) R = CH₃



A sample of the dextrorotatory, (-)-tartaric acid salt of (+)-(II) (Soares & Hite, 1975) [m.p. 149–150°; $[\alpha]_D^{25}$ (95% ethanol) +27.4 ± 0.5° (*c* 1.025)] was converted to the (+)-free base; R.D. (Fig. 1) in 0.1 *N* hydrochloric acid (*c* 0.0033), 25°, positive Cotton effect curve: $[\alpha]_{400} + 123^\circ$, $[\alpha]_{375} + 184^\circ$, $[\alpha]_{365} + 306^\circ$, $[\alpha]_{355} + 582^\circ$, $[\alpha]_{345} + 920^\circ$, $[\alpha]_{332} + 1240^\circ$, $[\alpha]_{325} + 1010^\circ$, $[\alpha]_{320} + 645^\circ$, $[\alpha]_{315} + 153^\circ$, $[\alpha]_{310} - 36^\circ$, $[\alpha]_{305} - 950^\circ$, $[\alpha]_{300} - 1350^\circ$, $[\alpha]_{295} - 1590^\circ$. A sample of the levorotatory,

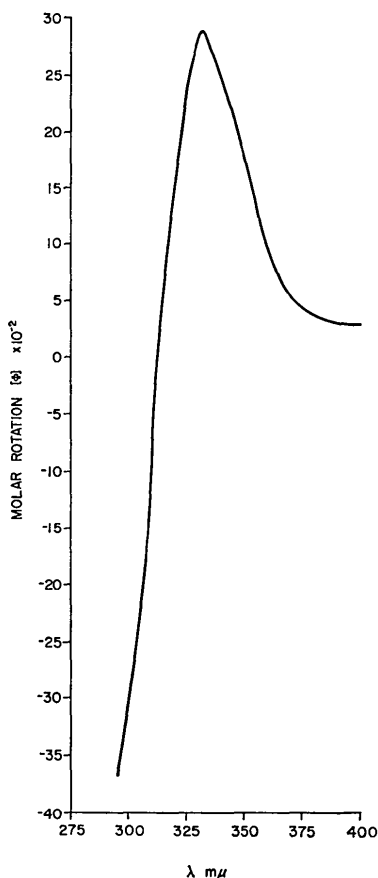


Fig. 1. Rotatory dispersion curve of (+)-[1-methyl-3-ethyl-3-benzoylpiperidine] in 0.1 *N* HCl.

(+)-tartaric acid salt of (-)-(II), which is antipodal to that described above, was recrystallized from acetone to constant melting point and specific rotation [m.p. 154–155°; $[\alpha]_D^{25}$ (95% ethanol) -31.1 ± 0.6° (*c* 1.00)]. A crystal (0.17 × 0.22 × 0.35 mm) of this (-)-salt was mounted on a Nonius CAD-4 automatic diffractometer equipped for data collection with graphite-mono-chromated Cu *K*α radiation ($\lambda = 1.5418 \text{ \AA}$). The cell parameters were refined on 50 automatically centered reflections ($30 \leq \theta \leq 90^\circ$). The intensities of 2086 independent reflections for which $\theta \leq 75^\circ$ were measured in the $\theta/2\theta$ mode. Other than systematic absences, there were 186 unobservably weak reflections [$I \leq \sigma(I)$] which were assigned values of $I = \sigma(I)$. Three standard reflections remained constant [$\pm 2\sigma(I)_{av}$] throughout data collection.

The structure was solved using *MULTAN* (Germain, Main & Woolfson, 1971). Of four acceptable solutions obtained using 272 of the highest (≥ 1.4) re-normalized $|E|$'s, one was chosen to provide an *E* map from which the positions of all but one of the non-hydrogen atoms could be determined. After one cycle of structure-factor calculation and Fourier synthesis, the remaining non-hydrogen atom was located. Full-matrix refinement, first isotropically, then anisotropically, followed by difference Fourier synthesis, revealed the positions of all except the six methyl hydrogen atoms. These were located after subsequent refinement and difference Fourier synthesis. The final stage of refinement, using isotropic thermal parameters for hydrogen, was accomplished in segments, first refining the positional and thermal parameters for the cation and then refining the positional and thermal parameters for the tartrate ion, together with all except the benzoyl and ethyl substituents of the cation. The solution converged at $R_w = 0.041$ ($w = 1/\sigma^2$). The maximum shift in a parameter was 0.3σ . No peaks greater than 0.239 e \AA^{-3} were seen in the final difference Fourier map. A table of observed and calculated structure factors, and a listing of intramolecular distances, angles and torsion angles, and intermolecular hydrogen-bonded and electrostatic distances more complete than that provided in Fig. 2 are available.* The final atomic and thermal parameters are listed in Table 1. Since these define the correct (Bijvoet, Peerdeman & van Bommel, 1951; Bijvoet, 1955) absolute configuration (*R*:*R*) for the (+)-tartaric acid moiety, the *R* configuration provided by the atomic parameters of Table 1 for the (-)-amine component is also correct. The atomic scattering factors for carbon, nitrogen and oxygen were taken from *International Tables for X-ray Crystallography* (1968). Those for hydrogen are from Stewart, Davidson & Simpson (1965). Computer

* These data have been deposited with the British Library Lending Division as Supplementary Publication No. SUP 31161 (26 pp., 1 microfiche). Copies may be obtained through The Executive Secretary, International Union of Crystallography, 13 White Friars, Chester CH1 1NZ, England.

programs used in this study were written or modified for the IBM 1130 and DEC 1070 systems by Shiono (1963-73).

Discussion

The bond distances, angles and torsion angles for the bitartrate ion (Hite & Soares, 1973) and for the cation (see previous papers in this series) are unexceptional (Fig. 2). The benzoyl group is *a*. The O-C(9)-C(3)-C(2) and C(8)-C(7)-C(3)-C(4) torsion angles are -1.1° and 173.2° , respectively (Fig. 3). The benzoyl group in (-)-(I) methiodide is *e* (Ruble, Blackmond & Hite, 1976). This difference in conformation is in accord with the role suggested for the ether oxygen in stabilizing

the benzoyl-*e* conformer of (-)-(I) methiodide. This, and the conformational similarity (benzoyl-*a*) between this structure and (+)-(III) methiodide also provide support for the suggested electrostatic role played by carbonyl oxygen atoms in stabilizing selected conformations of members of this series of compounds (see previous papers in this series). In this structure, intramolecular electrostatic interactions are indicated by the short O...C(2) and O...H(N) distances of 2.67 and 2.40 Å, respectively.

In this conformation (Fig. 3) the effects of C(5), C(4), C(7) and C(8) on the CEC cancel by reflection through the plane of the carbonyl group. Since C(2) and C(3) are in this nodal plane, and C(6) and N are virtually in an orthogonal nodal plane, the only apparent contrib-

Table 1. Atomic parameters

Positional parameters are given as fractions of the lattice translations. Anisotropic and isotropic temperature factors correspond, respectively, to the expressions $T = \exp[-2\pi^2(U_{11}h^2a^{*2} + U_{22}k^2b^{*2} + U_{33}l^2c^{*2} + 2U_{12}hka^*b^* + 2U_{13}hla^*c^* + 2U_{23}klb^*c^*)]$ and $T = \exp(-B \sin^2 \theta/\lambda^2)$. Estimated standard deviations are given in parentheses. Positional parameters for nonhydrogen atoms $\times 10^4$, for hydrogen atoms $\times 10^3$; thermal parameters for nonhydrogen atoms $\times 10^3$, for hydrogen atoms $\times 10$.

	<i>x</i>	<i>y</i>	<i>z</i>	U_{11}	U_{22}	U_{33}	U_{12}	U_{13}	U_{23}
O(1) <i>T</i>	1091 (2)	-2452 (0)	-1133 (1)	32 (1)	34 (1)	40 (1)	10 (1)	2 (1)	6 (1)
O(2) <i>T</i>	-1080 (2)	-2243 (3)	-2099 (1)	36 (1)	25 (1)	38 (1)	0 (1)	-3 (1)	-1 (1)
O(3) <i>T</i>	1310 (2)	1319 (3)	-910 (1)	31 (1)	36 (1)	43 (1)	-9 (1)	-2 (1)	4 (1)
O(4) <i>T</i>	-1907 (2)	679 (3)	-527 (1)	46 (1)	35 (1)	40 (1)	-7 (1)	21 (1)	-1 (1)
O(5) <i>T</i>	-1236 (2)	4238 (3)	-2085 (1)	57 (1)	24 (1)	33 (1)	1 (1)	11 (1)	-1 (1)
O(6) <i>T</i>	-1998 (2)	4480 (3)	-776 (1)	64 (1)	33 (1)	38 (1)	11 (1)	16 (1)	-6 (1)
C(1) <i>T</i>	32 (3)	-1532 (3)	-1572 (1)	26 (1)	24 (1)	27 (1)	2 (1)	9 (1)	2 (1)
C(2) <i>T</i>	61 (3)	622 (4)	-1516 (2)	25 (1)	20 (1)	29 (1)	-1 (1)	4 (1)	1 (1)
C(3) <i>T</i>	-1529 (3)	1384 (4)	-1324 (2)	24 (1)	23 (1)	30 (1)	-2 (1)	5 (1)	-2 (1)
C(4) <i>T</i>	-1582 (3)	3544 (4)	-1361 (2)	28 (1)	23 (1)	31 (1)	2 (1)	1 (1)	-1 (1)
N	5902 (2)	1802 (3)	1416 (1)	22 (1)	29 (1)	24 (1)	0 (1)	1 (1)	0 (1)
O	7521 (2)	4160 (3)	2807 (1)	52 (1)	44 (1)	32 (1)	-17 (1)	3 (1)	6 (1)
C(1)	5119 (3)	2423 (5)	540 (2)	36 (1)	51 (2)	25 (1)	4 (1)	0 (1)	6 (1)
C(2)	4920 (3)	2377 (4)	2095 (2)	26 (1)	34 (1)	28 (1)	7 (1)	4 (1)	-1 (1)
C(3)	5622 (2)	1808 (4)	3023 (1)	23 (1)	29 (1)	24 (1)	1 (1)	4 (1)	-2 (1)
C(4)	6056 (3)	-306 (4)	3046 (2)	36 (1)	28 (1)	30 (1)	-2 (1)	3 (1)	4 (1)
C(5)	7043 (3)	-837 (4)	2339 (2)	35 (1)	27 (1)	37 (1)	6 (1)	1 (1)	-2 (1)
C(6)	6241 (3)	-273 (4)	1440 (2)	30 (1)	29 (1)	33 (1)	1 (1)	3 (1)	-6 (1)
C(7)	4357 (3)	2159 (5)	3622 (2)	31 (1)	54 (2)	32 (1)	0 (1)	11 (1)	-4 (1)
C(8)	3951 (4)	4218 (6)	3745 (2)	58 (2)	63 (2)	47 (2)	21 (2)	15 (2)	-5 (2)
C(9)	7097 (3)	3013 (4)	3308 (1)	31 (1)	27 (1)	25 (1)	-1 (1)	6 (1)	-3 (1)
C(10)	8094 (3)	2734 (4)	4177 (2)	35 (1)	28 (1)	29 (1)	-6 (1)	0 (1)	-1 (1)
C(11)	9703 (3)	2491 (5)	4165 (2)	37 (1)	38 (2)	40 (1)	0 (1)	1 (1)	-1 (1)
C(12)	10709 (3)	2299 (5)	4938 (2)	44 (1)	41 (2)	56 (2)	-1 (1)	-12 (1)	3 (1)
C(13)	10149 (4)	2393 (5)	5723 (2)	60 (2)	41 (2)	40 (2)	-15 (2)	-19 (1)	10 (1)
C(14)	8575 (4)	2690 (6)	5746 (2)	68 (2)	56 (2)	27 (1)	-22 (2)	0 (1)	2 (1)
C(15)	7541 (3)	2840 (5)	4974 (2)	45 (1)	53 (2)	28 (1)	-9 (1)	3 (1)	2 (1)

	<i>x</i>	<i>y</i>	<i>z</i>	<i>B</i>		<i>x</i>	<i>y</i>	<i>z</i>	<i>B</i>
H(O3) <i>T</i>	133 (4)	57 (6)	-48 (2)	40 (8)	H2 (C5)	805 (3)	-14 (5)	245 (2)	26 (6)
H(O4) <i>T</i>	-150 (4)	135 (5)	-18 (2)	34 (8)	H1 (C6)	694 (3)	-51 (4)	98 (2)	26 (5)
H(O5) <i>T</i>	-118 (5)	563 (8)	-211 (3)	70 (11)	H2 (C6)	520 (4)	-94 (6)	129 (2)	36 (7)
H(C2) <i>T</i>	20 (3)	111 (4)	-210 (2)	23 (5)	H1 (C7)	469 (4)	141 (6)	420 (2)	35 (7)
H(C3) <i>T</i>	-232 (3)	99 (4)	-180 (2)	22 (5)	H2 (C7)	332 (3)	134 (4)	337 (2)	23 (5)
H(N)	678 (3)	228 (5)	153 (2)	28 (6)	H1 (C8)	487 (5)	501 (7)	396 (2)	65 (9)
H1 (C1)	409 (3)	173 (4)	42 (2)	28 (6)	H2 (C8)	358 (5)	490 (7)	315 (3)	66 (10)
H2 (C1)	583 (3)	211 (5)	13 (2)	36 (7)	H3 (C8)	329 (5)	438 (7)	424 (2)	68 (9)
H3 (C1)	499 (4)	383 (6)	57 (2)	49 (9)	H (C11)	1011 (3)	248 (4)	358 (2)	27 (5)
H1 (C2)	388 (3)	165 (4)	192 (2)	21 (5)	H (C12)	1191 (4)	199 (6)	490 (2)	57 (9)
H2 (C2)	480 (4)	386 (5)	207 (2)	34 (7)	H (C13)	1084 (5)	230 (8)	625 (3)	51 (11)
H1 (C4)	662 (3)	-62 (5)	365 (2)	26 (5)	H (C14)	814 (4)	272 (7)	632 (2)	50 (8)
H2 (C4)	507 (4)	-103 (6)	297 (2)	39 (7)	H (C15)	640 (4)	309 (6)	500 (2)	37 (8)
H1 (C5)	726 (3)	-220 (6)	233 (2)	33 (6)					

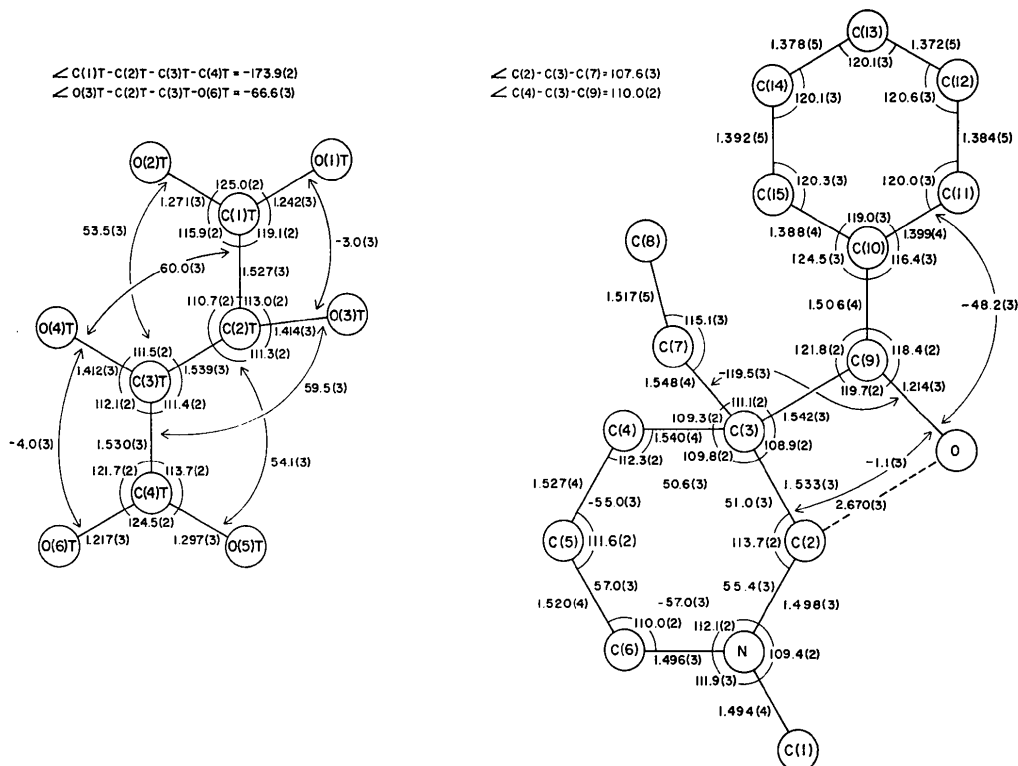


Fig. 2. Bond distances (Å) and angles (°), piperidine internal ring torsion angles (°), and other pertinent torsion angles (°) with standard deviations for (-)-[(-)-1-methyl-3-ethyl-3-benzoylpiperidine *R:R*-(+)-bitartrate].

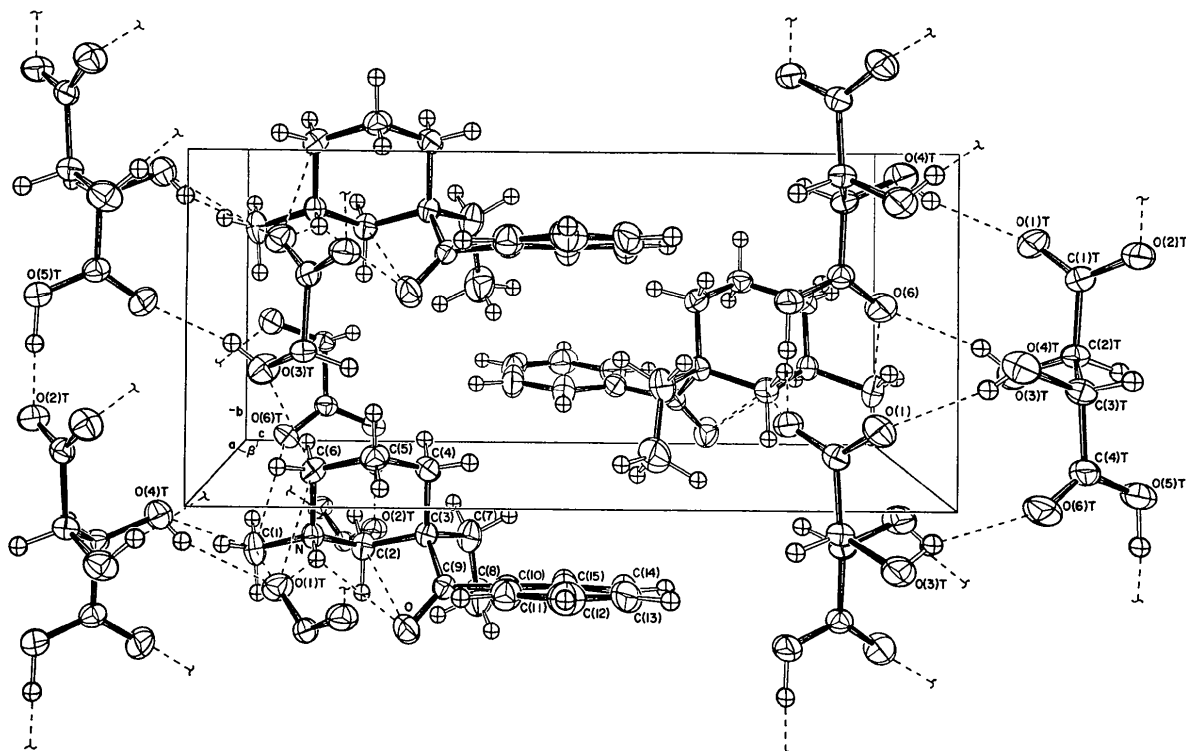


Fig. 3. Unit-cell diagram of (-)-[(-)-1-methyl-3-ethyl-3-benzoylpiperidine *R:R*-(+)-bitartrate], showing the conformation, hydrogen bonding and electrostatic interactions.

utor to the sign of the CEC is C(1), which lies in the lower, right, front, negative octant. This, and the negative CEC which would be observed (*cf.*, Fig. 1) for (-)-(II) in aqueous acid is consistent with octant behavior. This is the first of the protonated amines in this series to exhibit octant behavior. However, aspects of this crystal structure suggest that the observed conformation may not be indicative of the conformation of the molecule in aqueous solution.

Ring stacking not observed in other analogs in this series, and electrostatic repulsion between O(1)T and O appear to impose a -1.1° O-C(9)-C(3)-C(2) torsion angle. Since these conformational restrictions observed in the solid state will not be characteristic of the salt in aqueous solution, the -20° rotamer is a rational choice which may be stabilized by shortening of the O...H(N) 2.4 Å distance to afford a hydrogen bond. On this basis, the observed negative CEC for (-)-(II) in aqueous acid is consistent with antiocant behavior and this conclusion is consistent with previous studies. Since two reasonable explanations provide opposite answers to the o.r.d. behavior, interest in crystal structures of other protonated analogs of (II) continues.

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The Crystal Structure of *cis*-Catena- μ -sulphato-aquotris(imidazole)cadmium(II)

BY MINO R. CAIRA, LUIGI R. NASSIMBENI AND GUY ORPEN

Department of Physical Chemistry, University of Cape Town, South Africa

(Received 19 May 1975; accepted 22 May 1975)

The structure of $\text{Cd}(\text{C}_3\text{H}_4\text{N}_2)\text{SO}_4 \cdot \text{H}_2\text{O}$ has been determined from diffractometer data and refined by full-matrix least-squares calculations to a final R of 0.069 for 1856 independent reflexions. The crystals are monoclinic, space group $P2_1/n$, with $a = 11.85(1)$, $b = 9.00(1)$, $c = 14.32(1)$ Å, $\beta = 95.5(2)^\circ$, $Z = 4$. Cd exhibits distorted octahedral coordination, being bonded to three imidazole N atoms, a water molecule and two O atoms from bridging sulphates. The latter groups link the coordination polyhedra in infinite chains with Cd-O 2.32(1) and 2.37(1) Å. The mean Cd-N is 2.26(1) and the water Cd-O 2.43(1) Å. All H atoms were located in difference maps; intra- and inter-chain hydrogen bonding (O-H...O and N-H...O) is present.

Introduction

As part of a programme investigating metal ion-imidazole interaction by potentiometric and X-ray methods, we have synthesized crystals with the composition $\text{Cd}(\text{imidazole})_3\text{SO}_4 \cdot \text{H}_2\text{O}$. In view of the presence of imidazole in biological systems (*e.g.* the histidyl residue in proteins), it is of interest to establish metal-binding sites in the ligand.

The importance of Cd as a pollutant has been pointed out (Shaikh & Lucis, 1971). The metal probably functions by interactions with proteins in biological systems.

The stoichiometry of the complex suggests a four-coordinate species. However, the various possible binding modes of the sulphato group could lead to several structures and the X-ray analysis was undertaken in order to determine the Cd coordination.