The Crystal Structure of 2-Hydroxymethylpyridine *N*-Oxide

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The structure of 2-hydroxymethylpyridine *N*-oxide was determined from X-ray diffractometer data by a direct method. The compound crystallizes in the monoclinic space group $P2_1/c$ with cell dimensions a = 7.079, b = 8.046, c = 10.599 Å, cosβ = -0.2252. A total of 1241 independent reflections were refined to an R value of 0.06. The N-O dative bond has a length of 1.321 Å and the dative oxygen is bonded to a hydroxyl group on a symmetry related molecule by an intermolecular hydrogen bond. The structure corroborates recent findings concerning the relationship between the strength of hydrogen bonding to a dative oxygen and the length of the N-O dative bond.

Introduction.

2-Hydroxymethylpyridine *N*-oxide, 2HMPNO (Figure 1) is one of a series of substituted quinoline and pyridine *N*-oxides being studied in our laboratory in order to investigate the roles of exocyclic groups and hydrogen bonding on the N-O dative bond. Crystal structures of pyridine *N*-oxides reported in the literature have been rather limited in the variety of substituent groups studied. Also, structural studies of these compounds thus far have not been concerned with the effects of inter- or intramolecular hydrogen bonding. The crystal structure analysis of 2HMPNO was carried out since this compound could provide data on both substituent effects and hydrogen bonding. This is a somewhat unique compound in that it could potentially exhibit either inter- or intramolecular hydrogen bonding. There is also general chemical interest in 2HMPNO as a biological inhibitor (1) and as a precursor to other biologically active compounds (2).

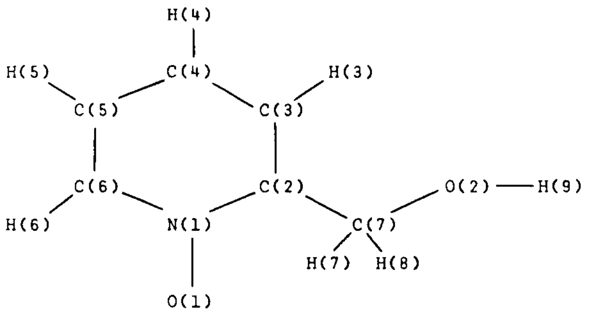

Figure 1. Atom numbering system in 2HMPNO.

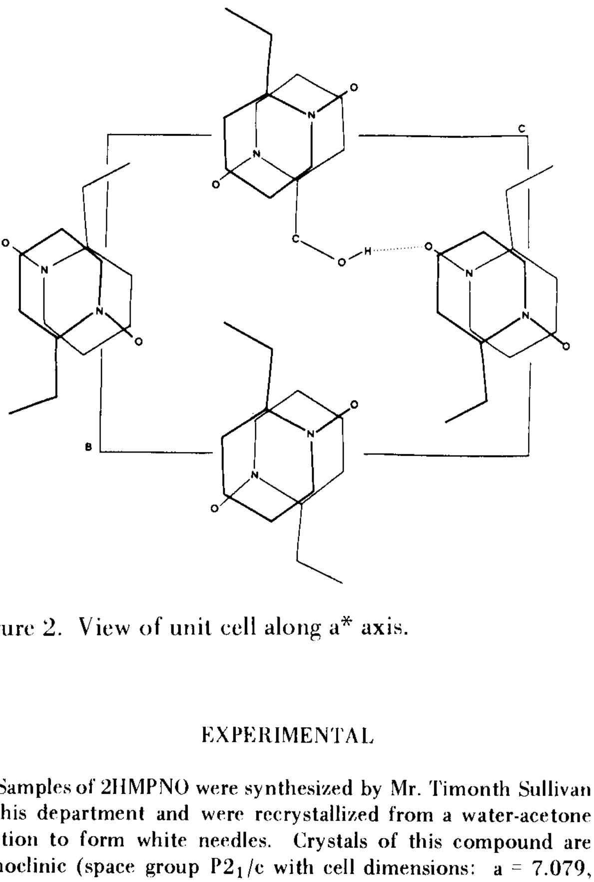

Figure 2. View of unit cell along a* axis.

EXPERIMENTAL

Samples of 2HMPNO were synthesized by Mr. Timonth Sullivan of this department and were recrystallized from a water-acetone solution to form white needles. Crystals of this compound are monoclinic (space group $P2_1/c$ with cell dimensions: a = 7.079, b = 8.046, c = 10.599 Å, cosβ = -0.2252. There are four molecules per unit cell. A suitable crystal was shaped with dimensions 0.37, 0.11, 0.08 mm and mounted on the Oak Ridge computer-controlled diffractometer for data collection. Intensity data to the limit sinθ/λ = 0.64 were collected using CuKα radiation.

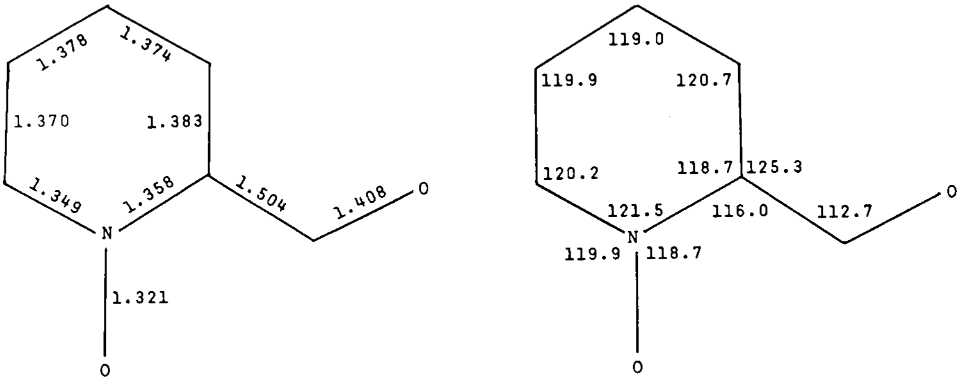

Figure 3. Bond distances (Å) and angles (°) in 2HMPNO.

TABLE I

Atomic and Thermal Parameters (with Estimated Standard Deviation). Thermal parameters are in the form: $\exp[-(\beta_{11}h^2 + \ldots + 2\beta_{23}k\ell)]$. All parameters are multiplied by 10^4 except for the hydrogen parameters which are multiplied by 10^3.

Atom	x	y	z	β_{11}	β_{22}	β_{33}	β_{12}	β_{13}	β_{23}
N(1)	1846(2)	643(2)	3877(1)	179(4)	122(3)	65(1)	11(2)	16(2)	4(1)
C(2)	2617(2)	1444(2)	5002(2)	174(4)	118(3)	68(2)	1(2)	27(2)	0(2)
C(3)	3258(3)	512(2)	6113(2)	202(5)	162(3)	69(2)	3(3)	22(2)	15(2)
C(4)	3119(3)	-1192(2)	6079(2)	219(5)	163(4)	107(2)	25(3)	34(2)	48(2)
C(5)	2317(3)	-1961(2)	4920(2)	231(5)	102(3)	151(3)	0(3)	48(3)	17(2)
C(6)	1677(3)	-1028(2)	3827(2)	197(5)	133(3)	103(2)	-8(3)	21(2)	-18(2)
C(7)	2675(3)	3310(2)	4930(2)	290(6)	116(3)	82(2)	-11(3)	44(3)	-5(2)
O(1)	1241(2)	1533(2)	2815(1)	297(4)	173(3)	63(1)	41(2)	9(2)	21(1)
O(2)	3504(3)	4049(2)	6131(1)	367(6)	159(3)	102(2)	-69(3)	56(2)	-38(2)
H(3)	380(3)	113(3)	690(2)	31(6)	25(5)	7(2)	-3(4)	4(3)	-4(3)
H(4)	360(3)	-191(3)	689(2)	36(7)	27(5)	22(4)	17(5)	8(4)	16(4)
H(5)	217(3)	-310(3)	481(2)	23(6)	12(4)	19(3)	2(4)	3(3)	2(3)
H(6)	102(4)	-147(2)	301(2)	79(10)	14(4)	16(3)	-2(5)	-3(5)	-12(3)
H(7)	132(3)	369(2)	456(2)	26(5)	13(3)	8(2)	4(3)	6(3)	1(2)
H(8)	346(3)	364(2)	430(2)	28(6)	14(4)	10(2)	-2(3)	7(3)	0(2)
H(9)	258(3)	388(3)	663(3)	15(6)	18(5)	39(6)	-13(4)	8(4)	-16(4)

TABLE II

Some bond lengths and angles in 8-hydroxyquinoline *N*-oxide (8HQNO), myxin, iodinin, and 2HMPNO.

Compound	N-O	O. . .O	<O-H. . .O
8HQNO	1.333 Å	2.48 Å	158°
myxin	1.323	2.50	159
iodinin	1.306	2.53	147
2HMPNO	1.321	2.69	170

A total of 1241 independent reflections were collected with 188 of these having net counts less than their standard deviations. The appropriate Lorentz, polarization, and absorption corrections were applied. The observed F's were scaled by a Wilson plot and then converted to normalized E values. A total of 192 reflections with magnitudes greater than 1.25 were selected for input to a computer program for direct sign determination (3). The E-maps synthesized using these signed reflections revealed an arrangement of peaks indicating plausible atomic positions for the heavy (non-hydrogen) atoms. Calculated structure factors based on these coordinates (with an overall temperature factor, B, of 4.17) agreed well with the observed structure factors, giving a reliability index (R) of 0.42. The entire data set (1421 reflections) was included in a full matrix least squares refinement, the quantity minimized being $\Sigma w[|Fo|^2-K|Fc|^2]^2$. The weight, w, applied to each reflection was derived as follows: to the $\sigma^2(F^2)$ obtained from counting statistics, a quantity $(0.03F^2)^2$ was added in order to attenuate the weights on very strong reflections. The weight applied to F^2 was $1/\sigma^2(F^2)$. Atomic form factors were taken from the International Tables for X-ray Crystallography. After a series of isotropic and anisotropic refinements, R was reduced to 0.11. The hydrogen parameters which were located from difference Fourier maps were refined anisotropically together with all other atoms and the four scale factors to reduce R to a final value of 0.06. The final atomic and thermal parameters are shown in Table I. Tables of observed and calculated structure factors are available from the first-named author (R.D.) on request.

Results and Discussion.

A view of the unit cell along the a* axis is shown in Figure 2. The pyridine moiety is quite planar, the largest deviation from the least squares best plane being 0.005 Å (atom N(1)). The exocyclic atoms, C(7), O(1), and O(2) deviate from this plane by 0.024, 0.012, and 0.020 Å, respectively. Bond distances and angles are shown in Figure 3. Bond lengths between non-hydrogen atoms have estimated standard deviations (e.s.d.'s) between 0.002 and 0.003 Å. The e.s.d.'s of the various bond angles (non-hydrogen) have an average value of 0.16°. The average of the six C-H distances is 0.98 Å with an average e.s.d. of 0.02 Å. The O(2)-H(9) distance is 0.94(2) Å. Of special interest are an intermolecular hydrogen bond and the N-O dative bond distance. The hydrogen bonding is between H(9) of one molecule and O(1)′ of another molecule related by the *c* glide. The H(9). . .O(1)′ distance is 1.75(3) Å and the O(2)-H(9). . . O(1)′ angle is 170(3)°. The N-O bond distance of 1.321 Å is consistent with N-O dative bond distances found in other compounds such as 1.34 Å in tetra-(pyridine oxide)-copper(II) perchlorate (4), 1.323 Å in myxin (5), 1.33 Å in pyridine *N*-oxide (6), 1.306 Å in iodinin (7), and 1.333 Å in 8-hydroxyquinoline *N*-oxide (8). An examination of atomic distances in four compounds containing N-O dative bonds to which hydrogen bonds are directed suggests an inverse relationship between the lengths of these two types of bonds. These data apparently support the observation of Hanson and Huml (7) that as the hydrogen bond to the *N*-oxide is strengthened, the N-O distance is lengthened. Such evidence is not conclusive, however, since in all the studies cited including this one the relatively large standard deviations associated with the hydrogen atom coordinates result in large uncertainties in the O-H bond length and the H. . .O intra- or intermolecular contacts. A more precise indication of this correlation is the comparison of N-O bond distances *vs.* O. . .O intramolecular contacts (8). This correlation is apparent for the three *N*-oxide compounds discussed - - myxin, iodinin, and 8-hydroxyquinoline *N*-oxide - - but not for 2HMPNO (Table II). The failure of 2HMPNO to conform to the relationship is probably due to the fact that hydrogen bonding in this compound is intermolecular in nature (as opposed to intramolecular for the other three compounds). In the intramolecular hydrogen bond examples, the geometric consideration of two oxygen atoms on the same molecule impose severe limitations on the range of O. . .O distances. This limitation is not experienced in 2HMPNO and, consequently, one does not necessarily expect the same correlation between the N-O bond distance and the intermolecular O. . .O contact in 2HMPNO.

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