

The Molecular and Crystal Structure of 8-Hydroxyquinoline-*N*-oxide

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The structure of 8-hydroxyquinoline-*N*-oxide was determined from diffractometer data by a direct method. The compound crystallizes in the monoclinic system with space group $P2_1/c$. The cell data are: $a = 12.1364(4)$, $b = 4.9211(2)$, $c = 13.1384(4)$ Å, $\beta = 109.26(1)^\circ$, $D_{\text{calc}} = 1.449$ g.cm⁻³, $D_{\text{exp}} = 1.46$ g.cm⁻³, $Z = 4$. The structure was solved by a direct method. A total of 1528 reflections were used in a full-matrix least-squares refinement. R was reduced to a final value of 0.053. Bond lengths between non-hydrogen atoms have e.s.d.'s between 0.002 and 0.003 Å. The e.s.d.'s of the various bond angles (non-hydrogen atoms) range from 0.01 to 0.02°. Distances and angles involving the hydrogen atoms have e.s.d.'s of 0.02 Å and 1°, respectively. The two C-N distances of the quinoline ring are unusually long and the quinoline moiety is surprisingly similar to naphthalene in terms of bond distances and angles. It is believed that the inductive effect of the N-O group may in part be responsible for the C-N lengthenings. The hydroxyl hydrogen atom is bonded to the dative oxygen atom *via* a short intramolecular hydrogen bond. The direct relationship between the N-O dative bond distance and the strength of a hydrogen bond to the dative oxygen atom appears to be substantiated in this study.

Introduction

The compound, 8-hydroxyquinoline-*N*-oxide, 8HQNO (Fig. 1), closely resembles myxin (Hanson, 1968) and

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iodinin (Hanson & Huml, 1969) in its arrangement of the *N*-oxide and hydroxyl moieties. Also, infrared studies of 8HQNO indicate that intramolecular hydrogen bonding is present (Ramaiah & Srinivasan, 1962). Of general chemical interest is the fact that 8HQNO is a bacterial inhibitor (Koshimura, Sabura, Hamada, Otaki & Degucki, 1954) and is a precursor to a number of antimalarial and cancer drugs (Sakai, Minoda, Saito, Akagi, Ueno & Fukuoka, 1955).

Crystal data

8-Hydroxyquinoline-*N*-oxide, C₉H₇O₂N, M.W. 161.16
Monoclinic, space group $P2_1/c$
 $a = 12.1364(4)$, $b = 4.9211(2)$, $c = 13.1384(4)$ Å,
 $\beta = 109.26(1)^\circ$
 $D_{\text{calc}} = 1.449$ g.cm⁻³, $D_{\text{exp}} = 1.46$ g.cm⁻³, $Z = 4$.

Experimental

Samples of pure 8HQNO were provided by Dr S. M. Sax of the Department of Pathology, Western Pennsylvania Hospital, Pittsburgh, Pennsylvania, and Mr Larry Smith of the Department of Chemistry, North Texas State University, Denton, Texas. Further recrystallization or purification of the long yellow needles was not deemed necessary. Cell data were obtained from Weissenberg and precession photographs. Diffractometer data were used for the refinement of cell constants and diffractometer angle settings. The dimensions of a suitable crystal mounted along the *b* axis were: 0.17, 0.22, and 0.15 mm in the *a*, *b*, and *c** directions, respectively. The intensity data were recorded to the limit $\sin \theta/\lambda = 0.64$ on the Oak Ridge computer-controlled diffractometer utilizing Cu $K\alpha$

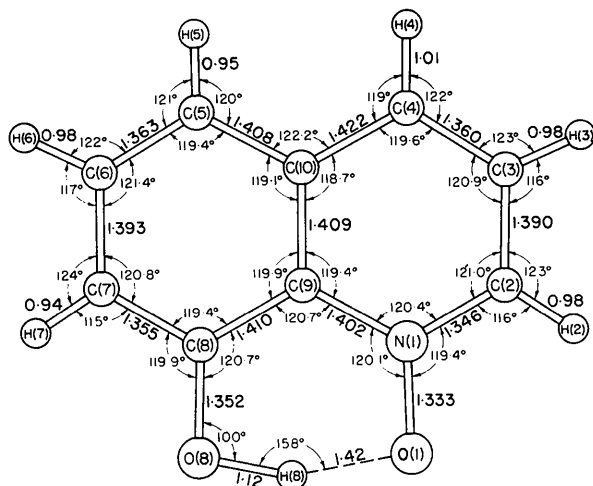


Fig. 1. Atom numbering, bond lengths and angles in 8-hydroxyquinoline-*N*-oxide. Bond lengths between non-hydrogen atoms have e.s.d.'s between 0.002 and 0.003 Å. The e.s.d.'s of the various bond angles (non-hydrogen) range from 0.01 to 0.02°. Distances and angles involving the hydrogen atoms have e.s.d.'s of 0.02 Å and 1°, respectively.

Table 1. Observed and calculated structure factors for 8-hydroxyquinoline-N-oxide

The column heading by OBS and CALC represent values of $10|F_o|$ and $10F_c$, respectively.

Table with multiple columns containing numerical data for structure factors, labeled with 'OBS' and 'CALC' for observed and calculated values. The table includes various indices and values for different reflections.

radiation (1.5418 Å). The following modes were used for data collection: ω step scans for the 0 to 53° range in 2θ , and $\theta-2\theta$ step scans for the 48 to 159° range in 2θ . Two reference reflections, $60\bar{4}$ and $\bar{1}3$, 0,2, were checked periodically to measure instrument and crystal stabilities. A total of 1528 independent reflections were collected with 64 of these having net counts less than their respective standard deviations. The data were corrected for geometric effects (Lorentz and polarization) and for absorption.

Structure determination and refinement

The entire data set was scaled by a Wilson plot and normalized structure factors (E 's) were calculated assuming an overall temperature factor of 4.75 Å². A symbolic sign procedure (Beurskens, 1966) was applied to the set of E 's with magnitude equal to or greater than 1.00. A total of 217 signs were generated by the procedure with two symbolic signs remaining. Of the four possible solutions, only one clearly revealed the quinoline ring when the E maps were synthesized. The atomic coordinates of the quinoline ring atoms and the two exocyclic oxygen atoms were used in a structure factor calculation which resulted in a reliability index (R) of 0.36. The entire data set was included in a full-matrix least-squares refinement using the computer program, *XFLS*, a modification of *ORFLS* (Busing, Martin & Levy, 1962). The atomic factors used are from *International Tables for X-ray Crystallography* (1962). The quantity minimized was $\sum w[|F_o|^2 - k|F_c|^2]^2$. The weighting scheme was derived as follows: to the $\sigma^2(F^2)$ obtained from counting statistics, a quantity $(0.03 F^2)^2$ was added in order to attenuate the weights on very strong reflections. The weight applied to F^2 was $1/\sigma^2(F^2)$. For the initial cycles of least squares, a single scale factor, an overall temperature factor, and atomic coordinates for all non-hydrogen atoms were refined. All the ring atoms were assigned carbon form factors since, at this stage, it had not been determined whether the ring nitrogen atom should be assigned to

ring position (1) or (8). After three cycles of refinement, R was reduced to 0.20. Individual anisotropic parameters for each atom were then calculated and refined for three cycles reducing R to 0.12. Atomic coordinates for the ring hydrogen atoms were then calculated assuming a planar triangular configuration (sp^2) about each ring carbon and a C-H distance of 1.0 Å. The hydrogen atoms were given the anisotropic temperature factors of the ring atoms to which they were attached. The location of the nitrogen atom in the ring was determined by testing each of the two possible nitrogen atom positions in a structure factor calculation. The R factor was calculated for each of the two structures in which the ring atoms attached to an oxygen were alternately assigned as nitrogen. The two R 's thus calculated were 0.068 and 0.078. The position of the nitrogen atom giving the lower R value was accepted as correct. A difference Fourier map was calculated which clearly indicated the position of the hydroxyl atom. Three further cycles of anisotropic refinement in which all the atoms were included reduced R to a final value of 0.053. The observed and calculated structure factors are listed in Table 1. The atomic coordinates and their thermal parameters together with their (estimated standard deviations) e.s.d.'s are listed in Tables 2 and 3, respectively. The projection of the unit cell along b is shown in Fig. 2.

Table 2. Atomic coordinates and e.s.d.'s

| | Fractional coordinates $\times 10^4$ | | |
|-------|--------------------------------------|------------|-----------|
| | x | y | z |
| N(1) | 3472 (1) | 8165 (3) | 4475 (1) |
| O(2) | 3632 (1) | 6591 (3) | 5339 (1) |
| C(2) | 4185 (2) | 7885 (4) | 3889 (2) |
| C(3) | 4041 (2) | 9483 (4) | 2981 (2) |
| C(4) | 3176 (2) | 11376 (4) | 2662 (1) |
| C(5) | 1515 (2) | 13699 (4) | 2988 (2) |
| C(6) | 0804 (2) | 13926 (4) | 3595 (2) |
| C(7) | 0948 (2) | 12263 (4) | 4488 (2) |
| C(8) | 1813 (1) | 10381 (3) | 4789 (1) |
| C(9) | 2569 (1) | 10094 (3) | 4184 (1) |
| C(10) | 2416 (1) | 11747 (3) | 3270 (1) |
| O(8) | 1937 (1) | 8781 (3) | 5657 (1) |
| H(8) | 2648 (34) | 7400 (50) | 5614 (21) |
| H(2) | 4810 (16) | 6533 (40) | 4148 (14) |
| H(3) | 4584 (17) | 9122 (43) | 2582 (15) |
| H(4) | 3052 (17) | 12531 (40) | 2001 (12) |
| H(5) | 1421 (18) | 14863 (37) | 2388 (16) |
| H(6) | 0188 (22) | 15309 (43) | 3442 (18) |
| H(7) | 0489 (18) | 12386 (41) | 4936 (15) |

Discussion

Bond distances and angles are listed in Fig. 1. It is surprising to note that the bond distances and angles in the quinoline ring are unusually similar to those in naphthalene (Cruickshank, 1957). One would expect shortened lengths for the N(1)-C(2) and N(1)-C(9) bonds in view of previous experimental results (see Table 4), and simple valence bond theory calculations (Pauling, 1960) which give values of 1.36 and 1.29 Å for the N(1)-C(9) and N(1)-C(2) bond lengths, respec-

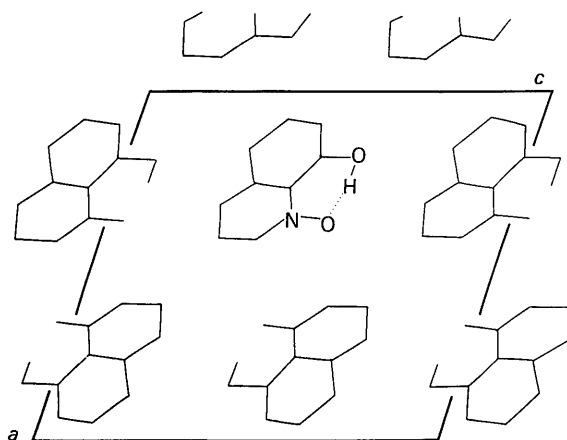


Fig. 2. View of unit cell along b axis.

Table 3. Anisotropic parameters ($\times 10^4$) for 8-hydroxyquinoline-*N*-oxide

The expression used in the form $\exp[-2\pi^2(h^2a^{*2}U_{11} \dots + klb^*c^*U_{23})]$

| | U_{11} | U_{22} | U_{33} | U_{12} | U_{13} | U_{23} |
|-------|------------|------------|------------|------------|------------|------------|
| N(1) | 503 (7) | 534 (9) | 527 (7) | 33 (6) | 171 (5) | 18 (6) |
| O(1) | 681 (7) | 713 (9) | 597 (6) | 189 (6) | 257 (5) | 202 (6) |
| C(2) | 503 (8) | 595 (21) | 646 (9) | 693 (7) | 241 (7) | -2 (8) |
| C(3) | 606 (9) | 649 (12) | 667 (9) | 2 (3) | 333 (8) | -1 (8) |
| C(4) | 636 (9) | 589 (11) | 556 (9) | -45 (8) | 248 (7) | 24 (8) |
| C(5) | 579 (9) | 490 (10) | 644 (10) | 30 (8) | 129 (8) | 25 (8) |
| C(6) | 584 (9) | 530 (11) | 836 (12) | 112 (8) | 190 (9) | -33 (9) |
| C(7) | 598 (9) | 607 (11) | 790 (11) | 55 (8) | 329 (9) | -98 (9) |
| C(8) | 522 (7) | 479 (9) | 502 (8) | -4 (6) | 216 (6) | -86 (6) |
| O(8) | 849 (9) | 766 (10) | 677 (8) | 109 (8) | 447 (7) | 25 (7) |
| C(9) | 430 (7) | 429 (8) | 494 (7) | -18 (6) | 146 (6) | -72 (6) |
| C(10) | 488 (7) | 444 (9) | 511 (8) | -54 (6) | 146 (6) | -47 (7) |
| H(2) | 641 (125) | 795 (113) | 610 (113) | 23 (118) | 246 (99) | 79 (109) |
| H(3) | 990 (161) | 1158 (169) | 977 (152) | -76 (143) | 828 (143) | -161 (135) |
| H(4) | 1094 (169) | 967 (159) | 279 (90) | -143 (140) | 122 (98) | 115 (107) |
| H(5) | 894 (147) | 668 (143) | 780 (139) | 262 (118) | 331 (116) | 74 (116) |
| H(6) | 1572 (224) | 877 (173) | 1181 (178) | 817 (165) | 750 (168) | 400 (139) |
| H(7) | 1179 (172) | 851 (150) | 1174 (165) | 243 (134) | 1045 (156) | 32 (130) |
| H(8) | 4356 (615) | 962 (216) | 1197 (215) | 1301 (299) | 1438 (310) | 464 (171) |

tively. It is possible that the increased lengths of the two C-N bonds (1.402 and 1.346 Å) are due to the existence of the N-O dative bond which undoubtedly is responsible for a strong inductive effect. We are uncertain at this point as to how an inductive effect would cause a lengthening of the C-N bonds if indeed this is the proper correlation. An additional feature of interest is the presence of an intramolecular hydrogen bond and the apparent effect of this bond on the N-O distance. As is shown in Fig. 2, the hydroxyl hydrogen atom is intramolecularly bonded to the *N*-oxide oxygen atom. Table 5 gives the lengths of the *N*-oxide bonds and the intramolecular O...O contacts for 8HQNO and two phenazine compounds, myxin and iodinin. There appears to be an inverse relationship between the N-O and O...O bond lengths as given in the Table.* This trend is reasonable if the O...O bond lengths are at all indicative of hydrogen bond strength, since a stronger hydrogen bond will delocalize the electrons on the *N*-oxide oxygen atom more than a weak hydrogen bond. This is also consistent with the theory of Caron, Palenik, Goldish & Donohue (1964) that a decrease in one of the formal charges across the N-O bond will result in an increase in bond length.

The thermal ellipsoids of all the atoms in the 8HQNO molecule are shown in Fig. 3. The outstanding feature in this diagram is the unusually large thermal ellipsoid for H(8). The thermal motion for this atom is highly anisotropic, the root-mean-square (r.m.s.) deviations along the three principle axes of the ellipsoid being 0.21, 0.36, and 0.70 Å. The axis with

the largest r.m.s. deviation is very nearly perpendicular to the quinoline moiety. That this is so is not unexpected, although the r.m.s. deviation of 0.70 Å is certainly unusually large. In view of the wide range of ellipsoidal shapes for the other hydrogen atoms, the authors are hesitant to infer any additional information from the hydrogen ellipsoids and r.m.s. deviations without the benefit and aid of neutron diffraction data. No anomalous or unusual thermal motions are exhibited by the heavy (non-hydrogen) atoms.

Table 4. Bond lengths (Å) of some quinoline compounds

The following abbreviations are used: 8HQNO for 8-hydroxyquinoline-*N*-oxide (this study); Cu-8HQNO for copper-8-hydroxyquinolinolate (Palenik, 1964a); Zn-8HQNO for zinc-8-hydroxyquinolinolate dihydrate (Palenik, 1964b); AMNQN for 5-acetoxy-6-methoxy-8-nitroquinoline (Sax & Desiderato, 1967); and MNQ for 6-methoxy-8-nitro-5(1*H*)-quinolone (Sax, Desiderato, & Dakin, 1969).

| | 8HQNO | Cu-8HQNO | Zn-8HQNO | AMNQN | MNQ |
|------------|-------|----------|----------|-------|-------|
| N(1)-C(2) | 1.354 | 1.324 | 1.328 | 1.314 | 1.311 |
| C(2)-C(3) | 1.398 | 1.403 | 1.394 | 1.408 | 1.367 |
| C(3)-C(4) | 1.368 | 1.354 | 1.361 | 1.365 | 1.393 |
| C(4)-C(10) | 1.430 | 1.414 | 1.426 | 1.416 | 1.398 |
| C(10)-C(5) | 1.416 | 1.399 | 1.407 | 1.422 | 1.477 |
| C(5)-C(6) | 1.371 | 1.364 | 1.359 | 1.379 | 1.433 |
| C(6)-C(7) | 1.402 | 1.435 | 1.388 | 1.410 | 1.359 |
| C(7)-C(8) | 1.363 | 1.375 | 1.386 | 1.371 | 1.411 |
| C(8)-C(9) | 1.418 | 1.428 | 1.448 | 1.416 | 1.408 |
| C(9)-C(10) | 1.417 | 1.418 | 1.423 | 1.423 | 1.418 |
| C(9)-N(1) | 1.409 | 1.355 | 1.342 | 1.371 | 1.368 |

Table 5. Some bond lengths and angles in 8HQNO, myxin, and iodinin

| | 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 |

* This correlation was suggested to us by the referee who reviewed the original draft of this manuscript. We had at first contended that the correlation was between the N-O and H...O bond lengths. However, as was pointed out by the referee, the relatively high e.s.d.'s of the hydrogen atom coordinates essentially rendered such a correlation meaningless.

Table 6 gives the equation for the least-squares best plane (Schomaker, Waser, Marsh & Bergman, 1959) for the quinoline moiety and the deviations of the atoms from this plane. The ring is quite planar, the largest deviation, 0.014 Å, being due to C(4). The two exocyclic atoms, O(1) and O(8), are off the plane by 0.013 and 0.028 Å, respectively.

Table 6. Distances of atoms from least-squares best plane through quinoline moiety

Equation of plane: $0.4541X + 0.6781Y + 0.3902Z - 6.9269 = 0$
Coefficients are referred to crystallographic axes (X, Y, Z in Å)

| Deviations from the plane (Å × 10 ³) | | | |
|--|-----|-------|-----|
| N(1) | 7 | C(7) | -11 |
| C(2) | 7 | C(8) | -7 |
| C(3) | -5 | C(9) | 3 |
| C(4) | -14 | C(10) | 2 |
| C(5) | 12 | O(1) | 13 |
| C(6) | 7 | O(8) | -28 |

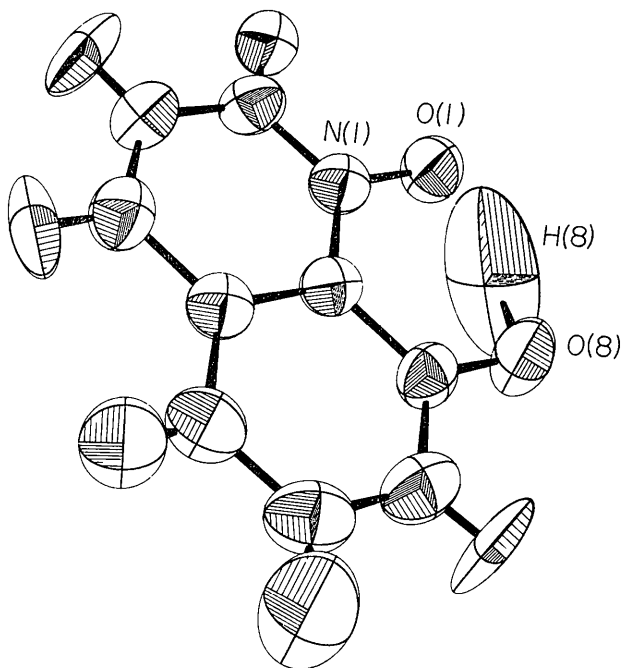


Fig. 3. Thermal motion in 8HQNO. The thermal ellipsoids are scaled to enclose 50% probability.

The only pair of atoms that have an intermolecular distance shorter than the sum of their van der Waals radii is O(1) of one molecule and H(2) of another molecule related by a center of symmetry. This distance is 2.35 Å and is close to 2.52 Å, the normal C-H van der Waals distance.

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