# THE HYDROGEN BOND IN 2-(*N,N*-DIMETHYLAMINO-*N*-OXYMETHYL)-4,6-DIMETHYLOPHENOL

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#### ABSTRACT

The X-ray diffraction studies have been carried out on the monohydrate of 2-(N,N-dimethylamino-N-oxymethyl)-4,6-dimethylophenol (I). The crystals are monoclinic, space group  $P2_1/c$ , with a=21.921(6) Å, b=5.058(2) Å, c=11.748(3) Å;  $\beta=113.66(4)^{\circ}$ , V=1193.1(4) Å<sup>3</sup>, Z=4. The length of the intramolecular OH···O hydrogen bond is 2.541(6) Å. The crystallographic data and the UV and IR absorption spectra indicate that this bond is considerably weaker than that reported previously for 2-(N,N-diethylamino-N-oxymethyl)-4,6-dichlorophenol (II), where a quasisymmetric bridge was found.

## INTRODUCTION

In a previous paper [1] we reported on the formation of a very short intramolecular OHO hydrogen bond in the N-oxide of ortho Mannich base represented by 2-(N,N-diethylamino-N-oxymethyl)-4,6-dichlorophenol (II). This bond shows features of a symmetric bridge from both crystallographic and spectroscopic points of view in spite of the chemical non-equivalence of the oxygen bridge atoms. The great stability of the hydrogen bonds in II are reflected in the  $pK_a$  values as well as in the absence of solvent effects upon the electronic and IR absorption spectra.

As a continuation of our structural studies on *ortho* Mannich bases and their N-oxides we have looked at the N-oxide of 2-(N,N-dimethylaminomethyl)-4,6-dimethylophenol (**III**) as one of the weakest proton donors (the p $K_a$  of the parent phenol is 10.61). X-ray diffraction studies have been performed on the monohydrate crystal which can be grown easily from a water-methanol solution. We have not found conditions for growing anhydrous (**I**). The results obtained in the present paper yield a possibility to discuss the cooperative effects caused by a water molecule attached via one OH group to the oxygen atom of the N-oxy group.

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## EXPERIMENTAL

The compound (I) was synthesized by oxidation of the parent Mannich base (III) in perhydrol. Crystals of the monohydrate were grown from water-methanol solutions; m.p. 120 °C. The density of crystals was measured using the flotation method in chloroethane/1,2-dichloroethane solution.

The IR spectra recorded on a Perkin-Elmer spectrophotometer type 180 and FTIR Bruker 80, and the UV spectra were recorded using a Carl-Zeiss Jena Specord UV VIS spectrophotometer. For X-ray diffraction studies a specimen of  $0.20 \times 0.35 \times 0.60$  mm was cut from a large crystal. The space group and approximate cell dimensions were determined from rotation and Weissenberg photographs. More accurate unit-cell parameters were obtained by least-squares refinement of the observed setting angles  $(22.0 < 2 \theta < 31.0^{\circ})$  for 15 high-order reflections measured with Mo $K_{\alpha}$  radiation on a Syntex P2<sub>1</sub> computer-controlled four-circle diffractometer equipped with a scintillation counter and a graphite monochromator. The diffraction data were collected at room temperature with the  $\theta$ -2 $\theta$  scan technique to  $2\theta_{max} = 50^{\circ}$ . Two check reflections measured after each 50 reflections indicated no decomposition of the crystal. The

#### TABLE 1

Space group Cell constants	$\begin{array}{rcl} P2_{1}/c \\ a = & 21.921(6) \text{ \AA} \\ b = & 5.058(2) \text{ \AA} \\ c = & 11.748(3) \text{ \AA} \\ \beta = & 113.66 & (4)^{\circ} \\ V = & 1193.1 & (4) \text{ \AA}^{3} \end{array}$
Molecular formula	$C_{11}H_{19}NO_3$
Molecular weight	213.3
Molecules per cell	Z=4
Density $(g \text{ cm}^{-3})$	$D_{\rm m} = 1.18$
	$D_{\rm c} = 1.19$
Absorption coefficient $(MoK_{\alpha})$ , $(cm^{-1})$	$\mu = 0.9$
Unique data collected	2076
Data with $l > 3 \sigma(l)$	1333
Total variables	212
$R = \Sigma( F_0  -  F_c ) / \Sigma  F_0 $	0.050
$R_w = [\Sigma w ( F_0  -  F_c )^2 / \Sigma w (F_0)^2]^{1/2}$	0.043
$S = [\Sigma w( F_0  -  F_c )^2 / (n-p)]^{1/2}$	3.548
Final $\Delta \sigma$	$\pm 0.25$
Final $(\Delta/\sigma)_{\rm max}$	0.02 for non-H atoms
	0.025 for H atoms

Summary of data collection and processing parameters

	X	Y	Z	$B_{ m eq}(B_{ m iso})$
0(1)	0.7785(1)	0.3866(4)	0.1142(2)	4.4(2)
0(2)	0.8730(1)	0.4289(3)	0.3277(2)	4.1(2)
O(3)	0.9708(2)	0.4117(9)	0.2411(5)	9.3(5)
N	0.8598(1)	0.6540(4)	0.3847(2)	3.6(2)
C(1)	0.7270(2)	0.4830(5)	0.1401(3)	3.4(3)
C(2)	0.7385(2)	0.6814(5)	0.2300(3)	3.3(2)
C(3)	0.6850(2)	0.7729(6)	0.2540(3)	4.0(3)
C(4)	0.6214(2)	0.6819(6)	0.1917(3)	4.4(3)
C(5)	0.6117(2)	0.4858(7)	0.1021(3)	4.2(3)
C(6)	0.6633(2)	0.3848(6)	0.0759(3)	3.8(3)
C(7)	0.8049(2)	0.8153(6)	0.2880(3)	3.6(3)
C(8)	0.9225(2)	0.8152(7)	0.4365(4)	4.8(4)
C(9)	0.8398(2)	0.5668(8)	0.4851(4)	5.1(4)
C(10)	0.5638(3)	0.7909(12)	0.2177(5)	6.5(5)
C(11)	0.6506(3)	0.1710(9)	-0.0218(5)	5.0(4)
H(1W)	0.937(2)	0.420(9)	0.274(4)	10.8(14)
H(2W)	0.968(2)	0.250(9)	0.210(4)	11.1(15)
H(1)	0.828(2)	0.408(7)	0.197(3)	6.2(9)
H(2)	0.694(1)	0.903(6)	0.321(3)	4.6(7)
H(3)	0.566(2)	0.427(6)	0.053(3)	4.7(8)
H(4)	0.797(1)	0.955(6)	0.333(3)	4.1(7)
H(5)	0.826(1)	0.855(6)	0.225(3)	4.3(7)
H(6)	0.933(2)	0.863(7)	0.365(3)	6.1(9)
H(7)	0.963(2)	0.722(7)	0.508(3)	6.4(9)
H(8)	0.915(2)	0.971(8)	0.481(4)	7.5(12)
H(9)	0.796(2)	0.486(6)	0.439(3)	5.4(9)
<b>H</b> (10)	0.874(2)	0.439(7)	0.550(3)	7.1(10)
H(11)	0.837(2)	0.729(9)	0.539(4)	8.8(11)
H(12)	0.528(2)	0.689(8)	0.179(4)	8.6(15)
<b>H</b> (13)	0.545(2)	0.969(9)	0.170(4)	9.8(17)
H(14)	0.572(2)	0.809(9)	0.301(4)	9.7(18)
H(15)	0.654(2)	0.214(8)	-0.105(4)	8.4(12)
H(16)	0.602(2)	0.123(8)	-0.054(4)	8.8(12)
H(17)	0.683(2)	0.048(8)	0.026(4)	8.7(13)

Positional parameters with  $B_{\rm eq}$  values for non-hydrogen atoms and  $B_{\rm iso}$  for hydrogen atoms

TABLE 2

raw intensity data were corrected for Lorentz and polarization effects, but no absorption or extinction corrections were taken into account. The crystallographic data and the refinement procedures are given in Table 1.

The structure was solved by the direct-phase determination method using the program MULTAN [2] and refined by a full-matrix least-squares technique. The non-hydrogen atoms were recognized from an E-map (calculated for the starting set having the highest combined FOM of 3.0) and the Fourier synthesis. The positions of all hydrogen atoms were determined from the difference Fourier synthesis. A several-cycle refinement of coordinates and thermal parameters (anisotropic for non-hydrogen and isotropic for hydrogen atoms) reduced the R value to 0.043 for the 1333 significant independent reflections with  $F > 6.0 \cdot \sigma(F)$ . The minimized function was  $\sum w(|F_0| - |F_c|)^2$  with  $w = 1/\sigma^2$  (F). Neutral atomic scattering factors for all atoms were taken from a standard source [3], while all calculations were performed on a NOVA 1200 minicomputer with the SYNTEX XTL/XTLE structure determination system [4]. The positional parameters together with the  $B_{eq}$  values for the non-hydrogen atoms, and  $B_{iso}$  for hydrogen atoms are given in Table 2.

# **RESULTS AND DISCUSSION**

The arrangement of molecules in the lattice and the configuration of molecules with numbering of atoms are shown in Figs. 1 and 2. The positional parameters for atoms, the bond lengths, the bond angles and some important torsion angles are collected in Tables 2–5.

In the unit cells there are four equivalent molecules of I which are bound





Fig. 1. Stereoview of the packing in the unit cell.



Fig. 2. Structure of monohydrated molecule I and numbering of atoms.

#### TABLE 3

0(1)-C(1)	1.372(5)	C(7)-N	1.518(4)
C(1)-C(2)	1.405(4)	N-O(2)	1.410(3)
C(2)-C(3)	1.390(5)	N-C(8)	1.501(5)
C(3)-C(4)	1.369(5)	N-C(9)	1.479(5)
C(4) - C(5)	1.400(5)	O(1) - H(1)	1.13(4)
C(4) - C(10)	1.516(7)	O(3) - H(1W)	0.97(5)
C(5)-C(6)	1.384(6)	O(3) - H(2W)	0.89(5)
C(6)-C(1)	1.386(5)		. ,
C(6)-C(11)	1.519(6)		
C(2) - C(7)	1.500(5)		

Bond lengths (Å) with the estimated standard deviations in parentheses

## **TABLE 4**

Bond angles (°) with the estimated standard deviations in parentheses

O(1)-C(1)-C(2)	120.4(3)	C(1)-C(6)-C(11)	120.4(3)
O(1)-C(1)-C(6)	119.4(3)	C(5)-C(6)-C(11)	120.9(4)
C(2)-C(1)-C(6)	120.2(3)	N-C(7)-C(2)	115.5(3)
C(1)-C(2)-C(3)	118.7(3)	O(2)-N-C(7)	109.4(2)
C(1)-C(2)-C(7)	120.9(3)	O(2) - N - C(8)	107.6(3)
C(3)-C(2)-C(7)	120.1(3)	O(2) - N - C(9)	108.7(3)
C(2)-C(3)-C(4)	122.7(3)	C(7) - N - C(8)	109.4(3)
C(3)-C(4)-C(5)	117.1(3)	C(7) - N - C(9)	111.0(3)
C(3)-C(4)-C(10)	121.4(4)	C(8) - N - C(9)	110.7(3)
C(5)-C(4)-C(10)	121.5(4)	H(1W)-O(3)-H(2W)	105(4)
C(4)-C(5)-C(6)	122.6(3)	C(1)-O(1)-H(1)	111(2)
C(1)-C(6)-C(5)	118.7(3)		

with water molecules through the N–O group. The length of the  $O_2 \cdots H - O_3$  hydrogen bond is 2.716(6) Å, which is very close to that found for monohydrate of *N*-methylmorpholine-*N*-oxide [5]. The second OH group of each molecule of water is linked with a neighbouring water molecule via the hydrogen bonding of 2.807(6) Å.

The length of the intramolecular  $O_1 H \cdots O_2$  hydrogen bond is 2.541(6) Å; this corresponds to strong hydrogen bonds. On the other hand, it seems evident that such a bond is markedly weaker than those in the previous *N*-oxide, **II**, where two different hydrogen bonds, 2.40 and 2.42 Å, were detected (two different molecules in the unit cell). The hydrogen bond in **I** is asymmetric; the bridge proton is located closer to oxygen atom  $O_1$ . Furthermore, the remaining bond lengths in the phenolic part of molecule indicate undoubtedly a negligible disturbance of the  $\pi$ -electron charge distribution with respect to free phenol molecule. Most informative is the length of the  $C_1-O_1$  bond which is equal to 1.372(5) Å. It is very close to that of the free phenol molecule and very different

TABLE	5
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Torsion angles (°) with the estimated standard deviations in parentheses

O(1)-C(1)-C(2)-C(7)	7.6(11)
C(1)-C(2)-C(7)-N	- 75.5(10)
C(2)-C(7)-N-C(8)	-178.6(10)
C(2)-C(7)-N-C(9)	- 56.1(10)
C(2)-C(7)-N-O(2)	63.8(10)
C(7)-N-O(2)-H(1)	- 4.1(17)
N-O(2)-H(1)-O(1)	-62(7)
O(2)-H(1)-O(1)-C(1)	27(6)
H(1)-O(1)-C(1)-C(2)	27(3)
C(8)-N-O(2)-H(1)	-123(2)
C(9)-N-O(2)-H(1)	117(2)
C(3)-C(2)-C(7)-N	111.8(10)
C(6)-C(1)-O(1)-H(1)	-154(2)

from that which could be expected for a symmetric OHO bridge (1.32 Å for the previously studied N-oxide, II).

The stability and symmetry of  $O_1 H \cdots O_2$  hydrogen bond is affected by the water molecule. Some competition causes the oxygen atom of the *N*-oxide group to become a weaker proton acceptor. This effect is important in that, in addition to the low acidity of the phenolic moiety itself, the solvent effect on the electronic spectra and the IR spectra in the solid state and in solution can be determined on the basis of the study of acid-base equilibria.



The acid-base equilibria are seen very well in the UV spectra at varying pH, where isosbestic points are clearly visible, and on the potentiometric titration curves in the range of the absorption band for the ionic form (c) (Figs. 3 and 4).

Similarly to the previous N-oxide II, the intramolecular hydrogen bond remains stable in water solution and the stability range of pH is expanded with respect to the  $pK_a$  values of the respective phenol and N-oxide. The  $pK_a$  of the acidic group amounts to 11.1 as compared to 10.61 for phenol, while the  $pK_a$  of the protonated N-oxide group amounts to 3.3 as compared to 4.78 for benzylamine. These shifts are markedly smaller than for the previous N-oxide which formed much stronger hydrogen bonds. This result proves that the attachment of a water molecule is not the unique and, presumably, not the crucial reason



Fig. 3. UV spectra of I at varying pH values in water solutions. pH: (1) 11.7; (2) 11.4; (3) 11.25; (4) 11.20; (5) 11.66; (6) 10.42; (7) 7.87; (8) 1 N HCl.



Fig. 4. Extinction at 34500 cm<sup>-1</sup> (1) and 35500 cm<sup>-1</sup> (2) as a function of pH. The arrows correspond to  $pK_a$  values for 2,4-dimethylphenol [6] and tribenzylamine N-oxide [7].

for a weakening of the hydrogen bonding in **I**. The acidity of the OH group seems to be more important.

An additional confirmation of such a statement results from the solvent effect upon the electronic long-wavelength absorption band. Let us remind readers that, in the case of II, no solvent effect was revealed. In Fig. 5 the correlation between the position of long-wavelength band for I and the acceptor number (AN) [8] of a solvent is presented and compared with that of the Mannich base III.

This result can be interpreted by assuming that solvent molecules attack the lone electron pair and weaken the intramolecular hydrogen bonding. As a consequence, a hypsochromic shift of the absorption band takes place. Interestingly, no solvent effect is observed on the position of the long-wavelength band of the Mannich base itself as the OH…N bridge is less susceptible to a penetration of solvent molecules. The correlation of the band shift with other indices of solvent polarity gives a similar picture, but scattering of experimental points is much greater. This seems to be obvious in the light of the accepted mechanism of interaction in which a particular role is ascribed to the interaction of lone electron pair of the oxygen atom in N–O group with solvent molecules. The studies of the solvent effect clearly show that the OHO hydrogen bond in I is considerably weaker than that in II, independently of the fact that in the crystal of monohydrate I this bond undergoes further weakening by the attached molecule of water.

In the IR spectra of the monohydrate (Fig. 6) one observes a broad absorption above 1700 cm<sup>-1</sup>. The doublet at 3190 and 3340 cm<sup>-1</sup> should be ascribed to water molecules. After deuteration these bands are shifted to 2500 and 2380 cm<sup>-1</sup> (isotopic ratio 1.34). The broad band in the range 2000–3100 cm<sup>-1</sup> with a maximum at about 2300 cm<sup>-1</sup> is related to the OHO intramolecular hydrogen bond. This band is shifted after deuteration to 1750 cm<sup>-1</sup> with an isotopic ratio 1.31. No absorption characteristic for short hydrogen bonds in the low-frequency range was detected. At 1800 cm<sup>-1</sup> an intense overtone band of  $\gamma_{OH}$ 



Fig. 5. Position of the long-wavelength band as a function of acceptor number (AN) [8] of a solvent for the Mannich base (A) and its *N*-oxide (B). (1) CH<sub>3</sub>OH; (2) 2-propanol; (3) CHCl<sub>3</sub>; (4) CH<sub>2</sub>Cl<sub>2</sub>; (5) CH<sub>3</sub>CN; (6) dioxan; (7) CCl<sub>4</sub>; (8) diethylether.



Fig. 6. IR spectrum of monohydrate I in KBr.

vibrations should be distinguished (fundamental band is located at 950 cm<sup>-1</sup>). The  $\delta_{OH}$  band is located at 1270 cm<sup>-1</sup> (after deuteration is shifted to 1010 cm<sup>-1</sup>).

After dehydration the doublet at 3190 and 3340 cm<sup>-1</sup> vanishes while the  $\nu_{OH}$  band ascribed to the intramolecular OHO bridge shifts to lower frequencies and is accompanied by an intensification of the  $\gamma_{OH}$  overtone band at 1800 cm<sup>-1</sup>. It is interesting to note that the IR spectra in chloroform and dichloromethane show the  $\nu_{OH}$  bands with maxima located between those for the monohydrate and CCl<sub>4</sub>. This result is consistent with the solvent effects on the electronic spectra. The strengthening of the OHO hydrogen bonds in I after deuteration is not significant enough to effect the absorption in the fingerprint region which is characteristic of the strongest hydrogen bonds.

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