Fig. 3. Torsion angles in the dioxaphospholane ring (°).

accordance with recent cyclic phosphate structures which have revealed endocyclic C—O distances 0·03–0·04 Å longer than the aliphatic C—O single-bond distance of 1·43 Å. A value of about 120° has been observed for the P—O—C angles in a large number of acyclic phosphate esters (Newton & Campbell, 1974). In contrast to this are the P—O—C ring angles of 111·1 (3) and 111·0 (3)° in (Ig). This contraction of the P—O—C angles is one of the most significant differences between five-membered-ring phosphate esters and larger-ring or acyclic esters. The O(2)—C(2)—C(1) and O(3)—C(1)—C(2) angles of 103·1 (3) and 102·9 (4)° are much smaller than for undistorted tetrahedral coordination. The value of 1·946 (1) Å for the length of the P=S bond, which is axially sited at an angle of 55·9° to the equatorial dioxaphospholane ring, is within the range (1·85–1·96 Å) normally observed for substituted phosphates (Corbridge, 1974, p. 218). P—O(1) is 1·502 (3) Å at an angle of 57·8° to the ring.

The imidazole ring is planar [distances from the best least-squares plane: N(1) −0·008, N(2) −0·004, C(3) 0·007, C(4) −0·001, C(5) 0·005 Å]. Two strong hydrogen bonds are observed in the crystal lattice, O(1)⋯H(1)—N(1) 2·72 and O(1)—H(2)⋯N(2) 2·79 Å, which connect the dioxaphospholane and imidazole systems into chains along c. The O⋯N distances are short for such hydrogen bonds, which have been observed in the range 2·64–3·18 Å (Corbridge, 1974, p. 252).

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# 3-Aminomethyl-5-isoxazolol Monohydrate (Isomuscimol)

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**Abstract.** $C_4H_6N_2O_2 \cdot H_2O$, $M_r = 132 \cdot 12$, m.p. 183·5 °C, orthorhombic, Pbca, $a = 16 \cdot 426$ (5), $b = 10 \cdot 205$ (2), $c = 7 \cdot 568$ (2) Å, $V = 1268 \cdot 6$ Å³, $Z = 8$, $D_m$ (flotation) $= 1 \cdot 39$, $D_x = 1 \cdot 383$ g cm⁻³. The structure was solved by direct methods and refined by least squares to $R = 0 \cdot 045$. The isomuscimol molecules

are zwitterions, and the crystal structure is stabilized by hydrogen bonds.

**Introduction.** 3-Aminomethyl-5-isoxazolol mono-hydrate (isomuscimol) (Hjeds & Krogsgaard-Larsen, 1978) was synthesized as part of an investigation of structure–activity relationships of semi-rigid compounds structurally related to $\gamma$-aminobutyric acid (GABA) and 5-aminomethyl-3-isoxazolol (muscimol) (Krogsgaard-Larsen & Johnston, 1975; Krogsgaard-Larsen, Johnston, Curtis, Game & McCulloch, 1975). Isomuscimol did not inhibit either the GABA metabolizing enzymes (GAD and GABA-T) or the GABA uptake system (Krogsgaard-Larsen, 1978a) and showed no activity with respect to GABA receptors (Krogsgaard-Larsen, 1978b). This X-ray analysis has been carried out in order to confirm the proposed molecular structure and to determine a low-energy conformation of the aminomethyl side chain.

The best crystals of 3-aminomethyl-5-isoxazolol monohydrate were obtained in the last step of the synthesis (Hjeds & Krogsgaard-Larsen, 1978). A crystal (0·22 × 0·22 × 0·50 mm) was sealed in a Lindemann capillary, to avoid dehydration, and mounted on a Nonius CAD-3 diffractometer. The unit-cell parameters were obtained from a least-squares refinement of the $2\theta$ values of 51 automatically centered reflections [Mo $K\alpha$ ($\lambda = 0·71069$ Å)]. Intensity data were measured using graphite-monochromated Mo $K\alpha$ radiation and the $\omega$-scan technique. Of the 1110 independent reflections measured in the range $2·5 \leq \theta \leq 25·0°$, 549 had net intensities $>2·5\sigma(I)$, where $\sigma(I)$ is the standard deviation from counting statistics. These were regarded as observed reflections and were used in the refinement procedure. Lorentz and polarization corrections were applied, but no absorption corrections were made [$\mu$(Mo $K\alpha$) = 1·27 cm$^{-1}$].

Table 1. *Final positional parameters* (*for* C, N, O × 10$^4$, *for* H × 10$^3$)

Numbers in parentheses here and throughout this paper are the estimated standard deviations of the last significant digits.

| | $x$ | $y$ | $z$ |
|---|---|---|---|
| O(1) | 4310 (1) | 8522 (2) | 8443 (3) |
| O(2) | 3220 (1) | 9669 (2) | 9403 (3) |
| O($W$) | 3775 (2) | 1851 (2) | 7546 (4) |
| N(1) | 3327 (2) | 4408 (3) | 7857 (4) |
| N(2) | 4551 (2) | 7195 (3) | 8230 (4) |
| C(3) | 3940 (2) | 6501 (3) | 8803 (4) |
| C(4) | 3290 (2) | 7278 (3) | 9373 (5) |
| C(5) | 3536 (2) | 8539 (3) | 9139 (4) |
| C(6) | 4019 (2) | 5048 (3) | 8781 (6) |
| H(41) | 279 (2) | 705 (3) | 980 (4) |
| H(61) | 451 (2) | 485 (3) | 812 (5) |
| H(62) | 401 (2) | 471 (3) | 998 (5) |
| H(71) | 340 (2) | 349 (4) | 777 (4) |
| H(72) | 286 (2) | 464 (3) | 840 (5) |
| H(73) | 328 (2) | 476 (3) | 670 (5) |
| H($W$1) | 432 (3) | 190 (3) | 747 (5) |
| H($W$2) | 366 (2) | 117 (4) | 818 (5) |

The structure was solved using the *MULTAN* system (Main, Woolfson, Lessinger, Germain & Declercq, 1974), which unambiguously revealed the complete non-hydrogen-atom skeleton. The positions of the eight H atoms were obtained from a difference electron-density map (0·4–0·9 e Å$^{-3}$). Full-matrix least-squares refinement of this model employing anisotropic temperature factors for the non-hydrogen atoms, fixed isotropic temperature factors for the H atoms and an overall scale factor converged at $R = 0·045$ ($R_w = 0·048$).

Refinement was carried out minimizing $\sum w(|F_o| - |F_c|)^2$, where $w = 1/\sigma^2(I)$. The X-ray atomic scattering factors for O, N and C were those of Cromer & Mann (1968) and for H those of Stewart, Davidson & Simpson (1965). All calculations were carried out using the *XRAY* system (1972). The final atomic coordinates are given in Table 1.*
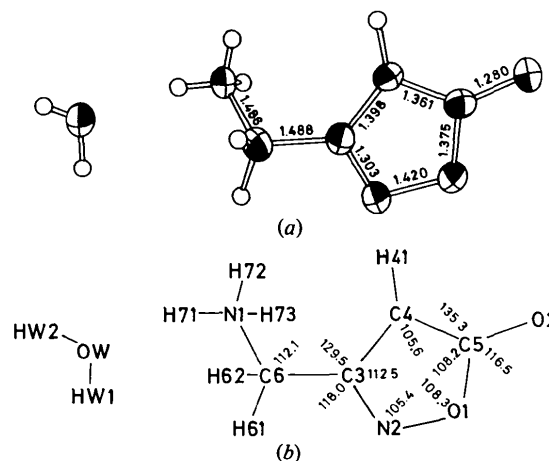
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Fig. 1. (a) Bond lengths (Å) between non-hydrogen atoms. The intramolecular distances (Å) from N(1) to O(1), O(2) and N(2) are 4·520 (4), 5·498 (4) and 3·494 (4), respectively. E.s.d.'s are 0·003–0·005 Å. Thermal ellipsoids for non-hydrogen atoms scale to 50% probability; hydrogen atoms are represented as spheres of arbitrary radius. Drawings were made by *ORTEP* II (Johnson, 1971). (b) The atomic numbering and bond angles (°) between non-hydrogen atoms. E.s.d.'s are 0·2–0·5°.
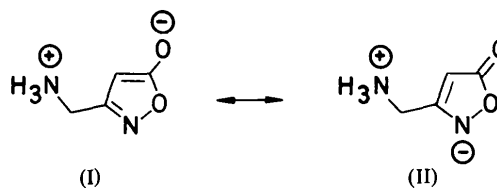


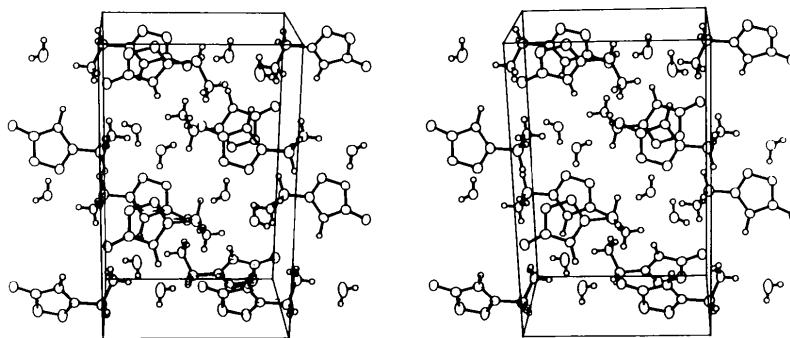Fig. 2. The two main resonance structures contributing to the hybrid molecule.

Fig. 3. Stereodiagram illustrating the molecular packing. The view is down $c$, with $b\leftarrow$ and $a\uparrow$.

Table 2. *Deviations* (Å) *of non-hydrogen atoms from the least-squares plane*

The atoms marked with an asterisk were used to calculate the plane of the isoxazole ring.

Equation: $6\cdot3178x + 0\cdot0752y + 6\cdot9856z - 8\cdot6828 = 0$

| | | | |
|---|---|---|---|
| O(1)* | 0·002 | O(2) | −0·007 |
| N(2)* | −0·004 | N(1) | −1·058 |
| C(3)* | 0·004 | C(6) | 0·029 |
| C(4)* | −0·002 | | |
| C(5)* | −0·001 | | |

Table 3. *Selected interatomic distances* (Å) *and angles* (°)

Symmetry code
(i)   $x, y, z$
(ii)  $\frac{1}{2} - x, -\frac{1}{2} + y, z$
(iii) $x, 1\frac{1}{2} - y, -\frac{1}{2} + z$
(iv) $1 - x, -\frac{1}{2} + y, \frac{1}{2} - z$
(v)  $x, -1 + y, z$

| $A-H\cdots B$ | $A-H$ | $H\cdots B$ | $A\cdots B$ | $\angle AHB$ |
|---|---|---|---|---|
| N(1)–H(71)$\cdots$O($W^i$) | 0·95 (4) | 1·79 (4) | 2·720 (4) | 167 (3) |
| N(1)–H(72)$\cdots$O(2$^{ii}$) | 0·90 (3) | 1·93 (3) | 2·811 (4) | 164 (3) |
| N(1)–H(73)$\cdots$O(2$^{iii}$) | 0·95 (4) | 1·83 (4) | 2·784 (4) | 176 (3) |
| O($W$)–H($W$1)$\cdots$N(2$^{iv}$) | 0·90 (4) | 1·95 (4) | 2·833 (4) | 166 (4) |
| O($W$)–H($W$2)$\cdots$O(2$^v$) | 0·86 (4) | 1·93 (4) | 2·787 (3) | 170 (4) |

**Discussion.** The conformation of the molecule, the molecular dimensions, the thermal ellipsoids and the atomic numbering are shown in Fig. 1. As anticipated from its p$Ka$ values (2·6 and 9·0) (Hjeds & Krogsgaard-Larsen, 1978) the compound crystallizes in the zwitterionic form. From the bond length values it is evident that there is a significant resonance effect within the isoxazolol ring, the two forms (I) and (II) (Fig. 2) making important contributions to the hybrid molecule. Table 2 lists the displacements of the non-hydrogen atoms from the least-squares plane through the isoxazole ring. The torsion angle C(4)—C(3)—C(6)—N(1) is ±53·2 (5)°. The corresponding torsion angles found in three crystallographically independent muscimol molecules are ±120·8 (Brehm, Hjeds &

Krogsgaard-Larsen, 1972), ±113·7 and ±109·5° (Brehm, 1978). The packing of the molecules in the crystals is illustrated in Fig. 3. The dimensions of the hydrogen bonds are summarized in Table 3. Each water molecule is hydrogen bonded to three different isomuscimol molecules, two of which act as acceptors and one as a donor. The crystal structure is further stabilized by hydrogen bonding between one iso-muscimol molecule and two symmetry-related iso-muscimol molecules. All other intermolecular contacts correspond to van der Waals interactions.

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