

Crystal Structures of the Reaction Product from Ethyl Acetoacetate and Hydroxylamine, $C_8H_8N_2O_3 \cdot H_2O$, and its Hexaaquamagnesium Salt, $Mg(H_2O)_6^{2+}(C_8H_7N_2O_2^-)_2 \cdot 4H_2O$

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Simonsen, O., Møgelmoose, M.-L. H. and la Cour, A., 1999. Crystal Structures of the Reaction Product from Ethyl Acetoacetate and Hydroxylamine, $C_8H_8N_2O_3 \cdot H_2O$, and its Hexaaquamagnesium Salt, $Mg(H_2O)_6^{2+}(C_8H_7N_2O_2^-)_2 \cdot 4H_2O$. Acta Chem. Scand. 53: 432–435. © Acta Chemica Scandinavica 1999.

The crystal structures of the two title compounds were determined by single crystal X-ray diffraction. The space group for the reaction product from the reaction between ethyl acetoacetate and hydroxylamine [3-methyl-4-(3-methylisoxazol-5-yl)isoxazol-5(2*H*)-one monohydrate] is $P2_1/c$, No. 14, $Z=4$. At 293 K $a=7.102(1)$, $b=13.113(2)$, $c=10.502(1)$ Å, $\beta=107.180(8)^\circ$ and $V=934.3(1)$ Å³. The space group for the hexaaquamagnesium salt [hexaaquamagnesium 3-methyl-4-(3-methylisoxazol-5-yl)-5-oxo-5*H*-isoxazol-2-ate tetrahydrate] is $C2/m$, No. 12, $Z=2$. At 293 K $a=18.213(1)$, $b=6.8125(3)$, $c=10.8623(4)$ Å, $\beta=101.516(4)^\circ$, $V=1320.6$ Å³. The structure of the isoxazolone compound previously determined from IR and UV spectra has been confirmed. The anion in the hexaaquamagnesium salt has a twisted conformation compared with the corresponding protonated form.

The reaction between ethyl acetoacetate and hydroxylamine has been known for more than a century. In 1891. Hantzsch¹ wrongly assigned the product from the reaction between ethyl acetoacetate and hydroxylamine as 3-methyl-5-isoxazolone (**1**) (Fig. 1). Later on, various salts of the reaction product were prepared and investigated by Uhlenhuth,² who proposed that the salts were dimers formed from 2 mol equiv. of **1** by release of water;

no structure was proposed for the dimeric product anion $C_8H_7N_2O_3^-$. The reaction was reinvestigated by Donleavy and Gilbert³ in 1937. They concluded that **1** was not prepared as described by Hantzsch and stated that the only possible reaction product from ethyl acetoacetate and hydroxylamine was 3-methyl-4-(3-methyl-2,5-dihydroisoxazol-4-ylidene)isoxazol-5(4*H*)-one **2** (Fig. 1). Later, Khromov⁴ identified the reaction product as com-

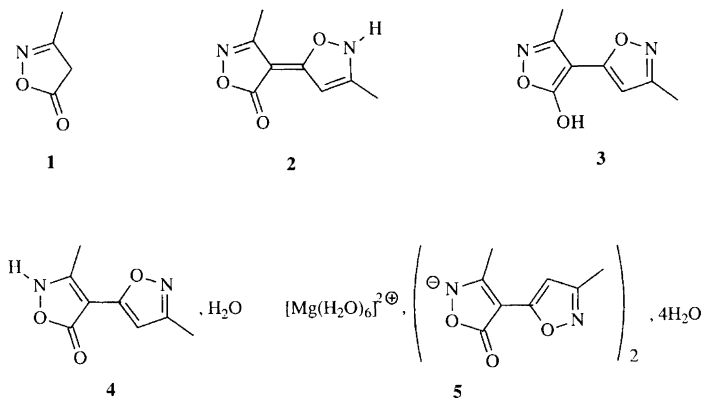


Fig. 1. Structural formulas for **1**, **2**, **3**, **4** and **5**.

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pound 3. In 1963 Inoue and Iguchi⁵ again reinvestigated the reaction, and from IR and UV spectra they assigned the structure 4 (Fig. 1) to the reaction product. In a project aimed at preparing new ligands, we carried out the reaction between ethyl acetoacetate and hydroxylamine. As a result of the present structure determination, the product was identified as 4 in agreement with the conclusion drawn by Inoue and Iguchi. Compound 4 may be deprotonated during the formation of salts such as the hexaaquamagnesium salt 5 (Fig. 1) reported herein.

Results and discussion

Selected bond lengths and angles for 4 are given in Table 1, the molecular structure is shown in Fig. 2, and the packing diagram in Fig. 3.

Compound 4 is an acid, the pK_a value of which was established to be 2.3 by titration. Its acidic hydrogen atom is attached to N in the isoxazolone moiety. The linkage C(2)–C(4) (Fig. 2) is a formal single bond. In each ring, the ring atoms have distances less than 0.007(4) Å from the two least-squares planes which they define. The dihedral angle between the ring planes of 1.4(1)° shows that the molecule is almost planar; thus π electron delocalization between the two five-membered rings is possible.

The bond distance C(2)–C(4) of 1.442(4) Å indicates weak π -electron delocalization and is in good agreement with the standard bond distance for a C_{sp^2} – C_{sp^2} conjugated bond given by Allen *et. al.*⁶ [C_{sp^2} – C_{sp^2} , conjugated: 1.455(11) Å].

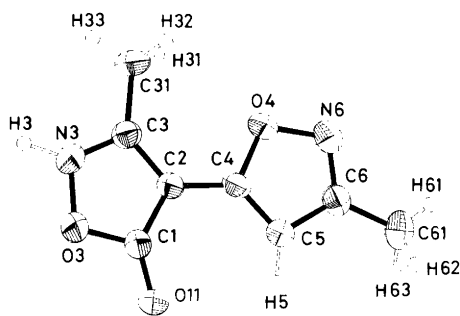


Fig. 2. Displacement ellipsoid drawing of 4 with ellipsoids drawn at the 50% probability level.

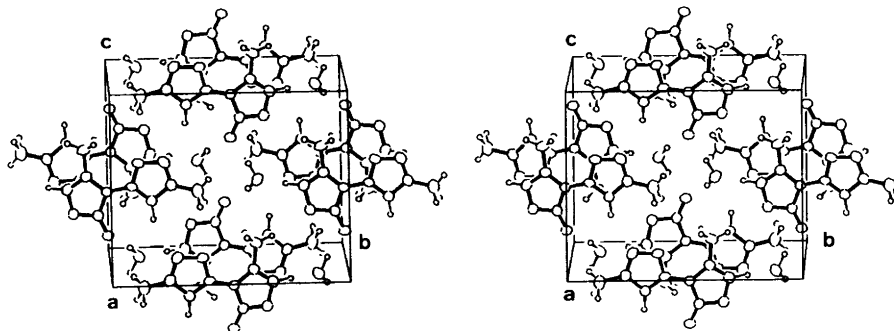


Fig. 3. Stereo drawing of one unit cell of 4.

Table 1. Selected bond distances (Å) and a bond angle (°) for 4 and 5.

Bond/angle	4	5
N(3)–O(3)	1.400(3)	1.425(8)
O(3)–C(1)	1.390(3)	1.364(7)
C(1)–O(11)	1.226(4)	1.243(8)
C(1)–C(2)	1.411(4)	1.411(9)
C(2)–C(3)	1.390(4)	1.410(8)
C(3)–N(3)	1.323(4)	1.324(9)
C(3)–C(31)	1.495(4)	1.48(1)
C(2)–C(4)	1.442(4)	1.445(8)
C(4)–O(4)	1.359(3)	1.346(7)
O(4)–N(6)	1.431(3)	1.435(6)
N(6)–C(6)	1.309(4)	1.298(9)
C(6)–C(5)	1.415(4)	1.405(8)
C(5)–C(4)	1.349(4)	1.367(9)
C(6)–C(61)	1.495(5)	1.51(1)
O(3)–N(3)–C(31)	110.5(2)	104.9(5)

The crystal structure of 4 (Fig. 3) is stabilized by the crystal water $H_2O(8)$; O(8) is a hydrogen bond acceptor for a short hydrogen bond involving the acidic H(3). Both in 4 and 5 carbonyl oxygen O(11) is a hydrogen bond acceptor for two hydrogen bonds (Table 2).

Crystallization trials on several salts (Na^+ , K^+ , NH_4^+ , Cu^{2+} , Ni^{2+} , anilinium, 2-pyridylammonium, 4-pyridylammonium) of the basic form of 4 were tried; however, only the hexaaquamagnesium salt 5 gave crystals suitable for single crystal diffraction experiments. Selected bond distances and angles are given in Table 1, the structure of the anion is shown in Fig. 4 and the packing diagram in Fig. 5.

The hexaaquamagnesium ion is required to have crystallographic $2/m$ symmetry; the anion is required to have crystallographic m symmetry. The release of a proton from 4 has a drastic influence on the overall structure; since as a result of formation of the anion one of the five-membered rings is rotated 180° about the C(2)–C(4) bond. Significant changes in bond lengths as a result of deprotonation (Table 1) indicate displacement of electron density in the ring with the negative charge, probably a shift of negative charge from N(3) to O(11). The ring angle O(3)–N(3)–C(3) is diminished by the proton release (Table 1) corresponding to a similar observa-

Table 2. Distances (Å) and angles (°) in the hydrogen bonds in **4** and **5**.

D-H...A;(D,A)=O/N	D...A	D-H	H...A	∠(D-H...A)
4				
O(8) ^a -H(81) ^b ...O(11) ^c	2.773(3)	0.92(4)	1.93(4)	168(4)
O(8) ^a -H(82)...O(11) ^d	2.838(3)	1.02(5)	1.75(5)	175(4)
N(3) ^a -H(3) ^a ...O(8) ^a	2.643(4)	1.04(4)	1.60(4)	177(3)
5				
O(7) ^e -H(71) ^e ...O(7) ^f	2.957(5)	0.70	2.44	133
O(7) ^e -H(72) ^e ...N(6) ^f	2.856(6)	0.99	2.07	135
O(8) ^e -H(81) ^e ...N(3) ^g	2.861(7)	0.89	1.92	171
O(8) ^e -H(82) ^e ...O(11)	2.861(7)	0.75	2.12	166
O(9) ^e -H(91) ^e ...O(11)	2.764(6)	1.01(5)	1.81(5)	156(4)
O(9) ^e -H(92) ^e ...O(9) ^h	2.861(7)	0.74(5)	2.13(5)	175(5)

^a(*x*, 3/2 - *y*, 1/2 + *z*). ^b(1 - *x*, 1 - *y*, 1 - *z*). ^c(*x*, *y*, 1 + *z*). ^d(1 - *x*, 1 - *y*, *z*). ^e(1 + *x*, 1/2 + *y*, *z*). ^f(1/2 - *x*, 1/2 + *y*, -*z*). ^g(*x*, 1 - *y*, *z*). ^h(*x*, 1 + *y*, *z*). ⁱ(1 - *x*, *y*, 1 - *z*).

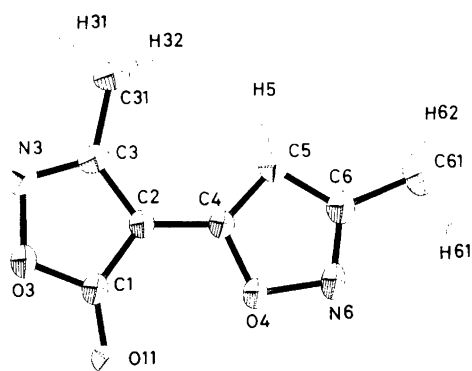


Fig. 4. Displacement ellipsoid drawing of the anion in **5** with ellipsoids drawn at the 50% probability level.

tion for 3-amino-4-nitro-1,2-dihydro-5-pyrazolone⁷ [109.5(1)°, 108.7(1)° → 105.3(1)°].

The crystal structure of **5** (Fig. 5) is stabilized by

hydrogen bonds involving all water molecules and N(6), O(11) in the anion (Table 2). O(7) and O(8) are oxygen atoms in the hexaaquamagnesium ion and H₂O(9) is the crystal water.

The Mg²⁺-O coordination distances [Mg²⁺-O(7), 2.052(4) Å; Mg²⁺-O(8), 2.072(4) Å] are in agreement with corresponding distances found in other hexaaquamagnesium salts.⁸⁻¹² In the crystal structure of **5** the cations and the anions form alternating layers which stack parallel to the plane (001).

Experimental

Crystal preparation of 4. A 33% aqueous solution of NaOH (50 ml) was added to 23.04 g of hydroxylamine hydrochloride. The mixture was heated to 43 °C. Ethyl acetoacetate (23 ml) was added with stirring. The temperature rose to 73 °C. The mixture was refluxed 48 h at

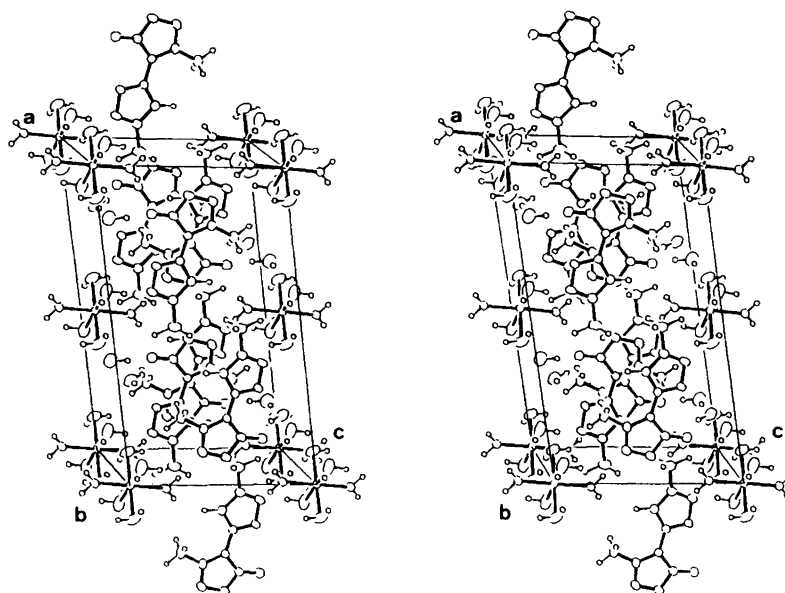


Fig. 5. Stereo drawing of one unit cell of **5**.

Table 3. Crystallographic data for **4** and **5**.

	4	5
Formula	C ₈ H ₈ N ₂ O ₂ , H ₂ O	Mg ²⁺ , (C ₈ H ₇ N ₂ O ₂ ⁻) ₂ , 10H ₂ O
Formula weight	198.178	530.77
λ/Å	1.54178	1.54178
T/K	293	293
Crystal dimension/ mm	0.16 × 0.17 × 0.37	0.16 × 0.14 × 0.092
Crystal system	Monoclinic	Monoclinic
Space group	P2 ₁ /c	C2/m
a/Å	7.102(1)	18.213(1)
b/Å	13.113(2)	6.8125(3)
c/Å	10.502(1)	10.8623(4)
β/°	107.180(8)	101.516(4)
V/Å ³	934.3(1)	1320.6(1)
Z	4	2
D _c /g cm ⁻³	1.409	1.335
μ/cm ⁻¹	11.35	12.91
Transmission factor min./max.	0.7618/ 0.8632	0.8504/ 0.9444
No. of independent reflections	1777	1458
No. of observed reflections ^a	1537	1132
Standard intensity reflection every 90 min	I(33̄5)	I(82̄1)
Standard intensity decrease (%)	12	5
R(F _o) ^b	0.049	0.070
R _w (F _o) ^c	0.051	0.078
Weighting w	1	1
No. of parameters refined	167	125
Max. and min. Δρ/e Å ⁻³	0.21/−0.19	1.20/−0.43

^aCriteria for observed reflections $I > 2.5\sigma(I)$. ^b $R = \sum(|F_o| - |F_c|) / \sum|F_o|$. ^c $R_w = [\sum w|F_o - F_c|^2 / \sum wF_o^2]^{1/2}$.

45 °C, after which it was cooled in an ice–water bath. Aqueous HCl (12 M) was added until pH 1 was reached. Crystals of **4** separated, and were recrystallized from hot water. Crystals of **4** suitable for single crystal work were obtained by slow cooling.

Crystal preparation of 5. An aqueous solution of **4** was added to an excess of magnesium hydroxide carbonate [Mg(OH)₂, 4MgCO₃, 5H₂O]. The suspension was stirred and heated to boiling for about 5 min, after which it was cooled and centrifuged. The liquid phase was then allowed to evaporate at room temperature. Very thin needles separated. Recrystallization from water gave crystals suitable for single crystal work.

Structure determination. Crystal data and parameters of the data collection are compiled in Table 3. Unit cell parameters were determined by centering of 22 reflections (**4**) or 21 reflections (**5**). The data were collected

on an Enraf–Nonius CAD4-F diffractometer, using graphite monochromated Cu Kα radiation and ω/2θ scans. The reflections were collected within the ranges 2 ≤ θ ≤ 70°, +h, +k, ±l (**4**) and 2 ≤ θ ≤ 74°, +h, +k, ±l (**5**) and corrected for Lp-effects, absorption¹³ and decay¹³ as the intensity of a standard reflection decreased by 12% (**4**) and 5% (**5**) during the data collection.

The structures of **4** and **5** were solved by direct methods using SHELXS 86.¹⁴ The non-H atoms were refined anisotropically by full-matrix least-squares methods. Initial positional parameters for all H-atoms were from Δρ maps and H-atoms were refined isotropically for **4**.

The positions of the H-atoms in the water molecules in **5** were not well defined. Fixed temperature factors were used for all H-atoms in **5**, along with fixed H-atom positions [except for H(91) and H(92)]. Refinements and geometric calculations were performed with the Xtal 3.2 program suite.¹⁵ The least-squares refinements were based on *F* with atomic scattering factors taken from *International Tables for X-ray Crystallography*.¹⁶

Acknowledgements. The authors thank Rita Hazell, Department of Chemistry, Aarhus University, and Oren P. Anderson, Department of Chemistry, Colorado State University, for good advice.

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Received November 24, 1998.