Oximation of Acetyl(hydroxyimino)acetone: Nuclear Magnetic Resonance Spectroscopic, Chemical, and *X*-Ray Crystallographic Studies of the Reaction Products

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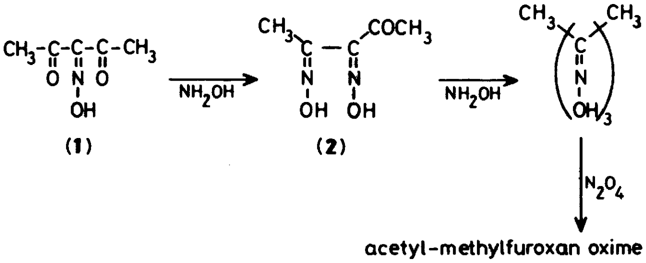
The oximation of acetyl(hydroxyimino)acetone (**1**) with hydroxylamine affords a mixture of oxime derivatives. The products obtained by the action of an equimolar amount of hydroxylamine on (**1**) are the two 3,5-dimethyl-5-hydroxy-4-hydroxyimino-2-isoxazoline isomers (**3a** and **b**). The main products obtained by the action of an excess of hydroxylamine on (**1**) are two pentane-2,3,4-trione trioxime isomers (**4a** and **b**) and a little amount of 4-acetyl-3-methylfuroxan oxime (**5**). N.m.r. and chemical data of all these derivatives are discussed in order to determine both structures and configuration. *X*-Ray analysis of (**3a**), (**4a**), and (**5**) are also reported.

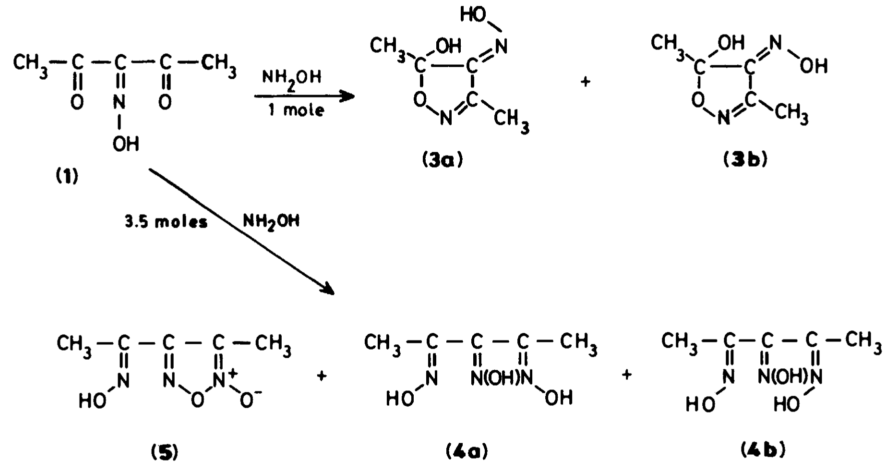
Our continuing interest in the chemistry of furoxans led us to investigate the structures of the intermediates involved in their formation. As early reported by Tappi,[1] an oxime derivative of acetyl(methyl)furoxan can be prepared according to the synthetic pathway shown in Scheme 1. In this paper a ^{13}C n.m.r. and *X*-ray study of the products obtained by reacting (**1**) with the amounts of hydroxylamine indicated in Scheme 2 is reported. We demonstrate that (a) the product obtained by the action of an equimolar amount of hydroxylamine on acetyl(hydroxyimino)acetone (**1**) is not acetylmethylglyoxime (**2**) as previously reported,[2,3] but a mixture of the two (*Z*)-(**3a**) and (*E*)-(**3b**) isomers of 3,5-dimethyl-5-hydroxy-4-hydroxyimino-2-isoxazoline and (b) the product obtained with an excess of reagent is a mixture of three compounds (**4a**), (**4b**), and (**5**). This latter reaction was previously studied but only one trioxime was described.[2,4] The products formed upon Ce^{4+} oxidation of (**3a** and **b**) and (**4a** and **b**), and N_2O_4 oxidation of (**4a** and **b**), are also briefly discussed.



Scheme 1.

Results and Discussion

(a) *Chemical and N.m.r. Studies.*—The reaction between (**1**) and an equimolar amount of hydroxylamine hydrochloride in water containing sodium acetate afforded, after one night at 5 °C, crystals which were collected by filtration. Additional product was recovered by ether extraction of the neutralized reaction solution. T.l.c. of the individual crops showed the



Scheme 2.

Table 1. ^{1}H and ^{13}C n.m.r. data ([^{2}H$_6$]DMSO) of (**3a**) (second eluted)

δ_H		δ_C(p.p.m.)	
1.65	(3 H, s, CH_3–C–O)	9.7	(q, $^{1}J_{C-H}$ 130.0 Hz, 3-CH_3)
1.96	(3 H, s, CH_3–C=N)	21.7	(dq, $^{1}J_{C-H}$ 129.0, $^{3}J_{C-C-OH}$ 5.5 Hz, 5-CH_3)
7.20	(1 H, s, HO–C–O)		
12.05	(1 H, s, HO–N=)	100.9	(dq, $^{2}J_{C-CH_3}$ 5.0, $^{2}J_{C-OH}$ 3.9 Hz, 5-C)
		151.8	(q, $^{2}J_{C-CH_3}$ 7.7 Hz, 3-C)
		157.8	(m, 4-C)

^{1}H and ^{13}C n.m.r. data ([^{2}H$_6$]DMSO) of (**3b**) (first eluted)

1.46	(3 H, s, CH_3–C–O)	14.4	(q, $^{1}J_{C-H}$ 130.5 Hz, 3-CH_3)
2.28	(3 H, s, CH_3–C=N)	24.5	(dq, $^{1}J_{C-H}$ 128.6, $^{3}J_{C-C-OH}$ 5.5 Hz, 5-CH_3)
7.27	(1 H, s, HO–C–O)		
12.15	(1 H, s, HO–N=)	102.5	(dq, $^{2}J_{C-CH_3}$ 5.0, $^{2}J_{C-OH}$ 3.9 Hz, 5-C)
		147.5	(q, $^{2}J_{C-CH_3}$ 7.7 Hz, 3-C)
		154.8	(m, 4-C)

Table 2. ^{1}H and ^{13}C n.m.r. data ([^{2}H$_6$]DMSO) of (**4a**)

δ_H		δ_C(p.p.m.)	
1.84	(3 H, s, 5-CH_3–C=N)	9.8	(q, $^{1}J_{C-H}$ 129.4 Hz, 1-CH_3)
1.97	(3 H, s, 1-CH_3–CN)	14.1	(q, $^{1}J_{C-H}$ 129.4 Hz, 5-CH_3)
10.94	(1 H, s, 4-C=N–OH)	149.3	(dq, $^{3}J_{C=NOH}$ 8.0, $^{2}J_{C-C-H}$ 7.0 Hz, 4-C)
11.60	(1 H, s, 3-C=N–OH)		
11.63	(1 H, s, 2-C=N–OH)	152.7	(dq, $^{3}J_{C=NOH}$ 8.0, $^{2}J_{C-C-H}$ 7.0 Hz, 2-C)
		153.1	(m, 3-C)

^{1}H and ^{13}C n.m.r. data ([^{2}H$_6$]DMSO) of (**4b**)

1.87	(3 H, s, 5-CH_3–C=N)	9.5	(q, $^{1}J_{C-H}$ 128.9 Hz, 1-CH_3)
1.95	(3 H, s, 1-CH_3–C=N)	18.3	(q, $^{1}J_{C-H}$ 129.5 Hz, 5-CH_3)
10.34	(1 H, s, 4-C=N–OH)	148.2	(qt, $^{2}J_{C-C=H} = {}^{3}J_{C=NOH}$ 7.0 Hz, 4-C)
11.48	(1 H, s, 2-C=N–OH)		
11.54	(1 H, s, 3-C=N–OH)	150.7	(qt, $^{2}J_{C-C-H} = {}^{3}J_{C=NOH}$ 7.0 Hz, 2-C)
		152.6	(m, 3-C)

^{1}H and ^{13}C n.m.r. data ([^{2}H$_6$]DMSO) of (**5**)

2.19	(3 H, s, CH_3)	10.1	(q, $^{1}J_{C-H}$ 133.3 Hz, CH_3)
2.28	(3 H, s, CH_3)	10.4	(q, $^{1}J_{C-H}$ 130.0 Hz, CH_3)
12.36	(1 H, s br, OH)	112.0	(q, $^{2}J_{C-C-H}$ 7.7 Hz, $C=\overset{+}{N}-O^-$)
		146.9	(dq, $^{2}J_{C-C-H}$ 6.6, $^{3}J_{C=N-OH}$ 8.8 Hz, C=N–OH)
		154.8	(qt, $^{3}J_{C-C-CH_3} = {}^{3}J_{C-C-CH_3} = 3.0$ Hz, C=N–O–)

presence of two main components. Flash chromatography of the combined crops gave pure compounds (19%, first eluted, R_F 0.44; 81%, second eluted, R_F 0.35). We obtained similar results by reacting hydroxylamine hydrochloride and (**1**) in water.

The main product of the reaction (the second eluted) recrystallized from ether–light petroleum (b.p. 40—60 °C) as crystals. The m.p. (with decomposition) of this product, measured on a capillary apparatus, was erratic in the range 115—130 °C depending on the heating rate* (see Experimental section). The analytical data and mass spectrum, *m/e* 144 (M^+), were in keeping with the molecular formula $C_5H_8N_2O_3$. The i.r. spectrum (KBr, CH_3CN) showed hydroxy group absorption (3 500—2 500 cm^{-1}) but did not show any absorption in the carbonyl region (1 600—1 800 cm^{-1}). Further evidence that this product would not have structure (**2**) came from the detection of a signal at δ 7.20 (1 H) in the ^{1}H n.m.r. spectrum (see Table 1). Although this proton was easily exchangeable with D_2O it could not be assigned to an oxime proton (unlike the signal at δ 12.05) since it has been shown for a variety of α-dioximes and mono-oximes (including hydroxyiminoketones) that this resonance ranges, in [^{2}H$_6$]DMSO, between δ 13.3 and 8.6.[6–8]

In order to elucidate the structure a detailed ^{13}C n.m.r. study was undertaken (see Table 1). The resonance at δ 100.9 p.p.m. can be assigned to an *sp*^{3} –O–C–O–,[9] and is central to our argument. The signals at δ 157.8 and 151.8 p.p.m. are in agreement with the presence of –C=N–O functions, and finally the signals at δ 21.7 and 9.7 p.p.m. can be assigned to two methyl groups. On the basis of the multiplicity patterns observed in the ^{1}H coupled and ^{1}H selectively decoupled spectra, we suggest for the main product the structure (**3a**). This compound is, in our opinion, the same as that isolated by Wolff[3] and by Ponzio,[2] to which structure (**2**) was assigned. The discrepancy between the m.p.s quoted by these authors [lit.,[3] 128 °C (decomp.) from water; lit.,[2] m.p. 141 °C (decomp.) from ether–light petroleum] can be explained by a difference in crystallization solvent[2] and the rate of measurement.*

The minor product, recrystallized from ether–light petroleum (b.p. 40—60 °C), gave crystals. The m.p. (with decomposition) of this compound was erratic in the range 105—115 °C again depending on the heating rate* (see Experimental section). Analytical data and the mass spectrum, *m/e* 144 (M^+), were in keeping with the molecular formula $C_5H_8N_2O_3$. In this case too the i.r. spectrum (KBr, CH_3CN) showed the presence of OH groups, and the absence of a C=O function. The ^{1}H n.m.r. and ^{13}C coupled, decoupled, and ^{1}H selectively decoupled spectra of this latter compound were very similar to those of the main product of the reaction apart from small differences in the chemical shifts. On these bases we suggest structure (**3b**) for it.

Thus, the two products obtained in the oximation of acetyl(hydroxyimino)acetone (**1**) are the two possible geometrical isomers of 3,5-dimethyl-5-hydroxy-4-hydroxyimino-2-isoxazoline. The reaction of (**1**) with 3.5 mol of hydroxylamine·HCl in water containing sodium acetate, after 16 h at 80 °C, afforded a mixture of three compounds. Column chromatography [silica gel 60; 70—230 mesh ASTM; Merck; eluant light petroleum (b.p. 40—60 °C) containing tetrahydrofuran 0—30%] gave the pure components: (**5**) (8%, first eluted, R_F 0.90), (**4a**) (40%, second eluted, R_F 0.51), (**4b**) (52%, third eluted, R_F 0.43).

Similar results with the exception that (**5**) was not found among the reaction products were also obtained by reacting (**3a** or **b**) under the conditions reported by Ponzio for the oximation of his 'acetylmethylglyoxime'.[2] Analytical data and routine spectroscopy were consistent with trioxime structures for (**4a** and **b**) and with a furoxan oxime structure for (**5**). The ^{1}H and ^{13}C n.m.r. spectra of these compounds are reported in Table 2.

Trioxime (**4a**) is probably the compound described by Ponzio and Ruggeri in ref. 2. The discrepancy between the m.p. with

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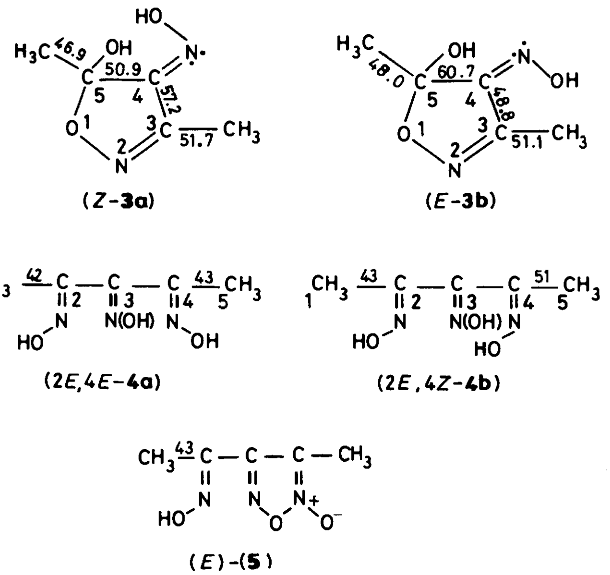
* Differential scanning calorimetric measurements indicate that the sample undergoes decomposition prior to melting. This decomposition is exothermic and exhibits a high activation energy. It is displaced to higher temperature upon increasing the heating rate, with variation of the m.p. (decomp.).[5]



(Z-**3a**)   (E-**3b**)

(2E,4E-**4a**)   (2E,4Z-**4b**)

(E)-(**5**)

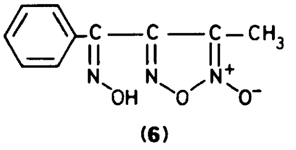
Figure 1. $^1J_{CC}$ coupling constants for the oxime derivatives

decomposition we have found, 155—156 °C [from ether–light petroleum (b.p. 40—60 °C)], and that quoted by the earlier authors, m.p. 175 °C (decomp.) (from water), can be explained by a difference in crystallization solvent and in rate of measurement.*

Oxime (**5**) was identical (i.r., mixed m.p.) to the acetyl(methyl)furoxan oxime described by Tappi,[1] to which earlier[10] we assigned a 3-methyl structure. The ^{13}C spectra are in keeping with this attribution. The resonance at δ 112.0 p.p.m. is particularly informative in this respect. It has been assigned to C-3 of the heterocyclic system[11] and appears as a quartet in the coupled spectrum as is in the parent ketone.[10]

We determined the exact configuration of the oxime groups in the two isoxazoline isomers (**3a** and **b**), that of the C-2 and C-4 oxime groups in the trioxime isomers (**4a** and **b**), and that in the furoxan oxime (**5**), by a $^1J_{CC}$ coupling constant study according to the suggestion of Krivdin *et al.*[12] These authors noted in fact that the *syn*-orientation of the nitrogen lone pair to a C–C bond results in an increase of ^{13}C–^{13}C coupling constant of the bond itself by comparison with the value found for *anti*-orientation. In this light we assigned the *Z* configuration to the isoxazoline isomer (**3a**) and the *E* configuration to the isomer (**3b**) (see Figure 1). By the same criterion the (2*E*,4*E*) configuration for isomer (**4a**) and (2*E*,4*Z*) for (**4b**) were assigned (Figure 1).

The relative resonance positions[13] and spin lattice relaxation times found for the methyl groups in these two latter stereoisomers also agree with our assignments. In fact we find similar ^{13}C T_1 values for isomer (**4a**) (1-CH$_3$, T_1 1.55; 5-CH$_3$, T_1 1.62 s), but different values for isomer (**4b**) (1-CH$_3$, T_1 2.13; 5-CH$_3$, T_1 1.37 s).



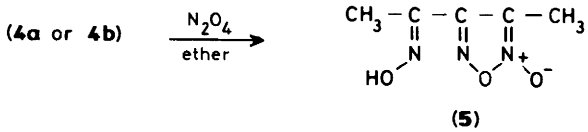
(**6**)

Unfortunately the difficulty in measuring *J*(C-2–C-3) and *J*(C-3–C-4) in the two trioxime derivatives prevented us from assigning the configuration of the central C=N–OH group. This prevents us on the one hand from completing the stereochemical assignment of (**4b**) and on the other hand from placing fully the n.m.r. parameters in (**4a**).

Oxime (**5**) does not rearrange in base,[1] unlike 4-benzoyl-3-methylfuroxan oxime (**6**).[14] This suggests an *E*-configuration for the oxime; the *J*(H$_3$C–C=NOH) value (43 Hz) confirms this hypothesis.

To provide chemical evidence for our structural assignment, we carried out the Ce^{4+} oxidation of (**3a** and **b**) in aqueous acetic acid. In this medium interconversion of the two isomers was observed. In effect in both cases we isolated in similar yields (*ca.* 20%) a product, m.p. 60 °C (from dilute ethanol), which proved to be 3,5-dimethyl-4-nitroisoxazole (**8**). The formation of this compound can be explained by the reaction pathway of Scheme 3. The presence of the intermediate 3,5-dimethyl-4-nitrosoisoxazole (**7**) in the acid reaction medium is suggested by the green colour that instantly appears when both (**3a** and **b**) are treated with cold sulphuric acid or with warm glacial acetic acid. Analogously, the action of Ce^{4+} on (**4a** or **b**) in aqueous acetic acid affords in poor yield 3,5-dimethyl-4-nitroisoxazole (**8**).

Since Ce^{4+} oxidation can also convert oximes into parent carbonyl compounds,[15] it is possible to explain these results by an initial conversion of the trioximes into acetylmethylglyoxime followed by its rearrangement to 3,5-dimethyl-5-hydroxy-4-hydroxyimino-2-isoxazoline derivatives (**3**). Finally we obtained (**5**) in quite different yield by the action of N$_2$O$_4$ in ether, on either (**4a**) or (**4b**). This result is in line with earlier data showing that different stereoisomeric oximes can give the same furoxan on oxidation.[16] (see Scheme 4).

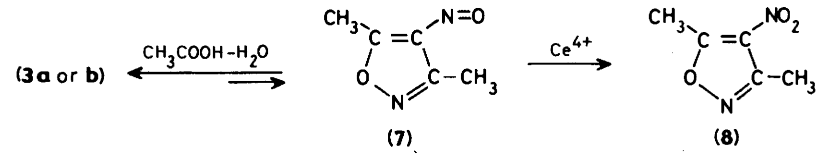


(**5**)

Scheme 4.

(b) *X-Ray Analysis.*—In order to confirm the structural hypothesis suggested by the n.m.r. parameters, an *X*-ray study of the above compounds was undertaken. Unfortunately it was not possible to obtain single crystals suitable for *X*-ray analysis in the cases of (**3b**) and (**4b**). Therefore the crystal and molecular structures of (**3a**), (**4a**), and (**5**) only are reported. The *X*-ray data confirmed the structural hypothesis formulated on the basis of ^{13}C n.m.r. spectroscopy. Tables 3—5 show the atomic parameters for the non-hydrogen atoms and Tables 6—8 list the bond distances and angles for the above compounds, using the numbering scheme of Figure 2. These values show no significant variation with respect to those normally found for this type of compound, except for the values involving the disordered part of (**3a**), as expected. In Table 9 the torsion angles among non-hydrogen atoms for (**4a**) are reported.

(*Z*)-3,5-*Dimethyl*-5-*hydroxy*-4-*hydroxyimino*-2-*isoxazoline* (**3a**). The proposed structure of (**3a**) and the *Z* configuration of



(**7**)   (**8**)

Scheme 3.

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* See footnote on p. 524

Table 3. Atomic co-ordinates for (**3a**)

Atom	x	y	z
O(1)	0	0.183 5(2)	0.269 8(2)
O(2)	0	0.161 6(2)	0.578 1(2)
O(3)	−0.149 9(12)	0.083 9(4)	0.382 0(5)
N(2)	0	0.279 7(2)	0.273 1(2)
N(3)	0	0.243 4(2)	0.527 1(2)
C(3)	0	0.307 2(2)	0.362 9(2)
C(4)	0	0.231 8(2)	0.433 0(2)
C(5)	0	0.145 6(3)	0.370 9(3)
C(6)	0	0.405 8(3)	0.388 4(3)
C(7)	0.232 3(9)	0.109 6(5)	0.382 2(8)

Table 4. Atomic co-ordinates for (**4a**)

Atom	x	y	z
O(1)	0.920 8(3)	0.723 5(4)	−0.208 2(8)
O(2)	0.796 4(3)	0.351 7(4)	−0.231 1(8)
O(3)	0.603 9(3)	0.629 5(4)	0.379 7(9)
N(1)	0.829 2(3)	0.646 2(4)	−0.207 6(9)
N(2)	0.720 6(3)	0.369 3(4)	−0.093 6(9)
N(3)	0.677 2(3)	0.609 0(4)	0.235 7(9)
C(1)	0.916 8(5)	0.545 6(6)	0.223(1)
C(2)	0.831 4(4)	0.561 9(5)	0.001(1)
C(3)	0.738 9(4)	0.474 9(4)	0.012(1)
C(4)	0.663 4(4)	0.497 6(5)	0.163(1)
C(5)	0.580 9(5)	0.397 1(6)	0.224(1)
O(11)	0.997 3(3)	0.108 9(4)	−0.272 7(8)
O(12)	0.796 2(3)	−0.161 0(3)	−0.698 1(8)
O(13)	0.604 8(3)	0.137 5(4)	−0.134 6(9)
N(11)	0.910 4(3)	0.026 9(4)	−0.248 1(9)
N(12)	0.722 2(3)	−0.139 1(4)	−0.559 4(9)
N(13)	0.682 1(3)	0.108 2(4)	−0.254 5(9)
C(11)	0.849 6(5)	0.147 3(6)	−0.680(1)
C(12)	0.841 0(4)	0.045 4(5)	−0.448(1)
C(13)	0.746 5(4)	−0.038 0(4)	−0.438(1)
C(14)	0.668 6(4)	−0.007 5(5)	−0.306(1)
C(15)	0.583 3(5)	−0.102 0(6)	−0.244(1)

Table 5. Atomic co-ordinates for (**5**)

Atom	x	y	z
O(1)	0.25	0.806 6(3)	0.331 6(2)
O(2)	0.25	0.891 2(3)	0.163 1(2)
O(3)	0.25	0.141 9(3)	0.304 5(2)
N(2)	0.25	0.775 3(3)	0.222 2(2)
N(5)	0.25	0.664 6(3)	0.382 4(2)
N(8)	0.25	0.295 5(3)	0.265 6(2)
C(3)	0.25	0.623 2(4)	0.208 4(3)
C(4)	0.25	0.557 6(4)	0.309 7(3)
C(5)	0.25	0.556 5(5)	0.102 2(3)
C(6)	0.25	0.392 6(4)	0.341 4(3)
C(7)	0.25	0.355 6(5)	0.455 4(3)

Table 6. Bond distances (Å) and angles (°) for (**3a**)

O(1)–N(2)	1.420(4)	N(2)–O(1)–C(5)	110.6(2)
O(1)–C(5)	1.471(4)	O(1)–N(2)–C(3)	110.3(3)
O(2)–N(3)	1.389(4)	O(2)–N(3)–C(4)	111.9(3)
O(3)–C(5)	1.380(8)	N(2)–C(3)–C(4)	111.7(3)
N(2)–C(3)	1.275(4)	N(2)–C(3)–C(6)	121.8(3)
N(3)–C(4)	1.277(4)	C(4)–C(3)–C(6)	126.5(3)
C(3)–C(4)	1.459(4)	N(3)–C(4)–C(3)	122.6(3)
C(3)–C(6)	1.495(5)	N(3)–C(4)–C(5)	131.0(3)
C(4)–C(5)	1.522(5)	C(3)–C(4)–C(5)	106.4(3)
C(5)–C(7)	1.684(7)	O(1)–C(5)–O(3)	110.5(3)
		O(1)–C(5)–C(4)	100.9(3)
		O(3)–C(5)–C(4)	119.5(3)
H(2) ··· N(2)	1.774*	O(1)–C(5)–C(7)	101.7(4)
O(2) ··· N(2)	2.762*	O(3)–C(5)–C(7)	119.0(5)
		C(4)–C(5)–C(7)	102.4(3)

* Refers to the position: x, $0.5 - y$, $z - 0.5$.

Table 7. Bond distances (Å) and angles (°) for (**4a**)

O(1)–N(1)	1.409(6)	O(11)–N(11)	1.395(6)
O(2)–N(2)	1.402(7)	O(12)–N(12)	1.400(7)
O(3)–N(3)	1.405(7)	O(13)–N(13)	1.409(7)
N(1)–C(2)	1.294(7)	N(11)–C(12)	1.282(6)
N(2)–C(3)	1.304(7)	N(12)–C(13)	1.305(7)
N(3)–C(4)	1.290(7)	N(13)–C(14)	1.296(7)
C(1)–C(2)	1.496(8)	C(11)–C(12)	1.504(8)
C(2)–C(3)	1.474(7)	C(12)–C(13)	1.476(7)
C(3)–C(4)	1.461(9)	C(13)–C(14)	1.458(9)
C(4)–C(5)	1.496(8)	C(14)–C(15)	1.487(8)
O(1)–N(1)–C(2)	111.5(5)	O(11)–N(11)–C(12)	112.8(5)
O(2)–N(2)–C(3)	112.2(6)	O(12)–N(12)–C(13)	112.6(6)
O(3)–N(3)–C(4)	112.7(6)	O(13)–N(13)–C(14)	112.4(6)
N(1)–C(2)–C(1)	126.7(6)	N(11)–C(12)–C(11)	124.3(6)
C(1)–C(2)–C(3)	118.6(5)	C(11)–C(12)–C(13)	119.4(5)
N(1)–C(2)–C(3)	114.8(5)	N(11)–C(12)–C(13)	116.3(5)
N(2)–C(3)–C(2)	123.7(6)	N(12)–C(13)–C(12)	124.0(6)
C(2)–C(3)–C(4)	121.3(5)	C(12)–C(13)–C(14)	121.7(5)
N(2)–C(3)–C(4)	114.9(5)	N(12)–C(13)–C(14)	114.2(6)
N(3)–C(4)–C(3)	113.3(6)	N(13)–C(14)–C(13)	112.9(6)
C(3)–C(4)–C(5)	121.2(5)	C(13)–C(14)–C(15)	121.9(5)
N(3)–C(4)–C(5)	125.5(6)	N(13)–C(14)–C(15)	125.2(6)
O(2) ··· N(13)	2.872(6)	H(20) ··· N(13)	2.03(8)
O(3) ··· N(12)^{a}	2.806(6)	H(30) ··· N(12)^{a}	2.00(7)
O(12) ··· N(3)^{b}	2.802(6)	H(120) ··· N(3)^{b}	1.92(8)
O(13) ··· N(2)	2.783(6)	H(130) ··· N(2)	1.96(7)
O(1) ··· O(11)^{c}	3.255(7)	H(10) ··· O(11)^{c}	2.38(8)
O(1) ··· O(12)^{d}	2.994(6)	H(10) ··· O(12)^{d}	2.41(7)
O(11) ··· O(12)^{e}	2.844(6)	H(110) ··· O(12)^{e}	2.20(6)
O(11) ··· N(11)^{f}	3.008(6)	H(110) ··· N(11)^{f}	2.35(9)

^{a} Superscripts refer to the following positions: ^{a} x, $1 + y$, $1 + z$; ^{b} x, $y - 1$, $z - 1$; ^{c} $1 - x$, $1 - y$, $1 - z$; ^{d} $2 - x$, $1 - y$, $-1 - z$; ^{e} $2 - x$, $-y$, $-1 - z$; ^{f} $2 - x$, $-y$, $-z$.

the oxime function were confirmed. The crystal structure is characterized by the fact that, although the molecule itself does not have *m* symmetry, it is located in a special position on the mirror plane orthogonal to the *a* axis. The hydroxy group O(3) and the methyl group C(7) are out of the plane, occupying a disordered position with an occupancy factor of 1/2. The two enantiomers present in the racemic solution are therefore statistically distributed, in the solid state, on the same site (Figures 2a and 3a show only one of the two enantiomers). The disordered distribution of the two molecules on the same position may be favoured by the lack of intermolecular hydrogen bonds involving O(3); the location of O(3) and C(7) on one or the other side of the plane is therefore irrelevant to the packing, which is dictated by the rest of the molecule. From Figure 3a and Table 6 it can be seen that a hydrogen bond of medium strength is formed[17] between O(2) acting as donor and N(2) acting as acceptor. This causes the formation of infinite chains along the *Z* axis which are connected to each other by van der Waals forces only.

(E,E)-*Pentane*-2,3,4-*trione trioxime* (**4a**). The crystal structure is based on two independent molecules, both with an *E,E* configuration, which differ in the orientation of one oxime group [C(2) and C(12) respectively], with respect to the plane defined by the other two oxime groups of each molecule (Figure

Table 8. Bond distances (Å) and angles (°) for (**5**)

O(1)–N(2)	1.431(4)	N(2)–O(1)–N(5)	107.2(2)
N(2)–C(3)	1.320(4)	O(1)–N(2)–C(3)	108.5(2)
C(3)–C(4)	1.417(4)	N(2)–C(3)–C(4)	105.8(3)
C(4)–N(5)	1.310(4)	C(3)–C(4)–N(5)	112.0(3)
N(5)–O(1)	1.384(4)	C(4)–N(5)–O(1)	106.5(2)
O(2)–N(2)	1.253(4)	O(1)–N(2)–O(2)	116.4(2)
C(3)–C(5)	1.480(5)	O(2)–N(2)–C(3)	135.1(3)
C(4)–C(6)	1.477(5)	N(2)–C(3)–C(5)	120.5(3)
C(6)–C(7)	1.498(5)	C(4)–C(3)–C(5)	133.7(3)
C(6)–N(8)	1.283(5)	C(3)–C(4)–C(6)	129.5(3)
N(8)–O(3)	1.412(4)	N(5)–C(4)–C(6)	118.5(3)
		C(4)–C(6)–C(7)	118.3(3)
		C(4)–C(6)–N(8)	114.6(3)
H(3)···O(2)	1.927*	C(7)–C(6)–N(8)	127.1(3)
O(3)···O(2)	2.819*	C(6)–N(8)–O(3)	110.0(3)

* Refers to the position: x, $1 + y$, z.

Table 9. Torsion angles (°) for (**4a**)

O(1)–N(1)–C(2)–C(3)	−178.4(5)
O(1)–N(1)–C(2)–C(1)	1.6(9)
O(2)–N(2)–C(3)–C(4)	−178.9(5)
O(2)–N(2)–C(3)–C(2)	−3.3(9)
O(3)–N(3)–C(4)–C(5)	−1.2(9)
O(3)–N(3)–C(4)–C(3)	179.8(5)
N(1)–C(2)–C(3)–N(2)	89.7(8)
C(1)–C(2)–C(3)–N(2)	−90.3(8)
C(1)–C(2)–C(3)–C(4)	85.0(8)
N(1)–C(2)–C(3)–C(4)	−95.0(7)
N(2)–C(3)–C(4)–N(3)	−171.9(6)
C(2)–C(3)–C(4)–N(3)	12.5(9)
C(2)–C(3)–C(4)–C(5)	−166.6(6)
N(2)–C(3)–C(4)–C(5)	9.1(9)
O(11)–N(11)–C(12)–C(13)	179.7(5)
O(11)–N(11)–C(12)–C(11)	−2.2(9)
O(12)–N(12)–C(13)–C(14)	176.1(5)
O(12)–N(12)–C(13)–C(12)	0.7(9)
O(13)–N(13)–C(14)–C(15)	−1.2(9)
O(13)–N(13)–C(14)–C(13)	178.2(5)
N(11)–C(12)–C(13)–N(12)	−96.9(8)
C(11)–C(12)–C(13)–N(12)	85.0(8)
C(11)–C(12)–C(13)–C(14)	−90.2(8)
N(11)–C(12)–C(13)–C(14)	88.0(8)
N(12)–C(13)–C(14)–N(13)	−161.7(6)
C(12)–C(13)–C(14)–N(13)	13.9(9)
C(12)–C(13)–C(14)–C(15)	−166.7(6)
N(12)–C(13)–C(14)–C(15)	17.8(9)

2b). The 'non-planar' oxime groups in both molecules are almost perpendicular to these planes, but the torsion angles N(1)–C(2)–C(3)–N(2) and N(11)–C(12)–C(13)–N(12) have opposite signs (89.7 and −96.9°, respectively). The 'planar' moieties of the two independent molecules form a dihedral angle of 3.5(1)° and a highly stabilized cyclic hydrogen bond system with the oxime oxygens acting as donors and the nitrogen atoms acting as acceptors (Table 7). As shown in Figure 3b, this causes the formation of infinite chains whose packing in the crystal is mainly determined, besides van der Waals interactions between the methyl groups, by bifurcated hydrogen bonds involving as donor the oxygen atoms [O(1) to O(11)] of the 'non-planar' oxime groups. These hydrogen bonds (see Table 7) are in the range of values reported in the literature.[17] The presence in the crystal structure of the two independent molecules can be explained on the basis of molecular packing; in the sequence of molecules along the chain, an alternate position of the 'non-planar' oxime group, with respect to the plane of the chain, leads in fact to a minimization of steric hindrance.

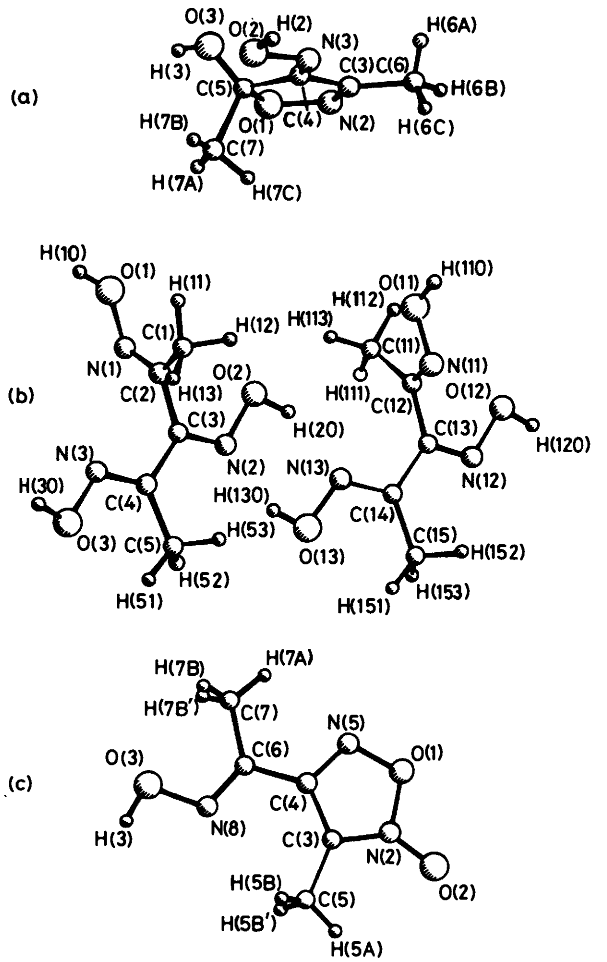

Figure 2. The molecular structures of: (a) (**3a**); (b) (**4a**); (c) (**5**)

(E)-4-*Acetyl*-3-*methylfuroxan oxime* (**5**). The proposed *E* configuration for the oxime group was confirmed. The molecule is planar, lying on the mirror plane orthogonal to the *a* axis. In the furoxan ring the distance O(1)–N(2) is longer than O(1)–N(5) (ΔNO 0.047 Å), a feature common to most substituted furoxans (see refs. 16 and 18 and references therein). The packing is characterized by the formation of infinite chains in the direction of the *y* axis, due to the presence of a hydrogen bond having the oxygen of the oxime group as donor and the exocyclic oxygen of the furoxan as acceptor. These chains are connected by van der Waals interactions only (Figure 3c).

Experimental

M.p.s were observed on a capillary Buchi 512 apparatus and are uncorrected. The decomposition of (**3a** and **b**) and (**4a** and **b**) was taken on a Dupon 900 differential thermal analyser. I.r. spectra were recorded on a Perkin-Elmer 781 spectrophotometer. ^{1}H and ^{13}C n.m.r. data were recorded on a JEOL GX 270/89 operating at 270.05 and 67.80 MHz, respectively. The samples were dissolved in [^{2}H$_6$]DMSO (Merck) and were contained in a 5 mm tube. The 90° pulses width were 15 (^{1}H probe) and 18 μs (^{13}C probe), respectively. ^{1}H and ^{13}C shifts are reported relative to tetramethylsilane. The detection of J_{CC} as satellites flanking the main isotopomer resonances were obtained by adding 10 000—15 000 transients in overnight accumulation; by using the INADEQUATE pulse sequence,[19] variable 1/4 J_{CC} values in the range of 0.0045 ± 0.0013 s were

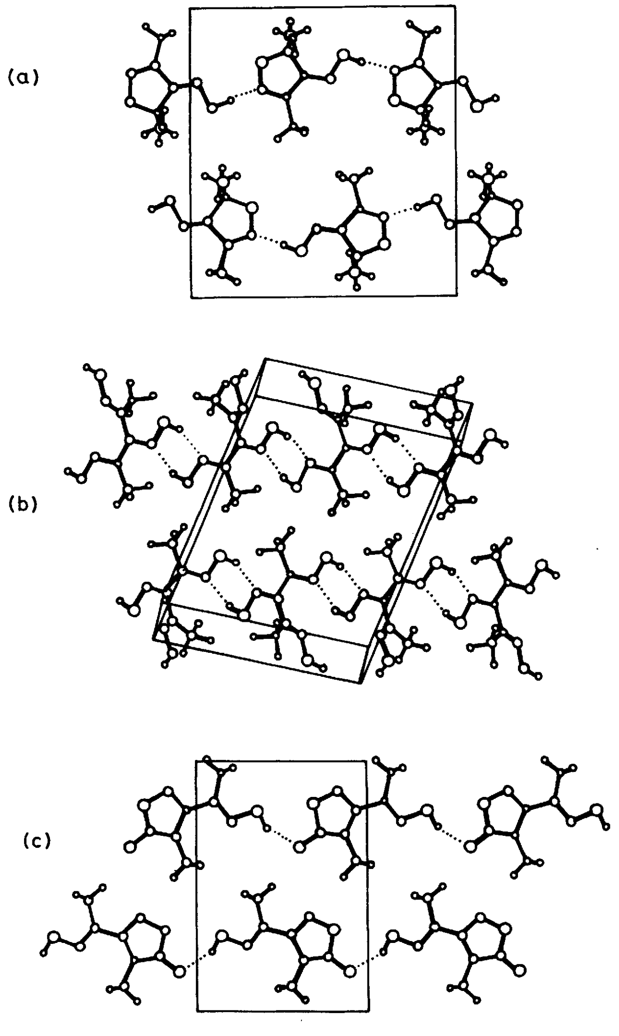

Figure 3. Packing diagram of: (a) (**3a**); (b) (**4a**); (c) (**5**)

employed. Mass spectra were obtained with a Varian CH7 MAT mass spectrometer. T.l.c. was carried out on 5 × 20 plates pre-coated with Merck silica gel 60 F_{254}, layer thickness 0.25 mm. Anhydrous magnesium sulphate was used as drying agent.

Acetyl(hydroxyimino)acetone (**1**).—This compound was prepared according to ref. 3, δ_C 25.5 (CH_3), 30.4 (CH_3), 156.4 (C=NOH), 194.9 (C=O), and 200.2 (C=O); δ_H 2.26 (CH_3), 2.53 (CH_3), and 12.95 p.p.m. (OH).

Oximation of Acetyl(hydroxyimino)acetone.—(a) To a stirred and externally ice–water-cooled solution of (**1**) (2.0 g, 15.4 mmol) dissolved in a minimal quantity of water (10 ml), sodium acetate trihydrate (2.1 g, 15.4 mmol) and then hydroxylamine hydrochloride (1.0 g, 15.4 mmol) were added. The solution was kept for 17 h at 5 °C. The precipitate was collected by filtration and the solid was shown by t.l.c. [light petroleum (b.p. 40—60 °C)–tetrahydrofuran (7:3)] to contain two components (R_F 0.44 minor component; R_F 0.35 main component). Neutralization of the filtered solution with 2N-NaOH, followed by several extractions with ether, gave another crop containing two components. Flash chromatography of the combined crops gave the pure compounds (silica gel 60; 230—400 mesh ASTM; Merck, eluant light petroleum (b.p. 40—60 °C) containing tetrahydrofuran 0—30%, overall yield 80%; (**3b**) first eluted, 19%; (**3a**) second eluted, 81%. (*E*)-3,5-Dimethyl-5-hydroxy-4-hydroxyimino-2-isoxazoline (**3b**) had m.p. 112 °C (decomp.) (sample introduced into the bath at 100 °C, heating rate 3 °C min^{-1}) (Found: C, 41.9; H, 5.5; N, 19.6%; *m/e* 144. $C_5H_8N_2O_3$ requires C, 41.7; H, 5.6; N, 19.4%; *M*, 144). (*Z*)-3,5-Dimethyl-5-hydroxy-4-hydroxyimino-2-isoxazoline (**3a**) had m.p. 123 °C (decomp.) (sample introduced into the bath at 100 °C, heating rate 3 °C min^{-1}) (Found: C, 41.8; H, 5.6; N, 19.3%; *m/e* 144).

(b) To a stirred solution of (**1**) (1.0 g, 7.74 mmol) in water (13 ml), sodium acetate trihydrate (3.68 g, 27.09 mmol) and hydroxylamine hydrochloride (1.88 g, 27.09 mmol) were added. The mixture was kept for 16 h at 80 °C. After cooling, the solution was neutralized with 2N-NaOH and then extracted with ethyl ether. The solid obtained after removal of solvent was shown by t.l.c. [light petroleum (b.p. 40—60 °C)–tetrahydrofuran (6:4)] to contain three components (R_F 0.91, 0.51, and 0.43, respectively). Column chromatography afforded the pure compounds [silica gel 60; 70—230 mesh ASTM; Merck; eluant light petroleum (b.p. 40—60 °C containing tetrahydrofuran 0—30%)] in an overall yield of 80%; (**5**) (first eluted) 8%; (**4a**) (second eluted) 40%; (**4b**) (third eluted) 52%. (*E*)-4-Acetyl-3-methylfuroxan oxime (**5**) had δ_C 10.08, 10.39 (CH_3), 146.90 (C=NOH), 154.84 (C=N–O), and 111.96 p.p.m. $(C{=}\overset{+}{N}<^{O^-}_{O})$, m.p. 129—130 °C (from benzene) [lit.,[1] 130—131 °C (from benzene)]. This compound was identical (i.r., mixed m.p.) with a sample of 4-acetyl-3-methylfuroxan oxime prepared by action of N_2O_4 on (**3a** or **b**) (see below). (*E,E*)-Pentane-2,3,4-trione trioxime (**4a**) had m.p. 155—156 °C (decomp.) (sample introduced into the bath at 140 °C, heating rate 3 °C min^{-1}) from ether–light petroleum (b.p. 40—60 °C) (Found: C, 37.6; H, 5.6; N, 26.2. $C_5H_9N_3O_3$ requires C, 37.7; H, 5.7; N, 26.4%). (2*E*,4*Z*)-Pentane-2,3,4-trione trioxime (**4b**) had m.p. 135—137 °C (decomp.) (sample introduced into the bath at 120 °C, heating rate 3 °C min^{-1}) from ether–light petroleum (b.p. 40—60 °C) (Found: C, 37.7; H, 5.6; N, 26.3. $C_5H_9N_3O_3$ requires C, 37.7; H, 5.7; N, 26.4%).

(E)-4-*Acetyl*-3-*methylfuroxan Oxime* (**5**).—According to ref. 1, a stirred and externally ice–water cooled solution of (**4a**) (1.0 g, 6.3 mmol) in anhydrous ether (13 ml) was treated with dinitrogen tetraoxide (0.3 g, 3.3 mmol). After 2 h the mixture was washed with 10% aqueous Na_2CO_3 solution and then with water. The organic layer was dried and distilled *in vacuo*. The residue was filtered on a short column of silica gel (eluant chloroform) to give a product (yield 61%), m.p. 129—130 °C (from benzene). Similar results were obtained working with (**4b**) under the same conditions (yield 21%).

3,5-*Dimethyl*-4-*nitroisoxazole* (**8**).—To a stirred solution of (**3a**) (2.0 g, 13.9 mmol) dissolved in 90% acetic acid (50 ml) a solution of cerium(IV) ammonium nitrate (15.2 g, 27.8 mmol) in water (15 ml) was added dropwise. Stirring was continued for 2 h at room temperature and then the solution, with added water, was extracted with ethyl ether. The combined organic layers were successively washed with 3% aqueous sodium hydrogencarbonate and water. Solvent removal and column chromatography [silica gel 60; 70—230 mesh ASTM; Merck; eluant light petroleum (b.p. 40—60 °C) containing chloroform 0—30%] gave crystals (20%), m.p. 60—61 °C (from aqueous ethanol). This compound was identical (i.r., mixed m.p.) with a sample of 3,5-dimethyl-4-nitroisoxazole prepared according to ref. 20. Similar results were obtained working with (**3b**) and (**4a** and **b**). In the case of (**4a** and **b**) a 1:4 ratio of trioxime:Ce^{4+} was adopted.

Crystal Structure of (Z)-3,5-*Dimethyl*-5-*hydroxy*-4-*hydroxyimino*-2-*isoxazoline* (**3a**).—*Crystal data*. $C_5H_8N_2O_3$, orthorhombic, space group *Cmca*, $a = 6.848(2)$, $b = 14.758(2)$, $c = 13.451(3)$ Å, $V = 1\,359.4(6)$ Å^3, $Z = 8$, $D_x = 1.40$ mg m^{-3}, Mo-K_α, $\mu = 0.11$ mm^{-1}, $F(000) = 608$, room temperature. The cell parameters were obtained and refined from 25 diffractometric reflections, 16° ⩽ 2θ ⩽ 36°.

Data collection. Poor quality crystals (0.4 × 0.25 × 0.13 mm) were mounted on a Nicolet R3 diffractometer, using graphite-monochromated Mo-K_α radiation and the θ–2θ scan technique at variable speed (2—15° min^{-1}); one standard remeasured every 50 reflections did not show a significant decrease in intensity. 1 340 Reflections were collected in two equivalent octants of which 604 unique reflections, with $I \geq 2\sigma(I)$, were considered observed. The five strongest reflections, measured with an attenuator, were used for the solution but excluded from the refinement. Data were corrected for background, Lorentz-polarization effect, and an empirical absorption correction based on the ψ-scan method[21] was applied.

Structure solution and refinement. For all computations use was made of the SHELXTL system.[22] The structure was solved by direct methods (program RANTAN[23]); the solution with the best figure of merit showed 80% of the non-hydrogen atoms, corresponding to the isoxazoline ring lying in a special position on the mirror plane orthogonal to the *a* axis. The two missing atoms, O(3) and C(7), are disordered and were located on a difference Fourier map calculated after a few cycles of refinement.

The refinement was carried out by full matrix least-squares methods; all non-hydrogen atoms are anisotropic; the hydrogen atoms were found on a difference Fourier map and refined under the constraint O–H = 0.98 ± 0.02 Å, with the exception of the disordered methyl group C(7), which was refined as a rigid group with the hydrogens in calculated positions; one overall isotropic temperature factor, common to all hydrogen atoms, converged to 0.125(9) Å^2. Even though the distance C(5)–C(7) was constrained to the value 1.54 ± 0.02 Å, it refined to the much too high value of 1.684(7) Å, due to the disorder. The C(5)–O(3) distance was normal, with constraints. Unit weights proved to be satisfactory. At convergence *R* was 0.055 for 599 reflections and 81 parameters. The maximum residual peak in the final difference Fourier maps was 0.28 e Å^{-3}.

Crystal Structure of (E,E)-*Pentane*-2,3,4-*trione Trioxime* (**4a**).—*Crystal data.* $C_5H_9N_3O_3$, triclinic, space group $P\bar{1}$, a = 13.776(3), b = 10.820(2), c = 5.083(2) Å, α = 81.8(1), β = 100.0(1), γ = 98.4(1)°, V = 732.8(5) Å^3, Z = 4, D_x = 1.44 mg m^{-3}, Cu-K_α, μ = 0.098 mm^{-1}, $F(000)$ = 336, room temperature. The cell parameters were obtained and refined from 20 diffractometric reflections, 30° ⩽ 2θ ⩽ 50°.

Data collection. The intensity data were collected from a prismatic crystal on an automated Simens AED diffractomer, using the θ–2θ scan technique at variable speed (6—24 s deg^{-1}). The integrated intensities were obtained from the diffracton profile by a modification[24] of the Lehman–Larsen procedure.[25] Periodic remeasurements of one standard reflection did not show significant variations. 2 176 Reflections were collected of which 1 561 having $I \geqslant 3\sigma(I)$ were considered observed and, corrected for Lorentz-polarization effects, used in the structure analysis.

Structure solution and refinement. All calculations were performed using the SHELX 76 system of programs.[26] The structure was solved by direct methods and refined by full matrix least-squares procedure. All the hydrogen atoms were located on a difference Fourier map at an advanced stage of the anisotropic refinement. Convergence was attained at *R* = 0.063 for 1 561 reflections and 270 parameters.

Crystal Structure of (E)-4-*Acetyl*-3-*methylfuroxan Oxime* (**5**).—*Crystal data.* $C_5H_7N_3O_3$, orthorhombic, space group *Pmcn*, a = 6.486(1), b = 8.601(2), c = 12.839(3) Å, V = 716.2(3) Å^3, Z = 4, D_x = 1.46 mg m^{-3}, Mo-K_α, μ = 0.13 mm^{-1}, $F(000)$ = 328, room temperature. The cell parameters were obtained and refined from 25 diffractometeric reflections, 17° ⩽ 2θ ⩽ 39°.

Data collection. Intensity data were collected from a crystal (0.30 × 0.23 × 0.08 mm), using the Nicolet R3 diffractometer, Mo-K_α radiation, and the ω–2θ scan technique at variable speed (1.5—10° min^{-1}). No evidence of crystal decay was noted. 690 Reflections were collected of which 559 were observed; the three strongest were excluded from the refinement. No absorption correction was applied. The data were treated as for (**3a**).

Structure solution and refinement. A few attempts at solving the structure by direct methods in the space group *Pmcn* did not produce any interpretable map. The solution was attained by program RANTAN[23] in the non-centrosymmetric subgroup $P2_12_12_1$ in which the solution with the best figure of merit showed all non-hydrogen atoms. The refinement was then carried out by full matrix least-squares methods in the true space group *Pmcn*, with unit weights, after correcting the *y* co-ordinate to take into consideration the shift of 1/4 of the origin in the direction of the *y* axis, passing from one space group to the other. All non-hydrogen atoms were anisotropic; hydrogen atoms were treated as for (**3a**), with overall temperature factor 0.121(7) Å. At convergence *R* was 0.042 for 556 reflections and 80 parameters. The maximum residual peak was 0.12 e Å^{-3}.

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