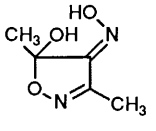
X-Ray and Nuclear Magnetic Resonance Structural Study of Acylglyoximes and Related Substances

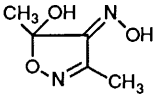
Roberta Fruttero,[a] Rosella Calvino,[a] Bruno Ferrarotti,[a] Alberto Gasco *,[a] and Piera Sabatino *,[b]
[a] *Dipartimento di Scienza e Tecnologia del Farmaco, Via Giuria 9, 10125 Torino, Italy*
[b] *Dipartimento di Chimica 'G. Ciamician,' Via Selmi 2, 40126 Bologna, Italy*

A series of reactions used in the literature to synthesize acylglyoximes were reinvestigated and the mixtures of products obtained resolved by chromatography. NMR spectroscopy revealed that some of the derivatives described in literature as dioximes actually have an isoxazoline structure. X-Ray analysis was employed to establish unequivocally the structures of *syn*-diacetylglyoxime and the (*Z*)-3-acetyl-5-hydroxy-4-hydroxyimino-5-methyl-4,5-dihydroisoxazole hemihydrate. In addition, the structure of the derivative produced by treatment of 5-hydroxy-4-hydroxyimino-3-methyl-5-phenyl-4,5-dihydroisoxazole with dinitrogen tetraoxide in dry diethyl ether is also described.

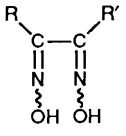
In recent work[1] we showed that the product obtained by the action of an equimolar amount of hydroxylamine on isonitrosoacetylacetone is not acetylmethylglyoxime, as previously reported, but a mixture of the two isomers (*Z*)-**1a** and (*E*)-**1b** of 5-hydroxy-4-hydroxyimino-3,5-dimethyl-4,5-dihydroisoxazole.



(*Z*)-**1a**

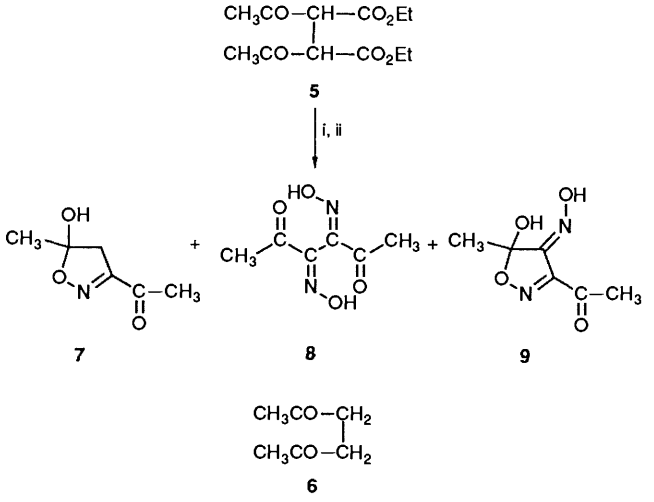


(*E*)-**1b**



2; R = R′ = $COCH_3$
3; R = R′ = COC_6H_5
4; R = COC_6H_5, R′ = CH_3

In the light of this result, we have reinvestigated the preparation and the structure of 'diacetylglyoxime' **2**,[2] 'dibenzoylglyoxime' **3**[3] and 'benzoylmethylglyoxime' **4**.[4]



Scheme 1 *Reagents:* i, KOH; ii, H_2SO_4, $NaNO_2$

Results and Discussion

'Diacetylglyoxime.'—We obtained 'diacetylglyoxime' **2**, starting from diethyl 2,3-diacetylsuccinate **5** according to the method reported by Thal[5] and modified by Alessandri[6] (Scheme 1). From 5 g of starting material we obtained a crude product, which was separated and purified by column chromatography to give compounds **7**, **8** and **9**.

Analytical data and mass spectrometry of the first eluted compound were in keeping with the molecular formula $C_6H_9NO_3$ (yield 0.94 g). The IR spectrum (KBr) showed hydroxy- and carbonyl-group absorptions (ν_{max} 3320br and 1660 cm^{-1}). ^1H and ^{13}C NMR spectra of this derivative are reported in Table 1.

The presence in the structure of a methylene group was evident by the ^{13}C absorption at δ_C 42.3. This group appears as an AB system centred at δ_C 3.31 (δ_A 3.38, δ_B 3.25, *J* 18 Hz) in the ^1H spectrum.

The spectral data of Table 1, very similar to those of compounds **1a** and **1b** with the exception of the oxime absorptions,[1] suggest that this product has the 3-acetyl-5-hydroxy-5-methyl-4,5-dihydroisoxazole structure **7**.

The formation of this derivative could arise from the partial nitrosation of the possible intermediate **6** to (*E*)-hexane-2,3,5-trione 3-oxime, which would immediately cyclize to compound **7**. Another possibility is that the intermediate on the way to **7** is the nitroso derivative of the unstable 2,3-diacetylsuccinic acid. Anyway, additional work is necessary to clarify this point. The ^1H NMR system suggested the presence, in dimethyl sulfoxide (DMSO), of minor amounts of the open form ($\leq 3\%$) (feeble signals at δ 3.6, 2.3 and 12.8 could be attributable to the CH_2CO, MeCO and NOH resonances. The lack of a second MeCO signal could be due to overlap with that of the corresponding acetyl of the closed form.)

The isoxazoline **7** melts at 74–75 °C and is the same compound that was obtained by Thal (m.p. 75 °C)[5] as a by-product in the reaction. To this product Thal assigned the open form of the isoxazoline **7**.

Analytical data and mass spectra of the second (**8**, 0.16 g) and third eluted products (**9**, 0.94 g), were in keeping with the molecular formula $C_6H_8N_2O_4$. The IR spectra (KBr) of these derivatives showed the presence of both carbonyl and hydroxy groups **8**: ν_{max} 1670 and 3200br cm^{-1}; **9**: ν_{max} 1690 and 3300br cm^{-1}).

Table 1 ^{13}C and ^{1}H NMR data of compounds **7**, **8**, **9**, **11**, **13**, **14** and **16** (solvent [$^{2}H_6$]DMSO; δ in ppm from $SiMe_4$)

	δ_C	δ_H
7	C=O 192.8 C-3 158.5 C-5 110.4 C-4 42.2 *Me*CO 26.0 *Me*C(OH) 25.2	OH 7.54 (1 H, s) CH_2 3.31 (2 H, AB system) MeCO 2.78 (3 H, s) *Me*C(OH) 1.97 (3 H, s)
8	C=O 194.1 C=N(OH) 150.3 Me 25.3	N(OH) 12.76 (1 H, s) Me 2.36 (3 H, s)
9	C=O 190.9 C-4 153.4 C-3 152.1 C-5 106.2 *Me*C=O 28.2 Me 21.9 $^{1}J_{C5-C4}$ 50.4 Hz	N(OH) 12.49 (1 H, s) OH 7.86 (1 H, s) MeCO 2.47 (3 H, s) *Me*C(OH) 1.73 (3 H, s)
11	C=O 185.7 C-3 154.9 C-4 152.2 C-5 105.0 Ph 137.0, 135.8, 134.7, 130.0, 129.0, 128.2, 126.3	N(OH) 12.47 (1 H, s) OH 8.66 (1 H, s) Ph 8.13–7.44 (5 H, m)
13	C=O 193.8 *C*=N(OH)(CO) 155.1 *C*=N(OH)(Me) 152.5 Me 9.5 Ph 128.7, 129.1, 134.1, 135.9	N(OH)(CO), N(OH)(Me) 11.82 (1 H, s), 11.77 (1 H, s)
14	C-4 157.7 C-3 151.7 C-5 101.9 Me 9.9 Ph 126.3, 127.8, 128.4, 138.2 $^{1}J_{C4-C3}$ 58.7 Hz, $^{1}J_{C5-C4}$ 51.3 Hz	N(OH) 11.91 (1 H, s) OH 7.88 (1 H, s) Ph 7.4–7.3 (5 H, m) Me 2.05 (3 H, s)
16[a]	C=O 162.3 C=N(OC)/C=N(OH) 153.4/151.9 Me 17.3 Ph 129.3, 129.6, 129.6, 134.4	N(OH) 14.25 (1 H, s) Me 2.40 (3 H, s) Ph 8.1–7.6 (5 H, m)

[a] It was not possible to get a ^{13}C coupled spectrum of this compound because of its easy decomposition in DMSO; therefore the C=N resonances were not assigned.

The ^{13}C NMR spectrum of compound **8** (see Table 1) exhibits only three signals. This is in keeping with a two-fold molecular symmetry for this product. In particular, the signal at δ_C 150.3 in the ^{13}C spectrum and the signal at δ_H 12.76 in the ^{1}H spectrum indicate the presence of –C=N–OH functions, while the other absorptions confirm the presence of an acetyl group. Consequently, we can assign to compound **8** a diacetylglyoxime structure, *syn* or *anti*,* *i.e.* that of (*E*,*E*)- or (*Z*,*Z*)-hexane-2,3,4,5-tetraone 3,4-dioxime.

X-Ray analysis has unequivocally established a *syn*-structure for compound **8**. This is in keeping with the inability of compound **8** to give any 2:1 Ni^{2+} complex.

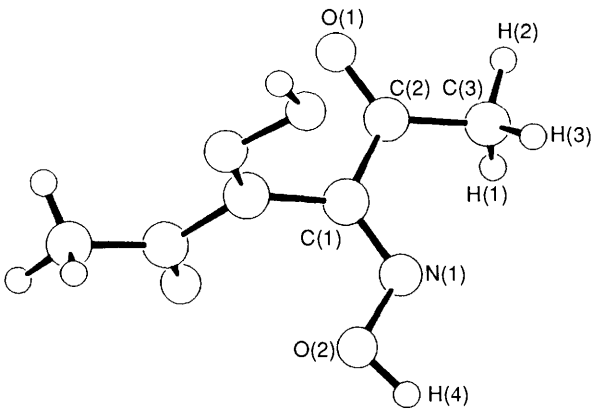


Fig. 1 The molecular structure of compound **8** with the atom labelling. *N.B.* The crystallographic numbering does not correspond to the systematic nomenclature.

Table 2 Bond distances/Å and angles/° and some relevant torsion angles/° for compound **8** with estimated standard deviations in parentheses

C(1)–N(1)	1.276(3)
N(1)–O(2)	1.381(3)
C(1)–C(2)	1.494(4)
C(2)–O(1)	1.220(3)
C(2)–C(3)	1.494(4)
C(1)–C(1′)	1.498(5)
C(1)–C(2)–O(1)	119.3(2)
C(2)–C(1)–N(1)	116.7(2)
C(1)–N(1)–O(2)	111.7(2)
O(1)–C(2)–C(3)	121.9(2)
C(1)–C(2)–C(3)	118.7(2)
N(1)–C(1)–C(1′)	123.5(2)
C(2)–C(1)–C(1′)	119.8(2)
O(2)–N(1)–C(1)–C(2)	179.0
N(1)–C(1)–C(2)–O(1)	176.4
N(1)–C(1)–C(1′)–N(1′)	101.0
N(1)–C(1)–C(2)–C(3)	−3.9

The molecular structure of compound **8** is shown in Fig. 1, together with the atom labelling. As shown, only half the molecule is independent, the second half being related by the crystallographic *c*-glide plane present in the lattice through the C(1)–C(1′) bond.

Each moiety is approximately planar: N(1) represents the maximum deviation from the least-squares plane passing through the six independent non-H atoms (0.034 Å below the plane), while H(4) deviates 0.20 Å from the same plane. The pairs of half, symmetry-related, molecules thus form crossed ribbons approximately perpendicular to each other: the dihedral angle between the two planar moieties is 99.5°.

Considering the molecule in itself, it possesses an idealized C_2 symmetry, through the C(1)–C(1′) bond; thus the symmetry observed in solution (see above) is preserved in the solid state.

Bond distances and angles fall in the range of values observed for similar oxime derivatives[1,7,8] and are reported in Table 2. Torsion angles, in the same Table, show the overall conformation of the molecule.

Intermolecular interactions involve essentially van der Waals forces and a hydrogen bond between the oxime oxygen, O(2), as a donor, and the carbonyl O(1) as an acceptor (symmetry operation 0.5 + *x*, 0.5 + *y*, 0.5 − *z*). The separation between the two oxygens is 2.703 Å, while the H(4)···O(1) contact is

* The old authors frequently used two different methods to name α-dioximes. In the first, glyoxime [the dioxime of glyoxal HC(=NOH)-CH(=NOH)] was taken as the parent compound. α-Dioximes were therefore named by citing as prefix to the name 'glyoxime' the substituting groups attached to it. In the second, the word 'dioxime' followed the name of the α-dicarbonyl compound, using, if necessary, arabic numbers to indicate the location of the oxime functions. This point can be a source of confusion. For example, in a recent Chemical Abstract (1982, **96**, 142774m, under the empirical formula $C_6H_8N_2O_4$ corresponding to hexane-2,3,4,5-tetraone 3,4-dioxime (diacetylglyoxime), is reported a reference in which, instead, dimethylglyoxime (diacetyl dioxime, butane-2,3-dione dioxime) is the compound actually studied.

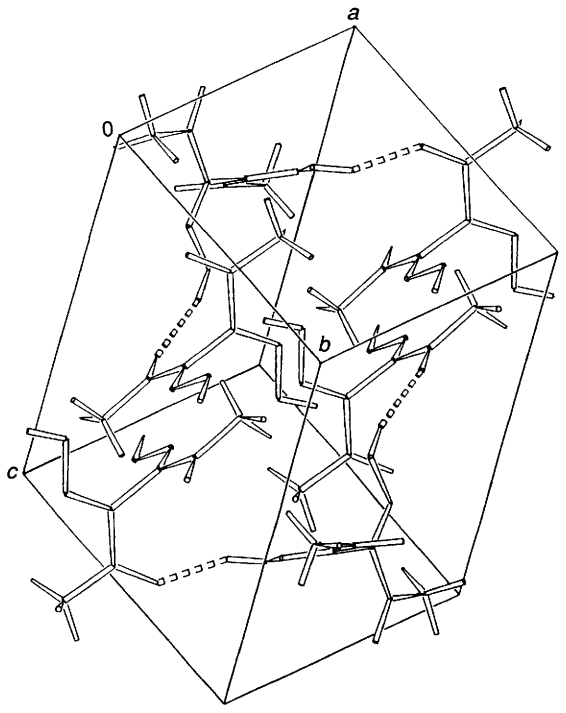


Fig. 2 Packing diagram of compound **8** showing the hydrogen-bonding network

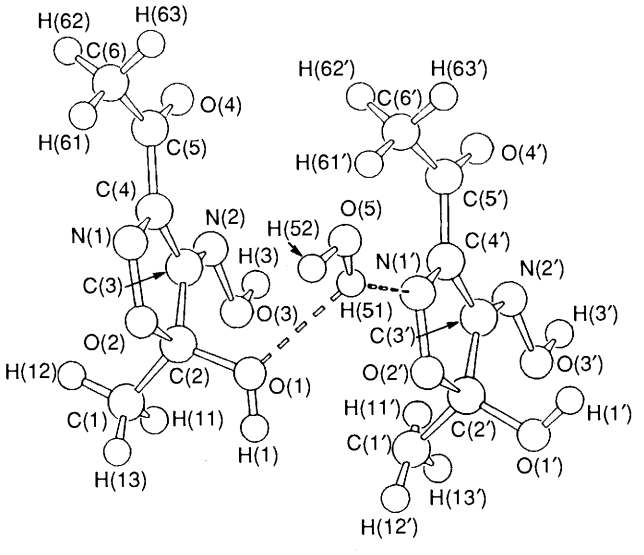


Fig. 3 The molecular structure of the two independent molecules of compound **9** together with the water molecule of crystallization. *N.B.* The crystallographic numbering does not correspond to the systematic nomenclature.

1.79 Å, the O(2)–H(4)–O(1) angle being 152.9°. The hydrogen-bonding scheme creates an infinite two-dimensional network along the directions 110 and 100 (Fig. 2).

For the third product, which showed six ^{13}C NMR signals, reasonable hypotheses were either the *amphi*-diacetylglyoxime [(*Z*,*E*)-hexane-2,3,4,5-tetraone 3,4-dioxime] or the 3-acetyl-5-hydroxy-4-hydroxyimino-5-methyl-4,5-dihydroisoxazole structures. The second structure, **9**, for this product is supported by the NMR data reported in Table 1 and, in particular, by the presence, in the ^{13}C spectrum, of a signal at δ_C 106.2, and, in the ^1H spectrum, by the presence of the OH signal at δ_H 7.86.[1]

We determined the configuration of the oxime group in this derivative by a ^1J coupling-constant study. We found a value of 50.4 Hz for the $^1J_{C4-C5}$, but difficulties in the measurements prevented us from calculating $^1J_{C3-C4}$. However, a comparison of the ^1J-value with those obtained for the corresponding coupling constants in compounds **1a** and **1b**[1] allowed us to assign a *Z* configuration to compound **9**.*

The X-ray analysis confirmed the hypothesized isoxazoline structure and the *Z* configuration of the oxime group. In the crystal structure of compound **9**, the asymmetric unit comprises two independent molecules, I and II, which have been labelled with the same numbering but adding a prime to molecule II, and one molecule of water. Both independent molecules present the same configuration of the oxime group (Fig. 3), but differ in the orientation of the hydroxy group at C(2). In molecule I this group is oriented towards the methyl substituent, while in molecule II it is directed away. Both hydrogen atoms, as well as the oxime ones, were located by difference Fourier maps, but, of course, the most significant evidence for a different conformation lies in the width of the O(1)–C(2)–C(1) angle, 114.3(2)° in I, 109.5(2)° in II, and of the C(3)–C(2)–O(1) angle, 110.8(2)° and 114.9(2)° in I and II, respectively.

The isoxazoline ring is planar, with the maximum deviation in C(2) and C(2') (0.013 and 0.004 Å, respectively, away from the least-squares plane), as already seen in the parent species 5-hydroxy-4-hydroxyimino-3,5-dimethyl-4,5-dihydroisoxazole.[1] The oxime group is almost coplanar, with the five-membered ring (the dihedral angle between the least-squares planes passing through the ring and the –C=N–OH fragment is 1.7°, in both molecules I and II).

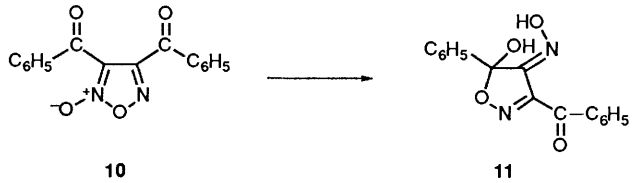
Bond distances and angles are reported in Table 3 together with some relevant torsion angles.

The water molecule is involved in three possible hydrogen bonds as a donor (D): in a bifurcated bond[10] with O(1) and N(1'); *via* H(51), thus bridging the two independent molecules (Fig. 3); and with N(1), *via* H(52). It is also involved in two probable H-bonds as an acceptor (A), with O(1') and C(6'), *via* H(61'). This latter interaction meets the criteria denoted by Berkovitch-Yellin and Leiserowitz.[11] The complex three-dimensional network of hydrogen bonds is completed by five other possible 'classical' D–A interactions, which involve the two hydroxy groups of both molecules as donors. Additionally, five C–H • • • O interactions occur, as shown in Table 4.

In molecule I, the orientation of the methyl hydrogen H(11), synperiplanar to O(3), suggests the possibility of an intramolecular hydrogen bond between C(1) and the oxime oxygen, with an angle at the hydrogen of 111.9°.

Atomic co-ordinates are given in Tables 5 and 6 for compounds **8** and **9**, respectively.

'*Dibenzoylglyoxime*'.—We synthesized 'dibenzoylglyoxime' **3** according to the method reported by Angeli[12] (see Scheme 2).



10 **11**

Scheme 2 *Reagents:* Zn, AcOH

From this reaction we obtained a product with the same m.p. as that reported by Angeli. NMR spectral characterization (see Table 1) is fully in agreement with structure **11**. We were unable to determine the stereochemistry of the oxime group. However,

* We also prepared 'diacetylglyoxime' according to Piloty's procedure[9] starting from dimethylpyrrole and nitrous acid. In this case we obtained, in poor yield, a mixture of compounds **8** and **9** in an approximate ratio of 1:1.

Table 3 Bond distances/Å, angles/° and some relevant torsion angles/° for compound **9**, with estimated standard deviations in parentheses

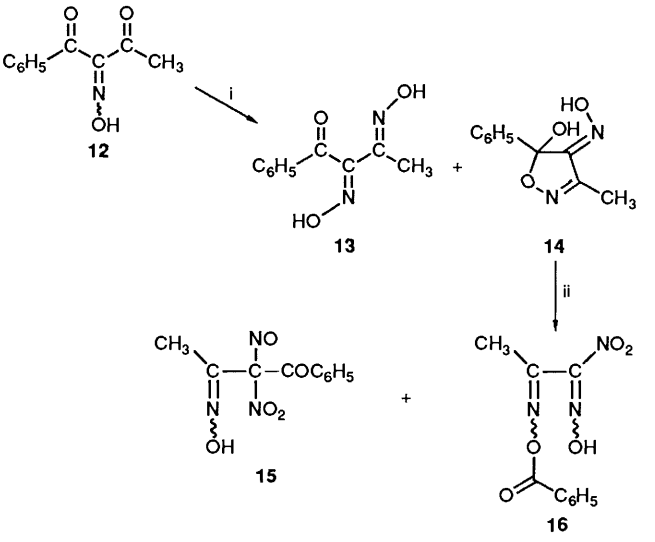
	I	II
O(1)–C(2)	1.382(3)	1.379(3)
O(2)–N(1)	1.382(3)	1.380(3)
O(2)–C(2)	1.477(3)	1.474(3)
O(3)–N(2)	1.383(3)	1.384(3)
O(4)–C(5)	1.209(3)	1.213(3)
N(1)–C(4)	1.284(3)	1.284(3)
N(2)–C(3)	1.278(3)	1.281(3)
C(1)–C(2)	1.511(4)	1.518(4)
C(2)–C(3)	1.507(3)	1.509(3)
C(3)–C(4)	1.450(4)	1.448(4)
C(4)–C(5)	1.489(3)	1.494(3)
C(5)–C(6)	1.500(4)	1.492(4)
C(2)–O(2)–N(1)	111.1(2)	111.1(2)
C(4)–N(1)–O(2)	110.1(2)	110.0(2)
C(3)–N(2)–O(3)	112.8(2)	112.7(2)
O(2)–C(2)–O(1)	107.4(2)	108.3(2)
C(1)–C(2)–O(1)	114.3(2)	109.5(2)
C(1)–C(2)–O(2)	106.8(2)	107.4(2)
C(3)–C(2)–O(1)	110.8(2)	114.9(2)
C(3)–C(2)–O(2)	100.9(2)	101.0(2)
C(3)–C(2)–C(1)	115.4(2)	114.9(2)
C(2)–C(3)–N(2)	131.1(2)	131.3(2)
C(4)–C(3)–N(2)	123.0(2)	123.0(2)
C(4)–C(3)–C(2)	106.1(2)	105.7(2)
C(3)–C(4)–N(1)	111.9(2)	112.1(2)
C(5)–C(4)–N(1)	119.9(2)	120.0(2)
C(5)–C(4)–C(3)	128.2(2)	127.8(2)
C(4)–C(5)–O(4)	119.1(2)	118.9(2)
C(6)–C(5)–O(4)	122.7(2)	122.4(2)
C(6)–C(5)–O(4)	118.2(2)	118.6(2)
N(1)–O(2)–C(2)–C(1)	−123.1	−120.0
O(1)–C(2)–C(3)–N(2)	67.4	63.7
O(3)–N(2)–C(3)–C(2)	1.2	0.0
N(1)–C(4)–C(5)–O(4)	174.9	173.5
N(1)–C(4)–C(5)–C(6)	−5.9	−6.8

Table 4 Scheme of potential hydrogen bonds in compound **9**

Donor–H ··· Acceptor	D ··· A	H ··· A	D–H ··· A
O(1)–H(1) ··· O(1′)[a]	2.789	1.845	174.1
O(3)–H(3) ··· O(4′)[b]	2.842	2.164	127.4
O(3)–H(3) ··· N(2′)[b]	2.901	2.059	146.9
O(5)–H(51) ··· O(1)	3.072	2.381	120.0
O(5)–H(51) ··· N(1′)	2.991	2.112	136.1
O(5)–H(52) ··· N(1)[c]	2.890	2.109	136.7
O(1′)–H(1′) ··· O(5)[d]	2.615	1.670	176.8
O(3′)–H(3′) ··· O(4)[b]	2.856	2.184	126.7
O(3′)–H(3′) ··· N(2)[b]	2.905	2.066	146.2
C(1)–H(11) ··· O(3)	3.122	2.553	111.9
C(1)–H(12) ··· O(4)[e]	3.437	2.548	139.0
C(1)–H(13) ··· O(2)[f]	3.653	2.598	165.4
C(1′)–H(11′) ··· O(4′)[b]	3.421	2.515	140.8
C(1′)–H(12′) ··· O(2′)[a]	3.540	2.471	170.4
C(6′)–H(61′) ··· O(5)	3.494	2.466	158.6

[a] $-x, -y, 1-z$. [b] $1-x, 1-y, 1-z$. [c] $1-x, -y, 2-z$. [d] $1-x, -y, 1-z$. [e] $1-x, 1-y, 2-z$. [f] $-x, -y, 2-z$.

in our opinion, this product probably has the *Z* configuration. This stereochemistry is supported by the synthetic pathway used. If no isomerization occurs during the reaction, the intermediate dioxime obtained by reduction of the furoxan **10** must have the *amphi* (*Z*,*E*) configuration [(*Z*,*E*)-1,4-diphenylbutane-1,2,3,4-tetraone 2,3-dioxime] and, consequently, compound **11** should have the *Z* configuration, as indicated.



Scheme 3 *Reagents:* i, NH_2OH·HCl; ii, N_2O_4, dry Et_2O

'*Benzoylmethylglyoxime*.'—We obtained 'benzoylmethylglyoxime,' **4**, according to the method reported by Ponzio[13] (see Scheme 3). By this reaction, Ponzio obtained a mixture of the two derivatives, 'β-methylbenzoylglyoxime' and 'α-methylbenzoylglyoxime,' to which Beilsteins Handbuch, according to Meisenheimer, gave the *anti* and *amphi* configurations [namely, (2*Z*,3*E*)- and (2*E*,3*E*)-1-phenylbutane 1,2,3-trione 2,3-dioxime], respectively.[4] The first derivative gave a red 2:1 Ni^{2+} complex, while the second one did not give any Ni^{2+} complex. We obtained similar results after resolution of the reaction mixture by column chromatography.

NMR spectral data (see Table 1) and the ability to give a red Ni^{2+} complex confirm Meisenheimer's view of the 'β' isomer, namely structure **13**.

To the α-isomer we assigned structure **14**, with *Z* stereochemistry, on the basis of the spectral data in Table 1 and the absence, in the IR region 1600–1800 cm^{-1} (KBr), of any strong absorption attributable to a carbonyl group. In addition, ^{13}C coupled spectra confirmed that the attack of hydroxylamine occurred on the acetyl moiety of compound **12** as already reported in the literature on the basis of chemical evidence (see ref. 8 and the literature therein). Indeed, the C-3 resonance at δ_C 151.7 appears as a quartet ($^2J_{CH}$ 6.6 Hz), while the C-5 resonance at δ_C 101.9 appears as a multiplet.

Reaction of compound **14** with N_2O_4 in dry diethyl ether afforded, according to Ponzio,[13] 'α-oximino-β-pseudonitrile-γ-ketophenylbutane' **15**. However, the absence of any visible absorption rules out the presence of a nitroso group, while ^{13}C and ^1H NMR spectra (Table 1) suggest, for this compound, structure **16**. The presence of two strong ion peaks in the mass spectrum, at *m*/*z* 105 $(C_6H_5CO)^+$ and 122 $(C_6H_5CO_2H)^+$, and the high $\nu_{C=O}$ frequency (1775 cm^{-1})[14] tend to confirm this hypothesis. This derivative probably arises through a reaction pathway similar to that involved in the formation of the methyl analogue described in an earlier paper.[15]

In conclusion, the results of this work and those reported in ref. 1 show that the possibility for an 'acylglyoxime' to exist either in the isoxazoline closed form or in the dioxime open form depends not only on the correct orientation of the acyl and the oxime OH groups involved in ring formation, but also on a fine balance of steric and electronic effects. The derivatives studied in the present work, with the probable exception of compound **7**, did not show, in DMSO at room temperature, any detectable equilibrium between closed and open structures, although tautomerism could be present under different experimental conditions.

Table 5 Fractional atomic coordinates for compound **8**, with esds in parentheses

Atom	*x*	*y*	*z*
O(1)	0.0007(2)	0.3786(2)	0.1007(2)
O(2)	0.1834(3)	0.7351(3)	0.3429(1)
C(1)	0.0924(3)	0.5645(3)	0.2252(2)
N(1)	0.2284(3)	0.6468(3)	0.2578(2)
C(2)	0.1234(3)	0.4657(3)	0.1321(2)
C(3)	0.3045(4)	0.4776(4)	0.0798(2)

Table 6 Fractional atomic coordinates for compound **9**, with esds in parentheses

Atom	*x*	*y*	*z*
O(1)	0.2009(2)	0.0639(2)	0.7861(2)
O(2)	0.2801(2)	0.0862(2)	0.9891(2)
O(3)	0.2892(2)	0.3821(2)	0.7307(2)
O(4)	0.7708(2)	0.4498(2)	0.9591(2)
N(1)	0.4532(3)	0.1535(2)	1.0386(2)
N(2)	0.4296(3)	0.3859(2)	0.8169(2)
C(1)	0.0645(3)	0.2032(3)	0.9099(3)
C(2)	0.2276(3)	0.1595(3)	0.8852(2)
C(3)	0.3933(3)	0.2828(3)	0.8851(2)
C(4)	0.5194(3)	0.2638(3)	0.9820(2)
C(5)	0.7064(3)	0.3525(3)	1.0183(2)
C(6)	0.8064(4)	0.3183(3)	1.1285(3)
O(5)	0.5598(4)	0.0108(3)	0.7543(2)
O(1′)	0.1581(2)	0.0585(2)	0.2979(2)
O(2′)	0.2631(2)	0.0895(2)	0.4986(2)
O(3′)	0.2803(2)	0.3703(2)	0.2273(2)
O(4′)	0.7611(2)	0.4388(2)	0.4549(2)
N(1′)	0.4367(3)	0.1560(2)	0.5469(2)
N(2′)	0.4203(3)	0.3756(2)	0.3144(2)
C(1′)	0.0549(3)	0.2153(3)	0.4194(3)
C(2′)	0.2108(3)	0.1606(3)	0.3937(2)
C(3′)	0.3808(3)	0.2774(3)	0.3871(2)
C(4′)	0.5051(3)	0.2614(3)	0.4862(2)
C(5′)	0.6944(3)	0.3481(3)	0.5194(2)
C(6′)	0.7943(4)	0.3205(3)	0.6315(3)

Experimental

M.p.s were observed on a Buchi 512 capillary apparatus and are uncorrected (heating rate 3 °C min^{-1}). IR spectra were recorded on a Perkin-Elmer 781 spectrophotometer. ^1H and ^{13}C NMR data were recorded on a JEOL GX 270/89 operating at 270.05 and 67.80 MHz, respectively. The samples were dissolved in [$^2H_6$]DMSO (Merck) and were contained in a 5 mm o.d. tube. ^{13}C Assignments were made on the basis of coupled and undecoupled spectra. In a few cases the INEPT sequence was employed to detect long-range J_{CH} coupling constants. The detection of J_{CC} couplings as satellites flanking the main isotopomer resonances were obtained by collecting 10 000–15 000 transients in overnight accumulation or by using the INADEQUATE pulse sequence.[16] Mass spectra were obtained with a Varian CH7 Mat mass spectrometer. TLC [eluent chloroform–tetrahydrofuran (THF) (9:1)] was carried out on 5 × 20 plates precoated with Merck silica gel 60 F_{254}, layer thickness 0.25 mm. Anhydrous magnesium sulfate was used as drying agent.

Compounds **5**,[17] **10**[18] and **12**[19] were prepared according to the literature methods. Light petroleum refers to the fraction boiling in the range 40–60 °C.

Action of Nitrous Acid on Diethyl 2,3-*Diacetylsuccinate.*—The reaction was carried out according to ref. 6 starting from compound **5** (5 g). The crude product obtained was purified by column chromatography [eluent chloroform–THF (9:1)] gave compounds **7**, **8** and **9** (overall yield 2 g). TLC, **7** R_f 0.45; **8** R_f 0.33; **9** R_f 0.09.

3-Acetyl-5-hydroxy-5-methyl-4,5-dihydroisoxazole **7** was eluted first (yield 0.94 g, 46%); m.p. 74–75 °C (from diethyl ether–light petroleum) [lit.,[5] 75 °C (from chloroform)] (Found: C, 50.0; H, 6.3%; M^+, 143. Calc. for $C_6H_9NO_3$: C, 50.35; H, 6.3%; M, 143).

(E,E)-*Hexane*-2,3,4,5-*tetraone* 3,4-*dioxime* (syn-*diacetylglyoxime*) **8** was eluted second (yield 0.16 g, 8%); m.p. 193–194 °C (decomp.) (from diethyl ether–light petroleum) (Found: C, 41.9; H, 4.5%; M^+, 172. $C_6H_8N_2O_4$ requires C, 41.9; H, 4.7%; M, 172).

3-Acetyl-5-hydroxy-4-hydroxyimino-5-methyl-4,5-dihydroisoxazole **9** was eluted third (yield 0.94 g, 46%); m.p. 160–161 °C (decomp.) [lit.,[5] 152.5 °C, lit.,[6] 150–152 °C (decomp.) (from diethyl ether–light petroleum)] (Found: C, 41.5; H, 4.8%; M^+, 172. Calc. for $C_6H_9NO_3$: C, 41.9; H, 4.7%; M, 172).

3-*Benzoyl*-5-*hydroxy*-4-*hydroxyimino*-5-*phenyl*-4,5-*dihydroisoxazole* **11**.—This product was prepared according to ref. 12 (yield 90%), m.p. 169 °C (decomp.) (from aq. ethanol) [lit.,[11] 168 °C (decomp.) (from aq. ethanol)].

Oximation of α-*Benzoyl*-α-*isonitrosoacetone.*—The reaction was carried out according to ref. 13 starting from compound **12** (5 g). The crude product obtained, purified by column chromatography (silica gel 60; 70–230 mesh ASTM, Merck; eluent chloroform containing THF 0–10%), gave compounds **13** and **14** (overall yield 4.2 g). TLC **13**, R_f 0.51; **14**, R_f 0.21.

(2*Z*,3*E*)-1-phenylbutane-1,2,3-trione 2,3-dioxime ('*anti-methylbenzoylglyoxime*') **13** (yield 2.9 g, 69%); m.p. 184 °C (decomp.) (from diethyl ether–light petroleum) [lit.,[13] 194 °C (decomp.)* (from diethyl ether–light petroleum)] (Found: C, 58.3; H, 4.9%; M^+, 206. Calc. for $C_{10}H_{10}N_2O_3$: C, 58.25; H, 4.9%; M, 206).

(*Z*)-5-Hydroxy-4-hydroxyimino-3-methyl-5-phenyl-4,5-dihydroisoxazole **14** (yield 1.27 g, 31%); m.p. 146 °C (decomp.) (from diethyl ether–light petroleum) [lit.,[13] 135 °C (decomp.)* (from toluene)].

2-(*Benzoyloxyimino*)-1-*nitropropanal Oxime* **16**.—This product was prepared according to ref. 13 by the action of dry dinitrogen tetraoxide on a solution of compound **14** in dry diethyl ether (yield 36%), m.p. 101 °C (decomp.) (from diethyl ether–light petroleum) [lit.,[13] 111 °C (decomp.)* (from diethyl ether–light petroleum)] [Found: C, 48.1; H, 3.7%; (mass spectrum lacks the parent ion at M^+, 251). Calc. for $C_{10}H_9N_3O_5$: C, 47.8; H, 3.6%; M, 251].

Crystal Structure of Compound **8**.—*Crystal data.* $C_6H_8N_2O_4$, orthorhombic, space group *Pbcn*, a = 7.293(3), b = 8.225(2), c = 13.239(1) Å, V = 794.1(4) Å^3, Z = 4, D_x = 1.44 Mg m^{-3}, Mo-Kα (λ = 0.710 69 Å), μ = 1.1 cm^{-1}, $F(000)$ = 360, room temperature. The cell parameters were obtained from 25 reflections with 16 < 2θ < 24°.

Data collection. The crystal (0.2 × 0.4 × 0.15 mm), grown from diethyl ether, was mounted on an Enraf-Nonius CAD-4 diffractometer, which used graphite-monochromated Mo-Kα radiation and the $\omega/2\theta$ scan technique; three standard reflections measured every 160 minutes did not show any significant decrease in intensity. 844 Reflections were collected ($+h, +k, +l$), of which 468 unique reflections, with $I > 2\sigma(I)$, were considered observed. Data were corrected for background and Lorentz-polarization effects.

Structure solution and refinement. For all calculations the SHELX86[20] and SHELX76[21] systems of programs were used.

* Probably different heating rates in the measurements of m.p.s of compounds **13**, **14** and **16** may partially account for the discrepancies in m.p.s with those quoted in ref. 13.

The structure was solved by direct methods which showed all the non-H atoms of the independent half-molecule. Full-matrix least-squares refinement was used, the minimized function being $\Sigma w(|F_o| - |F_c|)^2$. The weighting scheme employed was $w = k/[\sigma^2(F_o) + |g|F_o^2]$, where g was refined (final value 0.000 525). Thermal vibrations were treated anisotropically for all non-H atoms. The hydrogen atoms were found on difference Fourier maps and were refined under the constraints O–H = 0.97 ± 0.01 Å and C–H = 1.08 ± 0.01 Å, *i.e.* the values of distances from the 'heavy' atoms where they were localized. An overall isotropic temperature factor, common to all hydrogen atoms, converged to 0.091(6) Å^2. The final R- and R_w-values were 0.037 and 0.039 for the 68 parameters refined. The maximum residual peak in the final difference Fourier map was 0.16 e Å^{-3}.

Crystal Structure of Compound **9**.—*Crystal data.* $C_6H_8N_2O_4 \cdot \frac{1}{2}H_2O$, triclinic, space group $P\bar{1}$, a = 7.894(1), b = 9.626(1), c = 11.372(8) Å, α = 92.49(3), β = 96.68(4), γ = 105.85(1)°, V = 823.1(6) Å^3, Z = 4, D_x = 1.46 Mg m^{-3}, Mo-Kα, μ = 1.2 cm^{-1}, $F(000)$ = 380, T = 293 K. The cell parameters were obtained and refined from 25 reflections with 16° < 2θ < 28°.

Data collections. Crystal (0.2 × 0.25 × 0.15 mm), grown from water, was mounted on an Enraf-Nonius CAD-4 diffractometer which used graphite-monochromatized Mo-Kα radiation and the $\omega/2\theta$ scan technique; three standard reflections measured every 160 minutes did not show any significant variation. 2690 Reflections collected ($\pm h$, $\pm k$, $+l$), 1805 of which, having $I > 2\sigma(I)$, were considered observed.

Structure solution and refinement. SHELX76 and SHELX86 were used for all the calculations. Solution of the structure was not straightforward: all attempts in space group $P\bar{1}$ were unsuccessful. Assuming symmetry $P1$, it was possible to locate four complete molecules of compound **9** plus two oxygen atoms belonging to the water molecules, being quasi symmetry-related. The co-ordinates were then referred to the centroid as origin and were satisfactorily refined with least-squares methods. All thermal vibrations were treated anisotropically for the non-H atoms. The hydroxy hydrogen atoms and those belonging to the water molecule were found on difference Fourier maps and were refined under the constraints O–H = 0.97 ± 0.01 Å. Methyl hydrogens were positioned geometrically and were refined 'riding' on their C-atoms, with C–H = 1.08 Å. Three overall temperature factors were refined for the H-atoms, which converged at 0.12, 0.15 and 0.16 Å^2, respectively. Final R- and R_w-values = 0.048 and 0.052 for 255 parameters refined. The maximum residual peak in the final difference Fourier was 0.26 e Å^{-3}.

Geometrical calculations were made using the program Platon.[22]

Supplementary data (see section 5.6.3 of Instructions for Authors, Issue 1, 1992). Complete listings of bond lengths, angles and contacts, together with H-atom co-ordinates and thermal parameters, are available on request from the Cambridge Crystallographic Data Centre.

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Paper 1/03530D
Received 11*th July* 1991
Accepted 18*th September* 1991