Crystal Structure and Tautomerism in 4-Phenylisoxazoles with Two Potential Hydroxyl Groups at Positions 3 and 5

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The crystal structure of 4-phenyl-3-hydroxyisoxazol-5-one semihydrate exhibits an exceptional hydrogen bonded polymeric structure with a unit cell of 8 molecules. The hydrogen bonds stretch out, using the oxo-hydroxy groups in positions 3 and 5 in the direction of one axis and along a perpendicular direction the layers are stitched together by water molecules. The layers are stitched by using four hydrogen bridges of water molecules, the heterocyclic ring nitrogen as well as the oxygen at position 5. Tautomerism of this moiety in solution is discussed, in light of some new dialkylation products. The state in which these products exist in solution depends on the solvent. A zwitterionic tautomer is present in ether. In some alkylation conditions, the predominant dialkylation product is the *N,N*-disubstituted betaine (Anhydro-2,2-dialkyl-3(5)-oxo-5(3)hydroxy-4-phenylisoxazolonium hydroxide). Study of tautomerism in polar and protic solvent is unreliable owing to associations and dissociation phenomena.

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Although the isoxazole derivative containing two oxygen functions in positions 3 and 5 as well as three of its dimethylation products were available [1] there was a lot of confusion in the assignment of tautomeric structure in solution as well as in the solid state [2]. The uv spectra of the three dimethylation products corresponding to three neutral tautomeric forms (**1a-1c**) in solution did not differ from one another to permit a doubtless conclusion about the predominant tautomer in solution.

Using our previous data [1] it was concluded that the 3-hydroxyisoxazolin-5-one structure **1c**, is predominant both in solution and in the solid state [2]. For reasons of convenience such derivatives were and still are named 4-aryl-3,5-dihydroxyisoxazoles [1,3] or "disic acids" as they exhibit high acidity [4], having p*K*a's between 0 and 2. The absence of both free OH, NH or C=O stretching absorptions in the ir spectrum in the solid anhydrous powder prompted the suggestion of a dipolar structure **1d** [1]. The ir spectrum of the stable semihydrate showed an associated OH absorption and suggested intermolecular hydrogen bonding, evidence for which is now presented by means of single crystal X-ray analysis.

X-Ray Analysis.

i. Structure of Unit Cell and Polymeric Crystal.

There are 8 molecules in a unit cell [Figure 1], four of which face one another with their heterocyclic rings, in alternation. Diagonally each pair is in the same plane and perpendicularly in a slightly removed plane. The oxygen of the water molecule is located at the face of the unit cell using its tetrahedral coordination for inter cellular hydrogen bonding [Figure 2]. Two of its bonds adhere to one diagonal pair at the heterocyclic nitrogens; the other two are attached diagonally to another pair in a neighbouring unit cell, at the oxygens at position 5. Thus creating successive bridging along the Y axis. On the other hand there is a continuous hydrogen bridging along the X axis involving oxygens at positions 3 and 5. One extended thread in the X direction and another in the -X, reciprocally.

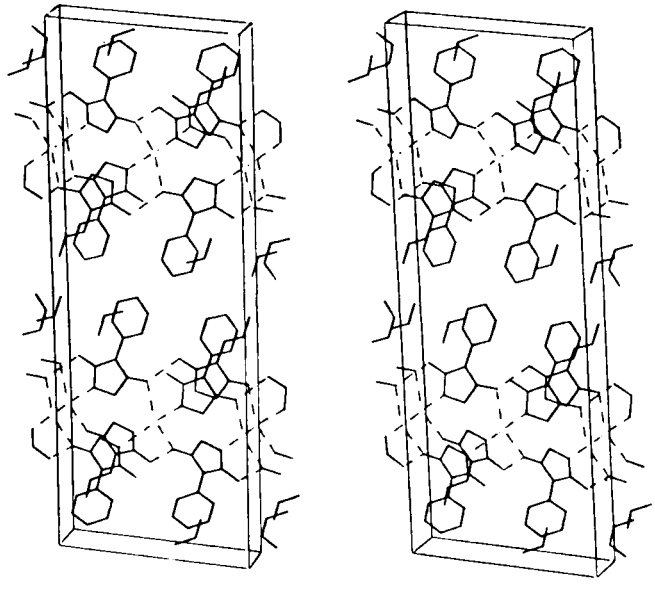


Figure 1. Stereoscopic drawing of molecular packing and hydrogen bridging of the semihydrate of **1**, excluding hydrogen atoms, in the unit cell.

By viewing carefully Figure 1 or looking at a model, one can visualize an extended hydrogen bonded conglomerate. Along such a conglomerate is situated another one of the same features with an inverted image (see the other four molecules in a unit cell, in Figure 1). Such an image is achieved by inversion of the whole structure, *e.g.* in the direction of -Y axis instead of +Y.

The continuous "half cell" conglomerates (along X axis) face each other only with the benzene rings, probably with some hydrophobic interactions.

Interestingly, the width of the unit cell (along Y axis) is only 3.78 Å quite a small distance for a polyatomic structure. The unit cell is quite large at its two other dimensions *e.g.*, 12.51 and 34.78 Å respectively. Each unit cell shares four halves and eight quarters of a molecule of water at the faces and edges. Elucidation of the crystal structure of **1** explains why all its known derivatives [4] crystallize out as semihydrates, even after recrystallization from organic solvents.

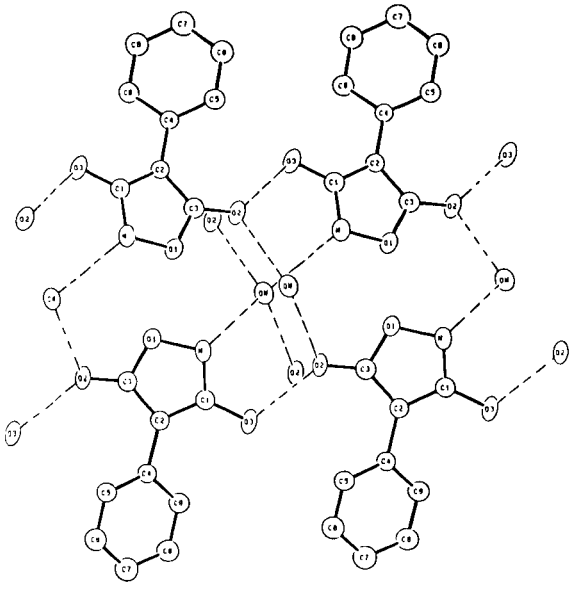


Figure 2. Half a unit cell containing four molecules with intra- and intercellular hydrogen bridges.

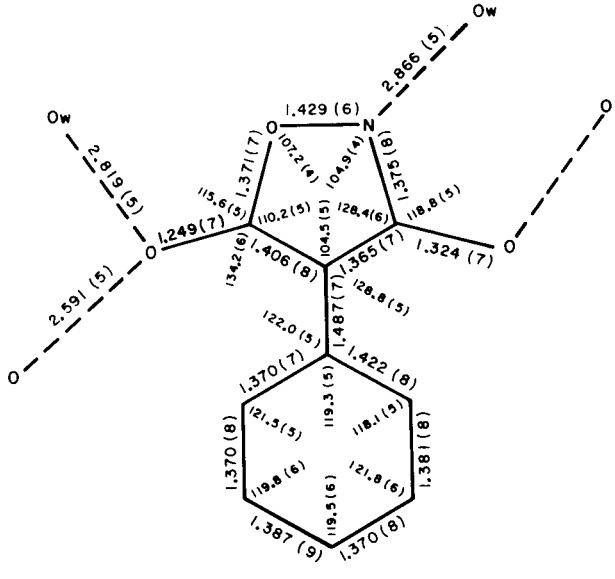
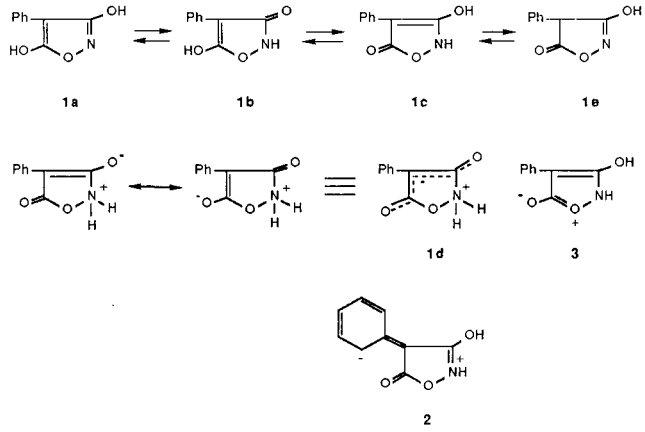


Figure 3. Bond Lengths (Å) and angles (°) in a molecule of 4-phenyldisic acid.

ii. Intramolecular Structural Features.

Considering the bond lengths in the heterocyclic ring [Figure 3] it may be concluded that the electron distribution is a result of a hybride in which several resonative and tautomeric forms must be considered.

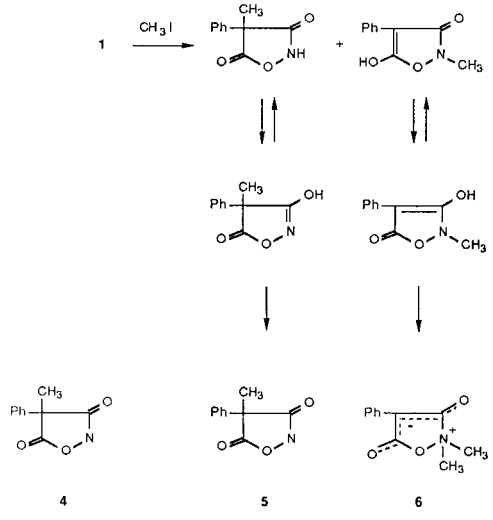


The C-N and C_3-C_4-C_5 distances are intermediate between single and double bonds. They are 1.373, 1.365 and 1.407 Å for C-N, C_3-C_4 and C_4-C_5 respectively. It seems that the contribution of the various tautomeric forms is in a decreasing order: **1c** > **1b** > **1a**. There must be some contribution of a resonance species **2** which involves dipolar delocalization, extended to the benzene ring. Besides its contribution to the shortening of the C-N bond it is expressed also in the relatively long bond in the benzene ring (1.422 Å), and in shortening of the distance between the two rings. A dihedral angle of 146° between the heterocyclic ring and the phenyl ring still permits such delocalization. The hydrogen at the nitrogen is thus donated easily to the hydrogen bridging.

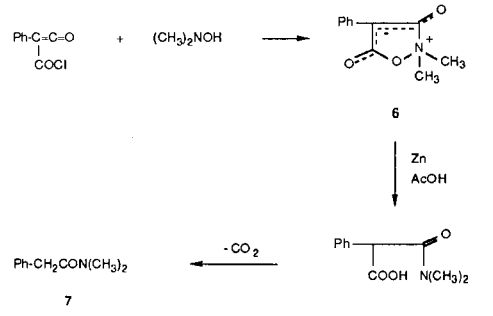
There is a slight difference between the C-O bonds lengths in positions 3 and 5, *e.g.* 1.25 and 1.32 Å for positions 3 and 5 respectively. This suggests a somewhat more carbonyl character to position 5. O-H distances indicate the same trend. 1.092 Å is quite a long bond for an OH group while 1.62 Å is quite short for merely a hydrogen bridge. The shortening of the C_5-O_1 bond must be attributed to another charged resonance species **3**, involving the ring oxygen as could be expected from an ester bond. The partial positive charge on this oxygen is probably the reason why this oxygen is the only heteroatom which is not involved in hydrogen bonding. On the other hand the partial negative charge on the exo oxygen explains its sharing two hydrogen bonds. One has O_3-O_5 distance of 2.59 Å and the second O_5-O_w distances of 2.89 Å (Figure 3).

Dialkylation on Nitrogen *vs.* Other Sites.

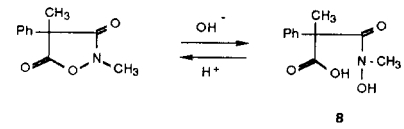
In an earlier publication [1] alkylation by diazomethane was reported to yield three isomers of dimethylation corresponding to the three neutral tautomers **1a-1c**. At present we have observed by using methyl iodide in acetone three additional dimethylation products **4-6**. Although 4-phenyldisic acid was reported to react with acetone, it is essentially a reversible reaction and in the presence of potassium carbonate it did not interfere with the alkylation. Alkylation at carbon is not so common but as a thermodynamically stable alkylation site and as a malonic acid derivative it is not surprising. Initial alkylation on carbon leads to products **4** and **5**. Initial substitution at the nitrogen leads immediately to a stable betain **6** (see scheme). Stability of betaines derived from 3,5-dioxoisoxazoles and pyrazoles were shown previously [5,6]. Structure **6** was proved spectroscopically, by independent synthesis from phenyl(chlorocarbonyl)ketene [9] as well as by zinc reduction to *N,N*-dimethylphenylacetamide (**7**). The latter was compared with an authentic preparation from dimethyl amine. In reexamining the previously described reaction with diazomethane the formation of **6** was also observed in addition



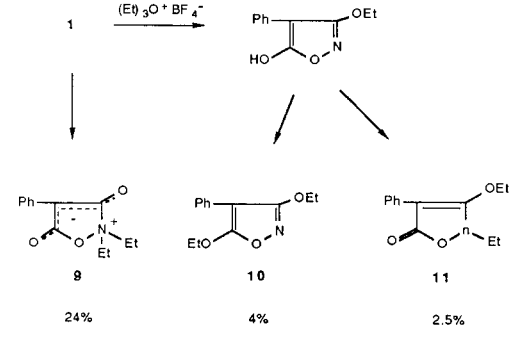
to its three isomers: 3-methoxy-4-phenyl-1-methylisoxazolin-5-one and 5-methoxy-4-phenyl-1-methylisoxazolin-3-one and 3,5-dimethyoxy-4-phenylisoxazole.



Interestingly, compound **4** exhibits γ-lactone properties. The ring is hydrolysed by titration with base to 2-phenyl-2,*N*-dimethylmalonohydroxamic acid **8**. Upon titration with acid ring reclosure occurs back to 4-phenyl-4,*N*-dimethylisoxazoline-3,5-dione (**4**).

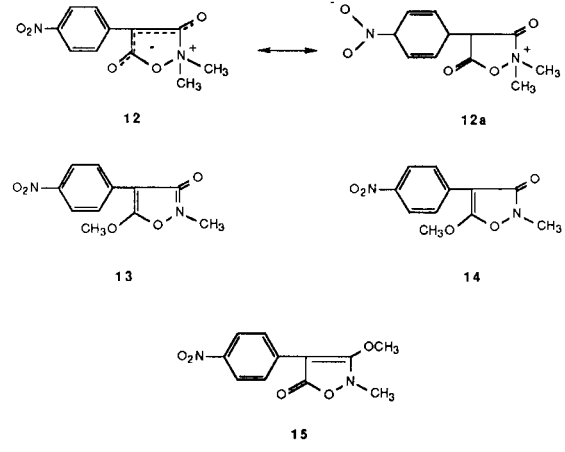


Using triethyloxonium fluoroborate (Meerwein reagent) for alkylation of **1** resulted mainly in the formation of the *N,N*-dimethyl zwitterion **9**. In this reaction the initial alkylation is mainly at the nitrogen to yield by further alkylation the betaine **9**. Initial alkylation (to a smaller extent) on the oxygen at position 3 leads to products **10** and **11**. The predominance of alkylation on nitrogen over oxygen in the case of this reagent, is contrary to what is generally known [8]. It can be explained only in terms of the thermodynamically stable betaine **6**.



Unlike methyl iodide this reagent does not attack carbon at position 4. It probably does not alkylate the oxygen at position 5 at the initial mono alkylation step as evident from the absence of a 5-methoxy-*N*-methyl derivative which is obtained, however, by using diazomethane [1].

On applying methyl iodide to 4-nitrophenyl derivative of **1**, the only isolable product was the betaine derivative,



12. The reason is probably that the nitro group reduces the nucleophilicity of the carbon at position 4 and on the other hand stabilizes the charged product by delocalization (**12a**).

p-Nitrophenyldisic acid gives with diazomethane in ethanol-ether only the three neutral dimethylation products **13-15**, owing probably to the acidic conditions. Although products **14** and **15** were isolated as a mixture, it permitted us to determine their spectral data.

UV Absorption and Tautomerism in Solution.

Having the six isomeric dimethylation products of this isoxazole derivative **1** and four dimethylation products of the *p*-nitrophenyl derivative, and by studying their spectra we could now reassess tautomerism. Tautomers with a saturated carbon at position 4 were excluded as their uv maxima were in very short wavelengths. Studying the spectra in ethanol proved again to be useless as the maxima did not differ considerably. There were two products with close maxima but rather different intensities. Having in mind interaction with protic ethanol it was advisable to switch to ether. A comparison of the uv spectra in ether is shown in Figure 4. Although it is hard to judge which of the isomers is similar to the parent compound, looking at the longer wavelength range where the betainic product has a typical pattern, it was possible to arrive at certain conclusions. First, that a zwitterionic structure cannot be excluded and second an aromatic species is present as well. Certainly, there is not one predominant tautomer.

By comparison of the *p*-nitrophenyl derivatives in ether [Figure 5] it is possible to conclude that the zwitterionic tautomer is predominant as none of the other dimethylation products absorbs in the same range of the parent *p*-nitrophenyl substituted free acid, whereas it is very close to that of the betaine **12**. Turning back to ethanol, the free acid of the *p*-nitro derivatives gave a spectrum so much different from all the fixed structures because it turned out that it tends to dissociate to an anion. The λ max of the latter depends considerably on the concentration, probably due to solvation or perhaps further dissociation. It is shifted, for instance, from 370 nm to 390 nm upon dilution from 1.4×10^{-4} to 0.5×10^{-4} *M*, in ethanol.

It turns out that in the case of compound **1** the monoanion absorbs at the same range as the neutral species. Whereas in the *p*-nitro derivative the difference between the λ max of the monoanion and the neutral acid is large enough to enable the detection of its dissociation.

Undoubtedly all experiments higherto to assign a predominant tautomeric structure in ethanol, water or in any other polar or protic solvent, failed due to dissociation, which was not taken into consideration [2].

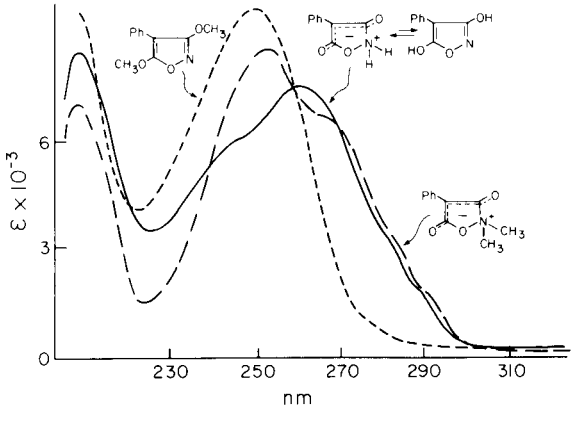


Figure 4. Uv Spectra of 4-phenyl disic acid derivatives in ether.

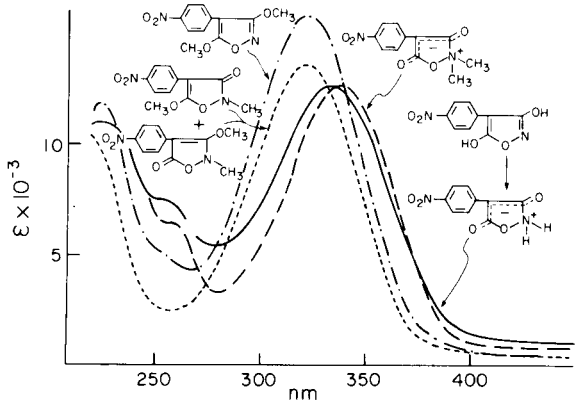


Figure 5. Uv Spectra of 4-(*p*-nitrophenyl)disic acid derivatives in ether.

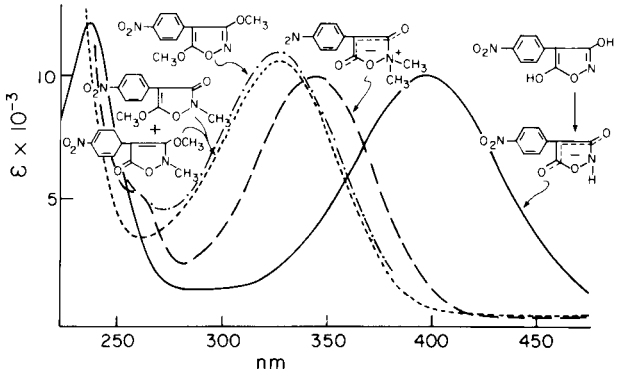


Figure 6. Uv Spectra of 4-(*p*-nitrophenyl)disic acid derivatives in ethanol.

EXPERIMENTAL

The uv spectra were taken either with a Varian Techtron Model 635 spectrophotometer or with a Bosch and Lomb Spectronic 2000. The ir with a Perkin Elmer Model 157, the ^{1}H-nmr with a Varian T-60 and the ^{13}C-nmr with a Bruker WH-300 spectrometer. Single crystal X-ray analyses were observed on a 4 circle automatic difractometer Philips PW 1100.

Table 1

Fractional Atomic Coordinates and Thermal Parameters (The estimated standard deviations are given in parentheses and refer to the last positions of respective values). The expression for the thermal parameters with U values in $Å^2$ is:

$$T = \exp\{-2\pi^2(U_{11}h^2a^{*2} + U_{22}k^2b^{*2} + U_{33}\ell^2c^{*2} + 2U_{12}hka^*b^* + 2U_{13}h\ell a^*c^* + 2U_{23}k\ell b^*c^*\}$$

Atom	X	Y	Z	U11 OR U.A^2	U22	U33	U12	U13	U23
OW	0.00000	0.796(2)	0.25000	0.026(3)	0.059(5)	0.040(4)	0.000000	0.005(3)	0.000000
O(1)	0.7268(3)	0.527(1)	0.2155(1)	0.024(2)	0.066(4)	0.033(2)	0.005(3)	0.007(2)	0.004(3)
O(2)	0.5689(3)	0.691(1)	0.1878(1)	0.020(2)	0.070(4)	0.043(3)	0.012(3)	0.011(2)	0.008(3)
O(3)	0.9163(3)	0.516(1)	0.1474(1)	0.022(2)	0.071(4)	0.046(3)	0.008(3)	0.014(2)	0.006(3)
N	0.8313(3)	0.448(2)	0.2039(1)	0.022(3)	0.056(4)	0.039(3)	0.006(3)	0.004(2)	0.006(3)
C(1)	0.8278(5)	0.543(2)	0.1657(2)	0.031(2)					
C(2)	0.7276(4)	0.642(2)	0.1513(2)	0.027(1)					
C(3)	0.6651(5)	0.628(2)	0.1831(2)	0.032(2)					
C(4)	0.6888(4)	0.720(2)	0.1106(2)	0.027(2)					
C(5)	0.5874(4)	0.634(2)	0.960(2)	0.031(2)					
C(6)	0.5534(5)	0.701(2)	0.0583(2)	0.039(2)					
C(7)	0.6229(5)	0.856(2)	0.0341(2)	0.042(2)					
C(8)	0.7248(5)	0.943(2)	0.0482(2)	0.038(2)					
C(9)	0.7599(5)	0.888(2)	0.0864(2)	0.034(2)					
H(3)	0.9863(3)	0.479(1)	0.1677(1)						
HN	0.8930(3)	0.545(2)	0.2220(1)						
H(5)	0.5369(4)	0.483(2)	0.116(2)						
H(6)	0.4754(5)	0.617(2)	0.0464(2)						
H(7)	0.5994(5)	0.896(2)	0.0074(2)						
H(8)	0.7766(5)	1.088(2)	0.0316(2)						
H(9)	0.8395(5)	0.930(2)	0.0989(2)						

Crystallographic data: Chemical formula $C_9H_7O_3N \cdot \frac{1}{2}H_2O$

Molecular weight:	162.2
Crystal system:	monoclinic
Space group:	C2/c
Unit cell dimensions:	a = 12.510 Å
	b = 3.776 Å
	c = 34.786 Å
	β = 94.47°
	v = 1638.2 $Å^3$
No. of molecules in unit cell:	8
Density (calculated):	1.315 g cm^{-3}
Linear absorption coefficient	$\mu(MoK_\alpha)$ = 0.74 cm^{-1}
Number of unique reflections	1037
Disagreement index R	0.071
Weighted disagreement index Rw	0.086

Table 1

Methylation of 4-Phenyldisic Acid with Methyl Iodide.

To a solution of 4-phenyldisic acid (1.86 g) in acetone (50 ml), potassium carbonate (5 g) and methyl iodide (22 ml) were added. The mixture was refluxed for 6 hours with stirring, cooling and filtered. The filtrate was evaporated to dryness *in vacuo* and redissolved in ether. Filtered from some impurities and dried on sodium sulfate. After concentration *in vacuo* to 15 ml a first crop of anhydro 2,2-dimethyl-4-phenyl-3(5)-oxo-5(3)-hydroxyisoxazolium hydroxide (**6**), was obtained. Recrystallization from 2-propanol gave 0.29 g (14%) of a pure product, mp 145°; ir (Nujol): ν max 1800 s, 1715, 1610 cm^{-1}; uv (ethanol): λ max 253 (ϵ = 17660), 268 sh; ^{1}H nmr (deuteriochloroform): δ 8.00-7.16 m (Ph), 3.33 s ($2CH_3$); ^{13}C nmr (DMSO-d_6): δ 169.03, 167.83 (CO), 131.14, 128.45, 125.25, 124.25 (Ph), 69.10 (C_4), 50.44 ($2CH_3$).

Anal. Calcd. for $C_{11}H_{11}NO_3$: C, 64.38; H, 5.40; N, 6.83. Found: C, 64.60; H, 5.18; N, 6.95.

The etheral filtrate (A) was extracted 3 times with 0.3 *M* sodium hydroxide (10 ml each). The combined aqueous solution was acidified to *p*H 2 with hydrochloric acid (32%) and extracted 3 times with ether (15 ml each). This etheral solution (B) was evaporated to dryness *in vacuo*. The residue consisted of an oily product identified as 2,4-dimethyl-4-phenyl-isoxazolidin-3,5-dione (**4**), 0.6 g (29%); ir (neat): ν max 1800, 1700 cm^{-1}; uv (ethanol): λ max 219 nm (ϵ = 4255); ^{1}H nmr (deuteriochloroform): δ 7.63-7.33 m (Ph), 3.43 s (NCH_3), 1.78 s (CH_3); ^{13}C nmr (DMSO-d_6): δ 172.51, 171.96 (C), 135.66-126.89 (Ph), 50.05 (C_9), 33.44 (CH_3), 20.08 (CH_3).

Anal. Found: C, 64.62; H, 5.49; N, 7.03.

The etheral solution (A) was evaporated and the residue subjected to column chromatography on silica-gel and eluted with a mixture of ethyl acetate and petroleum ether (3:1). First came another crop of **4** and then another oily product which was identified as 4-methyl-3-methoxy-4-phenylisoxazolin-5-one (**5**); ir (neat): ν max 1790 cm^{-1}; uv (ethanol): λ max 212 nm (ϵ = 69.93); ^{1}H nmr (deuteriochloroform): δ 7.26 s (Ph), 3.93 s (CH_3O), 1.75 s (CH_3).

Anal. Found: C, 64.41; H, 5.56; N, 6.58.

Independent Synthesis of Anhydro-2,2-dimethyl-4-phenyl-3(5)-oxo-5(3)-hydroxyisoxazolium Hydroxide **6**.

N,N-Dimethylhydroxylamine hydrochloride (1.0 g) was boiled in THF (30 ml) together with triethylamine (1.2 ml) in tetrahydrofuran (30 ml). The solution was cooled, filtered and introduced dropwise (10 minutes) into a solution of (chlorocarbonyl)phenylketene (3 g) [5], in dry ether (10 ml) at 15°. The precipitate which was formed was collected, washed with aqueous sodium bicarbonate (5%), recrystallized from 2-propanol (1.0 g), 48%, Spectral data (nmr, uv and ir) were identical with the product obtained above.

Reduction of Anhydro-2,2-dimethyl-4-phenyl-3(5)-oxo-5(3)-hydroxyisoxazolium Hydroxide (**6**) by Zinc in Acetic Acid.

Compound **6** (0.2 g) was dissolved and boiled in acetic acid (4 ml) and Zn powder (1 g), was added in small portions while boiling and stirring during 30 minutes. The mixture was cooled, filtered and 5% aqueous sodium bicarbonate (50 ml) was added to the filtrate. After cooling overnight at 4° it was extracted with 3 portions of chloroform (30 ml), dried on sodium sulfate and evaporated to dryness *in vacuo*. The oily residue proved to be *N,N*-dimethylphenylacetamide **7** by comparison (ir), with an authentic sample prepared from phenylacetyl chloride and dimethylamine.

Anhydro-2,2-dimethyl-4-(*p*-nitrophenyl)-3(5)-oxo-5(3)-hydroxyisoxazolium Hydroxide (**9**).

4-(*p*-Nitrophenyl)disic acid (2 g) which was obtained by a previously described method [4], was boiled in acetone (120 ml) with potassium carbonate (5 g) and methyl iodide (22 ml) for 10 hours with stirring. The mixture cooled, filtered and evaporated to dryness *in vacuo*. The residue was triturated in ether, the solid collected, washed with water and 5% aqueous sodium bicarbonate. It was recrystallized from acetic acid (0.6 g), 26% yield, mp 206°; ir (Nujol): ν max 1700 cm^{-1}; uv (ethanol): λ max 345 nm (ϵ = 9285), 262 nm (ϵ = 4795), 234 nm (ϵ = 7450); ^{1}H nmr (DMSO-d_6): 8.16 s (C_6H_4), 3.56 ($2CH_3$).

Anal. Calcd. for $C_{11}H_{10}N_2O_5$: C, 52.80; H, 4.13; N, 11.20. Found: C, 52.54; H, 3.98; N, 10.80.

Ethylation of 4-Phenyldisic Acid (**1**) with Meerwein Reagent.

4-Phenyldisic acid (**1**, 1.86 g) was dissolved in 5% aqueous sodium bicarbonate (100 ml). Triethyl oxonoium fluoroborate (8 g) was added in small portions (5 minutes), while cooling and with stirring. The solution was stirred for additional 1 hour and extracted 3 times with chloroform (30 ml). After drying on sodium sulfate and evaporation of the solvent *in vacuo*, the oily residue was subjected to silica gel column chromatography. Elution with ethyl acetate-petroleum ether (3:1) enabled the separation of three products: 2-ethyl-3-ethoxy-4-phenylisoxazol-5-one (**10**) came out with first fraction, 0.05 g (2.5%) of an oily product; ir (neat): ν max 1730 cm^{-1}; uv (ethanol): λ max 269 nm (ϵ = 11700), 247 nm (ϵ = 5212); ^{1}H nmr (deuteriochloroform): δ 7.66-7.16 m (Ph), 4.13 q (CH_2), 3.56 q (CH_2), 1.46-1.113 2t ($2CH_3$).

Anal. Calcd. for $C_{13}H_{15}NO_3$: C, 66.94; H, 6.48; N, 6.00. Found: C, 66.72; H, 6.67; N, 6.25.

Next fraction contained 3,5-diethoxy-4-phenylisoxazole (**11**) which recrystallized from cyclohexane (0.1 g), 5% yield, mp 56°; ir (Nujol): ν max 1615 cm^{-1}; uv (ethanol): λ max 248 nm (ϵ = 14780); ^{1}H nmr (deuteriochloroform): δ 8.06-7.83, 7.53-7.16 m (Ph), 4.33 q (CH_2), 3.86 q (CH_2), 1.34 2t ($2CH_3$).

Anal. Found: C, 66.98; H, 6.48; N, 5.96.

The last and major fraction was of anhydro-2,2-diethyl-4-phenyl-3(5)-oxo-5(3)-hydroxyisoxazolium hydroxide (**11**). It was eluted from the column with ethanol and recrystallized from cyclohexane-chloroform (1:1), mp 121°, 0.5 g (24%); ir (Nujol): ν max 1780, 1680, 1600 cm^{-1}; uv (ethanol): λ max 270 nm sh (ϵ = 13095), 254 nm (ϵ = 17160); ^{1}H-nmr (deuteriochloroform): δ 8.7-7.13 m (Ph), 3.79-3.50 m ($2CH_2$), 1.34 t ($2CH_3$).

Anal. Calcd. for $C_{13}H_{15}NO_3$: C, 66.94; H, 6.48; N, 6.00. Found: C, 67.23; H, 6.57; N, 5.96.

This product has been prepared and identified previously from the reaction of (chlorocarbonyl)phenylketene with *N,N*-diethyl hydroxylamine [9].

Methylation of 4-(*p*-Nitrophenyl)disic Acid with Diazomethane.

4-(*p*-Nitrophenyl)disic acid (2.3 g) was dissolved in ethanol. Into this solution an etheral solution of 0.03 moles of diazomethane was added while stirring. The solution stirred at room temperature overnight and acetic acid (1 ml) was added. Some impurities were filtered off and the filtrate evaporated to dryness *in vacuo*. The residue was redissolved in ethyl acetate (30 ml), washed twice with 5% aqueous sodium bicarbonate (20 ml), dried on magnesium sulfate and the solvent evaporated *in vacuo*. The residue was subjected to column chromatography, eluting with a mixture of ethyl acetate and petroleum ether (3:1). The first fraction contained 3,5-dimethoxy-4-(*p*-nitrophenyl)isoxazole (**13**) which was recrystallized from 2-propanol (0.25 g), 10% yield, mp 137°; ir (Nujol): ν max 1630 cm^{-1}; uv (ethanol): λ max 330 nm (ϵ = 16530); ^{1}H nmr (deuteriochloroform): δ 8.26-7.65 q (Ph), 4.16 s (CH_3), 4.00 s (CH_3).

Anal. Calcd. for $C_{11}H_{10}N_2O_5$: C, 52.80; H, 4.03; N, 11.20. Found: C, 52.74; H, 4.22; N, 11.15.

The second fraction contained 0.2 g (8%) of a mixture of 2-methyl-5-methoxy-4-(*p*-nitrophenyl)isoxazolin-5-one (**14**) and 2-methyl-3-methoxy-4-(*p*-nitrophenyl)isoxazolin-3-one (**15**). The mixture was recrystallized from isopropanol without any change (mp 112°). The ratio and features of the two isomers in solution could be determined by nmr and ir; ir (Nujol): ν max 1750 cm^{-1} (CO of **14**), 1680 cm^{-1} (CO of **15**); ^{1}H nmr (deuteriochloroform): δ 8.30-7.93 q (C_6H_4), 4.23 s (5-OCH_3), 4.06 (3-OCH_3), 3.36 (N-CH_3), 3.45 (N-CH_3).

Anal. Found: C, 52.61; H, 4.04; N, 11.18.

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