HETEROCYCLES, Vol 26, No 4, 1987

MOLECULAR STRUCTURE AND STABILITY OF ISOXAZOLIUM ENOLATES[1]

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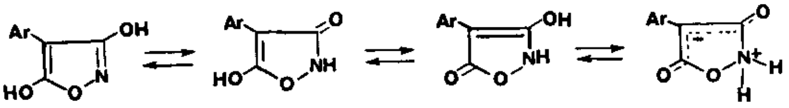
Abstract - Single crystal X-ray diffraction analysis, spontaneous formation and solvolytic stability of the dipolar Schiff base isoxazolium enolate, derived from aldehydes and ketones were studied. The cross conjugated betaine (V) derived from 2,4-dimethoxybenzaldehyde by condensation with 4-phenyl disic acid (II), showed coplanarity and cis configuration. The X-ray results revealed exceptionally long bonds between the two units, that of the anion and that of the cation. Results obtained by omega beta calculations were in line with the experimental observations. Cyclopentanone was the only ketone that gave a stable dipolar condensation product. Derivatives of aromatic aldehydes are generally more stable probably for the reason the coplanarity of the cationic part of the molecule is more feasible. There is evidence for attractive C-H···O interactions which might contribute to stability in aldehyde derivatives (IIIa). Ketisates (IIIb), which were synthesized by an alternative route were found to hydrolyze spontaneously when dissolved in moist solvents. Analogous betaines that have N^1-substituted pyrazole instead of isoxazole were also studied, leading to a scheme for facile decomposition of oximes and hydrazones.

The spontaneous condensation of aromatic aldehydes with 3,5-dihydroxyisoxazole derivatives (I) to produce red solid dipolar products (IIIa) were reported in earlier publications.[2-4] They were also named aldisates, a name which was derived from aldehydes and disic acids. The latter is a name given[4] to the highly acidic heterocyclic system (I). These acids exist as mixtures of tautomeric forms (Ia-d).

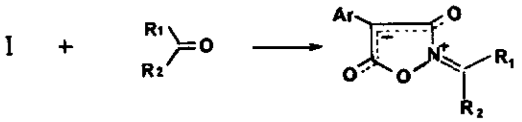
There is a great difference in stability between products derived from aromatic aldehydes and those derived from aromatic ketones. Whereas, for instance, 2,4-dimethoxybenzaldehyde reacts spontaneously with disic acids (I) to yield red crystalline aldisates[3,4], 2,4-dimethoxyacetophenone fails to give even the slightest coloration.

Most of the aliphatic carbonyl compounds give unstable products, which could not be isolated. The ketisate derived from acetone was shown[3,5] to be unstable and the isolated products were mesityl oxide derivatives. In the presence of primary and secondary alcohols (R'OH), derivative of isoxazolooxazine (IV) were obtained.[5] With α,β-unsaturated ketones a noncatalyzed Michael addition was observed, either at the nitrogen or both at the nitrogen and carbon. α,β-Unsaturated aldehydes yielded polymers.[5]



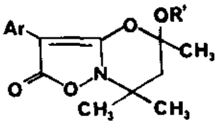
Ia Ib Ic Id

II Ar = Ph



IIIa R₁ = H, R₂ = Aryl

IIIb R₁ and R₂ ≠ H



IV

The single crystal X-ray structure determination of compound (V) which is described here provides information about the molecular and steric features of this group of dipolar products which was hitherto incomplete. The stereochemistry around the C=$\overset{+}{N}$ double bond was found to be cis, e.g., the one with the aldehydic hydrogen closer to the carbonyl oxygen (see Fig. 1). The other important features which were deduced from the X-ray study were coplanarity, exceptionally long bonds inside the isoxazolium ring and evidence for C-H···O hydrogen bonding.

The hemihedral angle between the heterocyclic ring and the 2,4-dimethoxyphenyl ring is 4.37° (Figs. 1, 2). That which is between the heterocyclic ring and the phenyl attached to the anion is 9.84°. The angle between these two aromatic rings is about 5°. The noticeable findings concerning the bond distances are as follows: a) Both the amidic C-N bond and the esteric C-O single bond are very long. Therefore any conjugation between the negative half and the positive half of the molecule as shown for instance in structure Va should be excluded. The distance between the carbon and the oxygen in a single C-O bond is considered to be 1.42 Å. Moreover this distance is even shorter in esters. Here we have a C_3-O distance of 1.469 Å (Figs. 1, 2), much longer than expected for a single bond. The C_1-N distance (Figs.1, 2) is also longer than expected for a single C-N bond. In the parent compound, e.g. disic acid, the C-O and C-N bonds are considerably shorter.

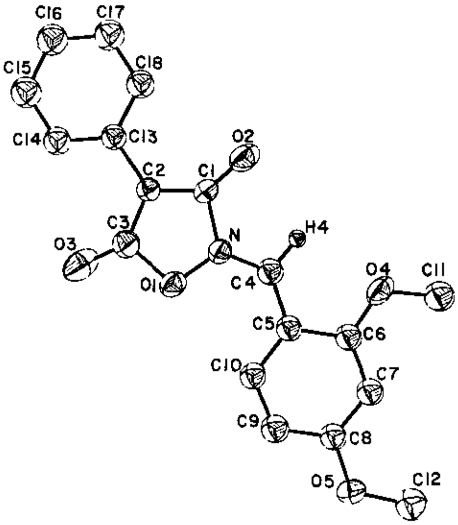


Fig. 1. Molecular structure of compound V by X-ray diffraction.

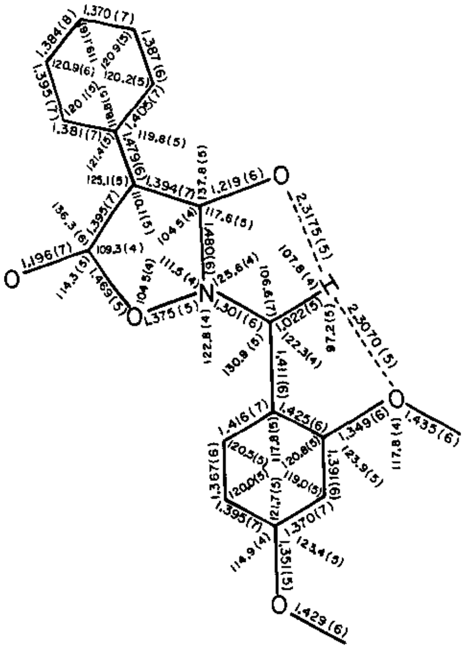
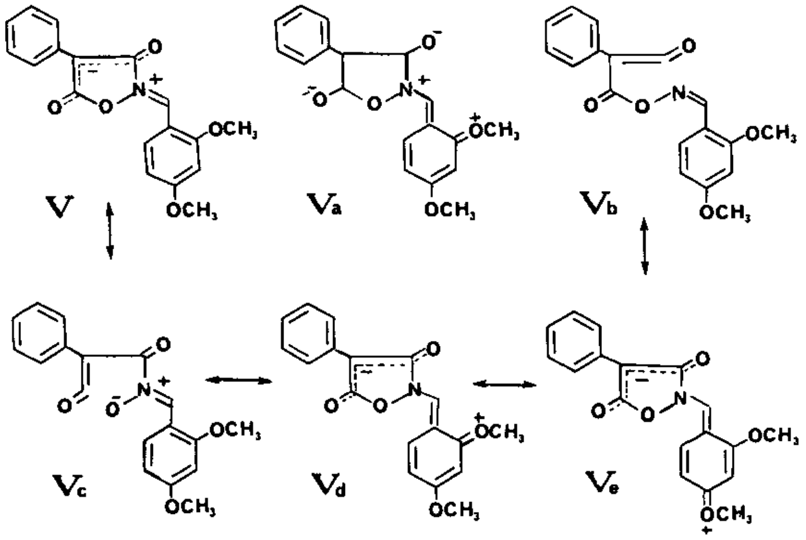


Fig. 2. Bond lengths (Å) and angles (°) in compound V by X-ray analysis.

They are 1.371 Å and 1.375 Å respectively.[4b] Although resonative structures as Vb and Vc look hypothetical they cannot be excluded. These structures (Vb and Vc) point at a decreased sigma character of the C_3-O and C_1-N bonds, while π-n orbital overlap is still possible. b) The two carbonyl $C\cdots O$ distances are shorter than expected from delocalized structure V. The shortening of these bonds is in line with the stretching of the C_3-O and C_1-N as expected from contribution from the resonance structure Vb and Vc. The C_1-C_2 and C_2-C_3 (Figs. 1, 2) distances are similar to aromatic $C\cdots C$ bonds as would be expected from the delocalized structures such as V. c) The delocalization of electrons in the cationic part is exhibited in the short distance of the C_4-C_5 (Figs. 1, 2) bond, being also in the range of an aromatic $C\cdots C$ bond. The shortest C-C bond e.g. 1.367 Å in the phenyl group (C_9-C_{10}, Figs. 1, 2) and the longest aromatic C-C bond (e.g. 1.425 Å for C_5-C_6) are in agreement with such delocalizations as shown in structures Vd and Ve. It is evident that the positive charge has a more extended delocalization than the negative.

It was also interesting to do HMO calculations in order to try to evaluate the π electron energy and bond orders of this unusual structure. This is permitted as all atoms in the molecule have either π or n electrons. The method used was a modified, self-consistent, version of Huckel



method (the ωβ technique).[6] The primary structure of this dipolar aldisate is expected to be stable as it consists of a filled shell system with a delocalization energy of 0.304 β electron. The calculated partial charges for a system not containing methoxy groups are shown in Fig. 3 and are in agreement with the delocalized structure which is assumed from the bond lengths. The bond orders are in line with the experimental bond lengths (see Table 1). The gap between the HOMO and LUMO levels was found to be of the order of 0.1 βunits which is in line with the red colours observed for these compounds. In such calculations a bond order of 0.4 complies with a single bond. Values calculated for C_3-O_1 and C_1-N were 0.2872 and 0.3158, respectively. This is in line with the unusually long bonds observed by X-ray diffraction. Where short bonds were observed, e.g. C_1-C_2-C_3 and C_4-C_5, the calculated bond orders were similar to $C\overset{\cdots}{-}C$ aromatic bonds.

The separation of charges in the molecule is well illustrated also in the calculated electron densities (Fig. 3). All the atoms in the cationic half are positive and all those in the negative half are negative (except for a small positive charge in the $C\overset{\cdots}{-}O$ carbons). The charges on both benzylic carbons (C_4 and C_2 in Fig. 3) explain the dramatic influence of substituents on the spectra and stability of these compounds.[4] The calculated results after introduction of two electron donating groups in ortho and para showed a considerable shift of the positive charge to these positions, accompanied by a relevant change of calculated bond orders in the phenyl ring (see Table 1 and Fig. 3).

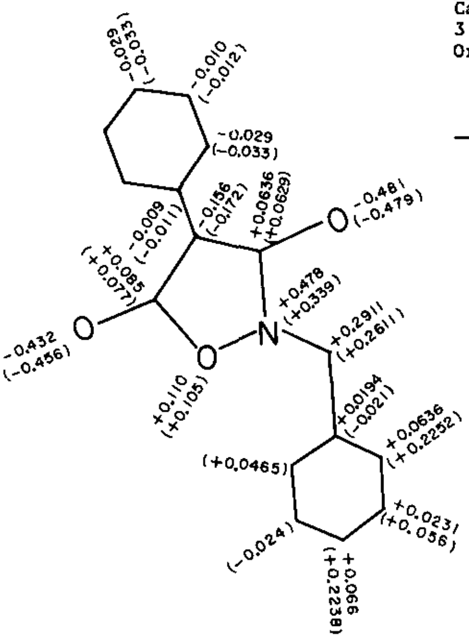


Fig. 3. Calculated partial charges. (The numbers in parentheses are the calculated values with electron donating substituents in positions ortho and para).

Table 1. Experimental Bond Lengths in Compound V and Calculated Bond Orders for the System Shown in Fig. 3 (The numbering of atoms is given in Fig. 1). Bond Order of C $\overset{...}{-}$ C in Benzene is 0.6667.

Bond	Experimental bond length (Å)	Calculated bond orders[a] System A	System B
C_3-O_1	1.469	0.2866	0.2878
C_1-N	1.480	0.3164	0.3108
N-O_1	1.375	0.1344	0.1211
C_3-O_3	1.196	0.7343	0.7288
C_1-O_2	1.219	0.7068	0.7075
C_4-N	1.301	0.6089	0.5585
C_1-C_2	1.394	0.5372	0.5524
C_2-C_3	1.395	0.5485	0.5430
C_2-C_{13}	1.479	0.4074	0.4061
C_4-C_5	1.411	0.5279	0.6087
C_5-C_6	1.425	0.5600	0.5742
C_5-C_{10}	1.416	0.5600	0.5130
C_6-C_7	1.391	0.6991	0.6905
C_7-C_8	1.370	0.6420	0.6570
C_8-C_9	1.395	0.6420	0.5842
C_9-C_{10}	1.367	0.6991	0.7471

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[a] System A and System B are those with and without electron donating groups at carbons 6 and 8 respectively.

The presence of C-H•••O attractive forces provides an explanation why aromatic aldehydes react spontaneously to yield solid aldisates while aromatic ketones do not. By examining Fig. 1, it is possible to see that coplanarity of the cationic half of the molecule requires overcrowding around the C=$\overset{+}{N}$ bond. The distance between the oxygen (O_2) and hydrogen (H_4) is shorter than the sum of the van der Waals radii (e.g. 2.3175 Å). It may be assumed therefore that the forces between these two atoms are attractive rather than repulsive. This phenomenon which was called C-H•••O hydrogen bonding[7] is known to exist often when the C-H is adjacent to a positive nitrogen.[7] The C_4-H_4-O_2 angle which was found to be 107.8° is large enough to fulfill the requirements suggested in the literature.[7] Moreover, the ortho methoxy group chooses to be positioned in such a way that it can form another hydrogen bond. Both the observed distance (2.31 Å) and the angle (97.18°) are also within the required range. Such "bifurcated" hydrogen bonds were described earlier.[8]

Cyclopentanone gave a relatively stable ketisate (VI) by its reaction with phenyl disic acid (II). The orange-yellow crystals are stable on the shelf for a few days and decompose in a few minutes in moist solvents. It was the only ketisate that its nmr could be determined (Fig. 4). A pronounced deshielding of the α protons in the cyclopentane ring is seen and a remarkable difference between the two α pairs is observed. These facts suggest a considerable electronic influence of the heterocyclic ring and that one pair of hydrogens is in a very close proximity to the oxygen. Therefore, some kind of association of the α-hydrogens cannot be excluded as an explanation for the relative stability in this case.

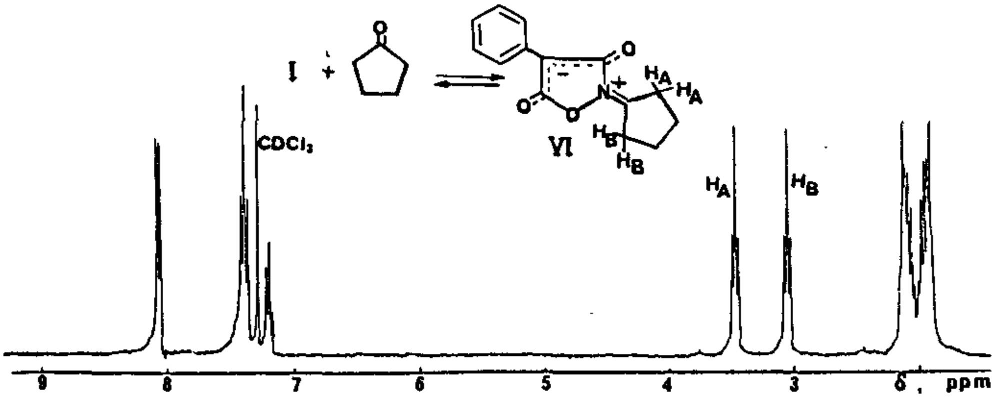
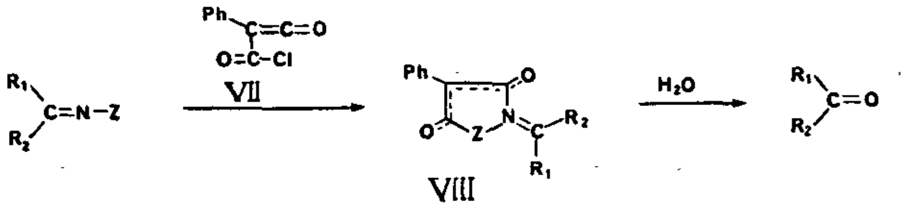


Fig. 4. Hnmr of VI

The failure of aromatic ketones to react with disic acid must therefore be attributed to the instability of the products, due to steric effects and the lack of C-H•••O association. Such ketisates which were prepared by an alternative way,[9] by applying the very reactive (chlorocarbonyl)phenyl ketene (VII) to ketoxime,[9] decomposed readily even in relatively dry solvents. Hydrolysis in wet solvents yielded either the starting material ketoxime or mostly the ketone; depending on the groups and on the solvent. The ketisates VIIIa and VIIIb decomposed in wet chloroform to benzophenone and 9-fluorenone respectively, but in wet acetonitrile they decomposed to the corresponding oximes.

We wish to propose here the following scheme for a gentle regeneration of ketones and aldehydes from their oximes and hydrazones by applying (chlorocarbonyl)phenyl ketene (VII) and subsequent mild hydrolysis by dissolution in wet solvents. Difficulties in hydrolyzing oximes and hydrazones in mild conditions were often reported,[10] and this proposed procedure should be adequate.



EXPERIMENTAL

Single crystal X-ray analysis was carried out with a 4 circle automatic diffractometer Philips PW 1100. Crystallographic data for N-(2,4-dimethoxylphenyl)methylidene-4-phenyl-3(5)-oxoisoxazolium-5(3)-enolate (V):

Chemical formula	$C_{18}H_{15}O_5N$
Molecular weight	325.3
Space group	$P2_1/n$
Unit cell dimensions	a = 14.663 (2) Å
	b = 11.878 (1) Å
	c = 8.776 (1) Å
	β = 100.07 Å
	ν = 1504 Å
No. of molecules in units cell:	4
Density (calculated):	1.436 g/cm^{-3}
Linear absorption coefficient:	$\mu(MoK_\alpha) = 0.64\ cm^{-1}$
No. of unique reflections:	1921
Disagreeement index R:	0.069
Weighted disagreement factor Rw:	0.090

IR spectra were taken with Perkin Elmer spectrophotometer Model 157. NMR spectra were taken with a Bruker WH-300 spectrometer.

Crystallization of N-(2,4-Dimethoxyphenyl)methylidene-4-phenyl-3(5)-oxoisoxazolium-5(3)-enolate (V).

4-Phenyldisic acid (II) semihydrate[11] (0.185 g) was dissolved in tetrahydrofurane (30 ml). A solution of 2,4-dimethoxybenzaldehyde (0.30 g) in tetrahydrofurane (30 ml) was added and the resulting red solution was kept until crystals of V separated. mp 262°C.

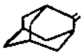
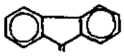
N-Cyclopentylidene-4-phenyl-3(5)-oxoisoxazolium-5(3)-enolate (VI).

4-Phenyldisic acid (II) (1.45 g) semihydrate[11] was dissolved in tetrahydrofurane (2 ml). Cyclopentanone (3 ml) was added and the solution shaken until all the solid dissolved. After 10 min an orange-yellow precipitate started to crystallize. The resulting ketisate (VI) was collected by filtration and washed with dry ether. 0.7 g (35%), mp 132°C. On dissolution in $CDCl_3$ a partial decomposition to cyclopentanone and phenyl disic acid (II) occurred. Nmr is shown in Fig. 4. Ir (ν , cm^{-1}): 1790, 1715, 1630 (typical for CO absorption of aldisates[1,2]). Anal. Calcd for $C_{14}H_{13}NO_3$: C, 69.12; H, 5.39; N, 5.76. Found: C, 69.00; H, 5.42; N, 5.94.

General Procedures for the Preparation of VIII from Oximes and Hydrazones by Reaction with (Chlorocarbonyl)phenyl Ketene (VII).

(chlorocarbonyl)phenyl ketene (VII)[12] (0.9 g) was dissolved in dry ether (5 ml) and cooled on ice. A solution of the oxime of hydrazone (1 to 1.5 nmoles) in ether (15-35 ml) was added with stirring for 5-10 min. The solid was collected after 5-30 min and washed with dry ether. In the case where the hydrazone did not dissolve in ether, dry tetrahydrofurane (5-10 ml) was used. Experimental results for a few relatively stable products are given in Table 2.

Table 2. Experimental Results and Ir of VIII, Derived by Reaction of (Chlorocarbonyl)phenyl ketene (VII) with Oximes and Hydrozones.

No. of compound	R_1	R_2	Z	Yield %	mp °C	Ir(CO) ν(cm⁻¹)	Formula	Analysis Found (Calcd)		
								% C	% H	% N
VIII a	C_6H_5	C_6H_5	O	91	136	1720	$C_{22}H_{15}NO_3$	77.24(77.41)	4.51(4.43)	4.45(4.10)
VIII b			O	92	155	1750,1680	$C_{22}H_{13}NO_3$	77.69(77.87)	4.33(3.86	4.21(4.13)
VIII c	CH_3	$C_6H_5CH=CH$	O	92	158	1780,1700	$C_{19}H_{13}NO_3$	74.87(74.74)	4.83(4.95)	4.81(4.59)
VIII d			O	62	158	1720	$C_{19}H_{19}NO_3$	73.67(73.77)	6.54(6.19)	4.60(4.53)
VIII e	- " -		C_6H_5-N	82	207	1770,1690	$C_{26}H_{24}N_2O_3$	75.77(75.71)	6.03(5.86)	6.89(6.79)
VIII f			C_6H_5CO-N	69	155	1690	$C_{29}H_{18}N_2O_3$	78.62(78.22)	4.30(4.10)	6.49(6.33)
VIII g	- " -		4-$CH_3C_6A_4SO_2$-N	50	140	1670	$C_{29}H_{20}N_2O_4S\cdot H_2O$	68.86(68.23)	4.22(4.31)	5.35(5.49)
VIII h	H	2.4-$(CH_3))_2C_6H_4$	C_6H_5-N	92	199	1680	$C_{25}H_{22}N_2O_4$	72.67(72.45)	5.55(5.35)	6.85(6.76)

ACKNOWLEDGEMENT

We wish to thank Professor G.V. Boyd from Kings College, London, for performing the ωβ technique calculations and to Shmuel Cohen for his help with the X-ray structure determination.

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Received, 13th November, 1986