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SYNTHESIS AND REACTIVITY OF 2-DIMETHYLAMINO-4-ALKENYL-1,3-OXAZIN-6-ONES

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Abstract - The Vilsmeier-Haack reaction on 4-alkylideneisoxazolin-5-ones gives 2-dimethylamino-4-alkenyl-1,3-oxazin-6-ones. Depending on substitution pattern, from these oxazinones, α-pyrones, 2-pyridones and pyridines may be obtained. The results confirm the thermal equilibrium between 2-dialkylamino-1,3-oxazin-6-ones, iminoketenes and vinylisocyanates.

We recently reported on the synthesis and reactivity of 2-dialkylamino--1,3-oxazin-6-ones[1], and now report the synthesis and reactivity of 2-dimethylamino-4-alkenyl-1,3-oxazin-6-ones **2**, heterocycles which we have obtained by a Vilsmeier-Haack type reaction from 4-alkylideneisoxazolin-5-ones **1**. The starting isoxazolones **1a-h** have been reported (see Table I) while compounds **1i,j** were prepared according to known methods[2,3] (see Experimental).

As is well known for isoxazol-5-ones[4], the 4-alkylideneisoxazol-5-ones may exist in CH and NH tautomeric forms[5].

When the Vilsmeier-Haack reaction is carried out on 4-alkylideneisoxazol-5-ones **1a-j**, the corresponding 2-dimethylamino-4-alkenyl-1,3-oxazin-6-ones **2a-j** are readily obtained in good yields (Scheme I and Table I). The reaction path is analogous with that previously reported for the Vilsmeier-Haack reaction of isoxazol-5-ones[1].

On compound **1g** the reaction has been carried out in DMF solution (see Experimental). In this case, besides the oxazinone **2g**, the derivative **3** has been obtained. The structure of compound **3** was assigned on the basis of single-crystal X-ray diffraction analysis and Figure I shows the molecular shape and numbering scheme.

Scheme I

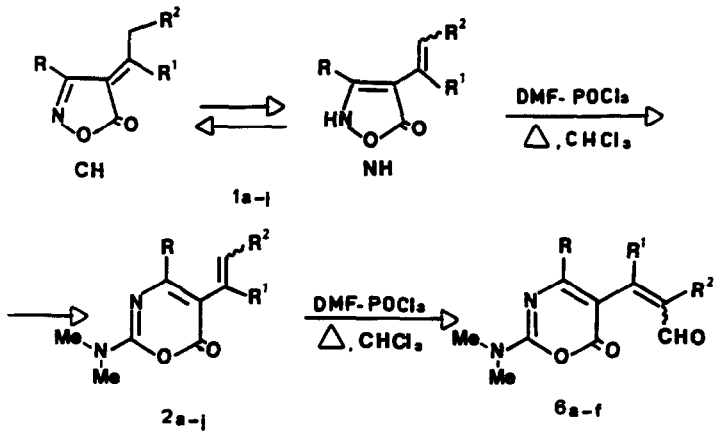


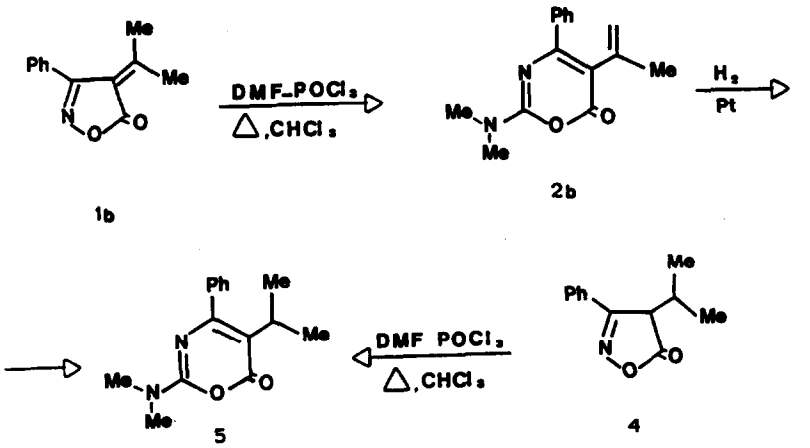
Table I. 2-Dimethylamino-4-alkenyl-1,3-oxazin-6-ones 2 from 4-Alkylideneisoxazol-5-ones 1.

Starting Material	R	R^1	R^2	Products (% Yield)	Eluant	mp, °C	Reacn. time (h)
1a[5]	Ph	$(CH_2)_3$		2a (74)	hexane-CH_2Cl_2 (2:1)	145[a]	1.5
1b[5]	Ph	Me	H	2b (57)	hexane-CH_2Cl_2 (1:1)	149-150[b]	6
1c[8]	Ph	Ph	H	2c (65)	hexane-CH_2Cl_2 (1:1)	166-167[c]	5
1d[6]	n-C_3H_7	$(CH_2)_3$		2d (67)	hexane-CH_2Cl_2 (2:1)	87[a]	5
1e[6]	Ph	H	Ph	E-2e (72)	hexane-CH_2Cl_2 (1:1)	219-220[c]	2.5
1f[2]	Ph	$(CH_2)_4$		2f (75)	hexane-CH_2Cl_2 (2:1)	144-145[a]	2
1g[5]	Me	CH_2-Ph		2g (47)	CH_2Cl_2	181-182[c]	1[e]
				3 (15)	CH_2Cl_2-MeOH (100:1)	171-172[c]	
1h[3]	Ph	Me	COOEt	E-2h (51)	CH_2Cl_2-Et_2O (30:1)	122-123[a]	3
				Z-2h (28)		116-117[a]	
1i[9]	Me	Me	COOEt	E-2i (82)	hexane-Et_2O (3:1)	oil	3
				Z-2i (8)		64-65[a]	
1j[9]	n-C_3H_7	Me	COOMe	E-2j (80)	CH_2Cl_2-Et_2O (30:1)	74-75[d]	3
				Z-2j (14)		oil	

[a] Et_2O-hexane. [b] Et_2O. [c] CH_2Cl_2-Et_2O. [d] hexane. [e] This reaction has been carried out at 80°C in DMF.

The structures of the new compounds are based on analytical and spectroscopic data as well as chemical behaviour. Indeed, catalytic hydrogenation of the unsaturated oxazinone **2b** gives the same oxazinone **5** as is obtained by the Vilsmeier-Haack reaction of 4-isopropyl-3-phenyl-isoxazol-5-one **4**[6] (Scheme II).

Scheme II



The structures of the E-isomer of the oxazinone **2h** and of the Z-isomer of the oxazinone **2i** were determined by X-ray diffraction analysis[7]. Pure E and Z isomers of the oxazinones **2h-j** were obtained by silica gel column chromatography (see Table I).

Table II. Products from Vilsmeier-Haack Reaction of Oxazinones 2.

Starting Material	Products (% Yield)	Eluant	mp, °C	Reacn. time (h)	E/Z ratio[f]
2a	6a (69)	CH_2Cl_2-Et_2O (20:1)	125[a]	5	---
2b	E,Z-6b (45)	CH_2Cl_2-Et_2O (20:1)	112-117[a]	6.5	40/60
2c	E,Z-6c (90)	CH_2Cl_2-Et_2O (20:1)	133-135[b]	5	26/74
2d	6d (50)	CH_2Cl_2	91-92[c]	7	---
E-2e	E-6e (40)	CH_2Cl_2-Et_2O (20:1)	178-179[b]	8	---
2f	6f (25)[d]	CH_2Cl_2-Et_2O (30:1)	112-113[c]	5	---
2g	3 (80)[e]	CH_2Cl_2-MeOH (50:1)	171-172[b]	5	---

[a] Et_2O. [b] CH_2Cl_2-Et_2O. [c] Et_2O-hexane. [d] Reaction solvent CCl_4; 50% of unreacted start. mat. was recovered. [e] Reaction solvent, DMF at 70 °C. [f] By ^{1}H-NMR.

When the oxazinones **2a-f** react with the Vilsmeier reagent, formylation at C_{13} of the unsaturated side chain occurs to give aldehydooxazinones **6a-f**. No reaction was observed in the case of the oxazinones **2h-j**. The aldehydooxazinones **6b,c** are formed as a mixture of E/Z isomers; the E/Z ratio has been determined by ^1H NMR (Scheme I and Table II). From **2g** compound **3** was obtained (Table II).

When a dioxane solution of the aldehydooxazinones **6a,d** is heated under reflux, the rapid formation of the corresponding α-pyrone derivatives **7a,d** is observed (Scheme III and Table III).

Scheme III

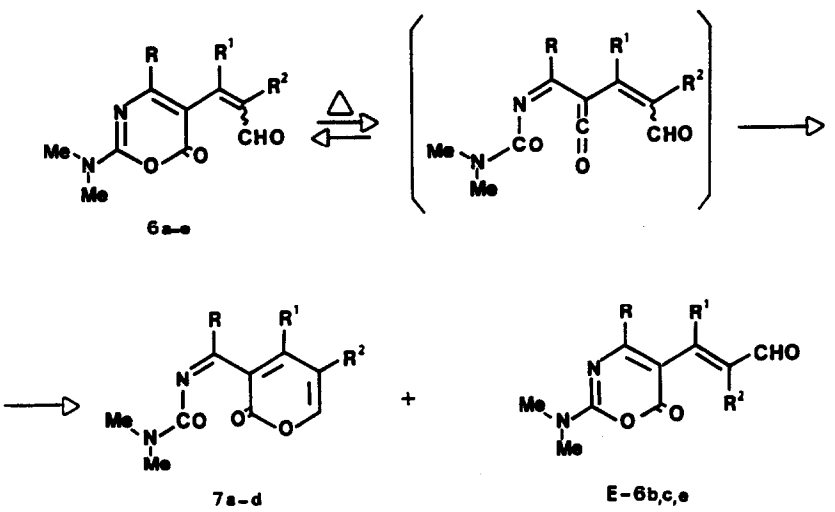


Table III. Products of reaction of aldehydooxazinones 6.

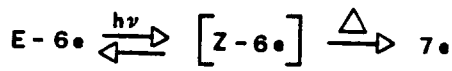
Starting Material	Products (% Yield)	Eluant	mp, °C	Reacn. time (h)
6a	7a (97)	----	135[a]	5
E,Z-6b	7b (55)	CH_2Cl_2-Et_2O (20:1)	95-96[b]	5
	E-6b (39)		157-158[a]	
E,Z-6c	7c (69)	CH_2Cl_2-Et_2O (10:1)	164-165[c]	10
	E-6c (23)		149-150[c]	
6d	7d (60)	CH_2Cl_2-Et_2O (20:1)	50-51[b]	5
E-6e	7e (65)	CH_2Cl_2-Et_2O (20:1)	157-158[c]	-[d]

[a] CH_2Cl_2-Et_2O. [b] Et_2O-hexane. [c] Et_2O. [d] Thermal cyclisation was achieved after UV irradiation (see Experimental).

The structure of compound **7a** was confirmed by X-ray diffraction analysis and Figure 2 shows the molecular shape and numbering scheme. From compounds **6b,c**, α-pyrones **7b,c** are also obtained but, in this case, only one isomer reacts while the other is recovered unchanged and then isolated in the pure state. To the unreacted isomers the structure of E-isomers was assigned and therefore the same configuration must be assigned to **6e** as no thermal reaction to **7e** was observed.

7e was easily obtained after UV irradiation of a CH_2Cl_2 solution of **6e** (see Experimental, Scheme IV).

Scheme IV

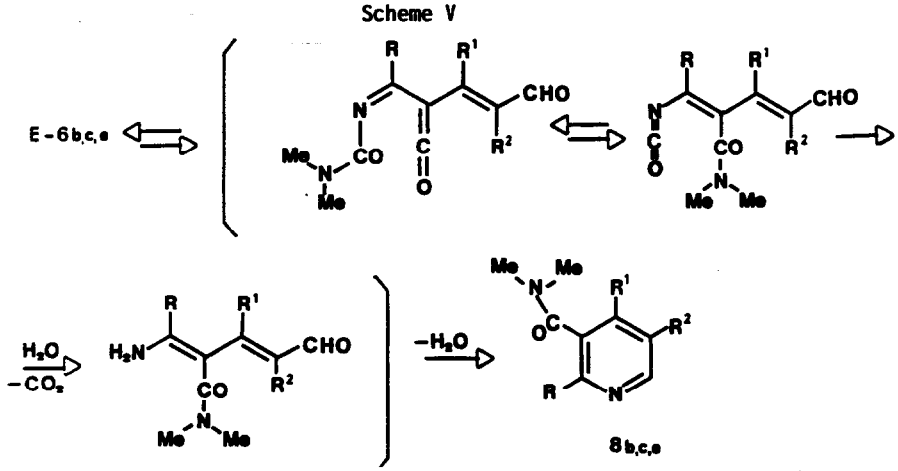


We presume that E-**6e** isomerizes to Z-**6e** and this is then transformed to **7e**. These reactions are very fast in refluxing dioxane but the α-pyrone formation is also observed in $CDCl_3$ solution at room temperature and may be followed by ^1H NMR (100% conversion in 24 h).

In our opinion the formation of α-pyrones **7** implies cycloreversion to a ketene aldehyde and subsequent electrocyclization as shown in Scheme III.

The aldehydooxazinones E-**6b,c,e**, refluxed in dioxane-water solution, give the pyridine derivatives **8b,c,e** (Scheme V and Table IV). In view of the results previously reported on the reactivity of 2-dialkylamino-1,3-oxazin-6-ones bearing an electron-withdrawing group in position 5[1], this reaction must occur via isomerization and the intramolecular cyclisation of the enaminoaldehyde arising from the addition of water to the

Scheme V



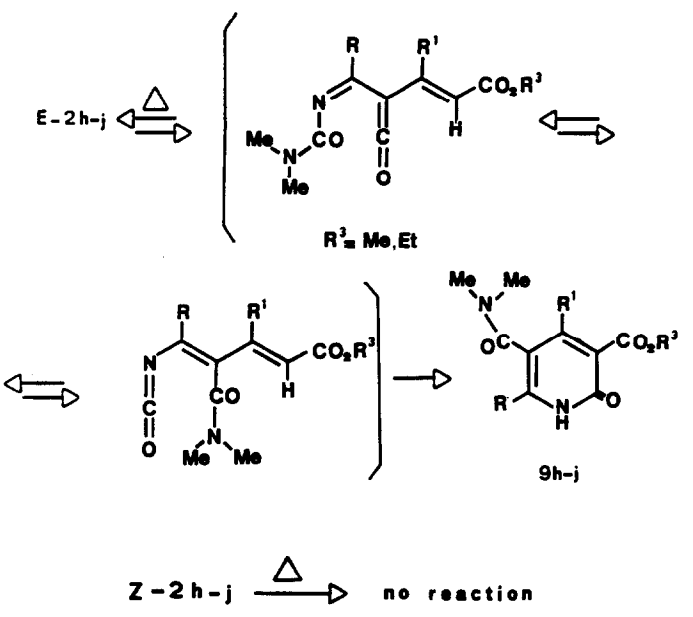
intermediate vinyl isocyanate as shown in Scheme V. The structure of compounds **8** is confirmed by X-ray diffraction analysis of compound **8c**. Figure III shows the molecular shape and the numbering scheme. Analytical and spectroscopic data agree with the reported structures.

Table IV. Products from reaction with H_2O of E-Aldehydooxazinones **6b,c,e.**

Starting Material	Products (% Yield)	mp,°C [bp,°C(mmHg)]	Eluant
E-6b	8b (51)	[135-140 (0.1)]	CH_2Cl_2-Et_2O (8:1)
E-6c	8c (65)	116-117[a]	CH_2Cl_2-Et_2O (10:1)
E-6e	8e (60)	109-110[a]	CH_2Cl_2-Et_2O (20:1)

[a] Et_2O-hexane.

Scheme VI



Z-2h-j $\xrightarrow{\Delta}$ no reaction

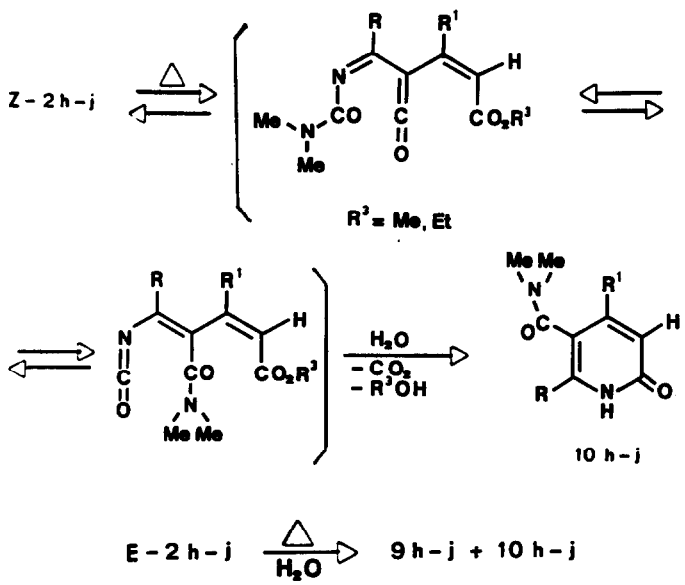
The Z-**6b,c,e** compounds only give α-pyrones when heated in dioxane-water solution.

As reported above the oxazinones **2h-j**, bearing an ester group, do not react further with

the Vilsmeier reagent. The E-isomers of these compounds give the pyridones **9h-j** when heated in a sealed tube in anhydrous dioxane (see Experimental). The formation of the pyridones **9**, with retention of the ester functionality, clearly involves the electrocyclization of the intermediate vinyl isocyanate as shown in Scheme VI. Under the same experimental conditions the corresponding isomers Z-**2h-j** do not react.

When the oxazinones **2h-j** are heated in dioxane-water solution, the new pyridones **10h-j**, lacking the ester functions are formed. The structure of compounds **10** is confirmed by X-ray diffraction analysis on compound **10h**. Figure IV shows the molecular shape and the numbering scheme. The formation of pyridones **10** parallels the formation of pyridines **8** since they are formed by intramolecular cyclization of the enamino ester, arising from hydrolysis of the intermediate vinylisocyanate (Scheme VII). It is to be stressed that compunds E-**2h-j** afford pyridones **10h-j** accompanied by a minor amount of pyridones **9h-j**, whereas the corresponding Z-**2h-j** produce only derivatives **10h-j**. This differences in behaviour is in fair agreement with the thermal reactivity in absence of water (see Scheme VI).

Scheme VII



Both reactions going to α-pyrones **7** and pyridones **9** are thermally-induced 6π-electrocyclisation of conjugated heterocumulenes and relatively few examples of these reactions have been reported[13]. Our results are consistent with the hypothesis that the initial stage of the thermal reactivity of the 2-dialkylamino-1,3-oxazin-6-ones is a

Table V. Products from reaction with H_2O of E- and Z-oxazinones 2h-j.

Starting Material	Products (% Yield)	mp,°C	Eluant
Z-2h	10h (75)	184-186[a]	---
Z-2i	10i (65)	215-217[a]	---
Z-2j	10j (60)	124-125[b]	---
E-2h	10h (65)	---	CH_2Cl_2-MeOH (30:1)
	9h (5)	190-192[c]	
E-2i	10i (60)	---	CH_2Cl_2-MeOH (30:1)
	9i (4)	159-160[c]	
E-2j	10j (70)	---	CH_2Cl_2-Et_2O (1:1)
	9j (6)	174-176[b]	

[a] CH_2Cl_2-Et_2O. [b] Et_2O-hexane. [c] Et_2O

cycloreversion reaction to an iminoketene followed by a [1.5]-shift of the dialkylamino group to form a vinylisocyanate. From both these intermediates, if an appropriate substituent is present at position of 5 of the oxazinone nucleus, easy transformation to the new heterocyclic systems is achieved. The photochemical behaviour of the 2-dimethylamino-1,3-oxazin-6-ones and 2-dimethylamino-4-alkenyl-1,3-oxazin-6-ones is also being studied.

EXPERIMENTAL

Melting and boiling points are uncorrected. IR spectra were determined with Perkin Elmer 298 instrument, in Nujol mull for solids and liquid film for oils. NMR spectra were recorded on a Varian EM-390 or on a Bruker WP80SY spectrometer with tetramethylsilane as an internal standard. Column chromatography was performed on Merck Kieselgel 60, 0.063-0.2 mn. Sodium sulfate was used as drying agent. Evaporation was carried out under vacuum in a rotary evaporator. Satisfactory combustion analysis (± 0.3%) for C, H and N were obtained for all new compounds.

Isoxazolin-5-one 1i

A mixture of ethyl 3-morpholino-2-butenoate[10] (25 mmol) and 3-methylisoxazol-5-one (20 mmol)(obtained from the corresponding morpholinium salt[11]) in diethyl ether (80 mL) was stirred under reflux for 3h. The mixture was allowed to stand for 15 h and then filtered and washed with Et_2O. The solid was treated with 4% HCl (80 mL) and the mixture extracted with Et_2O (2x50 mL). The organic layer was dried, filtered and evaporated to give pure 1i as an oil 3.5 g (82% crude yield).

Isoxazolin-5-one **1j**

Starting from methyl 3-aminobutenoate (40 mmol) and 3-propylisoxazol-5-one[12] (30 mmol) in Et_2O (100 mL) and working as reported for **1i**, pure **1j** was obtained, 3.7 g (54%); mp 60-61°C from Et_2O.

2-Dimethylamino-4-alkenyl-1,3-oxazin-6-ones **2a-j** from Isoxazolin-5-ones **1a-j**. General Procedure

To a solution in $CHCl_3$ (80 mL, EtOH free) of dimethylformamide (11 mmol) and phosphorus oxychloride (11 mmol), the isoxazolin-5-one **1** (10 mmol) was added at room temperature under stirring. The reaction mixture was stirred under reflux for the reported time (Table I). After cooling, the reaction mixture was evaporated, ice-water (70 mL) added, and the mixture neutralized with $NaHCO_3$ and extracted with CH_2Cl_2 (2x50 mL). The organic layer was dried, filtered, and evaporated. The residue was purified by column chromatography and by crystallization (see Table I). In the case of the isoxazolin-5-one **1g**, the reaction was carried out in dimethylformamide at 80°C.

2-Dimethylamino-4-phenyl-5-isopropyl-1,3-oxazin-6-one **5** from oxazinone **2b**

The oxazinone **2b** (1 mmol) was dissolved in AcOEt (30 mL) PtO_2 (40 mg) was added, and the mixture hydrogenated under ordinary pressure and temperature. After 4h the catalyst was filtered off, the solvent evaporated, and the residue crystallized from Et_2O-hexane to give pure **5** (88%); mp 133-134°C.

2-Dimethylamino-4-phenyl-5-isopropyl-1,3-oxazin-6-one **5** from 3-Phenyl-4-isopropylisoxazolin-5-one **4**

The 3-phenyl-4-isopropylisoxazolin-5-one **4**[6] (1 mmol) was reacted with dimethylformamide (2 mmol) and phosphorus oxychloride (2 mmol) the Vilsmeier reagent (2 mmol) in $CHCl_3$ (30 mL). The mixture was stirred under reflux for 4h. Working up as previously described[1] gives compound **5** in 61% yield.

Aldehydooxazinones **6a-f** from oxazinones **2a-f**. General Procedure

To $CHCl_3$ (EtOH free, 50 mL) were added dimethylformamide (4.5 mmol) and phosphorus oxychloride (4.5 mmol) and then the oxazinone **2** (3.5 mmol). The reaction was stirred under reflux for the reported time (Table II). Workup as described previously, column chromatography and crystallization give pure aldehydooxazinones **6** (Table II). For **2f** the reaction was carried out in CCl_4; for **2g** in DMF at 70°C.

α-Pyrones **7a-d** and aldehydooxazinones **E-6b,c** from aldehydooxazinones **6a-d**. General procedure

A solution of the aldehydooxazinone **6** (1 mmol) in dioxane (25 mL) was heated under reflux for the reported time (Table III). The residue from the solvent evaporation was purified by column chromatography and crystallized to obtaine derivatives **7** and unreacted

aldehydooxazinones E-**6b,c** (Table III).

α-Pyrone **7e** from E-**6e**

A solution of the aldehydooxazinone E-**6e** (1 mmol) in CH_2Cl_2 (50 mL) was irradiated (pyrex vessel) with a high pressure Hg lamp (Philips HPK 125W) for 30 min. The residue from the solvent evaporation was purified by column chromatography to give pure α-pyrone **7e** (Table III).

Pyridines **8b,c,e** from aldehydooxazinones E-**6b,c,e**. General Procedure

The aldehydooxazinone **6** (0.5 mmol) was dissolved in dioxane (15 mL), and then H_2O (5 mL) was added. The reaction mixture was heated under reflux for 3h. The residue from the solvent evaporation was purified by column chromatography to give pure compounds **8b,c,e** (Table IV).

2-Pyridones **9h-j** by thermal reaction of oxazinones E-**2h-j**. General Procedure

The oxazinone **2** (300 mg) was dissolved in anhydrous dioxane (5 mL) and the reaction was carried out in a sealed tube at 115°C for 72h. After solvent evaporation, the residue was crystallized (for the crystallization solvents see Table V) to give pure **9h** (67%), **9i** (64%) and **9j** (57%).

2-Pyridones **10h-j** by reaction with H_2O of the oxazinone Z-**2h-j**. General Procedure

The oxazinone **2** (200 mg) was dissolved in dioxane (4 mL) and then H_2O (2 mL) was added. The reaction was carried out at 110°C for 15h in a sealed tube. After solvent evaporation, the residue was crystallized to give pure pyridones **10h-j** (Table V).

2-Pyridones **9h-j** and **10h-j** by reaction with H_2O of the oxazinones E-**2h-j**. General Procedure

The reactions were carried out as described above and after 15h at 110°C pure pyridones **9h-j** and **10h-j** were obtained after columnu chromatography (Table V).

X-ray Structure Determination.

All single crystal X-ray measurements were performed on a Nonius CAD-4 diffractometer. The used radiation was graphite monochramated MoKα, λ =0.71069Å. The structures were solved by direct methods (program MULTAN[14]). The refinements were made by minimizing the function $\Sigma w(|F_o|F_c|)^2$ with weights $w=4I_o/[\sigma^2(I_o)+0.0004I^2_o]$. Crystal data and some details of data collection and of full-matrix least-squares refinement are given in Table VII.

(A) oxazinone 3 (XR-1). Single crystals of XR-1 suitable for X-ray difraction study were grown from methylene chloride. The compound co-crystallizes with the solvent and the crystal formula is $C_{20}H_{21}N_3O_3.1/6CH_2Cl_2$ with formula weight 365.6. The molecules, essentially by means of electrostatic interactions involving the nitrogen atoms, the oxygen atom bonded to the oxazine ring and the carbon atoms of the dimethylimido group, make layers parallel to the c axis. Between couple of layers, around a $\bar{3}$ crystallographic point, a hole is formed that include solvent. Such a structure is quite stable a do not change by changing the

solvent. The interaction between the solvent and the layers is responsible of the colour of the crystals. For example crystals obtained by pure methylene chloride are dark red by reflected light and emerald green by transmitted light, but the crystals obtained from technical acetone (cell parameters α=18.162(2), c=29.870(4)Å), are orange. The solvent cavity do not have any outlet and the solvent is strictly kept in it, so that crystals are stable for months. In spite of the solvent disorder, the refinement of the structure do not give any problem, solvent coordinates and thermal parameters included; only a hydrogen atom of a methyl group was fixed in calculated position; the final difference Fourier map do not show any deviations greater than $0.3eÅ^{-3}$.

The quite distorted planes through the indene and the oxazine groups form a dihedral angle of 77.19(4)° due to the steric interactions among the substituents at the rings. In spite of this, the bond between these two groups is only 1.486(3)Å, showing a noticeable electronic interaction between the two system. The molecule is shown in Figure 1.

(B) α-Pyrone 7a (XR-2). $C_{18}H_{18}N_2O_3$, F.w. 310.4. Colourless crystals were obtained from CH_2Cl_2 The molecule is shown in Figure 2.

(C) Pyridine 8e (XR-3). $C_{20}H_{18}N_3O$, F.w. 302.4. Colourless crystals were obtained from CH_2Cl_2 The molecule is shown in Figure 3.

(D) Pyridone 10h (XR-4). Single crystals were obtained from methylene chloride that co-crystallizes; the crystal formula is $C_{15}H_{16}N_2O_2 \cdot CH_2Cl_2$ with formula weight 341.2. Crystals quickly loss solvent with complete destruction of the structure. In a first attempt to collect data, we had a loss of 65% of check reflection intensity in about a day. A second collection was performed on a fresh crystal sealed in a glass capillary, without loss of intensity. The solvent is ordered but presents high thermal parameters. Because of this and/or the missing of absorption correction (the crystal was quite anisotropic), the final difference Fourier map presents a peak of $0.45eÅ^{-3}$ near a chlorine atom. The crystal structure shows molecule coupled through a crystallographic center of symmetry by strong hydrogen bonds involving N(1) and O(19) of pyridone. The hydrogen atoms is clearly bonded to N(1). The distance N(1)-H(1)...O(19) are in fact 0.87(3) and 1.92(3)Å respectively; the angle at H(1) is 173(3)°. A second, weaker hydrogen bond binds the solvent to the oxygen atoms of the carbonylamino group. The molecule is shown in Figure 4.

Tables of observed and calculated structure amplitudes and anisotropic thermal parameters are available on request (T.P.).

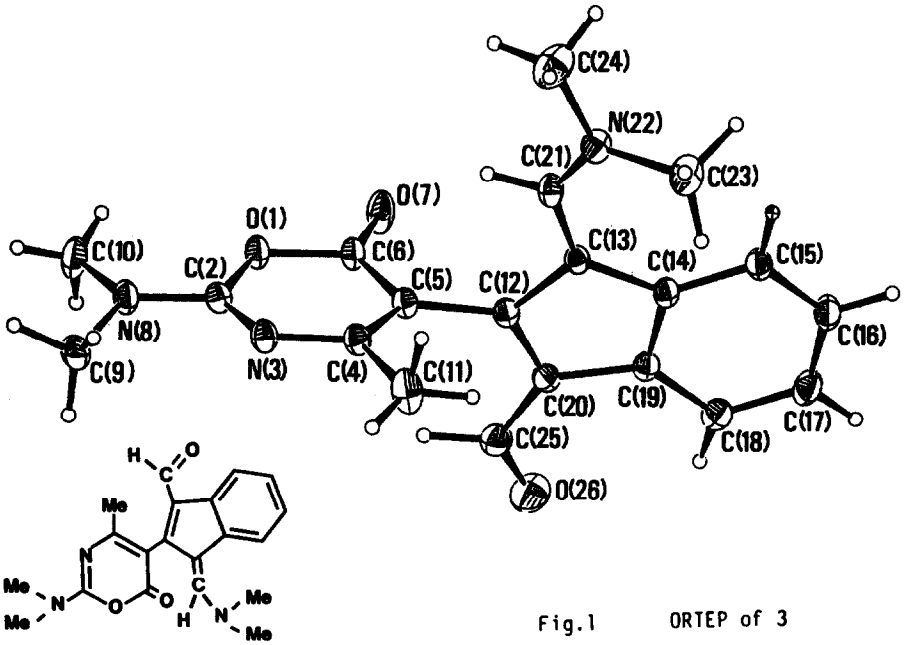


Fig.1 ORTEP of 3

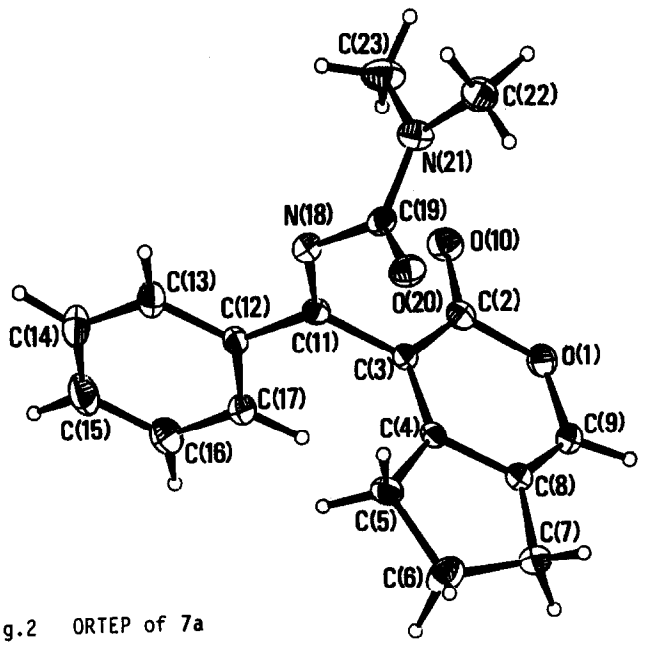


Fig.2 ORTEP of 7a

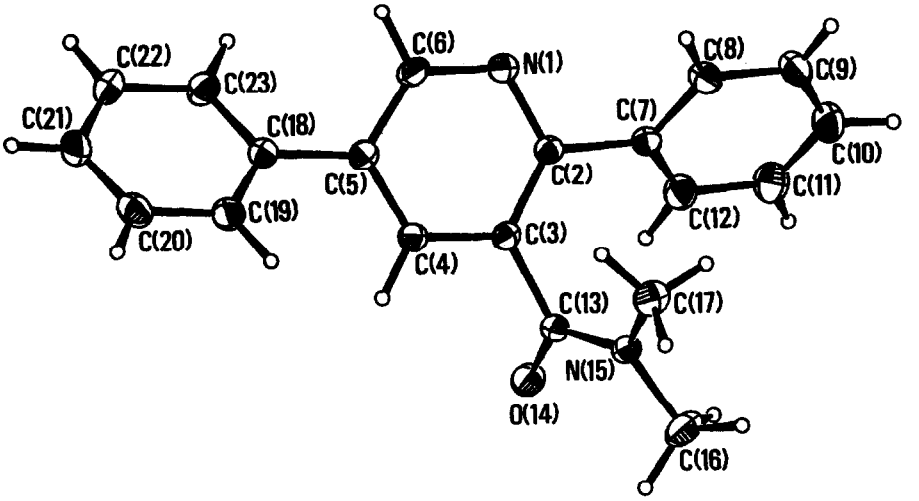


Fig.3 ORTEP of 8e

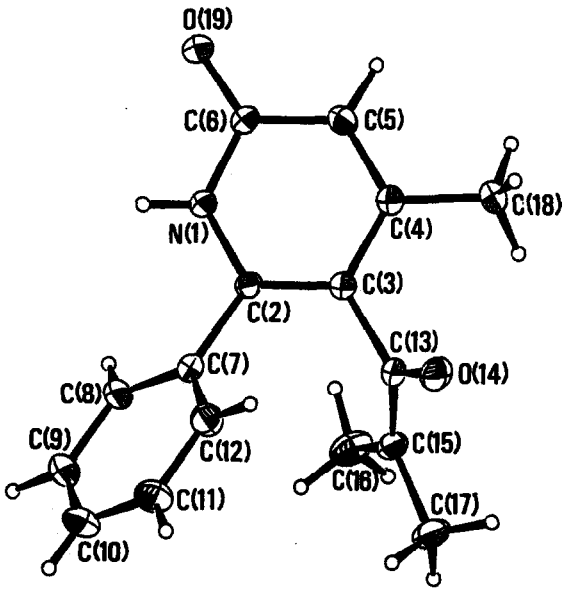


Fig.4 ORTEP of 10h

Table VI. Spectral data of new compounds.

Product	IR (cm^{-1})	^{1}H-NMR($CDCl_3$) δ, J(Hz)
1i	1750, 1733	4.23(2H,m), 4.11(1.6H,s), 3.7(0.4H,s), 2.63(1.2H,s), 2.44(4.8H,s), 1.3(3H,m), [CH form][c].
1j	3400br, 1752, 1738	10(1H,bs)[a], 6.18(1H,s), 3.64(3H,s), 2.7(2H,m), 2.43(3H,s), 1.6(2H,m), 0.95(3H,m), [NH form].
2a	1725, 1613	7.6(2H,m), 7.35(3H,m), 5.78(1H,m), 3.22(6H,s), 2.35(4H,m), 1.82(2H,m).
2b	1710, 1593	7.7(2H,m),7.38(3H,m), 5.17(1H,m), 4.9(1H,bs), 3.22(6H,s), 1.93(3H,s).
2c	1732, 1615	7.6(2H,m), 7.4-7.1(8H,m), 5.61(1H,s),5.16(1H,s), 3.23(6H,s).
2d	1735, 1605	5.6(1H,m), 3.16(6H,s), 2.43(6H,m), 2(2H,m), 1.65(2H,m), 0.93(3H,m).
E-2e	1732, 1600	7.7-7.2(11H,m), 6.83(1H,d, 17), 3.26(6H,s).
2f	1726, 1593	7.7 (2H,m), 7.33(3H,m), 5.5(1H,m), 3.2(6H,s), 2.1(4H,m), 1.63(4H,m).
2g	1739, 1605	7.25(4H,m), 6.77(1H,m), 3.83(2H,s), 3.19(6H,s), 2.32(3H,s).
E-2h	1722, 1706, 1600	7.53(2H,m), 7.35(3H,m), 5.76(1H,d,1.5), 4.13(2H,q,7.5), 3.25(6H,s), 2.28(3H,d,1.5), 1.25(3H,t,7.5).
Z-2h	1730, 1708,1600	7.63(2H,m), 7.36(3H,m), 5.94(1H,d,1.5), 4.1(2H,q,7.5), 3.23(6H,s), 1.9(3H,d,1.5), 1.22(3H,t,7.5).
E-2i	1743, 1712, 1605	5.73(1H,d,1.5), 4.23(2H,q,7), 3.2(6H,s), 2.4(3H,d,1.5), 2.18(3H,s), 1.31(3H,t,7).
Z-2i	1742, 1717, 1605	6(1H,d,1.5), 4.1(2H,q,7), 3.18(6H,s), 2.11(3H,d,1.5), 2.05(3H,s), 1.23(3H,t,7).
E-2j	1730, 1712, 1600	5.75(1H,d,1.5), 3.78(3H,s), 3.22(6H,s), 2.42(5H,m), 1.67(2H,m), 0.97(3H,t,7).
Z-2j	1735br, 1605	6.02(1H,d,1.5), 3.68(3H,s), 3.2(6H,s), 2.2(2H,m), 2.12(3H,d,1.5), 1.65(2H,m), 0.9(3H,t,7).
3	1722, 1600	9.68(1H,s), 8.15(1H,m), 7.79(1H,s), 7.6(1H,m), 7.1(2H,m), 3.48(6H,s), 3.19(6H,s), 1.92(3H,s)[b].
5	1715, 1595	7.42(5H,s), 3.18(6H,s), 2.87(1H,m), 1.28(6H,d,7).
6a	1725, 1650, 1595	9.63(1H,s), 7.45(5H,m), 3.29(6H,s), 2.6(4H,m), 1.9(2H,m).
E,Z-6b	1725, 1655, 1605	10(0.4H,d,8), 9.67(0.6H,d,8), 7.57(2H,m), 7.39(3H,m), 5.9(1H,m), 3.28(6H,m), 2.33(1.2H,d,1.5), 2.13(1.8H,d,1.5).
E,Z-6c	1727, 1663, 1612	9.7(1H,d,8), 7.6-7.1(10H,m), 6.4(1H,d,8), 3.3(6H,s).

6d	1735, 1661, 1597	9.65(1H,s), 3.22(6H,s), 2.7(4H,m), 2.2(4H,m), 1.62(2H,m), 0.9(3H,t,7).
E-6e	1732, 1667	9.65(1H,s), 7.5(11H,m), 3.22(6H,s).
6f	1726, 1666, 1615	9.7(1H,s), 7.6(2H,m), 7.33(3H,m), 3.3(6H,s), 2.5(2H,m), 2.2(2H,m), 1.65(4H,m).
7a	1690, 1637, 1627	7.8(2H,m), 7.42(4H,m), 3.04(3H,s), 2.99(3H,s), 2.73(4H,m), 2.05(2H,m).
7b	1690, 1635, 1622	7.8(2H,m), 7.42(4H,m), 6.2(1H,d,5), 3.01(3H,s), 2.97(3H,s), 2.13(3H,s).
7c	1700, 1650, 1637	7.55(5H,m), 7.25(6H,m), 6.36(1H,d,6), 3.02(3H,s), 2.92(3H,s).
7d	1690, 1652, 1632	7.33(1H,m), 3.02(3H,s), 2.95(3H,s), 2.7(4H,m), 2.06(4H,m), 1.6(2H,m), 0.98(3H,t,7).
7e	1704, 1645, 1630	7.86(4H,m), 7.4(8H,m), 3.05(3H,s), 3.02(3H,s).
8b	1642, 1630	8.57(1H,d,6), 7.65(2H,m), 7.4(3H,m), 7.12(1H,d,6), 2.95(3H,s), 2.47(3H,s), 2.31(3H,s).
8c	1642	8.73(1H,d,6), 7.66(2H,m), 7.42(8H,m), 7.26(1H,d,6), 2.73(3H,s), 2.49(3H,s).
8e	1615	9.01(1H,d,1.5), 7.99(1H,d,1.5), 7.6(10H,m), 3(3H,s), 2.5(3H,s).
9h	3400br, 1728, 1635	7.35(5H,m), 4.23(2H,q,7.5), 2.78(3H,s), 2.42(3H,s), 2.18(3H,s), 1.23(3H,t,7.5).
9i	1721, 1650, 1630	13.3(1H,bs)[a], 4.4(2H,q,7), 3.18(3H,s), 2.97(3H,s), 2.31(3H,s), 2.19(3H,s), 1.4(3H,t,7).
9j	1710, 1653, 1630	3.93(3H,s), 3.18(3H,s), 2.95(3H,s), 2.5(2H,m), 2.18(3H,s), 1.73(2H,m), 1(3H,t,7).
10h	3400br, 1662, 1630	7.48(5H,m), 6.35(1H,s), 2.88(3H,s), 2.53(3H,s), 2.23(3H,s).
10i	3300br, 1653, 1630	13.4(1H,bs)[a], 6.25(1H,s), 3.18(3H,s), 2.97(3H,s), 2.33(3H,s), 2.18(3H,s).
10j	3400br, 1660, 1640	6.29(1H,s), 6.18(3H,s), 2.95(3H,s), 2.5(2H,m), 2.16(3H,s), 1.73(2H,m), 1(3H,t,7).

[a] Exchange with D_2O. [b] DMSO. [c] 4:1 mixture of the stereoisomers.

Table VII. *Details of crystallographic data, data collection, and structure refinement.*

	XR-1	XR-2	XR-3	XR-4
system	trigonal	monoclinic	monoclinic	monoclinic
space group	$R\bar{3}$	$P2_1/c$.	$P2_1$.	$P2_1/c$.
a, Å.	18.174(2)	14.582(5)	8.460(1)	9.227(1)
b, Å.		13.533(3)	11.687(1)	12.693(1)
c, Å.	29.795(3)	8.265(1)	8.533(1)	15.105(1)
β, deg		102.47(2)	105.12(1)	106.16(1)
Z	18	4	2	4
D_x, g cm^{-3}	1.275	1.294	1.230	1.306
ϑ range of reflections, deg	16-19	16-18	15-18	16-20
range ϑ	0,25	0,27.5	0,27.5	0,26
no. of unique reflections collected	3337	3656	1959	3398
no. of refined reflections [if $I > \sigma(I)$]	2410	2909	1688	2573
R	0.047	0.033	0.033	0.059
R_w	0.044	0.034	0.031	0.058

REFERENCES

1) Beccalli, E.M., Marchesini, A. J. Org. Chem., 1987, 52, 3426.

2) Knowles, A.M., Lawson, A. J. Chem. Soc., Perkin Trans. 1, 1972, 1240.

3) Maquestiau, A., Vanden Eynde, J.J., Manderlier, R. Bull. Soc. Chim. Belg.,1984,93, 1073.

4) Katritzky, A.R., Lagowski, J.M. Adv. Heterocyclic Chem., 1963, 2, 36-39.
Elguero, J., Marzin, C., Katritzky, A.R., Linda, P. Adv. Heterocyclic Chem., 1976,S 1, 300-308.

5) Wollweber, H-J., Wentrup, C. J. Org. Chem., 1985, 50, 2041, and ref. cited therein.

6) Beccalli, E.M., Benincori, T., Marchesini, A. Synthesis, 1988, 886.

7) Pilati, T. unpublished results.

8) Maquestiau, A., Van Haverbeke, Y., Muller, R.N. Tetrahedron Lett., 1972, 1147.

9) Present work.

10) Couturier, P., Blanc, P., Frajdenrajch, S. Bull. Soc. Chim. Fr., 1962, 594.

11) Katritzky, A.R., Oksne, S., Boulton, A.J. Tetrahedron, 1962, 18, 777.

12) Kurkov, V.P. (Chevron Research Co.) US P 4504486, 1985, Chem. Abstr., 1985, 103, P54064.

13) Molina, P., Arques, A. Vinader, M.V. Becher, J. Brondum, K. J. Org. Chem., 1988, 53, 4654 and ref. cited therein.
Eloy, F., Deryckere, A. J. Heterocycl. Chem., 1970, 7, 1191.

14) Main, P., Fiske, S., Hull, S.E., Lessinger, L., Germain, G., Declerq, J.-P. & Woolfson, M.M. (1980). Multanll/82. A System of Computer Programs for Automatic Solution of Crystal Structures from X-Ray Diffraction Data. Univs. of York, England and Louvain,Belgium.