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1,3-Dipolar Cycloaddition of Imidate Ylides on Imino-Alcohols : Synthesis of New Imidazolones Using Solvent Free Conditions.

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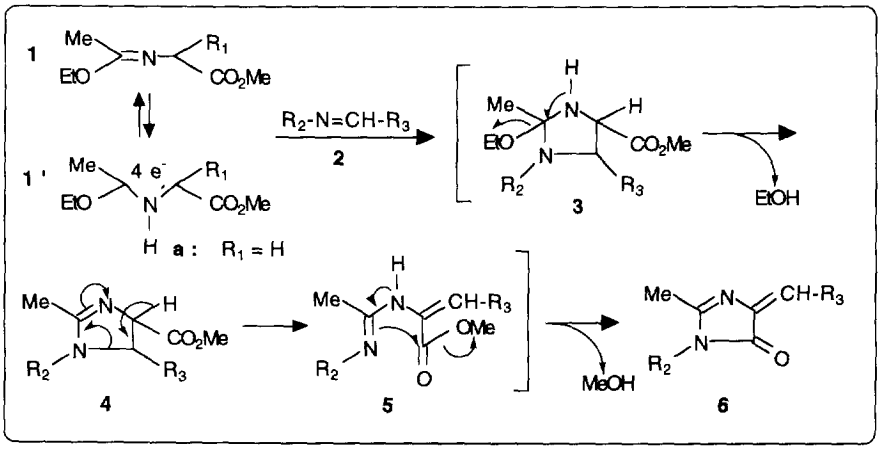
Abstract : Imidates derived from α-amino esters as potential azomethine ylides, undergo 1,3-dipolar cycloaddition with imino-alcohols, in tautomeric equilibrium with 1,3-oxazolidines, without solvent at 70°C or under microwave irradiation. This reaction leads to a wide range of novel polyfunctionalized 4-yliden-2-imidazolin-5-ones in good yields with short reaction times. The reactivity of these imidates derived from α-amino esters with imino-alcohols is rationalized from the energy of the Frontier Molecular Orbitals (FMO) determined by semi-empirical PM3 calculations : the reaction is controlled by the interaction $HOMO_{(1,3\text{-dipole})}$ - $LUMO_{(dipolarophile)}$ and the second order pertubation energy calculations are in agreement with the experimental reaction orientation.

INTRODUCTION

Imidazolones exhibit various biological properties[1] and most of the synthesis reported in the literature involve the condensation of aryl amines[2], acyl hydrazides[3], mercapto-acetyl hydrazides[4], chloramphenicol base[5] with arylidene azalactones[6]. Accordingly, we were stimulated to develop a synthetic program for new imidazolones with biological potential.

Scheme 1



Our interest in this field has been focused on the synthetic utilization of imidates derived from α-amino esters and imino-alcohols as dipolarophiles in 1,3-dipolar cycloaddition. The choice of imino-alcohols was guided by their use as "prodrugs"[7]. In a preliminary account[8], we have shown that imidates **1a** (R_1 = H) are in equilibrium with azomethine ylides **1a'** and undergo regioselective

cycloaddition with aldimines **2** at 70°C, without solvent (Scheme 1). The reaction leads to imidazolones **6** after the successive loss of ethanol and methanol via an intramolecular rearrangement.

As part of our program related to the study of organic synthesis in dry media[9], eventually under microwave irradiation[10], we have developed a fast synthesis of some new imidazolones **6** under irradiation in a focused open vessel microwave digestion system[11a].

We now report the results of our studies which describe the reactivity of imidate **1a** (R_1 = H) with a range of imino-alcohols. Here, we first report preparative procedures, including the full characterization of these new compounds and then, a Frontier Molecular Orbital Analysis (FMO) is described with the results of PM3 calculations using MOPAC program (version 6.0)[12].

RESULTS AND DISCUSSION

The starting imidate **1a** (R_1 = H) was readily obtained as described by the procedure of *Cornforth et al.*[13] from ethyl acetimidate hydrochloride[14] and methyl glycinate hydrochloride with potassium carbonate in water (method A, yield 70%). On large scale, the reaction is realized in methylene chloride at 40°C with triethylamine in 87% yield (method B). For the purpose of these investigations a variety of imino-alcohols **2** were synthesized (Scheme 2).

Scheme 2

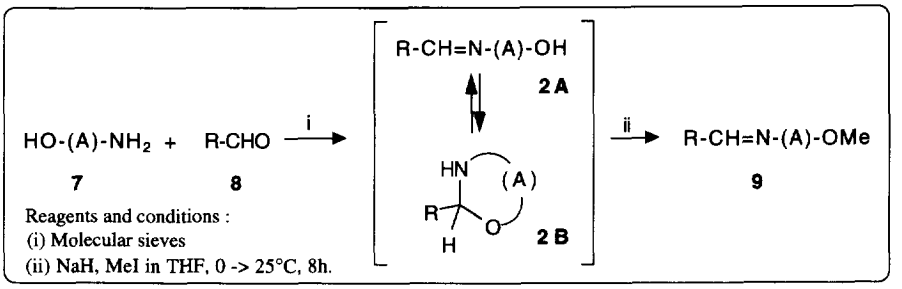
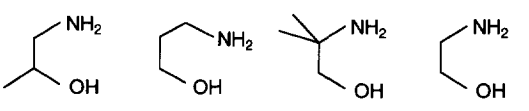


Table 1 : Synthesis of imino-alcohols **2A**/1,3-oxazolidines **2B** and imines **9.**

amino-alcohol	-(A)-	R	compound	Yield (%)	**2A/2B** ratio
7a	-CH_2-CH-Me	Ph	**2a**	95	93 : 7[15a]
7b	-$(CH_2)_3$-	Ph	**2b**	83	69 : 31
7a	-CH_2-CH-Me	Furyl	**2c**	92	100 : 0
7a	-CH_2-CH-Me	(2-OH) C_6H_4	**2d**	60	100 : 0
7c	-CMe_2-CH_2-	Ph	**2e**	93	42 : 58
7d	-$(CH_2)_2$-	iPr	**2f**	77	15 : 85
7d	-$(CH_2)_2$-	Ph	**2g**	79	100 : 0
7a	-CH_2-CH-Me	Ph	**9a**	93	-
7b	-$(CH_2)_3$-	Ph	**9b**	72	-



7a **7b** **7c** **7d**

The amino alcohols **7** were condensed with the corresponding aldehydes **8** on powdered 3Å molecular sieves in good yields (Table 1). It is known from ^1H NMR spectroscopy analysis that these compounds **2,** in solution ($CDCl_3$), exist as a tautomeric mixture of imino-alcohols **2A** and 1,3-oxazolidines **2B**[16]. The hydroxy group of imino-alcohols **2a, 2b** was protected by alkylation[17] with methyl iodide and sodium hydride in dry THF at 0°C, to give the desired imines **9** in 72-93% yield.

Cycloaddition reactions of imidate **1a** with imino-alcohols **2** were carried out at 70°C, without solvent. After removal of the alcohol, ^1H NMR analysis of the crude product indicated the formation of a major component which is the desired imidazolone **10** in good yields (Table 2) together with a by-product **11** (Scheme 3). In all cases, addition of imidate **1a** to imino-alcohols **2** leads to a single regioisomer.

Scheme 3

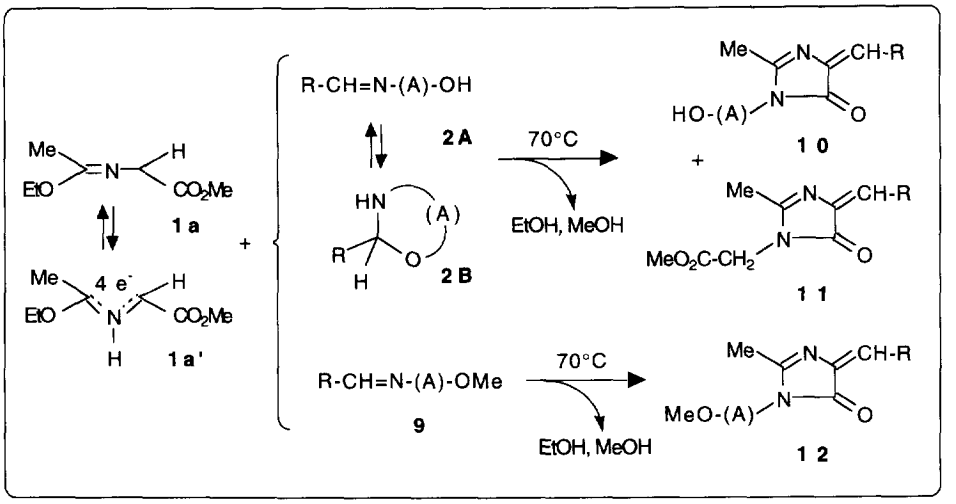


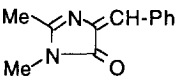
Table 2 : Synthesis of Imidazolones **10** and **12** by 1,3-dipolar cycloaddition.

compound	R	-(A)-	Yield (%)	Yield of **11**[(a)]	Reaction time (h)
10a	Ph	$-CH_2-CH-Me$	(76)[(a)] 67[(b)]	**11a** : 14	1
10b	Ph	$-(CH_2)_3-$	(85) 80	**11a** : 9	1.5
10c	Furyl	$-CH_2-CH-Me$	(84) 71	**11c** : 10[(c)]	2
10d	(2-OH) C_6H_4	$-CH_2-CH-Me$	(94) 85	**11d** : 5	1.5
10e[18]	Ph	$-CMe_2-CH_2-$	-	-	-
10f	iPr	$-(CH_2)_2-$	(77) 65	**11g** : 15[(c)]	2.5
10g	Ph	$-(CH_2)_2-$	(90) 85	**11a** : 5	1.5
12a	Ph	$-CH_2-CH-Me$	(98) 61	-	165
12b	Ph	$-(CH_2)_3-$	(98) 65	-	160

(a) Yield (%) for crude product by ^1H NMR spectroscopy.(b) Isolated product.(c) estimated by ^1H NMR on the CO_2Me group signal but not fully characterized.

These results show that azomethine ylide formation by thermal 1,2-prototropy[19] of imidate **1a** activated by an electron withdrawing group opens a simple route to a wide range of novel polyfunctionalized imidazolones **10** in a short reaction time (Table 2). We have also studied the effect of catalysts on the cycloaddition of imidate **1a** to N-benzyliden methylamine **2h**[20] (Table 3).

Table 3 : Effect of catalysts on reaction time for the formation of **6h** (R_2 = Me, R_3 = Ph, Scheme 1)



6 h

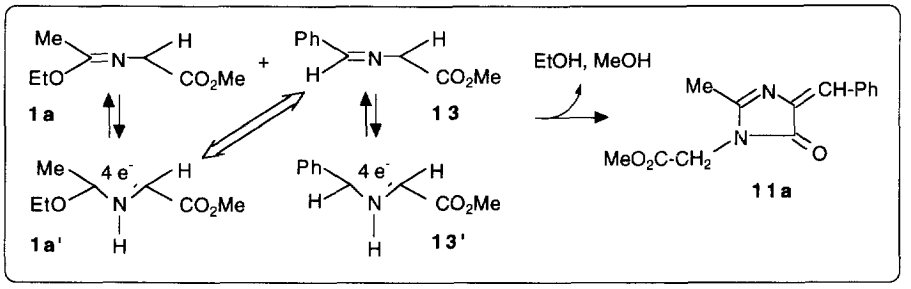
Entry	Catalyst	Conditions[a]	Reaction time	Yield of **6h** (%)[b]
1	-	70°C	46	98
2	Aliquat 336®, 8, 21	70°C, 10%[c]	19	94
3	$MeCO_2H$	70°C, 10%[c]	1,75	90

(a) reactions were run in a thermostated oil bath, temperature variation ± 1°C (b) estimated by ^1H NMR spectroscopy (c) catalyst amount.

The reactions proceeded cleanly in high yields with no evidence of decomposition of imidate **1a** and dipolarophile imine **2h**. This cycloaddition was controlled by ^1H NMR spectroscopy and the spectral data of compound **6h** were assigned on the basis of our earlier study[8]. These results show that the fastest rate is observed with Brönsted acid[22] (entry 3, Table 3) as catalyst.

For the synthesis of imidazolones **10** (from imidate **1a** and imino-alcohols **2**), the reactions were carried out at 70°C with shorter reaction times (Table 2). The hydroxy group of imino-alcohols **2** promotes an accelerating effect. This observation was confirmed by reacting imidate **1a** with O-alkylated imines **9a** and **9b** : in each case, reaction times are very long (Table 2, entry **12a** : 165 h, entry **12b** : 160 h), and without formation of by-product **11.**

Scheme 4



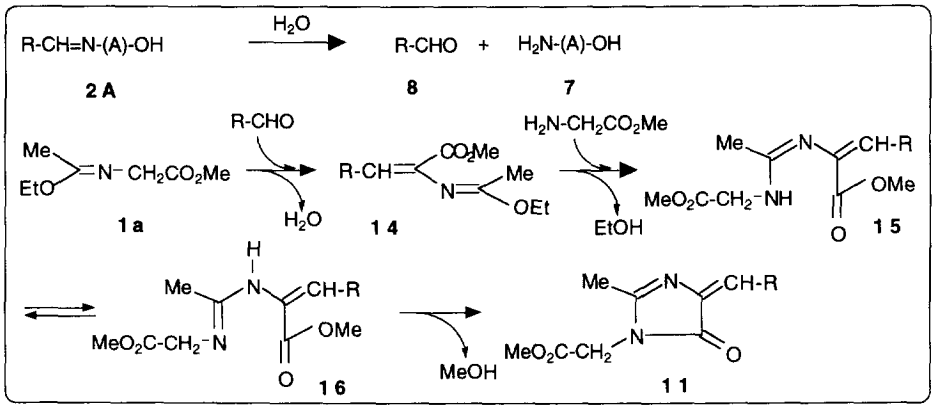
Identification of compounds 11 - For instance after the reaction of **1a** with **2a**, gravity column chromatography of the crude reaction mixture, on silica gel 60 Merck (4:1 / CH_2Cl_2-ether) provided two fractions (Table 2). The first fraction gave **11a** (Rf = 0.71, in 14% yield) and the second one (Rf = 0.24) afforded **10a** in 67% yield. The structure of **11a** (R = Ph) is established on the basis of spectral data, for example **11a** (see experimental part) exhibits a singlet at δ = 7.11 ppm in ^1H NMR, and in ^{13}C NMR two signals at δ = 130.26 ppm (CH=), and 138.04 ppm (C-4) which can be assigned to the exo C,C double bond, **11a** also exhibits three others singlets : one at δ = 3.74 ppm for the methyl ester group and the others appear at δ = 2.29 ppm (imidic methyl, Me-C=N) and the CH_2 group at 4.36 ppm. The structure of **11a** was further confirmed by mass spectrometry.

Two distinct mechanistic pathways may account for the formation of imidazolone **11a.** In path A (Scheme 4), the retrosynthetic analysis of **11a** involves an initial (3+2) cycloaddition of

imidate **1a** with the suitable Schiff's base of methyl glycinate **13**[23] and leads to imidazolone **11a** via an intramolecular rearrangement. In this process, imine **13** should react as dipolarophile. Experimentally, the equimolar mixture of compounds **1a** and **13** was carried out in an oil bath at 70°C without solvent during 4h (reaction time was monitored by ^{1}H NMR spectroscopy) and leads to **11a** in 50% yield with decomposition of by-products. So the dipolarophile imine[24] **13** can arise from the displacement ability[25] of imino-alcohols **2** with methyl glycinate (with **2a**, reaction time : 48h, crude yield = 56% by ^{1}H NMR spectroscopy) after initial hydrolysis of imidate **1a**. Another possibility (path B : Scheme 5) for the formation of **11a** (R = Ph) is the hydrolysis of imino-alcohols **2**. Then carbonyl addition of the resulting aldehyde **8** with the active methylene of imidate **1a** leads to the 1,3-aza diene **14**[26], the amino-alcohol **7** acting as a base catalyst[27]. Then compound **14** may be converted into **15** by addition of methyl glycinate (arising from hydrolysis of **1a**) on imidate function[13b,28], which undergo ring closure to **11a** with methanol elimination (**11a** was independently synthesized in 96% yield from a mixture of benzaldehyde and imidate **1a** at 70°C without solvent, reaction time : 3.5 h).

In summary, each path begins by *in situ* hydrolysis of imidate **1a** (path A) or imino-alcohols **2** (path B).

Scheme 5



*Synthesis of imidazolones **10** under microwave irradiation* - Finally, we tried to accelerate this process by microwave irradiation[29]. Recently in our laboratory, we have observed that microwave irradiation leads to considerable enhancements in the rate of 1,3-dipolar cycloaddition[29e]. Experiments were performed in open vessels in a Maxidigest focused microwave digester[11a]. As a typical experiment, the equimolar mixture of imidate **1a** (10 mmol.) and imino-alcohol **2** (see Scheme 3) is introduced in a Maxidigest MX 350 in a open Pyrex reactor. Microwave irradiation is carried out for 9-18 minutes at 45-180W. The crude residue is analysed by ^{1}H NMR spectroscopy. The main results are summarized in Table 4.

Table 4 : Synthesis of imidazolones **10** under microwave irradiation.

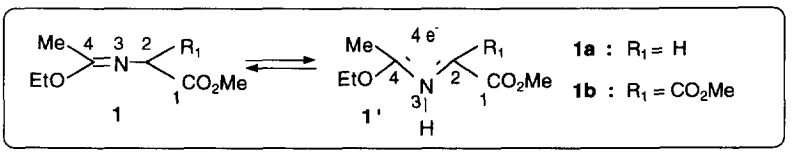
Entry	R	-(A)-	Yield ratio **10/11**[(a)] at 70°C[(b)]	Yield ratio **10/11**[(a)] by MW[(c)]	Power (Watt)	Reaction time (min.)
1	Ph	$-CH_2-CH-Me$	76 : 14	88 : 6	45	9
2	Ph	$-(CH_2)_3-$	85 : 9	95 : 4	75	14
3	Furyl	$-CH_2-CH-Me$	84 : 10	90 : 6	180	14
4	iPr	$-(CH_2)_2-$	77 : 15	88 : 10	120	18

(a) in %, from the crude residue by ^1H NMR spectroscopy (b) reactions were run in a thermostated oil bath, temperature variation ± 1°C, for the appropriate reaction time see Table 2 (c) MW : Microwave irradiation.

Comparison of the two methods clearly shows an acceleration of the 1,3-dipolar cycloaddition and yield enhancements for synthesis of imidazolones **10** under irradiation (see ratio **10/11** in Table 4). In fact, moisture elimination (from imino-alcohols **2**) is achieved by microwave irradiation and limits the formation of **11** according to path A or B.

A Frontier Molecular Orbital (FMO) Analysis - The use of a chemical reactivity analysis based on the frontier orbitals theory gave us the tools to account for these results. These calculations were performed using a quantum mechanical semi-empirical method (PM3)[12a]. All the reactant structures were then optimized at this level by the MOPAC package[12b]. In the frontier molecular orbital (FMO) treatment of [3+2] cycloadditions, the relative reactivity of the 1,3- dipoles (Table 5) **1a'** (R_1 = H), **1b'** (R_1 = CO_2Me) towards a series of imines **2**, **9** and **13** is determined primarily by the stabilization afforded in the transition state by interaction of the $HOMO_{(1,3\text{-dipole})}$ and the $LUMO_{(dipolarophile)}$.

Table 5 : Calculated frontier orbital energies, HOMO and LUMO coefficients, net atomic charges for imidates **1(a-b)**, **1(a-b)'** and imine **13**, **13'**.



	HOMO			LUMO			Net Atomic Charge		ΔHf
Compound	(eV)	C-2	C-4	(eV)	C-2	C-4	C-2	C-4	(Kcal)
1a'	-7.97	-0.711	0.533	-0.25	-0.313	-0.600	-0.722	-0.312	-103.95
1b'	-8.42	0.687	-0.383	-0.60	0.274	0.512	-0.682	-0.244	-181.39
13'	-8.19	-0.622	0.546	-0.85	0.339	0.369	-0.674	-0.498	-035.03
Compound	(eV)	N-3	C-4	(eV)	N-3	C-4	N-3	C-4	(Kcal)
1a	-10.11	-0.446	-0.368	0.59	-0.535	0.591	-0.146	0.064	-118.88
1b	-10.29	-0.342	-0.416	0.33	0.502	-0.594	-0.155	0.090	-196.82
13	-9.50	-0.391	-0.206	-0.43	0.451	0.400	-0.117	-0.007	-041.26

In this dipolar cycloaddition (see Scheme 1 for the mechanism), formation of intermediate **3** (which is not isolated experimentally) involves azomethine ylide **1a'** by thermal 1,2-prototropy[19].

Cycloaddition with imidate **1b** - In previous work[8], we have shown that imidate **1b** ($R_1 = CO_2Me$) in equilibrium with azomethine ylide **1b'** undergoes regioselective cycloaddition to dipolarophile imines **2** via the intermediate **17** (Scheme 6). After ethanol elimination, the reaction leads to a single regioisomer **18**. Elimination of this leaving group from the cycloadduct **17** gives formal nitrile ylide cycloadduct. In Table 6, we report calculated properties of a series of dipolarophiles **2(a-j)**. For compounds **2(h-j)**, that we have reacted with imidate **1b**, we report in Table 7, the FO interaction and the second order perturbation energy E_2. Inspection of Table 7 and Scheme 8, shows that the favourable frontier orbitals interaction between **1b'** and imines **2(h-j)** as dipolarophiles, is controlled by the interaction $HOMO_{(1,3\text{-dipole})}$ - $LUMO_{(dipolarophile)}$ (see column ΔE_1). Then, we have also developed calculations of second order perturbation energy E_2[30] with two possible approaches (Scheme 7). Values obtained in column $E_2(1)$ show that the favoured orientation[31] results (Table 7) from approach (1), and this is in agreement with the experimental results.

Scheme 6

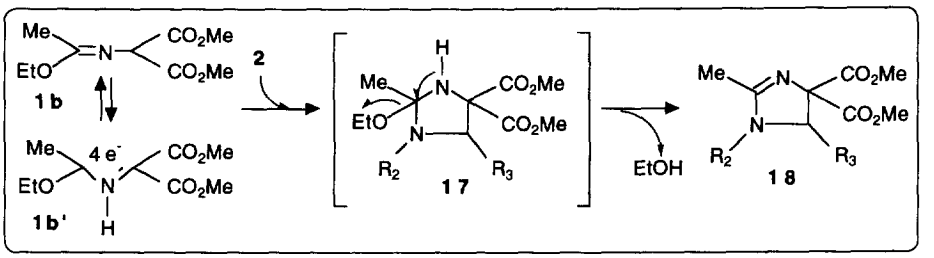


Table 6 : Calculated frontier orbital energies, HOMO and LUMO coefficients, net atomic charges for imino-alcohols **2a-g**, imines **2h-j** and **9**.

R-CH=N-(A)-OH	R-CH=N-(A)-OMe	R_2-N=CH-R_3	**2 h** R_2 = Me, R_3 = Ph
2a-g	**9a-b**	**2h-j**	**2 i** R_2 = iPr, R_3 = Ph
			2 j R_2 = $iPrCH_2$, R_3 = Ph

	HOMO			LUMO			Net Atomic Charge		ΔHf
Compound	(eV)	N	CH=	(eV)	N	CH=	N	CH=	(Kcal)
2a	-9.47	-0.394	-0.231	-0.36	0.446	-0.370	-0.124	-0.038	-13.06
2b	-9.33	-0.401	-0.242	-0.24	-0.445	0.360	-0.107	0.041	-10.08
2e[18]	-9.45	0.391	0.214	-0.31	0.441	-0.371	-0.115	-0.022	-17.33
2f	-10.01	-0.139	-0.007	0.87	-0.317	0.346	-0.113	-0.086	-49.10
2h[20]	-9.31	0.405	0.249	-0.21	0.441	-0.354	-0.110	-0.048	38.07
2i[32a]	-9.37	-0.396	-0.225	-0.20	-0.436	0.356	-0.113	-0.033	29.33
2j[32a]	-9.31	0.405	0.251	-0.21	0.442	-0.353	-0.104	-0.047	22.93
9a	-9.35	0.404	0.243	-0.26	0.445	-0.359	-0.109	-0.041	-06.46
9b	-9.34	-0.401	-0.241	-0.23	0.445	-0.361	-0.107	-0.041	-06.30

Table 7 : Frontier orbitals (FO) interaction and second order perturbation energy E_2 between imidate **1b** and imines **2(h-j)** via the intermediate **17**.

	ΔE_1(a)	ΔE_2(b)	$E_2(1)$(c)	$E_2(2)$(d)
Imine	(eV)	(eV)	(kcal./mole)	(kcal./mole)
2h[20]	8.21	8.71	0.980	0.886
2i[32a]	8.22	8.77	0.957	0.848
2j[32a]	8.21	8.71	0.980	0.889

(a) ΔE_1 = $HOMO_{\mathbf{1b}'}$ - $LUMO_{\mathbf{2}}$. (b) ΔE_2 = $HOMO_{\mathbf{2}}$ - $LUMO_{\mathbf{1b}'}$ (c) $E_2(1)$ = second order perturbation energy according to approach (1) (d) $E_2(2)$ = second order perturbation energy according to approach (2).

Cycloaddition with imidate **1a** - We now describe the extension of our FMO analysis to the cycloaddition reaction of imidate **1a** (R_1 = H) with imino-alcohols **2**, imines **2j**, **9a**, **9b** and **13** as dipolarophiles. PM3 calculations are developed only to explain the first step (via the intermediate **3**) in Scheme 1 according to FMO theory. Calculated properties of a series of imines **2** and **9** as dipolarophiles are given in Table 6. The calculated energies of the lower unoccupied molecular orbitals (LUMO) are relatively low and in the range of -0.36 eV to 0.87 eV.

Scheme 7

Different possible approaches

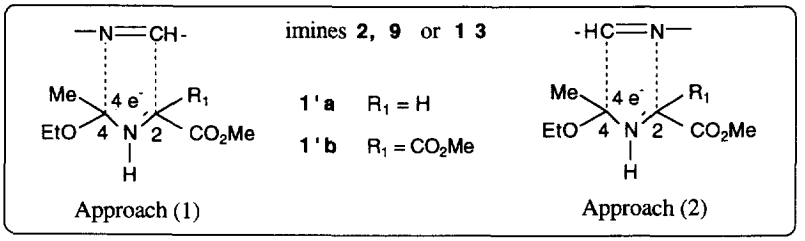


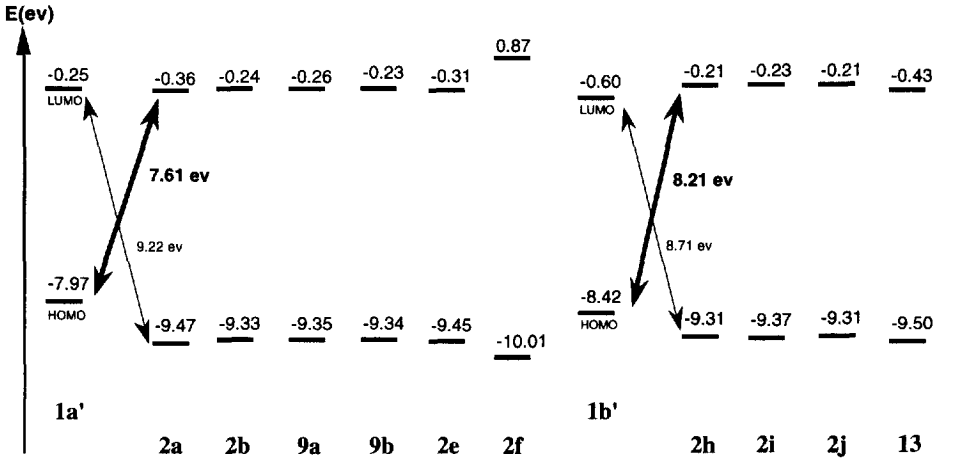
Table 8 : Frontier Orbitals (FO) energy differences and second order perturbation energy E_2 between imidate **1a** and imino-alcohols **2**, imines **2(h-j)**, **13** via the intermediate **3**.

	ΔE_1(a)	ΔE_2(b)	$E_2(1)$(c)	$E_2(2)$(d)
Imine	(eV)	(eV)	(kcal./mole)	(kcal./mole)
2a	7.61	9.22	1.399	1.305
2b	7.74	9.08	1.361	1.282
2e[18]	7.67	9.20	1.371	1.271
2f	8.84	9.76	0.722	0.614
2h[20]	7.77	9.06	1.338	1.266
2i[32a]	7.77	9.12	1.306	1.218
2j[32b]	7.76	9.06	1.338	1.269
9a	7.72	9.10	1.368	1.294
9b	7.74	9.09	1.363	1.282
13	7.55	9.25	1.516	1.377

(a) ΔE_1 = $HOMO_{\mathbf{1a}'}$ - $LUMO_{\mathbf{Imine}}$. (b) ΔE_2 = $HOMO_{\mathbf{Imine}}$ - $LUMO_{\mathbf{1a}'}$ (c) $E_2(1)$ = second order perturbation energy according to approach (1) (d) $E_2(2)$ = second order perturbation energy according to approach (2).

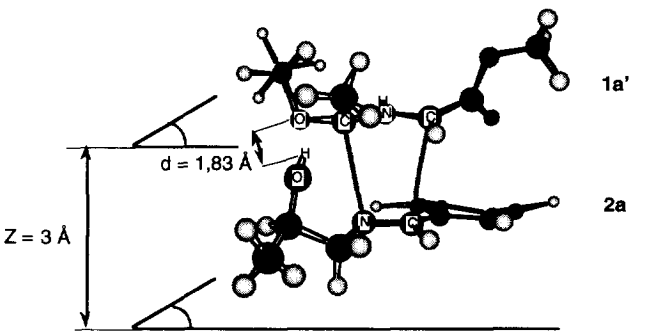
The results in Table 8 and in Scheme 8, show that the cycloaddition is also controlled by the interaction $HOMO_{1a'}$ - $LUMO_{(dipolarophile)}$ (column ΔE_1) and not surprisingly, all the second order perturbation energy E_2 calculations give results which accord with experiment (approach (1)). Furthermore it is interesting to notice that for the cycloaddition of **1a** with dipolarophiles **2a**, **9a** and **2j**, the ΔE_1 are very similar, but the reaction times are very different (**2a** : 1h; **9a** : 165h; **2j** : 170h).

Scheme 8 : Frontier Orbitals energy diagram.



This situation is analogous for compound **2b** (reaction time = 1.5h, LU_{2b} = - 0.24 eV, ΔE_1 = 7.74 eV) and **9b** (reaction time = 160h, $LUMO_{6b}$ = - 0.23 eV, ΔE_1 = 7.74 eV). In fact, the FMO interaction cannot describe the absolute reactivities of these dipolarophiles in this cycloaddition. We suggest that the particularly short reaction times observed in Table 2 with the imino-alcohols **2(a-g)** are due to interaction between the OH group of dipolarophile **2** and the EtO group of dipole **1a'** : for example with dipolarophile **2a** in Scheme 9.

Scheme 9



In Scheme 9, the two entities approach in two parallel planes (Z = 3Å, according to perturbation theory). The geometry of the reactants in this approach is optimized by the MOPAC

package : the centers C-2 and C-4 of **1a'** molecule interact with CH= and N of **2a** molecule respectively. This scheme shows, qualitatively, the distance between the OH group of **2a** and the EtO group of **1a'**. This average value (d = 1.83Å) is evaluated from one of the lowest energy approach. According to this model, it is surprising that no reaction is observed with the imino-alcohol **2e**[18] as dipolarophile ($LUMO_{2e}$ = - 0.31 eV, ΔE_1 = 7.67 eV), this may be due to the steric restriction provided by the two Me groups near the C=N towards this intermolecular interaction.

Finally, this intermolecular interaction is a possible explanation for the enhancement of the reactivity between the two entities and may contribute to the outcome of the reaction when HOMO - LUMO interactions are not large enough to dominate.

CONCLUSION

In summary, 1,3-dipolar cycloaddition of imidate **1a** on imino-alcohols dipolarophiles **2(a-g)**, leads to novel functionalized heterocyclic systems **10** in short reaction times using solvent free conditions. Results obtained with these dipolarophiles indicate that the hydroxy group of imino-alcohols **2(a-g)** exert an acceleration by an intermolecular interaction. In the same manner, the reaction time can be reduced by Brönsted acid catalysis or by microwave irradiation. The chemical reactivity in this cycloaddition is analysed according the FMO theory. PM3 calculations show that the reaction is controlled by the interaction $HOMO_{(1,3\text{-dipole})}$ - $LUMO_{(dipolarophile)}$. The second order perturbation energy E_2 calculations predict the reaction orientation and are in agreement with the experimental results. Further investigation of the biological activities and their synthetic utility is underway. Related applications of activated imidate cycloadditions to the synthesis of five membered nitrogen rings are being investigated.

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Experimental Section

General. Melting points were determined on a Kofler melting point apparatus and are uncorrected. IR spectra were taken with a PERKIN-ELMER 157G spectrometer. ^1H NMR spectra were recorded on BRUKER WP 80 CW (80 MHz), BRUKER AC 300 P (300 MHz) spectrometers and ^{13}C NMR spectra on BRUKER AC 300 P (75 MHz) spectrometer. Chemical shifts are expressed in parts per million downfield from tetramethylsilane as an internal standard. The mass spectra (MS) were taken on a VARIAN MAT 311 at an ionizing potential of 70 eV in the Centre de Mesures Physiques de l'Ouest (CRMPO, Rennes). Elemental analyses were performed at the Laboratoire Central de Microanalyses-CNRS (Lyon). Thin-layer chromatography (TLC) was accomplished on 0.2-mm precoated plates of silica gel 60 F-254 (Merck). Visualization was made with ultraviolet light (254 and 365 nm). For preparative column chromatography, silica gel 60 Merck (230-240 Mesh ASTM) is used. Reactions under microwave irradiation were performed into a Maxidigest MX 350™ (Prolabo) microwave reactor with a single focused system. All solvents and reagents were purchased from Janssen Chimica and Aldrich Chimie and used without further purification. Tetrahydrofuran (THF) was distilled from sodium benzophenone ketyl under a nitrogen atmosphere. Solvents were evaporated with a BUCHI rotary evaporator.

Methyl 2-(1-ethoxyethyliden)amino ethanoate (1a)

Method A : To a suspension of ethyl acetimidate hydrochloride (5 g - 40.5 mmol.) and methyl glycinate hydrochloride (5.64 g - 40.5 mmol.) in 200 mL of dry methylene chloride, cooled to 0°C with vigorous stirring, a solution of dry triethylamine (4.51 g - 44.6 mmol.) in 50 mL of dry methylene chloride was added dropwise during 0.5 h. Then, the resulting mixture was heated at 40°C during 18 h. The solvent was removed *in vacuo*, ether (150 mL) was added to the reaction mixture, and the suspension was filtered on filter paper. The filtrate was concentrated *in vacuo* to an oil (yield = 98%) distilled under reduced pressure, bp = 93-94°C/16 torr, in 87% yield. Compound **1a** can be stored under nitrogen at 0°C for several weeks without decomposition. - ^{1}H NMR ($CDCl_3$) δ : 1.25 (t, 3H, J = 7.2 Hz) ; 1.87 (s, 3H) ; 3.72 (s, 3H) ; 4.04 (s, 2H) ; 4.09 (q, 2H, J = 7.2 Hz); ^{13}C NMR ($CDCl_3$) δ : 14.22 (qt, J = 126 Hz) ; 15.19 (q, J = 129 Hz) ; 51.09 (t, J = 136 Hz) ; 51.18 (q, J = 147 Hz) ; 60.97 (tq, J = 146 Hz) ; 164.80 (C=N) ; 171.60 (C=O).

Method B : A suspension of potassium carbonate (6.9 g - 50 mmol.) and methyl glycinate hydrochloride (6.28 g - 50 mmol.) in ether (200 mL) was covered with water (20 mL), then treated with ethyl acetimidate hydrochloride (6.18 g - 50 mmol.). The mixture was shaken for 6 min, the ether decanted, and the mixture shaken with a further portion of ether (100 mL). The combined extracts were dried over anhydrous $MgSO_4$ and were evaporated to an oil which was distilled *in vacuo* to give 5.56 g of **1a**, in 70% yield, Lit.[13a] = 68%.

General procedure for the preparation of imino-alcohols (2) :

The carbonyl compound **8** (10 mmol.) and the amino-alcohol **7** (10 mmol.) were dispersed on 5 g of powdered 3Å molecular sieves (max. grain-size 50 micrometer). After standing for 8 h at room temperature, compound **2** was extracted with 3 x 30 mL of methylene chloride. The extract was filtered and the solvent removed *in vacuo*. The crude residue was purified by crystallization or by distillation under reduced pressure. The compounds **2** are known to exist in solution as a tautomeric mixture of imino-alcohol **2A** and 1,3-oxazolidine or 1,3-oxazinane **2B**, respectively. The ratio of each form was determined, in $CDCl_3$, by ^{1}H NMR integration of the imino proton (N=CH) and the aminal proton (NCHO).

N-Benzylidene-2-hydroxypropylamine (2a)

Colourless needles, mp = 70-71°C. Yield = 95% (93 : 7 mixture). - ^{1}H NMR[15b] ($CDCl_3$) δ : 1.24 (d, 3H, J = 6.3 Hz) ; 3.16 (br s, 1H, OH) ; 3.66 (ddd, 1H, J = 12, 4, 1 Hz) ; 3.45 (ddd, 1H, J = 12, 8, 1 Hz) ; 4.08 (m, 1H) ; 7.34-7.40 (m, 3H, Ar) ; 7.66-7.71 (m, 2H, Ar) 8.25 (s, 1H) ; ^{13}C NMR[15b] ($CDCl_3$) δ : 20.69 (qd, J = 124, 2 Hz) ; 67.31 (d, J = 146 Hz) ; 68.75 (t, J = 134 Hz) ; 128.19, 128.55, 130.80, 135.83 (Ar) ; 162.76 (d, J = 158 Hz) ; I.R. (cm^{-1}, CCl_4) = 3210 br., 2960, 2870, 1630, 1440. $C_{10}H_{13}NO$[33].

N-Benzylidene-3-hydroxypropylamine (2b)

Colourless viscous oil, bp = 92-93°C/0.5 torr. Yield = 83% (69 : 31 mixture) - ^{1}H NMR ($CDCl_3$) δ : major component : 1.89 (quint., 2H, J = 6 Hz) ; 3.33 (br s, 1H, OH) ; 3.72 (td, 2H, J = 6, 1 Hz) ; 3.78 (t, 2H, J = 6 Hz) ; 7.25-7.39 (m, 3H, Ar) ; 7.64-7.70 (m, 2H, Ar) ; 8.21 (s, 1H) ; minor component : 1.37 (dm, 1H, J = 13 Hz) ; 1.80 (dm, 1H, J = 13.4 Hz) ; 3.05 (ddd, 1H, J = 14, 12, 3 Hz) ; 3.20 (dddd, 1H, J = 14, 5, 2, 2 Hz) ; 3.33 (br s, 1H, NH) ; 3.88 (ddd, 1H, J = 12, 12, 2 Hz) ; 4.21 (dddd, 2H, J = 12, 5, 2, 2 Hz); 7.25-7.39 (m, 3H, Ar) ; 7.64-7.70 (m, 2H, Ar) ; ^{13}C NMR ($CDCl_3$) δ : major component : 33.37 (t, J = 126 Hz) ; 59.51 (t, J = 145 Hz) ; 67.87 (t, J = 145 Hz) ; 125.76, 128.05, 128.61, 135.72 (Ar) ; 161.42 (d, J = 157 Hz), minor component : 27.03 (t, J = 126 Hz) ; 44.46 (t, J = 145 Hz) ; 67.87 (t, J =

145 Hz) ; 88.82 (d, J= 152 Hz) ; 125.05, 128.61, 130.78, 140.57 (Ar). I.R. (cm^{-1}, nujol) = 3320, 2930, 2840, 1630, 1570, 1440. (Found : C, 73.3 ; H, 8.15 ; N, 8.70 ; O, 9.85. $C_{10}H_{13}NO$ requires C, 73.62 ; H, 7.97 ; N, 8.59 ; O, 9.82%).

N-Furylidene-2-hydroxypropylamine (2c)

Viscous oil which crystallized from ether on standing, mp = 67-68°C. Yield = 92%. - ^1H NMR ($CDCl_3$) δ : 1.24 (d, 3H, J = 6 Hz) ; 3.42 (ddd, 1H, J = 12, 8, 1 Hz) ; 3.50 (br. s, 1H, OH); 3.67 (ddd, 1H, J = 12, 4, 1 Hz) ; 4.13 (m, 1H) ; 6.45 (dd, 1H, J = 3, 2 Hz) ; 6.74 (d, 1H, J = 3 Hz) ; 7.50 (s, 1H) ; 8.06 (s, 1H) ; ^{13}C NMR ($CDCl_3$) δ : 20.70 (q, J = 126 Hz) ; 67.44 (d, J = 142 Hz) ; 69.15 (t, J = 139 Hz) ; 111.68 (dd, J =175, 13 Hz) ; 114.39 (d, J= 177 Hz) ; 144.80 (ddd, J = 203, 11, 8 Hz) ; 151.30 (s) ; 151.32 (dt, J =161, 9 Hz). I.R. (cm^{-1}, nujol) = 3180 br., 3120, 2920, 2840, 1630, 1565, 1465. (Found : C, 62.40 ; H, 7.30 ; N, 9.55 ; O, 20.75. $C_8H_{11}NO_2$ requires C, 62.72 ; H, 7.24 ; N, 9.14; O, 20.88%).

N-(2-Hydroxybenzylidene)-2-hydroxypropylamine (2d)

Colourless viscous oil, bp = 130°C/0.2 torr. Yield = 60%. - ^1H NMR ($CDCl_3$) δ : 1.23 (d, 3H, J = 6 Hz) ; 3.16 (br. s, 1H, OH) ; 3.42 (ddd, 1H, J = 12, 3, 1) ; 3.63 (ddd, 1H, J = 12, 3, 1 Hz) ; 4.04 (m, 1H) ; 6.79-6.92 (m, 2H, Ar) ; 7.17-7.29 (m, 2H, Ar) ; 8.26 (s, 1H) ; ^{13}C NMR ($CDCl_3$) δ : 20.83 (qd, J = 126, 2 Hz) ; 66.61 (t, J = 136 Hz) ; 66.90 (dq, J = 144, 4 Hz) ; 117.08, 118.46, 118.53, 131.49, 132.50, 161.61 (Ar) ; 166.63 (dq, J = 161, 8 Hz). I.R. (cm^{-1}, nujol) = 3030 br., 2920, 2845, 1620, 1590, 1480. (Found : C, 66.85 ; H, 7.45 ; N, 7.9 ; O, 17.8. $C_{10}H_{12}NO_2$ requires C, 67.0 ; H, 7.3 ; N, 7.8 ; O, 17.85%).

N-Benzylidene-1,1-dimethyl-2-hydroxyethylamine (2e)

Colourless needles, mp = 66°C. Yield = 93% (58 : 42 mixture) - ^1H NMR ($CDCl_3$) δ : major component : 1.27 (s, 3H) ; 1.29 (s, 3H) ; 3.53 (d, 1H, J = 7.5 Hz) ; 3.70 (d, 1H, J = 7.5 Hz) ; 5.53 (br. s, 1H) ; 7.29-7.38 (m, 3H, Ar) ; 7.45-7.49 (m, 2H, Ar) ; minor component : 1.23 (s, 6H) ; 2.38 (br. s, 1H) ; 3.50 (s, 2H) ; 7.29-7.38 (m, 3H, Ar) ; 7.69-7.73 (m, 2H, Ar) ; 8.28 (s, 1H); ^{13}C NMR ($CDCl_3$) δ : major component : 23.92 (qq, J = 126, 4 Hz) ; 26.62 (q, J = 126 Hz) ; 59.83 (s) ; 77.84 (t, J = 146 Hz) ; 92.03 (d, J = 167 Hz) ; 125.90, 128.41 ; 139.90 (Ar) ; minor component : 26.08 (qq, J = 126, 4 Hz) ; 60.72 (s) ; 71.57 (t, J = 143 Hz) ; 128.04, 128.50, 130.58, 136.60 (Ar) ; 157.58 (dt, J = 156, 5 Hz, C=N). I.R. (cm^{-1}, nujol) = 3220 br., 2920, 2850, 1625, 1565. (Found : C, 74.45 ; H, 8.5 ; N, 8.0 ; O, 9.05. $C_{11}H_{14}NO$ requires C, 74.57 ; H, 8.47 ; N, 7.9 ; O, 9.05%).

N-(2-Methylpropylidene)-2-hydroxyethylamine (2f)

Viscous oil, bp = 70°C/15 torr. Yield = 77% (15 : 85 mixture). - ^1H NMR ($CDCl_3$) δ : major component : 0.99 (d, 3H, J = 6 Hz) ; 1.01 (d, 3H, J = 6 Hz) ; 2.50 (br. s, 1H, OH) ; 3.55 (m, 1H) ; 2.96-3.05 (m, 1H) ; 3.19-3.27 (m, 1H) ; 3.62-3.74 (m, 2H) ; 4.08 (d, 1H, J = 6 Hz) ; minor component : 1.08 (d, 6H, J = 7 Hz) ; 2.44 (m, 1H) ; 2.50 (br. s, 1H, NH) ; 3.49 (t, 2H, J = 6 Hz) ; 3.76 (t, 2H, J = 5 Hz) ; 7.59 (d, 1H, J = 5 Hz) ; ^{13}C NMR ($CDCl_3$) δ : major component : 18.15 (q, J = 125 Hz) ; 18.16 (q, J = 125 Hz) ; 31.94 (d, J = 125 Hz) ; 46.28 (t, J = 141 Hz) ; 64.90 (t, J = 134 Hz) ; 96.88 (d, J = 156 Hz) ; minor component : 19.17 (q, J = 126 Hz) ; 33.94 (d, J = 125 Hz) ; 61.74 (t, J = 139 Hz) ; 63.04 (td, J = 132, 12 Hz) ; 171.67 (d, J = 153 Hz). I.R. (cm^{-1}, nujol) = 3300 br., 2960, 2870, 1660, 1460. $C_6H_{13}NO$[33].

N-Benzylidene-2-hydroxyethylamine (2g)

Colourless viscous oil, bp = 80-81°C/0.15 torr. Yield = 79%. - ^1H NMR ($CDCl_3$) δ : 3.46 (br s, 1H, OH) ; 3.69 (td, 2H, J = 5, 1 Hz) ; 3.87 (t, 2H, J = 5 Hz) ; 7.35-7.35 (m, 3H, Ar) ; 7.63-7.66 (m, 2H, Ar) ; 8.21 (s, 1H) ; ^{13}C NMR ($CDCl_3$) δ : 62.01 (tt, J = 143, 5 Hz) ; 63.47 (td, J = 123, 10 Hz) ; 128.23 (d, J = 158 Hz) ; 128.56 (d, J = 166 Hz) ; 130.81 (dt, J = 160, 8 Hz) ; 135.70 (s) ; 163.32 (d, J = 157 Hz). I.R. (cm^{-1}, nujol) = 3320 br., 2920, 2865, 1630,

1570, 1440. (Found : C, 72.0 ; H, 7.6 ; N, 9.6 ; O, 10.8. $C_9H_{11}NO$ requires C, 72.45 ; H, 7.43 ; N, 9.39 ; O, 10.7%).

N-Benzylidene-2-methylpropylamine (2j)

Colourless viscous oil, bp = 34-35°C/0.1 torr. Yield = 90%. - ^1H NMR ($CDCl_3$) δ : 0.96 (d, 6H, J = 6, 7 Hz) ; 2.01 (m, 1H) ; 3.42 (dd, 2H, J = 6.6, 1.3 Hz) ; 7.35-7.38 (m, 3H, Ar) ; 7.70-7.74 (m, 2H, Ar) ; 8.21 (s, 1H) ; ^{13}C NMR ($CDCl_3$) δ : 20.69 (qm, J = 125 Hz) ; 29.58 (dm, J = 127, 5 Hz) ; 62.01 (tt, J = 143, 5 Hz) ; 69.81 (tm, J = 133 Hz) ; 128.04, 128.53, 130.38, 136.40 (Ar) ; 160.74 (dm, J = 156 Hz). I.R. (cm^{-1}, nujol) = 3060, 3020, 2960, 2870, 2820, 1670, 1570, 1440.

Typical procedure for alkylation of imino-alcohols (2a) and (2b) :

N-Benzylidene-2-methoxypropylamine (9a)

A mixture of sodium hydride (60% dispersion in mineral oil, 0.48 g, 20 mmol.) and methyl iodide (3.55 g, 25mM) in dry THF (30 mL) was cooled to 0°C. A solution of the compound **2a** (1.63 g, 10 mmol.) in dry THF (15 mL) was added dropwise during 0.5 h. The solution was allowed to warm to room temperature and stirred overnight. After slow addition of water (15 mL), the mixture was extracted with ethyl acetate. Drying of the organic layer over anhydrous $MgSO_4$ and removal of the solvent by rotary evaporation, gave a viscous oil (yield = 98%), which was distilled under reduced pressure, bp = 47-48°C/0.03 torr, (1.65 g, 93%) - ^1H NMR ($CDCl_3$) δ : 1.21 (d, 3H, J = 6 Hz) ; 3.36 (s, 3H) ; 3.59-3.70 (m, 1H+2H) ; 7.36-7.39 (m, 3H, Ar) ; 7.70-7.74 (m, 2H, Ar) ; 8.25 (s, 1H) ; ^{13}C NMR ($CDCl_3$) δ : 17.89 (qt, J = 126, 3 Hz) ; 56.69 (qd, J = 141, 4 Hz) ; 66.77 (t, J = 134 Hz) ; 76.60 (d, J = 142 Hz) ; 128.13, 128.51, 130.23, 136.56 (Ar) ; 162.26 (d, J = 152 Hz). I.R. (cm^{-1}, nujol) = 2970, 2920, 2870, 2820, 1630, 1570, 1445. (Found : C, 74.15 ; H, 8.60 ; N, 7.85 ; O, 9.4. $C_{11}H_{15}NO$ requires C, 74.57 ; H, 8.47 ; N, 7.9 ; O, 9.05%).

N-Benzylidene-3-methoxypropylamine (9b)

This compound was prepared according to the method used for the synthesis of **9a** from compound **2b** in 72% yield, bp = 71-72°C/0.2 torr. - ^1H NMR ($CDCl_3$) δ : 1.98 (quint., 2H, J = 7 Hz) ; 3.33 (s, 3H) ; 3.46 (t, 2H, J = 6 Hz) ; 3.68 (t, 2H, J = 6 Hz) ; 7.36-7.43 (m, 3H, Ar) ; 7.68-7.76 (m, 2H, Ar) ; 8.28 (s, 1H) ; ^{13}C NMR ($CDCl_3$) δ : 30.78 (t, J = 127 Hz) ; 58.13 (t, J = 135 Hz) ; 58.54 (q, J = 140 Hz) ; 70.31 (t, J = 140 Hz) ; 128.04, 128.57, 130.5, 136.26 (Ar) ; 161.35 (d, J = 156 Hz). I.R. (cm^{-1}, nujol) = 2915, 2840, 1630, 1570, 1440. (Found : C, 74.15 ; H, 8.55 ; N, 7.9 ; O, 9.40. $C_{11}H_{15}NO$ requires C, 74.57 ; H, 8.47 ; N, 7.91 ; O, 9.05%).

Typical synthesis of 1,4-disubstituted 2-imidazolin-5-ones (10), (11a), (11d) and (6j) :

1-(2-Hydroxypropyl)-2-methyl-4-benzylidene-2-imidazolin-5-one (10a)

A mixture of imidate **1a** (1 g - 6.3 mmol.) and imino-alcohol **2a** (1.03 g - 6.3 mmol.) was heated at 70°C during 1 h under magnetic stirring. After removal of alcohols *in vacuo*, gravity column chromatography on silica gel 60 Merck (20 g) provided two fractions, after elution with methylene chloride/ether (4:1). The first fraction gave **11a*** (Rf = 0.71) and the second fraction (Rf = 0.24) gave the desired compound **10a** (1.6 g, 67%) as a colourless viscous oil which crystallized on standing (mp = 102-103°C). - ^1H NMR ($CDCl_3$) δ : 1.16 (d, 3H, J = 6 Hz) ; 2.31 (s, 3H) ; 3.33 (dd, 1H, J = 14, 9 Hz) ; 3.58 (dd, 1H, J = 14, 3 Hz) ; 3.93 (m, 1H) ; 4.15 (br s, 1H, OH) ; 6.98 (s, 1H) ; 7.32-7.40 (m, 3H, Ar) ; 8.02-8.08 (m, 2H, Ar) ; ^{13}C NMR ($CDCl_3$) δ : 15.90 (q, J = 130 Hz) ; 20.77 (q, J = 126 Hz) ; 48.24 (td, J = 134, 5 Hz) ; 65.42 (dt, J = 144, 5 Hz) ;

121.21, 128.61, 132.12, 134.00 (Ar) ; 130.08 (dt, J = 160, 8 Hz, CH=) ; 138.22 (s, C-4) ; 163.75 (s, C-2) ; 170.90 (s, C-5). I.R. (cm^{-1}, nujol) = 3380 br., 2920, 2830, 1680, 1630, 1560, 1450, 1395. MS, *m/z* = 244.1203 found (calculated for $C_{14}H_{16}N_2O_2$: 244.1212). (Found : C, 68.45 ; H, 6.55 ; N, 11.80 ; O, 13.20. $C_{14}H_{16}N_2O_2$ requires C, 68.85 ; H, 6.55 ; N, 11.47 ; O, 13.11%).

(*) : spectral properties of **11a** are given below.

The following compounds (**10, b, c, d, f, g**) were prepared according to the standard procedure described for **10a** .

1-(3-Hydroxypropyl)-2-methyl-4-benzylidene-2-imidazolin-5-one (10b)

Purification by chromatography (eluent : AcOEt) provided two fractions, the first fraction gave **11a** (Rf = 0.62) and the second fraction (Rf = 0.32) gave the desired compound **10b** (yield = 80%) as a colourless viscous oil which crystallized on standing (mp = 60-61°C). - ^1H NMR ($CDCl_3$) δ : 1.81 (quint., 2H, J = 6 Hz) ; 2.39 (s, 3H) ; 3.35 (br s, 1H, OH) ; 3.59 (t, 2H, J = 6 Hz) ; 3.76 (t, 2H, J = 6 Hz) ; 7.12 (s, 1H) ; 7.36-7.45 (m, 3H, Ar) ; 8.09-8.15 (m, 2H, Ar) ; ^{13}C NMR ($CDCl_3$) δ : 15.54 (q, J = 129 Hz) ; 31.67 (t, J = 126 Hz) ; 36.92 (t, J = 134 Hz) ; 58.20 (t, J = 138 Hz) ; 128.19, 128.75, 132.27, 133.99 (Ar) ; 130.35 (dt, 161, 8 Hz, CH=) ; 138.31 (s, C-4) ; 162.33 (s, C-2) ; 171.75 (s, C-5). I.R. (cm^{-1}, nujol) = 3480, 3340 br., 2920, 2840, 1665, 1625, 1560, 1440, 1400. MS, *m/z* = 244.1206 found (calculated for $C_{14}H_{16}N_2O_2$: 244.1212). (Found : C, 68.45 ; H, 6.65 ; N, 11.35 ; O, 13.55. $C_{14}H_{16}N_2O_2$ requires C, 68.85 ; H, 6.55 ; N, 11.47 ; O, 13.1%).

1-(2-Hydroxypropyl)-2-methyl-4-furylidene-2-imidazolin-5-one (10c)

Removal of alcohols *in vacuo* gave an oily residue which was crystallized from ether (yield = 71%), mp = 124-125°C. - ^1H NMR ($CDCl_3$) δ : 1.20 (d, 3H, J = 6 Hz) ; 2.36 (s, 3H) ; 3.37 (dd, 1H, J = 14, 9 Hz) ; 3.59 (dd, 1H, J = 14, 3 Hz) ; 4.00 (m, 1H) ; 4.08 (br s, 1H, OH) ; 6.55 (dd, 1H, J = 3, 2 Hz) ; 6.87 (s, 1H) ; 7.18 (sd, 1H, J = 3 Hz) ; 7.63 (sd, 1H, J = 2 Hz) ; ^{13}C NMR ($CDCl_3$) δ : 15.98 (q, J = 130 Hz) ; 20.83 (q, J = 126 Hz) ; 48.42 (td, J = 139, 5 Hz) ; 65.50 (dt, J = 144, 5 Hz) ; 113.40 (ddd, J = 177, 13, 4 Hz) ; 114.34 (d, J = 159 Hz, CH=) ; 118.87 (dq, J = 178, 5 Hz) ; 135.12 (s, C-4) ; 146.16 (ddd, J = 204, 11, 8 Hz) ; 150.69 (sq, J = 7 Hz) ; 163.12 (s, C-2) ; 170.47 (s, C-5). I.R. (cm^{-1}, nujol) = 3350 br , 3100, 2920, 2840, 1685, 1630, 1540, 1450 . MS, *m/z* = 234.1016 found (calculated for $C_{12}H_{14}N_2O_3$: 234.1004). (Found : C, 61.3 ; H, 5.9 ; N, 11.7 ; O, 21.1. $C_{12}H_{14}N_2O_3$ requires C, 61.54 ; H, 5.98 ; N, 11.96 ; O, 20.5%).

1-(2-Hydroxypropyl)-2-methyl-4-(2-hydroxybenzylidene)-2-imidazolin-5-one (10d)

Purification by chromatography (eluent : methylene chloride/methyl alcohol = 10/1) provided two fractions. The first fraction gave **11d*** (Rf = 0.86) and the second fraction (Rf = 0.32) gave the desired compound **10d** (yield = 85%) as a colourless viscous oil which crystallized on standing (mp = 50-51°C) - ^1H NMR ($CDCl_3$) δ : 1.22 (d, 3H, J = 6 Hz) ; 2.33 (s, 3H) ; 3.64 (dd, 1H, J = 14, 2 Hz) ; 3.38 (dd, 1H, J = 14, 9 Hz) ; 4.06 (m, 1H) ; 6.79-6.90 (m, 3H, Ar) ; 7.17-7.34 (m, 2H, Ar) ; 6.97 (s, 1H) ; 13.83 (br s, 1H, OH) ; ^{13}C NMR ($CDCl_3$) δ : 15.50 (q, J = 130 Hz) ; 20.93 (q, J = 127 Hz) ; 48.39 (t, J = 144 Hz) ; 65.81 (d, J = 144 Hz) ; 119.56 (st, J = 7 Hz, Ar) ; 119.56 (dd, J = 162, 8 Hz, Ar) ; 119.11, 134.21, 136.47, 158.33 (Ar) ; 132.42 (s, C-4) ; 158.39 (s, C-2) ; 168.38 (s, C-5). I.R. (cm^{-1}, nujol) = 3400 br., 3200 br., 2920, 2845, 1680, 1630, 1565, 1450. MS, *m/z* = 260.1159 found (calculated for $C_{14}H_{16}N_2O_3$: 260.1161). (Found : C, 64.7 ; H, 6.4 ; N, 10.45 ; O, 18.45. $C_{14}H_{16}N_2O_3$ requires C, 64.65 ; H, 6.2 ; N, 10.77 ; O, 18.45%).

(*) : spectral properties of **11d** are given below.

1-(2-Hydroxyethyl)-2-methyl-4-(2-methylpropylidene)-2-imidazolin-5-one (10f)
Removal of alcohols *in vacuo* gave an oily residue which was crystallized from acetonitrile (yield = 65%), mp = 138°C - ^{1}H NMR ($CDCl_3$) δ : 1.10 (d, 6H, J = 7 Hz) ; 2.35 (s, 3H) ; 3.16 (m, 1H) ; 3.70 (t, 2H, J = 5 Hz) ; 3.76 (t, 2H, J = 5 Hz) ; 4.23 (br s, 1H, OH) ; 6.29 (d, 1H, J = 10 Hz, CH=) ; ^{13}C NMR ($CDCl_3$) δ : 15.65 (q, J = 129 Hz), 22.14 (q, J = 127 Hz) ; 27.50 (d, J = 131 Hz) ; 43.35 (t, J = 139 Hz) ; 60.20 (t, J = 143 Hz) ; 138.43 (sd, J = 4 Hz, C-4) ; 141.13 (d, J = 156 Hz, CH=) ; 161.99 (s, C-2) ; 169.77 (s, C-5). I.R. (cm^{-1}, nujol) = 3200 br., 2910, 2845, 1705, 1650, 1565, 1440, 1405. MS, *m/z* = 196.1221 found (calculated for $C_{10}H_{16}N_2O_2$: 196.1212). (Found : C, 61.1 ; H, 8.3 ; N, 14.25 ; O, 16.35. $C_{10}H_{16}N_2O_2$ requires C, 61.2 ; H, 8.16 ; N, 14.28 ; O, 16.3%).

1-(2-Hydroxyethyl)-2-methyl-4-benzylidene-2-imidazolin-5-one (10g)
Purification by chromatography (eluent : methylene chloride/ethyl acetate = 1/1) provided two fractions. The first fraction gave **8a** (Rf = 0.70) and the second fraction (Rf = 0.22) gave the desired compound **10g** (yield = 85%) as a colourless viscous oil which crystallized on standing (mp = 78°C) - ^{1}H NMR ($CDCl_3$) δ : 2.27 (s, 3H) ; 3.66 (d, 2H, J = 5 Hz) ; 3.60 (d, 2H, J = 5 Hz) ; 4.08 (br. s, 1H, OH) ; 6.97 (s, 1H) ; 7.34-7.48 (m, 3H, Ar) ; 8.02-8.05 (m, 2H, Ar) ; ^{13}C NMR ($CDCl_3$) δ : 15.76 (q, J = 130 Hz) ; 43.52 (t, J = 139 Hz) ; 60.11 (t, J = 143 Hz) ; 127.63, 128.69, 132.21, 133.97 (Ar) ; 130.22 (dt, J = 161, 8 Hz, CH=) ; 138.11 (s, C-4) ; 163.52 (s, C-2) ; 170.91 (s, C-5). I.R. (cm^{-1}, nujol) = 3380 br. ; 2920 ; 2850 ; 1700 ; 1670 ; 1630 ; 1560 ; 1440 ; 1400. MS, *m/z* = 230.1020 found (calculated for $C_{13}H_{14}N_2O_2$: 230.1055). (Found : C, 67.60 ; H, 6.15 ; N, 12.1 ; O, 14.15. $C_{13}H_{14}N_2O_2$ requires C, 67.8 ; H, 6.08 ; N, 12.17 ; O, 13.9%).

1-(2-Methylpropyl)-2-methyl-4-benzylidene-2-imidazolin-5-one (6j)
A mixture of imidate **1a** (1 g - 6.3 mmol.) and imine **2j** (1.03 g - 6.3 mmol.) was heated at 70°C during 90 h under magnetic stirring. After removal of alcohols *in vacuo*, gravity column chromatography on silica gel 60 Merck (20 g) provided one fraction (Rf = 0.19), after elution with methylene chloride, which gave the desired compound **6j** (1.6 g, 76%) as a colourless viscous oil which crystallized on standing (mp = 81°C). - ^{1}H NMR ($CDCl_3$) δ : 0.93 (d, 6H, J = 6.7 Hz) ; 1.01 (m, 1H) ; 2.35 (s, 3H) ; 3.38 (d, 2H, J = 7.6 Hz) ; 1.10 (s, 1H) ; 7.34-7.42 (m, 3H, Ar) ; 8.11-8.14 (m, 2H, Ar) ; ^{13}C NMR ($CDCl_3$) δ : 15.93 (q, J = 129 Hz) ; 19.99 (qm, J = 125 Hz) ; 28.43 (dm, J = 128 Hz) ; 47.98 (tm, J = 144 Hz) ; 127.09, 128.68, 132.08, 134.23 (Ar) ; 129.99 (dt, J = 155, 8 Hz) ; 138.55 (s, C-4) ; 162.85 (s, C-2) ; 170.93 (s, C-5). I.R. (cm^{-1}, nujol) = 2920, 2825, 1690, 1630, 1440, 1390. MS, *m/z* = 242.1422 found (calculated for $C_{15}H_{18}N_2O$: 242.1419).

1-Methoxycarbonylmethyl-2-methyl-4-benzylidene-2-imidazolin-5-one (11a)
mp = 119-120°C. - ^{1}H NMR ($CDCl_3$) δ : 2.29 (s, 3H) ; 3.74 (s, 3H) ; 4.36 (s, 2H) ; 7.11 (s, 1H, CH=) ; 7.33-7.43 (m, 3H, Ar) ; 8.12-8.14 (m, 2H, Ar) ; ^{13}C NMR ($CDCl_3$) δ : 15.44 (q, J = 148 Hz) ; 40.20 (t, J = 141 Hz) ; 52.75 (q, J = 148 Hz) ; 127.98, 128.69, 132.21, 133.96 (Ar) ; 130.26 (dt, J = 161, 8 Hz) ; 138.04 (s, C-4) ; 161.46 (s, C-2) ; 168.03 (s, C=O) ; 170.00 (s, C-5). I.R. (cm^{-1}, nujol) = 2920 , 2840 , 1730 , 1705 , 1630 , 1560 , 1430. MS, *m/z* = 258.0990 found (calculated for $C_{14}H_{14}N_2O_3$: 258.1004). (Found : C, 65.1 ; H, 5.25 ; N, 10.7 ; O, 18.95. $C_{14}H_{14}N_2O_3$ requires C, 65.1 ; H, 5.4 ; N, 10.85 ; O, 18.6%).

1-Methoxycarbonylmethyl-2-methyl-4-(2-hydroxybenzylidene)-2-imidazolin-5-one (11d)
mp = 70-71°C. - ^{1}H NMR ($CDCl_3$) δ : 2.31 (s, 3H) ; 3.77 (s, 3H) ; 4.38 (s, 2H) ; 6.82-6.95 (m, 2H, Ar) ; 7.16 (s, 1H) ; 7.26-7.37 (m, 2H, Ar) ; 13.63 (br s, 1H, OH) ; ^{13}C NMR ($CDCl_3$) δ :

15.01 (q, J = 130 Hz) ; 41.29 (t, J =142 Hz) ; 52.92 (q, J = 148 Hz) ; 119.21, 119.52, 119.54, 134.34, 136.53, 156.77 (Ar) ; 130.90 (dd, J = 156, 7 Hz, CH=) ; 132.15 (s, C-4) ; 158.62 (s, C-2) ; 167.23 (s, C=O) ; 167.69 (s, C-5). I.R. (cm^{-1}, nujol) = 2920 , 2870 , 1760 , 1720 , 1650 , 1600 , 1560 , 1400 . MS, *m/z* = 274.0944 found (calculated for $C_{14}H_{14}N_2O_4$: 274.0953).

Typical procedure for the preparation of alkylated imidazolones (12)

1-(2-Methoxypropyl)-2-methyl-4-benzylidene-2-imidazolin-5-one (12a)
A mixture of imidate **1a** (1 g - 6.3 mmol.) and compound **9a** (1.11 g - 6.3 mmol.) was heated at 70°C during 165 h under magnetic stirring. After removal of alcohols *in vacuo*, the crude residue was purified by flash chromatography on silica gel 60 Merck (methylene chloride/ethyl acetate = 10/1, Rf = 0.32). Solvent evaporation gave a nearly pure oil (0.99 g, 61%) which crystallized on standing (mp = 60-61°C) - ^1H NMR ($CDCl_3$) δ : 1.16 (d, 3H, J = 6 Hz) ; 2.39 (s, 3H) ; 3.25 (s, 3H) ; 3.42 (dd, 1H, J = 14, 9 Hz) ; 3.68 (dd, 1H, J = 14, 3 Hz) ; 3.54 (m, 1H) ; 7.07 (s, 1H) ; 7.31-7.42 (m, 3H, Ar) ; 8.12-8.15 (m, 2H, Ar) ; ^{13}C NMR ($CDCl_3$) δ : 16.06 (q, J = 129 Hz) ; 16.59 (q, J = 126 Hz) ; 46.38 (t, J = 139 Hz) ; 56.68 (q, J = 141 Hz) ; 75.27 (d, J = 144 Hz) ; 126.87, 128.68, 132.13, 134.29 (Ar) ; 129.98 (dt, J = 160, 8 Hz, CH=) ; 138.62 (s, C-4) ; 163.76 (s, C-2) ; 170.86 (s, C-5). I.R. (cm^{-1}, nujol) = 2970, 2930, 2820, 1700, 1630, 1540, 1440, 1400. MS, *m/z* = 258.1355 found (calculated for $C_{15}H_{18}N_2O_2$: 258.1368). (Found : C, 69.2 ; H, 7.3 ; N, 10.95 ; O, 12.55. $C_{15}H_{18}N_2O_2$ requires C, 69.74 ; H, 7.0 ; N, 10.84 ; O, 12.38%).

1-(3-Methoxypropyl)-2-methyl-4-benzylidene-2-imidazolin-5-one (12b)
This compound was prepared according to the method described for the synthesis of **12a** with a reaction time of 160 h. Purification by chromatography on silica gel 60 Merck (ethyl acetate, Rf = 0.67) gave the desired product **12b** in 65% yield as viscous oil which crystallized on standing (mp = 160-161°C). - ^1H NMR ($CDCl_3$) δ : 1.90 (quint., 2H, J = 6 Hz) ; 2.38 (s, 3H) ; 3.32 (s, 3H) ; 3.37 (t, 2H, J = 6 Hz) ; 3.69 (t, 2H, J = 7 Hz) ; 7.08 (s, 1H) ; 7.34-7.40 (m, 3H, Ar) ; 8.11-8.14 (m, 2H, Ar) ; ^{13}C NMR ($CDCl_3$) δ : 15.52 (q, J = 129 Hz) ; 28.89 (t, J = 128 Hz) ; 37.87 (t, J =140 Hz) ; 58.60 (qt, J = 141, 3 Hz) ; 69.07 (t, J = 140 Hz) ; 127.03, 128.69, 132.09, 134.19 (Ar) ; 130.02 (dt, J = 160, 8 Hz, CH=) ; 138.60 (s, C-4) ; 162.88 (s, C-2) ; 170.85 (s, C-5). I.R. (cm^{-1}, nujol) = 2920, 2845, 1690, 1630, 1565, 1455, 1400. MS, *m/z* = 258.1331 found (calculated for $C_{15}H_{18}N_2O_2$: 258.1368). (Found : C, 69.4 ; H, 7.2 ; N, 10.75 ; O, 12.65 $C_{15}H_{18}N_2O_2$ requires C, 69.74 ; H, 7.03 ; N, 10.85 ; O, 12.39%).

Transamination reaction of imino-alcohols (2a) :
To a suspension of methyl glycinate hydrochloride (0.39 g - 3.06 mmol.) in 5 mL of dry methylene chloride, cooled to 0°C with vigorous stirring, a solution of dry triethylamine (0.38 g - 3.67 mmol.) in 5 mL of dry methylene chloride was added dropwise during 10 min.. Then, to the resulting mixture, a solution of imino-alcohol **2a** (0.5 g - 3.06 mmol.) in 5 mL of dry methylene chloride was added dropwise during 10 min. After the mixture was stirred vigorously at room temperature during 48 h (reaction time was monitored by TLC on precoated plates of silica gel 60F-254 Merck), it was washed rapidly with 5 mL of cooled water and the organic layer was dried (anhydrous $MgSO_4$), filtered and the filtrate concentrated *in vacuo* to a viscous oil (0.3 g, 56%) which was analysed by ^1H NMR. - ^1H NMR ($CDCl_3$, 80 MHz) δ 3.72 (s, 3H) ; 4.35 (s, 2H) ; 7.36 (m, 3H, Ar) ; 7.75 (m, 2H, Ar) ; 8.23 (s, 1H).

Typical procedure for microwave reaction :
A mixture of imidate **1a** (0.5 g - 3.15 mmol.) and imino-alcohols **2** (3.15 mmol.) was placed in a Pyrex tube. Then, the tube was introduced into a Maxidigest MX 350™ Prolabo microwave reactor fitted with a rotational system (2.45 GHz, adjustable power within the range 0-300 W and a wave guide (monomode T_{01})). Microwave irradiation was carried with a suitable power for an appropriate time (see Table 4). The mixture was cooled to room temperature and the crude residue was characterized by ^1H NMR and comparison with samples synthesized according to the standard procedure described for the compounds **10** and **11**.

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33 For these compounds, we could not get satisfactory analysis owing to partial hydrolysis. These compounds were used without further purification to give adducts which show satisfactory analysis.

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