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Synthesis of 4-(4-Pyridyl)oxazoles

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Abstract: Dimerization products and oxazoles have been synthesized from 4-acylaminomethyl-1-alkylpyridinium salts by heating with acetic anhydride at 100°C and 140°C respectively. One explanation is the formation of an anhydrobase as an intermediate; therefore, a new series of anhydrobase have been prepared to carry out the reaction, achieving a good synthetic procedure to obtain 4-(4-pyridyl)oxazoles.

INTRODUCTION

The 4-acylaminomethylpyridine *N*-oxides **1** show interesting behavior in their reaction with acetic anhydride. Small differences of temperature yield very different compounds. When the reaction is carried out at 100°C, acetoxylation in the methylene group takes place, and the compounds **2** are formed.[1] The acetoxy group can easily undergo nucleophilic substitution yielding **3** when there is a nucleophile in the reaction medium.[2] This reaction provides a good procedure for preparation of compounds of structure **3**. However, when the reaction is performed at 140°C the main products are the dimers **4** (Scheme 1).[3]

The experimental findings described above with the *N*-oxides, led us to study the behavior of pyridinium salts **5**. We have found that oxazoles **7** or dimeric products* **6** are formed in the reaction.

In this paper we report the results obtained. Additionally, we describe a new procedure to obtain trisubstituted oxazoles with a 4-pyridyl group in 4 position **12** from the anhydrobases **14**.

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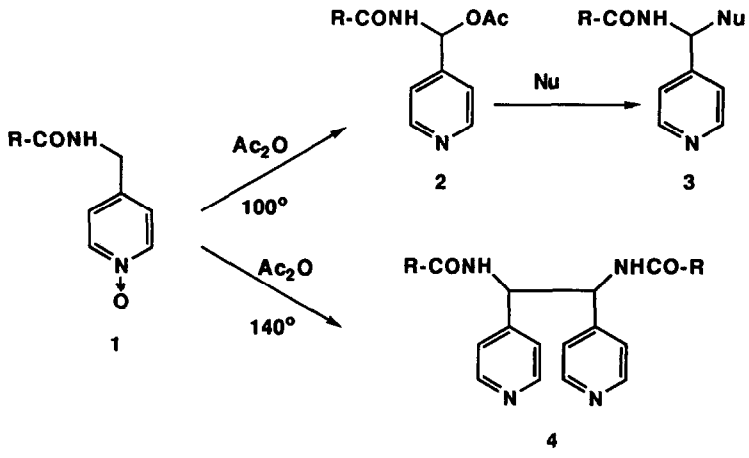
*An additional interest of the compounds obtained by this way, is their potential ganglion-blocking properties.

Scheme 1



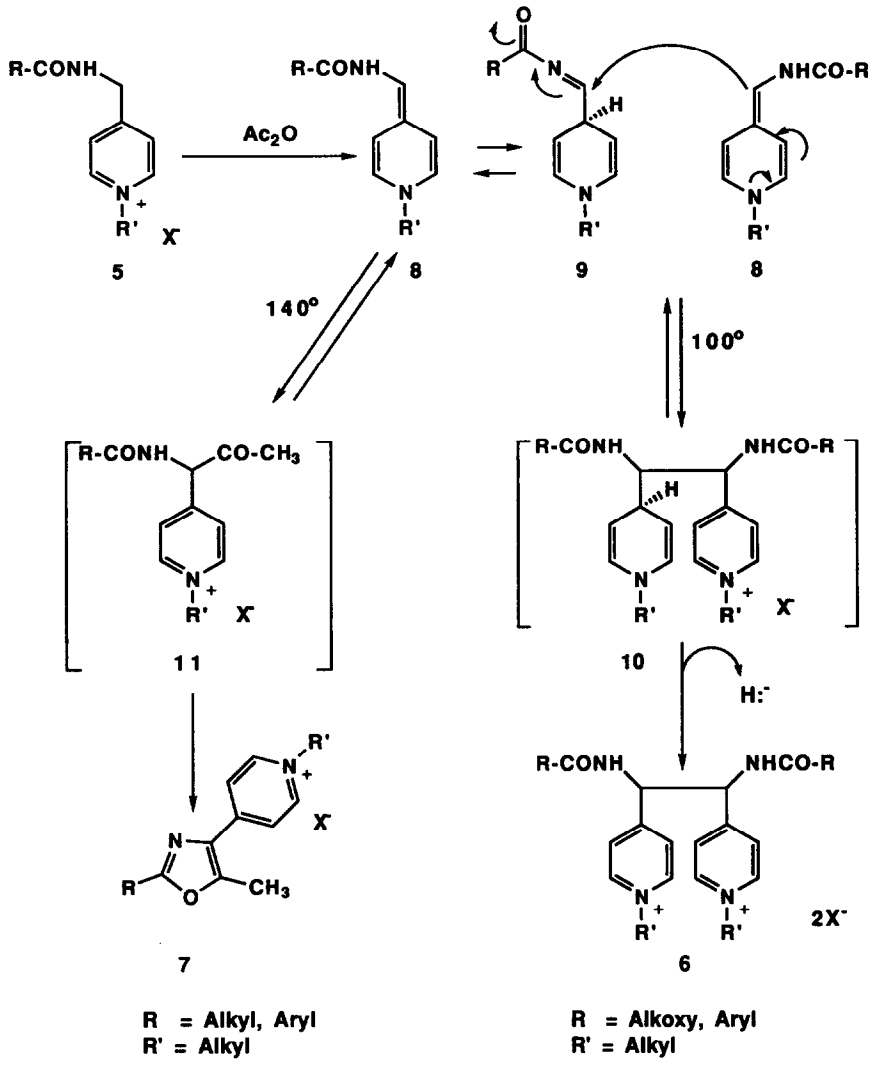
RESULTS AND DISCUSSION

Reaction of **5** with acetic anhydride at 100°C gave the dimer **6**, but oxazole **7** was the exclusive product when the reaction was performed at reflux (140°C). However, when **5** bears a carbamate instead of an acylamine group, the only compound isolated was the dimer; its formation is independent of reaction temperature. This result could be due to the strong -I effect of the alkoxy group. The structures of the dimeric products prepared are shown in Table 1.

The dimerization could be explained through a mechanism that supposes the initial formation of the anhydrobase **8**, which would be in equilibrium with the corresponding acylimine **9**. The nucleophilic attack of **8** on **9** would give the Michael type adduct **10**, which could lose a hydride ion, traped by electrophilic acetic anhydride of medium, to afford **6** (Scheme 2). The structure **6** was confirmed by unambiguous synthesis by methylation of **4** (R = OEt) to yield **6b**.

On the other hand, at higher temperatures, the anhydrobases **8** can be electrophilically attacked by the acetic anhydride to yield the α-acetyl derivative **11**, which undergoes a cyclization process usual in α-acylamides[4] to yield the corresponding oxazole **7** (Scheme 2).[5] This reaction is general, because when the propionic anhydride is used the corresponding 5-ethyloxazole **7c** is obtained. Structures of the oxazoles which have been prepared are shown in Table 2.

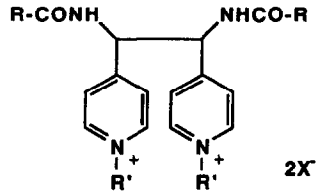
This hypothetic mechanism could explain the different behavior of pyridinium salts with temperature, because the dimerization products would be the kinetically controlled and the oxazoles the products of thermodynamic control.



Scheme 2

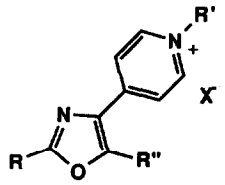
Disappointingly, all attempts to isolate and synthesize the intermediate anhydrobase **8** or acylimine **9** failed. To justify the mechanism and the intermediacy of anhydrobase **8** during the dimerization process, we decided to carry out the reaction under conditions where **8** would be formed "in situ". When we treated the pyridinium salt **5** with piperidine as base[6] in the presence of an oxidant, nitrobenzene, the dimers **6** are obtained in improved yields.

TABLE 1. *N,N'*-Diacyl-1,2-di(1-alkyl-4-pyridinium)ethylenediamine Dihalides



Compd.	R	R'	X	Method	Yield %
6a	MeO	Me	I	A	72
6b	EtO	Me	I	A	64
				B	72
6c	EtO	Et	Br	B	45
6d	EtO	*i*-Pr	Br	B	20
6e	EtO	Bu	Br	B	10
6f	EtO	Pentyl	Br	B	18
6g	EtO	Hexyl	Br	B	15
6h	EtO	Heptyl	Br	B	35
6i	EtO	Bn	Br	B	74
6j	BuO	Me	I	B	63
6k	BuO	Bu	Br	B	43
6l	*i*-BuO	Me	I	B	60
6m	2-Cl-C_6H_4	Me	I	A	52
6n	3-Cl-C_6H_4	Me	I	A	60
6o	4-Cl-C_6H_4	Me	I	A	32
6p	2-Me-C_6H_4	Me	I	A	35
6q	3,5-Me_2-C_6H_3	Me	I	A	30
6r	3,5-Me_2-C_6H_3	Bn	Cl	A	26

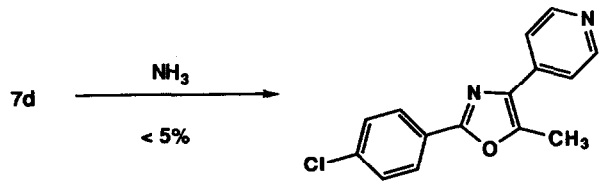
TABLE 2. 1-Alkyl-4-(2,5-disubstituted-4-oxazolyl)pyridinium Halides



Compd.	R	R'	R"	X	Yield %
7a	3-Cl-C_6H_4	Me	Me	I	42
7b	2-Cl-C_6H_4	Me	Me	I	37
7c	3-Cl-C_6H_4	Me	Et	I	69
7d	4-Cl-C_6H_4	Bn	Me	Cl	35
7e	2,4-Cl_2-C_6H_3	Me	Me	I	37
7f	2,4-Cl_2-C_6H_3	Bn	Me	Cl	19
7g	2-Me-C_6H_4	Me	Me	I	35
7h	3,5-Me_2-C_6H_3	Me	Me	I	24
7i	3,5-Me_2-C_6H_3	Bn	Me	Cl	88
7j	Me	Me	Me	I	44
7k	4-MeO-C_6H_4	Me	Me	I	34
7l	4-MeCONH-C_6H_4	Me	Me	I	11

On the other hand, we have been interested in the dequaternization of the pyridinium salts as a way to get the oxazole pyridine derivative. The dequaternization of the pyridinium salt **7d** (R = 4-Cl-C_6H_4, R' = Bn), using the van der Plas procedure[7] was tried but although **12e** was obtained the yield was very low (less than 5%) (Scheme 3).

Scheme 3

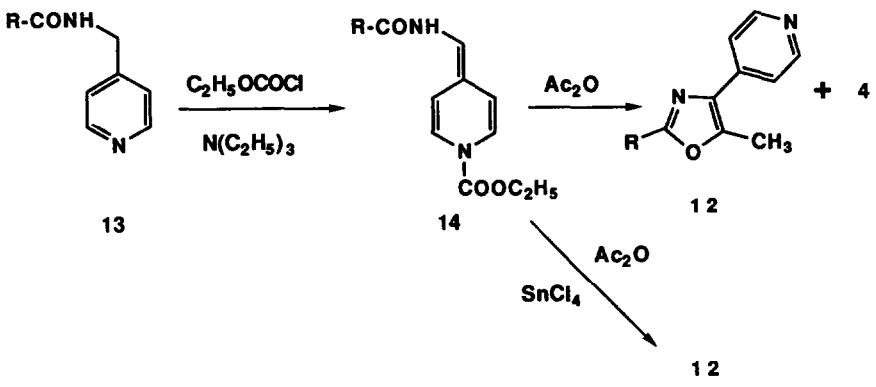


12e

Consequently, we decided to synthesize some stable anhydrobases. Andersand Will[8] have shown that anhydrobases of the *N*-benzoyl-1,4-dihydropyridine type behave as nucleophiles in the presence of carbonyl compounds.

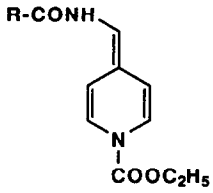
We have prepared the anhydrobases of structure **14** (see Table 3), using a carbethoxy group as better acyl leaving group. So, by reaction of the 4-acylaminomethylpyridine **13** with ethyl chloroformate in the presence of triethylamine, the anhydrobases **14** were obtained with good yields. When **14h** was refluxed with acetic anhydride the oxazole **12i**, together the corresponding dimerization product **4** (R = 3,5-Me_2-C_6H_3), were obtained in poor yields (30% and 18%, respectively). However, the yield of oxazole can be improved by carrying out the reaction in the presence of a Lewis acid ($SnCl_4$) as catalyst, to enhance the electrophilicity of the anhydride. Indeed, **12i** is the only product obtained under these conditions (Scheme 4). To find out how general the reaction is, other analogues were prepared with propionic anhydride, **12f** and **12j**, and trifluoroacetic anhydride **12k**. In all the cases, the expected oxazole was formed as listed in Table 4.

Scheme 4



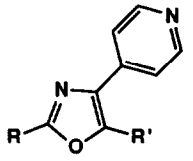
13 **14** **12** **12**

TABLE 3. *N*-(1,4-Dihydropyridylmethylene-1-ethoxycarbonyl)acylamines



Compd.	R	Yield %
14a	Me	86
14b	C_6H_5	62
14c	2-Me-C_6H_4	90
14d	2-Cl-C_6H_4	78
14e	3-Cl-C_6H_4	68
14f	4-Cl-C_6H_4	60
14g	4-NO_2-C_6H_4	62
14h	3,5-Me_2-C_6H_3	76
14i	4-MeCONH-C_6H_4	73

TABLE 4. 2,5-Disubstituted-4-(4-pyridyl)oxazoles



Compd.	R	R'	Yield %
12a	Me	Me	24
12b	C_6H_5	Me	32
12c	2-Cl-C_6H_4	Me	30
12d	3-Cl-C_6H_4	Me	38
12e	4-Cl-C_6H_4	Me	40
12f	2-Cl-C_6H_4	Et	35
12g	4-NO_2-C_6H_4	Me	30
12h	4-NH_2-C_6H_4	Me	90[a]
12i	3,5-Me_2-C_6H_3	Me	55
12j	3,5-Me_2-C_6H_3	Et	22
12k	3,5-Me_2-C_6H_3	CF_3	32
12l	4-MeCONH-C_6H_4	Me	57

([a]) Obtained by reduction of 12g

CONCLUSIONS

The reaction of 4-acylaminomethylpyridinium salts with acetic anhydride at 100°C affords dimeric compounds. In contrast, at 140°C only oxazoles by cyclization of a ketoamide intermediate, were isolated.

Recognizing an anhydrobase in both reactions as intermediate, we have studied their reaction in two ways: their formation "in situ" from 4-acylaminomethylpyridine under basic mild conditions and by synthesis

of more stable homologue. From the former, dimers are the only products obtained in improved yield, and from the latter dimers and oxazoles were formed. Oxazoles only are obtained when stannic chloride is used as catalyst.

We believe that this procedure to obtain 4-(4-pyridyl)oxazoles is a particularly important synthetic method for this kind of product.

EXPERIMENTAL

Melting points were determined on a Büchi 510 capillary melting point apparatus and are uncorrected. Infrared (IR) spectra were recorded on a Perkin-Elmer 257 spectrophotometer. ^1H and ^{13}C NMR spectra were recorded on a Varian T-60 (60 MHz) and a FT-80 (20 MHz) spectrometers respectively. Chemical shifts (δ) are reported in ppm downfield of tetramethylsilane as internal reference; coupling constants are given in Hertz. Microanalyses were performed by Centro Nacional de Química Orgánica (CSIC). Reaction progress was monitored by TLC, using silica gel as adsorbent and ethyl acetate as the eluent. 4-Acylaminomethylpyridines, and the corresponding pyridinium salts, were prepared according to literature methods[1,9].

Preparation of N,N'-diacyl-1,2-di(1-alkyl-4-pyridinium)ethylenediamine dihalides (6) General Procedures.

Method A: a solution containing 6 mmol of pyridinium salt, 7 mL of acetic anhydride, and 3 drops of pyridine, was heated at 100°C for 90 minutes. After cooling, the obtaining solid was filtered and recrystallized (**6a**, **6b**, **6m-6r**).

Method B: a solution containing 3.4 mmol of pyridinium salt, 15 mL of absolute ethanol, 4 drops of piperidine, and 4 drops of nitrobenzene, was heated at reflux for 4 hours. After cooling, the solid was filtered and purified by recrystallization (**6b-6l**).

N,N'-Di(methoxycarbonyl)-1,2-di(1-methyl-4-pyridinium)ethylenediamine diiodide (6a). This compound was prepared according to the general method **A**. Yield 72%; mp 260-262°C (methanol); ^1H NMR (d_6-DMSO) δ 3.4 (s, 6H, $2CH_3$ methoxy), 4.4 (s, 6H, $2CH_3$-N^+), 5.2-5.4 (m, 2H, 2CH), 8.1-8.3 (m, 6H, 2NH, 2H-3 and 2H-5 pyridine), 9.0 (d, J=6.0, 4H, 2H-2 and 2H-6 pyridine) ppm; IR (KBr) 3260 (NH), 1710 (C=O), 1250 and 1020 (O=C-O) cm^{-1}. Anal. Calcd for $C_{18}H_{24}I_2N_4O_4$: C, 35.19; H, 3.93; N, 9.12; I, 41.32. Found: C, 35.15; H, 3.70; N, 9.04; I, 41.33.

N,N'-Di(ethoxycarbonyl)-1,2-di(1-methyl-4-pyridinium)ethylenediamine diiodide (6b). This compound was prepared according to the general method **A**. Yield 64%; mp 257-259°C (methanol). Method **B**. Yield 72%; ^1H NMR (d_6-DMSO) δ 1.0 (t, J=7.0, 6H, $2CH_3$ ethoxy), 3.8 (q, J=7.0, 4H, $2CH_2$), 4.4 (s, 6H, $2CH_3$-N^+), 5.2-5.4 (m, 2H, 2CH), 8.1-8.3 (m, 6H, 2NH, 2H-3 and 2H-5 pyridine), 8.9 (d, J=6.0, 4H, 2H-2 and 2H-6 pyridine) ppm; IR (KBr) 3200 (NH), 1710 (C=O), 1250 and 1030 (O=C-O) cm^{-1}. Anal. Calcd for $C_{20}H_{28}I_2N_4O_4$: C, 37.40; H, 4.39; N, 8.72; I, 39.51. Found: C, 37.05; H, 4.09; N, 8n75; I, 39.33.

N,N'-Diethoxycarbonyl-1,2-di(1-ethyl-4-pyridinium)ethylenediamine dibromide (6c). This compound was prepared according to the general method **B**. Yield 45%; mp 234-236°C (methanol); ^1H NMR (d_6-DMSO) δ 0.9 (t, J=6.9, 6H, $2CH_3$ ethoxy), 1.5 (t, J=7.5, 6H, $2CH_3$ ethyl), 3.8 (q, J=6.9, 4H, $2CH_2$ ethoxy), 4.6 (q, J=7.5, 4H, $2CH_2$-N^+), 5.2-5.4 (m, 2H, 2CH), 8.2-8.4 (m, 6H, 2NH, 2H-3 and 2H-5 pyridine), 9.2 (d, J=6.0, 4H, 2H-2 and 2H-6 pyridine) ppm; IR (KBr) 3200 (NH), 1700 (C=O), 1260 and 1030 (O=C-O) cm^{-1}. Anal. Calcd for $C_{22}H_{32}Br_2N_4O_4$: C, 45.85; H, 5.56; N, 9.72; Br, 27.75. Found: C, 45.45; H, 5.54; N, 9.60; Br, 27.89.

N,N'-Di(ethoxycarbonyl)-1,2-di(1-isopropyl-4-pyridinium) ethylenediamine dibromide (6d). This compound was prepared according to the general method **B**. Yield 20%; mp 260-262°C (isopropanol); ^1H NMR (d_6-DMSO) δ 1.0 (t, J=6.9, 6H, $2CH_3$ ethoxy), 1.6 (d, J=7.5, 12H, $4CH_3$ isopropyl), 3.8 (q, J=6.9, 4H, $2CH_2$), 4.9-5.2 (m, 2H, 2CH-N^+), 5.3-5.5 (m, 2H, 2CH-N), 8.3-8.5 (m, 6H, 2NH, 2H-3 and 2H-5 pyridine), 9.3 (d, J=6.0, 4H, 2H-2 and 2H-6 pyridine) ppm; IR (KBr) 3190 (NH), 1700 (C=O), 1250 and 1035 (O=C-O) cm^{-1}. Anal. Calcd for $C_{24}H_{36}Br_2N_4O_4$: C, 47.68; H, 5.96; N, 9.27; Br, 26.49. Found: C, 47.41; H, 5.91; N, 8.92; Br, 26,40.

1,2-Di(1-butyl-4-pyridinium)-N,N'-di(ethoxycarbonyl)ethylenediamine dibromide (6e). This compound was prepared according to the general method **B**. Yield 10%; mp 236-238°C (ethanol-ether); ^1H NMR (d_6-DMSO) δ 0.7-1.5 (m, 16H, $2CH_3$ butyl, $2CH_3$ ethoxy and $2CH_2$ butyl), 1.8-2.1 (m, 4H, $2CH_2$ butyl), 3.8 (q, J=6.9, 4H, $2CH_2$ ethoxy), 4.6 (t, J=7.0, 4H, $2CH_2$-N^+), 5.2-5.5 (m, 2H, 2CH), 8.3-8.5 (m, 6H, 2NH, 2H-3 and 2H-5 pyridine), 9.3 (d, J=6.0, 4H, 2H-2 and 2H-6 pyridine) ppm; IR (KBr) 3220 (NH), 1710 (C=O), 1260 and 1030 (O=C-O) cm^{-1}. Anal. Calcd for $C_{26}H_{40}Br_2N_4O_4$: C, 49.38; H, 6.33; N, 8.86; Br, 25.29. Found: C, 49.07; H, 6.45; N, 8.58; Br, 25.57.

N,N'-Di(ethoxycarbonyl)-1,2-di(1-pentyl-4-pyridinium)ethylenediamine dibromide (6f). This compound was prepared according to the general method **B**. Yield18%; mp 249-251°C (ethanol-ether); ^1H NMR (d_6-DMSO) δ 0.7-1.4 (m, 20H, $4CH_3$ and $4CH_2$ pentyl), 1.8-2.1 (m, 4H, $2CH_2$ pentyl), 3.8 (q, J=6.9, 4H, $2CH_2$ ethoxy), 4.6 (t, J=7.0, 4H, $2CH_2$-N^+), 5.2-5.4 (m, 2H, 2CH), 8.2-8.4 (m, 6H, 2NH, 2H-3 and 2H-5 pyridine), 9.2 (d, J=6.0, 4H, 2H-2 and 2H-6 pyridine) ppm; IR(KBr) 3200 (NH), 1695 (C=O), 1250 and 1030 (O=C-O) cm^{-1}. Anal. Calcd for $C_{28}H_{44}Br_2N_4O_4$: C, 50.92; H, 6.67; N, 8.49; Br, 24.22. Found: C, 51.31; H, 6.86; N, 8.19; Br, 23.93.

N,N'-Di(ethoxycarbonyl)-1,2-di(1-hexyl-4-pyridinium)ethylenediamine dibromide (6g). This compound was prepared according to the general method **B**. Yield 15%; mp 239-241°C (ethanol-ether); ^1H NMR (d_6-DMSO) δ 0.7-1.4 (m, 24H, $4CH_3$ and

$6CH_2$ hexyl), 1.7-2.1 (m, 4H, $2CH_2$ hexyl), 3.8 (q, J=6.9, 4H, $2CH_2$ ethoxy), 4.6 (t, J=7.0, 4H, $2CH_2$-N^+), 5.3-5.5 (m, 2H, 2CH), 8.3-8.5 (m, 6H, 2NH, 2H-3 and 2H-5 pyridine), 9.3 (d, J=6.0, 4H, 2H-2 and 2H-6 pyridine) ppm; IR (KBr) 3210 (NH), 1700 (C=O), 1260 and 1030 (O=C-O) cm^{-1}. Anal. Calcd for $C_{30}H_{48}Br_2N_4O_4$: C, 52.34; H, 6.98; N, 8.14; Br, 23.23. Found: C, 52.10; H, 7.10; N, 7.88; Br, 23.16.

N,N'-Di(ethoxycarbonyl)-1,2-di(1-heptyl-4-pyridinium)ethylenediamine dibromide (6h). This compound was prepared according to the general method **B**. Yield 35%; mp 246-248°C (ethanol-ether); ^1H NMR (d_6-DMSO) δ 0.6-1.5 (m, 28H, $4CH_3$ and $8CH_2$ heptyl), 1.7- 2.2 (m, 4H, $2CH_2$ heptyl), 3.8 (q, J=6.9, 4H, $2CH_2$ ethoxy), 4.7 (t, J=7.0, 4H, $2CH_2$-N^+), 5.3-5.5 (m, 2H, 2CH), 8.4-8.6 (m, 6H, 2NH, 2H-3 and 2H-5 pyridine), 9.3 (d, J=6.0, 4H, 2H-2 and 2H-6 pyridine) ppm; IR (KBr) 3200 (NH), 1710 (C=O), 1260 and 1030 (O=C-O) cm^{-1}. Anal. Calcd for $C_{32}H_{52}Br_2N_4O_4$: C, 53.64; H, 7.26; N, 7.82; Br, 22.18. Found: C, 53.68; H, 7.47; N, 7.79; Br, 22.18.

1,2-Di(1-benzyl-4-pyridinium)-N,N'-di(ethoxycarbonyl)ethylenediamine dibromide (6i). This compound was prepared according to the general method **B**. Yield 74%; mp 274-276°C (ethanol); ^1H NMR (d_6-DMSO) δ 0.9 (t, J=6.9, 6H, $2CH_3$), 3.6 (q, J=6.9, 4H, $2CH_2$ ethoxy), 5.2-5.4 (m, 2H, 2CH), 5.9 (s, 4H, $2CH_2$-N^+), 7.3-7.6 (m, 10H, 2Ph), 8.5-8.6 (m, 6H, 2NH, 2H-3 and 2H-5 pyridine), 9.4 (d, J=6.0, 4H, 2H-2 and 2H-6 pyridine) ppm; IR (KBr) 3210 (NH), 1700 (C=O), 1260 and 1030 (O=C-O) cm^{-1}. Anal. Calcd for $C_{32}H_{36}Br_2N_4O_4$: C, 54.89; H, 5.14; N, 7.99; Br, 22.82. Found: C, 54.59; H, 5.12; N, 7.71; Br, 22.90.

N,N'-Di(butoxycarbonyl)-1,2-di(1-methyl-4-pyridinium)ethylenediamine diiodide (6j). This compound was prepared according to the general method **B**. Yield 63%; mp 209-211°C (methanol-ether); ^1H NMR (d_6-DMSO) δ 0.8 (t, J=6.9, 6H, $2CH_3$ butoxy), 1.1-1.6 (m, 8H, $4CH_2$ butoxy), 3.8 (t, J=6.9, 4H, $2CH_2$ butoxy), 4.4 (s, 6H, $2CH_3$-N^+), 5.2-5.4 (m, 2H, 2CH), 7.9-8.1 (m, 2H, 2NH), 8.2 (d, J=6.0, 4H, 2H-3 and 2H-5 pyridine), 9.2 (d, J=6.0, 4H, 2H-2 and 2H-6 pyridine) ppm; IR (KBr) 3220 (NH), 1710 (C=O), 1255 and 1025 (O=C-O) cm^{-1}. Anal. Calcd for $C_{24}H_{36}I_2N_4O_4$: C, 41.27; H, 5.16; N, 8.02; I, 36.37. Found: C, 40.96; H, 5.26; N, 7.86; I, 36.21.

N,N'-Di(butoxycarbonyl)-1,2-Di(1-butyl-4-pyridinium)ethylenediamine dibromide (6k). This compound was prepared according to the general method **B**. Yield 43%; mp 206-208°C (methanol-ether); ^1H NMR (d_6-DMSO) δ 0.7-1.6 (m, 24H, $4CH_3$, $4CH_2$ butoxy and $2CH_2$ butyl), 1.7-2.2 (m, 4H, $2CH_2$ butyl), 3.8 (t, J=6.9, 4H, $2CH_2$ butoxy), 4.7 (t, J=6.6, 4H, $2CH_2$-N^+), 5.3-5.5 (m, 2H, 2CH), 8.1-8.3 (m, 2H, 2NH), 8.5 (d, J=6.0, 4H, 2H-3 and 2H-5 pyridine), 9.3 (d, J=6.0, 4H, 2H-2 and 2H-6 pyridine) ppm; IR (KBr) 3250 (NH), 1695 (C=O), 1250 and 1030 (O=C-O) cm^{-1}. Anal. Calcd for $C_{30}H_{48}Br_2N_4O_4$: C, 52.34; H, 6.98; N, 8.14; Br, 23.23. Found: C, 52.06; H, 7.18; N, 7.98; Br, 23.04.

N,N'-Di(isobutoxycarbonyl)-1,2-di(1-methyl-4-pyridinium)ethylenediamine diiodide (6l). This compound was prepared according to the general method **B**. Yield 60%; mp 237-239°C (methanol-ether); ^1H NMR (d_6-DMSO) δ 0.9 (d, J=6.9, 12H, $4CH_3$ isobutoxy), 1.1-1.9 (m, 2H, 2CH isobutoxy), 3.7 (d, J=6.9, 4H, $2CH_2$), 4.5 (s, 6H, $2CH_3$-N^+), 5.3-5.5 (m, 2H, 2CH-N), 8.2-8.4 (m, 6H, 2NH, 2H-3 and 2H-5 pyridine), 9.3 (d, J=6.0, 4H, 2H-2 and 2H-6 pyridine) ppm; IR (KBr) 3220 (NH), 1710 (C=O), 1250 and 1025 (O=C-O) cm^{-1}. Anal. Calcd for $C_{24}H_{36}I_2N_4O_4$: C, 41.27; H, 5.16; N, 8.02; I, 36.37. Found: C, 40.95; H, 5.43; N, 7.69; I, 36.16.

N,N'-Di(2-chlorobenzoyl)-1,2-di(1-methyl-4-pyridinium)ethylenediamine diiodide (6m). This compound was prepared according to the general method **A**. Yield 52%; mp 251-253°C (water); ^1H NMR (d_6-DMSO) δ 4.4 (s, 6H, $2CH_3$-N^+), 5.8-6.0 (m, 2H, 2CH), 7.3 (s, 8H, 2Ph), 8.2 (d, J=6.0, 4H, 2H-3 and 2H-5 pyridine), 8.9 (d, J=6.0, 4H, 2H-2 and 2H-6 pyridine), 9.1-9.3 (m, 2H, 2NH) ppm; IR (KBr) 3180 (NH), 1665 (C=O) cm^{-1}. Anal. Calcd for $C_{28}H_{26}Cl_2I_2N_4O_2$: C, 43.38; H, 3.38; N, 7.22. Found: C, 43.34; H, 3.36; N, 7.23.

N,N'-Di(3-chlorobenzoyl)-1,2-di(1-methyl-4-pyridinium)ethylenediamine diiodide (6n). This compound was prepared according to the general method **A**. Yield 60%; mp 279-281°C (ethanol); ^1H NMR (d_6-DMSO) δ 4.1 (s, 6H, $2CH_3$-N^+), 5.8-6.0 (m, 2H, 2CH), 7.3-7.5 (m, 8H, 2Ph), 8.0 (d, J=6.0, 4H, 2H-3 and 2H-5 pyridine), 8.7 (d, J=6.0, 4H, 2H-2 and 2H-6 pyridine), 8.9-9.1 (m, 2H, 2NH) ppm; IR (KBr) 3220 (NH), 1660 (C=O) cm^{-1}. Anal. Calcd for $C_{28}H_{26}Cl_2I_2N_4O_2$: C, 43.38; H, 3.38; N, 7.22. Found: C, 43.33; H, 3.35; N, 7.22.

N,N'-Di(4-chlorobenzoyl)-1,2-di(1-methyl-4-pyridinium)ethylenediamine diiodide (6o). This compound was prepared according to the general method **A**. Yield 32%; mp 282-284°C (water); ^1H NMR (d_6-DMSO) δ 4.2 (s, 6H, $2CH_3$-N^+), 5.8-6.0 (m, 2H, 2CH), 7.3-7.5 (m, 8H, 2Ph), 8.1 (d, J=6.0, 4H, 2H-3 and 2H-5 pyridine), 8.8 (d, J=6.0, 4H, 2H-2 and 2H-6 pyridine), 9.0-9.2 (m, 2H, 2NH) ppm; IR (KBr) 3220 (NH), 1670 (C=O) cm^{-1}. Anal. Calcd for $C_{28}H_{26}Cl_2I_2N_4O_2$: C, 43.38; H, 3.38; N, 7.22. Found: C, 43.35; H, 3.35; N, 7.22.

N,N'-Di(2-methylbenzoyl)-1,2-di(1-methyl-4-pyridinium)ethylenediamine diiodide (6p). This compound was prepared according to the general method **A**. Yield 35%; mp 289-291°C (water);^1H NMR (TFA) δ 2.2 (s, 6H, $2CH_3$ phenyl), 4.5 (s, 6H, $2CH_3$-N^+), 6.9 (s, 2H, 2CH), 7.1-7.5 (m, 8H, 2Ph), 8.8-9.0 (m, 8H, 2pyridine) ppm; IR (KBr) 3160 (NH), 1670 (C=O) cm^{-1}. Anal. Calcd for $C_{30}H_{32}I_2N_4O_2$: C, 48.92; H, 4.65; N, 7.60; I, 34.59. Found: C, 48.95; H, 4.54; N, 7.54; I, 34.61.

N,N'-Di(3,5-dimethylbenzoyl)-1,2-di(1-methyl-4-pyridinium)ethylenediamine diiodide (6q). This compound was prepared according to the general method **A**. Yield 30%; mp 269-271°C (water);^1H NMR (TFA) δ 2.3 (s, 12H, $4CH_3$ Ph), 4.5 (s, 6H, $2CH_3$-N^+), 7.1 (s, 2H, 2CH), 7.3 (s, 2H, 2H-4 Ph), 7.4 (s, 4H, 2H-2 and 2H-6 Ph) 8.7-8.9 (m, 8H, 2pyridine) ppm; IR (KBr) 3240 (NH), 1650 (C=O) cm^{-1}. Anal. Calcd for $C_{32}H_{36}I_2N_4O_2$: C, 50.40; H, 4.75; N, 7.34; I, 33.31. Found: C, 50.12; H, 4.70; N, 7.03; I, 33.40.

1,2-Di(1-benzyl-4-pyridinium)-N,N'-di(3,5-dimethylbenzoyl)ethylenediamine dichloride (6r). This compound was prepared according to the general method **A**. Yield 26%; mp 258-260°C (water); ^1H NMR (TFA) δ 2.3 (s, 12H, $4CH_3$), 5.6 (s, 4H, $2CH_2$), 6.5-6.7(m, 2H, 2CH), 7.1-7.4 (m, 16H, 4Ph), 8.5-8.7 (m, 10H, 8H pyridine and 2NH) ppm; IR (KBr) 3230(NH), 1640(C=O) cm^{-1}. Anal. Calcd for $C_{44}H_{44}Cl_2N_4O_2$: C, 72.24; H, 6.02; N, 7.66. Found: C, 72.28; H, 6.05; N, 7.67.

Preparation of 1-alkyl-4-(2,5-disubstituted-4-oxazolyl)piridinium halides (7). General procedure. A solution containing 10 mmol of 4-acylaminomethylpyridinium halide, 25 mL of the corresponding anhydride, and 1 mL of pyridine was heated at reflux conditions for 3 hours. After cooling the reaction mixture, the obtained solid was filtered and purified by recrystallization.

4-(2-(3-Chlorophenyl)-5-methyl-4-oxazolyl)-1-methylpyridinium iodide (7a). This compound was prepared according to the general procedure. Yield 42%; mp 239-241°C (ethanol); ^{1}H NMR (d_6-DMSO) δ 2.8 (s, 3H, CH_3 oxazole), 4.3 (s, 3H, CH_3-N^+), 7.4-7.6 (m, 2H, H-4 and H-5 Ph), 7.6-7.8 (m, 2H, H-2 and H-6 Ph), 8.1 (d, J=6.0, 2H, H-3 and H-5 pyridine), 8.8 (d, J=6.0, 2H, H-2 and H-6 pyridine) ppm; IR (KBr) 1640 (C=N pyridine), 1610 (C=N oxazole), 1470 (C=C-C=N) cm^{-1}. Anal. Calcd for $C_{16}H_{14}ClIN_2O$: C, 46.56; H, 3.42; N, 6.79. Found: C, 46.39; H, 3.31; N, 6.93.

4-(2-(2-Chlorophenyl)-5-methyl-4-oxazolyl)-1-methylpyridinium iodide (7b). This compound was prepared according to the general procedure. Yield 37%; mp 252-254°C (water); ^{1}H NMR (d_6-DMSO) δ 2.8 (s, 3H, CH_3 oxazole), 4.3 (s, 3H, CH_3-N^+), 7.3-7.5 (m, 3H, H-3, H-4 and H-6 Ph), 7.7-7.9 (m, 1H, H-5 Ph), 8.2 (d, J=6.0, 2H, H-3 and H-5 pyridine), 8.8 (d, J=6.0, 2H, H-2 and H-6 pyridine) ppm; IR (KBr) 1640 (C=N pyridine), 1610 (C=N oxazole), 1470 (C=C-C=N) cm^{-1}. Anal. Calcd for $C_{16}H_{14}ClIN_2O$: C, 46.56; H, 3.42; N, 6.79. Found: C, 46.52; H, 3.37; N, 6.98.

4-(2-(3-Chlorophenyl)-5-ethyl-4-oxazolyl)-1-methylpyridinium iodide (7c). This compound was prepared according to the general procedure. Yield 69%; mp 245-247°C (water); ^{1}H NMR (d_6-DMSO) δ 1.3 (t, J=7.0, 3H, CH_3 ethyl), 3.2 (q, J=7.0, 2H, CH_2 ethyl), 4.2 (s, 3H, CH_3-N^+), 7.3-7.5 (m, 2H, H-3 and H-5 Ph), 7.6-7.8 (m, 2H, H-2 and H-6 Ph), 8.1 (d, J=6.0, 2H, H-3 and H-5 pyridine), 8.7 (d, J=6.0, 2H, H-2 and H-6 pyridine) ppm; IR (KBr) 1640 (C=N pyridine), 1610 (C=N oxazole), 1460 (C=C-C=N) cm^{-1}. Anal. Calcd for $C_{17}H_{16}ClIN_2O$: C, 47.85; H, 3.78; N, 6.56. Found: C, 47.58; H, 3.73; N, 6.81.

1-Benzyl-4-(2-(4-chlorophenyl)-5-methyl-4-oxazolyl)pyridinium chloride (7d) . This compound was prepared according to the general procedure. Yield 35%; mp 113-115°C (water); ^{1}H NMR (TFA) δ 2.9 (s, 3H, CH_3), 5.8 (s, 2H, CH_2-N^+), 7.3-8.1 (m, 11H, 5H benzyl, 4H Ph, H-3 and H-5 pyridine), 8.8 (d, J=5.0, 2H, H-2 and H-6 pyridine) ppm; IR (KBr) 1640 (C=N pyridine), 1610 (C=N oxazole), 1470 (C=C-C=N) cm^{-1}. Anal. Calcd for $C_{22}H_{18}Cl_2N_2O$: C, 66.50; H, 4.53; N, 7.05; Cl, 17.88. Found: C, 66.30; H, 4.35; N, 7.19; Cl, 17.99.

4-(2-(2,4-Dichlorophenyl)-5-methyl-4-oxazolyl)-1-methylpyridinium iodide (7e). This compound was prepared according to the general procedure. Yield 37%; mp 264-266°C (water); ^{1}H NMR (TFA) δ 2.5 (s, 3H, CH_3 oxazole), 4.1 (s, 3H, CH_3-N^+), 7.1-7.3 (m, 2H, H-3 and H-5 Ph), 7.6-7.8 (m, 1H, H-6 Ph), 8.0 (d, J=6.0, 2H, H-3 and H-5 pyridine), 8.5 (d, J=6.0, 2H, H-2 and H-6 pyridine) ppm; IR (KBr) 1640 (C=N pyridine), 1620 (C=N oxazole), 1470 (C=C-C=N) cm^{-1}. Anal. Calcd for $C_{16}H_{13}Cl_2IN_2O$: C, 42.90; H, 2.91; N, 6.26. Found: C, 42.99; H, 2.88; N, 6.05.

1-Benzyl-4-(2-(2,4-dichlorophenyl)-5-methyl-4-oxazolyl)pyridinium chloride (7f). This compound was prepared according to the general procedure. Yield 19%; mp 190-192°C (water); ^{1}H NMR (TFA) δ 3.0 (s, 3H, CH_3 oxazole), 5.9 (s, 2H, CH_2-N^+), 7.4-7.6 (m, 7H, 5H benzyl, H-3 and H-5 Ph), 8.0-8.2 (m, 1H, H-6 Ph), 8.5 (d, J=6.0, 2H, H-3 and H-5 pyridine), 8.8 (d, J=6.0, 2H, H-2 and H-6 pyridine) ppm; IR (KBr) 1640(C=N pyridine), 1610(C=N oxazole), 1470(C=C-C=N) cm^{-1}. Anal. Calcd for $C_{22}H_{17}Cl_3N_2O$: C, 61.20; H, 3.94; N, 6.49. Found: C, 61.30; H, 4.01; N, 6.53.

4-(5-Methyl-2-(2-methylphenyl)-4-oxazolyl)-1-methylpyridinium iodide (7g). This compound was prepared according to the general procedure. Yield 35%; mp 232-234°C (water); ^{1}H MNR (TFA) ? 2.8 (s, 3H, CH_3 Ph), 3.1 (s, 3H, CH_3 oxazole), 4.7 (s, 3H, CH_3-N^+), 7.5-7.7 (m, 3H, H-3, H-4 and H-5 Ph), 8.1-8.3 (m, 1H, H-6 Ph), 8.7 (d, J=6.0, 2H, H-3 and H-5 pyridine), 9.0 (d, J=6.0, 2H, H-2 and H-6 pyridine) ppm; IR (KBr) 1640 (C=N pyridine), 1610 (C=N oxazole), 1470 (C=C-C=N) cm^{-1}. Anal. Calcd for $C_{17}H_{17}IN_2O$: C, 52.05; H, 4.36; N, 7.14; I, 32.35. Found: C, 51.89; H, 4.34; N, 7.20; I, 32.44.

4-(2-(3,5-Dimethylphenyl)-5-methyl-4-oxazolyl)-1-methylpyridinium iodide (7h). This compound was prepared according to the general procedure. Yield 24%; mp 261-263°C (water); ^{1}H NMR (TFA) δ 2.4 (s, 6H, $2CH_3$ Ph), 2.8 (s, 3H, CH_3 oxazole), 4.4 (s, 3H, CH_3-N^+), 7.5 (s, 1H, H-4 Ph), 7.7 (s, 2H, H-2 and H-6 Ph), 8.3 (d, J=6.0, 2H, H-3 and H-5 pyridine), 8.7 (d, J=6.0, 2H, H-2 and H-6 pyridine) ppm; IR (KBr) 1640 (C=N pyridine), 1620 (C=N oxazole), 1470 (C=C-C=N) cm^{-1}. Anal. Calcd for $C_{18}H_{19}IN_2O$: C, 53.21; H, 4.71; N, 6.89; I, 31.23. Found: C, 53.31; H, 4.78; N, 6.95; I, 31.38.

1-Benzyl-4-(2-(3,5-dimethylphenyl)-5-methyl-4-oxazolyl)pyridinium chloride (7i). This compound was prepared according to the general procedure. Yield 88%; mp 203-205°C (water); ^{1}H NMR (TFA) δ 2.4 (s, 6H, $2CH_3$ Ph), 2.9 (s, 3H, CH_3 oxazole), 5.8 (s, 2H, CH_2-N^+), 7.5 (s, 6H, 5H benzyl and H-4 Ph), 7.9 (s, 2H, H-2 and H-6 Ph), 8.4 (d, J=6.0, 2H, H-3 and H-5 pyridine), 8.9 (d, J=6.0, 2H, H-2 and H-6 pyridine) ppm; IR (KBr) 1640 (C=N pyridine), 1620 (C=N oxazole), 1470 (C=C-C=N) cm^{-1}. Anal. Calcd for $C_{24}H_{23}ClN_2O$: C, 73.76; H, 5.89; N, 7.17. Found: C, 73.79; H, 5.80; N, 7.10.

4-(2,5-Dimethyl-4-oxazolyl)-1-methylpyridinium iodide (7j). This compound was prepared according to the general procedure. Yield 44%; mp 169-171°C (ethanol-ether); ^{1}H NMR (TFA) δ 2.9 (s, 3H, CH_3-5 oxazole), 3.0 (s, 3H, CH_3-2 oxazole), 4.5 (s, 3H, CH_3-N^+), 8.4 (d, J=6.0, 2H, H-3 and H-5 pyridine), 8.9 (d, J=6.0, 2H, H-2 and H-6 pyridine) ppm; IR (KBr) 1640 (C=N pyridine), 1620 (C=N oxazole), 1470 (C=C-C=N) cm^{-1}. Anal. Calcd for $C_{11}H_{13}IN_2O$: C, 41.77; H, 4.14; N, 8.86. Found: C, 41.76; H, 4.21; N, 8.57.

4-(2-(4-Methoxyphenyl)-5-methyl-4-oxazolyl)-1-methylpyridinium iodide (7k). This compound was prepared according to the general procedure. Yield 34%; mp 283-285°C (water); ^{1}H NMR (TFA) δ 3.0 (s, 3H, CH_3 oxazole), 4.1 (s, 3H, CH_3 methoxy), 4.6 (s, 3H, CH_3-N^+), 7.3-7.5 (m, 2H, H-3 and H-5 Ph), 8.5-8.7 (m, 4H, H-2 and H-6 Ph, H-3 and H-5 pyridine), 9.2 (d, J=6.0, 2H, H-2 and H-6 pyridine) ppm; IR (KBr) 1640 (C=N), 1620 (C=N oxazole), 1470 (C=C-C=N) cm^{-1}. Anal. Calcd for $C_{17}H_{17}IN_2O_2$: C, 50.01; H, 4.19; N, 6.86; I, 31.08. Found: C, 50.03; H, 4.25; N, 6.70; I, 31.21.

4-(2-(4-Acetamidophenyl)-5-methyl-4-oxazolyl)-1-methylpyridinium iodide (7l). This compound was prepared according to the general procedure. Yield 11%. mp 300°C (methanol); ^{1}H NMR (d_6-DMSO) δ 2.0 (s, 3H, CH_3), 2.7 (s, 3H, CH_3-oxazole), 4.3

(s, 3H, CH_3), 7.8 (q, 4H,Ph), 8.4 (d, 2H, H-3 and H-5 pyridine), 8.8 (d, 2H, H-2 and H-6 pyridine) ppm; IR (KBr) cm^{-1}. Anal. Calcd for $C_{18}H_{18}IN_3O_2$: C,49.67; H, 4.16; N,9.65. Found: C,49.46; H, 4.22; N, 9.67.

Preparation of N-(1,4-Dihydropyridylmethylene-1-ethoxycarbonyl)acylamine (14). General procedure. A solution of 4.74 mL (50 mmol) of ethyl chloroformiate in 50 mL of dry acetone was added dropwise with magnetic stirring, to a mixture of 50 mmol of the corresponding 4-acylaminomethylpyridine and 10.3 g of triethylamine in 200 mL of dry acetone at -10°C. The suspension was stirred at -10°C for 1 hour, then the mixture was allowed to warm to room temperature. The solid was filtered, and washed with acetone until colourless. The solvent was evaporated to dryness, and the remaining residue was purified by recrystallization.

N-(1,4-Dihydropyridylmethylen-1-ethoxycarbonyl)acetamide (14a). This compound was prepared according to the general procedure. Yield 86%; mp 130-132°C (toluene); ^1H NMR ($CDCl_3$) δ 1.2 (t, J=6.2, 3H, CH_3 ethoxy), 2.4 (s, 3H, CH_3CO), 4.0 (q, J=6.2, 2H, CH_2), 5.2-5.6 (m, 2H, 2CH dihydropyridine), 6.0 (d, J=9.2, 1H, CH=), 6.1-6.5 (m, 2H, 2CH dihydropyridine), 8.3 (d, J=9.2, 1H, NH) ppm; IR (KBr) 3270(NH), 1720 (C=O ester), 1660 (C=O amide), 1610 (C=C) cm^{-1}. Anal. Calcd for $C_{11}H_{14}N_2O_3$: C, 59.46; H, 6.31; N, 12.61. Found: C, 59.31; H, 5.83; N, 12.70.

N-(1,4-Dihydropyridylmethylen-1-ethoxycarbonyl)benzamide (14b). This compound was prepared according to the general procedure. Yield 62%; mp 88-90°C (benzene); ^1H NMR ($CDCl_3$) δ 1.3 (t, J=6.1, 3H, CH_3 ethoxy), 4.1 (q, J=6.0, 2H, CH_2), 5.2-5.7 (m, 2H, 2CH dihy-dropyridine), 6.1 (d, J=9.1, 1H, CH=), 6.4-6.7 (m, 2H, 2CH dihydropyridine), 6.9-7.5 (m, 5H, Ph), 8.5 (d, J=9.1, 1H, NH) ppm; IR (KBr) 3290(NH), 1710 (C=O ester), 1680 (C=O amide), 1620 (C=C) cm^{-1}. Anal. Calcd for $C_{16}H_{16}N_2O_3$: C, 67.60; H, 5.63; N, 9.56. Found: C, 67.69; H, 5.53; N, 9.50.

N-(1,4-Dihydropyridylmethylen-1-ethoxycarbonyl)-2-methylbenzamide (14c). This compound was prepared according to the general procedure. Yield 90%; mp 118-120°C (toluene); ^1H NMR ($CDCl_3$) δ 1.3 (t, J=6.5, 3H, CH_3 ethoxy), 2.3 (s, 3H, CH_3), 4.2 (q, J=6.5, 2H, CH_2), 5.4-5.8 (m, 2H, 2CH dihydropyridine), 6.2 (d, J=9.6, 1H, CH=), 6.5-6.8 (m, 2H 2CH dihydropyridine), 6.9-7.3 (m, 4H, Ph), 7.6 (d, J=9.6, 1H, NH) ppm; IR (KBr) 3350 (NH), 1710 (C=O ester), 1680 (C=O amide), 1610 (C=C) cm^{-1}. Anal. Calcd for $C_{17}H_{18}N_2O_3$: C, 68.45; H, 6.04; N, 9.40. Found: C, 68.50; H, 5.95; N, 9.30.

2-Chloro-N-(1,4-dihydropyridylmethylen-1-ethoxycarbonyl)benzamide (14d). This compound was prepared according to the general procedure. Yield 78%; mp 154-156°C (toluene); ^1H NMR ($CDCl_3$) δ 1.3 (t, J=6.0, 3H, CH_3), 4.2 (q, J=6.0, 2H, CH_2), 5.4-5.8 (m, 2H, 2CH dihydropyridine), 6.2 (d, J=9.6, 1H, CH=), 6.5-6.9 (m, 2H, 2CH dihydropyridine), 7.0-7.6 (m, 4H, Ph), 8.2 (d, J=9.6, 1H, NH) ppm; IR (KBr) 3280 (NH), 1720 (C=O ester), 1680 (C=O amide), 1610 (C=C) cm^{-1}. Anal. Calcd for $C_{16}H_{15}ClN_2O_3$: C, 60.28; H, 4.71; Cl, 11.15; N, 8.79. Found: C, 60.31; H, 4.83; Cl, 11.20; N, 8.68.

3-Chloro-N-(1,4-dihydropyridylmethylen-1-ethoxycarbonyl)benzamide (14e). This compound was prepared according to the general procedure. Yield 68%; mp 104-106°C (toluene); ^1H NMR ($CDCl_3$) δ 1.3 (t, J=6.0, 3H, CH_3), 4.2 (q, J=6.0, 2H, CH_2), 5.6 (d, J=9.0, 1H, CH=), 5.9-6.4 (m, 2H, 2CH dihydropyridine), 6.5-6.9 (m, 2H, 2CH dihydropyridine), 7.1-7.8 (m, 4H, Ph), 8.7 (d, J=9.6, 1H, NH) ppm; IR (KBr) 3260(NH), 1720 (C=O ester), 1680 (C=O amide), 1620 (C=C) cm^{-1}. Anal. Calcd for $C_{16}H_{15}ClN_2O_3$: C, 60.28; H, 4.71; Cl, 11.15; N, 8.79. Found: C, 60.25; H, 4.63; Cl, 11.22; N, 8.85.

4-Chloro-N-(1,4-dihydropyridylmethylen-1-ethoxycarbonyl)benzamide (14f). This compound was prepared according to the general procedure. Yield 60%; mp 127-129°C (toluene); ^1H NMR ($CDCl_3$) δ 1.3 (t, J=6.1, 3H, CH_3), 4.3 (q, J=6.1, 2H, CH_2), 5.5-5.9 (m, 2H, 2CH dihydropyridine), 6.3 (d, J=9.5 1H, CH=), 6.6-7.0 (m, 2H, 2CH dihydropyridine), 7.1-8.1 (m, 5H, 4HPh, NH) ppm; IR (KBr) 3300(NH), 1710 (C=O ester), 1670 (C=O amide), 1630 (C=C) cm^{-1}. Anal. Calcd for $C_{16}H_{15}ClN_2O_3$: C, 60.28; H, 4.71; Cl, 11.15; N, 8.79. Found: C, 60.30; H, 4.63; Cl, 11.10; N, 8.78.

N-(1,4-Dihydropyridylmethylen-1-ethoxycarbonyl)-4-nitrobenzamide (14g). This compound was prepared according to the general procedure. Yield 62%; mp 132-134°C (toluene); ^1H NMR ($CDCl_3$) δ 1.3 (t, J=6.4, 3H, CH_3), 4.2 (q, J=6.4, 2H, CH_2), 5.4-8.5 (m, 10H, 4CH dihydropyridine, CH=, 4HPh, NH) ppm; IR (KBr) 3300 (NH), 1720 (C=O ester), 1670 (C=O amide), 1630 (C=C) cm^{-1}. Anal. Calcd for $C_{16}H_{15}N_3O_5$: C, 58.30; H, 4.55; N, 12.76. Found: C, 58.40; H, 4.62; N, 12.65.

N-(1,4-Dihydropyridylmethylen-1-ethoxycarbonyl)-3,5-dimethylbenzamide (14h). This compound was prepared according to the general procedure. Yield 76%; mp 167-169°C (ethyl acetate); ^1H NMR ($CDCl_3$) δ 1.3 (t, J=6.5, 3H, CH_3 ethoxy), 2.2 (s, 6H, $2CH_3$ Ph), 4.1 (q, J=6.5, 2H, CH_2 ethoxy), 5.6 (d, J=9.5, 1H, CH=), 6.1-6.3 (m, 2H, 2CH dihydropyridine), 6.4-6.8 (m, 2H, 2CH dihydropyridine), 6.9 (s, 1H, H-4 Ph), 7.3 (s, 2H, H-2 and H-6 Ph), 9.4 (d, J=9.5, 1H, NH) ppm; IR (KBr) 3260(NH), 1720 (C=O esther), 1630 (C=O amide), 1610 (C=C) cm^{-1}. Anal. Calcd for $C_{18}H_{20}N_2O_3$: C, 69.15; H, 6.40; N, 8.96. Found: C, 69.21; H, 6.31; N, 9.04.

4-Acetamido-N-(1,4-dihydropyridylmethylen-1-ethoxycarbonyl)benzamide (14i). This compound was prepared according to the general procedure. Yield 73%; mp 217-218°C (ethyl acetate); ^1H NMR ($CDCl_3$) δ 1.3 (t, J=7.0, 3H, CH_3 ethoxy), 4.2 (q, J=7.0, 2H, CH_2), 5.8 (d, J=7.0, 1H, CH=), 6.4 (m, 2H, 2CH dihydropyridine), 7.7 (d, J=8, 2H, Ph), 7.8 (d, J=8, 2H, Ph), 9.6 (d,1H, NH), 10.2 (d,1H, NH) ppm; IR (KBr) 3290 (NH), 1700 (C=O ester), 1640 (C=O amide), 1600 (C=C) cm^{-1}. Anal. Calcd for $C_{18}H_{19}N_3O_4$: C, 63.33; H, 5.61; N, 12.30. Found: C, 62.89; H, 5.56; N,12.22.

Preparation of 4-(4-pyridyl)oxazoles (12). General procedure. A solution composed of 15 mmol of 4-acylaminomethylen-*N*-ethoxycarbonyl-1,4-dihydropyridine and 0.5 mL of $SnCl_4$, in 50 mL of the anhydride was heated at reflux for 4 hour. The solvent was evaporated to dryness, and the resulting oil was washed with a 5% sodium bicarbonate solution and purified by flash chromatography, using ethyl acetate as eluent. Further purification can be accomplished by recrystallization of the obtained solid.

2,5-Dimethyl-4-(4-pyridyl)oxazole (12a). This compound was prepared according to the general procedure. Yield 24%; mp 54-56°C (water); ^{1}H NMR ($CDCl_3$) δ 2.5 (s, 3H, CH_3), 2.6 (s, 3H, CH_3), 7.5 (d, J=6.5, 2H, H-3 and H-5 pyridine), 8.6 (d, J=6.5, 2H, H-2 and H-6 pyridine) ppm; ^{13}C NMR ($CDCl_3$) δ 11.77 (CH_3), 13.39 (CH_3), 120.23 (C-3 and C-5 pyri-dine), 131.79 (C-4 oxazole), 139.66 (C-5 oxazole), 145.79 (C-4 pyridine), 149.69 (C-2 and C-6 pyridine), 159.36 (C-2 oxazole) ppm; IR (KBr) 1620 (C=N pyridine), 1610 (C=N oxazole) cm^{-1}. Anal. Calcd for $C_{10}H_{10}N_2O$: C, 68.95; H, 5.78; N, 16.08. Found: C, 68.86; H, 5.81; N, 16.18.

5-Methyl-2-phenyl-4-(4-pyridyl)oxazole (12b). This compound was prepared according to the general procedure. Yield 32%; mp 110-112°C (methanol-water); ^{1}H NMR ($CDCl_3$) δ 2.5 (s, 3H, CH_3), 7.2-7.6 (m, 5H, H-3 and H-5 pyridine, 3H Ph), 7.8-8.1 (m, 2H, Ph), 8.5 (d, J=5.0, 2H, H-2 and H-6 pyridine) ppm; ^{13}C NMR ($CDCl_3$) δ 11.83 (CH_3), 120.21 (C-3 and C-5 pyridine), 125.73 (C-4 oxazole), 126.66, 128.29, 129.86, 133.08 (Ph), 139.37 (C-5 oxazole), 146.01 (C-4 pyridine), 149.60 (C-2 and C-6 pyridine), 159.23 (C-2 oxazole) ppm; IR (KBr) 1620(C=N pyridine), 1610(C=N oxazole) cm^{-1}. Anal. Calcd for $C_{15}H_{12}N_2O$: C, 76.27; H, 5.08; N, 11.86. Found: C, 76.10; H, 5.19; N, 11.59.

2-(2-Chlorophenyl)-5-methyl-4-(4-pyridyl)oxazole (12c). This compound was prepared according to the general procedure. Yield, 30%; mp 108-110°C (methanol-water); ^{1}H NMR (TFA) δ 2.9 (s, 3H, CH_3), 7.6-8.0 (m, 4H, Ph), 8.3 (d, J=5.7, 2H, H-3 and H-5 pyridine), 8.8 (d, J=5.7, 2H, H-2 and H-6 pyridine) ppm; ^{13}C NMR (TFA) δ 12.11 (CH_3), 120.50 (C-3 and C-5 pyridine), 125.80 (C-4 oxazole), 126.57, 130.54, 130.82, 130.92, 132.25, 133.32 (Ph), 139.42 (C-5 oxazole), 146.75 (C-4 pyridine), 149.89 (C-2 and C-6 pyridine), 157.55 (C-2 oxazole) ppm; IR (KBr) 1620 (C=N pyridine), 1610 (C=N oxazole) cm^{-1}. Anal. Calcd for $C_{15}H_{11}ClN_2O$: C, 66.54; H, 4.06; Cl, 13.12; N, 10.35. Found: C, 66.49; H, 4.20; Cl, 13.10; N, 10.15.

2-(3-Chlorophenyl)-5-methyl-4-(4-pyridyl)oxazole (12d). This compound was prepared according to the general procedure. Yield, 38%; mp 124-126°C (methanol-water); ^{1}H NMR ($CDCl_3$) δ 2.6 (s, 3H, CH_3), 7.2-8.1 (m, 6H, H-3 and H-5 pyridine, 4HPh), 8.6 (d, J=5.5, 2H, H-2 and H-6 pyridine) ppm; ^{13}C NMR ($CDCl_3$) δ 12.07 (CH_3), 120.38 (C-3 and C-5 pyridine), 125.91 (C-4 oxazole), 123.94, 128.41, 129.81, 130.00, 133.53, 134.57 (Ph), 139.31 (C-5 oxazole), 146.66 (C-4 pyridine), 149.79 (C-2 and C-6 pyridine), 158.11 (C-2 oxazole) ppm; IR (KBr) 1615 (C=N pyridine), 1605 (C=N oxazole) cm^{-1}. Anal. Calcd for $C_{15}H_{11}ClN_2O$: C, 66.54; H, 4.06; Cl, 13.12; N, 10.35. Found: C, 66.23; H, 4.30; Cl, 13.10; N, 10.55.

2-(4-Chlorophenyl)-5-methyl-4-(4-pyridyl)oxazole (12e). This compound was prepared according to the general procedure. Yield, 40%; mp 173-175°C (methanol); ^{1}H NMR ($CDCl_3$) δ 2.9 (s, 3H, CH_3), 7.6-7.8 (m, 4H, H-3 and H-5 pyridine, H-3 and H-5 Ph), 8.2 (d, J=7.5, 2H, H-2 and H-6 Ph), 8.8 (d, J=5.0, 2H, H-2 and H-6 pyridine) ppm; ^{13}C NMR ($CDCl_3$) δ 12.14 (CH_3), 120.57 (C-3 and C-5 pyridine), 125.38 (C-4 oxazole), 127.29, 128.87, 133.54, 136.28 (Ph), 139.73 (C-5 oxazole), 146.60 (C-4 pyridine), 149.63 (C-2 and C-6 pyridine), 158.71 (C-2 oxazole) ppm; IR (KBr) 1620 (C=N pyridine), 1605 (C=N oxazole) cm^{-1}. Anal. Calcd for $C_{15}H_{11}ClN_2O$: C, 66.54; H, 4.06; Cl, 13.12; N, 10.35. Found: C, 66.10; H, 3.98; Cl, 13.25; N, 10.16.

2-(2-Chlorophenyl)-5-ethyl-4-(4-pyridyl)oxazole (12f). This compound was prepared according to the general procedure. Yield, 35%; mp 234-236°C (acetic acid); ^{1}H NMR (TFA) δ 1.3 (t, J=6.8, 3H, CH_3), 3.2 (q, J=6.8, 2H, CH_2), 7.2-8.2 (m, 6H, H-3 and H-5 pyridine, 4HPh), 8.8 (d, J=5.0, 2H, H-2 and H-6 pyridine) ppm; IR (KBr) 1625 (C=N pyridine), 1610 (C=N oxazole) cm^{-1}. Anal. Calcd for $C_{16}H_{13}ClN_2O$: C, 67.49; H, 4.57; Cl, 12.48; N, 9.84. Found: C, 67.51; H, 4.30; Cl, 12.50; N, 9.90.

5-Methyl-2-(4-nitrophenyl)-4-(4-pyridyl)oxazole (12g). This compound was prepared according to the general procedure. Yield, 30%; mp 168-170°C (cyclohexane); ^{1}H NMR ($CDCl_3$) δ 2.7 (s, 3H, CH_3), 7.5 (d, J=6.0, 2H, H-3 and H-5 pyridine), 7.9-8.3 (m, 4H, Ph), 8.5 (d, J=6.0, 2H, H-2 and H-6 pyridine) ppm; IR (KBr) 1620 (C=N pyridine), 1610 (C=N oxazole) cm^{-1}. Anal. Calcd for $C_{15}H_{11}N_3O_3$: C, 64.05; H, 3.94; N, 14.93. Found: C, 63.96; H, 4.03; N, 14.83.

2-(4-Aminophenyl)-5-methyl-4-(4-pyridyl)oxazole (12h). This compound was prepared by reduction of **12g** with hydrazine hydrate (80%) in the presence of palladium on charcoal (10%). Yield, 90%; mp 194-196°C (methanol-water); ^{1}H NMR (d_6-DMSO) δ 2.6 (s, 3H, CH_3), 6.6 (d, J=7.9, 2H, H-3 and H-5 Ph), 7.5-7.7 (m, 4H, H-2 and H-6 Ph, H-3 and H-5 pyridine), 8.4 (d, J=5.2, 2H, H-2 and H-6 pyridine) ppm; IR (KBr) 3380 and 3320(NH_2), 1620 (C=N pyridine), 1610 (C=N oxazole) cm^{-1}. Anal. Calcd for $C_{15}H_{13}N_3O$: C, 71.62; H, 5.17; N, 16.72. Found: C, 71.59; H, 5.26; N, 16.80.

2-(3,5-Dimethylphenyl)-5-methyl-4-(4-pyridyl)oxazole (12i). Yield 55%; mp 156-158°C (cyclohexane); ^{1}H NMR ($CDCl_3$) δ 2.2 (s, 6H, $2CH_3$), 2.5 (s, 3H, CH_3), 6.8 (s, 1H, H-4 Ph), 7.4 (d, J=5.0, 2H, H-3 and H-5 pyridine), 7.7 (s, 2H, H-2 and H-6 Ph), 8.4 (d, J=5.0, 2H, H-2 and H-6 pyridine) ppm; ^{13}C NMR ($CDCl_3$) δ 11.99 (CH_3), 20.94 ($2CH_3$ Ph), 120.48 (C-3 and C-5 pyridine), 126.77 (C-4 oxazole), 123.76, 135.85, 133.23, 138.11 (Ph), 139.76 (C-5 oxazole), 145.95 (C-4 pyridine), 149.70 (C-2 and C-6 pyridine), 159.90 (C-2 oxazole) ppm; IR (KBr) 1620 (C=N pyridine), 1610 (C=N oxazole) cm^{-1}. Anal. Calcd for $C_{17}H_{16}N_2O$: C, 77.24; H, 6.10; N, 10.59. Found: C, 77.34; H, 6.16; N, 10.69.

2-(3,5-Dimethylphenyl)-5-ethyl-4-(4-pyridyl)oxazole (12j). This compound was prepared according to the general procedure. Yield 22%; mp 110-112°C (acetone-water); ^{1}H NMR ($CDCl_3$) δ 1.4 (t, J=8.0, 3H, CH_3 ethyl), 2.2 (s, 6H, $2CH_3$ Ph), 2.9 (q, J=8.0, 2H, CH_2 ethyl), 6.8 (s, 1H, H-4 Ph), 7.3-7.6 (m, 4H, H-3 and H-5 pyridine, H-2 and H-6 Ph), 8.4 (d, J=6.0, 2H, H-2 and H-6 pyridine) ppm; IR (KBr) 1620 (C=N pyridine), 1610 (C=N oxazole) cm^{-1}. Anal. Calcd for $C_{18}H_{18}N_2O$: C, 77.70; H, 6.52; N, 10.07. Found: C, 77.60; H, 6.56; N, 10.17.

2-(3,5-Dimethylphenyl)-4-(4-pyridyl)-5-trifluormethyloxazole (12k). This compound was prepared according to the general procedure. Yield 32%; mp 108-110°C (ethanol-water); ^{1}H NMR ($CDCl_3$) δ 2.4 (s, 6H, $2CH_3$), 7.1 (s, 1H, H-4 Ph), 7.3-7.6 (m, 4H, H-3 and H-5 pyridine, H-2 and H-6 Ph), 8.5 (d, J=6.0, 2H, H-2 and H-6 pyridine) ppm; IR (KBr) 1620 (C=N pyridine), 1610 (C=N oxazole) cm^{-1}. Anal. Calcd for $C_{17}H_{13}F_3N_2O$: C, 63.55; H, 4.07; N, 8.71; Found: C, 63.65; H, 4.16; N, 8.68.

2-(4-Acetamidophenyl)-5-methyl-4-(4-pyridyl)oxazole (12l). This compound was prepared according to the general procedure. Yield 57%; mp 211-213°C (methanol-water); ^{1}H NMR ($CDCl_3$) δ 2.2 (s, 3H, CH_3-CO), 2.7 (s, 3H, CH_3-5 oxazole), 7.5-7.7 (m,

4H, Ph), 7.9-8.1 (m, 2H, H-3 and H-5 pyridine), 8.5-8.7 (m, 2H, H-2 and H-6 pyridine) ppm; IR (KBr) 1650(C=O), 1620(C=N pyridine), 1610(C=N oxazole) cm^{-1}. Anal. Calcd for $C_{17}H_{15}N_3O_2$: C, 69.61; H, 5.15; N, 14.32. Found: C, 70.00; H, 5.01; N, 14.66.

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