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ALUMINA SUPPORTED POTASSIUM FLUORIDE PROMOTED REACTION OF NITROALKANES WITH ELECTROPHILIC ALKENES : SYNTHESIS OF 4,5-DIHYDRO FURANS AND ISOXAZOLINE N-OXIDES.

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Abstract - The reaction of secondary nitro alkanes **1** with α,β-unsaturated ketones **2** in the presence of alumina-supported potassium fluoride in acetonitrile gave 4,5-dihydrofurans **3** in high yields ; 1-nitropropane reacted with **2** to give a mixture of 4,5-dihydrofurans and furans. Nitroalkenes **17** reacted with nitroalkanes to give isoxazoline N-oxides **18** and **19** in good overall yields.

It has been reported that nitronate anions undergo Michael reaction with α,β-unsaturated α-cyano esters and α,β-unsaturated α-cyano nitriles to afford cyclopropanes [1-4]. We have shown that alumina supported potassium fluoride [5] is a good catalyst to carry out the Michael reaction and the preparation of cyclopropanes [6].

As part of our continuing program to study anionic activation by alumina-supported potassium fluoride [6-9], we have explored the reaction of nitroalkanes **1** with α,β-unsaturated ketones **2** and α,β-unsaturated nitro compounds **17**.

It is well known that alumina supported potassium fluoride promoted Michael reactions of nitroalkanes with α,β-unsaturated carbonyl compounds to give γ-nitro carbonyl compounds [10]. However, reaction of nitro alkanes **1** with very electrophilic alkenes **2** or **17** had not been reported yet.

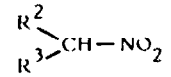
I - Reaction of nitroalkanes 1a-c with ketones 2

The reaction of the ketones **2a-j** with the nitroalkanes **1a-c** in the presence of alumina supported potassium fluoride in acetonitrile did not give cyclopropane **7**, as previously described for the reaction of **1** with α,β-unsaturated esters as **2m**, but 4,5-dihydrofurans **3a-l**, **4** and **5a**, **f**, **h**, in good yields (table 1). Alumina or potassium fluoride used alone were ineffective to promote this reaction.

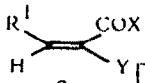
The structures of dihydrofurans **3**, **4** and **5** were established by ^{1}H and ^{13}C NMR spectroscopy. The proton H-4 of **3a** appeared as a quartet at 3.96 ppm, the coupling constant with Me-2 is 1.5 Hz. Two isomers **5A** and **5B** are obtained.

The Me-5 of isomers **5aA** and **5bA**, in cis position with the phenyl group, is more shielded than in the isomers B.

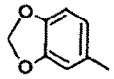
When the extent of the reaction of nitroalkanes with **2** at room temperature or at 80°C was monitored by ^{1}H NMR spectroscopy, we did not detect any cyclopropane **7** during early stages of the dihydrofuran forming reaction. If the reaction of **1a** with **2a** is allowed to proceed at room temperature, the corresponding Michael adduct **8** [11], mixed with a small amount of dihydrofuran **3a** are observed by ^{1}H NMR spectroscopy. In boiling acetonitrile, the Michael adduct **8** was not observed. It should be converted into **3a**. Although very fast isomerization of cyclopropane keto esters to dihydrofurans in the reaction system is conceivable [11,14], it seems more likely that dihydrofuran are obtained directly, without preliminary formation of cyclopropane (scheme I).

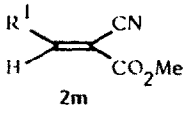


1	R^2	R^3
a	Me	Me
b	Me	Et
c	Et	Et
d	Et	H

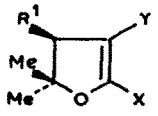


2

2	R^1	X	Y
a	Ph	Me	COMe
b	Ph	Me	CO_2Me
c	i.Pr	Me	COMe
d	Ph	Me	COPh
e	Ph	Ph	COPh
f	Ph	Ph	CO_2Et
g	4.Cl-C_6H_4	Me	CO_2Et
h		Me	COMe
i	Ph	Ph	SO_2Ph
j		Me	$SO_2C_6H_4$-Me.4
k	Ph	Ph	CN

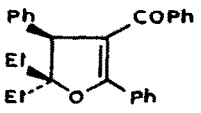


2m

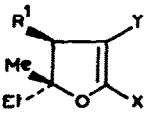


3a-k

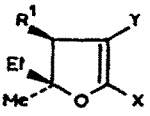
3l, R^1 = X = Ph, Y = COMe



4

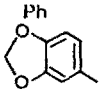


5A (a, f, h)



5B (a, f, h)

Table 1 - 4,5-dihydrofurans prepared.

Educts	Product	R^1	X	Y	Time (h)	Yield % [a]
2a + 1a	3a	Ph	Me	COMe	13	88
2b + 1a	3b	Ph	Me	CO_2Me	13	91
2c + 1a	3c	i.Pr	Me	COMe	11	45
2d + 1a	3d	Ph	Me	COPh	13	98 [b]
	3l	Ph	Ph	COMe		
2e + 1a	3e	Ph	Ph	COPh	12	80
2f + 1a	3f	Ph	Ph	CO_2Et	15	95
2g + 1a	3g	4.Cl-C_6H_4	Me	CO_2Et	13	93
2h + 1a	3h		Me	COMe	13	92
2i + 1a	3i	Ph	Ph	SO_2Ph	15	91
2j + 1a	3j		Me	$SO_2C_6H_4$ Me-4	15	73
2e + 1c	4	Ph	Ph	COPh	13	50
2a + 1b	5a	Ph	Me	COMe	12	90 [c]
2f + 1b	5f	Ph	Ph	CO_2Et	13	98 [d]
2h + 1b	5h		Me	COMe	13	77 [d]

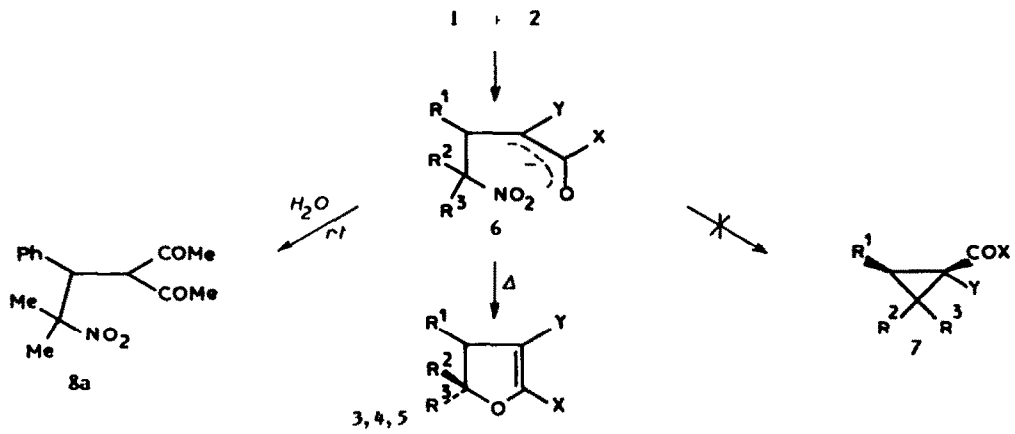
a Yield of isolated pure product after distillation or recrystallization.

b Mixture of 3d + 3l (50 : 50).

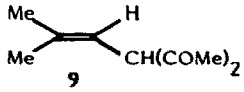
c Two isomers 5A (50 %) + 5B (50 %).

d Two isomers 5A (70 %) + 5B (30 %).

Scheme I

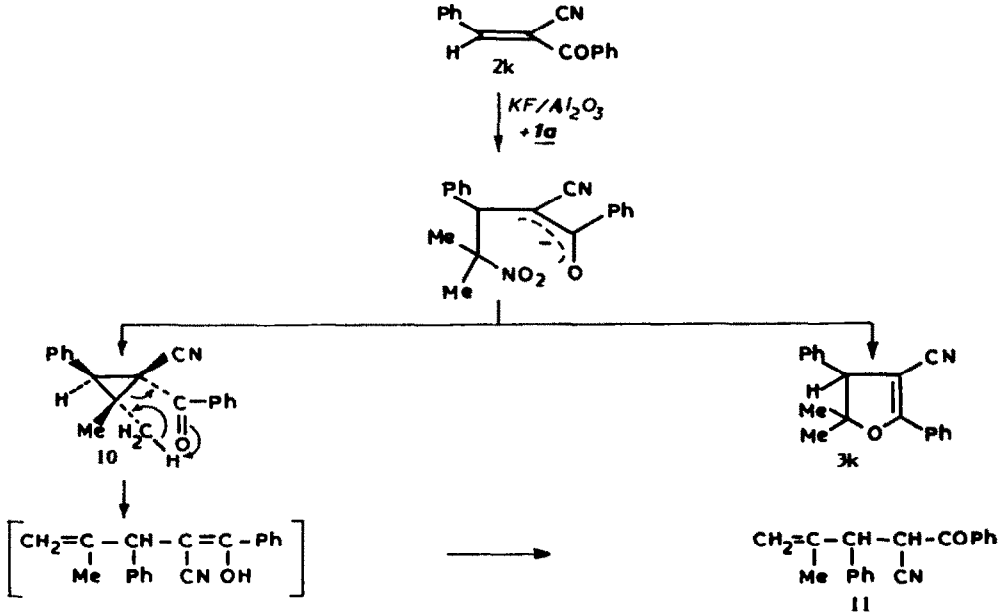


Alkene **2c** was slowly isomerized into **9** upon standing at room temperature [23]. So, the corresponding dihydrofuran **3c** was obtained in 45% yield.



Alkene **2d** reacted with 2-nitropropane **1a** to give a 50:50 mixture of dihydrofurans **3d** and **3l**. These two isomers were not separable by distillation or chromatography. Fractional crystallization of this mixture gave pure **3d**.

The reaction of 2-benzoylcinnamonitrile **2k** with **1a** is more complex. Analysis of the crude mixture along the reaction time by ^{1}H NMR spectroscopy showed that three products were formed : the dihydrofuran **3k**, the cyclopropane **10** and the pentenitrile **11** (scheme II), the product ratios varying during the progress of the reaction (table 2). After 13 h at 80°C, the cyclopropane **10** has disappeared. When a mixture of **3k**, **10** and **11** in acetonitrile with stirred at 80°C, without alumina-potassium fluoride, **10** was converted into **11**. Presumably, the formation of **11** is analogous to the thermal rearrangement of methyl cis-2-alkyl cyclopropane carboxylate into γ,δ-unsaturated ester through a 1,5 hydrogen shift [15] (scheme II). The pentenenitrile **11** was obtained in 42 % yield from the crude reaction mixture by distillation followed by fractionnal crystallization.



Scheme II

Table 2 - Reaction of **1a** with **2k** at 80°C : products mixture [a]

Time, h	3k %	10 %	11 %
2	13	70	17
4	15	37	48
6	16	33	51
10[b]	16	13	71
17[b]	16	6	78

a Products ratios determined by ^{1}H NMR.

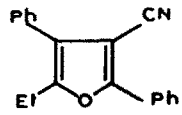
b The starting material **2k** has disappeared.

II - Reaction of 1-nitropropane 1d with ketones 2

The reaction of 1-nitropropane **1d** with **2a** gave a mixture of dihydrofuran **12** (30 %) and furan **13** (60 %). The ratio **12/13** (1:2) is independent of the reaction conditions, particularly of the reaction time. Furan **13** does not result from the oxidation of dihydrofuran **12** by an excess of 1-nitropropane : indeed, addition of an excess of 1-nitropropane or sodium nitrite to the reaction mixture did not change the ration **12/13**. Consequently, **12** and **13** were formed by two independent pathways (scheme III).

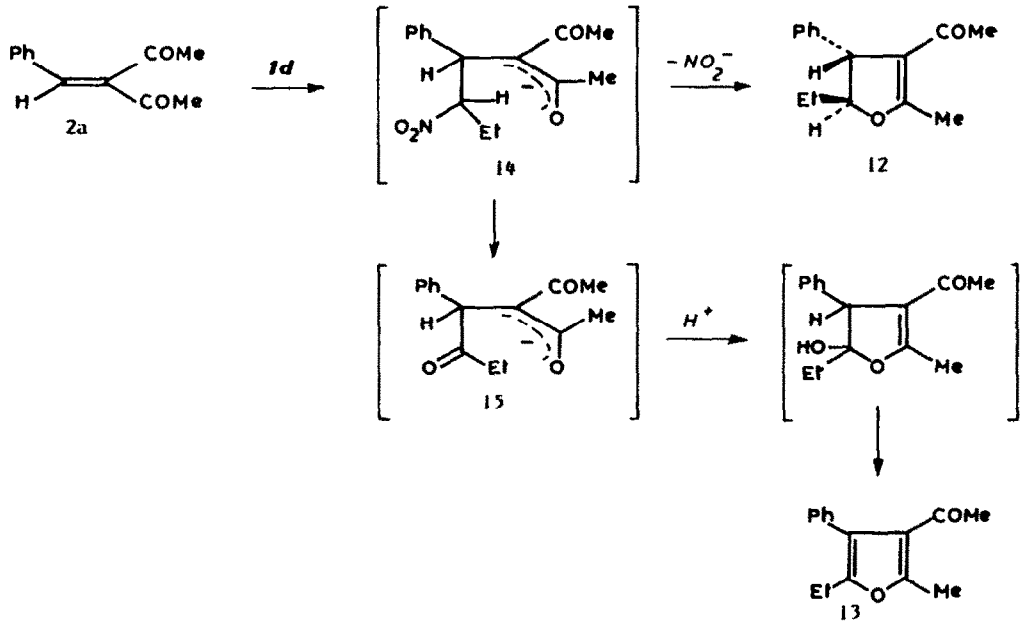
The first step of the reaction is the formation of the Michael adduct **14**. Moreover, it is known that secondary nitro compounds can be converted into ketones by nitrous oxide and nitrite esters [16]. Nitrite esters and nitrous oxide, as by products, in the reaction mixture, could cause the conversion of **14** to **15**, which is the precursor of **13**. The formation of dihydrofurans and furans from nitroalkenes and ketoesters has previously been reported [17,18,19]. A mechanism involving the Nef reaction (formation of **15**) has been also postulated to explain the formation of furan [17].

Reaction of 2-benzoyl cinnamonitrile **2k** with **1d** yielded the 3-cyanofuran **16** in good yield.



16

Scheme III



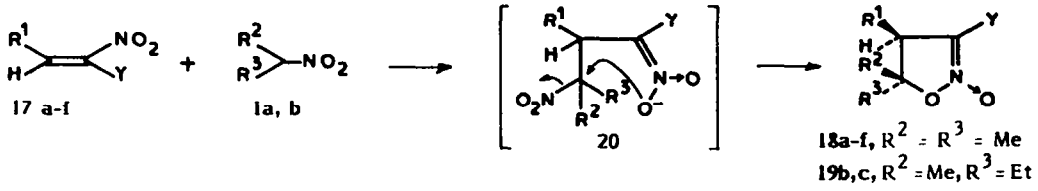
Syntheses of dihydrofuran rings have been the focus of a large number of studies. One of the most common procedure is the coupling reactions of olefins with β-ketoesters or β-diketones in the presence of thallic (III) acetate [20], mercuric acetate [21], manganese (III) acetate [22-25], cupric halide [26] or lead (IV) oxide [27]. The acid catalyzed ring closure of α-acyl α,β-unsaturated ketones into dihydrofurans has been reported [28]. Dihydrofurans have been prepared by the reaction of 3-diazo 2,4-pentadione or alkyl-2 diazo oxobutyrates with alkylvinylether [29-30] and by the reaction of sodium formate with cyclopropyltriphenyl phosphonium tetrafluoroborate [31]. Dihydrofurans were also generated, although most of all in minor amounts next to other compounds, by the acid catalyzed rearrangement of 1,1-diacylcyclopropanes [32], thermolysis of diacetylpyrazolines [33], electrochemical oxidative addition of acetylacetonate to olefins [34]. Recently, the reaction of S-ethenylsulfoximines with acetylacetone [35] and the addition of Grignard reagents on 2-diphenyl methylsilylbutanolides [36] are original ways giving dihydrofurans. The synthetic route to dihydrofurans described here is unprecedented.

III - Reaction of nitro alkanes with unsaturated nitro compounds 17

Reaction of nitroacetonitrile with gem-bromonitroolefins has been reported ; 3-cyano 5-nitro isoxazoline N-oxides were obtained in moderate yields [37].

Nitroalkanes **1a** and **1b** reacted with nitroolefins **17a-f** in acetonitrile, in the presence of potassium fluoride-alumina. Isoxazoline N-oxides **18a-f** and **19b, c** were obtained in moderate to good yields (table 3). The reaction was complete within few hours, but yields were lowered by the tendency of nitroalkenes **17** to undergo base catalyzed polymerization. The mechanism involves the elimination of nitrite ion by the oxygen atom of the nitronate ion. The reaction of nitroketone (**17f**) with **1a** gave only the isoxazoline N-oxide **18f** : the oxygen atom of the keto group does not participate to the elimination of the nitrite ion.

Scheme IV



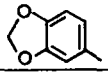
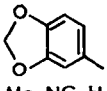
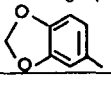
	a	b	c	d	e	f
Y	CO_2Me	CO_2Me	CO_2Me	CO_2Me	CO_2Me	COPh
R^1	Ph	4.MeO-C_6H_4		4.Me_2N.C_6H_4		Ph

Table 3 - Isoxazoline N-oxides **18** and **19** prepared.

Educts	Product	R^1	Y	Yield % [a]
17a + 1a	**18a**	Ph	CO_2Me	63
17b + 1a	**18b**	4.$MeOC_6H_4$	CO_2Me	74
17c + 1a	**18c**		CO_2Me	66
17d + 1a	**18d**	4.$Me_2NC_6H_4$	CO_2Me	60
17e + 1a	**18e**		CO_2Me	42
17f + 1a	**18f**	Ph	COPh	61
17b + 1b	**19b**	4.$MeOC_6H_4$	CO_2Me	55 [b]
17c + 1b	**19c**		CO_2Me	55 [b]

a Yield of pure product. b Two diastereoisomers **19A** (R^1 and 4-Me in cis position) and **19B**.

Discussion

The orientation of the reaction of electrophilic alkenes with nitroalkanes is subject to the nature of the electron withdrawing substituants of the alkene. The cyclization of the Michael adducts **6** and **20** is a charge controlled reaction [38], which proceed with the carbon center when the starting alkene is a cyano ester (**2**, X = OMe, Y = CN) to give the cyclopropane **7** [6]. This cyclization proceeds with the oxygen center of the keto group of **2** to give the dihydrofurans **3** or with the oxygen center of the nitro group of **17** to give the isoxazoline N-oxides **18** and **19**. However, other pathway as electron transfer is likely.

In summary, the reactions described here are convenient and simple methods for the synthesis of 4,5-dihydrofurans and isoxazoline N-oxydes from nitroalkanes and electrophilic alkenes in solid-liquid media.

Experimental section

Proton magnetic resonance spectra were measured in $CDCl_3$ solution on a Bruker WP 80 and Bruker 300 WB spectrometers. Chemical shifts are reported as δ values relative to tetramethylsilane as an internal standard. Infrared spectra are obtained with a Perkin Elmer 157 spectrometer. Mass spectra are obtained on a Varian Mat 311 spectrometer.

Alumina-supported potassium fluoride. Potassium fluoride (Aldrich, 8 g) in methanol (200 ml) was mixed with alumina (Merck 60, type E, Art. 1103, 16 g). After stirring for 5 min., the methanol was removed under reduced pressure. The impregnated alumina was further dried in a desiccator for 5 h. This reagent may be kept in a desiccator, without loss of activity, during several weeks. We have found that the addition of potassium fluoride and alumina in the solvent of the reaction (acetonitrile) gave a reagent which has the same efficiency as that previously prepared.

Reagents. 1-nitropropane and 2-nitropropane were obtained commercially and used without purification. 2-nitrobutane and 3-nitropentane were prepared by literature methods [39]. Following literature procedures, alkenes **2a, b, e-f, k** [40], **2c** [41] and **2d, i, j** [42] were prepared from aldehydes and β-dicarbonyl compounds, benzoylacetonitrile [44] and β-ketosulfones [43].

Ethyl 2-benzoylcinnamate **2f**. 80 % ; mp 98°C (EtOH). ^{1}H NMR : 1.20 (t, 3H, J = 7 Hz) ; 4.18 (q, 2H, J = 7 Hz) ; 7.1 - 8.1 (m, 10H) ; 7.95 (s, 1H). IR (Nujol) ν : 1620, 1675, 1720 cm^{-1}.

4-(2-furyl) 3-acetyl 3-buten 2-one **2h**. 65 % ; bp 102°C (0.05 mm). ^{1}H NMR : 2.38 (s, 3H) 2.45 (s, 3H) ; 6.53 (m, 1H) ; 6.80 (d, 1H, J = 3 Hz) ; 7.21 (s, 1H) ; 7.55 (d, 1H, J = 3 Hz). IR (neat) : 1650, 1680 cm^{-1}.

β-benzoyl β-phenylsulfonylstyrene **2i**. 84 % ; mp 139°C (EtOH). ^{1}H NMR : 7.0 - 8.0 (m, 15H) ; 8.05 (s, 1H). IR (Nujol) : 1145, 1305, 1600, 1620, 1660 cm^{-1}.

4-piperonyl 3-paratolylsulfonyl 3-buten 2-one **2j**. 66 % ; mp 144°C (EtOH). ^{1}H NMR : 2.35 (s, 3H) ; 2.47 (s, 3H) ; 6.00 (s, 2H) ; 6.7 - 7.9 (m, 7H) ; 7.70 (s, 1H). IR (Nujol) : 1150, 1310, 1625, 1660 cm^{-1}.

Dihydrofurans **3**. To a solution or a suspension of alkene **2** (10 mmol) and nitroalkane **1** (15 mmol) in acetonitrile (9 ml) was added potassium fluoride (1.33 g) and alumina (2.67 g). After stirring at 80°C for 13 h (15 h for **3f, i, j**) the reaction mixture was cooled to room temperature, filtered through a layer of celite. The solid was washed with acetonitrile (2 x 10 ml). Evaporation of the solvent in vacuo gave the crude dihydrofuran which was purified either by short path bulb to bulb distillation or by recrystallization.

3-acetyl 4,5-dihydro 4-phenyl 2,5,5-trimethylfuran **3a**. 88 % ; bp 60°C (0.023 mm). IR (neat) 1625, 1668 cm^{-1}. ^{1}H NMR 0.90 (s, 3H) ; 1.46 (s, 3H) ; 1.84 (s, 3H) ; 2.34 (d, 3H, J = 1.5 Hz) ; 3.96 (q, 1H, J = 1.5 Hz) ; 7.0 - 7.4 (m, 5H). Anal. calcd for $C_{15}H_{18}O_2$: C, 78.23 ; H, 7.88. Found : C, 77.85 ; H, 8.10.

When the reaction of **2a** with **1a** was performed at room temperature, the Michael adduct **8a** was observed in a mixture of **8a**, **2a** and **3a**. **8a** ^{1}H NMR : 4.32 ; 4.79 (AB, J = 11 Hz).

4,5-dihydro 3-methoxycarbonyl 4-phenyl 2,5,5-trimethylfuran **3b**. 91 % ; bp 65°C (0.03 mm), mp 55°C ($CHCl_3$/Petrol. ether). IR (Nujol) : 1640, 1710 cm^{-1}. ^{1}H NMR 0.90 (s, 3H) ; 1.50 (s, 3H) ; 2.35 (d, 3H, J = 1.5 Hz) ; 3.54 (s, 3H) ; 3.95 (q, 1H, J = 1.5 Hz) ; 7.0 - 7.4 (m, 5H). Anal. calcd for $C_{15}H_{18}O_3$: C, 73.15 ; H, 7.37. Found : C, 73.40 ; H, 7.52.

3-acetyl 4,5-dihydro 4-isopropyl 2,5,5-trimethylfuran **3c**. 40 % ; bp 40°C (0.03 mm). ^{1}H NMR 0.85 (d, 3H, J = 6 Hz) ; 0.98 (d, 3H, J = 6 Hz) ; 1.29 (s, 3H) ; 1.48 (s, 3H) ; 2.00 (m, 1H) ; 2.20 (s, 3H) ; 2.29 (s, 3H) ; 2.72 (d, 1H, J = 3 Hz).

3-benzoyl 4,5-dihydro 4-phenyl 2,5,5-trimethylfuran **3d**. By cooling at -20°C a solution of a distilled mixture of **3d** and **3l** in ether-hexane, **3d** crystallized ; 40 % ; mp 80°C (ether-hexane). IR (Nujol) 1620, 1640 cm^{-1}. ^{1}H NMR 0.98 (s, 3H) ; 1.60 (s, 3H) ; 1.96 (s, 3H) ; 4.30 (s, 1H) ; 7.0 - 7.7 (m, 10H). Anal. calcd for $C_{20}H_{20}O_2$: C, 82.16 ; H, 6.90. Found : C, 81.91 ; H, 6.71.

3-benzoyl 4,5-dihydro 5,5-dimethyl 2,4-diphenylfuran **3e**. 80 % ; mp 98°C (ether - petrol. ether). IR (Nujol) 1600, 1610, 1620 cm^{-1}. ^1H NMR 1.10 (s, 3H) ; 1.69 (s, 3H) ; 4.44 (s, 1H) ; 6.9 - 7.55 (m, 15H). Anal. calcd for $C_{24}H_{22}O_2$: C, 84.71 ; H, 6.26. Found : C, 84.51 ; H, 6.46.

4,5-dihydro 5,5-dimethyl 2,4-diphenyl 3-ethoxycarbonylfuran **3f**. 95 % ; bp 115°C (0.025 mm). IR (neat) 1625, 1700 cm^{-1}. ^1H NMR 0.90 (t, 3H, J = 7 Hz) ; 1.02 (s, 3H) ; 1.60 (s, 3H) ; 3.91 (q, 2H, J = 7 Hz) ; 4.10 (s, 1H) ; 7.1 - 8.0 (m, 10H). Anal. calcd for $C_{21}H_{22}O_3$: C, 78.23 ; H, 6.88. Found : C, 78.48 ; H, 6.99.

4-(4-chlorophenyl) 4,5-dihydro-3-ethoxycarbonyl 2,5,5-trimethylfuran **3g** ; 93 % ; bp 70°C (0.02 mm). IR (neat) : 1635, 1705 cm^{-1}. ^1H NMR 0.90 (s, 3H) ; 1.00 (t, 3H, J = 7 Hz) ; 1.46 (s, 3H) ; 2.30 (s, 3H) ; 3.82 - 4.20 (m, 3H) ; 6.9 - 7.4 (m, 4H). Anal. calcd for $C_{16}H_{19}O_3Cl$: C, 65.19 ; H, 6.50 ; Cl, 12.03. Found : C, 65.33 ; H, 6.22 ; Cl, 11.92.

3-acetyl 4,5-dihydro 4-(2-furyl) 2,5,5-trimethylfuran **3h** ; 92 % ; bp 50°C (0.02 mm). IR neat 1625, 1670 cm^{-1}. ^1H NMR 1.07 (s, 3H) ; 1.45 (s, 3H) ; 1.94 (s, 3H) ; 2.27 (s, 3H) ; 4.07 (s, 1H) ; 6.05 (d, 1H, J = 3 Hz) ; 6.30 (q, 1H, J = 3 Hz, J = 1 Hz) ; 7.35 (d, 1H, J = 1 Hz). Anal. calcd for $C_{13}H_{16}O_3$: C, 70.88 ; H, 7.32. Found : C, 71.01 ; H, 7.29.

4,5-dihydro 5,5-dimethyl 2,4-diphenyl 3-phenylsulfonylfuran **3i** ; 92 % ; mp 109°C (EtOH). IR (Nujol) 1150, 1305, 1620 cm^{-1}. ^1H NMR 1.03 (s, 3H) ; 1.55 (s, 3H) ; 4.03 (s, 1H) ; 7.9 - 8.9 (m, 15H). Anal. calcd for $C_{24}H_{22}O_3S$: C, 73.82 ; H, 5.68 ; S, 8.21. Found : C, 74.10 ; H, 5.61 ; S, 8.33.

4,5-dihydro 4-piperonyl 3-paratolylsulfonyl 2,5,5-trimethylfuran **3j** ; 73 % ; mp 146°C (EtOH). IR 1140, 1300, 1620 cm^{-1}. ^1H NMR 0.94 (s, 3H) ; 1.40 (s, 3H) ; 2.31 (s, 3H) ; 2.35 (s, 3H) ; 3.79 (s, 1H) ; 5.82 (m, 2H) ; 6.5 (m, 3H) ; 6.90 - 7.5 (m, 4H). Anal. calcd for $C_{21}H_{22}O_5S$: C, 65.26 ; H, 5.74 ; S, 8.30. Found : C, 65.34 ; H, 5.64 ; S, 8.43.

3-acetyl 4,5-dihydro 5,5-dimethyl 2,4-diphenylfuran **3l** (in a mixture with **3d**). ^1H NMR 1.01 (s, 3H) ; 1.62 (s, 3H) ; 1.85 (s, 3H) ; 4.15 (s, 1H) ; 7.0 - 7.7 (m, 10H).

3-benzoyl 4,5-dihydro 5,5-diethyl 2,4-diphenylfuran **4** ; 50 % ; mp 149°C (ether - petrol. ether). IR 1600, 1620 cm^{-1}. ^1H NMR 0.79 (t, 3H, J = 7 Hz) ; 1.10 (t, 3H, J = 7 JHz) ; 1.35 - 1.75 (m, 2H); 2.01 (q, 2H, J = 7 Hz) ; 4.51 (s, 1H) ; 6.85 - 7.60 (m, 15H). Anal. calcd for $C_{27}H_{26}O_2$: C, 84.78 ; H, 6.85. Found : C, 85.01 ; H, 6.96.

3-acetyl 4,5-dihydro 2,5-dimethyl 5-ethyl 4-phenylfuran **5a** (mixture of isomers 50 : 50) 80 % bp 65 - 70°C (0.02 mm). IR (neat) 1620, 1670 cm^{-1}. ^1H NMR, isomer A : 0.83 (s, 3H) ; 1.02 (t, 3H, J = 7 Hz) ; 1.70 (m, 2H) ; 1.85 (s, 3H) ; 2.35 (s, 3H) ; 4.07 (s, 1H) ; 6.95 - 7.6 (m). Isomer B : 0.75 (t, 3H, J = 7 Hz) ; 1.10 (m, 2H) ; 1.42 (s, 3H) ; 2.35 (s, 3H) ; 3.96 (s, 1H) ; 6.95 - 7.5 (m). Anal. calcd for $C_{16}H_{20}O_2$: C, 78.65 ; H, 8.25. Found : C, 78.47 ; H, 8.28.

4,5-dihydro 2,4-diphenyl 5-ethyl 3-ethoxycarbonyl 5-methylfuran **5f** (mixture of isomers) 98 % bp 100°C (0.02 mm). IR (neat) 1625, 1700 cm^{-1}. ^1H NMR. Isomer A (70 %) : 0.80 - 2.10 (m) ; 1.01 (s, 3H) ; 3.95 (q, J = 7.5 Hz) ; 4.24 (s, 1H) ; 7.0 - 8.0 (m). Isomer B (30 %) : 0.8 - 1.6 (m) ; 1.55 (s, 3H) ; 3.95 (q, J = 7.5 JHz) ; 4.13 (s, 1H) ; 7.0 - 8.0 (m). Anal. calcd for $C_{22}H_{24}O_3$: C, 78.54 ; H, 7.19. Found : C, 78.80 ; H, 7.11.

3-acetyl 4,5-dihydro 2,5-dimethyl 5-ethyl 4-(2-furyl) furan **5h** ; 77 % ; bp 50°C (0.018 mm). IR (neat) 1625, 1670 cm^{-1}. ^1H NMR. Isomer A (70 %) : 1.02 (s, 3H) ; 1.03 (t, 3H, J = 7 Hz) ; 1.70 (m, 2H) ; 1.96 (s, 3H) ; 2.34 (s, 3H) ; 4.15 (s, 1H) ; 6.07 (m, 1H) ; 6.32 (m, 1H) ; 7.32 (m, 1H). Isomer B (30 %) : 0.86 (t, 3H, J = 7 Hz) ; 1.42 (m, 2H) ; 1.43 (s, 3H) ; 1.96 (s, 3H) ; 2.34 (d, 3H) ; 4.08 (q, 1H) ; 6.07 (m, 1H) ; 6.32 (m, 1H) ; 7.32 (m, 1H). Anal. calcd for $C_{14}H_{18}O_3$: C, 71.77 ; H, 7.74. Found : C, 71.70 ; H, 7.93.

Reaction of 2-benzoylcinnamonitrile **2k** with 2-nitropropane. To a solution of **2k** (10 mmol) and 2-nitropropane (15 mmol) in acetonitrile (9 ml) was added alumina supported potassium fluoride (4 g). The mixture was refluxed for 17 h. The reaction mixture, cooled to room temperature, was filtered through a layer of celite. Evaporation of the solvent in vacuo gave a mixture of **3k** and **11** which were separated by distillation.

2-benzoyl 4-methyl 3 -phenyl 4-pentenitrile **11** ; 42 % ; bp 135°C (0.02 mm) ; mp 94-95°C (dichloromethane/hexane 10/90). IR (Nujol) : 1655, 1685, 2230 cm^{-1}. ^1H NMR (300 MHz) 1.65 (s, 3H) ; 4.13 (d, 1H, J = 9.8 Hz) ; 4.90 (d, 1H, J = 9.8 Hz) ; 4.85 (m, 2H) ; 7.3 - 8.0 (m, 10H). MS exact mass calcd for $C_{19}H_{17}NO$ 275.1310. Obsd 275.1304.

When the reaction of **2k** with 2-nitropropane is allowed to proceed for 2 h at 80°C, a mixture of **3k**, **10** and **11** is produced in 13/70/17 ratios.

3k ^1H NMR 0.99 (s, 3H) ; 1.62 (s, 3H) ; 4.15 (s, 1H) ; 7.5 (m).

10 ^1H NMR 1.25 (s, 3H) ; 1.53 (s, 3H) ; 3.31 (s, 1H) ; 7.5 (m).

This mixture (1.8 g) in 4 ml of acetonitrile was heated at reflux without KF/Al_2O_3 for 17 h. The solvent was removed and the residue was analyzed by ^1H NMR. The products formed were **3k** and **11** in a 17/83 ratio. The cyclopropane **10** has disappeared.

3-acetyl 4,5-dihydro 5-ethyl 2-methyl 4-phenylfuran **12** (in the mixture **12/13** 33/66), 30 % : bp 90°C (0.03 mm). ^1H NMR 1.02 (t, 3H, J = 7 Hz) ; 1.72 (m, 2H) ; 1.90 (s, 3H) ; 2.38 (m, 3H) ; 2.47 (s, 3H) ; 4.02 (m, 1H) ; 4.31 (m, 1H) ; 7.25 (m, 5H).

3-Acetyl 5-ethyl 2-methyl 4-phenyl furan **13** (in the mixture **12/13**), 60 % : bp 90°C (0.03 mm). ^{1}H NMR 1.16 (t, 3H, J = 7 Hz) ; 1.93 (s, 3H) ; 2.55 (s, 3H) ; 2.56 (m) ; 7.2 (m). MS exact mass calcd for **12** $C_{15}H_{18}O_2$ 230.1306, obsd 230.1318. Exact mass calcd for **13** $C_{15}H_{16}O_2$ 228.1159, obsd 228.1159.

3-Cyano 2,4-diphenyl 5-ethylfuran **16**. The reaction of 2-benzoylcinnamonitrile **2k** with 1-nitropropane was performed as above to give **16**. 58 % ; bp 110°C (0.03 mm) ; mp 124°C (EtOH). IR (Nujol) 1650, 2215 cm^{-1}. ^{1}H NMR 1.38 (t, 3H, J = 7.5 Hz) ; 2.85 (q, 2H, J = 7.5 Hz) ; 7.35 - 8.15 (m, 10H). MS, m/z (relative intensity) 77 (50) ; 105 (51) ; 258 (100) ; 273 (78). Exact mass calcd for $C_{19}H_{15}NO$ 273.1154, obsd 273.1153.

Unsaturated nitro compounds **17**. α,β-unsaturated nitro esters **17a-e** and β-benzoyl β-nitrostyrene **17f** were respectively prepared from aromatic aldehydes and methylnitroacetate [45] or ω-nitroacetophenone [46] following a modified procedure of Lehnert method [47] which is described below :

A 2000 ml, three necked, round bottom flask was fitted with a reflux condenser, a powerful magnetic stirring unit and a pressure equalizing dropping funnel. The system was filled with dry nitrogen and dry THF (500 ml) was added in the flask, at 0°C. To the stirred cold solvent was then added a solution of $TiCl_4$ (0,4 mol, 44 ml) in dry CCl_4 (50 ml) within 30 min. To the resulting yellow suspension was quickly added a solution of methylnitroacetate -or ω-nitroacetophenone for **17f**- (0,2 mol) and aromatic aldehyde (0.25 mol) in THF (50 ml). The mixture was then stirred at 0°C for 3 h and a solution de N-methyl morpholine (0.8 mol, 88 ml) in THF (100 ml) was very slowly added under powerful stirring within 2 h. After 8 h at 0°C, the mixture was stirred overnight at ambient temperature. Water was added (100 ml, except for **17d** where hydrolysis was performed with 200 ml of 5 M NaOH solution) and the organic phase separated. The aqueous phase was extracted with ether, the combined organic phases washed with saturated NaCl solution (100 ml), dried over $MgSO_4$ and solvents evaporated under reduced pressure. The alkene **17** was purified by crystallization at low temperature in benzene or ethanol.

Methyl 2-nitro cinnamate **17a** : 69 %.(Two isomers, crystallised from EtOH at-40°C). IR (Nujol) : 1735, 1645, 1535 cm^{-1}. ^{1}H NMR : 3.92, 3.98 (ss, 3H) ; 7.40, 7.43 (ss, 5H) ; 7.49, 8.05 (ss, 1H).

Methyl 2-nitro 3-(p-methoxyphenyl)-acrylate **17b** : 60 %. mp 87°C (one isomer obtained from EtOH). ^{1}H NMR : 3.90 (s, 3H) ; 3.96 (s, 3H) ; 6.90-7.40 (m, 4H) ; 7.50 (s, 1H).

Methyl 2-nitro 3-piperonyl acrylate **17c** : 63 %. mp 105°C (benzene, 2 isomers). ^{1}H NMR : 3.89, 4.00 (ss, 3H) ; 6.04 (s, 2H) ; 6.75-7.20 (m, 3H) ; 7.41, 7.97 (ss, 1H).

Methyl 2-nitro 3-(p-dimethylaminophenyl)-acrylate **17d** : 63 %. mp 90°C (EtOH, 2 isomers). ^{1}H NMR : 3.03, 3.05 (ss, 6H) ; 3.85, 4.00 (ss, 3H) ; 6.50 - 7.40 (m, 4H) ; 7.38, 7.96 (ss, 1H).

Methyl 2-nitro 3-(2-furyl) acrylate **17e** : 60 %. mp 70°C (EtOH at -10°C, 2 isomers). ^{1}H NMR : 3.91, 4.00 (ss, 3H) ; 6.60 (m, 1H) ; 7.00 (m, 1H) ; 7.30 - 7.90 (m, 2H).

β-Benzoyl β-nitrostyrene **17f** : 76 %. mp 90°C (EtOH). ^{1}H NMR : 7.25 - 8.05 (m, 10H) ; 8.30 (s, 1H).

Isoxazoline N-oxydes **18** and **19**.

The mixture of nitroalkene **17a-f** (10 mmol) and nitroalkane **1a** or **1b** (20 mmol) was dissolved in acetonitrile (15 ml). Potassium fluoride (2 g) and alumina (4 g) was added. The mixture was stirred for 5 h at room temperature and then refluxed for 2.5 h. After cooling, the solid was filtered on celite, washed with acetonitrile (2 x 10 ml) and the solvent was evaporated in vacuo. Products **18** and **19** were crystallized from ethanol.

5,5-dimethyl 3-methoxy carbonyl 4-phenyl isoxazoline N-oxide **18a** : 63 %. mp 136°C. ^{1}H NMR : 1.04 (s, 3H) ; 1.67 (s, 3H) ; 3.69 (s, 3H) ; 4.31 (s, 1H) ; 7.05 - 7.45 (m, 5H). ^{13}C NMR : 22.1 ; 28.0 ; 52.3 ; 48.1 ; 84.1 ; 113.1 ; 128.0 ; 129.0 ; 136.3 ; 159.6. Anal. calcd for $C_{13}H_{15}NO_4$: C, 62.64 ; H, 6.07 ; N, 5.62. Found : C, 62.47 ; H, 6.05 ; N, 5.64.

5,5-Dimethyl 3-methoxycarbonyl 4-(4-methoxyphenyl) isoxazoline N-oxide **18b** : 74 %. mp 131°C. ^{1}H NMR : 1.02 (s, 3H) ; 1.62 (s, 3H) ; 3.70 (s, 3H) ; 3.80 (s, 3H) ; 4.25 (s, 1H) ; 6.80 - 7.20 (m, 4H). Anal. calcd for $C_{14}H_{17}NO_5$: C, 60.20 ; H, 6.14 ; N, 5.02. Found : C, 59.92 ; H, 6.15 ; N, 5.16.

5,5-Dimethyl 3-methoxycarbonyl 4-piperonyl isoxazoline N-oxide **18c** : 66 %. mp 185°C (dec). ^{1}H NMR : 1.05 (s, 3H) ; 1.59 (s, 3H) ; 3.71 (s, 3H) ; 4.20 (s, 1H) ; 5.96 (s, 2H) ; 6.70 (m, 3H). Anal. calcd for $C_{14}H_{15}NO_6$: C, 57.33 ; H, 5.16 ; N, 4.78. Found : C, 57.25 ; H, 5.06 ; N, 4.74.

5,5-Dimethyl 3-methoxycarbonyl 4-(p.dimethylaminophenyl) isoxazoline N-oxide **18d** : 60 %. mp 139°C. ^{1}H NMR : 1.03 (s, 3H) ; 1.58 (s, 3H) ; 2.93 (s, 6H) ; 3.70 (s, 3H) ; 4.19 (s, 1H) ; 6.60 - 7.10 (m, 4H). Anal. calcd for $C_{15}H_{20}N_2O_4$: C, 61.63 ; H, 6.90 ; N, 9.61. Found : C, 61.66 ; H, 6.91 ; N, 9.40.

5,5-dimethyl 4-(2-furyl) 3-methoxycarbonyl isoxazoline N-oxide **18e** : 42 %. mp 126°C. ^{1}H NMR : 1.08 (s, 3H) ; 1.60 (s, 3H) ; 3.78 (s, 3H) ; 4.46 (s, 1H) ; 6.20 - 6.45 (m, 2H) ; 7.40 (d, 1H, J = 1.2 Hz). Anal. calcd for $C_{11}H_{13}NO_5$: C, 55.23 ; H, 5.48 ; N, 5.86. Found : C, 55.49 ; H, 5.39 ; N, 5.81.

5-ethyl 3-methoxycarbonyl 4-(4-methoxyphenyl) 5-methyl isoxazoline N-oxide **19b** : 55 %. mp 87°C (mixtures of isomers). ^{1}H NMR : isomer A (65 %) : 1.00 (s, 3H) ; 1.09 (t, 3H, J = 7 Hz) ; 1.90 (m, 2H) ; 3.73 (s, 3H) ; 3.82 (s, 3H) ; 4.35 (s, 1H) ; 6.80 - 7.20 (m, 4H). Isomer B (35 %) : 0.82 (t, 3H, J = 7 Hz) ; 1.25 (m, 2H) ; 1.60 (s, 3H) ; 3.72 (s, 3H) ; 3.82 (s, 3H) ; 4.27 (s, 1H) ; 6.80 - 7.20 (m, 4H). Anal. calcd for $C_{15}H_{19}NO_5$: C, 61.42 ; H, 6.53 ; N, 4.78. Found : C, 61.38 ; H, 6.57 ; N, 4.61.

5-ethyl 3-methoxycarbonyl 4-piperonyl 5-methyl isoxazoline N-oxide **19c** : 55 %. mp 135°C (mixture of isomers). ^{1}H NMR : isomer A (65 %) : 1.04 (s, 3H) ; 1.10 (t, 3H, J = 7 Hz) ; 1.90 (m, 2H) ; 3.74 (s, 3H) ; 4.27 (s, 1H) ; 5.97 (s, 2H) ; 6.70 (m, 3H). Isomer B (35 %) : 0.82 (t, 3H, J = 7 Hz) ; 1.25 (m, 2H) ; 1.59 (s, 3H) ; 3.74 (s, 3H) ; 4.20 (s, 1H) ; 5.97 (s, 2H) ; 6.70 (m, 3H). Anal. calcd for $C_{15}H_{17}NO_6$: C, 58.62 ; H, 5.58 ; N, 4.56. Found : C, 58.66 ; H, 5.50 ; N, 4.49.

Reaction of β-benzoyl β-nitrostyrene **17f** with 2-nitropropane

In a 500 ml, three necked flask, were placed acetonitrile (200 ml), 2-nitropropane (0.335 mol), alumina (50 g) and potassium fluoride (25 g). The mixture was refluxed with stirring and a solution of alkene **17f** (0.1 mol) in acetonitrile (100 ml) was added dropwise within 3 h. At the end of the addition, the mixture was further refluxed during 1 h, cooled to 25°C and filtered on celite. The solid was washed with acetonitrile (2 x 50 ml) and the solvent evaporated to afford an oil which was crystallised in ethanol.

3-benzoyl 4-phenyl 5,5-dimethyl isoxazoline N-oxide **18f** : 61 %. mp 159°C. ^{1}H NMR : 1.09 (s, 3H) ; 1.69 (s, 3H) ; 4.64 (s, 1H) ; 7.10 - 7.90 (m, 10H). Anal. calcd for $C_{18}H_{17}NO_3$: C, 73.20 ; H, 5.80; N, 4.74. Found : C, 73.25 ; H, 5.78 ; N, 4.62.

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