THE DIFFERENTIAL REACTIVITY OF 5- AND 3-METHYL GROUPS IN THE RE-
ACTION OF 4-SUBSTITUTED 2,3,5-TRIMETHYLISOXAZOLIUM   SALTS   WITH
AROMATIC ALDEHYDES.

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Abstract — 2,3,5-Trimethylisoxazolium salts with electron-withdra-
wing groups at C-4 react with aromatic aldehydes to give 3- and/
or 5-arylidene derivatives resulting from the condensation at CH_3
-3 and/or CH_3-5. The differential reactivity of 3- and 5-methyl
groups is markedly influenced by the nature of the substituent at
C-4 and varies in the same order as its kinetic acidity which was
estimated from studies on deuteriodeprotonation. The influence of
inductive, resonance and steric effects due to the 4-substituents
on the course of the reaction is shown.

INTRODUCTION

3,5-Dimethylisoxazoles substituted in the 4-position by electron-withdrawing groups
condense with aromatic aldehydes, in the presence of bases, exclusively at the me-
thyl group in 5-position to give 5- arylidene derivatives[1]. The strength of the ne-
cessary base depends on the nature of the groups attached at C-4. In the case of
3,5-dimethyl-4-nitroisoxazole, derivatives at the 5-methyl group (never at 3-posi-
tio) have also been obtained not only with aromatic aldehydes but also with their
anils, with N,N-diarylformamidines and p-nitrosodimethylaniline[1]. It also undergoes
Michael-type reactions with benzalacetophenone and acridine[1].
5-Alkylisoxazolium salts are deprotonated even more readily than the corresponding
isoxazoles and can undergo condensation reactions under the influence of comparati-
vely weak bases. In these compounds, however, deprotonation of 3-alkyl and 5-alkyl
compete and the ratio of the deprotonation depends on the nature of the base[1]. Fur-
thermore, α-deprotonation of the N-alkyl and 3-alkyl groups of N-alkylisoxazolium
salts takes place also competitively[1].
More recently we found[2] that 5-unsubstituted 3-alkylisoxazolium salts do not con -
dense with aromatic aldehydes, in the presence of bases, but undergo ring cleavage
leading to β-iminoesters via a ketene intermediate.
Taking this into consideration, the behavior of 2,3,5-trimethylisoxazolium salts
with electron-withdrawing groups at C-4 toward oxo compounds is impossible to pre-
dict. In this paper, the differential reactivity of the methyl groups at C-3 and
C-5 of some isoxazolium salts (Ia-e) is studied in function with the inductive, re-
sonance and steric effect of the substituent at C-4.
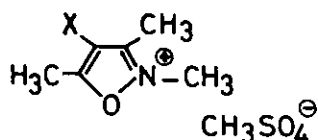
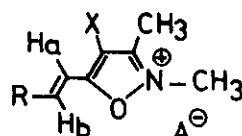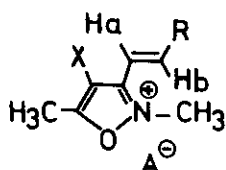$$\text{Ia, X=NO}_2 \quad \text{Id, X= CN}$$
$$\text{Ib, X= Cl} \quad \text{Ie, X= COC}_6\text{H}_5$$
$$\text{Ic, X= COCH}_3$$

RESULTS AND DISCUSSION

4-Substituted 2,3,5-trimethylisoxazolium methosulfates (Ia-d) react with aromatic aldehydes in the presence of bases and lead to only one product of monocondensation (II or III) or to a mixture of monocondensated products (II and III) (table 1).

IIa, X=NO$_2$ R=C$_6$H$_5$

IIb, X=NO$_2$ R=C$_6$H$_5$CH=CH

IIc, X=NO$_2$ R=p(CH$_3$)$_2$NC$_6$H$_4$

IId, X=Cl R=C$_6$H$_5$

IIe, X=Cl R=C$_6$H$_5$CH=CH

IIf, X=Cl R=HO–C$_6$H$_3$(CH$_3$O)–

IIIa, X=Cl R=C$_6$H$_5$

IIIb, X=Cl R=C$_6$H$_5$CH=CH

IIIc, X=Cl R=HO–C$_6$H$_3$(CH$_3$O)–

IIId, X=COCH$_3$ R= (furyl)

IIIe, X=COCH$_3$ R=C$_6$H$_5$CH=CH

IIIf, X=COCH$_3$ R=p(CH$_3$)$_2$NC$_6$H$_4$

IIIg, X=CN R=C$_6$H$_5$

IIa-c, A$^\ominus$ = SO$_4^\ominus$

IId-f, IIIa-g, A$^\ominus$ = F$_4$B$^\ominus$

Ia-d do not react with aliphatic aldehydes or ketones. 2,3,5-Trimethyl-4-benzoyl-isoxazolium (Ie) methosulfate or perchlorate was proven to be totally inactive toward oxo compounds in all possible conditions. Ia is also inactive toward p-nitro-benzaldehyde.

The nature of the arylidene derivatives obtained in each case, the utilized base and the conditions of the reactions are listed in table 1.

The high reactivity of the 2,3,5-trimethyl-4-nitroisoxazolium methosulfate (Ia) requires the use of ethanol as the base; pyridine and piperidine cause the cleavage of the ring and the polymerization of the resulting products. In the remaining cases pyridine has proven to be the most satisfactory base; secondary amines cause

Table 1

The reaction of 4-substituted 2,3,5-trimethylisoxazolium
methosulfates with aromatic aldehydes

4-Subst.	R-CHO	Base	Time (min.)	Products[a] II(%)	III (%)
NO_2	C_6H_5CHO	C_2H_5OH	120	IIa (36)	–
NO_2	$C_6H_5CH=CHCHO$	C_2H_5OH	60	IIb (67)[b]	–
NO_2	$p(CH_3)_2NC_6H_4CHO$	C_2H_5OH	1	IIc (80)	–
Cl	C_6H_5CHO	C_5H_5N	180	IId (36)	IIIa (9)
Cl	$C_6H_5CH=CHCHO$	C_5H_5N	120	IIe (18)	IIIb (18)
Cl	Vanillin	C_5H_5N	120	IIf (10)	IIIc (5)
$COCH_3$	Furfural	C_5H_5N	60	–	IIId (85)
$COCH_3$	$C_6H_5CH=CHCHO$	C_5H_5N	120	–	IIIe (68)
$COCH_3$	$p(CH_3)_2NC_6H_4CHO$	C_5H_5N	180	–	IIIf (11)
CN	C_6H_5CHO	C_5H_5N	60	–	IIIg (42)

[a] IIa-c were isolated as sulfates; IId-f and IIIa-g were isolated
as tetrafluoroborates.

[b] Yield corresponding to the mixture of geometric isomers ZE-IIb
and EE-IIb, isolated in the ratio 1:3 respectively.

the partial degradation of the ring and the final yields decrease notably. The be-
havior of Ie is remarkable because pyridine does not seem strong enough for the
reaction to be effective whereas piperidine degrades the ring.
In the reaction of Ia with cinnamaldehyde, two geometric isomers (EZ-IIb and EE-
IIb) in relative proportions 1:3 have been isolated. EZ-IIb spontaneously trans-
form itself into EE-IIb. The conversion is complete after being subjected to room
temperature for eigth months.

EE-IIb   ZE-IIb
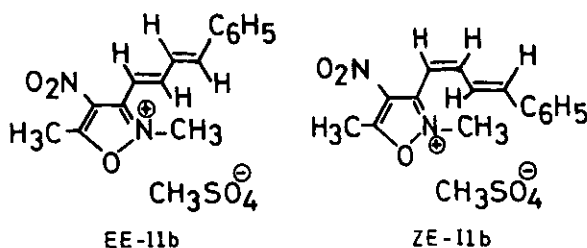
Since the reactivity of Ia-e toward aromatic aldehydes in the presence of bases must depend on the ease with which the respective carbanions are generated in CH_3-3 or CH_3-5, the study of the hydrogen-deuterium exchange of Ia-d when treated with D_2O should shed some light on the relative reactivity of the methyl groups. Ia-d exchange regioselectively in the methyl groups at C-3 and/or C-5 depending on the nature of the group attached at C-4 (table 2). Reaction of these salts with aldehydes occurs only at the methyl group in which the hydrogen-deuterium exchange takes place. Deuteriodeprotonation reactions have been followed by ^{1}H-NMR spectroscopy in order to determine the influence of the substituent at C-4 upon the kinetic acidity of the 3- and 5-methyl groups. The expected signal for the $N-CH_3$ protons remains unchanged and no evidence for hydrogen exchange was found. However, the 3- and/or 5-methyl groups underwent exchange at rates which depend on the substituent at C-4. The variation of the intensities of the ^{1}H-NMR absorption bands associated with the 3- and 5-methyl groups, when time and temperature were held constant are shown in table 2.

Table 2

Hydrogen-deuterium exchange rates for 3- and 5-methyl groups of 4-substituted 2,3,5-trimethylisoxazolium salts[a]

4-Subst.	Time (min.)	t (ºC)	NMR signals final intensities (%)[b]		
			$N-CH_3$	CH_3-5	CH_3-3
NO_2	5[c]	20[c]	100	98	0
Cl	40	100	100	10	11
$COCH_3$	40	100	100	11	94
CN	40	100	100	3	90
COC_6H_5	40	100	100	98	100

[a]In D_2O. Basic catalized exchange sharply reduces the exposure to deuterium oxide.

[b]Referred to the initial intensities.

[c]The high reactivity of Ia does not permit exchange experiences to be carried in the same conditions as Ib-e.

The nature of the compounds obtained in the preceding reactions and the results of the experiments of hydrogen-deuterium exchange suggest that the influence of the electron-withdrawing substituents at C-4 upon the reactivity of the 3- and 5-methyl groups depens on the inductive, resonance and steric effects of these substituents. With regard to the influence that the resonance effects have on the reactivity of the 5-methyl group, the steric hindrance of the groups attached at C-4 is of consi-

derable importance. Thus, introduction of a bulky substituent at C-4 (nitro, ben-
zoyl) can result in the non-planarity of the substituent and the isoxazole ring as
well as the non-planarity of the members of the ring[3]. In the first case, the ac-
tion of the substituent at C-4 upon the 5-methyl group decreases and can be negli-
gible. In the second case, the activation of the 5-methyl group due to the positi-
vely charged nitrogen *is also very small or non-existent.*

The inductive effect of the nitro group, especially strong (the constants of Taft[4]
are $\sigma_I = 0.65$, $\sigma_R = 0.47$) and the steric factors which were mentioned before ($-E_S = 2.52$) determine the preferential increase of the reactivity of the 3-methyl group
of Ia due to the sum of the factor σ_I plus the influence of the charged heterocy-
clic nucleus.

On the other hand, the moderate steric exigencies of the chlorine atom ($\sigma_I = 0.46$,
$\sigma_R = -0.23$, $-E_S = 0.97$) do not cause an appreciable distorsion of the ring and
both methyl groups of Ib are activated by the positively charged nitrogen and the
inductive effect of the chlorine atom.

The acetyl and cyano groups ($\sigma_I = 0.28$, $\sigma_R = 0.47$ and $\sigma_I = 0.56$, $\sigma_R = 0.33$, respec-
tively), *less bulky*, increase the acidity of the 5-methyl group because their reso-
nance effect —M is added to the one which originates in the ring[5]. The small hin-
drance of the cyano group ($-E_S = 0.51$) derived from its lineal geometry should cau-
se the acidity of the 5-methyl group of Id to be superior to the acidity of the sa-
me methyl group of Ic (table 2) in spite of their differences in *the resonance*
constants.

The strong steric distorsion in Ie due to the hindrance of the benzoyl group can be
the origin of the non-reactivity of this compound toward the studied bases. The
lack of planarity between the benzoyl group and the ring in Ie can also be deduced
from its IR carbonylic absorption (1687 cm^{-1}) which is higher than the expected for
a diaryl ketone.

Ketones fail to react with Ia-d and do not seem to show enough electrophilic cha -
racter. Nevertheless, the readily condensation of these salts with aromatic aldehy-
des (but not with the aliphatic ones) suggests that these reactions are subjected
to thermodynamic control. Aromatic aldehydes with electron-withdrawing groups as
p-nitrobenzaldehyde *seem to unstabilize the positively* charged heterocyclic nucleus
and Ia does not condense with the mentioned aldehyde. The absence of dicondensed
compounds in all the studied reactions (even when working with an excess of aldehy-
de) must be attributed to the decrease in the acidity of the remaining methyl group
when an arylidene group is introduced in the 3- or 5-position.

EXPERIMENTAL

All mp are uncorrected. Diethyl ether, toluene and ethanol were dried. 4-Nitro-3,5-
dimethylisoxazole[6], 4-chloro-3,5-dimethylisoxazole[7], 4-benzoyl-3,5-dimethylisoxazo-
le[8], 4-cyano-3,5-dimethylisoxazole[9] and 4-acetyl-3,5-dimethylisoxazole[10] were pre-
pared by established procedures. IR spectra were recorded on a Pye-Unicam SP-1100
spectrometer equipped with NaCl optics. A Pye-Unicam SP-1700 was used to obtain UV
spectra. ^{1}H-NMR spectra were determined at 60 MHz on a Varian T-60A spectrometer
using $Cl_3CD-(CD_3)_2SO$ solutions and TMS as standard reference; chemical shifts were
measured in the δ scale.

Quaternization of 4-substituted 3,5-dimethylisoxazole derivatives (general procedure). A mixture of 4-substituted 3,5-dimethylisoxazole and redistilled dimethyl sulfate (molar ratio 1:1.1) in toluene (100 ml) was refluxed for 11 h. On cooling the product solidified to a yellow-brown glass. This was decanted from the toluene layer, repeatedly extracted with ether and used directly. It could be crystallized by trituration with ether, but purification was difficult because the methosulfate was exceedingly hygroscopic; yield, 85-95%. The structure of the isoxazolium salts resulting from the above reaction has been elucidated througt their ^{1}H NMR spectroscopic characteristics (table 3). Ia-e show IR ring stretching bands in the 1635 - 1615 cm^{-1} range.

Table 3

NMR chemical shifts for 4-substituted 2,3,5-trimethylisoxazolium methosulfates (δ, 60 MHz, $Cl_3CD - (CD_3)_2SO$)

4-Subst.	CH_3-3	CH_3-5	N-CH_3	SO_4CH_3
COC_6H_5[a]	2.60	2.75	4.20	3.75
NO_2	3.00	3.15	4.40	3.80
Cl	2.65	2.70	4.30	3.80
$COCH_3$[b]	2.70	2.80	4.20	3.80
CN	2.80	2.90	4.20	3.80

[a]COC_6H_5, 7.5-7.9; [b]$COCH_3$, 2.45.

Reaction of Ia-e with aromatic aldehydes in the presence of bases (general procedure). An ethanol solution of the aldehyde (50 mM) and the required organic base (30 mM) was added to a strirred solution of Ia-e (25 mM) in 60 ml of ethanol and the mixture was refluxed during a determinated number of hours (table 1). When the isoxazolium salt used was the 4-nitro derivative (Ia), coloured crystals from the ethanol solution were collected by cooling at 0ºC, recrystallized from water and proven to be, in each case, IIa-c. After evaporation of the ethanol (reactions in which Ib-d are involved) the crude product was dissolved in a small amount of water, extracted with ether and added to a saturated solution of sodium tetrafluoborate in water to which a little of tetrafluoboric acid had been added (pH = 2-3) and the precipitated fluoborate salt was filtered off, washed with water, dried and recrystallized from water to give, in each case, IId-f or IIIa-g. Separation of the mixture of geometric isomers EE-IIb and ZE-IIb could be achieved by fractional recrystallization (ethanol). The reaction of Ib with aromatic aldehydes led to a mixture of 3- and 5-monocondensated products (table 1) which could not be seperated due to the analogy in their chemical properties. Quantitative estimations of these mixtures (IId-IIIa, IIe-IIIb and IIf-IIIc) were achieved by ^{1}H NMR.
Physical and spectroscopic data of II and III are given below.
2,5-Dimethyl-4-nitro-3-styrylisoxazolium sulfate (IIa): yellow crystals from water, mp 190ºC (d). Anal. Calcd. for $(C_{13}H_{13}O_3N_2)_2SO_4$: C, 53.22; H, 4.43; N, 9.55. Found:

C, 52.96; H, 4.37; N, 9.71. IR (nujol): 1635, 1605, 1570, 1350, 985, 770, 700 cm^{-1}. ^{1}H NMR (Cl$_3$CD-(CD$_3$)$_2$SO): 2.90 (3H, s, CH$_3$-5), 4.25 (3H, s, N-CH$_3$), 7.10-7.70 (6H, m, H$_a$ and aromatic protons), 7.90 (1H, d, J=15 Hz, H$_b$).

2,5-Dimethyl-4-nitro-3-(4-phenyl-1,3-butadienyl)isoxazolium sulfate (EE-IIb, trans-trans): red crystals (water), mp 175-176º (d). <u>Anal</u>. Calcd. for (C$_{15}$H$_{15}$O$_3$N$_2$)$_2$SO$_4$: C, 56.42; H, 4.70; N, 8.77. Found: C, 56.67; H, 4.68; N 8.82. UV: λ_{max}(EtOH-H$_2$O) 215 (ϵ=20500) and 408 (ϵ=25000). IR (nujol): 1620, 1600, 1560, 995, 770, 700 cm^{-1}. ^{1}H NMR (Cl$_3$CD-(CD$_3$)$_2$SO): 2.85 (3H, s, CH$_3$-5), 4.20 (3H, s, N-CH$_3$), 7.00-7.60 (9H, m, olefinic and aromatic protons).

2,5-Dimethyl-4-nitro-3-(4-phenyl-1,3-butadienyl)isoxazolium sulfate (ZE-IIb, cis-trans): orange crystals (water), mp 194º (d). <u>Anal</u>. Calcd. for (C$_{15}$H$_{15}$O$_3$N$_2$)$_2$SO$_4$: C, 56.42; H, 4.70; N, 8.77. Found: C, 56.63; H, 4.76; N, 8.88. UV: λ_{max}(EtOH-H$_2$O) 208 (ϵ=18000) and 401 (ϵ=21000). IR (nujol): 1620, 1600, 1560, 1000, 770, 740, 710 cm^{-1}. ^{1}H NMR (Cl$_3$CD-(CD$_3$)$_2$SO): 2.90 (3H, s, CH$_3$-5), 4.20 (3H, s, N-CH$_3$), 6.90-7.40 (9H, m, olefinic and aromatic protons).

2,5-Dimethyl-4-nitro-3-(2-p-dimethylaminophenylethenyl)isoxazolium sulfate (IIc): violet crystals from water, mp 196º (d). <u>Anal</u>. Calcd. for (C$_{15}$H$_{18}$O$_3$N$_2$)$_2$SO$_4$: C, 53.57; H, 5.35; N, 12.50. Found: C, 53.79; H, 5.41; N, 12.81. IR (nujol): 1610, 1600, 1575, 1365, 995, 825 cm^{-1}. ^{1}H NMR (Cl$_3$CD-(CD$_3$)SO): 2.85 (3H, s, CH$_3$-5), 3.20 (6H, s, (CH$_3$)$_2$N), 4.25 (3H, s, N-CH$_3$), 6.80 (2H, d, J=8 Hz, β-aromatic protons), 7.05 (1H, d, J=15 Hz, H$_a$), 7.45 (2H, d, J=8 Hz, α-aromatic protons), 7.75 (1H, d, J=15 Hz, H$_b$).

Mixture of 2,5-dimethyl-4-chloro-3-styrylisoxazolium tetrafluoroborate (IId) and 2,3-dimethyl-4-chloro-5-styrylisoxazolium tetrafluoroborate (IIIa) (molar ratio 4:1): yellowish crystals from water, mp 156-163º. <u>Anal</u>. Calcd. for C$_{13}$H$_{13}$ONClF$_4$B: C, 48.55; H, 4.04; N, 4.36. Found: C, 48.49; H, 4.10; N, 4.29. IR (nujol): 1640, 1600, 980, 770, 740, 710 cm^{-1}. ^{1}H NMR (Cl$_3$CD-(CD$_3$)$_2$SO): 2.50 (3H, s, IId CH$_3$-5), 2.60 (3H, s, IIIa CH$_3$-3), 4.25 (6H, s, IId and IIIa N-CH$_3$), 6.95 (2H, d, J=15 Hz, IId and IIa H$_a$), 7.20-7.60 (10 H, m, IId and IIIa aromatic protons), 7.85 (2H, d, J=15 Hz, IId and IIIa H$_b$).

Mixture of 2,5-dimethyl-4-chloro-3-(4-phenyl-1,3-butadienyl)isoxazolium tetrafloroborate (IIe) and 2,3-dimethyl-4-chloro-5-(4-phenyl-1,3-butadienyl)isoxazolium tetrafluoroborate (IIIb) (molar ratio 1:1): yellow crystals from water, mp 170-176º. <u>Anal</u>. Calcd. for C$_{15}$H$_{15}$ONClF$_4$B: C, 51.82; H, 4.32; N, 4.03. Found: C, 51.59; H, 4.11; N, 3.88. IR (nujol): 1630, 1600, 1000, 780, 740, 710 cm^{-1}. ^{1}H NMR (Cl$_3$CD-(CD$_3$)$_2$SO): 2.55 (3H, s, IIe CH$_3$-5), 2.65 (3H, s, IIIb CH$_3$-3), 4.30 (6H, s, IIe and IIIb N-CH$_3$), 6.60-7.50 (18H, m, IIe and IIIb aromatic and olefinic protons).

Mixture of 2,5-dimethyl-4-chloro-3-2-(4-hydroxy-3-methoxyphenyl)ethenyl isoxazolium tetrafluoroborate (IIf) and 2,3-dimethyl-4-chloro-5-2-(4-hydroxy-3-methoxyphenyl)ethenyl isoxazolium tetrafluoroborate (IIIc) (molar ratio 2:1): yellowish crystals from water, mp 181-187º. <u>Anal</u>. Calcd. for C$_{14}$H$_{15}$O$_3$NClF$_4$B: C, 45.73; H, 4.08; N, 3.81. Found: C, 46.05; H, 4.27; N, 3.91. IR (nujol): 3460, 1650, 1615, 985, 820 cm^{-1}. ^{1}H NMR (Cl$_3$CD-(CD$_3$)$_2$SO): 2.55 (3H, s, IIf CH$_3$-5), 2.65 (3H, s, IIIc CH$_3$-3), 3.85 (6H, s, IIf and IIIc O-CH$_3$), 4.30 (6H, s, IIf and IIIc N-CH$_3$), 6.60-7.25 (8H, m, IIf and IIIc aromatic and H$_a$ protons), 7.45 (1H, d, J=15 Hz, IIIc H$_b$), 7.90 (1H, d, J=14 Hz, IIf H$_b$).

2,3-Dimethyl-4-acetyl-5-(2--furylethenyl)isoxazolium tetrafluoroborate (IIId): yellow crystals from water, mp 134-135°. Anal. Calcd. for $C_{13}H_{14}O_3NF_4B$: C, 48.93; H, 4.39; N, 4.39. Found: C, 49.01; H, 4.36; N, 4.54. IR (nujol): 1695, 1625, 1570, 960 cm^{-1}. ^{1}H NMR ($Cl_3D-(CD_3)_2SO$): 2.60 (3H, s $COCH_3$), 2.80 (3H, s, CH_3-3), 4.25 (3H, s, N-CH_3), 6.50 (1H, dd, J=2 Hz and 3 Hz, 4-furylic proton), 6.95 (1H, d, J=3 Hz, 3-furylic proton), 7.10 (1H, d, J=15 Hz, H_a), 7.60 (1H, d, J=15 Hz, H_b), 7.65 (1H, d, J=2 Hz, 5-furylic proton).

2,3-Dimethyl-4-acetyl-5-(4-phenyl-1,3-butadienyl)isoxazolium tetrafluoroborate (IIIe): orange crystals from water, mp 173-175°. Anal. Calcd. for $C_{17}H_{18}O_2NF_4B$: C, 57.49; H, 5.07; N, 3.94. Found: C, 57.19; H, 4.78; N, 3.73. IR (nujol): 1695, 1605, 1590, 980, 770, 690 cm^{-1}. ^{1}H NMR ($Cl_3CD-(CD_3)_2SO$): 2.60 (3H, s, $COCH_3$), 2.80 (3H, s, CH_3-3), 4.20 (3H, s, N-CH_3), 7.00-7.50 (9H, m, aromatic and olefinic protons).

2,2-Dimethyl-4-acetyl-5-(2-p-dimethylaminophenylethenyl)isoxazolium tetrafluoroborate (IIIf): violet crystals from water, mp 148-150°. Anal. Calcd. for $C_{17}H_{21}O_2N_2F_4B$: C, 54.86; H, 5.65; N, 7.53. Found: C, 54.58; H, 5.60; N, 7.50. IR (nujol): 1690, 1600, 985, 840 cm^{-1}. ^{1}H NMR ($Cl_3CD-(CD_3)_2SO$): 2.60 (3H, s, $COCH_3$), 2.75 (3H, s, CH_3-3), 3.10 (6H, s, $(CH_3)_2$N), 4.20 (3H, s, N-CH_3), 6.55 (2H, d, J=8 Hz, β-aromatic protons), 7.05 (1H, d, J=15 Hz, H_a), 7.40 (2H, d, J=8 Hz, α-aromatic protons), 7.60 (1H, d, J=15 Hz, H_b).

2,3-Dimethyl-4-cyano-5-styrylisoxazolium tetrafluoroborate (IIIg): yellow crystals from water, mp 171°. Anal. Calcd. for $C_{14}H_{13}ON_2F_4B$: C, 53.87; H, 4.17; N, 8.98. Found: C, 53.60; H, 3.90; N, 8.68. IR (nujol): 2215, 1635, 1600, 900, 760, 695 cm^{-1}. ^{1}H NMR ($Cl_3CD-(CD_3)_2SO$): 2.80 (3H, s, CH_3-3), 4.20 (3H, s, N-CH_3), 7.05 (1H, d, J=14 Hz, H_a), 7.05-7.60 (5H, m, aromatic protons), 7.80 (1H, d, J=14 Hz, H_b).

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3. The constructions of these compounds with molecular models or their design based on the lengths and bond angles determinated by Stietvater[11] prove these facts to be valid.

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5. We found[2] that 3,5-dimethyl-4-acetylisoxazole (IV) reacts with benzaldehyde, in the presence of sodium ethoxide to give 3,5-dimethyl-4-cinnamoylisoxazole (V). This points to the large influence of the positively charged nitrogen of Ic upon the selective activation of CH_3-5. Formation of V rather than the condensation product at CH_3-5, in the above reaction, must be interpreted on the basis of the higher thermodynamic stability of V.

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