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A comparative study of reactions of 3-methyl-5-phenylisoxazole and 3-methyl-5-phenylisothiazole with electrophilic compounds in the presence of *n*-BuLi, LICA or LICA-TMEDA is reported. By using LICA-TMEDA, regioselective reactions of the heterocyclic compounds at the C-3 methyl group are obtained. With *n*-BuLi or LICA and the isoxazole derivative a product mixture at the C-4 position and the C-3 methyl group is found. In the case of isothiazole compound, only with methyl iodide and *n*-BuLi, the dialkylated product at both positions is formed.

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In the hydrogen-lithium exchange reactions it is generally accepted that the principal factors which determine the site of lithiation in the heterocyclic compounds are the acidities of the hydrogens, which depend mainly on the inductive effects in the ring [1] and coordination of the lithiating agent to the endo- or exocyclic heteroatoms [2]. Replacement of the most "acidic" proton by lithium can result in lithiation of the ring or lateral lithiation of a substituent on the ring.

Alkyl groups at the 3- and 5-positions of isoxazole and isothiazole rings are slightly activated and can be deprotonated by strong bases. This reaction is specially useful in the isoxazole series since methyl groups in the 3- and 5-positions can be further substituted before the ring is reductively cleaved [3].

We have previously investigated the reactivity of methyl groups of 3-methyl-5-phenylisoxazole (**1**) [4] and 3-methyl-5-phenylisothiazole (**2**) [5], with several bases in the presence of different electrophiles.

In the case of substrate **1**, we found a competitive reaction from the vinylic and allylic carbanions giving rise to a mixture of the products of reaction at the C-4 position and at the C-3 methyl group, depending on the base used.

The reactions of 3-methyl-5-phenylisothiazole led exclusively to the reaction product at the C-3 methyl group.

On the basis of these principles, in the present paper we wish to extend our studies to the reactions of these compounds **1** and **2** with other electrophiles.

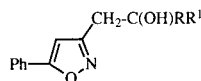
Results and Discussion.

The bases used in the study of the reactivity of substrates **1** and **2** with electrophiles were *n*-butyllithium, lithium isopropylcyclohexylamide (LICA) and lithium isopropylcyclohexylamide - *N,N,N',N'*-tetramethylethylenediamine

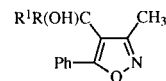
(LICA-TMEDA).

When the 3-methyl-5-phenylisoxazole reacts with oxo compounds, chlorotrimethylsilane and carboxylic acid derivatives in the presence of *n*-BuLi, and the isoxazole is added into the *n*-BuLi solution, both reaction products at the C-4 position and the C-3 methyl group were found, except in the case of the reaction with *N,N*-dimethylformamide, where the only product found was that substituted at the C-4 position (Table 1).

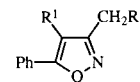
Scheme I



- 3: R = H, R' = CH₂-CH₃
 5: R = H, R' = Ph
 7: R = CH₃, R' = CH₃
 9: R = CH₃, R' = Ph
 11: R = H, R' = CH=CH₂
 12: R = CH₃, R' = CH=CH₂
 13: R = Ph, R' = Ph



- 4: R = H, R' = CH₂-CH₃
 6: R = H, R' = Ph
 8: R = CH₃, R' = CH₃
 10: R = CH₃, R' = Ph



- 14: R = H, R' = Si(CH₃)₃
 15: R = Si(CH₃)₃, R' = H
 16: R = H, R' = CON(CH₃)₂
 17: R = CON(CH₃)₂, R' = H
 18: R = H, R' = CHO
 19: R = H, R' = COCH₃
 20: R = COCH₃, R' = H
 21: R = COCH=CH-Ph, R' = H

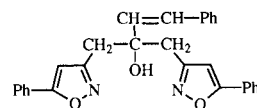


Table 1

Reactions of 3-Methyl-5-Phenylisoxazole (1) with Electrophiles in the Presence of *n*-BuLi

Electrophile	Reaction Conditions [a]		Products (%)
	Time (hours)		
	(-78°C)	(25°C)	
Propionaldehyde	5	1	3 (21), 4 (47)
Benzaldehyde	5	1	5 (13), 6 (30)
Acetone	5	1	7 (13), 8 (17)
Acetophenone	5	1	9 (22), 10 (25)
Chlorotrimethylsilane	5	1	14 (18), 15 (12)
<i>N,N</i> -dimethylcarbamoyl Chloride	5	1	16 (48), 17 (23)
<i>N,N</i> -dimethylformamide	5	1	18 (36)
Ethyl Acetate	5	1	19 (<2), 20 (16)

[a] The molar ratio used in all cases was: *n*-BuLi:isoxazole:electrophile = 1, 1, 1.

In the reactions with the LICA-TMEDA system the deprotonation is regioselective at the C-3 methyl group, as we previously reported [4]. With carbonyl compounds, alcohol derivatives were found. In the case of esters as substrates, the products were the oxo compound together the tertiary alcohol (Table 2).

The yields of the reaction products at C-3 methyl group are always higher when the system LICA-TMEDA is used.

Table 2

Reactions of 3-Methyl-5-Phenylisoxazole (1) with Electrophiles in the Presence of LICA-TMEDA

Electrophiles	Reaction Conditions[a]		Products (%)
	Time(hours)		
	(-78°C)	(25°C)	
Propionaldehyde	5	1	3 (38)
Acetone	5	1	7 (39)
Acrolein	5	1	11 (19)
Methyl Vinyl Ketone	5	1	12 (27)
Benzophenone	5	1	13 (31)
Chlorotrimethylsilane	5	1	15 (61)
<i>N,N</i> -dimethylcarbamoyl Chloride	5	1	17 (31)
Ethyl Cinnamate	5	1	21 (12), 22 (32)

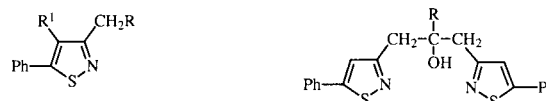
[a] The molar ratio used in all cases was LICA:TMEDA:isoxazole:electrophile = 1, 1.67, 1, 1.

We also report the results of the reactions of 3-methyl-5-phenylisothiazole (2) with alkyl halides, chlorotrimethylsilane and carboxylic acid derivatives in the presence of the aforementioned bases.

In the reactions with alkyl halides, the alkylation product was found at the C-3 methyl group in all the cases, except when methyl iodide was used and the isoxazole solution was added to the *n*-BuLi solution. In this case,

the dialkylated product was formed. This could be due to its small size, which allows it to approach all the carbanionic sites. Similar results were found in the reaction with 3-methyl-5-phenylisoxazole [4], but unlike the isoxazole analogue no monoalkylation products at the C-4 position were detected. The highest yields were found when *n*-BuLi was used. This can be explained on the basis of its higher basicity compared to the LICA and LICA-TMEDA systems. However the use of TMEDA greatly increased the basicity of LICA, by chelating the cation, as is shown in Table 3.

Scheme II



- 23: R = CH₃, R¹ = H
 24: R = CH₂Ph, R¹ = H
 25: R = (CH₂)₃CH₃, R¹ = H
 26: R = CH₃, R¹ = CH₃
 27: R = COCH₃, R¹ = H
 29: R = CO(CH₂)₂CH₃, R¹ = H
 31: R = COCH=CH-Ph, R¹ = H
 33: R = COPh, R¹ = H
 34: R = Si(CH₃)₃, R¹ = H

- 28: R = CH₃
 30: R = (CH₂)₂CH₃
 32: R = CH=CH-Ph

Table 3

Reactions of 3-Methyl-5-Phenylisothiazole (2) with Alkyl Halides

Alkyl Halide	Base	Products (%)
Methyl Iodide	<i>n</i> -BuLi[a,b]	23 (83)
Methyl Iodide	<i>n</i> -BuLi[a,c]	23 (69), 26 (5)
Methyl Iodide	LICA[a]	23 (15)
Methyl Iodide	LICA-TMEDA[d]	23 (62)
Benzyl Bromide	<i>n</i> -BuLi[a,b]	24 (83.5)
Benzyl Bromide	<i>n</i> -BuLi[a,c]	24 (75)
Benzyl Bromide	LICA[a]	24 (27)
Benzyl Bromide	LICA-TMEDA[d]	24 (60)
Butyl Bromide	<i>n</i> -BuLi[a,b]	25 (73.5)
Butyl Bromide	<i>n</i> -BuLi[a,c]	25 (63)
Butyl Bromide	LICA[a]	25 (20)
Butyl Bromide	LICA-TMEDA[d]	25 (14)

[a] The molar ratio used in all cases was base: isothiazole: alkyl halide = 1, 1, 1. [b] The base is added to the isothiazole solution. [c] The isothiazole solution is added to the *n*-BuLi solution. [d] The molar ratio used in all cases was: LICA:TMEDA:isothiazole:alkyl halide = 1, 1.67, 1, 1.

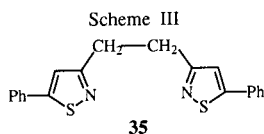
The reactions of compound 2 with chlorotrimethylsilane and carboxylic acid derivatives were carried out with LICA-TMEDA (Table 4). When esters were used as electrophiles, carbonyl compound and the tertiary alcohol were found. In all the cases, 1,2-bis(3-methyl-5-phenylisothiazolyl)ethane was found. Its presence could be explained by a free radical coupling mechanism [5].

Table 4

Reactions of 3-Methyl-5-Phenylisothiazole (2) with Electrophiles in the Presence of LICA-TMEDA

Electrophiles	Reactions Conditions[a]		Products (%)
	Time(hours) (-78°C)	Time(hours) (25°C)	
Ethyl Acetate	5	1	27 (36), 28 (32)
Ethyl Butyrate	5	1	29 (27), 30 (32)
Ethyl Cinnamate	5	1	31 (15), 32 (22)
Benzonitrile	5	1	33 (33)
Chlorotrimethylsilane	5	1	34 (75)

[a] The molar ratio used in all cases was LICA:TMEDA:isothiazole:electrophile = 1, 1.67, 1, 1.



In conclusion, these results and those found in our previous studies allow us to establish that the LICA-TMEDA system leads to regioselective reaction of 3-methyl-5-phenylisoxazole and 3-methyl-5-phenylisothiazole at the C-3 methyl group with different electrophiles: alkyl halides, oxo compounds, chlorotrimethylsilane and carboxylic acid derivatives. On the other hand, when *n*-BuLi or LICA were used with the isoxazole derivative **1**, a mixture of reaction products at the C-4 and the C-3 methyl group was found. In the case of isothiazole compound **2**, only with methyl iodide, the dialkylated product at C-4 and C-3 methyl group could be detected when *n*-BuLi was used.

EXPERIMENTAL

Melting points are uncorrected. 3-Methyl-5-phenylisoxazole and 3-methyl-5-phenylisothiazole were prepared by established procedures [6,7]. Nuclear magnetic resonance spectra were obtained with Bruker AC 80 and AC 300 spectrometers using deuteriochloroform and carbon tetrachloride solutions and TMS as the standard reference; chemical shifts were measured on the δ scale. Electron ionization mass spectra were obtained using a Hewlett-Packard GC/MS system 5988A. Elemental analyses were carried out with a Perkin-Elmer 240 B analyser. Merck silicagel 60 was used for column chromatography. Solvents and reagents were purified by conventional methods.

The general procedure was that previously reported [4,5].

3-(2-Hydroxybutyl)-5-phenylisoxazole (3).

This compound was obtained as a white solid, mp 72-73° (from ethanol-water); ¹H-nmr (deuteriochloroform): 7.78-7.61 (m, 2H), 7.47-7.32 (m, 3H), 6.49 (s, 1H), 4.06-3.84 (m, 1H), 2.86-2.76 (d, 2H), 1.70-1.39 (m, 2H), 1.06-0.88 (t, 3H); ¹³C-nmr (deuteriochloroform): 168.9, 161.9, 129.5, 128.4, 126.9, 125.2, 99.9, 70.9, 33.1, 29.4, 9.5; ms: m/z (relative intensity): 217 (M⁺, 12), 199 (25), 188 (41), 160 (23), 159 (100), 131 (31), 130

(20), 105 (76), 77 (58), 51 (15).

Anal. Calcd. for C₁₃H₁₅NO₂: C, 71.86; H, 6.96; N, 6.45. Found: C, 71.89; H, 6.93; N, 6.48.

4-(1-Hydroxypropyl)-3-methyl-5-phenylisoxazole (4).

This compound was obtained as a white solid, mp 70-71° (from ethanol) [8].

3-(2-Phenyl-2-hydroxyethyl)-5-phenylisoxazole (5).

This compound was obtained as a white solid, mp 99-100° (from ethanol-water) [4].

4-(Hydroxybenzyl)-3-methyl-5-phenylisoxazole (6).

This compound was obtained as a white solid, mp 95-96° (from ethanol) [8].

3-(2-Hydroxy-2-methylpropyl)-5-phenylisoxazole (7).

This compound was obtained as a white solid, mp 67-68° (from ethanol); ¹H-nmr (deuteriochloroform): 7.83-7.70 (m, 2H), 7.50-7.38 (m, 3H), 6.49 (s, 1H), 2.89 (s, 2H), 2.42 (s, 1H), 1.33 (s, 6H); ¹³C-nmr (deuteriochloroform): 169.5, 161.6, 130.0, 128.9, 127.5, 125.8, 100.8, 70.1, 40.0, 29.4; ms: m/z (relative intensity): 217 (M⁺, 3), 202 (6), 159 (70), 131 (16), 130 (9), 105 (39), 77 (47), 59 (100), 54 (15), 51 (22), 43 (39).

Anal. Calcd for C₁₃H₁₅NO₂: C, 71.86; H, 6.96; N, 6.45. Found: C, 71.93; H, 6.97; N, 6.42

4-(1-Hydroxy-1-methylethyl)-3-methyl-5-phenylisoxazole (8).

This compound was obtained as white solid, mp 60-61° (from ethanol); ¹H-nmr (deuteriochloroform): 7.45-7.34 (m, 5H), 2.45 (s, 3H), 1.46 (s, 6H); ¹³C-nmr (deuteriochloroform): 165.1, 159.0, 129.9, 129.7, 128.9, 128.1, 96.1, 68.7, 31.3, 12.8; ms: m/z (relative intensity): 217 (M⁺, 10), 202 (100), 160 (26), 145 (7), 105 (46), 82 (17), 77 (34), 51 (8), 43 (10).

Anal. Calcd. for C₁₃H₁₅NO₂: C, 71.86; H, 6.96; N, 6.45. Found: C, 71.88; H, 6.98; N, 6.44.

3-(2-Phenyl-2-hydroxypropyl)-5-phenylisoxazole (9).

This compound was obtained as a white solid, mp 113-114° (from ethanol-water) [4].

4-(1-Phenyl-1-hydroxyethyl)-5-phenyl-3-methylisoxazole (10).

This compound was obtained as a mixture with **9** and was identified from the ¹H-nmr and ¹³C-nmr. It was previously reported at literature [8].

3-(2-Hydroxy-3-butenyl)-5-phenylisoxazole (11).

This compound was obtained as a white solid, mp 56-57° (from ethanol); ¹H-nmr (deuteriochloroform): 7.79-7.60 (m, 2H), 7.48-7.26 (m, 3H), 6.47 (s, 1H), 6.18-5.77 (m, 1H), 5.42-5.06 (m, 2H), 4.64-4.40 (m, 1H), 2.97-2.89 (d, 2H); ¹³C-nmr (deuteriochloroform): 169.5, 161.4, 139.4, 129.9, 128.8, 127.3, 125.6, 115.4, 100.1, 70.9, 33.9; ms: m/z (relative intensity): 215 (M⁺, 6), 198 (35), 186 (10), 159 (47), 143 (8), 131 (27), 130 (18), 105 (76), 103 (11), 102 (12), 77 (100), 63 (10), 57 (46), 55 (18), 54 (22), 53 (15), 51 (49), 50 (16), 43 (13).

Anal. Calcd. for C₁₃H₁₃NO₂: C, 72.53; H, 6.09; N, 6.51. Found: C, 72.59; H, 6.11; N, 6.49.

3-(2-Hydroxy-2-methyl-3-butenyl)-5-phenylisoxazole (12).

This compound was obtained as a white solid, mp 46-47° (from ethanol); ¹H-nmr (deuteriochloroform): 7.78-7.66 (m, 2H), 7.42-7.33 (m, 3H), 6.51 (s, 1H), 6.19-5.84 (dd, 1H), 5.37-

4.98 (m, 2H), 3.03 (s, 1H), 2.95 (s, 2H), 1.37 (s, 3H); ¹³C-nmr (deuteriochloroform): 169.2, 161.0, 143.9, 129.8, 128.7, 127.3, 125.6, 112.6, 100.9, 38.7, 27.6; ms: m/z (relative intensity): 229 (M⁺, 3), 212 (13), 159 (53), 131 (18), 130 (14), 105 (44), 77 (70), 71 (33), 63 (10), 55 (28), 54 (11), 53 (16), 52 (11), 51 (41), 50 (15), 43 (100), 42 (11), 41 (23).

Anal. Calcd for C₁₄H₁₅NO₂: C, 73.34; H, 6.59; N, 6.11. Found: C, 73.36; H, 6.56; N, 6.09.

3-(2,2-Diphenyl-2-hydroxyethyl)-5-phenylisoxazole (13).

This compound was obtained as a white solid, mp 162-163^o (from ethanol); ¹H-nmr (DMSO-d₆): 7.71-7.17 (m, 15H), 6.23 (s, 1H), 3.74 (s, 2H); ¹³C-nmr (DMSO-d₆-deuteriochloroform): 169.1, 161.8, 146.8, 130.2, 129.2, 128.3, 127.1, 126.4, 125.8, 101.3, 39.1; ms: m/z (relative intensity): 341 (M⁺, 1), 236 (25), 222 (8), 183 (31), 159 (51), 105 (100), 77 (64), 51 (12).

Anal. Calcd. for C₂₃H₁₉NO₂: C, 80.92; H, 5.61; N, 4.10. Found: C, 80.89; H, 5.63; N, 4.09.

3-Methyl-5-phenyl-4-trimethylsilylisoxazole (14).

This compound was obtained as a white solid, mp 55-56^o (from ethanol); ¹H-nmr (deuteriochloroform): 7.50-7.39 (m, 5H), 2.36 (s, 3H), 0.16 (s, 9H); ¹³C-nmr (deuteriochloroform): 175.0, 163.3, 129.6, 128.8, 127.9, 107.9, 12.9, -0.06; ms: m/z (relative intensity): 231 (M⁺, 25), 217 (19), 216 (100), 200 (31), 142 (36), 135 (15), 127 (10), 105 (14), 77 (32), 73 (11), 51 (13), 45 (12), 43 (15).

Anal. Calcd for C₁₃H₁₇NOSi: C, 67.50; H, 7.41; N, 6.06. Found: C, 67.49; H, 7.43; N, 6.03.

5-Phenyl-3-trimethylsilylmethylisoxazole (15).

This compound was obtained as a white solid, mp 59-60^o (from ethanol); ¹H-nmr (deuteriochloroform): 7.85-7.81 (m, 2H), 7.52-7.30 (m, 3H), 6.31 (s, 1H), 2.21 (s, 2H), 0.20 (s, 9H); ¹³C-nmr (deuteriochloroform): 168.8, 162.2, 129.5, 128.8, 128.6, 125.4, 99.6, 15.9, -1.90; ms: m/z (relative intensity): 231 (M⁺, 42), 189 (7), 140 (6), 115 (11), 105 (7), 102 (6), 77 (27), 73 (100), 43 (9).

Anal. Calcd. for C₁₃H₁₇NOSi: C, 67.50; H, 7.41; N, 6.06. Found: C, 67.52; H, 7.42; N, 6.04.

4-(*N,N*-Dimethylcarbamoyl)-3-methyl-5-phenylisoxazole (16).

This compound was obtained as a white solid, mp 49-50^o (from ethanol); ¹H-nmr (deuteriochloroform): 7.68-7.66 (m, 2H), 7.45-7.42 (m, 3H), 3.12 (s, 3H), 2.78 (s, 3H), 2.32 (s, 3H); ¹³C-nmr (deuteriochloroform): 165.1, 163.5, 158.8, 130.6, 129.1, 126.2, 111.0, 37.9, 34.8, 10.3; ms: m/z (relative intensity): 230 (M⁺, 20), 229 (12), 186 (44), 105 (100), 77 (68), 72 (10), 51 (20).

Anal. Calcd for C₁₃H₁₅N₂O₂: C, 67.50; H, 6.54; N, 12.11. Found: C, 67.52; H, 6.51; N, 12.07.

3-(*N,N*-Dimethylcarbamoylmethyl)-5-phenylisoxazole (17).

This compound was obtained as a white solid, mp 76-77^o (from ethanol); ¹H-nmr (deuteriochloroform): 7.77-7.74 (m, 2H), 7.44-7.41 (m, 3H), 6.63 (s, 1H), 3.81 (s, 2H), 3.09 (s, 3H), 2.97 (s, 3H); ¹³C-nmr (deuteriochloroform): 169.9, 168.1, 159.2, 130.1, 128.9, 127.3, 125.7, 100.2, 37.7, 35.7, 31.8; ms: m/z (relative intensity): 230 (M⁺, 7), 186 (7), 159 (12), 130 (9), 105 (35), 102 (8), 77 (55), 72 (100), 51 (21).

Anal. Calcd. for C₁₃H₁₅N₂O₂: C, 67.50; H, 6.54; N, 12.11. Found: C, 67.59; H, 6.55; N, 12.07.

3-Methyl-5-phenylisoxazole-4-carbaldehyde (18).

This compound was obtained as a white solid, mp 85-87^o

(from ethanol) [9].

3-Methyl-4-(1-oxoethyl)-5-phenylisoxazole (19).

This compound was obtained in a very low yield and it could only be detected by ms: m/z (relative intensity): 201 (M⁺, 36), 200 (17), 186 (48), 105 (100), 77 (40), 51 (12).

3-(2-Oxopropyl)-5-phenylisoxazole (20).

This compound was obtained as a white solid, mp 80-81^o (from ethanol-water) [4].

3-(2-Oxo-4-phenyl-3-butenyl)-5-phenylisoxazole (21).

This compound was obtained as a white solid, mp 134-135^o (from ethanol); ¹H-nmr (deuteriochloroform): 7.75-7.35 (m, 11H), 6.85-6.80 (d, 1H), 6.56 (s, 1H), 4.09 (s, 2H); ¹³C-nmr (deuteriochloroform): 194.4, 170.1, 158.5, 144.6, 133.9, 130.9, 130.1, 128.9, 128.8, 128.5, 128.3, 128.1, 127.8, 127.6, 126.6, 125.7, 124.8, 100.2, 38.2; ms: m/z (relative intensity): 289 (M⁺, 2), 261 (8), 144 (5), 132 (10), 131 (100), 105 (20), 103 (58), 102 (9), 77 (60), 57 (7), 51 (20), 43 (20).

Anal. Calcd. for C₁₉H₁₅NO₂: C, 78.87; H, 5.23; N, 4.84. Found: C, 78.83; H, 5.24; N, 4.82.

1,1-Bis(5-phenyl-3-isoxazolymethyl)-3-phenyl-2-propen-1-ol (22).

This compound was obtained as a white solid, mp 182-183^o (from toluene); ¹H-nmr (DMSO-d₆): 7.79-7.19 (m, 15H), 6.88 (s, 2H), 6.59-6.41 (dd, 2H), 3.09 (s, 4H); ¹³C-nmr (DMSO-d₆): 167.9, 160.8, 136.6, 134.3, 129.9, 129.0, 128.4, 128.1, 127.2, 126.1, 125.3, 101.7, 72.7, 37.3; ms: m/z (relative intensity): 448 (M⁺, 2), 343 (7), 291 (21), 290 (99), 159 (27), 158 (69), 131 (61), 130 (14), 105 (100), 103 (54), 91 (11), 77 (64), 51 (10).

Anal. Calcd. for C₂₉H₂₄N₂O₃: C, 77.66; H, 5.39; N, 6.25. Found: C, 77.58; H, 5.41; N, 6.26.

3-Ethyl-5-phenylisothiazole (23).

This compound was obtained as a yellow liquid, bp 100-102^o at 1.5 mm; ¹H-nmr (deuteriochloroform): 7.53-7.27 (m, 5H), 7.14 (s, 1H), 2.96-2.68 (q, 2H), 1.41-1.22 (t, 3H); ¹³C-nmr (deuteriochloroform): 173.1, 167.0, 130.8, 129.0, 128.8, 126.2, 118.8, 26.4, 12.8; ms: m/z (relative intensity): 190 (M⁺, +1, 14), 189 (M⁺, 77), 134 (16), 121 (13), 89 (6), 77 (19), 63 (11), 51 (19).

Anal. Calcd. for C₁₁H₁₁NS: C, 69.80; H, 5.86; N, 7.40. Found: C, 69.84; H, 5.85; N, 7.43.

3-(2-Phenylethyl)-5-phenylisothiazole (24).

This compound was obtained as a yellow solid, mp 90-91^o (from ethanol); ¹H-nmr (deuteriochloroform): 7.58-7.25 (m, 10H), 7.12 (s, 1H), 3.12 (s, 4H); ¹³C-nmr (deuteriochloroform): 171.2, 167.3, 141.0, 130.8, 129.3, 129.0, 128.2, 126.4, 126.0, 119.6, 57.8, 34.9; ms: m/z (relative intensity): 266 (M⁺, +1, 22), 265 (M⁺, 100), 264 (17), 188 (33), 144 (12), 134 (18), 121 (14), 91 (69), 77 (19), 65 (18), 51 (12).

Anal. Calcd. for C₁₇H₁₅NS: C, 76.94; H, 5.70; N, 5.28. Found: C, 76.98; H, 5.68; N, 5.30.

3-Pentyl-5-phenylisothiazole (25).

This compound was obtained as a yellow liquid, bp 175^o at 0.9 mm; ¹H-nmr (deuteriochloroform): 7.55-7.23 (m, 5H), 7.09 (s, 1H), 2.85-2.67 (t, 2H), 1.82-1.21 (m, 6H), 0.95-0.88 (t, 3H); ¹³C-nmr (deuteriochloroform): 171.6, 166.3, 130.4, 128.4, 125.7, 118.7, 32.7, 30.9, 22.0, 21.8, 13.3; ms: m/z (relative

intensity): 231 (M^+ , 14), 202 (10), 189 (10), 188 (36), 175 (100).

Anal. Calcd. for $C_{14}H_{17}NS$: C, 72.68; H, 7.41; N, 6.05. Found: C, 72.66; H, 7.37; N, 6.06.

3,4-Dimethyl-5-phenylisothiazole (26).

This compound was obtained as a mixture with **23** and was identified from the 1H -nmr, ^{13}C -nmr and ms spectra; 1H -nmr (deuteriochloroform): 7.63-7.34 (m, 5H), 2.45 (s, 3H), 2.21 (s, 3H); ^{13}C -nmr (deuteriochloroform): 167.5, 167.3, 129.1, 128.8, 128.6, 126.5, 18.5, 12.1, ms: m/z (relative intensity): 189 (M^+ , 28), 148 (10), 147 (30), 121 (12), 115 (96), 103 (14), 89 (18), 77 (43), 69 (31), 63 (28), 51 (48), 42 (100).

3-(2-Oxopropyl)-5-phenylisothiazole (27).

This compound was obtained as a yellow solid, mp 67-68° (from ethanol); 1H -nmr (deuteriochloroform): 7.65-7.22 (m, 6H), 3.96 (s, 2H), 2.25 (s, 3H); ^{13}C -nmr (deuteriochloroform): 203.9, 167.7, 163.8, 129.7, 128.3, 126.8, 125.6, 120.3, 48.1, 29.8; ms: m/z (relative intensity): 217 (M^+ , 12), 175 (100), 134 (21), 115 (10), 102 (10), 77 (15), 51 (12), 43 (45).

Anal. Calcd. for $C_{12}H_{11}NOS$: C, 66.33; H, 5.10; N, 6.45. Found: C, 66.39; H, 5.08; N, 6.45.

1,3-Bis(5-phenyl-3-isothiazolyl)-2-methyl-2-propanol (28).

This compound was obtained as a yellow solid, mp 105-106° (from ethanol); 1H -nmr (deuteriochloroform): 7.56-7.28 (m, 12H), 4.37 (s, 1H), 3.07 (s, 4H), 1.31 (s, 3H); ^{13}C -nmr (deuteriochloroform): 169.0, 167.0, 130.7, 129.4, 129.1, 126.5, 121.5, 72.4, 44.4, 27.6; ms: m/z (relative intensity): 392 (M^+ , 8), 391 (30), 348 (100), 347 (80), 218 (96), 188 (29), 175 (97), 134 (44), 121 (30), 102 (17), 77 (23).

Anal. Calcd. for $C_{22}H_{20}N_2OS_2$: C, 67.30; H, 5.14; N, 7.14. Found: C, 67.39; H, 5.13; N, 7.11.

3-(2-Oxopentyl)-5-phenylisothiazole (29).

This compound was obtained as a yellow solid, mp 44-45° (from ethanol); 1H -nmr (deuteriochloroform): 7.60-7.28 (m, 6H), 3.90 (s, 2H), 2.59-2.51 (t, 2H), 1.83-1.47 (m, 2H), 0.97-0.79 (t, 3H); ^{13}C -nmr (deuteriochloroform): 205.6, 167.7, 163.8, 130.4, 129.2, 128.8, 126.2, 120.1, 46.9, 44.1, 16.7, 13.3; ms: m/z (relative intensity): 245 (M^+ , 9), 175 (100), 134 (18), 77 (13), 71 (30), 51 (10), 43 (74).

Anal. Calcd. for $C_{14}H_{15}NOS$: C, 68.54; H, 6.16; N, 5.71. Found: C, 68.53; H, 6.13; N, 5.74.

1,1-Bis(5-phenyl-3-isothiazolylmethyl)-1-butanol (30).

This compound was obtained as a white solid, mp 80-81° (from ethanol) 1H -nmr (deuteriochloroform): 7.59-7.27 (m, 12H), 4.38 (s, 1H), 3.06 (s, 4H), 1.54-1.25 (m, 4H), 0.95-0.85 (t, 3H); ^{13}C -nmr (deuteriochloroform): 169.1, 166.9, 130.7, 129.4, 129.0, 126.5, 121.6, 74.5, 42.7, 42.1, 17.1, 14.5; ms: m/z (relative intensity): 420 (M^+ , 1), 246 (100), 176 (20), 175 (48), 134 (19), 43 (10).

Anal. Calcd. for $C_{24}H_{24}N_2OS_2$: C, 68.54; H, 5.75; N, 6.66. Found: C, 68.48; H, 5.76; N, 6.64.

3-(2-Oxo-4-phenyl-3-butenyl)-5-phenylisothiazole (31).

This compound was obtained as a yellow solid, mp 128-129° (from ethanol); 1H -nmr (deuteriochloroform): 7.81-7.13 (m, 11H), 6.97-6.65 (dd, 2H), 4.21 (s, 2H); ^{13}C -nmr (deuteriochloroform): 195.2, 167.3, 164.1, 144.3, 134.2, 130.7, 129.5, 129.1, 128.9, 128.4, 126.6, 125.2, 120.3, 45.7; ms: m/z (relative inten-

sity): 305 (M^+ , 17), 277 (57), 228 (19), 175 (16), 147 (16), 131 (100), 121 (14), 115 (21), 103 (98), 102 (37), 89 (13), 77 (97), 76 (18), 63 (12), 51 (28), 43 (15).

Anal. Calcd. for $C_{19}H_{15}NOS$: C, 74.72; H, 4.95; N, 4.59. Found: C, 74.77; H, 4.94; N, 4.56.

1,1-Bis(5-phenyl-3-isothiazolylmethyl)-3-phenyl-2-propenol (32).

This compound was obtained as a white solid, mp 175-176° (from ethanol); 1H -nmr (deuteriochloroform): 7.58-7.14 (m, 17H), 6.71-6.24 (dd, 2H), 5.26 (s, 1H), 3.22 (s, 4H); ^{13}C -nmr (deuteriochloroform): 165.6, 163.1, 134.1, 132.2, 127.8, 126.3, 125.5, 125.1, 124.2, 123.4, 119.1, 71.3, 41.4; ms: m/z (relative intensity): 480 (M^+ , 3), 307 (23), 306 (100), 202 (10), 175 (72), 174 (98), 147 (24), 134 (32), 131 (33), 121 (13), 115 (19), 103 (58), 77 (30).

Anal. Calcd. for $C_{29}H_{24}N_2OS_2$: C, 72.47; H, 5.03; N, 5.83. Found: C, 72.46; H, 5.05; N, 5.84.

3-Benzoylmethyl-5-phenylisothiazole (33).

This compound was obtained as a yellow solid, mp 66-67° (from ethanol); 1H -nmr (deuteriochloroform): 8.10-7.98 (m, 2H), 7.53-7.33 (m, 8H), 7.28 (s, 1H), 4.49 (s, 2H); ^{13}C -nmr (deuteriochloroform): 195.3, 167.8, 164.1, 136.1, 133.2, 130.5, 129.3, 128.9, 128.5, 126.3, 120.7, 43.3; ms: m/z (relative intensity): 279 (M^+ , 2), 251 (12), 105 (100), 77 (50), 51 (14).

Anal. Calcd. for $C_{17}H_{13}NOS$: C, 73.09; H, 4.69; N, 5.01. Found: C, 73.04; H, 4.71; N, 5.00.

5-Phenyl-3-trimethylsilylmethylisothiazole (34).

This compound was obtained as a colourless liquid, bp 210° at 0.9 mm; 1H -nmr (deuteriochloroform): 7.60-7.29 (m, 5H), 6.99 (s, 1H), 2.38 (s, 2H), 0.08 (s, 9H); ^{13}C -nmr (deuteriochloroform): 169.9, 166.4, 131.0, 128.9, 126.2, 119.4, 25.0, -1.7; ms: m/z (relative intensity): 247 (M^+ , 33), 232 (39), 115 (21), 77 (10), 73 (100), 72 (13), 45 (29).

Anal. Calcd. for $C_{13}H_{17}NSSi$: C, 63.10; H, 6.92; N, 5.66. Found: C, 63.12; H, 6.93; N, 5.64.

1,2-Bis(5-phenyl-3-isothiazolyl)ethane (35).

This compound was obtained as a white solid, mp 182-183° (from ethanol) [5].

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