The Reaction of Carbanions from 3-Methyl-5-phenylisoxazole with Electrophilic Compounds

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The reactivity of 3-methyl-5-phenylisoxazole against electrophilic compounds in the presence of different bases is studied. With *n*-BuLi, alkylated products at C-4 position and C-3 methyl group, and, in a few cases, dialkylated isoxazoles are obtained. When the reactions are carried out with LICA, the nature of the alkylated products depends on the alkyl halide used. By using LICA-TMEDA, as deprotonating system, regioselective reaction at the C-3 methyl group is found.

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Although 3,5-dimethylisoxazole has three reaction sites in the electrophilic substitution reactions in the presence of bases, the results of deuterium exchange reaction have shown the stereoselective reaction with electrophiles on C-5 methyl group [1] or first at the 5-methyl group and then at the C-3 methyl group in a sequential manner [2]. Electron withdrawing 4-substituents accelerate deprotonation, while electron-donating 4-substituents retard it [3,4].

5-Alkylisoxazolium salts are deprotonated even more readily than the corresponding isoxazoles and can undergo condensation reactions under the influence of comparatively weak bases. In these compounds, however, the 3-methyl group might compete; the ratio of deprotonation at C-3 and/or C-5 is markedly influenced by the nature of the base [5].

In this paper, we have chosen a substrate without acidic properties at the C-5 position, 3-methyl-5-phenylisoxazole, in order to study the reactivity of the C-3 methyl group, and the possible reaction at C-4 position, with electrophiles in the presence of different bases.

Results and Discussion.

3-Methyl-5-phenylisoxazole (**1**) reacts with alkyl halides in the presence of different bases to lead to products whose nature depends on the base used. When *n*-butyllithium is used and the base is added into the isoxazole derivative followed by the reaction with an equimolar amount of alkyl halide, the corresponding alkylated products on the C-4 position and the C-3 methyl group are obtained, we found similar results in previous reactions of this substrate with *n*-BuLi and oxo compounds [6]. But if the isoxazole compound is added into *n*-BuLi and then treated with the alkyl halide not only the aforementioned products are obtained, but in some cases dialkylated isoxazoles at both positions are found. In this reaction, it is suggested that the dianion is formed when the substrate is added into an excess amount of base.

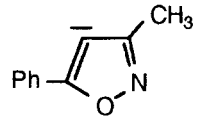
By the treatment of **1** with lithium isopropylcyclohexylamide (LICA) as the deprotonating agent no dialkylated derivatives can be detected and only a small proportion of alkylated product at C-4 position is found when methyl iodide is used. In contrast with the results described above, by using lithium isopropylcyclohexylamide and *N,N,N',N'*-tetramethylethylendiamine (TMEDA) exclusively the product at the C-3 methyl group is obtained.

The observations suggest that the reactivity of 3-methyl-5-phenylisoxazole against halo compounds in the presence of each base used is quite different.

In compound **1** two reaction sites, the C-3 methyl group and the C-4 position, can be deprotonated and both anions are stabilized.

The lithiation of 3-methyl-5-phenylisoxazole at the C-4 position implies the formation of a vinylic carbanion **10** where the negative charge is directly placed on a carbon atom of the double bond while the lithiation at the C-3 methyl group leads to an allylic carbanion **11**.

Scheme I



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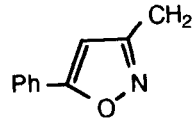

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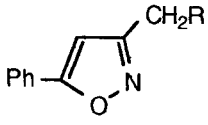
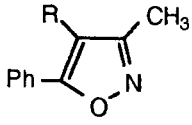
Studies of equilibrium constants in the exchange reactions between organolithium compounds and halo compounds show the different stability of carbanions [7].

The vinylic carbanion **10** is considerably more stable than the corresponding saturated carbanion since the anion is on a carbon atom with sp^2 hybridation and the anion stability increases simultaneously with the amount of s character at the carbanion atom. The allylic carbanion **11** is more stable than the vinylic one due to the additional resonance possibility and so the vinylic carbanion will be

more reactive with electrophile agents to give the alkylation products.

Scheme II

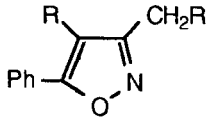




2 : R = CH_3 **3** : R = CH_3

5 : R = $CH_2C_6H_5$ **6** : R = $CH_2C_6H_5$

7 : R = $(CH_2)_3CH_3$ **8** : R = $(CH_2)_3CH_3$



4 : R = CH_3

9 : R = $(CH_2)_3CH_3$

Among the bases examined, *n*-BuLi is found to give the highest yields of alkylation at the C-4 position since it is the sterically smallest base used. Lithium isopropylcyclohexylamide (LICA) is a hindered base and it has a difficult approach to the C-4 position.

The basicity of lithium reagents is greatly increased by complexing agents such as TMEDA which chelates the cation leaving a greater negative charge on the carbanionic site. The organolithium compounds-TMEDA complexes are capable of rapidly removing protons from allylic positions [8-10] and this can explain the stereoselective formation of the alkylated products at the C-3 methyl group with all the alkyl halides used when the 5-methyl-3-phenylisoxazole is treated with the LICA-TMEDA system.

Methyl iodide leads to higher yields than the other alkyl halides. It can be interpreted by its high reactivity and its small size which allows it to approach all the carbanionic sites.

When the electrophile used is the benzyl bromide and the base *n*-BuLi the major products are 1,2-diphenylethane (30%) and 1,2-diphenylethene (25%). This can be explained by a lithium-bromide exchange reaction between the benzyl bromide and *n*-BuLi followed by the reaction of this compound with benzyl bromide.

On the basis of the results described above, the LICA-TMEDA system is particularly effective and allows highly stereoselective formation of the carbanion on C-3 methyl group and so we have chosen it for studying the reactivity of the 5-phenyl-3-isoxazolylmethyl carbanion with different electrophiles.

In the case of carbonyl compounds, as the electrophile reagents, under the conditions mentioned above, **1** gives hydroxy derivatives of the isoxazole compound. When the reaction with benzaldehyde is carried out with LICA as base without TMEDA the yield is lower (37%) than using the system LICA-TMEDA (70%) but no product on the C-4 position could be detected.

The results of these reactions are shown in Table 1.

The chemical behavior of the 5-phenyl-3-isoxazolylmethyl carbanion against α,β-unsaturated carbonyl compounds is observed to be similar with Grignard reagents. That is,

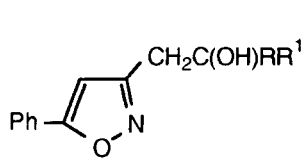
Table 1

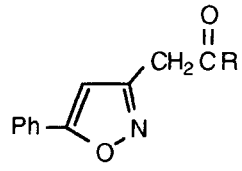
Reactions of 3-Methyl-5-phenylisoxazole with Halo Compounds

Halo Compounds	Base	Reaction Conditions Time (hours) (-78°C)	Time (hours) (25°C)	Products (%)
CH_3I	*n*-BuLi [a]	2.5	2	**2** (20), **3** (39)
CH_3I	*n*-BuLi [b]	4	1	**2** (12), **3** (78), **4** (4)
CH_3I	LICA	4	1	**2** (33), **3** (8)
CH_3I	LICA-TMEDA	5	–	**2** (27)
$C_6H_5CH_2Br$	*n*-BuLi [a]	4	2	**5** (9), **6** (3)
$C_6H_5CH_2Br$	*n*-BuLi [b]	4	1	**5** (7), **6** (3)
$C_6H_5CH_2Br$	LICA	4	1	**5** (31)
$C_6H_5CH_2Br$	LICA-TMEDA	5	–	**5** (23)
$CH_3(CH_2)_3Br$	*n*-BuLi [a]	5	2	**7** (12), **8** (4)
$CH_3(CH_2)_3Br$	*n*-BuLi [b]	4	1	**7** (16), **8** (17), **9** (8)
$CH_3(CH_2)_3Br$	LICA	4	1	**7** (13)
$CH_3(CH_2)_3Br$	LICA-TMEDA	5	–	**7** (27)

[a] The base is added into the isoxazole solution. [b] The isoxazole solution is added into the *n*-BuLi solution.

Scheme III





12 : R = H , $R^1 = C_6H_5$

13 : R = H , $R^1 = CH{=}CHC_6H_5$

14 : $R = CH_3$, $R^1 = C_6H_5$

15 : $R = CH_3$, $R^1 = CH{=}CHC_6H_5$

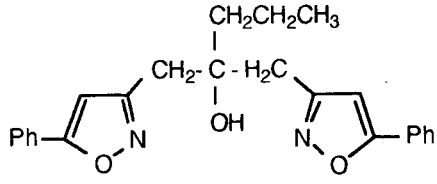
16 : R , $R^1 = (CH_2)_4$

17 : R , $R^1 = (CH_2)_5$

18 : $R = CH_3$

19 : $R = (CH_2)_2CH_3$

20 : $R = C_6H_5$



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the carbanion attacks on the carbonyl carbon to give a corresponding alcohol derivative. The results of these reactrions are summarized in Table 2.

Table 2

Reaction of 3-Methyl-5-phenylisoxazole with Oxo Compounds in the Presence of LICA-TMEDA

Oxo Compound	Reaction Conditions [a] Time (hours)	Temp (°C)	Products (%)
Benzaldehyde	5	-78	**12** (70)
Benzaldehyde [b]	5	-78	**12** (30)
Cinnamaldehyde	5	-78	**13** (39)
Acetophenone	5	-78	**14** (87)
Bencylidenacetophenone	5	-78	**15** (64)
Cyclopentanone	5	-78	**16** (80)
Cyclohexanone	5	-78	**17** (58)

[a] The molar ratio used in all these cases was LICA:TMEDA:isox:electroph = 1, 1.67, 1, 1. [b] This reaction has been carried out without using TMEDA.

Reactions of **1** with esters give the respective oxo compounds. In the case of the reaction with ethyl butyrate, the tertiary alcohol, 1,1-di(5-phenyl-3-isoxazolylmethyl)-1-hydroxybutane (**21**), is obtained together with the oxo compound 3-(2-oxopentyl)-5-phenylisoxazole (**19**), as a result of the introduction of two isoxazole rings in the carbonyl group.

Finally, under the same conditions, treatment of compound **1** with nitriles leads to carbonyl compounds after acidic hydrolysis of respective imines. These results are summarized in Table 3.

Table 3

Reation of 5-Phenyl-3-methylisoxazoyl Carbanoin (**1**) with Esters and Nitriles

Electrophile	Reaction Conditions Time (hours)	Temp (°C)	Products (%)
CH_3CO_2Et	5	-78	**18** (49)
$CH_3(CH_2)_2CO_2Et$	5	-78	**19** (24), **21** (21)
C_6H_5CN	5	-78	**20** (33)
CH_3CN	5	-78	**18** (30)

In conclusion, by using the LICA-TMEDA system as the deprotonating agent, we have found the regioselective reaction of 5-phenyl-3-methylisoxazole (**1**) at the C-3 methyl group with different electrophiles. In addition to this, the highest yields can be obtained with this system and when carbonyl compounds are used as electrophile reagent.

EXPERIMENTAL

Melting points are uncorrected. 3-Methyl-5-phenylisoxazole was prepared by established procedures [11]. The infrared spectra were recorded in potassium bromide pellets in the case of solids or as a film in the case of liquids, using a Perkin-Elmer Model 577 or a Pye Unicam SP-1100 spectrophotometers. Nuclear magnetic resonance spectra were determined at 60 MHz on a Hitachi-Perkin-Elmer R-24 B or a Bruker A.C.80 spectrometers using deuteriochloroform or carbon tetrachloride solutions and with TMS as the standard reference; chemical shifts were measured on the δ scale. Electron ionization mass spectra were obtained on a Hewlett-Packard GC/MS system 5988A. Elemental analyses were determined on 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.

1. By the Use of *n*-Butyllithium.

The reaction with *n*-BuLi has been carried out following two different methods.

a) A solution of isoxazole (0.010 mole) in dry tetrahydrofurane (10 ml) was cooled to -78°. An hexane solution (1.6 *M*) of *n*-butyllithium (0.011 mole) was added slowly under dry nitrogen. The solution was stirred and kept at -78° for 1 hour and then was treated with a solution of the halo compound (0.011 mole) in 10 ml of dry THF. The reaction mixture was stirred at -78° for a suitable time (Table 1). After two hours at room temperature, the mixture was hydrolysed with dilute hydrochloric acid (1:10). Then the layers were separated and the aqueous layer extracted with ether. The combined extracts were dried (magnesium sulfate) and evaporated to give the crude products. The products were separated and purified by flash column chromatography with hexane-ethyl acetate (8:1) as the eluent.

b) An hexane solution (1.6 *M*) of *n*-butyllithium (0.011 mole) in dry THF (10 ml) was cooled at -78°. A solution of isoxazole (0.010 mole) in dry THF (10 ml) was added over a period of 1 hour under dry nitrogen. After cooling and stirring for 1 hour, a solution of the halo derivative (0.011 mole) in 10 ml of dry THF was added. The reaction mixture was kept at -78° for four hours and then was allowed to warm at room temperature. One hour later the mixture was hydrolysed with dilute hydrochloric acid (1:10). The layers were separated and the aqueous layer extracted with ether. After being dried over anhydrous magnesium sulfate, the organic layer was evaporated to give the crude products which were purified by flash chromatography using hexane-ethyl acetate (8:1) as eluent.

2. By the Use of Lithium Isopropylcyclohexylamide (LICA).

To a solution of isopropylcyclohexylamine (0.011 mole) in 10 ml of dry THF at -78°, an hexane solution (1.6 *M*) of *n*-BuLi (0.011 mole) was added. The solution was stirred for 15 minutes at -78°. Then the system was allowed to warm at room temperature. After 30 minutes the reaction mixture was cooled at -78° and a solution of isoxazole (0.010 mole) in 10 ml of dry THF was slowly added. After being stirred for 1 hour the electrophile compound (0.011 mole) in 10 ml of dry THF was added, cooling and stirring was continued for 4 hours. The system was allowed to reach room temperature and stirred for another hour. After a usual work-up, the residue was purified by flash column chromatography on silicagel with an hexane-ethyl acetate mixture (8:1).

3-Ethyl-5-phenylisoxazole (**2**).

This compound was obtained as a yellow liquid, bp 100-102° at 0.8 mm; ^{1}H-nmr (deuteriochloroform): 7.86-7.24 (m, 5H), 6.29 (s, 1H), 2.64 (q, 2H), 1.22 (t, 3H); ^{13}C-nmr (deuteriochloroform): 168.9, 165.2, 129.3-125.1, 98.4, 19.1, 12.1; ms: m/z (relative intensity) 173 ($M^{+\cdot}$, 86), 144 (60), 105 (100), 96 (15), 77 (63), 68 (18), 51 (15).

Anal. Calcd. for $C_{11}H_{11}NO$: C, 76.27; H, 6.40; N, 8.09. Found: C, 76.37; H, 6.37; N, 8.05.

3,4-Dimethyl-5-phenylisoxazole (**3**).

This compound was obtained as a white solid, mp 47-48° (from ethanol); ^{1}H-nmr (deuteriochloroform): 7.67-7.63 (m, 5H), 2.27 (s, 3H), 2.15 (s, 3H); ^{13}C-nmr (deuteriochloroform): 169.0, 160.8, 129.1-126.4, 109.1, 10.0, 8.0; ms: m/z (relative intensity) 173 ($M^{+\cdot}$, 100), 144 (15), 105 (53), 104 (74), 68 (16), 77 (68).

Anal. Calcd. for $C_{11}H_{11}NO$: C, 76.27; H, 6.40; N, 8.09. Found: C, 76.31; H, 6.38; N, 8.10.

3-Ethyl-4-methyl-5-phenylisoxazole (**4**).

This compound could not be isolated but it was separated by gc/ms; ms: m/z (relative intensity) 187 ($M^{+\cdot}$, 61), 117 (28), 105 (99), 103 (50), 82 (19), 77 (100), 51 (31). It was also identified from the ^{1}H-nmr of the mixture **4** and **3**; ^{1}H-nmr (deuteriochloroform): 7.86-7.24 (m, 5H), 2.20 (q, 2H), 2.22 (s, 3H), 1.35 (t, 3H).

3-(2-Phenylethyl)-5-phenylisoxazole (**5**).

This compound was obtained as a white solid, mp 69-70° (from ethanol); ^{1}H-nmr (deuteriochloroform): 7.75-7.32 (m, 5H), 7.19 (s, 5H), 6.2 (s, 1H), 2.98 (s, 4H); ^{13}C-nmr (deuteriochloroform): 169.4, 163.7, 124.9-125.6, 94.2, 34.3, 27.9; ms: m/z (relative intensity) 249 ($M^{+\cdot}$, 71), 144 (58), 105 (100), 91 (99), 77 (71), 65 (18), 51 (21).

Anal. Calcd. for $C_{17}H_{15}NO$: C, 81.90; H, 6.06; N, 5.62. Found: C, 81.85; H, 6.07; N, 5.64.

4-Benzyl-3-methyl-5-phenylisoxazole (**6**).

This compound was obtained as a white solid, mp 56-57° (from ethanol); ^{1}H-nmr (deuteriochloroform): 7.70-7.06 (m, 10H), 3.95 (s, 2H), 2.13 (s, 3H); ^{13}C-nmr (deuteriochloroform): 168.2, 161.2, 129.6-126.8, 111.8, 28.5, 10.3; ms: m/z (relative intensity) 249 ($M^{+\cdot}$, 80), 207 (36), 179 (21), 144 (27), 105 (73), 77 (100), 51 (2).

Anal. Calcd. for $C_{17}H_{15}NO$: C, 81.90; H, 6.06; N, 6.42. Found: C, 81.91; H, 6.06; N, 5.60.

3-Pentyl-5-phenylisoxazole (**7**).

This compound was obtained as a yellow liquid, bp 158-160° at 0.3 mm; ^{1}H-nmr (deuteriochloroform): 7.82-7.36 (m, 5H), 6.33 (s, 1H), 2.70 (t, 2H), 1.83-1.20 (m, 6H), 0.95 (t, 3H); ^{13}C-nmr (deuteriochloroform): 168.9, 164.0, 129.4-125.2, 98.7, 30.9, 27.6, 25.6, 21.9, 13.5; ms: m/z (relative intensity) 215 ($M^{+\cdot}$, 6), 172 (37), 159 (100), 131 (17), 105 (43), 77 (25).

Anal. Calcd. for $C_{14}H_{17}NO$: C, 78.10; H, 7.96; N, 6.51. Found: C, 78.12; H, 7.93; N, 6.48.

4-Butyl-3-methyl-5-phenylisoxazole (**8**).

This compound was obtained as a yellow liquid, bp 150-152° at 0.3 mm; ^{1}H-nmr (deuteriochloroform): 7.71-7.35 (m, 5H), 2.54 (t, 2H), 2.24 (s, 3H), 1.71-1.15 (m, 4H), 0.91 (t, 3H); ^{13}C-nmr (deuteriochloroform): 164.3, 160.6, 129.2-126.6, 114.0, 31.8, 22.5, 13.7, 10.2; ms: m/z (relative intensity) 215 ($M^{+\cdot}$, 44), 172 (100), 118 (6), 105 (58), 103 (12), 77 (20).

Anal. Calcd. for $C_{14}H_{17}NO$: C, 78.10; H, 7.96; N, 6.51. Found: C, 78.17; H, 7.95; N, 6.48.

4-Butyl-3-pentyl-5-phenylisoxazole (**9**).

This compound could not be isolated but it was separated by gc/ms; ms: m/z (relative intensity) 271 ($M^{+\cdot}$, 6), 228 (41), 200 (13), 158 (11), 144 (42), 130 (31), 105 (100), 77 (73); It was also identified from the ^{1}H-nmr of the mixture **8** and **9**; ^{1}H-nmr (deuteriochloroform): 7.86-7.30 (m, 5H), 2.65 (t, 2H), 2.55 (t, 2H), 1.90-1.10 (m, 10H), 0.95 (t, 6H).

3. By the Use of Lithium Isopropylcyclohexylamide and *N,N,N',N'*-Tetramethylethylendiamine.

A solution of isopropylcyclohexylamine (0.011 mole) in dry THF (10 ml) was cooled at -78°. An hexane solution (1.6 *M*) of *n*-BuLi (0.011 mole) was added and after 15 minutes at -78°, the system was allowed to reach room temperature and stirred for 30 minutes. Then a solution of TMEDA (0.016 mole) in 10 ml of dry THF was added. After 5 minutes the system was cooled at -78° and a solution of the isoxazole (0.010 mole) in 10 ml of dry THF was added dropwise. The resulting solution was stirred for 30 minutes and then the corresponding electrophile (0.011 mole) in dry THF (10 ml) was added. Five hours later the reaction mixture was allowed to warm to room temperature over a 30 minute period.

A saturated ammonium chloride solution (50 ml) was added, the organic layer was separated and the aqueous layer extracted with diethyl ether, the combined extracts were dried with anhydrous magnesium sulfate and evaporated to give a residue which was purified by flash column chromatography or crystallization.

3-(2-Phenyl-2-hydroxyethyl)-5-phenylisoxazole (**12**).

This compound was obtained as a white solid, mp 99-100° (from ethanol-water); ^{1}H-nmr (deuteriochloroform): 7.81-7.76 (m, 5H), 7.72-7.66 (m, 5H), 6.36 (s, 1H), 5.15 (t, 1H), 3.17 (d, 2H); ^{13}C-nmr (deuteriochloroform): 169.8, 162.9, 129.8-125.6, 100.2, 72.3, 35.9; ms: m/z (relative intensity) 265 ($M^{+\cdot}$, 7), 159 (100), 131 (14), 105 (41), 79 (31), 77 (66), 51 (16).

Anal. Calcd. for $C_{17}H_{15}NO_2$: C, 76.96; H, 5.70; N, 5.28. Found: C, 76.94; H, 5.70; N, 5.25.

3-(4-Phenyl-2-hydroxy-3-butenyl)-5-phenylisoxazole (**13**).

This compound was obtained as a yellow solid, mp 120-121° (from ethanol); ^{1}H-nmr (deuteriochloroform): 7.83-7.43 (m, 10H), 6.49-6.35 (m, 2H), 4.70 (q, 1H), 3.05 (d, 2H); ^{13}C-nmr (deuteriochloroform): 169.7, 162.9, 130.9-124.8, 99.7, 69.9, 33.5; ms: m/z (relative intensity) 291 ($M^{+\cdot}$, 10), 246 (4), 186 (10), 159 (100), 131 (32), 115 (27), 105 (50), 77 (68), 51 (20).

Anal. Calcd. for $C_{19}H_{17}NO_2$: C, 78.33; H, 5.88; N, 4.81. Found: C, 78.25; H, 5.91; N, 4.83.

5-Phenyl-3-(2-phenyl-2-hydroxypropyl)isoxazole (**14**).

This compound was obtained as a white solid, mp 113-114° (from ethanol-water); ^{1}H-nmr (deuteriochloroform): 7.70-7.24 (m, 10H), 6.10 (s, 1H), 3.22 (s, 2H), 1.64 (s, 3H); ^{13}C-nmr (deuteriochloroform): 169.8, 162.7, 129.5-124.5, 100.6, 73.0, 40.2, 29.3; ms: m/z (relative intensity) 279 ($M^{+\cdot}$, 1), 236 (16), 159 (100), 131 (15), 121 (33), 105 (51), 77 (55), 42 (53).

Anal. Calcd. for $C_{18}H_{17}NO_2$: C, 77.40; H, 6.13; N, 5.01. Found: C, 77.44; H, 6.15; N, 4.99.

3-(2-Hydroxy-2-methyl-4-phenyl-3-butenyl)-5-phenylisoxazole (**15**).

This compound was obtained as a white solid, mp 98-99° (from ethanol-water); ^{1}H-nmr (deuteriochloroform): 7.78-7.73 (m, 5H), 7.43-7.39 (m, 5H), 6.60-6.49 (m, 2H), 3.08 (s, 2H), 1.48 (s, 3H); ^{13}C-nmr (deuteriochloroform): 170.0, 162.3, 135.4, 130.0-125.7, 100.8, 72.2, 39.3, 28.2; ms: m/z (relative intensity) 305 ($M^{+\cdot}$, 9), 200 (11), 159 (100), 147 (77), 129 (30), 105 (71), 91 (17), 77 (71), 51 (18), 43 (53).

Anal. Calcd. for $C_{20}H_{19}NO_2$: C, 78.66; H, 6.27; N, 4.59. Found: C, 78.67; H, 6.30; N, 4.58.

3-(1-Hydroxycyclopentyl)methyl-5-phenylisoxazole (**16**).

This compound was obtained as a white solid, mp 93-94° (from ethanol); ^{1}H-nmr (deuteriochloroform): 7.82-7.37 (m, 5H), 6.50 (s, 1H), 2.99 (s, 2H), 1.73 (m, 10H); ^{13}C-nmr (deuteriochloroform): 169.1, 161.9, 129.8-125.5, 100.5, 80.8, 39.6, 37.6, 23.6; ms: m/z (relative intensity) 243 ($M^{+\cdot}$, 14), 224 (7), 214 (10), 201 (37), 186 (10), 159 (100), 131 (18), 105 (40), 85 (11), 77 (35), 55 (11), 51 (9).

Anal. Calcd. for $C_{15}H_{17}NO_2$: C, 74.05; H, 7.04; N, 5.76. Found: C, 74.04; H, 7.02; N, 5.74.

3-(1-Hydroxycyclohexyl)methyl-5-phenylisoxazole (**17**).

This compound was obtained as a white solid, mp 100-101° (from ethanol-water); ^{1}H-nmr (deuteriochloroform): 7.82-7.32 (m, 5H), 6.49 (s, 1H), 2.87 (s, 2H), 1.55 (m, 10H); ^{13}C-nmr (deuteriochloroform): 257 ($M^{+\cdot}$, 7), 214 (9), 201 (6), 159 (100), 131 (13), 105 (25), 99 (9), 81 (13), 77 (22), 51 (5).

Anal. Calcd. for $C_{16}H_{19}NO_2$: C, 74.69; H, 7.44; N, 5.44. Found: C, 74.72; H, 7.41; N, 5.46.

5-Phenyl-3-(2-oxopropyl)isoxazole (**18**).

This compound was obtained as a white solid, mp 80-81° (from ethanol-water); ^{1}H-nmr (deuteriochloroform): 7.74-7.39 (m, 5H), 6.52 (s, 1H), 3.85 (s, 2H), 2.28 (s, 3H); ^{13}C-nmr (deuteriochloroform): 203.3, 170.0, 157.9, 130.0-125.6, 100.0, 40.7, 29.6; ms: m/z (relative intensity) 201 ($M^{+\cdot}$, 27), 159 (100), 131 (22), 105 (29), 89 (5), 77 (44), 51 (17), 43 (39).

Anal. Calcd. for $C_{12}H_{11}NO_2$: C, 71.63; H, 5.51; N, 6.96. Found: C, 71.54; H, 5.53; N, 6.98.

5-Phenyl-3-(2-oxopentyl)isoxazole (**19**).

This compound was obtained as a white solid, mp 51-52° (from ethanol-water); ^{1}H-nmr (deuteriochloroform): 7.90-7.10 (m, 5H), 6.50 (s, 1H), 3.80 (s, 2H), 2.50 (t, 2H), 1.90-1.20 (m, 2H), 0.95 (t, 3H).

Anal. Calcd. for $C_{14}H_{15}NO_2$: C, 73.34; H, 6.59; N, 6.11. Found: C, 73.39; H, 6.61; N, 6.08.

3-Benzoylmethyl-5-phenylisoxazole (**20**).

This compound was obtained as a white solid, mp 115-116° (from petroleum ether); ^{1}H-nmr (deuteriochloroform): 8.13-7.39 (m, 10H), 6.59 (s, 1H), 4.42 (s, 2H); ^{13}C-nmr (deuteriochloroform): 194.6, 170.0, 158.3, 135.9-125.7, 100.3, 36.2; ms: m/z (relative intensity) 263 ($M^{+\cdot}$, 15), 186 (3), 158 (2), 105 (100), 103 (10), 77 (50), 51 (10).

Anal. Calcd. for $C_{17}H_{13}NO_2$: C, 77.55; H, 4.98; N, 5.32. Found: C, 77.47; H, 4.99; N, 5.35.

1,1-Bis(5-phenyl-3-isoxazolylmethyl)-1-butanol (**21**).

This compound was obtained as a white solid, mp 143-144° (from ethanol-water); ^{1}H-nmr (deuteriochloroform): 7.84-7.38 (m, 10H), 6.55 (s, 2H), 2.97 (s, 4H), 1.56-1.52 (m, 4H), 1.10 (t, 3H);

^{13}C-nmr (deuteriochloroform): 169.5, 161.5, 130.0-125.7, 101.7, 73.4, 41.9, 36.6, 35.9, 17.0, 14.4; ms: m/z (relative intensity) 388 (M^+, 1), 345 (3), 283 (2), 230 (100), 159 (16), 105 (18), 77 (14).

Anal. Calcd. for $C_{24}H_{24}N_2O_3$: C, 74.2; H, 6.23; N, 7.21. Found: C, 74.27; H, 6.24; N, 7.19.

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