Pergamon

Tetrahedron, Vol. 52, No. 2, pp. 605-616, 1996

0040-4020/96 $15.00 + 0.00

0040-4020(95)00899-3

Selective Formation of Aminoxyls or Oxaziridines by Oxidation of 2,2,4,4-tetrasubstituted Oxazolidines

Mourad Hamdani,[a] Denise Scholler,[b] James Bouquant[b] and Alexandre Feigenbaum*[a]

[a]INRA, 23 rue C Ader, 51100 Reims

[b]URA 459 CNRS, 51062 Reims Cedex, France

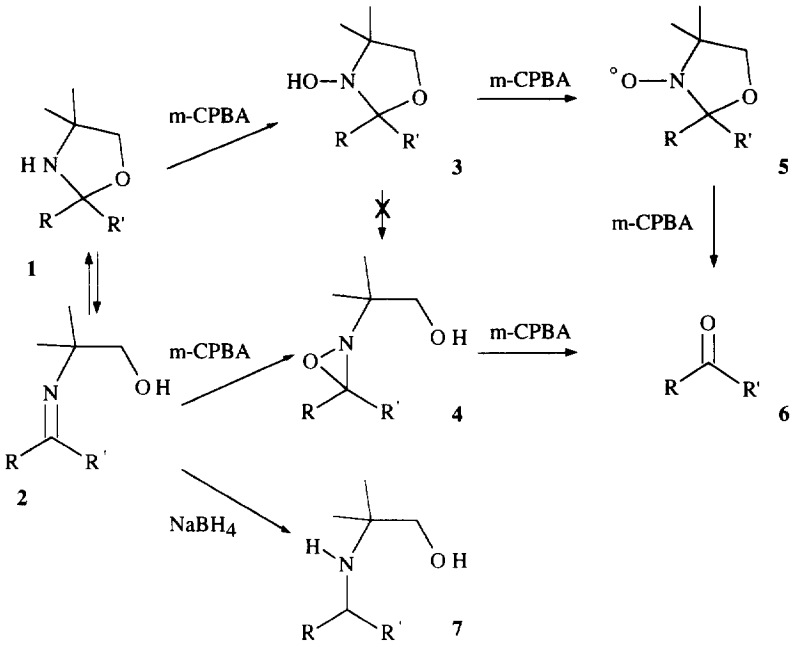
ABSTRACT: The reactivity of 2,2,4,4-tetrasubstituted-1,3-oxazolidines **1** with m-chloroperbenzoic acid was reinvestigated. Aminoxyls **5** are isolated in good yields in ether at -15 °C, or in anhydrous dichloromethane at 0 °C. Oxaziridines **4** are promoted at room temperature, or in the presence of an acid. In any case, short reaction times prevented the degradation of aminoxyls and oxaziridines. The competition between oxaziridines **4** and aminoxyls **5** is ruled by the oxazolidine imine equilibrium.

INTRODUCTION

In the presence of peracids, oxazolidines **1** are known to be converted in moderate to bad yields into hydroxylamines **3** and to aminoxyls **5** (Scheme 1)[1-5] which are widely used as spin probes in biological membranes and in polymers studies.[6,7]

On the other hand, oxazolidines **1** can be in equilibrium with N-(2-hydroxyalkyl)imines **2** (Scheme I).[8] They could be used as a convenient starting point for the chemistry of imines **2**, if experimental conditions for the control of the equilibrium could be defined. If peracids could react with the imine form **2**, one could expect the formation of N-(2-hydroxyalkyl)oxaziridines **4**, which are interesting intermediates in organic synthesis.[9]

We decided to reinvestigate the oxidation of oxazolidines **1** by m-chloroperbenzoic acid (m-CPBA), with two objectives : improve the yields of aminoxyls **5** and obtain selectively oxaziridines **4**. This could be achieved by shifting the oxazolidine imine equilibrium through a control of the temperature, of the nature of the solvent and the presence of acid.

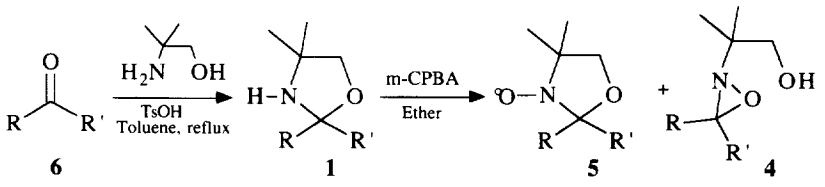


Reported yields for the oxidation of **1** into **5** :
R = CH_3 ; R' = n-C_5H_{11} : 26 %[1], 11 %[2] ; R, R' = -$(CH_2)_5$-) : 42 %[1], 30 %[2]
R = CH_3 ; R' = $(CH_2)_2$-COOEt : 63 %[3] ; R = n-C_6H_{13} ; R' = $(CH_2)_{10}$-COOMe : 35 %[4], 15 %[5]

Scheme 1: Reactivity of oxazolidines 1 and its derivatives

RESULTS AND DISCUSSIONS

Oxazolidines **1a - i** were prepared quantitatively and with high purity (≥ 95% evaluated by ^1H NMR), by condensation of the parent ketones **6a - i** with 2-amino-2-methylpropanol (Scheme 2).[3]



a [1,2] : R = CH_3 ; R' = n-C_5H_{11} f : R = R' = n-C_3H_7
b : R = CH_3 ; R' = n-C_6H_{13} g : R = R' = n-C_4H_9
c : R = CH_3 ; R' = n-C_7H_{15} h : R = R' = n-C_5H_{11}
d : R = CH_3 ; R' = n-C_8H_{17} i : R = R' = n-C_9H_{19}
e : R = CH_3 ; R' = n-C_9H_{19}

Scheme 2: Synthesis of oxaziridines 4 and aminoxyls 5

When oxazolidines **1a**, **1e** (unsymmetrical), **1h** and **1i** (symmetrical) were treated in the usual conditions described in literature (1.5 equiv of m-CPBA added to an ice-cold solution of oxazolidine in ether, the resulting solution being allowed to stand at room temperature for 24 h),[1] the corresponding aminoxyls **5a**, **5e**, **5h**, **5i** and oxaziridines[10] **4a**, **4e**, **4h**, **4i** were obtained respectively (Entry A, table 1). However, in these reactions, the parent ketone **6** was by far the major product (Entry A, table 1). When aminoxyl **5i** and oxaziridine **4i** were treated by m-CPBA in ether at room temperature they were quantitatively converted into the starting ketone **6**. These results show that **6** arises from the degradation of aminoxyl **5** and oxaziridine **4**.

The possibility that competition between aminoxyls **5** and oxaziridines **4** could involve hydroxylamine **3** was ruled out as follows : **3a** was isolated by using only 1 equiv. of m-CPBA and was then allowed to react with m-CPBA. This gave only aminoxyl **5a** (Scheme 1). The rel.ative amounts of aminoxyl and oxaziridine seem to be ruled by the oxazolidine imine equilibrium.

The oxazolidine imine equilibrium constant is strongly dependent on the structure of the oxazolidine ring, on the temperature and on the solvents,[8] the oxazolidine form being strongly favoured in case of 2,2,4,4-tetrasubstituted oxazolidines like **1**. When **1g** was heated in NMR spectrometer, the corresponding imine **2g** could not even be detected even in d_6-DMSO at temperatures up to 70°C, conditions which favour the imine.[8a] However **2g** could be trapped by treating **1g** with sodium borohydride, which lead to a slow and clean conversion into amine **7g**.

We decided to investigate for reaction conditions where **4** and **5** could be obtained by shifting the oxazolidine imine equilibrium, but would not be degradated into **6**.

By keeping the reaction mixture at 0 °C for 1 hour, the formation of ketone **6** was completely suppressed (Entry B, table 1). These conditions appeared to be suitable for the formation of symmetrical (R=R') aminoxyls **3f-3i** (Entry B, table 1). With unsymmetrical ($R \neq R'$) oxazolidines, small amounts of oxaziridines were still formed at 0 °C. Since the competition between aminoxyls **5** and oxaziridines **4** seems to be influenced by temperature (compare entries A and B, table 1), we lowered the temperature down to -15 °C ; unsymmetrical ($R \neq R'$) aminoxyls **5a-5e** were then obtained in good yields as the only reaction products (Entry C, table 1).

Another factor which could shift the equilibrium is the presence of m-chlorobenzoic acid (m-CBA) in the reaction medium. When the reaction was carried out in methylene chloride at 0 °C,

aminoxyl **5a** was selectively obtained in 74 % yield. In these reaction conditions m-CBA is insoluble and precipitates before protonation of the oxazolidine takes place. A similar yield was obtained in ether in presence of 2-dimethylaminopyridine (used as base). A sterical hindrance to protonation could also explain the lower tendency of symmetrical oxazolidines to yield oxaziridines at 0 °C.

It was thus possible to define conditions which allowed the selective formation of aminoxyls **5** on a preparative scale, the yields of literature being strongly improved. The oxazolidines can also be converted into aminoxyls by dimethyldioxirane.[11]

Entry	Starting substance	Aminoxyl **5** Yield[a] (%)	Oxaziridine **4** Yield[a] (%)	Ketone **6** Yield[a](%)
A	**1a**	10	8	45
	1e	14	12	43
	1h	15	13	39
	1i	28	11	30
B	**1f**	66	6	b
	1g	70	b	b
	1h	66	b	b
	1i	70	b	b
C	**1a**	68	b	b
	1b	68	b	b
	1c	72	b	b
	1d	74	b	b
	1e	76		
D	**1a**	74	b	b

(A) : addition of m-CPBA to an ice cold solution of **1** in ether, followed by 24 h at RT
(B) : addition like (A) but followed by 1 h at 0 °C
(C) : addition of m-CPBA to a solution of **1** in ether at -15 °C followed by 1 h at -15 °C
(D): like (B), but ether was replaced by CH_2Cl_2
[a] after purification by flash chromatography [b] Not observed

Table 1 : Yields of reactions of oxazolidines 1 with m-CPBA

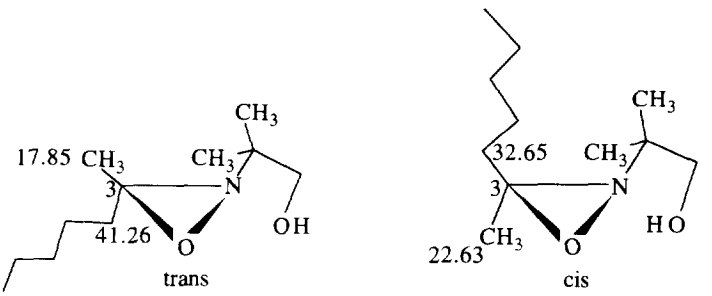
Having now strongly improved the yield of aminoxyls **5**, we then investigated for selective obtention of oxaziridines **4**. The formation of oxaziridines **4** from oxazolidines **1** had never been reported in literature. Conducting the reaction at room temperature promotes oxaziridine, but unfortunately also its decomposition into the ketone **6**. We thought that increasing the concentration of an acid in the medium could shift the equilibrium towards the imine, even at lower temperatures. This hypothesis was confirmed by the following experiments : when the oxidation of **1a** in ether was

carried out in the presence of 0.5 equiv. of p-toluenesulfonic acid (TsOH), the yield of oxaziridine **4a** was strongly improved. However, it markedly depended on the rate of addition. **4a** was obtained in a 60% yield when the peracid was added over one hour and in 37% yield over 20 min. During the slow addition of peracid, protonation of **1a** had time to take place, confirming once more that the competition between aminoxyls and oxaziridines could be controlled.

It was thus possible to define conditions which allowed the selective obtention of oxaziridines **4** on a preparative scale.

Oxaziridines **4a**, **4e**, **4h**, and **4i** could be stored at room temperature for months, without any detectable decomposition. This can be explained by the presence of two structural features : the tertiary alkyl group[12-14] and an intramolecular hydrogen bond with the OH group (**4a**, CCl_4 : 3550 cm^{-1}, independant of the dilution).

Unsymmetrical oxaziridines **4a** and **4e** were isolated as mixtures of cis/trans diastereoisomers (in a 10/90 ratio), which were separated by flash chromatography. The structures of these isomers were attributed on the basis of ^1H and ^{13}C NMR data. The carbon atom linked to the position 3 of oxaziridine ring is expected to be shifted upfield when it is cis to the alkyl substituent of the nitrogen (Scheme 3).[15,16,17]. In addition a slight nuclear Overhauser effect on ($C\underline{H}_3$)$_2$-N (1.03 and 1.21 ppm) (0,5%) was observed when the 3-$C\underline{H}_3$ group (1.63 ppm) of trans **4a** was irradiated. This effect was not observed for the cis isomer. Each pure diastereoisomer was converted slowly into a cis/trans mixture. A 10/90 equilibrium was reached after four days at room temperature in both cases, as a result of a slow inversion of the nitrogen atom.[18]



Scheme 3: ^{13}C Chemical shift of oxaziridines 4a cis and trans

CONCLUSION

We have found conditions which orient the oxidation of oxazolidines by m-CPBA selectively towards the oxaziridines **4** or aminoxyls **5**. Oxaziridines **4** are largely promoted when the reaction is conducted at room temperature, or in the presence of TsOH at 0 °C. Aminoxyls **5** were isolated in good yields at -15 °C in ether or at 0 °C in anhydrous dichloromethane. In any case, short reaction times prevented the degradation of **4** and **5** into the starting ketone **6**.

EXPERIMENTAL SECTION

NMR spectra were recorded in $CDCl_3$ on a BRUKER AC 250 spectometer (250 MHz for ^1H and 62.9 MHz for ^{13}C). Chemical shifts of ^1H NMR spectra were expressed in parts per million downfield rel.ative to internal TMS ($\delta = 0$). Mass spectra were recorded on a JEOL D 300 mass spectrometer at 70 eV.

NMR spectra of aminoxyls were recorded after in situ reduction of their $CDCl_3$ solutions into the corresponding N-hydroxylamines with freshly distilled phenylhydrazine.[19]

All reactions were monitored by thin-layer chromatography carried out on 0.25 mm E. Merck Silicagel plates (60 F_{254}). Flash chromatography was performed on Silicagel Merck 60 (particle size 0.04 - 0.063 mm). Toluene, methylene chloride and 2-amino-2-methylpropan-1-ol were purified by distillation from calcium hydride. Commercial ketones **6** (Aldrich) and 3-chloroperbenzoic acid (70-75%, balance 3-chlorobenzoic and water, Janssen) were used as received.

Preparation of Oxazolidines. According to the procedure of Joseph *et al.*[3] the ketone **6** (20 mmol), 2-amino-2-methyl-1-propanol (3.6 g, 40 mmol) and p-toluenesulfonic acid (50 mg) were refluxed in dry toluene (15 ml) for 24 to 60 hours with azeotropic water removal by means of a Dean-Stark apparatus. The resulting liquid was diluted in ether (50 ml), washed with a saturated $NaHCO_3$ aqueous solution (15 ml) then with water (3 x 25 ml) and dried over $MgSO_4$. Evaporation of the solvent gave quantitatively the crude oxazolidine derivative, which was used without purification.

2,4,4-Trimethyl-2-pentyloxazolidine (1a). ^1H NMR ($CDCl_3$) δ 3.58 (d, J = 8.0 Hz, 1H, OCH_2), 3.51 (d, J = 8.0 Hz, 1H, OCH_2), 1.65 - 1.55 (m, 2H, CH_2), 1.45 - 1.20 (m, 6H, 3 CH_2), 1.33 (s, 3H, CH_3), 1.27 (s, 3H, CH_3), 1.24 (s, 3H, CH_3), 0.90 (t, J = 6.5 Hz, 3H, CH_3); ^{13}C

NMR ($CDCl_3$) δ 97.21 (O<u>C</u>N), 76.83 (O<u>C</u>H_2), 59.04 (<u>C</u>$(CH_3)_2$), 41.58 (<u>C</u>H_2), 38.23 (<u>C</u>H_2), 28.40 (<u>C</u>H_3), 28.18 (<u>C</u>H_3), 26.21 (<u>C</u>H_3), 24.48 (<u>C</u>H_2), 22.59 (<u>C</u>H_2), 13.58 (<u>C</u>H_3).

2-Hexyl-2,4,4-trimethyloxazolidine (1b). ^1H NMR ($CDCl_3$) δ 3.57 (d, J = 8.0 Hz, 1H, OCH_2), 3.51 (d, J = 8.0 Hz, 1H, OCH_2), 1.65 - 1.55 (m, 2H, CH_2), 1.43 - 1.20 (m, 8H, 4 CH_2), 1.33 (s, 3H, CH_3), 1.26 (s, 3H, CH_3), 1.24 (s, 3H, CH_3), 0.90 (t, J = 6.5 Hz, 3H, CH_3); ^{13}C NMR ($CDCl_3$) δ 97.30 (O<u>C</u>N), 76.88 (O<u>C</u>H_2), 59.14 (<u>C</u>$(CH_3)_2$), 41.70 (<u>C</u>H_2), 31.87 (<u>C</u>H_2), 29.77 (<u>C</u>H_2), 28.46 (<u>C</u>H_3), 28.24 (<u>C</u>H_3), 26.27 (<u>C</u>H_3), 24.83 (<u>C</u>H_2), 22.63 (<u>C</u>H_2), 14.12 (<u>C</u>H_3).

2-Heptyl-2,4,4-trimethyloxazolidine (1c). ^1H NMR ($CDCl_3$) δ 3.52 (d, J = 8.0 Hz, 1H, OCH_2), 3.56 (d, J = 8.0 Hz, 1H, OCH_2), 1.65 - 1.55 (m, 2H, CH_2), 1.40 - 1.20 (m, 10H, 5 CH_2), 1.32 (s, 3H, CH_3), 1.26 (s, 3H, CH_3), 1.24 (s, 3H, CH_3), 0.90 (t, J = 6.5 Hz, 3H, CH_3); ^{13}C NMR ($CDCl_3$) δ 97.47 (O<u>C</u>N), 76.76 (O<u>C</u>H_2), 59.53 (<u>C</u>$(CH_3)_2$), 41.38 (<u>C</u>H_2), 31.82 (<u>C</u>H_2), 29.97 (<u>C</u>H_2), 29.27 (<u>C</u>H_2), 28.06 (<u>C</u>H_3), 27.88 (<u>C</u>H_3), 25.96 (<u>C</u>H_3), 24.77 (<u>C</u>H_2), 22.98 (<u>C</u>H_2), 14.09 (<u>C</u>H_3).

2,4,4-Trimethyl-2-octyloxazolidine (1d). ^1H NMR ($CDCl_3$) δ 3.52 (d, J = 8.0 Hz, 1H, OCH_2), 3.56 (d, J = 8.0 Hz, 1H, OCH_2), 1.60 - 1.50 (m, 2H, CH_2), 1.40 - 1.20 (m, 12H, 6 CH_2), 1.32 (s, 3H, CH_3), 1.26 (s, 3H, CH_3), 1.24 (s, 3H, CH_3), 0.90 (t, J = 6.5 Hz, 3H, CH_3); ^{13}C NMR ($CDCl_3$) δ 97.35 (O<u>C</u>N), 76.95 (O<u>C</u>H_2), 59.19 (<u>C</u>$(CH_3)_2$), 41.75 (<u>C</u>H_2), 31.99 (<u>C</u>H_2), 30.16 (<u>C</u>H_2), 29.65 (<u>C</u>H_2), 29.36 (<u>C</u>H_2), 28.52 (<u>C</u>H_3), 28.29 (<u>C</u>H_3), 26.33 (<u>C</u>H_3), 24.93 (<u>C</u>H_2), 22.76 (<u>C</u>H_2), 14.18 (<u>C</u>H_3).

2,4,4-Trimethyl-2-nonyloxazolidine (1e). ^1H NMR ($CDCl_3$) δ 3.55 (d, J = 8.0 Hz, 1H, OCH_2), 3.48 (d, J = 8.0 Hz, 1H, OCH_2), 1.60 - 1.45 (m, 2H, CH_2), 1.35 - 1.10 (m, 14H, 7 CH_2), 1.33 (s, 3H, CH_3), 1.26 (s, 3H, CH_3), 1.24 (s, 3H, CH_3), 0.90 (t, J = 6.5 Hz, 3H, CH_3); ^{13}C NMR ($CDCl_3$) δ 97.22 (O<u>C</u>N), 76.79 (O<u>C</u>H_2), 59.08 (<u>C</u>$(CH_3)_2$), 41.58 (<u>C</u>H_2), 31.86 (<u>C</u>H_2), 30.02 (<u>C</u>H_2), 29.52 (<u>C</u>H_2), 29.30 (<u>C</u>H_2), 28.33 (<u>C</u>H_3), 28.11 (<u>C</u>H_3), 26.17 (<u>C</u>H_3), 24.79 (<u>C</u>H_2), 22.63 (2 <u>C</u>H_2), 14.50 (<u>C</u>H_3).

4,4-Dimethyl-2,2-dipropyloxazolidine (1f). ^1H NMR ($CDCl_3$) δ 3.51 (s, 2H, OCH_2), 1.65 - 1.50 (m, 4H, 2 CH_2), 1.35 - 1.20 (m, 4H, 2 CH_2), 1.15 (s, 6H, 2 CH_3), 0.90 (t, J = 6.5 Hz, 6H, 2 CH_3); ^{13}C NMR ($CDCl_3$) δ 99.17 (O<u>C</u>N), 76.73 (O<u>C</u>H_2), 58.77 (<u>C</u>$(CH_3)_2$), 40.94 (2 <u>C</u>H_2), 28.46 (2 <u>C</u>H_3), 17.77 (2 <u>C</u>H_2), 14.50 (2 <u>C</u>H_3).

2,2-Dibutyl-4,4-dimethyloxazolidine (1g). ^1H NMR ($CDCl_3$) δ 3.50 (s, 2H, OCH_2), 1.62 - 1.50 (m, 4H, 2 CH_2), 1.40 - 1.20 (m, 8H, 4 CH_2), 1.15 (s, 6H, 2 CH_3), 0.90 (t, J = 6.5 Hz, 6H, 2 CH_3); ^{13}C NMR ($CDCl_3$) δ 99.10 (O<u>C</u>N), 76.91 (O<u>C</u>H_2), 59.24 (<u>C</u>$(CH_3)_2$), 38.63 (2 <u>C</u>H_2), 28.88 (2 <u>C</u>H_2), 27.08 (2 <u>C</u>H_3), 23.53 (2 <u>C</u>H_2), 14.41 (2 <u>C</u>H_3).

4,4-Dimethyl-2,2-dipentyloxazolidine (1h). ^1H NMR ($CDCl_3$) δ 3.50 (s, 2H, OCH_2), 1.65 - 1.50 (m, 4H, 2CH_2), 1.40 - 1.20 (m, 12H, 6 CH_2), 1.15 (s, 6H, 2 CH_3), 0.90 (t, J = 6.5 Hz,

6H, 2 CH_3); ^{13}C NMR ($CDCl_3$) δ 99.33 (O<u>C</u>N), 76.63 (O<u>C</u>H_2), 58,86 (<u>C</u>$(CH_3)_2$), 38.51 (2 <u>C</u>H_2), 31.49 (2 <u>C</u>H_2), 28.55 (2 <u>C</u>H_3), 24.08 (2 <u>C</u>H_2), 22.50 (2 <u>C</u>H_2), 14.06 (2 <u>C</u>H_3).

4,4-Dimethyl-2,2-dinonyloxazolidine (1i). ^1H NMR ($CDCl_3$) δ 3.49 (s, 2H, OCH_2), 1.65 - 1.50 (m, 4H, 2CH_2), 1.40 - 1.20 (m, 14H, 7 CH_2), 1.15 (s, 6H, 2 CH_3), 0.90 (t, J = 6.5 Hz, 6H, 2 CH_3); ^{13}C NMR ($CDCl_3$) δ 99.36 (O<u>C</u>N), 76.62 (O<u>C</u>H_2), 58,85 (<u>C</u>$(CH_3)_2$), 38.60 (2 <u>C</u>H_2), 31.95 (2 <u>C</u>H_2), 30.14 (2 <u>C</u>H_2), 29.62 (2 <u>C</u>H_2), 29.50 (2 <u>C</u>H_2), 29.37 (2 <u>C</u>H_2), 28.58 (2 <u>C</u>H_3), 24.58 (2 <u>C</u>H_2), 22.72 (2 <u>C</u>H_2), 14.13 (2 <u>C</u>H_3).

Oxidation of oxazolidines into aminoxyls : A solution of 70-75% m-CPBA (2.96 g, 15 mmol) in ether (50 ml) is added dropwise over 20 min. to a cold solution of the appropriate oxazolidine (10 mmol) in ether (50 ml) at -15 °C for **1a-e** and 0 °C for **1f-i**. After one hour the resulting solution was washed with a 4% Na_2CO_3 aqueous solution (4 x 20 ml) and once with saturated aqueous sodium chloride solution. The ether layer was dried over $MgSO_4$ and evaporated under vaccum to produce a yellow liquid which is purified by flash chromatography (pentane 95% - ethyl acetate 5%).

2,4,4-Trimethyl-2-pentyloxazolidine-N-oxyl (5a). ^1H NMR ($CDCl_3$, as N-hydroxyamine) δ 3.64 (d, J = 8.4 Hz, 1H, OCH_2), 3.55 (d, J = 8.4 Hz, 1H, OCH_2), 1.65 - 1.50 (m, 2H, CH_2), 1.40 - 1.20 (m, 6H, 3 CH_2), 1.30 (s, 3H, CH_3), 1.16 (s, 3H, CH_3), 1.13 (s, 3H, CH_3), 0.90 (t, J = 6.5 Hz, 3H, CH_3); ^{13}C NMR ($CDCl_3$, as N-hydroxyamine) δ 100.21 (O<u>C</u>N), 74.29 (O<u>C</u>H_2), 63.64 (<u>C</u>$(CH_3)_2$), 41.19 (<u>C</u>H_2), 32.37 (<u>C</u>H_2), 25.16 (<u>C</u>H_3), 23.80 (<u>C</u>H_2), 22.66 (<u>C</u>H_2), 21.99 (2 <u>C</u>H_3), 14.04 (<u>C</u>H_3); MS m/z (rel. intensity) 200 (M^+, (6%)), 144 (16%), 129 (30%), 115 (100%), 97 (14%), 71 (26%), 56 (100%), 55 (60%). Anal. Calcd for $C_{11}H_{22}NO_2$: C, 65.95; H, 11.08; N, 7.00. Found: C, 65.79; H, 10.97; N, 6.96.

2-Hexyl-2,4,4-trimethyloxazolidine-N-oxyl (5b). ^1H NMR ($CDCl_3$, as N-hydroxyamine) δ 3.62 (d, J = 8.4 Hz, 1H, OCH_2), 3.54 (d, J = 8.0 Hz, 1H, OCH_2), 1.65 - 1.55 (m, 2H, CH_2), 1.4 - 1.20 (m, 8H, 4 CH_2), 1.31 (s, 3H, CH_3), 1.17 (s, 3H, CH_3), 1.12 (s, 3H, CH_3), 0.90 (t, J = 6.5 Hz, 3H, CH_3); ^{13}C NMR ($CDCl_3$, as N-hydroxyamine) δ 99.74 (O<u>C</u>N), 74.26 (O<u>C</u>H_2), 63.21 (<u>C</u>$(CH_3)_2$), 40.47 (<u>C</u>H_2), 31.84 (<u>C</u>H_2), 29.78 (<u>C</u>H_2), 25.13 (<u>C</u>H_3), 24.08 (<u>C</u>H_2), 22.80 (<u>C</u>H_2), 21.85 (<u>C</u>H_3), 21.68 (<u>C</u>H_3), 14.05 (<u>C</u>H_3); MS m/z (rel. intensity) 214 (M^+, (10%)), 158 (54%), 129 (100%), 115 (22%), 86 (30%), 71 (45%), 69 (100%), 58 (96%), 56 (100%), 55 (60%). Anal. Calcd for $C_{12}H_{24}NO_2$: C, 67.23; H, 11.29; N, 6.45. Found: C, 67.35; H, 11.28; N, 6.48.

2-Heptyl-2,4,4-trimethyloxazolidine-N-oxyl (5c). ^1H NMR ($CDCl_3$, as N-hydroxyamine) δ 3.62 (d, J = 8.4 Hz, 1H, OCH_2), 3.55 (d, J = 8.4 Hz, 1H, OCH_2), 1.65 - 1.55 (m, 2H, CH_2), 1.40 - 1.20 (m, 10H, 5 CH_2), 1.32 (s, 3H, CH_3), 1.25 (s, 3H, CH_3), 1.18 (s, 3H, CH_3), 0.90 (t, J = 6.5 Hz, 3H, CH_3); ^{13}C NMR ($CDCl_3$, as N-hydroxyamine) δ 99.91 (O<u>C</u>N), 74.24 (O<u>C</u>H_2),

63.41 ($\underline{C}(CH_3)_2$), 40.37 ($\underline{C}H_2$), 31.83 ($\underline{C}H_2$), 30.27 ($\underline{C}H_2$), 29.47 ($\underline{C}H_2$), 25.22 ($\underline{C}H_3$), 24.30 ($\underline{C}H_2$), 22.73 ($\underline{C}H_2$), 22.00 ($\underline{C}H_3$), 21.93 ($\underline{C}H_3$), 14.21 ($\underline{C}H_3$); MS m/z (rel. intensity) 228 (M^+, (4%)), 172 (20%), 143 (85%), 129 (24%), 82 (24%), 69 (45%), 69 (100%), 56 (100%), 55 (30%). Anal. Calcd for $C_{13}H_{26}NO_2$: C, 68.38; H, 11.48; N, 6.14. Found: C, 68.37; H, 11.87; N, 6.16.

2,4,4-Trimethyl-2-octyloxazolidine-N-oxyl (5d). ^1H NMR ($CDCl_3$, as N-hydroxyamine) δ 3.60 (d, J = 8.4 Hz, 1H, OCH_2), 3.54 (d, J = 8.4 Hz, 1H, OCH_2), 1.65 - 1.55 (m, 2H, CH_2), 1.40 - 1.20 (m, 12H, 6 CH_2), 1.32 (s, 3H, CH_3), 1.22 (s, 3H, CH_3), 1.19 (s, 3H, CH_3), 0.85 (t, J = 6.5 Hz, 3H, CH_3); ^{13}C NMR ($CDCl_3$, as N-hydroxyamine) δ 99.60 (O$\underline{C}$N), 74.16 (O$\underline{C}H_2$), 63.14 ($\underline{C}(CH_3)_2$), 40.42 ($\underline{C}H_2$), 31.76 ($\underline{C}H_2$), 30.07 ($\underline{C}H_2$), 29.51 ($\underline{C}H_2$), 29.19 ($\underline{C}H_2$), 25.06 ($\underline{C}H_3$), 24.06 ($\underline{C}H_2$), 22.54 ($\underline{C}H_2$), 21.81 ($\underline{C}H_3$), 21.61 ($\underline{C}H_3$), 13.98 ($\underline{C}H_3$); MS m/z (rel. intensity) 242 (M^+, (4%)), 186 (20%), 157 (88%), 139 (34%), 97 (20%), 83 (40%), 71 (20%), 56 (100%), 55 (34%). HRMS Calcd for $C_{14}H_{28}NO_2$: 242.2120. Found: 242.2116.

2,4,4-Trimethyl-2-nonyloxazolidine-N-oxyl (5e). ^1H NMR ($CDCl_3$, as N-hydroxyamine) δ 3.55 (d, J = 8.4 Hz, 1H, OCH_2), 3.48 (d, J = 8.4 Hz, 1H, OCH_2), 1.65 - 1.55 (m, 2H, CH_2), 1.40 - 1.20 (m, 14H, 7 CH_2), 1.25 (s, 3H, CH_3), 1.20 (s, 3H, CH_3), 1.15 (s, 3H, CH_3), 0.85 (t, J = 6.5 Hz, 3H, CH_3); ^{13}C NMR ($CDCl_3$, as N-hydroxyamine) δ 99.36 (O$\underline{C}$N), 73.38 (O$\underline{C}H_2$), 62.80 ($\underline{C}(CH_3)_2$), 39.26 ($\underline{C}H_2$), 31.00 ($\underline{C}H_2$), 30.02 ($\underline{C}H_2$), 29.24 ($\underline{C}H_2$), 29.06 ($\underline{C}H_2$), 28.36 ($\underline{C}H_2$), 28.43 ($\underline{C}H_2$), 24.24 ($\underline{C}H_3$), 23.24 (2 $\underline{C}H_2$), 21.77 ($\underline{C}H_3$), 21.02 ($\underline{C}H_3$), 14.50 ($\underline{C}H_3$); MS m/z (rel. intensity) 256 (M^+, (8%)), 200 (30%), 171 (88%), 130 (50%), 97 (25%), 83 (25%), 71 (20%), 56 (100%), 55 (32%). Anal. Calcd for $C_{15}H_{30}NO_2$: C, 70.30; H, 11.80; N, 5.47. Found: C, 70.47; H, 12.00; N, 5.20.

4,4-Dimethyl-2,2-dipropyloxazolidine-N-oxyl (5f). ^1H NMR ($CDCl_3$, as N-hydroxyamine) δ 3.55 (s, 2H, OCH_2), 1.70 - 1.60 (m, 4H, 2 CH_2), 1.40 - 1.20 (m, 4H, 2 CH_2), 1.15 (s, 6H, 2 CH_3), 0.90 (t, J = 6.5 Hz, 6H, 2 CH_3); ^{13}C NMR ($CDCl_3$, as N-hydroxyamine) δ 101.04 (O$\underline{C}$N), 74.52 (O$\underline{C}H_2$), 63.39 ($\underline{C}(CH_3)_2$), 38.24 (2 $\underline{C}H_2$), 23.63 (2 $\underline{C}H_3$), 17.22 (2 $\underline{C}H_2$), 14.50 (2 $\underline{C}H_3$); MS m/z (rel. intensity) 200 (M^+, (4%)), 157 (20%), 144 (20%), 129 (45%), 115 (100%), 71 (95%), 56 (60%), 55 (60%). Anal. Calcd for $C_{11}H_{22}NO_2$: C, 65.96; H, 11.08; N, 7.00. Found: C, 66.00; H, 11.01; N, 7.17.

2,2-Dibutyl-4,4-dimethyloxazolidine-N-oxyl (5g). ^1H NMR ($CDCl_3$, as N-hydroxyamine) δ 3.55 (s, 2H, OCH_2), 1.70 - 1.60 (m, 4H, 2 CH_2), 1.40 - 1.20 (m, 8H, 4 CH_2), 1.15 (s, 6H, 2 CH_3), 0.90 (t, J = 6.5 Hz, 6H, 2 CH_3); ^{13}C NMR ($CDCl_3$, as N-hydroxyamine) δ 101.18 (O$\underline{C}$N), 74.44 (O$\underline{C}H_2$), 63.36 ($\underline{C}(CH_3)_2$), 35.60 (2 $\underline{C}H_2$), 26.08 (2 $\underline{C}H_2$), 23.64 (2 $\underline{C}H_3$), 23.30 (2 $\underline{C}H_2$), 14.08 (2 $\underline{C}H_3$); MS m/z (rel. intensity) 228 (M^+, 6(%)), 172 (80%), 143 (100%), 129 (88%), 99 (40%), 85 (76%), 69 (46%), 56 (100%), 55 (76%). Anal. Calcd for $C_{13}H_{26}NO_2$: C, 68.38; H, 11.48; N, 6.14. Found: C, 68.54; H, 11.68; N, 5.84.

4,4-Dimethyl-2,2-dipentyloxazolidine-N-oxyl (5h). ^1H NMR ($CDCl_3$, as N-hydroxyamine) δ 3.55 (s, 2H, OCH_2), 1.70 - 1.60 (m, 4H, 2 CH_2), 1.55 - 1.20 (m, 12H, 6 CH_2),

1.12 (s, 6H, 2 CH_3), 0.90 (t, J = 6.5 Hz, 6H, 2 CH_3); ^{13}C NMR ($CDCl_3$, as N-hydroxyamine) δ 101.13 (O<u>C</u>N), 74.47 (O<u>C</u>H_2), 63,42 (<u>C</u>$(CH_3)_2$), 35.81 (2 <u>C</u>H_2), 32.94 (2 <u>C</u>H_2), 24.79 (2 <u>C</u>H_3), 23.98 (2 <u>C</u>H_2), 22.70 (2 <u>C</u>H_2), 14.09 (2 <u>C</u>H_3); MS m/z (rel. intensity) 256 (M^+, (5%)), 200 (42%), 186 (70%), 171 (100%), 129 (40%), 99 (80%), 71 (36%), 56 (36%), 55 (30%). HRMS Calcd for $C_{15}H_{30}NO_2$: 256.2276. Found: 256.2281.

4,4-Dimethyl-2,2-dinonyloxazolidine-N-oxyl (5i). ^1H NMR ($CDCl_3$, as N-hydroxyamine) δ 3.51 (s, 2H, OCH_2), 1.65 - 1.50 (m, 4H, 2 CH_2), 1.40 - 1.20 (m, 4H, 2 CH_2), 1.05 (s, 6H, 2 CH_3), 0.80 (t, J = 6.5 Hz, 6H, 2 CH_3); ^{13}C NMR ($CDCl_3$, as N-hydroxyamine) δ 99.98 (O<u>C</u>N), 73.10 (O<u>C</u>H_2), 62,15 (<u>C</u>$(CH_3)_2$), 34.40 (2 <u>C</u>H_2), 30.65 (2 <u>C</u>H_2), 30.49 (2 <u>C</u>H_2), 28.49 (2 <u>C</u>H_2), 28.23 (2 <u>C</u>H_2), 27.92 (2 <u>C</u>H_2), 22.58 (2 <u>C</u>H_2), 22.26 (2 <u>C</u>H_3), 21.26 (2 <u>C</u>H_2), 12.69 (2 <u>C</u>H_3); MS m/z (rel. intensity) 368 (M^+, (6%)), 283 (100%), 242 (30%), 155 (40%), 129 (40%), 71 (20%), 56 (100%), 55 (32%). HRMS Calcd for $C_{123}H_{46}NO_2$: 368.3528. Found: 368.3525.

Oxidation of oxazolidines into oxaziridines : A solution of 70-75% m-CPBA (2.96 g, 15 mmol) in ether (50 ml) is added dropwise over 1 hour at room temperature to a solution of the appropriate oxazolidine (10 mmol) in ether (50 ml) with p-Toluenesulphonic acid (0.95 g, 0.5 mmol). After one hour further stirring at room temperature, the resulting solution was treated as described above for the obtention of aminoxyls.

2-(1-Hydroxy-2-methylpropan-2-yl)-3-methyl-3-pentyloxaziridine (4a).
<u>Cis isomer</u>: ^1H NMR ($CDCl_3$) δ 3.51 (d, J = 10.5 Hz, 1H, OCH_2), 3.29 (d, J = 10.5 Hz, 1H, OCH_2), 1.95 - 1.80 (m, 2H, CH_2), 1.65 - 1.20 (m, 6H, 3 CH_2), 1.40 (s, 3H, CH_3), 1.22 (s, 3H, CH_3), 1.04 (s, 3H, CH_3), 0.90 (t, J = 6.5 Hz, 3H, CH_3); ^{13}C NMR ($CDCl_3$) δ 83.62 (O<u>C</u>N), 72.44 (O<u>C</u>H_2), 60.16 (<u>C</u>$(CH_3)_2$), 32.65 (<u>C</u>H_2), 32.15 (<u>C</u>H_2), 25.70 (<u>C</u>H_2), 25.05 (<u>C</u>H_3), 22.63 (<u>C</u>H_2), 21.41 (<u>C</u>H_3), 20.59 (<u>C</u>H_3), 14.05 (<u>C</u>H_3).
<u>Trans isomer</u>: ^1H NMR ($CDCl_3$) δ 3.51 (d, J = 10.5 Hz, 1H, OCH_2), 3.29 (d, J = 10.5 Hz, 1H, OCH_2), 1.50 - 1.20 (m, 8H, 4 CH_2), 1.63 (s, 3H, CH_3), 1.21 (s, 3H, CH_3), 1.03 (s, 3H, CH_3), 0.90 (t, J = 6.5 Hz, 3H, CH_3); ^{13}C NMR ($CDCl_3$) δ 82.93 (O<u>C</u>N), 72.23 (O<u>C</u>H_2), 60.16 (<u>C</u>$(CH_3)_2$), 41.26 (<u>C</u>H_2), 32.93 (<u>C</u>H_2), 24.12 (<u>C</u>H_2), 22.63 (<u>C</u>H_2), 21.41 (<u>C</u>H_3), 20.59 (<u>C</u>H_3), 17.85 (<u>C</u>H_3), 14.05 (<u>C</u>H_3).
IR ν max (neat) : 3550, 2950, 1455, 1371, 1062 cm^{-1}. MS m/z (rel. intensity) 202 (M^+, (8%)), 170 (6%), 130 (32%), 88 (100%), 86 (25%), 73 (100%), 70 (70%), 58 (88%), 56 (95%), 55 (54%). Anal. Calcd for $C_{11}H_{23}NO_2$: C, 65.62; H, 11.52; N, 6.96. Found: C, 65.94; H, 11.87; N, 7.01.

2-(1-Hydroxy-2-methylpropan-2-yl)-3-methyl-3-nonyloxaziridine (4e).
<u>Cis isomer</u>: ^1H NMR ($CDCl_3$) δ 3.50 (d, J = 10.5 Hz, 1H, OCH_2), 3.28 (d, J = 10.5 Hz, 1H, OCH_2), 1.90 - 1.80 (m, 2H, CH_2), 1.65 - 1.20 (m, 14H, 7 CH_2), 1.40 (s, 3H, CH_3), 1.25 (s, 3H, CH_3), 1.04 (s, 3H, CH_3), 0.90 (t, J = 6.5 Hz, 3H, CH_3); ^{13}C NMR ($CDCl_3$) δ 82.90 (O<u>C</u>N), 72.31 (O<u>C</u>H_2), 60.11 (<u>C</u>$(CH_3)_2$), 32.53 (<u>C</u>H_2), 31.84 (<u>C</u>H_2), 29.86 (<u>C</u>H_2), 29.63 (<u>C</u>H_2), 29.49

($\underline{C}H_2$), 25.89 ($\underline{C}H_2$), 24.93 ($\underline{C}H_3$), 22.66 ($\underline{C}H_2$), 21.41 ($\underline{C}H_2$), 21.25 ($\underline{C}H_3$), 20.42 ($\underline{C}H_3$), 14.01 ($\underline{C}H_3$).

Trans isomer: RMN ^1H ($CDCl_3$) δ 3.50 (d, J = 10.5 Hz, 1H, OCH_2), 3.28 (d, J = 10.5 Hz, 1H, OCH_2), 1.55 - 1.20 (m, 16H, 8 CH_2), 1.63 (s, 3H, CH_3), 1.21 (s, 3H, CH_3), 1.02 (s, 3H, CH_3), 0.90 (t, J = 6.5 Hz, 3H, CH_3); ^{13}C NMR ($CDCl_3$) δ 82.90 (O$\underline{C}$N), 72.19 (O$\underline{C}H_2$), 60.11 ($\underline{C}(CH_3)_2$), 41.31 ($\underline{C}H_2$), 31.97 ($\underline{C}H_2$), 29.76 $\underline{C}H_2$), 29.62 (2 $\underline{C}H_2$), 29.40 ($\underline{C}H_2$), 24.35 ($\underline{C}H_2$), 22.66 ($\underline{C}H_2$), 21.25 ($\underline{C}H_3$), 20.42 ($\underline{C}H_3$), 17.71 ($\underline{C}H_3$), 14.01 ($\underline{C}H_3$); MS m/z (rel. intensity) 258 (M^+, (5%)), 190 (25%), 104 (8%), 100 (8%), 88 (75%), 73 (100%), 59 (40%), 50 (50%), 55 (40%). Anal. Calcd for : $C_{15}H_{31}NO_2$: C, 69.67; H, 12.15; N, 5.44. Found: C, 69.73; H, 12.86; N, 5.40. HRMS Calcd for $C_{15}H_{31}NO_2$: 257.2354. Found: 256.2369.

2-(1-Hydroxy-2-methylpropan-2-yl)-3,3-Dipentyloxaziridine (4h). ^1H NMR ($CDCl_3$) δ 3.48 (d, J = 10.5 Hz, 1H, OCH_2), 3.25 (d, J = 10.5 Hz, 1H, OCH_2), 2.00 - 1.70 (m, 3H), 1.40 - 1.20 (m, 2H, CH_2), 1.40 - 1.20 (m, 11H), 1.20 (s, 3H, CH_3), 1.04 (s, 3H, CH_3), 0.89 (t, J = 6.5 Hz, CH_3), 0,87 (t, J = 6.5 Hz, CH_3); ^{13}C NMR ($CDCl_3$) δ 85.29 (O$\underline{C}$N), 72.32 (O$\underline{C}H_2$), 59.79 ($\underline{C}(CH_3)_2$), 41.28 ($\underline{C}H_2$), 37.26 ($\underline{C}H_2$), 32.06 ($\underline{C}H_2$), 31.89 ($\underline{C}H_2$), 29.59 ($\underline{C}H_2$), 25.23 ($\underline{C}H_2$), 23.98 ($\underline{C}H_2$), 22.50 (2 $\underline{C}H_2$), 21.19 ($\underline{C}H_3$), 20.51 ($\underline{C}H_3$), 13.92 ($\underline{C}H_3$); IR ν_{max} (neat) : 3550, 2950, 1455, 1371, 1062 cm^{-1}. MS m/z (rel. intensity) 258 (M^+, (4%)), 226 (8%), 186 (25%), 142 (24%), 98 (22%), 73 (100%), 58 (40%), 56 (55%), 55 (40%). Anal. Calcd for $C_{15}H_{31}NO_2$: C, 69.97; H, 12.15; N, 5.44. Found: C, 69.69; H, 12.00; N, 5.61.

2-(1-Hydroxy-2-methylpropan-2-yl)-3,3-dinonyloxaziridine (4i). ^1H NMR ($CDCl_3$) δ 3.50 (d, J = 10.5 Hz, 1H, OCH_2), 3.26 (d, J = 10.5 Hz, 1H, OCH_2), 2.00 - 1.70 (m, 3H), 1.60 - 1.45 (m, 2H, CH_2), 1.40 - 1.20 (m, 27H), 1.19 (s, 3H, CH_3), 1.03 (s, 3H, CH_3), 0.89 (t, J = 6.5 Hz, CH_3), 0.88 (t, J = 6.5 Hz, CH_3); ^{13}C NMR ($CDCl_3$) δ 85.82 (O$\underline{C}$N), 72.20 (O$\underline{C}H_2$), 59.74 ($\underline{C}(CH_3)_2$), 37.30 ($\underline{C}H_2$), 31.82 ($\underline{C}H_2$), 29.95 ($\underline{C}H_2$), 29.88 (2 $\underline{C}H_2$), 29.70 ($\underline{C}H_2$), 29.43 ($\underline{C}H_2$), 29.23 ($\underline{C}H_2$), 25.53 ($\underline{C}H_2$), 24.30 ($\underline{C}H_2$), 22.61 ($\underline{C}H_2$), 21.19 ($\underline{C}H_3$), 20.49 ($\underline{C}H_3$), 14.01 ($\underline{C}H_3$); MS m/z (rel. intensity) 370 (M^+, (10%)), 348 (10%), 298 (30%), 186 (20%), 89 (70%), 88 (100%), 78 (100%), 58 (80%), 56 (100%), 55 (80%). Anal. Calcd for $C_{23}H_{47}NO_2$: C, 74.72; H, 12.82; N, 3.79. Found: C, 75.02; H, 12.90; N, 3.69.

Reduction of oxazolidine with sodium borohydride: A solution of oxazolidine **1g** (0.400 g, 2 mmol) and sodium borohydride (75 mg, 2 mmol) in ethanol (5 ml) was stirred at room temperature for 48 h.. Evaporation of the solvent gave quantitatively **7g** which was purified by column chromatography on silica gel (ethyl acetate).

2-((Nonan-5-yl)amino)-2-methylpropan-1-ol (7g). ^1H NMR ($CDCl_3$) δ 3.21 (s, 2H, OCH_2), 2.56 (q, J = 5.5 Hz, 1H, CH), 1.40 - 1.24 (m, 12H, 6 CH_2), 1.06 (s, 6H, 2 CH_3), 0.88 (t, J = 6.5 Hz, 6H, 2 CH_3); ^{13}C NMR ($CDCl_3$) δ 69.71 (O$\underline{C}H_2$), 54.58 ($\underline{C}(CH_3)_2$), 51,45 ($\underline{C}H$),36.28 (2 $\underline{C}H_2$), 28.10 (2 $\underline{C}H_2$), 24.70 (2 $\underline{C}H_3$), 23.01 (2 $\underline{C}H_2$), 14.15 (2 $\underline{C}H_3$).

REFERENCES AND NOTES

1. Keana, J. F. W.; Keana, S. B.; Beetham, D. *J. Am. Chem. Soc.* **1967**, 89, 3055.
2. Nelson, J. A.; Chou, S.; Spencer, T. A. *J. Org. Chem.* **1974**, 39, 2356.
3. Joseph, J.; Lai, C. S. *J. Lipids Res.* **1988**, 29, 1101.
4. Waggoner, A. S.; Kingzett, T. J.; Rottschaefer, S.; Griffith, O. H. *Chem. Phys. Lipids* **1969**, 3, 245.
5. Singhatta, D.; Venkatamaru, S. D.; Person, D.E.; Beth, A. H.; Park, C. R.; Park, J. H. *Tetrahedron Lett.* **1985**, 26, 1403.
6. *Spin labelling theory and applications;* Berliner, L.J. Ed.; Academic Press: New York, 1976, p. 526.
7. Keana, J. F. W. *Chem. Rev.* **1978**, 78, 37.
8. a) Paukstelis, J. V.; Hammaker, R. M. *Tetrahedron Lett.* **1968**, 3557.
   b) Bergman, E. D. *Chem. Rev.* **1953**, 53, 309.
9. Davis, A. F.; Sheppard, A. C. *Tetrahedron* **1989**, 45, 5703.
10. *The structures of oxaziridines **4** were established through analytical data : mass spectrometry and element analysis were in agreement with the proposed structure, iodometric titration with potassium iodide indicated a highly active oxygen content*[13]. *^{13}C NMR indicated that all the carbon atoms of the starting oxazolidine were present ; ^{1}H NMR showed an ABX spectrum coresponding to the two geminal protons (CH_2OH), which simplified to an AB in presence of D_2O. The IR spectroscopy (CCl_4) confirmed the presence of a hydroxyl group with a strong intramolecular hydrogen band and shows an absorption at 1455 cm^{-1} (characteristic of oxaziridine).*[14]
11. Murray, R. W.; Singh, M. *Tetrahedron Lett.* **1988**, 29, 4677.
12. Lamchen, M. *Mecanismes of Molecular Migrations*, Thyagarayam, B. S. Ed.; John Wiley: New York, 1968, p. 8.
13. Emmons, W. D. *J. Am. Chem. Soc.* **1957**, 79, 5739.
14. Schmidz, E. *Comprehensive Heterocyclic Chemistry ;* Lwowski, W., Ed.; Pergamon Press ; Vol. 7, 1984 ; p. 195.
15. Wehrli, F. W. and Wirthlin, T. *Interpretation of Carbon-13 NMR Spectra* ; Ed.; Heyden and Son London, 1976.
16. Linsz, J. *Liebigs Ann. Chem.* **1969**, 727.
17. Jordan, G. J.; Grist, D. R. *Org. Magn. Reson.* **1977**, 9, 322.
18. Boyd, D. R.; Spratt, R.; Jerina, D. M. *J. Chem. Soc.(C)* **1969**, 2650.
19. Lee, T. D.; Keana, J. F. W. *J. Org. Chem.* **1975**, 40, 3145.

(*Received in Belgium* 14 *November* 1994; *accepted* 5 *October* 1995)