Pergamon

Tetrahedron 57 (2001) 2807–2812

TETRAHEDRON

# Microwave-assisted ring expansion of *N*-acetyl 3′-unsubstituted aziridine in the presence of Lewis acids

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Received 2 November 2000; revised 2 January 2001; accepted 18 January 2001

**Abstract**—The microwave-assisted ring expansion of *N*-acetyl 3′-unsubstituted aziridine-2-imides and *N*-acetyl 3′-unsubstituted aziridine-2-esters to oxazolines is reported. The regioselectivities of the rearrangements depend upon the reaction conditions, such as the Lewis acid selected and the solvent. © 2001 Elsevier Science Ltd. All rights reserved.

## 1. Introduction

In recent years there has been an increasing interest in the use of aziridine-2-carboxylates[1] as intermediates for the synthesis of biologically active compounds, such as α- and β-amino acids or β-lactam antibiotics.

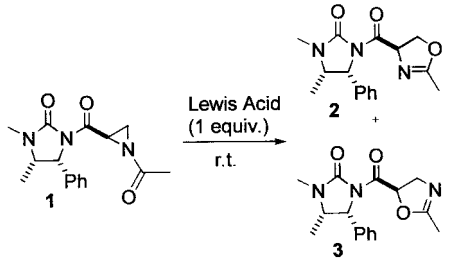
In this field we have developed a new strategy towards the synthesis of stereodefined aziridines. Indeed, we obtained aziridine-2-carboxylate derivatives following several synthetic pathways, such as the well known Gabriel–Cromwell reaction performed on unsaturated chiral imides[2] or the 1,4-addition of *O*-benzylhydroxylamine to α,β-unsaturated imides, followed by cyclization to the corresponding *trans* aziridine.[3] The stereochemical results of both these reactions were controlled using 1,5-dimethyl-4-phenylimidazolidin-2-one as a chiral auxiliary. This heterocycle is available in both enantiomerically pure forms, starting from (+)- or (−)-ephedrine.[4]

*N*-Acyl activated aziridines easily afford ring opening in the presence of a nucleophile through an $S_N2$ mechanism[1] or can be transformed into the corresponding oxazolines through a ring expansion reaction in the presence of Lewis acids.[5] The ring expansion of activated aziridines promoted by azaphilic Lewis acids has recently been the object of attention and both chemical evidence and ab initio calculations show that this reaction occurs with retention of the pre-existing stereogenic centers.[5,6] These results have been confirmed by us through $^1$H NMR experiments[7a] and chemical transformations,[7b] performed on the optically active *trans N*-acyl-3-substituted aziridine-2-imides. These compounds spontaneously rearrange in $CHCl_3$, in the absence of Lewis acid, affording exclusively *trans* oxazoline-4-imides, under complete regiocontrol and with retention of the configurations. These results show that the presence of an alkyl substituent at C3′ of the imide derivative strongly favors the formation of oxazoline-4-imides. The same protocol, carried out on 3′-unsubstituted aziridines, afforded a mixture of regioisomers, whose ratio strongly depended on the Lewis acid selected for the activation and on the reaction conditions. These observations prompted us to further investigate the ring expansion of 3′-unsubstituted-aziridines.

## 2. Results and discussion

The aziridine **1** was synthesized following the procedure reported elsewhere.[2,3] The ring expansion of **1** to afford **2** or **3** was performed in the presence of several Lewis acids in equimolar amounts with respect to **1**, in different solvents, under normal conditions at room temperature (Scheme 1). The results obtained are reported in Table 1.

The selected data, reported in Table 1, show that $MgBr_2{\cdot}Et_2O$ favors the formation of oxazoline **2**, while $BF_3{\cdot}Et_2O$ gives oxazoline **3** as the major product. This result shows that the reaction could occur via attack of the carbonyl at both C3′ and C2′ ring carbon atoms, depending




**Scheme 1.**

*Keywords*: aziridine; oxazoline; microwaves; Lewis acids; rearrangement.

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PII: S0040-4020(01)00123-5

**Table 1.** Ring expansion of aziridine **1** to oxazolines **2** and **3**

| Entry | Lewis acid (1 equiv.) | Solvent | Yield **2**+**3** (%) | **2**:**3** (%)[a] |
|---|---|---|---|---|
| 1 | $BF_3{\cdot}Et_2O$ | THF | 70 | 30:70 |
| 3 | $Cu(OTf)_2$ | THF | 60[b] | 40:60 |
| 5 | $MgBr_2{\cdot}Et_2O$ | Toluene | 70[c] | 70:30 |
| 6 | $MgBr_2{\cdot}Et_2O$ | THF | 50[d] | 99:1 |

[a] Determined on the basis of $^1$H NMR analysis of the crude reaction mixture.
[b] Traces of products deriving from aziridine ring opening and starting material were detected in the crude reaction mixture.
[c] A 30% amount of starting material was recovered.
[d] Conversion >95%. A 50% amount of ring opening products was detected in the reaction mixture.

on the Lewis acid. Anyway, although all reactions go to complete conversion of the starting aziridine, a careful product analysis showed the presence of regioisomeric oxazolines and ring opening products, deriving from hydrolysis to esters or amides, or halo compounds, deriving from nucleophilic attack by metal halides.[8]

In order to avoid complex product mixtures, we performed this reaction following a microwave-assisted methodology.[9] In fact, it is reported that some reactions proceed faster when submitted to microwave irradiation in comparison with conventional heating and the presence of byproducts is strongly reduced.[10]

The ring expansion was then performed promoting the reaction with microwave irradiation at 240 W for 10 min. Under these conditions, the reaction temperatures were 55–60°C. Comparative experiments have been carried out in different solvents and in the presence of Lewis acids. The results obtained are reported in Table 2.

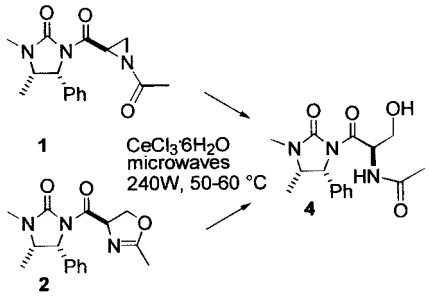
The regioisomeric oxazolines have been separated by flash chromatography performed on alumina, eluting with cyclohexane/ethyl acetate 7:3. Compound **3** is quite unstable and was not isolated in pure form.[11]

The results obtained confirm the trend observed in the reactions performed at room temperature. In fact, complete regioselectivity was observed when the reaction was promoted by $MgBr_2{\cdot}Et_2O$ in THF (entry 6), the oxazoline

**Table 2.** Microwave-assisted ring expansion of aziridine **1** to oxazolines **2** and **3**

| Entry | Lewis acid (1 equiv.) | Solvent | Yield **2**+**3** (%) | **2**:**3** (%)[a] |
|---|---|---|---|---|
| 1 | $BF_3{\cdot}Et_2O$ | THF | >95 | 15:85 |
| 2 | $BF_3{\cdot}Et_2O$ | Toluene | 85 | 30:70 |
| 3 | $Cu(OTf)_2$ | Toluene | >95 | 30:70 |
| 4 | $Zn(OTf)_2$ | THF | >95 | 56:44 |
| 5 | $MgBr_2{\cdot}Et_2O$[b] | Toluene | 70 | 65:45 |
| 6 | $MgBr_2{\cdot}Et_2O$ | THF | >95 | 99:1 |
| 7 | $AlMe_2Cl$[c] | THF | 50[c] | 25:75 |

[a] Determined on the basis of $^1$H NMR analysis of the crude reaction mixture.
[b] Although the reaction mixture appeared very clean, the yield and regioselectivity were not always reproducible, for the low solubility of the Lewis acid.
[c] Conversion >95%. Several products deriving from aziridine ring opening were detected in the crude reaction mixture.




**Scheme 2.**

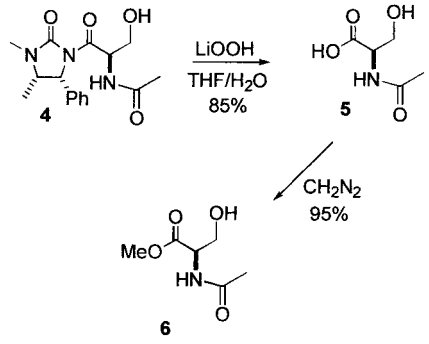
**3** not being detected in the crude reaction mixture. A lower yield and diastereoselectivity was obtained in toluene (entry 5). When the ring expansion of aziridine **1** was performed in the presence of an equimolar amount of $BF_3{\cdot}Et_2O$, we observed the preferential formation of oxazoline **3** both in toluene (entry 2) and in THF (entry 1).

When the aziridine **1** was subjected to microwave irradiation in the presence of 1 equiv. of $CeCl_3{\cdot}6H_2O$, compound **4** was exclusively obtained in quantitative yield. Furthermore, when oxazoline **2** was treated under the same conditions, **4** was quantitatively recovered (Scheme 2). These results show that both ring expansion and ring opening by means of water as nucleophile can occur on aziridine **1**.

Compound **4** was even obtained when we tried to purify oxazoline **2** by flash chromatography on silica gel. The structure of **4** was determined through the $^1$H NMR signal multiplicity and confirms the regiochemistry attributed to oxazoline **2**.

The non-destructive removal of the chiral auxiliary under Evans' conditions,[12] by means of LiOOH in $THF/H_2O$, followed by treatment with $CH_2N_2$, furnished (*R*)-*N*-acetylserine methyl ester **6** (Scheme 3). The regio- and stereochemistry of both the acid **5** and the ester **6** were confirmed by comparison with the data reported in the literature.[13]

Finally, the (2*S*)-*N*-acetylaziridine methyl ester **7**, prepared as reported in the literature starting from *N*-trityl-(*S*)-serine,[14] was submitted to ring expansion under microwave-assisted conditions (Scheme 4).




**Scheme 3.**


**Scheme 4.**

The reaction was carried out in toluene and in the presence of several Lewis acids such as $MgBr_2{\cdot}Et_2O$, $BF_3{\cdot}Et_2O$, $Cu(OTf)_2$ and $Zn(OTf)_2$. After 45 min the crude mixtures showed oxazoline **8** as the major product, the presence of traces of the starting aziridine and byproducts deriving from oxazoline ring opening. The structure of oxazoline **8** was confirmed on the basis of $^1H$ NMR[15] and MS analysis.

These results show that the aziridine-2-imide **1** rearranges to oxazoline faster than the aziridine-2-ester **7**, suggesting the possibility that the oxazolidin-2-one substituent could exert a neighboring group participation effect.[16]

To rationalize the regiochemistry reversal observed in the ring expansion of **1** in the presence of different Lewis acids, and in particular in the presence of $BF_3$ and $MgBr_2$, we investigated the properties of the $MgBr_2$–**1** and the $BF_3$–**1** complexes, and the reaction intermediates, by means of semi-empirical calculations.[17]

The $MgBr_2$–**1** complex was evaluated by means of semi-empirical PM3 calculations, and its more stable structure among a set of 100 conformations generated by a Monte-carlo procedure[18] is reported in Fig. 1. In this $MgBr_2$–**1** structure,[19] the Lewis acid coordinates both the carbonyl oxygen and the aziridine nitrogen and for this reason the aziridine ring is turned towards the exocyclic carbonyl. We also considered $MgBr_2$ coordination at different positions, but each calculated complex resulted higher in energy.

It is generally accepted that the *N*-acetyl aziridine ring opening in the presence of a Lewis acid coordinated to aziridinic nitrogen occurs via a first C–N break, leading to a carbocationic-like transition state,[5a] or to a carbocationic intermediate,[6] followed by the ring closure to oxazoline. According to this mechanism, we increased the C3–N distances to simulate the ring opening at the C3 position, and to find out a possible role of oxazolin-2-one carbonyl.

The minimization of this high energy structure gave the intermediate **9**.[20] This structure is only 2.4 kcal/mol higher in energy with respect to the $MgBr_2$–**1** complex, and shows the presence of a six-membered ring with a highly delocalized positive charge, for the formation of a new imidazolidin-2-one carbonyl oxygen–C3 bond.

To simulate the following ring closure to oxazoline, we shortened the *N*-acetyl carbonyl oxygen–C3 distance and increased the imidazolidin-2-one carbonyl oxygen–C3 distance in intermediate **9**. Minimization of this structure gave the stable oxazoline-4-imide $MgBr_2$ complex **10**, which is 16.9 kcal/mol more stable than the $MgBr_2$–**1** complex.

These findings allow us to deduce the existence of a neighboring group participation effect exerted by the imidazolidin-2-one carbonyl oxygen, which gives a strong contribution to the stability of the incoming positive charge on C3 during the aziridine ring opening, leading to the formation of a stable carbocationic intermediate. The stabilizing effect is also present in the following ring closure to oxazoline, on the whole determining an acceleration of the ring expansion of aziridine-2-imide with respect to the ring expansion of aziridine-2-ester, in agreement with our observations.

On the contrary, ring opening at C2 gave rise to the very unstable intermediate complex **11**, which is 19.8 kcal/mol higher in energy than $MgBr_2$–**1**, and shows the presence of a five-membered ring, for the interaction of imidazolidin-2-one carbonyl with C2. The following cyclization gave oxazoline-5-imide complex **12**. This compound results rather high in energy, +2.8 kcal/mol with respect to $MgBr_2$–**1**, probably due to an unfavorable chelation geometry.

According to the mechanistic model proposed, the high regioselectivity observed experimentally for aziridine ring opening in the presence of $MgBr_2$ can be attributed to the marked difference both in the energies of intermediates **9** and **11**, and in the energies of the oxazoline complexes **10** and **12**.

Next we studied the effect of $BF_3$ on the regiochemistry of the ring expansion of **1**. To perform semiempirical AM1 calculations, $BF_3$ was replaced by $BH_3$, and the preferred conformation of the $BH_3$–**1** complex was evaluated by minimization of a 200 conformation set generated by a Montecarlo procedure. The lower minimum obtained

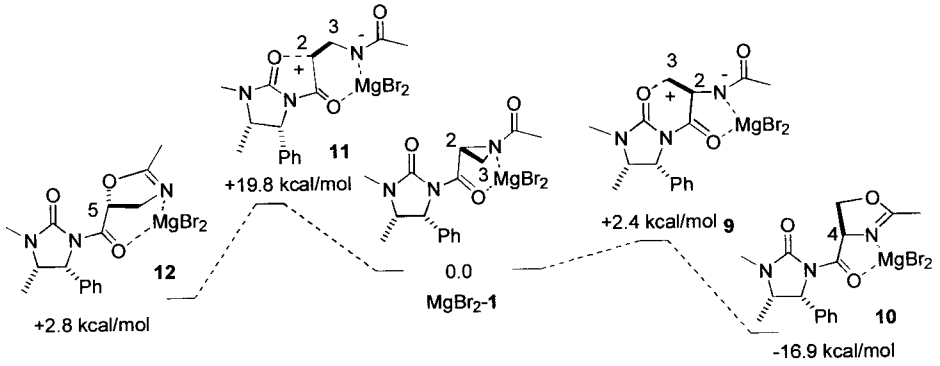



**Figure 1.**

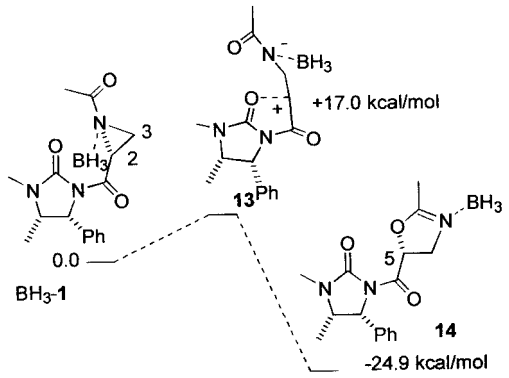



**Figure 2.**

resulted in the structure shown in Fig. 2[21] which, with respect to the the $MgBr_2$–**1** complex, shows the aziridine ring and the exocyclic carbonyl turned away from each other. Also in this case alternative complexes were calculated. Actually, the alternative coordination of $BH_3$ to the acetyl oxygen gave a slightly more stable compound, but this situation does not allow the proper aziridine activation, which is necessary for the ring expansion.[5,6] Indeed, it has been suggested that $BF_3$ should preferably complex the acetyl oxygen rather than the aziridinic nitrogen, but the two complexes are in equilibrium.[5,6]

To simulate the ring opening at the C2 position, we increased the C2–N distance. The minimization of this high energy structure gave the intermediate **13**.[22] This structure is 17 kcal/mol higher in energy with respect to the $BH_3$–**1** complex, and shows the formation of a five-membered ring with a highly delocalized positive charge. To simulate the following ring closure to oxazoline, we shortened the *N*-acetyl carbonyl oxygen–C2 distance and increased the imidazolidin-2-one carbonyl oxygen–C2 distance in intermediate **13**. Minimization of this structure gave the stable oxazoline-5-imide $BH_3$ complex **14**, which is 24.9 kcal/mol more stable than the $BH_3$–**1** complex.

In the alterative ring opening at the C3 position to give oxazoline-4-imide, the neighboring group participation of the imidazolidin-2-one carbonyl oxygen seems more difficult. Indeed, no stable intermediate leading to oxazoline-4-imide could be calculated after breaking the C3–N bond, starting from the preferred conformation of $BH_3$–**1** reported in Fig. 2. This mechanism gives a rationale for the experimental observation that the ring opening of aziridine **1** in the presence of $BF_3$ affords preferentially oxazoline-5-imide **3**.

## 3. Conclusion

In this paper we describe the microwave-assisted ring expansion of 3-unsubstituted aziridine-2-imide **1** and aziridine-2-ester **7** to oxazoline in the presence of several Lewis acids. This reaction occurs with different reaction rates and regioselectivities. In particular, in the presence of $MgBr_2$, aziridine-2-imide **1** gave after 10 min the oxazoline-4-imide **2** as the only regioisomer, while in the presence of $BF_3$ it gave after 10 min a mixture of **2** and oxazoline-5-imide **3** in 15:85 ratio. On the other hand, aziridine-2-ester **7** gave after 45 min only oxazoline-4-ester **8**. On the basis of semi-empirical calculations, the different reaction rates observed for the ring expansion of the aziridine-2-imide and the aziridine-2-ester can be attributed to the existence of a neighboring group participation effect exercised by the imidazolidin-2-one chiral auxiliary. In the same way, the regioselectivity reversal observed in the ring expansion of **1** to oxazoline **2** or **3** in the presence of $MgBr_2$ or $BF_3$ can be attributed to the different geometries assumed by the two Lewis acid–**1** complexes, which allow the imidazolidin-2-one to exert its neighboring group participation effect in the C3 or in the C2 aziridine position, respectively.

## 4. Experimental

### 4.1. General

Unless stated otherwise, chemicals were obtained from commercial sources and used without further purification. $CH_2Cl_2$ was distilled from $P_2O_5$. Toluene was distilled from molecular sieves. Flash chromatography was performed on Merck silica gel 60 (230–400 mesh) or Alumina $PF_{254}$ (Typ E). NMR Spectra were recorded with a Gemini Varian spectrometer at 300 or 200 MHz ($^1$H NMR) and at 75 MHz ($^{13}$C NMR). Chemical shifts are reported as $\delta$ values relative to the solvent peak of $CDCl_3$ set at $\delta$=7.27 ($^1$H NMR) or $\delta$=77.0 ($^{13}$C NMR). Infrared spectra were recorded with an FT-IR Nicolet 205 spectrometer. Aziridine **1** was prepared following a previously reported methodology.[2,3] (2*S*)-*N*-Acetylaziridine methyl ester **7** was prepared as reported in the literature starting from the trityl derivative.[11] Focused microwave irradiations were carried out with a Synthwave™ 402 Prolabo microwave reactor (monomode system, 300 W) which has a variable spin rotation, visual control, irradiation monitored by PC, infrared measurement and continuous feedback of the temperature control.

**4.1.1. (4*R*,5*S*,3′*R*)-1,5-Dimethyl-3-[(1′-acetyl-2′-aziridinyl)-carbonyl]-4-phenylimidazolidin-2-one (1).** White waxy solid; IR (nujol) 1728, 1703, 1699 cm$^{-1}$; $^1$H NMR ($CDCl_3$) $\delta$ 0.80 (d, 3H, *J*=6.9 Hz), 1.88 (s, 3H), 2.48 (m, 2H), 2.83 (s, 3H), 3.93 (dq, 1H, *J*=6.9, 8.7 Hz), 4.74 (dd, 1H, *J*=3.0, 5.4 Hz), 5.27 (d, 1H, *J*=8.7 Hz), 7.1–7.4 (m, 5H); $^{13}$C NMR ($CDCl_3$) $\delta$ 14.9, 23.9, 28.2, 31.3, 34.5, 54.2, 59.5, 126.8, 128.2, 128.5, 135.7, 155.2, 166.8, 181.0; $[\alpha]_D^{20}$=−144 (*c* 1.2 in $CHCl_3$); $C_{16}H_{19}N_3O_3$ (301.34): calcd C 63.77, H 6.36, N 13.94; found C 63.74, H 6.37, N 13.92.

### 4.2. General procedure for the ring expansion of aziridine 1 to oxazolines 2 and 3

To a stirred solution of aziridine **1** (30 mg, 0.1 mmol) in toluene (3 mL) the Lewis acid (1 equiv., 0.1 mmol) was added and the mixture was submitted to microwave irradiation (Power 80%, 240 W) for 10 min. The solution was then diluted with EtOAc (5 mL), washed with water, dried over $Na_2SO_4$ and the solvent removed under reduced pressure. Compounds **2** and **3** were separated by flash chromatography on alumina (cyclohexane/EtOAc 7:3 as eluent) and obtained as yellow oils with the yield reported in

Table 2. Compound **3** is quite unstable and was not isolated in pure form.[11]

**4.2.1. (4*R*,4′*R*,5′*S*)-4,5-Dihydro-2-methyl-4-[(1′,5′-dimethyl-4′-phenylimidazolidin-2′-on-3′yl)carbonyl]oxazole (2).** IR (film) 1728, 1702, 1686 $cm^{-1}$; $^1H$ NMR ($CDCl_3$) $\delta$ 0.82 (d, 3H, *J*=6.6 Hz), 2.05 (s, 3H), 2.85 (s, 3H), 3.94 (dq, 1H, *J*=6.6, 8.7 Hz), 4.42 (m, 1H), 4.46 (dd, 1H, *J*=8.9, 12.3 Hz), 5.33 (d, 1H, *J*=8.7 Hz), 5.89 (t, 1H, *J*=8.9 Hz), 7.1–7.4 (m, 5H); $^{13}C$ NMR ($CDCl_3$) $\delta$ 14.0, 15.2, 28.3, 54.2, 59.3, 68.3, 69.7, 127.0, 128.1, 128.4, 135.8, 153.9, 165.8, 170.0; $[\alpha]_D^{20}=-61.8$ (*c* 0.3 in $CHCl_3$); $C_{16}H_{19}N_3O_3$ (301.34): calcd C 63.77, H 6.36, N 13.94; found C 63.78, H 6.32, N 13.95.

**4.2.2. (5*R*,4′*R*,5′*S*)-4,5-Dihydro-2-methyl-5-[(1,5-dimethyl-4-phenylimidazolidin-2′-on-3′yl)carbonyl]oxazole (3).** IR (film) 1732, 1704, 1666 $cm^{-1}$; $^1H$ NMR ($CDCl_3$) $\delta$ 0.82 (d, 3H, *J*=6.6 Hz), 1.99 (s, 3H), 2.84 (s, 3H), 3.87 (dd, 1H, *J*=6.2, 13.5 Hz), 3.97 (dq, 1H, *J*=6.6, 8.8 Hz), 4.29 (dd, 1H, *J*=13.5, 10.8 Hz), 5.26 (d, 1H, *J*=8.8 Hz), 5.96 (dd, 1H, *J*=6.2, 10.8 Hz), 7.05–7.4 (m, 5H). $^{13}C$ NMR ($CDCl_3$) $\delta$ 13.7, 15.0, 28.2, 29.7, 54.6, 59.3, 59.9, 126.8, 128.3, 128.6, 135.8, 151.8, 159.7, 169.6.

**4.2.3. (4*R*,5*S*,3′*R*)-1,5-Dimethyl-3-(2′-acetamido-3′-hydroxypropionyl)-4-phenylimidazolidin-2-one (4).** To a stirred solution of aziridine **1** (30 mg, 0.1 mmol) or oxazoline **2** (30 mg, 0.1 mmol) in toluene (3 mL), $CeCl_3{\cdot}6H_2O$ (1 equiv., 36 mg) was added and the mixture was submitted to microwave irradiation (Power 80%, 240 W) for 10 min. The solution was then diluted with EtOAc (5 mL), washed with water, dried over $Na_2SO_4$ and the solvent removed under reduced pressure. Compound **4** was purified by flash chromatography on silica gel (cyclohexane/EtOAc 8:2 as eluent) and isolated as colorless oil in 96% yield (31 mg). IR (film) 3353, 1730, 1702, 1662 $cm^{-1}$; $^1H$ NMR ($CDCl_3$) $\delta$ 0.81 (d, 3H, *J*=6.6 Hz), 1.93 (s, 3H), 2.84 (s, 3H), 3.95 (m, 2H), 4.05 (dq, 1H, *J*=6.6, 8.1 Hz), 5.27 (d, 1H, *J*=8.1 Hz), 6.03 (dt, 1H, *J*=7.5, 4.5 Hz), 6.58 (d, 1H, *J*=7.5 Hz), 7.1–7.4 (m, 5H); $^{13}C$ NMR ($CDCl_3$) $\delta$ 14.9, 23.2, 28.2, 54.1, 54.5, 59.9, 64.5, 126.7, 128.2, 128.6, 135.8, 155.0, 170.2, 172.9; $[\alpha]_D^{20}=-45.0$ (*c* 0.4 in $CHCl_3$); MS *m/z* 319 ($M^+$, 5), 262 (100), 183 (77), 108 (55), 51 (26); $C_{16}H_{21}N_3O_4$ (319.36): calcd C 60.17, H 6.63, N 13.16; found C 60.14, H 6.59, N 13.09.

**4.2.4. (2*R*)-*N*-Acetylserine (5), (2*R*)-*N*-acetylserine methyl ester (6).** Hydrogen peroxide (0.4 mmol, 40 μl 30% p/v soln.) and LiOH (5 mg, 0.22 mmol) were added at 0°C to a solution of **4** (31 mg, 0.1 mmol) in THF (4 mL) and water (1 mL). After 2 h, the reaction was quenched with sat. $Na_2SO_3$ and the mixture extracted with EtOAc. The organic layer was dried over $Na_2SO_4$ and the solvent was removed under reduced pressure to give (4*R*,5*S*)-1,5-dimethyl-4-phenylimidazolidin-2-one (17 mg, 90%). The aqueous layer was acidified to pH 2, extracted twice with EtOAc and the solvent removed under reduced pressure. (2*R*)-*N*-Acetylserine **5** was obtained in 85% yield (15 mg) as a white solid. The residue was diluted with $Et_2O$ (2 mL) and treated with an excess of $CH_2N_2$ in $Et_2O$ for 2 h. The solvent was then removed under reduced pressure to afford methyl ester **6** in 95% yield (16 mg) as a waxy solid.

**5.** Mp 119–121; $^1H$ NMR ($D_2O$) $\delta$ 1.98 (s, 3H), 3.75 (dd, 1H, *J*=12.0, 6.6 Hz), 3.81 (dd, 1H, *J*=12.0, 3.7 Hz), 4.30 (dd, *J*=6.6, 3.7 Hz); $^{13}C$ NMR ($D_2O$) $\delta$ 25.3, 60.2, 65.4, 177.1, 179.0; $[\alpha]_D^{20}=-13.9$ (*c* 1.2 in EtOH); MS *m/z* 147 ($M^+$, 22), 105 (100), 60 (42); $C_5H_9NO_4$ (147.13): calcd C 40.82, H 6.17, N 9.52; found C 40.77, H 6.16, N 9.52.

**6.** $^1H$ NMR ($CDCl_3$) $\delta$ 2.09 (s, 3H), 3.81 (s, 3H), 3.94 (dd, 1H, *J*=11.2, 3.6 Hz), 4.02 (dd, 1H, *J*=11.2, 4.0 Hz), 4.70 (ddd, *J*=3.6, 4.0 Hz, 7.4 Hz), 6.54 (d, 1H, *J*=7.4 Hz); $^{13}C$ NMR ($CDCl_3$) $\delta$ 23.2, 50.9, 54.8, 63.6, 171.8, 173.6; $C_6H_{11}NO_4$ (161.16): calcd C 44.72, H 6.88, N 8.69; found C 44.75, H 6.89, N 8.72.

### 4.3. General procedure for the ring expansion of aziridine 7 to oxazoline 8

To a stirred solution of aziridine **7** (30 mg, 0.2 mmol) in toluene (3 mL) the Lewis acid (1 equiv., 0.2 mmol) was added and the mixture was submitted to microwave irradiation (Power 80%, 240 W) for 45 min. The solution was then diluted with EtOAc (5 mL), washed with water, dried over $Na_2SO_4$ and the solvent removed under reduced pressure. Compound **8** was obtained as a yellow oil by flash chromatography on silica gel (cyclohexane/EtOAc 3:7 as eluent). The yield depends upon the Lewis acid selected (40–75%).

**4.3.1. (4*S*)-2-Methyl-4-methoxycarbonyloxazoline (8).** IR (film) 1732, 1704, 1666 $cm^{-1}$; $^1H$ NMR ($CDCl_3$) $\delta$ 2.07 (s, 3H), 3.79 (s, 3H). 4.35 (dd, 1H, *J*=3.8, 11.8 Hz), 4.48 (dd, 1H, *J*=4, 11.8 Hz), 4.87 (dd, 1H, *J*=3.8, 4 Hz); $^{13}C$ NMR ($CDCl_3$) $\delta$ 13.7, 53.2, 68.6, 69.4, 166.9, 171.3; MS *m/z* 143 ($M^+$, 29), 133 (20), 111 (30), 105 (26), 101 (69), 91 (73), 85 (74), 83 (100), 79 (42); $C_6H_9NO_3$ (143.14): calcd C 50.35, H 6.34, N 9.79; found C 50.37, H 6.33, N 9.82.

## Acknowledgements

We thank M. U. R. S. T. (60% and Cofin '98) and Bologna University (Funds for Selected Topics) for financial support of this research.

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17. Performed by means of HYPERCHEM 5.1 Release Pro for Windows Molecular Modeling System (Hypercube Inc., Copyright © 1999).
18. Performed by means of CHEMPLUSTM™ Release (Hypercube Inc., Copyright © 1993–1997).
19. For $MgBr_2$–**1** interatomic distances: C3–N=1.50 Å, C2–N=1.51 Å, imidazolidin-2-one carbonyl oxygen–C2=2.73 Å, imidazolidin-2-one carbonyl oxygen–C3=3.85 Å.
20. For **9** interatomic distances: C3–N=2.50 Å, imidazolidin-2-one carbonyl oxygen–C3=1.54 Å, *N*-acetyl carbonyl oxygen–C3=3.31 Å.
21. For $BH_3$–**1** interatomic distances: C2–N and C3–N=1.48 Å, imidazolidin-2-one carbonyl oxygen–C2=2.73 Å, imidazolidin-2-one carbonyl oxygen–C3=4.07 Å.
22. For **13** interatomic distances: C2–N=2.53 Å, imidazolidin-2-one carbonyl oxygen–C2=1.50 Å, *N*-acetyl carbonyl oxygen–C2=3.08 Å.