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Asymmetric Synthesis of 2-(2-Pyridyl)aziridines from 2-Pyridineimines Bearing Stereogenic *N*-Alkyl Substituents and Regioselective Opening of the Aziridine Ring

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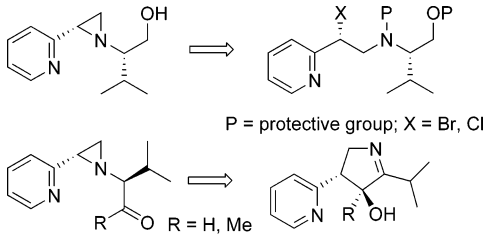

The addition of chloromethyllithium to the imine derived from 2-pyridinecarboxaldehyde and (*S*)-valinol, protected as its *O*-trimethylsilyl ether, gave the 1,2-disubstituted aziridine with good yield and diastereoselectivity. The analogous reaction performed on the imine derived from (*S*)-valine methyl ester gave the product containing the aziridine ring and the α-chloro ketone group coming from the attack of chloromethyllithium to the ester function. Other stereogenic alkyl substituents at nitrogen gave less satisfactory results. Moreover, the aziridination protocol did not work on other aromatic imines which were not capable of bidentate chelation, e.g., 3- and 4-pyridineimine and benzaldimine. Preliminary studies showed the possibility to carry out regio- and stereospecific opening reactions of 2-(2-pyridyl)aziridines by attack of internally generated or external nucleophiles.

Introduction

Enantiopure aziridines have gained considerable importance over a number of years as chiral ligands in transition-metal-catalyzed asymmetric syntheses.[1] Following our previous studies on enantioselective Pd-catalyzed allylic substitution reactions using 1-(2-pyridyl)alkylaziridines as ligands,[2] we directed our interest to the asymmetric synthesis of 2-(2-pyridyl)aziridines **2** from chiral 2-pyridineimines **1** bearing a stereogenic center at the nitrogen atom, aiming to assess their potential as bidentate ligands in a variety of enantioselective catalytic transformations. The envisioned route involved the addition of halomethylmetal reagents to the imine function. Recently, the *N*-(*tert*-butylsulfinyl)aziridine **2** (R = (*R*)-*t*-BuSO) has been prepared by the Corey−Chaykovsky sulfonium ylide aziridination protocol.[3] Moreover, an *N*-substituted 2-phenyl-3-(2-pyridyl)aziridine was obtained by Darzens-type reaction of lithiated 2-(chloromethyl)-pyridine with (*R*)- and (*S*)-*N*-benzylidene-*O*-methylphenylglycinol.[4] However, in both reports, removal of the aziridine nitrogen substituent (chiral auxiliary) has not been described. Apparently, this is a difficult task that should be accomplished by selective procedures to preserve the integrity of the aziridine ring and the configuration of the benzylic stereocenter. In this regard, it should be underlined that the aziridine **2** can easily undergo ring-opening by hydrogenolysis and nucleophilic attack, especially through *N*-activation by protic or Lewis acids. Hence, in order to prepare the *N*-unsubstituted 2-(2-pyridyl)aziridine **2**

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(1) (a) Tanner, D. *Angew. Chem., Int. Ed. Engl.* **1994**, *33*, 599−619. (b) Osborn, H. M. I.; Sweeney, J. B. *Tetrahedron: Asymmetry* **1997**, *8*, 1693−1715. (c) Li, A. H.; Dai, L. X.; Aggarwal, V. K. *Chem. Rev.* **1997**, *97*, 2341−2372. (d) Mc Coull, W.; Davis, F. A. *Synthesis* **2000**, 1347−1365.

(2) (a) Fiore, K.; Martelli, G.; Monari, M.; Savoia, D. *Tetrahedron: Asymmetry* **1999**, *10*, 4803−4810. (b) Savoia, D.; Alvaro, G.; Di Fabio, R.; Fiorelli, C.; Gualandi, A.; Monari, M.; Piccinelli, F. *Adv. Synth. Catal.* **2006**, *348*, 1883−1893.

(3) Morton, D.; Pearson, D.; Field, R. A.; Stockman, R. A. *Synlett* **2003**, 1985−1988.

(4) De Vitis, L.; Florio, S.; Granito, C.; Ronzini, L.; Troisi, L.; Capriati, V.; Luisi, R.; Pilati, T. *Tetrahedron* **2004**, *60*, 1175−1182.

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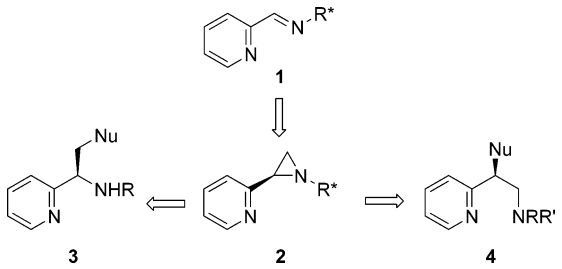
SCHEME 1



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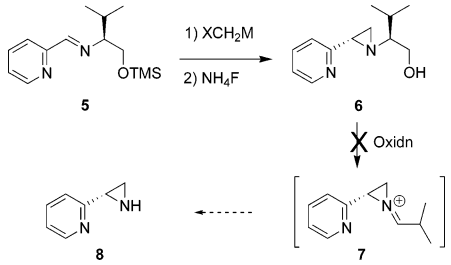


(R = H), it should be possible to remove the *N*-(*tert*-butyl)-sulfinyl substituent R in the aziridine **2** by treatment with methyllithium at low temperature,[5] rather than by the usual treatment with HCl/dioxane or HCl/methanol.

We envisioned that the 2-(2-pyridyl)aziridines **2** would be useful intermediates for the regioselective preparation of 1-(2-pyridyl)alkylamines **3** and/or 2-(2-pyridyl)alkylamines **4**, taking advantage of the propensity of the aziridine ring to undergo ring-opening reactions by attack of nucleophilic reagents (Scheme 1). Herein, we describe an aziridination procedure for 2-pyridineimines derived from β-amino alcohols and α-aminoacid esters. The *N*-substituent could not be removed from the obtained aziridines, e.g., by direct oxidative cleavage of the β-amino alcohol moiety or even through manipulation of the chemical functionality present in it. Furthermore, we have explored the possibility to exploit the reactivity of the aziridine ring toward external nucleophiles. Moreover, an unusual rearrangement involving aziridine ring opening was observed when an enolate was generated in the *N*-substituent.

Results and Discussion

Addition of "Carbenoid" Reagents to Chiral Aromatic Imines. Initial reactions were performed on the known imine **5**, which is available by condensation of 2-pyridinecarboxaldehyde with (*S*)-valinol and subsequent protection of the hydroxyl function as its trimethylsilyl ether.[6] As a matter of fact, our previous studies on the asymmetric synthesis of enantiopure 1-(2-pyridyl)alkylamines showed that *O*-trimethylsilyl valinol is the preferred chiral auxiliary for the diastereoselective addition of organometallic reagents to 2-pyridineimines, providing the desired amines with higher diastereoselectivities compared to valine esters and phenylglycinol.[6] Hence, a number of halogenomethylmetal reagents were added to the imine **5** under different experimental conditions, in order to optimize the synthesis of the 1,2-disubstituted aziridine **6**, which was isolated following routine desilylation procedures (Scheme 2).

It should be observed that electron-withdrawing *N*-substituents are generally required to achieve the addition of carbenoid reagents to the azomethine function. We hoped, however, that the electron-withdrawing pyridine ring would provide sufficient activation of the imine **5**. So, in the first experiment, we used the zinc reagent that is formed in situ from diethylzinc and chloroiodomethane and was previously used for the cyclopropanation of alkenes.[7] This reagent was added to the TMSO-protected imine **5** at −30 °C, but no desired product was formed, even when the reaction mixture was allowed to reach room temperature (Table 1, entry 1). No reaction was observed even when chloroiodomethane was replaced with diiodomethane (entry 2). We then moved to reagents that have previously been used for the preparation of halohydrins from aldehydes. We observed that a smooth reaction occurred at room temperature using the samarium reagent formed in situ by reaction of samarium with diiodomethane;[8] the desired aziridine **6** was isolated in good yield but very low diastereoselectivity (entry 3) after desilylation of the crude reaction product with ammonium fluoride and column chromatography. No improvement was achieved by carrying out the reaction at 0 °C, as the yield and diastereomeric ratio (dr) were slightly lower (entry 4). The use of chloroiodomethane in place of diiodomethane in the samarium-mediated procedure gave a complex mixture of products (entry 5).

The reagent formed in situ from diiodomethane and methyllithium[9] also gave a mixture of products, which was abandoned (entry 6). Good results were instead obtained with chloromethyllithium, which was formed in situ by adding methyllithium to a mixture of chloroiodomethane and lithium bromide in THF at −78 °C in the presence of the imine **5**[10] and then slowly raising the temperature to 20 °C. In this case, the aziridine **6** was obtained with excellent yield and high stereocontrol (dr 87:13, entry 7), following desilylation with ammonium fluoride in a MeOH−H_2O mixture. The positive influence of lithium bromide on the stability of the carbenoid reagent should be similar to that of lithium dialkylamides, which, on the basis of DFT calculations,[11] form mixed dimer aggregates with chloromethyllithium in THF solution. Better diastereoselectivity (dr 92:8) was finally obtained by using a greater excess of reagents (3.6 equiv) with respect to the imine, and the pure diastereomer (*S*,*S*)-**6** was isolated in 65% yield following chromatography on a silica gel column (entry 8). In the latter reactions (entries 7 and 8), small amounts (up to 8%) of the *O*-methyl ether of **6** were detected by GC−MS analysis and this compound was isolated by repeated chromatography of the

(5) Kells, K.; Chong, J. M. *Org. Lett.* **2003**, *5*, 4215−4218.

(6) (a) Basile, T.; Bocoum, A.; Savoia, D.; Umani-Ronchi, A. *J. Org. Chem.* **1994**, *59*, 7766−7773. (b) Alvaro, G.; Boga, C.; Savoia, D.; Umani-Ronchi, A. *J. Chem. Soc., Perkin Trans. 1* **1996**, 875−882. (c) Alvaro, G.; Savoia, D. *Tetrahedron: Asymmetry* **1996**, *7*, 2083−2092. (d) Alvaro, G.; Savoia, D.; Valentinetti, M. R. *Tetrahedron* **1996**, *38*, 12571−12586. (e) Alvaro, G.; Pacioni, P.; Savoia, D. *Chem. Eur. J.* **1997**, *3*, 726−731. (f) Alvaro, G.; Martelli, G.; Savoia, D. *J. Chem. Soc., Perkin Trans. 1* **1998**, 775−783. (g) Alvaro, G.; Savoia, D. *Synlett* **2002**, 651−673.

(7) Furukawa, J.; Kawabata, N.; Nishimura, J. *Tetrahedron Lett.* **1966**, 3353−3356.

(8) Concellón, J. M.; Bernad, P. L.; Pérez-Andrés, J. A. *J. Org. Chem.* **1997**, *62*, 8902−8906.

(9) (a) Barluenga, J.; Baragaña, B.; Concellón, J. M. *J. Org. Chem.* **1999**, *64*, 2843−2846. (b) Bessieres, B.; Morin, C. *Synlett* **2000**, 1691−1693. (c) Concellón, J. M.; Cuervo. H.; Fernández-Fano, R. *Tetrahedron* **2001**, *57*, 8983−8987. (d) Bessieres, B.; Morin, C. *J. Org. Chem.* **2003**, *68*, 4100−4103.

(10) (a) Barluenga, J.; Baragaña, B.; Alonso, A.; Concellón, J. M. *J. Chem. Soc., Chem. Commun.* **1994**, 969−970. (b) Barluenga, J.; Baragaña, B.; Concellón, J. M. *J. Org. Chem.* **1995**, *60*, 6696−6699.

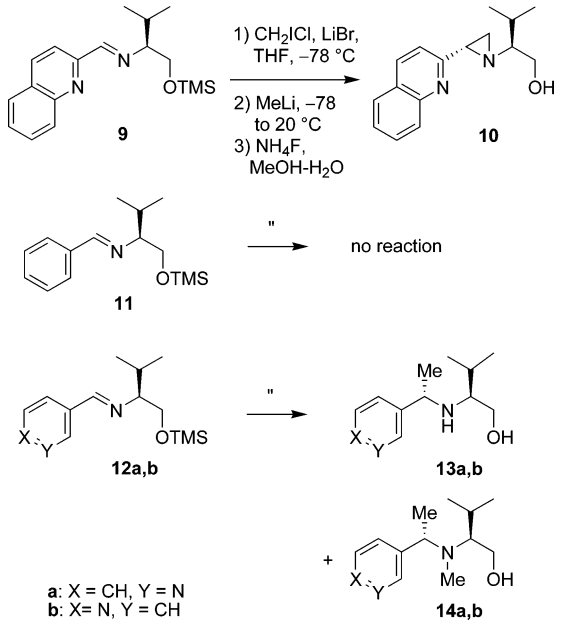
(11) Pratt, L. M.; Lê, L. T.; Truong, T. N. *J. Org. Chem.* **2005**, *70*, 8298−8302.

TABLE 1. Addition of Halomethylmetal Reagents to the Imine 5 in THF

entry	reagents (equiv)	*T* (°C)	time (h)	**6** (yield, %)[a]	**6** (*S*,*S*)/(*R*,*S*)[b]
1	Et_2Zn (2), CH_2ICl (4) [c]	−30 to 20	3	0[d]	
2	Et_2Zn (2), CH_2I_2 (4) [c]	−30 to 20	3	0[d]	
3	Sm (3), CH_2I_2 (2)	20	3	72	56:44
4	Sm (3), CH_2I_2 (2)	0	3	70	52:48
5	Sm (3), CH_2ICl (2)	20	3	*e*	
6	MeLi (2), CH_2I_2 (2)	−78 to 0	4	*e*	
7	MeLi (1.8), CH_2ICl (1.8), LiBr (1)	−78 to 20	8	93[f]	87:13
8	MeLi (3.6), CH_2ICl (3.6), LiBr (2)	−78 to 20	8	95[f] (65)[g]	92:8 (>99:1)[g]

[a] Yield of the crude reaction product. [b] Determined by GC−MS and ^1H NMR analyses. [c] The reaction was performed in toluene. [d] The starting imine was recovered, [e] A complex mixture of products was obtained. [f] The *O*-methyl derivative of **6** (ca. 8% yield) was observed by GC−MS analysis in the reaction mixture. [g] Yield and dr of **6** after column chromatography (SiO_2).

SCHEME 3



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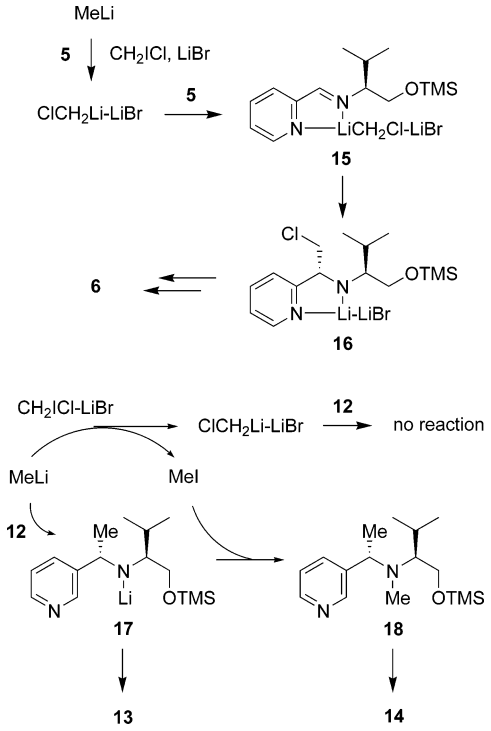


impure compound obtained by pooling enriched chromatographic fractions coming from different reaction runs.

Removal of the nitrogen substituent from the aziridine **6** to give the 1-unsubstituted aziridine **8** proved to be impossible by the routine procedures generally used to cleave *β*-amino alcohols. In fact, the aziridine **6** was unreactive toward oxidizing agents, such as periodic acid/methylamine and lead tetraacetate, in different solvents and experimental conditions (Scheme 2). In our opinion, this failure can be ascribed to the strain associated with the formation of the intermediate iminium ion **7**, which features an exocyclic N═C double bond. This hypothesis is supported by the recent observation of the peculiar reactivity of 1-alkenylaziridines, which do not display nucleophilic character at the exocyclic C2-alkenyl carbon as is usually observed in enamines.[12]

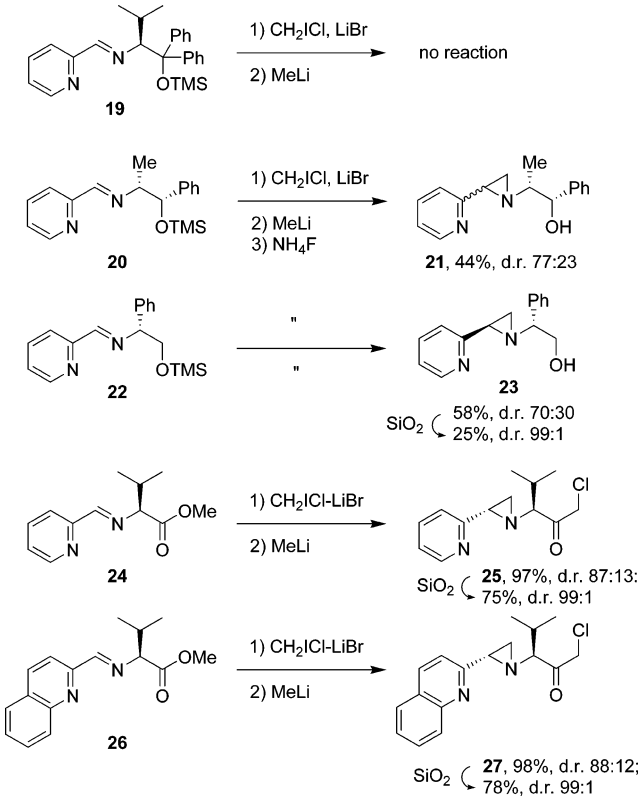
The scope of the described aziridination procedure exploiting chloromethyllithium was then investigated on a range of different aromatic imines derived from the same chiral auxiliary, (*S*)-valinol (Scheme 3). We readily recognized that the presence of the 2-pyridineimine moiety is a requisite for the successful aziridination. As a matter of fact, the 2-quinolineimine **9** proved to be less reactive than the 2-pyridineimine **5**, as the corresponding aziridine **10** was obtained with low yield (51%) and the benzaldimine **11** did not react at all. Surprisingly, the reactions of the 3- and 4-pyridineimines **12a** and **12b**, respectively, lead to the secondary amines **13a**,**b**, which were isolated in small amounts and identified by comparison with authentic specimen, and mainly the tertiary amines **14a**,**b**. All of the products **13a**,**b** and **14a**,**b** were obtained with complete diastereoselectivity.

It is noteworthy that the direct attack of methyllithium on the imine **5** was not observed. Moreover, when the reaction mixture was quenched at low temperature, we did not detect the presumed intermediate *β*-chloro amine. The outcome of a modified experimental procedure was also instructive. When methyllithium was added to the mixture of chloroiodomethane and lithium bromide in THF at −78 °C and then the imine **5** was added to the cold mixture after 15 min, no product was formed after the temperature was allowed to slowly reach room temperature. This result demonstrated that the actual reagent must be formed in situ in the presence of the imine.

The proposed rationale for the different behavior of the 2- and 3-pyridineimines in this reaction is described in Scheme 4. The reactivity of the bidentate imines **5** and **9** can be associated

(12) (a) Dalili, S.; Yudin, A. K. *Org. Lett.* **2005**, *7*, 1161−1164. (b) Similarly, *N*-formylaziridine displays basic properties at nitrogen rather than at oxygen, this has been associated with nitrogen pyramidalization: Alkorta, I.; Cativiela, C.; Elguero, J.; Gil, A. M.; Jiménez, A. I. *New J. Chem.* **2005**, *29*, 1450−1453.

SCHEME 5



to their chelating ability, allowing formation of the stable chelate complex **15** with the organometallic reagent $ClCH_2Li$ generated in situ. At the same time, the bidentate ligand (imine) enhances the nucleophilic character of the organolithium reagent and promotes the intramolecular C−C bond-forming reaction leading to the β-chloro lithium amide **16**. Then, this intermediate undergoes intramolecular substitution to give the aziridine **6**, after deprotection of the hydroxyl group.

On the other hand, when methyllithium is added to the mixture of chloroiodomethane and 3-pyridineimine **12**, it reacts with both of them at comparable rates. Apparently, the chloromethyllithium generated in situ is less reactive or unreactive toward the imine **12**. The amide **17**, formed by attack of methyllithium on the imine **12**, is converted to the secondary amine **13** by proton quenching and desilylation, and to the tertiary amine **14** by reaction with methyl iodide, which is formed in the first halogen-metal exchange step, and desilylation.

We also examined the effect of different chiral auxiliaries, either β-aminoalcohols or α-aminoesters available from the "chiral pool", on the reactivity/diastereoselectivity of the corresponding 2-pyridineimines (Scheme 5). The imine **19** derived from 1,1-diphenylvalinol was found to be unreactive, presumably owing to the bulkiness of the *N*-substituent, and the (+)-norephedrine-derived imine **20** reacted sluggishly to give a mixture of products containing the diastereomeric aziridines **21** in 44% yield and 77:23 ratio (GC−MS). Moreover, the imine **22** prepared from (*R*)-phenylglycinol, gave the expected aziridine **23** with low diastereoselectivity and the major (*R*,*R*)-diastereomer was isolated in 25% yield after column chromatography. As found for aziridine **6**, the *N*-substituent in **23** could not be removed by oxidative procedures, and hydrogenolysis over different Pd catalysts was unsatisfactory due to concomitant cleavage of the pyridyl-substituted aziridine C−N bond.

Then we assessed (*S*)-valine methyl ester as the chiral auxiliary and carried out the aziridination procedure on the derived imine **24**. In this way, we obtained the product **25**, coming from organometallic additions to both the imine and ester functions, in good yield and dr 87:13. Selective attack to the azomethine functionality could not be accomplished by working with equimolar amounts of reagents (imine, chloroiodomethane, and methyllithium), as the same product **25** was formed, albeit in low yield. This result apparently demonstrates that chloromethyllithium, rather than a carbene, is the active intermediate in the reaction. Moreover, products coming from the attack of methyllithium to the ester function were not observed either in the crude reaction mixture or in chromatographic fractions. Similarly, the 2-quinolineimine **26** gave the corresponding aziridine-α-chloroketone **27**, in comparable yield and dr 88:12.

Further efforts were devoted to find alternative procedures for the removal of the *N*-substituent in the aziridine **6**, through modification of the hydroxyl functionality. Initial attempts were directed to the transformation of the primary alcohol to halides or phenylsulfide by Mitsunobu procedures, because these compounds were expected to undergo β-amide elimination by treatment with a metal or a reducing agent (e.g., LiDBB and SmI_2).[13] Unfortunately, we met with no success, because the reaction mixtures were generally complex and the desired product was never isolated by column chromatography. Even the preparation of the bromide via the tosylate in different experimental conditions failed, probably because of the instability of any eventual bromide formed.

Treatment of the chloroketone **25** with tributylstannyl hydride in refluxing benzene in the presence of AIBN gave the ketone **28**, on which Wolff−Kishner reactions with hydrazine or phenylhydrazine and KOH in ethylene glycol or dimethylsulfoxide at high temperature were carried out; however, no fragmentation to aziridine was observed, as we had hoped to achieve by analogy with previous reports of α-heterosubstituted ketones.[14] Instead a new product was formed by rearrangement of **28** in the basic medium (vide supra).

Swern oxidation of the aziridine alcohol **6** smoothly led to the aziridine aldehyde **29** (Scheme 6), which was reduced with SmI_2 at low temperature. β-Fragmentation of the intermediate ketyl radical anion was expected to occur, thus giving the desired NH-aziridine. Instead, several unidentified products were observed by TLC analysis, presumably due to competitive side reactions, probably including pinacol coupling and most likely cleavage of the aziridine C−N bond. Indeed, it has been reported that acetoxymethylpyridine can be coupled with carbonyl compounds through cleavage of the benzylic C−O bond, driven by chelation of samarium to the pyridine nitrogen and the acetate.[15]

Considerable efforts were then devoted to find suitable reagents and conditions for the regioselective and stereoselective ring opening of the aziridine ring.[16] For example, aziridine

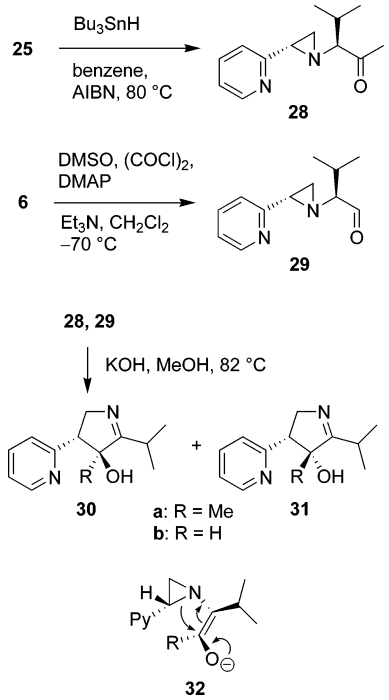
(13) This procedure has been used to remove the *N*-substituent (chiral auxiliary) from 1-(2-hydroxy-1-phenylethyl)-2-arylpyrrolidines: (a) Meyers, A. I.; Burgess, L. E. *J. Org. Chem.* **1991**, *56*, 2294−2296. (b) Higashiyama, K.; Inoue, H.; Takahashi, H. *Tetrahedron* **1994**, *50*, 1083−1092.

(14) (a) Leonard, N. J.; Gelfand, S. *J. Am. Chem. Soc.* **1955**, *77*, 3269−3271. (b) Caglioti, L.; Rosini, G.; Rossi, F. *J. Am. Chem. Soc.* **1966**, *88*, 3865−3866.

(15) Weitgenant, J. A.; Mortison, J. D.; Helquist, P. *Org. Lett.* **2005**, *7*, 3609−3612.

(16) (a) Sweeney, J. *Chem. Soc. Rev.* **2002**, *31*, 247−258. (b) Hu, X. E. *Tetrahedron* **2004**, *60*, 2701−2743.

SCHEME 6



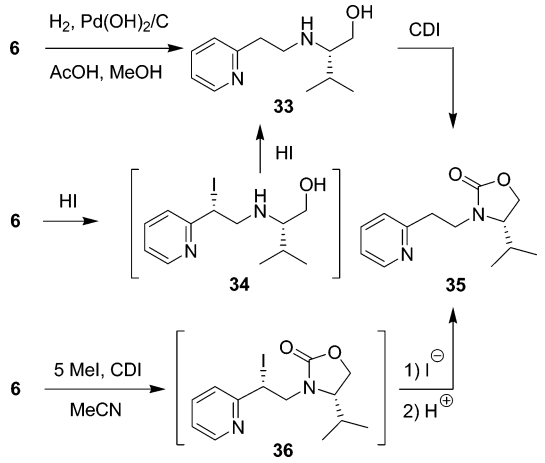
ketone **28** was reacted with methanolic KOH at the reflux temperature of methanol; unfortunately, formation of a highly prevalent compound, to which the structure **30a** (Scheme 6) was tentatively assigned on the basis of mass-spectrometric and spectroscopic analyses, was observed. Although several structures could be hypothesized for this product, only the depicted structure fits with all the analytical data. In particular, the stereochemistry of the two ring stereocenters was determined by a NOE experiment: irradiation of the pyridyl-substituted ring proton only caused a response of the adjacent methylene hydrogen, not the ring methyl substituent. Although another compound, probably the diastereomer **31a**, was present (ca. 15% by ^{1}H NMR) in the crude reaction mixture, it was not isolated by column chromatography, perhaps because it can undergo dehydration more readily.

We suggest that compound **30a** is formed by the concerted mechanism depicted in structure **32**, featuring the cleavage of the aziridine C−N bond, wherein the two electrons unusually move from nitrogen to carbon. We assume that the configuration of the pyridyl-substituted stereocenter is maintained throughout this rearrangement. This supposition is in agreement with the reported stereoselective rearrangement of a 1,2,3-trisubstituted aziridine to 1-pyrroline by generation of a carbanion at the propargyl *N*-substituent.[17] Analogously, when aldehyde **29** was subjected to the same conditions a 55:45 mixture of two compounds was observed, presumably the diastereomers **30b** and **31b**, as evidenced by the ^{1}H NMR spectrum of the crude reaction mixture. However, only the major product was isolated by column chromatography, as the minor one probably decomposed by dehydration. Conversely, no product was formed by heating the sodium alkoxide derived from the aziridine alcohol **6** in THF.

Other methodologies to achieve ring opening reactions of the aziridine ring in the aziridine alcohol **6** were then studied

(17) Åhman, J.; Jarevång, T.; Somfai, P. *J. Org. Chem.* **1996**, *61*, 8148−8159.

SCHEME 7



(Scheme 7). The secondary amine **33** was obtained by hydrogenolysis of the more substituted C−N bond of the aziridine alcohol **6** in the presence of $Pd(OH)_2/C$. Surprisingly, treatment of **6** with an excess of hydroiodic acid gave the same amine **33**. A literature survey showed that hydroiodic acid displays reducing properties toward many organic compounds.[18] In particular, reductions of α-halo ketones by iodide ion and hydroiodic acid have been reported.[19] Based on these reports, we propose that ring opening occurs first to give the iodide **34**, which is then reduced by iodide attack.

The reactions of aziridine-alcohol **6** with an excess of both carbonyldiimidazole (CDI) and reactive alkyl halides were then carried out, as these reactions were expected to give halogenated products coming from the ring opening of the aziridine by halide ion.[20] Presumably, the halide ion is generated by *N*-alkylation of one imidazole ring of CDI or a reaction intermediate.[21] However, when methyl iodide was used the only product observed was the imidazolidinone **35**, which was also prepared by reaction of the amino alcohol **33** with CDI. In order to account for this result, the iodide **36** is proposed as an intermediate in the formation of **35** from **6**. In this case, the regioselectivity of the aziridine ring-opening by iodide attack is presumed on the basis of the following results.

The bromide **37** was obtained by reaction of **6** with CDI and an excess of allyl bromide in acetonitrile at room temperature (Scheme 8). The diastereomeric bromide was detected in 10% in the crude reaction mixture. It showed the ^{1}H NMR absorption of the CHBr proton at lower field with respect to the major diastereomer, and its amount increased to 33% when the reaction was carried out at reflux temperature. Interestingly, analogous reactions of 2-(2-hydroxyalkyl)aziridines described in the

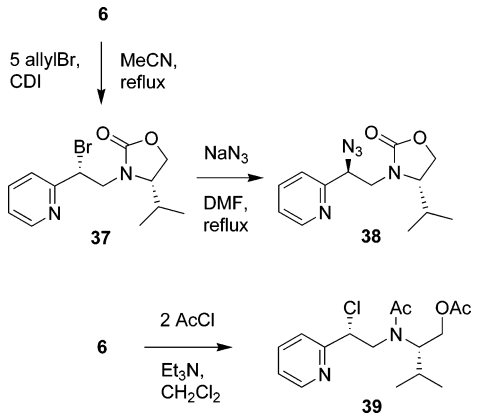
(18) (a) Deno, N. C.; Friedman, N.; Hodge, J. D.; MacKay, F. P.; Saines, G. *J. Am. Chem. Soc.* **1962**, *84*, 4713−4715. (b) Konieczny, M.; Harvey, R. G. *J. Org. Chem.* **1979**, *26*, 4813−4816. (c) Zoeller, J. R.; Ackerman, C. J. *J. Org. Chem.* **1989**, *55*, 1354−1356. (d) Duddek, H.; Rosenbaum, *J. Org. Chem.* **1991**, *56*, 1707−1713. (e) Davies, I. W.; Taylor, M.; Hughes, D.; Reider, P. J. *Org. Lett.* **2000**, *2*, 3385−3387. (f) D. Kumar, J. S. D.; Ho, M. M.; Toyokuni, T. *Tetrahedron Lett.* **2001**, *42*, 5601−5603. (g) Kamal, A.; Reddy, P. S. M. M.; Reddy, D. R. *Tetrahedron Lett.* **2002**, *43*, 6629−6631.

(19) Gemal, A. L.; Luche, J. L. *Tetrahedron Lett.* **1980**, 3195−3198.

(20) (a) Pyun, D. K.; Lee, C. H.; Ha, H-J.; Park, C. S.; Chang, J.-W.; Lee, W. K. *Org. Lett.* **2001**, *3*, 4197−4199. (b) Park, C. S.; Kim, M. S.; Sim, T. B.; Pyun, D. K.; Lee, C. H.; Choi, D.; Lee, W. K.; Chang, J.-W.; Ha, H.-J. *J. Org. Chem.* **2003**, *68*, 43−49.

(21) Kamijo, T.; Harada, H.; Iizuka. K. *Chem. Pharm. Bull.* **1983**, *31*, 4189−4193.

SCHEME 8



literature gave compounds coming from attack of halide ions to the unsubstituted aziridine carbon.[20] The bromine in **37** could be easily substituted by reaction with sodium azide in refluxing DMF to give the azido-oxazolidinone **38** as a single stereoisomer. Finally, reaction of **6** with 2 equiv of acetyl chloride gave the polyfunctional compound **39** by *N*,*O*-diacetylation and concomitant aziridine ring-opening by chloride ion. The complete or very high stereoselectivity observed in the described transformations of both the aziridine **6** and the bromide **37** involving cleavage of the benzylic C−N and C−Br bonds, respectively, points to an S_N2 mechanism operating with inversion of configuration.

Conclusion

An aziridination protocol for 2-pyridineimines has been achieved, making use of the reagent formed in situ from methyllithium and chloroiodomethane in the presence of lithium bromide. Good stereocontrol has been obtained with the imine derived from *O*-trimethylsilyl-(*S*)-valinol. On the other hand, when (*S*)-valine methyl ester was used, the carbenoidic organometallic reagent also attacked the ester function to give the corresponding aziridine α-chloroketone. The nitrogen substituent could not be removed, in order to prepare the optically pure *N*-H 2-(2-pyridyl)aziridine. However, the chemical functionality present in the nitrogen substituent can be exploited to achieve regioselective and stereoselective ring opening reactions by halide ions and an unusual rearrangement to a substituted pyrroline. For example, the halides **37** and **39** appear to be useful intermediates for the preparation of a variety of diversely functionalized pyridine derivatives, owing to their benzylic nature, that makes them highly electrophilic reagents in S_N2-type reactions. We are also currently investigating other regioselective and stereoselective ring-opening reactions of the optically pure *N*-unactivated 2-(2-pyridyl)aziridines.

Experimental Section

The imines **12a**, **12b**, **20**, and **26** were prepared from the corresponding aldehydes and enantiopure amines in almost quantitative yield by the procedures previously described for the preparation of the 2-pyridineimines **5**, **9**, **22**, and **24**.[2,6] All the crude imines (>95% pure by ^{1}H NMR analysis) were used immediately as obtained to avoid purification. However, the imine **26**, obtained as a solid, could be easily purified for analytical purpose by crystallization from an Et_2O−pentane mixture.

***N*-(3-Pyridylmethylidene)-*O*-trimethylsilyl-(*S*)-valinol (12a):** yellow oil; $[\alpha]^{20}_D$ −20.8 (*c* 1.0, $CHCl_3$); IR (neat) ν = 2958, 2929, 2868, 1646, 1591, 1575, 1470, 1422, 1388, 1250, 1026, 839, 805, 708; ^{1}H NMR (300 MHz, $CDCl_3$) δ = 8.87 (s, 1 H), 8.63 (d, J = 4.7 Hz, 1 H), 8.24 (s, 1 H), 8.12 (dt, J = 1.8 Hz, J = 7.9 Hz, 1 H), 7.33 (dd, J = 4.8 Hz, J = 7.8 Hz, 1 H), 3.87 (dd, J = 3.9 Hz, J = 10.3 Hz, 1 H), 3.66 (dd, J = 8.2 Hz, J = 10.3 Hz, 1 H), 3.02 (m, 1 H), 1.95 (sept, J = 6.8 Hz, 1 H), 0.93 (d, J = 6.8 Hz, 3 H), 0.92 (d, J = 6.8 Hz, 3 H), 0.03 (s, 9 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 157.8 (C=N), 151.2, 150.2, 134.5, 134.5, 131.9, 123.5, 78.8, 64.2, 29.9, 20.0, 18.6, −0.4; MS (EI) m/z = 264 (M^+, 6), 249 (5), 221 (4), 161 (100), 73 (27), 55 (16).

***N*-(4-Pyridylmethylidene)-*O*-trimethylsilyl-(*S*)-valinol (12b):** yellow oil; $[\alpha]^{20}_D$ −43.0 (*c* 0.4, $CHCl_3$); IR (neat) ν = 3081, 3032, 2958, 2872, 1650, 1593, 1462, 1405, 1251, 1115, 882, 841; ^{1}H NMR (300 MHz, $CDCl_3$) δ = 8.67 (dd, J = 1.6 Hz, J = 4.5 Hz, 1 H), 8.18 (s, 1 H), δ = 7.60 (dd, J = 1.6 Hz, J = 4.5 Hz, 1 H), 3.86 (dd, J = 3.6 Hz, J = 10.5 Hz, 1 H), 3.64 (dd, J = 7.8 Hz, J = 10.5 Hz, 1 H), 3.03 (dd, J = 3.6 Hz, J = 7.8 Hz, 1 H), 1.95 (sept, J = 6.9 Hz, 1 H), 0.93 (d, J = 6.9 Hz, 3 H), 0.91 (d, J = 6.9 Hz, 3 H), 0.02 (s, 9 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 158.8, 150.3, 143.1, 121.9 (PyH), 78.7, 64.0, 29.9, 19.9, 18.6, −0.4; MS (EI) m/z = 264 (M^+, 11), 249 (10), 221 (3), 161 (100), 131 (4), 103 (9), 73 (35).

***N*-(2-Pyridylmethylidene)-*O*-trimethylsilyl-1(*R*),2(*S*)-norephedrine (20):** colorless oil; $[\alpha]^{20}_D$ +98.0 (*c* 1.9, $CHCl_3$); IR (neat) ν = 3054, 2958, 2872, 1650, 1588, 1568, 1468, 1436, 1367, 1251, 1107, 973, 878, 774; ^{1}H NMR (300 MHz, $CDCl_3$) δ = 8.64 (ddd, J = 0.9 Hz, J = 1.7 Hz, J = 4.9 Hz, 1 H), 8.08 (s, 1 H), 7.90 (dt, J = 1.0 Hz, J = 7.9 Hz, 1 H), 7.69 (ddt, J = 1.0 Hz, J = 1.7 Hz, J = 7.9 Hz, 1 H), 7.15−7.33 (m, 6 H), 4.78 (d, J = 6.4 Hz, 1 H), 7.90 (quint, J = 6.4 Hz, 1 H), 1.33 (d, J = 6.4 Hz, 3 H), 0.07 (s, 9 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 159.4, 153.6, 150.1, 138.0, 136.8, 128.4, 128.0, 127.2, 126.5, 123.8, 78.5, 65.8, 16.2, 2.1; MS (EI) m/z = 297 (6), 179 (100), 133 (44), 92 (19), 73 (48).

***N*-(2-Quinolylmethylidene)-(*S*)-valine methyl ester (26):** white powder; mp = 57−58 °C (Et_2O−pentane); $[\alpha]^{20}_D$ −113.7 (*c* 1.1, $CHCl_3$); IR (Nujol) ν = 1735, 1639, 1595, 1463, 1376, 1193, 1142, 975, 842, 760, 734; ^{1}H NMR (300 MHz, $CDCl_3$) δ = 8.52 (s, 1 H), 8.28 (d, J = 8.5 Hz, 1 H), 8.21 (d, J = 8.6 Hz, 1 H), 8.14 (d, J = 8.5 Hz, 1 H), 7.87 (d, J = 8.0 Hz, 1 H), 7.77 (dt, J = 1.4 Hz, J = 8.1 Hz, 1 H), 7.77 (dt, J = 1.4 Hz, J = 8.0 Hz, 1 H), 3.86 (d, J = 7.0 Hz, 1 H), 3.78 (s, 3 H), 2.45 (dsept, J = 6.8 Hz, J = 7.0 Hz, 1 H), 1.01 (d, J = 6.8 Hz, 3 H), 0.98 (d, J = 6.8 Hz, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 172.0, 164.7, 154.2, 147.7, 136.4, 129.7, 129.5, 128.8, 127.6, 127.5, 118.6, 79.8, 51.9, 31.8, 19.4, 18.5; MS (EI) m/z = 270 (M^+, 2), 255 (2), 238 (3), 227 (14), 212 (15), 211 (100), 195 (30), 169 (28), 168 (25), 142 (42), 128 (13), 115 (15). Anal. Calcd for $C_{16}H_{18}N_2O_2$: C, 71.09; H, 6.71; N, 10.36. Found: C, 71.15; H, 6.73; N, 10.34.

Reaction of Imines with Methyllithium/Chloroiodomethane. General Procedure. Lithium bromide (0.66 g, 7.6 mmol) and chloroiodomethane (0.99 mL, 13.6 mmol) were added to the solution of the imine **5** (1.00 g, 7.6 mmol) in anhydrous THF (20 mL) under an inert atmosphere. The magnetically stirred mixture was cooled at −78 °C, and MeLi (1.6 M in Et_2O, 8.5 mL, 13.6 mmol) was slowly added; meanwhile, the mixture assumed a dark red color. The temperature was allowed to rise to 20 °C over 6 h, and then the mixture was quenched with saturated aqueous sodium hydrogen carbonate (20 mL). The organic phase was extracted with Et_2O (3 × 20 mL), and the combined organic layers were concentrated at reduced pressure. For reactions of imines derived from *O*-TMS-*β*-amino alcohols, the residue was taken up in MeOH−H_2O (1:1, 20 mL), NH_4F (2.5 g) was added, the mixture was stirred overnight, NaOH pellets were added until pH 11 was achieved, MeOH was removed at reduced pressure, and the organic phase was extracted with Et_2O (3 × 20 mL). The combined organic layers were washed with brine (20 mL), dried (Na_2SO_4), and concentrated at reduced pressure. The dark oily residue was purified via SiO_2 column chromatography eluting with 20:80 cyclohexane/EtOAc and then with 90:10 EtOAc/MeOH mixtures.

3-Methyl-2(*S*)-[2(*S*)-(2-pyridyl)-1-aziridinyl]-1-butanol (6): 0.509 g, 65%; red oil; $[\alpha]^{20}_D$ −105.6 (*c* 0.5, $CHCl_3$); IR (neat) ν = 3373, 2960, 1595, 1570, 1479, 1436, 1387, 1077, 762; ^{1}H NMR (300 MHz, $CDCl_3$) δ = 8.54 (ddd, *J* = 1.0 Hz, *J* = 1.8 Hz, *J* = 4.8 Hz, 1 H), 7.63 (dt, *J* = 1.2 Hz, *J* = 7.8 Hz, 1 H), 7.24 (dt, *J* = 0.9 Hz, *J* = 7.8 Hz, 1 H), 7.16 (ddd, *J* = 1.2 Hz, *J* = 4.9 Hz, *J* = 7.5 Hz, 1 H), 3.83 (d, *J* = 3.6 Hz, 2 H), 2.69 (dd, *J* = 3.2 Hz, *J* = 6.6 Hz, 1 H), 2.07 (d, *J* = 3.2 Hz, 1 H), 2.04 (sept, *J* = 6.9 Hz, 1 H), 1.95 (d, *J* = 6.5 Hz, 1 H), 1.66 (bs, 1 H), 1.50 (q, *J* = 3.6 Hz, 1 H), 0.98 (d, *J* = 6.9 Hz, 3 H), 0.96 (d, *J* = 6.9 Hz, 6 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 159.5, 149.9, 136.5, 121.9, 120.3, 75.6, 63.3, 42.9, 35.6, 29.9, 19.5, 19.4; MS (ES) *m*/*z* = 207.3 (M + H)$^+$, 229.2 (M + Na)$^+$, 413.3 [(2 M + H)$^+$], 435.3 (2 M + Na)$^+$. Anal. Calcd for $C_{12}H_{18}N_2O$: C, 69.87; H, 8.80; N, 13.58. Found: C, 69.60; H, 8.85; N, 13.28.

Whereas the minor diastereomer of **6** was not isolated by column chromatography, a sample of the *O*-methyl ether of **6** was obtained by column chromatography of several pooled fractions containing it, coming from different reaction runs: red oil; $[\alpha]^{20}_D$ −82.6 (*c* 4.6, $CHCl_3$); IR (neat) ν = 2968, 1590, 1578, 1482, 1431, 1391, 1075, 767; ^{1}H NMR (300 MHz, $CDCl_3$) δ = 8.49 (ddd, *J* = 0.7 Hz, *J* = 1.6 Hz, *J* = 4.9 Hz, 1 H), 7.59 (dt, *J* = 1.4 Hz, *J* = 7.9 Hz, 1 H), 7.24 (d, *J* = 7.9 Hz, 1 H), 7.12 (ddt, *J* = 0.9 Hz, *J* = 4.7 Hz, *J* = 7.9 Hz, 1 H), 3.55 (d, *J* = 6.7 Hz, 1 H), 3.54 (d, *J* = 4.5 Hz, 1 H), 3.38 (s, 3 H), 2.56 (dd, *J* = 3.3 Hz, *J* = 6.5 Hz, 1 H), 2.02 (d, *J* = 3.3 Hz, 1 H), 2.00 (d, *J* = 6.5 Hz, 1 H), 1.94 (sept, *J* = 6.9 Hz, 1 H), 1.65 (dd, *J* = 4.5 Hz, *J* = 6.7 Hz, 1 H), 0.95 (d, *J* = 6.9 Hz, 3 H), 0.94 (d, *J* = 6.9 Hz, 6 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 160.1, 148.9, 136.4, 120.7, 120.0, 74.4, 73.8, 59.0, 41.9, 30.1, 19.2, 18.9; MS (EI) *m*/*z* = 220 (M, 1), 219 (2), 175 (31), 145 (22), 133(10), 119 (100), 106 (69), 92 (55), 79 (21), 65 (16). Anal. Calcd for $C_{13}H_{20}N_2O$: C, 70.87; H, 9.15; N, 12.72. Found: C, 70.58; H, 9.18; N, 12.42.

3(*S*)-Methyl-2-[2(*S*)-(2-quinolyl)-1-aziridinyl]-1-butanol (10): Compound **10** was obtained from the imine **9** (1.1 g, 3.5 mmol): 0.457 g (51%); red oil; $[\alpha]^{20}_D$ −115.7 (*c* 1.6, $CHCl_3$); IR (neat) ν = 3370, 2964, 1589, 1574, 1428, 1388, 1070, 770; ^{1}H NMR (300 MHz, $CDCl_3$) δ = 8.10 (d, *J* = 8.5 Hz, 1 H), 8.07 (d, *J* = 8.5 Hz, 1 H), 7.80 (d, *J* = 8.1 Hz, 1 H), 7.71 (ddd, *J* = 1.5 Hz, *J* = 6.9 Hz, *J* = 8.4 Hz, 1 H), 7.52 (ddd, *J* = 1.2 Hz, *J* = 7.0 Hz, *J* = 8.5 Hz, 1 H), 7.36 (d, *J* = 8.5 Hz, 1 H), 3.86 (d, *J* = 3.9 Hz, 2 H), 2.92 (dd, *J* = 3.3 Hz, *J* = 6.8 Hz, 1 H), 2.13 (sept, *J* = 6.9 Hz, 1 H), 2.10 (d, *J* = 3.3 Hz, 1 H), 2.05 (d, *J* = 6.8 Hz, 1 H), 1.58 (q, *J* = 4.0 Hz, 1 H), 0.98 (d, *J* = 6.9 Hz, 3 H), 0.96 (d, *J* = 6.9 Hz, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 160.4, 147.6, 136.8, 129.5, 128.8, 127.6, 127.5, 126.0, 117.9, 75.4, 63.5, 42.7, 35.7, 30.1, 19.7, 19.4; MS (ES) *m*/*z* = 256.4 (M + H)$^+$, 279.3 (M + Na)$^+$, 535.6 (2 M + Na)$^+$. Anal. Calcd for $C_{16}H_{20}N_2O$: C, 74.97; H, 7.86; N, 10.93. Found: C, 74.71; H, 7.88; N, 10.90.

1(*R*)-Phenyl-2(*S*)-[2(*R*)- and 2(*S*)-(2-pyridyl)-1-aziridinyl]-1-propanol 21. The reaction of the imine **20** (0.936 g, 3 mmol) gave a mixture of the diastereomeric aziridines **21** (0.335 g, 44%) with a 77:23 ratio (^{1}H NMR), which could not be separated by column chromatography. The different absorptions for the two diastereomers were evidenced from enriched chromatographic fractions. Major diastereomer: yellow oil; ^{1}H NMR (300 MHz, $CDCl_3$) δ = 8.49 (m, 1 H), 7.60 (m, 2 H), 7.38−7.12 (m, 6 H), 4.95 (d, *J* = 3.9 Hz, 1 H), 4.55 (d, *J* = 6.3 Hz, 1 H), 2.82 (dd, *J* = 3.9 Hz, *J* = 6.3 Hz, 1 H), 2.61 (dd, *J* = 3.3 Hz, *J* = 6.4 Hz, 1 H), 2.06 (d, *J* = 3.3 Hz, 1 H), 1.86 (d, *J* = 6.6 Hz, 1 H), 1.00 (d, *J* = 6.4 Hz, 1 H). Minor diastereomer: yellow oil; ^{1}H NMR (300 MHz, $CDCl_3$) δ = 8.60 (m, 1 H, PyH), 7.66 (m, 2 H), 7.38−7.12 (m, 6 H), 4.88 (d, *J* = 3.9 Hz, 1 H), 4.39 (d, *J* = 6.5 Hz, 1 H), 2.84 (dd, *J* = 3.9 Hz, *J* = 6.5 Hz, 1 H), 2.61 (dd, *J* = 3.2 Hz, *J* = 6.6 Hz, 1 H), 2.17 (d, *J* = 3.3 Hz, 1 H), 1.91 (d, *J* = 6.6 Hz, 1 H), 0.88 (d, *J* = 6.5 Hz, 1 H). Anal. Calcd for $C_{16}H_{18}N_2O$: C, 75.56; H, 7.13; N, 11.01. Found: C, 75.98; H, 7.17; N, 10.98.

2(*R*)-Phenyl-2-[2(*R*)-(2-pyridyl)-1-aziridinyl]ethanol (23). Compound **23** was obtained from the imine **22** (1.04 g, 3.5 mmol): 0.210 g (25%); red oil; $[\alpha]^{20}_D$ −87.3 (*c* 0.7, $CHCl_3$); IR (neat) ν = 3365, 3052, 3019, 2933, 2853, 1595, 1570, 1480, 1389, 1354, 1216, 1150, 1067, 756, 701; ^{1}H NMR (300 MHz, $CDCl_3$) δ = 8.51 (ddd, *J* = 0.9 Hz, *J* = 1.7 Hz, *J* = 4.9 Hz, 1 H), 7.61 (dt, *J* = 1.9 Hz, *J* = 7.7 Hz, 1 H), 7.38 (dd, *J* = 1.6 Hz, *J* = 7.9 Hz, 1 H), 7.34−7.10 (m, 6 H), 4.01 (dd, *J* = 5.5 Hz, *J* = 11.3 Hz, 1 H), 3.94 (dd, *J* = 5.5 Hz, *J* = 11.3 Hz, 1 H), 2.95 (t, *J* = 5.5 Hz, 1 H); 2.72 (bs, 1 H), 2.61 (dd, *J* = 3.2 Hz, *J* = 6.6 Hz, 1 H), 2.39 (d, *J* = 3.3 Hz, 1 H), 2.19 (d, *J* = 6.6 Hz, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 159.1, 149.1, 139.9, 136.4, 128.3, 127.5, 127.4, 121.9, 120.7, 75.6, 67.6, 39.7, 38.6; MS (EI) *m*/*z* = 312 (M$^+$, 1), 297 (5), 177 (10), 144 (31), 119 (63), 106 (100), 92 (30), 73 (43). Anal. Calcd for $C_{15}H_{16}N_2O$: C, 74.97; H, 6.71; N, 11.66. Found: C, 75.12; H, 6.88; N, 11.48.

(*S*)-1-Chloro-4-methyl-3-[2(*S*)-(2-pyridyl)-1-aziridinyl]-2-pentanone (25). Compound **25** was obtained from the imine **24** (0.792 g, 3.6 mmol): 0.60 g (75%); red oil; $[\alpha]^{20}_D$ −59.3 (*c* 1.2, $CHCl_3$); IR (neat) ν = 2967, 2865, 1734, 1593, 1465, 1436, 1389; ^{1}H NMR (300 MHz, $CDCl_3$) δ = 8.44 (dd, *J* = 0.9 Hz, *J* = 4.8 Hz, 1 H), 7.58 (tt, *J* = 1.7 Hz, *J* = 7.8 Hz, 1 H), 7.19 (dd, *J* = 0.9 Hz, *J* = 7.8 Hz, 1 H), 7.14 (ddt, *J* = 1.2 Hz, *J* = 4.8 Hz, *J* = 7.8 Hz, 1 H), 4.60 (d, *J* = 17.0 Hz, 1 H), 4.51 (d, *J* = 17.0 Hz, 1 H), 2.68 (dd, *J* = 3.4 Hz, *J* = 6.7 Hz, 1 H), 2.25 (d, *J* = 6.5 Hz, 1 H), 2.06 (dsept, *J* = 6.5 Hz, *J* = 6.6 Hz, 1 H), 2.00 (d, *J* = 3.4 Hz, 1 H), 1.68 (d, *J* = 6.7 Hz, 1 H), 0.91 (d, *J* = 6.6 Hz, 3 H), 0.85 (d, *J* = 6.6 Hz, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 202.0, 158.1, 148.9, 136.5, 122.2 , 119.9, 83.9, 47.6, 43.6, 34.9, 32.1, 19.1, 19.0; MS (ES) *m*/*z* = 253.2 (M + H)$^+$, 275.1 (M + Na)$^+$. Anal. Calcd for $C_{13}H_{17}ClN_2O$: C, 61.78; H, 6.78; Cl, 14.03; N, 11.08. Found: C, 61.48; H, 6.88; Cl, 13.99; N, 11.03.

(*S*)-1-Chloro-4-methyl-3-[2(*S*)-(2-quinolyl)-1-aziridinyl]-2-pentanone (27). Compound **27** was obtained starting from of the imine **26** (0.621 g, 2.3 mmol): 0.514 g (78%); red oil; $[\alpha]^{20}_D$ −71.2 (*c* 1.2, $CHCl_3$); IR (neat) ν = 3052, 2964, 2926, 2875, 1733, 1618, 1600, 1505, 1430, 1428, 1389, 1313, 1030, 829, 756, 628; ^{1}H NMR (300 MHz, $CDCl_3$) δ = 8.13 (d, *J* = 8.6 Hz, 1 H), 8.04 (d, *J* = 8.4 Hz, 1 H), 7.80 (d, *J* = 8.1 Hz, 1 H), 7.71 (dt, *J* = 1.4 Hz, *J* = 8.4 Hz, 1 H), 7.57 (dt, *J* = 1.4 Hz, *J* = 8.0 Hz, 1 H), 7.35 (d, *J* = 8.5 Hz, 1 H), 4.68 (d, *J* = 16.7 Hz, 1 H), 4.60 (d, *J* = 16.7 Hz, 1 H), 2.99 (dd, *J* = 3.3 Hz, *J* = 6.7 Hz, 1 H), 2.42 (d, *J* = 6.3 Hz, 1 H), 2.19 (dsept, *J* = 6.3 Hz, *J* = 6.8 Hz, 1 H), 2.12 (d, *J* = 3.3 Hz, 1 H), 1.79 (d, *J* = 6.7 Hz, 1 H), 1.00 (d, *J* = 6.8 Hz, 3 H), 0.96 (d, *J* = 6.8 Hz, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 201.1, 158.9, 147.4, 136.9, 129.6, 128.6, 127.5, 127.4, 126.1, 117.0, 83.7, 47.7, 44.2, 35.2, 32.4, 19.2, 19.1; MS (ES) *m*/*z* = 303.1 (M + H)$^+$, 325.0 (M + Na)$^+$. Anal. Calcd for $C_{17}H_{19}ClN_2O$: C, 67.43; H, 6.32; Cl, 11.71; N, 9.25. Found: C, 67.40; H, 6.36; Cl, 11.67; N, 9.20.

(*S*)-4-Methyl-3-[2(*S*)-(2-pyridyl)-1-aziridinyl]-2-pentanone (28). A solution of compound **25** (0.102 g, 0.4 mmol), tri(*n*-butyl)tin hydride (0.12 mL, 0.6 mmol), and AIBN (10 mg) in benzene (5 mL) was heated at reflux temperature under an inert atmosphere for 3 h. Evaporation of the solvent at reduced pressure gave an oily residue that was subjected to chromatography on a SiO_2 column eluting with cyclohexane−ethyl acetate (70:30) to obtain **28** as a red-brown oil: 0.076 g (88%); red-brown oil; $[\alpha]^{20}_D$ −20.2 (*c* 1.0, $CHCl_3$); IR (neat) ν = 2936, 2932, 2874, 1710, 1594, 1565, 1436, 1353, 1212, 996, 776, 748; ^{1}H NMR (300 MHz, $CDCl_3$) δ = 8.50 (ddd, *J* = 1.0 Hz, *J* = 1.7 Hz, *J* = 4.9 Hz, 1 H), 7.62 (dt, *J* = 1.7 Hz, *J* = 7.7 Hz, 1 H), 7.21 (td, *J* = 1.0 Hz, *J* = 7.7 Hz, 1 H), 7.14 (ddd, *J* = 1.2 Hz, *J* = 4.9 Hz, *J* = 7.7 Hz, 1 H), 2.68 (dd, *J* = 3.3 Hz, *J* = 6.6 Hz, 1 H), 2.31 (s, 3 H), 2.12 (dsept, *J* = 6.2 Hz, *J* = 6.6 Hz, 1 H), 2.07 (d, *J* = 6.2 Hz, 1 H), 2.02 (d, *J* = 3.3 Hz, 1 H), 1.69 (d, *J* = 6.6 Hz, 1 H), 0.97 (d, *J* = 6.6 Hz, 3 H), 0.90 (d, *J* = 6.6 Hz, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 210.1, 159.0, 149.0, 136.6, 122.1, 120.0, 85.9, 44.0, 34.7, 31.7, 27.1, 19.4, 19.2; MS (ES) *m*/*z* = 219.4 (M + H)$^+$, 241.4 (M + Na)$^+$. Anal. Calcd for $C_{13}H_{18}N_2O$: C, 71.53; H, 8.31; N, 12.83. Found: C, 71.21; H, 8.38; N, 12.64.

(*S*)-3-Methyl-2-[2(*S*)-(2-pyridyl)-1-aziridinyl]butanal (29). To a solution of oxalyl chloride (68 mg, 45 μL, 0.53 mmol) in CH_2Cl_2 (2 mL) at −60 °C was added dropwise a solution of DMSO (83 mg, 76 μL, 1.1 mmol) in CH_2Cl_2 (2 mL). After 10 min, a solution of aziridine **6** (100 mg, 0.49 mmol) in CH_2Cl_2 (2 mL) was added dropwise, followed, after 15 min, by triethylamine (246 mg, 0.34 mL, 2.4 mmol). The temperature was slowly raised to 20 °C, and the mixture was further stirred for 2 h and then quenched with H_2O (5 mL). The organic phase was extracted with CH_2Cl_2 (3 × 10 mL), and the combined organic phases was concentrated. The residue was subjected to chromatography on a SiO_2 column eluting with EtOAc to give **29** as a red oil: 74 mg (74%); $[\alpha]^{20}_D$ −24.6 (*c* 0.33, $CHCl_3$); IR (neat) ν = 3059, 2964, 2919, 2868, 1733, 1669, 1592, 1572, 1472, 1436, 1260, 1079, 804, 753; ^{1}H NMR (300 MHz, $CDCl_3$) δ = 9.78 (d, *J* = 2.8 Hz, 1 H), 8.48 (ddd, *J* = 0.9 Hz, *J* = 1.8 Hz, *J* = 4.9 Hz, 1 H), 7.61 (dt, *J* = 1.8 Hz, *J* = 7.6 Hz, 1 H), 7.32 (d, *J* = 8.7 Hz, 1 H), 7.21 (ddd, *J* = 0.9 Hz, *J* = 3.9 Hz, *J* = 7.6 Hz, 1 H), 2.64 (dd, *J* = 3.5 Hz, *J* = 6.7 Hz, 1 H), 2.25 (dsept, *J* = 5.7 Hz, *J* = 6.6 Hz, 1 H), 2.23 (d, *J* = 3.5 Hz, 1 H), 2.08 (dd, *J* = 2.8 Hz, *J* = 5.7 Hz, 1 H), 1.82 (d, 1 H, *J* = 6.7 Hz), 0.98 (d, *J* = 6.8 Hz, 3 H), 0.95 (d, *J* = 6.8 Hz, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 202.9, 158.8, 149.2, 136.6, 122.2, 120.2, 83.1, 42.3, 35.1, 30.6, 19.2, 18.9; MS (ES) *m*/*z* = 205.4 $(M + H)^+$, 227.3 $(M + Na)^+$. Anal. Calcd for $C_{12}H_{16}N_2O$: C, 70.56; H, 7.90; N, 13.71; Found: C, 70.32; H, 7.93; N, 13.66.

3(*S*),4(*S*)-3-Hydroxy-2-isopropyl-3-methyl-4-(2-pyridyl)-1-pyrroline (30a): To a solution of **28** (300 mg, 1.4 mmol) in MeOH (10 mL) was added KOH (0.118 g, 2.1 mmol). The mixture was heated at the reflux temperature for 2 h, and then the solvent was evaporated at reduced pressure, H_2O (5 mL) was added, and the organic phase was extracted with CH_2Cl_2 (2 × 20 mL). The combined organic layers was washed with brine (10 mL), dried (Na_2SO_4), and concentrated at reduced pressure. The dark oily residue was subjected to chromatography on a SiO_2 column eluting with EtOAc, then with a 90:10 EtOAc/MeOH mixture, to give **30a** as a yellowish oil: 0.186 g (61%); $[\alpha]^{20}_D$ −120.2 (*c* 0.9, $CHCl_3$); IR (neat) ν = 3245, 2967, 2931, 2871, 1641, 1594, 1569, 1473, 1436, 1370, 1151, 1112, 987, 788, 751; ^{1}H NMR (300 MHz, $CDCl_3$) δ = 8.49 (d, *J* = 4.3 Hz, 1 H), 7.66 (t, *J* = 7.7 Hz), 7.19 (dd, *J* = 4.3 Hz, *J* = 7.7 Hz, 2 H), 6.22 (bs, 1 H), 4.17 (dd, *J* = 7.9 Hz, *J* = 15.5 Hz, 1 H), 3.82 (dd, *J* = 6.9 Hz, *J* = 15.5 Hz, 1 H), 3.22 (dd, *J* = 6.9 Hz, *J* = 7.9 Hz, 1 H), 2.82 (sept, *J* = 6.6 Hz, 1 H), 1.43 (s, 3 H), 1.29 (d, *J* = 6.9 Hz, 3 H), 1.22 (d, *J* = 6.9 Hz, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 185.3, 160.1, 148.4, 137.1, 124.7, 121.8, 84.6, 64.0, 53.4, 28.0, 24.6, 21.8, 21.3; MS (EI) *m*/*z* = 218 (M, 4), 175 (5), 149 (6), 120 (3), 121 (10), 106 (100), 92 (8), 78 (15); MS (ES) *m*/*z* = 219.3 $(M + H)^+$, 241.4 $(M + Na)^+$. Anal. Calcd for $C_{13}H_{18}N_2O$: C, 71.53; H, 8.31; N, 12.83. Found: C, 71.56; H, 8.34; N, 12.80.

3(*S*),4(*S*)-3-Hydroxy-2-isopropyl-4-(2-pyridyl)-1-pyrroline (30b). Compound **30b** was obtained from **29** (0.300 g, 1.45 mmol) by the same procedure used for **30a**: 148 mg (52%); yellowish oil; $[\alpha]^{20}_D$ −98.7 (*c* 1.4, $CHCl_3$); IR (neat) ν = 3241, 2977, 2927, 2864, 1647, 1597, 1578, 1471, 1430, 1378, 1141, 988, 784, 757; ^{1}H NMR (300 MHz, $CDCl_3$) δ = 8.54 (dt, *J* = 1.7 Hz, *J* = 4.6 Hz, 1 H), 7.64 (td, *J* = 1.9 Hz, *J* = 7.7 Hz, 1 H), 7.17 (m, 2 H), 5.14 (d, *J* = 8.3 Hz, 1 H), 4.30 (dt, *J* = 8.3 Hz, *J* = 14.9 Hz, 1 H), 3.76 (dt, *J* = 8.6 Hz, *J* = 14.9 Hz, 1 H), 3.50 (dt, *J* = 8.3 Hz, *J* = 8.4 Hz, 1 H), 2.87 (sept, *J* = 6.8 Hz, 1 H), 1.26 (d, *J* = 6.8 Hz, 3 H), 1.22 (d, *J* = 6.8 Hz, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 183.4, 160.4 (Py), 149.5, 136.7, 123.9, 122.5, 83.0, 61.7, 55.6, 29.4, 20.0, 19.0; the product decomposed during GC−MS analysis. Anal. Calcd for $C_{12}H_{16}N_2O$: C, 70.56; H, 7.90; N, 13.71.Found: C, 70.54; H, 7.93; N, 13.77.

***N*-[2-(2-Pyridyl)]ethyl-(*S*)-valinol (33).** Compound **33** was obtained from the aziridine **6** by hydrogenation over $Pd(OH)_2$/C (91% yield) and by reduction with HI (62% yield, see the Supporting Information): $[\alpha]^{20}_D$ +16.8 (*c* 2.0, $CHCl_3$); IR (neat) ν = 3334, 2962, 2925, 2872, 1651, 1589, 1467, 1427, 1384, 1274, 1070, 813, 716; ^{1}H NMR (300 MHz, $CDCl_3$) δ = 8.49 (ddd, *J* = 1.0 Hz, *J* = 1.8 Hz, *J* = 4.9 Hz, 1 H), 7.59 (ddt, *J* = 1.3 Hz, *J* = 1.8 Hz, *J* = 7.7 Hz, 1 H), 7.59 (dd, *J* = 0.9 Hz, *J* = 7.8 Hz, 1 H), 7.11 (ddd, *J* = 1.3 Hz, *J* = 4.9 Hz, *J* = 7.7 Hz, 1 H), 3.63 (dd, *J* = 4.1 Hz, *J* = 10.9 Hz, 1 H), 3.34 (dd, *J* = 7.5 Hz, *J* = 10.9 Hz, 1 H), 2.90 (bs, 2 H, OH + NH), 3.15−2.92 (m, 4 H), 2.40 (dd, *J* = 4.1 Hz, *J* = 10.9 Hz, 1 H), 1.76 (sept, *J* = 6.7 Hz, 1 H), 0.90 (d, *J* = 6.7 Hz, 3 H), 0.85 (d, *J* = 6.7 Hz, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 160.1 (Py), 149.0, 136.5, 123.4, 121.3, 64.6, 60.8, 46.5, 38.0, 29.1, 19.4, 18.5; MS (EI) *m*/*z* = 204 (6), 191 (8), 177 (46), 165 (21), 135 (11), 121 (10), 106 (55), 94 (100), 84 (20), 78 (15). Anal. Calcd for $C_{12}H_{20}N_2O$: C, 69.19; H, 9.68; N, 13.45. Found: C, 69.41; H, 9.83; N, 13.42.

(*S*)-3-[2-(2-Pyridyl)ethyl]-1,3-oxazolidin-2-one (35). To a solution of **33** (50 mg, 0.24 mmol) in dry CH_2Cl_2 (10 mL) was added CDI (40 mg, 0.24 mmol) in one portion. After the mixture was stirred overnight, H_2O (5 mL) was added. The organic phase was extracted with CH_2Cl_2 (3 × 10 mL), and the combined organic phases was dried (Na_2SO_4) and concentrated at reduced pressure. The red oily residue was subjected to chromatography on a SiO_2 column, eluting with EtOAc then with a 90:10 EtOAc/MeOH mixture to give **35** as a red oil: 0.047 g (84%); $[\alpha]^{20}_D$ +29.0 (*c* 1.9, $CHCl_3$); IR (neat) ν = 2961, 2929, 2869, 1733, 1593, 1566, 1427, 1259, 1009, 759; ^{1}H NMR (300 MHz, $CDCl_3$) δ = 8.52 (d, *J* = 4.9 Hz, 1 H, PyH), 7.62 (td, *J* = 1.8 Hz, *J* = 7.7 Hz, 1 H), 7.23 (d, *J* = 7.8 Hz, 1 H), 7.15 (dd, *J* = 4.9 Hz, *J* = 7.8 Hz, 1 H), 4.11 (dd, *J* = 8.8 Hz, *J* = 8.9 Hz, 1 H), 4.01 (dd, *J* = 5.4 Hz, *J* = 8.9 Hz, 1 H), 3.87 (ddd, *J* = 6.9 Hz, *J* = 7.1 Hz, *J* = 14.4 Hz, 1 H), 3.61 (ddd, *J* = 3.6 Hz, *J* = 5.4 Hz, *J* = 8.8 Hz, 1 H), 3.42 (ddd, *J* = 6.2 Hz, *J* = 7.9 Hz, *J* = 14.4 Hz, 1 H), 3.07 (m, 2 H), 2.87 (dsept, *J* = 3.5 Hz, *J* = 6.8 Hz, 1 H), 0.83 (d, *J* = 7.0 Hz, 3 H), 0.84 (d, *J* = 7.0 Hz, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 158.5, 157.5, 149.3, 136.6, 136.6, 123.5, 121.7, 62.7, 59.3, 41.5, 35.9, 27.4, 17.6, 14.1; MS (ES) *m*/*z* = 235.2 $(M + H)^+$, 491.1 $(2M + Na)^+$. Anal. Calcd for $C_{13}H_{18}N_2O_2$: C, 66.64; H, 7.74; N, 11.96. Found: C, 66.72; H, 7.77; N, 11.92.

3-[2(*R*)-Bromo-2-(2-pyridyl)ethyl]-4(*S*)-isopropyl-1,3-oxazolidin-2-one (37). To the aziridine **6** (0.100 g, 0.48 mmol) dissolved in anhydrous MeCN (10 mL) were added, in order, CDI (0.080 g, 0.48 mmol) and allyl bromide (0.21 mL, 2.4 mmol). The mixture was stirred at room temperature for 2 h and then quenched with H_2O (10 mL). The organic phase was extracted with Et_2O (2 × 10 mL) and CH_2Cl_2 (2 × 10 mL). The combined organic phases was washed with saturated aq $NaHCO_3$, combined, dried (Na_2SO_4), and concentrated at reduced pressure. The oily residue was subjected to chromatography on a SiO_2 column eluting with cyclohexane−EtOAc (1:1) to give **37** as a whitish solid: 0.108 g (72%); mp = 107−108 °C; $[\alpha]^{20}_D$ + 41.5 (*c* 1.2, $CHCl_3$); IR (KBr) ν = 3050, 3013, 2953, 2874, 1728, 1588, 1487, 1436, 1258, 1159, 1050, 932, 788, 751, 706, 597; ^{1}H NMR (300 MHz, $CDCl_3$) δ = 8.57 (ddd, *J* = 0.9 Hz, *J* = 1.7 Hz, *J* = 4.8 Hz, 1 H), 7.59 (dt, *J* = 1.8 Hz, *J* = 7.7 Hz, 1 H), 7.38 (td, *J* = 0.9 Hz, *J* = 7.8 Hz, 1 H), 7.22 (ddd, *J* = 1.0 Hz, *J* = 4.8 Hz, *J* = 7.7 Hz, 1 H), 5.21 (dd, *J* = 6.3 Hz, *J* = 9.0 Hz, 1 H), 4.12 (dd, *J* = 6.3 Hz, *J* = 14.2 Hz, 1 H), 3.89 (m, 3 H), 3.08 (ddd, *J* = 1.0 Hz, *J* = 6.1 Hz, *J* = 7.6 Hz, 1 H), 2.09 (dsept, *J* = 3.6 Hz, *J* = 6.9 Hz, 1 H), 0.76 (d, *J* = 6.9 Hz, 3 H), 0.72 (d, *J* = 6.9 Hz, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 158.1, 157.2, 149.5, 137.1, 123.6, 123.5, 62.8, 59.1, 48.0, 46.4, 27.1, 17.3, 14.0; MS (ES); *m*/*z* = 313.2 $(M + H)^+$, 336.9 $(M + H + Na)^+$. Anal. Calcd for $C_{13}H_{17}BrN_2O_2$: C, 49.85; H, 5.47; Br, 25.51; N, 8.94. Found: C, 49.98; H, 5.41; Br, 25.43; N, 8.90.

3-[2(*S*)-Azido-2-(2-pyridyl)ethyl]-4(*S*)-isopropyl-1,3-oxazolidin-2-one (38). The bromide **37** (40 mg, 0.13 mmol) was dissolved in dry DMF (5 mL), and sodium azide (48 mg, 0.73 mmol) was added. The mixture was heated at the reflux temperature for 8 h, and then brine (5 mL) and EtOAc (10 mL) were added. The organic phase was extracted with EtOAc (3 × 10 mL), and the combined organic phases were concentrated at reduce pressure. The yellowish residue was subjected to chromatography on a SiO_2 column eluting

with cyclohexane, then with a 80:20 cyclohexane/EtOAc mixture to give the azide **38** as a yellowish oil: 28 mg (78%); $[\alpha]^{20}_D$ +12.8 (*c* 1.1, $CHCl_3$); IR (neat) ν = 2964, 2935, 2874, 2102, 1738, 1597, 1560, 1425, 1268, 1001, 757; ^{1}H NMR (300 MHz, $CDCl_3$) δ = 8.62 (ddd, *J* = 0.8 Hz, *J* = 1.6 Hz, *J* = 4.6 Hz, 1 H), 7.74 (dt, *J* = 1.8 Hz, *J* = 7.7 Hz, 1 H), 7.39 (d, *J* = 7.8 Hz, 1 H), 7.28 (ddd, *J* = 0.8 Hz, *J* = 4.9 Hz, *J* = 7.7 Hz, 1 H), 4.95 (dd, *J* = 4.6 Hz, *J* = 9.1 Hz, 1 H), 4.27 (dd, *J* = 8.8 Hz, *J* = 8.9 Hz, 1 H), 4.09 (dd, *J* = 4.8 Hz, *J* = 8.8 Hz, 1 H), 3.97 (ddd, *J* = 3.5 Hz, *J* = 4.8 Hz, *J* = 8.8 Hz, 1 H), 3.85 (dd, *J* = 4.6 Hz, *J* = 14.6 Hz, 1 H), 3.45 (dd, *J* = 9.1 Hz, *J* = 14.5 Hz, 1 H), 2.16 (dsept, *J* = 3.5 Hz, *J* = 6.9 Hz, 1 H), 0.89 (d, *J* = 6.9 Hz, 3 H), 0.82 (d, *J* = 6.9 Hz, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 158.3, 155.7, 149.8 (PyH), 137.2, 123.6, 122.3, 64.4, 63.1, 60.4, 45.4, 27.4, 17.6, 14.1; MS (ES) *m*/*z* = 276.1 $(M + H)^+$, 298.2 $(M + Na)^+$. Anal. Calcd for $C_{14}H_{21}N_5O_2$: C, 57.71; H, 7.27; N, 24.04. Found: C, 57.56 ; H, 7.29; N, 23.94.

***N*-[(2(*R*)-Chloro-2-(2-pyridyl)ethyl]-*N*,*O*-diacetyl-(*S*)-valinol (39).** To a stirred solution of **6** (100 mg, 0.49 mmol) in CH_2Cl_2 (4 mL) at 0 °C was added dropwise acetyl chloride (76 mg, 69 μL, 0.97 mmol), followed by triethylamine (59 mg, 82 μL, 0.59 mmol), and the temperature was raised to room temperature. After 2 h, aq $NaHCO_3$ (5 mL) was added to the mixture, and the organic phase was extracted with CH_2Cl_2 (3 × 10 mL). The combined organic phases were dried (Na_2SO_4) and concentrated at reduced pressure. The red oily residue was subjected to chromatography on a SiO_2 column eluting with EtOAc/cyclohexane (90:10) to give **39** as a yellow oil: 113 mg (74%); $[\alpha]^{20}_D$ −23.1 (*c* 2.3, $CHCl_3$); IR (neat) ν = 2958, 2926, 2874, 1739, 1647, 1599, 1470, 1438, 1373, 1225, 1039, 746; ^{1}H NMR (300 MHz, $CDCl_3$) δ = 8.58 (ddd, *J* = 1.1 Hz, *J* = 1.7 Hz, *J* = 4.9 Hz, 1 H), 7.67 (dt, *J* = 1.7 Hz, *J* = 7.7 Hz, 1 H), 7.33 (d, *J* = 7.7 Hz, 1 H), 7.20 (ddd, *J* = 1.1 Hz, *J* = 4.9 Hz, *J* = 7.5 Hz, 1 H), 5.85 (dd, *J* = 5.2 Hz, *J* = 7.3 Hz, 1 H), 4.11 (dd, *J* = 4.5 Hz, *J* = 11.3 Hz, 1 H), 3.97 (dd, *J* = 6.5 Hz, *J* = 11.3 Hz, 1 H), 3.20 (dd, *J* = 7.3 Hz, *J* = 13.0 Hz, 1 H), 3.11 (dd, *J* = 5.2 Hz, *J* = 13.0 Hz, 1 H), 3.11 (ddd, *J* = 4.5 Hz, *J* = 5.4 Hz, *J* = 6.5 Hz, 1 H), 2.15 (s, 3 H), 2.04 (s, 3 H), 1.79 (dsept, *J* = 5.4 Hz, *J* = 6.8 Hz, 1 H), 0.89 (d, *J* = 6.8 Hz, 3 H), 0.87 (d, *J* = 6.8 Hz, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 171.0, 170.3, 158.0, 149.3, 136.5, 122.8, 121.5, 75.9, 64.7, 61.1, 50.9, 29.2, 21.1, 20.9, 18.5; the product decomposed during GC/MS analysis. Anal. Calcd for $C_{16}H_{23}ClN_2O_3$: C, 58.80; H, 7.09; Cl, 10.85; N, 8.57. Found: C, 58.56; H, 7.12; Cl, 10.82; N, 8.55.

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Supporting Information Available: Experimental procedures for compound **33**. Analytical data for compounds **13a**,**b** and **14a**,**b**. Copies of the ^{1}H NMR spectra of the imines **12a**,**b**, **20**, and **26**, aziridines **6**, **10**, **21**, **23**, **25**, **27**, **28**, and **29**, amines **13a**,**b** and **14a**,**b**, pyrrolines **30a**,**b**, oxazolidinone **35**, bromide **37**, azide **38**, and chloride **39**. This material is available free of charge via the Internet at http://pubs.acs.org.

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