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Studies on the Reaction of Aziridines with Nitriles and Carbonyls: Synthesis of Imidazolines and Oxazolidines

Shikha Gandhi, Alakesh Bisai, B. A. Bhanu Prasad, and Vinod K. Singh*

Department of Chemistry, Indian Institute of Technology, Kanpur 208 016, India

vinodks@iitk.ac.in

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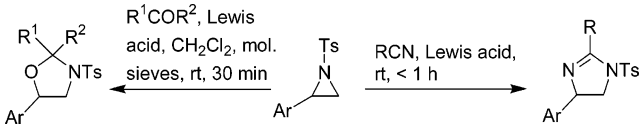
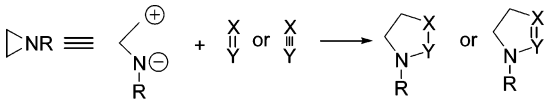


Reaction of *N*-tosylaziridines with nitriles and carbonyls to produce imidazolines and oxazolidines has been studied in the presence of a variety of Lewis acids. The reaction is efficient with 1 equiv of $BF_3{\cdot}Et_2O$ or Et_3OBF_4 in CH_2Cl_2. However, it is catalytic with metal triflates that give the best results for cycloaddition of *N*-tosylaziridine with nitriles under solvent free conditions. The same reaction with carbonyls proceeds best in CH_2Cl_2 in the presence of molecular sieves. Among various triflates, $Zn(OTf)_2$ has been found to be the best. The cleavage of the *N*-Ts bond of the cyclized products has been studied in order to make it more versatile in synthesis. The mechanistic aspect of the reaction has been studied by using chiral aziridines as substrates. These formal [3 + 2] cycloaddition reactions of aziridines with nitriles and carbonyls proceed in a Ritter fashion.

Introduction

Aziridine, a three-membered cyclic amine, has been extensively exploited in organic synthesis due to high strain energy associated with the ring.[1] The reactivity of this strained heterocyclic ring system depends on whether the substituents are electron withdrawing (activated) or electron donating (nonactivated). Its electrostatic potential is very different in the nitrogen and carbon of the ring.[2] Thus, the most common reactions reported with aziridines are ring cleavage by various kinds of nucleophiles. Activated aziridines react with nucleophiles to yield ring-opened products.[3] However, nonactivated aziridines are inert toward nucleophiles and require prior activation with a Lewis acid.[4] In any case, the nucleophilic opening proceeds via cleavage of the C−N bond. Thus, aziridine can be considered as a masked 1,3-dipole that can undergo a formal [3 + 2] cycloaddition with a range of dipolarophiles to provide five-membered nitrogen containing heterocycles which are useful in organic synthesis (Scheme 1). Most of these reactions involve alkenes and alkynes as dipolarophiles[5] leading to the formation of pyrrolidine derivatives. The use of CO_2 and CS_2 in cycloaddition to aziridines forming 1,3-oxazolidin-2-ones and urethanes, respectively, has also been reported.[6] Certain reports have also appeared on the cycloaddition of aziridines to heterocumulenes, carbodiimides, ketenimines, and isocyanates leading to five-membered heterocycles.[7]

SCHEME 1



While the chemistry of aziridines in cycloaddition reactions has been explored to some extent, not many reports involving

* To whom correspondence should be addressed. Fax: +91-512-2597436.

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nitriles as dipolarophiles have found sizable entry into the literature. This is mainly because most nitriles are known to be poor dipolarophiles for intermolecular [3 + 2] cycloaddition reaction. The seminal contribution to this reaction was made by Hiyama and co-workers,[8] who reported the reaction of acetonitrile or benzonitrile with *N*-alkoxycarbonylaziridine in the presence of a Lewis acid to provide an imidazoline in good yield. A similar reaction was also reported by Zwanenburg and his group.[9] Reported methods required harsh conditions like higher temperature and excess of nitrile (as solvent) and were limited to only acetonitrile or benzonitrile. As a preliminary communication, we showed that the reaction can be extended to a variety of nitriles under mild conditions.[10] In this paper, we report full details of our study for the reaction of *N*-tosyl aziridines with nitriles. Since imidazolines, formed in this reaction, are useful intermediates for the synthesis of molecules with pharmacological activities,[11] we have also synthesized stereodefined imidazolines from chiral aziridines. We have further extended the work to aldehydes and ketones as dipolarophiles in the cycloaddition reaction with chiral and achiral aziridines so as to provide suitable oxazolidines, which are useful in organic synthesis.[12]

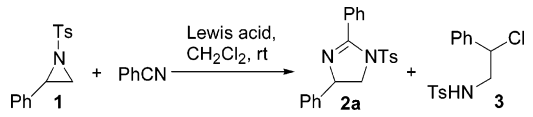
Results and Discussion

Formal [3 + 2] Cycloaddition of *N*-Tosylaziridines with Nitriles. We were interested to see the versatility of nitriles as dipolarophiles in the formal [3 + 2] cycloaddition reaction with aziridines. At the outset, the reaction of 2-phenyl-*N*-tosylaziridine with benzonitrile was studied in the presence of Lewis acids such as $Sn(OTf)_2$, $Cu(OTf)_2$, $Sc(OTf)_3$, $InCl_3$, $CeCl_3$, $ErCl_3$, $YbCl_3$, $LiClO_4$, $BF_3{\cdot}Et_2O$, and Et_3OBF_4 in CH_2Cl_2 at room temperature. Out of these Lewis acids, $BF_3{\cdot}Et_2O$ and Et_3OBF_4 were found to be the most efficient (Table 1). The reaction was complete in less than 10 min at ambient temperature. It was essential to use a stoichiometric amount of $BF_3{\cdot}Et_2O$ or Et_3OBF_4 for achieving high yields of imidazolines. On the use of 10 mol % of the Lewis acids, the reaction was incomplete even after 2 days. Some Lewis acids, instead of giving the desired imidazolines, gave ring-opened products (entries 11−13). No effort was made toward optimization of this reaction sequence.

Several nitriles were used for the above formal [3 + 2] cycloaddition reaction, and the results are summarized in Table 2. High yields of imidazolines were obtained with aliphatic nitriles (entries 2−4), whereas benzonitrile (entry 1) and various substituted phenyl acetonitriles (entries 5−14) gave only moderate yields. Reactive nitriles such as TMSCN, benzoyl cyanide, and hydroxyl cyanides gave a complex mixture of products which could not be characterized. However, chloro- and bromo-substituted acetonitriles gave products in moderate yields (entries 15 and 16).

The versatility of the reaction was extended to a few more *N*-tosylaziridines using acetonitrile and benzonitrile as dipolarophiles (Table 3). In all the cases, a moderate yield (51−60%) of imidazolines was obtained. In the case of an aziridine derived from 1,2-dihydronaphthalene, tricyclic imidazolines **4e** and **5e** were obtained in modest yields (entry 5). The structure was confirmed by taking a single-crystal X-ray structure of **5e**.[13] It was observed that the imidazoline **4e** derived from acetonitrile

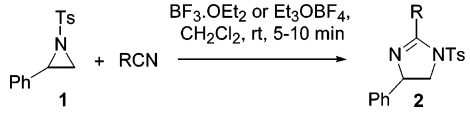
TABLE 1. Screening of Lewis Acids in the Reaction of Aziridines with Benzonitrile[a]



entry	Lewis acid	time	yield (%) 2a	yield (%) 3
1	$BF_3.OEt_2$	5 min	67	00
2	Et_3OBF_4	5 min	65	00
3	$Zn(OTf)_2$	24 h	34	00
4	$Cu(OTf)_2$	12 h	39	00
5	$Sn(OTf)_2$	12 h	22	00
6	$Sc(OTf)_3$	12 h	41	00
7	$Yb(OTf)_3$	12 h	22	00
8	$In(OTf)_3$	12 h	31	00
9	$LiClO_4$	12 h	15	00
10	$Cu(MeCN)_4PF_6$	12 h	23	00
11	$InCl_3$	0.5 h	00	80[b]
12	$ErCl_3$	24 h	00	15
13	$YbCl_3$	24 h	00	33

[a] 1 equiv of Lewis acid was used in all cases. [b] The product was isolated as a mixture of regioisomers in a ratio of 4:1 (only the major regioisomer is shown).

TABLE 2. Formal [3 + 2] Cycloaddition of 2-Phenyl-*N*-tosylaziridine with Various Nitriles in the Presence of $BF_3{\cdot}OEt_2$ or Et_3OBF_4



entry	R	product	yield[a] (%) $BF_3{\cdot}OEt_2$	yield[a] (%) Et_3OBF_4[b]
1	Ph	**2a**	67	65
2	Me	**2b**	75	74
3	Et	**2c**	72	72
4	^{i}Pr	**2d**	76	74
5	$PhCH_2$	**2e**	63	59
6	2-methylbenzyl	**2f**	65	65
7	3-methylbenzyl	**2g**	49	50
8	2,5-dimethylbenzyl	**2h**	55	49
9	3-methoxybenzyl	**2i**	60	56
10	4-fluorobenzyl	**2j**	51	50
11	2-trifluoromethylbenzyl	**2k**	49	47
12	3-trifluoromethylbenzyl	**2l**	46	48
13	3,4-methylenedioxybenzyl	**2m**	53	49
14	2,4-dichlorobenzyl	**2n**	48	47
15	chloromethyl	**2o**	48	49
16	bromomethyl	**2p**	47	46

[a] 1 equiv of Lewis acid was used in all cases. [b] 1 M solution of Et_3OBF_4 in CH_2Cl_2 was used.

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(11) (a) *The Pharmacological Basis of Therapeutics*, 10th ed.; Gilman, A. G., Goodman, L. S., Eds.; Macmillan: New York, 2001. (b) Ueno, M.; Imaizumi, K.; Sugita, T.; Takata, I.; Takeshita, M. *Int. J. Immunopharmacol.* **1995**, *17*, 597−603.

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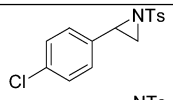
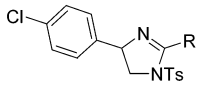
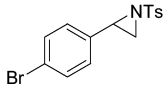
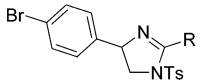
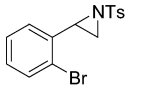
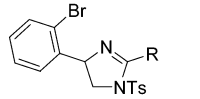
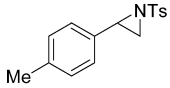
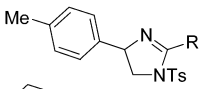
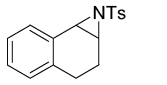
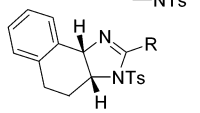
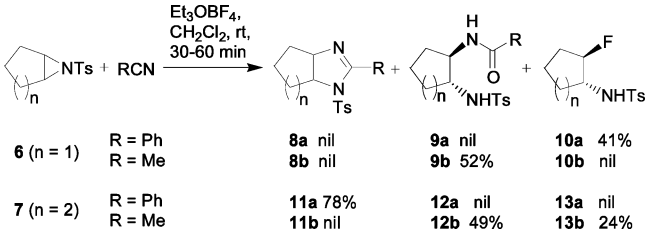
TABLE 3. Formal [3 + 2] Cycloaddition of Nitriles with a Few Selected Aziridines[a]

Entry	Aziridine	Product	Yield (%) R = Me	Yield (%) R = Ph
1			52 (**4a**)	59 (**5a**)
2			54 (**4b**)	60 (**5b**)
3			52 (**4c**)	55 (**5c**)
4			51 (**4d**)	54 (**5d**)
5			54 (**4e**)	56 (**5e**)

[a] 1 equiv of BF_3·OEt_2 was used, and the reactions were complete in less than 5 min.

SCHEME 2. Reaction of *N*-Tosylcycloalkylaziridines with Nitriles

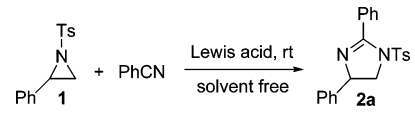


slowly hydrolyzed to the corresponding α-acetamido *β*-sulfonamide on standing. However, the imidazoline **5e** derived from benzonitrile was stable at room temperature.

The results obtained from 2-aryl-*N*-tosylaziridines prompted us to study the reaction on aliphatic cyclic *N*-tosylaziridines. In the presence of Et_3OBF_4, these aziridines gave imidazolines (**8** or **11**) or hydrolyzed α-acetamido *β*-sulfonamide (**9** or **12**) and/or ring-opened products (**10** or **13)** by fluoride ion (Scheme 2). The imidazoline derived from cyclopentene *N*-tosylaziridine **6** and acetonitrile was unstable, and only hydrolyzed product **9b** was isolated. However, in the case of cyclohexene *N*-tosylaziridine **7**, a mixture of the hydrolyzed product **12b** and ring-opened product **13b** was isolated. The latter was due to ring cleavage of the aziridine by fluoride ion of triethyloxonium tetrafluoroborate. The results were different when the same reaction was carried out using benzonitrile as a dipolarophile. Whereas cyclopentene *N*-tosylaziridine **6** gave only the ring-opened product **10a**, the expected Ritter product **11a** was obtained in the case of cyclohexene *N*-tosylaziridine **7**. It was observed that BF_3·Et_2O gave a complex mixture for the same reaction.

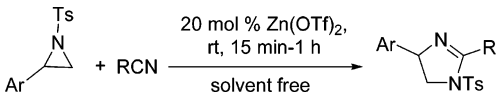
The formal [3 + 2] cycloaddition of aziridines with nitriles would be very useful if they can be performed using a catalytic amount of Lewis acids. Since satisfactory results could not be obtained on using 10−30 mol % of Lewis acids in solvents, we resorted to solvent-free conditions. Several Lewis acids such as BF_3.OEt_2, Et_3OBF_4, $Cu(OTf)_2$, $Sn(OTf)_2$, $In(OTf)_3$, $Sc(OTf)_3$, $Yb(OTf)_3$, and $Zn(OTf)_2$ were screened in a catalytic amount for the reaction of *N*-tosylaziridine and benzonitrile in the absence of any solvent. To our delight, all the metal triflates (20−30 mol %) gave satisfactory results (Table 4). The reaction was complete in less than 30 min. Since $Zn(OTf)_2$ was found to be slightly superior to other triflates, it was further used for the reaction of 2-aryl-substituted *N*-tosylaziridines with various nitriles under solvent-free conditions (Table 5). Reasonably good yield of imidazolines was obtained in almost all of the cases. The reaction worked with aliphatic and aromatic nitriles equally well.

TABLE 4. Screening of Lewis Acids for Reaction of an Aziridine with Benzonitrile under Solvent-Free Conditions



entry	Lewis acid (mol %)	time	yield (%)
1	BF_3·OEt_2 (20)	1 h	40
2	Et_3OBF_4 (20)	1 h	32
3	$Cu(OTf)_2$ (20)	20 min	65
4	$Sn(OTf)_2$ (20)	30 min	60
5	$In(OTf)_3$ (20)	30 min	58
6	$Sc(OTf)_3$ (20)	30 min	60
7	$Yb(OTf)_3$ (20)	35 min	50
8	$Zn(OTf)_2$ (20)	15 min	68
9	$Zn(OTf)_2$ (30)	15 min	67
10	$Zn(OTf)_2$ (10)	1 h	30

TABLE 5. $Zn(OTf)_2$-Catalyzed Reaction of *N*-Tosylaziridines and Nitriles under Solvent-Free Conditions



entry	Ar	R	product	yield (%)
1	Ph	Ph	**2a**	67
2	Ph	Me	**2b**	63
3	Ph	^{i}Pr	**2d**	51
4	Ph	$PhCH_2$	**2e**	80
5	Ph	4-$FC_6H_4CH_2$	**2j**	85
6	Ph	$ClCH_2$	**2o**	64
7	Ph	$BrCH_2$	**2p**	61
8	2-bromophenyl	Me	**4c**	58
9	4-chlorophenyl	Ph	**5a**	79
10	2-bromophenyl	Ph	**5c**	56
11	4-chlorophenyl	$PhCH_2$	**14a**	76
12	2-bromophenyl	$PhCH_2$	**14b**	60

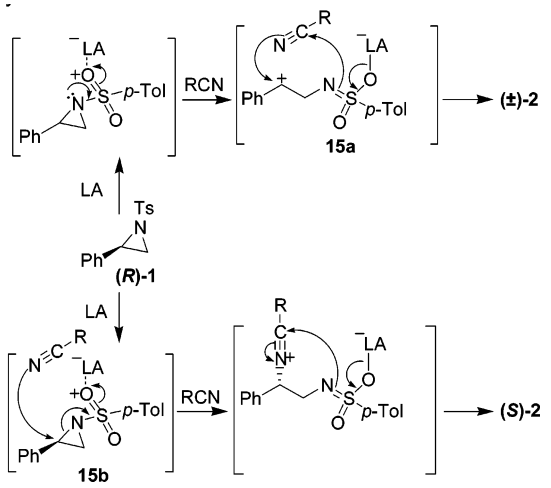
The current reaction may proceed predominantly via either S_N1 or S_N2 mechanism as depicted in Scheme 3. In order to ascertain it, a chiral aziridine (*R*)-**1**[14] was allowed to react with benzonitrile in the presence of Lewis acids [$Sc(OTf)_3$, $Cu(OTf)_2$, $Sn(OTf)_2$, $Zn(OTf)_2$, $In(OTf)_3$)] (Scheme 3). The isolated imidazoline from each experiment was found to be racemic in nature (2−5% ee by chiral HPLC column).[15] Based on these results, it is proposed that the reaction involves a stabilized zwitterionic intermediate **15a** derived from the aziridine. The

(13) Crystallographic data has been deposited with the Cambridge Crystollographic Data Centre as supplementary publication no CCDC-210538. This data can be obtained free of charge via the internet www.ccdc.cam.ac.uk/conts/ retrieving .html or by sending an email to deposit@ccdc.cam.ac.uk.

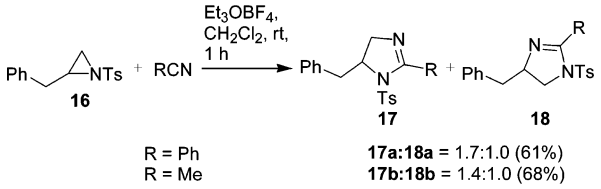
(14) Alonso, D. A.; Andersson, P. G. *J. Org. Chem.* **1998**, *63*, 9455−9461.

(15) The optical purity was determined by HPLC on chiralpak AD-H column [hexane/2-propanol 90.0:10.0]; flow rate 1.0 mL/min; t_R = 19.17 min (major), 24.82 min (minor).

SCHEME 3. Proposed Mechanism for the Formal [3 + 2] Cycloaddition of an Aziridine with a Nitrile



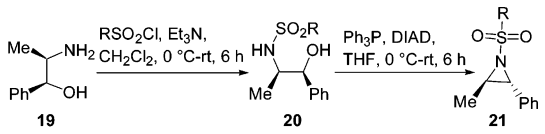
SCHEME 4. Reaction of Terminal *N*-Tosylalkylaziridine with Nitriles



chelation of the Lewis acid to the sulfonyl oxygen gives rise to a discrete stable benzylic carbocation that reacts with the nitrile in a Ritter fashion to provide (±)-**2**. On the basis of this concept, very recently Yadav and Sriramurthy have used silylmethyl-substituted aziridine for formal [3 + 2] cycloaddition reaction with nitriles where silicon stabilizes the β-carbocation to form the stable zwitterion intermediate.[16] Ghorai et al. and Wu et al. have proposed an alternative S_N2 mechanism where attack of the nitrile at the benzylic carbon and the cleavage of C−N bond of aziridine (cf. **15b**) takes place at the same time.[17] In our opinion, it is either less likely or operates to a small extent in this particular case. However, the mechanism would depend upon the substituents on the substrates and effective power of Lewis acids. This is the reason why alkyl substituted aziridine **16** gave a mixture of imidazolines **17** and **18** where the former predominates due to a major portion of the reaction possibly going via S_N2 mode where the nitrile attacks the aziridinic carbon from the less hindered side (Scheme 4).

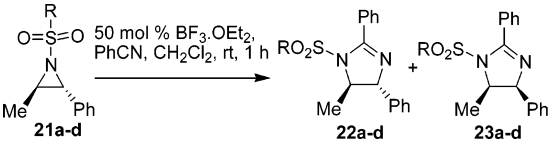
In order to focus more light on the mechanism, chiral disubstituted *N*-tosylaziridines **21** were synthesized from (1*S*,2*R*)-norephedrine **19** (Table 6). Reaction of these aziridines was studied with benzonitrile in the presence of $BF_3{\cdot}OEt_2$ in dichloromethane at room temperature (Table 7). A stoichiometric amount of $BF_3{\cdot}OEt_2$ gave the same yield as 50 mol %, so the latter amount was used for all of the reactions. A mixture of diastereomeric imidazolines **22** and **23** was obtained and the ratio varied depending upon substituents on *N*-sulfonyl group. In most of the cases, the former predominated in the reaction mixture where the nitrile attacked the benzylic carbon with

TABLE 6. Synthesis of Chiral Aziridines from (1*S*,2*R*)-Norephedrine



entry	R	product (**20**)	yield (%)	product (**21**)	yield (%)
1	4-methylphenyl	**20a**	95	**21a**	99
2	4-bromophenyl	**20b**	85	**21b**	85
3	4-fluorophenyl	**20c**	96	**21c**	77
4	Me	**20d**	70	**21d**	99
5	Ph	**20e**	99	**21e**	89

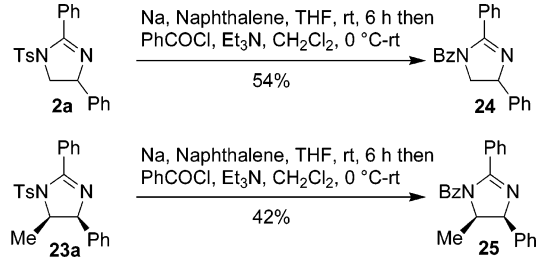
TABLE 7. Diastereoselective Synthesis of Chiral Imidazolines



entry	R	yield (%)	dr **22**/**23**[a]
1	4-MeC_6H_4	70	73:27 (**22a**/**23a**)
2	4-BrC_6H_4	69	53:47 (**22b**/**23b**)
3	4-FC_6H_4	75	61:39 (**22c**/**23c**)
4	Me	94	62:38 (**22d**/**23d**)

[a] Diastereomeric ratio was determined with the help of ^1H NMR spectra.

SCHEME 5. Cleavage of *N*-Tosyl Bond in Imidazolines



retention of configuration. This could be due to higher stability of the trans diastereomer. This result supports the SN^1 mechanism.

In order to show effectiveness of the method, cleavage of *N*-Ts was studied with various reagents. There was no reaction with Mg in MeOH even under reflux conditions.[14] Use of Na and amyl alcohol did not give a clean reaction. However, Na in naphthalene was found to be effective for the cleavage of *N*-Ts bond.[18] The free detosylated imidazoline formed, in situ, was derivatized as a benzoate (Scheme 5). This was nicely shown by converting **2a** into **24** and **23a** into **25** in modest yields.

Formal [3 + 2] Cycloaddition of *N*-Tosylaziridine with Carbonyls. Motivated by the above results, the cycloaddition of *N*-tosylaziridine was extended to carbonyls as dipolarophiles for the synthesis of oxazolidines.[19] At the outset, the reaction of 2-phenyl *N*-tosylaziridine **1** with cyclohexanone was studied. Initial attempts with $Zn(OTf)_2$ as a Lewis acid in CH_2Cl_2 failed since the expected product was formed only in poor yield. This

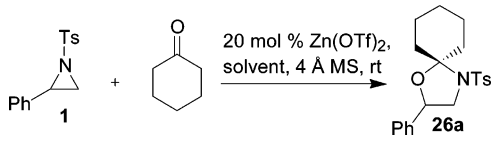
(16) Yadav, V. K.; Sriramurthy, V. *J. Am. Chem. Soc.* **2005**, *127*, 16366−16367.

(17) (a) Ghorai, M. K.; Ghosh, K.; Das, K. *Tetrahedron Lett.* **2006**, *47*, 5399−5403. (b) Wu, J.; Sun, X.; Xia, H.-G. *Tetrahedron Lett.* **2006**, *47*, 1509−1512.

(18) Bergmeier, S. C.; Seth, P. P. *Tetrahedron Lett.* **1999**, *40*, 6181−6184.

(19) The work was presented in a DST Group Monitoring Workshop on July 25, 2005 at RRL Trivandrum.

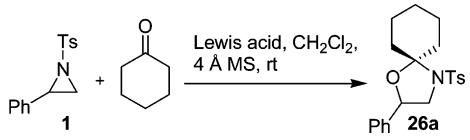
TABLE 8. Solvent Study for Formal [3 + 2] Cycloaddition of an Aziridine with Cyclohexanone



entry	solvent	time	yield[a] (%)
1	$CHCl_3$	45 min	89
2	toluene	45 min	87
3	DCE	45 min	93
4	hexane	2 h	95
5	ethyl acetate	45 min	70
6	THF	48 h	17
7	MTBE[b]	45 min	93
8	diethyl ether	45 min	76
9	CH_2Cl_2	30 min	96

[a] Isolated yield after column chromatography. [b] MTBE = methyl *tert*-butyl ether.

TABLE 9. Screening of Lewis Acids for Formal [3 + 2] Cycloaddition of Aziridine with Cyclohexanone



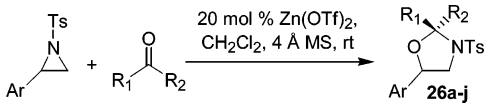
entry	MX_Y (mol %)	yield[a] (%)	time
1	$Zn(OTf)_2$ (20 mol %)	96	30 min
2	$Zn(OTf)_2$ (10 mol %)	90	1.5 h
3	$Sn(OTf)_2$ (20 mol %)	27	3 h
4	$Yb(OTf)_3$ (20 mol %)	58	1 h
5	$Cu(MeCN)_4PF_6$ (20 mol %)	52	4 h
6	$YbCl_3$ (20 mol %)	19	16 h
7	$InCl_3$ (20 mol %)	30	4 h
8	$CuCl_2$ (20 mol %)	09	4 h
9	$BF_3{\cdot}OEt_2$ (20 mol %)	35	12 h
10	$BF_3{\cdot}OEt_2$ (100 mol %)	82	1.5 h
11	Et_3OBF_4 (20 mol %)	29	12 h
12	Et_3OBF_4 (100 mol %)	86	1.5 h

[a] Isolated yield after column chromatography

could be due to unstability of the product to the residual moisture as the hydrolysis product was formed along with the cycloaddition product. In search of a stabilized condition for this reaction, we decided to add molecular sieves to the reaction mixture. To our delight, the addition of 4 Å molecular sieves (crushed) resulted in an excellent yield of the desired oxazolidine **26a** (Table 8). Among several solvents evaluated for the reaction, CH_2Cl_2 gave the best results (entry 9). Although most of the nonpolar solvents were suitable for the reaction, polar solvent such as THF gave very poor yields (entry 6). Having settled for CH_2Cl_2 as a suitable solvent, the reaction was evaluated in the presence of other Lewis acids (Table 9). It was observed that 20 mol % of $Zn(OTf)_2$ was optimum for the best results (entry 1). Other metal triflates and metal halides gave poor yields in this reaction (entries 3−8). Classical Lewis acids such as $BF_3{\cdot}Et_2O$ and Et_3OBF_4 were effective only when used in stoichiometric amounts (entries 9−12).

The formal [3 + 2] cycloaddition of 2-aryl-substituted *N*-tosylaziridines was then studied with various carbonyl compounds as dipolarophiles (Table 10). With 2-phenyl-*N*-tosylaziridine, aliphatic symmetrical ketones (entries 1, 2 and

TABLE 10. Scope of Substrate for $Zn(OTf)_2$-Catalyzed Formal [3 + 2] Cycloaddition of Aziridines with Carbonyls



entry	Ar	R_1	R_2	product	time	yield[a] (%)
1	Ph	$-(CH_2)_5-$		**26a**	30 min	96
2	Ph	Me	Me	**26b**	2 h	80
3	Ph	^{i}Pr	H	**26c**	4 h	59
4	Ph	Ph	H	**26d**	3.5 h	52
5	Ph	Ph	Ph	**26e**	5 h	58
6	Ph	Et	Et	**26f**	1.5 h	62
7	Ph	Me	H	**26g**	4 h	76
8	4-ClPh	Me	Me	**26h**	4 h	40
9	4-ClPh	$-(CH_2)_5-$		**26i**	3 h	75
10	2-BrPh	$-(CH_2)_5-$		**26j**	4 h	32

[a] Isolated yield after column chromatography.

SCHEME 6. Proposed Mechanism for [3 + 2] Cycloaddition of Aziridine with Carbonyls

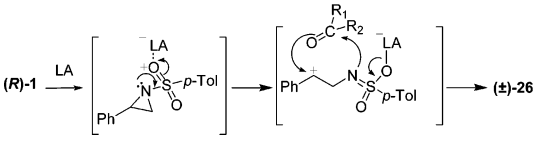
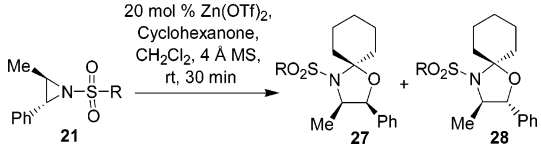


TABLE 11. Highly Diastereoselective Synthesis of Chiral Oxazolidines



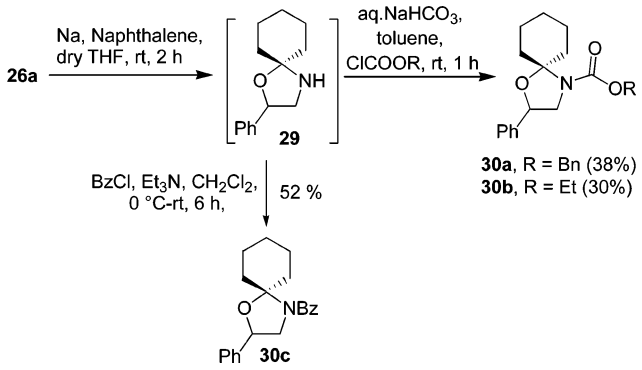
entry	R	yield (%)	diastereomeric ratio (**27**/**28**)
1	4-MeC_6H_4	97	94:6 (**27a**/**28a**)
2	4-BrC_6H_4	99	98:2 (**27b**/**28b**)
3	4-FC_6H_4	98	95:5 (**27c**/**28c**)
4	Me	84	94:6 (**27d**/**28d**)
5	Ph	97	93:7 (**27e**/**28e**)

6) reacted faster than aliphatic and aromatic aldehydes (entries 3, 4, and 7). The reaction with benzophenone was slightly slow (entry 5).

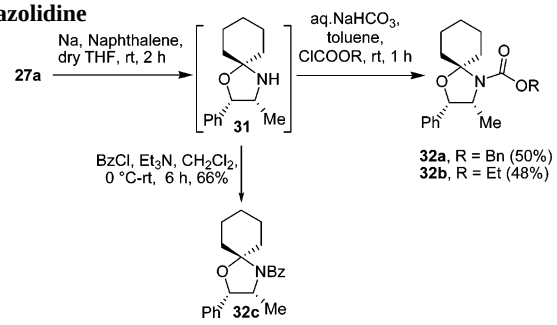
In order to explore the mechanism, the reaction was studied with chiral aziridines. A chiral aziridine (*R*)-**1**, as in the above case, was allowed to react with cyclohexanone in the presence of various Lewis acids (Scheme 6). This resulted in the formation of a racemic oxazolidine **26a**[20] which indicated that the reaction proceeds via a benzyl carbocation intermediate in this case (Scheme 6). In the case of disubstituted chiral aziridines **21**, the product spirooxazolidines **27** and **28** were formed with excellent diastereoselectivities (Table 11). The structure of the major diastereomer **27** was determined by ^{1}H NMR and further confirmed with the help of NOE spectra. On irradiating the proton at benzylic carbon, an enhancement in the peak intensity of adjacent proton was observed and vice-versa. This confirmed the cis stereochemistry at these two carbon atoms. The predominant formation of **27** can be explained by the attack of the carbonyl oxygen at the benzylic carbon atom from a less

(20) The optical purity was determined by HPLC on chiralpak OD-H column [hexane/2-propanol 97.5:2.5]; flow rate 1.0 mL/min; t_R = 10.73 min (minor), 12.88 min (major).

SCHEME 7. Cleavage of *N*-Tosyl Bond in Racemic Oxazolidine



SCHEME 8. Cleavage of *N*-Tosyl Bond in Chiral Oxazolidine



hindered side, i.e., away from the methyl group. Due to high diastereoselectivities achieved in this type of cases, the reaction can be widely exploited for the synthesis of stereodefined oxazolidines.

As in the case of imidazolines (Scheme 5), the *N*-Ts bond in oxazolidines could also be cleaved using Na in naphthalene to provide detosylated oxazolidines, which in turn could be derivatized using benzylchloroformate, ethyl chloroformate, and benzoyl chloride (Schemes 7 and 8). Although reasonably good yields were obtained in benzoylation reaction, the yields were poor for chloroformate reactions.

Conclusion

In conclusion, we have described a good method for the synthesis of imidazolines through a formal [3 + 2] cycloaddition of *N*-tosylaziridines with nitriles. The reaction proceeds in a Ritter fashion. On the basis of the results from chiral aziridines, it was concluded that the reaction can proceed via either S_N1 (2-aryl-*N*-sulfonylaziridines) or S_N2 (alkyl-*N*-tosylazidines) fashion. The reaction of aziridines was also extended to carbonyls for the synthesis of oxazolidines. The cleavage of *N*-Ts bond of the imidazolines and oxazolidines has been studied in order to make them more versatile in synthesis.

Experimental Section

General Procedure for the Reaction of *N*-Tosylaziridines with Nitriles Using Lewis Acids in CH_2Cl_2. A solution of an *N*-tosylaziridine (0.5 mmol) and a nitrile (0.5 mmol) in anhydrous dichloromethane (2 mL) was treated with a Lewis acid (0.5 mmol). After completion of the reaction, as monitored by TLC, saturated aqueous $NaHCO_3$ solution (2 mL) was added. The organic layer was separated, and the aqueous layer was extracted with dichloromethane. The organic layers were mixed, washed with water and brine, dried over anhydrous Na_2SO_4, and concentrated to give the crude product. Purification by column chromatography (30% EtOAc in petroleum ether) gave the substituted imidazoline.

General Procedure for [3 + 2] Cycloaddition Reaction of Aziridines with Nitriles Using Metal Triflates. A metal triflate (0.2 mmol; 20 mol %) was added to a stirred mixture of an *N*-tosylaziridine (1 mmol) and nitrile (5.0 mmol) at rt. After completion of the reaction, as monitored by TLC, the reaction mixture was purified by column chromatography (30% EtOAc in petroleum ether) to provide the substituted imidazoline.

2-Benzyl-4-(4-chlorophenyl)-1-(toluene-4-sulfonyl)-4,5-dihydro-1*H*-imidazole (14a): yield 76%; dense liquid; R_f 0.39 (30% EtOAc in petroleum ether); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.29 (m, 11H), 6.91 (m, 2H), 5.01 (dd, J = 10.2, 7.6 Hz, 1H), 4.16 (s, 2H), 4.12 (t, J = 10.3 Hz, 1H), 3.54 (m, 1H), 2.40 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 158.8, 144.6, 140.2, 135.2, 134.6, 133.3, 129.8, 129.3, 128.7, 128.5, 127.7, 127.1, 127.0, 66.0, 55.4, 35.6, 21.5. Anal. Calcd for $C_{23}H_{21}ClN_2O_2S$: C, 65.01; H, 4.98; N, 6.59. Found: C, 64.89; H, 4.86; N, 6.65.

2-Benzyl-4-(2-bromophenyl)-1-(toluene-4-sulfonyl)-4,5-dihydro-1*H*-imidazole (14b): yield 60%; colorless paste; R_f 0.41 (30% EtOAc in petroleum ether); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.50 (m, 2H), 7.34 (m, 7H), 7.16 (d, J = 7.6 Hz, 2H), 7.10 (m, 1H), 6.99 (m, 1H), 5.33 (m, 1H), 4.27 (t, J = 10.2 Hz, 1H), 4.21 (s, 2H), 3.48 (dd, J = 10.0, 7.6 Hz, 1H), 2.39 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 159.7, 144.5, 141.4, 135.3, 134.9, 132.5, 129.8, 129.3, 128.9, 128.6, 127.7, 127.6, 127.1, 126.9, 122.3, 66.0, 54.8, 35.8, 21.5; MS (FAB) 470 ($M^+ + 1$). Anal. Calcd for $C_{23}H_{21}BrN_2O_2S$: C, 58.85; H, 4.51; N, 5.97. Found: C, 59.03; H, 4.62; N, 5.90.

5-Benzyl-2-phenyl-1-(toluene-4-sulfonyl)-4,5-dihydro-1*H*-imidazole (17a): yield 35%; colorless gel. Analytical data were in accordance with those reported in the literature.[17a]

4-Benzyl-2-phenyl-1-(toluene-4-sulfonyl)-4,5-dihydro-1*H*-imidazole (18a): yield 21%; colorless gel. Analytical data were in accordance with those reported in the literature.[17a]

5-Benzyl-2-methyl-1-(toluene-4-sulfonyl)-4,5-dihydro-1*H*-imidazole (17b): colorless gel; isolated as an inseparable mixture with **18b**. Analytical data were in accordance with those reported in the literature.[17a]

4-Benzyl-2-methyl-1-(toluene-4-sulfonyl)-4,5-dihydro-1*H*-imidazole (18b): colorless gel; isolated as an inseparable mixture with **17b**. Analytical data were in accordance with those reported in the literature.[17a]

General Procedure for Sulfonylation of Norephedrine. Sulfonyl chloride (1.05 mmol) was added slowly to a solution of norephedrine (1 mmol) and triethylamine (4 mmol) in CH_2Cl_2 (10 mL) at 0 °C. The ice bath was then removed, and the reaction was allowed to warm to rt and further stirred for 6 h. The reaction mixture was then washed with water and brine and dried over anhydrous Na_2SO_4. The organic layer was then concentrated to give the crude product. Purification by column chromatography provided the sulfonylated norephedrine.

(1*R*,2*S*)-*N*-(2-Hydroxy-1-methyl-2-phenylethyl)-4-methylbenzenesulfonamide (20a): yield 95%; mp 79−81 °C; R_f 0.32 (30% EtOAc in petroleum ether); $[\alpha]^{25}_D$ = +13.40 (*c* 1.0, $CHCl_3$); FT IR (KBr) 3500, 3278, 1494, 1326, 1159, 1088 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.77 (d, J = 8.3 Hz, 2H), 7.29 (m, 7H), 5.05 (br, 1H, NH), 4.79 (br, 1H), 3.57 (m, 1H), 2.62 (br, 1H, OH), 2.42 (s, 3H), 0.83 (d, J = 6.8 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 143.5, 140.2, 137.7, 129.8, 128.3, 127.6, 126.9, 126.0, 75.7, 54.9, 21.5, 14.6. Anal. Calcd for $C_{16}H_{19}NO_3S$: C, 62.93; H, 6.27; N, 4.59. Found: C, 62.78; H, 6.36; N, 4.49.

(1*R*,2*S*)-4-Bromo-*N*-(2-Hydroxy-1-methyl-2-phenylethyl)benzenesulfonamide (20b): yield 85%; mp 149−150 °C; R_f 0.37 (20% EtOAc in petroleum ether); $[\alpha]^{25}_D$ = +8.80 (*c* 0.25, $CHCl_3$); FT IR (KBr) 3499, 3286, 1492, 1326, 1160, 1087, 1009 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.73 (m, 2H), 7.64 (m, 2H), 7.29 (m, 5H), 4.76 (m, 1H), 4.74 (br, 1H, NH), 3.61 (m, 1H), 2.32 (d, J = 3.9

Hz, 1H, OH), 0.90 (d, J = 6.8 Hz, 3H). Anal. Calcd for $C_{15}H_{16}BrNO_3S$: C, 48.66; H, 4.36; N, 3.78. Found: C, 48.89; H, 4.29; N, 3.69.

(1*R*,2*S*)-4-Fluoro-*N*-(2-hydroxy-1-methyl-2-phenylethyl)benzenesulfonamide (20c): yield 96%; viscous liquid; R_f 0.66 (40% EtOAc in petroleum ether); $[\alpha]^{25}_D$ = +25.80 (*c* 1.0, $CHCl_3$); FT IR (neat) 3509, 3280, 1493, 1328, 1236, 1153, 1091 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.81 (dd, J = 8.8, 5.1 Hz, 2H), 7.21 (m, 5H), 7.09 (m, 2H), 5.07 (d, J = 8.8 Hz, 1H, NH), 4.73 (br, 1H), 3.49 (m, 1H), 2.73 (br, 1H, OH), 0.78 (d, J = 6.8 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 166.2, 163.7, 140.1, 136.8, 129.7, 128.4, 127.8, 126.0, 116.4, 116.2, 75.9, 55.0, 14.7. Anal. Calcd for $C_{15}H_{16}FNO_3S$: C, 58.24; H, 5.21; N, 4.53. Found: C, 58.43; H, 5.29; N, 4.45.

(1*R*,2*S*)-*N*-(2-Hydroxy-1-methyl-2-phenylethyl)methanesulfonamide (20d): yield 70%; mp 102−106 °C; R_f 0.36 (40% EtOAc in petroleum ether); $[\alpha]^{25}_D$ = +34.33 (*c* 0.6, $CHCl_3$); FT IR (KBr) 3498, 3334, 1492, 1317, 1146, 1075 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.34(m, 5H), 4.87 (br, 1H, NH), 4.57 (br, 1H), 3.51 (m, 1H), 2.79 (br, 1H, OH), 0.76 (d, J = 6.8 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 140.2, 128.4, 127.9, 126.3, 76.3, 55.1, 41.6, 16.2. Anal. Calcd for $C_{10}H_{15}NO_3S$: C, 52.38; H, 6.59; N, 6.11. Found: C, 52.58; H, 6.50; N, 6.03.

(1*R*,2*S*)-*N*-(2-Hydroxy-1-methyl-2-phenylethyl)benzenesulfonamide (20e): yield 99%; viscous liquid; R_f 0.52 (40% EtOAc in petroleum ether); $[\alpha]^{25}_D$ = +15.57 (*c* 0.7, $CHCl_3$); FT IR (neat) 3505, 3277, 1492, 1325, 1161, 1089 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.82 (d, J = 8.1 Hz, 2H), 7.46 (m, 3H), 7.21 (m, 5H), 5.08 (br, 1H, NH), 4.72 (br, 1H), 3.51 (m, 1H), 2.79 (br, 1H, OH), 0.76 (d, J = 6.8 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 140.7, 140.2, 132.6, 129.1, 128.3, 127.6, 126.9, 125.9, 75.7, 55.0, 14.4. Anal. Calcd for $C_{15}H_{17}NO_3S$: C, 61.83; H, 5.88; N, 4.81. Found: C, 62.04; H, 5.82; N, 4.73.

General Procedure for the Synthesis of Chiral Aziridines from *N*-Sulfonyl-Substituted Norephedrine. Triphenylphosphine (1.5 mmol) was added to a solution of an *N*-sulfonyl-substituted norephedrine (1 mmol) in THF (5 mL) at rt. The reaction mixture was then cooled to 0 °C and treated slowly with diisopropyl azodicarboxylate. The ice bath was removed, and the yellow solution was stirred for 6 h. THF was evaporated, and the crude product was purified by column chromatography to yield the chiral aziridine.

(2*R*,3*R*)-2-Methyl-3-phenyl-1-(toluene-4-sulfonyl)aziridine (21a): yield 99%; yellow liquid; R_f 0.54 (20% EtOAc in petroleum ether); $[\alpha]^{25}_D$ = −64.64 (*c* 1.3, $CHCl_3$); FT IR (neat) 1321, 1159 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.82 (d, J = 8.3 Hz, 2H), 7.25 (m, 5H), 7.15 (m, 2H), 3.79 (d, J = 4.4 Hz, 1H), 2.91 (m, 1H), 2.39 (s, 3H), 1.84 (d, J = 6.1 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 143.9, 137.9, 135.5, 129.5, 128.5, 128.0, 127.2, 126.3, 49.2, 49.1, 21.5, 14.1. Anal. Calcd for $C_{16}H_{17}NO_2S$: C, 66.87; H, 5.96; N, 4.87. Found: C, 67.08; H, 5.85; N, 4.78.

(2*R*,3*R*)-1-(4-Bromobenzenesulfonyl)-2-methyl-3-phenylaziridine (21b): yield 85%; yellow liquid; R_f 0.55 (15% EtOAc in petroleum ether); $[\alpha]^{25}_D$ = −42.13 (*c* 1.6, $CHCl_3$); FT IR (neat) 1322, 1160, 1009 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.79 (d, J = 8.3 Hz, 2H), 7.59 (d, J = 8.6 Hz, 2H), 7.26 (m, 3H), 7.13 (m, 2H), 3.81 (d, J = 4.4 Hz, 1H), 2.96 (m, 1H), 1.84 (d, J = 6.1 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 139.8, 135.1, 132.2 (2C), 128.6 (2C), 128.3, 126.2, 49.5 (2C), 14.3. Anal. Calcd for $C_{15}H_{14}BrNO_2S$: C, 51.15; H, 4.01; N, 3.98. Found: C, 51.36; H, 4.11; N, 3.85.

(2*R*,3*R*)-1-(4-Fluorobenzenesulfonyl)-2-methyl-3-phenylaziridine (21c): yield 77%; viscous liquid; R_f 0.59 (20% EtOAc in petroleum ether); $[\alpha]^{25}_D$ = −69.80 (*c* 1.0, $CHCl_3$); FT IR (neat) 1324, 1156, 1235 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.96 (dd, J = 6.6, 2.9 Hz, 2H), 7.27 (m, 3H), 7.13 (m, 4H), 3.80 (d, J = 4.4 Hz, 1H), 2.95 (m, 1H), 1.85 (d, J = 5.8 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 166.3, 163.8, 136.7, 135.0, 129.9, 129.8, 128.4, 128.1, 126.1, 116.1, 115.9, 49.3 (2C), 14.0. Anal. Calcd for $C_{15}H_{14}FNO_2S$: C, 61.84; H, 4.84; N, 4.81. Found: C, 62.04; H, 4.96; N, 4.88.

(2*R*,3*R*)-1-Methanesulfonyl-2-methyl-3-phenylaziridine (21d): yield 99%; dense yellow liquid; R_f 0.84 (40% EtOAc in petroleum ether); $[\alpha]^{25}_D$ = −168.00 (*c* 1.5, $CHCl_3$); FT IR (neat) 1313, 1149 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.32 (m, 5H), 3.71 (d, J = 2.9 Hz, 1H), 3.08 (s, 3H), 2.91 (m, 1H), 1.79 (d, J = 4.12 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 135.5, 128.7, 128.3, 126.2, 49.1, 48.9, 42.6, 14.1. Anal. Calcd for $C_{10}H_{13}NO_2S$: C, 56.85; H, 6.20; N, 6.63. Found: C, 56.98; H, 6.12; N, 6.71.

(2*R*,3*R*)-1-Benzenesulfonyl-2-methyl-3-phenylaziridine (21e): yield 89%; dense yellow liquid; R_f 0.54 (20% EtOAc in petroleum ether); $[\alpha]^{25}_D$ = −78.00 (*c* 1.0, $CHCl_3$); FT IR (neat) 1318, 1161 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.94 (d, J = 8.0 Hz, 2H), 7.55 (m, 1H), 7.47 (m, 2H), 7.26 (m, 3H), 7.14 (m, 2H), 3.82 (d, J = 4.4 Hz, 1H), 2.94 (m, 1H), 1.85 (d, J = 6.1 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 140.7, 135.3, 133.0, 128.9, 128.5, 128.1, 127.1, 126.2, 49.3 (2C), 14.2. Anal. Calcd for $C_{15}H_{15}NO_2S$: C, 65.91; H, 5.53; N, 5.12. Found: C, 66.12; H, 5.49; N, 5.01.

General Procedure for Synthesis of Chiral Imidazolines Using BF_3·OEt_2. The procedure was same as used for the synthesis of achiral imidazolines (Table 1) except that 0.5 mmol of BF_3·OEt_2 was used instead of 1 mmol.

(4*R*,5*R*)-5-Methyl-2,4-diphenyl-1-(toluene-4-sulfonyl)-4,5-dihydro-1*H*-imidazole (22a). Nonpolar diastereomer: yield 51%; mp 60−63 °C; R_f 0.40 (20% EtOAc in petroleum ether); $[\alpha]^{25}_D$ = −69.14 (*c* 1.0, $CHCl_3$); FT IR (KBr) 1627, 1356, 1164 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.85 (d, J = 7.8 Hz, 2H), 7.60 (d, J = 8.0 Hz, 2H), 7.53 (m, 1H), 7.45 (m, 2H), 7.24 (m, 7H), 4.73 (d, J = 8.5 Hz, 1H), 4.61 (m, 1H), 2.43 (s, 3H), 0.92 (d, J = 6.8 Hz, 3H). Anal. Calcd for $C_{23}H_{22}N_2O_2S$: C, 70.74; H, 5.68; N, 7.17. Found: C, 70.95; H, 5.60; N, 7.09.

(4*S*,5*R*)-5-Methyl-2,4-diphenyl-1-(toluene-4-sulfonyl)-4,5-dihydro-1*H*-imidazole (23a). Polar diastereomer: yield 19%; mp 112−114 °C; R_f 0.31 (20% EtOAc in petroleum ether); $[\alpha]^{25}_D$ = +9.50 (*c* 1.0, $CHCl_3$); FT IR (KBr) 1627, 1362, 1169 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.82 (d, J = 7.1 Hz, 2H), 7.54 (m, 1H), 7.45 (m, 2H), 7.28 (m, 3H), 7.16 (m, 1H), 7.06 (m, 3H), 6.63 (m, 2H), 4.71 (d, J = 4.2 Hz, 1H), 4.10 (m, 1H), 2.37 (s, 3H), 1.67 (d, J = 6.4 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 159.2, 144.4, 141.8, 134.2, 131.1, 130.5, 129.9, 129.6, 128.3, 127.6, 127.5, 126.9, 125.5, 75.4, 65.7, 23.5, 21.5; MS (ES+) 391 (M^+ + 1). Anal. Calcd for $C_{23}H_{22}N_2O_2S$: C, 70.74; H, 5.68; N, 7.17. Found: C, 70.92; H, 5.61; N, 7.07.

(4*R*,5*R*)-1-(4-Bromobenzenesulfonyl)-5-methyl-2,4-diphenyl-4,5-dihydro-1*H*-imidazole (22b). Nonpolar diastereomer: yield 37%; gummy solid; R_f 0.68 (20% EtOAc in petroleum ether); $[\alpha]^{25}_D$ = +6.67 (*c* 0.6, $CHCl_3$); FT IR (KBr) 1647, 1326, 1162, 1031 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.81 (d, J = 6.8 Hz, 2H), 7.66 (d, J = 8.0 Hz, 2H), 7.56 (m, 3H), 7.46 (d, J = 7.3 Hz, 2H), 7.24 (m, 5H), 4.83 (d, J = 8.3 Hz, 1H), 4.63 (m, 1H), 0.94 (d, J = 6.6 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 159.2, 137.9, 136.6, 132.8, 132.7, 131.6, 130.4, 129.9, 129.7, 128.7, 128.6, 128.3, 127.9, 127.5, 127.4, 72.1, 62.0, 17.7. Anal. Calcd for $C_{22}H_{19}BrN_2O_2S$: C, 58.03; H, 4.21; N, 6.15. Found: C, 58.21; H, 4.12; N, 6.07.

(4*S*,5*R*)-1-(4-Bromobenzenesulfonyl)-5-methyl-2,4-diphenyl-4,5-dihydro-1*H*-imidazole (23b). Polar diastereomer: yield 32%; mp 150−153 °C; R_f 0.60 (20% EtOAc in petroleum ether); $[\alpha]^{25}_D$ = −7.00 (*c* 0.5, $CHCl_3$); FT IR (KBr) 1629, 1359, 1173, 1021 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.83 (d, J = 7.3 Hz, 2H), 7.56 (m, 1H), 7.47 (m, 2H), 7.34 (d, J = 8.5 Hz, 2H), 7.18 (m, 5H), 6.66 (d, J = 7.3 Hz, 2H), 4.76 (d, J = 3.7 Hz, 1H), 4.09 (m, 1H), 1.67 (d, J = 6.6 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 178.8, 175.2, 144.7, 137.6, 137.2, 134.6, 133.8, 133.1, 132.3, 129.5, 127.6, 126.5, 126.2, 125.9, 121.1, 78.6, 21.2, 18.1. Anal. Calcd for $C_{22}H_{19}BrN_2O_2S$: C, 58.03; H, 4.21; N, 6.15. Found: C, 58.21; H, 4.18; N, 6.07.

(5*R*)-1-(4-Fluorobenzenesulfonyl)-5-methyl-2,4-diphenyl-4,5-dihydro-1*H*-imidazole: diastereomeric ratio (**22c**/**23c**) 61:39; total yield 75%; mp 149−152 °C; R_f (nonpolar, major) 0.35, (polar, minor), 0.33 (20% EtOAc in petroleum ether); ^{1}H NMR ($CDCl_3$, 400 MHz) (for major diastereomer) δ 7.81 (d, J = 7.6 Hz, 3H), 7.46 (m, 3H), 7.29 (m, 2H), 7.17 (m, 4 H), 6.89 (m, 1H), 6.70 (d, J = 7.3 Hz, 1H), 4.76 (m, 1H), 4.11 (m, 1H), 0.93 (d, J = 6.8 Hz, 3H); (for minor diastereomer) δ 7.71 (d, J = 7.6 Hz, 3 H), 7.53 (m, 3H), 7.29 (m, 4H), 7.17 (m, 4H), 4.85 (m, 1H), 4.64 (m, 1H), 1.68 (d, J = 6.6 Hz, 3H). Anal. Calcd for $C_{22}H_{19}FN_2O_2S$: C, 66.99; H, 4.85; N, 7.10. Found: C, 67.24; H, 4.80; N, 7.02.

(5*R*)-1-Methanesulfonyl-5-methyl-2,4-diphenyl-4,5-dihydro-1*H*-imidazole: diastereomeric ratio (**22d**/**23d**) 62:38; total yield 94%; sticky solid; R_f (nonpolar, major) 0.11, (polar, minor), 0.09 (20% EtOAc in petroleum ether); ^{1}H NMR ($CDCl_3$, 400 MHz) (for major diastereomer) δ 7.82 (m, 2H), 7.38 (m, 8H), 4.90 (d, J = 4.2 Hz, 1H), 4.28 (m, 1H), 2.60 (s, 3H), 1.64 (d, J = 6.3 Hz, 3H); (for minor diastereomer) δ 7.82 (m, 2H), 7.38 (m, 8H), 5.53 (d, J = 8.6 Hz, 1H), 4.80 (m, 1H), 2.98 (s, 3H), 0.93 (d, J = 6.6 Hz, 3H). Anal. Calcd for $C_{17}H_{18}N_2O_2S$: C, 64.94; H, 5.77; N, 8.91. Found: C, 65.14; H, 5.82; N, 8.83.

General Procedure for the Cleavage of *N*-Tosyl Bond in Imidazolines. A solution of naphthalene anion radical was prepared as follows: Naphthalene (4.5 mmol) was dissolved in THF (10 mL) in a round-bottom flask under argon atmosphere. Sodium (4.5 mmol) cut into small pieces was then added. The mixture was stirred at room temperature for 1 h. To the deep-green solution of the radical anion was then added a solution of imidazoline (1 mmol) dissolved in THF (4 mL). The reaction mixture was stirred for 1 h. Water was then added until a colorless solution was obtained. The mixture was stirred until the residual small pieces of sodium had dissolved. THF was then evaporated and the reaction mixture was basified (pH = 9.0) with 4 N NaOH. Ethyl acetate was then added and organic layer washed with water, brine and dried over anhydrous Na_2SO_4. The organic layer was concentrated and the crude product directly used for the next step.

A solution of the crude detosylated product (1 mmol) and triethylamine (3 mmol) in CH_2Cl_2 (5 mL) was treated with benzoyl chloride (1.2 mmol) at 0 °C for 6 h. The solution was washed with water, brine and dried over anhydrous Na_2SO_4. The organic layer was concentrated, and the crude material was purified over silica gel by column chromatography.

(2,4-Diphenyl-4,5-dihydroimidazol-1-yl)phenylmethanone (24): yield 54%; sticky solid; R_f 0.17 (30% EtOAc in petroleum ether); FT IR (neat) 1634, 1528 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.57 (dd, J = 15.2, 7.3 Hz, 3H), 7.38 (m, 6H), 7.27 (m, 6H), 5.32 (t, J = 8.3 Hz, 1H), 4.52 (m, 1H), 4.09 (m, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 169.3, 161.1, 141.1, 134.6, 131.7, 130.8, 130.4, 128.5 (2C), 128.2, 128.1, 127.9, 126.7, 68.4, 58.2. Anal. Calcd for $C_{22}H_{18}N_2O$: C, 80.96; H, 5.56; N, 8.58. Found: C, 80.50; H, 5.70; N, 8.46.

(5-Methyl-2,4-diphenyl-4,5-dihydroimidazol-1-yl)phenylmethanone (25): yield 42%; mp 242−245 °C; R_f 0.07 (10% EtOAc in petroleum ether); $[\alpha]^{25}_D$ = −35.85 (c 0.65, $CHCl_3$); FT IR (KBr) 1627, 1530 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.58 (m, 2H), 7.40 (m, 11 H), 7.13 (m, 2H), 4.95 (d, J = 3.4 Hz, 1H), 4.22 (m, 1H), 1.45 (d, J = 6.8 Hz, 3H). Anal. Calcd for $C_{23}H_{20}N_2O$: C, 81.15; H, 5.92; N, 8.23. Found: C, 81.34; H, 5.90; N, 8.16.

General Procedure for the Reaction of *N*-Tosylaziridines with Carbonyls Using Metal Triflates. A carbonyl compound (1.5 mmol) was slowly added to the mixture of an *N*-tosylaziridine (1 mmol), metal triflate (0.2 mmol), and ground 4 Å molecular sieves in anhydrous solvent (5 mL) at rt. After the completion of reaction, as monitored by TLC, the solvent was evaporated to give the crude product. Purification by column chromatography (10% EtOAc in petroleum ether) yielded the desired oxazolidine.

2-Phenyl-4-(toluene-4-sulfonyl)-1-oxa-4-azaspiro[4.5]decane (26a): yield 96%; mp 121−122 °C; R_f 0.62 (20% EtOAc in petroleum ether); FT IR (KBr) 1335, 1211, 1121, 1096 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.74 (d, J = 8.0 Hz, 2H), 7.28 (m, 7H), 5.06 (dd, J = 9.5, 5.6 Hz, 1H), 3.89 (dd, J = 8.5, 5.6 Hz, 1H), 3.12 (t, J = 9.2 Hz, 1H), 2.41 (s, 3H), 2.27 (m, 2H), 1.92 (m, 1H), 1.62 (m, 6H), 1.27 (m, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 143.2, 137.7, 129.5, 128.5, 128.3, 127.2, 126.1, 98.9, 75.8, 53.9, 36.1, 35.4, 24.5, 23.6, 23.4, 21.4; MS (FAB) 372 (M^+ + 1). Anal. Calcd for $C_{21}H_{25}NO_3S$: C, 67.89; H, 6.78; N, 3.77. Found: C, 68.12; H, 6.85; N, 3.68.

2,2-Dimethyl-5-phenyl-3-(toluene-4-sulfonyl)oxazolidine (26b): yield 80%; mp 80−82 °C; R_f 0.57 (20% EtOAc in petroleum ether); FT IR (KBr) 1331, 1243, 1153, 1098 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.65 (d, J = 8.3 Hz, 2H), 7.29 (m, 7H), 5.10 (dd, J = 9.5, 5.6 Hz, 1H), 3.87 (dd, J = 8.8, 5.8 Hz, 1H), 3.14 (t, J = 8.8 Hz, 1H), 2.42 (s, 3H), 1.74 (s, 3H), 1.68 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 143.4, 137.2, 137.1, 129.6, 128.5, 128.4 127.3, 126.2 , 97.3, 76.3, 53.9, 27.5, 27.0, 21.5. Anal. Calcd for $C_{18}H_{21}NO_3S$: C, 65.23; H, 6.39; N, 4.23. Found: C, 65.42; H, 6.35; N, 4.18.

2-Isopropyl-5-phenyl-3-(toluene-4-sulfonyl)oxazolidine (26c): yield 59%; sticky solid; R_f 0.60 (20% EtOAc in petroleum ether); $[\alpha]^{25}_D$ = +1.33 (c 0.8, $CHCl_3$); FT IR (neat) 1352, 1232, 1162, 1093 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) (NMR for major diastereomer) δ 7.82 (d, J = 8.3 Hz, 2H), 7.39 (d, J = 8.3 Hz, 2H), 7.30 (m, 3H), 7.16 (m, 2H), 5.11 (d, J = 4.4 Hz, 1H), 4.05 (dd, J = 10.1, 5.5 Hz, 1H), 3.95 (dd, J = 12.2, 5.4 Hz, 1H), 3.10 (dd, J = 12.2, 10.2 Hz, 1H), 2.47 (s, 3H), 2.12 (m, 1H), 1.08 (d, J = 5.6 Hz, 6H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 144.3, 137.1, 135.2, 130.0, 128.6, 128.4, 127.8, 125.9, 95.7, 78.3, 54.1, 33.9, 21.6, 18.2, 15.9. Anal. Calcd for $C_{19}H_{23}NO_3S$: C, 66.06; H, 6.71; N, 4.05. Found: C, 66.24; H, 6.82; N, 4.15.

2,5-Diphenyl-3-(toluene-4-sulfonyl)oxazolidine (26d): yield 52%; dense liquid; R_f 0.50 (20% EtOAc in petroleum ether); $[\alpha]^{25}_D$ = +0.87 (c 1.5, $CHCl_3$); FT IR (neat) 1352, 1210, 1161, 1093 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) (NMR for major diastereomer) δ 7.73 (d, J = 8.3 Hz, 2H), 7.57 (m, 2H), 7.27 (m, 10H), 6.29 (s, 1H), 4.47 (dd, J = 10.2, 5.6 Hz, 1H), 4.12 (ddd, J = 11.7, 5.6, 0.7 Hz, 1H), 3.28 (t, J = 11.0 Hz, 1H), 2.44 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 144.3, 138.6, 136.6, 135.3, 129.9, 128.9, 128.5 (2C), 128.3, 127.6, 126.9, 126.2, 91.6, 79.6, 53.6, 21.5. Anal. Calcd for $C_{22}H_{21}NO_3S$: C, 69.63; H, 5.58; N, 3.69. Found: C, 69.92; H, 5.48; N, 3.62.

2,2,5-Triphenyl-3-(toluene-4-sulfonyl)oxazolidine (26e): yield 58%; mp 149−150 °C; R_f 0.56 (20% EtOAc in petroleum ether); FT IR (KBr) 1342, 1206, 1155, 1091 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.66 (dd, J = 8.1, 2.0 Hz, 2H), 8.33 (m, 2H), 8.20 (m, 9H), 8.07 (t, J = 7.6 Hz, 2H), 7.87 (d, J = 8.0 Hz, 2H), 7.70 (d, J = 8.0 Hz, 2H), 5.85 (dd, J = 9.8, 6.0 Hz, 1H), 5.13 (dd, J = 8.3, 5.9 Hz, 1H), 4.38 (t, J = 8.8 Hz, 1H), 3.2 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 142.7, 141.8, 138.2, 137.1, 136.2, 130.2, 128.9, 128.7 (2C), 128.6, 128.5, 128.4, 127.8, 127.2, 126.9, 126.1, 100.3, 75.6, 55.4, 21.5; MS (FAB) 456 (M^+ + 1). Anal. Calcd for $C_{28}H_{25}NO_3S$: C, 73.82; H, 5.53; N, 3.07. Found: C, 73.99; H, 5.47; N, 3.17.

2,2-Diethyl-5-phenyl-3-(toluene-4-sulfonyl)oxazolidine (26f): yield 62%; yellow liquid; R_f 0.65 (20% EtOAc in petroleum ether); FT IR (neat) 1328, 1157, 1091 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.76 (m, 2H), 7.29 (m, 7H), 5.07 (dd, J = 9.8, 5.9 Hz, 1H), 3.85 (dd, J = 8.5, 5.8 Hz, 1H), 3.16 (t, J = 10.4 Hz, 1H), 2.42 (s, 3H), 2.09 (m, 4H), 0.99 (t, J = 7.3 Hz, 3H), 0.92 (t, J = 7.3 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 143.3, 137.7, 129.5, 128.6, 128.5, 127.1 (2C), 126.2, 103.3, 77.3, 54.5, 31.7, 30.4, 21.5, 8.7, 8.0. Anal. Calcd for $C_{20}H_{25}NO_3S$: C, 66.82; H, 7.01; N, 3.90. Found: C, 66.98; H, 6.95; N, 3.87.

2-Methyl-5-phenyl-3-(toluene-4-sulfonyl)oxazolidine (26g): yield 76%; sticky solid; R_f 0.53 (20% EtOAc in petroleum ether); $[\alpha]^{25}_D$ = +0.60 (c 1.0, $CHCl_3$); FT IR (neat) 1347, 1211, 1164, 1090 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) (NMR for major diastereomer) δ 7.8 (d, J = 8.1 Hz, 2H), 7.38 (d, J = 8.1 Hz, 2H), 7.29 (m, 3H), 7.20 (m, 2H), 5.32 (q, J = 5.4 Hz, 1H), 4,18 (dd, J = 10.0, 5.6 Hz, 1H), 3.89 (dd, J = 10.2, 5.6 Hz, 1H), 3.23 (t, J =

10.7 Hz, 1H), 2.46 (s, 3H), 1.62 (d, J = 5.4 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 144.3, 136.8, 134.8, 129.9, 128.6, 128.5, 127.7, 126.0, 88.8, 78.7, 53.3, 22.7, 21.6. Anal. Calcd for $C_{17}H_{19}NO_3S$: C, 64.33; H, 6.03; N, 4.41. Found: C, 64.54; H, 6.12; N, 4.34.

5-(4-Chlorophenyl)-2,2-dimethyl-3-(toluene-4-sulfonyl)oxazolidine (26h): yield 40%; mp 89−91 °C; R_f 0.57 (20% EtOAc in petroleum ether); FT IR (KBr) 1343, 1216, 1155, 1092, 1014 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.74 (d, J = 8.3 Hz, 2H), 7.27 (m, 6H), 5.07 (dd, J = 9.3, 5.6 Hz, 1H), 3.85 (dd, J = 8.8, 5.8 Hz, 1H), 3.09 (t, J = 9.0 Hz, 1H), 2.40 (s, 3H), 1.73 (s, 3H), 1.67 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 143.5, 137.0, 135.9, 134.3, 129.6 , 128.8 , 127.5, 127.3, 97.4, 75.5, 53.9, 27.5, 26.9, 21.5. Anal. Calcd for $C_{18}H_{20}ClNO_3S$: C, 59.09; H, 5.51; N, 3.83. Found: C, 59.32; H, 5.55; N, 3.88.

2-(4-Chlorophenyl)-4-(toluene-4-sulfonyl)-1-oxa-4-azaspiro-[4.5]decane (26i): yield 75%; mp 132−134 °C; R_f 0.60 (20% EtOAc in petroleum ether); FT IR (KBr) 1331, 1221, 1152, 1096, 1005 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.73 (d, J = 8.3 Hz, 2H), 7.28 (m, 6H), 5.03 (dd, J = 9.5, 5.9 Hz, 1H), 3.88 (dd, J = 8.8, 5.6 Hz, 1H), 3.07 (t, J = 9.0 Hz, 1H), 2.42 (s, 3H), 2.33 (td, J = 12.2, 4.2 Hz, 1H), 2.22 (td, J = 13.4, 4.7 Hz, 1H), 1.95 (m, 1H), 1.62 (m, 6H), 1.29 (m, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 143.3, 137.7, 136.4, 134.1, 129.6, 128.7, 127.5, 127.3, 99.2, 75.2, 53.9, 36.2, 35.4, 24.6, 23.6, 23.4, 21.5; MS (ES+) 429 (M^+ + Na^+). Anal. Calcd for $C_{21}H_{24}ClNO_3S$: C, 62.13; H, 5.96; N, 3.45. Found: C, 62.31; H, 5.86; N, 3.37.

2-(2-Bromophenyl)-4-(toluene-4-sulfonyl)-1-oxa-4-azaspiro-[4.5]decane (26j): yield 32%; mp 133−135 °C; R_f 0.64 (20% EtOAc in petroleum ether); FT IR (KBr) 1336, 1208, 1161, 1096, 1001 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.73 (d, J = 8.1 Hz, 2H), 7.52 (t, J = 8.7 Hz, 2H), 7.31 (m, 3H), 7.16 (td, J = 7.8, 1.7 Hz, 1H), 5.31 (dd, J = 9.0, 5.9 Hz, 1H), 4.22 (dd, J = 8.8, 5.9 Hz, 1H), 2.98 (t, J = 8.8 Hz, 1H), 2.41 (s, 3H), 2.35 (m, 1H), 2.20 (td, J = 13.4, 4.4 Hz, 1H), 1.97 (m, 1H), 1.62 (m, 6H), 1.28 (m, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 143.2, 137.8, 132.6 (2C), 129.5, 127.7 (2C), 127.2 (2C), 121.6, 100.5, 98.7, 75.0, 52.4, 36.2, 35.3, 24.6, 23.6, 23.6, 21.5. Anal. Calcd for $C_{21}H_{24}BrNO_3S$: C, 56.00; H, 5.37; N, 3.11. Found: C, 56.22; H, 5.30; N, 3.04.

(2*S*,3*R*)-3-Methyl-2-phenyl-4-(toluene-4-sulfonyl)-1-oxa-4-azaspiro[4.5]decane: diastereomeric ratio (**27a**/**28a)** 94:6; total yield 97%; dense liquid; R_f 0.57 (20% EtOAc in petroleum ether); $[\alpha]^{25}_D$ = −11.00 (c 1.5, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 400 MHz) (NMR for major diastereomer) δ 7.82 (d, J = 8.0 Hz, 2H), 7.28 (m, 7H), 4.96 (d, J = 5.4 Hz, 1H), 4.04 (m, 1H), 2.43 (s, 3H), 2.33 (m, 2H), 1.75 (m, 6H), 1.32 (m, 2H), 0.80 (d, J = 6.6 Hz, 3H). Anal. Calcd for $C_{22}H_{27}NO_3S$: C, 68.54; H, 7.06; N, 3.63. Found: C, 68.72; H, 6.90; N, 3.69.

(2*S*,3*R*)-4-(4-Bromobenzenesulfonyl)-3-methyl-2-phenyl-1-oxa-4-azaspiro[4.5]decane: diastereomeric ratio (**27b**/**28b)** 98:2; total yield 99%; viscous yellow liquid; R_f 0.50 (20% EtOAc in petroleum ether); $[\alpha]^{25}_D$ = −11.83 (c 1.2, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 400 MHz) (NMR for major diastereomer) δ 7.81 (m, 2H), 7.66 (m, 2H), 7.31 (m, 5H), 4.97 (d, J = 5.1 Hz, 1H), 4.01 (m, 1H), 2.38 (m, 2H), 2.23 (m, 1H), 1.76 (m, 6H), 1.29 (m, 1H), 0.82 (d, J = 6.6 Hz, 3H). Anal. Calcd for $C_{21}H_{24}BrNO_3S$: : C, 56.00; H, 5.37; N, 3.11. Found: C, 56.19; H, 5.31; N, 3.03.

(2*S*,3*R*)-4-(4-Fluorobenzenesulfonyl)-3-methyl-2-phenyl-1-oxa-4-azaspiro[4.5]decane: diastereomeric ratio (**27c**/**28c)** 95:5; total yield 98%; viscous yellow liquid; R_f 0.61 (20% EtOAc in petroleum ether); $[\alpha]^{25}_D$ = +0.50 (c 1.7, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 400 MHz) (NMR for major diastereomer) δ 7.95 (m, 2H), 7.30 (m, 5H), 7.17 (m, 2H), 4.98 (d, J = 5.1 Hz, 1H), 4.00 (m, 1H), 2.30 (m, 3H), 1.74 (m, 6H), 1.34 (m, 1H), 0.81 (br, 3H). Anal. Calcd for $C_{21}H_{24}FNO_3S$: C, 64.76; H, 6.21; N, 3.60. Found: C, 64.94; H, 6.29; N, 3.55.

(2*S*,3*R*)-4-Methanesulfonyl-3-methyl-2-phenyl-1-oxa-4-azaspiro-[4.5]decane: diastereomeric ratio (**27d**/**28d)** 94:6; total yield 84%; dense liquid; R_f 0.39 (20% EtOAc in petroleum ether); $[\alpha]^{25}_D$ = +51.72 (c 1.5, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 400 MHz) (NMR for major diastereomer) δ 7.35 (m, 5H), 5.20 (d, J = 5.4 Hz, 1H), 4.08 (m, 1H), 3.03 (s, 3H), 2.24 (m, 3H), 1.97 (m, 1H), 1.89 (m, 1H), 1.76 (m, 1H), 1.64 (m, 3H), 1.25 (m, 1H), 0.90 (d, J = 6.6 Hz, 3H). Anal. Calcd for $C_{16}H_{23}NO_3S$: C, 62.11; H, 7.49; N, 4.53. Found: C, 62.30; H, 7.36; N, 4.58.

(2*S*,3*R*)-4-Benzenesulfonyl-3-methyl-2-phenyl-1-oxa-4-azaspiro-[4.5]decane: diastereomeric ratio (**27e**/**28e)** 93:7; total yield 97%; viscous liquid; R_f 0.57 (20% EtOAc in petroleum ether); $[\alpha]^{25}_D$ = −1.00 (c 1.5, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 400 MHz) (NMR for major diastereomer) δ 7.95 (m, 2H), 7.54 (m, 3H), 7.30 (m, 5H), 4.97 (d, J = 5.1 Hz, 1H), 4.05 (m, 1H), 2.30 (m, 3H), 1.61 (m, 7H), 0.80 (d, J = 6.6 Hz, 3H). Anal. Calcd for $C_{21}H_{25}NO_3S$: C, 67.89; H, 6.78; N, 3.77. Found: C, 67.72; H, 6.80; N, 3.75.

General Procedure for the Cleavage of *N*-Tosyl Bond in Oxazolidines. For **30a**, **30b**, **32a**, and **32b**, the same procedure, as described above for the detosylation of imidazolines (Scheme 5), was followed up to the formation of crude detosylated product. To the crude detosylated product were added a saturated solution of $NaHCO_3$ (4 mL) and toluene (4 mL). This was followed by the addition of substituted chloroformate (1.5 mmol), and the reaction mixture was subsequently stirred for 1 h. The organic layer was then separated and the aqueous layer extracted with ethyl acetate. The combined organic layers were then washed with water and brine, dried over anhydrous Na_2SO_4, and concentrated to give the crude product. Purification by column chromatography gave the desired product.

2-Phenyl-1-oxa-4-azaspiro[4.5]decane-4-carboxylic acid benzyl ester (30a): yield 38%; yellow liquid; R_f 0.35 (5% EtOAc in petroleum ether); FT IR (neat) 1705, 1409, 1209, 1133, 1070 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.34 (m, 10H), 5.13 (m, 2H), 5.02 (dd, J = 9.8, 5.8 Hz, 1H), 4.02 (dd, J = 9.3, 6.1 Hz, 1H), 3.29 (t, J = 9.8 Hz, 1H), 2.55 (m, 1H), 2.29 (m, 1H), 1.67 (m, 7H), 1.28 (m, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 152.0, 138.3, 136.6, 128.5, 128.4, 128.2, 127.9, 127.8, 126.2, 95.5, 75.5, 66.4, 52.8, 34.4, 31.7, 24.6, 23.2 (2C); MS (FAB) 352 (M^+ + 1). Anal. Calcd for $C_{22}H_{25}NO_3$: C, 75.19; H, 7.17; N, 3.99. Found: C, 75.36; H, 7.12; N, 3.91.

2-Phenyl-1-oxa-4-azaspiro[4.5]decane-4-carboxylic acid ethyl ester (30b): yield 30%; yellow liquid; R_f 0.33 (5% EtOAc in petroleum ether); FT IR (neat) 1707, 1413, 1210, 1127, 1068 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.30 (m, 5H), 5.03 (dd, J = 9.8, 5.8 Hz, 1H), 4.12 (br, 2H), 3.27 (br, 1H), 3.32 (m, 1H), 2.52 (m, 1H), 2.29 (m, 1H), 1.72 (m, 8H), 1.28 (br, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 152.4, 138.5, 128.5, 128.2, 126.2, 95.3, 75.5, 60.6, 52.8, 34.4, 31.8, 24.7, 23.2 (2C), 14.6; MS (ES+) 290 (M^+ + 1). Anal. Calcd for $C_{17}H_{23}NO_3$: C, 70.56; H, 8.01; N, 4.84. Found: C, 70.78; H, 7.95; N, 4.91.

Phenyl (2-phenyl-1-oxa-4-azaspiro[4.5]dec-4-yl)methanone (30c): yield 52%; mp 144−147 °C; R_f 0.20 (10% EtOAc in petroleum ether); FT IR (KBr) 1630, 1417, 1217, 1078 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.45 (m, 2H), 7.34 (m, 8H), 5.03 (dd, J = 10.0, 5.6 Hz, 1H), 3.74 (br, 1H), 3.44 (t, J = 10.0 Hz, 1H), 2.76 (m, 1H), 1.75 (m, 9H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 167.4, 138.0, 137.7, 129.6, 128.5, 128.3, 128.2, 126.3, 126.1, 97.0, 75.6, 56.3, 34.0, 31.0, 24.5, 23.1, 23.0. Anal. Calcd for $C_{21}H_{23}NO_2$: C, 78.47; H, 7.21; N, 4.36. Found: C, 78.68; H, 7.15; N, 4.31.

3-Methyl-2-phenyl-1-oxa-4-azaspiro[4.5]decane-4-carboxylic acid benzyl ester (32a): yield 50%; viscous liquid; R_f 0.44 (10% EtOAc in petroleum ether); $[\alpha]^{25}_D$ = +33.16 (c 1.6, $CHCl_3$); FT IR (neat) 1708, 1408, 1206, 1124, 1055 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.26 (m, 10H), 5.19 (m, 2H), 4.22 (m, 1H), 2.57 (m, 1H), 2.37 (m, 1H), 1.63 (m, 9H), 0.77 (d, J = 6.6 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 152.1, 136.8, 128.5, 128.1 (2C), 127.9, 127.8, 127.5, 126.1, 94.6, 77.7, 66.4, 56.3, 35.9, 32.1, 25.7, 23.4, 23.3, 15.9; MS (FAB) 366 (M^+ + 1). Anal. Calcd for $C_{23}H_{27}NO_3$: C, 75.59; H, 7.45; N, 3.83. Found: C, 75.78; H, 7.40; N, 3.88.

3-Methyl-2-phenyl-1-oxa-4-azaspiro[4.5]decane-4-carboxylic acid ethyl ester (32b): yield 48%; viscous liquid; R_f 0.14 (5%

EtOAc in petroleum ether); $[\alpha]^{25}_D = +44.41$ (*c* 1.5, $CHCl_3$); FT IR (neat) 1705, 1410, 1206, 1125, 1063 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 7.32 (m, 5H), 5.19 (m, 1H), 4.17 (m, 2H), 2.55 (m, 1H), 2.36 (m, 1H), 1.70 (br, 8H), 1.38 (m, 1H), 1.28 (m, 3H), 0.78 (m, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 152.4, 136.9, 128.0, 127.4, 126.1, 94.4, 60.4, 56.2, 35.9, 30.9, 24.7 (2C), 23.4 (2C), 15.8, 14.6; MS (ES+) 304 ($M^+ + 1$). Anal. Calcd for $C_{18}H_{25}NO_3$: C, 71.26; H, 8.31; N, 4.62. Found: C, 71.45; H, 8.25; N, 4.66.

(3-Methyl-2-Phenyl-1-oxa-4-azaspiro[4.5]dec-4-yl)methanone (32c): yield 56%; mp 183−185 °C; R_f 0.19 (10% EtOAc in petroleum ether); $[\alpha]^{25}_D = +6.50$ (*c* 1.0, $CHCl_3$); FT IR (KBr) 1622, 1412, 1203, 1067 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 7.40 (br, 4H), 7.32 (d, $J = 4.4$ Hz, 4H), 7.27 (m, 2H), 5.27 (d, $J = 4.9$ Hz, 1H), 4.11 (br, 1H), 2.94 (br, 1H), 2.66 (br, 1H), 1.79 (m, 7H), 1.37 (br, 1H), 0.59 (d, $J = 5.1$ Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 168.3, 138.4, 136.5, 128.9, 128.4, 128.2, 127.6, 126.1, 125.9, 96.1, 77.7, 58.3, 35.9, 30.7, 24.5, 23.3, 23.2, 16.7; MS (FAB) 336 ($M^+ + 1$). Anal. Calcd for $C_{22}H_{25}NO_2$: C, 78.77; H, 7.51; N, 4.18. Found: C, 78.98; H, 7.45; N, 4.23.

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Supporting Information Available: Characterization data for some of the compounds, crystal structure and data of compound **5e**. Crystallographic information file for compound **5e**. This material is available free of charge via the Internet at http://pubs.acs.org.

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