JOC The Journal of Organic Chemistry

Article

pubs.acs.org/joc

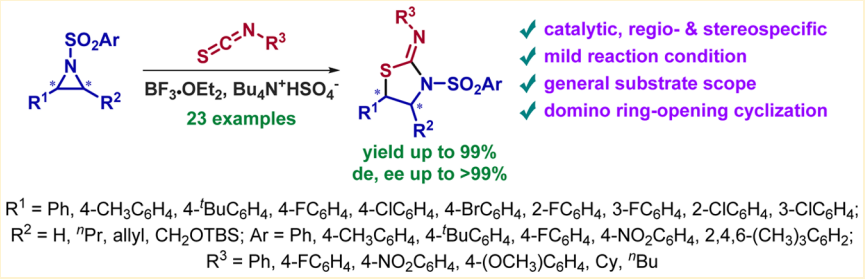
Stereospecific Synthesis of 2-Iminothiazolidines via Domino Ring-Opening Cyclization of Activated Aziridines with Aryl- and Alkyl Isothiocyanates

Aditya Bhattacharyya,[†] C. V. Kavitha,[‡] and Manas K. Ghorai*[,†]

[†]Department of Chemistry, Indian Institute of Technology, Kanpur 208016, India

[‡]Department of Chemistry, Government College for Women, Mandya 571401, Karnataka India

Supporting Information



ABSTRACT: Lewis acid catalyzed domino ring-opening cyclization of activated aziridines with aryl and alkyl isothiocyanates has been accomplished leading to the formation of a wide variety of highly substituted and functionalized 2-iminothiazolidines with excellent diastereo- and enantiospecificity (de, ee up to >99%). The reaction proceeds via a Lewis acid catalyzed S_N2-type ring-opening of the activated aziridine followed by a concomitant 5-*exo*-*dig* cyclization in a domino fashion to furnish the 2-iminothiazolidine derivative in excellent yields (up to 99%).

INTRODUCTION

The thiazolidines, especially the 2-iminothiazolidines and their derivatives, are pervasive molecular frameworks in various drug candidates and natural products with immense biological potencies.[1] Some of the representative examples of the biologically and pharmaceutically active compounds with 2-iminothiazolidines as their core are given in the Figure 1. While compounds **I** and **II** are used as progesterone receptor binding agents,[1a] **III** is used as an anti-inflammatory agent.[1b] 2-(Tetrahydronaphthalen-1-yl)iminothiazolidine (**IV**) and EGYT-4201 (**V**) exhibit pronounced antidepressant activity.[1c,d]

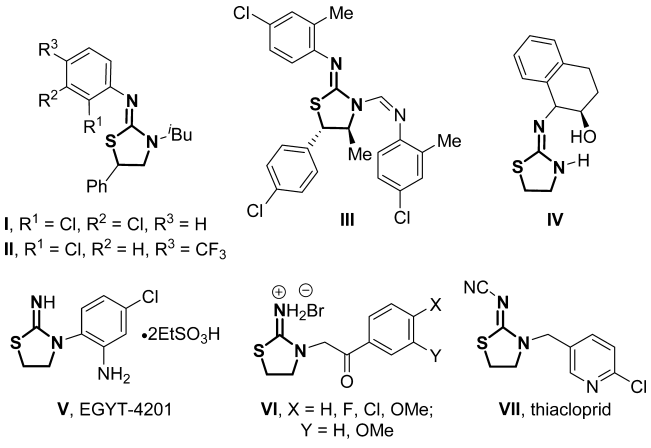


Figure 1. Some biologically active 2-iminothiazolidine derivatives.

A series of 2-iminothiazolidine derivatives (**VI**) have been found to be active as radioprotector agents.[1e,f] Thiacloprid (**VII**), another 2-iminothiazolodine derivative, is an neonicotinoid insecticide.[1g]

Considering the synthetic utility and immense biological activities, a large number of synthetic routes have been developed for the synthesis of 2-iminothiazolidines.[2−4] The synthesis of 2-iminothiazolidines are reported from acylthioureas and allylic bromides via a base-mediated [3 + 2] annulation strategy,[2a] Fe(III)-catalyzed [3 + 2] cycloaddition reaction of aziridines with heterocumulenes,[2b] organophosphine-catalyzed ring-opening reaction of activated aziridines with isothiocyanates,[2c] and Pd(II)-catalyzed reaction of 1,2,3-trisubstituted aziridines with heterocumulenes,[2d] etc. A concise report by D'hooghe et al. comprehensively describes various methodologies available for the synthesis of 2-iminothiazolidine derivatives,[3] and as pointed out in their review, a general and direct method for the regio- and stereoselective synthesis of 2-iminothiazolidines bearing diverse substituents at the 2-, 3-, 4-, or 5-positions of the aza-heterocyclic moiety is greatly desirable.

Aziridines have emerged as one of the most useful building blocks in organic synthesis of late. The ring-opening trans-

Received: June 28, 2016
Published: July 16, 2016

DOI: 10.1021/acs.joc.6b01551
J. Org. Chem. 2016, 81, 6433−6443

formations of activated aziridines have been carried out with a variety of carbon and heteroatomic nucleophiles delivering a diverse array of nitrogen-containing acyclic and cyclic compounds with immense biological importance.[5] Although a few reports are available for the synthesis of 2-iminothizolidines from aziridines,[2b−d,3,4a−c] most of them employed racemic aziridines as the substrate, and they also suffer from limited substrate scope. Recently, Stoltz and co-workers have reported a synthetic protocol for the synthesis of racemic and nonracemic 2-iminothiazolidines from the corresponding aziridines[4a] employing a superstoichiometric amount of metal salt as the activating Lewis acid. Therefore, there is a conspicuous requirement of a general, catalytic, regio- and stereoselective strategy for the synthesis of enantioenriched 2-iminothiazolidines with a wide substrate scope.

Over the years, we have been exploring the Lewis acid assisted S_N2-type ring-opening reactions of activated chiral aziridines and azetidines with a wide range of functionalized nucleophiles to synthesize various enantiomerically enriched bioactive molecular targets.[6] Moreover, we demonstrated that the racemization process of the chiral aziridines and azetidines in the presence of various Lewis acids during the reactions could be successfully controlled by using quaternary ammonium salts along with catalytic amount of Lewis acids and the corresponding ring-opened products were obtained with excellent stereoselectivities (de, ee up to >99%).[6e,f] We have further extended this chemistry by developing several one-pot multistep strategies that involve ring opening of aziridines and donor−acceptor cyclopropanes with functionalized nucleophiles followed by concomitant cyclization in a domino fashion for the syntheses of various aza-hetero- and carbacycles, and we termed this protocol domino ring-opening cyclization (DROC).[6d,h] Stoltz and co-workers have also reported Lewis acid mediated [3 + 2] cycloaddition of heterocumulenes with donor−acceptor cyclopropanes that have reactivity similar to that of aziridines.[7] In this vein, we envisaged that a variety of chiral substituted 2-iminothiazolidines could be easily synthesized via Lewis acid catalyzed quaternary ammonium salt-mediated ring opening of chiral activated aziridines employing various isothiocyanates as the nucleophiles followed by intramolecular cyclization in a domino fashion.

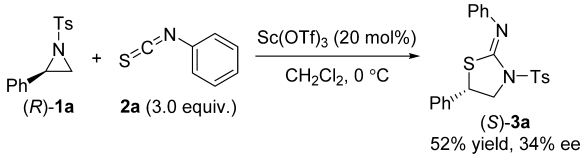
In this paper, we wish to describe in detail an efficient and operationally simple procedure for the stereospecific synthesis of various nonracemic and racemic substituted 2-iminothiazolidines via Lewis acid catalyzed domino ring-opening cyclization (DROC) of activated aziridines with aryl and alkyl isothiocyanates in excellent yields (up to 99%) and stereospecificity (de, ee up to >99%).

RESULTS AND DISCUSSION

Initial study commenced with the reaction of (*R*)-2-phenyl-*N*-tosylaziridine (*R*)-**1a** with phenyl isothiocyanate (**2a**, 3.0 equiv) as the nucleophile in the presence of a catalytic amount of scandium(III) triflate (20 mol %) as the Lewis acid in dichloromethane at 0 °C. The reaction proceeded sluggishly, and the corresponding product iminothiazolidine **3a** was obtained as the single regioisomer in moderate yield and poor enantiomeric excess (34% ee, Scheme 1). The structure of the product **3a** was ascertained by spectroscopic analysis.

Next, we aimed to optimize the reaction conditions for improved yield and enantiospecificity. Altering the solvent from dichloromethane to dichloroethane resulted in diminution of stereospecificity of the transformation (entries 2 and 3, Table 1). We inferred that the enantiopure starting material (*R*)-**1a** underwent partial racemization under the reaction conditions as we previously reported.[6e] Therefore, we introduced the quaternary ammonium salt as an additive into the reaction mixture with a view to reducing the extent of partial racemization of the starting material before the nucleophilic ring-opening step.[6e,f] When we performed the reaction in the presence of a superstoichiometric amount (200 mol %) of tetrabutylammonium hydrogen sulfate (TBAHS) and 5 mol % of $Sc(OTf)_3$ in dichloromethane at 0 °C, we were delighted to observe the formation of the corresponding product **3a** with higher ee (70%, entry 4, Table 1). Next, we screened other Lewis acids, and by employing $BF_3{\cdot}OEt_2$ we obtained the product with 73% ee at 0 °C (entry 8, Table 1). In order to further increase the enantiospecificity of the reaction, we continued to decrease the temperature, and to our great pleasure, the product could be obtained in excellent yield (97%) with excellent enantiomeric excess (98% ee) in the presence of 20 mol % of $BF_3{\cdot}OEt_2$ and 1.0 equiv of TBAHS at −30 °C (entry 10, Table 1). Decreasing the temperature further caused freezing of the reaction mixture. In addition, no product was formed when the loading of quaternary ammonium salt was increased from 100 to 200 mol % (entries 11 and 12, Table 1). All of the results are detailed in Table 1.

Scheme 1. Domino Ring-Opening Cyclization of (*R*)-2-Phenyl-*N*-tosylaziridine 1a with Phenyl Isothiocyanate 2a

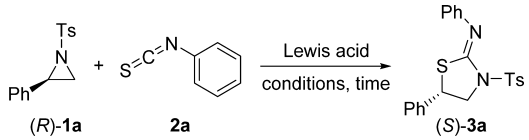


With the optimal DROC conditions in hand, we next aimed at generalizing the synthetic strategy and expanding the substrate scope by employing enantiopure 2-phenyl-*N*-tosylaziridine (*S*)-**1a** and various aryl and alkyl isothiocyanates **2a−f** (Scheme 2). While (*S*)-**1a** upon reaction with phenyl isothiocyanate (**2a**) at −30 °C furnished the corresponding iminothiazolidine (*R*)-**3a** with excellent enantiospecificity (98%, entry 1, Table 2), the other aryl isothiocyanates **2b−d** afforded the products with reduced ee, possibly due to the partial racemization of the enantiopure starting material under the reaction conditions (entries 2−4, Table 2). As the reactions were carried out using the isothiocyanates as the solvent, the extent of racemization of the enantiopure starting materials might vary depending on the nature and reactivity of different isothiocyanates resulting in the formation of the products with reduced ee in some cases.[6e] On the other hand, while cyclohexyl isothiocyanate (**2e**) yielded the corresponding iminothiazolidine (*R*)-**3e** with moderate ee (entry 5, Table 2), *n*-butyl isothiocyanate (**2f**) provided the iminothiazolidine (*R*)-**3f** with excellent enantiomeric excess (93% ee, entry 6, Table 2). The structures of the products were unambiguously ascertained by spectroscopic analysis. As a representative example, single-crystal X-ray analysis of **3b** also confirmed the molecular structure with the configuration of the double bond at the 2-position as *Z*.[8] All of the results are shown in Table 2.

Next, to study the electronic effect of the arylsulfonyl groups on our developed synthetic methodology, a variety of enantiopure *N*-arylsulfonylaziridines (*R*)-**1b−f** (ee >99%) with diverse electron-withdrawing capability on the nitrogen atom of the aziridine rings were reacted with phenyl

DOI: 10.1021/acs.joc.6b01551
J. Org. Chem. 2016, 81, 6433−6443

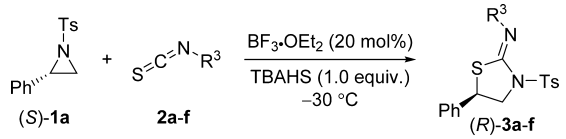
Table 1. Optimization Studies for Domino Ring-Opening Cyclization of (*R*)-2-Phenyl-*N*-tosylaziridine 1a with Phenyl Isothiocyanate 2a



entry	Lewis acid (mol %)	quaternary ammonium salt (mol %)	solvent	temp (°C)	time	yield of **3a** (%)	ee[a] (%)
1	$Sc(OTf)_3$ (20)		CH_2Cl_2	0	6 h	52	34
2	$Sc(OTf)_3$ (10)		$(CH_2)_2Cl_2$	0	18 h	26	24
3	$Sc(OTf)_3$ (20)		$(CH_2)_2Cl_2$	0	10 h	30	30
4	$Sc(OTf)_3$ (5)	TBAHS (200)	CH_2Cl_2	0	30 min	56	70
5	$Cu(OTf)_2$ (5)	TBAHS (200)	CH_2Cl_2	0	30 min	45	42
6	$BF_3{\cdot}OEt_2$ (20)	TBAHS (100)	CH_2Cl_2	0	30 min	88	52
7	$BF_3{\cdot}OEt_2$ (20)	TBAHS (100)		RT	20 min	78	62
8	$BF_3{\cdot}OEt_2$ (20)	TBAHS (100)		0	45 min	90	73
9	$BF_3{\cdot}OEt_2$ (20)	TBAHS (100)		−15	1 h	93	83
10	$BF_3{\cdot}OEt_2$ (20)	TBAHS (100)		−30	40 min	97	98
11	$BF_3{\cdot}OEt_2$ (10)	TBAHS (200)		−30	6 h	nr	
12	$BF_3{\cdot}OEt_2$ (20)	TBAHS (200)		−30	6 h	nr	

[a]Enantiomeric excess (ee) was determined by chiral HPLC analysis.

Scheme 2. Domino Ring-Opening Cyclization of (*S*)-2-Phenyl-*N*-tosylaziridine 1a with Aryl and Alkyl Isothiocyanates



R^3 = Ph, 4-FC_6H_4, 4-$NO_2C_6H_4$, 4-$OMeC_6H_4$, cyclohexyl, ^{n}Bu

isothiocyanate (**2a**), serving as both nucleophile and solvent, in the presence of 20 mol % of $BF_3{\cdot}OEt_2$ as the Lewis acid and 1.0 equiv of tetrabutylammonium hydrogen sulfate at −30 °C (Scheme 3). Gratifyingly, we observed the formation of the corresponding 2-iminothiazolidines (*S*)-**3g−k** in excellent yield (up to 98%) and with good to excellent enantioselectivity (ee up to >99%). All of the results are shown in Table 3.

The synthetic versatility of the developed methodology was illustrated by engaging a range of racemic 2-aryl-*N*-tosylaziridines as the substrate. When aziridines **1g−n** were reacted with phenyl isothiocyanate (**2a**) in the presence of 20 mol % of $BF_3{\cdot}OEt_2$ as the Lewis acid and stoichiometric amount of tetrabutylammonium hydrogen sulfate (TBAHS, 1.0 equiv) in dichloromethane at 0 °C, the corresponding 2-iminothiazolidines **3l−s** were obtained as single regioisomers in excellent yield (up to 99%, Scheme 4). All of the results are detailed in Table 4. As a representative example, single-crystal X-ray analysis of **3j** reaffirmed the molecular structure.[8]

To further demonstrate the substrate scope and generality of the synthetic methodology, we studied the domino ring-opening cyclization (DROC) of *trans*-2,3-disubstituted aziridines **1o−q** with aryl isothiocyanates (Scheme 5). When enantio- and diastereopure disubstituted aziridines **1o,p** (de, ee >99%) were subjected to DROC with phenyl isothiocyanate **2a** in the presence of 40 mol % of $BF_3{\cdot}OEt_2$ and 1.0 equiv of TBAHS at 0 °C, the corresponding 2-iminothiazolidines **3t,u** were obtained as single diastereomers (de, ee >99%) in excellent yield (up to 90%, Table 5, entries 1 and 2). Similarly, subjection of racemic diastereopure *trans*-2,3-disubstituted aziridine **1q** (de >99%) to phenyl isothiocyanate **2a** and 4-methoxyphenyl isothiocyanate **2d** under identical reaction conditions also afforded the corresponding 2-iminothiazolidines **3v** and **3w** as single diastereomers (de >99%) in excellent yields (entries 3 and 4). All of the results are described in Table 5.

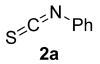
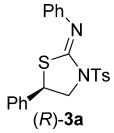
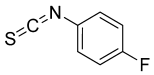
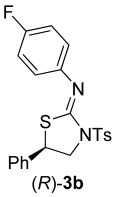
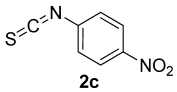
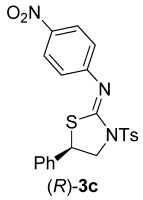
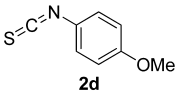
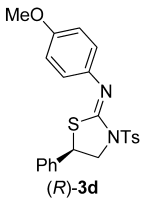
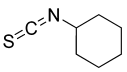
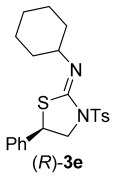
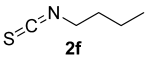
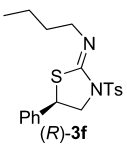
The 4,5-relative stereochemistry of the 2-iminothiazolidines **3t−w** obtained from the corresponding *trans*-2,3-disubstituted aziridines **1o−q** was determined by NOESY experiments of **3t** and **3v** as representative examples. When proton H_a was irradiated in both compounds **3t** and **3v**, peak enhancement of the *ortho*-protons of the 4-phenyl ring was observed but the peaks corresponding to H_c and H_d were not enhanced. On the other hand, when proton H_b was irradiated, peak enhancements for the protons H_c and H_d were observed as expected, but no enhancement was found for the *ortho*-protons of the 4-phenyl ring. Moreover, for compound **3v**, when proton H_c was irradiated, peak enhancement for the proton H_e was observed.[8] All of these diagnostic NOE observations evidently suggest that the relative stereochemistry at the 4,5-postitions of the 2-iminothiazolidines is *cis*. The spatial interactions of the protons are shown in Figure 2.

MECHANISM

A mechanistic rationale is offered in Scheme 6 to explain the formation of the desired products. Experimental evidence indicates that the Lewis acid catalyzed DROC of activated aziridines with aryl and alkyl isothiocyanates follows an S_N2-type pathway as described in our previous reports.[6e] At first, the Lewis acid ($BF_3{\cdot}OEt_2$) along with the quaternary ammonium salt (TBAHS) activate the *N*-arylsulfonylaziridine to produce a highly reactive intermediate **A**, which successively undergoes an S_N2-type attack on the benzylic carbon by the isothiocyanate functionality to afford the corresponding ring-opened intermediate **B** with inverted stereochemistry. Subsequently, the incipient negatively charged nitrogen of **B** attacks the carbon of the isothiocyanato group in a domino fashion resulting in a 5-*exo-dig* cyclization to afford the corresponding 2-iminothiazolidine **3** in excellent yield and enantioselectivity.

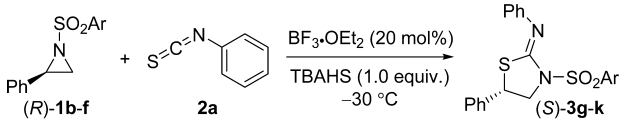
DOI: 10.1021/acs.joc.6b01551
J. Org. Chem. 2016, 81, 6433−6443

Table 2. Domino Ring-Opening Cyclization of (*S*)-2-Phenyl-*N*-tosylaziridine 1a with Aryl- and Alkyl Isothiocyanates 2a−f[a]

entry	isothiocyanate (**2**)	iminothiazolidine (**3**)	time	yield (%)	ee (%)[b]
1	 **2a**	 (*R*)-**3a**	40 min	97	98
2[c]	 **2b**	 (*R*)-**3b**	50 min	98	66
3[d]	 **2c**	 (*R*)-**3c**	45 min	95	ND[e]
4	 **2d**	 (*R*)-**3d**	1 h	94	20
5[f]	 **2e**	 (*R*)-**3e**	2 h	96	63
6[f]	 **2f**	 (*R*)-**3f**	3 h	94	93

[a]All of the reactions were carried out using the corresponding aryl and alkyl isothiocyanates as solvent at −30 °C unless otherwise noted. [b]The enantiomeric excess (ee) was determined by chiral HPLC analysis. [c]The reaction was performed at 25 °C. [d]The reaction was performed using CH_2Cl_2 as the solvent at −30 °C. [e]ee could not be determined. [f]The reaction was performed at 0 °C.

Scheme 3. Domino Ring-Opening Cyclization of (*R*)-2-Phenyl-*N*-arylsulfonylaziridines 1b−f with Phenyl Isothiocyanate 2a



Ar = Ph, 4-FC_6H_4, 4-$NO_2C_6H_4$, 4-$^tBuC_6H_4$, 2,4,6-$(CH_3)_3C_6H_2$

CONCLUSION

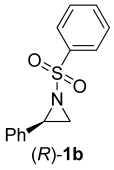
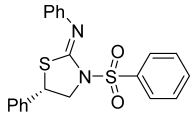
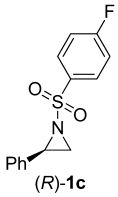
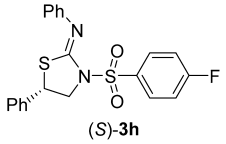
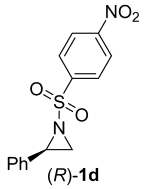
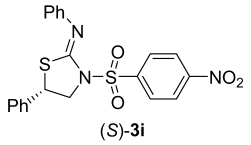
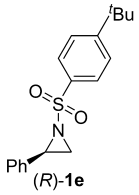
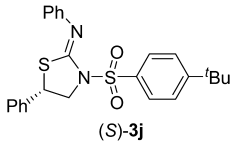
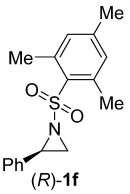
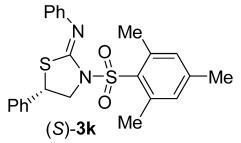
We have developed a simple and straightforward synthetic protocol for the synthesis of a wide range of 2-iminothiazolidines via Lewis acid catalyzed DROC of various racemic and nonracemic aziridines with aryl and alkyl isothiocyanates. The high regio- and stereospecificity observed in the products and the wide range of substrate tolerance make the strategy superior to other existing synthetic protocols for the synthesis of 2-iminothiazolidines.

EXPERIMENTAL SECTION

General Procedures. Analytical thin-layer chromatography (TLC) was carried out for monitoring the progress of the reactions using silica gel 60 F_{254} precoated plates. Visualizations of the spots were accomplished with a UV lamp or I_2 stain. Silica gel 100−200 and 230−400 mesh sizes were used for flash column chromatographic purification using a combination of ethyl acetate and petroleum ether as the eluent. Unless otherwise mentioned, all of the reactions were carried out in oven-dried glassware under an atmosphere of nitrogen using anhydrous solvents. Where appropriate, the solvents and all of the reagents were purified prior to use following the guidelines of

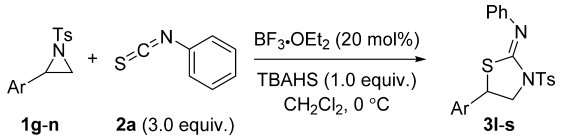
DOI: 10.1021/acs.joc.6b01551
J. Org. Chem. 2016, 81, 6433−6443

Table 3. Domino Ring-Opening Cyclization of (*R*)-2-Phenyl-*N*-sulfonylaziridines with Phenyl Isothiocyanate 2a[a]

entry	aziridine (**1**)	iminothiazolidine (**3**)	time (min)	yield (%)	ee (%)[b]
1	 (*R*)-**1b**	 (*S*)-**3g**	40	96	80
2	 (*R*)-**1c**	 (*S*)-**3h**	35	98	>99
3	 (*R*)-**1d**	 (*S*)-**3i**	30	94	ND[c]
4	 (*R*)-**1e**	 (*S*)-**3j**	45	97	86
5	 (*R*)-**1f**	 (*S*)-**3k**	35	95	76

[a]Phenyl isothiocyanate was used as the solvent unless otherwise noted. [b]The enantiomeric excess (ee) was determined by chiral HPLC analysis. [c]ee could not be determined.

Scheme 4. Domino Ring-Opening Cyclization of Racemic 2-Aryl-*N*-tosylaziridines 1g−n with Phenyl Isothiocyanate 2a



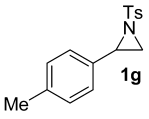
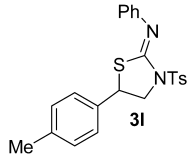
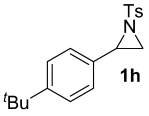
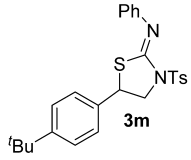
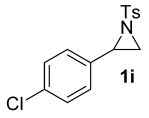
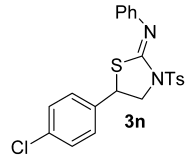
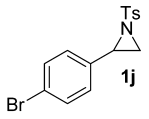
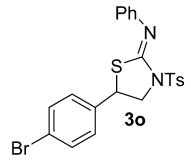
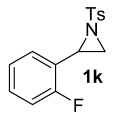
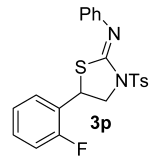
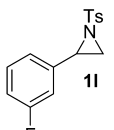
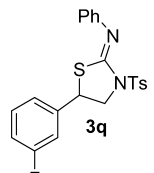
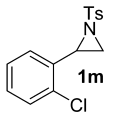
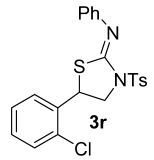
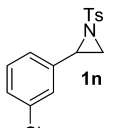
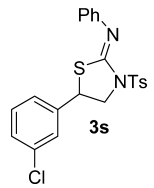
1g-n **2a** (3.0 equiv.) **3l-s**

Armarego and Chai.[9] The monosubstituted *N*-Ts aziridines,[10] the *N*-sulfonylaziridines, and disubstituted aziridines[6f] were prepared by following the previous reports. All of the commercial reagents were used as received without further purification unless otherwise mentioned. Proton nuclear magnetic resonance (^{1}H NMR) was recorded at 400 or 500 MHz. The chemical shifts were recorded in parts per million (ppm, δ) using tetramethylsilane (δ 0.00) as the internal standard. Splitting patterns of the ^{1}H NMR are mentioned as singlet (s), doublet (d), doublet of doublet (dd), triplet (t), quartet (q), multiplet (m), etc. Carbon nuclear magnetic resonance (^{13}C{^{1}H} NMR) spectra were recorded at 100 or 125 MHz. HRMS were obtained using an (ESI) mass spectrometer (TOF). KBr plates were used for IR spectra of solid compounds, whereas liquid compounds were recorded neat. The melting point measurements were made using a hot-stage apparatus and are reported as uncorrected. The enantiomeric excess (ee) was determined by chiral HPLC using a Chiralcel OD-H or Chiralpak AD-H, AS-H, or cellulose-1, cellulose-2, or amylose-2 column (detection at 254 nm). Optical rotations were measured using a 6.0 mL cell with a 1.0 dm path length and are reported as $[\alpha]^{25}_{D}$ (*c* in g per 100 mL solvent) at 25 °C.

General Experimental Procedure for the BF_3·OEt_2-Catalyzed TBAHS-Mediated Domino Ring-Opening Cyclization of Aziridines with Isothiacyanates. *Method A.* To a solution of 1.0 equiv of the aziridine (*S*)-**1a** (for Table 2, 50.0 mg, 0.183 mmol, 1.0 equiv) or (*R*)-**1b−f** (for Table 3) and tetrabutylammonium hydrogen sulfate (TBAHS, 62.1 mg, 0.183 mmol, 1.0 equiv) in liquid aryl or alkyl isothiocyanate (for entry 1, Table 2, 0.8 mL of PhNCS; for entry 3, Table 2, 5.0 equiv of solid 1-isothiocyanato-4-nitrobenzene was added, and 1.0 mL of CH_2Cl_2 was used as the solvent), trifluoroborane diethyerate (BF_3·OEt_2, 5 μL, 0.037 mmol, 0.2 equiv) was added at the appropriate temperature under an argon atmosphere. Then the reaction mixture was stirred at the same temparature until the reaction was complete. After complete consumption of the aziridine

DOI: 10.1021/acs.joc.6b01551
J. Org. Chem. 2016, 81, 6433−6443

Table 4. Domino Ring-Opening Cyclization of Racemic 2-Aryl-*N*-tosylaziridines 1g−n with Phenyl Isothiocyanate 2a[a]

entry	aziridine (**1**)	iminothiazolidine (**3**)	time	yield (%)
1	 **1g**	 **3l**	35 min	98
2	 **1h**	 **3m**	50 min	95
3	 **1i**	 **3n**	45 min	96
4	 **1j**	 **3o**	45 min	95
5	 **1k**	 **3p**	1 h	92
6	 **1l**	 **3q**	45 min	94
7	 **1m**	 **3r**	1 h	90
8	 **1n**	 **3s**	50 min	92

[a]Unless otherwise noted, all of the reactions were carried out in the presence of 20 mol % of $BF_3{\cdot}OEt_2$, 1.0 equiv of TBAHS, and 3.0 equiv of PhNCS in CH_2Cl_2 at 0 °C.

(monitored by TLC), the reaction was quenched by aqueous saturated $NaHCO_3$ solution at the same temperature. The organic phase was separated, and the aqueous phase was extracted with dichloromethane (3 × 5.0 mL). The combined organic layers were washed with brine solution and dried over anhydrous Na_2SO_4. After removal of the organic solvent under reduced pressure, the crude reaction mixture was purified by flash column chromatography on silica gel (230−400 mesh) using 10% ethyl acetate in petroleum ether as the eluent to afford the corresponding pure 2-iminothiazolidines.

Method B. To a solution of the 2-aryl-*N*-tosylaziridine **1g−n** (for entry 1, Table 4, 50.0 mg, 0.174 mmol, 1.0 equiv), tetrabutylammonium hydrogen sulfate (TBAHS, 59.1 mg, 0.174 mmol, 1.0 equiv), and phenyl isothiocyanate (for entry 1, Table 4, 63 μL, 0.522 mmol, 3.0 equiv) in dichloromethane (2.0 mL), trifluoroborane diethyl etherate ($BF_3{\cdot}OEt_2$, 5 μL, 0.037 mmol, 0.2 equiv) was added at the appropriate

DOI: 10.1021/acs.joc.6b01551
J. Org. Chem. 2016, 81, 6433−6443

Scheme 5. Domino Ring-Opening Cyclization of *trans*-2,3-Disubstituted *N*-Tosylaziridines 1o−q with Aryl Isothiocyanates

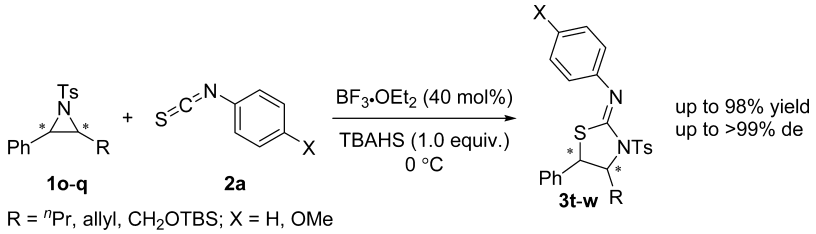
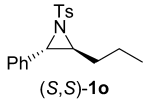
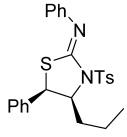
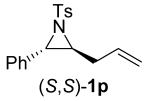
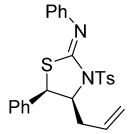
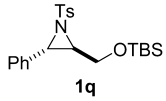
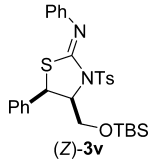
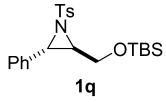
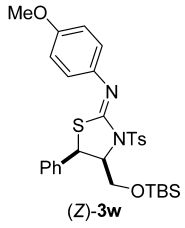


Table 5. Domino Ring-Opening Cyclization of *trans*-2,3-Disubstituted *N*-Tosylaziridines 1o−q with Phenyl Isocyanate 2a[a]

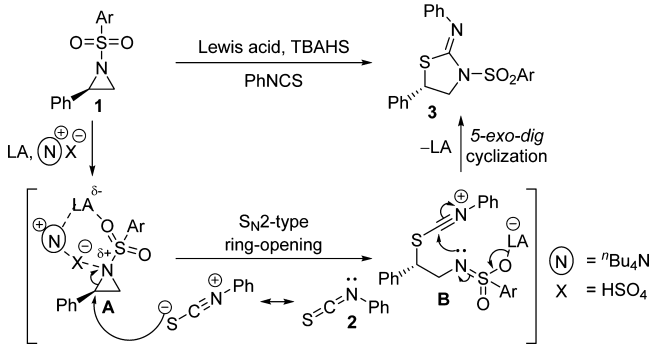
entry	Aziridine (**1**)	iminothiazolidine (**3**)	time (min)	yield (%)	dr (%)[b]
1	 (*S*,*S*)-**1o**	 (*S*,*R*,*Z*)-**3t**	2.5 h	88	>99
2	 (*S*,*S*)-**1p**	 (*S*,*R*,*Z*)-**3u**	2 h	90	>99
3	 **1q**	 (*Z*)-**3v**	1.5 h	94	>99
4	 **1q**	 (*Z*)-**3w**	1.5 h	91	>99

[a]Phenyl isothiocyanate was used as the solvent unless otherwise noted. [b]The diastereomeric ratio (dr) was determined by ^{1}H NMR.

Figure 2. Diagnostic NOE observations for the 2-iminothiazolidines (*S*,*R*,*Z*)-**3t** and (*Z*)-**3v**.

temperature under an argon atmosphere. Then the reaction mixture was stirred at the same temparature until the reaction was complete. After complete consumption of the starting compound (monitored by TLC), the reaction was quenched by aqueous saturated $NaHCO_3$ solution. The organic phase was separated, and the aqueous phase was extracted with dichloromethane (3 × 5.0 mL). The combined organic layers were washed with brine solution and dried over anhydrous Na_2SO_4. After removal of the organic solvent under reduced pressure,

Scheme 6. Plausible Mechanistic Pathway for the Lewis Acid Catalyzed Domino Ring-Opening Cyclization of Activated Aziridines with Isothiocyanates



DOI: 10.1021/acs.joc.6b01551
J. Org. Chem. 2016, 81, 6433−6443

the crude reaction mixture was purified by flash column chromatography on silica gel (230−400 mesh) using 10% ethyl acetate in petroleum ether as the eluent to give pure 2-iminothiazolidines.

Method C. To a solution of the 2,3-disubstituted aziridine **1o−q** (for entry 1, Table 5, 50 mg, 0.158 mmol, 1.0 equiv) and tetrabutylammonium hydrogen sulfate (TBAHS, 53.6 mg, 0.158 mmol, 1.0 equiv) in the liquid aryl isothiocyanate (for entry 1, Table 5, 0.8 mL of PhNCS) was added trifluoroborane diethyerate ($BF_3{\cdot}OEt_2$, 8 μL, 0.063 mmol, 0.4 equiv) at the appropriate temperature under an argon atmosphere. Then the reaction mixture was stirred at the same temparature until the reaction was complete. After complete consumption of the starting compound (monitored by TLC), the reaction was quenched by aqueous saturated $NaHCO_3$ solution. The organic phase was separated, and the aqueous phase was extracted with dichloromethane (3 × 5.0 mL). The combined organic layers were washed with brine solution and dried over anhydrous Na_2SO_4. After removal of the organic solvent under reduced pressure, the crude reaction mixture was purified by flash column chromatography on silica gel (230−400 mesh) using 10% ethyl acetate in petroleum ether as the eluent to give pure 2-iminothiazolidines as single diastereomer.

*(R,Z)-N,5-Diphenyl-3-tosylthiazolidin-2-imine ((R)-**3a**).*[2b] General method A described above was followed when (*S*)-**1a** (50.0 mg, 0.183 mmol, 1.0 equiv) was reacted with phenyl isothiocyanate **2a** to afford (*R*)-**3a** (72.5 mg, 0.177 mmol) as a white solid in 97% yield: mp 86−88 °C; $[\alpha]^{25}_D$ −64.1 (*c* 0.42 in $CHCl_3$) for a 98% ee sample. Optical purity was determined by chiral HPLC analysis (Cellulose 1 column), hexane−2-propanol, 98:2; flow rate = 1.0 mL/min; t_R 1:48.58 min (minor), t_R 2:59.45 min (major): R_f 0.50 (ethyl acetate/petroleum ether, 1:4); IR $\tilde{\nu}_{max}$ (KBr, cm^{-1}) 3030, 2924, 1642, 1591, 1488, 1453, 1361, 1288, 1247, 1186, 1171, 1136, 1101, 1019; ^1H NMR (500 MHz, $CDCl_3$) δ 7.97 (d, 2H, *J* = 8.1 Hz), 7.36−7.32 (m, 7H), 7.27−7.23 (m, 2H), 7.07−7.04 (m, 1H), 6.77 (d, 2H, *J* = 6.9 Hz), 4.79 (dd, 1H, *J* = 8.6, 6.3 Hz), 4.59 (dd, 1H, *J* = 10.3, 6.3 Hz), 4.05 (dd, 1H, *J* = 10.3, 8.6 Hz), 2.48 (s, 3H); $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$) δ 152.2, 150.1, 147.7, 144.9, 136.5, 134.7, 129.3, 129.2, 129.1, 129.0, 128.8, 128.6, 127.5, 124.4, 120.8, 56.8, 47.0, 21.8; HRMS (ESI-TOF) calcd for $C_{22}H_{21}N_2O_2S_2$ $(M + H)^+$ 409.1044, found 409.1046.

*(R,Z)-N-(4-Fluorophenyl)-5-phenyl-3-tosylthiazolidin-2-imine ((R)-**3b**).* The general method A described above was followed when (*S*)-**1a** (50.0 mg, 0.183 mmol, 1.0 equiv) was reacted with 1-fluoro-4-isothiocyanatobenzene **2b** (0.8 mL) to afford (*R*)-**3b** (76.4 mg, 0.179 mmol) as a white solid in 98% yield: mp 74−76 °C; $[\alpha]^{25}_D$ −44.2 (*c* 0.435 in $CHCl_3$) for a 66% ee sample. Optical purity was determined by chiral HPLC analysis (Chiralpak AS-H column), hexane−2-propanol, 90:10; flow rate = 1.0 mL/min; t_R 1:25.89 min (major), t_R 2:45.02 min (minor): R_f 0.44 (ethyl acetate/petroleum ether, 1:4); IR $\tilde{\nu}_{max}$ (KBr, cm^{-1}) 2923, 2865, 1650, 1595, 1501, 1455, 1355, 1290, 1211, 1187, 1167, 1137, 1102; ^1H NMR (500 MHz, $CDCl_3$) δ 7.96 (d, 2H, *J* = 8.6 Hz), 7.36−7.33 (m, 7H), 6.94 (t, 2H, *J* = 8.6 Hz), 6.75−6.72 (m, 2H), 4.80 (dd, 1H, *J* = 8.6, 6.7 Hz), 4.59 (dd, 1H, *J* = 10.4, 6.4 Hz), 4.05 (dd, 1H, *J* = 10.4, 8.6 Hz), 2.48 (s, 3H); $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$) δ 159.9 (d, $^1J_{C-F}$ = 242.6 Hz), 152.8, 146.2, 145.1, 136.5, 134.7, 129.4, 129.2, 129.1, 128.9, 127.6, 122.3, 122.2, 115.8, 115.7, 56.9, 47.1, 21.9; HRMS (ESI-TOF) calcd for $C_{22}H_{20}FN_2O_2S_2$ $(M + H)^+$ 427.0950, found 427.0953.

*(R,Z)-N-(4-Nitrophenyl)-5-phenyl-3-tosylthiazolidin-2-imine ((R)-**3c**).* The general method A described above was followed when (*S*)-**1a** (50.0 mg, 0.183 mmol, 1.0 equiv) was reacted with 1-isothiocyanato-4-nitrobenzene **2c** (164.8 mg, 0.915 mmol, 5.0 equiv) to afford (*R*)-**3c** (78.8 mg, 0.173 mmol) as a gummy liquid in 95% yield: $[\alpha]^{25}_D$ −29.8 (*c* 0.40 in $CHCl_3$); R_f 0.42 (ethyl acetate/petroleum ether, 1:4); IR $\tilde{\nu}_{max}$ (neat, cm^{-1}) 3064, 2924, 1640, 1585, 1512, 1494, 1454, 1400, 1339, 1305, 1290, 1258, 1187, 1172, 1105, 1019; ^1H NMR (500 MHz, $CDCl_3$) δ 8.13 (d, 2H, *J* = 8.9 Hz), 7.95 (d, 2H, *J* = 8.3 Hz), 7.38−7.32 (m, 7H), 6.86 (d, 2H, *J* = 8.9 Hz), 4.87 (dd, 1H, *J* = 8.3, 6.6 Hz), 4.64 (dd, 1H, *J* = 10.3, 6.3 Hz), 4.12 (dd, 1H, *J* = 10.3, 8.3 Hz), 2.49 (s, 3H); $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$) δ 155.6, 153.9, 145.5, 144.3, 135.9, 134.3, 129.7, 129.5, 129.3, 129.2, 129.1, 128.8, 128.3, 127.5, 127.2, 127.1, 126.7, 125.1, 121.5, 57.1, 47.4, 21.9; HRMS (ESI-TOF) calcd for $C_{22}H_{20}N_3O_4S_2$ $(M + H)^+$ 454.0895, found 454.0891.

*(R,Z)-N-(4-Methoxyphenyl)-5-phenyl-3-tosylthiazolidin-2-imine ((R)-**3d**).*[2b] The general method A described above was followed when (*S*)-**1a** (50.0 mg, 0.183 mmol, 1.0 equiv) was reacted with 1-isothiocyanato-4-methoxybenzene **2d** to afford (*R*)-**3d** (75.4 mg, 0.172 mmol) as a thick liquid in 94% yield. $[\alpha]^{25}_D$ −14.2 (*c* 0.386 in $CHCl_3$) for a 20% ee sample. Optical purity was determined by chiral HPLC analysis (Chiralpak AS-H column), hexane−2-propanol, 80:20; flow rate =1.0 mL/min; t_R 1:28.28 min (major), t_R 2:52.22 min (minor): R_f 0.40 (ethyl acetate/petroleum ether, 1:4); IR $\tilde{\nu}_{max}$ (neat, cm^{-1}) 3032, 2927, 1639, 1597, 1504, 1454, 1400, 1359, 1289, 1242, 1186, 1168, 1136, 1101, 1032; ^1H NMR (500 MHz, $CDCl_3$) δ 7.97 (d, 2H, *J* = 8.6 Hz), 7.35−7.31 (m, 7H), 6.80−6.73 (m, 4H), 4.78 (dd, 1H, *J* = 8.6, 6.3 Hz), 4.57 (dd, 1H, *J* = 10.3, 6.3 Hz), 4.03 (dd, 1H, *J* = 10.3, 8.6 Hz), 3.75 (s, 3H), 2.47 (s, 3H); $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$) δ 156.6, 151.9, 144.9, 143.4, 136.6, 134.7, 129.9, 129.8, 129.3, 129.2, 129.1, 128.8, 128.7, 127.6, 127.1, 126.6, 121.9, 114.2, 56.7, 55.5, 47.0, 21.8; HRMS (ESI-TOF) calcd for $C_{23}H_{23}N_2O_3S_2$ $(M + H)^+$ 439.1150, found 439.1151.

*(R,Z)-N-Cyclohexyl-5-phenyl-3-tosylthiazolidin-2-imine ((R)-**3e**).*[2b] The general method A described above was followed when (*S*)-**1a** (50.0 mg, 0.183 mmol, 1.0 equiv) was reacted with isothiocyanatocyclohexane **2e** to afford (*R*)-**3e** (72.7 mg, 0.175 mmol) as a white solid in 96% yield: mp 134−136 °C; $[\alpha]^{25}_D$ − 0.52 (*c* 0.47 in $CHCl_3$) for a 63% ee sample. Optical purity was determined by chiral HPLC analysis (Chiralpak AS-H column), hexane−2-propanol, 90:10; flow rate = 1.0 mL/min; t_R 1:12.21 min (major), t_R 2:17.65 min (minor): R_f 0.65 (ethyl acetate/petroleum ether, 1:4); IR $\tilde{\nu}_{max}$ (KBr, cm^{-1}) 2927, 2852, 1654, 1597, 1493, 1450, 1361, 1286, 1170, 1099; ^1H NMR (500 MHz, $CDCl_3$) δ 7.90 (d, 2H, *J* = 10.3 Hz), 7.37−7.31 (m, 5H), 7.27 (d, 2H, *J* = 9.8 Hz), 4.74 (dd, 1H, *J* = 10.3, 7.4 Hz), 4.44 (dd, 1H, *J* = 13.2, 8.0 Hz), 3.85 (dd, 1H, *J* = 12.6, 10.3 Hz), 2.78−2.72 (m, 1H), 2.43 (s, 3H), 1.73−1.54 (m, 5H), 1.42−1.33 (m, 2H), 1.28−1.20 (m, 3H); $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$) δ 147.2, 144.4, 137.1, 134.9, 129.3, 129.1, 128.9, 128.7, 127.6, 65.4, 56.0, 46.9, 33.5, 33.3, 25.7, 24.4, 21.7; HRMS (ESI-TOF) calcd for $C_{22}H_{27}N_2O_2S_2$ $(M + H)^+$ 415.1514, found 415.1515.

*(R,Z)-N-Butyl-5-phenyl-3-tosylthiazolidin-2-imine ((R)-**3f**).*[2b] The general method A described above was followed when (*S*)-**1a** (50.0 mg, 0.183 mmol, 1.0 equiv) was reacted with 1-isothiocyanatobutane **2f** to afford (*R*)-**3f** (66.8 mg, 0.172 mmol) as a white solid in 94% yield. mp 84−86 °C; $[\alpha]^{25}_D$ −7.2 (*c* 0.538 in $CHCl_3$) for a 93% ee sample. Optical purity was determined by chiral HPLC analysis (cellulose-1 column), hexane−2-propanol, 90:10; flow rate =1.0 mL/min; t_R 1:10.47 min (major), t_R 2:12.32 min (minor): R_f 0.58 (ethyl acetate/petroleum ether, 1:4); IR $\tilde{\nu}_{max}$ (KBr, cm^{-1}) 2955, 2927, 2870, 1656, 1597, 1494, 1454, 1357, 1286, 1185, 1169, 1094; ^1H NMR (500 MHz, $CDCl_3$) δ 7.88 (d, 2H, *J* = 7.5 Hz), 7.36−7.33 (m, 5H), 7.29−7.25 (m, 2H), 4.78−4.75 (m, 1H), 4.47 (dd, 1H, *J* = 10.3, 6.3 Hz), 3.91−3.88 (m, 1H), 3.21−3.16 (m, 1H), 3.08−3.03 (m, 1H), 2.43 (s, 3H), 1.51−1.45 (m, 2H), 1.24−1.16 (m, 2H), 0.85 (t, 3H, *J* = 6.3 Hz); $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$) δ 144.5, 138.1, 135.1, 134.7, 129.1, 128.7, 127.7, 127.6, 126.3, 56.4, 56.0, 46.9, 32.8, 21.8, 20.4, 13.9; HRMS (ESI-TOF) calcd for $C_{20}H_{25}N_2O_2S_2$ $(M + H)^+$ 389.1357, found 389.1350.

*(S,Z)-N,5-Diphenyl-3-(phenylsulfonyl)thiazolidin-2-imine ((S)-**3g**).*[2b] The general method A described above was followed when (*R*)-**1b** (50.0 mg, 0.193 mmol, 1.0 equiv) was reacted with isothiocyanatobenzene **2a** to afford (*S*)-**3g** (73.0 mg, 0.185 mmol) as a thick liquid in 96% yield: $[\alpha]^{25}_D$ +36.7 (*c* 0.395 in $CHCl_3$) for an 80% ee sample. Optical purity was determined by chiral HPLC analysis (cellulose 2 column), hexane−2-propanol, 98:2; flow rate = 1.0 mL/min; t_R 1:71.21 min (major), t_R 2:78.44 min (minor): R_f 0.48 (ethyl acetate/petroleum ether, 1:4); IR $\tilde{\nu}_{max}$ (neat, cm^{-1}) 3062, 2924, 2853, 1723, 1643, 1591, 1487, 1447, 1361, 1288, 1248, 1170, 1135, 1101, 1024; ^1H NMR (500 MHz, $CDCl_3$) δ 8.08 (d, 2H, *J* = 8.6 Hz), 7.68 (t, 1H, *J* = 6.8 Hz), 7.56 (t, 2H, *J* = 7.3 Hz), 7.33−7.20 (m, 7H), 7.05 (t, 1H, *J* = 7.4 Hz), 6.75 (d, 2H, *J* = 8.6 Hz), 4.80 (t, 1H, *J* = 8.6 Hz), 4.61 (dd, 1H, *J* = 10.3, 7.3 Hz), 4.08 (t, 1H, *J* = 10.4 Hz); $^{13}C\{^1H\}$ NMR

DOI: 10.1021/acs.joc.6b01551
J. Org. Chem. 2016, 81, 6433−6443

(125 MHz, $CDCl_3$) δ 152.2, 150.0, 137.6, 136.4, 133.9, 129.2, 129.1, 129.0, 128.8, 128.7, 127.9, 127.5, 126.6, 124.4, 120.7, 56.9, 47.1; HRMS (ESI-TOF) calcd for $C_{21}H_{19}N_2O_2S_2$ $(M + H)^+$ 395.0888, found 395.0883.

*(S,Z)-3-((4-Fluorophenyl)sulfonyl)-N,5-diphenylthiazolidin-2-imine ((S)-**3h**).* The general method A described above was followed when (*R*)-**1c** (50.0 mg, 0.180 mmol, 1.0 equiv) was reacted with isothiocyanatobenzene **2a** to afford (*S*)-**3h** (72.8 mg, 0.176 mmol) as a white solid 98% yield): mp 142−144 °C; $[\alpha]^{25}_D$ +77.8 (*c* 0.528 in $CHCl_3$) for a > 99% ee sample. Optical purity was determined by chiral HPLC analysis (cellulose 2 column), hexane−2-propanol, 98:2; flow rate = 1.0 mL/min; t_R 1:14.14 min (minor), t_R 2:18.68 min (major): R_f 0.52 (ethyl acetate/petroleum ether, 1:4); IR $\tilde{\nu}_{max}$ (KBr, cm^{-1}) 3429, 3104, 3052, 2924, 2863, 1651, 1590, 1533, 1490, 1453, 1406, 1364, 1291, 1254, 1239, 1213, 1182, 1152, 1137, 1105, 1047, 1028, 1015; ^1H NMR (400 MHz, $CDCl_3$) δ 8.11−8.08 (m, 2H), 7.35−7.30 (m, 4H), 7.28−7.19 (m, 5H), 7.09−7.04 (m, 1H), 6.77−6.75 (m, 2H), 4.80 (dd, 1H, *J* = 8.3, 6.4 Hz), 4.59 (dd, 1H, *J* = 10.1, 6.4 Hz), 4.05 (dd, 1H, *J* = 10.1, 8.2 Hz); $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$) δ 166.0 (d, $^1J_{C-F}$ = 257.1 Hz), 152.2, 149.8, 136.4, 133.6, 132.2, 132.1, 129.2, 129.1, 128.9, 127.5, 124.6, 120.7, 116.0, 115.8, 56.8, 47.1; HRMS (ESI-TOF) calcd for $C_{21}H_{18}FN_2O_2S_2$ $(M + H)^+$ 413.0794, found 413.0797.

*(S,Z)-3-((4-Nitrophenyl)sulfonyl)-N,5-diphenylthiazolidin-2-imine ((S)-**3i**).* The general method A described above was followed when (*R*)-**1d** (50.0 mg, 0.164 mmol, 1.0 equiv) was reacted with isothiocyanatobenzene **2a** to afford (*S*)-**3i** (67.8 mg, 0.154 mmol) as a white solid in 94% yield: mp 124−126 °C; $[\alpha]^{25}_D$ +2.1 (*c* 0.33 in $CHCl_3$). R_f 0.50 (ethyl acetate/petroleum ether, 1:4); IR $\tilde{\nu}_{max}$ (KBr, cm^{-1}) 3105, 3064, 3032, 2884, 1643, 1606, 1592, 1530, 1487, 1454, 1402, 1349, 1313, 1289, 1248, 1176, 1134, 1104, 1013; ^1H NMR (500 MHz, $CDCl_3$) δ 8.41−8.37 (m, 2H), 8.29−8.26 (m, 2H), 7.41−7.32 (m, 5H), 7.31−7.25 (m, 2H), 7.13−7.07 (m, 1H), 6.81−6.72 (m, 2H), 4.85 (dd, 1H, *J* = 8.3, 6.3 Hz), 4.63 (dd, 1H, *J* = 10.6, 6.6 Hz), 4.09 (dd, 1H, *J* = 10.6, 8.6 Hz); $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$) δ 152.1, 150.8, 149.3, 143.4, 136.0, 130.6, 129.2, 129.1, 128.3, 127.5, 127.2, 124.9, 124.5, 123.8, 120.6, 56.7, 47.4; HRMS (ESI-TOF) calcd for $C_{21}H_{18}N_3O_4S_2$ $(M + H)^+$ 440.0739, found 440.0740.

*(S,Z)-3-((4-tert-Butylphenyl)sulfonyl)-N,5-diphenylthiazolidin-2-imine ((S)-**3j**).* The general method A described above was followed when (*R*)-**1e** (50.0 mg, 0.158 mmol, 1.0 equiv) was reacted with isothiocyanatobenzene **2a** to afford (*S*)-**3j** (69.2 mg, 0.153 mmol) as a white solid in 97% yield: mp 100−102 °C; $[\alpha]^{25}_D$ +65.1 (*c* 0.465 in $CHCl_3$) for an 86% ee sample. Optical purity was determined by chiral HPLC analysis (Chiralcel OD-H column), hexane−2-propanol, 95:5; flow rate = 1.0 mL/min; t_R 1:15.79 min (minor), t_R 2:19.82 min (major): R_f 0.55 (ethyl acetate/petroleum ether, 1:4); IR $\tilde{\nu}_{max}$ (KBr, cm^{-1}) 3061, 2963, 1643, 1592, 1488, 1463, 1399, 1363, 1289, 1249, 1197, 1173, 1136, 1112, 1101, 1085, 1024; ^1H NMR (500 MHz, $CDCl_3$) δ 8.00 (d, 2H, *J* = 8.6 Hz), 7.56−7.54 (m, 2H), 7.36−7.30 (m, 5H), 7.26−7.23 (m, 2H), 7.07−7.03 (m, 1H), 6.74 (d, 2H, *J* = 8.6 Hz), 4.80 (dd, 1H, *J* = 8.5, 7.0 Hz), 4.61 (dd, 1H, *J* = 10.4, 6.7 Hz), 4.07 (dd, 1H, *J* = 10.3, 8.6 Hz), 1.38 (s, 9H); $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$) δ 157.9, 152.3, 150.1, 136.4, 134.6, 129.1, 129.0, 128.8, 127.6, 125.7, 124.4, 120.8, 56.8, 47.1, 35.4, 31.2; HRMS (ESI-TOF) calcd for $C_{25}H_{27}N_2O_2S_2$ $(M + H)^+$ 451.1514, found 451.1510.

*(S,Z)-3-(Mesitylsulfonyl)-N,5-diphenylthiazolidin-2-imine ((S)-**3k**).* The general method A described above was followed when (*R*)-**1f** (50.0 mg, 0.165 mmol, 1.0 equiv) was reacted with isothiocyanatobenzene **2a** to afford (*S*)-**3k** (68.8 mg, 0.157 mmol) as a white solid in 95% yield: mp 128−130 °C; $[\alpha]^{25}_D$ +55.6 (*c* 0.486 in $CHCl_3$) for a 76% ee sample. Optical purity was determined by chiral HPLC analysis (cellulose 2 column), hexane−2-propanol, 90:10; flow rate = 1.0 mL/min; t_R 1:8.11 min (minor), t_R 2:10.34 min (major): R_f 0.63 (ethyl acetate/petroleum ether, 1:4); IR $\tilde{\nu}_{max}$ (KBr, cm^{-1}) 3030, 2939, 1644, 1592, 1488, 1455, 1342, 1188, 1164, 1098; ^1H NMR (500 MHz, $CDCl_3$) δ 7.44−7.35 (m, 5H), 7.21 (t, 2H, *J* = 7.3 Hz), 7.02 (t, 1H, *J* = 7.3 Hz), 6.95 (s, 2H), 6.68 (d, 2H, *J* = 8.3 Hz), 4.85 (dd, 1H, *J* = 9.2, 6.7 Hz), 4.67 (dd, 1H, *J* = 11.0, 6.7 Hz), 4.23 (t, 1H, *J* = 9.8 Hz), 2.65 (s, 6H), 2.32 (s, 3H); $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$) δ 151.6, 149.6, 143.3, 141.0, 136.3, 133.3, 131.8, 129.2, 128.9, 127.8, 127.4, 124.2, 120.9, 55.4, 47.5, 22.8, 21.2; HRMS (ESI-TOF) calcd for $C_{24}H_{25}N_2O_2S_2$ $(M + H)^+$ 437.1357, found 437.1351.

*(Z)-N-Phenyl-5-(p-tolyl)-3-tosylthiazolidin-2-imine (**3l**).*[2c] The general method B described above was followed when **1g** (50.0 mg, 0.174 mmol, 1.0 equiv) was reacted with isothiocyanatobenzene **2a** (63 μL, 0.522 mmol, 3.0 equiv) to afford **3l** (72.0 mg, 0.170 mmol) as a white solid in 98% yield: mp 106−108 °C; R_f 0.52 (EtOAc/petroleum ether, 1:4); IR $\tilde{\nu}_{max}$ (KBr, cm^{-1}) 3023, 2922, 2863, 1719, 1651, 1593, 1512, 1489, 1458, 1380, 1355, 1302, 1288, 1252, 1213, 1186, 1167, 1136, 1100, 1043, 1018; ^1H NMR (500 MHz, $CDCl_3$) δ 7.98 (d, 2H, *J* = 8.3 Hz), 7.35 (d, 2H, *J* = 8.2 Hz), 7.28−7.21 (m, 4H), 7.13 (d, 2H, *J* = 7.9 Hz), 7.08−7.04 (m, 1H), 6.78 (d, 2H, *J* = 7.4 Hz), 4.77 (dd, 1H, *J* = 8.6, 6.5 Hz), 4.57 (dd, 1H, *J* = 10.4, 6.4 Hz), 4.01 (dd, 1H, *J* = 10.4, 8.9 Hz), 2.48 (s, 3H), 2.33 (s, 3H); $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$) δ 152.4, 150.1, 144.9, 138.8, 134.7, 133.4, 129.8, 129.6, 129.34, 129.32, 129.27, 129.25, 129.0, 127.5, 126.9, 124.4, 120.9, 56.9, 46.9, 21.8, 21.2; HRMS (ESI-TOF) calcd for $C_{23}H_{23}N_2O_2S_2$ $(M + H)^+$ 423.1201, found 423.1200.

*(Z)-5-(4-tert-Butylphenyl)-N-phenyl-3-tosylthiazolidin-2-imine (**3m**).* The general method B described above was followed when **1h** (50.0 mg, 0.152 mmol, 1.0 equiv) was reacted with isothiocyanatobenzene **2a** (55 μL, 0.455 mmol, 3.0 equiv) to afford **3m** (67.0 mg, 0.144 mmol) as a white solid in 95% yield: mp 108−110 °C; R_f 0.51 (EtOAc/petroleum ether, 1:4); IR $\tilde{\nu}_{max}$ (KBr, cm^{-1}) 3024, 2964, 1723, 1651, 1592, 1512, 1491, 1463, 1391, 1365, 1289, 1249, 1215, 1191, 1167, 1137, 1102, 1047, 1021; ^1H NMR (500 MHz, $CDCl_3$) δ 7.98 (d, 2H, *J* = 8.6 Hz), 7.41−7.30 (m, 5H), 7.28−7.24 (m, 3H), 7.06 (t, 1H, *J* = 7.5 Hz), 6.79 (d, 2H, *J* = 7.4 Hz), 4.78 (dd, 1H, *J* = 8.6, 6.3 Hz), 4.58 (dd, 1H, *J* = 10.3, 6.3 Hz), 4.05 (dd, 1H, *J* = 9.8, 8.6 Hz), 2.48 (s, 3H), 1.30 (s, 9H); $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$) δ 152.4, 151.9, 150.1, 144.9, 134.7, 133.4, 129.3, 129.2, 129.0, 127.3, 126.0, 125.8, 125.7, 124.3, 120.8, 56.9, 46.8, 34.7, 31.3, 21.8; HRMS (ESI-TOF) calcd for $C_{26}H_{29}N_2O_2S_2$ $(M + H)^+$ 465.1670, found 465.1673.

*(Z)-5-(4-Chlorophenyl)-N-phenyl-3-tosylthiazolidin-2-imine (**3n**).* The general method B described above was followed when **1i** (50.0 mg, 0.162 mmol, 1.0 equiv) was reacted with isothiocyanatobenzene **2a** (59 μL, 0.487 mmol, 3.0 equiv) to afford **3n** (69.0 mg, 0.155 mmol) as a white solid in 96% yield: mp 90−92 °C; R_f 0.33 (EtOAc/petroleum ether, 1:4); IR $\tilde{\nu}_{max}$ (KBr, cm^{-1}) 3060, 2924, 1717, 1643, 1592, 1576, 1486, 1478, 1448, 1432, 1400, 1360, 1305, 1279, 1250, 1186, 1171, 1137, 1102, 1024; ^1H NMR (500 MHz, $CDCl_3$) δ 7.96 (d, 2H, *J* = 8.6 Hz), 7.35 (d, 2H, *J* = 8.0 Hz), 7.31−7.21 (m, 6H), 7.07 (t, 1H, *J* = 7.7 Hz), 6.79−6.76 (m, 2H), 4.73 (dd, 1H, *J* = 7.6, 6.4 Hz), 4.58 (dd, 1H, *J* = 10.4, 6.4 Hz), 4.04 (dd, 1H, *J* = 10.4, 7.9 Hz), 2.47 (s, 3H); $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$) δ 151.6, 150.0, 145.1, 138.9, 135.0, 134.5, 130.4, 129.3, 129.1, 129.0, 127.7, 125.8, 124.5, 120.7, 56.6, 46.3, 21.8; HRMS (ESI-TOF) calcd for $C_{22}H_{20}ClN_2O_2S_2$ $(M + H)^+$ 443.0655, found 443.0651.

*(Z)-5-(4-Bromophenyl)-N-phenyl-3-tosylthiazolidin-2-imine (**3o**).*[2c] The general method B described above was followed when **1j** (50.0 mg, 0.142 mmol, 1.0 equiv) was reacted with isothiocyanatobenzene **2a** (51 μL, 0.426 mmol, 3.0 equiv) to afford **3o** (65.7 mg, 0.134 mmol) as a white solid in 95% yield: mp 120−122 °C; R_f 0.44 (EtOAc/petroleum ether, 1:4); IR $\tilde{\nu}_{max}$ (KBr, cm^{-1}) 3024, 2923, 2867, 1720, 1653, 1594, 1489, 1457, 1404, 1380, 1353, 1292, 1279, 1251, 1212, 1186, 1165, 1139, 1095, 1072, 1041, 1010; ^1H NMR (400 MHz, $CDCl_3$) δ 7.95 (d, 2H, *J* = 8.2 Hz), 7.45−7.42 (m, 2H), 7.33 (d, 2H, *J* = 8.4 Hz), 7.26−7.19 (m, 4H), 7.07−7.03 (m, 1H), 6.77−6.75 (m, 2H), 4.71 (dd, 1H, *J* = 7.8, 6.4 Hz), 4.54 (dd, 1H, *J* = 10.5, 6.4 Hz), 4.03 (dd, 1H, *J* = 10.5, 8.2 Hz), 2.47 (s, 3H); $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$) δ 151.7, 150.0, 145.1, 135.9, 134.6, 132.2, 129.4, 129.3, 129.2, 129.1, 124.5, 122.8, 120.8, 56.7, 46.3, 21.8; HRMS (ESI-TOF) calcd for $C_{22}H_{20}BrN_2O_2S_2$ $(M + H)^+$ 487.0150, found 487.0153.

*(Z)-5-(2-Fluorophenyl)-N-phenyl-3-tosylthiazolidin-2-imine (**3p**).* The general method B described above was followed when **1k** (50.0 mg, 0.172 mmol, 1.0 equiv) was reacted with isothiocyanatobenzene **2a** (62 μL, 0.515 mmol, 3.0 equiv) to afford **3p** (67.3 mg, 0.157 mmol) as a white solid in 92% yield: mp 94−96 °C; R_f 0.44 (EtOAc/petroleum ether, 1:4); IR $\tilde{\nu}_{max}$ (KBr, cm^{-1}) 1643, 1592, 1489, 1456,

DOI: 10.1021/acs.joc.6b01551
J. Org. Chem. 2016, 81, 6433−6443

1364, 1291, 1232, 1187, 1171, 1137, 1104, 1092, 1019; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.96 (d, 2H, J = 8.3 Hz), 7.45 (t, 1H, J = 7.6 Hz), 7.38−7.23 (m, 5H), 7.16−7.03 (m, 3H), 6.78 (d, 2H), 5.06 (t, 1H, J = 6.4 Hz), 4.53 (dd, 1H, J = 10.7, 6.4 Hz), 4.22 (dd, 1H, J = 10.7, 6.4 Hz), 2.48 (s, 3H); ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) δ 160.3 (d, $^1J_{C-F}$ = 248.7 Hz), 151.9, 150.1, 145.1, 134.6, 130.3, 129.2, 129.1, 128.4, 128.3, 124.9, 124.8, 124.7, 124.6, 124.5, 120.8, 115.9, 115.7, 55.6, 39.3, 21.9; HRMS (ESI-TOF) calcd for $C_{22}H_{20}FN_2O_2S_2$ (M + H)$^+$ 427.0950, found 427.0952.

*(Z)-5-(3-Fluorophenyl)-N-phenyl-3-tosylthiazolidin-2-imine (**3q**).* The general method B described above was followed when **1l** (50.0 mg, 0.172 mmol, 1.0 equiv) was reacted with isothiocyanatobenzene **2a** (62 μL, 0.515 mmol, 3.0 equiv) to afford **3q** (68.8 mg, 0.161 mmol) as a white solid in 94% yield: mp 88−90 °C; R_f 0.44 (EtOAc/petroleum ether, 1:4); IR $\tilde{\nu}_{max}$ (KBr, cm^{-1}) 3426, 2923, 2863, 1721, 1647, 1614, 1591, 1488, 1462, 1449, 1356, 1303, 1282, 1261, 1222, 1208, 1187, 1169, 1134, 1101, 1046, 1018; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.97 (d, 2H, J = 8.3 Hz), 7.35 (d, 2H, J = 7.9 Hz), 7.32−7.25 (m, 3H), 7.13−6.99 (m, 4H), 6.78 (d, 2H), 4.76 (t, 1H, J = 7.1 Hz), 4.59−4.56 (m, 1H), 4.05 (dd, 1H, J = 10.4, 7.6 Hz), 2.48 (s, 3H); ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) δ 162.9 (d, $^1J_{C-F}$ = 247.5 Hz), 151.7, 150.0, 145.1, 139.4, 134.5, 130.7, 129.3, 129.2, 129.1, 127.1, 124.5, 123.3, 120.8, 115.9, 115.7, 114.7, 114.5, 56.7, 46.3, 21.8; HRMS (ESI-TOF) calcd for $C_{22}H_{20}FN_2O_2S_2$ (M + H)$^+$ 427.0950, found 427.0954.

*(Z)-5-(2-Chlorophenyl)-N-phenyl-3-tosylthiazolidin-2-imine (**3r**).* The general method B described above was followed when **1m** (50.0 mg, 0.162 mmol, 1.0 equiv) was reacted with isothiocyanatobenzene **2a** (58 μL, 0.487 mmol, 3.0 equiv) to afford **3r** (64.7 mg, 0.146 mmol) as a white solid in 90% yield: mp 134−136 °C; R_f 0.44 (EtOAc/petroleum ether, 1:4); IR $\tilde{\nu}_{max}$ (KBr, cm^{-1}) 3284, 2920, 2859, 2118, 1597, 1411, 1328, 1159, 1086; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.99 (d, 2H, J = 8.3 Hz), 7.36−7.31 (m, 7H), 7.28−7.25 (m, 1H), 7.07 (t, 1H, J = 7.4 Hz), 6.79 (d, 2H, J = 7.7 Hz), 4.79 (dd, 1H, J = 8.3, 6.5 Hz), 4.61−4.58 (m, 1H), 4.06 (dd, 1H, J = 10.4, 8.9 Hz), 2.48 (s, 3H); ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) δ 152.3, 150.1, 145.0, 136.6, 134.7, 129.4, 129.3, 129.2, 129.1, 128.9, 127.6, 124.4, 120.9, 56.9, 47.0, 21.9; HRMS (ESI-TOF) calcd for $C_{22}H_{20}ClN_2O_2S_2$ (M + H)$^+$ 443.0655, found 443.0651.

*(Z)-5-(3-Chlorophenyl)-N-phenyl-3-tosylthiazolidin-2-imine (**3s**).*[2c] The general method B described above was followed when **1n** (50.0 mg, 0.162 mmol, 1.0 equiv) was reacted with isothiocyanatobenzene **2a** (58 μL, 0.487 mmol, 3.0 equiv) to afford **3s** (66.2 mg, 0.149 mmol) as a gummy liquid in 92% yield: R_f 0.44 (EtOAc/petroleum ether, 1:4); IR $\tilde{\nu}_{max}$ (neat, cm^{-1}) 3059, 2924, 1643, 1592, 1486, 1432, 1360, 1279, 1186, 1171, 1137, 1102, 1024; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.96 (d, 2H, J = 8.6 Hz), 7.35 (d, 2H, J = 7.9 Hz), 7.32−7.21 (m, 6H), 7.07 (t, 1H, J = 7.3 Hz), 6.77 (d, 2H, J = 7.3 Hz), 4.73 (dd, 1H, J = 7.9, 6.1 Hz), 4.58 (dd, 1H, J = 10.4, 6.7 Hz), 4.04 (dd, 1H, J = 10.4, 7.9 Hz), 2.48 (s, 3H); ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) δ 151.6, 150.0, 145.1, 138.9, 135.0, 134.5, 130.4, 129.3, 129.2, 129.1, 129.0, 127.7, 125.8, 124.5, 120.8, 56.6, 46.3, 21.8; HRMS (ESI-TOF) calcd for $C_{22}H_{20}ClN_2O_2S_2$ (M + H)$^+$ 443.0655, found 443.0654.

*(4S,5R,Z)-N,5-Diphenyl-4-propyl-3-tosylthiazolidin-2-imine (**3t**).* The general method C described above was followed when (*S,S*)-**1o** (50.0 mg, 0.166 mmol, 1.0 equiv) was reacted with isothiocyanatobenzene **2a** to afford (*S,R,Z*)-**3t** (63.7 mg, 0.146 mmol) as a gummy liquid in 88% yield: $[\alpha]^{25}_D$ +57.1 (*c* 0.26 in $CHCl_3$); R_f 0.42 (EtOAc/petroleum ether, 1:4); IR $\tilde{\nu}_{max}$ (neat, cm^{-1}) 3060, 2960, 2925, 2872, 1640, 1592, 1488, 1451, 1351, 1242, 1186, 1168, 1143, 1104, 1086; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.02 (d, 2H, J = 8.6 Hz), 7.36 (d, 2H, J = 7.9 Hz), 7.34−7.30 (m, 4H), 7.27−7.24 (m, 3H), 7.08−7.05 (m, 1H), 6.73 (dd, 2H, J = 8.6, 1.2 Hz), 5.10 (d, 1H, J = 6.1 Hz), 4.96−4.92 (m, 1H), 2.47 (s, 3H), 1.75−1.67 (m, 1H), 1.51−1.46 (m, 1H), 1.40−1.34 (m, 1H), 1.15−1.09 (m, 1H), 0.79 (t, 3H, J = 7.3 Hz); ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) δ 152.4, 150.3, 144.7, 136.4, 133.4, 129.3, 129.2, 129.0, 128.9, 128.6, 128.4, 124.4, 120.7, 65.9, 54.3, 31.6, 21.8, 19.3, 13.9; HRMS (ESI-TOF) calcd for $C_{25}H_{27}N_2O_2S_2$ (M + H)$^+$ 451.1514, found 451.1514.

*(4S,5R,Z)-4-Allyl-N,5-diphenyl-3-tosylthiazolidin-2-imine (**3u**).* The general method C described above was followed when (*S,S*)-**1p** (50.0 mg, 0.167 mmol, 1.0 equiv) was reacted with isothiocyanatobenzene **2a** to afford (*S,R,Z*)-**3u** (65.3 mg, 0.150 mmol) as a gummy liquid in 90% yield: $[\alpha]^{25}_D$ + 117.3 (*c* 0.475 in $CHCl_3$); R_f 0.44 (EtOAc/petroleum ether, 1:4); IR $\tilde{\nu}_{max}$ (neat, cm^{-1}) 3064, 2922, 2851, 1737, 1642, 1594, 1495, 1451, 1405, 1327, 1305, 1291, 1239, 1185, 1162, 1091; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.88 (d, 2H, J = 8.0 Hz), 7.35−7.31 (m, 4H), 7.27−7.21 (m, 7H), 6.75 (d, 1H, J = 8.0 Hz), 5.58−5.47 (m, 1H), 4.96−4.89 (m, 2H), 3.99 (d, 1H, J = 7.5 Hz), 3.12−3.08 (m, 1H), 2.43 (s, 3H), 2.03−1.91 (m, 2H); ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) δ 144.6, 135.0, 133.2, 132.9, 132.6, 129.7, 129.3, 129.2, 129.0, 128.9, 128.7, 128.4, 128.3, 128.1, 127.9, 127.6, 124.4, 120.8, 118.7, 117.4, 65.7, 53.7, 34.4, 21.8; HRMS (ESI-TOF) calcd for $C_{25}H_{25}N_2O_2S_2$ (M + H)$^+$ 449.1357, found 449.1358.

*(Z)-4-(((tert-Butyldimethylsilyl)oxy)methyl)-N,5-diphenyl-3-tosylthiazolidin-2-imine (**3v**).* The general method C described above was followed when **1q** (50.0 mg, 0.119 mmol, 1.0 equiv) was reacted with isothiocyanatobenzene **2a** to afford (*Z*)-**3v** (62.2 mg, 0.112 mmol) as a gummy liquid in 94% yield: R_f 0.44 (EtOAc/petroleum ether, 1:4); IR $\tilde{\nu}_{max}$ (neat, cm^{-1}) 3061, 3031, 2953, 2926, 2854, 2138, 1725, 1642, 1593, 1543, 1489, 1470, 1463, 1452, 1389, 1359, 1325, 1306, 1254, 1212, 1185, 1170, 1125, 1100, 1064, 1029, 1004; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.05 (d, 2H, J = 8.0 Hz), 7.43−7.41 (m, 2H), 7.33−7.30 (m, 5H), 7.26−7.23 (m, 2H), 7.06−7.03 (m, 1H), 6.77 (d, 2H, J = 8.0 Hz), 5.19 (d, 1H, J = 6.8 Hz), 4.94−4.90 (m, 1H), 3.87 (dd, 1H, J = 11.5, 4.6 Hz), 3.56−3.53 (m, 1H), 2.45 (s, 3H), 0.79 (s, 9H), − 0.08 (s, 6H); ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) δ 152.9, 152.6, 150.2, 144.4, 136.7, 133.2, 129.6, 129.2, 128.9, 128.8, 128.7, 128.6, 127.2, 125.6, 124.2, 124.1, 120.9, 65.9. 61.6, 51.5, 25.8, 21.7, 18.1, −5.7; HRMS (ESI-TOF) calcd for $C_{29}H_{37}N_2O_3S_2Si$ (M + H)$^+$ 553.2015, found 553.2010.

*(4S,5R,Z)-4-(((tert-Butyldimethylsilyl)oxy)methyl)-N-(4-methoxyphenyl)-5-phenyl-3-tosylthiazolidin-2-imine (**3w**).* The general method C described above was followed when **1q** (50.0 mg, 0.119 mmol, 1.0 equiv) was reacted with 1-isothiocyanato-4-methoxybenzene **2d** to afford **3w** (63.5 mg, 0.108 mmol) as a dense colorless liquid in 91% yield: R_f 0.40 (EtOAc/petroleum ether, 1:4); IR $\tilde{\nu}_{max}$ (neat, cm^{-1}) 2927, 2854, 1641, 1504, 1463, 1358, 1290, 1241, 1168, 1100, 1064, 1033; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.04 (d, 2H, J = 8.1 Hz), 7.45−7.41 (m, 2H), 7.34−7.29 (m, 5H), 6.82−6.78 (m, 2H), 6.76−6.72 (m, 2H), 5.17 (d, 1H, J = 7.5 Hz), 4.92−4.87 (m, 1H), 3.86 (dd, 1H, J = 11.5, 4.6 Hz), 3.76 (s, 3H), 3.54 (dd, 1H, J = 10.9, 2.9 Hz), 2.45 (s, 3H), 0.78 (s, 9H), − 0.10 (s, 6H); ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) δ 156.4, 144.4, 143.6, 136.7, 133.3, 129.2, 128.8, 128.7, 128.6, 122.0, 114.1, 65.7, 61.6, 55.5, 51.5, 25.8, 21.8, 18.1, −5.7; HRMS (ESI-TOF) calcd for $C_{30}H_{39}N_2O_4S_2Si$ (M + H)$^+$ 583.2121, found 583.2121.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.6b01551.

NMR spectra for all the compounds; HPLC chromatograms for ee determination (PDF)

X-ray crystallographic data of **3b** (CCDC 1000585) (CIF)

X-ray crystallographic data of **3j** (CCDC 1000586) (CIF)

■ AUTHOR INFORMATION

Corresponding Author

*Fax: (+91)-512-2597436. Phone: (+91)-512-2597518. E-mail: mkghorai@iitk.ac.in.

Notes

The authors declare no competing financial interest.

DOI: 10.1021/acs.joc.6b01551
J. Org. Chem. 2016, 81, 6433−6443

■ ACKNOWLEDGMENTS

A.B. thanks CSIR, India, for a research fellowship. M.K.G. is grateful to IIT-Kanpur and CSIR, India.

■ DEDICATION

Dedicated to Professor Ganesh Pandey on the occasion of his 62nd Birthday.

■ REFERENCES

(1) (a) Dixon, B. R.; Bagi, C. M.; Brennan, C. R.; Brittelli, D. R.; Bullock, W. H.; Chen, J.; Collibee, W. L.; Dally, R.; Johnson, J. S.; Kluender, H. C. E. Substituted 2-Arylimino Heterocycles and Compositions Containing Them, for Use as Progesterone Receptor Binding Agents. U.S. Patent 6,353,006, Mar 5, 2002. (b) Takagi, M.; Ishimitsu, K.; Nishibe, T. Oxa(thia)zolidine Derivative and Anti-Inflammatory Drug. U.S. Patent 6,762,200, Jul 13, 2004. (c) Shukla, U. K.; Singh, R.; Khanna, J. M.; Saxena, A. K.; Singh, H. K.; Sur, R. N.; Dhawan, B. N.; Anand, N. *Collect. Czech. Chem. Commun.* **1992**, *57*, 415. (d) Gyertyan, I.; Petocz, L.; Gacsalyi, I.; Fekete, M. I. K.; Tekes, K.; Kapolnai, L. *Drug Dev. Res.* **1991**, *22*, 385. (e) Hosseinimehr, S. J.; Shafiee, A.; Mozdarani, H.; Akhlagpour, S. *J. Radiat. Res.* **2001**, *42*, 401. (f) Hosseinimehr, S. J.; Shafiee, A.; Mozdarani, H.; Akhlagpour, S.; Froughizadeh, M. *J. Radiat. Res.* **2002**, *43*, 293. (g) Wakita, T.; Kinoshita, K.; Yamada, E.; Yasui, N.; Kawahara, N.; Naoi, A.; Nakaya, M.; Ebihara, K.; Matsuno, H.; Kodaka, K. *Pest Manage. Sci.* **2003**, *59*, 1016.

(2) (a) Ferreira, M.; Sá, M. M. *Adv. Synth. Catal.* **2015**, *357*, 829 and references cited therein. (b) Sengoden, M.; Punniyamurthy, T. *Angew. Chem., Int. Ed.* **2013**, *52*, 572. (c) Wu, J.-Y.; Luo, Z.-B.; Dai, L.-X.; Hou, X.-L. *J. Org. Chem.* **2008**, *73*, 9137. (d) Baeg, J.-O.; Bensimon, C.; Alper, H. *J. Am. Chem. Soc.* **1995**, *117*, 4700.

(3) D'hooghe, M.; De Kimpe, N. *Tetrahedron* **2006**, *62*, 513 and references cited therein.

(4) (a) Craig, R. A., II; O'Connor, N. R.; Goldberg, A. F. G.; Stoltz, B. M. *Chem. - Eur. J.* **2014**, *20*, 4806 and references cited therein. (b) Gao, L.; Fu, K.; Zheng, G. *RSC Adv.* **2016**, *6*, 47192 and references cited therein. (c) Nadir, U. K. J.; Susan. *Indian J. Chem., Sect B* **2003**, *42B*, 1531. (d) Zhou, H.-B.; Dong, C.; Alper, H. *Chem. - Eur. J.* **2004**, *10*, 6058.

(5) (a) Ghorai, M.; Bhattacharyya, A.; Das, S.; Chauhan, N. *Top. Heterocycl. Chem.* **2015**, *41*, 49 and references cited therein. (b) Ghorai, M. K.; Shahi, C. K.; Bhattacharyya, A.; Sayyad, M.; Mal, A.; Wani, I. A.; Chauhan, N. *Asian J. Org. Chem.* **2015**, *4*, 1103 and references cited therein. (c) Dolfen, J.; De Kimpe, N.; D'hooghe, M. *Synlett* **2016**, *27*, 1486. (d) Takeda, Y.; Kuroda, A.; Sameera, W. M. C.; Morokuma, K.; Minakata, S. *Chem. Sci.* **2016**, DOI: 10.1039/C6SC01120A. (e) Takeda, Y.; Ikeda, Y.; Kuroda, A.; Tanaka, S.; Minakata, S. *J. Am. Chem. Soc.* **2014**, *136*, 8544. (f) Callebaut, G.; Meiresonne, T.; De Kimpe, N.; Mangelinckx, S. *Chem. Rev.* **2014**, *114*, 7954 and references cited therein. (g) Schneider, C. *Angew. Chem., Int. Ed.* **2009**, *48*, 2082.

(6) (a) Sayyad, M.; Nanaji, Y.; Ghorai, M. K. *J. Org. Chem.* **2015**, *80*, 12659. (b) Ghorai, M. K.; Sahoo, A. K.; Bhattacharyya, A. *J. Org. Chem.* **2014**, *79*, 6468. (c) Ghorai, M. K.; Tiwari, D. P. *J. Org. Chem.* **2010**, *75*, 6173. (d) Ghorai, M. K.; Tiwari, D. P. *J. Org. Chem.* **2013**, *78*, 2617. (e) Ghorai, M. K.; Shukla, D.; Bhattacharyya, A. *J. Org. Chem.* **2012**, *77*, 3740. (f) Ghorai, M. K.; Kumar, A.; Tiwari, D. P. *J. Org. Chem.* **2010**, *75*, 137. (g) Ghorai, M. K.; Talukdar, R.; Tiwari, D. P. *Chem. Commun.* **2013**, *49*, 8205. (h) Talukdar, R.; Tiwari, D. P.; Saha, A.; Ghorai, M. K. *Org. Lett.* **2014**, *16*, 3954.

(7) Goldberg, A. F. G.; O'Connor, N. R.; Craig, R. A.; Stoltz, B. M. *Org. Lett.* **2012**, *14*, 5314.

(8) See the Supporting Information for details.

(9) Armarego, W. L. F.; Chai, C. *Purification of Laboratory Chemicals*, 7th ed.; Butterworth-Heinemann: Oxford, 2012.

(10) Cernerud, M.; Adolfsson, H.; Moberg, C. *Tetrahedron: Asymmetry* **1997**, *8*, 2655.

DOI: 10.1021/acs.joc.6b01551
J. Org. Chem. 2016, 81, 6433−6443