

Telluronium Salts Mediated Aziridination of Chiral *N*-*tert*-Butylsulfinylimines: Highly Stereoselective Synthesis of Optically Active Vinylaziridines

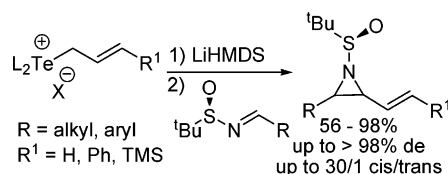
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Received August 9, 2005

ABSTRACT



Optically active *cis*-2-substituted vinylaziridines are synthesized by the reaction of *N*-*tert*-butylsulfinylimines with telluronium ylides with excellent diastereoselectivity in good to excellent yields.

Vinylaziridines are important subunits in a number of biologically active compounds¹ and versatile intermediates for the synthesis of nitrogen-containing compounds, such as alkaloids, amino acids, amino alcohols, and β -lactamic antibiotics.² Although carbene^{3,4} and nitrene⁴ approaches are recognized as two of the most efficient methods for the

preparation of aziridines, they are generally less effective for vinyl-type aziridines due to the difficulty associated with the regioselectivity control. Darzens-type reaction is also well-documented to prepare aziridines,⁵ but few direct synthesis involved vinylaziridines in the literature. Of the synthetic methods developed for vinylaziridines, the reaction between ylide and imines proved to be one of the most convenient ways.⁶ By an ylide approach, to access optically active vinylaziridines, Aggarwal et al. reported that silylated chiral sulfur allylide could react with *N*-SES phenylimine to afford *trans*-phenylvinylaziridine in 94% ee with moderate

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cis/trans selectivity (*cis/trans* = 22/78),^{7a} and Saito et al. also described the synthesis of nonracemic chiral vinylaziridines via a chiral ylide route, but the enantioselectivity was poor (enantiomeric excess up to 42%).^{7b} Very recently, Stockman et al. documented the reaction of *tert*-butylsulfynylimines⁸ with sulfur ylide and found that the desired optically active vinylaziridines could be obtained with high diastereoselectivity (85–95% de, *cis/trans* up to 1/4.8, *trans* favored) in moderate to good yield (44–82%).⁹ As described above, although the reaction of imines with ylide provided a good access to vinylaziridines, the stereoselectivity, in particular, the *cis/trans* selectivity, is generally not good.^{6,7,9} Furthermore, few reports appeared in the literature on the preparation of optically active *cis*-disubstituted aziridines via an ylide route.¹⁰ In this paper, we wish to report a highly efficient protocol for the synthesis of optically active 2-substituted vinylaziridines with high *cis*-selectivity and excellent diastereoselectivity via telluronium allylides.

In a previous study on ylide chemistry,¹¹ we found that the nature of ylide influenced the stereochemistry in ylide cyclopropanation.¹² Considering that the match of ylide and substrate is very important for achieving good stereoselectivity in ylide reaction,^{6–12} we tried the aziridination of telluronium allylide with chiral *N-tert*-butylsulfynylimines.¹³ Fortunately, it was found that this reaction proceeded well to give the desired *cis*-2-substituted vinylaziridines. As shown in Table 1, telluronium salt **1a**, after deprotonation by LDA, reacted with enantiopure imine **2a** at –78 °C in THF to afford the desired aziridine with high *cis*-selectivity and excellent diastereoselectivity (>99/1) in 55% yield (entry 1). The yield was improved to good when NaHMDS or KHMDS was used as a base instead of LDA (entries 3 and 4), however, the stereoselectivity deteriorated greatly. In our

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Table 1. Effects of Base, Solvent, and Telluronium Salt on the Aziridination of *tert*-Butylsulfynylimines (ref 14)^a

entry	solvent	base	yield (%) ^b	<i>cis/trans</i> ^c	de (%) ^c
1	THF	LDA	55	20/1	>98
2	THF	^t BuOK	trace		
3	THF	NaHMDS	85	2.5/1	78
4	THF	KHMDS	85	1/2.5	5
5	THF	LiTMP	55	6/1	95
6	THF	LiHMDS	83	17/1	97
7	PhMe	LiHMDS	84	16/1	97
8 ^d	PhMe	LiHMDS	82	1/4	9

^a **2a**/1/base = 1.0/1.5/1.5. ^b Isolated yield. ^c Determined by ¹H NMR, and de was assigned for the *cis*-isomer. ^d **1b** was used instead of **1a**.

screened conditions, the best base was LiHMDS. In this case, the desired product was obtained in good yield (83%) with a good *cis/trans* ratio and excellent diastereoselectivity. Toluene as a solvent instead of THF also gave the similar yield and stereoselectivity (entry 7). The anion of the telluronium salt was also found to influence both the yield and stereoselectivity. Tetraphenylborate decreased the yield as well as the diastereoselectivity greatly under the same conditions (entry 8, Table 1).

Additives also proved to influence the aziridination. As shown in Table 2, the addition of TMEDA or HMPA

Table 2. Effects of Addition Sequence and Additives on the Aziridination of *tert*-Butylsulfynylimines¹⁴

entry	additive	sequence ^a	yield (%) ^b	<i>cis/trans</i> ^c	de (%) ^c
1 ^d	TMEDA ^e	A	57	12/1	95
2 ^d	HMPA ^e	A	52	1/2.6	56
3 ^d	LiBr ^f	A	68	20/1	>98
4 ^d	LiBr ^f	B	75	20/1	>98
5 ^g	MgBr ₂ ^f	B	85	20/1	>98
6 ^h	Ti(OEt) ₄ ^f	B	98	20/1	>98

^a A: additive was added after the addition of base (LiHMDS). B: additive was added before the addition of base. ^b Isolated yield. ^c Determined by ¹H NMR, and de was assigned for the *cis*-isomer. ^d With 1.5 equiv of base used. ^e With 3 equiv used. ^f With 2 equiv used. ^g With 1.9 equiv of base used. ^h With 4 equiv of base used.

deteriorated both the yield and the diastereoselectivity (entries 1 and 2). In the presence of LiBr or MgBr₂, high *cis/trans* selectivity was achieved and the diastereoselectivity maintained. The best result was obtained when Lewis acid Ti(OEt)₄ was used. In this case, the desired aziridine **3a** was isolated in 98% yield with a good *cis/trans* selectivity

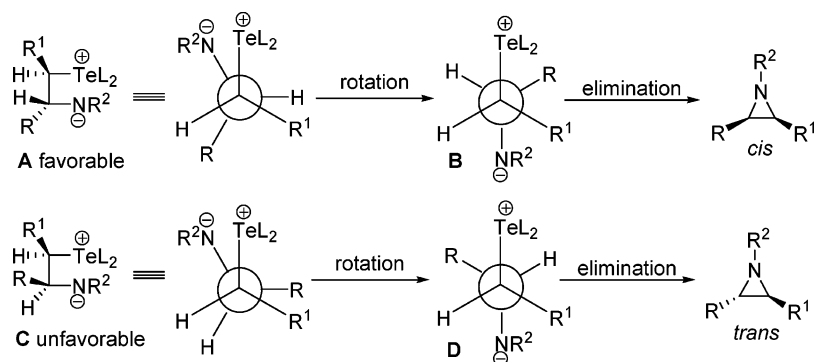
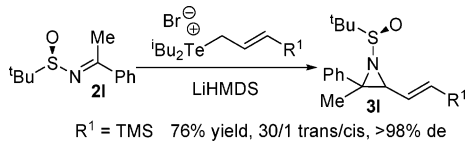


Figure 1. Proposed mechanism for the aziridination mediated by telluronium salt.

(*cis/trans* = 20/1) and excellent diastereoselectivity (*dr* > 99/1, entry 6).

Having established optimal conditions, a survey of the scope of imines suitable for this aziridination was carried out. As summarized in Table 3, the reaction displayed good generality with respect to the substituents of imines. Various aryl and heteroaryl aldimines (entries 1–7) as well as alkyl and α,β -unsaturated aldimines (entries 8–12) all worked well to afford the desired products with high diastereoselectivity in good to excellent yields, providing an easy access to optically active *cis*-2-substituted vinylaziridines. Furthermore, ketimines, usually less active than aldimines in ylide reactions,¹⁵ worked well in this aziridination. For example, phenylmethylketimine **2l** could react with silylated telluronium allylide to afford the corresponding aziridine in 76% yield with excellent diastereoselectivity (*cis/trans* > 30/1 and >98% *de*, Scheme 1).

Scheme 1. Stereoselective Aziridination of Ketimine **2l**¹⁴



Further study showed that the reaction of the simple allylic telluronium salt **1c** with imine **2a** also proceeded well to give the desired *cis*-vinylaziridine with high diastereoselectivity in high yield (*cis/trans* = 14/1, 95% *de*, entries 1 and 2 in Table 4), completely different from *cis/trans* selectivity in the reaction of the corresponding sulfur ylide in which a *trans*-isomer was favored. This result demonstrated that telluronium ylide, compared with the corresponding sulfur ylide,⁹ was unique. Noticeably, although cinnamyl sulfonium ylide was reported to be inert to *tert*-butylsulfonylimines,^{6c} the corresponding telluronium ylide worked well to afford

the desired cinnamyl aziridine with excellent selectivity in high yield (entry 3, Table 4), suggesting that telluronium ylide is more active than the corresponding sulfur ylide.

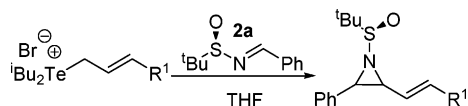
Table 3. Stereoselective Aziridination of Enantiopure *N-tert*-Butylsulfonylimines¹⁴

entry	2, R	method ^a	yield (%) ^b	<i>cis/trans</i> ^c	<i>de</i> (%) ^c
1	2a	A	83	17/1	97
2	2a	B	98	20/1	>98
3	2b	B	96	20/1	>98
4	2c	B	98	20/1	>98
5	2d	B	98	20/1	97
6	2e	B	98	22/1	>98
7	2f	B	93	19/1	94
8 ^d	2g	A	83	9/1	>98
9 ^d	2h	A	53	>30/1	>98
10	2i	B	88	10/1	88
11	2j	B	98	25/1	87
12	2k	B	91	12/1	86

^a A: **2l**/LiHMDS = 1.0/1.5/1.5. B: Ti(OEt)₄ was added, **2l**/Ti(OEt)₄/LiHMDS = 1.0/1.5/2/4. ^b Isolated yield. ^c Determined by ¹H NMR, and *de* was assigned for the *cis*-isomer. ^d Salt **1b** was used instead of **1a**.

(14) For detailed procedure, please see Supporting Information.
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Table 4. Aziridination of **2a** Mediated by Different Telluronium Salts¹⁴



entry	1 (R ¹)	method ^a	yield (%) ^b	<i>cis/trans</i> ^c	de (%) ^c
1	1c (H)	A	75	9/1	95
2	1c (H)	B	91	14/1	96
3	1d (Ph)	B	89	>30/1	>98

^a A: **2a**/LiHMDS = 1.0/1.5/1.5. B: Ti(OEt)₄ was added, **2a**/Ti(OEt)₄/LiHMDS = 1.0/1.5/2.0/4.0. ^b Isolated yield. ^c Determined by ¹H NMR, and de was assigned for the *cis*-isomer.

In the literature, the ylide aziridination is regarded as a two-step reaction.^{6e,16} Although the detailed mechanistic pathway is not clear, Figure 1 could account for the selectivity of the aziridination. The telluronium ylide attacks the imine to form intermediates **A** and **C**. Transformation of intermediates **A** and **C** into the corresponding **B** and **D**

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by rotation was followed by an intramolecular *anti*-elimination to afford the vinylaziridine. Obviously, intermediate **A** is favored over **C** due to steric hindrance and thus, *cis*-aziridine formed preferably.

In conclusion, on the basis of the reaction of enantiopure *N*-tert-butylsufinylimines with various allylic telluronium ylides, a highly stereoselective and efficient ylide aziridination has been developed. This aziridination provided an easy access to optically active *cis*-2-substituted vinylaziridines and 2,2-disubstituted vinylaziridines directly from imines. The excellent diastereoselectivity, good *cis/trans* selectivity, as well as high yield make this reaction potentially useful in organic synthesis.

Acknowledgment. We are grateful for the financial support from the Natural Sciences Foundation of China and the Science and Technology Commission of Shanghai Municipality.

Supporting Information Available: General synthetic procedures and characterization and spectral data for key compounds. This material is available free of charge via the Internet at <http://pubs.acs.org>.

OL051921N