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Highly Diastereoselective Strecker Reaction of Enolizable Aliphatic Sulfinimines

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Received April 15, 2003

The reaction of chiral sulfinimines **1c**−**g** derived from aliphatic aldehydes with TMSCN in the presence of CsF gave α-amino nitriles in high diastereoselectivity and yield. α,*β*-Diamino acid derivatives were also obtained in high diastereoselectivity from the reaction of 2-aziridinesulfinimines **1h** and **1i** followed by ring-opening of the products with thiophenol. The presence of hydrogen at the α-position of the C═N double bond is crucial in this TMSCN addition reaction.

The growing interest in nonproteinogenic α-amino acids in a variety of scientific disciplines has prompted the development of numerous methods for the asymmetric synthesis of nonnatural α-amino acids.[1] The addition of HCN to imines (Strecker reaction) is one of the most direct and viable strategies for the asymmetric synthesis of α-amino acid derivatives.[2] Chiral imines are often used as substrates and cyanotrimethylsilane (TMSCN) is a promising alternative to HCN and is a safer source of cyanide anion.[3] Many catalyzed procedures have also recently been developed.[4] However, most of these are only suitable for aryl imine substrates, and the aliphatic examples give low yields and low selectivity.[4c]

There have been numerous reports on enantiopure sulfinimines in recent years.[5] Sulfinimines are stable compounds. The sulfinyl group is an excellent chiral auxiliary and activator of the C═N bond for nucleophilic addition. It is easily removed from the product. Therefore, the addition of TMSCN to readily available enantiopure sulfinimines may be a good method for obtaining diastereomerically enriched α-amino nitriles. However, Davis and co-workers, who pioneered research on sulfinimines, recently reported that when *N*-(benzylidene)-*p*-toluenesulfinamide was treated with TMSCN and CsF in THF, no desired α-amino nitrile was obtained.[6] They therefore used ethylaluminum cyanide and isopropyl alcohol as an alternative, and found that extreme care was needed with this reaction, since it is strongly influenced by moisture.[7]

In the course of our research on the reactions of imines[8] and aziridines,[9] we discovered that fluoride anion served as a trigger to initiate the addition of silicon reagents, such as allyltrimethylsilane, TMSCN, and $TMSN_3$, to imines[8a] and aziridines,[9a] and the corresponding products were obtained in excellent yields. Upon further study, we surprisingly found that in the presence of fluoride

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(1) Williams, R. M. *Synthesis of Optically Active α-Amino Acids*; Pergamon: Oxford, UK, 1989.

(2) Strecker, A. *Ann. Chem. Pharm.* **1850**, *75*, 27.

(3) For representative recent examples, see: (a) Duthaler, O. R. *Tetrahedron* **1994**, *50*, 1539. (b) Kunz, H.; Rick, C. *Angew. Chem., Int. Ed. Engl.* **1993**, *32*, 336. (c) Kobayashi, S.; Ishitani, H.; Ueno, M. *Synlett* **1997**, 115. (d) Meyers, A. G.; Gleason, J. L.; Yoon, T.; Kung, D. W. *J. Am. Chem. Soc.* **1997**, *119*, 656.

(4) For representative recent examples, see: (a) Sigman, M. S.; Jacobsen, E. N. *J. Am. Chem. Soc.* **1998**, *120*, 5315. (b) Krueger, C. A.; Kuntz, K. W.; Dzierba, C. D.; Wirschun, W. G.; Gleason, J. D.; Snapper, M. L.; Hoveyda, A. H. *J. Am. Chem. Soc.* **1999**, *121*, 4284. (c) Iyer, M. S.; Gigstad, K. M.; Namdev, N. D.; Lipton, M. *J. Am. Chem. Soc.* **1996**, *118*, 4910. (d) Corey, E. J.; Grogan, M. J. *Org. Lett.* **1999**, *1*, 157. (e) Ishitani, H.; Komiyama, S.; Hasegawa, Y.; Kobayashi, S. *J. Am. Chem. Soc.* **2000**, *122*, 762.

(5) For examples, see: (a) Davis, F. A.; Wu, Y.; Yan, H.; McCoull, W.; Prasad, K. R. *J. Org. Chem.* **2003**, *68*, 2410. (b) Davis, F. A.; Mohanty, P. K. *J. Org. Chem.* **2002**, *67*, 1290. (c) Davis, F. A.; Zhang, Y.; Andemichael, Y.; Fang, T.; Fanelli, D. L.; Zhang, H. *J. Org. Chem.* **1999**, *64*, 1403. (d) Davis, F. A.; Chen, B. C. *Chem. Soc. Rev.* **1998**, *27*, 13. (e) Dragoli, D. R.; Burdett, M. T.; Ellman, J. A. *J. Am. Chem. Soc.* **2001**, *123*, 10127. (f) Tang, T. P.; Volkman, S. K.; Ellman, J. A. *J. Org. Chem.* **2001**, *66*, 8772. (g) Liu, G.; Cogan, D. A.; Owens, T. D.; Tang, T. D.; Ellman, J. A. *J. Org. Chem.* **1999**, *64*, 1278. (h) Cogan, D. A.; Liu, G.; Kim, K.; Backes, B. J.; Ellman, J. A. *J. Am. Chem. Soc.* **1998**, *120*, 8011. (i) Lefebvre, I. M.; Evans, S. A., Jr. *J. Org. Chem.* **1997**, *62*, 7532.

(6) Davis, F. A.; Reddy, R. E.; Portonovo, P. *Tetrahedron Lett.* **1994**, *35*, 9351.

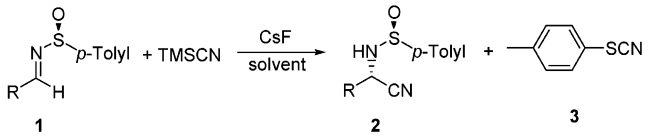
(7) (a) Davis, F. A.; Portonovo, P. S.; Reddy, R. E.; Chiu, Y. H. *J. Org. Chem.* **1996**, *61*, 440. (b) Davis, F. A.; Fanelli, K. L. *J. Org. Chem.* **1998**, *63*, 1981. (c) Davis, F. A.; Srirajan, V.; Titus, D. D. *J. Org. Chem.* **1999**, *64*, 6931. (d) Davis, F. A.; Srirajan, V. *J. Org. Chem.* **2000**, *65*, 3248. (e) Davis, F. A.; Srirajan, V.; Fanelli, D. L.; Portonovo, P. *J. Org. Chem.* **2000**, *65*, 7663. (f) Davis, F. A.; Lee, S.; Zhang, H.; Fanelli, D. L. *J. Org. Chem.* **2000**, *65*, 8704.

(8) (a) Wang, D. K.; Zhou, Y. G.; Tang, Y.; Hou, X. L.; Dai, L. X. *J. Org. Chem.* **1999**, *64*, 4233. (b) Li, A. H.; Dai, L. X.; Hou, X. L. *Chem. Commun.* **1996**, 491. (c) Wang, D. K.; Dai, L. X.; Hou, X. L. *Chem. Commun.* **1997**, 1231. (d) Hou, X. L.; Yang, X. F.; Dai, L. X.; Chen, X. F. *Chem. Commun.* **1998**, 747. (e) Hou, X. L.; Zheng, X. L.; Dai, L. X. *Tetrahedron Lett.* **1998**, *39*, 6949. (f) Li, B. F.; Zhang, M. J.; Hou, X. L.; Dai, L. X. *J. Org. Chem.* **2002**, *67*, 2902. (g) Yang, X. F.; Zhang, M. J.; Hou, X. L.; Dai, L. X. *J. Org. Chem.* **2002**, *67*, 8097.

(9) (a) Wu, J.; Hou, X. L.; Dai, L. X. *J. Org. Chem.* **2000**, *65*, 1344. (b) Wu, J.; Hou, X. L.; Dai, L. X. *J. Chem. Soc., Perkin Trans. 1* **2001**, 1314. (c) Hou, X. L.; Fan, R. H.; Dai, L. X. *J. Org. Chem.* **2002**, *67*, 5295. (d) Fan, R. H.; Hou, X. L. *J. Org. Chem.* **2003**, *68*, 726. (e) Fan, R. H.; Hou, X. L. *Org. Biomol. Chem.* **2003**, *1*, 1565.

10.1021/jo034477f CCC: $25.00
Published on Web 07/18/2003

SCHEME 1



a. R = *p*-MeOC$_6$H$_4$; **b.** R = Bu^t; **c.** R = Pr^i; **d.** R = Pr^n; **e.** R = Bu^i; **f.** R = cyclohexyl; **g.** R = Hexyl^n.

TABLE 1. Results of Reaction of TMSCN with Sulfinimines[a]

entry	sulfinimine	solvent	temp (°C)	yield of **2** (%)	de[c]
1[b]	**1a**	THF	25	86% of **3**[d]	
2[b]	**1b**	THF	25	71% of **3**	
3	**1c**	THF	25	95	18
4	**1c**	*n*-hexane	25	96	80
5	**1c**	*n*-hexane	−50	98	90
6	**1d**	*n*-hexane	−50	92	82
7	**1e**	*n*-hexane	−50	97	86
8	**1f**	*n*-hexane	−50	99	>98
9	**1g**	*n*-hexane	−50	95	>98

[a] Reaction conditions: Sulfinimine (0.1 M in solvent), TMSCN (1.05 equiv), CsF (1.05 equiv). [b] TMSCN (2 equiv), CsF (2.05 equiv), 12 h. [c] The diastereoselectivity was determined by ^{1}H NMR. [d] Reference 6.

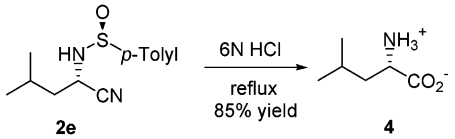
anion, TMSCN is also successfully added to the C═N bond of sulfinimines when there is a hydrogen atom at the α-position of the C═N bond. Herein we would like to report our results with the Strecker reaction of aliphatic imines to give high diastereoselectivity and high yield.

The reaction of sulfinimines[5a] with TMSCN in the presence of CsF gave rise to α-amino nitrile **2** or *p*-toluenethiocyanate (**3**) (Scheme 1), and the results are presented in Table 1. When (*S*)-(+)-*N*-(*p*-methoxybenzylidene)-*p*-toluenesulfinamide (**1a**) reacted with TMSCN and CsF in THF for 12 h, *p*-toluenethiocyanate (**3**) was isolated in 86% yield and no addition product aminonitrile **2a** was detected (entry 1).[6] The reaction of (*S*)-(+)-*N*-(*tert*-butylidene)-*p*-toluenesulfinamide (**1b**) gave similar results (entry 2). However, α-amino nitrile **2c** was obtained from (*S*)-(+)-*N*-(isopropylidene)-*p*-toluenesulfinamide (**1c**) in almost quantitative yield (95%). The NMR spectrum of the product showed two peaks at δ 3.97 (dd, J_1 = 7.9 Hz, J_2 = 5.6 Hz) and 3.75 (dd, J_1= 8.9 Hz, J_2 = 5.6 Hz) with a ratio of 59:41, which corresponds to 18% de (entry 3).

The solvent had an important impact on the stereochemistry of the reaction, although it can proceed in almost any aprotic solvent. Among the solvents tested, the highest diastereoselectivity (80% de) was realized in *n*-hexane (entry 4), while it was lower in CH_2Cl_2 (16% de), toluene (12% de), CH_3CN (14% de, more syn-product), Et_2O (8% de), and Et_3N (52% de). When the concentration of the substrate in *n*-hexane was lowered from 0.1 to 0.01 M, the diastereoselectivity decreased from 80% de to 12% de. The reaction at a concentration of 0.25 M gave the same diastereoselectivity as that at 0.1 M.

A catalytic amount of CsF (0.1 equiv) also promoted the addition of TMSCN to (*S*)-(+)-*N*-(isopropylidene)-*p*-toluenesulfinamide (**1c**), although the yield (91%) and diastereoselectivity (70%) were slightly lower. The best results were obtained when the reaction temperature was lowered to −50 °C (entry 5). This addition reaction was almost suppressed at −78 °C.

SCHEME 2



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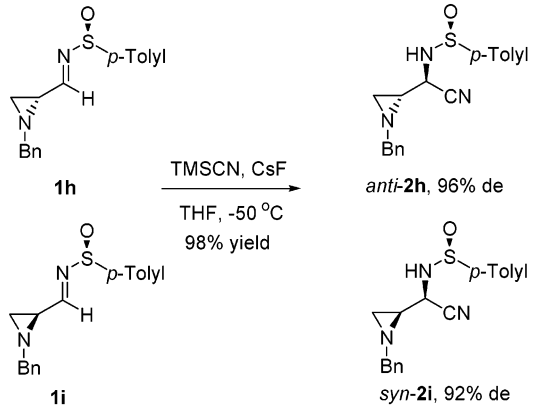

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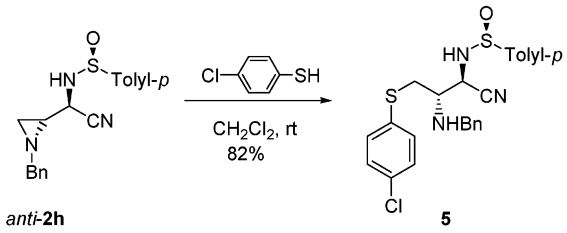
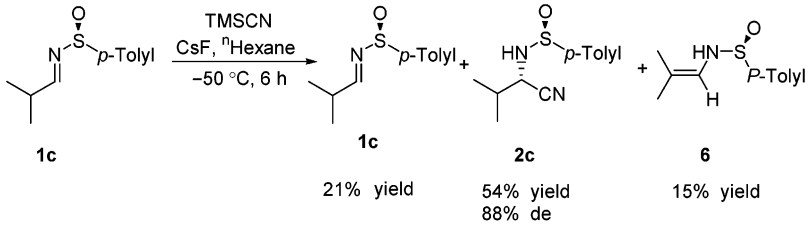


Various enolizable sulfinimines **1c**−**g** were evaluated in *n*-hexane at −50 °C. The addition of (*S*)-(+)-*N*-(cyclohexylidene)-*p*-toluenesulfinamide **1f** and (*S*)-(+)-*N*-(hexylidene)-*p*-toluenesulfinamide **1g** gave the best results (entries 8 and 9). They also give some of the best results in the Strecker reaction involving aliphatic imines by means of chiral imines[3] or chiral catalysts.[4] A similar diastereoselectivity and yield were achieved (90% de, 93% yield) even at a 3-g scale for imine **1c**. The absolute configuration of the major diastereomeric α-amino nitriles was determined to be (*S*,*S*$_s$) by comparison with authentic samples.[6] There have been many reports on the hydrolysis of sulfinylamino nitriles to the corresponding α-amino acids without racemization.[6,10] Thus, the α-amino nitrile **2e** was converted to the corresponding L-leucine **4** in 85% yield. Chiral HPLC analysis of product **4** showed that no racemization took place.[10b]

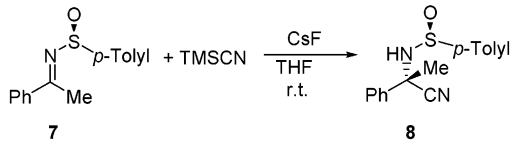
2-Aziridinesulfinimines **1h** and **1i**[8f] were also suitable substrates in this reaction and provided the desired products in excellent diastereoselectivity and yield (Scheme 3). Simple crystallization from CH_2Cl_2/ethyl acetate provided optically pure amino nitriles **2h** and **2i**. The best solvent in this reaction is THF. Davis reported the asymmetric Strecker reaction of β-hydroxyl sulfinimines,[7f] and the results suggested the influence of a double stereodifferentiation effect where the chirality of the resident hydroxyl moiety influences asymmetric induc-

(10) (a) DeWitt, H. D.; Ingersoll, A. W. *J. Am. Chem. Soc.* **1951**, *73*, 3359. (b) Wang, M X.; Lin, S. J. *J. Org. Chem.* **2002,** *67,* 6542. (c) Reference 7f and references therein.

SCHEME 5



SCHEME 6



tion. In our case, the stereochemistry was controlled by the chiral sulfinyl group.

The products **2h** and **2i** were α,β-diamino nitriles and also intermediates for the preparation of a variety of α,β-diamino acids by ring-opening of the aziridine with various nucleophiles. To explore this point, the ring-opening reaction of *anti*-**2h** with 4-chlorothiophenol was carried out, and the corresponding product, α-(*N*-sulfinylamino)-β-benzylamino nitrile **5**, was obtained in 82% yield (Scheme 4). Since the enantiomers of **2h** and **2i** are conveniently prepared from (*R*)-(−)-*p*-toluenesulfinamide and 1-benzyl-2-aziridinecarboxaldehyde,[8f] the combination of the Strecker reaction of 2-aziridinesulfinimines followed by ring-opening of the products provided a potential facile route to all four diastereoisomers of α,β-diamino acid derivatives.[11]

In the reaction of imines with TMSCN, the presence of hydrogen at the α-position of the C═N bond was crucial because the reaction of arylimine **1a** and tertiary butyl imine **1b**, which have no α-H, gave *p*-toluenethiocyanate (**3**) as the product while all other substrates **1c**−**i** with a hydrogen at the α-position of the C═N bond provided α-amino nitriles **2c**−**i** in high yields. The following experiment supported our hypothesis. When the reaction of TMSCN with (*S*)-(+)-*N*-(isopropylidene)-*p*-toluenesulfinamide **1c** at −50 °C proceeded for 6 h and was then stopped, a new compound was isolated in 15% yield in addition to the substrate **1c** (21% recovery) and product **2c** (54% yield and 88% de). On the basis of IR and ^{1}H NMR spectra, we deemed it was an enamine **6** (Scheme 5). When the above mixture of **1c**, **2c**, and **6** was re-exposed to the reaction conditions, α-amino nitrile **2c** was obtained in almost quantitative yield and 88% de. The reaction of ketimine **7** provided further evidence to support our hypothesis. In contrast to the result with methoxy-phenylimine **1a**, the reaction of ketosulfinimine **7** under the above Strecker reaction conditions gave rise to α-amino nitrile **8** in 90% yield. The NMR spectrum of the product in benzene-d_6 showed two singlet peaks at δ 5.25 and 4.98 with a ratio of 11:89, which corresponds to 78% de. After chromatograph purification, enantiopure product **8** was obtained in 72% yield (Scheme 6).[7f]

In summary, we have developed an effective and facile route to aliphatic α-amino acid derivatives with high diastereoselectivity that involves the addition of TMSCN to chiral enolizable sulfinimines. The combination of the Strecker reaction and the ring-opening reaction of 2-aziridinesulfinimines provides a convenient route to chiral α,β-diamino acids. This CsF-promoted addition complements Davis' protocol and is attractive on several points: higher yields, better diastereoselectivities, milder reaction conditions, and no need for strict moisture-free and oxygen-free conditions. Further studies on the mechanism and application of this reaction to asymmetric synthesis are in progress.

Experimental Section

General. The commercially available reagents were used without further purification. The solvents were treated by using standard methods. Compounds **1c**−**f**,[12] **1h**−**i**,[8f] α-amino acid **4**,[6,10] and **7**[7f] were synthesized according to the literature procedures. All reactions were performed under a nitrogen atmosphere. ^{1}H NMR spectra were recorded in $CDCl_3$ and the chemical shifts were referenced to $CHCl_3$ (δ 7.27). Optical rotations were measured with a thermally jacketed 10-cm cell at 25 °C (concentration *c* given as g/100 mL). IR spectra were measured in cm^{-1}.

Preparation of (*S*)-*N*-Heptylidene-*p*-toluenesulfinamide (1g). To a solution of heptyl aldehyde (685 mg, 6 mmol) and (*S*)-*p*-toluenesulfinamide (775 mg, 5 mmol) in CH_2Cl_2 (50 mL) was added $Ti(OEt)_4$ (5.3 mL, 5.76 g, 25 mmol). The mixture was refluxed and monitored by TLC. After completion, the reaction mixture was quenched at 0 °C by addition of H_2O (50 mL). The solution was filtered through Celite, and the filter cake was washed with CH_2Cl_2 (3 × 30 mL). The aqueous phase was extracted with CH_2Cl_2 (2 × 20 mL), and the combined organic portions were dried over Na_2SO_4, concentrated, and purified by column chromatography over silica gel (petroleum ether:EtOAc 10:1) to give (*S*)-*N*-heptylidene-*p*-toluenesulfinamide (**1g**): 1.155 g, 92% yield. ^{1}H NMR ($CDCl_3$/TMS, 300 MHz) δ 0.86 (t, J = 6.2 Hz, 3H), 1.27−1.33 (m, 6H), 1.57−1.62 (m, 2H), 2.38 (s, 3H), 2.44−2.51 (m, 2H), 7.29 (d, J = 7.9 Hz, 2H), 7.56 (d, J = 7.9 Hz, 2H), 8.22 (t, J = 4.8 Hz, 1H). IR (neat) 1621, 1099 cm^{-1}. EI-MS *m*/*z* (%) 139 (100). Anal. Calcd for $C_{14}H_{21}NOS$: C, 66.89; H, 8.42; N, 5.57. Found: C, 66.56; H, 8.11; N, 5.34.

General Procedure for the Addition of TMSCN to Sulfinimines 1c−g in the Presence of CsF. To a solution of sulfinimine (0.2 mmol) and CsF (32 mg, 0.21 mmol) in *n*-hexane (2 mL) at −50 °C was added TMSCN (21 mg, 0.028 mL, 0.21 mmol) dropwise via syringe. The resulting mixture was stirred at −50 °C and monitored by TLC. After completion, the reaction mixture was quenched with a saturated solution of NH_4Cl and extracted with ethyl acetate (2 × 5 mL). The organic phase was dried over Na_2SO_4. Removal of solvent in a vacuum afforded the corresponding α-amino nitrile. The diastereoselectivity was determined by ^{1}H NMR.

(S_s,*S*)-1-(*p*-Toluenesulfinylamino)-2-methylbutyronitrile (2c): 46 mg, 98% yield, 90% de. ^{1}H NMR ($CDCl_3$/TMS,

(11) For example, see: Luo, Y.; Blaskovich, M. A.; Lajoie, G. A. *J. Org. Chem.* **1999**, *64*, 6106 and references therein.

(12) Davis, F. A.; Reddy, R. E.; Szewczyk, J. M.; Reddy, G. V.; Portonovo, P. S.; Zhang, H.; Fanelli, D.; Reddy, R. T.; Zhou, P.; Carroll, P. J. *J. Org. Chem.* **1997**, *62*, 2555.

300 MHz) (major product) δ 1.06 (d, J = 6.7 Hz, 3 H), 1.11 (d, J = 6.7 Hz, 3 H), 2.06−2.13 (m, 1 H), 2.42 (s, 3 H), 3.97 (dd, J_1 = 7.9 Hz, J_2 = 5.6 Hz, 1 H), 4.76 (d, J = 7.9 Hz, 1 H), 7.35 (d, J = 8.2 Hz, 2 H), 7.60 (d, J = 8.2 Hz, 2 H); (minor product) δ 1.06 (d, J = 6.7 Hz, 3 H), 1.11 (d, J = 6.7 Hz, 3 H), 2.06−2.13 (m, 1 H), 2.42 (s, 3 H), 3.75 (dd, J_1 = 8.9 Hz, J_2 = 5.6 Hz, 1 H), 4.76 (d, J = 7.9 Hz, 1 H), 7.35 (d, J = 8.2 Hz, 2 H), 7.60 (d, J = 8.2 Hz, 2 H). IR (KBr) 3040, 1052 cm^{-1}. EI-MS m/z (%) 236 (M, 1), 139 (100). Anal. Calcd for $C_{12}H_{16}N_2OS$: C, 60.98; H, 6.82; N, 11.85. Found: C, 61.07; H, 6.78; N, 11.92.

(S_s,*S*)-1-(*p*-Toluenesulfinylamino)pentanenitrile (2d):[6] 44 mg, 92% yield, 82% de. ^{1}H NMR ($CDCl_3$/TMS, 300 MHz) (major product) δ 0.97 (t, J = 7.3 Hz, 3 H), 1.48−1.57 (m, 2 H), 1.81−1.89 (m, 2 H), 2.43 (s, 3 H), 4.07−4.14 (m, 1 H), 4.87 (d, J = 7.3 Hz, 1 H), 7.36 (d, J = 8.0 Hz, 2 H), 7.61 (d, J = 8.0 Hz, 2 H); (minor product) δ 0.97 (t, J = 7.3 Hz, 3 H), 1.48−1.57 (m, 2 H), 1.81−1.89 (m, 2 H), 2.43 (s, 3 H), 3.97−4.03 (m, 1 H), 4.87 (d, J = 7.3 Hz, 1 H), 7.36 (d, J = 8.0 Hz, 2 H), 7.61 (d, J = 8.0 Hz, 2 H).

(S_s,*S*)-1-(*p*-Toluenesulfinylamino)-3-methylpentanenitrile (2e):[6] 48 mg, 97% yield, 86% de. ^{1}H NMR ($CDCl_3$/TMS, 300 MHz) (major product) δ 0.94 (d, J = 6.3 Hz, 3 H), 0.98 (d, J = 6.3 Hz, 3 H), 1.70−1.88 (m, 3 H), 2.43 (s, 3 H), 4.10−4.17 (m, 1 H), 4.60 (s, br, 1 H), 7.36 (d, J = 7.8 Hz, 2 H), 7.61 (d, J = 7.8 Hz, 2 H); (minor product) δ 0.94 (d, J = 6.3 Hz, 3 H), 0.98 (d, J = 6.3 Hz, 3 H), 1.70−1.88 (m, 3 H), 2.43 (s, 3 H), 3.96−4.03 (m, 1 H), 4.60 (s, br, 1 H), 7.36 (d, J = 7.8 Hz, 2 H), 7.61 (d, J = 7.8 Hz, 2 H).

(S_s,*S*)-α-(*p*-Toluenesulfinylamino)-α-cyclohexylacetonitrile (2f): 54 mg, 99% yield, >98% de. $[\alpha]^{20}_D$ +72.9 (*c* 1.33, $CHCl_3$). mp 98−99 °C. ^{1}H NMR ($CDCl_3$/TMS, 300 MHz) δ 1.10−1.24 (m, 5 H), 1.68−1.90 (m, 6 H), 2.42 (s, 3 H), 3.90−3.94 (m, 1 H), 4.82 (s, br, 1 H, NH), 7.34 (d, J = 8.0 Hz, 2 H), 7.60 (d, J = 8.0 Hz, 2 H). IR (KBr) 3309, 1091 cm^{-1}. EI-MS m/z (%) 259 (26), 139 (100). Anal. Calcd for $C_{15}H_{20}N_2OS$: C, 65.18; H, 7.29; N, 10.14. Found: C, 65.14; H, 7.28; N, 10.13.

(S_s,*S*)-1-(*p*-Toluenesulfinylamino)octanenitrile (2g): 53 mg, 95% yield, >98% de. ^{1}H NMR ($CDCl_3$/TMS, 300 MHz) δ 0.88 (t, J = 7.1 Hz, 3H), 1.25−1.34 (m, 6H), 1.44−1.49 (m, 2H), 1.81−1.89 (m, 2H), 2.43 (s, 3H), 4.06−4.13 (m, 1H), 4.54 (d, J = 7.3 Hz, 1H), 7.36 (d, J = 7.9 Hz, 2H), 7.61 (d, J = 7.9 Hz, 2H). IR (KBr) 3044, 1088 cm^{-1}. EI-MS m/z (%) 261 (2), 139 (100). Anal. Calcd for $C_{15}H_{20}N_2OS$: C, 64.71; H, 7.96; N, 10.06. Found: C, 64.68; H, 7.78; N, 9.99.

General Procedure for the Addition of TMSCN to Sulfinimines 1h−i in the Presence of CsF. To a solution of sulfinimine (0.2 mmol) and CsF (32 mg, 0.21 mmol) in THF (2 mL) at −50 °C was added TMSCN (21 mg, 0.028 mL, 0.21 mmol) dropwise via syringe. The resulting mixture was stirred at −50 °C and monitored by TLC. After completion, the reaction mixture was quenched with a saturated solution of NH_4Cl and extracted with ethyl acetate (2 × 5 mL). The organic phase was dried over Na_2SO_4. Removal of solvent in a vacuum afforded the corresponding α-amino nitrile. The diastereoselectivity was determined by ^{1}H NMR.

(2*R*,S_s,α*R*)-α-(*p*-Toluenesulfinylamino)-α-(1-benzaziridinyl-2)-acetonitrile (2h): 65 mg, 99% yield, 96% de. Crystallization from CH_2Cl_2/hexane provided pure **2h**: 56 mg, 84% yield. $[\alpha]^{20}_D$ −11.8 (*c* 1.0, $CHCl_3$). mp 135−136 °C. ^{1}H NMR ($CDCl_3$/TMS, 300 MHz) δ 1.58 (d, J = 6.2 Hz, 1 H), 1.97−2.01 (m, 1 H), 2.09 (d, J = 3.0 Hz, 1 H), 2.42 (s, 3 H), 3.51, 3.60 (AB, J = 13.2 Hz, 2 H), 4.12 (dd, J_1 = 6.8 Hz, J_2 = 2.1 Hz, 1 H), 7.26−7.39 (m, 7 H), 7.57 (d, J = 8.2 Hz, 2 H). IR (KBr) 3188, 2247, 1091, 1069 cm^{-1}. EI-MS m/z (%) 325 (10), 234 (46), 91 (100). Anal. Calcd for $C_{18}H_{19}N_3OS$: C, 66.43; H, 5.88; N, 12.91. Found: C, 66.10; H, 5.75; N, 12.68.

(2*S*,S_s,α*R*)-α-(*p*-Toluenesulfinylamino)-α-(1-benzaziridinyl-2)-acetonitrile (2i): 65 mg, 99% yield, 92% de. Crystallization from CH_2Cl_2/hexane provided pure **2i**: 48 mg, 74% yield. $[\alpha]^{20}_D$ +63.1 (*c* 0.9, $CHCl_3$). mp 89−90 °C. ^{1}H NMR ($CDCl_3$/TMS, 300 MHz) δ 1.66−1.70 (m, 1 H), 2.03−2.12 (m, 2 H), 2.41 (s, 3 H), 3.14, 3.86 (AB, J = 12.6 Hz, 2 H), 4.23 (dd, J_1 = 7.7 Hz, J_2 = 4.5 Hz, 1 H), 4.46 (d, J = 7.7 Hz, 1 H), 7.26−7.42 (m, 7 H), 7.51−7.54 (m, 2 H). IR (KBr) 3062, 2234, 1736 cm^{-1}. EI-MS m/z (%) 325 (M, 15), 234 (42), 91 (100). Anal. Calcd for $C_{18}H_{19}N_3OS$: C, 66.43; H, 5.88; N, 12.91. Found: C, 66.23; H, 5.89; N, 12.93.

Preparation of (S_s,*S*)-2-(*p*-Toluenesulfinylamino)-2-phenylpropionitrile (8).[7f] To a solution of sulfinimine **7** (52 mg, 0.2 mmol) and CsF (32 mg, 0.21 mmol) in *n*-hexane (2 mL) at −50 °C was added TMSCN (21 mg, 0.028 mL, 0.21 mmol) dropwise via syringe. The resulting mixture was stirred at −50 °C and monitored by TLC. After completion, the reaction mixture was quenched with a saturated solution of NH_4Cl and extracted with ethyl acetate (2 × 5 mL×). The organic phase was dried over Na_2SO_4. Removal of solvent in a vacuum afforded the corresponding α-amino nitrile **8**: 51 mg, 90% yield, 78% de. After flash chromatography (Et_2O:CH_2Cl_2 5:95), 41 mg, 72% yield. $[\alpha]^{20}_D$ 72.0 (*c* 0.6, $CHCl_3$). ^{1}H NMR ($CDCl_3$/TMS) δ 2.07 (s, 3H), 2.39 (s, 3H), 4.78 (s, 1H), 7.25−7.29 (m, 2H), 7.42−7.46 (m, 3H), 7.56 (d, J = 8.1 Hz, 2H), 7.68−7.72 (m, 2H). EI-MS m/z (%) 284 (M, 1.5), 154 (59) 139 (100).

Ring-Opening Reaction of *anti*-2h with 4-Chlorothiophenol. To a solution of *anti*-**2h** (66 mg, 0.2 mmol) in CH_2Cl_2 (5 mL) was added 4-chlorothiophenol (87 mg, 0.6 mmol); after being stirred overnight at room temperature, the solvent was removed by evaporation under vacuum and purified by column chromatography over silica gel (petroleum ether:EtOAc 3:1) to give thioether **5**: 77 mg, 82% yield. $[\alpha]^{20}_D$ +85.7 (*c* 1.1, $CHCl_3$). mp 103−104 °C. ^{1}H NMR ($CDCl_3$−D_2O, 300 MHz) δ 2.42 (s, 3H), 2.90 (dd, J_1 = 12.9 Hz, J_2 = 6.3 Hz, 1H), 2.97−3.02 (m, 1H), 3.08 (dd, J_1 = 12.9 Hz, J_2 = 5.8 Hz, 1H), 3.78, 3.89 (AB, J = 13.2 Hz, 2H), 4.15 (d, J = 2.8 Hz, 1H), 7.11−7.36 (m, 11H), 7.59 (d, J = 8.3 Hz, 2H). IR (KBr) 3330, 1058 cm^{-1}. EI-MS m/z (%) 276 (35), 91 (100). Anal. Calcd for $C_{24}H_{24}ClN_3OS_2$: C, 61.33; H, 8.94; N, 5.15. Found: C, 61.18; H, 9.00; N, 5.17.

Mechanistic Study: (a) The Formation of Enamine 6. To a solution of sulfinimines **1c** (209 mg, 1 mmol) and CsF (160 mg, 1.05 mmol) in hexane (10 mL) was added TMSCN (0.14 mL, 105 mg, 1.05 mmol) at −50 °C. The mixture was stirred for 6 h and quenched with a saturated solution of NH_4Cl and extracted with EtOAc (2 × 10 mL×). The organic phase was dried over Na_2SO_4. Removal of solvent in a vacuum and chromatography provided **2c** (127 mg, 54% yield, 88% de), recovered **1c** (44 mg, 21% recovery), and enamine **6** (31 mg, 15% yield). ^{1}H NMR ($CDCl_3$/TMS) δ 1.30−1.32 (m, 6 H), 2.38 (s, 3 H), 3.46 (s, 1 H, NH), 7.22−7.42 (m, 4 H), 7.70 (s, 1 H). IR (neat) 3411 (br, S), 1611 cm^{-1}. EI-MS m/z (%) 209 (M^+, 27), 166 (100). Anal. Calcd for $C_{11}H_{15}NOS$: C, 63.12; H, 7.22; N, 6.69. Found: C, 63.23; H, 7.33; N, 6.73.

(b) Reaction of Sulfinimines 1c, Amino Nitrile 2c, and Enamine 6 with TMSCN in Strecker Reaction Conditions. The crude product from procedure **a** was not purified and dissolved in hexane (10 mL). After the solution cooled to −50 °C, TMSCN (0.14 mL, 105 mg, 1.05 mmol) was added. The mixture was stirred for an additional 6 h. After the same workup procedure, product **2c** was isolated in 95% yield and 88% de.

Acknowledgment. This research was financially supported by the National Natural Science Foundation of China, the Major Basic Research Development Program (grant No. G2000077506), the National Outstanding Youth Fund, the Chinese Academy of Sciences, and the Shanghai Committee of Science and Technology.

Supporting Information Available: Experimental procedure for hydrolysis of α-amino nitrile **2e** as well as spectral and analytical data for reaction product **4**. This material is available free of charge via the Internet at http://pubs.acs.org.

JO034477F