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# Lewis acid mediated nucleophilic ring opening followed by cycloaddition of 2-aryl-*N*-tosylaziridines with carbonyl compounds: further support towards an $S_N2$-type mechanism

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**Abstract**—A highly regioselective $S_N2$-type ring opening of 2-aryl-*N*-tosylaziridines with carbonyl compounds in the presence of a Lewis acid to afford various 1,3-oxazolidines and 1,2-amino alcohols in excellent yields and moderate to high enantioselectivity is described. The formation of non-racemic products provides convincing evidence for the $S_N2$-type ring opening mechanism.


Aziridines are important as well as versatile building blocks used in the synthesis of various natural products and bioactive molecules.[1] The synthetic importance of these molecules is due to their ability to undergo nucleophilic ring opening reactions with a variety of nucleophiles.[2] Nucleophilic ring opening of 2-alkyl-*N*-activated aziridines[3a,b] and in situ generated aziridinium ions from non-activated aziridines[3c–e] is known to proceed via an $S_N2$ pathway. Aziridines can readily undergo a formal [3+2] cycloaddition reaction with a range of dipolarophiles leading to five-membered nitrogen-containing heterocycles.[4–6] $BF_3{\cdot}OEt_2$-mediated nucleophilic ring opening or [3+2] cycloaddition of 2-aryl-*N*-tosylaziridines is known where the reaction is believed to proceed through a stable 1,3-dipolar intermediate.[6] As a result, the enantioselective version of this reaction is not expected to be realized through nucleophilic ring opening of chiral 2-aryl-*N*-tosylaziridines. In contrast to the earlier reports, we have observed the formation of non-racemic products via nucleophilic ring opening of chiral 2-phenyl-*N*-tosyl aziridine with various nucleophiles.[7] We have proposed a new mechanism and have shown that the ring opening processes proceed through an $S_N2$-type pathway[7] instead of a 1,3-dipole as invoked earlier in the literature.[6] In continuation of our mechanistic investigations in this area, herein, we report a highly regioselective nucleophilic ring opening of 2-aryl-*N*-tosylaziridines with a variety of aliphatic and aromatic carbonyl compounds followed by a [3+2] cycloaddition to afford non-racemic 1,3-oxazolidines. These oxazolidines could easily be transformed into the corresponding non-racemic 1,2-amino alcohols. Syntheses of 1,3-oxazolidines are well documented in the literature starting from amino alcohols[8] or other precursors.[9] Surprisingly, there are only a few reports where carbonyl compounds have been utilized as dipolarophiles for [3+2] cycloaddition with N-activated aziridines in the presence of a Lewis acid (LA) to construct 1,3-oxazolidine derivatives.[5] 1,3-Oxazolidines exhibit biological activities such as antibacterial, antimicrobial and antitumour.[10] They can also be used as synthetic intermediates,[11] chiral auxilaries[12] and as precursors for synthetically and pharmaceutically important 1,2-amino alcohols[13] which are present in several natural products.[14] Very few methods are available in the literature for the synthesis of 2-amino-1-phenylethanol with high enantiopurity.[15] Most of these methods require expensive catalysts or ligands for the chiral induction. Utilizing our strategy,[16a–c] we synthesized 1-phenyl-2-amino-ethanol in up to 68% ee starting from the corresponding chiral aziridine.[17] By choosing the appropriate (*R*)- or (*S*)-aziridine, the corresponding (*S*)- or (*R*)-isomer of the amino alcohol could be prepared.

In order to provide further evidence for our proposed $S_N2$-type mechanism, we have explored the nucleophilic

*Keywords*: 2-Aryl-*N*-tosylaziridine; $Cu(OTf)_2$; $Zn(OTf)_2$; $BF_3{\cdot}OEt_2$; Nucleophilic ring opening; $S_N2$ pathway; Mechanism; Carbonyl; 1,3-Oxazolidine; 1,2-Amino alcohol.
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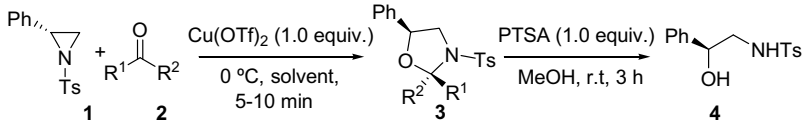
ring opening of activated aziridines with carbonyl compounds. When 2-phenyl-*N*-tosylaziridine **1** was treated with acetone in the presence of $Cu(OTf)_2$ as the Lewis acid at 0 °C, the reaction proceeded very smoothly and 2,2-dimethyl-5-aryl-3-tosyloxazolidine **3a** was obtained in high yield within a very short period of time (5 min) via a [3+2] cycloaddition reaction with acetone (Scheme 1). Similar results were obtained when the reaction was performed in dichloromethane with 4–5 equiv of acetone. This strategy was generalized with other aziridines using aldehydes or ketones in dichloromethane. In all the cases, the corresponding substituted oxazolidines **3** were produced in very high yields and the results are shown in Scheme 2. When aldehydes were used the reaction was found to be highly diastereoselective in favour of the *cis*-1,3-oxazolidines in most of the cases. The cis/trans stereochemistry was determined by NOE experiments.

To investigate the mechanism of the cycloaddition we carried out the reaction of enantiomerically pure (*R*)-2-phenyl-*N*-tosylaziridine **1** with carbonyl compounds. The enantioselectivity for the cycloaddition of (*R*)-**1** with acetone in $CH_2Cl_2$ or cyclopentane as the solvent was found to be poor (ee 36%). However, when acetone was used as the solvent the corresponding oxazolidine **3a** was obtained in high ee (62%). A small enhancement in the enantioselectivity was observed when $BF_3{\cdot}OEt_2$ (ee 74%) or $Zn(OTf)_2$ (ee 64%) was used as the Lewis acid (Table 1). Similarly, when (*R*)-**1** was subjected to our reaction conditions[16a,b] with benzaldehyde, product **3f** was formed as a single diastereomer (dr > 99% cis:trans) with moderate ee (Table 2). The reaction was generalized with various aliphatic as well as aromatic carbonyl compounds (Scheme 1) and in all the cases non-racemic 1,3-oxazolidines **3** were obtained in good yields with moderate to high ee (Tables 1 and 2). With aldehydes, the reaction was found to be highly diastereoselective in most of the cases at 0 °C (Table 2). The cis/trans selectivity of the product varies depending on the aldehyde and the reaction conditions.[18a] These observations provide convincing evidence that the cycloaddition reaction proceeds through an $S_N2$-type pathway.[7] The mechanism is illustrated in Scheme 3 where the reactive species **6** undergoes an $S_N2$-type nucleophilic ring opening reaction followed by cyclization with the carbonyl compound to produce **3**. The reduced enantioselectivity in all the cases was rationalized through partial racemization of the starting aziridine (*R*)-**1** before the nucleophilic ring opening step (Scheme 3).

These chiral 1,3-oxazolidines could easily be hydrolyzed to the corresponding non-racemic 1,2-amino alcohols[16c] in quantitative yields using PTSA in MeOH as shown in Schemes 1 and 2. After work-up, slightly decreased enantioselectivity (up to 68%) was observed compared to the starting oxazolidine.[18b] Starting from (*R*)-**1** we obtained (*S*)-1-phenyl-2-(tosylamino)-ethanol (**4**) as the major product. The absolute configuration of **4** was assigned by comparing the optical rotation and chiral HPLC analysis with an authentic sample prepared from (*S*)-mandelic acid.[16c] The inverted stereochemistry of **4** further supports the $S_N2$-type mechanism.

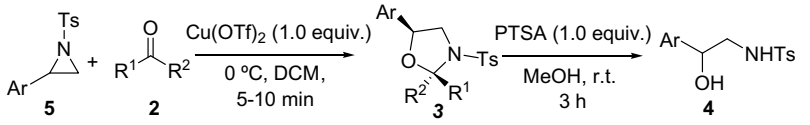
In conclusion, we have demonstrated that nucleophilic ring opening of 2-aryl-*N*-tosylaziridines proceeds through an $S_N2$ pathway. We believe that the reaction medium plays a key role in this type of nucleophilic ring opening reaction. The non-racemic 1,3-oxazolidines prepared via this method could easily be transformed into the corresponding 1,2-amino alcohols. Further applications of this methodology with chiral disubstituted aziridines is under active investigation in our laboratory.




**a**: $R^1 = R^2 = CH_3$; **b**: $R^1 = R^2 = -(CH_2)_5-$; **c**: $R^1 = R^2 = Ph$; **d**: $R^1 = C_2H_5$, $R^2 = H$;
**e**: $R^1 = C_3H_7$, $R^2 = H$; **f**: $R^1 = Ph$, $R^2 = H$; **g**: $R^1 = CH_2Ph$, $R^2 = H$;
**h**: $R^1 = H$, $R^2$ = cinnamyl; **i**: $R^1 = H$, $R^2$ = furyl

solvent: $CH_2Cl_2$ or carbonyl compounds; racemic **3** and **4** are obtained from racemic **1**

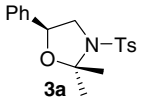
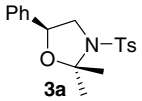
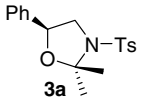
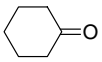
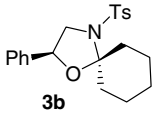
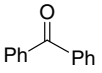
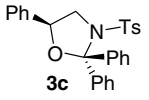
**Scheme 1.** $Cu(OTf)_2$ promoted [3+2] cycloaddition of (*R*)-2-phenyl-*N*-tosylaziridine **1** with carbonyl compounds.




**j**: Ar = 4-$ClC_6H_4$, $R^1 = R^2 = CH_3$; Yield: 71%
**k**: Ar = 4-$ClC_6H_4$, $R^1$ = Et, $R^2 = H$; Yield: 77%, *dr*: 91: 9 *(cis: trans)*
**l**: Ar = 4-$MeC_6H_4$, $R^1 = R^2 = CH_3$; Yield: 50%
**m**: Ar = 4-$MeC_6H_4$, $R^1$ = Pr, $R^2 = H$; Yield: 89%; *dr*: 88:12 *(cis: trans)*

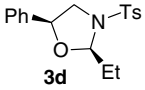
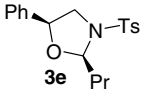
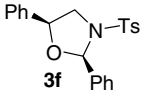
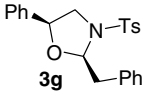
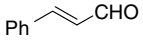
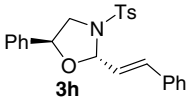
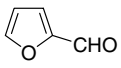
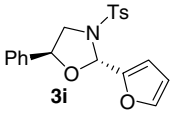
**Scheme 2.** $Cu(OTf)_2$ promoted [3+2] cycloaddition of racemic 2-aryl-*N*-tosylaziridines **5** with carbonyl compounds.

**Table 1.** Lewis acid promoted [3+2] cycloaddition of (*R*)-2-phenyl-*N*-tosylaziridine (**1**) with ketones[a]

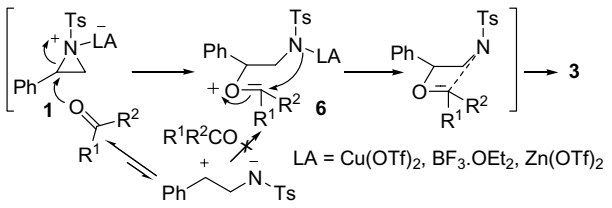
| Entry | Carbonyl **2** | Product[b] **3** | Lewis acid | Yield[c] (%) | $[\alpha]_D^{25}$ (*c* $CHCl_3$) | ee[d] (%) |
|---|---|---|---|---|---|---|
| 1 | $(CH_3)_2CO$ |  **3a** | $Cu(OTf)_2$ | 90 | +17 (*c* 1.0) | 62 |
| 2 | $(CH_3)_2CO$ |  **3a** | $Zn(OTf)_2$ | 81 | +18 (*c* 1.0) | 64 |
| 3 | $(CH_3)_2CO$ |  **3a** | $BF_3{\cdot}OEt_2$ | 80 | +21 (*c* 0.21) | 74 |
| 4 |  |  **3b** | $Cu(OTf)_2$ | 65 | +12 (*c* 1.0) | 56 |
| 5 |  |  **3c** | $Cu(OTf)_2$ | 60 | — | 22[e] |

[a] 1.0 equiv of $Cu(OTf)_2$, in ketone, the reactions were conducted for 5–10 min at 0 °C.
[b] Absolute stereochemistry of the major enantiomer is shown.
[c] Yield of isolated products.
[d] ee Determined by chiral HPLC.
[e] 5.0 equiv of Benzophenone was used in dichloromethane.

**Table 2.** $Cu(OTf)_2$ promoted [3+2] cycloaddition of (*R*)-2-phenyl-*N*-tosylaziridine (**1**) with aldehydes

| Entry | Carbonyl **2** | Product[a] **3** | ee[b,c] (%) | Yield[d] (%) | dr[e,f] cis:trans (%) | $[\alpha]_D^{25}$ (*c*, $CHCl_3$)[g] |
|---|---|---|---|---|---|---|
| 1 | EtCHO |  **3d** | 56 | 78 | 95:5 | −11.4 (*c* 0.70) |
| 2 | PrCHO |  **3e** | 54 | 82 | 93:7 | −7.0 (*c* 1.0) |
| 3 | PhCHO |  **3f** | 62[h] | 88 | >99 | +23.6 (*c* 0.55) |
| 4 | $PhCH_2CHO$ |  **3g** | 50 | 68 | 94:6 | +4.2 (*c* 0.95) |
| 5 |  |  **3h** | 68 | 75 | 40:60 | +21.43 (*c* 0.70) |
| 6 |  |  **3i** | 72 | 78 | 40:60 | +8.75 (*c* 0.80) |

[a] Absolute stereochemistry of the major isomer is shown.
[b] 1.0 equiv of $Cu(OTf)_2$, in aldehyde, the reactions were conducted for 5–10 min at 0 °C.
[c] ee Determined by chiral HPLC.
[d] Yields of isolated products.
[e] Stereochemistry was confirmed by NOE measurements and dr was determined by $^1H$ NMR analysis of the crude reaction mixture.
[f] Diastereoselectivity is dependant on the temperature and solvent.
[g] $[\alpha]_D^{25}$ was measured from **3** as a mixture of diastereomers.
[h] The reaction was carried out at −25 °C (at 0 °C, ee 54%).




**Scheme 3.** Proposed mechanism for the formation of the 1,3-oxazolidine from **1**.

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## References and notes

1. (a) Takano, S.; Iwabuchi, Y.; Ogasawara, K. *J. Am. Chem. Soc.* **1987**, *109*, 5523–5524; (b) Sisko, J.; Weinreb, S. M. *J. Org. Chem.* **1991**, *56*, 3210–3211; (c) Sisko, J.; Henry, J. R.; Weinreb, S. M. *J. Org. Chem.* **1993**, *58*, 4945–4951; (d) Tanner, D. *Angew. Chem., Int. Ed. Engl.* **1994**, *33*, 599–619; (e) McCoull, W.; Davis, F. A. *Synthesis* **2000**, 1347–1365; (f) Yeung, Y.-Y.; Hong, S.; Corey, E. J. *J. Am. Chem. Soc.* **2006**, *128*, 6310–6311.
2. (a) Hu, X. E. *Tetrahedron* **2004**, *60*, 2701–2743, and references cited therein; (b) Minakata, S.; Okoda, Y.; Oderaotoshi, Y.; Komatsu, M. *Org. Lett.* **2005**, *7*, 3509–3512; (c) Ding, C. H.; Dai, L. X.; Hou, X. L. *Tetrahedron* **2005**, *61*, 9586–9593; (d) Zhu, W.; Cai, G.; Ma, D. *Org. Lett.* **2005**, *7*, 5545–5548; (e) Fukuta, Y.; Mita, T.; Fukudam, N.; Kanai, M.; Shibasaki, M. *J. Am. Chem. Soc.* **2006**, *128*, 6312–6313.
3. (a) Bergmeier, S. C.; Seth, P. P. *J. Org. Chem.* **1997**, *62*, 2671–2674; (b) Sweeney, J. B.; Cantrill, A. A. *Tetrahedron* **2003**, *59*, 3677–3690; (c) Sim, T. B.; Kang, S. H.; Lee, K. S.; Lee, W. K. *J. Org. Chem.* **2003**, *68*, 104–108; (d) D'hooghe, M.; Van Speybroeck, V.; Waroquier, M.; De Kimpe, N. *Chem. Commun.* **2006**, 1554–1556; (e) Couturier, C.; Blanchet, J.; Schlama, T.; Zhu, J. *Org Lett.* **2006**, *8*, 2183–2186.
4. (a) Bucciarelli, M.; Forni, A.; Moretti, I.; Prati, F.; Torre, G. *Tetrahedron: Asymmetry* **1995**, *6*, 2073–2080; (b) Concellón, J. M.; Riego, E.; Suárez, J. R.; García-Granda, S.; Díaz, M. R. *Org. Lett.* **2004**, *6*, 4499–4501; (c) Prasad, B. A. B.; Pandey, G.; Singh, V. K. *Tetrahedron Lett.* **2004**, *45*, 1137–1141, and references cited therein; (d) Wu, J.; Sun, X.; Xia, H.-G. *Tetrahedron Lett.* **2006**, *47*, 1509–1512; (e) Ney, J. E.; Wilfe, J. P. *J. Am. Chem. Soc.* **2006**, *128*, 15415–15422; (f) Ishii, K.; Sone, T.; Shigeyama, T.; Noji, M.; Sugiyama, S. *Tetrahedron* **2006**, *62*, 10865–10878.
5. (a) Yadav, V. K.; Sriramurthy, V. *J. Am. Chem. Soc.* **2005**, *127*, 16366–16367; (b) Lee, S.-H.; Han, T.-D.; Yu, K.; Ahn, K.-H. *Bull. Korean Chem. Soc.* **2001**, *22*, 449–450; (c) Gandhi, S.; Bisai, A.; Bhanu Prasad, B. A.; Singh, V. K. *J. Org. Chem.* **2007**. doi:10.1021/jo062564c. During the revision of our manuscript, this report appeared as an ASAP article where the authors proposed an $S_N1$ mechanism for the cycloaddition reaction of 2-aryl-*N*-tosylaziridines with carbonyl compounds.
6. (a) Ungureanu, I.; Bologa, C.; Chayer, S.; Mann, A. *Tetrahedron Lett.* **1999**, *40*, 5315–5318; (b) Ungureanu, I.; Klotz, P.; Mann, A. *Angew. Chem., Int. Ed.* **2000**, *39*, 4615–4617; (c) Ungureanu, I.; Klotz, P.; Schoenfelder, A.; Mann, A. *Tetrahedron Lett.* **2001**, *42*, 6087–6091.
7. (a) Ghorai, M. K.; Das, K.; Kumar, A.; Ghosh, K. *Tetrahedron Lett.* **2005**, *46*, 4103–4106; (b) Ghorai, M. K.; Ghosh, K.; Das, K. *Tetrahedron Lett.* **2006**, *47*, 5399–5403.
8. (a) Galvez-Ruiz, J. C.; Jaen-Gaspar, J. C.; Castellanos-Arzola, I. G.; Contreras, R.; Flores-Parra, A. *Heterocycles* **2004**, *63*, 2269–2285; (b) Cintrat, J. C.; Leat-Crest, V.; Parrain, J. L.; Le Grognee, E.; Beaudet, I.; Quintard, J. P. *Eur. J. Org. Chem.* **2004**, 4251–4267; (c) Huo, C. D.; Wei, R.; Zhang, W.; Yang, L.; Liu, Z. L. *Synlett* **2005**, 161–163; (d) Braga, A. L.; Sehnem, J. A.; Lüdtke, D. S.; Zeni, G.; Silveira, C. C.; Marchi, M. I. *Synlett* **2005**, 1331–1333.
9. (a) Calaza, M. I.; Paleo, M. R.; Sardina, F. J. *J. Am. Chem. Soc.* **2001**, *123*, 2095–2096; (b) Lee, S.-H.; Kim, Y. H. *Bull. Korean Chem. Soc.* **2005**, *26*, 225–226; (c) Tejedor, D.; Santos-Expósito, A.; González-Cruz, D.; Marrero-Tellado, J. J.; Gracía-Tellado, F. *J. Org. Chem.* **2005**, *70*, 1042–1045; (d) He, P.; Zhu, S. *Tetrahedron* **2005**, *61*, 6088–6096.
10. (a) Sriharsha, S. N.; Shashikanth, S. *Heterocycl. Commun.* **2006**, *12*, 213–218; (b) Li, Y. J.; Ye, F. *Chin. Chem. Lett.* **2006**, *17*, 891–894.
11. (a) Reddy, S. H. K.; Lee, S.; Datta, A.; Georg, G. I. *J. Org. Chem.* **2001**, *66*, 8211–8214; (b) Yoo, D.; Oh, J. S.; Kim, Y. G. *Org. Lett.* **2002**, *4*, 1213–1215; (c) Choi, W. J.; Ahn, H. S.; Kim, H. O.; Kim, S.; Chun, M. W.; Jeong, L. S. *Tetrahedron Lett.* **2002**, *43*, 6241–6243; (d) Huguenot, F.; Brigaud, T. *J. Org. Chem.* **2006**, *71*, 2159–2162.
12. (a) Agami, C.; Couty, F. *Eur. J. Org. Chem.* **2004**, 677–685; (b) Pastor, A.; Adam, W.; Wirth, T.; Gabor, T. *Eur. J. Org. Chem.* **2005**, 3075–3084; (c) Wünnemann, S.; Fröhlich, R.; Hoppe, D. *Org. Lett.* **2006**, *8*, 2455–2458.
13. (a) Soai, K.; Niwa, S. *Chem. Rev.* **1992**, *92*, 833–856; (b) Guangyou, Z.; Yuquing, L.; Zhaohui, W.; Nohira, H.; Hirose, T. *Tetrahedron: Asymmetry* **2003**, *14*, 3297–3300, and references cited therein; (c) Kim, S.-G.; Kim, K.-H.; Kim, Y. K.; Shin, S. K.; Ahn, K. H. *J. Am. Chem. Soc.* **2003**, *125*, 13819–13824; (d) Kamal, A.; Khanna, G. B. R.; Krishnaji, T.; Tekumalla, V.; Ramu, R. *Tetrahedron: Asymmetry* **2005**, *16*, 1485–1494, and references cited therein.
14. (a) Howe, R.; Rao, B. S. *J. Med. Chem.* **1968**, *11*, 1118–1120, and references cited therein; (b) Horri, S.; Fukase, H.; Matsuo, T.; Kameda, Y.; Asano, N.; Matsui, K. *J. Med. Chem.* **1986**, *29*, 1038–1046; (c) Knapp, S. *Chem. Rev.* **1995**, *95*, 1859–1876.
15. (a) Izumi, T.; Fukaya, K. *Bull. Chem. Soc. Jpn.* **1993**, *66*, 1216–1221; (b) Lohse, O.; Spöndlin, C. *Org. Process Res. Dev.* **1997**, *1*, 247–249; (c) Andersson, M. A.; Epple, R.; Fokin, V. V.; Sharpless, K. B. *Angew. Chem., Int. Ed.* **2002**, *41*, 472–475; (d) Watanabe, M.; Murata, K.; Ikariya, T. *J. Org. Chem.* **2002**, *67*, 1712–1715.
16. (a) Experimental procedure for the $Cu(OTf)_2$ mediated [3+2] cycloaddition of (*R*)-2-phenyl-*N*-tosylaziridine with carbonyl compounds: A solution of (*R*)-**1** (0.091 mmol) in aldehyde or ketone (0.5 mL) was added to a suspension of anhydrous $Cu(OTf)_2$ (0.091 mmol) in the same carbonyl compound at 0 °C under an argon atmosphere. The mixture was stirred for 5–10 min and then the reaction was quenched with saturated $NaHCO_3$ solution at the same temperature. The aqueous layer was extracted with $CH_2Cl_2$ ($3 \times 5.0$ mL) and dried over anhydrous $Na_2SO_4$. The crude product was purified by flash column chromatography on silica gel (230–400 mesh) using a mixture of ethyl acetate in petroleum ether to provide the corresponding 1,3-oxazolidine. With solid carbonyl compounds or racemic aziridines, the reaction was performed in dry $CH_2Cl_2$ using 5 equiv of the carbonyl compound.

Spectral data of **3a** ($R^1$, $R^2 = CH_3$): White solid; mp: 98–101 °C; $^1$H NMR (400 MHz, $CDCl_3$): $\delta$ (ppm) 1.61 (s, 3H), 1.66 (s, 3H), 2.35 (s, 3H), 3.04–3.09 (m, 1H), 3.79 (dd, $J = 8.8$, 5.6 Hz, 1H), 5.03 (dd, $J = 9.5$, 5.6 Hz, 1H), 7.19–7.28 (m, 7H), 7.67 (d, $J = 8.0$ Hz, 2H); $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$ (ppm) 21.5, 27.0, 27.5, 54.0, 76.2, 97.3, 126.2, 127.3, 128.5, 128.6, 129.6, 137.3, 137.4, 143.4; IR $\nu_{max}$ (KBr, $cm^{-1}$) 3068, 3034, 2985, 2935, 2877, 1774, 1753, 1569, 1430, 1335, 1295, 1249, 1213, 1153, 1095, 1022, 951; FAB mass: *m/z* 332 ($M^+$+1). Anal. Calcd (%) for $C_{18}H_{21}NO_3S$: C, 65.23; H, 6.39; N, 4.23. Found (%): C, 65.25, H, 6.67, N, 4.28; $[\alpha]_D^{25}$ +21 (*c* 0.21, $CHCl_3$); The enantiomeric excess was determined by chiral HPLC analysis (Chiralcel OD-H column, *i*PrOH/hexane, 3:97, 0.80 mL $min^{-1}$), 74% (ee).

Spectral data of **3l** (Ar = 4-$MeC_6H_4$; $R^1$, $R^2 = CH_3$): $^1$H NMR (400 MHz, $CDCl_3$): $\delta$ 1.59 (s, 3H), 1.66 (s, 3H), 2.25 (s, 3H), 2.35 (s, 3H), 3.03–3.07 (m, 1H), 3.76 (dd, $J = 8.6$, 5.6 Hz, 1H), 5.00 (dd, $J = 9.5$, 5.6 Hz, 1H), 7.05–7.23 (m, 6H), 7.67 (d, $J = 8.3$ Hz, 2H); $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$ 21.2, 21.5, 27.1, 27.5, 54.0, 76.2, 97.3, 126.2, 127.3, 129.2, 129.6, 134.3, 137.3, 138.4, 143.4.; ES mass: *m/z* 346 ($M^+$+1). Anal. Calcd (%) for $C_{19}H_{23}NO_3S$: C, 66.06, H, 6.71, N, 4.05. Found (%): C, 66.18, H, 6.69, N, 4.25.; (b) The decreased yield of isolated 1,3-oxazolidine was due to hydrolysis during work-up or column chromatographic purification which was necessary for preparing an analytical sample; (c) General experimental procedure for the cleavage of 1,3-oxazolidines: The 1,3-oxazolidines derived from (*R*)-**1** with various carbonyl compounds were hydrolyzed using PTSA in MeOH at room temperature, to give **4** in quantitative yields. Compound **3a** (ee 74%) gave (*S*)-1-phenyl-2-(tosylamino)-ethanol (**4**) in quantitative yield with 68% ee. Spectral data of **4** (Ar = Ph): IR $\nu_{max}$ (KBr, $cm^{-1}$) 3429, 3276, 3175, 2922, 2856,1597, 1491, 1448, 1407, 1323, 1151, 1093, 1063, 1029, 925; $^1$H NMR (400 MHz, $CDCl_3$): $\delta$ (ppm) 2.34 (s, 3H), 2.94 (dd, $J = 13.2$, 8.8 Hz, 1H), 3.16 (dd, $J = 13.2$, 3.4 Hz, 1H), 4.72 (dd, $J = 8.7$, 3.6 Hz, 1H), 5.1 (s, 1H) 7.18–7.27 (m, 7H), 7.65 (d, $J = 8.3$ Hz, 2H); $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$ (ppm) 21.5, 50.2, 72.7, 125.8, 127.0, 128.2, 128.6, 129.7, 136.6, 140.7, 143.6; ES mass: *m/z* 292 ($M^+$+1). Anal. Calcd (%) for $C_{15}H_{17}NO_3S$: C, 61.83, H, 5.88, N, 4.81; Found (%): C, 61.80, H, 5.86, N, 4.82, $[\alpha]_D^{25}$ +33.2 (*c* 0.50, $CHCl_3$). The enantiomeric excess was determined by chiral HPLC analysis (Chiralcel OD-H column, *i*PrOH/hexane, 10:90, 1.0 mL $min^{-1}$).

17. (a) McKennon, M. J.; Meyers, A. I. *J. Org. Chem.* **1993**, *58*, 3568–3571; (b) Cernerud, M.; Adolfsson, H.; Moberg, C. *Tetrahedron: Asymmetry* **1997**, *8*, 2655–2662.
18. (a) As the reaction of **1** with benzaldehyde approaches rt, the initially formed cis isomer was converted to the trans isomer and the dr (cis:trans) changes to 72:38 (at ~10 °C). When the reaction was performed in aldehyde medium at rt, the observed dr was 1.22:1.0 (cis:trans). The enantioselectivity of product **3f** increased up to 62% when the reaction was carried out at −25 °C. There was no change in ee upon further lowering of the reaction temperature; (b) Decrease in ee is probably due to partial racemization of the product at the benzylic position in acidic medium.