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Enantioselective aziridination reaction of α,β-unsaturated aldehydes using an organocatalyst and *tert*-butyl *N*-arenesulfonyloxycarbamates

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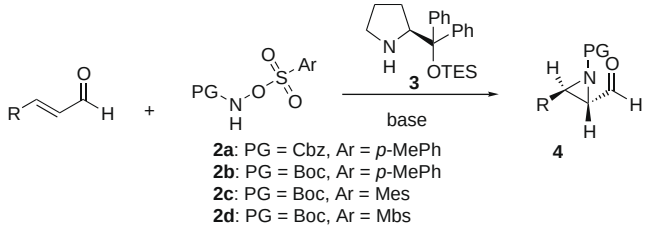
ABSTRACT

An organocatalytic enantioselective aziridination reaction of α,β-unsaturated aldehydes including aromatic substrates using *N*-arenesulfonyloxycarbamates in the presence of diphenylprolinol triethylsilyl ether and sodium carbonate or sodium acetate is described.

Chiral aziridines are useful synthetic intermediates with one stereogenic center or two stereogenic centers, which are effectively used for the synthesis of amino acids, natural products, and pharmaceuticals.[1–3] In this context, the development of a method for the simple preparation of chiral aziridines from commercially available starting materials is of significant interest.[4,5] Recently, the organocatalytic asymmetric aziridination of α,β-unsaturated aldehydes using *N*-acetyloxycarbamate has been reported.[6,7] This method is an efficient procedure with a high enantioselectivity. However, the yields and diastereoselectivities are insufficient and need to be improved. In addition, the range of the substrates is restricted to aliphatic α,β-unsaturated aldehydes, and the reaction of aromatic α,β-unsaturated aldehydes has never been reported.

We have been working on the synthesis of functionalized amino acids and naturally occurring cyclodepsipeptides.[8] As part of this research, we now describe an organocatalytic enantioselective aziridination reaction of α,β-unsaturated aldehydes including aromatic substrates using *N*-arenesulfonyloxycarbamates[9] as a source of nitrogen (Scheme 1). These carbamates are mostly stable crystalline solids and have been already used in aziridination reactions via nitrene addition reactions, base-catalyzed tandem Michael-substitution reactions, and metal-catalyzed aziridination reactions.[10] However, there are no reports on the use of *N*-arenesulfonyloxycarbamates in secondary amine-catalyzed enantioselective aziridination reactions.



Scheme 1. Enantioselective aziridination reaction using *N*-arenesulfonyloxycarbamates.

Our investigation commenced with the optimization of the aziridination reaction using 2-hexen-1-al (**1a**), benzyl *N*-toluenesulfonyloxycarbamate (**2a**), and (*S*)-diphenylprolinol triethylsilyl ether[11] (**3**), and the results are summarized in Table 1. Since the presence of a base was essential for this aziridination reaction (entry 2), we examined the background reaction without the organocatalyst. The reaction was sluggish, but gave the racemic aziridine **4a** in low yield with a trans/cis ratio of 86/14 (entry 1). Fortunately, the aziridination reaction using 20 mol % (*S*)-**3** in the presence of sodium carbonate (3 equiv) in methylene chloride at room temperature proceeded in a stereoselective manner to afford the aziridine **4a** in 38% yield and in an enantiomeric excess of 99% ee with a high level of diastereoselectivity[12] (entry 3). The enantiomeric excess was determined after derivatization of **4a** into the ester **5a** in two steps by its HPLC analysis. Since there was a poor reproducibility for the chemical yield, we carried out the optimization of the reaction conditions. For the examination of the reaction solvents, methylene chloride was the solvent of choice for this aziridination reaction and toluene also gave the product with a comparable stereoselectivity (entries 4–7). A slight excess of the substrate was essential for a smooth reaction and good chemical yield. Other bases, such as sodium acetate and potassium acetate, produced comparable results (entries 8–9). Finally, the serious problem of the reproducibility was solved using *tert*-butyl *p*-toluenesulfonyloxycarbamate (**2b**) as the nucleophile (entry 10). Although the second channel, the background sodium carbonate-catalyzed reaction, exists and should cause a low enantioselectivity, it is very interesting that the asymmetric aziridination reaction proceeds with a high enantioselectivity and diastereoselectivity.

Using the conditions of entry 10 in Table 1, other aliphatic α,β-unsaturated aldehydes were examined, and the results are summa-

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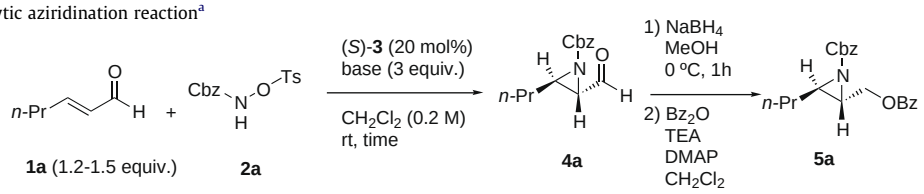
Table 1
Optimization of organocatalytic aziridination reaction[a]

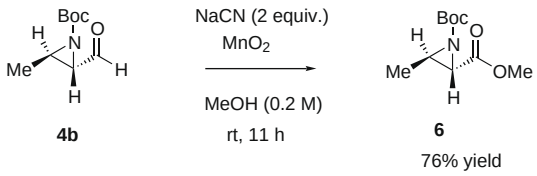


1a (1.2-1.5 equiv.) **2a** **4a** **5a**

Entry	Base	Solvent	Time (h)	Yield (%)	Trans/cis	% ee[b]
1[c]	Na_2CO_3	CH_2Cl_2	25	—[d]	86/14	—
2	—	CH_2Cl_2	24	nr[e]	—	—
3	Na_2CO_3	CH_2Cl_2	3.5	38	>99/1	99
4	Na_2CO_3	DMSO	2	26	91/9	52.7
5	Na_2CO_3	CH_3CN	24	36	88/12	30.5
6	Na_2CO_3	THF	23	8	83/17	—
7	Na_2CO_3	$PhCH_3$	4	54	95/5	94.4
8	NaOAc	CH_2Cl_2	0.5	69	94/6	97.8
9	KOAc	CH_2Cl_2	0.5	48	96/4	99.4
10[f]	Na_2CO_3	CH_2Cl_2	3.5	60	97/3	98

[a] The reaction was carried out using 2-hexen-1-al (excess) and the carbamate **2a** (1 equiv) in the presence of (*S*)-**3** (0.2 equiv) and base (3 mol equiv).
[b] The enantiomeric excess was determined after conversion of **4a**–**5a**.
[c] The reaction was carried out without (*S*)-**3**.
[d] A 1:6.2 mixture of **4a** and **1a** was obtained.
[e] No reaction.
[f] *tert*-Butyl *p*-toluenesulfonyloxycarbamate (**2b**) was used instead of **2a**.

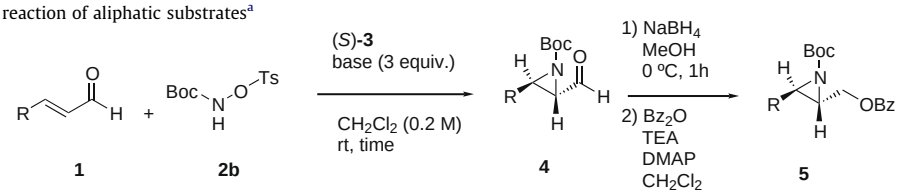
rized in Table 2. The crotonaldehyde (**1b**) afforded aziridine **4b** in good yield and 96.4% ee as an inseparable trans/cis mixture of 91/9 (entry 2). An excess amount of the substrate was again essential for a smooth reaction. Under the conditions using a large excess amount of crotonaldehyde, the reaction proceeded even at the 5 mol % amount of (*S*)-**3** to afford **4b** in a similar yield and stereoselectivity (entry 3). The obtained aziridine **4b** was directly oxidized with activated manganese dioxide in the presence of sodium cyanide in methanol to give the methyl ester **6** in good yield (Scheme 2). Although the preparation of esters by the oxidation of α,β-unsaturated aldehydes and benzylic aldehydes with activated manganese dioxide is a well-known procedure,[13] to the best of our knowledge, this is the first example of the directed formation of an ester from an aziridine aldehyde, a saturated aldehyde, using activated manganese dioxide. The fumaric acid methyl ester half aldehyde (**1c**), a substrate with an electron-withdrawing



4b **6** 76% yield

Scheme 2.

Table 2
Enantioselective aziridination reaction of aliphatic substrates[a]



1 **2b** **4** **5**

Entry	**1** (equiv)	Cat. (*S*)-**3** (mol %)	Base	Time (h)	Yield[b] (%)	Trans/cis	% ee[c]
1	**1a**: R = *n*-Pr (1.5)	20	Na_2CO_3	3.5	60[d]	97/3	98
2	**1b**: R = Me (2.5)	20	Na_2CO_3	3	62[d]	91/9	96.4
3	**1b**: R = Me (5)	5	NaOAc	3	73[d]	91/9	97.8
4	**1c**:R = CO_2Me (1)	10	Na_2CO_3	11	61[e]	>99/1	98
5	**1c**: R = CO_2Me (1)	30	NaOAc	2.5	71[e]	>99/1	92.3
6	**1d**: R = cyclohexyl (1)	30	NaOAc	4	51[d]	90/10	92
7	**1e**: R = H (5.2)	20	Na_2CO_3	6	58		91
8	**1e**: R = H (2.2)	20	K_2CO_3	2	37		48
9	**1e**: R = H (5.2)	20	NaOAc	2	58		72
10[f]	**1e**: R = H (5.2)	20	Na_2CO_3	2.5	66		94

[a] The reaction was carried out using α,β-unsaturated aldehyde (excess) and *p*-toluenesulfonyloxycarbamate (1 equiv) in the presence of (*S*)-**3** (0.05–0.3 equiv, see table) and base (3 mol equiv) in methylene chloride at room temperature.
[b] Yield based on **2b**.
[c] Enantiomeric excess after conversion to ester **5**.
[d] Yield of a trans/cis mixture.
[e] Yield after reduction with sodium borohydride in two steps.
[f] Compound **2c** was used instead of **2b**.

group, was reactive for the present aziridination reaction and produced the aziridine **4c**, which was isolated after the conversion to the corresponding alcohol in 61% yield and 98% ee with complete diastereoselectivity (entry 4). 3-Cyclohexyl-2-propenal (**1d**) with a secondary alkyl group had a low reactivity. In the case of a slow reacting substrate, sodium acetate was the base of choice for avoiding the decomposition of the carbamate. In the presence of a 30 mol % catalyst and sodium acetate (3 equiv), the reaction of **1d** afforded the aziridine **4d** in 51% yield and 92% ee as an inseparable trans/cis mixture of 90/10 (entry 6).

We next examined the asymmetric aziridination reaction of acrolein (**1e**), the simplest substrate. The enantioselectivity was dependent on the base and the nitrogen source. Sodium carbonate was again the base of choice (entries 7–9), and the bulky *tert*-butyl mesitylenesulfonyloxycarbamate (**2c**) maximized the enantioselectivity to afford the product **4e** in 66% yield and 94% ee (entry 10). The result of the enantioselective aziridination reaction of **1e** is noteworthy because the obtained **4e** is a useful building block for the preparation of unusual amino acids and natural products, which has been conventionally prepared from serine in several steps.[14]

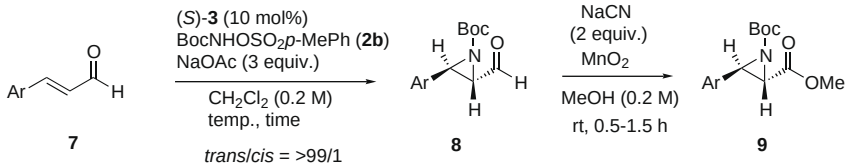
Next, the enantioselective aziridination of aromatic α,β-unsaturated aldehydes were examined as shown in Table 3. Although we first examined the reaction of cinnamaldehyde (**7a**) and **2b** using the above optimized conditions, **7a** was a difficult substrate due to the low reactivity. In addition, the corresponding aziridine **8a** was sensitive to silica gel, which resulted in the decomposition of **8a** during the silica gel purification. To avoid this inherent problem, **8a** was directly converted to the corresponding methyl ester **9a** by oxidation using activated manganese dioxide in the presence of sodium cyanide and methanol, which was stable to silica gel purification.

After some experiments, the use of sodium acetate and *tert*-butyl *N*-*p*-methoxybenzenesulfonyloxycarbamate (**2d**) instead of sodium carbonate and **2b** affected the reaction to afford **9a** in a good yield with an excellent stereoselectivity (entry 2). The absolute stereochemistry of **9a** was unambiguously confirmed after the hydrogenolysis of **9a** to the *N*-*tert*-butoxycarbonyl-(*S*)-phenylalanine methyl ester by its comparisons to the authentic sample.

The substrate with an electron-donating group at an aromatic nucleus did not react under the above conditions (entry 3). The reaction of *p*-methoxycinnamaldehyde (**7b**) with **2b** in the presence of sodium acetate resulted in the recovery of the starting aldehyde and in the complete decomposition of **2b**. However, the substituted cinnamaldehydes with an electron-withdrawing group at an aromatic nucleus were excellent substrates, and they smoothly reacted with **2b** in the presence of sodium acetate to yield the corresponding aziridines in good to excellent yields with high levels of diastereoselectivity and enantioselectivity (entries 4–18), which could be isolated by silica gel chromatographic purification. In particular, the nitrocinnamaldehydes (**7e**–**7g**) reacted with 1–1.2 equivalent of **2b** to furnish the corresponding aziridines **8e**–**8g** in high yields (entries 8–12).[15] The aziridination reaction of the β-(3-pyridyl)-α,β-unsaturated aldehyde (**7j**) with **2b** (1.2 equiv) also proceeded to give the product **8j** in a 77% yield and 98.7% ee.

In conclusion, we have succeeded in the development of the enantioselective aziridination reaction of α,β-unsaturated aldehydes using *N*-arenesulfonyloxycarbamates in the presence of sodium carbonate or sodium acetate. The present reaction is an

Table 3
Enantioselective aziridination reaction of aromatic substrates[a]



7 8 9

Entry	Ar	Equiv of **2b**	Temp (°C)	Time (h)	Yield (%) of 8[b]	Yield (%) of 9	% ee[c]
1	Ph (**7a**)	1.2	rt	1.2	–	14[d]	97.9
2	Ph (**7a**)	1.2[e]	rt	2	–	41[d]	97
3[f]	*p*-MeOPh (**7b**)	1	rt	1.5	–[g]	–	–
4[h]	*p*-TfOPh (**7c**)	1	4	1	68	38	93.6[i]
5	*p*-TfOPh (**7c**)	1	−20	7.5	75	57	99
6[h]	*p*-TsOPh (**7d**)	1	4	1	48	49	95.5[i]
7	*p*-TsOPh (**7d**)	1	−20	22.5	57	52	94.7
8	*p*-NO_2Ph (**7e**)	1	−20	8	82	55	98.1
9[h]	*m*-NO_2Ph (**7f**)	1.2	4	2.5	99	49	95.8[i]
10	*m*-NO_2Ph (**7f**)	1.2	−20	13	97	46	98.7
11[h]	*o*-NO_2Ph (**7g**)	1.2	4	2.5	77	43	97.2[i]
12	*o*-NO_2Ph (**7g**)	1.2	−20	23.5	90	40	96.7
13[h]	*p*-FPh (**7h**)	1.2	4	6.5	61	37	84.4[i]
14	*p*-FPh (**7h**)	1.2	−20	18.5	32	30	94.2
15[h]	*p*-CF_3Ph (**7i**)	1.2	4	1.5	84	63	84.5[i]
16	*p*-CF_3Ph (**7i**)	1.2	−20	23	72	58	97.2
17[h]	3-Pyridyl (**7j**)	1.2	4	3	94	66	90.4[i]
18	3-Pyridyl (**7j**)	1.2	−20	14	77	62	98.7

[a] The reaction was carried out using the α,β-unsaturated aldehyde (1 equiv) and the carbamate (1–1.2 equiv) in the presence of the catalyst (0.1 equiv) and sodium acetate (3 equiv) in methylene chloride.
[b] Yield based on **7**.
[c] Enantiomeric excess after the conversion to the methyl ester **9**.
[d] Yield in two steps.
[e] The carbamate **2d** was used instead of **2b**.
[f] The reaction was carried out using the substrate (1.8 equiv) and the catalyst (19 mol %) in $CHCl_3$.
[g] The substrate was recovered.
[h] (*R*)-Catalyst **3** was used instead of the (*S*)-catalyst.
[i] The (2*R*,3*R*)-isomer **8** was obtained.

efficient method applicable to aliphatic aldehydes, acrolein, and aromatic aldehydes, and it proceeds with a high diastereoselectivity and excellent enantioselectivity. Further investigations on the applications to the synthesis of unusual amino acids and natural products are now underway.

References and notes

1. For a review of aziridines, see: Sweeney, J. B. *Chem. Soc. Rev.* **2002**, *32*, 247–248.
2. For reviews on the synthesis of aziridines, see: (a) Halfen, J. A. *Curr. Org. Chem.* **2005**, *9*, 657–669; (b) Muller, P.; Fruit, C. *Chem. Rev.* **2003**, *103*, 2905–2919; (c) Osborn, H. M. I.; Sweeney, J. B. *Tetrahedron: Asymmetry* **1997**, *8*, 1693–1715.
3. For synthetic applications of aziridines, see: (a) Hu, X. E. *Tetrahedron* **2004**, *60*, 2701–2743; (b) McCoull, M.; Davis, F. A. *Synthesis* **2000**, *10*, 1347–1365; (c) Zwanenburg, B.; ten Holte, P. *Top. Curr. Chem.* **2001**, *216*, 93–124.
4. For recent examples of enantioselective aziridination, see: (a) Yamawaki, M.; Tanaka, M.; Abe, T.; Anada, M.; Hashimoto, S. *Heterocycles* **2007**, *72*, 709–721; (b) Wang, X.; Ding, K. *Chem. Eur. J.* **2006**, *12*, 4568–4575; (c) Ma, L.; Jiao, P.; Zhang, Q.; Xu, J. *Tetrahedron: Asymmetry* **2005**, *16*, 3718–3734; (d) Ma, L.; Du, D.-M.; Xu, J. *J. Org. Chem.* **2005**, *70*, 10155–10158; (e) Xu, J.; Ma, L.; Jiao, P. *Chem. Commun.* **2004**, 1616–1617; (f) Omura, K.; Murakami, M.; Uchida, T.; Irie, R.; Katsuki, T. *Chem. Lett.* **2003**, *32*, 354–355.
5. For recent examples of organocatalytic aziridinations, see: (a) Shen, Y.-M.; Zhao, M.-X.; Xu, J.; Shi, Y. *Angew. Chem., Int. Ed.* **2006**, *45*, 8005–8008; (b) Armstrong, A.; Baxter, C. A.; Lamon, S. G.; Pape, A. R.; Wincewics, R. *Org. Lett.* **2007**, *9*, 351–353; (c) Minakata, S.; Murakami, Y.; Tsuruoka, R.; Kitanaka, S.; Komatsu, M. *Chem. Commun.* **2008**, 6363–6365.
6. Vesely, J.; Ibrahem, I.; Zhao, G.-L.; Rios, R.; Cordova, A. *Angew. Chem., Int. Ed.* **2007**, *46*, 778–781.
7. For reviews on organocatalysts, see: (a) Pellissier, H. *Tetrahedron* **2007**, *63*, 9267–9331; (b) Kotsuki, H.; Ikishima, H.; Okuyama, A. *Heterocycles* **2008**, *75*, 493–529; Kotsuki, H.; Ikishima, H.; Okuyama, A. *Heterocycles* **2008**, *75*, 757–797; (c) Mielgo, A.; Palomo, C. *Chem. Asian J.* **2008**, *3*, 922–948;.
8. For recent examples, see: (a) Hara, S.; Makino, K.; Hamada, Y. *Pept. Sci. 2005* **2006**, 39–42; (b) Hara, S.; Makino, K.; Hamada, Y. *Tetrahedron Lett.* **2006**, *47*, 1081–1085; (c) Makino, K.; Jiang, H.; Suzuki, T.; Hamada, Y. *Tetrahedron: Asymmetry* **2006**, *17*, 16441649; (d) Yoshitomi, Y.; Makino, K.; Hamada, Y. *Org. Lett.* **2007**, *9*, 2457–2460; (e) Hara, S.; Nagata, E.; Makino, K.; Hamada, Y. *Pept. Sci. 2007* **2008**, 27–30.
9. Carpino, L. A. *J. Am. Chem. Soc.* **1960**, *82*, 3133–3135.
10. For aziridinations using *N*-arenesulfonyloxycarbamates, see: (a) Lwowski, W.; Mairich, T. J. *J. Am. Chem. Soc.* **1965**, *87*, 3630–3637; (b) Banks, M. R.; Blake, A. J.; Cadogan, J. I. G.; Dawson, I. M.; Gosney, I.; Grant, K. J.; Gaur, S.; Hodgson, P. K. G.; Knight, K. S.; Smith, G. W. *Tetrahedron* **1992**, *48*, 7979–8006; (c) Fioravanti, S.; Morreale, A.; Pellacani, L.; Tardella, P. A. *Synthesis* **2001**, *13*, 1975–1978; (d) Fioravanti, S.; Morreale, A.; Pellacani, L.; Tardella, P. A. *Eur. J. Org. Chem.* **2003**, *23*, 4549–4552; (e) Fioravanti, S.; Morreale, A.; Pellacani, L.; Tardella, P. A. *Synlett* **2004**, 1083–1085; (f) Fioravanti, S.; Colantoni, D.; Pellacani, L.; Tardella, P. A. *J. Org. Chem.* **2005**, *70*, 3296–3298; (g) Mohr, F.; Binfield, S. A.; Fettinger, J. C.; Vedernikov, A. N. *J. Org. Chem.* **2005**, *70*, 4833–4839; (h) Lebel, H.; Huard, K.; Lectard, S. *J. Am. Chem. Soc.* **2005**, *127*, 14198–14199; (i) Lebel, H.; Lectard, S.; Parmentier, M. *Org. Lett.* **2007**, *9*, 4797–4800; (j) Pesciaioli, F.; De Vincentiis, F.; Galzerano, P.; Bencivenni, G.; Bartoli, G.; Mazzanti, A.; Melchiorre, P. *Angew. Chem., Int. Ed.* **2008**, *47*, 8703–8706.
11. Hayashi, Y.; Gotoh, H.; Hayashi, T.; Shoji, M. *Angew. Chem., Int. Ed.* **2005**, *44*, 4212–4215.
12. Although *N*-arenesulfonyloxycarbamates afforded aziridine aldehydes with a high diastereoselectivity, the origin of the high diastereoselectivity is unclear.
13. Corey, E. J.; Gilman, N. W.; Ganem, B. E. *J. Am. Chem. Soc.* **1968**, *90*, 5616–5617.
14. For ester derivatives of **4e**, see: Nakajima, K.; Takai, F.; Tanaka, T.; Okawa, K. *Bull. Chem. Soc. Jpn* **1978**, *51*, 1577–1578. and; Sato, K.; Kozikowski, A. P. *Tetrahedron Lett.* **1989**, 4073–4076.
15. Typical procedure: To a stirred solution of (*S*)-**3** (7.4 mg, 0.02 mmol), 3-nitrocinnamaldehyde (**7f**, 35.4 mg, 0.20 mmol), and sodium acetate (49.3 mg, 0.60 mmol) in methylene chloride (1.0 mL) at −20 °C was added *tert*-butyl *p*-toluenesulfonyloxycarbamate (**2b**, 69.0 mg, 0.24 mmol). After stirring the mixture at −20 °C for 13 h, the reaction mixture was diluted with ethyl acetate, washed with saturated aqueous sodium hydrogen carbonate and brine, dried over sodium sulfate, filtered, and concentrated in vacuo. The residue was purified by silica gel column chromatography (*n*-hexane/ethyl acetate = 4/1) to give aziridine **8f** (56.8 mg, 97%) as a yellow oil: $[\alpha]_D^{21}$ +95.5 (*c*0.54, $CHCl_3$); IR (neat) 1727, 1532, 1351, 1155 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.50 (9H, s), 3.31 (1H, dt, *J* = 1.1, 2.4 Hz), 3.94 (1H, d, *J* = 2.2 Hz), 7.56 (1H, dt, *J* = 1.1, 8.8 Hz), 7.67 (1H, dd, *J* = 1.1, 7.7 Hz), 8.19–8.21 (2H, m), 9.49 (1H, dd, *J* = 1.1, 3.3 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 27.8, 44.3, 49.9, 83.4, 121.4, 123.5, 129.7, 132.5, 137.2, 148.4, 157.6, 193.2; HRMS (FAB, NPOE) calcd for $C_{14}H_{17}N_2O_5$ 293.1137 ($M+H^+$), found 293.1158. The enantiomeric excess was determined after conversion into the corresponding methyl ester **9f**. To a stirred solution of **8f** (51.0 mg, 0.17 mmol) and sodium cyanide (17.3 mg, 0.35 mmol) in methanol (0.87 mL) at 0 °C was added activated manganese dioxide (255 mg). After stirring the mixture at 0 °C for 40 min, the reaction mixture was diluted with ethyl acetate and filtered through a pad of Celite. The filtrate was concentrated in vacuo. The residue was diluted with ether, washed with saturated aqueous ammonium chloride and brine, dried over sodium sulfate, filtered, and concentrated in vacuo. The residue was purified by silica gel chromatography (*n*-hexane/ethyl acetate = 9/1) to give aziridine methyl ester **9f** (25.7 mg, 46%, 99% ee, dr >99/1) as a colorless oil: $[\alpha]_D^{19}$ +45.4 (*c*1.05, $CHCl_3$); IR (neat) 1729, 1532, 1439, 1350, 1208, 1149 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.49 (9H, s), 3.09 (1H, d, *J* = 2.4 Hz), 3.84 (3H, s), 3.93 (1H, d, *J* = 2.2 Hz), 7.54 (1H, t, *J* = 7.7 Hz), 7.67 (1H, dt, *J* = 1.1, 7.7 Hz), 8.16–8.20 (2H, m); ^{13}C NMR (100 MHz, $CDCl_3$) δ 27.9, 43.6, 44.3, 52.9, 82.8, 121.5, 123.3, 129.6, 132.6, 137.7, 148.5, 157.7, 167.2; HRMS (FAB, NBA) calcd for $C_{15}H_{18}N_2NaO_6$ 345.1063 ($M+Na^+$), found 345.1086. HPLC analysis: CHIRALCEL OD-H, (*n*-hexane/*i*-PrOH = 90/10, 1.0 mL/min), t_R = 10.7 min (minor) and 13.6 min (major).