JACS
JOURNAL OF THE AMERICAN CHEMICAL SOCIETY

Communication

pubs.acs.org/JACS

Catalytic Asymmetric Ring Openings of Meso and Terminal Aziridines with Halides Mediated by Chiral 1,2,3-Triazolium Silicates

Kohsuke Ohmatsu, Yuta Hamajima, and Takashi Ooi*

Department of Applied Chemistry, Graduate School of Engineering, Nagoya University, Nagoya, 464-8603, Japan

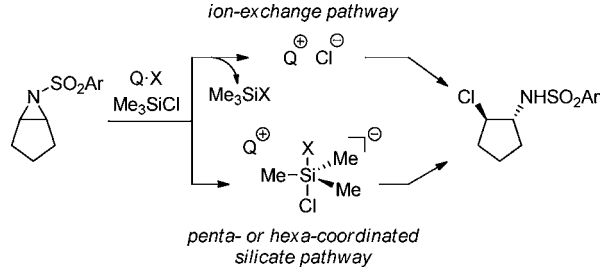
Supporting Information

ABSTRACT: Catalytic asymmetric chloride and bromide ring openings of meso aziridines with trimethylsilyl halides have been developed using modular chiral 1,2,3-triazolium chlorides as catalysts. Control experiments suggest the reaction pathway involving hypervalent silicate ions as reactive intermediates. The application of this system to the efficient kinetic resolution of terminal aziridines is also reported.

Extra-coordinated silicon species, called hypervalent silicates, play important roles as reagents and intermediates in synthetic organic chemistry.[1] Owing to their enhanced reactivity, significant progress has been made in the development of catalytic asymmetric reactions that proceed through the intermediacy of penta- or hexacoordinated silicates.[2] One of the attractive features of the silicate-based methodologies is the allowance of asymmetric transformations with otherwise difficult-to-use nucleophiles, such as halide ions,[3,4] under mild conditions, making it feasible to rapidly construct optically active halogen-containing organic molecules.[5] For instance, the combined use of chlorosilanes and chiral Lewis base catalysts offers the fruitful opportunity of employing chloride ions as nucleophiles for asymmetric bond-forming processes.[6,7] In fact, since the pioneering work by Denmark and co-workers,[6a] several elegant studies have been reported on the design of chiral catalysts for chlorosilicate-mediated stereoselective reactions. However, despite the potential synthetic utility of halosilicates, their successful applications have been limited to the asymmetric ring openings of meso epoxides using the highly reactive silicon tetrachloride ($SiCl_4$). Herein, we describe the highly enantioselective chloride and bromide ring openings of aziridines based on the use of trimethylsilyl halides as a stoichiometric halide source in combination with chiral 1,2,3-triazolium chlorides as catalysts.[8] This new catalytic system is effective not only for the desymmetrization of meso aziridines[4,9] but also for the kinetic resolution of terminal aziridines,[10,11] including the hitherto unknown kinetic resolution of differently 2,2-disubstituted aziridines. In addition, this study shows the importance of chiral triazolium halosilicates as a reactive intermediate, thereby providing mechanistic insight into ion-pair catalysis with silicon-based nucleophiles.

Ring opening of *N*-protected aziridines with trimethylsilyl chloride can be promoted by tetrabutylammonium fluoride (TBAF), affording *trans*-β-chloroamine derivatives in nearly quantitative yields.[12] In the reactions of silicon-based nucleophiles catalyzed by onium salts possessing relatively hard, basic anions such as fluoride or phenoxide ions, there are two possible mechanistic scenarios (Scheme 1). One is the ion-exchange reaction pathway, where the interaction of the silyl compound with Lewis basic anions (X) leads to the exclusion of Me_3SiX, generating requisite yet reactive ion pairs. The other mechanism involves the formation of onium silicate as a key intermediate.[1,13] Although the latter, silicate-mediated pathway is conceivable, reactions of this type are often believed to proceed through the ion-exchange pathway.[14] If this ion-exchange mechanism is operative in the chloride ring opening of aziridines, onium chloride itself should be reactive enough to effect C−N bond cleavage by the chloride ion transfer. To examine this possibility, we attempted the reaction of *N*-*p*-*tert*-butylbenzenesulfonyl aziridine **2a** with L-phenylalanine-derived, chiral 1,2,3-triazolium chloride **1a**·Cl (see the scheme for Table 1).[8] As shown in Scheme 2, treatment of **2a** with 1 equiv of **1a**·Cl in toluene at −40 °C for 12 h did not result in the formation of a detectable amount of the desired ring-opening product **3a**. The exposure of **2a** to a stoichiometric quantity of trimethylsilyl chloride (Me_3SiCl) led to an essentially quantitative recovery of the starting material. In contrast, the ring-opening reaction of **2a** was promoted by the combined use of a catalytic amount of **1a**·Cl and Me_3SiCl (1.2 equiv), giving **3a** in 35% isolated yield even with an appreciable level of enantioselectivity (65% ee). These results indicate that the hypervalent chlorosilicate acts as a reactive intermediate in this desymmetrization reaction. The intervention of the chlorosilicate was also supported by the ^{29}Si NMR spectroscopic analysis of a 1:1 mixture of **1a**·Cl and Me_3SiCl in toluene-d_8; this showed a single peak at δ = 6.6 ppm, which is considerably shifted upfield from the original signal of Me_3SiCl (29.5

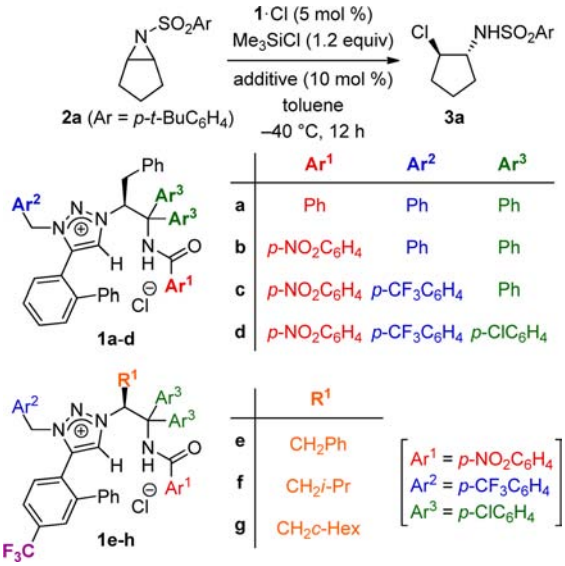
Scheme 1. Two Possible Reaction Pathways for Chloride Ring Opening of Aziridines Catalyzed by Onium Salts (Q·X)



Received: March 24, 2012
Published: May 14, 2012

   dx.doi.org/10.1021/ja3028668 | *J. Am. Chem. Soc.* 2012, 134, 8794−8797

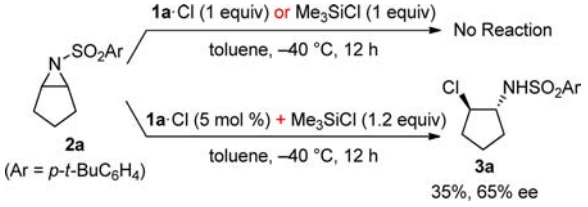
Table 1. Screening of the Structure of Triazolium Ions and Reaction Conditions for Enantioselective Chloride Ring Opening of Meso Aziridine 2a[a]



entry	1	additive	% yield[b]	% ee[c]
1	**1a**	none	35	65
2	**1b**	none	24	81
3	**1c**	none	26	84
4	**1d**	none	42	87
5	**1e**	none	35	92
6	**1f**	none	49	93
7	**1g**	none	31	95
8	**1g**	MeOH	44	89
9	**1g**	PhOH	41	94
10	**1g**	Me_3SiOH	49	95
11[d]	**1g**	Me_3SiOH	85	95
12[e]	**1g**	Me_3SiOH	55	90
13[f]	**1g**	Me_3SiOH	NA	NA

[a]Reactions were carried out with 0.10 mmol of **2a**, 0.12 mmol of Me_3SiCl, and 5 mol % of **1**·Cl in 1 mL of toluene. [b]Isolated yield. [c]Determined by chiral HPLC analysis. [d]Reaction was performed with 1 equiv of Me_3SiOH. [e]With 1.2 equiv of Et_3SiCl instead of Me_3SiCl. [f]With 1.2 equiv of *t*-$BuMe_2SiCl$ instead of Me_3SiCl. NA, not available.

Scheme 2. Control Experiments for Chloride Ring Opening of Meso Aziridine 2a



ppm).[15] When tetrabutylammonium chloride was mixed with an equimolar amount of Me_3SiCl, a single peak was also detected at $\delta = 6.7$ ppm, thereby suggesting the generation of a silicate species through the interaction of chloride ions with Me_3SiCl.[16]

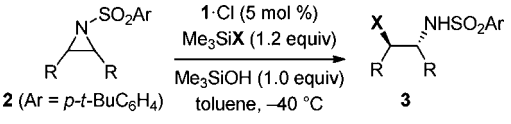
Based on this preliminary information, we next focused on improving the reaction efficiency and stereoselectivity of the asymmetric chloride ring opening reaction of the meso aziridine. For this purpose, we undertook a systematic modification of the structure of chiral triazolium ion **1** by taking advantage of its modularity (Table 1).[17] Initial screening of the amide substituent (Ar^1) revealed that the introduction of a strongly electron-withdrawing *p*-nitrophenyl group (**1b**) delivered a notable enhancement in enantioselectivity (entry 2). The property of the benzylic appendage at the triazolium N(3) (Ar^2) was also important for stereocontrol, and the *p*-trifluoromethylphenyl group was optimal (**1c**, entry 3). This set of aromatic substituents would impart an increased anion-binding ability to the triazolium ion **1** rendering its ion pairing with the silicate ion tight, which might be beneficial in terms of attaining a higher asymmetric induction. On the basis of this assumption, the electronic attribute of **1** was further tuned by installing a *p*-chlorophenyl group as Ar^3 (**1d**), leading to a slight increase in the enantiomeric excess (entry 4). Furthermore, the incorporation of a trifluoromethyl group into the *para* position of the C(4) phenyl ring (**1e**) brought critical improvement in the selectivity (entry 5). We then turned our attention to the effect of the substituent attached to the stereogenic carbon of the amino acid origin (R^1) on the reaction profile. Interestingly, the appropriate choice of parent α-amino acid appeared to be crucial for eliciting the full potential of the catalyst, and **1g**·Cl prepared from L-cyclohexylalanine exerted excellent stereocontrolling ability (entries 6 and 7). Throughout these fruitful investigations, however, the conversion of aziridine **2a** into the product **3a** remains insufficient; this seems to be associated with the difficulty in facile regeneration of the active triazolium chlorosilicate, probably because of the relatively weak Lewis basicity of the *p*-*tert*-butylbenzenesulfonamide ion formed after the ring opening. Therefore, we considered the use of alcoholic additives to possibly facilitate this process by the generation of alkoxide ions through a proton transfer. Fortunately, among the several candidates examined, trimethylsilanol (Me_3SiOH) was identified to be suitable for increasing the catalyst turnover without loss of enantioselectivity (entry 10).[18] Eventually, the addition of 1 equiv of Me_3SiOH allowed the reaction to proceed smoothly in the presence of **1g**·Cl as a catalyst, affording **3a** in 85% yield with 95% ee (entry 11). It should be added that the attempted reaction with triethylsilyl chloride (Et_3SiCl) instead of Me_3SiCl proceeded slowly to give **3a** in moderate yield with slightly lower enantioselectivity (entry 12). Use of *tert*-butyldimethylsilyl chloride (*t*-$BuMe_2SiCl$) resulted in no detectable formation of **3a** (entry 13). The observed dependence of the reactivity and selectivity on the structure of silyl substituents was consistent with the intermediacy of the silicate in the chloride ring-opening event.

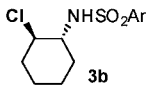
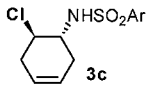
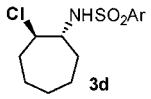
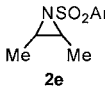
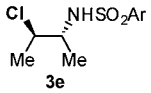
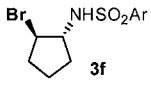
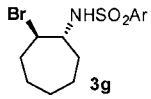
The optimized conditions thus established were used for reactions with a variety of meso aziridines (Table 2). A near-quantitative yield was obtained in the chlorination of **2a** simply by extending the reaction time (entry 1). A cyclohexene-derived substrate **2b** was also employable for this desymmetrization, in which the chiral triazolium salt **1f**·Cl was found to be more effective than **1g**·Cl (entries 2 and 3). Other bicyclic and simple aziridines were well accommodated, and high stereoselectivities were uniformly observed (entries 4–6).[19] It is noteworthy that the present system was successfully applied to the bromide ring opening of the aziridines using trimethylsilyl bromide, providing the corresponding β-bromoamine derivatives in high chemical yields with excellent enantiomeric excesses (entries 7 and 8).[20]

The potential utility of the chiral 1,2,3-triazolium chloride **1**·Cl-catalyzed, asymmetric halide ring-opening protocol was further demonstrated by its successful application to the kinetic

dx.doi.org/10.1021/ja3028668 | J. Am. Chem. Soc. 2012, 134, 8794–8797

Table 2. Enantioselective Chloride and Bromide Ring Openings of Meso Aziridines[a]

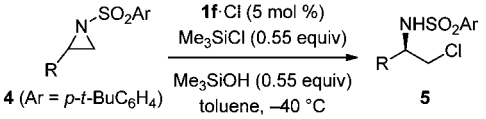


entry	2	3	1	time (h)	% yield[b]	% ee[c]
1	**2a**	**3a**	**1g**	24	97	95
2	 **2b**	 **3b**	**1g**	12	83	95
3			**1f**	12	88	97
4	 **2c**	 **3c**	**1f**	72	96	86
5[d]	 **2d**	 **3d**	**1f**	72	90	93
6	 **2e**	 **3e**	**1g**	24	90	87
7[e]	 **2a**	 **3f**	**1g**	30	99	95
8[d,e]	 **2d**	 **3g**	**1f**	72	93	93

[a]Unless otherwise noted, reactions were carried out with 0.10 mmol of **2**, 0.12 mmol of trimethylsilyl halide, 0.10 mmol of Me_3SiOH, and 5 mol % of **1**·Cl in 1 mL of toluene at −40 °C. [b]Isolated yield. [c]Determined by chiral HPLC analysis. Absolute configuration of the product **3b** was determined after conversion to the known compound, and the stereochemistries of other examples were assumed by analogy. For details, see the Supporting Information. [d]With 10 mol % of **1f**·Cl. [e]Reaction was performed at −78 °C.

resolution of racemic, terminal aziridines **4** (Scheme 3). For instance, the reaction of the vinylcyclohexane-derived aziridine

Scheme 3. Kinetic Resolution of Terminal Aziridines 4

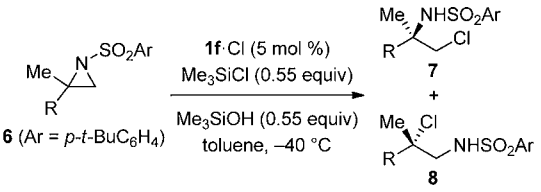


4	% conv.	% yield/% ee 5	4	S
4a: R = *c*-Hex	56	51/80 (**5a**)	44/94	23
4b: R = *t*-Bu	53	49/85 (**5b**)	43/92	32
4c: R = Me_3Si	49	40/88 (**5c**)	47/89	78

4a with Me_3SiCl (0.55 equiv) in the presence of **1f**·Cl (5 mol %) and Me_3SiOH (0.55 equiv) in toluene at −40 °C gave rise to the ring-opening product **5a** exclusively in 51% yield with 80% ee, and **4a** was recovered in 44% yield with 94% ee (selectivity factor: s = 23).[21] Even higher selectivities were observed with terminal aziridines bearing sterically demanding *tert*-butyl and trimethylsilyl substituents (**4b** and **4c**).[22]

Another distinct feature of this approach is an unprecedented kinetic resolution of differently 2,2-disubstituted aziridines **6**, which exhibited impressive levels of selectivity factors, enabling the preparation of enantiomerically pure **6**, otherwise not readily accessible by conventional asymmetric methodologies (Scheme 4).[23] When **6a** was exposed to reaction conditions

Scheme 4. Kinetic Resolution of 2,2-Disubstituted Aziridines 6



6	% conv.	% yield/% ee of 7 7+8 (7:8)	% yield/% ee 6	S
6a: R = *i*-Pr	54	48 (80:20)/90 (**7a**)	46/99	61
6b: R = *c*-Hex	56	53 (67:33)/94 (**7b**)	41/96	27
6c: R = *t*-Bu	49	48 (67:33)/97 (**7c**)	51/98	470

similar to those of the kinetic resolution of **4**, a regioisomeric mixture of the chlorinated products was isolated in 48% combined yield (**7a**/**8a** = 80:20) and the enantiomeric excess of the major β-chloro-*tert*-amine derivative **7a** was 90% ee.[24] Importantly, the starting **6a** was recovered in 46% yield in an essentially enantiopure form. While the regioselectivity was dependent on the substrate structure, an almost complete discrimination of the two enantiomers of **6** was consistently realized.

In conclusion, we developed highly enantioselective chloride and bromide ring openings of meso aziridines with trimethylsilyl halides catalyzed by chiral 1,2,3-triazolium chlorides under mild conditions. The potential utility of the asymmetric halide ring-opening strategy has also been demonstrated by its application to the kinetic resolution of racemic, terminal aziridines. These catalytic asymmetric nucleophilic halogenations based on the use of trimethylsilyl halides rely on the ability of the appropriately modified, chiral 1,2,3-triazolium chloride to generate the requisite halosilicates and extend precise stereocontrol over the halide ion transfer. We believe that the present study adds a new dimension to the development of silicate-based asymmetric methodologies.

■ ASSOCIATED CONTENT

Supporting Information

Representative experimental procedures, spectral and analytical data for all new compounds, and crystallographic data for **7a** (CIF). This material is available free of charge via the Internet at http://pubs.acs.org.

■ AUTHOR INFORMATION

Corresponding Author

tooi@apchem.nagoya-u.ac.jp

Notes

The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

This work was supported by the Funding Program for Next Generation World-Leading Researchers, the Grant-in-Aid for Young Scientists (B) from JSPS, the Global COE Program in Chemistry of Nagoya University, and Program for Leading

Graduate Schools "Integrative Graduate Education and Research Program in Green Natural Sciences" in Nagoya University.

REFERENCES

(1) Chuit, C.; Corriu, R. J. P.; Reye, C.; Young, J. C. *Chem. Rev.* **1993**, *93*, 1371.

(2) (a) Rendler, S.; Oestreich, M. *Synthesis* **2005**, 1727. (b) Orito, Y.; Nakajima, M. *Synthesis* **2006**, 1391. (c) Benaglia, M.; Guizzetti, S.; Pignataro, L. *Coord. Chem. Rev.* **2008**, *252*, 492.

(3) For examples of asymmetric ring openings of epoxides with stoichiometric or catalytic amounts of chiral Lewis acid halides, see: (a) Joshi, N. N.; Srebnik, M.; Brown, H. C. *J. Am. Chem. Soc.* **1988**, *110*, 6246. (b) Naruse, Y.; Esaki, T.; Yamamoto, H. *Tetrahedron* **1988**, *44*, 4747. (c) Nugent, W. A. *J. Am. Chem. Soc.* **1998**, *120*, 7139. (d) Bruns, S.; Haufe, G. *Tetrahedron: Asymmetry* **1999**, *10*, 1563. For recent reports on asymmetric nucleophilic fluorinations, see: (e) Kalow, J. A.; Doyle, A. G. *J. Am. Chem. Soc.* **2010**, *132*, 3268. (f) Katcher, M. H.; Doyle, A. G. *J. Am. Chem. Soc.* **2010**, *132*, 17402. For asymmetric dichlorination of cyclopropanecarbaldehyde, see: (g) Sparr, C.; Gilmour, R. *Angew. Chem., Int. Ed.* **2011**, *50*, 8391.

(4) For a single example of asymmetric chloride ring opening of meso aziridines, in which hydrogen chloride was employed as a chloride source, see: Mita, T.; Jacobsen, E. N. *Synlett* **2009**, 1680.

(5) (a) Ibrahim, H.; Togni, A. *Chem. Commun.* **2004**, 1147. (b) Ueda, M.; Kano, T.; Maruoka, K. *Org. Biomol. Chem.* **2009**, *7*, 2005. (c) Shibatomi, K. *Synthesis* **2010**, 2679.

(6) (a) Denmark, S. E.; Barsanti, P. A.; Wong, K.-T.; Stavenger, R. A. *J. Org. Chem.* **1998**, *63*, 2428. (b) Tao, B.; Lo, M. M.-C.; Fu, G. C. *J. Am. Chem. Soc.* **2001**, *123*, 353. (c) Nakajima, M.; Saito, M.; Uemura, M.; Hashimoto, S. *Tetrahedron Lett.* **2002**, *43*, 8827. (d) Paek, S. H.; Shim, S. C.; Cho, C. S.; Kim, T.-J. *Synlett* **2003**, 849. (e) Tokuoka, E.; Kotani, S.; Matsunaga, H.; Ishizuka, T.; Hashimoto, S.; Nakajima, M. *Tetrahedron: Asymmetry* **2005**, *16*, 2391. (f) Takenaka, N.; Sarangthem, R. S.; Captain, B. *Angew. Chem., Int. Ed.* **2008**, *47*, 9708. (g) Chelucci, G.; Baldino, S.; Pinna, G. A.; Benaglia, M.; Buffa, L.; Guizzetti, S. *Tetrahedron* **2008**, *64*, 7574. (h) Pu, X.; Qi, X.; Ready, J. M. *J. Am. Chem. Soc.* **2009**, *131*, 10364. (i) Malkov, A. V.; Gordon, M. R.; Stončius, S.; Hussain, J.; Kočovský, P. *Org. Lett.* **2009**, *11*, 5390. (j) Denmark, S. E.; Barsanti, P. A.; Beutner, G. L.; Wilson, T. W. *Adv. Synth. Catal.* **2007**, *349*, 567.

(7) For asymmetric ring opening of terminal aziridine using a stoichiometric amount of chiral amine and trimethysilyl cyanide or iodide, see: Minakata, S.; Murakami, Y.; Satake, M.; Hidaka, I.; Okada, Y.; Komatsu, M. *Org. Biomol. Chem.* **2009**, *7*, 641.

(8) Ohmatsu, K.; Kiyokawa, M.; Ooi, T. *J. Am. Chem. Soc.* **2011**, *133*, 1307.

(9) For representative references of desymmetrization of aziridines with azide, see: (a) Li, Z.; Fernández, M.; Jacobsen, E. N. *Org. Lett.* **1999**, *1*, 1611. (b) Fukuta, Y.; Mita, T.; Fukuda, N.; Kanai, M.; Shibasaki, M. *J. Am. Chem. Soc.* **2006**, *128*, 6312. (c) Rowland, E. B.; Rowland, G. B.; Rivera-Otero, E.; Antilla, J. C. *J. Am. Chem. Soc.* **2007**, *129*, 12084. (d) Nakamura, S.; Hayashi, M.; Kamada, Y.; Sasaki, R.; Hiramatsu, Y.; Shibata, N.; Toru, T. *Tetrahedron Lett.* **2010**, *51*, 3820. With cyanide, see: (e) Mita, T.; Fujimori, I.; Wada, R.; Wen, J.; Kanai, M.; Shibasaki, M. *J. Am. Chem. Soc.* **2005**, *127*, 11252. (f) Fujimori, I.; Mita, T.; Maki, K.; Shiro, M.; Sato, A.; Furusho, S.; Kanai, M.; Shibasaki, M. *J. Am. Chem. Soc.* **2006**, *128*, 16438. (g) Wu, B.; Gallucci, J. C.; Parquette, J. R.; RajanBabu, T. V. *Angew. Chem., Int. Ed.* **2009**, *48*, 1126. With other nucleophiles, see: (h) Müller, P.; Nury, P. *Org. Lett.* **1999**, *1*, 439. (i) Arai, K.; Lucarini, S.; Salter, M. M.; Ohta, K.; Yamashita, Y.; Kobayashi, S. *J. Am. Chem. Soc.* **2007**, *129*, 8103. (j) Della Sala, G.; Lattanzi, A. *Org. Lett.* **2009**, *11*, 3330. (k) Larson, S. E.; Baso, J. C.; Li, G.; Antilla, J. C. *Org. Lett.* **2009**, *11*, 5186. (l) Xu, Y.; Lin, L.; Kanai, M.; Matsunaga, S.; Shibasaki, M. *J. Am. Chem. Soc.* **2011**, *133*, 5791.

(10) For palladium-catalyzed asymmetric alcoholysis of terminal aziridines, see: Leung, W.-H.; Mak, W.-L.; Chan, E. Y. Y.; Lam, T. C. H.; Lee, W.-S.; Kwong, H.-L.; Yeung, L.-L. *Synlett* **2002**, 1688.

(11) For regiodivergent kinetic resolution of terminal aziridines with trimethylsilyl azide, see: Wu, B.; Parquette, J. R.; RajanBabu, T. V. *Science* **2009**, *326*, 1662.

(12) Wu, J.; Hou, X.-L.; Dai, L.-X. *J. Org. Chem.* **2000**, *65*, 1344.

(13) Gawronski, J.; Wascinska, N.; Gajewy, J. *Chem. Rev.* **2008**, *108*, 5227.

(14) For selected examples, see: (a) Michida, M.; Mukaiyama, T. *Chem. Lett.* **2008**, *37*, 890. (b) Michida, M.; Mukaiyama, T. *Chem.—Asian J.* **2008**, *3*, 1592.

(15) For details, see the Supporting Information.

(16) (a) Damrauer, R.; Burggraf, L. W.; Davis, L. P.; Gordon, M. S. *J. Am. Chem. Soc.* **1988**, *110*, 6601. (b) Hao, C.; Kaspar, J. D.; Check, C. E.; Lobring, K. C.; Gilbert, T. M.; Sunderlin, L. S. *J. Phys. Chem. A* **2005**, *109*, 2026.

(17) The reactions with aziridine bearing *p*-toluenesulfonyl group (Ts) exhibited a similar level of reaction efficiency and slightly lower enantioselectivity. For details, see Table S1 in the Supporting Information.

(18) To interrogate the possibility of concomitant generation of hydrogen chloride (HCl) and its participation as a reactive promoter, the reaction of **2a** was conducted with 10 mol% of a proton scavenger, 2,6-di-*tert*-butylpyridine, under otherwise identical conditions with those of entry 7 in Table 1; this revealed that the differences in chemical yield and ee were marginal and thus HCl was irrelevant to the present catalytic system, even if it was generated.

(19) The present system seems to be ineffective for aziridines having aromatic substituents. For instance, the reaction of *cis*-stilbene-derived aziridine proceeded sluggishly even at 0 °C, resulting in the formation of the desired product in 14% yield with 48% ee after 24 h.

(20) The chlorinated product was not obtained even in the reaction with 30 mol% of **1f**·Cl.

(21) $S = k_{fast}/k_{slow} = \ln[(1 - C/100)(1 - ee/100)]/\ln[(1 - C/100)(1 + ee/100)]$ (C = conversion, ee = enantiomeric excess of recovered **4** or **6**).

(22) The ring opening of styrene-derived aziridine showed an opposite regioselectivity and diminished stereoselectivity. For details, see the Supporting Information.

(23) (a) Morton, D.; Pearson, D.; Fielda, R. A.; Stockman, R. A. *Chem. Commun.* **2006**, 1833. (b) Colpaert, F.; Mangelinckx, S.; Leemans, E.; Denolf, B.; De Kimpe, N. *Org. Biomol. Chem.* **2010**, *8*, 3251.

(24) The absolute configuration of **7a** was determined to be *R* by X-ray diffraction analysis. The minor regioisomers **8** were also obtained in enantioenriched form (**8a**: 64% ee, **8b**: 62% ee, **8c**: 80% ee). These products would arise from the stereo-invertive ring opening of (*R*)-aziridines, and the stereochemistry of **8** shown in Scheme 4 is based on this assumption. For stereo-invertive nucleophilic substitution at the disubstituted carbon of aziridine, see: Forbeck, E. M.; Evans, C. D.; Gilleran, J. A.; Li, P.; Joullie, M. M. *J. Am. Chem. Soc.* **2007**, *129*, 14463.