JACS
JOURNAL OF THE AMERICAN CHEMICAL SOCIETY
Communication
pubs.acs.org/JACS

Tungsten-Catalyzed Regioselective and Stereospecific Ring Opening of 2,3-Epoxy Alcohols and 2,3-Epoxy Sulfonamides

Chuan Wang[†] and Hisashi Yamamoto*[,†,‡]

[†]Department of Chemistry, The University of Chicago, 5735 South Ellis Avenue, Chicago, Illinois 60637, United States
[‡]Molecular Catalyst Research Center, Chubu University, 1200 Matsumoto, Kasugai, Aichi 487-8501, Japan

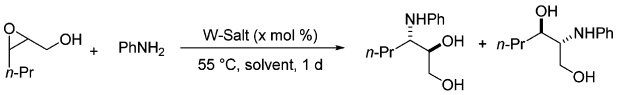
Supporting Information

ABSTRACT: The first catalytic, highly C3-selective, stereosepecific ring-opening reaction of 2,3-epoxy alcohols and 2,3-epoxy sulfonamides has been accomplished. This process was efficiently promoted by W-salts, and the developed method was applicable to various epoxides with diverse N- and O-nucleophiles affording the products in good to excellent yields (up to 95%) and generally with high regioselectivities (C3:C2 up to >99:1).

As 2,3-epoxy alcohols are readily available in highly enantioenriched form through asymmetric epoxidation of allylic alcohols,[1,2] regioselective and stereospecific ring opening of these compounds with various nucleophiles provides a direct access to versatile chiral building blocks for the synthesis of natural products and synthetic analogues with biological activities.[3−8] Nucleophilic addition at the C-3 position of 2,3-epoxy alcohols by amines affords 3-amino 1,2-diols as products, which are synthetic intermediates of cardiovascular,[9] antibacterial,[10] and sedative agents.[11] Although regioselective ring opening of epoxides using amines, phenols, and alcohols as nucleophiles has been intensively studied in the past decades and tremendous progress has been achieved, excellent regioselectivities are usually obtained in the case of terminal epoxides, while regiocontrol is generally difficult to realize for the ring opening of trisubstituted, *cis*-, and *trans*-disubstituted oxiranes, especially the aliphatic analogues.[12,13] For the C-3 regioselective ring opening of 2,3-epoxy alcohols employing amines as nucleophiles, only a few direct and practical approaches have been reported.[4a,c,5d,g,h] The pioneering progress in this field was achieved by Sharpless et al., who developed a $Ti(OiPr)_4$-mediated C3-selective ring opening of 2,3-epoxy alcohols using a variety of nucleophiles including secondary amines, alcohols, and phenol.[4a,c] Nevertheless, all these reported protocols utilize stoichiometric amounts of promoters and thus the development of a catalytic version of this type of reaction is highly desirable. Furthermore, a large number of biological active compounds bearing anti-HIV-activities contain 1,3-diaminoalkan-2-ol as a structural subunit,[14] which could be accessed through regioselective addition of amines to 2,3-epoxy amines or amides. To the best of our knowledge, this type of reaction utilizing nonterminal epoxides as precursors remains elusive.[15] Herein, we report a tungsten-catalyzed C-3 regioselective and stereospecific ring opening of structurally diverse 2,3-epoxy alcohols and 2,3-epoxy sulfonamides using amines, alcohols, and phenol as nucleophiles.

For optimization of the reaction conditions we used racemic *cis*-2,3-epoxy hexane-1-ol (**1a**) and aniline (**2a**) as standard substrates. Initially, a background reaction in the absence of W-salt was carried out and no ring-opening reaction occurred (Table 1, entry 1). Encouragingly, when the reaction was performed in $PhCF_3$ at rt employing WO_2Cl_2 as the catalyst (10 mol %), the desired product **3a** was obtained in a yield of 31% with moderate regioselectivity (C3:C2 = 82:18, entry 2). In order to improve the conversion, the reaction was conducted at 55 °C with 20 mol % catalyst leading to an increase of the yield to 93%, while the regioselectivity did not diminish significantly (entry 3). Subsequently, three other W-salts were investigated as catalysts for this reaction (entries 4−6) and the best outcome with respect to both yield and regioselectivity was obtained in the case of

Table 1. W-Salts and Solvents Screening for the Regioselective Ring Opening with Aniline as the Nucleophile[a]



1a **2a** **3a-I** **3a-II**

entry	W-salt	*x*	solvent	yield (%)[b]	C3:C2[c]
1	–	0	$PhCF_3$	0	–
2[d]	WO_2Cl_2	10	$PhCF_3$	31	82:18
3	WO_2Cl_2	20	$PhCF_3$	93	81:19
4	$WOCl_4$	20	$PhCF_3$	95	86:14
5	$WO_2(acac)_2$	20	$PhCF_3$	81	79:21
6	$W(OEt)_6$	20	$PhCF_3$	96	90:10
7	$W(OEt)_6$	20	DCE	87	89:11
8	$W(OEt)_6$	20	toluene	95	85:15
9	$W(OEt)_6$	20	EtOAc	85	87:13
10	$W(OEt)_6$	20	THF	73	83:17
11	$W(OEt)_6$	20	MeCN	94	93:7
12	**$W(OEt)_6$**	**15**	**MeCN**	**94**	**93:7**
13	$W(OEt)_6$	10	MeCN	84	93:7
14	$W(OEt)_6$	10	$PhCF_3$	91	90:10

[a]Unless otherwise specified, reactions were performed on a 0.25 mmol scale of racemic *cis*-2,3-epoxy hexane-1-ol (**1a**) using 2.0 equiv of aniline (**2a**), *x* mol % W-salt at 55 °C in 0.6 mL of solvent. [b]Combined yields of the isolated C3- and C2-regioisomers. [c]Determined by ^{1}H-spectroscopy of the reaction mixtures. [d]Reaction was performed at rt.

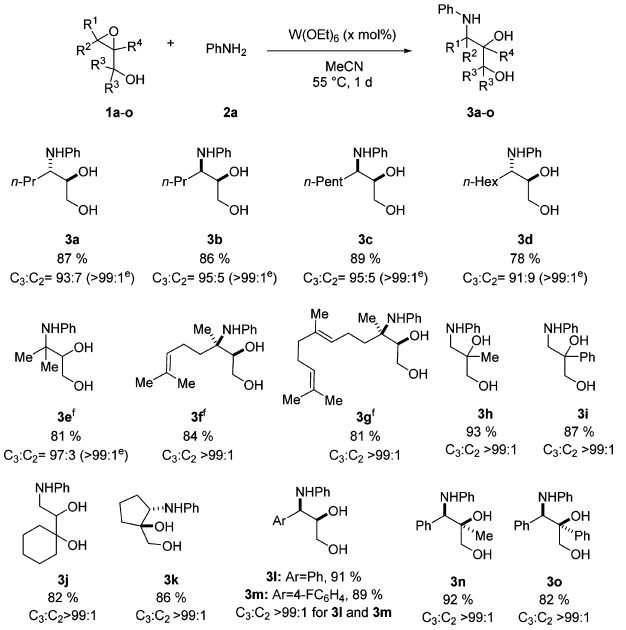
Received: March 24, 2014
Published: April 29, 2014

   dx.doi.org/10.1021/ja5029809 | J. Am. Chem. Soc. 2014, 136, 6888−6891

$W(OEt)_6$ (entry 6). Next, a brief solvent screening was undertaken (entries 7−11) and the best regioselectivity (C3:C2 = 93:7) was achieved in the case of MeCN (entry 11). No decrease of the yield was observed when the catalyst loading was reduced to 15 mol % (entry 12). Lowering the amount of $W(OEt)_6$ further to 10 mol % resulted in a lower yield (entry 13). Furthermore, the ring-opening reaction turned out to be more efficient in $PhCF_3$, although the regioselectivity was relatively low (entry 14). Notably, the resulting two regioisomers **3a-I** and **3a-II** of the ring-opening reaction could be easily separated through column chromatography affording both compounds in regiomerically pure form.

After optimizing the reaction conditions we started to evaluate the substrate scope of this reaction. We first explored a variety of 2,3-epoxy alcohols **1a−o** with different substituted patterns, and the results are summarized in Chart 1. Generally, all the reactions

Chart 1. Regioselective Ring-Opening Reactions of 2,3-Epoxy Alcohols with Aniline as Nucelophile[16,a−d]

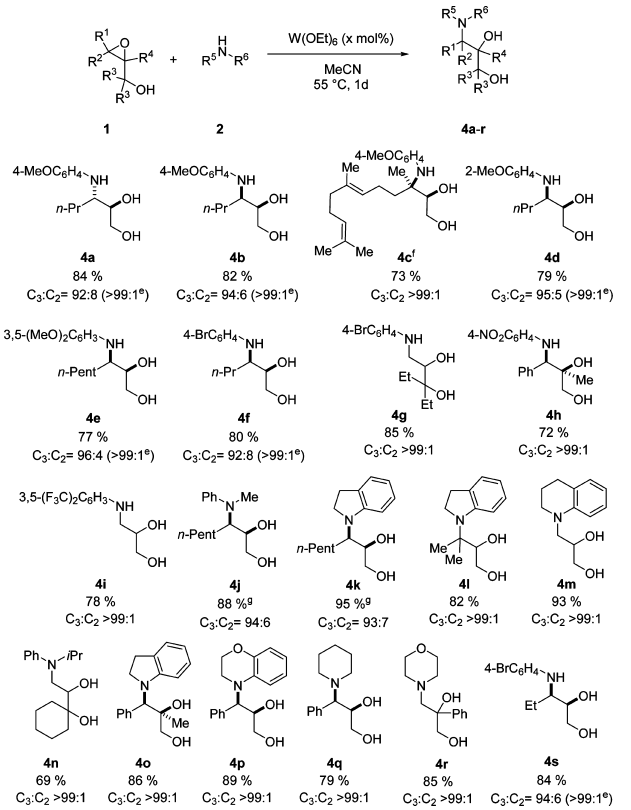


[a]Unless otherwise specified, reactions were performed on a 0.50 mmol scale of racemic 2,3-epoxy alcohols **1** using 2.0 equiv of aniline (**2a**) and *x* mol % $W(OEt)_6$ at 55 °C in 1.2 mL of MeCN. [b] Catalyst loading: 2 mol % for **3h**, **3i**, and **3l−n**; 5 mol % for **3j**, **3k**, and **3o**; 7.5 mol % for **3b** and **3c**; 15 mol % for **3a**, **3d**, and **3e−g**. [c] Yields of the isolated C-3-regioisomer. [d] All regiomeric ratios were determined by ^{1}H-spectroscopy. [e] C-3/C-2 ratios after separation through column chromatography. [f] $PhCF_3$ was used as solvent.

proceeded smoothly at 55 °C affording the products **3a−o** in good to excellent yields (78−93%) with high to complete regioselectivities (C3:C2 = 91:9 → 99:1) in favor of the formation C-3-regioisomers irrespective of the substitution patterns at the C-3 position of the epoxy alcohols. Moreover, the results obtained show clearly the following trend of the reactivity of different substrates: terminal epoxides ≈ aromatic epoxides > aliphatic *trans*-disubstituted epoxides > aliphatic *cis*-disubstituted epoxides > aliphatic trisubstituted epoxides. Remarkably, even sterically demanding trisubstituted epoxides **1f** and **1g** turned out to be competent substrates for the ring-opening reaction furnishing the products **3f** and **3g** bearing two consecutive quaternary and tertiary stereocenters in good yields (81 and 84%) and complete regioselectivities (C3:C2 > 99:1). Furthermore, all the C-3-regioisomers of **3a−e** could be readily separated from the corresponding minor C-2-regioisomers through simple column chromatography.

Subsequently, we studied the substrate spectrum further by variation of structure of the N-nucleophiles. Various substituted anilines bearing electron-withdrawing or -donating substituents at different positions, secondary aromatic amines, and aliphatic amines were reacted with structurally diverse 2,3-epoxy alcohols **1** (Chart 2). Generally, the products **4** were obtained in high to

Chart 2. Regioselective Ring-Opening Reactions of 2,3-Epoxy Alcohols with Various Amines as Nucelophiles[16,a−d]



[a]Unless otherwise specified, reactions were performed on a 0.50 mmol scale of racemic 2,3-epoxy alcohols **1** using 2.0 equiv of amines **2** and *x* mol % $W(OEt)_6$ at 55 °C in 1.2 mL of MeCN. [b] Catalyst load: 5 mol % for **4m**, **4o**, **4p**, and **4r**; 7.5 mol % for **4b**, **4d**, **4e**, and **4s**; 10 mol % for **4f**, **4g**, and **4i**; 15 mol % for **4a**, **4c**, **4j−l**, and **4n**; 20 mol % for **4h** and **4q**. [c] Yields of the isolated C-3-regioisomer. [d] All regiomeric ratios were determined by ^{1}H-spectroscopy. [e] C-3/C-2 ratios after separation through column chromatography. [f] $PhCF_3$ was used as solvent. [g] Combined yield of the C-3- and C-2-regioisomers.

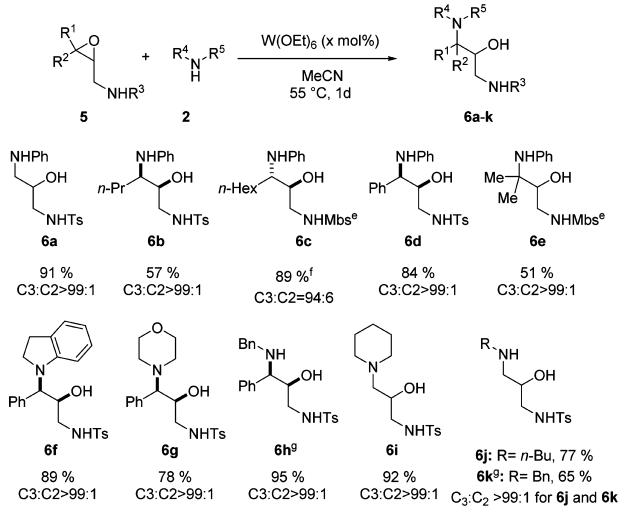
complete regioselectivities (C3:C2 = 92:8 → 99:1). Methoxy- and Br-substituted anilines and secondary aromatic amines demonstrated similar reactivity and regioselectivities compared with aniline. Strong electron-withdrawing groups such as NO_2 and CF_3 lowered the nucleophilicity of the NH_2 moiety. Also, aliphatic amines were less reactive than their aromatic analogues. Thus, a higher catalyst loading was necessary for these substrates to achieve good yields. Importantly, all the products except **4j** and **4k** could be isolated in regiomerically pure form after column chromatography.

Moreover, we are also interested in the regioselective aminolysis of 2,3-epoxy sulfonamides, which can be synthesized

dx.doi.org/10.1021/ja5029809 | J. Am. Chem. Soc. 2014, 136, 6888−6891

in a highly enantioselective manner using our Hf-bishydroxamic acid catalytic system.[17] To our delight, the sulfonamide moiety turned out to be a good directing group for the ring-opening process (Chart 3). All the reactions proceeded smoothly affording the products **6** in 51−95% yields and in most cases with complete regioselectivities.

Chart 3. Regioselective Ring-Opening Reactions of 2,3-Epoxy Sulfonamides with Amines[16,a−d]

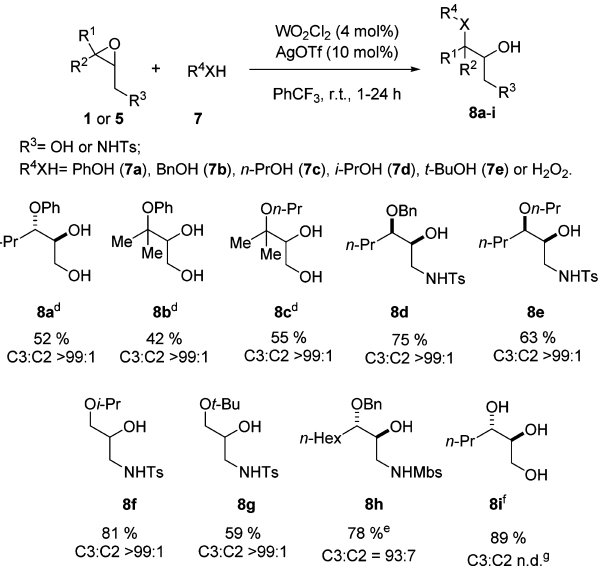


[a]Unless otherwise specified, reactions were performed on a 0.50 mmol scale of racemic 2,3-epoxy sulfonamides **5** using 2.0 equiv of amines **2** and *x* mol % $W(OEt)_6$ at 55 °C in 1.2 mL of MeCN. [b] Catalyst loading: 5 mol % for **6a** and **6i−k**; 10 mol % for **6d** and **6f**; 20 mol % for **6b**, **6c**, **6e**, **6g**, and **6h**. [c] Yields of the isolated C-3-regioisomer. [d] All regiomeric ratios were determined by ^{1}H-spectroscopy. [e] Mbs: 4-methoxybenzenesulfonyl. [f] Combined yields of the C-3- and C-2-regioisomers. [g] $PhCF_3$ was used as solvent.

Furthermore, we have also studied the use of various O-nucleophiles for this ring-opening reaction. Unfortunately, the protocol developed for amines could not be applied to phenol or alcohols. Nonetheless, we found that the use of AgOTf as an additive showed a crucial influence on the outcome of this reaction (Chart 4). Under the optimum conditions both alcohols and phenol were successfully employed as nucleophiles for the ring opening of various 2,3-epoxy alcohols and 2,3-epoxy sulfonamides furnishing the products **8** in moderate to high yields (42−81%) and generally with complete regioselectivities. Moreover, the use of aqueous hydrogen peroxide as a nucleophile resulted in the formation of two regioisomers of the corresponding hydroperoxide and the triol **8i**. Upon treatment with aqueous Na_2SO_3 solution the triol **8i** was obtained as the sole product in excellent yield (89%).

To gain more insight into the effect of the OH and NH-sulfonyl groups on the regioselectivity, we performed some control reactions using unfunctionalized epoxides.[18] In the case of the *trans*-2,3-epoxy octane both the aminolysis and alcoholysis proceeded without regioselectivity. When styrene oxide was employed as the substrate, the ring-opening reactions occurred only at the more substituted site. Further, the reaction using 1,2-epoxy 3-methylpropane as a precursor also proceeded in favor of the more substituted position, but the regioselectivity (70:30) was only moderate. By comparing these results with 2,3-epoxy alcohols and 2,3-epoxy sulfonamides demonstrated in Charts 2−4, we can conclude that the OH and NH-sulfonyl moieties

Chart 4. Regioselective Ring-Opening Reactions of 2,3-Epoxy Alcohols and 2,3-Epoxy Sulfonamides with O-Nucleophiles[16,a−c]



[a]Unless otherwise specified, reactions were performed on a 0.50 mmol scale of racemic 2,3-epoxy alcohols **1** or racemic 2,3-epoxy sulfonamides **5** using 10 equiv of phenol (**7a**) or 5 equiv of alcohols **7b−e**, 4 mol % WO_2Cl_2, and 10 mol % AgOTf at rt in 1.2 mL of $PhCF_3$. [b] Yields of the isolated C-3-regioisomer. [c] All regiomeric ratios were determined by ^{1}H-spectroscopy. [d] Reaction was performed with 2 mol % WO_2Cl_2 and 5 mol % AgOTf. [e] Combined yields of the C-3- and C-2-regioisomers. [f] Reaction was performed with 2 mol % WO_2Cl_2 in absence of AgOTf using 2 equiv of 30% H_2O_2 as nucleophile. After completion of the conversion the reaction mixture was treated with saturated aqueous NaS_2O_3 solution to reduce the hydroperoxide to a triol. [g] Not determined.

play a significant role as a directing group for the site preference of the W-catalyzed ring-opening reactions.

Since the utility of ring-opening reactions relies on both the regioselectivity and stereospecificity, we investigated whether our W-catalyzed ring-opening reactions proceed in a stereospecific pathway. Several reactions using enantioenriched substrates were conducted under the same reaction conditions used for the racemic epoxides.[18] To our delight, the products **3c**, **4j**, **6c**, and **8a** were all furnished with identical enantiomeric excesses in comparison to their epoxide precursors indicating the stereospecificity of this W-catalyzed reaction.

In summary, we developed a W-catalyzed regioselective ring-opening reaction, with the following advantages and breakthroughs: (1) first catalytic version of a C-3 selective ring-opening reaction of 2,3-epoxy alcohols and 2,3-epoxy sulfonamides; (2) excellent regioselectivities obtained for diverse epoxides with various N- and O-nucleophiles, especially, the successful use of challenging trisubstituted epoxides allowing the construction of two consecutive quaternary and tertiary stereocenters; (3) stereospecificity of the ring-opening process allowing preparation of enantioenriched highly functionalized compounds starting from readily available chiral epoxides without racemization; (4) commercial availability of the W-catalysts easing the practical use of this method.

dx.doi.org/10.1021/ja5029809 | J. Am. Chem. Soc. 2014, 136, 6888−6891

■ ASSOCIATED CONTENT

Supporting Information

Representative experimental procedures and necessary characterization data for all new compounds are provided. This material is available free of charge via the Internet at http://pubs.acs.org.

■ AUTHOR INFORMATION

Corresponding Author

yamamoto@uchicago.edu

Notes

The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

The National Institutes of Health (NIH) is greatly appreciated for providing financial support (2R01GM068433). C.W. thanks the Alexander von Humboldt Foundation for his postdoctoral fellowship. We would also like to thank Dr. Antoni Jurkiewicz, Dr. Ian Steele, and Dr. Jin Qin for their expertise in NMR-spectroscopy, X-ray crystallography, and mass spectrometry, respectively.

■ REFERENCES

(1) For recent selected general reviews on asymmetric epoxidation, see: (a) Katsuki, T.; Martin, V. S. *Org. React.* **1996**, *48*, 1. (b) Katsuki, T. In *Comprehensive Asymmetric Catalysis*, Jacobsen, E. N., Pfaltz, A., Yamamoto, H., Eds.; Springer: Berlin, 1999; Vol. *2*, p 621. (c) McGarrigle, E. M.; Gilheany, D. G. *Chem. Rev.* **2005**, *105*, 1563. (d) Xia, Q.-H.; Ge, H.-Q.; Ye, C.-P.; Liu, Z.-M.; Su, K.-X. *Chem. Rev.* **2005**, *105*, 1603. (e) Wong, O. A.; Shi, Y. *Chem. Rev.* **2008**, *108*, 3958.

(2) For selected examples on asymmetric epoxidation of allylic alcohols: (a) Katsuki, T.; Sharpless, K. B. *J. Am. Chem. Soc.* **1980**, *102*, 5974. (b) Zhang, W.; Basak, A.; Kosugi, Y.; Hoshino, Y.; Yamamoto, H. *Angew. Chem., Int. Ed.* **2005**, *44*, 4389. (c) Egami, H.; Ogama, T.; Katsuki, T. *J. Am. Chem. Soc.* **2010**, *132*, 5886. (d) Olivares-Romero, J. L.; Li, Z.; Yamamoto, H. *J. Am. Chem. Soc.* **2013**, *135*, 3411. (e) Wang, C.; Yamamoto, H. *J. Am. Chem. Soc.* **2014**, *136*, 1222.

(3) For a review on regioselective ring opening of 2,3-epoxy alcohols, see: Hanson, R. M. *Chem. Rev.* **1991**, *91*, 437.

(4) For examples on C3 selective ring opening of 2,3-epoxy alcohols with a variety of nucleophiles, see: (a) Caron, M.; Sharpless, K. B. *J. Org. Chem.* **1985**, *50*, 1557. (b) Behrens, C. H.; Sharpless, K. B. *J. Org. Chem.* **1985**, *50*, 5696. (c) Ko, S. Y.; Sharpless, K. B. *J. Org. Chem.* **1986**, *51*, 5413. (d) Chini, M.; Crotti, P.; Flippin, L. A.; Gardelli, C.; Giovani, E.; Macchia, F.; Pineschi, M. *J. Org. Chem.* **1993**, *58*, 1221.

(5) For examples on C3 selective ring opening of 2,3-epoxy alcohols with N-nucleophiles, see: (a) Maruoka, K.; Sano, H.; Yamamoto, H. *Chem. Lett.* **1985**, *14*, 599. (b) Onaka, M.; Sugita, K.; Izumi, Y. *Chem. Lett.* **1986**, *15*, 1327. (c) Caron, M.; Carlier, P. R.; Sharpless, K. B. *J. Org. Chem.* **1988**, *53*, 5185. (d) Canas, M.; Poch, M.; Verdaguer, X.; Moyano, A.; Pericàs, M. A.; Riera, A. *Tetrahedron Lett.* **1991**, *32*, 6931. (e) Benedetti, F.; Berti, F.; Norbedo, S. *Tetrahedron Lett.* **1998**, *39*, 7971. (f) Martín, R.; Islas, G.; Moyano, A.; Pericàs, M. A.; Riera, A. *Tetrahedron* **2001**, *57*, 6367. (g) Pastó, M.; Rodríguez, B.; Riera, A.; Pericàs, M. A. *Tetrahedron Lett.* **2003**, *44*, 8369. (h) Surendra, K.; Krishnaveni, N. S.; Rao, K. R. *Synlett* **2004**, *36*, 506.

(6) For examples on C3 selective ring opening of 2,3-epoxy alcohols with C-nucleophiles, see: (a) Suzuki, T.; Saimoto, H.; Tomioka, H.; Oshima, K.; Nozaki, H. *Tetrahedron Lett.* **1982**, *23*, 3597. (b) Mulzer, J.; Schöllhorn, B. *Angew. Chem., Int. Ed.* **1990**, *29*, 1476. (c) Ahn, K. H.; Kim, J. S.; Jin, C. S.; Kang, D. H.; Han, D. S.; Shin, Y. S.; Kim, D. H. *Synlett* **1992**, *24*, 306.

(7) For examples on C3 selective ring opening of 2,3-epoxy alcohols with O, S, and halide-nucleophiles, see: (a) Onaka, M.; Sugita, K.; Takeuchi, H.; Izumi, Y. *J. Chem. Soc., Chem. Commun.* **1988**, 117. (b) Narender, M.; Reddy, M. S.; Nageswar, Y. V. D.; Rao, K. R. *Helv. Chim. Acta* **2007**, *90*, 1107.

(8) For examples on C2 selective ring opening of 2,3-epoxy alcohols, see: (a) Chakraborty, T. K.; Reddy, G. V. *Tetrahedron Lett.* **1991**, *32*, 679. (b) Sasaki, M.; Tanino, K.; Miyashita, M. *Org. Lett.* **2001**, *3*, 1765. (c) Sasaki, M.; Tanino, K.; Hirai, A.; Miyashita, M. *Org. Lett.* **2003**, *5*, 1789. (d) Tomata, Y.; Sasaki, M.; Tanino, K.; Miyashita, M. *Tetrahedron Lett.* **2003**, *44*, 8975. (e) Chakraborty, T. K.; Samanta, R.; Das, S. *J. Org. Chem.* **2006**, *71*, 3321.

(9) Manoury, P. M.; Binet, J. L.; Rousseau, J.; Lefevre-Borg, F. M.; Cavero, I. G. *J. Med. Chem.* **1987**, *30*, 1003.

(10) (a) Wang, C.-L. J.; Gregory, W. A.; Wuonola, M. A. *Tetrahedron* **1989**, *45*, 1323. (b) Gregory, W. A.; Brittelli, D. R.; Wang, C.-L. J.; Wuonola, M. A.; McRipley, R. J.; Eustice, D. C.; Eberly, V. S.; Bartholomew, P. T.; Slee, A. M.; Forbes, M. *J. Med. Chem.* **1989**, *32*, 1673.

(11) Giani, R.; Marinone, E.; Melillo, G.; Borsa, M.; Tonon, G. C. *Arzneim.-Forsch.* **1988**, *38*, 1139.

(12) For examples on regioselective ring opening of epoxides without directing groups using amines as nucleophiles, see: (a) Sekar, G.; Sing, V. K. *J. Org. Chem.* **1999**, *64*, 287. (b) Rampalli, S.; Chaudhari, S. S.; Akamanchi, K. G. *Synthesis* **2000**, *32*, 78. (c) Rodríguez, J. R.; Navarro, A. *Tetrahedron Lett.* **2004**, *45*, 7495. (d) Sundararajan, G.; Vijayakrishna, K.; Varghese, B. *Tetrahedron Lett.* **2004**, *45*, 8253. (e) Chakraborti, A. K.; Kondaskar, A.; Rudrawar, S. *Tetrahedron* **2004**, *60*, 9085. (f) Bartoli, G.; Bosco, M.; Carlone, A.; Locatelli, M.; Massaccesi, M.; Melchiorre, P.; Sambri, L. *Org. Lett.* **2004**, *6*, 2173. (g) Williams, D. B. G.; Lawton, M. *Tetrahedron Lett.* **2006**, *47*, 6557. (h) Shivani; Pujala, B.; Chakraborti, A. K. *J. Org. Chem.* **2007**, *72*, 3713. (i) Robinson, M. W. C.; Timms, D. A.; Williams, S. M.; Graham, A. E. *Tetrahedron Lett.* **2007**, *48*, 6249. (j) Arai, K.; Lucarini, S.; Salter, M. M.; Ohta, K.; Yamashita, Y.; Kobayashi, S. *J. Am. Chem. Soc.* **2007**, *129*, 8103. (k) Procopio, A.; Gaspari, M.; Nardi, M.; Oliverio, M.; Rosati, O. *Tetrahedron Lett.* **2008**, *49*, 2289. (l) Chimni, S. S.; Bala, N.; Dixit, V. A.; Bharatam, P. V. *Tetrahedron* **2010**, *66*, 3042. (m) Pathare, S. P.; Akamanchi, K. G. *Tetrahedron Lett.* **2013**, *54*, 6455.

(13) For examples on regioselective ring-opening of epoxides without directing groups using alcohols or phenols as nucleophiles, see: (a) Iida, T.; Yamamoto, N.; Matsunaga, S.; Woo, H.-G.; Shibasaki, M. *Angew. Chem., Int. Ed.* **1998**, *37*, 2223. (b) Matsunaga, S.; Das, J.; Roels, J.; Vogl, E. M.; Yamamoto, N.; Iida, T.; Yamaguchi, K.; Shibasaki, M. *J. Am. Chem. Soc.* **2000**, *122*, 2252. (c) Ready, J.-M.; Jacobsen, E. N. *J. Am. Chem. Soc.* **2001**, *123*, 2687. (d) Ready, J.-M.; Jacobsen, E. N. *Angew. Chem., Int. Ed.* **2002**, *41*, 1374. (e) Pineschi, M.; Bertolini, F.; Haak, R. M.; Crotti, P.; Macchia, F. *Chem. Commun.* **2005**, *41*, 1426.

(14) (a) Getman, D. P.; DeCrescenzo, G. A.; Heintz, R. M.; Reed, K. L.; Talley, J. J.; Bryant, M. L.; Clare, M.; Houseman, K. A.; Marr, J. J.; Mueller, R. A.; Vazquez, M. L.; Shieh, H.-S.; Stallings, W. C.; Stegeman, R. A. *J. Med. Chem.* **1993**, *36*, 288. (b) Beaulieu, P. L.; Wernic, D. *J. Org. Chem.* **1996**, *61*, 3635. (c) Beaulieu, P. L.; Lavallée, P.; Abraham, A.; Anderson, P. C.; Boucher, C.; Bousquet, Y.; Duceppe, J.-S.; Gillard, J.; Gorys, V.; Grand-Maître, C.; Grenier, L.; Guindon, Y.; Guse, I.; Plamondon, L.; Soucy, F.; Valois, S.; Wernic, D.; Yoakim, C. *J. Org. Chem.* **1997**, *62*, 3440.

(15) For examples on regioselective ring-opening reaction using terminal 2,3-epoxy amines, see: (a) Concellón, J. M.; Suárez, J. R.; del Solar, V. *J. Org. Chem.* **2005**, *70*, 7447. (b) Concellón, J. M.; Suárez, J. R.; del Solar, V.; Llavova, R. *J. Org. Chem.* **2005**, *70*, 10348.

(16) The relative configurations of **3l** (CCDC-999510) and **4s** (CCDC-999511) were assigned to be *erythro* unambiguously by X-ray crystal structure analysis (Supporting Information (SI), p 23). The supplementary crystallographic data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac. uk/data_request/cif. The *erythro* configuration of **3l** was confirmed by NOESY-measurements on its oxazolidine derivative **10** (SI, pp 20−21 and 137−139). The other ring-opening products were assigned by analogy assuming a common S_N2-type reaction pathway.

(17) Olivares-Romero, J. L.; Li, Z.; Yamamoto, H. *J. Am. Chem. Soc.* **2012**, *134*, 5440.

(18) For detailed reaction conditions and results, see SI (p 24).