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Kinetic Resolution of 2,3-Epoxy 3-Aryl Ketones via Catalytic Asymmetric Ring-Opening with Pyrazole Derivatives

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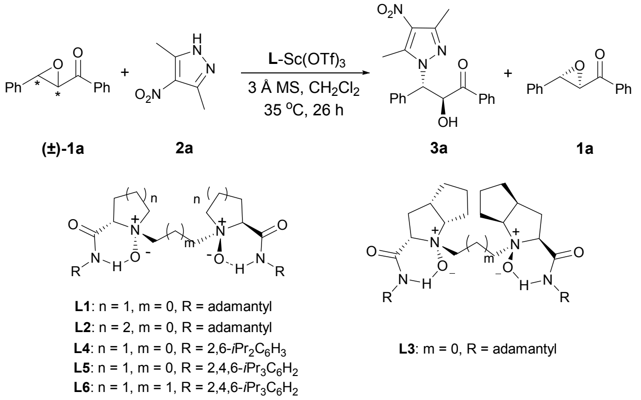
A highly efficient catalytic kinetic resolution of 2,3-epoxy 3-aryl ketones via asymmetric ring-opening with pyrazole derivatives has been achieved by using a chiral *N,N'*-dioxide–Sc(III) complex as the catalyst. A wide variety of substrates were readily scoped, and the selectivity factors were excellent (up to > 300).

Kinetic resolution (KR) is thought as one of the most general methods to obtain enantiopure molecules. The main types of functional compounds that have been resolved involve alcohols, epoxides, amines, alkenes and so on.[1-2] On the other hand, catalytic asymmetric epoxide ring-opening reactions by nucleophiles[3] attract much attention due to the high ring strain of epoxide and the convenient synthesis of useful optically enriched 1,2-difunctionalized compounds with two adjacent stereocenters. Although numerous reports on catalytic asymmetric epoxide ring-opening reactions have been appeared,[4] most of them are desymmetrization of *meso*-epoxides. Comparatively, the kinetic resolution of racemic epoxides via enantioselective catalytic ring-opening version continues to be relatively rare.[5-6] Meanwhile, only terminal unfunctionalized epoxides can give excellent results and the catalysts are focused on Salen based complexes.[7] Hence, developing new catalytic systems for the ring opening of 1,2-disubstituted epoxides is meaningful and imperative.

Besides, as one of the 1,2-disubstituted epoxides, 2,3-epoxy 3-aryl ketones, to the best of our knowledge, have never been applied in the catalytic asymmetric ring-opening reaction to date, due to not only the difficulty in controlling the regioselectivity, but also the hardness of KR caused by the high activity of 2,3-epoxy 3-aryl ketones. Moreover, the kinetic resolution of racemic 2,3-epoxy 3-aryl ketones via asymmetric ring-opening by pyrazole derivatives can afford both β-pyrazole-substituted alcohols and optically pure epoxides[8] simultaneously. In addition, β-pyrazole-substituted alcohols have emerged as potential neuromuscular blocking agents and compounds possessing proneurogenic activity,[9] while optically pure epoxides are among the most versatile compounds in organic chemistry, because their derivatives have been found broad applications in synthetic and biological technology.[10] Also, encouraged by the success of *N,N'*-

Table 1. Optimization of the reaction conditions.



Entry[a]	L:M	L	Conv. (%)[b]	Yield (%)[c]		*ee* (%)[d]		*s*[e]
				3a	**1a**	**3a**	**1a**	
1	1:1	**L1**	59	55	40	53	77	7
2	1.2:1	**L1**	56	50	42	66	71	10
3	1.5:1	**L1**	41	39	55	71	50	10
4	2:1	**L1**	21	19	70	95	26	50
5	2:1	**L2**	14	14	84	89	17	20
6	2:1	**L3**	33	18	60	93	47	44
7	2:1	**L4**	53	43	52	86	96	51
8	2:1	**L5**	51	46	49	93	97	116
9	2:1	**L6**	41	39	60	95	67	78
10[f]	2:1	**L5**	50	47	49	95	94	139
11[g]	2:1	**L5**	39	38	60	96	61	91

[a] Unless otherwise noted, the reactions were performed with **L**-Sc(OTf)$_3$ (10 mol%), 30 mg 3 Å MS and **2a** (0.1 mmol) with (±)-**1a** (0.1 mmol) under nitrogen in CH$_2$Cl$_2$ (0.5 mL) at 35 °C for 26 h. All the diastereoselectivities were up to > 19:1, determined by ^{1}H NMR analysis of the product **3a**. [b] Conv. = $ee^{\mathbf{1a}}/(ee^{\mathbf{1a}} + ee^{\mathbf{3a}})$. [c] Isolated yield. [d] Determined by HPLC analysis. [e] $s = \ln[(1 - \text{Conv.})(1 - ee^{\mathbf{1a}})]/\ln[(1 - \text{Conv.})(1 + ee^{\mathbf{1a}})]$. [f] 5 mol% catalyst loading, **2a** (0.2 mmol). [g] Without 3 Å MS.

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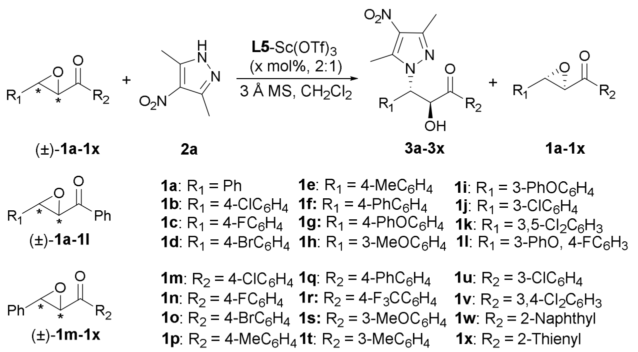
Table 2. Evaluation of the scope of epoxides



Entry[a]	**1**	t (h)	Conv. (%)[b]	Yield (%)[c]		*ee* (%)[d]		*s*[e]
				3	**1**	**3**	**1**	
1	**1a**	26	50	47	49	95	94	139
2[f,g]	**1b**	44	50	50	49	94	95	120
3	**1c**	16	48	48	51	96	91	156
4[f,g]	**1d**	48	48	48	52	93	85	75
5[j]	**1e**	24	52	50	43	91	> 99	111
6	**1f**	12	50	49	48	95	98	179
7[j]	**1g**	12	52	50	46	91	> 99	111
8[f,h]	**1h**	50	50	48	48	91	93	72
9[f,i]	**1i**	72	47	42	52	93	83	72
10[f,g]	**1j**	72	37	32	63	97	54	113
11[f,g]	**1k**	72	33	28	66	98	49	160
12[f,g]	**1l**	72	49	43	47	92	88	71
13[f]	**1m**	27	51	50	49	95	> 99	206
14[f]	**1n**	46	51	51	49	95	> 99	206
15[f]	**1o**	19	51	51	47	96	> 99	259
16[f,g]	**1p**	48	52	48	42	82	90	31
17	**1q**	31	48	46	50	95	89	117
18[j,k]	**1r**	12	50	50	49	97	> 99	> 300
19[f,h]	**1s**	48	51	49	47	91	95	78
20[f,g]	**1t**	30	50	46	47	90	89	57
21[f]	**1u**	40	51	46	49	85	87	35
22[j,k]	**1v**	12	50	48	49	95	96	153
23[f,g]	**1w**	72	48	48	47	83	79	25
24[f,g]	**1x**	72	45	35	65	82	44	16

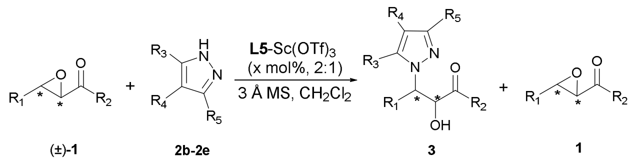
[a] Unless otherwise noted, the reactions were performed with **L5**-Sc(OTf)$_3$ (5 mol%, 2:1), 30 mg 3 Å MS and **2a** (0.2 mmol) with (±)-**1** (0.1 mmol) under nitrogen in CH$_2$Cl$_2$ (0.5 mL) at 35 ºC. [b] Conv. = $ee^1/(ee^1 + ee^3)$. [c] Isolated yield. [d] Determined by HPLC analysis. [e] $s = \ln[(1 - \text{Conv.})(1 - ee^1)]/\ln[(1 - \text{Conv.})(1 + ee^1)]$. [f] 10 mol% catalyst loading. [g] **2a** (0.5 mmol). [h] **2a** (0.3 mmol). [i] **2a** (0.4 mmol). [j] At 25 ºC. [k] **2a** (0.1 mmol).

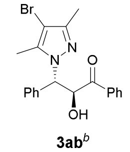
dioxide–Sc(III) complex catalyzed desymmetrization of *meso*-epoxides using pyrazole derivatives as nucleophiles,[11] herein, we decide to develop *N,N'*-dioxide–metal complexes[12] to furnish the first kinetic resolution of racemic 2,3-epoxy 3-aryl ketones via asymmetric ring-opening by employing pyrazole derivatives as the aza-nucleophiles.

Our investigation began with the ring-opening of phenyl(3-phenyloxiran-2-yl)methanone (±)-**1a** by 3,5-dimethyl-4-nitro-*1H*-pyrazole **2a** as the model reaction to optimize the reaction conditions. A screen of metal salts showed that Sc(OTf)$_3$ was the potentially optimal metal salt (see ESI for details). With chiral *N,N'*-dioxide **L1**-Sc(OTf)$_3$ complex as the catalyst, the desired product **3a** was obtained in 55% yield with 53% *ee*, meanwhile, the substrate **1a** was recovered in 40% yield with 77% *ee* (Table 1, entry 1). The molar ratio of ligand **L1** to Sc(OTf)$_3$ was an important factor in determining the selectivity factor of the reaction. As shown in Table 1, an excess of ligand **L1** over Sc(OTf)$_3$ had a positive effect on the selectivity factor (Table 1, entries 1-4). When the ratio of ligand **L1** to Sc(OTf)$_3$ was 2:1, a better *s* factor of 50 was obtained. When the structure of chiral ligand was examined, it was found that the chiral backbone, the amide moiety and the linker of the ligand all affected the selectivity of the process. As for the chiral backbone, the ligand **L1** derived from *L*-proline exhibited a slight superiority on the *s* factor compared with ligand **L2** and **L3** (Table 1, entries 4-6). In addition, the steric hindrance of the amide subunits had a crucial influence on both the yield and the stereoselectivity. The use of ligand **L4** with aromatic substituent on the amine moiety gave the result with the *s* factor of 51 (Table 1, entry 7). Excitingly, ligand **L5** containing 2,4,6-triisopropyl aniline provided a better result, giving rise to an *s* factor of 116. When ligand **L6** with a three-carbonic linkage was used, the *s* factor dropped sharply to 78 (Table 1, entries 8-9). To our delight, when reducing the catalyst loading from 10 mol% to 5 mol% and increasing the amount of **2a** to 2 equiv (Table 1, entry 10), the product **3a** could be obtained in 47% yield with 95% *ee*, and substrate **1a** was retrieved in 49% yield with 94% *ee* simultaneously with an *s* factor of 139. Furthermore, when we conducted this transformation without 3 Å molecular sieves (Table 1, entry 11), the yield of **3a** reduced to 38% and the enantiomeric excess of **1a** decreased to 61%, which confirmed that the molecular sieves was an indispensable part of the catalytic system.

With the optimized conditions in hand (Table 1, entry 10), the substrate scope of racemic epoxides (±)-**1** was examined firstly. As shown in Table 2, regardless of the electronic nature or position of the substituents on the aryl ring of R$_1$ and R$_2$, racemic epoxides could undergo the KR process smoothly. Both the β-pyrazole-substituted alcohols and the recovered epoxides were obtained in excellent yields with high to excellent enantioselectivities (up to 50% yield, > 99:1 d.r. and 99% *ee*), and the selectivity factors were also excellent (up to > 300) (Table 2, entries 1-10, 13-21). Furthermore, fused-ring chalcone epoxide (±)-**1w** as well as heteroaromatic (±)-**1x** and multi-substituted ones (±)-**1k**, (±)-**1l**, (±)-**1v** were also suitable candidates for the reaction (*s* factors of 16-160; Table 2, entries11-12, 22-24). In all cases, up to > 19:1 diastereomeric

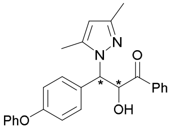
Table 3. Asymmetric ring-opening of epoxides with different pyrazole derivatives.[a]





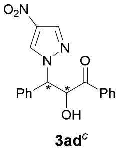
3ab[b]

s: 50% yield, 91% *ee*
p: 49% yield, 90% *ee*
> 19:1 d.r., *s* = 60
25 h



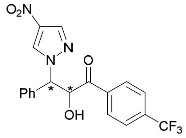
3gc

s: 49% yield, 90% *ee*
p: 40% yield, 88% *ee*
d.r. = 12:1, *s* = 48
22 h



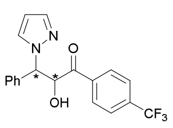
3ad[c]

s: 65% yield, 33% *ee*
p: 28% yield, 90% *ee*
s = 26
26 h



3rd[c]

s: 50% yield, 90% *ee*
p: 44% yield, 95% *ee*
> 19:1 d.r., *s* = 120
22 h



3re[c]

s: 50% yield, 84% *ee*
p: 40% yield, 57% *ee*
> 19:1 d.r., *s* = 10
22 h

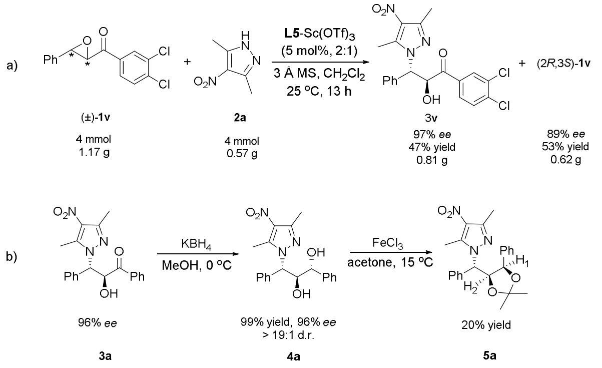
[a] Unless otherwise noted, the reactions were performed with **L5**-Sc(OTf)$_3$ (5 mol%, 2:1), 30 mg 3 Å MS and **2** (0.2 mmol) with (±)-**1** (0.1 mmol) under nitrogen in CH$_2$Cl$_2$ (0.5 mL) at 35 °C; Isolated yield; $s = \ln[(1 - \text{Conv.})(1 - ee^1)]/\ln[(1 - \text{Conv.})(1 + ee^1)]$; $\text{Conv.} = ee^1/(ee^1 + ee^3)$; **s** = starting material; **p** = product. [b] At 25 °C. [c] 10 mol% catalyst loading.

ratios were obtained and almost no other byproducts were detected for all evaluated substrates (see ESI for details). To investigate the substrates **1** with the alkyl substituent, we tried (3-isobutyloxiran-2-yl)(phenyl)methanone under the optimized condition, but no desired product was detected. The absolute configuration of the product **3f** (Table 2, entry 6) was determined to be (2*S*,3*S*) by X-ray crystallography,[13] and the others were assigned by comparing the Cotton effect of the CD spectra with that of **3f**.

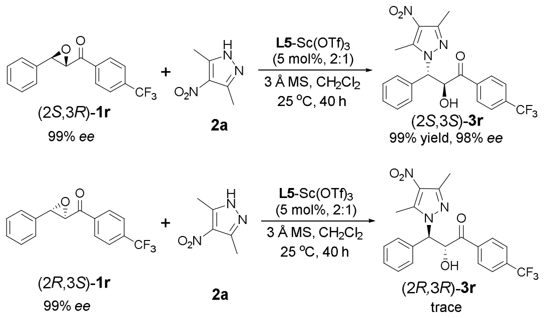
Given the remarkable efficiency of present catalytic system, various pyrazole derivatives were also examined. As shown in Table 3, **2b** and **2c** proceeded the reaction smoothly, providing the products **3ab**, **3gc** in 40-49% yields with 88-90% *ee*, as well as the starting material **1ab**, **1gc** in 49-50% yields with 90-91% *ee*. Significantly, the 3,5-dimethyl substituent on 1*H*-pyrazole had a momentous influence on the conversion of the reaction. When the standard substrate (±)-**1a** was chosen to react with **2d**, the yield of the product **3ad** reduced sharply. In the mind of speeding up the resolution rate, we changed (±)-**1a** to (±)-**1r**, and got the result with a better *s* factor of 120. Unfortunately, 1*H*-pyrazole (**2e**) did not fit the resolution system, even though we had explored some other epoxides.

To show the synthetic application of the current system, the reaction of (±)-**1v** was enlarged to a gram scale (1.17 g, 4.0 mmol) under the optimized reaction condition, and gave the product **3v** in 47% yield with 97% *ee*, **1v** was retrieved in 53% yield with 89% *ee* (Scheme 1a). Meanwhile, the products (2*S*,3*S*)-**3a** could be easily transformed into pinacol (1*R*,2*S*,3*S*)-**4a**,[14] which is a valuable and versatile intermediate in organic synthesis, by reduction in excellent yield (99%) without any loss of enantioselectivity (Scheme 1b).

To identify the "matched/mismatched" effect of the epoxide clearly, we investigated the reaction of **2a** with both enantiomeric forms of the epoxide **1r**. The comparative experiments gave very impressive stereo differentiation. The matched epoxide (2*S*,3*R*)-**1r** went through the reaction smoothly, and gave the product (2*S*,3*S*)-**3r** in 99% yield with 98% *ee* while the mismatched (2*R*,3*S*)-**1r** gave only trace amount of product (Scheme 2).



Scheme 1. a) Gram version of the reaction; b) Conversion of **3a** to **4a**.



Scheme 2. Control Experiments

Conclusions

In conclusion, we have developed an efficient ring-opening and kinetic resolution of racemic 2,3-epoxy 3-aryl ketones by using pyrazole derivatives for synthesizing the optically active epoxides, as well as chiral β-pyrazole-substituted alcohols. The excellent chemical and optical yields, broad substrate generality, operational simplicity, and mild reaction conditions highlighted the efficiency of the chiral *N*,*N*'-dioxide–Sc(III) complex system.

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Notes and references

1 For a review, see: J. C. Fiaud, H. B. Kagan, *Topics in Stereochemistry*, 1988, **18**, 249.
2 E. Vedejs, M. Jure, *Angew. Chem.,* 2005, **117**, 4040; *Angew. Chem. Int. Ed*., 2005, **44**, 3974.
3 For reviews, see: (*a*) E. N. Jacobsen, *Acc. Chem. Res.,* 2000, **33**, 421; (*b*) H. C. Kolb, M. G. Finn, K. B. Sharpless, *Angew. Chem.,* 2001, **113**, 2056; *Angew. Chem. Int. Ed*., 2001, **40**, 2004; (*c*) M. Pineschi, *Eur. J. Org. Chem*., 2006, 4979; (*d*) A. Gansäuer, C.-A. Fan, F. Keller, P. Karbaum, *Chem. Eur. J.*, 2007, **13**, 8084; (*e*) H. Pellissier, *Adv. Synth. Catal*., 2011, **353**, 1613.

4 Selected examples of ring-opening reactions of epoxides with a cyanide nucleophile: (*a*) B. M. Cole, K. D. Shimizu, C. A. Krueger, J. P. A. Harrity, M. L. Snapper, A. H. Hoveyda, *Angew. Chem.*, 1996, **108**, 1776; *Angew. Chem. Int. Ed. Engl*., 1996, **35**, 1668; (*b*) S. E. Schaus, E. N. Jacobsen, *Org. Lett*., 2000, **2**, 1001; (*c*) C. J. Zhu, F. Yuan, W. J. Gu, Y. Pan, *Chem. Commun*., 2003, 692; Selected examples of ring-opening reactions of epoxides with alcohols: (*d*) S. Matsunaga, J. Das, J. Roels, E. M. Vogl, N. Yamamoto, T. Iida, K. Yamaguchi, M. Shibasaki, *J. Am. Chem. Soc*., 2000, **122**, 2252; (*e*) C. Schneider, A. R. Sreekanth, E. Mai, *Angew. Chem.,* 2004, **116**, 5809; *Angew. Chem. Int. Ed*., 2004, **43**, 5691; Selected examples of ring-opening reactions of epoxides with thiols: (*f*) T. Iida, N. Yamamoto, H. Sasai, M. Shibasaki, *J. Am. Chem. Soc*., 1997, **119**, 4783; (*g*) J. Wu, X.-L. Hou, L.-X. Dai, L.-J. Xia, M.-H. Tang, *Tetrahedron: Asymmetry*, 1998, **9**, 3431; (*h*) M. V. Nandakumar, A. Tschöp, H. Krautscheid, C. Schneider, *Chem. Commun*., 2007, 2756; (*i*) Z. Wang, W. K. Law, J. Sun, *Org. Lett*., 2013, **15**, 5964; Selected examples of ring-opening reactions of epoxides with azides: (*j*) W. A. Nugent, *J. Am. Chem. Soc*., 1992, **114**, 2768; (*k*) L. E. Martínez, J. L. Leighton, D. H. Carsten, E. N. Jacobsen, *J. Am. Chem. Soc*., 1995, **117**, 5897; (*l*) K. B. Hansen, J. L. Leighton, E. N. Jacobsen, *J. Am. Chem. Soc*., 1996, **118**, 10924; Selected examples of ring-opening reactions of epoxides with amines: (*m*) X.-L. Hou, J. Wu, L.-X. Dai, L.-J. Xia, M.-H. Tang, *Tetrahedron: Asymmetry*, 1998, **9**, 1747; (*n*) F. Carrée, R. Gil, J. Collin, *Org. Lett*., 2005, **7**, 1023; (*o*) S. Azoulay, K. Manabe, S. Kobayashi, *Org. Lett*., 2005, **7**, 4593; (*p*) K. Arai, S. Lucarini, M. M. Salter, K. Ohta, Y. Yamashita, S. Kobayashi, *J. Am. Chem. Soc*., 2007, **129**, 8103; (*q*) K. Arai, M. M. Salter, Y. Yamashita, S. Kobayashi, *Angew. Chem.,* 2007, **119**, 973; *Angew. Chem. Int. Ed*., 2007, **46**, 955; (*r*) E. Mai, C. Schneider, *Chem. Eur. J*., 2007, **13**, 2729; (*s*) H. Bao, J. Zhou, Z. Wang, Y. Guo, T. You, K. Ding, *J. Am. Chem. Soc*., 2008, **130**, 10116; (*t*) B. Gao, Y. H. Wen, Z. G. Yang, X. Huang, X. H. Liu, X. M. Feng, *Adv. Synth. Catal.,* 2008, **350**, 385; (*u*) B. Plancq, T. Ollevier, *Chem. Commun*., 2012, **48**, 3806; (*v*) M. Kumar, R. I. Kureshy, S. Saravanan, S. Verma, A. Jakhar, N. H. Khan, S. H. R. Abdi, H. C. Bajaj, *Org. Lett*., 2014, **16**, 2798; Selected examples of ring-opening reactions of epoxides by a halide: (*w*) W. A. Nugent, *J. Am. Chem. Soc*., 1998, **120**, 7139; (*x*) B. Tao, M. M.-C. Lo, G. C. Fu, *J. Am. Chem. Soc*., 2001, **123**, 353; (*y*) N. Takenaka, R. S. Sarangthem, B. Captain, *Angew. Chem.,* 2008, **120**, 9854; *Angew. Chem. Int. Ed*., 2008, **47**, 9708; (*z*) X. Pu, X. Qi, J. M. Ready, *J. Am. Chem. Soc*., 2009, **131**, 10364.

5 Selected examples of kinetic resolution of racemic epoxides: (*a*) J. F. Larrow, S. E. Schaus, E. N. Jacobsen, *J. Am. Chem. Soc*., 1996, **118**, 7420; (*b*) M. Bandini, P. G. Cozzi, P. Melchiorre, A. Umani-Ronchi, *Angew. Chem.,* 2004, **116**, 560; *Angew. Chem. Int. Ed*., 2004, **43**, 84; (*c*) G. Bartoli, M. Bosco, A. Carlone, M. Locatelli, M. Massaccesi, P. Melchiorre, L. Sambri, *Org. Lett*., 2004, **6**, 2173; (*d*) G. Bartoli, M. Bosco, A. Carlone, M. Locatelli, P. Melchiorre, L. Sambri, *Org. Lett*., 2005, **7**, 1983; (*e*) A. Berkessel, E. Ertürk, *Adv. Synth. Catal*., 2006, **348**, 2619; (*f*) R. I. Kureshy, S. Singh, N. H. Khan, S. H. R. Abdi, S. Agrawal, R. V. Jasra, *Tetrahedron: Asymmetry,* 2006, **17**, 1638; (*g*) J. A. Kalow, A. G. Doyle, *J. Am. Chem. Soc*., 2010, **132**, 3268; (*h*) R. I. Kureshy, K. J. Prathap, M. Kumar, P. K. Bera, N. H. Khan, S. H. R. Abdi, H. C. Bajaj, *Tetrahedron,* 2011, **67**, 8300.

6 (*a*) X. M. Feng, L. H. Shu, Y. Shi, *J. Am. Chem. Soc.,* 1999, **121**, 11002; (*b*) X. M. Feng, L. H. Shu, Y. Shi, *J. Org. Chem.,* 2002, **67**, 2831.

7 The 1,2-disubstituted epoxides can't give the product with good *s* factor as well as the scope of the substrates is poor. During the period we were preparing our issue, H. Yamamoto reported Tungsten-catalyzed regio- and enantioselective aminolysis of *trans*-2,3-epoxy alcohols: C. Wang, H. Yamamoto, *Angew. Chem.,* 2014, **126**, 14140; *Angew. Chem. Int. Ed*., 2014, **53**, 13920.

8 Y. Y. Chu, X. H. Liu, W. Li, X. L. Hu, L. L. Lin, X. M. Feng, *Chem. Sci*., 2012, **3**, 1996.

9 A. A. Pieper, S. H. Xie, E. Capota, S. J. Estill, J. Zhong, J. M. Long, G. L. Becker, P. Huntington, S. E. Goldman, C. H. Shen, M. Capota, J. K. Britt, T. Kotti, K. Ure, D. J. Brat, N. S. Williams, K. S. MacMillan, J. Naidoo, L. Melito, J. Hsieh, J. D. Brabander, J. M. Ready, S. L. McKnight, *Cell*, 2010, **142**, 39.

10 (*a*) A. K. Yudin, *Aziridines and Epoxides in Organic Synthesis*, Wiley-VCH, Weinheim 2006; (*b*) W. Zhang, J. L. Loebach, S. R. Wilson, E. N. Jacobsen, *J. Am. Chem. Soc*., 1990, **112**, 2801; (*c*) Z.-X. Wang, Y. Tu, M. Frohn, J.-R. Zhang, Y. Shi, *J. Am. Chem. Soc*., 1997, **119**, 11224; (*d*) V. K. Aggarwal, C. Lopin, F. Sandrinelli, *J. Am. Chem. Soc*., 2003, **125**, 7596; (*e*) L. Kürti, M. M. Blewett, E. J. Corey, *Org. Lett*., 2009, **11**, 4592.

11 X. L. Hu, B. Gao, Y. Y. Chu, W. Li, X. H. Liu, L. L. Lin, X. M. Feng, *Chem. Eur. J*., 2012, **18**, 3473.

12 For recent reviews on *N*,*N*'-dioxide–metal complexes, see: (*a*) X. H. Liu, L. L. Lin, X. M. Feng, *Acc. Chem. Res.,* 2011, **44**, 574; (*b*) K. Shen, X. H. Liu, L. L. Lin, X. M. Feng, *Chem. Sci.,* 2012, **3**, 327; (*c*) X. H. Liu, L. L. Lin, X. M. Feng, *Org. Chem. Front.,* 2014, **1**, 298.

13 CCDC 1034676 (**3f**).

14 To determine the absolute configuration of **4a**, we convert **4a** to **5a**. Based on NOESY spectra, we deduce the absolute configuration of **4a** is (1*R*,2*S*,3*S*).