DOI: 10.1002/cctc.201402811

Asymmetric Organocatalyzed Epoxidation of 2-Oxoindoline-3-ylidene Acetaldehydes

Takasuke Mukaiyama, Kento Ogata, Tsuyoshi Ono, and Yujiro Hayashi*[a]

The asymmetric epoxidation of 2-oxoindoline-3-ylidene acetaldehydes, catalyzed by diarylprolinol silyl ether, has been developed. The reaction provides oxindole derivatives possessing chiral epoxides in good yield with good diastereoselectivity and excellent enantioselectivity.

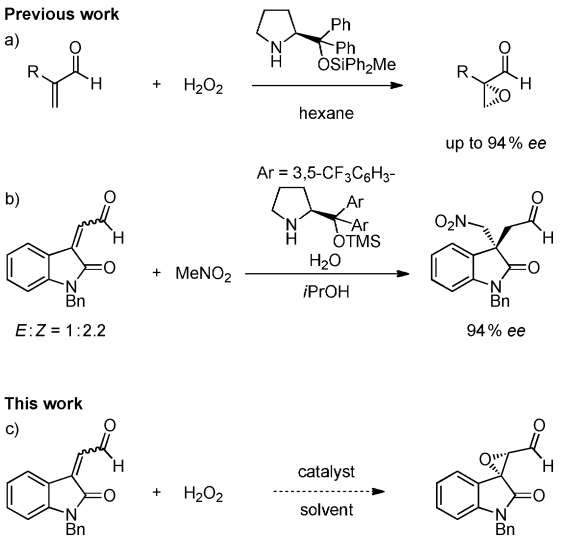
Introduction

Chiral epoxides are often used as intermediates of pharmaceutical products and natural products because they can react with a plethora of nucleophiles to generate a variety of chiral compounds. Owing to this importance, many research groups have developed methods to achieve asymmetric epoxidation. Since the discovery of Sharpless asymmetric epoxidation of allyl alcohols,[1] chiral metal catalysts have largely contributed to the development of asymmetric epoxidation methods, including manganese-salen complex mediated epoxidations as developed independently by Jacobsen[2] and Katsuki.[3] Shibasaki also developed lanthanoid-BINOL complexes for asymmetric epoxidation reactions.[4]

Organocatalysts have also been applied to effect asymmetric epoxidations, and the field of organocatalysis is still expanding today.[5] For instance, Shi developed a sugar derived organocatalyst for asymmetric epoxidations.[6] A pyrrolidine-based catalyst,[7] chiral iminium salt,[8] and chiral tripeptide[9] have also been found to be effective. For electron deficient olefins such as α,β-unsaturated carbonyl compounds, a number of asymmetric epoxidations have been developed using organocatalysts.[10] Examples include the epoxidation of α,β-unsaturated aldehydes as catalyzed by diarylprolinol silyl ethers,[11] chiral phosphoric amine salts,[12] diphenylfluoromethylpyrrolidines,[13] and imidazolidinones,[14] whereas α-substituted-α,β-unsaturated aldehydes have been catalyzed by cinchona-based amines and chiral phosphoric acids.[15] The diphenylprolinol,[16] amino alcohol,[17] guanidine-based,[18] and cinchona-based[19] amine catalysts have all been used for the asymmetric epoxidation of α,β-unsaturated ketones. Although α,β-unsaturated aldehydes have been frequently used as starting materials, reports of β,β-disubstituted-α,β-unsaturated aldehydes have been limited to iminium-ion mediated nucleophilic epoxidation methods.[2,12,20]

Pertinent to our current investigation is the asymmetric synthesis of oxindole derivatives via epoxides. These have attracted attention because they show a variety of bioactivities, for example, as lead compounds for cancer treatment.[21] Hirama's group synthesized the oxindole derivative TMC-95A, a potent proteasome inhibitor, via a chiral epoxide intermediate.[22] Gasperi's group reported the asymmetric epoxidation of oxindole derivatives possessing β,β-disubstituted-α,β-unsaturated esters when catalyzed by diarylprolinol.[23]

In 2010, we reported the asymmetric epoxidation of α-substituted-α,β-unsaturated aldehydes by using diphenylprolinol silyl ether as the chiral catalyst.[24] This organocatalyst was developed independently by our group[25] and Jørgensen's group[26] [Scheme 1a]. Recently, we have also reported the asymmetric Michael addition of nitromethane to 2-oxoindoline-3-ylidene acetaldehydes as catalyzed by diarylprolinol silyl ether to construct all-carbon quaternary stereogenic centers with excellent enantioselectivity [Scheme 1b].[27] As 2-oxoindo-



Scheme 1.

[a] T. Mukaiyama, K. Ogata, T. Ono, Prof. Y. Hayashi
Department of Chemistry, Graduate School of Science
Tohoku University
6-3 Aramaki-Aza Aoba, Aoba-ku, Sendai 980-8578 (Japan)
Fax: (+81) 22-795-6566
Tel: (+81) 22-795-3554
E-mail: yhayashi@m.tohoku.ac.jp
Homepage: http://www.ykbsc.chem.tohoku.ac.jp/

Supporting information for this article is available on the WWW under http://dx.doi.org/10.1002/cctc.201402811.

line-3-ylidene acetaldehydes have been successfully employed in the Michael reaction of indoles and malonates,[28] we expected that hydrogen peroxide would function as a nucleophile to form chiral epoxides of the oxindole [Scheme 1c].

Herein, we report the organocatalyzed asymmetric epoxidation of 2-oxoindoline-3-ylidene acetaldehydes, possessing β,β-disubstituted-α,β-unsaturated aldehydes, with hydrogen peroxide to afford chiral epoxides in excellent yield and enantioselectivity.

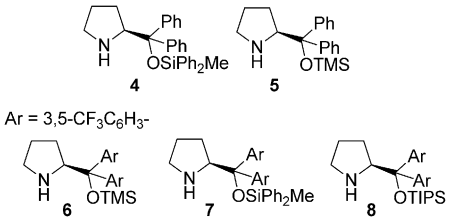
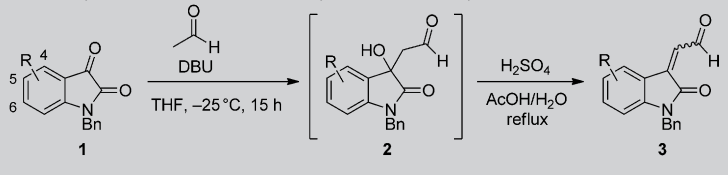


Figure 1. Organocatalysts used in the asymmetric epoxidation.

Results and Discussions

We have very recently reported the preparation of the 2-oxoindoline-3-ylidene acetaldehyde **3a** from the isatin derivative **1a** with acetaldehyde during a three "one-pot" sequential synthesis of (−)-horsfiline and (−)-coerulescine.[27] Herein, we explored this procedure to prepare other 2-oxoindoline-3-ylidene acetaldehydes, including **3b**, **3c**, and **3d** (Table 1). The isatin derivatives **1** were thus mixed with acetaldehyde in the presence of a catalytic amount of DBU to give β-hydroxyaldehyde **2**, followed by dehydration under acidic conditions, to afford the 2-oxoindoline-3-ylidene acetaldehydes **3** in excellent yield. Although **3a**, **3c**, and **3d** were obtained as a mixture of *E*/*Z* isomers (entry 1, 3, 4), only the *Z*-isomer **3b** was generated in case of the 4-Br substrate **1b** (entry 2).

Table 1. Synthesis of 2-oxoindoline-3-ylidene acetaldehydes.[a]



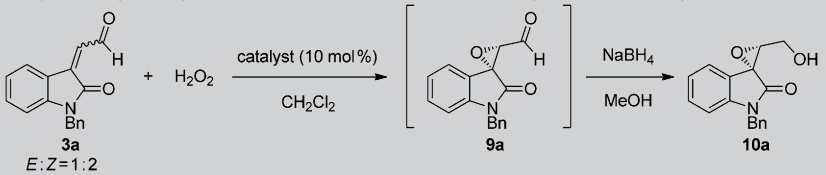
Entry	R	*E*:*Z*[b]	Yield of **3** [%][c]
1	H (**1a**)	1:2	89 (**3a**)
2	4-Br (**1b**)	*Z* only	99 (**3b**)
3	5-Me (**1c**)	1:2	89 (**3c**)
4	6-Br (**1d**)	1:2	90 (**3d**)

[a] Unless noted otherwise, the reaction was performed by employing isatin derivative **1** (4.2 mmol), acetaldehyde (21 mmol), and DBU (0.42 mmol) in THF (8 mL) at −25 °C for 15 h. After evaporation, H_2O (1 mL), AcOH (3 mL), and H_2SO_4 (0.21 mL) were added and the mixture was refluxed until completion of reaction. [b] *E*/*Z* ratio was determined by ^{1}H NMR. [c] Yield after isolation of the product.

The organocatalyzed asymmetric epoxidation was investigated next (Table 2). The 2-oxoindoline-3-ylidene acetaldehyde, **3a**, was treated with hydrogen peroxide in the presence of various catalysts (Figure 1). The yield, diastereo- and enantioselectivities were determined after reduction of the epoxy aldehyde **9a** to the epoxy alcohol **10a**. Since the *O*-silyl prolinol **4** is known to be effective for the asymmetric epoxidation of α-substituted-α,β-unsaturated alkenes,[24] the organocatalyst **4** was tried first. The epoxy aldehyde **9a** was generated as a mixture of diastereomers in a ratio of 1:1.8; subsequent aldehyde reduction provided the epoxy alcohol **10a** in 56% yield with moderate enantioselectivity (entry 1). A change of the silyl substituents to a trimethylsilyl (TMS) group increased the diastereoselectivity, but decreased the yield and enantioselectivity (entry 2). When the Michael addition of nitromethane to **3a** was performed, the trfluoromethylated diarylprolinol silyl ether **6** was found to be optimal. Therefore, diarylprolinol catalysts like **6** were explored more. Eventually, the yield, diastereo and enantioselectivity were all improved (entry 3). In case of catalyst **7**, the enantioselectivity and yield increased slightly, although the diastereoselectivity decreased (entry 4). The bulky triisopropyl silyl (TIPS) group gave the best enantioselectivity, but the reaction was very slow (entry 5). We thus selected **7** as the best organocatalyst by considering the balance of yield and stereoselectivity. It should be noted that the diastereomeric ratio of epoxy alcohol **10a** was 1:3.8 with excellent enantioselectivity (90% *ee* for major isomer) even though the *E*/*Z* ratio of **3a** was 1:2. Stereoselectivity issues will be discussed later.

Solvent screening was performed using the catalyst **7** (Table 3). As the epoxy aldehyde **9a** was found to be stable enough for isolation, the yield, diastereo- and enantiose-

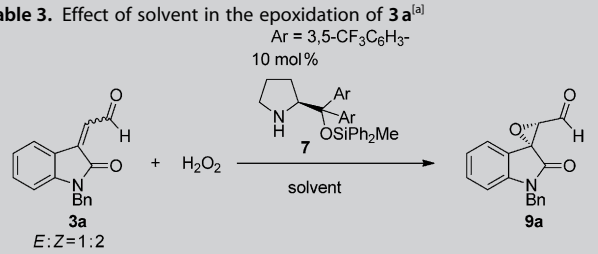
Table 2. Organocatalyzed asymmetric epoxidation of 2-oxoindoline-3-ylidene acetaldehyde **3a**[a]



Entry	Catalyst	Temp. [°C]	Time [h]	Yield of **10a** [%][b]	*dr*[c]	*ee* [%][d]
1	**4**	0	1.5	56	1:1.8	46/79
2	**5**	0	1.5	49	1:3.7	38/67
3	**6**	RT	2.5	63	1:6	68/86
4	**7**	RT	6	68	1:3.8	64/90
5	**8**	RT	7	26	1:6	80/98

[a] Unless otherwise noted, the reaction was performed by employing **3a** (0.1 mmol), hydrogen peroxide (0.3 mmol), and catalyst (0.01 mmol) in CH_2Cl_2 (1 mL) at indicated temperature and time. [b] Yield after isolation of the product. [c] The diastereomeric ratio was determined by ^{1}H NMR. [d] The enantiomeric excess was determined by HPLC analysis on a chiral phase.

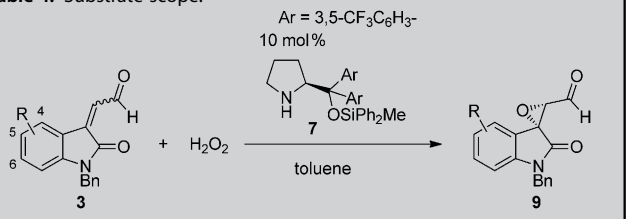
Table 3. Effect of solvent in the epoxidation of **3a**[a]



Entry	Solvent	Time [h]	Yield [%][b]	*dr*[c]	*ee* [%][d]
1	CH_2Cl_2	6	83	1:4.8	62/85
2	$CHCl_3$	7	74	1:4.2	72/78
3	MeCN	60	46	1:3.1	20/80
4	*i*PrOH	120	31	1:1.9	64/81
5	toluene	7	80	1:5.0	70/90

[a] Unless noted otherwise, the reaction was performed by employing **3a** (0.1 mmol), hydrogen peroxide (0.3 mmol), and catalyst (0.01 mmol) in solvent (1 mL) at room temperature for the indicated time. [b] Yield after isolation of the product. [c] The diastereomeric ratio was determined by ^{1}H NMR. [d] The enantiomeric excess was determined by HPLC analysis on a chiral phase.

Table 4. Substrate scope.[a]



Entry	R	*E*:*Z* of **3**	Time [h]	Yield [%][b]	*dr*[c]	*ee* [%][d]
1	H (**3a**)	1:2	7	80 (**9a**)	1:5.0	70/90
2	4-Br (**3b**)	*Z* only	28	61 (**9b**)	1:>20	–/94
3	5-Me (**3c**)	1:2	9	81 (**9c**)	1:4.4	73/91
4	6-Br (**3d**)	1:2	24	68 (**9d**)	1:3.6	69/98
5	6-OMe (**3e**)	1:1.3	6	55 (**1e**)[e]	–	–

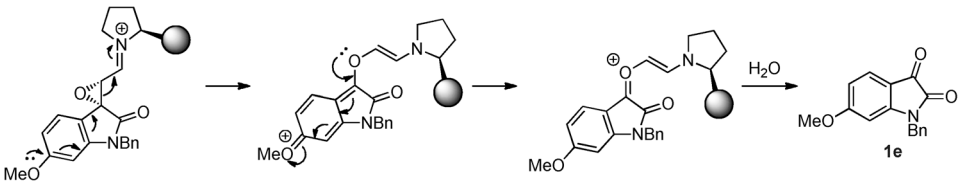
[a] Unless otherwise noted, the reaction was performed by employing **3a** (0.1 mmol), hydrogen peroxide (0.3 mmol), and catalyst **7** (0.01 mmol) in toluene (1 mL) at room temperature for the indicated time. [b] Yield after isolation of the product. [c] The diastereomeric ratio was determined by ^{1}H NMR. [d] The enantiomeric excess was determined by HPLC analysis on a chiral phase. [e] Isolated yield of **1e**, epoxy aldehyde **9e** was not isolated.

lectivities were determined at the stage of **9a**. When halogenated solvents such as CH_2Cl_2 or $CHCl_3$ were used, good yield, diastereo- and enantioselectivities were observed (entry 1, 2). In case of MeCN or *i*PrOH, the enantioselectivity was good, but the reaction progressed very slowly (entry 3, 4). Toluene was found to be the best in terms of diastereo- and enantioselectivity (entry 5).

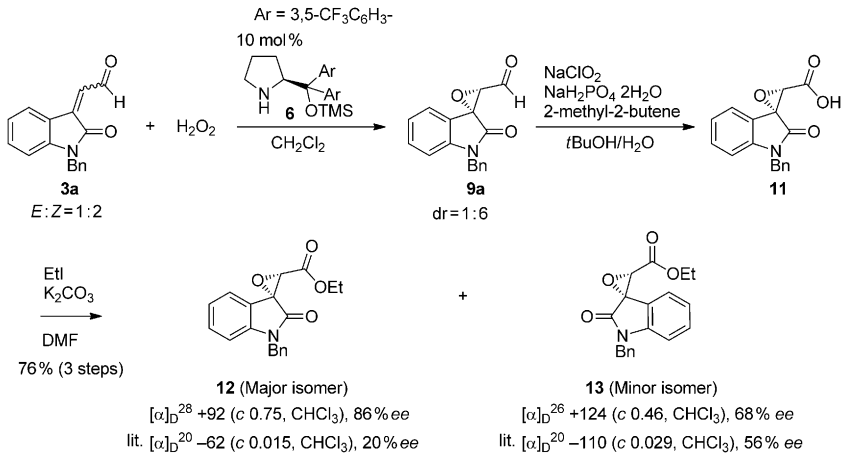
As the optimum condition was identified, substrate scope was investigated next (Table 4). An *E*/*Z* mixture of 2-oxoindoline-3-ylidene acetaldehyde **3** was thus treated with hydrogen peroxide in the presence of catalyst **7** in toluene. With no aromatic substituents, the epoxy aldehyde **9a** was obtained in 80% yield as a diastereomeric mixture (*dr* = 1:5) with excellent enantioselectivity (90% *ee*, major isomer) (entry 1). When the *Z*-isomer of 4-Br substrate **3b** was used, excellent diastereo- and enantioselectivities were observed (entry 2). Excellent enantioselectivity was also realized with both an electron donating 5-Me substrate **3c** and an electron withdrawing 6-Br substrate **3d** (entry 3, 4). In case of the 6-OMe substrate **3e**, isatin **1e** was obtained in 55% yield. The isatin **1e** is likely generated via its epoxide by C–C bond cleavage by virtue of the electron donating OMe group [Scheme 2]. It is noteworthy that better diastereoselectivity (1:3.6 to 5.0) was obtained even though a mixture of *E*/*Z* isomer **3** (1:2) was used as starting material (entry 1, 3, 4). In addition, the reaction time increased when the electron withdrawing Br group is appended to the aromatic ring (entry 2, 4).

The relative and absolute configuration of epoxy aldehyde **9a** was determined as follows (Scheme 3). After the asymmetric epoxidation of **3a** with hydrogen peroxide and catalyst **6**, the aldehyde **9a** was oxidized to carboxylic acid **11** and ethyl ester formation provided **12** and **13**. The relative and absolute configuration of **12** and **13** were determined by comparison of the NMR spectra and optical rotation to reported data.[23]

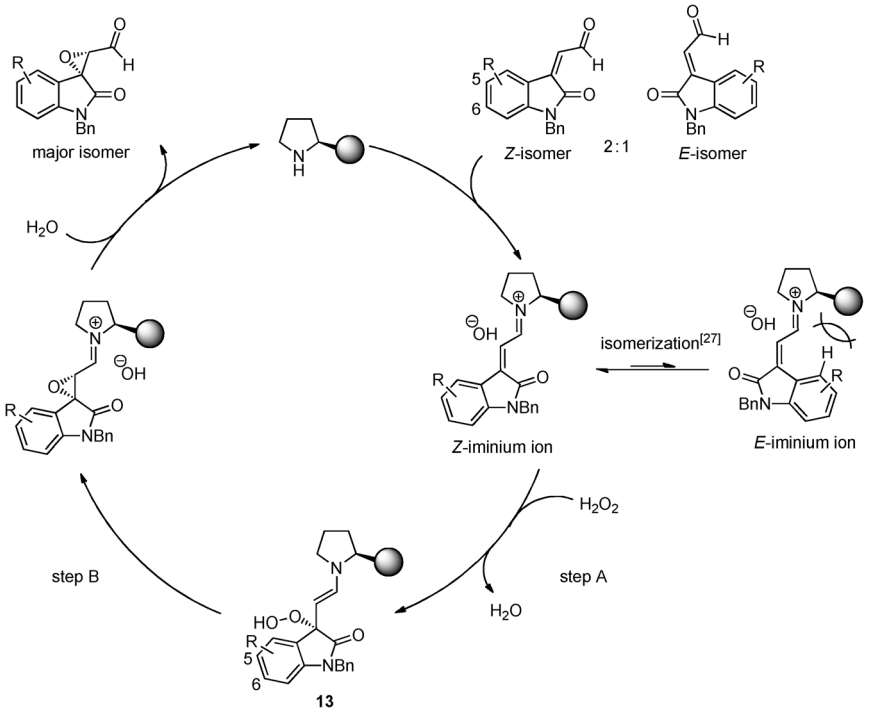
A postulated reaction mechanism is shown in Scheme 4. Both *E*/*Z* iminium ions would be formed from by combination of the amino-catalyst with the *E*/*Z*-mixture of 2-oxoindoline-3-ylidene acetaldehydes. As reported already,[27] isomerization of *E*/*Z*-iminium ions would exist via an addition/elimination process to the iminium ion by a hydroxyl ion or hydroperoxide anion. Owing to the steric repulsion between the bulky substituents on the pyrrolidine and the aromatic hydrogen atom, the *Z*-iminium ion would likely predominate. Hydroperoxide anion attack onto the *Z*-iminium ion, facially-opposite to the bulky substituents on the pyrrolidine, would then form a chiral enamine. Intramolecular carbon-attack of the enamine to the oxygen atom, expelling hydroxide, forms the epoxide. Subsequent hydrolysis then generates the major epoxy aldehyde stereoisomer. Here, good diastereo- and enantioselectivities were observed from a mixture of *E*/*Z* isomers of the 2-oxoindoline-3-ylidene acetaldehyde. We propose the electron withdrawing Br atom on the 6-position lowers the LUMO of the iminium ion, thus accelerating the addition step of the hydroperoxide anion (step A). However, the reaction time increased when the 5- or 6-position of aromatic ring was substituted by a Br atom, as compared to hydrogen (Table 4, entry 2, 4 vs 1). Here, the reactivity of enamine **13** is anticipated to decrease with Br substi-



Scheme 2.



Scheme 3. Determination of absolute configuration.



Scheme 4. Postulated reaction mechanism.

tution at 5- or 6-position of aromatic ring because the HOMO of the enamine **13** would lower, owing to an electron withdrawing Br atom. This would be the reason for the unexpected reactivity of Br substituted substrates.

Conclusions

We have developed an organocatalyzed asymmetric epoxidation of 2-oxoindoline-3-ylidene acetaldehydes with hydrogen peroxide in good yield. Good to excellent diastereo- and enantioselectivities were realized even though the starting material 2-oxoindoline-3-ylidene acetaldehydes pre-existed as a mixture of *E*/*Z*-isomers.

Acknowledgements

This work was supported by Mitsubishi Foundation and a Grant-in-Aid for Scientific Research on Innovative Areas "Advanced Molecular Transformations by Organocatalysts" from The Ministry of Education, Culture, Sports, Science and Technology, Japan.

Keywords: asymmetric reaction · epoxide · organocatalysis · oxindole

[1] a) K. Katsuki, K. B. Sharpless, *J. Am. Chem. Soc.* **1980**, *102*, 5974; b) R. M. Hanson, K. B. Sharpless, *J. Org. Chem.* **1986**, *51*, 1992.

[2] a) W. Zhang, J. L. Loebach, S. R. Wilson, E. N. Jacobsen, *J. Am. Chem. Soc.* **1990**, *112*, 2801; b) E. N. Jacobsen, W. Zhang, A. R. Muci, J. R. Ecker, L. Deng, *J. Am. Chem. Soc.* **1991**, *113*, 7063; c) For a review, see: E. N. Jacobsen in *Catalytic Asymmetric Synthesis* (Ed.: I. Ojima), VCH, New York, **1993**, pp. 159–202.

[3] R. Irie, K. Noda, Y. Ito, N. Matsumoto, T. Katsuki, *Tetrahedron Lett.* **1990**, *31*, 7345.

[4] a) M. Bougauchi, S. Watanabe, T. Arai, H. Sasai, M. Shibasaki, *J. Am. Chem. Soc.* **1997**, *119*, 2329; b) T. Nemoto, T. Ohshima, K. Yamaguchi, M. Shibasaki, *J. Am. Chem. Soc.* **2001**, *123*, 2725; c) T. Nemoto, T. Ohshima, M. Shibasaki, *J. Am. Chem. Soc.* **2001**, *123*, 9474.

[5] Selected reviews on organocatalysis: a) *Enantioselective Organocatalysis* (Ed.: P. I. Dalko), Wiley-VCH, Weinheim, **2007**; b) S. Mukherjee, J. W. Yang, S. Hoffmann, B. List, *Chem. Rev.* **2007**, *107*, 5471; c) A. M. Walji, D. W. C. MacMillan, *Synlett* **2007**, 1477; d) D. W. C. MacMillan, *Nature* **2008**, *455*, 304; e) C. F. Barbas III, *Angew. Chem. Int. Ed.* **2008**, *47*, 42; *Angew. Chem.* **2008**, *120*, 44; f) A. Dondoni, A. Massi, *Angew. Chem. Int. Ed.* **2008**, *47*, 4638; *Angew. Chem.* **2008**, *120*, 4716; g) P. Melchiorre, M. Marigo, A. Carlone, G. Bartoli, *Angew. Chem. Int. Ed.* **2008**, *47*, 6138; *Angew. Chem.* **2008**, *120*, 6232; h) S. Bertelsen, K. A. Jørgensen, *Chem. Soc. Rev.* **2009**, *38*, 2178; i) E. Marqués-López, R. P. Herrera, M. Christmann, *Nat. Prod. Rep.* **2010**, *27*, 1138; j) *Science of Synthesis Asymmetric Organocatalysis 1, Lewis Base and Acid Catalysts* (Ed.: B. List), Georg Thieme, Stuttgart, **2012**; k) *Science of Synthesis Asymmetric Organocatalysis 2, Brønsted Base and Acid Catalysts, and Additional Topics* (Ed.: K. Maruoka), Georg Thieme, Stuttgart, **2012**; l) *Comprehensive Enantioselective Organocatalysis, Vol. 1–3* (Ed.: P. I. Dalko), Wiley-VCH, Weinheim, **2013**.

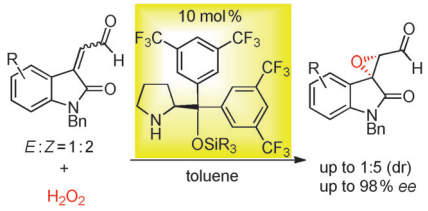
[6] a) Z. X. Wang, W. Tu, M. Frohn, J. R. Zhang, Y. Shi, *J. Am. Chem. Soc.* **1997**, *119*, 11224; Review, see; b) M. Frohn, Y. Shi, *Synthesis* **2000**, 1979; c) Y. Shi, *Acc. Chem. Res.* **2004**, *37*, 488.
[7] M. F. Adamo, V. A. Aggarwal, M. A. Sage, *J. Am. Chem. Soc.* **2000**, *122*, 8317.
[8] a) P. C. B. Page, B. R. Buckley, A. J. Blacker, *Org. Lett.* **2004**, *6*, 1543; b) P. C. B. Page, B. R. Buckley, M. M. Farah, A. J. Blacker, *Eur. J. Org. Chem.* **2009**, 3413.
[9] G. C. E. Peris, S. Jakobsche, J. Miller, *J. Am. Chem. Soc.* **2007**, *129*, 8710.
[10] *Science of Synthesis Asymmetric Organocatalysis 1, Lewis Base and Acid Catalysts* (Ed.: B. List), Georg Thieme, Stuttgart, **2012**, pp. 392 – 396.
[11] a) M. Marigo, J. Franzen, T. B. Poulsen, W. Zhuang, K. A. Jørgensen, *J. Am. Chem. Soc.* **2005**, *127*, 6964; b) W. Zhuang, M. Marigo, K. A. Jørgensen, *Org. Biomol. Chem.* **2005**, *3*, 3883; c) H. Sundén, I. Ibrahem, A. Córdova, *Tetrahedron Lett.* **2006**, *47*, 99; d) G. L. Zhao, I. Ibrahem, H. Sunden, A. Cordova, *Adv. Synth. Catal.* **2007**, *349*, 1210.
[12] X. Wang, B. List, *Angew. Chem. Int. Ed.* **2008**, *47*, 1119; *Angew. Chem.* **2008**, *120*, 1135.
[13] C. Sparr, W. B. Schweizer, H. M. Senn, R. Gilmour, *Angew. Chem. Int. Ed.* **2009**, *48*, 3065; *Angew. Chem.* **2009**, *121*, 3111.
[14] S. Lee, D. W. C. MacMillan, *Tetrahedron* **2006**, *62*, 11413.
[15] O. Lifchits, C. M. Reisinger, B. List, *J. Am. Chem. Soc.* **2010**, *132*, 10227.
[16] a) A. Lattanzi, *Org. Lett.* **2005**, *7*, 2579; b) A. Lattanzi, *Chem. Commun.* **2009**, 1452; c) A. Russo, A. Lattanzi, *Synthesis* **2009**, *9*, 1551; For a review, see: d) S. Meninno, A. Lattanzi, *Chem. Commun.* **2013**, *49*, 3821.
[17] J. Lu, Y. H. Xu, F. Liu, T. P. Loh, *Tetrahedron Lett.* **2008**, *49*, 6007.
[18] S. Tanaka, K. Nagasawa, *Synlett* **2009**, *4*, 667.
[19] a) C. M. Reisinger, X. Wang, B. List, *Angew. Chem. Int. Ed.* **2008**, *47*, 8112; *Angew. Chem.* **2008**, *120*, 8232; b) X. Lu, Y. Liu, B. Sun, B. Cindric, L. Deng, *J. Am. Chem. Soc.* **2008**, *130*, 8134.
[20] a) H. Jiang, K. S. Halskov, T. K. Johansen, K. A. Jørgensen, *Chem. Eur. J.* **2011**, *17*, 3842; b) E. M. Tanzer, L. E. Zimmer, W. B. Schweizer, R. Gilmour, *Chem. Eur. J.* **2012**, *18*, 11334.
[21] B. Yu, D. Q. Yu, H. M. Liu, *Eur. J. Med. Chem*. in press. DOI: 10.1016/j.ejmech.2014.06.056.
[22] M. Inoue, H. Sakazaki, H. Furuyama, M. Hirama, *Angew. Chem. Int. Ed.* **2003**, *42*, 2654; *Angew. Chem.* **2003**, *115*, 2758.
[23] C. Palumbo, G. Mazzeo, A. Mazziotta, A. Gambacorta, M. A. Loreto, A. Migliorini, S. Superchi, D. Tofani, T. Gasperi, *Org. Lett.* **2011**, *13*, 6248.
[24] B. P. Bondzic, T. Urushima, H. Ishikawa, Y. Hayashi, *Org. Lett.* **2010**, *12*, 5434.
[25] a) Y. Hayashi, H. Gotoh, T. Hayashi, M. Shoji, *Angew. Chem. Int. Ed.* **2005**, *44*, 4212; *Angew. Chem.* **2005**, *117*, 4284; b) H. Gotoh, Y. Hayashi in *Sustainable Catalysis: Challenges and Practices for the Pharmaceutical and Fine Chemical Industries* (Eds.: P. J. Dunn, K. K. Hii, M. J. Krische, M. T. Williams), Wiley, Hoboken, **2013**, Chap. 13, pp. 287 – 316.
[26] M. Marigo, T. C. Wabnitz, D. Fielenbach, K. A. Jørgensen, *Angew. Chem. Int. Ed.* **2005**, *44*, 794; *Angew. Chem.* **2005**, *117*, 804.
[27] T. Mukaiyama, K. Ogata, I. Sato, Y. Hayashi, *Chem. Eur. J.* **2014**, *20*, 13583.
[28] a) R. Liu, J. Zhang, *Org. Lett.* **2013**, *15*, 2266; b) R. Liu, J. Zhang, *Chem. Eur. J.* **2013**, *19*, 7319.

Received: October 11, 2014
Published online on ■■ ■■, 0000

*T. Mukaiyama, K. Ogata, T. Ono, Y. Hayashi**

■■ – ■■

Asymmetric Organocatalyzed Epoxidation of 2-Oxoindoline-3-ylidene Acetaldehydes



Giving metal catalysis the slip: The asymmetric epoxidation of 2-oxoindoline-3-ylidene acetaldehydes with hydrogen peroxide, catalyzed by diarylprolinol silyl ether, has been developed. Good to excellent diastereo- and enantioselectivities were realized even though the starting material 2-oxoindoline-3-ylidene acetaldehydes pre-existed as a mixture of *E*/*Z*-isomers.