

## RESEARCH ARTICLE

View Article Online

View Journal | View Issue



Cite this: *Org. Chem. Front.*, 2015, 2, 811

Received 26th March 2015,  
Accepted 28th April 2015

DOI: 10.1039/c5qo00099h

rs.c.li/frontiers-organic

# Efficient catalytic enantioselective Nazarov cyclizations of divinyl ketoesters†

Zhou Xu,<sup>a,b</sup> Hai Ren,<sup>a</sup> Lijia Wang<sup>\*a</sup> and Yong Tang<sup>\*a</sup>

An efficient catalytic enantioselective Nazarov cyclization of divinyl ketoesters was developed using a chiral BOX/Cu(II) complex, which provides facile access to a variety of optically active multi-substituted cyclopent-2-enone esters in 78–95% yields with 78–90% ee.

Multi-substituted five membered carbocyclic skeletons are widely found in natural products and other biologically active compounds.<sup>1</sup> Nazarov cyclization reaction<sup>2–4</sup> represents one of the most effective methods for the construction of five membered carbocyclic rings, and it has been applied in the total synthesis of many useful natural products.<sup>5</sup> However, in the asymmetric catalytic Nazarov reaction, which has attracted increasing attention from chemists, it is quite difficult to achieve high enantioselectivity. Only a few successful examples have been reported.<sup>6–9</sup> In 2004, Trauner *et al.* developed the first highly efficient scandium–pybox catalyzed asymmetric Nazarov reactions of divinyl ketones bearing an oxygen at the  $\alpha$ -position of the vinyl nucleophile (Type A, Fig. 1).<sup>6b</sup> In 2013, Rawal *et al.* documented the Cr(III)/salen promoted enantioselective Nazarov cyclizations of dienones (Type A, Fig. 1), giving rise to cyclopentenoids in 80–96% ee.<sup>6f</sup> In 2010, an elegant bifunctional thiourea promoted organocatalytic asymmetric Nazarov cyclization of diketoesters (Type B, Fig. 1) was realized by Tius *et al.*, affording the  $\alpha$ -hydroxycyclopentenones in 42–95% yields with 80–97% ee.<sup>7a</sup> In the same year, our group reported a highly regio-, diastereo-, and enantioselective

Nazarov reaction of alkoxy divinyl ketoesters (Type C, Fig. 1) catalyzed by a chiral trisoxazoline/copper(II) system.<sup>8</sup>

On the other hand, for acyclic divinyl ketoesters (Type D, Fig. 1) as substrates,<sup>10d,e</sup> the racemic studies on the Nazarov cyclization<sup>10</sup> have achieved important breakthrough in recent years; however, successful examples of an asymmetric version are still limited. In 2003, Aggarwal *et al.* developed the first asymmetric Nazarov cyclization promoted by stoichiometric or semi-stoichiometric chiral Cu(II)–pybox complexes, achieving up to 88% enantiomeric excess (eqn (1), Scheme 1).<sup>9a</sup> Togni *et al.* reported a chiral tridentate phosphine Pigiphos/Ni(II) catalyzed process of divinyl ketoesters containing an activated trimethoxyphenyl (TMP) group or a 4-methoxyphenyl (PMP) group, affording the products in 32–97% yields with 45–88% ee after 4–15 days (eqn (2), Scheme 1).<sup>9b</sup> Despite these great efforts, challenging problems, such as reactivity, stereo-selectivity and substrate scope generality in this process, have

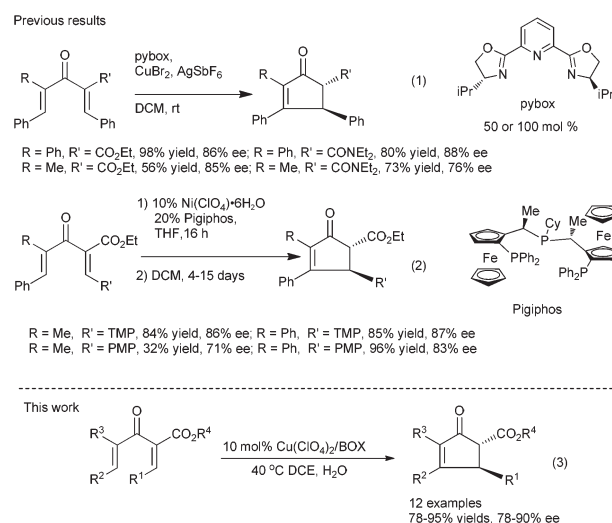


Fig. 1 Representative substrate types used in Nazarov reaction.

<sup>a</sup>State Key Laboratory of Organometallic Chemistry, Shanghai Institute of Organic Chemistry, Chinese Academy of Sciences, 345 Lingling Lu, Shanghai 200032, China. E-mail: tangy@mail.sioc.ac.cn, wanglijia@sioc.ac.cn

<sup>b</sup>Xuzhou Medical College, 209 Tongshan Road, Xuzhou 221004, China

†Electronic supplementary information (ESI) available: Experimental procedures and the characterization data of new compounds. See DOI: 10.1039/c5qo00099h



Scheme 1 Asymmetric Nazarov cyclization of divinyl ketoesters (Type D).

not been well resolved yet. Recently, we have developed an efficient catalytic enantioselective Nazarov cyclization of divinyl ketoesters, which provides facile access to the optically active multi-substituted cyclopent-2-enones in high yields with good to excellent ee values (eqn (3), Scheme 1). In this communication, we wish to report the preliminary results.

Initially, the enantioselective Nazarov cyclization of substrate **1a** was carried out with 20 mol% of copper complex in a chloroform solution at 40 °C. The pyridyl bisoxazolines were documented as effective chiral ligands in the asymmetric Nazarov reactions.<sup>6b,e,9a,c</sup> However, as to substrate **1a**,<sup>11</sup> with **L1** the reaction could not occur (entry 1, Table 1). Then we tried to use BOX ligand **L2**, and found that the cyclization proceeded smoothly producing **2a** in 86% yield with 51% ee (entry 2). Changing the solvent to 1,2-dichloroethane (DCE) led to a better level of enantioselectivity (61% ee, entry 3). Next, we turned to investigate a series of BOX ligands bearing various chiral backbones.<sup>12</sup> With the L-Ala derived BOX ligand **L3**, the product **2a** was obtained in 84% yield with 47% ee (entry 4). A more hindered <sup>i</sup>Pr group was beneficial to the enantioselectivity (67% ee, entry 5). However, on continuing to increase the hindrance, **L5** led to a dramatic drop of the enantioselectivity (23% ee entry 6). Meanwhile, when the L-Phe derived BOX ligand **L6** was employed, **2a** was produced in 93% yield with 58% ee (entry 7). Under optimal conditions, we

finally found that chiral ligand **L7** could promote the reaction very efficiently, affording **2a** in 92% yield with 90% ee after 10 h (entry 8), better than pybox/Cu(SbF<sub>6</sub>)<sub>2</sub> in both selectivity and catalyst loading. We also examined the counter ion effect of this reaction. As shown in entries 8–10, ClO<sub>4</sub><sup>−</sup> proved to be the best one. However, when the catalyst loading was further reduced to 10 mmol%, the ee value dropped to 84% ee (entry 11). In order to raise the efficiency of this reaction system, additives were examined. Interestingly, 4 Å molecular sieves destroyed the reaction, while a trace amount of water could promote the reaction to give 92% yield and 90% ee (entry 12 vs. 13).<sup>13</sup>

Under the optimized reaction conditions (entry 8, Table 1), we next investigated the substrate scope (Table 2). Divinyl ketoesters **1b–d** bearing the R<sup>1</sup> group with –Br substituted at the *para*-, *meta*- and *ortho*- positions underwent cyclization with high enantioselectivity (85–88% ee) and a decline of the reactivity (entries 2–4). When R<sup>1</sup> was a 4-PhC<sub>6</sub>H<sub>5</sub>– group, 20% catalyst loading was required to produce the cyclization product **2e** in 92% yield with 88% ee (entry 5). Cyclic enone products **2g** and **2h** bearing both 1- and 2-naphthyl groups could be easily accessed in 89% yield with 86% ee, and in 93% yield with 87% ee, respectively (entries 7 and 8). The catalyst system was even competent with electron deficient substrate **1f**, affording the product **2f** in 83% yield with 84% ee (entry 6). As to the electron-rich substrates **1i** and **1j**, the reactions proceeded very fast and were complete within 2 h at room temperature, giving the corresponding products **2i** and **2j** in high yields with good enantioselectivities (entries 9 and 10). Thus, the current cata-

Table 1 Reaction optimization<sup>a</sup>

| Entry             | Metal salts                                           | L         | Solvent           | Time (h) | Yield <sup>b</sup> (%) | ee <sup>c</sup> (%) |
|-------------------|-------------------------------------------------------|-----------|-------------------|----------|------------------------|---------------------|
| 1                 | Cu(ClO <sub>4</sub> ) <sub>2</sub> ·6H <sub>2</sub> O | <b>L1</b> | CHCl <sub>3</sub> | 24       | 0                      | —                   |
| 2                 | Cu(ClO <sub>4</sub> ) <sub>2</sub> ·6H <sub>2</sub> O | <b>L2</b> | CHCl <sub>3</sub> | 17       | 86                     | 51                  |
| 3                 | Cu(ClO <sub>4</sub> ) <sub>2</sub> ·6H <sub>2</sub> O | <b>L2</b> | DCE               | 14       | 90                     | 62                  |
| 4                 | Cu(ClO <sub>4</sub> ) <sub>2</sub> ·6H <sub>2</sub> O | <b>L3</b> | DCE               | 12       | 84                     | 47                  |
| 5                 | Cu(ClO <sub>4</sub> ) <sub>2</sub> ·6H <sub>2</sub> O | <b>L4</b> | DCE               | 14       | 90                     | 67                  |
| 6                 | Cu(ClO <sub>4</sub> ) <sub>2</sub> ·6H <sub>2</sub> O | <b>L5</b> | DCE               | 16       | 95                     | 23                  |
| 7                 | Cu(ClO <sub>4</sub> ) <sub>2</sub> ·6H <sub>2</sub> O | <b>L6</b> | DCE               | 14       | 93                     | 58                  |
| 8                 | Cu(ClO <sub>4</sub> ) <sub>2</sub> ·6H <sub>2</sub> O | <b>L7</b> | DCE               | 10       | 92                     | 90                  |
| 9                 | Cu(SbF <sub>6</sub> ) <sub>2</sub>                    | <b>L7</b> | DCE               | 8        | 94                     | 89                  |
| 10                | Cu(OTf) <sub>2</sub>                                  | <b>L7</b> | DCE               | 10       | 86                     | 88                  |
| 11 <sup>d</sup>   | Cu(ClO <sub>4</sub> ) <sub>2</sub> ·6H <sub>2</sub> O | <b>L7</b> | DCE               | 14       | 91                     | 84                  |
| 12 <sup>d,e</sup> | Cu(ClO <sub>4</sub> ) <sub>2</sub> ·6H <sub>2</sub> O | <b>L7</b> | DCE               | 24       | 0                      | —                   |
| 13 <sup>d,f</sup> | Cu(ClO <sub>4</sub> ) <sub>2</sub> ·6H <sub>2</sub> O | <b>L7</b> | DCE               | 24       | 92                     | 90                  |

<sup>a</sup> Reactions were carried out with metal salts (0.04 mmol), ligand (0.04 mmol) and **1a** (0.2 mmol) in solvent (4.0 mL) under an Ar atmosphere. <sup>b</sup> Isolated yield. <sup>c</sup> Determined by chiral HPLC. <sup>d</sup> The reaction was carried out with 10 mol% catalyst loading. <sup>e</sup> 4 Å molecular sieves were added. <sup>f</sup> H<sub>2</sub>O (0.12 mmol, 2.3 μL) was added.

Table 2 Substrate scope<sup>a</sup>

| Entry           | R <sup>1</sup> ; R <sup>2</sup> ; R <sup>3</sup> ; R <sup>4</sup> | 2         | Time (h) | Yield <sup>b</sup> (%) | ee <sup>c</sup> (%)  |
|-----------------|-------------------------------------------------------------------|-----------|----------|------------------------|----------------------|
| 1               | Ph; Ph; Ph; Et                                                    | <b>2a</b> | 24       | 92                     | 90 <sup>e</sup>      |
| 2               | 4-BrC <sub>6</sub> H <sub>5</sub> ; Ph; Ph; Et                    | <b>2b</b> | 45       | 81                     | 88                   |
| 3               | 3-BrC <sub>6</sub> H <sub>5</sub> ; Ph; Ph; Et                    | <b>2c</b> | 55       | 80                     | 85                   |
| 4               | 2-BrC <sub>6</sub> H <sub>5</sub> ; Ph; Ph; Et                    | <b>2d</b> | 60       | 78                     | 86                   |
| 5               | 4-PhC <sub>6</sub> H <sub>5</sub> ; Ph; Ph; Et                    | <b>2e</b> | 22       | 92                     | 84 (88) <sup>d</sup> |
| 6               | 4-CF <sub>3</sub> C <sub>6</sub> H <sub>5</sub> ; Ph; Ph; Et      | <b>2f</b> | 72       | 83                     | 84                   |
| 7               | 1-Naphthyl; Ph; Ph; Et                                            | <b>2g</b> | 24       | 89                     | 86                   |
| 8               | 2-Naphthyl; Ph; Ph; Et                                            | <b>2h</b> | 24       | 93                     | 87                   |
| 9 <sup>f</sup>  | Ph; 4-MeOC <sub>6</sub> H <sub>5</sub> ; Ph; Et                   | <b>2i</b> | 2        | 91                     | 78                   |
| 10 <sup>f</sup> | Ph; 4-MeOC <sub>6</sub> H <sub>5</sub> ; Et                       | <b>2j</b> | 2        | 90                     | 82                   |
| 11              | Ph; Ph; Ph; Me                                                    | <b>2k</b> | 20       | 95                     | 90                   |
| 12              | 4-IC <sub>6</sub> H <sub>5</sub> ; Ph; Ph; Me                     | <b>2l</b> | 30       | 87                     | 90                   |

<sup>a</sup> Reactions were carried out with Cu(ClO<sub>4</sub>)<sub>2</sub>·6H<sub>2</sub>O (0.02 mmol), **L7** (0.02 mmol), **1** (0.2 mmol) and H<sub>2</sub>O (0.12 mmol) in DCE (4.0 mL) under an Ar atmosphere. <sup>b</sup> Isolated yield. <sup>c</sup> Determined by chiral HPLC. <sup>d</sup> The reaction was carried out with 20 mol% catalyst loading. <sup>e</sup> The absolute configuration of the major enantiomer is (1*R*,5*S*) by the comparison of the reported data. <sup>f</sup> The reaction was carried out at rt.

Scheme 2 Control experiment of **1a'**.

Scheme 3 Product transformation.

lyst system is tolerated for both electron rich and poor substrates. In addition, by changing the ester group from ethyl to methyl, both the reactivity and the enantioselectivity are maintained (entry 11). Moreover, for the 4-IC<sub>6</sub>H<sub>5</sub> substituted divinyl ketoester **1l**, a pleasing result of 87% yield with 90% ee was obtained (entry 12).

Interestingly, when substrate **1a'** was employed with the current catalytic system, the absolute configuration of the major enantiomer reversed to (1*S*,5*R*), leading to the product **2a'** in 72% ee (Scheme 2). Thus, under the same catalyst system, both the enantiomers could be obtained in terms of changing the *Z/E* configuration of substrates.

Fluorine-containing chiral cyclic ketoesters are potentially useful building blocks for the synthesis of natural products and medicines. Ma *et al.* reported an elegant copper-catalyzed tandem Nazarov cyclization–electrophilic fluorination reaction in the stereoselective synthesis of highly substituted indanones.<sup>14</sup> We found that under mild reaction conditions, compound **2a** was easily transferred to fluorine substituted ketoester **3a** in 87% yield without loss of optical purity with stereospecific diastereoselectivity (Scheme 3).<sup>7,9c</sup>

## Conclusions

In conclusion, we have developed an efficient catalytic enantioselective Nazarov cyclization of divinyl ketoesters by a chiral BOX/Cu(II) complex, which provides facile access to the optically active cyclopent-2-enone esters with functional diversity in 78–95% yields with 78–90% ee. There are several remarkable features of the method, such as mild reaction conditions, high catalytic efficiency and simple procedure, that make the current reaction practically useful. A study on the application of this method to the total synthesis of natural products is ongoing in our lab.

## Acknowledgements

We are grateful for the financial support from the National Natural Sciences Foundation of China (no. 21121062 and 21272250), and the Chinese Academy of Sciences. We thank Dr Xue-bing, Leng (SIOC) and Mr Jie, Sun (SIOC) for X-ray crystal analysis.

## Notes and references

- For recent reviews on five-membered carbocycles, see: (a) S. E. Gibson, S. E. Lewis and N. Mainolfi, *J. Organomet. Chem.*, 2004, **689**, 3873; (b) V. B. Kurteva and C. A. M. Afonso, *Chem. Rev.*, 2009, **109**, 6809.
- For books and reviews on the Nazarov reaction: (a) S. E. Denmark, in *Comprehensive Organic Synthesis*, ed. B. M. Trost and I. Fleming, Pergamon, Oxford, 1991, vol. 5, p. 751; (b) C. Santelli-Rouvier and M. Santelli, *Synthesis*, 1983, 429; (c) M. Ramaiah, *Synthesis*, 1984, 529; (d) K. L. Habermas, S. E. Denmark and T. K. Jones, *Org. React.*, 1994, **45**, 1; (e) M. A. Tius, *Acc. Chem. Res.*, 2003, **36**, 284; (f) H. Pellissier, *Tetrahedron*, 2005, **61**, 6479; (g) A. J. Frontier and C. Collison, *Tetrahedron*, 2005, **61**, 7577; (h) M. A. Tius, *Eur. J. Org. Chem.*, 2005, 2193; (i) N. Grant, C. J. Rieder and F. G. West, *Chem. Commun.*, 2009, 5676; (j) S. Thompson, A. G. Coyne, P. C. Knipe and M. D. Smith, *Chem. Soc. Rev.*, 2011, **40**, 4217; (k) C. Schotes and A. Mezzetti, *ACS Catal.*, 2012, **2**, 528.
- For selected racemic examples, see: (a) S. E. Denmark and T. K. Jones, *J. Am. Chem. Soc.*, 1982, **104**, 2642; (b) T. K. Jones and S. E. Denmark, *Helv. Chim. Acta*, 1983, **66**, 2397; (c) T. K. Jones and S. E. Denmark, *Helv. Chim. Acta*, 1983, **66**, 2377; (d) W. He, X. F. Sun and A. J. Frontier, *J. Am. Chem. Soc.*, 2003, **125**, 14278; (e) M. Janka, W. He, A. J. Frontier and R. Eisenberg, *J. Am. Chem. Soc.*, 2004, **126**, 6864; (f) A. R. Banaag and M. A. Tius, *J. Org. Chem.*, 2008, **73**, 8133; (g) A. K. Basak and M. A. Tius, *Org. Lett.*, 2008, **10**, 4073; (h) T. N. Grant and F. G. West, *J. Am. Chem. Soc.*, 2006, **128**, 9348; (i) M. Janka, W. He, I. E. Haedicke, F. R. Fronczek, A. J. Frontier and R. Eisenberg, *J. Am. Chem. Soc.*, 2006, **128**, 5312; (j) D. Song, A. Rostami and F. G. West, *J. Am. Chem. Soc.*, 2007, **129**, 12019; (k) F. Dhoro, T. E. Kristensen, V. Stockmann, G. P. A. Yap and M. A. Tius, *J. Am. Chem. Soc.*, 2007, **129**, 7256; (l) A. R. Banaag and M. A. Tius, *J. Am. Chem. Soc.*, 2007, **129**, 5328; (m) J. Huang and A. J. Frontier, *J. Am. Chem. Soc.*, 2007, **129**, 8060; (n) W. He, I. R. Herrick, T. A. Atesin, P. A. Caruana, C. A. Kellenberger and A. J. Frontier, *J. Am. Chem. Soc.*, 2008, **130**, 1003.
- (a) P. Cordier, C. Aubert, M. Malacria, E. Lacte and V. Gandon, *Angew. Chem., Int. Ed.*, 2009, **48**, 8757; (b) C. J. Rieder, K. J. Winberg and F. G. West, *J. Am. Chem. Soc.*, 2009, **131**, 7504; (c) P. Cao, X.-L. Sun, B.-H. Zhu, Q. Shen, Z. Xie and Y. Tang, *Org. Lett.*, 2009, **11**, 3048; (d) F. De Simone, J. Gertsch and J. Waser, *Angew. Chem., Int.*

- Ed.*, 2010, **49**, 5767; (e) V. M. Marx and D. J. Burnell, *J. Am. Chem. Soc.*, 2010, **132**, 1685; (f) J. L. Brooks, P. A. Caruana and A. J. Frontier, *J. Am. Chem. Soc.*, 2011, **133**, 12454; (g) C. J. Hastings, M. P. Backlund, R. G. Bergman and K. N. Raymond, *Angew. Chem., Int. Ed.*, 2011, **50**, 10570; (h) V. M. Marx, R. L. Stoddard, G. S. Heverly-Coulson and D. J. Burnell, *Chem. – Eur. J.*, 2011, **17**, 8098; (i) J. Barluenga, A. Alvarez-Fernandez, A. L. Suarez-Sobrinio and M. Tomas, *Angew. Chem., Int. Ed.*, 2012, **51**, 183; (j) J. L. Brooks and A. J. Frontier, *J. Am. Chem. Soc.*, 2012, **134**, 16551; (k) D. J. Kerr, M. Miletic, J. H. Chaplin, J. M. White and B. L. Flynn, *Org. Lett.*, 2012, **14**, 1732; (l) L. H. Zhu, Z. G. Xi, J. Lv and S. Z. Luo, *Org. Lett.*, 2013, **15**, 4496.
- 5 For selected examples, see: (a) G. O. Berger and M. A. Tius, *J. Org. Chem.*, 2007, **72**, 6473; (b) L. Wan and M. A. Tius, *Org. Lett.*, 2007, **9**, 647; (c) W. He, J. Huang, X. Sun and A. J. Frontier, *J. Am. Chem. Soc.*, 2007, **129**, 498; (d) D. R. Williams, L. A. Robinson, C. R. Nevill and J. P. Reddy, *Angew. Chem., Int. Ed.*, 2007, **46**, 915; (e) W. He, J. Huang, X. Sun and A. J. Frontier, *J. Am. Chem. Soc.*, 2008, **130**, 300; (f) J. A. Malona, K. Cariou and A. J. Frontier, *J. Am. Chem. Soc.*, 2009, **131**, 7560; (g) S. Gao, Q. Wang and C. Chen, *J. Am. Chem. Soc.*, 2009, **131**, 1410; (h) A. Y. Bitar and A. J. Frontier, *Org. Lett.*, 2009, **11**, 49; (i) H. M. Cheng, W. W. Tian, P. A. Peixoto, B. Dhudshia and D. Y. K. Chen, *Angew. Chem., Int. Ed.*, 2011, **50**, 4165; (j) D. J. Kerr and B. L. Flynn, *Org. Lett.*, 2012, **14**, 1740; (k) P. Magnus, W. A. Freund, E. J. Moorhead and T. Rainey, *J. Am. Chem. Soc.*, 2012, **134**, 6140; (l) J. A. Malona, K. Cariou, W. T. Spencer and A. J. Frontier, *J. Org. Chem.*, 2012, **77**, 1891; (m) J. C. P. Reyes and D. Romo, *Angew. Chem., Int. Ed.*, 2012, **51**, 6870; (n) C. J. Song, H. Liu, M. L. Hong, Y. Y. Liu, F. F. Jia, L. Sun, Z. L. Pan and J. B. Chang, *J. Org. Chem.*, 2012, **77**, 704; (o) D. H. Dethe and G. Murhade, *Org. Lett.*, 2013, **15**, 429; (p) D. J. Kerr, M. Miletic, N. Manchala, J. M. White and B. L. Flynn, *Org. Lett.*, 2013, **15**, 4118; (q) B. J. Moritz, D. J. Mack, L. C. Tong and R. J. Thomson, *Angew. Chem., Int. Ed.*, 2014, **53**, 2988; (r) A. Shvartsbart and A. B. Smith, *J. Am. Chem. Soc.*, 2014, **136**, 870.
- 6 (a) G. Liang, S. N. Gradl and D. Trauner, *Org. Lett.*, 2003, **5**, 4931; (b) G. Liang and D. Trauner, *J. Am. Chem. Soc.*, 2004, **126**, 9544; (c) M. Rueping, W. Ieawsuwan, A. P. Antonchick and B. J. Nachtsheim, *Angew. Chem., Int. Ed.*, 2007, **46**, 2097; (d) M. Rueping and W. Ieawsuwan, *Adv. Synth. Catal.*, 2009, **351**, 78; (e) K. Yaji and M. Shindo, *Synlett*, 2009, 2524; (f) G. E. Hutson, Y. E. Türkmen and V. H. Rawal, *J. Am. Chem. Soc.*, 2013, **135**, 4988.
- 7 (a) A. K. Basak, N. Shimada, W. F. Bow, D. A. Vicic and M. A. Tius, *J. Am. Chem. Soc.*, 2010, **132**, 8266; (b) N. Shimada, C. Stewart, W. F. Bow, A. Jolit, K. Wong, Z. Zhou and M. A. Tius, *Angew. Chem., Int. Ed.*, 2012, **51**, 5727; (c) A. Jolit, S. Vazquez-Rodriguez, G. P. A. Yap and M. A. Tius, *Angew. Chem., Int. Ed.*, 2013, **52**, 11102; (d) A. Jolit, P. M. Walleiser, G. P. A. Yap and M. A. Tius, *Angew. Chem., Int. Ed.*, 2014, **53**, 6180.
- 8 P. Cao, C. Deng, Y. Y. Zhou, X. L. Sun, J. C. Zheng, Z. W. Xie and Y. Tang, *Angew. Chem., Int. Ed.*, 2010, **49**, 4463.
- 9 (a) V. K. Aggarwal and A. J. Belfield, *Org. Lett.*, 2003, **5**, 5075; (b) I. Walz and A. Togni, *Chem. Commun.*, 2008, 4315; (c) M. Kawatsura, K. Kajita, S. Hayase and T. Itoh, *Synlett*, 2010, 1243.
- 10 (a) W. He, I. R. Herrick, T. A. Atesin, P. A. Caruana, C. A. Kellenberger and A. J. Frontier, *J. Am. Chem. Soc.*, 2008, **130**, 1003; (b) T. Vaidya, A. C. Atesin, I. R. Herrick, A. J. Frontier and R. Eisenberg, *Angew. Chem., Int. Ed.*, 2010, **49**, 3363; (c) J. Huang, D. Leboeuf and A. J. Frontier, *J. Am. Chem. Soc.*, 2011, **133**, 6307; (d) D. Leboeuf, V. Gandon, J. Ciesielski and A. J. Frontier, *J. Am. Chem. Soc.*, 2012, **134**, 6296; (e) Y. Kwon, R. McDonald and F. G. West, *Angew. Chem., Int. Ed.*, 2013, **52**, 8616.
- 11 CCDC 1029676 (2a) contains the supplementary crystallographic data for this paper. See the ESI.†
- 12 For recent reviews on bisoxazoline and oxazoline-containing ligands in asymmetric catalysis, see: (a) C. Foltz, B. Stecker, G. Marconi, S. Bellemin-Laponnaz, H. Wadepohl and L. H. Gade, *Chem. – Eur. J.*, 2007, **13**, 9912; (b) S. Bellemin-Laponnaz and L. H. Gade, *Actual. Chim.*, 2007, 16; (c) G. C. Hargaden and P. J. Guiry, *Chem. Rev.*, 2009, **109**, 2505; (d) G. Desimoni, G. Faita and K. A. Jørgensen, *Chem. Rev.*, 2011, **111**, 284; (e) J. Zhou and Y. Tang, *Top. Organomet. Chem.*, 2011, **36**, 287; (f) S. H. Liao, X. L. Sun and Y. Tang, *Acc. Chem. Res.*, 2014, **47**, 2260; (g) Q.-H. Deng, R. L. Melen and L. H. Gade, *Acc. Chem. Res.*, 2014, **47**, 3162. For selected recent studies, see: (h) J. Choi and G. C. Fu, *J. Am. Chem. Soc.*, 2012, **134**, 9102; (i) J. Li, S. Liao, H. Xiong, Y.-Y. Zhou, X.-L. Sun, Y. Zhang, X.-G. Zhou and Y. Tang, *Angew. Chem., Int. Ed.*, 2012, **51**, 8838; (j) C. Deng, L. Wang, J. Zhu and Y. Tang, *Angew. Chem., Int. Ed.*, 2012, **51**, 11620; (k) D. Leboeuf, V. Gandon, J. Ciesielski and A. J. Frontier, *J. Am. Chem. Soc.*, 2012, **134**, 6296; (l) Y.-Y. Zhou, L. Wang, J. Li, X.-L. Sun and Y. Tang, *J. Am. Chem. Soc.*, 2012, **134**, 9066; (m) X.-G. Song, S.-F. Zhu, X.-L. Xie and Q.-L. Zhou, *Angew. Chem., Int. Ed.*, 2013, **52**, 2555; (n) H. Xiong, H. Xu, S. Liao, Z. Xie and Y. Tang, *J. Am. Chem. Soc.*, 2013, **135**, 7851; (o) T. Kusakabe, T. Takahashi, R. Shen, A. Y. Ikeda, D. Dhage, Y. Kanno, Y. Inouye, H. Sasai, T. Mochida and K. Kato, *Angew. Chem., Int. Ed.*, 2013, **52**, 7845; (p) J. Choi, P. Martin-Gago and G. C. Fu, *J. Am. Chem. Soc.*, 2014, **136**, 12161; (q) X.-L. Xie, S.-F. Zhu, J.-X. Guo, Y. Cai and Q.-L. Zhou, *Angew. Chem., Int. Ed.*, 2014, **53**, 2978; (r) J.-J. Shen, S.-F. Zhu, Y. Cai, H. Xu, X.-L. Xie and Q.-L. Zhou, *Angew. Chem., Int. Ed.*, 2014, **53**, 13188.
- 13 For details, see the ESI.†
- 14 J. Nie, H.-W. Zhu, H.-F. Cui, M.-Q. Hua and J.-A. Ma, *Org. Lett.*, 2007, **9**, 3053.