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Asymmetric addition of benzothiazole to *N-tert*-butanesulfinyl imine for the synthesis of chiral α-branched heteroaryl amines

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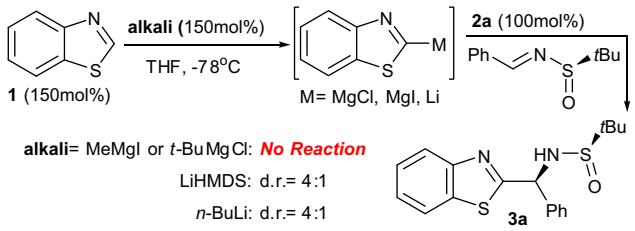
ABSTRACT

This work concerns the asymmetric additions of benzothiazole to a variety of *N-tert*-butanesulfinyl imines with excellent diastereoselectivities (d.r. up to >99:1). Amino alkoxyl lithium was the key additive to obtain the excellent diastereoselectivity. More functionalized 4-methyl-5-vinyl thiazole and alkyl imines which can isomerize to enamines are also compatible substrates to the present protocol.

Heteroaromatic compounds always exhibit broad bioactivity and pharmacodynamic value. These compounds are also important synthetic intermediates in organic chemistry. The most attractive and challenging way for their structural diversity is direct functionalization of arene via new bond construction. In recent years, expanding progress has been developed in the direct functionalization of benzothiazole at C2 position.[1] These studies mainly focused on the direct cross coupling strategy for the benzothiazole arylation,[2] alkylation,[3] alkynylation,[4] carbonylation,[5] iodination,[6] amination,[7] and sulfuration.[8] Besides, limited studies were reported in the addition of benzothiazole to alkyne,[9] aldehyde[10] as well as ketone.[11] However, the addition of benzothiazole to aldimine for chiral heteroaromatic substituted amine synthesis has rarely been reported. Asymmetric synthesis of chiral diaryl-methylamines has attracted growing attentions,[12] since these frameworks always perform as key building blocks as well as important synthetic intermediates for a series of bioactive compounds. As the formation of one C–C bond and one chiral center can be achieved in one step, direct aryl transfer approach is considered to be the most facile strategy. The present efforts mainly focused on the rhodium catalysis for the synthesis of diarylmethylamine via new C–C bond formation.[13] While the use of chiral sulfinyl as the chiral auxiliary has been widely exploited in various synthetic approaches,[14] the additions of aryl-Grignard reagent[15] and aryl-lithium reagent[16] to *N-tert*-butanesulfinyl imine were recognized to be reliable alternative methods. However, to obtain excellent diastereoselectivity still remains the most challenging issue. Although very limited cases have disclosed the addition of benzothiazole to ketimine for achiral tertiary amine synthesis,[17] to the best of our knowledge, the direct asymmetric addition of benzothiazole to imine to afford chiral α-branched aryl-heteroaryl amine has not yet reported. Herein, we report a highly diastereoselective synthesis of chiral α-branched heteroaryl amines. The direct asymmetric addition of benzothiazole to a series of *N-tert*-butanesulfinyl imines was carried out with excellent diastereoselectivities. Amplification of the chiral auxiliary effect was also observed with the aid of the amino alkoxyl lithium additive chelation with *N-tert*-butanesulfinyl imine.

The preliminary study indicated that the benzothiazole-metallic reagents exhibit distinctly different nucleophilicity (Scheme



Scheme 1. Preliminary study for the addition of **1** to imine **2a**.

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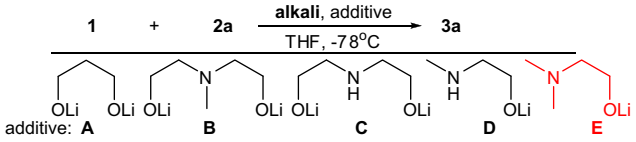
1). While using either MeMgI or *t*-BuMgCl as the deprotonating alkali,[18] no addition product of **3a** was observed. It seemed that the benzothiazol-2-yl-magnesium halides were not active species in the addition to imine **2a** due to the low nucleophilicity. In the replacement of Grignard reagent with either LiHMDS or *n*-BuLi, the model reaction favorably accomplished and afforded the desired **3a** immediately after inducing **2a** into the priorly prepared benzothiazole-lithium reagent. Although the reaction proceeded very rapidly, only a low diastereoselectivity of 4:1 d.r. was observed due to the difficulty in stereocontrol for the mono-lithium species. Therefore, a series of reaction conditions were optimized for the reaction diastereoselectivity improvement.

As a general strategy, various additives were explored to deactivate the nucleophile (Table 1).[19] Using TMEDA had no effect on diastereoselectivity improvement (entry 1). Impressive lithium salt effect on fine tuning the nucleophilicity and stereoselectivity of the organometallic reagent was disclosed in recent years.[20] However, poor conversion of **1** and only a trace of **3a** that were observed in the model reaction (Method A), may be due to the nucleophilicity of benzothiazol-2-yl sodium generated via 1 and NaHMDS was well restrained by the lithiated amino alcohols (**A**–**E**, entry 2). Then different types of alkali as well as a combination order of the reaction components were attempted to improve the diastereoselectivity. While di-lithium additive **A** with **2a** were firstly combined and added to the benzothiazol-2-yl potassium solution prepared in advance, diarylmethylamine **3a** was afforded with an increased d.r. value of 10:1 in 38% yield (Method B) (entry 3). Chiral lithium complex was probably formed with the combination of chiral imine **2a** and the lithium additive, and the chiral auxiliary effect of the *N*-*tert*-butanesulfinyl might be amplified. Thus, method B was employed in the subsequent studies as the general procedure.

Table 1
Model reaction optimization[a]



Entry	Method [b]	Alkali	Additive[c]	d.r.[d]	Yield[e]
1	Method A	NaHMDS	TMEDA	4:1	77%
2[f]	Method A	NaHMDS	[g]	N. D.	Trace
3	Method B	KHMDS	**A**	10:1	38%
4	Method B	KHMDS	**B**	17:1	61%
5	Method B	KHMDS	**C**	30:1	59%
6	Method B	KHMDS	**D**	52:1	32%
7	Method B	KHMDS	**E**	>99:1	81%
8	Method A	KHMDS	**E**	14:1	51%
9	Method B	LiHMDS	**E**	4:1	53%
10	Method B	*n*-BuLi	**E**	5:1	61%
11	Method B	NaHMDS	**E**	13:1	50%
12[f,h]	Method B	KHMDS	**E**	N. D.	Trace
13[i]	Method B	KHMDS	**E**	2:1	74%
14[j]	Method B	KHMDS	**E**	24:1	42%
15	Method B	KHMDS	**LiCl**	5:1	70%

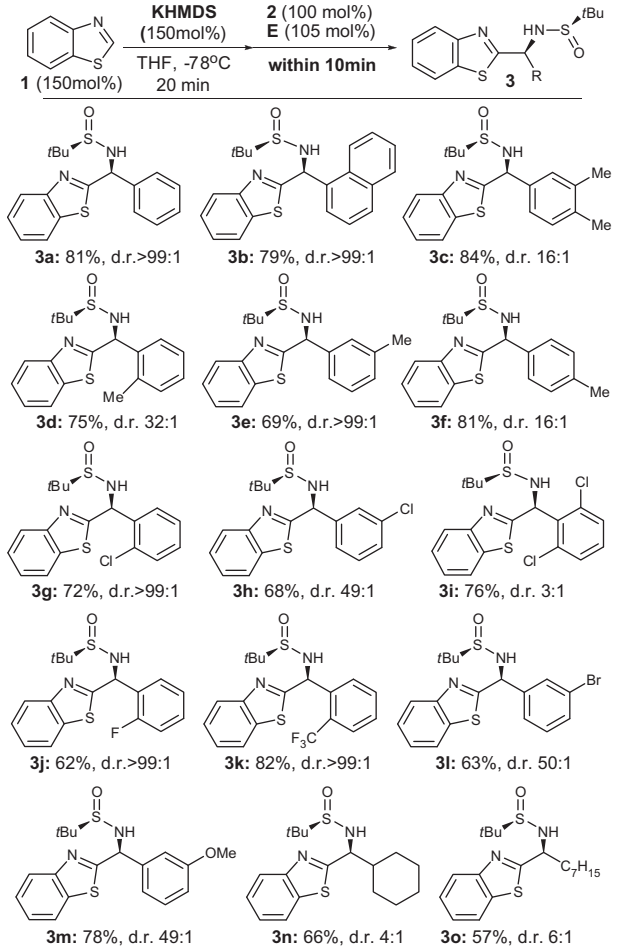
[a] Unless otherwise noted, reactions were carried out with **1** (0.45 mmol), **2a** (0.3 mmol), and alkali (0.45 mmol) in THF at −78 °C.
[b] Method A: **2a** was added to the mixture of **1**, additive (0.45 mmol), and alkali. Method B: **2a** and additive (0.315 mmol) in 3 mL THF were added to the mixture of **1** and alkali.
[c] Prepared and stored as solid.
[d] Determined by ^{1}H NMR analysis.
[e] Isolated yield of the two diastereomers.
[f] Poor conversion of **2a**; d.r. was not determined.
[g] Similar results were observed while using additives **A**–**E**, respectively.
[h] The solvent was *t*-BuOMe.
[i] The solvent was toluene.
[j] Carried out at −40 °C.

Using di-lithium B (entry 4) and **C** (entry 5) as the additive, the model reaction proceeded smoothly and gave **3a** with moderate yields and high d.r. values (17:1 and 30:1, respectively). Although the diastereoselectivity was greatly improved to 52:1, only a low yield (32%) of **3a** was obtained (entry 6). Amino alkoxyl lithium **E** was found to be an ideal additive. A single diastereomer (d.r. >99:1) of the desired **3a** was afforded in a high yield of 81% (entry 7). The reaction diastereoselectivity was also greatly affected by different types of alkali used for the C2 de-protonation of benzothiazole. While using KHMDS and additive **E** in method A, the model reaction proceeded smoothly to give **3a** in moderate yield (51%) with dr value of 14:1 (entry 8). The additive effect was not observed while using either LiHMDS (entry 9) or *n*-BuLi (entry 10) instead of KHMDS. The addition of benzothiazol-2-yl sodium to **2a** gave **3a** with moderate d.r. value (13:1) and 50% yield (entry 11). No reaction occurred while using *t*-BuOMe as the solvent due to the poor solubility of the benzothiazol-2-yl potassium (entry 12). Good yield (74%) of **3a** was obtained but with poor diastereoselectivity (d.r. 2:1) when the reaction was carried out in toluene (entry 13). Both the yield and the diastereoselectivity of **3a** decreased sharply at a higher reaction temperature (−40 °C) (entry 14). Non-basic lithium salt such as LiCl was explored in the model reaction but displayed no effect in dr enhancement (entry 15).

Under the optimal conditions, the substrate scope for the asymmetric benzothiazole addition was studied, and results are summarized in scheme 2. After adding the mixture of aldimine **2** and additive **E** to the priorly prepared benzothiazol-2-yl potassium solution, the asymmetric addition was favourably accomplished within 10 min. This approach can tolerate either electron-donating or electron withdrawing substituted aryl aldimines, and readily afford the desired diarylmethylamines with high yields and excellent diastereoselectivities. In general, just one single diastereomer (d.r. >99:1) was obtained in several cases. The asymmetric additions of benzothiazole to *p*-substituted phenyl imine **2h**, **2l**, and **2m** proceeded favourably to give **3h**, **3l**, and **3m** with excellent diastereoselectivities (d.r. of 49:1, 50:1, and 49:1, respectively). The diastereo-selectivity slightly decreased to 16:1 in the addition to aldimine **2c**, which contained a 3, 4-dimethyl substituted phenyl group. High d.r. value (32:1) of **3d** was obtained in 75% yield. Diarylmethylamine **3f** bearing a 4-methyl phenyl was also obtained with a high d.r. value (16:1). Much hindered **3i** was afforded with a moderate diastereoselectivity (d.r. 3:1) in good yield (76%), due to the great steric hindrance of the 2, 6-dichloro substituted phenyl. Alkyl-substituted imines, which can easily isomerize to enamines under basic condition, were also compatible substrates. However, the asymmetric additions to **2n** and **2o** were well restrained while using additive **E** under standard conditions due to the enamine formation. Thus, lithium additive **E** was avoided in the asymmetric synthesis of **3n–o**. Accordingly, the diastereoselectivities decreased to 4:1 and 6:1 for **3n** and **3o**.

Under the standard conditions, the asymmetric addition of 6-methyl benzothiazole and 4-methyl-5-vinyl thiazole to **2a** proceeded favourably to give diarylmethylamine **5** and **6** with excellent diastereoselectivities (d.r. of 34:1 and 61:1) in moderate yields (57% and 55%) (Fig. 1). However, it was found that the addition activity was significantly affected by the substitutes of the thiazole ring in the following study.[21] Thiazole as well as 4-methyl thiazole was also examined in the addition to imine **2a** under standard conditions, but with very poor conversion.

To illustrate the significant effect of the lithium additive in enhancing the reaction diastereoselectivity, possible transition states of the intermediate directed by amino alkoxyl lithium **E** were proposed (Fig. 2). While using (*Rs*)-**2a** in the reaction, the intermediate **X** might be favourably formed under the chelation of additive **E** with **2a** and benzothiazol-2-yl potassium. Thus, the addition of benzothiazol-2-yl to the imine group preferred *Si*-face



Scheme 2. Asymmetric benzothiazole addition. Imine **2** (0.3 mmol) and **E** (0.315 mmol) in 3 mL THF were added to a pre-stirred THF solution (3 mL) of **1** and KHMDS at −78 °C. All reactions were accomplished within 10 min. The stated yield was isolated yield of the two diastereomers. The d.r. was determined by ^{1}H NMR analysis of the crude product. No additive **E** was used in the synthesis of **3n** or **3o**.

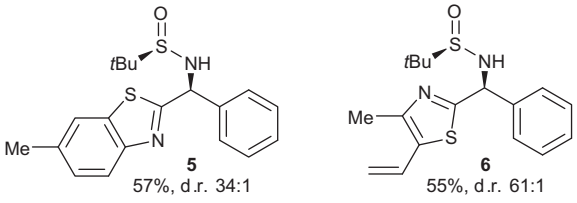


Figure 1. Asymmetric addition of 4-methyl-5-vinyl thiazole **4** to imine **2a**.

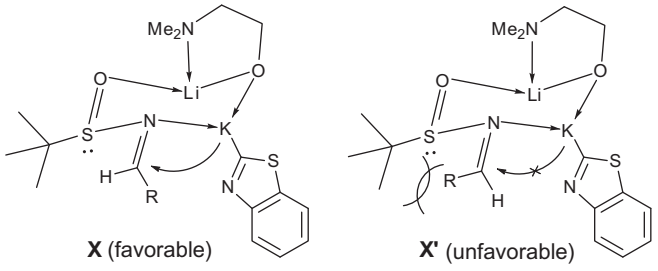


Figure 2. Proposed transition states of the intermediate directed by amino alkoxyl lithium **E**.

attack. In contrast, *Re*-face attack was unfavorable due to the high steric hindrance. This hypothesis was reliably proved by the absolute configuration of the product. The absolute configuration of product **3b** was confirmed to be (*Rs*, *S*) via X-ray crystal analysis (Fig. 3).[22]

In summary, we developed a facile and reliable approach for the asymmetric synthesis of chiral α-branched heteroaromatic amine. Using *N-tert*-butanesulfinyl as the chiral auxiliary, the asymmetric addition of benzothiazol-2-yl potassium reagent to *N-tert*-butanesulfinyl imines gave the chiral diarylmethylamines with excellent diastereoselectivities in high yields. Amino alkoxyl lithium was explored as an essential additive to amplify the chiral auxiliary effect of the *N-tert*-butanesulfinyl via chelating with chiral imine. It is considered to be a meaningful protocol for the diastereoselectivity improvement in *N-tert*-butanesulfinyl directed asymmetric transformations. The more challenging alkyl substituted imines, which can isomerize to enamines, were also compatible substrates to the present protocol. The asymmetric addition of more functionalized 4-methyl-5-vinyl thiazole was successfully carried out under standard conditions. The asymmetric addition of other thiazoles as well as oxazoles is under investigation.

Typical Experimental Procedure

Method A: To a stirred solution of benzothiazole **1** (0.45 mmol) and the additive (0.45 mmol) in 3 mL THF, NaHMDS (0.45 mmol, 1.0 M in THF) was added drop-wise at −78 °C. After the mixture being stirred for 20 min, imine **2a** (0.3 mmol) in 3 mL THF was added in. Poor conversion of both benzothiazole **1** and imine **2a** as well as the trace product **3a** was observed by TLC. No further workup was treated.

Method B (General procedure): At room temperature, (*Rs*) imine **2** (0.3 mmol) and the additive (0.315 mmol) was dissolved in 3 mL THF with vigorous stirring for about half an hour. The resulted clear solution was added to the priorly prepared benzothiazol-2-yl metallic reagent (0.45 mmol in 3 mL THF) at −78 °C. The reaction was accomplished rapidly within 10 min (monitored by TLC). Then the reaction was quenched with aqueous saturated NH_4Cl, extracted with DCM (10 mL × 3), washed by brine (10 mL), dried over Na_2SO_4, and concentrated under vacuum. The crude product was purified by silica gel column chromatography (petroleum ether/ethyl acetate 3:1–1:1). The diastereoselectivity was determined by ^{1}H NMR analysis of the crude product.

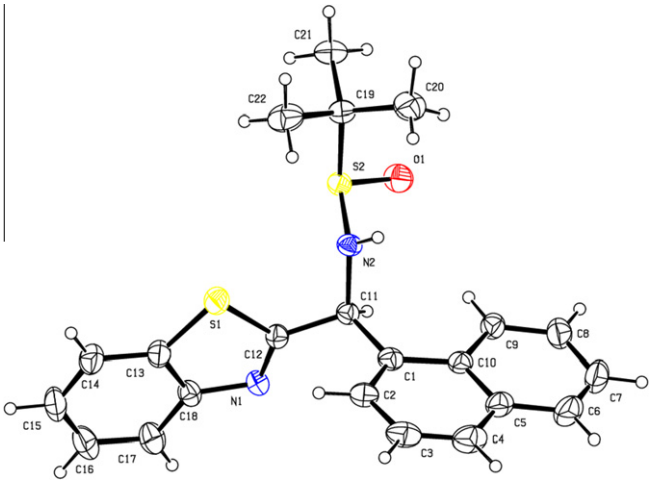


Figure 3. X-Ray structure of **3b**.

Acknowledgements

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Supplementary data

Supplementary data (Experimental procedure, characterization data and NMR spectra of the products can be founded in the Supplementary data) associated with this article can be found, in the online version, at http://dx.doi.org/10.1016/j.tetlet.2012.09.131.

References and notes

1. Over one hundred literatures have been reported in recent three years in C2 direct functionalization of benzothiazole. Only recent examples were cited in the following related areas.
2. Recent examples (a) Yang, F.; Xu, Z.; Wang, Z.; Yu, Z.; Wang, R. *Chem. Eur. J.* **2011**, *17*, 6321–6325; (b) Liu, B.; Guo, Q.; Cheng, Y.; Lan, J.; You, J. *Chem. Eur. J.* **2011**, *17*, 13415–13419; (c) Zhang, M.; Zhang, S.; Liu, M.; Cheng, J. *Chem. Commun.* **2011**, *47*, 11522–11524; (d) Yamamoto, T.; Muto, K.; Komiyama, M.; Canivet, J.; Yamaguchi, J.; Itami, K. *Chem. Eur. J.* **2011**, *17*, 10113–10122; (e) Han, W.; Mayer, P.; Ofial, A. R. *Chem. Eur. J.* **2011**, *17*, 6904–6908; (f) Baghbanzadeh, M.; Pilger, C.; Kappe, C. O. *J. Org. Chem.* **2011**, *76*, 8138–8142; (g) Han, W.; Mayer, P.; Ofial, A. R. *Angew. Chem., Int. Ed.* **2011**, *50*, 2178–2182; (h) Truong, T.; Daugulis, O. *J. Am. Chem. Soc.* **2011**, *133*, 4243–4245; (i) Ranjit, S.; Liu, X. *Chem.-Eur. J.* **2011**, *17*, 1105–1108; (j) Shibahara, F.; Yamaguchi, E.; Murai, T. *Chem. Commun.* **2010**, *46*, 2471–2473; (k) Huang, J.; Chan, J.; Chen, Y.; Borths, C. J.; Baucom, K. D.; Larsen, R. D.; Faul, M. M. *J. Am. Chem. Soc.* **2010**, *132*, 3674–3675.
3. (a) He, T.; Yu, L.; Zhang, L.; Wang, L.; Wang, M. *Org. Lett.* **2011**, *13*, 5016–5019; (b) Zhao, X.; Wu, G.; Zhang, Y.; Wang, J. *J. Am. Chem. Soc.* **2011**, *133*, 3296–3299; (c) Yao, T.; Hirano, K.; Satoh, T.; Miura, M. *Chem. Eur. J.* **2010**, *16*, 12307–12311; (d) Vechorkin, O.; Proust, V.; Hu, X. *Angew. Chem., Int. Ed.* **2010**, *49*, 3061–3064; (e) Nakao, Y.; Kashihara, N.; Kanyiva, K. S.; Hiyama, T. *Angew. Chem., Int. Ed.* **2010**, *49*, 4451–4454.
4. (a) Patil, S. S.; Jadhav, R. P.; Patil, S. V.; Bobade, V. D. *Tetrahedron Lett.* **2011**, *52*, 5617–5619; (b) Kim, S. H.; Yoon, J.; Chang, S. *Org. Lett.* **2011**, *13*, 1474–1477; (c) Pacheco Berciano, B.; Lebrequier, S.; Besselièvre, F. O.; Piguel, S. *Org. Lett.* **2010**, *12*, 4038–4041; (d) Kim, S. H.; Chang, S. *Org. Lett.* **2010**, *12*, 1868–1871.
5. (a) He, T.; Li, H.; Li, P.; Wang, L. *Chem. Commun.* **2011**, *47*, 8946–8948; (b) Wu, X.-F.; Anbarasan, P.; Neumann, H.; Beller, M. *Angew. Chem., Int. Ed.* **2010**, *49*, 7316–7319; (c) Boogaerts, I. I. F.; Fortman, G. C.; Furst, M. R. L.; Cazin, C. S. J.; Nolan, S. P. *Angew. Chem., Int. Ed.* **2010**, *49*, 8674–8677; (d) Boogaerts, I. I. F.; Nolan, S. P. *J. Am. Chem. Soc.* **2010**, *132*, 8858–8859.
6. Selected examples: (a) Do, H.-Q.; Daugulis, O. *J. Am. Chem. Soc.* **2011**, *133*, 13577–13586; (b) Snégaroff, K.; L'Helgoual'ch, J.-M.; Bentabed-Ababsa, G.; Nguyen, T. T.; Chevallier, F.; Yonehara, M.; Uchiyama, M.; Derdour, A.; Mongin, F. *Chem. Eur. J.* **2009**, *15*, 10280–10290.
7. Recent examples (a) Kienle, M.; Wagner, A. J.; Dunst, C.; Knochel, P. *Chem. Asian J.* **2011**, *6*, 517–523; (b) Matsuda, N.; Hirano, K.; Satoh, T.; Miura, M. *Org. Lett.* **2011**, *13*, 2860–2863; (c) Kim, J. Y.; Cho, S. H.; Joseph, J.; Chang, S. *Angew. Chem., Int. Ed.* **2010**, *49*, 9899–9903; (d) Guo, S.; Qian, B.; Xie, Y.; Xia, C.; Huang, H. *Org. Lett.* **2010**, *13*, 522–525.
8. (a) Dai, C.; Xu, Z.; Huang, F.; Yu, Z.; Gao, Y.-F. *J. Org. Chem.* **2012**, *77*, 4414–4419; (b) Ranjit, S.; Lee, R.; Heryadi, D.; Shen, C.; Wu, J. E.; Zhang, P.; Huang, K.-W.; Liu, X. *J. Org. Chem.* **2011**, *76*, 8999–9007; (c) Zhou, A.-X.; Liu, X.-Y.; Yang, K.; Zhao, S.-C.; Liang, Y.-M. *Org. Biomol. Chem.* **2011**, *9*, 5456–5462.
9. (a) Ding, Z.; Yoshikai, N. *Synthesis* **2011**, 2561–2566; (b) Ding, Z.; Yoshikai, N. *Org. Lett.* **2010**, *12*, 4180–4183.
10. Rohbogner, C. J.; Wunderlich, S. H.; Clososki, G. C.; Knochel, P. *Eur. J. Org. Chem.* **2009**, 1781–1795.
11. (a) Hirono, Y.; Kobayashi, K.; Yonemoto, M.; Kondo, Y. *Chem. Commun.* **2010**, *46*, 7623–7624; (b) Boga, C.; Micheletti, G. *Eur. J. Org. Chem.* **2010**, 5659–5665; (c) Wunderlich, S. H.; Knochel, P. *Chem. Eur. J.* **2010**, *16*, 3304–3307.
12. Schmidt, F.; Stemmler, R. T.; Rudolph, J.; Bolm, C. *Chem. Soc. Rev.* **2006**, *35*, 454–470.
13. For review see: Tian, P.; Dong, H.-Q.; Lin, G.-Q. *ACS Catal.* **2012**, *2*, 95–119. And references cited in.
14. For reviews see (a) Robak, M. T.; Herbage, M. A.; Ellman, J. A. *Chem. Rev.* **2010**, *110*, 3600–3740; (b) Ferreira, F.; Botuha, C.; Chemla, F.; Perez-Luna, A. *Chem. Soc. Rev.* **2009**, *38*, 1162–1186; (c) Lin, G.-Q.; Xu, M.-H.; Zhong, Y.-W.; Sun, X.-W. *Acc. Chem. Res.* **2008**, *41*, 831–840; (d) Ellman, J. A.; Owens, T. D.; Tang, T. P. *Acc. Chem. Res.* **2002**, *35*, 984–995.
15. (a) Han, Z.; Busch, R.; Fandrick, K. R.; Meyer, A.; Xu, Y.; Krishnamurthy, D. K.; Senanayake, C. H. *Tetrahedron* **2011**, *67*, 7035–7041; (b) Pflum, D. A.; Krishnamurthy, D.; Han, Z.; Wald, S. A.; Senanayake, C. H. *Tetrahedron Lett.* **2002**, *43*, 923–926; (c) Plobeck, N.; Powell, D. *Tetrahedron: Asymmetry* **2002**, *13*, 303–310.
16. (a) Qiu, X.-L.; Zhu, J.; Wu, G.; Lee, W.-H.; Chamberlin, A. R. *J. Org. Chem.* **2009**, *74*, 2018–2027; (b) Cheng, L.; Liu, L.; Sui, Y.; Wang, D.; Chen, Y.-J. *Tetrahedron: Asymmetry* **2007**, *18*, 1833–1843; (c) Rajapakse, H. A.; Young, M. B.; Zhu, H.; Charlton, S.; Tsou, N. N. *Tetrahedron Lett.* **2005**, *46*, 8909–8912.
17. (a) Hamzik, P. J.; Brubaker, J. D. *Org. Lett.* **2010**, *12*, 1116–1119; (b) Nitta, A.; Fujii, H.; Sakami, S.; Nishimura, Y.; Ohyama, T.; Satoh, M.; Nakaki, J.; Satoh, S.; Inada, C.; Kozono, H.; Kumagai, H.; Shimamura, M.; Fukazawa, T.; Kawai, H. *Bioorg. Med. Chem. Lett.* **2008**, *18*, 5435–5438.
18. (a) Kenney, B. D.; Breslav, M.; Chang, R.; Glaser, R.; Harris, B. D.; Maryanoff, C. A.; Mills, J.; Roessler, A.; Segmuller, B.; Villani, F. J. *J. Org. Chem.* **2007**, *72*, 9798–9801; (b) Pippel, D. J.; Mapes, C. M.; Mani, N. S. *J. Org. Chem.* **2007**, *72*, 5828–5831.
19. Selected examples (a) Salvi, L.; Kim, J. G.; Walsh, P. J. *J. Am. Chem. Soc.* **2009**, *131*, 12483–12493; (b) Salvi, L.; Jeon, S.-J.; Fisher, E. L.; Carroll, P. J.; Walsh, P. J. *J. Am. Chem. Soc.* **2007**, *129*, 16119–16125; (c) Kim, J. G.; Walsh, P. J. *Angew. Chem., Int. Ed.* **2006**, *45*, 4175–4178; (d) Rudolph, J.; Hermanns, N.; Bolm, C. *J. Org. Chem.* **2004**, *69*, 3997–4000.
20. Selected examples: (a) Liu, M.; Shen, A.; Sun, X.-W.; Deng, F.; Xu, M.-H.; Lin, G.-Q. *Chem. Commun.* **2010**, *46*, 8460–8462; (b) Hatano, M.; Ito, O.; Suzuki, S.; Ishihara, K. *Chem. Commun.* **2010**, *46*, 2674–2676; (c) Piller, F. M.; Metzger, A.; Schade, M. A.; Haag, B. A.; Gavryushin, A.; Knochel, P. *Chem. Eur. J.* **2009**, *15*, 7192–7202.
21. Different types of thiazole and oxazole always display distinct reactivity in various transformations. For similar observations see selected Refs. 2c, 2j-k, 3c, 4b-d, 7c, 9b
22. CDC 901054 (**3b**) contains the supplementary crystallographic data for this Letter. These data can be obtained free of charge from the Cambridge Crystallographic Data Centre via http://www.ccdc.cam.ac.uk/data_request/cif.