Enantioselective Access to *S*-Chiral 1,2-Benzothiazines by Cp^{x}Rh(III)-Catalyzed C–H Functionalization of Sulfoximines

Yang Sun[a] and Nicolai Cramer*[a]

Abstract: Sulfoximines with stereogenic sulfur atoms are attractive structural motifs in drug discovery. A direct catalytic enantioselective method accessing *S*-chiral 1,2-benzothiazines from readily accessible diarylsulfoximines is presented. Rhodium(III) complexes equipped with chiral cyclopentadienyl ligands and paired with suitable carboxylic acid additives engage in an enantiodetermining C-H activation directed by the sulfoximine group. Subsequent trapping of the rhodacycle by a broad range of diazoketones gives access to *S*-chiral 1,2-benzothiazines with synthetically highly attractive substitution patterns in good yields and enantioselectivities.

Over the past decade, the sulfoximine class of compounds received a steadily growing interest from the pharmaceutical and agrochemical industry.[1] Sulfoxmines have a high chemical stability and can provide several strategic advantages over the corresponding and ubiquitous sulfone and sulfonamide derivatives.[2] Besides the acyclic sulfoximine motif, examplified by roniciclib,[3] ceralasertib,[4] and sulfoxaflor,[5] rigid cyclic benzannulated sulfoximine scaffolds such as Lilly's prazosin analogue,[6] Gö 4962[7] and NSC 287474[8] have recently gained attention. Despite these examples, 1,2,4-benzothiadiazine and 1,2-benzothiazines are still underrepresented heterocyclic scaffolds with significant upside potential for the discovery of compounds with potential medical applications. A characteristic trait of sulfoximines is their stereogenic sulfur atom.[9] Embedded in a rigid cyclic structure, this provides the additional benefit of a directed and functionalizable exit vector.[10]

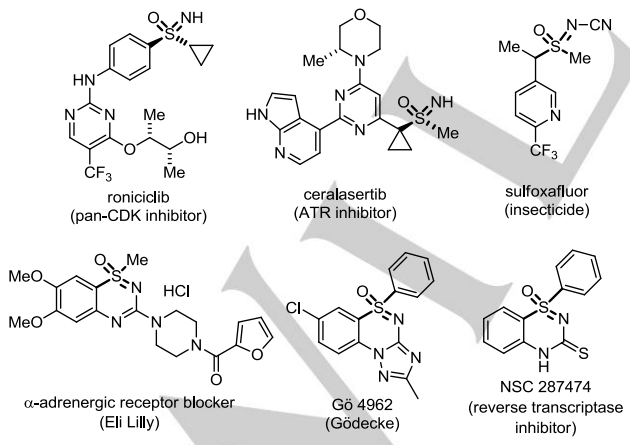
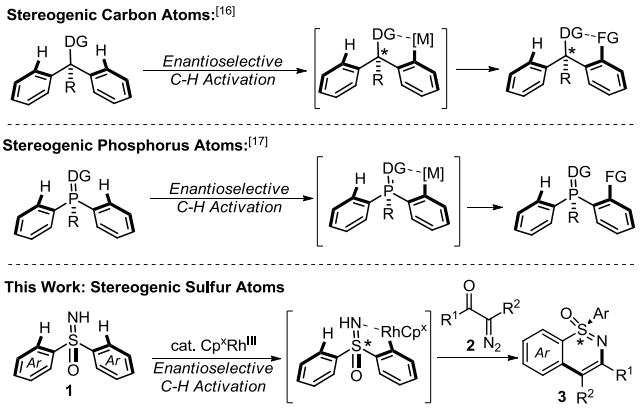


Figure 1. Biologically active molecules with a sulfoximine functionality.

Recent synthetic advances have improved the access to sulfoximines and have largely broadened its available structural diversity.[11] In particular, Bolm and others demonstrated the suitability of the sulfoximine moiety to as *ortho*-directing group for Rh(III)-catalyzed C-H functionalizations.[12] However, the thin arsenal of catalytic enantioselective methods to selectively access optically pure sulfoximines remains a limiting factor. Besides few approaches by kinetic resolution,[13] only multi-step strategies focusing on stereoselective imidation or oxidation are available.[14] Frequently, enantiopure chiral sulfoximines are obtained by resolution techniques. Therefore, the development of catalytic enantioselective sulfoximine syntheses remains a relevant target for asymmetric catalysis.

Desymmetrization strategies by the selective C-H functionalization of one C(sp^2)-H bond of enantiotopic aryl groups have been successfully implemented for the generation of stereogenic carbon atoms (Scheme 1).[15, 16] Examples using this concept to create stereogenic phosphorus[17] or silicon atoms[18] are more scarce. Related methods to access chiral sulfur atomsare to best of our knowledge elusive except a single example for chiral sulfoxides reported by Wang.[19] On the basis of our findings of creating *P*-chirality with chiral cyclopentadienyl (Cp^x) rhodium and iridium catalysts, compounds,[17f,h,j] we explored the suitability of these for the generation of chiral sulfur atoms of sulfoximines. Herein, we report an asymmetric annulative C–H functionalization approach of sulfoximines **1** providing an efficient access to *S*-chiral 1,2-benzothiazines **3**.



Scheme 1. Enantioselective C–H functionalization strategies for the creation of stereogenic carbon, phosphorus and sulfur atoms by desymmetrization. DG=directing group.

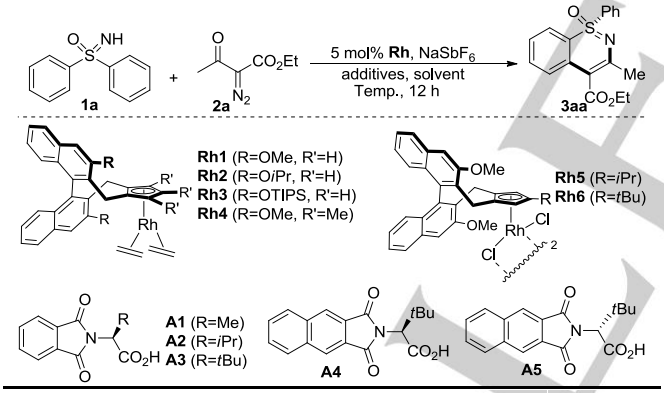
[a] Y. Sun, Prof. Dr. N. Cramer
Laboratory of Asymmetric Catalysis and Synthesis
EPFL SB ISIC LCSA, BCH 4305
CH-1015 Lausanne (Switzerland)
E-mail: nicolai.cramer@epfl.ch
Homepage: http://isic.epfl.ch/lcsa

Supporting information for this article is given via a link at the end of the document.

The envisaged functionalization / cyclization sequence was investigated and optimized with diphenyl sulfoximine (**1a**) and ethyl diazo acetylacetate (**2a**) as the prototype substrate combination (Table 1). First, our most general chiral Cp^x ligands[20] were surveyed (Entries 1-7). Under the initial

conditions (toluene at 100 °C), disubstituted version **Rh1**-**Rh3** gave modest selectivities and yields (Entries 1-3). Fully pentasubstituted versions **Rh4** resulted in an increased yield (Entry 4). Complexes having trisubstituted Cp^x ligands were directly used at the +III-oxidation state (Entries 5 and 6). **Rh5** provided with sodium benzoate as additive **3aa** in 80:20 e.r. and 78 % yield at 50 °C (Entry 5). Notably, the trisubstituted ligands led to the opposite major enantiomer compared to the di- and pentasubstituted congeners. Moreover, the transformation was found to be sensitive to the carboxylic acid / carboxylate additive (Entries 7-14). A brief evaluation showed that *tert*-leucine derived acid **A4**[17h] performed best and gave **3aa** in 95 % yield with 87.5:12.5 e.r. in the matching combination (Entry 13). The mismatched enantiomer **A5** was less efficient, but still gave the same major enantiomer of **3aa** (Entry 14). Switching the solvent from toluene to *t*BuOH allowed for a reaction temperature of 35 °C and additionally increased the enantioselectivity of **3aa** to 95.5:4.5 (Entries 15-16). The added K_3PO_4 can be omitted by increasing the acid additive from 5 to 30 mol%. The use of TFE caused a significant reduction in the enantioselectivity which dropped to 70:30 e.r. (Entry 17). Notably, HFIP was found to have an even more profound effect on the selectivity, giving the opposite enantiomer of **3aa** majorly with 28.5:71.5 e.r. (Entries 18, 19). The very high sensitivity of the enantioselectivity in this transformation towards external effects like solvents and additives besides the direct influence of the chiral Cp^x ligands opens opportunities but poses as well some caution flags in terms of robustness.

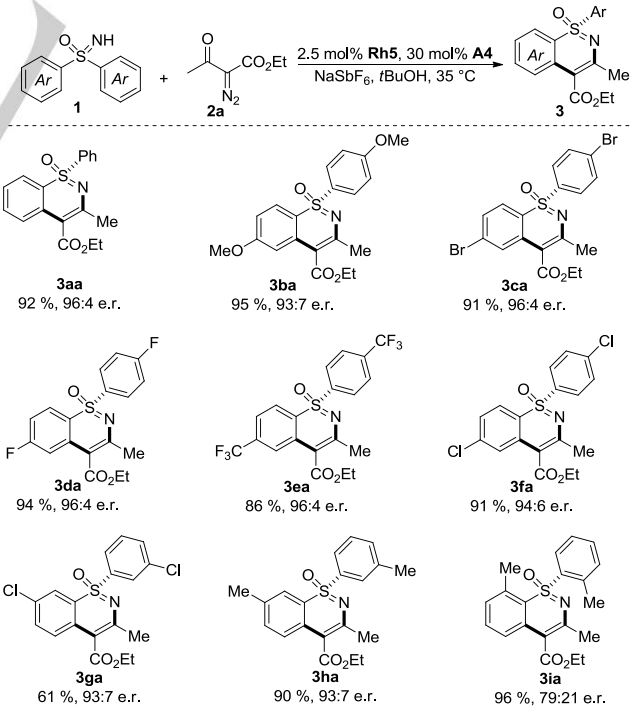
Table 1. Optimization of the enantiotopic functionalization of sulfoximine **1a**.[a]



Entry	Rh	Additive	Solvent	T [° C]	yield [%][b]	e.r.[c]
1[d]	**Rh1**	$(BzO)_2$	toluene	100	75	54:46
2[d]	**Rh2**	$(BzO)_2$	toluene	100	35	23:77
3[d]	**Rh3**	$(BzO)_2$	toluene	100	48	24:76
4[d]	**Rh4**	$(BzO)_2$	toluene	100	99	35:65
5	**Rh5**	NaOBz	toluene	50	78	80:20
6	**Rh6**	NaOBz	toluene	50	14	81:19
7	**Rh5**	HOBz	toluene	50	93	78:22
8	**Rh5**	NaOAc	toluene	50	99	74:26
9	**Rh5**	NaOPiv	toluene	50	87	61:39
10	**Rh5**	**A1**	toluene	50	89	80.5:19.5
11	**Rh5**	**A2**	toluene	50	88	81:19
12	**Rh5**	**A3**	toluene	50	75	87:13
13	**Rh5**	**A4**	toluene	50	95	87.5:12.5
14	**Rh5**	**A5**	toluene	50	82	71.5:28.5
15[e,f]	**Rh5**	**A4**	*t*BuOH	35	99 (92)[g]	95.5:4.5
16[h,i]	**Rh5**	**A4**[j]	*t*BuOH	35	92[g]	96:4
17[e,i]	**Rh5**	**A4**	TFE	35	95	70:30
18[e,i]	**Rh5**	**A4**	HFIP	35	94	28.5:71.5
19[i]	**Rh5**	**A4**	HFIP	35	85	32.5:67.5

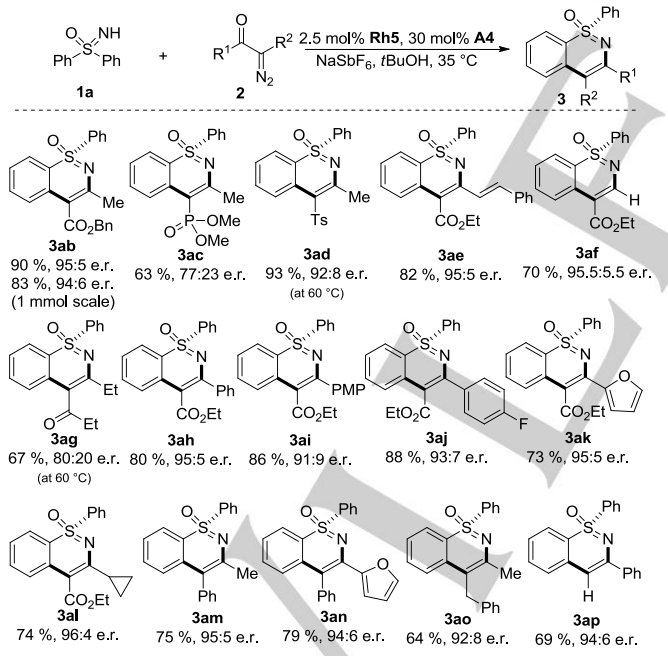
[a] Conditions: 0.05 mmol **1a**, 0.05 mmol **2a**, 5 mol% **Rh** (2.5 mol% dimer), 5 mol% additive, 50 mol% $NaSbF_6$, 0.2 M in solvent. [b] Determined by ^{1}H-NMR with an internal standard. [c] Determined by HPLC with a chiral stationary phase. [d] for 6 h. [e] with 50 mol% K_3PO_4. [f] for 48 h. [g] isolated yield. [h] 0.1 mmol scale. [i] for 30 h. [j] with 30 mol% **A4**. TFE=2,2,2-trifluoroethanol; HFIP=hexafluoroisopropanol.

We next investigated the scope of the developed transformation (Scheme 2). A variety of *para*-substituted diary sulfoximines **1** underwent efficient C–H functionalization and allowed for the synthesis of annulated sulfoximines **3** in a highly enantioselective fashion. Substrates with either electron-donating groups (**1b**) or those with electron-withdrawing groups (**1c**-**1f**) reacted well and gave the corresponding cyclized products **3** in excellent yields and good enantioselectivities.



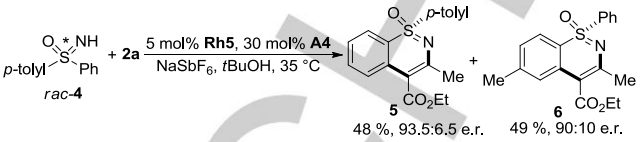
Scheme 2. Scope of the sulfoximine substrates. Conditions: 0.1 mmol **1**, 0.1 mmol **2a**, 2.5 µmol **Rh5**, 30 µmol **A4**, 50 µmol $NaSbF_6$, 0.2 M in *t*BuOH at 35 °C for 30-72 h.

Sulfoximine substrates with *meta*-substituted aryl groups underwent selective functionalization at the more accessible *ortho* C-H group and gave product **3ga** and **3ha**. *Ortho*-substitution does not compromise the yield but influences the selectivity and caused a reduction in e.r. of **3ia**. Besides R^2 being the standard ethyl ester, benzyl ester bearing diazo compound **1b** reacts equally well, allowing to determine the absolute configuration by X-ray crystallography[21] (Scheme 3). A ten-fold increase in scale resulted in 83 % yield 94:6 e.r. Replacing the ester by a phosphonate gave cyclized product **3ac**. A *p*-tosyl group reacted in high yields and selectivities at 60 °C (**3ad**). While the enantioselectivity is somewhat lower, the obtained particular substitution pattern is synthetically attractive. The substituent R^1 offers a broad variability. For instance, alkyl groups, a cyclopropyl unit (**3al**), aromatic and heteroaromatic moieties (**3ah**-**3ak**) as well as a styryl unit (**3ae**) can be used for the cyclization with very little influence on the reaction outcome. Uniformly, high yields and selectivities are obtained. The reaction with diazo ethyl formyl acetate (R^1=H) gives rise to **3af** with a free 3-position at the ring. Notably, besides the described acceptor/acceptor substituted diazo species, diazo ketones *without* an additional electron-withdrawing group participated very well in the enantioselective annulation. For instance, diazo ketones having aryl or benzyl groups as the R^2 substituent can be used. These provide cyclized product **3am**, **3an** and **3ao** in good yields and selectivities. Moreover, diazoacetophenone (R^2=H) gives rise to **3ap** with a free 4-position at the ring.



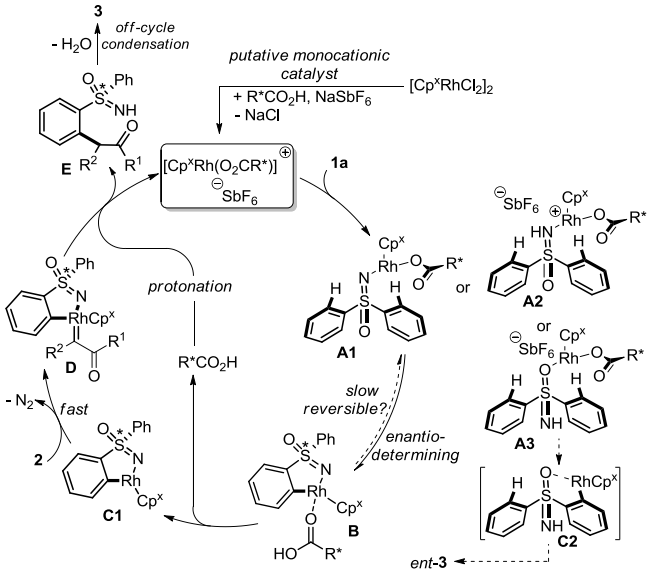
Scheme 3. Scope of the diazo compounds in the sulfoximine functionalization. Conditions: 0.1 mmol **1a**, 0.1 mmol **2**, 2.5 µmol **Rh5**, 30 µmol **A4**, 50 µmol $NaSbF_6$, 0.2 M in *t*BuOH at 35 °C for 24-72 h.

A parallel kinetic resolution of racemic sulfoximines bearing two different aromatic groups was attempted next (Scheme 4). Substrate **4** having a minimal steric and electronic bias, we observed the formation of products **5** and **6** in virtually the same yield. The observed enantiomeric ratios were for 93.5:6.5 for the phenyl functionalization and 90:10 for the *p*-tolyl activation, indicating a smooth parallel kinetic resolution.



Scheme 4. Parallel kinetic resolution of racemic diaryl sulfoximine *rac*-**4**.

Mechanistically, the transformation very likely proceeds by the pathway proposed by Bolm for the corresponding achiral reaction (Scheme 5).[12b] Coordination of the sulfoximine to the Rh^{III} center initiates *ortho*-C-H activation by a concerted metalation deprotonation.[22] Coordination of the diazo species leads to formation of carbenoid intermediate **D**, which in turn undergoes subsequent insertion and protonation to produce ketone **E**. An off-cycle cyclocondensation delivers 1,2-benzothiazine **3**. However, the mechanism of the enantioselection remains a complex question with several interplaying variables. Theoretically, for transformations with a trapping step *after* the enantiodetermining step (**A**→**B**), the observed enantioselectivities of the products **3** should be *completely* independent of the intercepting reagent, unless the enantiodetermining step has some reversible character. Indeed, most used diazo compounds are very reactive interceptors and react fast enough so that the potential reversibility of the C-H activation by the CMD-pathway becomes rather negligible. However, the lower selectivity of difficult diazo compounds such as phosphonate **2c** and ketone **2g** implicates reversibility which can become an issue for the development of related transformations with less reactive trapping agents. The pronounced responsiveness of the enantioselectivity towards solvents and especially the solvent may be linked to a potential ambiguity in the catalyst-substrate binding and orientation. The initial coordination of the rhodium to the free sulfoximine directing group classically suggested[12a] to occur *via* its deprotonated nitrogen atom (**A1**). However, depending on the reaction conditions, the metal center may alternatively initiate cyclometalation from a coordination of the oxygen atom as for **A3** (or the non-deprotonated *NH*-group, **A2**). Mono-cationic Cp* metal complexes of group 9 metals with a single carboxylate were found to be typically most suited for non-deprotonatable directing groups (**A3**-mode) whereas neutral *bis*-carboxylate bound congeners are superior for deprotonable directing groups (**A1**-mode). With all other factors constant, a switch from *N*- to *O*-coordination would result in an inversion of the attacked enantiotopic aryl group (**C2**) and consequently lead to *ent*-**3**. The exact catalyst binding and enantioselection warrants further detailed computational studies which could provide valuable insights for the development of related transformations.



Scheme 5. Suggested mechanism and their potentially critical steps for the enantioselectivity.

In conclusion, we have developed an enantiotopic C-H functionalization of sulfoximines resulting in a stereogenic sulfur atom. The enantio-determining activation step is enabled by a combination of a Rh(III) complex bearing a chiral Cp^x ligand. Carboxylic acid additives were found to have a profound effect on the selectivity. A matching chiral carboxylic acid additive interacts synergistically and enhances the selectivity. The transformation proceeds with high enantioselectivity for a diverse range of sulfoximines. A broad range of diazo compounds are suitable acceptors and allow for a wide variability in the substitution pattern of the newly formed heterocycle.

Acknowledgements

This work is supported by the Swiss National Science Foundation (n° 157741).

Keywords: Asymmetric Catalysis • C–H Activation • Chiral Cyclopentadienyl • Sulfoximine • Rhodium

[1] a) U. Lücking, *Angew. Chem. Int. Ed.* **2013**, *52*, 9399; b) J. A. Sirvent, U. Lücking, *Chem. Med. Chem.* **2017**, *12*, 487.

[2] M. Frings, C. Bolm, A. Blum, C. Gnamm, *Eur. J. Med. Chem.* **2017**, *126*, 225.

[3] G. Siemeister, U. Lücking, A. M. Wengner, P. Lienau, W. Steinke, C. Schatz, D. Mumberg, K. Ziegelbauer, *Mol. Cancer Ther.* **2012**, *11*, 2265.

[4] F. P. Vendetti, A. Lau, S. Schamus, T. P. Conrads, M. J. O'Conner, C. J. Bakkenist, *Oncotarget* **2015**, *6*, 44289.

[5] G. B. Watson, M. R. Loso, J. M. Babcock, J. M. Hasler, T. J. Letherer, C. D. Young, Y. Zhu, J. E. Casida, T. C. Sparks, *Insect Biochem. Mol. Biol.* **2011**, *41*, 432.

[6] R. D. Dillard, T. T. Yen, P. Stark, D. E. Pavey, *J. Med. Chem.* **1980**, *23*, 717.

[7] G. D. Bartoszyk, D. J. Dooley, H. Barth, J. Hartenstein, G. Satzinger, *J. Pharm. Pharmacol.* **1987**, *39*, 407.

[8] R. W. Buckheit Jr, V. Fliakas-Boltz, W. D. Decker, J. L. Roberson, C. A. Pyle, E. L. White, B. J. Bowdon, J. B. McMahon, M. R. Boyd, J. P. Bader, D. G. Nickell, H. Barth, T. K. Antonucci, *Antiviral Res.* **1994**, *25*, 43.

[9] a) C. Bolm in *Asymmetric Synthesis with Chemical and Biological Methods* (Eds.: D. Enders, K.-E. Jaeger), Wiley-VCH, Weinheim, 2007, p. 149; b) C. Worch, A. Mayer, C. Bolm in *Organosulfur Chemistry in Asymmetric Synthesis* (Eds.: T. Toru, C. Bolm),Wiley-VCH, Weinheim, 2008, p. 209.

[10] F. Lovering, J. Bikker, C. Humblet, *J. Med. Chem.* **2009**, *52*, 6752.

[11] a) V. Bizet, R. Kowalczyk, C. Bolm, *Chem. Soc. Rev.* **2014**, *43*, 2426; b) F. W. Goldberg, J. G. Kettle, J. Xiong, D. Lin, *Tetrahedron* **2014**, *70*, 6613; c) V. Bizet, C. M. M. Hendriks, C. Bolm, *Chem. Soc. Rev.* **2015**, *44*, 3378; d) A. Tota, M. Zenzola, S. J. Chawner, S. S. John-Campbell, C. Carlucci, G. Romanazzi, L. Degennaro, J. A. Bull, R. Luisi, *Chem. Comm.* **2017**, *53*, 348.

[12] a) W. Dong, L. Wang, K. Parthasarathy, F. Pan, C. Bolm, *Angew. Chem. Int. Ed.* **2013**, *52*, 11573; b) Y. Cheng, C. Bolm, *Angew. Chem. Int. Ed.* **2015**, *127*, 12526; c) K. Parthasarathy, C. Bolm, *Chem. Eur. J.* **2014**, *20*, 4896; d) W. Dong, K. Parthasarathy, Y. Cheng, F. Pan, C. Bolm, *Chem. Eur. J.* **2014**, *20*, 15732; e) W. H. Jeon, J.-Y. Son, J. E. Kim, P. H. Lee, *Org. Lett.* **2016**,*18*, 3498; f) Y. Deng, W. Dong, H .Wang, C. Bolm, *Chem. Eur. J.* **2016**, *22*, 10821; g) Y. Deng, W. Dong, K. Parthasarathy, C. Bolm, *Org. Lett.* **2017**, *19*, 726; h) G. H. Ko, J.-Y. Son, H. Kim, C. Y. Maeng, Y. Baek, B. Seo, K. Um, P. H. Lee, *Adv. Synth. Catal.* **2017**, *359*, 3362; i) G. Zheng, M. Tian, Y. Xu, X. Chen, X. Li, *Org. Chem. Front.* **2018**, *5*, 998; with other metals: j) M. R. Yadav, R. K. Rit, A. K. Sahoo, *Chem. Eur. J.* **2012**, *18*, 5541; k) M. R. Yadav, R. K. Rit, A. K. Sahoo, *Org. Lett.* **2013**, *15*, 1638; l) M. R. Yadav, R. K. Rit, M. Shankar, A. K. Sahoo, *J. Org. Chem*. **2014**, *79*, 6123; m) K. Ghosh, R. K. Rit, E. Ramesh, A. K. Sahoo, *Angew. Chem. Int. Ed.* **2016**, *55*, 7821; n) R. K. Chinnagolla, A. Vijeta, M. Jeganmohan, *Chem. Commun.* **2015**, *51*, 12992; o) K. Raghuvanshi, D. Zell, L. Ackermann, *Org. Lett.* **2017**, *19*, 1278; p) Y. N. Aher, D. M. Lade, A. B. Pawar, *Chem. Commun.* **2018**, *54*, 6288.

[13] a) J. Wang, M. Frings, C. Bolm, *Chem. Eur. J.* **2014**, *20*, 966; b)S. Dong, M. Frings, H. Cheng, J. Wen, D. Zhang, G. Rabe, C. Bolm, *J. Am. Chem. Soc.* **2016**, *138*, 2166.

[14] a) T. Bach, C. Körber, *Eur. J. Org. Chem.* **1999**, 1033; b) H. Okamura, C. Bolm, *Org. Lett.* **2004**, *6*, 1305; c) F. Collet, R. H. Dodd, P. Dauban, *Org. Lett.* **2008**, *10*, 5473; d) J. Wang, C. Bolm, *Angew. Chem. Int. Ed.* **2013**, *52*, 8661.

[15] Recent reviews on enantioselective C–H functionalizations: a) J. Wencel-Delord, F. Colobert, *Chem. Eur. J.* **2013**, *19*, 14010-14017; b) C. Zheng, S.-L. You, *RSC Advances* **2014**, *4*, 6173-6214; c) D.-W. Gao, J. Zheng, K.-Y. Ye, C. Zheng., S.-L. You in *Asymmetric Functionalization of C–H Bonds*, (Ed.: S.-L. You), Royal Society of Chemistry, Cambridge, U. K., **2015**, p. 141. d) C. G. Newton, S.-G. Wang, C. C. Oliveira, N. Cramer, *Chem. Rev.* **2017**, *117*, 8908-8976; e) T. G. Saint-Denis, R.-Y. Zhu, G. Chen, Q.-F. Wu, J.-Q. Yu, *Science* **2018**, *359*, 759.

[16] a) B.-F. Shi, N. Maugel, Y.-H. Zhang, J.-Q. Yu, *Angew. Chem. Int. Ed.* **2008**, *47*, 4882; b) M. R. Albicker, N. Cramer, *Angew. Chem. Int. Ed.* **2009**, *48*, 9139; c) B.-F. Shi, Y.-H. Zhang, J. K. Lam, D.-H. Wang, J.-Q. Yu, *J. Am. Chem. Soc.* **2010**, *132*, 460; d) T. Saget, N. Cramer, *Angew. Chem. Int. Ed.* **2013**, *52*, 7865; e) X. F. Cheng, Y. Li, Y. M. Su, F. Yin, J. Y. Wang, J. Sheng, H. U. Vora, X. S. Wang, J. Q. Yu, *J. Am. Chem. Soc.* **2013**, *135*, 1236; f) L. Chu, X. C. Wang, C. E. Moore, A. L. Rheingold, J. Q. Yu, *J. Am. Chem. Soc.* **2013**, *135*, 16344; g) T. Lee, T. W. Wilson, R. Berg, P. Ryberg, J. F. Hartwig, *J. Am. Chem. Soc.* **2015**, *137*, 6742; h) B. N. Laforteza, K. S. L. Chan, J. Q. Yu, *Angew. Chem. Int. Ed.* **2015**, *54*, 11143; i) D. Grosheva, N. Cramer, *ACS Catal.* **2017**, *7*, 7417; j) J. Wang, D.-W. Gao, J. Huang, S. Tang, Z. Xiong, H. Zu, S.-L. You, Q. Zhu, *ACS Catal.* **2017**, *7*, 3832; k) H. Shi, A. N. Herron, Y. Shao, Q. Shao, J.-Q. Yu, *Nature* **2018**, *558*, 581; l) L. Yang, M. Neuburger, O. Baudoin, *Angew. Chem. Int. Ed.* **2018**, *57*, 1394; m) L.

Lin, S. Fukagawa, D. Sekine, E. Tomita, T. Yoshino, S. Matsunaga, *Angew. Chem. Int. Ed.* **2018**. *57*, 12048; n) N. Cramer, D. Grosheva, *Angew. Chem. Int. Ed.* **2018**, *57*, 13644.

[17] a) D. Gwon, S. Park, S. Chang, *Tetrahedron*, **2015**, *71*, 4504; b) Z.-Q. Lin, W.-Z. Wang, S.-B. Yan, W.-L. Duan, *Angew. Chem. Int. Ed*., **2015**, *54*, 6265; c) L. Liu, A.-A. Zhang, Y. Wang, F. Zhang, Z. Zuo, W.-X. Zhao, C.-L. Feng, W. Ma, *Org. Lett*., **2015**, *17*, 2046; d) G. Xu, M. Li, S. Wang, W. Tang, *Org. Chem. Front*., **2015**, *2*, 1342; e) Z.-J. Du, J. Guan, G.-J. Wu, P. Xu, L.-X. Gao, F.-S. Han, *J. Am. Chem. Soc.*, **2015**, *137*, 632; f) Y. Sun, N. Cramer, *Angew. Chem., Int. Ed*., **2017**, *56*, 364; *Angew. Chem*. **2017**, *129*, 370; g) S.-X. Li, Y.-N. Ma, S.-D. Yang, *Org. Lett.* **2017**, *19*, 1842; h) Y.-S. Jang, M. Dieckmann, N. Cramer, Angew. *Chem. Int. Ed.*, **2017**, *56*, 15088; i) Z. Wang T. Hayashi, *Angew. Chem. Int. Ed*. **2018**, *57*, 1702; j) Y.-S. Jang, Ł. Woźniak, J. Pedroni, N. Cramer, *Angew. Chem. Int. Ed.* **2018**, DOI:10.1002/anie.201807749.

[18] a) R. Shintani, H. Otomo, K. Ota, T. Hayashi, *J. Am. Chem. Soc.* **2012**, *134*, 7305; b) Y. Kuninobu, K. Yamauchi, N. Tamura, T. Seiki, K. Takai, *Angew. Chem. Int. Ed.* **2013**, *52*, 1520; c) M. Murai, Y. Takeuchi, K. Yamauchi, Y. Kuninobu, K. Takai, *Chem. Eur. J.* **2016**, *22*, 6048.

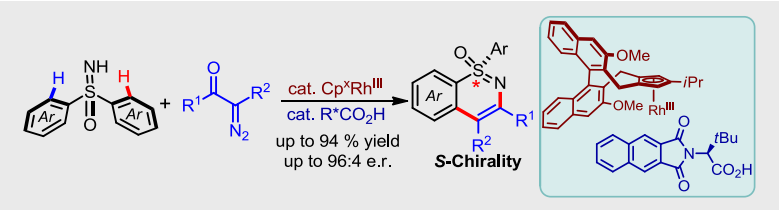
[19] Y.-C. Zhu, Y. Li, B.-C. Zhang, F.-X. Zhang, Y.-N. Yang, X.-S. Wang, *Angew. Chem. Int. Ed.* **2018**, *57*, 5129.

[20] For reviews see: a) B. Ye, N. Cramer, *Acc. Chem. Res.* **2015**, *48*, 1308; b) C. G. Newton, D. Kossler, N. Cramer, *J. Am. Chem. Soc.* **2016**, *138*, 3935; seminal reports detailing the ligand synthesis: c) B. Ye, N. Cramer, *Science* **2012**, *338*, 504; d) B. Ye, N. Cramer, *J. Am. Chem. Soc*. **2013**, *135*, 636; e) J. Zheng, W.-J. Cui, C. Zheng, S.-L. You, *J. Am. Chem. Soc.* **2016**, *138*, 5242; f) Z.-J. Jia, C. Merten, R. Gontla, C. G. Daniliuc, A. P. Antonchick, H. Waldmann, *Angew. Chem. Int. Ed*. **2017**, *56*, 2429; *Angew. Chem*. **2017**, *129*, 2469; g) S. Wang, S. Hwan Park, N. Cramer, *Angew. Chem. Int. Ed*. **2018**, *57*, 5459; h) E. A. Trifonova, N. M. Ankudinov, A. A. Mikhaylov, D. A. Chusov, Y. V. Nelyubina, D. S. Perekalin, *Angew. Chem. Int. Ed*. **2018**, *57*, 7714.

[21] CCDC 1872022 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

[22] a) L. Ackermann, *Chem. Rev.* **2011**, *111*, 1315; b) D. L. Davies, S. A. Macgregor, C. L. McMullin, *Chem. Rev.* **2017**, *117*, 8649.

COMMUNICATION



Sulfoximines with stereogenic sulfur atoms are attractive structural motifs in drug discovery. A catalytic enantioselective method accessing *S*-chiral 1,2-benzothiazines is reported. Cp^xRh^{III} catalysts paired with suitable carboxylic acid additives engage in enantiodetermining C-H activation. Trapping of the rhodacycle by a broad range of diazoketones yields *S*-chiral 1,2-benzothiazines with synthetically highly attractive substitution patterns in good yields and enantioselectivities.

*Yang Sun, Nicolai Cramer**

Page No. – Page No.
Enantioselective Access to *S*-Chiral 1,2-Benzothiazines by $Cp^xRh(III)$ Catalyzed C–H Functionalization of Sulfoximines