Letter

Chiral Brønsted Acid Catalyzed Asymmetric Oxidation of Sulfenamide by Using H2O2: A Versatile Access to Sulfinamide and Sulfoxide with High Enantioselectivity

Long-jun Ma, Shu-sen Chen, Guang-xun Li, Jin Zhu, Qi-Wei Wang, and Zhuo Tang

ACS Catal., **Just Accepted Manuscript** • Publication Date (Web): 22 Jan 2019

Chiral Brønsted Acid Catalyzed Asymmetric Oxidation of Sulfenamide by Using H_2O_2: A Versatile Access to Sulfinamide and Sulfoxide with High Enantioselectivity

Long-jun Ma [a], Shu-sen Chen[c], Guang-xun Li*[a], Jin Zhu[b], Qi-wei Wang[b], Zhuo Tang*[a]

[a] Natural Products Research Center Chengdu Institute of Biology, Chinese Academy of Sciences, Chengdu, Sichuan 610041(China)

[b] Chengdu Institute of Organic Chemistry, Chinese Academy of Sciences, Chengdu, Sichuan 610041 (China).

[c] Department of Chemistry, University of Science and Technology of China, Hefei 230026 (China)

.

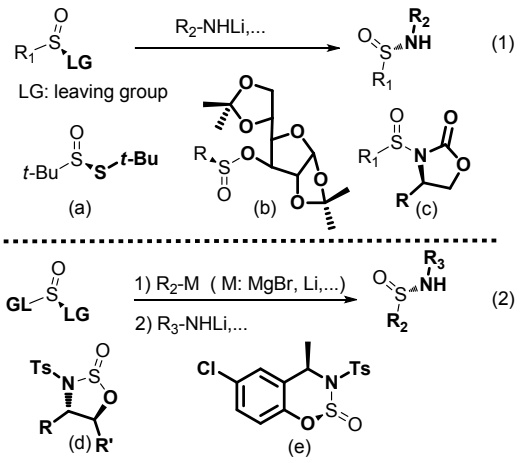
ABSTRACT: Herein we describe an example of catalytic asymmetric synthesis of sulfinamides. Aromatic sulfenamides were chosen as useful substrates due to the indispensable N-H bond, which could form an efficient hydrogen bond with chiral phosphoric acid. H_2O_2 (35%) was used as the terminal oxidant for preparation of sulfinamides in high yields and enantioselectivities, which could be easily derivatized to sulfoxides and other sulfinamides without loss the enantioselectivity.

KEYWORDS: *Sulfinamide; Sulfoxide; Asymmetric oxidation; Sulfenamide; Chiral Brønsted acid*

The demand for optically pure complex organic molecules is continuously growing due to their pervasive applications in agrochemicals, fragrances, cosmetics, fine chemical synthesis, and especially in worldwide-sold drugs. Asymmetric catalysis, capable of creating hundreds or thousands of molecules of the chiral product per catalyst molecule, has emerged as a new, exciting and environmentally friendly methodology in modern synthetic chemistry, complementing bio- and metal catalysis. Catalytic asymmetric oxidations, particularly those involving oxygen atom transfer, constitute an important class of enantioselective reactions, which have propelled the development of asymmetric catalysis during the last several decades. For example, intensive effort has been devoted to asymmetric oxygenative transformations such as epoxidations[1], sulfoxidations[2], Baeyer−Villiger oxidations[3], olefin *cis*-dihydroxylation reactions[4], α-Hydroxylation of carbonyl compounds[5], etc.

In view of the importance of the asymmetric oxidations as well as the continuous interest of highly atom-efficient and green reagent(s) that co-produce only innocuous waste, H_2O_2 is a desirable terminal oxidant because it is inexpensive and does not produce environmentally toxic byproducts. Meanwhile, most of the asymmetric oxidations with H_2O_2, actually rely on the nucleophilic properties of H_2O_2, forming covalent adducts with catalysts or electrophilic substrates. Recently List and co-workers proposed an alternative scenario, in which H_2O_2 could be electrophilically activated toward prochiral nucleophilic sulfides with a confined chiral Brønsted acid catalyst, affording sulfoxides in high enantioselectivity.[6]

Scheme 1. Selected examples for preparation of sulfinamides from different types of chiral reagent

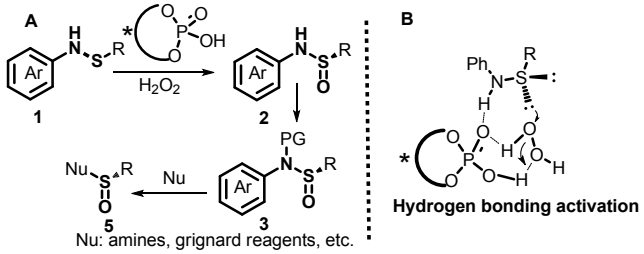


Actually, sulfoxides have widespread applications in modern organic synthesis such as auxiliaries, ligands, and constitute important biologically active compounds, including several marketed drugs. Therefore, chemists have been pursuing a general, metal-free, and highly enantioselective catalytic sulfoxidation reaction since the first enantioselective catalysts for the oxidation of sulfide in 1984. Meanwhile, sulfinamide as an important pharmaceutical intermediate can mediate the synthesis of compounds containing chiral amine

functionalities[7]. Moreover, their utility has been extended to be used as chiral ligands for many catalytic asymmetric transformatios[8]. Although the power of chiral sulfinamide reagents in synthetic chemistry has long been recognized, methods for their synthesis have emerged slowly.

In 1997, Ellman's group reported catalytic asymmetric oxidation of *tert*-butyl disulfide to *tert*-butyl *tert*-butanethiosulfinate intermediate by vanadium catalysts[9] , which have been widely used for preparation of *tert*-butanesulfinamide until now,[10] (**a**, Scheme 1, eq. 1). The inadequacy lies in the odorous mercaptan byproduct which is neither in line with atomic economics nor consistent with the requirements of green chemistry. In fact, chiral auxiliaries were frequently used for preparation of chiral sulfinamides in high enantioselectivities. For example, diacetone-d-glucose[11](**b**), Menthol,[12] and Quinine,[13] amino alchol[14](**c**), were efficiently used to prepare optically pure sulfoxides or sulfinamides. Moreover, chiral sulfinyl transfer reagents which could be used for obtaining different types of sulfoxides or sulfinamides via two sequential nucleophilic additions, were developed[15](**d**, **e**, scheme 1, eq. 2). In this method, Grignard reagent was initially used to nucleophilic attack sulfinyl group by cleavage of N-S bound. Then the resulting intermediate reacted with lithium amide by amino-ester exchange and afforded the corresponding chiral sulfinamides. Auxiliary-based approaches possess obvious disadvantages in comparison with asymmetric catalytic synthesis. Herein we envisioned an efficient approach for directly asymmetric oxidation of sulfenamides to sulfinamides with H_2O_2 as terminal oxidant.

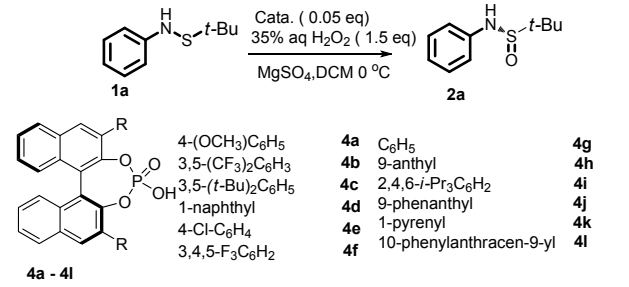
Scheme 2. Direct oxidation of sulfenamide for obtaining sulfinamides and their derivatives



As we know, sulfenamides **1** with a sulfur–nitrogen bond, has garnered great attention in the chemical community over the years due to their unique bond properties and widespread applications, (Scheme 2 **A**). As a result, the availability of them is supported by many synthetic approaches developed by our and others' groups. [16] Based on the work of List[6] and Sunoj[17], we envisioned that the N-H of the substrate sulfenamide **1** can make a great difference due to the additional hydrogen bonds with bi-functional phosphoric acid (Scheme 2, **B**). On the one hand, the phosphoric acid catalyst could form hydrogen bond with H_2O_2 and increase its electrophilic property towards the nucleophilic sulfur[16]. On the other hand, the hydrogen bond between phosphoric acid and sulfenamide could efficiently reduce the spatial distance between hydrogen peroxide and sulfenamide, which could not only promotes the reaction but also increase the enantioselectivity of the product. Here we demonstrated that this is an inexpensive and environmentally friendly process for obtaining sulfinamides **2** with high enantioselectivities. Moreover, chiral sulfoxides **5** or other sulfinamides could be easily derived from the obtained sulfinamides without losing the enantioselectivities (Scheme 2).

To begin with our research, we investigated asymmetric oxidation of sulfenamide **1a** by using BINOL-derived phosphoric acid catalysts **4a**. To our satisfaction, the reaction was clean without the formation of over-oxidation byproduct sulfonamide. Encouraged by this initial result, we performed an extensive screening of reaction temperature, oxidant equivalent, and additive (see the Supporting Information). The yield and enantiomeric excess (ee) value could be efficiently increased when the reaction was run with DCM as solvent, 1.5 eq. H_2O_2 as oxidant, and magnesium sulfate as moisture absorbent (Table 1). The result demonstrated that a catalytic amount of phosphoric acid **4a** promoted the oxidation of **1a** to sulfinamide **2a** in moderate yield (57%) and low ee (27 %) (entry 1). Then we screened other BINOL-derived phosphoric acid catalysts. Fortunately, both the enantioselectivity and yield were improved with **4j** as catalyst (entries 2-10). Therefore, we re-screened the reaction solvents with **4j** (see the Supporting Information, Table S II). The results demonstrated that the mixture of CCl_4: n-hexane (3:1) was the optimal solvent (entry 11). Finally, we found **4k** was the optimal catalyst with better yield and ee value (entries 12-13). Based on the above screening experiments, we obtained sulfinamide **2a** in 85% yield and 92% ee. The final optimal reaction condition is as following: 1 eq. sulfenamide and 1.5 eq H_2O_2 reacted at 0 °C with CCl_4: *n*-hexane (3: 1) as solvent, $MgSO_4$ as additive, and 5 mol % **4k** as catalyst.

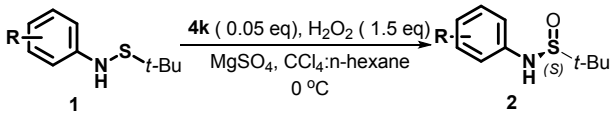
Table 1. Catalyst screening



entry[a]	catalyst	yield (%)[c]	ee (%)[d]
1	**4a**	57	27
2	**4b**	64	37
3	**4c**	60	31
4	**4d**	62	31
5	**4e**	69	24
6	**4f**	65	25
7	**4g**	54	22
8	**4h**	72	41
9	**6i**	62	39
10	**4j**	75	66
11[b]	**4j**	77	81
12[b]	**4k**	85	92
13[b]	**4l**	74	79

[a]Performed at 0 °C in CH_2Cl_2 (0.1 M), 5% Catalyst, $MgSO_4$ (30 mg). [b]Performed in 0.1 M CCl_4: n-hexane (3:1). [c]Isolated yield. [d] Determined by chiral HPLC.

Table 2. Investigation of the aromatic amine scopes



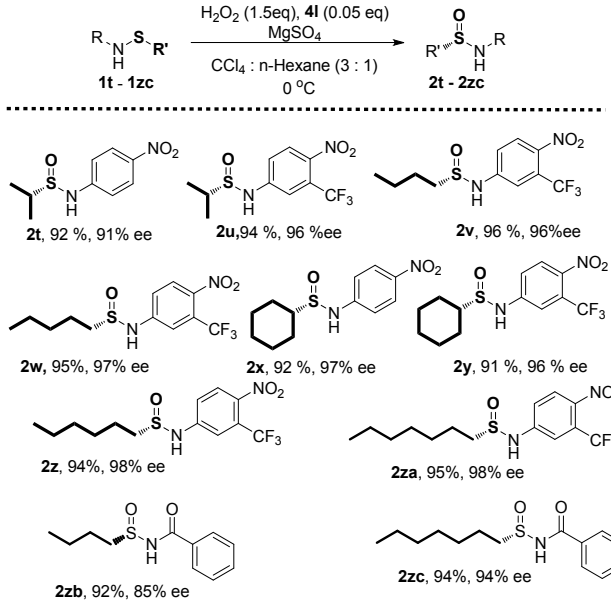
entry	R	2	yield(%)[a]	ee[b] (%)
1	H	**2a**	85	92
2	4-CH_3	**2b**	87	93
3	2-CH_3	**2c**	76	91
4	4-CH_3O	**2d**	71	54
5	4-C_2H_5O	**2e**	65	78
6	4- CF_3	**2f**	92	93
7	3,5-$(CF_3)_2$	**2g**	87	95
8	4-NO_2	**2h**	88	91
9	4-$CO_2C_2H_5$	**2i**	82	90
10	4-Cl	**2j**	94	93
11	3-Cl	**2k**	95	94
12	4-Br	**2l**	88	95
13	3-Br	**2m**	91	93
14	2-F	**2n**	77	87
15	4-F	**2o**	89	93
16	4-I	**2p**	92	93
17	3,5-Cl_2	**2q**	96	99
18	2-Cl-4-CF_3	**2r**	82	99
19	2-CH_3O-4-Cl	**2s**	83	95

[a] Isolated yield on 0.1 mmol scale. [b]Configuration according to literature[18].

Then we began to investigate the substrates scopes with different aromatic amines under the optimal reaction condition. A remarkably broad range of sulfenamides could be converted to the corresponding sulfenamides with high yield and enantioselectivity (Table 2). Electronic effect was reflected obviously after various electron-poor substrates and electron-rich substrates were examined. For aromatic amines with methyl substituents, the high enantioselectivity and pleasant yield were obtained (**2b** and **2c**). The slightly lower yield of **2c** (compared with **2b**) indicates that the ortho-methyl group on the benzene ring may have a steric effect which inhibits the progress of the reaction. When there was a stronger electron-donating substituent like methoxy or ethoxy (entries 4-5), both the yield and ee value of the product decreased (**2d** and **2e**). We speculated that the acidity of the protons on the sulfenamides was weakened due to the electron donating group on the aromatic ring. Therefore the hydrogen bonding ability between the N-H and P=O was greatly crippled. For this reason, we envisioned that sulfenamides with electron-withdrawing substituent on the benzene ring like trifluoromethyl or nitro, could afford the desired product with pleasant results due to the improved acidity of the N-H and the enhanced the hydrogen bonding property between N-H and P=O. Expectedly, high enantioselectivity and yield were obtained, (entries 6-9). Finally halogen-substituents whether it is ortho, meta or para position on the benzene ring were explored (entries 10-17). The pleasant yield (77-96%) and good ee value (87-99%) were obtained. Interestingly when halogen substituent on the phenyl ring, both electron withdrawing or electron donating groups were contained, pleasant enantioselectivity and yield were also obtained (entries 18-19). Meanwhile, sulfenamides prepared from aliphatic amine cannot be oxidized to the corresponding product (data not shown), presumably due to the decreased acidity of the N-H proton.

On the other hand, sulfenamides with different substituents on the sulfur were also screened. The results demonstrated that the enantioselectivity dropped slightly when the *tert*-butyl group on the sulfur atom was replaced with small alkyl group. Therefore we optimized the reaction conditions based on these substrates (see supporting information). The results showed that pleasant yield and enantioselectivity were obtained simply by replacing the catalyst **4k** with **4l** (scheme 3). Then we tried to investigate the substrates scopes with different substituents such as butyl, pentyl, cyclohexyl, hexyl or heptyl on the sulfur. Sulfenamides with short chain (**2v, 2w**) or long chain (**2z, 2za)**, straight chain (**2t, 2u, 2x, 2y**) or branched chain (**2v, 2w, 2z, 2za**), could be smoothly transformed to the corresponding sulfonamides with high yields (91-96%) and ee values (91-98%). Based on the above reaction results, we found the acidity of the N-H of the aromatic sulfenamides were critical for the reaction. Therefore, sulfenamides prepared from benzamide were investigated under the optimal reaction condition. To our delight, the corresponding sulfinamides (**2zb, 2zc**) were obtained with high yield and good enantioselectivity.

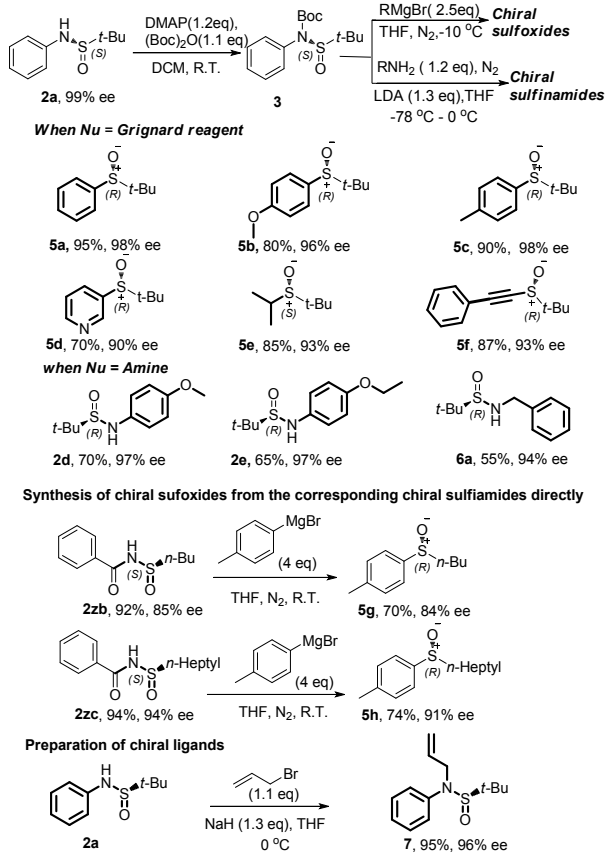
Scheme 3. Substrate scopes of the sulfenamides with different alkyl substituents



Then our attentions were turned to derivatize the obtained sulfinamides, (Scheme 4). Inspired by the work of chiral sulfinyl transfer reagent[15], we envisioned that the aromatic

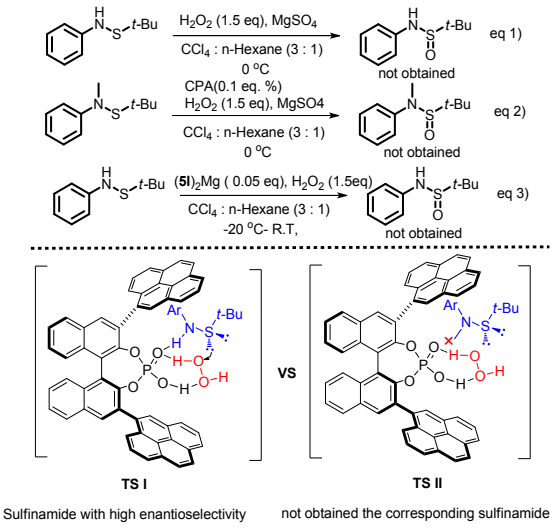
amine with a protection group might be regarded as leaving group when reacted with nucleophiles such as Grignard reagent or amine metal salt. Therefore, the obtained sulfinamide **2a** was transformed to **3** with Boc protection group in quantitative yield. Then different types of Grignard reagent were used to react with **3** and afforded the corresponding sulfoxides (**5a-5f**) easily with high yield (70-95%). Moreover, enantioselectivity was maintained except **5d** and **5e** with a slight decrease. On the other hand, when LDA was used as a base, sulfinamide **3** could be smoothly transformed to the corresponding sulfinamide **2d** and **2e** in high yield and ee with converse configuration. Interestingly, it's difficult to obtain them with pleasant ee by direct oxidation of the corresponding sulfenamide (Entries 4-5, Table 2). What's more, Benzylamine could be easily used to produce N-benzyl sulfinamide **6a** in moderate yield and pleasant ee. It should be pointed out that sulfinamides **2t-2za** were difficult to derivatize into the corresponding sulfoxides due to the failure to add a protection group or degraded during reaction with Grignard reagent. However, we found that the sulfinamides with benzamide (**2zb, 2zc**) could be easily transformed to the corresponding sulfoxides directly without the protection group. The corresponding sulfoxides (**5g, 5h**) were obtained with moderate yield and good enantioselectivity. Finally, chiral ligand **7** that has been applied as catalyst in the 1,4-addition of boronic acids to α， β-unsaturated ketones[19] could be easily prepared and used.

Scheme 4. Derivatization of sulfinamides



Finally, our attentions were focused on the exploration of the possible reaction mechanism. We proposed that the H_2O_2 was activated by chiral phosphoric acid according to our experiments and other researcher's work[6, 20]. First of all, H_2O_2 couldn't oxidize sulfenamide without the addition of phosphoric catalyst (eq. 1, Scheme 5). Secondly, the hydrogen bonding between the chiral phosphoric acid and the substrate N-H is also critical because the N-CH_3 substrate couldn't be oxidized (eq. 2, Scheme 5). Moreover, the ee values and yields were reduced when the acidity of the protons on the arylamine was weakened (entries 4-5, Table 2). Therefore, we proposed a probable oxidation transition state (**TSI**, Scheme 5): The hydrogen bond was formed by phosphoric acid and H_2O_2 to fix and activate H_2O_2; another hydrogen bond between the P=O of phosphoric acid and N-H of sulfenamide help sulfenamide to approach the reaction site.

Scheme 5. Mechanism investigations



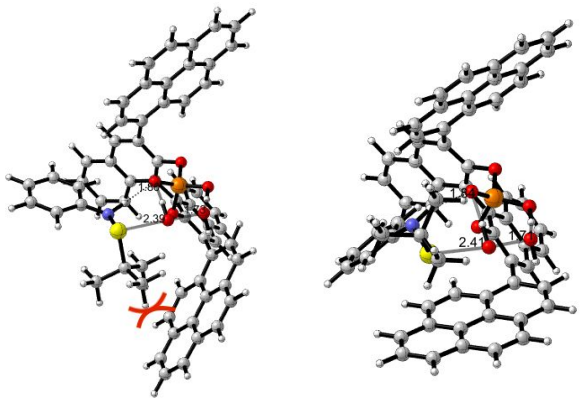


Figure 1. Located transition state structures with relative energies in $\Delta\Delta E_{sol}$ (blue) and $\Delta\Delta G_{sol}$ (red) in kcal mol^{-1}. DFT-computed energies were applied at the M06-2X/def2tzvp//B3LYP-D3/6-31G** level of theory.

To verify our proposal, DFT calculations[22] were performed on this catalytic model. After conformer searching, two preferred transition states which can obtain *R*- and *S*- products with lowest energy barriers were located (Figure 1). There is a strong hydrogen bond between the N-H of sulfenamide and the

P=O of phosphoric acid due to the length of this bond is around 1.84-1.86 Å which can help substrate approach catalyst. Comparing two transition states, TS **I-*re*** leads to a higher free energy barrier than TS **I-*si*** by 5.5 kcal mol^{-1} as the result of steric compulsion between *tert*-butyl of sulfenamide and 3,3'-aromatic substituent of catalyst **4l** (Figure 1). These calculated results indicate that the (*S*)-products should be formed preferentially, which is consistent with the experimental observations. As a result, the activation and the transfer of oxygen atom from H_2O_2 to sulfenamide was controlled by phosphoric acid simultaneously so as to keep the stereoselectivity of the product. Therefore, the methylated sulfenamide could not be oxidized due to the missing of the hydrogen bond (**TS II**). Meanwhile, to determine that the catalytic action comes from phosphoric acid rather than Mg-phosphate, chiral Mg-phosphate **$(4l)_2$Mg** was prepared from **4l** and $Mg(O\text{-}t\text{-}Bu)_2$. [21] However, the corresponding sulfinamide was not formed even at room temperature, (eq. 3, Scheme 5). Moreover, we found that the reaction yield and ee could be improved and finally maintained after the addition of excess anhydrous $MgSO_4$, which might preclude the possibility that water takes part in the transition state [20], (see supporting information).

In summary, we have developed an efficient method for obtaining chiral sulfinamides through asymmetric oxidation of sulfenamides with aqueous H_2O_2 as terminal oxidant. To the best of our knowledge, this is unprecedented for preparation of chiral sulfinamides due to the fact that they were prepared indirectly through resolving, chiral reagent, or chiral auxiliaries up to the present. Meanwhile, this procedure is more in line with atomic economic benefits and green chemistry considering the following advantages: environmentally benign aqueous H_2O_2 (35%) as the oxidant, organocatalysis, very clean reaction without over-oxidation byproduct, high levels of yield (up to 96%) and enantioselectivity (up to 98%), easy workup, etc. Moreover, the chiral sulfinamide obtained could be easily derivatized to most of the chiral sulfoxides or other sulfinamides in high yields and enantioselectivities.

ASSOCIATED CONTENT

Supporting Information.
Experimental procedures and compound characterization. This material is available free of charge via the Internet at http://pubs.acs.org.

AUTHOR INFORMATION

Corresponding Author

ligx@cib.ac.cn; tangzhuo@cib.ac.cn

Acknowledgement.

We are grateful for financial support from the Youth Innovation Promotion Association CAS (2018402); the Natural Science Foundation of Sichuan province, China (2017JY0055); the Innovative Team of Sichuan Province (grant numbers 2017TD0021, 2012SZ0219). The numerical calculations in this paper have been done on the supercomputing system in the Supercomputing Center of University of Science and Technology of China.

REFERENCES

(1) (a) Gelalcha, F. G.; B. Bitterlich, G.; Anilkumar, M. K.; Tse, M.; Beller, M. Iron-Catalyzed Asymmetric Epoxidation of Aromatic Alkenes Using Hydrogen Peroxide. *Angew. Chem., Int. Ed.* **2007**, *46*, 7293-7296. (b) Lane, B. S.; Vogt, M.; DeRose, V. J.; Burgess, K. Manganese-Catalyzed Epoxidations of Alkenes in Bicarbonate Solutions. *J. Am. Chem. Soc.* **2002**, *124*, 11946-11954. (c) Meunier, B. Metalloporphyrins as versatile catalysts for oxidation reactions and oxidative DNA cleavage. *Chem. Rev.* **1992**, *92*, 1411-1456.

(2) (a) O'Mahony, G. E.; Eccles, K. S.; Morrison, R. E.; Ford, A.; Lawrence, S. E. Investigation of steric and electronic effects in the copper-catalysed asymmetric oxidation of sulfides. *Tetrahedron* **2013**, *69*, 10168-10184. (b) Tanaka, K.; Kubo, K.; Iida, K.; Otani, K.; Murase, T.; Yanamoto, M.; Shiro, M. Asymmetric Catalytic Sulfoxidation with H_2O_2 using Chiral Copper Metal–Organic Framework Crystals. *Asian. J. Org. Chem.* **2013**, *2*, 1055-1060.

(3) (a) Gusso, A.; Baccin, C.; Pinna, F.; Strukul, G. Platinum-Catalyzed Oxidations with Hydrogen Peroxide: Enantiospecific Baeyer-Villiger Oxidation of Cyclic Ketones. *Organometallics* **1994**, *13*, 3442-3451. (b) Murahashi, S. I.; Ono, S.; Imada, Y. Asymmetric Baeyer-Villiger Reaction with Hydrogen Peroxide Catalyzed by a Novel Planar-Chiral Bisflavin. *Angew. Chem., Int. Ed.* **2002**, *41*, 2366-2368. (c) Xu, S.; Wang, Z.; Zhang, X.; Zhang, X.; Ding, K. Chiral Brønsted Acid Catalyzed Asymmetric Baeyer-Villiger Reaction of 3-Substituted Cyclobutanones by Using Aqueous H_2O_2. *Angew. Chem., Int. Ed.* **2008**, *47*, 2840-2843. (d) Romney, D. K.; Colvin, S. M.; Miller, S. J. Catalyst Control over Regio- and Enantioselectivity in Baeyer–Villiger Oxidations of Functionalized Ketones. *J. Am. Chem. Soc.* **2004**, *136*, 14019-14022. (e) Bataille, C. J. R.; Donohoe, T. J. Osmium-free direct *syn*-dihydroxylation of alkenes. *Chem. Soc. Rev.* **2011**, *40*, 114-128. (f) Suzuki, K.; Oldenburg, P. D.; Lawrence, Q. J. Iron-Catalyzed Asymmetric Olefin *cis*-Dihydroxylation with 97% Enantiomeric Excess. *Angew. Chem., Int. Ed.* **2008**, *47*, 1887-1889. (g) Zang, C.; Liu,Y.; Xu, Z.-J.; Tse, C.; Guan, X.; Wei, J.; Huang, J.-S. Highly Enantioselective Iron-Catalyzed *cis*-Dihydroxylation of Alkenes with Hydrogen Peroxide Oxidant via an Fe III-OOH Reactive Intermediate. *Angew. Chem., Int. Ed.* **2016**, *55*, 10253-10257.

(4) (a) Chen, K.; Lawrence, Q. J. *cis*-Dihydroxylation of Olefins by a Non‐Heme Iron Catalyst: A Functional Model for Rieske Dioxygenases. *Angew. Chem., Int. Ed.* **1999**, *38*, 2227-2229. (b) Boer, J. W.; Browne, W. R.; Harutyunyan, S. R.; Bini, L. Manganese catalysed asymmetric *cis*-dihydroxylation with H_2O_2. *Chem.Commun.* **2008**, 3747-3749.

(5) (a) Cordova, A.; Sunden, H.; Engqvist, M.; Ibrahem, I.; Casas, J. The Direct Amino Acid-Catalyzed Asymmetric Incorporation of Molecular Oxygen to Organic Compounds. *J. Am. Chem. Soc.* **2004**, *126*, 8914-8915. (b) Sunden, H.; Engqvist, M.; Casas, J.; Ibrahem, I.; Cordova, A. Direct Amino Acid Catalyzed Asymmetric α Oxidation of Ketones with Molecular Oxygen. *Angew. Chem., Int. Ed.* **2004**, *43*, 6532-6535.

(6) Liao, S.; Čorić, I.; Wang, Q.-G.; List, B. Activation of H_2O_2 by Chiral Confined Brønsted Acids: A Highly Enantioselective Catalytic Sulfoxidation. *J. Am. Chem. Soc.* **2012**, *134*, 10765-10768.

(7) (a) Han, Z.; Reeves, D. C.; Krishnamurthy, D.; Senanayake, C. H. Synthetically Derived Auxiliaries: Sulfur Derivatives (including Sulfilamines and Sulfoximines). *Comprehensive Chirality* **2012**, *3*, 560-600. (b) Robak, M. T.; Herbage, M. A.; Ellman, J. A. Synthesis and Applications of *tert*-Butanesulfinamide. *Chem. Rev.* **2010**, *110*, 3600-3740. (c) Senanayake, C. H.; Krishnamurthy, D.; Lu, Z.-H.; Han, Z.; Gallou, I.; Enantiopure Sulfoxides and Sulfinamides: Recent Developments in Their Stereoselective Synthesis and Applications to Asymmetric Synthesis. *Aldrichim. Acta.* **2005**, *38*, 106-128. (d) C. H. Senanayake, Z. Han, D. Krishnamurthy, Synthesis and Ues of Chiral Sulfinamides. *Organosulfur Chemistry in Asymmetric Synthesis* **2008**, 234-264.

(8) (a) Zhu, T.-S.; Jin, S.-S.; Xu, M.-H. Rhodium-Catalyzed, Highly Enantioselective 1,2-Addition of Aryl Boronic Acids to α-Ketoesters and α-Diketones Using Simple, Chiral Sulfur-Olefin Ligands. *Angew. Chem. Int. Ed.* **2012**, *51*, 780-783. (b) Kimmel, K. L.; Weaver, J. D.;

Lee, M.; Ellman, J. A. Catalytic Enantioselective Protonation of Nitronates Utilizing an Organocatalyst Chiral Only at Sulfur. *J. Am. Chem. Soc.* **2012**, *134*, 9058-9061. (c) Wang, Y.; Feng, X.; Du, H. Kinetic Resolution of Hindered Morita–Baylis–Hillman Adducts by Rh(I)-Catalyzed Asymmetric 1,4-Addition/β-Hydroxyelimination. *Org. Lett* **2011**, *13*, 4954-4957. (d) Wang, C.; Wu, X.; Zhou, L.; Sun, J. A Highly Enantioselective Organocatalytic Method for Reduction of Aromatic N-Alkyl Ketimines. *Chem. Eur. J.* **2008**, *14*, 8789-8792; (e) Ye, J.; Wang, C.; Chen, L.; Wu, X.; Zhou, L.; Sun, J. Chiral Lewis Base-Catalyzed Enantioselective Reduction of Unprotected β-Enamino Esters with Trichlorosilane. *Adv. Synth. Catal.* **2016**, *358*, 1042-1047.

(9) Liu, G. D.; Cogan, A.; Ellman, J. A. Catalytic Asymmetric Synthesis of *tert*-Butanesulfinamide. Application to the Asymmetric Synthesis of Amines. *J. Am. Chem. Soc.* **1997**, *119*, 9913-9914.

(10) Weix, D. J.; Ellman, J. A. Improved Synthesis of *tert*-Butanesulfinamide Suitable for Large-Scale Production. *Org. Lett.* **2003**, *5*, 1317-1320.

(11) Chelouan, A.; Recio, R..; Alcudia, A.; Khiar, N.; Fernández, I. DMAP-Catalysed Sulfinylation of Diacetone-D-Glucose: Improved Method for the Synthesis of Enantiopure *tert*-Butyl Sulfoxides and *tert*-Butanesulfinamides. *Eur. J. Org. Chem.* **2014**, *2014*, 6935-6944.

(12) Andersen, K. K.; Gaffield, W.; Papanikolaou, N. E.; Foley, J. W.; Perkins, R. I. Optically Active Sulfoxides. The Synthesis and Rotatory Dispersion of Some Diaryl Sulfoxides[2]. *J. Am. Chem. Soc*. **1964**, *86*, 5637-5646.

(13) Zhang, Y.; Chitale, S.; Goyal, N.; Li, G.; Han, Z.; Shen, S.; Ma, S.; Grinberg, N.; Lee, H.; Lu, B.; Senanayake, C. H.; Asymmetric Synthesis of Sulfinamides Using (−)-Quinine as Chiral Auxiliary, *J. Org. Chem.* **2012**, *77*, 690-695.

(14) Evans, D. A.; Faul, M. M.; Colombo, L.; Bisaha, J. J.; Clardy, J.; Cherry, D. Asymmetric synthesis of chiral organosulfur compounds using N-sulfinyloxazolidinones. *J. Am. Chem. Soc.* **1992**, *114*, 5977-5985.

(15) (a) Han, Z.; Krishnamurthy, D.; Grover, P.; Fang, K.; Senanayake, C. H. Properly Designed Modular Asymmetric Synthesis for Enantiopure Sulfinamide Auxiliaries from N-Sulfonyl-1,2,3-oxathiazolidine-2-oxide Agents. *J. Am. Chem. Soc.* **2002**, *124*, 7880-7881. (b) Qin, Y; Wang, C.; Huang, Z.; Xiao, X.; Jiang, Y. Synthesis of Enantiopure *tert*-Butanesulfinamide from *tert*-Butanesulfinyloxazolidinone, *J. Org. Chem.* **2004**, *69*, 8533-8536. (c) Han, Z.; Krishnamurthy, D.; Grover, P.; Fang, Q.; Su, X.; Wilkinson, H. S.; Lu, Z.; Magierab, D.; Senanayakea, C. H. Practical and highly stereoselective technology for preparation of enantiopure sulfoxides and sulfinamides utilizing activated and functionally differentiated N-sulfonyl-1,2,3-oxathiazolidine-2-oxide derivatives, *Tetrahedron* **2005**, *61*, 6386-6408. (d) Han, Z.; Meyer, A. M.; Xu, Y.; Zhang, Y.; Busch, R.; Shen, S.; Grinberg, N.; Lu, B.; Krishnamurthy, D.; Senanayake, C. H. Enantioselective Synthesis of Diverse Sulfinamides and Sulfinylferrocenes from Phenylglycine-Derived Chiral Sulfinyl Transfer Agent. *J. Org. Chem* **2011**, *76*, 5480-5484. (e) Han, Z.; Herbage, M. A. H.; Mangunuru, P. R.; Xu, Y.; Zhang, L.; Reeves, J. T.; Sieber, J. D.; Li, Z.; DeCroos, P.; Zhang, Y.; Li, G.; Li, N.; Ma, S.; Grinberg, N.; Wang, X.; Goyal, N.; Krishnamurthy, D.; Lu, B.; Song, J. ; Wang, G.; Senanayake, C. H. Design and Synthesis of Chiral Oxathiozinone Scaffolds: Efficient Synthesis of Hindered Enantiopure Sulfinamides and Sulfinyl Ketimines. *Angew. Chem. Int. Ed.* **2013**, *52*, 6713-6717.

(16) (a) Ma, L.-J.; Li, G.-X.; Huang, J.; Zhu, J.; Tang, Z. Using sulfinamides as high oxidation state sulfur reagent for preparation of sulfonamides. *Tetrahedron Lett.* **2018**, *59*, 1600-1603. (b) Craine, L.; Raban, M. The chemistry of sulfonamides. *Chem. Rev.* **1989**, *89*, 689-712. (c) Oka, K.; Hara, S. Conversion of α-chlorosulfenyl chlorides to ketones via α-chlorosulfen-amides. Use of thionyl chloride for oxidation of active methylene compounds. *Tetrahedron Lett.* **1977**, *18*, 695-698. (d) Raban, M.; Hu, C.; Craine, L. H. Stereochemistry in trivalent nitrogen compounds. 40. Torsional barriers in N-2,4-dinitrobenzenesulfenyl benzimidazoles, *Tetrahedron Lett.* **1984**, *25*, 1337-1340. (e) Peng, L.; Turesky, R. J. Capturing Labile Sulfenamide and Sulfinamide Serum Albumin Adducts of Carcinogenic Arylamines by Chemical Oxidation. *Anal. Chem.* **2013**, *85*, 1065-1072.

(17) Jindal, G.; Sunoj, R. B. Axially Chiral Imidodiphosphoric Acid Catalyst for Asymmetric Sulfoxidation Reaction: Insights on Asymmetric Induction. *Angew. Chem., Int. Ed.* **2014**, *126*, 4521-4525.

(18) Sun, X.; Tu, X.; Dai, C.; Zhang, X.; Zhang, B.; Zeng, Q. Palladium-Catalyzed C–N Cross Coupling of Sulfinamides and Aryl Halides, *J. Org. Chem.* **2012**, *77*, 4454-4459.

(19) Khiar, N.; Salvador, Á.; Chelouan, A.; Alcudiab, A.; Fernández, I. "Sulfolefin": Highly modular mixed S/Olefin ligands for enantioselective Rh-catalyzed 1,4-addition. *Org. Biomol. Chem.* **2012**, *10*, 2366-2368.

(20) Gupta, V.; Santra, B.; Mandal, D.; Jana, A. Neutral and anionic phosphate-diesters as molecular templates for the encapsulation of a water dimer. *Chem. Commun.* **2018**, *54*, 11913-11916.

(21) Ingle, G. K.; Liang, Y.; Mormino, M. G.; Li, G.; Fronczek, F. R.; Antilla, J. C. Chiral Magnesium BINOL Phosphate Catalyzed Phopshination of Imines: Access to Enantioenriched α-Amino Phosphine Oxides. *Org. Lett.* **2011**, *13,* 2054-2057.

(22) See calculation details in Supporting Information.

Chiral Brønsted Acid Catalyzed Asymmetric Oxidation of Sulfenamide by Using H_2O_2: A Versatile Access to Sulfinamide and Sulfoxide with High Enantioselectivity