Organic LETTERS

Letter

Cite This: Org. Lett. XXXX, XXX, XXX−XXX

pubs.acs.org/OrgLett

Catalytic Enantioselective Reaction of 2*H*-Azirines with Thiols Using Cinchona Alkaloid Sulfonamide Catalysts

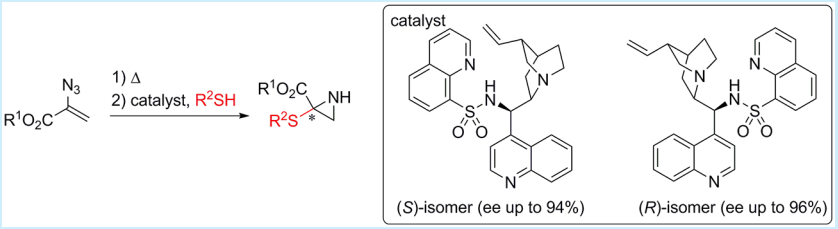
Shuichi Nakamura,*[,†,‡] Daiki Hayama,[†] Masataka Miura,[†] Tsubasa Hatanaka,[§] and Yasuhiro Funahashi[§]

[†]Department of Life Science and Applied Chemistry, Graduate School of Engineering, Nagoya Institute of Technology, Gokiso, Showa-ku, Nagoya 466-8555, Japan

[‡]Frontier Research Institute for Material Science, Nagoya Institute of Technology, Gokiso, Showa-ku, Nagoya 466-8555, Japan

[§]Department of Chemistry, Graduate School of Science, Osaka University 1-1 Machikaneyama, Toyonaka, Osaka 560-0043, Japan

Supporting Information

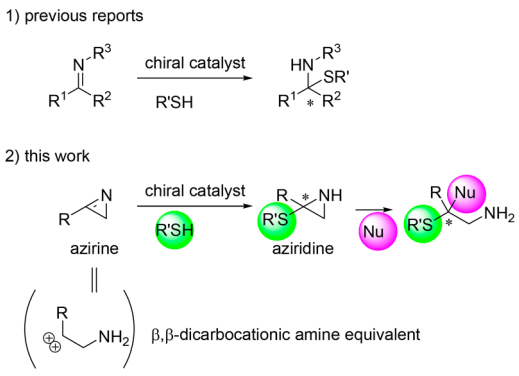


ABSTRACT: The first catalytic enantioselective reaction of 2*H*-azirines with thiols has been developed. The obtained aziridines can be converted to optically active oxazolines, aziridylamides, or α-sulfonyl esters. Transformation of these optically active aziridines showed that 2*H*-azirines act as β,β-dicarbocationic amine synthons.

The reaction of ketimines with some nucleophiles is recognized as one of the most powerful and atom-economical synthetic methods for chiral amines having a tetrasubstituted chiral carbon center. Therefore, there are many papers that describe enantioselective nucleophilic reactions for ketimines, although these reactions are not easy because of their low reactivity and difficulties associated with their enantiofacial control of ketimines.[1] Among these, the enantioselective reaction of ketimines with *S*-nucleophiles has not been very fruitful, although the reaction gives chiral *N*,*S*-acetals, which are attractive as biologically active compounds.[2] The first enantioselective reaction of ketimines with thiols was reported by us[3] and by the Enders group[4] independently. These reports described the reaction of ketimines derived from isatins with alkyl or aryl thiols using chiral cinchona alkaloid sulfonamide catalysts or phosphoric acid catalysts, respectively, to give products with high enantioselectivity. Gredičak[5] and Singh[6] also reported that the enantioselective reaction of *N*-acyl cyclic ketimines with thiols using chiral phosphoric acid catalysts gave products in good yields with high enantioselectivities.[7] On the other hand, the enantioselective reaction of 2*H*-azirines as ketimines with nucleophiles is also an important reaction because it provides chiral aziridines, which can act as chiral building blocks[8] or biologically active compounds.[9] However, the enantioselective reaction of 2*H*-azirines with nucleophiles is rare. We recently reported the first highly enantioselective reaction of 2*H*-azirines with phosphites as nucleophiles using bis(imidazoline)zinc(II) catalysts.[10] However, there have been no reports on the enantioselective nucleophilic reaction of 2*H*-azirines with thiols, although the aziridines that were obtained also accept some other reactions with other nucleophiles, namely, 2*H*-azirines act as β,β-dicarbocationic amine equivalents (Scheme 1). Herein our ongoing interest was extended to the enantioselective reaction of 2*H*-azirines with thiols using our original chiral catalysts.

The reaction of 2*H*-azirines **2**, which were prepared in situ by heating α-azidoacrylates **1** in dichloromethane at 150 °C in a sealed tube, with *p*-bromobenzenethiol **3a** (1.0 equiv) was carried out in the presence of 10 mol % loadings of various chiral catalysts **4a**−**g**. The results are shown in Table 1. The reaction of **1a** with **3a** using cinchonine **4a** afforded product

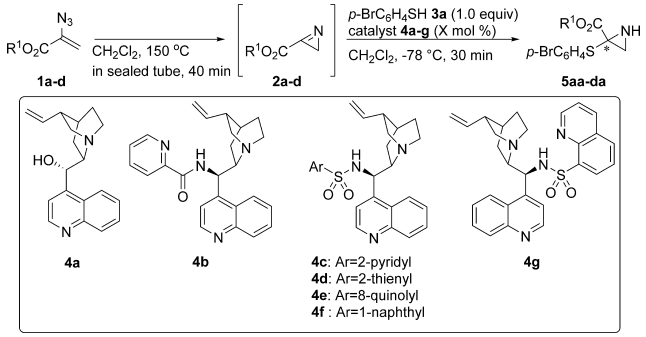
Scheme 1. Enantioselective Reaction of 2*H*-Azirines as Ketimines with Thiols and Synthetic Utility of the Obtained Aziridines



Received: December 26, 2017

DOI: 10.1021/acs.orglett.7b04022
Org. Lett. XXXX, XXX, XXX−XXX

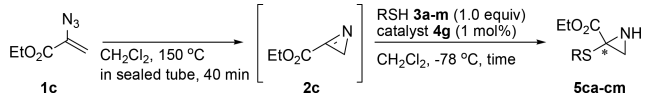
Table 1. Enantioselective Reaction of Azirines 2 with Thiol 3a Using Various Chiral Catalysts 4a–g[a]



entry	1	R^1	4	X	yield (%)	% ee[b] (config.)
1	**1a**	Bn	**4a**	10	89	30 (*R*)
2	**1a**	Bn	**4b**	10	87	58 (*S*)
3	**1a**	Bn	**4c**	10	87	81 (*S*)
4	**1a**	Bn	**4d**	10	98	78 (*S*)
5	**1a**	Bn	**4e**	10	88	92 (*S*)
6	**1a**	Bn	**4f**	10	83	74 (*S*)
7	**1b**	Me	**4e**	10	99	92 (*S*)
8	**1c**	Et	**4e**	10	94	93 (*S*)
9	**1d**	*t*Bu	**4e**	10	87	92 (*S*)
10	**1c**	Et	**4g**	10	96	94 (*R*)
11	**1c**	Et	**4g**	1	96	94 (*R*)
12	**1c**	Et	**4g**	0.5	95	93 (*R*)

[a]Reaction conditions: **1a–d** (0.12 mmol), **3a** (0.10 mmol), and catalyst **4a–g** (1 mol %) were used. [b]Enantiomeric excess was determined by HPLC analysis using a chiral column.

Table 2. Enantioselective Reaction of Azirine 2c with Various Thiols Using Catalysts 4[a]



entry	3	R	5	time (min)	yield (%)	% ee[b] (config.)
1	**3a**	4-BrC_6H_4	**5ca**	30	96	94 (*R*)
2	**3b**	4-ClC_6H_4	**5cb**	60	88	94 (*R*)
3	**3c**	4-FC_6H_4	**5cc**	30	86	92 (*R*)
4	**3d**	3-FC_6H_4	**5cd**	30	80	93 (*R*)
5	**3e**	2-FC_6H_4	**5ce**	30	93	96 (*R*)
6	**3f**	4-$CF_3C_6H_4$	**5cf**	30	89	90 (*R*)
7	**3g**	C_6H_5	**5cg**	30	93	92 (*R*)
8	**3h**	3-$CH_3OC_6H_4$	**5ch**	30	97	93 (*R*)
9	**3i**	3-$CH_3C_6H_4$	**5ci**	30	90	90 (*R*)
10	**3j**	2-naphthyl	**5cj**	75	97	93 (*R*)
11[c]	**3k**	benzothiazole	**5ck**	60	95	93 (*R*)
12[d]	**3b**	4-ClC_6H_4	**5cb**	90	93	93 (*S*)
13[d]	**3c**	4-FC_6H_4	**5cc**	30	93	91 (*S*)
14[d]	**3d**	3-FC_6H_4	**5cd**	30	97	91 (*S*)
15[d]	**3e**	2-FC_6H_4	**5ce**	30	88	94 (*S*)
16[d]	**3j**	2-naphthyl	**5cj**	75	91	93 (*S*)
17[c,d]	**3k**	benzothiazole	**5ck**	120	91	91 (*S*)
18[c,d]	**3l**	benzoxazole	**5cl**	120	93	91 (*S*)
19[e]	**3m**	benzyl	**5cm**	120	87	72 (*R*)

[a]Reaction conditions: **1c** (0.12 mmol), **3a–m** (0.10 mmol) and catalyst **4g** (1 mol %) were used. [b]Enantiomeric excess was determined by HPLC analysis using a chiral column. [c]Catalyst (10 mol %) was used. [d]Catalyst **4e** was used. [e]Catalyst (20 mol %) was used.

5aa in good yield but with low enantioselectivity (entry 1).[11] To our delight, the reaction using picolinamide catalyst **4b** gave product **5aa** with better enantioselectivity than that obtained with catalyst **4a** (entry 2). Encouraged by this result, we examined the reaction using chiral catalysts **4c–e** having various arenesulfonyl groups (entries 3–5). The reaction using 8-quinolinesulfonylated 9-amino-9-deoxy-*epi*-cinchonine catalyst **4e**[12] afforded product **5aa** with high enantioselectivity (entry 5). On the other hand, the reaction using 1-naphthalenesulfonylated 9-amino-9-deoxy-*epi*-cinchonine catalyst **4f** gave **5aa** in high yield but with lower enantioselectivity than that obtained using catalyst **4e** (entry 6). The reactions using methyl, ethyl, and *tert*-butyl esters **1b–d** showed almost the same enantioselectivity (entries 7–9). On the other hand, the reaction of **2c** with **3a** using 8-quinolinesulfonamide catalyst **4g** derived from cinchonidine gave the opposite enantiomer of **5ca** with good enantioselectivity (entry 10). Good enantioselectivity was still observed even when the catalyst loading was decreased to 1 or 0.5 mol % (entries 11 and 12).

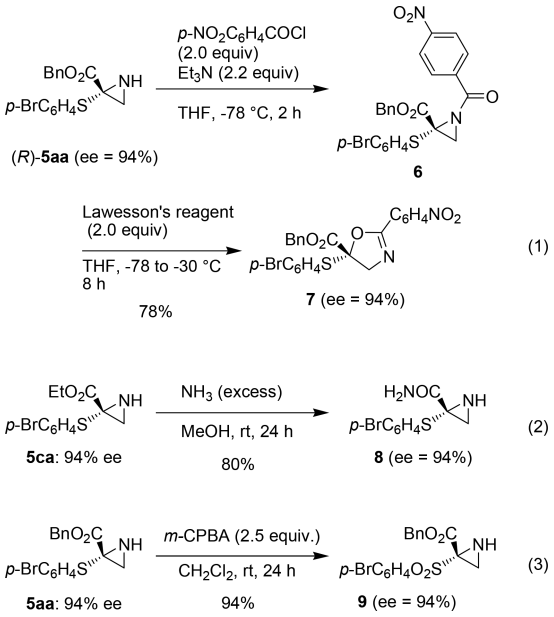
Under these optimized conditions, we next examined the nucleophilic reaction of azirine **2c** with various thiols **3a–m** using catalyst **4g** (Table 2). The reaction of azirine **2c** with thiols **3a–f** having electron-withdrawing groups such as bromo, chloro, fluoro, and trifluoromethyl groups at the *ortho*, *meta*, or *para* position gave the corresponding products **5ca–cf** in good yield with high enantioselectivity (80–96% yield, 90–96% ee; entries 1–6). The reaction of benzenethiol (**3g**) and electron-rich thiols **3h** and **3i** having methyl or methoxy groups also gave products **5cg–ci** with good enantioselectivity (entries 7–9). Various bulky thiols such as 2-naphthalenethiol and benzothiazolethiol were also applicable nucleophiles in this reaction (entries 10 and 11). In addition, the reaction of **2c** with various thiols **3b–e,j–l** using catalyst **4e** afforded the opposite enantiomer of the products compared with the reaction using catalyst **4g** with high enantioselectivity (entries 12–18). The reaction of azirine **2c** with benzyl mercaptan (**3m**) as an alkyl thiol also gave product **5cm** in high yield with good enantioselectivity (entry 19).[13] These results are the first examples of a highly enantioselective reaction of azirines with sulfur nucleophiles.

We next examined the transformation of various aziridines **5** obtained (Scheme 2). The reaction of **5aa** with *p*-nitrobenzoyl chloride gave *N*-benzoylated aziridine **6**, which reacted with 2.0 equiv of Lawesson's reagent in situ to give oxazoline compound **7** (Scheme 2, eq 1). Although the role of Lawesson's reagent is not clear, it could activate the carbonyl oxygen and act as a weak Lewis acid.[14] These reactions implied that azirines act as *β*,*β*-dicarbocationic amine synthons. The reaction of **5ca** with NH_3 in methanol gave aziridylamide **8** without loss of enantiopurity (Scheme 2, eq 2). The absolute configuration of **8** was assigned as *R* by X-ray crystallographic analysis, and the configurations of other products were tentatively assumed by analogy. Furthermore, chiral *α*-amino sulfones, *β*-amino sulfones, and *α*-sulfonyl esters are important classes of synthetic targets because they often exhibit a broad range of biological activities.[15] Therefore, we next examined the oxidation of sulfides to sulfones. The reaction of **5aa** with *m*-CPBA in dichloromethane at rt gave *α*-sulfonyl ester **9** in high yield (Scheme 2, eq 3).

Next, we examined the gram-scale synthesis of aziridine **5aa**. The preparation of azirine **2a** was carried out in toluene at

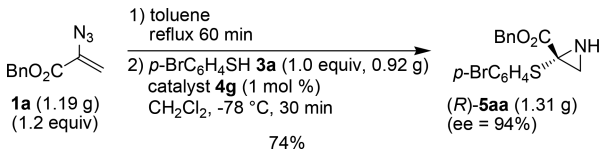
DOI: 10.1021/acs.orglett.7b04022
Org. Lett. XXXX, XXX, XXX–XXX

Scheme 2. (1) Transformation of 5aa to Chiral Oxazoline Compound 7 Using Lawesson's Reagent; (2) Transformation of 5ca to Aziridylamide 8; (3) Transformation of 5aa to α-Sulfonyl Ester 9 Using *m*-CPBA



reflux because the large-scale reaction using azide compound **1g** in a sealed tube in CH_2Cl_2 was dangerous. The reaction was accomplished using 1.19 g of **1a**, 0.92 g of **3a**, and 1 mol % catalyst **4g** to give **5aa** in 74% yield with 94% ee (Scheme 3).

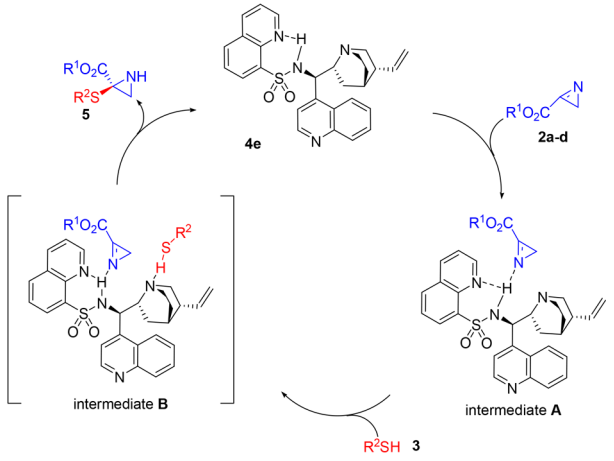
Scheme 3. Large-Scale Synthesis of (*R*)-5aa Using 1 mol % 4g



The reaction of azirines **2** with thiols **3** using catalyst **4e**, which has heteroarenesulfonyl groups, gave products **5** with higher enantioselectivity than that obtained using naphthalenesulfonylated catalyst **4f** (Table 1, entries 5 vs 6). Therefore, the heteroarenesulfonyl groups play an important role in enhancing the enantioselectivity of the reaction. On the basis of these results, a proposed catalytic cycle for the reaction of azirines **2** with thiols **3** is shown in Scheme 4. The acidic proton of 8-quinolinesulfonamide in catalyst **4e** can activate azirine **2** by hydrogen bonding to give intermediate **A**, and the quinuclidine moiety in catalyst **4e** could also activate the thiol by hydrogen bonding. The reaction of activated thiol **3** with azirine leads to an adduct, which undergoes protonation and decomplexation to give product **5** and regenerate catalyst **4e**. In order to clarify the assumed reaction cycle, we conducted a spectroscopic analysis. ESI-MS analysis of the reaction mixture of **2c** and **4e** showed intermediate **A** (cation mode; calcd for $C_{33}H_{36}N_5O_4S^+$ as $[\mathbf{A} + H]^+$ 598.3, found 598.3). This signal supports our proposed reaction mechanism.

The assumed transition state for the reaction of an azirine **2** with a thiol **3** using catalyst **4e** is shown in Figure 1. The reaction of **2** with **3** proceeds in the coordination sphere of the

Scheme 4. Assumed Reaction Cycle for the Enantioselective Reaction of Azirines 2 with Thiols 3 Using Catalyst 4e



chiral catalyst **4e**, and therefore, the thiol approaches the *Si* face of the azirine to avoid steric repulsion, giving the *S* isomer of the product.

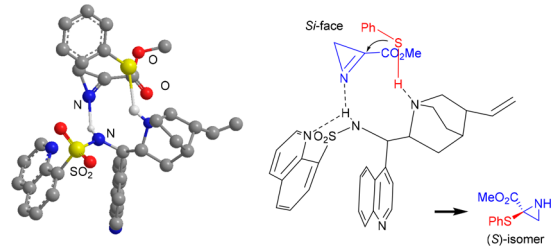


Figure 1. Assumed transition state of the reaction of azirine **2** with thiol **3** using **4e**. H atoms have been omitted for clarity.

In conclusion, we have developed a highly enantioselective reaction of azirines with various thiols. The reaction was screened for a broad range of thiols. This approach is the first example of a highly enantioselective reaction of azirines with sulfur nucleophiles. The obtained aziridines can be converted to various chiral compounds having a tetrasubstituted carbon center without loss of enantioselectivity. Further studies of the potential of these catalytic systems for other processes and the enantioselective reaction of azirines are in progress.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.orglett.7b04022.

^{1}H and ^{13}C NMR spectra and experimental procedures for all new compounds (PDF)

Accession Codes

CCDC 1588168 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge via www.ccdc.cam.ac.uk/data_request/cif, or by e-mailing data_request@ccdc.cam.ac.uk, or by contacting The Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, U.K.; fax: +44 1223 336033.

DOI: 10.1021/acs.orglett.7b04022
Org. Lett. XXXX, XXX, XXX−XXX

AUTHOR INFORMATION

Corresponding Author

*E-mail: snakamur@nitech.ac.jp.

ORCID

Shuichi Nakamura: 0000-0001-5633-8367

Notes

The authors declare no competing financial interest.

ACKNOWLEDGMENTS

This work was supported by a Grant-in-Aid for Scientific Research on Innovative Areas "Advanced Molecular Transformations by Organocatalysts" from MEXT (26105727) and the Tatematsu Foundation.

REFERENCES

(1) For selected reviews, see: (a) Shibasaki, M.; Kanai, M. *Org. Biomol. Chem.* **2007**, *5*, 2027. (b) Riant, O.; Hannedouche, J. *Org. Biomol. Chem.* **2007**, *5*, 873. (c) Cozzi, P. G.; Hilgraf, R.; Zimmermann, N. *Eur. J. Org. Chem.* **2007**, *2007*, 5969. (d) Shibasaki, M.; Kanai, M. For selected recent examples, see. *Chem. Rev.* **2008**, *108*, 2853. (e) Chen, Q. G.; Xie, L. H.; Li, Z. J.; Tang, Y.; Zhao, P.; Lin, L. L.; Feng, X. M.; Liu, X. H. *Chem. Commun.* **2018**, *54*, 678.

(2) For β-lactam antibiotics, see: (a) Sammes, P. G. *Chem. Rev.* **1976**, *76*, 113. (b) *The Organic Chemistry of β-Lactams*; Georg, G. I., Ed.; VCH: New York, 1993. For fusaperazine A, see: (c) Usami, Y.; Aoki, S.; Hara, T.; Numata, A. *J. Antibiot.* **2002**, *55*, 655. For the fungal metabolite (+)-11,11′-dideoxyverticillin A, see: (d) Kim, J.; Ashenhurst, J. A.; Movassaghi, M. *Science* **2009**, *324*, 238. (e) Bertamino, A.; Soprano, M.; Musella, S.; Rusciano, M. R.; Sala, M.; Vernieri, E.; Di Sarno, V.; Limatola, A.; Carotenuto, A.; Cosconati, S.; Grieco, P.; Novellino, E.; Illario, M.; Campiglia, P.; Gomez-Monterrey, I. *J. Med. Chem.* **2013**, *56*, 5407.

(3) (a) Nakamura, S.; Takahashi, S.; Nakane, D.; Masuda, S. *Org. Lett.* **2015**, *17*, 106. For recent studies on enantioselective reactions with ketimines from our group, see: (b) Nakamura, S.; Hayashi, M.; Hiramatsu, Y.; Shibata, N.; Funahashi, Y.; Toru, T. *J. Am. Chem. Soc.* **2009**, *131*, 18240. (c) Hara, N.; Nakamura, S.; Sano, M.; Tamura, R.; Funahashi, Y.; Shibata, N. *Chem. - Eur. J.* **2012**, *18*, 9276. (d) Hayashi, M.; Sano, M.; Funahashi, Y.; Nakamura, S. *Angew. Chem., Int. Ed.* **2013**, *52*, 5557. (e) Hayashi, M.; Iwanaga, M.; Shiomi, N.; Nakane, D.; Masuda, H.; Nakamura, S. *Angew. Chem., Int. Ed.* **2014**, *53*, 8411. (f) Nakamura, S.; Sano, M.; Toda, A.; Nakane, D.; Masuda, H. *Chem. - Eur. J.* **2015**, *21*, 3929. (g) Nakamura, S.; Yamaji, R.; Hayashi, M. *Chem. - Eur. J.* **2015**, *21*, 9615. (h) Nakamura, S.; Takahashi, S. *Org. Lett.* **2015**, *17*, 2590. (i) Nakamura, S.; Matsuda, N.; Ohara, M. *Chem. - Eur. J.* **2016**, *22*, 9478. (j) Nakamura, S.; Yamaji, R.; Iwanaga, M. *Chem. Commun.* **2016**, *52*, 7462.

(4) Beceño, C.; Chauhan, P.; Rembiak, A.; Wang, A.; Enders, D. *Adv. Synth. Catal.* **2015**, *357*, 672.

(5) Suć, J.; Dokli, I.; Gredičak, M. *Chem. Commun.* **2016**, *52*, 2071.

(6) Unhale, R. A.; Molleti, N.; Rana, N. K.; Dhanasekaran, S.; Bhandary, S.; Singh, V. K. *Tetrahedron Lett.* **2017**, *58*, 145.

(7) There have been several reports on the enantioselective reaction of aldimines with thiols. See: (a) Ingle, G. K.; Mormino, M. G.; Wojtas, L.; Antilla, J. C. *Org. Lett.* **2011**, *13*, 4822. (b) Fang, X.; Li, Q.-H.; Tao, H.-Y.; Wang, C.-J. *Adv. Synth. Catal.* **2013**, *355*, 327. (c) Wang, H.-Y.; Zhang, J.-X.; Cao, D.-D.; Zhao, G. *ACS Catal.* **2013**, *3*, 2218. (d) Qian, H.; Sun, J. *Asian J. Org. Chem.* **2014**, *3*, 387. (e) Feng, B.-X.; Wang, B.; Li, X. *Org. Biomol. Chem.* **2016**, *14*, 9206.

(8) (a) Tanner, D. *Angew. Chem., Int. Ed. Engl.* **1994**, *33*, 599. (b) McCoull, W.; Davis, F. A. *Synthesis* **2000**, *2000*, 1347. (c) Hu, X. E. *Tetrahedron* **2004**, *60*, 2701. (d) Pineschi, M. *Eur. J. Org. Chem.* **2006**, *2006*, 4979. (e) Schneider, C. *Angew. Chem., Int. Ed.* **2009**, *48*, 2082.

(9) For mitomycin C, see: (a) Hata, T.; Hoshi, T.; Kanamori, K.; Matsumae, A.; Sano, Y.; Shima, T.; Sugawara, R. *J. Antibiot.* **1956**, *9*, 141. (b) Mao, Y.; Varoglu, M.; Sherman, D. H. *Chem. Biol.* **1999**, *6*, 251. For azicemicins A and B, see: (c) Tsuchida, T.; Iinuma, H.; Kinoshita, N.; Ikeda, T.; Sawa, R.; Takahashi, Y.; Naganawa, H.; Sawa, T.; Hamada, M.; Takeuchi, T. *J. Antibiot.* **1993**, *46*, 1772. (d) Tsuchida, T.; Iinuma, H.; Kinoshita, N.; Ikeda, T.; Sawa, T.; Hamada, M.; Takeuchi, T. *J. Antibiot.* **1995**, *48*, 217. (e) Tsuchida, T.; Sawa, R.; Takahashi, Y.; Iinuma, H.; Sawa, T.; Naganawa, H.; Takeuchi, T. *J. Antibiot.* **1995**, *48*, 1148. For miraziridine A, see: (f) Nakao, Y.; Fujita, M.; Warabi, K.; Matsunaga, S.; Fusetani, N. *J. Am. Chem. Soc.* **2000**, *122*, 10462. (g) Konno, H.; Kubo, K.; Makabe, H.; Toshiro, E.; Hinoda, N.; Nosaka, K.; Akaji, K. *Tetrahedron* **2007**, *63*, 9502. For reviews of other biological active compounds, see: (h) Ismail, F. M. D.; Levitsky, D. O.; Dembitsky, V. M. *Eur. J. Med. Chem.* **2009**, *44*, 3373. (i) Singh, G. S. *Mini-Rev. Med. Chem.* **2016**, *16*, 892.

(10) (a) Nakamura, S.; Hayama, D. *Angew. Chem., Int. Ed.* **2017**, *56*, 8785. For pioneering works on enantioselective nucleophilic addition reactions with 2*H*-azirines, see: (b) Risberg, E.; Somfai, P. *Tetrahedron: Asymmetry* **2002**, *13*, 1957. (c) An, D.; Guan, X.; Guan, R.; Jin, L.; Zhang, G.; Zhang, S. *Chem. Commun.* **2016**, *52*, 11211. For kinetic resolution of 2*H*-azirines, see: (d) Hu, H.; Liu, Y.; Lin, L.; Zhang, Y.; Liu, X.; Feng, X. *Angew. Chem., Int. Ed.* **2016**, *55*, 10098. For diastereoselective reactions of 2*H*-azirines with thiols, see: (e) Álvares, Y. S. P.; Alves, M. J.; Azoia, N. G.; Bickley, J. F.; Gilchrist, T. L. *J. Chem. Soc. Perkin Trans. 1* **2002**, *1*, 1911. (f) Palacios, F.; Ochoa de Retana, A. M.; Alonso, J. M. *J. Org. Chem.* **2005**, *70*, 8895.

(11) The reaction without catalyst gave the product in 80% yield. We also examined the reaction using a bis(imidazoline)zinc(II) catalyst, which was a good catalyst for the enantioselective reaction of azirines with phosphites, but the enantioselectivity of the product was low (5% ee, 88% yield). See ref 10a.

(12) For *N*-heteroarenesulfonylated cinchona alkaloid amide catalysts, see: (a) Hara, N.; Nakamura, S.; Funahashi, Y.; Shibata, N. *Adv. Synth. Catal.* **2011**, *353*, 2976. (b) Hara, N.; Nakamura, S.; Sano, M.; Tamura, R.; Funahashi, Y.; Shibata, N. *Chem. - Eur. J.* **2012**, *18*, 9276. (c) Nakamura, S.; Toda, A.; Sano, M.; Hatanaka, T.; Funahashi, Y. *Adv. Synth. Catal.* **2016**, *358*, 1029. Also see refs 3f and 3h.

(13) We also examined the reactions of azirine **2a** with *p*-chlorophenol and benzyl alcohol, but the yield or enantioselectivity was low.

(14) For activation of cyclopropane cleavage by Lawesson's reagent as a Lewis acid, see: (a) Kaschel, J.; Schmidt, C. D.; Mumby, M.; Kratzert, D.; Stalke, D.; Werz, D. B. *Chem. Commun.* **2013**, *49*, 4403. (b) Hadj-Abo, F.; Bienz, S.; Hesse, M. *Tetrahedron* **1994**, *50*, 8665. For a review of Lawesson's reagent, see: (c) Jesberger, M.; Davis, T. P.; Barner, L. *Synthesis* **2003**, *2003*, 1929. For the synthesis of oxazolines from aziridines using Lewis acids, see: (d) Heine, H. W.; Proctor, Z. *J. Org. Chem.* **1958**, *23*, 1554. (e) Ferraris, D.; Drury, W. J.; Cox, C.; Lectka, T. *J. Org. Chem.* **1998**, *63*, 4568. (f) Cardillo, G.; Gentilucci, L.; Tolomelli, A. *Tetrahedron* **1999**, *55*, 15151. (g) Cockrell, J.; Wilhelmsen, C.; Rubin, H.; Martin, A.; Morgan, J. B. *Angew. Chem., Int. Ed.* **2012**, *51*, 9842.

(15) For α- or β-aminosulfones, see: (a) Micetich, R. G.; Maiti, S. N.; Spevak, P.; Hall, T. W.; Yamabe, S.; Ishida, N.; Tanaka, M.; Yamazaki, T.; Nakai, A.; Ogawa, K. *J. Med. Chem.* **1987**, *30*, 1469. (b) Vintonyak, V. V.; Warburg, K.; Kruse, H.; Grimme, S.; Hübel, K.; Rauh, D.; Waldmann, H. *Angew. Chem., Int. Ed.* **2010**, *49*, 5902. (c) Miller, B. E.; Mistry, S.; Smart, K.; Connolly, P.; Carpenter, D. C.; Cooray, H.; Bloomer, J. C.; Tal-Singer, R.; Lazaar, A. L. *BMC Pharmacol. Toxicol.* **2015**, *16*, 18. For α-sulfonyl esters, see: (d) León, L. G.; Machín, R. P.; Rodríguez, C. M.; Ravelo, J. L.; Martín, V. S.; Padrón, J. M. *Bioorg. Med. Chem. Lett.* **2008**, *18*, 5171.

DOI: 10.1021/acs.orglett.7b04022
Org. Lett. XXXX, XXX, XXX−XXX