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Enantioselective Construction of Sulfur-Containing Tetrasubstituted Stereocenters via Asymmetric Functionalizations of α-Sulfanyl Cyclic Ketones

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Abstract. Asymmetric functionalizations of α-sulfanyl cyclic ketones were realized via chiral phosphoric acid catalyzed enantioselective addition reactions with aldimines, azodicarboxylates and allenamides. A series of chiral organosulfur compounds possessing sulfur-containing tetrasubstituted stereocenters were accessed via these methods, with excellent regioselectivities and high stereoselectivities.

Keywords: asymmetric catalysis; organic catalysis; α-sulfanyl cyclic ketones; Mannich-type reaction; azodicarboxylates; allenamides

Organosulfur compounds are widely present in a series of bioactive natural products and pharmaceuticals[1]. Accordingly, the catalytic enantioselective synthesis of optically active organosulfur compounds has received considerable research interest[2]. However, the asymmetric synthesis of sulfur-containing tetrasubstituted stereocenters is still a challenging task, due to the relatively low reactivities and difficulties in stereoselectivity control.[3] In spite of these challenges, a number of elegant asymmetric methods have been developed for enantioselective construction of sulfur-containing tetrasubstituted stereocenters recently, using the strategies of asymmetric addition of sulfur-based nucleophiles[4], asymmetric electrophilic sulfenylation[5] and asymmetric functionalization of sulfur-containing substrates[6]. Although the enantioselective C-S bond formation provided a straightforward method for asymmetric synthesis of chiral organosulfur compounds, the alternative strategy based on asymmetric functionalizations of sulfur-containing substrates has also proved to be fruitful, because of the more extensive reaction types. Among various reactions developed via this strategy, the asymmetric functionalizations of α-sulfanyl substituted cyclic carbonyl compounds represent as the most versatile one. Shibasaki and co-workers reported the chiral Ag(I) catalyzed enantioselective aldol[7] and Mannich-type reactions[8] of α-sulfanyl lactones (Figure 1, a). Zhou group and others developed a series asymmetric catalytic reactions of 3-thioxindoles, including asymmetric aminations with azodicarboxylates[9], Michael additions with nitrolefines[10] and enals[11] and electrophilic sulfenylations[12] (Figure 1, b). In addition, Secci and co-workers disclosed the asymmetric Michael additions of 2-arylthio substituted cyclobutanones with nitrolefines by chiral amine-thiourea catalyst, however, expanding the scope to five and six membered cyclic ketones led to the generation of products in moderate yields[13] (Figure 1, c).

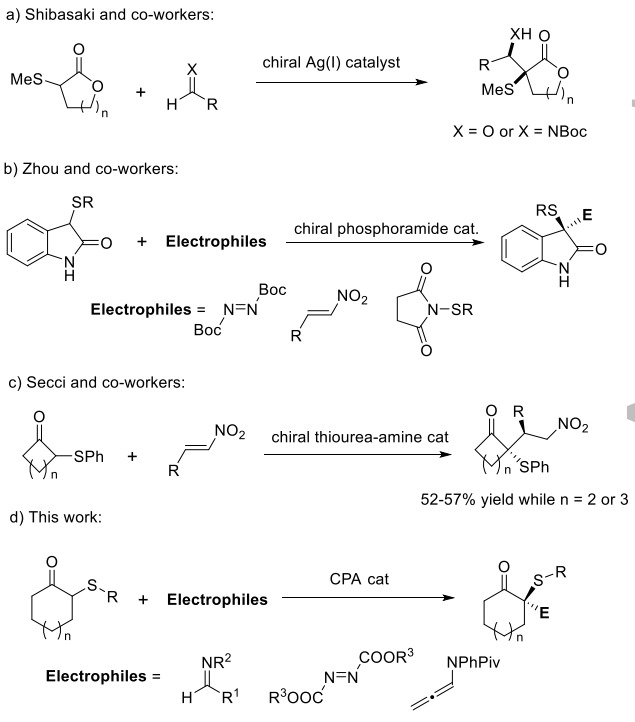

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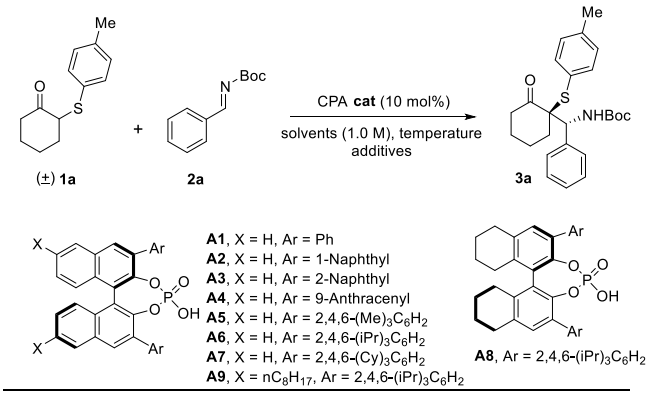
Figure 1. Enantioselective construction of sulfur-containing tetrasubstituted stereocenters via asymmetric functionalizations of α-sulfanyl carbonyl compounds.

The chiral phosphoric acid[14] (CPA) catalyzed asymmetric functionalizations of α-substituted cyclic ketones have become a versatile strategy for construction of quaternary stereocenters on cyclic ketones, which were independently developed by List[15] and Toste[16] group. Recently, we reported the asymmetric Mannich-type reactions of α-azido cyclic ketones under CPA catalysis, generating chiral azides possessing α-quaternary stereocenters[17]. With our continuous interest on developing asymmetric reactions for construction of chiral quaternary stereocenters[18], herein we report a general protocol for enantioselective construction of sulfur-containing tetrasubstituted stereocenters via asymmetric functionalizations of α-sulfanyl cyclic ketones, including asymmetric Mannich-type reactions[19], aminations with azodicarboxylates[16a, 20] and additions with allenamides[16b, 21] (Figure 1, d).

We commenced our study by choosing racemic α-sulfanyl substituted cyclohexanone **1a** and aldimine **2a** as substrates under the catalysis of CPA catalysts (Table 1). The reaction between these two substrates under the catalysis of cat **A1** (10 mol%) in DCM (1.0 M) at 40 °C in the presence of 4 Å molecular sieves provided the desired Mannich-type product **3a** with excellent diastereomeric ratio (dr) and moderate enantiomeric excess (ee), albeit in low yield (Table 1, entry 1). Next, a series of BINOL-derived CPA catalysts were screened in this reaction (entries 2-7), and encouragingly the TRIP catalyst (cat **A6**) provided the optimal results, generating **3a** in 68% yield with 99% ee (entry 6). Switching the chiral scaffold of catalyst to H8-BINOL-type led to improved yield, but with decreased ee (entry 8). A range of solvents were also examined in this reaction, which indicated DCM was still the optimal one (entries 9-11). The role of molecular sieve was also investigated (entries 12-13). Interestingly, in the absence of 4 Å MS, the yield of this reaction diminished to 25%; while switching 4 Å MS to acid-wash molecular sieves (AW-300 MS) gave an improved yield of 82% with retained stereoselectivity (entry 13).

Table 1. Optimizations of reaction conditions.[a]



Entry	Cat.	Sol.	Yield (%)[b]	Dr[c]	Ee (%)[d]
1	**A1**	DCM	16	>20:1	54
2	**A2**	DCM	21	>20:1	94
3	**A3**	DCM	31	>20:1	49
4	**A4**	DCM	52	>20:1	94
5	**A5**	DCM	45	>20:1	95
6	**A6**	DCM	68	>20:1	99
7	**A7**	DCM	54	>20:1	98
8	**A8**	DCM	78	>20:1	97
9	**A6**	Tol	44	>20:1	98
10	**A6**	$CHCl_3$	42	>20:1	94
11	**A6**	THF	29	>20:1	95
12[e]	**A6**	DCM	25	>20:1	88
13[f]	**A6**	DCM	82	>20:1	99

[a] Reactions were performed with **1a** (0.1 mmol), **2a** (0.2 mmol), CPA catalysts (0.01 mmol) in solvents (0.1 mL) with 4 Å MS (150 mg) at 40 °C for 16 h. [b] Isolated yield. [c] Dr value was determined by crude ^{1}H NMR analysis. [d] Ee value was determined by HPLC analysis on a chiral stationary phase. [e] Without 4 Å MS. [f] With AW-300 MS.

Having the optimized reaction conditions established, the scope of this reaction was studied with CPA catalyst (*R*)-**A6** (Scheme 1). A series of *para*- and *meta*-substituted benzaldimins (with various electron-donating, electron-withdrawing and electron-neutral substitutions) were well tolerated under the optimal conditions, generating the Mannich-type products with excellent diastereoselectivities and enantioselectivities (**3b**-**3f)**. The absolute configurations of these products were assigned by analogy to product **3b**, whose structure was unambiguously confirmed by X-ray crystallography[22]. The sterically demanding *ortho* substituted benzaldimins was also compatible under the standard conditions (**3k**). 2-Naphthyl group (**3l**) and heteroaryl groups, like 2-furanyl group (**3m**) and 3-thienyl group (**3n**), were also amenable variants. Switching the *N*-Boc aldimine to *N*-Cbz aldimine led to the formation of product with high enantioselectivity as well, albeit in moderate yield (**3o**). Next, the scope for cyclic ketones was investigated. Using α-sulfanyl substituted cyclopentanone (**3p**) and other six-membered cyclic ketones (**3r** and **3s**) as substrates afforded the Mannich-type products with good yields and high

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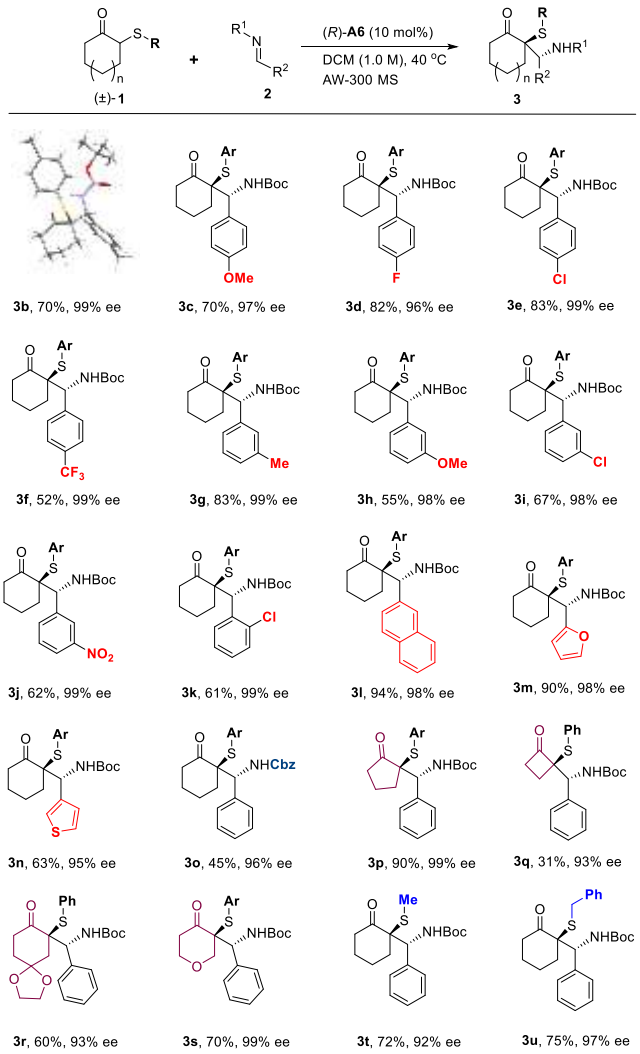
stereoselectivities under the optimal conditions. Additionally, the α-sulfanyl substituted cyclobutanone could produce the product with high stereoselectivity as well, albeit in low yield (**3q**). Finally, the scope for the sulfanyl groups was also examined; switching the arylsulfanyl group to methylsulfanyl (**3t**) and benzylsulfanyl group (**3u**) was well tolerated, giving access to Mannich-type products with comparable results.

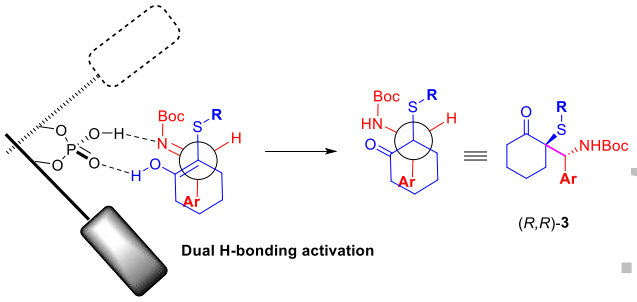
Scheme 1. Substrate scope for direct Mannich-type reactions of α-sulfanyl cyclic ketones with aldimines.[a]



[a]Reactions were performed with **1** (0.1 mmol), **2** (0.2 mmol), CPA catalysts (*R*)-**A6** (0.01 mmol) in DCM (0.1 mL) with AW-300 MS (150 mg) at 40 °C for 16 h. Yields were isolated yield. The dr values were >20:1 as determined by ^{1}H NMR analysis. Ee values were determined by HPLC analysis on a chiral stationary phase. **Ar** = 4-methylphenyl.

To account for the observed stereochemical outcome of these reactions, we propose that the CPA catalyst acts as a bifunctional catalyst to activate both the imine substrates and the enol form of α-sulfanyl cyclic ketones through dual H-bonding interactions (Scheme 2). Under the guidance of CPA (*R*)-**A6**, the *Re*-face the enol intermediate attacks the *Si*-face of imine through this transition state to give the (*R*,*R*)-addition product **3**, as was observed.

Scheme 2. Postulated transition state that accounts for the observed stereoselectivity.



To extend the applicability of this strategy for asymmetric construction of sulfur-containing tetrasubstituted stereocenters, the asymmetric functionalization of α-sulfanyl cyclic ketones with other electrophiles was investigated. Satisfyingly, the asymmetric amination of **1a** with di-*tert*-butyl azodicarboxylate **4a** under the catalysis of (*S*)-**A7** catalyst provided the *S*,*N*-acetal **5a** in 64% yield with 91% ee[23], which was an important motif in biologically active small molecules[24] (Scheme 3). Switching the cyclohexanone scaffold to cyclopentanone (**5b**) and other six-membered cyclic ketone (**5c**) were well compatible with the optimal conditions, generating *S*,*N*-acetal products with high enantioselectivities. The scope for azodicarboxylates was also studied; however, using dibenzyl and diisopropyl azodicarboxylates as amination reagent under the standard conditions gave products with diminished enantioselectivities (**5d** and **5e**). Switching the aryl sulfanyl substitution of benzyl sulfanyl group was also investigated, however, which led to the generation of product in both diminished yield and ee (**5f**).

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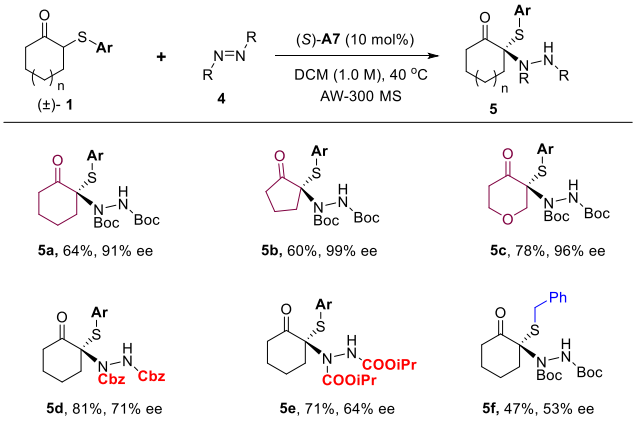
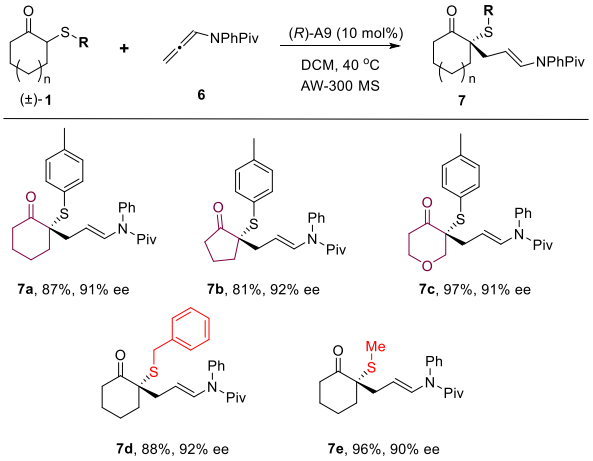
Scheme 3. Substrate scope for asymmetric aminations of α-sulfanyl cyclic ketones with azodicarboxylate.[a]



[a]Reactions were performed with **1** (0.1 mmol), **4** (0.2 mmol), CPA catalysts (*S*)-**A7** (0.01 mmol) in DCM (0.1 mL) with AW-300 MS (150 mg) at 40 °C for 16 h. Yields were isolated yield. Ee values were determined by HPLC analysis on a chiral stationary phase. **Ar** = 4-methylphenyl.

The chiral phosphoric acid catalyzed asymmetric additions of α-sulfanyl cyclic ketones with allenamides for the construction of sulfur-containing tetrasubstituted stereocenters was also studied (Scheme 4). Encouragingly, in the presence of C_8-TRIP catalyst (*R*)-**A9** (10 mol%), the reaction between **1a** and allenamide **6** proceeded smoothly to give the addition product **7a** in 87% yield with 91% ee[25]. The scope of this reaction was investigated, which indicated that the α-sulfanyl cyclopentanone and other six-membered cyclic ketones were well tolerated under these conditions, giving products with high yields and enantioselectivities (**7b** and **7c**). The scope for sulfanyl substituents were also examined; switching the arylsulfanyl group to alkylsulfanyl groups were amenable to the standard conditions, generating products with high enantioselectivities as well (**7d** and **7e**).

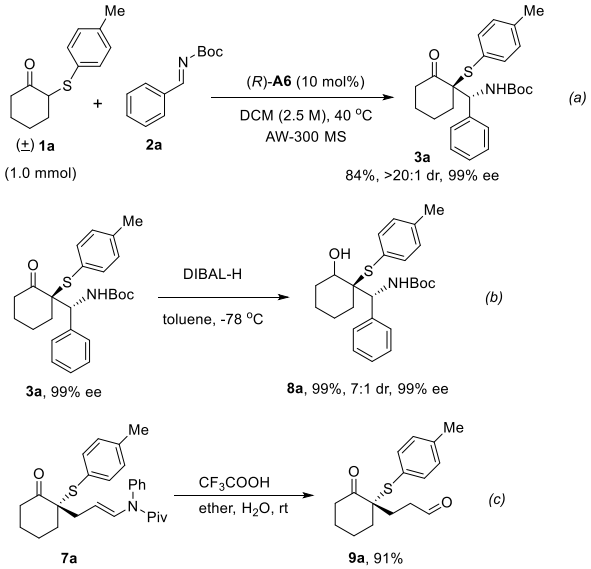
Scheme 4. Substrate scope for asymmetric addition reactions of α-sulfanyl cyclic ketones with allenamides.



[a] Reactions were performed with **1** (0.1 mmol), **6** (0.2 mmol), CPA catalysts (*R*)-**A9** (0.01 mmol) in DCM (0.1 mL) with AW-300 MS (150 mg) at 40 °C for 16 h. Yields were isolated yield. Ee values were determined by HPLC analysis on a chiral stationary phase.

To demonstrate the practicability of these methods, a large-scale reaction between **1a** (1.0 mmol) and **2a** was performed with the standard conditions, which provided the product **3a** in high yield with excellent stereoselectivity, without exception (Scheme 5, a). The derivatizations of the chiral products were also carried out to showcase the potential applications of these methods. Stereoselective reduction of the ketone motif in **3a** with DIBAL-H at -78 °C gave the alcohol **8a** in 99% yield with 7:1 dr and retained ee (Scheme 5, b). Facile hydrolysis of enamide motif in **7a** in the presence of TFA generated the 5-keto aldehyde **9a** without erosion of optical purity, which would be a valuable building block for further transformations (Scheme 5, c).

Scheme 5. Large-scale reaction and derivatizations of the chiral products.



In conclusion, we disclose the asymmetric functionalizations of α-sulfanyl cyclic ketones enabled by chiral phosphoric acid catalysis, which generated a series of chiral cyclic ketone derivatives possessing a sulfur-containing chiral tetrasubstituted stereocenter. A range of aldimines, azodicarboxylates and allenamides were well compatible in these reactions, as well as various cyclic ketones and sulfanyl groups. The facile and diverse transformations of the chiral products demonstrate the utilities of these methods in asymmetric synthesis of optically active organosulfur compounds.

Experimental Section

To a 4 ml reaction tube was added α-sulfanyl cyclic ketone **1** (0.10 mmol), aldimine **2** (0.20 mmol), (*R*)-cat **A6** (0.01 mmol) and AW-300 MS (150 mg). Subsequently, DCM (0.1 ml) was added to dissolve the reagents, and the reaction mixture was warmed to 40 °C under N_2 atmosphere. After stirring at 40 °C for 16 h, the reaction mixture was cooled to room temperature and directly purified by flash column chromatography to afford the desired product **3**.

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References

[1] a) A. Nudelman, *Phosphorus and Sulfur and the Related Elements* **1976**, *2*, 51-94; b) J. Westley, *Chemistry, Biochemistry and Toxicology, Vol. 2, Part B, Analytical, Biochemical and Toxicological Aspects of Sulfur Xenobiochemistry* **1989**.

[2] P. Chauhan, S. Mahajan, D. Enders, *Chem. Rev.* **2014**, *114*, 8807-8864.

[3] a) J. Clayden, P. MacLellan, *Beilstein. J. Org. Chem.* **2011**, *7*, 582-595; b) J.-S. Yu, H.-M. Huang, P.-G. Ding, X.-S. Hu, F. Zhou, J. Zhou, *ACS Catal.* **2016**, *6*, 5319-5344.

[4] a) E. Emori, T. Arai, H. Sasai, M. Shibasaki, *J. Am. Chem. Soc.* **1998**, *120*, 4043-4044; b) H.-H. Lu, F.-G. Zhang, X.-G. Meng, S.-W. Duan, W.-J. Xiao, *Org. Lett.* **2009**, *11*, 3946-3949; c) Y. Su, J.-B. Ling, S. Zhang, P.-F. Xu, *J. Org. Chem.* **2013**, *78*, 11053-11058; d) J. Chen, S. Meng, L. Wang, H. Tang, Y. Huang, *Chem. Sci.* **2015**, *6*, 4184-4189.

[5] a) M. Jereb, A. Togni, *Org. Lett.* **2005**, *7*, 4041-4043; b) S. Sobhani, D. Fielenbach, M. Marigo, T. C. Wabnitz, K. A. Jørgensen, *Chem. Eur. J.* **2005**, *11*, 5689-5694; c) L. Fang, A. Lin, H. Hu, C. Zhu, *Chem. Eur. J.* **2009**, *15*, 7039-7043; d) Y. Cai, J. Li, W. Chen, M. Xie, X. Liu, L. Lin, X. Feng, *Org. Lett.* **2012**, *14*, 2726-2729; e) S. Shirakawa, T. Tokuda, A. Kasai, K. Maruoka, *Org. Lett.* **2013**, *15*, 3350-3353; f) B. Qiao, X. Liu, S. Duan, L. Yan, Z. Jiang, *Org. Lett.* **2014**, *16*, 672-675; g) L. Huang, J. Li, Y. Zhao, X. Ye, Y. Liu, L. Yan, C.-H. Tan, H. Liu, Z. Jiang, *J. Org. Chem.* **2015**, *80*, 8933-8941.

[6] a) V. K. Aggarwal, E. S. Anderson, D. Elfyn Jones, K. B. Obierey, R. Giles, *Chem. Commun.* **1998**, 1985-1986; b) Y. Fujiwara, G. C. Fu, *J. Am. Chem. Soc.* **2011**, *133*, 12293-12297; c) A. Sakakura, H. Yamada, K. Ishihara, *Org. Lett.* **2012**, *14*, 2972-2975; d) W. Wu, H. Huang, X. Yuan, K. Zhu, J. Ye, *Chem. Commun.* **2012**, *48*, 9180-9182; e) F. Yu, H. Hu, X. Gu, J. Ye, *Org. Lett.* **2012**, *14*, 2038-2041; f) S. Diosdado, J. Etxabe, J. Izquierdo, A. Landa, A. Mielgo, I. Olaizola, R. López, C. Palomo, *Angew. Chem. Int. Ed.* **2013**, *52*, 11846-11851; *Angew. Chem.* **2013**, *125*, 12062 –12067 g) K. Zhu, H. Huang, W. Wu, Y. Wei, J. Ye, *Chem. Commun.* **2013**, *49*, 2157-2159; h) E. Badiola, B. Fiser, E. Gómez-Bengoa, A. Mielgo, I. Olaizola, I. Urruzuno, J. M. García, J. M. Odriozola, J. Razkin, M. Oiarbide, C. Palomo, *J. Am. Chem. Soc.* **2014**, *136*, 17869-17881; i) W. Chen, J. F. Hartwig, *J. Am. Chem. Soc.* **2014**, *136*, 377-382; j) H. Zhang, B. Wang, L. Cui, Y. Li, J. Qu, Y. Song, *Org. Bio. Chem.* **2014**, *12*, 9097-9100; k) T. Wang, Z. Yu, D. L. Hoon, K.-W. Huang, Y. Lan, Y. Lu, *Chem. Sci.* **2015**, *6*, 4912-4922; l) L. Yu, X. Wu, M. J. Kim, V. Vaithiyanathan, Y. Liu, Y. Tan, W. Qin, C. E. Song, H. Yan, *Adv. Synth. Catal.* **2017**, *359*, 1879-1891.

[7] S. Takechi , S. Yasuda, N. Kumagai, M. Shibasaki, *Angew. Chem. Int. Ed.* **2012**, *51*, 4218-4222; *Angew. Chem.* **2012**, *124*, 4294-4298.

[8] S. Takechi, N. Kumagai, M. Shibasaki, *Org. Lett.* **2013**, *15*, 2632-2635.

[9] F. Zhou, X.-P. Zeng, C. Wang, X.-L. Zhao, J. Zhou, *Chem. Commun.* **2013**, *49*, 2022-2024.

[10] a) X. Dou, B. Zhou, W. Yao, F. Zhong, C. Jiang, Y. Lu, *Org. Lett.* **2013**, *15*, 4920-4923; b) W.-M. Gao, J.-S. Yu, Y.-L. Zhao, Y.-L. Liu, F. Zhou, H.-H. Wu, J. Zhou, *Chem. Commun.* **2014**, *50*, 15179-15182.

[11] S. Wang, Y. Jiang, S. Wu, G. Dong, Z. Miao, W. Zhang, C. Sheng, *Org. Lett.* **2016**, *18*, 1028-1031.

[12] K. Liao, F. Zhou, J.-S. Yu, W.-M. Gao, J. Zhou, *Chem. Commun.* **2015**, *51*, 16255-16258.

[13] A. Luridiana, A. Frongia, D. J. Aitken, R. Guillot, G. Sarais, F. Secci, *Org. Bio. Chem.* **2016**, *14*, 3394-3403.

[14] a) T. Akiyama, J. Itoh, K. Yokota, K. Fuchibe, *Angew. Chem. Int. Ed.* **2004**, *43*, 1566-1568; *Angew. Chem.* **2004**, *116*, 1592-1594; b) D. Uraguchi, M. Terada, *J. Am. Chem. Soc.* **2004**, *126*, 5356-5357; c) T. Akiyama, *Chem. Rev.* **2007**, *107*, 5744-5758; d) M. Terada, *Synthesis* **2010**, *2010*, 1929-1982; e) D. Parmar, E. Sugiono, S. Raja, M. Rueping, *Chem. Rev.* **2014**, *114*, 9047-9153; f) T. Akiyama, K. Mori, *Chem. Rev.* **2015**, *115*, 9277-9306; g) A. Rahman, X. Lin, *Org. Bio. Chem.* **2018**, *16*, 4753-4777; h) X. Li, Q. Song, *Chin. Chem. Lett.* **2018**, 1181-1192.

[15] a) G. A. Shevchenko, B. Oppelaar, B. List, *Angew. Chem. Int. Ed.* **2018**, *57*, 10756-10759; *Angew. Chem.* **2018**, *130*, 10916-10919; b) G. A. Shevchenko, G. Pupo, B. List, *Synlett* **2019**, *30*, 49-53; c) I. Felker, G. Pupo, P. Kraft, B. List, *Angew. Chem. Int. Ed.* **2015**, *54*, 1960-1964; *Angew. Chem.* **2015**, *127*, 1983-1987; d) G. Pupo, R. Properzi, B. List, *Angew. Chem. Int. Ed.* **2016**, *55*, 6099-6102; *Angew. Chem.* **2016**, *128*, 6204-6207; e) G. A. Shevchenko, G. Pupo, B. List, *Synlett* **2015**, *26*, 1413-1416.

[16] a) X. Yang, F. D. Toste, *J. Am. Chem. Soc.* **2015**, *137*, 3205-3208; b) X. Yang, F. D. Toste, *Chem. Sci.* **2016**, *7*, 2653-2656.

[17] X. Ye, Y. Pan, X. Yang, *Chem. Commun.* **2020**, *56*, 98-101.

[18] a) W. Liu, S. Rajkumar, W. Wu, Z. Huang, X. Yang, *Org. Lett.* **2019**, *21*, 3563-3567; b) S. Rajkumar, S. He, X. Yang, *Angew. Chem. Int. Ed.* **2019**, *58*, 10315-10319; *Angew. Chem.* **2019**, *131*, 10421-10425; c) S. Rajkumar, M. Tang, X. Yang, *Angew. Chem. Int. Ed.* **2020**, *59*, 2333-2337; *Angew. Chem.* **2020**, *132*, 2353-2357.

[19] a) Q.-X. Guo, H. Liu, C. Guo, S.-W. Luo, Y. Gu, L.-Z. Gong, *J. Am. Chem. Soc.* **2007**, *129*, 3790-3791; b) Y.-Y. Chen, Y.-J. Jiang, Y.-S. Fan, D. Sha, Q. Wang,

G. Zhang, L. Zheng, S. Zhang, *Tetrahedron: Asymmetry* **2012**, *23*, 904-909; c) J.-S. Li, Y.-J. Liu, S. Li, J.-A. Ma, *Chem. Commun.* **2018**, *54*, 9151-9154; d) S. Tong, Q. Wang, M.-X. Wang, J. Zhu, *Tetrahedron* **2018**, *74*, 5143-5149; e) M. Shang, M. Cao, Q. Wang, M. Wasa, *Angew. Chem. Int. Ed.* **2017**, *56*, 13338-13341.

[20] F. Drouet, C. Lalli, H. Liu, G. Masson, J. Zhu, *Org. Lett.* **2011**, *13*, 94-97; b) M. Shang, X. Wang, S. M. Koo, J. Youn, J. Z. Chan, W. Yao, B. T. Hastings, M. Wasa, *J. Am. Chem. Soc.* **2017**, *139*, 95-98.

[21] a) C. Romano, M. Jia, M. Monari, E. Manoni, M. Bandini, *Angew. Chem. Int. Ed.* **2014**, *53*, 13854-13857; *Angew. Chem.* **2014**, *126*, 14074-14077; b) B. Yang, X. Zhai, S. Feng, D. Hu, Y. Deng, Z. Shao, *Org. Lett.* **2019**, *21*, 330-334; c) S. Biswas, H. Kim, K. Le Anh Cao, S. Shin, *Adv. Synth. Catal.* **2020**, DOI: *10.1002/adsc.202000083*.

[22] For details see Supporting Information.

[23] The absolute structures of products **5** were assigned via analogy to products in ref 15e and 16a.

[24] a) H. J. Khoury, G. Garcia-Manero, G. Borthakur, T. Kadia, M. C. Foudray, M. Arellano, A. Langston, B. Bethelmie-Bryan, S. Rush, K. Litwiler, S. Karan, H. Simmons, A. I. Marcus, M. Ptaszynski, H. Kantarjian, *Cancer* **2012**, *118*, 3556-3564; b) A. Mertens, H. Zilch, B. Koenig, W. Schaefer, T. Poll, W. Kampe, H. Seidel, U. Leser, H. Leinert, *J. Med. Chem.* **1993**, *36*, 2526-2535.

[25] The absolute structures of products **7** were assigned via analogy to products in ref 16b.

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Enantioselective Construction of Sulfur-Containing Tetrasubstituted Stereocenters via Asymmetric Functionalizations of α-Sulfanyl Cyclic Ketones

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