Advanced Synthesis & Catalysis

## Accepted Article

**Title:** Asymmetric Construction of Bispiro-Cyclopropane-Pyrazolones via a [2 + 1] Cyclization Reaction by Dipeptide-Based Phosphonium Salt Catalysis

**Authors:** Dongming Lu, Xin Liu, Jia-Hong Wu, Song Zhang, Jian-Ping Tan, xiaojun yu, and Tianli Wang



**To be cited as:** *Adv. Synth. Catal.* 10.1002/adsc.202000073

**Link to VoR:** http://dx.doi.org/10.1002/adsc.202000073

VERY IMPORTANT PUBLICATION **COMMUNICATION**

**DOI: 10.1002/adsc.201**((will be filled in by the editorial staff))

# Asymmetric Construction of Bispiro-Cyclopropane-Pyrazolones via a [2 + 1] Cyclization Reaction by Dipeptide-Based Phosphonium Salt Catalysis

Dongming Lu,[a] Xin Liu,[a] Jia-Hong Wu,[a] Song Zhang,[a] Jian-Ping Tan,[a] Xiaojun Yu,[a,b] and Tianli Wang[a,*]

[a] Key Laboratory of Green Chemistry & Technology of Ministry of Education, College of Chemistry, Sichuan University, Chengdu 610064, People's Republic of China
E-mail: wangtl@scu.edu.cn

[b] Department of Chemistry, School of Basic Medical Sciences, Southwest Medical University, Luzhou 646000, People's Republic of China

Received: ((will be filled in by the editorial staff))

Supporting information for this article is available on the WWW under http://dx.doi.org/10.1002/ ((Please delete if not appropriate))

**Abstract.** We reported herein an efficient alternative for asymmetric synthesis of structurally complicated chiral bispiro-cyclopropane-pyrazolones via dipeptide-based phosphonium salt catalyzed [2 + 1] cyclization of 2,3-dioxopyrrolidines and halogenated pyrazolones. With this catalytic asymmetric protocol, a broad range of bispiro heterocyclic compounds bearing a pyrazolone unit were prepared in high yields with excellent diastereo- and enatioselectivities. Of note, this transformation proceeds in a really short time under mild reaction conditions.

**Keywords:** dipeptide-based phosphonium salts; [2+1] cyclization; bispiro-cyclopropane-pyrazolones; asymmetric synthesis; hydrogen-bonding interaction

Asymmetric organocatalysis has been a frontier in the realm of asymmetric catalysis, which shows powerful capability in building a range of chiral molecules. Among the manifold organogatalysts, chiral phase-transfer catalyst (PTC) is one type of fundamental organocatalysts.[1] Over the past decades, quaternary ammonium salts, being regarded as privileged components in PTC, have been widely employed in asymmetric synthesis. By contrast, PTCs involving phosphonium salts just began to flourish until very recently.[2] Outstanding contributions in this field have been made by the research groups of Ooi[3] and Marouka.[4] Later, Ma and co-workers disclosed a binol-derived *P*-spiro-phosphonium salt and realized its application in asymmetric amination of benzofuranones[5]. Recently, Zhao[6] and Lu[7] pioneered the development of bifunctional phosphonium catalysts derived from natural amino acids, and demonstrated their effectiveness in many organic transformations. Quite recently, our group developed an novel pattern of dipeptide-based phosphonium salt catalysts and fulfilled its utilization in the asymmetric synthesis of challenging *tetra*-

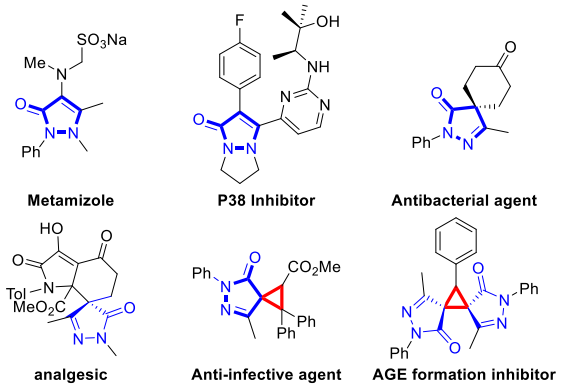
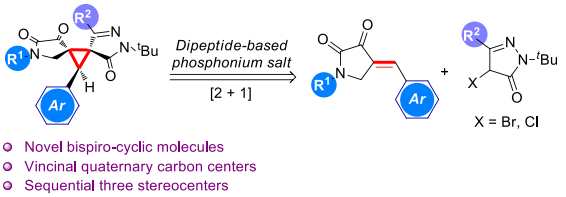



**Figure 1.** Selected bioactive molecules containing (spiro-) pyrazolone core.

Substituted aziridines[8] and other biologically momentous hetercyclic molecules.[9,10] Of note, such dipeptide-based phosphonium catalyst possesses remarkably high tunability, and further, this catalyst with an ion-pairing moiety and peptide backbone that captures essential features of enzymatic active sites with hydrogen-donating characteristics becomes a multifunctional phase-transfer catalyst, which can be advantageous for asymmetric induction.[11] However, its applications in asymmetric synthesis are still in its infancy.

On the other hand, pyrazolone unit is widespread in both natural products and pharmaceutical targets (Figure 1).[12] Particularly, structurally spiro

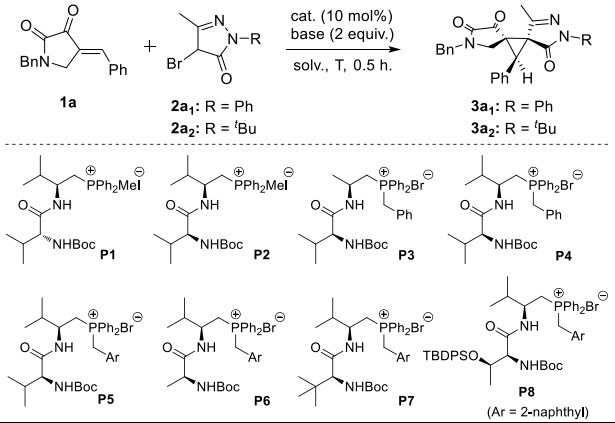



**Scheme 1.** Asymmetric synthesis of bispiro-cyclopropane-pyrazolones via [2 + 1] reaction by dipeptide-based phosphonium salt catalysis.

10.1002/adsc.202000073

pyrazolone frameworks are an interesting and important subclass of bioactive agents, and these ring systems are always displayed in numerous drug leads and pharmaceuticals.[13] In this context, catalytic asymmetric construction of chiral spiro-pyrazolones has stimulated considerable interest among synthetic chemists, and a number of methods have been developed for preparing such scalffords.[14] It should be noted that the catalytic asymmetric construction of structurally rigid bispiro-cyclopropane-pyrazolone molecules is still rare. To the best of our knowledge, only one example related to this issue has been reported so far. In 2015, Du and co-workers disclosed a cascade reaction of arylidenepyrazolones and 3-chlorooxindoles to provide such compounds in moderate stereoselectivities (2.4:1–6.7:1 d.r. and 40–74% ee).[15] From our review, the main challenge, lying on controlling the enantio- and diastereo-

**Table 1.** Optimization of reaction conditions. [a]




| entry | cat. | solvent | base | **3**, yield (%)[b] | ee (%) | d.r. |
|---|---|---|---|---|---|---|
| 1 | **P1** | toluene | $K_2CO_3$ | **3a₁**, 75 | 3 | 1:1 |
| 2 | **P2** | toluene | $K_2CO_3$ | **3a₁**, 83 | 6 | 1:1 |
| 3 | **P3** | toluene | $K_2CO_3$ | **3a₁**, 82 | 16 | 1:1 |
| 4 | **P4** | toluene | $K_2CO_3$ | **3a₁**, 88 | 34 | 1.3:1 |
| 5 | **P5** | toluene | $K_2CO_3$ | **3a₁**, 89 | 38 | 1.3:1 |
| 6 | **P6** | toluene | $K_2CO_3$ | **3a₁**, 86 | 34 | 1.3:1 |
| 7 | **P7** | toluene | $K_2CO_3$ | **3a₁**, 78 | 39 | 1.3:1 |
| 8 | **P8** | toluene | $K_2CO_3$ | **3a₁**, 93 | 46 | 1.3:1 |
| 9 | **P8** | toluene | $Cs_2CO_3$ | **3a₁**, 91 | 59 | 1.3:1 |
| 10 | **P8** | toluene | $K_3PO_4$ | **3a₁**, 87 | 43 | 1.3:1 |
| 11 | **P8** | toluene | PhONa | **3a₁**, 94 | 13 | 1.3:1 |
| 12 | **P8** | toluene | $(NH_4)_2CO_3$ | **3a₁**, 96 | 73 | 1:1.6 |
| 13[c] | **P8** | toluene | $(NH_4)_2CO_3$ | **3a₁**, 95 | 94 | 4.5:1 |
| 14[c] | **P8** | toluene | $(NH_4)_2CO_3$ | **3a₂**, 95 | 95 | >20:1 |

[a] All reactions were performed with **1a** (0.1 mmol), **2a₁**/**2a₂** (0.12 mmol), and catalyst (10 mol%) in solvent for 0.5 h. The d.r. values were determined by $^1$H NMR analysis and ee values were determined by HPLC analysis.

[b] Isolated yield.

[c] The reaction was performed at -20 °C.

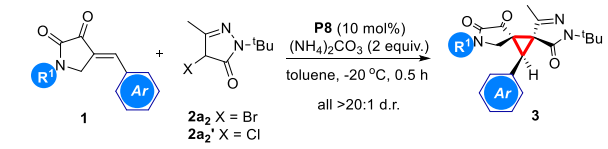
selectivities of this transformations, may due to the strongly steric hindrance of final products. In continuation of our major interest in bifunctional organocatalysis involving phosphonium salt catalysts, we questioned whether our dipiptide-based phosphonium salt catalysis can be an efficient alternative for achieving high stereoinduction, and thus prepare structurally rigid and optically pure bispiro-cyclopropane-pyrazolone molecules (Scheme 1). Herein, we describe a highly stereoselective [2 + 1] cyclization reaction between 2,3-dioxopyrrolidines and halogenated pyrazolones under dipeptide-based phosphonium salt catalytic conditions, providing an efficient and complementary way to bispiro-cyclopropane-pyrazolone derivatives.

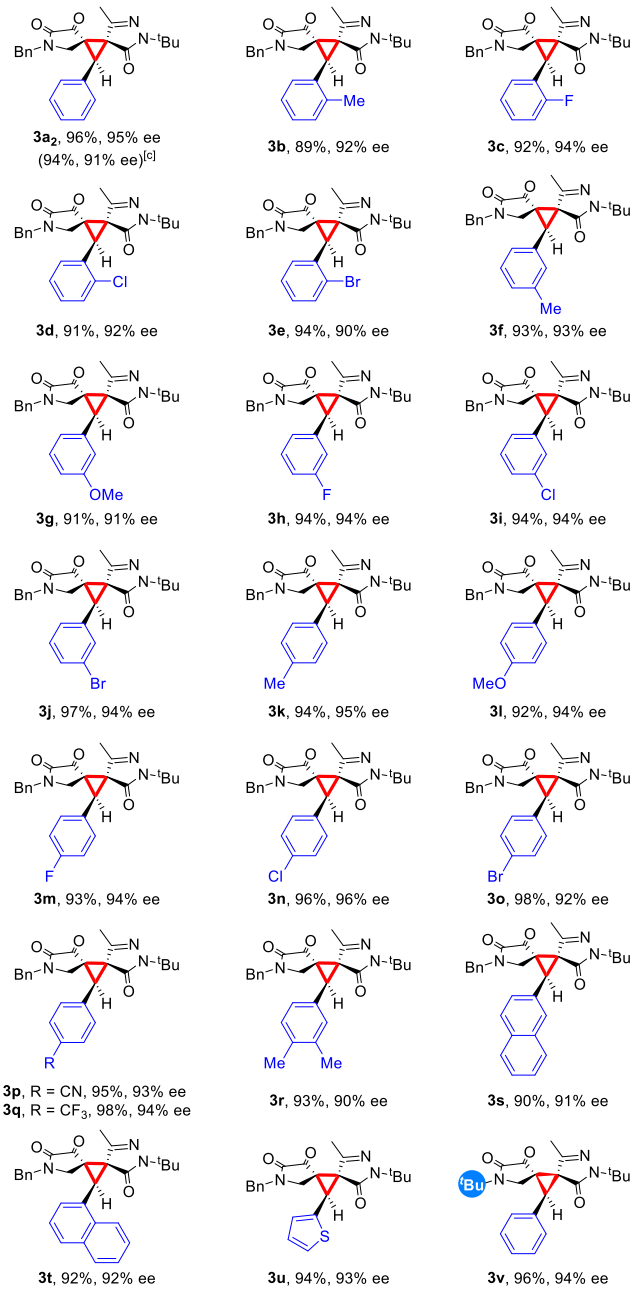
Initially, the cyclization between 2,3-dioxopyrrolidine **1a** and 4-bromo-pyrazolone **2a₁** was chosen as a model reaction for optimizing reaction conditions. The reaction was performed with different bifunctional phosphonium salt catalysts in the presence of $K_2CO_3$ in toluene at room temperature. Pleasingly, the model reaction proceeded swiftly while dipeptide-based phosphonium salts were employed as catalysts (entries 1–8).[16a] Both L- and D-valine-based dipeptide-phosphonium iodides could promote this reaction, affording the cycloadduct in good yield but with poor enantioselectivities (entries 1–2). By contrast, the dipeptide-phosphonium bromides were found to be slighly more favorable in asymmetric induction (entries 3–4). Accordingly, several dipeptide-based phosphonium bromides were prepared and evaluated (entries 5–8), and the *L*-Val-*L*-OTBDPS-Thr-derived phosphonium salt **P8** was found to be the best catalyst, furnishing the desired product in moderate enantioselectivity (entry 8). With a promising ee value in hand, a series of bases were tested (entries 8–10),[16b] and the relatively weak base of $(NH_4)_2CO_3$ proved to be a suitable choice with affording the adduct in excellent yield and good enantioselectivity (entry 12). The solvent screening was explored, and none of the solvents were shown to be superior to toluene.[16c] Subsequently, it was found that decreasing reaction temperature led to a better diastereoselectivity and enantioselectivity without sacrificing the isolated yield (entry 13). Moreover, the desired product **3a₂** could be isolated in 95% yield with >20:1 d.r. and 95% ee when pyrazolone **2a₂** was used instead of **2a₁** (entry 14).

With the optimized conditions identified, the generality protocol for different 2,3-dioxopyrrolidines was investigated. Generally, a diverse array of 2,3-dioxopyrrolidine derivatives bearing different aromatic substituents were found to be well tolerated under the standard reaction conditions (**3a**–**r**). 2,3-dioxopyrrolidines bearing either electron-neutral, -withdrawing or -donating groups in the *ortho*-, *meta*-,

10.1002/adsc.202000073

**Table 2.** Scope of 2,3-dioxopyrrolidines **1**.[a,b]




[a] All reactions were performed with **1** (0.1 mmol), **2a$_2$** /**2a$_2$'** (0.12 mmol), catalyst **P8** (10 mol%) and $(NH_4)_2CO_3$ (0.2 mmol) in 0.5 mL toluene at -20 °C for 0.5 h. The d.r. values were determined by $^1$H NMR analysis and ee values were determined by HPLC analysis.

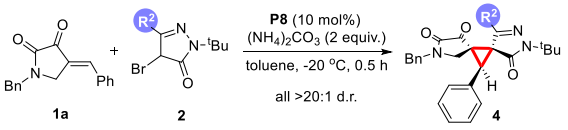
[b] Isolated yield.

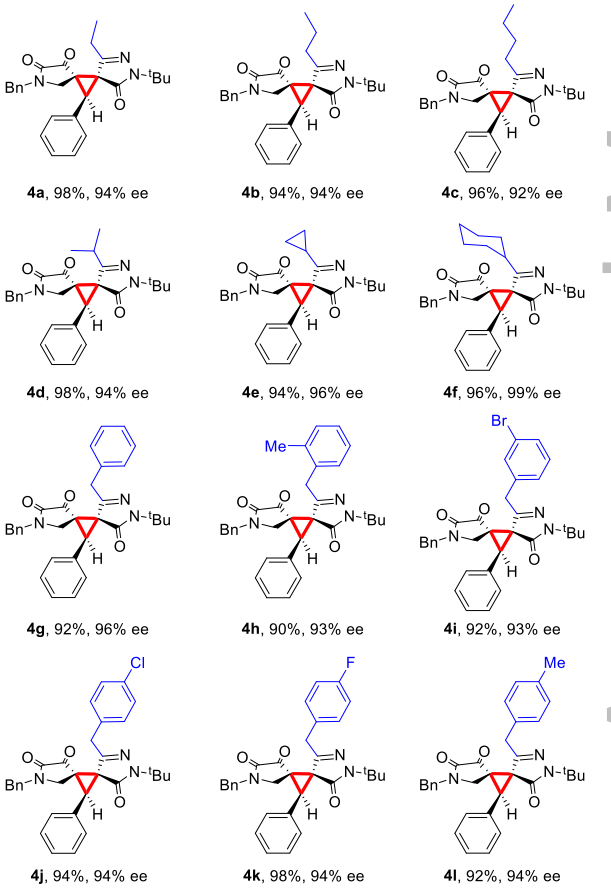
[c] **2'** was used.

or *para*-position of the phenyl ring could deliver the corresponding products in high yields (89–98%) with excellent stereoselectivities (all >20:1 d.r. and 90–96% ee). Of note, chlorogenated pyrazolones was also well tolerated in this catalytic process and provided the corresponding product in good yield and stereoselectivities. Surprisingly, both naphthyl and thienyl substituted dioxopyrrolidines were also compatible with the reaction conditions for giving the desired product in quantitive yields with excellent d.r. and ee values (**3s**–**u**). Moreover, the *N*-*tert*-butyl substituted dioxopyrrolidine was also tolerated, affording the desired product **3v** in 96% yield with >20:1 d.r. and 94% ee.

Encouraged by these results, we turned our attention to the scope of halogenated pyrazolones. The results were outlined in Table 3. Varies pyrazolones bearing linear aliphatic chains were found to be suitable, irrelevant with the length of these chains, producing the desired cycloadducts (**4a**–**c**) in high yields with excellent stereoselectivities.

**Table 3**. Scope of halogenated pyrazolones **2**. [a,b]

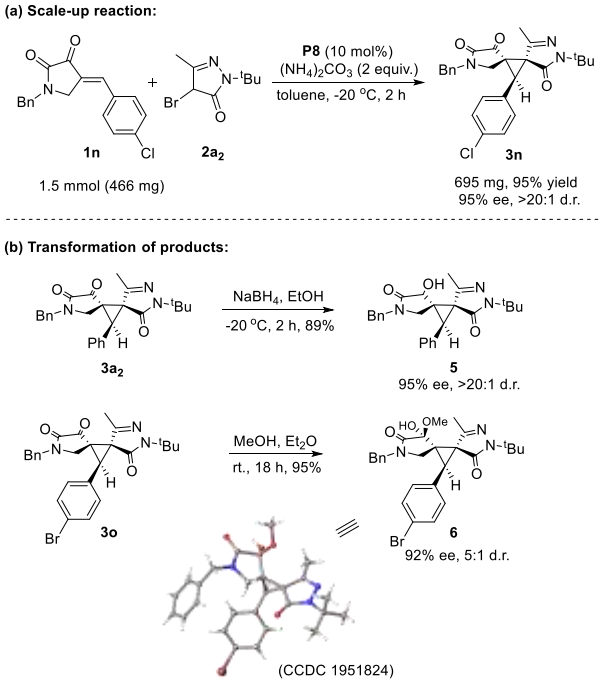



[a] All reactions were performed with **1a** (0.1 mmol), **2** (0.12 mmol), catalyst **P8** (10 mol%) and $(NH_4)_2CO_3$ (0.2 mmol) in 0.5 mL toluene at -20 °C for 0.5 h. The d.r. values were determined by $^1$H NMR analysis and ee values were determined by HPLC analysis.

[b] Isolated yield.

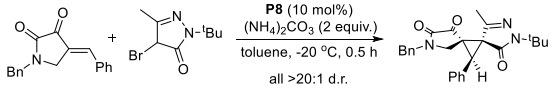
Both acyclic and cyclic branched aliphatic pyrazolones were also suitable reactants and resulted in corresponding adducts with satisfying yields and stereoselectivities (**4d**–**f**). The pyrazolone substrates bearing different benzyl substituents, regardless of their steric hindrance or electron properties, could be readily transformed into the expected adducts in parallel yields with no loss of diastereoselectivities and enantioselectivities (**4g**–**l**). To illustrate the robustness and utility of this catalytic protocol, the scaled-up reaction was conducted and corresponding adduct **3n** was obtained in satisfying yield with >20:1 d.r. and 95% ee (Scheme 2a). Besides, the optically active products were readily converted into other bioactive compounds (**5** and **6**) in high yields (Scheme 2b). The relative and absolute configuration of the above [2 + 1] annulation products were assigned on the basis of X-ray crystallographic analysis of derivative compound **6** (CCDC 1951824).[17]




**Scheme 2.** Scale-up synthesis and transformation of chiral product.

To gain some insights into the dual activation of this dipeptide-based catalytic system, the control experiments were performed (Table 4). The methylated catalysts **P8-1** and **P8-2** were further prepared and applied to the model [2 + 1] cyclization, respectively. It was found that their enantioselectivities decreased sharply (entries 1–3). Notably, when methanol was used as solvent, racemic product was obtained (entry 4). These preliminary results clearly verified the significance of the H-bonding as well as ion-pair interactions in such catalytic system. Based on these experimental

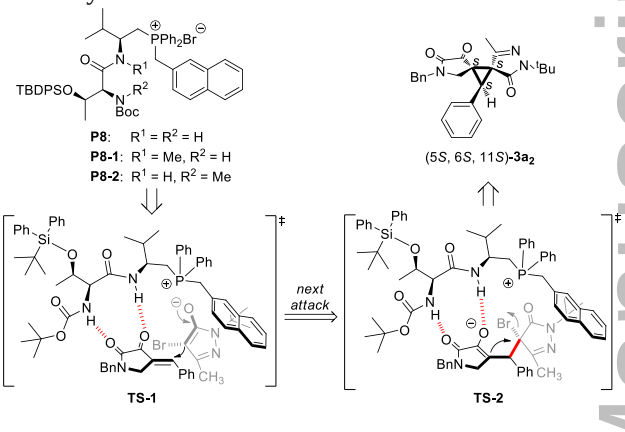
**Table 4.** Preliminary investigation of the reaction mechanism and proposed transition state models.[a,b]




| entry | solvent | cat. | t (h) | yield (%)[b] | ee (%) |
|---|---|---|---|---|---|
| 1 | toluene | **P8** | 0.5 | 96 | 95 |
| 2 | toluene | **P8-1** | 0.5 | 94 | 18 |
| 3 | toluene | **P8-2** | 0.5 | 93 | 23 |
| 4 | MeOH | **P8** | 1 | 23 | 0 |

[a] All reactions were performed with **1a** (0.1 mmol), **2a2** (0.12 mmol), catalyst (10 mol%) and $(NH_4)_2CO_3$ (0.2 mmol) in 0.5 mL solvent at -20 °C for 0.5 h. The d.r. values were determined by $^1H$ NMR analysis and ee values were determined by HPLC analysis.

[b] Isolated yield.




observations and our previous studies, the plausible transition state models were presented (**TS-1** and **TS-2**) in Table 4.

In conclusion, we have disclosed a highly efficient and stereoselective [2 + 1] annulation reaction between 2,3-dioxopyrrolidines and halogenated pyrazolones under dipeptide-based phosphonium salt catalytic conditions. This method represented an efficient and complementary approach for the construction of optically active bispiro-cyclopropane-pyrazolone derivatives in high yields with excellent diastereo- and enantioselectivities. Of note, these results indicated that such type of highly tunable dipeptided phosphonium salt catalysis was a practicable approach for constructing structurally complex chiral molecules, and further investigation is ongoing in our laboratory.

# Experimental Section General

## Procedure for [2+1] Annulation

To a flame-dried round bottle flask with a magnetic stirring bar were added the 2,3-dioxopyrrolidines **1** (0.1 mmol), halogenated pyrazolones **2** (0.12 mmol), phosphonium salt **P8** (0.005 mmol) and $(NH_4)_2CO_3$ (0.4 mmol), followed by the addition of toluene (0.5

mL). The reaction mixture was stirred at -20 °C for 0.5 h. The solvent was then removed under reduced pressure, and the residue was purified by column chromatography on silica gel (petroleum ether/ethyl acetate = 10:1 to 3:1) to afford **3**/**4** as a white solid.

## Acknowledgements

We acknowledge financial support from the National Key R&D Program of China (2018YFA0903500), the National Natural Science Foundation of China (21971165, 21921002), the "1000-Youth Talents Program" (YJ201702) and the Fundamental Research Funds for the Central Universities. We also acknowledge the comprehensive training platform of the Specialized Laboratory in the College of Chemistry at Sichuan University and the Analytical & Testing Center of Sichuan University for compound testing.

## References

[1] For selected reviews, see: a) E. V. Dehmlow, S. S. Dehmlow, *Phase Transfer Catalysis*, 3rd. ed., Wiley-VCH, Weinheim, **1993**; b) A. Nelson, *Angew. Chem. Int. Ed.* **1999**, *38*, 1583–1585; *Angew. Chem.* **1999**, *111*, 1685–1687; c) M. J. O`Donnell, *Acc. Chem. Res*. **2004**, *37*, 506–517; d) B. Lygo, B. I. Andrews, *Acc. Chem. Res*. **2004**, *37*, 518–525; e) T. Ooi, K. Maruoka, *Angew. Chem. Int. Ed.* **2007**, *46*, 4222–4266; *Angew. Chem.* **2007**, *119*, 4300–4345; f) T. Hashimoto, K. Maruoka, *Chem. Rev*. **2007**, *107*, 5656–5682; g) S.-s. Jew, H.-g. Park, *Chem. Commun.* **2009**, *46*, 7090–7103; h) D. Qian, J. Sun, *Chem. Eur. J.* **2019**, *25*, 3740–3751.

[2] For recent reviews, see: a) T. Werner, *Adv. Synth. Catal*. **2009**, *351*, 1469–1481; b) S. Liu, Y. Kumatabara, S. Shirakawa, *Green Chem.* **2016**, *18*, 331–341; c) A. Golandaj, A. Ahmad, D. Ramjugernath, *Adv. Synth. Catal.* **2017**, *359*, 3676–3706; d) M. Selva, M. Noe, A. Perosa, M. Gottardo, *Org. Biomol. Chem*. **2012**, *10*, 6569–6578. For previously reported work, see: a) T. Shioiri, A. Ando, M. Masui, T. Miura, T. Tatematsu, A. Bohsako, M. Higashiyama, C. Asakura in Phase-Transfer Catalysis: Use of Chiral Quaternary Salts in Asymmetric Synthesis (Ed.: M. E. Halpern), ACS Symposium Series, American Chemical Society, Washington, DC, **1997**, and references therein; b) K. Manabe, *Tetrahedron Lett.* **1998**, *39*, 5807–5810; c) K. Manabe, *Tetrahedron* **1998**, *54*, 14465–14476.

[3] For the pioneering work of Ooi and co-workers, see: a) D. Uraguchi, S. Sakaki, T. Ooi, *J. Am. Chem. Soc*. **2007**, *129*, 12392–12393; b) D. Uraguchi, Y. Ueki, T. Ooi, *J. Am. Chem. Soc.* **2008**, *130*, 14088–14089; c) D. Uraguchi, D. Nakashima, T. Ooi, *J. Am. Chem. Soc*. **2009**, *131*, 7242–7243; d) D. Uraguchi, T. Ito, T. Ooi, *J. Am. Chem. Soc*. **2009**, *131*, 3836–3837; e) D. Uraguchi, Y. Asai, T. Ooi, *Angew. Chem. Int. Ed.* **2009**, *48*, 733–737; *Angew. Chem*. **2009**, *121*, 747–751; f) D. Uraguchi, N. Kinoshita, T. Kizu, T. Ooi, *J. Am. Chem. Soc*. **2015**, *137*, 13768–13771.

[4] For the pioneering work of Maruoka and co-workers, see: a) R. He, X. Wang, T. Hashimoto, K. Maruoka, *Angew. Chem. Int. Ed.* **2008**, *47*, 9466–9468; *Angew.Chem.* **2008**, *120*, 9608–9610; b) R. He, C. Ding, K. Maruoka, *Angew. Chem. Int. Ed.* **2009**, *48*, 4559–4561; *Angew. Chem.* **2009**, *121*, 4629–4631; c) R. He, K. Maruoka, *Synthesis* **2009**, *13*, 2289–2292; d) C. J. Abraham, D. H. Paull, C. Dogo-Isonagie, T. Lectka, *Synlett* **2009**, 1651–1654; e) S. Shirakawa, A. Kasai, T. Tokuda, K. Maruoka, *Chem. Sci*. **2013**, *4*, 2248–2252; f) S. Shirakawa, K. Koga, T. Tokuda, K. Yamamoto, K. Maruoka, *Angew. Chem. Int. Ed*. **2014**, *53*, 6220–6223; *Angew. Chem*. **2014**, *126*, 6334–6337.

[5] C.-L. Zhu, F.-G. Zhang, W. Meng, J. Nie, D. Cahard, J.-A. Ma, *Angew. Chem. Int. Ed.* **2011**, *50*, 5869–5872; *Angew. Chem.* **2011**, *123*, 5991–5994.

[6] For recent review on phosphonium salt catalyzed asymmetric reactions , see: a) H. Wang, C. Zheng, G. Zhao, *Chin. J. Chem.* **2019**, *37*, 1111–1119; For selected examples by Zhao and co-workers, see: b) D. Cao, Z. Chai, J. Zhang, Z. Ye, H. Xiao, H. Wang, J. Chen, X. Wu, G. Zhao, *Chem. Commun*. **2013**, *49*, 5972–5974; c) X. Wu, Q. Liu, Y. Liu, Q. Wang, Y. Zhang, J. Chen, W. Cao, G. Zhao, *Adv. Synth. Catal*. **2013**, *355*, 2701–2708; d) D. Cao, J. Zhang, H. Wang, G. Zhao, *Chem. Eur. J*. **2015**, *21*, 9998–10002; e) L. Ge, X. Lu, C. Cheng, J. Chen, W. Cao, X. Wu, G. Zhao, *J. Org. Chem*. **2016**, *81*, 9315–9325; f) D. Cao, G. Fang, J. Zhang, H. Wang, C. Zheng, G. Zhao, *J. Org. Chem.* **2016**, *81*, 9973–9982; g) H. Wang, K. Wang, Y. Ren, N. Li, B. Tang, G. Zhao, *Adv. Synth. Catal*. **2017**, *359*, 1819–1826; h) X. Xia, Q. Zhu, J. Wang, J. Chen, W. Cao, B. Zhu, X. Wu, *J. Org. Chem.* **2018**, *83*, 14617–14625; i) G. Fang, C. Zheng, D. Cao, L. Pan, H. Hong, H. Wang, G. Zhao, *Tetrahedron* **2019**, *75*, 2706–2716; j) J. Zhang, G. Zhao, *Tetrahedron* **2019**, *75*, 1697–1705; k) L. Pan, C.-W. Zheng, G.-S. Fang, H.-R. Hong, J. Liu, L.-H. Yu, G. Zhao, *Chem. Eur. J.* **2019**, *25*, 6306–6310.

[7] For selected reviews on amino acid based bifunctional phosphine catalysis, see: a) T. Wang, X. Han, F. Zhong, W. Yao, Y. Lu, *Acc. Chem. Res.* **2016**, *49*, 1369–1378; b) H. Ni, W.-L. Chan, Y. Lu, *Chem. Rev.* **2018**, *118*, 9344–9411; For selected examples, see: c) T. Wang, Z. Yu, D. L. Hoon, C. Y. Phee, Y. Lan, Y. Lu, J. *Am. Chem. Soc*. **2016**, *138*, 265–271; d) T. Wang, Z. Yu, D. L. Hoon, K.-W. Huang, Y. Lan, Y. Lu, *Chem. Sci*. **2015**, *6*, 4912–4922; e) T. Wang, W. Yao, F. Zhong, G. H. Pang, Y. Lu, *Angew. Chem. Int. Ed*. **2014**, *53*, 2964–2968; f) T. Wang, D. L. Hoon, Y. Lu, *Chem. Commun*. **2015**, *51*, 10186–10189; g) S. Wen, X. Li, Y. Lu, *Asian J. Org. Chem*. **2016**, *5*,1457–1460.

[8] J. Pan, J.-H. Wu, H. Zhang, X. Ren, J.-P. Tan, L. Zhu, H.-S. Zhang, C. Jiang, T. Wang, *Angew. Chem. Int. Ed.* **2019**, *58*, 7425–7432.

[9] a) J.-P. Tan, P. Yu, J.-H. Wu, Y. Chen, J. Pan, C. Jiang, X. Ren, H.-S. Zhang, T. Wang, *Org. Lett*. **2019**, *21*, 7298–7303; b) S. Zhang, X. Yu, J. Pan, C. Jiang, H.S.

Zhang, T. Wang, *Org. Chem. Front*. **2019**, *6*, 3799; c) L. Zhu, X. Ren, Z. Liao, J. Pan, C. Jiang, T. Wang, *Org. Lett*. **2019**, *21*, 8667; d) G. Huang, X. Ren, C. Jiang, J.-H. Wu, G. Gao, T. Wang, *Org. Chem. Front.* **2019**, *6*, 2872–2876; e) C. Jiang, Y. Chen, G. Huang, C. Ni, X. Liu, H. Lu, *Asian J. Org. Chem.* **2019**, *8*, 257–260; f) X. Liu, D. Lu, J.-H. Wu, J.-P, Tan, C. Jiang, G. Gao, T. Wang, *Adv. Synth. Catal.* **2020**, DOI:10.1002/adsc.202000001.

[10] a) J.-P. Tan, H. Zhang, Z. Jiang, Y. Chen, X. Ren, C. Jiang, T. Wang, *Adv. Synth. Catal.* **2020**, *362*, 1–7; b) J.-H. Wu, J. Pan, J. Du, X. Wang, X. Wang, C. Jiang, T. Wang, *Org. Lett*. **2020**, *22*, 2, 395−399.

[11] For selected reviews, see: a) M. S. Taylor, E. N. Jacobsen, *Angew. Chem. Int. Ed.* **2006**, *45*, 1520–1543; *Angew. Chem.* **2006**, *118*, 1550–1573; b) Z. Zhang, P. R. Schreiner, *Chem. Soc. Rev.* **2009**, *38*, 1187–1198; c) J.-F. Brière, S. Oudeyer, V. Dalla, V. Levacher, *Chem. Soc. Rev.* **2012**, *41*, 1696–1707; d) O.-V. Serdyuk, C.-M. Heckel S. B. Tsogoeva, *Org. Biomol. Chem.* **2013**, *11*, 7051–7071; e) T. -J. Auvil, A.-G. Schafer, A.-E. Mattson, *Eur. J. Org. Chem.* **2014**, 2633–2646; f) Y. Nishikawa, *Tetrahedron Lett.* **2018**, *59*, 216–223.

[12] For selected review, see: a) H. Yoshida, H. Yanai, Y. Namiki, K. FukatsuSasaki, N. Furutani, N. Tada, *CNS Drug Rev*. **2006**, *12*, 9; b) S. Liu, X. Bao, B. wang, *Chem. Commun*. **2018**, *54*, 11515−11529; For selected examples, see: c) B. Hinz, O. Cheremina, J. Bachmakov, B. Renner, O. Zolk, M. F. Fromm, K. Brune, *FASEB J.* **2007**, *21*, 2343–2351; d) A. Wong, A. Sibbald, F. Ferrero, M. Plager, M. E. Santolaya, A. M. Escobar, S. Campos, S. Barragan, M. D. L. Gonzalez, G. L. F. Kesselring, *Clin. Pediatr*. **2001**, *40*, 313–324; e) I. Schlemminger, B. Schmidt, D. Flockerzi, H. Tenor, C. Zitt, A. Hatzelmann, D. Marx, C. Braun, R. Kglzer, A. Heuser, H. P. Kley, G. J. Sterk 2 (NycomedGmbH, Germany), WO2010055083, 2010.

[13] For selected examples, see: a) M. S. Chande,P. A. Barve and V. Suryanarayan, *J. Heterocyclic. Chem*. **2007**, *44*, 49–53; b) H. Maruoka, N. Kashige, T. Eishima, F. Okabe, R. Tanaka, T. Fujioka, F. Miake, K. Yamagata. *J. Heterocyclic Chem.* **2008**, *45*, 1883−1887; c) P. Chauhan, S. Mahajan, C. C. J. Loh, G. Raabe, D. Enders, *Org. Lett*. **2014**, *16*, 2954−2957; d) M. Liu, C.-F. Liu, J. Zhang, Y.-J. Xu, L. Dong, *Org. Chem. Front.* **2019**, *6*, 664–668.

[14] For selected examples, see: a) M.-M. Chu, S.-S. Qi, Y.-F. Wang, B. Wang, Z.-H. Jiang, D.-Q. Xu, Z. Xu, *Org. Chem. Front.* **2019**, *6*, 1977–1982; b) B.-B. Sun, J.-Q. Zhang, J.-B. Chen, W.-T. Fan, J.-Q. Yu, J.-M. Hu, X. Wang, *Org. Chem. Front.* **2019**, *6*, 1842–1857; c) C. Zhao, K. Shi, G. He, Q. Gu, Z. Ru, L. Yang, G. Zhong, *Org. Lett.* **2019**, *21*, 7943–7947; d) H.-J. Leng, Q.-Z. Li, R. Zeng, Q.-S. Dai, H.-P. Zhu, Y. Liu, W. Huang, B. Han, J.-L. Li, *Adv. Synth. Catal*. **2018**, *360*, 229–234; e) J. Zhou, W.-J. Huang, G.-F. Jiang, Org. Lett. 2018, 20, 1158−1161; f) W. Yang, W. Sun, C. Zhang, Q. Wang, Z. Guo, B. Mao, J. Liao, H. Guo, *ACS Catal.* **2017**, *7*, 3142−3146; g) S. Mondal, S. Mukherjee, S. R. Yetra, R. G. Gonnade, A. T. Biju, *Org. Lett.* **2017**, *19*, 4367−4370; h) S. R. Yetra, S. Mondal, S. Mukherjee, R. G. Gonnade, A. T. Biju, *Angew. Chem. Int. Ed*. **2016**, *55*, 268–272; i) P. Chauhan, S. Mahajan, C. C. J. Loh, G. Raabe, D. Enders, *Org. Lett*. **2014**, *16*, 2954−2957.

[15] J.-H. Li, T.-F. Feng, D.-M. Du, *J. Org. Chem*. **2015**, *80*, 11369−11377.

[16] a) See the Table S1 in Supporting Information for more details; b) See the Table S2 in Supporting Information for more details; c) See the Table S3 in Supporting Information for more details.

[17] CCDC 1951824 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre.

10.1002/adsc.202000073

COMMUNICATION

# Asymmetric Construction of Bispiro-Cyclopropane-Pyrazolones via a [2 + 1] Cyclization Reaction by Dipeptide-Based Phosphonium Salt Catalysis

*Adv. Synth. Catal.* **Year**, *Volume*, Page – Page

D. Lu, X. Liu, J.-H. Wu, S. Zhang, J.-P. Tan, X. Yu and T. Wang*