

Development of C₂-Symmetric Chiral Spirocyclic Phase-Transfer Catalysts: Synthesis and Application to Asymmetric Alkylation of Glycinate Schiff Base

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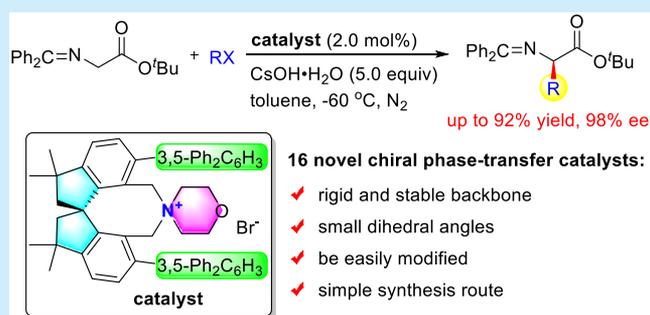
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ABSTRACT: A class of C₂-symmetric chiral spirocyclic phase-transfer catalysts based on tetramethyl-1,1'-spirobiindane scaffold was synthesized from commercially available bisphenol A in 12 steps with 22–25% total yields, which features a more rigid and stable backbone and smaller dihedral angles and can be easily modified. These catalysts show high catalytic performance in the asymmetric alkylation of *tert*-butyl glycinate Schiff base at only 2 mol % catalyst loading, giving the target products with up to 92% yield and 98% ee.



Since the Merck research group reported the first highly efficient asymmetric alkylation reaction using cinchona alkaloid-derived quaternary ammonium salt as a phase-transfer catalyst (PTC),¹ asymmetric phase-transfer catalysis has been developed rapidly over the past three decades due to its simple experimental procedures, mild reaction conditions, and large-scale production.² Inspired by this pioneering work, several similar cinchona alkaloid-derived phase-transfer catalysts (PTCs) had also been reported for the alkylation of glycinate Schiff bases.³ However, the major drawback of these PTCs is the difficulty in structural modification for further improving the enantioselectivity and reactivity in other reactions. To address these issues, Maruoka,⁴ Nagasawa,⁵ Shibasaki,⁶ Ooi,⁷ Tan,⁸ and Zhao⁹ et al. designed a series of catalysts derived from different chiral backbones and succeeded in alkylations, conjugate additions, Mannich reactions, aldol reactions, and so on. Despite great advances in this field, there still remain a few unresolved challenges. In some important reactions, such as Neber rearrangement,¹⁰ intramolecular conjugate addition of nitroalkanes,¹¹ [3 + 2] cycloaddition of allylic sulfones,¹² desymmetrization of meso-aziridines,¹³ and synthesis of planar chiral cyclic amines,¹⁴ the observed enantioselectivities were unsatisfactory using known PTCs. It is well-known that the reaction enantioselectivities are highly substrate dependent. Therefore, the development of new structurally well-designed chiral PTCs is still highly desirable.

In the field of asymmetric metal catalysis, the C₂-symmetric BINAP has proven to be one of the prominent ligands.¹⁵ It should also be noted that C₂-symmetric chiral spiro diphosphine ligand (SDP) based on the 1,1'-spirobiindane backbone was viewed as a perfect complement and alternative to BINAP due to its more rigid backbone and smaller dihedral angles (Figure

1a).¹⁶ Moreover, the C₂-symmetric chiral spiroketal bisphosphine ligands (SKP) developed by the Ding group recently also exhibit unique and outstanding performance in several types of asymmetric transformations.¹⁷

Similarly, Maruoka PTCs with binaphthyl structure have displayed outstanding performance in asymmetric phase-transfer catalysis because they are easier to modify and diversify for accommodating substrates (Figure 1b, left).⁴ To our knowledge, C₂-symmetric chiral quaternary ammonium salt containing 1,1'-spirobiindane has not been reported to date, although 1,1'-spirobiindane-based chiral ligands and phosphoric acids are prevalent in asymmetric catalysis.¹⁸ We think that 1,1'-spirobiindane-based chiral PTCs may also be complementary to Maruoka PTCs. Herein, we report this novel class of C₂-symmetric chiral spirocyclic PTCs based on the tetramethyl-1,1'-spirobiindane backbone (Figure 1b, right). It is noteworthy that introducing four methyl groups into this type PTCs is advantageous to their stability, especially under strongly basic conditions in asymmetric phase-transfer catalysis, because the benzyl positions of 1,1'-spirobiindane are completely protected.

The synthetic route to tetramethyl-1,1'-spirobiindane-based PTCs are shown in Scheme 1. First, racemic 3,3',3'-tetramethyl-1,1'-spirobiindane-7,7'-diol ((±)-1) was synthesized from low-cost, commercially available bisphenol A via acid-

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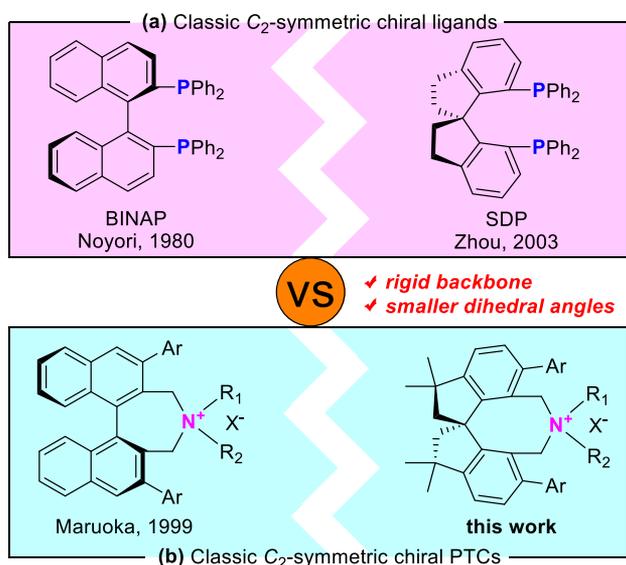
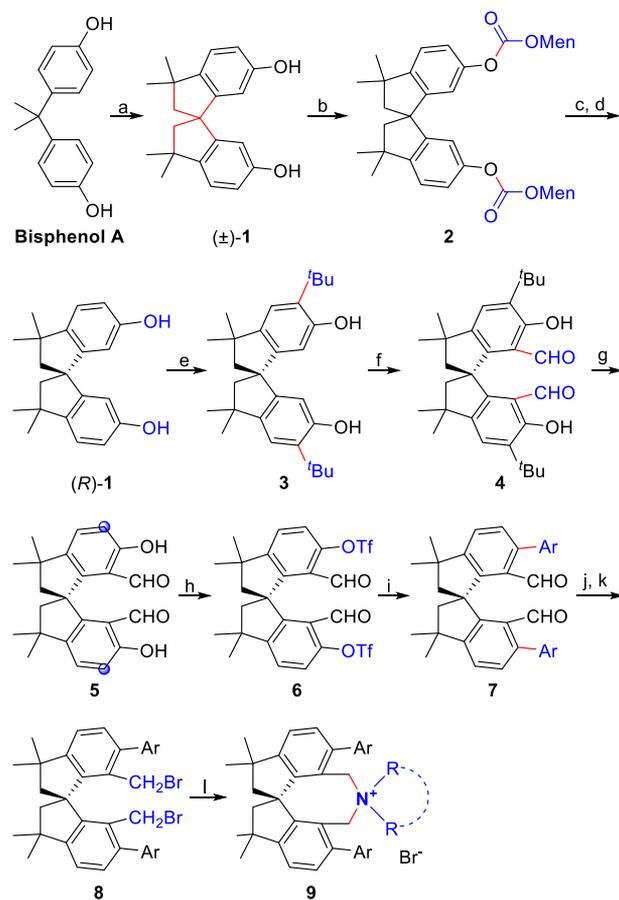


Figure 1. Classic C_2 -symmetric chiral ligands and PTCs.

promoted cascade reactions with 91% yield. Subsequently, an optical resolution was conducted using L-menthyl chloroformate as a resolving agent, giving enantioenriched (*R*)-1 with >99% ee. After that, Friedel–Crafts reaction, Duff reaction, retro-Friedel–Crafts reaction, and esterification were performed sequentially with high to excellent yields, and the desired bistriflate **6** was obtained successfully. The above-mentioned reactions were run according to the reported procedures in the literature¹⁹ with slight modifications. Then the Pd-catalyzed Suzuki coupling of bistriflate **6** with several arylboronic acids afforded compounds **7** with 92–99% yields. In this step, three different methods were used to introduce nine aryl groups at the 6,6'-positions of intermediates **7**. The 3,5-bis(trifluoromethyl)phenyl and 3,4,5-trifluorophenyl were installed using method A, the phenyl, 2-naphthyl, 4-phenylphenyl, 3,5-diphenylphenyl, and 4-(2-naphthyl)phenyl were installed using method B, and the 3,5-di-*tert*-butylphenyl and 4-*tert*-butylphenyl were installed using method C. The subsequent reduction of **7** with NaBH_4 followed by bromination of bromides **8** gave bromides **8** in almost quantitative yields, respectively. It was found that using either PBr_3 or $\text{CBr}_4/\text{PPh}_3$ as bromination reagents gave the brominated products in low yields only. Finally, the reactions of bromides **8** with secondary amines, including di-*n*-butylamine, morpholine, and tetrahydropyrrole, delivered the corresponding spirocyclic quaternary ammonium salts **9** with excellent yields. Notably, employing NaHCO_3 as base is key to this step, and when using either K_2CO_3 or Na_2CO_3 instead of NaHCO_3 , the compounds **8** will be decomposed. Considering the solubility of compounds **8**, the mixed solvents were used in some cases (method E for **9c** and **9n**). Thus, 16 new spirocyclic PTCs **9a–9p** were synthesized successfully in 12 steps from bisphenol A with 22–25% total yields (Figure 2a), and every step can be conducted on a multigram scale. The X-ray crystal structures of **9c** and **9n** clearly indicate that the absolute configuration of this type PTCs is *R* and their dihedral angles are 65.3° and 64.5°, respectively (Figure 2b), which are smaller than that of Maruoka PTCs.²⁰

In order to evaluate the catalytic performance of the newly synthesized spirocyclic PTCs, we applied them to the enantioselective alkylation of *tert*-butyl glycinate Schiff base (**10**) with benzyl bromide (**11a**), which was an entry to optically

Scheme 1. Synthesis Route to Chiral PTCs **9a**



^aConditions: (a) $\text{CH}_3\text{SO}_3\text{H}$, rt, 91%; (b) Et_3N , DMAP, L-menthyl chloroformate, CH_2Cl_2 , rt, 95%; (c) recrystallization for three times at -18°C , 56%; (d) KOH , EtOH , reflux, 99%; (e) $t\text{-BuOH}$, $\text{CH}_3\text{SO}_3\text{H}$, CH_2Cl_2 , rt, 99%; (f) HMTA, TFA, AcOH, 4 M aq HCl, H_2O , reflux, 71%; (g) AlCl_3 , CH_3NO_2 , toluene, rt, 83%; (h) Tf_2O , pyridine, CH_2Cl_2 , rt, 94%; (i) Method A: $\text{ArB}(\text{OH})_2$, $\text{Pd}(\text{PPh}_3)_4$, KBr , $\text{K}_3\text{PO}_4 \cdot 3\text{H}_2\text{O}$, $\text{DME}/\text{H}_2\text{O} = 3/1$, reflux, 92–95%; Method B: $\text{ArB}(\text{OH})_2$, $\text{Pd}(\text{PPh}_3)_4$, K_2CO_3 , DMF, 70°C , 92–99%; Method C: $\text{ArB}(\text{OH})_2$, $\text{Pd}(\text{PPh}_3)_4$, $\text{CH}_3\text{OH}/2\text{ M aq K}_2\text{CO}_3/\text{THF} = 1/2.5/2.5$, reflux, 99%; (j) NaBH_4 , $\text{THF}/\text{CH}_3\text{OH} = 1/1$, 0°C ; (k) 33 wt % HBr in AcOH, reflux; (l) Method D: R_2NH , NaHCO_3 , CH_3CN , 70°C , 93–99%; Method E: R_2NH , NaHCO_3 , $\text{CH}_3\text{CN}/\text{CHCl}_3 = 1/1$, 70°C , 92–98%.

active unnatural α -amino acids²¹ and viewed as a benchmark reaction in asymmetric phase-transfer catalysis.^{2e} Initially, the PTCs **9a–9i** bearing two *n*-butyl groups attached to the N atom were tested at 2 mol % catalyst loading in Et_2O using 50% aq KOH as base at 0°C (Table 1, entries 1–9). To our disappointment, the target product **12a** was delivered with moderate to high yields but in low enantioselectivities. Even worse, the enantioselectivities seemed so elusive. Consequently, it was imperative to adjust the PTCs's alkyl substituents at N atom. When the catalyst was changed to **9j** derived from morpholine, the enantioselectivity of **12a** was elevated dramatically from 4% ee to 60% ee (entry 8 vs entry 10). Then the use of toluene as solvent instead of Et_2O gave a slightly increased ee value (entry 11). To our surprise, the tetrahydropyrrole-derived catalyst **9k** containing similar rigid N-spirocycle was found to be invalid for enhancing the stereoselectivity (entry 12). Next, the morpholine-derived catalysts **9l–9p** were screened (entries 13–17), and it was

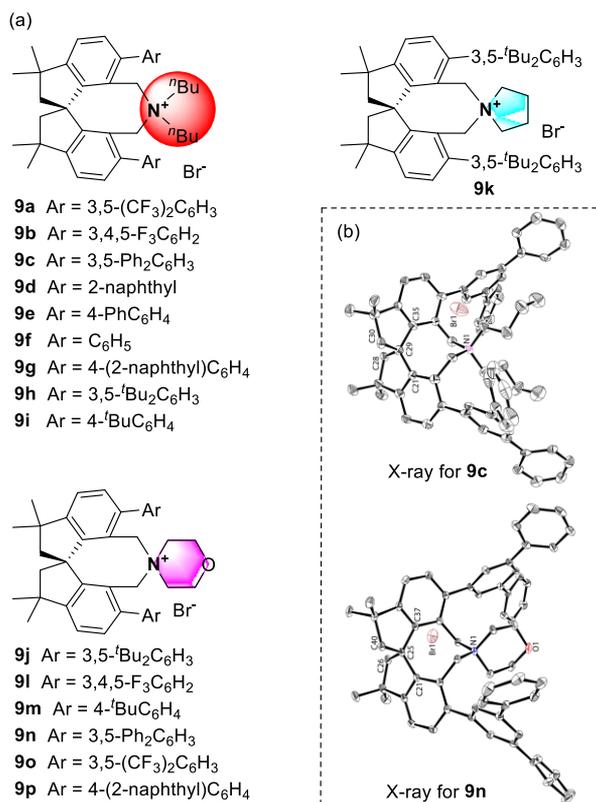


Figure 2. (a) Structure of PTCs **9a–9p**; (b) X-ray crystal structures of **9c** and **9n**. (The ellipsoids are drawn at 30% probability; solvent and hydrogen atoms were removed.)

found that catalyst **9n** delivered **12a** in high yield and improved enantioselectivity (82% yield, 72% ee; entry 15). It was puzzling that the 3,5-bis(trifluoromethyl)phenyl substituted catalyst **9o** showed almost no catalytic activity (entry 16). To our delight, when the temperature was lowered from 0 °C to –40 or –50 °C, the reaction proceeded smoothly to afford the desired product **12a** in comparable yields and with up to 92% ee (entries 18 and 19). Further decreasing the temperature to –60 °C resulted in inactivity of this catalytic system (entry 20), but employing solid CsOH·H₂O as base instead of 50% aq KOH at –60 °C produced **12a** with 84% yield and 98% ee (entry 21). Absolute configuration of **12a** was determined by comparison of the HPLC retention time with the reported literature.^{4b}

Under the optimized conditions, the asymmetric alkylations of **10** with different alkyl halides were examined (Table 2). Both aryl- and alkyl- as well as fluoro-substituted benzyl bromides could be employed in the reaction to provide the products with high yields and high to excellent enantioselectivities (entries 1–5). The 3,5-bis(trifluoromethyl)benzyl bromide also underwent smooth conversion to give **12f** in high yield and moderate ee value (entry 6). Remarkably, functionalized alkyl halides, such as *tert*-butyl bromoacetate, allyl bromide, and propargyl bromide, worked equally well and delivered the desired products in high yields and enantioselectivities (entries 7–9). The less reactive methyl iodide could also participate in the reaction to afford the corresponding product **12j** in moderate yield and ee (entry 10). In order to accelerate the reaction rate, the temperature was slightly elevated to –50 °C and/or the amounts of alkyl halides were increased to 5 equiv in some cases. When the reaction was scaled up 10 times and the catalyst loading was reduced to 1 mol % simultaneously, the substrate underwent smooth conversion

Table 1. Optimization of Reaction Conditions^a

entry	catalyst	solvent	time (h)	yield ^b (%)	ee ^c (%)
1	9a	Et ₂ O	8	42	12
2	9b	Et ₂ O	8	61	33
3	9c	Et ₂ O	5	70	–9
4	9d	Et ₂ O	4	81	–21
5	9e	Et ₂ O	1.5	90	–35
6	9f	Et ₂ O	4	83	–21
7	9g	Et ₂ O	5	91	–40
8	9h	Et ₂ O	8	79	4
9	9i	Et ₂ O	6	85	–31
10	9j	Et ₂ O	4	84	60
11	9j	toluene	9	81	65
12	9k	toluene	5	92	18
13	9l	toluene	12	74	32
14	9m	toluene	5.5	91	40
15	9n	toluene	9	82	72
16	9o	toluene	24	trace	
17	9p	toluene	8	71	32
18 ^d	9n	toluene	25	83	90
19 ^e	9n	toluene	41	81	92
20 ^f	9n	toluene	50	trace	
21 ^{f,g}	9n	toluene	31	84	98

^aUnless otherwise illustrated, the reactions were carried out with 0.17 mmol of **10**, 0.20 mmol of **11a**, 2.0 mol % of catalyst, and 50% aqueous KOH (0.3 mL) in solvent (2.0 mL) at 0 °C. ^bIsolated yield. ^cDetermined by chiral HPLC analysis. ^dAt –40 °C. ^eAt –50 °C. ^fAt –60 °C. ^gUse of solid CsOH·H₂O (5.0 equiv) as base.

Table 2. Substrate Scope^a

entry	RX (11)	time (h)	12	yield ^b (%)	ee ^c (%)
1	C ₆ H ₅ CH ₂ Br	31	12a	84	98
2	<i>p</i> -Ph-C ₆ H ₄ CH ₂ Br	14	12b	92	97
3	1-naphthyl-CH ₂ Br	14	12c	87	96
4 ^d	2,6-Me ₂ C ₆ H ₃ CH ₂ Br	19	12d	83	88
5	<i>m</i> -F-C ₆ H ₄ CH ₂ Br	27	12e	84	90
6 ^d	3,5-(CF ₃) ₂ C ₆ H ₃ CH ₂ Br	15	12f	91	63
7 ^d	BrCH ₂ CO ₂ ^t Bu	19	12g	77	97
8 ^d	CH≡CCH ₂ Br	15	12h	81	79
9 ^e	CH ₂ =CHCH ₂ Br	12	12i	92	85
10 ^{d,e}	CH ₃ I	27	12j	74	71
11 ^f	C ₆ H ₅ CH ₂ Br	30	12a	84	94

^aUnless otherwise illustrated, the reactions were implemented with **10** (0.17 mmol), **11** (0.20 mmol), **9n** (2.0 mol %), and CsOH·H₂O (5.0 equiv) in toluene (2.0 mL) at –60 °C. ^bIsolated yield. ^cDetermined by chiral HPLC analysis. ^dAt –50 °C. ^eUse of 5.0 equiv of alkyl halide. ^fThe reaction was performed on 1.7 mmol scale at 1 mol % catalyst loading.

to give **12a** in 84% yield and 94% ee (entry 11). We also studied the reactivity of α -methyl-substituted glycinate Schiff base derived from benzophenone and found that it did not work

under standard conditions and underwent decomposition when the temperature was elevated to $-20\text{ }^{\circ}\text{C}$.

In conclusion, we have designed and synthesized a type of structurally well-defined C_2 -symmetric spirocyclic quaternary ammonium salts based on tetramethyl-1,1'-spirobiindane as chiral PTCs, which possess more rigid and stable backbones and smaller dihedral angles and can be modified easily. A total 16 new chiral PTCs were synthesized on multigram-scale in 12 steps with 22–25% total yields, and only four steps need purification via column chromatography. Their catalytic performance was examined in the benchmark reaction, asymmetric alkylation of *tert*-butyl glycinate Schiff base, and the morpholine-based catalyst **9n** exhibited high reactivity (up to 92% yield and 98% ee) at only 2 mol % catalyst loading. This type of PTCs is expected to be a complement and alternative to binaphthyl-based Maruoka PTCs. Studies on taming those unsuccessful reactions^{10–14} in asymmetric phase-transfer catalysis using new spirocyclic PTCs are in progress.

■ ASSOCIATED CONTENT

SI Supporting Information

The Supporting Information is available free of charge at <https://pubs.acs.org/doi/10.1021/acs.orglett.1c00535>.

Experimental procedures; ^1H NMR and ^{13}C NMR spectra; HPLC spectra; crystallographic data (PDF)

Accession Codes

CCDC 2047923 and 2047925 contain 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 emailing data_request@ccdc.cam.ac.uk, or by contacting The Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK; fax: +44 1223 336033.

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Notes

The authors declare no competing financial interest.

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■ REFERENCES

- (1) Dolling, U.-H.; Davis, P.; Grabowski, E. J. J. Efficient Catalytic Asymmetric Alkylations. 1. Enantioselective Synthesis of (+)-Indacrinone via Chiral Phase-Transfer Catalysis. *J. Am. Chem. Soc.* **1984**, *106*, 446–447.
- (2) For selected reviews, see: (a) Maruoka, K.; Ooi, T. Enantioselective Amino Acid Synthesis by Chiral Phase-Transfer Catalysis. *Chem. Rev.* **2003**, *103*, 3013–3028. (b) Ooi, T.; Maruoka, K. Recent Advances in Asymmetric Phase-Transfer Catalysis. *Angew. Chem., Int. Ed.* **2007**, *46*, 4222–4266. (c) Hashimoto, T.; Maruoka, K. Recent Development and Application of Chiral Phase-Transfer Catalysts. *Chem. Rev.* **2007**, *107*, 5656–5682. (d) Jew, S.; Park, H. Cinchona-Based Phase-Transfer Catalysts for Asymmetric Synthesis. *Chem. Commun.* **2009**, 7090–7103. (e) Shirakawa, S.; Maruoka, K. Recent Developments in Asymmetric Phase-Transfer Reactions. *Angew. Chem., Int. Ed.* **2013**, *52*, 4312–4348. (f) Novacek, J.; Waser, M. Bifunctional Chiral Quaternary Ammonium Salt Catalysts: A Rapidly Emerging Class of Powerful Asymmetric Catalysts. *Eur. J. Org. Chem.* **2013**, 2013, 637–648.
- (3) (a) O'Donnell, M. J.; Bennett, W. D.; Wu, S. The Stereoselective Synthesis of α -Amino Acids by Phase-Transfer Catalysis. *J. Am. Chem. Soc.* **1989**, *111*, 2353–2355. (b) O'Donnell, M. J.; Wu, S.; Huffman, J. C. A New Active Catalyst Species for Enantioselective Alkylation by Phase-Transfer Catalysis. *Tetrahedron* **1994**, *50*, 4507–4518. (c) Corey, E. J.; Xu, F.; Noe, M. C. A Rational Approach to Catalytic Enantioselective Enolate Alkylation Using a Structurally Rigidified and Defined Chiral Quaternary Ammonium Salt under Phase Transfer Conditions. *J. Am. Chem. Soc.* **1997**, *119*, 12414–12415. (d) Lygo, B.; Wainwright, P. G. A New Class of Asymmetric Phase-Transfer Catalysts Derived from Cinchona Alkaloids — Application in the Enantioselective Synthesis of α -Amino Acids. *Tetrahedron Lett.* **1997**, *38*, 8595–8598.
- (4) For selected examples, see: (a) Ooi, T.; Kameda, M.; Maruoka, K. Molecular Design of a C_2 -Symmetric Chiral Phase-Transfer Catalyst for Practical Asymmetric Synthesis of α -Amino Acids. *J. Am. Chem. Soc.* **1999**, *121*, 6519–6520. (b) Ooi, T.; Kameda, M.; Maruoka, K. Design of N-Spiro C_2 -Symmetric Chiral Quaternary Ammonium Bromides as Novel Chiral Phase-Transfer Catalysts: Synthesis and Application to Practical Asymmetric Synthesis of α -Amino Acids. *J. Am. Chem. Soc.* **2003**, *125*, 5139–5151.
- (5) For a selected example, see: Kita, T.; Georgieva, A.; Hashimoto, Y.; Nakata, T.; Nagasawa, K. C_2 -Symmetric Chiral Pentacyclic Guanidine: A Phase-Transfer Catalyst for the Asymmetric Alkylation of *tert*-Butyl Glycinate Schiff Base. *Angew. Chem., Int. Ed.* **2002**, *41*, 2832–2834.
- (6) For a selected example, see: Ohshima, T.; Shibuguchi, T.; Fukuta, Y.; Shibasaki, M. Catalytic Asymmetric Phase-Transfer Reactions Using Tartrate-Derived Asymmetric Two-Center Organocatalysts. *Tetrahedron* **2004**, *60*, 7743–7754.
- (7) For selected examples, see: (a) Uruguchi, D.; Asai, Y.; Ooi, T. Site-Directed Asymmetric Quaternization of a Peptide Backbone at a C-Terminal Azlactone. *Angew. Chem., Int. Ed.* **2009**, *48*, 733–737. (b) Ohmatsu, K.; Kiyokawa, M.; Ooi, T. Chiral 1,2,3-Triazoliums as New Cationic Organic Catalysts with Anion-Recognition Ability: Application to Asymmetric Alkylation of Oxindoles. *J. Am. Chem. Soc.* **2011**, *133*, 1307–1309.

(8) For a selected example, see: Ma, T.; Fu, X.; Kee, C. W.; Zong, L.; Pan, Y.; Huang, K.-W.; Tan, C.-H. Pentanidium-Catalyzed Enantioselective Phase-Transfer Conjugate Addition Reactions. *J. Am. Chem. Soc.* **2011**, *133*, 2828–2831.

(9) For selected examples, see: (a) Wang, H.-Y.; Chai, Z.; Zhao, G. Novel Bifunctional Thiourea-Ammonium Salt Catalysts Derived from Amino Acids: Application to Highly Enantio- and Diastereoselective aza-Henry Reaction. *Tetrahedron* **2013**, *69*, 5104–5111. (b) Wu, X.; Liu, Q.; Liu, Y.; Wang, Q.; Zhang, Y.; Chen, J.; Cao, W.; Zhao, G. Amino Acid-Derived Phosphonium Salts-Catalyzed Michael Addition of 3-Substituted Oxindoles. *Adv. Synth. Catal.* **2013**, *335*, 2701–2706. (c) Cao, D.; Chai, Z.; Zhang, J.; Ye, Z.; Xiao, H.; Wang, H.; Chen, J.; Wu, X.; Zhao, G. Thiourea-Phosphonium Salts From Amino Acids: Cooperative Phase-Transfer Catalysis in Enantioselective aza-Henry Reaction. *Chem. Commun.* **2013**, *49*, 5972–5974.

(10) Ooi, T.; Takahashi, M.; Doda, K.; Maruoka, K. Asymmetric Induction in the Neber Rearrangement of Simple Ketoxime Sulfonates under Phase-Transfer Conditions: Experimental Evidence for the Participation of an Anionic Pathway. *J. Am. Chem. Soc.* **2002**, *124*, 7640–7641.

(11) Nodes, W. J.; Shankland, K.; Rajkumar, S.; Cobb, A. J. A. Asymmetric Phase-Transfer-Catalyzed Synthesis of Five-Membered Cyclic γ -Amino Acid Precursors. *Synlett* **2010**, 3011–3014.

(12) Gembus, V.; Postikova, S.; Levacher, V.; Brière, J.-F. Highly Regio- and Diastereoselective Anionic [3 + 2] Cycloaddition under Phase Transfer Catalytic Conditions. *J. Org. Chem.* **2011**, *76*, 4194–4199.

(13) (a) Luo, Z.-B.; Hou, X.-L.; Dai, L.-X. Enantioselective Desymmetrization of *meso*-N-Sulfonylaziridines with Thiols. *Tetrahedron: Asymmetry* **2007**, *18*, 443–446. (b) Zhang, J.; Cao, D.; Wang, H.; Zhao, G.; Shang, Y. Enantioselective Desymmetrization of *meso*-Aziridines with Aromatic Thiols Catalyzed by Chiral Bifunctional Quaternary Phosphonium Salts Derived from α -Amino Acids. *Tetrahedron* **2015**, *71*, 1785–1791.

(14) Tomooka, K.; Uehara, K.; Nishikawa, R.; Suzuki, M.; Igawa, K. Enantioselective Synthesis of Planar Chiral Organonitrogen Cycles. *J. Am. Chem. Soc.* **2010**, *132*, 9232–9233.

(15) Miyashita, A.; Yasuda, A.; Takaya, H.; Toriumi, K.; Ito, T.; Souchi, T.; Noyori, R. Synthesis of 2,2'-Bis(diphenylphosphino)-1,1'-binaphthyl (BINAP), an Atropisomeric Chiral Bis(triaryl)phosphine, and Its Use in the Rhodium(I)-Catalyzed Asymmetric Hydrogenation of α -(Acylamino)acrylic Acids. *J. Am. Chem. Soc.* **1980**, *102*, 7932–7934.

(16) For selected examples, see: (a) Xie, J.-H.; Wang, L.-X.; Fu, Y.; Zhu, S.-F.; Fan, B.-M.; Duan, H.-F.; Zhou, Q.-L. Synthesis of Spiro Diphosphines and Their Application in Asymmetric Hydrogenation of Ketones. *J. Am. Chem. Soc.* **2003**, *125*, 4404–4405. (b) Xie, J.-H.; Duan, H.-F.; Fan, B.-M.; Cheng, X.; Wang, L.-X.; Zhou, Q.-L. Application of SDP Ligands for Pd-Catalyzed Allylic Alkylation. *Adv. Synth. Catal.* **2004**, *346*, 625–632. (c) Cheng, X.; Zhang, Q.; Xie, J.-H.; Wang, L.-X.; Zhou, Q.-L. Highly Rigid Diphosphane Ligands with a Large Dihedral Angle Based on a Chiral Spirobifluorene Backbone. *Angew. Chem., Int. Ed.* **2005**, *44*, 1118–1121.

(17) For a review, see: (a) Wang, X.; Han, Z.; Wang, Z.; Ding, K. A Type of Structurally Adaptable Aromatic Spiroketal Based Chiral Diphosphine Ligands in Asymmetric Catalysis. *Acc. Chem. Res.* **2021**, *54*, 668–684. For selected examples, see: (b) Cao, Z.-Y.; Wang, X.; Tan, C.; Zhao, X.-L.; Zhou, J.; Ding, K. Highly Stereoselective Olefin Cyclopropanation of Diazoindoles Catalyzed by a C_2 -Symmetric Spiroketal Bisphosphine/Au(I) Complex. *J. Am. Chem. Soc.* **2013**, *135*, 8197–8200. (c) Wang, X.; Guo, P.; Han, Z.; Wang, X.; Wang, Z.; Ding, K. Spiroketal-Based Diphosphine Ligands in Pd-Catalyzed Asymmetric Allylic Amination of Morita–Baylis–Hillman Adducts: Exceptionally High Efficiency and New Mechanism. *J. Am. Chem. Soc.* **2014**, *136*, 405–411. (d) Liu, J.; Han, Z.; Wang, X.; Wang, Z.; Ding, K. Highly Regio- and Enantioselective Alkoxy-carbonylative Amination of Terminal Allenes Catalyzed by a Spiroketal-Based Diphosphine/Pd(II) Complex. *J. Am. Chem. Soc.* **2015**, *137*, 15346–15349.

(18) For a review, see: (a) Xie, J.-H.; Zhou, Q.-L. Chiral Diphosphine and Monodentate Phosphorus Ligands on a Spiro Scaffold for Transition-Metal-Catalyzed Asymmetric Reactions. *Acc. Chem. Res.* **2008**, *41*, 581–593. For selected examples, see: (b) Zheng, Z.; Cao, Y.; Chong, Q.; Han, Z.; Ding, J.; Luo, C.; Wang, Z.; Zhu, D.; Zhou, Q.-L.; Ding, K. Chiral Cyclohexyl-Fused Spirobiindanes: Practical Synthesis, Ligand Development, and Asymmetric Catalysis. *J. Am. Chem. Soc.* **2018**, *140*, 10374–10381. (c) Wu, M.; Han, Z.; Li, K.; Wu, J.; Ding, K.; Lu, Y. Cyclohexyl-Fused, Spirobiindane-Derived, Phosphine-Catalyzed Synthesis of Tricyclic γ -Lactams and Kinetic Resolution of γ -Substituted Allenates. *J. Am. Chem. Soc.* **2019**, *141*, 16362–16373. (d) Luo, J.; Zhang, T.; Wang, L.; Liao, G.; Yao, Q.-J.; Wu, Y.-J.; Zhan, B.-B.; Lan, Y.; Lin, X.-F.; Shi, B.-F. Enantioselective Synthesis of Biaryl Atropisomers by Pd-Catalyzed C–H Olefination using Chiral Spiro Phosphoric Acid Ligands. *Angew. Chem., Int. Ed.* **2019**, *58*, 6708–6712.

(19) Zhou, Q.; Pan, R.; Shan, H.; Lin, X. Synthesis and Optical Resolution of 3,3,3',3'-Tetramethyl-1,1'-spirobiindane-7,7'-diol. *Synthesis* **2019**, *51*, 557–563.

(20) Kano, T.; Lan, Q.; Wang, X.; Maruoka, K. Effects of Aromatic Substituents on Binaphthyl-Based Chiral Spiro-Type Ammonium Salts in Asymmetric Phase-Transfer Reactions. *Adv. Synth. Catal.* **2007**, *349*, 556–560.

(21) For selected examples about asymmetric α -functionalization of glycine esters, see: (a) Xu, B.; Shi, L.-L.; Zhang, Y.-Z.; Wu, Z.-J.; Fu, L.-N.; Luo, C.-Q.; Zhang, L.-X.; Peng, Y.-G.; Guo, Q.-X. Catalytic Asymmetric Direct α -Alkylation of Amino Esters by Aldehydes via Imine Activation. *Chem. Sci.* **2014**, *5*, 1988–1991. (b) Jörres, M.; Aceña, J. L.; Soloshonok, V. A.; Bolm, C. Asymmetric Carbon–Carbon Bond Formation under Solventless Conditions in Ball Mills. *ChemCatChem* **2015**, *7*, 1265–1269. (c) Chen, J.; Gong, X.; Li, J.; Li, Y.; Ma, J.; Hou, C.; Zhao, G.; Yuan, W.; Zhang, B. *Science* **2018**, *360*, 1438–1442. (d) Wen, W.; Chen, L.; Luo, M.-J.; Zhang, Y.; Chen, Y.-C.; Ouyang, Q.; Guo, Q.-X. Chiral Aldehyde Catalysis for the Catalytic Asymmetric Activation of Glycine Esters. *J. Am. Chem. Soc.* **2018**, *140*, 9774–9780. Ma, J.; Zhou, Q.; Song, G.; Song, Y.; Zhao, G.; Ding, K.; Zhao, B. Enantioselective Synthesis of Pyroglutamic Acid Esters from Glycinate via Carbonyl Catalysis. *Angew. Chem., Int. Ed.* **2021**, DOI: 10.1002/anie.202017306.