How to cite: *Angew. Chem. Int. Ed.* **2021**, *60*, 27241 – 27246
International Edition: doi.org/10.1002/anie.202111137
German Edition: doi.org/10.1002/ange.202111137

Asymmetric Catalysis

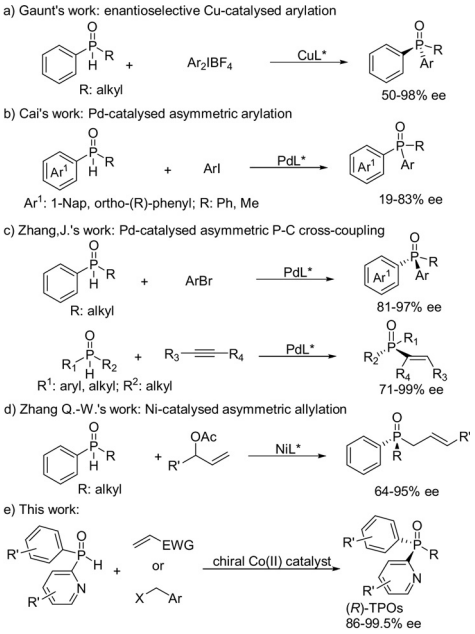
Cobalt-Catalysed Asymmetric Addition and Alkylation of Secondary Phosphine Oxides for the Synthesis of *P*-Stereogenic Compounds

Zeng-Hua Wu, An-Qi Cheng, Meng Yuan, Ya-Xuan Zhao, Huai-Lan Yang, Li-Hua Wei, Huai-Yu Wang, Tao Wang, Zunting Zhang, and Wei-Liang Duan**

Abstract: *The catalytic asymmetric synthesis of P-chiral phosphorus compounds is an important way to construct P-chiral ligands. Herein, we report a new strategy that adopts the pyridinyl moiety as the coordinating group in the cobalt-catalysed asymmetric nucleophilic addition/alkylation of secondary phosphine oxides. A series of tertiary phosphine oxides were generated with up to 99 % yield and 99.5 % ee, and with broad functional-group tolerance. Mechanistic studies reveal that (R)-secondary phosphine oxides preferentially interact with the cobalt catalysts to produce P-stereogenic compounds.*

Chiral phosphorus compounds play important roles as ligands[1] or organic catalysts[2] in asymmetric catalysis. Compared to the synthesis of axial-, planar-, and carbon-centered chiral phosphorus compounds, the synthesis of *P*-stereogenic phosphines has been less investigated. The main recent strategies for the preparation of *P*-chiral compounds involve the use of chiral auxiliary materials or the resolution of racemates.[3] These classical methods require stoichiometric chiral agents or generate an equivalent amount of compound with an opposite configuration.[4] Recently, several asymmetric catalytic methods were developed based on the desymmetrization of phosphine oxides via C–H bond activation,[5] asymmetric addition,[6] ring-closing metatheses,[7] and [2+2+2] cycloaddition processes.[8] In addition, secondary phosphines have been used as nucleophiles in asymmetric conjugate addition,[9] alkylation,[10] and arylation reactions.[11] However, in this process, the strong coordination ability of the secondary phosphines may lead to deactivation of the metal catalyst, thereby reducing the enantioselectivity. Therefore, the development of alternative methods for the synthesis of *P*-chiral compounds is still highly necessary.

Compared with secondary phosphines, secondary phosphine oxides (SPOs) are more stable in air and have low toxicity to metal catalysts. Nonetheless, only a few synthetic examples have been reported for the preparation of optically active tertiary phosphine oxides (TPOs) from SPOs. In 2016, Gaunt and co-workers reported a new strategy in which Cu combined with chiral pyridine-2,6-bis(oxazolines) ligand (pybox) was applied for the enantioselective arylation of SPOs with diaryliodonium salt, affording *P*-chiral tertiary phosphorus compounds with up to 98 % *ee* (Scheme 1 a).[12] The Cai group reported a Pd-catalysed arylation of SPOs with aryl iodides with moderate to high *ee* (Scheme 1 b).[13] Recently, Zhang and co-workers also reported Pd-catalysed asymmetric arylation and alkenylation reactions of SPOs (Scheme 1 c), in which products were obtained in up to 99 % *ee*.[14] In addition to the above examples, the Qing-Wei Zhang group developed a Ni-catalysed kinetic resolution of SPOs via an allylic substitution process, providing a series of P-stereogenic compounds with high enantioselectivity (Scheme 1 d).[15] However, the SPOs in the abovementioned examples usually contain one aryl and one alkyl group. Substrates bearing two similar aryl moieties on the phosphorus atom are rarely explored due to the obvious difficulty in distinguishing two aryl groups of similar size. Hence, we envisioned that introducing a 2-pyridinyl moiety into the SPOs could cause the phosphine oxide to coordinate to the metal catalyst in a bidentate chelating form, which will make it easier to distinguish two aromatic rings on the SPO and achieve high stereoselectivity control. It is worth pointing out



Scheme 1. Reported examples of catalytic asymmetric coupling of secondary phosphine oxides.

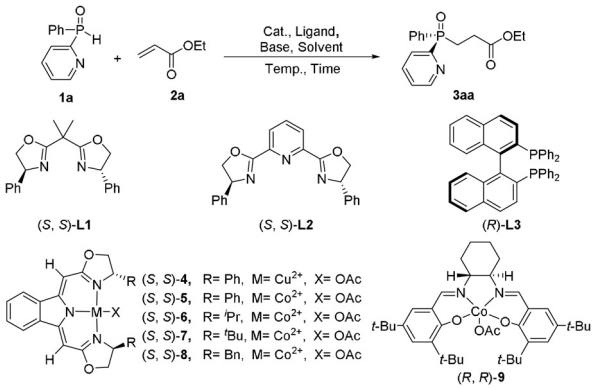
[*] Z.-H. Wu, A.-Q. Cheng, M. Yuan, Y.-X. Zhao, H.-L. Yang, L.-H. Wei, H.-Y. Wang, Dr. T. Wang, Prof. Dr. Z. Zhang, Prof. Dr. W.-L. Duan
School of Chemistry and Chemical Engineering, Shaanxi Normal University, 620 Xi Changan Street, Xi'an 710119 (China)
E-mail: zhangzt@snnu.edu.cn
wlduan@snnu.edu.cn
Prof. Dr. W.-L. Duan
College of Chemistry and Chemical Engineering, Yangzhou University
180 Siwangting Road, Yangzhou 225002 (China)
Supporting information and the ORCID identification number(s) for the author(s) of this article can be found under: https://doi.org/10.1002/anie.202111137.

that according to the work of Beller's group in recent years, tertiary-substituted phosphorus compounds containing a 2-pyridinyl group have great potential in catalysis.[16] 2-Pyridinyl has been introduced into the bisphosphine ligand to achieve remarkable selectivity in the carbonylation of alkenes and alkynes.[16] For example, pyridyl-substituted bidentate phosphine ligands were used not only to enable the formation of adipate diesters with 97% selectivity and 100% atom economy under industrially viable and scalable conditions but also for the first time to realize the stereoselective synthesis of conjugated dienes via the alkoxycarbonylation of easily available 1,3-diynes.[16h,i] Based on the above proposal, we reported a cobalt-catalysed pyridinyl-directed enantioselective nucleophilic addition and alkylation reaction, providing a new pathway for the synthesis of novel pyridyl-substituted bidentate phosphorus ligands.

Initially, we investigated the addition reaction of **1a** to ethyl acrylate **2a** in the presence of copper salt and nitrogen- or phosphorus-based chiral ligand (Table 1). The use of a bidentate or tridentate oxazoline ligand, (*S*,*S*)-**L1** or (*S*,*S*)-pybox **L2**, afforded only the racemic product **3aa** in 16% and 62% yields, respectively (entries 1 and 2). In addition to the screening of oxazoline ligands, chiral bisphosphine ligands, such as (*R*)-binap **L3**, were examined to generate **3aa** with 21% *ee* (entry 3). In further exploration of the reaction, the copper complex of boxmi[17] ligand **4** designed by the Gade group was found to be an effective catalyst for the formation of **3aa** with 43% *ee*, albeit with a low yield (12%) (entry 4). Then, changing the metal to cobalt increased the enantioselectivity to 71% (entry 5).[18] Moreover, the different substituent groups on the ligand framework were further investigated, and the Ph group was found to be the best one for the control of enantioselectivity (compared to *i*Pr, *t*Bu, and Bn) (entries 6–8). In addition, the chiral salen cobalt complex **9** was examined, and the desired product was formed in high yield but with low *ee* (entry 9). Next, changing the solvent to methanol significantly improved the enantioselectivity, generating **3aa** in 89% *ee* and 92% yield (entry 10). By changing the base in the reaction to DIPEA, the *ee* of product **3aa** was further increased to 92% (entry 11). Moreover, lowering the reaction temperature from room temperature to 0°C and using EtOH as the solvent further increased *ee* to 96% (entry 12).

The substrate scope was examined under the optimized conditions obtained (Table 2). First, different substituents on the pyridinyl groups of the phosphine oxides were investigated. Electron-rich or electron-deficient moieties were all tolerated well, affording products **3aa**–**3ha** in high yields (87–99%) and excellent enantioselectivities (91–99% *ee*). A

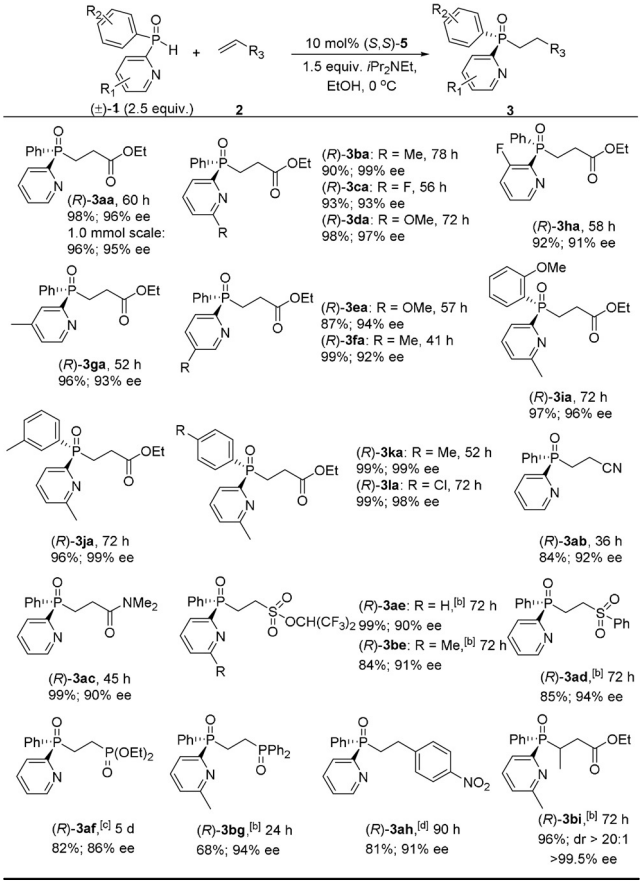
Table 1: Optimization of the enantioselective addition of **1a** to **2a**.[a]



Entry	Cat	Base	Solvent	Yield [%][b]	*ee* [%][c]
1	$Cu(OTf)_2$/**L1**	Et_3N	THF	16	–
2	$Cu(OTf)_2$/**L2**	Et_3N	THF	62	–
3	$Cu(MeCN)_4BF_4$/**L3**	Et_3N	Toluene	40	21
4	(*S*,*S*)-**4**	Et_3N	Toluene	12	43
5	(*S*,*S*)-**5**	Et_3N	Toluene	83	71
6	(*S*,*S*)-**6**	Et_3N	Toluene	99	5
7	(*S*,*S*)-**7**	Et_3N	Toluene	99	23
8	(*S*,*S*)-**8**	Et_3N	Toluene	99	17
9	(*R*,*R*)-**9**	Et_3N	Toluene	99	13
10[d]	(*S*,*S*)-**5**	Et_3N	MeOH	92	89
11[d]	(*S*,*S*)-**5**	iPr_2NEt	MeOH	70	92
12[e]	(*S*,*S*)-**5**	iPr_2NEt	EtOH	99	96

[a] Reaction conditions unless otherwise noted: **1a** (0.25 mmol), **2a** (0.10 mmol), catalyst (0.01 mmol), base (0.15 mmol), solvent (3 mL) under a N_2 atmosphere at room temperature for 48 h. [b] Yield was determined by ^1H NMR using CH_2Br_2 as the internal standard. [c] Determined by chiral HPLC. [d] 96 h. [e] Yields of isolated products, at 0°C for 60 h monitored by TLC.

Table 2: Substrate scope for the addition reaction.[a]



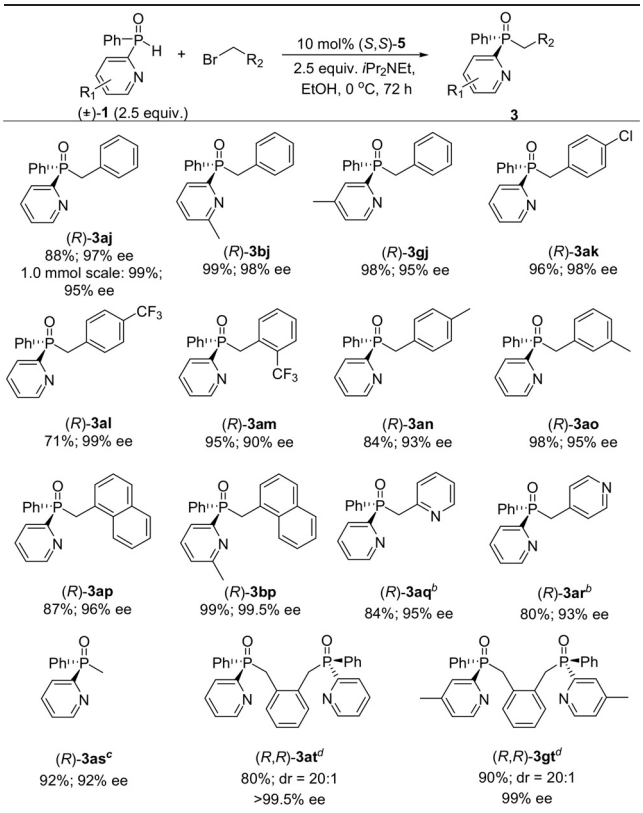
[a] Reaction conditions unless otherwise noted: **1** (0.25 mmol), **2** (0.10 mmol), (*S*,*S*)-**5** (0.01 mmol), iPr_2NEt (0.15 mmol), in EtOH (3 mL) under a N_2 atmosphere at 0°C. Yields of isolated products and the *ee* were determined by chiral HPLC. dr were determined by ^{31}P NMR analysis of the crude reaction mixture. [b] −20°C. [c] RT. [d] −30°C.

substrate bearing an electron-rich group (Me) at the *ortho*-position of the pyridinyl ring needed a longer reaction time (72 h) than a substrate with no substituent or electron-withdrawing group (F) due to the steric hindrance effect (**1b**–**1d**). The substrates containing the F group on the pyridyl ring at the 3- and 6-positions (**1c**, **1h**) exhibited lower enantioselectivity than the others, affording products **3ca** and **3ha** in 93% and 91% *ee*. The substrate scope of the SPOs on the aromatic ring was further investigated, and all moieties, such as *o*-OMe, *p*-Me, *m*-Me, and *p*-Cl, were compatible with excellent yield and enantioselectivity (**3ia**–**3la**, 96–99%). After that, different electrophiles (**2**) were explored. In addition to acrylate ester, acrylonitrile **2b** and acrylamide **2c** were smoothly converted to the corresponding products (**3ab**, **3ac**) with good yields (84%, 99%) and *ee* values (92%, 90%) under standard conditions. For other electron-deficient alkenes, such as sulfonate, arylsulfoxide, phosphine oxide, and phosphinate, the reaction was carried out at a lower temperature (−20 °C), furnishing the desired products with high enantioselectivity (86 to 94% *ee*). It is worth pointing out that the absolute configuration of product **3bg** was determined to be *R* by single-crystal XRD analysis.[19] In addition, substituted styrene **2h** was also found to be reactive, generating product **3ah** with 91% *ee* at −30 °C. β-Methyl-substituted acrylate was also examined, and the desired *P*-chiral compound **3bi** was obtained with excellent diastereo- and enantioselectivity (> 20:1 dr and > 99.5% *ee*).

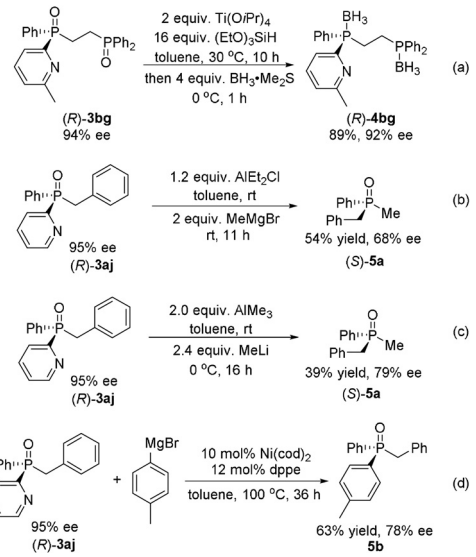
In subsequent attempts, substituted alkyl bromides were used as reaction partners with SPOs to obtain the corresponding nucleophilic substitution products (Table 3). When benzyl bromide was involved in the reaction, either template substrates **1a** or the substrate with methyl substituents on the pyridine rings of phosphine atoms afforded the products **3aj**, **3bj**, and **3gj** with high efficiency (88–99%) and excellent enantioselectivity (> 95% *ee*). For substituents on the benzyl bromides, both the electron-donating and electron-withdrawing groups were well tolerated, delivering the products (**3ak**–**3bp**) in good yield (71–99%) with high *ee* (90–99.5%). It is particularly noteworthy that benzyl bromides containing coordinating pyridinyl groups are also tolerated to obtain the product (**3aq**–**3ar**) in more than 80% yield with 95% and 93% *ee*. We next investigated alkyl halides and found that iodomethane was also a suitable electrophilic reagent, and the target product **3as** could be obtained with excellent yield and enantioselectivity (92% *ee*). Finally, *o*-dibenzyl bromide was used as the substrate to synthesize the corresponding bisphosphine oxides (**3at** and **3gt**) with remarkably high diastereoselectivity and enantiomeric excess (dr = 20:1, > 99% *ee*).

To demonstrate the utility of the obtained product, the phosphine oxide **3bg** was reduced to the trivalent phosphorus compound, followed by protection with borane. A bisphosphine borane complex was obtained in good yield with almost the same level of *ee* (Scheme 2a).[20] The success of this transformation revealed that a series of pyridinyl substituted *P*-chiral phosphine compounds can be readily prepared via the current protocol. In addition, the pyridinyl moiety in the product can be removed by nucleophilic attack of MeMgBr or MeLi in the presence of additives, or through a Ni-catalysed cross-coupling reaction. The corresponding products were obtained in moderate yields with a partial loss of enantioselectivity (Scheme 2b–d).

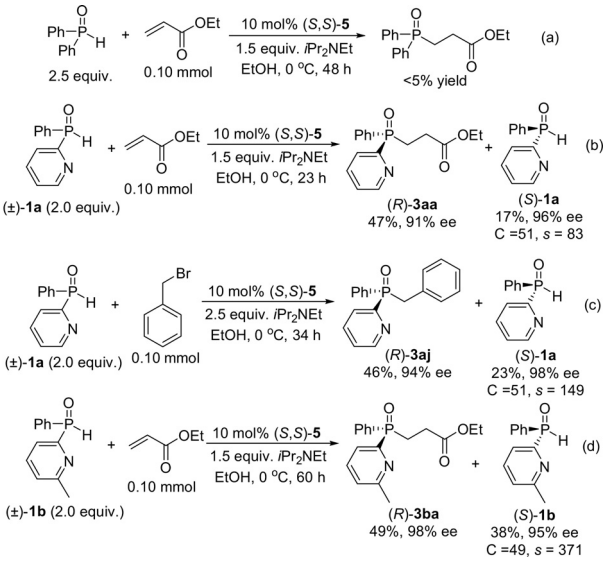
Table 3: Substrate scope for the substitution reaction.[a]



[a] Reaction conditions unless otherwise noted: **1** (0.25 mmol), alkyl bromide (0.10 mmol), (*S*,*S*)-**5** (0.01 mmol), iPr_2NEt (0.25 mmol), in EtOH (3 mL) under a N_2 atmosphere at 0 °C. Yields of the isolated products and the *ee* were determined by chiral HPLC. dr were determined by ^{31}P NMR analysis of the crude reaction mixture. [b] iPr_2EtN (0.35 mmol). [c] Methyl iodide was used. [d] alkyl bromide (0.05 mmol).



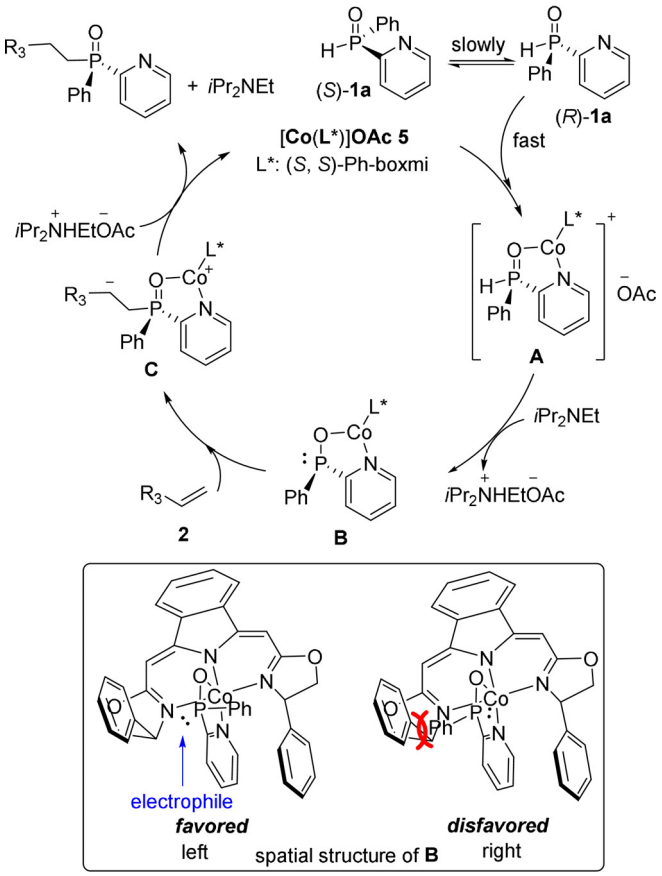
Scheme 2. The product transformation.



Scheme 3. Mechanistic study.

To understand the reaction mechanism, diphenylphosphine oxide was used as the reactant instead of **1a**, and the corresponding product was not generated at all (Scheme 3a). The results indicated that the presence of a pyridinyl group is essential for the progress of the reaction. It was obvious that this reaction involved a kinetic resolution process, while the configuration of the product was determined to be *R*. The three reactions were conducted to determine the selectivity factors of the reaction and which configuration of **1a** is preferentially transformed (Scheme 3b–d). The remaining substrate **1a** with the *S*-configuration[21] was isolated in low yields due to its partial decomposition under reaction conditions and during the purification step. The *s* values[22] were in the range of 83–371, which indicates (*R*)-**1a** reacts much faster than (*S*)-**1a**. Based on the above results, a proposed catalytic cycle is shown in Scheme 4. First, (*R*)-**1a** preferentially coordinates with cobalt catalyst (*S*,*S*)-**5** to generate P^V intermediate **A**. Then, the presence of the base enables the formation of P^{III} intermediate **B**. To avoid the steric repulsion between the Ph group on the *P*-atom and the Ph ring in the oxazolinyl unit, nucleophilic addition to alkenes preferentially occurs via **B** (left), followed by a protonolysis process, releases the product with (*R*)-configuration and regenerates the original Co catalyst.

In summary, we have developed a method for the synthesis of *P*-chiral phosphine oxides (TPOs) using secondary phosphine oxides (SPOs) as substrates with high enantioselectivities. The strategy of using pyridine-assisted coordination effectively distinguishes two aryl groups on the phosphorus atom, realizing a highly stereoselective transformation and affording a series of pyridinyl group-containing *P*-chiral compounds. Further expansion of this method and application of synthesized chiral phosphorus compounds in catalysis is underway.



Scheme 4. Proposed catalytic cycle.

Acknowledgements

This work was financially supported by the NSFC (22071139 and 21871168), and the Fundamental Research Funds for the Central Universities (2019TS034), Shaanxi Normal University.

Conflict of Interest

The authors declare no conflict of interest.

Keywords: asymmetric catalysis · cobalt · *P*-stereogenic compound · tridentate ligand

[1] a) W. Tang, X. Zhang, *Chem. Rev.* **2003**, *103*, 3029–3070; b) *Phosphorus Ligands in Asymmetric Catalysis: Synthesis and Applications*, *Vols. 1–3* (Eds.: A. Börner), Wiley-VCH, Weinheim, **2008**; c) H. Fernández-Pérez, P. Etayo, A. Panossian, A. Vidal-Ferran, *Chem. Rev.* **2011**, *111*, 2119–2176; d) *Privileged Chiral Ligands and Catalysts*, *Vol. 6* (Eds.: Q.-L. Zhou), Wiley-VCH, Weinheim, **2011**; e) "The Use of New Phosphines as Powerful Tools in Asymmetric Synthesis of Biologically Active Compounds": C. A. Busacca, C. H. Senanayake, *Comprehensive Chirality*, *Vol. 1* (Eds.: E. M. Carreira, H. Yamamoto), Elsevier, Amsterdam, **2012**, pp. 167–216; f) *Phosphorus(III) Ligands in Homogeneous Catalysis: Design and Synthesis* (Eds.: P. C. J. Kamer, P. W. N. M. van Leeuwen), Wiley, Chichester, **2012**; g) M. Dutartre, J. Bayardon, S. Juge, *Chem. Soc. Rev.* **2016**, *45*, 5771–5794.

[2] a) J. L. Methot, W. R. Roush, *Adv. Synth. Catal.* **2004**, *346*, 1035 – 1050; b) J. Seayad, B. List, *Org. Biomol. Chem.* **2005**, *3*, 719 – 724; c) S. J. Connon, *Angew. Chem. Int. Ed.* **2006**, *45*, 3909 – 3912; *Angew. Chem.* **2006**, *118*, 4013 – 4016; d) E. Remond, S. Juge, *Chim. Oggi* **2014**, *32*, 49 – 55; e) H. Guo, Y. C. Fan, Z. Sun, Y. Wu, O. Kwon, *Chem. Rev.* **2018**, *118*, 10049 – 10293; f) H. Ni, W.-L. Chan, Y. Lu, *Chem. Rev.* **2018**, *118*, 9344 – 9411; g) T. Ayad, A. Gernet, J.-L. Pirat, D. Virieux, *Tetrahedron* **2019**, *75*, 4385 – 4418.

[3] For recent reviews, see: a) K. M. Pietrusiewicz, M. Zablocka, *Chem. Rev.* **1994**, *94*, 1375 – 1411; b) A. Grabulosa, J. Granell, G. Muller, *Coord. Chem. Rev.* **2007**, *251*, 25 – 90; c) O. I. Kolodiazhnyi, *Tetrahedron: Asymmetry* **2012**, *23*, 1 – 46; For recent examples, see: d) E. Bergin, C. T. O'Connor, S. B. Robinson, E. M. McGarrigle, C. P. O'Mahony, D. G. Gilheany, *J. Am. Chem. Soc.* **2007**, *129*, 9566 – 9567; e) Z.-S. Han, N. Goyal, M. A. Herbage, J. D. Sieber, B. Qu, Y. Xu, Z. Li, J. T. Reeves, J.-N. Desrosiers, S. Ma, N. Grinberg, H. Lee, H. P. R. Mangunuru, Y. Zhang, D. Krishnamurthy, B. Z. Lu, J. Song, G. Wang, C. H. Senanayake, *J. Am. Chem. Soc.* **2013**, *135*, 2474 – 2477; f) S. Rast, B. Mohar, M. Stephan, *Org. Lett.* **2014**, *16*, 2688 – 2691; g) Z. S. Han, H. Wu, Y. Xu, Y. Zhang, B. Qu, Z. Li, D. R. Caldwell, K. R. Fandrick, L. Zhang, F. Roschangar, J. Song, C. H. Senanayake, *Org. Lett.* **2017**, *19*, 1796 – 1799.

[4] For reviews on the synthesis of *P*-chiral phosphines, see: a) D. S. Glueck, *Chem. Eur. J.* **2008**, *14*, 7108 – 7117; b) J. S. Harvey, V. Gouverneur, *Chem. Commun.* **2010**, *46*, 7477 – 7485; c) D. Zhao, R. Wang, *Chem. Soc. Rev.* **2012**, *41*, 2095 – 2108; d) Z. Li, W.-L. Duan, *Chin. J. Org. Chem.* **2016**, *36*, 1805 – 1813; e) R.-Y. Zhu, K. Liao, J.-S. Yu, J. Zhou, *Huaxue Xuebao* **2020**, *78*, 193 – 216; f) D. S. Glueck, *Synlett* **2021**, *32*, 875 – 884; g) D. S. Glueck, *Synthesis* **2021**, https://doi.org/10.1055/a-1582-0169.

[5] a) Z.-J. Du, J. Guan, G.-J. Wu, P. Xu, L.-X. Gao, F.-S. Han, *J. Am. Chem. Soc.* **2015**, *137*, 632 – 635; b) Z.-Q. Lin, W.-Z. Wang, S.-B. Yan, W.-L. Duan, *Angew. Chem. Int. Ed.* **2015**, *54*, 6265 – 6269; *Angew. Chem.* **2015**, *127*, 6363 – 6367; c) Y. S. Jang, M. Dieckmann, N. Cramer, *Angew. Chem. Int. Ed.* **2017**, *56*, 15088 – 15092; *Angew. Chem.* **2017**, *129*, 15284 – 15288; d) Y. S. Jang, L. Wozniak, J. Pedroni, N. Cramer, *Angew. Chem. Int. Ed.* **2018**, *57*, 12901 – 12905; *Angew. Chem.* **2018**, *130*, 13083 – 13087; e) Z. Li, Z.-Q. Lin, C.-G. Yan, W.-L. Duan, *Organometallics* **2019**, *38*, 3916 – 3920; f) Y. H. Chen, X.-L. Qin, F.-S. Han, *Chem. Commun.* **2017**, *53*, 5826 – 5829; g) Y. Sun, N. Cramer, *Chem. Sci.* **2018**, *9*, 2981 – 2985.

[6] For selected examples, see: a) K. M. Lim, T. Hayashi, *J. Am. Chem. Soc.* **2017**, *139*, 8122 – 8125; b) Y. Zheng, L. Guo, W. Zi, *Org. Lett.* **2018**, *20*, 7039 – 7043; c) Y. Zhang, F. Zhang, L. Chen, J. Xu, X. Liu, X. Feng, *ACS Catal.* **2019**, *9*, 4834 – 4840.

[7] J. S. Harvey, S. J. Malcolmson, K. S. Dunne, S. J. Meek, A. L. Thompson, R. R. Schrock, A. H. Hoveyda, V. Gouverneur, *Angew. Chem. Int. Ed.* **2009**, *48*, 762 – 766; *Angew. Chem.* **2009**, *121*, 776 – 780.

[8] G. Nishida, K. Noguchi, M. Hirano, K. Tanaka, *Angew. Chem. Int. Ed.* **2008**, *47*, 3410 – 3413; *Angew. Chem.* **2008**, *120*, 3458 – 3461.

[9] a) Y. Huang, Y. Li, P.-H. Leung, T. Hayashi, *J. Am. Chem. Soc.* **2014**, *136*, 4865 – 4868; b) C. Li, Q.-L. Bian, S. Xu, W.-L. Duan, *Org. Chem. Front.* **2014**, *1*, 541 – 545; c) W.-J. Yue, J.-Z. Xiao, S. Zhang, L. Yin, *Angew. Chem. Int. Ed.* **2020**, *59*, 7057 – 7062; *Angew. Chem.* **2020**, *132*, 7123 – 7128; d) Y.-B. Li, H. Tian, L. Yin, *J. Am. Chem. Soc.* **2020**, *142*, 20098 – 20106; e) C. Wang, K. Huang, J. Ye, W.-L. Duan, *J. Am. Chem. Soc.* **2021**, *143*, 5685 – 5690.

[10] a) V. S. Chan, I. C. Stewart, R. G. Bergman, F. D. Toste, *J. Am. Chem. Soc.* **2006**, *128*, 2786 – 2787; b) C. Scriban, D. S. Glueck, *J. Am. Chem. Soc.* **2006**, *128*, 2788 – 2789; c) B.-J. Anderson, M. A. Guino-O, D. S. Glueck, J. A. Golen, A. G. DiPasquale, L. M. Liable-Sands, A. L. Rheingold, *Org. Lett.* **2008**, *10*, 4425 – 4428; d) B.-J. Anderson, M. A. Guino-O, D. S. Glueck, A. G. Dipasquale, A. L. Rheingold, *Organometallics* **2008**, *27*, 4992 – 5001; e) V. S. Chan, M. Chiu, R. G. Bergman, F. D. Toste, *J. Am. Chem. Soc.* **2009**, *131*, 6021 – 6032; f) B. J. Anderson, S. C. Reynolds, M. A. Guino-o, Z. Xu, D. S. Glueck, *ACS Catal.* **2016**, *6*, 8106 – 8114; g) S. Zhang, J.-Z. Xiao, Y.-B. Li, C.-Y. Shi, L. Yin, *J. Am. Chem. Soc.* **2021**, *143*, 9912 – 9921.

[11] a) J. R. Moncarz, N. F. Laritcheva, D. S. Glueck, *J. Am. Chem. Soc.* **2002**, *124*, 13356 – 13357; b) V. S. Chan, R. G. Bergman, F. D. Toste, *J. Am. Chem. Soc.* **2007**, *129*, 15122 – 15123; c) N. F. Blank, J. R. Moncarz, T. J. Brunker, C. Scriban, B. J. Anderson, O. Amir, D. S. Glueck, L. N. Zakharov, J. A. Golen, C. D. Incarvito, A. L. Rheingold, *J. Am. Chem. Soc.* **2007**, *129*, 6847 – 6858; d) T. J. Brunker, B. J. Anderson, N. F. Blank, D. S. Glueck, A. L. Rheingold, *Org. Lett.* **2007**, *9*, 1109 – 1112.

[12] R. Beaud, R. J. Phipps, M. J. Gaunt, *J. Am. Chem. Soc.* **2016**, *138*, 13183 – 13186.

[13] Y. Zhang, H. He, Q. Wang, Q. Cai, *Tetrahedron Lett.* **2016**, *57*, 5308 – 5311.

[14] a) Q. Dai, B. Li, M. Li, L. Zhang, *J. Am. Chem. Soc.* **2019**, *141*, 20556 – 20564; b) Q. Dai, L. Liu, Y. Qian, W. Li, J. Zhang, *Angew. Chem. Int. Ed.* **2020**, *59*, 20645 – 20650; *Angew. Chem.* **2020**, *132*, 20826 – 20831; c) H. Qiu, Q. Dai, J. He, W. Li, J. Zhang, *Chem. Sci.* **2020**, *11*, 9983 – 9988.

[15] X.-T. Liu, Y.-Q. Zhang, X.-Y. Han, S.-P. Sun, Q.-W. Zhang, *J. Am. Chem. Soc.* **2019**, *141*, 16584 – 16589.

[16] a) K. Dong, X. Fang, S. Gülak, R. Franke, A. Spannenberg, H. Neumann, R. Jackstell, M. Beller, *Nat. Commun.* **2017**, *8*, 14117 – 14123; b) K. Dong, R. Sang, R. Franke, A. Spannenberg, H. Neumann, R. Jackstell, M. Beller, *Angew. Chem. Int. Ed.* **2017**, *56*, 5267 – 5271; *Angew. Chem.* **2017**, *129*, 5351 – 5355; c) K. Dong, R. Sang, J. Liu, R. Razzaq, R. Franke, R. Jackstell, M. Beller, *Angew. Chem. Int. Ed.* **2017**, *56*, 6203 – 6207; *Angew. Chem.* **2017**, *129*, 6299 – 6303; d) L. Wang, H. Neumann, M. Beller, *Angew. Chem. Int. Ed.* **2018**, *57*, 6910 – 6914; *Angew. Chem.* **2018**, *130*, 7026 – 7030; e) R. Sang, P. Kucmierczyk, K. Dong, R. Franke, H. Neumann, R. Jackstell, M. Beller, *J. Am. Chem. Soc.* **2018**, *140*, 5217 – 5223; f) J. Liu, K. Dong, R. Franke, H. Neumann, R. Jackstell, M. Beller, *J. Am. Chem. Soc.* **2018**, *140*, 10282 – 10288; g) J. Yang, J. Liu, H. Neumann, R. Franke, R. Jackstell, M. Beller, *Science* **2019**, *366*, 1514 – 1517; h) J. Liu, J. Yang, W. Baumann, R. Jackstell, M. Beller, *Angew. Chem. Int. Ed.* **2019**, *58*, 10683 – 10687; *Angew. Chem.* **2019**, *131*, 10793 – 10797; i) R. Sang, P. Kucmierczyk, R. Dühren, R. Razzaq, K. Dong, J. Liu, R. Franke, R. Jackstell, M. Beller, *Angew. Chem. Int. Ed.* **2019**, *58*, 14365 – 14373; *Angew. Chem.* **2019**, *131*, 14503 – 14511; j) J.-W. Liu, C.-L. Schneider, J. Yang, Z.-H. Wei, H.-J. Jiao, R. Franke, R. Jackstell, M. Beller, *Angew. Chem. Int. Ed.* **2021**, *60*, 371 – 379; *Angew. Chem.* **2021**, *133*, 375 – 383; k) J.-W. Liu, J. Yang, C. Schneider, R. Franke, R. Jackstell, M. Beller, *Angew. Chem. Int. Ed.* **2020**, *59*, 9032 – 9040; *Angew. Chem.* **2020**, *132*, 9117 – 9125.

[17] a) Q.-H. Deng, H. Wadepohl, L. H. Gade, *Chem. Eur. J.* **2011**, *17*, 14922 – 14928; b) Q.-H. Deng, H. Wadepohl, L. H. Gade, *J. Am. Chem. Soc.* **2012**, *134*, 2946 – 2949; c) Q.-H. Deng, H. Wadepohl, L. H. Gade, *J. Am. Chem. Soc.* **2012**, *134*, 10769 – 10772; d) Q.-H. Deng, T. Bleith, H. Wadepohl, L. H. Gade, *J. Am. Chem. Soc.* **2013**, *135*, 5356 – 5359; e) Q.-H. Deng, C. Rettenmeier, H. Wadepohl, L. H. Gade, *Chem. Eur. J.* **2014**, *20*, 93 – 97; f) T. Bleith, H. Wadepohl, L. H. Gade, *J. Am. Chem. Soc.* **2015**, *137*, 2456 – 2459; g) T. Bleith, L. H. Gade, *J. Am. Chem. Soc.* **2016**, *138*, 4972 – 4983; h) T. Bleith, Q.-H. Deng, H. Wadepohl, L. H. Gade, *Angew. Chem. Int. Ed.* **2016**, *55*, 7852 – 7856; *Angew. Chem.* **2016**, *128*, 7983 – 7987; i) V. Vasilenko, C. K. Blasius, H. Wadepohl, L. H. Gade, *Angew. Chem. Int. Ed.* **2017**, *56*, 8393 – 8397; *Angew. Chem.* **2017**, *129*, 8513 – 8517; j) C. K. Blasius, V.

Vasilenko, L.-H. Gade, *Angew. Chem. Int. Ed.* **2018**, *57*, 10231 – 10235; *Angew. Chem.* **2018**, *130*, 10388 – 10392; k) C. K. Blasius, N. F. Heinrich, V. Vasilenko, L. H. Gade, *Angew. Chem. Int. Ed.* **2020**, *59*, 15974 – 15977; *Angew. Chem.* **2020**, *132*, 16108 – 16111.
[18] C. K. Blasius, H. Wadepohl, L. H. Gade, *Eur. J. Inorg. Chem.* **2020**, 2335 – 2342.
[19] Deposition Number 2059262 (for **3bg**) contains the supplementary crystallographic data for this paper. These data are provided free of charge by the joint Cambridge Crystallographic Data Centre and Fachinformationszentrum Karlsruhe Access Structures service www.ccdc.cam.ac.uk/structures.
[20] A. Hu, H. Ngo, W. Lin, *Angew. Chem. Int. Ed.* **2004**, *43*, 2501 – 2504; *Angew. Chem.* **2004**, *116*, 2555 – 2558.
[21] Q. Xu, C.-Q. Zhao, L.-B. Han, *J. Am. Chem. Soc.* **2008**, *130*, 12648 – 12655.
[22] a) E. Vedejs, M. Jure, *Angew. Chem. Int. Ed.* **2005**, *44*, 3974 – 4001; *Angew. Chem.* **2005**, *117*, 4040 – 4069; b) M. D. Greenhalgh, J. E. Taylor, A. D. Smith, *Tetrahedron* **2018**, *74*, 5554 – 5560.

Manuscript received: August 18, 2021
Revised manuscript received: October 21, 2021
Version of record online: November 22, 2021

