Chemical Science

EDGE ARTICLE

View Article Online
View Journal | View Issue

Check for updates

Cite this: *Chem. Sci.*, 2018, **9**, 2981

Tailored trisubstituted chiral Cp^xRh^{III} catalysts for kinetic resolutions of phosphinic amides†

Y. Sun and N. Cramer *

Received 21st December 2017
Accepted 3rd February 2018

DOI: 10.1039/c7sc05411d

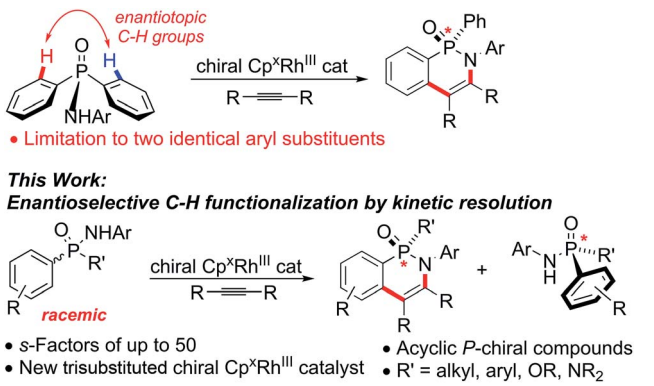
rsc.li/chemical-science

A trisubstituted chiral Cp^x ligand family is introduced. Based on the disubstituted atropchiral Cp^x ligand scaffold, the introduction of a bulky third substituent at the central position of the Cp ring leads to substantially increased selectivities for rhodium(III)-catalyzed kinetic resolutions and allowed for *s*-factors of up to 50. Their superiority is demonstrated by kinetic resolutions of phosphinic amides providing access to compounds with stereogenic phosphorus(V) atoms. The unreacted acyclic phosphinic amide and the cyclized product are both obtained in good yields and enantioselectivities. The ligand synthesis capitalizes on a late stage modification and expands the accessible ligand Cp^x ligand portfolio.

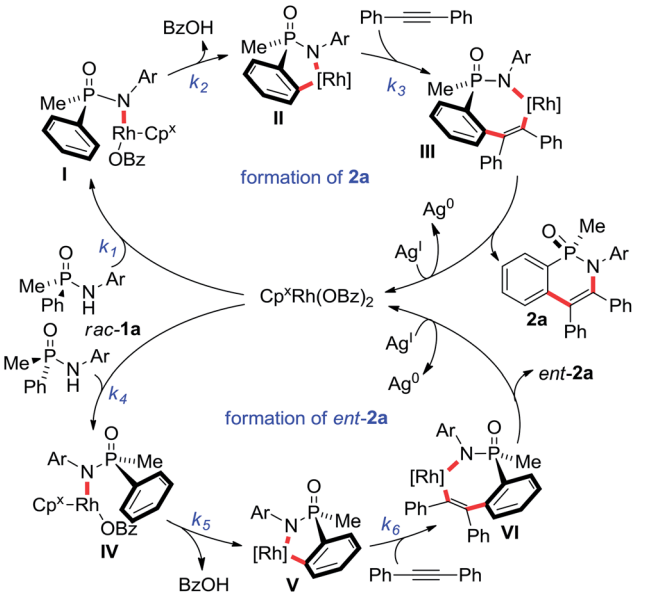
Introduction

Molecules possessing a chiral phosphorus(III)[1] as well as phosphorus(V) center[2] are important compounds classes with widespread applications. The catalytic and stereoselective synthesis of molecules with chiral phosphorus centers received significant attention,[3] but remains a challenging task. Additional and complementary methods for their selective preparations are highly desirable and would be synthetically very valuable. In this respect, catalytic enantioselective C–H functionalizations have emerged a complementary tactic to access chiral building blocks from simple starting materials.[4] To the best of our knowledge, the synthesis of P-stereogenic centers by catalytic C–H functionalizations is so far limited to desymmetrization reactions of achiral precursors.[5] For instance, we have recently reported the formation of cyclic phosphinic amides catalyzed by chiral Cp^xRh^{III}-catalysts.[5g,6,7] This desymmetrization approach is only suitable for substrates containing the same two aromatic substituents with identical prochiral C–H groups, thus restricting the obtainable structural diversity. Notably, acyclic P-stereogenic phosphinic amides[8] are not accessible by this approach.

Herein, we report a flexible route to new trisubstituted Cp^x ligands. We showcase their potential for an enantioselective



Scheme 1 Rh^{III}-catalyzed desymmetrization and kinetic resolution approaches for the synthesis P-chiral compounds.



Scheme 2 Kinetic resolution by a difference in the cyclometalation rates $k_2 > k_5$.

Laboratory of Asymmetric Catalysis and Synthesis, EPFL SB ISIC LCSA, BCH 4305, CH-1015, Lausanne, Switzerland. E-mail: nicolai.cramer@epfl.ch

† Electronic supplementary information (ESI) available: Experimental procedures and characterisation of all new compounds. CCDC 1588292 and 1588293. For ESI and crystallographic data in CIF or other electronic format see DOI: 10.1039/c7sc05411d

Cp^xRh^{III}-catalyzed C–H functionalization of racemic phosphinic amides through a kinetic resolution[9] (Scheme 1). *s*-Factors of up to 50 were realized with the new tri-substituted Cp^x ligands, largely outperforming any previous Cp^x ligand.

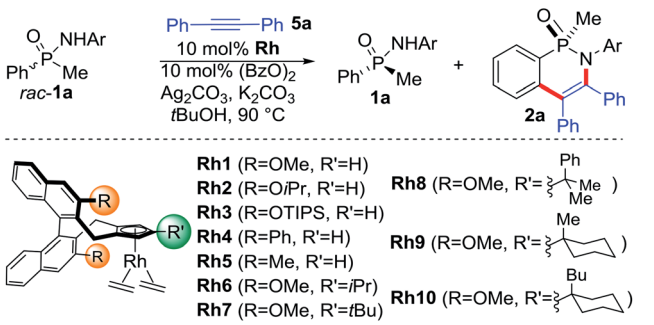
Conceptually, both acyclic starting material enantiomers can coordinate to the Cp^xRh^{III} catalyst forming diastereomeric intermediates **I** and **IV** (Scheme 2). In the subsequent – likely rate-limiting step of the process – the matching enantiomer would undergo C–H activation leading to rhodacycle **II** much faster than **IV** to **V**, corresponding to $k_2 \gg k_5$. Experimental support of this assumption consists in the absence of *ortho*-C-deuteration of unreacted starting material (see ESI† for details). Rhodacycle **II** can further react with alkyne *via* **III** to deliver cyclic phosphinic amide **2a**. The unreactive complex **IV** reverts back to the Rh^{III}-catalyst and substrate **1a**. Over time, the reacting enantiomer is removed from the starting material, get enriched over time.

Results and discussion

The initial feasibility of the kinetic resolution was explored with racemic phenyl methyl phosphinic amide *rac*-**1a** and diphenyl acetylene (Table 1). Complex **Rh1** with our standard second generation Cp^x ligand (R = OMe)[10a] caused a moderate rate difference in the reaction of the two starting material enantiomers, correlating to an *s*-factor of 14 (entry 1).[11,12] Cp^x ligands with other substitutions R[10] were largely inferior (entries 2–5). We hypothesized that a new trisubstituted Cp^x ligand class with increased bulk may enhance the selection between matched and mismatched substrate. These ligands are straightforward prepared from **L1** by condensation with a ketone forming the corresponding fulvenes **3** and **4** (Scheme 3).[13] Reduction of **3** with $LiAlH_4$ gave isopropyl-substituted ligand **L6**. X-ray crystallographic analysis of $[\mathbf{L6}RhCl_2]_2$ showed the orientation of the installed isopropyl group.[14] Moreover, facile addition of lithium organometallics across the fulvene double bond provided access to ligands **L7**-**L10** with bulky *tert*-butyl analogues as third Cp substituent. The corresponding rhodium complexes were subsequently evaluated for the kinetic resolution. In this respect, **Rh6** with an isopropyl group R′ largely improved the *s*-value to 32 (entry 6). **Rh7** featuring a larger *tert*-butyl group further improved the selectivity to an *s*-value of 42 (entry 7). **Rh8** and **Rh9** were slightly inferior (entries 8 and 9). **Rh10** featuring a 1-butylcyclohexyl group R′ allowed for a significant reduction in reaction time to 3 h maintaining a high *s* value of 41 (entry 10). Moreover, the amount of diphenyl acetylene could be lower to 0.6 equivalents, improving the selectivity further (entries 11–12).

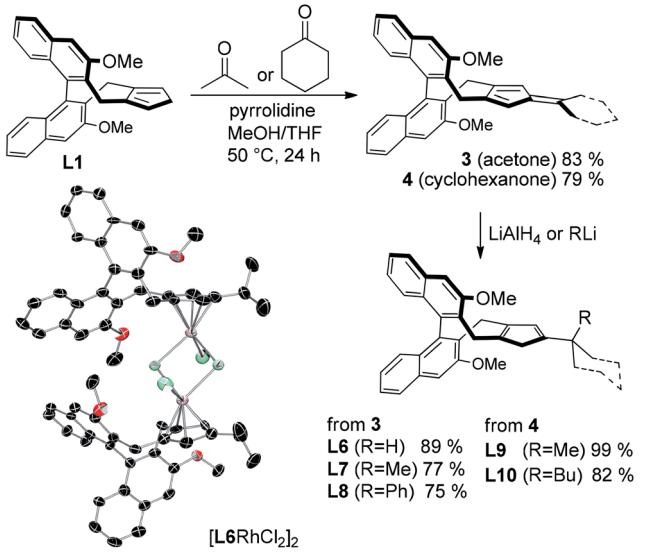
Next, the scope of the kinetic resolution procedure was evaluated (Table 2). Steric and electronic variations of R on the aryl group in the *para*- and *meta*-position had little influence on the reaction performance (entries 1–8). In all cases, the reaction of *rac*-**1a–1h** could be stopped at around 50% conversion. Both products were isolated in good to excellent enantioselectivities, resulting in *s*-values ranging from 26–50. An *ortho*-substituted aryl group (*rac*-**1i**) largely equalled the reaction rates of both starting material enantiomers and reduced the *s*-values. Besides variations of the aryl group, substituent R′ can be varied, maintaining synthetically useful selectivities (entries 10–11). In addition to phosphinic amides, we evaluated phosphonodiamidates *rac*-**1l** and *rac*-**1m** (entries 12–13) as well as phosphonamidate esters *rac*-**1n** and *rac*-**1o** towards the

Table 1 Screening of the Cp^x ligands for the kinetic resolution[a]



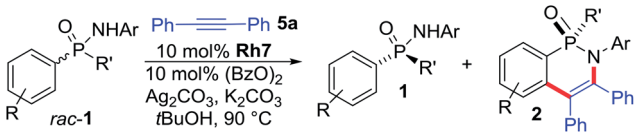
Entry	Rh	*T* [h]	% Conv.[b]	er **1a**[c] (% yield)	er **2a**[c] (% yield)	*s*
1	**Rh1**	8	54	91 : 9 (40)	85 : 15 (46)	14
2	**Rh2**	10	60	78 : 22 (35)	81 : 19 (46)	4
3	**Rh3**	32	30	63.5 : 36.5 (63)	84 : 16 (23)	4
4	**Rh4**	32	18	57 : 43 (78)	77 : 23 (17)	5
5	**Rh5**	32	54	68 : 32 (42)	76 : 24 (32)	3
6	**Rh6**	10	55	98 : 2 (42)	89 : 11 (48)	32
7	**Rh7**	8.5	51	95 : 5 (46)	93 : 7 (46)	42
8	**Rh8**	5	55	98.5 : 1.5 (42)	89 : 11 (50)	36
9	**Rh9**	3	53	96 : 4 (44)	90.5 : 9.5 (48)	32
10	**Rh10**	3	55	99 : 1 (42)	90.5 : 9.5 (48)	41
11[d]	**Rh7**	8.5	52	97 : 3 (44)	93 : 7 (48)	50
12[d]	**Rh10**	4	51	95.5 : 4.5 (46)	94 : 6 (46)	47

[a] Conditions: 50 μmol **1a**, 75 μmol **5a**, 5.0 μmol **Rh7**, 5.0 μmol $(BzO)_2$, 0.10 mmol Ag_2CO_3, 50 μmol K_2CO_3, 0.25 M in *t*BuOH at 90 °C for the indicated time; Ar = 3,5-$(CF_3)C_6H_3$. [b] By 1H-NMR. [c] By chiral HPLC, (isolated yield). [d] With 30 μmol **5a**.



Scheme 3 Synthesis of trisubstituted **L6**–**L10** from **L1**.

Table 2 Kinetic resolution of aryl phosphinic amides *rac*-**1**[a]



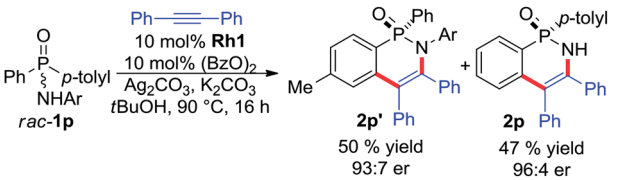
Entry	*rac*-**1**	R/R′	*T* [h]	Conv.[b] [%]	er **1**[c] (% yield)	er **2**[c] (% yield)	*s*
1	*rac*-**1a**	H/Me	8.5	51	95 : 5 (46)	93 : 7 (46)	42
2	*rac*-**1b**	4-Me/Me	10.5	55	98 : 2 (42)	89 : 11 (50)	32
3	*rac*-**1c**	4-F/Me	10.5	55	98 : 2 (40)	90 : 10 (48)	32
4	*rac*-**1d**	4-Cl/Me	10.5	55	97 : 3 (40)	89 : 11 (45)	29
5	*rac*-**1e**	4-OMe/Me	8.5	54	99 : 1 (42)	91 : 9 (48)	50
6	*rac*-**1f**	4-NMe_2/Me	9.5	42	83 : 17 (50)	95 : 5 (36)	43
7	*rac*-**1g**	3-Me/Me	10.5	58	99 : 1 (38)	85 : 15 (53)	26
8	*rac*-**1h**	3-Br/Me	14	55	99 : 1 (38)	91 : 9 (42)	49
9	*rac*-**1i**	2-Me/Me	10	53	79 : 21 (44)	77 : 23 (42)	5
10	*rac*-**1j**	H/Bn	4	59	99.5 : 0.5 (37)	84 : 16 (53)	27
11	*rac*-**1k**	H/$(CH_2)_2OBn$	6.5	51	93 : 7 (44)	93 : 7 (47)	29
12	*rac*-**1l**	H/pyrrolidinyl	5	57	89 : 11 (40)	79 : 21 (52)	9
13	*rac*-**1m**	H/morpholinyl	3.5	61	95 : 5 (37)	79 : 21 (55)	11
14[d]	*rac*-**1n**	H/OMe	24	60	97 : 3 (37)	81 : 19 (55)	15
15[d]	*rac*-**1o**	H/OPh	14	53	91 : 9 (44)	86 : 14 (48)	16

[a] Conditions: 0.10 mmol **1a**, 0.15 mmol **5a**, 10 μmol **Rh7**, 10 μmol $(BzO)_2$, 0.20 mmol Ag_2CO_3, 0.10 mmol K_2CO_3, 0.25 M in *t*BuOH at 90 °C; Ar = 3,5-$(CF_3)C_6H_3$. [b] By ^{1}H-NMR. [c] By chiral HPLC, (isolated yield). [d] At 70 °C.

resolutions conditions.[15] The additional hetero atom on the phosphorus center had only a weak influence on the reactivity, whereas the *s*-values were lower with the current ligand system.

The nature of alkyne **5** can be varied as well (Table 3). Whereas electron-rich diaryl alkyne **5b** reacted less selective, unsymmetrically substituted internal alkynes such as **5c**, **5d** and **5e** provided comparable selectivities. Moreover, they are incorporated in a highly regioselective manner, giving **2ac**, **2ad** and **2ae** with excellent regioselectivities.

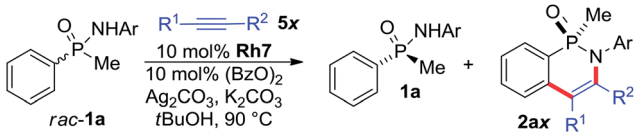
In addition, we have as well investigated racemic phosphinic amide substrate *rac*-**1p** having two different aryl groups (eqn (1)). In this case, a parallel kinetic resolution[16] becomes operative, yielding the two cyclic phosphinic amide products **2p** and **2p′** in excellent yield and good enantioselectivity.

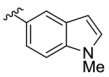


(1)

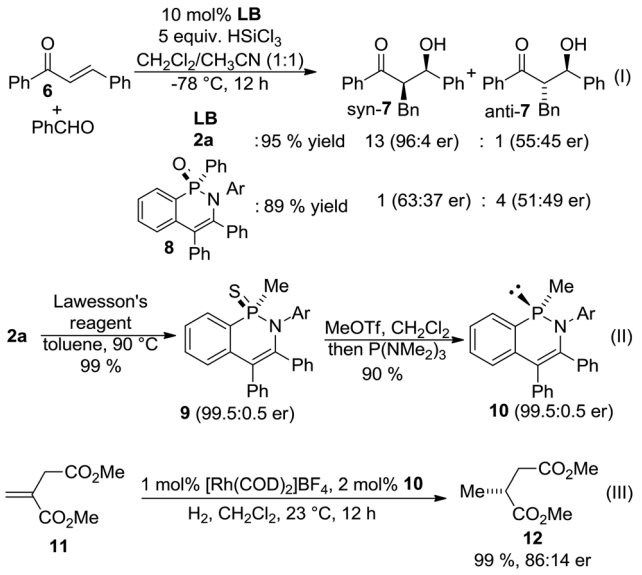
The P-chiral phosphinic amides were subsequently evaluated as chiral Lewis-bases in enantioselective reductive aldol

Table 3 Variation of the alkyne **5**[a]



Entry	**5x**	R^1	R^2	Conv.[b] [%]	er **1a**[c] (% yield)	er **2ax**[c] (% yield)	*s*
1	**5a**	Ph	Ph	51	95 : 5 (46)	93 : 7 (46)	42
2	**5b**	PMP	PMP	51	90 : 10 (46)	89 : 11 (46)	18
3	**5c**	Bu	PMP	50	94 : 6 (46)	95 : 5 (46)[d]	45
4	**5d**	iPr	PMP	43	82 : 18 (52)	94 : 6 (37)[e]	23
5	**5e**	Bu		54	98 : 2 (43)	96 : 4 (48)[e]	39

[a] Conditions: 0.10 mmol **1a**, 0.15 mmol **5a–d**, 10 μmol **Rh7**, 10 μmol $(BzO)_2$, 0.20 mmol Ag_2CO_3, 0.10 mmol K_2CO_3, 0.25 M in *t*BuOH at 90 °C for 8.5 h; Ar = 3,5-$(CF_3)C_6H_3$. [b] By ^{1}H-NMR. [c] By chiral HPLC, (isolated yield). [d] rs = 18 : 1. [e] rs ≥ 20 : 1.



Scheme 4 (I) Comparison of phosphinamides **2a** and **8** in enantioselective reductive aldol reactions. (II) Enantiospecific reduction of **2a** (**2a**: >99.5 : 0.5 er). (III) Rh-catalyzed asymmetric hydrogenation with **10** as chiral ligand.

additions[17] between enone **6** and benzaldehyde (Scheme 4). Aldol adduct *syn*-**7** was obtained in 96 : 4 er with 13 : 1 *syn*/*anti* ratio using methyl-substituted **2a** as the catalyst. In stark contrast, related phenyl-substituted phosphinic amide **8** obtained by the previous desymmetrization method[5g] provided isomer *anti*-**7** preferentially (1 : 4 *syn*/*anti*), with almost no enantioselectivity. Moreover, an enantiospecific access to corresponding P^{III}-compound was achieved by transfer reduction with $P(NMe_2)_3$ *via* its thiophosphinic amide **9**,[18] providing **10** in 90% yield and 99.5: 0.5 er with retention of the configuration. Subsequent use of **10** as a ligand in rhodium catalyzed asymmetric hydrogenation[19] of **11** provided reduced product **12** in 99% yield and 86 : 14 er.

Conclusions

In summary, we have developed a new trisubstituted Cp^x ligand family. Based on our atropchiral Cp^x ligand scaffold, we have shown that the introduction of a bulky third substituent at the central position of the Cp ring leads to substantially increased selectivities for kinetic resolutions and allowed for *s*-factors of up to 50. The superiority of them are showcased by kinetic resolutions amides providing access to compounds with stereogenic phosphorus(v) atoms. The ligand synthesis capitalizes on a late stage modification and expands the accessible ligand Cp^x ligand portfolio for further catalytic-enantioselective transformations with additional metals.

Conflicts of interest

There are no conflicts of interest to declare.

Acknowledgements

This work is supported by the Swiss National Science Foundation (no 157741). We thank Dr R. Scopelliti and Dr F. Fadaei Tirani for X-ray crystallographic analysis of compounds $[\mathbf{L6}RhCl_2]_2$ and (*S*)-**1a**.

Notes and references

1 (*a*) *P-Stereogenic Ligands in Enantioselective Catalysis* ed. A. Grabulosa, RSC, Cambridge, 2011; (*b*) *Phosphorus(III) Ligands in Homogeneous Catalysis: Design and Synthesis*, ed. P. C. J. Kamer and P. W. N. M. v. Leeuwen, Wiley, Hoboken, 2012.

2 (*a*) S. E. Denmark and G. L. Beutner, *Angew. Chem., Int. Ed.*, 2008, **47**, 1560; (*b*) Phosphorus Chemistry I: Asymmetric Synthesis and Bioactive Compounds, *Top. Curr. Chem.*, ed. J. L. Montchamp, 2015, vol. 360; (*c*) U. Pradere, E. C. Garnier-Amblard, S. J. Coats, F. Amblard and R. F. Schinazi, *Chem. Rev.*, 2014, **114**, 9154.

3 Recent overviews: (*a*) D. S. Glueck, *Chem.–Eur. J.*, 2008, **14**, 7108; (*b*) J. S. Harvey and V. Gouverneur, *Chem. Commun.*, 2010, **46**, 7477; (*c*) M. Dutarte, J. Bayardon and S. Jugé, *Chem. Soc. Rev.*, 2016, **45**, 5771; (*d*) *Asymmetric Synthesis in Organophosphorus Chemistry*, ed. O. I. Kolodiazhnyi, Wiley-VCH, Weinheim, 2016; selected examples: chiral auxilliary-based: (*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. J. Song, G. Wang and C. H. Senanayake, *J. Am. Chem. Soc.*, 2013, **135**, 2474; desymmetrization with a chiral base: (*f*) J. J. Gammon, V. H. Gessner, G. R. Barker, J. Granander, A. C. Whitwood, C. Strohmann, P. O'Brien and B. Kelly, *J. Am. Chem. Soc.*, 2010, **132**, 13922; desymmetrization of enantiotopic alkyne groups: (*g*) G. Nishida, K. Noguchi, M. Hirano and K. Tanaka, *Angew. Chem., Int. Ed.*, 2008, **47**, 3410; organocatalytic esterification of enantiotopic phenols: (*h*) Z. Huang, X. Huang, B. Li, C. Mou, S. Yang, B.-A. Song and Y. R. Chi, *J. Am. Chem. Soc.*, 2016, **138**, 7524; enantioselective addition to secondary phosphines and phosphine oxides: (*i*) C. Scriban and D. S. Glueck, *J. Am. Chem. Soc.*, 2006, **128**, 2788; (*j*) V. S. Chan, M. Chiu, R. G. Bergman and F. D. Toste, *J. Am. Chem. Soc.*, 2009, **131**, 6021; (*k*) Y. Huang, Y. Li, P.-H. Leung and T. Hayashi, *J. Am. Chem. Soc.*, 2014, **136**, 4865; (*l*) R. Beaud, R. J. Phipps and M. J. Gaunt, *J. Am. Chem. Soc.*, 2016, **138**, 13183.

4 (*a*) R. Giri, B.-F. Shi, K. M. Engle, N. Maugel and J.-Q. Yu, *Chem. Soc. Rev.*, 2009, **38**, 3242; (*b*) J. Wencel-Delord and F. Colobert, *Chem.–Eur. J.*, 2013, **19**, 14010; (*c*) C. Zheng and S.-L. You, *RSC Adv.*, 2014, **4**, 6173; (*d*) *Asymmetric Functionalization of C–H Bonds*, ed. S.-L. You, RSC, Cambridge, 2015; (*e*) C. G. Newton, S.-G. Wang, C. C. Oliveira and N. Cramer, *Chem. Rev.*, 2017, **117**, 8908.

5 (*a*) Z.-Q. Lin, W.-Z. Wang, S.-B. Yan and W.-L. Duan, *Angew. Chem., Int. Ed.*, 2015, **54**, 6265; (*b*) L. Liu, A.-A. Zhang, Y. Wang, F. Zhang, Z. Zuo, W.-X. Zhao, C.-L. Feng and

W. Ma, *Org. Lett.*, 2015, **17**, 2046; (*c*) G. Xu, M. Li, S. Wang and W. Tang, *Org. Chem. Front.*, 2015, **2**, 1342; (*d*) Z.-J. Du, J. Guan, G.-J. Wu, P. Xu, L.-X. Gao and F.-S. Han, *J. Am. Chem. Soc.*, 2015, **137**, 632; (*e*) D. Gwona, S. Park and S. Chang, *Tetrahedron*, 2015, **71**, 4504; (*f*) T. T. Nguyen, L. Grigorjeva and O. Daugulis, *ACS Catal.*, 2016, **6**, 551; (*g*) Y. Sun and N. Cramer, *Angew. Chem., Int. Ed.*, 2017, **56**, 364; (*h*) Y.-S. Jang, M. Dieckmann and N. Cramer, *Angew. Chem., Int. Ed.*, 2017, **56**, 15088.

6 Seminal work and overviews of chiral Cp^x-metal catalyst for asymmetric C–H functionalization: (*a*) T. K. Hyster, L. Knörr, T. R. Ward and T. Rovis, *Science*, 2012, **338**, 500; (*b*) B. Ye and N. Cramer, *Science*, 2012, **338**, 504; (*c*) B. Ye and N. Cramer, *Acc. Chem. Res.*, 2015, **48**, 1308; (*d*) C. G. Newton, D. Kossler and N. Cramer, *J. Am. Chem. Soc.*, 2016, **138**, 3935.

7 Recent examples of catalytic applications in Rh-catalysis: (*a*) B. Ye, P. A. Donets and N. Cramer, *Angew. Chem., Int. Ed.*, 2014, **53**, 507; (*b*) B. Ye and N. Cramer, *Angew. Chem., Int. Ed.*, 2014, **53**, 7896; (*c*) J. Zheng and S.-L. You, *Angew. Chem., Int. Ed.*, 2014, **53**, 13244; (*d*) J. Zheng, S.-B. Wang, C. Zheng and S.-L. You, *J. Am. Chem. Soc.*, 2015, **137**, 4880; (*e*) S. R. Chidipudi, D. J. Burns, I. Khan and H. W. Lam, *Angew. Chem., Int. Ed.*, 2015, **54**, 13975; (*f*) M. V. Pham and N. Cramer, *Chem.–Eur. J.*, 2016, **22**, 2270; (*g*) J. Zheng, W.-J. Cui, C. Zheng and S.-L. You, *J. Am. Chem. Soc.*, 2016, **138**, 5242; (*h*) J. Zheng, S.-B. Wang, C. Zheng and S.-L. You, *Angew. Chem., Int. Ed.*, 2017, **56**, 4540; (*i*) Z.-J. Jia, C. Merten, R. Gontla, C. G. Daniliuc, A. P. Antonchick and H. Waldmann, *Angew. Chem., Int. Ed.*, 2017, **56**, 2429; (*j*) G. Smits, B. Audic, M. D. Wodrich, C. Corminboeuf and N. Cramer, *Chem. Sci.*, 2017, **8**, 7174.

8 For the pharmaceutical relevance of acyclic P-stereogenic compounds, see: (*a*) S. Pikul, K. L. McDow Dunham, N. G. Almstead, B. De, M. G. Natchus, M. V. Anastasio, S. J. McPhail, C. E. Snider, Y. O. Taiwo, L. Chen, C. M. Dunaway, F. Gu and G. E. Mieling, *J. Med. Chem.*, 1999, **42**, 87; (*b*) M. J. Sofia, D. Bao, W. Chang, J. Du, D. Nagarathnam, S. Rachakonda, P. G. Reddy, B. S. Ross, P. Wang, H. R. Zhang, *et al.*, *J. Med. Chem.*, 2010, **53**, 7202; (*c*) F.-R. Alexandre, A. Amador, S. Bot, C. Caillet, T. Convard, J. Jakubik, C. Musiu, B. Poddesu, L. Vargiu, M. Liuzzi, A. Roland, M. Seifer, D. standring, R. storer and C. B. Dousson, *J. Med. Chem.*, 2011, **54**, 392; (*d*) D. A. DiRocco, Y. Ji, E. C. Sherer, A. Klapars, M. Reibarkh, J. Dropinski, R. Mathew, P. Maligres, A. M. Hyde, J. Limanto, A. Brunskill, R. T. Ruck, L. C. Campeau and I. W. Davies, *Science*, 2017, **356**, 426.

9 Recent examples in C–H functionalization: (*a*) C. González-Rodríguez, S. R. Parsons, A. L. Thompson and M. C. Willis, *Chem.–Eur. J.*, 2010, **16**, 10950; (*b*) D.-W. Gao, Q. Gu and S.-L. You, *ACS Catal.*, 2014, **4**, 2741; (*c*) L. Chu, K.-J. Xiao and J.-Q. Yu, *Science*, 2014, **346**, 451; (*d*) K.-J. Xiao, L. Chu, G. Chen and J.-Q. Yu, *J. Am. Chem. Soc.*, 2016, **138**, 7796; (*e*) K. J. Xiao, L. Chu and J.-Q. Yu, *Angew. Chem., Int. Ed.*, 2016, **55**, 2856.

10 (*a*) B. Ye and N. Cramer, *J. Am. Chem. Soc.*, 2013, **135**, 636; (*b*) B. Ye and N. Cramer, *Synlett*, 2015, **26**, 1490; (*c*) D. Kossler and N. Cramer, *Chem. Sci.*, 2017, **8**, 1862.

11 Definition *s*-factor: $s = \ln[(1 - c)(1 - ee)]/\ln[(1 - c)(1 + ee)]$ (c: conversion; ee: recovered substrate' see).

12 The absolute configuration of recovered **1a** was determined to be (*S*) by X-ray-crystallographic analysis.

13 N. Cokun and I. Erden, *Tetrahedron*, 2011, **67**, 8607.

14 CCDC 1588292 ((*S*)-**1a**) and 1588293 ($[\mathbf{L6}RhCl_2]_2$) contain the supplementary crystallographic data for this paper.†

15 For examples of the biological properties of these P(V)-compounds, see: (*a*) M. Sawa, T. Kiyoi, K. Kurokawa, H. Kumihara, M. Yamamoto, T. Miyasaka, Y. Ito, R. Hirayama, T. Inoue, Y. Kirii, E. Nishiwaki, H. Ohnoto, Y. Maeda, F. Ishibushi, Y. Inoae, K. Yoshino and H. Kondo, *J. Med. Chem.*, 2002, **45**, 919; (*b*) G. Ruiz-Gómez, A. Francesch, M. J. Iglesias, F. López-Ortiz, C. Cuevas and M. Serrano-Ruiz, *Org. Lett.*, 2008, **10**, 3981.

16 For a review, see: (*a*) J. R. Dehli and V. Gotor, *Chem. Soc. Rev.*, 2002, **31**, 365; for selected recent examples in C–H functionalization: (*b*) K. Tanaka and G. C. Fu, *J. Am. Chem. Soc.*, 2003, **125**, 8078; (*c*) D. Katayev, M. Nakanishi, T. Bürgi and E. P. Kündig, *Chem. Sci.*, 2012, **3**, 1422; (*d*) T. Lee, T. W. Wilson, R. Berg, P. Ryberg and J. F. Hartwig, *J. Am. Chem. Soc.*, 2015, **137**, 6742; (*e*) D. Grosheva and N. Cramer, *ACS Catal.*, 2017, **7**, 7417; (*f*) J. Pedroni and N. Cramer, *J. Am. Chem. Soc.*, 2017, **139**, 12398.

17 M. Sugiura, N. Sato, Y. Sonoda, S. Kotani and M. Nakajima, *Chem.–Asian J.*, 2010, **5**, 478.

18 Y.-H. Chen, X.-L. Qin and F.-S. Han, *Chem. Commun.*, 2017, **53**, 5826.

19 T. Jerphagnon, J.-L. Renaud and C. Bruneau, *Tetrahedron: Asymmetry*, 2004, **15**, 2101.