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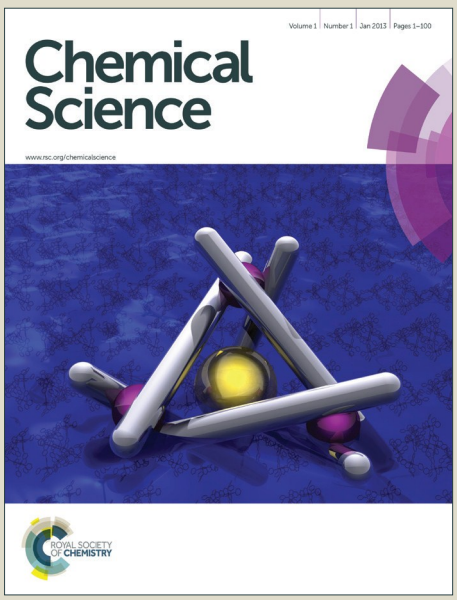

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EDGE ARTICLE

A Supramolecularly Tunable Chiral Diphosphine Ligand: Application to Rh and Ir-Catalyzed Enantioselective Hydrogenation

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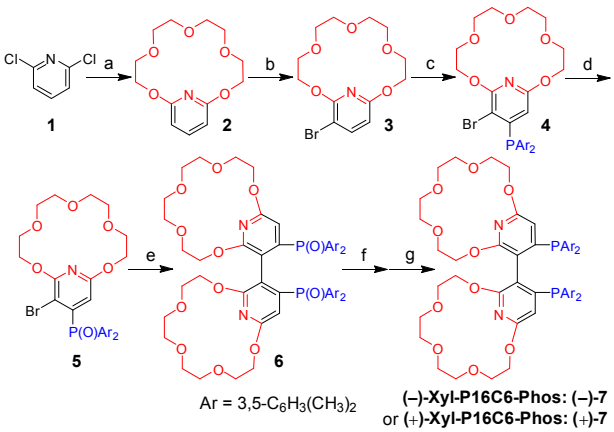
A supramolecularly tunable chiral bisphosphine ligand bearing two pyridyl-containing crown ethers, (–) or (+)-Xyl-P16C6-Phos was fabricated and utilized in the Rh-catalyzed asymmetric hydrogenation of α-dehydroamino acid esters and Ir-catalyzed asymmetric hydrogenation of quinolines in high yields with excellent enantioselectivities (90–99% ee). Up to 22% enhancement in enantioselectivities was achieved by the addition of certain amounts of alkali ions (Li^+, Na^+ or K^+), which could be selectively recognized and effectively complexed by the crown ethers on chiral Xyl-P16C6-Phos.

Introduction

The design and synthesis of new chiral ligands plays a pivotal role in the field of transition metal-catalyzed asymmetric reactions.[1] It is well known that the performance of transition metal catalysts can be remarkably affected by the subtle variations in either geometric or electronic properties of chiral ligands. For instance, when chiral atropisomeric diphosphines[2] are used as ligands, without altering the backbone structure, the catalytic properties can be tuned by attaching various P-substituents. Another strategy is the development of diphosphine ligands with adjustable dihedral angles,[2d,2e,3] such as *o*-Ph-hexaMeO-BIPHEP,[4] Cn-TunaPhos[5] and PQ-Phos,[6] for different substrates or reactions. Although good-to-excellent results were obtained in some asymmetric catalytic reactions, these ligands often required individual and unique syntheses and thus are not really tunable by simply changing the catalytic reaction conditions.

In the past decade, supramolecular chiral catalysis has attracted the growing attention and exhibited the fascination in both forming catalyst libraries and mimicking enzymes to achieve unexpected activities and stereoselectivities in relevant reactions.[7] Some elegant supramolecular or combinatorial chiral catalyst systems have been designed, such as the self-assembled bidentate ligands via intermolecular hydrogen bonding,[8] ion pair catalysts,[9] Co(II)-salen with a hydrogen-bonding network,[10] the bidentate ligands based on Zn(II) porphyrins,[11] Zn(II) salphen[12] or $Zn(box)_2$ complexes[13] via metal-ligand interactions, the supramolecular ligands based on a crown-ether appended phosphate or phosphoramidite skeleton,[14,15] the bisphosphite ligands with oligo(ethylene-glycol) as backbone,[16] as well as self-supported chiral catalysts with coordination polymer frameworks.[17]

Employing supramolecular methods to impart tunable conformations, steric bulk and electronic properties to a given atropisomeric diphosphine is conceptually appealing since it could avoid aforementioned individual tedious procedures associated with traditional syntheses of covalent bonds for acquiring enantiomerically pure ligands. To the best of our knowledge, examples for tunable ligands or catalysts illustrating this concept remained rare. Herein, we describe our research on introducing crown ethers, as host sites for



Scheme 1 Synthesis of (–) or (+)-Xyl-P16C6-Phos (**7**). Reagents and conditions: (a) tetraethylene glycol, NaH, KPF_6, THF, reflux, 65% yield; (b) NBS, CH_2Cl_2, –78 °C, 85% yield; (c) LDA, THF, then $(3,5\text{-}Me_2C_6H_3)_2PCl$, –78 °C, 73% yield; (d) H_2O_2, acetone, 0 °C, 85% yield; (e) Cu, DMF, 140 °C, 50% yield; (f) i. (*L* or *D*)-DBTA, EtOAc/$CHCl_3$; ii. NaOH aq; 54–55% yield for two steps; (g) $HSiCl_3$, Et_3N, toluene, reflux, 87% yield for (–)-**7**, 91% yield for (+)-**7**.

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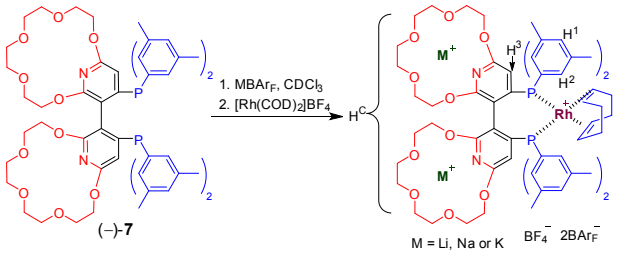
recognition, to the scaffold of a well-established chiral dipyridylphosphine ligand Xyl-P-Phos[2c, 18, 19] to form new ligands, (–) or (+)-Xyl-P16C6-Phos ((–) or (+)-**7**, Scheme 1). Utilizing the selective recognition and strong complexation between the crown ethers on **7** and different alkali cations,[20] supramolecularly tunable chiral catalysts (Scheme 2) have been constructed and applied in both the Rh-catalyzed asymmetric hydrogenation of α-dehydroamino acid derivatives and the Ir-catalyzed asymmetric hydrogenation of quinolines.

Results and discussion

The new ligand Xyl-P16C6-Phos (**7**) was synthesized as shown in Scheme 1.[18] The cyclization of tetraethylene glycol and 2,6-dichloropyridine (**1**) afforded 2,6-pyrido-16-crown-6 (**2**), which was then brominated to yield **3**. The regioselective lithiation of **3** followed by the substitution with di(3,5-dimethylphenyl)phosphine chloride produced **4** in 73% yield. The oxidation of **4** furnished **5**, which was further converted to the racemic diphosphine oxide **6** via the copper-mediated Ullman coupling protocol. The resolution of racemate (±)-**6** was realized by the use of (*D*) or (*L*)-*O,O'*-dibenzoyltartaric acid (DBTA). The enantiomerically pure (–) or (+)-**6** was then reduced to the targeted atropisomeric ligand (–) or (+)-**7**, respectively.



Scheme 2 Preparation of Rh complexes with alkali ions.

With the new, crown ether-attached chiral diphosphine ligand **7** in hand, the complexation of (–)-**7** with alkali ions and coordination with $[Rh(COD)_2]BF_4$ (Scheme 2) were systematically investigated by ^1H and ^{31}P NMR spectra. As compared with the ^1H NMR spectrum of (–)-**7** (Figure 1a), the spectra of [(–)-**7** + $[Rh(COD)_2]BF_4$] (Figure 1b) and [(–)-**7** + $[Rh(COD)_2]BF_4$ + $MBAr_F$ (M= Li, Na or K, BAr_F^- = $(3,5\text{-}(CF_3)_2C_6H_3)_4B^-$)] (Figure 1c–e) displayed significant differences in either chemical shifts or peak shapes. After coordination with $[Rh(COD)_2]BF_4$, the signal of protons H^3 on the pyridyl shifted downfield sharply (Figure 1b vs 1a). Upon further binding alkali ions, the chemical shift of H^3 changed slightly (Figures 1c–e vs 1b), while the signals of oxyethylene protons (H^c) changed as expected (Figures 1c–e vs 1a and 1b), owing to the complexation between crown ethers and alkali ions. The peaks of the oxyethylene protons exhibited marginal differences due to the effects of the different sizes and electronic properties of alkali ions. The ^{31}P NMR spectra also showed substantial shifts upon coordination of (–)-**7** with $[Rh(COD)_2]BF_4$ (Supporting Information, Figure S1). The lone singlet peak of free ligand split into a doublet due to the coupling between Rh-P (Figures S1b–e vs S1a). The obvious changes of both chemical shift and peak shapes in the ^1H NMR spectra of [(–)-**7** + $NaBAr_F$] also directly confirmed the complexation between (–)-**7** and alkali ions (Figure S2c vs S2a). Moreover, with the molar ratio of NaBArF to ligand increased from 1:1 to 10:1, the ^1H NMR peaks of oxyethylene protons and ^{31}P NMR spectra did not show distinct changes (Figures S2e–g vs S2d, Figures S3e and S3f vs S3d). Additionally, the stoichiometries of the complexations of (±)-**7** with $LiBAr_F$ and (±)-**6** with $NaBAr_F$ or $KBAr_F$ in solution were all determined to be 1:2 by Job plots using proton NMR data (Figure S4–S6). This binding ratio was further confirmed by low-resolution electrospray ionization mass spectroscopy (Figure S7–S9).

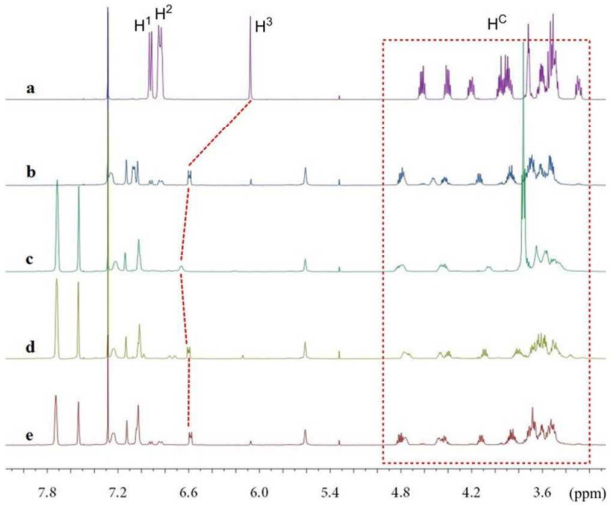


Fig 1 Partial ^1H NMR (500 MHz, $CDCl_3$) spectra of (a) (–)-**7**; (b) (–)-**7** + $[Rh(COD)_2]BF_4$ (1:1 molar ratio); (c) (–)-**7** + $[Rh(COD)_2]BF_4$ + $LiBAr_F$(1:1:2 molar ratio); (d) (–)-**7** + $[Rh(COD)_2]BF_4$ + $NaBAr_F$ (1:1:2 molar ratio); (e) (–)-**7** + $[Rh(COD)_2]BF_4$ + $KBAr_F$ (1:1:2 molar ratio).

After the self-assembled chiral Rh complexes of **7** were prepared, these complexes were applied as catalysts for the asymmetric hydrogenation of α-dehydroamino acid derivatives to assess the host-guest effect between alkali ions and crown ethers on the catalytic reactions. The $[Rh((–)\text{-}7)(COD)]BF_4$ complex was an effective catalyst for the enantioselective hydrogenation of model substrate methyl-(*Z*)-2-acetamido-cinnamate (**8a**). The reaction proceeded smoothly in CH_2Cl_2 at ambient temperature with 1 atm of initial H_2 pressure for 6 h, resulting in full conversion to the chiral product (*R*)-**9a** with 82% ee (Table 1, entry 1).

Interestingly, the addition of certain amounts of alkali salts $MBAr_F$ (M = Li, Na, K) as guests for the crown ethers on **7** had an obviously beneficial influence on the enantioselectivities of catalysts while no abate in activities was observed (Table 1, entries 3–10 vs entry 1). Na^+ or K^+ appeared to be the preferred choice of cationic additives in terms of enantioselectivities (entries 4, 5, 8 and 9 vs entries 6 and 7). Elevated ratios of alkali salts to (–)-**7** facilitated an enhancement in the enantiomeric purity of the product

(entries 4 and 5 vs entry 3, entry 9 vs entry 8). Finally, upon increasing the $NaBAr_F$ loading to 10 mol %, 93% ee was achieved (entry 10). The lower reaction temperature (0 °C) did not render a higher ee (entry 11 vs entry 10). Next, when using 10 mol % of Na^+ as guest, various counter-ions were tested and the results indicated that the presence of sterically bulker and more weakly coordinating anion BAr_F^- possessed superior levels of activity and asymmetric induction to those of BF_4^- and PF_6^- (entries 12 and 13 vs entry 10), probably owing to the impact of anions on the complexation between crown ethers and Na^+.

Table 1 Effect of additives on Rh-catalyzed asymmetric hydrogenation of methyl-(*Z*)-2-acetamidocinnamate **8a**.[a]

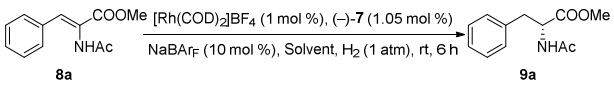
Entry	Additive [mol %]	Conv [%][b]	ee [%][c]
1	none	>99	82
2[d]	none	>99	88
3	$NaBAr_F$ (1)	>99	84
4	$NaBAr_F$ (2)	>99	88
5	$NaBAr_F$ (5)	>99	91
6	$LiBAr_F$ (2)	>99	84
7	$LiBAr_F$ (5)	>99	84
8	$KBAr_F$ (2)	>99	86
9	$KBAr_F$ (5)	>99	90
10	$NaBAr_F$ (10)	>99	93
11[e]	$NaBAr_F$ (10)	>99	93
12	$NaBF_4$ (10)	68	81
13	$NaPF_6$ (10)	96	83
14	$(nBu)_4NBAr_F$ (10)	91	84
15[d]	$NaBAr_F$ (10)	>99	88

[a] Reaction conditions: 0.05–0.09 mol•L^{-1} in CH_2Cl_2. [b] The conversions were determined by NMR and GC analysis. [c] The ee values were determined by chiral GC analysis. [d] (*S*)-Xyl-P-Phos was used as ligand. [e] The reaction was carried out at 0 °C.

It is well-known that the counter-ions may affect the outcomes of transition metal-mediated asymmetric reactons.[19b, 21] In order to investigate the contribution of anions on the present catalytic system, $(nBu)_4NBAr_F$ was used as a controlled additive (Table 1, entry 14), wherein the much more sterically demanding $(nBu)_4N^+$ cation could not complex with the pyridyl-containing crown ethers. When replacing Na^+ with $(nBu)_4N^+$ cation, only a slight increase in ee was observed (entry 14 vs entry 1), which demonstrated that the host–guest interaction between (–)-**7** and alkali ions played a crucial role on the increase of stereoselectivities. Additionally, a side by side comparison study showed that either cationic or anionic additives had no pronounced effect on the reaction outcomes in the case of (*S*)-Xyl-P-Phos as the chiral ligand (entry 15 vs entry 2).

Moreover, the present self-assembled catalyst system was strongly solvent-dependent (Table 2) and nonpolar *c*-hexane was much more conductive in either reactivity or enantioselectivity than other solvents, such as CH_2Cl_2, MeOH and THF. Thus, 97% ee and full conversion were attained when the reaction was carried out in *c*-hexane (Table 2, entry 8), probably due to the stronger association between Na^+ and (–)-**7** in nonpolar solvents. In the absence of alkali additives, (*R*)-**9a** was furnished in 82% conversion with only 77% ee (Table 2, entry 9 vs entry 8) in *c*-hexane under otherwise identical reaction conditions, which furtherly confirmed the impact of the host-guest interaction between Na^+ cations and crown ethers on the asymmetric induction.

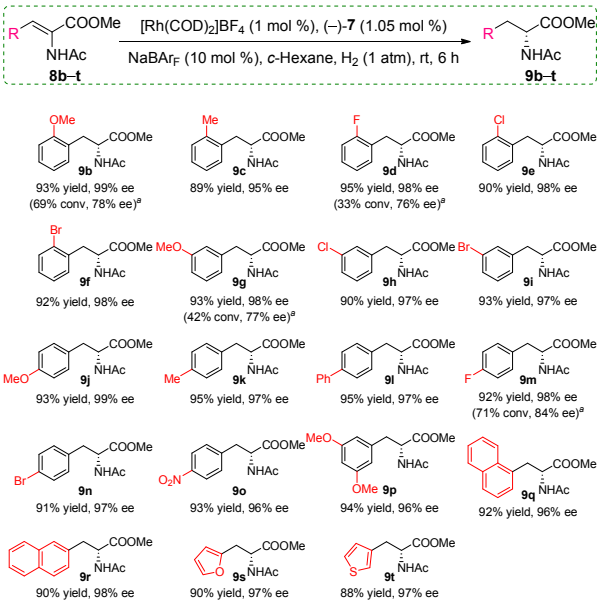
Table 2 The effect of solvent on the Rh-catalyzed asymmetric hydrogenation of methyl-(*Z*)-2-acetamidocinnamate **8a**.[a]



8a 9a

Entry	Solvent	Conv [%][b]	ee [%][c]
1	CH_2Cl_2	>99	93
2	Acetone	<2	n.d.[d]
3	MeOH	<10	n.d.[d]
4	Toluene	>99	96
5	THF	>99	90
6	Ethyl acetate	>99	90
7	*n*-Hexane	97	96
8[e]	*c*-Hexane	>99	97
9[f]	*c*-Hexane	82	77

[a] Reaction conditions: 0.05–0.09 mol•L^{-1} in solvent. [b] The conversions were determined by NMR and GC analysis. [c] The ee values were determined by chiral GC analysis. The absolute configuration was determined by comparing the retention times with the known data. [d] n.d. = not determined. [e] The isolated yield was 94%. [f] No $NaBAr_F$ was added.



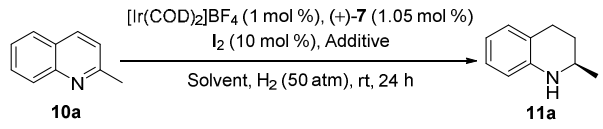
Scheme 3 Asymmetric hydrogenation of α-dehydroamino acid esters **8b–t** with the self-assembled chiral Rh catalyst. Reaction conditions: 0.05–0.09 mol•L^{-1} in *c*-hexane; >99% conversions were observed in all cases. [a] No $NaBAr_F$ was added.

Having identified the optimized conditions, we set out to evaluate the general applicability of the self-assembled catalyst. As the findings in Scheme 3 depicted, the asymmetric hydrogenation of a wide assortment of α-dehydroamino acid esters **8b–t** proceeded to afford desired products **9b–t** neatly

in *c*-hexane under 1 atm of H_2 at room temperature with excellent catalytic activities and enantioselectivities (95–99% ee). These results showed that the present supramolecular catalyst system was rather competitive by comparison with similar catalytic systems.[16a,16c,19a] Further comparison between catalysts with or without the alkali salts for a few selected substrates indicated that only poor or moderate conversions and enantioselectivities were acquired when no $NaBAr_F$ was added (Scheme 3, **9b**, **9d**, **9g**, and **9m**). For example, in the absence of Na^+ as additives, **8d** was hydrogenated to (*R*)-**9d** in only 33% conversion with 76% ee. Whereas, full conversion and up to 22% enhancement in ee were achieved when 10 mol % $NaBAr_F$ was added under otherwise identical conditions (Scheme 3).

Optically active tetrahydroquinoline derivatives are important synthetic intermediates and structural units for some natural products and biologically active compounds.[22] The enantioselective hydrogenation of heteroaromatic compounds is a great challenge as harsh reaction conditions are usually necessary to overcome the aromaticity of the substrates. Although the asymmetric hydrogenation of aromatic compounds has been explored since 1987,[23] there are but several elegant catalytic systems with high activity and enantioselectivity.[24] As such, we were interested in the extension of our self-assembled catalyst design to the Ir-catalyzed asymmetric hydrogenation of substituted quinolines (Table 3 and Table 4).

Table 3: The effects of solvent and alkali ion on the Ir-catalyzed asymmetric hydrogenation of 2-methylquinoline **10a**.[a]

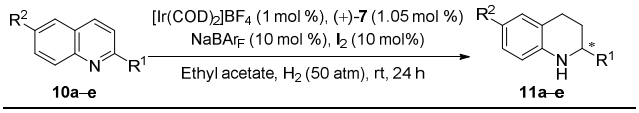


Entry	Solvent	Additive [mol %]	Conv [%][b]	ee [%][c]
1	*c*-Hexane	$NaBAr_F$ (10)	37	93
2	CH_2Cl_2	$NaBAr_F$ (10)	87	95
3	Ethyl acetate	$NaBAr_F$ (10)	98[d]	97
4	Ethyl acetate	None	97	87

[a] Reaction conditions: 0.2 mol•L^{-1} in solvent. [b] The conversions were determined by NMR and GC analysis. [c] The ee values were determined by chiral HPLC analysis and the absolute configuration was determined by comparing the rotation sign with the literature data. [d] The isolated yield was 96%.

As the data in entry 3 of Table 3 indicated, when the model substrate 2-methylquinoline (**10a**) was submitted to the self-assembled Ir catalyst generated from $[Ir(COD)_2]BF_4$, (+)-**7** and $NaBAr_F$ (1:1:10 molar ratio, Figure S10 and S11), the hydrogenation was completed in ethyl acetate in the presence of 10 mol % of I_2 under 50 atm of H_2 at ambient temperature in 24 h to furnish the chiral product in 96% yield and 97% ee, which were superior to those obtainable in the case of other solvents, such as *c*-hexane and CH_2Cl_2 (entry 3 vs entries 1 and 2). In contrast, 87% ee was obtained if no $NaBAr_F$ was added (entry 4 vs entry 3). Further investigations (Table 4) showed that the present self-assembled Ir catalyst system gave rise to the formation of chiral tetrahydroquinolines **11b–e** of high optical purities (90–97% ee*)* in quantitative yields (96–98%).

Table 4: Asymmetric hydrogenation of substituted quinolines **10a–e** with the self-assembled chiral Ir catalyst.[a]



Entry	R^2/R^1 (substrate)	Yield [%][b]	ee [%][c]
1	H/*n*-Pr (**10b**)	98	97 (*R*)
2	H/*n*-Bu (**10c**)	97	96 (*R*)
3	H/*n*-Pentyl (**10d**)	97	96 (*R*)
4	F/Me (**10e**)	96	90 (*R*)

[a] Reaction conditions: 0.2 mol•L^{-1} in ethyl acetate. [b] Isolated yields. [c] The ee values were determined by chiral HPLC analysis.

Conclusions

In conclusion, a supramolecularly tunable chiral bisphosphine ligand bearing two pyridyl-containing crown ethers, (–) or (+)-Xyl-P16C6-Phos was synthesized and successfully applied in the Rh-catalyzed asymmetric hydrogenation of α-dehydroamino acid esters and Ir-catalyzed asymmetric hydrogenation of quinolines, in the presence of certain amounts of alkali ion, in quantitative yields and with excellent enantioselectivities (90–99% ee). By finely regulating the host-guest interactions between the crown ethers of the chiral ligand and the alkali ion additives, up to 22% enhancement in enantioselectivities was achieved in comparison with those obtainable from the catalyst systems in the absence of crown ether/alkali-metal ions recognition motifs. Studies aimed at elucidating the reaction mechanism and expanding these supramolecular catalysts to other asymmetric reactions are in progress in our laboratory.

Acknowledgements

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Notes and references

1 (*a*) *Asymmetric Catalysis in Organic Synthesis*, ed. R. Noyori, Wiley, New York, 1994; (*b*) *Comprehensive Asymmetric Catalysis*, ed. E. N. Jacobsen, A. Pfaltz, H. Yamamoto, Springer, Berlin, Germany, 1999; (*c*) G. Q. Lin, Y. M. Li and A. S. C. Chan, *Principles and Applications of Asymmetric*

Synthesis, Wiley & Sons, New York, 2001; (*d*) *Catalytic Asymmetric Synthesis, 3rd ed.*, ed. I. Ojima, John Wiley & Sons, New Jersey, 2010.

2 For some reviews, see: (*a*) W. Tang and X. Zhang, *Chem. Rev.*, 2003, **103**, 3029–3070; (*b*) H. Shimizu, I. Nagasaki and T. Saito, *Tetrahedron*, 2005, **61**, 5405–5432; (*c*) J. Wu and A. S. C. Chan, *Acc. Chem. Res.*, 2006, **39**, 711–720; (*d*) W. Zhang, Y. Chi and X. Zhang, *Acc. Chem. Res.*, 2007, **40**, 1278–1290; (*e*) H. Shimizu, I. Nagasaki, K. Matsumura, N. Sayo and T. Saito, *Acc. Chem. Res.*, 2007, **40**, 1385–1393.

3 (*a*) T. Saito, T. Yokozawa, T. Ishizaki, T. Moroi, N. Sayo, T. Miura and H. Kumobayashi, *Adv. Synth. Catal.*, 2001, **343**, 264–267; (*b*) P. Dierkes and P. W. N. M. Van Leeuwen, *J. Chem. Soc., Dalton Trans.*, 1999, 1519–1530; (*c*) L. A. Van der Veen, M. D. K. Boele, F. R. Bregman, P. C. J. Kamer, P. W. N. M. Van Leeuwen, K. Goubitz, J. Fraanje, H. Schenk and C. Bo, *J. Am. Chem. Soc.*, 1998, **120**, 11616–11626.

4 W. Tang, Y. Chi and X. Zhang, *Org. Lett.*, 2002, **4**, 1695–1698.

5 (*a*) Z. Zhang, H. Qian, J. Longmire and X. Zhang, *J. Org. Chem.*, 2000, **65**, 6223–6226; (*b*) S. Wu, W. Wang, W. Tang, M. Lin and X. Zhang, *Org. Lett.*, 2002, **4**, 4495–4497.

6 L. Q. Qiu, F. Y. Kwong, J. Wu, W. H. Lam, S. S. Chan, W.-Y. Yu, Y.-M. Li, R. W. Guo, Z. Y. Zhou and A. S. C. Chan, *J. Am. Chem. Soc.*, 2006, **128**, 5955–5965.

7 For some recent books, reviews and selected examples on supramolecular catalysis, see: (*a*) P. W. N. M. van Leeuwen, Supramolecular Catalysis, Wiley-VCH, 2008; (*b*) B. Breit, *Angew. Chem. Int. Ed.*, 2005, **44**, 6816–6825; (*c*) P. E. Goudriaan, P. W. N. M. van Leeuwen, M. N. Birkholz and J. N. H. Reek, *Eur. J. Inorg. Chem.*, 2008, **19**, 2939–2958; (*d*) J. Meeuwissen and J. N. H. Reek, *Nature Chem.*, 2010, **2**, 615–621; (*e*) M. Raynal, P. Ballester, A. Vidal-Ferran and P. W. N. M. van Leeuwen, *Chem. Soc. Rev.*, 2014, **43**, 1660–1733; (*f*) M. Raynal, P. Ballester, A. Vidal-Ferran and P. W. N. M. van Leeuwen, *Chem. Soc. Rev.*, 2014, **43**, 1734–1787; (*g*) D. A. Leigh, V. Marcos and M. R. Wilson, *ACS Catal.*, 2014, **4**, 4490−4497; (*h*) K. Ohmatsu and T. Ooi, *Tetrahedron Lett.*, 2015, **56**, 2043–2048; (*i*) V. Blanco, D. A. Leigh and V. Marcos, *Chem. Soc. Rev.*, 2015, **44**, 5341–5370; (*j*) J.-B. Wang and B. L. Feringa, *Science*, 2011, **331**, 1429–1432; (*k*) V. Blanco, A. Carlone, K. D. Hanni and D. A. Leigh, *Angew. Chem. Int. Ed.*, 2012, **51**, 5166–5169; (*l*) M. Schmittel, S. De and S. Pramanik, *Angew. Chem. Int. Ed.*, 2012, **51**, 3832–3836; (*m*) S. De, S. Pramanik and M. Schmittel, *Angew. Chem. Int. Ed.*, 2014, **53**, 14255–14259; (*n*) V. Blanco and D. A. Leigh, *J. Am. Chem. Soc.*, 2014, **136**, 4905–4908.

8 (*a*) B. Breit and W. Seiche, *J. Am. Chem. Soc.*, 2003, **125**, 6608–6609; (*b*) Y. Liu, C. A. Sandoval, Y. Yamaguchi, X. Zhang, Z. Wang, K. Kato and K. Ding, *J. Am. Chem. Soc.*, 2006, **128**, 14212–14213; (*c*) J. Wieland and B. Breit, *Nature Chem.*, 2010, **2**, 832–837; (*d*) V. Agabekov, W. Seiche and B. Breit, *Chem. Sci.*, 2013, **4**, 2418–2422.

9 (*a*) D. Uraguchi, Y. Ueki and T. Ooi, *Science*, 2009, **326**, 120–123; (*b*) F. W. Patureau, C. Worch, M. A. Siegler, A. L. Spek, C. Bolm and J. N. H. Reek, *Adv. Synth. Catal.*, 2012, **354**, 59–64.

10 J. Park, K. Lang, K. A. Abboud and S. Hong, *J. Am. Chem. Soc.*, 2008, **130**, 16484–16485.

11 (*a*) V. F. Slagt, M. Roder, P. C. J. Kamer, P. W. N. M. van Leeuwen and J. N. H. Reek, *J. Am. Chem. Soc.*, 2004, **126**, 4056–4057; (*b*) T. Besset, D. W. Norman and J. N. H. Reek, *Adv. Synth. Catal.*, 2013, **355**, 348–352.

12 (*a*) M. Kuil, P. E. Goudriaan, P. W. N. M. van Leeuwen and J. N. H. Reek, *Chem. Commun.* 2006, 4679–4681; (*b*) T. Gadzikwa, R. Bellini, H. L. Dekker and J. N. H. Reek, *J. Am. Chem. Soc.*, 2012, **134**, 2860−2863.

13 (*a*) J. M. Takacs, D. S. Reddy, S. A. Moteki, D. Wu and H. Palencia, *J. Am. Chem. Soc.*, 2004, **126**, 4494–4495; (*b*) N. C. Thacker, S. A. Moteki and J. M. Takacs, *ACS Catal.*, 2012, **2**, 2743−2752.

14 G. Hattori, T. Hori, Y. Miyake. and Y. Nishibayashi, *J. Am. Chem. Soc.*, 2007, **129**, 12930–12931.

15 Y. Li, Y. Feng, Y. M. He, F. Chen, J. Pan and Q. H. Fan, *Tetrahedron Lett.*, 2008, **49**, 2878–2881.

16 (*a*) Y. Li, B. Ma, Y. He, F. Zhang and Q.-H. Fan, *Chem. Asian J.*, 2010, **5**, 2454–2458; (b) G.-H. Ouyang, Y.-M. He and Q.-H. Fan, *Chem. Eur. J.*, 2014, **20**, 16454–16457; (*c*) G.-H. Ouyang, Y.-M. He, Y. Li, J.-F. Xiang and Q.-H. Fan, *Angew. Chem. Int. Ed.*, 2015, **54**, 4334–4337; (*d*) A. Vidal-Ferran, I. Mon, A. Bauzá, A. Frontera and L. Rovira, *Chem. Eur. J.*, 2015, **21**, 11417–11426.

17 (*a*) Z. Wang, G. Chen and K. Ding, *Chem. Rev.*, 2009, **109**, 322–359; (*b*) L. Yu, Z. Wang, J. Wu, S. Tu and K. Ding, *Angew. Chem. Int. Ed.*, 2010, **49**, 3627–3630.

18 Xyl-P-Phos = 2,2′,6,6′-tetramethoxy-4,4′-bis[di(3,5-dimethyl-phenyl)phosphino]-3,3′-3,3hino]-3,3etramethoxy-4,4′-bis- [di(3,5-dimethyl- phenyl)phosphino], J. Wu, H. Chen, W.-H. Kwok, C.-H. K.-H. Lam, Z.-Y. Zhou, C.-H. Yeung and A. S. C. Chan, *Tetrahedron Lett.*, 2002, **43**, 1539–1543.

19 For some representative applications of Xyl-P-Phos ligand in asymmetric catalytic reactions: (*a*) J. Wu, C. C. Pai, W. H. Kwok, R. W. Guo, T. T. L. Au-Yeung, C. H. Yeung and A. S. C. Chan, *Tetrahedron: Asymmetry*, 2003, **14**, 987–992; (*b*) J. Wu, J. X. Ji and A. S. C. Chan, *Proc. Natl. Acad. Sci. U.S.A.*, 2005, **102**, 3570–3575; (*c*) X.-C. Zhang, Y. Wu, F. Yu, F.-F. Wu, J. Wu and A. S. C. Chan, *Chem. Eur. J.*, 2009, **15**, 5888–5891; (*d*) F. Yu, X.-C. Zhang, F.-F. Wu, J.-N. Zhou, W. Fang, J. Wu and A. S. C. Chan, *Org. Biomol. Chem.*, 2011, **9**, 5652–5654; (*e*) F.-F. Wu, J.-N. Zhou, Q. Fang, Y.-H. Hu, S. Li, X.-C. Zhang, A. S. C. Chan and J. Wu, *Chem.–Asian J.*, 2012, **7**, 2527–2530; (*f*) M. Li, B. Li, H.-F. Xia, D. Ye, J. Wu and Y. Shi, *Green Chem.*, 2014, **16**, 2680–2688.

20 (*a*) M. Ewcomb, J. M. Timko, D. M. Walba and D. J. Cram, *J. Am. Chem. Soc.*, 1977, **99**, 6392–6398; (*b*) D. J. Cram and J. M. Cram, *Acc. Chem. Res.*, 1978, **11**, 8–14; (*c*) B. M. Trost and R. Radinov, *J. Am. Chem. Soc.*, 1997, **119**, 5962–5963.

21 (*a*) I. Krossing and I. Raabe, *Angew. Chem. Int. Ed.*, 2004, **43**, 2066–2090; (*b*) K. Kallstrom, I. Munslow and P. G. Andersson, *Chem. Eur. J.*, 2006, **12**, 3194–3200; (*c*) R. Schwenk and A. Togni, *Dalton Trans.*, 2015, **44**, 19566–19575.

22 D. H. Barton, K. Nakanishi and O. Meth-Cohn, In *Comprehensive Natural Products Chemistry, Vol. 1-9*, Elsevier, Oxford, 1999.

23 (*a*) C. W. Bird, *Tetrahedron*, 1992, **48**, 335–340; (*b*) S. Murata, T. Sugimoto and S. Matsuura, *Heterocycles*, 1987, **26**, 763–766.

24 (*a*) W.-B. Wang, S.-M. Lu, P.-Y. Yang, X.-W. Han and Y.-G. Zhou, *J. Am. Chem. Soc.*, 2003, **125**, 10536–10537; (*b*) Y.-G. Zhou, *Acc. Chem. Res.*, 2007, **40**, 1357–1366. (*c*) R. Kuwano, *Heterocycles*, 2008, **76**, 909–922; (*d*) D.-S. Wang, Q.-A. Chen, S.-M. Lu and Y.-G. Zhou, *Chem. Rev.*, 2012, **112**, 2557–2590; (*e*) C.-X. Zhuo, W. Zhang and S.-L. You, *Angew. Chem. Int. Ed.*, 2012, **51**, 12662–12686; (*f*) L. Shi, Z.-S. Ye, L.-L. Cao, R.-N. Guo, Y. Hu and Y.-G. Zhou, *Angew. Chem. Int. Ed.*, 2012, **51**, 8286–8289; (*g*) T. Nagano, A. Iimuro, R. Schwenk, T. Ohshima, Y. Kita, A. Togni and K. Mashima, *Chem. Eur. J.*, 2012, **18**, 11578–11592; (*h*) S. Urban, B. Beiring, N. Ortega, D. Paul and F. Glorius, *J. Am. Chem. Soc.*, 2012, **134**, 15241−15244; (*i*) A. Iimuro, K. Yamaji, S. Kandula, T. Nagano, Y. Kita and K. Mashima, *Angew. Chem. Int. Ed.*, 2013, **52**, 2046–2050; (*j*) Z.-S. Ye, R.-N. Guo, X.-F. Cai, M.-W. Chen, L.

Shi and Y.-G. Zhou, *Angew. Chem. Int. Ed.*, 2013, **52**, 3685–3689.