Tetrahedron: *Asymmetry* 22 (2011) 769–774

Contents lists available at ScienceDirect

Tetrahedron: *Asymmetry*

journal homepage: www.elsevier.com/locate/tetasy

Readily available and recoverable chiral ionic phosphite ligands for the highly enantioselective hydrogenation of functionalized olefins

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ARTICLE INFO

Article history:
Received 18 March 2011
Accepted 11 April 2011

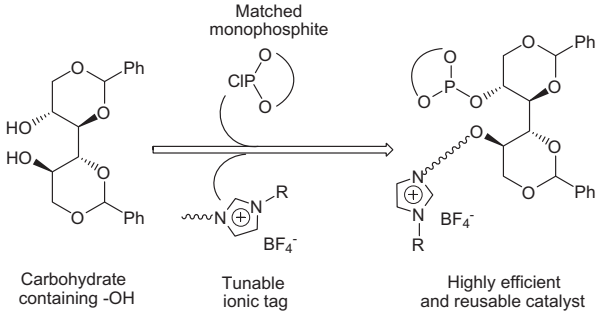
ABSTRACT

A series of novel ionic phosphite ligands bearing carbohydrate groups were conveniently synthesized and successfully applied in the asymmetric hydrogenation of enamides, α-dehydroamino acid esters, and dimethyl itaconate. High efficiency and excellent reusability were obtained in an ionic liquid–toluene biphasic system.

1. Introduction

The reutilization of chiral catalysts and reaction media is very important for developing sustainable chemistry.[1,2] Among the many strategies developed,[3–8] catalytic reactions carried out in ionic liquid or ionic liquid–organic solvent biphasic system is a promising approach toward achieving this goal, which has received considerable attentions both from academia and industry.[9–12] To achieve higher efficiency for this method, making the structure of the catalysts similar to that of the ionic liquids is needed in order to improve the immobilization of catalysts in ionic liquids, according to the theory of similarity and intermiscibility. The direct approach to this problem is to incorporate an ionic tag to the parent catalyst structure,[13–20] which has been successfully applied in asymmetric hydrogenations. Lee et al. introduced an imidazolium moiety onto a 1,4-bisphosphine ligand and obtained good results in recyclable asymmetric hydrogenations.[21] Similar work was also carried out by Reetz,[22] Blaser,[23] and others.[24–27] However, only a few good catalysts could be recycled more than ten times with no or minimal loss of activity.[23,28] Moreover, the synthetic procedure for most of the reported ionic ligands was tedious and their catalytic efficiencies were often inferior to those of non-ionic ones.[25,29]

Several years ago, one of us synthesized a series of monophosphite ligands based on carbohydrates, which exhibited high efficiency in asymmetric hydrogenations.[30] The hydroxyl groups contained in the backbone of these ligands inspired us to incorporate ionic tags on them and thus make them more convenient and tunable. Moreover, since no major change was exerted on the backbone, excellent performance in asymmetric hydrogenation could be expected (Scheme 1).



Scheme 1. Design of the ionic tagged chiral phosphite ligands.

2. Results and discussion

A facile synthetic route for chiral ionic monophosphites **1a**–**1e** is outlined in Scheme 2. Starting from the readily available D-mannitol, chiral diol **3** was conveniently obtained according to the reported method.[31] Selective *mono*-*O*-alkylation of the chiral diol **3** was successfully controlled to give **4** in moderate yield. Quaternarization of *N*-alkylimidazole with **4** afforded chiral alcohol **5**, which was then subjected to anion-exchange with $NaBF_4$ to give compound **6**. The reaction of (*R*)-BINOL-derived chlorophosphite with **6** in the presence of pyridine led to ionic chiral phosphites **1a**–**1e** [our previous work has demonstrated that the (*R*)-BINOL matched cooperatively to the corresponding D-mannitol-derived backbone[30]]. Using a similar procedure, chiral biphosphite **1f** was also successfully obtained (see Section 4.4). The corresponding rhodium complexes were obtained through the reaction of the chiral ionic ligands with $[Rh(COD)_2]BF_4$ at room temperature. All of the complexes and ligands were air-stable and fully characterized. They are insoluble in hexane, ether, ethyl acetate, and toluene, but soluble in CH_2Cl_2, THF, and other commonly used ionic liquids.

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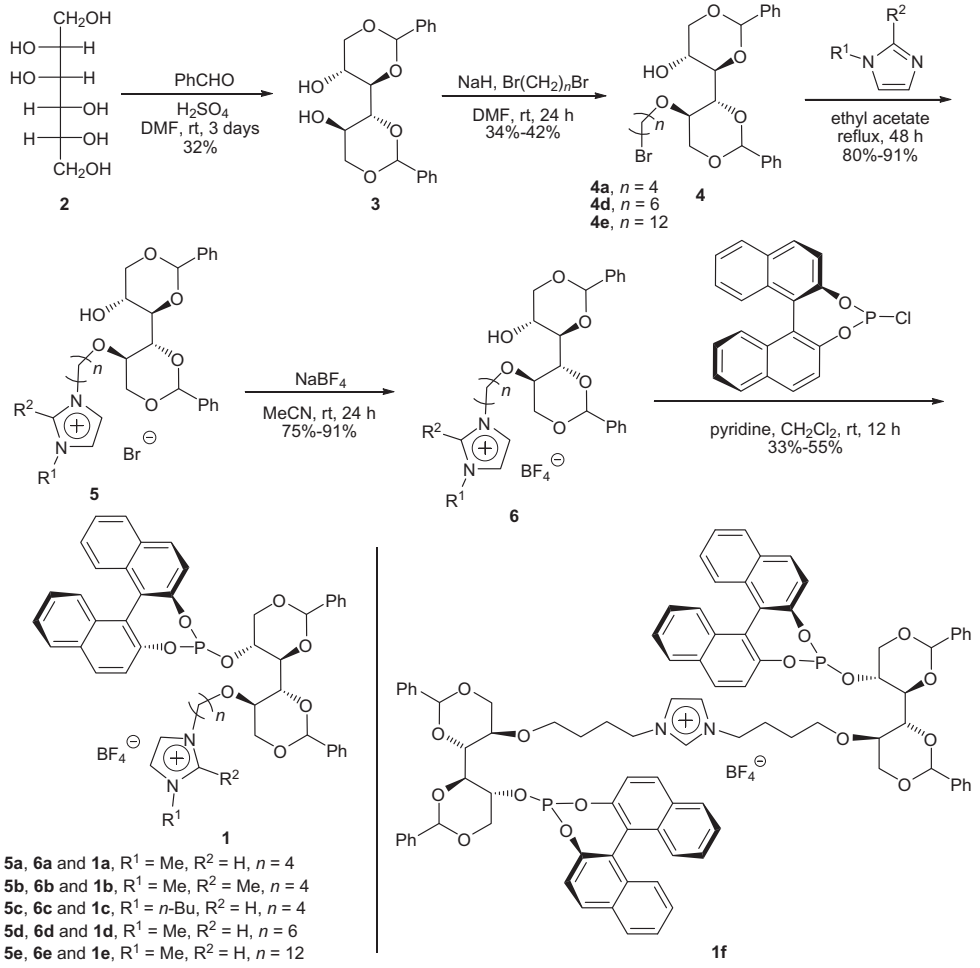
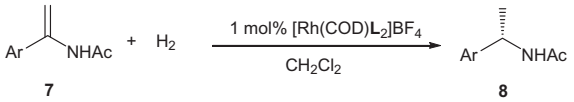
doi:10.1016/j.tetasy.2011.04.011



Scheme 2. Synthesis of ionic monophosphites.

Table 1
Asymmetric hydrogenation of enamides in CH_2Cl_2[a]



Entry	Ar (substrate)	Ligand	Ee[b] (%)
1	Ph **7a**	**1a**	>99
2	Ph **7a**	**1b**	>99
3	Ph **7a**	**1c**	>99
4	Ph **7a**	**1d**	>99
5	Ph **7a**	**1e**	>99
6	Ph **7a**	**1f**	99
7	4-BrC_6H_4 **7b**	**1d**	>99
8	4-FC_6H_4 **7c**	**1d**	>99
9	4-ClC_6H_4 **7d**	**1d**	>99
10	4-$MeOC_6H_4$ **7e**	**1d**	>99
11	2-Naphthyl **7f**	**1d**	>99

[a] Enamide 0.25 mmol; $[Rh(COD)\mathbf{L}_2]BF_4$ 0.0025 mmol; H_2 pressure: 10 atm; rt; reaction time: 1 h; CH_2Cl_2: 1 mL; 100% conversions obtained in all cases.

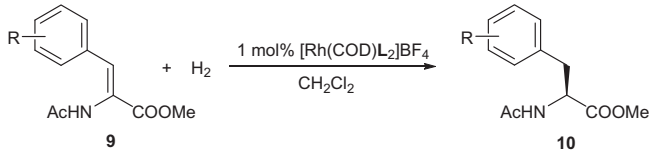
[b] Ee values were determined by GC with CP-Chiralsil Dex CB column and the absolute configuration was assigned as (*S*) by comparison of the specific rotation with reported data.[32]

With these ligands in hand, we first examined their catalytic performance on the asymmetric hydrogenation of *N*-acetylphenylethenamine **7a** with CH_2Cl_2 as the solvent under 10 atm of H_2, which were the same reaction conditions previously used for the parent ligands;[30] the results are summarized in Table 1. It was found that all the ionic catalysts showed high activities (100% conversions were obtained in 1 h) and excellent enantioselectivities (99% or >99% ee). These results indicated that the ionic tag moiety has no significant effect on the conformations of native ligands or transition states in Rh-catalyzed reactions. To explore the general utilities of these ionic ligands, we employed one of the ionic ligands **1d** in the asymmetric hydrogenation of a variety of enamides under the same reaction conditions. Uniformly excellent enantioselectivities (over 99% ee) were obtained in producing the corresponding chiral amines from all of the substituted enamides with different electronic properties **7b**–**7f** (Table 1, entries 7–11).

The efficacy of these types of ligands for the hydrogenation of enamides encouraged us to examine other functionalized olefins. The catalyst precursor with these ionic ligands produced high ee values for α-dehydroamino acid ester **9a** (Table 2, entries 1–6). With ligand **1d**, excellent enantioselectivities (92–99% ee) were observed for almost all α-dehydroamino acid esters **9a**–**9f** tested here, which bear different substituents in the phenyl ring, indicating their minimal electronic effects. Furthermore, dimethyl itaconate (**11**) was also applicable for this catalyst system, with full conversion and an ee value of up to 98% being obtained by employing the catalyst precursor containing ligand **1d** (Scheme 3).

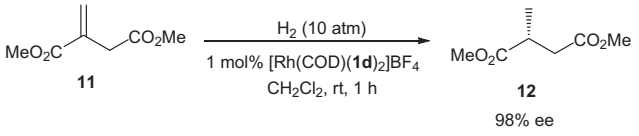
Encouraged by these preliminary results, we then turned our attention to the role of the ionic moiety in the reusability of the catalysts derived from these ionic ligands. The reactions were performed in an ionic liquid [bmim][BF_4]/toluene ([bmim]$^+$ = 1-

Table 2
Asymmetric hydrogenation of α-dehydroamino acid esters in CH_2Cl_2[a]



Entry	R (substrate)	Ligand	Ee[b] (%)
1	4-Cl **9a**	**1a**	97
2	4-Cl **9a**	**1b**	97
3	4-Cl **9a**	**1c**	94
4	4-Cl **9a**	**1d**	97
5	4-Cl **9a**	**1e**	94
6	4-Cl **9a**	**1f**	96
7	4-Me **9b**	**1d**	98
8	2-Cl **9c**	**1d**	92
9	4-MeO **9d**	**1d**	99
10	2-MeO **9e**	**1d**	96
11	3-MeO **9f**	**1d**	96

[a] α-Dehydroamino acid ester 0.25 mmol; $[Rh(COD)\mathbf{L}_2]BF_4$ 0.0025 mmol; H_2 pressure: 10 atm; rt; reaction time: 1 h; CH_2Cl_2: 1 mL; 100% conversions obtained in all cases.
[b] Ee values were determined by chiral GC using CP-Chiralsil Dex CB column or by HPLC using Chiralcel OJ-H column and the absolute configuration was assigned as (*S*) by comparison of the specific rotation with reported data.[33]

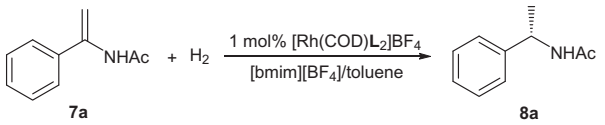


Scheme 3. Asymmetric hydrogenation of dimethyl itaconate in CH_2Cl_2.

methyl-3-butylimidazolium) biphasic system and after completion of the hydrogenation, the toluene layer was separated automatically from the ionic liquid layer. Simple extraction under an Ar atmosphere afforded the products and the catalyst remaining in the ionic liquid layer was then directly subjected to the next catalytic reaction to examine the reusability.

The results are summarized in Table 3 and show that the ionic tagged chiral monophosphites are efficient ligands for reutilization in asymmetric hydrogenation. However, the reusability proved to be significantly influenced by the structure of the ionic tag moiety. A comparison of the results in Table 3 shows that the reusability depends strongly on the structure of the cation contained in the chiral ligands. In general, *N*-methylimidazolium cation tagged ligands **1a** and **1d** demonstrated better reusability than ligands **1b** and **1c** with 1,2-dimethylimidazolium and *N*-butylimidazolium as the cation, respectively. We speculated that the structures of the ionic ligands containing *N*-methylimidazolium cations **1a** and **1d** are more similar to that of ionic liquid [bmim][BF_4], which showed a higher affinity of these ligands with the ionic liquid, and thus displayed good reusability. On the other hand, the length of the alkyl-chain (*n*), which links the cationic tag and the ligand backbone, also affects the reusability of ionic catalysts. It seems that longer alkyl-chains are better, for example, the results obtained by **1d** ($n = 6$) are better than those of **1a** ($n = 4$). However, increasing the length of alkyl-chain of the methylene group to 12 (ligand **1e**) led to a significant catalytic efficiency decrease, which suggests that if the long alkyl-chain is too long, it might weaken the immobilization ability of the ionic ligand in ionic liquids. The reusability of the ionic tagged biphosphite **1f** is lower, and which could only be recycled twice. With ligand **1d**, the best reusability was observed (it could be recycled seven times with only a slight loss of enantioselectivity).

Table 3
Asymmetric hydrogenation of an enamide in [bmim][BF_4]/toluene biphasic solvent system[a]



Run	Conversion[b] (%)/ee[c] (%)					
	L = **1a**	L = **1b**	L = **1c**	L = **1d**	L = **1e**	L_2 = **1f**
1	100/>99	100/98	100/>99	**100/>99**	100/95	100/98
2	100/98	100/97	100/>99	**100/99**	100/93	100/97
3	100/97	96/94	89/99	**100/99**	100/91	84/95
4	100/97	95/93	63/98	**100/98**	100/92	67/90
5	100/96	92/91	46/97	**100/98**	98/87	57/88
6	99/96	82/90	37/95	**99/97**	94/85	46/83
7	94/93	77/89	28/94	**97/97**	90/83	39/81

[a] Enamide 0.25 mmol; $[Rh(COD)\mathbf{L}_2]BF_4$ 0.0025 mmol; [bmim][BF_4]/toluene = 1 mL/1 mL; H_2: 40 atm; rt; reaction time: 1 h;
[b] Conversions were determined by GC using AT FFAP column.
[c] Ee values were determined by GC with CP-Chiralsil Dex CB column.

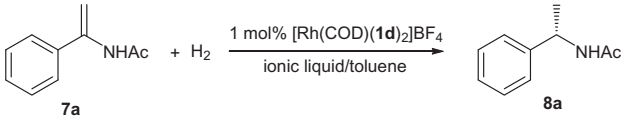
To rationalize the deactivation of the catalyst during the recycle, we checked catalyst leaching by ICP-AES analysis of the toluene layers, which were separated from the first run. For these chiral ligands, nearly no leaching of the Rh catalysts (<0.1%) was observed, indicating their good immobilization in the ionic liquid. These results together with the preliminary investigation on the ligand structure/enantioselectivity/reusability relationship shown in Table 3 indicate that a possible reason for the catalyst deactivation may be due to some contamination with oxygen during the recycling of the catalyst, which means that the ligands which have a high affinity for the ionic liquid should be better protected against reaction with oxygen.[23]

To further improve the reusability of these ionic tagged chiral catalysts, the reactions were also carried out in two other commonly used ionic liquids using toluene as a co-solvent. The results in Table 4 show that the observed reusability of the catalyst was again sensitive to the structure of the cations contained in the ligands, which further confirmed that structure similarity between the ionic tag of the chiral catalyst and the ionic liquid media used in the reaction is crucial for the reutilization of the catalyst. The best reusability was observed when using ionic liquid [bmim][PF_6] as the reaction media, in which the reusability of the Rh-catalyst derived from ligand **1d** was further enhanced compared to the reaction performed in [bmim][BF_4]: 95% conversion and 97% ee were still obtained in the tenth run. Prolonging the reaction time would further increase the reusability and prevent the decrease of the conversions in the next two runs and only a slight loss of enantioselectivity was observed.

3. Conclusion

In conclusion, we have designed and synthesized a series of ionic monophosphite ligands based on D-mannitol and successfully applied them in the Rh-catalyzed asymmetric hydrogenation of enamides, α-dehydroamino acid esters and dimethyl itaconate. These ionic tagged monophosphites have the advantages of being readily available and can be easily recovered from the reaction mixture, and can be recycled more than ten times in the biphasic system without a significant loss of catalytic efficiency. The pronounced effect of the ionic tags in these ligands on the reusability of catalysts indicates that the structural similarity between the ionic tag of the chiral catalyst and the ionic liquid media is crucial for improving the reusability.

Table 4
Asymmetric hydrogenation of an enamide in ionic liquid/toluene biphasic solvent system[a]



Run	Conversion[b] (%)/ee[c] (%)		
	[bmim][BF_4]	[bmmim][BF_4][d]	[bmim][PF_6]
1	100/>99	100/99	100/>99
2	100/99	99/98	100/>99
3	100/99	99/98	100/>99
4	100/98	99/97	100/99
5	100/98	99/97	100/99
6	99/97	97/96	100/98
7	97/97	91/95	100/98
8	96/94	84/94	99/98
9	ND	ND	98/97
10	ND	ND	95/97
11[e]	ND	ND	95/96
12[f]	ND	ND	96/94

[a] Enamide 0.25 mmol; [Rh(COD)(**1d**)$_2$]BF_4 0.0025 mmol; IL/toluene = 1 mL/1 mL; H_2: 40 atm, rt; reaction time: 1 h.
[b] Conversions were determined by GC with AT FFAP column.
[c] Ee values were determined by GC with CP-Chiralsil Dex CB column.
[d] [bmmim]$^+$ = 1,2-dimethyl-3-butylimidazolium.
[e] The reaction time was prolonged to 2 h.
[f] The reaction time was prolonged to 4 h.

4. Experimental

4.1. General

All solvents were dried and degassed by standard methods and stored under nitrogen. The ionic liquids and dimethyl itaconate were purchased from Alfa Aesar. Enamides, α-dehydroamino esters and [Rh(COD)$_2$]BF_4 were synthesized according to previous articles.[34–37] All other starting materials and solvents were commercially available. ^{1}H, ^{13}C, and ^{31}P NMR spectra were recorded with a Bruker Avance III 400 MHz NMR spectrometer. HRMS were recorded with a Bruker Daltonics APEX II mass spectrometer. GC and HPLC analyses were carried out on an HP 6890 system and an Agilent 1200 system, respectively. Optical rotations were determined on a PerkinElmer Model 341 LC polarimeter at 25 °C.

4.2. 1,3:4,6-Di-*O*-benzylidene-2-*O*-(4-bromobutyl)-D-mannitol 4a

Chiral diol **3** (7.16 g, 20 mmol) was dissolved in 100 mL of dry DMF. To this solution was slowly added sodium hydride (80% oil suspension, 600 mg, 20 mmol) under ice-bath. The resulting mixture was stirred at room temperature for 1 h, and then 1,4-dibromobutane (20 mmol) was added dropwise under ice-bath. The reaction mixture was stirred for 24 h at room temperature, quenched by 200 mL of water, and extracted with ether. The combined extracts were washed with water and brine, dried over Na_2SO_4, and concentrated. The residue was purified by chromatography on silica gel with ethyl acetate/petroleum ether (1:10) to give the product. Yield: 42%, mp 30–32 °C. $[\alpha]_D^{25} = -29.5$ (*c* 0.95, CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.64–1.71 (m, 2H), 1.86–1.94 (m, 2H), 3.36 (t, *J* = 6.8 Hz, 2H), 3.47–3.53 (m, 1H), 3.61–3.68 (m, 3H), 3.83–3.89 (m, 1H), 3.93 (d, *J* = 9.2 Hz, 1H), 4.02 (d, *J* = 9.2 Hz, 1H), 4.14–4.20 (m, 1H), 4.30 (q, *J* = 5.2 Hz, 1H), 4.42 (q, *J* = 5.2 Hz, 1H), 5.49 (s, 1H), 5.51 (s, 1H), 7.33–7.39 (m, 6H), 7.48–7.52 (m, 4H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 28.7, 29.5, 33.4, 33.4, 60.3, 67.5, 69.6, 71.2, 78.8, 101.2, 101.3, 126.2, 126.2, 128.2, 128.9, 129.0, 137.6, 137.7. HRMS: Calcd: for $C_{24}H_{29}BrO_6Na$ ([M+Na]$^+$) 515.1040 and 517.1021. Found: 515.1045 and 517.1032.

The synthetic procedures for **4d** and **4e** are similar to that of **4a**.

4.3. 1-(4-((4*R*,4′*R*,5*R*,5′*R*)-5′-Hydroxy-2,2′-diphenyl-4,4′-bi(1,3-dioxan)-5-yloxy)butyl)-3-methyl-1*H*-imidazol-3-ium bromide 5a

The chiral alcohol **4a** (6 mmol), *N*-methylimidazole (12 mmol), and ethyl acetate (20 mL) were heated at reflux with stirring for 48 h. Upon cooling, the precipitate was filtered off, washed with ether (3 × 10 mL), and dried in vacuum to give **5a** as white foam-like solid. Yield: 86%, mp 73–76 °C. $[\alpha]_D^{25} = -22.1$ (*c* 1.00, CH_2Cl_2). ^{1}H NMR (400 MHz, DMSO-d_6): δ 1.49–1.52 (m, 2H), 1.81–1.92 (m, 2H), 3.51–3.70 (m, 5H), 3.84 (s, 5H), 4.00–4.03 (m, 1H), 4.18–4.26 (m, 3H), 4.39–4.43 (m, 1H), 5.43 (s, 1H), 5.55–5.57 (m, 2H), 7.36–7.44 (m, 10H), 7.72–7.80 (m, 2H), 9.17–9.24 (m, 1H). ^{13}C NMR (100 MHz, DMSO-d_6): δ 26.0, 26.2, 26.5, 35.7, 35.8, 47.9, 48.5, 58.7, 67.1, 68.7, 69.3, 70.8, 76.5, 78.3, 99.9, 100.1, 122.1, 122.2, 123.6, 125.9, 126.0, 127.9, 128.0, 128.6, 136.5, 136.6, 138.0, 138.9. ESI-MS: *m*/*z* (+) = 495.0; *m*/*z* (−) = 78.4, 80.4. HRMS: Calcd: for $C_{28}H_{35}N_2O_6$ ([M−Br]$^+$) 495.2490. Found: 495.2491.

The synthetic procedures of **5b**, **5c**, **5d** and **5e** are similar to that of **5a**.

4.4. 3-(4-((4*R*,4′*R*,5*R*,5′*R*)-5′-Hydroxy-2,2′-diphenyl-4,4′-bi(1,3-dioxan)-5-yloxy)butyl)-1-(5-((4*R*,4′*R*,5*R*,5′*R*)-5′-hydroxy-2,2′-diphenyl-4,4′-bi(1,3-dioxan)-5-yloxy)pentyl)-1*H*-imidazol-3-ium bromide 5f[38]

A solution of imidazole (0.34 g, 10.5 mmol) in dry THF was added dropwise to an ice-cooled stirred solution of NaH (0.21 g of 60% dispersion in mineral oil, 5.25 mmol) in dry THF. The mixture was stirred for 1 h at room temperature and for 1 h at 55 °C under an argon atmosphere. The formation of hydrogen gas could be observed by the formation of bubbles in the solution. Next, a solution of **4a** (5.2 g, 10.5 mmol) in dry THF was added dropwise, and the mixture was refluxed for 48 h under an argon atmosphere. The solvent was removed under reduced pressure, and the resulting solid was washed with ethyl acetate (2 × 20 mL) and then dissolved in dichloromethane. The insoluble NaBr was filtered off and the filtrate washed with water, dried over $MgSO_4$, and concentrated under reduced pressure. A white foam-like solid was obtained in 43% yield. Mp 117–119 °C. $[\alpha]_D^{25} = -30.6$ (*c* 0.54, CH_2Cl_2). ^{1}H NMR (400 MHz, DMSO-d_6): δ 1.44–1.51 (m, 4H), 1.75–1.91 (m, 4H), 3.50–3.70 (m, 10H), 3.83 (s, 4H), 3.99–4.01 (m, 2H), 4.15–4.19 (m, 6H), 4.41 (q, *J* = 4.8 Hz, 2H), 5.46 (s, 2H), 5.53 (s, 2H), 5.55 (s, 2H), 7.36–7.44 (m, 20H), 7.78 (s, 2H), 9.22–9.25 (m, 1H). ^{13}C NMR (100 MHz, DMSO-d_6): δ 26.2, 26.4, 48.6, 58.7, 67.1, 68.7, 69.3, 70.8, 76.5, 78.3, 99.9, 100.1, 122.4, 125.9, 126.0, 128.0, 128.1, 128.6, 135.9, 137.9, 138.0. ESI-MS: *m*/*z* (+) = 893.1; *m*/*z* (−) = 79.4, 80.4. HRMS: Calcd: for $C_{51}H_{61}N_2O_{12}$ ([M−Br]$^+$) 893.4219. Found: 893.4220.

4.5. 1-(4-((4*R*,4′*R*,5*R*,5′*R*)-5′-Hydroxy-2,2′-diphenyl-4,4′-bi(1,3-dioxan)-5-yloxy)butyl)-3-methyl-1*H*-imidazol-3-ium tetrafluoroborate 6a

A mixture of **5a** (3 mmol), $NaBF_4$ (0.44 g, 4 mmol) and dry acetonitrile (5 mL) was stirred at room temperature for 24 h. The white precipitate (NaBr) was then filtered off and washed with dichloromethane. The filtrate was concentrated in vacuum to give **5a** as a white foam-like (which absorbs moisture easily) solid.

Yield: 87%, $[\alpha]_D^{25} = -25.8$ (c 0.65, CH_2Cl_2). ^{1}H NMR (400 MHz, DMSO-d_6): δ 1.46–1.53 (m, 2H), 1.77–1.91 (m, 2H), 3.51–3.70 (m 5H), 3.82–3.85 (m, 5H), 3.99 (d, J = 9.2 Hz, 1H), 4.15–4.20 (m, 3H), 4.40 (q, J = 4.8 Hz, 1H), 5.42 (s, 1H), 5.53 (s, 1H), 5.55 (s, 1H), 7.35–7.44 (m, 10H), 7.67 (s, 1H), 7.74 (t, J = 2.0 Hz, 1H), 9.08 (s, 1H). ^{13}C NMR (100 MHz, DMSO-d_6): δ 26.0, 26.2, 26.4, 35.7, 48.0, 48.6, 58.7, 67.1, 68.7, 69.3, 70.8, 76.6, 78.3, 99.9, 100.2, 122.2, 123.6, 125.9, 126.0, 127.9, 128.0, 128.6, 136.4, 137.9, 138.0. ESI-MS: m/z (+) = 495.0; m/z (−) = 86.4. HRMS: Calcd: for $C_{28}H_{35}N_2O_6$ ($[M-BF_4]^+$) 495.2490. Found: 495.2488.

The synthetic procedures for **6b**, **6c**, **6d**, **6e** and **6f** are similar to that of **6a**.

4.6. 1-(4-((4*R*,4′*S*,5*R*,5′*R*)-5′-(Dinaphtho[2,1-*d*:1′,2′-*f*][1,3,2]dioxaphosphepin-4-yloxy)-2,2′-diphenyl-4,4′-bi(1,3-dioxan)-5-yloxy) butyl)-3-methyl-1*H*-imidazol-3-ium tetrafluoroborate 1a

A solution of (*R*)-BINOL-derived chlorophosphite (1.5 mmol) in CH_2Cl_2 (5 mL) was added dropwise to a vigorously stirred solution of ionic chiral alcohol **6a** (1 mmol) and pyridine (4 mmol) in CH_2Cl_2 (5 mL). The mixture was stirred at room temperature for an additional 12 h, and then concentrated. The residue was purified by flash chromatography on silica gel with CH_2Cl_2/THF (1:1) to give the ligand **1a** as a white foam-like solid. Yield: 33%, mp 142–143 °C. $[\alpha]_D^{25} = -224.4$ (c 0.45, CH_2Cl_2). ^{1}H NMR (400 MHz, DMSO-d_6): δ 1.42–1.47 (m, 2H), 1.75–1.84 (m, 2H), 3.46–3.58 (m, 3H), 3.65–3.72 (m, 1H), 3.77 (s, 3H), 3.84–3.92 (m, 2H), 4.06–4.11 (m, 3H), 4.39–4.24 (m, 1H), 4.58–4.61 (m, 1H), 4.66–4.72 (m, 1H), 5.56 (s, 1H), 5.67 (s, 1H), 7.21 (t, J = 7.2 Hz, 2H), 7.35–7.40 (m, 10H), 7.47–7.68 (m, 7H), 7.69 (s, 1H), 8.07–8.17 (m, 4H), 9.00 (s, 1H). ^{13}C NMR (100 MHz, DMSO-d_6): δ 26.2, 26.4, 35.6, 48.5, 62.9, 63.1, 66.8, 67.0, 68.5, 68.8, 69.2, 76.2, 76.5, 99.9, 100.0, 121.5, 121.9, 122.0, 122.1, 123.3, 123.5, 125.3, 125.5, 125.8, 125.9, 126.0, 126.7, 126.9, 128.1, 128.2, 128.6, 128.7, 128.8, 130.3, 130.8, 130.9, 131.2, 131.7, 132.0, 136.4, 137.3, 137.6, 146.6, 146.9, 147.0. ^{31}P NMR (162 MHz, DMSO-d_6): δ 153.0. HRMS: Calcd: for $C_{48}H_{46}N_2O_8P$ ($[M-BF_4]^+$) 809.2986. Found: 809.2991.

The synthetic procedures for **1b**, **1c**, **1d**, **1e** and **1f** are similar to that of **1a**.

Compound **1b** was obtained as a white foam-like solid (55%) from the reaction of **6b** and (*R*)-BINOL-derived chlorophosphite. Mp 148–149 °C. $[\alpha]_D^{25} = -225.0$ (c 0.52, CH_2Cl_2). ^{1}H NMR (400 MHz, DMSO-d_6): δ 1.43–1.50 (m, 2H), 1.64–1.72 (m, 2H), 2.47 (s, 3H), 3.48–3.54 (m, 2H), 3.59–3.61 (m, 1H), 3.66 (s, 3H), 3.69–3.71 (m, 1H), 3.82–3.92 (m, 2H), 4.01–4.08 (m, 3H), 4.39–4.42 (m, 1H), 4.58–4.62 (m, 1H), 4.68–4.74 (m, 1H), 5.56 (s, 1H), 5.67 (s, 1H), 7.19–7.23 (m, 2H), 7.35–7.40 (m, 10H), 7.47–7.59 (m, 8H), 8.07–8.17 (m, 4H). ^{13}C NMR (100 MHz, DMSO-d_6): δ 9.0, 26.1, 26.2, 34.5, 47.2, 62.9, 63.1, 66.7, 67.0, 68.5, 68.8, 69.4, 76.2, 76.5, 99.9, 100.0, 120.7, 121.5, 121.9, 122.0, 122.2, 123.3, 123.4, 125.3, 125.5, 125.8, 125.9, 126.0, 126.7, 126.9, 128.1, 128.2, 128.6, 128.7, 128.8, 130.3, 130.8, 130.9, 131.2, 131.7, 132.0, 137.3, 137.6, 144.1, 146.6, 146.9, 147.0. ^{31}P NMR (162 MHz, DMSO-d_6): δ 153.0. HRMS: Calcd: for $C_{49}H_{48}N_2O_8P$ ($[M-BF_4]^+$) 823.3143. Found: 823.3148.

Compound **1c** was obtained as a white foam-like solid (47%) from the reaction of **6c** and (*R*)-BINOL-derived chlorophosphite. Mp 116–118 °C. $[\alpha]_D^{25} = -213.3$ (c 0.48, CH_2Cl_2). ^{1}H NMR (400 MHz, DMSO-d_6): δ 0.86 (t, J = 7.2 Hz, 3H), 1.16–1.25 (m, 2H), 1.42–1.47 (m, 2H), 1.65–1.76 (m, 2H), 3.46–3.72 (m, 5H), 3.82–3.96 (m, 2H), 4.07–4.13 (m, 4H), 4.39–4.43 (m, 1H), 4.58–4.62 (m, 1H), 4.66–4.75 (m, 1H), 5.56 (s, 1H), 5.67 (s, 1H), 7.20–7.24 (m, 2H), 7.35–7.40 (m, 10H), 7.48–7.56 (m, 6H), 7.71 (s, 1H), 7.72 (s, 1H), 8.07–8.17 (m, 4H), 9.10 (s, 1H). ^{13}C NMR (100 MHz, DMSO-d_6): δ 13.2, 18.7, 25.1, 26.2, 26.4, 31.2, 48.5, 48.6, 62.9, 63.1, 66.8, 67.0, 68.6, 68.8, 69.2, 76.2, 76.5, 100.0, 100.1, 121.5, 121.9, 122.0, 122.3, 122.4, 123.3, 123.4, 125.3, 125.5, 125.8, 125.9, 126.7, 126.9, 128.1, 128.2, 128.6, 128.7, 128.8, 130.3, 130.8, 130.9, 131.2, 131.7, 132.0, 135.8, 137.3, 137.6, 146.6, 146.9. ^{31}P NMR (162 MHz, DMSO-d_6): δ 153.0. HRMS: Calcd: for $C_{51}H_{52}N_2O_8P$ ($[M-BF_4]^+$) 851.3456. Found: 851.3427.

Compound **1d** was obtained as a white foam-like solid (47%) from the reaction of **6d** and (*R*)-BINOL-derived chlorophosphite. Mp 129–131 °C. $[\alpha]_D^{25} = -216.0$ (c 0.42, CH_2Cl_2). ^{1}H NMR (400 MHz, DMSO-d_6): δ 1.14–1.20 (m, 2H), 1.23–1.29 (m, 2H), 1.41–1.46 (m, 2H), 1.66–1.71 (m, 2H), 3.43–3.67 (m, 5H), 3.81 (s, 3H), 3.83–3.92 (m, 1H), 4.03–4.07 (m, 3H), 4.37–4.40 (m, 1H), 4.57–4.60 (m, 1H), 4.67–4.70 (m, 1H), 5.55 (s, 1H), 5.66 (s, 1H), 7.19–7.23 (m, 2H), 7.35–7.42 (m, 10H), 7.46–7.70 (m, 8H), 8.08–8.18 (m, 4H), 9.03 (s, 1H). ^{13}C NMR (100 MHz, DMSO-d_6): δ 24.8, 25.2, 29.1, 29.2, 35.7, 48.6, 62.8, 63.0, 66.5, 68.6, 68.8, 69.7, 76.1, 76.5, 100.0, 121.6, 121.9, 122.0, 122.2, 123.3, 123.5, 125.3, 125.5, 125.8, 125.9, 126.0, 126.7, 126.9, 128.1, 128.2, 128.6, 128.7, 128.8, 130.3, 130.8, 130.9, 131.2, 131.7, 132.0, 136.4, 137.4, 137.6, 146.6, 146.9. ^{31}P NMR (162 MHz, DMSO-d_6): δ 152.8. HRMS: Calcd: for $C_{50}H_{50}N_2O_8P$ ($[M-BF_4]^+$) 837.3299. Found: 837.3291.

Compound **1e** was obtained as a white foam-like solid (38%) from the reaction of **6e** and (*R*)-BINOL-derived chlorophosphite. Mp 103–105 °C. $[\alpha]_D^{25} = -194.4$ (c 0.43, CH_2Cl_2). ^{1}H NMR (400 MHz, DMSO-d_6): δ 1.15–1.21 (m, 16H), 1.40–1.45 (m, 2H), 1.73–1.76 (m, 2H), 3.40–3.68 (m, 4H), 3.78–3.91 (m, 5H), 4.06 (d, J = 9.6 Hz, 1H), 4.12 (t, J = 7.2 Hz, 2H), 4.35–4.39 (m, 1H), 4.55–4.59 (m, 1H), 4.63–4.70 (m, 1H), 5.50 (s, 1H), 5.65 (s, 1H), 7.18–7.23 (m, 2H), 7.33–7.60 (m, 16H), 7.68 (s, 1H), 7.74 (s, 1H), 8.07–8.17 (m, 4H), 9.07 (s, 1H). ^{13}C NMR (100 MHz, DMSO-d_6): δ 25.4, 25.5, 28.3, 28.7, 28.8, 28.9, 29.2, 29.3, 35.7, 48.7, 62.8, 63.0, 66.5, 67.0, 68.6, 68.8, 69.7, 76.1, 76.6, 100.0, 121.6, 121.9, 122.0, 122.2, 123.4, 123.6, 125.3, 125.4, 125.8, 125.9, 126.0, 126.7, 126.8, 128.0, 128.1, 128.6, 128.7, 128.8, 130.2, 130.8, 131.2, 131.7, 132.0, 136.4, 137.4, 137.6, 146.6, 146.9. ^{31}P NMR (162 MHz, DMSO-d_6): δ 152.4. HRMS: Calcd: for $C_{56}H_{62}N_2O_8P$ ($[M-BF_4]^+$) 921.4238. Found: 921.4204.

Compound **1f** was obtained as a white foam-like solid (53%) from the reaction of **6f** and (*R*)-BINOL-derived chlorophosphite. Mp 158–160 °C. $[\alpha]_D^{25} = -230.7$ (c 0.44, CH_2Cl_2). ^{1}H NMR (400 MHz, DMSO-d_6): δ 1.37–1.40 (m, 4H), 1.66–1.73 (m, 4H), 3.43–3.55 (m, 6H), 3.65–3.67 (m, 2H), 3.80–3.89 (m, 4H), 4.01–4.06 (m, 6H), 4.36–4.39 (m, 2H), 4.57–4.60 (m, 2H), 4.65–4.71 (m, 2H), 5.54 (s, 2H), 5.64 (s, 2H), 7.15–7.25 (m, 5H), 7.31–7.40 (m, 20H), 7.47–7.64 (m, 13H), 8.05–8.10 (m, 6H), 8.14 (s, 1H), 8.16 (s, 1H), 9.01 (s, 1H). ^{13}C NMR (100 MHz, DMSO-d_6): δ 26.1, 26.3, 48.6, 62.9, 63.1, 66.8, 68.5, 68.8, 69.2, 76.1, 76.5, 100.0, 100.1, 115.4, 118.5, 121.5, 121.9, 122.0, 122.2, 122.3, 123.3, 123.4, 124.4, 125.3, 125.5, 125.8, 125.9, 126.0, 126.7, 126.9, 127.8, 128.1, 128.2, 128.6, 128.7, 128.8, 130.2, 130.8, 130.9, 131.2, 131.7, 132.0, 134.1, 135.8, 137.3, 137.6, 146.6, 146.9, 147.0, 153.0. ^{31}P NMR (162 MHz, DMSO-d_6): δ 153.0. HRMS: Calcd: for $C_{91}H_{83}N_2O_{16}P_2$ ($[M-BF_4]^+$) 1521.5212. Found: 1521.5150.

4.7. Hydrogenation reaction in CH_2Cl_2

To a mixture of substrate (enamide, α-dehydroamino ester or dimethyl itaconate) (0.25 mmol) and Rh complex catalyst (2.5×10^{-3} mmol) was added degassed CH_2Cl_2 (1 mL) and stirred vigorously for 10 min. Hydrogenation was carried out in a stainless autoclave at room temperature for 1 h. After releasing the H_2, the reaction mixture was passed through a short silica gel column to remove the catalyst. The resulting solution was used directly for GC or HPLC analysis.

4.8. Hydrogenation in the [bmim][BF_4]/toluene system

To a mixture of enamide or α-dehydroamino acid ester (0.25 mmol) and Rh complex catalyst (2.5×10^{-3} mmol) were added ionic liquid [bmim][BF_4] (1 mL) and toluene (1 mL). Hydrogenation was carried out in a stainless autoclave at room temperature. After releasing the H_2, the toluene layer was separated in a glovebox and subjected to GC analysis without any purification. For catalyst recycling, enamide (0.25 mmol), and toluene (1 mL) were added again to the ionic liquid layer remaining in the reaction vessel.

Acknowledgments

This work was supported by the Chinese Academy of Sciences, the National Natural Science Foundation of China (20802085), and the Research Foundation for the Returned Overseas Chinese Scholars, State Education Ministry.

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