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A new kind of organophosphorus compounds as an efficient catalyst for asymmetric C–C bond formation reactions

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ABSTRACT

A new class of chiral pyrrolidine-phosphite organocatalysts, available from commercially starting materials, has been synthesized and shown to be good catalytic activity for asymmetric Michael and Aldol reactions. The reactions proceeded to give the products in good yield and in a highly selective manner. Ionic liquid [Bmim][BF_4] as an efficient green solvent has been employed in the Michael addition.

1. Introduction

Organocatalyzed asymmetric synthesis has received great attention due to it being environmentally benign and fundamentally interesting. Asymmetric carbon–carbon bond-forming reactions play a very important role in organocatalyzed asymmetric synthesis.[1] Over the past few years, there has been a tremendous increase in research activities on the development of organocatalysts for asymmetric carbon–carbon bond-forming reactions.[2] Within this field, the organocatalyzed asymmetric Michael and Aldol reactions remain an important challenge,[3] the products of these two kind carbon–carbon bond-forming reactions are particularly interesting and challenging because they can generate two contiguous stereocenters in a single step. The development of efficient organocatalysts for this type of transformation, therefore, is fundamental importance. Since L-proline and pyrrolidine-based catalytic systems for asymmetric carbon–carbon bond-forming were reported,[4] a great number of pyrrolidine-type organocatalysts have been synthesized and successfully used in Michael and Aldol reactions.[5,6]

Recently, the application of α-aminophosphonates and phosphinyl oxide compounds as chiral pyrrolidine-type organocatalysts have been introduced for asymmetric carbon–carbon bond formation. In 2006, Amedjkouh and Dinér first reported chiral α-aminophosphonate pyrrolidines as a new class of efficient organocatalysts for the asymmetric direct aldol reaction.[7] The reaction proceeded smoothly to give the adduct in high enantioselectivity, but low yield. Tang et al.[8a] and Ding and co-workers[8b] reported the asymmetric Michael addition of cyclohexanone to nitroolefins directly catalyzed by these simple chiral α-aminophosphonate organocatalysts with good yields and moderate to good diastereoselectivities and enantioselectivities. The chiral α-aminophosphonate organocatalysts also could catalyze the asymmetric conjugate additions of nitroalkanes to α,β-unsaturated carbonyls with enantioselectivity up to 81% ee[9] Liu co-workers first synthesized chiral phosphinyl oxide pyrrolidines and used them as organocatalysts for Aldol reaction with moderate yield and good enantioselectivity.[10] Most recently, Zhong and co-workers successfully used the same chiral phosphinyl oxide organocatalysts in Michael reaction of *cyclo* ketones to nitroolefins with both excellent yield and stereoselectivity.[5h]

Well, these organocatalysts still have some drawbacks, such as they are not readily available from starting materials. They often need several steps to be synthesized. When they were used in asymmetric reactions, low yield and moderate enantioselectivity were often obtained.

As a part of our continuing interests in asymmetric small-molecule catalysis,[11] here, we report the asymmetric organocatalytic Michael and Aldol reactions, which are promoted by simple chiral pyrrolidine-phosphite organocatalysts.

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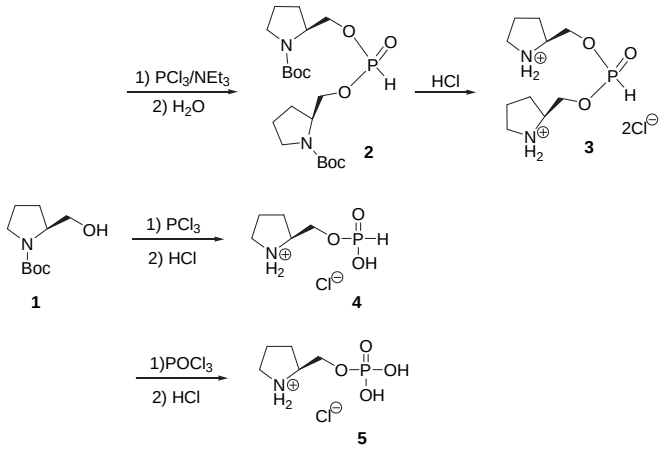
2. Results and discussion

The hydrochloric acid salts of newly designed chiral pyrrolidine-phosphite catalysts **3**, **4**, and **5** were synthesized from commercially available starting materials *N*-Boc-L-prolinol (Scheme 1). They were obtained through only one or two steps. For example, compound **2** was prepared from *N*-Boc-L-prolinol by treating with 0.5 equiv PCl_3 in presence of triethylamine at 0 °C. Next, the deprotection of the Boc-group was carried out using 5 M HCl in ethanol to give the desired organocatalyst **3** in 96% total yield. We kept these catalysts in their hydrochloride form, because they were easy to handle and could be stored for a long time without loss any catalytic activity.



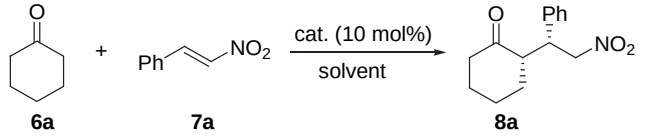
Scheme 1. Synthesis of the catalysts **3**–**5**.

With these organocatalysts in hand, we first investigated the effect of the solvents on the catalytic performance with the Michael addition of cyclohexanone (**6a**) to nitrostyrene (**7a**) as a model reaction. As can be seen from the results summarized in Table 1, when compounds **3**, **4**, and **5** were directly used as catalysts in their hydrochloride form, nearly no product was obtained (Table 1, entries 1–3). Then $NaHCO_3$ was added as a base to generate the organocatalysts. The pyrrolidine-phosphite catalyst **3** promoted the Michael addition reaction with high diastereoselectivity and enantioselectivity (Table 1, entry 4). Chiral catalysts **4** and **5** gave good yields, but lower diastereoselectivities and enantioselectivities were obtained than with **3** (Table 1, entries 5 and 6).

Compound **3** was used as the catalyst of choice and evaluated in different solvents (Table 1, entries 7–16). The yields and enantioselectivities of the product differed significantly. The catalyst **3** displayed excellent catalytic efficiency in THF at room temperature for 96 h, affording Michael adduct **8a** in 99% yield with moderate enantioselectivity (68% ee) and high diastereoselectivity (*syn*/*anti* 99/1) (Table 1, entry 7). When H_2O was used as the solvent, no product was obtained. Other polar solvents, such as CH_3OH, *i*-PrOH, and DMF, gave good yields with high diastereoselectivities but with moderate enantioselectivities (Table 1, entries 9–11). When the reaction was carried out in ionic liquid [Bmin][BF_4], the best result was observed. The reaction could be finished in 45 h with excellent yield (99% yield) and good stereoselectivity (*syn*/*anti* 99/1, 84% ee) (Table 1, entry 12). Other classical organic solvents were also tested in the model reaction. They all gave the products with good diastereoselectivities, but lower enantioselectivities were obtained than with [Bmin][BF_4] (Table 1, entries 13–16).

Having identified ionic liquid [Bmin][BF_4] to be the best solvent for the Michael reaction of cyclohexanone (**6a**) and nitrostyrene (**7a**), other factors influencing the reaction were further thoroughly investigated. The results are summarized in Table 2. The enantioselectivities are lower with organic base such as triethylamine, tributylamine, and aqueous ammonia than with inorganic base, such as NaOH and Na_2CO_3. We found that $NaHCO_3$ was the best base in combination with catalyst **3** (Table 2, entry 1: *syn*/*anti* 99/1, 84% ee). If reduced or increased the amount of $NaHCO_3$, the product **8a** was also formed in high yields and diastereoselectivities, but low with enantioselectivities (Table 2, entries 7 and 8).

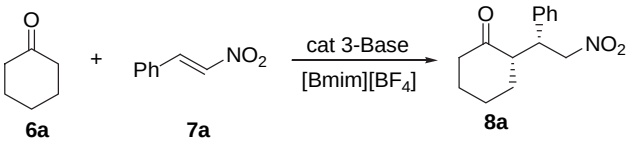
Table 1
The effect of catalysts in asymmetric Michael additions of cyclohexanone **6a** and nitrostyrene **7a**[a]



Entry	cat-base[b] (mol %)	Solvent	Time (h)	Yield[c] (%)	dr[d] (*syn*/*anti*)	ee[e] (%)
1	3	*t*-BuOH	48	<5	—	—
2	4	*t*-BuOH	46	<5	—	—
3	5	*t*-BuOH	46	<5	—	—
4	3-$NaHCO_3$ (50)	*t*-BuOH	48	78	94/6	82
5	4-$NaHCO_3$ (50)	*t*-BuOH	46	95	87/13	63
6	5-$NaHCO_3$ (50)	*t*-BuOH	48	91	90/10	71
7	3-$NaHCO_3$ (50)	THF	96	99	99/1	68
8	3-$NaHCO_3$ (50)	H_2O	96	—	—	—
9	3-$NaHCO_3$ (50)	CH_3OH	45	99	94/6	72
10	3-$NaHCO_3$ (50)	*i*-PrOH	120	83	95/5	63
11	3-$NaHCO_3$ (50)	DMF	48	86	94/6	74
12	3-$NaHCO_3$ (50)	[Bmin][BF_4]	45	99	99/1	84
13	3-$NaHCO_3$ (50)	$CHCl_3$	72	99	97/3	83
14	3-$NaHCO_3$ (50)	DCE	144	95	99/1	82
15	3-$NaHCO_3$ (50)	CH_2Cl_2	96	89	98/2	82
16	3-$NaHCO_3$ (50)	Toluene	72	50	90/10	81

[a] All reactions were conducted in solvent (0.5 mL) using **6a** (0.1 mL, 1.0 mmol) and **7a** (15 mg, 0.1 mmol) in the presence the catalyst.
[b] The amount of the base used for this reaction is relative to substrate **7a.**
[c] Isolated yield.
[d] Determined by ^{1}H NMR spectroscopy.
[e] Determined by HPLC analysis (Chiralcel AD-H column).

Table 2
Asymmetric Michael addition reactions of cyclohexanone and nitrostyrene catalyzed by **3** with different bases[a]

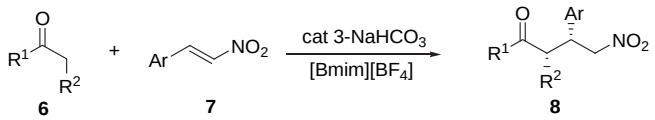


Entry	Base[b] (mol %)	Time (h)	Yield[c] (%)	dr[d] (*syn*/*anti*)	ee[e] (%)
1	$NaHCO_3$ (50)	45	99	99/1	84
2	Et_3N (50)	48	96	92/8	70
3	Bu_3N (50)	61	40	91/9	72
4	NH_3H_2O (50)	60	85	85/15	58
5	NaOH (25)	24	95	95/5	79
6	Na_2CO_3 (50)	63	99	97/3	81
7	$NaHCO_3$ (30)	120	92	98/2	66
8	$NaHCO_3$ (100)	120	98	99/1	74

[a] All reactions were conducted in [Bmin][BF_4] (0.5 mL) using **6a** (0.1 mL, 1.0 mmol) and **7a** (15 mg, 0.1 mmol) in the presence of 10 mol % of the catalyst **3**.
[b] The amount of the base used for this reaction is relative to substrate **7a**.
[c] Isolated yield.
[d] Determined by ^{1}H NMR spectroscopy.
[e] Determined by HPLC analysis (Chiralcel AD-H column).

Having established the optimal reaction conditions, we then examined the reactions of other nitroolefins to establish the general scope of this asymmetric transformation. As shown in Table 3 (entries 1–10), high isolated yields were obtained for all the products, regardless of the electronic nature of the aromatic substituents, and in most of the cases we obtained the *syn* products with high diastereoselectivities (>94% *syn*/*anti*) and good enantioselectivities (up to 88% ee).

Table 3
Asymmetric Michael addition reaction of ketones to nitroolefins[a]



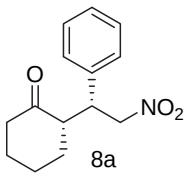
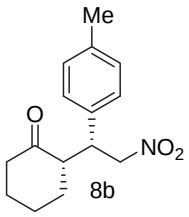
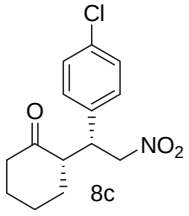
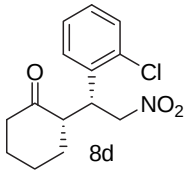
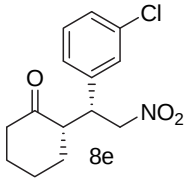
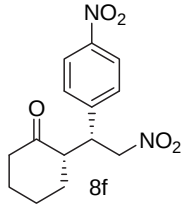
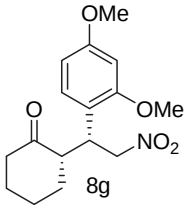
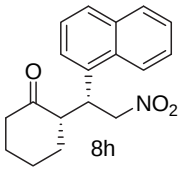
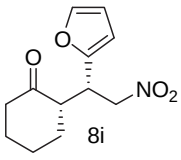
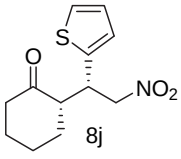
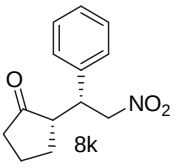
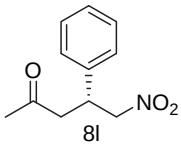
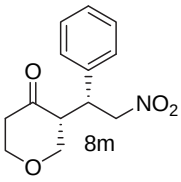
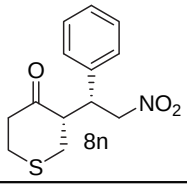
Entry	Product	Time (h)	Yield[b] (%)	dr[c] (*syn*/*anti*)	ee[d] (%)
1	 8a	45	99	99/1	84
2	 8b	65	99	98/2	84
3	 8c	64	99	95/5	84
4	 8d	64	99	99/1	87
5	 8e	64	99	94/6	70
6	 8f	40	99	94/6	78
7	 8g	112	92	98/2	88

Table 3 (*continued*)

Entry	Product	Time (h)	Yield[b] (%)	dr[c] (*syn*/*anti*)	ee[d] (%)
8	 8h	112	95	99/1	84
9	 8i	88	99	89/11	78
10	 8j	88	99	85/15	70
11	 8k	40	99	75/25	56
12	 8l	48	97	—	9.3
13	 8m	17	98	98/2	91
14	 8n	40	99	96/4	81

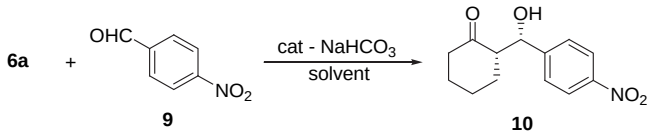
[a] All reactions were conducted in [Bmin]BF_4 (0.5 mL) using **6** (1.0 mmol) and **7** (0.1 mmol) in the presence of 10 mol % of the catalyst **3** and 50 mol %$NaHCO_3$.
[b] Isolated yield.
[c] Determined by ^1H NMR spectroscopy.
[d] Determined by HPLC analysis (Chiralcel AD-H or OD-H column).

Other cyclic ketones were also found to be compatible with **7a** under the optimized conditions (Table 3, entries 11–14). Reactions with six-membered ring ketone gave the Michael adducts with high enantioselectivities (81–91% ee) (Table 3, entries 13 and 14). However, when cyclopentanone was used as substrate, only moderate enantioselectivity was obtained (Table 3, entry 11). Acetone worked well to give the desired products in good yield, but poor enantioselectivity (9.3% ee) (Table 3, entry 12).

After the above success, we sought to extend the catalytic activity of chiral pyrrolidine-phosphite organocatalysts in an Aldol reaction. The results of enantioselective aldol reaction of

cyclohexanone with 4-nitrobenzaldehyde are shown in Table 4. Initial screening studies with pyrrolidine-phosphite organocatalyst 3 identified DMSO as the optimal solvent for the reaction (Table 4, entries 1–4). Other chiral pyrrolidine-phosphite organocatalysts were also test in the reaction; they all proceeded efficiently to give the corresponding product **10** in high yields (87–95%). However, the enantioselectivity of this reaction was moderate (Fig. 1).

Table 4
Asymmetric aldol reaction of 4-nitrobenzaldehyde with cyclohexanone using organocatalysts **3**–**5**[a]



9 **10**

Entry	cat. (%)	Solvent	Time (h)	Yield[b] (%)	*syn*/*anti*[c]	ee[d] (%) *syn*	ee[d] (%) *anti*
1	3-$NaHCO_3$	[Bmim][BF_4]	48	<5	—	—	—
2	3-$NaHCO_3$	DMF	24	90	48/52	51	30
3	3-$NaHCO_3$	Neat	36	92	40/60	40	40
4	3-$NaHCO_3$	DMSO	24	95	37/63	54	38
5	4-$NaHCO_3$	DMSO	24	91	54/46	30	22
6	5-$NaHCO_3$	DMSO	48	87	52/48	26	4

[a] All reactions were conducted in solvent (0.5 mL) using **6a** (0.1 mL, 1.0 mmol) and **9** (15 mg, 0.1 mmol) in the presence of 10 mol % of the catalyst and 50 mol %$NaHCO_3$.
[b] Isolated yield.
[c] Determined by ^{1}H NMR spectroscopy.
[d] Determined by HPLC analysis (Chiralcel AD-H column).

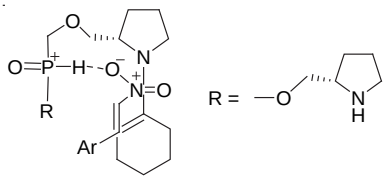


Fig. 1. Proposed transition state model for **3** catalyzed cyclohexanone to nitroolefins.

The high stereoselectivity may be tentatively explained by acyclic synclinal transition state model originally proposed by Seebach and Golinski.[12] The phosphite group occupies a larger space than a pyrrolidine to more efficiently shield the *si*-face of an enamine double bond, which might be a possible reason for the high stereochemical outcome. The hydrogen bond between the P–H and the nitro group activates the nitroolefins effectively.

3. Conclusions

We have developed a new class of chiral pyrrolidine-phosphite organocatalysts, which were easily prepared from *N*-Boc-L-prolinol, for the asymmetric Michael addition reaction of ketones to nitroolefins and for the Aldol reaction. The reactions were highly efficient in terms of yield and selectivity for Michael addition. In the case of direct Aldol reaction, the products were obtained with low enantioselectivity. Further investigation into the applications of these organocatalysts in asymmetric catalysis is in progress.

4. Experimental section

4.1. General information

All the solvents were purified according to standard procedures. The ^{1}H NMR and spectra was recorded at 300 MHz or 400 MHz, ^{13}C NMR was recorded at 75 MHz or 100 MHz. ^{1}H and ^{13}C NMR Chemical shifts were calibrated to tetramethylsilane as an external reference. ^{31}P NMR spectra were obtained with 85% H_3PO_4 (δ 0.0) as an external standard. Coupling constants are given in hertz. The following abbreviations are used to indicate the multiplicity: s, singlet; d, doublet: t, triplet; q, quartet; m, multiplet; HRMS were recorded on an IonSpec FT-ICR mass spectrometer with ESI resource. Optical rotations were measured on a Perkin–Elmer 341 Polarimeter at 20 °C. HPLC analysis was performed on Shimadzu CTO-10AS by using a Chiralpak AD-H or OD-H column purchased from Daicel Chemical Industries. The chemicals were purchased from commercial suppliers (Aldrich, USA and Shanghai Chemical Company, China) and were used without purification prior to use.

4.2. Synthesis of organocatalysts

*4.2.1. Bis(((S)-1-(tert-butoxycarbonyl)pyrrolidin-2-yl)methyl) phosphonate **2**.* To a dry round-bottom flask with magnetic stir bar were added 20 mL dry CH_2Cl_2, *N*-Boc-L-prolinol (2.0 g, 10.0 mmol), and triethylamine (1.4 mL, 10.0 mmol) at 0 °C via an ice bath. To this solution was added a solution of PCl_3 (0.66 g, 5.0 mmol) in 10 mL CH_2Cl_2 via cannula, dropwise, under argon at 0 °C. The reaction was allowed to stir at the same temperature for 2 h. Then the reaction mixture was heated to reflux and stir for 1 h. To the resulting solution was added H_2O (10 mL) at room temperature and stir for another hour. The organic solution was washed with brine (10 mL), and dried over Na_2SO_4, then filtered. The CH_2Cl_2 was concentrated under reduced pressure. The crude product was purified by column chromatography with petroleum ether/ethyl acetate (5:1) to afford 2.15 g (96% yield) of **2** as colorless oil. ^{1}H NMR (300 MHz, $CDCl_3$): δ (ppm) 1.44 (s, 18H), 1.56–1.71 (m, 2H), 1.73–1.89 (m, 4H), 1.95–2.06 (m, 2H), 3.29–3.35 (m, 2H), 3.41–3.46 (m, 2H), 3.55–3.61 (m, 3H), 3.88–3.97 (m, 2H), 4.13–4.21 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$,): δ (ppm) 23.84, 28.43, 28.65, 47.36, 59.86, 67.00, 80.09, 162.35; ^{31}P NMR (162 MHz, $CDCl_3$): δ 8.16; HRMS calcd for $C_{20}H_{37}N_2O_7PNa^+$ $(M+Na)^+$ 471.2231, found 471.2227; $[\alpha]_D^{20}$ −115.2° (*c* 0.5, CH_2Cl_2).

*4.2.2. Hydrochloric acid salts of bis(((S)-pyrrolidin-2-yl)methyl) phosphonate **3**.* To a solution of **2** (2.0 g, 4.5 mmol) in ethanol (8 mL) was added dropwise a solution of HCl (8 mL) in 8 mL ethanol at 0 °C. The mixture was warmed to room temperature and stirred overnight. After the removal of the organic solvents and more HCl under vacuo, the catalyst **3** was given as colorless oil (1.47 g, 100% yield). ^{1}H NMR (300 MHz, D_2O): δ (ppm) 1.56–1.63 (m, 2H), 1.82–2.01 (m, 6H), 3.14–3.26 (m, 4H), 3.47–3.78 (m, 6H); ^{13}C NMR (75 MHz, D_2O,): δ (ppm) 23.36, 25.83, 45.72, 60.32, 61.38; ^{31}P NMR (162 MHz, D_2O) δ 4.63; HRMS calcd for $C_{10}H_{22}N_2O_3P^+$ M^+ 249.1363, found 249.1364; $[\alpha]_D^{20}$ +38.4° (*c* 0.5, CH_3OH).

*4.2.3. Hydrochloric acid salts of ((S)-pyrrolidin-2-yl)methyl hydrogen phosphonate **4**.* To a dry round-bottom flask with magnetic stir bar were added 180 mL dry CH_2Cl_2 and PCl_3 (10.9 g, 80 mmol) at 0 °C via an ice bath. To this solution was added a solution of *N*-Boc-L-prolinol (1.6 g, 8.0 mmol) in 20 mL CH_2Cl_2 via cannula, dropwise, under argon at 0 °C. The reaction was allowed to stir at the same temperature for 2 h. Then the reaction mixture was warmed to room temperature and stirred overnight. The organic solvents and PCl_3 was evaporated at room temperature to give a colorless oil, which was used without further purification. To a solution of the oil in CH_2Cl_2 (20 mL) was added dropwise 8 mL HCl at 0 °C, and stirring was continued at room temperature overnight. The solvent was removed, and the residue was purified by chromatography (ethyl acetate/MeOH 6:1 then 2:1) to give 1.45 g (90% yield) of **4** as a wax. ^{1}H NMR (400 MHz, D_2O):

δ (ppm) 1.24–1.31 (m, 1H), 1.49–1.73 (m, 3H), 2.87 (t, 2H, J=7.2 Hz), 3.15–3.31 (m, 2H), 3.40 (dd, 1H, J_1=3.2 Hz, J_2=12.0 Hz); ^{13}C NMR (100 MHz, D_2O): δ (ppm) 22.97, 25.39, 45.21, 59.88, 60.91; ^{31}P NMR (162 MHz, D_2O) δ 4.29; HRMS calcd for $C_5H_{13}NO_3P^+$ M^+ 166.0628, found 166.0628; $[\alpha]_D^{20}$ +34.4° (*c* 0.5, CH_3OH).

4.2.4. Hydrochloric acid salts of ((S)-pyrrolidin-2-yl)methyl dihydrogen phosphate ***5***. To a dry round-bottom flask with magnetic stir bar were added 180 mL dry CH_2Cl_2 and $POCl_3$ (12.1 g, 80 mmol) at 0 °C via an ice bath. To this solution was added a solution of *N*-Boc-L-prolinol (1.6 g, 8.0 mmol) in 20 mL CH_2Cl_2 via cannula, dropwise, under argon at 0 °C. The reaction was allowed to stir at the same temperature for 2 h. Then the reaction mixture was warmed to room temperature and stirred overnight. The organic solvents and $POCl_3$ was evaporated to give a colorless oil, which was used without further purification. To a solution of the oil in CH_2Cl_2 (20 mL) was added dropwise 8 mL HCl at 0 °C, and stirring was continued at room temperature overnight. The solvent was removed, and the residue was purified by chromatography (ethyl acetate/MeOH 6:1 then 2:1) to give 1.26 g (73% yield) of **5** as a wax; ^{1}H NMR (400 MHz, D_2O): δ (ppm) 1.73–1.90 (m, 1H), 1.94–2.20 (m, 3H), 3.30 (t, 2H, J=7.6 Hz), 3.73–3.90 (m, 2H), 4.01–4.13 (m, 1H); ^{13}C NMR (100 MHz, D_2O): δ (ppm) 24.07, 25.91, 45.56, 60.39, 62.73; ^{31}P NMR (162 MHz, D_2O) δ 4.32; HRMS calcd for $C_5H_{13}NO_4P^+$ M^+ 182.0577, found 182.0578; $[\alpha]_D^{20}$ +25.9° (*c* 0.5, CH_3OH).

4.3. Representative procedure for the Michael reaction

To a mixture of catalyst **3** (6.4 mg, 0.02 mmol) in [Bmin][BF_4] (0.5 mL) $NaHCO_3$ (1.0 mg, 0.01 mmol) was added at room temperature under air. The reaction mixture was stirred for 10 min, then cyclohexanone (208 μL, 2.0 mmol) and *trans*-β-nitrostyrene (30 mg, 0.2 mmol) were added. The homogeneous reaction mixture was stirred at room temperature for 45 h. 5 mL H_2O was added, the mixture was extracted with ethyl acetate three times (5 mL×3) and the combined extracts were washed with brine, then dried over anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure. The residue was purified by flash silica gel chromatography (ethyl acetate/hexane 1:6) to afford the Michael adduct **8a** (49 mg, 99% yield) as white solid. *syn*/*anti*=99/1 (by ^{1}H NMR), The ee was determined by HPLC analysis (Chiralpak AD-H, *i*-PrOH/hexane=10/90, 0.5 mL/min, 254 nm, t_r (minor)=24.0 min, t_r (major)=31.5 min), 84% ee.

4.4. Representative procedure for the Aldol reaction

To a mixture of catalyst **3** (6.4 mg, 0.02 mmol) in DMSO (0.5 mL) $NaHCO_3$ (1.0 mg, 0.01 mmol) was added at room temperature under air. The reaction mixture was stirred for 10 min, then cyclohexanone (208 μL, 2.0 mmol) and 4-nitrobenzaldehyde (30 mg, 0.2 mmol) were added. The homogeneous reaction mixture was stirred at room temperature for 24 h. H_2O (5 mL) was added, the mixture was extracted with ethyl acetate three times (5 mL×3) and the combined extracts were washed with brine, then dried over anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure. The residue was purified by flash silica gel chromatography (ethyl acetate/hexane 1:6) to afford the pure Aldol product **10** (48 mg, 95% yield). *syn*/*anti*=37/63 (by ^{1}H NMR), The ee was determined by HPLC analysis (Chiralpak AD-H, *i*-PrOH/hexane=8/92, 1.0 mL/min, 254 nm, *syn*: t_1=23.8, t_2=27.4, 54% ee; *anti*: t_1=30.8, t_2=41.77), 38% ee.

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Supplementary data

Supplementary data associated with this article can be found in the online version at doi:10.1016/j.tet.2010.09.062.

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