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Highly enantioselective Michael addition reactions in water catalyzed by an insoluble MPS-supported 4-sulfonamidyl prolinol *tert*-butyldiphenylsilyl ether

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ABSTRACT

The development of a highly efficient, insoluble, and non-swelling MPS-supported organocatalyst for the direct asymmetric Michael reaction of ketones and aldehydes to nitrostyrenes at room temperature in water is described. Excellent yields (up to 100%) and high stereoselectivities (up to 94% dr and 93% ee) were achieved with 10 mol % of the catalyst. The resin-bound catalyst was simply separated and recovered by filtration, and reused for six consecutive trials without significant loss of activity and enantioselectivity.

Environmental concerns associated with chemical processes have encouraged the development of more environmentally friendly methodologies for organic reactions. Recently, organic reactions that took place in water have attracted a great deal of attention because water is safe, economical, and environmentally benign, and is considered to be a substitute for conventional organic solvents.[1] The synthesis of enantiopure molecules is another important issue.[2] In this field, asymmetric organocatalytic reactions have been proven to be very effective for achieving this goal and have witnessed a tremendous growth in recent years.[3] Organocatalysts are environmentally benign due to avoidance of use of heavy metals, inexpensiveness, and good stability to moisture and air.[4b] Thus, the development of organocatalysts that catalyze asymmetric reactions in water is currently a highly sought-after goal for green chemistry.[4]

However, organocatalysts still suffer drawbacks such as the requirement of high catalyst loading, sophisticated, and time-consuming process in final separation.[5l] To solve these difficulties, the development of easily recoverable and reusable polymer-supported catalysts appears attractive.[5] Recently, recyclable chiral organocatalysts have attracted considerable interest among organic chemists and have been developed to catalyze asymmetric organic reactions.[5] Amongst them, some recoverable organocatalyst (both non-supported and supported) have been developed for the asymmetric Michael addition of ketones or aldehydes to nitrostyrenes, such as fluorous pyrrolidine sulfonamide,[6] ionic liquid-supported pyrrolidine-based catalyst,[7] polymer-supported pyrrolidine,[8] and thiourea catalyst.[9] Although many good results have been achieved using supported organocatalysts, the catalysis is mainly performed under homogeneous conditions. Heterogeneous catalysis by polymer-supported organocatalysts has rarely been documented.[8a] Moreover, compared with soluble polymer-supported organocatalysts, insoluble polymer-supported ones have shown advantages such as product purification and catalyst recovery. Hence, development of highly effective insoluble polymer-supported organocatalysts is highly desirable.

On the other hand, Michael addition of carbonyl compounds to nitroalkenes affording versatile bifunctional products in an atom-economical manner has been extensively studied and considerable efforts have been directed toward the development of an organocatalytic asymmetric version over recent years.[10,11] With an interest in developing an efficient chiral organocatalytic system to achieve high yield and enantioselectivity in Michael addition, we have developed prolinol tert-butyldiphenylsilyl ether as organocatalysts for direct Michael reaction of ketones to nitroalkenes. Although high levels of enantioselectivity (73–95% ee) and diastereoselectivity ($\geqslant$20:1 dr) were achieved, the catalytic efficiency was low (up to 20 mol % catalyst loading).[12] It is therefore of importance to recover and reuse this kind of organocatalyst, which will make the reactions more economical and environmentally friendly.

For optimal performance, we have designed and introduced trans-4-amino substituent on the pyrrolidine ring of the prolinol *tert*-butyldiphenylsilyl ether, which could play a double role. On the one hand, the formation of thiourea or sulfonamide bond provides a convenient way to graft the chiral pyrrolidine monomer onto the polystyrene backbone. On the other hand, the thiourea or sulfonamide proton could activate the nitrostyrene by hydrogen bond effectively. In this Letter, we report that those novel insoluble and non-swelling MPS-supported organocatalysts catalyzed Michael addition of ketones to nitrostyrene in water in excellent yields and high enantioselectivities.

Four of the MPS-supported organocatalysts **1a–d** (Fig. 1) were synthesized and screened in asymmetric Michael addition of cyclohexanone to nitrostyrene under various conditions (Table 1). Initial

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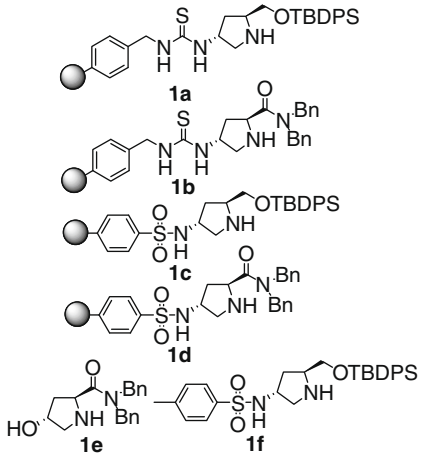


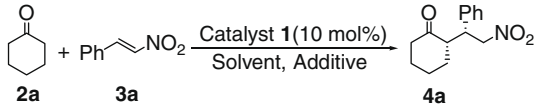
Figure 1. Chiral organocatalysts tested.

tests showed that the performance of catalysts **1a** and **1c**[13] was superior to that of **1b** and **1d** especially the enantioselectivities of the products. (*trans*-4-hydroxyprolylamide **1e**, which is the similar monomer of **1b** and **1d**, has also shown good results when it was used to catalyze the asymmetric Michael addition of aldehydes to nitroalkene).[11c] Good yield (89%) was achieved when the reaction was catalyzed by **1a** in the presence of PhCOOH as an additive in hexane at 10 °C after 3 d (Table 1, entry 1). When **1c** was used as the catalyst, the reactivity decreased; leading to 71% yield after 5 d (Table 1, entry 3). However, the enantioselectivity increased slightly from 89% ee to 92% ee. The reaction proceeded smoothly to give the product in 83% and 50% yields, respectively, in the presence of **1b** or **1d**. However, the enantioselectivity decreased dramatically and only 30% ee and 19% ee were obtained, respectively (Table 1, entries 2 and 4). These results indicated that the dibenzylamide was not as effective as the bulky group $CH_2OTBDPS$ in shielding the si-face of enamine double bond.

In order to achieve high reactivity and enantioselectivity, various reaction conditions were examined; a series of solvents including hexane, pentane, toluene, DCM, $CHCl_3$, Et_2O, THF, DMF, i-PrOH, and H_2O were screened using **1c** as catalyst in the presence of 10 mol % benzoic acid as additive (Table 1, entries 3, 5–14). Good enantioselectivities were obtained in hexane, pentane, and H_2O (Table 1, entries 3, 5, and 14). To our delight, the reactivity was increased when the reaction proceeded in water in comparison with that in hexane. The yields increased from 71% to 78% and the reaction time was shortened from 5 d to 4 d. The enantioselectivity slightly decreased from 92% ee to 90% ee (Table 1, entries 3 and 14). We also studied the influence of acid additive and reactive temperature on the reaction. When the additive was changed from benzoic acid into p-nitrobenzoic acid, the yield and the enantioselectivity increased from 78% to 89% and from 90% ee to 93% ee, respectively (Table 1, entries 14 and 15). When the reaction ran at rt, the reaction time was shortened from 4 d to 2 d. The yield increased from 89% to 94% and the enantioselectivity decreased slightly from 93% ee to 91% ee (Table 1, entries 15 and 19). Control experiment has shown that the influence of insoluble polystyrene part of catalyst **1c** was only on the reactivity, not on selectivity or diastereoselectivity. Under the same reaction conditions, when the reaction catalyzed by the non-supported catalyst **1f**, the same selectivity and diastereoselectivity were obtained, the reaction time was shortened from 2 d to 0.5 d (Table 1, entries 19 and 20).

With the optimal conditions in hand, a variety of nitrostyrenes with different substitutions were investigated and the results are summarized in Table 2.[14] Generally, nitrostyrenes bearing both electron-withdrawing (Table 2, entries 2–11, 17) and electron-donating (Table 2, entries 12–16, 20) aryl groups and heterocyclic groups (Table 2, entries 18 and 19) gave the desired products with high selectivities (dr up to 97/3 and ee up to 93%) in excellent yields. The substitution position of β-nitrostyrenes in some

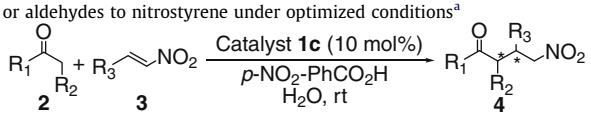
Table 1
Optimization of the reaction conditions

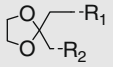


Entry	Catalyst	Solvent	Additive	Temperature (°C)	Time (d)	Yield (%)[c]	ee (%)[d] *syn*	dr[e] (*syn*/ *anti*)
1[a]	**1a**	Hexane	PhCOOH	10	3	89	89	97/3
2[a]	**1b**	Hexane	PhCOOH	10	3	83	30	95/5
3[a]	**1c**	Hexane	PhCOOH	10	5	71	92	94/6
4[a]	**1d**	Hexane	PhCOOH	10	4	50	19	94/6
5[a]	**1c**	Pentane	PhCOOH	10	4	91	88	93/7
6[a]	**1c**	Cyclohexane	PhCOOH	10	6.5	68	90	94/6
7[a]	**1c**	Toluene	PhCOOH	10	5.5	86	86	93/7
8[a]	**1c**	DCM	PhCOOH	10	6	87	87	92/8
9[a]	**1c**	$CHCl_3$	PhCOOH	10	6	44	82	91/9
10[a]	**1c**	Et_2O	PhCOOH	10	5	70	78	93/7
11[a]	**1c**	THF	PhCOOH	10	7	68	86	93/7
12[a]	**1c**	DMF	PhCOOH	10	4	Trace	—	—
13[a]	**1c**	*i*-PrOH	PhCOOH	10	4	Trace	—	—
14[b]	**1c**	H_2O	PhCOOH	10	4	78	90	94/6
15[b]	**1c**	H_2O	*p*-NO_2–PhCOOH	10	4	89	93	95/5
16[a]	**1c**	H_2O	*p*-NO_2–PhCOOH	rt	1	84	90	93/7
17[a]	**1c**	H_2O	PhCOOH	rt	1	91	88	93/7
18[a]	**1c**	H_2O	CH_3COOH	rt	1	55	87	92/8
19[b]	**1c**	H_2O	*p*-NO_2–PhCOOH	rt	2	94	91	93/7
20[b]	**1f**	H_2O	*p*-NO_2–PhCOOH	rt	0.5	100	91	93/7

[a] All reactions performed with 10 equiv cyclohexanone, 20 mol % additive, and 0.25 mmol nitrostyrene in the presence of 10 mol % 1 in 1 mL solvent.
[b] Using 10 mol % additive, 0.5 mL H_2O.
[c] Isolated yield.
[d] Determined by chiral HPLC analysis.
[e] Determined by ^1H NMR of the crude products

Table 2
Catalytic asymmetric Michael addition of ketones or aldehydes to nitrostyrene under optimized conditions[a]



Entry	R_1	R_2	R_3	Note	Time (h)	Yield (%)[b]	dr (*syn*/*anti*)[c]	ee (%)[d]
1		$-(CH_2)_4-$	Ph	**4a**	48	94	93/7	91
2		$-(CH_2)_4-$	2-ClPh	**4b**	24	95	95/5	90
3		$-(CH_2)_4-$	4-ClPh	**4c**	48	94	94/6	85
4		$-(CH_2)_4-$	2-BrPh	**4d**	47	96	95/5	93
5		$-(CH_2)_4-$	3-BrPh	**4e**	57	93	94/6	92
6		$-(CH_2)_4-$	4-BrPh	**4f**	71	98	95/5	91
7		$-(CH_2)_4-$	2-FPh	**4g**	28	97	97/3	93
8		$-(CH_2)_4-$	4-FPh	**4h**	71	92	93/7	91
9		$-(CH_2)_4-$	2-NO_2Ph	**4i**	42	100	96/4	90
10		$-(CH_2)_4-$	3-NO_2Ph	**4j**	72	95	93/7	92
11		$-(CH_2)_4-$	4-NO_2Ph	**4k**	48	100	94/6	90
12		$-(CH_2)_4-$	4-CH_3Ph	**4l**	55	95	94/6	92
13		$-(CH_2)_4-$	2-CH_3OPh	**4m**	71	97	95/5	90
14		$-(CH_2)_4-$	4-CH_3OPh	**4n**	72	87	88/12	87
15		$-(CH_2)_4-$	1-Naphthyl	**4o**	72	96	95/5	91
16		$-(CH_2)_4-$	2-Naphthyl	**4p**	72	86	94/6	93
17		$-(CH_2)_4-$	2,4-Cl_2Ph	**4q**	29	90	96/4	93
18		$-(CH_2)_4-$	2-Furyl	**4r**	48	91	89/11	88
19		$-(CH_2)_4-$	2-Thienyl	**4s**	72	98	89/11	86
20		$-(CH_2)_4-$		**4t**	72	84	93/7	91
21			Ph	**4u**	72	57	90/10	84
22	CH_3	H	Ph	**4v**	72	39	—	90
23[e]	H	C_2H_5	Ph	**4w**	12	99	97/3	77
24[e]	H	C_3H_7	Ph	**4x**	19	95	97/3	74
25[e]	H	C_6H_{13}	Ph	**4y**	19	94	88/12	74
26[e,f]	H	C_2H_5	Ph	**4w**	72	76	97/3	81
27[g]		$-(CH_2)_4-$	*n*-Bu	**4z**	86	42	5/95	89

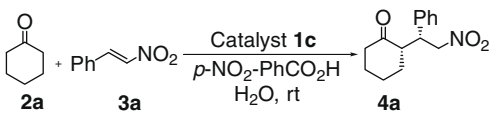
[a] All reactions performed with 10 equiv cyclohexanone, 10 mol % additive, and 0.25 mmol nitrostyrenes in the presence of 10 mol % **1c** in 0.5 mL H_2O at room temperature.
[b] Isolated yield.
[c] Determined by ^1H NMR of the crude products.
[d] Determined by chiral HPLC analysis.
[e] 20 equiv aldehyde.
[f] 0 °C.
[g] 20 mol % catalyst **1c** and 20 mol % additive.

substrates had a slight influence on the diastereoselectivities and enantioselectivities as well as on the yields. For example, when the methoxyl group position of nitrostyrene was changed from ortho to *para*, the yield decreased from 97% to 87% and the enantioselectivity decreased from 90% ee to 87% ee (Table 2, entries 13 and 14). However, the influence of bromo and nitro substituents on the aryl ring was on the diastereoselectivities and enantioselectivities (Table 2, entries 4–6, and 9–11). Other ketone and aldehyde substrates were investigated as well. Acetone gave the desired product in high enantioselectivities (90% ee) with poor yield (39%) (Table 2, entry 22). Good enantioselectivity (74–81% ee) and diastereoselectivity (76–94% dr) were obtained when aldehydes were used as donors (Table 2, entries 23–26). These results are better than those of the reactions catalyzed by the insoluble PS-supported pyrrolidine catalyst reported previously.[8a]

In addition, the recyclability of the MPS-supported sulfonamidyl prolinol tert-butyldiphenylsilyl ether was investigated. When the reaction was complete, the catalyst was filtered using a sintered glass funnel and washed with ethyl acetate followed by dichloromethane. After being dried in vacuo, **1c** was reused directly without further purification, and it was recovered and reused for six consecutive trials without significant loss of activity and enantioselectivity (Table 3, entries 1–6).

The high stereoselectivity may be tentatively explained by acyclic synclinal transition state model originally proposed by Seebach and Golinski.[15] As shown in Figure 2, for cyclohexanone, the bulky group ($-CH_2OTBDPS$) should effectively shield the si-face

Table 3
Recycling and reuse of catalyst in Michael addition of cyclohexanone to nitrostyrene[a]



Entry	Time (d)	Yield[b] (%)	ee[c] *syn* (%)	dr[d] *syn*:*anti*
1	1.4	92	92	93/7
2	2.5	94	92	93/7
3	2	91	92	93/7
4	3	92	91	93/7
5	3	89	92	92/8
6	4	82	91	92/8

[a] All reactions performed with 10 equiv cyclohexanone, 20 mol % additive, and 0.25 mmol nitrostyrenes in the presence of 20 mol % **1c** in 0.5 mL H_2O at room temperature.
[b] Isolated yield.
[c] Determined by chiral HPLC analysis.
[d] Determined by ^1H NMR of the crude products.

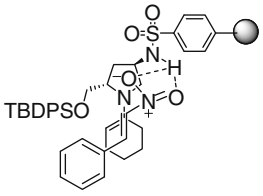


Figure 2. Proposed transition state model.

of an enamine double bond, which would make nitrostyrene acceptors approach from the non-shielded side to give the observed major enantiomer. The hydrogen bond between the sulfonamide proton and the nitro group activates the nitrostyrene effectively.

In conclusion, we have developed a novel MP-sulfonyl chloride resin-supported sulfonamidyl prolinol tert-butyldiphenylsilyl ether catalytic system. Only 10 mol % catalyst loading was needed for good yields (up to 100%) and high stereoselectivities (up to 97/3 dr and 93% ee). When used in the Michael reaction at room temperature in water, the catalyst can be reused for at least six times in subsequent reactions. Further investigations of the applications of this organocatalytic system in other asymmetric reactions are in progress.

Acknowledgments

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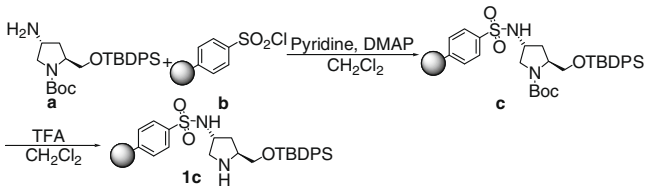
Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.tetlet.2009.04.011.

References and notes

1. For reviews on organic synthesis in water, see: (a) Lindstrom, U. M. *Chem. Rev.* **2002**, *102*, 2751; (b) Li, C. J. *Chem. Rev.* **2005**, *105*, 3095; (c) Kobayashi, S.; Manabe, K. *Acc. Chem. Res.* **2002**, *35*, 209; (d) Grieco, P. A. *Organic Synthesis in Water*; Blackie Academic & Professional: New York, 1998; (e) Li, C. J.; Chan, T. H. *Organic Reactions in Aqueous Media*; Wiley: New York, 1997.
2. Reviews see: (a) Tomioka, K.; Nagaoka, Y.; Yamaguchi, M. In *Comprehensive Asymmetric Catalysis*; Jacobsen, E. N., Pfaltz, A., Yamamoto, H., Eds.; Springer: New York, 1999; (b) Berner, O. M.; Tedeschi, L.; Enders, D. *Eur. J. Org. Chem.* **2002**, 1877; (c) Krause, N.; Hoffmann-Röder, A. *Synthesis* **2001**, *2*, 171; (d) Christoffers, J.; Koripelly, G.; Rosiak, A.; Rössle, M. *Synthesis* **2007**, *9*, 1279; (e) Tsukamoto, M.; Kagan, H. B. *Adv. Synth. Catal.* **2002**, *344*, 453; (f) Satyanarayana, T.; Kagan, H. B. *Adv. Synth. Catal.* **2005**, *347*, 737.
3. Reviews see: (a) Dalko, P. I.; Moisan, L. *Angew. Chem., Int. Ed.* **2004**, *43*, 5138; (b) Seayad, J.; List, B. *Org. Biomol. Chem.* **2005**, *3*, 719; (c) Berkessel, A.; Groger, H. *Asymmetric Organocatalysis: From Biomimetic Concepts to Applications in Asymmetric Synthesis*; Wiley-VCH Verlag GmbH & Co. KGaA: Weinheim, Germany, 2005; (d) Tsogoeva, S. B. *Eur. J. Org. Chem.* **2007**, *11*, 1701; (e) Connon, S. J. *Chem. Commun.* **2008**, 2499; (f) Vicario, J. L.; Badía, D.; Carrillo, L. *Synthesis* **2007**, *14*, 2065; (g) Almaşi, D.; Alonso, D. A.; Nájera, C. *Tetrahedron: Asymmetry* **2007**, *18*, 299; (h) Pellissier, H. *Tetrahedron* **2007**, *63*, 9267; (i) Notz, W.; Tanaka, F.; Barbas, C. F., III *Acc. Chem. Res.* **2004**, *37*, 580; (j) List, B. *Acc. Chem. Res.* **2004**, *37*, 548.
4. For selected examples of organocatalyzed reactions in pure water; see: (a) Mase, N.; Nakai, Y.; Ohara, N.; Yoda, H.; Takabe, K.; Tanaka, F.; Barbas, C. F., III *J. Am. Chem. Soc.* **2006**, *128*, 734; (b) Hayashi, Y.; Sumiya, T.; Takahashi, J.; Gotoh, H.; Urushima, T.; Shoji, M. *Angew. Chem., Int. Ed.* **2006**, *45*, 958; (c) Tang, Z.; Yang, Z. H.; Cun, L. F.; Gong, L. Z.; Mi, A. Q.; Jiang, Y. Z. *Org. Lett.* **2004**, *6*, 2285; (d) Dickerson, T. J.; Janda, K. D. *J. Am. Chem. Soc.* **2002**, *124*, 3220; (e) Mase, N.; Watanabe, K.; Yoda, H.; Takabe, K.; Tanaka, F.; Barbas, C. F., III *J. Am. Chem. Soc.* **2006**, *128*, 4966; (f) Vishnumaya Singh, V. K. *Org. Lett.* **2007**, *9*, 1117; (g) Zhu, S. L.; Yu, S. Y.; Ma, D. W. *Angew. Chem., Int. Ed.* **2008**, *47*, 545; (h) Yan, Z. Y.; Niu, Y. N.; Wei, H. L.; Wu, L. Y.; Zhao, Y. B.; Liang, Y. M. *Tetrahedron: Asymmetry* **2006**, *17*, 3288; (i) Luo, S. Z.; Mi, X. L.; Liu, S.; Xu, H.; Cheng, J. P. *Chem. Commun.* **2006**, 3687.
5. (a) Benaglia, M.; Puglisi, A.; Cozzi, F. *Chem. Rev.* **2003**, *103*, 3401; (b) Cozzi, F. *Adv. Synth. Catal.* **2006**, *348*, 1367; (c) Bannwarth, W.; Bergbreiter, D. E.; Desai, B.; End, N. Immobilized Catalysts: Solid, Phases, Immobilization and Applications. In *Topics in Current Chemistry*; Kirschning, A., Ed.; Springer GmbH: Berlin, 2004; Vol. 1, p 242; (d) Dickerson, T. J.; Reed, N. N.; Janda, K. D. *Chem. Rev.* **2002**, *102*, 3325; (e) Bergbreiter, D. E. *Chem. Rev.* **2002**, *102*, 3345; (f) Benaglia, M. *New J. Chem.* **2006**, *30*, 1525; (g) Font, D.; Jimeno, C.; Pericàs, M. A. *Org. Lett.* **2006**, *8*, 4653; (h) Wu, Y. Y.; Zhang, Y. Z.; Yu, M. L.; Zhao, G.; Wang, S. W. *Org. Lett.* **2006**, *8*, 4417; (i) Giacalone, F.; Gruttadauria, M.; Marculescu, A. M.; Noto, R. *Tetrahedron Lett.* **2007**, *48*, 255; (j) Yamaguchi, K.; Imago, T.; Ogasawara, Y.; Kasai, J.; Kotani, M.; Mizuno, N. *Adv. Synth. Catal.* **2006**, *348*, 1516; (k) Kehat, T.; Portnoy, M. *Chem. Commun.* **2007**, 2823; (l) Zhang, Y. G.; Zhao, L.; Lee, S. S.; Ying, J. Y. *Adv. Synth. Catal.* **2006**, *348*, 2027.
6. (a) Zu, L. S.; Wang, J.; Li, H.; Wang, W. *Org. Lett.* **2006**, *8*, 3077; (b) Wang, J.; Li, H.; Lou, B.; Zu, L. S.; Guo, H.; Wang, W. *Chem. Eur. J.* **2006**, *12*, 4321.
7. (a) Luo, S. Z.; Mi, X. L.; Zhang, L.; Liu, S.; Xu, H.; Cheng, J. P. *Angew. Chem., Int. Ed.* **2006**, *45*, 3093; (b) Ni, B. K.; Zhang, Q. Y.; Headley, A. D. *Green Chem.* **2007**, *9*, 737; (c) Ni, B. K.; Zhang, Q. Y.; Headley, A. D. *Tetrahedron Lett.* **2008**, *49*, 1249; (d) Siyutkin, D. E.; Kucherenko, A. S.; Struchkova, M. I.; Zlotin, S. G. *Tetrahedron Lett.* **2008**, *49*, 1212; (e) Wu, L. Y.; Yan, Z. Y.; Xie, Y. X.; Niu, Y. N.; Liang, Y. M. *Tetrahedron: Asymmetry* **2007**, *18*, 2086; (f) Li, P. H.; Wang, L.; Zhang, Y. C.; Wang, G. W. *Tetrahedron* **2008**, *64*, 7633.
8. (a) Alza, E.; Cambeiro, X. C.; Jimeno, C.; Pericàs, M. A. *Org. Lett.* **2007**, *9*, 3717; (b) Miao, T.; Wang, L. *Tetrahedron Lett.* **2008**, *49*, 2173; (c) Lv, G. H.; Jin, R. Z.; Mai, W. P.; Gao, L. X. *Tetrahedron: Asymmetry* **2008**, *19*, 2568.
9. Miyabe, H.; Tuchida, S.; Yamauchi, M.; Takemoto, Y. *Synthesis* **2006**, 3295.
10. For selected publications, see: (a) List, B.; Pojarliev, P.; Martin, H. J. *Org. Lett.* **2001**, *3*, 2423; (b) Tsogoeva, S. B.; Wei, S. W. *Chem. Commun.* **2006**, 1451; (c) Huang, H. B.; Jacobsen, E. N. *J. Am. Chem. Soc.* **2006**, *128*, 7170; (d) Lalonde, M. P.; Chen, Y. G.; Jacobsen, E. N. *Angew. Chem., Int. Ed.* **2006**, *45*, 6366; (e) Xu, Y. M.; Córdova, A. *Chem. Commun.* **2006**, 460; (f) Xu, Y. M.; Zou, W. B.; Sundén, H.; Ibrahem, I.; Córdova, A. *Adv. Synth. Catal.* **2006**, *348*, 418; (g) McCooey, S. H.; Connon, S. J. *Org. Lett.* **2007**, *9*, 599; (h) Liu, K.; Cui, H. F.; Nie, J.; Dong, K. Y.; Li, X. J.; Ma, J. A. *Org. Lett.* **2007**, *9*, 923; (i) Luo, S. Z.; Xu, H.; Mi, X. L.; Li, J. Y.; Zheng, X. X.; Cheng, J. P. *J. Org. Chem.* **2006**, *71*, 9244; (j) Cobb, A. J. A.; Longbottom, D. A.; Shaw, D. M.; Ley, S. V. *Chem. Commun.* **2004**, 1808; (k) Betancort, J. M.; Barbas, C. F., III *Org. Lett.* **2001**, *3*, 3737; (l) Pansare, S. V.; Pandya, K. *J. Am. Chem. Soc.* **2006**, *128*, 9624; (m) Alexakis, A.; Andrey, O. *Org. Lett.* **2002**, *4*, 3611; (n) Mossé, S.; Laars, M.; Kriis, K.; Kanger, T.; Alexakis, A. *Org. Lett.* **2006**, *8*, 2559; (o) Mossé, S.; Alexakis, A. *Org. Lett.* **2006**, *8*, 3577; (p) Wang, W.; Wang, J.; Li, H. *Angew. Chem., Int. Ed.* **2005**, *44*, 1369; (q) Diez, D.; Gil, M. J.; Moro, R. F.; Marcos, I. S.; García, P.; Basabe, P.; Garrido, N. M.; Broughton, H. B.; Urones, J. G. *Tetrahedron* **2007**, *63*, 740; (r) Cao, C. L.; Ye, M. C.; Sun, X. L.; Tang, Y. *Org. Lett.* **2006**, *8*, 2901; (s) Hayashi, Y.; Gotoh, H.; Hayashi, T.; Shoji, M. *Angew. Chem., Int. Ed.* **2005**, *44*, 4212; (t) Albertshofer, K.; Thayumanavan, R.; Utsumi, N.; Tanaka, F.; Barbas, C. F., III *Tetrahedron Lett.* **2007**, *48*, 693; (u) Xiong, Y.; Wen, Y. H.; Wang, F.; Gao, B.; Liu, X. H.; Huang, X.; Feng, X. M. *Adv. Synth. Catal.* **2007**, *349*, 2156; (v) Yang, Z. G.; Liu, J.; Liu, X. H.; Wang, Z.; Feng, X. M.; Su, Z. S.; Hu, C. W. *Adv. Synth. Catal.* **2008**, *350*, 2001; (w) Chen, H. B.; Wang, Y.; Wei, S. Y.; Sun, J. *Tetrahedron: Asymmetry* **2007**, *18*, 1308.
11. Selected publications, see: (a) García-García, P.; Ladépêhe, A.; Halder, R.; List, B. *Angew. Chem., Int. Ed.* **2008**, *47*, 4719; (b) Hayashi, Y.; Itoh, T.; Ohkubo, M.; Ishikawa, H. *Angew. Chem., Int. Ed.* **2008**, *47*, 4722; (c) Palomo, C.; Vera, S.; Mielgo, A.; Gómez-Bengoa, E. *Angew. Chem., Int. Ed.* **2006**, *45*, 5984; (d) Clarke, M. L.; Fuentes, J. A. *Angew. Chem., Int. Ed.* **2007**, *46*, 930; (e) Barros, M. T.; Phillips, A. M. F. *Eur. J. Org. Chem.* **2007**, 178; (f) Li, P. H.; Wang, L.; Wang, M.; Zhang, Y. C. *Eur. J. Org. Chem.* **2008**, 1157.
12. Liu, F. Y.; Wang, S. W.; Wang, N.; Peng, Y. G. *Synlett* **2007**, 2415.
13. *Synthesis of catalyst* **1c**:



Pyridine (2 mL) and **a** (1.1 g) in CH_2Cl_2 (2 mL) were added to a suspension solution of MP-sulfonyl resin **b** (0.5 g, f = 1.2 mmol/g) and DMAP 37 mg in CH_2Cl_2 (3 mL) at 0 °C. The resulting mixture was gently stirred for 24 h at room temperature. The mixture was filtered and the resin was washed successively with CH_2Cl_2, CH_3OH, and CH_2Cl_2 (three times) and then dried under vacuum to afford resin **c** (0.659 g, f = 0.58 mmol/g). IR (KBr): 3418, 3218, 3062, 3025, 2924, 2854, 2364, 2342, 2137, 1798, 1776, 1700, 1603, 1490, 1171, 1123, 1034, 1007, 756, 700, 506 cm^{-1}.Elemental Anal. N, 2.02; C, 72.58; H, 6.63. Trifluoroacetic acid (2 mL) was added to a suspension of resin **c** (0.659 g) in CH_2Cl_2 (5 mL) at 0 °C and then the mixture was warmed to room temperature and gently stirred overnight. The mixture was filtered and washed successively with 20% Et_3N/THF, CH_2Cl_2, CH_3OH, THF, and CH_2Cl_2 (three times). The solid was dried under vacuum to afford catalyst **1c** (0.58 g, f = 0.43 mmol/g). IR (KBr): 3418, 3218, 3062, 3025, 2924, 2854, 2364, 2342, 2137, 1798, 1776, 1700, 1603, 1490, 1171, 1123, 1034, 1007, 756, 700, 506 cm^{-1}. Elemental Anal. N, 2.2; C, 72.29; H, 6.68.
14. *General procedure for asymmetric Michael addition of ketones or aldehydes to nitroolefins catalyzed by* **1c**: The catalyst **1c** (f = 0.45 mmol/g, 56 mg, 10 mol %),

p-nitrobenzoic acid (4.2 mg, 10 mmol %), and cyclohexanone (10 equiv, 0.26 mL) were mixed in 0.5 mL water at room temperature. After stirring for 10 min, the nitroolefin (37.3 mg, 0.25 mmol) was added. The resulting suspension was gently stirred at room temperature for 1–3 d and then directly filtered. The solid resin was washed with ethyl acetate and the organic filtrate was washed with saturated $NaHCO_3$ and NaCl solution, dried over anhydrous Na_2SO_4, and concentrated under reduced pressure. The residue was purified by flash chromatography on silica gel (ethyl acetate/petroleum ether as eluent) to afford the Michael addition product (58 mg, 94%) as a white solid. The enantiomeric excess was determined by HPLC on a chiral phase chiralpak AD-H/AS-H column (91% ee).

15. Seebach, D.; Golinski, J. *Helv. Chim. Acta* **1981**, *64*, 1413.