JOC*Article*

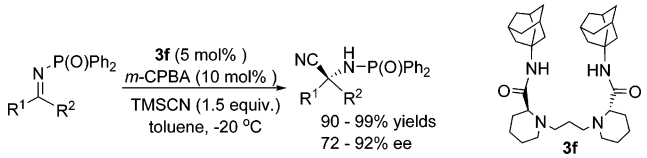
Enantioselective Strecker Reaction of Phosphinoyl Ketoimines Catalyzed by in Situ Prepared Chiral *N*,*N*′-Dioxides

Jinglun Huang,[†] Xiaohua Liu,[†] Yuehong Wen,[†] Bo Qin,[†] and Xiaoming Feng*[,†,‡]

Key Laboratory of Green Chemistry & Technology (Sichuan University), Ministry of Education, College of Chemistry, Sichuan University, Chengdu 610064, China, and State Key Laboratory of Biotherapy, West China Hospital, Sichuan University, Chengdu 610041, China

xmfeng@scu.edu.cn

Received September 28, 2006



The enantioselective Strecker reaction of *N*-diphenylphosphinoyl ketoimines has been achieved by use of in situ prepared chiral *N*,*N*′-dioxide catalyst from L-piperidinamide **3f** and *m*-chloroperoxybenzoic acid (*m*-CPBA). Excellent yields (up to 99%) and high enantioselectivities (up to 92% ee) were obtained. In particular, in situ prepared catalyst with readily available chiral material made the procedure more convenient. Moreover, the L-piperidinamide **3f**-derived *N*,*N*′-dioxide **9** could be recycled and reused at least five times without any loss of either catalytic activity or enantioselectivity.

Introduction

The Strecker reaction is one of the most attractive methods for the synthesis of α-amino acids and their derivatives.[1] Effective catalytic asymmetric cyanation of various aldimines has been achieved, leading to efficient formation of monosubstituted chiral α-amino nitriles.[2] However, relatively fewer systems have been developed for catalytic asymmetric cyanation of ketoimines, which is very useful for the generation of quaternary α-amino acids. Reported methods include metal-catalyzed cyanations with chiral heterobimetallic complex catalyst[3] and gadolinium complex catalyst.[4] Only a metal-free chiral urea catalyst has been reported to be effective for the aryl methyl ketoimines and *t*-butyl methyl ketomine.[5] Then, we expect to find another new organocatalyst, which can enantioselectively catalyze the Strecker reaction of ketoimine.

Chiral *N*-oxide has been disclosed as having high efficiency in many asymmetric procedures.[6] We previously reported that chiral *N*,*N*′-dioxide was a highly efficient catalyst for the cyanation of aldimines and aldehydes with moderate to high

[†] Key Laboratory of Green Chemistry & Technology.
[‡] State Key Laboratory of Biotherapy.

(1) Strecker, A. *Ann. Chem. Pharm.* **1850**, *75*, 27−45.
(2) (a) Iyer, M. S.; Gigstad, K. M.; Namdev, N. D.; Lipton, M. *J. Am. Chem. Soc.* **1996**, *118*, 4910−4911. (b) Sigman, M. S.; Jacobsen, E. N. *J. Am. Chem. Soc.* **1998**, *120*, 4901−4902. (c) Ishitani, H.; Komiyama, S.; Kobayashi, S. *Angew. Chem., Int. Ed.* **1998**, *37*, 3186−3188. (d) Corey, E. J.; Grogan, M. J. *Org. Lett.* **1999**, *1*, 157−160. (e) Krueger, C. A.; Kuntz, K. W.; Dzierba, C. D.; Wirschun, W. G.; Gleason, J. D.; Snapper, M. L.; Hoveyda, A. H. *J. Am. Chem. Soc.* **1999**, *121*, 4284−4285. (f) Porter, J. R.; Wirschun, W. G.; Kuntz, K. W.; Snapper, M. L.; Hoveyda, A. H. *J. Am. Chem. Soc.* **2000**, *122*, 2657−2658. (g) Sigman, M. S.; Vachal, P.; Jacobsen, E. N. *Angew. Chem., Int. Ed.* **2000**, *39*, 1279−1281. (h) Takamura, M.; Hamashima, Y.; Usuda, H.; Kanai, M.; Shibasaki, M. *Angew. Chem., Int. Ed.* **2000**, *39*, 1650−1652. (i) Yet, L. *Angew. Chem., Int. Ed.* **2001**, *40*, 875−877. (j) Mansawat, W.; Bhanthumnavin, W.; Vilaivan, T. *Tetrahedron Lett.* **2003**, *44*, 3805−3808. (k) Nakamura, S.; Sato, N.; Sugimoto, M.; Toru, T. *Tetrahedron: Asymmetry* **2004**, *15*, 1513−1516. (l) Huang, J.; Corey, E. J. *Org. Lett.* **2004**, *6*, 5027−5029. (m) Spino, C. *Angew. Chem., Int. Ed.* **2004**, *43*, 1764−1766. (n) Ooi, T.; Uematsu, Y.; Maruoka, K. *J. Am. Chem. Soc.* **2006**, *128*, 2548−2549. (o) Rueping, M.; Sugiono, E.; Azap, C. *Angew. Chem., Int. Ed.* **2006**, *45*, 2617−2619.
(3) (a) Byrne, J. J.; Chavarot, M.; Chavant, P.-Y.; Vallée, Y. *Tetrahedron Lett.* **2000**, *41*, 873−876. (b) Chavarot, M.; Byrne, J. J.; Chavant, P. Y.; Vallée, Y. *Tetrahedron: Asymmetry* **2001**, *12*, 1147−1150.
(4) (a) Masumoto, S.; Usuda, H.; Suzuki, M.; Kanai, M.; Shibasaki, M. *J. Am. Chem. Soc.* **2003**, *125*, 5634−5635. (b) Kato, N.; Suzuki, M.; Kanai, M.; Shibasaki, M. *Tetrahedron Lett.* **2004**, *45*, 3147−3151. (c) Kato, N.; Suzuki, M.; Kanai, M.; Shibasaki, M. *Tetrahedron Lett.* **2004**, *45*, 3153−3155.
(5) (a) Vachal, P.; Jacobsen, E. N. *Org. Lett.* **2000**, *2*, 867−870. (b) Vachal, P.; Jacobsen, E. N. *J. Am. Chem. Soc.* **2002**, *124*, 10012−10014.
(6) (a) Tao, B.; Lo, M. M.-C.; Fu, G. C. *J. Am. Chem. Soc.* **2001**, *123*, 353−354. (b) Denmark, S. E.; Fan, Y. *J. Am. Chem. Soc.* **2002**, *124*, 4233−4235. (c) Shimada, T.; Kina, A.; Hayashi, T. *J. Org. Chem.* **2003**, *68*, 6329−6337. (d) Traverse, J. F.; Zhao, Y.; Hoveyda, A. H.; Snapper, M. L. *Org. Lett.* **2005**, *7*, 3151−3154. (e) Malkov, A. V.; Bell, M.; Castelluzzo, F.; Kočovsý, P. *Org. Lett.* **2005**, *7*, 3219−3222.
(7) (a) Liu, B.; Feng, X. M.; Chen, F. X.; Zhang, G. L.; Cui, X.; Jiang, Y. Z. *Synlett* **2001**, 1551−1554. (b) Jiao, Z. G.; Feng, X. M.; Liu, B.; Chen, F. X.; Zhang, G. L.; Jiang, Y. Z. *Eur. J. Org. Chem.* **2003**, 3818−3826. (c) Wen, Y. H.; Huang, X.; Huang, J. L.; Xiong, Y.; Qin, B.; Feng, X. M. *Synlett* **2005**, 2445−2448.

10.1021/jo062006y CCC: $37.00
Published on Web 12/07/2006

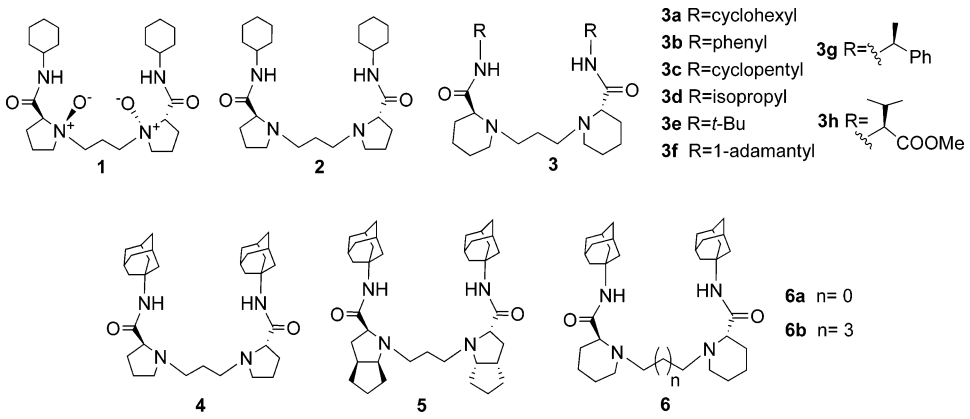
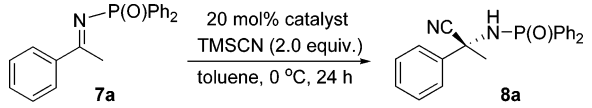


FIGURE 1. Catalysts evaluated in this study.

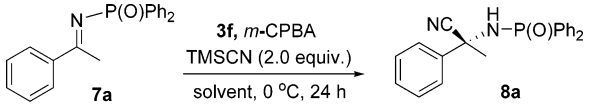
TABLE 1. Asymmetric Strecker Reaction Catalyzed by Various Catalysts[a]



	catalyst			
entry	precursor (mol %)	*m*-CPBA mol %	conversion,[b] %	ee,[c] %
1	**1** (20)	0	28	42
2	**2** (20)	40	29	43
3	**3a** (20)	40	56	65
4	**3b** (20)	40	15	51
5	**3c** (20)	40	45	66
6	**3d** (20)	40	20	64
7	**3e** (20)	40	50	77
8	**3f** (20)	40	64	80
9	**3g** (20)	40	28	74
10	**3h** (20)	40	10	44
11	**4** (20)	40	95	58
12	**5** (20)	40	<5	55
13	**6a** (20)	40	68	13
14	**6b** (20)	40	22	0

[a] All reactions were carried out in the air; concentration of ketoimine was 0.1 M; see Supporting Information for details. [b] Conversions were determined by chiral HPLC. [c] Determined by HPLC on Chiralcel OD column and the absolute configuration was determined to be *R* by comparison with literature data.[4]

TABLE 2. Solvent and Catalyst Loading Effects on the Strecker Reaction of Ketoimine 7a[a]



	catalyst				
entry	**3f** (mol %)	*m*-CPBA (mol %)	solvent	conversion,[b] %	ee,[c] %
1	20	40	toluene	64	80
2	20	40	THF	60	65
3	20	40	CH_3CN	50	3
4	20	40	CH_2Cl_2	<5	27
5	20	40	MeOH	NR	
6	40	80	toluene	99	64
7	5	10	toluene	38	80

[a–c] See Table 1 footnotes.

enantioselectivity.[7] However, our subsequent study has shown that the cyanation of ketones with the chiral *N*,*N*′-dioxide required the presence of a metal.[8] Herein, we report a highly enantioselective Strecker reaction of ketoimines by a metal-free system with a readily available chiral C_2-symmetric *N*,*N*′-dioxide as catalyst.

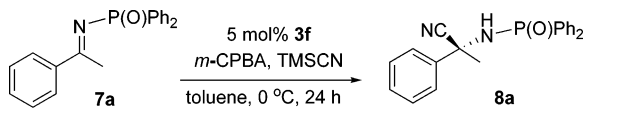
Results and Discussion

Reaction Condition Optimization. We initiated our search for the Strecker reaction between *N*-diphenylphosphinoyl ketoimine **7a** and trimethylsilyl cyanide (TMSCN) by using 20 mol % L-prolinamide-derived *N*,*N*′-dioxide **1** (Figure 1). As shown in Table 1, organocatalyst **1** gave moderate enantioselectivity (42% ee) (Table 1, entry 1). Interestingly, a similar result was obtained when chiral *N*,*N*′-dioxide **1** was generated in situ with 20 mol % prolinamide **2** and 40 mol % *m*-chloroperoxybenzoic acid (*m*-CPBA) (Table 1, entry 2) (no reaction was observed with prolinamide **2** as the catalyst alone). To optimize the catalyst, various in-situ-generated chiral *N*,*N*′-dioxides were then examined for the Strecker reaction. As shown in Table 1, significantly higher ee values were obtained with piperidinamide **3**-derived *N*,*N*′-dioxides (Table 1, entries 3−10). The enantioselectivity was increased to 80% ee with the bulky 1-adamantylamine-based (**3f**) catalyst (Table 1, entry 8). Other changes to the catalysts, such as replacing piperidinamide (Table 1, entries 11 and 12) or decreasing or increasing the length of carbon chain (Table 1, entries 13 and 14) resulted in lower enantioselectivity.

Then, we selected the catalyst precursor **3f** to investigate other parameters. As shown in Table 2, the yields and enantioselectivities were very much dependent on the solvent. Of the solvents screened, toluene was the best (Table 2, entry 1). Tetrahydrofuran (THF) and CH_3CN also provided good yields, but the enantioselectivities were notably diminished (Table 2, entries 2 and 3). When CH_2Cl_2 was used, a rather low yield was obtained (Table 2, entry 4). However, no product was observed in MeOH as solvent, which was probably due to the fact that the TMSCN and MeOH generated hydrogen cyanide (Table 2, entry 5). In addition, higher catalyst loading could result in complete conversion, but the enantioselectivity decreased to 64% ee (Table 2, entry 6). Fortunately, when the catalyst loading was reduced to 5 mol %, there was no loss in enantioselectivity (Table 2, entry 7).

(8) Li, Q. H.; Liu, X. H.; Wang, J.; Shen, K.; Feng, X. M. *Tetrahedron Lett.* **2006**, *47*, 4011−4014.

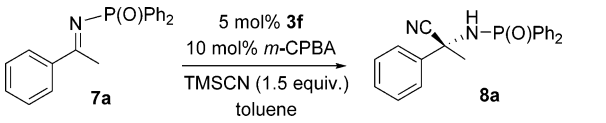
TABLE 3. Amount of TMSCN and *m*-CPBA Effects on the Strecker Reaction of Ketoimine 7a[a]



entry	TMSCN (equiv)	*m*-CPBA (mol %)	conversion,[b] %	ee,[c] %
1	2.0	15	35	75
2	2.0	5	17	73
3	2.0	10	38	80
4	3.0	10	75	79
5	2.5	10	66	79
6	1.5	10	34	80

[a] –[c]See Table 1 footnotes.

TABLE 4. Temperature and Concentration Effects on the Strecker Reaction of Ketoimine 7a[a]



entry	temp, °C	ketoimine concn, M	time, h	conversion,[b] %	ee,[c] %
1	25	0.1	24	99	73
2	0	0.1	24	34	80
3	−20	0.1	48	38	90
4	−45	0.1	48	NR	
5	−20	0.05	48	16	92
6	−20	0.2	48	68	84
7	−20	0.25	48	77	83
8	−20	0.1	196	>99	90

[a] All reaction were performed in the air; see Supporting Information for details. [b,c]See Table 1 footnotes.

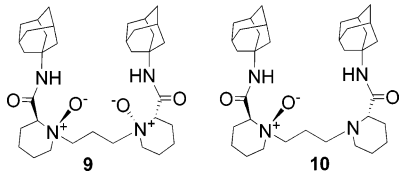
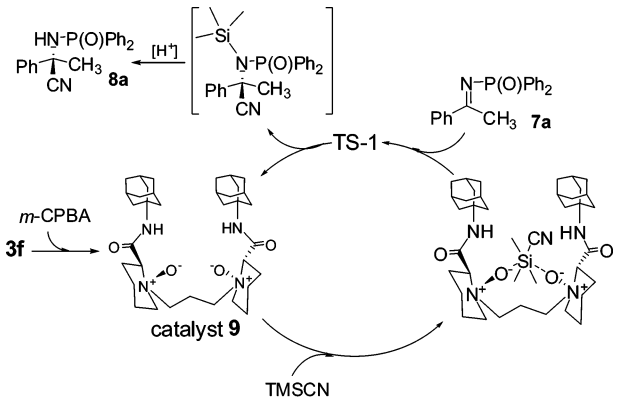


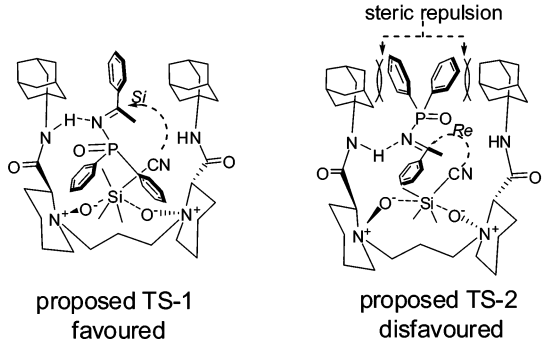
FIGURE 2. *N*-oxides of piperidinamide **3f**.

With 5 mol % **3f** in toluene, we next examined the amount of *m*-CPBA and TMSCN with results summarized in Table 3. When the *m*-CPBA loading was increased, the yield and enantioselectivity somewhat dropped (Table 3, entry 1 vs 3). However, lowering the *m*-CPBA loading greatly decreased the yield, which was probably due to the fact that the piperidinamide **3f** was not completely oxidized into the effective *N*,*N*-dioxide (Table 3, entry 2 vs 3). There was a tendency that higher amounts of TMSCN resulted in higher yields (Table 3, entries 3−6). In order to use less reagent, we chose 1.5 equiv of TMSCN in the subsequent optimization.

Under the conditions of 5 mol % **3f**, 10 mol % *m*-CPBA, and 1.5 equiv of TMSCN, the reaction temperature and ketoimine concentration were investigated and the results are presented in Table 4. The reaction temperature was found to be the key factor in the yields and enantioselectivities. Lowering the temperature led to a dramatic drop in reactivity (Table 4, entries 1−4). Fortunately, the product was obtained with up to 90% ee in moderate conversion at −20 °C (Table 4, entry 3).

SCHEME 1. Proposed Catalytic Cycle





However, further decreasing the temperature to −45 °C led to no product (Table 4, entry 4). With the concentration of ketoimine increasing, the yields were improved, while the enantioselectivities decreased from 92% to 83% ee (Table 4, entries 3−7). When the concentration of ketoimine was 0.1 M, the appropriate conversion and enantioselectivity were obtained (38% conversion, 90% ee). Complete conversion could be obtained by prolonging the reaction time and high enantioselectivity remained (Table 4, entry 8).

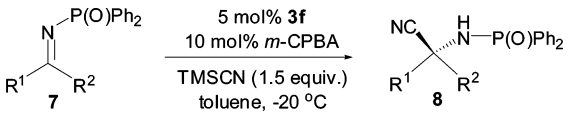
Hence, the optimal conditions were 5 mol % **3f**, 10 mol % *m*-CPBA, concentration of ketoimine 0.1 M, 1.5 equiv of TMSCN, toluene, and −20 °C.

Substrate Generality. Encouraged by these results, we investigated a variety of *N*-diphenylphosphinoyl ketoimines. As shown in Table 5, excellent yields (90−99%) were obtained with all substrates. High enantioselectivities were obtained for aryl methyl ketoimines (Table 5, entries 1−12). In some cases, essentially optically pure products can be obtained by recrystallization from CH_2Cl_2/hexane (Table 5, entries 6 and 7). The reaction can also extend to cyclic ketoimine with 90% ee (Table 5, entry 13). Somewhat lower ee values were obtained with aryl propyl ketoimine **7n**, propiophenone-derived ketoimine **7o,** and alkyl-substituted ketoimine **7p,** as well as heteroaromatic ketoimines **7q** and **7r** (Table 5, entries 14−18). Most of the products **8** in Table 5 can be directly subjected to acid hydrolysis to produce the corresponding amino acids.[4]

To check the reusability of the catalyst, the chiral piperidinamide **3f**-derived *N*,*N*′-dioxide **9** was isolated (Figure 2). From the results in Table 6, it was clearly demonstrated that catalyst **9** could be recycled and reused at least five times without any loss of either catalytic activity or enantioselectivity. In addition, chiral catalyst **9** was quantitatively recovered from the reaction mixture by using flash silica gel column chromatography.

Mechanistic Consideration. To gain preliminary insight into the mechanism, some experiments were tested: (1) The in-situ-

TABLE 5. Scope of the Enantioselective Strecker Reaction of Ketoimine 7[a]



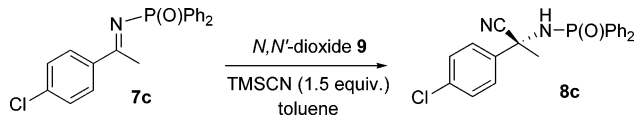
entry	ketoimines **7**	products **8**	yield (%) [b]	ee (%) [c]
1	**7a** R= H	**8a**	91	90 (*R*)
2	**7b** R= *p*-F	**8b**	95	90 (*R*)
3	**7c** R= *p*-Cl	**8c**	98	89 (*R*)
4	**7d** R= *p*-Br	**8d**	92	91 (*R*)
5 [d]	**7e** R= *p*-MeO	**8e**	93	89 (*R*)
6 [e]	**7f** R= *p*-Me	**8f**	97 (55)[f]	92 (>99)[f] (*R*)
7	**7g** R= *m*-Cl	**8g**	95 (63)[f]	88 (>99)[f] (*R*)
8	**7h** R= *m*-NO_2	**8h**	94	88 (*R*)
9	**7i** R= *o*-F	**8i**	98	81
10 [e]	**7j**	**8j**	90	92
11 [e]	**7k**	**8k**	91	89
12 [d]	**7l**	**8l**	99	88 (*R*)
13	**7m**	**8m**	91	90 (*R*)
14 [e]	**7n**	**8n**	91	78
15	**7o**	**8o**	97	76 (*R*)
16	**7p**	**8p**	98	80
17	**7q**	**8q**	92	77
18 [e]	**7r**	**8r**	91	72

[a] Unless other specified, reactions were run with 0.1 mmol of ketoimine, 0.15 mmol of TMSCN, and 5 mol % catalyst in 1 mL of toluene for 60−196 h in the air; see Supporting Information for details. [b] Isolated yields. [c] The ee values were determined by chiral HPLC. The absolute configuration of **8a** was determined by comparison with literature data[4] and other configurations were compared with the Cotton effect in their CD spectra (see Supporting Information for details). [d] 10 mol % **3f** and 20 mol % *m*-CPBA were used, and the reaction was at −10 °C. [e] 10 mol % **3f** and 20 mol % *m*-CPBA were used. [f] Product was recrystallized from CH_2Cl_2/hexane.

generated **9** and isolated **9** gave the same enantioselectivities and conversions (see Supporting Information), whereas no product was detected with piperidinamide **3f** or *m*-CPBA alone as the catalyst. This result revealed that the *N*-oxide played the role of actual catalyst. (2) The single *N*-oxide **10** derived from L-piperidinamide **3f** could not catalyze the addition of TMSCN to ketoimine (Figure 2), which suggested that TMSCN was likely to be activated by the two donors (N−O) of catalyst **9.**[9] (3) The nucleophilicity of the cyano group was enhanced, which can be proved by simple ^{29}Si NMR spectra. Another strong silicon signal was found at $\delta = 0.51$ ppm when chiral *N*,*N*′-dioxide **9** and TMSCN were mixed (see Supporting Information). (4) No product was found when HCN replaced TMSCN, which suggested that the attacking group was not CN^- ion but activated TMSCN. On the basis of these observations, we proposed a possible catalytic cycle (Scheme 1). The chiral *N*,*N*′-dioxide **9** was first generated from piperidinamide **3f** and *m*-CPBA. Then chiral *N*,*N*′-dioxide **9** coordinated with the TMSCN to form the possible hypervalent silicate, enhancing

(9) (a) Tian, S.-K.; Deng, L. *J. Am. Chem. Soc.* **2001**, *123*, 6195−6196. (b) Tian, S.-K.; Hong, R.; Deng, L. *J. Am. Chem. Soc.* **2003**, *125*, 9900−9901. (c) Kato, N.; Tomita, D.; Maki, K.; Kanai, M.; Shibasaki, M. *J. Org. Chem.* **2004**, *69*, 6128−6130. (d) Hamashima, Y.; Kanai, M.; Shibasaki, M. *J. Am. Chem. Soc.* **2000**, *122*, 7412−7413. (e) Ryu, D. H.; Corey, E. J. *J. Am. Chem. Soc.* **2005**, *127*, 5384−5387. (f) Knudsen, K. R.; Risgaard, T.; Nishiwaki, N.; Gothelf, K. V.; Jørgensen, K. A. *J. Am. Chem. Soc.* **2001**, *123*, 5843−5844.

TABLE 6. Recycling and Reuse of the Chiral *N,N′*-Dioxide 9 in Strecker Reaction [a]



	cycle				
	1	2	3	4	5
yield,[b] %	95	96	95	93	96
ee,[c] %	87	90	89	88	89

[a] The reaction were performed with 5 mol % *N,N′*-dioxide **9** at −20 °C for 68 h. [b] Isolated yield. [c] Determined by HPLC on Chiralcel OJ column.

the nucleophilicity of TMSCN and creating a fixed chiral pocket. On the other hand, hydrogen bonding,[10] between the amide moiety and the ketoimine **7a**, may also play a role in activating the ketoimine and controlling the reaction conformation. The cyano group prefered to attack the *si* face of the hydrogen-bond-activated ketoimine (proposed TS-1), affording enantiomer *R*-**8a** as major product, since the *re*-face attack was likely to disfavor the steric repulsion between the phenyl group of phosphinoyl and the bulky 1-adamantylamine of catalyst in proposed TS-2.

Conclusion

In summary, we have developed a new strategy for asymmetric Strecker reaction of ketoimines using in-situ-formed *N,N′*-dioxide catalyst. High yields and moderate to excellent enantioselectivities have been obtained for a wide variety of substrates. Attractive features of the present method include the simple in situ catalyst preparation with readily available material, mild reaction conditions, and convenient procedure with the tolerance of moisture and air. Moreover, the chiral *N,N′*-dioxide can be easily recovered and reused at least five times without any loss in either catalytic activity or enantioselectivity.

Experimental Section

Typical Procedure for Catalyst Preparation (3f). To a solution of (*S*)-1-*N*-Boc-piperidine-2-carboxylic acid (917 mg, 4 mmol) in CH_2Cl_2 (40 mL) were added Et_3N (0.62 mL, 4.4 mmol) and isobutyl carbonochloridate (576 mg, 4.4 mmol) at 0 °C under stirring. After 15 min, amine (666 mg, 4.4 mmol) was added. The reaction was allowed to warm to ambient temperature and detected by thin-layer chromatography (TLC). The mixture was washed with 1 M $KHSO_4$, saturated $NaHCO_3$, and brine, dried over anhydrous $MgSO_4$, and concentrated. To the residue in CH_2Cl_2 (4 mL) was added TFA (4 mL), and the mixture was stirred until the reaction was finished. Then the solvent was evaporated, and H_2O (10 mL) was added. The pH value of the mixture was brought into the range of 8−10 by the addition of 1 M NaOH. The aqueous phase was extracted with CH_2Cl_2 (5 × 20 mL). The combined organic phase was washed with brine, dried over anhydrous $MgSO_4$, and evaporated in vacuo. The residue was directly used for next step. To a solution of (*S*)-1-*N*-Boc-piperidine-2-carbonamide in CH_3CN (4 mL) were added K_2CO_3 (608 mg, 4.4 mmol) and 1,3-dibromopropane (204 μL, 2 mmol) under stirring. It was kept at 80 °C and monitored by TLC. Then K_2CO_3 was removed by filtration. The residue was concentrated and purified by silica gel column chromatography (EtOAc) to give a white product **3f** (1.060 g, 94% yield): mp 74−76 °C; $[\alpha]_D^{25} = -103.60$ ($c = 0.50$ in $CHCl_3$); ^{1}H NMR [400 MHz, $CDCl_3$, 25 °C, tetramethylsilane (TMS)] δ 6.38 (s, 2H), 3.05 (d, J = 11.2 Hz, 2H), 2.46−2.52 (m, 4H), 2.16−2.22 (m, 2H), 2.07−2.10 (m, 8H), 1.92−1.98 (m, 14H), 1.65−1.68 (m, 18H), 1.34−1.45 (m, 4H), 1.22−1.28 (m, 2H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C, TMS) δ 173.7, 69.2, 54.7, 51.4, 50.9, 41.6, 36.2, 30.8, 29.3, 25.0, 24.5, 23.5 ppm; EI-HRMS calcd for $C_{35}H_{56}N_4O_2$ (M^+) 564.4403, found 564.5426.

Typical Experimental Procedure for the Catalytic Enantioselective Strecker Reaction (7a). The chiral piperidinamide **3f** (2.8 mg, 0.005 mmol) and *m*-CPBA (1.8 mg, 0.01 mmol) in toluene (0.4 mL) were stirred in a tube at ambient temperature for 0.5 h. Then ketoimine **7a** (31.9 mg, 0.1 mmol), dissolved in toluene (0.6 mL), was added. Subsequently, TMSCN (20.2 μL, 0.15 mmol) was added at −20 °C. When ketoimine **7a** disappeared (monitored by HPLC), the reaction mixture was directly purified by column chromatography on silica gel eluted with ethyl acetate/petroleum ether (1:1 v/v) to afford product **8a** as an off-white solid: mp 122−124 °C; $[\alpha]_D^{25} = +14.02$ ($c = 0.214$ in $CHCl_3$, 90% ee); ^{1}H NMR (400 Hz, $CDCl_3$, 25 °C, TMS) δ 8.01−8.07 (m, 2H), 7.81−7.86 (m, 2H), 7.73−7.76 (m, 2H), 7.33−7.60 (m, 9H), 3.68 (d, J = 7.6 Hz, 1H, NH), 2.29 (s, 3H) ppm; HPLC (Chiralcel OD, hexane/2-propanol = 95/5, 0.6 mL/min), t_R (minor) = 40.63 min, t_R (major) = 45.66 min, 91% yield, 90% ee.

Acknowledgment. This work was financially supported by the National Natural Science Foundation of China (20225206, 20390055, and 20372050) and the Ministry of Education, People's Republic of China (104209). We also thank Sichuan University Analytical and Testing Center for CD spectra analysis.

Supporting Information Available: Experimental procedures and structural proofs for catalysts and racemates, CD spectra, ^{1}H NMR and ^{13}C NMR spectra, and HPLC results. This material is available free of charge via the Internet at http://pubs.acs.org.

JO062006Y

(10) (a) Huang, Y.; Rawal, V. H. *J. Am. Chem. Soc.* **2002**, *124*, 9662−9663. (b) Roitzsch, M.; Lippert, B. *J. Am. Chem. Soc.* **2004**, *126*, 2421−2424. (c) Pihko, P. M. *Angew. Chem., Int. Ed.* **2004**, *43*, 2062−2064. (d) Unni, A. K.; Takenaka, N.; Yamamoto, H.; Rawal, V. H. *J. Am. Chem. Soc.* **2005**, *127*, 1336−1337. (e) Kim, K. M.; Park, H.; Kim, H.-J.; Chin, J.; Nam, W. *Org. Lett.* **2005**, *7*, 3525−3527. (f) Taylor, M. S.; Jacobsen, E. N. *Angew. Chem., Int. Ed.* **2006**, *45*, 1520−1543.