Enantioselective Strecker Reactions between Aldimines and Trimethylsilyl Cyanide Promoted by Chiral *N*,*N*′-Dioxides

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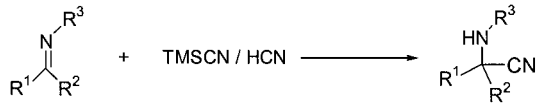
Axially chiral *N*,*N*′-dioxide Lewis base promoters have been developed and have for the first time been applied to the asymmetric synthesis of α-amino nitriles through cyanide addition to aldimines. The chiral 3,3′-dimethyl-2,2′-biquinoline *N*,*N*′-dioxide **2** exhibited high enantioselectivity for asymmetric Strecker reactions between *N*-benzhydrylimines and trimethylsilyl cyanide. In the presence of 1 equiv. of chiral promoter **2**, the cyanosilylation of aldimines afforded the corresponding α-amino nitriles with *ee* values of up to 95%. Optically pure products (99% *ee*) were obtained simply by recrystallization in the cases of some of the products. Moreover, the promoter **2** could be recovered and reused at least four times without any loss of enantioselectivity and reactivity. A putative mechanism for the enantioselective Strecker reactions is also discussed.

Introduction

Because of the significance of α-amino acids in chemistry and biology, the development of efficient synthetic methods for the preparation of various α-amino acids has attracted considerable attention. Recently, the ever-increasing demand for the non-proteinogenic α-amino acids in a variety of scientific disciplines has promoted the development of novel methods for the asymmetric syntheses of α-amino acids.[1] Together with the classic Strecker reaction,[2] one of the most important reactions for the production of α-amino nitriles − key intermediates for the synthesis of α-amino acids − is asymmetric cyanation of imines (Scheme 1).[3] Several procedures requiring the use of chiral auxiliaries have been reported to afford α-amino nitriles with high selectivity.[4] However, the enantioselective addition of cyanide to imine through the employment of chiral ligands[5,6] and chiral promoters can be regarded as one of the most attractive strategies.[7] Despite the progress achieved, a more general and practical procedure for its application to a wide range of imines is still highly desirable.



Scheme 1. Cyanation of imines

Because chiral molecules play key roles in asymmetric synthesis, the rational design and synthesis of new chiral molecules have currently become the focus of attention.[8] In this context, a great number of homochiral molecules containing amines, ethers, and phosphanes as electron-pair donors have been employed as asymmetric controllers in many enantioselective reactions.[9] It is well known that amine *N*-oxides possess a notable electron-pair donor property, which allows them to form different complexes with a variety of metal ions,[10] but few reports have dealt with the application of chiral *N*-oxides as chiral ligands[11] or as chiral promoters.[12] The axially chiral biquinoline *N*,*N*′-dioxide **2**, one of the chiral *N*-oxides, attracted our attention because of its highly skewed chiral environment. Nakajima and co-workers have employed the chiral biquinoline *N*,*N*′-dioxide in asymmetric reactions.[12b][12c,13] Intrigued by the feasibility of these catalytic asymmetric processes based on the chiral biquinoline *N*,*N*′-dioxide **2**, we surmised that it may also have a positive effect on promoting asymmetric cyanosilylation of aldimines. We have recently reported our preliminary studies,[14] and detailed investigations into the enantioselective Strecker reaction with the use of the axially chiral biquinoline *N*,*N*′-dioxide **2** as a promoter are reported here.

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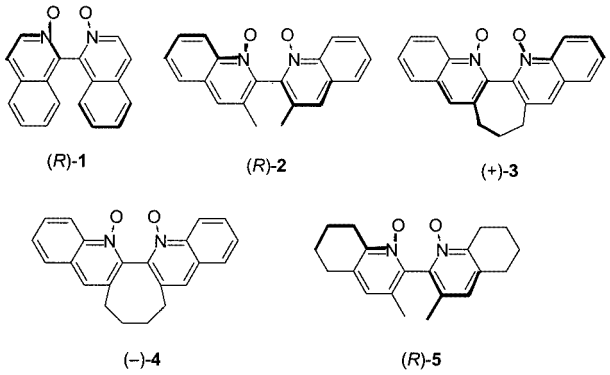
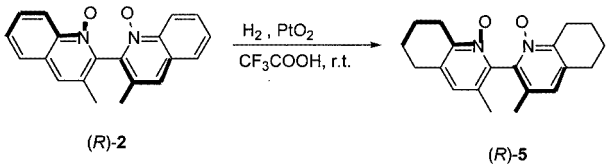
Results and Discussion

Promoter Survey

A series of axially chiral *N*,*N*′-dioxides **1**−**5** (Scheme 2) were examined as promoters for the enantioselective Strecker reaction. The racemic *N*,*N*′-dioxides **1**−**4** were prepared by reported procedures.[15,16] Racemates *rac*-**1** and *rac*-**2** were resolved by Nakajima's method,[17,18] while (+)-**3** and (−)-**4** were obtained by resolution of *rac*-**3** and *rac*-**4** with L-dibenzoyltartaric acid (L-DBTA) and D-DBTA, respectively. The absolute configuration of (+)-**3** was determined to be (*S*) by crystal X-ray analysis of its complex with L-DBTA.[19] Compound (*R*)-**5** was prepared in excellent yield by hydrogenation of (*R*)-**2** in the presence of PtO_2 in CF_3COOH (Scheme 3). To investigate the effects of chiral *N*,*N*′-dioxides on the Strecker reaction, the compounds **1**−**5** were evaluated by the addition of benzaldehyde *N*-benzhydrylimine **6a** to HCN.[20] The results listed in Table 1 indicated that the chiral promoters **1**−**5** showed surprising differences in chiral induction, although each of them possesses a C_2-symmetric axis. (*R*)-BINOL has been found to be an excellent chiral inducer in many asymmetric reactions, but the similar molecule (*R*)-**1** exhibited poor asymmetric inductive abilities in the Strecker reaction (Table 1, Entry 1). The highest *ee* value (62%) was recorded on employment of (*R*)-**2**, whereas its analogues (+)-**3** and (−)-**4** gave no meaningful enantioselectivities (Table 1, Entries 2−4). H_8-BINOL, a hydrogenation product of BINOL, has proven to be a ligand superior to BINOL in some cases.[21] However, (*R*)-**5** showed poorer abilities than the unsaturated dioxide (*R*)-**2** in promoting the asymmetric Strecker reaction (Table 1, Entry 5).

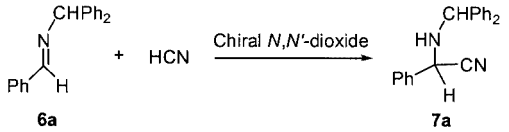


Scheme 2. Chiral *N*,*N*′-dioxides investigated in this study



Scheme 3. Synthesis of (*R*)-**5**

Table 1. Effects of chiral promoters on the enantioselective Strecker reaction between benzaldehyde *N*-benzhydrylimine and HCN



Entry[a]	Promoter	Yield[b] [%]	*ee*[c] [%]	Config.[d]
1	(*R*)-**1**	7	13	(*S*)
2	(*R*)-**2**	20	62	(*S*)
3	(+)-**3**	31	20	(*R*)
4	(−)-**4**	NR[e]	–	–
5	(*R*)-**5**	17	53	(*S*)

[a] Conditions: 1 equiv. of chiral *N*,*N*′-dioxide, concentration of imine = 0.05 M in CH_2Cl_2, −25 °C, 24 h, ratio imine/HCN = 1:1. [b] Isolated yield. [c] Determined by HPLC analysis on Daicel Chiralpak AD. [d] The configuration was determined by comparison of the elution order of the chiral HPLC assay with literature values.[7a] [e] NR = no reaction.

Optimization of the Reaction Conditions

Since we had found that the *N*,*N*′-dioxide (*R*)-**2** was the best promoter among the screened *N*,*N*′-dioxides under the employed conditions, the solvent effects on the reaction between **6a** and TMSCN in the presence of (*R*)-**2** were studied (Table 2).[22] Only traces of product were detected by TLC when the reaction was run in diethyl ether (Table 2, Entry 1). With THF and CH_3CN as solvents, the reaction provided the product with poor enantioselectivity and in low to moderate yields. Moreover, (*R*)-**2** was found to be insoluble in Et_2O, THF, and CH_3CN during the course of the experiments. Toluene and benzene were also found to afford results as poor as those obtained with ether-type solvents (Table 2, Entries 4, 5). When DMF and MeOH were employed, the reaction proceeded smoothly, and afforded the racemic product. Although the yields in CH_2Cl_2 and $CHCl_3$ were relatively low, the cyanosilylation of imine afforded moderate *ee* values (Table 2, Entries 8, 9). In terms of enantioselectivity, CH_2Cl_2 appeared to be the best solvent among the solvents tested, affording the product with 61% *ee*.

Table 2. Solvent effects on the enantioselective Strecker reaction between benzaldehyde *N*-benzhydrylimine and TMSCN

Entry[a]	Solvent	Yield[b] [%]	*ee*[c] [%]
1	Et_2O	trace	–
2	THF	30	6
3	CH_3CN	57	7
4	toluene	10	18
5	benzene	10	12
6	DMF	78	0
7	MeOH[d]	94	0
8	CH_2Cl_2	64	61
9	$CHCl_3$	60	59

[a] Conditions: 1 equiv. of chiral *N*,*N*′-dioxide **2**, concentration of imine = 0.2 M, 0 °C, 24 h, ratio imine/TMSCN = 1:2. [b] Isolated yield. [c] Determined by HPLC analysis on Daicel Chiralpak AD-H. [d] Carried out at −25 °C.

To improve the enantioselectivity, the effect of promoter loading was investigated in detail. The results, described in Table 3, indicated that the enantioselectivity and yield were influenced by the amount of the chiral *N*,*N*′-dioxide **2**. On increasing of the promoter loading from 5 to 50 mol %, the *ee* value was sharply enhanced from 14 to 58% (Table 3, Entries 1−4). The highest *ee* value (61%) was obtained when stoichiometric amounts of the promoter were used (Table 3, Entry 5), suggesting that the background reaction, which would be able to take in the process, could have led to the diminution in the *ee* value. When over 1 equiv. of promoter was used, the yield increased significantly but without any improvement in the observed enantioselectivity (Table 3, Entry 6).

Table 3. Effect of the amount of promoter on the enantioselective Strecker reaction between benzaldehyde *N*-benzhydrylimine and TMSCN

Entry[a]	Promoter loading [mol %]	Time [h]	Yield[b] [%]	*ee*[c] [%]
1	5	39	79	14
2	10	39	73	39
3	20	39	81	42
4	50	24	54	58
5	100	24	64	61
6	120	24	84	60

[a] Conditions: concentration of imine = 0.2 M in CH_2Cl_2, 0 °C, 24 h, ratio imine/TMSCN = 1:2. [b] Isolated yield. [c] Determined by HPLC analysis on Daicel Chiralpak AD-H.

The concentration of substrate was also found to be another important factor for yield and enantioselectivity. The results, listed in Table 4, indicated that the enantioselectivity increased rapidly from 45 to 59% with a change of the concentration of the imine **6a** from 0.025 to 0.05 M (Table 4, Entries 1, 2). The highest enantioselectivity was observed when the reaction was carried out at 0.2 M. When the concentration of substrate and promoter was changed from 0.2 to 0.1 M, both yield and *ee* decreased (Table 4, Entries 3, 4). At a higher concentration, the yield was improved, but the *ee* value was lowered (Table 4, Entry 5).

Table 4. Effects of the concentration of substrate on the enantioselective Strecker reaction between benzaldehyde *N*-benzhydrylimine and TMSCN

Entry[a]	Concentration of substrate [mol·L^{-1}]	Yield[b] [%]	*ee*[c] [%]
1	0.025	60	45
2	0.05	41	59
3	0.1	52	52
4	0.2	64	61
5	0.4	75	56

[a] Conditions: 1 equiv. of chiral *N*,*N*′-dioxide **2**, CH_2Cl_2, 0 °C, 24 h, ratio imine/TMSCN = 1:2. [b] Isolated yield. [c] Determined by HPLC analysis on Daicel Chiralpak AD-H.

An examination of the temperature effects, shown in Table 5, revealed that the temperature clearly affected the yield, but not the enantioselectivity. At slightly higher temperatures, the yield increased without significant impact on enantioselectivity (Table 5, Entries 1−3). When, however, the reaction was carried out below 0 °C, α-amino nitrile was obtained with low conversion and enantioselectivity (Table 5, Entries 4, 5). The highest *ee* value was obtained at 0 °C. It should be noted that enantiomeric excesses similar (60%) to those obtained at 0 °C were also observed at 19−25 °C, which made the procedure more attractive, since most previous enantioselective Strecker reactions required rather low temperatures (−78 to −20 °C) in order to provide good levels of enantioselectivity.

Table 5. Effects of temperature on the enantioselective Strecker reaction between benzaldehyde *N*-benzhydrylimine and TMSCN

Entry[a]	Temperature [°C]	Time [h]	Yield[b] [%]	*ee*[c] [%]
1	23−27	48	85	56
2	19−25	24	80	60
3	0	24	64	61
4	−25	48	77	57
5	−78	96	80	59

[a] Conditions: 1 equiv. of chiral *N*,*N*′-dioxide **2**, concentration of imine = 0.2 M in CH_2Cl_2, ratio imine/TMSCN = 1:2. [b] Isolated yield. [c] Determined by HPLC analysis on Daicel Chiralpak AD-H.

In order to find the optimal reaction conditions, the effects of the molar ratio of **6a** to TMSCN were investigated (Table 6). The reaction between **6a** and 1 equiv. of TMSCN gave a low yield and moderate enantioselectivity (Table 6, Entry 1). With molar ratios of 1:1.2 or 1:1.5 the reaction gave better *ee* values (65 and 66% *ee*, respectively) than seen with the higher molar ratio of 1:2 (Table 6, Entries 2−4), which was not consistent with reported results.[6,7] A further increase in the molar ratio to 1:3 disrupted the reaction enantioselectivity (Table 6, Entry 5).

Table 6. Effects of the ratio of imine to TMSCN on the enantioselective Strecker reaction between benzaldehyde *N*-benzhydrylimine and TMSCN

Entry[a]	Ratio imine/TMSCN	Time [h]	Yield[b] [%]	*ee*[c] [%]
1	1:1	36	43	58
2	1:1.2	24	67	65
3	1:1.5	24	67	66
4	1:2	24	64	61
5	1:3	36	64	35

[a] Conditions: 1 equiv. of chiral *N*,*N*′-dioxide **2**, concentration of imine = 0.2 M in CH_2Cl_2, 0 °C. [b] Isolated yield. [c] Determined by HPLC analysis on Daicel Chiralpak AD-H.

The effects of potential recycling of the promoter were also studied. The chiral *N*,*N*′-dioxide **2** could be recovered quantitative by chromatography. Furthermore, the results in Table 7 showed that the chiral *N*,*N*′-dioxide **2** could be reused at least four times without any loss of enantioselectivity and reactivity.

Table 7. Effects of recovery of promoter on the enantioselective Strecker reaction between benzaldehyde *N*-benzhydrylimine and TMSCN

Entry[a]	Recovery	Yield[b] [%]	*ee*[c] [%]
1	0	64	61
2	1	71	62
3	2	71	57
4	3	67	64
5	4	60	61

[a] Conditions: 1 equiv. of chiral *N*,*N*′-dioxide **2**, concentration of imine = 0.2 M in CH_2Cl_2, 24 h, 0 °C, ratio imine/TMSCN = 1:2. [b] Isolated yield. [c] Determined by HPLC analysis on Daicel Chiralpak AD-H.

Substrate Generality

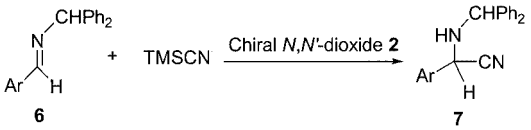
A series of *N*-benzhydrylimines was tested under the optimal conditions. As shown in Table 8, aromatic, heteroaromatic, and conjugated aldimines afforded the corresponding α-amino nitriles with moderate to excellent *ee* values and in considerable yields. The results suggested that there was a positive *ortho*-substitution effect on enantioselectivity except in the case of an *o*-methoxy substituent (Table 8, Entries 1−5). The electron-withdrawing *o*-nitro- and *o*-chloro-substituted imines underwent the enantioselective cyanide addition to afford α-amino nitriles with excellent enantioselectivities. The *o*-chlorobenzaldehyde derivative **6c** provided the highest enantioselectivity and yield (95% *ee*, 96% yield) (Table 8, Entry 3). Notably, the *o*-nitro-substituted substrate **6e** first afforded the Strecker adduct in 85% yield with 89% *ee* in the molar ratio of imine to TMSCN = 1:2 (Table 8, Entry 5). On the other hand, the electron-donating *o*-methyl- and *o*-methoxy-substituted substrates provided the Strecker products with 71 and 12% *ee*, respectively (Table 8, Entries 2, 4). On the whole, the electron-deficient imines were able to provide higher enantioselectivity than the electron-rich imines, and the electronic effects of substrates were more significant than steric effects in terms of enantioselectivity.

As illustrated in Entries 6−9 in Table 8, the electron-donating *m*-methyl- and *m*-methoxy-substituted imines also participated in the chiral *N*-oxide-promoted addition reaction, albeit with lower enantioselectivities (66 and 71% *ee*, respectively). The electron-withdrawing *m*-chloro and *m*-nitro derivatives were more suitable for asymmetric cyanide addition to imines to afford α-amino nitriles with high *ee* values and excellent yields. It could be concluded that the electronic effects were still the most important factors on enantioselectivity. It is worthwhile to mention that the asymmetric reaction of the *m*-nitro-substituted substrate **6i** gave an 88% *ee* and an 87% yield (Table 8, Entry 9), while an essentially racemic product was obtained on employment of a cyclic dipeptide catalyst.[7a]

All *para*-substituted *N*-benzhydrylimines gave moderate to good enantioselectivities, indicating little influence deriving from electronic effects (Table 8, Entries 10−14). The *p*-cyano-substituted Strecker product **7n** could be isolated in only 30% yield, however.

Chiral promoter **2** was adapted to promote the reaction of the heteroaromatic and conjugated aromatic aldimines under general reaction conditions. In contrast with the previous examples, a low enantioselectivity (49% *ee*) was observed for the *o*-furyl derivative **7o**, showing poor compatibility of the asymmetric reaction with a heteroaromatic im-

Table 8. Enantioselective Strecker reactions between aldimines and TMSCN



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Entry[a]	Ar in imine **6**	Aldimine/TMSCN	Time [h]	Yield[b] [%]	*ee*[c] [%]
1	**a**: Ph	1:1.5	24	67	66
2	**b**: *o*-MeC_6H_4	1:1.5	72	70	71 (99)[c]
3	**c**: *o*-ClC_6H_4	1:1.5	96	96	95 (99)[d]
4	**d**: *o*-$MeOC_6H_4$	1:2	94	67	12[e]
5	**e**: *o*-$O_2NC_6H_4$	1:2	96	85	89[e] (99)[d]
6	**f**: *m*-MeC_6H_4	1:1.5	72	83	66
7	**g**: *m*-ClC_6H_4	1:1.5	96	90	81
8	**h**: *m*-$MeOC_6H_4$	1:2	94	69	71[e]
9	**i**: *m*-$O_2NC_6H_4$	1:2	96	87	88[e]
10	**j**: *p*-MeC_6H_4	1.1.5	72	72	75 (99)[d]
11	**k**: *p*-ClC_6H_4	1:1.5	96	93	78 (99)[d]
12	**l**: *p*-$MeOC_6H_4$	1:2	96	90	62[e]
13	**m**: *p*-FC_6H_4	1:1.5	96	95	72 (99)[d]
14	**n**: *p*-NCC_6H_4	1:1.5	72	30	61
15	**o**: *o*-furyl	1:1.5	72	86	49
16	**p**: PhCH=CH	1:1.5	96	88	67

[a] Conditions: 1 equiv. of chiral *N*,*N*′-dioxide **2**, concentration of imine = 0.2 M in CH_2Cl_2, 0 °C. [b] Isolated yield. [c] Determined by HPLC analysis on Daicel Chiralpak AD-H/AS-H and Chiralcel OD. [d] Purified by recrystallization. [e] Nitro- and methoxy-substituted imines gave better results under the molar ratio of imine to TMSCN = 1:2.

ine (Table 8, Entry 15). Nevertheless, aromatic α,β-unsaturated imine **6p** underwent asymmetric cyanosilylation to provide the corresponding α-amino nitrile with moderate enantioselectivity (67% *ee*) and in 88% yield (Table 8, Entry 16).

Furthermore, some of the Strecker products, such as the *o*-methyl-, *o*-chloro-, *o*-nitro-, *p*-methyl-, *p*-chloro-, and *p*-fluoro-substituted α-amino nitriles, could be recrystallized from *n*-hexane to afford optically pure materials (99% *ee*).

To elucidate the significant nucleophilic effect of the *N*-oxides on the silicon atoms and their potential role in the reaction, *rac*-**2**, *rac*-3,3′-dimethyl-2,2′-biquinoline *N*-oxide (*N*-monoxide), and 3,3′-dimethyl-2,2′-biquinoline were chosen for investigation of the promotion of the Strecker reaction between benzaldehyde *N*-benzhydrylimine and TMSCN under the general reaction conditions, affording 88, 76, and 60% yields, respectively. The different yields indicated that the strong donor (N−O) could play the most important role in enhancing reactivity and nucleophilicity of TMSCN, but that the weak donor (N) could have only a small effect on the silicon atom in the process. This is in agreement with Feng's reports that TMSCN could be activated by an achiral *N*-oxide.[11f][11g] We therefore assumed that the transition states of the chiral *N*-oxide-promoted Strecker reactions should be hypervalent silicates.[23] In order to confirm the hypothesis, ^{29}Si NMR (300 MHz) analyses were carried out at 25 °C in $CDCl_3$. Firstly, all experiments were performed in $CDCl_3$, as detailed in the Exp. Sect. The ^{29}Si NMR spectra were then recorded and scaled from tetramethylsilane (TMS). As illustrated in Entry 1 in Table 9, TMSCN affords a signal at δ = −11.5 ppm. When TMSCN is added to the solution of *rac*-**2**, another strong signal is found at δ = 7.1 ppm (Table 9, Entry 2). The spectral changes strongly indicate that the environments around the silicon atoms of some TMSCN species are changed when *rac*-**2** is present. It is very possible that these silicon atoms of TMSCN could form five- or six-coordinate hypervalent silicate species by coordination to *N*-oxides. Furthermore, when *rac*-*N*-monoxide, possessing only one N−O dipolar moiety, is employed instead of *rac*-**2**, the same ^{29}Si NMR spectroscopic data are recorded, but the signal at δ = 7.1 ppm is weakened and that at δ = −11.5 ppm strengthened. The similar ^{29}Si spectra of *rac*-**2** and *rac*-*N*-monoxide suggest that it is easier for the silicon atom of TMSCN to form a six-coordinate silicate because the hexacoordinate silicate is more stable than pentacoordinate silicate. The different results are also consistent with the effects of the strong donor (N−O) and the weak donor (N) on TMSCN in the process. When imine is added to the solution of *rac*-**2** and TMSCN, an almost identical spectrum is observed (Table 9, Entry 4). The spectra suggest that a six-coordinate hypervalent silicate also exists after imine has been added, but there is a small difference between its transition state and that of Entry 2 according to the chemical shift.

Table 9. ^{29}Si NMR chemical shifts of several systems

Entry[a]	Components	δ [ppm]
1	TMSCN	−11.5
2	TMSCN+ *rac*-**2**	7.1, −11.5
3	TMSCN+ *rac*-*N*-monoxide	7.1, −11.5
4	TMSCN+ *rac*-**2**+imine	7.2, −11.5

[a] Conditions: $CDCl_3$, 25 °C. Imine/*rac*-**2**/TMSCN = 1:1:1.5. TMS (δ = 0.1 ppm) as internal standard.

^{1}H NMR (600 MHz) analysis in $CDCl_3$ at 25 °C was also carried out to support the hypothesis further. The ^{1}H NMR spectrum of Entry 4 in Table 9 shows that the representative signals of the Strecker adduct at δ = 5.28 ($HCPh_2$) and 4.64 (HCCN) ppm are observed, but that there is no corresponding signal at δ = 2.18 (NH) ppm. The ^{1}H NMR spectroscopic data suggest that the N atom of the imine probably coordinates to the silicon atom of the hypervalent silicate and ultimately forms an N−Si bond.

On the basis of these observations, it is possible to propose reaction transition states to account for the observed asymmetric induction of (*S*)-**2**, as shown in Figure 1. The mechanistic hypothesis suggests that when TMSCN is added to the solution of (*S*)-**2** and CH_2Cl_2, the strong electron donors (N−O) of (*S*)-**2** coordinate to the silicon atom of TMSCN to form hexacoordinate hypervalent silicate **A**, so the nucleophilicity of the cyano group of **A** is enhanced. The highly reactive cyano group then attacks the imine from the *Re* face, and the nitrogen atom simultaneously coordinates to the silicon atom to produce another hexacoordinate hypervalent silicate **B**, which ultimately forms the desired Strecker adduct with (*R*) configuration.

Conclusion

In conclusion, efficient, enantioselective Strecker reactions between aromatic aldimines and TMSCN promoted by 1 equiv. of axially chiral promoter **2** are documented. A

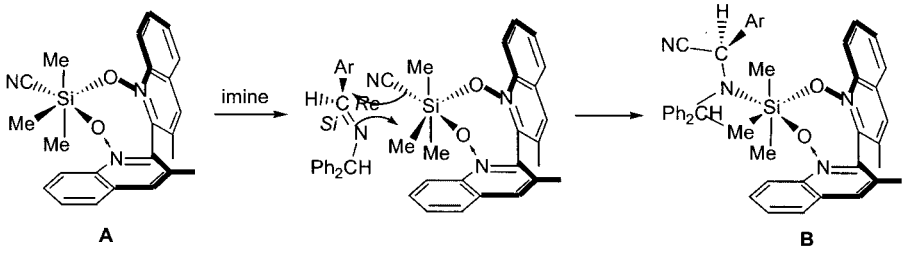

Figure 1. Proposed transition states

wide range of aromatic *N*-benzhydrylimines can be employed to obtain the corresponding α-amino nitriles in high yields and with moderate to excellent enantioselectivities (up to 95% *ee*) under mild and practical conditions. In addition, some of the products can be obtained with up to 99% *ee* after recrystallization. Future efforts will be directed towards the design and syntheses of novel chiral ligands and chiral molecules for enantioselective Strecker reactions of aldimines and ketoimines.

Experimental Section

General: Analytical TLC was carried out with 0.25 mm precoated plates from Yan-Tai (SIL G-60 UV254 60-F), and spots were viewed by use of UV light. ^{1}H NMR, ^{13}C NMR, and ^{29}Si NMR spectra were recorded on 400 MHz (Inova), 600 MHz (Bruker), or 300 MHz. (Bruker) spectrometers with $CDCl_3$ as standard; Chemical shifts (δ) are reported in ppm, and coupling constants (*J*) are reported in Hz. Melting points are uncorrected. Elemental analyses were performed with a Carlo-1160 instrument. Enantiomeric excesses were determined by chiral HPLC analysis on Daicel Chiralcel OJ/OD and Daicel Chiralpak AD/AD-H/AS-H equipment. Optical rotations were measured with a Perkin−Elmer 341 instrument. HRMS data were measured with a Finnigan MA$^+$ mass spectrometer. The Strecker reactions were performed under nitrogen with the use of oven-dried glassware (at 140 °C for at least 4 h, then stored in the drybox) and magnetic stirring. Reaction solvents were distilled under nitrogen from appropriate agents immediately prior to use: toluene, benzene, THF, and Et_2O from Na/benzophenone, CH_2Cl_2 and $CHCl_3$ from CaH_2, and methanol from Mg/I_2. DMF and CH_3CN were distilled under nitrogen by standard methods just prior to use. Commercially available reagents were used without further purification. The following compounds are available by literature procedures: (*R*)-**1**,[15,17] 3,3′-dimethyl-2,2′-biquinoline,[16] (*R*)-**2**,[16,18] *rac*-**3**,[16] *rac*-**4**,[16] and **6a**−**6p**.[24]

Preparation of (+)-3, (−)-4, (*R*)-5, and *rac*-3,3′-Dimethyl-2,2′-biquinoline *N*-Oxide

(+)-3,3′-Trimethylene-2,2′-biquinoline *N*,*N*′-Dioxide [(+)-3]: A solution of racemic 3 (81 mg, 0.25 mmol) in CH_2Cl_2 (5.6 mL) was added to a solution of L-DBTA (47 mg, 0.13 mmol) in EtOH (0.28 mL). The resulting clear solution was allowed to stand at room temp. for 30 min to afford yellow prisms. The mother liquor was washed with CH_2Cl_2 (10 mL) and a satd. solution of $NaHCO_3$ (3×10 mL) and dried with anhydrous Na_2SO_4. After filtration and removal of solvent, the residue was chromatographed on silica gel, with elution with ethyl acetate, to afford optically pure (+)-3 (> 99% *ee*) as a yellow solid (31 mg, 38%). The absolute configuration of (+)-3 was determined to be (*S*) by X-ray crystal structure analysis of its complex with L-DBTA; m.p 163−165 °C. $[\alpha]_D^{20}$ = +1263 (*c* = 0.24 in $CHCl_3$); *ee* was determined by chiral HPLC column (Daicel Chiralcel OJ, *n*-hexane/*i*PrOH, 65:35, 1.0 mL/min, UV: 254 nm). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.87 (d, *J* = 8.8 Hz, 2 H; H-8 and H-8′), 7.85 (d, *J* = 7.6 Hz, 2 H; H-5 and H-5′), 7.74 (td, *J* = 1.2, 8.0 Hz, 2 H; H-7 and H-7′), 7.67 (td, *J* = 1.2 Hz, 2 H; H-6 and H-6′), 7.56 (s, 2 H, H-4 and H-4′), 2.88 (dt, *J* = 4.0, 14.0 Hz, 2 H; CH_2), 2.55 (dt, *J* = 6.0, 14.0 Hz, 2 H; CH_2), 2.15 (m, 2 H, CH_2) ppm.

(−)-3,3′-Tetramethylene-2,2′-biquinoline *N*,*N*′-Dioxide [(−)-4]: Compound (−)-4 was obtained with *O*,*O*′-dibenzoyl-D-tartaric acid (D-DBTA) by a procedure similar to that used for the preparation of (+)-3, as a yellow solid with 97% *ee*; m.p. 205−207 °C. $[\alpha]_D^{20}$ = −1247 (*c* = 0.22 in $CHCl_3$); *ee* was determined by chiral HPLC column (Daicel Chiralcel OJ, *n*-hexane/*i*PrOH, 65:35, 1.0 mL/min, UV: 254 nm). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.82 (d, *J* = 8.8 Hz, 2 H, H-8 and H-8′), 7.87 (d, *J* = 8.0 Hz, 2 H; H-5 and H-5′), 7.73 (m, 2 H, H-7 and H-7′), 7.68 (s, 2 H, H-4 and H-4′), 7.67 (m, 2 H, H-6 and H-6′), 3.01 (dd, *J* = 8.0, 13.6 Hz, 2 H; CH_2), 2.35 (dd, *J* = 11.6, 14.0 Hz, 2 H; CH_2), 2.26 (t, *J* = 8.8 Hz, 2 H; CH_2),1.64 (m, 2 H, CH_2) ppm.

(*R*)-3,3′-Dimethyl-5,5′,6,6′,7,7′,8,8′-octahydro-2,2′-biquinoline *N*,*N*′-Dioxide [(*R*)-5]: Compound (*R*)-2 (100 mg, 0.32 mmol) was dissolved in CF_3COOH (2 mL), PtO_2 (12 mg) was added, the solution was connected to the hydrogenator, the air was removed, 0.34 MPa pressure was applied, and the mixture was hydrogenated for 4 h. It was then diluted with H_2O (10 mL), neutralized with 10% NaOH, extracted with CH_2Cl_2 (3 × 10 mL) and brine (10 mL), and dried with anhydrous Na_2SO_4. After filtration and removal of solvent, the residue was chromatographed on silica gel. Compound (*R*)-5 (96 mg, 94%) was obtained as a colorless solid; m.p. 190−192 °C. $[\alpha]_D^{20}$ = +41.3 (*c* = 0.54 in $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.94 (s, 2 H, H-4 and H-4′), 2.99 (tt, *J* = 6.0, 19.2 Hz, 2 H; H-8 or H-8′), 2.84 (tt, *J* = 6.4, 19.2 Hz, 2 H; H-8′ or H-8), 2.76 (t, *J* = 6.0 Hz, 4 H; H-5 and H-5′), 2.03 (s, 6 H, CH_3), 1.91−1.73 (m, 8 H, H-6 and H-6′ and H-7 and H-7′) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 146.1, 140.1, 135.4, 132.4, 127.0, 28.5, 24.3, 21.9, 21.7, 17.4 ppm. ESI-HRMS for $C_{20}H_{24}N_2O_2$+Na: calcd. 325.1915; found 325.1909.

***rac*-3,3′-Dimethyl-2, 2′-biquinoline *N*-Oxide:** A solution of *m*-chloroperbenzoic acid (*m*-CPBA, 130 mg, 0.75 mmol) in CH_2Cl_2 (10 mL) was slowly added at 0 °C to a stirred solution of 3,3′-dimethyl-2,2′-biquinoline (210 mg, 0.75 mmol) in CH_2Cl_2 (10 mL). The resulting yellow solution was stirred at room temperature for 6 h and was then diluted with CH_2Cl_2 (20 mL), washed with 5% Na_2CO_3 (3 × 20 mL), and dried with anhydrous $MgSO_4$. After filtration and removal of solvent, the residue was chromatographed on silica gel, with elution by petroleum ether/ethyl acetate (1:2) to afford the mono-*N*-oxide (170 mg, 77%), which was recrystallized from ethyl acetate to afford thin yellow crystals: m.p. 232−234 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.73 (d, *J* = 8.8 Hz, 1 H; aromatic H), 8.11 (d, *J* = 10.8 Hz, 2 H; aromatic H), 7.84 (d, *J* = 8.0 Hz, 2 H; aromatic H), 7.73−7.55 (m, 5 H, aromatic H), 2.35 (s, 3 H, CH_3), 2.19 (s, 3 H,CH_3) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 153.6, 146.8, 140.2, 136.3, 131.1, 130.6, 129.7, 129.4, 129.3, 128.73, 128.66, 128.3, 127.3, 127.1, 127.0, 125.8, 119.8, 19.2, 17.6 ppm. ESI-HRMS for $C_{20}H_{16}N_2O$+Na: calcd. 301.1335; found 301.1333.

General Enantioselective Strecker Procedure: A mixture of (*S*)-2 (31.6 mg, 0.1 mmol) and imine 6 (0.1 mmol) was kept in vacuo for 30 min, after which CH_2Cl_2 (0.5 mL) was added. The resulting solution was then cooled to 0 °C, and TMSCN (0.15 or 0.2 mmol) was added. When the reaction was complete (24−96 h), the solvent was evaporated directly and the crude residue was purified by flash column chromatography on silica gel to afford compounds (*R*)-7 as white solids or oils.

α-[(Diphenylmethyl)amino]-α-phenylacetonitrile (7a):[7a] The crude material was purified by flash chromatography on silica gel (Et_2O/light petroleum ether, 1:60) to afford the product in 67% yield as a white solid. The chromatographed material was determined to be of 66% *ee* by chiral HPLC analysis [Chiralpak AD-H, 80:20 *n*-hexane/*i*PrOH, 1.0 mL/min, *t*(minor) = 7.96 min, *t*(major) = 13.31 min]; m.p. 94−96 °C. $[\alpha]_D^{20}$ = −3.9 (*c* = 0.36 in $CHCl_3$). ^{1}H

NMR (400 MHz, $CDCl_3$): δ = 7.58−7.20 (m, 15 H, aromatic H), 5.25 (s, 1 H, $HCPh_2$), 4.60 (d, *J* = 12.4 Hz, 1 H; HCCN), 2.14 (d, *J* = 12.0 Hz, 1 H; NH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 142.7, 141.0, 134.9, 129.03, 129.00, 128.98, 128.8, 127.9, 127.7, 127.4, 127.2, 127.1, 118.7, 65.6, 52.4 ppm.

α-[(Diphenylmethyl)amino]-α-(2-methylphenyl)acetonitrile (7b):[7c] The crude material was purified by flash chromatography on silica gel (Et_2O/light petroleum ether, 1:60) to afford the product in 70% yield as a white solid. The chromatographed material was determined to be of 71% *ee* by chiral HPLC analysis [Chiralpak AD-H, *n*-hexane/*i*PrOH, 80:20, 1.0 mL/min, *t* (minor) = 4.80 min, *t* (major) = 6.89 min], after recrystallization from *n*-hexane to afford colorless needle crystals [> 99% *ee* by chiral HPLC analysis, Chiralpak AD-H, *n*-hexane/*i*PrOH, 80:20, 1.0 mL/min, t(minor) = 4.17 min, t(major) = 6.32 min]; m.p. 106−108 °C. $[\alpha]_D^{20}$ = −11.6 (*c* = 0.53 in $CHCl_3$, 99% *ee*). ^1H NMR (400 MHz, $CDCl_3$): δ = 7.56 (d, *J* = 7.2 Hz, 3 H; aromatic H), 7.45 (d, *J* = 7.2 Hz, 2 H; aromatic H), 7.37 (t, *J* = 7.2 Hz, 2 H; aromatic H), 7.31−7.20 (m, 7 H, aromatic H), 5.26 (s, 1 H, $HCPh_2$), 4.60 (d, *J* = 12.0 Hz, 1 H; HCCN), 2.27 (s, 3 H, CH_3), 1. 99 (d, *J* = 11.6 Hz, 1 H; NH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 142.7, 140.9, 136.4, 133.1, 131.1, 129.2, 128.9, 128.7, 128.0, 127.8, 127.6, 127.4, 126.9, 126.6, 118.7, 65.7, 50.3, 18.9 ppm.

α-(2-Chlorophenyl)-α-[(diphenylmethyl)amino]acetonitrile (7c):[6c] The crude material was purified by flash chromatography on silica gel (Et_2O/light petroleum ether, 1:30) to afford the product in 96% yield as a white solid. The chromatographed material was determined to be of 95% *ee* by chiral HPLC analysis [Chiralpak AS-H, *n*-hexane/*i*PrOH, 90:10, 1.0 mL/min, *t*(minor) = 10.31 min, *t*(major) = 11.66 min], after recrystallization from *n*-hexane to afford colorless crystals (99% *ee*); m.p. 100−102 °C. $[\alpha]_D^{20}$ = −10.2 (*c* = 0.56 in $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$): δ = 7.58−7.55 (m, 3 H, aromatic H), 7.45−7.42 (m, 3 H, aromatic H), 7.38−7.20 (m, 8 H, aromatic H), 5.22 (s, 1 H, $HCPh_2$), 4.89 (d, *J* = 12.0 Hz, 1 H; HCCN), 2.19 (d, *J* = 11.6 Hz, 1 H; NH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 142.5, 140.7, 133.4, 132.7, 130.5, 130.4, 129.2, 128.8, 128.7, 127.9, 127.7, 127.64, 127.55, 127.1, 118.1, 65.6, 50.2 ppm.

α-[(Diphenylmethyl)amino]-α-(2-methoxyphenyl)acetonitrile (7d): The crude material was purified by flash chromatography on silica gel (Et_2O/light petroleum ether, 1:20) to afford the product in 67% yield as a white solid. The chromatographed material was determined to be of 12% *ee* by chiral HPLC analysis [Chiralpak AD-H, *n*-hexane/*i*PrOH, 90:10, 1.0 mL/min, *t*(minor) = 6.57 min, *t*(major) = 8.14 min]; m.p. 98−100 °C. $[\alpha]_D^{20}$ = −0.4 (*c* = 0.92 in $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$): δ = 7.52 (d, *J* = 7.2 Hz, 2 H; aromatic H), 7.43 (d, *J* = 7.6 Hz, 2 H; aromatic H), 7.38−7.20 (m, 8 H, aromatic H), 6.97 (d, *J* = 7.6 Hz, 1 H; aromatic H), 6.93 (d, *J* = 8.0 Hz, 1 H; aromatic H), 5.18 (s, 1 H, $HCPh_2$), 4.66 (d, *J* = 12.0 Hz, 1 H; HCCN), 3.85 (s, 3 H, OCH_3), 2.55 (d, *J* = 12.0 Hz, 1 H; NH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 157.0, 142.9, 141.4, 130.5, 128.9, 128.71, 128.67, 127.7, 127.5, 127.4, 127.2, 123.3, 120.9, 119.0, 111.3, 65.3, 55.5, 48.5 ppm. $C_{22}H_{20}N_2O$ (328.2): calcd. C 80.46, H 6.14, N 8.53; found C 80.56, H 6.11, N 8.49.

α-[(Diphenylmethyl)amino]-α-(2-nitrophenyl)acetonitrile (7e): The crude material was purified by flash chromatography on silica gel (Et_2O/light petroleum ether, 1:10) to afford the product in 85% yield as a white solid. The chromatographed material was determined to be of 89% *ee* by chiral HPLC analysis [Chiralpak AD-H, *n*-hexane/*i*PrOH, 95:5, 1.0 mL/min, *t*(minor) = 11.88 min, *t*(major) = 13.35 min], after recrystallization from *n*-hexane to afford of a colorless needle crystal (> 99% *ee*); m.p. 88−90 °C. $[\alpha]_D^{20}$ = −17.8 (*c* = 1.1 in $CHCl_3$, 99% *ee*). ^1H NMR (400 MHz, $CDCl_3$): δ = 7.95 (d, *J* = 8.0 Hz, 1 H; aromatic H), 7.76 (d, *J* = 8.0 Hz, 1 H; aromatic H), 7.64 (t, *J* = 8.0 Hz, 1 H; aromatic H), 7.55 (t, *J* = 8.0 Hz, 1 H; aromatic H), 7.47 (d, *J* = 7.6 Hz, 2 H; aromatic H), 7.39−7.19 (m, 8 H, aromatic H), 5.29 (d, *J* = 12.0 Hz, 1 H; HCCN), 5.20 (s, 1 H, $HCPh_2$), 2.38 (d, *J* = 11.6 Hz, 1 H; NH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 148.4, 142.2, 140.1, 133.4, 130.2, 129.8, 129.2, 128.9, 128.7, 128.1, 127.74, 127.68, 127.0, 125.4, 117.1, 65.8, 49.6 ppm. $C_{21}H_{17}N_3O_2$ (343.1): calcd. C 73.45, H 4.99, N 12.24; found C 73.56, H 5.12, N 11.98.

α-[(Diphenylmethyl)amino]-α-(3-methylphenyl)acetonitrile (7f): The crude material was purified by flash chromatography on silica gel (Et_2O/light petroleum ether, 1:60) to afford the product in 83% yield as a liquid. The chromatographed material was determined to be of 66% *ee* by chiral HPLC analysis [Chiralpak AD-H, *n*-hexane/*i*PrOH, 95:5, 1.0 mL/min, *t*(minor) = 6.55 min, *t*(major) = 8.68 min]. $[\alpha]_D^{20}$ = −4.1 (*c* = 1.1 in $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$): δ = 7.61 (d, *J* = 8.0 Hz, 2 H; aromatic H), 7.49 (d, *J* = 8.0 Hz, 2 H; aromatic H), 7.43−7.21 (m, 10 H, aromatic H), 5.28 (s, 1 H, $HCPh_2$), 4.59 (s, 1 H, HCCN), 2.42 (s, 3 H, CH_3), 2.15 (br. s, 1 H; NH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 142.8, 141.2, 138.9, 134.9, 129.8, 129.0, 128.9, 128.8, 127.90, 127.86, 127.7, 127.5, 127.2, 124.4, 118.9, 65.6, 52.4, 21.4 ppm. $C_{22}H_{20}N_2$ (312.2): calcd. C 84.58, H 6.45, N 8.97; found C 84.48, H 6.36, N 8.84.

α-(3-Chlorophenyl)-α-[(diphenylmethyl)amino]acetonitrile (7g):[7a] The crude material was purified by flash chromatography on silica gel (Et_2O/light petroleum ether, 1:30) to afford the product in 90% yield as a white solid. The chromatographed material was determined to be of 81% *ee* by chiral HPLC analysis [Chiralpak AD-H, *n*-hexane/*i*PrOH, 80:20, 1.0 mL/min, *t*(major) = 4.96 min, *t*(minor) = 5.67 min]; m.p. 101−103 °C. $[\alpha]_D^{20}$ = −4.1 (*c* = 0.83 in $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$): δ = 7.57−7.55 (m, 3 H, aromatic H), 7.46−7.22 (m, 11 H, aromatic H), 5.23(s, 1 H, $HCPh_2$), 4.58 (d, *J* = 12.4 Hz, 1 H, HCCN), 2.16 (d, *J* = 12.8 Hz, 1 H, NH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 142.4, 140.7, 136.7, 134.9, 130.2, 129.3, 129.1, 128.8, 128.0, 127.8, 127.43, 127.39, 127.0, 125.4, 118.2, 65.6, 51.8 ppm.

α-[(Diphenylmethyl)amino]-α-(3-methoxyphenyl)acetonitrile (7h):[7a] The crude material was purified by flash chromatography on silica gel (Et_2O/light petroleum ether, 1:20) to afford the product in 69% yield as a white solid. The chromatographed material was determined to be of 71% *ee* by chiral HPLC analysis [Chiralpak AD-H, *n*-hexane/*i*PrOH, 80:20, 1.0 mL/min, *t*(minor) = 6.16 min, *t*(major) = 6.67 min]; m.p. 82−84 °C. $[\alpha]_D^{20}$ = −2.8 (*c* = 0.76 in $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$): δ = 7.57−7.55 (m, 2 H, aromatic H), 7.46−7.44 (m, *J* = 8.0 Hz, 2 H, aromatic H), 7.38−7.21 (m, 7 H, aromatic H), 7.19 (dd, *J* = 0.8, 7.6 Hz, 1 H, aromatic H), 7.08 (d, *J* = 2.0 Hz, 1 H, aromatic H), 6.91 (dd, *J* = 2.0, 8.0 Hz, 1 H, aromatic H), 5.23(s, 1 H, $HCPh_2$), 4.56 (d, *J* = 12.4 Hz, 1 H, HCCN), 3.83 (s, 3 H, OCH_3), 2.15 (d, *J* = 12.4 Hz, 1 H, NH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 160.0, 142.7, 141.0, 136.3, 130.1, 129.0, 128.8, 127.9, 127.7, 127.4, 127.1, 119.4, 118.7, 114.3, 113.1, 65.5, 55.4, 52.2 ppm.

α-[(Diphenylmethyl)amino]-α-(3-nitrophenyl)acetonitrile (7i):[7a] The crude material was purified by flash chromatography on silica gel (Et_2O/light petroleum ether, 1:10) to afford the product in 87% yield as a white solid. The chromatographed material was determined to be of 88% *ee* by chiral HPLC analysis [Chiralpak AD-H, *n*-hexane/*i*PrOH, 80:20, 1.0 mL/min, *t*(minor) = 6.16 min,

t(major) = 7.01 min]; m.p. 101−103 °C. $[\alpha]_D^{20}$ = −4.1 (*c* = 0.48 in $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.45 (s, 1 H, aromatic H), 8.25 (dd, *J* = 1.6, 8.0 Hz, 1 H; aromatic H), 7.92 (d, *J* = 6.0 Hz, 1 H, aromatic H), 7.64−7.23 (m, 11 H, aromatic H), 5.27 (s, 1 H, $HCPh_2$), 4.72 (d, *J* = 12.4 Hz, 1 H, HCCN), 2.27 (d, *J* = 12.4 Hz, 1 H, NH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 148.5, 142.1, 140.4, 136.9, 133.2, 130.1, 129.2, 128.9, 128.2, 127.9, 127.4, 127.0, 124.1, 122.4, 117.7, 65.7, 51.7 ppm.

α-[(Diphenylmethyl)amino]-α-(4-methylphenyl)acetonitrile (7j):[7c] The crude material was purified by flash chromatography on silica gel (Et_2O/light petroleum ether, 1:60) to afford the product in 72% yield as a white solid. The chromatographed material was determined to be of 75% *ee* by chiral HPLC analysis [Chiralpak AD-H, *n*-hexane/*i*PrOH, 80:20, 1.0 mL/min, *t*(minor) = 10.39 min, *t*(major) = 23.68 min], after recrystallization from *n*-hexane to afford of a colorless crystal (> 99% *ee*); m.p. 104−106 °C. $[\alpha]_D^{20}$ = −2.5 (*c* = 1.0 in $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.55 (d, *J* = 7.6 Hz, 2 H; aromatic H), 7.45−7.19 (m, 12 H, aromatic H), 5.22 (s, 1 H, $HCPh_2$), 4.54 (d, *J* = 12.0 Hz, 1 H, HCCN), 2.36 (s, 3 H, CH_3), 2.10 (d, *J* = 12.4 Hz, 1 H, NH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 142.7, 141.1, 138.9, 132.0, 129.6, 128.9, 128.7, 127.8, 127.6, 127.4, 127.10, 127.06, 118.9, 65.5, 52.1, 21.1 ppm.

α-(4-Chlorophenyl)-α-[(diphenylmethyl)amino]acetonitrile (7k):[7a] The crude material was purified by flash chromatography on silica gel (Et_2O/light petroleum ether, 1:30) to afford the product in 93% yield as a white solid. The chromatographed material was determined to be of 78% *ee* by chiral HPLC analysis [Chiralpak AD-H, *n*-hexane/*i*PrOH, 80:20, 1.0 mL/min, *t*(minor) = 8.31 min, *t*(major) = 19.38 min], after recrystallization from *n*-hexane to afford of a colorless crystal (> 99% *ee*); m.p. 102−104 °C. $[\alpha]_D^{20}$ = −4.5 (*c* = 0.61 in $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.56−7.21 (m, 14 H, aromatic H), 5.22 (s, 1 H, $HCPh_2$), 4.57 (d, *J* = 12.4 Hz, 1 H; HCCN), 2.14 (d, *J* = 12.8 Hz, 1 H, NH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 142.5, 140.8, 135.0, 133.4, 129.2, 129.1, 128.8, 128.6, 128.0, 127.8, 127.4, 127.0, 118.4, 65.6, 51.8 ppm.

α-[(Diphenylmethyl)amino]-α-(4-methoxyphenyl)acetonitrile (7l):[7a] The crude material was purified by flash chromatography on silica gel (Et_2O/light petroleum ether, 1:10) to afford the product in 90% yield as a liquid. The chromatographed material was determined to be of 62% *ee* by chiral HPLC analysis [Chiralpak AD-H, *n*-hexane/*i*PrOH, 80:20, 1.0 mL/min, *t*(major) = 11.62 min, *t*(minor) = 30.15 min]. $[\alpha]_D^{20}$ = −1.5 (*c* = 1.6 in $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.58−7.56 (m, 2 H, aromatic H), 7.48−7.22 (m, 10 H, aromatic H), 6.96−6.92 (m, 2 H, aromatic H), 5.23 (s, 1 H, $HCPh_2$), 4.55 (s, 1 H, HCCN), 3.83 (s, 3 H, OCH_3), 2.11 (br. s, 1 H, NH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 160.0, 142.6, 141.1, 128.8, 128.6, 128.4, 127.7, 127.5, 127.3, 127.0, 118.8, 114.2, 65.4, 55.2, 51.7 ppm.

α-[(Diphenylmethyl)amino]-α-(4-fluorophenyl)acetonitrile (7m):[7c] The crude material was purified by flash chromatography on silica gel (Et_2O/light petroleum ether, 1:30) to afford the product in 95% yield as a white solid. The chromatographed material was determined to be of 72% *ee* by chiral HPLC analysis [Chiralpak AD-H, 80:20 n-hexane/*i*PrOH, 1.0 mL/min, *t*(major) = 6.71 min, *t*(minor) = 13.15 min] after recrystallization from *n*-hexane to afford colorless crystals [> 99% *ee* by chiral HPLC analysis, Chiralpak AS-H, *n*-hexane/*i*PrOH, 90:10, 1.0 mL/min, *t*(major) = 10.37 min, *t*(minor) = 13.38 min]; m.p. 84−86 °C. $[\alpha]_D^{20}$ = +2.6 (*c* = 0.45 in $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.57−7.07 (m, 14 H, aromatic H), 5.22 (s, 1 H, $HCPh_2$), 4.57 (d, *J* = 12.4 Hz, 1 H; HCCN), 2.13 (d, *J* = 12.4 Hz, 1 H; NH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 142.5, 140.9, 130.74, 130.70, 129.1, 129.03, 129.01, 128.8, 128.0, 127.7, 127.4, 127.0, 118.5, 116.1, 115.8, 65.6, 51.7 ppm.

α-(4-Cyanophenyl)-α-[(diphenylmethyl)amino]acetonitrile (7n): The crude material was purified by flash chromatography on silica gel (Et_2O/light petroleum ether, 1:8) to afford the product in 30% yield as a white solid. The chromatographed material was determined to be of 61% *ee* by chiral HPLC analysis [Chiralcel OD, *n*-hexane/*i*PrOH, 80:20, 1.0 mL/min, *t*(minor) = 13.31 min, *t*(major) = 16.34 min]; m.p. 109−110 °C. $[\alpha]_D^{20}$ = −1.3 (*c* = 0.39 in $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.71 (s, 3 H, aromatic H), 7.56 (d, *J* = 7.2 Hz, 2 H; aromatic H), 7.45−7.24 (m, 9 H, aromatic H), 5.24 (s, 1 H, $HCPh_2$), 4.66 (d, *J* = 12.4 Hz, 1 H; HCCN), 2.22 (d, *J* = 12.4 Hz, 1 H; NH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 142.2, 140.4, 139.7, 132.7, 129.2, 128.9, 128.2, 128.0, 127.9, 127.4, 127.0, 118.1, 117.7, 113.1, 65.7, 52.0 ppm. $C_{22}H_{17}N_3$ (323.1): calcd. C 81.71, H 5.30, N 12.99; found C 81.76, H 5.33, N 13.16.

α-[(Diphenylmethyl)amino]-α-furylacetonitrile (7o):[7a] The crude material was purified by flash chromatography on silica gel (Et_2O/light petroleum ether, 1:15) to afford the product in 86% yield as a white solid. The chromatographed material was determined to be of 49% *ee* by chiral HPLC analysis [Chiralpak AS-H, *n*-hexane/*i*PrOH, 95:5, 1.0 mL/min, *t*(minor) = 12.18 min, *t*(major) = 13.14 min]; m.p. 99−101 °C. $[\alpha]_D^{20}$ = −1.7 (*c* = 1.2 in $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.55−7.24 (m, 11 H, aromatic H and furyl H), 6.47 (d, *J* = 3.6 Hz, 1 H; furyl H), 6.40 (dd, *J* = 1.6, 3.2 Hz, 1 H, furyl H), 5.19 (s, 1 H, $HCPh_2$), 4.67 (s, 1 H, HCCN), 2.35 (br. s, 1 H, NH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 147.3, 143.6, 142.3, 140.9, 129.0, 128.8, 127.9, 127.7, 127.4, 127.2, 116.9, 110.6, 108.8, 65.1, 46.2 ppm.

***trans*-2-[(Diphenylmethyl)amino]-4-phenylbut-3-enenitrile (7p):**[6e] The crude material was purified by flash chromatography on silica gel (Et_2O/light petroleum ether, 1:10) to afford the product in 88% yield as a white solid. The chromatographed material was determined to be of 67% *ee* by chiral HPLC analysis [Chiralpak AD-H, *n*-hexane/*i*PrOH, 80:20, 1.0 mL/min, *t*(minor) = 5.27 min, *t*(major) = 6.93 min]; m.p. 90−92 °C. $[\alpha]_D^{20}$ = −1.1 (*c* = 0.51 in $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.55 (d, *J* = 7.6 Hz, 2 H, aromatic H), 7.48 (d, *J* = 7.6 Hz, 2 H; aromatic H), 7.44−7.25 (m, 11 H, aromatic H), 6.93 (d, *J* = 16 Hz, 1 H, =CHPh), 6.25 (qd, *J* = 1.2, 5.2, 16.0 Hz, 1 H, =CH−), 5.24 (s, 1 H, $HCPh_2$), 4.27 (s, 1 H, HCCN), 2.02 (br. s, 1 H, NH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 142.8, 141.1, 135.3, 133.8, 128.9, 128.8, 128.75, 128.70, 128.55, 127.8, 127.7, 127.4, 127.1, 126.8, 122.4, 118.3, 65.3, 50.1 ppm.

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[1] [1a] R. M. Williams, *Synthesis of Optically Active* α-*Amino Acids*, Pergamon, Oxford, **1989**. [1b]R. M. Williams, J. A. Hendrix, *Chem. Rev.* **1992**, *92*, 889−917. [1c] R. O. Duthaler, *Tetrahedron* **1994**, *50*, 1539−1650. [1d] M. Arend, *Angew. Chem.* **1999**, *111*, 3047−3049; *Angew. Chem. Int. Ed.* **1999**, *38*, 2873−2874.
[2] A. Strecker, *Ann. Chem. Pharm.* **1850**, *75*, 27−45.

[3] Y. M. Shafran, V. A. Bakulev, V. S. Mokrushin, *Russ. Chem. Rev.* **1989**, *58*, 148−162.
[4] For representative recent examples, see: [4a] W. H. J. Boesten, J.-P. G. Seerden, B. Lange, H. J. A. Dielemans, H. L. M. Elsenberg, B. Kaptein, H. M. Moody, R. M. Kellogg, Q. B. Broxterman, *Org. Lett.* **2001**, *3*, 1121−1124. [4b] S. P. Vincent, A. Schleyer, C.-H. Wong, *J. Org. Chem.* **2000**, *65*, 4440−4443. [4c] J. Wede, F.-J. Volk, A. W. Frahm, *Tetrahedron: Asymmetry* **2000**, *11*, 3231−3252. [4d] E. Juaristi, J. L. León-Romo, A. Reyes, J. Escalante, *Tetrahedron: Asymmetry* **1999**, *10*, 2441−2495. [4e] R. H. Dave, B. D. Hosangadi, *Tetrahedron* **1999**, *55*, 11295−11308. [4f] D.-W. Ma, H.-Q. Tian, G.-X. Zhou, *J. Org. Chem.* **1999**, *64*, 120−125. [4g] F. A. Davis, D. L. Fanelli, *J. Org. Chem.* **1998**, *63*, 1981−1985. [4h] H. Kunz, W. Sager, *Angew. Chem.* **1987**, *99*, 595−597; *Angew. Chem. Int. Ed. Engl.* **1987**, *26*, 557−559. [4i] H. Kunz, W. Sager, D. Schanzenbach, M. Decker, *Liebigs Ann. Chem.* **1991**, 649−654. [4j] K. Weinges, K-P. Klotz, H. Droste, *Chem. Ber.* **1980**, *113*, 710−721. [4k] K. Weinges, H. Brachmann, P. Stahnecker, H. Rodewald, M. Nixdorf, H. Irngartinger, *Liebigs Ann. Chem.* **1985**, 566−578. [4l] F. A. Davis, P. S. Portonovo, R. E. Ready, Y. Chiu, *J. Org. Chem.* **1996**, *61*, 440−441. [4m] J. Zhu, C. Deur, L. S. Hegedus, *J. Org. Chem.* **1997**, *62*, 7704−7710. [4n] A. G. Myers, J. L. Gleason, T. Yoon, D. W. Kung, *J. Am. Chem. Soc.* **1997**, *119*, 656−673. [4o] T. K. Chakraborty, K. A. Hussain, G. V. Reddy, *Tetrahedron* **1995**, *51*, 9179−9190. [4p] J. C. Speelman, A. G. Talma, R. M. Kellogg, A. Meetsma, J. L. de Boer, P. T. euriskens, W. P. Bosman, *J. Org. Chem.* **1989**, *54*, 1055−1062. [4q] D. M. Stout, L. A. Black, W. L. Matier, *J. Org. Chem.* **1983**, *48*, 5369−5373.
[5] For a review, see: [5a] S. Kobayashi, H. Ishitani, *Chem. Rev.* **1999**, *99*, 1069−1094. [5b] L. Yet, *Angew. Chem.* **2001**, *113*, 900−902; *Angew. Chem. Int. Ed.* **2001**, *40*, 875−877.
[6] For examples of asymmetric Strecker reactions catalyzed by chiral metal complexes, see: [6a] M. S. Sigman, E. N. Jacobsen, *J. Am. Chem. Soc.* **1998**, *120*, 5315−5316. [6b] H. Ishitani, S. Komiyama, S. Kobayashi, *Angew. Chem.* **1998**, *110*, 3369−3372; *Angew. Chem. Int. Ed.* **1998**, *37*, 3186−3188. [6c] C. A. Krueger, K. W. Kuntz, C. D. Dzierba, W. G. Wirschun, J. D. Gleason, M. L. Snapper, A. H. Hoveyda, *J. Am. Chem. Soc.* **1999**, *121*, 4284−4285. [6d] H. Ishitani, S. Komiyama, Y. Hasegawa, S. Kobayashi, *J. Am. Chem. Soc.* **2000**, *122*, 762−766. [6e] J. R. Porter, W. G. Wirschun, K. W. Kuntz, M. L. Snapper, A. H. Hoveyda, *J. Am. Chem. Soc.* **2000**, *122*, 2657−2658. [6f] M. Takamura, Y. Hamashima, H. Usuda, M. Kanai, M. Shibasaki, *Angew. Chem.* **2000**, *112*, 1716−1718; *Angew. Chem. Int. Ed.* **2000**, *39*, 1650−1652. [6g] J. J. Byrne, M. Chavarot, P. Y. Chavant, Y. Vallée, *Tetrahedron Lett.* **2000**, *41*, 873−876. [6h] H. Nogami, S. Matsunaga, M. Kanai, M. Shibasaki, *Tetrahedron Lett.* **2001**, *42*, 279−283. [6i] M. Takamura, H. Yamashima, H. Usuda, M. Kanai, M. Shibasaki, *Chem. Pharm. Bull.* **2000**, *48*, 1586−1592. [6j] M. Chavarot, J. J. Byrne, P. Y. Chavant, Y. Vallée, *Tetrahedron: Asymmetry* **2001**, *12*, 1147−1150. [6k] N. S. Josephsohn, K. W. Kuntz, M. L. Snapper, A. H. Hoveyda, *J. Am. Chem. Soc.* **2001**, *123*, 11594−11599.
[7] For asymmetric Strecker reaction catalyzed by chiral molecule, see: [7a] M. S. Iyer, K. M. Gigstad, N. D. Namdev, M. Lipton, *J. Am. Chem. Soc.* **1996**, *118*, 4910−4911. [7b] M. S. Sigman, E. N. Jacobsen, *J. Am. Chem. Soc.* **1998**, *120*, 4901−4902. [7c] E. J. Corey, M. J. Grogan, *Org. Lett.* **1999**, *1*, 157−160. [7d] P. Vachal, E. N. Jacobsen, *Org. Lett.* **2000**, *2*, 867−870. [7e] M. S. Sigman, P. Vachal, E. N. Jacobsen, *Angew. Chem.* **2000**, *112*, 1336−1338; *Angew. Chem. Int. Ed.* **2000**, *39*, 1279−1281.
[8] [8a] *Catalytic Asymmetric Synthesis* (Ed.: I. Ojima), VCH, New York, **1993**. [8b] R. Noyori, *Asymmetric Catalysis in Organic Synthesis*, Wiley, New York, **1994**.
[9] H. B. Kagan, Chiral Ligands for Asymmetric Catalysis, in *Asymmetric Synthesis*, vol. 5 (Ed.: J. D. Morrison), Academic Press, London, **1985**, pp. 1−39.
[10] N. M. Karayannis, L. L. Pytlewski, C. M. Mikulski, *Coord. Chem. Rev.* **1973**, *11*, 93−159.
[11] [11a] I. A. O'Neil, C. D. Turner, S. B. Kalindjian, *Synlett* **1997**, 777−780. [11b] G. Dyker, B. Hölzer, G. Henkel, *Tetrahedron: Asymmetry* **1999**, *10*, 3297−3307. [11c] V. Derdau, S. Laschat, E. Hupe, W. A. König, I. Dix, P. G. Jones, *Eur. J. Inorg. Chem.* **1999**, 1001−1007. [11d] Y.-C. Shen, X.-M. Feng, Y. Li, G.-L. Zhang, Y.-Z. Jiang, *Synlett* **2002**, 793−795. [11e] Y.-C. Shen, X.-M. Feng, G.-L. Zhang, Y.-Z. Jiang, *Synlett* **2002**, 1353−1355; *N*-oxides have also been employed in double activation catalysis. See: [11f] F.-X. Chen, X.-M. Feng, B. Qin, G.-L. Zhang, Y.-Z. Jiang, *Synlett* **2003**, 558−560. [11g] F.-X. Chen, X.-M. Feng, B. Qin, G.-L. Zhang, Y.-Z. Jiang, *Org. Lett.* **2003**, *5*, 949−952.
[12] [12a] M. B. Diana, M. Marchetti, G. Melloni, *Tetrahedron: Asymmetry* **1995**, *6*, 1175−1179. [12b] M. Nakajima, M. Saito, M. Shiro, S. Hashimoto, *J. Am. Chem. Soc.* **1998**, *120*, 6419−6420. [12c] M. Nakajima, M. Saito, S. Hashimoto, *Chem. Pharm. Bull.* **2000**, *48*, 306−307. [12d] B. Tao, M. M. C. Lo, G. C. Fu, *J. Am. Chem. Soc.* **2001**, *123*, 353−354. [12e] A. V. Malkov, M. Orsini, D. Pernazza, K. W. Muir, V. Langer, P. Meghani, P. Kocovský, *Org. Lett.* **2002**, *4*, 1047−1049. [12f] S. E. Denmark, Y. Fan, *J. Am. Chem. Soc.* **2002**, *124*, 4233−4235. [12g] T. Shimada, A. Kina, S. Ikeda, T. Hayashi, *Org. Lett.* **2002**, *4*, 2799−2801.
[13] [13a] M. Saito, M. Nakajima, S. Hashimoto, *Chem. Commun.* **2000**, 1851−1852. [13b] M. Saito, M. Nakajima, S. Hashimoto, *Tetrahedron* **2000**, *56*, 9589−9594. [13c] M. Nakajima, Y. Yamaguchi, S. Hashimoto, *Chem. Commun.* **2001**, 1596−1597.
[14] B. Liu, X.-M. Feng, F.-X. Chen, G.-L. Zhang, X. Cui, Y.-Z. Jiang, *Synlett* **2001**, 1551−1554.
[15] For preparation of *rac*-**1**, see: M. Fuji, A. Honda, *J. Heterocycl. Chem.* **1992**, *29*, 931−933.
[16] For preparation of racemic **2**−**4**, see: R. P. Thummel, F. Lefoulon, *J. Org. Chem.* **1985**, *50*, 666−670.
[17] For the resolution of *rac*-**1**, see: Supporting Information of ref.[12b]
[18] For the resolution of *rac*-**2**, see: M. Nakajima, Y. Sasaki, M. Shiro, S. Hashimoto, *Tetrahedron: Asymmetry* **1997**, *8*, 341−344.
[19] CCDC-217323 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge at www.ccdc.cam.ac.uk/conts/retrieving.html [or from the Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK; Fax: (internat.) + 44-1223/336-033; E-mail: deposit@ccdc.cam.ac.uk].
[20] With 1 equiv. of HCN in the absence of chiral *N*,*N*′-dioxides, the reaction gave traces of product after 24 h; and with 2 equiv. of HCN under the same conditions, the product was obtained in 39% yield after 30 h.
[21] [21a] B. Wang, X.-M. Feng, X. Cui, H. Liu, Y.-Z. Jiang, *Chem. Commmun.* **2000**, 1605−1606. [21b] B. Wang, X.-M. Feng, Y.-Z. Huang, H. Liu, X. Cui, Y.-Z. Jiang, *J. Org. Chem.* **2002**, *67*, 2175−2182. [21c] A. S. C. Chan, F. Zhang, C. Yip, *J. Am. Chem. Soc.* **1997**, *119*, 4080−4081.
[22] We found that TMSCN could act as another effective cyanide source in the presence of chiral *N*,*N*′-dioxide **2** and that the reaction with use of TMSCN instead of HCN at 0 °C afforded the product in better yield with similar enantioselectivity.
[23] [23a] S. Kobayashi, K. Nishio, *Tetrahedron Lett.* **1993**, *34*, 3453−3456. [23b] S. Kobayashi, K. Nishio, *J. Org. Chem.* **1994**, *59*, 6620−6628. [23c] S. E. Denmark, D. M. Coe, N. E. Pratt, B. D. Griedel, *J. Org. Chem.* **1994**, *59*, 6161−6163. [23d] K. Sato, M. Kira, H. Sakurai, *Tetrahedron Lett.* **1989**, *30*, 4375−4378. [23e] I. P. Holmes, H. B. Kagan, *Tetrahedron Lett.* **2000**, *41*, 7453−7456. [23f] T. Mukaiyama, H. Fujisawa, T. Nakagawa, *Helv. Chim. Acta* **2002**, *85*, 4518−4531.
[24] For preparation of imines, see: Supporting Information of ref.[6c]

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