Effective Activation of the Chiral Salen/Ti(O*i*Pr)$_4$ Catalyst with Achiral Phenolic *N*-Oxides as Additives in the Enantioselective Cyanosilylation of Ketones

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The activation of chiral titanium(IV) complexes with phenolic *N*-oxides additives has been found to provide an alternative strategy for the asymmetric cyanosilylation of ketones. By using 10 mol % of chiral salen–titanium(IV) complex in combination with 1 mol % achiral phenolic *N*-oxide as an additive, aromatic, aliphatic and heterocyclic ketones have been converted into the corresponding cyanohydrin trimethylsilyl ethers in 58–96% yields with 56–82% *ee*. Several factors concerning the reactivity and enantioselectivity have been discussed. A catalytic cycle based on experimental phenomena and studies has been proposed to explain the origin of this activation and the asymmetric induction.

Introduction

Optically pure cyanohydrins are important chiral building blocks for a wide variety of chiral products such as α-hydroxy acids, α-hydroxy carbonyl compounds, α-hydroxy amines, α-amino alcohols and α-amino acid derivatives.[1] Therefore, the catalytic asymmetric addition of cyanide to carbonyl compounds is currently being studied intensively. Though there have been some advances in this field,[2] reactions involving ketones remain a great challenge because of their low reactivity and the difficulty in controlling facial stereoselectivity in state-of-the-art asymmetric synthetic methodologies. Much research has been carried out in an effort to overcome these difficulties. Belokon et al. have reported the Ti-catalyzed cyanosilylation of aromatic ketones in which a C_2-symmetric Schiff base was used as the chiral ligand.[3] Shibashaki and co-workers have developed a novel bifunctional catalyst in which a carbohydrate-derived bifunctional ligand and Ti(O*i*Pr)$_4$ promote the asymmetric addition of TMSCN to aromatic and aliphatic ketones.[4] Deng and co-workers have outlined a method for the addition of cyanide to ketones using cyanoformate and catalytic amounts of cinchona alkaloids.[5] Recently, Snapper and co-workers reported a new approach to asymmetric cyanosilylation of both aromatic and aliphatic ketones by using a recyclable chiral peptide as ligand.[6]

In the mean time, a number of important observations have been made recently regarding the effect of additives on asymmetric catalytic reactions.[7] The addition of suitable achiral additives and co-catalysts, which support the asymmetric catalyst system, enhances the yield and, surprisingly, in many cases also enhances the enantioselectivity very efficiently. Furthermore, chiral *N*-oxides have been extensively used in asymmetric synthesis, for example, in the allylation of aldehydes,[8] the addition of Et_2Zn to aldehydes,[9] in the Strecker[10] and aldol reactions[11] and in the reduction of ketones.[12] However, only a few achiral *N*-oxides have been used as additives in asymmetric reactions.[13]

Looking back at our group's research, we have found that *N*-oxides play a key role in the activation of TMSCN in the catalytic asymmetric cyanosilylation of ketones. Initially, we developed a new catalytic system for the asymmetric cyanosilylation of ketones that was based on bifunctional titanium complexes and chiral *N*-oxides.[14] Recently, we improved this reaction by developing a catalytic double-activation method (CDAM) in which the salen−Ti^{IV} complex was used as the Lewis acid and an achiral *N*-oxide as the Lewis base to activate the ketones and TMSCN, respectively.[15] Subsequently, by introducing achiral *N*-oxides as additives into the catalytic system, we developed an alternative activation strategy for the asymmetric cyanosilylation of ketones based on a chiral salen−Ti(O*i*Pr)$_4$ catalyst with a phenolic *N*-oxide as the additive.[16]

In this paper we describe the results of studies of the relationship between catalyst efficiency and the structures of the ligands and *N*-oxides, substrate generality and the reaction mechanism.

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Results and Discussion

By contrast to the reactions involving aldehydes, the cyanosilylation of ketones remains a great challenge owing to their low reactivity and greater steric hindrance. Based on the understanding of the chiral inductive capabilities of salen−Ti^{IV} complexes in the asymmetric cyanosilylation of aldehydes,[17] and of the N−O dipolar activation of TMSCN, an alternative activation strategy has been developed in which achiral phenolic *N*-oxides **3a**−**l**, **4** and **5** are introduced as additives to the titanium complexes of ligands **1a**−**m** and **2** (Scheme 1). In this way, enhanced reactivity and chiral inductivity were achieved in the enantioselective addition of TMSCN to ketones.

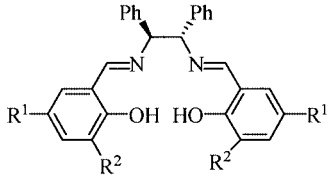
Optimization of the Catalyst: To optimize the catalytic reactivity and enantioselectivity of the reaction, phenolic *N*-oxides **3a**−**l**, **4** and **5** were tested as additives to promote cyanosilylation of acetophenone by using **1m**−Ti(O*i*Pr)$_4$ as the catalyst. The results, shown in Table 1, illustrate that to some extent the structure of the *N*-oxides affects the reactivity and enantioselectivity of the reaction.

In general, the *N*-oxides with electron-donating substituents on the aromatic ring were more active than those with electron-withdrawing substituents (Table 1, Entries 1−3 and 8−12 vs. Entries 4, 6 and 7). In terms of the enantioselectivity, of the simplest *N*-oxides **3a**−**l**, *N*-oxide **3e** with no substituents on the aromatic ring gave the lowest *ee* value (Table 1, Entry 5). The *N*-oxides with only *para* substituents had enantioselectivities of 66−67% *ee* (Table 1, Entries 1−4) and the *ortho*-substituted *N*-oxides also had similar enantioselectivities of 68−70% *ee* (Table 1, Entries 6−12). The best result was obtained with **3l** (*ee* = 70%; Table 1, Entry 12). Further efforts to improve the enantioselectivity

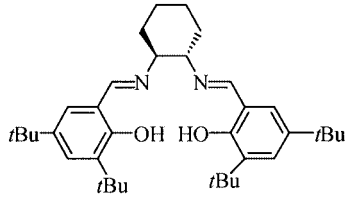
Table 1. Asymmetric cyanosilylation of acetophenone catalyzed by the **1m**−Ti(O*i*Pr)$_4$ complex in the presence of achiral phenolic *N*-oxides as additives

Entry[a]	Additives	Time [h]	Yield [%][b]	*ee* [%][c]
1	**3a**	72	95	66
2	**3b**	72	90	67
3	**3c**	72	88	66
4	**3d**	96	70	67
5	**3e**	96	73	60
6	**3f**	96	36	69
7	**3g**	96	75	68
8	**3h**	80	88	69
9	**3i**	80	90	68
10	**3j**	96	83	68
11	**3k**	68	93	69
12	**3l**	68	92	70
13	**4**	96	82	56
14	**5**	96	50	68

[a] All reactions were carried out at 0 °C under the following conditions: 10 mol % **1m**−Ti(O*i*Pr)$_4$ complex, 1 mol % *N*-oxide, 0.5 M acetophenone in CH_2Cl_2. [b] Isolated yield. [c] Determined by chiral GC analysis on Chirasil DEX CB.



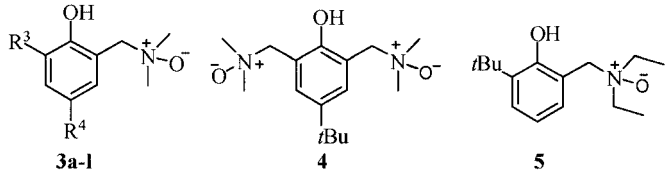
(1*S*,2*S*)-**1a-m**



(1*S*,2*S*)-**2**

	1a	**1b**	**1c**	**1d**	**1e**	**1f**	**1g**	**1h**	**1i**	**1j**	**1k**	**1l**	**1m**
R^1	MeO	Me	Cl	Br	NO_2	Cl	H	H	H	H	Me	*t*Bu	*t*Bu
R^2	H	H	H	H	H	Cl	H	Me	Ph	*t*Bu	*t*Bu	Ada[a]	*t*Bu

[a] Ada = adamantanyl



3a-l **4** **5**

	3a	**3b**	**3c**	**3d**	**3e**	**3f**	**3g**	**3h**	**3i**	**3j**	**3k**	**3l**
R^3	H	H	H	H	H	Cl	F	*t*Bu	MeO	Me	Ph	*t*Bu
R^4	MeO	Me	*t*Bu	NO_2	H	Cl	F	*t*Bu	H	H	H	H

Scheme 1. Chiral Salen ligands and achiral phenolic *N*-oxides

by modifying the structure of the *N*-oxides had no effect (Table 1, Entries 13 and 14).

The effect of temperature is shown in Table 2. As the reaction temperature was lowered from 0 to −20 °C, the enantioselectivity increased from 70% to 81% *ee* (Table 2, Entries 1 and 2). However, further decreases in the reaction temperature led to a dramatic reduction in reactivity and a remarkable drop in the enantioselectivity (Table 2, Entries 3 and 4).

Table 2. Effect of temperature on the asymmetric addition of TMSCN to acetophenone

Entry[a]	Temp. [°C]	Time [h]	Yield [%][b]	*ee* [%][c]
1	0	68	92	70
2	−20	96	94	81
3	−40	168	23	72
4	−78	168	12	70

[a] All reactions were carried out at the indicated temperature under the following conditions: 10 mol % **1m**−Ti(O*i*Pr)$_4$ complex, 1 mol % **3l**, 0.5 M acetophenone in CH_2Cl_2. [b] Isolated yield. [c] Determined by chiral GC analysis on Chirasil DEX CB.

An increase in the catalyst loading had a slight effect on the reactivity and enantioselectivity of the asymmetric cyanosilylation of acetophenone (Table 3, Entries 1−3). However, when the catalyst loading was reduced to 5 mol % the yield dropped to 46% and the enantioselectivity also decreased to 71% *ee* (Table 3, Entry 4). Hence the optimal catalyst loading is 10 mol % (Table 3, Entry 3). Further studies indicated that the concentration of acetophenone had a slight impact on the enantioselectivity, but a larger effect on the yield (Table 3, Entries 3, 5 and 6). The best result was obtained when the concentration of acetophenone was 0.5 M (Table 3, Entry 3). Lowering the concentration of acetophenone to less than 0.5 M led to a dramatic drop in the reaction's reactivity and a decrease in the enantioselectivity (Table 3, Entry 6).

The effect of the amount of additive *N*-oxide **3l** on the asymmetric cyanosilylation of acetophenone was then examined, and it was found that the amount had some effect on the enantioselectivity. Decreasing the amount of **3l** from 10 to 0.5 mol % led to increases in enantioselectivity (Table 4, Entries 1−5). The best result was obtained when 1 mol % of **3l** was used (Table 4, Entry 4).

Table 4. Effect of the amount of additive *N*-oxide **3l** on the asymmetric addition of TMSCN to acetophenone

Entry[a]	Amount of *N*-oxide **3l** [mol %]	Yield [%][b]	*ee* [%][c]
1	10	96	69
2	5	94	76
3	2.5	93	79
4	1	94	81
5	0.5	81	80

[a] All reactions were carried out at −20 °C under the following conditions: 10 mol % **1m**−Ti(O*i*Pr)$_4$ complex, the indicated amount of **3l**, 0.5 M acetophenone in CH_2Cl_2. [b] Isolated yield. [c] Determined by chiral GC analysis on Chirasil DEX CB.

To assess the asymmetric catalytic ability of the ligands **1a**−**m** and **2**, their complexes with Ti(O*i*Pr)$_4$ were used to catalyze the enantioselective addition of TMSCN to acetophenone. The results indicate that the substituents on the salicylidene phenolic rings of the ligands play an important role in determining the enantioselectivity of the reaction. Both electron-withdrawing and electron-donating ligands as well as the unsubstituted ligand decreased the enantioselectivity considerably (Table 5, Entries 1−7). On the other hand, steric alkyl-substituted catalysts increased of the *ee* value (Table 5, Entries 8−11). However, the sterically most hindered substituent, adamantyl, did not show this steric benefit (Table 5, Entry 12). Ligand **1m** was found to have the highest enantioselective capability of the ligands tested (Table 5, Entry 13). In addition, the structurally similar Jacobsen's ligand **2** gave a lower enantioselectivity than ligand **1m** (Table 5, Entry 14). In agreement with the work of Belokon et al.,[3] we used ligand (1*S*,2*S*)-**2** and obtained (*R*)-**7a**. Hence we have shown that the chiral backbone of (1*S*,2*S*)-1,2-diphenylethane-1,2-diamine is superior to that of (1*S*,2*S*)-cyclohexane-1,2-diamine in this catalytic system.

A series of **1m**−metal complexes were screened for use as catalysts in the asymmetric cyanosilylation of acetophenone (Table 6, Entries 1−6). It was found that Ti(O*i*Pr)$_4$ was the best choice (Table 6, Entry 4). We also examined the effect of solvent on this reaction (Table 7, Entries 1−6). Although

Table 3. Effects of catalyst loading and acetophenone concentration on the asymmetric addition of TMSCN to acetophenone

Entry[a]	Catalyst loading [mol %]	Acetophenone conc. [M]	Yield [%][b]	*ee* [%][c]
1	20	0.5	96	79
2	15	0.5	94	79
3	10	0.5	94	81
4	5	0.5	46	71
5	10	0.75	96	77
6	10	0.25	31	73

[a] All reactions were carried out at −20 °C under the following conditions: the indicated amount of **1m**−Ti(O*i*Pr)$_4$ complex, corresponding 0.1 equiv. **3l** compared to **1m**−Ti(O*i*Pr)$_4$, the indicated concentration of acetophenone in CH_2Cl_2. [b] Isolated yield. [c] Determined by chiral GC analysis on Chirasil DEX CB.

Table 5. Structural effect of the ligands **1a**−**m** and **2** on the asymmetric addition of TMSCN to acetophenone in the presence of achiral *N*-oxide **3l** as additive

Entry[a]	Ligand	Yield [%][b]	*ee* [%][c]
1	**1a**	42	53
2	**1b**	78	50
3	**1c**	51	28
4	**1d**	74	55
5	**1e**	73	18
6	**1f**	65	35
7	**1g**	71	47
8	**1h**	54	48
9	**1i**	56	32
10	**1j**	63	73
11	**1k**	70	75
12	**1l**	27	12
13	**1m**	94	81
14	**2**	90	70

[a] All reactions were carried out at −20 °C under the following conditions: 10 mol % indicated ligand−Ti(O*i*Pr)$_4$ complex, 1 mol % **3l**, 0.5 M acetophenone in CH_2Cl_2. [b] Isolated yield. [c] Determined by chiral GC analysis on Chirasil DEX CB.

a similar *ee* value was obtained when the reaction was carried out in THF, the reactivity was clearly inferior to that in CH_2Cl_2 (Table 7, Entry 3). Therefore, the optimal solvent is CH_2Cl_2 (Table 7, Entry 6).

Table 6. Effect of different **1m**−metal complexes on the asymmetric addition of TMSCN to acetophenone

Entry[a]	Metal	Yield [%][b]	*ee* [%][c]
1	Al(O*i*Pr)$_4$	53	16
2	La(O*i*Pr)$_4$	64	1.2
3	Zr(O*i*Pr)$_4$	40	0.4
4	Ti(O*i*Pr)$_4$	94	81
5	Ti(O*i*Pr)$_2$Cl$_2$	–	–
6	$TiCl_4$	–	–

[a] All reactions were carried out at −20 °C under the following conditions: 10 mol % **1m**−indicated metal complex, 1 mol % **3l**, 0.5 M acetophenone in CH_2Cl_2. [b] Isolated yield. [c] Determined by chiral GC analysis on Chirasil DEX CB.

Table 7. Effect of solvent on the asymmetric addition of TMSCN to acetophenone

Entry[a]	Solvent	Yield [%][b]	*ee* [%][c]
1	toluene	53	69
2	Et_2O	trace	65
3	THF	12	79
4	CH_3CN	86	44
5	$CHCl_3$	84	70
6	CH_2Cl_2	94	81

[a] All reactions were carried out at −20 °C under the following conditions: 10 mol % **1m**−Ti(O*i*Pr)$_4$ complex, 1 mol % **3l**, 0.5 M acetophenone in the indicated solvent. [b] Isolated yield. [c] Determined by chiral GC analysis on Chirasil DEX CB.

We also examined the influence of counter ions on the enantioselectivity. The results, listed in Table 8, indicate that the addition of counter ions led to a decrease in the enantioselectivity. Notably, the addition of the phenolic ion led to a sharp decrease in yield and a distinct drop in the enantioselectivity (Table 8, Entry 5).

Table 8. Effect of the counter ion on the enantioselectivity

Entry[a]	Counter ion	Yield [%][b]	*ee* [%][c]
1	–	94	81
2	MeO^-	67	66
3	EtO^-	88	79
4	$iPrO^-$	90	77
5	PhO^-	19	67

[a] All reactions were carried out at −20 °C under the following conditions: 10 mol % **1m**−Ti(O*i*Pr)$_4$ complex, 1 mol % **3l**, 0.5 M acetophenone in CH_2Cl_2, 96 hours. [b] Isolated yield. [c] Determined by chiral GC analysis on Chirasil DEX CB.

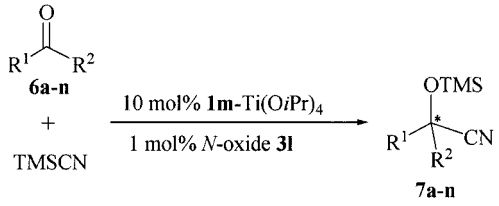
Substrate Generality: Encouraged by the results obtained with acetophenone, we investigated a number of other ketones to probe their behavior under the optimized conditions (Scheme 2). As shown in Table 9, major observations are in accord with those afforded by CDAM.[15a] Most of the aromatic, α,β-unsaturated, α,β-saturated, heterocyclic and aliphatic ketones were converted into the corresponding cyanohydrin trimethylsilyl ethers in 58−95% yields and with 56−82% *ee*. While the use of *para*-substituted acetophenone led to lower enantioselectivities and, in general, lower yields than was the case with acetophenone, the cyanohydrin derived from the *meta*-chloro-substituted ketone had a similar enantioselectivity and yield to that from acetophenone (Table 9, Entries 1−6). Curiously, the electron-deficient 4-nitroacetophenone was converted into the corresponding product with a higher chemical yield and enantioselectivity in the absence of **3l** than in its presence (Table 9, Entry 7). β-Acetonaphthone afforded a lower *ee* value than acetophenone (Table 9, Entry 8). Steric cyclic ketones such as α-tetralone and 1-indanone afforded the corresponding products with similar enantioselectivities (Table 9, Entries 9 and 10). Interestingly, the product derived from the α,β-saturated ketone has a higher *ee* value than that derived from the α,β-unsaturated one (Table 9, Entries 11 and 12) in contrast with Snapper and co-workers' report,[6] but in agreement with Shibasaki and co-workers' results.[4] However, the heterocyclic and aliphatic ketones gave the corresponding products with relatively low chemical yields and *ee* values (Table 9, Entries 13 and 14).

Mechanistic Studies and Suggestion: To identify a reasonable mechanism, we carried out control experiments with acetophenone as the standard substrate under the optimal conditions. As shown in Table 10, neither Ti(O*i*Pr)$_4$ nor *N*-oxide **3l** alone was effective enough to promote the addition of TMSCN to acetophenone (Table 10, Entries 1 and 2). In addition, it was shown that no background reaction occurred in the presence of the non-coordinated Ti(O*i*Pr)$_4$

Table 9. Asymmetric cyanosilylation of ketones catalyzed by **1m**−Ti(O*i*Pr)$_4$ in the presence of **3l**

Entry[a]	Ketone **6**	Yield [%][b]	*ee* [%][c]	Config.[d]
1	Acetophenone (**6a**)	94	81	*R*
2	4′-Methoxyacetophenone (**6b**)	70	75	
3	4′-Methylacetophenone (**6c**)	87	77	
4	4′-Chloroacetophenone (**6d**)	95	75	
5	3′-Chloroacetophenone (**6e**)	93	82	
6	4′-Fluoroacetophenone (**6f**)	90	77	
7[e]	4′-Nitroacetophenone (**6g**)	23(93)[f]	15(65)[f]	
8	β-Acetonaphthone (**6h**)	90	72	
9	α-Tetralone (**6i**)	75	77	
10	1-Indanone (**6j**)	96	79	
11	*trans*-4-Phenyl-3-buten-2-one (**6k**)	93	56[g]	
12	Benzylacetone (**6l**)	95	77	
13	2-Acetylthiophene (**6m**)	58	59	
14	2-Heptanone (**6n**)	71	69	*R*

[a] Reaction conditions: 10 mol % **1m**−Ti(O*i*Pr)$_4$ complex, 1 mol % **3l** (unless otherwise indicated), 0.5 M ketone in CH_2Cl_2, −20 °C, 96 h. [b] Isolated yield. [c] Determined by chiral GC analysis on Chirasil DEX CB (unless otherwise indicated). [d] Determined by comparison with the reported values of the optical rotation (see ref.[4a]). [e] The yield and *ee* are given in parentheses for the reaction conducted in the absence of **3l**. [f] Determined by HPLC on Chiralcel AD-H. [g] Determined by HPLC on Chiralcel OD.



Scheme 2. Asymmetric cyanosilylation of ketones

and *N*-oxide **3l** (Table 10, Entry 3). While 10 mol % of **1m**−Ti(O*i*Pr)$_4$ catalyzed this reaction to give a yield of 31% and 72% *ee*, the use of 1 mol % *N*-oxide **3l** as an additive in this catalytic system led to an increase in both the reactivity and enantioselectivity of this reaction (up to 94% yield and 81% *ee*; Table 10, Entries 4 and 5). Hence we have shown that the use of achiral phenolic *N*-oxide **3l** as an additive provides an effective activation strategy for the chiral salen/Ti(O*i*Pr)$_4$ catalyst in the asymmetric cyanosilylation of ketones.

Table 10. Control experiments for the investigation of catalytic mechanism

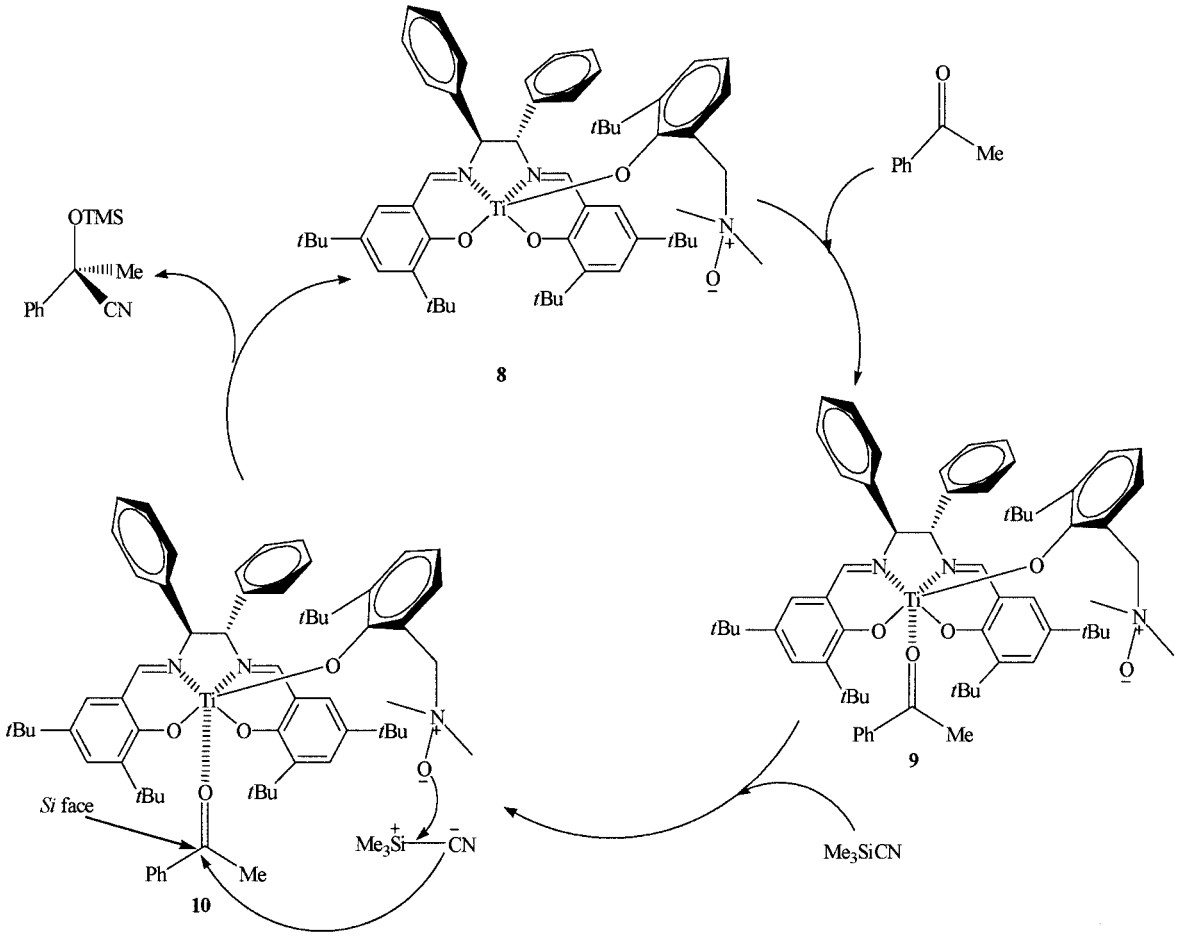
Entry[a]	Lewis acid	Additive	Yield [%][b]	*ee* [%][c]
1	Ti(O*i*Pr)$_4$	−	0	−
2	−	**3l**	0	−
3	Ti(O*i*Pr)$_4$	**3l**	0	−
4	**1m**−Ti(O*i*Pr)$_4$	−	31	72
5	**1m**−Ti(O*i*Pr)$_4$	**3l**	94	81

[a] All reactions were carried out at −20 °C under the following conditions: 10 mol % **1m**−Ti(O*i*Pr)$_4$ complex and/or 1 mol % **3l**, 0.5 M acetophenone in CH_2Cl_2, 96 h. [b] Isolated yield. [c] Determined by chiral GC analysis on Chirasil DEX CB.

Based on the above observations, we proposed the preliminary catalytic cycle shown in Scheme 3. We considered that different complexes were formed that exhibited different reactivities when Ti(O*i*Pr)$_4$, salen and phenolic *N*-oxide were mixed directly. Among these different complexes, complex **8**, a bifunctional catalyst, was expected to form. Complex **8** then interacted with acetophenone to form complex **9**. Thus, a combination of complex **9** and TMSCN would generate the key intermediate **10** that contains both the activated ketone and the activated TMSCN. Intramolecular transfer of cyanide within intermediate **10** and subsequent intramolecular trimethylsilylation would give the *O*-TMS cyanohydrin product and complex **8**. In the study of the effect of counter ions on the reaction, it was found that the presence of the phenolic ion made the formation of the effective catalyst **8** more difficult, leading to a sharp decrease in the yield and a distinct reduction of the enantioselectivity (Table 8, Entry 5). The catalytic cycle presented here also correctly predicts the sense of asymmetric induction; acetophenone is coordinated to the catalyst so as to minimize the interactions between the acetophenone and the phenyl group of the ligand, which results in an orientation in which the *Si* face of the acetophenone is exposed to intramolecular attack by the cyanide of the activated TMSCN to produce the *R* enantiomer of the *O*-TMS cyanohydrin.

Conclusions

In summary, by introducing achiral phenolic *N*-oxides as additives into the asymmetric cyanosilylation of ketones, we achieved results comparable to those afforded by CDAM.[15a] Under the optimized conditions, most aromatic, α,β-unsaturated, α,β-saturated, heterocyclic and aliphatic ketones were converted into the corresponding cy-



Scheme 3. Proposed catalytic cycle

anohydrin trimethylsilyl ethers in 58−95% yields and with 56−82% *ee*. As a result of control experiments a mechanism for the catalytic cycle has been proposed for the asymmetric cyanosilylation of ketones and the probable effective catalyst has been suggested. Moreover, the use of additives simplified the procedure and provides a method for the effective screening of efficient catalyst systems.

Experimental Section

General Remarks: ^{1}H NMR spectra were recorded with a Varian Unity INOVA 400 (400 MHz) or with a Bruker (300 MHz) spectrometer. Chemical shifts are reported in ppm relative to tetramethylsilane with the solvent resonance as the internal standard ($CDCl_3$, δ = 7.26). Data are reported as follows: Chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, m = multiplet), coupling constants (Hz), integration. ^{13}C NMR spectroscopic data were collected with a Varian Unity INOVA 400 (100 MHz) or with a Bruker (75 MHz) spectrometer with complete proton decoupling. Chemical shifts are reported in ppm relative to tetramethylsilane with the solvent resonance as internal standard ($CDCl_3$, δ = 77.0 ppm). Elemental analyses were performed on a Carlo-1160 apparatus. Enantiomeric ratios were determined by chiral GC analysis on a Varian Chirasil DEX CB instrument or by chiral HPLC analysis on a Daicel Chiralcel OD/OJ apparatus in comparison with authentic racemates. Optical rotations were recorded with a Perkin−Elmer Polarimeter-341. HRMS was recorded on BRUKER-APEX-2. All ketones, TMSCN and substituted salicylal were purchased from Acros, Aldrich and Fluka, and used directly without further purification. Solvents were purified by the usual methods. CH_2Cl_2 was distilled over CaH_2. $CHCl_3$ was passed through a column of basic alumina. Other solvents were dried with Na.

Preparation of Achiral Phenolic *N*-Oxides: The synthesis of phenolic *N*-oxides **3a**−**l**, **4** and **5** were carried out according to the methods reported in the literature.[18]

General Procedure: Formaldehyde and dimethylamine (or diethylamine) were added to a solution of the various phenols in EtOH. The solution was then refluxed and the reaction monitored by TLC. After completion, the reaction mixture was concentrated under reduced pressure to remove the surplus formaldehyde and the resulting mixture was extracted with CH_2Cl_2. The extract was washed with brine and dried with anhydrous sodium sulfate; the solvents were evaporated under reduced pressure to give a residue, which was purified by silica gel column chromatography to give the corresponding Mannich-type product. Next, *m*CPBA was added at −78 °C to a solution of the Mannich-type product and anhydrous K_2CO_3 in CH_2Cl_2. The resulting mixture was stirred at the same temperature and the reaction monitored by TLC. After completion, the mixture was allowed to warm slowly to room temperature and filtered, and the solvents were evaporated under reduced pressure.

Purification of the residue by silica gel column chromatography afforded the corresponding *N*-oxides **3a**−**l**, **4** and **5**.

***N*,*N*-Dimethyl-(2-hydroxy-5-methoxybenzyl)amine *N*-Oxide (3a):** M.p. 130−132 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.24 (s, 6 H), 3.77 (s, 3 H), 4.46 (s, 2 H), 6.58−6.93 (m, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 56.15, 58.42, 73.58, 117.25, 117.82, 118.05, 119.60, 152.00, 154.35 ppm.

***N*,*N*-Dimethyl-(2-hydroxy-5-methylbenzyl)amine *N*-Oxide (3b):** M.p. 100−101 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.26 (s, 3 H), 3.24 (s, 6 H), 4.46 (s, 2 H), 6.80−7.11 (m, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 20.43, 58.29, 73.77, 117.28, 118.77, 127.43, 132.75, 132.74, 158.16 ppm.

***N*,*N*-Dimethyl-(5-*tert*-butyl-2-hydroxybenzyl)amine *N*-Oxide (3c):** M.p. 123−125 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.29 (s, 9 H), 3.25 (s, 6 H), 4.51 (s, 2 H), 6.94−7.34 (m, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 31.78, 34.06, 38.29, 74.26, 116.73, 118.54, 128.95, 129.24, 141.17, 158.07 ppm.

***N*,*N*-Dimethyl-(2-hydroxy-5-nitrobenzyl)amine *N*-Oxide (3d):** M.p. 176−178 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.34 (s, 6 H), 4.61 (s, 2 H), 6.94−8.20 (m, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 58.06, 73.45, 116.94, 119.75, 128.73, 128.99, 137.92, 169.83 ppm.

***N*,*N*-Dimethyl-(2-hydroxybenzyl)amine *N*-Oxide (3e):** M.p. 97−99 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.25 (s, 6 H), 4.51 (s, 2 H), 6.77−7.32 (m, 4 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 58.26, 73.78, 117.60, 118.36, 119.06, 132.19, 132.53, 160.69 ppm.

***N*,*N*-Dimethyl-(3,5-dichloro-2-hydroxybenzyl)amine *N*-Oxide (3f):** M.p. 148−149 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.29 (s, 6 H), 4.49 (s, 2 H), 6.91−7.40 (m, 2 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 59.36, 74.14, 120.55, 122.40, 125.96, 131.45, 133.17, 158.25 ppm.

***N*,*N*-Dimethyl-(3,5-difluoro-2-hydroxybenzyl)amine *N*-Oxide (3g):** M.p. 155−156 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.28 (s, 6 H), 4.52 (s, 2 H), 6.58−6.92 (m, 2 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 58.33, 72.83, 106.93, 113.02, 119.06, 146.51, 152.60, 154.20 ppm.

***N*,*N*-Dimethyl-(3,5-di-*tert*-butyl-2-hydroxybenzyl)amine *N*-Oxide (3h):** M.p. 145−150 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.29 (s, 9 H), 1.44 (s, 9 H), 3.24 (s, 6 H), 4.48 (s, 2 H), 6.84−7.36 (m, 2 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 31.05, 33.07, 35.50, 36.54, 59.43, 75.34, 118.79, 127.51, 128.05, 139.79, 141.23, 158.46 ppm.

***N*,*N*-Dimethyl-(2-hydroxy-3-methoxybenzyl)amine *N*-Oxide (3i):** M.p. 123−125 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.24 (s, 6 H), 3.88 (s, 3 H), 4.52 (s, 2 H), 6.61−6.91 (m, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 56.09, 58.19, 73.55, 113.71, 117.79, 117.80, 124.09, 150.58, 150.93 ppm.

***N*,*N*-Dimethyl-(2-hydroxy-3-methylbenzyl)amine *N*-Oxide (3j):** M.p. 98−99 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.28 (s, 3 H), 3.24 (s, 6 H), 4.49 (s, 2 H), 6.69−7.18 (m, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 16.66, 58.26, 73.75, 116.90, 117.97, 127.97, 130.11, 133.06, 158.90 ppm.

***N*,*N*-Dimethyl-(2-hydroxy-3-phenylbenzyl)amine *N*-Oxide (3k):** M.p. 144−146 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.29 (s, 6 H), 4.56 (s, 2 H), 6.86−7.66 (m, 8 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 58.18, 73.77, 118.23, 118.41, 126.96, 128.19, 129.67, 131.48, 131.93, 133.13, 139.07, 158.35 ppm.

***N*,*N*-Dimethyl-(3-*tert*-butyl-2-hydroxybenzyl)amine *N*-Oxide (3l):** M.p. 95−97 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.43 (s, 9 H), 3.24 (s, 6 H), 4.49 (s, 2 H), 6.72−7.33 (m, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 30.94, 36.33, 59.45, 74.99, 118.85, 119.64, 130.27, 131.73, 140.76, 161.13 ppm.

4-*tert*-Butyl-2,6-bis[(dimethylamino)methyl]phenol Di-*N*-oxide (4): M.p. 70−72 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.30 (s, 9 H), 3.21 (s, 12 H), 4.51 (s, 4 H), 7.30 (s, 2 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 31.70, 34.09, 58.17, 72.09, 118.62, 132.79, 140.89, 158.18 ppm.

(3-*tert*-Butyl-2-hydroxybenzyl)-*N*,*N*-diethylamine *N*-Oxide (5): M.p. 107−109 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.37 (m, 6 H), 1.43 (s, 9 H), 3.30 (m, 4 H), 4.40 (s, 2 H), 6.70−7.31 (m, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 9.06, 29.72, 35.13, 59.44, 68.79, 117.27, 117.88, 128.71, 130.28, 139.39, 160.20 ppm.

Preparation of Salen Ligands:

Salen ligands **1a**−**m** and **2** were prepared according to the methods reported in the literature.[19]

(1*S*,2*S*)-*N*,*N*′-Bis[(5-methoxy-2-hydroxyphenyl)methylene]-1,2-diphenylethylenediamine (1a): M.p. 89−91 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.70 (s, 6 H), 4.71 (s, 2 H), 6.64 (s, 2 H), 6.89 (m, 4 H), 7.16−7.21 (m, 10 H), 8.26 (s, 2 H), 12.82 (s, 2 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 55.8, 80.3, 114.9, 117.6, 118.1, 119.8, 127.6, 127.8, 128.4, 139.3, 152.0, 155.1, 165.9 ppm.

(1*S*,2*S*)-*N*,*N*′-Bis[(5-methyl-2-hydroxyphenyl)methylene]-1,2-diphenylethylenediamine (1b): M.p. 55−56 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.21 (s, 6 H), 4.69 (s, 2 H), 6.86 (m, 2 H), 6.92 (m, 2 H), 7.06−7.09 (m, 2 H), 7.16−7.21 (m, 10 H), 8.26 (s, 2 H), 13.07 (s, 2 H) ppm. HRMS (ESI): calcd. for $C_{30}H_{28}N_2O_2$: 449.2224; found 449.2222 $[M + H]^+$.

(1*S*,2*S*)-*N*,*N*′-Bis[(5-chloro-2-hydroxyphenyl)methylene]-1,2-diphenylethylenediamine (1c): M.p. 86−88 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 4.75 (s, 2 H), 6.92 (d, J = 8.8 Hz, 2 H), 7.10 (d, J = 2.8 Hz, 2 H), 7.16−7.25 (m, 12 H), 8.18 (s, 2 H), 13.26 (s, 2 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 80.0, 118.6, 119.2, 123.4, 127.7, 127.9, 128.6, 130.7, 132.6, 138.8, 159.5, 165.1 ppm.

(1*S*,2*S*)-*N*,*N*′-Bis[(5-bromo-2-hydroxyphenyl)methylene]-1,2-diphenylethylenediamine (1d): M.p. 156−158 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 4.75 (s, 2 H), 6.87 (d, J = 8.8 Hz, 2 H), 7.16−7.26 (m, 12 H), 7.34−7.37 (m, 2 H), 8.18 (s, 2 H), 13.29 (s, 2 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 80.0, 110.3, 119.0, 119.8, 127.7, 127.9, 128.6, 133.7, 135.4, 138.8, 160.0, 165.0 ppm.

(1*S*,2*S*)-*N*,*N*′-Bis[(2-hydroxy-5-nitrophenyl)methylene]-1,2-diphenylethylenediamine (1e): M.p. 150−152 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 4.89 (s, 2 H), 7.07 (m, 2 H), 7.20−7.30 (m, 12 H), 8.13−8.21 (m, 2 H), 8.31 (s, 2 H), 14.39 (s, 2 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 79.3, 117.3, 118.3, 127.6, 128.0, 128.3, 128.4, 128.9, 137.9, 138.0, 165.1, 166.8 ppm.

(1*S*,2*S*)-*N*,*N*′-Bis[(3,5-dichloro-2-hydroxyphenyl)methylene]-1,2-diphenylethylenediamine (1f): M.p. 109−110 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 4.76 (s, 2 H), 7.09 (d, J = 2.4 Hz, 2 H), 7.12−7.15 (m, 4 H), 7.20−7.23 (m, 6 H), 7.38 (d, J = 2.8 Hz, 2 H), 8.27 (s, 2 H), 14.07 (s, 2 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 80.0, 119.4, 122.5, 123.4, 127.7, 128.1, 128.7, 129.5, 132.6, 138.0, 155.6, 164.6 ppm. HRMS (ESI): calcd. for $C_{28}H_{20}Cl_4N_2O_2$: 557.0352; found 557.0356 $[M + H]^+$.

(1*S*,2*S*)-*N*,*N*′-Bis[(2-hydroxyphenyl)methylene]-1,2-diphenylethylenediamine (1g): M.p. 155−156 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 4.73 (s, 2 H), 6.81 (td, J = 8.4, J = 2.0 Hz, 2 H), 6.95 (d, J = 8.4 Hz, 2 H), 7.11−7.28 (m, 14 H), 8.29 (s, 2 H), 13.32 (s, 2 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 80.2, 116.9, 118.5, 118.7, 127.6, 127.8, 128.3, 131.7, 132.5, 139.3, 160.9, 166.1 ppm.

(1*S*,2*S*)-*N*,*N*′-Bis[(2-hydroxy-3-methylphenyl)methylene]-1,2-diphenylethylenediamine (1h): M.p. 52−54 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.29 (s, 6 H), 4.74 (s, 2 H), 6.73 (m, 2 H), 7.03 (m, 2 H), 7.15−7.27 (m, 12 H), 8.35 (s, 2 H), 13.53 (s, 2 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 15.71, 80.61, 118.08, 118.49, 125.95, 127.78, 128.12, 128.57, 129.69, 133.80, 139.71, 159.38, 166.53 ppm. HRMS (ESI): calcd. for $C_{30}H_{28}N_2O_2$: 449.2224; found 449.2232 $[M + H]^+$.

(1*S*,2*S*)-*N*,*N*′-Bis[(2-hydroxy-3-phenylphenyl)methylene]-1,2-diphenylethylenediamine (1i): M.p. 94−96 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 4.72 (s, 2 H), 6.91 (m, 2 H), 7.15−7.21 (m, 12 H), 7.36−7.39 (m, 4 H), 7.47 (m, 4 H), 7.61 (d, J = 7.08, 4 H), 8.44 (s, 2 H), 13.83 (s, 2 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 80.72, 118.99, 127.37, 127.86, 128.13, 128.38, 128.60, 129.56, 129.86, 131.52, 133.81, 137.93, 139.40, 158.39, 166.53 ppm.

(1*S*,2*S*)-*N*,*N*′-Bis[(3-*tert*-butyl-2-hydroxyphenyl)methylene]-1,2-diphenylethylenediamine (1j): M.p. 109−110 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.43 (s, 18 H), 4.74 (s, 2 H), 6.72 (m, 2 H), 7.00 (m, 2 H), 7.19−7.27 (m, 12 H), 8.37 (s, 2 H), 13.79 (s, 2 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$), δ = 29.53, 35.00, 80.37, 118.05, 118.76, 127.74, 128.22, 128.54, 129.81, 130.30, 137.35, 139.74, 160.46, 167.07 ppm. HRMS (ESI): calcd. for $C_{36}H_{40}N_2O_2$: 533.3163; found 533.3155 $[M + H]^+$.

(1*S*,2*S*)-*N*,*N*′-Bis[(3-*tert*-butyl-5-methyl-2-hydroxyphenyl)-methylene]-1,2-diphenylethylenediamine (1k): M.p. 69−71 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.41 (s, 18 H), 2.18 (s, 6 H), 4.68 (s, 2 H). 6.77 (d, J = 1.6 Hz, 2 H), 7.05 (d, J = 1.6 Hz, 2 H), 7.17−7.21 (m, 10 H), 8.30 (s, 2 H), 13.50 (s, 2 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 20.6, 29.3, 34.7, 80.2, 118.2, 126.5, 127.4, 128.0, 128.3, 130.0, 130.6, 136.7, 140.0, 157.9, 166.9 ppm.

(1*S*,2*S*)-*N*,*N*′-Bis[(3-adamantyl-5-*tert*-butyl-2-hydroxyphenyl)-methylene]-1,2-diphenylethylenediamine (1l): M.p. 190−192 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.22 (s, 18 H), 1.57 (s, 4 H), 1.84 (m, 10 H), 2.08−2.16 (m, 16 H), 4.72 (s, 2 H), 6.97 (s, 2 H), 7.18 (m, 10 H), 7.26 (d, J = 1.2 Hz, 2 H), 8.40 (s, 2 H), 13.52 (s, 2 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 29.1, 31.4, 34.1, 37.2, 40.2, 80.1, 117.9, 126.3, 127.1, 127.3, 128.0, 128.2, 136.6, 139.8, 140.0, 158.2, 167.4 ppm. HRMS (ESI): calcd. for $C_{56}H_{68}N_2O_2$: 801.5354; found 801.5374 $[M + H]^+$.

(1*S*,2*S*)-*N*,*N*′-Bis[(3,5-di-*tert*-butyl-2-hydroxyphenyl)methylene]-1,2-diphenylethylenediamine (1m): M.p. 195−197 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.22 (d, J = 1.6 Hz, 18 H), 1.42 (d, J = 2.0 Hz, 18 H), 4.73 (d, J = 1.6 Hz, 2 H), 6.98 (m, 2 H), 7.16−7.20 (m, 10 H), 7.31 (d, J = 2.4 Hz, 2 H), 8.40 (d, J = 1.2 Hz, 2 H), 13.60 (d, J = 2.0 Hz, 2 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 29.4, 31.4, 34.0, 35.0, 80.1, 117.8, 126.3, 127.1, 127.4, 128.0, 128.2, 136.3, 139.8, 140.0, 157.9, 167.2 ppm.

(1*S*,2*S*)-*N*,*N*′-Bis[(3,5-di-*tert*-butyl-2-hydroxyphenyl)methylene]-1,2-cyclohexanediamine (2): M.p. 206−207 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.23 (s, 18 H), 1.41 (s, 18 H), 1.48 (m, 2 H), 1.72−1.96 (m, 6 H), 3.30−3.33 (m, 2 H), 6.98 (d, J = 2.4 Hz, 2 H), 7.30 (d, J = 2.0 Hz, 2 H), 8.30 (s, 2 H), 13.72 (s, 2 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 24.3, 29.4, 31.4, 33.3, 34.0, 34.9, 72.4, 117.8, 126.0, 126.7, 136.3, 139.8, 158.0, 165.8 ppm.

Preparation of Optically Active Trimethylsilyl Cyanohydrin Ethers. General Procedure: Ti(O*i*Pr)$_4$ (1 M solution in toluene, 50 μL, 0.05 mmol) was added to a solution of **1m** (32.2 mg, 0.05 mmol) and *N*-oxide **3l** (1.1 mg, 0.005 mmol) in CH_2Cl_2 (1 mL) at room temperature, and the mixture was stirred at 35 °C for 1 h under N_2. The ketone (0.5 mmol) was added to this solution at −20 °C, followed by the addition of TMSCN (137 μL, 1 mmol). After 96 h, the solution was concentrated and the residue was purified by silica gel column chromatography to give the corresponding cyanohydrin trimethylsilyl ethers.

2-Phenyl-2-(trimethylsilyloxy)propanenitrile (7a): The title compound **7a** (100.3 mg, 94%) was obtained as a colorless oil. $[\alpha]_D^{20}$ = +16.7 (c = 0.85 in $CHCl_3$, 81% *ee*) {ref.[4a] $[\alpha]_D^{24}$ = +21.9 (c = 1.18 in $CHCl_3$, 93% *ee*)}. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.19 (s, 9 H), 1.87 (s, 3 H), 7.38−7.58 (m, 5 H) ppm. GC [Varian, CP-Chirasil DEX CB (0.25 mm × 25 m), column temperature: 110 °C (isothermal), injection temperature: 200 °C, detector temperature: 250 °C, inlet pressure: 5.516 × 10^4 Pa]: t_r[minor, (*S*)] = 20.27 min, t_r[major, (*R*)] = 20.87 min.

2-(4-Methoxyphenyl)-2-(trimethylsilyloxy)propanenitrile (7b): The title compound **7b** (87.2 mg, 70%) was obtained as a colorless oil. $[\alpha]_D^{20}$ = +18.1 (c = 1.67 in $CHCl_3$, 75% *ee*) {ref.[6] $[\alpha]_D^{20}$ = +22.6 (c = 1.09 in $CHCl_3$, 91% *ee*)}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.19 (s, 9 H), 1.87 (s, 3 H), 3.85 (s, 3 H), 6.93 (m, 2 H), 7.49 (m, 2 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 33.41, 55.33, 71.28, 113.89, 121.81, 126.06, 134.04, 159.80 ppm. GC [Varian, CP-Chirasil DEX CB (0.25 mm × 25 m), column temperature: 105 °C (isothermal), injection temperature: 200 °C, detector temperature: 250 °C, inlet pressure: 5.516 × 10^4 Pa]: t_r(minor) = 118.13 min, t_r(major) = 120.27 min.

2-(4-Methylphenyl)-2-(trimethylsilyloxy)propanenitrile (7c): The title compound **7c** (101.8 mg, 87%) was obtained as a colorless oil. $[\alpha]_D^{20}$ = +19.8 (c = 1.91 in $CHCl_3$, 77% *ee*) {ref.[4a] $[\alpha]_D^{25}$ = +21.3 (c = 1.28 in $CHCl_3$, 90% *ee*)}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.16 (s, 9 H), 1.84 (s, 3 H), 2.36 (s, 3 H), 7.21 (m, 2 H), 7.43 (m, 2 H) ppm. $C_{13}H_{19}NOSi$: C 66.90, H 8.21, N 6.00; found C 66.78, H 8.03, N 6.39. GC [Varian, CP-Chirasil DEX CB (0.25 mm × 25 m), column temperature: 100 °C (isothermal), injection temperature: 200 °C, detector temperature: 250 °C, inlet pressure: 5.516 × 10^4 Pa]: t_r(minor) = 55.33 min, t_r(major) = 56.27 min.

2-(4-Chlorophenyl)-2-(trimethylsilyloxy)propanenitrile (7d): The title compound **7d** (120.6 mg, 95%) was obtained as a colorless oil. $[\alpha]_D^{20}$ = +17.2 (c = 2.18 in $CHCl_3$, 75% *ee*) {ref.[4a] $[\alpha]_D^{25}$ = +29.5 (c = 1.04 in $CHCl_3$, 92% *ee*)}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.19 (s, 9 H), 1.83 (s, 3 H), 7.38 (m, 2 H), 7.48 (m, 2 H) ppm. $C_{12}ClH_{16}NOSi$: C 56.79, H 6.35, N 5.52; found C 56.82, H 6.41, N 5.93. GC [Varian, CP-Chirasil DEX CB (0.25 mm × 25 m), column temperature: 105 °C (isothermal), injection temperature: 200 °C, detector temperature: 250 °C, inlet pressure: 5.516 × 10^4 Pa]: t_r(minor) = 73.73 min, t_r(major) = 76.67 min.

2-(3-Chlorophenyl)-2-(trimethylsilyloxy)propanenitrile (7e): The title compound **7e** (118.0 mg, 93%) was obtained as a colorless oil. $[\alpha]_D^{20}$ = +19.1 (c = 1.11 in $CHCl_3$, 82% *ee*) {ref.[14d] $[\alpha]_D^{26}$ = +7.1 (c = 0.34 in $CHCl_3$, 33% *ee*)}. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.22 (s, 9 H), 1.86 (s, 3 H), 7.34−7.55 (m, 4 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 1.0, 33.4, 70.9, 121.0, 122.7, 124.8, 128.8, 129.9, 134.6, 144.0 ppm. $C_{12}ClH_{16}NOSi$ (421.0): C 56.79, H 6.35, N 5.52; found C 56.61, H 6.39, N 5.90. GC [Varian, CP-Chirasil DEX CB (0.25 mm × 25 m), column temperature: 105 °C (isothermal), injection temperature: 200 °C, detector temperature: 250

°C, inlet pressure: 5.516×10^4 Pa]: t_r(minor) = 56.13 min, t_r(major) = 57.07 min.

2-(4-Fluorophenyl)-2-(trimethylsilyloxy)propanenitrile (7f): The title compound **7f** (106.8 mg, 90%) was obtained as a colorless oil. $[\alpha]_D^{20}$ = +15.9 (*c* = 2.01 in $CHCl_3$, 77% *ee*) {ref.[15a] $[\alpha]_D^{22}$ = −18.6 (*c* = 1.47 in $CHCl_3$, 83% *ee*)}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.18 (s, 9 H), 1.84 (s, 3 H), 7.08 (m, 2 H), 7.52 (m, 2 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 1.0, 33.5, 71.0, 115.6 (d, $^2J_{CCF}$ = 21.9 Hz), 121.4, 126.5 (d, $^3J_{CCCF}$ = 8.5 Hz), 138.0, 162.2 (d, $^1J_{C,F}$ = 246.4 Hz) ppm. GC [Varian, CP-Chirasil DEX CB (0.25 mm × 25 m), column temperature: 115 °C (isothermal), injection temperature: 200 °C, detector temperature: 250 °C, inlet pressure: 5.516×10^4 Pa]: t_r(minor) = 17.13 min, t_r(major) = 17.70 min.

2-(4-Nitrophenyl)-2-(trimethylsilyloxy)propanenitrile (7g): The title compound **7g** (122.9 mg, 93%) was obtained as white crystals. $[\alpha]_D^{22}$ = +1.5 (*c* = 1.15 in CH_2Cl_2, 65% *ee*) {ref.[6] $[\alpha]_D^{20}$ = +16.2 (*c* = 1.67 in $CHCl_3$, 88% *ee*)}. ^{1}H NMR (300 MHz, $CDCl_3$), δ = 0.26 (s, 9 H), 1.89 (s, 3 H), 7.75 (d, *J* = 9.0 Hz, 2 H), 8.30 (d, *J* = 9.0 Hz, 2 H, aromatic H) ppm. HPLC (Chiralcel AD-H, *i*PrOH/*n*-hexane, 1:99, flow: 1.0 mL·min^{-1}): t_r(minor) = 5.68 min, t_r(major) = 6.78 min.

2-Naphthyl-2-(trimethylsilyloxy)propanenitrile (7h): The title compound **7h** (121.3 mg, 90%) was obtained as white crystals. $[\alpha]_D^{20}$ = +10.3 (*c* = 2.45 in CH_2Cl_2, 72% *ee*) {ref.[4a] $[\alpha]_D^{25}$ = +15.6 (*c* = 1.9 in $CHCl_3$, 95% *ee*)}. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.22 (s, 9 H), 1.97 (s, 3 H), 7.54−7.66 (m, 3 H), 7.90−7.93 (m, 3 H), 8.07 (d, *J* = 1.8 Hz, 1 H) ppm. HPLC (Chiralcel OJ, *i*PrOH/*n*-hexane, 1:99, flow: 1.0 mL·min^{-1}): t_r(minor) = 7.48 min, t_r(major) = 8.29 min.

1-(Trimethylsilyloxy)-1,2,3,4-tetrahydronaphthalene-1-carbonitrile (7i): The title compound **7i** (102.5 mg, 75%) was obtained as a colorless oil. $[\alpha]_D^{20}$ = +11.9 (*c* = 1.97 in CH_2Cl_2, 77% *ee*). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.24 (s, 9 H), 2.06 (m, 2 H), 2.23 (m, 1 H), 2.35 (m, 1 H), 2.85 (m, 2 H), 7.13 (m, 1 H), 7.29 (m, 2 H), 7.67 (m, 1 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 1.3, 18.6, 28.2, 37.6, 69.8, 122.0, 126.6, 127.9, 129.0, 129.2, 135.6, 136.0 ppm. $C_{14}H_{19}NOSi$ (245.4): C 68.52, H 7.80, N 5.71; found C 68.30, H 7.70, N 6.11. GC [Varian, CP-Chirasil DEX CB (0.25 mm × 25 m), column temperature: 120 °C (isothermal), injection temperature: 200 °C, detector temperature: 250 °C, inlet pressure: 5.516×10^4 Pa]: t_r(major) = 73.87 min, t_r(minor) = 75.20 min.

1-(Trimethylsilyloxy)indane-1-carbonitrile (7j): The title compound **7j** (111.1 mg, 96%) was obtained as a colorless oil. $[\alpha]_D^{20}$ = +29.1 (*c* = 2.056 in CH_2Cl_2, 79% *ee*) {ref.[4a] $[\alpha]_D^{23}$ = +24.5 (*c* = 2.18 in CH_2Cl_2, 65% *ee*)}. ^{1}H NMR (400 MHz, $CDCl_3$), δ = 0.20 (s, 9 H), 2.43−2.47 (m, 1 H), 2.70−2.74 (m, 1 H), 2.97−3.02 (m, 1 H), 3.10−3.15 (m, 1 H), 7.28 (d, *J* = 7.2 Hz, 1 H), 7.31 (t, *J* = 14.4 Hz, 1 H), 7.36 (td, *J* = 1.2, *J* = 14.4 Hz, 1 H), 7.55 (d, *J* = 7.2 Hz, 1 H) ppm. GC [Varian, CP-Chirasil DEX CB (0.25 mm × 25 m), column temperature: 110 °C (isothermal), injection temperature: 200 °C, detector temperature: 250 °C, inlet pressure: 5.516×10^4 Pa]: t_r(major) = 62.13 min, t_r(minor) = 63.33 min.

2-Methyl-4-phenyl-2-(trimethylsilyloxy)-3-butenenitrile (7k): The title compound **7k** (114.1 mg, 93%) was obtained as a colorless oil. $[\alpha]_D^{20}$ = +35.5 (*c* = 2.32 in CH_2Cl_2, 56% *ee*) {ref.[4a] $[\alpha]_D^{25}$ = +21.3 (*c* = 1.34 in $CHCl_3$, 91% *ee*)}. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.27 (s, 9 H), 1.77 (s, 3 H), 6.15 (d, *J* = 15.9 Hz, 1 H), 6.91 (d, *J* = 15.9 Hz, 1 H), 7.33−7.45 (m, 5 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 1.3, 30.8, 69.9, 120.6, 126.8, 128.5, 128.7, 129.5, 130.9, 135.1 ppm. HPLC (Chiralcel OD, *i*PrOH/*n*-hexane, 1:99, flow: 1.0 mL·min^{-1}): t_r(minor) = 4.55 min, t_r(major) = 5.15 min.

2-Methyl-4-phenyl-2-(trimethylsilyloxy)butanenitrile (7l): The title compound **7l** (117.8 mg, 95%) was obtained as a colorless oil. $[\alpha]_D^{20}$ = +10.0 (*c* = 2.26 in CH_2Cl_2, 77% *ee*) {ref.[4a] $[\alpha]_D^{25}$ = +13.3 (*c* = 1.15 in $CHCl_3$, 81% *ee*)}. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.29 (s, 9 H), 1.65 (s, 3 H), 2.02−2.08 (m, 2 H), 2.80−2.91 (m, 2 H), 7.22−7.33 (m, 5 H) ppm. GC [Varian, CP-Chirasil DEX CB (0.25 mm × 25 m), column temperature: 135 °C (isothermal), injection temperature: 200 °C, detector temperature: 250 °C, inlet pressure: 5.516×10^4 Pa]: t_r(major) = 28.33 min, t_r(minor) = 28.87 min.

2-(2-Thienyl)-2-(trimethylsilyloxy)propanenitrile (7m): The title compound **7m** (66.0 mg, 58%) was obtained as a colorless oil. $[\alpha]_D^{20}$ = +47.2 (*c* = 0.41 in CH_2Cl_2, 59% *ee*) {ref.[4a] $[\alpha]_D^{24}$ = +13.3 (*c* = 1.15 $CHCl_3$, 81% *ee*)}. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.20 (s, 9 H), 2.00 (s, 3 H), 7.00 (m), 7.21−7.34 (m) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 0.78, 33.40, 68.24, 120.82, 124.70, 125.97, 126.61, 146.27 ppm. $C_{10}H_{15}NOSSi$ (225.4): C 53.29, H 6.71, N 6.21; found C 53.48, H 6.94, N 6.43. GC [Varian, CP-Chirasil DEX CB (0.25 mm × 25 m), column temperature: 80 °C (isothermal), injection temperature: 200 °C, detector temperature: 250 °C, inlet pressure: 5.516×10^4 Pa]: t_r(minor) = 20.20 min, t_r(major) = 20.87 min.

2-Methyl-2-(trimethylsilyloxy)heptanenitrile (7n): The title compound **7n** (75.9 mg, 71%) was obtained as a colorless oil. $[\alpha]_D^{20}$ = +9.1 (*c* = 1.05 in CH_2Cl_2, 69% *ee*) {ref.[4a] $[\alpha]_D^{24}$ = +1.8 (*c* = 2.63 $CHCl_3$, 76% *ee*)}. ^{1}H NMR (300 MHz, $CDCl_3$), δ = 0.25 (s, 9 H), 0.92 (t, *J* = 6.9 Hz, 3 H), 1.34 (m, 4 H), 1.42 (m, 1 H), 1.50 (m, 2 H), 1.58 (s, 3 H), 1.70 (m, 2 H) ppm. GC [Varian, CP-Chirasil DEX CB (0.25 mm × 25 m), column temperature: 80 °C (isothermal), injection temperature: 200 °C, detector temperature: 250 °C, inlet pressure: 5.516×10^4 Pa]: t_r[major, (*R*)] = 36.40 min, t_r[minor, (*S*)] = 38.33 min.

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