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Lewis Acid-Lewis Base Bifunctional Schiff Base-Titanium, Vanadium Catalysis for Enantioselective Cyanosilylation of Benzaldehyde and Oxidation of Sulfides to Chiral Sulfoxides

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Abstract: New bifunctional asymmetric catalysts containing a Lewis acid Ti(IV)/V(IV) and a Lewis base were developed and applied to the catalytic asymmetric cyanosilylation of benzaldehyde and oxidation of sulfides to chiral sulfoxides. The products were obtained with moderate to low enantiomeric excess.
Key words: Lewis acid; Lewis base; asymmetric catalyst; cyanosilylation; chiral sulfoxide.

Resumen: Se han desarrollado nuevos catalizadores asimétricos bifuncionales que contienen un ácido de Lewis y una base de Lewis, y se han aplicado a las reacciones asimétricas catalíticas de cianosililación de benzaldehído y oxidación de sulfuros a sulfóxidos quirales. Los productos se obtuvieron con excesos enantioméricos de moderados a bajos.
Palabras clave: Ácido de Lewis; Base de Lewis; catalizador asimétrico; cianosililación; sulfóxido quiral.

Introduction

It is well established that the addition of trimethylsilylcyanide (TMSCN) to aldehydes is catalyzed by Lewis acids [1] as well as Lewis bases [2] to afford trimethylsilylated cyanohydrins. Cyanohydrins are highly versatile synthetic intermediates, which can be easily converted to various important building blocks including α-hydroxy carbonyl derivatives and β-amino alcohols [3]. In view of their importance, there is currently considerable focus in developing methods for the asymmetric synthesis of cyanohydrins, especially using chiral catalysts [4, 5]. Impressive enantiomeric excesses have been obtained in the cyanation of aldehydes catalyzed by heterocyclic organic molecules, organometallics complexes and enzymes [4a,b; 5, 6]. Following this, researcher's interest has been focused in designing ligands to prepare metal complexes as catalysts that would mimic the enzymes. Shibasaki and coworkers have elegantly demonstrated this concept by designing bifuctional catalysts with built-in Lewis acid and Lewis base receptor sites (Figure 1) [7]. Following this, Feng an coworkers used pyrrolidine-N-oxide-titanium complex as acatalytic double-activation method to add TMSCN to acetophenone [5e]. In the transition state, the substrate and the reactant are held together by the complex and the nucheophilic nitrile is delivered enantioselectively to the benzaldehyde carbonyl bound to the metal.

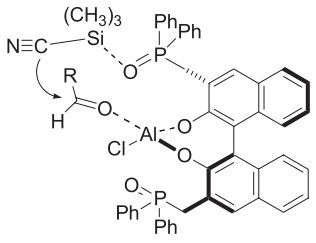
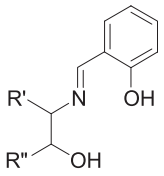


Fig. 1

During the course of our study of asymmetric silylcyanation of benzaldehyde, using Schiff base ligands [5b,k,n], we were interested in substituting R' with a Lewis base entity **1** and evaluate its effect on the enantioselectivity of the reaction. We selected Schiff bases as a scaffold for arranging the Lewis acid and Lewis base moieties as shown in Figure 2. Having a Lewis base group tethered to the ligand, we expected a strong interaction with the TMSCN, thus helping to deliver the -CN to the benzaldehyde coordinated to the metal in the transition state, mimicking an enzyme reaction.



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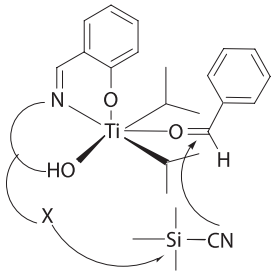
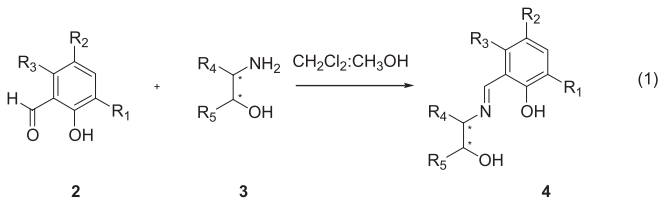


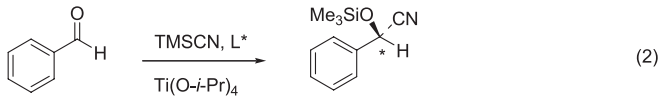
Fig. 2

Results and discussion

To test our hypothesis a number of Schiff base ligands **4** were synthesized by condensing chiral amino alcohols with benzaldehyde as shown in Equation 1, and tested for catalytic activity in Equation 2. Our results are shown in Table 1.



a) R_1= COOH, R_2=R_3= H, R_4-R_5= $CH_2C_6H_4$
b) R_1=R_2= $C(CH_3)_3$, R_3= H, R_4= CH_2OH, R_5= Ph
c) R_1= H, R_2= Br, R_3= H, R_4= CH_2OH, R_5= Ph
d) R_1= $C(CH_3)_3$, R_2=R_3= H, R_4=CH_2OH, R_5= Ph
e) R_1=R_2=R_3=H, R_4= CH_2SCH_2Ph, R_5= H
f) R_1=R_2= $C(CH_3)_3$, R_3=H, R_4= CH_2SCH_2Ph, R_5= H
g) R_1= H, R_2=R_3= C_6H_4, R_4= CH_2OCH_3, R_5= Ph
h) R_1=R_2=R_3= H, R_4= CH_2OCH_3, R_5= Ph
i) R_1=R_2= $C(CH_3)_3$, R_3= H, R_4= CH_2OCH_3, R_5= Ph
j) R_1= $C(CH_3)_3$, R_2=R_3= H, R_4= $(CH_2)_2SCH_3$, R_5= H
k) R_1=R_2=R_3=H, R_4= $(CH_2)_2SCH_3$, R_5= H

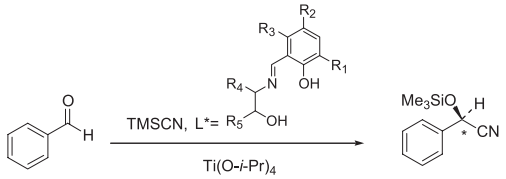


Ligands **4b-d** with primary alcohol groups were tested in Equation 2. However, this strong Lewis base (-OH) led to poor enantioselectivities and moderate yields (entries 2-4), most likely due to the alcohols forming a sterically less hindered dimeric titanium complex. The stronger carboxylic acid bearing ligand (entry 1, Table 1) gave a racemic mixture of the cyanohydrin product. This prompted the replacement of the hard hydroxyl with a soft Lewis base such as thio- and alkyl ethers in Schiff base ligand (entries 5-11). This lead to moderate enantioselectivities and yields in the trimethylsilylcyanation of benzaldehyde. In a previous study using computational modeling of the trimethylsilylcyanide-benzaldehyde transition state and experimental data we established that having bulky substituents at position R_1 and R_4 on the Schiff base ligand favors high enantioselectivity [5b]. Bulky sustituent R_1 prevents the formation of the catalytically inactive 2:1 ligand-titanium complex as observed by Oguni and Somanathan [5n,o] and substituent R_4 creates the needed steric crowding around the titanium-benzaldehyde to induce a more favorable transition state [5b]. Based on these observations, results obtained with ligands bearing substituent R_4 (**4e-k**) (Entries 5-11) may be attributed to steric rather than Lewis base interaction with TMSCN. However, some bifunctional Lewis base-Lewis acid interaction cannot be ruled out.

Our results are compatible with the recent report by Pericás and co-workers, who used Schiff base ligands derived from 3-amino-1,2-propanediol, where the primary alcohol functional group is derivatized as methyl, benzyl, trityl and isopropylsilyl and used in the TMSCN reaction with aldehydes [8].

Having failed to observe rate enhancement or high enantioselectivities with tethered Lewis bases, the use of these ligands in the asymmetric sulfide to sulfoxide oxidation with H_2O_2/$VO(acac)_2$ [9] was explored. In a previous work, we reported the synthesis of a library of chiral Schiff base ligands and their catalytic application in the oxidation of sulfide to sulfoxide using vanadium [10]. The tethered ligand-vanadium complexes gave moderate yields and enantioselectivities in the sulfide to sulfoxide oxidation. Replacing vanadium with

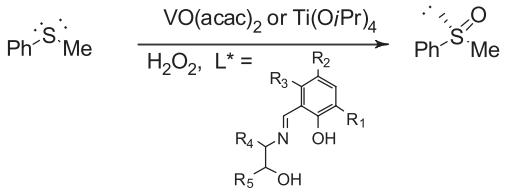
Table 1. Enantioselective addition of trimethylsilylcyanide to benzaldehyde promoted by chiral Schiff base-titanium complexes[a]



Entry	Schiff base	R_1	R_2	R_3	R_4	R_5	Yields (%)	e.e (%)[b] (Configuration)[c]
1	**4a** (*S,R*)	COOH	H	H	$CH_2C_6H_4$		65	Racemic
2	**4b** (*S,S*)	$C(CH_3)_3$	$C(CH_3)_3$	H	CH_2OH	Ph	70	20(*R*)
3	**4c** (*R,R*)	H	Br	H	CH_2OH	Ph	65	10(*S*)
4	**4d** (*S,S*)	$C(CH_3)_3$	H	H	CH_2OH	Ph	72	25(*R*)
5	**4e** (*S*)	H	H	H	CH_2SCH_2Ph	H	30	20(*R*)
6	**4f** (*S*)	$C(CH_3)_3$	$C(CH_3)_3$	H	CH_2SCH_2Ph	H	60	55(*R*)
7	**4g** (*S,S*)	H	C_6H_4	CH_2OCH_3	Ph	22	15(*R*)	
8	**4h** (*S,S*)	H	H	H	CH_2OCH_3	Ph	15	12(*R*)
9	**4i** (*S,S*)	$C(CH_3)_3$	$C(CH_3)_3$	H	CH_2OCH_3	Ph	65	54(*R*)
10	**4j** (*S*)	$C(CH_3)_3$	H	H	$(CH_2)_2SCH_3$	H	70	65(*R*)
11	**4k** (*S*)	H	H	H	$(CH_2)_2SCH_3$	H	20	12(*R*)

[a] All reactions were performed using 20% mol titanium tetraisopropoxide at -78 °C in dichloromethane for 36 h.
[b] Each e.e. value is the result of a minimum of two runs.
[c] Configuration of the cyanohydrin was established from previous work [5n,o].

Table 2. Enantioselective catalytic oxidation of sulfide to sulfoxides promoted by chiral Schiff base-vanadium(IV) and Schiff base-Titanium(IV) complexes derived from β-aminoalcohols.[a]



Entry	Schiff base	R_1	R_2	R_3	R_4	R_5	Yields (%) V	e.e. (%) V[b] (Config.)[c]	Yields (%) Ti	e.e.(%) Ti[b] (Config.)[c]
1	**4c** (*R,R*)	H	Br	H	CH_2OH	Ph	60	35(*R*)	58	40(*S*)
2	**4d** (*R,R*)	$C(CH_3)_3$	H	H	CH_2OH	Ph	80	40(*S*)	65	44(*S*)
3	**4e** (*S*)	H	H	H	CH_2SCH_2Ph	H	51	45(*S*)		
4	**4f** (*S*)	$C(CH_3)_3$	$C(CH_3)_3$	H	CH_2SCH_2Ph	H	75	52(*S*)	78	64(*S*)
5	**4i** (*S,S*)	$C(CH_3)_3$	$C(CH_3)_3$	H	CH_2OCH_3	Ph	60	42(*S*)	78	60 (*S*)
6	**4j** (*S*)	$C(CH_3)_3$	H	H	$(CH_2)_2SCH_3$	H	65	45(*S*)		
7	**4k** (*S*)	H	H	H	$(CH_2)_2SCH_3$	H	48	40(*S*)		

[a] All reactions were performed using 20% mol titanium tetraisopropoxide at -78 °C in dichloromethane for 36 h.
[b] Each e.e. value is the result of a minimum of two runs.
[c] Configuration of sulfoxide was established from previous work [10].

titanium tetraisopropoxide ligands **4c, d, f, i** (entries 1, 2, 4, 5) gave similar results (Table 2).

Conclusion

In conclusion we have synthesized a series of ligands tethered with Lewis base substituents and tested with titanium as catalyst in the trimethylsilylcyanation of benzaldehyde. Cyanohydrins were obtained in moderate yields and enanatioselctivities. Although we do not have conclusive chemical evidence for a bifunctional catalytic activity in the above reactions, based on our previous work with similar ligands, we believe the moderate cyanohydrin formation is probably controlled more by steric factors. However, some Lewis base interaction with the TMSCN can not be ruled out. Application of the same ligands with vanadium or titanium also catalysed the sulfide to sulfoxide oxidation in moderate enanatioselectivities and yields. Further studies towards the synthesis of Schiff base ligands with more efficient Lewis base group are currently in progress.

Experimental

General. Unless otherwise specified, all reagents were purchased from Aldrich Chemical Co. and used without further purification. Methanol and dichloromethane were dried by standard methods and stored over molecular sieves 4Å under argon. Titanium tetraisopropoxide and benzaldehyde were distilled under vacuum and stored in glass reaction vessels fitted with Teflon stopcocks. NMR spectra were recorded on a Varian Varian 500 MHz and 200 MHz Gemini 2000-BB FT. ^1H (200 MHz) and $^{13}C\{^1H\}$ NMR (50 MHz) are reported in ppm relative to Me_4Si as an internal standard. Coupling constants *J* are given in hertz (Hz). IR spectra were recorded on a Perkin-Elmer Model 1605 FT-IR spectrometer. Mass spectra were obtained with a HP-5890 II gas chromatograph (SUPELCO 2-4028, SPβ™ -1, and 30M X 0.25mm, column #5366-05A) coupled to a HP-5971 mass detector. Optical rotation measurements were determined in CH_2Cl_2 in a 10 cm path length cell using Rudolph Research Flanders automatic polarimeter. Elemental analyses were performed at NuMega Resonance Labs, Inc. All samples for elemental analysis and MS were dried under vacuum at room temperature for at least 24 h. All manipulations involving titanium complexes were carried out under inert atmosphere using standard Schlenk and vacuum line techniques. Enantiomeric excesses were determined using a Hewlett-Packard 6890 gas chromatograph with a 30 m Supelco β-DEX column, or a Hewlett-Packard liquid chromatograph (UV diodes detector at 254 nm), with a (*R,R*)-WHELK-01 chiral column.

General procedure for the synthesis of the ligands 4a-k: Synthesis of (*S,S*)-1-[(2-hydroxy-1-methoxymethyl-2-phenyl-ethylimino)-methyl]-phenol, (4h). A mixture of dry CH_2Cl_2/methanol (3:1) (20 mL), (*1S, 2S*)-(+)-2-amino-3-methoxy-1-phenyl-1-propanol (0.56 g, 3.35 mmol), 2-hydroxybenzaldehyde (0.41 g, 3.35 mmol) and anhydrous Na_2SO_4 (2 g) was refluxed for 4 h. The solution was filtered and the solvent

was evaporated under reduced pressure, giving **4h** as a yellow solid (0.28 g, 89.5 %).

General procedure for the trimethylsilylcyanation to benzaldehyde promoted by chiral Schiff base-titanium complexes. Schiff Base **4i** (0.17 g, 0.43 mmol) was dissolved in dry CH_2Cl_2 (20 mL), then titanium tetraisopropoxide (0.12 g, 0.43 mmol) was added and the mixture stirred at room temperature for 1 h. The mixture was then cooled to -78 °C and added trimethylsilylcyanide (0.23 g, 0.36 mL, 2.33 mmol) followed by benzaldehyde (0.24 g, 0.24 mL, 2.33 mmol). The mixture was maintained at -78 °C for 36 h. The reaction mixture was allowed to warm to room temperature. The mixture was passed through a short silica gel column and the solvent removed under reduced pressure. The residue was treated with HCl (1N) for 4 h, followed by acetylation with acetic anhydride and the final crude product was analyzed by GC. The retention times of the enantiomers were 10.0 min (*R*) and 10.7 min (*S*), in agreement with previously reported data [5n,o]. The rotations are based on concentrations of g/100 mL.

General procedure for the oxidation of methyl phenylsulfide to sulfoxide using vanadyl acetylacetonate. In a 25 mL flask were placed vanadyl acetylacetonate (5.2 mg, 0.02 mmol), the Schiff base (0.012 g, 0.03 mmol) and with 4 mL CH_2Cl_2. The solution was stirred for 5 min at room temperature. To the stirring solution methylphenylsulfide was added (0.240 g, 2 mmol) and the mixture was then cooled to 0 °C, adding 30% H_2O_2 (0.124 g, 1.1 mmol) slowly. The mixture was stirred for 20 h at 0 °C, after which a second portion of $[VO(acac)_2]$ (5.2 mg, 0.02 mmol) was added, more ligand (12 mg, 0.03 mmol) and 30% H_2O_2 (124 mg, 1.1 mmol), stirring for an additional 20 h period at 0 °C. The mixture was then extracted with CH_2Cl_2 (2 x 5 mL), the organic extracts were combined and washed with H_2O, brine and dried over Na_2SO_4. The solvent was removed under reduced pressure to give a dark brown liquid. HPLC retention times for the methylphenyl sulfoxides (*R*)= 26.9 min and (*S*)= 29.2 min (hexane: 2-propanol, 95:5) [10].

General procedure for the oxidation of methyl phenylsulfide to sulfoxide using titanium tetraisopropoxide. Sulfide (0.1 mmol) was added to a magnetically stirred solution of $Ti(OiPr)_4$ and Schiff Base (1:1) in dichloromethane (1 mL) at 0 °C. 30% hydrogen peroxide (0.11 mmol) was added and the mixture stirred for 19 h at 0 °C. The mixture was processed and analyzed as described above.

(*S,R*)-2-Hydroxy-3-[(2-hydroxy-indan-1-imino)-methyl]benzoic acid (4a). IR (KBr) 3500, 2958, 1680, 1630 cm^{-1}; $[\alpha]^{25}_D$ = +364° (*c* = 0.45, MeOH); ^{1}H NMR (500 MHz, $CDCl_3$): δ 13.37 (1H, brs), 8.97 (1H, s), 8.12 (1H, dd, *J* = 9.5 Hz, *J* = 2.5 Hz), 7.78 (1H, dd, *J* = 9.5 Hz, *J* = 2.5 Hz), 7.38-7.26 (4H, m), 6.72 (1H, t, *J* = 9.5 Hz,), 5.86 (1H, brs), 5.36 (1H, d, *J* = 5.0 Hz), 4.71-4.67 (1H, m), 3.21 (1H, dd, *J* = 21.0 Hz, *J* = 7.0 Hz,), 2.94 (1H, dd, *J* = 20.5 Hz, *J* = 3.0 Hz,); ^{13}C NMR (125 MHz, $CDCl_3$): δ 175.2, 168.1, 167.6, 141.3, 136.5, 128.9, 126.9, 125.5, 124.5, 119.2, 113.8, 71.9, 67.5, 39.2. Anal. Calcd for $C_{17}H_{15}NO_4$: C, 68.68, H, 5.08; Found: C, 68.24, H 5.03.

(*S,S*)-2-[3,5-Di-*tert*-butyl-2-hydroxy-benzylidene)-aminol]-3-phenyl-propane-1,3-diol (4b). IR (KBr) 3383, 2889, 1633, 1581, 1454, 1277, 1129, 1014, 835, 763 cm^{-1}; $[\alpha]^{25}_D$ = +111 ° (*c* = 0.16, CH_2Cl_2); ^{1}H NMR (500 MHz, $CDCl_3$): δ 13.26 (1H, brs), 8.44 (1H, s), 7.42 (1H, d, *J* = 2.4 Hz), 7.33-7.31 (5H, m), 7.12 (1H, d, *J* = 2.4 Hz), 4.89 (1H, d, *J* = 6.9 Hz,), 3.69 (1H, dd, *J* = 11.4 Hz, *J* = 7.2 Hz), 3.61 (1H, dd, *J* = 11.4 Hz, *J* = 3.8 Hz), 3.50 (1H, dt, *J* = 7.1 Hz, *J* = 3.8 Hz), 1.46 (9H, s), 1.31 (9H, s); ^{13}C NMR (125 MHz, $CDCl_3$): δ 169.5, 158.0, 140.6, 140.5, 136.9, 128.7, 128.3, 127.7, 126.8, 126.5, 117.7, 77.5, 74.8, 63.7, 35.1, 34.2, 31.5, 29.5. MS 285. Anal. Calcd for $C_{24}H_{33}NO_3$: C, 75.16, H, 8.67; Found: C, 75.36, H, 8.78.

(*R,R*)-2-[5-bromo-2-hydroxy-benzylidene)-aminol]-3-phenyl-propane-1,3-diol (4c). IR (KBr) 3309, 3057, 2872, 1647, 1509, 1491, 1338, 1164, 1092, 1072, 831 cm^{-1}; $[\alpha]^{25}_D$ = -296° (*c* = 0.05, MeOH); ^{1}H NMR (200 MHz, $CDCl_3$-DMSO-d_6): δ 14.00 (1H, brs), 8.25 (1H, s), 7.38-7.21 (7H, m), 6.77 (1H, d, *J* = 8.8 Hz), 5.38 (1H, brs), 4.81-4.80 (1H, m), 4.61 (1H, brs), 3.52 (2H, dd, *J* = 16.8 Hz, *J* = 9.6 Hz,); ^{13}C NMR (50 MHz, $CDCl_3$-DMSO-d_6): δ 163.3, 159.5, 141.3, 132.9, 131.9, 126.4, 125.6, 125.1, 118.7, 117.6, 107.2, 74.8, 71.3, 60.6. Anal. Calcd for $C_{16}H_{16}BrNO_3$: C, 54.87, H, 4.60; Found: C, 54.91, H, 4.64.

(*S,S*)-2-[3-*tert*-butyl-2-hydroxy-benzylidene)-aminol]-1-phenyl-propane-1,3-diol (4d). IR (KBr) 3410, 2957, 1630, 1436, 1308, 1086, 467 cm^{-1}; $[\alpha]^{25}_D$ = +153 ° (*c* = 2.4 g/ml, CH_2Cl_2); H^1 NMR(500 MHz, $CDCl_3$): δ 13.60 (1H, s), 8.25 (1H, s), 7.33 (1H, dd, *J* = 7.8 Hz, *J* = 1.6 Hz,), 7.30-7.26 (5H, m), 7.05 (1H, dd, *J* = 7.6 Hz, *J* = 1.5 Hz,), 6.79 (1H, t, *J* = 7.6 Hz), 4.80 (d, 1H, *J* = 6.7 Hz), 3.60-3.52 (2H, m), 3.40 (1H, dt, *J* = 6.7 Hz, *J* = 2.4 Hz), 1.43 (9H, s); ^{13}C NMR (125 MHz, $CDCl_3$): 168.7, 160.4, 140.6, 137.5, 130.2, 129.9, 128.5, 128.2, 126.7, 118.5, 118.1, 76.9, 74.6, 63.5, 34.8, 29.4. Anal. Calcd for $C_{20}H_{25}NO_3$: C, 73.37, H, 7.70; Found: C, 73.32, H, 7.64.

(*S*)-2-[(2-hydroxy-1-phenylsulfanylmethylethyllimino)-methyl]-phenol (4e). IR (KBr) 3451, 2917, 1632, 1494, 1271, 1057, 763, 700 cm^{-1}; $[\alpha]^{25}_D$ = -107° (*c* = 0.6, CH_2Cl_2). ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.29 (1H, s), 7.35-7.20 (7H, m), 6.93 (2H, dt, *J* = 7.6 Hz, *J* = 0.9 Hz), 3.82-3.75 (2H, m), 3.69 (2H, S), 3.40-3.29 (1H, m) 2.66 (2H, dq, *J* = 13.5 Hz, *J* = 5.2 Hz); ^{13}C NMR (125 MHz, $CDCl_3$): δ 166.4, 160.8, 137.9, 132.5, 131.6, 128.8, 128.7, 128.4, 126.9, 118.7, 118.3, 116.9, 71.1, 65.3, 36.9, 33.7. MS 301 (39), 179(91), 107(48), 91(100). Anal. Calcd for $C_{16}H_{17}NO_2S$: C, 68.87, H, 5.96; Found: C, 68.19, H 6.26.

(*S*)-2,4-Di-*tert*-butyl-6[(1-hydroxymethyl-3-phenyl-sulfanyl-propylimino)-methyl]-phenol, (4f). IR (KBr) 3413, 2956, 1628, 1453, 1361, 1250, 1173, 1029, 700 cm^{-1}; $[\alpha]^{25}_D$ = -98° (*c*

= 0.4, CH_2Cl_2); ^1H NMR (500 MHz, $CDCl_3$): δ 8.32 (1H, s), 7.41 (1H, d, *J* = 2.0 Hz), 7.29-7.26 (5H, m), 7.10 (1H, d, *J* = 2.0 Hz), 3.78-3.74 (2H, m), 3.69 (2H, s), 3.38-3.35 (1H, m) 2.66 (2H, dq, *J* = 13.5 Hz, *J* = 5.3 Hz), 1.44 (9H, s), 1.32 (9H, s); ^{13}C NMR (125 MHz, $CDCl_3$): δ 167.9, 158.3, 140.5, 138.2, 136.9, 136.0, 129.0, 128.6, 127.5, 127.2, 126.4, 122.7, 117.7, 71.3, 65.6, 53.7, 37.0, 34.9, 34.1, 31.5, 29.3. MS 413 (76), 398(21), 291(32), 274(29), 260(60), 91(100). Anal. Calcd for $C_{25}H_{35}NO_2S$: C, 72.60, H, 8.53; Found: C, 73.01, H 8.82.

(*S,S*)-1-[(2-hydroxy-1-methoxymethyl-2-phenyl-ethylimino)-methyl]-naphthalene-2-ol, (4g). IR (KBr) 3383, 2990, 2888, 1632, 1581, 1495, 1453, 1413, 1276, 1187, 1129, 1014, 908, 835, 762 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ 8.62 (1H, s), 7.70 (1H, d, *J* = 8.3 Hz), 7.49-7.32 (9H, m), 7.31 (1H, d, *J* = 7.9 Hz), 6.54 (1H, d, *J* = 7.9 Hz), 5.05 (1H, d, *J* = 6.1 Hz), 3.57-3.49 (3H, m), 3.32 (3H, s); ^{13}C NMR (50 MHz, $CDCl_3$): δ 158.1, 140.6, 137.2, 133.7, 128.7, 128.2, 127.6, 127.3, 126.3, 125.5, 124.7, 121.9, 117.5, 105.8, 73.2, 71.8, 68.6, 59.2. MS 285(24), 178(63), 147(100), 132(56), 118(48), 105(36). Anal. Calcd for $C_{21}H_{21}NO_3$: C, 75.20, H, 6.3; Found: C, 75.60, H 6.60.

(*S,S*)-1-[(2-hydroxy-1-methoxymethyl-2-phenyl-ethylimino)-methyl]-phenol (4h). IR (KBr) 3383, 2889, 1633, 1581, 1454, 1277, 1129, 1014, 835, 763 cm^{-1}; $[\alpha]^{25}_D$ = +138 ^{o} (*c* = 5.0, CH_2Cl_2); ^1H NMR (200 MHz, $CDCl_3$): δ 8.28 (1H, s), 7.35-7.20 (7H, m), 6.95 (1H, d, *J* = 7.9 Hz), 6.86 (1H, t, *J* = 7.9 Hz), 4.91 (1H, d, *J* = 6.0 Hz), 3.65-3.55 (1H, m), 3.50-3.40 (2H, m), 3.28 (3H, s); ^{13}C NMR (50 MHz, $CDCl_3$): δ 167.0, 160.9, 140.6, 132.4, 131.5, 128.3, 127.9, 127.6, 126.5, 126.2, 118.5, 116.9, 74.6, 73.3, 59.1, 58.9. MS 285. Anal. Calcd for $C_{17}H_{19}NO_3$: C, 71.56, H, 6.71; Found: C, 71.82, H 6.91.

(*S,S*)-2,4-Di-*tert*-butyl-6-[(2-hydroxy-1-methoxymethyl-2-phenyl-ethylimino)- methyl]-phenol (4i). IR (KBr) 3420, 2957, 2879, 1630,1469, 1389, 1249,1201, 1123, 1026, 768, 703 cm^{-1}; $[\alpha]^{25}_D$ = +111.5^o (c = 0.6, CH_2Cl_2); ^1H NMR (500 MHz, $CDCl_3$): δ 8.34 (1H, s), 7.39 (1H, d, *J* = 2.4 Hz), 7.37-7.35 (5H, m), 7.09 (1 H, d, *J* = 2.2 Hz,), 4.89 (1H, d, *J* = 6.0 Hz), 3.58 (1H, q, *J* = 5.4 Hz), 3.42 (2H, d, *J* = 5.4 Hz), 3.27 (3H, s), 1.47 (9H, s), 1.30 (9H, s); ^{13}C NMR (125 MHz, $CDCl_3$): δ 168.6, 158.2, 141.0, 140.2, 136.8, 128.5, 128.0, 127.3, 126.8, 126.4, 117.9, 74.9, 74.8, 73.4, 59.1, 34.9, 34.0, 31.4, 29.4. MS 397. Anal. Calcd for $C_{25}H_{35}NO_3$: C, 75.83, H, 8.87; Found: C, 75.82, H 8.90.

(*S*)-2-*tert*-Butyl-6-[(1-hydroxymethyl-3-methyl-sulfanyl-propylimino)-methyl]-phenol (4j). IR (KBr) 3412, 2954, 1629, 1453 cm^{-1}; $[\alpha]^{25}_D$ = -355^o (*c* = 0.4, CH_2Cl_2); ^1H NMR (500 MHz, $CDCl_3$): δ 8.30 (1H, s), 7.40 (1H, d, *J* = 8.0 Hz), 7.20 (1H, d, *J* = 8.0 Hz), 6.80 (1H, t, *J* = 8.0 Hz), 3.70 (2H, dq, *J* = 10.0 Hz, *J* = 4.0 Hz), 3.42 (1H, dt, *J* = 10.0 Hz, *J* = 4.0 Hz), 2.53 (1H, dq, *J* = 10.0 Hz, *J* = 4.0 Hz), 2.40 (1H, dq, *J* = 10.0 Hz, *J* = 4.0 Hz), 2.03 (3H, s), 1.94-1.84 (2H, m), 1.4 (9H, s); ^{13}C NMR (125 MHz, $CDCl_3$): δ 167.3, 160.5, 137.6, 130.2, 129.9, 118.6, 118.2, 70.3, 66.1, 34.9, 31.2, 30.8, 29.6, 15.5. Anal. Calcd for $C_{16}H_{25}NO_2S$: C, 65.05, H, 8.53; Found: C, 65.36, H 8.80.

(*S*)-2-[(1-hydroxymethyl-3-methyl-sulfanyl-propylimino)-methyl]-phenol (4k). IR (KBr) 3189, 2912, 2861, 1625, 1574, 1487, 1394, 1276, 1051, 912, 830, 759 cm^{-1}; $[\alpha]^{25}_D$ = -181^o (*c* = 1.0, CH_2Cl_2); ^1H NMR (500 MHz, $CDCl_3$): δ 8.40 (1H, s), 7.32-7.25 (2H, m), 6.92 (2H, dq, *J* = 7.5 Hz, *J* = 1.1 Hz), 3.74-3.69 (2H, m), 3.47 (1H, q, *J* = 6.8 Hz), 2.52 (2H, dq, *J* = 10.0 Hz, *J* = 7.9 Hz), 2.07 (3H, s), 1.94 (2H, q, *J* = 6.4 Hz); ^{13}C NMR (50 MHz, $CDCl_3$): δ 166.0, 160.6, 132.2, 131.2, 118.4, 118.2, 116.6, 69.8, 65.6, 30.7, 30.4, 15.1. Anal. Calcd for $C_{12}H_{17}NO_2S$: C, 60.22, H, 7.16; Found: C, 60.54, H 7.38.

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