Tetrahedron: *Asymmetry* 20 (2009) 2788–2794

Contents lists available at ScienceDirect

Tetrahedron: *Asymmetry*

journal homepage: www.elsevier.com/locate/tetasy

Catalytic asymmetric hydrosilylation of acetophenone with new chiral thiourea ligands containing the (*S*)-α-phenylethyl group

Ericka Santacruz [a], Gabriela Huelgas [a], Sandra K. Angulo [a], Virginia M. Mastranzo [a,b], Simón Hernández-Ortega [b], Judit A. Aviña [c], Eusebio Juaristi [c], Cecilia Anaya de Parrodi [a,*], Patrick J. Walsh [d]

[a] *Departamento de Ciencias Químico-Biológicas, Universidad de las Américas-Puebla, Sta. Catarina Mártir, 72820 Cholula, Mexico*
[b] *Instituto de Química, Universidad Nacional Autónoma de Mexico, 04510 D.F., Mexico*
[c] *Departamento de Química, Centro de Investigación y de Estudios Avanzados del Instituto Politécnico Nacional, 07000 D.F., Mexico*
[d] *Department of Chemistry, University of Pennsylvania, Philadelphia, PA 19104-6323, USA*

ARTICLE INFO

Article history:
Received 23 September 2009
Accepted 27 November 2009
Available online 6 January 2010

ABSTRACT

New chiral thioureas **1–8** containing 1,2-ethylendiamine or *trans*-1,2-diaminocyclohexane as the carbon skeleton, and containing an (*S*)-α-phenylethyl group have been prepared (79–98% yield). Thioureas **1–8** were used as ligands for the zinc-based catalyzed asymmetric hydrosilylation of acetophenone with polymethylhydrosiloxane (PMHS). The best result was achieved with monothiourea **1** (up to 75% ee), in toluene and a catalyst load of 5 mol %.

1. Introduction

The search for more economical and environmentally friendly methods for the enantioselective reduction of prochiral ketones is a rewarding goal. Asymmetric hydrosilylation of arylketones catalyzed by transition metals with chiral nitrogen and sulfur-containing ligands is a useful synthetic route to optically active alcohols.[1–5]

Polymethylhydrosiloxane (PMHS), a polymer coproduct of the silicone industry, is a safe and inexpensive hydrosilylating agent, which can transfer its hydride to a variety of inexpensive and non-toxic metal catalysts (Ti, Zn, and Cu).[2,3] The enantioselective hydrosilylation of prochiral ketones and imines in the presence of PMHS as a reducing reagent with zinc-based catalysts in the presence of bidentate *N,N*-ligands[6–12] and *N,S*-ligands[13,14] had been reported by several groups.

Considerable attention has been focused on the development of chiral thioureas, which are air and moisture stable and have been used as ligands in asymmetric catalysis.[15–25] Chiral thiourea **A** has been employed in the asymmetric reduction of acetophenone by ruthenium- and rhodium-catalyzed hydride transfer with 87% and 63% ee, respectively, in 98% yield.[17,18,21] Additionally, the hydrosilylation of acetophenone using thiourea **B** with iridium-based catalysts and diphenylsilane has been reported. Enantioselectivities as high as 74% were achieved, although only 30% conversion was reported (Scheme 1).[21]

Our goal is the design of new ligands using the α-phenylethylamino group as an economic chiral moiety.[26] Herein we report the preparation of new thioureas **1–8** (Chart 1) containing 1,2-ethylendiamine or *trans*-1,2-diaminocyclohexane as the backbone, and (*S*)-α-phenylethyl groups as chiral appendages. We also report the use of ligands **1–8** in the catalytic asymmetric hydrosilylation of acetophenone with PMHS and diethylzinc.

2. Results and discussion

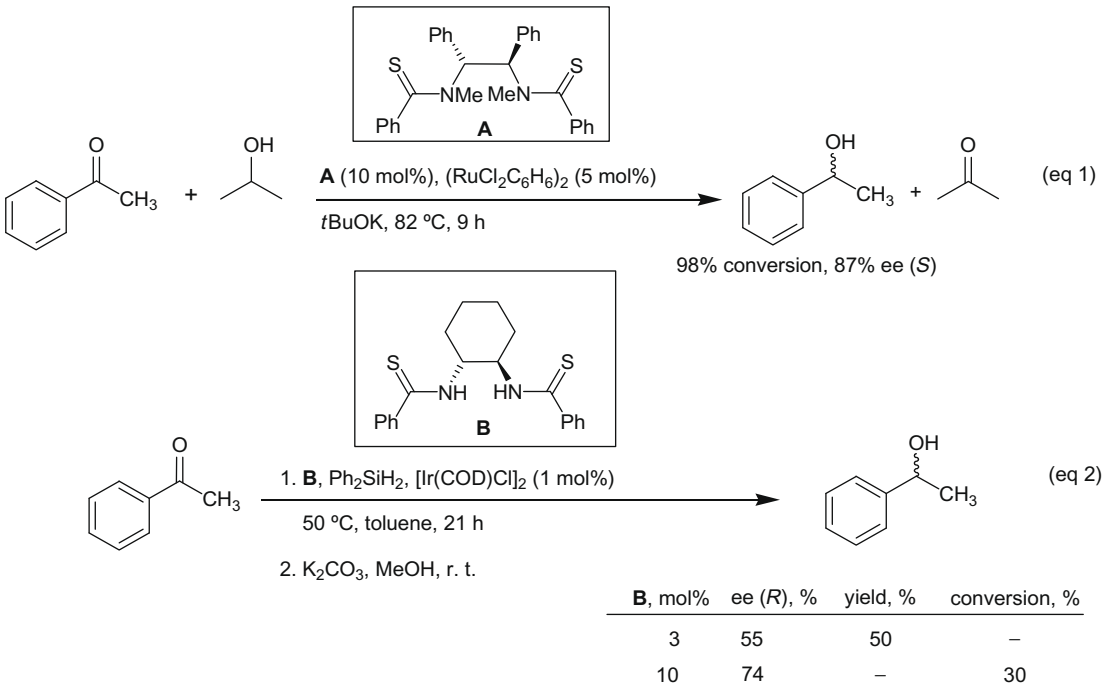
2.1. Preparation of chiral thioureas 1–8

Thioureas **1–8** were prepared in dichloromethane at 25 °C with 1.0 equiv of 1,2-diamines **9–11**[10] and 2 equiv of isothiocyanates **12–16**.[27,28] Diamine **9** afforded monothioureas **1–4** in 79–80% yield after purification by column chromatography on silica gel [hexanes/EtOAc; 12:1] (Scheme 2, Eq. 1). Thioureas **1–4** did not react with the second equivalent of isothiocyanate. The dithioureas were obtained with 1,2-diamines **10** and **11** affording **5** in 98% yield, and **6–8** in 79–80% yield (Scheme 2, Eqs. 2 and 3), respectively.

We observed dynamic phenomena in the NMR spectra of chiral thioureas **1–8** in $CDCl_3$ at 25 °C, and so we recorded the spectra in DMSO-d_6 at 50–110 °C. Monothioureas **1–3** formed suitable crystals for X-ray diffraction analysis. ORTEP diagrams are shown in Figures 1–3. The structures of **1–3** show that the secondary amines are sterically crowded. The congested environment about the secondary amines might explain the formation of the monothioureas **1–4** as the major product, instead of the corresponding dithioureas as in the case of **6–8**, even though an excess of isothiocyanate was used in all reactions.

* Corresponding author. Fax: +52 222 229 2419.
E-mail address: cecilia.anaya@udlap.mx (Cecilia Anaya de Parrodi).

0957-4166/$ - see front matter © 2009 Elsevier Ltd. All rights reserved.
doi:10.1016/j.tetasy.2009.11.027



B, mol%	ee (*R*), %	yield, %	conversion, %
3	55	50	–
10	74	–	30

Scheme 1.

2.2. Enantioselective reduction of acetophenone

With a series of new ligands in hand, we optimized the asymmetric reduction of acetophenone with diethylzinc, PMHS, and the substrate. We observed the best yields and enantioselection in the hydrosilylation of 1 equiv of acetophenone with 1.2 equiv of PMHS in the presence of toluene as a solvent, 5 mol % thiourea ligand and 5 mol % Et_2Zn for 48 h at room temperature.[10] Thioureas **1–4**, containing the *trans*-1,2-diaminocyclohexane backbone, afforded higher yields and enantioselectivities compared with thiourea **5–8** with the 1,2-ethylendiamine backbone (Table 1). The highest enantioselectivities were observed with a catalyst formed from thiourea **1**, affording 1-phenylethanol with 75% ee. In all cases, the yields were low (Table 1) and no side reaction was observed. Higher loadings of the catalysts or long reaction times led to a higher conversion with a reduction in the enantioselectivity. Unfortunately, the use of different solvents did not afford better results (Table 2).

Compounds **1–4** are bifunctional ligands that presumably bind through the amine and thiourea groups. The basic nitrogen of the amine is normally a good ligand for zinc.[6,9,10] We surmise that

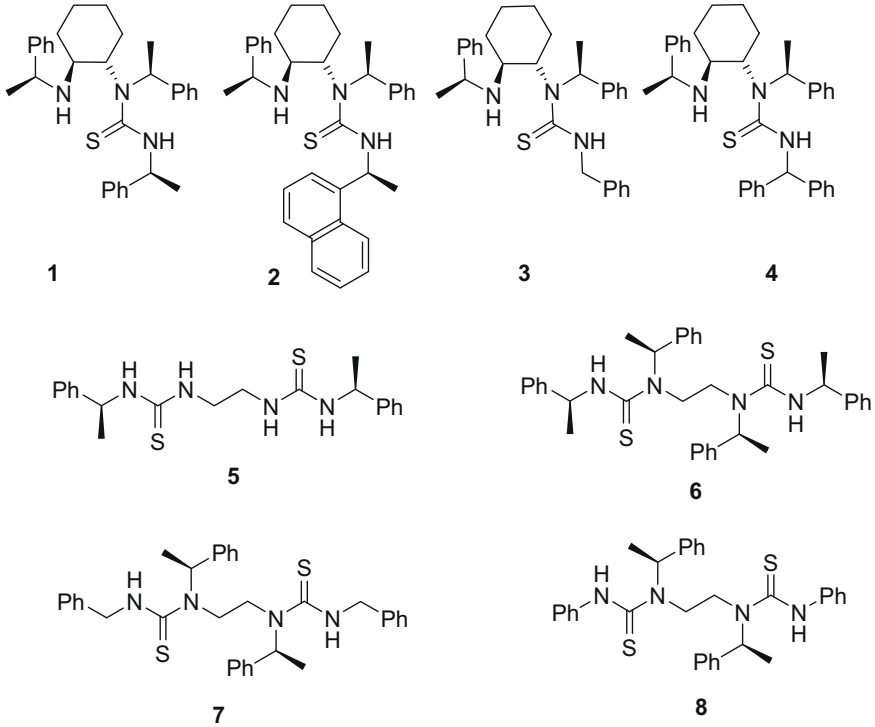
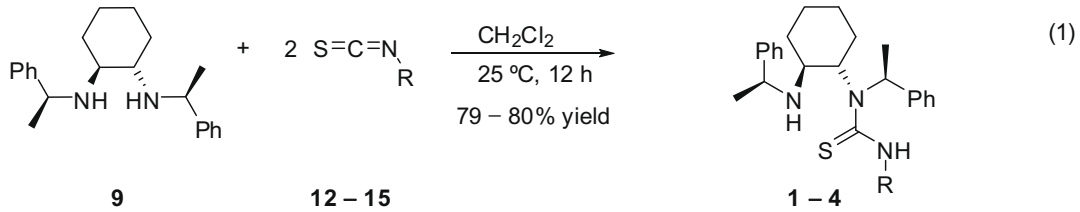
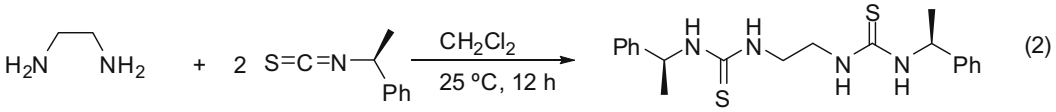
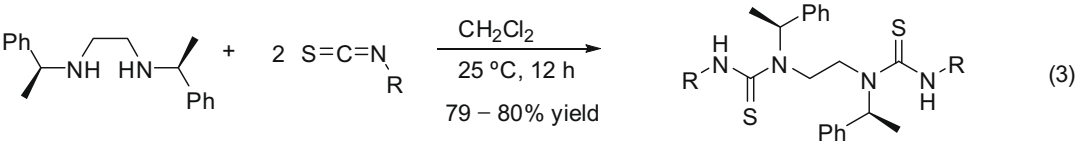


Chart 1.



1, **12**; R = (*S*)-CHCH$_3$Ph
2, **13**; R = (*S*)-CHCH$_3$-1-Naphthyl
3, **14**; R = CH$_2$Ph
4, **15**; R = CHPh$_2$





6, **12**; R = (*S*)-CHCH$_3$Ph
7, **14**; R = CH$_2$Ph
8, **16**; R = Ph

Scheme 2.

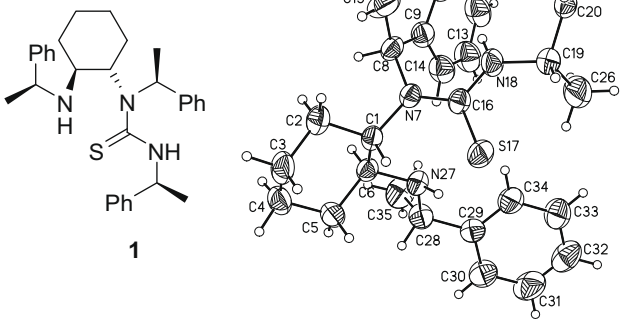


Figure 1. Solid-state structure of (1*S*,2*S*)-*N*,*N*′,*N*″-tris[(*S*)-α-phenylethyl]-1,2-diaminocyclohexylthiourea **1**.

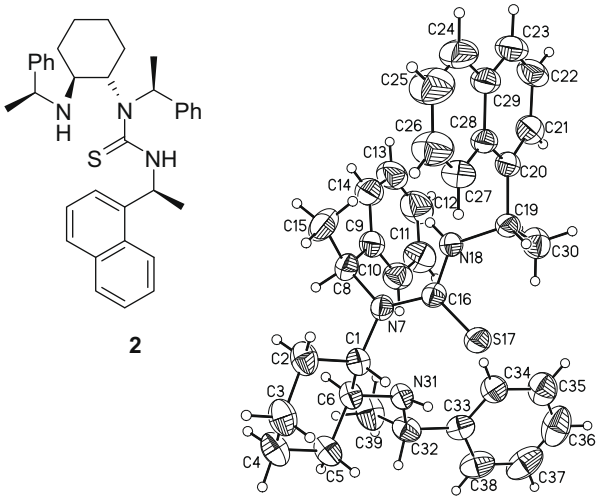


Figure 2. Solid-state structure of (1*S*,2*S*)-*N*,*N*′-bis[(*S*)-1-phenylethyl]-*N*́-[(*S*)-1-naphthylethyl)-1,2-diaminocyclohexylthiourea **2**.

the low conversion and moderate enantioselectivities observed with compounds **1–4** are due to the congestion around the basic nitrogen atoms (Fig. 4). On the other hand, the poor results with ligands **5–8**, which are dithiourea ligands, might be caused by two factors: (a) the presence of only weakly coordinating nitrogen atoms and (b) coordination of the sulfur atoms with zinc would result in the formation of a nine-membered metallocycle with very conformationally flexible rings.

We also observed the presence of intramolecular interactions N–H···S in the structures of thioureas **1–3** (Figs. 1–3), which are shown in Table 3. A shorter N–H···S hydrogen bond is observed in compound **1** in comparison with compounds **2** and **3**. Furthermore, we found a weak intermolecular interaction involving C–H···S along the *c* axis in **1** and **2** and along the *b* axis in compound **3** (Table 3).

3. Conclusion

In conclusion, new chiral thiourea ligands **1–8** have been prepared in good yields (79–98%). They have been used as zinc-based

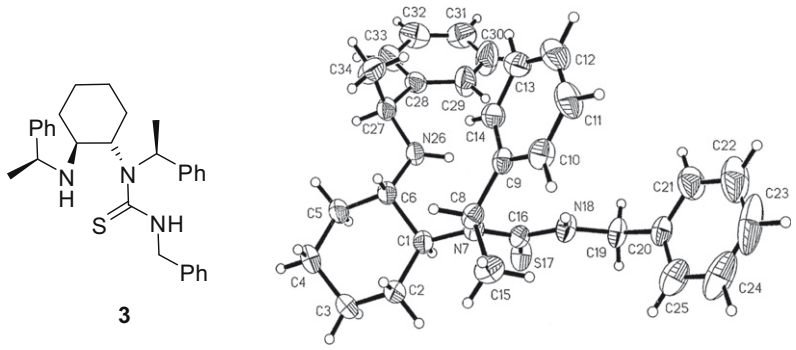
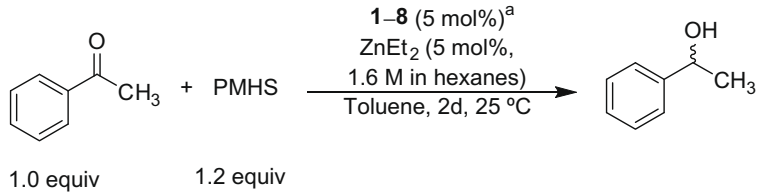


Figure 3. Solid-state structure of (1*S*,2*S*)-*N*,*N*′-bis[(*S*)-α-phenylethyl]-*N*″-(benzyl)-1,2-diaminocyclohexylthiourea **3**.

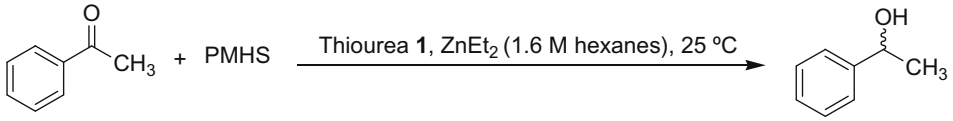
Table 1
Enantioselective reduction of acetophenone in the presence of diethylzinc and thioureas **1**–**8**



Entry	Thiourea	Yield[b] (%)	ee (config.)[c] (%)
1	1	33	75 (*R*)
2	2	38	46 (*R*)
3	3	54	38 (*R*)
4	4	31	57 (*R*)

[a] Thioureas **5**–**8** gave low enantioselectivities (1–39%) and low yields (20–53%).
[b] Yields were measured after column chromatography on silica gel (hexanes/EtOAc; 12:1 as eluent).
[c] The enantiomeric excesses were determined by HPLC with a Chiralcel OD column.

Table 2
Enantioselective reduction of acetophenone in the presence of diethylzinc and thiourea 1 under different reaction conditions



Entry	PMHS (equiv)	$ZnEt_2$ (mol %)	Thiourea **1** (mol %)	Solvent	Time (d)	Yield[a] (%)	ee (config.)[b] (%)
1	5.0	5	5	Toluene	4	50	70 (*R*)
2	1.2	10	10	Toluene	2	60	59 (*R*)
3	1.2	10	10	Hexanes	2	87	52 (*R*)
5	1.2	10	5	Hexanes	2	62	65 (*R*)
5	1.2	5	5	Solvent-free	2	36	58 (*R*)

[a] Yields were measured after column chromatography on silica gel (hexanes/EtOAc; 12:1 as eluent).
[b] The enantiomeric excesses were determined by HPLC with a Chiralcel OD column.

catalysts in the hydrosilylation of acetophenone with polymethylhydrosiloxane (PMHS) as the hydride source with enantioselectivities reaching 75%. Based on these results, we are currently working on the design of new chiral thiourea-based catalyst for the asymmetric hydrosilylations of prochiral ketones.

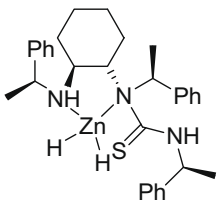


Figure 4.

Table 3
Hydrogen bonds for thioureas **1**–**3** (Å and °)

Thiourea	D–H···A	*d*(D–H)	*d*(H···A)	*d*(D···A)	∠(DHA)
1	N(26)–H(26)···S(17)	0.889(9)	2.80(2)	3.496(2)	136.1(17)
2	N(31)–H(31)···S(17)	0.88(1)	3.07(2)	3.672(2)	127(2)
3	N(26)–H(26)···S(17)	0.90(1)	3.20(1)	3.881(2)	133.8(2)
1	C(4)–H(4)···S(17)	0.97	2.95	3.82	150.6
2	C(23)–H(23)···S(17)	0.93	2.86	3.78	171.6
3	C(23)–H(23)···S(17)	0.93	2.86	3.80	164.4

4. Experimental

4.1. General methods

All manipulations involving diethylzinc were carried out under an argon atmosphere. Benzaldehyde was distilled prior to use. NMR spectra were obtained on a Varian 200 and 400 MHz Fourier transform spectrometer. ^{1}H NMR spectra were referenced to tetramethylsilane; ^{13}C{^{1}H} NMR spectra were referenced to the solvent resonances.

4.2. General procedure for the preparation of chiral thioureas 1–8

1,2-Diamines (2.0 mmol) **9–11** and isothiocyanates **12–16** (4.0 mmol) were dissolved in CH_2Cl_2 (10 mL). The mixture was stirred for 12 h at 25 °C. The reaction mixture was concentrated in vacuo and the residue was purified by column chromatography on silica gel [hexanes/EtOAc/CH_2Cl_2, (2:1:1)].

4.2.1. (1*S*,2*S*)-*N*,*N*′,*N*″-Tris[(*S*)-α-phenylethyl]-1,2-diaminocy clohexylthiourea 1

Affording colorless crystals (1.8 g, 90% yield); mp 105.0–107.0 °C; $[\alpha]_D^{20} = +18$ (*c* 1.0, $CHCl_3$). ^{1}H NMR (200 MHz, DMSO-d_6, 105 °C) δ: 1.05 (m, 6H), 1.26 (d, 6H, *J* = 6.6 Hz), 1.58 (m, 7H), 2.26 (m, 2H), 3.81 (q, 2H, *J* = 6.2 Hz), 5.18 (q, 1H, *J* = 7.0 Hz), 7.17–7.39 (m, 14H), 7.80 (d, 1H, *J* = 6.0 Hz). ^{13}C NMR (50 MHz, $CDCl_3$) δ: 19.2, 21.8, 23.2, 25.4, 26.5, 32.2, 33.4, 53.6, 54.3, 55.3, 56.3, 65.2, 125.8, 126.1, 126.2, 126.6, 126.8, 127.2, 127.4, 127.9, 128.4, 140.1, 142.7, 147.0, 180.4. IR-FT (KBr): 3394, 3295, 3059, 3027, 2968, 2929, 2857, 1602, 1584, 1519, 1448, 1413, 1347, 1229, 1204, 1142, 1083, 1044, 1030, 999, 963, 913, 871, 855, 804, 761, 699 cm^{-1}. Recrystallized from hexanes/CH_2Cl_2 (3:1), colorless prism 0.30 × 0.17 × 0.16 mm; $C_{31}H_{39}N_3S$. Orthorhombic, $P2_12_12_1$, *a* = 12.486 (1) Å, *b* = 13.984 (1) Å, *c* = 16.422 (2) Å, *Z* = 4, δ_{calcd} = 1.125 mg/m^3, *V* = 2867.4(5)Å^3 μ = 0.136 mm^{-1}, *F*(0 0 0) = 1048 A set of 31776 reflections was collected at *T* = 298(2) K, 5329 independent reflections [R_{int} = 0.0688]. (Brucker Smart diffractometer, APEX AXS CCD area detector, omega scans). The structure was solved by direct methods (SHELXTL-2008) and refined with all data by full matrix least squares using SHELXTL-2008.[30b] All non-hydrogen atoms were localized from the difference electron density map and refined anisotropically. H atoms were placed in geometrically idealized positions [0.97 Å(CH_2) and 0.96 Å (CH_3)] tied to the parent atom with Uiso(H) = 1.2 UeqC(sp2) and 1.5 UeqC(sp2) and were refined using the riding model. The absolute configuration was established by stereogenic centers C1(*S*) and C6(*S*), as a reference and was confirmed by anomalous dispersion effects in diffraction measurements on the crystal. The other stereogenic centers were assigned as C8(*S*), C19(*S*), and C28(*S*). Flack parameter −0.02(7). A phenyl ring fragment was disordered and was refined anisotropically in two major contributors. Final *R* indices: R_1 = 0.0413 and wR_2 = 0.0611 for all data. CCDC deposition number: 747611. Structure factors and raw files are available on request to the authors. Elemental Anal. Calcd for $C_{31}H_{39}N_3S$: C, 76.65; H, 8.09; N, 8.65. Found: C, 76.81; H, 7.98; N, 8.68.

4.2.2. (1*S*,2*S*)-*N*,*N*′-Bis[(*S*)-1-phenylethyl]-*N*″-(1-naphthylethyl)-1,2-diaminocyclohexyl-thiourea 2

Affording colorless crystals (0.300 g, 70% yield); mp 164–165 °C; $[\alpha]_D$ = +12 (*c* 1.0, $CHCl_3$); ^{1}H NMR (200 MHz, DMSO-d_6, 105 °C) δ: 1.04 (m, 6H), 1.30 (d, 6H, *J* = 6.6 Hz), 1.53 (m, 3H), 1.81 (m, 4H), 2.33 (m, 2H), 3.86 (q, 2H, *J* = 6.6 Hz), 5.83 (q, 1H, *J* = 6.6 Hz), 7.12–8.08 (m, 17H). ^{13}C NMR (50 MHz, $CDCl_3$) δ: 19.1, 20.1, 23.3, 25.5, 26.6, 32.2, 33.5, 51.3, 53.8, 54.4, 56.5, 65.3, 122.3, 124.0, 124.8, 125.4, 126.1, 126.3, 126.4, 127.4, 127.5, 127.8, 128.0, 128.2, 128.4, 130.9, 133.4, 138.0, 140.2, 147.2, 180.3. IR-FT (KBr): 3379, 3302, 3053, 3027, 2969, 2928, 2856, 1599, 1519, 1449, 1410, 1347, 1297, 1263, 1227, 1118, 1083, 1036, 999, 961, 913, 863, 804, 781, 751, 732, 701, 650, 622, 538, 498, 442 cm^{-1}. Recrystallized from hexanes/CH_2Cl_2 (5:1), colorless prism 0.34 × 0.18 × 0.08 mm; $C_{35}H_{41}N_3S$. Monoclinic, $P2_1$, *a* = 7.672(2) Å, *b* = 19.080 (5) Å, *c* = 10.763 (3) Å, β = 95.022(4)°, *Z* = 2, δ_{calcd} = 1.134 mg/m^3, *V* = 1569.5(7)Å^3, μ = 0.130 mm^{-1}. A set of 12930 reflections was collected at *T* = 298(2) K, 5760 independent reflections [R_{int} = 0.0369]. (Brucker Smart diffractometer, APEX AXS CCD area detector, omega scans). The structure was solved by direct methods (SHELXTL-2008) and was refined with all data by full matrix least squares using SHELXTL-2008.[30b] All non-hydrogen atoms were localized from the difference electron density map and refined anisotropically. H atoms were placed in geometrically idealized positions [0.97 Å (CH_2) and 0.96 Å (CH_3)] tied to the parent atom with Uiso(H) = 1.2 UeqC(sp2) and 1.5 UeqC(sp2) and were refined using the riding model. The absolute configuration was established by stereogenic centers C1(*S*) and C6(*S*), as reference and was confirmed by anomalous dispersion effects in diffraction measurements on the crystal. The other stereogenic centers were assigned as C8(*S*), C19(*S*), and C28(*S*). Flack parameter −0.11(7). Final *R* indices: R_1 = 0.0478 and wR_2 = 0.0922 for all data CCDC deposition number: 747612. Structure factors and raw files are available on request to the authors. FAB-MS: *m*/*z* [M+H]$^+$ calcd 536.3099 for $C_{35}H_{42}N_3S$; found 536.3109.

4.2.3. (1*S*,2*S*)-*N*,*N*′-Bis[(*S*)-1-phenylethyl]-*N*″-(benzyl)-1,2-diaminocyclohexylthiourea 3

Affording colorless crystals (0.60 g, 85% yield); mp 104–106 °C; $[\alpha]_D$ = +13 (*c* 1.0, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 1.05 (m, 1H), 1.16 (d, 3H, *J* = 6.4 Hz), 1.36 (m, 1H), 1.47–1.69 (m, 5H), 1.73 (d, 3H, *J* = 6.9 Hz), 2.05 (d, 1H, *J* = 12.0 Hz), 2.15 (d, 1H, *J* = 10.8 Hz), 2.84 (dt, 1H, *J* = 10.2 Hz, *J* = 3.6 Hz), 3.94 (q, 1H, *J* = 6.4 Hz), 4.54 (dd, 1H, *J* = 14.6 Hz, *J* = 4.2 Hz), 4.78 (dd, 1H, *J* = 14.6 Hz, *J* = 4.6 Hz), 5.15 (m, 1H), 5.69 (m, 1H), 5.92 (br, 1H), 6.85 (m, 2H), 7.16–7.37 (m, 11H), 7.88 (d, 2H, *J* = 7.2 Hz). ^{13}C NMR (100 MHz, $CDCl_3$): 18.4, 22.7, 24.7, 25.7, 31.4, 33.0, 50.3, 53.4, 54.3, 56.2, 65.5, 126.3, 126.5, 126.9, 127.2, 127.3, 127.5, 128.1, 128.2, 128.6, 137.5, 140.4, 147.2, 182.8; IR-FT (KBr): 3397, 3297, 3060, 3027, 2930, 2857, 1602, 1584, 1518, 1495, 1449, 1415, 1369, 1320, 1273, 1230, 1203, 1160, 1142, 1075, 1029, 1000, 962, 913, 872, 857, 804, 761, 741, 699 cm^{-1}. Recrystallized from hexanes/CH_2Cl_2 (7:1), colorless irregular, 0.78 × 0.61 × 0.44 mm^3, $C_{30}H_{37}N_3S$. Orthorhombic, $P2_12_12_1$, *a* = 7.549(2) Å, *b* = 10.857(2) Å, *c* = 33.203(7) Å, *Z* = 4, ρ_{calcd} = 1.151 g cm^{-3}. A set of 6080 reflections was collected at *T* = 293(2) K using Mo Kα radiation (λ = 0.71073 Å, Enraf-Nonius CAD4 diffractometer), corresponding to $2\theta_{max}$ = 52.40°. 5382 independent reflections (R_{int} = 0.0738) were used for the refinement of 308 parameters (SHELXL-86).[30a] H atoms were placed in idealized positions and were refined using a standard riding model. The absolute configuration of the chiral centers was assigned as *S*-C8, *S*-C27, and confirmed by refinement of a Flack parameter, *x* = −0.11(15), based on non-merged Friedel pairs. Final *R* indices: R_1 = 0.0530 for 2864 reflections with $I > 2\sigma(I)$ and wR_2 = 0.1448 for all data. CCDC deposition number: 748359. Structure factors and raw files are available on request to the authors. Elemental Anal. Calcd for $C_{30}H_{37}N_3S$: C, 76.39; H, 7.91; N, 8.91. Found: C, 76.44; H, 7.90; N, 8.91.

4.2.4. (1*S*,2*S*)-*N*,*N*′-Bis[(*S*)-1-phenylethyl]-*N*″-[di(phenyl)methylene]-1,2-diaminocyclo-hexylthiourea 4

Affording a pale white solid (0.500 g, 80% yield); mp 150–155 °C; $[\alpha]_D$ = +19 (*c* 1.0, $CHCl_3$); ^{1}H NMR (200 MHz, DMSO-d_6, 105 °C) δ: 1.06 (m, 6H), 1.26 (d, 6H, *J* = 6.2 Hz), 1.61 (m, 3H), 2.26 (m, 2H), 3.81 (q, 2H, *J* = 6.6 Hz), 5.66 (d, 1H, *J* = 0.8 Hz), 6.41 (s, 1H), 6.82 (m, 1H), 7.03–7.45 (m, 18H), 7.79 (m, 1H). ^{13}C NMR

(50 MHz, $CDCl_3$) δ: 18.1, 23.3, 25.4, 26.5, 31.0, 33.4, 53.9, 54.2, 56.1, 63.5, 65.5, 126.1, 126.2, 126.6, 126.8, 127.2, 127.4, 127.6, 127.7, 128.0, 128.1, 128.6, 140.0, 141.0, 141.6, 147.1, 181.1. IR-FT (KBr): 3401, 3301, 3055, 3027, 2996, 2926, 2857, 1598, 1519, 1493, 1449, 1412, 1343, 1291, 1222, 1145, 1078, 1030, 962, 911, 859, 838, 806, 748, 698, 649, 637, 611, 536, 467 cm^{-1}. FAB-MS: m/z $[M+H]^+$; calcd 548.3099 for $C_{36}H_{42}N_3$; found 548.3094.

4.2.5. *N,N′*-Bis[(*S*)-α-phenylethyl]-1,2-diaminoethylendithiourea 5

Affording a white solid (0.76 g, 98% yield), mp 75.0–77.0 °C; $[\alpha]_D^{20} = +37$ (*c* 1.0, $CHCl_3$). ^1H NMR (200 MHz, DMSO-d_6, 50 °C) δ: 1.40 (d, 6H, *J* = 7.0 Hz), 3.24 (s, 2H), 3.51 (m, 4H), 5.41 (m, 2H, *J* = 7.0 Hz), 7.17–7.38 (m, 10H), 7.81 (d, 2H, *J* = 8.0 Hz). ^{13}C NMR (50 MHz, DMSO-d_6, 50 °C) δ: 22.3, 42.7, 52.2, 125.1, 125.7, 127.2, 143.0, 180.3. IR-FT (KBr): 3228, 3060, 2972, 2871, 2820, 1545, 1494, 1448, 1355, 1249, 1217, 1140, 1084, 1019, 913, 761, 736, 699 cm^{-1}. Elemental Anal. Calcd for $C_{20}H_{26}N_4S_2$: C, 62.14; H, 6.78. Found: C, 61.90; H, 6.93.

4.2.6. *N,N′,N″,N‴*-Tetraquis-[(*S*)-α-phenylethyl]-1,2-diaminoethylendithiourea 6

Affording a white solid (0.70 g, 80% yield); mp 76.0–78.0 °C; $[\alpha]_D^{20} = -0.7$ (*c* 1.0, $CHCl_3$). ^1H NMR (200 MHz, DMSO-d_6, 100 °C) δ: 1.28 (d, 6H, *J* = 7.0 Hz), 1.46 (d, 6H, *J* = 7.0 Hz), 3.00 (s, 2H), 3.35 (s, 4H), 5.78 (m, 2H), 6.22 (q, 2H, *J* = 7.0 Hz), 7.09–7.38 (m, 18H), 8.00 (d, 2H, *J* = 7.6 Hz). ^{13}C NMR (50 MHz, DMSO-d_6, 100 °C) δ: 16.4, 21.3, 43.7, 54.3, 55.3, 124.9, 125.1, 125.3, 126.0, 126.7, 127.1, 139.1, 142.6, 179.8. IR-FT (KBr): 3228, 3029, 2974, 2936, 1603, 1541, 1494, 1449, 1356, 1263, 1240, 1205, 1156, 1126, 1084, 1027, 986, 788, 758, 698 cm^{-1}. HRMS-FAB$^+$: m/z $[M+H]^+$ calcd for $C_{36}H_{43}N_4S_2$: 595.2929; found: 595.2924.

4.2.7. *N,N′*-Bis[(*S*)-α-phenylethyl]-*N″,N‴*-bis(benzyl)-1,2-diaminoethylendithiourea 7

Affording a pale yellow solid (0.31 g, 79% yield); mp 67.0–69.0 °C; $[\alpha]_D^{20} = -68$ (*c* 1.0, $CHCl_3$). ^1H NMR (200 MHz, DMSO-d_6, 100 °C): δ = 1.29 (d, 6H, *J* = 7.0 Hz), 3.00 (s, 2H), 3.29 (m, 4H), 4.82 (m, 4H), 6.17 (q, 2H, *J* = 7.0 Hz), 7.10–7.39 (m, 18H), 8.43 (t, 2H, *J* = 5.1 Hz). ^{13}C NMR (50 MHz, DMSO-d_6, 100 °C): δ = 16.3, 43.7, 48.3, 55.4, 125.3, 125.5, 125.9, 126.0, 126.7, 127.2, 137.7, 138.9, 180.8. IR-FT (KBr): 3216, 3030, 2976, 2940, 2906, 1603, 1551, 1526, 1495, 1452, 1380, 1340, 1224, 1152, 1094, 1028, 1069, 987, 963, 901, 787, 736, 698 cm^{-1}. FABS-MS: m/z $[M+H]^+$calcd for $C_{34}H_{39}N_4S_2$: 567.2616; found: 567.2620.

4.2.8. *N,N′*-Bis[(*S*)-α-phenylethyl]-*N″,N‴*-bis(phenyl)-1,2-ethylendithiourea 8

Affording a pale yellow solid (2.8 g, 80% yield); mp 95.0–97.0 °C; $[\alpha]_D^{20} = -120$ (*c* 1.0, $CHCl_3$). ^1H NMR (200 MHz, DMSO-d_6, 80 °C) δ: 1.35 (d, 6H, *J* = 7.0 Hz), 3.41 (m, 4H), 6.35 (q, 2H, *J* = 6.6 Hz), 7.10–7.45 (m, 20H), 9.62 (s, 2H). ^{13}C NMR (50 MHz, DMSO-d_6, 80 °C) δ: 16.2, 43.8, 55.8, 124.0, 125.4, 125.7, 126.3, 126.8, 127.0, 127.4, 138.8, 139.2, 180.5. IR-FT (KBr): 3174, 3118, 3027, 2976, 2936, 2908, 2791, 1595, 1534, 1496, 1449, 1344, 1249, 1204, 1130, 1111, 1097, 1072, 1003, 987, 984, 915, 830, 786, 763, 746, 694, 668 cm^{-1}. FABS-MS: m/z $[M+H]^+$ calcd for $C_{32}H_{35}N_4S_2$: 539.2303; found: 539.2298.

4.2.9. *N,N′*-Bis[(*S*)-α-phenylethyl]-1,2-ethylendiamine 10

1,2-Diamine **10** was prepared from 1,2-dichloroethane and (*S*)-1-phenylethylamine, according to the literature procedure.[6]

4.2.10. (1*S*,2*S*)-*N,N′*-Bis[(*S*)-α-phenylethyl]-1,2-cyclohexanodiamine 11

1,2-Diamine **11** was prepared from cyclohexene oxide and (*S*)-1-phenylethylamine, according to the literature procedure.[10]

4.3. Enantioselective reduction of acetophenone

In a Schlenk flask Et_2Zn (0.05 mL, 1 M in hexanes, 0.05 mmol) and the chiral ligand (0.05 mmol) were dissolved in 1 mL of hexane and stirred under a nitrogen atmosphere for 10 min. Then 1.0 mmol of acetophenone was added, and PMHS (0.78 g, 1.2 mmol) was added slowly to the mixture. The reaction was kept at rt for two days. The reaction mixture was poured on to 15% aqueous KOH solution (5 mL) and extracted three times with EtOAc (3 mL). The organic layer was washed with water (3 mL), dried over $MgSO_4$, and concentrated in vacuo. The product was purified by column chromatography on silica gel, with hexanes/EtOAc, 10:1, as eluent.

4.4. Conditions for the determination of the enantiomeric excess

Chiral HPLC: Chiralcel OD column, 254 nm UV detector, 97:3 hexanes/IPA, flow rate 5 mL/min, retention time (*R*): 15 min, retention time (*S*): 18 min. Specific rotations of the secondary alcohols were measured and compared with those reported on the literature to assign configuration.[29] *rac*-1-Phenyl-1-ethanol was obtained by the addition of $NaBH_4$ to acetophenone in MeOH.

Acknowledgments

This work was supported by ACS-Petroleum Research Fund (PRF # 46222-B) and CONACYT, Consejo Nacional de Ciencia y Tecnología (Project No. 55802. G.H. and S.K.A. thank CONACYT for postdoctoral scholarships. We also acknowledge Instituto de Química of the Universidad Nacional Autónoma de México for mass spectra. P.J.W. also thanks the U.S. NSF for support (CHE 0848460).

References

1. *Hydrosilylation of Carbonyl and Imino Groups*; Nishiyama, H., Ed.; Springer: Berlin, 1999. Vol. Chapter 63.
2. Carpentier, J. F.; Bette, V. *Curr. Org. Chem.* **2002**, *6*, 913–936.
3. Riant, O.; Mostefai, N.; Courmarcel, J. *Synthesis* **2004**, *18*, 2943–2958.
4. Zhang, W. H.; Cai, Y.; Liu, X.; Fang, Y.; Xu, J. H. *Prog. Chem.* **2007**, *19*, 1537–1552.
5. Roy, A. K. *Adv. Organomet. Chem.* **2008**, *55*, 1–59.
6. Mimoun, H.; de Saint Laumer, J. Y.; Giannini, L.; Scopelliti, R.; Floriani, C. *J. Am. Chem. Soc.* **1999**, *121*, 6158–6166.
7. Bette, V.; Mortreux, A.; Lehmann, C. W. *Chem. Commun.* **2003**, 332–333.
8. Bette, V.; Mortreux, A.; Ferioli, F.; Martelli, G.; Savoia, D.; Carpentier, J.-F. *Eur. J. Org. Chem.* **2004**, 3040–3045.
9. Bette, V.; Mortreux, A.; Savoia, D.; Carpentier, J. F. *Tetrahedron* **2004**, *60*, 2837–2842.
10. Mastranzo, V. M.; Quintero, L.; de Parrodi, C. A.; Juaristi, E.; Walsh, P. J. *Tetrahedron* **2004**, *60*, 1781–1789.
11. Ushio, H.; Mikami, K. *Tetrahedron Lett.* **2005**, *46*, 2903–2906.
12. Park, B. M.; Mun, S.; Yun, J. *Adv. Synth. Catal.* **2006**, *348*, 1029–1032.
13. Gerard, S.; Pressel, Y.; Riant, O. *Tetrahedron: Asymmetry* **2005**, *16*, 1889–1891.
14. Some recent examples: (a) Bandini, M.; Melucci, M.; Piccinelli, F.; Sinisi, R.; Tommasi, S.; Umani-Ronchi, A. *Chem. Commun.* **2007**, 4519–4521; (b) Gajewy, J.; Kwit, M.; Gawronski, J. *Adv. Synth. Catal.* **2009**, *351*, 1055–1063; (c) Inagaki, T.; Yamada, Y.; Phong, L. T.; Furuta, A.; Ito, J.-I.; Nishiyama, H. *Synlett* **2009**, 253–256.
15. Jacobsen, E. N.; Pfaltz, A.; Yamamoto, H. *Comprehensive Asymmetric Catalysis*; Springer: Berlin, 1999.
16. Walsh, P. J.; Li, H.; de Parrodi, C. A. *Chem. Rev.* **2007**, *107*, 2503–2545.
17. Touchard, F.; Fache, F.; Lemaire, M. *Tetrahedron Lett.* **1997**, *38*, 2275–2278.
18. Touchard, F.; Fache, F.; Lemaire, M. *Tetrahedron: Asymmetry* **1997**, *8*, 3319–3326.
19. Breuzard, J. A. J.; Tommasino, M. L.; Touchard, F.; Lemaire, M.; Bonnet, M. C. *J. Mol. Catal. A: Chem.* **2000**, *156*, 223–232.
20. Bernard, M.; Debecq, F.; Fache, F.; Sautet, P.; Lemaire, M. *Eur. J. Org. Chem.* **2001**, 1589–1596.

21. Karamé, I. M.; Tommasino, L.; Lemaire, M. *J. Mol. Catal. A: Chem.* **2003**, *196*, 137–143.
22. Dai, M. J.; Liang, B.; Wang, C. H.; You, Z. J.; Xiang, J.; Dong, G. B.; Chen, J. H.; Yang, Z. *Adv. Synth. Catal.* **2004**, *346*, 1669–1673.
23. Yang, D.; Chen, Y. C.; Zhu, N. Y. *Org. Lett.* **2004**, *6*, 1577–1580.
24. (a) Pan, J. H.; Yang, M.; Gao, Q.; Zhu, N. Y.; Yang, D. *Synthesis* **2007**, 2539–2544; (b) Seidel, D.; Klauber, E. G.; Kanta De, C. *J. Am. Chem. Soc.* **2009**.
25. (a) Hernández-Rodríguez, M.; Avila-Ortiz, C. G.; Martín del Campo, J.; Hernández-Romero, D.; Rosales-Hoz, M. J.; Juaristi, E. *Aust. J. Chem.* **2008**, *61*, 364–375; (b) Juaristi, E.; Hernández-Rodríguez, M.; López-Ruiz, H.; Aviña, J. *Helv. Chim. Acta* **2002**, *85*, 1999–2008.
26. (a) Juaristi, E.; Escalante, J.; León-Romo, J. L.; Reyes, A. *Tetrahedron: Asymmetry* **1998**, *9*, 715–740; (b) Juaristi, E.; León-Romo, J. L.; Reyes, A. *Tetrahedron: Asymmetry* **1999**, *10*, 2441–2495.
27. Isobe, T.; Fukuda, K.; Tokunaga, T.; Seki, H.; Yamaguchi, K.; Ishikawa, T. *J. Org. Chem.* **2000**, *65*, 7774–7778.
28. Molina, P.; Alajarin, M.; Arques, A. *Synthesis* **1982**, 596–597.
29. Naemura, K.; Murata, M.; Tanaka, R.; Yano, M.; Hirose, K.; Tobe, Y. *Tetrahedron: Asymmetry* **1996**, *7*, 3285–3294.
30. (a) Sheldrick, G. M. SHELXL-*86 Program for Crystal Structure Determination*; University of Gottingen: Federal Republic of Germany, 1986; (b) Sheldrick, G. M. *Acta Crystallogr., Sect. A* **2008**, *64*, 112–122.