A Novel Bis-Thiourea Organocatalyst for the Asymmetric Aza-Henry Reaction.

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SUPPORTING INFORMATION

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General procedure for the preparation of the bis-thioureas 1 and 12.

![Chemical structure diagram](image_url)

**bis-Thiourea 12:** 3,5-Bis-trifluoromethylphenyl isothiocyanate 19 (8.12 mmol, 1.48 mL) was added to a solution of (R)-BINAM (R)-18 (1.26 g, 4.00 mmol) in 7 mL THF at rt and the mixture was stirred overnight. The volatiles were evaporated and the product was purified by crystallization from dichloromethane/hexanes to afford 3.22 g (3.89 mmol) of (R)-12 in 96% isolated yield. White crystals, mp 120-122 °C. Spectral data for (R)-12: 1H NMR (CDCl3, 300 MHz) δ 7.09 (d, J = 8.7 Hz, 2H), 7.26 (t, J = 6.9 Hz, 2H), 7.48 (m, 4H), 7.54 (m, 2H), 7.67 (br s, 4H), 7.81 (d, J = 8.7 Hz, 2H), 8.10 (d, J = 8.7 Hz, 2H); 13C NMR (CDCl3, 300 MHz) δ 119.2, 122.8 (q, J = 272.9 Hz), 124.6, 125.3, 125.6, 125.7, 127.5, 127.6, 128.5, 129.7, 131.7 (q, J = 33.7 Hz), 132.3, 132.8, 134.4, 139.1, 180.4; IR (neat) 3265, 1688, 1498, 980 cm\(^{-1}\); HRMS (ESI) calcd for C\(_{38}\)H\(_{23}\)N\(_4\)F\(_{12}\)S\(_2\) m/z 827.1179, meas 827.1172; [a]\(\text{D}^2\) +103.8 (c 1.0, acetone).

![Chemical structure diagram](image_url)

**bis-Thiourea 1:** This compound was prepared according to the above procedure starting with 468 mg (4.10 mmol) of (S,S)-1,2-cyclohexyldiamine 20 and purified by crystallization from EtOAc/hexanes to afford 1.99 g of (S,S)-1 as white crystals (3.03 mmol, 74%). Spectral data for (S,S)-1: 1H NMR (300 MHz, CDCl3) δ 1.35 (br s, 4H), 1.81 (br s, 2H), 2.20 (br s, 2H), 4.38 (br s, 2H), 7.07 (br s, 2H), 7.69 (s, 2H), 7.81 (s, 4H), 8.12 (br s, 2H). This data is in agreement with that reported in the literature.\(^1\)
The preparation of the bis-thioureas 6 and 13.

**bis-Thiourea 13:** A solution of 365 mg (1 mmol) (R)-2,2'-bis(isothiocyanato)-2,2'-binaphthyl diamines (R)-21² and 281 mg (1 mmol) of (R)-1,1'-binaphthyl-2,2'-diamine 18 in THF at rt was allowed to stir overnight. The volatiles were evaporated and the product purified by crystallization from acetone/hexanes to afford 351 mg (55%) of (R,R)-13 as white crystals, mp 230-231 °C. Spectral data for (R,R)-13: ¹H NMR (CDCl₃, 300 MHz) δ 6.68 (d, J = 8.7 Hz, 2H), 6.82 (s, 4H), 6.87 (s, 2H), 7.02 (d, J = 8.4 Hz, 2H), 7.15 (t, J = 6.9 Hz, 2H), 7.40 (q, J = 6.9 Hz, 6.9Hz, 4H), 7.57 (s, 2H), 7.67 (t, J = 6.9 Hz, 2H), 7.76 (d, J = 8.1Hz, 2H), 7.90 (d, J = 8.1Hz, 2H), 8.02 (d, J = 9.3 Hz, 2H), 9.41 (d, J = 9.3 Hz, 2H); ¹³C NMR (CDCl₃, 300 MHz) δ 119.8, 120.8, 123.1, 125.4, 125.5, 125.9, 127.1, 127.2, 127.8, 128.2, 128.6, 128.8, 129.3, 130.2, 131.1, 132.2, 132.3, 132.5, 133.7, 135.7, 177.6; IR (KBr) 3154, 1595 cm⁻¹; mass spectrum (FAB⁺) m/z (% rel intensity) 653 [M+H]⁺ (18), 619 (4), 460 (5), 307 (40), 252 (45) 154 (100), 136 (84), 102 (38). This compound was also characterized by X-ray diffraction (See Appendix).

**bis-Thiourea 6:** This thioureas was synthesized according to the above procedure starting with 0.50 g (1.3 mmol) (R)-2,2'-bis(isothiocyanato)-2,2'-binaphthyl 21² and 302 mg (2.71 mmol) of histamine to afford 540 mg (0.91 mmol, 100% from 21) of (R)-6 as an off-white solid. Spectral data for (R)-6: ¹H NMR (DMSO-d₆, 300 MHz) δ 2.55 (br. s, 4H), 3.47 (br. s, 4H), 6.62 (br. s, 2H), 7.07-7.17 (m, 4H), 7.40 (m, 4H), 7.73 (m, 4H), 7.95 (t, J = 9.3, 4H), 8.61 (br. s, 2H), 11.71 (br. s, 2H); ¹³C NMR (DMSO-d₆, 300 MHz) δ 27.0, 44.5, 55.4, 126.1, 126.2, 126.7, 127.2, 128.3, 128.7, 131.9, 133.1, 135.1, 136.4, 181.3; two carbons are not located; mass spectrum (FAB⁺) m/z (% rel intensity) 591 [M+H]⁺
(17), 307 (14); IR (neat) 3150, 1595, 1490 cm⁻¹; HRMS (FAB⁺) calcd for C₃₂H₃₁N₈S₂ m/z 591.2113, meas 591.2117.

General procedure for the preparation of thioureas catalysts 7 – 11.

The appropriate isothiocyanate (2 equiv) was added to a solution of (R)-BINAM 18 in THF (0.6 M in BINAM) and the mixture was stirred overnight at rt. The volatiles were evaporated and the products were purified by column chromatography on silica gel with 30% acetone in hexanes as eluent.

bis-thiourea (R)-7: This compound was synthesized from (R)-BINAM 18 (300 mg, 1.05 mmol) and isolated as a white solid (277 mg, 0.50 mmol, 50%, mp 128-130 °C) along with 210 mg of (R)-22 which was also a white solid (0.50 mmol, 50%, mp 108-110 °C). Spectral data for (R)-7: ¹H NMR (CDCl₃, 300 MHz) δ 6.12 (d, J = 7.2 Hz, 4H), 6.92 (t, J = 7.2 Hz, 4H), 7.03 (t, J = 7.5 Hz, 2H), 7.35-7.28 (m, 4H), 7.58-7.53 (m, 4H), 7.89 (d, J = 8.7 Hz, 2H), 8.02 (dd, J = 8.1, 2.7 Hz, 4H), 8.30 (br. s, 2H); ¹³C-NMR (CDCl₃, 300 MHz) δ 125.30, 125.33, 126.4, 127.23, 127.29, 128.0, 128.1, 129.2, 129.5, 132.31, 132.33, 135.0, 135.6, 179.7, one C not located; IR (neat) 3159, 1593, 1535 cm⁻¹; mass spectrum (FAB⁺) m/z (% rel intensity) 555 [M+H]⁺, (26), 462 (17), 307 (30), 154 (100), 136 (60); α²⁵D +60.0 (c 1.0, dichloromethane). Spectral data for (R)-22: ¹H NMR (CDCl₃, 300 MHz) δ 3.66 (s, 2H), 6.46 (d, J = 9 Hz, 2H), 6.83 (d, J = 7.8 Hz, 1H), 7.07-6.92 (m, 4H), 7.31-7.24 (m, 3H), 7.13 (td, J = 1.5, 6.9 Hz, 1H), 7.51-7.41 (m, 1H), 7.52 (br s, 1H), 7.85 (d, J = 8.7 Hz, 2H), 7.78 (d, J = 8.4 Hz, 1H), 8.02 (d, J = 8.7 Hz, 1H) 8.36 (d, J = 9 Hz, 1 H), 8.40 (br s, 1H); ¹³C NMR (CDCl₃, 300 MHz) δ 111.5, 118.3, 122.5, 122.9, 124.5, 125.6, 125.8, 126.0, 126.7, 126.7, 126.9, 127.2, 127.4, 127.9, 128.1, 129.6, 132.3, 132.4, 133.4, 135.2, 135.3, 142.7, 179.0, 2 C’s not located; mass spectrum (FAB⁺) m/z (% rel intensity) 420 [M+H]⁺ (40), 307 (30), 154 (100), 136 (65); IR (neat) 3352, 3186, 1626, 1510; α²⁵D +24.2 (c 1.0, dichloromethane).
bis-thiourea (R)-8: This compound was synthesized from (R)-BINAM 18 (300 mg, 1.05 mmol) according to the procedure above and was isolated as a white solid (32 mg, 0.05 mmol, 5%) in a form not pure enough to completely characterize. The major product was the mono-thiourea (R)-24 which was isolated in 55% yield (259 mg, 0.55 mmol) and a white solid, mp 126-128 °C. Spectral data for (R)-8: ¹H NMR (CDCl₃, 300 MHz) δ 5.91 (d, J = 7.2 MHz, 2H), 6.85 (t, J = 8.1 MHz, 2H), 7.59-7.14 (m, 16 H), 7.73 (dd, J = 8.7, 17.4 MHz, 4H), 7.88 (t, J = 8.4 MHz, 4 H); 2 exchangeable H’s can not be located; Rᵣ = 0.17 (30% acetone in hexanes); mass spectrum (FAB⁺) m/z (% rel intensity) 655 [M+H]⁺ (40), 512 (37), 436 (20), 391 (18). Spectral data for (R)-24: ¹H NMR (CDCl₃, 300 MHz) δ 3.1 (br. s, 2H), 6.42 (d, J = 7.2 Hz, 1H), 6.71 (d, J = 8.4 Hz, 1H), 6.76 (d, J = 8.7 Hz, 1H), 6.92 (t, J = 7.8 Hz, 3H), 7.01 (t, J = 7.2 Hz, 1H), 7.21 (t, J = 8.1 Hz, 3H), 7.56-7.43 (m, 3H), 7.63 (d, J = 6.0 Hz, 1H), 7.66 (d, J = 9.0 Hz, 1H), 7.76 (d, J = 8.1Hz, 1H), 7.81 (d, J = 8.1 Hz, 1H), 7.93 (d, J = 8.1 Hz, 1H), 8.01 (d, J = Hz, 1H), 8.53 (d, J = 9 Hz, 1H), 8.63 (br. s, 1H); ¹³C NMR (CDCl₃, 300 MHz) δ 110.9, 117.8, 122.0, 122.3, 122.7, 124.3, 125.00, 125.05, 125.5, 125.8, 126.5, 126.6, 126.9, 127.1, 127.6, 127.94, 127.99, 128.03, 128.05, 128.4, 129.4, 129.5, 130.8, 132.1, 132.2, 133.0, 134.1, 135.3, 142.3, 179.9; 1 C not located; mass spectrum (FAB⁺) m/z (% rel intensity) 470 (60) [M+H]⁺, 307 (20), 284 (40); IR (neat) 3350, 2959, 1620, 1531 cm⁻¹; [α]²⁵ D +4.7 (c 1.0, dichloromethane).

bis-thiourea (R)-9: This compound was synthesized from (R)-BINAM 18 (300 mg, 1.05 mmol) according to the procedure above and isolated as a white solid (104 mg, 0.17 mmol, 17%, mp 124-125 °C) along with a 50% yield (224 mg, 0.50 mmol) of the mono-thiourea (R)-23 also as a white solid, mp 114-116 °C. Spectral data for (R)-9: ¹H NMR (CDCl₃, 300 MHz) δ 3.77 (s, 6H), 6.18 (d, 6.9 Hz, 4H), 6.47 (d, 6.9 Hz, 8H), 7.27-7.56 (m, 8H), 8.02-8.15 (m, 4H); ¹³C NMR (CDCl₃, 300 MHz) δ
55.5, 114.9, 125.2, 126.4, 127.3, 127.6, 127.9, 128.1, 128.2, 132.3, 135.9, 158.9, 180.7, 3 C’s not located; mass spectrum (FAB⁺) m/z 615 [M+H]⁺, 492, 307, 154; IR (neat) 3163, 2953, 1508, 1244, 860 cm⁻¹; [α]⁰ D +15.3 (c 1.0, acetone). Spectral data for (R)-23: ¹H NMR (CDCl₃, 300 MHz) δ 3.68 (s, 3H), 3.74 (br. s, 2H), 6.45-6.38 (m, 4H), 6.81 (d, J = 8.4 Hz, 1H), 7.15-7.09 (m, 2H), 7.29-7.22 (m, 3H), 7.37 (br. s, 1H), 7.50-7.45 (m, 1H), 7.83 (d, J = 8.7 Hz, 2H), 7.94 (d, J = 8.4 Hz, 1H), 8.02 (d, J = 9.0 Hz, 1H), 8.15 (br. s, 1H), 8.49 (d, J = 8.7 Hz, 1H); ¹³C NMR (CDCl₃, 300 MHz) δ 55.6, 111.6, 115.5, 123.3, 125.6, 125.9, 126.3, 127.0, 127.1, 127.6, 127.8, 128.3, 128.43, 128.47, 128.5, 130.0, 132.6, 132.7, 133.7, 133.8, 135.8, 143.2, 158.7, 179.9, 122.7, 118.7; IR (neat) 3350, 3184, 3055, 2961, 2837, 1620, 1531 cm⁻¹; mass spectrum (FAB⁺) m/z (% rel intensity) 450 [M+H]⁺ (98), 416 (20), 284, (100), 154 (70), 136 (50); [α]⁰ D +66.2 (c 1.0, dichloromethane).

![Chemical structure](image1)

**bis-thiourea (R)-10:** This compound was synthesized from (R)-BINAM (300 mg, 1.05 mmol) according to the above procedure and isolated as a white solid (644 mg, 1.00 mmol, 100%), mp 134-136 °C. Spectral data for (R)-10: ¹H NMR (CDCl₃, 300 MHz) δ 6.69 (d, J = 9 Hz, 4H), 7.18 (d, J = 8.7 Hz, 2H), 7.31 (t, J = 8.0 Hz, 2H), 7.53 (t, J = 8.0 Hz, 2H), 7.82 (d, J = 9 Hz, 4H), 7.98 (d, J = 8.1 Hz, 2H), 8.06 (s, 4H), 4 exchangeable H’s are not located; ¹³C NMR (CDCl₃, 300 MHz) δ 112.8, 122.1, 124.7, 126.3, 126.6, 126.9, 127.1, 127.6, 128.5, 132.3, 133.1, 136.4, 142.9, 145.9, 180.0; mass spectrum (FAB⁺) m/z 645 [M+H]⁺, 507, 460, 307, 154, 136; IR (neat) 3410, 1702, 1594, 1500, 1388, 1268 cm⁻¹; [α]⁰ D −56.7 (c 1.0, acetone).

![Chemical structure](image2)

**bis-thiourea (R)-11:** This compound was synthesized from (R)-BINAM (300 mg, 1.05 mmol) according to the above procedure and isolated as a white solid (692 mg, 1.00 mmol, 100%), mp 116-120 °C. Spectral data for (R)-11: ¹H NMR (CDCl₃, 300 MHz) δ 6.69 (d, J = 9 Hz, 4H), 7.18 (d, J = 8.7 Hz, 2H), 7.31 (t, J = 8.0 Hz, 2H), 7.53 (t, J = 8.0 Hz, 2H), 7.82 (d, J = 9 Hz, 4H), 7.98 (d, J = 8.1 Hz, 2H), 8.06 (s, 4H), 4 exchangeable H’s are not located; ¹³C NMR (CDCl₃, 300 MHz) δ 112.8, 122.1, 124.7, 126.3, 126.6, 126.9, 127.1, 127.6, 128.5, 132.3, 133.1, 136.4, 142.9, 145.9, 180.0; mass spectrum (FAB⁺) m/z 645 [M+H]⁺, 507, 460, 307, 154, 136; IR (neat) 3410, 1702, 1594, 1500, 1388, 1268 cm⁻¹; [α]⁰ D +15.3 (c 1.0, acetone).
°C. Spectral data for (R)-11: 1H NMR (CDCl₃, 300 MHz) δ 6.50 (s, 4H), 7.04-7.03 (m, 2H), 7.30-7.22 (m, 4H), 7.55-7.48 (m, 2H), 7.74 (s, 2H), 7.88 (d, J = 9Hz, 4H), 8.00 (t, J = 9 Hz, 4H), 8.57 (br. s, 2H); 13C NMR (CDCl₃, 300 MHz) δ 179.8, 137.5, 135.2, 134.9, 132.12, 132.11, 128.9, 128.5, 128.2, 127.2, 127.0, 126.6, 126.3, 125.1, 123.6; IR (neat) 3434, 1644 cm⁻¹; mass spectrum (FAB⁺) m/z (% rel intensity) 693 [M+H]⁺ (19, 3 x 35Cl, 1 x 37Cl ), 691 [M+H]⁺ (8, 4 x 35Cl), 530 (11), 154 (100), 136 (60); [α]²⁵D +106.8 (c 1.0, dichloromethane).

The Synthesis of Thiourea 5.

Preparation of (R)-N-(1-(2-Aminonaphthalen-1-yl)naphthalen-2-yl)acetamide 25. To a solution of (R)-(+)1,1'-Binaphthyl-2,2'-diamine 18 (284 mg, 1.0 mmol) and AcOH (0.6 mL, 10 mmol) in 10 mL of dried CH₂Cl₂ was added acetic anhydride (104 µL, 1.0 mmol) at 0 °C under N₂. The resulting solution was stirred overnight at room temperature, then 2N NaOH aqueous solution was added until pH ≈ 7. The reaction mixture was extracted with CH₂Cl₂ (3 x 50 mL) and the combined organic phases were washed with saturated brine and dried over MgSO₄. The solvent was removed under reduced pressure and the crude product was purified by flash chromatography (ethyl acetate/hexane = 2/1) to afford (R)-25 as a colorless oil in 77% yield (0.25 g, 0.77 mmol). Spectral data for (R)-25: 1H NMR (CDCl₃, 300 MHz) δ 1.85 (s, 3H), 6.91-7.42 (m, 8H), 7.81-8.03 (m, 4H), 8.58 (d, J = 9.0 Hz, 2H). This data agreed with that reported in the literature³.

(R)-N-(1-(2-(Dimethylamino)naphthalen-1-yl)naphthalen-2-yl)acetamide 26. N-(1-(2-Aminonaphthalen-1-yl)naphthalen-2-yl)acetamide 25 (0.25 g, 0.77 mmol) and aqueous formaldehyde (37%, 0.75 mL, 9.0 mmol) were combined in 10 mL of THF and stirred for 15 min. Then NaBH₃CN
(200 mg, 5.3 mmol) was added, followed 15 min later by AcOH (1.0 mL). The resulting solution was stirred for 4 h at room temperature and then 1N aqueous NaOH was added until pH ≈ 7. The reaction mixture was extracted with CH₂Cl₂ (3 × 50 mL) and the combined organic phases were washed with saturated brine and dried over MgSO₄. The solvent was removed under reduced pressure and the crude product was purified by flash chromatography (ethyl acetate/hexane = 1/5) to afford (R)-26 as a brown powder in quantitative yield (272 mg, 0.77 mmol). Spectral data for (R)-26: ¹H NMR (CDCl₃, 300 MHz) δ 1.88 (s, 3H), 2.58 (s, 6H), 6.95 (d, J = 8.7 Hz, 1H), 7.12-7.55 (m, 6H), 7.84-7.80 (m, 4H), 8.49 (d, J = 9.0 Hz, 1H), 1 exchangeable H not located. This data is in agreement with that reported in the literature.³.

(R)-1-(2-(Dimethylamino)naphthalen-1-yl)naphthalen-2-amine 27. To a solution of N-(1-(2-(dimethylamino)naphthalen-1-yl)naphthalen-2-yl)acetamide 26 (0.18 g, 0.51 mmol) in 15 mL of EtOH was added 4M HCl (6 mL). The resulting solution was stirred overnight at room temperature and then 1N aqueous NaOH was added until pH ≈ 7. The reaction mixture was extracted with CH₂Cl₂ (3 × 50 mL) and the combined organic phase was washed with saturated brine and dried over MgSO₄. The solvent was removed under reduced pressure and the crude product was purified by flash chromatography (ethyl acetate/hexane = 1/10) to afford (R)-27 as a colorless oil in 93% yield (148 mg, 0.47 mmol). Spectral data for (R)-27: ¹H NMR (CDCl₃, 300 MHz) δ 2.59 (s, 2Me), 7.0-7.29 (m, 7H), 7.47 (d, J = 9.0 Hz, 1H), 7.74-7.91 (m, 4H).

(R)-1-(3,5-Bis(trifluoromethyl)phenyl)-3-(1-(2-(dimethylamino)naphthalen-1-yl)naphthalen-2-yl)thiourea 5. To a solution of 1-(2-(dimethylamino)naphthalen-1-yl)naphthalen-2-amine 27 (36 mg, 0.12 mmol) in 2 mL of dried CH₂Cl₂ was added 3,5-bis(trifluoromethyl)phenyl isothiocyanate (22 mg,
0.132 mmol) at 0 °C under N₂. The resulting solution was stirred overnight at room temperature. The reaction was concentrated in vacuo and the product was purified by flash chromatography on silica gel (ethylacetate/hexane = 1/10) to afford (R)-5 as a light yellow solid in 91% yield (64 mg, 0.11 mmol).

Spectral data for (R)-5: ¹H NMR (300 MHz, CDCl₃) δ 2.59 (s, 6H), 6.90 (d, 1H, J = 7.5 Hz), 7.09 (t, 1H, J = 7.5 Hz), 7.26 (m, 2H), 7.36 (s, 2H), 7.41 (s, 1H), 7.56-7.50 (m, 4H), 7.71 (d, 1H, J = 8.5 Hz), 7.82 (d, 2H, J = 9.0 Hz), 8.06 (d, 1H, J = 8.5 Hz), 8.37 (s, 1H); mass spectrum (FAB⁺) m/z (% rel intensity) 355 (100), 252 (30), 157 (37), 140 (47), 123 (37), 73 (60). These data are in agreement with that reported for this compound.

General procedure for the synthesis of aminosulfones 28 and Boc-imines 14.

The appropriate aldehyde (1.20 equiv 20.48 mmol) was added to a mixture of 1 equiv (2.00 g, 17.07 mmol) of NH₂Boc and 2.0 equiv (5.6 g, 34.1 mmol) of PhSO₂Na (TolSO₂Na in the case of 28f and 28g) in 50 mL of water and MeOH (2:1 v/v) and stirred at rt for 3 days. After this time the resultant white suspension was filtered, washed with water and diethyl ether and then triturated with diethyl ether overnight. The product 28 was dried under vacuum.

Subsequently 1 equiv of 28 (2 mmol) was refluxed in THF for an overnight period in the presence of 1.60 g (12 mmol) of K₂CO₃ and ~2 g Na₂SO₄ (drying agent). The resulting mixture was filtered through a clean white fritted funnel through Celite and the volatiles were evaporated. The resulting imine was transferred carefully under nitrogen to a dry flask dried under high vacuum. Cautious handling of the imine is required to prevent decomposition and/or hydrolysis. The imines were used in the aza-Henry reaction without further purification. Imines 14a, e-f and h-j have previously been described in the literature.

N-(tert-butoxycarbonyl)-α-(phenylsulfonyl)benzylamine 28a. This compound was synthesized from 2.00 g (17.07 mmol) of NH₂Boc to afford 5.89 g (17 mmol, 100%) of 28a as a white solid.
Spectral data for 28a: $^1$H NMR (300 MHz, CDCl$_3$) $\delta$ 1.24 (9H, s), 5.72 (1H, br d, $J = 10.3$ Hz), 7.49-7.38 (5H, m), 5.90 (1H, br d, $J = 11.0$ Hz), 7.52 (2H, m), 7.62-7.60 (1H, m), 7.89 (2H, d, $J = 7.3$ Hz).

$N$-(tert-butoxycarbonyl)-$\alpha$-(phenylsulfonyl)-4-chlorobenzylamine 28b. This compound was synthesized from 2.00 g (17.07 mmol) of NH$_2$Boc to afford 1.48 g (3.91 mmol, 23%) of 28b as a white solid. Spectral data for 28b: $^1$H NMR (300 MHz, CDCl$_3$) $\delta$ 1.25 (9H, s), 5.63 (1H, br d, $J = 10.1$ Hz), 5.86 (1H, br d, $J = 10.1$ Hz), 7.36 (4H, s), 7.52 (2H, t, $J = 7.8$ Hz), 7.63 (1H, t, $J = 7.5$ Hz), 7.88 (2H, d, $J = 8.4$ Hz).

$N$-(tert-butoxycarbonyl)-$\alpha$-(phenylsulfonyl)-3-chlorobenzylamine 28c. This compound was synthesized from 2.00 g (17.07 mmol) of NH$_2$Boc to afford 4.98 g (13.9 mmol, 77%) of 28c as a white solid. Spectral data for 28c: $^1$H NMR (300 MHz, CDCl$_3$) $\delta$ 1.23 (9H, s), 5.69 (1H, br d, $J = 10.5$ Hz), 5.87 (1H, br d, $J = 10.5$ Hz), 7.32-7.41 (4H, m), 7.54 (2H, t, $J = 7.5$ Hz), 7.62 (1H, t, $J = 7.2$ Hz), 7.90 (2H, d, $J = 7.2$ Hz).

$N$-(tert-butoxycarbonyl)-$\alpha$-(phenylsulfonyl)-2-chlorobenzylamine 28d. This compound was synthesized from 2.00 g (17.07 mmol) of NH$_2$Boc to afford 4.66 g (12.24 mmol, 77%) of 28d as a white solid. Spectral data for 28d: $^1$H NMR (300 MHz, CDCl$_3$) $\delta$ 1.32 (9H, s), 5.85 (1H, br d, $J = 10.2$ Hz), 6.65 (1H, br d, $J = 10.2$ Hz), 7.37-7.48 (3H, m), 7.55-7.58 (3H, m), 7.69 (1H, t, $J = 6.9$ Hz), 7.97 (2H, d, $J = 7.5$ Hz).
**N-(tert-butoxycarbonyl)-α-(phenylsulfonyl)-4-bromobenzylamine 28e.** This compound was synthesized using 2.00 g (17.07 mmol) of NH₂Boc to afford 2.24 g (5.27 mmol, 31%) of 28e as a white solid. Spectral data for 28e: ^1^H NMR (300 MHz, CDCl₃) δ 1.25 (9H, s), 5.70 (1H, br d, J = 10.7 Hz), 5.89 (1H, br d, J = 10.7 Hz), 7.28 (2H, d, J = 8.2 Hz), 7.58-7.51 (4H, m), 7.72-7.62 (1H, m), 7.91 (2H, d, J = 7.6 Hz).

**N-(tert-butoxycarbonyl)-α-(4-methyltoluenesulfonyl)-4-methoxybenzylamine 28f.** This compound was synthesized using 2.00 g (17.07 mmol) of NH₂Boc to afford 5.83 g (14.28 mmol, 84%) of 28f as a white solid. Spectral data for 28f: ^1^H NMR (300 MHz, CDCl₃) δ 1.25 (9H, s), 2.41 (3H, s), 3.81 (3H, s), 5.79 (1H, br d, J = 10.6 Hz), 5.85 (1H, br d, J = 11.0 Hz), 6.92 (2H, d, J = 8.8 Hz), 7.31 (2H, d, J = 8.1 Hz), 7.36 (2H, d, J = 8.8 Hz), 7.78 (2H, d, J = 7.7 Hz).

**N-(tert-butoxycarbonyl)-α-(4-methyltoluenesulfonyl)-2-methoxybenzylamine 28g.** This compound was synthesized from 2.00 g (17.07 mmol) of NH₂Boc to afford 5.76 g (15.3 mmol, 90%) of 28g as a white solid, mp 160-162 °C. Spectral data for 28g: ^1^H NMR (300 MHz, CDCl₃) δ 1.28 (9H, s), 2.37 (3H, s), 3.70 (3H, s), 6.16-6.27 (2H, m), 6.84 (1H, d, J = 8.1 Hz), 6.96 (1H, t, J = 7.2 Hz), 7.22-7.35 (4H, m), 7.68 (1H, d, J = 8.1 Hz), NH not located; ^1^C NMR (300 MHz, CDCl₃) δ 21.6, 28.1, 55.9, 71.1, 80.8, 111.5, 118.9, 120.9, 129.4, 129.5, 130.3, 131.1, 134.6, 144.6, 154.5, 157.9; IR (CHCl₃) 3344, 2978, 2358, 1704, 1493, 1141; mass spectrum (FAB⁺) m/z (% rel intensity) 307 (10), 236 (100), 180 (100), 136 (90).
N-(tert-butoxycarbonyl)-α-(phenylsulfonyl)-4-methylbenzylamine 28h. This compound was synthesized using 2.00 g (17.07 mmol) of NH₂Boc to afford 4.54 g (12.58 mmol, 74%) of 28h as a white solid. Spectral data for 28h: ¹H NMR (300 MHz, CDCl₃) δ 1.28 (9H, s), 2.40 (3H, s), 5.77 (1H, d, J = 10.6 Hz), 5.90 (1H, br d, J = 10.6 Hz), 7.27 (2H, d, J = 8.0 Hz), 7.34 (2H, d, J = 7.7 Hz), 7.53 (2H, t, J = 7.6 Hz), 7.64 (1H, t, J = 7.0 Hz), 7.93 (2H, d, J = Hz).

N-(tert-butoxycarbonyl)-α-(phenylsulfonyl)-C-naphthalen-1-yl-methylamine 28i. This compound was synthesized from 2.00 g (17.07 mmol) of NH₂Boc to afford 3.98 g (10.03 mmol, 59%) of 28i as a white solid. Spectral data for 28i: ¹H NMR (300 MHz, CDCl₃) δ 1.27 (9H, s), 5.98 (1H, br d, J = 10.6 Hz), 6.88 (1H, br d, J = 10.6 Hz), 7.66-7.48 (6H, m), 7.79 (1H, d, J = 7.0 Hz), 7.88 (1H, d, J = 8.1 Hz), 7.94 (1H, d, J = 8.1 Hz,), 7.99 (2H, d, J = 7.7 Hz), 8.14 (1H, d, J = 8.4 Hz).

N-(tert-butoxycarbonyl)-α-(phenylsulfonyl)-C-pyridin-3-yl-methylamine 28j. This compound was synthesized from 2.00 g (17.07 mmol) of NH₂Boc to afford 4.02 g (11.56 mmol, 68%) of 28j as a white solid. Spectral data for ¹H NMR (300 MHz, CDCl₃) δ 1.25 (9H, s), 5.97 (2H, br), 7.39-7.35 (1H, m), 7.57 (2H, t, J = 7.5 Hz), 7.68 (1H, t, J = 7.0 Hz), 7.86-7.83 (1H, m), 7.92 (2H, d, J = 8.3 Hz), 8.70-8.63 (2H, m).
Benzaldehyde N-(tert-butoxycarbonyl)imine 14a. This compound was synthesized from 5.89 g (17 mmol) of 28a to afford 4.40 g (16.66 mmol, 98%) of 14a as a colorless liquid. Spectral data for 14a: $^1$H NMR (300 MHz, CDCl$_3$) $\delta$ 1.59 (9H, s), 7.49-7.43 (2H, m), 7.57-7.54 (1H, m), 7.93-7.90 (2H, m), 8.88 (1H, s).

$p$-Chlorobenzaldehyde N-(tert-butoxycarbonyl)imine 14b. This compound was synthesized from 1.48 g (3.91 mmol) of 28b to afford 0.91 g (3.83 mmol, 98%) of 14b as a colorless liquid. Spectral data for 14b: $^1$H NMR (300 MHz, CDCl$_3$) $\delta$ 1.57 (9H, s), 7.42 (2H, d, $J = 8.4$ Hz), 7.85 (2H, d, $J = 8.4$ Hz), 8.81 (1H, s).

$m$-Chlorobenzaldehyde N-(tert-butoxycarbonyl)imine 14c. This compound was synthesized from 4.98 g (13.9 mmol) of 28c to afford 3.32 g (13.76, 99%) 14c as a clear oil. $^1$H-NMR (300 MHz, CDCl$_3$): $\delta$ = 1.56 (9H, s) 7.39 (1H, t, $J = 7.5$ Hz), 7.48-7.52 (1 H, m), 7.73 (1H, dd, $J = 1.2$ Hz, $J = 7.5$ Hz), 8.77 (1H, s), 7.93 (1H, s).

$o$-Chlorobenzaldehyde N-(tert-butoxycarbonyl)imine 14d. This compound was synthesized from 4.66 g (12.24 mmol) of 28d to afford 2.86 g (11.99 mmol, 99%) 14d as a clear oil. Spectral data
for 14d: $^1$H NMR (300 MHz, CDCl$_3$) δ 1.63 (9H, s), 7.37 (1H, t, $J = 6.0$ Hz), 7.47-7.50 (2H, m), 8.22 (1H, d, $J = 6.0$ Hz), 9.31 (1H, s).

$p$-Bromobenzaldehyde $N$-($\text{ tert-butoxycarbonyl}$)imine 14e. This compound was synthesized from 2.24 g (5.27 mmol) of 28e to afford 0.95 g (3.37 mmol, 64%) 14e as a white solid. Spectral data for $^1$H NMR (300 MHz, CDCl$_3$) δ 1.57 (9H, s), 7.60 (2H, d, $J = 8.4$ Hz), 7.77 (2H, d, $J = 8.4$ Hz), 8.81 (1H, s).

$p$-Methoxybenzaldehyde $N$-($\text{ tert-butoxycarbonyl}$)imine 14f. This compound was synthesized using 5.83 g (14.28 mmol) of 28f to afford 2.58 g (10.99 mmol, 77%) 14f as a clear oil. Spectral data for 14f: $^1$H NMR (300 MHz, CDCl$_3$) δ 1.56 (9H, s), 3.86 (3H, s), 6.96 (2H, d, $J = 8.8$ Hz), 7.88 (2H, d, $J = 8.8$ Hz), 8.88 (1H, s).

$o$-Methoxybenzaldehyde $N$-($\text{ tert-butoxycarbonyl}$)imine 14g. This compound was synthesized from 5.76 g (15.3 mmol) of 28g to afford 3.41 g (14.53 mmol, 95%) 14g as a clear oil. Spectral data for 14g: $^1$H NMR (300 MHz, CDCl$_3$) δ 1.56 (9H, s), 3.88 (3H, s), 6.90-7.00 (2H, m), 7.49 (1H, t, $J = 9.0$ Hz), 8.09 (1H, d, $J = 7.8$ Hz), 9.35 (1H, s); $^{13}$C NMR (300 MHz, CDCl$_3$) δ 27.9, 55.6, 81.9, 111.27, 120.77, 122.6, 128.3, 135.2, 160.9, 165.8, 163.2; IR (CHCl$_3$) 2978, 1711, 1600, 1237, 1153 cm$^{-1}$; mass spectrum (FAB$^+$) m/z (% rel intensity) 236 [M+H]$^+$ (60), 180 (100), 136 (95).
p-Tolualdehyde \(N\)-(tert-butoxycarbonyl)imine 14h. This compound was synthesized from 4.54 g (12.58 mmol) of 28h to afford 2.67 g (12.20 mmol, 97%) 14h as a white solid. Spectral data for 14h: \(^1H\) NMR (300 MHz, CDCl\(_3\)) \(\delta\) 1.58 (9H, s), 2.41 (3H, s), 7.26 (2H, \(d, J = 7.7 \text{ Hz}\)), 7.81 (2H, \(d, J = 8.1 \text{ Hz}\)), 8.87 (1H, s).

1-Naphthaldehyde \(N\)-(tert-butoxycarbonyl)imine 14i. This compound was synthesized from 3.98 g (10.03 mmol) of 28i to afford 2.55 g (10.00 mmol, 99%) 14i as a white solid. Spectral data for 14i: \(^1H\) NMR (300 MHz, CDCl\(_3\)) \(\delta\) 1.61 (9H, s), 7.60-7.54 (2H, m), 7.68-7.63 (1H, m), 7.90 (1H, \(d, J = 7.7 \text{ Hz}\)), 8.05 (1H, \(d, J = 8.4 \text{ Hz}\)), 8.17 (1H, \(d, J = 7.0 \text{ Hz}\)), 8.92 (1H, \(d, J = 8.4 \text{ Hz}\)), 9.53 (1H, s).

3-pyridinecarboxaldehyde \(N\)-(tert-butoxycarbonyl)imine 14j. This compound was synthesized from 4.02 g (11.56 mmol) of 28j to afford 2.32 g 14j (11.3 mmol, 98%) as a clear oil. Spectral data for 14j: \(^1H\) NMR (300 MHz, CDCl\(_3\)) \(\delta\) 1.58 (9H, s), 7.40 (1H, \(dd, J = 4.8, 8.1 \text{ Hz}\)), 8.25-8.28 (1H, dt, \(J = 1.8, 8.1 \text{ Hz}\)), 8.76 (1H, \(dd, J = 1.83, 4.8 \text{ Hz}\)), 8.87 (1H, s), 9.00 (1H, \(d, J = 2.2 \text{ Hz}\)).
General procedure for the asymmetric aza-Henry reaction (Table 3).

A flame-dried round bottom flask was loaded with 0.2 equiv. of catalyst 12 (0.2 mmol, 160 mg) and 1 equiv of imine 14a-j (1 mmol). The solid mixture was dissolved in 4 mL of toluene and then RCH$_2$NO$_2$ (10 equiv., 0.52 mL) was added at –35 °C. After 5 minutes, Et$_3$N (0.4 equiv, 56 µL) was added and then the mixture was stirred at –35 °C for 17-36 hours. The volatiles were evaporated and the crude product was purified by column chromatography on silica gel (20% acetone in hexanes) to afford products 16a – 16l.

For all the optimization studies of the aza-Henry reaction detailed in Tables 1 and 2, the experimental procedure is the same with slight modifications that are indicated in each Table. Whenever a % conversion is mentioned, this means the product was not purified, and the % conversion was determined from the $^1$H NMR spectrum of the crude reaction mixture by integration of product peaks versus the C(=N)H proton if the imine. The only species observed in the crude $^1$H NMR spectrum of the crude reaction mixture was the catalyst, the desired product and the starting imine.

** tert-Butyl (R)-2-nitro-1-phenylethylcarbamate 16a. ** According to the general procedure, imine 14a (1.00 mmol, 205 mg) and MeNO$_2$ were stirred for 36 h and the product 16a was isolated in 55% yield (146 mg, 0.55 mmol) as a white solid, mp 107-108 °C. The % ee was determined to be 86% by HPLC analysis (Chiralpak OJ-H, hexane/2-PrOH 95/5, flow rate = 1.0 mL/min, l = 210 nm): t$_r$ (minor) = 32.3, t$_r$ (major) = 36.8 min. Spectral data for (R)-16a: $^1$H NMR (300 MHz, CDCl$_3$) δ 1.40 (s, 9H), 4.64–4.81 (m, 2 H), 4.80 (br s, 1H), 5.34 (br s, 1 H), 7.37-7.23 (m, 5 H); $^{13}$C NMR (300 MHz, CDCl$_3$) δ 28.3, 52.9, 78.9, 80.7, 126.4, 128.7, 129.2, 137.0, 154.9; [α]$^D_{25}$ –18.0 (c 1.0, CHCl$_3$) on 86% ee material

Johnston’s group$^8$ reported that the (R)-configuration of 16a has a negative optical rotation, while Takemoto’s group$^6$ assigned the same absolute configuration (R) to 16a with a positive optical rotation. Both groups made their assignments on the basis of a chemical correlation with the same chemical compound. Takemoto’s group appears to have made an error in translating the sign of the
optical rotation from the original literature. On the basis of the assignment made by the Johnston group for the adduct 16a, the rest of the aza-Henry adducts in this work were assumed to occur with the same face selectivity of addition to the imine as observed for imine 14a. For references to others who have characterized this compound, see references 5, 7, 10-13.

\[ \text{[R]-16b} \]

**1-(p-Chlorophenyl)-2-nitroethyl carbamic acid t-butyl ester 16b.** Following the general procedure, 239 mg (1.00 mmol) of imine 14b was reacted to give compound 16b as a white solid in 62% yield (0.62 mmol, 182 mg) after chromatographic purification. The ee of the product was determined to be 85% by HPLC using a Daicel Chiralpak OJ-H column (n-hexane/i-PrOH = 97/3, flow rate = 1.0 mL/min, t_r (minor) = 68.6 min; t_r (major) = 74.1 min. Spectral data for (R)-16b: \(^1\)H NMR (300 MHz, CDCl\(_3\)) \(\delta\) 1.47 (s, 9H), 4.72–4.90 (m, 1H), 4.73 (dd, \(J = 5.0, 12.6\) Hz, 1H), 5.40 (br s, 2H), 7.28–7.30 (m, 2H), 7.34–7.41 (m, 2H); \(^{13}\)C NMR (300 MHz, CDCl\(_3\)) \(\delta\) 28.2, 52.3, 78.7, 80.9, 127.8, 129.4, 134.6, 135.6, 154.8; \([\alpha]^{25}_D\) –44.0 (c 1.0, CHCl\(_3\)) on 85% ee material. This data is in agreement with that previously reported.\(^5,7,13\)

\[ \text{[R]-16c} \]

**1-(m-Chlorophenyl)-2-nitroethyl carbamic acid t-butyl ester 16c.** Following the general procedure, 239 mg (1.00 mmol) of imine 14c was reacted to give after chromatographic purification a 53% yield (161 mg, 0.53 mmol) of compound 16c as a white solid, mp 98-100 °C. The ee of the product was determined to be 91% by HPLC using a Daicel Chiralpak AD column (n-hexane/i-PrOH = 97/3, flow rate = 1 mL/min, t_r (minor) = 23.2 min; t_r (major) = 33.6 min. Spectral data for (R)-16c: \(^1\)H NMR (300 MHz, CDCl\(_3\)) \(\delta\) 1.46 (s, 9H), 4.80–4.90 (br s, 1H), 4.72 (m, 1H), 5.42 (br s, 1H), 5.70 (br s, 1H), 7.21–7.35 (m, 4H); \(^{13}\)C-NMR (300 MHz, CDCl\(_3\)) \(\delta\) 28.2, 52.2, 78.6, 80.9, 124.6, 126.7, 128.8, 130.4, 135.0, 139.2, 154.9; IR (neat) 3370, 2980, 1686, 1556, 1368, 1165 cm\(^{-1}\); mass spectrum (FAB\(^+\)) m/z (% rel intensity) 303 [M+H\(^+\)] (3, \(^{37}\)Cl), 301 [M+H\(^+\)] (10, \(^{35}\)Cl), 245 (90), 184 (90) 154 (82); \([\alpha]^{25}_D\) –24.4 (c 1.0, acetone) on 91% ee material.
1-(o-Chlorophenyl)-2-nitroethyl carbamic acid t-butyl ester 16d. Following the general procedure, 239 mg (1.00 mmol) of imine 14d were reacted to give after chromatographic purification a 61% yield (179 mg, 0.61 mmol) of compound 16d as a white solid, mp 106-108 °C. The ee of the product was determined to be 74% by HPLC using a Daicel Chiralpak AD column (n-hexane/i-PrOH = 99/1, flow rate = 1 mL/min, t_r (major) = 69.1 min; t_r (minor) = 92.3 min. Spectral data for (R)-16d: 1H NMR (300 MHz, CDCl_3) δ 1.47 (s, 9H), 4.84 (m, 2H), 5.78 (m, 2H), 7.31–7.46 (m, 4H); 13C NMR (300 MHz, CDCl_3) δ 28.2, 50.6, 77.5, 80.8, 127.5, 128.0, 129.9, 130.3, 132.6, 134.4, 154.6; IR (neat) 3355, 2982, 2935, 1712, 1685, 1555, 1367, 1253 cm⁻¹; mass spectrum (FAB⁺) m/z (% rel intensity) 303 [M+H]^+ (3, 37Cl), 301 [M+H]^+ (10, 35Cl), 245 (90), 184 (90) 154 (82); [α]^{25}_D +19.0 (c 1.0, acetone).

1-(p-Bromophenyl)-2-nitroethyl carbamic acid t-butyl ester 16e. Following the general procedure, the reaction of imine 14e gave after chromatographic purification a 50% yield (172 mg, 0.50 mmol) of compound 16e as a white solid, mp 140-142 °C. The ee of the product was determined to be 78% by HPLC using a Daicel Chiralpak OJ-H column (n-hexane/i-PrOH = 95/5, flow rate = 1.0 mL/min, t_r (minor) = 51.1 min; t_r (major) = 54.9 min). Spectral data for (R)-16e: 1H NMR (300 MHz, CDCl_3) δ 1.47 (s, 9H), 4.75 (m, 1H), 4.76–4.90 (br s, 1H), 5.40 (br s, 2H), 7.23 (d, J = 6.9 Hz, 2H), 7.53 (d, J = 6.9 Hz, 2H); 13C NMR (300 MHz, CDCl_3) δ 28.2, 52.2, 78.6, 80.9, 122.7, 128.1, 132.3, 136.1, 154.7; IR (neat) 3338, 2981, 2935, 2363, 1687, 1527, 1166 cm⁻¹; mass spectrum (FAB⁺) m/z (% rel intensity) 347 [M+H]^+ (10, 81Br), 345 [M+H]^+ (10, 79Br), 289 (60), 228 (65), 154 (100).

tert-Butyl (R)-2-nitro-1-(p-methoxyphenyl)ethylcarbamate 16f. According to the general procedure, 235 mg (1.00 mmol) of imine 14f was reacted and after chromatographic purification the
product 16f was obtained in 50% yield (145 mg, 0.49 mmol) as a white solid. The % ee was determined to be 89% by HPLC analysis (Chiralpak OJ-H, hexane/EtOH 95/5, flow rate = 1.0 mL/min, l = 210 nm): t<sub>r</sub> (minor) = 65.8, t<sub>r</sub> (major) = 72.0 min. Spectral data for (R)-16f: <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>) δ 1.47 (s, 9H), 3.82 (s, 3 H), 4.69 (dd, <sup>J</sup> = 12.0, 5.3 Hz, 1 H), 5.36 (m, 1H), 4.83 (s, 1H), 5.42 (s, 1 H), 6.92 (d, <sup>J</sup> = 8.6 Hz, 2 H), 7.25 (d, <sup>J</sup> = 8.6 Hz, 2H); <sup>13</sup>C NMR (300 MHz, CDCl<sub>3</sub>) δ 28.3, 52.4, 55.3, 78.9, 80.6, 114.5, 127.7, 129.0, 154.9, 159.8; [a]<sub>25</sub><sup>D</sup> –31.0 (c 1.00, CHCl<sub>3</sub>) on 89% ee material. These data are in agreement with those previously reported.<sup>5-7, 11-13</sup>

![Image of (R)-16g]

**tert-Butyl (R)-2-nitro-1-(o-methoxyphenyl)ethylcarbamate 16g.** According to the general procedure, 235 mg (1 mmol) of imine 14g was reacted to give after chromatographic purification a 40% yield (116 mg, 0.40 mmol) of the product 16g as a white solid, mp 138-140 °C. The % ee was determined to be 65% by HPLC analysis (Chiralpak OJ-H, hexane/2-PrOH = 90/10, flow rate = 1.0 mL/min): t<sub>r</sub> (major) = 17.2 min, t<sub>r</sub> (minor) = 20.8 min. Spectral data for (R)-16g: <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>) δ 1.48 (s, 9H), 2.37 (s, 3H), 4.70 (dd, <sup>J</sup> = 12.4, 5.7 Hz, 1H), 4.83 (s, 1H), 5.40 (br s, 1 H), 5.55 (m, 1H), 7.22 (s, 4 H); <sup>13</sup>C NMR (300 MHz, CDCl<sub>3</sub>) δ 28.3, 51.0, 55.5, 77.9, 80.3, 111.0, 121.19, 124.4, 129.1, 130.9, 154.8, 156.8; IR (neat) 3433, 2358, 2105, 1646 cm<sup>-1</sup>; mass spectrum (FAB<sup>+</sup>) m/z (% rel intensity) 297 [M+H]<sup>+</sup> (5), 252 (100), 140 (100).

![Image of (R)-16h]

**tert-Butyl (R)-2-nitro-1-(4-methylphenyl)ethylcarbamate 16h.** According to the typical procedure, 219 mg (1.00 mmol) of imine 14h was reacted and after chromatographic purification the product 16h was obtained in 48% yield (134 mg) as a white solid. The % ee was determined to be 86% by HPLC analysis (Chiralpak AD, hexane/2-PrOH 98/2, flow rate = 1.0 mL/min, l = 210 nm): t<sub>r</sub> (minor) = 50.5, t<sub>r</sub> (major) = 59.0 min. Spectral data for (R)-16h: <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>) δ 1.48 (s, 9H), 2.37 (s, 3H), 4.70 (dd, <sup>J</sup> = 12.4, 5.7 Hz, 1H), 4.83 (s, 1H), 5.40 (br s, 1 H), 5.55 (m, 1H), 7.22 (s, 4 H); <sup>13</sup>C NMR (300 MHz, CDCl<sub>3</sub>) δ 21.1, 28.3, 52.7, 79.0, 80.5, 126.3, 129.8, 133.1, 138.5, 154.9; [a]<sub>25</sub><sup>D</sup> –26.0 (c 1.00, CHCl<sub>3</sub>) on 86% ee material. These data are in agreement with those previously reported.<sup>6,7</sup>
tert-Butyl (R)-2-nitro-1-(1-naphthyl)ethylcarbamate 16i. According to the general procedure, 255 mg (1 mmol) of imine 14i was reacted and after chromatographic purification the product 16i was obtained in 65% yield (165 mg, 0.65 mmol) as a white solid. The % ee was determined to be 85% by HPLC analysis (Chiralpak OJ-H, hexane/2-PrOH 95/5, flow rate = 1.0 mL/min, l = 210 nm): tₘ (minor) = 35.9, tₘ (major) = 50.7 min. Spectral data for (R)-16i: ¹H NMR (300 MHz, CDCl₃) δ 1.43 (s, 9H), 4.88 (br s, 2 H), 5.25 (m, 2H), 7.45 (m, 2H), 7.54 (t, J = 7.5 Hz, 1 H), 7.61 (t, J = 7.3 Hz, 1H), 7.84 (dd, J = 5.7, 3.5 Hz, 1H), 7.90 (d, J = 8.2 Hz, 1 H), 8.12 (d, J = 8.2 Hz, 1H); ¹³C NMR (300 MHz, CDCl₃) δ 28.3, 49.3, 78.3, 81.0, 123.8, 133.1, 134.2, 148.1, 149.9, 154.7; [α]²⁵_D –8.1 (c 0.5, CHCl₃) on 85% ee material. These data are in agreement with those previously reported⁵⁻⁷,₁²,₁³.

tert-Butyl (R)-2-nitro-1-(3-pyridyl)ethylcarbamate 16j. According to the general procedure, 206 mg (1.00 mmol) of imine 14j was reacted and after chromatographic purification the product 16j was obtained in 63% yield (168 mg, 0.63 mmol) as a white solid. The % ee was determined to be 81% by HPLC analysis (Chiralpak AD, hexane/2-PrOH 90/10, flow rate = 1.0 mL/min, l = 210 nm): tₘ (major) = 16.7, tₘ (minor) = 17.9 min. Spectral data for (R)-16j: ¹H NMR (300 MHz, CDCl₃) δ 1.42 (s, 9H), 4.76 (d, J=8.9 Hz, 1H), 4.90 (s, 1 H), 5.40 (s, 2H), 7.32 (dd, J = 7.5, 4.7 Hz, 1 H), 7.65 (d, J = 7.9 Hz, 1H), 8.62 (d, J = 21.4 Hz, 2H); ¹³C-NMR (300 MHz, CDCl₃) δ 28.2, 50.7, 78.3, 81.0, 123.8, 133.1, 134.2, 148.1, 149.9, 154.8; [α]²⁵_D –33.5 (c 1.00, acetone). These data are in agreement with those previously reported⁶ except for the sign of the optical rotation (see discussion on data for (R)-16a).
**tert-Butyl (1R,2S)-2-nitro-1-phenylpropylcarbamate 16k.** According to the general procedure, 205 mg (1 mmol) of imine 14a and excess nitroethane (10 equiv) were reacted and after chromatographic purification the product 16k was obtained in 59% yield (165 mg, 0.59 mmol) as a white solid and as a 77/23 mixture of diastereomers as determined by the $^1$H-NMR spectrum. The major diastereomer was determined to be 70% ee by chiral HPLC analysis and identification of enantiomeric pairs by UV absorption spectrum (Chiralpak AD, hexane/iPrOH 92/8, flow rate = 0.8 mL/min, $l = 210$ nm): Syn isomer: $t_r$ (minor) = 13.8 min, $t_r$ (major) 15.9 min; anti isomer: $t_r$ (major) = 17.8 min, $t_r$ (minor) = 21.8 min;). Spectral data for the syn isomer was extracted from the data of the mixture, and are in agreement with that previously reported.5,6,8,10 Spectral data for syn-(1R,2S)-16k: $^1$H NMR (300 MHz, CDCl$_3$) $\delta$ 1.40 (s, 9H), 1.50 (d, $J = 6.7$ Hz, 3H), 4.91 (br s, 1 H), 5.18 (dd, $J = 8.8$, 5.8 Hz, 1 H), 5.32 (br s, 1H), 7.18–7.24 (m, 2H), 7.37–7.34 (m, 3 H); $^{13}$C NMR (300 MHz, CDCl$_3$) $\delta$ 15.2, 28.3, 57.7, 80.0, 85.8, 126.4, 126.8, 128.7, 129.0, 136.7, 154.9.

**tert-Butyl (1R,2S)-2-nitro-1-phenylbutylcarbamate 16l.** According to the general procedure, 205 mg (1 mmol) of imine 14a was reacted with excess 1-nitropropane and after chromatographic purification the product 16l was obtained as white solid in 63% yield (185 mg, 0.62 mmol) and as an 80/20 mixture of diastereomers as determined by HPLC analysis (enantiomeric pairs were identified by comparison with a racemic sample). The % ee of major diastereomer 16l was determined to be 80% by chiral HPLC analysis (Chiralpak OJ-H, hexane/2-PrOH 97/3, flow rate = 0.8 mL/min, $l = 210$ nm); Syn isomer: $t_r$ (major) = 28.1 min, $t_r$ (minor) = 50.1 min. The spectral data for the syn-isomer was extracted by the 1H NMR spectrum of the mixture. Spectral data for syn-(1R,2S)-16l: $^1$H NMR (300 MHz, CDCl$_3$) $\delta$ 0.96–1.03 (t, $J = 3.5$ Hz, 3H), 1.43 (s, 9 H), 1.84–1.92 (m, 2H), 5.10–5.14 (m, 1 H), 4.74 (br s, 1H), 5.14–5.20 (br s, 1H), 7.22–7.26 (m, 2 H), 7.30–7.40 (m, 3 H); $^{13}$C NMR (300 MHz, CDCl$_3$) $\delta$ 10.4, 24.8, 28.2, 56.8, 80.0, 93.0, 126.9, 128.7, 129.0, 136.7, 154.9. These data are in agreement with those previously reported.5,10
References:


Appendix

Crystal Structure of bis-thiourea 13.
ORTEP for bis-thiourea 13.
S24
Table 1. Crystal data and structure refinement for 13.

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