Kinetic Resolutions of Azomethine Imines via Copper-Catalyzed [3+2] Cycloadditions

Andrés Suárez, C. Wade Downey, and Gregory C. Fu*

*Department of Chemistry, Massachusetts Institute of Technology, Cambridge, Massachusetts
02139*

Supporting Information

I. General

All air- and moisture-sensitive reactions were carried out under nitrogen in a glovebox or under argon using Schlenk techniques.

CH₂Cl₂ was purified by passage through a neutral alumina column under argon. CHCl₃ and Cy₂NMe (Aldrich) were distilled from CaH₂ prior to use. CuI (99.999%, Strem) was used as received. Ethyl propiolate (Aldrich) was distilled under vacuum.

II. Synthesis of Substrates

The yields have not been optimized.

1-Benzylidene-3-oxo-5-phenylpyrazolidin-1-ium-2-ide. Benzaldehyde (0.72 mL, 7.08 mmol) was added to a solution of 5-phenyl-3-pyrazolidinone (1.00 g, 6.17 mmol) in MeOH (2.0 mL). The mixture was stirred for 2 h at rt, and then the solvent was removed under vacuum. The residue was chromatographed on silica gel (10% MeOH/EtOAc) to afford the desired product as a white solid (1.08 g; 71%).

¹H NMR (400 MHz, CD₂Cl₂): δ 2.28 (dd, *J* = 16.8, 5.2 Hz, 1H), 3.25 (dd, *J* = 16.4, 9.6 Hz, 1H), 5.60 (dd, *J* = 9.6, 5.6 Hz, 1H), 5.89 (s, 1H), 7.38-7.51 (m, 8H), 8.25 (m, 2H).

¹³C NMR (101 MHz, CDCl₃): δ 39.5, 74.5, 127.3, 129.2, 129.6, 130.1, 130.2, 132.1, 132.4, 133.7, 138.7, 183.6.

IR (nujol): 3057, 3032, 1674, 1584, 1448, 1294, 761, 694.

HRMS (ESI): *m/z* 251.1179, [M+H]⁺ (calcd for C₁₆H₁₅N₂O: 251.1179).

Mp 202-203 °C.

1-(((5-Methyl)2-furyl)methylene)-3-oxo-5-phenylpyrazolidin-1-ium-2-ide. This was synthesized from 5-methyl-2-furaldehyde and 5-phenyl-3-pyrazolidinone following the procedure for 1-benzylidene-3-oxo-5-phenylpyrazolidin-1-ium-2-ide. Pale-yellow solid. 54% yield.

^1H NMR (400 MHz, CD_2Cl_2): δ 2.31 (s, 3H), 2.88 (dd, $J = 16.8, 6.0$ Hz, 1H), 3.30 (dd, $J = 16.8, 10.0$ Hz, 1H), 5.47 (dd, $J = 9.6, 6.0$ Hz, 1H), 6.26 (d, $J = 3.2$ Hz, 1H), 6.82 (s, 1H), 7.32-7.43 (m, 5H), 7.89 (d, $J = 3.2$ Hz, 1H).

^{13}C NMR (101 MHz, CDCl_3): δ 14.1, 40.0, 72.3, 111.0, 122.0, 123.7, 127.2, 129.8, 129.9, 138.1, 144.9, 157.8, 182.6.

IR (nujol): 3091, 1674, 1595, 1519, 1460, 1302, 823, 697, 679.

HRMS (ESI): m/z 255.1131, $[\text{M}+\text{H}]^+$ (calcd for $\text{C}_{15}\text{H}_{15}\text{N}_2\text{O}_2$: 255.1128).

Mp 195-197 °C.

1-(((1-Methyl)pyrrol-2-yl)methylene)-3-oxo-5-phenylpyrazolidin-1-ium-2-ide. *N*-Methyl-2-pyrrolicarboxaldehyde (0.21 mL, 2.06 mmol) was added to a solution of 5-phenyl-3-pyrazolidinone (303 mg, 1.87 mmol) in MeOH (7.0 mL). The mixture was heated at 70 °C for 48 h. The solvent was then removed under vacuum, and the residue was chromatographed on silica gel (10% MeOH/EtOAc) and then recrystallized (MeOH/EtOAc). The desired product was obtained as a pale-pink microcrystalline solid (356 mg; 75%).

^1H NMR (400 MHz, CDCl_3): δ 2.82 (dd, $J = 16.8, 6.0$ Hz, 1H), 3.22 (dd, $J = 16.4, 10.0$ Hz, 1H), 3.55 (s, 3H), 5.47 (dd, $J = 9.6, 6.0$ Hz, 1H), 6.33 (dd, $J = 3.6, 2.4$ Hz, 1H), 6.73 (s, 1H), 6.84 (dd, $J = 2.0, 2.0$ Hz, 1H), 7.32-7.36 (m, 2H), 7.39-7.45 (m, 3H), 7.98 (dd, $J = 4.0, 1.6$ Hz, 1H).

^{13}C NMR (101 MHz, CDCl_3): δ 34.7, 40.5, 72.5, 111.2, 122.4, 122.8, 124.7, 127.2, 129.8, 130.1, 130.3, 139.2, 182.5.

IR (nujol): 3114, 3100, 1646, 1603, 1420, 1329, 1245, 759, 679.

HRMS (ESI): m/z 254.1291, $[\text{M}+\text{H}]^+$ (calcd for $\text{C}_{15}\text{H}_{16}\text{N}_3\text{O}$: 254.1288).

Mp 219 °C (dec.).

1-(Cyclohex-1-enylmethylene)-3-oxo-5-phenylpyrazolidin-1-ium-2-ide. This was synthesized from 1-cyclohexene-1-carboxaldehyde and 5-phenyl-3-pyrazolidinone following the procedure for 1-benzylidene-3-oxo-5-phenylpyrazolidin-1-ium-2-ide. White solid. 55% yield.

^1H NMR (400 MHz, CD_2Cl_2): δ 1.58 (m, 4H), 2.21 (m, 2H), 2.51 (m, 2H), 2.71 (dd, J = 16.4, 5.6 Hz, 1H), 3.17 (dd, J = 16.8, 10.0 Hz, 1H), 5.37 (dd, J = 9.6, 5.2 Hz, 1H), 6.27 (s, 1H), 6.99 (s, 1H), 7.27-7.29 (m, 2H), 7.34-7.41 (m, 3H).

^{13}C NMR (101 MHz, CDCl_3): δ 21.2, 22.2, 26.9, 27.8, 39.3, 73.4, 126.8, 129.5, 129.7, 131.0, 136.6, 138.7, 144.9, 182.7.

IR (nujol): 3051, 3032, 1661, 1644, 1580, 1458, 1430, 1327, 1307, 702, 682.

HRMS (ESI): m/z 255.1495, $[\text{M}+\text{H}]^+$ (calcd for $\text{C}_{16}\text{H}_{19}\text{N}_2\text{O}$: 255.1492).

Mp 183 °C (dec.).

1-(Cyclohexylmethylene)-3-oxo-5-phenylpyrazolidin-1-ium-2-ide. This was synthesized from cyclohexanecarboxaldehyde and 5-phenyl-3-pyrazolidinone following the procedure for 1-benzylidene-3-oxo-5-phenylpyrazolidin-1-ium-2-ide, except that the product was purified by recrystallization from MeOH/EtOAc. White solid. 42% yield.

^1H NMR (400 MHz, CD_2Cl_2): δ 1.05-1.43 (m, 5H), 1.66-2.02 (m, 5H), 2.70 (dd, J = 16.8, 5.6 Hz, 1H), 3.09 (m, 1H), 3.18 (dd, J = 16.8, 10.0 Hz, 1H), 5.37 (dd, J = 10.0, 5.6 Hz, 1H), 6.12 (dd, J = 7.6, 0.8 Hz, 1H), 7.28-7.31 (m, 2H), 7.39-7.46 (m, 3H).

^{13}C NMR (101 MHz, CD_2Cl_2): δ 25.4, 25.5, 26.1, 28.4, 29.0, 38.5, 40.5, 72.5, 127.1, 129.8, 130.0, 139.3, 144.2, 181.7.

IR (nujol): 3034, 1670, 1600, 1458, 1335, 1296, 766, 698, 687.

HRMS (ESI): m/z 257.1652, $[\text{M}+\text{H}]^+$ (calcd for $\text{C}_{16}\text{H}_{21}\text{N}_2\text{O}$: 257.1648).

Mp 154 °C.

1-Benzylidene-3-oxo-5-(3-bromophenyl)pyrazolidin-1-ium-2-ide. Benzaldehyde (0.380 mL, 3.74 mmol) was added to a solution of 5-(3-bromophenyl)-3-pyrazolidinone (1.21 g, 3.74 mmol) in MeOH (3 mL). The mixture was stirred at reflux for 15 min, by which time a solid had precipitated. The mixture was cooled, and the pale-yellow solid was isolated by filtration. The solid was chromatographed on silica gel (10% MeOH/CH₂Cl₂), then precipitated from CH₂Cl₂ with diethyl ether to provide the product as a pale-yellow powder (589 mg; 48%).

¹H NMR (500 MHz, CDCl₃): δ 2.86 (dd, *J* = 5.3, 16.9 Hz, 1H), 3.36 (dd, *J* = 10.0, 16.9 Hz, 1H), 5.54 (dd, *J* = 5.1, 9.7 Hz, 1H), 6.88 (s, 1H), 7.30-7.38 (m, 2H), 7.46-7.62 (m, 5H), 8.31 (dd, *J* = 1.4, 7.4 Hz, 2H).

¹³C NMR (101 MHz, CDCl₃): δ 39.4, 73.8, 124.1, 125.6, 129.3, 129.5, 130.4, 131.9, 132.2, 132.6, 133.3, 133.7, 140.9, 183.1.

IR (film): 1673, 1588, 1567, 1451, 1293, 1089, 688, 669.

MS (EI): *m/z* 327.0127, [M-H]⁺ (calcd for C₁₆H₁₂BrN₂O: 327.0206).

Mp 245 °C (dec.).

1-Benzylidene-3-oxo-5-(2-thienyl)pyrazolidin-1-ium-2-ide. Benzaldehyde (1.00 mL, 9.89 mmol) was added to a solution of 5-(2-thiophenyl)-3-pyrazolidinone (1.70 g, 10.1 mmol) in MeOH (10 mL), and the resulting mixture was stirred for 20 h. The solvent was then removed under vacuum, and the residue was chromatographed on silica gel (10% MeOH/CH₂Cl₂). The yellow solid was ground to a fine powder and washed with acetone, then dried in vacuo (1.82 g; 70%).

¹H NMR (500 MHz, CDCl₃): δ 3.05 (dd, *J* = 16.8, 6.7 Hz, 1H), 3.36 (dd, *J* = 16.8, 9.8 Hz, 1H), 5.85 (dd, *J* = 9.2, 7.0 Hz, 1H), 7.00 (s, 1H), 7.09 (dd, *J* = 3.4, 4.9 Hz, 1H), 7.26-7.30 (m, 2H), 7.44-7.50 (m, 3H), 8.27 (dd, *J* = 1.22, 7.63 Hz, 2H).

¹³C NMR (101 MHz, CDCl₃): δ 39.7, 69.6, 128.0, 128.4, 129.2, 129.4, 132.2, 132.5, 133.3, 139.8, 182.7.

IR (nujol): 1666, 1590, 1568, 1451, 1294, 1082, 711, 679.

MS (EI): *m/z* 256.06, [M]⁺ (calcd for C₁₄H₁₂N₂OS: 256.067).

Mp 189 °C (dec.).

1-Benzylidene-3-oxo-5-isopropylpyrazolidin-1-ium-2-ide. Benzaldehyde (0.420 mL, 4.13 mmol) was added to a solution of 5-isopropyl-3-pyrazolidinone (501 mg, 3.93 mmol) in MeOH (2 mL), and the resulting mixture was stirred for 20 h. The solvent was then removed under vacuum, and the residue was chromatographed on silica gel (3% MeOH/CH₂Cl₂). The resulting pale-yellow solid was crystallized from Et₂O/CH₂Cl₂ (715 mg; 80%).

¹H NMR (500 MHz, CDCl₃): δ 0.92 (d, *J* = 6.7 Hz, 3H), 1.09 (d, *J* = 7.0 Hz, 3H), 2.30-2.41 (m, 1H), 2.56 (dd, *J* = 4.0, 16.8 Hz, 1H), 2.81 (dd, *J* = 9.5, 16.8 Hz, 1H), 4.61 (dt, *J* = 4.0, 9.8 Hz, 1H), 7.08 (s, 1H), 7.46-7.52 (m, 3H), 8.32-8.37 (m, 2H).

¹³C NMR (101 MHz, CDCl₃): δ 14.9, 19.3, 31.1, 33.4, 75.6, 129.2, 129.7, 132.1, 132.2, 184.5.

IR (film): 2964, 1676, 1655, 1588, 1452, 1297, 1101, 683.

HRMS (ESI): *m/z* 217.1337, [M+H]⁺ (calcd for C₁₃H₁₇N₂O: 217.1335).

Mp 169 °C (dec.).

1-Benzylidene-3-oxo-5-tert-butylpyrazolidin-1-ium-2-ide. Benzaldehyde (0.227 mL, 2.23 mmol) was added to a solution of 5-tert-butyl-3-pyrazolidinone (362 mg, 2.23 mmol) in MeOH (2 mL). Diethyl ether (5 mL) was added, and the mixture was stirred for 20 h. Then, the solvent was removed under vacuum, and the residue was chromatographed on silica gel (10% MeOH/CH₂Cl₂) and then precipitated from Et₂O/CH₂Cl₂. White microcrystalline solid (324 mg; 58%).

¹H NMR (500 MHz, CDCl₃): δ 1.07 (s, 9H), 2.62 (d, *J* = 16.5 Hz, 1H), 2.90 (dd, *J* = 8.9, 16.5 Hz, 1H), 4.36 (d, *J* = 8.9 Hz, 1H), 7.14 (s, 1H), 7.44-7.51 (m, 3H), 8.32-8.38 (m, 2H).

¹³C NMR (101 MHz, CDCl₃): δ 26.6, 34.3, 36.0, 80.8, 129.3, 132.4, 132.5, 135.2, 184.6.

IR (film): 1674, 1655, 1588, 1453, 1296, 1283, 1091, 684.

HRMS (ESI): *m/z* 231.1494, [M+H]⁺ (calcd for C₁₄H₁₉N₂O: 231.1492).

Mp 248 °C (dec.).

III. Kinetic Resolutions

General Procedure. A solution of CuI (1.5 mg, 8.0 μ mol) and ligand **3** (3.9 mg, 8.8 μ mol) in CH₂Cl₂ (2.0 mL) was stirred for 1 h, at which time the CuI had completely dissolved. A portion (1.0 mL) of this solution was filtered through an acrodisc and added to a mixture of the azomethine imine (0.40 mmol) and Cy₂NMe (42.8 μ L, 0.20 mmol) in CH₂Cl₂ (1.0 mL). The alkyne (0.20-0.24 mmol) was added, and then the resulting solution was stirred for 12 h at rt. An aliquot was removed to determine the approximate conversion by ¹H NMR, and the remainder of the mixture was directly chromatographed on silica gel (pretreated with NEt₃; the reaction product was eluted with 50% $\rightarrow$ 100% Et₂O/hexanes; the unreacted dipole was eluted with 10% MeOH/EtOAc).

The ee of the recovered dipole was determined by chiral HPLC after either hydrogenation or reduction with NaBH₄ by the following procedures.

Hydrogenation: A mixture of the azomethine imine (~0.20 mmol) and PtO₂·xH₂O (Adam's catalyst) (3.0 mg) in MeOH (1.0 mL) was stirred for 1 h under an atmosphere of H₂. The solvent was removed in vacuo, and then the residue was chromatographed on silica gel (50% $\rightarrow$ 100% EtOAc).

Reduction with NaBH₄: A solution of the azomethine imine (~0.20 mmol) in MeOH (1.0 mL) was treated with NaBH₄ (8.3 mg, 0.22 mmol). The reaction mixture was stirred for 1 h, and then the solvent was removed in vacuo, and the residue was chromatographed on silica gel (50% $\rightarrow$ 100% EtOAc).

The conversion (C) was calculated by the equation:

$$C = [\text{ee (recovered dipole)}] / [\text{ee (recovered dipole)} + \text{ee (product)}].^1$$

The selectivity factor ($s = k_{\text{fast}}/k_{\text{slow}}$) was determined by the equation:

$$s = \ln [(1 - C)(1 - \text{ee (recovered dipole)})] / \ln [(1 - C)(1 + \text{ee (recovered dipole)})].^1$$

Table 1, entry 1. Conversion according to ¹H NMR: 57%.

Recovered dipole: 42% yield; 99% ee; $[\alpha]_{\text{D}}^{20} -19^\circ$ (*c* 1.05, MeOH). The ee was determined by chiral HPLC after hydrogenation of the dipole (viscous oil; 92% yield), using a Daicel Chiralpak AD-H column with hexanes/ⁱPrOH = 90:10, flow = 1.0 mL/min, detection at 210 nm, reference at 360 nm. Retention times: 17.6 min (major), 22.6 min (minor).

$[\alpha]_{\text{D}}^{20} -163^\circ$ (*c* 0.90, CH₂Cl₂).

^1H NMR (400 MHz, CDCl_3): δ 2.56 (dd, $J = 16.8, 9.1$ Hz, 1H), 2.98 (dd, $J = 16.8, 8.4$ Hz, 1H), 3.61 (d, $J = 12.8$ Hz, 1H), 4.02 (d, $J = 12.8$ Hz, 1H), 4.23 (t, $J = 8.8$ Hz, 1H), 7.24 (br s, 1H), 7.27-7.48 (m, 10H).

^{13}C NMR (101 MHz, CDCl_3): δ 39.6, 62.3, 67.3, 127.3, 128.2, 128.3, 128.9, 129.0, 129.3, 136.3, 139.7, 172.8.

IR (nujol): 1695, 1608, 1456, 1376, 752, 699.

HRMS (ESI): m/z 275.1160, $[\text{M}+\text{Na}]^+$ (calcd for $\text{C}_{16}\text{H}_{16}\text{N}_2\text{ONa}$: 275.1155).

White solid; 54% yield; 80% ee. The ee of the product was determined by chiral HPLC, using a Daicel Chiralpak OD-H column with hexanes/ $^i\text{PrOH} = 90:10$, flow = 1.0 mL/min, detection at 330 nm, reference at 380 nm. Retention times: 25.6 min (minor), 34.8 min (major).

$[\alpha]_D^{20} -392^\circ$ (c 1.01, CH_2Cl_2).

Mp 111°C .

^1H NMR (400 MHz, CD_2Cl_2): δ 1.16 (t, $J = 7.2$ Hz, 3H), 2.90 (dd, $J = 16.0, 7.2$ Hz, 1H), 2.99 (dd, $J = 16.4, 12.0$ Hz, 1H), 4.07 (m, 2H), 4.47 (dd, $J = 12.0, 7.2$ Hz, 1H), 5.24 (d, $J = 1.6$ Hz, 1H), 7.15-7.27 (m, 10H), 7.60 (d, $J = 2.0$ Hz, 1H).

^{13}C NMR (101 MHz, CD_2Cl_2): δ 14.4, 44.8, 60.9, 72.2, 73.5, 117.4, 128.0, 128.1, 128.4, 128.8, 128.9, 130.2, 136.8, 141.4, 163.9, 166.9.

IR (nujol): 3184, 3062, 1695, 1603, 1495, 1455, 758, 698.

HRMS (ESI): m/z 371.1376, $[\text{M}+\text{Na}]^+$ (calcd for $\text{C}_{21}\text{H}_{20}\text{N}_2\text{O}_3\text{Na}$: 371.1376).

Calculated conversion: 0.55; **s** = **49**.

Second run: **s** = **57** (42% conversion; dipole: 68% ee, 52% yield; product: 93% ee, 44% yield).

Table 1, entry 2. Conversion according to ^1H NMR: 56%.

Recovered dipole: 42% yield; 91% ee; $[\alpha]_D^{20} -37^\circ$ (c 0.49, CH_2Cl_2). The ee was determined by chiral HPLC after hydrogenation of the dipole (viscous oil; 95% yield), using a Daicel Chiralpak AD-H column with hexanes/ $^i\text{PrOH} = 90:10$, flow = 1.0 mL/min, detection at 210 nm, reference at 360 nm. Retention times: 17.6 min (major), 22.6 min (minor).

Yellow oil; 52% yield; 77% ee. The ee of the product was determined by chiral HPLC, using a Daicel Chiralcel IA column with hexanes/ⁱPrOH = 80:20, flow = 0.9 mL/min, detection at 330 nm, reference at 380 nm. Retention times: 26.3 min (minor), 58.5 min (major).

$[\alpha]_D^{20}$ -449° (*c* 0.95, CH₂Cl₂).

¹H NMR (500 MHz, CDCl₃): δ 2.80 (dd, *J* = 7.0, 16.1 Hz, 1H), 2.87 (dd, *J* = 12.5, 16.5 Hz, 1H), 3.20 (s, 3H), 4.23 (dd, *J* = 7.0, 12.5 Hz, 1H), 5.04 (d, *J* = 1.5 Hz, 1H), 6.31 (d, *J* = 1.8 Hz, 1H), 6.93-6.98 (m, 2H), 7.07-7.23 (m, 10H), 7.33-7.41 (m, 3H).

¹³C NMR (101 MHz, CDCl₃): δ 38.2, 44.9, 72.2, 75.1, 121.4, 125.4, 127.6, 127.8, 128.1, 128.3, 128.5, 128.7, 128.8, 130.1, 136.5, 140.4, 144.1, 164.6, 166.1.

IR (film): 1712, 1634, 1495, 1353, 1301, 1269, 761, 742, 698.

HRMS (EI): *m/z* 409.1792, [M]⁺ (calcd for C₂₆H₂₃N₃O₂: 409.1785).

Calculated conversion: 54%; **s** = 25.

Second run: **s** = 35 (55% conversion; dipole: 96% ee, 35% yield; product: 80% ee, 51% yield).

Table 1, entry 3.

Recovered dipole: 39% yield; 99% ee; $[\alpha]_D^{20}$ -38° (*c* 0.61, CH₂Cl₂). The ee was determined by chiral HPLC after hydrogenation of the dipole (viscous oil; 74% yield), using a Daicel Chiralpak AD-H column with hexanes/ⁱPrOH = 90:10, flow = 1.0 mL/min, detection at 210 nm, reference at 360 nm. Retention times: 17.6 min (major), 22.6 min (minor).

Yellow solid; 51% yield; 89% ee. The ee of the product was determined by chiral HPLC, using a Daicel Chiralcel AD-H column with hexanes/ⁱPrOH = 90:10, flow = 1.0 mL/min, detection at 330 nm, reference at 380 nm. Retention times: 20.1 min (major), 32.6 min (minor).

$[\alpha]_D^{20}$ -162° (*c* 0.99, CH₂Cl₂).

¹H NMR (400 MHz, CDCl₃): δ 2.91-3.05 (m, 2H), 4.50 (dd, *J* = 7.4, 12.1 Hz, 1H), 5.38 (d, *J* = 1.7 Hz, 1H), 7.01-7.24 (m, 12H), 7.41 (app dd, *J* = 2.7, 4.6 Hz, 3H).

^{13}C NMR (125 MHz, CDCl_3): δ 45.3, 72.2, 75.2, 119.2, 123.1, 124.8, 125.3, 125.6, 125.7, 126.7, 127.6, 128.2, 128.5, 128.6, 128.9, 135.9, 136.6, 139.5, 163.8.

IR (film): 1699, 1608, 1433, 1414, 1325, 1166, 1114, 1070, 761, 698.

HRMS (EI): m/z 420.1459, $[\text{M}]^+$ (calcd for $\text{C}_{25}\text{H}_{19}\text{F}_3\text{N}_2\text{O}$: 420.1444).

Calculated conversion: 53%; **s** = **49**.

Second run: **s** = **56** (49% conversion; dipole: 84% ee, 47% yield; product: 91% ee, 47% yield).

Table 2, entry 2. Conversion according to ^1H NMR: 52%.

Recovered dipole: 48% isolated yield; 95% ee; $[\alpha]_{\text{D}}^{20} -90^\circ$ (c 0.88, MeOH). The ee was determined by chiral HPLC after reaction of hydrogenation of the dipole (viscous oil; 82% yield), using a Daicel Chiralcel OJ-H column with hexanes/ $^i\text{PrOH}$ = 80:20, flow = 0.9 mL/min, detection at 210 nm, reference at 360 nm. Retention times: 8.5 min (minor), 9.2 min (major).

$[\alpha]_{\text{D}}^{20} -169^\circ$ (c 0.53, MeOH).

^1H NMR (400 MHz, CDCl_3): δ 2.24 (s, 3H), 2.52 (dd, J = 16.8, 9.2 Hz, 1H), 2.84 (dd, J = 16.8, 8.0 Hz, 1H), 3.61 (d, J = 14.0 Hz, 1H), 3.85 (d, J = 14.0 Hz, 1H), 4.20 (t, J = 8.8 Hz, 1H), 5.87 (d, J = 2.8 Hz, 1H), 6.10 (d, J = 2.8 Hz, 1H), 7.19 (br s, 1H), 7.23-7.36 (m, 5H).

^{13}C NMR (101 MHz, CDCl_3): δ 13.8, 39.4, 54.3, 67.2, 106.6, 110.8, 127.4, 128.4, 129.0, 139.3, 148.2, 153.0, 172.7.

IR (nujol): 3178, 3063, 1694, 1556, 1455, 788, 760, 700.

HRMS (ESI): m/z 257.1291, $[\text{M}+\text{H}]^+$ (calcd for $\text{C}_{15}\text{H}_{17}\text{N}_2\text{O}_2$: 257.1285).

White solid; 50% yield; 93% ee. The ee of the product was determined by chiral HPLC, using a Daicel Chiralcel AS-H column with hexanes/ $^i\text{PrOH}$ = 80:20, flow = 0.9 mL/min, detection at 330 nm, reference at 380 nm. Retention times: 21.4 min (major), 30.6 min (minor).

$[\alpha]_D^{20} -315^\circ$ (*c* 1.12, CH₂Cl₂).

Mp 99-100 °C.

¹H NMR (400 MHz, CDCl₃): δ 1.20 (t, *J* = 7.2 Hz, 3H), 2.15 (d, *J* = 0.8 Hz, 3H), 2.91 (dd, *J* = 16.4, 6.8 Hz, 1H), 3.00 (dd, *J* = 16.0, 12.0 Hz, 1H), 4.13 (m, 2H), 4.40 (dd, *J* = 12.4, 6.8 Hz, 1H), 5.24 (d, *J* = 1.6 Hz, 1H), 5.74 (m, 2H), 7.27-7.33 (m, 5H), 7.60 (d, *J* = 1.6 Hz, 1H).

¹³C NMR (101 MHz, CDCl₃): δ 13.7, 14.3, 44.5, 60.7, 66.5, 71.7, 106.4, 109.1, 114.6, 127.7, 128.7, 128.8, 130.5, 136.2, 149.8, 152.1, 163.5, 166.0.

IR (nujol): 3103, 1693, 1610, 1457, 780, 770, 702.

HRMS (ESI): *m/z* 353.1498, [M+H]⁺ (calcd for C₂₀H₂₁N₂O₄: 353.1496).

Calculated conversion: 0.51; **s** = **97**.

Second run: **s** = **94** (52% conversion; dipole: 96% ee; product: 90% ee).

Table 2, entry 3. The reaction of this substrate was carried out according to the General Procedure, except that CHCl₃ was employed as the solvent (due to solubility considerations; [dipole] = 0.13 M).

Conversion according to ¹H NMR: 59%.

Recovered dipole: 31% yield; >99% ee; $[\alpha]_D^{20} -137^\circ$ (*c* 1.23, MeOH). The ee was determined by chiral HPLC after hydrogenation of the dipole (viscous oil; 88% yield), using a Daicel Chiralcel AD-H column with hexanes/ⁱPrOH = 90:10, flow = 1.0 mL/min, detection at 210 nm, reference at 360 nm. Retention times: 15.3 min (minor), 21.9 (major).

$[\alpha]_D^{20} -202^\circ$ (*c* 0.94, CH₂Cl₂).

¹H NMR (400 MHz, CD₂Cl₂): δ 2.53 (dd, *J* = 16.8, 8.8 Hz, 1H), 2.98 (dd, *J* = 16.4, 8.4 Hz, 1H), 3.05 (s, 3H), 3.62 (d, *J* = 13.2 Hz, 1H), 3.89 (d, *J* = 13.2 Hz, 1H), 4.20 (t, *J* = 8.8 Hz, 1H), 6.00 (dd, *J* = 3.2, 2.8 Hz, 1H), 6.11 (dd, *J* = 3.6, 1.6 Hz, 1H), 6.60 (dd, *J* = 2.4, 2.0 Hz, 1H), 7.10 (br s, 1H), 7.32-7.46 (m, 5H).

¹³C NMR (101 MHz, CDCl₃): δ 33.9, 40.0, 53.8, 67.5, 107.0, 110.6, 123.8, 126.8, 127.5, 128.4, 128.9, 139.4, 172.0.

IR (nujol): 3187, 3063, 1694, 1496, 1456, 1301, 701.

HRMS (ESI): *m/z* 256.1441, [M+H]⁺ (calcd for C₁₅H₁₈N₃O: 256.1444).

White solid; 55% yield; 69% ee. The ee of the product was determined by chiral HPLC, using a Daicel Chiralcel AD-H column with hexanes/ⁱPrOH = 80:20, flow = 0.9 mL/min, detection at 330 nm, reference at 380 nm. Retention times: 11.6 min (major), 13.8 min (minor).

$[\alpha]_D^{20} -142^\circ$ (*c* 0.98, CH₂Cl₂).

Mp 104 °C (dec.).

¹H NMR (400 MHz, CDCl₃): δ 1.26 (t, *J* = 7.2 Hz, 3H), 3.02 (m, 2H), 3.33 (s, 3H), 4.19 (m, 2H), 4.49 (dd, *J* = 11.2, 8.0 Hz, 1H), 5.37 (d, *J* = 1.6 Hz, 1H), 5.98 (m, 2H), 6.46 (t, *J* = 2.4 Hz, 1H), 7.28-7.35 (m, 5H), 7.66 (d, *J* = 1.6 Hz, 1H).

¹³C NMR (101 MHz, CDCl₃): δ 14.3, 33.9, 44.8, 60.7, 65.7, 71.6, 107.1, 109.4, 116.3, 123.1, 127.3, 128.7, 128.9, 129.6, 129.7, 136.5, 163.6, 166.5.

IR (nujol): 3108, 1712, 1688, 1457, 1410, 1356, 803, 769, 720, 701.

HRMS (ESI): *m/z* 352.1655, [M+H]⁺ (calcd for C₂₀H₂₂N₃O₃: 352.1656).

Calculated conversion: 59%; **s** = **27**.

Second run: **s** = **27** (59% conversion; dipole: >99% ee; product: 69% ee).

Table 2, entry 4. Conversion according to ¹H NMR: 57%.

Recovered dipole: 36% yield; 95% ee; $[\alpha]_D^{20} -64^\circ$ (*c* 0.84, MeOH). The ee was determined by chiral HPLC after reaction of the dipole with NaBH₄ (viscous oil; 93% yield), using a Daicel Chiralpak OD-H column with hexanes/ⁱPrOH = 95:5, flow = 1.0 mL/min, detection at 230 nm, reference at 360 nm. Retention times: 12.7 min (minor), 14.9 min (major).

$[\alpha]_D^{20} -142^\circ$ (*c* 1.09, MeOH).

¹H NMR (400 MHz, CDCl₃): δ 1.47-1.84 (m, 5H), 2.00-2.13 (m, 3H), 2.54 (dd, *J* = 16.8, 10.0 Hz, 1H), 2.96 (m, 2H), 3.24 (d, *J* = 12.4 Hz, 1H), 4.06 (t, *J* = 10.0 Hz, 1H), 5.71 (s, 1H), 7.25 (br s, 1H), 7.27-7.42 (m, 5H).

¹³C NMR (101 MHz, CDCl₃): δ 22.4, 22.7, 25.3, 27.1, 40.3, 65.3, 67.5, 127.1, 127.3, 128.1, 128.9, 134.1, 139.9, 171.8.

IR (nujol): 3168, 3063, 1698, 1495, 1456, 1307, 758, 699.

HRMS (ESI): m/z 257.1654, $[M+H]^+$ (calcd for $C_{16}H_{21}N_2O$: 257.1648).

Yellow oil; 48% yield; 82% ee. The ee of the product was determined by chiral HPLC, using a Daicel Chiralpak OD-H column with hexanes/ i PrOH = 90:10, flow = 1.0 mL/min, detection at 330 nm, reference at 380 nm. Retention times: 16.5 min (minor), 24.9 min (major).

$[\alpha]_D^{20}$ -167° (c 0.79, CH_2Cl_2).

1H NMR (400 MHz, $CDCl_3$): δ 1.24 (t, J = 6.8 Hz, 3H), 1.31-1.84 (m, 7H), 2.14 (m, 1H), 2.95 (m, 2H), 4.10 (m, 1H), 4.18-4.28 (m, 2H), 4.59 (d, J = 1.6 Hz, 1H), 5.22 (m, 1H), 7.26-7.39 (m, 5H), 7.47 (d, J = 2.0 Hz, 1H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 14.4, 22.3, 22.7, 24.6, 25.3, 45.3, 60.5, 71.1, 77.2, 117.1, 127.7, 127.9, 128.5, 128.6, 129.4, 134.4, 137.3, 163.8, 164.6.

IR (nujol): 3064, 3032, 1706, 1599, 1436, 1364, 766, 700.

Calculated conversion: 0.54; **s** = 35.

Second run: **s** = 35 (53% conversion; dipole: 93% ee; product: 82% ee).

Table 2, entry 5. Conversion according to 1H NMR: 63%.

Recovered dipole: We were unable to obtain completely pure material (approximate yield: 36%); 91% ee. The ee was determined by chiral HPLC after hydrogenation of the dipole (viscous oil; ~78% yield; 27% yield over two steps from the racemic dipole), using a Daicel Chiralpak OD-H column with hexanes/ i PrOH = 97:3, flow = 1.0 mL/min, detection at 210 nm, reference at 360 nm. Retention times: 17.6 min (major), 19.9 min (minor).

$[\alpha]_D^{20}$ -181° (c 1.03, MeOH).

^1H NMR (400 MHz, CDCl_3): δ 0.82-0.83 (m, 2H), 0.86-1.22 (m, 3H), 1.35 (m, 1H), 1.63 (m, 4H), 1.90 (m, 1H), 2.50 (m, 3H), 2.95 (dd, J = 16.8, 8.4 Hz, 1H), 4.02 (t, J = 8.8 Hz, 1H), 7.23-7.38 (m, 5H), 7.79 (br s, 1H).

^{13}C NMR (101 MHz, CDCl_3): δ 25.9, 26.0, 26.7, 31.3, 31.7, 36.6, 39.9, 65.5, 68.2, 127.2, 128.0, 128.9, 140.3, 173.2.

IR (nujol): 3160, 3059, 1686, 1497, 1447, 1377, 758, 667.

HRMS (ESI): m/z 259.1812, $[\text{M}+\text{H}]^+$ (calcd for $\text{C}_{16}\text{H}_{23}\text{N}_2\text{O}$: 259.1805).

White solid; 58% yield; 64% ee. The ee of the product was determined by chiral HPLC, using a Daicel Chiralpak AD-H column with hexanes/ i PrOH = 90:10, flow = 1.0 mL/min, detection at 330 nm, reference at 380 nm. Retention times: 7.3 min (minor), 8.2 min (major).

$[\alpha]_D^{20}$ -221° (c 1.12, CH_2Cl_2).

Mp 124-126 °C.

^1H NMR (400 MHz, CDCl_3): δ 0.45 (m, 1H), 0.82 (m, 1H), 0.92-1.05 (m, 4H), 1.29 (t, J = 7.2 Hz, 3H), 1.40-1.50 (m, 4H), 1.64 (m, 1H), 2.77 (dd, J = 16.4, 6.0 Hz, 1H), 3.10 (dd, J = 16.0, 13.2 Hz, 1H), 4.16-4.28 (m, 4H), 7.34-7.42 (m, 3H), 7.44-7.47 (m, 3H).

^{13}C NMR (101 MHz, CDCl_3): δ 14.5, 26.4, 26.5, 26.6, 26.9, 29.4, 41.2, 42.8, 60.6, 72.6, 73.4, 114.2, 128.8, 128.9, 129.3, 132.4, 136.2, 164.5, 171.0.

IR (nujol): 3085, 3031, 1716, 1685, 1611, 1456, 1385, 770, 703.

HRMS (ESI): m/z 355.2026, $[\text{M}+\text{H}]^+$ (calcd for $\text{C}_{21}\text{H}_{27}\text{N}_2\text{O}_3$: 355.2016).

Calculated conversion: 0.59; **s** = **14**.

Second run: **s** = **16** (58% conversion; dipole: 94% ee; product: 66% ee).

Table 3, entry 2. Due to the very low solubility of the dipole, 40 mL of CH_2Cl_2 was employed in the reaction (under these conditions, the reaction mixture was homogeneous). The reaction was performed at 0 °C with 2% CuI/2.2% **3** (the kinetic resolution was reproducible at 0 °C, but it was not always reproducible at rt).

Conversion according to ^1H NMR: 52%.

Recovered dipole: Because we could not purify the dipole to homogeneity, it was reduced with NaBH_4 (see below); 99% ee. The ee was determined by chiral HPLC after reduction of the dipole, using a Daicel Chiralpak AD-H column with hexanes/ i PrOH =

90:10, flow = 1.0 mL/min, detection at 210 nm, reference at 360 nm. Retention times: 11.9 min (major), 14.6 min (minor).

The recovered, impure dipole (0.20 mmol; estimated) and NaBH₄ (7.4 mg, 0.20 mmol) were dissolved in MeOH (6 mL). The reaction mixture was stirred for 10 min, and then the solvent was removed in vacuo and the residue was chromatographed (1:1 EtOAc:pentane) to provide the product as a colorless oil (44% yield over two steps from the racemic dipole).

$[\alpha]_D^{20} -132^\circ$ (*c* 1.00, CH₂Cl₂).

¹H NMR (500 MHz, CDCl₃): δ 2.51 (dd, *J* = 8.4, 16.7 Hz, 1H), 3.02 (dd, *J* = 8.3, 16.8 Hz, 1H), 3.67 (d, *J* = 12.7 Hz, 1H), 4.03 (d, *J* = 12.7 Hz, 1H), 4.23 (t, *J* = 8.3 Hz, 1H), 7.19-7.49 (m, 9H), 7.63 (br s, 1H).

¹³C NMR (101 MHz, CDCl₃): δ 39.6, 62.8, 66.6, 123.3, 126.0, 128.6, 129.2, 129.5, 130.5, 130.8, 131.6, 136.2, 142.6, 172.6.

IR (film): 3062, 1692, 1337, 1070, 783, 698.

HRMS (ESI): *m/z* 353.0262, [M]⁺ (calcd for C₁₆H₁₅BrN₂O: 353.0260).

Yellow powder; 51% yield; 79% ee. The ee of the product was determined by chiral HPLC, using a Daicel Chiralcel IA column with hexanes/ⁱPrOH = 80:20, flow = 0.9 mL/min, detection at 330 nm, reference at 380 nm. Retention times: 39.5 min (minor), 81.8 min (major).

$[\alpha]_D^{20} -311^\circ$ (*c* 0.97, CH₂Cl₂).

¹H NMR (500 MHz, CDCl₃): δ 2.80 (app d, *J* = 3.1 Hz, 1H), 2.82 (app s, *J* = 12.8, 1H), 3.19 (s, 3H), 4.20 (dd, *J* = 8.6, 11.0 Hz, 1H), 5.00 (d, *J* = 1.8 Hz, 1H), 6.30 (d, *J* = 1.8 Hz, 1H), 6.94-7.00 (m, 3H), 7.01-7.05 (m, 1H), 7.10-7.15 (m, 2H), 7.20-7.28 (m, 5H), 7.33-7.43 (m, 3H).

¹³C NMR (101 MHz, CDCl₃): δ 38.2, 44.9, 72.0, 75.3, 121.6, 122.8, 125.2, 126.2, 127.6, 128.36, 128.38, 128.6, 130.2, 130.3, 130.9, 131.7, 139.0, 140.0, 142.5, 144.0, 164.4, 165.1.

IR (film): 1710, 1632, 1592, 1494, 1404, 1357, 1301, 1272, 743, 698.

HRMS (ESI): m/z 510.0805, $[M]^+$ (calcd for $C_{26}H_{22}BrN_3O_2$: 510.0788).

Calculated conversion: 56%; **s** = **47**.

Second run: **s** = **61** (54% conversion; dipole: >99% ee, 39% yield; product: 86% ee, 54% yield).

Table 3, entry 3. Due to the low solubility of the dipole, 4 mL of CH_2Cl_2 was employed in the reaction (under these conditions, the reaction mixture was homogeneous). The reaction was performed at 0 °C (at rt, **s** = 8).

Conversion according to 1H NMR: not determined, due to the low solubility of the dipole.

Recovered dipole: 31% yield; 98% ee; $[\alpha]_D^{20} +41^\circ$ (c 0.61, CH_2Cl_2). The ee was determined by chiral HPLC after reduction of the dipole, using a Daicel Chiralpak AD-H column with hexanes/ iPrOH = 90:10, flow = 1.0 mL/min, detection at 210 nm, reference at 360 nm. Retention times: 18.5 min (major), 25.7 min (minor).

The dipole (29.9 mg, 0.117 mmol) and $NaBH_4$ (4.2 mg, 0.111 mmol) were dissolved in MeOH (4 mL). The reaction mixture was stirred for 10 min, and then the solvent was removed in vacuo, and the residue was chromatographed (1:1 EtOAc:pentane) to provide the product as a colorless oil, which solidified under vacuum (91% yield; 98% ee).

$[\alpha]_D^{20} -134^\circ$ (c 0.42, CH_2Cl_2).

1H NMR (500 MHz, $CDCl_3$): δ 2.65 (dd, J = 8.2, 16.8 Hz, 1H), 3.04 (dd, J = 8.2, 16.8 Hz, 1H), 3.66 (d, J = 12.8 Hz, 1H), 4.13 (d, J = 12.8 Hz, 1H), 4.53 (app t, J = 8.2 Hz, 1H), 6.94 (br s, 1H), 7.00 (dd, J = 3.7, 5.2 Hz, 1H), 7.04 (dt, J = 0.9, 3.3 Hz, 1H), 7.29-7.39 (m, 6H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 39.9, 62.5, 63.2, 125.6, 126.0, 127.4, 128.6, 129.2, 129.5, 136.3, 144.0, 172.9.

IR (film): 3181, 1693, 1320, 697.

HRMS (EI): m/z 258.0819, $[M]^+$ (calcd for $C_{14}H_{14}N_2OS$: 258.0821).

Mp 104 °C.

Yellow solid; 58% yield; 50% ee. The ee of the product was determined by chiral HPLC, using a Daicel Chiralcel AD-H column with hexanes/ⁱPrOH = 90:10, flow = 1.0 mL/min, detection at 330 nm, reference at 380 nm. Retention times: 17.1 min (major), 19.8 min (minor).

$[\alpha]_D^{20} -159^\circ$ (*c* 0.98, CH₂Cl₂).

¹H NMR (400 MHz, CDCl₃): δ 1.14 (t, *J* = 7.1 Hz, 3H), 2.96 (dd, *J* = 6.6, 16.3 Hz, 1H), 3.06 (dd, *J* = 12.3, 16.3 Hz, 1H), 4.07 (app dddd, *J* = 7.1, 10.8, 14.3, 36.1 Hz, 2H), 4.73 (dd, *J* = 6.6, 12.3 Hz, 1H), 5.28 (d, *J* = 1.6 Hz, 1H), 6.84 (dd, *J* = 3.5, 5.1 Hz, 1H), 6.95 (dd, *J* = 0.8, 3.5 Hz, 1H), 7.13-7.24 (m, 6H), 7.58 (d, *J* = 1.7 Hz, 1H).

¹³C NMR (101 MHz, CDCl₃): δ 14.2, 45.2, 60.7, 67.3, 73.1, 117.6, 126.4, 126.6, 126.7, 127.9, 128.0, 128.2, 129.7, 139.4, 140.5, 163.6, 166.2.

IR (film): 1738, 1700, 1608, 1363, 1325, 1244, 1211, 1089, 752, 697.

HRMS (EI): *m/z* 354.1024, [M]⁺ (calcd for C₁₉H₁₈N₂O₃S: 354.1033).

Mp 189 °C (dec.).

Calculated conversion: 65%; **s** = 13.

Second run: **s** = 16 (65% conversion; dipole: 99% ee, 39% yield; product: 54% ee, 58% yield).

Table 3, entry 4. Conversion according to ¹H NMR: 51%.

Recovered dipole: Because we could not purify the dipole to homogeneity, it was reduced with NaBH₄ (see below); 95% ee. The ee was determined by chiral HPLC after reduction of the dipole, using a Daicel Chiralpak OD-H column with hexanes/ⁱPrOH = 98:2, flow = 1.0 mL/min, detection at 210 nm, reference at 360 nm. Retention times: 30.2 min (minor), 34.7 min (major).

The recovered, impure dipole (0.22 mmol, estimated) and NaBH₄ (8.5 mg, 0.22 mmol) were dissolved in MeOH (3 mL). The reaction mixture was stirred for 10 min, and then the solvent was removed in vacuo and the residue was chromatographed (1:1 EtOAc:pentane) to provide the product as a colorless oil, which solidified under vacuum (40% yield over two steps from the racemic dipole).

$[\alpha]_D^{20} -133^\circ$ (*c* 0.99, CH₂Cl₂).

¹H NMR (500 MHz, CDCl₃): δ 0.91 (d, *J* = 6.7 Hz, 3H), 0.95 (d, *J* = 6.7 Hz, 3H), 1.78 (app dsept, *J* = 6.7, 6.7 Hz, 1H), 2.20 (dd, *J* = 4.3, 17.4 Hz, 1H), 2.77 (dd, *J* = 8.9, 17.4 Hz, 1H), 3.05 (ddd, *J* = 4.0, 6.7, 8.9 Hz, 1H), 3.77 (d, *J* = 12.2 Hz, 1H), 3.95 (d, *J* = 12.2 Hz, 1H), 6.82 (br s, 1H), 7.28-7.39 (m, 5H).

¹³C NMR (101 MHz, CDCl₃): δ 18.4, 18.9, 31.9, 32.2, 64.5, 68.3, 128.1, 128.8, 129.6, 136.5, 174.3.

IR (film): 3182, 2958, 1690, 1347, 725, 698.

HRMS (ESI): *m/z* 241.1308, [M+Na]⁺ (calcd for C₁₃H₁₈N₂O: 241.1311).

Mp 91-92 °C.

Yellow oil; 52% yield; 89% ee. The ee of the product was determined by chiral HPLC, using a Daicel Chiralcel IA column with hexanes/ⁱPrOH = 80:20, flow = 0.9 mL/min, detection at 330 nm, reference at 380 nm. Retention times: 17.3 min (minor), 37.2 min (major).

$[\alpha]_D^{20} -670^\circ$ (*c* 1.01, CH₂Cl₂).

¹H NMR (400 MHz, CDCl₃): δ 0.63 (d, *J* = 6.8 Hz, 3H), 0.75 (d, *J* = 6.9 Hz, 3H), 1.62 (app dsept, *J* = 4.4, 6.8 Hz, 1H), 2.38 (dd, *J* = 6.7, 16.3 Hz, 1H), 2.63 (dd, *J* = 12.9, 16.3 Hz, 1H), 3.18 (s, 3H), 3.23 (ddd, *J* = 4.3, 6.7, 12.8 Hz, 1H), 5.20 (d, *J* = 1.5 Hz, 1H), 6.06 (d, *J* = 1.7 Hz, 1H), 6.87 (d, *J* = 1.7 Hz, 2H), 7.20-7.57 (m, 8H).

¹³C NMR (101 MHz, CDCl₃): δ 16.4, 19.9, 28.4, 36.1, 38.0, 73.6, 75.8, 121.7, 124.1, 127.5, 128.1, 128.3, 128.6, 128.7, 130.1, 140.9, 144.3, 164.6, 166.2.

IR (film): 1713, 1635, 1495, 1403, 1354, 1302, 1157, 742, 699.

HRMS (EI): *m/z* 375.1934, [M]⁺ (calcd for C₂₃H₂₅N₃O₂: 375.1941).

Calculated conversion: 49%; **s** = 25.

Second run: **s** >100 (49% conversion; dipole: 95% ee, 49% yield; product: 97% ee, 51% yield).

Table 3, entry 5. Due to the low solubility of the dipole, 4 mL of CH₂Cl₂ was employed in the reaction (under these conditions, the reaction mixture was homogeneous).

Conversion according to ¹H NMR: 50%.

Recovered dipole: 48% yield; 93% ee; $[\alpha]_D^{20} -590^\circ$ (*c* 0.96, CH₂Cl₂). The ee was determined by chiral HPLC after reduction of the dipole, using a Daicel Chiralpak OD-

H column with hexanes/ⁱPrOH = 98:2, flow = 1.0 mL/min, detection at 210 nm, reference at 360 nm. Retention times: 24.4 min (minor), 31.7 min (major).

The dipole (21.8 mg, 0.0900 mmol) and NaBH₄ (3.7 mg, 0.098 mmol) were dissolved in MeOH (0.5 mL). The reaction mixture was stirred for 10 min, and then the solvent was removed in vacuo, and the residue was chromatographed (1:1 EtOAc:pentane) to provide the product as a colorless oil, which solidified under vacuum (77% yield; 93% ee).

$[\alpha]_D^{20} -110^\circ$ (*c* 1.05, CH₂Cl₂).

¹H NMR (500 MHz, CDCl₃): δ 0.91 (s, 9H), 2.25 (dd, *J* = 2.7, 17.7 Hz, 1H), 2.79 (dd, *J* = 10.1, 17.7 Hz, 1H), 3.02 (dd, *J* = 2.4, 9.8 Hz, 1H), 3.82 (d, *J* = 12.2 Hz, 1H), 3.94 (d, *J* = 12.2 Hz, 1H), 6.76 (br s, 1H), 7.29-7.39 (m, 5H).

¹³C NMR (101 MHz, CDCl₃): δ 25.8, 30.7, 35.4, 66.1, 71.3, 128.4, 129.0, 130.0, 136.8, 174.6.

IR (film): 3178, 2954, 1692, 1361, 698.

HRMS (EI): *m/z* 232.1564, [M]⁺ (calcd for C₁₄H₂₀N₂O: 232.1570).

Mp 108 °C.

Yellow powder; 51% yield; 85% ee. The ee of the product was determined by chiral HPLC, using a Daicel Chiralcel IA column with hexanes/ⁱPrOH = 80:20, flow = 0.9 mL/min, detection at 330 nm, reference at 380 nm. Retention times: 12.7 min (minor), 33.8 min (major).

$[\alpha]_D^{20} -631^\circ$ (*c* 0.97, CH₂Cl₂).

¹H NMR (400 MHz, CDCl₃): δ 0.73 (s, 9H), 2.45 (dd, *J* = 7.0, 16.5 Hz, 1H), 2.70 (dd, *J* = 12.8, 16.5 Hz, 1H), 3.18 (s, 3H), 3.19 (dd, *J* = 7.0, 12.8 Hz, 1H), 5.37 (s, 1H), 5.80 (s, 1H), 6.71 (d, *J* = 5.2 Hz, 2H), 7.22-7.47 (m, 8H).

¹³C NMR (101 MHz, CDCl₃): δ 27.2, 33.2, 37.3, 37.9, 76.0, 77.8, 121.7, 123.2, 127.3, 127.95, 127.99, 128.65, 128.68, 130.0, 141.3, 144.3, 164.8, 167.7.

IR (film): 2960, 1716, 1639, 1593, 1494, 1399, 1356, 1302, 1266, 1157, 741, 699.

HRMS (EI): *m/z* 389.2095, [M]⁺ (calcd for C₂₄H₂₇N₃O₂: 389.2098).

Calculated conversion: 52%; **s** = **44**.

Second run: **s** = **57** (49% conversion; dipole: 87% ee, 49% yield; product: 94% ee, 49% yield).

As noted in the text, side reactions are occasionally observed during cycloadditions of ethyl propiolate. These side reactions are accompanied by a change in color in the reaction mixture (from yellow-gold to red).

IV. Synthesis of Ligand 3

In an oven-dried round-bottom flask, *n*-BuLi (2.53 M in hexanes; 2.91 mL, 7.36 mmol) was added to a $-78\text{ }^{\circ}\text{C}$ solution of (*S*)-phenylglycine (505 mg, 3.68 mmol) in THF (20 mL) under argon. The forest-green reaction mixture was warmed to $0\text{ }^{\circ}\text{C}$ and stirred for 1 h, and then it was warmed to room temperature and stirred for 2 h. The resulting pale-yellow mixture (containing a white precipitate) was cooled to $-78\text{ }^{\circ}\text{C}$, and a solution of the trifluoroacetylated phosphoferrocene² in THF (5 mL) was added. The reaction mixture was allowed to slowly warm to room temperature overnight. After 16 h, the reaction was heated to reflux for 2 h. The reaction was then cooled to room temperature, and NH_4Cl (0.50 g) was added. The mixture was stirred for 1 h, and then the solvent was removed under vacuum, and the residue was chromatographed on silica gel to yield a mixture of diastereomeric amides (orange foam; 357 mg, 84%).

The amides were dissolved in CH_2Cl_2 (10 mL), and the resulting solution was cooled to $-78\text{ }^{\circ}\text{C}$ and treated with 4-dimethylaminopyridine (20 mg, 0.16 mmol), Et_3N (0.200 mL, 1.43 mmol), and methanesulfonyl chloride (0.110 mL, 1.42 mmol). The resulting solution was stirred for 30 min at $0\text{ }^{\circ}\text{C}$. The mixture was then warmed to room temperature, and additional Et_3N (500 mL, 3.59 mmol) was added. After 20 h, the reaction mixture was concentrated to a volume of 5 mL under a stream of N_2 . The mixture was chromatographed on silica gel (1:8 Et_2O :hexane). The desired, slower-eluting diastereomer was isolated in 33% overall yield from the racemic trifluoroacetylated phosphoferrocene (orange powder; 129 mg, 33%).

^1H NMR (500 MHz, CDCl_3): δ 1.79 (s, 15H), 2.07 (s, 3H), 2.34 (s, 3H), 3.47 (d, $J = 36.9$ Hz, 1H), 3.99 (app t, $J = 9.5$ Hz, 1H), 4.67 (dd, $J = 8.3, 10.1$ Hz, 1H), 5.25 (app t, $J = 9.5$ Hz, 1H), 7.26–7.31 (m, 1H), 7.34–7.38 (m, 4H).

^{13}C NMR (101 MHz, CDCl_3): δ 10.7, 13.0, 14.6, 70.7, 73.5, 83.9, 84.5, 84.6, 91.8, 97.9, 127.1, 127.5, 128.9, 143.2.

IR (film): 2952, 2904, 1626, 1475, 1450, 1376, 1267, 1114, 1019, 699.

HRMS (EI): m/z 447.1420, $[\text{M}]^+$ (calcd for $\text{C}_{25}\text{H}_{30}\text{NOPFe}$: 447.1420).

$[\alpha]_D^{20} -195^{\circ}$ (c 0.34, CH_2Cl_2).

Mp $121\text{--}124\text{ }^{\circ}\text{C}$ (dec.).

V. Reactions of the Enantioenriched Dipoles (eq 3-5)

Eq 3. The dipole (29.9 mg, 0.117 mmol) and NaBH₄ (4.2 mg, 0.11 mmol) were dissolved in MeOH (4 mL) and stirred for 10 min. The solvent was then removed in vacuo, and the residue was chromatographed (1:1 EtOAc:pentane) to provide the product as a colorless oil, which solidified under vacuum (91% yield, 98% ee).

The ee was determined by chiral HPLC, using a Daicel Chiralpak AD-H column with hexanes/ⁱPrOH = 90:10, flow = 1.0 mL/min, detection at 210 nm, reference at 360 nm. Retention times: 18.5 min (major), 25.7 min (minor).

$[\alpha]_D^{20}$ -134° (*c* 0.42, CH₂Cl₂).

¹H NMR (500 MHz, CDCl₃): δ 2.65 (dd, *J* = 8.2, 16.8 Hz, 1H), 3.04 (dd, *J* = 8.2, 16.8 Hz, 1H), 3.66 (d, *J* = 12.8 Hz, 1H), 4.13 (d, *J* = 12.8 Hz, 1H), 4.53 (app t, *J* = 8.2 Hz, 1H), 6.94 (br s, 1H), 7.00 (dd, *J* = 3.7, 5.2 Hz, 1H), 7.04 (dt, *J* = 0.9, 3.3 Hz, 1H), 7.29-7.39 (m, 6H).

¹³C NMR (101 MHz, CDCl₃): δ 39.9, 62.5, 63.2, 125.6, 126.0, 127.4, 128.6, 129.2, 129.5, 136.3, 144.0, 172.9.

IR (film): 3181, 1693, 1320, 697.

HRMS (EI): *m/z* 258.0819, [M]⁺ (calcd for C₁₄H₁₄N₂OS: 258.0821).

Mp 104 °C.

Eq 4. *i*-PrMgCl (90 μL, 0.18 mmol; 2.0 M in THF) was added dropwise to a suspension of the azomethine imine (30.0 mg, 0.120 mmol) in THF (1.5 mL) at -78 °C. The reaction mixture was allowed to warm to room temperature, and then the reaction was quenched with MeOH (100 μL). The reaction mixture was passed through a plug of silica gel (eluant: EtOAc), and the solvent was removed in vacuo. Chromatography on silica gel (50 → 100% EtOAc/hexanes) provided the product as a white foam (29.6 mg, 83%).

Second run (with racemic dipole): 83% yield.

$[\alpha]_D^{20}$ -127° (*c* 1.48, CH₂Cl₂).

¹H NMR (400 MHz, CDCl₃): δ 0.85 (d, *J* = 6.7 Hz, 3H), 0.90 (d, *J* = 6.7 Hz, 3H), 2.23 (dd, *J* = 1.5, 16.8 Hz, 1H), 2.26-2.36 (m, 1H), 3.03 (dd, *J* = 8.5, 16.8 Hz, 1H), 3.81 (d, *J* = 5.2 Hz, 1H), 4.35 (d, *J* = 8.2 Hz, 1H), 7.22-7.32 (m, 10H), 8.50 (s, 1H).

¹³C NMR (101 MHz, CDCl₃): 16.7, 20.9, 29.7, 37.0, 63.1, 76.9, 126.6, 127.5, 128.1, 128.3, 128.9, 129.8, 137.3, 142.7, 175.8.

IR (film): 3172, 3062, 2963, 1690, 1494, 1452, 1421, 1367, 1030, 704.

HRMS (ESI): *m/z* 317.1624, [M+Na]⁺ (calcd for C₁₉H₂₂N₂ONa: 317.1634).

Mp 149 °C.

The assignment of the stereochemistry of the product of eq 4 is based on the assumption that the nucleophile adds to the less hindered face of the dipole.

Eq 5. To a suspension of CuI (1.7 mg, 8.9 μmol ; the high catalyst loading is due to the small scale of the reaction) in CH_2Cl_2 (100 μL) was added Cy_2NMe (4.8 μL , 22 μmol). The mixture was treated with the azomethine imine (11.0 mg, 45.4 μmol) and the alkyne (8.6 mg, 54 μmol) and then diluted with CH_2Cl_2 (400 μL). The resulting mixture was stirred for 16 h. The mixture was then purified, without workup, by chromatography on silica gel (pretreated with NEt_3 ; 50 $\rightarrow$ 100% Et_2O /hexanes), which furnished the desired product (14.6 mg, 80%; dr = 94:6), which was identical by ^1H NMR spectroscopy with the product from Table 3, entry 5.

Second run: 75% yield (dr = 96:4).

VI. X-Ray Crystal Structures: Relative and Absolute Configuration

General. X-ray structure data were collected using a Siemens SMART CCD-based diffractometer equipped with an LT-2 low-temperature apparatus operating at 213 K. A suitable crystal was chosen and mounted on a fiberglass loop using grease. Data were measured using omega scans of 0.3° per frame for 30 seconds (unless otherwise noted) such that a hemisphere was collected. A total of 1271 frames were collected with a final resolution of 0.80-0.90 Å. The first 50 frames were re-collected at the end of data collection to monitor for decay. Cell parameters were retrieved using SMART software and refined using SAINT on all observed reflections. Data reduction was performed using the SAINT software supplied by George Sheldrick. The structures were solved by the direct method using the SHELXS-90 program and refined by least squares method on F^2 with SHELXL-93. The structures were solved in the indicated space group by analysis of systematic absences. All non-hydrogen atoms were refined anisotropically. Hydrogens were calculated by geometrical methods and refined as a riding model. The crystals used for the diffraction studies showed no decomposition during data collection.

Recovered dipole: Table 3, entry 2.

Table 1. Crystal data and structure refinement for gcf105t.

Identification code	gcf105t	
Empirical formula	C ₁₆ H ₁₃ Br N ₂ O	
Formula weight	329.19	
Temperature	193(2) K	
Wavelength	0.71073 Å	
Crystal system	Orthorhombic	
Space group	P2(1)2(1)2(1)	
Unit cell dimensions	a = 6.1369(14) Å	$\alpha = 90^\circ$.
	b = 13.672(3) Å	$\beta = 90^\circ$.
	c = 16.152(4) Å	$\gamma = 90^\circ$.
Volume	1355.3(5) Å ³	
Z	4	
Density (calculated)	1.613 Mg/m ³	
Absorption coefficient	3.029 mm ⁻¹	
F(000)	664	
Crystal size	0.29 x 0.05 x 0.03 mm ³	
Theta range for data collection	1.95 to 28.26°.	
Index ranges	-7 ≤ h ≤ 8, -18 ≤ k ≤ 16, -21 ≤ l ≤ 12	
Reflections collected	9811	
Independent reflections	3345 [R(int) = 0.0574]	
Completeness to theta = 28.26°	99.8 %	
Absorption correction	None	
Refinement method	Full-matrix least-squares on F ²	
Data / restraints / parameters	3345 / 0 / 181	
Goodness-of-fit on F ²	0.892	
Final R indices [I > 2σ(I)]	R1 = 0.0280, wR2 = 0.0569	
R indices (all data)	R1 = 0.0356, wR2 = 0.0583	
Absolute structure parameter	-0.018(9)	
Largest diff. peak and hole	0.512 and -0.294 e.Å ⁻³	

Table 2. Atomic coordinates ($\times 10^4$) and equivalent isotropic displacement parameters ($\text{\AA}^2 \times 10^3$) for gcf105t. $U(\text{eq})$ is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U(eq)
Br(1)	2636(1)	3368(1)	6554(1)	34(1)
O(1)	6041(2)	6564(1)	9613(1)	35(1)
C(2)	2515(4)	6656(2)	8936(1)	31(1)
N(2)	1503(3)	5184(2)	9577(1)	23(1)
C(4)	27(4)	5435(2)	8163(2)	23(1)
N(1)	3617(3)	5322(2)	9794(1)	26(1)
C(10)	256(4)	4494(2)	9852(2)	26(1)
C(8)	-2590(5)	5153(2)	7077(1)	30(1)
C(6)	785(4)	4305(2)	7060(2)	25(1)
C(16)	-895(4)	3054(2)	10601(2)	33(1)
C(14)	1352(5)	2221(2)	11581(2)	44(1)
C(1)	4247(4)	6193(2)	9478(2)	27(1)
C(9)	-1993(4)	5618(2)	7807(2)	28(1)
C(5)	1435(4)	4776(2)	7782(2)	26(1)
C(7)	-1217(4)	4487(2)	6701(2)	28(1)
C(11)	760(4)	3731(2)	10444(2)	25(1)
C(15)	-597(5)	2309(2)	11161(2)	41(1)
C(3)	631(4)	5933(2)	8965(2)	26(1)
C(12)	2749(4)	3637(2)	10870(1)	30(1)
C(13)	3007(4)	2886(2)	11438(2)	38(1)

Table 3. Bond lengths [Å] and angles [°] for gcf105t.

Br(1)-C(6)	1.897(2)
O(1)-C(1)	1.232(3)
C(2)-C(1)	1.515(3)
C(2)-C(3)	1.521(3)
N(2)-C(10)	1.295(3)
N(2)-N(1)	1.357(3)
N(2)-C(3)	1.521(3)
C(4)-C(9)	1.390(3)
C(4)-C(5)	1.393(3)
C(4)-C(3)	1.509(3)
N(1)-C(1)	1.352(3)
C(10)-C(11)	1.448(3)
C(8)-C(7)	1.381(3)
C(8)-C(9)	1.388(3)
C(6)-C(7)	1.381(3)
C(6)-C(5)	1.390(3)
C(16)-C(15)	1.374(4)
C(16)-C(11)	1.397(3)
C(14)-C(15)	1.381(4)
C(14)-C(13)	1.382(4)
C(11)-C(12)	1.407(3)
C(12)-C(13)	1.387(3)
C(1)-C(2)-C(3)	104.13(18)
C(10)-N(2)-N(1)	125.3(2)
C(10)-N(2)-C(3)	120.45(19)
N(1)-N(2)-C(3)	114.3(2)
C(9)-C(4)-C(5)	119.1(2)
C(9)-C(4)-C(3)	119.6(2)
C(5)-C(4)-C(3)	121.3(2)
C(1)-N(1)-N(2)	107.3(2)
N(2)-C(10)-C(11)	128.7(2)
C(7)-C(8)-C(9)	121.0(2)
C(7)-C(6)-C(5)	121.6(2)

C(7)-C(6)-Br(1)	118.26(18)
C(5)-C(6)-Br(1)	120.10(17)
C(15)-C(16)-C(11)	120.9(2)
C(15)-C(14)-C(13)	119.8(3)
O(1)-C(1)-N(1)	123.5(2)
O(1)-C(1)-C(2)	123.8(2)
N(1)-C(1)-C(2)	112.69(19)
C(8)-C(9)-C(4)	120.3(2)
C(6)-C(5)-C(4)	119.5(2)
C(6)-C(7)-C(8)	118.4(2)
C(16)-C(11)-C(12)	118.8(2)
C(16)-C(11)-C(10)	116.2(2)
C(12)-C(11)-C(10)	125.0(2)
C(16)-C(15)-C(14)	120.2(3)
C(4)-C(3)-N(2)	109.86(19)
C(4)-C(3)-C(2)	117.0(2)
N(2)-C(3)-C(2)	100.94(17)
C(13)-C(12)-C(11)	119.3(2)
C(14)-C(13)-C(12)	120.9(2)

Symmetry transformations used to generate equivalent atoms:

Table 4. Anisotropic displacement parameters ($\approx^2 \times 10^3$) for gcf105t. The anisotropic displacement factor exponent takes the form: $-2\pi^2 [h^2 a^{*2} U^{11} + \dots + 2 h k a^* b^* U^{12}]$

	U^{11}	U^{22}	U^{33}	U^{23}	U^{13}	U^{12}
Br(1)	42(1)	32(1)	30(1)	-4(1)	-2(1)	10(1)
O(1)	26(1)	44(1)	36(1)	-5(1)	4(1)	-10(1)
C(2)	35(1)	26(1)	33(1)	-2(1)	0(1)	-3(2)
N(2)	22(1)	27(1)	21(1)	-2(1)	1(1)	0(1)
C(4)	27(1)	22(1)	21(1)	5(1)	3(1)	-1(1)
N(1)	21(1)	33(1)	24(1)	0(1)	1(1)	-3(1)
C(10)	23(1)	32(1)	25(1)	-4(1)	0(1)	-2(1)
C(8)	24(1)	36(1)	29(1)	9(1)	-5(1)	-2(1)
C(6)	28(1)	21(1)	25(1)	2(1)	5(1)	4(1)
C(16)	34(1)	36(1)	28(1)	-1(1)	1(1)	-7(1)
C(14)	62(2)	38(2)	30(1)	8(1)	-1(2)	-2(1)
C(1)	27(1)	32(1)	22(1)	-3(1)	5(1)	-1(1)
C(9)	25(1)	28(1)	30(1)	6(1)	3(1)	3(1)
C(5)	22(1)	27(1)	28(1)	4(1)	-1(1)	4(1)
C(7)	32(1)	30(1)	22(1)	2(1)	-3(1)	-4(1)
C(11)	30(1)	26(1)	20(1)	-3(1)	3(1)	-2(1)
C(15)	48(2)	40(2)	35(2)	5(1)	3(1)	-12(1)
C(3)	22(1)	28(1)	27(1)	3(1)	2(1)	4(1)
C(12)	35(1)	30(1)	24(1)	-3(1)	0(1)	-2(1)
C(13)	44(2)	41(2)	29(1)	-3(1)	-5(1)	2(1)

Table 5. Hydrogen coordinates ($\times 10^4$) and isotropic displacement parameters ($\approx \times 10^{-3}$) for gcf105t.

	x	y	z	U(eq)
H(2A)	3050	6742	8363	38
H(2B)	2069	7301	9158	38
H(10A)	-1185	4486	9637	32
H(8A)	-3962	5295	6833	35
H(16A)	-2245	3110	10317	39
H(14A)	1554	1706	11968	52
H(9A)	-2970	6064	8063	33
H(5A)	2830	4648	8013	31
H(7A)	-1640	4161	6207	33
H(15A)	-1736	1853	11258	49
H(3A)	-684	6260	9203	31
H(12A)	3903	4084	10769	35
H(13A)	4340	2827	11733	46

Table 6. Torsion angles [$^{\circ}$] for gcf105t.

C(10)-N(2)-N(1)-C(1)	-170.8(2)
C(3)-N(2)-N(1)-C(1)	8.5(3)
N(1)-N(2)-C(10)-C(11)	0.7(4)
C(3)-N(2)-C(10)-C(11)	-178.6(2)
N(2)-N(1)-C(1)-O(1)	174.9(2)
N(2)-N(1)-C(1)-C(2)	-5.5(3)
C(3)-C(2)-C(1)-O(1)	-179.8(2)
C(3)-C(2)-C(1)-N(1)	0.6(3)
C(7)-C(8)-C(9)-C(4)	1.3(3)
C(5)-C(4)-C(9)-C(8)	-0.3(3)
C(3)-C(4)-C(9)-C(8)	-178.9(2)
C(7)-C(6)-C(5)-C(4)	1.1(3)
Br(1)-C(6)-C(5)-C(4)	-177.60(17)
C(9)-C(4)-C(5)-C(6)	-0.8(3)
C(3)-C(4)-C(5)-C(6)	177.7(2)
C(5)-C(6)-C(7)-C(8)	-0.1(3)
Br(1)-C(6)-C(7)-C(8)	178.59(17)
C(9)-C(8)-C(7)-C(6)	-1.1(3)
C(15)-C(16)-C(11)-C(12)	0.0(4)
C(15)-C(16)-C(11)-C(10)	-179.1(2)
N(2)-C(10)-C(11)-C(16)	-177.4(2)
N(2)-C(10)-C(11)-C(12)	3.5(4)
C(11)-C(16)-C(15)-C(14)	0.3(4)
C(13)-C(14)-C(15)-C(16)	0.0(4)
C(9)-C(4)-C(3)-N(2)	131.0(2)
C(5)-C(4)-C(3)-N(2)	-47.5(3)
C(9)-C(4)-C(3)-C(2)	-114.7(2)
C(5)-C(4)-C(3)-C(2)	66.8(3)
C(10)-N(2)-C(3)-C(4)	-64.3(3)
N(1)-N(2)-C(3)-C(4)	116.3(2)
C(10)-N(2)-C(3)-C(2)	171.6(2)
N(1)-N(2)-C(3)-C(2)	-7.8(3)
C(1)-C(2)-C(3)-C(4)	-115.2(2)
C(1)-C(2)-C(3)-N(2)	3.9(2)

C(16)-C(11)-C(12)-C(13)	-0.7(4)
C(10)-C(11)-C(12)-C(13)	178.3(2)
C(15)-C(14)-C(13)-C(12)	-0.6(4)
C(11)-C(12)-C(13)-C(14)	1.0(4)

Symmetry transformations used to generate equivalent atoms:

Product: Table 3, entry 3 (racemic crystal).

Note: Data were measured using omega scans of 0.3° per frame for 45 seconds, and data collected beyond $2\theta = 45^\circ$ were omitted due to crystal and data quality.

Table 1. Crystal data and structure refinement for gcf205t.

Identification code	gcf205t	
Empirical formula	C ₁₉ H ₁₈ N ₂ O ₃ S	
Formula weight	354.41	
Temperature	193(2) K	
Wavelength	0.71073 $\approx$	
Crystal system	Monoclinic	
Space group	P2(1)/n	
Unit cell dimensions	a = 5.9566(8) $\approx$	$\alpha = 90^\circ$.
	b = 18.493(3) $\approx$	$\beta = 95.980(3)^\circ$.
	c = 16.122(2) $\approx$	$\gamma = 90^\circ$.
Volume	1766.3(4) $\approx^3$	
Z	4	
Density (calculated)	1.333 Mg/m ³	
Absorption coefficient	0.203 mm ⁻¹	
F(000)	744	
Crystal size	0.15 x 0.14 x 0.03 mm ³	
Theta range for data collection	1.68 to 22.49 $^\circ$.	
Index ranges	-6 $\leq$ h $\leq$ 6, -19 $\leq$ k $\leq$ 19, -11 $\leq$ l $\leq$ 17	
Reflections collected	7516	
Independent reflections	2313 [R(int) = 0.0434]	
Completeness to theta = 22.49 $^\circ$	100.0 %	
Absorption correction	None	
Refinement method	Full-matrix least-squares on F ²	
Data / restraints / parameters	2313 / 0 / 226	
Goodness-of-fit on F ²	1.238	
Final R indices [I $\geq$ 2 σ (I)]	R1 = 0.0725, wR2 = 0.1346	
R indices (all data)	R1 = 0.0960, wR2 = 0.1434	
Largest diff. peak and hole	0.204 and -0.160 e. $\approx^3$	

Table 2. Atomic coordinates ($\times 10^4$) and equivalent isotropic displacement parameters ($\text{\AA}^2 \times 10^3$) for gcf205t. $U(\text{eq})$ is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	$U(\text{eq})$
S(1)	-9100(2)	-221(1)	-6104(1)	57(1)
O(3)	-6606(5)	1567(1)	-9282(2)	42(1)
N(2)	-10109(5)	36(2)	-7952(2)	29(1)
O(2)	-9591(5)	1542(2)	-10258(2)	51(1)
O(1)	-14797(4)	-791(2)	-9058(2)	47(1)
N(1)	-11888(5)	-21(2)	-8631(2)	33(1)
C(16)	-7576(7)	1064(2)	-7617(2)	31(1)
C(9)	-9520(6)	792(2)	-9070(2)	29(1)
C(17)	-8622(7)	1328(2)	-9605(3)	35(1)
C(1)	-13104(7)	-643(2)	-8599(3)	37(1)
C(10)	-8322(6)	501(2)	-8261(2)	28(1)
C(4)	-8393(7)	-785(2)	-6884(2)	34(1)
C(11)	-9062(7)	1577(2)	-7391(3)	40(1)
C(5)	-6775(7)	-1265(2)	-6582(3)	42(1)
C(8)	-11523(6)	465(2)	-9242(3)	34(1)
C(3)	-9573(6)	-731(2)	-7744(2)	33(1)
C(2)	-11931(7)	-1067(2)	-7883(3)	39(1)
C(13)	-6207(10)	2091(3)	-6419(3)	64(2)
C(15)	-5375(7)	1070(2)	-7235(3)	45(1)
C(12)	-8391(9)	2092(2)	-6792(3)	55(1)
C(14)	-4703(9)	1582(3)	-6632(3)	64(2)
C(19)	-3890(7)	2502(2)	-9114(3)	62(1)
C(6)	-6132(8)	-1168(3)	-5721(3)	59(1)
C(18)	-5604(8)	2155(2)	-9715(3)	53(1)
C(7)	-7235(8)	-634(3)	-5390(3)	59(1)

Table 3. Bond lengths [Å] and angles [°] for gcf205t.

S(1)-C(7)	1.697(5)
S(1)-C(4)	1.720(4)
O(3)-C(17)	1.333(5)
O(3)-C(18)	1.453(5)
N(2)-N(1)	1.446(4)
N(2)-C(3)	1.484(5)
N(2)-C(10)	1.494(5)
O(2)-C(17)	1.211(4)
O(1)-C(1)	1.218(4)
N(1)-C(1)	1.363(5)
N(1)-C(8)	1.368(5)
C(16)-C(11)	1.373(5)
C(16)-C(15)	1.389(5)
C(16)-C(10)	1.503(5)
C(9)-C(8)	1.340(5)
C(9)-C(17)	1.452(5)
C(9)-C(10)	1.519(5)
C(1)-C(2)	1.507(6)
C(4)-C(5)	1.362(5)
C(4)-C(3)	1.492(5)
C(11)-C(12)	1.385(6)
C(5)-C(6)	1.413(6)
C(3)-C(2)	1.531(5)
C(13)-C(14)	1.368(7)
C(13)-C(12)	1.375(6)
C(15)-C(14)	1.386(6)
C(19)-C(18)	1.479(6)
C(6)-C(7)	1.329(6)
C(7)-S(1)-C(4)	91.7(2)
C(17)-O(3)-C(18)	117.3(3)
N(1)-N(2)-C(3)	103.1(3)
N(1)-N(2)-C(10)	106.3(3)
C(3)-N(2)-C(10)	118.8(3)

C(1)-N(1)-C(8)	135.0(3)
C(1)-N(1)-N(2)	112.5(3)
C(8)-N(1)-N(2)	109.8(3)
C(11)-C(16)-C(15)	118.8(4)
C(11)-C(16)-C(10)	120.6(3)
C(15)-C(16)-C(10)	120.6(4)
C(8)-C(9)-C(17)	124.0(4)
C(8)-C(9)-C(10)	110.3(3)
C(17)-C(9)-C(10)	125.7(3)
O(2)-C(17)-O(3)	124.0(4)
O(2)-C(17)-C(9)	124.5(4)
O(3)-C(17)-C(9)	111.5(3)
O(1)-C(1)-N(1)	125.2(4)
O(1)-C(1)-C(2)	129.6(4)
N(1)-C(1)-C(2)	105.2(3)
N(2)-C(10)-C(16)	109.8(3)
N(2)-C(10)-C(9)	101.7(3)
C(16)-C(10)-C(9)	115.3(3)
C(5)-C(4)-C(3)	128.6(4)
C(5)-C(4)-S(1)	110.7(3)
C(3)-C(4)-S(1)	120.7(3)
C(16)-C(11)-C(12)	120.9(4)
C(4)-C(5)-C(6)	112.2(4)
C(9)-C(8)-N(1)	110.6(3)
N(2)-C(3)-C(4)	110.1(3)
N(2)-C(3)-C(2)	100.5(3)
C(4)-C(3)-C(2)	116.4(3)
C(1)-C(2)-C(3)	104.2(3)
C(14)-C(13)-C(12)	120.4(4)
C(14)-C(15)-C(16)	120.5(4)
C(13)-C(12)-C(11)	119.7(5)
C(13)-C(14)-C(15)	119.8(5)
C(7)-C(6)-C(5)	113.2(4)
O(3)-C(18)-C(19)	107.6(4)
C(6)-C(7)-S(1)	112.2(4)

Symmetry transformations used to generate equivalent atoms:

Table 4. Anisotropic displacement parameters ($\approx \times 10^3$) for gcf205t. The anisotropic displacement factor exponent takes the form: $-2\pi^2 [h^2 a^{*2} U^{11} + \dots + 2 h k a^* b^* U^{12}]$

	U^{11}	U^{22}	U^{33}	U^{23}	U^{13}	U^{12}
S(1)	77(1)	57(1)	36(1)	-6(1)	3(1)	11(1)
O(3)	48(2)	42(2)	34(2)	5(1)	2(1)	-11(1)
N(2)	26(2)	30(2)	31(2)	-2(2)	-2(2)	-1(2)
O(2)	56(2)	56(2)	39(2)	15(2)	-4(2)	5(2)
O(1)	32(2)	51(2)	58(2)	-15(2)	-1(2)	-5(1)
N(1)	28(2)	33(2)	36(2)	-1(2)	-3(2)	-1(2)
C(16)	32(2)	34(2)	27(2)	5(2)	2(2)	-6(2)
C(9)	30(2)	29(2)	27(2)	-5(2)	2(2)	3(2)
C(17)	45(3)	31(2)	27(2)	-3(2)	4(2)	6(2)
C(1)	30(2)	40(3)	42(3)	-17(2)	11(2)	-3(2)
C(10)	26(2)	29(2)	30(2)	0(2)	4(2)	2(2)
C(4)	39(2)	30(2)	36(2)	5(2)	7(2)	-7(2)
C(11)	50(3)	38(2)	32(2)	-8(2)	-1(2)	4(2)
C(5)	40(3)	49(3)	39(3)	7(2)	10(2)	1(2)
C(8)	35(3)	33(2)	33(2)	-3(2)	-2(2)	7(2)
C(3)	37(2)	29(2)	35(2)	1(2)	10(2)	-3(2)
C(2)	44(3)	34(2)	40(3)	-5(2)	7(2)	-8(2)
C(13)	87(4)	61(3)	42(3)	-12(3)	4(3)	-35(3)
C(15)	38(3)	62(3)	33(3)	1(2)	3(2)	-7(2)
C(12)	78(4)	44(3)	43(3)	-6(2)	9(3)	-3(3)
C(14)	55(3)	94(4)	41(3)	-7(3)	-2(3)	-30(3)
C(19)	55(3)	42(3)	88(4)	-4(3)	9(3)	-10(2)
C(6)	48(3)	81(4)	48(3)	18(3)	2(3)	12(3)
C(18)	77(3)	35(3)	50(3)	1(2)	15(3)	-13(2)
C(7)	66(3)	75(4)	36(3)	3(3)	-1(3)	-10(3)

Table 5. Hydrogen coordinates ($\times 10^4$) and isotropic displacement parameters ($\text{\AA}^2 \times 10^{-3}$) for gcf205t.

	x	y	z	U(eq)
H(10A)	-7005	198	-8381	34
H(11A)	-10570	1580	-7650	49
H(5A)	-6152	-1624	-6913	50
H(8A)	-12547	559	-9722	41
H(3A)	-8596	-936	-8154	40
H(2A)	-11843	-1586	-8026	47
H(2B)	-12734	-1017	-7378	47
H(13A)	-5741	2447	-6012	76
H(15A)	-4323	721	-7388	54
H(12A)	-9435	2444	-6639	66
H(14A)	-3202	1579	-6367	77
H(19A)	-3175	2901	-9390	92
H(19B)	-2742	2146	-8915	92
H(19C)	-4617	2691	-8641	92
H(6A)	-5023	-1456	-5410	71
H(18A)	-6777	2510	-9920	64
H(18B)	-4891	1966	-10198	64
H(7B)	-7005	-499	-4818	71

Table 6. Torsion angles [°] for gcf205t.

C(3)-N(2)-N(1)-C(1)	27.4(4)
C(10)-N(2)-N(1)-C(1)	153.2(3)
C(3)-N(2)-N(1)-C(8)	-136.8(3)
C(10)-N(2)-N(1)-C(8)	-11.0(4)
C(18)-O(3)-C(17)-O(2)	4.6(6)
C(18)-O(3)-C(17)-C(9)	-174.4(3)
C(8)-C(9)-C(17)-O(2)	0.7(6)
C(10)-C(9)-C(17)-O(2)	178.4(4)
C(8)-C(9)-C(17)-O(3)	179.7(4)
C(10)-C(9)-C(17)-O(3)	-2.6(5)
C(8)-N(1)-C(1)-O(1)	-27.5(7)
N(2)-N(1)-C(1)-O(1)	173.8(4)
C(8)-N(1)-C(1)-C(2)	153.9(4)
N(2)-N(1)-C(1)-C(2)	-4.8(4)
N(1)-N(2)-C(10)-C(16)	133.2(3)
C(3)-N(2)-C(10)-C(16)	-111.4(3)
N(1)-N(2)-C(10)-C(9)	10.6(3)
C(3)-N(2)-C(10)-C(9)	126.1(3)
C(11)-C(16)-C(10)-N(2)	-63.4(4)
C(15)-C(16)-C(10)-N(2)	116.1(4)
C(11)-C(16)-C(10)-C(9)	50.7(5)
C(15)-C(16)-C(10)-C(9)	-129.8(4)
C(8)-C(9)-C(10)-N(2)	-7.4(4)
C(17)-C(9)-C(10)-N(2)	174.6(3)
C(8)-C(9)-C(10)-C(16)	-126.1(4)
C(17)-C(9)-C(10)-C(16)	55.9(5)
C(7)-S(1)-C(4)-C(5)	-0.1(3)
C(7)-S(1)-C(4)-C(3)	177.4(3)
C(15)-C(16)-C(11)-C(12)	-0.2(6)
C(10)-C(16)-C(11)-C(12)	179.3(4)
C(3)-C(4)-C(5)-C(6)	-177.2(4)
S(1)-C(4)-C(5)-C(6)	0.0(5)
C(17)-C(9)-C(8)-N(1)	178.9(3)
C(10)-C(9)-C(8)-N(1)	0.9(4)

C(1)-N(1)-C(8)-C(9)	-152.7(4)
N(2)-N(1)-C(8)-C(9)	6.4(4)
N(1)-N(2)-C(3)-C(4)	-159.9(3)
C(10)-N(2)-C(3)-C(4)	83.0(4)
N(1)-N(2)-C(3)-C(2)	-36.5(4)
C(10)-N(2)-C(3)-C(2)	-153.7(3)
C(5)-C(4)-C(3)-N(2)	-147.1(4)
S(1)-C(4)-C(3)-N(2)	35.9(4)
C(5)-C(4)-C(3)-C(2)	99.4(5)
S(1)-C(4)-C(3)-C(2)	-77.6(4)
O(1)-C(1)-C(2)-C(3)	162.5(4)
N(1)-C(1)-C(2)-C(3)	-19.0(4)
N(2)-C(3)-C(2)-C(1)	34.4(4)
C(4)-C(3)-C(2)-C(1)	153.2(3)
C(11)-C(16)-C(15)-C(14)	0.6(6)
C(10)-C(16)-C(15)-C(14)	-178.9(4)
C(14)-C(13)-C(12)-C(11)	-0.6(7)
C(16)-C(11)-C(12)-C(13)	0.2(7)
C(12)-C(13)-C(14)-C(15)	0.9(7)
C(16)-C(15)-C(14)-C(13)	-0.9(7)
C(4)-C(5)-C(6)-C(7)	0.1(6)
C(17)-O(3)-C(18)-C(19)	159.5(4)
C(5)-C(6)-C(7)-S(1)	-0.2(6)
C(4)-S(1)-C(7)-C(6)	0.2(4)

Symmetry transformations used to generate equivalent atoms:

References

- (1) Kagan, H. B.; Fiaud, J. C. *Top. Stereochem.* **1988**, *18*, 249-330.
- (2) For syntheses of related planar-chiral ligands, see: Shintani, R.; Lo, M. M.-C.; Fu, G. C. *Org. Lett.* **2000**, *2*, 3695–3697.