**A New Copper-Catalyzed [3+2] Cycloaddition:
Enantioselective Coupling of Terminal Alkynes with Azomethine Imines to Generate
Five-Membered Nitrogen Heterocycles**

Ryo Shintani and Gregory C. Fu*

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

Supporting Information

I. General

CH₂Cl₂ was purified by passing through a neutral alumina column under argon.

Cy₂NMe (Aldrich) was distilled over KOH under vacuum. CuI (99.999% Cu; Strem) was used as received. Ethyl propiolate (Aldrich), 3-butyne-2-one (Aldrich), 4-ethynyl- α,α,α -trifluorotoluene (Aldrich), 2-ethynylpyridine (Aldrich), and phenylacetylene (Avocado) were distilled under vacuum prior to use. Pyrazolidin-3-one (commercially available from Acros and Pfaltz & Bauer as the HCl salt) and 5,5-dimethylpyrazolidin-3-one were synthesized following a literature procedure.¹

All other chemicals and solvents were purchased from Aldrich, Mallinckrodt, EM Science, or J. T. Baker and used as received.

All air- and moisture-sensitive manipulations were carried out under argon with standard Schlenk techniques or under nitrogen in a glove box.

II. Synthesis of Substrates

The yields have not been optimized.

1-Benzylidene-3-oxopyrazolidin-1-ium-2-ide. Benzaldehyde (1.07 mL, 10.5 mmol) was added to a solution of pyrazolidin-3-one (861 mg, 10.0 mmol) in methanol (1.0 mL). The mixture was stirred for 10 min at room temperature and then diluted with Et₂O (5.0 mL). The precipitate was collected by filtration, washed with Et₂O, and dried under vacuum to afford 1-benzylidene-3-oxopyrazolidin-1-ium-2-ide as a white solid (1.26 g, 7.24 mmol; 72%).

¹H NMR (CDCl₃): δ 8.27-8.24 (m, 2H), 7.44-7.41 (m, 3H), 7.17 (s, 1H), 4.54-4.49 (m, 2H), 2.78-2.73 (m, 2H). ¹³C NMR (CDCl₃): δ 184.9, 132.9, 131.8, 131.5, 129.1, 128.8, 58.0, 29.6. FTIR (neat) 3059, 2985, 1669, 1651, 1590, 1567, 1453, 1341, 1315, 1292, 1107, 952, 754, 687 cm⁻¹. M.p. 196-198 °C. HRMS (ESI) calcd for C₁₀H₁₁N₂O (M+H⁺) 175.0866, found 175.0869.

This was synthesized from 2-fluorobenzaldehyde and pyrazolidin-3-one following the procedure for 1-benzylidene-3-oxopyrazolidin-1-ium-2-ide. White solid, 76% yield.

¹H NMR (DMSO-*d*₆): δ 9.05-9.01 (m, 1H), 7.70 (s, 1H), 7.61-7.53 (m, 1H), 7.41-7.34 (m, 2H), 4.66-4.60 (m, 2H), 2.61-2.55 (m, 2H). ¹³C NMR (DMSO-*d*₆): δ 184.9, 160.3 (d, ¹J_{CF} = 254.1

Hz), 133.1 (d, $^3J_{\text{CF}} = 9.1$ Hz), 131.2, 124.9 (d, $^4J_{\text{CF}} = 3.6$ Hz), 123.2 (d, $^3J_{\text{CF}} = 9.4$ Hz), 118.1 (d, $^2J_{\text{CF}} = 8.8$ Hz), 115.4 (d, $^2J_{\text{CF}} = 21.1$ Hz), 58.2, 29.1. FTIR (neat) 3069, 3000, 1673, 1656, 1609, 1599, 1562, 1474, 1460, 1438, 1241, 1190, 1111, 956, 795, 759 cm^{-1} . M.p. 230-231 $^{\circ}\text{C}$ (dec). HRMS (ESI) calcd for $\text{C}_{10}\text{H}_{10}\text{FN}_2\text{O}$ ($\text{M}+\text{H}^+$) 193.0772, found 193.0775.

This was synthesized from 3-bromobenzaldehyde and pyrazolidin-3-one following the procedure for 1-benzylidene-3-oxopyrazolidin-1-ium-2-ide. White solid, 72% yield.

^1H NMR ($\text{DMSO}-d_6$): δ 8.70-8.69 (m, 1H), 8.12-8.10 (m, 1H), 7.72-7.66 (m, 2H), 7.53-7.47 (m, 1H), 4.61-4.56 (m, 2H), 2.60-2.55 (m, 2H). ^{13}C NMR ($\text{DMSO}-d_6$): δ 184.7, 133.4, 132.5, 132.1, 130.9, 129.93, 129.90, 121.9, 57.8, 29.1. FTIR (neat) 3052, 2982, 1671, 1652, 1592, 1437, 1398, 1345, 1306, 1108, 1090, 956, 785, 680 cm^{-1} . M.p. 235-236 $^{\circ}\text{C}$. HRMS (ESI) calcd for $\text{C}_{10}\text{H}_{10}\text{BrN}_2\text{O}$ ($\text{M}+\text{H}^+$) 252.9971, found 252.9980.

This was synthesized from 4-trifluoromethylbenzaldehyde and pyrazolidin-3-one following the procedure for 1-benzylidene-3-oxopyrazolidin-1-ium-2-ide. White solid, 76% yield.

^1H NMR ($\text{DMSO-}d_6$): δ 8.46 (d, $^3J_{\text{HH}} = 8.2$ Hz, 2H), 7.87 (d, $^3J_{\text{HH}} = 8.3$ Hz, 2H), 7.77 (s, 1H), 4.66-4.60 (m, 2H), 2.63-2.58 (m, 2H). ^{13}C NMR ($\text{DMSO-}d_6$): δ 185.0, 133.5 (q, $^4J_{\text{CF}} = 1.6$ Hz), 131.1, 129.9 (q, $^2J_{\text{CF}} = 32.1$ Hz), 129.8, 125.6 (q, $^3J_{\text{CF}} = 3.8$ Hz), 123.9 (q, $^1J_{\text{CF}} = 272.4$ Hz), 58.0, 29.1. FTIR (neat) 3065, 2991, 1678, 1659, 1615, 1590, 1565, 1444, 1342, 1313, 1287, 1157, 1114, 1071, 959, 892, 668 cm^{-1} . M.p. 231-233 $^{\circ}\text{C}$. HRMS (ESI) calcd for $\text{C}_{11}\text{H}_{10}\text{F}_3\text{N}_2\text{O}$ ($\text{M}+\text{H}^+$) 243.0740, found 243.0743.

This was synthesized from 1-cyclohexene-1-carboxaldehyde and pyrazolidin-3-one following the procedure for 1-benzylidene-3-oxopyrazolidin-1-ium-2-ide. Pale-yellow solid, 73% yield.

^1H NMR (CDCl_3): δ 7.12-7.09 (m, 1H), 6.61 (s, 1H), 4.39-4.33 (m, 2H), 2.75-2.69 (m, 2H), 2.61-2.56 (m, 2H), 2.37-2.28 (m, 2H), 1.72-1.58 (m, 4H). ^{13}C NMR (CDCl_3): δ 184.5, 144.4, 135.9, 130.8, 57.4, 29.6, 27.9, 26.9, 22.3, 21.2. FTIR (neat) 3062, 2999, 2951, 2929, 2860, 1660, 1616, 1590, 1448, 1338, 1297, 1264, 1114, 1099, 962, 919, 903, 658 cm^{-1} . M.p. 177-178 $^{\circ}\text{C}$ (dec). HRMS (ESI) calcd for $\text{C}_{10}\text{H}_{15}\text{N}_2\text{O}$ ($\text{M}+\text{H}^+$) 179.1179, found 179.1178.

This was synthesized from 1-hexanal and pyrazolidin-3-one following the procedure

for 1-benzylidene-3-oxopyrazolidin-1-ium-2-ide. White solid, 35% yield.

^1H NMR (CDCl_3): δ 6.58-6.52 (m, 1H), 4.40-4.33 (m, 2H), 2.85-2.66 (m, 4H), 1.66-1.56 (m, 2H), 1.42-1.27 (m, 4H), 0.92-0.88 (m, 3H). ^{13}C NMR (CDCl_3): δ 183.7, 140.5, 56.1, 31.6, 30.4, 29.6, 25.3, 22.4, 14.0. FTIR (neat) 3383, 3026, 2956, 2929, 2859, 1672, 1589, 1412, 1355, 1303, 1265, 1085, 956, 731, 667 cm^{-1} . M.p. 75-76 $^\circ\text{C}$. HRMS (ESI) calcd for $\text{C}_9\text{H}_{17}\text{N}_2\text{O}$ ($\text{M}+\text{H}^+$) 169.1335, found 169.1339.

This was synthesized from cyclohexanecarboxaldehyde and pyrazolidin-3-one following the procedure for 1-benzylidene-3-oxopyrazolidin-1-ium-2-ide. White solid, 64% yield.

^1H NMR (CDCl_3): δ 6.40-6.37 (m, 1H), 4.36-4.32 (m, 2H), 3.25-3.15 (m, 1H), 2.80-2.74 (m, 2H), 2.02-1.94 (m, 2H), 1.82-1.69 (m, 3H), 1.44-1.19 (m, 5H). ^{13}C NMR (CDCl_3): δ 183.8, 144.0, 56.2, 37.9, 30.2, 28.6, 25.6, 24.9. FTIR (neat) 3381, 3288, 3031, 2988, 2928, 2852, 1672, 1591, 1447, 1416, 1352, 1285, 1080, 960, 898, 669 cm^{-1} . M.p. 160-161 $^\circ\text{C}$. HRMS (ESI) calcd for $\text{C}_{10}\text{H}_{17}\text{N}_2\text{O}$ ($\text{M}+\text{H}^+$) 181.1335, found 181.1338.

This was synthesized from benzaldehyde and 5,5-dimethylpyrazolidin-3-one following the procedure for 1-benzylidene-3-oxopyrazolidin-1-ium-2-ide. White solid, 81% yield.

^1H NMR (CDCl_3): δ 8.38-8.35 (m, 2H), 7.51-7.49 (m, 3H), 7.04 (s, 1H), 2.79 (s, 2H), 1.76 (s, 6H). ^{13}C NMR (CDCl_3): δ 181.8, 131.82, 131.76, 130.3, 129.5, 128.7, 73.9, 44.4, 28.9. FTIR (neat) 3054, 2973, 2934, 2876, 1659, 1588, 1567, 1451, 1419, 1336, 1319, 1303, 1088, 948, 759, 692, 676 cm^{-1} . M.p. 140-142 $^\circ\text{C}$. HRMS (ESI) calcd for $\text{C}_{12}\text{H}_{15}\text{N}_2\text{O}$ ($\text{M}+\text{H}^+$) 203.1179, found 203.1181.

4,4-Dimethylpyrazolidin-3-one. (CAS 2941-18-6)² Et_3N (4.18 mL, 30.0 mmol) was added to a solution of 3-chloropivaloyl chloride (3.88 mL, 30.0 mmol) in ethanol (absolute; 10 mL) at 0 $^\circ\text{C}$. The mixture was stirred for 5 min at room temperature and then extracted with Et_2O /aqueous NaCl . The organic layer was dried over Na_2SO_4 , filtered, and concentrated. The residue was placed into a Schlenk tube with ethanol (absolute; 30 mL). Et_3N (4.18 mL, 30.0 mmol) and hydrazine monohydrate (1.60 mL, 33.0 mmol) were added, and the mixture was stirred for 43 h at 120 $^\circ\text{C}$. After cooling to room temperature, the volatiles were removed under vacuum, and the residue was chromatographed on silica gel with methanol/chloroform = 1/9 to afford 4,4-dimethylpyrazolidin-3-one as a white solid (1.04 g, 9.10 mmol; 30%).

^1H NMR (CDCl_3): δ 8.12 (br s, 1H), 4.49 (br s, 1H), 3.21 (s, 2H), 1.20 (s, 6H). ^{13}C NMR (CDCl_3): δ 181.7, 60.4, 40.5, 21.9.

This was synthesized from benzaldehyde and 4,4-dimethylpyrazolidin-3-one following the procedure for 1-benzylidene-3-oxopyrazolidin-1-ium-2-ide. White solid, 74% yield.

^1H NMR (CDCl_3): δ 8.34-8.32 (m, 2H), 7.49-7.47 (m, 3H), 7.13 (s, 1H), 4.33 (s, 2H), 1.38 (s, 6H). ^{13}C NMR (CDCl_3): δ 190.3, 132.5, 132.0, 131.8, 129.4, 129.0, 71.4, 40.6, 24.6. FTIR (neat) 3055, 2972, 2956, 2869, 1666, 1589, 1569, 1452, 1427, 1382, 1345, 1322, 1296, 1103, 943, 933, 758, 751, 690 cm^{-1} . M.p. 184-185 $^\circ\text{C}$. HRMS (ESI) calcd for $\text{C}_{12}\text{H}_{15}\text{N}_2\text{O}$ ($\text{M}+\text{H}^+$) 203.1179, found 203.1184.

III. Dipolar Cycloaddition Reactions

Because the yields that are reported in the paper are the average of two runs, the yields that are given below for a specific experiment may differ from the values in the paper.

Note: The use of a glove box is not required (see the final experimental in this section).

General procedure for Table 1. In a glove box, a solution of CuI (1.9 mg, 10 μ mol) and ligand (11 μ mol) in CH₂Cl₂ (1.0 mL) was stirred for 30 min at room temperature to obtain a Cu(I)/ligand complex. This solution was added to a vial containing azomethine imine **2** (34.8 mg, 0.200 mmol) and Cy₂NMe (21.4 μ L, 0.100 mmol), with the aid of additional CH₂Cl₂ (0.5 mL). A solution of ethyl propiolate (24.3 μ L, 0.240 mmol) in CH₂Cl₂ (0.5 mL) was added dropwise to the vial over 30 sec, and the resulting mixture was stirred for 20 h at room temperature. This mixture was loaded directly onto a column of silica gel (pretreated with Et₃N to deactivate it) and chromatographed with Et₂O/hexane = 3/1 $\rightarrow$ Et₂O to afford the desired product (**4**).

The ee was determined on a Daicel Chiralpak AD column with hexanes : isopropanol = 85 : 15, flow = 1 mL/min, detection at 330 nm, reference at 380 nm. Retention times: 11.2 min [(*R*)-enantiomer], 12.9 min [(*S*)-enantiomer].

¹H NMR (CDCl₃): δ 7.52 (d, ⁴*J*_{HH} = 0.5 Hz, 1H), 7.40-7.25 (m, 5H), 5.14 (d, ⁴*J*_{HH} = 1.7 Hz, 1H), 4.14-3.95 (m, 2H), 3.43-3.36 (m, 1H), 3.08-3.00 (m, 1H), 2.95-2.83 (m, 1H), 2.79-2.70 (m, 1H), 1.13 (t, ³*J*_{HH} = 7.2 Hz, 3H). ¹³C NMR (CDCl₃): δ 164.6, 163.3, 138.4, 128.6, 128.49, 128.47, 128.2, 118.4, 73.5, 60.6, 51.9, 36.0, 14.3. FTIR (neat) 3401, 3088, 3031, 2982, 2933, 2848, 1725, 1699, 1602, 1434, 1416, 1387, 1364, 1321, 1251, 1196, 1171, 1104, 1027, 843, 752, 700 cm⁻¹. HRMS (ESI) calcd for C₁₅H₁₆N₂O₃Na (M+Na⁺) 295.1053, found 295.1061.

General procedure for Table 2. In a glove box, a solution of CuI (2.9 mg, 15 μ mol) and ligand **6a** (6.8 mg, 16 μ mol) in CH₂Cl₂ (1.5 mL) was stirred for 30 min at room

temperature to obtain a Cu(I)/**6a** complex. This solution was added to a vial containing the azomethine imine (0.30 mmol) and Cy₂NMe (32 μ L, 0.15 mmol), with the aid of additional CH₂Cl₂ (0.7 mL). A solution of ethyl propiolate (36.5 μ L, 0.360 mmol) in CH₂Cl₂ (0.8 mL) was added dropwise to the vial over 30 sec, and the resulting mixture was stirred for 20 h at room temperature. This mixture was loaded directly onto a column of silica gel (pretreated with Et₃N to deactivate it) and chromatographed to afford the desired product.

Table 2, entry 1. Eluant for chromatography: Et₂O/hexane = 3/1 $\rightarrow$ Et₂O. Yellow oil. 98% yield. 91% ee. $[\alpha]_D^{20}$ -442 (*c* 1.06, CHCl₃). The absolute configuration was assigned by analogy with Table 3, entry 6.

Table 2, entry 2. Eluant for chromatography: Et₂O/hexane = 2/1 $\rightarrow$ Et₂O. Yellow oil. 99% yield. The ee was determined on a Daicel Chiralpak AD column with hexanes : isopropanol = 85 : 15, flow = 1 mL/min, detection at 330 nm, reference at 380 nm. Retention times: 10.6 min [(*R*)-enantiomer], 12.0 min [(*S*)-enantiomer]. 79% ee. $[\alpha]_D^{20}$ -242 (*c* 1.05, CHCl₃). The absolute configuration was assigned by analogy with Table 3, entry 6.

¹H NMR (CDCl₃): δ 7.57-7.56 (m, 1H), 7.36-7.25 (m, 2H), 7.17-7.03 (m, 2H), 5.55 (d, ⁴*J*_{HH} = 1.7 Hz, 1H), 4.17-3.99 (m, 2H), 3.48-3.41 (m, 1H), 3.19-3.10 (m, 1H), 2.94-2.71 (m, 2H), 1.14 (t, ³*J*_{HH} = 6.9 Hz, 3H). ¹³C NMR (CDCl₃): δ 164.8, 163.2, 161.0 (d, ¹*J*_{CF} = 247.4 Hz), 130.1 (d, ³*J*_{CF} = 8.5 Hz), 129.5 (d, ³*J*_{CF} = 3.8 Hz), 129.4, 125.5 (d, ²*J*_{CF} = 12.5 Hz), 124.5 (d, ⁴*J*_{CF} = 3.6 Hz), 116.8, 115.6 (d, ²*J*_{CF} = 21.7 Hz), 66.1 (d, ³*J*_{CF} = 3.2 Hz), 60.7, 52.1, 35.9, 14.3. FTIR (neat) 3406, 3087, 2983, 2934, 2851, 1727, 1699, 1605, 1491, 1434, 1388, 1364, 1322, 1252, 1200, 1171, 1105, 1026, 926, 842, 760 cm⁻¹. HRMS (ESI) calcd for C₁₅H₁₅FN₂O₃Na (M+Na⁺) 313.0959, found 313.0967.

Table 2, entry 3. Eluant for chromatography: Et₂O/hexane = 2/1 $\rightarrow$ Et₂O. Yellow oil. 99% yield. The ee was determined on a Daicel Chiralpak AD column with hexanes : isopropanol = 85 : 15, flow = 1 mL/min, detection at 330 nm, reference at 380 nm. Retention times: 10.7 min [(*R*)-enantiomer], 12.4 min [(*S*)-enantiomer]. 84% ee. $[\alpha]_D^{20}$ -384

S-9

(c 1.05, CHCl₃). The absolute configuration was assigned by analogy with Table 3, entry 6.

¹H NMR (CDCl₃): δ 7.55-7.51 (m, 2H), 7.45-7.41 (m, 1H), 7.35-7.31 (m, 1H), 7.24-7.19 (m, 1H), 5.09 (d, ⁴J_{HH} = 1.7 Hz, 1H), 4.16-3.97 (m, 2H), 3.50-3.45 (m, 1H), 3.10-2.88 (m, 2H), 2.78-2.70 (m, 1H), 1.16 (t, ³J_{HH} = 7.2 Hz, 3H). ¹³C NMR (CDCl₃): δ 164.7, 163.2, 141.2, 131.5, 131.3, 130.0, 128.8, 127.1, 122.6, 117.7, 73.2, 60.7, 52.4, 35.8, 14.4. FTIR (neat) 3408, 3086, 2981, 2932, 2847, 2250, 1728, 1699, 1600, 1430, 1387, 1364, 1319, 1248, 1198, 1171, 1105, 1024, 761, 731 cm⁻¹. HRMS (ESI) calcd for C₁₅H₁₅BrN₂O₃Na (M+Na⁺) 373.0158, found 373.0157.

Table 2, entry 4. Eluant for chromatography: Et₂O/hexane = 2/1 → Et₂O. Yellow oil. 97% yield. The ee was determined on a Daicel Chiralpak AD column with hexanes : isopropanol = 80 : 20, flow = 1 mL/min, detection at 330 nm, reference at 380 nm. Retention times: 7.8 min [(R)-enantiomer], 10.8 min [(S)-enantiomer]. 94% ee. [α]_D²⁰ -410 (c 1.22, CHCl₃). The absolute configuration was assigned by analogy with Table 3, entry 6.

¹H NMR (CDCl₃): δ 7.63-7.53 (m, 5H), 5.19 (d, ⁴J_{HH} = 1.7 Hz, 1H), 4.16-3.97 (m, 2H), 3.53-3.47 (m, 1H), 3.13-2.89 (m, 2H), 2.79-2.71 (m, 1H), 1.15 (t, ³J_{HH} = 7.2 Hz, 3H). ¹³C NMR (CDCl₃): δ 164.8, 163.2, 143.0, 130.5 (q, ²J_{CF} = 32.3 Hz), 128.9, 128.7, 125.5 (q, ³J_{CF} = 3.8 Hz), 124.1 (q, ¹J_{CF} = 271.7 Hz), 117.5, 73.5, 60.8, 52.6, 35.8, 14.3. FTIR (neat) 3408, 3086, 2985, 2938, 2847, 1729, 1699, 1603, 1419, 1389, 1365, 1325, 1251, 1198, 1169, 1122, 1067, 1019, 860, 773 cm⁻¹. HRMS (ESI) calcd for C₁₆H₁₅F₃N₂O₃Na (M+Na⁺) 363.0927, found 363.0921.

Table 2, entry 5. Eluant for chromatography: Et₂O/hexane = 2/1 → Et₂O. Yellow oil. 99% yield. The ee was determined on a Daicel Chiralpak AD column with hexanes : isopropanol = 90 : 10, flow = 1 mL/min, detection at 330 nm, reference at 380 nm. Retention times: 9.9 min [(R)-enantiomer], 11.2 min [(S)-enantiomer]. 92% ee. [α]_D²⁰ -376 (c 1.21, CHCl₃). The absolute configuration was assigned by analogy with Table 3, entry 6.

¹H NMR (CDCl₃): δ 7.41-7.40 (m, 1H), 5.70-5.68 (m, 1H), 4.49 (d, ⁴J_{HH} = 1.7 Hz, 1H), 4.27-4.05 (m, 2H), 3.58-3.50 (m, 1H), 3.00-2.87 (m, 2H), 2.76-2.65 (m, 1H), 2.17-2.03 (m, 3H), 1.84-1.77 (m, 1H), 1.70-1.53 (m, 4H), 1.25 (t, ³J_{HH} = 7.2 Hz, 3H). ¹³C NMR (CDCl₃): δ 164.6, 163.6, 134.5, 129.3, 127.5, 117.2, 77.1, 60.5, 52.4, 35.9, 25.5, 25.2, 22.8, 22.6, 14.5. FTIR (neat)

3401, 3086, 2980, 2929, 2857, 2836, 1727, 1699, 1600, 1434, 1417, 1387, 1364, 1249, 1200, 1171, 1103, 1026, 787 cm^{-1} . HRMS (ESI) calcd for $\text{C}_{15}\text{H}_{20}\text{N}_2\text{O}_3\text{Na}$ ($\text{M}+\text{Na}^+$) 199.1366, found 199.1377.

Table 2, entry 6. Eluant for chromatography: Et_2O /hexane = 1/1 $\rightarrow$ Et_2O . Pale-yellow oil. 92% yield. The ee was determined on a Daicel Chiralpak AD column with hexanes : isopropanol = 90 : 10, flow = 1 mL/min, detection at 330 nm, reference at 380 nm. Retention times: 6.6 min [(*R*)-enantiomer], 7.8 min [(*S*)-enantiomer]. 82% ee. $[\alpha]_{\text{D}}^{20}$ -412 (*c* 1.05, CHCl_3). The absolute configuration was assigned by analogy with Table 3, entry 6.

^1H NMR (CDCl_3): δ 7.36-7.35 (m, 1H), 4.27-4.09 (m, 3H), 3.65-3.62 (m, 1H), 3.04-2.90 (m, 2H), 2.70-2.58 (m, 1H), 1.97-1.88 (m, 1H), 1.71-1.62 (m, 1H), 1.43-1.27 (m, 6H), 1.29 (t, $^3J_{\text{HH}}$ = 6.9 Hz, 3H), 0.89 (t, $^3J_{\text{HH}}$ = 6.3 Hz, 3H). ^{13}C NMR (CDCl_3): δ 165.6, 163.9, 129.3, 117.6, 71.0, 60.6, 55.0, 35.6, 33.8, 31.9, 25.4, 22.9, 14.6, 14.4. FTIR (neat) 3409, 3090, 2956, 2929, 2858, 1728, 1699, 1603, 1416, 1387, 1364, 1324, 1255, 1232, 1199, 1171, 1105, 1025, 952, 822, 758 cm^{-1} .

Table 2, entry 7. Eluant for chromatography: Et_2O /hexane = 1/1 $\rightarrow$ Et_2O . Pale-yellow solid. 96% yield. The ee was determined on a Daicel Chiralcel OJ column with hexanes : isopropanol = 90 : 10, flow = 1 mL/min, detection at 330 nm, reference at 380 nm. Retention times: 8.6 min [(*R*)-enantiomer], 11.0 min [(*S*)-enantiomer]. 96% ee. $[\alpha]_{\text{D}}^{20}$ -448 (*c* 1.09, CHCl_3). The absolute configuration was assigned by analogy with Table 3, entry 6.

^1H NMR (CDCl_3): δ 7.37-7.36 (m, 1H), 4.28-4.10 (m, 2H), 4.05-4.03 (m, 1H), 3.60-3.55 (m, 1H), 3.03-2.88 (m, 2H), 2.66-2.54 (m, 1H), 2.04-1.95 (m, 1H), 1.80-1.07 (m, 10H), 1.28 (t, $^3J_{\text{HH}}$ = 7.2 Hz, 3H). ^{13}C NMR (CDCl_3): δ 166.5, 164.0, 129.7, 115.9, 75.9, 60.6, 56.4, 39.5, 35.4, 30.5, 27.0, 26.8, 26.6, 26.3, 14.6. FTIR (neat) 3116, 2981, 2928, 2853, 1728, 1698, 1606, 1415, 1387, 1363, 1326, 1301, 1257, 1194, 1107, 1023, 964, 755 cm^{-1} . M.p. 114-115 $^{\circ}\text{C}$. HRMS (ESI) calcd for $\text{C}_{15}\text{H}_{22}\text{N}_2\text{O}_3\text{Na}$ ($\text{M}+\text{Na}^+$) 301.1523, found 301.1529.

Procedure for Equation 3. In a glove box, a solution of CuI (2.9 mg, 15 μmol) and

S-11

ligand **6a** (6.8 mg, 16 μ mol) in CH_2Cl_2 (1.5 mL) was stirred for 30 min at room temperature to obtain a Cu(I)/**6a** complex. This solution was added to a vial containing the azomethine imine (0.30 mmol) and Cy_2NMe (32 μ L, 0.15 mmol), with the aid of additional CH_2Cl_2 (0.7 mL). A solution of ethyl propiolate (36.5 μ L, 0.360 mmol) in CH_2Cl_2 (0.8 mL) was added dropwise to the vial over 30 sec, and the resulting mixture was stirred for 20 h at room temperature. This mixture was loaded directly onto a column of silica gel (pretreated with Et_3N to deactivate it) and eluted with Et_2O /hexane = 1/2 $\rightarrow$ Et_2O to afford the desired product.

R = Me, R¹ = H. Yellow oil. 99% yield. The ee was determined on a Daicel Chiralpak AD column with hexanes : isopropanol = 90 : 10, flow = 1 mL/min, detection at 330 nm, reference at 380 nm. Retention times: 7.6 min [(*S*)-enantiomer], 8.5 min [(*R*)-enantiomer]. 98% ee. $[\alpha]_{\text{D}}^{20}$ -681 (*c* 1.31, CHCl_3). The absolute configuration was assigned by analogy with Table 3, entry 6.

^1H NMR (CDCl_3): δ 7.52 (d, $^4J_{\text{HH}} = 1.7$ Hz, 1H), 7.47-7.43 (m, 2H), 7.37-7.25 (m, 3H), 5.46 (d, $^4J_{\text{HH}} = 1.4$ Hz, 1H), 4.16-3.95 (m, 2H), 2.87 (d, $^2J_{\text{HH}} = 15.7$ Hz, 1H), 2.39 (d, $^2J_{\text{HH}} = 15.7$ Hz, 1H), 1.24 (s, 3H), 1.15 (t, $^3J_{\text{HH}} = 7.2$ Hz, 3H), 1.14 (s, 3H). ^{13}C NMR (CDCl_3): δ 166.6, 163.8, 142.2, 129.4, 128.5, 128.01, 127.95, 117.4, 64.7, 64.6, 60.5, 49.5, 25.1, 19.2, 14.2. FTIR (neat) 3587, 3088, 3031, 2978, 2932, 2872, 1732, 1699, 1603, 1435, 1385, 1363, 1323, 1256, 1227, 1207, 1119, 1099, 1045, 1029, 1010, 936, 848, 753, 699 cm^{-1} . HRMS (ESI) calcd for $\text{C}_{17}\text{H}_{20}\text{N}_2\text{O}_3\text{Na}$ ($\text{M}+\text{Na}^+$) 323.1366, found 323.1360.

R = H, R¹ = Me. Yellow oil. 100% yield. The ee was determined on a Daicel Chiralpak AD column with hexanes : isopropanol = 95 : 5, flow = 1 mL/min, detection at 330 nm, reference at 380 nm. Retention times: 14.6 min [(*S*)-enantiomer], 16.0 min [(*R*)-enantiomer]. 96% ee. $[\alpha]_{\text{D}}^{20}$ -371 (*c* 1.01, CHCl_3). The absolute configuration was assigned by analogy with Table 3, entry 6.

^1H NMR (CDCl_3): δ 7.54-7.53 (m, 1H), 7.42-7.30 (m, 5H), 5.14 (d, $^4J_{\text{HH}} = 1.7$ Hz, 1H), 4.15-3.96 (m, 2H), 3.12 (d, $^2J_{\text{HH}} = 8.5$ Hz, 1H), 2.81 (d, $^2J_{\text{HH}} = 8.5$ Hz, 1H), 1.29 (s, 3H), 1.27 (s,

S-12

3H), 1.13 (t, $^3J_{\text{HH}} = 6.9$ Hz, 3H). ^{13}C NMR (CDCl_3): δ 170.3, 163.6, 138.6, 128.7, 128.53, 128.48, 118.8, 73.0, 64.4, 60.5, 46.9, 22.7, 22.4, 14.2. FTIR (neat) 3404, 3088, 3032, 2974, 2933, 2871, 2825, 1699, 1602, 1427, 1389, 1364, 1320, 1249, 1217, 1164, 1099, 1014, 940, 831, 752, 719, 700 cm^{-1} . HRMS (ESI) calcd for $\text{C}_{17}\text{H}_{20}\text{N}_2\text{O}_3\text{Na}$ ($\text{M}+\text{Na}^+$) 323.1366, found 323.1372.

General procedure for Table 3. In a glove box, a solution of CuI (2.9 mg, 15 μmol) and ligand **6a** (6.8 mg, 16 μmol) in CH_2Cl_2 (1.5 mL) was stirred for 30 min at room temperature to obtain a Cu(I)/**6a** complex. This solution was added to a vial containing azomethine imine **2** (52.3 mg, 0.300 mmol) and Cy_2NMe (32 μL , 0.15 mmol), with the aid of additional CH_2Cl_2 (0.7 mL). A solution of the alkyne (0.36 mmol) in CH_2Cl_2 (0.8 mL) was added dropwise to the vial over 30 sec, and the resulting mixture was stirred for 20 h at room temperature. This mixture was loaded directly onto a column of silica gel (pretreated with Et_3N to deactivate it) and chromatographed to afford the desired product.

Table 3, entry 2. Eluant for chromatography: $\text{Et}_2\text{O} \rightarrow \text{Et}_2\text{O}/\text{EtOAc} = 1/1$. Yellow oil. 98% yield. The ee was determined on a Daicel Chiralpak AD column with hexanes : isopropanol = 75 : 25, flow = 1 mL/min, detection at 360 nm, reference at 390 nm. Retention times: 8.0 min [(*R*)-enantiomer], 8.7 min [(*S*)-enantiomer]. 89% ee. $[\alpha]_{\text{D}}^{20} -473$ (c 1.08, CHCl_3). The absolute configuration was assigned by analogy with Table 3, entry 6.

^1H NMR (CDCl_3): δ 7.51 (s, 1H), 7.37-7.25 (m, 5H), 5.20 (d, $^4J_{\text{HH}} = 1.4$ Hz, 1H), 3.41-3.34 (m, 1H), 3.08-2.99 (m, 1H), 2.95-2.83 (m, 1H), 2.80-2.71 (m, 1H), 2.21 (s, 3H). ^{13}C NMR (CDCl_3): δ 192.6, 165.5, 138.2, 128.6, 128.5, 128.4, 128.1, 127.2, 73.2, 51.7, 35.9, 27.1. FTIR (neat) 3414, 3075, 3031, 2927, 2850, 2248, 1713, 1653, 1581, 1432, 1415, 1363, 1320, 1253, 1196, 1172, 1107, 1080, 985, 906, 825, 750, 701 cm^{-1} . HRMS (ESI) calcd for $\text{C}_{14}\text{H}_{14}\text{N}_2\text{O}_2\text{Na}$ ($\text{M}+\text{Na}^+$) 265.0947, found 265.0951.

Table 3, entry 3. Eluant for chromatography: $\text{Et}_2\text{O}/\text{EtOAc} = 1/1 \rightarrow \text{EtOAc}$. Pale-yellow oil. 100% yield. The ee was determined on a Daicel Chiralpak AD column with hexanes :

isopropanol = 50 : 50, flow = 0.9 mL/min, detection at 330 nm, reference at 380 nm. Retention times: 10.6 min [(S)-enantiomer], 23.2 min [(R)-enantiomer]. 94% ee. $[\alpha]_{\text{D}}^{20}$ -540 (c 1.11, CHCl₃). The absolute configuration was assigned by analogy with Table 3, entry 6.

¹H NMR (CDCl₃): δ 7.40-7.28 (m, 8H), 6.97-6.94 (m, 2H), 6.23-6.22 (m, 1H), 4.93 (d, ⁴J_{HH} = 1.9 Hz, 1H), 3.39-3.34 (m, 1H), 3.18 (s, 3H), 2.92-2.74 (m, 2H), 2.67-2.57 (m, 1H). ¹³C NMR (CDCl₃): δ 164.1, 163.8, 143.5, 138.7, 129.8, 128.6, 128.4, 128.2, 127.9, 127.2, 124.5, 121.9, 75.5, 52.4, 38.0, 35.9. FTIR (neat) 3486, 3062, 3032, 2979, 2930, 2838, 2246, 1705, 1633, 1592, 1495, 1443, 1406, 1356, 1304, 1272, 1216, 1159, 1105, 1030, 913, 844, 739, 699 cm⁻¹. HRMS (ESI) calcd for C₂₀H₁₉N₃O₂Na (M+Na⁺) 356.1369, found 356.1358.

Table 3, entry 4. The reaction was stirred for 63 h. Eluant for chromatography: Et₂O → Et₂O/EtOAc = 1/1. Yellow solid. 78% yield. The ee was determined on a Daicel Chiralpak AD column with hexanes : isopropanol = 75 : 25, flow = 1 mL/min, detection at 360 nm, reference at 390 nm. Retention times: 12.5 min [(R)-enantiomer], 22.0 min [(S)-enantiomer]. 88% ee. $[\alpha]_{\text{D}}^{20}$ -103 (c 1.10, CHCl₃). The absolute configuration was assigned by analogy with Table 3, entry 6.

¹H NMR (CDCl₃): δ 7.85-7.81 (m, 2H), 7.37-7.27 (m, 6H), 7.16-7.12 (m, 2H), 5.35 (d, ⁴J_{HH} = 1.7 Hz, 1H), 4.30 (q, ³J_{HH} = 6.9 Hz, 2H), 3.31-3.24 (m, 1H), 3.14-3.05 (m, 1H), 2.93-2.77 (m, 2H), 1.33 (t, ³J_{HH} = 7.2 Hz, 3H). ¹³C NMR (CDCl₃): δ 166.0, 162.3, 136.9, 136.5, 129.8, 129.1, 128.9, 128.7, 126.6, 125.1, 118.2, 74.4, 61.1, 50.9, 36.3, 14.6. FTIR (neat) 3087, 2982, 2935, 2870, 2249, 1710, 1600, 1562, 1435, 1415, 1367, 1277, 1257, 1184, 1108, 1020, 914, 858, 770, 732, 702 cm⁻¹. M.p. 127-129 °C. HRMS (ESI) calcd for C₂₁H₂₀N₂O₃Na (M+Na⁺) 371.1366, found 371.1360.

Table 3, entry 5. The reaction was stirred for 63 h. Eluant for chromatography: Et₂O → Et₂O/EtOAc = 1/1. Pale-yellow solid. 94% yield. The ee was determined on a Daicel Chiralpak AD column with hexanes : isopropanol = 75 : 25, flow = 1 mL/min, detection at 360 nm, reference at 390 nm. Retention times: 8.9 min [(R)-enantiomer], 12.6 min [(S)-enantiomer]. 86% ee. $[\alpha]_{\text{D}}^{20}$ -82.5 (c 1.01, CHCl₃). The absolute configuration was assigned

by analogy with Table 3, entry 6.

^1H NMR (CDCl_3): δ 7.44-7.28 (m, 8H), 7.22-7.16 (m, 2H), 5.34 (d, $^4J_{\text{HH}} = 1.7$ Hz, 1H), 3.31-3.24 (m, 1H), 3.13-3.05 (m, 1H), 2.93-2.77 (m, 2H). ^{13}C NMR (CDCl_3): δ 162.5, 136.9, 135.8, 129.3, 129.14, 129.06 (q, $^2J_{\text{CF}} = 32.6$ Hz), 128.8, 126.2, 125.7 (q, $^3J_{\text{CF}} = 4.0$ Hz), 125.6, 124.1 (q, $^1J_{\text{CF}} = 271.9$ Hz), 118.3, 74.4, 50.8, 36.2. FTIR (neat) 3066, 2936, 2958, 2247, 1694, 1618, 1521, 1496, 1435, 1417, 1326, 1258, 1167, 1115, 1070, 1016, 910, 843, 736, 702 cm^{-1} . M.p. 97-99 $^{\circ}\text{C}$. HRMS (ESI) calcd for $\text{C}_{19}\text{H}_{15}\text{F}_3\text{N}_2\text{ONa}$ ($\text{M}+\text{Na}^+$) 367.1029, found 367.1023.

Table 3, entry 6. The reaction was stirred for 47 h. Eluant for chromatography: $\text{Et}_2\text{O}/\text{EtOAc} = 1/1 \rightarrow \text{EtOAc}/\text{Et}_3\text{N} = 20/1$. Yellow solid. 100% yield. The ee was determined on a Daicel Chiralpak AD column with hexanes : isopropanol = 50 : 50, flow = 0.9 mL/min, detection at 330 nm, reference at 380 nm. Retention times: 7.9 min [(R)-enantiomer], 8.9 min [(S)-enantiomer]. 85% ee. $[\alpha]_{\text{D}}^{20} -170$ (c 1.00, CHCl_3). The absolute configuration was determined by X-ray crystallographic analysis of the TfOH salt of the product.

^1H NMR (CDCl_3): δ 8.43-8.40 (m, 1H), 7.62 (d, $^4J_{\text{HH}} = 1.7$ Hz, 1H), 7.43-7.25 (m, 6H), 7.00-6.95 (m, 1H), 6.86-6.83 (m, 1H), 5.41 (d, $^4J_{\text{HH}} = 1.7$ Hz, 1H), 3.32-3.25 (m, 1H), 3.13-3.05 (m, 1H), 2.92-2.73 (m, 2H). ^{13}C NMR (CDCl_3): δ 162.7, 151.3, 149.7, 137.7, 136.1, 128.9, 128.64, 128.60, 127.6, 121.7, 120.2, 120.1, 73.7, 51.0, 36.3. FTIR (neat) 3392, 3063, 3030, 3004, 2928, 2852, 2243, 1693, 1612, 1586, 1560, 1441, 1411, 1327, 1260, 1205, 1173, 1109, 843, 776, 702 cm^{-1} . M.p. 149-151 $^{\circ}\text{C}$. HRMS (ESI) calcd for $\text{C}_{17}\text{H}_{15}\text{N}_3\text{ONa}$ ($\text{M}+\text{Na}^+$) 300.1107, found 300.1098.

Table 3, entry 7. The reaction was stirred for 67 h at 45 $^{\circ}\text{C}$. The unpurified product was a mixture of regioisomers (6.3/1). Eluant for chromatography: $\text{Et}_2\text{O}/\text{hexane} = 3/1 \rightarrow \text{Et}_2\text{O}/\text{CH}_2\text{Cl}_2 = 1/1$. White solid. 73% yield. The ee was determined on a Daicel Chiralpak AD column with hexanes : isopropanol = 80 : 20, flow = 1 mL/min, detection at 330 nm, reference at 380 nm. Retention times: 12.3 min [(R)-enantiomer], 16.0 min [(S)-enantiomer]. 89% ee. $[\alpha]_{\text{D}}^{20} -109$ (c 1.12, CHCl_3). The absolute configuration was assigned

by analogy with Table 3, entry 6.

^1H NMR (CDCl_3): δ 7.37-7.26 (m, 5H), 7.25 (d, $^4J_{\text{HH}} = 1.9$ Hz, 1H) 7.19-7.07 (m, 5H), 5.32 (d, $^4J_{\text{HH}} = 1.7$ Hz, 1H), 3.26-3.19 (m, 1H), 3.11-3.02 (m, 1H), 2.90-2.75 (m, 2H). ^{13}C NMR (CDCl_3): δ 161.8, 137.1, 131.9, 129.1, 128.7, 128.6, 127.9, 127.5, 125.5, 116.4, 74.3, 50.6, 36.3. FTIR (neat) 3061, 3030, 2928, 2850, 2245, 1683, 1608, 1448, 1436, 1416, 1285, 1258, 1215, 1174, 1111, 1076, 911, 758, 731, 700 cm^{-1} . M.p. 131-133 $^\circ\text{C}$. HRMS (ESI) calcd for $\text{C}_{18}\text{H}_{16}\text{N}_2\text{ONa}$ ($\text{M}+\text{Na}^+$) 299.1155, found 299.1148.

Table 3, entry 8. The reaction was stirred for 67 h at 45 $^\circ\text{C}$. The unpurified product was a mixture of regioisomers (8.0/1). Eluant for chromatography: Et_2O /hexane = 3/1 $\rightarrow$ Et_2O . Pale-yellow oil. 62% yield. The ee was determined on a Daicel Chiralpak AD column with hexanes : isopropanol = 85 : 15, flow = 1 mL/min, detection at 330 nm, reference at 380 nm. Retention times: 6.0 min [(*R*)-enantiomer], 6.8 min [(*S*)-enantiomer]. 74% ee. $[\alpha]_{\text{D}}^{20} -184$ (c 1.02, CHCl_3). The absolute configuration was assigned by analogy with Table 3, entry 6.

^1H NMR (CDCl_3): δ 7.41-7.28 (m, 5H), 6.52 (d, $^4J_{\text{HH}} = 1.4$ Hz, 1H), 4.66 (d, $^4J_{\text{HH}} = 1.7$ Hz, 1H), 3.45-3.38 (m, 1H), 3.01-2.87 (m, 2H), 2.76-2.65 (m, 1H), 1.81-1.74 (m, 2H), 1.40-1.15 (m, 6H), 0.83 (t, $^3J_{\text{HH}} = 6.6$ Hz, 3H). ^{13}C NMR (CDCl_3): δ 160.8, 138.1, 131.6, 128.8, 128.5, 128.4, 115.1, 77.1, 52.1, 36.6, 31.5, 26.53, 26.47, 22.6, 14.2. FTIR (neat) 3063, 3030, 2956, 2929, 2858, 1727, 1684, 1455, 1418, 1281, 1210, 1123, 1002, 914, 845, 757, 702 cm^{-1} .

Larger scale reaction (without using a glove box). A solution of CuI (38.1 mg, 0.200 mmol) and ligand **6a** (90.9 mg, 0.220 mmol) in CH_2Cl_2 (15 mL) was stirred for 30 min at

room temperature to obtain a Cu(I)/**6a** complex. This solution was added by cannula to a 0 °C solution of azomethine imine **2** (697 mg, 4.00 mmol) and Cy₂NMe (428 μL, 2.00 mmol) in CH₂Cl₂ (10 mL), with the aid of additional CH₂Cl₂ (5 mL). A solution of ethyl propiolate (486 μL, 4.80 mmol) in CH₂Cl₂ (10 mL) was then added by cannula, and the resulting mixture was stirred for 20 h at room temperature. The solvent was then removed under vacuum, and the residue was chromatographed on silica gel (pretreated with Et₃N to deactivate it) with Et₂O/hexane = 3/1 → Et₂O to afford the desired product (**4**) as a yellow oil (1.06 g, 3.89 mmol; 97% yield) in 84% ee. Ligand **6a** was recovered in 78% yield (71 mg, 0.17 mmol).

IV. Determination of Absolute Configuration

X-ray Crystal Structure of the Triflic Acid Salt of the Product of Table 3, Entry 6 (03149RS)

An orange CH_2Cl_2 solution of the compound was prepared. Crystals suitable for X-ray structural analysis were obtained by diffusion of pentanes at room temperature.

An orange plate of dimensions $0.4 \times 0.38 \times 0.1 \text{ mm}^3$ was mounted under STP and transferred to a Bruker AXS/CCD three-circle diffractometer (χ fixed at 54.78°) equipped with a cold stream of N_2 gas. An initial unit cell was determined by harvesting reflections $I > 20 \sigma(I)$ from 45×10 -s frames of 0.30° ω scan data with monochromated $\text{Mo K}\alpha$ radiation ($\lambda = 0.71073 \text{ \AA}$). The cell thus determined was orthorhombic.

A hemisphere of data was then collected using ω scans of 0.30° and 30-s frames. The raw data frames were integrated using the Bruker program SAINT+ for NT version 6.01. The data that were collected (8836 total reflections, 3212 unique, $R_{\text{int}} = 0.00414$) had the following Miller index ranges: -26 to 15 in h , -9 to 9 in k , and -11 to 10 in l . The data were corrected for Lorentz and polarization effects. No absorption correction was performed.

All aspects of the solution and refinement were handled by SHELXTL NT version 5.10. The structure was solved by direct methods in the chiral orthorhombic space group $P2_12_12$, $a = 23.483(2) \text{ \AA}$; $b = 8.8967(8) \text{ \AA}$; $c = 10.7240(9) \text{ \AA}$; $\alpha = 90^\circ$; $\beta = 90^\circ$; $\gamma = 90^\circ$, and refined using standard difference Fourier techniques. Final, full-matrix least-squares refinement (3212 data for 290 parameters) on F^2 yielded residual of R_1 and wR_2^3 of 0.0619 and 0.1796 for data $I > 2\sigma(I)$, and 0.0647 and 0.1832, respectively, for all data. During the final refinement, all non-hydrogen atoms were treated anisotropically. Hydrogen atoms were included in calculated positions and refined isotropically on a riding model. A secondary extinction coefficient of 0.005(2) was also included in the refinement. Residual electron density amounted to a maximum of $1.219 \text{ e/\AA}^3$ and a minimum of $-0.479 \text{ e/\AA}^3$.

The absolute structure (Flack) parameter for the correct enantiomer is 0.05(14). The structure was also inverted and refined in order to confirm the initial assignment of absolute stereochemistry.

Tables 1-5 provide the full crystallographic data for the X-ray structure.

Crystallographic data (excluding structure factors) have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication no. CCDC-213165. Copies of the data can be obtained free of charge on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK (fax: (+44)1223-336-033; E-mail: deposit@ccdc.cam.ac.uk).

Table 1. Crystal data and structure refinement for 03149rs.

Identification code	03149rs	
Empirical formula	C _{19.50} H ₁₉ Cl F ₃ N ₃ O ₄ S	
Formula weight	483.89	
Temperature	193(2) K	
Wavelength	0.71073 Å	
Crystal system	Orthorhombic	
Space group	P2(1)2(1)2	
Unit cell dimensions	a = 23.483(2) Å	$\alpha = 90^\circ$.
	b = 8.8967(8) Å	$\beta = 90^\circ$.
	c = 10.7240(9) Å	$\gamma = 90^\circ$.
Volume	2240.5(3) Å ³	
Z	4	
Density (calculated)	1.435 Mg/m ³	
Absorption coefficient	0.319 mm ⁻¹	
F(000)	996	
Crystal size	0.4 x 0.38 x 0.1 mm ³	
Theta range for data collection	2.45 to 23.28°.	
Index ranges	-26 ≤ h ≤ 15, -9 ≤ k ≤ 9, -11 ≤ l ≤ 10	
Reflections collected	8836	
Independent reflections	3212 [R(int) = 0.0414]	
Completeness to theta = 23.28°	99.8 %	
Refinement method	Full-matrix least-squares on F ²	
Data / restraints / parameters	3212 / 3 / 290	
Goodness-of-fit on F ²	1.107	
Final R indices [I > 2σ(I)]	R1 = 0.0619, wR2 = 0.1796	
R indices (all data)	R1 = 0.0647, wR2 = 0.1832	
Absolute structure parameter	0.05(14)	
Extinction coefficient	0.005(2)	
Largest diff. peak and hole	1.219 and -0.479 e.Å ⁻³	

Table 2. Atomic coordinates ($\times 10^4$) and equivalent isotropic displacement parameters ($\text{\AA}^2 \times 10^3$) for 03149rs. $U(\text{eq})$ is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	$U(\text{eq})$
C(1)	4306(2)	7554(6)	1260(5)	54(1)
C(2)	3781(2)	3227(6)	3072(5)	49(1)
C(3)	3710(3)	1714(6)	3250(5)	54(1)
C(4)	3478(3)	1206(6)	4357(5)	53(1)
C(5)	3334(2)	2208(5)	5265(4)	43(1)
C(6)	3404(2)	3746(5)	5080(4)	36(1)
C(7)	3245(2)	4895(5)	5986(4)	34(1)
C(8)	3150(2)	6354(5)	5748(4)	38(1)
C(9)	3094(2)	4548(5)	7347(4)	33(1)
C(10)	3504(2)	3616(5)	8084(4)	34(1)
C(11)	4071(2)	4031(7)	8199(6)	63(2)
C(12)	4442(3)	3187(8)	8902(7)	74(2)
C(13)	4265(3)	1913(6)	9484(5)	59(2)
C(14)	3703(2)	1489(6)	9390(5)	53(1)
C(15)	3323(2)	2325(6)	8700(4)	42(1)
C(16)	2649(2)	6563(6)	8752(4)	43(1)
C(17)	2617(2)	8261(5)	8516(5)	44(1)
C(18)	2753(2)	8409(5)	7157(4)	36(1)
C(1S')	4860(4)	7947(8)	5255(10)	183(4)
Cl(1)	4344(2)	8559(7)	6618(5)	123(2)
Cl(2)	4902(2)	5991(6)	5202(5)	106(1)
F(1)	4637(2)	6394(5)	1513(4)	88(1)
F(2)	4282(2)	7711(5)	26(3)	83(1)
F(3)	4549(2)	8807(5)	1696(4)	84(1)
N(1)	2993(2)	7076(4)	6819(3)	39(1)
N(2)	3094(2)	6122(4)	7869(3)	37(1)
N(3)	3631(2)	4176(4)	3995(3)	39(1)
O(1)	2665(2)	9451(4)	6424(3)	50(1)
O(2)	3416(2)	5938(4)	1400(4)	61(1)
O(3)	3724(2)	7238(4)	3244(3)	53(1)
O(5)	3306(2)	8643(4)	1532(4)	57(1)

S(1)

3605(1)

7327(1)

1921(1)

38(1)

Table 3. Bond lengths [Å] and angles [°] for 03149rs.

C(1)-F(1)	1.321(6)
C(1)-F(2)	1.332(6)
C(1)-F(3)	1.338(7)
C(1)-S(1)	1.803(5)
C(2)-N(3)	1.348(6)
C(2)-C(3)	1.370(8)
C(3)-C(4)	1.382(8)
C(4)-C(5)	1.362(7)
C(5)-C(6)	1.392(7)
C(6)-N(3)	1.335(6)
C(6)-C(7)	1.459(7)
C(7)-C(8)	1.341(7)
C(7)-C(9)	1.534(6)
C(8)-N(1)	1.367(6)
C(9)-C(10)	1.496(6)
C(9)-N(2)	1.508(6)
C(10)-C(11)	1.386(7)
C(10)-C(15)	1.392(6)
C(11)-C(12)	1.375(8)
C(12)-C(13)	1.359(8)
C(13)-C(14)	1.375(8)
C(14)-C(15)	1.378(7)
C(16)-N(2)	1.464(7)
C(16)-C(17)	1.534(7)
C(17)-C(18)	1.497(7)
C(18)-O(1)	1.233(6)
C(18)-N(1)	1.362(6)
C(1S')-Cl(2)	1.745(9)
C(1S')-Cl(1)	1.975(10)
Cl(2)-Cl(2)#1	1.822(10)
N(1)-N(2)	1.430(5)
O(2)-S(1)	1.426(4)
O(3)-S(1)	1.448(3)
O(5)-S(1)	1.428(4)

F(1)-C(1)-F(2)	108.1(5)
F(1)-C(1)-F(3)	109.1(5)
F(2)-C(1)-F(3)	106.1(5)
F(1)-C(1)-S(1)	111.7(4)
F(2)-C(1)-S(1)	111.4(4)
F(3)-C(1)-S(1)	110.3(4)
N(3)-C(2)-C(3)	118.8(5)
C(2)-C(3)-C(4)	119.3(5)
C(5)-C(4)-C(3)	119.8(5)
C(4)-C(5)-C(6)	120.8(5)
N(3)-C(6)-C(5)	116.9(4)
N(3)-C(6)-C(7)	118.8(4)
C(5)-C(6)-C(7)	124.3(4)
C(8)-C(7)-C(6)	126.5(4)
C(8)-C(7)-C(9)	109.7(4)
C(6)-C(7)-C(9)	123.5(4)
C(7)-C(8)-N(1)	109.9(4)
C(10)-C(9)-N(2)	108.6(3)
C(10)-C(9)-C(7)	117.8(4)
N(2)-C(9)-C(7)	99.6(3)
C(11)-C(10)-C(15)	118.2(4)
C(11)-C(10)-C(9)	121.1(4)
C(15)-C(10)-C(9)	120.7(4)
C(12)-C(11)-C(10)	120.7(5)
C(13)-C(12)-C(11)	120.9(6)
C(12)-C(13)-C(14)	119.2(5)
C(13)-C(14)-C(15)	120.9(5)
C(14)-C(15)-C(10)	120.1(5)
N(2)-C(16)-C(17)	101.1(4)
C(18)-C(17)-C(16)	103.7(4)
O(1)-C(18)-N(1)	123.6(4)
O(1)-C(18)-C(17)	130.6(4)
N(1)-C(18)-C(17)	105.7(4)
Cl(2)-C(1S')-Cl(1)	109.5(6)
C(1S')-Cl(2)-Cl(2)#1	168.4(5)

C(18)-N(1)-C(8)	138.1(4)
C(18)-N(1)-N(2)	112.1(3)
C(8)-N(1)-N(2)	109.7(3)
N(1)-N(2)-C(16)	103.4(3)
N(1)-N(2)-C(9)	105.0(3)
C(16)-N(2)-C(9)	119.3(4)
C(6)-N(3)-C(2)	124.3(4)
O(2)-S(1)-O(5)	116.3(2)
O(2)-S(1)-O(3)	113.4(2)
O(5)-S(1)-O(3)	115.2(2)
O(2)-S(1)-C(1)	103.1(3)
O(5)-S(1)-C(1)	104.0(2)
O(3)-S(1)-C(1)	102.5(3)

Symmetry transformations used to generate equivalent atoms:

#1 -x+1,-y+1,z

Table 4. Anisotropic displacement parameters ($\text{\AA}^2 \times 10^3$) for 03149rs. 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}
C(1)	49(3)	50(3)	63(3)	11(3)	15(2)	8(3)
C(2)	67(3)	38(3)	41(3)	0(2)	5(2)	7(2)
C(3)	83(4)	38(3)	40(3)	-5(2)	-6(3)	11(3)
C(4)	78(4)	32(3)	50(3)	4(2)	-10(3)	-2(2)
C(5)	59(3)	31(3)	38(2)	3(2)	-6(2)	-6(2)
C(6)	40(2)	34(2)	34(2)	6(2)	-10(2)	-2(2)
C(7)	34(2)	30(2)	36(2)	4(2)	-4(2)	-3(2)
C(8)	46(3)	39(3)	30(2)	4(2)	-2(2)	-5(2)
C(9)	37(2)	26(2)	37(2)	3(2)	-4(2)	-3(2)
C(10)	40(2)	28(2)	33(2)	4(2)	3(2)	-2(2)
C(11)	40(3)	58(3)	89(4)	40(3)	-20(3)	-14(3)
C(12)	44(3)	74(4)	104(5)	46(4)	-21(3)	-13(3)
C(13)	61(3)	50(3)	66(4)	25(3)	-27(3)	1(3)
C(14)	58(3)	41(3)	58(3)	23(2)	-13(3)	-4(2)
C(15)	41(2)	41(3)	43(2)	9(2)	-3(2)	-8(2)
C(16)	50(3)	46(3)	33(2)	4(2)	-3(2)	5(2)
C(17)	57(3)	38(3)	36(2)	-5(2)	2(2)	4(2)
C(18)	40(2)	25(2)	42(2)	7(2)	-5(2)	-6(2)
C(1S'')	142(7)	96(6)	310(12)	-27(7)	-60(8)	0(5)
Cl(1)	51(2)	175(5)	143(4)	78(4)	-8(2)	-36(2)
Cl(2)	78(2)	107(3)	133(3)	4(3)	-22(3)	-3(2)
F(1)	63(2)	81(3)	119(3)	24(2)	20(2)	34(2)
F(2)	94(3)	100(3)	56(2)	14(2)	34(2)	22(2)
F(3)	65(2)	71(3)	115(3)	8(2)	19(2)	-26(2)
N(1)	47(2)	33(2)	37(2)	6(2)	-1(2)	3(2)
N(2)	47(2)	30(2)	33(2)	6(2)	-4(2)	2(2)
N(3)	48(2)	30(2)	38(2)	2(2)	-3(2)	1(2)
O(1)	61(2)	34(2)	56(2)	6(2)	-1(2)	3(2)
O(2)	81(3)	43(2)	59(2)	6(2)	-19(2)	-10(2)
O(3)	74(2)	46(2)	39(2)	4(2)	6(2)	-10(2)
O(5)	53(2)	47(2)	72(2)	15(2)	14(2)	14(2)

S(1)	43(1)	32(1)	39(1)	7(1)	6(1)	0(1)
------	-------	-------	-------	------	------	------

Table 5. Hydrogen coordinates ($\times 10^4$) and isotropic displacement parameters ($\text{\AA}^2 \times 10^{-3}$)
for 03149rs.

	x	y	z	U(eq)
H(2)	3933	3601	2312	58
H(3)	3819	1021	2620	64
H(4)	3418	162	4484	64
H(5)	3185	1853	6033	51
H(8)	3187	6816	4954	46
H(9)	2703	4107	7400	40
H(11)	4204	4908	7787	75
H(12)	4827	3498	8981	89
H(13)	4526	1322	9951	71
H(14)	3576	608	9806	63
H(15)	2936	2019	8644	50
H(16A)	2761	6339	9623	52
H(16B)	2283	6061	8564	52
H(17A)	2231	8653	8700	52
H(17B)	2898	8809	9032	52
H(1S1)	4715	8335	4450	219
H(1S2)	5244	8375	5397	219
H(3A)	3687	5144	3876	46

References

- (1) Perri, S. T.; Slater, S. C.; Toske, S. G.; White, J. D. *J. Org. Chem.* **1990**, *55*, 6037–6047.
- (2) Kemp, D. S.; Sidell, M. D.; Shortridge, T. J. *J. Org. Chem.* **1979**, *44*, 4473–4476.
- (3) $R_1 = \Sigma ||F_o| - |F_c|| / \Sigma |F_o|$
 $wR_2 = [\Sigma[w(F_o^2 - F_c^2)^2] / \Sigma[w(F_o^2)^2]]^{1/2}$
 $w = 1 / [\sigma^2(F_o)^2 + (0.0743 * P)^2 + 1.72 * P]$
where $P = [\text{Max}(F_o^2, 0) + 2 * F_c^2] / 3$