# Kinetic Resolution and Double Stereodifferentiation in Catalytic Asymmetric C–H Activation of 2-Substituted Pyrrolidines

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## Supporting Information

**General Information:** $^{1}$H NMR spectra were recorded at either 400 or 500 MHz Varian spectrometers and $^{13}$C NMR at 125 MHz in $CDCl_3$ unless otherwise noted. Mass spectral determination were carried out at 70 eV. FTIR spectra were recorded using a Nicolet Impact spectrometer. Optical rotations were measured using a Jasco DIP-370 digital polariemeter. Glassware was flame dried prior to use. All reactions were carried out under an atmosphere of argon. Elemental analysis was performed by Atlantic Microlab Inc., Norcross Georgia. Column chromatography was carried out on silica gel 60 (230-400) mesh. Commercially available reagents were used without additional purification unless noted. Degassing was carried out by bubbling Ar gas through the solution for 10 –15 min.

**(*2R, 5R*)-5-[(*S*)-(Methoxycarbonyl(4-bromophenyl)methyl]proline methyl ester (3)**:

Methyl 4-bromo phenyldiazoacetate (222 mg, 0.87 mmol) in 2,2-dimethylbutane (10 mL) was added dropwise over 4 h using a syringe pump to a refluxing solution of $Rh_2$(*S*-DOSP)$_4$ (17 mg, 0.01mmol) and 1-(*tert*-butoxycarbonyl)-(*R*)-proline methyl ester[1] (100 mg, 0.44 mmol) in 2,2-dimethylbutane (10 mL). After the addition, the resulting solution was cooled to 23$^{o}$ C. The solvent was removed under reduced pressure and the residue was reconstituted in $CH_2Cl_2$ (8 mL) and TFA (0.84 mL) and stirred for 4 h at 23$^{o}$ C. The

solution was concentrated in *vacuo*, and the residue was dissolved in $Et_2O$ (20 mL), extracted with 10% HCl (4 x 15 mL). The combined aqueous layers were basified ($NaHCO_3$, 1M NaOH to pH 8-9) and extracted with EtOAc (3 x 20 mL). The combined organic layers were washed with water (1 x 20 mL), brine (1 x 20 mL), dried over $Na_2SO_4$ and concentrated to give the free amine in >94% de (by $^1H$ NMR). The product was purified by flash chromatography ($SiO_2$, $Et_2O$/Pentane/$NEt_3$= 49:49:2) to give the title compound (106 mg, 0.29 mmol, 68% yield). $[\alpha]^{25}_D = +6.9^o$ (c 1.1, $CHCl_3$); $^1H$ NMR (500 MHz, $CDCl_3$) δ 7.48 (d, *J* = 8.5 Hz, 2 H), 7.28 (d, *J* = 8.0 Hz, 2 H), 3.91 (m, 1 H), 3.78 (dd, *J* = 6.0, 8.5 Hz, 1 H), 3.68 (s, 3 H), 3.65 (s, 3 H), 3.42 (d, *J* = 9.5 Hz, 1 H), 2.24 - 2.18 (m, 1 H), 2.08 - 2.02 (m, 1 H), 1.94 - 1.88 (m, 1 H), 1.58 - 1.51 (m, 1 H); $^{13}C$ NMR (125 MHz, $CDCl_3$) 175.73 (C), 172.52 (C), 136.13 (C), 131.63 (CH), 130.14 (CH), 121.46 (C), 60.1 (CH), 58.65 (CH), 57.18 (CH), 51.94 ($CH_3$), 51.87 ($CH_3$), 29.54 ($CH_2$), 29.0 ($CH_2$); IR (neat): 3352, 2951, 2874, 1732, 1489, 1202, 1126, 1011 $cm^{-1}$; Anal. Calcd for $C_{15}H_{19}NBrClO_4$: C, 45.88; H, 4.88; N, 3.57. Found: C, 45.88; H, 4.96; N, 3.58.

**(*2S, 5 S*)-5-[(*R*)-(Methoxycarbonyl(4-bromophenyl)methyl] prolinemethylester (ent-3) and (*2S, 5S*)-5-[(*S*)-(Methoxycarbonyl(4-bromophenyl)methyl]prolinemethyl ester** (**4**): Methyl 4-bromo phenyldiazoacetate (1.23 g, 4.86 mmol) in 2,2-dimethylbutane (25 mL) was added dropwise over 7 h using a additional funnel to a refluxing solution of $Rh_2$(*S*-DOSP)$_4$ (90 mg, 0.01mmol) and 1-(*tert*-butoxycarbonyl)-(*S*)-prolinemethylester[1] (550 mg, 2.40 mmol) in 2,2-dimethylbutane (20 mL). After the addition, the resulting solution was cooled to 23° C. The solvent was removed under reduced pressure and the residue was reconstituted in $CH_2Cl_2$ (20 mL) and TFA (4.8 mL) and stirred for 4 h at 23°

C. The solution was concentrated in *vacuo*, and the residue was dissolved in $Et_2O$ (40 mL), extracted with 10% HCl (4 x 25 mL). The combined aqueous layers were basified ($NaHCO_3$, 1M NaOH to pH 8–9) and extracted with EtOAc (3 x 30 mL). The combined organic layers were washed with water (1 x 30 mL) and brine (1 x 30 mL) and dried over $Na_2SO_4$. The solvent was removed under reduced pressure to give the title diastereomers (d:r = 2.5:1). The two diastereomers were separated by preparative TLC ($SiO_2$, $Et_2O$/Pentane/$NEt_3$= 40:58:2).

**Major diastereomer: (*2S, 5 S*)-5-[(*R*)-(Methoxycarbonyl(4-bromophenyl)methyl] prolinemethyl ester** (**ent-3**): (260 mg, 0.73 mmol, 31% yield); $[\alpha]^{25}_D$ = -7.1° (c 5.3, $CHCl_3$); $^1$H NMR (500 MHz, $CDCl_3$) δ 7.48 (d, *J* = 9.0 Hz, 2 H), 7.28 (d, *J* = 8.0 Hz, 2 H), 3.91 (m, 1 H), 3.78 (dd, *J* = 5.5, 9.0 Hz, 1 H), 3.68 (s, 3 H), 3.65 (s, 3 H), 3.42 (d, *J* = 9.5 Hz, 1 H), 2.24 - 2.18 (m, 1 H), 2.08 - 2.02 (m, 1 H), 1.94 - 1.88 (m, 1 H), 1.58 - 1.51 (m, 1 H); $^{13}$C NMR (125 MHz, $CDCl_3$) 176.1 (C), 172.9 (C), 136.1 (C), 132.0 (CH), 130.5 (CH), 121.8 (C), 60.4 (CH), 59.0 (CH), 57.5 (CH) , 52.3 ($CH_3$), 52.2 ($CH_3$), 29.9 ($CH_2$), 29.3 ($CH_2$); IR (neat): 3353, 2951, 2874, 1734, 1489, 1201, 1163, 1011 $cm^{-1}$; Anal. Calcd for $C_{15}H_{19}NBrClO_4$: C, 45.88; H, 4.88; N, 3.57. Found: C, 45.88; H, 4.86; N, 3.27. The signal from the proton attached to nitrogen is not observed in the $^1$H NMR spectrum.

**Minor diastereomer: (*2S, 5 S*)-5-[(*S*)-(Methoxycarbonyl(4-bromophenyl)methyl] proline methyl ester** (**4**): (120 mg, 0.34 mmol, 14% yield); $[\alpha]^{25}_D$ = -46.1° (c 1.9, $CHCl_3$); $^1$H NMR (500 MHz, $CDCl_3$) δ 7.45 (d, *J* = 8.5 Hz, 2 H), 7.19 (d, *J* = 8.5 Hz, 2 H), 3.94 - 3.90 (m, 1 H), 3.89 - 3.80 (dd, *J* = 6.0, 7.5 Hz, 1 H), 3.73 (s, 3 H), 3.67 (s, 3 H), 3.39 (d, *J* = 10.0 Hz, 1 H), 2.8 (br, 1 H), 2.20 - 2.10 (m, 1 H), 1.84 - 1.77 (m, 1 H),

1.62 - 1.55 (m, 1 H), 1.38 - 1.31 (m, 1 H); $^{13}$C NMR (125 MHz, $CDCl_3$) 175.6 (C), 173.2 (C), 135.9 (C), 131.8 (CH), 129.8 (CH), 121.5 (C), 60.7 (CH), 59.7 (CH), 58.6 (CH) , 52.1 ($CH_3$), 52.0 ($CH_3$), 29.5 ($CH_2$), 29.1 ($CH_2$); IR (neat): 3353, 2951, 1734, 1488, 1434, 1201, 1164, 1011, 1073 $cm^{-1}$; Anal. Calcd for $C_{15}H_{19}NBrClO_4$: C, 45.88; H, 4.88; N, 3.57. Found: C, 45.71; H, 4.94; N, 3.48. The stereochemical assignment for the minor diastereomer **4** was based on the distinctive coupling constants and NOE enhancement studies. The stereochemistry at the C2 position for **4** was assigned to be *S*, assuming it was in unchanged from **L-1a**. A 2D correlation COSY experiment allowed assignment of the $^1$H resonances. The configuration at the C5 position was based on distinctive NOE enhancement. A large enhancement (8%) was observed between the cis protons $H_e$ and $H_d$ while smaller enhancement (1.8%) was observed between the trans protons $H_c$ and $H_e$. Enhancement of $H_b$ (0.9%) was observed on irradiation of $H_f$, but no enhancement of $H_b$ was observed on irradiation $H_e$. Similarly enhancement of $H_g$ (1.0%) was observed on irradiation of $H_d$, and no enhancement of $H_g$ was observed on irradiation $H_c$. Additionally, no enhancement of $H_b$ was observed on irradiation of $H_g$, suggesting that $H_b$ and $H_g$ are anti to each other (Figure 1). Based on this, the configuration at C5 position for **4** was assigned to be *R*. Based on the same argument, the diastereomers **ent-3** ands **4** have the same configuration at C2 and C5 position. The configuration at the $\alpha$ position for the minor diastereomer **4** has to be *S*, because it is known that the stereocenter for the major diastereomer **ent-3** is *R*. This is consistent with the model proposed by Davies and Ren.[2] The large coupling constant value between $H_a$ and $H_b$ ($J$ = 11 Hz) indicates that the protons preferentially exist in an antiperiplanar conformation (**A**, Figure 2). Furthermore the NMR signals for the $H_c$ and $H_d$ protons of **4** are shifted to $\delta$ 1.73 and $\delta$ 1.63 ppm

respectively, in comparison to **B**, from the major diastereomer **ent-3** ($H_c$ = δ 2.28 and $H_d$ = δ 1.92 ppm respectively). This clearly shows the shielding effect of the aromatic ring on $H_c$ and $H_d$ protons in **4** as shown in the Figure 2. Based on the above explanation, the configuration at the α position for the minor diastereomer **4** was assigned to be *S*.

**Figure 1**

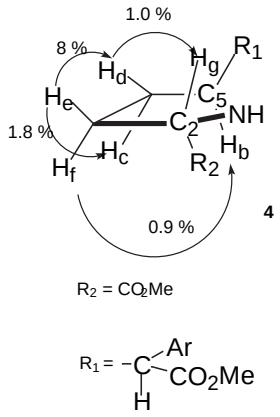
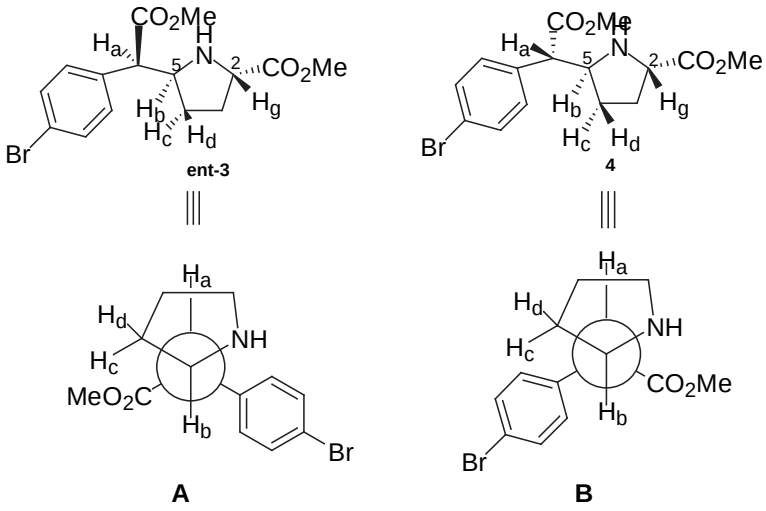



**Figure 2**




**1-(*tert*-Butoxycarbonyl)-*2R*-acetoxymethylpyrrolidine (1c):** To a solution of 1-(*tert*-butoxycarbonyl) prolin-*2R*-ol[3] (1.24 g, 6.2 mmol), pyridine (1 mL, 12.4 mmol) and acetic anhydride (0.73 mL, 7.7 mmol) in $CH_2Cl_2$ (20 mL) was added dimethylaminopyridine (152 mg, 20%). The reaction mixture was stirred at 23° C for 2 h and diluted with $CH_2Cl_2$ (30 mL) and washed with water (2 x 30 mL) and brine (3 x 25 mL). The organic layer was dried in $Na_2SO_4$ and removed in *vacuo*. The residue was purified by column chromatography ($SiO_2$, $Et_2O$/Pentane = 10:90) to give the title compound (1.38 g, 5.67 mmol, 91% yield). $[\alpha]^{25}_D$ = +48.9° (c 1.7, $CHCl_3$); $^1$H NMR (500MHz, $CDCl_3$) δ 4.15 - 4.10 (m, 2 H), 4.07 - 3.85 (m, 3 H), 2.06 (s, 3 H), 2.01 - 1.82 (m, 4 H), 1.46 (s, 9 H); IR

(neat): 2975, 2877, 1741, 1692, 1457, 1395, 1239, 1173, 1106 $cm^{-1}$; Anal. Calcd for $C_{12}H_{21}NO_4$: C, 59.24; H, 8.70; N, 5.76. Found: C, 59.28; H, 8.76; N, 5.59.

**1-(*tert*-Butoxycarbonyl)-*2R*-[*tert*-butyldiphenylsilyl)oxymethyl]pyrrolidine (1d):** To a solution of 1-(*tert*-butoxycarbonyl) prolin-*2R*-ol[3] (1.6 g, 8.1 mmol) and imidazole (1.1 g, 16.1 mmol) in DMF (3 mL) at 0 $^oC$ under Ar was added *tert*-butyldiphenylsilyl chloride (2.6 mL, 10.1 mmol). The ice bath was removed after 15 min, and the mixture was stirred at 23 $^oC$. After 16 h, the reaction mixture was diluted with $Et_2O$ (40 mL) and washed with water (3 x 30 mL) and brine (1 x 30 mL). Ether layer was dried over $Na_2SO_4$ and removed in *vacuo*. The residue was purified by column chromatography ($SiO_2$, EtOAc/hexane = 10:90) to give the title compound (3.36 g, 7.64 mmol, 95% yield). $[\alpha]^{25}_D$ = +30.2$^o$ (c 1.2, $CHCl_3$); $^1H$ NMR (500MHz, $CDCl_3$) $\delta$ 7.72 (d, *J* = 7.0 Hz, 2 H), 7.65 (t, *J* = 6.0 Hz, 3 H), 7.39 (m, 5 H), 3.96 - 3.71 (m, 2 H), 3.52 - 3.34 (m, 3 H), 2.2 - 1.79 (m, 4 H), 1.33 (s, 9 H), 1.97 (s, 9 H); IR (neat): 3070, 3049, 2930, 2857, 1695, 1671, 1473, 1427, 1393, 1169, 1112 $cm^{-1}$; MS (EI) *m/z* 366 $[M–C_4H_9O]^+$, 326, 280, 199; HRMS (EI) *m/z* calcd for $C_{22}H_{28}NO_2Si$ $[M–C_4H_9O]^+$ 366.1889, Found 366.1886.

**(*2R*, *5R*)-1-(*tert*-Butoxycarbonyl)-5-[(*S*)-(methoxycarbonyl(4-bromophenyl)methyl] proline methyl ester (5a):** Methyl 4-bromo phenyldiazoacetate (222 mg, 0.87 mmol) in 2,2-dimethylbutane (10 mL) was added dropwise over 4 h using a syringe pump to a refluxing solution of $Rh_2$(*S*-DOSP)$_4$ (17 mg, 0.01mmol) and 1-(*tert*-butoxycarbonyl)-(*R*)-prolinemethylester[1] (100 mg, 0.44 mmol) in 2,2-dimethylbutane (10 mL). After the addition, the resulting solution was cooled to 23$^o$ C. The solvent was removed under

reduced pressure to give **5a** in >94% de (by $^1$H NMR). The residue was purified by flash chromatography ($SiO_2$, $CH_2Cl_2$/Pentane = 50:50, then $Et_2O$/Pentane = 30:70) to give the title compound (330 mg, 0.72 mmol, 83% yield). $[\alpha]^{25}_D$ = +7.0$^o$ (c 1.1, $CHCl_3$); $^1$H NMR (500MHz, $CDCl_3$, rotomers 1:0.5) $\delta$ 7.44 (m, 2 H), 7.28 (d, *J* = 7.5 Hz, 2 H, major), 7.23 (d, *J* = 8.0 Hz, 2 H, minor), 4.52 (t, *J* = 6.0 Hz, 1 H, major), 4.39 (t, *J* = 7.5 Hz, 1 H, minor), 4.34 (d, *J* = 9.0 Hz, 1 H, minor), 4.21 (d, *J* = 8.5 Hz, 1 H, major), 4.15 (d, *J* = 5.5 Hz, 1 H, major), 4.0 (d, *J* = 6.5 Hz, 1 H, minor), 3.69 (m, 6H), 2.28 - 1.79 (m, 4 H), 1.34 (s, 9 H); IR (neat): 2975, 2952, 1738, 1701, 1489, 1436, 1366, 1167, 1125 cm$^{-1}$; Anal. Calcd for $C_{20}H_{26}NBrO_6$: C, 52.64; H, 5.74; N, 3.07. Found: C, 52.51; H, 5.77; N, 2.94.

**(*2 R , 5 R*)-1-(*tert*-Butoxycarbonyl)-5-[(*S*)-(4-bromophenyl)methyl]proline-*tert*-butyl ester (5b):** Methyl 4-bromo phenyldiazoacetate (188 mg, 0.74 mmol) in 2,2-dimethylbutane (8 mL) was added dropwise over 3 h using a syringe pump to a refluxing solution of $Rh_2$(*S*-DOSP)$_4$ (28 mg, 0.02mmol) and 1-(*tert*-butoxycarbonyl)-(*R*)-proline-*tert*-butylester[4] (100 mg, 0.37 mmol) in 2,2-dimethylbutane (10 mL). After the addition, the resulting solution was cooled to 23$^o$ C. The solvent was removed under reduced pressure to give **5b** in >94% de (by $^1$H NMR). The residue was purified by flash chromatography ($SiO_2$, $CH_2Cl_2$/Pentane = 50:50, then $Et_2O$/Pentane = 20:80) to give the title compound (157 mg, 0.32 mmol, 85% yield). $[\alpha]^{25}_D$ = +21.2$^o$ (c 1.38, $CHCl_3$); $^1$H NMR (500MHz, $CDCl_3$, rotomers 1.8:1.0) $\delta$ 7.42 (m, 2 H), 7.28 (d, *J* = 10.5 Hz, 2 H, major), 7.21 (d, *J* = 10.0 Hz, 2 H, minor), 4.48 (m, 1 H, major), 4.36 (m, 1 H, minor), 4.16 (m, 1 H), 3.93 (d, *J* = 10.0 Hz, 1 H, major), 3.92 (d, *J* = 9.0 Hz, 1 H, minor), 3.69 (m, 3 H), 2.30 - 1.70 (m, 4 H), 1.43 (m, 9 H), 1.37 (s, 9 H, major), 1.32 (s, 9 H, minor);

IR (neat): 2976, 1736, 1702, 1485, 1371, 1161, 1074, 1011 $cm^{-1}$; Anal. Calcd for $C_{23}H_{32}NBrO_6$: C, 55.43; H, 6.47; N, 2.81. Found: C, 55.55; H, 6.52; N, 2.80.

**(*2R*, *5R*)-1-(*tert*-Butoxycarbonyl)-5-[(*S*)-(methoxycarbonyl(4-bromophenyl)methyl]-2-acetoxypyrrolidine (5c):** Methyl 4-bromo phenyldiazoacetate (629 mg, 2.47 mmol) in 2,2-dimethylbutane (25 mL) was added dropwise over 2 h using a additional funnel to a refluxing solution of $Rh_2$(*S*-DOSP)$_4$ (93 mg, 0.02mmol) and 1-(*tert*-butoxycarbonyl)-*2R*-acetoxymethylpyrrolidine (303 mg, 1.23 mmol) in 2,2-dimethylbutane (25 mL). After the addition, the resulting solution was cooled to 23$^o$ C. The solvent was removed under reduced pressure to give **5c** in >94% de (by $^1$H NMR). The residue was purified by flash chromatography ($SiO_2$, $Et_2O$/Pentane = 20:80) to give the title compound (493 mg, 1.05 mmol, 85% yield). $[\alpha]^{25}_D$ = +40.2$^o$ (c 3.85, $CHCl_3$); $^1$H NMR (500MHz, $CDCl_3$) $\delta$ 7.45 (m, 2 H), 7.33 (m, 2 H), 4.38 - 3.80 (m, 5 H), 3.69 (s, 3 H), 2.02 (s, 3 H), 1.99 - 1.95 (m, 2 H), 1.89 - 1.83 (m, 1 H), 1.75 - 1.69 (m, 1 H), 1.45 (m, 9 H); IR (neat): 2974, 1740, 1694, 1489, 1389, 1229, 1170, 1124 $cm^{-1}$; Anal. Calcd for $C_{21}H_{28}NBrO_6$: C, 53.62; H, 6.00; N, 2.98. Found: C, 53.85; H, 5.91; N, 3.04.

**(*2R*, *5R*)-1-(*tert*-Butoxycarbonyl)-5-[(*S*)-(methoxycarbonyl(4-bromophenyl)methyl]-2-[*tert*-butyldiphenylsilyloxymethyl]pyrrolidine (5d):**

Methyl 4-bromo phenyldiazoacetate (202 mg, 0.79 mmol) in 2,2-dimethylbutane (10 mL) was added dropwise over 3 h using a syringe pump to a refluxing solution of $Rh_2$(*S*-DOSP)$_4$ (30 mg, 0.02mmol) and 1-(tert-butoxycarbonyl)-*2R*-[tert-butyldiphenylsilyloxy methyl]pyrrolidine (139 mg, 0.32 mmol) in 2,2-dimethylbutane (10 mL). After the

addition, the resulting solution was cooled to 23° C. The solvent was removed under reduced pressure to give **5d** in >94% de (by $^1$H NMR). The residue was purified by flash chromatography ($SiO_2$, $CH_2Cl_2$/Pentane = 60:40, then $Et_2O$/Pentane = 10:90) to give the title compound (181 mg, 0.27 mmol, 85% yield). $[\alpha]^{25}_D$ = +28.5° (c 2.26, $CHCl_3$); $^1$H NMR (500MHz, $CDCl_3$) δ 7.60 (m, 4 H), 7.36 (m, 10 H), 4.36 - 4.16 (m, 2 H), 3.98 - 3.77 (m, 1 H), 3.69 (s, 3 H), 3.66 - 3.46 (m, 2 H), 2.1 - 1.94 (m, 4 H), 1.27 (s, 9 H), 1.01 (s, 9 H); IR (neat): 3070, 3049, 2959, 2857, 1736, 1693, 1390, 1170, 1112, 1012 cm$^{-1}$; MS (EI) *m/z* 608 $[M–C_4H_9]^+$, 338, 338, 280; HRMS (EI) *m/z* calcd for $C_{31}H_{35}NO_5SiBr$ $[M–C_4H_9]^+$ 608.1468, Found 608.1488.

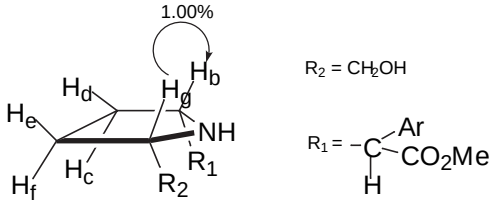
**(*2S*, *5R*)-1-(*tert*-Butoxycarbonyl)-5-[(*S*)-(methoxycarbonyl(4-bromophenyl)methyl]-2-acetoxypyrrolidine (6)**: Methyl 4-bromo phenyldiazoacetate (629 mg, 2.47 mmol) in 2,2-dimethylbutane (25 mL) was added dropwise over 2 h using a additional funnel to a refluxing solution of $Rh_2$(*S*-DOSP)$_4$ (93 mg, 0.02mmol) and 1-(*tert*-butoxycarbonyl)-*2S*-acetoxymethylpyrrolidine (303 mg, 1.23 mmol) in 2,2-dimethylbutane (25 mL). After the addition, the resulting solution was cooled to 23° C and the solvent was removed under reduced pressure. The crude was then purified by flash chromatography ($SiO_2$, $Et_2O$/Pentane = 20:80) to give the title compound as a mixture of inseparable diastereomers (114 mg, 0.24 mmol, 20% yield).

To a solution of the mixture of diastereomers (50 mg, 0.106 mmol) from above in methanol (3 mL), was added 0.05N NaOH (2.4 mL). The reaction mixture was stirred at 23° C for 3 h, then was concentrated, dissolved in EtOAc (5 mL). The EtOAc layer was washed with water (5 mL) and brine (5 mL), and dried over $Na_2SO_4$. The evaporation of

the solvent gave the crude alcohol that was used without further purification for the next step.

Crude alcohol was dissolved in 1M HCl in dioxane (2 mL) and stirred at 23° C. After 10 min the reaction mixture was diluted with $Et_2O$ (15 mL) and stirrred at 23° C. After 30 min the mixture was concentrated, dissolved in water (10 mL). The aqueous phase was basified with $NaHCO_3$, and 1M NaOH to pH 7–8, and extracted with EtOAc (3 x 5 mL). The combined organic layers were washed with water (5 mL) and brine (5 mL), and dried over $Na_2SO_4$. The product was purified by flash chromatography ($SiO_2$, EtOAc/Pentane/$NEt_3$ = 40:60:10) to give the major diastereomer, **(*2S,5R*)-5-[(*S*)-(Methoxycarbonyl(4-bromophenyl)methyl]-2-hydroxymethylpyrrolidine**. $[\alpha]^{25}_D$ = -68.7° (c 0.99, $CHCl_3$); $^1$H NMR (free amine, 500 MHz, $CDCl_3$) δ 7.49 (d, *J* = 8.5 Hz, 2 H), 7.28 (d, *J* = 8.5 Hz, 2 H), 3.78 - 3.74 (m, 1 H), 3.67 (s, 3 H), 3.47 - 3.45 (dd, *J* = 3.5, 7.5 Hz), 3.43 (d, *J* = 8.5 Hz, 1 H), 3.32 (m, 1H), 3.27 - 3.22 (dd, *J* = 5.5, 10.5 Hz, 1 H), 2.02 - 1.98 (m, 1 H), 1.92 - 1.82 (m, 2 H), 1.65 (m, 1 H), 1.5 (m, 1 H); $^{13}$C NMR (125 MHz, $CDCl_3$) 172.87 (C), 136.36 (C), 131.67 (CH), 130.23 (CH), 121.57 (C), 64.86 ($CH_2$), 61.08 (CH), 57.98 (CH), 57.43 (CH), 52.0 ($CH_3$), 29.82 ($CH_2$), 26.87 ($CH_2$); IR (neat): 3322, 2950, 2870, 1733, 1489, 1158, 1073, 1011 $cm^{-1}$; Anal. Calcd for $C_{14}H_{18}NBrO_3$: C, 50.68; H, 5.59; N, 4.22. Found: C, 50.77; H, 5.69; N, 4.14. The stereochemical assignment at C5 position was based on distinctive NOE enhancement, as summarized in Figure 3. Presaturation of the $H_b$ resonance resulted in the enhancement of the signal of the $H_g$ (1.00%) proton which suggested that they are on the same side. Based on this, configuration at C5 position was assigned as *R*.

**Figure 3**




The configuration at α position was once again assigned on the basis of the model.[2] The large coupling constant value between the two hydrogens at the newly formed stereogenic centers, indicates antiperiplanar arrangement. Since the proton NMR signals for the methylene group did not shift downfield, indicates the lack of shielding due to the aromatic ring. Based on this argument the configuration at α position was assigned as *S*.

**(*2R, 5R*)-5-[(*S*)-(Methoxycarbonyl(4-bromophenyl)methyl]proline methyl ester (5a):** Methyl 4-bromo phenyldiazoacetate (100 mg, 0.39 mmol) in 2,2-dimethylbutane (5 mL) was added dropwise over 4 h using a syringe pump to a refluxing solution of $Rh_2$(*S*-DOSP)$_4$ (15 mg, 0.02mmol) and 1-(*tert*-butoxycarbonyl)-(±)-prolinemethylester (180 mg, 0.78 mmol) in 2,2-dimethylbutane (10 mL). After the addition, the resulting solution was cooled to 23$^o$ C. The solvent and excess of 1-(*tert*-butoxycarbonyl)prolinemethyl ester was removed on a rotary evaporator and by Kugelrohr distillation. The crude was then purified by flash chromatography ($SiO_2$, $CH_2Cl_2$/Pentane = 50:50, then $Et_2O$/Pentane = 25:75) to give the title compound (228 mg, 0.50 mmol, 64% yield). $^1$H NMR (500MHz, $CDCl_3$, rotomers 1:0.5) δ 7.44 (m, 2 H), 7.28 (d, *J* = 7.5 Hz, 2 H, major), 7.23 (d, *J* = 8.0 Hz, 2 H, minor), 4.52 (t, *J* = 6.0 Hz, 1 H, major), 4.39 (t, *J* = 7.5 Hz, 1 H, minor), 4.34 (d, *J* = 9 Hz, 1 H, minor), 4.21 (d, *J* = 8.5 Hz, 1 H, major), 4.15 (d, *J* = 5.5 Hz, 1 H, major), 4.0 (d, *J* = 6.5 Hz, 1 H, minor), 3.69 (m, 6H), 2.28 - 1.79 (m, 4 H), 1.34

(s, 9 H). The mixture was then dissolved in $CH_2Cl_2$ (15 mL) and treated with TFA (1.5 mL) and stirred for 4 h at 23° C. The solution was concentrated in *vacuo*, and the residue was dissolved in $Et_2O$ (20 mL), extracted with 10% HCl (4 x 15 mL). The combined aqueous layers were basified ($NaHCO_3$, 1M NaOH to pH 8–9) and extracted with EtOAc (3 x 20 mL). The combined organic layers were washed with water (1 x 20 mL) and brine (1 x 20 mL) and dried over $Na_2SO_4$. The solvent was removed under reduced pressure to give free amine **3** in 86% de (by $^1$H NMR)**.** To measure the enantiomeric excess of the above compound, it was converted to its trifluoroacetamide. Trifluoroacetamide of **3**: Acylation of a small sample of the free amine from above with TFAA and $CH_2Cl_2$ followed by flash chromatography ($SiO_2$, $Et_2O$/Pet.ether = 20:80) gave the amide in 77% ee (HPLC, Chiracel-OD column, 1% 2-PrOH in hexanes, 1.0 mL/min, 1 mg/mL, $T_R$ = 13.75 and 16.84 min, UV 254 nm); $^1$H NMR (500 MHz, $CDCl_3$) δ 7.48 (d, *J* = 8.5 Hz, 2 H), 7.33 (d, *J* = 8.5 Hz, 2 H), 4.74 (dd, J = 4.0, 9.0 Hz, 1 H), 4.69 (d, *J* = 9.0 Hz, 1 H), 4.51 (d, *J* = 4.5 Hz, 1 H), 3.73 (s, 3 H), 3.69 (s, 3 H), 2.39 - 2.30 (m, 1 H), 2.18 - 2.13 (m, 1 H), 2.07 - 2.03 (m, 1 H), 1.95 - 1.86 (m, 1 H); $^{13}$C NMR (125 MHz, $CDCl_3$) 171.83 (C), 171.69 (C), 156.93 (C), 134.21 (CH), 131.78 (CH), 130.57 (CH), 121.94 (C), 114.71 (C), 63.31 (CH), 60.87 (CH), 52.94 (CH), 52.14 ($CH_3$), 49.63 ($CH_3$), 29.63 ($CH_2$), 24.05 ($CH_2$); IR (neat): 2955, 1740, 1696, 1490, 1437, 1205, 1167, 1011 $cm^{-1}$; Anal. Calcd for $C_{17}H_{17}NF_3BrO_5$: C, 45.15; H, 3.79; N, 3.10. Found: C, 45.15; H, 3.80; N, 3.06.

**(*2R, 5R*)-5-[(*S*)-Methoxycarbonyl(4-bromophenyl)methyl]proline-*tert*-butyl ester (5b):** Methyl 4-bromo phenyldiazoacetate (50 mg, 0.196 mmol) in 2,2-dimethylbutane (2

mL) was added dropwise over 2 h using a syringe pump to a refluxing solution of $Rh_2$(*S*-DOSP)$_4$ (8 mg, 0.02mmol) and 1-(*tert*-butoxycarbonyl)-(±)-proline-*tert*-butylester (106 mg, 0.392 mmol) in 2,2-dimethylbutane (10 mL). After the addition, the resulting solution was cooled to 23° C. The solvent and excess of and 1-(*tert*-butoxycarbonyl) proline-*tert*-butylester was removed on a rotary evaporator and by Kugelrohr distillation to give **5b** in >94% de (by $^1$H NMR). The crude was then purified by flash chromatography ($SiO_2$, $CH_2Cl_2$/Pentane = 50:50, then $Et_2O$/Pentane = 20:80) to give the title compound (58 mg, 0.12 mmol, 58% yield). 83% ee (HPLC, Whelk (R,R) column, 1% 2-PrOH in hexanes, 0.75 mL/min, 1 mg/mL, $T_R$ = 16.84 and 21.43 min, UV 254 nm); $^1$H NMR (500MHz, $CDCl_3$, rotomers 1.8:1.0) δ 7.42 (m, 2 H), 7.28 (d, *J* = 10.5 Hz, 2 H, major), 7.21 (d, *J* = 10.0 Hz, 2 H, minor), 4.48 (m, 1 H, major), 4.36 (m, 1 H, minor), 4.16 (m, 1 H), 3.93 (d, *J* = 10.0 Hz, 1 H, major), 3.92 (d, *J* = 9.0 Hz, 1 H, minor), 3.69 (m, 3 H), 2.30 - 1.70 (m, 4 H), 1.43 (m, 9 H), 1.37 (s, 9 H, major), 1.32 (s, 9 H, minor).

**(*2R*, *5R*)-1-(*tert*-Butoxycarbonyl)-5-[(*S*)-(methoxycarbonyl(4-bromophenyl)methyl]-2-acetoxypyrrolidine (5c):** Methyl 4-bromo phenyldiazoacetate (50 mg, 0.196 mmol) in 2,2-dimethylbutane (2 mL) was added dropwise over 2 h using a syringe pump to a refluxing solution of $Rh_2$(*S*-DOSP)$_4$ (8 mg, 0.02mmol) and 1-(*tert*-butoxycarbonyl)-2-(±)-acetoxymethylpyrrolidine (191 mg, 0.784 mmol) in 2,2-dimethylbutane (15 mL). After the addition, the resulting solution was cooled to 23° C. The solvent and excess of and 1-(*tert*-butoxycarbonyl)-2-acetoxymethylpyrrolidine was removed on a rotary evaporator and by Kugelrohr distillation. The diastereomeric ratio could not be determined here due to the rotomers. The residue was purified by flash chromatography ($SiO_2$,

$CH_2Cl_2$/Pentane = 50:50, then $Et_2O$/Pentane = 20:80) to give the title compound (55 mg, 0.12 mmol, 62% yield). $^1$H NMR (500MHz, $CDCl_3$) δ 7.45 (m, 2 H), 7.33 (m, 2 H), 4.38 - 3.80 (m, 5 H), 3.69 (s, 3 H), 2.02 (s, 3 H), 1.99 - 1.95 (m, 2 H), 1.89 - 1.83 (m, 1 H), 1.75 - 1.69 (m, 1 H), 1.45 (m, 9 H). The enantiomeric excess was determined by the hydrolysis of the acetate group from above with 0.05N NaOH in methanol to give the alcohol, purified through a plug of silica gel and subjected to HPLC analysis to give 94% ee (Whelk (R,R) column, 3% 2-PrOH in hexanes, 1.0 mL/min, 1 mg/mL, $T_R$ = 24.10 and 32.25 min, UV 254 nm). $^1$H NMR (500MHz, $CDCl_3$) δ 7.46 (d, *J* = 8.5 Hz, 2 H), 7.24 (d, *J* = 8.5 Hz, 2 H), 4.48 - 4.22 (m, 2 H), 3.98 - 3.94 (m, 1 H), 3.70 (s, 3 H), 3.7 - 3.55 (m, 2 H), 2.1 - 1.97 (m, 2 H), 1.84 - 1.79 (m, 2 H), 1.42 (s, 9 H); IR (neat): 3436, 2974, 2952, 1735, 1690, 1489, 1392, 1367, 1168, 1123 $cm^{-1}$; MS (EI) *m/z* 428, 372, 328, 296; HRMS (EI) *m/z* calcd for $C_{19}H_{26}NO_5Br$ 428.1072, Found 428.1042. The diastereomeric excess of the C–H insertion reaction was found to be 78% from $^1$H NMR after removal of the BOC group in the above alcohol with 1M HCl in dioxane.

**(*2R*, *5R*)-1-(*tert*-Butoxycarbonyl)-5-[(*S*)-(methoxycarbonyl(4-bromophenyl)methyl]-2-[*tert*-butyldiphenylsilyloxymethyl]pyrrolidine (5d):**

Methyl 4-bromo phenyldiazoacetate (50 mg, 0.196 mmol) in 2,2-dimethylbutane (2 mL) was added dropwise over 2 h using a syringe pump to a refluxing solution of $Rh_2$(*S*-DOSP)$_4$ (8 mg, 0.02mmol) and-1-(*tert*-butoxycarbonyl)-2-(±)-[*tert*-butyldiphenylsilyloxy methyl]pyrrolidine (172 mg, 0.392 mmol) in 2,2-dimethylbutane (10 mL). After the addition, the resulting solution was cooled to 23$^o$ C. The solvent was removed under reduced pressure and the residue was purified by flash chromatography ($SiO_2$,

$CH_2Cl_2$/pentane = 60:40, then $Et_2O$/pentane = 10:90) to give the title compound (111 mg, 0.17 mmol, 85% yield). $^1$H NMR (500 MHz, $CDCl_3$,) δ 7.60 (m, 4 H), 7.36 (m, 10 H), 4.36 - 4.16 (m, 2 H), 3.98 - 3.77 (m, 1 H), 3.69 (s, 3 H), 3.66 - 3.46 (m, 2 H), 2.1 - 1.94 (m, 4 H), 1.27 (s, 9 H), 1.01 (s, 9 H). The enantiomeric excess of the above was determined by the removal of the -OTBDPS group with HF.Py in acetonitrile, purified through a plug of silica gel and subjected to HPLC analysis to give 98% ee (Whelk (R,R) column, 3% 2-PrOH in hexanes, 1.0 mL/min, 1 mg/mL, $T_R$ = 24.92 and 32.04 min, UV 254 nm). The diastereomeric excess of the C–H insertion reaction was found to be >94% from $^1$H NMR after removal of the BOC group from the above alcohol to free amine with 1M HCl in dioxane.

**(*2 R , 5R*)-2,5-Bis[(*S*)-Methoxycarbonyl(phenyl)methyl] pyrrolidine (9):** Methyl phenyldiazoacetate (59 mg, 0.33 mmol) in 2,2-dimethylbutane (4 mL) was added dropwise over 4 h using a syringe pump to a refluxing solution of $Rh_2$(*S*-DOSP)$_4$ (7 mg, 0.01mmol) and (±)-1-(tert-Butoxycarbonyl)-2-(methoxycarbonyl(phenyl)methyl]-pyrrolidine[5] (215 mg, 0.67 mmol) in 2,2-dimethylbutane (5 mL). After the addition, the resulting solution was cooled to 23$^o$ C. The solvent was removed under reduced pressure and the residue was reconstituted in $CH_2Cl_2$ (10 mL) and TFA (1.0 mL) and stirred for 2 h at 23$^o$ C. The solution was concentrated in *vacuo*, and the residue was dissolved in $Et_2O$ (15 mL), extracted with 10% HCl (3 x 15 mL). The combined aqueous layers were basified ($NaHCO_3$, 1M NaOH to pH 8–9) and extracted with EtOAc (3 x 15 mL). The combined organic layers were washed with water (1 x 20 mL), brine (1 x 20 mL), dried over $Na_2SO_4$ and concentrated to give the free amine **9** in >94% de (by $^1$H NMR). The

product was purified by flash chromatography ($SiO_2$, $Et_2O$/Pentane/$NEt_3$= 50:49:1) to give the title compound (55 mg, 0.15 mmol, 45% yield). $^1$H NMR (400 MHz, $CDCl_3$) δ 7.23 (m, 10 H), 3.75 - 3.72 (m, 2 H), 3.63 (s, 6 H), 3.43 (d, *J* = 12.0 Hz, 2 H), 2.2 - 2.1 (m, 2 H), 1.6 - 1.5 (m, 3 H). The spectroscopic data are consistent with previously reported data.[5] Trifluoroacetamide of **9**: A small sample of the free amine **9** was dissolved in $CH_2Cl_2$, treated with TFAA, purified through a plug of silica gel and subjected to HPLC analysis to give 91% ee (Whelk (R,R) column, 2% 2-PrOH in hexanes, 1.0 mL/min, 1 mg/mL, $T_R$ = 13.46 and 18.92 min, UV 254 nm).

**Determination of relative stereochemistry of 5a, 5b, 5c and 5d:**

The relative stereochemsitry of **5a** was determined by converting **5a** into **3** by deprotection of the BOC group with TFA in $CH_2Cl_2$.

**(*2 R , 5 R* ) - 2 - (hydroxymethyl)-5-[(*1S*)-(4-bromophenyl)-2-(hydroxyeth-1-yl)] pyrrolidine:** To a solution of **3** (105 mg, 0.29 mmol) in toluene (4 mL) at 0$^o$ C under Ar was added DIBAL-H in toluene (1.8 mL, 1M). The ice bath was removed after 15 min, and the mixture was stirred at 23$^o$ C. After 3 h, anhydrous methanol (2 mL) was added and when the evolution of gas was complete, aqueous 1N NaOH (15 mL) was added. The organic layer was extracted with EtOAc, dried over $Na_2SO_4$, filtered and evaporated under reduced pressure. The crude was then purified by flash chromatography ($SiO_2$, EtOAc/methanol/$NEt_3$ = 90:5:5) to give diol as thick oil (54 mg, 0.18 mmol, 61% yield). $^1$H NMR (free amine, 500 MHz, $CDCl_3$) δ 7.45 (d, *J* = 8.0 Hz, 2 H), 7.12 (d, *J* = 8.5 Hz, 2 H), 4.05 - 4.01 (dd, *J* = 7.0, 11.0 Hz, 1 H), 3.81 - 3.78 (dd, *J* = 6.0, 11.0 Hz, 1 H), 3.49 - 3.45 (m, 2 H), 3.33 - 3.29 (m, 2 H), 2.97 - 2.93 (dd, *J* = 6.5, 13.0 Hz, 1 H), 1.97 - 1.86 (m, 2 H), 1.66 - 1.62 (m, 1 H), 1.47 - 1.42 (m, 1 H); $^{13}$C NMR (125 MHz, $CDCl_3$)

139.28, 131.76, 130.09, 120.89, 64.54, 64.52, 60.09, 58.58, 50.64, 28.8, 27.22; IR (neat) 3320, 2963, 2926, 2872, 1487, 1407, 1070, 1042, 1009 $cm^{-1}$; MS (EI) *m/z* 298, 268, 237; HRMS (EI) *m/z* calcd for $C_{13}H_{18}NO_2Br$: 298.0442, Found 298.0433.

The relative stereochemistry of **5b** was determined by reduction of the diester group with $LiAlH_4$ followed by the deprotection of the BOC group to the same diastereomer of the diol above. The relative stereochemistry of **5c** was determined by the removal of the acetate group to alcohol, followed by the deprotection of the BOC group with 1M HCl which was then reduced by DIBAl-H to the same diastereomer of the diol above. The relative stereochemistry of **5d** was determined by the removal of the BOC group and TBDPS group with TFA in $CH_2Cl_2$ followed by the reduction of the ester group with DIBAL-H to the same diastereomer of the diol above.

**References:**


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**Table 1. X-ray crystallographic data for 3.**

| | | |
|---|---|---|
| Identification code | SP007 | |
| Empirical formula | C15 H19 Br Cl N O4 | |
| Formula weight | 392.67 | |
| Temperature | 90(1) K | |
| Wavelength | 0.71073 Å | |
| Crystal system | Triclinic | |
| Space group | P1 | |
| Unit cell dimensions | a = 11.1214(14) Å | _= 104.506(2)°. |
| | b = 14.1305(18) Å | _= 100.221(2)°. |
| | c = 16.934(2) Å | _ = 99.042(3)°. |
| Volume | 2478.0(5) Å3 | |
| Z | 6 | |
| Density (calculated) | 1.579 Mg/m3 | |
| Absorption coefficient | 2.666 mm-1 | |
| F(000) | 1200 | |
| Crystal size | 0.3 x 0.2 x 0.05 mm3 | |
| Theta range for data collection | 1.90 to 28.61°. | |
| Index ranges | -13<=h<=14, -18<=k<=18, -22<=l<=22 | |
| Reflections collected | 13637 | |
| Independent reflections | 13520 [R(int) = 0.0387] | |
| Completeness to theta = 28.61° | 77.3 % | |
| Refinement method | Full-matrix least-squares on F2 | |
| Data / restraints / parameters | 13520 / 3 / 1185 | |
| Goodness-of-fit on F2 | 0.875 | |
| Final R indices [I>2sigma(I)] | R1 = 0.0550, wR2 = 0.1158 | |
| R indices (all data) | R1 = 0.0937, wR2 = 0.1271 | |
| Absolute structure parameter | 0.015(9) | |
| Extinction coefficient | 0.00214(18) | |
| Largest diff. peak and hole | 1.380 and -1.140 e.Å-3 | |

**Table 2.** Atomic coordinates ( x 104) and equivalent isotropic displacement parameters (Å2x 103) for SP007. U(eq) is defined as one third of the trace of the orthogonalized Uij tensor.

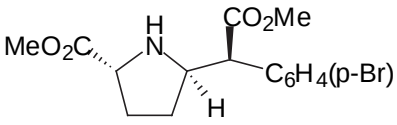
| | x | y | z | U(eq) |
|---|---|---|---|---|
| C(1) | 482(10) | 2746(7) | 4540(6) | 20(2) |
| C(2) | 5598(11) | 924(7) | 7950(6) | 26(3) |
| O(1) | 9027(6) | 2437(4) | 8658(4) | 20(2) |
| Br(1) | 1449(1) | 3392(1) | 3281(1) | 31(1) |
| Br(2) | -1073(1) | 7842(1) | -1659(1) | 39(1) |
| Br(3) | 6026(1) | 4461(1) | -1879(1) | 38(1) |
| Br(4) | 7708(1) | 664(1) | 3322(1) | 35(1) |
| Br(5) | 2578(1) | 576(1) | -1484(1) | 27(1) |
| Br(6) | 4266(1) | 6996(1) | 3399(1) | 39(1) |
| Cl(6) | 2958(3) | 1989(2) | 1927(2) | 19(1) |
| O(2) | 4317(7) | 1845(5) | 6582(4) | 22(2) |
| O(3) | 1021(6) | 10433(4) | 4283(4) | 21(2) |
| O(4) | 21(7) | 7058(5) | 6211(5) | 26(2) |
| O(5) | 1276(7) | 8574(5) | 6822(4) | 25(2) |
| O(6) | 9686(7) | 1356(5) | 9304(4) | 25(2) |
| O(7) | -1910(7) | 5296(5) | 6550(4) | 25(2) |
| O(8) | 4593(7) | 8206(5) | 1719(4) | 29(2) |
| O(9) | 3176(7) | 3555(5) | 8385(5) | 28(2) |
| O(10) | 2910(7) | 4871(5) | 9377(4) | 28(2) |
| O(11) | 5554(7) | 9009(5) | 8741(4) | 24(2) |
| C(3) | -23(9) | 4591(7) | 5311(6) | 17(2) |
| C(4) | 7096(10) | 646(7) | 4303(5) | 21(2) |
| O(12) | 11249(7) | 4796(5) | 1464(4) | 23(2) |
| O(13) | 5296(7) | 2629(5) | 3765(4) | 29(2) |
| C(5) | 4209(11) | 863(7) | 6182(6) | 16(2) |
| O(14) | 7243(8) | 7502(6) | 3382(5) | 33(2) |
| O(15) | 4666(7) | 4019(5) | 4365(4) | 25(2) |
| N(1) | 905(7) | 3845(5) | 7366(4) | 14(2) |
| C(6) | 10147(9) | 6087(6) | 1378(6) | 18(2) |
| N(6) | 5574(7) | 3427(5) | 2431(4) | 15(2) |
| N(10) | 4321(8) | 7257(5) | 7466(4) | 15(2) |
| C(7) | 180(10) | 9007(7) | 6694(7) | 26(3) |
| C(8) | 6223(10) | 1094(7) | 7245(6) | 19(2) |
| O(16) | 8396(7) | 7221(5) | 4493(4) | 28(2) |
| C(9) | 8896(10) | 1618(7) | 8765(6) | 18(2) |
| C(10) | -971(10) | 3880(6) | 6337(6) | 18(2) |
| O(17) | 3270(7) | 339(5) | 5728(5) | 28(2) |
| C(11) | 3348(9) | 9368(6) | 1431(6) | 17(2) |
| O(18) | 12149(8) | 6039(5) | 1019(5) | 33(2) |

| | | | | |
|---|---|---|---|---|
| C(12) | 1594(9) | 9873(7) | 3779(6) | 14(2) |
| O(19) | 6468(6) | 8065(4) | 9453(4) | 20(2) |
| C(13) | 3208(10) | 7750(6) | 7415(6) | 18(2) |
| O(20) | -3017(8) | 3885(5) | 5652(5) | 38(2) |
| C(14) | 6665(10) | 2909(7) | 2382(6) | 18(2) |
| C(15) | 3362(10) | 7933(8) | 4797(6) | 29(3) |
| C(16) | 2748(10) | 7147(7) | 5816(6) | 17(2) |
| O(21) | 8201(7) | 1648(5) | 1753(4) | 21(2) |
| C(17) | 6436(9) | 1487(7) | 5476(6) | 16(2) |
| C(18) | 6255(11) | -295(7) | 5136(7) | 23(3) |
| N(5) | 8882(8) | 6704(5) | 2403(4) | 16(2) |
| C(19) | 2925(10) | 7983(7) | 5519(6) | 24(3) |
| C(20) | 5553(11) | 7671(9) | 1579(8) | 38(3) |
| C(21) | 3081(10) | 6272(7) | 5405(7) | 21(3) |
| C(22) | 4148(14) | 9855(11) | 3030(8) | 61(5) |
| C(23) | 551(9) | 4478(6) | 4603(6) | 18(2) |
| C(24) | 6965(9) | 2832(6) | 1524(5) | 16(2) |
| C(25) | 2262(11) | 8990(7) | 706(6) | 19(3) |
| C(26) | 10791(10) | 6252(8) | 2968(6) | 25(3) |
| C(27) | 7314(10) | 8960(7) | 10020(7) | 28(3) |
| C(28) | 3660(10) | 7069(8) | 4397(6) | 26(3) |
| N(3) | 7399(7) | 676(5) | 7428(4) | 13(2) |
| O(22) | 8809(8) | 2637(6) | 998(5) | 43(2) |
| C(29) | 12321(11) | 4357(8) | 1410(7) | 29(3) |
| C(30) | 1690(10) | 9629(8) | 364(6) | 19(3) |
| C(31) | 1148(11) | 3952(8) | 8309(6) | 20(3) |
| C(32) | 6923(10) | 1514(7) | 4794(6) | 21(2) |
| C(33) | 11297(11) | 5655(7) | 1264(6) | 19(3) |
| N(4) | 2121(8) | 10013(5) | 2429(4) | 19(2) |
| C(34) | 7769(10) | 826(7) | 8358(6) | 17(3) |
| C(35) | 8641(10) | 4658(7) | 244(6) | 24(3) |
| C(36) | 792(10) | 7643(7) | -350(6) | 19(2) |
| C(37) | 3060(11) | 9373(7) | 2283(6) | 26(3) |
| C(38) | 5890(10) | 2285(7) | 808(6) | 19(2) |
| C(39) | 9756(9) | 5994(6) | 2185(5) | 15(2) |
| C(40) | 319(13) | 9937(9) | 4766(8) | 46(4) |
| C(41) | 3917(10) | 1281(7) | -544(6) | 18(2) |
| C(42) | 9273(11) | 7153(8) | 3349(6) | 21(3) |
| C(43) | 5752(12) | 4083(8) | 3302(6) | 23(3) |
| C(44) | 1054(12) | 7562(7) | 6518(6) | 23(3) |
| C(45) | 4334(10) | 2277(7) | -398(6) | 20(2) |
| C(46) | 2509(11) | 4108(7) | 8665(6) | 24(3) |
| C(47) | 6072(10) | 590(7) | 5677(6) | 15(2) |
| C(48) | 5415(10) | 538(6) | 6360(5) | 16(2) |
| C(49) | 2256(9) | 7188(6) | 6601(5) | 15(2) |
| C(50) | -61(9) | 4444(6) | 7168(5) | 15(2) |

| | | | | |
|---|---|---|---|---|
| C(51) | 7669(11) | 3505(8) | 3155(6) | 24(3) |
| C(52) | -2956(12) | 5761(7) | 6392(7) | 36(3) |
| C(53) | -621(10) | 4648(7) | 7949(5) | 20(2) |
| C(54) | 7449(12) | 7343(9) | 4971(7) | 42(3) |
| C(55) | 4416(10) | 752(7) | -32(6) | 19(2) |
| C(56) | 5405(10) | 1260(6) | 646(6) | 20(2) |
| C(57) | -89(10) | 2875(8) | 5226(6) | 22(3) |
| C(58) | 7650(10) | 5969(7) | -496(7) | 24(3) |
| C(59) | -343(10) | 3773(7) | 5620(6) | 14(2) |
| C(60) | -2080(11) | 4331(7) | 6135(6) | 21(3) |
| C(61) | 283(11) | 8287(8) | -679(6) | 29(3) |
| C(62) | 7741(11) | 4301(7) | -468(7) | 27(3) |
| C(63) | 4387(11) | 8799(7) | 1248(7) | 21(3) |
| C(64) | 7250(10) | 4940(8) | -852(6) | 26(3) |
| C(65) | 1768(10) | 7946(7) | 329(6) | 18(2) |
| C(66) | 4161(11) | 5067(8) | 9837(7) | 35(3) |
| C(67) | 5333(11) | 2775(8) | 254(6) | 21(3) |
| O(23) | 4921(8) | 8895(6) | 700(5) | 40(2) |
| C(68) | 5228(10) | 3475(8) | 3827(6) | 23(2) |
| C(69) | 8570(11) | 6315(8) | 215(7) | 21(3) |
| C(70) | 693(10) | 9304(7) | -338(6) | 22(3) |
| C(71) | 7175(10) | 4409(7) | 3579(6) | 24(3) |
| C(72) | 3187(10) | 2217(7) | 6433(7) | 25(3) |
| C(73) | 4768(11) | 7244(7) | 8354(6) | 15(2) |
| C(74) | 4150(11) | 3543(8) | 4935(7) | 33(3) |
| C(75) | 10754(11) | 2133(8) | 9800(7) | 32(3) |
| C(76) | 5625(9) | 8201(7) | 8853(6) | 16(2) |
| C(77) | 9178(11) | 1139(8) | 1593(7) | 30(3) |
| C(78) | 531(10) | 4802(8) | 8647(6) | 26(3) |
| C(79) | 2347(12) | 10507(7) | 3377(6) | 22(3) |
| C(80) | 8168(11) | 7311(8) | 3711(7) | 23(2) |
| C(81) | 3542(10) | 6213(7) | 4676(6) | 24(3) |
| C(82) | 746(9) | 3575(7) | 4240(6) | 20(2) |
| C(83) | 10105(10) | 6540(8) | 3676(6) | 24(3) |
| C(84) | 3701(11) | 10539(9) | 3678(7) | 35(3) |
| Cl(1) | 6281(3) | 5255(2) | 1784(2) | 24(1) |
| Cl(2) | 9467(3) | 8661(2) | 1895(2) | 22(1) |
| Cl(3) | 3199(3) | 4956(2) | 6931(2) | 21(1) |
| Cl(4) | 9683(3) | 1557(2) | 6805(2) | 20(1) |
| Cl(5) | 6445(2) | 8341(2) | 6836(2) | 20(1) |
| O(24) | 1571(7) | 8987(5) | 3688(4) | 22(2) |
| C(85) | 6743(9) | -277(7) | 4448(6) | 19(2) |
| C(86) | 3528(11) | 7125(7) | 8660(6) | 26(3) |
| C(87) | 2774(12) | 7737(8) | 8227(7) | 30(3) |
| C(88) | 9117(11) | 5685(7) | 598(6) | 17(2) |
| C(89) | 8091(10) | 2381(7) | 1401(7) | 20(3) |

| | | | | |
|---|---|---|---|---|
| C(90) | 6657(10) | 1135(8) | 8707(6) | 22(3) |

**Ortep drawing of structure 3**




**3**