Stereoselective Synthesis of Morpholines Via Copper-Promoted Oxyamination of Alkenes

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Supporting Information I

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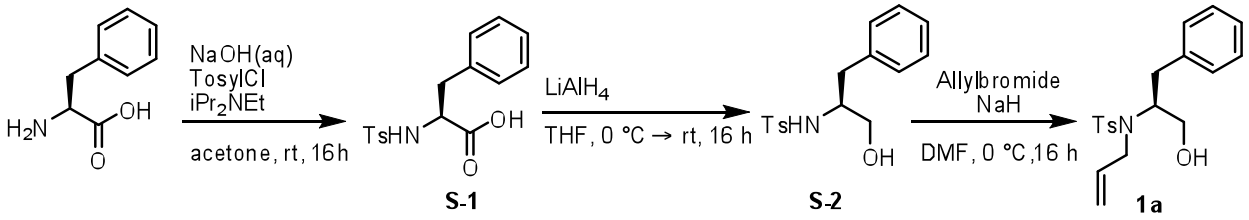
General experimental information: All reagents were used out of the bottle as purchased from the supplier without further purification unless otherwise noted. Solvents were dried using a commercial solvent filtration system. ^{1}H NMR spectra were recorded in $CDCl_3$ (using 7.26 ppm for reference of residual $CHCl_3$) at 300, 400 or 500 MHz. ^{13}C NMR spectra were recorded in $CDCl_3$ (using 77.0 ppm as internal reference) at 75 or 125.7 MHz. IR spectra were taken neat using a Nicolet-Impact 420 FTIR. Wave numbers in cm^{-1} are reported for characteristic peaks. High resolution mass spectra were obtained at SUNY Buffalo's mass spec. facility on a ThermoFinnigan MAT XL spectrometer. Optical rotations were obtained using a Rudolph Autopol 1 fitted with a micro cell with a 100 mm path length. Melting points are reported as uncorrected. The reactions involving sodium azide were run on 50 mg scale and no adverse reactivity was detected. Precautions such as a blast shield should be taken when heating sodium azide in the presences of metal, especially on larger reaction scales.

Synthesis of N-allyl alcohols from amino acids:

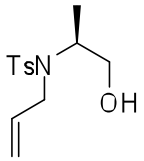


(*S*)-N-allyl-N-(1-hydroxy-3-phenylpropan-2-yl)-4-methylbenzenesulfonamide (1a) (Representative Procedure)

L-Phenylananine (1.50 g, 9.08 mmol) was placed in a dry round-bottomed flask equipped with a stir bar and was treated with 4.5 mL of 2 M NaOH at room temperature. Tosyl choride (1.79 g, 9.44 mmol, 1.05 equiv), *N*,*N*-diisopropylethylamine (1.52 mL, 9.08 mmol, 1 equiv) and 4.5 mL of acetone were added. The reaction was stirred for 16 h. The reaction mixture was placed in a separtory funnel and was washed with Et_2O (20mL). The layers were separated and the organic layer was washed with 2 M NaOH. The aqueous layers were combined, cooled to 0 °C and slowly acidified with HCl (pH<1). The mixture was then extracted with EtOAc (2x) and the combined organic extracts were dried over anhydrous Na_2SO_4, filtered and concentrated in vacuo. The crude product **S-1** was obtained as a solid and used without further purification.

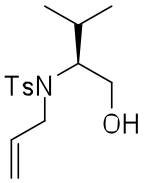
A portion of the crude *(S)*-4-methyl-N-(1-oxo-3-phenylpropan-2-yl)benzenesulfonamide **S-1** (0.98 g, 3.06 mmol) was dissolved in 27.0 mL of THF and was slowly added to a stirred dispersion of $LiAlH_4$ (0.31 g, 8.17 mmol) in 81.0 mL of THF at 0 °C. The reaction was allowed to come to room temperature and was stirred for 16 h. The reaction mixture was cooled to 0 °C and quenched slowly with NaOH (1 M), producing a white precipitate. The reaction was stirred for an additional 30 min and then was filtered through a Celite plug. The filtrate was dried over anhydrous Na_2SO_4 and then filtrated and concentrated in vacuo. The crude residue **S-2** was carried immediately to the next reaction. The residue was dissolved in 5.4 mL of DMF in a

round-bottomed flask equipped with a stir bar and placed into a 0 °C ice water bath. Sodium hydride (99%) (0.07 g, 2.92 mmol) was added to the solution. After 20 min, allylbromide (0.27 mL, 3.12 mmol) was added and the reaction was stirred at room temperature for 16 h. This mixture was concentrated in vacuo to give a crude oil. Flash chromatography on SiO_2 (0-20% EtOAc/hexanes gradient) provided (*S*)-*N*-allyl-*N*-(1-hydroxy-3-phenylpropan-2-yl)-4-methylbenzenesulfonamide **1a** (820 mg, 78% yield over 3 steps) as a colorless oil. The ^{1}H NMR was in agreement with literature values.[1] ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.56 (d, 2H, J = 8.2 Hz), 7.18-7.11 (m, 5H), 6.97-6.95 (m, 2H), 5.89-5.76 (m, 1H), 5.24-5.08 (m, 2H), 4.10-4.04 (m, 1H), 3.81 (d, J = 5.6 Hz, 1H), 3.89-3.83 (m, 1H), 3.63-3.49 (m, 2H), 2.73-2.56 (m, 2H), 2.43(s, 3H), 2.04 (br s,1H).



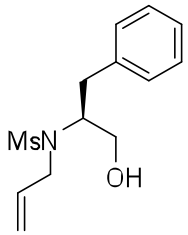
(S)-N-allyl-N-(1-hydroxypropan-2-yl)-4-methylbenzenesulfonamide (1c)

Following the above procedure, alcohol **1c** was isolated as colorless oil in 78% yield (1.10 g) from L-alanine. The ^{1}H NMR spectrum were in agreement the reported.[2] ^{1}H NMR (400 MHz, CDCl3) δ 7.73 (d, J = 8.4 Hz, 2H), 7.30-7.29 (m, 2H), 5.84 (m, 1H), 5.27-5.83 (m, 2H), 4.03-3.95 (m, 2H), 3.75-3.72 (m, 1H), 3.61-3.47 (m, 2H), 2.42 (s, 3H), 1.93 (br s, 1H), 0.94 (d, J = 6.9 Hz,3H).



(S)-N-allyl-N-(1-hydroxy-3-methylbutan-2-yl)-4-methylbenzenesulfonamide (1d)

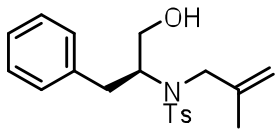
Following the above procedure, L-valine was converted to *N*-allyl sulfonamide alcohol **1d** (0.83 g) in 71% yield. The ^{1}H NMR spectrum were in agreement the reported.[2] ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.72 (d, J=8.4 Hz, 2H), 7.32 (d, J=8.8 Hz, 2H), 5.98-5.80 (m, 1H) 5.18 (dd, J=6.8, 16.0 Hz, 2H), 4.01 (m, 1H), 3.98-3.81 (m, 2H), 3.10 (dd, J=6.0, 14.8 Hz, 1H), 2.97 (d, J=3.2 Hz, 1H), 2.44 (s, 3H), 1.85-1.80 (m, 1H), 0.83 (d, J = 6.5 Hz, 3H), 0.61 (d, J= 6.6 Hz, 3H).



(S)-N-allyl-N-(1-hydroxy-3-phenylpropan-2-yl)methanesulfonamide (1h):

Alcohol **1h** was obtained as a colorless oil in a 48% yield (180 mg) following the above procedure except methanesulfonyl chloride was used instead of tosyl chloride. $[\alpha]_D^{22}$ = -16.8° (c = 1.0, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.34-7.23 (m, 5H), 5.94 (m, 1H) 5.28 (dd, J=17.2, 46.0 Hz, 2H), 4.19-4.15 (m, 1H), 3.91-3.89 (m, 2H), 3.73-3.71 (m, 2H), 2.87 (dd, J=1.6, 7.6 Hz, 1H), 2.51 (s, 3H), 1.82 (bs, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 137.9, 135.6, 129.2, 128.7,

126.9, 118.3, 62.8, 62,5, 46.8, 400.3, 36.5; IR (neat, thin film) ν 3468, 2903, 2358, 1321, 1136, 1013, 792, 705 cm^{-1}; HRMS (ESI) calcd for $C_{13}H_{19}O_3N_1Na_1S_1$ $[M+Na]^+$ 292.0978, found 292.0985.



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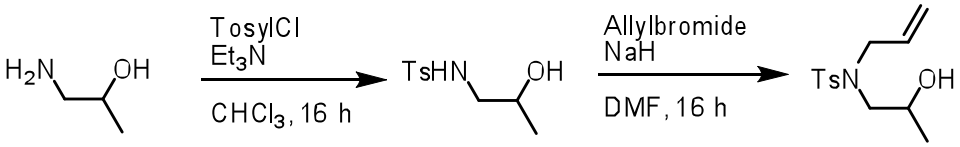
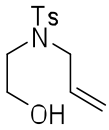
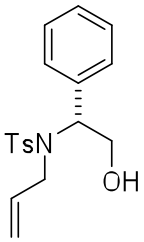
(*S*)-N-(1-hydroxy-3-phenylpropan-2-yl)-4-methyl-N-(2-methylallyl)benzenesulfonamide (5)
Alcohol **5** was obtained as a colorless oil in a 12% yield (60 mg, unoptimized) following the above procedure except 3-bromo-2methyl-propene was used instead of allylbromide.
$[\alpha]_D^{22}$ = -23.5° (*c* 1.0, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.80 (d, J=1.8 Hz, 2H), 7.36-7.25 (m, 5H), 7.05 (d, J=1.8 Hz, 2H), 5.11 (d, J=22.5 Hz, 2H), 3.99 (ABq, J_{ab}=15.9 Hz, Δν=1.5 Hz, 2H), 4.05-3.87 (overlapping m, 1H), 3.80-3.70 (m, 1H), 3.70-3.60 (m, 1H), 2.84 (dd, J=10.5, 13.5 Hz, 1H), 2.70 (dd, J=4.8 13.5 Hz, 1H), 2.49 (s, 3H), 2.10 (t, J=5.1 Hz, 1H), 1.87 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 143.5, 142.8, 137.8, 137.6, 129.7, 129.0, 128.0, 128.6, 127.3, 126.6, 114.0, 62.3, 62.1, 51.6, 35.8, 21.5, 20.0; IR (neat, thin film) ν 3468, 2903, 2358, 1659, 1492, 1329, 1102, 1039, 995 cm-1; HRMS (ESI) calcd for $C_{20}H_{26}O_3N_1S_1$ $[M+1]^+$ 360.1628, found 360.1625.



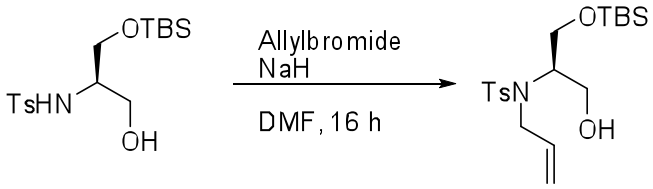
(±)-N-allyl-N-(2-hydroxypropyl)-4-methylbenzenesulfonamide (3)
1-Aminopropan-2-ol (1.0 mL, 13.0 mmol) was placed in a round-bottomed flask and dissolved in CH_2Cl_2 (8 mL). The solution was treated with tosyl choride (2.70 g, 14.6 mmol, 1.1 equiv), triethylamine (3.60 mL, 26.0 mmol, 2 equiv) and stirred at room temperature overnight. The reaction mixture was then diluted with water and extracted with CH_2Cl_2. The combined organic layers were dried over Na_2SO_4 and concentrated *in vacuo* to give the crude sulfonamide in quantitative yield. The crude sulfonamide in 26 mL of DMF in a round-bottom flask equipped was treated with NaH (0.36 g, 15.6 mmol, 1.2 equiv) at 0 °C. After 20 min, allylbromide (1.36 mL, 15.6 mmol, 1.2 equiv) was added and the reaction was stirred at room temperature for 16 h. The mixture was concentrated and the crude oil was flash chromatographed on SiO_2 (30%-50% EtOAc/hexanes) to provide *N*-allyl-*N*-(2-hydroxypropyl)-4-methylbenzenesulfonamide **(3)** as a colorless oil (1.13g, 32% yield over 2 steps).
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.72 (d, J=8.4 Hz, 2H), 7.32 (d, J=8.8 Hz, 2H), 5.64 (m, 1H), 5.18 (dd, J=6.8, 16.0, 2H), 4.03-3.99 (m, 1H), 3.98-3.81 (m, 2H), 3.10 (dd, J=6.0, 14.8, 1H), 2.97 (dd, J= 11.6, 3.2 Hz, 1H), 2.44 (s, 3H), 2.28 (br s, 1H), 1.15 (d, J=6.0 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 143.5, 136.0, 132.8, 129.7, 127.17, 119.3, 65.9, 54.9, 52.4, 21.4, 20.3. IR (neat, thin film) ν 3493, 2924, 1591, 1315, 1164, 1090, 1025, 930, 816, 761, 662 cm^{-1}. HRMS (ESI) calcd for $C_{13}H_{19}O_3N_1Na_1S_1$ $[M+Na]^+$ 292.0978, found 292.0968.



N-allyl-N-(2-hydroxyethyl)-4-methylbenzenesulfonamide (1b):
Using the method above, the alcohol **1b** was isolated as colorless oil in 88% yield (5.5 g) from 2-aminoethanol. This product was isolated as colorless oil. The ^{1}H NMR spectrum in agreement with literature values.[1] ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.71 (d, J=8.8 Hz, 2H), 7.32 (d, J=8.4 Hz, 2H), 5.74-5.64 (m, 1H), 5.21-5.16 (m, 2H), 3.82 (d, J=6.0 Hz, 2H), 3.74 (t, J=5.6 Hz, 2H), 3.29 (t, J=5.2, 2H), 2.44 (s, 3H).

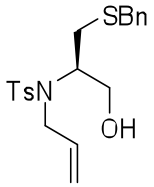


(R)-N-allyl-N-(2-hydroxy-1-phenylethyl)-4-methylbenzenesulfonamide (1i)
Using the method above, alcohol **(1i)** was isolated as colorless oil in 87% yield (2.38 g) from D-2-phenylglycine; $[\alpha]_D^{22}$ = -78.8° (*c* 1.0, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.72 (d, J=8.4 Hz, 2H), 7.29-7.21 (m, 5H), 7.00 (dd, J=1.5, 5.5 Hz, 2H), 5.80-5.75 (m, 1H), 5.11-5.04 (m, 2H), 4.14-4.03 (m, 2H), 3.98-3.92 (m, 1H), 3.52 (dd, J=7.6, 16.4 Hz), 2.45 (s, 3H), 2.11 (br s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 143.5, 137.9, 135.7, 135.4, 129.6, 128.6, 128.2, 128.2, 127.4, 117.8, 62.3, 47.4, 21.5; IR (neat, thin film) ν 3521, 3050, 2923, 1592, 1497, 1447, 1320, 1153, 1094, 1003 cm^{-1}; HRMS (ESI) calcd for $C_{18}H_{21}O_3N_1Na_1S_1$ $[M+Na]^+$ 354.1143, found 354.1113.



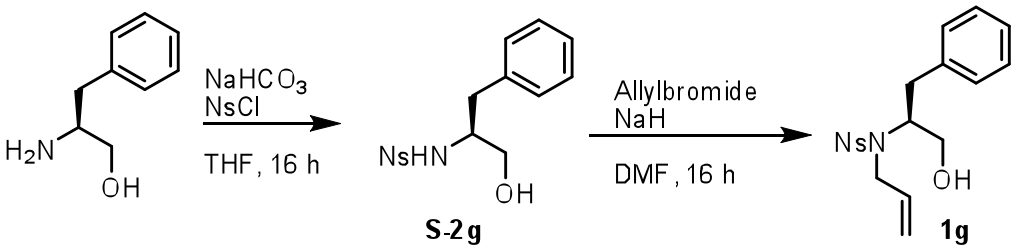
(R)-N-allyl-N-(1-(tert-butyldimethylsilyloxy)-3-hydroxypropan-2-yl)-4-methylbenzenesulfonamide (1e)
(R)-N-(1-(tert-butyldimethylsilyloxy)-3-hydroxypropan-2-yl)-4-methylbenzenesulfonamide[3] (0.81 g, 2.0 mmol) in a round-bottom flask equipped with a stir bar was dissolved in DMF (20 mL) at 0 °C was treated with NaH (0.057 g, 2.40 mmol). After being stirred for 20 min, allylbromide (0.58 mL, 6.71 mmol) was added and the reaction was stirred at room temperature for 16 h. This mixture was concentrated then in vacuo to give a crude oil, that was chromatographed on SiO_2 (EtOAc/hexanes gradient) to provide **1e** (495 mg, 62% yield).
$[\alpha]_D^{22}$ = 13.2° (*c* 1.0, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.74 (d, J= 8.0 Hz, 2H), 7.28 (d, J=8.4 Hz, 2H), 5.89-5.82 (m,1H), 5.24-5.12 (m, 2H), 3.95-3.88 (m, 3H), 3.79-3.70 (m, 2H), 3.70-3.66 (m, 2H), 2.42 (s, 3H), 0.83 (s, 9H), -0.12(s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 143,3, 137.9, 135.9, 129.7, 127.2, 117.6, 62.6, 62.1, 60.8, 48.0, 25.7, 21.5, 18.1, -5.7; IR (neat, thin

film) ν 3516, 2927, 2360, 1598, 1331, 1259, 1159, 1090, 922, 837 cm^{-1}; HRMS (ESI) calcd for $C_{19}H_{34}O_4N_{11}S_1Si_1$ $[M+H]^+$ 400.1972, found 400.1970.



(R)-N-allyl-N-(1-(benzylthio)-3-hydroxypropan-2-yl)-4-methylbenzenesulfonamide (1f)

Using the method above, alcohol (**1f)** was obtained as colorless oil in 41% yield (208 mg) from D-2-((R)-N-(1-(benzylthio)-3-hydroxypropan-2-yl)-4-methylbenzenesulfonamide.[4] $[\alpha]_D^{22}$ = 36.9° (*c* 1.0, $CHCl_3$); ^1H NMR (500 MHz, $CDCl_3$) δ 7.71 (dd, J=1.6, 6.4 Hz, 2H), 7.32-7.23 (m, 7H), 5.83-5.77 (m, 1H), 5.10 (m, 2H), 3.95-3.88 (m, 1H), 3.82 (dd, J=1.2, 6.0 Hz, 1H), 3.78-3.65 (m, 3H), 3.61 (s, 2H), 2.53 (dd, J=5.6, 7.6 Hz, 2H), 2.41 (s, 3H), 1.82 (br s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 143.5, 137.8, 137.6, 135.6, 129.6, 128.9, 128.6, 127.4, 127.2, 118.0, 62.9, 59.4, 47.6, 36.5, 31.1, 21.6; IR (neat, thin film) ν 3547, 2888, 1330,1160, 1069, 706, 660, 535 cm^{-1}; HRMS (ESI) calcd for $C_{20}H_{25}O_3N_1Na_1S_2$ $[M+Na]^+$ 414.1179, found 414.1173.



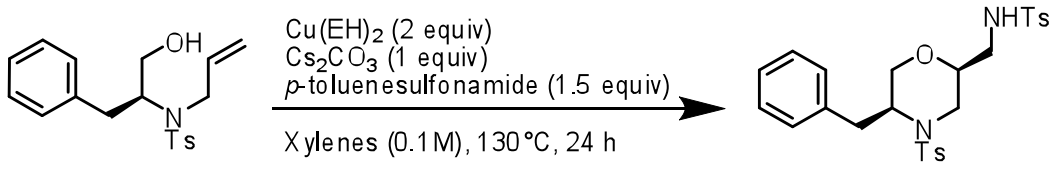
(2S)-2-benzyl-3-(4-nitrophenylsulfonyl)hex-5-en-1-ol (1g):

This is a modification of an existing procedure.[5] A solution of p-nitrobenzenesulfonyl chloride (3.16 g, 14.4 mmol, 1.1 equiv) in THF (8.9 mL) was added dropwise to a mixture of the (S)-2-amino-3-phenyl-1-propanol (1.72 g, 13.0 mmol) and $NaHCO_3$ (3.48g, 44.0 mmol, 4 equiv) in THF (8.9 mL) at 0 °C. The resulting mixture was stirred at room temperature for 16 h. The solution was concentrated and the yellow solid obtained was taken up in EtOAc/H_2O (7:3 v/v, 100 mL). The layers were separated, and the aqueous phase was back-extracted with EtOAc (3 x 100 mL). The combined organic layers were dried over anhydrous Na_2SO_4, filtered, and concentrated. The crude **S-2g** was used in the next reaction. The residue was dissolved in DMF (11 mL) in a round-bottom flask equipped with a stir bar and placed into a 0 °C bath, followed by the addition of NaH (0.25 g, 10.5 mmol, 1.2 equiv). After 20 min, allylbromide (0.94 mL, 10.9 mmol) was added and the reaction was stirred at room temperature for 16 h. This mixture was concentrated in vacuo to give a crude oil that was chromatographed on SiO_2 (0-20% EtOAc/hexanes gradient) to provide (S)-N-allyl-N-(1-hydroxy-3-phenylpropan-2-yl)-4-nitrobenzenesulfonamide **(1g)** (500 mg, 14% yield over 2 steps).

$[\alpha]_D^{22}$ = -12.0° (*c* 1.0, $CHCl_3$); ^1H NMR (500 MHz, $CDCl_3$) δ 8.14 -7.96 (m, 2H), 7.81-7.76 (m, 2H). 7.32-7.09 (m, 5H), 5.95-5.90 (m, 1H), 5.40-5.26 (m, 2H) 4.29-4.08 (m, 1H), 4.09-3.99 (m, 2H) 3.81-3.73 (m, 2H), 2.90 (dd, J=7.5, 14.5 Hz, 1H), 2.82 (dd, J=7.5, 14.0 Hz, 1H), 1.76 (br s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 149.7, 146.5, 137.4, 135.1, 129.0, 128.7, 128.3, 126.9, 124.0, 118.7, 62.8, 62.6, 47.2, 36.3; IR (neat, thin film) ν 3557, 3104, 2950, 2335, 1601, 1524,

1343, 1162, 1098, 1026 cm^{-1}; HRMS (ESI) calcd for $C_{18}H_{20}O_5N_2Na_1S_1$ $[M+Na]^+$ 399.0985, found 399.0980.

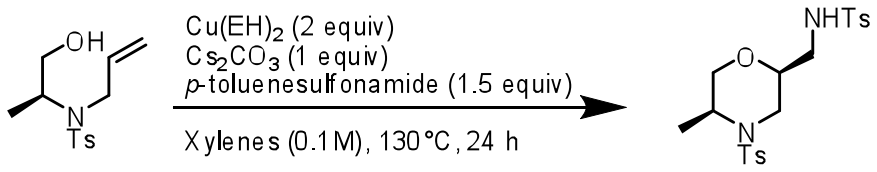
Copper-Promoted Oxyamination Reaction Procedure:



1a **2a**

***N*-(((2S,5S)-5-benzyl-4-tosylmorpholin-2-yl)methyl)-4-methylbenzenesulfonamide (2a)**

(S)-4-Methyl-N-(1-oxo-3-phenylpropan-2-yl)benzenesulfonamide **(1a)** (40.0 mg, 0.116 mmol, 1 equiv) in a glass pressure tube equipped with a magnetic stir bar was treated with Cs_2CO_3 (37.0 mg, 0.150 mmol, 1 equiv), *p*-toluenesulfonamide (29 mg, 0.174 mmol, 1.5 equiv) and Cu(II) 2-ethylhexanoate (81.0 mg, 0.232 mmol, 2 equiv) in 1.2 mL of xylenes. The tube was capped and the reaction mixture was stirred at 130 °C for 24 h. The reaction mixture was allowed to cool to room temperature and was diluted with EtOAc (10 mL). This mixture was then washed with sat. aq. $EDTANa_2$ (2 x 10 mL) and 2M NaOH (2 x 10 mL). The combined aqueous layers were washed with EtOAc, dried over Na_2SO_4, filtered and concentrated *in vacuo*. The resulting oil was purified by flash chromatography on SiO_2 (0 – 40% EtOAc in hexanes gradient) to give morpholine **2a** in 85% yield (50.6 mg, 0.099 mmol) as a yellow oil. The diastereomeric ratio was >20:1 based on analysis of the crude ^1H NMR spectrum. $[\alpha]_D^{22}$ = -15.6 ° (*c* 1.0, $CHCl_3$); ^1H NMR (500 MHz, $CDCl_3$) δ 7.73 (d, J=8.5 Hz, 2H), 7.77 (d, J=7.5 Hz, 2H), 7.32 (d, J= 8.0 Hz, 2H), 7.29-7.22 (m, 5H), 7.13 (d, J=7.0 Hz, 2H), 4.81 (br s, 1H), 3.99-3.97 (m, 1H), 3,62 (d, J=11.5 Hz, 1H), 3.54 (dd, J=3.0, 13.0 Hz, 1H), 3.47 (m, 1H), 3.35 (dd, J=3.0, 12.0 Hz, 2H), 3.14-3.10 (m, 1H), 3.08-3.02 (m, 1H), 3.00-2.91 (m, 2H), 2.65 (dd, J=5.0, 13 Hz, 1H)), 2.45 (s, 3H), 2.42 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 143.8, 143.7, 137.5, 137.1, 136.5, 129.9, 129.8, 129.4, 128.7, 127.1, 126.7, 73.4, 67.4, 53.9, 45.0, 42.5, 34.0, 21.6, 21.5; IR (neat, thin film) ν 3267, 2914, 1601, 1325, 1166, 155, 1085 cm^{-1}; HRMS (ESI) calcd for $C_{26}H_{31}O_5N_2S_2$ $[M+H]^+$ 515.1669, found 515.1676.

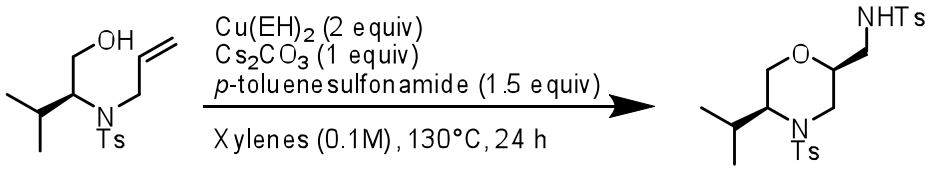


1c **2c**

4-methyl-N-(((2S,5R)-5-methyl-4-tosylmorpholin-2-yl)methyl)benzenesulfonamide (2c)

Morpholine **2c (**47 mg) was obtained as an oil (73%, dr >20:1) from 40 mg of **1c** using the conditions above. $[\alpha]_D^{22}$ = -36.9 ° (*c* 1.5, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 7.72 (d, J=7.2 Hz, 2H), 7.64 (d, J=6.4 Hz, 2H), 7.32-7.26 (m, 4H), 4.73 (t, J=5.6 Hz, 1H), 3.96 (d, J=7.2 Hz, 1H), 3.54-3.49 (m, 2H), 3.45 (dd, J=2.0, 12.8 Hz, 1H), 3.46-3.40 (m, 1H), 3.10-3.02 (m, 1H), 2.92-2.87 (m, 2H), 2.42 (s, 6H), 1.01 (d, J=7.2 Hz, 3H);^{13}C NMR (75 MHz, $CDCl_3$) δ 143.7, 137.5, 137.3, 129.9, 129.4, 128.7, 127.1, 126.7, 74.2, 67.3, 54.0, 52.5, 42.4, 33.8, 21.5; IR (neat,

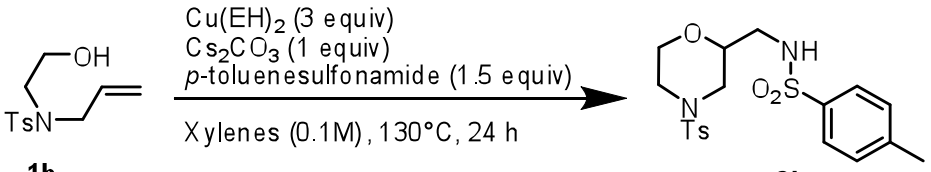
thin film) ν 3392, 2333, 1628, 1310, 1253, 1140 cm^{-1}; HRMS (ESI) calcd for $C_{20}H_{27}O_5N_2S_2$ $[M+H]^+$ 439.1356, found 439.1361.



1d **2d**

***N*-(((2*S*,5*S*)-5-isopropyl-4-tosylmorpholin-2-yl)methyl)-4-methylbenzenesulfonamide (2d)**

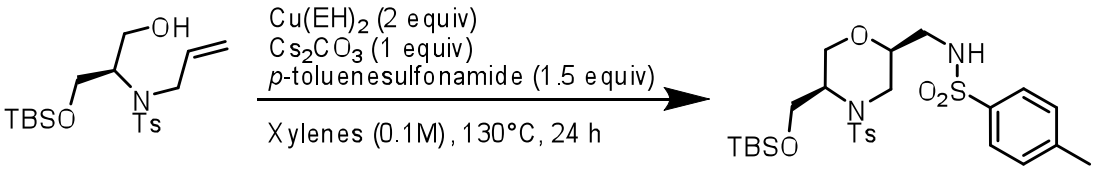
Morpholine **2d** (52 mg) was obtained as an oil (82%, dr >20:1) from 40 mg of **1d** using the conditions above. $[\alpha]_D^{22}$ = 6.02 ° (*c* 1.0, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.69 (apparent t, J=8.5 Hz, 4H), 7.31-7.29 (m, 4H), 4.70 (t, J=2.4 Hz, 1H), 3.80 (d, J=11.6, 1H), 3.57 (dd, J= 2.8, 14.4 Hz, 1H), 3.30-3.18 (m, 3H), 3.02-2.95 (m, 1H), 2.95 (dd, J=11.2, 14.4 Hz, 1H), 2.91-2.73 (m, 1H), 2.43 (s, 3H), 2.42 (s, 3H), 2.12-2.07 (m, 1H), 0.91 (d, J=0.7 Hz, 3H) 0.86 (d, J= 0.7 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 143.7, 143.5, 138.2, 136.4, 129.9, 129.8, 127.0, 126.9, 72.2, 66.3, 58.8, 45.0, 42.8, 25.26, 21.5, 19.9, 19.7; IR (neat, thin film) ν 3442, 1161, 1341, 1153, 1087, 690, 557 cm^{-1}; HRMS (ESI) calcd for $C_{22}H_{30}O_5N_2NaS_2$ $[M+Na]^+$ 489.1488, found 489.1483.



1b **2b**

(±)-4-methyl-N-((4-tosylmorpholin-2-yl)methyl)benzenesulfonamide (2b)

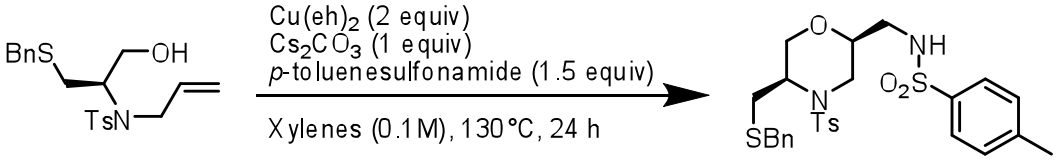
Morpholine **2b** (53 mg) was obtained as an oil (80%) from 40 mg of **1b** using the conditions above except that 3 equivalents of $Cu(eh)_2$ was used. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.69 (d, J= 8.4 Hz, 2H), 7.59 (d, J= 8.0, 2H), 7.35-7.30 (m, 4H), 4.68 (t, J= 6.4 Hz, 1H), 3.83 (dd, J=2.0, 9.6 Hz, 1H), 3.57- 3.49 (m, 4H), 3.06-3.03 (m, 1H), 2.91-2.86 (m, 1H), 2.44 (s, 3H), 2.43 (s, 3H), 2.36-2.32 (m, 1H), 2.20-2.04 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 144.2, 143.7, 136.4, 131.9, 129.9, 129.8, 127.8, 127.1, 73.0, 65.9, 47.6, 45.3, 44.9, 21.6; IR (neat, thin film) ν 3417.1, 3220.1, 2953.8, 2359.9, 1642.3, 1334.8, 1251.9, 1154.2, 841.5, 792.2, 756.2, 700.2 cm^{-1}; HRMS (ESI) calcd for $C_{19}H2_4O_5N_2NaS_2$ $[M+Na]^+$ 447.1019, found 447.1036.



1e **2e**

***N*-(((2*S*,5*S*)-5-((tert-butyldimethylsilyloxy)methyl)-4-tosylmorpholin-2-yl)methyl)-4-methylbenzenesulfonamide (2e)**

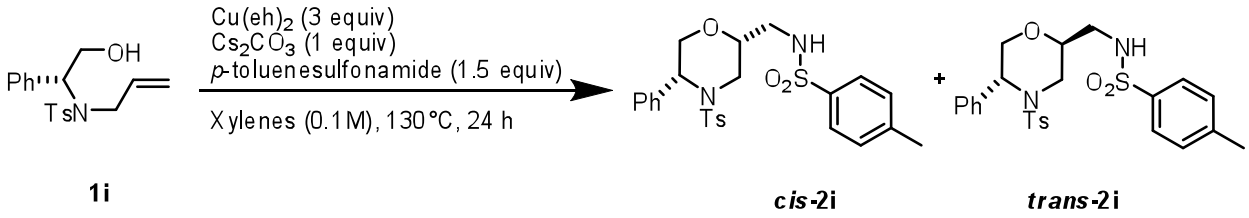
Morpholine **2e (**41 mg, dr >20:1) was obtained as an oil (72%) from 40 mg of **1e** using the conditions above. $[\alpha]_D^{22}$ = 3.9° (*c* 1.0, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.69 (dd, J=6.8, 10.0 Hz, 4H), 7.30 (d, J= 8.0 Hz, 4H), 4.71-4.68 (m, 1H), 4.02 (d, J=12.0 Hz, 1H), 3.74-3.62 (m, 2H), 3.53 (dd, J=10.4, 13.2 Hz, 1H), 3.43 (d, J= 2.0 Hz, 1H), 3.36-3.29 (m, 2H), 3.07-3.04 (m, 1H), 2.88-2.80 (m, 2H), 2.40 (s, 3H), 2.43 (s, 3H), 0.84 (s, 9H), 0.01 (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 143.7, 137.5,136.4, 129.9, 129.8, 127.0, 127.0, 72.9, 65.4, 58.4, 52.9, 45.0, 43.1, 25.8, 21.5, 18.2, -5.4, -5.5; IR (neat, thin film) ν 2359, 1326, 1254, 1162, 838 552 cm^{-1}; HRMS (ESI) calcd for $C_{26}H_{40}O_6N_2NaS_2Si$ $[M+Na]^+$ 591.1989, found 591.1978.



1f **2f**

***N*-(((2*S*,5*R*)-5-(benzylthiomethyl)-4-tosylmorpholin-2-yl)methyl)-4-methylbenzenesulfonamide (2f)**

Morpholine **2f (**24 mg, dr >20:1) was obtained as an oil (42%) from 40 mg of **II-12f** using the conditions above. $[\alpha]_D^{22}$ = 21.4 ° (*c* 0.5, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.72-7.68 (m, 2H), 7.60-7.56 (m, 2H), 7.35-7.26 (m, 9H), 4.65-4.60 (m, 1H), 4.08 (dd, J=7.5, 12.0 Hz, 1H), 3.87-3.80 (m, 1H), 3.69 (d, J=8.4, 2H), 3.47-3.42 (m, 1H), 3.37-3.33 (m, 2H), 3.06-3.02 (m, 1H), 3.01-2.78 (m, 2H), 2.67 (m, 1H), 2.62 (s, 3H), 2.43 (s, 3H), 2.40 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 143.8, 137.8, 137.1, 136.4, 130.0, 129.8, 129.0, 128.6, 127.2, 127.0, 73.0, 66.8, 51.4, 44.9, 42.3, 36.1, 28.9, 21.5; IR (neat, thin film) ν 3200, 1654, 1452, 1332, 1160, 813, 670, 549 cm^{-1}; HRMS (ESI) calcd for $C_{26}H_{40}O_6N_2NaS_2Si$ $[M+Na]^+$ 583.1366, found 583.1363.

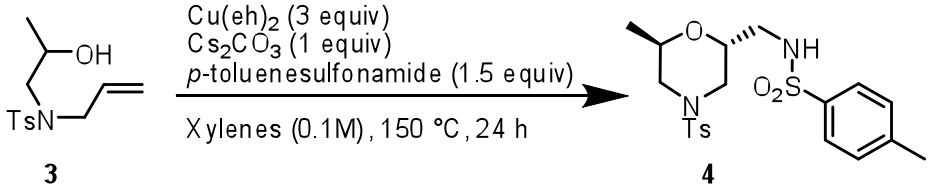


1i ***cis*-2i** ***trans*-2i**

dr = 6:1 *cis:tras*

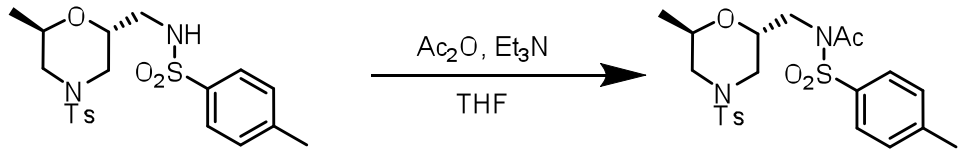
4-methyl-N-(((2R,5R)-5-phenyl-4-tosylmorpholin-2-yl)methyl)benzenesulfonamide (*cis/trans* 2i):

Morpholine **2i (**40 mg) was obtained as an oil (67%) from 40 mg of **1i** as an inseperable mixture of *cis/trans* diasteromers in 6:1 ratio. Data for the major product is reported. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.67 (d, J= 8.4 Hz, 2H), 7.57 (d, J= 8.4, 2H), 7.30-7.27 (m, 9H), 4.92 (d, J=3.6 Hz, 1H), 4.64 (dd, J=4.4, 8.0 Hz, 1H), 4.25 (d, J=12 Hz, 1H), 3.69 (dd, J=5.0, 8.2 Hz, 1H), 3.58 (dd, J=1.2, 13.6 Hz, 1H), 3.50-3.42 (m, 1H), 3.09-3.04 (m, 1H), 2.86 (dd, J=10.8, 13.6 Hz, 1H), 2.80-2.75 (m, 1H), 2.42 (s, 3H), 2.42 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 143.7, 137.3, 137.2, 129.8, 129.4, 128.1, 127.7, 127.0, 73.2, 68.7, 60.6, 54.3, 45.0, 43.1, 21.5; IR (neat, thin film) ν 3286, 28.45, 2315, 1429, 1340, 1153, 1098, 1020, 811 cm^{-1}; HRMS (ESI) calcd for $C_{25}H_{28}O_5N_2NaS_2$ $[M+Na]^+$ 523.1332, found 523.1332.



3 **4**

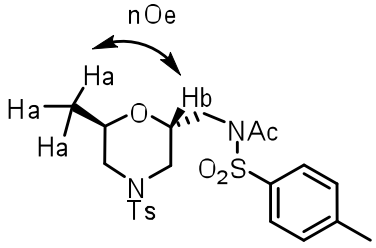
(±)-4-Methyl-N-(((2S,6R)-6-methyl-4-tosylmorpholin-2-yl)methyl)benzenesulfonamide (4)
Morpholine **4** (29 mg) was obtained as an oil (48%, dr >20:1) from 40 mg of **3** using the conditions above except 3 equivalents of $Cu(eh)_2$ was used and the reaction was run at 150 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.72 (d, J= 8.0 Hz, 2H), 7.56 (d, J= 8.0, 2H), 7.35-7.30 (m, 4H), 4.67-4.64 (m, 1H), 3.92-3.87 (m, 1H), 3.86-3.82 (m, 1H), 3.20-3.08 (m, 1H), 3.08-3.04 (m, 1H), 3.00-2.91 (m, 2H), 2.82 (dd, J= 5.6, 12.0 Hz, 1H), 2.57 (dd, J= 6.0, 11.2 Hz, 1H), 2.44 (s, 3H), 2.43 (s, 3H), 1.39 (d, J=6.0 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 144.1, 143.7, 136.5, 131.9, 129.8, 127.7, 127.1, 68.1, 66.3, 50.3, 46.7, 43.0, 21.5, 17.4. IR (neat, thin film) ν 3414, 2300, 1639, 1469, 1333, 1162, 1071, 799, 731, 674 cm^{-1}; HRMS (ESI) calcd for $C_{20}H_{26}O_5N_2NaS_2$ $[M+Na]^+$ 461.1175, found 461.1183.
We had difficulty obtaining an nOe of **4** due to overlapping peaks in ^{1}H NMR. Therefore, morpholine **4** was acetylated to form **S-3**.

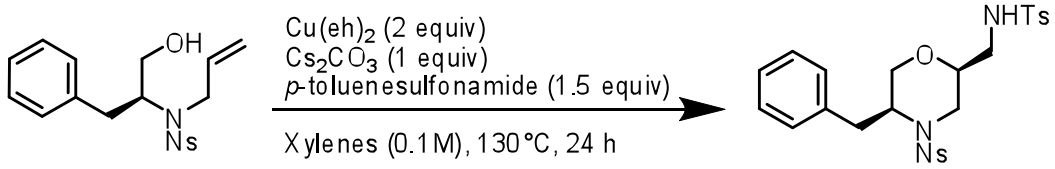


4 **S-3**

(±)-*N*-(((2R,6R)-6-methyl-4-tosylmorpholin-2-yl)methyl)-N-tosylacetamide (S-3)
Morpholine **4** (30 mg, 0.068 mmol) was treated with acetic anhydride (0.29 mL, 3.1 mmol), and triethylamine (0.027 mL, 0.207 mmol) in THF (4.3 mL). The reaction was allowed to stir for 3 h at rt. The reaction mixture was diluted in Et_2O, and then washed with brine. The combined organic layers were dried over Na_2SO_4, filtered and concentrated *in vacuo*. Purification by flash chromatography on SiO2 afforded 25 mg (78%) of amide **S-3**. ^{1}H NMR (400 MHz, benzene) δ 7.70 (d, J= 6.5 Hz, 2H), 7.52 (d, J= 8.5, 2H), 7.25 (d, J=7.0 Hz, 4H), 4.37 (dd, J=8.5, 14.0 Hz, 1H), 4.22-4.15 (m, 1H), 3.66 (dd, J=3.0, 14.5 Hz, 1H), 3.17 (d, J=10.5 Hz, 1H), 3.07 (dd, J=3.0, 11.5 Hz, 1H), 2.71 (dd, J=4.0, 11.5 Hz, 1H), 2.36 (s, 3H), 2.24 (dd, J=8.5, 11.5 Hz, 1H), 2.19 (s, 3H), 1.05 (d, J=6.5 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.5, 145.1, 144.1, 136.8, 131.8, 130.0, 129.8, 127.9, 127.4, 69.6, 65.7, 51.1, 47.4, 47.4, 46.5, 29.7, 25.0, 21.6, 21.5, 17.8; IR (neat, thin film) ν 2928, 1688, 1342, 1159, 1080, 802 cm^{-1}; HRMS (ESI) calcd for $C_{20}H_{26}O_5N_2NaS_2$ $[M+Na]^+$ 461.1175, found 461.1183.

The relative stereochemistry of morpholine **S-3** was determined by a 1D nOe experiment that showed a signal between Ha (0.87 ppm) and Hb (4.48 ppm).

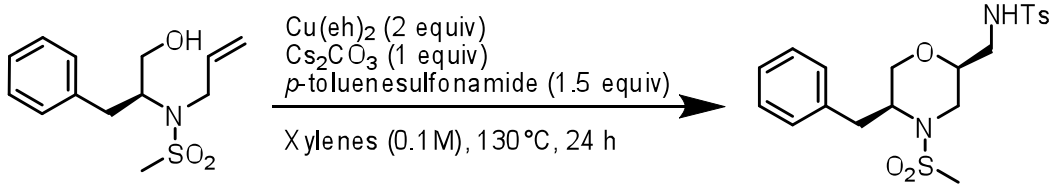




1g **2g**

N-(((2S,5S)-5-benzyl-4-(4-nitrophenylsulfonyl)morpholin-2-yl)methyl)-4-methylbenzenesulfonamide (2g):

Morpholine **2g (**48 mg) was obtained as an oil (83%, dr >20:1) from 40 mg of **1g** using the conditions above. $[\alpha]_D^{22}$ = -14.4 ° (*c* 0.5, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.19 (d, J= 8.5 Hz, 2H), 7.73 (d, J= 8.0 Hz, 2H), 7.66 (d, J=8.0 Hz, 2H), 7.32 (d, J= 7.5 Hz, 2H), 7.22-7.21 (m, 3H), 7.07-7.06 (m, 2H), 4.83 (t, J=6.5 Hz, 1H), 4.08 (m, 1H), 3.73 (d, J=12.0 Hz, 1H), 3.60 (d, J= 13.0 Hz, 1H), 3.55-3.54 (m, 1H), 3.49 (dd, J= 3.0 11.5 Hz, 1H), 3.18-3.09 (m, 2H) 3.00 (m, 1H), 2.97 (dd, J=8.0, 13.5 Hz, 1H), 2.88 (dd, J= 7.5, 14.0, 1H), 2.44 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 150.2, 145.6, 143.8, 137.4, 137.0, 129.9, 129.3, 128.8, 128.3, 127.1, 126.8, 124.5, 73.4, 67.5, 63.5, 53.9, 45.1, 42.4, 34.0, 21.5. IR (neat, thin film) ν 3437.5, 1643.5, 1529.7, 1349.3, 1161.8, 736.3, 665.5 cm^{-1}; HRMS (ESI) calcd for $C_{25}H_{27}O_7N_3NaS_2$ $[M+H]^+$ 439.1356, found 439.1361.

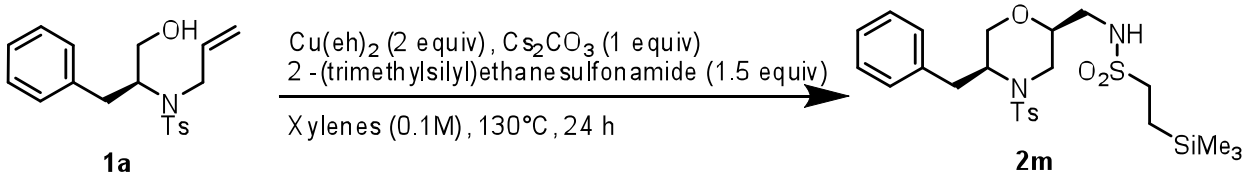


1h **2h**

N-(((2S,5S)-5-benzyl-4-(methylsulfonyl)morpholin-2-yl)methyl)-4-methylbenzenesulfonamide (2h):

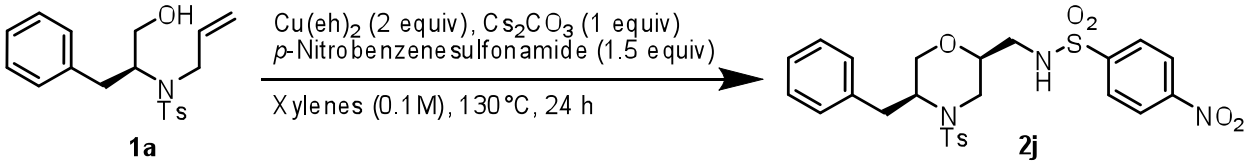
Morpholine **2h (**52 mg) was obtained as an oil (79%, dr >20:1) from 40 mg of **1h** using the conditions above. $[\alpha]_D^{22}$ = -14.9 ° (*c* 1.0, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.76 (d, J= 8.0 Hz, 2H), 7.35-7.8 (m, 4H), 7.25-7.20 (m, 4H), 4.92 (t, J=6.4 Hz, 1H), 4.03 (dt, J= 2.8, 8.0 Hz, 1H), 3.76 (d, J=11.6 Hz, 1H), 3.58 (d, J= 3.2 Hz, 1H), 3.55-3.51 (m, 2H), 3,17-2.98 (m, 4H), 2.94 (dd, J=8.0 14.0, 1H), 2.44 (s, 3H), 2.32 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 143.8, 137.8, 136.6, 129.9, 129.4, 128.8, 127.1, 127.0, 73.9, 69.2, 54.2, 44.9, 42.1, 40.0, 34.9, 21.6. IR (neat,

thin film) ν 3430, 2095, 1642, 1326, 1159 cm^{-1}; HRMS (ESI) calcd for $C_{20}H_{26}O_5N_2NaS_2$ $[M+Na]^+$ 461.1175, found 461.1156.



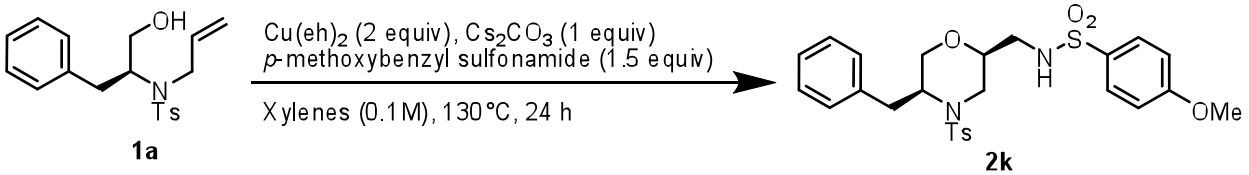
***N*-(((2S,5*S*)-5-benzyl-4-tosylmorpholin-2-yl)methyl)-2-(trimethylsilyl)ethanesulfonamide (2m)**

Morpholine **2m** (53 mg, dr >20:1) was obtained as an oil (98%) from 40 mg of **1a** using the conditions above. $[\alpha]_D^{22}$ = -69.4 ° (*c* 1.5, $CHCl_3$); ^{1}H NMR (500 MHz, C_6D_6) δ 7.58 (d, J=8.5 Hz, 2H), 7.29-7.22 (m, 5H), 7.15 (d, J=7.0 Hz, 2H), 4.63 (t, J=6.5 Hz, 1H), 4.02 (m, 1H), 3.65(d, J= 11.5 Hz, 1H), 3.60 (d, J=13.5 Hz, 1H), 3.58-3.52 (m, 1H), 3.45 (dd, J=2.5, 11.5 Hz, 1H), 3.29-3.26 (m, 1H) 3.17-3.12 (m, 1H), 3.08-2.96 (m, 4H), 2.94-2.68 (dd, J=5.0, 13.0 Hz, 1H), 2.40 (s, 3H), 1.03-1.00 (m, 2H), 0.54 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$): δ =136.6, 130.4, 130.0, 122.8, 122.3, 121.6, 120.0, 119.6, 67.0, 60.3, 46.9, 42.1, 38.1, 35.3, 27.0, 14.4, 3.5, -9.1; IR (neat, thin film) ν 3294, 2954, 1598, 1495, 1451, 1325, 1160, 994, 842, 738, 701 cm^{-1}; HRMS (ESI) calcd for $C_{24}H_{36}O_5N_2NaS_2Si$ $[M+Na]^+$ 547.1727, found 547.1727.



***N*-(((2*S*,5*S*)-5-benzyl-4-tosylmorpholin-2-yl)methyl)-4-nitrobenzenesulfonamide (2j)**

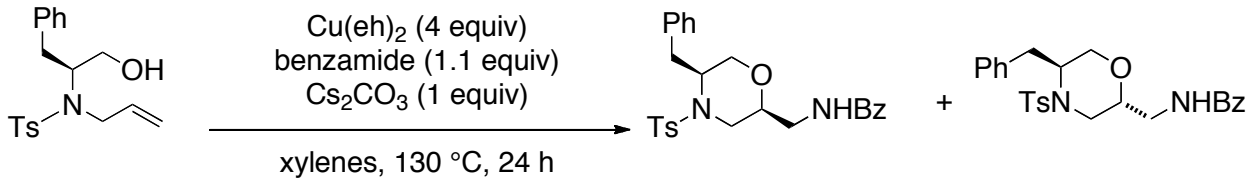
Morpholine **2j (**52 mg) was obtained as an oil (82%, dr >20:1) from 40 mg of **1a** using the conditions above. $[\alpha]_D^{22}$ = -30.9 ° (*c* 1.0, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.37-8.34 (m, 2H), 8.05-8.02 (m, 2H), 7.55 (d, J=8.8 Hz, 2H), 7.28-7.21 (m, 5H), 7.10 (d, J=8.0 Hz, 2H), 5.01-4.98 (m, 1H), 3.99-3.87 (m, 1H), 3.59 (dd, J=12, 2.5 Hz, 2H), 3.55 (d, J=10.8 Hz, 1H), 3.57-3.49 (m, 1H), 3.37 (dd, J= 12.0, 15.2 Hz, 1H), 3.21-3.16 (m, 1H), 3.03-2.97 (m, 1H), 2.88 (dd, J=12.0, 13.2 Hz, 1H), 2.67 (dd, J=4.8, 13.2 Hz, 1H), 2.41 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 150.2, 145.6, 143.8, 137.4, 137.0, 129.9, 129.2, 128.8, 128.3, 127.1, 126.8, 124.5, 73.4, 67.5, 53.8, 45.1, 42.4, 34.1, 21.50; IR (neat, thin film) ν 3265, 2867, 2359, 1517, 1351, 1164, 1075, 722, 678 cm^{-1}; HRMS (ESI) calcd for $C_{26}H_{40}O_6N_2NaS_2Si$ $[M+Na]^+$ 583.1366, found 583.1363.



***N*-(((2*S*,5*S*)-5-benzyl-4-tosylmorpholin-2-yl)methyl)-4-methoxybenzenesulfonamide (2k)**:

Morpholine **2k (**50 mg) was obtained as an oil (82%, dr >20:1) from 40 mg of **1a** using the conditions above. $[\alpha]_D^{22}$ = -19.7 ° (*c* 1.0, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.88 (d, J=8.7

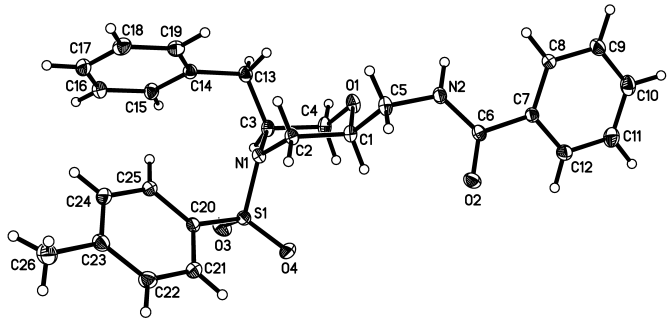
Hz, 2H), 7.57 (d, J=8.4 Hz, 2H), 7.29-7.19 (m, 5H), 7.12 (d, J=6.3 Hz, 2H), 6.99 (d, J=8.7 Hz, 2H), 4.80 (br s, 1H), 3.98-3.90 (m, 1H), 3.88 (s, 3H), 3.65 (d, J=11.7, 1H), 3.55 (dd, J=2.4, 11.7 Hz, 1H), 3.50-3.40 (m, 1H), 3.35 (dd, J=3.0, 11.7 Hz, 1H), 3.12-2.95 (m, 4H), 2.67 (dd, J=5.1, 13.5 Hz, 1H), 2.41 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 163.1, 143.7, 137.5, 137.2, 129.9, 129.4, 129.2, 128.7,127.1, 126.7, 114.4, 73.4, 67.4, 55.6, 53.9, 45.0, 42.5, 34.0, 21.5; IR (neat, thin film) ν 3267, 2914, 1601, 1325, 1166, 1155, 1085 cm^{-1}; HRMS (ESI) calcd for $C_{26}H_{30}O_6N_2NaS_2$ $[M+Na]^+$ 553.1437, found 553.1449.



***N*-((5-benzyl-4-tosylmorpholin-2-yl)methyl)benzamide (2n):**

The procedure for the diastereoselective aminooxygenation of **1a** was the same as above except 4 equiv of $Cu(eh)_2$ was used with benzamide (1.1 equiv) as the nucleophile. The 10:1 ratio of ***cis*-2n** and ***trans*-2n** was determined from the analysis of the crude ^{1}H NMR spectrum. Flash chromatography on SiO_2 afforded 47 mg of **2n** (dr = 10:1) as a white solid (87% yield). The diastereomers were separated by HPLC (EtOAc in hexanes, 30-60% gradiant), where the major *cis*-isomer eluted first. The major diastereomer was recrystallized from CH_2Cl_2 in hexanes to provide X-ray quality crystals for analysis. *N*-(((2*S*,5*S*)-5-benzyl-4-tosylmorpholin-2-yl)methyl)benzamide ***(cis*-2n)**: mp=196 °C; $[\alpha]_D^{22}$ = -20.3 ° (*c* 1.5, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.76 (d, J= 7.5 Hz, 2H), 7.68 (d, J=8.5 Hz, 2H), 7.61-7.50 (m, 1H), 7.45 (m, 2H),7.30-7.23 (m, 5H), 7.17 (d, J=7.5 Hz, 2H, 6.49 (m, 1H), 4.05 (m, 1H), 3.84-3.81 (m, 1H), 3.72 (d, J=11.5, 1H), 3.62 (d, J= 15.0 Hz, 1H), 3.60-3.59 (overlapping m, 1H), 3.47 (d, J=11.5 Hz, 1H), 3.37 (m, 1H), 3.50 (dd, J=11.5, 24.5 Hz, 1H), 2.76 (dd, J=5.0, 13.5 Hz, 1H), 2.40 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 167.5, 144.1, 134.2, 132.0, 131.6, 129.8, 128.6, 127.8, 127.0, 74.0, 65.9, 48.1, 45.4, 41.7, 21.6. IR (neat, thin film) ν 3346, 2920, 2360, 1644, 1538, 1338, 1159, 1119, 801, 695, 547 cm^{-1}. HRMS (ESI) calcd for $C_{26}H_{28}O_4N_2NaS_1$ $[M+Na]^+$ 487.1662, found 487.1652.

The X-ray structure of cis-**2n** was obtained by William Brennessel at the University of Rochester X-ray Crystallography facility:

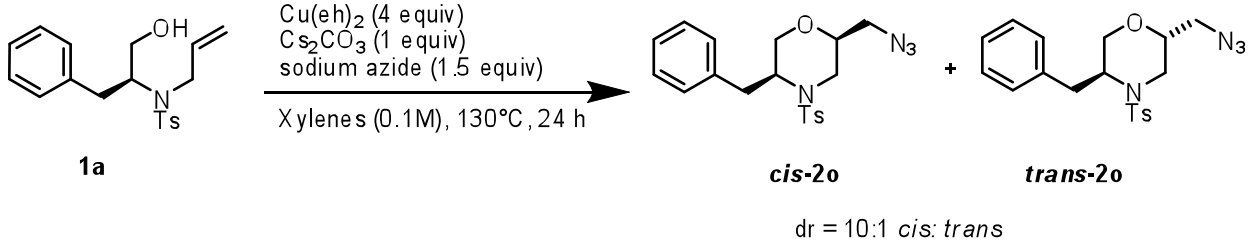


N-(((2*R*,5*S*)-5-benzyl-4-tosylmorpholin-2-yl)methyl)benzamide ***(trans*-2n)**: $[\alpha]_D^{22}$ = 8.4 ° (*c* 0.25, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.76 (dd, J= 1.8, 4.5 Hz, 2H), 7.68 (d, J=8.1 Hz, 2H), 7.51-7.41 (m, 3H), 7.31-7.25 (m, 2H), 6.47 (br s, 1H), 4.01 (d, J=6.0, 1H), 3.73 (dd, J= 3.0, 6.9

Hz, 1H), 3.66 (d, J=2.4, 2H), 3.59-3.51 (m, 2H), 3.33 (dd, J=6.6, 13.5 Hz, 1H), 2.93 (dd, J=11.7, 13.5 Hz, 1H), 2.42 (s, 3H), 1.13 (d, J=6.6 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 167.5, 143.8, 137.4, 136.4, 134.1, 131.6, 129.9, 129.2, 128.7, 129.6, 127.1, 126.9, 126.7, 70.1, 61.8, 55.2, 42.1, 38.2, 34.3, 21.6. IR (neat, thin film) ν 3456, 2161, 1648, 1160, 706, 546 cm^{-1}; HRMS (ESI) calcd for $C_{26}H_{28}O_4N_2NaS_1$ $[M+Na]^+$ 487.1662, found 487.1661.

Table S-1, Oxyamination of 1a with Benzamide as a Function of Copper Loading

Entry	Equiv $Cu(eh)_2$	Equiv $PhC(O)NH_2$	Yield (%)	dr (cis : trans)
1	2	1.5	94	5:1
2	2	1.1	93	7:1
3	3	1.1	86	8:1
4	4	1.1	87	10:1



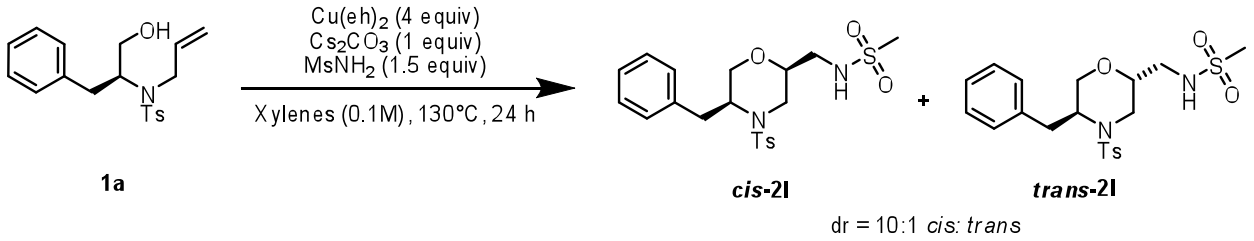
1a ***cis*-2o** ***trans*-2o**

dr = 10:1 *cis: trans*

2-(azidomethyl)-5-benzyl-4-tosylmorpholine (2o):

The procedure for the diastereoselective aminooxygenation of **1a** was the same as above expect 4 equivalents of $Cu(eh)_2$ was used and the nucleophile was NaN_3. The 10:1 ratio of ***cis*-2o** *to* ***trans*-2o** was determined from the analysis of the crude ^{1}H NMR spectrum. Flash chromatography afforded a mixture of **2o** diastereomers in 53% yield (24 mg), obtained as an oil. The diastereomers were separated by HPLC (EtOAc in hexanes, 0-30% gradient) where ***cis*-2o** eluted first. (2*S*,5*S*)-2-(azidomethyl)-5-benzyl-4-tosylmorpholine **(*cis*-2o)**: $[\alpha]_D^{22}$ = 38.2 ° (*c* 1.0, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.62 (d, J= 7.5 Hz, 2H), 7.30-7.18 (m, 4H), 7.17 (d, J=5.0 Hz, 2H), 4.02-4.00 (m, 1H), 3.71 (d, J= 11.5 Hz, 2H), 3.58 (d, J=7.0 Hz, 2H), 3.46-3.38 (m, 2H), 3.72 (dd, J=5.5, 13.5 Hz, 1H), 3.13 (t, J=11.5, 1H), 3.02 (t, J= 11.0 Hz, 1H), 2.68 (dd, J= 5.0, 8.5 Hz, 1H), 2.41 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 143.7, 137.5, 129.9, 129.4, 128.7, 127.1, 126.7, 74.2, 67.3, 54.5, 52.5, 42.4, 33.8, 21.5; IR (neat, thin film) ν 3397, 2094, 1638, 1451, 1319, 1263, 1142, 977, 690, 535 cm^{-1}; HRMS (ESI) calcd for $C_{19}H_{22}O_3N_4NaS_1$ $[M+Na]^+$ 409.1305, found 409.1314.

(2*R*,5*S*)-2-(azidomethyl)-5-benzyl-4-tosylmorpholine **(trans-2o)**: $[\alpha]_D^{22}$ = -23.6 ° (*c* 0.5, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.68 (d, J= 8.4 Hz, 2H), 7.33-7.14 (m, 4H), 7.13 (d, J=8.0 Hz, 2H), 3.95-3.74 (m, 1H), 3.79 (d, J= 4.0 Hz, 2H), 3.64-3.28 (m, 5H), 3.28 (dd, J=8.0, 11.2 Hz, 1H), 2.83 (dd, J= 4.0, 13.2 Hz, 1H), 2.44 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 143.9, 136.3, 129.9, 129.3, 128.7, 127.1, 126.8, 70.3, 62.1, 55.2, 49.5, 42.0, 34.4, 21.6; IR (neat, thin film) ν 3397, 2337, 2094, 1638, 1329, 1175, 745, 679, 557 cm^{-1}; HRMS (ESI) calcd for $C_{19}H_{22}O_3N_4NaS_1$ $[M+Na]^+$ 409.1305, found 409.1297.



1a ***cis*-2l** ***trans*-2l**

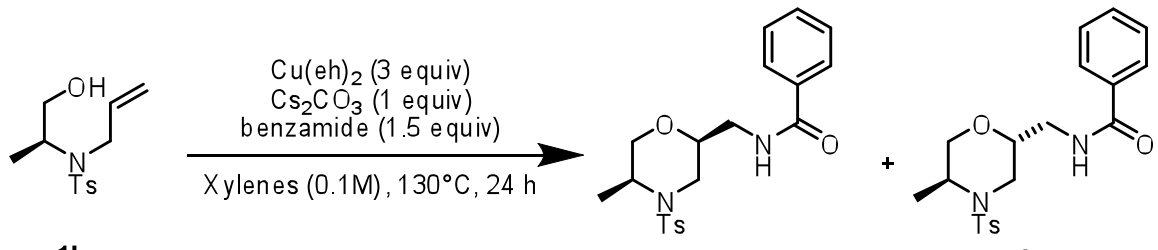
dr = 10:1 *cis*: *trans*

***N*-((5-benzyl-4-tosylmorpholin-2-yl)methyl)methanesulfonamide (2l)**

The procedure for the diastereoselective aminooxygenation of **1a** was the same as above except 4 equiv $Cu(eh)_2$ was used and $MsNH_2$ was the nucleophile. The 10:1 ratio of ***cis*-2l and *trans*-2l** was determined from the analysis of the crude ^1H NMR spectrum. The flash chromatographed mixture of **2l** provided a 43% yield (36 mg, oil). The diastereomers were then separated by HPLC (EtOAc in hexanes 30-60% gradient) where the **cis-2l** eluted first.

N-(((2*S*,5*S*)-5-benzyl-4-tosylmorpholin-2-yl)methyl)methanesulfonamide (***cis*-2l**): $[\alpha]_D^{22}$ = 15.0 ° (*c* 0.5, $CHCl_3$). ^1H NMR (500 MHz, $CDCl_3$) δ 7.58 (d, J= 8.4 Hz, 2H), 7.30-7.23 (m, 5H), 7.15 (d, J=8.0 Hz, 2H), 4.70 (t, J=6.0 Hz, 1H), 4.05-4.02 (m, 1H), 3.69 (d, J=12.0, 1H), 3.61-3.55 (m, 2H), 3.45 (dd, J=3.0, 11.5 Hz, 1H), 3.32-3.29 (m, 1H), 3.17 (dd, J=6.5, 12.5 Hz, 1H), 3.09 (dd, J= 10.5, 13.0 Hz, 1H), 3.01-2.92 (overlapping m, 1H), 2.98 (s, 3H), 2.19 (dd, J=5.5, 13.5 Hz, 1H), 2.41 (s 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 143.7, 137.5, 137.0, 129.9, 129.3, 128.7, 127.1, 126.7, 73.8, 67.4, 53.9, 45.1, 42.4, 40.5, 34.1, 21.5; IR (neat, thin film) ν 3284, 1598, 1333, 1160, 1091, 999, 815, 756 cm^{-1}; HRMS (ESI) calcd for $C_{20}H_{26}O_5N_2NaS_2$ $[M+Na]^+$ 461.1175, found 461.1183.

N-(((2*R*,5*S*)-5-benzyl-4-tosylmorpholin-2-yl)methyl)methanesulfonamide (***trans*-2l**): $[\alpha]_D^{22}$ = 6.1 ° (*c* 0.25, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 7.62 (d, J= 7.2 Hz, 2H), 7.28-7.16 (m, 5H), 7.09 (d, J=7.6 Hz, 2H), 4.56 (t, J=6.0 Hz, 1H), 4.05-3.97 (m, 1H), 3.92-3.80 (d, J=6.4, 1H), 3.64 (dd, J=3.2, 12.0, 1H), 3.54 (dd, J=3.0, 11.5 Hz, 1H), 3.41-3.41 (m, 3H), 3.32-3.29 (m, 1H), 2.99 (s, 3H) 2.99-2.97 (overlapping m, 1H), 2.80-2.76 (m, 1H), 2.43 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 143.9, 137.2, 136.4, 130.0, 129.3, 128.8, 127.0, 126.8, 70.6, 62.1, 55.1, 41.7, 41.4, 40.5, 34.2, 21.5; IR (neat, thin film) ν 3256, 2342, 1660, 1398, 1092, 796, 683, 535 cm^{-1}; HRMS (ESI) calcd for $C_{20}H_{26}O_5N_2NaS_2$ $[M+Na]^+$ 461.1175, found 461.1169.



1b ***cis*-2p** ***trans*-2p**

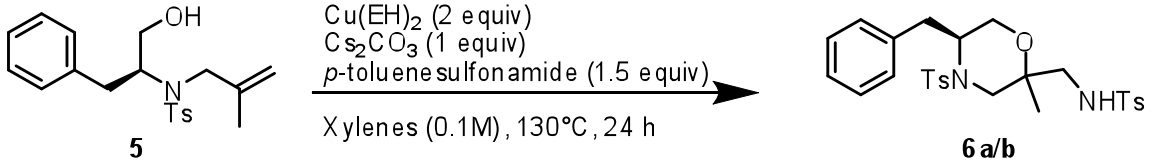
dr = 10:1 *cis*: *trans*

N-((5-methyl-4-tosylmorpholin-2-yl)methyl)benzamide (2p):

The procedure for the diastereoselective aminooxygenation of **1b** was the same as above except 3 equivalents of $Cu(eh)_2$ was used and benzamide was the nucleophile. The 10:1 ratio of ***cis*-2p to *trans*-2p** was determined from the analysis of the crude ^1H NMR spectrum. Flash chromatography afforded the 10:1 diastereomeric mixture **2p** as an oil (36 mg, 63% yield). The diastereomers were separated by HPLC (EtOAc in hexanes, 40-80% gradient) where the *cis*-isomer eluted first.

N-(((2*S*,5*S*)-5-methyl-4-tosylmorpholin-2-yl)methyl)benzamide **(*cis*-2p)**: $[\alpha]_D^{22}$ = 38.2 ° (*c* 1.00, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.76 (dd, J= 1.8, 4.5 Hz, 2H), 7.68 (d, J=8.1 Hz, 2H), 7.51-7.41 (m, 3H), 7.31-7.25 (m, 2H), 6.50-6.45 (m, 1H), 4.01 (d, J=6.0, 1H), 3.73 (dd, J= 3.0, 6.9 Hz, 1H), 3.66 (d, J=2.4, 2H), 3.59-3.51 (m, 2H), 3.33 (dd, J=6.6, 13.5 Hz, 1H), 2.93 (dd, J=11.7, 13.5 Hz, 1H), 2.42 (s, 3H), 1.13 (d, J=6.6 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 167.3, 143.6, 137.1, 134.1, 131.7, 129.9, 128.6, 127.1, 126,9, 74.3, 71.4, 48.2, 42.1, 41.7, 21.5, 13.8. IR (neat, thin film) ν 3397, 2316, 1639, 1551, 1319, 1164, 679, 557 cm^{-1}; HRMS (ESI) calcd for $C_{20}H_{24}O_4N_2NaS_1$ $[M+Na]^+$ 411.1349, found 461.1361.

N-(((2*R*,5*S*)-5-methyl-4-tosylmorpholin-2-yl)methyl)benzamide **(*trans*-2p)**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.76 (d, J= 7.5 Hz, 2H), 7.68 (d, J= 8.5 Hz, 2H),7.51 (t, J=7.5 Hz, 1H), 7.42 (apparent triplet, J=7.4 Hz, 1H), 7.36-7.39 (m, 2H), 6.42-6.35 (m, 1H), 4.03-4.00 (m, 1H), 3.81 (dd, J= 3.5, 12.0 Hz, 1H), 3.78-3.66 (m, 2H), 3.57 (m, 2H), 3.36 (dd, J=6.5, 11.5 Hz, 1H), 3.16 (m, 1H), 2.75 (m,1H), 2.42 (s, 3H), 1.24 (d, J=6.5 Hz, 3H).



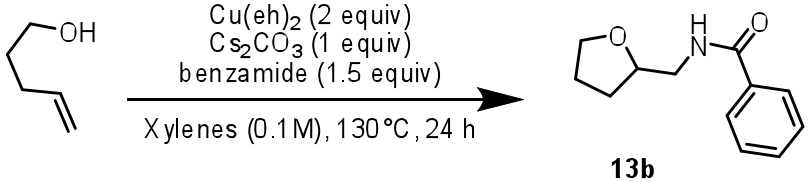
5 **6 a/b**

N-(((5S)-5-benzyl-2-methyl-4-tosylmorpholin-2-yl)methyl)-4-methylbenzenesulfonamide (6a/b):

Morpholine **6a** (24 mg) and morpholine **6b** (12 mg) were obtained as oils (91% combined yield) from 40 mg of **5** using the conditions above. The 2:1 ratio of **6** was determined from the analysis of the crude ^{1}H NMR and the diastereomers were separated by flash chromatography on SiO_2 (0-45% EtOAc in hexanes gradient).

6a-major: ^{1}H NMR spectrum.^{1}H NMR (500 MHz, $CDCl_3$) δ 7.77 (d, J= 8.0 Hz, 2H), 7.68 (d, J= 8.5 Hz, 2H), 7.37-7.12 (m, 7H), 7.10 (d, J=7.5 Hz, 2H), 4.89-4.86 (m,1H), 3.92 (dt, J=3.5 10.5 Hz, 1H), 3.68 (dd, J=2.5 11.4 Hz, 1h). 3.45-3.32 (m, 2H), 3.03-2.90 (m, 3H), 2.46 (s, 3H), 2.44 (s, 3H), 1.25 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 143.6, 143.6, 137.5, 137.2, 136.5, 129.9, 129.8, 129.3, 128. 6, 127.0, 126.9, 126.6, 71.8, 61.0, 53.8, 50.9, 45.1, 33.2, 21.5, 18.4 cm^{-1}. IR (neat, thin film) ν 3316, 1639, 1494, 1456, 1238, 1159, 1088, 1028, 1003 cm^{-1}. HRMS (ESI) calcd for $C_{27}H_{32}O_5N_2NaS_2$ $[M+Na]^+$ 551.1645, found 551.1642.

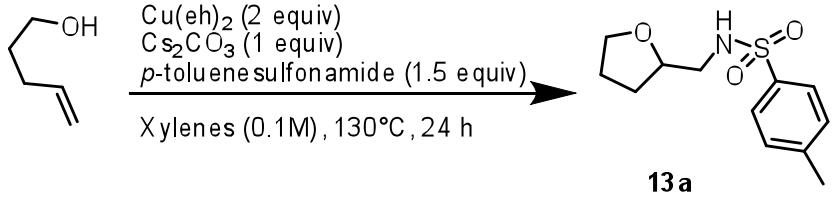
6b-minor: ^{1}H NMR spectrum.^{1}H NMR (400 MHz, $CDCl_3$) δ 7.71 (d, J= 6.8 Hz, 2H), 7.59 (d, J= 6.4 Hz, 2H), 7.32-7.17 (m, 7H), 7.08 (d, J=8.0 Hz, 2H), 4.62 (t, J= 8.0 Hz, 2H), 3.87 (d, J=10.4 Hz, 1H), 3.45-3.24 (m, 3H), 3.26 (dd, J=5.2, 12.8 Hz, 1H), 3.03-2.91 (m, 3H), 2.48 (dd, J=5.2, 13.2 Hz, 1H), 2.44 (s, 3H), 2.42 (s, 3H), 1.24 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 143.7, 143.6, 137.5, 137.3, 136.9, 136.7, 129.9, 129.8, 129.3, 128.7, 127.0, 126.8, 126.7, 71.6, 61.3, 53.7, 46.1, 43.3, 33.2, 23.4, 21.5 cm^{-1}. IR (neat, thin film) ν 3316, 1652, 1597, 1497, 1453, 1328, 1106, 1093, 1033, 1004 cm^{-1}. HRMS (ESI) calcd for $C_{27}H_{33}O_5N_2S_2$ $[M+1]^+$ 529.1825, found 529.1820.



13b

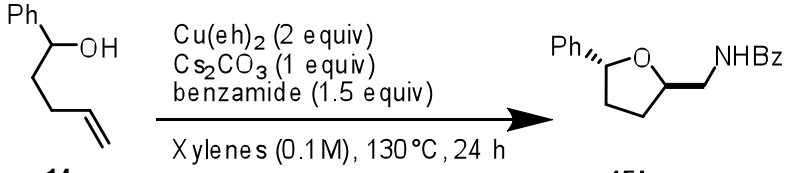
(±)-N-((tetrahydrofuran-2-yl)methyl)benzamide (13b):

Tetrahydrofuran **13b (**80 mg) was obtained as an oil (85%) from 40 mg of 4-pentenol using the conditions above. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.76 (d, J= 6.9 Hz, 2H), 7.49-7.37 (m, 3H), 6.61 (br s, 1H), 4.09-3.92 (m,1H), 3.85 (dd, J=6.6, 7.8 Hz, 1H), 3.80-3.71 (m, 2H), 3.37-3.28 (m, 1H), 2.03-1.85 (m, 3H), 1.65-1.56 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 167.5, 134.5, 131.3, 128.4, 126.8, 68.1, 43.5, 28.6, 25.8; IR (neat, thin film) ν 3309 2934, 2338, 1644, 1538, 1294, 1074, 695 cm^{-1}; HRMS (ESI) calcd for $C_{12}H_{16}O_2N_1$ $[M+]^+$ 206.1176, found 206.1178.



13a

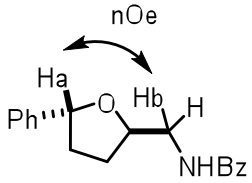
4-Methyl-N-((tetrahydrofuran-2-yl)methyl)benzenesulfonamide (13a):
Tetrahydrofuran **13a (**123 mg) was obtained as an oil (83%) from 50 mg of 4-pentenol using the conditions above. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.73 (d, J= 8.4 Hz, 2H), 7.73 (d, J= 8.1 Hz, 2H), 4.84 (t, J= 6.0, Hz, 1H), 3.95-3.78 (m, 1H), 3.80-3.64 (m, 1H), 3.14-3.07 (m, 1H), 2.92-2.84 (m, 1H), 2.41 (s, 3H), 1.95-1.81 (m, 3H), 1.60 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 143.3, 136.9, 129.7, 127.0, 76.99 68.3, 46.7, 28.3, 25.8, 21.5; IR (neat, thin film) ν 3274, 2928, 2844, 2351, 1316, 1164 cm^{-1}. HRMS (ESI) calcd for $C_{12}H_{17}O_3N_1NaS$ $[M+Na]^+$ 278.0821, found 278.0819.

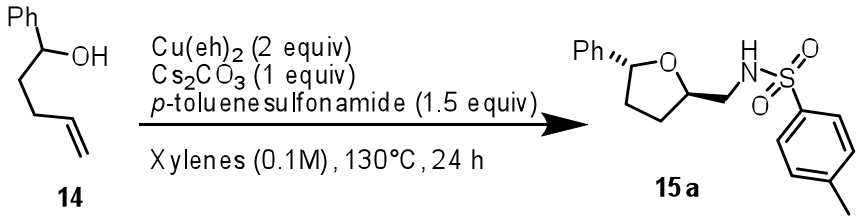


14 **15b**

(±)-N-(((2R,5R)-5-phenyltetrahydrofuran-2-yl)methyl)benzamide (15b):
Tetrahydrofuran **15b (**52 mg) was obtained as an oil (77%, >20:1 dr) from 40 mg of **14** using the conditions above. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.75 (d, J=8.0 Hz, 2H), 7.34-7.24 (m, 7H), 4.92 (t, J=5.0 Hz, 1H), 4.29 (dd, J=2.8, 6.0 Hz, 1H), 3.82-3.76 (m, 1H), 3.41-3.34 (m, 1H). 2.42 (s, 3H), 2.35-2.28 (m, 1H), 2.15-2.09 (m, 1H), 1.88-1.68 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 167.5, 142.8, 134.5, 131.4, 128.5, 128.4, 127.5, 127.0, 125.6, 80.9, 78.7, 43.9, 35.3, 29.6; IR (neat, thin film) ν 3316, 2928, 1651, 1531, 1494, 1290, 1070, 703 cm^{-1}; HRMS (ESI) calcd for $C_{18}H_{20}O_2N[M+H]^+$ 282.1489, found 282.1485.

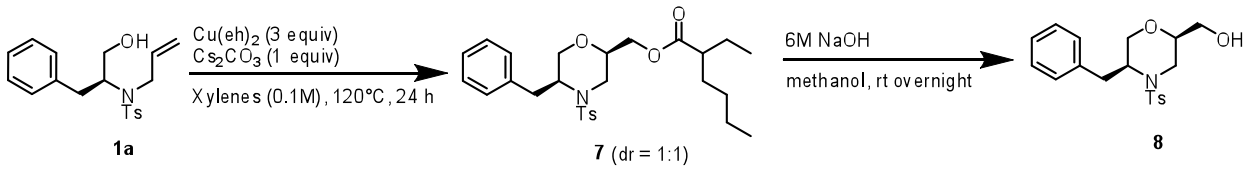
The relative stereochemistry of the diamination product **15b** was determined by a 1D nOe experiment that showed a signal between Ha (4.91 ppm) and Hb (3.35 ppm).





14 **15a**

(±)-4-methyl-N-(((2R,5R)-phenyltetrahydrofuran-2-yl)methyl)benzenesulfonamide (15a): Compound **15a (**50 mg) was obtained as an oil (62%, >20:1 dr) from 40 mg of **14** using the conditions above. The 2,5-trans relative stereochemistry of **15a** is assigned by analogy to **15b**. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.75 (d, J=8.0 Hz, 2H), 7.34-7.24 (m, 7H), 4.92 (t, J=5.0 Hz, 1H), 4.29 (dd, J=2.8, 6.0 Hz, 1H), 3.21-3.16 (m, 1H), 3.01-2.95 (m, 1H). 2.42 (s, 3H), 2.34-2.31 (m, 1H), 2.08-2.05 (m, 1H), 1.85-1.78 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 143.3, 142.5, 136.8, 129.6, 128.3, 127.4, 127.0,125.4, 80.9, 77.7, 47.0, 35.2, 29.2, 21.5; IR (neat, thin film) ν 3274, 2907, 1604, 1452, 1332, 1154, 1070, 661 cm^{-1}. HRMS (ESI) calcd for $C_{24}H_{36}O_5N_2NaS_2Si$ $[M+Na]^+$ 354.1134, found 354.1127.



1a **7** (dr = 1:1) **8**

((2R,5S)-5-benzyl-4-tosylmorpholin-2-yl)methanol (8):
Compound **8 (**33 mg) was obtained as an oil (64%, 2 steps) from 50 mg of **1a** using the conditions above expect 3 equivalents of $Cu(eh)_2$ was used and the nitrogen nucleophile was omitted. **(2R,5S)-5-benzyl-4-tosylmorpholin-2-yl)methyl 2-ethylhexanoate (7):** 1:1 mixture of diastereomers. Characterized as the mixture. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.63 (d, J=8.4 Hz, 2H), 7.31-7.15 (m, 7H), 4.17-4.02 (m, 2H), 4.01 (m, 1H), 3.73-3.45 (m, 5H), 3.13 (m, 1H), 3.00 (dd, J=10.5, 12.9 Hz, 1H), 2.67 (dd, J=5.4 13.5 Hz, 1H), 2.67 (dd, J=5.4 13.5 Hz, 1H), 2.34 (s, 3H), 2.31 (m, 1H). 1.65-1.43 (m, 1H), 1.32-1.23 (m, 5H). 0.93-0.85 (m, 7H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 176.0, 143.6, 137.7, 129.9, 129.8, 129.4, 128.7, 127.1, 126.6, 73.2, 67.2, 54.1, 47.1, 42.2, 34.0, 31.7, 31.6, 29.6, 25.4, 22.6, 21.5, 13.9, 11.8; IR (neat, thin film) ν 2992, 1732, 1455, 1345, 1162 cm^{-1}. HRMS (ESI) calcd for $C_{27}H_{37}O_5N_1NaS$ $[M+Na]^+$ 384.1240, found 384.1231.

The ester was hydrolyzed to establish the alcohol was one diastereomer. The major diastereomer is assigned by analogy to **2n**. The ester obtained in 74% yield was dissolved in 1.41 mL of methanol in a round bottomed flask equipped with a stir bar. The solution was then treated with 0.46 mL of 6M NaOH. The mixture was stirred at room temperature for 24 h. The reaction was concentrated *in vacuo* and partitioned between water and ethyl acetate. The organic extract was washed with brine (10 mL). The organic layer was dried over Na_2SO_4, filtered and concentrated *in vacuo* and the residue was chromatographed on SiO_2 column, using EtOAc/hexanes to provide ((2R,5S)-5-benzyl-4-tosylmorpholin-2-yl)methanol **(8)** as a colorless oil (67% yield).
$[\alpha]_D^{22}$ = 8.40 ° (c = 0.25, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.63 (d, J=8.1 Hz, 2H), 7.28-7.55 (m, 5H), 7.18 (d, J= 6.0 Hz, 2H), 4.03-4.00 (m, 1H), 3.71 (d, J=11.1 Hz, 2H). 3.62 (d, J=11.7 Hz, 2H), 3.48 (d, 2H), 3.13 (t, J=10.5 Hz, 1H), 2.95 (t, J=10.8 Hz, 1H), 2.70 (dd, J=5.4, 13.5 Hz, 1H), 2.41 (t, 3H), 1.80 (br s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 143.5, 137.7, 129.9, 129.4, 128.7, 127.1, 126.7, 67.2, 63.5, 54.2, 41.7, 34.0, 21.5; IR (neat, thin film) ν 3500, 2923,

2251,1598, 1495, 1454, 1336, 1160, 1093, 993, 912, 815, 678 cm^{-1}; HRMS (ESI) calcd for $C_{19}H_{23}O_4N_1NaS$ $[M+Na]^+$ 384.1240, found 384.1231.

X-ray Data for Structure of cis-**2n**.

Table 1. Crystal data and structure refinement for ubsc13.

Identification code	ubsc13	
Empirical formula	C26 H28 N2 O4 S	
Formula weight	464.56	
Temperature	100.0(5) K	
Wavelength	0.71073 Å	
Crystal system	Orthorhombic	
Space group	$P2_12_12_1$	
Unit cell dimensions	a = 9.6487(14) Å	α = 90°
	b = 12.0714(17) Å	β = 90°
	c = 19.866(3) Å	γ = 90°
Volume	2313.8(6) $Å^3$	
Z	4	
Density (calculated)	1.334 Mg/m^3	
Absorption coefficient	0.176 mm^{-1}	
F(000)	984	
Crystal color, morphology	colorless, block	
Crystal size	0.26 x 0.24 x 0.20 mm^3	
Theta range for data collection	1.97 to 37.78°	
Index ranges	$-16 \le h \le 16$, $-20 \le k \le 20$, $-34 \le l \le 34$	
Reflections collected	85203	
Independent reflections	12399 [R(int) = 0.0531]	
Observed reflections	10873	
Completeness to theta = 37.78°	100.0%	
Absorption correction	Multi-scan	
Max. and min. transmission	0.9657 and 0.9557	
Refinement method	Full-matrix least-squares on F^2	

Data / restraints / parameters	12399 / 0 / 410
Goodness-of-fit on F^2	1.040
Final R indices [I>2sigma(I)]	$R1$ = 0.0385, $wR2$ = 0.0927
R indices (all data)	$R1$ = 0.0476, $wR2$ = 0.0983
Absolute structure parameter	-0.02(3)
Largest diff. peak and hole	0.517 and -0.220 e.Å^{-3}

Table 2. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters ($Å^2$x 10^3) for ubsc13. U_{eq} is defined as one third of the trace of the orthogonalized U_{ij} tensor.

	x	y	z	U_{eq}
S1	-725(1)	1572(1)	1880(1)	15(1)
O1	1649(1)	1758(1)	3582(1)	18(1)
O2	-1738(1)	1862(1)	4857(1)	18(1)
O3	-168(1)	737(1)	1441(1)	23(1)
O4	-1821(1)	1254(1)	2336(1)	22(1)
N1	575(1)	2123(1)	2282(1)	13(1)
N2	408(1)	2601(1)	4748(1)	16(1)
C1	322(1)	2265(1)	3516(1)	14(1)
C2	230(1)	2871(1)	2842(1)	14(1)
C3	1879(1)	1494(1)	2370(1)	14(1)
C4	1869(1)	954(1)	3066(1)	18(1)
C5	151(1)	3084(1)	4091(1)	17(1)
C6	-566(1)	2039(1)	5088(1)	14(1)
C7	-158(1)	1628(1)	5771(1)	13(1)
C8	835(1)	2171(1)	6158(1)	18(1)
C9	1178(1)	1773(1)	6796(1)	22(1)
C10	542(1)	823(1)	7043(1)	21(1)
C11	-451(1)	281(1)	6659(1)	21(1)
C12	-810(1)	686(1)	6028(1)	17(1)
C13	3141(1)	2262(1)	2293(1)	16(1)
C14	3099(1)	2963(1)	1666(1)	14(1)
C15	3264(1)	2504(1)	1027(1)	17(1)
C16	3190(1)	3166(1)	454(1)	21(1)
C17	2952(1)	4296(1)	514(1)	21(1)
C18	2770(1)	4762(1)	1147(1)	20(1)
C19	2852(1)	4102(1)	1718(1)	17(1)
C20	-1365(1)	2686(1)	1398(1)	14(1)
C21	-2790(1)	2867(1)	1370(1)	17(1)
C22	-3299(1)	3687(1)	945(1)	18(1)
C23	-2408(1)	4322(1)	550(1)	17(1)
C24	-987(1)	4143(1)	598(1)	18(1)

C25	-456(1)	3322(1)	1018(1)	16(1)
C26	-2983(1)	5194(1)	87(1)	26(1)

Table 3. Bond lengths [Å] and angles [°] for ubsc13.

S(1)-O(3)	1.4368(8)	C(9)-H(9)	0.983(19)
S(1)-O(4)	1.4431(8)	C(10)-C(11)	1.3890(16)
S(1)-N(1)	1.6285(8)	C(10)-H(10)	0.953(18)
S(1)-C(20)	1.7616(9)	C(11)-C(12)	1.3890(14)
O(1)-C(1)	1.4254(12)	C(11)-H(11)	0.979(17)
O(1)-C(4)	1.4277(12)	C(12)-H(12)	0.928(18)
O(2)-C(6)	1.2396(12)	C(13)-C(14)	1.5060(13)
N(1)-C(2)	1.4707(12)	C(13)-H(13A)	0.965(16)
N(1)-C(3)	1.4800(12)	C(13)-H(13B)	0.958(17)
N(2)-C(6)	1.3418(13)	C(14)-C(15)	1.3944(13)
N(2)-C(5)	1.4508(12)	C(14)-C(19)	1.3983(13)
N(2)-H(2N)	0.933(17)	C(15)-C(16)	1.3931(14)
C(1)-C(5)	1.5193(13)	C(15)-H(15)	0.927(15)
C(1)-C(2)	1.5280(13)	C(16)-C(17)	1.3892(16)
C(1)-H(1)	0.971(15)	C(16)-H(16)	0.957(17)
C(2)-H(2A)	0.970(15)	C(17)-C(18)	1.3882(17)
C(2)-H(2B)	0.966(15)	C(17)-H(17)	0.915(17)
C(3)-C(4)	1.5279(13)	C(18)-C(19)	1.3882(15)
C(3)-C(13)	1.5378(14)	C(18)-H(18)	0.962(15)
C(3)-H(3)	0.959(16)	C(19)-H(19)	0.983(17)
C(4)-H(4A)	0.951(16)	C(20)-C(25)	1.3899(13)
C(4)-H(4B)	1.024(16)	C(20)-C(21)	1.3934(14)
C(5)-H(5A)	0.964(16)	C(21)-C(22)	1.3895(14)
C(5)-H(5B)	0.941(17)	C(21)-H(21)	0.903(17)
C(6)-C(7)	1.4974(12)	C(22)-C(23)	1.3941(15)
C(7)-C(8)	1.3926(13)	C(22)-H(22)	0.936(18)
C(7)-C(12)	1.3957(13)	C(23)-C(24)	1.3913(15)
C(8)-C(9)	1.3950(14)	C(23)-C(26)	1.5033(15)
C(8)-H(8)	0.987(19)	C(24)-C(25)	1.3930(14)
C(9)-C(10)	1.3895(17)	C(24)-H(24)	0.906(15)

C(25)-H(25)	0.960(18)	O(1)-C(4)-H(4A)	110.2(10)
C(26)-H(26A)	0.95(2)	C(3)-C(4)-H(4A)	108.9(10)
C(26)-H(26B)	0.93(3)	O(1)-C(4)-H(4B)	106.1(9)
C(26)-H(26C)	0.83(3)	C(3)-C(4)-H(4B)	106.9(9)
O(3)-S(1)-O(4)	117.91(5)	H(4A)-C(4)-H(4B)	113.6(12)
O(3)-S(1)-N(1)	107.19(5)	N(2)-C(5)-C(1)	113.36(8)
O(4)-S(1)-N(1)	111.43(5)	N(2)-C(5)-H(5A)	106.6(9)
O(3)-S(1)-C(20)	109.65(5)	C(1)-C(5)-H(5A)	109.1(9)
O(4)-S(1)-C(20)	106.66(5)	N(2)-C(5)-H(5B)	107.7(10)
N(1)-S(1)-C(20)	102.99(4)	C(1)-C(5)-H(5B)	109.7(10)
C(1)-O(1)-C(4)	111.06(7)	H(5A)-C(5)-H(5B)	110.3(14)
C(2)-N(1)-C(3)	114.65(7)	O(2)-C(6)-N(2)	122.66(8)
C(2)-N(1)-S(1)	116.55(6)	O(2)-C(6)-C(7)	121.24(9)
C(3)-N(1)-S(1)	120.28(6)	N(2)-C(6)-C(7)	116.10(8)
C(6)-N(2)-C(5)	122.45(8)	C(8)-C(7)-C(12)	119.40(8)
C(6)-N(2)-H(2N)	121.7(11)	C(8)-C(7)-C(6)	121.69(9)
C(5)-N(2)-H(2N)	115.7(11)	C(12)-C(7)-C(6)	118.90(8)
O(1)-C(1)-C(5)	107.93(8)	C(7)-C(8)-C(9)	120.19(10)
O(1)-C(1)-C(2)	109.82(7)	C(7)-C(8)-H(8)	121.3(11)
C(5)-C(1)-C(2)	109.94(8)	C(9)-C(8)-H(8)	118.4(11)
O(1)-C(1)-H(1)	111.2(8)	C(10)-C(9)-C(8)	120.00(10)
C(5)-C(1)-H(1)	108.0(8)	C(10)-C(9)-H(9)	122.4(11)
C(2)-C(1)-H(1)	109.8(8)	C(8)-C(9)-H(9)	117.5(11)
N(1)-C(2)-C(1)	110.81(7)	C(11)-C(10)-C(9)	119.97(9)
N(1)-C(2)-H(2A)	109.6(9)	C(11)-C(10)-H(10)	120.8(11)
C(1)-C(2)-H(2A)	109.2(9)	C(9)-C(10)-H(10)	119.1(11)
N(1)-C(2)-H(2B)	105.4(9)	C(12)-C(11)-C(10)	120.08(10)
C(1)-C(2)-H(2B)	111.4(9)	C(12)-C(11)-H(11)	118.4(10)
H(2A)-C(2)-H(2B)	110.3(12)	C(10)-C(11)-H(11)	121.5(9)
N(1)-C(3)-C(4)	108.72(7)	C(11)-C(12)-C(7)	120.33(9)
N(1)-C(3)-C(13)	110.66(7)	C(11)-C(12)-H(12)	117.8(11)
C(4)-C(3)-C(13)	110.68(8)	C(7)-C(12)-H(12)	121.9(11)
N(1)-C(3)-H(3)	109.3(9)	C(14)-C(13)-C(3)	113.59(8)
C(4)-C(3)-H(3)	105.6(9)	C(14)-C(13)-H(13A)	109.1(10)
C(13)-C(3)-H(3)	111.7(9)	C(3)-C(13)-H(13A)	108.1(10)
O(1)-C(4)-C(3)	111.07(8)	C(14)-C(13)-H(13B)	111.6(10)

C(3)-C(13)-H(13B)	108.0(10)	C(21)-C(20)-S(1)	119.22(7)
H(13A)-C(13)-H(13B)	106.1(14)	C(22)-C(21)-C(20)	119.03(9)
C(15)-C(14)-C(19)	118.50(9)	C(22)-C(21)-H(21)	120.0(11)
C(15)-C(14)-C(13)	121.72(8)	C(20)-C(21)-H(21)	120.9(11)
C(19)-C(14)-C(13)	119.76(9)	C(21)-C(22)-C(23)	121.06(10)
C(16)-C(15)-C(14)	120.66(9)	C(21)-C(22)-H(22)	122.0(10)
C(16)-C(15)-H(15)	117.0(10)	C(23)-C(22)-H(22)	116.9(10)
C(14)-C(15)-H(15)	122.4(10)	C(24)-C(23)-C(22)	118.91(9)
C(17)-C(16)-C(15)	120.13(9)	C(24)-C(23)-C(26)	120.94(10)
C(17)-C(16)-H(16)	123.2(10)	C(22)-C(23)-C(26)	120.15(10)
C(15)-C(16)-H(16)	116.6(10)	C(23)-C(24)-C(25)	120.93(9)
C(18)-C(17)-C(16)	119.76(9)	C(23)-C(24)-H(24)	118.1(10)
C(18)-C(17)-H(17)	122.5(10)	C(25)-C(24)-H(24)	120.9(10)
C(16)-C(17)-H(17)	117.7(10)	C(20)-C(25)-C(24)	119.14(9)
C(17)-C(18)-C(19)	120.01(10)	C(20)-C(25)-H(25)	121.1(10)
C(17)-C(18)-H(18)	119.6(9)	C(24)-C(25)-H(25)	119.7(10)
C(19)-C(18)-H(18)	120.3(9)	C(23)-C(26)-H(26A)	111.0(13)
C(18)-C(19)-C(14)	120.93(9)	C(23)-C(26)-H(26B)	115.9(16)
C(18)-C(19)-H(19)	121.0(10)	H(26A)-C(26)-H(26B)	107.2(19)
C(14)-C(19)-H(19)	118.0(10)	C(23)-C(26)-H(26C)	107.7(18)
C(25)-C(20)-C(21)	120.90(9)	H(26A)-C(26)-H(26C)	112(2)
C(25)-C(20)-S(1)	119.74(7)	H(26B)-C(26)-H(26C)	103(2)

Table 4. Anisotropic displacement parameters ($Å^2 x\ 10^3$) for ubsc13. The anisotropic displacement factor exponent takes the form: $-2\pi^2[\ h^2\ a^{*2}U_{11} + ... + 2\ h\ k\ a^*\ b^*\ U_{12}\ ]$

	U_{11}	U_{22}	U_{33}	U_{23}	U_{13}	U_{12}
S1	18(1)	12(1)	14(1)	2(1)	-2(1)	-3(1)
O1	20(1)	20(1)	13(1)	1(1)	0(1)	6(1)
O2	15(1)	21(1)	17(1)	-1(1)	-4(1)	0(1)
O3	31(1)	15(1)	22(1)	-5(1)	-5(1)	1(1)
O4	19(1)	26(1)	22(1)	9(1)	-1(1)	-8(1)
N1	14(1)	13(1)	11(1)	0(1)	-1(1)	1(1)
N2	16(1)	20(1)	11(1)	0(1)	0(1)	0(1)
C1	16(1)	16(1)	12(1)	1(1)	1(1)	2(1)
C2	15(1)	14(1)	11(1)	0(1)	0(1)	2(1)
C3	17(1)	13(1)	13(1)	2(1)	1(1)	3(1)
C4	24(1)	15(1)	14(1)	3(1)	3(1)	6(1)
C5	23(1)	17(1)	11(1)	1(1)	1(1)	3(1)
C6	16(1)	14(1)	12(1)	-2(1)	0(1)	2(1)
C7	13(1)	16(1)	11(1)	0(1)	0(1)	1(1)
C8	17(1)	26(1)	12(1)	0(1)	0(1)	-7(1)
C9	16(1)	35(1)	14(1)	-1(1)	-3(1)	-2(1)
C10	21(1)	29(1)	15(1)	4(1)	0(1)	6(1)
C11	27(1)	19(1)	18(1)	5(1)	2(1)	1(1)
C12	20(1)	16(1)	16(1)	0(1)	-1(1)	-3(1)
C13	15(1)	19(1)	14(1)	2(1)	-1(1)	2(1)
C14	13(1)	15(1)	14(1)	1(1)	0(1)	1(1)
C15	21(1)	16(1)	14(1)	0(1)	2(1)	0(1)
C16	23(1)	25(1)	14(1)	0(1)	1(1)	-4(1)
C17	18(1)	25(1)	20(1)	8(1)	-3(1)	-3(1)
C18	19(1)	15(1)	26(1)	4(1)	-1(1)	0(1)
C19	16(1)	16(1)	18(1)	-1(1)	0(1)	0(1)
C20	16(1)	14(1)	11(1)	1(1)	-2(1)	-2(1)
C21	15(1)	20(1)	17(1)	2(1)	0(1)	-2(1)
C22	15(1)	20(1)	20(1)	1(1)	-2(1)	0(1)
C23	20(1)	15(1)	17(1)	1(1)	-4(1)	0(1)
C24	18(1)	18(1)	18(1)	6(1)	-3(1)	-2(1)

C25	15(1)	18(1)	16(1)	4(1)	-2(1)	-2(1)
C26	26(1)	21(1)	30(1)	9(1)	-9(1)	1(1)

Table 5. Hydrogen coordinates (x 10^4) and isotropic displacement parameters ($Å^2$ x 10^3) for ubsc13.

	x	y	z	U(eq)
H1	-416(15)	1721(12)	3548(7)	13(3)
H2A	-702(16)	3155(12)	2783(7)	15(3)
H2B	896(16)	3467(13)	2816(7)	15(3)
H3	1904(16)	894(13)	2055(8)	17(3)
H4A	1159(17)	408(13)	3078(8)	20(4)
H4B	2842(17)	639(13)	3145(8)	19(3)
H5A	811(17)	3677(13)	4036(8)	19(4)
H5B	-758(18)	3366(14)	4091(8)	26(4)
H8	1330(20)	2830(15)	5987(10)	37(5)
H9	1820(20)	2218(15)	7068(9)	35(5)
H10	750(20)	585(15)	7489(9)	36(5)
H11	-922(17)	-383(14)	6824(8)	27(4)
H12	-1482(19)	307(14)	5787(9)	31(4)
H13A	3181(17)	2740(14)	2682(8)	22(4)
H13B	3960(18)	1814(14)	2309(8)	24(4)
H15	3435(17)	1756(13)	962(8)	21(4)
H16	3370(19)	2809(14)	33(9)	26(4)
H17	2950(17)	4710(14)	128(8)	23(4)
H18	2633(16)	5548(12)	1189(7)	17(3)
H19	2763(18)	4423(14)	2171(9)	28(4)
H21	-3382(18)	2443(14)	1610(8)	25(4)
H22	-4247(19)	3835(13)	908(8)	23(4)
H24	-417(16)	4575(13)	349(7)	17(3)
H25	526(19)	3192(14)	1032(8)	26(4)
H26A	-2360(20)	5344(17)	-271(11)	44(6)
H26B	-3200(30)	5870(20)	287(12)	65(7)

H26C	-3750(30)	4970(20)	-49(13)	68(8)
H2N	1317(17)	2657(14)	4905(9)	28(4)

Table 6. Torsion angles [°] for ubsc13.

O3-S1-N1-C2	-170.18(6)	C7-C8-C9-C10	0.85(17)
O4-S1-N1-C2	-39.81(8)	C8-C9-C10-C11	-1.06(17)
C20-S1-N1-C2	74.18(7)	C9-C10-C11-C12	0.06(17)
O3-S1-N1-C3	-23.90(8)	C10-C11-C12-C7	1.16(16)
O4-S1-N1-C3	106.48(7)	C8-C7-C12-C11	-1.35(15)
C20-S1-N1-C3	-139.53(7)	C6-C7-C12-C11	179.75(9)
C4-O1-C1-C5	178.50(8)	N1-C3-C13-C14	-50.08(10)
C4-O1-C1-C2	-61.66(10)	C4-C3-C13-C14	-170.67(8)
C3-N1-C2-C1	-49.90(10)	C3-C13-C14-C15	-69.86(12)
S1-N1-C2-C1	98.27(8)	C3-C13-C14-C19	108.42(10)
O1-C1-C2-N1	53.94(10)	C19-C14-C15-C16	0.22(15)
C5-C1-C2-N1	172.55(8)	C13-C14-C15-C16	178.52(9)
C2-N1-C3-C4	49.74(10)	C14-C15-C16-C17	0.14(16)
S1-N1-C3-C4	-97.15(8)	C15-C16-C17-C18	-0.85(17)
C2-N1-C3-C13	-72.02(9)	C16-C17-C18-C19	1.19(17)
S1-N1-C3-C13	141.09(7)	C17-C18-C19-C14	-0.84(16)
C1-O1-C4-C3	63.36(10)	C15-C14-C19-C18	0.13(15)
N1-C3-C4-O1	-55.18(11)	C13-C14-C19-C18	-178.21(10)
C13-C3-C4-O1	66.57(10)	O3-S1-C20-C25	-65.05(9)
C6-N2-C5-C1	-83.58(11)	O4-S1-C20-C25	166.22(8)
O1-C1-C5-N2	-52.53(11)	N1-S1-C20-C25	48.81(9)
C2-C1-C5-N2	-172.29(8)	O3-S1-C20-C21	110.71(9)
C5-N2-C6-O2	2.36(14)	O4-S1-C20-C21	-18.02(9)
C5-N2-C6-C7	-177.77(8)	N1-S1-C20-C21	-135.43(8)
O2-C6-C7-C8	-151.79(10)	C25-C20-C21-C22	1.07(15)
N2-C6-C7-C8	28.33(13)	S1-C20-C21-C22	-174.64(8)
O2-C6-C7-C12	27.07(13)	C20-C21-C22-C23	0.10(16)
N2-C6-C7-C12	-152.80(9)	C21-C22-C23-C24	-1.52(16)
C12-C7-C8-C9	0.35(15)	C21-C22-C23-C26	179.15(10)
C6-C7-C8-C9	179.21(10)	C22-C23-C24-C25	1.83(16)

C26-C23-C24-C25	-178.85(10)
C21-C20-C25-C24	-0.78(15)
S1-C20-C25-C24	174.91(8)
C23-C24-C25-C20	-0.70(16)

Table 7. Hydrogen bonds and close contacts for ubsc13 [Å and °].

D-H...A	d(D-H)	d(H...A)	d(D...A)	<(DHA)
N2-H2N...O2#1	0.933(17)	2.020(17)	2.9358(12)	166.4(15)

Symmetry transformations used to generate equivalent atoms:

#1 x+1/2,-y+1/2,-z+1

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