Supporting information for

**Enantioselective Addition of Oxazolones to N-Protected Imines Catalyzed by Chiral Thioureas**

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**1. General Information**

All reactions were carried out in oven-dried glassware under argon. The commercially available chemicals were used without purification. THF, toluene and dioxane were distilled from Na/benzophenone, CH₂Cl₂ and MeCN from CaH₂ under argon at 760 Torr. Thin layer chromatography (TLC) was performed on pre-coated aluminium-backed plates (Merck Kieselgel 60 F254) and visualized by ultraviolet irradiation, potassium permanganate or phosphomolybdic acid solution dip. Column and flash chromatography were performed on silica gel with particle size 0.040-0.065 mm in diameter.

NMR spectra were acquired on Varian NMR System 300 and 600 spectrometers, running at 300 or 600 MHz for ¹H and 75 or 150 MHz for ¹³C and DEPT, respectively. Chemical shifts (δ) are reported in ppm relative to tetramethylsilane (TMS) as an internal standard. The following abbreviations are used to indicate the multiplicity in ¹H NMR spectra: s, singlet; bs, broad singlet; d, doublet; dd, double doublet; ddd, double double doublet; t, triplet; dt, double triplet; q, quartet; dq, double quartet; p, pentet; m, multiplet. IR spectra were measured at Nikolet IS10 spectrometer. HRMS was measured on a mass spectrometer with H-ESI Orbitrap ionization in positive mode. HPLC was performed on Daicel Chiralpak AD-H and IA columns.
with UV detection at 240 nm. Optical rotation measurements were performed on Jasco P-2000 polarimeter. CD spectra were measured on Jasco J-815 CD spectrometer.

Catalysts 1a, 1b, 2a, 2b, 3, 4 – 5, 6, 7 and 8 were synthesized following the corresponding literature procedures.

Azlactones 9a and 9b were synthesized from the corresponding N-benzoxy amino acids. N-benzoxy alanine, N-benzoxy phenylalanine and N-benzoxy valine were prepared following the literature procedures.

N-benzyldiene-ethanesulfonamide, N-benzylidene-2,4,6-trimethylbenzenesulfonamide, N-benzylidene-2,4,6-tris(isopropyl)benzenesulfonamide and N-benzylidenenaphthalene-2-sulfonamide were synthesized utilizing the corresponding literature procedures.

2. General Procedure for the Mannich Reaction

An oven-dried Schlenk tube was charged with imine (0.1 mmol), azlactone (0.12 mmol, 1.2 eq.), catalyst (0.01 mmol, 10 mol %) and acid co-catalyst (0.01 mmol, 10 mol %) if not stated otherwise. The solvent (0.5 mL) was then added. After stirring at room temperature for 18 h, the solution was concentrated in vacuo and the residue was purified by silica gel column chromatography (eluant petroleum ether/EtOAc) to afford the product.

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Following the general procedure, 10a was isolated after silica gel chromatography (eluant petroleum ether/EtOAc 4:1 - 3:1) as a white solid. 

**1H NMR (300 MHz, CDCl₃):** \( \delta \) 7.95 – 7.85 (m, 2H), 7.65 – 7.48 (m, 2H), 7.48 – 7.31 (m, 4H), 7.18 – 7.04 (m, 4H), 6.96 (d, \( J = 8.0 \) Hz, 2H), 5.37 – 5.23 (m, 1H), 4.68 (d, \( J = 10.8 \) Hz, 1H), 2.29 (s, 3H), 1.33 (s, 3H). 

**13C NMR (75 MHz, CDCl₃):** 179.2 (Cq), 161.8 (Cq), 143.2 (Cq), 136.7 (Cq), 135.3 (Cq), 133.1 (CH), 129.1 (CH), 129.0 (CH), 128.7 (CH), 128.2 (CH), 128.1 (CH), 127.9 (CH), 127.1 (CH), 125.3 (Cq), 72.9 (Cq), 62.3 (CH), 21.7 (CH₃), 21.4 (CH₃). 

**IR (cm⁻¹):** 3257, 2959, 2920, 1819, 1651, 1451, 1328, 1292, 1162, 1089, 1001, 911, 874, 811. 

**MS:** \( m/z 457.1 \ [M+Na]^+ \).

**HPLC:** Chiralpak AD-H column, eluant = hexane/i-PrOH 85:15, flow rate = 0.8 mL.min⁻¹; \( t \) (major) = 19.8 min; \( t \) (minor) = 22.5 min.

The spectral data are in agreement with the literature data.¹⁵

Following the general procedure, 10b was isolated after silica gel chromatography (eluant petroleum ether/EtOAc 6:1 – 5:1) as a white solid. 

**[α]D²⁰** = +38.5 (c 1.4, CHCl₃, 90:10 er). 

**1H NMR (300 MHz, CDCl₃):** \( \delta \) 7.87 – 7.80 (m, 2H), 7.58 – 7.50 (m, 1H), 7.46 – 7.35 (m, 4H), 7.07 – 6.92 (m, 7H), 5.48 (d, \( J = 10.7 \) Hz, 1H), 4.98 (d, \( J = 10.8 \) Hz, 1H), 2.45 – 2.34 (m, 1H), 2.27 (s, 3H), 1.10 (d, \( J = 6.8 \) Hz, 3H), 0.90 (d, \( J = 6.8 \) Hz, 3H). 

**13C NMR (75 MHz, CDCl₃):** \( \delta \) 179.2 (Cq), 161.2 (Cq), 143.0 (Cq), 137.2 (Cq), 135.1 (Cq), 132.9 (CH), 129.1 (CH), 128.7 (CH), 128.0 (CH), 127.9 (CH), 127.83 (CH), 127.78

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(CH), 126.9 (CH), 125.1 (Cq), 79.9 (Cq), 59.4 (CH), 32.1 (CH), 21.4 (CH₃), 16.6 (CH₃), 16.3 (CH₃). IR (cm⁻¹): 3266, 2961, 1816, 1646, 1455, 1334, 1262, 1159, 1095, 1081, 1022, 944, 861. MS: m/z 485.2 [M+Na]⁺. HPLC: Chiralpak AD-H column, eluant = hexane/i-PrOH 85:15, flow rate = 0.8 mL.min⁻¹; t (major) = 17.9 min; t (minor) = 22.1 min.

The spectral data are in agreement with the literature data.¹⁶

\[ \text{N-((S)-(R)-4-methyl-5-oxo-2-phenyl-4,5-dihydrooxazol-4-yl)(phenyl)methyl)} \]
\[ \text{methanesulfonamide (10c)} \]

Following the general procedure, 10c was isolated after silica gel chromatography (eluant petroleum ether/EtOAc 3:1 – 2:1) as a white solid. Rₐ = 0.13 (petroleum ether/EtOAc 3:1). 

**¹H NMR (300 MHz, DMSO-\text{d₆}):** δ 8.08 – 7.96 (m, 3H), 7.76 – 7.58 (m, 5H), 7.49 – 7.32 (m, 3H), 4.69 (d, J = 10.8 Hz, 1H), 2.30 (s, 3H), 1.20 (s, 3H). 

**¹³C NMR (75 MHz, DMSO-\text{d₆}):** 179.6 (Cq), 160.8 (Cq), 136.7 (Cq), 133.5 (CH), 129.6 (CH), 129.4 (CH), 128.8 (CH), 128.7 (CH), 128.6 (CH), 126.2 (Cq), 73.7 (Cq), 63.2 (CH), 41.4 (CH₃), 21.3 (CH₃). IR (cm⁻¹): 3273, 3031, 2936, 1827, 1652, 1454, 1441, 1307, 1298, 1162, 1004, 976, 901, 877, 703. MS: m/z 381.1 [M+Na]⁺. HRMS: calcd. for [C₁₈H₁₈N₂O₄S+H]⁺ ([M+H]⁺): m/z 359.1066, found: 359.1053. HPLC: Daicel IA column, eluant = hexane/i-PrOH 85:15, flow rate = 1.0 mL.min⁻¹; t (major) = 8.2 min; t (minor) = 10.6 min.

\[ \text{N-((S)-(R)-4-isopropyl-5-oxo-2-phenyl-4,5-dihydrooxazol-4-yl)(phenyl)methyl)} \]
\[ \text{methanesulfonamide (10d)} \]

Following the general procedure, 10d was isolated after silica gel chromatography (eluant petroleum ether/EtOAc 3:1) as a white solid. Rₐ = 0.50 (petroleum ether/EtOAc 3:1). 

**¹H NMR (300 MHz, CDCl₃):** δ 7.90 (d, J = 7.3 Hz, 2H), 7.62 – 7.51 (m, 1H), 7.50 – 7.40 (m, 4H), 7.36

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\(-7.27\) (m, 3H), 5.40 (d, \(J = 10.6\) Hz, 1H), 5.04 (d, \(J = 10.7\) Hz, 1H), 2.53 (s, 3H), 2.40 – 2.26 (m, 1H), 1.07 (d, \(J = 6.8\) Hz, 3H), 0.97 (d, \(J = 6.8\) Hz, 3H). \(^{13}\)C NMR (75 MHz, CDCl\(_3\)): \(\delta\) 179.1 (Cq), 161.5 (Cq), 136.2 (Cq), 133.0 (CH), 128.8 (CH), 128.7 (CH), 128.1 (CH), 128.0 (CH), 125.1 (Cq), 79.9 (Cq), 59.6 (CH), 41.7 (CH\(_3\)), 32.1 (CH), 16.5 (CH\(_3\)), 16.3 (CH\(_3\)). IR (cm\(^{-1}\)): 3288, 2968, 2915, 2881, 1811, 1652, 1460, 1320, 1289, 1153, 1093, 1065, 1013, 969, 881, 763, 705, 696. MS: \(m/z\) 409.1 [M+Na\(^+\)]. HRMS: calcd. for \([C_{20}H_{22}N_2O_4S+H]\): \(m/z\) 409.1379, found: 409.1367.

HPLC: Daicel IA column, eluant = hexane/i-PrOH 80:20, flow rate = 1 mL.min\(^{-1}\); \(t\) (major) = 6.8 min; \(t\) (minor) = 14.6 min.

\(N\)-((S)-((R))-4-benzyl-5-oxo-2-phenyl-4,5-dihydrooxazol-4-yl)(phenyl)methyl)methanesulfonamide (10e)

Following the general procedure, 10e was isolated after silica gel chromatography (eluant petroleum ether/EtOAc 3:1) as a white solid. \(R_F = 0.41\) (petroleum ether/EtOAc 3:1). \(^{1}H\) NMR (300 MHz, CDCl\(_3\)): \(\delta\) 7.79 (d, \(J = 7.3\) Hz, 2H), 7.61 – 7.48 (m, 3H), 7.45 – 7.32 (m, 5H), 7.15 – 6.99 (m, 5H), 5.37 (d, \(J = 10.8\) Hz, 1H), 4.98 (d, \(J = 10.8\) Hz, 1H), 3.21 (d, \(J = 13.4\) Hz, 1H), 2.86 (d, \(J = 13.3\) Hz, 1H), 2.50 (s, 3H). \(^{13}\)C NMR (75 MHz, CDCl\(_3\)): \(\delta\) 178.3 (Cq), 161.9 (Cq), 136.4 (Cq), 133.3 (Cq), 133.0 (CH), 130.1 (CH), 129.1 (CH), 129.0 (CH), 128.7 (CH), 128.2 (CH), 128.1 (CH), 128.0 (CH), 127.3 (CH), 125.0 (Cq), 78.2 (Cq), 62.1 (CH), 41.7 (CH\(_3\)), 41.3 (CH\(_2\)). IR (cm\(^{-1}\)): 3273, 3030, 2922, 1816, 1651, 1495, 1320, 1289, 1157, 1057, 980, 878, 710. MS: \(m/z\) 435.1 [M+H\(^+\)]. HRMS: calcd. for \([C_{24}H_{22}N_2O_4S+H]\): \(m/z\) 435.1379, found: 435.1371. HPLC: Daicel IA column, eluant = hexane/i-PrOH 80:20, flow rate = 1 mL.min\(^{-1}\); \(t\) (major) = 9.4 min; \(t\) (minor) = 11.3 min.

\(N\)-((S)-((R))-4-methyl-5-oxo-2-phenyl-4,5-dihydrooxazol-4-yl)(phenyl)methyl)naphthalene-2-sulfonamide (10f)
Following the general procedure, 10f was isolated after silica gel chromatography (eluant petroleum ether/EtOAc 3:1) as a white solid. \( R_f = 0.20 \) (petroleum ether/EtOAc 3:1). \( ^1H \) NMR (300 MHz, CDCl\(_3\)): \( \delta 8.05 \) (d, \( J = 1.3 \) Hz, 1H), 7.83 – 7.76 (m, 2H), 7.76 – 7.69 (m, 2H), 7.63 – 7.30 (m, 7H), 7.01 – 6.94 (m, 2H), 6.81 – 6.68 (m, 3H), 5.66 (d, \( J = 10.8 \) Hz, 1H), 5.04 (d, \( J = 10.8 \) Hz, 1H), 2.42 – 2.28 (m, 1H), 1.07 (d, \( J = 6.8 \) Hz, 3H), 0.91 (d, \( J = 6.8 \) Hz, 3H). \( ^{13}C \) NMR (150 MHz, CDCl\(_3\)): \( \delta 179.2 \) (Cq), 161.3 (Cq), 137.0 (Cq), 134.8 (Cq), 134.5 (Cq), 132.9 (CH), 131.8 (Cq), 129.1 (CH), 128.9 (CH), 128.7 (CH), 128.54 (CH), 128.53 (CH), 128.0 (CH), 127.9 (CH), 127.8 (CH), 127.63 (CH), 127.61 (CH), 127.1 (CH), 125.1 (Cq), 122.0 (CH), 79.8 (Cq), 59.6 (CH), 32.1 (CH), 16.6 (CH\(_3\)), 16.4 (CH\(_3\)). IR (cm\(^{-1}\)): 3253, 3059, 2972, 2928, 1827, 1812, 1653, 1494, 1329, 1294, 1160, 1132, 1060, 1021, 939, 881, 710, 864. MS: \( m/z \) 521.2 [M+Na\(^+\)]. HRMS: calcd. for [C\(_{29}\)H\(_{26}\)N\(_2\)O\(_4\)S]+ ([M+H\(^+\)]: \( m/z \) 499.1692, found: 499.1685. HPLC: Chiralpak AD-H column, eluant = hexane/i-PrOH 85:15, flow rate = 1.0 mL.min\(^{-1}\); \( t_R \) (major) = 17.6 min; \( t_R \) (minor) = 21.8 min.

2,4,6-trimethyl-N-((S)-((R)-4-methyl-5-oxo-2-phenyl-4,5-dihydrooxazol-4-yl)(phenyl)methyl)benzenesulfonamide (10g)

Following the general procedure, 10g was isolated after silica gel chromatography (eluant petroleum ether/EtOAc 6:1) as a white solid. \( R_f = 0.21 \) (petroleum ether/EtOAc 6:1). \( ^1H \) NMR (300 MHz, CDCl\(_3\)): \( \delta 8.00 – 7.93 \) (m, 2H), 7.63 – 7.56 (m, 1H), 7.53 – 7.45 (m, 2H), 7.19 – 7.11 (m, 5H), 6.75 (s, 2H), 5.30 (d, \( J = 10.4 \) Hz, 1H), 4.56 (d, \( J = 10.4 \) Hz, 1H), 2.47 (s, 6H), 2.22 (s, 3H), 1.31 (s, 3H). \( ^{13}C \) NMR (75 MHz, CDCl\(_3\)): \( \delta 179.2 \) (Cq), 161.7 (Cq), 142.2 (Cq), 138.7 (Cq), 135.7 (Cq), 133.7 (Cq), 133.1 (CH), 131.7 (CH), 128.8 (CH), 128.3 (CH), 128.2 (CH), 128.1 (CH), 127.6 (CH), 125.3 (Cq), 72.8 (Cq), 62.3 (CH), 22.9 (CH\(_3\)), 21.7 (CH\(_3\)), 20.8 (CH\(_3\)). IR (cm\(^{-1}\)): 3317, 3033, 2937, 1818, 1654, 1450, 1330, 1319, 1158, 1001, 913, 685, 661. MS: \( m/z \) 485.2 [M+Na\(^+\)]. HRMS: calcd. for [C\(_{29}\)H\(_{26}\)N\(_2\)O\(_4\)S]+ ([M+H\(^+\)]: \( m/z \) 463.1692, found: 463.1686. HPLC: Daicel IA column, eluant = hexane/i-PrOH 95:5, flow rate = 0.8 mL.min\(^{-1}\); \( t_R \) (minor) = 17.7 min; \( t_R \) (major) = 19.1 min.
Following the general procedure, 10h was isolated after silica gel chromatography (eluant petroleum ether/EtOAc 6:1) as a white solid. R_f = 0.30 (petroleum ether/EtOAc 6:1). ¹H NMR (300 MHz, CDCl₃): δ 7.88 – 7.81 (m, 2H), 7.59 – 7.50 (m, 1H), 7.47 – 7.39 (m, 2H), 7.14 – 6.92 (m, 5H), 6.70 (s, 2H), 5.56 (d, J = 10.4 Hz, 1H), 4.89 (d, J = 10.4 Hz, 1H), 2.47 (s, 6H), 2.38 – 2.24 (m, 1H), 2.19 (s, 3H), 1.01 (d, J = 6.8 Hz, 3H), 0.90 (d, J = 6.8 Hz, 3H). ¹³C NMR (75 MHz, CDCl₃): δ 179.1 (Cq), 161.3 (Cq), 141.9 (Cq), 138.3 (Cq), 135.5 (Cq), 134.5 (Cq), 132.9 (CH), 131.6 (CH), 128.7 (CH), 127.9 (2xCH), 127.8 (CH), 127.5 (CH), 125.2 (Cq), 79.8 (Cq), 59.5 (CH), 32.1 (CH₃), 20.8 (CH₃), 16.4 (CH₃), 16.3 (CH₃). IR (cm⁻¹): 3030, 2935, 1809, 1651, 1452, 1331, 1291, 1175, 1021, 882, 701, 660. MS: m/z 513.2 [M+Na]⁺. HRMS: calcd. for [C₂₈H₃₀N₂O₄S+H]⁺ (M+H)⁺: m/z 491.2005, found: 491.1998. HPLC: Daicel IA column, eluant = hexane/i-PrOH 97:3, flow rate = 0.75 mL.min⁻¹; t (major) = 14.6 min; t (minor) = 15.9 min.

Following the general procedure, 10i was isolated after silica gel chromatography (eluant petroleum ether/EtOAc 6:1) as a colorless oil. R_f = 0.35 (petroleum ether/EtOAc 6:1). ¹H NMR (300 MHz, CDCl₃): δ 7.85 – 7.78 (m, 2H), 7.60 – 7.51 (m, 1H), 7.50 – 7.38 (m, 2H), 7.07 – 6.83 (m, 7H), 5.66 (d, J = 9.5 Hz, 1H), 4.86 (d, J = 9.5 Hz, 1H), 4.06 – 3.88 (m, 2H), 2.88 – 2.69 (m, 1H), 1.77 (s, 3H), 1.21 (d, J = 6.7 Hz, 6H), 1.17 (d, J = 6.9 Hz, 12H). ¹³C NMR (75 MHz, CDCl₃): δ 179.3 (Cq), 161.7 (Cq), 152.7 (Cq), 149.6 (Cq), 135.8 (Cq), 133.3 (Cq), 132.1
(CH), 128.8 (CH), 128.4 (CH), 128.3 (CH), 128.1 (CH), 125.3 (Cq), 123.4 (CH), 72.8 (Cq), 62.0 (CH), 34.1 (CH), 30.0 (CH), 24.8 (CH3), 24.7 (CH3), 23.6 (CH3), 21.9 (CH3).

**IR (cm⁻¹):** 3061, 2956, 2926, 1821, 1650, 1600, 1451, 1321, 1293, 1178, 1004, 875, 700, 661.

**MS:** *m/z* 569.3 [M+Na]⁺. **HRMS:** calc. for [C₃₂H₃₈N₂O₄S+H]⁺ ([M+H]⁺): *m/z* 547.2631, found: 547.2623.

**HPLC:** Daicel IA column, eluant = hexane/i-PrOH 94:6, flow rate = 0.8 mL.min⁻¹; *t* (minor) = 8.9 min; *t* (major) = 9.6 min.

\[
\text{N-((S)-(R)-4-isopropyl-5-oxo-2-phenyl-4,5-dihydrooxazol-4-yl)(4-methoxyphenyl)methyl)-4-methylbenzenesulfonamide (10j)}
\]

Following the general procedure, 10k was isolated after silica gel chromatography (eluant petroleum ether/EtOAc 5:1 to 4:1) as a white solid. **Rf** = 0.29 (petroleum ether/EtOAc 3:1). **1H NMR (300 MHz, CDCl₃):** δ 7.91 – 7.81 (m, 2H), 7.56 – 7.52 (m, 1H), 7.45 – 7.36 (m, 4H), 6.99 (d, *J* = 8.1 Hz, 2H), 6.96 (d, *J* = 8.3 Hz, 2H), 6.50 (d, *J* = 8.5 Hz, 2H), 5.40 (d, *J* = 1.5 Hz, 1H), 4.93 (d, *J* = 10.7 Hz, 1H), 3.65 (s, 3H), 2.38 – 2.31 (m, 1H), 2.29 (s, 3H), 1.05 (d, *J* = 6.7 Hz, 3H), 0.90 (d, *J* = 6.8 Hz, 3H). **13C NMR (150 MHz, CDCl₃):** δ 179.2 (Cq), 161.3 (Cq), 159.1 (Cq), 142.9 (Cq), 137.4 (Cq), 132.9 (CH), 129.1 (CH), 129.0 (CH), 128.0 (CH), 127.3 (Cq), 127.0 (CH), 125.2 (Cq), 113.3 (CH), 80.0 (Cq), 59.0 (CH), 55.1 (CH3), 32.1 (CH), 21.4 (CH3), 16.4 (CH3), 16.3 (CH3). **IR (cm⁻¹):** 3242, 2957, 2931, 1815, 1647, 1612, 1513, 1324, 1241, 1159, 1023, 945, 849, 690. **MS:** 515.1 [M+Na]⁺. **HRMS:** calc. for [C₂₇H₂₈N₂O₅S+H]⁺ ([M+H]⁺): *m/z* 493.1797, found: 493.1788. **HPLC:** Daicel IA column, eluant = hexane/i-PrOH 90:10, flow rate = 1 mL.min⁻¹; *t* (major) = 21.8 min; *t* (minor) = 26.1 min.

The spectral data are in agreement with the literature data.¹⁶

\[
\text{N-((S)-(4-chlorophenyl)((R)-4-isopropyl-5-oxo-2-phenyl-4,5-dihydrooxazol-4-yl)methyl)-4-methylbenzenesulfonamide (10k)}
\]
Following the general procedure, 10k was isolated after silica gel chromatography (eluant petroleum ether/EtOAc 5:1 to 4:1) as a white solid. \( R_F = 0.47 \) (petroleum ether/EtOAc 3:1). \( ^1 \)H NMR (600 MHz, CDCl\(_3\)): \( \delta \) 7.81 (d, \( J = 8.1 \) Hz, 2H), 7.52 (t, \( J = 7.4 \) Hz, 1H), 7.40 (t, \( J = 7.7 \) Hz, 2H), 7.35 (d, \( J = 8.1 \) Hz, 2H), 6.99 – 6.89 (m, 6H), 5.61 (d, \( J = 10.7 \) Hz, 1H), 4.93 (d, \( J = 10.7 \) Hz, 1H), 2.36 – 2.26 (m, 2H), 1.03 (d, \( J = 6.7 \) Hz, 3H), 0.90 (d, \( J = 6.8 \) Hz, 3H). \( ^{13} \)C NMR (150 MHz, CDCl\(_3\)): \( \delta \) 178.8 (Cq), 161.5 (Cq), 143.4 (Cq), 137.1 (Cq), 133.9 (Cq), 133.7 (Cq), 133.0 (CH), 129.3 (CH), 129.1 (CH), 128.7 (CH), 128.1 (CH), 128.0 (CH), 126.9 (CH), 124.9 (Cq), 79.6 (Cq), 58.8 (CH), 32.1 (CH), 21.4 (CH\(_3\)), 16.4 (CH\(_3\)), 16.3 (CH\(_3\)). IR (cm\(^{-1}\)): 3263, 2968, 2924, 1809, 1493, 1450, 1331, 1290, 1160, 1090, 1014, 880, 696. MS: 519.1 [M+Na]\(^+\). HRMS: calcd. for \( [\text{C}_{26}\text{H}_{25}\text{ClN}_2\text{O}_4\text{S}+\text{H}]^+ \): \( m/z \) 497.1302, found: 497.1293.

HPLC: Daicel IA column, eluant = hexane/i-PrOH 90:10, flow rate = 1 mL.min\(^{-1}\); \( t \) (major) = 16.1 min; \( t \) (minor) = 26.1 min.

The spectral data are in agreement with the literature data.\(^6\)

\((S)-2-[[1R,2R]-2-(N’-(p-toluenesulfonyl)cyclohexyl)thioureido]-N-benzyl-N,3,3-trimethylbutanamide (1c)\)

\((S)-2-(3-((1R,2R)-2-aminocyclohexyl)thioureido)-N-benzyl-N,3,3-trimethylbutanamide \) (100 mg, 0.26 mmol) was dissolved in dry THF (3.5 mL) and Et\(_3\)N (43 \( \mu \)L, 0.31 mmol, 1.2 eq.) was added. A solution of TsCl (53.7 mg, 0.28 mmol, 1.1 eq.) in THF (1 mL) was added dropwise and the reaction was stirred at room temperature. After 2 hours, the solvent was evaporated \textit{in vacuo} and the residue was purified by silica gel column chromatography (petroleum ether/ethyl acetate 1.2:1) to give thiourea \( \textbf{1c} \) (120 mg, 86 % yield) as a white crystalline solid.
Mp. 109 – 113 °C. [α]D20 = +5.2 (c 1.00, CHCl3). 1H NMR (300 MHz, CDCl3; compound exists as a 2.4:1 mixture of rotamers, the major rotamer is denoted by *): 7.70 (d, J = 8.2 Hz, 2H*), 7.65 (d, J = 8.1 Hz, 2H), 7.45 – 7.27 (m, 4H* + 4H), 7.26 – 7.19 (m, 3H* + 3H), 6.83 (d, J = 9.4 Hz, 1H*), 6.80 – 6.70 (m, 1H* + 1H), 6.36 (d, J = 8.3 Hz, 1H*), 6.18 (d, J = 8.1 Hz, 1H), 5.82 (s, 1H), 5.76 (d, J = 9.4 Hz, 1H*), 5.18 (d, J = 14.9 Hz, 1H*), 5.05 (d, J = 15.3 Hz, 1H), 4.53 (d, J = 15.6 Hz, 1H), 4.27 (ddd, J = 13.8, 11.3, 3.6 Hz, 1H* + 1H), 4.06 (d, J = 15.0 Hz, 1H*), 3.19 (s, 3H*), 2.86 (s, 3H), 2.85 – 2.77 (m, 1H* + 1H), 2.41 (s, 3H*), 2.39 (s, 3H), 2.07 – 1.80 (m, 4H* + 4H), 1.64 – 1.49 (m, 3H* + 3H), 1.34 – 1.14 (m, 4H* + 3H), 1.08 (s, 9H*), 1.03 (s, 9H), 0.98 – 0.83 (m, 2H* + 2H). 13C NMR (75 MHz, CDCl3): δ 183.8 (Cq), 183.4 (Cq), 172.4 (Cq), 171.9 (Cq), 143.0 (Cq), 143.0 (Cq), 138.4 (Cq), 138.2 (Cq), 136.5 (Cq), 135.8 (Cq), 129.6 (CH), 129.5 (CH), 129.0 (CH), 128.8 (CH), 128.1 (CH), 128.0 (CH), 127.9 (CH), 127.6 (CH), 127.0 (CH), 127.0 (CH), 60.0 (CH), 59.7 (CH), 59.1 (CH), 58.8 (CH), 56.7 (CH), 54.5 (CH2), 51.27 (CH2), 37.0 (Cq), 36.7 (Cq), 36.3 (CH3), 33.9 (CH2), 33.7 (CH2), 33.4 (CH3), 32.7 (CH2), 32.6 (CH2), 27.0 (CH3), 24.6 (CH2), 24.2 (CH2), 21.7 (CH3), 21.6 (CH3). IR (cm⁻¹): 3320, 3086, 2933, 2859, 1619, 1527, 1495, 1449, 1416, 1398, 1317, 1234, 1155, 1091, 1071, 961, 899, 700, 661. MS: m/z 567.2 [M+Na]+. HRMS: calcd. for [C28H40N4O3S+Na]+ ([M+Na]+): m/z 567.2440, found: 567.2430.
3. Hydrolysis of the adduct 10b

(R)-2-benzamido-3-methyl-2-((S)-(4-methylphenylsulfonamido)(phenyl)methyl)butanoic acid (11)

Adduct 10b (50 mg, 1.1 mmol, 1 eq.) was dissolved in MeCN (1.0 mL) and conc. HCl (0.17 ml, 2.2 mmol, 2 eq.) was added. The mixture was stirred at rt for 3 h, then rinsed with MeCN (1 mL). The solvent was evaporated to give 11 as a pale yellow solid (52 mg, quantitative yield).

\[^{[α]}D_{20} = +85.5\ (c 0.5, \text{EtOH})\].

\[^{1}H\ NMR\ (600\ MHz, DMSO-\text{d}_6)\]: \(δ\ 8.36\ (bs, 1H), 7.66\ (d, J = 7.5\ Hz, 2H), 7.56 – 7.52\ (m, 2H), 7.46\ (t, J = 7.6\ Hz, 2H), 7.31\ (d, J = 8.0\ Hz, 2H), 7.06 – 6.91\ (m, 7H), 6.67\ (bs, 1H), 5.66\ (d, J = 7.8\ Hz, 1H), 2.45\ (bs, 1H), 2.21\ (s, 3H), 1.07\ (d, J = 6.6\ Hz, 3H), 1.02\ (d, J = 6.7\ Hz, 3H)\].

\[^{13}C\ NMR\ (150\ MHz, DMSO-\text{d}_6)\]: \(δ\ 172.0, 168.3, 142.0, 138.8, 137.4, 135.6, 132.0, 129.1, 129.0, 128.4, 127.8, 127.5, 127.4, 126.9, 71.4, 32.6, 21.3, 18.9, 18.7\].

\(IR\ (\text{cm}^{-1})\): 3351 (broad), 3060, 2969, 2932, 1713, 1652, 1599, 1516, 1487, 1318, 1148, 1089, 809, 702, 667. \(MS\): 481.2 \([\text{M}+\text{H}]^{+}\).

The spectral data are in agreement with the literature data.\(^{16}\)
4. Copies of NMR spectra

$^1$H NMR (300 MHz, CDCl$_3$) spectrum of 10a

$^{13}$C NMR (75 MHz, CDCl$_3$) spectrum of 10a
$^1$H NMR (300 MHz, CDCl$_3$) spectrum of 10b

$^{13}$C NMR (75 MHz, CDCl$_3$) spectrum of 10b
$^1$H NMR (300 MHz, DMSO-$d_6$) spectrum of 10c

$^{13}$C NMR (75 MHz, DMSO-$d_6$) spectrum of 10c
$^1$H NMR (300 MHz, CDCl$_3$) spectrum of 10d

$^{13}$C NMR (75 MHz, CDCl$_3$) spectrum of 10d
$^1$H NMR (300 MHz, CDCl$_3$) spectrum of 10e

$^{13}$C NMR (75 MHz, CDCl$_3$) spectrum of 10e
$^{1}$H NMR (300 MHz, CDCl$_3$) spectrum of 10f

$^{13}$C NMR (75 MHz, CDCl$_3$) spectrum of 10f
$^1$H NMR (300 MHz, CDCl$_3$) spectrum of 10g

$^{13}$C NMR (75 MHz, CDCl$_3$) spectrum of 10g
$^1$H NMR (300 MHz, CDCl$_3$) spectrum of 10h

$^{13}$C NMR (75 MHz, CDCl$_3$) spectrum of 10h
$^{1}$H NMR (300 MHz, CDCl$_3$) spectrum of 10i

$^{13}$C NMR (75 MHz, CDCl$_3$) spectrum of 10i
$^1$H NMR (300 MHz, CDCl$_3$) spectrum of 10j

$^{13}$C NMR (150 MHz, CDCl$_3$) spectrum of 10j
$^1$H NMR (600 MHz, CDCl$_3$) spectrum of 10k

$^{13}$C NMR (150 MHz, CDCl$_3$) spectrum of 10k
$^{1}H$ NMR (300 MHz, CDCl$_3$) spectrum of 1c

$^{13}C$ NMR (75 MHz, CDCl$_3$) spectrum of 1c
$^1$H NMR (600 MHz, DMSO-$d_6$) spectrum of 11

$^{13}$C NMR (150 MHz, DMSO-$d_6$) spectrum of 11
5. HPLC Spectra

HPLC Trace of 10a

[Graph showing UV, Retention Time, Area Percent with peaks at specific times and retention values]
HPLC Trace of 10b
HPLC Trace of 10c
HPLC Trace of 10d
HPLC Trace of 10e
HPLC Trace of 10f
HPLC Trace of 10g
HPLC Trace of 10h
HPLC Trace of 10i

### Signal 3: VWD1 A, Wavelength=240 nm

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**Totals:**

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**UV Retention Time**

**Area Percent**
HPLC Trace of 10k

Signal 2: VWD1 A, Wavelength=240 nm

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### Signal 3: VWD1 A, Wavelength=240 nm

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6. Computational data

CD spectra

Comparison of theoretical and experimental ECD spectra of derivate (S,R)-10b; red curve - experimental spectrum; blue curve - calculated conformationally averaged spectrum (DFT, M06, def2_TZVP).

Comparison of theoretical and experimental ECD spectra of derivate (S,R)-10a; red curve - experimental spectrum; blue curve - calculated conformationally averaged spectrum (DFT, M06, def2_TZVP).

Method:

The structure of derivates 10a,b were drawn and optimized by AM1 method in Spartan 8. Then the conformation search was done using AM1 method. The conformers with ΔE<20 kJ/mol were optimized at HF level using base 3-21G. After geometry optimization, which

---

17 Spartan '08, Wavefunction, Inc., Irvine, CA.
was done at DFT,\textsuperscript{19} B3-LYP, def2-TZVP level in Turbomole\textsuperscript{20}, calculation of Boltzmann distribution of conformers was performed.\textsuperscript{20} Two most stable conformers accounted for 88\% and 7\% (more than 95\% all conformers) for compound (\textit{S,R})-\textbf{10a} and 86\% and 9\% for compound (\textit{S,R})-\textbf{10b}. ECD spectra of these conformers were calculated at DFT level using functional M06 and basis set def2-TZVP.\textsuperscript{21} The resulted calculated ECD spectrum is conformationally averaged spectrum. The transition states \textbf{TS1} and \textbf{TS2} were pre-optimized by AM1 method and then optimized by HF using 3-21G bases set in program Spartan 8.\textsuperscript{17} They were confirmed by one negative vibration corresponding to formation of C-C bond.


TURBOMOLE V6.6, TURBOMOLE GmbH, Karlsruhe, 2014.


\((S,R)-10a\) confl

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Transition state model:

The observed stereochemistry of the products can be rationalized by the help of quantum chemical calculations. Based on Hartree-Fock calculations (HF, 3-21G), following model of the transition state was devised. The anion of oxazolone approaches imine in synclinal arrangement due to steric interactions in the transition state. The oxazolone attacks imine from re-face via its re-face. The catalyst and benzoic acid helps in activating the imine through oxygen atoms.

Transition state was optimized at AM1 level in Spartan and finally it was refined at HF level using 3-21G base. The transition state was confirmed by one negative vibration corresponding to formation of C-C bond (verified by visualisation).

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