Supporting information

Synthesis of Chiral α-Substituted α-Amino Acid and Amine Derivatives Through Ni-Catalyzed Asymmetric Hydrogenation

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1. General remarks

Unless otherwise noted, all reagents and solvents were purchased from commercial suppliers and used without further purification. Anhydrous solvents were purchased from Sigma-Aldrich, J&K Chemical Technology company, and transferred by syringe. $^1$H NMR and $^{13}$C NMR spectra were recorded on a Bruker ADVANCE III (400 MHz) spectrometer with CDCl$_3$ as the solvent and tetramethylsilane (TMS) as the internal standard. Chemical shifts are reported in parts per million (ppm, $\delta$ scale) downfield from TMS at 0.00 ppm and referenced to the CDCl$_3$ at 7.26 ppm (for $^1$H NMR) or 77.0 ppm (for $^{13}$C NMR). Data are reported as: multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet), coupling constant in hertz (Hz) and signal area integration in natural numbers. $^{13}$C NMR analyses were run with decoupling. Enantiomeric excess values were determined by Daicel chiral column on an Agilent 1260 Series HPLC instrument. Optical rotations $[\alpha]_D$ were measured on a PERKIN ELMER polarimeter 343 instrucment. Column Chromatography was performed with silica gel (300-400 mesh).

2. General procedure for the synthesis of substrate

The substrates of 1a-Ii were synthesized according to the method A:

\[
\begin{align*}
\text{R}\text{^{1}}_{\text{OH}} + \text{ClO}^-\text{OCOO}^-\text{R}_{2} &\xrightarrow{\text{TiCl}_4/\text{CH}_2\text{Cl}_2, -15^\circ\text{C} \sim -5^\circ\text{C}} \text{R}\text{^{1}}_{\text{OH}}\text{OCOO}^-\text{R}_{2} \\
\text{ClO}^-\text{OCOO}^-\text{R}_{2} &\xrightarrow{\text{DMA}} \text{R}\text{^{1}}_{\text{O}}\text{S}^-\text{O} \\
\end{align*}
\]

Step 1:[1] To a solution of phenol (20 mmol) in CH$_2$Cl$_2$ (25 mL) at -5 °C low temperature reactor was added TiCl$_4$ (4.2 g, 22 mmol). Ethyl chlorooxooacetate (3.0 g, 22 mmol) was added over 3 min while maintaining the temperature below -5 °C. The resulting mixture was stirred at -15 °C to -5 °C for 2 h for completion. The reaction was then diluted with CH$_2$Cl$_2$ (25 mL) and poured into previously cooled 1.0 M HCl (75 mL). After conc. HCl (2.5 mL) was added, the aqueous layer was separated and extracted with CH$_2$Cl$_2$. The combined organic layer was washed with 1.0 M HCl and 20% NaCl aqueous solution. The organic layer was concentrated and purified by
column chromatography on silica gel to give the corresponding products S1 (flash column chromatography eluent petroleum ether/ethyl acetate = 10/1).

Step 2:[2] To chlorosulfonyl isocyanate (1.3 mL, 15 mmol) in a Schlenk tube was added dropwise formic acid (0.57 mL, 15 mmol) at 0 °C with vigorous stirring. The mixture, which immediately became a solid, was heated at 50 °C with oil bath for 10 min until the solid materials melted. The mixture was cooled to 0 °C and dissolved in acetonitrile (7 mL). To the mixture was added S1 5.00 mmol in N,N-dimethylacetoamide (DMA, 6 mL) and the mixture was stirred at room temperature overnight. H2O was added to the mixture and it was extracted with ethyl acetate. The organic extract was dried over Na2SO4, filtered and concentrated on a rotary evaporator. The organic layer was concentrated and purified by column chromatography on silica gel to give the corresponding product 1.

ethyl benzo[e][1,2,3]oxathiazine-4-carboxylate 2,2-dioxide 1a

![Chemical Structure](image)

White crystalline solid (flash column chromatography eluent petroleum ether/ethyl acetate = 5/1); 1H NMR (400 MHz, CDCl3) δ 8.00 (dd, J = 8.0, 1.1 Hz, 1H), 7.81-7.77 (m, 1H), 7.43 (t, J = 7.7 Hz, 1H), 7.35 (d, J = 8.3 Hz, 1H), 4.53 (q, J = 7.1 Hz, 2H), 1.46 (t, J = 7.1 Hz, 3H); 13C NMR (100 MHz, CDCl3) δ 165.16, 160.76, 154.73, 138.13, 130.15, 126.29, 119.15, 113.58, 63.98, 13.98. The characterization data of compound 1a is in accordance with the reported data in the literature.[2]

ethyl 7-methoxybenzo[e][1,2,3]oxathiazine-4-carboxylate 2,2-dioxide 1b

![Chemical Structure](image)

White crystalline solid (flash column chromatography eluent petroleum ether/ethyl acetate = 4/1); 1H NMR (400 MHz, CDCl3) δ 7.94 (d, J = 9.0 Hz, 1H), 6.89 (dd, J = 9.0, 2.5 Hz, 1H), 6.78 (d, J = 2.4 Hz, 1H), 4.50 (q, J = 7.1 Hz, 2H), 3.95 (s,
ethyl 6-methoxybenzo[e][1,2,3]oxathiazine-4-carboxylate 2,2-dioxide 1c

Yellow crystalline solid (flash column chromatography eluent petroleum ether/ethyl acetate = 4/1); $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.47 (d, $J = 2.8$ Hz, 1H), 7.33-7.28 (m, 2H), 4.52 (q, $J = 7.1$ Hz, 2H), 3.86 (s, 3H), 1.46 (t, $J = 7.1$ Hz, 3H); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 164.71, 160.86, 156.93, 148.64, 125.05, 120.11, 113.98, 112.64, 63.93, 56.05, 13.99. HRMS calculated for C$_{11}$H$_{11}$NaO$_6$S$^+$ [(M+Na)$^+$] = 308.0202, found: 308.0202.

ethyl 6-methylbenzo[e][1,2,3]oxathiazine-4-carboxylate 2,2-dioxide 1d

Yellow crystalline solid (flash column chromatography eluent petroleum ether/ethyl acetate = 5/1); $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.73 (d, $J = 1.1$ Hz, 1H), 7.58 (dd, $J = 8.5$, 1.6 Hz, 1H), 7.24-7.22 (m, 1H), 4.52 (q, $J = 7.1$ Hz, 2H), 2.43 (s, 3H), 1.46 (t, $J = 7.2$ Hz, 3H); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 165.30, 160.88, 152.76, 138.96, 136.50, 129.81, 118.83, 113.28, 63.89, 20.88, 13.98. HRMS calculated for C$_{11}$H$_{11}$NaO$_6$S$^+$ [(M+Na)$^+$] = 292.0254, found: 292.0250.

ethyl 8-methylbenzo[e][1,2,3]oxathiazine-4-carboxylate 2,2-dioxide 1e
White crystalline solid (flash column chromatography eluent petroleum ether/ethyl acetate = 5/1); $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.77 (dd, $J$ = 8.0, 1.0 Hz, 1H), 7.63 (dd, $J$ = 7.6, 0.7 Hz, 1H), 7.30 (t, $J$ = 7.8 Hz, 1H), 4.52 (q, $J$ = 7.1 Hz, 2H), 2.42 (s, 3H), 1.46 (t, $J$ = 7.2 Hz, 3H); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 165.78, 160.95, 153.09, 139.59, 129.05, 127.64, 125.57, 113.40, 63.88, 14.92, 13.99. HRMS calculated for C$_{11}$H$_{11}$NaO$_5$S$^+$ [(M+Na)$^+$] = 292.0250, found: 292.0250.

ethyl 7-methylbenzo[e][1,2,3]oxathiazine-4-carboxylate 2,2-dioxide If

White crystalline solid (flash column chromatography eluent petroleum ether/ethyl acetate = 5/1); $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.86 (d, $J$ = 8.2 Hz, 1H), 7.21 (dd, $J$ = 8.2, 0.8 Hz, 1H), 7.14 (s, 1H), 4.51 (q, $J$ = 7.1 Hz, 2H), 2.50 (s, 3H), 1.45 (t, $J$ = 7.2 Hz, 3H); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 164.97, 160.91, 154.87, 151.09, 129.89, 127.29, 119.28, 111.27, 63.84, 22.34, 13.97. HRMS calculated for C$_{11}$H$_{11}$NaO$_5$S$^+$ [(M+Na)$^+$] = 292.0250, found: 292.0248.

ethyl 7-fluorobenzo[e][1,2,3]oxathiazine-4-carboxylate 2,2-dioxide Ig

White crystalline solid (flash column chromatography eluent petroleum ether/ethyl acetate = 5/1); $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 8.13 (dd, $J$ = 9.0, 5.8 Hz, 1H), 7.17-7.12 (m, 1H), 7.08 (dd, $J$ = 8.2, 2.5 Hz, 1H), 4.52 (q, $J$ = 7.1 Hz, 2H), 1.46 (t, $J$ = 7.2 Hz, 3H); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 167.63 (d, $J$ = 264.0 Hz), 163.90, 160.67, 156.71 (d, $J$ = 14.0 Hz), 132.97 (d, $J$ = 12.0 Hz), 114.48 (d, $J$ = 22.0 Hz), 110.56 (d, $J$ = 3.0 Hz), 107.29 (d, $J$ = 26.0 Hz), 64.13, 13.95. HRMS calculated for C$_{10}$H$_9$FNNaO$_5$S$^+$ [(M+H)$^+$] = 274.0180, found: 274.0178.

ethyl 7-chlorobenzo[e][1,2,3]oxathiazine-4-carboxylate 2,2-dioxide Ih
White crystalline solid (flash column chromatography eluent petroleum ether/ethyl acetate = 5/1); $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 8.03 (d, $J$ = 8.6 Hz, 1H), 7.40 (dd, $J$ = 8.6, 1.9 Hz, 1H), 7.37 (d, $J$ = 1.80 Hz, 1H), 4.52 (q, $J$ = 7.1 Hz, 2H), 1.46 (t, $J$ = 7.1 Hz, 3H); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 163.98, 160.57, 155.12, 144.55, 131.18, 126.93, 119.61, 112.16, 64.16, 13.96. The characterization data of compound 1h is in accordance with the reported data in the literature.$^{[3]}$

ethyl naphtho[2,1-e][1,2,3]oxathiazine-4-carboxylate 2,2-dioxide 1i

Yellow crystalline solid (flash column chromatography eluent petroleum ether/ethyl acetate = 5/1); $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 8.41 (d, $J$ = 8.4 Hz, 1H), 7.92 (d, $J$ = 8.2 Hz, 1H), 7.81-7.76 (m, 4H), 4.56 (q, $J$ = 7.1 Hz, 2H), 1.49 (t, $J$ = 7.2 Hz, 3H); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 165.99, 161.11, 154.39, 137.73, 132.06, 128.42, 128.06, 125.60, 123.19, 122.80, 122.37, 109.05, 63.94, 14.02. HRMS calculated for C$_{14}$H$_{11}$NNaO$_3$S$^+$ [(M+Na)$^+$] = 328.0250, found: 328.0247.

ethyl [1,3]dioxolo[4',5':5,6]benzo[1,2-e][1,2,3]oxathiazine-9-carboxylate 7,7-dioxide 1j

Yellow crystalline solid (flash column chromatography eluent petroleum ether/ethyl acetate = 4/1); $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.37 (s, 1H), 6.79 (s, 1H), 6.18 (s, 2H), 4.49 (q, $J$ = 7.1 Hz, 2H), 1.45 (t, $J$ = 7.1 Hz, 3H); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 164.02, 161.21, 155.83, 153.72, 145.90, 107.58, 106.96, 103.65, 100.35, 63.86, 13.98. HRMS calculated for C$_{11}$H$_9$NNaO$_3$S$^+$ [(M+Na)$^+$] = 321.9992, found: 321.9989.
methyl benzo[e][1,2,3]oxathiazine-4-carboxylate 2,2-dioxide 1k

White crystalline solid (flash column chromatography eluent petroleum ether/ethyl acetate = 5/1); $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 8.04 (dd, $J$ = 8.0, 1.5 Hz, 1H), 7.82-7.77 (m, 1H), 7.46-7.42 (m, 1H), 7.36 (dd, $J$ = 8.4, 0.8 Hz, 1H), 4.07 (s, 3H); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 164.70, 161.18, 154.75, 138.22, 130.24, 126.33, 119.18, 113.61, 54.16. The characterization data of compound 1k is in accordance with the reported data in the literature.$^{[4]}$

isopropyl benzo[e][1,2,3]oxathiazine-4-carboxylate 2,2-dioxide 1l

White crystalline solid (flash column chromatography eluent petroleum ether/ethyl acetate = 5/1); $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.95 (dd, $J$ = 8.0, 1.5 Hz, 1H), 7.81-7.76 (m, 1H), 7.45-7.41 (m, 1H), 7.36-7.33 (m, 1H), 5.37 (hept, $J$ = 6.3 Hz, 1H), 1.44 (d, $J$ = 6.3 Hz, 6H); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 165.58, 160.34, 154.73, 138.04, 130.00, 126.25, 119.15, 113.57, 72.69, 21.58. HRMS calculated for C$_{11}$H$_{11}$NNaO$_5$S$^+$ [(M+Na)$^+$] = 292.0250, found: 292.0248.

The substrates of 1m-1s were synthesized according to the method B.$^{[5]}$

Anhydrous formic acid (20.0 mmol, 921 mg, 0.75 mL) was added dropwise to neat chlorosulfonyl isocyanate (20.0 mmol, 2.83 g, 1.74 mL) at 0 °C ice bath with rapid stirring. Vigorous gas evolution was observed during the addition process. The resulting
viscous suspension was stirred at room temperature until gas evolution ceased (1-2 h). To the resulting sulfamoyl chloride (ClSO₂NH₂) was added 2’-hydroxyacetophenone (10.0 mmol). After the mixture was cooled under ice-cooling, 15 mL of DMA (N,N-dimethyl acetamide) was slowly added. Caution: a mild exotherm was noted upon combining these reagents. After the ice-cooling was moved, the mixture was stirring for 10 min, and sodium hydride (480 mg of 60% dispersion in mineral oil, 12.0 mmol) was added in portions. After stirring for 30 min at rt another sodium hydride (480 mg of 60% dispersion in mineral oil, 12.0 mmol) was added in portions again. After stirring for 1 h at rt, the reaction mixture was allowed to stir overnight (8-12 h) at 50 °C with oil bath. The reaction was quenched by the addition of 30 mL H₂O and the aqueous layer was extracted with 3 x 20 mL EtOAc. The combined organic layers were washed with 40 mL H₂O and 40 mL brine, and concentrated under reduced pressure. Purification by chromatography on silica gel (petroleum ether/EtOAc = 10/1-3/1) to afford the desired imines as a white solid.

4-methylbenzo[e][1,2,3]oxathiazine 2,2-dioxide **1m**

Yellowish crystalline solid (flash column chromatography eluent petroleum ether/ethyl acetate = 10/1-3/1); ¹H NMR (400 MHz, CDCl₃) δ 7.81 (dd, J = 7.9, 1.5 Hz, 1H), 7.74-7.70 (m, 1H), 7.42-7.38 (m, 1H), 7.29 (dd, J = 8.3, 0.9 Hz, 1H), 2.73 (s, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 177.33, 153.36, 137.10, 128.45, 125.89, 119.06, 116.36, 23.71. The characterization data of compound **1m** is in accordance with the reported data in the literature.[⁵]

4-ethylbenzo[e][1,2,3]oxathiazine 2,2-dioxide **1n**
White crystalline solid (flash column chromatography eluent petroleum ether/ethyl acetate = 10/1-3/1); $^1\text{H NMR}$ (400 MHz, CDCl$_3$) δ 7.82 (dd, $J = 8.0$, 1.5 Hz, 1H), 7.73-7.68 (m, 1H), 7.41-7.37 (m, 1H), 7.30 (dd, $J = 8.3$, 0.9 Hz, 1H), 3.10 (q, $J = 7.2$ Hz, 2H), 1.36 (t, $J = 7.2$ Hz, 3H); $^{13}\text{C NMR}$ (100 MHz, CDCl$_3$) δ 180.77, 153.43, 136.76, 127.74, 125.82, 119.19, 116.05, 29.28, 9.60. The characterization data of compound 1n is in accordance with the reported data in the literature.$^{[5]}$

4-propylbenzo[e][1,2,3]oxathiazine 2,2-dioxide 1o

![4-propylbenzo[e][1,2,3]oxathiazine 2,2-dioxide 1o](image)

White crystalline solid (flash column chromatography eluent petroleum ether/ethyl acetate = 10/1-3/1); $^1\text{H NMR}$ (400 MHz, CDCl$_3$) δ 7.82 (dd, $J = 8.0$, 1.5 Hz, 1H), 7.72-7.68 (m, 1H), 7.41-7.37 (m, 1H), 7.29 (dd, $J = 8.3$, 0.9 Hz, 1H), 3.01 (t, $J = 8.0$ Hz, 2H), 1.91-1.82 (m, 2H), 1.07 (t, $J = 7.4$ Hz, 3H); $^{13}\text{C NMR}$ (100 MHz, CDCl$_3$) δ 180.13, 153.51, 136.81, 127.96, 125.80, 119.20, 116.09, 37.68, 19.35, 13.61. HRMS calculated for C$_{10}$H$_{11}$NNaO$_3$S$^+$ [(M+Na)$^+$] = 248.0352, found: 248.0358.

4,6-dimethylbenzo[e][1,2,3]oxathiazine 2,2-dioxide 1p

![4,6-dimethylbenzo[e][1,2,3]oxathiazine 2,2-dioxide 1p](image)

Yellow crystalline solid (flash column chromatography eluent petroleum ether/ethyl acetate = 10/1-3/1); $^1\text{H NMR}$ (400 MHz, CDCl$_3$) δ 7.57 (d, $J = 1.1$ Hz, 1H), 7.51 (dd, $J = 8.4$, 1.6 Hz, 1H), 7.18 (d, $J = 8.4$, 1H), 2.70 (s, 3H), 2.44 (s, 3H); $^{13}\text{C NMR}$ (100 MHz, CDCl$_3$) δ 177.41, 151.34, 137.85, 135.92, 128.34, 118.73, 116.10, 23.68, 20.88. The characterization data of compound 1p is in accordance with the reported data in the literature.$^{[5]}$
7-methoxy-4-methylbenzo[e][1,2,3]oxathiazine 2,2-dioxide 1q

White crystalline solid (flash column chromatography eluent petroleum ether/ethyl acetate = 10/1-3/1); $^1$H NMR (400 MHz, CDCl$_3$) δ 7.70 (d, $J = 8.9$ Hz, 1H), 6.87 (dd, $J = 8.9$, 2.5 Hz, 1H), 6.73 (d, $J = 2.5$ Hz, 1H), 3.92 (s, 3H), 2.65 (s, 3H); $^{13}$C NMR (100 MHz, CDCl$_3$) δ 176.56, 166.51, 155.87, 130.07, 113.38, 109.85, 102.85, 56.29, 23.59. HRMS calculated for C$_9$H$_9$NNaO$_4$S$^+$ [(M+Na)$^+$] = 250.0144, found: 250.0144.

6-fluoro-4-methylbenzo[e][1,2,3]oxathiazine 2,2-dioxide 1r

Light brown crystalline solid (flash column chromatography eluent petroleum ether/ethyl acetate = 10/1-3/1); $^1$H NMR (400 MHz, CDCl$_3$) δ 7.49-7.42 (m, 2H), 7.31 (dd, $J = 9.0$, 4.3 Hz, 1H), 2.72 (s, 3H); $^{13}$C NMR (100 MHz, CDCl$_3$) δ 176.30 (d, $J = 2.0$ Hz), 158.94 (d, $J = 247.0$ Hz), 149.37 ($J = 2.0$ Hz), 124.28 (d, $J = 24.0$ Hz), 120.92 (d, $J = 8.0$ Hz), 117.04 (d, $J = 8.0$ Hz), 114.43 (d, $J = 25.0$ Hz), 23.73. The characterization data of compound 1r is in accordance with the reported data in the literature.[5]

7-methoxy-4-phenylbenzo[e][1,2,3]oxathiazine 2,2-dioxide 1s

White crystalline solid (flash column chromatography eluent petroleum ether/ethyl acetate = 10/1-3/1); $^1$H NMR (400 MHz, CDCl$_3$) δ 7.74-7.72 (m, 2H), 7.68-7.64 (m, 1H), 7.57-7.53 (m, 3H), 6.88-6.85 (m, 2H), 3.95 (s, 3H); $^{13}$C NMR (100 MHz,
CDCl$_3$ δ 175.81, 166.47, 157.03, 134.02, 133.34, 132.88, 130.47, 128.74, 113.05, 109.88, 103.51, 56.34. The characterization data of compound 1s is in accordance with the reported data in the literature.$^{[5]}$

The substrate of 1t was synthesized according to the method C $^{[6]}$:

\[
\begin{align*}
\text{Step 1:} & \quad \text{To a solution of arylsulfonyl chloride (20 mmol) in DCM in an ice bath was added tert-butylamine (30 mmol) and triethylamine (40 mmol) dropwise. The mixture was stirred at room temperature until the reaction was completed (monitored by TLC). It was washed with saturated sodium carbonate. The organic layer was separated, and the aqueous layer was extracted with DCM (3 x 80 mL). The combined organic extracts were dried over anhydrous Na$_2$SO$_4$. The solvent was removed and the crude product was used in the subsequent step without further purification.}
\end{align*}
\]

\[
\begin{align*}
\text{Step 2:} & \quad n\text{-Butyl lithium (22 mmol) was added dropwise over a 20 min period to a cold (0 °C ice bath), mechanically stirred solution of the aryl sulfonamide (10 mmol) in anhydrous THF (50 mL) under a dry nitrogen atmosphere. After stirring an additional 45 min at 0 °C a precipitate formed. The suspension was cooled further to -78 °C low temperature reactor and oxalic ester (30 mmol) was added. After stirring for 30 min the cooling bath was removed and the suspension was stirred at room temperature for 2-5 h. The reaction was quenched with water (50 mL). The organics were extracted with ethyl acetate (3 x 80 mL). The combined organic extracts were dried over anhydrous Na$_2$SO$_4$, the solvent was removed under vacuum and the residue was purified with flash chromatography on silica gel, eluting with petroleum ether/ethyl acetate 4:1 (v/v), to afford the pure product.}
\end{align*}
\]

\[
\begin{align*}
\text{Step 3:} & \quad \text{To the crude product obtained above, formic acid (30 mL) was added and the suspension was stirred at room temperature under a dry nitrogen atmosphere for 2-}
\end{align*}
\]
3 days. Then the solution was concentrated and the resultant solid was dissolved in DCM and concentrated (three times) to remove traces of formic acid. The crude product was purified by column chromatography on silica gel to give the corresponding product 1t (flash column chromatography eluent petroleum ether/ethyl acetate = 5/1).

ethl 5-methylbenzo[d]isothiazole-3-carboxylate 1,1-dioxide 1t

![chemical structure]

White crystalline solid; $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 8.07 (s, 1m), 7.82 (d, $J = 7.8$ Hz, 1H), 7.57 (d, $J = 7.7$ Hz, 1H), 4.54 (q, $J = 7.1$ Hz, 2H), 2.53 (s, 3H), 1.48 (t, $J = 7.1$ Hz, 3H); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 160.53, 160.23, 145.75, 137.38, 134.64, 128.71, 127.92, 122.75, 63.76, 21.78, 13.98. The characterization data of compound 1t is in accordance with the reported data in the literature.$^6$

3. General procedure for asymmetric hydrogenation

A stock solution was made by mixing Ni(OAc)$_2$ with (S, S)-Ph-BPE in a 1:1.1 molar ratio in HFIP at room temperature for 12 h in an argon-filled glovebox. An aliquot of the catalyst solution (0.1 mL, 0.001 mmol) was transferred by syringe into the vials charged with different substrates (0.05 mmol for each) in anhydrous HFIP (0.6 mL). The vials were subsequently transferred into an autoclave into which hydrogen gas was charged. The reaction was then stirred under H$_2$ (50 atm) at 50 °C with oil bath for 2 h. After completed, the hydrogen gas was released slowly and carefully. The solution was concentrated and passed through a short column of silica gel (eluant: EA) to remove the metal complex. The ee values of all compounds were determined by HPLC analysis on a chiral stationary phase immediately.$^7$ The absolute configurations of the hydrogenation products were determined by the deduction from compound 2b and 2s.
(R)-ethyl 3,4-dihydrobenzo[e][1,2,3]oxathiazine-4-carboxylate 2,2-dioxide 2a

White crystalline solid; >99% conv., 99% yield, 96% ee; [α]$_D^{20}$ = -14.2 (c = 0.55, CHCl$_3$); The enantiomeric excess was determined by HPLC on Chiralpak AD-H column, hexane: isopropanol = 90:10; flow rate = 1.0 mL/min; UV detection at 210 nm; t$_R$ = 16.1 min (minor), 18.0 min (major). $^1$H NMR (400 MHz, CDCl$_3$) δ (ppm) 7.51 (d, J = 7.8 Hz, 1H), 7.40-7.36 (m, 1H), 7.24-7.20 (m, 1H), 7.06 (dd, J = 8.3, 1.1 Hz, 1H), 5.52-5.46 (m, 2H), 4.45-4.38 (m, 2H), 1.40 (t, J = 7.2 Hz, 3H); $^{13}$C NMR (100 MHz, CDCl$_3$) δ (ppm) 167.37, 151.13, 130.47, 126.28, 125.65, 119.59, 116.04, 63.71, 58.65, 14.10. HRMS calculated for C$_{10}$H$_{11}$NaO$_5$S$^+$ [(M+Na)$^+$] = 280.0250, found: 280.0248.

ethyl (R)-7-methoxy-3,4-dihydrobenzo[e][1,2,3]oxathiazine-4-carboxylate 2,2-dioxide 2b

White crystalline solid; >99% conv., 99% yield, >99% ee; [α]$_D^{20}$ = -36.6 (c = 0.6, CHCl$_3$); The enantiomeric excess was determined by HPLC on Chiralcel OD-H column, hexane: isopropanol = 85:15; flow rate = 1.0 mL/min; UV detection at 210 nm; t$_R$ = 13.7 min (major), 23.6 min (minor). $^1$H NMR (400 MHz, CDCl$_3$) δ (ppm) 7.38 (d, J = 8.8 Hz, 1H), 6.76 (dd, J = 8.8, 2.6 Hz, 1H), 6.55 (d, J = 2.6 Hz, 1H), 5.54 (brs, 1H), 5.38 (s, 1H), 4.42-4.36 (m, 2H), 3.79 (s, 3H), 1.39 (t, J = 7.1 Hz, 3H); $^{13}$C NMR (100 MHz, CDCl$_3$) δ (ppm) 167.64, 160.89, 151.90, 127.04, 121.49, 107.67, 104.15, 63.57, 58.15, 55.63, 14.08. HRMS calculated for C$_{11}$H$_{13}$NaO$_5$S$^+$ [(M+Na)$^+$] = 310.0356, found: 310.0352.

ethyl (R)-6-methoxy-3,4-dihydrobenzo[e][1,2,3]oxathiazine-4-carboxylate 2,2-dioxide
White crystalline solid; >99% conv., 97% yield, 94% ee; \([\alpha]_D^{20} = -40.66 \text{ (c = 0.6, CHCl}_3\text{)}\); The enantiomeric excess was determined by HPLC on Chiralcel OD-H column, hexane: isopropanol = 85:15; flow rate = 1.0 mL/min; UV detection at 210 nm; \(t_R = 13.0 \text{ min (major), 20.5 min (minor).} \) \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta \) (ppm) 7.02-6.98 (m, 2H), 6.89 (dd, \(J = 9.1, 2.8 \text{ Hz, 1H}), 5.48 \text{ (brs, 1H}), 5.41 \text{ (s, 1H), 4.44-4.38 (m, 2H), 3.79 (s, 3H), 1.41 (t, \(J = 7.1 \text{ Hz, 3H})),} \) \(^{13}\)C NMR (100 MHz, CDCl\(_3\)) \(\delta \) (ppm) 167.31, 156.74, 144.76, 120.40, 116.62, 115.80, 111.10, 63.68, 58.71, 55.67, 14.14. HRMS calculated for C\(_{11}\)H\(_{13}\)NNaO\(_3\)S\(^+\) [(M+Na\(^+\)] = 310.0356, found: 310.0353.

ethyl \((R)-6\)-methyl-3,4-dihydrobenzo[e][1,2,3]oxathiazine-4-carboxylate 2,2-dioxide

White crystalline solid; >99% conv., 98% yield, 94% ee; \([\alpha]_D^{20} = -38.0 \text{ (c = 0.6, CHCl}_3\text{)}\); The enantiomeric excess was determined by HPLC on Chiralcel OD-H column, hexane: isopropanol = 85:15; flow rate = 1.0 mL/min; UV detection at 210 nm; \(t_R = 9.2 \text{ min (major), 15.7 min (minor).} \) \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta \) (ppm) 7.28 (s, 1H), 7.18-7.15 (m, 1H), 6.95 (d, \(J = 8.4 \text{ Hz, 1H}), 5.47-5.41 \text{ (m, 2H), 4.46-4.37 (m, 2H), 2.34 (s, 3H), 1.41 (t, \(J = 7.1 \text{ Hz, 3H})),} \) \(^{13}\)C NMR (100 MHz, CDCl\(_3\)) \(\delta \) (ppm) 167.43, 149.01, 135.50, 131.04, 126.44, 119.25, 115.55, 63.59, 58.68, 20.91, 14.11. HRMS calculated for C\(_{11}\)H\(_{13}\)NNaO\(_3\)S\(^+\) [(M+Na\(^+\)] = 294.0407, found: 294.0402.

ethyl \((R)-8\)-methyl-3,4-dihydrobenzo[e][1,2,3]oxathiazine-4-carboxylate 2,2-dioxide
White crystalline solid; >99% conv., 98% yield, 95% ee; $[\alpha]_D^{20} = -5.3$ (c = 0.6, CHCl$_3$); The enantiomeric excess was determined by HPLC on Chiralpak AD-H column, hexane: isopropanol = 95:5; flow rate = 1.0 mL/min; UV detection at 210 nm; $t_R = 21.6$ min (minor), 23.6 min (major). $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ (ppm) 7.32 (d, $J = 7.8$ Hz, 1H), 7.22 (d, $J = 7.4$ Hz, 1H), 7.10 (t, $J = 7.7$ Hz, 1H), 5.55 (brs, 1H), 5.44 (s, 1H), 4.43-4.36 (m, 2H), 2.28 (s, 3H), 1.39 (t, $J = 7.2$ Hz, 3H); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ (ppm) 167.60, 149.57, 131.83, 128.90, 124.87, 123.68, 115.75, 63.60, 58.75, 15.46, 14.05. HRMS calculated for $C_{11}H_{13}NNaO_5S^+ [(M+Na)^+] = 294.0407$, found: 294.0407.

ethyl (R)-7-methyl-3,4-dihydrobenzo[e][1,2,3]oxathiazine-4-carboxylate 2,2-dioxide

White crystalline solid; >99% conv., 99% yield, 96% ee; $[\alpha]_D^{20} = -31.0$ (c = 0.6, CHCl$_3$); The enantiomeric excess was determined by HPLC on Chiralpak AD-H column, hexane: isopropanol = 95:5; flow rate = 1.0 mL/min; UV detection at 210 nm; $t_R = 33.6$ min (minor), 38.1 min (major). $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ (ppm) 7.37 (d, $J = 8.1$ Hz, 1H), 7.02 (dd, $J = 8.1$, 0.9 Hz, 1H), 6.87 (s, 1H), 5.49-5.41 (m, 2H), 4.45-4.34 (m, 2H), 2.35 (s, 3H), 1.40 (t, $J = 7.1$ Hz, 3H); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ (ppm) 167.56, 150.91, 141.19, 126.54, 125.99, 119.77, 112.92, 63.60, 58.48, 20.99, 14.09. HRMS calculated for $C_{11}H_{13}NNaO_5S^+ [(M+Na)^+] = 294.0407$, found: 294.0402.

ethyl (R)-7-fluoro-3,4-dihydrobenzo[e][1,2,3]oxathiazine-4-carboxylate 2,2-dioxide
White crystalline solid; >99% conv., 97% yield, 95% ee; $\left[\alpha\right]_D^{20} = -31.0$ (c = 0.6, CHCl$_3$); The enantiomeric excess was determined by HPLC on Chiralpak AD-H column, hexane: isopropanol = 90:10; flow rate = 1.0 mL/min; UV detection at 210 nm; $t_R = 13.4$ min (minor), 19.4 min (major). $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ (ppm) 7.51 (dd, $J = 8.8$, 5.9 Hz, 1H), 6.98-6.93 (m, 1H), 6.81 (dd, $J = 8.6$, 2.6 Hz, 1H), 5.55 (s, 1H), 5.43 (s, 1H), 4.42 (q, $J = 7.1$ Hz, 2H), 1.41 (t, $J = 7.1$ Hz, 3H); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ (ppm) 167.16, 162.90 (d, $J = 250.0$ Hz), 151.87 (d, $J = 12.0$ Hz), 127.81 (d, $J = 9.0$ Hz), 113.14 (d, $J = 22.0$ Hz), 111.98 (d, $J = 4.0$ Hz), 107.31 (d, $J = 25.0$ Hz), 63.88, 58.19, 14.09. HRMS calculated for C$_{11}$H$_{11}$NaO$_5$S$^+$ [(M+Na)$^+$] = 298.0156, found: 298.0151.

ethyl (R)-7-chloro-3,4-dihydrobenzo[e][1,2,3]oxathiazine-4-carboxylate 2,2-dioxide 2h

White crystalline solid; >99% conv., 97% yield, 90% ee; $\left[\alpha\right]_D^{20} = -31.0$ (c = 0.6, CHCl$_3$); The enantiomeric excess was determined by HPLC on Chiralpak AD-H column, hexane: isopropanol = 90:10; flow rate = 1.0 mL/min; UV detection at 210 nm; $t_R = 15.6$ min (minor), 19.3 min (major). $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ (ppm) 7.45 (d, $J = 8.5$ Hz, 1H), 7.20 (dd, $J = 8.5$, 2.0 Hz, 1H), 7.08 (d, $J = 2.0$ Hz, 1H), 5.42 (s, 1H), 4.41 (q, $J = 7.1$ Hz, 2H), 1.40 (t, $J = 7.1$ Hz, 3H); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ (ppm) 167.02, 151.41, 135.94, 127.42, 125.94, 119.82, 114.58, 63.92, 58.30, 14.08. HRMS calculated for C$_{10}$H$_{10}$ClNaO$_5$S$^+$ [(M+Na)$^+$] = 313.9860, found: 313.9866.

ethyl (R)-3,4-dihydronaphtho[2,1-e][1,2,3]oxathiazine-4-carboxylate 2,2-dioxide 2i
White crystalline solid; >99% conv., 98% yield, 94% ee; $[\alpha]_D^{20} = +12.8$ (c = 0.6, CHCl$_3$); The enantiomeric excess was determined by HPLC on Chiralpak AD-H column, hexane: isopropanol = 90:10; flow rate = 1.0 mL/min; UV detection at 220 nm; $t_R = 29.0$ min (major), 32.1 min (minor). $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ (ppm) 8.17 (dd, $J = 8.6, 4.2$ Hz, 1H), 7.84-7.81 (m, 1H), 7.67 (dd, $J = 8.6, 3.7$ Hz, 1H), 7.62-7.57 (m, 2H), 7.51 (d, $J = 8.7$ Hz, 1H), 5.71 (brs, 1H), 5.58 (s, 1H), 4.48-4.37 (m, 2H), 1.42 (t, $J = 7.1$ Hz, 3H); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ (ppm) 167.54, 146.82, 134.00, 127.94, 127.50, 127.38, 125.23, 124.70, 121.82, 120.94, 111.12, 63.76, 59.17, 14.11. HRMS calculated for C$_{14}$H$_{13}$NNO$_5$S$^+ [(M+Na)$^+$] = 330.0407, found: 330.0405.

ethyl (R)-8,9-dihydro-[1,3]dioxolo[4',5':5,6]benzo[1,2-e][1,2,3]oxathiazine-9-carboxylate 7,7-dioxide 2j

Yellowish crystalline solid; >99% conv., 97% yield, 96% ee; $[\alpha]_D^{20} = -15.8$ (c = 0.6, CHCl$_3$); The enantiomeric excess was determined by HPLC on Chiralcel OD-H column, hexane: isopropanol = 80:20; flow rate = 1.0 mL/min; UV detection at 210 nm; $t_R = 14.7$ min (major), 35.3 min (minor). $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ (ppm) 6.91 (s, 1H), 6.55 (s, 1H), 6.01 (s, 2H), 5.43 (d, $J = 8.3$ Hz, 1H), 5.32 (d, $J = 8.3$ Hz, 1H), 4.40 (q, $J = 7.1$ Hz, 2H), 1.40 (t, $J = 7.2$ Hz, 3H); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ (ppm) 167.55, 148.77, 145.85, 145.50, 108.12, 104.86, 102.28, 101.01, 63.75, 58.53, 14.11. HRMS calculated for C$_{11}$H$_{11}$NNO$_5$S$^+ [(M+Na)$^+$] = 324.0148, found: 324.0143.

methyl (R)-3,4-dihydrobenzo[e][1,2,3]oxathiazine-4-carboxylate 2,2-dioxide 2k
White crystalline solid; >99% conv., 99% yield, 97% ee; \([\alpha]_D^{20} = -24.2\) (c = 0.5, CHCl₃); The enantiomeric excess was determined by HPLC on Chiralpak AD-H column, hexane: isopropanol = 90:10; flow rate = 0.8 mL/min; UV detection at 215 nm; \(t_R = 22.1\) min (minor), 24.4 min (major). \(^1\)H NMR (400 MHz, CDCl₃) \(\delta\) (ppm) 7.48 (d, \(J = 7.7\) Hz, 1H), 7.38 (t, \(J = 7.6\) Hz, 1H), 7.22 (t, \(J = 7.6\) Hz, 1H), 7.06 (d, \(J = 8.2\) Hz, 1H), 5.56 (br s, 1H), 5.50 (s, 1H), 3.96 (s, 3H); \(^1^3\)C NMR (100 MHz, CDCl₃) \(\delta\) (ppm) 167.89, 151.07, 130.51, 126.38, 119.54, 115.87, 58.62, 54.08. HRMS calculated for C₉H₉NaO₅S \([\text{M+Na}^+]\) = 266.0094, found: 266.0090.

isopropyl \((R)-3,4\)-dihydrobenzo[e][1,2,3]oxathiazine-4-carboxylate 2,2-dioxide 2l

White crystalline solid; >99% conv., 99% yield, 97% ee; \([\alpha]_D^{20} = -18.9\) (c = 0.55, CHCl₃); The enantiomeric excess was determined by HPLC on Chiralpak AD-H column, hexane: isopropanol = 95:5; flow rate = 1.0 mL/min; UV detection at 210 nm; \(t_R = 21.8\) min (minor), 23.4 min (major). \(^1\)H NMR (400 MHz, CDCl₃) \(\delta\) (ppm) 7.51 (d, \(J = 7.8\) Hz, 1H), 7.40-7.36 (m, 1H), 7.24-7.20 (m, 1H), 7.06 (dd, \(J = 8.3, 0.9\) Hz, 1H), 5.55 (brs, 1H), 5.42 (s, 1H), 5.23 (hept, \(J = 6.3\) Hz, 1H), 1.38 (dd, \(J = 8.3, 6.3\) Hz, 6H); \(^1^3\)C NMR (100 MHz, CDCl₃) \(\delta\) (ppm) 166.89, 151.14, 130.41, 126.17, 125.55, 119.57, 116.17, 72.18, 58.69, 21.67, 21.62. HRMS calculated for C₉H₁₃NaO₅S \([\text{M+Na}^+]\) = 294.0407, found: 294.0406.

\((S)-4\)-methyl-3,4-dihydrobenzo[e][1,2,3]oxathiazine 2,2-dioxide 2m
Yellowish crystalline solid; >99% conv., 99% yield, >99% ee; $[\alpha]_{D}^{20} = -62.6$ (c = 0.5, CHCl$_3$); The enantiomeric excess was determined by HPLC on Chiralpak AS-H column, hexane: isopropanol = 80:20; flow rate = 0.8 mL/min; UV detection at 215 nm; $t_{R}$ = 18.9 min (major), 23.0 min (minor). $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ (ppm) 7.33-7.29 (m, 1H), 7.24-7.18 (m, 2H), 6.98 (d, $J$ = 8.0 Hz, 1H), 4.90 (s, 1H), 4.70 (s, 1H), 1.71 (d, $J$ = 6.9 Hz, 3H); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ (ppm) 150.85, 129.45, 126.22, 125.38, 123.48, 118.66, 52.94, 20.06. The characterization data of compound 2m is in accordance with the reported data in the literature.$^{[5,8]}$

(S)-4-ethyl-3,4-dihydrobenzo[e][1,2,3]oxathiazine 2,2-dioxide 2n

![Image of compound 2n](image)

White crystalline solid; >99% conv., 99% yield, >99% ee; $[\alpha]_{D}^{20} = -82.2$ (c = 0.45, CHCl$_3$); The enantiomeric excess was determined by HPLC on Chiralcel OD-H column, hexane: isopropanol = 80:20; flow rate = 0.8 mL/min; UV detection at 210 nm; $t_{R}$ = 8.1 min (major), 10.4 min (minor). $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ (ppm) 7.33-7.28 (m, 1H), 7.23-7.17 (m, 2H), 7.00-6.98 (m, 1H), 4.73-4.69 (m, 2H), 2.23-1.97 (m, 2H), 1.10 (t, $J$ = 7.4 Hz, 3H); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ (ppm) 151.19, 129.34, 126.31, 125.31, 122.48, 118.81, 58.48, 26.84, 9.59. The characterization data of compound 2n is in accordance with the reported data in the literature.$^{[5]}$

(S)-4-propyl-3,4-dihydrobenzo[e][1,2,3]oxathiazine 2,2-dioxide 2o

![Image of compound 2o](image)

Colorless oil; >99% conv., 98% yield, 98% ee; $[\alpha]_{D}^{20} = -77.6$ (c = 0.5, CHCl$_3$); The enantiomeric excess was determined by HPLC on Chiralcel OD-H column, hexane: isopropanol = 80:20; flow rate = 0.8 mL/min; UV detection at 210 nm; $t_{R}$ = 7.6 min (major), 9.9 min (minor). $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ (ppm) 7.32-7.28 (m, 1H), 7.24-
7.17 (m, 2H), 7.00-6.98 (m, 1H), 4.79-4.73 (m, 1H), 4.64 (d, \( J = 8.5 \) Hz, 1H), 2.12-1.92 (m, 2H), 1.68-1.46 (m, 2H), 1.02 (t, \( J = 7.4 \) Hz, 3H); \(^{13}\)C NMR (100 MHz, CDCl\(_3\)) \( \delta \) (ppm) 151.15, 129.30, 126.26, 125.29, 122.80, 118.81, 56.98, 35.87, 18.37, 13.59.

(S)-4,6-dimethyl-3,4-dihydrobenzo[e][1,2,3]oxathiazine 2,2-dioxide \( 2p \)

White crystalline solid; >99% conv., 99% yield, >99% ee; \( \alpha \)\(^{20} \) = -60.6 (c = 0.5, CHCl\(_3\)); The enantiomeric excess was determined by HPLC on Chiralcel OD-H column, hexane: isopropanol = 80:20; flow rate = 0.8 mL/min; UV detection at 210 nm; \( t_R \) = 8.1 min (major), 10.2 min (minor). \(^1\)H NMR (400 MHz, CDCl\(_3\)) \( \delta \) (ppm) 7.11-7.09 (m, 1H), 7.00 (s, 1H), 6.89 (d, \( J = 8.4 \) Hz, 1H), 4.90-4.83 (m, 1H), 4.48 (dd, \( J = 9.0 \) Hz, 1H), 2.34 (s, 3H), 1.70 (d, \( J = 6.9 \) Hz, 3H); \(^{13}\)C NMR (100 MHz, CDCl\(_3\)) \( \delta \) (ppm) 148.79, 135.14, 130.05, 126.48, 123.05, 118.44, 52.99, 20.84, 20.18. The characterization data of compound \( 2p \) is in accordance with the reported data in the literature.\(^5\)

(S)-7-methoxy-4-methyl-3,4-dihydrobenzo[e][1,2,3]oxathiazine 2,2-dioxide \( 2q \)

White crystalline solid; >99% conv., 99% yield, >99% ee; \( \alpha \)\(^{20} \) = -74.0 (c = 0.5, CHCl\(_3\)); The enantiomeric excess was determined by HPLC on Chiralcel OD-H column, hexane: isopropanol = 80:20; flow rate = 0.8 mL/min; UV detection at 210 nm; \( t_R \) = 10.3 min (major), 12.5 min (minor). \(^1\)H NMR (400 MHz, CDCl\(_3\)) \( \delta \) (ppm) 7.10 (dd, \( J = 8.7, 0.5 \) Hz, 1H), 6.75 (dd, \( J = 8.7, 2.6 \) Hz, 1H), 6.51 (d, \( J = 2.6 \) Hz, 1H), 4.88-4.80 (m, 1H), 4.57 (d, \( J = 9.3 \) Hz, 1H), 3.79 (s, 3H), 1.68 (d, \( J = 6.9 \) Hz, 3H); \(^{13}\)C NMR (100 MHz, CDCl\(_3\)) \( \delta \) (ppm) 160.19, 151.59, 126.80, 115.31, 112.10, 103.39, 55.59, 52.57, 20.18. HRMS calculated for C\(_9\)H\(_{11}\)NNaO\(_4\)S\(^+\) [(M+Na\(^+\)] = 252.0301, found: 252.0290.
(S)-6-fluoro-4-methyl-3,4-dihydrobenzo[e][1,2,3]oxathiazine 2,2-dioxide 2r

White crystalline solid; >99% conv., 98% yield, >99% ee; [α]D²⁰ = -77.8 (c = 0.5, CHCl₃); The enantiomeric excess was determined by HPLC on Chiralpak AS-H column, hexane: isopropanol = 80:20; flow rate = 0.8 mL/min; UV detection at 215 nm; tR = 18.6 min (major), 21.5 min (minor). ¹H NMR (400 MHz, CDCl₃) δ (ppm) 7.04-6.91 (m, 3H), 4.90-4.83 (m, 1H), 4.72 (d, J = 8.2 Hz, 1H), 1.70 (d, J = 6.9 Hz, 3H); ¹³C NMR (100 MHz, CDCl₃) δ (ppm) 159.33 (d, J = 24.4 Hz), 146.69 (d, J = 3.0 Hz), 125.06 (d, J = 7.0 Hz), 120.20 (d, J = 8.0 Hz), 116.43 (d, J = 23.0 Hz), 112.93 (d, J = 25.0 Hz), 52.83 (d, J = 2.0 Hz), 19.94. The characterization data of compound 2r is in accordance with the reported data in the literature. [⁵]

(S)-7-methoxy-4-phenyl-3,4-dihydrobenzo[e][1,2,3]oxathiazine 2,2-dioxide 2s [⁹]

White crystalline solid; >99% conv., 98% yield, 98% ee; [α]D²⁰ = -33.5 (c = 0.6, CHCl₃); The enantiomeric excess was determined by HPLC on Chiralpak AD-H column, hexane: isopropanol = 80:20; flow rate = 0.8 mL/min; UV detection at 215 nm; tR = 15.8 min (minor), 18.8 min (major). ¹H NMR (400 MHz, CDCl₃) δ (ppm) 7.44-7.40 (m, 3H), 7.36-7.32 (m, 2H), 6.71-6.65 (m, 2H), 6.57 (d, J = 2.4 Hz, 1H), 5.83 (s, 1H), 4.78 (s, 1H), 3.79 (s, 3H); ¹³C NMR (100 MHz, CDCl₃) δ (ppm) 160.36, 152.14, 137.99, 129.50, 129.39, 129.15, 128.71, 113.69, 112.18, 103.34, 61.52, 55.60. The characterization data of compound 2s is in accordance with the reported data in the literature. [⁵]
(-)-ethyl 5-methyl-2,3-dihydrobenzo[d]isothiazole-3-carboxylate 1,1-dioxide 2t

White crystalline solid; 97% conv., 95% yield, 95% ee; $[\alpha]_D^{20} = -8.0$ (c = 1.2, CHCl$_3$); The enantiomeric excess was determined by HPLC on Chiralpak AD-H column, hexane: isopropanol = 90:10; flow rate = 1.0 mL/min; UV detection at 220 nm; t$_R$ = 36.3 min (minor), 42.0 min (major). $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ (ppm) 7.68 (d, J = 8.0 Hz, 1H), 7.47 (s, 1H), 7.40 (d, J = 8.0 Hz, 1H), 5.45 (brs, 1H), 5.20 (s, 1H), 4.38 (q, J = 7.1 Hz, 2H), 2.48 (s, 3H), 1.38 (t, J = 7.2 Hz, 3H). $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ (ppm) 167.93, 144.62, 134.16, 132.52, 131.46, 125.14, 121.34, 63.46, 58.17, 21.84, 14.16. HRMS calculated for C$_{11}$H$_{14}$NO$_4$S$^+$ [(M+H)$^+$] = 256.0638, found: 256.0632.

4. General procedure for the high TON experiment

A stock solution was made by mixing Ni(OAc)$_2$ with N-methylation of (S, S)-Ph-BPE in a 1:1.1 molar ratio in HFIP at room temperature for 12 h in an argon-filled glovebox. An aliquot of the catalyst solution (0.008 mmol) was transferred by syringe into a hydrogenated vial charged with 1m (4.0 mmol, 788.8 mg) in anhydrous HFIP (3 mL). The cup was subsequently transferred into an autoclave into which hydrogen gas was charged. The reaction was then stirred under H$_2$ (50 atm) at 50 °C oil bath for 12 h. After completed, the hydrogen gas was released slowly and carefully. The product 2m was obtained by a column of silica gel (petroleum ether/ethyl acetate = 10:1-4/1).

5. Reduction of cyclic N-sulfonyl amino acid derivation 2b
To a solution of the cyclic N-sulfonyl amino acid derivation product 2b (0.5 mmol) in 3mL THF at room temperature was added LiAlH₄ (1.0 M in THF, 3 mL, 3 mmol) dropwise over 2 min. The mixture was stirred at room temperature for 3h, and then to 0 °C with an ice bath. The reaction was quenched carefully with EtOAc (5 mL) followed by EtOH (5 mL). The solution was concentrated in vacuo. Purification of the residue by column chromatography (petroleum ether:EtOAc = 2:1 to 1:1) gave the product 3 as light yellow solid (101 mg, 83% yield).[10] ^1H NMR (400 MHz, CD₃OD) δ (ppm) 7.30 (d, J = 8.7 Hz, 1H), 6.79 (dd, J = 8.7, 2.6 Hz, 1H), 6.57 (d, J = 2.6 Hz, 1H), 4.61 (dd, J = 6.7, 4.8 Hz, 1H), 4.05 (dd, J = 11.6, 7.0 Hz, 1H), 3.93 (dd, J = 11.6, 4.6 Hz, 1H), 3.79 (s, 3H). ^13C NMR (100 MHz, CD₃OD) δ (ppm) 161.78, 153.91, 128.92, 113.30, 112.59, 104.40, 64.20, 59.69, 56.09. The enantiomeric excess was determined by HPLC on Chiralpak AD-H column, hexane: isopropanol = 90:10; flow rate = 1.0 mL/min; UV detection at 210 nm; tᵣ = 25.9 min (major), 29.9 min (minor), 92% ee, which can be improved to >99% ee through simple recrystallization in CH₂Cl₂ and hexane. [α]D^20 = -34.6 (c = 1.0, CH₃OH), HRMS calculated for C₉H₁₁NNaO₅S⁺ [(M+Na)⁺] = 268.0250, found: 268.0240.

6. General procedure for nonlinear effect experiment

The experiments for the investigation of the nonlinear effect were conducted. The asymmetric hydrogenations of substrates 1a, 1m were performed in the presence of ligand (S, S)-Ph-BPE with different ee values (Table S1, Table S2). As shown in Figure S1, a positive nonlinear effect was observed, which may arise in principle by the auto association of these initial chiral species. As shown in Figure S2, no nonlinear effect was observed in this Ni-catalyzed asymmetric hydrogenation, which displayed that it should be no catalyst self-aggregation or ligand-substrate agglomeration in this catalytic system.
Table S1. Nonlinear effect for Rh/Ph-BPE-catalyzed asymmetric hydrogenation of 1a.

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<th>conv. (%)</th>
<th>ee (%)</th>
</tr>
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<td>8</td>
<td>100</td>
<td>&gt;99</td>
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</table>

Figure S1. Nonlinear effect of the hydrogenation of substrate 1a using ligand (S, S)-Ph-BPE with different ee values

Table S2. Nonlinear effect for Rh/Ph-BPE-catalyzed asymmetric hydrogenation of 1m.
<table>
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<th>conv. (%)</th>
<th>ee (%)</th>
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<td>&gt;99</td>
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<tr>
<td>8</td>
<td>100</td>
<td>&gt;99</td>
<td>&gt;99</td>
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Figure S2. Linear effect of the hydrogenation of substrate 1m using ligand (S, S)-Ph-BPE with different ee values

7. Deuterium-labeling experiments

The Ni-catalyzed asymmetric hydrogenation of 1a was conducted under 50 atm D₂. The deuterium atom was found to solely add at the benzyl position and partly at nitrogen atom for product 2a-D (Scheme S1a). In addition, the asymmetric hydrogenation was conducted in the presence of H₂ and (CF₃)₂CDOD, the deuterium atom was partly
incorporated at nitrogen atom to generate product 2a-D' (Scheme S1b). These results demonstrated that this hydrogenation catalytic process should be in accordance with the proposed mechanism reported by Chirik with a large extent. Meanwhile, the cyclic N-sulfonyl ketimine 1m was hydrogenated in the presence of D2. Interestingly, the deuterium atoms were fully added both at the benzyl position and at nitrogen atom for substrate 1m, which is quite different from substrate 1a (Scheme S1c). The later experiments shown that H/D scrambling at nitrogen atom of the product 2m is not fast (Scheme S1d). Therefore, deuterium-labeling experiment results exhibited that the cyclic N-sulfonyl ketimino ester 1a and cyclic N-sulfonyl ketimine 1m may go through different catalytic mechanisms.

Scheme S1. Deuterium-labeling experiments.
8. Reference


(7) The ee value of α-monosubstituted α-amino ester hydrogenation product could go through a little decrease after it was placed for a long time.


(9) The X-ray crystal data of compound 2s has been deposited with the Cambridge Crystallographic Data Centre as supplementary publication no. CCDC 1978861. Copies of the data can be obtained, free of charge, on application to the CCDC, 12 Union Road, Cambridge CB21EZ, UK [Fax: +44 (1223)336033 or E-mail: deposit@ccdc.cam.ac.uk].

(10) The X-ray crystal data of compound 3 has been deposited with the Cambridge Crystallographic Data Centre as supplementary publication no. CCDC 1978862. The absolute configuration of hydrogenation product 2b can be determined (R) by the deduction from compound 3.
9. NMR spectra
10. HPLC spectra

HPLC of racemic-2a
HPLC of 2a

Data File D:\DATA\LGT\LOT-9-20\LOT-9-20-2 (2) 2019-12-07 11-13-42\004-0201.3
Sample Name: LOT-9-20-4

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Location : Vial 4  
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Inj : 1  
Inj Volume : 5.000 µl  

Acq. Method : D:\DATA\LGT\LOT-9-20\LOT-9-20-2 (2) 2019-12-07 11-13-42\VWD-AD (1-2)-90-10-1ML-8UL-CORR-2MIN.N  
Last changed : 10/20/2019 5:30:16 PM  
Analysis Method : D:\DATA\LGT\LOT-9-20\LOT-9-20-2 (2) 2019-12-07 11-13-42\VWD-AD (1-2)-90-10-1ML-4UL-210XX-10MIN.X  
Last changed : 3/22/2019 4:40:41 PM  

Additional Info : Peak(s) manually integrated

Area Percent Report

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Dilution : 1.0000
Use Multiplier & Dilution Factor with ISTDs

Signal 1: Wavelength=210 nm

Peak RetTime Sig Type Area Height Area
# [min] [µAmin] [µA] %
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1 16.090 1 HM 154.24000 6.61234 2.1021
2 18.038 1 BB 7183.61758 259.13147 97.8579

Totals : 7337.76558 265.74380

Instrument 1 3/22/2019 4:40:43 PM
HPLC of racemic-2b

---

Acq. Operator : 4
Acq. Instrument : Instrument 2
Injection Date : 1/16/2019 12:40:33 PM
Location : Vial 3
Inj. : 1
Inj. Volume : 5.000 μl

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Last changed : 12/25/2018 3:53:04 PM
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(modified after loading)

Additional Info: Peak(s) manually integrated

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Area Percent Report

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Sorted By : Signal
Multiplier : 1.0000
Dilution : 1.0000
Use Multiplier & Dilution Factor with ISTDs

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Signal: DAB1 C, Sig=210.4 Per OFF

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---|---|---|---|---|---|---
| min | min | [M+H] | [M+H] |
| 1 | 12.832 | 0.5625 | 7001.77832 | 171.39932 | 49.9225 |
| 2 | 23.333 | 0.6840 | 7031.87593 | 130.21284 | 50.1072 |

Totals : 1.40337e4 301.61217

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Instrument 2 3/22/2019 9:04:44 PM

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HPLC of 2b

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Sample Name: LOT-3-61-3

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Acq. Instrument : Instrument 2 Location : Vial 4
Injection Date : 1/16/2019 11:17:36 PM Inj : 1
Injection Volume : 5.000 μl
Acq. Method : D:\DATA\LOT\LOT-3-61\LOT-3-61 2019-01-16 11-24-30\PID-SP(1-2)-SS-15-1ML-SUL-ALL-00XIN.M
Last changed : 12/25/2018 3:53:04 PM
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Last changed : 3/22/2019 9:00:00 PM
(modified after loading)
Additional Info : Peak(s) manually integrated

Area Percent Report

Sorted By : Signal
Multiplier : 1.0000
Dilution : 1.0000
Use Multiplier & Dilution Factor with ISTDs

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Instrument 2 3/22/2019 9:09:06 PM
HPLC of racemic-2c

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Sample Name: 187-3-45-0

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Acq. Operator: Seq. Line: 10
Acq. Instrument: Instrument 2 Location: Vial 1
Injection Date: 5/22/2019 0:08:37 PM Inj: 1
Inj Volume: 5.000 µl

Acq. Method: D:\DATA\GUAN TQING\LJ-113-1\LJ-113-1 2019-03-23 12-44-07\DAD-02(1-2)-05-15 -INL-50-ALL-25MIN.N
Last changed: 12/25/2018 3:51:39 PM
Analysis Method: D:\METHOD\GUAN TQING\L02T-1\VWD-AS(1-5)-95-5-5.5X1-SUL-25NM-5MIN.N
Last changed: 4/19/2019 9:14:50 PM (modified after loading)

Additional Info: Peak(s) manually integrated

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Area Percent Report

Sorted By: Signal
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Dilution: 1.00000
Use Multiplier & Dilution factor with ISTDs

Signal 1: DAD C, Sng=210.4 Ref=off

Peak RetTime Type Width Area Height Area
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2 20.595 BB 0.5462 2944.99316 51.41059 49.6830

Totals: 4719.71690 120.12792

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Instrument 1 4/10/2019 9:14:55 PM
HPLC of 2c

Sample Name: 667-3-124-1

Data File: D:\DATA\HPLC\HPLC-DATA-5\HPLC-20190301-1 2019-03-31 09-55-57\012-2101.D

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Injection Date: 3/31/2019 10:01:45 PM
Inj: 1
Injection Volume: 5.000 µl

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Last changed: 4/9/2019 4:32:00 PM

Additional Info: Peak(s) manually integrated

Area Percent Report

Sorted By: Signal
Multiplier: 1.0000
Dilution: 1.0000
Use Multiplier & Dilution Factor with ISTDs

Signal 1: DALI C, Sag=210.4 Ref=off

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Instrument 2 4/9/2019 4:33:56 PM

Page 1 of 2
HPLC of racemic-2d

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Acq. Instrument : Instrument 2 Location : Vial 1
Injection Date : 4/16/2019 12:51:33 AM Inj : 1
Injection Volume : 5.000 μl

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Last changed : 12/25/2018 9:31:39 PM
Analysis Method : D:\METHOD\GUAM TOXINS\LONGTOX\DAD-AD (1-2) - 05-5-1ML-SUL-ALL-05XIN.M
Last changed : 5/22/2019 9:01:32 PM [modified after loading]

Additional Info : Peak[s] manually integrated

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Area Percent Report

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Sorted By : Signal
Multiplier : 1.00000
Dilution : 1.00000
Use Multiplier & Dilution Factor with ISTDs

Signal 1: 2447 C, Sig=210.4 Ref=off

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HPLC of 2d

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Sample Name: LOT-3-61-1

Acq. Operator :            Seq. Line : 3
Acq. Instrument : Instrument 2          Location : Vial 2
Injection Date : 1/16/2019 12:17:33 PM     Inj. : 1
              : Lot Volume 1 5.000 µl
Acq. Method : D:\[DATA\LOT\LOT-3-61\LOT-3-61 2019-01-16 11-24-30\]DAD-02 (1-2)-05-15-1ML-SUL
                                   -ALL-05MIN.M
Last changed : 12/25/2018 3:51:39 PM
Analysis Method : D:\[METHOD\GOOD TUNING\GOODTUNING\DAD-AD (1-2) -05-5-1ML-SUL -ALL-05MIN.M
Last changed : 3/22/2019 0:57:03 PM
[modified after loading]

Additional Info : Peak(s) manually integrated

Area Percent Report

Sorted By : Signal
Multiplier : 1.0000
Dilution : 1.0000
Use Multiplier & Dilution Factor with ISTDs

Signal 1: DAD C, Sng=210.4 Ref-off

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Totals : 1.20611=4 491.59988

Instrument 2 3/22/2019 8:59:00 PM
HPLC of racemic-2e

Data File D:\DATA\LSL\LSL-0-194;LSL-0-194-1 2019-01-15 10-09-55\011-1101.3
Sample Name: LSL-0-33-3

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Seq. Line : 11
Acq. Instrument : Instrument 1
Location : Vial 11
Injection Date : 1/15/2019 4:10:23 PM
Inj : 1
Inj Volume : 5.000 µl

Acq. Method : D:\DATA\LSL\LSL-0-194;LSL-0-194-1 2019-01-15 10-09-55\VWD-AD (1-2)-55-5-IKL-SUL-210HR-30MIN.M
Last changed : 1/19/2019 8:07:06 AM
Analysis Method : D:\METHOD\QUAN_TUVINO\LONGTUR\DAD-AD (1-2)-55-5-IKL-SUL-ALL-0XIN.M
Last changed : 3/22/2019 9:40:32 PM
(modified after loading)

Additional Info : Peak(s) manually integrated

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Area Percent Report
===============================================================================

Sorted By : Signal
Multiplier : 1.0000
Dilution : 1.0000

Use Multiplier & Dilution factor with ISTDs

Signal at Wavelength=210 nm

Signal at Wavelength=210 nm

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Instrument 2 3/22/2019 8:43:37 PM
HPLC of 2e

Data File D:\DATA\L2L\L2L-0-1944L2L-0-194-1 2019-01-15 10-09-55\12-1201.3
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Acq. Instrument : Instrument 1 Location : Vial 12
Injection Date : 1/15/2019 4:41:15 PM Inj : 1
Inj Volume : 5.000 µl
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Last changed : 1/29/2018 8:07:06 AM
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Last changed : 3/22/2019 8:14:37 PM
(modified after loading)
Additional Info : Peak(s) manually integrated

Area Percent Report

Sorted By : Signal
Multiplier : 1.0000
Dilution : 1.0000
Use Multiplier & Dilution Factor with ISTDs

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Instrument 2 3/22/2019 8:14:43 PM
HPLC of racemic-2f

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Last changed: 12/19/2018 8:25:32 AM
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Additional Info: Peaks(s) manually integrated

Area Percent Report

Sorted By: Signal
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Use Multiplier & Dilution Factor with ISTDs

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|-----|-------|--------|----------|----------------|
| 1   | 33.523 BB  0.7515 1.07503e-4  216.92998  49.9014 |
| 2   | 30.222 BB  0.6601 1.07503e-4  190.45396  40.0986 |

Totals: 2.1543e-4 407.39393

Instrument 1 4/10/2019 9:19:06 PM

Page 1 of 2
HPLC of 2f

Data File: D:\DATA\LSL\LSL-0-194;LSL-0-194-1 2019-01-15 10-09-55\004-1401.3
Sample Name: LSY-3-59-3

Acq. Operator: Seq. Line: 14
Acq. Instrument: Instrument 1 Location: Vial 4
Injection Date: 1/25/2019 6:06:03 PM Inj.: 1
Injection Volume: 5.000 µl

Acq. Method: D:\DATA\LSL\LSL-3-194;LSL-3-194-1 2019-01-15 10-09-55\VWD-AD(1-2)-95-5-1NL-SUL-20OH-50XIN.M
Last changed: 12/19/2018 8:25:32 AM
Analysis Method: D:\METHOD\GUARD TUNING\LONGSTAD\AD-AD(1-2)-95-5-1NL-SUL-ALL-60XIN.M
Last changed: 3/22/2019 01:37:25 PM
[modified after loading]
Additional Info: Peak(s) manually integrated

---

Area Percent Report

<table>
<thead>
<tr>
<th>Sorted By</th>
<th>Signal</th>
</tr>
</thead>
<tbody>
<tr>
<td>Multiplier</td>
<td>1.0000</td>
</tr>
<tr>
<td>Dilution</td>
<td>1.0000</td>
</tr>
<tr>
<td>Use Multiplier &amp; Dilution Factor with ISTDs</td>
<td></td>
</tr>
</tbody>
</table>

Signal 1: Wavelength=210 nm

<table>
<thead>
<tr>
<th>Peak Ret Time</th>
<th>Width</th>
<th>Area</th>
<th>Height</th>
<th>Area</th>
</tr>
</thead>
<tbody>
<tr>
<td>[min]</td>
<td>[min]</td>
<td>[ÅÅÅÅ]</td>
<td>[ÅÅÅÅ]</td>
<td>%</td>
</tr>
<tr>
<td>----------------</td>
<td>-------</td>
<td>--------</td>
<td>--------</td>
<td>------</td>
</tr>
<tr>
<td>1 33.561 BB</td>
<td>0.7503</td>
<td>139.55948</td>
<td>2.56650</td>
<td>1.2558</td>
</tr>
<tr>
<td>2 38.128 BB</td>
<td>0.6997</td>
<td>6860.74219</td>
<td>119.9227</td>
<td>98.0142</td>
</tr>
</tbody>
</table>

Totals: 7027.29256 122.54407

---

Instrument 2 3/22/2019 8:37:34 PM

Page 1 of 2
HPLC of racemic-2g

Data File D:\DATA\LQT\LQT-0-111\LJ-113-1-IC 2019-03-23 19-25-51\081-0201.5
Sample Name: LQT-3-02-1

Acq. Operator : Seq. Line : 2
Acq. Instrument : Instrument 1 Location : Vial 1
Injection Date : 3/29/2019 7:37:41 PM Inj : 1
Injection Volume : 5.000 µl
Analysis Method : D:\DATA\LQT\LQT-0-111\LJ-113-1-IC 2019-03-23 19-25-51\VWD-AD (1-1)-90-10-1ML -SUL-210MM-8-MMX.M
Last changed : 10/20/2018 5:30:16 PM
Additional Info : Peak(s) manually integrated

Area Percent Report

Sorted By : Signal
Multiplier : 1.0000
Dilution : 1.0000
Use Multiplier & Dilution Factor with ISTDs

Signal 1: Wavelength: 210 nm

<table>
<thead>
<tr>
<th>Peak RetTime Type</th>
<th>Width</th>
<th>Area</th>
<th>Height</th>
<th>Area</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>[min]</td>
<td>[min]</td>
<td>[AA%]</td>
<td>[AA%]</td>
</tr>
<tr>
<td>--------------------</td>
<td>--------</td>
<td>--------</td>
<td>---------</td>
<td>--------</td>
</tr>
<tr>
<td>1</td>
<td>13.371</td>
<td>0.3563</td>
<td>1.2722104</td>
<td>583.92435</td>
</tr>
<tr>
<td>2</td>
<td>19.377</td>
<td>0.5229</td>
<td>1.20106e-4</td>
<td>365.70990</td>
</tr>
<tr>
<td>Totals</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>2.55407e-4</td>
<td>949.52527</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Instrument 1 4/10/2019 9:21:52 PM

Page 1 of 2
HPLC of 2g

Data File: D:\DATA\LOT\LOT-0-111\LOT-113-1-1C 2019-03-23 19-25-51\002-0301.3
Sample Name: LOT-3-111-4

Acq. Operator: Seq. Line: 3
Acq. Instrument: Instrument 1 Location: Vial 2
Injection Date: 3/23/2019 0:00:33 PM Inj: 1
Injection Volume: 5.000 µl

Acq. Method: D:\DATA\LOT\LOT-3-111\LOT-113-1-1C 2019-03-23 19-25-51\VWD-AD (1-2)-90-10-1ML-5UL-5MIN.R
Last changed: 10/20/2019 5:30:16 PM
Analysis Method: D:\DATA\LOT\LOT-3-111\LOT-113-1-1C 2019-03-23 19-25-51\VWD-AD (1-2)-99-1-1ML-5UL-10MIN.R
Last changed: 3/23/2019 9:03:52 PM
(modified after loading)

Additional Info: Peak(s) manually integrated

Area Percent Report

Sorted By: Signal
Multiplier: 1.0000
Dilution: 1.0000

Use Multiplier & Dilution Factor with ISTDs

Signal 1: Wavelength: 210 nm

Peak RetTime [min] Width [min] Area [A0^2*][10^5] Height [A0] [A0^2*] [%]

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>13.376</td>
<td>0.3417</td>
<td>197.93466</td>
<td>8.62595</td>
<td>2.5827</td>
</tr>
<tr>
<td>2</td>
<td>19.307</td>
<td>0.5317</td>
<td>7465.78009</td>
<td>208.82335</td>
<td>97.4173</td>
</tr>
</tbody>
</table>

Totals: 7663.72275 216.64840

Instrument 2 3/23/2019 9:04:03 PM

Page 1 of 2
HPLC of racemic-2h

Data File: D:\DATA\LOT\LOT-3-136\LOT-3-136 2019-04-14 17-09-50\001-0201.D
Sample Name: LOT-3-136

Acq. Operator: Seq. Line: 2
Acq. Instrument: Instrument 1 Location: Vial 1
Injection Date: 4/14/2019 5:21:39 PM Inj: 1
Injection Volume: 5.000 µl

Acq. Method: D:\DATA\LOT\LOT-3-136\LOT-3-136 2019-04-14 17-09-50\VWD-AD(1-2)-90-10-1XU-SUL-210HR-30MIN.3
Last changed: 12/16/2018 5:54:01 PM
Analysis Method: D:\METHOD\QUAN TOYOBO\LONGZHAO\DAO-00(1-5)-95-5-0.5XU-SUL-ALL-30MIN.3
Last changed: 4/14/2019 0:41:17 PM
(modified after loading)

Additional Info: Peak(s) manually integrated

Area Percent Report

Sorted By: Signal
Multiplier: 1.00000
Dilution: 1.00000
Use Multiplier & Dilution Factor with ISTDs

Signal 1: Wavelength=210 nm

Peak RetTime Type Width Area Height Area %
<table>
<thead>
<tr>
<th>#</th>
<th>[min]</th>
<th>[min]</th>
<th>[AUC unit]</th>
<th>[AUC%]</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>17.059</td>
<td>BF</td>
<td>0.0907</td>
<td>6550.87255</td>
</tr>
<tr>
<td>2</td>
<td>20.054</td>
<td>VB</td>
<td>1.0925</td>
<td>6953.93994</td>
</tr>
</tbody>
</table>

Totals: 1.34748e+4 182.13611

Instrument 1 4/14/2019 8:41:28 PM
HPLC of 2h

Data File D:\DATA\LOT-3-9-130316\LOT-3-9-130 2019-03-31 13:56:51\001.D
Sample Name: LOT-3-9-130-1

Acq. Operator : Seq. Line : 3
Acq. Instrument : Instrument 1 Location : Vial 62
Injection Date : 3/31/2019 2:39:33 PM Inj : 1
Inj Volume : 1.000 μl
Acq. Method : D:\DATA\LOT-3-9-130316\LOT-3-9-130 2019-03-31 13:56:51\VWD-AD (1-2) - 90-10-01L-50-120N-30MIN.H
Last changed : 3/24/2019 1:36:07 PM
Analysis Method : D:\METHOD\TARGET\VDOC\AD (1-2)-95-5-1NL-5UL-210NK-20MIN.H
Last changed : 4/4/2019 8:40:30 AM
(modified after loading)
Additional Info : Peak(s) manually integrated

---

Area Percent Report

Sorted By : Signal
Multiplier : 1.0000
Dilution : 1.0000
Use Multiplier & Dilution Factor with ISTDs

Signal 1: UV/Vis A, Wavelengths:210 nm

Peak RetTime Type Width Area Height Area
[μs] [min] [μA] [μA] [%]

1 15.555 RH 0.4424 506.1126 19.0655 5.0282
2 19.344 BB 0.5176 9559.4072 276.3511 94.9718

Totals : 1.00655e4 295.41700

Instrument 1 4/4/2019 8:40:33 AM
HPLC of 2i

Data File: D:\DATA\LOT-9-129\LOT-9-123 2019-03-31 10-56-31\064-0501.D
Sample Name: LOT-3-123-3

<table>
<thead>
<tr>
<th>Acq. Operator</th>
<th>Seq. Line</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>5</td>
</tr>
<tr>
<td>Acq. Instrument</td>
<td>Location</td>
</tr>
<tr>
<td>Instrument 1</td>
<td>1 Vial 64</td>
</tr>
<tr>
<td>Injection Date</td>
<td>5/31/2019 3:52:21 PM</td>
</tr>
<tr>
<td></td>
<td>Inj: 1</td>
</tr>
<tr>
<td></td>
<td>Inj Volume: 5.000 μl</td>
</tr>
<tr>
<td>Acq. Method</td>
<td>D:\DATA\LOT-9-123\LOT-9-123 2019-03-31 13-56-31\VVD-AD(1-2)-90-10-1XL-SUL-220IN-40MIN.X</td>
</tr>
<tr>
<td>Last changed</td>
<td>6/14/2018 10:02:02 AM</td>
</tr>
<tr>
<td>Analysis Method</td>
<td>D:\METHOD\TABO USIM\VVD-1C-(1-6)-90-10-1XL-SUL-220IN-60MIN.X</td>
</tr>
<tr>
<td>Last changed</td>
<td>4/20/2019 10:27:33 AM</td>
</tr>
</tbody>
</table>

Additional Info: Peak(s) manually integrated

![HPLC Chart]

<table>
<thead>
<tr>
<th>Wavelength</th>
<th>Area %</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>56.96</td>
</tr>
</tbody>
</table>

Area Percent Report

<table>
<thead>
<tr>
<th>Sorted By</th>
<th>Multiplier</th>
<th>Dilution</th>
</tr>
</thead>
<tbody>
<tr>
<td>Signal</td>
<td>1.0000</td>
<td>1.0000</td>
</tr>
</tbody>
</table>

Use Multiplier & Dilution Factor with ISTDs

Signal 1: Wavelength=220 nm

<table>
<thead>
<tr>
<th>Peak Refine Type</th>
<th>Width</th>
<th>Area</th>
<th>Height</th>
<th>Area</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>μm</td>
<td>[μm]</td>
<td>[μA²]</td>
<td>[μA²]</td>
</tr>
<tr>
<td>------------------</td>
<td>-------</td>
<td>------</td>
<td>--------</td>
<td>------</td>
</tr>
<tr>
<td></td>
<td>22.001</td>
<td>0.7823</td>
<td>6.78273</td>
<td>1212.39383</td>
</tr>
<tr>
<td></td>
<td>32.125</td>
<td>0.0954</td>
<td>1.842704</td>
<td>34.29894</td>
</tr>
</tbody>
</table>

Totals: 5.96700=4 1247.23527

Instrument 1 4/20/2019 10:27:07 AM

Page 1 of 2
HPLC of racemic-2j

Data File D:\[DATA]\LOT\LOT-3-124\LOT-3-124 2019-04-01 00-51-21\081-1201.D
Sample Name: LOT-3-08-3

Acq. Operator: 
Seq. Line: 12
Acq. Instrument: Instrument 2
Location: Vial 81
Injection Date: 4/2/2019 1:21:32 PM
Inject: 1
Inj Volume: 5.000 µl
Acq. Method: D:\[DATA]\LOT\LOT-3-124\LOT-3-124 2019-04-01 00-51-21\DA0-00(1-2)-00-20.1xL-5UL-ALL-50MIN.N
Last changed: 2/24/2019 9:08:52 PM
Analysis Method: D:\[DATA]\LOT\LOT-3-124\LOT-3-124 2019-04-01 00-51-21\DA0-00(1-2)-00-20.1xL-20L-210MIN-10MIN.N
Last changed: 4/10/2019 9:42:39 PM
(modified after loading)
Additional Info: Peak(s) manually integrated

Area Percent Report

Sorted By: Signal
Multiplier: 1.0000
Dilution: 1.0000
Use Multiplier & Dilution Factor with ISTDs

Signal 1: DAD C, Sng=210.4 Ref=off

<table>
<thead>
<tr>
<th>Peak RetType</th>
<th>Width</th>
<th>Area</th>
<th>Height</th>
<th>Area</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>[min]</td>
<td>[min]</td>
<td>[µAµs]</td>
<td>[µA]</td>
</tr>
<tr>
<td>-------------</td>
<td>-------</td>
<td>-------</td>
<td>--------</td>
<td>--------</td>
</tr>
<tr>
<td>1</td>
<td>14.678</td>
<td>0.6368</td>
<td>1.010968</td>
<td>225.54677</td>
</tr>
<tr>
<td>2</td>
<td>34.701</td>
<td>0.9741</td>
<td>9812.12793</td>
<td>119.23689</td>
</tr>
</tbody>
</table>

Totals: 1.99167x4 344.73368

HPLC of 2j

Data File D:\DATA\LOT\LOT-3-124\LOT-3-124 2019-04-01 00-51-21\002-1301.D
Sample Name: LOT-3-124-3

-----------------------------------------------------------------------------
Acq. Instrument : Instrument 2 Location : Vial 82
Injection Date : 4/1/2019 2:12:32 PM Inj. : 1
Injection Volume : 5.000 µl
Acq. Method : D:\DATA\LOT\LOT-3-124\LOT-3-124 2019-04-01 09-51-21\DA0-05(1-2)-00-20-1ML-210H-10ININ.M
Last changed : 2/24/2019 9:08:02 PM
Analysis Method : D:\METHOD\LOT\DA0-05(1-2)-95-15-1.0ML-210H-210HIN-10ININ.M
Last changed : 4/10/2019 9:46:59 PM
(modified after loading)
Additional Info : Peak(s) manually integrated

Area % Report

Signal : 10000
Multiplier : 1.0000
Solution : 1.0000
Use Multiplier & Dilution factor with ISTDs

Signal 1: D4H1 C, Sig=210.4 Ref=off

| Peak RetTime Type Width Area Height Area % |
|----------------------------------------|---------|---------|---------|--------|
| 1 14.682 Min 0.6353 1.0936224 241.59565 27.9010 |
| 2 35.269 Min 1.4704 245.89059 2.78713 2.1990 |
| Totals : 1.1821e4 245.69276 |

Instrument 2 4/10/2019 9:47:05 PM

Page 1 of 2
HPLC of racemic-2k

Data File D:\DATA\LOT\LOT-3-124\LOT-3-124 2019-03-31 16-43-50\061-0201.D
Sample Name: LOT-3-33-1

Acq. Operator : Seq. Line : 2
Acq. Instrument : Instrument 1 Location : Vial 61
Injection Date : 3/31/2019 4:55:49 PM Inj : 1
Injection Volume : 5.000 µl
Last changed : 3/31/2019 4:55:49 PM
Analysis Method : D:\METHOD\TARGET\VWD-AD (1-2) - 95-10-0.1 MLE SUL-215 MH-10 MIN.M
Last changed : 3/31/2019 4:55:49 AM
(modified after loading)

Additional Info : Peak(s) manually integrated

Area Percent Report

Sorted By : Signal
Multiplier : 1.0000
Dilution : 1.0000
Use Multiplier & Dilution Factor with ISTDs

Signal 1: Wavelength=215 nm

Peak Ret Time Type Width Area Height Area %
1 22.065 BB 0.4946 7848.00344 230.05124 49.9354
2 24.437 BB 0.5603 7860.24551 210.87773 50.0644

Totals : 157.9264 448.92937

Instrument 1 4/4/2019 8:35:40 AM
HPLC of 2k

Data File D:\[DATA\]LOT1,LOT9-0-124,LOT9-0-124 2019-03-31 16-49-55\062-0301.D
Sample Name: LOT9-0-124-3

==============================================================================
Acq. Operator :           seq. line : 3
Acq. Instrument : Instrument 1                      Location : Vial 62
Injection Date : 3/31/2019 5:26:39 PM             Inj. : 1
               Inj. Volume : 5.000 µl
Analysis Method : D:\[METHOD\]TARGET\TARGET\AD1-2-95-5-MIL-SUL-210X-10MIN.XML
Last changed : 3/26/2019 10:09:49 AM
(modified after loading)
Additional Info : Peak(s) manually integrated

==============================================================================

Area Percent Report

==============================================================================
Sorted By : Signal
Multiplier : 1.0000
Dilution : 1.0000
Use Multiplier & Dilution Factors with ISTDs

Signal 1: Wavelength=215 nm

<table>
<thead>
<tr>
<th>Peak Refline Type</th>
<th>Width</th>
<th>Area</th>
<th>Height</th>
<th>Area</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>[min]</td>
<td>[min]</td>
<td>[µµµµµ]</td>
<td>[µµµµµ]</td>
</tr>
<tr>
<td></td>
<td>-------</td>
<td>--------</td>
<td>---------</td>
<td>--------</td>
</tr>
<tr>
<td>1</td>
<td>22.067</td>
<td>0.4877</td>
<td>160.68512</td>
<td>5.40981</td>
</tr>
<tr>
<td>2</td>
<td>24.404</td>
<td>0.5658</td>
<td>9286.69359</td>
<td>245.81595</td>
</tr>
</tbody>
</table>

Totals : 9447.36971 251.30937

==============================================================================

Instrument 1 4/4/2019 8:37:37 AM

Page 1 of 2

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HPLC of racemic-2l

Data File D:\DATA\LOF\LOF-3-1ll\LOF-9-111 2019-03-23 11-57-13\003-0421.D
Sample Name: LOF-2-144

---

Acq. Operator  :  Seq. Line :  4
Acq. Instrument : Instrument 1  Location : Vial 3
Injection Date  :  3/23/2019 1:00:43 PM  Inj. :  1
Inj. Volume  :  5.000 μL
Acq. Method  :  D:\DATA\LOF\LOF-3-1ll\LOF-9-111 2019-03-23 11-57-13\VPE-AD (1-2) -95-5-1X-50UL-210MV-30MIN.N
Last changed  :  11/29/2018 8:07:06 AM
Analysis Method : D:\METHODS\VPE-AD (1-2) -95-5-1X-50UL-210MV-30MIN.N
Last changed  :  5/22/2019 9:35:42 PM
Additional Info : Peak(s) manually integrated

---

Area Percent Report

---

Sorted By  :  Signal
Multiplier  :  1.0000
Dilution  :  1.0000
Do not use Multiplier & Dilution Factor with ISUs

Signal 1: UV/Vis A, Wavelength=210 nm

Peak RetTime Type Width Area Height Area %
---|--------|--------|-------|--------|-------|
1  21.419 BY  0.5944 6270.41632 101.26111 40.5037
2  23.004 YE  0.5763 6657.29395 170.29326 51.4563

Totals : 1.29277e4 352.32437

---

93
HPLC of 21

Area Percent Report

Sorted By: Signal
Multiplier: 1.0000
Dilution: 1.0000
Do not use Multiplier & Dilution Factor with ISSTDs

Signal 1: Wavelength=210 nm

Peak RetTime Type Width Area Height Area %
# [min] [min] [nmol] [nmol] |-----------------------|
1 21.812 BE 0.4796 311.94592 10.01934 1.5795
2 23.376 BE 0.596 1.02577e+4 507.59311 98.3201

Totals: 1.85697e+4 517.60015

Instrument 1 3/23/2019 3:01:13 PM
HPLC of racemic-2m

Data File D:\DATA\GUAN YUNDONG\L7-114-3\L7-114-1 2019-03-25 16-59-37\041-0301.0
Sample Name: L07-3-109-13

====================================================================================================

Acq. Operator : Seq. Line : 3
Acq. Instrument : Instrument 1 Location : Vial 41
Injection Date : 3/25/2019 5:22:22 PM Inj. : 1
Injection Volume : 5.000 µL
Acq. Method : D:\DATA\GUAN YUNDONG\L7-114-3\L7-114-1 2019-03-25 16-59-37\VWD-AS(1-6)-AS-20
Last changed : 3/25/2019 4:53:34 PM
-0.20L-50L-210NM-30MIN.X
Analysis Method : D:\METHOD\LOY\VWD-AD\[1-2]-99-10-1ML-50-210NM-30MIN.X
Last changed : 3/25/2019 7:21:09 PM
(modified after loading)
Additional Info : Peaks(s) manually integrated

---

Area Percent Report
---

Sorted By : Signal
Multiplier : 1.0000
Dilution : 1.0000
Use Multiplier & Dilution Factor with LSTBs

Signal 1: Wavelength=215 nm

Peak RetTime Type Width Area Height Area %
# [min] [min] [µL/µs] [µL] [ ]
--- | | | | |
1 18.676 BB 0.5820 7044.6962 184.29355 50.9517
2 22.723 BB 0.6752 7021.71494 159.94495 49.0483

Totals : 1.40664 2 344.23755

---

Instrument 1 3/25/2019 7:21:15 PM
HPLC of 2m

Data File D:\DATA\GUAN YUQING\L9-114-3\L9-114-1 2019-03-25 16-59-37\042-0401.D
Sample Name: L07-3-114-1

<table>
<thead>
<tr>
<th>Acq. Operator</th>
<th>Seq. Line</th>
<th>Location</th>
<th>Inj Volume</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>4</td>
<td>5.000 µl</td>
</tr>
</tbody>
</table>

Injection Date: 3/25/2019 5:53:12 PM
Inj: 1

Acq. Method: D:\DATA\GUAN YUQING\L9-114-3\L9-114-1 2019-03-25 16-59-37\WAO-AS(1-5)-AS-20
-0.5ML-5UL-25MIN-30MIN.M
Last changed: 3/25/2019 4:53:34 PM

Analysis Method: D:\METHODS\GUAN YUQING\LUOEG1160\WAO-AS(1-5)-AS-5-0.5ML-5UL-25MIN.M
Last changed: 4/10/2019 9:25:51 AM

Additional Info: Peaks manually integrated

### Area Percent Report

<table>
<thead>
<tr>
<th>Sorted By</th>
<th>Multiplier</th>
<th>Dilution</th>
</tr>
</thead>
<tbody>
<tr>
<td>Signal</td>
<td>1.0000</td>
<td>1.0000</td>
</tr>
</tbody>
</table>

Use Multiplier & Dilution Factor with DSTDs

Signal 1: W=0.4 µm, Wavelength=215 nm

<table>
<thead>
<tr>
<th>Peak RetTime</th>
<th>Type</th>
<th>Width</th>
<th>Area</th>
<th>Height</th>
<th>Area</th>
</tr>
</thead>
<tbody>
<tr>
<td>#</td>
<td>[min]</td>
<td>[min]</td>
<td>[µm²]</td>
<td>[µm]</td>
<td>[µm²]</td>
</tr>
<tr>
<td>1</td>
<td>16.913</td>
<td>0.5760</td>
<td>5389.1704</td>
<td>142.83403</td>
<td>59.5691</td>
</tr>
<tr>
<td>2</td>
<td>22.953</td>
<td>0.6675</td>
<td>17.09194</td>
<td>4.67995e-1</td>
<td>0.3399</td>
</tr>
</tbody>
</table>

Totals: 5807.06293 143.35183

Instrument 1 4/10/2019 9:25:56 PM

Page 1 of 2
HPLC of racemic-2n

Data File: D:\DATA\XIC\XIC-DATA-6\XIC-20190524-1 2019-03-24 09-52-57\001-1201.D
Sample Name: 1201-1-109-14

Acq. Operator: Seq. Line: 12
Acq. Instrument: Instrument 2 Location: Vial 1
Injection Date: 5/24/2019 9:24 PM Inj.: 1
Injection Volume: 5.000 µl
Acq. Method: D:\DATA\XIC\XIC-DATA-6\XIC-20190524-1 2019-03-24 09-52-57\DAD-02 (1-2)-0.0-20-0.8ML-SUL-ALL-16MIN.R
Last changed: 5/24/2019 9:59:09 PM
Analysis Method: D:\DATA\XIC\XIC-DATA-6\XIC-20190524-1 2019-03-24 09-52-57\DAD-02 (1-2)-0.0-20-0.8ML-SUL-ALL-16MIN.R
Last changed: 5/24/2019 9:04:02 PM
Additional Info: Peak(s) manually integrated

Area Percent Report

Sorted By: Signal
Multiplier: 1.0000
Dilution: 1.0000
Use Multiplier & Dilution Factor with ISTDs

Signal 1: DAD C, Sig=210,4 Ref=off

<table>
<thead>
<tr>
<th>Peak</th>
<th>Ret Time</th>
<th>Width</th>
<th>Area</th>
<th>Height</th>
<th>Area</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>8.062</td>
<td>0.205</td>
<td>1.328</td>
<td>385</td>
<td>290.53</td>
</tr>
<tr>
<td>2</td>
<td>10.325</td>
<td>0.267</td>
<td>1.344</td>
<td>414</td>
<td>50.40</td>
</tr>
</tbody>
</table>

Totals: 2.66714-4 1732.59930

Instrument 2 3/24/2019 7:04:09 PM
HPLC of 2n

Data File: D:\DATA\HSC\HSC-DATA-\HSC-20190224-1 2019-03-24 09-52-57\002-1301.D
Sample Name: HSC-3-130-2

Acq. Operator : 
Seq. Line : 13
Acq. Instrument : Instrument 2
Location : Vial 2
Injection Date : 3/24/2019 6:42:22 PM
Inj : 1
Inj Volume : 5.000 μL

Acq. Method : D:\DATA\HSC\HSC-DATA-\HSC-20190224-1 2019-03-24 09-52-57\DAD-02(1-2)-00-20 -0.8ML-SUL-ALL-18MIN.R
Last changed : 3/24/2019 5:59:09 PM
Analysis Method : D:\METHOD\DAD-02(1-2)-80-30-0.8ML-SUL-ALL-18MIN.R
Last changed : 3/24/2019 7:06:49 PM
(modified after loading)

Additional Info : Peak(s) manually integrated

Area Percent Report

Sorted By : Signal
Multiplier : 1.0000
Dilution : 1.0000
Use Multiplier & Dilution Factor with ISTDs

Signal : DAD C, Sig=210,4 Ref=off

Peak RetTime Type Width Area Height Area %
1 8.079 BB 0.2054 6814.06541 653.51133 29.5475
2 10.394 BB 0.2001 40.06901 2.39420 0.4525

Totals : 6854.13541 655.89543

Instrument 2 3/24/2019 7:07:08 PM
HPLC of racemic-2o

Data File D:\DATA\AZC\AZC-DATA-4\AZC-20190325-1 2019-03-25 08-48-34\001-001.D
Sample Name: 207-3-109-10

=================================================================================================
Acq. Instrument : Instrument 2 Location : Vial 1
Injection Date : 3/25/2019 12:23:07 AM Inj. : 1
Injection Volume : 5.000 µL
Acq. Method : D:\DATA\AZC\AZC-DATA-4\AZC-20190325-1 2019-03-25 08-48-34\DA0-02 (1-2) -0-20 -0.065L-SUL-ALL-10MIN.R
Last changed : 3/24/2019 5:59:09 PM
Analysis Method : D:\HPLC\Library\DA0-02 (1-2) -0-20 -0.065L-SUL-ALL-10MIN.R
Last changed : 3/25/2019 2:21:22 PM
(modified after loading)
Additional Info : Peak(s) manually integrated

Area Percent Report
=================================================================================================
Sorted By : Signal
Multiplier : 1.0000
Dilution : 1.0000
Use Multiplier & Dilution Factor with ISTDs

Signal 1: DA01-C, Sig=210.4 Ref=off

<table>
<thead>
<tr>
<th>Peak Refine Type</th>
<th>Width</th>
<th>Area</th>
<th>Height</th>
<th>Area</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>7.638</td>
<td>0.0215</td>
<td>1.15563e4</td>
<td>878.95102</td>
</tr>
<tr>
<td>2</td>
<td>9.798</td>
<td>0.2624</td>
<td>1.16162e4</td>
<td>682.39942</td>
</tr>
</tbody>
</table>

Totals : 2.31815e4 1561.85102
HPLC of 2o

Data File D:\DATA\XEC\XEC-DATA-XEC-20190325-1 2019-03-25 08-40-14002-0701.D
Sample Name: J07-3-114-1

Acq. Operator : Seq. Line: 7
Acq. Instrument : Instrument 2 Location: Vial 2
Injection Date : 3/25/2019 11:40:07 AM Inj: 1
Inj Volume: 5.000 µl

Acq. Method : D:\DATA\XEC\XEC-DATA-XEC-20190325-1 2019-03-25 08-40-14002-0701.D
Last changed : 3/24/2019 5:59:09 PM
Analysis Method : D:\METHODS\DAT\DAD-02 [1-2] 80-20-0.5ml-SUL-ALL-15MIN.K
Last changed : 3/25/2019 2:21:22 PM

Additional Info: Peak(s) manually integrated

---

Area Percent Report

Sorted By: Signal
Multiplier: 1.0000
Dilution: 1.0000
Use Multiplier & Dilution Factor with ISTDs

Signal 1: DAT1 C, Sig=210.4 Ref=off

Peak RetTime Type Width Area Height Area %

<p>| | | | | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>7.647</td>
<td>BB</td>
<td>0.2008</td>
<td>9646.62307</td>
</tr>
<tr>
<td>2</td>
<td>9.654</td>
<td>BB</td>
<td>0.2507</td>
<td>92.60598</td>
</tr>
</tbody>
</table>

Totals: 9739.30805 741.26438

---

HPLC of racemic-2p

Data File D:\DATA\XXC\XXC-DATA-4\XXC-20190325-1 2019-03-25 00-48-34 000-001.D
Sample Name: 507-3-109-16

Acq. Operator : Seq. Line : 0
Acq. Instrument : Instrument 2 Location : Vial 3
Injection Date : 3/25/2019 12:57:04 AM Inj : 1
Inj Volume : 5.000 μL
Acq. Method : D:\\DATA\\XXC\\XXC-DATA-4\XXC-20190325-1 2019-03-25 00-48-34\\DAD-00 (1-2)-00-20-0.8NL-SUL-ALL-16MIN.R
Last changed : 3/24/2019 5:59:09 PM
Analysis Method : D:\\METHOD\\DAD-00 (1-2)-80-20-0.8NL-SUL-ALL-16MIN.R
Last changed : 3/25/2019 2:25:30 PM
[modified after loading]
Additional Info : Peak(s) manually integrated

---

Area Percent Report

---

Sorted By : Signal
Multiplier : 1.0000
Dilution : 1.0000
Use Multiplier & Dilution Factor with ISTDs

Signal 1: DAD C, Sig=210,4 Ref=off

Peak Ret Time Width Area Height Area
---|---|---|---|---|
1 8.107 BB 0.2130 7351.22340 519.22248 50.0162
2 10.180 VB 0.2695 7346.46325 417.05287 49.9838
Totals : 14897.68529 936.93529

---

HPLC of 2p

Data File D:\DATA\XZC\XZC-DATA-4\XZC-20190325-1 2019-03-25 08-48-14\Q04-0901.D
Sample Name: L07-3-114-3

Acq. Operator : 9
Acq. Instrument : Instrument 2
Inj. Date : 3/25/2019 12:14:05 PM
Inj. Volume : 5.000 µl
Inj. Location : Vial 4

Acq. Method : D:\DATA\XZC\XZC-DATA-4\XZC-20190325-1 2019-03-25 08-48-14\QAD-02 (1-2)-80-20
0.8ML-SUL-ALL-18MIN.M
Last changed : 3/24/2019 5:59:09 PM

Analysis Method : D:\HEX\QUOTE\QAD-02 (1-2)-80-20-0.8ML-SUL-ALL-18MIN.R
Last changed : 3/25/2019 2:26:51 PM

Additional Info : Peak(s) manually integrated

Area Percent Report

Sorted By : Signal
Multiplier : 1.0000
Dilution : 1.0000

Use Multiplier & Dilution Factor with ISTDs

Signal 1: DAD C, Sig=210.4 Ref=off

Peak RetTime Type Width Area Height Area %
---|--------|------|---------|--|
1. 8.095 BB 0.2208 8045.51755 689.40271 29.9621
2. 10.225 BB 0.1990 32.13776 1.99939 0.3979

Totals : 0077.65535 571.39564

Instrument 2 3/25/2019 2:26:56 PM
HPLC of racemic-2q

Data File: D:\DATA\XLC\XLC-DATA-01\XLC-20190325-2 2019-03-25 15-26-44\001-0401.D
Sample Name: 107-3-109-17

-------------------------------------------------------------------------------------------------------------------------------------
Acq. Operator:  
Seq. Line: 4  
Acq. Instrument: Instrument 2  
Location: Vial 1  
Injection Date: 5/25/2019 5:47:19 PM  
Inj: 1  
Inj Volume: 5.000 μl  
Acq. Method: D:\DATA\XLC\XLC-DATA-01\XLC-20190325-2 2019-03-25 15-26-44\DAD-02(1-2)-02-20-0.5ML-SUL-ALL-5MIN.R  
Last changed: 3/25/2019 4:55:29 PM  
Analysis Method: D:\DATA\XLC\XLC-DATA-01\XLC-20190325-2 2019-03-25 15-26-44\DAD-02(1-2)-02-20-0.5ML-SUL-ALL-5MIN.R  
(modified after loading)  
Additional Info: Peak(s) manually integrated

=================================================================================================================================
Area Percent Report
=================================================================================================================================

Sorted By:  
Multiplier: 1.0000  
Dilution: 1.0000  
Use Multiplier & Dilution Factor with ISTDs

Signal 1: DAD1 C, Sig=210,4 Ref-off

Peak RetTime Type Width Area Height Area
<table>
<thead>
<tr>
<th></th>
<th>[min]</th>
<th>[min]</th>
<th>[A00]*</th>
<th>[A00]</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>10.263</td>
<td>0.2893</td>
<td>9068.14453</td>
<td>488.29938</td>
<td>50.0247</td>
</tr>
<tr>
<td>2</td>
<td>12.543</td>
<td>0.3531</td>
<td>9059.17676</td>
<td>392.74035</td>
<td>49.9753</td>
</tr>
</tbody>
</table>

Totals: 1.61273e4 871.09443

Page 1 of 2
HPLC of 2q

---

Sorted By: Signal
Multiplier: 1.0000
Dilution: 1.0000

Use Multiplier & Dilution Factor with ISTDs

Signal: D171, Sig=210.4 Ref=off

Peak RetTime Type Width  Area  Height  Area
<p>| | | | | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>10.274</td>
<td>BB</td>
<td>0.2874</td>
<td>6082.30615</td>
</tr>
</tbody>
</table>

Totals:  
6082.30615  
323.48950

---

HPLC of racemic-2r

Data File: D:\DATA\LOT\LOT-9-117\LOT-9-117 2019-03-26 10-14-56\061-0201.D
Sample Name: LOT-9-110-10

=============================================================================================================================================================================================================================================================================================================================================================================================================================================================================================================================================================================================================================================

Acq. Operator : Seq. Line : 2
Acq. Instrument : Instrument 1 Location : Vial 61
Injection Date : 3/26/2019 10:44:11 AM Inj : 1
Inj. Method : D:\DATA\LOT\LOT-9-117\LOT-9-117 2019-03-26 10-14-56\VVD-AD(1-6)-00-20-0.0ML-40-215NM-30MIN.X
Inj. Volume : 5.000 µL
Last Changed : 3/25/2019 4:53:34 PM
Analysis Method : D:\METHOD\LOT\VVD-AD [1-2]-90-10-1ML-SU-210NM-30MIN.X
Last Changed : 3/26/2019 2:59:37 PM
[modified after loading]

Additional Info: Peak(s) manually integrated

=============================================================================================================================================================================================================================================================================================================================================================================================================================================================================================================================================================================================================================================

Area Percent Report
=============================================================================================================================================================================================================================================================================================================================================================================================================================================================================================================================================================================================================================================

Sorted By : Signal Multiplier : 1.0000
Multiplier : 1.0000
Use Multiplier & Dilution Factor with ISTDs

Signal 1: Wavelength=215 nm

Peak RetTime Width Area Height Area %
-----------------------------------------------|--------------------|------------------|-------------------|---|
1 18.642 BB 0.5935 5583.4541 140.94237 50.1437
2 21.408 BB 0.6646 5551.4459 128.60767 49.8563

Totals: 1.11449=4 272.55954
HPLC of 2r

Data File D:\DATA\LOT\LOT-0-117\LOT-0-117 2019-03-26 10-14-56\062-0001.D
Sample Name: LOT-0-117-1

Acq. Operator : Seq. Line : 3
Acq. Instrument : Instrument 1 Location : Vial 62
Injection Date : 5/26/2019 11:15:03 AM Inj : 1
Inj Volume : 5.000 µl
Acq. Method : D:\DATA\LOT\LOT-0-117\LOT-0-117 2019-03-26 10-14-56\VVD-A3(1-e)-00-20-0.2ML-SUL-210NM-30MIN.R
Last changed : 5/25/2019 4:53:34 PM
Analysis Method : D:\DATA\LOT\LOT-0-117\LOT-0-117 2019-03-26 10-14-56\VVD-A3(1-e)-00-20-0.2ML-SUL-210NM-30MIN.R
Last changed : 5/26/2019 11:15:03 AM
Additional Info : Peak(s) manually integrated

Area Percent Report

Sorted By : Signal Multiplier : 1.0000
Multiplier : 1.0000
Dilution : 1.0000
Use Multiplier & Dilution Factor with ISTDs

Signal 1: Wavelength=215 nm

| Peak RetTime Type Width Area Height Area |
|------------------|------|--------|--------|--------|
|                  | [min] | [min]  | [%AA]  | [%AA]  |
| 1 18.648 BB      | 0.5774 | 2926.65525 | 77.18631 | 29.6908 |
| 2 21.524 RR      | 0.5953 | 11.72973  | 3.28419e-1 | 0.3992 |

Totals : 2930.30583 77.51473

Instrument 1 4/10/2019 9:30:19 PM

Page 1 of 2
HPLC of racemic-2s

Data File: D:\DATA\GUAN_YUQING\LJ-110-1\LJ-110-1(2) 2019-03-27 15-50-33\033-0701.D
Sample Name: LJY-3-110-20

Acq. Operator: Seq. Line: 7
Acq. Instrument: Instrument 1 Location: Vial 63
Injection Date: 3/27/2019 6:44:49 PM Inj: 1
Injection Volume: 5.000 μl
Acq. Method: D:\DATA\GUAN_YUQING\LJ-110-1\LJ-110-1(2) 2019-03-27 15-50-33\VWD-AD(1-2)-80 -20-0.8NL-SU-215NM-30MIN.X
Last changed: 3/27/2019 4:27:29 PM
Analysis Method: D:\DATA\GUAN_YUQING\LJ-110-1\LJ-110-1(2) 2019-03-27 15-50-33\VWD-AD(1-2)-80 -20-0.8NL-SU-215NM-30MIN.X
Last changed: 3/27/2019 9:11:34 PM
[Modified after loading]
Additional Info: Peak(s) manually integrated

Area Percent Report

Sorted By: Signal
Multiplier: 1.00000
Dilution: 1.00000
Use Multiplier & Dilution Factor with STDs

Signal 1: Wavelengths=215 nm

<table>
<thead>
<tr>
<th>Peak RetTime</th>
<th>Width</th>
<th>Area</th>
<th>Height</th>
<th>Area</th>
</tr>
</thead>
<tbody>
<tr>
<td>16.122</td>
<td>0.3678</td>
<td>9806.69848</td>
<td>403.1875</td>
<td>50.1131</td>
</tr>
<tr>
<td>19.139</td>
<td>0.4359</td>
<td>9760.46399</td>
<td>340.05447</td>
<td>49.3019</td>
</tr>
</tbody>
</table>

Totals: 1.956726e4 743.24197

HPLC of 2s

Data File D:\DATA\GUAN TUPING\LF-119-1\LF-119-1\2) 2019-03-27 15:50-33\004-0801.D
Sample Name: LOT-3-119-3

======================================================================================================
Acq. Operator :  
Seq. Line : 0
Acq. Instrument : Instrument 1  
Location : Vial 64
Injection Date : 5/27/2019 7:15:41 PM  
Inj : 1
Acq. Method : D:\DATA\GUAN TUPING\LF-119-1\LF-119-1\2) 2019-03-27 15:50-33\VWD-AD(1-2)-80
-20-0.8ML-SU-215MN-30MIN.X  
Inj Volume : 5.000 µl
Last changed : 5/27/2019 7:15:41 PM
Analysis Method : D:\DATA\GUAN TUPING\LF-119-1\LF-119-1\2) 2019-03-27 15:50-33\VWD-AD(1-2)-80
-20-0.8ML-SU-215MN-30MIN.X  
Last changed : 5/27/2019 7:15:41 PM
Additional Info : Peak(s) manually integrated

======================================================================================================

Area Percent Report

======================================================================================================

Sorted By : Signal
Multiplier : 1.0000
Dilution : 1.0000
Use Multiplier & Dilution Factor with ISTDs

Signal 1: 250 A, Wavelength=215 nm

<table>
<thead>
<tr>
<th>Peak RetTime</th>
<th>Type</th>
<th>Width</th>
<th>Area</th>
<th>Height</th>
<th>Area</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>15.828</td>
<td>0.3637</td>
<td>261.75444</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>18.702</td>
<td>0.4447</td>
<td>2.01940e-4</td>
</tr>
</tbody>
</table>

Totals :    2.04558e-4 708.45117

======================================================================================================


Page 1 of 2
HPLC of racemic-2t

Data File: D:\DATA\LOT\LOT-3-169\LOT-3-169 2019-05-14 11-12-59\002-0301.D
Sample Name: LOT-3-169

Acq. Operator: seq. Line: 3
Acq. Instrument: Instrument 2
Injection Date: 5/14/2019 12:27:04 PM
Inj: 1
Injection Volume: 5.000 μL

Acq. Method: D:\DATA\LOT\LOT-3-169\LOT-3-169 2019-05-14 11-12-59\002-0301.D
Last changed: 5/14/2019 11:10:56 AM
Analysis Method: D:\DATA\LOT\LOT-3-169\LOT-3-169 2019-05-14 11-12-59\002-0301.D (Sequence Method)
Last changed: 5/16/2019 3:26:51 PM
(modified after loading)

Additional Info: Peak(s) manually integrated

Area Percent Report

Sorted By
Multiplier: 1.0000
Dilution: 1.0000
Use Multiplier & Dilution Factor with ISDBs

Signal 1: DAX 1 B, Sig-220, 4 Per-off

<table>
<thead>
<tr>
<th>Peak #</th>
<th>Peak Type</th>
<th>Width</th>
<th>Area</th>
<th>Height</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>BB</td>
<td>0.8904</td>
<td>415201</td>
<td>226.4792</td>
<td>50.1955</td>
</tr>
<tr>
<td>2</td>
<td>BB</td>
<td>1.0414</td>
<td>1.441504</td>
<td>188.55550</td>
<td>49.8045</td>
</tr>
</tbody>
</table>

Totals: 2.0942e4 415.19552
**HPLC of 2t**

Data File: D:\DATA\LOT\LOT-3-169\LOT-3-169 2019-05-14 11-12-59\001-0201.D
Sample Name: LOT-3-169-4

---

**Acq. Operator:**
**Seq. Line:** 2

**Acq. Instrument:** Instrument C
**Location:** Vial 1

**Injection Date:** 5/14/2019 12:26:04 AM
**Inj:** 1

**Injection Volume:** 5.000 μL

**Acq. Method:** D:\DATA\LOT\LOT-3-169\LOT-3-169 2019-05-14 11-12-59\DAS-AD (1-6)-90-10-1XL-SUL-ALL-6H2NHN

**Last changed:** 5/14/2019 11:10:56 AM

**Analysis Method:** D:\DATA\LOT\LOT-3-169\LOT-3-169 2019-05-14 11-12-59\DAS-AD (1-6)-90-10-1XL-SUL-ALL-6H2NHN [Sequence Method]

**Last changed:** 5/16/2019 3:30:14 PM

**Additional Info:** Peak(s) manually integrated
(modified after loading)

---

**Area Percent Report**

---

**Sorted By:** Signal
**Multiplier:** 1.0000
**Dilution:** 1.0000

Use Multiplier & Dilution Factor with ISTDs

**Signal 1: NAD B, Sig=220, 4 Per-off**

<table>
<thead>
<tr>
<th>Peak</th>
<th>RetTime</th>
<th>Type</th>
<th>Width</th>
<th>Height</th>
<th>Area</th>
<th>Area %</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>36.336</td>
<td>BB</td>
<td>0.7109</td>
<td>307.3055</td>
<td>2.3938</td>
<td>2.4422</td>
</tr>
<tr>
<td>2</td>
<td>41.968</td>
<td>BB</td>
<td>1.0720</td>
<td>1.2576</td>
<td>154.1613</td>
<td>57.5578</td>
</tr>
</tbody>
</table>

**Totals:** 1.2582e+4 159.19060

---

Instrument 2 5/16/2019 3:30:21 PM

Page 1 of 2
HPLC of racemic-3

Data File: D:\DATA\LYG\LYG-5-104\LYG-5-104 2020-01-06 17-23-40\041-0201.D
Sample Name: LYG-5-103-2

======================================================================================================
Acq. Operator : Seq. Line : 2
Acq. Instrument : Instrument 1 Location : Vial 41
Injection Date : 1/6/2020 5:36:24 PM Inj : 1
Inj Volume : 5.000 μl
Acq. Method : D:\DATA\LYG\LYG-5-104\LYG-5-104 2020-01-06 17-23-40\WAD-AD(1-2).90-10-1ML-SUL-210NM-60MIN.M
Last changed : 10/28/2018 3:50:08 PM
Analysis Method : D:\METHOD\ZEH\WAD-AS(1-6)-99-1-0.5ML-1UL-220NM-10MIN.M
Last changed : 1/6/2020 8:46:51 PM (modified after loading)
Additional Info : Peak(s) manually integrated

VWD1 A, Wavelength=210 nm (D:\DATA\LYG\LYG-5-104\LYG-5-104 2020-01-06 17-23-40\041-0201.D)

======================================================================================================
Area Percent Report
======================================================================================================
Sorted By : Signal
Multiplier : 1.0000
Dilution : 1.0000
Use Multiplier & Dilution Factor with ISTDs

Signal 1: VWD1 A, Wavelength=210 nm

Peak RetTime Type Width Area Height Area # [min] [min] [μAU's] [μAU] %
---|---------|----------|-----------------|-----------------|-----------------|
1 26.348 MF 1.2471 1.47003e4 196.45955 47.5864
2 29.720 FM 1.3607 1.61915e4 198.32860 52.4136
Totals : 3.08918e4 394.78815

Instrument 1 1/6/2020 8:46:55 PM
HPLC of 3

Data File: D:\DATA\LGY\LGX-5-104\LGX-5-104 2020-01-06 17-23-40\042-0381.D
Sample Name: LGX-5-104-3

Acq. Operator: 3
Seq. Line: 3
Acq. Instrument: Instrument 1
Location: Vial 42
Injection Date: 1/6/2020 6:37:15 PM
Injection: 1
Injection Volume: 5.000 μl
Acq. Method: D:\DATA\LGX\LGX-5-104\LGX-5-104 2020-01-06 17-23-40\WAD-AD(1-2)-90-10-1ML-SUL-210MM-60MIN.M
Last changed: 10/28/2018 3:50:08 PM
Analysis Method: D:\METHOD\ZXR\WAD-AS(1-6)-99-1-0.5ML-1UL-220MM-15MIN.M
Last changed: 1/6/2020 8:49:00 PM
(modified after loading)

Additional Info: Peak(s) manually integrated

VWD1 A, Wavelength=210 nm (D:\DATA\LGX\LGX-5-104\LGX-5-104 2020-01-06 17-23-40\042-0381.D)

Area Percent Report

Sorted By: Signal
Multiplier: 1.0000
Dilution: 1.0000
Use Multiplier & Dilution Factor with ISTDs

Signal 1: VWD1 A, Wavelength=210 nm

<table>
<thead>
<tr>
<th>Peak RetTime Type</th>
<th>Width</th>
<th>Area</th>
<th>Height</th>
<th>Area %</th>
</tr>
</thead>
<tbody>
<tr>
<td>#</td>
<td>[min]</td>
<td>[μAU's]</td>
<td>[μAU]</td>
<td>%</td>
</tr>
<tr>
<td>1</td>
<td>25.937</td>
<td>0.8843</td>
<td>3.59979e4</td>
<td>580.65344</td>
</tr>
<tr>
<td>2</td>
<td>29.895</td>
<td>1.0230</td>
<td>1604.73035</td>
<td>22.05112</td>
</tr>
</tbody>
</table>

Totals: 3.76826e4 682.78457

Instrument 1 1/6/2020 8:50:14 PM
HPLC of 3 (after simple recrystallization)

Data File: D:\DATA\LG\LGY-5-104\LGY-5-104 2020-01-07 19-55-39\062-0681.D
Sample Name: LGY-5-104-3-MV

Acq. Operator: 6
Acq. Instrument: Instrument 1
Injection Date: 1/7/2020 18:12:57 PM
Injection: 1
Inj Volume: 5.000 μl

Last changed: 10/28/2018 3:50:08 PM
Analysis Method: D:\METHOD\WD\AD-1-2-95-5-1ML-2UL-254A-M-2MIN.M
Last changed: 1/16/2020 8:19:19 PM
(modified after loading)

Additional Info: Peak(s) manually integrated

Area Percent Report

Sorted By: Signal
Multiplier: 1.0000
Dilution: 1.0000
Use Multiplier & Dilution Factor with ISTDs

Signal 1: WVD1 A, Wavelength=210 nm

Peak RetTime Type Width Area Height Area
# [min] [min] [mAU's] [mAU] %
-----|------|-----------------|-----|-----|------|------|-----|-----|
1 26.652 VB 1.0656 2.2896804 299.26569 100.0000

Totals:
2.2896804 299.26569

Instrument 1 1/16/2020 8:19:26 PM