

Supporting Information

for

Efficient, highly diastereoselective MS 4 Å-promoted one-pot, three-component synthesis of 2,6-disubstituted-4-tosyloxytetrahydropyrans via Prins cyclization

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Experimental details and characterization data of synthesized compounds, ¹H and ¹³C NMR spectra

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1. General methods

Organic solvents were dried by standard methods, the reagents (chemicals) were purchased from commercial sources, and used without further purification. All reactions were monitored by TLC using precoated silica gel aluminum plates. Visualization of TLC plates was accomplished with an UV lamp. Column chromatography was performed using silica gel 100–200 mesh size (SD Fine-Chem Limited) with EtOAc–hexanes as eluent. Melting points were recorded on Perfit apparatus and are uncorrected. All products were characterized by NMR, IR and MS spectra. ^1H and ^{13}C NMR spectra were recorded in deuterated chloroform (CDCl_3) on a 500 MHz and 125 MHz spectrometer (Bruker), respectively. Chemical shifts were reported in parts per million (ppm, δ) downfield from tetramethylsilane. Proton coupling patterns are described as singlet (s), doublet (d), triplet (t), quartet (q), triplet of triplet (tt), multiplet (m), and broad (br). Elemental analysis was performed by using Perkin-Elmer 2400 series CHNS/O analyzer.

2. General procedure for the synthesis of 4-tosyloxytetrahydropyrans: Aldehyde (1 mmol) and *p*-toluenesulfonic acid (PTSA, 1.4 mmol) were dissolved in dichloromethane (2 mL) and stirred for 5 min at 40 °C. Then, aromatic homoallylic alcohol (1 mmol, dissolved in 2 mL DCM) followed by MS 4 \AA were added to the stirred reaction mixture. Furthermore, the reaction mixture was stirred at the same temperature for a specified time (Table 2). TLC monitoring, after completion of the reaction the reaction mixture was cooled and aq. NaHCO_3 solution was added. The product was extracted with dichloromethane (3 x 10 mL). The combined organic layer was washed with brine (5 mL) and water (5 mL) followed by drying with anhyd. Na_2SO_4 . After evaporation of the solvent in vacuo, the pure product was obtained. In some cases, purification by silica gel column chromatography using hexane:EtOAc as eluent was necessary.

3. General procedure for the synthesis of 4-hydroxytetrahydropyrans from toluenesulfonates using Mg–MeOH: 4-Tosyloxytetrahydropyran (0.5 mmol) and magnesium (120 mg, 5 mmol) in dry methanol (5 mL) in a round bottom flask fitted with a condenser and calcium chloride guard tube was stirred at room temperature with a keeping flask in a water bath for 6 h. After the reaction was complete, the reaction mixture was neutralized with chilled 5% HCl and extracted with diethyl ether (3 x 8 mL). The combined organic layers were washed with water, brine and dried over anhydrous Na₂SO₄ and concentrated. Crystallization from ethanol yielded pure tetrahydropyran-4-ol.

4. General procedure for the preparation of homoallylic alcohols: To a cooled (–78 °C) solution of aromatic aldehyde (5 mmol) in THF (30 mL) was added CH₂=CHCH₂MgBr (10 mL, 1.0 M in THF, 10 mmol). After the reaction mixture was stirred for 2 h at the same temperature, it was quenched with saturated aqueous NH₄Cl and diluted with EtOAc. The layers were separated and the aqueous layer was extracted with EtOAc. The combined organic layers were washed with brine, dried over anhydrous Na₂SO₄, and concentrated in vacuo. The residue was purified by column chromatography (silica gel, hexanes/EtOAc, 10/1 v/v) to afford the known homoallylic alcohol.

5. Characterization data for 4-tosyloxytetrahydropyrans, 4-hydroxytetrahydropyrans and homoallylic alcohols:

(2*R*,4*s*,6*S*)-2,6-diphenyl-4-tosyloxytetrahydropyran (1b)

Yellow solid; yield: 376 mg (92%); mp 100-102 °C. ¹H NMR (500 MHz, CDCl₃): δ = 7.88 (d, *J* = 8 Hz, 2 H, Ar-H), 7.43-7.37 (m, 10 H, Ar-H), 7.34-7.31 (m, 2 H, Ar-H), 5.03 (tt, *J* = 4.5 and 11.5 Hz, 1 H, H-C-OTs), 4.59 (d, *J* = 11.5 Hz, 2 H, Ar-CH-O), 2.48 (s, 3 H, Me), 2.34 (dd, *J* = 4.5 and 12.5 Hz, 2 H, C-CH_{eq}-C), 1.90 (q, *J* = 11.5 Hz, 2 H, C-CH_{ax}-C). ¹³C NMR (125 MHz,

CDCl₃): δ = 144.75, 140.91, 134.20, 129.84, 128.34, 127.75, 127.5, 125.78, 78.18, 77.41, 39.94, 21.56. IR (KBr): 3056, 3039, 2923, 2852, 2373, 1717, 1629, 1454, 1379, 1178, 1065, 945, 903, 757, 699 cm⁻¹. Anal. Calcd for C₂₄H₂₄O₄S (408.5): C, 70.56; H, 5.92; S, 7.85. Found: C, 70.49; H, 5.91; S, 7.68.

(2*R*,4*R*,6*S*)-2-(4-bromophenyl)-6-(3,4,5-trimethoxyphenyl)-4-tosyloxypyrrolidine (2b)

Yellow semisolid; yield: 473.5 mg (82%). ¹H NMR (500 MHz, CDCl₃): δ = 7.81 (d, J = 8.5 Hz, 2 H, Ar-H), 7.45 (d, J = 8.5 Hz, 2 H, Ar-H), 7.34 (d, J = 8.5 Hz, 2 H, Ar-H), 7.22 (d, J = 8.5 Hz, 2 H, Ar-H), 6.56 (s, 2 H, Ar-H), 4.94 (tt, J = 5.0 and 11.0 Hz, 1 H, H-C-OTs), 4.50-4.44 (m, 2 H, Ar-CH-O), 3.85 (s, 6 H, OMe), 3.81 (s, 3 H, OMe), 2.44 (s, 3 H, Me), 2.32-2.25 (m, 2 H, C-CH_{eq}-C), 1.85 (q, J = 11.5 Hz, 1 H, C-CH_{ax}-C), 1.79 (q, J = 11.5 Hz, 1 H, C-CH_{ax}-C). ¹³C NMR (125 MHz, CDCl₃): δ = 153.31, 144.96, 139.84, 137.73, 136.29, 134.23, 131.61, 129.96, 127.62, 121.77, 103.15, 77.89, 77.73, 71.81, 60.84, 56.18, 39.82, 21.7. IR (KBr): 2960, 2925, 2843, 1726, 1594, 1461, 1382, 1175, 1126, 1010, 953, 904, 817 cm⁻¹. Anal. Calcd for C₂₇H₂₉BrO₇S (577.48): C, 56.16; H, 5.06; S, 5.55. Found: C, 56.03; H, 5.49; S, 5.65.

(2*R*,4*s*,6*S*)-2,6-bis(4-chlorophenyl)-4-tosyloxypyrrolidine (3b)

Yellow solid; yield: 439.2 mg (92%); mp 106-108 °C. ¹H NMR (500 MHz, CDCl₃): δ = 7.81 (d, J = 8 Hz, 2 H, Ar-H), 7.35-7.26 (m, 10 H, Ar-H), 4.93 (tt, J = 4.5 and 11.5 Hz, 1 H, H-C-OTs), 4.50 (dd, J = 1.5 and 11.5 Hz, 2 H, Ar-CH-O), 2.44 (s, 3 H, Me), 2.27 (dd, J = 4.5 and 11.5 Hz, 2 H, C-CH_{eq}-C), 1.75 (q, J = 11.5 Hz, 2 H, C-CH_{ax}-C). ¹³C NMR (125 MHz, CDCl₃): δ = 145.0, 139.3, 134.2, 133.7, 130.0, 128.7, 127.6, 127.2, 77.6, 76.9, 39.9, 21.7. IR (KBr): 3051, 2956, 2924, 2853, 1721, 1634, 1596, 1491, 1353, 1293, 1171, 1089, 1014, 950, 908, 859, 828, 665 cm⁻¹. Anal. Calcd for C₂₄H₂₂Cl₂O₄S (477.4): C, 60.38; H, 4.64; S, 6.72. Found: C, 60.45; H, 4.65; S, 6.55.

(2*R*,4*S*,6*S*)-2-(4-bromophenyl)-6-(4-methoxyphenyl)-4-tosyloxytetrahydropyran (4b)

yellow semisolid; yield: 455.3 mg (88%). ¹H NMR (500 MHz, CDCl₃): δ = 7.81 (d, *J* = 8.5 Hz, 2 H, Ar-H), 7.45 (d, *J* = 8.5 Hz, 2 H, Ar-H), 7.34 (d, *J* = 8.5 Hz, 2 H, Ar-H), 7.27 (d, *J* = 9 Hz, 2 H, Ar-H), 7.22 (d, *J* = 8.5 Hz, 2 H, Ar-H), 6.87 (d, *J* = 9 Hz, 2 H, Ar-H), 4.92 (tt, *J* = 4.5 and 11.5 Hz, 1 H, H-C-OTs), 4.48 (t, *J* = 10 Hz, 2 H, Ar-CH-O), 3.79 (s, 3 H, OMe), 2.45 (s, 3 H, Me), 2.29-2.22 (m, 2 H, C-CH-C_{eq}), 1.83 (q, *J* = 11.5 Hz, 1 H, C-CH_{ax}-C), 1.76 (q, *J* = 11.5 Hz, 1 H, C-CH_{ax}-C). ¹³C NMR (125 MHz, CDCl₃): δ = 158.2, 143.8, 139.0, 133.2, 131.8, 130.5, 128.9, 126.5, 126.2, 120.6, 112.8, 76.9, 75.7, 54.2, 38.9, 38.7, 20.6. IR (KBr): 2920, 2850, 1631, 1499, 1383, 1299, 1248, 1175, 1073, 904, 813, 730, 721, 669 cm⁻¹. Anal. Calcd for C₂₅H₂₅BrO₅S (517.43): C, 58.03; H, 4.87; S, 6.20. Found: C, 58.11; H, 4.90; S, 6.28.

(2*S*,4*R*,6*R*)-2-(4-chlorophenyl)-6-phenyl-4-tosyloxytetrahydropyran (5b)

Yellow solid; yield: 398.65 mg (90%); mp 95-97 °C. ¹H NMR (500 MHz, CDCl₃): δ = 7.82 (dd, *J* = 2 and 8.5 Hz, Ar-H), 7.38-7.261 (m, 10 H, Ar-H), 4.96 (tt, *J* = 5.5 and 11 Hz, 1 H, H-C-OTs), 4.55-4.50 (m, 2 H, Ar-CH-O), 2.48 (s, 3 H, Me), 2.30 (m, 2 H, C-CH_{eq}-C), 1.85 (m, 2 H, C-CH_{ax}-C). ¹³C NMR (125 MHz, CDCl₃): δ = 144.9, 140.9, 139.4, 134.3, 133.5, 129.9, 128.6, 128.4, 128.0, 127.6, 127.2, 125.9, 78.0, 77.6, 77.6, 40.0, 39.9, 21.7. IR (KBr): 3056, 2962, 1600, 1149, 1356, 1261, 1172, 1095, 1022, 802, 560 cm⁻¹. Anal. Calcd for C₂₄H₂₃ClO₄S (442.95): C, 65.08; H, 5.23; S, 7.24. Found: C, 64.18; H, 5.25; S, 7.30.

(2*R*,4*R*,6*S*)-2-(4-bromophenyl)-6-(3,4-dimethoxyphenyl)-4-tosyloxytetrahydropyran (6b)

Yellow solid; yield: 465.33 mg (85%); mp 111-113 °C. ¹H NMR (500 MHz, CDCl₃): δ = 7.81 (d, *J* = 8 Hz, 2 H, Ar-H), 7.45 (d, *J* = 8 Hz, 2 H, Ar-H), 7.34 (d, *J* = 8 Hz, 2 H, Ar-H), 7.22 (d, *J* = 8.5 Hz, 2 H, Ar-H), 6.90-6.82 (m, 3 H, Ar-H), 4.93 (tt, *J* = 4.5 and 11.5 Hz, 1 H, H-C-OTs), 4.48 (t, *J* = 11.5 Hz, 2 H, Ar-CH-O), 3.87 (s, 3H, OMe), 3.86 (s, 3H, OMe), 2.45 (s, 3 H, Me),

2.27 (dd, $J = 4.0$ and 12.0 Hz, 2 H, C-CH_{eq}-C), 1.86 (q, $J = 11.5$ Hz, 1 H, C-CH_{ax}-C), 1.76 (q, $J = 12$ Hz, 1 H, C-CH_{ax}-C). ¹³C NMR (125 MHz, CDCl₃): $\delta = 149.2, 145.1, 140.2, 133.5, 131.7, 130.1, 127.8, 118.5, 111.3, 109.6, 78.1, 77.7, 77.0, 56.1, 40.1, 39.9, 21.9$. IR (KBr): 3010, 2965, 2924, 2852, 1734, 1630, 1516, 1460, 1361, 1265, 1174, 1070, 1028, 949, 904, 846, 813.7, 668.37 cm⁻¹. Anal. Calcd for C₂₆H₂₇BrO₆S(547.45): C, 57.04; H, 4.97; S, 5.86. Found: C, 56.98; H, 4.95; S, 5.75.

(2*S*,4*S*,6*R*)-2-(4-bromophenyl)-6-(3,4,5-trimethoxyphenyl)-4-tosyloxytetrahydropyran (7b)

Yellow semisolid; yield: 415.8 mg (72%). ¹H NMR (500 MHz, CDCl₃): $\delta = 7.81$ (d, $J = 8$ Hz, 2 H, Ar-H), 7.46 (d, $J = 8.5$ Hz, 2 H, Ar-H), 7.35 (d, $J = 8$ Hz, 2 H, Ar-H), 7.24-7.22 (m, 2 H, Ar-H), 6.57 (s, 2 H, Ar-H), 4.95 (tt, $J = 4.5$ and 11.5 Hz, 1 H, H-C-OTs), 4.50-4.47 (m, 2 H, Ar-CH-O), 3.86 (s, 6 H, OMe), 3.82 (s, 3 H, OMe), 2.45 (s, 3 H, Me), 2.32-2.26 (m, 2 H, C-CH_{eq}-C), 1.84 (q, $J = 12$ Hz, 1 H, C-CH_{ax}-C), 1.79 (q, $J = 11.5$ Hz, 1 H, C-CH_{ax}-C). ¹³C NMR (125 MHz, CDCl₃): $\delta = 153.2, 144.9, 139.8, 137.6, 136.2, 134.2, 131.5, 129.9, 127.6, 121.7, 103.1, 77.8, 77.7, 76.7, 60.8, 56.1, 39.8, 39.7, 21.6$. IR (KBr): 2960, 2925, 2843, 1726, 1594, 1461, 1382, 1175, 1126, 1010, 953, 904, 817 cm⁻¹. Anal. Calcd for C₂₇H₂₉BrO₇S (577.48): C, 56.16; H, 5.06; S, 5.55. Found: C, 56.20; H, 5.03; S, 5.42.

(2*R*,4*S*,6*S*)-2,6-bis(4-bromophenyl)-4-tosyloxytetrahydropyran (8b)

Pale yellow solid; yield: 438 mg (95%); mp 110-112 °C. ¹H NMR (500 MHz, CDCl₃): $\delta = 7.73$ (d, $J = 8$ Hz, 2 H, Ar-H), 7.38 (m, 4 H, Ar-H), 7.26 (d, $J = 8$ Hz, 2 H, Ar-H), 7.13 (d, $J = 8.5$ Hz, 4 H, Ar-H), 4.84 (tt, $J = 4.5$ and 11.5 Hz, 1 H, H-C-OTs), 4.40 (d, $J = 10$ Hz, 2 H, Ar-CH-O), 2.37 (s, 3 H, Me), 2.18 (dd, $J = 4.5$ and 12.5 Hz, 2 H, C-CH_{eq}-C), 1.68 (q, $J = 11.5$ Hz, 2 H, C-CH_{ax}-C). ¹³C NMR (125 MHz, CDCl₃): $\delta = 145.0, 139.8, 134.2, 131.6, 129.98, 127.6, 121.8, 77.5, 76.8, 39.8, 21.7$. IR (KBr): 3100, 2960, 2908, 2843, 1895, 1726, 1595, 1489, 1353, 1172,

1073, 1011, 950, 908, 811, 682, 664 cm^{-1} . Anal. Calcd for $\text{C}_{24}\text{H}_{22}\text{Br}_2\text{O}_4\text{S}$ (566.30): C, 50.90; H, 3.92; S, 5.66. Found: C, 50.82; H, 3.94; S, 5.55.

(2*S*,4*R*,6*R*)-2-(4-bromophenyl)-6-(4-methoxyphenyl)-4-tosyloxypyrrolidine (9b)

Yellow semisolid; yield: 388 mg (75%). ^1H NMR (500 MHz, CDCl_3): δ = 7.74 (d, J = 8.5 Hz, 2 H, Ar-H), 7.38 (dd, J = 2 and 7 Hz, 2 H, Ar-H), 7.27 (d, J = 8.5 Hz, 2 H, Ar-H), 7.21-7.14 (m, 4 H, Ar-H), 6.80 (dd, J = 2 and 6.5 Hz, 2 H, Ar-H), 4.84 (tt, J = 4.5 and 11 Hz, 1H, H-C-OTs), 4.41 (t, J = 11 Hz, 2 H, Ar-CH-O), 3.72 (s, 3 H), 2.38 (s, 3 H, Me), 2.22-2.15 (m, 2 H, C- CH_{eq} -C), 1.77 (q, J = 12 Hz, 1H, C-CH- C_{ax}), 1.73 (q, J = 11.5 Hz, 1H, C- CH_{ax} -C). ^{13}C NMR (125 MHz, CDCl_3): δ = 159.3, 144.9, 140.1, 139.8, 137.0, 134.3, 132.9, 131.6, 129.97, 127.6, 127.6, 127.3, 113.9, 78.0, 77.5, 76.8, 55.3, 40.0, 39.8, 21.7. IR (KBr): 2920, 2850, 1631, 1499, 1383, 1299, 1248, 1175, 1073, 904, 813, 730, 721, 669 cm^{-1} . Anal. Calcd for $\text{C}_{25}\text{H}_{25}\text{BrO}_5\text{S}$ (517.43): C, 58.03; H, 4.87; S, 6.20. Found: C, 58.10; H, 4.85; S, 6.10.

(2*S*,4*R*,6*R*)-2-(4-bromophenyl)-6-(4-chlorophenyl)-4-tosyloxypyrrolidine (10b)

Pale yellow solid; yield: 495 mg (95%); mp 110-112 $^{\circ}\text{C}$. ^1H NMR (500 MHz, CDCl_3): δ = 7.78 (d, J = 8 Hz, 2 H, Ar-H), 7.42 (d, J = 8.5 Hz, 2 H, Ar-H), 7.31 (d, J = 8 Hz, 2 H, Ar-H), 7.28-7.23 (m, 4 H, Ar-H), 7.18 (d, J = 8.5 Hz, 2 H, Ar-H), 4.9 (tt, J = 4.5 and 11.5 Hz, 1 H, H-C-OTs), 4.46 (t, J = 10 Hz, 2 H, Ar-CH-O), 2.40 (s, 3 H, Me), 2.22 (dd, J = 3 and 12.5 Hz, 2 H, C- CH_{eq} -C), 1.72 (qd, J = 2.5 and 11 Hz, 2 H, C- CH_{ax} -C). ^{13}C NMR (125MHz, CDCl_3): δ = 144.9, 139.7, 139.2, 134.1, 133.5, 131.5, 129.9, 128.5, 127.5, 127.1, 121.7, 77.5, 76.7, 39.74, 39.7, 21.6. IR (KBr): 3078, 2965, 2921, 2856, 1908, 1708, 1630, 1591, 1489, 1354, 1171, 1081, 948, 908, 831, 669 cm^{-1} . Anal. Calcd for $\text{C}_{24}\text{H}_{22}\text{BrClO}_4\text{S}$ (521.85): C, 55.24; H, 4.25; S, 6.14. Found: C, 55.16; H, 4.20; S, 6.22.

(2*R*,4*R*,6*S*)-2-(4-chlorophenyl)-6-(3-nitrophenyl)-4-tosyloxypyrans (11b)

Yellow solid; yield: 468.43 mg (96%); mp 118-120 °C. ¹H NMR (500 MHz, CDCl₃): δ = 8.62 (s, 1 H, Ar-H), 8.4 (dd, *J* = 3 and 8 Hz, 1 H, Ar-H), , 8.14 (d, *J* = 7.5 Hz, 1 H, Ar-H), 7.72 (d, *J* = 8.5 Hz, 2 H, Ar-H), 7.67 (t, *J* = 8 Hz, 1 H, Ar-H), 7.26 (d, *J* = 8 Hz, 2 H, Ar-H), 7.229-7.186 (m, 4 H, Ar-H), 4.85 (tt, *J* = 4.5 and 11 Hz, 1 H, H-C-OTs), 4.43 (dd, *J* = 1 and 11.5 Hz, 2 H, Ar-CH-O), 2.36 (s, 3 H, Me), 2.18 (dd, *J* = 4.5 and 12.5 Hz, 2 H, C-CH_{eq}-C), 1.68 (q, *J* = 11.5 Hz, 2 H, C-CH_{ax}-C). ¹³C NMR (125 MHz, CDCl₃): δ = 148.5, 144.9, 139.0, 137.1, 134.6, 133.7, 133.4, 130.3, 129.8, 128.5, 127.4, 127.1, 124.4, 77.4, 76.7, 39.7, 21.6. IR (KBr): 3069.6, 2960.87, 2926.1, 1703.7, 1596, 1533, 1352, 1171, 1090, 970.9, 908.8, 841, 700, 666 cm⁻¹. Anal. Calcd for C₂₄H₂₂ClNO₆S (487.95): C, 59.07; H, 4.54; N, 2.87; S, 6.57. Found: C, 58.93; H, 4.58; N, 2.82; S, 6.40.

(2*R*,4*R*,6*S*)-2-phenyl-6-(3,4,5-trimethoxyphenyl)-4-tosyloxypyrans (12b)

Dark yellow solid; yield: 413.8 mg (83%); mp 116-118 °C. ¹H NMR (500 MHz, CDCl₃): δ = 7.85 (d, *J* = 8 Hz, 2 H, Ar-H), 7.38 (m, 7 H, Ar-H), 6.6 (s, 2 H, Ar-H), 4.99 (tt, *J* = 4.5 and 11 Hz, 1 H, H-C-OTs), 4.52 (ddd, *J* = 2, 11.5 and 25.5 Hz, 2 H, Ar-CH-O), 3.9 (s, 6 H, OMe), 3.84 (s, 3 H, OMe), 2.47 (s, 3 H, Me), 2.34-2.29 (m, 2 H, C-CH_{eq}-C), 1.93-1.84 (m, 2 H, C-CH_{ax}-C). ¹³C NMR (125 MHz, CDCl₃): δ = 152.3, 143.8, 143.1, 139.8, 136.5, 135.5, 128.9, 127.5, 126.9, 126.6, 124.9, 102.2, 77.1, 76.8, 75.7, 59.8, 55.1, 39.0, 38.9, 20.6. IR (KBr): 2962, 2926, 2852, 1634, 1595, 1456, 1417, 1261, 1178, 1096, 1023, 803, 873, 708 cm⁻¹. Anal. Calcd for C₂₇H₃₀O₇S (498.6): C, 65.05; H, 6.06; S, 6.43. Found: C, 65.10; H, 6.08; S, 6.38.

(2*R*,4*S*,6*S*)-2-(4-chlorophenyl)-6-(4-methoxyphenyl)-4-tosyloxypyrans (13b)

Yellow semisolid; yield: 416 mg (88%). ¹H NMR (500 MHz, CDCl₃): δ = 7.74 (d, *J* = 8.5 Hz, 2 H, Ar-H), 7.28-7.19 (m, 8 H, Ar-H), 6.8 (d, *J* = 9 Hz, 2 H, Ar-H), 4.85 (tt, *J* = 4.5 and 11.5 Hz, 1

H, H-C-OTs), 4.45-4.39 (ddd, $J = 1.5, 11.5$ and 16.5 Hz, 2 H, Ar-CH-O), 3.72 (s, 3 H, OMe), 2.38 (s, 3 H, Me), 2.22-2.15 (m, 2 H, C-CH_{eq}-C), 1.76 (q, $J = 11.5$ Hz, 2 H, C-CH_{ax}-C), 1.7 (q, $J = 11.5$ Hz, 2 H, C-CH_{ax}-C). ¹³C NMR (125 MHz, CDCl₃): $\delta = 159.3, 144.8, 141.0, 133.2, 129.9, 128.5, 128.4, 127.9, 127.6, 127.3, 126.0, 113.8, 78.38, 76.8, 55.3, 40.1, 39.9, 39.6, 21.7$. IR (KBr): 3010, 2956, 2921, 2847, 1721, 1633, 1508, 1456, 1386, 1252, 1178, 1082, 1026, 904, 813 cm⁻¹. Anal. Calcd for C₂₅H₂₅ClO₅S (472.9): C, 63.48; H, 5.33; S, 6.78. Found: C, 63.45; H, 5.36; S, 6.69.

(2*S*,4*R*,6*R*)-2-(4-bromophenyl)-6-phenyl-4-tosyloxytetrahydropyran (14b)

Pale yellow solid; yield: 463 mg (95%); mp 104-106 °C. ¹H NMR (500 MHz, CDCl₃): $\delta = 7.84$ -7.22 (m, 2 H, Ar-H), 7.47 (dd, $J = 2$ and 8.5 Hz, 2 H, Ar-H), 7.39-7.22 (m, 9 H, Ar-H), 4.95 (m, 1 H, H-C-OTs), 4.56-4.48 (m, 2 H, Ar-CH-O), 2.45 (s, 3 H, Me), 2.30-2.27 (m, 2 H, C-CH-C_{eq}), 1.89-1.74 (m, 2 H, C-CH-C_{ax}). ¹³C NMR (125MHz, CDCl₃): $\delta = 143.9, 139.7, 139.0, 133.2, 130.5, 128.9, 127.4, 126.9, 126.6, 124.8, 120.7, 76.8, 76.51, 75.79, 38.9, 38.8, 20.6$. IR (KBr): 2921.7, 1630, 1486, 1352, 1182, 1065, 1008, 900, 817, 756 cm⁻¹. Anal. Calcd for C₂₄H₂₃BrO₄S (487.4): C, 59.14; H, 4.76; S, 6.58. Found: C, 59.12; H, 4.79; S, 6.49.

(2*R*,4*S*,6*S*)-2-(4-chlorophenyl)-6-*p*-tolyl-4-tosyloxytetrahydropyran (15b)

Yellow solid; yield: 425 mg (93%); mp 104-106 °C. ¹H NMR (500MHz, CDCl₃): $\delta = 7.81$ (d, $J = 8$ Hz, 2 H, Ar-H), 7.34 (d, $J = 8.5$ Hz, 2 H, Ar-H), 7.30- 7.22 (m, 6 H, Ar-H), 7.146 (d, $J = 7.5$ Hz, 2 H, Ar-H), 4.92 (tt, $J = 4.5$ and 11 Hz, 1 H, H-C-OTs), 4.49 (td, $J = 2$ and 11 Hz, 2 H, Ar-CH-O), 2.45 (s, 3 H), 2.33 (s, 3 H, Me), 2.29-2.26 (m, 2 H, C-CH_{eq}-C), 1.84-1.76 (m, 2 H, C-CH_{ax}-C). ¹³C NMR (125MHz, CDCl₃): $\delta = 144.9, 139.6, 137.8, 134.3, 133.5, 129.96, 129.2, 128.6, 127.6, 127.3, 125.9, 78.0, 77.54, 40.4, 39.8, 21.7, 21.2$. IR (KBr): 3047, 2982, 2916, 2843,

2373, 1639, 1369, 1265, 1169, 1117, 738 cm^{-1} . Anal. Calcd for $\text{C}_{25}\text{H}_{25}\text{ClO}_4\text{S}$ (456.98): C, 65.71; H, 5.51; S, 7.02. Found: C, 65.76; H, 5.49; S, 7.15.

(2*S*,4*R*,6*R*)-2-(furan-2-yl)-6-phenyl-4-tosyloxytetrahydropyran (16b)

Yellow solid; yield: 330 mg (83%); mp 123-125 °C. ^1H NMR (500MHz, CDCl_3): δ = 7.82 (d, J = 7.5 Hz, 2 H, Ar-H), 7.41 (d, J = 7.5 Hz, 2 H, Ar-H), 7.31 (m, 1 H, Ar-H), 7.21 (m, 5 H, Ar-H), 6.43-6.25 (m, 2 H, Ar-H), 5.15 (t, J = 12Hz 1H,), 4.95 (tt, J = 4.5 and 11 Hz, 1 H, H-C-OTs), 4.53 (td, J = 2 and 11.5 Hz, 1 H, Ar-CH-O), 2.45 (s, 3 H), 2.25-2.21 (m, 2 H, C- CH_{eq} -C), 1.90-1.86 (m, 2 H, C- CH_{ax} -C). ^{13}C NMR (125MHz, CDCl_3): δ = 153.2, 144.5, 142.2, 139.8, 138.4, 132.7, 130.9, 128.6, 128.5, 127.0, 112.4, 111.6, 78.0, 75.2, 40.7, 39.9, 22.5. IR (KBr): 3021, 2986, 2355, 1696, 1432 cm^{-1} . Anal. Calcd for $\text{C}_{22}\text{H}_{22}\text{O}_5\text{S}$ (398.47): C, 66.31; H, 5.56; S, 8.05. Found: C, 66.24; H, 5.52; S, 8.20.

(2*S*,4*R*,6*R*)-2-phenyl-6-(1*H*-pyrrol-2-yl)-4-tosyloxytetrahydropyran (17b)

Yellow semi solid; yield: 341 mg (86%); ^1H NMR (500MHz, CDCl_3): δ = 8.21 (s, br, D_2O exchangeable, 1H, NH), 7.81 (d, J = 7.5 Hz, 2 H, Ar-H), 7.44 (d, J = 7.5 Hz, 2 H, Ar-H), 7.19 (m, 5 H, Ar-H), 6.43 (m, 1 H, Ar-H), 5.95-5.7 (m, 2H, Ar-H), 4.93 (tt, J = 4.5 and 11.5 Hz, 1 H, H-C-OTs), 4.87 (td, J = 2 and 11.5 Hz, 2 H, Ar-CH-O), 2.41 (s, 3 H), 2.25-2.21 (m, 2 H, C- CH_{eq} -C), 1.90-1.86 (m, 2 H, C- CH_{ax} -C). ^{13}C NMR (125MHz, CDCl_3): δ = 144.3, 140.3, 139.1, 133.6, 130.8, 128.9, 128.2, 127.2, 118.5, 108.6, 107.4, 77.6, 72.1, 59.8, 41.4, 40.2, 21.3. IR (KBr): 3451, 3069.6, 2960.87, 1703.7, 1596, 1533, 1352 cm^{-1} . Anal. Calcd for $\text{C}_{22}\text{H}_{23}\text{NO}_4\text{S}$ (397.13): C, 66.48; H, 5.83; N, 3.52; S, 8.07. Found: C, 66.40; H, 5.81; N, 3.60; S, 8.20.

(2*R*,4*S*,6*S*)-2-methyl-6-phenyl-4-tosyloxytetrahydropyran (18b):

Yellow solid; yield: 307 mg (89%); mp 92-94 °C. ^1H NMR (500 MHz, CDCl_3): δ = 7.88 (d, J = 8 Hz, 2 H, Ar-H), 7.34-7.31 (d, J = 8 Hz, 2 H, Ar-H), 7.22 (m, 5H), 5.03 (tt, J = 4.5 and 11.5 Hz, 1

H, H-C-OTs), 4.59 (t, $J = 11.5$ Hz, 1 H, Ar-CH-O), 3.92 (m, 1 H), 2.48 (s, 3 H, Me), 2.33-2.37 (dd, $J = 4.5$ and 11.5 Hz, 2 H, C-CH_{eq}-C), 1.88 (q, $J = 7.5$ Hz, 2 H, C-CH_{ax}-C). 1.56 (m, 3H). ¹³CNMR (125 MHz, CDCl₃): $\delta = 144.7, 140.9, 134.2, 129.8, 128.3, 127.7, 127.5, 125.82, 77.4, 68.21, 61.2, 39.9, 24.3, 21.6$. IR (KBr): 3056, 2923, 2852, 1717, 1629, 1454, 1379 cm⁻¹. Anal. Calcd for C₁₉H₂₂O₄S (346.12): C, 65.87; H, 6.40; S, 9.26. Found: C, 65.85; H, 6.36; S, 9.20.

(2R,4s,6S)-2,6-bis(4-chlorophenyl)tetrahydropyran-4-ol (1c)

Yellow solid; yield: 297 mg (92%); mp 110-112 °C. ¹H NMR (500 MHz, CDCl₃): $\delta = 7.29-7.24$ (m, 8 H, Ar-H), 4.47 (d, $J = 11.5$ Hz, 2 H, Ar-CH-O), 4.06 (tt, $J = 4.5$ and 11 Hz, 1 H, H-C-OH), 2.19 (dd, $J = 4$ and 12 Hz, 2 H, C-CH_{eq}-C), 1.48 (q, $J = 11.5$ Hz, 2 H, C-CH_{ax}-C). ¹³C NMR (125 MHz, CDCl₃): $\delta = 139.2, 132.3, 127.5, 126.2, 67.4, 41.9$. IR (KBr): 3447.1, 2960.87, 2886, 1652, 1543, 1088, 804 cm⁻¹. GC-MS: m/z (%) = 323 (65, [M⁺]), 138(100).

(2R,4s,6S)-2,6-diphenyltetrahydropyran-4-ol (2c)

Yellow solid; yield: 241.3 mg (95%); mp 102-103 °C. ¹H NMR (500 MHz, CDCl₃): $\delta = 7.42$ (d, $J = 7$ Hz, 4 H, Ar-H), 7.35 (t, $J = 7.5$ Hz, 4 H, Ar-H), 7.28 (m, 2 H, Ar-H), 4.57 (d, $J = 11.5$ Hz, 2 H, Ar-CH-O), 4.16 (tt, $J = 4.5$ and 11 Hz, 1 H, H-C-OH), 2.29 (dd, $J = 2$ and 10 Hz, 2 H, C-CH_{eq}-C), 2.23 (s, br, D₂O exchangeable, 1 H, OH), 1.60 (q, $J = 11.5$ Hz, 2 H, C-CH_{ax}-C). ¹³C NMR (125 MHz, CDCl₃): $\delta = 141.8, 128.2, 127.4, 125.7, 77.8, 68.6, 42.96$. IR (KBr): 3434, 3010, 2922, 2843, 1734, 1626, 1456, 1386, 1256, 1069, 808.8 cm⁻¹. GC-MS: m/z (%) = 254 (38, [M⁺]), 104(100).

(2R,4s,6S)-2,6-bis(4-bromophenyl)tetrahydropyran-4-ol (3c)

Yellow solid; yield: 385 mg (94%); mp 122-123 °C. ¹H NMR (500 MHz, CDCl₃): $\delta = 7.19-7.41$ (m, 8 H, Ar-H), 4.51-4.43 (m, 2 H, Ar-CH-O), 4.07 (tt, $J = 4.5$ and 11.5 Hz, 1 H, H-C-OH), 2.28 (s, br, D₂O exchangeable, 1 H, OH), 2.21 (m, 2 H, C-CH_{eq}-C), 1.53 (m, 2 H, C-CH_{ax}-C). ¹³C

NMR (125 MHz, CDCl₃): δ = 131.4, 128.3, 127.5, 125.8, 77.8, 68.6, 43.0, 42.8. IR (KBr): 3433.8, 2965.2, 2921.7, 2852.1, 1634.8, 1452.1, 1382.6, 1265.2, 1156.5, 1065.2, 900.0, 760.87, 700 cm⁻¹. GC-MS: m/z (%) = 410 (48, [M⁺]), 104 (100).

1-Phenylbut-3-en-1-ol (1a)¹

Color less oil; yield: 782.5 mg (86%). ¹H NMR (500 MHz, CDCl₃): δ = 7.3 (d, J = 4 Hz, 2 H, Ar-H), 7.2 (d, J = 4 Hz, 2 H, Ar-H), 5.7 (m, 1 H, C=C-H), 5.1 (m, 2 H, C=C-H₂), 4.6 (t, J = 5 Hz, 1 H, Ar-CH-OH), 3.2 (s, br, D₂O exchangeable, 1 H, OH), 2.4 (m, 2 H, =C-CH-C). ¹³C NMR (125 MHz, CDCl₃) δ = 143.8, 134.4, 128.4, 127.6, 125.8, 125.8, 118.5, 73.3, 43.9. IR (KBr): 3450, 3070, 2935, 2917, 1639, 1491, 1417, 1260, 1099, 1012, 917, 835, 739 cm⁻¹. GC-MS: m/z (%) = 148 (53, [M⁺]), 107(100).

1-(4-chlorophenyl)but-3-en-1-ol (2a)²

Pale yellow oil; yield: 651 mg (88%). ¹H NMR (500 MHz, CDCl₃): δ = 7.19 (m, 1 H, Ar-H), 5.7 (m, 1 H, C=C-H), 5.0 (m, 1 H, C=C-H₂), 4.6 (t, J = 5 Hz, 1 H, Ar-CH-OH), 2.4 (m, 2 H, =C-CH-C), 2.3 (s, br, D₂O exchangeable, 1 H, OH). ¹³C NMR (125 MHz, CDCl₃): δ = 143.8, 134.5, 128.4, 127.6, 125.8, 125.8, 118.5, 73.3, 43.9. IR (KBr): 3425, 3072, 2923, 2852, 1638, 1443, 1262, 1094, 1030, 804, 701 cm⁻¹. GC-MS: m/z (%) = 182 (74, [M⁺]), 141(100).

1-(4-methoxyphenyl)but-3-en-1-ol (3a)³

Pale yellow oil. Yield: 756 mg (85%). ¹H NMR (500 MHz, CDCl₃): δ = 7.28 (d, J = 9 Hz, 2 H, Ar-H), 6.88 (d, J = 8.5 Hz, 2 H, Ar-H), 5.82 (m, 2 H, C=C-H), 4.68 (t, J = 6.5 Hz, 1 H, Ar-CH-OH), 2.49 (t, J = 7 Hz, 2 H, =C-CH-C), 2.1 (s, br, D₂O exchangeable, 1H, OH). ¹³C NMR (125 MHz, CDCl₃): δ = 158.2, 135.4, 133.9, 126.3, 117.0, 113.2, 72.0, 54.0, 42.0. IR (KBr): 3421.5,

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3073.7, 2998.0, 2925.9, 1617, 1508, 1447, 1299, 1247, 1178, 1039, 926, 830, 739 cm^{-1} . GC-MS: m/z (%) = 178 (38, $[\text{M}^+]$), 137(100).

1-(4-bromophenyl)but-3-en-1-ol (4a)⁴

Pale yellow oil; yield: 995 mg (88%). ¹H NMR (500 MHz, CDCl_3): δ = 7.4 (d, J = 7 Hz, 2 H, Ar-H), 7.1 (d, J = 10.5 Hz, 2 H, Ar-H), 5.7 (m, 1 H), 5.1 (m, 2 H), 4.6 (td, J = 6.5, 17 Hz, 1 H), 2.49 (m, 2 H), 2.49 (s, br, D_2O exchangeable, 1H, OH). ¹³C NMR (125 MHz, CDCl_3) δ = 143.8, 134.4, 128.4, 127.6, 125.8, 125.8, 118.5, 73.3, 43.9. IR (KBr): 3406.2, 3077.4, 2978.2, 2928.6, 1640.3, 1591.3, 1487.7, 1405, 1068.6, 1008.6, 910, 825.7, 735.9, 649.27, 535.1 cm^{-1} . GC-MS: m/z (%) = 226 (48, $[\text{M}^+]$), 78(100).

1-(3,4,5-trimethoxyphenyl)but-3-en-1-ol (5a)⁵

Pale yellow oil; yield: 1046 mg (82%). ¹H NMR (500 MHz, CDCl_3) δ = 6.57 (s, 2 H, Ar-H), 5.8 (m, 1 H), 5.16 (m, 2 H), 4.64 (m, 1 H), 2.49 (m, 2 H), 2.2 (s, broad-OH, D_2O exchangeable, 1 H). ¹³C NMR (125 MHz, CDCl_3): δ = 153.0, 140.0, 136.9, 134.6, 118.0, 102.6, 73.5, 60.7, 56.0, 43.9. IR (KBr): 3442, 3100, 2934.8, 2847.83, 1637.1, 1593.9, 1460.3, 1421.7, 1330.4, 1233.9, 1126.2, 1060.9, 1004.35, 913.04, 834.8, 669.57 cm^{-1} . GC-MS: m/z (%) = 238 (64, $[\text{M}^+]$), 197(100).

⁴ Mosher, M. D.; Emmerich, L. G.; Frost, K. S.; Anderson, B. J. *Heterocycl. Chem.* **2006**, *43*, 535-539.

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6. ¹H data for 4-tosyloxy and 4-hydroxytetrahydropyran:



































