Stereochemistry of Nucleophilic Substitution Reactions Depending Upon Substituent: Evidence for Electrostatic Stabilization of Pseudoaxial Conformers of Oxocarbenium Ions by Heteroatom Substituents

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Note: Details for experiments that were reported in the Communication of this work (J. A. C. Romero, S. A. Tabacco, K. A. Woerpel, J. Am. Chem. Soc. 2000, 122, 168-169) have already been published on the Web as Supporting Information. Consequently, that information was not duplicated in the Supporting Information for this Article.

I. General Information

$^1$H NMR and $^{13}$C NMR spectra were recorded at ambient temperature at 500 MHz and 125 MHz, respectively, using a Nicolet Omega 500 or a GN 500 spectrometer. All chemical shifts are reported in ppm relative to tetramethylsilane on the $\delta$ scale, multiplicity (br = broad, s = singlet, d = doublet, t = triplet, q = quartet, quint = quintet, and m = multiplet), coupling constants
in Hz, and integration. The $^{19}$F NMR spectra were recorded in ppm downfield from internal standard CFCl$_3$ in CDCl$_3$ at 376 MHz using a Bruker DRX 400. Infrared (IR) spectra were obtained using a MIDAC Prospect FT-IR spectrometer. High resolution mass spectra were acquired on a VG Analytical 7070E or Fisons Autospec spectrometer. Elemental analyses were performed by Atlantic Microlab, Atlanta, GA. Analytical gas-liquid chromatography (GC) analyses were performed on a Hewlett Packard 5890 Level 4 Chromatograph, equipped with a split-mode injection system and a flame ionization detector. Fused silica capillary column (30 m $\times$ 0.32 mm) wall coated with DB-1 (J & W Scientific) was used with helium as the carrier gas (16 psi column head pressure). Liquid chromatography was performed using force flow (flash chromatography) with the indicated solvent on 60 Å SiliTech silica gel (SiO$_2$). All reactions were carried out under nitrogen atmosphere in flame-dried glassware using standard syringe/septa techniques. Unless otherwise stated, all reagents were used unpurified from the supplier. CH$_2$Cl$_2$ and THF were dried non-pyrophorically as in the method of Grubbs.$^1$ All other solvents were dried and distilled. NaH was washed with hexanes and dried under reduced pressure.

II. Synthesis of Acetates

IIA. Synthesis of 4-(tert-Butyldiphenylsilyloxy)tetrahydropyran-1-acetate (14a)
4-(tert-Butyldiphenylsilyloxy)-1-methoxytetrahydropyran (S2): Triethylamine (8.39 mL, 60.2 mmol) and 4-dimethylaminopyridine (0.886 g, 7.22 mmol) were added to a cooled (0 °C) solution of 4-hydroxy-1-methoxytetrahydropyran in CH$_2$Cl$_2$ (12 mL), followed by slow addition of tert-butylchlorodiphenylsilane (8.14 mL, 31.3 mmol). The mixture was warmed slowly to room temperature and stirred for 15 h before addition of water (100 mL) to dissolve the white precipitate. The layers were separated, and the aqueous layer was extracted with Et$_2$O (3 × 50 mL). The combined organic layers were washed with 1 N HCl (30 mL), saturated aqueous NaHCO$_3$ (30 mL), and brine (30 mL), dried over MgSO$_4$, filtered and concentrated in vacuo. The resulting oil was purified by flash chromatography (9:1 to 4:1 EtOAc/hexanes) to afford the product (as a 3.3:1 mixture of anomers) as a colorless oil (7.41 g, 83%).

1H NMR (500 MHz, CDCl$_3$) δ 7.68–7.64 (m, 17.2H), 7.44–7.41 (m, 8.6H), 7.38–7.35 (m, 17.2H), 4.54 (dd, $J = 4.8, 2.9, 3.3$H), 4.46 (dd, $J = 3.1, 2.0, 1$H), 3.77–3.67 (m, 7.6H), 3.52 (t, $J = 10.1, 1$H), 3.42 (ddd, $J = 10.7, 4.8, 1.9, 1$H), 3.37 (s, 9.9H), 3.34 (s, 3H), 3.32 (ddd, $J = 10.3, 5.2, 1.2, 3.3$H), 2.08 (ddd, $J = 13.4, 9.9, 4.6, 3.3, 3.3$H), 1.88 (ddt, $J = 13.2, 8.8, 4.4, 3.3$H), 1.81 (m, 1H), 1.76–1.67 (m, 2H), 1.58 (m, 3.3H), 1.51 (dt, $J = 13.4, 3.8, 1$H), 1.44 (ddt, $J = 12.1, 7.8, 4.7, 3.3$H), 1.07 (s, 29.7H), 1.05 (s, 9H); 13C NMR (125 MHz, CDCl$_3$) δ 135.9, 135.7, 134.8, 134.13, 134.09, 134.0, 129.69, 129.65, 129.4, 127.8, 127.6, 127.5, 127.4, 99.9, 97.2, 67.1, 66.51, 66.46, 64.4, 55.3, 54.6, 28.6, 28.0, 27.6, 27.0, 26.9, 26.7, 19.2, 19.1; IR (thin film) 3071, 2932, 1428, 1216, 1109, 823, 703 cm$^{-1}$; HRMS (Cl/isobutane) m / z calcd for C$_{21}$H$_{27}$O$_2$Si (M – CH$_3$O)$^+$ 339.1780, found 339.1771. Anal. Calcd for C$_{22}$H$_{30}$O$_3$Si: C, 71.31; H, 8.16. Found: C, 71.15; H, 8.28.

4-(tert-Butyldiphenylsilyloxy)tetrahydropyran-1-ol (S3): An aqueous (10%) solution of HCl (10 mL) was added slowly to a solution of 4-(tert-butyldiphenylsilyloxy)-1-
methoxytetrahydropyran in THF (20 mL). After 36 h, the mixture was neutralized with saturated aqueous NaHCO₃. The THF was removed in vacuo, and the remaining aqueous layer was extracted with Et₂O (3 × 25 mL), dried over MgSO₄, filtered, and concentrated in vacuo. The resulting oil was purified by flash chromatography (1:9 to 2:3 EtOAc/hexanes) to afford the product (as a 1:1 mixture of anomers) as a colorless oil (0.898 g, 96%).

\[ \text{1H NMR (500 MHz, CDCl}_3\text{)} \delta 7.68–7.64 (m, 8H), 7.46–7.44 (m, 4H), 7.43–7.35 (m, 8H), 4.97 (dd, } J = 7.2, 3.5, 1H), 4.91 (ddd, } J = 7.1, 4.8, 2.3, 1H), 3.83 (dd, } J = 11.3, 3.7, 1.7, 1H), 3.79–3.68 (m, 3H), 3.45 (ddd, } J = 10.8, 3.8, 1.6, 1H), 3.34 (dd, } J = 11.4, 7.1, 1H), 2.56 (d, } J = 5.0, 1H), 2.46 (dd, } J = 1.4, 4.2, 1H), 2.02 (m, 1H), 1.99–1.77 (m, 3H), 1.66 (m, 1H), 1.61–1.52 (m, 2H), 1.38 (m, 1H), 1.06 (s, 18H); 13C NMR (125 MHz, CDCl₃) δ 135.71, 135.68, 135.65, 134.1, 134.01, 133.96, 129.73, 129.70, 129.67, 127.8, 127.64, 127.62, 127.59, 94.4, 91.8, 68.1, 66.7, 66.5, 65.8, 29.0, 28.9, 28.7, 27.8, 27.0, 26.9, 19.2, 19.1; IR (thin film) 3390, 2931, 2360, 1427, 1111, 822, 701 cm⁻¹; HRMS (Cl/isobutane) m / z calcd for C₂₁H₂₈O₃SiNa (M + Na)⁺ 379.1705, found 379.1708. Anal. Calcd for C₂₁H₂₈O₃Si: C, 70.74; H, 7.92. Found: C, 70.89; H, 7.90.

**4-(tert-Butyldiphenylsilyloxy)tetrahydropyran-1-acetate (14a):** A solution of 4-(tert-butyldiphenylsilyloxy)tetrahydropyran-1-ol (0.411 g, 1.15 mmol), acetic anhydride (0.544 mL, 5.76 mmol), pyridine (0.373 mL, 4.61 mmol) and 4–dimethylaminopyridine (0.170 g, 1.38 mmol) in CH₂Cl₂ (20 mL) was stirred for 24 h. Saturated aqueous NH₄Cl (10 mL) was added, and CH₂Cl₂ was removed in vacuo. The residue was dissolved in MTBE (75 mL), and the layers were separated. The organic layer was washed with saturated aqueous Na₂HPO₄ (4 × 20 mL), NaH₂PO₄ (4 × 20 mL), and CuSO₄ (5 × 20 mL), filtered through Na₂SO₄, and concentrated in vacuo. The resulting oil was purified by flash chromatography (1:9 to 1:2 EtOAc/hexanes) to afford the product (as a 1.1:1 mixture of anomers) as a colorless oil (0.402
IIB. Synthesis of 4-Methanesulfoxytetrahydropyran-1-acetate (14b)

4-Methanesulfoxy-1-methoxymethoxytetrahydropyran (S4): Alcohol 4-hydroxy-1-methoxymethoxytetrahydropyran was dissolved in CH₂Cl₂ (183 mL) and cooled to 0 °C. Triethylamine (10.1 mL, 72.6 mmol) was added, followed by slow addition of methanesulfonyl chloride (6.56 mL, 84.7 mmol). The mixture was stirred at 0 °C for 3 h and poured into a solution of 1 N HCl (300 mL). The layers were separated, and the aqueous layer was extracted with Et₂O (3 × 100 mL). The combined organic layers were washed with saturated aqueous NaHCO₃ (200 mL), dried over MgSO₄, filtered and concentrated in vacuo. The resulting oil was purified by flash
chromatography (1:4 to 3:2 Et₂O/pentane) to afford the product (as a 1.4:1 mixture of anomers) as a colorless oil (11.85 g, 93%).

\[ ^1H\text{ NMR (500 MHz, CDCl}_3\text{) } \delta \text{ 4.77 (br s, 1.4H), 4.72–4.68 (m, 2.4H), 4.55 (t, } J = 3.2, \text{ 1H), 3.94 (dd, } J = 12.9, 0.6, \text{ 1.4H), 3.82–3.73 (m, 3.4H), 3.396 (s, 3H), 3.392 (s, 4.2H), 3.08 (s, 4.2H), 3.04 (s, 3H), 2.19–1.85 (m, 7.2H), 1.77 (m, 1H), 1.62 (m, 1.4H); } ^{13}C\text{ NMR (125 MHz, CDCl}_3\text{) } \delta \text{ 97.8, 97.7, 77.2, 75.0, 74.1, 62.3, 61.6, 55.0, 38.8, 38.6, 28.0, 25.576, 25.582, 23.4; IR (thin film) 2940, 1443, 1352, 920 cm}^{-1}\text{; HRMS (Cl/isobutane) } m / z \text{ calcd for C}_7\text{H}_{13}\text{O}_5\text{S (M – H) }^+ \text{ 209.0484, found 209.0488. Anal. Calcd for C}_7\text{H}_{14}\text{O}_5\text{S: } C, 39.99; H, 6.71. \text{ Found: C, 40.12; H, 6.61.}

4-Methanesulfoxytetrahydropyran-1-acetate (14b): An aqueous (10%) solution of HCl (100 mL) was added slowly to a solution of 4-methanesulfoxy-1-methoxytetrahydropyran (2.90 g, 13.8 mmol) in THF (200 mL). After 12 h, the mixture was neutralized with saturated aqueous NaHCO₃. The solvent was removed \textit{in vacuo}, and the remaining aqueous layer was extracted with Et₂O (4 × 150 mL), dried over MgSO₄, filtered, and concentrated \textit{in vacuo} to afford the product as a mixture of closed hemiacetal and open aldehyde isomers. A small amount of residual starting material (0.987 g, 4.69 mmol) was removed by flash chromatography (1:9 to 9:1 Et₂O/pentane). A solution of the hemiacetal/aldehyde mixture (0.558 g, 2.84 mmol), acetic anhydride (1.34 mL, 14.2 mmol), pyridine (0.920 mL, 11.4 mmol) and 4–dimethylaminopyridine (0.419 g, 3.41 mmol) in CH₂Cl₂ (14 mL) was stirred for 24 h. Saturated aqueous NH₄Cl (10 mL) was added, and CH₂Cl₂ was removed \textit{in vacuo}. The residue was dissolved in MTBE (100 mL), and the layers were separated. The organic layer was washed with saturated aqueous Na₂HPO₄ (4 × 25 mL), NaH₂PO₄ (4 × 25 mL), and CuSO₄ (5 × 25 mL), filtered through Na₂SO₄, and concentrated \textit{in vacuo}. The resulting oil was purified by flash chromatography (9:1 to 1:4 pentane/Et₂O) to afford the product (as a 1.1:1 mixture of anomers)
as a colorless oil. The product was prone to hydrolysis and elimination, and decomposition was observed upon concentration and warming above 23 °C (0.643 g, 30% over two steps, based on recovered starting material): ¹H NMR (500 MHz, CDCl₃) δ 6.11 (t, J = 2.3, 1H), 5.94 (t, J = 3.5, 1.1H), 4.84 (m, 1H), 4.74 (ddd, J = 13.4, 7.5, 4.9, 1.1H), 4.03 (dd, J = 13.2, 1.7, 1H), 3.92–3.84 (m, 3.2H), 3.10 (s, 3H), 3.09 (s, 3.3H), 2.21–2.15 (m, 2H), 2.14–2.10 (m, 8.5H), 2.06 (m, 1H), 1.97 (m, 1.1H), 1.88 (m, 1.1H), 1.70 (m, 1H); ¹³C NMR (125 MHz, CDCl₃) δ 169.4, 169.3, 90.8, 90.5, 73.8, 73.2, 64.2, 63.5, 38.9, 38.7, 26.8, 25.6, 23.4, 23.2, 21.01, 20.97; IR (thin film) 2942, 1747, 1348, 1172, 920 cm⁻¹; HRMS (Cl/isobutene) m / z calcd for C₆H₁₁O₅S (M – C₂H₃O)+ 195.0327, found 195.0327.

**IIC. Synthesis of 4-Benzoyloxytetrahydropyran-1-acetate (14c)**

4-Benzoyloxy-1-methoxytetrahydropyran (S6): To a solution of 4-hydroxy-1-methoxytetrahydropyran (0.798 g, 5.96 mmol) in CH₂Cl₂ (32 mL) was added benzoyl chloride
(0.692 mL, 5.96 mmol), pyridine (1.90 mL, 23.8 mmol), and 4-dimethylaminopyridine (1.60 g, 7.15 mmol). The reaction mixture was allowed to stir at 23 °C for 15 h. Ethylenediamine (12 mL) was added, and the mixture was stirred for 2 h. Saturated aqueous NH$_4$Cl (16 mL) was added, and the CH$_2$Cl$_2$ was removed in vacuo. The residue was dissolved in MTBE (30 mL), and the layers were separated. The organic layer was washed with saturated aqueous Na$_2$HPO$_4$ (3 × 50 mL), NaH$_2$PO$_4$ (3 × 50 mL), and CuSO$_4$ (4 × 50 mL), filtered through Na$_2$SO$_4$, and concentrated in vacuo. The resulting oil was purified by flash column chromatography (hexanes to 1:9 EtOAc/hexanes) to afford the product (as a 1:2 mixture of isomers) as a colorless oil (1.25 g, 89%):³ ¹H NMR (500 MHz, CDCl$_3$) δ 8.09 (m, 2H), 8.04 (m, 2H), 7.57 (m, 3H), 7.46 (m, 3H), 5.08 (m, 2H), 4.72 (m, 2H), 4.04 (dd, J = 12.6, 2.0, 2H), 3.85 (m, 1H), 3.74 (m, 1H), 3.44 (s, 3H), 3.42 (s, 3H), 2.22 (m, 2H), 2.02 (m, 2H), 1.86 (m, 2H), 1.66 (m, 2H); ¹³C NMR (125 MHz, CDCl$_3$) δ 166.0, 165.8, 133.01, 132.95, 130.5, 129.7, 128.3, 98.6, 98.2, 68.1, 67.9, 62.7, 61.8, 55.2, 55.0, 28.1, 25.4, 24.8, 22.5; IR (thin film) 3624, 2939, 1724, 1602, 1274 cm$^{-1}$; HRMS (EI/GCMS) m / z calcd for C$_{12}$H$_{13}$O$_3$ (M – CH$_3$O)$^+$ 205.0865, found 205.0868. Anal. Calcd for C$_{13}$H$_{16}$O$_4$: C, 66.09; H, 6.83. Found: C, 65.14; H, 6.83.

4-Benzoxytetracyclopentene-1-ol (S7): A mixture of 4-benzoxy-tetrahydropyran (1.50 g, 6.35 mmol) and 80:20 AcOH:H$_2$O (65 mL) was stirred at 90 °C for 24 h. The reaction mixture was cooled to 23 °C and the solvent was removed in vacuo as an azeotrope with toluene. The resulting oil was purified by flash column chromatography (hexanes to 1:3 EtOAc/hexanes) to afford the product (as a 1:1 mixture of isomers) as a colorless oil (1.15 g, 82%):³ ¹H NMR (500 MHz, CDCl$_3$) δ 8.07 (m, 4H), 7.57 (m, 2H), 7.45
4-Benzoyloxytetrahydropyran-1-acetate (14c): To a stirring solution of 4-benzoyl-tetrahydropyran-1-ol (0.972 g, 4.37 mmol) in CH₂Cl₂ (44 mL) was added pyridine (1.40 mL, 17.5 mmol) followed by 4-dimethylaminopyridine (1.19 g, 5.25 mmol). Acetic anhydride (2.06 mL, 21.9 mmol) was added drop wise to the solution by syringe, and the mixture was stirred for 38 h. Saturated aqueous NH₄Cl (30 mL) was added, and the CH₂Cl₂ was removed in vacuo. The residue was dissolved in MTBE (150 mL), and the organic layer was washed with saturated aqueous Na₂HPO₄ (4 × 50 mL), NaH₂PO₄ (4 × 50 mL), and CuSO₄ (5 × 50 mL), filtered through Na₂SO₄, and concentrated in vacuo. The resulting oil was purified by flash column chromatography (hexanes to 1:9 EtOAc/hexanes) to afford the product (as a 1:1 mixture of diastereomers) as a colorless oil (0.913 g, 79%):³ ¹H NMR (500 MHz, C₆D₆) δ 8.07 (m, 4H), 7.57 (m, 2H), 7.45 (m, 4H), 6.16 (bs, 1H), 5.98 (t, J = 3.6, 1H), 5.14 (m, 2H), 4.10 (dd, J = 12.7, 1.9, 1H), 3.91 (m, 3H), 2.20 (m, 2H), 2.14 (s, 3H), 2.13 (s, 3H), 1.98 (m, 5H), 1.73 (m,1H); ¹³C NMR (125 MHz, CDCl₃) δ 170.3, 170.1, 166.5, 166.2, 133.73, 133.70, 130.7, 130.5, 130.2, 129.0, 128.9, 91.9, 91.8, 67.80, 67.77, 64.9, 64.2, 27.5, 25.2, 24.6, 22.7, 21.71, 21.69; IR (thin film) 2961, 1748, 1719 cm⁻¹; HRMS (EI/GCMS) m/z calcd for C₁₂H₁₃O₃ (M + Na)⁺ 245.0790, found 245.0793. Anal. Calcd for C₁₂H₁₄O₄: C, 64.85; H, 6.35. Found: C, 64.64; H, 6.46.
205.0865, found 205.0868. Anal. calcd for C_{14}H_{16}O_5: C, 63.63; H, 6.10. Found: C, 63.70; H,
6.21.

IID. Synthesis of 4-(p-Anisoyloxy)tetrahydroxyran-1-acetate (14d)

4-(p-Anisoyloxy)-1-methoxytetrahydroxyran (S8): To a solution of 4-hydroxy-1-
methoxytetrahydroxyran (0.050 g, 0.38 mmol) in CH_2Cl_2 (3 mL) was added p-anisoyl chloride
(0.065 g, 0.38 mmol), pyridine (0.121 mL, 1.51 mmol), and 4-dimethylaminopyridine (0.102 g,
0.454 mmol). The reaction mixture was allowed to stir at 23 °C for 15 h. Ethylenediamine
(0.750 mL) was added, and the mixture was stirred for 1 h. Saturated aqueous NH_4Cl (10 mL)
was added, and the CH_2Cl_2 was removed in vacuo. The residue was dissolved in MTBE (15
mL), and the layers were separated. The organic layer was washed with saturated aqueous
Na_2HPO_4 (3 × 25 mL), NaH_2PO_4 (3 × 25 mL), and CuSO_4 (4 × 25 mL), filtered through


Na$_2$SO$_4$, and concentrated in vacuo. The resulting oil was purified by flash column chromatography (hexanes to 1:9 EtOAc/hexanes) to afford the product (as a 1:1 mixture of isomers) as a colorless oil (0.070 g, 69%).$^3$ $^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 7.94 (m, 4H), 6.85 (m, 4H), 4.97 (m, 2H), 4.64 (m, 2H), 3.92 (dd, $J = 12.5, 4.6$, 1H), 3.79 (s, 3H), 3.78 (s, 3H), 3.65 (m, 2H), 3.37 (m, 1H), 3.36 (s, 3H), 3.35 (s, 3H), 2.07 (m, 2H), 1.93–1.76 (m, 3H), 1.58 (m, 3H); $^{13}$C NMR (125 MHz, CDCl$_3$) $\delta$ 166.2, 163.9, 132.1, 123.0, 114.0, 99.1, 98.7, 68.1, 68.0, 63.2, 62.3, 55.8, 55.5, 55.4, 29.0, 25.9, 25.3, 23.0; IR (thin film) 2957, 1711, 1607, 1511, 1258 cm$^{-1}$; HRMS (EI/GCMS) $m/z$ calcd for C$_{14}$H$_{18}$O$_5$ (M)$^+$ 266.1154, found 266.1159. Anal. Calcd for C$_{14}$H$_{18}$O$_5$: C, 63.15; H, 6.81. Found: C, 63.27; H, 6.83.

4-($p$-Anisoyl)tetrahydropyran-1-ol (S9): A mixture of 4-($p$-anisoyl)-1-methoxytetrahydropyran (1.21 g, 4.54 mmol) and 80:20 AcOH:H$_2$O (40 mL) was stirred at 90 °C for 48 h. The reaction mixture was cooled to 23 °C and the solvent was removed in vacuo as an azeotrope with toluene. The resulting oil was purified by flash column chromatography (hexanes to 3:7 EtOAc/hexanes) to afford the product (as a 1:1 mixture of isomers) as a colorless oil (0.872 g, 76%):$^3$ $^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 8.03 (m, 4H), 6.92 (m, 4H), 5.21 (m, 1H), 5.04 (m, 3H), 4.23 (dd, $J = 12.6, 2.1$, 1H), 4.09 (ddd, $J = 11.8, 5.7, 1.3$, 1H), 3.86 (s, 3H), 3.85 (s, 3H), 3.78 (m, 1H), 3.70 (dd, $J = 12.2, 4.0$, 1.6, 1H), 2.23 (m, 1H), 2.11 (m, 2H), 1.85 (m, 4H), 1.65 (m, 1H); $^{13}$C NMR (125 MHz, CDCl$_3$) $\delta$ 167.0, 164.0, 132.23, 132.19, 123.2, 123.1, 114.1, 94.0, 93.0, 68.0, 67.7, 65.3, 63.4, 55.9, 29.1, 27.2, 25.7, 23.5; IR (thin film) 3417, 2956, 1709, 1607, 1169, 1026 cm$^{-1}$; HRMS (EI/GCMS) $m/z$ calcd for C$_{13}$H$_{16}$O$_5$ (M)$^+$

4-($p$-Anisoyl)tetrahydropyran-1-acetate (14d): To a solution of 4-($p$-anisoyl)tetrahydropyran-1-ol (0.391 g, 1.55 mmol) in CH$_2$Cl$_2$ (32 mL) was added pyridine (0.497 mL, 6.20 mmol) followed by 4-dimethylaminopyridine (0.417 g, 1.86 mmol). Acetic anhydride (0.731 mL, 7.75 mmol) was added drop wise to the solution by syringe, and the mixture was stirred for 38 h. Saturated aqueous NH$_4$Cl (25 mL) was added, and the CH$_2$Cl$_2$ was removed in vacuo. The residue was dissolved in MTBE (20 mL), and the organic layer was washed with saturated aqueous Na$_2$HPO$_4$ (4 × 15 mL), NaH$_2$PO$_4$ (4 × 15 mL), and CuSO$_4$ (5 × 15 mL), filtered through Na$_2$SO$_4$, and concentrated in vacuo. The resulting oil was purified by flash column chromatography (hexanes to 1:9 EtOAc/hexanes) to afford the product (as a 1:1 mixture of diastereomers) as a colorless oil (0.366 g, 80%): $^{31}$H NMR (500 MHz, CDCl$_3$) δ 8.03 (m, 4H), 6.93 (m, 4H), 6.16 (m, 1H), 5.99 (t, $J$ = 3.6, 1H), 5.11 (m, 1H), 5.06 (m, 1H), 4.08 (dd, $J$ = 12.7, 1.9, 1H), 3.91 (m, 3H), 3.87 (s, 3H), 3.86 (s, 3H), 2.24 (m, 2H), 2.13 (s, 3H), 2.12 (s, 3H), 2.05 (m, 3H), 1.96 (m, 2H), 1.73 (m, 1H); IR (thin film) 2961, 2939, 1748, 1711, 1607, 1512 cm$^{-1}$; HRMS (EI/GCMS) $m/z$ calcd for C$_{13}$H$_{15}$O$_4$ (M – C$_2$H$_3$O$_2$)$^+$ 235.0970, found 235.0969. Anal. Calcd for C$_{15}$H$_{18}$O$_6$: C, 61.22; H, 6.16. Found: C, 61.48; H, 6.21.
**IIE. Synthesis of 4-(p-Nitrobenzoyloxy)tetrahydropyran-1-acetate (14e)**

![Diagram showing the synthesis of 4-(p-Nitrobenzoyloxy)tetrahydropyran-1-acetate (14e)](image)

4-(p-Nitrobenzoyloxy)-1-methoxytetrahydropyran (S10): To a solution of 4-hydroxy-1-methoxytetrahydropyran (0.506 g, 3.83 mmol) in CH$_2$Cl$_2$ (20 mL) was added 4-nitrobenzoyl chloride (0.711 g, 3.83 mmol), pyridine (1.23 mL, 15.3 mmol), and 4-dimethylaminopyridine (0.561 g, 4.59 mmol). The reaction mixture was allowed to stir at 23 °C for 15 h. Saturated aqueous NH$_4$Cl (25 mL) was added, and the CH$_2$Cl$_2$ was removed in vacuo. The residue was dissolved in MTBE (40 mL), and the layers were separated. The organic layer was washed with saturated aqueous Na$_2$HPO$_4$ (3 × 50 mL), NaH$_2$PO$_4$ (3 × 50 mL), and CuSO$_4$ (4 × 50 mL), filtered through Na$_2$SO$_4$, and concentrated in vacuo. The resulting oil was purified by flash column chromatography (hexanes to 1:9 EtOAc/hexanes) to afford the product as a colorless oil (0.909 g, 84%):$^3$ $^1$H NMR (500 MHz, CDCl$_3$) δ 8.29 (m, 4H), 5.17 (m, 1H), 4.80 (m, 1H), 4.09 (dd, $J = 12.7$, 1.9, 1H), 3.84 (dd, $J = 12.7$, 2.3, 1H), 3.40 (s, 3H), 2.28 (m, 1H), 2.17 (m, 1H),
1.97 (m, 1H), 1.76 (m, 1H); \(^{13}\text{C} \text{ NMR (125 MHz, CDCl}_3) \delta 164.6, 151.1, 136.3, 131.2, 124.0, 98.4, 69.8, 61.8, 55.5, 25.7, 22.8; \text{ IR (thin film) 2957, 1726, 1712, 1517, 1280 cm}^{-1}; \text{ HRMS (EI/GCMS) } m/z \text{ calcd for C}_{13}\text{H}_{16}\text{NO}_6 (M + H)^+ 282.0977, \text{ found 282.0969.} \text{ Anal. Calcd for } C_{13}H_{15}NO_6: \text{ C, 55.51; H, 5.38; N, 4.98. } \text{ Found: C, 55.74; H, 5.47; N, 4.87.}

\[ \text{S11} \]

**4-(\text{p-Nitrobenzoyloxy})tetrahydropyran-1-ol (S11):** A 10% aqueous solution of HCl (5 mL) was added slowly to a solution of 4-(\text{p-nitrobenzoyloxy})-1-methoxytetrahydropyran (0.105 g, 0.395 mmol) in THF (10 mL). The reaction mixture was stirred at 90 °C for 18 h and allowed to cool to 23 °C. The mixture was neutralized with saturated aqueous NaHCO\(_3\) (15 mL), extracted with Et\(_2\)O (5 \times 25 mL), dried over MgSO\(_4\), filtered, and concentrated \textit{in vacuo}. The colorless oil was purified by flash chromatography (hexanes to 3:7 EtOAc/hexanes) to afford the product (as a 1:1 mixture of isomers) as a colorless oil (0.093 g, 93%).\(^3\) \(^{1}\text{H NMR (500 MHz, CDCl}_3) \delta 8.30 (m, 8H), 5.27 (m, 1H), 5.13–5.04 (m, 3H), 4.27 (dd, J = 12.4, 2.3, 1H), 4.16 (dd, J = 12.1, 5.4, 1H), 3.85 (dd, J = 12.0, 3.0, 1H), 3.75 (dt, J = 12.4, 1.6, 1H), 2.33 (m, 1H), 2.21–2.01 (m, 3H), 1.90 (m, 3H), 1.74 (m, 3H); \(^{13}\text{C NMR (125 MHz, CDCl}_3) \delta 164.4, 164.3, 150.9, 150.8, 135.9, 135.8, 131.1, 131.0, 123.78, 123.77, 93.8, 92.3, 69.5, 68.9, 64.9, 62.4, 28.7, 26.5, 25.5, 22.8; \text{ IR (thin film) 3405, 2940, 1737, 1705, 1606 cm}^{-1}.}
4-(p-Nitrobenzoyloxy)tetrahydropryan-1-acetate (14e): To a solution of 4-(p-nitrobenzoyloxy)tetrahydropryan-1-ol (0.074 g, 0.277 mmol) in CH₂Cl₂ (5 mL) was added pyridine (0.889 mL, 1.11 mmol) followed by 4-dimethylaminopyridine (0.041 g, 0.34 mmol). Acetic anhydride (0.130 mL, 1.38 mmol) was added drop wise to the solution by syringe, and the mixture was stirred for 44 h. Saturated aqueous NH₄Cl (5 mL) was added, and the CH₂Cl₂ was removed in vacuo. The residue was dissolved in MTBE (20 mL), and the organic layer was washed with saturated aqueous Na₂HPO₄ (4 × 15 mL), NaH₂PO₄ (4 × 15 mL), and CuSO₄ (5 × 15 mL), filtered through Na₂SO₄, and concentrated in vacuo. The resulting oil was purified by flash column chromatography (hexanes to 1:9 EtOAc/hexanes) to afford the product (as a 1:1 mixture of diastereomers) as a colorless oil (0.054 g, 63%).

¹H NMR (500 MHz, CDCl₃) δ 8.31–8.21 (m, 8H), 6.18 (m, 1H), 5.99 (m, 1H), 5.18 (m, 2H), 4.69–4.12 (m, 2H), 4.14 (dd, J = 12.9, 1.7, 1H), 3.94 (m, 1H), 2.25–1.75 (m, 8H and s, 6H); ¹³C NMR (125 MHz, CDCl₃) δ 170.0, 169.9, 164.5, 164.3, 151.1, 136.0, 135.8, 131.3, 124.01, 123.98, 123.95, 91.7, 91.6, 69.0, 68.8, 64.8, 63.8, 27.3, 25.1, 24.5, 22.5, 21.52, 21.50; IR (thin film) 2962, 1722, 1608, 1527, 1348, 1272 cm⁻¹; HRMS (GCMS/EI) m/z calcd for C₁₂H₁₂NO₅ (M – C₂H₃O₂)+ 250.0715, found 250.0721. Anal. Calcd for C₁₄H₁₅NO₇: C, 54.37; H, 4.89; N, 4.53. Found: C, 54.42; H, 5.05; N, 4.31.
IIF. Synthesis of 4-Nitrotetrahydropyran-1-acetate (14f)

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\begin{align*}
H_2C=CH_2 + HO-\text{NO}_2 & \quad \text{1. Et}_3\text{N, HCO}_2\text{H, C}_6\text{H}_6 (\text{reflux}) \\
& \quad 2. \text{HCl, MeOH}
\end{align*}
\]

1-Methoxy-4-nitrotetrahydropyran (S12): 4 A 1:1.75 mol mixture of triethylamine and formic acid (0.150 mL) was added to a solution of acrolein (6.57 mL, 98.3 mmol) and 2-nitroethanol (25.1 g, 275 mmol) in benzene (50 mL). The mixture was heated to reflux and stirred for 20 h. The solvent was removed in vacuo, and the resulting brown oil was loaded on to a silica gel column packed with 9:1 hexanes/EtOAc. The reaction mixture was eluted (9:1 to 1:4 hexanes/EtOAc) to provide the product as a brown oil contaminated with inseparable byproducts. The oil was dissolved in methanol (65 mL). Concentrated HCl (0.650 mL) was added, and the mixture was stirred at 50 °C for 24 h. After neutralization with saturated aqueous NaHCO₃, solvent was removed in vacuo. The remaining aqueous layer was extracted with CH₂Cl₂ (3 × 50 mL), and the combined organic layers were filtered through Na₂SO₄ and concentrated in vacuo. The resulting oil was purified by flash chromatography (1:9 to 3:2 Et₂O/pentane) to afford the product (as a 1.1:1 mixture of anomers) as a colorless oil (7.38 g, 47%):³ ¹H NMR (500 MHz, CDCl₃) δ 4.66 (t, J = 2.8, 1.1H), 4.62 (t, J = 2.8, 1H), 4.51 (m, 1H), 4.38 (quint, J = 3.5, 1.1H), 4.26 (dt, J = 12.8, 2.5, 1.1H), 4.14 (dd, J = 11.8, 3.0, 1.1H), 4.11 (t, J = 10.2, 1H), 3.99 (ddd, J = 11.1, 4.5, 1.8, 1H), 3.40 (s, 3.3H), 3.39 (s, 3H), 2.44–2.36 (m, 2.1H), 2.31–2.19 (m, 2.1H), 2.02 (m, 1.1H), 1.93 (ddt, J = 13.9, 4.5, 2.6, 1H); ¹³C NMR
(125 MHz, CDCl₃) δ 98.0, 97.4, 79.1, 78.9, 60.3, 59.9, 55.2, 55.0, 28.0, 25.4, 23.2, 20.9; IR (thin film) 2942, 1549, 1050, 850 cm⁻¹; HRMS (Cl/isobutane) m / z calcd for C₅H₈NO₃ (M – CH₃O)⁺ 130.0504, found 130.0507. Anal. Calcd for C₆H₁₁NO₄: C, 44.72; H, 6.88; N, 8.69. Found: C, 44.89; H, 6.98; N, 8.71.

4-Nitrotetrahydropyran-1-ol (S13): An aqueous (10%) solution of HCl (50 mL) was added slowly to a solution of 1-methoxy-4-nitrotetrahydropyran (4.36 g, 27.1 mmol) in THF (100 mL). After 24 h, the mixture was neutralized with saturated aqueous NaHCO₃. The solvent was removed in vacuo, and the remaining aqueous layer was extracted with Et₂O (4 × 100 mL), dried over MgSO₄, filtered, and concentrated in vacuo. The resulting white solid was purified by flash chromatography (1:9 to 3:2 Et₂O/pentane) to afford the product (as a 3.8:1 mixture of anomers) as a white solid (3.67 g, 92%).³ mp 98-100 °C; ¹H NMR (500 MHz, CDCl₃) δ 5.16 (dd, J = 7.1, 3.7, 3.8H), 5.08 (dd, J = 7.5, 4.3, 1H), 4.48–4.41 (m, 5.8H), 4.38 (dd, J = 12.5, 3.2, 3.8H), 4.20 (dd, J = 12.5, 4.0, 3.8H), 3.98 (m, 1H), 2.74 (dd, J = 3.9, 1.5, 3.8H), 2.53 (m, 1H), 2.43–2.34 (m, 8.6H), 2.17 (m, 1H), 2.05 (m, 3.8H), 1.91 (m, 1H), 1.83 (m, 1H), 1.66 (ddd, J = 14.2, 9.0, 5.2, 3.8H)¹³C NMR (125 MHz, C₆D₆) δ 93.6, 92.6, 79.4, 79.1, 63.5, 61.3, 28.9, 27.2, 23.8, 22.0; IR (KBr pellet) 3360, 2948, 1543, 1060, 964, 850 cm⁻¹; HRMS (Cl/isobutene) m / z calcd for C₅H₉NO₃ (M – OH)⁺ 130.0504, found 130.0498. Anal. Calcd for C₅H₉NO₄: C, 40.82; H, 6.17; N, 9.52. Found: C, 41.02; H, 6.17; N, 9.54.

4-Nitrotetrahydropyran-1-acetate (14f): A solution of 4-nitrotetrahydropyran-1-ol (0.930 g, 6.32 mmol) in acetic anhydride (8.0 mL) was cooled to 0 °C. Pyridine (0.511 mL, 6.32 mmol)
was added slowly, and the mixture was stirred at 0 °C for 3 h and poured into a separatory funnel containing saturated aqueous NaHCO₃ (100 mL) and pentane (100 mL). The layers were separated, and the aqueous layer was extracted with pentane (2 × 100 mL). The combined organic layers were washed with H₂O (100 mL) and brine (100 mL), filtered through Na₂SO₄, and concentrated in vacuo. The resulting pale blue oil was purified by flash chromatography (1:9 to 2:3 EtOAc/hexanes) to afford the product (as a 1.2:1 mixture of anomers) as a colorless oil (0.486 g, 41%).³ ¹H NMR (500 MHz, CDCl₃) δ 6.04 (br s, 1H), 6.01 (t, J = 2.9, 1.2H), 4.56 (m, 1.2H), 4.45 (m, 1H), 4.41 (m, 1H), 4.23 (t, J = 2.9, 1H), 4.19 (m, 1.2H), 4.12 (m, 1.2H), 2.53 (m, 1H), 2.44 (m, 1.2H), 2.35–2.25 (m, 2.2H), 2.14 (s, 3H), 2.13 (m, 1H), 2.12 (s, 3.6H), 2.00 (m, 1.2H), 1.91 (m, 1.2H), 1.73 (ddd, J = 14.4, 7.2, 4.3, 1H); ¹³C NMR (125 MHz, CDCl₃) δ 169.10, 169.06, 90.5, 89.9, 78.1, 78.0, 62.2, 61.4, 26.5, 24.0, 22.9, 20.7, 20.2; IR (thin film) 2946, 1750, 1546, 1374, 1046, 935 cm⁻¹; HRMS (CI/isobutene) m / z calcd for C₅H₈NO₄ (M – C₂H₃O)+ 146.0453, found 146.0457. Anal. Calcd for C₇H₁₁NO₅: C, 44.45; H, 5.86; N, 7.40. Found: C, 44.26; H, 5.78; N, 7.34.

**IIG. Synthesis of 4-Azidotetrahydropyran-1-acetate (14g)**

4-Azido-1-methoxytetrahydropyran (S14): Sodium azide (1.55 g, 23.8 mmol) was added to a solution of 4-methanesulfoxy-1-methoxytetrahydropyran in DMF (50 mL), and the mixture
was stirred at 80 °C for 48 h, cooled to 22 °C, and poured into H2O (300 mL). The mixture was extracted with Et2O (4 × 100 mL), and the combined organic layers were dried over MgSO4, filtered, and concentrated in vacuo. The resulting oil was purified by flash chromatography (1:5 Et2O/pentane) to afford the product (as a 1.3:1 mixture of anomers) as a colorless oil (0.720 g, 95%): 1H NMR (500 MHz, CDCl3) δ 4.61–4.58 (m, 2.3H), 3.95 (dd, J = 12.0, 2.6, 1H), 3.63 (ddd, J = 10.9, 4.8, 1.6, 1.3H), 3.60–3.56 (m, 2.3H), 3.52 (ddd, J = 12.0, 4.0, 1.9, 1H), 3.47 (m, 1.3H), 3.40 (s, 3H), 3.37 (s, 3.9H), 2.12 (ddt, J = 13.5, 11.2, 4.0, 1H), 2.00 (ddddd, J = 13.6, 11.2, 4.2, 3.2, 1H), 1.94–1.83 (m, 3.6H), 1.76–1.67 (m, 2.3H), 1.57 (m, 1.3H); 13C NMR (125 MHz, CDCl3) δ 98.7, 97.3, 62.1, 61.9, 55.6, 55.5, 55.2, 54.8, 28.4, 25.9, 23.9, 23.1; IR (thin film) 2938, 2101, 1257, 1130 cm⁻¹; HRMS (Cl/isobutane) m / z calcd for C₆H₁₀N₃O₂ (M – H)⁺ 156.0773, found 156.0774.

**4-Azidotetrahydropyran-1-ol (S15):** An aqueous (10%) solution of HCl (10 mL) was added slowly to a solution of 1-azido-1-methoxytetrahydropyran (0.496 g, 3.16 mmol) in THF (20 mL). After 24 h, the mixture was neutralized with saturated aqueous NaHCO₃. The solvent was removed in vacuo, and the remaining aqueous layer was extracted with Et2O (4 × 50 mL), dried over MgSO4, filtered, and concentrated in vacuo. The resulting oil was purified by flash chromatography (1:4 to 1:2 Et₂O/pentane) to afford the product (as a 1:1 mixture of anomers) as a colorless oil (0.428 g, 95%): 1H NMR (500 MHz, CDCl₃) δ 5.07–5.02 (m, 2H), 4.12 (ddd, J = 11.8, 3.1, 0.9, 1H), 3.87 (dd, J = 11.4, 8.0, 1H), 3.67 (ddd, J = 11.4, 3.9, 1.4, 1H), 3.58 (ddd, J = 13.1, 6.7, 3.6, 1H), 3.51–3.46 (m, 2H), 3.03 (br s, 1H), 2.95 (br s, 1H), 2.18 (m, 1H), 2.06–1.81 (m, 4H), 1.80–1.65 (m, 2H), 1.58 (m, 1H); 13C NMR (125 MHz, CDCl₃) δ 93.1, 92.1, 63.8, 63.4, 55.3, 55.2, 28.6, 27.6, 24.2, 24.0; IR (thin film) 3399, 2951, 2103, 1259 cm⁻¹;
HRMS (Cl/isobutane) \( m/z \) calcd for \( C_5H_8N_3O \) (M – OH)\(^+\) 126.0667, found 126.0671. Anal. Calcd for \( C_5H_9N_3O_2 \) C, 41.95; H, 6.34. Found: C, 41.52; H, 6.39.

**4-Azidotetrahydropyran-1-acetate (14g):** A solution of 4-azidotetrahydropyra-1-ol (0.193 g, 1.35 mmol), acetic anhydride (0.636 mL, 6.74 mmol), pyridine (0.436 mL, 5.39 mmol) and 4–dimethylaminopyridine (0.199 g, 1.62 mmol) in \( CH_2Cl_2 \) (20 mL) was stirred for 24 h. Saturated aqueous \( NH_4Cl \) (10 mL) was added, and \( CH_2Cl_2 \) was removed in vacuo. The residue was dissolved in MTBE (75 mL), and the layers were separated. The organic layer was washed with saturated aqueous \( Na_2HPO_4 \) (4 × 20 mL), \( NaH_2PO_4 \) (4 × 20 mL), and \( CuSO_4 \) (5 × 20 mL), filtered through \( Na_2SO_4 \), and concentrated in vacuo. The resulting oil was purified by flash chromatography (1:4 \( Et_2O/pentane \)) to afford the product (as a 1:1 mixture of anomers) as a colorless oil (0.239 g, 96%).\(^3\) \(^1\)H NMR (500 MHz, \( CDCl_3 \)) \( \delta \) 6.02–5.99 (m, 2H), 4.02 (dd, \( J = 13.3, 3.6, 1H \)), 3.78 (ddd, \( J = 11.0, 4.4, 1.9, 1H \)), 3.70–3.62 (m, 3H), 3.55 (m, 1H), 2.18–2.06 (m, 8H), 2.02 (m, 1H), 1.94–1.79 (m, 4H), 1.65 (m, 1H); \(^{13}\)C NMR (125 MHz, \( CDCl_3 \)) \( \delta \) 169.5, 169.4, 91.5, 90.3, 63.9, 63.8, 55.1, 54.9, 27.3, 24.5, 23.9, 22.8, 21.0; IR (thin film) 2944, 2105, 1748, 1242, 1209 cm\(^{-1}\); HRMS (Cl/isobutane) \( m/z \) calcd for \( C_7H_{11}N_3O_3 \) (M – \( C_2H_5O_2 \))\(^+\) 126.0667, found 126.0664. Anal. Calcd for \( C_7H_{11}N_3O_3 \): C, 45.40; H, 5.99. Found: C, 45.67; H, 6.16.
III. Synthesis of 4–Fluorotetrahydropyran–1–acetate (21a)

Ethyl-2-fluoro-4-pentenoate (S16): Allyl bromide (57.01 g, 471.3 mmol) was added to a solution of ethyl fluoroacetate (50.00 g, 471.3 mmol) in benzene and HMPA (236 mL and 118 mL) respectively. Sodium hydride (11.31 g, 471.3 mmol) was washed with hexanes (3 × 150 mL) and added to the solution. The reaction mixture was stirred and heated at 80 °C for 12 h. The reaction mixture was cooled to 23 °C and H₂O was added (350 mL), and the layers were separated. The organic layer was washed with H₂O (3 × 150 mL), and the aqueous layer was neutralized with 0.1 M H₂SO₄. The aqueous layer was extracted with Et₂O (3 × 240 mL). The combined organic layers were washed with saturated aqueous NaCl (350 mL), dried over
MgSO₄, filtered, and concentrated in vacuo. The resulting yellow oil was purified by flash column chromatography (pentane to 1:9 Et₂O/pentane) to afford the product as a colorless oil (33.39 g, 48%): ¹H NMR (500 MHz, CDCl₃) δ 5.87–5.78 (m, 1H), 5.22–5.17 (m, 2H), 5.01–4.89 (ddd, J = 48.7, 6.9, 4.6, 1H), 4.26 (q, J = 7.1, 2H), 2.68–2.61 (m, 2H), 1.31 (t, J = 7.1, 3H); ¹³C NMR (125 MHz, CDCl₃) δ 169.8 (d, J = 24), 131.41 (d, J = 4), 119.7, 89.3 (d, J = 185), 61.9, 37.2 (d, J = 21), 14.6; ¹⁹F NMR (376 MHz, CDCl₃) δ –191.6 (m); IR (thin film) 2978, 1756, 1278, 1211, 1072, 750 cm⁻¹; HRMS (EI/GCMS) m/z calcd for C₇H₁₁FO₂ (M)⁺ 146.0743, found 146.0745.

OTBDPS

1-(tert-Butyldiphenylsilyloxy)-2-fluoropent-4-en (S17): A suspension of LiAlH₄ (6.08 g, 160 mmol) in Et₂O (1033 mL) was cooled to 0 °C, and a solution of ethyl-2-fluoro-4-pentenoate (15.71 g, 80.08 mmol) in Et₂O (235 mL) was added dropwise. The reaction mixture was warmed to 23 °C and stirred for 18 h before dropwise addition of H₂O (8.40 mL), 15% NaOH (8.40 mL), and H₂O (25.0 mL). Anhydrous Na₂SO₄ (15.7 g) was added, and the mixture was filtered, dried over MgSO₄, filtered, and concentrated in vacuo to afford a yellow oil. Because of the volatility of the alcohol, the impure oil was submitted to silylation conditions. To a solution of 2-fluoro-4-penten-1-ol in DMF (94 mL) were added tert-butyldiphenylsilyl chloride (24.2 g, 88.1 mmol) and imidazole (12.0 g, 176 mmol). After 12 h, the mixture was diluted with Et₂O (650 mL) and washed with H₂O (200 mL). The layers were separated, and the aqueous layer was extracted with Et₂O (3 × 250 mL), dried over MgSO₄, filtered and concentrated in vacuo. The resulting yellow oil was purified by flash column chromatography (pentane to 1:9 Et₂O/pentane) to afford the desired product as a colorless oil (13.17 g, 48% over two steps): ¹H NMR (500 MHz, CDCl₃) δ 7.69–7.67 (m, 4H), 7.43–7.36 (m, 6H), 5.78 (m, 1H), 5.14–5.10 (m, 1H), 5.08 (m, 1H), 4.63 (m, 1H), 3.78–3.74 (m, 2H), 2.49–2.43 (m, 2H), 1.07 (s, 9H); ¹³C NMR (125 MHz, CDCl₃)
δ 136.14, 136.12, 133.80, 133.4, 130.3, 128.3, 94.3 (d, J = 174), 65.6 (d, J = 24), 36.3 (d, J = 21), 27.3 (d, J = 14), 19.8; 19F NMR (376 MHz, CDCl3) δ –186.4 (dq, J = 51.2, 23.3); IR (thin film) 3067, 2922, 1422, 1111, 756, 700 cm⁻¹; HRMS (EI/GCMS) m / z calcd for C₁₇H₁₈FO₂Si (M – C₄H₉)+ 285.1111, found 285.1113. Anal. Calcd for C₂₁H₂₇FO₂Si: C, 73.64; H, 7.95. Found: C, 74.01; H, 8.37.

1-(tert-Butyldiphenylsilyloxy)-2-fluoropentan-5-ol (S18): To a solution of 1-(tert-butyldiphenylsilyloxy)-2-fluoropent-4-ene (9.00 g, 26.3 mmol) in THF (22 mL) at 0 °C was added 10 M BH₃·SMe₂ (1.1 mL). The reaction mixture was allowed to warm to 23 °C and stirred for 72 h. The reaction mixture was cooled to 0 °C and 10% NaOH (31 mL) followed by 30% H₂O₂ (15 mL) were added. The reaction mixture was allowed to warm to 23 °C and stirred for 48 h. Solid K₂CO₃ (45.6 g) was added and the mixture was stirred for an additional 2 h. The layers were separated, and the aqueous layer was extracted with Et₂O (3 × 50 mL). The combined organic phases were dried over MgSO₄, filtered and concentrated in vacuo. The resulting yellow oil was purified by flash column chromatography (1:9 Et₂O/pentane to 2:3 Et₂O/pentane) to afford a colorless oil (7.86 g, 83%): 1H NMR (500 MHz, CDCl₃) δ 7.68 (m, 4H), 7.41–7.35 (m, 6H), 4.64–4.51 (m, 1H), 3.78–3.72 (dd, J = 22.6, 4.5, 2H), 3.60 (m, 2H), 2.22 (bs, 1H), 1.75–1.58 (m, 4H), 1.07 (s, 9H); 13C NMR (125 MHz, CDCl₃) δ 135.9, 133.60, 133.57, 130.1, 128.1, 95.0 (d, J = 170), 66.1 (d, J = 24), 62.6, 28.4 (d, J = 4), 27.8 (d, J = 21), 27.1, 19.6; 19F NMR (376 MHz, CDCl₃) δ –186.8 (m); IR (thin film) 3389, 2944, 1428, 1113, 758, 703 cm⁻¹; HRMS (EI/GCMS) m / z calcd for C₁₇H₁₈FO₂Si (M – C₄H₉)+ 303.1217, found 303.1220. Anal. Calcd for C₂₁H₂₇FO₂Si: C, 69.96; H, 8.11. Found: C, 69.90; H, 8.23.
**5-(tert-Butyldiphenylsilyloxy)-4-fluoropentanal (S19):** Dess–Martin periodinane\(^6,7\) (0.828 g, 1.95 mmol) was added to a solution of 1-(tert-butyldiphenylsilyloxy)-2-fluoropentan-5-ol (0.502 g, 1.39 mmol) in CH\(_2\)Cl\(_2\) (13 mL). The mixture was stirred for 16 h. A saturated aqueous solution of NaHCO\(_3\) and Na\(_2\)S\(_2\)O\(_3\) (30 mL) was added. After stirring for 15 min, the layers were separated and the aqueous layer was extracted with CH\(_2\)Cl\(_2\) (3 \(\times\) 60 mL). The combined organic phases were washed with saturated aqueous NaHCO\(_3\) (30 mL), dried over Na\(_2\)SO\(_4\), and concentrated in vacuo. The resulting oil was purified by flash column chromatography (pentane to 1:4 Et\(_2\)O/pentane) to afford the product as a colorless oil (0.473 g, 95%): \(^1\)H NMR (500 MHz, CDCl\(_3\)) \(\delta\) 9.75 (s, 1H), 7.67 (m, 4H), 7.42–7.36 (m, 6H), 4.65–4.50 (m, 1H), 3.79–3.73 (m, 2H), 2.57 (m, 2H), 2.00 (m, 2H), 1.07 (s, 9H); \(^13\)C NMR (125 MHz, CDCl\(_3\)) \(\delta\) 201.8, 136.11, 136.09, 133.62, 133.60, 130.4, 128.3, 94.0 (d, \(J = 173\)), 65.9 (d, \(J = 24\)), 39.8 (d, \(J = 4\)), 27.3, 24.2 (d, \(J = 21\)), 19.8; \(^19\)F NMR (376 MHz, CDCl\(_3\)) \(\delta\) –189.0 (m); IR (thin film) 2932, 1726, 1428, 1113, 911, 735 cm\(^{-1}\); HRMS (EI/GCMS) \(m/\text{z}\) calcld for C\(_{17}\)H\(_{18}\)FO\(_2\)Si (M – C\(_4\)H\(_9\))\(^+\) 301.1060, found 301.1062. Anal. Calcld for C\(_{21}\)H\(_{27}\)FO\(_2\)Si: C, 70.35; H, 7.59. Found: C, 70.28; H, 7.59.

**5-(tert-Butyl(diphenylsilyloxy)-4-fluoropent-dibenzylaceal (S20):**\(^8\) A solution of 5-(tert-butyldiphenylsilyloxy)-4-fluoropentanal (0.672 g, 1.87 mmol), benzyl alcohol (0.446 g, 4.12 mmol), and \(p\)-toluenesulfonic acid monohydrate (0.004 g, 0.019 mmol) in benzene (24 mL)
was heated to 80 °C for 20 h employing a Dean Stark trap. The reaction mixture was cooled to 23 °C, washed with saturated aqueous NaHCO₃ (3 × 10 mL), dried over MgSO₄, filtered and concentrated in vacuo. The resulting oil was purified by flash column chromatography (pentane to 1:4 Et₂O/pentane) to afford the product as a colorless oil (1.38 g, 86%): ¹H NMR (500 MHz, CDCl₃) δ 7.67 (m, 4H), 7.42–7.27 (m, 16H), 4.75 (t, J = 5.4, 1H), 4.67 (d, J = 5.0, 1H), 4.64 (d, J = 4.9, 1H), 4.55 (m, 3H), 3.73 (m, 2H), 1.93–1.75 (m, 4H), 1.06 (s, 9H); ¹³C NMR (125 MHz, CDCl₃) δ 138.6, 136.1, 133.8, 130.2, 129.1, 128.93, 128.90, 128.3, 128.2, 128.12, 128.08, 102.3, 94.9 (d, J = 170), 68.0 (d, J = 26), 66.2 (d, J = 24), 29.3 (d, J = 4), 27.3, 27.1 (d, J = 21), 19.8; ¹⁹F NMR (376 MHz, CDCl₃) δ –187.6 (m); IR (thin film) 3067, 2922, 1422, 1111, 1022, 733 cm⁻¹; HRMS (EI/GCMS) m / z calcd for C₃₅H₄₁FO₃SiNa (M + Na)⁺ 579.2707, found 579.2709. Anal. Calcd for C₃₅H₄₁FO₃Si: C, 75.50; H, 7.42. Found: C, 75.50; H, 7.44.

4-Fluoro-1,1-dibenzyloxy-5-pentanol (S21): Tetrabutylammonium fluoride was added as a 1 M solution in THF (1.4 mL) to a solution of 5-(tert-butyldiphenylsilyloxy)-4-fluoropent-dibenzylacetal (0.638 g, 1.15 mmol) in THF (13 mL). The mixture was allowed to stir for 20 h at 23 °C. Saturated aqueous NH₄Cl (4 mL) was added, and the layers were separated. The aqueous layer was extracted with Et₂O (3 × 10 mL). The combined organic layers were washed with saturated aqueous NaCl (4 mL), dried over MgSO₄, filtered and concentrated in vacuo. The resulting oil was purified by flash column chromatography (1:8 Et₂O/pentane to 1:1 Et₂O/pentane) to afford the product as a colorless oil (0.314 g, 86%): ¹H NMR (500 MHz, CDCl₃) δ 7.32–7.25 (m, 10H), 4.73 (t, J = 5.5, 1H), 4.64 (dd, J = 11.7, 3.8, 4H), 4.53 (d, J = 11.7, 1H), 3.61–3.54 (m, 2H), 2.63 (bs, 1H), 1.94–1.89 (m, 1H), 1.83–1.71 (m, 3H); ¹³C NMR (125 MHz, CDCl₃) δ 138.8, 138.6, 129.00, 128.97, 128.9, 128.8, 128.6, 128.5, 128.4, 128.3, 128.2, 128.12, 128.05,
4-Fluoro-1-benzyloxytetrahydropyran (S22):" p-Toluenesulfonic acid monohydrate (0.005 g, 0.010 mmol) was added to a solution of 4-fluoro-1,1-dibenzyloxy-5-pentanol (0.314 g, 0.986 mmol) in CH$_2$Cl$_2$ (1.2 mL) at 0 °C. After 17 h, the solution was concentrated in vacuo to afford a yellow oil. The unpurified product was purified by flash column chromatography (1:9 Et$_2$O/pentane to 4:7 Et$_2$O/pentane) to afford the product (as a 3:5 mixture of isomers) as a colorless oil (0.168 g, 81%): $^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 7.36–7.25 (m, 10H), 4.91 (bs, 1H), 4.78 (d, $J$ = 12.0, 1H), 4.73 (d, $J$ = 12.0, 1H), 4.69 (m, 1H), 4.59–4.50 (m, 4H), 3.95–3.74 (m, 4H), 2.13–2.07 (m, 3H), 1.93–1.90 (m, 3H), 1.75 (m, 1H), 1.65 (m, 1H); $^{13}$C NMR (125 MHz, CDCl$_3$) $\delta$ 138.4, 138.2, 128.9, 128.3, 128.23, 128.16, 128.1, 96.9, 96.3, 87.3 (d, $J$ = 48), 85.9 (d, 49), 69.5, 69.4, 64.0 (d, $J$ = 25), 62.6 (d, $J$ = 20), 28.2 (d, $J$ = 6), 26.4 (d, $J$ = 20), 24.9 (d, $J$ = 1), 23.4 (d, $J$ = 21); $^{19}$F NMR (376 MHz, CDCl$_3$) $\delta$ –186.9 (m), –189.5 (m); IR (thin film) 2933, 1450, 1367, 1211, 1078, 1033, 978, 911, 728 cm$^{-1}$; HRMS (EI/GCMS) $m/z$ calcd for C$_{12}$H$_{15}$FO$_2$ (M) $^+$ 210.1056, found 210.1058. Anal. Calcd for C$_{12}$H$_{15}$FO$_2$: C, 68.55; H, 7.19. Found: C, 68.65; H, 7.16.
4-Fluorotetrahydropyran-1-acetate (21a): Palladium on carbon (10%, 0.153 g) was added to a solution of 4-fluoro-1-benzyloxytetrahydropyran (0.168 g, 0.801 mmol) in CD$_2$Cl$_2$ (4 mL) and the mixture was purged with H$_2$, then allowed to stir in a sealed vessel at 1 atm. After filtering the solution, acetic anhydride (0.378 g, 3.70 mmol), pyridine (0.259 mL, 3.20 mmol), and 4-dimethylaminopyridine (0.118 g, 0.962 mmol) were added. The reaction mixture was allowed to stir for 24 h. Saturated aqueous NH$_4$Cl (2 mL) was added and the CH$_2$Cl$_2$ was removed in vacuo. The residue was dissolved in MTBE (1.5 mL). The organic layer was washed with saturated aqueous Na$_2$HPO$_4$ (4 × 1 mL), NaH$_2$PO$_4$ (4 × 1 mL), and CuSO$_4$ (5 × 1 mL), filtered through Na$_2$SO$_4$, and concentrated in vacuo. The resulting oil was purified by flash column chromatography (pentane to 1:4 Et$_2$O/pentane) to afford the product (as a 1:1 mixture of isomers) as a colorless oil (0.085 g, 35%): $^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 6.13 (bs, 1H), 5.87 (m, 1H), 4.73–4.55 (m, 1H and dtt, $J = 47.9$, 7.6, 3.7, 1H), 4.00–3.81 (m, 4H), 2.20 (m, 1H), 2.11 (m, 3H), 2.10 (m, 3H), 1.97 (m, 5H), 1.81 (m, 1H), 1.64 (m, 1H); $^{13}$C NMR (125 MHz, CDCl$_3$) $\delta$ 169.6, 169.5, 91.21, 91.20, 85.9 (d, $J = 40$), 84.6 (d, $J = 40$), 65.2 (d, $J = 26$), 63.7 (d, $J = 21$), 26.3 (d, $J = 6$), 25.7 (d, $J = 20$), 23.2 (d, $J = 1$), 22.4 (d, $J = 21$), 21.1 (d, $J = 3$); $^{19}$F NMR (376 MHz, CDCl$_3$) $\delta$ -187.4 (m), -190.1 (m); IR (thin film) 2960, 1751, 1441, 1373, 1243, 1211, 1140, 1050 cm$^{-1}$; HRMS (EI/GCMS) $m/z$ calcd for C$_6$H$_4$FO$_3$ (M − CH$_3$)$^+$ 147.0457, found 147.0462. Anal. Calcd for C$_7$H$_{11}$FO$_3$: C, 51.85; H, 6.84. Found: C, 52.12; H, 6.74,
**III. Synthesis of 4-Chlorotetrahydropyran-1-acetate (21b)**

![Chemical reaction diagram]

4-Chlorotetrahydropyran-1-ol (S23): A solution of anhydrous zinc chloride (9.06 g, 66.5 mmol) in THF (600 mL) and a solution of diethyl azodicarboxylate (34.8 g, 200 mmol) in THF (120 mL) were added consecutively to a solution of 4-hydroxy-1-methoxytetrahydropyran (8.79 g, 66.5 mmol) and triphenylphosphine (52.3 g, 200 mmol) in THF (600 mL). The mixture was stirred at 23 °C for 10 h and concentrated *in vacuo*. The triphenylphosphine oxide was removed by flash chromatography (1:49 to 1:9 Et₂O/pentane) to afford the impure product as a volatile, colorless oil. Because inseparable impurities were present, the impure methyl acetal was submitted to hydrolysis conditions. A 10% aqueous solution of HCl (200 mL) was added slowly to a solution of methyl acetal in THF (400 mL). After 10 h, the mixture was neutralized with saturated aqueous NaHCO₃, extracted with Et₂O (4 × 150 mL), dried over MgSO₄, filtered, and concentrated *in vacuo*. The resulting oil was purified by flash chromatography (1:9 to 1:4 Et₂O/pentane) to afford the product (as a 1:1 mixture of anomers) as a volatile colorless oil (4.26 g, 47% over two steps): ³¹H NMR (500 MHz, CDCl₃) δ 5.12 (dd, J = 7.0, 3.3, 1H), 5.02 (dt, J = 7.6, 2.8, 1H), 4.21 (ddd, J = 11.9, 3.4, 1.2, 1H), 4.05 (m, 1H), 3.99–3.95 (m, 2H), 3.76 (m, 1H), 3.56 (ddd, J = 11.9, 6.7, 0.9, 1H), 2.81 (d, J = 3.3, 1H), 2.67 (s, 1H), 2.35 (m, 1H), 2.15–2.06 (m, 3H), 1.91 (m, 1H), 1.86–1.78 (m, 2H), 1.59 (m, 1H); ¹³C NMR (125 MHz, CDCl₃) δ 93.6, 91.5, 67.5, 65.5, 54.0, 53.8, 29.8, 29.3, 29.0, 28.7; IR (thin film) 3391, 2959, 1440 cm⁻¹; HRMS (CI/isobutane) m/z calcd for C₅H₉O₂Cl (M)+ 136.0291, found 136.0290.
4-Chlorotetrahydropyran-1-acetate (21b): A solution of 4-chlorotetrahydropyran-1-ol (2.53 g, 18.5 mmol), acetic anhydride (8.74 mL, 92.6 mmol), pyridine (5.99 mL, 74.1 mmol) and 4-dimethylaminopyridine (2.73 g, 22.2 mmol) in CH$_2$Cl$_2$ (250 mL) was stirred for 24 h. Saturated aqueous NH$_4$Cl (50 mL) was added, and CH$_2$Cl$_2$ was removed \textit{in vacuo}. The residue was dissolved in MTBE (250 mL), and the layers were separated. The organic layer was washed with saturated aqueous Na$_2$HPO$_4$ (4 × 50 mL), NaH$_2$PO$_4$ (4 × 50 mL), and CuSO$_4$ (5 × 50 mL), filtered through Na$_2$SO$_4$, and concentrated \textit{in vacuo}. The resulting oil was purified by flash chromatography (pentane to 1:4 Et$_2$O/pentane) to afford the product (as a 1:1 mixture of anomers) as a volatile, colorless oil (3.28 g, 99%):$^3$ $^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 6.03 (t, $J = 2.7$, 1H), 6.00 (t, $J = 3.5$, 1H), 4.18–4.14 (m, 2H), 4.00 (ddd, $J = 15.0$, 10.6, 4.5, 1H), 3.87 (ddd, $J = 11.2$, 4.6, 1.8, 1H), 3.78 (t, $J = 10.8$, 1H), 3.72 (m, 1H), 2.33 (m, 1H), 2.28–2.17 (m, 2H), 2.13 (s, 3H), 2.11 (s, 3H), 2.07 (m, 1H), 1.96–1.89 (m, 3H), 1.67 (m, 1H); $^{13}$C NMR (125 MHz, CDCl$_3$) $\delta$ 169.5, 169.3, 91.7, 90.0, 67.3, 66.1, 53.9, 52.7, 28.8, 28.7, 27.6, 25.1, 21.0; IR (thin film) 2965, 1738, 1371 cm$^{-1}$; HRMS (CI/isobutane) $m / z$ calcd for C$_5$H$_8$O$_2$Cl (M – C$_2$H$_3$O)$^+$ 135.0213, found 135.0211.

IIJ. Synthesis of 4-Bromotetrahydropyran-1-acetate (21c)
4-Bromotetrahydropyran-1-ol (S24): A solution of anhydrous zinc bromide (3.44 g, 15.3 mmol) in THF (150 mL) and a solution of diethyl azodicarboxylate (7.99 g, 45.9 mmol) in THF (30 mL) were added consecutively to a solution of 4-hydroxy-1-methoxytetrahydropyran (2.02 g, 15.3 mmol) and triphenylphosphine (12.0 g, 45.9 mmol) in THF (150 mL). The mixture was stirred at 23 °C for 24 h and concentrated in vacuo. The triphenylphosphine oxide was removed by flash chromatography (1:9 Et₂O/pentane) to afford the impure product as a colorless oil. Because inseparable impurities were present, the impure methyl acetal was submitted to hydrolysis conditions. An aqueous (10%) solution of HCl (100 mL) was added slowly to a solution of methyl acetal in THF (200 mL). After 36 h, the mixture was neutralized with saturated aqueous NaHCO₃, extracted with Et₂O (4 × 100 mL), dried over MgSO₄, filtered, and concentrated in vacuo. The product proved to be highly unstable, decomposing quickly upon concentration. The resulting oil could be quickly purified by flash chromatography (1:9 to 1:4 Et₂O/pentane) to afford the product (as a 1:1 mixture of anomers) as a volatile, colorless oil (2.67 g, 96% over two steps):³ ¹H NMR (500 MHz, CDCl₃) δ 5.19 (dd, J = 6.6, 3.2, 1H), 5.01 (m, 1H), 4.23 (ddd, J = 12.0, 3.6, 1.5, 1H), 4.20–4.07 (m, 3H), 3.78 (m, 1H), 3.64 (dd, J = 12.0, 7.2, 1H), 2.80 (d, J = 4.8, 1H), 2.63 (dd, J = 3.8, 1.7, 1H), 2.39 (m, 1H), 2.28 (m, 1H), 2.22–2.07 (m, 2H), 1.98–1.79 (m, 3H), 1.61 (m, 1H); ¹³C NMR (125 MHz, CDCl₃) δ 93.9, 91.3, 68.3, 65.4, 46.1, 45.8, 31.0, 30.64, 30.61, 29.3; IR (thin film) 3396, 2957, 1451, 1057, 735 cm⁻¹; HRMS (Cl/isobutane) m/z calcd for C₅H₉O₂Br (M)⁺ 179.9786, found 179.9785.
4-Bromotetrahydropyran-1-acetate (21c): A solution of 4-bromotetrahydropyran-1-ol (1.88 g, 10.4 mmol), acetic anhydride (4.90 mL, 51.9 mmol), pyridine (3.36 mL, 41.5 mmol) and 4–dimethylaminopyridine (1.53 g, 12.5 mmol) in CH₂Cl₂ (52 mL) was stirred for 24 h. Saturated aqueous NH₄Cl (25 mL) was added, and CH₂Cl₂ was removed in vacuo. The residue was dissolved in MTBE (150 mL), and the layers were separated. The organic layer was washed with saturated aqueous Na₂HPO₄ (4 × 30 mL), NaH₂PO₄ (4 × 30 mL), and CuSO₄ (5 × 30 mL), filtered through Na₂SO₄, and concentrated in vacuo. The resulting oil was purified by flash chromatography (pentane to 1:4 Et₂O/pentane) to afford the product (as a 1:1 mixture of anomers) as a volatile, colorless oil (1.69 g, 73%): ¹H NMR (500 MHz, CDCl₃) δ 6.09 (t, J = 2.7, 1H), 5.98 (dd, J = 4.6, 3.1, 1H), 4.25 (m, 1H), 4.19 (dd, J = 12.5, 3.0, 1H), 4.10 (m, 1H), 3.91 (s, 1H), 3.89 (s, 1H), 3.78 (dd, J = 12.5, 5.1, 1.4, 1H), 2.37 (m, 1H), 2.30–2.17 (m, 3H), 2.13 (s, 3H), 2.10 (s, 3H), 2.01 (m, 1H), 1.95–1.90 (m, 2H), 1.69 (ddt, J = 13.9, 6.7, 4.4, 1H); ¹³C NMR (125 MHz, CDCl₃) δ 169.5, 169.3, 91.7, 89.9, 68.1, 66.2, 46.1, 44.3, 30.0, 29.3, 28.8, 26.5, 21.01, 21.00; IR (thin film) 2939, 1749, 1372, 1220, 1009, 737 cm⁻¹; HRMS (Cl/isobutane) m / z calcd for C₅H₇BrO₂ (M – C₂H₅O)⁺ 178.9708, found 178.9704. Anal. Calcd for C₇H₁₁BrO₃: C, 37.69; H, 4.97. Found: C, 37.90; H, 5.05.

IIK. Synthesis of 4–Iodotetrahydropyran–1–acetate (21d)
4-Iodo-1-methoxymethyltetrahydropyran (S25): A solution of anhydrous zinc iodide (2.41 g, 7.57 mmol) in THF (26 mL) and a solution of diethyl azodicarboxylate (3.95 g, 22.7 mmol) in THF (5 mL) were added consecutively to a solution of 4-hydroxy-1-methoxymethyltetrahydropyran (1.00 g, 7.57 mmol) and triphenylphosphine (5.95 g, 22.7 mmol) in THF (26 mL). The mixture was stirred at 25 °C for 12 h and concentrated in vacuo. The resulting oil was purified by flash column chromatography (pentane to 1:9 Et₂O/pentane) to afford one isomer as a colorless oil (0.751 g, 41%): ¹H NMR (500 MHz, CDCl₃) δ 4.76 (m, 1H), 4.22 (m, 1H), 3.97 (t, J = 11.1, 1H), 3.78 (m, 1H), 3.36 (s, 3H), 2.38 (m, 1H), 2.21 (m, 1H), 1.87 (m, 1H), 1.73 (m, 1H); ¹³C NMR (125 MHz, CDCl₃) δ 97.0, 66.0, 54.8, 32.9, 31.3, 24.2; IR (thin film) 2929, 1123, 1050, 1019 cm⁻¹; HRMS (EI/GCMS) m/z calcd for C₆H₁₁IO₂ (M⁺) 241.9804, found 241.9803. Anal. Calcd for C₆H₁₁O₂: C, 29.77; H, 4.58. Found: C, 29.85; H, 4.55.

4-Iodotetrahydropyran-1-ol (S26): A 10% aqueous solution of HCl (41 mL) was added slowly to a solution of 4-iodo-1-methoxymethyltetrahydropyran (1.83 g, 0.008 mmol) in THF (81 mL). The reaction mixture was stirred at 55 °C for 12 hr and allowed to cool to 23 °C. The mixture was neutralized with saturated aqueous NaHCO₃ and extracted with Et₂O (3 × 30 mL). The organic layers were dried over MgSO₄, filtered, and concentrated in vacuo. The resulting oil was purified by flash column chromatography (1:9 Et₂O/pentane to 3:2 Et₂O/pentane) to afford
the product (as a 1:1 mixture of anomers) as a colorless oil (0.76 g, 45\%): $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 5.29 (d, $J = 3.1$, 1H), 4.95 (m, 1H) 4.24–4.15 (m, 4H), 3.77–3.68 (m, 2H), 3.02 (m, 1H) 2.78 (m, 1H), 2.43–2.35 (m, 2H), 2.20–2.16 (m, 1H), 2.07–2.00 (m, 2H), 1.89–1.80 (m, 2H), 1.65–1.60 (m, 1H); $^{13}$C NMR (125 MHz, CDCl$_3$) $\delta$ 94.4, 91.1, 71.0, 66.8, 32.4, 32.6, 30.9, 24.4, 24.3; IR (thin film) 3391, 2952, 1449, 1270, 1133, 1050 cm$^{-1}$; HRMS (EI/GCMS) $m / z$ calcd for C$_5$H$_9$IO$_2$ (M)$^+$ 227.9649, found 227.9641.

4-Iodotetrahydropyran-1-acetate (21d): A solution of 4-iodotetrahydropyran-1-ol (0.779 g, 3.42 mmol), acetic anhydride (1.61 mL, 17.1 mmol), pyridine (1.10 mL, 13.7 mmol), and 4-dimethylaminopyridine (0.500 g, 4.09 mmol) in CH$_2$Cl$_2$ (34 mL) was stirred for 12 h. Saturated aqueous NH$_4$Cl (10 mL) was added and the CH$_2$Cl$_2$ layer was separated and removed in vacuo. The residue was dissolved in MTBE (34 mL) and washed with aqueous Na$_2$HPO$_4$ (3 $\times$ 10 mL), NaH$_2$PO$_4$ (3 $\times$ 10 mL), and CuSO$_4$ (5 $\times$ 10 mL). The organic phases were filtered through Na$_2$SO$_4$ and concentrated in vacuo. The resulting oil was purified by flash chromatography (pentane to 1:10 Et$_2$O/pentane) to afford the product (as a 2:3 mixture of isomers) as a colorless oil (0.776 g, 84\%): $^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 6.18 (t, $J = 2.0$, 1H), 5.90 (m, 1H) 4.33–4.30 (m, 1H), 4.26–4.20 (m, 1H), 4.10–4.06 (dd, $J = 12.4$, 3.3, 1H) 4.02 (t, $J = 11.3$, 1H), 3.90–3.87 (ddd, $J = 11.3$, 4.5, 1.8, 1H), 3.81–3.70 (ddd, $J = 12.4$, 6.4, 1H), 2.35–2.25 (m, 3H), 2.13 (s, 3H and m, 1H), 2.09 (s, 3H), 2.07 (m, 1H), 2.05 (m, 1H), 1.83 (m, 1H), 1.75 (m, 1H); $^{13}$C NMR (125 MHz, CDCl$_3$) $\delta$ 170.0, 169.7, 92.5, 90.5, 71.0, 68.3, 32.1, 32.0, 31.5, 29.7, 24.7, 22.7, 21.6, 21.5; IR (thin film) 2959, 1749, 1371, 1242, 1129, 1049 cm$^{-1}$; HRMS (EI/GCMS) $m / z$ calcd for C$_5$H$_3$IO$_1$ (M – C$_2$H$_3$O$_2$)$^+$ 210.9620, found 210.9622.
III. Synthesis of 2–Isopropyltetrahydropyran–1–acetate (32c)

Ethyl 2-isopropyl-4-pentenoate (S27):\textsuperscript{12} To a stirred solution of diisopropylamine (11.9 mL, 72.2 mmol) in THF (91 mL) at –78 °C was added a solution of \textit{n}-BuLi in hexanes (34 mL, 2.5 M). The resultant pale solution was allowed to stir at –78 °C for 1 h. A solution of isovalerate (10.10 g, 77.6 mmol) in THF (24 mL) was added, and the mixture was allowed to stir for 4 h at –78 °C. Allyl bromide (31 mL, 82 mmol) was added, and the mixture was allowed to warm to 23 °C and stirred for 16 h before addition of 2 N HCl (100 mL). The mixture was poured into Et\textsubscript{2}O (200 mL) and the layers were separated. The aqueous layer was extracted with Et\textsubscript{2}O (3 × 200 mL) and the combined organic layers were washed with saturated aqueous NaHCO\textsubscript{3} (65 mL), dried over MgSO\textsubscript{4}, filtered, and concentrated \textit{in vacuo}. The resulting oil was purified by distillation (100 °C, 760 mmHg) to afford the product as a colorless oil (7.78 g, 63\%): \textsuperscript{1}H NMR (500 MHz, CDCl\textsubscript{3}) \( \delta \) 5.78–5.70 (m, 1H), 5.07–5.03 (ddd, \( J = 17.1, 3.3, 1.4, 1H \)), 4.98 (m, 1H), 4.15–4.10 (m, 2H), 2.36–2.25 (m, 2H), 2.22–2.17 (ddd, \( J = 13.1, 7.3, 4.4, 1H \)), 1.92–1.85 (m, 1H), 1.25 (t, \( J = 7.1, 3H \)), 0.96 (d, \( J = 6.8, 3H \)), 0.93 (d, \( J = 6.8, 3H \)); \textsuperscript{13}C NMR (125 MHz, CDCl\textsubscript{3}) \( \delta \) 175.1, 136.2, 116.4, 60.1, 52.6, 34.1, 30.4, 20.5, 20.4, 14.5; IR
Ethyl 2-isopropyl-5-ol-pentanoate (S28): To a solution of ethyl 2-isopropyl-4-pentenoate (8.88 g, 52.2 mmol) in THF (43 mL) at 0 °C was added 10 M BH₃·SMe₂ (2.1 mL). The reaction mixture was allowed to warm to 23 °C and stirred for 72 h. The reaction mixture was cooled to 0 °C and 10% NaOH (24 mL) followed by 30% H₂O₂ (12 mL) were added. The reaction mixture was allowed to warm to 23 °C and stirred for 48 h before K₂CO₃ (25 g) was added and the mixture was stirred for an additional 2 h. The layers were separated, and the aqueous layer was extracted with Et₂O (3 × 50 mL). The combined organic phases were dried over MgSO₄, filtered, and concentrated in vacuo. The resulting yellow oil was purified by flash column chromatography (1:9 Et₂O/pentane to 2:3 Et₂O/pentane) to afford the product as a colorless oil (4.81 g, 49%): ¹H NMR (400 MHz, CDCl₃) δ 4.21–4.15 (m, 2H), 3.66 (m, 2H), 2.18–2.13 (ddd, J = 9.9, 7.3, 4.4, 1H), 1.92–1.87 (m, 1H), 1.68–1.57 (m, 5H), 1.30 (t, J = 7.1, 3H), 0.97 (d, J = 6.9, 3H), 0.95 (d, J = 6.8, 3H); ¹³C NMR (125 MHz, CDCl₃) δ 176.1, 62.8, 60.2, 52.7, 31.2, 31.0, 25.9, 20.7, 20.4, 14.6; IR (thin film) 3431, 2961, 1731, 1467, 1376, 1194, 1029 cm⁻¹; HRMS (EI/GCMS) m/z calcd for C₁₀H₁₈O₃ (M + H)⁺ 189.1491, found 189.1478.
2-Isopropyltetrahydropyran-1-one (S29): To a solution of ethyl 2-isopropyl-5-ol-pentenoate (0.691 g, 3.67 mmol) in benzene (122 mL) was added camphorsulfonic acid (0.069 g, 0.30 mmol). The mixture was stirred at 80 °C for 24 h, cooled to 23 °C and concentrated in vacuo. The resulting oil was purified by flash column chromatography (pentane to 1:4 Et₂O/pentane) to afford the product as a light yellow oil (0.370 g, 71%): ¹H NMR (500 MHz, CDCl₃) δ 4.33 (m, 1H), 4.23 (ddd, J = 11.1, 7.9, 4.6, 1H), 2.40 (m, 2H), 1.92 (m, 3H), 1.62 (m, 1H), 1.00 (d, J = 6.8, 3H), 0.94 (d, J = 6.7, 3H); ¹³C NMR (125 MHz, CDCl₃) δ 173.8, 68.8, 46.1, 28.8, 22.6, 20.3, 20.1, 18.3; IR (thin film) 2962, 1731, 1465, 1389, 1273, 1155, 1085 cm⁻¹; HRMS (EI/GCMS) m/z calcd for C₈H₁₄O₂ (M)+ 142.0994, found 142.0993. Anal. Calcd for C₈H₁₄O₂: C, 67.57; H, 9.92. Found: C, 67.27; H, 10.03.

2-Isopropyltetrahydropyran-1-acetate (32c): A solution of 2-isopropyl-tetrahydropyran-1-one (0.367 g, 2.57 mmol) in CH₂Cl₂ (26 mL) was cooled to –78 °C and a 1.5 M solution of DIBAL-H in toluene (2.06 mL, 3.09 mmol) was added dropwise. After 5 h, acetic anhydride (1.21 mL, 12.9 mmol), pyridine (0.83 mL, 10.3 mmol), and 4-dimethylaminopyridine (0.474 g, 3.86 mmol) were added. The reaction mixture was allowed to warm slowly over 0.5 h to 23 °C and it was stirred for 24 h. Saturated aqueous NH₄Cl (18 mL) was added, and the CH₂Cl₂ was removed in vacuo. The residue was dissolved in MTBE (28 mL). The organic layer was washed with saturated aqueous Na₂HPO₄ (4 × 12 mL), NaH₂PO₄ (4 × 12 mL), and CuSO₄ (5 × 12 mL), filtered through Na₂SO₄, and concentrated in vacuo. The resulting oil was purified by flash
column chromatography (pentane to 1:4 Et₂O/pentane) to afford the product (as a 1:2 mixture of isomers) as a colorless oil: (0.196 g, 41%): ¹H NMR (500 MHz, CDCl₃) δ 6.13 (d, J = 2.1, 1H), 5.70 (d, J = 6.4, 1H), 3.94 (m, 1H), 3.72 (td, J = 11.2, 3.1, 1H), 3.67 (m, 1H), 3.57 (ddd, J = 11.4, 8.2, 3.5, 1H), 2.11, (s, 6H), 1.86 (m, 4H), 1.67 (m, 2H), 1.53–1.37 (m, 6H), 0.95 (d, J = 6.9, 3H), 0.89 (d, J = 6.4, 3H), 0.88 (d, J = 6.3, 3H), 0.87 (d, J = 6.9, 3H); ¹³C NMR (125 MHz, CDCl₃) δ 170.3, 170.0, 95.4, 92.6, 65.2, 61.2, 45.4, 44.4, 29.2, 26.7, 25.5, 23.8, 22.2, 21.43, 21.36, 21.2, 20.9, 20.5, 20.4, 18.6; IR (thin film) 2960, 2876, 1751, 1371, 1232 cm⁻¹; HRMS (EI/GCMS) m/z calcd for C₈H₁₅O (M – C₂H₃O₂)+ 126.1045, found 126.1046. Anal. Calcd for C₁₀H₁₈O₃:  C, 64.49; H, 9.74. Found:  C, 64.40; H, 9.84.

**IIM. Synthesis of 2-tert-Butyltetrahydropyran–1–acetate (32d)**

![Chemical diagram](image)

**Ethyl 3,3-dimethyl-butanoate (S30):** To a solution of ethyl 2-tert-butylacetic acid (13.0 g, 112 mmol) in EtOH (75 mL) was added 36 N H₂SO₄ (3.4 mL). The reaction mixture was heated to 84 °C for 24 h. The reaction mixture was cooled to 23 °C, and the acid was quenched with saturated aqueous NaHCO₃ and the layers were separated. The aqueous layer was extracted with Et₂O (3 × 100 mL). The combined organic layers were washed with H₂O, dried
over MgSO₄, filtered, and concentrated *in vacuo*. The resulting oil was purified by distillation (83 °C, 760 mmHg) to afford the product as a colorless oil (12.0 g, 74%): ¹H NMR (500 MHz, CDCl₃) δ 4.12 (m, 2H), 2.18 (d, J = 1.8, 2H), 1.25 (m, 3H), 1.03 (s, 9H); ¹³C NMR (125 MHz, CDCl₃) δ 172.7, 60.2, 48.4, 31.1, 30.0, 14.7; IR (thin film) 2960, 1737, 1469, 1368, 1231, 1132, 1047 cm⁻¹; HRMS (EI/GCMS) m / z calcld for C₈H₁₆O₂ (M)⁺ 144.1150, found 144.1145. Anal. Calcld for C₈H₁₆O₂: C, 66.63; H, 11.18. Found: C, 66.38; H, 11.25.

![Chemical Structure](image)

**Ethyl 2-tert-butyl-4-pentenoate (S31):** To a stirred solution of diisopropylamine (13.4 mL, 88.7 mmol) in THF (94 mL) at −78 °C was added a solution of n-BuLi in hexanes (35 mL, 2.5 M). The resultant pale solution was allowed to stir at −78 °C for 1 h. A solution of ethyl 3,3-dimethyl-butanoate (11.62 g, 80.6 mmol) in THF (25 mL) was added, and the mixture was allowed to stir for 4 h at −78 °C. Allyl bromide (32 mL, 85 mmol) was added, and the mixture was allowed to warm to 23 °C and stirred for 16 h before addition of 2 N HCl (100 mL). The mixture was poured into Et₂O (200 mL) and the layers were separated. The aqueous layer was extracted with Et₂O (3 × 200 mL) and the combined organic layers were washed with saturated aqueous NaHCO₃ (65 mL), dried over MgSO₄, and filtered. The resulting oil was purified by distillation (115 °C, 760 mmHg) to afford the product as a colorless oil (11.75 g, 89%): ¹H NMR (500 MHz, CDCl₃) δ 5.71 (m, 1H), 5.05 (m, 1H), 4.96 (m, 1H), 4.11 (q, J = 7.2, 2H), 2.36 (m, 1H), 2.22 (m, 2H), 1.24 (t, J = 7.2, 3H), 0.98 (s, 9H); ¹³C NMR (125 MHz, CDCl₃) δ 174.7, 136.6, 116.3, 59.9, 56.2, 33.0, 32.3, 28.0, 14.6; IR (thin film) cm⁻¹ 2964, 1732, 1642, 1475, 1371, 1152; HRMS (EI/GCMS) m / z calcld for C₁₁H₂₁O₂ (M + H)⁺ 184.1542, found 185.1543.
Ethyl 2-tert-butyl-5-ol-pentanoate (S32): To a solution of ethyl 2-tert-butyl-4-pentenoate (5.02 g, 27.2 mmol) in THF (23 mL) at 0 °C was added 10 M BH₃·SMe₂ (1.1 mL). The reaction mixture was allowed to warm to 23 °C for 72 h. The reaction mixture was cooled to 0 °C, and 10% NaOH (13 mL) followed by 30% H₂O₂ (6.2 mL) were added. The reaction mixture was allowed to warm to 23 °C and stirred for 48 h before K₂CO₃ (14 g) was added and the mixture was stirred for an additional 2 h. The layers were separated, and the aqueous layer was extracted with Et₂O (3 × 40 mL). The combined organic phases were dried over MgSO₄, filtered, and concentrated in vacuo. The resulting yellow oil was purified by flash column chromatography (1:9 Et₂O/pentane to 2:3 Et₂O/pentane) to afford the product as a colorless oil (2.81 g, 51%): ¹H NMR (500 MHz, CDCl₃) δ 4.14 (q, J = 7.1, 2H), 3.63 (m, 2H), 2.14 (dd, J = 12.0, 2.9, 1H), 1.73 (m, 1H), 1.61 (m, 1H), 1.45 (m, 2H), 1.27 (t, J = 7.1, 3H), 0.96 (s, 9H); ¹³C NMR (125 MHz, CDCl₃) δ 175.7, 62.8, 60.0, 56.3, 33.2, 31.8, 28.0, 24.1, 14.6; IR (thin film) 3440, 2960, 1729, 1371, 1151, 1054 cm⁻¹; HRMS (EI/GCMS) m / z calcd for C₁₁H₂₂O₃ (M)⁺ 202.1569, found 202.1563. Anal. Calcd for C₁₁H₂₂O₃: C, 65.31; H, 10.96. Found: C, 65.24; H, 10.90.

2-tert-Butyltetrahydropyran-1-one (S33): To a solution of ethyl 2-tert-butyl-5-ol-pentenoate (1.22 g, 6.03 mmol) in benzene (201 mL) was added camphorsulfonic acid (0.560 g,
The mixture was stirred at 80 °C for 24 h, then it was cooled to 23 °C and concentrated in vacuo. The resulting oil was purified by flash column chromatography (pentane to 1:4 Et₂O/pentane) to afford the product as a colorless oil (0.763 g, 81%): \( ^1H \) NMR (500 MHz, CDCl₃) δ 4.27 (m, 1H), 4.23 (dt, \( J = 10.9, 5.9, 1H \)), 2.32 (dd, \( J = 11.5, 8.2, 1H \)), 2.09 (dq, \( J = 13.5, 7.1, 1H \)), 1.87 (m, 2H), 1.65 (m, 1H), 1.08 (s, 9H); \( ^{13}C \) NMR (125 MHz, CDCl₃) δ 173.3, 68.1, 49.3, 33.3, 28.0, 22.9, 21.5; IR (thin film) 2962, 1732, 1483, 1380, 1252, 1129, 1082 cm\(^{-1}\); HRMS (EI/GCMS) \( m/z \) calcd for C₅H₈O₂ (M – C₄H₈)+ 100.0524, found 100.0527. Anal. Calcd for C₉H₁₆O₂: C, 69.19; H, 10.32. Found: C, 68.76; H, 10.16.

**2-tert-Butyltetrahydropyran-1-acetate (32d):** A solution of 2-tert-butyltetrahydropyran-1-one, (0.759 g, 4.86 mmol) in CH₂Cl₂ (49 mL) was cooled to –78 °C, and a 1.5 M solution of DIBAL-H in toluene (3.9 mL, 5.8 mmol) was added dropwise. After 5 h, acetic anhydride (2.29 mL, 24.3 mmol), pyridine (1.57 mL, 19.4 mmol), and 4-dimethylaminopyridine (0.715 g, 5.83 mmol) were added. The reaction mixture was allowed to warm slowly over 0.5 h to 23 °C and it was stirred for 24 h. Saturated aqueous NH₄Cl (25 mL) was added, and the CH₂Cl₂ was removed in vacuo. The residue was dissolved in MTBE (34 mL). The organic layer was washed with saturated aqueous Na₂HPO₄ (4 × 15 mL), NaH₂PO₄ (4 × 15 mL), and CuSO₄ (5 × 15 mL), filtered through Na₂SO₄, and concentrated in vacuo. The resulting oil was purified by flash column chromatography (pentane to 1:4 Et₂O/pentane) to afford the product as a colorless oil (0.341 g, 35%): \( ^1H \) NMR (500 MHz, CDCl₃) δ 6.16 (d, \( J = 2.5, 1H \)), 3.75 (td, \( J = 11.4, 3.2, 1H \)), 3.67 (m, 1H), 2.12 (s, 3H), 1.73–1.67 (m, 4H), 1.57 (m, 1H), 0.89 (s, 9H); \( ^{13}C \) NMR (125 MHz, CDCl₃) δ 170.2, 92.9, 61.6, 48.7, 32.1, 28.4, 26.4, 21.8, 19.8; IR (thin film) 2957, 2874, 1751, 1474, 1084, 1011 cm\(^{-1}\); HRMS (EI/GCMS) \( m/z \) calcd for C₁₀H₁₇O₃ (M – CH₃)+
185.1178, found 185.1174. Anal. Calcd for C_{11}H_{20}O_{3}: C, 65.97; H, 10.07. Found: C, 66.27; H, 9.98.

IIIN. Synthesis of (4S, 5R)–2–Acetoxy–5–benzyloxy–4–methyltetrahydropyran (43)

2-(tert-Butyldiphenylsilyloxy)ethanol (S34): Sodium hydride (0.873 g, 36.4 mmol) was suspended in THF (70 mL) in a flame-dried flask after being washed with hexanes (3 × 5 mL). Ethylene glycol (2.03 mL, 36.4 mmol) was added at 22 °C, and the mixture was stirred for 45 min. tert-Butylchlorodiphenylsilane (9.5 mL, 37 mmol) was then added. After five days, the mixture was poured into diethyl ether (500 mL), washed with 10% aqueous K_{2}CO_{3} (170 mL) and brine (170 mL), dried over MgSO_{4}, filtered and concentrated in vacuo. The resulting oil was purified by flash chromatography (1:4 EtOAc/hexanes) to afford the product as a colorless oil (6.83 g, 62%): \(^1\)H NMR (500 MHz, CDCl_{3}) \(\delta\) 7.67 (dd, \(J = 7.9, 1.4\), 4H), 7.45–7.37 (m, 6H), 3.73 (m, 2H), 3.67 (m, 2H), 2.12 (t, \(J = 6.3\), 1H), 1.07 (s, 9H); \(^{13}\)C NMR (125 MHz,
(tert-Butyldiphenylsilyloxy)acetaldehyde (S35): Dess–Martin periodinane⁶,⁷ (11.08 g, 26.0 mmol) was added to a solution of 2-(tert-butyldiphenylsilyloxy)ethanol (6.00 g, 20.0 mmol) in CH₂Cl₂ (200 mL). The mixture was stirred for 12 h before adding 100 mL of a saturated aqueous solution of Na₂S₂O₃ and NaHCO₃. Stirring was continued for 40 min before the layers were separated. The organic layer was washed with saturated aqueous NaHCO₃ (100 mL) and water (100 mL) and dried over Na₂SO₄. Solvent was removed in vacuo, and the resulting oil was purified by flash chromatography (1:9 EtOAc/hexanes) to afford the known product as a colorless oil (4.63 g, 78%):¹³ ¹H NMR (500 MHz, CDCl₃) δ 9.73 (d, J = 0.8, 1H), 7.66 (m, 4H), 7.45–7.38 (m, 6H), 4.21 (d, J = 0.8, 2H), 1.10 (s, 9H); ¹³C NMR (125 MHz, CDCl₃) δ 201.7, 135.5, 132.5, 130.1, 127.9, 70.0, 26.7, 19.2; IR (thin film) 3071, 2958, 2932, 2858, 1738, 1114 cm⁻¹; HRMS (CI/isobutane) m / z calcd for C₁₄H₁₄O₂Si (M – t-Butyl)+ 241.0685, found 241.0686.
(2R,3S)-1-(tert-Butyldiphenylsilyloxy)-3-methylpent-4-en-2-ol (S36): (Z)-(2S,3S)-Diisopropyltartrate crotylboronate was added as a 0.44 M solution in toluene (85.0 mL, 37 mmol) to a suspension of crushed 4 Å molecular sieves (0.789 g) in toluene (50 mL). The mixture was cooled to –78 °C, and a solution of (tert-butyldiphenylsilyloxy)acetaldehyde (4.00 g, 13.4 mmol) in toluene (10 mL) was added dropwise over 15 min. After 4 h, 10% aqueous NaOH (50 mL) was added. The mixture was warmed to 0 °C, stirred for 45 min, and filtered through Celite. The layers were separated, and the aqueous layer was extracted with Et₂O (4 × 30 mL). The combined organic layers were dried over K₂CO₃ and concentrated in vacuo. The resulting oil was purified by flash chromatography (1:9 EtOAc/hexanes) to afford the product as a colorless oil (3.70 g, 78%, >95:5 diastereoselectivity, as determined based on GC analysis): [α]D²² +1.7° (c 0.72, CHCl₃); ¹H NMR (500 MHz, CDCl₃) δ 7.67–7.65 (m, 4H), 7.46–7.37 (m, 6H), 5.64 (ddd, J = 17.2, 10.3, 7.9, 1H), 4.99 (ddd, J = 17.2, 1.7, 1.2, 1H), 4.94 (ddd, J = 10.3, 1.8, 0.8, 1H), 3.70 (dd, J = 10.0, 3.3, 1H), 3.57 (dd, J = 10.0, 7.2, 1H), 3.53 (dt, J = 7.0, 3.5, 1H), 2.52 (d, J = 3.9, 1H), 2.31 (m, 1H), 1.06 (s, 9H), 1.05 (d, J = 6.8, 3H); ¹³C NMR (125 MHz, CDCl₃) δ 140.3, 135.5, 133.1, 129.8, 127.8, 115.0, 74.9, 66.1, 40.8, 26.8, 19.2, 15.8; IR (thin film) 3575, 3478, 3071, 2930, 1428, 1112, 917, 740, 702 cm⁻¹; HRMS (CI/isobutane) m/z calcd for C₁₈H₂₁O₂Si (M – t-Butyl)+ 297.1311, found 297.1303. Anal. Calcd for C₂₂H₃₀O₂Si: C, 74.53; H, 8.53. Found: C, 74.68; H, 8.66.
(2R,3S)-(2-Benzyloxy-3-methylpent-4-enyloxy)-tert-butyldiphenylsilane (S37): Freshly distilled benzyl trichloroacetimidate (0.311 mL, 1.67 mmol) was added to a solution of (2R,3S)-1-(tert-butyldiphenylsilyloxy)-3-methylpent-4-en-2-ol (0.100 g, 0.28 mmol) in CH₂Cl₂ (2 mL) and hexanes (3 mL), and the mixture was cooled to 0 °C. TMSOTf (0.011 mL, 0.06 mmol) was added dropwise, and the mixture was warmed to 22 °C and stirred for 12 h. Additional benzyl trichloroacetimidate (0.150 mL, 0.81 mmol) and TMSOTf (0.007 mL, 0.04 mmol) were added at 0 °C, and the mixture was warmed to 22 °C and stirred for 48 h. The solvent was removed in vacuo, and the residue was dissolved in 6:1 petroleum ether/Et₂O (20 mL) and filtered through a plug of silica gel. The silica gel was rinsed with Et₂O (2 × 2 mL), and the combined organic phases were washed with saturated aqueous NaHCO₃ (10 mL) and water (10 mL), dried over Na₂SO₄, and concentrated in vacuo. The resulting oil was purified by flash chromatography (2:1 hexanes/benzene) to afford the product as a colorless oil (0.103 g, 82%): [α]D²² -15.1° (c 0.36, CHCl₃); ¹H NMR (500 MHz, CDCl₃) δ 7.69–7.67 (m, 4H), 7.43–7.25 (m, 11H), 5.78 (ddd, J = 17.3, 10.3, 7.6, 1H), 5.01 (dt, J = 17.2, 1.5, 1H), 4.95 (d, J = 10.3, 1H), 4.71 (d, J = 11.6, 1H), 4.52 (d, J = 11.6, 1H), 3.74 (m, 2H), 3.37 (dd, J = 10.4, 5.7, 1H), 2.52 (m, 1H), 1.06 (s, 9H), 1.02 (d, J = 6.9, 3H); ¹³C NMR (125 MHz, CDCl₃) δ 141.3, 139.0, 135.7, 135.6, 133.6, 133.5, 129.6, 128.2, 127.7, 127.6, 127.3, 114.3, 83.6, 72.9, 64.6, 39.5, 26.8, 19.2, 15.3; IR (thin film) 3071, 2930, 1428, 1112, 823, 739, 701 cm⁻¹; HRMS (CI/isobutane) m/z calcd for C₂₉H₃₅O₂Si (M – H)⁺ 443.2406, found 443.2414. Anal. Calcd for C₂₉H₃₆O₂Si: C, 78.33; H, 8.16. Found: C, 78.61; H, 8.10.
(2R,3S)-2-Benzylxoy-1-(\textit{tert}-butyldiphenylsilyloxy)-3-methylpentan-5-ol (S38): A 1 M solution of BH$_3$·THF in THF (2.27 mL) was added to a solution of (2R,3S)-2-benzylxoy-3-methylpent-4-enyloxy)-\textit{tert}-butyldiphenylsilane (1.01 g, 2.27 mmol) in THF (20 mL). The mixture was stirred for 15 h before dropwise addition of water (1 mL), addition of 10% aqueous NaOH (1.5 mL), and dropwise addition of 30% aqueous H$_2$O$_2$ (1 mL). The mixture was stirred for 5 h before the solvent was removed \textit{in vacuo}. The residue was redissolved in Et$_2$O (100 mL), washed with water (50 mL) and brine (50 mL), dried over MgSO$_4$, and concentrated \textit{in vacuo}. The resulting oil was purified by flash chromatography (1:4 EtOAc/hexanes) to afford the product as a colorless oil (0.722 g, 69%): $\alpha$D$^2_2$-20.7° (c 0.09, CHCl$_3$); $^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 7.68 (m, 4H), 7.44–7.25 (m, 11H), 4.73 (d, $J = 11.7$, 1H), 4.53 (d, $J = 11.7$, 1H), 3.85 (dd, $J = 10.9$, 6.4, 1H), 3.73 (dd, $J = 10.9$, 4.5, 1H), 3.63 (m, 1H), 3.56 (m, 1H), 3.46 (m, 1H), 1.96 (m, 1H), 1.80 (t, $J = 5.4$, 1H), 1.63 (m, 1H), 1.43 (m, 1H), 1.06 (s, 9H), 0.86 (d, $J = 7.0$, 3H); $^{13}$C NMR (125 MHz, CDCl$_3$) $\delta$ 138.8, 135.6, 133.5, 129.7, 128.3, 128.3, 127.7, 127.5, 83.5, 72.8, 64.4, 61.3, 36.3, 32.3, 26.9, 19.2, 15.5; IR (thin film) 3399, 3070, 2931, 1428, 1112, 738, 701 cm$^{-1}$; HRMS (CI/isobutane) $m/z$ calcd for C$_{29}$H$_{39}$O$_3$Si (M + H)$^+$ 463.2668, found 463.2656. Anal. Calcd for C$_{29}$H$_{38}$O$_3$Si: C, 75.28; H, 8.28. Found: C, 74.99; H, 8.25.

(3S,4R)-4-Benzylxoy-5-(\textit{tert}-butyldiphenylsilyloxy)-3-methylpentanal (S39): Dess–Martin periodinane$^{46}$ (0.794 g, 1.87 mmol) was added to a solution of (2R,3S)-2-benzylxoy-1-(\textit{tert}-butyldiphenylsilyloxy)-3-methylpentan-5-ol (0.722 g, 1.56 mmol) in CH$_2$Cl$_2$
(50 mL). The mixture was stirred for 14 h. A saturated aqueous solution of NaHCO₃ and Na₂S₂O₃ (30 mL) was added. After stirring for 15 min, the layers were separated, and the aqueous layer was extracted with CH₂Cl₂ (3 × 15 mL). The combined organic phases were washed with saturated aqueous NaHCO₃ (30 mL), dried over Na₂SO₄, and concentrated in vacuo. The resulting oil was purified by flash chromatography (benzene) to afford the product as a colorless oil (0.606 g, 84%): [α]D²²−32.5° (c 0.04, CHCl₃); ¹H NMR (500 MHz, CDCl₃) δ 9.69 (dd, J = 2.3, 1.8, 1H), 7.68 (m, 4H), 7.46–7.25 (m, 11H), 4.62 (d, J = 11.8, 1H), 4.42 (d, J = 11.8, 1H), 3.78 (dd, J = 10.9, 5.7, 1H), 3.70 (dd, J = 10.9, 5.2, 1H), 3.43 (m, 1H), 2.54 (ddd, J = 16.3, 5.8, 1.7, 1H), 2.46 (m, 1H), 2.27 (ddd, J = 16.2, 7.4, 2.5, 1H), 1.06 (s, 9H), 0.93 (d, J = 6.9, 3H); ¹³C NMR (125 MHz, CDCl₃) δ 202.4, 138.7, 135.6, 133.4, 133.3, 129.7, 128.3, 127.4, 127.71, 127.5, 82.0, 72.5, 63.9, 47.7, 30.0, 26.8, 19.2, 14.8; IR (thin film) 3070, 2931, 1725, 1428, 1112, 740, 702 cm⁻¹; HRMS (Cl/isobutane) m/z calcd for C₂₅H₂₇O₃Si (M – t-Butyl)+ 403.1729, found 403.1730. Anal. Calcd. for C₂₉H₃₆O₃Si: C, 75.61; H, 7.88. Found: C, 74.53; H, 7.77.

![Diagram](image.png)

(4S,5R)-2-Acetoxy-5-benzyloxy-4-methyldihydropyran (43): Tetrabutylammonium fluoride was added as a 1 M solution in THF (26.3 mL) to (3S,4R)-4-Benzyl-5-(tert-butyldiphenylsilyl)-3-methylpentanal (0.606 g, 1.32 mmol) and stirred for 48 h. The solvent was removed in vacuo, and the majority of the tetrabutylammonium fluoride was removed by flash chromatography (4:1 hexanes/EtOAc). The resulting hemiacetal was isolated as a 45:55 (α : β) mixture of anomers with approximately 28 mol % of tetrabutylammonium fluoride, as determined based on analysis of ¹H NMR spectroscopy. The unpurified yellow oil was
dissolved in pyridine (32 mL) and acetic anhydride (16 mL, 170 mmol). 4-Dimethylaminopyridine (0.020 g, 0.16 mmol) was added, and the mixture was stirred for 48 h. The mixture was poured into a separatory funnel with tert-butyl methyl ether (100 mL), washed with saturated aqueous NaHSO₃ (30 mL), saturated aqueous Na₂HPO₄ (3 × 30 mL), saturated aqueous NaH₂PO₄ (3 × 30 mL), and saturated aqueous CuSO₄ (3 × 30 mL), dried over Na₂SO₄, and concentrated in vacuo. The resulting oil was purified by flash chromatography (1:9 EtOAc/hexanes) followed by a second flash chromatography (19:1 benzene/EtOAc) to afford the product (as a 1:1 mixture of anomers) as a colorless oil (0.244 g, 70%):

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1H NMR (500 MHz, CDCl₃) δ 7.38–7.18 (m, 10H), 6.02 (d, J = 2.1, 1H), 5.71 (dd, J = 8.9, 2.7, 1H), 4.61 (m, 2H), 4.54 (m, 2H), 4.07 (dd, J = 11.6, 4.3, 1H), 3.85 (dd, J = 10.9, 4.9, 1H), 3.56 (t, J = 10.7, 1H), 3.40 (dd, J = 11.5, 8.8, 1H), 3.14 (m, 2H), 2.08 (s, 3H), 2.07 (s, 3H), 1.99 (m, 2H), 1.84 (m, 2H), 1.50 (m, 1H), 1.40 (m, 1H), 1.09 (d, J = 6.6, 3H), 1.05 (d, J = 6.5, 3H); 13C NMR (125 MHz, CDCl₃) δ 169.8, 169.4, 138.23, 138.17, 128.7, 128.4, 128.2, 128.0, 127.8, 127.7, 93.6, 91.0, 78.6, 78.0, 72.5, 72.3, 66.4, 63.2, 36.0, 33.9, 30.9, 21.1, 18.2, 17.9; IR (thin film) 2928, 1749, 1235, 1075, 929, 699 cm⁻¹; HRMS (CI/isobutane) m / z calcd for C₁₃H₁₆O₂ (M – OAc)^+ 204.1150, found 204.1147.
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### III. Allylation Reactions

**Typical Allylation Procedure:** Allyltrimehylsilane (4.0 equiv) was added to a solution of acetate (0.15 M) in CH₂Cl₂, and the mixture was cooled to –78 °C and treated with the Lewis acid (1.2 equiv). The mixture was allowed to warm to 23 °C and quenched with saturated aqueous Na₂HPO₄ (1mL per mmol of acetate). The layers were separated, and the aqueous layer was extracted three times with CH₂Cl₂ (1 mL per mmol of acetate), dried over Na₂SO₄, and concentrated in vacuo. The unpurified product ratios were determined using GC and confirmed using GCMS. The reported yields are of purified material.
trans-1-Allyl-4-(tert-butyldiphenylsilyloxy)tetrahydropyran (16a): Under standard allylation conditions using SnBr₄ as a Lewis acid, 4-(tert-butyldiphenylsilyloxy)tetrahydropyran-1-acetate (0.109 g, 0.273 mmol) afforded the product (0.103 g, 99%) as a 94:6 trans:cis mixture of isomers. Under standard allylation conditions using BF₃·OEt₂ as a Lewis acid, 4-(tert-butyldiphenylsilyloxy)tetrahydropyran-1-acetate (0.040 g, 1.0 mmol) afforded the product (0.034 g, 89%) as an 83:17 trans:cis mixture of isomers. The oil was purified by flash chromatography (1:99 to 1:9 EtOAc/hexanes): GC tR(major) 10.8 min, tR(minor) 10.4 min (160 °C for 1 min, 10 °C/min to 250 °C); 1,4-trans isomer (major): $^1$H NMR (500 MHz, C₆D₆) δ 7.75–7.70 (m, 4H), 7.23–7.15 (m, 6H), 5.79 (m, 1H), 4.99–4.94 (m, 2H), 4.05 (ddd, J = 10.7, 4.9, 2.3, 1H), 3.80 (m, 1H), 3.23 (t, J = 10.3, 1H), 3.04 (m, 1H), 2.17 (m, 1H), 1.97 (m, 1H), 1.87 (m, 1H), 1.41 (tdd, J = 13.0, 10.7, 4.2, 1H), 1.23 (m, 1H), 1.14 (s, 9H), 0.92 (tdd, J = 13.6, 11.1, 3.9, 1H); $^{13}$C NMR (125 MHz, C₆D₆) δ 135.70, 135.65, 134.9, 134.2, 134.0, 129.7, 129.6, 127.61, 127.55, 116.7, 76.7, 72.9, 67.6, 40.2, 33.2, 30.2, 26.9, 19.1; IR (thin film) 3071, 2933, 1428, 702 cm⁻¹; HRMS (Cl/isobutane) m/z calcd for C₂₄H₃₁O₂Si (M – H)⁺ 379.2093, found 379.2080. Anal. Calcd for C₂₄H₃₂O₂Si: C, 75.74; H, 8.47. Found: C, 75.60; H, 8.46.
**trans-1-Allyl-4-methanesulfoxytetrahydropyran (16b):** Under standard allylation conditions using SnBr$_4$ as a Lewis acid, 4-methanesulfoxytetrahydropyran-1-acetate (0.115 g, 0.483 mmol) afforded the product (0.081 g, 76%) as a 96:4 trans:cis mixture of isomers. Under standard allylation conditions using BF$_3$·OEt$_2$ as a Lewis acid, 4-methanesulfoxytetrahydropyran-1-acetate (0.116 g, 0.487 mmol) afforded the product (0.075 g, 70%) as a 93:7 trans:cis mixture of isomers. The oil was purified by flash chromatography (1:9 to 1:2 EtOAc/hexanes): GC $t_R$ (major) 12.6 min, $t_R$ (minor) 12.4 min (50 °C for 1 min, 10 °C/min to 250 °C); 1,4-trans isomer (major): $^1$H NMR (500 MHz, C$_6$D$_6$) $\delta$ 5.73 (m, 1H), 5.00–4.96 (m, 2H), 4.42 (tt, $J$ = 10.3, 5.2, 1H), 4.03 (ddd, $J$ = 10.7, 5.0, 2.3, 1H), 3.03 (t, $J$ = 10.5, 1H), 2.84 (m, 1H), 2.12 (m, 1H), 2.08 (s, 3H), 1.97–1.89 (m, 2H), 1.27 (ttd, $J$ = 12.7, 11.4, 4.4, 1H), 1.16 (m, 1H), 0.94 (ttd, $J$ = 13.5, 11.0, 4.0, 1H); $^{13}$C NMR (125 MHz, C$_6$D$_6$) $\delta$ 134.5, 116.6, 76.4, 74.6, 69.5, 40.1, 37.6, 30.5, 29.9; IR (thin film) 3021, 1359, 1176, 1097, 858 cm$^{-1}$; HRMS (CI/isobutane) $m/z$ calcd for C$_9$H$_{17}$O$_4$S (M + H)$^+$ 221.0847, found 221.0852

![Chemical structure](image)

**1-Allyl-4-benzoyloxytetrahydropyran (16c):** Under standard allylation conditions using BF$_3$·OEt$_2$ as a Lewis acid, 4-benzoyloxytetrahydropyran-1-acetate (0.100 g, 0.378 mmol) afforded the product (0.077 g, 83%) as an 93:7 trans:cis mixture of isomers. The oil was purified by flash column chromatography (hexanes to 1:9 EtOAc/hexanes) to afford the 1,4-trans product as a colorless oil: $^1$H NMR (500 MHz, C$_6$D$_6$) $\delta$ 8.11 (m, 2H), 7.33–7.06 (m, 3H), 5.85 (m, 1H), 5.12 (tt, $J$ = 10.5, 5.4, 1H), 5.04 (m, 2H), 4.18 (ddd, $J$ = 10.6, 4.9, 2.2, 1H), 3.20 (t, $J$ = 10.4, 1H), 3.06 (m, 1H), 2.23 (m, 1H), 2.04 (m, 2H) 1.33 (m, 2H), 1.15 (m, 1H); $^{13}$C
NMR (125 MHz, CDCl$_3$) $\delta$ 165.4, 134.3, 132.7, 129.9, 129.3, 128.0, 116.7, 76.7, 69.2, 68.5, 39.7, 29.5, 29.0; IR (thin film) 2943, 2853, 1721, 1452, 1272, 1098 cm$^{-1}$; HRMS (EI/GCMS) $m/z$ calcd for C$_{15}$H$_{18}$O$_3$ (M)$^+$ 246.1256, found 246.1256. Anal. Calcd for C$_{15}$H$_{18}$O$_3$: C, 73.15; H, 7.37. Found: C, 73.34; H, 7.59.

1-allyl-4-(p-anisoyloxy)tetrahydropyran (16d): Under standard allylation conditions using BF$_3$·OEt$_2$ as a Lewis acid, 4-(p-anisoyloxy)tetrahydropyran-1-acetate (0.083 g, 0.282 mmol) afforded the product as a 96:4 trans:cis mixture of isomers. The oil was purified by flash column chromatography (hexanes to 1:9 EtOAc/hexanes) to afford the 1,4-trans product as a colorless oil (0.065 g, 85%): $^1$H NMR (500 MHz, C$_6$D$_6$) $\delta$ 8.13 (m, 2H), 6.67 (m, 2H), 5.84 (m, 1H), 5.14 (m, 1H), 5.03 (m, 2H), 4.23 (ddd, $J = 10.5, 4.9, 2.1$, 1H), 3.23 (t, $J = 10.4$, 1H), 3.20 (s, 3H), 3.07 (m, 1H), 2.27 (m, 1H), 2.08 (m, 2H), 1.31 (m, 2H) 1.19 (m, 1H); $^{13}$C NMR (125 MHz, CDCl$_3$) $\delta$ 165.5, 163.4, 135.7, 131.6, 122.6, 117.0, 113.6, 77.0, 69.6, 68.4, 55.4, 40.1, 29.8, 29.3; IR (thin film) 2944, 1714, 1606, 1511, 1168 cm$^{-1}$; HRMS (EI/GCMS) $m/z$ calcd for C$_{16}$H$_{20}$O$_4$ (M)$^+$ 235.0970, found 235.0972. Anal. Calcd for C$_{16}$H$_{20}$O$_4$: C, 69.54; H, 7.30. Found: C, 69.47; H, 7.46.
**1-Allyl-4-(p-nitrobenzoyloxy)tetrahydropyran. (16e):** Under standard allylation conditions using BF$_3$·OEt$_2$ as a Lewis acid, 4-(p-nitrobenzoyloxy)tetrahydropyran-1-acetate (0.047 g, 0.15 mmol) afforded the product (0.077 g, 83%) as an 81:19 trans:cis mixture of isomers. The oil was purified by flash column chromatography (hexanes to 1:9 EtOAc/hexanes) to afford the 1,4-trans product as a colorless oil (0.040 g, 90%): $^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 7.70 (m, 4H), 5.84 (m, 1H), 5.07 (m, 2H), 4.97 (m, 1H), 4.11 (ddd, $J = 10.5, 4.9, 2.3, 1H$), 3.16 (t, $J = 10.4, 1H$), 3.07 (m, 1H), 2.28 (m, 1H), 2.07 (m, 1H), 1.99 (m, 1H), 1.35–1.29 (m, 2H), 1.15 (m, 1H); $^{13}$C NMR (125 MHz, CDCl$_3$) $\delta$ 164.3, 151.0, 136.0, 135.0, 131.2, 124.0, 117.6, 77.4, 70.3, 69.6, 40.4, 30.1, 29.6; HRMS (EI/GCMS) $m/z$ calcd for C$_{12}$H$_{11}$NO$_5$ (M – C$_3$H$_6$)$^+$ 250.0715, found 250.0711. Anal. Calcd for C$_{15}$H$_{17}$NO$_5$: C, 61.85; H, 5.88; N, 4.81. Found: C, 61.98; H, 6.02; N, 4.70.

![1-Allyl-4-(p-nitrobenzoyloxy)tetrahydropyran](image)

**trans-1-Allyl-4-nitrotetrahydropyran (16f):** Under standard allylation conditions using SnBr$_4$ as a Lewis acid, 4-nitrotetrahydropyran1-1-acetate (0.364 g, 1.92 mmol) afforded the product (0.299 g, 91%) as a 85:15 trans:cis mixture of isomers. Under standard allylation conditions using BF$_3$·OEt$_2$ as a Lewis acid, 4-nitrotetrahydropyran1-1-acetate (0.094 g, 0.50 mmol) afforded the product (0.075 g, 88%) as an 80:20 trans:cis mixture of isomers. The oil was purified by flash chromatography (1:99 to 1:4 Et$_2$O/pentane): GC $t_R$(major) 8.5 min, $t_R$(minor) 9.2 min (50 °C for 1 min, 10 °C/min to 250 °C); 1,4-trans (major): $^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 5.80 (m, 1H), 5.12–5.07 (m, 2H), 4.51 (ddt, $J = 11.9, 10.5, 4.5, 1H$), 4.38 (ddd, $J = 10.9, 4.6, 2.4, 1H$), 3.66 (t, $J = 10.7, 1H$), 3.39 (m, 1H), 2.48 (m, 1H), 2.32 (m, 1H), 2.21 (m, 1H).
1H), 2.07 (qd, J = 12.7, 4.4, 1H), 1.88 (ddt, J = 13.9, 4.8, 2.4, 1H), 1.44 (tdd, J = 13.6, 11.2, 4.0, 1H); 13C NMR (125 MHz, CDCl3) δ 133.9, 117.4, 79.9, 76.7, 68.6, 39.7, 29.2, 28.3; IR (thin film) 3078, 1546, 1351, 1091, 768 cm⁻¹; HRMS (Cl/isobutane) m / z calcd for C₅H₈NO₃ (M – C₃H₅)+ 130.0504, found 130.0501. Anal. Calcd for C₈H₁₃NO₃: C, 56.13; H, 7.65; N, 8.18. Found: C, 56.04; H, 7.82; N, 8.21.

trans-1-allyl-4-azidotetrahydropyran (16g): Under standard allylation conditions using SnBr₄ as a Lewis acid, 4-azidotetrahydropyran-1-acetate (0.095 g, 0.51 mmol) afforded the product (0.081 g, 95%) as a 88:12 trans:cis mixture of isomers. Under standard allylation conditions using BF₃·OEt₂ as a Lewis acid, 4-azidotetrahydropyran-1-acetate (0.095 g, 0.51 mmol) afforded the product (0.081 g, 95%) as an 78:22 trans:cis mixture of isomers. The oil was purified by flash chromatography (99:1 to 4:1 pentane/Et₂O): GC tᵣ(major) 7.6 min, tᵣ(minor) 8.0 min (50 °C for 1 min, 10 °/min to 250 °C); 1,4-trans isomer (major): ¹H NMR (500 MHz, CDCl₃) δ 5.80 (m, 1H), 5.11–5.05 (m, 2H), 4.01 (ddd, J = 11.0, 4.7, 2.4, 1H), 3.41 (tt, J = 11.0, 4.7, 1H), 3.30 (m, 1H), 3.17 (t, J = 10.8, 1H), 2.29 (m, 1H), 2.23–2.15 (m, 2H), 1.78 (m, 1H), 1.51 (tdd, J = 12.8, 11.5, 4.0, 1H), 1.39 (tdd, J = 13.4, 10.9, 3.7, 1H); ¹³C NMR (125 MHz, CDCl₃) δ 134.3, 117.0, 76.7, 70.2, 56.1, 40.0, 29.8, 29.0; IR (thin film) 3077, 2850, 2104, 1271, 1119, 916 cm⁻¹; HRMS (Cl/isobutane) m / z calcd for C₈H₁₃N₃O (M)⁺ 167.1059, found 167.1060.
trans-1-(3-Hydroxypropyl)-4-fluorotetrahydropyran (S40): Allyltrimethylsilane (0.053 g, 0.466 mmol) was added to a solution of 4-fluorotetrahydropyran-1-acetate (0.018 g, 0.117 mmol) in CD$_2$Cl$_2$ (1 mL), and the mixture was cooled to –78 °C and treated with BF$_3$·OEt$_2$ (0.018 mL, 0.140 mmol). The reaction afforded a 95:5 trans:cis mixture of anomers, as determined based on GC and $^1$H NMR. After 3 h, the mixture was allowed to warm to 23 °C and the reaction was monitored by $^1$H NMR spectroscopy: $^1$H NMR (500 MHz, CD$_2$Cl$_2$) δ 4.70–4.45 (dtt, $J = 48.8, 10.3, 5.3, 1$H), 4.15 (ddt, $J = 10.7, 5.1, 2.5, 1$H), 3.43 (tdt, $J = 10.5, 6.0, 1.8 1$H), 3.37 (td, $J = 10.1, 3.7, 1$H). The solution was cooled to 0 °C and 10 M BH$_3$·SMe$_2$ (0.005 mL, 0.048 mmol) was added. The reaction mixture was stirred at 23 °C for 72 h and cooled to 0 °C before 10% NaOH (0.055 mL) followed by 30% H$_2$O$_2$ (0.028 mL) were added. The reaction mixture was allowed to warm to 23 °C and stirred for 48 h. Solid K$_2$CO$_3$ (0.049 g) was added, and the mixture was allowed to stir for an additional 2 h. The CD$_2$Cl$_2$ layer was washed with H$_2$O (10 mL) and the aqueous layer was extracted with CH$_2$Cl$_2$ (3 × 1 mL). The combined organic phases were filtered through Na$_2$SO$_4$, and concentrated in vacuo. The resulting yellow oil was purified by flash column chromatography (1:9 Et$_2$O/pentane to 3:2 Et$_2$O/pentane) to afford the 1,4-trans product as a colorless oil (0.009 g, 45%): $^1$H NMR (500 MHz, CDCl$_3$) δ 4.70–4.45 (dtt, $J = 48.8, 10.3, 5.3, 1$H), 4.12 (m, 1H), 3.65 (bm, 2H), 3.31–3.26 (td, $J = 10.4, 3.3, 1$H and m, 1H), 2.23 (m, 1H), 1.94 (bs, 1H), 1.68–1.64 (m, 1H), 1.60–1.55 (m, 5H), 1.43 (m, 1H); $^{13}$C NMR (125 MHz, CDCl$_3$) δ 87.2 (d, $J = 174$), 69.6 (d, $J =$
23), 62.8, 32.0 (d, J = 2), 30.2, 30.01 (d, J = 8), 29.95, 29.2; \(^{19}\)F NMR (376 MHz, CDCl\(_3\)) –187.5 (m); IR (thin film) 3352, 2946, 2866, 1446, 1377, 1092, 1038 cm\(^{-1}\); HRMS (EI/GCMS) \(m / z\) calcd for C\(_8\)H\(_{14}\)O\(_2\) (M – HF\(^+\)) 142.0994, found 142.0991.

\[
\begin{align*}
\text{trans-(4-Nitrophenyl)carbamic acid-4-fluorotetrahydropyran (S41):} & \quad \text{To a solution of trans-1-(1-Propanol)-4-fluorotetrahydropyran (0.026 g, 0.16 mmol) in 0.5 mL of THF at 0 °C was added 4-nitrophenyl isocyanate (0.028 g, 0.17 mmol). The reaction mixture was allowed to warm to 23 °C and stirred for 24 h. The layers were separated, and the aqueous layer was extracted with Et\(_2\)O (3 \times 2 mL), dried over MgSO\(_4\), filtered, and concentrated in vacuo. The resultant oil was purified by flash column chromatography (pentane to 1:1 Et\(_2\)O/pentane) to afford the product as a white solid (0.23 g, 44%).} & \quad \text{\^{1}H NMR (500 MHz, C\(_6\)D\(_6\))} \\
& \quad \delta 7.80 (m, 2H), 6.87 (m, 2H), 5.9 (bs, 1H), 4.35–4.19 (dtt, J = 48.8, 10.4, 5.2, 1H), 4.00 (m, 1H and t, J = 6.4, 2H), 3.10 (td, J = 10.3, 3.4, 1H), 2.78 (dddd, J = 10.8, 8.7, 3.9, 1.9, 1H), 1.88 (m, 1H), 1.67 (m, 1H), 1.48 (m, 1H), 1.35 (m, 2H), 1.15 (m, 2H), 0.93 (m, 1H); \^{13}\text{C NMR (125 MHz, C\(_6\)D\(_6\))} \\
& \quad \delta 152.3, 143.4, 124.67, 117.07, 86.8 (d, J = 175), 76.1, 69.4 (d, J = 28), 65.4, 31.4 (d, J = 2), 30.0 (d, J = 18), 29.8 (d, J = 9.4), 25.2; \(^{19}\text{F NMR (376 MHz, CDCl\(_3\))} –188.0 (m); IR (thin film) 3403, 2918, 1749, 1543, 1221, 1038 cm\(^{-1}\); HRMS (CI/GCMS) \(m / z\) calcd for C\(_{15}\)H\(_{19}\)FN\(_2\)O\(_5\) (M\(^+\)) 326.1278, found 326.1268.}
\end{align*}
\]
1-Allyl-4-chlorotetrahydropyran (22b, 23b): Under standard alkylation conditions using SnBr₄ as a Lewis acid, 4-chlorotetrahydropyran-1-acetate (1.02 g, 5.71 mmol) afforded 22b, 23b (0.828 g, 90%) as a separable 86:14 trans (23b):cis (22b) mixture of isomers. The oil was purified by flash chromatography (pentane to 1:49 to 1:9 Et₂O/pentane): GC ₜᵣ(major) 8.9 min, ₜᵣ(minor) 10.1 min (50 °C for 2 min, 5 °/min); 1,4-trans isomer (major): ¹H NMR (500 MHz, C₆D₆) δ 5.73 (m, 1H), 4.97 (m, 2H), 3.97 (ddd, ₇J = 10.9, 4.7, 2.3, 1H), 3.52 (tt, ₇J = 11.2, 4.6, 1H), 3.13 (t, ₇J = 10.8, 1H), 2.88 (m, 1H), 2.12 (m, 1H), 1.96–1.85 (m, 2H), 1.36 (qd, ₇J = 12.6, 4.2, 1H), 1.13 (m, 1H), 0.93 (qd, ₇J = 12.7, 3.8, 1H); ¹³C NMR (125 MHz, C₆D₆) δ 134.9, 116.8, 76.6, 73.1, 54.3, 40.3, 34.5, 31.7; IR (thin film) 2947, 1089, 765 cm⁻¹; HRMS (CI/isobutane) m/z calcd for C₈H₁₂ClO (M – H)⁺ 159.0577, found 159.0578. Anal. Calcd for C₈H₁₃ClO: C, 59.81; H, 8.16. Found: C, 59.97; H, 8.11; 1,4-cis isomer (minor): ¹H NMR (500 MHz, CDCl₃) δ 5.85 (m, 1H), 5.09 (m, 2H), 4.17 (br s, 1H), 4.02 (dt, ₇J = 12.7, 2.3, 1H), 3.77 (dd, ₇J = 12.7, 1.8, 1H), 3.39 (m, 1H), 2.40 (m, 1H), 2.24 (m, 1H), 2.11 (m, 1H), 1.99 (m, 1H), 1.86 (m, 1H), 1.48 (m, 1H); ¹³C NMR (125 MHz, CDCl₃) δ 134.5, 117.0, 77.4, 72.1, 55.9, 40.3, 31.2, 25.5; IR (thin film) 2952, 1064, 886 cm⁻¹; HRMS (CI/isobutane) m/z calcd for C₈H₁₂ClO (M – H)⁺ 159.0577, found 159.0578. Anal. Calcd for C₈H₁₃OCl: C, 59.81; H, 8.16. Found: C, 59.92; H, 8.11.
1-Allyl-4-bromotetrahydropyran (22c, 23c): Under standard allylation conditions using SnBr₄ as a Lewis acid, 4-bromotetrahydropyran-1-acetate (0.204 g, 0.928 mmol) afforded 22c, 23c (0.168 g, 87%) as a separable 71:29 trans (23c):cis (22c) mixture of isomers. Under standard allylation conditions using BF₃·OEt₂ as a Lewis acid, 4-bromotetrahydropyran-1-acetate (0.207 g, 0.914 mmol) afforded 22c, 23c (0.164 g, 88%) as a separable 58:42 trans (23c):cis (22c) mixture of isomers. The oil was purified by flash chromatography (pentane to 1:49 to 1:9 Et₂O/pentane): GC tᵣ(major) 7.1 min, tᵣ(minor) 7.8 min (100 °C for 1 min, 10 °C/min); 1,4-trans isomer (major): ¹H NMR (500 MHz, C₆D₆) δ 5.72 (m, 1H), 4.99–4.94 (m, 2H), 4.00 (ddd, J = 11.0, 4.6, 2.3, 1H), 3.61 (tt, J = 11.4, 4.6, 1H), 3.25 (t, J = 11.0, 1H), 2.89 (m, 1H), 2.11 (m, 1H), 1.96–1.89 (m, 2H), 1.51 (qd, J = 12.6, 4.2, 1H), 1.10 (m, 1H), 0.95 (tdd, J = 13.4, 11.1, 3.8, 1H); ¹³C NMR (125 MHz, C₆D₆) δ 135.2, 117.2, 76.9, 73.8, 46.9, 40.8, 35.7, 33.4; IR (thin film) 3076, 2850, 1642, 1083, 731 cm⁻¹; HRMS (Cl/isobutane) m/z calcd for C₅H₈BrO (M – C₃H₅)⁺ 162.9759, found 162.9756. Anal. Calcd for C₈H₁₅BrO: C, 46.85; H, 6.39. Found: C, 46.58; H, 6.44. 1,4-cis isomer (minor): ¹H NMR (500 MHz, CDCl₃) δ 5.85 (m, 1H), 5.02–4.99 (m, 2H), 3.79 (dt, J = 12.9, 2.2, 1H), 3.64 (d, J = 1.7, 1H), 3.12 (dd, J = 12.9, 1.9, 1H), 2.95 (m, 1H), 2.31 (m, 1H), 2.06 (m, 1H), 1.81–1.71 (m, 2H), 1.27 (m, 1H), 1.00 (m, 1H); ¹³C NMR (125 MHz, CDCl₃) δ 135.5, 117.2, 77.5, 72.7, 50.0, 41.0, 32.4, 26.7; IR (thin film) 3076, 2850, 1642, 1083, 731 cm⁻¹; HRMS (Cl/isobutane) m/z calcd for C₅H₈BrO (M – C₃H₅)⁺ 162.9759, found 162.9756. Anal. Calcd for C₈H₁₅BrO: C, 46.85; H, 6.39. Found: C, 47.10; H, 6.42.
**1-Allyl-4-iodotetrahydropyran (22d, 23d):** Under standard allylation conditions using BF$_3$·OEt$_2$ as a Lewis acid, 4-iodotetrahydropyran-1-acetate (0.055 g, 0.20 mmol) afforded 22d, 23d (0.050 g, 97%) as a 2:1 1,4-*cis:*trans mixture of isomers. The oil was purified by flash chromatography (pentane to 1:25 Et$_2$O/pentane) to afford the 1,4-*cis* product and a 2:1 *trans:*cis mixture of isomers:

**1,4-*cis* isomer (22d):** $^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 5.90–5.82 (m, 1H), 5.14–5.07 (m, 2H), 4.48 (m, 1H), 4.06 (d, $J = 13.0$, 1H), 3.56 (d, $J = 13.0$, 1H), 3.45–3.42 (m, 1H), 2.46–2.40 (m, 1H), 2.30–2.24 (m, 1H) 2.17–2.12 (m, 1H) 1.91–1.74 (m, 2H), 1.62–1.55 (m, 1H); $^{13}$C NMR (125 MHz, CDCl$_3$) $\delta$ 135.0, 117.5, 77.9, 74.5, 40.6, 34.0, 30.0, 28.2; IR (thin film) 2944, 2841, 1434, 1278, 1112, 757 cm$^{-1}$; HRMS (EI/GCMS) $m/z$ calcd for C$_8$H$_{13}$IO (M)$^+$ 252.0011. Submitted. Anal. Calcd for C$_8$H$_{13}$IO: C, 38.12; H, 5.20. Submitted.

**1,4-*cis* and 1,4-*trans* isomers (22d, 23d):** $^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 5.88–5.76 (m, 2H), 5.14–5.05 (m, 4H), 4.48 (m, 1H), 4.14–4.05 (m, 3H), 3.60 (dd, $J = 11.9$, 10.5, 1H and m, 1H), 3.46–3.41 (m, 2H), 2.49–2.40 (m, 2H), 2.30–2.24 (m, 2H) 2.17–2.05 (m, 3H) 1.88–1.81 (m, 2H), 1.65 (m, 1H) 1.60–1.50 (m, 2H); $^{13}$C NMR (125 MHz, CDCl$_3$) $\delta$ 134.8, 134.6, 117.4, 117.3, 77.7, 75.4, 74.3, 40.8, 40.4, 37.3, 35.0, 33.8, 29.9, 28.0, 25.2; IR (thin film) 2942, 2843, 1112, 1075, 917, 757; HRMS (EI/GCMS) $m/z$ calcd for C$_8$H$_{13}$IO (M)$^+$ 252.0011.

![Diagram](attachment:image.png)

**1-Allyl-2-isopropyltetrahydropyran (33c, 34c):** Under standard allylation conditions using BF$_3$·OEt$_2$ as the Lewis acid, 2-isopropyltetrahydropyran-1-acetate (0.161 g, 0.866 mmol) afforded 1 (0.064 g, 44%) as a 40:60 1,2-*cis:*trans mixture of isomers. The oil was purified by
flash chromatography (pentane to 1:9 Et₂O/pentane) to afford the 1,2-cis isomer (0.080 g) and the 1,2-trans isomer (0.077 g):

**1,2-cis (33c):** ¹H NMR (500 MHz, CDCl₃) δ 5.95–5.88 (m, 1H), 5.09–5.03 (m, 2H), 3.86 (m, 1H), 3.33 (m, 1H), 3.25 (ddd, J = 9.5, 7.8, 3.0, 1H), 2.45 (m, 1H), 2.18 (dt, J = 14.7, 7.4, 1H), 1.90 (m, 1H), 1.73 (m, 1H), 1.59 (m, 2H), 1.53 (m, 2H), 0.89 (d, J = 6.9, 3H), 0.77 (d, J = 6.9, 3H); ¹³C NMR (125 MHz, CDCl₃) δ 135.9, 116.5, 80.2, 68.6, 45.1, 37.6, 27.0, 26.8, 22.2, 21.3, 16.0; IR (thin film) 2959, 2850, 1641, 1464, 1099 cm⁻¹; HRMS (EI/GCMS) m/z calcd for C₁₁H₂₀O (M)+ 168.1514, found 168.1515.

**1,2-trans (34c):** ¹H NMR (500 MHz, CDCl₃) δ 5.95–5.88 (m, 1H), 5.09–5.03 (m, 2H), 3.94 (dt, J = 11.3, 3.9, 1H), 3.58 (m, 2H), 2.62 (ddd, J = 14.9, 11.3, 7.4, 1H), 2.03 (m, 1H), 1.75 (m, 1H), 1.65 (m, 2H), 1.40 (m, 3H), 0.91 (d, J = 6.4, 3H), 0.89 (d, J = 6.3, 3H); ¹³C NMR (125 MHz, CDCl₃) δ 136.3, 116.3, 75.8, 60.8, 45.7, 30.0, 29.2, 26.3, 22.9, 21.2, 21.0; IR (thin film) 2932, 2859, 1641, 1471, 1085, 910 cm⁻¹; HRMS (EI/GCMS) m/z calcd for C₁₁H₁₉O (M – H)⁺ 167.1436, found 167.1437. Anal. Calcd for C₁₁H₂₀O: C, 78.51; H, 11.98. Found: C, 78.38; H, 12.05.

**trans-1- Allyl-2-tert-butyldihydropyran (34d):** Under standard allylation conditions using BF₃·OEt₂ as a Lewis acid, 2-tert-butyldihydropyran-1-acetate (0.374 g, 1.87 mmol) afforded 69 (0.197 g, 58%) as a 1:99 1,2-cis:trans mixture of isomers. The oil was purified by
flash chromatography (pentane to 1:9 Et₂O/pentane) to afford the 1,2-\textit{trans} isomer as a colorless oil:

\textbf{1,2-\textit{trans}-isomer (34d):} \textsuperscript{1}H NMR (500 MHz, CDCl\textsubscript{3}) $\delta$ 5.93–5.88 (m, 1H), 5.09–5.03 (m, 2H), 3.86 (dddd, $J = 11.1, 5.1, 3.7, 1.2$, 1H), 3.41 (ddd, $J = 8.6, 7.4, 4.0$, 1H), 3.37 (td, $J = 11.0, 3.8$, 1H), 2.48 (m, 1H), 2.37 (m, 1H), 1.84 (dddd, $J = 13.2, 9.3, 4.1, 1.3$, 1H), 1.66 (m, 1H), 1.54 (m, 1H), 1.36 (td, $J = 11.1, 8.6, 4.2$, 1H), 1.19 (ddd, $J = 10.3, 7.3, 4.3$, 1H), 0.94 (s, 9H); $^{13}$C NMR (125 MHz, CDCl\textsubscript{3}) $\delta$ 136.8, 116.3, 79.4, 66.2, 48.4, 40.2, 33.1, 29.5, 26.2, 24.6; IR (thin film) 2958, 2870, 1112 cm$^{-1}$; HRMS (EI/GCMS) $m/z$ calcd for C\textsubscript{11}H\textsubscript{19}O (M – CH\textsubscript{3})$^+$ 167.1436, found 167.1432.

\begin{center}
\includegraphics[width=\textwidth]{reaction_diagram}
\end{center}

\textbf{(2S,4S,5R)-2-allyl-5-benzyloxy-4-methyltetrahydropyran (44):} Under standard allylation conditions using BF\textsubscript{3}·OEt\textsubscript{2} as a Lewis acid, (4S,5R)-2-acetoxy-5-benzyloxy-4-methyltetrahydropyran (0.098 g, 0.37 mmol) afforded the product (0.074 g, 81\%) as a 95:5 1,4-\textit{cis}:\textit{trans} mixture of isomers. The oil was purified by flash chromatography (1:9 EtOAc/hexanes) as eluent: \textsuperscript{1}H NMR (500 MHz, C\textsubscript{6}D\textsubscript{6}) $\delta$ 7.30 (d, $J = 7.6$, 2H), 7.18–7.08 (m, 3H), 5.94–5.86 (m, 1H), 5.03 (m, 2H), 4.39 (d, $J = 12.1$, 1H), 4.25 (d, $J = 12.1$, 1H), 3.77 (dd, $J = 12.4, 3.8$, 1H), 3.53 (m, 1H), 3.46 (dd, $J = 12.4, 2.3$, 1H), 2.76 (m, 1H), 2.40 (m, 1H), 2.08 (m, 1H), 1.97 (m, 1H), 1.85 (dd, $J = 13.3, 9.1, 4.9$, 1H), 1.11 (ddd, $J = 13.3, 4.6, 3.2$, 1H), 0.80 (d, $J = 7.2$, 3H); \textsuperscript{13}C NMR (125 MHz, CDCl\textsubscript{3}) $\delta$ 138.8, 135.2, 128.3, 127.6, 127.5, 116.7, 77.0, 71.6, 70.7, 64.4, 39.2, 33.5, 29.9, 17.3; IR (thin film) 3066, 2928, 1642, 1454, 1097, 698 cm$^{-1}$; HRMS
(Cl/isobutane) \( m / z \) calcd for \( C_{13}H_{17}O_2 \) (M – C\( \text{H}_{3}\))\(^+\) 205.1229, found 205.1219. Anal. Calcd. for \( C_{16}H_{22}O_2 \): C, 78.01; H, 9.00. Found: C, 78.05; H, 9.06.

IV. Nucleophilic Addition of Diethylzinc

![Reaction Diagram]

4-Benzylxoy-1-ethytltetrahydropyran (17a):\(^{15}\) A solution of 4-benzylxoytetrahydropyran-1-acetate (0.212 g, 0.85 mmol) in CH\(_2\)Cl\(_2\) (3.36 mL) was cooled to -78 °C. Diethyl zinc (0.209 g, 1.69 mmol) was added followed by TMSOTf (0.226 g, 1.01 mmol) and the mixture was stirred for 1 h. The reaction mixture was warmed to room temperature and triethylamine (0.5 mL) was added followed by saturated aqueous NaHCO\(_3\) (1 mL). The mixture was allowed to stir for 30 min, and then it was filtered. The organic layer was washed with ice cold 1N NaHSO\(_4\) (5 mL) and saturated aqueous NaHCO\(_3\) (5 mL), dried over MgSO\(_4\), and concentrated in vacuo to afford a 98:2 \textit{trans}:\textit{cis} mixture of anomers (as determined by GC analysis) as a yellow oil. The oil was purified by flash chromatography (pentane to 1:9 Et\(_2\)O/pentane) to afford the 1,4-\textit{trans} isomer as a colorless oil (0.164 g, 88%): \(^1\)H NMR (400 MHz, CDCl\(_3\)) \( \delta \) 7.39–7.28 (m, 5H), 4.62 (d, \( J = 11.8, 1H \)), 4.56 (d, \( J = 11.9, 1H \)), 4.14–4.10 (ddd, \( J = 10.7, 4.6, 2.3, 1H \)), 3.52–3.45 (m, 1H), 3.21 (t, \( J = 10.6, 1H \) and m, 1H), 2.22 (m, 1H), 1.76 (m, 1H), 1.56–1.42 (m, 3H), 1.41–1.28 (m, 1H), 0.94 (t, \( J = 7.5, 3H \)); \(^{13}\)C NMR \( \delta \) (125 MHz, CDCl\(_3\)) 139.1, 128.8, 128.7, 128.0, 79.3, 73.8, 71.18, 71.16, 30.6, 30.5, 29.1, 10.6; IR (thin film) 2937, 1454, 1374, 1249, 1098, 1028 cm\(^{-1}\); HRMS (EI/GCMS) \( m / z \) calcd for \( C_{14}H_{24}NO_2 \) (M + NH\(_3\))\(^+\) 238.1807, found 238.1807.
3-Benzyloxy-1-ethyltetrahydropyran (31/31a): A solution of 3-benzyloxy-tetrahydropyran-1-acetate (0.039 g, 0.157 mmol) in CH₂Cl₂ (0.66 mL) was cooled to –78 °C. Diethyl zinc (0.286 mL, 0.315 mmol) was added as a 1.1 M solution in toluene followed by TMSOTf (0.034 mL, 0.19 mmol) and the mixture was stirred for 3 h. The reaction mixture was warmed to room temperature and triethylamine (0.25 mL) followed by saturated aqueous NaHCO₃ (0.5 mL) were added. The mixture was allowed to stir for 30 min and filtered using CH₂Cl₂. The organic layer was washed with ice cold 1N NaHSO₄ (2 mL) and saturated aqueous NaHCO₃ (2 mL), dried over MgSO₄, and concentrated in vacuo. The reaction afforded a 78:22 cis:trans mixture of anomers, as determined based on GC. The resulting yellow oil was purified by flash column chromatography (pentane to 1:9 Et₂O/pentane) to afford the product (as a 9:1 cis:trans) as a colorless oil (g, %): ¹H NMR (400MHz, CDCl₃) δ 7.36–7.26 (m, 5H), 7.16 (m, 5H), 4.58 (m, 1H), 4.53 (m, 1H and m, 2H), 4.05–4.01 (ddd, J = 11.8, 4.8, 1.8, 1H and m, 1H), 3.91–3.78 (m, 2H), 3.63 (m, 1H), 3.57–3.50 (tt, J = 11.0, 4.5, 1H), 3.40–3.33 (td, J = 12.5, 2.1, 1H), 3.20–3.13 (dd, J = 11.2, 6.7, 5.5, 1.9, 1H), 2.08–2.03 (dd, J = 12.4, 4.5, 2.1, 1H), 2.00–1.95 (d, J = 12.4, 2.0, 1H), 1.86 (m, 1H), 1.76 (m, 1H), 1.62–1.37 (m, 2H and m, 2H), 1.29 (m, 2H and m, 2H), 0.93 (t, J = 7.5, 3H and m, 3H); ¹³C NMR δ 128.63, 128.59, 127.80, 127.76, 127.67, 127.6, 77.9, 75.0, 73.7, 71.2, 70.2, 69.7, 66.2, 63.1, 38.2, 36.0, 33.0, 30.4, 29.3, 10.1; IR (thin film) 2937, 1454, 1374, 1249, 1098, 1028 cm⁻¹; HRMS (EI/GCMS) m/z calcd for C₁₄H₂₀O₂ (M)⁺ 220.1462, found 220.1463.
IV. Nucleophilic Addition of 1-Phenyl-1-(trimethylsilyloxy)ethylene

\[
\begin{align*}
\text{BnO}^+ & \quad \text{Ph} \quad \text{EtCN} \\
\text{OSiMe}_3 & \quad \text{BF}_3\cdot\text{OEt}_2 \\
9c & \quad \rightarrow \quad 17b
\end{align*}
\]

4-Benzylxy-1-(2-oxo-2-phenylethyl)tetrahydropyran (17b): A solution of 4-benzyloxytetrahydropyran-1-acetate (0.050 g, 0.20 mmol) in \(n\)-propionitrile (2 mL) was cooled to −78 °C. 1-Phenyl-1-(trimethylsilyloxy)ethylene (0.041 mL, 0.20 mmol) was added followed by \(\text{BF}_3\cdot\text{OEt}_2\) (0.029 mL, 0.24 mmol) and the mixture was stirred for 5 min. The reaction mixture was quenched with \(\text{NaHCO}_3\) (4 mL) and the layers were separated. The aqueous layer was extracted with \(\text{CH}_2\text{Cl}_2\) (3 × mL), filtered through \(\text{Na}_2\text{SO}_4\), and concentrated in vacuo. The reaction afforded a 96:4 trans:cis mixture of anomers, as determined based on GC. The resulting oil was purified by flash column chromatography (10:90 EtOAc/hexanes) to afford the trans product as a colorless oil (0.046 g, 74%): \(^1\text{H} \text{NMR} (500 \text{ MHz, } \text{C}_6\text{D}_6) \delta 7.30 (d, J = 7.6, 2H), 7.18–7.08 (m, 3H), 5.94–5.86 (m, 1H), 5.03 (m, 2H), 4.39 (d, J = 12.1, 1H), 4.25 (d, J = 12.1, 1H), 3.77 (dd, J = 12.4, 3.8, 1H), 3.53 (m, 1H), 3.46 (dd, J = 12.4, 2.3, 1H), 2.76 (m, 1H), 2.40 (m, 1H), 2.08 (m, 1H), 1.97 (m, 1H), 1.85 (ddd, J = 13.3, 9.1, 4.9, 1H), 1.11 (ddd, J = 13.3, 4.6, 3.2, 1H), 0.80 (d, J = 7.2, 3H); \(^{13}\text{C} \text{NMR} (125 \text{ MHz, } \text{CDCl}_3) \delta 198.0, 138.5, 133.2, 128.6, 127.7, 127.6, 77.3, 74.0, 72.8, 70.8, 70.7, 44.5, 30.6, 30.0; \text{IR (thin film)} 2953, 2854, 1684, 1202, 1092, 753 \text{ cm}^{-1}; \text{HRMS (CI/isobutane) } m/z \text{ calcd for C}_{11}\text{H}_{16}\text{OSi} (M^+) 310.1568, \text{ found 310.1562. }}

\text{Anal. Calcd. for C}_{11}\text{H}_{16}\text{OSi: C, 77.39; H, 7.14. Found: C, 77.12; H, 7.20.} \]
VI. Stereochemical Proofs

VIA. $^1$H NMR Coupling Constant Data

**trans-1-Allyl-4-(tert-butyldiphenylsilyloxy)tetrahydropyran (16a)**

$\text{H}^\text{B}$: $t$, $J = 10.3$ (gem, ax$^\text{A}$–ax$^\text{C}$)

$\text{H}^\text{E}$: $dd$, $J = 10.7$ (gem), 4.9 (eq$^\text{B}$–ax$^\text{C}$), 2.3 (W–coupling to H$^\text{D}$)

$\text{H}^\text{G}$: $tt$, $J = 10.3$ (ax$^\text{C}$–ax$^\text{A}$, ax$^\text{C}$–ax$^\text{E}$), 5.2 (ax$^\text{C}$–eq$^\text{B}$, ax$^\text{C}$–eq$^\text{D}$)

**trans-Allyl-4-methanesulfoxytetrahydropyran (16b)**

$\text{H}^\text{B}$: $t$, $J = 10.5$ (gem, ax$^\text{A}$–ax$^\text{C}$)

$\text{H}^\text{E}$: $dd$, $J = 10.7$ (gem), 4.5 (eq$^\text{B}$–ax$^\text{C}$), 2.3 (W–coupling to H$^\text{D}$)

$\text{H}^\text{G}$: $tt$, $J = 10.5$ (ax$^\text{C}$–ax$^\text{A}$, ax$^\text{C}$–ax$^\text{E}$), 5.4 (ax$^\text{C}$–eq$^\text{B}$, ax$^\text{C}$–eq$^\text{D}$)

**trans-Allyl-4-benzoyloxytetrahydropyran (16c)**

$\text{H}^\text{B}$: $t$, $J = 10.6$ (gem, ax$^\text{A}$–ax$^\text{C}$)

$\text{H}^\text{E}$: $dd$, $J = 10.6$ (gem), 4.9 (eq$^\text{B}$–ax$^\text{C}$), 2.2 (W–coupling to H$^\text{D}$)

$\text{H}^\text{G}$: $tt$, $J = 10.5$ (ax$^\text{C}$–ax$^\text{A}$, ax$^\text{C}$–ax$^\text{E}$), 5.4 (ax$^\text{C}$–eq$^\text{B}$, ax$^\text{C}$–eq$^\text{D}$)
trans- Allyl-4-anisoyloxytetrahydropyran (16d)

H^a: t, J = 10.4 (gem, ax^A–ax^C)
H^b: ddd, J = 10.5 (gem), 4.9 (eq^B–ax^C), 2.1 (W–coupling to H^D)

trans- Allyl-4-nitrobenzyloxytetrahydropyran (16e)

H^a: t, J = 10.4 (gem, ax^A–ax^C)
H^b: ddd, J = 10.5 (gem), 4.9 (eq^B–ax^C), 2.3 (W–coupling to H^D)

trans-1-Allyl-4-nitrotetrahydropyran (16f)

H^a: t, J = 10.7 (gem, ax^A–ax^C)
H^b: ddd, J = 10.9 (gem), 4.6 (eq^B–ax^C), 2.4 (W–coupling to H^D)
H^c: ddt, J = 11.9 (ax^C–ax^{AE}), 10.5 (ax^C–ax^{AE}), 4.5 (ax^C–eq^B, ax^C–eq^D)
H^d: tdd, J = 13.6 (gem, ax^F–ax^{HE}), 11.2 (ax^F–ax^{HE}), 4.0 (ax^F–eq^D)
**trans-1-Allyl-4-azidotetrahydropyran (16g)**

- **H^A:** t, \( J = 10.8 \) (gem, ax^A–ax^C)
- **H^B:** ddd, \( J = 11.0 \) (gem), 4.7 (eq^B–ax^C), 2.4 (W–coupling to H^D)
- **H^C:** tt, \( J = 11.0 \) (ax^C–ax^A, ax^C–ax^E), 4.7 (ax^C–eq^B, ax^C–eq^D)
- **H^F:** tdd, \( J = 13.4 \) (gem, ax^F–ax^{HE}), 10.9 (ax^F–ax^{HE}), 3.7 (ax^F–eq^D)

**trans-1-Allyl-4-Fluorotetrahydropyran (23a, major)**

- **H^A:** td, \( J = 10.1 \) (gem, ax^A–ax^B), 3.7 (ax^A–Feq)
- **H^B:** ddt, \( J = 10.7 \) (gem), 5.1 (eq^B–ax^C), 2.5 (ax^B–Feq, W–coupling to H^D)
- **H^C:** dtt, \( J = 48.8 \) (ax^C–Feq), 10.3 (ax^C–ax^A, ax^C–ax^E), 5.3 (ax^C–eq^B, ax^C–eq^H)
- **H^D:** dtd, \( J = 10.5 \) (ax^D–ax^F), 6.0 (ax^D–ax^J, ax^D–ax^J), 21.8 (ax^D–eq^G)

**trans-1-(3-Hydroxypropyl)-4-fluorotetrahydropyran (S40)**

- **H^A:** td, \( J = 10.4 \) (gem, ax^A–ax^B), 3.3 (ax^A–Feq)
- **H^B:** dtt, \( J = 48.7 \) (ax^B–Feq), 10.4 (ax^B–ax^A, ax^B–ax^E), 5.3 (ax^B–eq^D, ax^B–eq^C)
**trans-(4-Nitrophenyl)carbamic acid-4-Fluorotetrahydropyran (trans-S41, major)**

H\(^A\): td, \(J = 10.4\) (gem, ax\(^A\)–ax\(^B\)), 3.4 (ax\(^A\)–Feq)

H\(^B\): dtt, \(J = 48.7\) (ax\(^B\)–Feq), 10.4 (ax\(^B\)–ax\(^A\), ax\(^B\)–ax\(^E\)), 5.2 (ax\(^B\)–eq\(^D\), ax\(^B\)–eq\(^F\))

H\(^C\): dddd, \(J = 10.8\) (ax\(^C\)–H\(^G\)), 8.7 (ax\(^C\)–ax\(^I\)), 3.9 (ax\(^C\)–eq\(^J\)), 2.3 (ax\(^C\)–eq\(^H\))

**cis-1–Allyl-4–Chlorotetrahydropyran (cis-22b, minor)**

H\(^A\): dd, \(J = 12.7\) (gem), 1.8 (ax\(^A\)–eq\(^C\))

H\(^B\): dt, \(J = 12.7\) (gem), 1.8 (eq\(^B\)–eq\(^C\), W–coupling to H\(^D\))
trans-1-Allyl-4-Chlorotetrahydropyran (trans-23b, major)

H^A: t, J = 10.8 (gem, ax^A–ax^C)
H^B: ddd, J = 10.9 (gem), 4.7 (eq^B–ax^C), 2.3 (W–coupling to H^D)
H^C: tt, J = 11.2 (ax^C–ax^A, ax^C–ax^E), 4.6 (ax^C–eq^B, ax^C–eq^D)

1-Allyl-4-bromotetrahydropyran (23c, major isomer)

H^A: t, J = 11.0 (gem, ax^A–ax^C)
H^B: ddd, J = 11.0 (gem), 4.6 (eq^B–ax^C), 2.3 (W–coupling to H^D)
H^C: tt, J = 11.4 (ax^C–ax^A, ax^C–ax^E), 4.6 (ax^C–eq^B, ax^C–eq^D)

trans-1-Allyl-4-iodotetrahydropyran (23d, the minor isomer)

H^A: dd, J = 11.9 (gem), 10.5 (ax^A–ax^C)
trans-1-Allyl-2-tert-butyltetrahydropyran (34d, major)

**H^A:** ddd, $J = 8.7$ (ax$^A$–ax$^B$), 7.4 (ax$^A$–ax$^G$), 4.0 (ax$^A$–eq$^H$)

**H^B:** ddd, $J = 10.3$ (ax$^B$–ax$^C$), 8.6 (ax$^B$–ax$^A$), 4.2 (ax$^B$–eq$^D$)

**H^C:** tdd, $J = 11.1$ (gem, ax$^C$–ax$^B$), 8.6 (ax$^C$–ax$^E$), 4.2 (ax$^C$–eq$^F$)

Disubstituted System (44)

**H^A:** dd, $J = 12.4$ (gem), 2.3 (ax$^A$–eq$^C$)

**H^B:** dd, $J = 12.4$ (gem), 3.8 (eq$^B$–eq$^C$)

**H^E:** ddd, $J = 13.3$ (gem), 9.1 (ax$^E$–ax$^D$), 4.9 (ax$^E$–eq$^D$)

**H^F:** ddd, $J = 13.3$ (gem), 4.6 (eq$^F$–eq$^D$/ax$^G$), 3.2 (eq$^F$–eq$^D$/ax$^G$)

VIB. DPFGSE–NOE Data

trans-1-Allyl-4-(tert-butylidiphenylsilyloxy)tetrahydropyran (16a)
H^A irradiated: H^E (4.13%)
H^B irradiated: H^C (8.33%), H^D (3.80%)
Mixing time was 2.0 s.

**trans-1-allyl-4-methanesulfoxytetrahydropyran (16b)**
H^A irradiated: H^E (2.18%)
H^B irradiated: H^C (4.45%), H^D (2.40%)
Mixing time was 2.0 s.

**trans-1-allyl-4-nitrotetrahydropyran (16f)**
H^A irradiated: H^C (3.85%), H^D (1.94%)
H^B irradiated: H^E (2.80%)
Mixing time was 2.0 s.
trans-1- Allyl-4- azidotetrahydropyran (16g)

\( H^A \) irradiated: \( H^C \) (3.36%)

\( H^B \) irradiated: \( H^D \) (2.34%)

Mixing time was 2.0 s.

cis–1–Allyl–4–Chlorotetrahydropyran (cis–22b, minor)

\( H^A \) irradiated: \( H^C \) (2.90%), \( H^D \) (1.72%)

\( H^B \) irradiated: \( H^C \) (2.21%), \( H^E \) (0.40%)

(Mixing time was 2.0 s.)
**trans–1–Allyl–4–Chlorotetrahydropyran (trans–23b, major)**

- $H^A$ irradiated: $H^D$ (1.97%), $H^E$ (2.77%)
- $H^B$ irradiated: $H^C$ (1.71%)
- $H^C$ irradiated: $H^F$ (0.92%)

Note: There was no NOE observed between $H^C$ and $H^E$. (Mixing time was 2.0 s.)

**1-Allyl-4-bromotetrahydropyran (23c, major isomer)**

- $H^A$ irradiated: $H^C$ (1.20%), $H^E$ (3.24%)
- $H^B$ irradiated: $H^D$ (1.46%)

Mixing time was 2.0 s.
**Cis-1-allyl-4-iodotetrahydropyran (22d, major isomer)**

- $H^A$ irradiated: $H^B$ (2.57%), $H^E$ (1.61%)
- $H^B$ irradiated: $H^C$ (4.55%), $H^D$ (0.77%)
- $H^C$ irradiated: $H^B$ (1.05%), $H^D$ (1.65%)
- $H^D$ irradiated: $H^C$ (1.10%), $H^B$ (2.20%)
- $H^F$ irradiated: $H^D$ (1.41%)

(Mixing time was two seconds.)

**Disubstituted Compound (44)**

- $Me$ irradiated: $H^A$ (0.4%), $H^C$ (0.5%)
- $H^C$ irradiated: $Me$ (1.4%)
- $H^D$ irradiated: $Me$ (1.3%), $H^F$ (1.7%)

(Mixing time was two seconds.)
VII. Bibliography


(3) The anomer ratio was determined using $^1$H NMR spectroscopy.


