Solvent Effects in the Nucleophilic Substitutions of Tetrahydropyran Acetals Promoted by Trimethylsilyl Trifluoromethanesulfonate: Trichloroethylene as Solvent for Stereoselective C- and O-Glycosylations

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I. General Procedures

Solvents were dried by filtration through alumina according to the procedure by Grubbs, except otherwise noted.\(^1\) Trichloroethylene was stored over molecular sieves (3 Å). Propionitrile was dried by distillation over CaH\(_2\) and stored over 3 Å molecular sieves. All reagents and starting materials were purchased from commercial sources and, where appropriate, purified before use. Reactions were conducted in flame-dried flasks under an inert nitrogen atmosphere using standard Schlenk techniques. \(^1\)H and \(^{13}\)C NMR spectra were obtained at ambient temperature at 400, 500, or 600 MHz and 100, 125, or 150 MHz, respectively. Chemical shifts are reported in ppm and referenced downfield to tetramethylsilane for \(^1\)H NMR spectra, or to the central peak in CDCl\(_3\) (δ 77.23) for \(^{13}\)C NMR spectra. The coupling constant values (\(J\)) are reported in Hertz (Hz), with the following abbreviations: s = singlet, d = doublet, t = triplet, q = quartet, sext = sextet, m = multiplet. Analytical gas chromatography (GC) analyses were performed using a fused silica capillary column (30 m x 32 mm x 0.25μm) wall-coated with DB-1 (J & W Scientific) with helium as the carrier gas (25 psi column-head pressure). The chromatographic method was the following: start temperature = 150 °C; ramp 10 °C/min; final temperature = 250 °C. Chromatographic purifications were performed using standard forced flow (flash chromatography) in the indicated solvent system with 40-63 μm, 230-400 mesh silica gel. Acetals 1, 4, and 8 were prepared as previously described.\(^2\)\(^-\)\(^4\) Nucleophiles 2 and 5 were prepared by reported methods.\(^5\) Characterization of products obtained from the nucleophilic addition to acetals 1 and 8 were previously reported.\(^2\)\(^-\)\(^4\)
II. Characterization of New Compounds

Previously unreported compounds were synthesized on a preparative scale. Characterization of these new compounds is described below.

**3,4,6-Tri-O-methyl-2-deoxy-β-D-glucopyranosyl-diethyl phosphite 11**

![Chemical Structure]

To a cooled (–78 °C) solution of S1 (0.11 g, 0.51 mmol) in CH₂Cl₂ (5.1 mL) was added NEt₃ (0.51 mL, 3.6 mmol) and diethyl chlorophosphite (0.15 mL, 1.0 mmol). After stirring for 30 minutes, ice was added to the reaction mixture and stirred at 0 °C for 1 h. The entire reaction mixture was poured into a flask containing a cooled (0 °C) mixture of EtOAc (50 mL), saturated NaHCO₃ (25 mL), and brine (25 mL). The phases were separated, and the aqueous phase was extracted with EtOAc (2 x 20 mL). The combined organic phase was dried over Na₂SO₄, filtered, and concentrated in vacuo. Flash chromatography of the crude mixture (50% EtOAc in hexanes, with 2% NEt₃) yielded 0.078 g (47%) of the product as a >95:5 mixture of anomers. ¹H NMR (400 MHz, CDCl₃) δ 5.64 (ddd, J = 7.5, 3.4, 1.4 Hz, 1H), 3.92 (ddq, J = 7.1, 4.1, 0.8 Hz, 4H), 3.87 (ddq, J = 7.1, 4.4, 1.0 Hz), 3.80 (ddq, J = 9.9, 3.2, 2.2 Hz Hz, 1H), 3.69 – 3.60 (m, 2H), 3.55 (s, 3H), 3.53 (dd, J = 8.7, 1.8 Hz, 1H), 3.45 (s, 3H), 3.40 (s, 3H), 3.25 (dd, J = 9.7, 9.2 Hz, 1H), 2.22 (dd, J = 13.0, 4.9, 1.4 Hz, 1H), 1.64 (dd, J = 13.0, 11.5, 3.4 Hz, 1H), 1.26 (td, J = 7.1, 4.7 Hz, 6H); ¹³C NMR (100 MHz, CDCl₃) δ 92.6 (²JCP = 15.9 Hz), 79.8, 78.4, 71.9, 71.2, 60.6, 59.3, 58.40 (²JCP = 10.9, 1.9 Hz), 57.5, 36.2 (³JCP = 4.0 Hz), 17.0 (³JCP = 5.0 Hz); IR (thin film) 2931, 2824, 1442, 1387, 1103, 1024, 900, 748 cm⁻¹; HRMS (TOF MS APCI+) m/z calcd for C₁₃H₂₈O₇P (M + H)⁺ 327.1567, found 327.1567.

**Standard procedure for nucleophilic additions**

Me₃SiOTf (1.6 equiv) was slowly added to a cooled (–78 °C) 0.1 M solution of tetrahydropyran acetal (0.075–0.105 mmol, 1 equiv) and nucleophile (4 equiv) in the indicated solvent. The reaction mixture was stirred at –78 °C for 2 h. A cooled (–78 °C) solution of 1:1:1 MeOH:Et₃N:CH₂Cl₂ (2 mL) was then added to the reaction mixture, and the reaction was allowed to warm to room temperature. Saturated aqueous NaHCO₃ (2
mL) was added, and the mixture was extracted into CH₂Cl₂ (3 x 2 mL). The combined organic layers were dried over Na₂SO₄ and concentrated in vacuo. Diastereomeric ratios of the crude oil were determined by gas chromatography and confirmed by ¹H NMR or ¹³C NMR spectroscopy. Cis- and trans- isomers were identified in ¹H NMR spectra by comparing to published spectroscopic data.

Phenyl 2-[6-(benzyloxymethyl)-tetrahydro-2H-pyran-2-yl] acetate 6

Following the standard procedure for nucleophilic additions, Me₃SiOTf (0.070 g, 0.32 mmol) was added dropwise to a cooled, −78 °C solution of acetal 4 (0.052 g, 0.20 mmol) and nucleophile 2 (0.17 g, 0.79 mmol) in trichloroethylene (2 mL) and stirred for 2 h. Purification of the crude mixture (48:52 cis/trans ratio) by flash chromatography (10% EtOAc in hexanes) yielded 0.032 g pure of cis-6 and 0.034 g of trans-6, for a combined 86% yield.

**cis-6**: ¹H NMR (500, CDCl₃) δ 7.35 – 7.25 (m, 7H), 7.21 – 7.16 (m, 1H), 7.08 – 7.04 (m, 2 H), 4.60 (d, J = 12.2 Hz, 1H), 4.56 (d, J = 12.2 Hz, 1H), 3.94 (dddd, J = 9.9, 7.8, 5.6, 2.0 Hz, 1H), 3.67 (dddd, J = 10.5, 6.1, 4.2, 2.0 Hz, 1 H), 3.53 (dd, J = 10.3, 6.1 Hz, 1H), 3.45 (dd, J = 10.3, 4.2 Hz, 1H), 2.81 (dd, J = 14.9, 7.8 Hz, 1H), 2.67 (dd, J = 14.9, 5.6 Hz, 1H), 1.93 – 1.87 (m, 1H), 1.75 (dddd, J = 12.6, 7.6, 5.6, 2.0 Hz, 1H), 1.65 – 1.60 (m, 1 H), 1.60 – 1.55 (m, 1H), 1.40 – 1.32 (m, 1H), 1.32 – 1.24 (m, 1H); ¹³C NMR (125 MHz, CDCl₃) δ 170.2, 150.9, 138.6, 129.6, 128.5, 127.9, 127.7, 125.9, 121.9, 77.6, 74.7, 73.9, 73.5, 42.0, 31.3, 27.9, 23.3; IR (thin film) 2934, 2851, 1758, 1734, 1088, 800 cm⁻¹; HRMS (TOF MS ES⁺) m / z calcd for C₂₁H₂₄NaO₄ (M + Na)⁺ 363.1567, found, 363.1545. Anal. Calcd for C₂₁H₂₄O₄: C, 74.09; H; 7.11. Found: C, 74.04; H, 7.02.

**trans-6**, characterized as an 11:1 mixture with the cis isomer: ¹H NMR (500 MHz, CDCl₃) δ 7.34 – 7.26 (m, 7H), 7.20 (m, 1H), 7.10 – 7.06 (m, 2H), 4.58 (d, J = 12.1 Hz, 1H), 4.54 (d, J = 12.1 Hz, 1H),
4.44 (dt, \( J = 8.6, 5.8, 4.3 \text{ Hz}, 1H \)), 4.04 (dddd, \( J = 7.0, 6.1, 5.2, 3.6 \text{ Hz}, 1H \)), 3.62 (dd, \( J = 10.0, 6.1 \text{ Hz}, 1H \)), 3.52 (dd, \( J = 10.0, 5.2 \text{ Hz}, 1H \)), 2.98 (dd, \( J = 14.6, 8.6 \text{ Hz}, 1H \)), 2.68 (dd, \( J = 14.6, 5.8 \text{ Hz}, 1H \)), 1.85 (ddt, \( J = 8.9, 6.5, 5.0 \text{ Hz}, 1H \)), 1.74 – 1.68 (m, 3H), 1.57 – 1.52 (m, 1H), 1.52 – 1.47 (m, 1H); \(^{13}C\) NMR (125 MHz, CDCl\(_3\)) \( \delta \) 170.2, 150.9, 138.5, 129.5, 128.5, 127.8, 127.7, 125.9, 121.8, 73.5, 71.9, 70.6, 69.3, 39.0, 29.6, 27.0, 18.5; IR (thin film) 2933, 1756, 1493, 1454, 1150, 1025, 799 cm\(^{-1}\). HRMS (TOF MS ES+) \( m / z \) calcd for \( C_{21}H_{24}NaO_4 \) (M + Na)\(^+\) 363.1567, found, 363.1559. Anal. Calcd for \( C_{21}H_{24}O_4 \): C, 74.09; H, 7.11. Found: C, 74.24; H, 7.12.

\textit{n-Butyl 2-[6-(benzyloxymethyl)-tetrahydro-2H-pyran-2-yl] acetate 7}

Following the standard procedure for nucleophilic additions, Me\(_3\)SiOTf (0.040 g, 0.18 mmol) was added dropwise to a cooled, –78 °C solution of acetal 4 (0.031 g, 0.11 mmol) and nucleophile 2 (0.10 g, 0.45 mmol) in propionitrile (1 mL) and stirred for 2 h. Purification of the crude mixture (40:60 mixture of cis- and trans- isomers) by flash chromatography (10% EtOAc in hexanes) yielded 0.010 g of \textit{cis}-7 and 0.011 g of \textit{trans}-7, for a combined 57% yield.

\textit{cis}-7: \(^1H\) NMR (400 MHz, CDCl\(_3\)) \( \delta \) 7.36 – 7.24 (m, 5H), 4.58 (d, \( J = 12.2 \text{ Hz}, 1H \)), 4.54 (d, \( J = 12.2 \text{ Hz}, 1H \)), 4.07 (t, \( J = 6.7 \text{ Hz}, 2H \)), 3.80 (dddd, \( J = 11.2, 7.1, 6.2, 2.0 \text{ Hz}, 1H \)), 3.60 (dddd, \( J = 11.6, 5.7, 4.6, 2.1 \text{ Hz}, 1H \)), 3.48 (dd, \( J = 10.2, 5.7 \text{ Hz}, 1H \)), 3.41 (dd, \( J = 10.2, 4.6 \text{ Hz}, 1H \)), 2.60 (dd, \( J = 15.0, 7.1 \text{ Hz}, 1H \)), 2.40 (dd, \( J = 15.0, 6.2 \text{ Hz}, 1H \)), 1.91 – 1.82 (m, 1H), 1.69 – 1.63 (m, 1H), 1.64 – 1.55 (m, 3H), 1.55 – 1.50 (m, 1H), 1.36 (tq, \( J = 9.4, 7.4 \text{ Hz}, 2H \)), 1.31 – 1.19 (m, 2H), 0.91 (t, \( J = 7.4 \text{ Hz}, 3H \)); \(^{13}C\) NMR (125 MHz, CDCl\(_3\)) \( \delta \) 171.7, 138.7, 128.5, 127.9, 127.7, 74.7, 73.7, 73.5, 64.5, 42.0, 30.9, 28.1, 19.3, 13.9; IR (thin film) 2934, 2862, 1735, 1454, 1089, 737 cm\(^{-1}\); HRMS (TOF MS ES+) \( m / z \) calcd for \( C_{19}H_{26}KO_4 \) (M + K)\(^+\) 359.1619, found, 359.1629.
trans-7: $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.38 – 7.26 (m, 5H), 4.57 (d, $J = 12.1$ Hz, 1H), 4.53 (d, $J = 12.1$ Hz, 1H), 4.27 (dtd, $J = 7.8$, 6.4, 4.3 Hz, 1H), 4.07 (t, $J = 6.7$ Hz, 2H), 3.94 (dddd, $J = 9.1$, 5.9, 5.6, 3.4 Hz, 1H), 3.56, (dd, $J = 9.9$, 5.9 Hz, 1H) 3.48 (dd, $J = 9.9$, 5.6 Hz, 1H), 2.71 (dd, $J = 14.6$, 7.8 Hz, 1H), 2.46 (dd, $J = 14.6$, 6.4 Hz, 1H), 1.79 – 1.69 (m, 1H), 1.69 – 1.62 (m, 3 H), 1.61 – 1.57 (m, 2H), 1.54 – 1.45 (m, 1H), 1.46 – 1.39 (m, 1H), 1.37 (sext, $J = 7.4$ Hz, 2H), 0.91 (t, $J = 7.4$ Hz, 3H); $^{13}$C NMR (125 MHz, CDCl$_3$) $\delta$ 171.7, 138.6, 128.5, 127.8, 127.7, 73.5, 71.8, 70.6, 69.3, 64.6, 39.0, 30.9, 29.4, 27.0, 19.3, 18.5, 13.9; IR (thin film) 2934, 2868, 1732, 1097, 1048, 736, 698 cm$^{-1}$; HRMS (TOF MS ES+) m/z calcd for C$_{19}$H$_{28}$KO$_4$ (M + K)$^+$ 359.1619; found, 359.1609.

$(2R,3S,4R,6R)$-6-Ethoxy-3,4-dimethoxy-2-(methoxymethyl)tetrahydro-2H-pyran 12

Following the standard procedure for nucleophilic additions, Me$_3$SiOTf (0.16 g, 0.74 mmol) was added dropwise to a cooled (–78 °C) solution of 11 (0.20 g, 0.61 mmol) and EtOH (0.056 g, 1.23 mmol) in trichloroethylene (6.1 mL). Purification by flash chromatography (50% EtOAc in hexanes) yielded 0.10 g (82%) of 12$\beta$ in a 90:10 ratio. This ratio of products is not consistent with the ratio expected by a thermodynamically controlled reaction, which favors the $\alpha$ product. Characterization data matched the reported literature values.$^9$

### III. Stereochemical Proofs of Nucleophilic Substitution Products

The stereochemical configuration of products 6 and 7 was determined by $^1$H NMR spectroscopy and compared with known compounds.$^{3,10}$ Diagnostic coupling constants of $^3$J $> 9$ Hz were observed for axial hydrogens ($H^A$–$H^C$; $H^F$–$H^D$). The observed downfield chemical shift displacements of the 1,5-trans products relative to the 1,5-cis products for $H^A$ and $H^F$ is consistent with observed chemical shifts in the 1,5-allyl substituted tetrahydropyrans.$^{3,10}$ The $^{13}$C NMR spectrum shows a characteristic chemical
shift $\delta$ of about 42 ppm for C1 in the 1,5-cis products 6 and 7, compared to a $\delta$ of $\sim$39 ppm for their 1,5-trans counterparts.

**Figure S1.** Diagnostic $^1$H-$^1$H coupling constants for cis-6

\[
\begin{align*}
\text{cis-6} & \\
\text{H}^A: \delta 3.94 \text{ ppm; } J = 9.9 \text{ Hz (ax}^A\text{–ax}^C\text{), } 2.0 \text{ Hz (ax}^A\text{–eq}^B\text{)} \\
\text{H}^F: \delta 3.67 \text{ ppm; } J = 10.5 \text{ Hz (ax}^F\text{–ax}^D\text{), } 2.0 \text{ Hz (ax}^F\text{–eq}^E\text{)}
\end{align*}
\]

Note: These coupling constants reflect the fact that two conformers of similar energy are present.

**Figure S2.** Diagnostic $^1$H-$^1$H coupling constants for trans-6

\[
\begin{align*}
\text{trans-6} & \\
\text{H}^A: \delta 4.44 \text{ ppm; } J = 5.7 \text{ Hz (eq}^A\text{–ax}^C\text{), } 4.3 \text{ Hz (eq}^A\text{–eq}^B\text{)} \\
\text{H}^F: \delta 3.67 \text{ ppm; } J = 7.0 \text{ Hz (ax}^F\text{–ax}^D\text{), } 3.6 \text{ Hz (ax}^F\text{–eq}^E\text{)}
\end{align*}
\]

Note: These coupling constants reflect the fact that two conformers of similar energy are present.

**Figure S3.** Diagnostic $^1$H-$^1$H coupling constants for cis-7

\[
\begin{align*}
\text{cis-7} & \\
\text{H}^A: \delta 3.80 \text{ ppm; } J = 11.2 \text{ Hz (ax}^A\text{–ax}^C\text{), } 2.0 \text{ Hz (ax}^A\text{–eq}^B\text{)} \\
\text{H}^F: \delta 3.60 \text{ ppm; } J = 11.6 \text{ Hz (ax}^F\text{–ax}^D\text{), } 2.1 \text{ Hz (ax}^F\text{–eq}^E\text{)}
\end{align*}
\]

**Figure S4.** Diagnostic $^1$H-$^1$H coupling constants for trans-7

\[
\begin{align*}
\text{trans-7} & \\
\text{H}^A: \delta 4.27 \text{ ppm; } J = 6.0 \text{ Hz (eq}^A\text{–ax}^C\text{), } 4.3 \text{ Hz (eq}^A\text{–eq}^B\text{)} \\
\text{H}^F: \delta 3.94 \text{ ppm; } J = 9.1 \text{ Hz (ax}^F\text{–ax}^D\text{), } 3.4 \text{ Hz (ax}^F\text{–eq}^E\text{)}
\end{align*}
\]

Note: These coupling constants reflect the fact that two conformers of similar energy are present.
IV. Correlation Between Selected Solvent Parameters and $S_N2$ Selectivity

![Chemical structure]

Table S1: Influence of solvent in $S_N2$ selectivity for the reaction between tetrahydropyran acetal 1 and nucleophile 2

| Order of selectivity | Solvent     | $\varepsilon$ (F/m)$^a$ | $\mu$ (D)$^b$ | $E_T$(30) (kcal/mol)$^c$ | cis : trans ratio | % $S_N2$ product cis-3 |
|----------------------|-------------|--------------------------|--------------|--------------------------|------------------|-----------------------|
| 1                    | Cl$_2$C=CHCl| 3.4                      | 0.8          | 35.9                     | 10.11 : 1        | 91                    |
| 2                    | PhMe        | 2.38                     | 0.37         | 33.9                     | 7.33 : 1         | 88                    |
| 3                    | CS$_2$      | 2.6                      | 0            | 32.8                     | 3.55 : 1         | 78                    |
| 4                    | CH$_2$Cl$_2$| 8.93                     | 1.6          | 40.7                     | 3.00 : 1         | 75                    |
| 5                    | Et$_2$O     | 4.33                     | 1.15         | 34.5                     | 1.86 : 1         | 65                    |
| 6                    | THF         | 7.58                     | 1.75         | 37.4                     | 1.22 : 1         | 55                    |
| 7                    | EtOAc       | 6.02                     | 1.78         | 38.1                     | 1 : 1.70         | 37                    |
| 8                    | EtCN        | 27.7                     | 4.05         | 43.6                     | 1 : 3.76         | 21                    |
| 9                    | H$_2$C=CCN  | 37.5                     | 3.87         | 46.7                     | 1 : 4.88         | 17                    |

$^a$Dielectric constant.$^{11}$ $^b$Dipole moment.$^{12}$ $^c$Empirical solvent polarity parameter.$^{13}$

No direct correlation was found between the different solvent parameters (dipole moment, dielectric constant, etc.) and selectivity towards the $S_N2$ product. This observation is consistent with Mayr's conclusions that none of the common solvent polarity parameters accurately predict relative ionizing power of aprotic solvents.$^{14}$ The closest correlation ($R^2 = 0.79$) was observed for the dipole moment.
**Figure S5:** Plot of the log (cis/trans product ratios) against dielectric constant

![Graph of log(cis/trans ratio) vs dielectric constant](image)

\[ y = -0.0392x + 0.6331 \]

\[ R^2 = 0.67732 \]

**Figure S6:** Plot of the log (cis/trans product ratios) against dipole moment

![Graph of log(cis/trans ratio) vs dipole moment](image)

\[ y = -0.3782x + 0.8412 \]

\[ R^2 = 0.79482 \]
Figure S7: Plot of the log (cis/trans product ratios) against the empirical solvent polarity parameter $E_T(30)$
Figure S8: $^1$H NMR spectrum (400 MHz) of 11
Figure S9: $^{13}$C NMR spectrum (100 MHz) of 11
Figure S10: $^1$H NMR spectrum (500 MHz) of cis-6
Figure S11: $^{13}$C NMR spectrum (125 MHz) of cis-6
Figure S12: $^1$H NMR spectrum (500 MHz) of trans-6
Figure S13: $^{13}$C NMR spectrum (125 MHz) of trans-6
Figure S14. $^1$H NMR spectrum (400 MHz) of cis-7
Figure S15: $^{13}$C NMR spectrum (100 MHz) of cis-7
Figure S16: $^1$H NMR spectrum (400 MHz) of trans-7
Figure S17: $^{13}$C NMR spectrum (100 MHz) of trans-7
VI. Determination of Diastereoselectivity of Selected Compounds

Figure S18: GC spectrum for Table 1, Entry 4
Figure S19: GC spectrum for Table 1, Entry 6

\[ \text{O}_2 \text{BnO}^+ \text{OAc} \xrightarrow{\text{OSiMe}_3} \text{Me}_3 \text{SiOTf} \xrightarrow{-78 \degree C} \text{CH}_2\text{Cl}_2 \xrightarrow{\text{cis-3} \text{ (S_N2-like)} \ + \ \text{trans-3} \text{ (S_N1)}} \]

Area Percent Report

| Sorted By   | Signal |
|-------------|--------|
| Multiplier  | 1.0000 |
| Dilution    | 1.0000 |

Signal 1: FID1A,

| Peak RetTime Type | Width | Area | Height | Area |
|-------------------|-------|------|--------|------|
|                    | [min] | [pA*min] | [pA] | % |
| 1                  | 21.402 | 4966.54 | 1110.44775 | 74.31116 |
| 2                  | 21.557 | 1716.89 | 613.65430 | 25.68884 |

Totals: 6683.43933 1724.10205
Figure S20: GC spectrum for Table 1, Entry 10

```
\begin{align*}
\text{BnO}^- & \xrightarrow{\text{CH}_2=\text{CHCN}} \text{Me}_3\text{SiOTf} \\
-78 \, ^\circ\text{C} & \xrightarrow{\text{OSiMe}_3} \text{cis-3} \\
\text{cis-3} & (\text{SN}_2 \text{-like}) \\
\text{trans-3} & (\text{SN}_1)
\end{align*}
```

Area Percent Report

| Sorted By   | Signal |
|-------------|--------|
| Multiplier  | 1.0000 |
| Dilution    | 1.0000 |

Signal 1: FID1 A,

| Peak Ret Time | Type | Width | Area  | Height | Area % |
|---------------|------|-------|-------|--------|--------|
| 1 21.321 MM   | MM   | 0.0470| 677.18823| 240.25647| 18.10798|
| 2 21.566 MM   | MM   | 0.0617| 3046.08423| 822.59149| 81.81202|

Totals: 3723.27246 1062.84796
Figure S21: GC spectrum for Table 2, Entry 2

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**Figure S22:** GC spectrum for Table 2, Entry 5
**Figure S23:** GC spectrum for Table 3, Entry 2

![GC spectrum diagram](image)

**Area Percent Report**

| Sorted By   | Signal |
|-------------|--------|
| Multiplier  | 1.0000 |
| Dilution    | 1.0000 |

**Signal 1: FID1 A,**

| Peak Ret Time | Width [min] | Area [pA*sec] | Height [pA] | Area % |
|---------------|-------------|---------------|-------------|--------|
| 1 17.936 MM   | 0.0472      | 1696.08997    | 598.29309   | 81.57045 |
| 2 18.137 MM   | 0.0376      | 383.20471     | 169.76398   | 18.42955 |

**Totals:**

| 2079.29468 | 768.05707 |
Figure S24: GC spectrum for Table 3, Entry 3

\[
\begin{align*}
\text{OMe} & \text{O} \text{O} \text{Me} \\
\text{OMe} & \text{O} \text{O} \text{Me} \\
\text{MeO} & 2 \text{Me}_3\text{SiOTf} \text{Cl}_2\text{C} = \text{CHCl} (-78 \text{ °C}) \text{MeO} \text{O} \text{O} \text{Me} \\
\text{OMe} & \text{O} \text{O} \text{Me} \\
\end{align*}
\]

---

**Area Percent Report**

| Sorted By | Multiplier | Dilution |
|-----------|------------|----------|
| Signal    | 1.0000     | 1.0000   |

Signal 1: FID1 A,

| Peak # | RetTime | Type | Width (min) | Area (pA*s) | Height (pA) | Area % |
|--------|---------|------|-------------|-------------|-------------|--------|
| 1      | 17.903  | MM   | 0.0381      | 608.37109   | 266.02127   | 87.01431 |
| 2      | 18.132  | MM   | 0.0419      | 90.79105    | 36.10112    | 12.98569 |

Totals: 699.16214 302.12239
Figure S25: GC spectrum for Scheme 5, with trichloroethylene as solvent

8 \[ \xrightarrow{\text{MeO}} \] 10β (SN2) + 10α (SN1)

\[
\begin{array}{c}
\text{MeO} \quad \text{OMe} \\
\text{OMe} \quad \text{MeO} \\
\text{OMe} \quad \text{OAc} \\
\end{array}
\]

5 \[ \xrightarrow{\text{On-Bu Me3SiOTf}} \] 8

\[
\begin{align*}
\text{Cl}_2\text{C}=&\text{CHCl} \\
\text{-78 °C} \\
\end{align*}
\]
Figure S26: GC spectrum for Scheme 6, with dichloromethane as solvent
Figure S27: GC spectrum for Scheme 6, with trichloroethylene as solvent
VII. Literature Cited

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