Gold- and Silver-Catalyzed Glycosylation with Pyranone Glycosyl Donors: An Efficient and Diastereoselective Synthesis of α-Anomers

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General Methods. Commercial reagents and solvents were used without further purification, unless
otherwise stated. PtCl₂ (98%) and PtCl₄ (98%) were purchased from Aldrich. AuCl₃ (99%), AuCl (99%), AgBF₄ (99.99%) and AgSbF₆ (99%) were purchased from Adamas. CH₂Cl₂ and ether were refluxed with CaH₂ and distilled prior to use. Toluene and THF were distilled from sodium. Flash chromatography was performed using the indicated solvent system on silica gel standard grade 60 (230-400 mesh). Optical rotations were obtained using a digital polarimeter at sodium D line (589 nm) and were reported in concentration of g/100 mL. ¹H NMR spectra were recorded on a 400 MHz spectrometer. ¹³C NMR spectra were recorded on a 100 MHz spectrometer. Chemical shifts are reported relative to CDCl₃ (δ 7.26 ppm) for ¹H NMR and CDCl₃ (δ 77.00 ppm) for ¹³C NMR. Melting points are uncorrected.

**General Procedure for Gold- and Silver-Catalyzed Glycosylation.** To a solution of glycosyl donor
L-3 (0.40 mmol) and the appropriate alcohol (0.80 mmol) in anhydrous THF (2.0 mL) was added AuCl3 or AgSbF6 (0.020 mmol) at –20 °C under nitrogen atmosphere. The mixture was stirred at –20 °C for 30 min. After removal of the solvent under reduced pressure, the residue was then purified by flash column chromatography on silica gel using an appropriate eluent to give the desired glycoside.


\[\alpha-L-5a\]

\(\alpha-L-5a\): colorless oil; \([\alpha]_D^{1} = +21.5 (c = 0.5, \text{CH}_2\text{Cl}_2)\); \(^1\text{H} NMR (400 MHz, CDCl_3) \delta 6.80 (dd, J = 10.2, 3.5 Hz, 1H), 6.05 \text{ (d, J = 10.2 Hz, 1H), 5.33 \text{ (d, J = 3.5 Hz, 1H), 4.59 \text{ (i, J = 6.8 Hz, 1H), 3.72–3.64 \text{ (m, 1H), 1.98–1.95 \text{ (m, 1H), 1.88–1.72 \text{ (m, 3H), 1.68–1.46 \text{ (m, 7H), 1.38–0.94 \text{ (m, 20H), 1.37 \text{ (d, J = 6.8 Hz, 3H), 0.89 \text{ (d, J = 6.4 Hz, 3H), 0.87 \text{ (d, J = 1.6 Hz, 3H), 0.85 \text{ (d, J = 1.6 Hz, 3H), 0.80 \text{ (s, 3H), 0.64 \text{ (s, 3H), }^{13}\text{C} NMR (100 MHz, CDCl}_3) \delta 197.29, 144.17, 127.20, 91.36, 77.89, 70.28, 56.48, 56.31, 54.38, 44.84, 42.61, 40.04, 39.53, 37.11, 36.19, 35.79, 35.62, 35.50, 34.54, 32.08, 29.34, 28.85, 28.25, 28.01, 24.22, 23.84, 22.81, 22.56, 21.25, 18.68, 15.27, 12.25, 12.08; ESI-MS: \text{m/z} = 499.2 (\text{M}^+ + \text{H})\].

\[(2S,6R)-6-(benzyloxy)-2-methyl-2H-pyran-3(6H)-one\]

\[\alpha-L-5b\]

\(\alpha-L-5b\): colorless oil; \([\alpha]_D^{1} = +53.4 (c = 0.5, \text{CH}_2\text{Cl}_2); \(^1\text{H} NMR (400 MHz, CDCl_3) \delta 7.38–7.32 \text{ (m, 5H), 6.83 \text{ (dd, J = 10.2, 3.5 Hz, 1H), 6.09 \text{ (d, J = 10.2 Hz, 1H), 5.28 \text{ (d, J = 3.4 Hz, 1H), 4.84 \text{ (d, J = 11.8 Hz, 1H), 4.69 \text{ (d, J = 11.8 Hz, 1H), 4.56 \text{ (q, J = 6.8 Hz, 1H), 1.37 \text{ (d, J = 6.8 Hz, 3H), }^{13}\text{C} NMR (100 MHz, CDCl}_3) \delta 196.98, 143.42, 137.21, 128.59, 128.16, 128.12, 127.51, 92.40, 70.85, 70.52, 15.21; ESI-MS: \text{m/z} = 219.0 (\text{M}^+ + \text{H})].

\[(2S,6R)-2-methyl-6-phenethoxy-2H-pyran-3(6H)-one\]
α-L-5c: colorless oil; [α]_D^20 = +30.1 (c = 0.5, CH₂Cl₂); ^1H NMR (400 MHz, CDCl₃) δ 7.37–7.30 (m, 5H), 6.86 (dd, J = 10.2, 3.5 Hz, 1H), 6.12 (d, J = 10.2 Hz, 1H), 5.21 (d, J = 3.5 Hz, 1H), 4.37 (t, J = 6.8 Hz, 1H), 4.20–4.07 (m, 1H), 3.92 (dt, J = 9.7, 6.7 Hz, 1H), 3.01 (t, J = 6.9 Hz, 2H), 1.37 (d, J = 6.8 Hz, 3H); ^13C NMR (100 MHz, CDCl₃) δ 197.08, 143.38, 138.58, 128.89, 128.44, 127.29, 126.44, 93.17, 70.38, 69.88, 36.29, 15.21; ESI-MS: m/z = 233.1 (M⁺ + H).

(2S,6R)-6-(cyclohexyloxy)-2-methyl-2H-pyran-3(6H)-one

α-L-5d: colorless oil; [α]_D^20 = +4.2 (c = 0.5, CH₂Cl₂); ^1H NMR (400 MHz, CDCl₃) δ 6.80 (dd, J = 10.2, 3.5 Hz, 1H), 6.05 (d, J = 10.2 Hz, 1H), 5.32 (d, J = 3.4 Hz, 1H), 4.58 (q, J = 6.8 Hz, 1H), 3.77–3.64 (m, 1H), 1.94–1.92 (m, 2H), 1.76–1.74 (m, 2H), 1.57–1.19 (m, 6H), 1.37 (d, J = 6.8 Hz, 3H); ^13C NMR (100 MHz, CDCl₃) δ 197.34, 144.24, 127.13, 91.46, 70.29, 33.47, 32.00, 25.52, 24.25, 15.24; ESI-MS: m/z = 211.0 (M⁺ + H).

(2S,6R)-6-(((1R,2S,5R)-2-isopropyl-5-methylcyclohexyl)oxy)-2-methyl-2H-pyran-3(6H)-one

α-L-5e: colorless oil; [α]_D^20 = -41.2 (c = 0.5, CH₂Cl₂); ^1H NMR (400 MHz, CDCl₃) δ 6.82 (dd, J = 10.2, 3.5 Hz, 1H), 6.05 (d, J = 10.2 Hz, 1H), 5.23 (d, J = 3.5 Hz, 1H), 4.60 (q, J = 6.8 Hz, 1H), 3.45 (td, J = 10.6, 4.4 Hz, 1H), 2.16–2.08 (m, 2H), 1.68–1.58 (m, 2H), 1.48–0.88 (m, 5H), 1.36 (d, J = 6.8 Hz, 3H), 0.92 (d, J = 4.0 Hz, 3H), 0.91 (d, J = 4.0 Hz, 3H), 0.79 (d, J = 6.8 Hz, 3H); ^13C NMR (100 MHz, CDCl₃) δ 197.17, 143.47, 127.02, 94.96, 81.51, 70.26, 48.68, 42.98, 34.21, 31.71, 25.77, 23.30, 22.27, 21.07, 16.31, 15.11; ESI-MS: m/z = 267.1 (M⁺ + H).
(2S,6S)-6-((3R,5R,7R)-adamantan-1-yloxy)-2-methyl-2H-pyran-3(6H)-one

\[ \text{H} \]
\[ \alpha-L-5f \]

\( \alpha-L-5f \): colorless oil; \([\alpha]_D^{25} = +27.7 \) (c = 0.5, CH\(_2\)Cl\(_2\)); \(^1\text{H} \) NMR (400 MHz, CDCl\(_3\)) \( \delta \) 6.75 (dd, \( J = 10.1 \), 3.6 Hz, 1H), 6.03 (d, \( J = 10.1 \) Hz, 1H), 5.59 (d, \( J = 3.6 \) Hz, 1H), 4.65 (q, \( J = 6.8 \) Hz, 1H), 2.22–2.17 (m, 3H), 1.93–1.81 (m, 6H), 1.75–1.60 (m, 6H), 1.34 (d, \( J = 6.8 \) Hz, 3H); \(^{13}\text{C} \) NMR (100 MHz, CDCl\(_3\)) \( \delta \) 197.85, 145.45, 126.88, 86.54, 75.18, 70.01, 42.46, 36.21, 30.75, 15.28; ESI-MS: \( m/z = 263.1 \) (M\(^+\) + H).

(2S,6R)-6-(((3aR,4R,6S,7S,7aR)-4-methoxy-2,2,6-trimethyltetrahydro-3aH-[1,3]dioxolo[4,5-c]pyran-7-yl)oxy)-2-methyl-2H-pyran-3(6H)-one

\[ \text{H} \]
\[ \alpha-L-5g \]

\( \alpha-L-5g \): white solid; mp: 126–127 °C; \([\alpha]_D^{25} = +105.3 \) (c = 0.5, CH\(_2\)Cl\(_2\)); \(^1\text{H} \) NMR (400 MHz, CDCl\(_3\)) \( \delta \) 6.82 (dd, \( J = 10.2 \), 3.5 Hz, 1H), 6.07 (d, \( J = 10.2 \) Hz, 1H), 5.28 (d, \( J = 3.5 \) Hz, 1H), 4.86–4.79 (m, 2H), 4.12–4.08 (m, 2H), 3.68–3.64 (m, 1H), 3.55–3.52 (m, 1H), 3.36 (s, 3H), 1.57 (s, 3H), 1.37 (d, \( J = 6.7 \) Hz, 3H), 1.34 (s, 3H), 1.30 (d, \( J = 6.3 \) Hz, 3H); \(^{13}\text{C} \) NMR (100 MHz, CDCl\(_3\)) \( \delta \) 197.62, 142.75, 127.51, 109.25, 98.04, 93.28, 80.21, 77.13, 76.15, 70.72, 64.75, 54.90, 28.15, 26.38, 17.48, 15.21; ESI-MS: \( m/z = 329.1 \) (M\(^+\) + H).

\(^1\text{H} \) NMR spectra of isomers L-5 for \( \alpha/\beta \) ratio in Table 2.
L-5e
α:β=99:1

L-5f
α:β=15:1
L-5g

α:β~99:1