Synthesis of 2,3-unsaturated glycosides and disaccharides via RuCl₃ catalyzed Ferrier glycosylation

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**Experimental**

**General Synthesis Information.** Reactions were run in screw capped glass vials (4 mL) stirred with Teflon®-coated magnetic stir bars. Moisture and air-sensitive reactions were performed in flame-dried round bottom flasks, fitted with rubber septa or glass gas adapters, under a positive pressure of nitrogen. Moisture and air-sensitive liquids or solutions were transferred via nitrogen-flushed syringe. Concentration of solvents was accomplished by rotary evaporation using a Büchi rotary evaporator at temperatures between 35 °C and 50 °C. Experiments were monitored by thin layer chromatography (TLC).

**Materials.** Unless otherwise noted, materials were obtained from commercial suppliers and used without purification. Removal of solvent under reduced pressure refers to distillation with a Büchi rotary evaporator attached to a vacuum pump (~3 mmHg). Products obtained as solids or high boiling oils were dried under vacuum (~1 mmHg).

**Chromatography.** Analytical TLC was performed using Whatman 250 micron aluminum backed UV F254 precoated silica gel flexible plates. Subsequent to elution, ultraviolet illumination at 254 nm allowed for visualization of UV active materials. Staining with p-anisaldehyde, basic potassium permanganate solution, or Molisch's reagents allowed for further visualization. The retardation factor (Rf) is the ratio of the distance traveled by the compound to the distance traveled by the eluent.

**Physical Data.** Proton nuclear magnetic resonance spectra (1H NMR) were recorded on Avance 300 or Avance 500 MHz nuclear magnetic resonance spectrometers. Chemical shifts for 1H NMR spectra are reported as δ in units of parts per million (ppm) relative to tetramethylsilane (δ 0.0) using the residual solvent signal as an internal standard or tetramethylsilane itself: chloroform-d (δ 7.26, singlet). The number of protons (n) for a given resonance is indicated by nH. IR spectra were recorded on Bruker Alpha spectrometer and mass analyses (ESI) were performed on Finnegan MAT 1020 mass spectrometer operating at 70 eV.
**General procedure for the RuCl₃-catalyzed Ferrier reaction.** To a stirred solution of 3,4,6-tri-O-acetyl-D-glucal 1 (1 equiv) and acceptor (1.2 equiv) in anhydrous acetonitrile (2 mL/mmol) under an atmosphere of argon was added RuCl₃ (2 mol%) at room temperature. The reaction mixture was stirred until the complete consumption of the starting material (glycal). The solvent was concentrated in vacuo, the crude residue was re-dissolved in dichloromethane and loaded on a silica gel column. The product was purified by silica gel chromatography using Hexane/EtOAc to afford the 2,3-unsaturated α-glycosides in excellent yields. All the Ferrier products were confirmed by IR, ¹H NMR, ¹³C NMR and MS/HRMS spectroscopy.
**$^1$H NMR Spectrum of compound 3a in CDCl$_3$ (300 MHz)**

13C NMR Spectrum of compound 3a in CDCl$_3$ (75 MHz)
\textsuperscript{1}H NMR Spectrum of compound 3b in CDCl\textsubscript{3} (500 MHz)

\textsuperscript{13}C NMR Spectrum of compound 3b in CDCl\textsubscript{3} (75 MHz)
$^1$H NMR Spectrum of compound 3c in CDCl$_3$ (300 MHz)

$^{13}$C NMR Spectrum of compound 3c in CDCl$_3$ (75 MHz)
$^1$H NMR Spectrum of compound 3d in CDCl$_3$ (300 MHz)

$^{13}$C NMR Spectrum of compound 3d in CDCl$_3$ (75 MHz)
$^1$H NMR Spectrum of compound 3e in CDCl$_3$ (500 MHz)

$^{13}$C NMR Spectrum of compound 3e in CDCl$_3$ (125 MHz)
\(^1\)H NMR Spectrum of compound 3f in CDCl\(_3\) (500 MHz)

\(^{13}\)C NMR Spectrum of compound 3f in CDCl\(_3\) (75 MHz)
$^1$H NMR Spectrum of compound 3g in CDCl$_3$ (500 MHz)

$^{13}$C NMR Spectrum of compound 3g in CDCl$_3$ (75 MHz)
$^1$H NMR Spectrum of compound 3h in CDCl$_3$ (500 MHz)

$^{13}$C NMR Spectrum of compound 3h in CDCl$_3$ (75 MHz)
$^1$H NMR Spectrum of compound 3i in CDCl$_3$ (500 MHz)

$^{13}$C NMR Spectrum of compound 3i in CDCl$_3$ (75 MHz)
$^1$H NMR Spectrum of compound 3j in CDCl$_3$ (500 MHz)

$^{13}$C NMR Spectrum of compound 3j in CDCl$_3$ (75 MHz)
\[ ^1H \text{NMR Spectrum of compound 3k in CDCl}_3 \ (500 \text{ MHz}) \]

\[ \begin{align*}
\text{FERRIER}_6\text{-OH GALACTOSE DIACETONIDE.ESP} \\
\end{align*} \]

\[ \begin{align*}
\text{Chemical Shift (ppm)} \\
\text{Normalized Intensity} \\
0.38 & 1.94 & 1.16 & 1.00 & 0.47 & 0.96 & 1.25 & 5.96 & 1.631 & 10.1 & 24 & 2 \ \\
0.76 & 0.63 & 0.5 & 0.43 & 0.39 & 0.34 & 0.31 & 0.28 & 0.25 & 0.22 & 0.19 & 0.16 \\
\end{align*} \]

\[ \begin{align*}
\text{13C NMR Spectrum of compound 3k in CDCl}_3 \ (75 \text{ MHz}) \]

\[ \begin{align*}
\text{FERRIER}_6\text{-OH GALACTOSE DIACETONIDE}_1\text{3C}_GNY.ESP \\
\end{align*} \]

\[ \begin{align*}
\text{Chemical Shift (ppm)} \\
\text{Normalized Intensity} \\
170.75 & 170.17 & 129.08 & 127.62 & 109.19 & 108.45 & 96.24 & 94.50 & 77.00 & 76.58 & 70.82 & 70.51 & 70.08 & 69.95 & 62.76 & 25.95 & 25.89 & 24.81 & 24.42 & 20.73 \\
\end{align*} \]
$^1$H NMR Spectrum of compound 3l in CDCl$_3$ (500 MHz)

$^{13}$C NMR Spectrum of compound 3l in CDCl$_3$ (125 MHz)
\(^1\)H NMR Spectrum of compound 3m in CDCl\(_3\) (500 MHz)

\[^{13}\text{C}\] NMR Spectrum of compound 3m in CDCl\(_3\) (75 MHz)
$^1$H NMR Spectrum of compound 3n in CDCl$_3$ (300 MHz)

$^{13}$C NMR Spectrum of compound 3n in CDCl$_3$ (75 MHz)
\(^1\)H NMR Spectrum of compound 3o in CDCl\(_3\) (500 MHz)

\(^1\)C NMR Spectrum of compound 3o in CDCl\(_3\) (75 MHz)
$^1$H NMR Spectrum of compound 3p in CDCl$_3$ (300 MHz)

$^{13}$C NMR Spectrum of compound 3p in CDCl$_3$ (75 MHz)
$^{1}H$ NMR Spectrum of compound 3q in CDCl$_3$ (500 MHz)

$^{13}C$ NMR Spectrum of compound 3q in CDCl$_3$ (75 MHz)
$^1$H NMR Spectrum of compound 3r in CDCl$_3$ (500 MHz)

$^{13}$C NMR Spectrum of compound 3q in CDCl$_3$ (75 MHz)