Supplementary Information For:

Synthesis of Enantiopure Chloroalcohols by Enzymatic Kinetic Resolution

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Table of contents

General procedure for the synthesis of substrates 1-7 ................................................................. 2
$^1$H and $^{13}$C(APT) spectra for substrates 1-7 .................................................................................. 3
1-Chloro-pent-3-en-2-ol (1) ........................................................................................................ 3
1-chloro-hex-3-en-2-ol (2) ............................................................................................................. 4
1-Chloro-oct-3-en-2-ol (3) ............................................................................................................. 5
1-Chloro-3,5-octadien-2-ol (4) ........................................................................................................ 6
(E)-1-Chloro-4-phenyl-but-3-en-2-ol (5) ......................................................................................... 7
2-Chloro-1-furan-2-yl-ethanol (6) ..................................................................................................... 8
2-Chloro-1-thiophen-2-yl-ethanol (7) .............................................................................................. 9
References .................................................................................................................................................. 10
General procedure for the synthesis of substrates 1-7

Substrates 1-7 were synthesized according to a literature procedure\(^1\).

\[
\begin{array}{c}
\text{CHO} \\ R \end{array} \xrightarrow{\text{ClCH}_2\text{I (1.5 eq)}} \xrightarrow{n-\text{BuLi (1.5 eq)}} \xrightarrow{\text{THF, -78ºC}} \begin{array}{c}
\text{OH} \\ R \end{array} \text{Cl}
\]

In a flamedried flask, a solution of aldehyde (typically 20 mmol) in freshly distilled THF (50 mL) was cooled down to \(-78\) °C. Chloroiodomethane (30 mmol) was then added, and subsequently \(n\)-butyllithium (30 mmol, 2.5 M in hexanes, 12 mL) was added dropwise to the solution over a period of 30 min. The reaction mixture was stirred until the starting material was fully converted (TLC), then quenched with \(\text{NH}_4\text{Cl}\) (sat.). After extraction with Et\(_2\)O (3x), the combined organic layers were washed with brine, dried over \(\text{Na}_2\text{SO}_4\), filtered, and solvents evaporated. The crude products thus obtained were further purified by flash chromatography.
$^1$H and $^{13}$C(APT) spectra for substrates 1-7

1-Chloro-pent-3-en-2-ol (I)$^2$

Prepared according to the general procedure, starting from 2.06 mL (1.75 g; 25 mmol) of crotonaldehyde. After flash chromatography over silica gel (pentane/Et$_2$O 4:1) a colorless oil was obtained (2.21 g; 18.3 mmol; 73%).

$^1$H NMR:

$^{13}$C NMR (APT):
1-chloro-hex-3-en-2-ol (2)

Prepared according to the general procedure, starting from 1.96 mL (1.68 g; 20 mmol) of pent-2-enal. After flash chromatography over silica gel (pentane/Et₂O 6:1, gradient to 4:1) a colorless oil was obtained (1.77 g; 13.2 mmol; 66%).

¹H NMR:

³¹C NMR (APT):
1-Chloro-oct-3-en-2-ol (3)\textsuperscript{1,3}

Prepared according to the general procedure, starting from 1.31 mL (1.12 g; 10 mmol) of hept-2-enal. After flash chromatography over silica gel (pentane/Et\textsubscript{2}O 6:1; \textit{R}_f = 0.32) a colorless oil was obtained (903 mg; 5.55 mmol; 56%).

\textsuperscript{1}H NMR:

\textsuperscript{13}C NMR (APT):

\[ \text{Diagram of chemical structure} \]
1-Chloro-3,5-octadien-2-ol (4)

Prepared according to the general procedure, starting from 1.25 mL (1.10 g; 10 mmol) of \textit{trans,trans}-hepta-2,4-dienal. After flash chromatography over silica gel (pentane/Et₂O 7:1; \(R_f = 0.26\)) a colorless oil was obtained (1.29 g; 8.0 mmol; 79%).

\(\text{\textsuperscript{1}H NMR:}\)

\(\text{\textsuperscript{13}C NMR (APT):}\)
(E)-1-Chloro-4-phenyl-but-3-en-2-ol (5)\textsuperscript{1,3,4,5,6}

Prepared according to the general procedure, starting from 2.52 mL (2.64 g; 20 mmol) of cinnamaldehyde. After flash chromatography over silica gel (pentane/Et\textsubscript{2}O 5:1; \( R_f = 0.24 \)) a colorless oil was obtained (2.34 g; 12.8 mmol; 64%), which crystallized upon standing.

\textsuperscript{1}H NMR:

\textsuperscript{13}C NMR (APT):
2-Chloro-1-furan-2-yl-ethanol (6)

Prepared according to the general procedure, starting from 1.66 mL (1.92 g; 20 mmol) of freshly distilled furfural. After flash chromatography over silica gel (pentane/Et₂O 4:1, gradient to 3:1; R<sub>f</sub> 3:1 = 0.40) a light yellow oil (1.87 g; 12.7 mmol; 64%) was obtained.

For the resolution on 2.3 g scale, different preparations were combined.

<sup>1</sup>H NMR:

![1H NMR spectrum](image)

<sup>13</sup>C NMR (APT):

![13C NMR spectrum](image)
2-Chloro-1-thiophen-2-yl-ethanol (7)\textsuperscript{4,8}

Prepared according to the general procedure, starting from 1.87 mL (2.24 g; 20 mmol) of 2-thiophene-carboxaldehyde. After flash chromatography over silica gel (pentane/Et\textsubscript{2}O 4:1; \( R_f = 0.33 \)) a colorless oil was obtained (2.86 g; 17.6 mmol; 88\%). For the 20 g scale resolution, this compound was prepared analogously (64\%).

\textsuperscript{1}H NMR:

\textsuperscript{13}C NMR (APT):

![NMR spectra](image-url)
References


