Supporting Information

Application of Sulfuryl Chloride for Quick Construction of β-Chlorotetrahydrofuran Derivatives from Homoallylic Alcohols under Mild Conditions

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1. General Methods

All chemicals were purchased as reagent grade and used without further purification, unless otherwise noted. Dichloromethane was distilled over calcium hydride. Nuclear magnetic resonance ($^1$H NMR and $^{13}$C NMR) spectra were obtained on a Bruker Avance III 400 MHz spectrometer. Chemical shifts ($\delta$) are reported in parts per million (ppm) downfield from internal TMS. HRMS (ESI) was determined on a Bruker Daltonics microTOF-Q II or a Bruker Daltonics APEX II 47e FT-ICR mass spectrometer. GC-MS was measured on Agilent 7890A/5975C spectrometer. Silica gel (200-300 mesh) was used for column chromatography and TLC inspection was on silica gel GF$_{254}$ plates.

2. General Procedure for the Synthesis of Compounds (1a-w)

2.1 Homoallylic alcohols 1a-q, 1t, 1u: $^1$

Lithium bis(trimethylsilyl)amide (10.5 mmol) added dropwise at -20 °C to a suspension of (3-propan-1-ol)triphenylphosphonium bromide (4.5 mmol) in 10 ml of tetrahydrofuran. The solution was stirred at -20°C for 1 hour and aldehyde (3.75 mmol) was added dropwise. After additional, the mixture was stirred at the same temperature for 2 hours. The mixture was warmed to room temperature and stirred for another 12 hours, then saturated aqueous NH$_4$Cl solution was added. The organic layer was dried over MgSO$_4$ and then concentrated under reduced pressure. The residue was purified by flash column chromatography (EtOAc/Petroleum = 1/5; v/v).

(E)-4-(2,6-dichlorophenyl)but-3-en-1-ol (1h) Colorless oil (634 mg, 78%). $^1$H NMR (CDCl$_3$, 400 MHz) $\delta$ = 7.27-7.31 (m, 2H), 7.05-7.09 (m, 1H), 6.45 (d, $J = 16.4$ Hz, 1H), 6.15 (dt, $J = 7.2$, 2.0 Hz, 1H), 3.76-3.79 (m, 2H), 2.54 (ddd, $J = 6.0$, 4.2, 1.2 Hz, 2H), 1.86 (s, 1H); $^{13}$C NMR (CDCl$_3$, 100 MHz) $\delta$ = 135.4, 134.3, 132.1, 128.3, 128.0, 126.6, 61.6, 36.8. HRMS (ESI-TOF) m/z: [M+Na]$^+$ Calcd for C$_{10}$H$_{10}$Cl$_{2}$ONa 239.0001; Found 239.0007.
**(E)-4-(3-bromophenyl)but-3-en-1-ol (1j)** Colorless oil (681 mg, 80%). \(^1\)H NMR (CDCl\(_3\), 400 MHz) \(\delta = 7.49\) (t, \(J = 1.6\) Hz, 1H), 7.30-7.33 (m, 1H), 7.22-7.25 (m, 1H), 7.12-7.16 (m, 1H), 6.39 (d, \(J = 16.0\) Hz, 1H), 6.02 (dt, \(J = 7.2, 1.2\) Hz, 1H), 3.73 (d, \(J = 6.4\) Hz, 2H), 2.44 (dddd, \(J = 6.4, 6.0, 4.2, 1.2\) Hz, 2H), 1.98 (s, 1H); \(^{13}\)C NMR (CDCl\(_3\), 100 MHz) \(\delta = 140.8, 131.1, 129.6, 128.9, 126.2, 125.49, 125.45, 125.41, 125.37, 61.8, 36.3\). HRMS (ESI-TOF) m/z: [M+Na]\(^+\) Calcd for C\(_{10}\)H\(_{11}\)BrONa 248.9885; Found 248.9888.

**(E)-4-(2-bromophenyl)but-3-en-1-ol (1k)** Colorless oil (723 mg, 85%). \(^1\)H NMR (CDCl\(_3\), 400 MHz) \(\delta = 7.46-7.53\) (m, 2H), 7.21-7.28 (m, 2H), 6.79-7.6.82 (d, \(J = 15.6\) Hz, 1H), 6.11-6.19 (m, 1H), 3.73-3.77 (m, 2H), 2.50-2.51 (m, 2H), 1.98 (s, 1H); \(^{13}\)C NMR (CDCl\(_3\), 100 MHz) \(\delta = 137.1, 132.9, 131.4, 129.7, 128.6, 127.8, 127.5, 127.0, 61.9, 36.4\). GC/MS (EI) m/z : 226.0.

**(E)-4-(4-(dimethylamino)phenyl)but-3-en-1-ol (1m)** Colorless oil (415 mg, 58%). \(^1\)H NMR (CDCl\(_3\), 400 MHz) \(\delta = 7.25\) (d, \(J = 8.8\) Hz, 2H), 6.68 (d, \(J = 8.8\) Hz, 2H), 6.40 (d, \(J = 16.0\) Hz, 1H), 5.97 (dt, \(J = 7.2, 1.2\) Hz, 1H), 3.71 (d, \(J = 5.6\) Hz, 2H), 2.94 (s, 6H), 2.44 (ddd, \(J = 6.0, 4.2, 1.2\) Hz, 2H), 1.59 (s, 1H); \(^{13}\)C NMR (CDCl\(_3\), 100 MHz) \(\delta = 149.9, 132.8, 127.0, 121.8, 112.6, 62.2, 40.7, 36.5\). HRMS (ESI-TOF) m/z: [M+H]\(^+\) Calcd for C\(_{12}\)H\(_{18}\)NO 192.1383; Found 192.1380.

**(E)-4-(naphthalen-1-yl)but-3-en-1-ol (1n)** Colorless oil (668 mg, 90%). \(^1\)H NMR (CDCl\(_3\), 400 MHz) \(\delta = 8.14-8.16\) (m, 1H), 7.86-7.88 (m, 1H), 7.77-7.78 (m, 1H), 7.45-7.53 (m, 4H), 7.26 (d, \(J = 15.6\) Hz, 1H), 6.23 (dt, \(J = 7.2, 1.2\) Hz, 1H), 3.82 (d, \(J = 6.4\) Hz, 2H), 2.58-2.63 (m, 2H), 1.85 (s, 1H); \(^{13}\)C NMR (CDCl\(_3\), 100 MHz) \(\delta =


(E)-4-(thiophen-2-yl)but-3-en-1-ol (1o) Colorless oil (467 mg, 81%). $^1$H NMR (CDCl$_3$, 400 MHz) $\delta$ = 7.10 (d, $J$ = 4.8 Hz, 1H), 6.93 (dd, $J$ = 3.6, 1.2 Hz, 1H), 6.89 (d, $J$ = 3.2 Hz, 1H), 6.61 (d, $J$ = 16.0 Hz, 1H), 6.02 (dt, $J$ = 7.2, 1.2 Hz, 1H), 3.72 (d, $J$ = 6.0 Hz, 2H), 2.41-2.46 (m, 2H), 1.81 (s, 1H); $^{13}$C NMR (CDCl$_3$, 100 MHz) $\delta$ = 142.4, 127.3, 126.3, 124.9, 123.6, 61.9, 36.2. HRMS (ESI-TOF) m/z: [M+Na]$^+$ Calcd for C$_8$H$_{10}$SONa 177.0345; Found 177.0349.

(E)-4-(pyridin-4-yl)but-3-en-1-ol (1p) Colorless oil (257 mg, 46%). $^1$H NMR (CDCl$_3$, 400 MHz) $\delta$ = 8.42-8.43 (m, 2H), 7.17-7.18 (m, 2H), 6.37-6.54 (m, 2H), 3.76-3.81 (m, 2H), 2.51-2.52 (m, 2H); $^{13}$C NMR (CDCl$_3$, 100 MHz) $\delta$ = 149.6, 145.1, 133.1, 129.6, 120.8, 61.3, 36.5. HRMS (ESI-TOF) m/z: [M+H]$^+$ Calcd for C$_9$H$_{12}$NO 150.0913; Found 150.0911.

2.2 (E)-2-methyl-5-phenylpent-4-en-2-ol (1r): 

To a solution of malonic acid (7.1 g, 68.2 mmol) in DMSO (25 mL), AcOH (0.04 mL, 0.04 g, 0.65 mmol) and piperidine (0.07 mL, 0.055 g, 0.65 mmol) in DMSO (2 mL) was added. The reaction solution was warmed to 65 °C and phenylacetaldehyde (4 mL, 3.7 g, 31 mmol) was added dropwise within 90 min. Then the reaction mixture was stirred for further 1.5 h at 65 °C. After the reaction was completed, the solution was cooled to room temperature, taken up in H$_2$O (75 mL) and extracted with Et$_2$O (1 x 25 mL and 3 x 20 mL). The combined organic extracts were washed with 5% aqueous KHSO$_4$ and brine, dried over MgSO$_4$, and evaporated to dryness. The oil residue was
purified by flash chromatography on silica gel (EtOAc:petroleum ether, 1:5 v/v) to give (E)-methyl 4-phenylbut-3-enoate as colourless oil (4.0 g, 41%).

Under an argon atmosphere, CH₃MgI (5.5 g, 33.0 mmol) in 10 mL dry THF was added dropwise to a solution of (E)-methyl 4-phenylbut-3-enoate (2.0 g, 11.3 mmol) in dry THF (20 mL) at 0 °C. And the resulting mixture was stirred for 10 h at room temperature. Then saturated aqueous NH₄Cl (10 mL) was added, the layers were separated and extracted three times with EtOAc (20 mL). The combined organic layers were dried over Na₂SO₄, and the solvent was removed in vacuum. Finally, the crude product was isolated by flash chromatography on silica gel (EtOAc:Petroleum ether, 1:3 v/v) to give the desired product 1r.

Yellow oil (755 mg, 38%). ¹H NMR (CDCl₃, 400 MHz) δ 7.18-7.37 (m, 5H), 6.44 (d, J = 15.2 Hz, 1H), 6.25-6.32 (m, 1H), 2.36 (d, J = 7.2 Hz, 2H), 1.25 (s, 6H); ¹³C NMR (CDCl₃, 100 MHz) δ = 137.4, 133.6, 128.6, 127.3, 126.2, 126.0, 71.0, 47.4, 29.3. GC/MS (EI) m/z: 176.1.

2.3 Compounds 1v-w:

Zn (3.25 g, 50 mmol) was placed in a 50-mL two-necked round bottom flask attached with a reflux condenser and septum. The reaction vessel was evacuated and flushed with argon. Anhydrous benzene–Et₂O (1:1, 60 mL) was added with vigorous stirring. Ethyl bromoacetate (2.5 mL, 22.7 mmol) was added dropwise, followed by a catalytic amount of I₂ to initiate the reaction. Cyclohexanone (2.1 mL, 20.4 mmol) or cyclopentanone (1.9 ml, 20.4 mmol) was added dropwise after 15 minutes and the reaction was refluxed at 80 °C for overnight. Then the mixture was quenched by the addition of HCl (10%, 20 mL). The compound was extracted with Et₂O (2 x 20 mL), washed with dil. HCl (5 mL), and water (2 x 10 mL). The combined organic layers were dried over anhydrous Na₂SO₄, filtered, and concentrated under vacuum.
Chromatography (EtOAc–Petroleum ether, 1:10 v/v) furnished β-hydroxyesters as a colorless oil.

Ethyl 1-(hydroxycyclopenta)acetate (1.7 g, 9.9 mmol) or ethyl 1-(hydroxycyclohexyl)acetate (1.5 g, 8.1 mmol) in anhydrous CH₂Cl₂ (40 mL) was placed in a 100 mL two-necked round bottom flask with an addition funnel and a guard tube attached. Anhydrous pyridine (0.77 g, 9.7 mmol) was added and the reaction mixture was cooled to 0 °C using an ice-salt mixture. After 10 min, SOCl₂ (0.65 mL) was added dropwise over 10 min. The progress of the reaction was monitored by TLC using EtOAc–petroleum ether (1:20). The reaction mixture was stirred for 30 min, quenched with ice-cold water (5 mL), and CH₂Cl₂ (20 mL) was added. The reaction mixture was washed with dilute HCl (5%, 2 x 20 mL), water (2x 20 mL), and NaHCO₃ (5%, 20 mL). The organic layer was dried over anhydrous Na₂SO₄, filtered, and concentrated in vacuo. Chromatography (EtOAc–Petroleum ether, 1:20 v/v) gave aim product as colorless oil.

Ethyl cyclopent-1-en-1-ylacetate (1.0 g, 6.5 mmol) or ethyl cyclohex-1-en-1-ylacetate (1.1 g, 6.5 mmol) was placed in a 100 mL dry two-necked round bottom flask. The round bottom flask was flushed with argon, anhydrous THF (30 mL) was added, and the mixture was cooled to 0 °C in a cryostat. LiAlH₄ (0.5 g, 13 mmol) was added and then the mixture was refluxed at 80 °C for further 12 h. The mixture was quenched by sat aqueous NH₄Cl. It was filtered through celite, concentrated in vacuo, and purified by flash column chromatography (EtOAc–Petroleum ether, 1:10 v/v) to furnish aim product as a colorless liquid.

2-cyclohexenylethanol (1v) Colorless liquid (500 mg, 60%). ¹H NMR (CDCl₃, 400 MHz) δ = 5.50 (s, 1H), 3.62-3.66 (m, 2H), 2.17-2.21 (m, 2H), 1.92-1.99 (m, 4H), 1.53-1.64 (m, 5H); ¹³C NMR (CDCl₃, 100 MHz) δ = 134.0, 124.3, 60.2, 41.1, 28.0, 25.3, 22.9, 22.4. GC/MS (EI) m/z: 126.1.

2-cyclopentenylethanol (1w) Colorless liquid (600 mg, 81%). ¹H NMR (CDCl₃, 400 MHz) δ = 5.46 (s, 1H), 3.71 (t, J = 6.4 Hz, 2H), 2.24-2.37 (m, 6H), 1.82-1.90 (m,
$^2$H;$^1$H NMR (CDCl$_3$, 100 MHz) $\delta = 140.8, 126.3, 60.5, 39.1, 34.9, 32.6, 23.3$. GC/MS (EI) m/z: 112.1.

3. References


4. Copies of NMR spectra for part of the substrates

Compound 1h
Compound 1m
Compound 1o
Compound 1p
5. Copies of NMR spectra for the desired products

Compound 2a
Compound 2b
Compound 2c
Compound 2e
Compound 2g
Compound 2h
Compound 2i
Compound 2j
Compound 2k
Compound 2l
Compound 2m
Compound 2n
Compound 2o
Compound 2p
Compound 2q
Compound 2r
Compound 2t (6-endo(cis/trans=1/1) / 5-exo(cis/trans=0.5/1) =1.3/1)
Compound 2u
Compound 2v
Compound 2w
Compound 2x