Supporting information

Chiral N,N'-Dioxide/In(OTf)₃-Catalyzed Asymmetric Vinylogous Mukaiyama Aldol Reactions

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1. General remarks

$^1$H NMR spectra were recorded on commercial instruments (400 MHz). Chemical shifts are recorded in ppm relative to tetramethylsilane and with the solvent resonance as the internal standard (CDCl$_3$, $\delta$ = 7.26). Spectra are reported as follows: chemical shift ($\delta$ = ppm), multiplicity ($s$ = singlet, $d$ = doublet, $t$ = triplet, $m$ = multiplet), coupling constants (Hz), integration and assignment. $^{13}$C NMR data were collected on commercial instruments (100 MHz) with complete proton decoupling. Chemical shifts are reported in ppm from the tetramethylsilane with the solvent resonance as internal standard (CDCl$_3$, $\delta$ = 77.0). Enantiomeric excesses (ee) were determined by chiral HPLC on corresponding commercial chiral column. Optical rotations were reported as follows: $[\alpha]^T_{D}$ (c: g/100 mL, in solvent). HRMS was recorded on a commercial apparatus (ESI Source). Reactions were carried out using commercial available reagents in oven dried apparatus. Acyclic silyl dienolate 1, were prepared from methyl crotonate according to a literature procedure.$^1$ The $N,N'$-dioxide ligands were synthesized by the same procedure in the literature.$^2$

2. General procedure for the catalytic asymmetric VMAR

$N,N'$-dioxide L-$\text{PiPr}_2$ (0.02 mmol), In(OTf)$_3$ (0.01 mmol), and 5-methylsalicylic acid (0.02 mmol) were stirred in 0.5 mL ethyl caproate solvent at 35 °C for 0.5 h under an N$_2$ atmosphere. Subsequently, acyclic silyl dienol ester 1 (0.15 mmol) and aldehydes 2 (0.1 mmol) were added under −20 °C. The mixture was stirred for further 48 h, and then was purified directly by column chromatography on silica gel (ethyl acetate/petroleum ether 1/7–1/4).

3. Other conditions of VMAR
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* Unless specified, all reactions were performed with L-metal (10 mol%, 2:1), 1 (0.15 mmol), 2a (0.10 mmol) in THF (0.5 mL). "Isolated yield. " Determined by HPLC analysis.

4. The analytical and spectral characterization data of the VMAR products

(S,2E,6E)-methyl 5-hydroxy-7-phenylhepta-2,6-dienoate 3a
A colorless oil; HPLC (Chiralcel IB, hexane/i-PrOH = 70/30, flow rate = 1.0 ml/min, λ = 254 nm), retention time: t\textsubscript{1} = 5.57 min, t\textsubscript{2} = 6.79 min, ee = 92%. [α\textsubscript{D}\textsuperscript{23.7}] = −3.57 (c = 0.42 in CHCl\textsubscript{3}). \textsuperscript{1}H NMR (400 MHz, CDCl\textsubscript{3}) δ 7.41 – 7.24 (m, 5H), 7.01 (dt, J = 15.5, 7.3 Hz, 1H), 6.61 (d, J = 15.9 Hz, 1H), 6.22 (dd, J = 15.9, 6.6 Hz, 1H), 5.95 (dt, J = 15.7, 1.4 Hz, 1H), 4.44 (q, J = 6.2 Hz, 1H), 3.72 (s, 3H), 2.56 – 2.52 (m, 2H), 2.04 (s, 1H). \textsuperscript{13}C NMR (101 MHz, CDCl\textsubscript{3}) 166.84, 144.83, 136.30, 131.09, 130.91, 128.65, 127.93, 126.58, 123.68, 71.37, 51.59, 40.11.

HRMS (SEI-TOF) calcd for C\textsubscript{14}H\textsubscript{16}NaO\textsubscript{3}+ ([M+Na\textsuperscript{+}]) = 255.0992, Found 255.0998.

Retention Time | % Area
--- | ---
1 | 5.472 | 3.65
2 | 6.733 | 96.35

(2E,6E)-methyl 5-hydroxy-7-(2-methoxyphenyl)hepta-2,6-dienoate 3b

A colorless oil; HPLC (Chiralcel IB, hexane/i-PrOH = 70/30, flow rate = 1.0 ml/min, λ = 254 nm), retention time: t\textsubscript{1} = 7.05 min, t\textsubscript{2} = 11.78 min, ee = 93%. [α\textsubscript{D}\textsuperscript{26.5}] = −2.67 (c = 0.60 in CHCl\textsubscript{3}). \textsuperscript{1}H NMR (400 MHz, CDCl\textsubscript{3}) δ 7.41 (dd, J = 7.6, 1.6 Hz, 1H), 7.26 – 7.21 (m, 1H), 7.06 – 6.97 (m, 1H), 6.96 – 6.84 (m, 3H), 6.24 (dd, J = 16.0, 6.8 Hz, 1H), 6.02 – 5.89 (m, 1H), 4.44 (q, J = 6.3 Hz, 1H), 3.84 (s, 3H), 3.72 (s, 3H), 2.62 – 2.46 (m, 2H), 1.98 (s, 1H). \textsuperscript{13}C NMR (101 MHz, CDCl\textsubscript{3}) 166.77, 156.84, 144.96, 131.62, 129.00, 127.02, 126.12, 125.30, 123.57, 120.67, 110.91, 72.01, 55.43, 51.48, 40.16. HRMS (SEI-TOF) calcd for C\textsubscript{15}H\textsubscript{18}NaO\textsubscript{4}+ ([M+Na\textsuperscript{+}]) = 285.1097, Found 285.1107.
(2E,6E)-methyl 7-(4-chlorophenyl)-5-hydroxyhepta-2,6-dienoate 3c

A colorless oil; HPLC (Chiralcel IB, hexane/i-PrOH = 90/10, flow rate = 1.0 ml/min, λ = 254 nm), retention time: $t_{r1} = 10.78$ min, $t_{r2} = 11.91$ min, ee = 90%. $[\alpha]_{D}^{22.6} = -7.62$ (c = 0.30 in CHCl$_3$). $^1$H NMR (400 MHz, CDCl$_3$) δ 7.33 – 7.23 (m, 4H), 7.09 – 6.90 (m, 1H), 6.58 (dd, $J = 15.9, 0.8$ Hz, 1H), 6.20 (dd, $J = 15.9, 6.4$ Hz, 1H), 5.99 – 5.91 (m, 1H), 4.45 (q, $J = 6.1$ Hz, 1H), 3.73 (s, 3H), 2.58 – 2.48 (m, 2H), 1.97 (s, 1H). $^{13}$C NMR (101 MHz, CDCl$_3$) 166.71, 144.45, 134.80, 133.57, 131.52, 129.85, 128.80, 127.77, 123.88, 71.32, 51.58, 40.11. HRMS (SEI-TOF) calcd for C$_{14}$H$_{15}$ClNaO$_3$+ ([M+Na$^+$]) = 289.0602, Found 289.0604; HRMS (SEI-TOF) calcd for C$_{14}$H$_{15}$ClNaO$_3$+ ([M+Na$^+$]) = 291.0583.
(2E,6E)-methyl 7-(furan-2-yl)-5-hydroxyhepta-2,6-dienoate 3d

A colorless oil; HPLC (Chiralcel IE, hexane/i-PrOH = 90/10, flow rate = 1.0 ml/min, λ = 254 nm), retention time: t₁ = 16.38 min, t₂ = 18.59 min, ee = 92%. [α]D<sup>27.3</sup> = −14.38 (c = 0.15 in CHCl₃). H NMR (400 MHz, CDCl₃) δ 7.36 (d, J = 1.5 Hz, 1H), 6.99 (dt, J = 15.5, 7.3 Hz, 1H), 6.49 – 6.41 (m, 1H), 6.38 (dd, J = 3.3, 1.8 Hz, 1H), 6.26 (d, J = 3.3 Hz, 1H), 6.17 (dd, J = 15.8, 6.3 Hz, 1H), 5.95 (dt, J = 15.7, 1.4 Hz, 1H), 4.46 – 4.37 (m, 1H), 3.73 (s, 3H), 2.63 – 2.42 (m, 2H), 1.82 (s, 1H). C NMR (101 MHz, CDCl₃) 166.70, 151.96, 144.51, 142.22, 129.38, 123.84, 119.31, 111.37, 108.66, 77.34, 77.03, 76.71, 71.08, 51.54, 40.14. HRMS (SEI-TOF) calcd for C₁₂H₁₄NaO₄⁺ (M+Na⁺) = 245.0784, Found 245.0788.
(2E,6Z)-methyl 6-bromo-5-hydroxy-7-phenylhepta-2,6-dienoate \(3e\)

A colorless oil; HPLC (Chiralcel IB, hexane/i-PrOH = 80/20, flow rate = 1.0 ml/min, \(\lambda = 254\) nm), retention time: \(t_{11} = 6.05\) min, \(t_{12} = 6.70\) min, ee = 92%. \([\alpha]_D^{28.1} = -13.30\) (c = 1.20 in CHCl\(_3\)). \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta 7.63 – 7.53\) (m, 2H), 7.42 – 7.28 (m, 3H), 7.10 (s, 1H), 6.98 (dt, \(J = 15.6, 7.3\) Hz, 1H), 5.98 (dt, \(J = 15.7, 1.4\) Hz, 1H), 4.46 – 4.38 (m, 1H), 3.72 (s, 3H), 2.79 – 2.61 (m, 3H). \(^1^3\)C NMR (101 MHz, CDCl\(_3\)) 166.75, 143.96, 134.80, 129.14, 128.69, 128.53, 128.34, 128.22, 123.89, 76.15, 51.60, 38.60. HRMS (SEI-TOF) calcd for \(\text{C}_{14}\text{H}_{15}\text{BrNaO}_3^+ ([M+Na^+]) = 333.0097\), Found 333.0100; HRMS (SEI-TOF) calcd for \(\text{C}_{14}\text{H}_{15}\text{BrNaO}_3^+ ([M+Na^+]) = 335.0077\), Found 335.0111.

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(S,E)-methyl 5-hydroxy-5-phenylpent-2-enoate \(3f\)

A colorless oil; HPLC (Chiralcel IE, hexane/i-PrOH = 90/10, flow rate = 1.0 ml/min, \(\lambda = 254\) nm), retention time: \(t_{11} = 14.17\) min, \(t_{12} = 15.37\) min, ee = 95%. \([\alpha]_D^{21.6} = -41.32\) (c = 0.48 in CHCl\(_3\)). \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta 7.39 – 7.25\) (m, 5H), 6.96 (dt, \(J = 15.5, 7.3\) Hz, 1H), 5.89 (dt, \(J = 15.7, 1.3\) Hz, 1H), 4.81 (dd, \(J = 7.6, 5.3\) Hz, 1H), 3.70 (s, 3H), 2.72 – 2.54 (m, 2H), 2.30 (s,
1H). $^{13}$C NMR (101 MHz, CDCl$_3$) 166.79, 145.08, 143.45, 128.63, 127.94, 125.74, 123.56, 73.07, 51.53, 41.84. HRMS (SEI-TOF) calcd for $\text{C}_{12}\text{H}_{14}\text{NaO}_3^+$ ([M+Na$^+$]) = 229.0835, Found 229.0843.

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(E)-methyl 5-hydroxy-5-(o-tolyl)pent-2-enoate 3g

A colorless oil; HPLC (Chiralcel IE, hexane/i-PrOH = 90/10, flow rate = 1.0 ml/min, $\lambda$ = 254 nm), retention time: $t_{r1} = 7.12$ min, $t_{r2} = 20.64$ min, ee = 86%. $[\alpha]_D^{22.1}$ = $-60.62$ (c = 0.39 in CHCl$_3$). $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.51 – 7.42 (m, 1H), 7.26 – 7.11 (m, 3H), 7.01 (dt, $J$ = 15.6, 7.3 Hz, 1H), 5.92 (dt, $J$ = 15.7, 1.4 Hz, 1H), 5.10 – 4.98 (m, 1H), 3.72 (s, 3H), 2.65 – 2.55 (m, 2H), 2.32 (s, 3H), 2.10 (d, $J$ = 3.2 Hz, 1H). $^{13}$C NMR (101 MHz, CDCl$_3$) 166.78, 145.35, 141.55, 134.27, 130.54, 127.61, 126.47, 125.06, 123.47, 69.42, 51.51, 40.73, 18.99. HRMS (SEI-TOF) calcd for $\text{C}_{13}\text{H}_{16}\text{NaO}_3^+$ ([M+Na$^+$]) = 243.0992, Found 243.0999.
(E)-methyl 5-hydroxy-5-(m-tolyl)pent-2-enoate 3h

A colorless oil; HPLC (Chiralcel IB, hexane/i-PrOH = 95/05, flow rate = 1.0 ml/min, λ = 254 nm), retention time: t₁ = 13.65 min, t₂ = 14.78 min, ee = 94%. [α]D²⁸ = −29.62 (c = 0.26 in CHCl₃). ¹H NMR (400 MHz, CDCl₃) δ 7.26 – 7.21 (m, 1H), 7.19 – 7.08 (m, 3H), 7.02 – 6.92 (m, 1H), 5.91 (d, J = 15.7 Hz, 1H), 4.78 (t, J = 5.8 Hz, 1H), 3.72 (s, 3H), 2.72 – 2.55 (m, 2H), 2.36 (s, 3H), 2.08 (s, 1H). ¹³C NMR (101 MHz, CDCl₃) 166.76, 145.13, 143.39, 138.36, 128.71, 128.55, 126.40, 123.54, 122.79, 73.14, 51.50, 41.81, 21.45. HRMS (SEI-TOF) calcd for C₁₃H₁₆NaO₃⁺ ([M+Na⁺]) = 243.0992, Found 243.1000.
A colorless oil; HPLC (Chiralcel IE, hexane/i-PrOH = 90/10, flow rate = 1.0 ml/min, λ = 254 nm), retention time: t_{r1} = 18.20 min, t_{r2} = 21.25 min, ee = 92%. \([\alpha]_D^{26.5} = -25.25\) (c = 0.80 in CHCl₃). ¹H NMR (400 MHz, CDCl₃) δ 7.32 (dd, J = 7.5, 1.6 Hz, 1H), 7.28 – 7.23 (m, 1H), 7.05 – 6.94 (m, 2H), 6.88 (d, J = 8.2 Hz, 1H), 5.88 (dt, J = 15.7, 1.4 Hz, 1H), 5.03 (dd, J = 12.4, 5.8 Hz, 1H), 3.84 (s, 3H), 3.70 (s, 3H), 2.76 (dd, J = 5.5, 2.1 Hz, 1H), 2.70 – 2.63 (m, 2H). ¹³C NMR (101 MHz, CDCl₃) 166.87, 156.30, 145.97, 131.26, 128.66, 126.76, 126.67, 122.98, 120.86, 110.52, 69.38, 55.27, 51.40, 40.12. HRMS (SEI-TOF) calcd for C₁₃H₁₆NaO₄⁺ ([M+Na⁺]) = 259.0941, Found 259.0946.

(E)-methyl 5-hydroxy-5-(3-methoxyphenyl)pent-2-enoate 3j

A colorless oil; HPLC (Chiralcel IC, hexane/i-PrOH = 80/20, flow rate = 1.0 ml/min, λ = 254 nm), retention time: t_{r1} = 11.80 min, t_{r2} = 14.62 min, ee = 95%. \([\alpha]_D^{28.7} = -33.33\) (c = 0.30 in CHCl₃). ¹H NMR (400 MHz, CDCl₃) δ 7.30 – 7.24 (m, 1H), 7.03 – 6.86 (m, 3H), 6.87 – 6.79 (m, 1H), 5.95 – 5.86 (m, 1H), 4.80 (t, J = 5.2 Hz, 1H), 3.81 (s, 3H), 3.71 (s, 3H), 2.72 – 2.55 (m, 2H), 2.22 (d, J = 8.8 Hz, 1H). ¹³C NMR (101 MHz, CDCl₃) 166.76, 159.85, 145.15, 145.00, 129.69, 123.58, 118.00, 113.38, 111.23, 73.01, 55.26, 51.53, 41.80. HRMS (SEI-TOF) calcd for C₁₃H₁₆NaO₄⁺
(E)-methyl 5-hydroxy-5-(4-methoxyphenyl)pent-2-enoate 3k

A colorless oil; HPLC (Chiralcel IE, hexane/i-PrOH = 90/10, flow rate = 1.0 ml/min, λ = 254 nm), retention time: tᵱ₁ = 25.62 min, tᵱ₂ = 27.41 min, ee = 95%. [α]ᵢ²⁸.⁷ = −7.84 (c = 0.10 in CHCl₃). ¹H NMR (400 MHz, CDCl₃) δ 7.30 – 7.23 (m, 2H), 7.02 – 6.83 (m, 3H), 5.89 (dt, J = 15.7, 1.3 Hz, 1H), 4.82 – 4.71 (m, 1H), 3.80 (s, 3H), 3.71 (s, 3H), 2.74 – 2.50 (m, 2H), 2.08 (s, 1H). ¹³C NMR (101 MHz, CDCl₃) 166.75, 159.31, 145.11, 135.58, 127.03, 123.49, 114.01, 72.74, 55.30, 51.48, 41.77. HRMS (SEI-TOF) calcd for C₁₃H₁₂O₄Na⁺ ([M+Na⁺]) = 259.0941, Found 259.0942.
(E)-methyl 5-hydroxy-5-(3-phenoxyphenyl)pent-2-enoate 3l

A colorless oil; HPLC (Chiralcel IE, hexane/i-PrOH = 90/10, flow rate = 1.0 ml/min, λ = 254 nm), retention time: $t_1 = 17.82$ min, $t_2 = 20.64$ min, ee = 96%. $[\alpha]_D^{25.1} = -19.69$ (c = 0.66 in CHCl$_3$). $^1$H NMR (400 MHz, CDCl$_3$) δ 7.36 – 7.25 (m, 3H), 7.14 – 7.05 (m, 2H), 7.04 – 6.87 (m, 5H), 5.88 (dt, $J = 15.7, 1.3$ Hz, 1H), 4.84 – 4.70 (m, 1H), 3.70 (s, 3H), 2.68 – 2.54 (m, 2H), 2.33 (d, $J = 3.4$ Hz, 1H). $^{13}$C NMR (101 MHz, CDCl$_3$) 166.71, 157.57, 157.00, 145.60, 144.77, 129.98, 129.82, 123.71, 123.42, 120.47, 118.96, 118.14, 116.12, 72.70, 51.53, 41.79. HRMS (SEI-TOF) calcd for C$_{18}$H$_{18}$NaO$_4$ ([M+Na$^+$]) = 321.1097, Found 321.1100.

(E)-methyl 5-(4-fluorophenyl)-5-hydroxypent-2-enoate 3m

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A colorless oil; HPLC (Chiralcel IE, hexane/i-PrOH = 90/10, flow rate = 1.0 ml/min, λ = 254 nm), retention time: \( t_{r1} = 11.20 \) min, \( t_{r2} = 12.51 \) min, ee = 87%. \([\alpha]_{D}^{27.8} = -40.00 \) (c = 0.40 in CHCl₃). \(^1\)H NMR (400 MHz, CDCl₃) \( \delta 7.47 \) (td, \( J = 7.5, 1.7 \) Hz, 1H), 7.30 – 7.23 (m, 1H), 7.16 (td, \( J = 7.5, 1.0 \) Hz, 1H), 7.08 – 6.91 (m, 2H), 5.91 (dt, \( J = 15.7, 1.4 \) Hz, 1H), 5.15 (t, \( J = 5.9 \) Hz, 1H), 3.71 (s, 3H), 2.76 – 2.59 (m, 2H), 2.30 (s, 1H). \(^{13}\)C NMR (101 MHz, CDCl₃) 166.71, 160.80, 158.36, 144.62, 130.45, 130.32, 129.28, 129.20, 127.13, 127.09, 124.44, 124.41, 123.79, 115.49, 115.28, 67.03, 67.01, 51.52, 40.60. HRMS (SEI-TOF) calcd for \( \text{C}_{12}\text{H}_{13}\text{FNaO}_3^+ \) ([M+Na⁺]) = 247.0741, Found 247.0746.

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\((E)\)-methyl 5-(3-fluorophenyl)-5-hydroxypent-2-enoate 3n

A colorless oil; HPLC (Chiralcel IB, hexane/i-PrOH = 95/05, flow rate = 1.0 ml/min, λ = 254 nm), retention time: \( t_{r1} = 15.27 \) min, \( t_{r2} = 16.21 \) min, ee = 94%. \([\alpha]_{D}^{28.4} = -20.83 \) (c = 0.36 in CHCl₃). \(^1\)H NMR (400 MHz, CDCl₃) \( \delta 7.36 – 7.28 \) (m, 1H), 7.14 – 7.06 (m, 2H), 7.01 – 6.90 (m, 2H), 5.95 – 5.86 (m, 1H), 4.87 – 4.80 (m, 1H), 3.72 (s, 3H), 2.67 – 2.59 (m, 2H), 2.29 (d, \( J = 3.2 \) Hz, 1H). \(^{13}\)C NMR (101 MHz, CDCl₃) 166.67, 164.23, 161.78, 146.12, 146.05, 144.42, 130.20, 130.12,
123.91, 121.31, 121.28, 114.86, 114.64, 112.79, 112.57, 72.41, 72.40, 51.57, 41.80. HRMS (SEI-TOF) calcd for $C_{12}H_{13}FNaO_3^+$ ([M+Na$^+$]) = 247.0741, Found 247.0746.

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$(E)$-methyl 5-((4-fluorophenyl)-5-hydroxypent-2-enoate 3o

![Graph of retention times and areas]

A colorless oil; HPLC (Chiralcel IE, hexane/i-PrOH = 90/10, flow rate = 1.0 ml/min, $\lambda$ = 254 nm), retention time: $t_{11} = 10.85$ min, $t_{12} = 11.85$ min, ee = 95%. $[\alpha]_D^{22.4} = -35.11$ (c = 0.54 in CHCl$_3$). $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.35 – 7.26 (m, 2H), 7.09 – 6.99 (m, 2H), 6.98 – 6.87 (m, 1H), 5.88 (dt, $J = 15.7$, 1.3 Hz, 1H), 4.80 (dd, $J = 7.5$, 5.4 Hz, 1H), 3.70 (s, 3H), 2.69 – 2.56 (m, 2H), 2.56 – 2.27 (m, 1H). $^{13}$C NMR (101 MHz, CDCl$_3$) 166.77, 163.53, 161.08, 144.76, 139.23, 139.20, 127.47, 127.39, 123.69, 115.54, 115.33, 72.38, 51.56, 41.92. HRMS (SEI-TOF) calcd for $C_{12}H_{13}FNaO_3^+$ ([M+Na$^+$]) = 247.0741, Found 247.0744.
(E)-methyl 5-(3-bromophenyl)-5-hydroxypent-2-enoate 3p

A colorless oil; HPLC (Chiralcel IC, hexane/i-PrOH = 80/20, flow rate = 1.0 ml/min, \( \lambda = 254 \) nm), retention time: \( t_{r1} = 7.61 \) min, \( t_{r2} = 10.16 \) min, ee = 96%. \([\alpha]_D^{28.6} = -29.69\) (\( c = 0.32 \) in CHCl\(_3\)).

\(^1\)H NMR (400 MHz, CDCl\(_3\)) \( \delta 7.52 \) (s, 1H), 7.44 – 7.39 (m, 1H), 7.28 – 7.19 (m, 2H), 7.02 – 6.85 (m, 1H), 5.90 (d, \( J = 15.7 \) Hz, 1H), 4.83 – 4.75 (m, 1H), 3.71 (s, 3H), 2.69 – 2.55 (m, 2H), 2.41 (d, \( J = 3.5 \) Hz, 1H). \(^1\)C NMR (101 MHz, CDCl\(_3\)) 166.70, 145.78, 144.45, 130.95, 130.19, 128.86, 124.38, 123.92, 122.75, 72.33, 51.59, 41.82. HRMS (SEI-TOF) calcld for C\(_{12}\)H\(_{13}\)BrNaO\(_3^+\) ([M+Na\(^+\)]) = 306.9940, Found 306.9941; HRMS (SEI-TOF) calcld for C\(_{12}\)H\(_{13}\)BrNaO\(_3^+\) ([M+Na\(^+\)]) = 308.9920, Found 308.9948.
(E)-methyl 5-(benzo[d][1,3]dioxol-5-yl)-5-hydroxypent-2-enoate 3q

A colorless oil; HPLC (Chiralcel IE, hexane/i-PrOH = 80/20, flow rate = 1.0 ml/min, $\lambda$ = 254 nm), retention time: $t_{r1} = 18.17$ min, $t_{r2} = 20.33$ min, ee = 98%. $[\alpha]_{D}^{22.3} = -16.84\, (c = 0.37$ in CHCl$_3$). $^1$H NMR (400 MHz, CDCl$_3$) $\delta 6.93$ (dt, $J = 15.5, 7.3$ Hz, 1H), 6.86 (s, 1H), 6.82 – 6.73 (m, 2H), 5.95 (s, 2H), 5.89 (dt, $J = 15.7, 1.4$ Hz, 1H), 4.73 (dd, $J = 7.6, 5.4$ Hz, 1H), 3.71 (s, 3H), 2.71 – 2.52 (m, 2H), 2.20 (s, 1H). $^{13}$C NMR (101 MHz, CDCl$_3$) 166.76, 147.92, 147.22, 144.93, 137.50, 123.54, 119.23, 108.20, 106.23, 101.10, 72.95, 51.53, 41.82. HRMS (SEI-TOF) calcld for C$_{13}$H$_{14}$NaO$_5$ $([M+Na^+] = 273.0733$, Found 273.0735.

(E)-methyl 5-(3,4-dichlorophenyl)-5-hydroxypent-2-enoate 3r

A colorless oil; HPLC (Chiralcel IE, hexane/i-PrOH = 95/05, flow rate =
1.0 ml/min, \( \lambda = 254 \text{ nm} \), retention time: \( t_{r1} = 19.81 \) min, \( t_{r2} = 20.93 \) min, ee = 93\%. \([\alpha]_D^{27.9} = -26.45 \) (c = 0.76 in CHCl\(_3\)).

\(^1\)H NMR (400 MHz, CDCl\(_3\)) \( \delta \) 7.44 (dd, \( J = 18.1, 5.1 \text{ Hz} \), 2H), 7.17 (dd, \( J = 8.3, 2.0 \text{ Hz} \), 1H), 6.92 (dt, \( J = 15.6, 7.3 \text{ Hz} \), 1H), 5.89 (dt, \( J = 15.7, 1.4 \text{ Hz} \), 1H), 4.79 (dd, \( J = 8.0, 6.6 \text{ Hz} \), 1H), 3.71 (s, 3H), 2.67 – 2.53 (m, 3H), 1.82 (s, 0H).

\(^{13}\)C NMR (101 MHz, CDCl\(_3\)) 166.69, 144.11, 143.71, 132.71, 131.68, 130.54, 127.79, 125.10, 124.08, 71.77, 51.62, 41.75.

HRMS (SEI-TOF) calcd for C\(_{12}\)H\(_{12}\)O\(_3\)Cl\(_2\)NaO\(_3\)= ([M+Na\(^+\)]) = 297.0056, Found 297.0063; HRMS (SEI-TOF) calcd for C\(_{12}\)H\(_{12}\)O\(_3\)Cl\(_2\)NaO\(_3\)= ([M+Na\(^+\)]) = 300.9996, Found 301.0003.

\( (E)\)-methyl 5-hydroxy-5-(naphthalen-1-yl)pent-2-enoate 3s

A colorless oil; HPLC (Chiralcel IB, hexane/i-PrOH = 90/10, flow rate = 1.0 ml/min, \( \lambda = 254 \text{ nm} \), retention time: \( t_{r1} = 12.24 \) min, \( t_{r2} = 14.95 \) min, ee = 94\%. \([\alpha]_D^{27.5} = -70.45 \) (c = 0.22 in CHCl\(_3\)).

\(^1\)H NMR (400 MHz, CDCl\(_3\)) \( \delta \) 8.04 (d, \( J = 8.1 \text{ Hz} \), 1H), 7.92 – 7.86 (m, 1H), 7.80 (d, \( J = 8.2 \text{ Hz} \), 1H), 7.67 (d, \( J = 7.1 \text{ Hz} \), 1H), 7.57 – 7.45 (m, 3H), 7.16 – 7.06 (m, 1H), 6.00 – 5.90 (m, 1H), 5.61 (dd, \( J = 8.0, 3.8 \text{ Hz} \), 1H), 3.73 (s, 3H), 2.90 – 2.72 (m, 2H), 2.19 (s, 1H). \(^{13}\)C NMR (101 MHz, CDCl\(_3\)) 166.77, 145.38, 138.94, 133.85, 130.05, 129.09, 128.40, 126.32, 125.71, 125.48, 123.53,
HRMS (SEI-TOF) calcd for C_{10}H_{14}NaO_{3}^+ ([M+Na^+]) = 279.0992, Found 279.0996.

(S,E)-methyl 5-(furan-2-yl)-5-hydroxypent-2-enoate 3t

A colorless oil; HPLC (Chiralcel IE, hexane/i-PrOH = 90/10, flow rate = 1.0 ml/min, λ = 254 nm), retention time: t_{11} = 15.80 min, t_{22} = 17.20 min, ee = 92%. [α]_D^{22.9} = −22.73 (c = 0.09 in CHCl₃), ^1H NMR (400 MHz, CDCl₃) δ 7.43 – 7.36 (m, 1H), 7.01 – 6.91 (m, 1H), 6.34 (dd, J = 3.2, 1.9 Hz, 1H), 6.27 (d, J = 3.2 Hz, 1H), 5.94 (dt, J = 15.7, 1.4 Hz, 1H), 4.84 (dd, J = 11.1, 6.4 Hz, 1H), 3.71 (s, 3H), 2.84 – 2.69 (m, 2H), 2.14 (d, J = 4.7 Hz, 1H). ^13C NMR (101 MHz, CDCl₃) 169.04, 166.66, 155.32, 144.12, 142.30, 123.85, 110.30, 106.50, 66.46, 51.55, 38.26. HRMS (SEI-TOF) calcd for C_{10}H_{14}NaO_{3}^+ ([M+Na^+]) = 219.0628, Found 219.0637.
### (E)-methyl 5-hydroxyoct-2-enoate 3u

A colorless oil; HPLC (Chiralcel IB, hexane/i-PrOH = 95/05, flow rate = 1.0 ml/min, λ = 254 nm), retention time: \( t_1 = 9.02 \text{ min} \), \( t_2 = 9.78 \text{ min} \), ee = 83%. \([\alpha]_D^{23.5} = -8.89 \) (c = 0.18 in CHCl₃). ¹H NMR (400 MHz, CDCl₃) \( \delta 7.08 – 6.92 \text{ (m, 1H)} \), 5.91 (d, \( J = 15.7 \text{ Hz, 1H} \)), 3.78 (s, 1H), 3.74 (s, 3H), 2.46 – 2.28 (m, 2H), 1.62 (s, 1H), 1.51 – 1.32 (m, 4H), 0.99 – 0.88 (m, 3H). ¹³C NMR (101 MHz, CDCl₃) 170.61, 166.79, 145.59, 123.43, 70.30, 51.51, 40.19, 39.26, 18.78, 13.97. HRMS (SEI-TOF) calcd for \( C_{9}H_{16}NaO_{3}^{+} ([M+Na^{+}]) = 195.0992 \), Found 195.0999.

### (R,E)-methyl 5-hydroxydec-2-enoate 3v

A colorless oil; HPLC (Chiralcel IB, hexane/i-PrOH = 98/02, flow rate = 1.0 ml/min, λ = 254 nm), retention time: \( t_1 = 15.66 \text{ min} \), \( t_2 = 17.76 \text{ min} \), ee = 93%. \([\alpha]_D^{25.1} = -6.25 \) (c = 0.40 in CHCl₃). ¹H NMR (400 MHz, CDCl₃) \( \delta 7.06 – 6.93 \text{ (m, 1H)} \), 5.91 (dt, \( J = 15.7, 1.3 \text{ Hz, 1H} \)), 3.81 – 3.72 (m, 4H), 2.45 – 2.24 (m, 2H), 1.68 (s, 1H), 1.51 – 1.26 (m, 8H), 0.89 (t, \( J = 6.8 \text{ Hz, 3H} \)). ¹³C NMR (101 MHz, CDCl₃) 166.81, 145.64, 123.40, 70.57, 51.50, 40.17, 37.11, 31.73, 25.26, 22.59, 14.01. HRMS (SEI-TOF) calcd for \( C_{16}H_{16}NaO_{3}^{+} ([M+Na^{+}]) = 223.1305 \), Found 223.1309.
(S,E)-methyl 5-hydroxy-6-methylhept-2-enoate 3w

A colorless oil; HPLC (Chiralcel IB, hexane/i-PrOH = 95/05, flow rate = 1.0 ml/min, λ = 254 nm), retention time: $t_{R1} = 7.68$ min, $t_{R2} = 9.00$ min, ee = 89%. $[\alpha]_{D}^{29.1} = -13.89$ (c = 0.18 in CHCl$_3$). $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.09 – 6.95 (m, 1H), 5.92 (dt, $J = 15.7$, 1.4 Hz, 1H), 3.73 (s, 3H), 3.57 – 3.45 (m, 1H), 2.51 – 2.21 (m, 2H), 1.76 – 1.68 (m, 1H), 1.66 (d, $J = 3.5$ Hz, 1H), 0.95 (d, $J = 1.1$ Hz, 3H), 0.94 (d, $J = 1.2$ Hz, 3H). $^{13}$C NMR (101 MHz, CDCl$_3$) 166.79, 146.20, 123.24, 75.34, 51.47, 37.17, 33.40, 18.69, 17.22. HRMS (SEI-TOF) calcd for C$_9$H$_{16}$NaO$_3$ $^+(\text{M+Na}^+)$ = 195.0992, Found 195.1000.
(S,E)-methyl 5-hydroxy-6,6-dimethylhept-2-enoate 3x

A colorless oil; HPLC (Chiralcel IE, hexane/i-PrOH = 90/10, flow rate = 1.0 ml/min, λ = 254 nm), retention time: t\textsubscript{r1} = 8.54 min, t\textsubscript{r2} = 9.68 min, ee = 98%. \([\alpha]_D^{23.9} = -10.00\) (c = 0.08 in CHCl\textsubscript{3}). \(^1\)H NMR (400 MHz, CDCl\textsubscript{3}) δ 7.12 – 6.97 (m, 1H), 5.93 (d, J = 15.7 Hz, 1H), 3.73 (s, 3H), 3.37 (d, J = 10.1 Hz, 1H), 2.52 – 2.35 (m, 1H), 2.25 – 2.10 (m, 1H), 1.56 (d, J = 2.7 Hz, 1H), 0.93 (s, 9H). \(^13\)C NMR (101 MHz, CDCl\textsubscript{3}) 166.83, 147.49, 122.97, 78.38, 51.47, 34.85, 25.60. HRMS (SEI-TOF) calcd for C\textsubscript{10}H\textsubscript{18}NaO\textsubscript{3}\textsuperscript{+} ([M+Na\textsuperscript{+}]) = 209.1148, Found 209.1153.

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methyl 5-hydroxydecanoate 5v

To a solution of 3v (3.7 mmol, 741.3 mg) in CH\textsubscript{3}OH (12 mL), 5% Pd/C (100 mg) was added. The mixture was stirred under H\textsubscript{2} atmosphere (5 MPa) at 25 °C until the reaction was finished (12 h). Then, Pd/C was removed by filtration and washed with CH\textsubscript{2}Cl\textsubscript{2}. The filtrate was concentrated and isolated via column chromatography (1/7, ethyl acetate/petroleum ether). A colorless oil; \(^1\)H NMR (400 MHz, CDCl\textsubscript{3}) δ 3.67 (s, 3H), 3.63 – 3.54 (m, 1H), 2.35 (t, J = 7.4 Hz, 2H), 1.84 – 1.61 (m, 3H), 1.54 – 1.38 (m, 5H), 1.34 – 1.22 (m, 5H), 0.89 (t, J = 6.9 Hz, 3H). \(^13\)C NMR (101 MHz, CDCl\textsubscript{3}) 174.26, 71.36, 51.53, 37.43, 36.68, 33.89, 31.86, 25.29, 22.61, 20.98, 14.02. HRMS (SEI-TOF) calcd for C\textsubscript{11}H\textsubscript{22}NaO\textsubscript{3}\textsuperscript{+} ([M+Na\textsuperscript{+}]) = 225.1461, Found 225.1465.
(R)-6-pentyltetrahydro-2H-pyran-2-one 6v

The product of 5v (0.665g) was dissolved in 12 mL DCM, 16.5 mg of p-TSA was added, and the mixture was stirred for 12 h. The mixture was subjected to chromatography using ethyl acetate/petroleum ether = 1/7. A colorless oil; ee = 94%. $[\alpha]_D^{20.0} = 39.00$ (c = 0.50 in CHCl$_3$), lit.$^3$ $[\alpha]_D^{25.0} = 52.20$ (c =1.00 in CHCl$_3$). $^1$H NMR (400 MHz, CDCl$_3$) δ 4.33 – 4.24 (m, 1H), 2.64 – 2.53 (m, 1H), 2.51 – 2.38 (m 1H), 1.98 – 1.83 (m, 3H), 1.75 – 1.65 (m, 1H), 1.62 – 1.44 (m, 3H), 1.42 – 1.25 (m, 5H), 0.89 (t, J = 6.8 Hz, 3H). $^{13}$C NMR (101 MHz, CDCl$_3$) 179.55, 80.57, 35.76, 31.55, 29.42, 27.75, 24.56, 22.47, 18.45, 13.94. HRMS (SEI-TOF) calcd for C$_{10}$H$_{18}$NaO$_2$+$^+$ ([M+Na$^+$]) = 193.1199, Found 193.1209.

5. The operando IR experiments of the reaction

The 3D ATR-FTIR profile of the reaction

The IR spectrum of diene 1
The IR spectrum of aldehyde 2a

The IR spectrum of product 3a

6. References


7. Copies of NMR spectra for VMAR products

*(S,2E,6E)-methyl 5-hydroxy-7-phenylhepta-2,6-dienoate 3a*
(2E,6E)-methyl 5-hydroxy-7-(2-methoxyphenyl)hepta-2,6-dienoate 3b
(2E,6E)-methyl 7-(4-chlorophenyl)-5-hydroxyhepta-2,6-dienoate 3c
(2E,6E)-methyl 7-(furan-2-yl)-5-hydroxyhepta-2,6-dienoate 3d
(2E,6Z)-methyl 6-bromo-5-hydroxy-7-phenylhepta-2,6-dienoate 3e
(S,E)-methyl 5-hydroxy-5-phenylpent-2-enoate 3f
(E)-methyl 5-hydroxy-5-(o-tolyl)pent-2-enoate 3g
(E)-methyl 5-hydroxy-5-((m-tolyl)pent-2-enoate 3h
(E)-methyl 5-hydroxy-5-(2-methoxyphenyl)pent-2-enoate 3i
(E)-methyl 5-hydroxy-5-(3-methoxyphenyl)pent-2-enoate 3j
(E)-methyl 5-hydroxy-5-(4-methoxyphenyl)pent-2-enoate 3k
(E)-methyl 5-hydroxy-5-(3-phenoxphenyl)pent-2-enoate 3l
(E)-methyl 5-(4-fluorophenyl)-5-hydroxypent-2-enoate 3m
(E)-methyl 5-(3-fluorophenyl)-5-hydroxypent-2-enoate 3n
(E)-methyl 5-(4-fluorophenyl)-5-hydroxypent-2-enoate 3o
(E)-methyl 5-(3-bromophenyl)-5-hydroxypent-2-enoate 3p
(E)-methyl 5-(benzo[d][1,3]dioxol-5-yl)-5-hydroxypent-2-enoate 3q
(E)-methyl 5-(3,4-dichlorophenyl)-5-hydroxypent-2-enoate 3r
(E)-methyl 5-hydroxy-5-(naphthalen-1-yl)pent-2-enoate 3s
(S,E)-methyl 5-(furan-2-yl)-5-hydroxypent-2-enoate 3t
(E)-methyl 5-hydroxyoct-2-enoate 3u
(S,E)-methyl 5-hydroxydec-2-enoate 3v
(S,E)-methyl 5-hydroxy-6-methylhept-2-enoate 3w
(S,E)-methyl 5-hydroxy-6,6-dimethylhept-2-enoate 3x
methyl 5-hydroxydecanoate 5v
(R)-6-pentyltetrahydro-2H-pyran-2-one 6v