Aniline mediated oxidative C-C bond cleavage of α-alkoxy aldehydes in air and a model reaction for the synthesis of α-(D)-amino acid derivatives

Supporting information

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1. General Information

All reagents and materials were purchased from commercial sources unless otherwise noted. All anhydrous solvents were prepared with standard procedures. Reactions were monitored by thin-layer chromatography (TLC) using commercial silica gel 60 F254 aluminum plates. Flash chromatography was performed using silica gel of particle size 0.040-0.063 mm. $^1$H NMR (400 MHz) and $^{13}$C NMR (100 MHz) spectra were recorded on Bruker AV400 spectrometers. Chemical shifts were reported in parts per million (ppm, $\delta$) relative to tetramethylsilane ($\delta = 0.00$) or chloroform ($\delta = 7.26$, singlet). $^1$H NMR splitting patterns are labeled as abbreviations s (singlet), d (doublet), dd (doublet of doublets), t (triplet), q (quartet), m (multiplets) and br (broad). The determination of ee was performed via chiral phase HPLC analysis using HPLC Chiralcel OD-H column. Optical rotations were measured using a 0.5 mL cell with a 10 mm path length on Optical Activity automatic polarimeter. The HR-ESI-MS data were measured on a Bruker Apex IV FTICR spectrometer.

2. Preparation of $\alpha$-alkoxy aldehydes

Procedure A for the synthesis of $\alpha$-benzoxyl aldehydes (1a, 1c, 1d, 1f, 1h, 1i, 1j)$^1$

![Chemical Structure]

To a solution of 1,3-dithiane (3.17 g, 26 mmol) in 25 mL anhydrous THF at -20 °C was added slowly 11.9 mL n-butyllithium (2.2 M in hexane, 26 mmol) and stirred for 1 h. Arylaldehyde (2.24 mL, 22 mmol) dissolved in THF was added dropwise, and the reaction mixture was stirred at 0 °C for 24 h. After quenching by saturated aqueous NH$_4$Cl, the solvent was removed under vacuo. Then the product was extracted with CH$_2$Cl$_2$ and dried over NaSO$_4$. Purification by column chromatography on silica gel (petroleum ether: ethyl acetate = 5:1) afforded SI-1 as light yellow oil, 3.74 g, 76%. SI-1 (3.74 g, 16 mmol) in 25 mL anhydrous THF cooled to 0 °C was added NaH (60%, 1.25 g, 31 mmol) and BnBr (3.9 mL, 33 mmol). The reaction was then warmed to room temperature, stirring for 2 h. Methanol was added and the mixture was concentrated followed by column chromatography on silica gel (petroleum ether: ethyl acetate = 10:1) to afford SI-2 as yellow oil, 4.76 g, 91%. To a solution of SI-2 (540 mg, 1.7 mmol) in acetone (34 mL) was added BaCO$_3$ (4.23 g, 21 mmol) at 0 °C. A solution of N-bromo-succinimide (590 mg, 3.3 mmol) in acetone (70 mL) was added and the mixture was stirred at 30 °C for 2 h. After decomposition of excessive N-bromosuccinimide by addition of saturated aqueous NaHCO$_3$, the solution was filtered and concentrated, extracted with ethyl acetate by three times. The organic layer was combined and then dried over anhydrous sodium sulfate. After evaporation in vacuo, the residue was purified by chromatography on silica gel (dichloromethane: hexane = 1:1), to give 1a as colorless oil, 319 mg, 83% yield.
Procedure B for the synthesis of 2-(benzylloxy)-2-(furanyl)acetaldehyde (1e)\(^{1,2}\)

\[
\begin{align*}
\text{CHO} & \xrightarrow{-20^\circ \text{C} \to 0^\circ \text{C}, \text{THF}} \text{OH} \\
\text{BnBr, NaH} & \xrightarrow{\text{THF, 0}^\circ \text{C} \to \text{rt}} \text{OBn} \\
\text{CaCO}_3, \text{MeI} & \xrightarrow{\text{CH}_2\text{CN/H}_2\text{O, 80}^\circ \text{C}} \text{1e}
\end{align*}
\]

SI-4 was obtained as in procedure A. To a solution of SI-4 (238 mg, 0.78 mmol) in MeCN (16 mL) and H\(_2\)O (4 mL) was added CaCO\(_3\) (386 mg, 3.9 mmol) and MeI (2.5 mL, 40.0 mmol). The reaction mixture was stirred at 80 °C for 8 h, then concentrated under reduced pressure, and extracted with CH\(_2\)Cl\(_2\) for three times. The combined organic extracts were washed with brine, dried over MgSO\(_4\) and concentrated. The residue was purified by column chromatography (dichloromethane: hexane = 8:1) to give aldehyde 1e as yellow oil, 56 mg, 33%.

Procedure C for the synthesis of \(\alpha\)-methyl oxy aldehydes (1b, 1g)

\[
\begin{align*}
\text{CHO} & \xrightarrow{-20^\circ \text{C} \to 0^\circ \text{C}, \text{THF}} \text{OH} \\
\text{Mel, NaH} & \xrightarrow{\text{THF, 0}^\circ \text{C} \to \text{rt}} \text{OMe}
\end{align*}
\]

SI-1 was obtained as in procedure A. SI-1 (217 mg, 0.96 mmol) in 10 mL anhydrous THF cooled to 0 °C was added NaH (60%, 73 mg, 1.8 mmol) and MeI (298 \(\mu\)L, 4.8 mmol). The reaction was then warmed to room temperature, stirring for 1 h. Methanol was added and the mixture was concentrated followed by column chromatography on silica gel (petroleum ether: ethyl acetate = 4:1) to afford SI-6 as yellow oil, 166 mg, 72%. 1b was obtained from SI-6 as procedure A.

3. Characterization of Substrates

2-(benzylloxy)-2-phenylacetaldehyde (1a):

\(^1\)H NMR (400 MHz, CDCl\(_3\)): \(\delta\) 9.63 (s, 1H), 7.36 (m, 10H), 4.80 (s, 1H), 4.68 (d, \(J = 11.8\) Hz, 1H), 4.55 (d, \(J = 11.8\) Hz, 1H). \(^{13}\)C NMR (101 MHz, CDCl\(_3\)): \(\delta\) 197.5, 136.2, 133.2, 128.2, 128.1, 127.7, 127.3, 127.2, 126.8, 84.7, 70.3. These data correspond to previously reported literature\(^{16}\).

2-methoxy-2-phenylacetaldehyde (1b):

$^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 9.59 (d, $J = 1.5$ Hz, 1H), 7.38 (m, 5H), 4.64 (s, 1H), 3.45 (s, 3H).

$^{13}$C NMR (101 MHz, CDCl$_3$): $\delta$ 198.3, 133.8, 129.0, 129.0, 127.5, 88.2, 57.3. These data correspond to previously reported literature$^{1a}$.

2-(benzlyoxy)-2-(4-chlorophenyl)acetaldehyde (1c):

$^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 9.61 (d, $J = 1.7$ Hz, 1H), 7.36 (m, 9H), 4.76 (d, $J = 1.6$ Hz, 1H), 4.67 (d, $J = 11.8$ Hz, 1H), 4.55 (d, $J = 11.8$ Hz, 1H). $^{13}$C NMR (101 MHz, CDCl$_3$): $\delta$ 198.2, 136.7, 135.0, 132.6, 129.3, 128.8, 128.7, 128.3, 128.1, 84.7, 71.4. HRMS (ESI) m/z calcld for C$_{15}$H$_{13}$ClNaO$_2$ [M + Na]$^+$: 283.0496, found: 283.0503.

2-(benzlyoxy)-2-(4-methoxyphenyl)acetaldehyde (1d):

$^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 9.61 (s, 1H), 7.32 (m, 7H), 6.95 (d, $J = 7.9$ Hz, 2H), 4.75 (s, 1H), 4.66 (d, $J = 12.0$ Hz, 1H), 4.52 (d, $J = 11.6$ Hz, 1H), 3.82 (s, 3H). $^{13}$C NMR (101 MHz, CDCl$_3$): $\delta$ 198.3, 160.2, 137.1, 129.1, 128.6, 128.1, 125.9, 114.6, 85.0, 70.8, 55.3. HRMS (ESI) m/z calcld for C$_{16}$H$_{16}$NaO$_3$ [M + Na]$^+$: 279.0992, found: 279.1000.

2-(benzlyoxy)-2-(furanyl)acetaldehyde (1e):

$^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 9.71 (d, $J = 1.2$ Hz, 1H), 7.49 (d, $J = 1.0$ Hz, 1H), 7.34 (m, 5H), 6.46 (d, $J = 3.2$ Hz, 1H), 6.42 (dd, $J = 3.2$, 1.9 Hz, 1H), 4.87 (s, 1H), 4.68 (d, $J = 11.8$ Hz, 1H), 4.53 (d, $J = 11.8$ Hz, 1H). $^{13}$C NMR (101 MHz, CDCl$_3$): $\delta$ 196.4, 147.6, 144.2, 136.7, 128.2, 111.4, 110.7, 78.6, 71.0. HRMS (ESI) m/z calcld for C$_{13}$H$_{12}$NaO$_3$ [M + Na]$^+$: 239.0679, found: 239.0679.

2-(benzlyoxy)-3-phenylpropanal (1f):

$^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 9.69 (d, $J = 1.9$ Hz, 1H), 7.25 (m, 10H), 4.59 (d, $J = 11.8$ Hz, 1H), 4.47 (d, $J = 11.8$ Hz, 1H), 3.97 (ddd, $J = 8.4$, 4.7, 1.9 Hz, 1H), 3.03 (dd, $J = 14.2$, 4.7 Hz, 1H), 2.93 (dd, $J = 14.2$, 8.4 Hz, 1H). $^{13}$C NMR (101 MHz, CDCl$_3$): $\delta$ 203.1, 137.1, 136.5, 129.6, 128.5, 128.0, 127.9, 126.8, 84.2, 72.8, 36.7. These data correspond to previously reported literature$^{3}$.

2-methoxy-3-phenylpropanal (1g):

$^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 9.69 (d, $J = 1.9$ Hz, 1H), 7.28 (m, 5H), 3.80 (ddd, $J = 7.9$, 4.9, 1.9 Hz, 1H), 3.40 (s, 3H), 3.01 (dd, $J = 14.3$, 4.9 Hz, 1H), 2.91 (dd, $J = 14.3$, 8.0 Hz, 1H). $^{13}$C NMR (101 MHz, CDCl$_3$): $\delta$ 203.3, 136.4, 129.4, 128.5, 126.8, 86.5, 58.6, 36.4. These data correspond to previously reported literature$^{4}$.

2-(benzlyoxy)pentanal (1h):

$^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 9.65 (d, $J = 2.1$ Hz, 1H), 7.32 (m, 5H), 4.67 (d, $J = 11.7$ Hz, 1H),
4.53 (d, J = 11.7 Hz, 1H), 3.76 (ddd, J = 7.5, 5.5, 2.1 Hz, 1H), 1.65 (m, 2H), 1.46 (m, 2H), 0.91 (t, J = 7.3 Hz, 3H). 13C NMR (101 MHz, CDCl3): δ 203.9, 137.4, 128.5, 128.1, 128.0, 83.3, 72.5, 32.1, 18.1, 13.9. HRMS (ESI) m/z calcld for C12H16NaO2 [M + Na]+: 215.1043, found: 215.1041.

2-(benzyloxy)-3-methylbutanal (1i):

1H NMR (400 MHz, CDCl3): δ 9.66 (d, J = 2.7 Hz, 1H), 7.31 (m, 5H), 4.68 (d, J = 11.8 Hz, 1H), 4.49 (d, J = 11.8 Hz, 1H), 3.47 (dd, J = 5.8, 2.7 Hz, 1H), 2.09 (m, 1H), 0.99 (t, J = 7.1 Hz, 6H).

13C NMR (101 MHz, CDCl3): δ 204.5, 137.5, 128.5, 128.0, 128.0, 88.1, 72.9, 39.6, 28.8, 28.0, 26.2, 26.0, 25.9. HRMS (ESI) m/z calcld for C12H17O2 [M + H]+: 193.1223, found: 193.1219.

2-(benzyloxy)-2-cyclohexylacetaldehyde (1j):

1H NMR (400 MHz, CDCl3): δ 9.66 (d, J = 2.8 Hz, 1H), 7.33 (m, 5H), 4.67 (d, J = 11.8 Hz, 1H), 4.47 (d, J = 11.8 Hz, 1H), 3.49 (dd, J = 5.7, 2.8 Hz, 1H), 1.77 (m, 4H), 1.64 (m, 2H), 1.20 (m, 5H).

13C NMR (101 MHz, CDCl3): δ 204.7, 137.5, 128.5, 128.0, 128.0, 87.8, 72.9, 39.6, 28.8, 28.0, 26.2, 26.0, 25.9. HRMS (ESI) m/z calcld for C15H20NaO2 [M + Na]+: 255.1356, found: 255.1358.

(2R,3S,4R)-2,3,4-Tris(benzyloxy)hex-5-enal (1k)5:  

1H NMR (400 MHz, CDCl3): δ 9.65 (d, J = 0.7 Hz, 1H), 7.29 (m, 15H), 5.82 (ddd, J = 16.9, 10.8, 7.7 Hz, 1H), 5.27 (m, 2H), 4.71 (dd, J = 11.7, 2.3 Hz, 2H), 4.58 (d, J = 11.7 Hz, 1H), 4.54 (d, J = 11.5 Hz, 1H), 4.49 (d, J = 11.8 Hz, 1H), 4.36 (d, J = 11.5 Hz, 1H), 4.15 (d, J = 5.0 Hz, 1H), 3.87 (dd, J = 4.4, 0.7 Hz, 1H), 3.80 (t, J = 4.7 Hz, 1H). 13C NMR (101 MHz, CDCl3): δ 201.6, 137.8, 137.7, 137.2, 134.8, 128.5, 128.4, 128.8, 128.3, 128.2, 128.2, 127.9, 127.6, 119.4, 82.4, 81.8, 80.0, 74.5, 73.3, 71.0. These data correspond to previously reported literature5.

4. General Procedure for oxidative C-C bond cleavage reaction

To a round-bottom flask charged with 2-(benzyloxy)-2-phenylacetaldehyde 1a (86 mg, 0.38 mmol) in solution of toluene (4 mL) was added aniline 3f (40 mg, 0.37 mmol). The reaction mixture was stirred at 50 °C for 2 h with a reflux condenser open to air. The solvent was then removed under vacuo, and the residue was purified by column chromatography on silica gel (dichloromethane: hexane = 2:3) to afford 2a as yellow oil, 65 mg, 81%.

5. Characterization of products

Benzyl benzoate (2a):
$^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 8.10 (m, 2H), 7.57 (m, 1H), 7.42 (m, 7H), 5.39 (s, 2H). $^{13}$C NMR (101 MHz, CDCl$_3$): $\delta$ 165.6, 135.3, 132.2, 129.3, 128.9, 127.8, 127.6, 127.4, 127.3, 65.9. These data correspond to previously reported literature.$^6$

Methyl benzoate (2b):

$^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 8.04 (d, $J = 7.3$ Hz, 2H), 7.54 (d, $J = 7.2$ Hz, 1H), 7.43 (t, $J = 6.9$ Hz, 2H), 3.91 (s, 1H). $^{13}$C NMR (101 MHz, CDCl$_3$): $\delta$ 167.1, 132.9, 130.2, 129.6, 128.4, 52.1. These data correspond to previously reported literature.$^7$

Benzyl 4-chlorobenzoate (2c):

$^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 8.01 (d, $J = 7.8$ Hz, 2H), 7.41 (m, 7H), 5.36 (s, 2H). $^{13}$C NMR (101 MHz, CDCl$_3$): $\delta$ 165.6, 139.5, 135.8, 131.1, 128.8, 128.7, 128.6, 128.4, 128.3, 67.0. These data correspond to previously reported literature.$^8$

Benzyl 4-methoxybenzoate (2d):

$^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 8.03 (m, 2H), 7.44 (m, 2H), 7.35 (m, 3H), 6.91 (m, 2H), 5.33 (s, 2H), 3.84 (s, 3H). $^{13}$C NMR (101 MHz, CDCl$_3$): $\delta$ 166.2, 163.5, 136.4, 131.8, 128.6, 128.4, 128.1, 128.1, 127.8, 122.6, 113.6, 66.4, 55.4. These data correspond to previously reported literature.$^8$

Benzyl furan-2-carboxylate (2e):

$^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 7.57 (d, $J = 0.8$ Hz, 1H), 7.43 (dd, $J = 7.8$, 1.2 Hz, 2H), 7.37 (m, 3H), 7.20 (d, $J = 3.5$ Hz, 1H), 6.49 (dd, $J = 3.5$, 1.7 Hz, 1H), 5.34 (s, 2H). $^{13}$C NMR (101 MHz, CDCl$_3$): $\delta$ 158.6, 146.5, 144.6, 135.6, 128.6, 128.4, 128.4, 118.2, 111.9, 66.6. These data correspond to previously reported literature.$^9$

Benzyl 2-phenylacetate (2f):

$^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 7.30 (m, 10H), 5.13 (s, 2H), 3.67 (s, 2H). $^{13}$C NMR (101 MHz, CDCl$_3$): $\delta$ 171.4, 135.9, 133.9, 129.3, 128.6, 128.2, 128.1, 127.1, 66.6, 41.4. These data correspond to previously reported literature.$^{10}$

Methyl 2-phenylacetate (2g):

$^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 7.30 (m, 5H), 3.69 (s, 3H), 3.63 (s, 2H). $^{13}$C NMR (101 MHz, CDCl$_3$): $\delta$ 172.1, 134.0, 129.3, 128.6, 127.1, 52.1, 41.2. These data correspond to previously reported literature.$^{11}$
Benzyl butyrate (2h):

$^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 7.33 (m, 5H), 5.11 (s, 2H), 2.34 (t, $J = 7.4$ Hz, 2H), 1.67 (m, 2H), 0.94 (t, $J = 7.4$ Hz, 3H). $^{13}$C NMR (101 MHz, CDCl$_3$): $\delta$ 173.5, 136.2, 128.6, 128.2, 66.06, 36.2, 18.5, 13.7. These data correspond to previously reported literature.$^{12}$

Benzy l isobutyrate (2i):

$^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 7.34 (m, 5H), 5.11 (s, 2H), 2.60 (dt, $J = 14.0$, 7.0 Hz, 1H), 1.19 (d, $J = 7.0$ Hz, 6H). $^{13}$C NMR (101 MHz, CDCl$_3$): $\delta$ 177.0, 136.3, 128.5, 128.1, 128.0, 65.9, 43.2, 29.0, 25.8, 25.5. These data correspond to previously reported literature.$^{13}$

Benzyl cyclohexanecarboxylate (2j):

$^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 7.33 (m, 5H), 5.10 (s, 2H), 2.35 (tt, $J = 11.4$, 3.6 Hz, 1H), 1.93 (dd, $J = 13.1$, 2.6 Hz, 2H), 1.75 (m, 2H), 1.63 (m, 1H), 1.46 (m, 2H), 1.25 (m, 4H). $^{13}$C NMR (101 MHz, CDCl$_3$): $\delta$ 175.9, 136.4, 128.5, 128.0, 128.1, 128.0, 65.9, 43.2, 29.0, 25.8, 25.5. These data correspond to previously reported literature.$^{14}$

$(2S,3R)$-benzyl 2,3-bis(benzyloxy)pent-4-enoate (2k):

$^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 7.31 (m, 15H), 5.94 (ddd, $J = 17.4$, 10.5, 8.0 Hz, 1H), 5.31 (dd, $J = 13.8$, 7.7 Hz, 2H), 5.21 (d, $J = 12.2$ Hz, 1H), 5.11 (d, $J = 12.2$ Hz, 1H), 4.84 (d, $J = 12.0$ Hz, 1H), 4.66 (d, $J = 12.2$ Hz, 1H), 4.53 (d, $J = 12.0$ Hz, 1H), 4.39 (d, $J = 12.2$ Hz, 1H), 4.20 (dd, $J = 7.9$, 4.4 Hz, 1H), 4.09 (d, $J = 4.4$ Hz, 1H). $^{13}$C NMR (101 MHz, CDCl$_3$): $\delta$ 170.0, 138.0, 137.3, 135.5, 134.2, 128.5, 128.4, 128.3, 128.3, 128.2, 127.9, 127.9, 127.6, 119.8, 81.0, 80.6, 73.0, 70.6, 66.7. HRMS (ESI) m/z calcd for C$_{26}$H$_{26}$NaO$_4$ [M + Na]$^+$: 425.1723, found: 425.1720.

1-benzylidene-2-(2,4-dinitrophenyl)hydrazine(2l)$^{15}$:

$^1$H NMR (400 MHz, DMSO) $\delta$ 11.68 (s, 1H), 8.87 (d, $J = 2.6$ Hz, 1H), 8.72 (s, 1H), 8.39 (dd, $J = 9.6$, 2.6 Hz, 1H), 8.12 (d, $J = 9.6$ Hz, 1H), 7.80 (dd, $J = 7.2$, 2.3 Hz, 2H), 7.50 (dd, $J = 8.4$, 3.1 Hz, 3H). $^{13}$C NMR (101 MHz, DMSO) $\delta$ 149.4, 144.5, 137.1, 133.8, 130.6, 129.8, 129.5, 129.0, 127.4, 123.0, 116.8. These data correspond to previously reported literature.$^{16}$

6. Procedure for mechanistic study
To a round-bottom flask charged with 2-(benzyloxy)-2-phenylacetaldehyde 1a (64 mg, 0.28 mmol) in solution of toluene (4 mL) was added aniline 3f (30 mg, 0.28 mmol) and 2,2,6,6-Tetramethyl-1-piperidinyloxy (22 mg, 0.14 mmol). The reaction mixture was stirred at 50 °C for 2 h with a reflux condenser open to air. Column chromatography on silica gel (dichloromethane: hexane = 2:3) gave recovered 1a.

To an aluminium-foil paper wrapped round-bottom flask charged with 2-(benzyloxy)-2-phenylacetaldehyde 1a (130 mg, 0.57 mmol) in solution of toluene (5 mL) was added aniline 3f (62 mg, 0.58 mmol). The reaction mixture was stirred at 50 °C for 2 h with a reflux condenser open to air. The solvent was then removed under vacuo, and the residue was purified by column chromatography on silica gel (dichloromethane: hexane = 2:3) to afford 2a, 25 mg, 18%.

7. One pot operation for Mannich reaction/Oxidative cleavage to serine derivative

To a flask containing 2-(benzyloxy)-acetaldehyde 4 (148 mg, 0.98 mmol) and 4-methyl aniline 3f (35 mg, 0.33 mmol) in anhydrous CH$_3$CN (1.3 mL) was added 30% mol of L-proline (11.4 mg, 0.099 mmol). After 48 h of vigorous stirring, the reaction was quenched by addition of phosphate buffer (pH ≈ 7.0), and the aqueous phase was extracted three times with CH$_2$Cl$_2$. The combined organic layers were dried with Na$_2$SO$_4$. After concentrating, the crude Mannich reaction mixture was dissolved in toluene (3 mL) followed by addition of 4-methyl aniline 3f (70 mg, 0.65 mmol). The reaction was stirred at 50 °C for 5 h with a reflux condenser open to air. Then solvent was removed under vacuo, and the residue was purified by column chromatography on silica gel (dichloromethane: hexane = 6:1) to afford 6 as dark yellow oil, 39 mg, 32%.

$^1$H NMR (400 MHz, CDCl$_3$) δ 7.26 (m, 10H), 6.96 (d, $J = 8.1$ Hz, 2H), 6.53 (d, $J = 8.4$ Hz, 2H), 5.18 (d, $J = 12.3$ Hz, 1H), 5.13 (d, $J = 12.3$ Hz, 1H), 4.53 (d, $J = 12.1$ Hz, 1H), 4.47 (d, $J = 12.2$ Hz, 1H), 4.25 (br, 1H), 3.88 (ddd, $J = 9.3$, 3.8 Hz, 1H), 3.78 (dd, $J = 9.3$, 4.1 Hz, 1H), 2.22 (s, 3H). $^{13}$C NMR (101 MHz, CDCl$_3$) δ 172.0, 144.3, 137.6, 135.6, 129.9, 128.6, 128.4, 128.3, 128.2, 127.8, 127.8, 127.6, 114.0, 73.4, 70.2, 67.0, 57.4, 20.4. The ee of 6 was 97% as determined by chiral-phase HPLC analysis (Chiralcel OD-H, hexanes/i-PrOH = 70: 30, flow rate 1 mL/min, λ = 254 nm): minor isomer: $t_R = 6.500$ min; major isomer: $t_R = 10.642$ min; $[\alpha]_D^{25} = -13.3^\circ$ (c = 1.5, CHCl$_3$). HRMS (ESI) m/z calcd for C$_{24}$H$_{28}$N$_3$O$_3$ [M + H]$^+$: 376.1907, found: 376.1900.
8. $^1$H NMR and $^{13}$C NMR spectra for substrates and products
Electronic Supplementary Material (ESI) for Organic & Biomolecular Chemistry
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9. HPLC spectra for ee determination

Detector A Ch1 254nm

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Detector A Ch1 254nm

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