Supporting Information
Highly Diastereoselective 1,3-Dipolar Cycloaddition
Reactions of Carbonyl Ylides with Aldimines to Steric
Disfavored cis-Oxazolidines

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General: HRMS (ESI) Mass spectra were recorded on Bruker micrOTOF-II mass spectrometer. NMR spectra were recorded on a Brucker-400 MHz and Brucker-500 MHz spectrometer. X-ray was performed on Buker SMART APEX-II. Optical rotational data were performed on PerkinElmer PL-343.

Materials: Dichloromethane was distilled from calcium hydride. Diazo compounds 1 were prepared according to the literature procedure.\[^1\] Aldehyde 2a was purified by recrystallization. Imines 3 were prepared by condensation of corresponding aldehydes and amines.\[^2\] Lewis acids were purchased from ACROS or Aldrich. Solvents for the column chromatography were distilled before using.
General Procedure for the selective 3+2 cycloaddition of diazo acetrate aldehydes and imines (Table 2 in the manuscript):

To an flame-dried vial was charged with 2 (0.22 mmol), 3 (0.20 mmol), 4Å MS (0.1 g), Rh$_2$(OAc)$_4$ (2.0 mol%), co-catalyst (10.0 mol%) and 1.5 mL CH$_2$Cl$_2$ under an argon atmosphere. The flask was cooled to 0 °C, and diazo 1 (0.22 mmol) in 0.5 mL CH$_2$Cl$_2$ was added to the reaction mixture over 1 h period of time via a syringe pump. After completion of the addition, the reaction mixture was stirred for additional 30mins. The crude products were subjected to $^1$H NMR spectroscopy analysis for the determination of diastereoselectivity. The reaction mixture was purified by flash chromatography on silica gel (eluent: EtOAc : light petroleum ether = 1:50 to 1:20) to give the pure products 4 or 6.

(4b): yield 87%; $^1$H NMR (CDCl$_3$, 500 MHz): δ (ppm) 1.00 (t, $J = 7.5$ Hz, 3H), 3.80-3.98 (m, 2H), 5.00 (d, $J = 6.0$ Hz, 1H), 5.34 (d, $J = 6.0$ Hz, 1H), 6.28 (d, $J = 8.5$ Hz, 2H), 6.56 (s, 1H), 6.66 (t, $J = 7.5$ Hz, 1H), 7.04 (m, 2H), 7.18 (d, $J = 8.0$ Hz, 2H), 7.33 (d, $J = 8.0$ Hz, 2H), 7.42 (d, $J = 8.0$ Hz, 2H), 7.51 (d, $J = 8.0$ Hz, 2H); $^{13}$C NMR (CDCl$_3$, 100 MHz): δ (ppm) 13.78, 61.38, 63.23, 78.14, 91.21, 113.98, 117.99, 122.33, 123.40, 128.87, 129.10, 129.60, 131.59, 131.97, 135.87, 136.86, 141.62, 166.78; HRMS (ESI) calcd for C$_{24}$H$_{21}$Br$_2$NNaO$_3$ (M+Na)$^+$ 553.9762, found 553.9761.

(4c): yield 83%; $^1$H NMR (CDCl$_3$, 500 MHz): δ (ppm) 0.99 (t, $J = 7.0$ Hz, 3H), 3.79-3.97 (m, 2H), 4.99 (d, $J = 6.0$ Hz, 1H), 5.35 (d, $J = 6.0$ Hz, 1H), 6.28 (d, $J = 8.0$ Hz, 2H), 6.56 (s, 1H), 6.65 (t, $J = 7.5$ Hz, 1H), 7.01-7.27 (m, 6H), 7.32 (d, $J = 7.5$ Hz, 2H), 7.51 (d, $J = 7.5$ Hz, 2H); $^{13}$C NMR (CDCl$_3$, 100 MHz): δ (ppm) 13.77, 61.34, 63.15, 78.19, 91.21, 113.97, 117.96, 123.37, 128.63 128.87, 129.07, 129.27, 131.96, 134.13, 135.33, 136.87, 141.63, 166.78; HRMS (ESI) calcd for C$_{24}$H$_{21}$BrClKNO$_3$ (M+K)$^+$ 524.0025, found 524.0048.
(4d): yield 82%; $^1$H NMR (CDCl$_3$, 400 MHz): $\delta$ (ppm) 1.04 (t, $J = 9.0$ Hz, 3H), 3.85-4.01 (m, 2H), 4.98 (d, $J = 7.5$ Hz, 1H), 5.32 (d, $J = 7.5$ Hz, 1H), 6.28 (d, $J = 11.0$ Hz, 2H), 6.57 (s, 1H), 6.68 (m, 1H), 7.04-7.52 (m, 9H); $^{13}$C NMR (CDCl$_3$, 100 MHz): $\delta$ (ppm) 13.80, 61.54, 62.72, 78.04, 91.21, 113.96, 118.25, 123.51, 128.97, 129.24, 129.88, 130.54, 132.03, 132.49, 136.62, 137.33, 141.41, 166.56; HRMS (ESI) calcd for C$_{24}$H$_{20}$BrCl$_2$NNaO$_3$ (M+Na)$^+$ 541.9896, found 541.9902.

(4e): yield 76%; $^1$H NMR (CDCl$_3$, 500 MHz): $\delta$ (ppm) 0.98 (t, $J = 7.0$ Hz, 3H), 3.78-3.96 (m, 2H), 4.98 (d, $J = 6.0$ Hz, 1H), 5.29 (d, $J = 6.0$ Hz, 1H), 6.20 (d, $J = 9.0$ Hz, 2H), 6.51 (s, 1H), 6.98 (m, 2H), 7.14 (d, $J = 8.5$ Hz, 2H), 7.26 (d, $J = 8.5$ Hz, 2H), 7.42 (d, $J = 8.5$ Hz, 2H), 7.51 (d, $J = 8.5$ Hz, 2H); $^{13}$C NMR (CDCl$_3$, 100 MHz): $\delta$ (ppm) 13.78, 61.46, 63.37, 78.21, 91.32, 115.08, 122.58, 123.64, 128.83, 129.07, 129.56, 131.72, 132.09, 135.37, 136.39, 140.26, 166.46; HRMS (ESI) calcd for C$_{24}$H$_{20}$Br$_2$ClNNaO$_3$ (M+Na)$^+$ 585.9391, found 585.9391.

(4f): yield 90%; $^1$H NMR (CDCl$_3$, 500 MHz): $\delta$ (ppm) 0.98 (t, $J = 7.0$ Hz, 3H), 3.62 (s, 3H), 3.78-3.96 (m, 2H), 5.01 (d, $J = 6.5$ Hz, 1H), 5.31 (d, $J = 6.5$ Hz, 1H), 6.23 (m, 2H), 6.51 (s, 1H), 6.62 (m, 2H), 7.15 (d, $J = 8.5$ Hz, 2H), 7.32 (d, $J = 8.5$ Hz, 2H), 7.40 (d, $J = 8.5$ Hz, 2H), 7.49 (d, $J = 8.5$ Hz, 2H); $^{13}$C NMR (CDCl$_3$, 100 MHz): $\delta$ (ppm) 13.75, 55.41, 61.27, 63.62, 78.34, 91.57, 114.69, 115.04, 122.21, 123.28, 128.91, 129.66, 131.51, 131.89, 135.84, 136.04, 137.27, 152.03, 166.98; HRMS (ESI) calcd for C$_{25}$H$_{23}$Br$_2$NNaO$_4$ (M+Na)$^+$ 581.9886, found 581.9896.

(4g): yield 78%; $^1$H NMR (CDCl$_3$, 500 MHz): $\delta$ (ppm) 1.02 (t, $J = 7.0$ Hz, 3H), 3.64 (s, 3H), 3.82-3.97 (m, 2H), 5.01 (d, $J = 6.0$ Hz, 1H), 5.31 (d, $J = 6.0$ Hz, 1H), 6.25 (d, $J = 9.0$ Hz, 2H), 6.53 (s, 1H), 6.63 (d, $J = 9.0$ Hz, 2H), 7.13-7.52 (m, 8H); $^{13}$C NMR (CDCl$_3$, 100 MHz): $\delta$ (ppm) 13.78, 55.46, 61.38, 63.59, 78.35, 91.58, 114.75, 114.96, 122.45, 123.33, 126.51, 128.93, 130.06, 131.01, 131.39, 131.93, 135.79, 137.19, 139.46, 152.06, 166.88; HRMS (ESI) calcd for C$_{25}$H$_{23}$Br$_2$NNaO$_4$ (M+Na)$^+$ 581.9886, found 581.9895.
(4h): yield 75%; $^1$H NMR (CDCl$_3$, 500 MHz): $\delta$ (ppm) 0.99 (t, $J = 7.0$ Hz, 3H), 3.63 (s, 3H), 3.74-3.96 (m, 2H), 5.10 (d, $J = 6.5$ Hz, 1H), 5.95 (d, $J = 6.5$ Hz, 1H), 6.26 (d, $J = 9.0$ Hz, 2H), 6.60 (s, 1H), 6.63 (d, $J = 9.0$ Hz, 2H), 7.07-7.55 (m, 8H); $^{13}$C NMR (CDCl$_3$, 100 MHz): $\delta$ (ppm) 13.66, 55.38, 61.22, 62.29, 77.99, 91.74, 114.66, 115.22, 123.23, 124.41, 128.02, 129.02, 129.33, 129.68, 131.85, 132.60, 135.76, 136.02, 137.30, 152.02, 167.20; HRMS (ESI) calcd for C$_{23}$H$_{23}$Br$_2$NNaO$_4$ (M+Na)$^+$ 581.9886, found 581.9905.

(4i): yield 89%; $^1$H NMR (CDCl$_3$, 500 MHz): $\delta$ (ppm) 0.99 (t, $J = 7.0$ Hz, 3H), 3.63 (s, 3H), 3.75 (s, 3H), 3.78-3.96 (m, 2H), 5.00 (d, $J = 6.0$ Hz, 1H), 5.32 (d, $J = 6.0$ Hz, 1H), 6.26 (d, $J = 9.0$ Hz, 2H), 6.52 (s, 1H), 6.60 (d, $J = 9.0$ Hz, 2H), 6.80 (d, $J = 8.5$ Hz, 2H), 7.20 (d, $J = 8.5$ Hz, 2H), 7.35 (d, $J = 8.5$ Hz, 2H), 7.50 (d, $J = 8.5$ Hz, 2H); $^{13}$C NMR (CDCl$_3$, 100 MHz): $\delta$ (ppm) 13.81, 55.13, 55.43, 61.10, 63.70, 78.60, 91.48, 113.75, 114.58, 115.01, 123.17, 128.68, 128.94, 129.10, 131.86, 136.24, 137.62, 151.77, 159.39, 167.28; HRMS (ESI) calcd for C$_{26}$H$_{26}$BrNNaO$_5$ (M+Na)$^+$ 534.0887, found 534.0899.

(4j): yield 78%; $^1$H NMR (CDCl$_3$, 500 MHz): $\delta$ (ppm) 0.97 (t, $J = 7.0$ Hz, 3H), 2.28 (s, 3H), 3.63 (s, 3H), 3.76-3.95 (m, 2H), 5.01 (d, $J = 6.0$ Hz, 1H), 5.33 (d, $J = 6.0$ Hz, 1H), 6.26 (d, $J = 9.0$ Hz, 2H), 6.52 (s, 1H), 6.61 (d, $J = 9.0$ Hz, 2H), 7.07 (d, $J = 7.5$ Hz, 2H), 7.15 (d, $J = 7.5$ Hz, 2H), 7.30 (d, $J = 8.0$ Hz, 2H), 7.49 (d, $J = 8.0$ Hz, 2H); $^{13}$C NMR (CDCl$_3$, 100 MHz): $\delta$ (ppm) 13.73, 21.12, 55.45, 61.10, 64.05, 78.60, 91.59, 114.61, 114.98, 123.18, 127.86, 128.96, 129.06, 131.89, 133.68, 136.30, 137.67, 137.85, 151.78, 167.28; HRMS (ESI) calcd for C$_{26}$H$_{26}$BrNNaO$_4$ (M+Na)$^+$ 518.0937, found 518.0961.

Hydrolysis of the oxazolidine product:

The oxazolidine 4a (0.20 mmol) was dissolved in MeOH : H$_2$O (4 mL, 95:5) and p-methylbenzene sulfonic acid ($p$-TSA, 0.25 mmol, in 0.5 mL MeOH) was added.
The resultant mixture was stirred at room temperature for about 1-2 h, and detected by TLC. Until the material was consumed, the solvents were removed under reduced pressure and the residue was dissolved in CH\textsubscript{2}Cl\textsubscript{2} and washed with NaHCO\textsubscript{3} (sat.). The aqueous phase was extracted twice with CH\textsubscript{2}Cl\textsubscript{2} and the combined organic extracts were dried (MgSO\textsubscript{4}) and concentrated under reduced pressure. The residue was purified by flash chromatography on silica gel (eluent: EtOAc : light petroleum ether = 1:80 to 1:30) to give the pure product 5\textit{a}. Yield 92%; \textsuperscript{1}H NMR (CDCl\textsubscript{3}, 500 MHz): \(\delta\) (ppm) 1.26 (t, \(J = 7.0\) Hz, 3H), 2.90 (d, \(J = 6.0\) Hz, 1H), 4.12-4.22 (m, 2H), 4.66(s, 1H), 4.87 (m, 2H), 6.61-7.30 (m, 10H); \textsuperscript{13}C NMR (CDCl\textsubscript{3}, 100 MHz): \(\delta\) (ppm) 14.08, 59.57, 61.94, 73.56, 113.85, 117.96, 127.50, 127.99, 128.42, 129.16, 137.20, 146.27, 172.07; HRMS (ESI) calcd for C\textsubscript{17}H\textsubscript{19}NO\textsubscript{3} (M)+ 285.1365, found 285.1368.

\(\text{6a}\): yield 62%; \([\alpha]_D^{20} = -42.5^\circ\) (c = 1, CH\textsubscript{2}Cl\textsubscript{2}); \textsuperscript{1}H NMR (CDCl\textsubscript{3}, 500 MHz): \(\delta\) (ppm) 0.53-1.60 (m, 19H), 4.49-4.54 (m, 1H), 4.99 (d, \(J = 6.0\) Hz, 1H), 5.36 (d, \(J = 6.0\) Hz, 1H), 5.31 (d, \(J = 8.0\) Hz, 2H), 6.55 (s, 1H), 6.59-7.53 (m, 12H); \textsuperscript{13}C NMR (CDCl\textsubscript{3}, 125 MHz): \(\delta\) (ppm) 15.95, 20.82, 21.84, 23.01, 25.65, 31.17, 33.99, 40.39, 46.70, 63.80, 75.44, 78.07, 91.06, 114.06, 117.64, 123.30, 128.31, 128.49, 128.96, 129.05, 131.98, 136.72, 137.31, 141.99, 166.51; HRMS (ESI) calcd for C\textsubscript{32}H\textsubscript{36}BrNNaO\textsubscript{3} (M+Na)+ 586.1756, found 586.1729.

\(\text{6b}\): yield 66%; \([\alpha]_D^{20} = -34.0^\circ\) (c = 1, CH\textsubscript{2}Cl\textsubscript{2}); \textsuperscript{1}H NMR (CDCl\textsubscript{3}, 500 MHz): \(\delta\) (ppm) 0.55-1.60 (m, 19H), 3.61 (s, 3H), 4.48-4.53 (m, 1H), 5.01 (d, \(J = 6.0\) Hz, 1H), 5.33 (d, \(J = 6.0\) Hz, 1H), 6.26 (d, \(J = 9.0\) Hz, 2H), 6.51 (s, 1H), 6.58 (d, \(J = 9.0\) Hz, 2H), 7.20-7.32 (m, 5H), 7.36 (d, \(J = 8.0\) Hz, 2H), 7.50 (d, \(J = 8.0\) Hz, 2H); \textsuperscript{13}C NMR (CDCl\textsubscript{3}, 125 MHz): \(\delta\) (ppm) 15.94, 20.76, 21.79, 22.99, 25.65, 31.11, 33.95, 40.29, 46.68, 55.41, 64.22, 75.29, 78.24, 91.38, 114.55, 115.07, 123.18, 128.19, 128.41, 128.51, 129.05, 131.89, 136.24, 136.83, 137.69, 151.80, 166.68; HRMS (ESI) calcd for C\textsubscript{33}H\textsubscript{38}BrNNaO\textsubscript{4} (M+Na)+ 614.1876, found 614.1917.
(6c): yield 73%; [α]_D^{20} = -44.2° (c = 1, CH₂Cl₂); \( ^1 \)H NMR (CDCl₃, 500 MHz): δ (ppm) 0.54-1.60 (m, 19H), 3.63 (s, 3H), 4.52-4.53 (m, 1H), 5.00 (d, \( J = 6.0 \) Hz, 1H), 5.30 (d, \( J = 6.0 \) Hz, 1H), 6.23 (d, \( J = 9.0 \) Hz, 2H), 6.49 (s, 1H), 6.60 (d, \( J = 9.0 \) Hz, 2H), 7.19 (d, \( J = 8.0 \) Hz, 2H), 7.33 (d, \( J = 8.0 \) Hz, 2H), 7.38 (d, \( J = 8.0 \) Hz, 2H), 7.50 (d, \( J = 8.0 \) Hz, 2H); \( ^{13} \)C NMR (CDCl₃, 125 MHz): δ (ppm) 15.93, 20.72, 21.89, 23.00, 25.76, 31.15, 33.95, 40.41, 46.63, 55.47, 63.62, 75.58, 78.20, 91.42, 114.70, 115.17, 122.35, 123.34, 129.07, 130.24, 131.69, 131.96, 135.94, 136.12, 137.42, 152.06, 166.69; HRMS (ESI) calcd for C₃₃H₃Br₂NNaO₄ (M+Na)+ 692.0982, found 692.0935.

Reduction and hydrolysis of the chiral oxazolidine product:

The oxazolidine 5 (0.50 mmol) was dissolved in anhydrous THF (8 mL), and LAH (1.50 mmol) was added in portion under Ar at 0°C. The resultant mixture was stirred at room temperature for about 1h, and detected by TLC. Until the material was consumed, the reaction was quenched by sodium sulfate decahydrate (until no bubble was formed) and diluted with ethyl acetate (20 mL). Then the solid was removed by filtration and the liquid phase was concentrated under reduced pressure. The residue was purified by flash chromatography on silica gel (eluent: EtOAc : light petroleum ether = 1:50 to 1:5) to give the pure product 7. Yield 70%; [α]_D^{20} = -7.0° (c = 1, EtOH) \( ^1 \)H NMR (CDCl₃, 500 MHz): δ (ppm) 3.20-3.38 (m, 2H), 4.58-4.62 (m, 1H), 5.17 (d, \( J = 5.8 \) Hz, 1H), 6.30 (d, \( J = 8.0 \) Hz, 2H), 6.31 (s, 1H), 6.57-7.45 (m, 12H); \( ^{13} \)C NMR (CDCl₃, 125 MHz): δ (ppm) 62.11, 63.49, 78.90, 91.54, 113.80, 116.93, 127.16, 127.48, 127.88, 128.72, 128.86, 128.92, 137.77, 142.42; HRMS (ESI) calcd for C₂₂H₂₁NNaO₂ (M+Na)^+ 354.1470, found 354.1478.

The reduce product 7 (0.25 mmol) was dissolved in MeOH : H₂O (5 mL, 95:5) and \( \rho \)-TSA (0.31 mmol, in 0.5 mL MeOH) was added. The resultant mixture was stirred
at room temperature for about 1-2 h, and detected by TLC. Until the material was consumed, the solvents were removed under reduced pressure and the residue was dissolved in CH$_2$Cl$_2$ and washed with NaHCO$_3$ (sat.). The aqueous phase was extracted twice with CH$_2$Cl$_2$ and the combined organic extracts were dried (MgSO$_4$) and concentrated under reduced pressure. The residue was purified by flash chromatography on silica gel (eluent: EtOAc : light petroleum ether = 1:10 to 1:1) to give the pure product 8. Yield 95%; $^1$H NMR (CDCl$_3$, 400 MHz): $\delta$ (ppm) 2.71 (bs, 1H), 3.53-3.68 (m, 2H), 4.00 (d, $J$ = 4.0 Hz, 1H), 4.61 (d, $J$ = 4.0 Hz, 1H), 6.55-7.34 (m, 10H); $^{13}$C NMR (CDCl$_3$, 125 MHz): $\delta$ (ppm) 60.63, 63.53, 73.92, 113.87, 117.94, 127.16, 127.71, 128.81, 129.13, 139.09, 146.78; HRMS (ESI) calcd for C$_{15}$H$_{17}$NNaO$_2$ (M+Na)$^+$ 266.1151, found 266.1171. $[\alpha]_{D}^{20}$ = + 4.0° (c = 1, EtOH); Reference Data.$^{[3]}$ $[\alpha]_{D}$ = + 4.0° (c =1, EtOH), so the absolute structure of the product was determined as (2S, 3S).

References:


X-ray analysis date of 4f

Bond precision: C-C = 0.0061Å  Wavelength=0.71073
Cell: a=5.8858(3)  b=9.0384(4)  c=23.4473(11)
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Temperature: 296 K

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wR2(reflections)= 0.1452( 4285)
S = 1.032
Npar= 289