Highly Enantioselective and Diastereoselective Cycloaddition of Cyclopropanes with Nitrones and Its Application in the Kinetic Resolution of 2-Substituted Cyclopropane-1,1-dicarboxylates
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General information.
All reactions were carried out under dry nitrogen atmosphere. Dimethoxyl ethane (DME) was distilled over calcium hydride prior to use. Activated molecular sieves powder 4Å (MS 4 Å) was dried at 250 °C in vacuum before use. All of the nitrones1 and 2-substituted cyclopropane-1,1-dicarboxylates2 were synthesized according to the literature. All glassware was oven-dried, assembled hot, and cooled under a stream of dry nitrogen before use.

1H NMR was recorded on a Varian Mercury-300 (300 MHz). Chemical shifts are reported in parts per million (ppm) down field from TMS, using residual CDCl3 (7.26 ppm) as an internal standard. 13C NMR was recorded on a Varian Mercury-300 (75 MHz) spectrometers using proton decoupling. Chemical shifts are reported in parts per million (ppm) down field from TMS, using the middle resonance of CDCl3 (77 ppm) as an internal standard.

A mixture of Ni(ClO4)2·6H2O (0.040 mmol) and trisoxazoline (0.044 mmol) in dimethoxyethane (1 mL) was stirred at 50 °C for 2 hours under nitrogen. The mixture was cooled to room temperature and then was transferred to cyclopropane diester (0.44 mmol) via a syringe. To the resulting solution was added activated molecular sieves 4Å (100 mg). The mixture was stirred at -30 °C for 30 minutes and then nitrone (0.20 mmol) was added. After the reaction was complete (monitored by TLC), the mixture was passed rapidly through a glass funnel with a thin layer (20 mm) of silica gel (300-400 mesh), washed with CH2Cl2 (50 mL). The filtrate was concentrated under reduced pressure and the residue was purified by flash chromatography.

(cis)-diethyl 2-phenyl-3,6-diphenyl-[1,2]oxazinane-4,4-dicarboxylate

Analytical data: 1H NMR (300 MHz, CDCl3) δ 7.61-7.55 (m, 4H), 7.49-7.39 (m, 3H), 7.20-7.09 (m, 7H), 6.83-6.80 (m, 1H), 5.79 (s, 1H), 5.04 (dd, J = 3.3, 14.4 Hz, 1H), 4.39 (dd, J = 7.2, 14.4 Hz, 2H), 3.91 (m, 2H), 2.88-2.81 (m, 2H), 1.36 (t, J = 7.2 Hz, 3H), 1.02 (t, J = 7.2 Hz, 3H); 13C NMR (75 MHz, CDCl3): 169.56, 167.88, 148.57, 139.56, 134.95, 130.56, 128.60, 128.48, 128.23, 127.98, 127.85, 126.38, 121.48, 115.71, 78.81, 65.74, 62.32, 61.79, 59.29, 31.81, 14.15, 13.68; IR (thin film, cm⁻¹) 2978, 1737, 1586, 1492, 1446, 1255, 1231, 747, 692; Anal. Calcd for C28H29NO5: C, 73.18%; H, 6.36%; N, 3.05%; Found: C, 72.92%, H, 6.42%, N, 3.13%; LRMS-EI (m/e): 459 (M⁺, 4.5), 198(100.0). The ees listed in table 1 were determined by HPLC analysis using a Chiralpak AD-H column with hexane/i-PrOH 90/10 as eluent, 254 nm.
(cis)-dimethyl 2-methyl-3,6-diphenyl-[1,2]oxazinane-4,4-dicarboxylate

-30°C, 3 days, 82% yield for cis-isomer, dr = 13/1, 90% ee. 43% conversion of cyclopropane (by 1H NMR). Analytical data:

1H NMR (300 MHz, CDCl3) δ 7.62-7.31 (m, 10H), 4.89 (dd, J = 2.8 Hz, 11.6 Hz, 1H), 4.85 (s, 1H), 3.89 (s, 3H), 3.39 (s, 3H), 2.78-2.60 (s, 2H), 2.54 (s, 3H); [α]D25 = +160.8° (c 1.0, CHCl3, 90% ee). 90% ee was determined by HPLC analysis using a Chiralpak AD-H column with hexane/i-PrOH 90/10 as eluent, 254 nm, tR1 = 6.10 min (minor), tR2 = 9.94 min (major). The absolute configuration for the cycloadducts has not been established and positive polar rotation was given, which was accorded with that of literature (+154.7°, same conditions).

(cis)-dibenzyl 2-methyl-3,6-diphenyl-[1,2]oxazinane-4,4-dicarboxylate

-40°C, 4 days, 62% yield for cis-isomer, dr = 10/1, 97% ee. 41% conversion of cyclopropane (by 1H NMR). Analytical data:

1H NMR (300 MHz, CDCl3) δ 7.56 (d, J = 6.6 Hz, 2H), 7.43-7.22 (m, 16H), 7.04-7.01 (m, 2H), 5.30 (s, 2H), 4.90 (dd, J = 3.4 Hz, 11.2 Hz, 1H), 4.86 (s, 1H), 4.77-4.65 (m, 2H), 2.79-2.63 (m, 2H), 2.52 (s, 3H); 13C NMR (75 MHz, CDCl3) δ 169.51, 167.69, 135.44, 134.75, 131.02, 128.55, 128.44, 128.35, 128.25, 128.20, 128.16, 128.05, 126.31, 77.98, 67.73 (2C), 67.26, 59.41, 43.31. IR (thin film, cm⁻¹) 3032, 2957, 2885, 1741, 1496, 1454, 1257, 1098, 749, 698; Anal. Calcd. For C33H31NO5: C, 75.99; H, 5.99; N, 2.69. Found: C, 75.66; H, 6.14; N, 2.66. LRMS-ESI: 522 (M + H⁺, 100). [α]D25 = +127.6° (c 1.0, CHCl3, 97% ee.), 97% ee was determined by HPLC analysis using a Chiralpak OD-H column with hexane/i-PrOH 90/10 as eluent, 1 mL/min, 254 nm, tR1 = 5.79 min (major), tR2 = 6.81 min (minor).

(cis)-diethyl 2-methyl-3,6-diphenyl-[1,2]oxazinane-4,4-dicarboxylate

-30°C, 4 days, 88% yield for cis-isomer, dr = 11/1, 95% ee. 48% conversion of cyclopropane (by 1H NMR). Analytical data:

1H NMR (300 MHz, CDCl3) δ 7.62-7.30 (m, 10H), 4.89 (dd, J = 3.3 Hz, 11.7 Hz, 1H), 4.84 (s, 1H), 4.40-4.33 (m, 2H), 3.92-3.72 (m, 2H), 2.78-2.60 (m, 2H), 2.53 (s, 3H), 1.33 (t, J = 7.2 Hz, 3H), 0.97 (t, J = 7.2 Hz, 3H); 13C NMR (75 MHz, CDCl3) δ 169.71, 169.79, 140.14, 134.59, 131.02, 128.47, 128.09, 127.96, 127.88, 126.25, 77.88, 67.73, 61.99, 61.49, 59.02, 43.26, 31.07, 14.02, 13.55. IR (thin film, cm⁻¹) 3029, 2984, 2885, 1738, 1494, 1453, 1366, 1253, 1099, 753, 700; Anal. Calcd. For C23H27NO5: C, 69.50; H, 6.85; N, 3.52. Found: C, 69.48; H, 7.09; N, 3.46. LRMS-ESI: 398 (M + H⁺, 100). [α]D25 = +160.3° (c 1.0, CHCl3, 95% ee.), 95% ee was determined by HPLC analysis using a Chiralpak AD-H column with hexane/i-PrOH 90/10 as eluent, 1 mL/min, 254 nm, tR1 = 6.48 min (minor), tR2 = 7.94 min (major).

(cis)-diethyl 3-(4-bromophenyl)-2-methyl-6-phenyl-[1,2]oxazinane-4,4-dicarboxylate
-30°C, 4 days, 85% yield for cis-isomer, dr = 12/1, 97% ee. 45% conversion of cyclopropane (by \(\text{H}^1\) NMR). Analytical data:

\(\text{H}^1\) NMR (300 MHz, CDCl\(_3\)) \(\delta\) 7.53-7.34 (m, 9H), 4.90 (t, \(J = 7.4\) Hz, 1H), 4.82 (s, 1H), 4.36 (q, \(J = 7.2\) Hz, 2H), 3.97-3.76 (m, 2H), 2.66-2.64 (m, 2H), 2.51 (s, 3H), 1.33 (t, \(J = 7.2\) Hz, 3H), 0.97 (t, \(J = 7.2\) Hz, 3H); \(\text{C}^{13}\) NMR (75 MHz, CDCl\(_3\)) \(\delta\) 169.48, 167.86, 139.93, 133.73, 132.66, 131.12, 128.57, 128.09, 126.22, 122.48, 77.87, 67.11, 62.17, 61.70, 58.93, 43.26, 30.93, 14.05, 13.68. IR (thin film, \(\text{cm}^{-1}\)) 2983, 2960, 2884, 1738, 1486, 1253, 1011, 968, 755, 698; LRMS-ESI: 476 (M + H\(^+\), 100). HRMS-ESI calcd. for C\(_{23}\)H\(_{27}\)BrNO\(_5\)+ is 476.1067; observed: 476.1076; \([\alpha]_D^{25}\) = +156.7° (c 1.0, CHCl\(_3\), 97% ee.), 97% ee was determined by HPLC analysis using a Chiralcel OD-H column with hexane/i-PrOH 50/1 as eluent, 1 mL/min, 254 nm, \(t_{R1}\) = 5.49 min (major), \(t_{R2}\) = 6.87 min (minor).

\[
\text{N O} \quad \text{Me} \quad \text{Ph} \quad \text{CO}_2\text{Et} \quad \text{CO}_2\text{Et}
\]

(cis)-diethyl 3-(4-(methoxycarbonyl)phenyl)-2-methyl-6-phenyl-[1,2]oxazinane-4,4-dicarboxylate

-30°C, 4 days, 97% yield, dr = 11/1, 97% ee. 46% conversion of cyclopropane (by \(\text{H}^1\) NMR). Analytical data:

\(\text{H}^1\) NMR (300 MHz, CDCl\(_3\)) \(\delta\) 8.00 (d, \(J = 8.4\) Hz, 2H), 7.73 (d, \(J = 8.4\) Hz, 2H), 7.48-7.32 (m, 5H), 4.95-4.90 (m, 1H), 4.91 (s, 1H), 4.41-4.34 (m, 2H), 3.90 (s, 3H), 2.74-2.63 (m, 2H), 2.52 (s, 3H), 1.33 (t, \(J = 6.9\) Hz, 3H), 0.99 (t, \(J = 6.9\) Hz, 3H; \(\text{C}^{13}\) NMR (75 MHz, CDCl\(_3\)) \(\delta\) 169.42, 167.76, 166.72, 140.06, 131.06, 129.82, 129.08, 128.56, 128.08, 126.21, 109.68, 77.92, 67.48, 62.18, 61.67, 58.93, 52.06, 43.27, 31.08, 14.03, 13.63. IR (thin film, \(\text{cm}^{-1}\)) 2984, 2956, 2885, 1725, 1436, 1279, 1186, 1105, 699; LRMS-ESI: 456 (M + H\(^+\), 100). HRMS-ESI calcd. for C\(_{25}\)H\(_{30}\)BrNO\(_7\)+ is 456.2017; observed: 456.2024; \([\alpha]_D^{25}\) = +144.1° (c 1.0, CHCl\(_3\), 97% ee.), 97% ee was determined by HPLC analysis using a Chiralpak AD-H column with hexane/i-PrOH 90/10 as eluent, 1 mL/min, 254 nm, \(t_{R1}\) = 8.53 min (minor), \(t_{R2}\) = 11.44 min (major).

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\text{N O} \quad \text{Me} \quad \text{Ph} \quad \text{CO}_2\text{Et} \quad \text{CO}_2\text{Et}
\]

MeO

(cis)-diethyl 2-methyl-6-phenyl-3-p-tolyl-[1,2]oxazinane-4,4-dicarboxylate

-30°C, 4 days, 97% yield, dr = 12/1, 96% ee. 41% conversion of cyclopropane (by \(\text{H}^1\) NMR). Analytical data:

\(\text{H}^1\) NMR (300 MHz, CDCl\(_3\)) \(\delta\) 7.52-7.33 (m, 7H), 7.12 (d, \(J = 7.8\) Hz, 2H), 4.90 (dd, \(J = 3.0\) Hz, 12.0 Hz, 1H), 4.81 (s, 1H), 4.36 (q, \(J = 6.9\) Hz, 1H), 3.95-3.73 (m, 2H), 2.77-2.53 (m, 2H), 2.52 (s, 3H), 2.32 (s, 3H), 1.32 (t, \(J = 7.2\) Hz, 3H), 1.01 (t, \(J = 7.2\) Hz, 3H); \(\text{C}^{13}\) NMR (75 MHz, CDCl\(_3\)) \(\delta\) 169.81, 168.06, 140.14, 137.73, 131.41, 130.91, 128.63, 128.49, 127.96, 126.31, 77.92, 67.47, 61.96, 61.47, 59.09, 43.25, 31.08, 21.03, 14.04, 13.62. IR (thin film, \(\text{cm}^{-1}\)) 2982, 2885, 1739, 1253, 1188, 1105, 698; LRMS-ESI: 412 (M + H\(^+\), 100). HRMS-ESI calcd. for C\(_{24}\)H\(_{30}\)BrNO\(_5\)+ is 412.2118; observed: 412.2123; \([\alpha]_D^{25}\) = +157.7° (c 1.0, CHCl\(_3\), 96% ee.), 96% ee was determined by HPLC analysis using a Chiralpak AD-H column with hexane/i-PrOH 90/10 as eluent, 1 mL/min, 254 nm, \(t_{R1}\) = 6.60 min (minor), \(t_{R2}\) = 9.67 min (major).

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\text{N O} \quad \text{Me} \quad \text{Ph} \quad \text{CO}_2\text{Et} \quad \text{CO}_2\text{Et}
\]

MeO

(cis)-diethyl 3-(4-methoxyphenyl)-2-methyl-6-phenyl-[1,2]oxazinane-4,4-dicarboxylate

S-3
-30°C, 4 days, 92% yield for cis-isomer, dr = 13/1, 90% ee. 47% conversion of cyclopropane (by \textsuperscript{1}H NMR). Analytical data: \textbf{\textsuperscript{1}H NMR} (300 MHz, CDCl\textsubscript{3}) \(\delta\) 7.55-7.31 (m, 7H), 6.85 (d, \(J = 9.0\) Hz, 2H), 4.90 (dd, \(J = 3.0\) Hz, 11.6 Hz, 1H), 4.80 (s, 1H), 4.37 (q, \(J = 7.2\) Hz, 1H), 3.96-3.80 (m, 2H), 3.79 (s, 3H), 2.84-2.59 (m, 2H), 2.51 (s, 3H), 1.33 (t, \(J = 7.2\) Hz, 3H), 1.02 (t, \(J = 7.2\) Hz, 3H); \textbf{\textsuperscript{13}C NMR} (75 MHz, CDCl\textsubscript{3}) \(\delta\) 169.84, 168.09, 159.30, 140.24, 132.24, 128.51, 127.98, 126.29, 113.24, 77.90, 67.08, 61.99, 59.14, 55.06, 43.22, 31.04, 14.05, 13.70. \textbf{IR} (thin film, cm\textsuperscript{-1}) 2983, 2885, 1738, 1511, 1252, 1180, 699; \textbf{LRMS-ESI}: 428 (M + H\textsuperscript{+}, 100). \textbf{HRMS-ESI} calcd. for C\textsubscript{24}H\textsubscript{30}BrNO\textsubscript{5}\textsuperscript{+} is 428.2068: observed: 428.2078; \([\alpha]_D^{25} = +150.9^\circ\) (c 1.0, CHCl\textsubscript{3}, 90% ee.), 90% ee was determined by HPLC analysis using a Chiralpak AD-H column with hexane/i-PrOH 19/1 as eluent, 1 mL/min, 254 nm, \(t_{R1} = 12.66\) min (minor), \(t_{R2} = 16.15\) min (major).

\[
\text{(cis)-diethyl 3-(furan-2-yl)-2-methyl-6-phenyl-[1,2]oxazinane-4,4-dicarboxylate}
\]

-30°C, 4 days, 99% yield, dr = 13/1, 93% ee. 45% conversion of cyclopropane (by \textsuperscript{1}H NMR). Analytical data: \textbf{\textsuperscript{1}H NMR} (300 MHz, CDCl\textsubscript{3}) \(\delta\) 7.45-7.25 (m, 6H), 6.49 (d, \(J = 3.3\) Hz, 1H), 6.38 (t, \(J = 1.5\) Hz, 1H), 4.98 (s, 1H), 4.93 (dd, \(J = 2.8\) Hz, 11.2 Hz, 1H), 4.40-4.30 (m, 2H), 4.09-3.92 (m, 2H), 2.70-2.53 (m, 2H), 2.51 (s, 3H), 1.33 (t, \(J = 7.0\) Hz, 3H), 1.05 (t, \(J = 7.2\) Hz, 3H); \textbf{\textsuperscript{13}C NMR} (75 MHz, CDCl\textsubscript{3}) \(\delta\) 168.94, 167.78, 148.5, 140.10, 128.42, 127.99, 126.42, 111.51, 110.15, 78.11, 62.11, 62.08, 61.64, 58.04, 42.97, 32.16, 14.00, 13.70. \textbf{IR} (thin film, cm\textsuperscript{-1}) 2982, 2884, 1738, 1257, 1187, 1099, 1016, 754, 700; \textbf{LRMS-ESI}: 388 (M + H\textsuperscript{+}, 100). \textbf{Anal. Calcd.} For C\textsubscript{21}H\textsubscript{25}NO\textsubscript{6}: C, 65.10; H, 6.50; N, 3.61. Found: C, 64.85; H, 6.64; N, 3.44. \([\alpha]_D^{25} = +130.6^\circ\) (c 1.0, CHCl\textsubscript{3}, 93% ee.), 93% ee was determined by HPLC analysis using a Chiralpak AD-H column with hexane/i-PrOH 50/1 as eluent, 1 mL/min, 254 nm, \(t_{R1} = 12.80\) min (minor), \(t_{R2} = 15.74\) min (major).

\[
\text{(cis,E)-diethyl 2-methyl-6-phenyl-3-styryl-[1,2]oxazinane-4,4-dicarboxylate}
\]

-30°C, 3 days, 76% yield for cis-isomer, dr = 4/1, 92% ee. 47% conversion of cyclopropane (by \textsuperscript{1}H NMR). Analytical data: \textbf{\textsuperscript{1}H NMR} (300 MHz, CDCl\textsubscript{3}) \(\delta\) 7.45-7.24 (m, 10H), 6.69-6.50 (m, 2H), 4.89 (dd, \(J = 2.4\) Hz, 12.0 Hz, 1H), 4.38-4.30 (m, 3H), 4.12-4.04 (m, 2H), 2.64 (s, 3H), 2.64-2.59 (m, 1H), 2.40 (dd, \(J = 12.0\) Hz, 14.4 Hz, 1H), 1.33 (t, \(J = 7.2\) Hz, 3H), 1.15 (t, \(J = 7.2\) Hz, 3H); \textbf{\textsuperscript{13}C NMR} (75 MHz, CDCl\textsubscript{3}) \(\delta\) 169.24, 167.78, 148.5, 140.10, 128.42, 127.99, 126.42, 111.51, 110.15, 78.11, 62.11, 62.08, 61.64, 58.04, 42.97, 32.16, 14.00, 13.70. \textbf{IR} (thin film, cm\textsuperscript{-1}) 2981, 2883, 1737, 1450, 697; \textbf{LRMS-ESI}: 424 (M + H\textsuperscript{+}, 100). \textbf{HRMS-ESI} calcd. for C\textsubscript{25}H\textsubscript{30}NO\textsubscript{5}\textsuperscript{+} is 424.2118: observed: 424.2127; \([\alpha]_D^{25} = +239.3^\circ\) (c 1.0, CHCl\textsubscript{3}, 93% ee.), 92% ee was determined by HPLC analysis using a Chiralcel OD-H column with hexane/i-PrOH 30/1 as eluent, 1 mL/min, 254 nm, \(t_{R1} = 4.86\) min (major), \(t_{R2} = 5.53\) min (minor).

\[
\text{(cis)-diethyl 2-methyl-3-phenyl-6-vinyl-[1,2]oxazinane-4,4-dicarboxylate}
\]

-40°C, 3 days, 88% yield for cis-isomer, dr = 6/1, 80% ee. 46% conversion of cyclopropane (by \textsuperscript{1}H NMR). Analytical data:
^1H NMR (300 MHz, CDCl\textsubscript{3}) \( \delta \) 7.54-7.51 (m, 2H), 7.30-7.27 (m, 3H), 6.04-5.93 (m, 1H), 5.39 (d, \( J = 17.1 \) Hz, 1H), 5.27 (d, \( J = 10.5 \) Hz, 1H), 4.74 (s, 1H), 4.40-4.29 (m, 3H), 3.91-3.71 (m, 2H), 2.46-2.43 (m, 5H), 1.31 (t, \( J = 7.2 \) Hz, 3H); \( [\alpha]_D^{25} = +155.2 \) (c 1.0, CHCl\textsubscript{3}, 80% ee.), 80% ee was determined by HPLC analysis using a Chiralpak AD-H column with hexane/i-PrOH 50/1 as eluent, 1 mL/min, 254 nm, \( t_{R1} = 6.89 \) min (major), \( t_{R2} = 9.59 \) min (minor).

\[
\begin{align*}
\text{(cis,E)-diethyl 2-methyl-3-phenyl-6-styryl-[1,2]oxazinane-4,4-dicarboxylate}\n\end{align*}
\]
-40°C, 5 hrs, 84% yield, dr = 5/1, 80% ee, 41% conversion of cyclopropane (by \(^1H\) NMR). Analytical data: \(^1H\) NMR (300 MHz, CDCl\textsubscript{3}) \( \delta \) 7.56-7.26 (m, 10H), 6.72 (d, \( J = 15.9 \) Hz, 1H), 6.34 (dd, \( J = 5.8 \) Hz, 15.8 Hz, 1H), 4.78 (s, 1H), 4.57-4.55 (m, 1H), 4.35 (q, \( J = 6.9 \) Hz, 2H), 3.93-3.72 (m, 2H), 2.62-2.50 (m, 2H), 2.50 (s, 3H), 1.33 (t, \( J = 7.2 \) Hz, 3H), 0.98 (t, \( J = 7.2 \) Hz, 3H); \(^{13}C\) NMR (75 MHz, CDCl\textsubscript{3}) \( \delta \) 169.77, 168.11, 136.49, 134.72, 132.16, 131.15, 128.54, 128.17, 127.94, 127.74, 126.60, 76.29, 68.02, 62.07, 61.56, 58.73, 43.34, 30.12, 14.08, 13.64. IR (thin film, cm\textsuperscript{-1}) 2981, 2885, 1738, 1252, 701; LRMS-ESI: 424 (M + H\textsuperscript{+}, 100). HRMS-ESI calcd. for C\textsubscript{25}H\textsubscript{30}NO\textsubscript{5}\textsuperscript{+} is 424.2118: observed: 424.2118; \([\alpha]_D^{25} = +121.9 \)° (c 1.0, CHCl\textsubscript{3}, 80% ee.), 80% ee was determined by HPLC analysis using a Chiralpak AD-H column with hexane/i-PrOH 19/1 as eluent, 1 mL/min, 254 nm, \( t_{R1} = 7.61 \) min (major), \( t_{R2} = 8.40 \) min (minor).

\[
\begin{align*}
\text{(cis)-diethyl 2-benzyl-3,6-diphenyl-[1,2]oxazinane-4,4-dicarboxylate}\n\end{align*}
\]
-30°C, 5 days, 74% yield for cis-isomer, dr = 11/1, 93% ee, 48% conversion of cyclopropane (by \(^1H\) NMR). Analytical data: \(^1H\) NMR (300 MHz, CDCl\textsubscript{3}) \( \delta \) 7.60-7.24 (m, 15H), 4.96 (t, \( J = 7.2 \) Hz, 1H), 4.90 (s, 1H), 4.42-4.25 (m, 2H), 3.92 (d, \( J = 13.8 \) Hz, 1H), 3.90-3.70 (m, 2H), 3.64 (d, \( J = 13.8 \) Hz, 1H), 2.74 (s, 1H), 2.71 (s, 1H), 1.30 (t, \( J = 7.2 \) Hz, 3H), 0.92 (t, \( J = 7.2 \) Hz, 3H); \(^{13}C\) NMR (75 MHz, CDCl\textsubscript{3}) \( \delta \) 169.53, 168.09, 140.21, 136.92, 134.89, 131.28, 128.79, 128.35, 128.10, 127.92, 127.88, 127.74, 126.74, 126.97, 126.09, 77.70, 65.70, 61.92, 61.44, 59.38, 59.28, 31.26, 14.05, 13.34. IR (thin film, cm\textsuperscript{-1}) 3062, 3030, 2981, 2937, 1739, 1453, 1253, 1199, 755, 699; LRMS-ESI: 474 (M + H\textsuperscript{+}, 100). HRMS-ESI calcd. for C\textsubscript{29}H\textsubscript{32}NO\textsubscript{5}\textsuperscript{+} is 474.2275: observed: 474.2266; \([\alpha]_D^{25} = +113.9 \)° (c 10.0, CHCl\textsubscript{3}, 93% ee.), 93% ee was determined by HPLC analysis using a Chiralpak AD-H column with hexane/i-PrOH 30/1 as eluent, 1 mL/min, 254 nm, \( t_{R1} = 8.27 \) min (minor), \( t_{R2} = 11.19 \) min (major). When this reaction scale was enlarged by 2 times, the results are similar as above: cyclopropane/nitrone = 0.88 mmol/0.40 mmol, -30°C, 7 days, 83% yield for cis-isomer, dr = 10/1, 94% ee, 49% conversion of cyclopropane (by \(^1H\) NMR).

**General procedure for kinetic resolution of cyclopropane-1,1-diester.**

\[
\begin{align*}
\text{Ni(ClO}_4\text{)}_2\cdot6\text{H}_2\text{O (0.040 mmol) and trisoxazoline 1e (0.044 mmol) in dimethoxyl ethane (1 mL) was stirred at 50 °C for 2 hours under nitrogen. The mixture was cooled to room temperature and then was transferred to cyclopropane diester (0.44 mmol) via a syringe. To the resulting solution was added activated molecular sieves 4Å (100 mg). The mixture}\n\end{align*}
\]
was stirred at -30°C for 30 minutes and then nitrone (0.23 mmol) was added. After the conversion of (±) 2 was higher than 50% (monitored by 1H NMR), the mixture was passed rapidly through a glass funnel with a thin layer (20 mm) of silica gel (300-400 mesh), washed with CH2Cl2 (50 mL). The filtrate was concentrated under reduced pressure and the residue was purified by flash chromatography. The absolute configuration for recovered cyclopropanes was assigned R by comparing its polar rotation with that reported in the reference.5

\[
\text{CO}_2\text{Me} \quad \text{CO}_2\text{Me} \\
\text{Br} \\
\text{F}_3\text{C} \\
\text{O}_2\text{N}
\]

(R)-dimethyl 2-phenylcyclopropane-1,1-dicarboxylate.5 Cyclopropane/nitrone = 0.4 mmol/0.4 mmol, at -40 °C, 30 hours, 55% conversion of cyclopropane by 1H NMR. Recovered yield: 43%. 1H NMR (CDCl3, 300 MHz) δ 7.30-7.17 (m, 5H), 3.78 (s, 3H), 3.35 (s, 3H), 3.23 (t, J = 8.7 Hz, 1H), 2.20 (dd, J = 5.1 Hz, 8.1 Hz, 1H), 1.74 (dd, J = 5.1 Hz, 9.3 Hz, 1H), [α]D25 = +131.9 (c 1.0, PhH), 91% ee determined by HPLC analysis using a Chiralcel OD-H with hexane/i-PrOH = 50/1 v/v, 1.0 mL/min, 254 nm, tR1 = 7.70 min (minor), tR2 = 8.14 min (major).

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\text{CO}_2\text{Me} \quad \text{CO}_2\text{Me} \\
\text{Me} \\
\text{CO}_2\text{Me} \\
\text{CO}_2\text{Me}
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(R)-dimethyl 2-p-tolylcyclopropane-1,1-dicarboxylate.5 Cyclopropane/nitrone = 0.4 mmol/0.25 mmol, at -40 °C, 48 hours, 50% conversion of cyclopropane by 1H NMR. Recovered yield: 49%. 1H NMR (CDCl3, 300 MHz) δ 7.07 (s, 4H), 3.78 (s, 3H), 3.38 (s, 3H), 3.19 (t, J = 8.6 Hz, 1H), 2.30 (s, 3H), 2.17 (dd, J = 5.1 Hz, 8.1 Hz, 1H), 1.72 (dd, J = 5.1 Hz, 9.3 Hz, 1H), [α]D25 = +119.3 ° (c 1.0, PhH), 96% ee determined by HPLC analysis using a Chiralcel OD-H with hexane/i-PrOH = 500/3 v/v, 0.6 mL/min, 254 nm, tR1 = 18.63 min (minor), tR2 = 19.86 min (major).

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\text{Br} \\
\text{F}_3\text{C} \\
\text{O}_2\text{N}
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(R)-dimethyl 2-(4-bromophenyl)cyclopropane-1,1-dicarboxylate.5 Cyclopropane/nitrone = 0.4 mmol/0.23 mmol, at -30 °C, 67 hours, 51% conversion of cyclopropane by 1H NMR. Recovered yield: 49%. 1H NMR (CDCl3, 300 MHz) δ 7.40 (d, J = 8.4 Hz, 2H), 7.07 (d, J = 7.8 Hz, 2H), 3.79 (s, 3H), 3.41 (s, 3H), 3.16 (t, J = 8.7 Hz, 1H), 2.15 (dd, J = 5.1 Hz, 8.0 Hz, 1H), 1.74 (dd, J = 5.1 Hz, 9.3 Hz, 1H), [α]D25 = +90.1 ° (c 1.0, PhH), 95% ee determined by HPLC analysis using a Chiralcel AD-H with hexane/i-PrOH = 50/1 v/v, 0.8 mL/min, 254 nm, tR1 = 12.02 min (minor), tR2 = 13.46 min (major).

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\text{O}_2\text{N} \\
\text{O}_2\text{N}
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(R)-dimethyl 2-(4-(trifluoromethyl)phenyl)cyclopropane-1,1-dicarboxylate.5 Cyclopropane/nitrone = 0.4 mmol/0.23 mmol, at 0 °C, 168 hours, 50% conversion of cyclopropane by 1H NMR. Recovered yield: 49%. 1H NMR (CDCl3, 300 MHz) δ 7.54 (d, J = 8.1 Hz, 2H), 7.31 (d, J = 8.1 Hz, 2H), 3.81 (s, 3H), 3.39 (s, 3H), 3.26 (t, J = 8.7 Hz, 1H), 2.21 (dd, J = 5.4 Hz, 8.2 Hz, 1H), 1.79 (dd, J = 5.4 Hz, 9.6 Hz, 1H), [α]D25 = +44.5 ° (c 1.0, PhH), 96% ee determined by HPLC analysis using a Chiralcel AD-H with hexane/i-PrOH = 50/1 v/v, 0.8 mL/min, 238 nm, tR1 = 7.91 min (minor), tR2 = 9.32 min (major).

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\text{CO}_2\text{Me} \quad \text{CO}_2\text{Me} \\
\text{O}_2\text{N} \\
\text{O}_2\text{N}
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(R)-dimethyl 2-(4-nitrophenyl)cyclopropane-1,1-dicarboxylate.6 Cyclopropane/nitrone = 0.4 mmol/0.23 mmol, at 0 °C, 96 hours, 53% conversion of cyclopropane by 1H NMR. Recovered yield: 45%. 1H NMR (CDCl3, 300 MHz) δ 8.14 (d, J = 9.0 Hz, 2H), 7.36 (d, J = 8.4 Hz, 2H), 3.81 (s, 3H), 3.41 (s, 3H), 3.28 (t, J = 8.7 Hz, 1H), 2.22 (dd, J = 5.4 Hz, 7.7 Hz, 1H), 1.83 (dd, J = 5.4 Hz, 9.3 Hz, 1H), [α]D25 = +100.5 ° (c 1.0, PhH), 97% ee determined by HPLC analysis.
using a Chiralcel AD-H with hexane/i-PrOH = 90/10 v/v, 0.7 mL/min, 254 nm, t<sub>R1</sub> = 11.82 min (minor), t<sub>R2</sub> = 14.63 min (major).

(R)-dimethyl 2-(4-chlorophenyl)cyclopropane-1,1-dicarboxylate. Cyclopropane/nitrone = 0.4 mmol/0.23 mmol, -30 °C, 72 hours, 50 % conversion of cyclopropane by <sup>1</sup>H NMR. Recovered yield: 49%. <sup>1</sup>H NMR (CDCl<sub>3</sub>, 300 MHz) δ 7.24 (d, J = 6.9 Hz, 2H), 7.13 (d, J = 8.4 Hz, 2H), 3.79 (s, 3H), 3.41 (s, 3H), 3.19 (t, J = 8.4 Hz, 1H), 2.16 (dd, J = 5.1 Hz, 8.0 Hz, 1H), 1.75 (dd, J = 5.1 Hz, 9.6 Hz, 1H). [α]<sub>D</sub><sup>25</sup> = +95.8° (c 1.0, PhH), 94% ee estimated on the basis of HPLC analysis using a chiral column: Diacel Chiralcel AD-H with hexane/i-PrOH = 50/1 v/v, 0.8 mL/min, 254 nm, t<sub>R1</sub> = 10.79 min (minor), t<sub>R2</sub> = 12.31 min (major).

(CO<sub>2</sub>Me)<sub>2</sub>C<sub>6</sub>H<sub>4</sub>Cl (R)-dimethyl 2-(4-chlorophenyl)cyclopropane-1,1-dicarboxylate. Cyclopropane/nitrone = 0.4 mmol/0.23 mmol, at -30°C, 48 hours, 57 % conversion of cyclopropane by <sup>1</sup>H NMR. Recovered yield: 40%. <sup>1</sup>H NMR (CDCl<sub>3</sub>, 300 MHz) δ 7.10 (d, J = 8.4 Hz, 2H), 6.79 (d, J = 8.7 Hz, 2H), 3.77 (s, 3H), 3.76 (s, 3H), 3.38 (s, 3H), 3.17 (t, J = 8.6 Hz, 1H), 2.14 (dd, J = 5.1 Hz, 8.0 Hz, 1H), 1.71 (dd, J = 5.1 Hz, 9.3 Hz, 1H). [α]<sub>D</sub><sup>25</sup> = +56.4° (c 1.0, PhH), 92% ee estimated on the basis of HPLC analysis using a chiral column: Diacel Chiralpak AD-H with hexane/i-PrOH = 20/1 v/v, 1.0 mL/min, 254 nm, t<sub>R1</sub> = 9.26 min (minor), t<sub>R2</sub> = 10.24 min (major).

**Procedure for cycloaddition of nitrone with (R)-dimethyl 2-phenyl cyclopropane-1,1-dicarboxylate.**

A mixture of (R)-dimethyl 2-phenylcyclopropane-1,1-dicarboxylate (91% ee, 0.1 mmol), nitrone (0.12 mmol), MS 4Å (100 mg) and Ni(ClO<sub>4</sub>)<sub>2</sub>·6H<sub>2</sub>O (0.01 mmol, absence of ligand) in dry CH<sub>2</sub>Cl<sub>2</sub> (1 mL) was stirred at room temperature for 48 hours under nitrogen. After the reaction was complete (monitored by TLC), the mixture was passed rapidly through a glass funnel with a thin layer (20 mm) of silica gel (300-400 mesh), washed with CH<sub>2</sub>Cl<sub>2</sub> (50 mL). The filtrate was concentrated under reduced pressure and the residue (used for the determination of the diastereomer ratio by <sup>1</sup>H NMR) was purified by flash chromatography. The ee was determined by HPLC analysis using a Chiralpak AD-H column with hexane/i-PrOH 20/1 as eluent, 254 nm, t<sub>R1</sub> = 13.19 min (major), t<sub>R2</sub> = 24.19 min (minor).

(R)-dimethyl 2-phenylcyclopropane-1,1-dicarboxylate. Room temperature, 48 hours, dr > 99/1, 83% yield, 90% ee, [α]<sub>D</sub><sup>25</sup> = -152.9° (CHCl<sub>3</sub>, c 1.0, 90% ee).

References

NMR spectra.
HPLC analytical spectra.