Supporting Information

Nitrile Biotransformation for Highly Enantioselective Synthesis of 3-Substituted 2,2-Dimethylcyclopropanecarboxylic Acids and Amides

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1. Biotransformations of (+/-)-nitriles and characterization of nitriles, amides and acids

**General Procedure for the Biotransformations of Nitriles and Amides.** To an Erlenmeyer flask (100 ml) with a screw cap were added *Rhodococcus* sp. AJ270 cells (Blakey, A. J.; Colby, J.; Williams, E.; O’Reilly, C. *FEMS Microbiology Lett.* **1995**, *129*, 57. Meth-Cohn, O.; Wang, M-X. *J. Chem. Soc. Perkin Trans. 1* **1997**, 1099.) (2 g wet weight) and potassium phosphate buffer (0.1 M, 50 ml) and the resting cells were activated at 30 °C for 30 min with orbital shaking. Racemic nitriles or amides were added in one potion to the flask and the mixture was incubated at 30 °C with the use of an orbital shaker (200 rpm). The reaction, monitored by TLC, was quenched after a specified period of time (see Tables 1 to 3) by removing the biomass through a Celite pad filtration. The resulting aqueous solution was basified to pH 12 with aqueous NaOH (2 M). Extraction with ethyl acetate gave, after drying and concentration, the amides and unconverted nitriles. Separation of amide and nitrile was effected by column chromatography. The aqueous solution was then acidified using aqueous HCl (2 M) to pH 2 and extracted with ethyl acetate. Acid was obtained after removal of the solvent. All products were characterized by their spectra data and comparison of the melting points and optical rotary power with that of the known compounds or by full characterization (see Supporting Information).

**Enzymatic Hydrolysis of (+/-)-trans-2,2-Dimethyl-3-phenylcyclopropanecarbonitrile (1a).**

(-)-(1S, 3S)-2,2-Dimethyl-3-phenylcyclopropanecarboxamide (2a): mp 174-175°C; \([\alpha]_{D}^{25} = -19\)
(+)-(1R, 3R)-2,2-Dimethyl-3-phenylcyclopropanecarboxylic acid (3a): mp 74-75°C; [α]25D +38 (c 1.0, CHCl3) [lit.1 [α]D20 +31.9 (c 4.93, ethanol)]; ee >99% (HPLC); 1H NMR (CDCl3) δ 11.00 (br s, 1H, COOH), 7.15-7.31 (m, 5H, Ar-H), 2.74 (d, J = 5.8 Hz, 1H, CH), 1.96 (d, J = 5.8 Hz, 1H, CH), 1.43 (s, 3H, CH3), 0.94 (s, 3H, CH3); 13C NMR (CDCl3) δ 178.9, 137.0, 128.6, 128.5, 127.2, 120.3, 37.7, 26.5, 23.8, 20.1, 15.1; IR (KBr) 2234 cm⁻¹; MS (EI) m/z 171 (M⁺, 74%), 156 (80), 129 (100). HRMS-EI Calcd. for C12H13N: 171.1042. Found: 171.1043.

(-)-(1S, 3S)-2,2-Dimethyl-3-phenylcyclopropanecarbonitrile 1a: 4h (40%), oil; [α]25D -102.3 (c 2.6, CHCl3); ee 99% (HPLC); 1H NMR (200Hz, CDCl3) δ 7.12-7.32 (m, 5H, Ar-H), 2.52 (d, J = 5.6 Hz, 1H, CH), 1.64 (d, J = 5.6 Hz, 1H, CH), 1.49 (s, 3H, CH3), 0.91 (s, 3H, CH3); 13C NMR (CDCl3) δ 135.3, 128.6, 128.5, 127.2, 120.3, 37.7, 26.5, 23.8, 20.1, 15.1; IR (KBr) 2234 cm⁻¹; MS (EI) m/z 171 (M⁺, 74%), 156 (80), 129 (100). HRMS-EI Calcd. for C12H13N: 171.1042. Found: 171.1043.

Enzymatic Hydrolysis of (+/-)-trans-2,2-Dimethyl-3-(4-fluorophenyl)cyclopropanecarbonitrile (1b). (-)-(1S, 3S)-2,2-Dimethyl-3-(4-fluorophenyl)cyclopropanecarboxamide (2b): mp 141-143°C;
ee >99% (HPLC); $[\alpha]_{D}^{25} -11$ (c 1.0, CHCl$_3$); $^1$H NMR (CDCl$_3$) δ 7.15 (dd, $J = 8.2, 2.4$ Hz, 2H, Ar-H) □ 7.00 (t, $J = 8.5$ Hz, 2H, Ar-H), 5.71 (br s, 2H, NH$_2$), 2.73 (d, $J = 5.5$ Hz, 1H, CH), 1.74 (d, $J = 5.6$ Hz, 1H, CH), 1.39 (s, 3H, CH$_3$), 0.95 (s, 3H, CH$_3$); $^{13}$C NMR (CDCl$_3$) δ 174.5, 161.4 (d, $J = 990$ Hz), 132.6, 130.1 (d, $J = 30$Hz), 114.9 (d, $J = 90$ Hz), 35.6, 32.6, 29.3, 21.9, 20.2; IR (KBr) 3388, 3196, 1651 cm$^{-1}$; MS (EI) $m/z$ 207 (M$^+$, 5%), 192 (8), 164 (20), 163 (100). Anal. Calcd for C$_{12}$H$_{14}$FNO: C, 69.55; H, 6.81; N, 6.76. Found: C, 69.09; H, 6.68; N, 6.69.

(+)-(1R, 3R)-2,2-Dimethyl-3-(4-fluorophenyl)cyclopropanecarboxylic acid (3b): mp 55-57°C; $[\alpha]_{D}^{25} +27.79$ (c 2.65, CHCl$_3$); ee 87% (HPLC); $^1$H NMR (CDCl$_3$) δ 7.13 (dd, $J = 8.0, 2.1$ Hz, 2H, Ar-H), 6.98 (t, $J = 8.4$ Hz, 2H, Ar-H), 2.70 (d, $J = 5.7$ Hz, 1H, CH), 1.92 (d, $J = 5.7$ Hz, 1H, CH), 1.42 (s, 3H, CH$_3$), 0.94 (s, 3H, CH$_3$); $^{13}$C NMR (CDCl$_3$) δ 178.0, 162.2 (d, $J = 990$ Hz), 132.7, 130.2 (d, $J = 60$ Hz), 115.1 (d, $J = 90$ Hz), 37.5, 31.6, 30.4, 22.1, 20.5; IR (KBr) 2250-3350, 1696, 1603 cm$^{-1}$; MS (EI) $m/z$ 208 (M$^+$, 15%), 193 (9), 164 (15), 163 (100). Anal. Calcd for C$_{12}$H$_{13}$FO$_2$: C, 69.22; H, 6.29. Found: C, 69.26; H, 6.49.

(-)-(1S, 3S)-2,2-Dimethyl-3-(4-fluorophenyl)cyclopropanecarbonitrile (1b): oil; $[\alpha]_{D}^{25} -52$ (c 1.0, CHCl$_3$); ee 86% (HPLC); $^1$H NMR (CDCl$_3$) δ 6.98-7.15 (m, 4H, Ar-H) □ 2.49 (d, $J = 5.5$ Hz, 1H, CH), 1.59 (d, $J = 5.6$ Hz, 1H, CH), 1.49 (s, 3H, CH$_3$), 0.91 (s, 3H, CH$_3$); $^{13}$C NMR (CDCl$_3$) δ 161.9 (d, $J = 960$ Hz), 131.1, 130.2 (d, $J = 30$ Hz), 120.1, 115.4 (d, $J = 90$ Hz), 36.9, 26.4, 23.6, 20.1, 15.4; IR (KBr) 2235 cm$^{-1}$; MS (EI) $m/z$ 189 (M$^+$, 56%), 174 (100), 147 (90). HRMS (EI) Calcd for C$_{12}$H$_{12}$FN: 189.0948. Found: 189.0951.
Enzymatic Hydrolysis of (+/-)-trans-2,2-Dimethyl-3-(4-chlorophenyl)cyclopropanecarbonitrile (1c). (-)-(1S, 3S)-2,2-Dimethyl-3-(4-chlorophenyl)cyclopropanecarboxamide (2c): mp 203-205°C; 

\[\alpha\]_D^25 -28 (c 1.0, CHCl_3); ee >99% (HPLC); \(^1\)H NMR (CDCl_3) \(\delta\) 7.25 (d, \(J = 8.2\) Hz, 2H, Ar-H)\(\square\) 7.09 (d, \(J = 8.2\) Hz, 2H, Ar-H)\(\square\) 5.60 (br s, 2H, NH_2), 2.69 (d, \(J = 5.5\) Hz, 1H, CH), 1.73 (d, \(J = 5.7\) Hz, 1H, CH), 1.36 (s, 3H, CH_3), 0.92 (s, 3H, CH_3); \(^1^3\)C NMR (CDCl_3) \(\delta\) 172.8, 136.2, 132.1, 130.2, 128.3, 35.3, 33.2, 28.6, 22.1, 20.3; IR (KBr) 3423, 3222, 1625 cm\(^{-1}\); MS (EI) \(m/z\) 225 (M^+ + 2, 2), 223 (M^+, 6%), 208 (7), 182 (7), 181 (33), 180 (20), 179 (100). Anal. Calcd for C\(_{12}\)H\(_{14}\)ClNO: C, 64.43; H, 6.31, N, 6.26. Found: C, 64.06; H, 6.26; N, 5.94.

(+)-(1R, 3R)-2,2-Dimethyl-3-(4-chlorophenyl)cyclopropanecarboxylic acid (3c): mp 128-131°C; \[\alpha\]_D^25 +26 (c 2.0, CHCl_3); ee 56% (HPLC); \(^1\)H NMR (CDCl_3) \(\delta\) 7.26 (d, \(J = 8.0\) Hz, 2H, Ar-H), 7.10 (d, \(J = 8.2\) Hz, 2H, Ar-H), 2.70 (d, \(J = 5.7\) Hz, 1H, CH), 1.93 (d, \(J = 5.9\) Hz, 1H, CH), 1.43 (s, 3H, CH_3), 0.94 (s, 3H, CH_3); \(^1^3\)C NMR (CDCl_3) \(\delta\) 178, 135.3, 132.2, 129.9, 128.2, 37.3, 31.3, 30.3, 21.9, 20.4; IR (KBr) 2250-3380, 1686; MS (EI) \(m/z\) 226 (M^+ + 2, 10), 224 (M^+, 24%), 211 (4), 209 (14), 181 (40), 180 (20), 179 (100). Anal. Calcd for C\(_{12}\)H\(_{13}\)ClO_2: C, 64.15; H, 5.83. Found: C, 64.26; H, 5.79.

trans-2,2-Dimethyl-3-(4-chlorophenyl)cyclopropanecarbonitrile (1c): oil; \[\alpha\]_D^25 0 (c 1.0, CHCl_3); \(^1\)H NMR (CDCl_3) \(\delta\) 7.28 (d, \(J = 8.2\) Hz, 2H, Ar-H)\(\square\) 7.08 (d, \(J = 8.1\) Hz, 2H, Ar-H)\(\square\) 2.47 (d, \(J = 5.5\) Hz, CH), 1.60 (d, \(J = 5.6\) Hz, 1H, CH), 1.48 (s, 3H, CH_3), 0.90 (s, 3H, CH_3); \(^1^3\)C NMR (CDCl_3) \(\delta\) 133.8, 130.0, 129.9, 128.6, 120.0, 36.9, 26.5,
23.6, 20.1; IR (KBr) 2235 cm\(^{-1}\); MS (EI) \(m/z\) 207 (M\(^+\) + 2, 23), 205 (M\(^+\), 71%), 192 (33), 190 (100), 170 (85), 165 (20), 163 (56). HRMS (EI) Calcd for C\(_{12}H_{12}ClN\): 205.0653. Found: 205.0653.

**Enzymatic Hydrolysis of**

\((+/-)-trans-2,2\)-Dimethyl-3-(3-chlorophenyl)cyclopropanecarbonitrile (1d). (-)-(1S, 3S)-2,2-Dimethyl-3-(3-chlorophenyl)cyclopropanecarboxamide (2d): mp 119-121\(^\circ\)C; 
\([\alpha]^{25}_D\) -22 (c 1.0, CHCl\(_3\)); ee >99% (HPLC); 
\(^1\)H NMR (CDCl\(_3\)) \(\delta\) 7.05-7.24 (m, 4H, Ar-H), 5.62 (br s, 2H, NH\(_2\)), 2.70 (d, \(J = 5.4\) Hz, 1H, CH), 1.76 (d, \(J = 5.5\) Hz, 1H, CH), 1.37 (s, 3H, CH\(_3\)), 0.94 (s, 3H, CH\(_3\)); 
\(^{13}\)C NMR (CDCl\(_3\)) \(\delta\) 172.7, 139.9, 134.0, 129.4, 128.8, 127.2, 126.5, 35.6, 33.1, 28.7, 22.1, 20.3; IR (KBr) 3414, 3200, 1650 cm\(^{-1}\); MS (EI) \(m/z\) 225 (M\(^+\) + 2, 3), 223 (M\(^+\), 8%), 182 (12), 181 (31), 180 (33), 179 (100). Anal. Calcd for C\(_{12}H_{14}ClNO\): C, 64.43; H, 6.31, N, 6.26. Found: C, 64.46; H, 6.35; N, 6.04.

\((-)-(1R, 3R)-2,2\)-Dimethyl-3-(3-chlorophenyl)cyclopropanecarboxylic acid (3d): 
mp 130-131\(^\circ\)C; \([\alpha]^{25}_D\) +34 (c 2.0, CHCl\(_3\)); ee 91% (HPLC); 
\(^1\)H NMR (CDCl\(_3\)) \(\delta\) 7.05-7.23 (m, 4H, Ar-H), 2.72 (d, \(J = 5.7\) Hz, 1H, CH), 1.96 (d, \(J = 5.9\) Hz, 1H, CH), 1.43 (s, 3H, CH\(_3\)), 0.96 (s, 3H, CH\(_3\)); 
\(^{13}\)C NMR (CDCl\(_3\)) \(\delta\) 176.6, 137.2, 132.2, 127.6, 127.0, 125.0, 124.9, 35.8, 29.6, 28.7, 20.2, 18.7; IR (KBr) 2250-3350, 1697 cm\(^{-1}\); MS (EI) \(m/z\) 226 (M\(^+\) + 2, 7), 224 (M\(^+\), 21%), 211 (5), 209 (15), 181 (37), 180 (19), 179 (100). Anal. Calcd for C\(_{12}H_{13}ClO_2\): C, 64.15; H, 5.83. Found: C, 64.14; H, 5.80.

\((-)-(1S, 3S)-2,2\)-Dimethyl-3-(3-chlorophenyl)cyclopropanecarbonitrile (1d): oil; 
\([\alpha]^{25}_D\) -62.86 (c 2.1, CHCl\(_3\)); ee 83% (HPLC); 
\(^1\)H NMR (CDCl\(_3\)) \(\delta\) 7.03-7.29 (m, 4H,
Ar-H), 2.50 (d, J = 5.6 Hz, 1H, CH), 1.64 (d, J = 5.7 Hz, 1H, CH), 1.50 (s, 3H, CH₃), 0.93 (s, 3H, CH₃); ¹³C NMR (CDCl₃) δ 137.4, 134.3, 129.8, 128.7, 127.4, 126.8, 119.9, 37.1, 26.6, 23.6, 20.1, 15.2; IR (KBr) 2235 cm⁻¹; MS (EI) m/z 207 (M⁺ + 2, 18), 205 (M⁺, 57%), 192 (19), 190 (51), 170 (100), 165 (16), 163 (35). HRMS (EI) Calcd for C₁₂H₁₂ClN: 205.0653. Found: 205.0655.

Enzymatic Hydrolysis of (+/-)-trans-2,2-Dimethyl-3-(2-chlorophenyl)cyclopropanecarbonitrile (1e). (-)-(1S,3S)-2,2-Dimethyl-3-(2-chlorophenyl)cyclopropanecarboxamide (2e): mp 126-128°C; [α]²⁵_D -8 (c 1.0, CHCl₃); ee 15% (HPLC); ¹H NMR (CDCl₃) δ 7.09-7.38 (m, 4H, Ar-H), 5.64 (br s, 2H, NH₂), 2.72 (d, J = 5.9 Hz, 1H, CH), 1.76 (d, J = 5.8 Hz, 1H, CH), 1.43 (s, 3H, CH₃), 0.89 (s, 3H, CH₃); ¹³C NMR (CDCl₃) δ 171.0, 134.4, 134.2, 127.7, 127.3, 125.9, 124.5, 33.3, 30.8, 26.8, 19.8, 17.9; IR (KBr) 3407, 3201, 1652 cm⁻¹; MS (EI) m/z 223 (M⁺, 3%), 208 (4), 188 (52), 181 (37), 179 (100). Anal. Calcd for C₁₂H₁₄ClNO: C, 64.43; H, 6.31, N, 6.26. Found: C, 64.50; H, 6.30; N, 6.47.

(+)-(1R,3R)-2,2-Dimethyl-3-(2-chlorophenyl)cyclopropanecarboxylic acid (3e): mp 121-123°C; [α]²⁵_D +20 (c 1.0, CHCl₃); ee >99% (HPLC); ¹H NMR (CDCl₃) δ 7.15-7.41 (m, 4H, Ar-H), 2.77 (d, J = 6.0 Hz, 1H, CH), 1.99 (d, J = 6.1 Hz, 1H, CH), 1.52 (s, 3H, CH₃), 0.93 (s, 3H, CH₃); ¹³C NMR (CDCl₃) δ 178.1, 135.8, 135.3, 129.5, 129.0, 127.8, 126.4, 37.2, 30.8, 30.6, 21.5, 19.8; IR (KBr) 2250-3350, 1691 cm⁻¹; MS (EI) m/z 226 (M⁺ + 2, 7), 224 (M⁺, 22%), 209 (8), 190 (13), 189 (87), 181 (42), 179 (100). Anal. Calcd for C₁₂H₁₃ClO₂: C, 64.15; H, 5.83. Found: C, 64.24; H, 5.81.
trans-2,2-Dimethyl-3-(2-chlorophenyl)cyclopropanecarbonitrile (1e): mp 62-63°C; 
\([\alpha]^{25}_D \) 0 (c 1.0, CHCl₃); \(^1\)H NMR (CDCl₃) \(\delta\) 7.09-7.42 (m, 4H, Ar-H), 2.52 (d, \(J = 5.8\) Hz, 1H, CH), 1.65 (d, \(J = 5.8\) Hz, 1H, CH), 1.56 (s, 3H, CH₃), 0.88 (s, 3H, CH₃); \(^{13}\)C NMR (CDCl₃) \(\delta\) 135.8, 133.9, 129.5, 128.7, 126.9, 120.0, 36.9, 26.9, 23.1, 19.7, 15.0; IR (KBr) 2235 cm\(^{-1}\); MS (EI) \(m/z\) 207 (M⁺ + 2, 20), 205 (M⁺, 59%), 192 (18), 190 (58), 170 (100). Anal. Calcd for C₁₂H₁₂ClN: C, 70.07; H, 5.88; N, 6.81. Found: C, 70.22; H, 5.90, N, 6.67.

Enzymatic Hydrolysis of (+/-)-trans-2,2-Dimethyl-3-(4-methoxylphenyl)cyclopropanecarbonitrile (1f).

(-)-(1S, 3S)-2,2-Dimethyl-3-(4-methoxylphenyl)cyclopropanecarboxamide (2f): mp 204-205°C; \([\alpha]^{25}_D \) -17 (c 1.0, CHCl₃); ee >99% (HPLC); \(^1\)H NMR (CDCl₃) \(\delta\) 7.08 (d, \(J = 8.3\) Hz, 2H, Ar-H), 6.82 (d, \(J = 8.3\) Hz, 2H, Ar-H), 5.70 (br s, 2H, NH₂), 3.79 (s, 3H, CH₃O), 2.67 (d, \(J = 5.5\) Hz, 1H, CH), 1.70 (d, \(J = 5.7\) Hz, 1H, CH), 1.36 (s, 3H, CH₃), 0.93 (s, 3H, CH₃); \(^{13}\)C NMR (CDCl₃) \(\delta\) 174.8, 157.9, 134.6, 129.5, 129.1, 113.4 55.0, 35.8, 32.6, 29.3, 21.9, 20.3; IR (KBr) 3420, 3221, 1623 cm\(^{-1}\); MS (EI) \(m/z\) 219 (M⁺, 11%), 176 (17), 175 (100). Anal. Calcd for C₁₃H₁₇NO₂: C, 71.21; H, 7.81, N, 6.39. Found: C, 71.13; H, 7.90; N, 6.40.

(+)-(1R, 3R)-2,2-Dimethyl-3-(4-methoxylphenyl)cyclopropanecarboxylic acid (3f): mp 111-113°C; \([\alpha]^{25}_D \) +40.5 (c 2.0, CHCl₃); ee 96% (HPLC); \(^1\)H NMR (CDCl₃) \(\delta\) 7.09 (d, \(J = 8.5\) Hz, 2H, Ar-H), 6.83 (d, \(J = 8.4\) Hz, 2H, Ar-H), 3.79 (s, 3H, CH₃O), 2.69 (d, \(J = 5.7\) Hz, 1H, CH), 1.90 (d, \(J = 5.7\) Hz, 1H, CH), 1.42 (s, 3H, CH₃), 0.95 (s, 3H, CH₃); \(^{13}\)C NMR (CDCl₃) \(\delta\) 178.7, 158.0, 129.5, 128.9, 113.4, 55.0, 37.5, 31.4,
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30.3, 21.9, 20.4; IR (KBr) 2240-3350, 1681 cm\(^{-1}\); MS (EI) \(m/z\) 220 (M\(^+\), 26%), 205 (25), 176 (16), 175 (100). Anal. Calcd for C\(_{13}\)H\(_{16}\)O\(_3\): C, 70.89; H, 7.23. Found: C, 71.03; H, 7.53.

\((-\)-(1\(S\), 3\(S\))-2,2-Dimethyl-3-(4-methoylphenyl)cyclopropanecarbonitrile (1\(f\)): oil; 
[\(\alpha\)]\(^{25}\)\(_D\) -13.3 (c 1.5, CHCl\(_3\)); ee 10\% (HPLC); \(^1\)H NMR (CDCl\(_3\)) \(\delta\) 7.06 (d, \(J = 8.5\) Hz, 2H, Ar-H)/6.85 (d, \(J = 8.6\) Hz, 2H, Ar-H)/3.80 (s, 3H, CH\(_3\)O), 2.47 (d, \(J = 5.6\) Hz, 1H, CH), 1.56 (d, \(J = 5.5\) Hz, 1H, CH), 1.47 (s, 3H, CH\(_3\)), 0.91 (s, 3H, CH\(_3\)); \(^13\)C NMR (CDCl\(_3\)) \(\delta\) 158.7, 129.6, 127.3, 120.5, 113.9, 55.2, 37.1, 26.3, 23.7, 20.1, 15.2; 
IR (KBr) 2233 cm\(^{-1}\); MS (EI) \(m/z\) 201 (M\(^+\), 51%), 186 (100). HRMS (EI) Calcd for C\(_{13}\)H\(_{15}\)NO: 201.1148. Found: 201.1148.

Enzymatic Hydrolysis of (+/-)-\textit{trans}-2,2-Dimethyl-3-(4-methylphenyl)cyclopropanecarbonitrile (1\(g\)).

\((-\)-(1\(S\), 3\(S\))-2,2-Dimethyl-3-(4-methylphenyl)cyclopropanecarboxamide (2\(g\)): mp 154-156\(^\circ\)C; [\(\alpha\)]\(^{25}\)\(_D\) -21 (c 1.0, CHCl\(_3\)); ee >99\% (HPLC); \(^1\)H NMR (CDCl\(_3\)) \(\delta\) 7.02 (d, \(J = 8.16\) Hz, 2H, Ar-H)/6.98 (d, \(J = 8.16\) Hz, 2H, Ar-H)/5.5 (br s, 2H, NH\(_2\)), 2.62 (d, \(J = 3.8\) Hz, 1H, CH), 2.25 (s, 3H, CH\(_3\)), 1.67 (d, \(J = 4.7\) Hz, 1H, CH), 1.30 (s, 3H, CH\(_3\)), 0.86 (s, 3H, CH\(_3\)); \(^13\)C NMR (CDCl\(_3\)) \(\delta\) 173.5, 135.8, 134.6, 128.8, 128.7, 35.8, 33.1, 28.6, 22.2, 21.0, 20.5; IR (KBr) 3426, 3221, 1624 cm\(^{-1}\); MS (EI) \(m/z\) 203 (M\(^+\), 6\%), 188 (7), 160 (18), 159 (100). Anal. Calcd for C\(_{13}\)H\(_{17}\)NO: C, 76.81; H, 8.43, N, 6.89. Found: C, 76.79; H, 8.48; N, 6.85.

\((+\)-(1\(R\), 3\(R\))-2,2-Dimethyl-3-(4-methylphenyl)cyclopropanecarboxylic acid (3\(g\)): 
mp 69-71\(^\circ\)C; [\(\alpha\)]\(^{25}\)\(_D\) +48.67 (c 3.0, CHCl\(_3\)); ee 96\% (HPLC); \(^1\)H NMR (CDCl\(_3\)) \(\delta\)
7.13 (d, \( J = 8.1 \) Hz, 2H, Ar-H), 7.08 (d, \( J = 8.1 \) Hz, 2H, Ar-H), 2.74 (d, \( J = 5.8 \) Hz, 1H, CH), 2.35 (s, 3H, CH3), 1.96 (d, \( J = 5.8 \) Hz, 1H, CH), 1.45 (s, 3H, CH3), 0.97 (s, 3H, CH3); \(^{13}\)C NMR (CDCl\(_3\)) \( \delta \) 178.4, 135.8, 133.7, 128.7, 128.4, 37.8, 31.2, 30.3, 21.9, 20.8, 20.4; IR (KBr) 2150-3300, 1689 cm\(^{-1}\); MS (EI) \( m/z \) 204 (M\(^{+}\), 25%), 189 (23), 160 (16), 159 (100). Anal. Calcd for C\(_{13}\)H\(_{16}\)O\(_2\): C, 76.44; H, 7.90. Found: C, 76.38; H, 7.98.

(−)-(1S, 3S)-2,2-Dimethyl-3-(4-methylphenyl)cyclopropanecarbonitrile (1g): oil; \([\alpha]_{25}^{25}\) -75 (c 2.5, CHCl\(_3\)); ee 81% (HPLC); \(^1\)H NMR (CDCl\(_3\)) \( \delta \) 7.10 (d, \( J = 7.9 \) Hz, 2H, Ar-H) \( \cap \) 7.01 (d, \( J = 7.9 \) Hz, 2H, Ar-H) \( \cap \) 2.46 (d, \( J = 5.6 \) Hz, 1H, CH), 2.31 (s, 3H, CH3), 1.58 (d, \( J = 5.6 \) Hz, 1H, CH), 1.46 (s, 3H, CH3), 0.89 (s, 3H, CH3); \(^{13}\)C NMR (CDCl\(_3\)) \( \delta \) 136.6, 132.0, 129.0, 128.2, 120.3, 37.2, 26.2, 23.5, 20.8, 19.9, 14.8; IR (KBr) 2233 cm\(^{-1}\); MS (EI) \( m/z \) 185 (M\(^{+}\), 55%), 170 (100). HRMS (EI) Calcd for C\(_{13}\)H\(_{15}\)N: 185.1198. Found: 185.1199.

**Enzymatic Hydrolysis of (+/-)-trans-2,2-Dimethyl-3-(2-methylphenyl)cyclopropanecarbonitrile (1h).**

(−)-(1S, 3S)-2,2-Dimethyl-3-(2-methylphenyl)cyclopropanecarboxamide (2h): mp 128-129°C; \([\alpha]_{25}^{25}\) -10 (c 0.5, CHCl\(_3\)); ee 51% (HPLC); \(^1\)H NMR (CDCl\(_3\)) \( \delta \) 7.01-7.18 (m, 4H, Ar-H) \( \cap \) 5.75 (br s, 2H, NH\(_2\)), 2.61 (d, \( J = 5.7 \) Hz, 1H, CH), 2.31 (s, 3H, CH3), 1.78 (d, \( J = 5.9 \) Hz, 1H, CH), 1.43 (s, 3H, CH3), 0.85 (s, 3H, CH3); \(^{13}\)C NMR (CDCl\(_3\)) \( \delta \) 173.5, 138.5, 136.4, 129.7, 127.8, 126.5, 125.5, 35.5, 32.4, 28.3, 21.8, 20.1, 19.8; IR (KBr) 3434, 3196 (NH\(_2\)), 1649 cm\(^{-1}\); MS (EI) \( m/z \) 203 (M\(^{+}\), 11%), 160 (21), 159 (100).
Anal. Calcd for C$_{13}$H$_{17}$NO: C, 76.81; H, 8.43, N, 6.89. Found: C, 76.98; H, 8.60; N, 6.67.

(+)-(1R, 3R)-2,2-Dimethyl-3-(2-methylphenyl)cyclopropanecarboxylic acid (3h): mp 129-131°C; $[\alpha]^{25}_D +31.4$ (c 0.7, CHCl$_3$); ee >99% (HPLC); $^1$H NMR (CDCl$_3$) $\delta$ 7.08-7.17 (m, 4H, Ar-H), 2.66 (d, $J$ = 5.9 Hz, 1H, CH), 2.33 (s, 3H, CH$_3$), 2.01 (d, $J$ = 5.8 Hz, 1H, CH), 1.52 (s, 3H, CH$_3$), 0.91 (s, 3H, CH$_3$); $^{13}$C NMR (CDCl$_3$) $\delta$ 178.3, 137.9, 135.5, 129.5, 127.7, 126.5, 125.5, 37.6, 30.6, 30.2, 21.5, 20.1, 19.5; IR (KBr) 2250-3300, 1695 cm$^{-1}$; MS (EI) $m/z$ 204 (M$^+$, 21%), 189 (44), 160 (15), 159 (100).

(-)-(1S, 3S)-2,2-Dimethyl-3-(2-methylphenyl)cyclopropanecarbonitrile (1h): mp 64-65°C; $[\alpha]^{25}_D$ -2.0 (c 3.0, CHCl$_3$); ee 17% (HPLC); $^1$H NMR (CDCl$_3$) $\delta$ 7.01-7.21 (m, 4H, Ar-H), 2.42 (d, $J$ = 5.7 Hz, 1H, CH), 2.31 (s, 3H, CH$_3$), 1.68 (d, $J$ = 5.8 Hz, 1H, CH), 1.56 (s, 3H, CH$_3$), 0.86 (s, 3H, CH$_3$); $^{13}$C NMR (CDCl$_3$) $\delta$ 138.0, 134.0, 130.0, 127.7, 127.4, 126.0, 120.4, 37.3, 26.4, 23.4, 19.7, 14.6; IR (KBr) 2233 cm$^{-1}$; MS (EI) $m/z$ 185 (M$^+$, 54%), 170 (100). Anal. Calcd for C$_{13}$H$_{16}$O$_2$: C, 76.44; H, 7.90. Found: C, 76.08; H, 7.62.

Enzymatic Hydrolysis of (+/-)-trans-2,2-dimethyl-3-(2',2'-dimethylvinyl)cyclopropanecarbonitrile (5a).

(-)-trans-(1S, 3S)-2,2-Dimethyl-3-(2',2'-dimethylvinyl)cyclopropanecarboxamide (6a) mp 115-116°C; $[\alpha]^{25}_D$ -21 (c 1.0, CHCl$_3$) [lit.$^2$ $[\alpha]_D$ -11.09 (c 0.361, alcohol)]; ee >99% (HPLC); $^1$H NMR (CDCl$_3$) $\delta$ 5.57 (br s, 2H, NH$_2$), 4.92 (d, $J$ = 7.6 Hz, 1H, vinyl-H), 2.10 (m, 1H, CH), 1.74 (s, 6H, 2CH$_3$), 1.29 (s, 3H, CH$_3$), 1.21 (d, $J$ = 5.3 Hz, 1H, vinyl-H), 1.10 (m, 1H, CH).
Hz, 1H, CH), 1.16 (s, 3H, CH₃); ¹³C NMR (CDCl₃) δ 173.8, 135.3, 121.3, 36.2, 31.1, 27.8, 25.5, 22.3, 20.1, 18.5; IR (KBr) 3393, 3188, 1647 cm⁻¹; MS (EI) m/z 167 (M⁺, 9%), 152 (10), 124 (16), 123 (100). Anal. Calcd for C₁₀H₁₇NO: C, 71.81; H, 10.25; N, 8.37. Found: C, 71.63; H, 10.46; N, 8.22.

(+)-trans-(1R, 3R)-2,2-Dimethyl-3-(2',2'-dimethylvinyl)cyclopropanecarboxylic acid (7a): oil; [α]²⁵ D +20.6 (c 1.65, CHCl₃) [lit.³ [α]²⁰ D +26.5 (c 1, CHCl₃)]; ee >99% (HPLC); ¹H NMR (CDCl₃) δ 11.30 (br s, 1H, COOH), 4.91 (d, J = 7.7 Hz, 1H, vinyl-H), 2.11 (dd, J = 6.1, 6.9 Hz, 1H, CH), 1.73 (s, 3H, CH₃), 1.72 (s, 3H, CH₃), 1.40 (d, J = 5.3 Hz, 1H, CH), 1.32 (s, 3H, CH₃), 1.17 (s, 3H, CH₃); ¹³C NMR (CDCl₃) δ 179.3, 135.8, 120.7, 34.6, 33.6, 29.8, 25.5, 22.2, 20.4, 18.5; IR (KBr) 2500-3500, 1692 cm⁻¹; MS (EI) m/z 168 (M⁺, 28%), 153 (25), 125 (18), 124 (11), 123 (100).

Enzymatic Hydrolysis of (+/-)-trans-2,2-Dimethyl-3-(2',2'-dichlorovinyl)cyclopropanecarbonitrile (6b).

(-)-trans-(1S, 3R)-2,2-Dimethyl-3-(2',2'-dichlorovinyl)cyclopropanecarboxamide (6b): mp 110-112°C; [α]²⁵ D -16 (c 1.0, CHCl₃); ee >99% (HPLC); ¹H NMR (CDCl₃) δ 6.12 (br s, 2H, NH₂), 5.64 (d, J = 8.4 Hz, 1H, vinyl-H), 2.27 (dd, J = 8.4, 5.2 Hz, 1H, CH), 1.49 (d, J = 5.2 Hz, 1H, CH), 1.30 (s, 3H, CH₃), 1.21 (s, 3H, CH₃); ¹³C NMR (CDCl₃) δ 172.7, 127.0, 121.9, 35.9, 31.6, 28.5, 22.7, 19.8; IR (KBr) 3442, 3326, 1654, 1608 cm⁻¹; MS (EI) m/z 209 (M⁺ + 2, 8), 207 (M⁺, 13%), 201 (3), 192 (5), 167 (14), 166 (31), 165 (69), 164 (41), 163 (100). Anal. Calcd for C₈H₁₇Cl₂NO: C, 46.18; H, 5.33; N, 6.73. Found: C, 46.34; H, 5.35; N, 6.66.
(+)-trans-(1R, 3S)-2,2-Dimethyl-3-(2',2'-dichlorovinyl)cyclopropanecarboxylic acid (7b): mp 70-72°C; $[\alpha]_{D}^{25} +25$ (c 0.8, CHCl$_3$); ee >99% (HPLC analysis of the corresponding amide); $^1$H NMR (CDCl$_3$) $\delta$ 7.23 (br s, 1H, COOH), 5.63 (d, $J$ = 8.2 Hz, 1H, vinyl-H), 2.28 (dd, $J$ = 8.2, 5.3 Hz, 1H, CH), 1.63 (d, $J$ = 5.3 Hz, 1H, CH), 1.34 (s, 3H, CH$_3$), 1.22 (s, 3H, CH$_3$); $^{13}$C NMR (CDCl$_3$) $\delta$ 177.6, 126.5, 122.5, 34.5, 33.6, 30.0, 22.7, 20.1; IR (KBr) 2570-3045, 1687 cm$^{-1}$; MS (EI) $m/z$ 210 (M$^+$ + 2, 5), 208 (M$^+$, 8%), 175 (34), 173 (100). Anal. Calcd for C$_8$H$_{10}$Cl$_2$O$_2$: C, 45.96; H, 4.82. Found: C, 45.86; H, 4.86.

Enzymatic Hydrolysis of (+/-)-cis-2,2-Dimethyl-3-(2',2'-dimethylvinyl)cyclopropanecarbonitrile (8a).

(-)-cis-(1S, 3R)-2,2-Dimethyl-3-(2',2'-dimethylvinyl)cyclopropanecarboxamide (9a): mp 60-62°C; $[\alpha]_{D}^{25} -70$ (c 1.0, CHCl$_3$); ee >99% (HPLC); $^1$H NMR (CDCl$_3$) $\delta$ 5.60 (br s, 2H, NH$_2$), 5.36 (d, $J$ = 8.0 Hz, 1H, vinyl-H), 1.77 (s, 3H, CH$_3$), 1.75 (dd, $J$ = 8.0, 8.7 Hz, 1H, CH), 1.72 (s, 6H, 2CH$_3$), 1.48 (d, $J$ = 8.7 Hz, 1H, CH), 1.23 (s, 3H, CH$_3$), 1.20 (s, 3H, CH$_3$); $^{13}$C NMR (CDCl$_3$) $\delta$ 174.4, 136.6, 119.4, 36.6, 31.4, 29.8, 26.8, 25.6, 19.3, 16.1; IR (KBr) 3451, 3397, 1658, 1615 cm$^{-1}$; MS (EI) $m/z$ 167 (M$^+$, 11%), 152 (10), 149 (14), 134 (930), 124 (14), 123 (100). Anal. Calcd for C$_{10}$H$_{17}$NO: C, 71.81; H, 10.25; N, 8.37. Found: C, 71.76; H, 10.15; N, 8.26.

(+)-cis-(1R, 3S)-2,2-Dimethyl-3-(2',2'-dimethylvinyl)cyclopropanecarboxylic acid (10a): mp 48-50°C [lit.$^4$ mp 50-51°C]; $[\alpha]_{D}^{25} +82.14$ (c 1.4, CHCl$_3$) [lit.$^4$ $[\alpha]_{D}^{24} +83.0$ (c 1.75, CHCl$_3$)]; ee >99% (HPLC analysis of the corresponding amide); $^1$H NMR (CDCl$_3$) $\delta$ 5.36 (d, $J$ = 8.6 Hz, 1H, vinyl-H), 1.96 (dd, $J$ = 8.6, 8.7 Hz, 1H, CH), 1.75
(s, 3H, CH₃), 1.70 (s, 3H, CH₃), 1.65 (d, J = 8.7 Hz, 1H, CH), 1.25 (s, 3H, CH₃), 1.21 (s, 3H, CH₃); ¹³C NMR (CDCl₃) δ 177.5, 134.8, 117.7, 33.0, 30.9, 28.7, 27.3, 25.7, 18.1, 14.5; IR (KBr) 2560-3500, 1696 cm⁻¹; MS (EI) m/z 168 (M⁺, 38%), 153 (28), 135 (5), 125 (16), 124 (12), 123 (100).

Enzymatic Hydrolysis of
(+/-)-cis-2,2-dimethyl-3-(2',2'-dichlorovinyl)cyclopropanecarbonitrile (8b).

(+)-cis-(1S, 3S)-2,2-Dimethyl-3-(2',2'-dichlorovinyl)cyclopropanecarboxamide (9b):
mp 75-76°C; [α]²⁵D +16 (c 1.0, CHCl₃); ee >99% (HPLC); ¹H NMR (CDCl₃) δ 6.36 (d, J = 9.1 Hz, 1H, vinyl-H), 5.94 (br s, 2H, NH₂), 1.98 (dd, J = 9.1, 8.4 Hz, 1H, CH), 1.63 (d, J = 8.4 Hz, 1H, CH), 1.28 (s, 3H, CH₃), 1.23 (s, 3H, CH₃); ¹³C NMR (CDCl₃) δ 173.2, 125.7, 120.4, 33.2, 32.7, 29.0, 27.4, 15.3; IR (KBr) 3489, 3333, 1680, 1658 cm⁻¹; MS (EI) m/z 209 (M⁺ + 2, 5), 207 (M⁺, 8%), 174 (10), 172 (24), 167 (11), 166 (31), 165 (65), 164 (40), 163 (94), 131 (28), 129 (100). Anal. Calcd for C₈H₁₁Cl₂NO: C, 46.18; H, 5.33; N, 6.73. Found: C, 46.44; H, 5.41; N, 6.67.

(+)-cis-(1R, 3R)-2,2-Dimethyl-3-(2',2'-dichlorovinyl)cyclopropanecarboxylic acid (10b): mp 82-84°C [lit.⁵ mp 90-91°C, ee 98%]; [α]²⁵D +26 (c 1.0, CHCl₃) [lit.⁵ [α]D +28.9 (c 1, CHCl₃); ee 98%]; ee >99% (HPLC analysis of the corresponding amide);
¹H NMR (CDCl₃) δ 9.25 (br s, 1H, COOH), 6.25 (d, J = 8.9 Hz, 1H, vinyl-H), 2.15 (t, J = 8.6 Hz, 1H, CH), 1.89 (d, J = 8.4 Hz, 1H, CH), 1.32 (s, 3H, CH₃), 1.31 (s, 3H, CH₃); ¹³C NMR (CDCl₃) δ 177.0, 124.4, 121.1, 33.4, 31.6, 28.5, 14.9; IR (KBr) 2560-3080, 1688 cm⁻¹; MS (EI) m/z 210 (M⁺ + 2, 5), 208 (M⁺, 7%), 175 (34), 173
(100), 165 (38), 163 (58). Anal. Calcd for C₉H₁₀Cl₂O₂: C, 45.96; H, 4.82. Found: C, 46.08; H, 4.94.

2. Biocatalytic Kinetic Resolution of (+/-)-Amides 2 and 6 and 9

Enzymatic Hydrolysis of (+/-)-trans-2,2-Dimethyl-3-phenylcyclopropanecarboxamide (2a). (-)-(1S, 3S)-2,2-Dimethyl-3-phenylcyclopropanecarboxamide (2a): 73h (46%); [α]ᵢ₂⁵ 20 (c 1.0, CHCl₃); ee >99% (HPLC).

(+)-(1R, 3R)-2,2-Dimethyl-3-phenylcyclopropanecarboxylic acid (3a): 73h (52%); [α]ᵢ₂⁵ +49.6 (c 2.5, CHCl₃) [lit.¹ [α]ᵢ₂⁰ +31.9 (c 4.93, ethanol)]; ee 92% (HPLC).

Enzymatic Hydrolysis of (+/-)-trans-2,2-Dimethyl-3-(4-fluorophenyl)cyclopropanecarboxamide (2b). (-)-(1S, 3S)-2,2-Dimethyl-3-(4-fluorophenyl)cyclopropanecarboxamide (2b): 52h (40%); [α]ᵢ₂⁵ -10 (c 1.0, CHCl₃); ee >99% (HPLC).

(+)-(1R, 3R)-2,2-Dimethyl-3-(4-fluorophenyl)cyclopropanecarboxylic acid (3a): 52h (57%); [α]ᵢ₂⁵ +24.4 (c 0.5, CHCl₃); ee 67% (HPLC).

Enzymatic Hydrolysis of (+/-)-trans-2,2-Dimethyl-3-(4-chlorophenyl)cyclopropanecarboxamide (2c). (-)-(1S, 3S)-2,2-Dimethyl-3-(4-chlorophenyl)cyclopropanecarboxamide (2c): 48h (30%); [α]ᵢ₂⁵ -15 (c 0.8, CHCl₃); ee 67% (HPLC).

(+)-(1R, 3R)-2,2-Dimethyl-3-(4-chlorophenyl)cyclopropanecarboxylic acid (3c): 48h (65%); [α]ᵢ₂⁵ +18.67 (c 1.5, CHCl₃); ee 31% (HPLC).
Enzymatic Hydrolysis of (+/-)-trans-2,2-Dimethyl-3-(3-chlorophenyl)cyclopropanecarboxamide (2d).

(-)-(1S, 3S)-2,2-Dimethyl-3-(3-chlorophenyl)cyclopropanecarboxamide (2d): 84h (44%); \([\alpha]_{D}^{25} -54 \ (c \ 1.0, \ CHCl_3)\); ee 91% (HPLC).

(+)-(1R, 3R)-2,2-Dimethyl-3-(3-chlorophenyl)cyclopropanecarboxylic acid (3d):
84h (49%); \([\alpha]_{D}^{25} +37.3 \ (c \ 1.5, \ CHCl_3)\); ee 74% (HPLC).

Enzymatic Hydrolysis of (+/-)-trans-2,2-Dimethyl-3-(2-chlorophenyl)cyclopropanecarboxamide (2e).

(-)-(1S, 3S)-2,2-Dimethyl-3-(2-chlorophenyl)cyclopropanecarboxamide (2e): 6d (85%); \([\alpha]_{D}^{25} -3.4 \ (c \ 1.75, \ CHCl_3)\); ee <5% (HPLC).

(+)-(1R, 3R)-2,2-Dimethyl-3-(2-chlorophenyl)cyclopropanecarboxylic acid (3e): 6d (13%); \([\alpha]_{D}^{25} +25.3 \ (c \ 0.75, \ CHCl_3)\); ee 80% (HPLC).

Enzymatic Hydrolysis of (+/-)-trans-2,2-Dimethyl-3-(4-methoxylphenyl)cyclopropanecarboxamide (2f).

(-)-(1S, 3S)-2,2-Dimethyl-3-(4-methoxylphenyl)cyclopropanecarboxamide (2f): 25h (45%); \([\alpha]_{D}^{25} -18 \ (c \ 1.0, \ CHCl_3)\); ee >99% (HPLC).

(+)-(1R, 3R)-2,2-Dimethyl-3-(4-methoxylphenyl)cyclopropanecarboxylic acid (3f):
25 (52%); \([\alpha]_{D}^{25} +32 \ (c \ 2.0, \ CHCl_3)\); ee 88% (HPLC).

Enzymatic Hydrolysis of (+/-)-trans-2,2-Dimethyl-3-(4-methylphenyl)cyclopropanecarboxamide (2g).

(-)-(1S, 3S)-2,2-Dimethyl-3-(4-methylphenyl)cyclopropanecarboxamide (2g): 44h (49%); \([\alpha]_{D}^{25} -18 \ (c \ 1.0, \ CHCl_3)\); ee 80% (HPLC).
(+)-(1R, 3R)-2,2-Dimethyl-3-(4-methylphenyl)cyclopropanecarboxylic acid (3g):
44h (47%); [α]D25 +30 (c 1.0, CHCl3); ee 57% (HPLC).

Enzymatic Hydrolysis of
(+/-)-trans-2,2-Dimethyl-3-(2-methylphenyl)cyclopropanecarboxamide (2h).

(-)-(1S, 2S)-2,2-Dimethyl-3-(2-methylphenyl)cyclopropanecarboxamide (2h): 7d (70%); [α]D25 -12 (c 1.0, CHCl3); ee 39% (HPLC).

(+)-(1R, 3R)-2,2-Dimethyl-3-(2-methylphenyl)cyclopropanecarboxylic acid (3h):
7d (26%); [α]D25 +28 (c 1.0, CHCl3); ee 95% (HPLC).

Enzymatic Hydrolysis of
(+/-)-trans-2,2-Dimethyl-3-(2',2'-dimethylvinyl)cyclopropanecarboxamide (6a).

(-)-(1S, 3S)-2,2-Dimethyl-3-(2',2'-dimethylvinyl)cyclopropanecarboxamide (6a): 73h (48%); [α]D25 -22 (c 1.0, CHCl3) [lit.2 [α]D -11.09 (c 0.361, alcohol)]; ee >99% (HPLC).

(+)-(1R, 3R)-2,2-Dimethyl-3-(2',2'-dimethylvinyl)cyclopropanecarboxylic acid (7a): 73h (51%); [α]D25 +16.5 (c 2.0, CHCl3) [lit.3 [α]D 20 +26.5 (c 1, CHCl3)]; ee 97% (HPLC).

Enzymatic Hydrolysis of
(+/-)-cis-2,2-dimethyl-3-(2',2'-dimethylvinyl)cyclopropanecarboxamide (9a).

(-)-(1S, 3R)-2,2-Dimethyl-3-(2',2'-dimethylvinyl)cyclopropanecarboxamide (9a): 66h (48%); [α]D25 = -70 (c 1.0, CHCl3); ee >99% (HPLC).
(+)-(1R, 3S)-2,2-Dimethyl-3-(2',2'-dimethylvinyl)cyclopropane carboxylic acid (10a): 66h (49%); [α]D 25 +69 (c 2.0, CHCl3) [lit.4 [α]D 24 +83.0 (c 1.75, CHCl3)]; ee 97% (HPLC).

Enzymatic Hydrolysis of (+/-)-trans-2,2-dimethyl-3-(2',2'-dichlorovinyl)cyclopropanecarboxamide (6b).

(-)-(1S, 3R)-2,2-Dimethyl-3-(2',2'-dichlorovinyl)cyclopropanecarboxamide (6b): 48h (47%); [α]D 25 -16 (c 1.0, CHCl3); ee >99% (HPLC).

(+)-(1R, 3S)-2,2-Dimethyl-3-(2',2'-dichlorovinyl)cyclopropanecarboxylic acid (7b): 48h (48%); [α]D 25 +25 (c 0.8, CHCl3); ee 89% (HPLC).

Enzymatic Hydrolysis of (+/-)-cis-2,2-dimethyl-3-(2',2'-dichlorovinyl)cyclopropanecarboxamide (9b).

(+)-(1S, 3S)-2,2-Dimethyl-3-(2',2'-dichlorovinyl)cyclopropanecarboxamide (9b): 48h (48%); [α]D 25 +16 (c 1.0, CHCl3); ee >99% (HPLC).

(+)-(1R, 3R)-2,2-Dimethyl-3-(2',2'-dichlorovinyl)cyclopropanecarboxylic acid (10b): 48h (47%); [α]D 25 +17.33 (c 0.75, CHCl3) [lit.5 [α]D +28.9 (c 1, CHCl3); ee 98%], ee 95% (HPLC).

3. Chemical Transformations of Optically Active Amides and Acids, and Determination of the Configurations of Biotransformation Products.

Preparation of Methyl (+)-trans-(1R, 3R)-2,2-Dimethyl-3-phenylcyclopropanecarboxylate.

To (+)-trans-2,2-dimethyl-3-phenylcyclopropanecarboxylic acid 3a [24 mg, 0.13 mmol, ee >99%
(HPLC)] was added an excess amount of CH₂N₂ ethereal solution. After keeping stirring for 0.5h, the solvent was removed under reduced pressure to afford pure methyl (+)-trans-(1R, 3R)-2,2-dimethyl-3-phenylcyclopropanecarboxylate: 100% yield; oil; [α]_D^{25} + 41.6 (c 1.25, CHCl₃) [lit. [α]_D^{22} − 36.0 (c 0.72, CHCl₃) for (-)-(1S, 3S)-enantiomer]; ee >99% (HPLC); ¹H NMR (300Hz, CDCl₃) δ 7.16-7.30 (m, 5H, Ar-H)/3.74 (s, 3H, CH₃), 2.72 (d, J = 5.9 Hz, 1H, CH), 1.98 (d, J = 5.7 Hz, 1H, CH), 1.40 (s, 3H, CH₃), 0.94 (s, 3H, CH₃); IR (KBr) 1729 cm⁻¹; MS (EI) m/z 204 (M⁺, 8%), 189 (4), 173 (6), 146 (12), 145 (100). HPLC: chiralcel OJ, Hexane : Isopropanol 9 : 1, 0.8 ml/min, (+) (1R, 3R) 6.117 min, (-) (1S, 3S) 7.528 min.

Preparation of (+)-trans-(1R, 3R)-2,2-Dimethyl-3-phenylcyclopropanecarboxamide (2a). A mixture of (+)-acid 3a (0.1 mmol, ee>99%) and freshly distilled SOCl₂ was stirred for 2h at room temperature. Then the excess amount of SOCl₂ was removed under reduced pressure. To the resulting solution was added 4 ml of cold ammonia while stirring at 0°C. After workup and purification as for (-)-amide-2a, (+)-trans-(1R, 3R)-2,2-dimethyl-3-phenylcyclopropanecarboxamide 2a was obtained in 86% yield. [α]_D^{25} + 18.75 (c 0.8, CHCl₃); ee >99% (HPLC). Identical spectra as for (-)-amide-2a were obtained.

Preparation of (-)-trans-(1S, 3S)-2,2-Dimethyl-3-phenylcyclopropanecarbonitrile (1a). Dehydration of (-)-amide 2a (ee>99%) to (-)-trans-(1S, 3S)-2,2-dimethyl-3-phenylcyclopropanecarbonitrile 1a was accomplished in 93% yield by the reaction with SOCl₂ in benzene and DMF at
room temperature. (-)-1a: [α]$_{D}^{25}$ –108.57 (c 1.05, CHCl$_3$); ee >99% (HPLC). Identical spectra as for (-)-1a obtained directly from biotransformation were obtained.

**Chemical Hydrolysis of (-)-trans-(1S, 3S)-2,2-Dimethyl-3-phenylcyclopropanecarboxamide (2a):**

(-)-trans-2,2-Dimethyl-3-phenylcyclopropanecarboxamide 2a (0.11 mmol, ee>99%) was refluxed in a mixture of methanol (1 ml) and KOH (10%, 2 ml) for 24h to give, after the workup, (-)-trans-(1S, 3S)-2,2-dimethyl-3-phenylcyclopropanecarboxylic 3a in 86% yield. [α]$_{D}^{25}$ –37 (c 0.75, CHCl$_3$); ee >99% (HPLC). Identical spectra as for (+)-3a were obtained.

**Preparation of (+)-trans-(1R, 3R)-2,2-Dimethyl-3-(2',2'-dimethylvinyl)cyclopropanecarboxamide (6a).** (+)-trans-(1R, 3R)-2,2-Dimethyl-3-(2',2'-dimethylvinyl)cyclopropanecarboxamide 6a was prepared from (+)-chrysanthemic acid 7a in 89% yield using the method for the preparation of (+)-2a. [α]$_{D}^{25}$ +18 (c 1.0, CHCl$_3$); ee >99% (HPLC). Identical spectra as for (-)-6a were obtained.

**Chemical Hydrolysis of (-)-trans-(1S, 3S)-2,2-Dimethyl-3-(2',2'-dimethylvinyl)cyclopropanecarboxamide (6a).** (-)-trans-(1S, 3S)-2,2-Dimethyl-3-(2',2'-dimethylvinyl)cyclopropanecarboxamide 6a (0.2mmol, e>99%) was refluxed in a mixture of methanol (2 ml) and KOH (10%, 4ml) for 22h to give, after the workup, (-)-trans-(1S, 3S)-chrysanthemic acid 7a in 91% yield. [α]$_{D}^{25}$ –23.3 (c 1.5, CHCl$_3$) [lit.$^2$ [α]$_{D}^{25}$ –14.07 (c 1.920, alcohol)]; ee >99% (HPLC). Identical spectra as for (+)-7a were obtained.

The enantiomeric excesses of all optically active compounds obtained were measured with the Shimadzu LC-10AVP HPLC system using chiral columns with hexane:2-propanol (9:1 or 20:1) as the mobile phase at a certain flow rate.

Table S1. Retention time of enantiomers of acids 3, 7 and 10.

<table>
<thead>
<tr>
<th>Racemic acids</th>
<th>Retention Time (min)</th>
<th>Configuration</th>
<th>Column</th>
<th>Mobile phase (Hex:IPA)/Flow rate (ml/min)</th>
</tr>
</thead>
<tbody>
<tr>
<td>3a</td>
<td>7.306 9.357</td>
<td>(+) (-)</td>
<td>Chiralcel OJ</td>
<td>9 : 1/0.8</td>
</tr>
<tr>
<td>3b</td>
<td>6.759 5.911</td>
<td>(+) (-)</td>
<td>Chiralcel OJ</td>
<td>9:1/0.8</td>
</tr>
<tr>
<td>3c</td>
<td>6.643 5.720</td>
<td>(+) (-)</td>
<td>Chiralcel OJ</td>
<td>9:1/0.8</td>
</tr>
<tr>
<td>3d</td>
<td>5.695 7.094</td>
<td>(+) (-)</td>
<td>Chiralpak AD</td>
<td>9:1/0.8</td>
</tr>
<tr>
<td>3e</td>
<td>5.521 6.108</td>
<td>(+) (-)</td>
<td>Chiralpak AD</td>
<td>9:1/0.8</td>
</tr>
<tr>
<td>3f</td>
<td>8.638 12.637</td>
<td>(+) (-)</td>
<td>Chiralpak AD</td>
<td>9:1/0.8</td>
</tr>
<tr>
<td>3g</td>
<td>9.287 6.697</td>
<td>(+) (-)</td>
<td>Chiralcel OJ</td>
<td>9:1/0.8</td>
</tr>
<tr>
<td></td>
<td>Retention Time (min)</td>
<td>Configuration</td>
<td>Column</td>
<td>Mobile phase (Hex:IPA)/Flow rate (ml/min)</td>
</tr>
<tr>
<td>---</td>
<td>----------------------</td>
<td>---------------</td>
<td>--------</td>
<td>-----------------------------------------</td>
</tr>
</tbody>
</table>
| **2a** | 8.312  
13.147 | (+) (1R, 3R)  
(-) (1S, 3S) | Chiracel OJ | 9:1/0.8 |
| **2b** | 8.028  
9.627 | (+) (1R, 3R)  
(-) (1S, 3S) | Chiracel OJ | 9:1/0.8 |
| **2c** | 8.248  
9.532 | (+) (1R, 3R)  
(-) (1S, 3S) | Chiracel OJ | 9:1/0.8 |
| **2d** | 7.206 | (+) (1R, 3R) | Chiracel OJ | 9:1/0.8 |

*: analysis of the corresponding amide

**Table S2.** Retention time of enantiomers of amides 2, 6 and 9.
Table S3. Retention time of enantiomers of nitriles 1.

<table>
<thead>
<tr>
<th>Racemic nitriles</th>
<th>Retention Time (min)</th>
<th>Configuration</th>
<th>Column</th>
<th>Mobile phase (Hex:IPA)/Flow rate (ml/min)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1a</td>
<td>18.601</td>
<td>(+) (1R, 3R)</td>
<td>Chiralcel</td>
<td>9:1/0.4</td>
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</table>

| 2e               | 8.330 (-) (1S, 3S)   | Chiracel OJ   | 9:1/0.8 |
| 2f               | 7.732 (+) (1R, 3R)   | Chiracel OJ   | 9:1/0.8 |
|                  | 8.929 (-) (1S, 3S)   | Chiracel OJ   | 9:1/0.8 |
| 2g               | 7.999 (+) (1R, 3R)   | Chiracel OJ   | 9:1/0.8 |
|                  | 14.963 (-) (1S, 3S)  | Chiracel OJ   | 9:1/0.8 |
| 2h               | 17.042 (+) (1R, 3R)  | Chiralpak AD  | 9:1/0.8 |
|                  | 14.823 (-) (1S, 3S)  | Chiralpak AD  | 9:1/0.8 |
| 6a               | 18.419 (+) (1R, 3R)  | Chiralcel OD  | 20:1/0.8 |
|                  | 16.231 (-) (1S, 3S)  | Chiralcel OD  | 20:1/0.8 |
| 6b               | 9.737 (+) (1R, 3S)   | Chiralcel OD  | 9:1/0.8 |
|                  | 8.682 (-) (1S, 3R)   | Chiralcel OD  | 9:1/0.8 |
| 9a               | 10.795 (+) (1R, 3S)  | Chiralcel OD  | 9:1/0.8 |
|                  | 8.614 (-) (1S, 3R)   | Chiralcel OD  | 9:1/0.8 |
| 9b               | 7.735 (+) (1S, 3S)   | Chiralcel OD  | 9:1/0.8 |
|                  | 9.328 (-) (1R, 3R)   | Chiralcel OD  | 9:1/0.8 |

**Table S3.** Retention time of enantiomers of nitriles 1.
### Table

<table>
<thead>
<tr>
<th></th>
<th>Retention Time</th>
<th>Enantiomeric Ratio</th>
<th>Stationary Phase</th>
<th>Resolution</th>
</tr>
</thead>
<tbody>
<tr>
<td>1b</td>
<td>9.190</td>
<td>(+) (1R, 3R)</td>
<td>Chiralcel OD</td>
<td>9:1/0.8</td>
</tr>
<tr>
<td></td>
<td>7.461</td>
<td>(-) (1S, 3S)</td>
<td>OD</td>
<td></td>
</tr>
<tr>
<td>1c</td>
<td>11.467</td>
<td>(+) (1R, 3R)</td>
<td>Chiralcel OD</td>
<td>9:1/0.8</td>
</tr>
<tr>
<td></td>
<td>8.695</td>
<td>(-) (1S, 3S)</td>
<td>OD</td>
<td></td>
</tr>
<tr>
<td>1d</td>
<td>9.321</td>
<td>(+) (1R, 3R)</td>
<td>Chiralcel OD</td>
<td>9:1/0.8</td>
</tr>
<tr>
<td></td>
<td>10.194</td>
<td>(-) (1S, 3S)</td>
<td>OD</td>
<td></td>
</tr>
<tr>
<td>1e</td>
<td>7.660</td>
<td></td>
<td>Chiralcel OD</td>
<td>9:1/0.8</td>
</tr>
<tr>
<td></td>
<td>8.648</td>
<td></td>
<td>OD</td>
<td></td>
</tr>
<tr>
<td>1f</td>
<td>11.018</td>
<td>(+) (1R, 3R)</td>
<td>Chiralcel OD</td>
<td>9:1/0.8</td>
</tr>
<tr>
<td></td>
<td>9.635</td>
<td>(-) (1S, 3S)</td>
<td>OD</td>
<td></td>
</tr>
<tr>
<td>1g</td>
<td>9.285</td>
<td>(+) (1R, 3R)</td>
<td>Chiralcel OD</td>
<td>9:1/0.8</td>
</tr>
<tr>
<td></td>
<td>7.970</td>
<td>(-) (1S, 3S)</td>
<td>OD</td>
<td></td>
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<tr>
<td>1h</td>
<td>11.257</td>
<td>(+) (1R, 3R)</td>
<td>Chiralcel OD</td>
<td>9:1/0.8</td>
</tr>
<tr>
<td></td>
<td>10.479</td>
<td>(-) (1S, 3S)</td>
<td>OD</td>
<td></td>
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</table>

### 5. Preparation of Racemic Nitriles 1 and 4, and Amides 2.

Nitriles 1 and 4 were synthesized from (E)-ethyl 2-cyano-3-aryl-2-propenoates according to the literature. Amides 2 were synthesized from the corresponding nitriles 1 according to the literature.

**Scheme 1. Preparation of Racemic Nitriles 1 and 4**
General Method for the Preparation of Ethyl 1-Cyano-2,2-dimethyl-3-arylcyclopropanecarboxylates: A mixture of equimolar amounts of ethyl (E)-2-cyano-3-aryl-2-propenoate, 2-nitropropane and anhydrous potassium carbonate in absolute ethanol (0.8 ml/mmol substrate) was under reflux until the material was disappeared (TLC). The product was isolated by column chromatography.

General Method for the Preparation of 1-Cyano-2,2-dimethyl-3-arylcyclopropanecarboxylic Acids: Treatment of ethyl 1-cyano-2,2-dimethyl-3-arylcyclopropanecarboxylate (1 mmol) with anhydrous potassium carbonate (1.2 mmol), water (1 ml) and methyl alcohol (4 ml) under reflux for about 0.5h. The product was isolated by cooling the mixture to room temperature, cautiously acidifying it by adding aqueous HCl (2M) solution, subsequent dilution with 20 ml of brine, and extraction with ether. The ether extracts were washed with brine, and then dried with anhydrous magnesium sulfate. After filtration and removal of the ether, the desired acid product was yielded.

General Method for the Preparation of trans- and cis-2,2-Dimethyl-3-arylcyclopropanecarbonitriles 1 and 4. A mixture of
1-cyano-2,2-dimethyl-3-aryl-cyclopropanecarboxylic acid (1 mmol), sodium bicarbonate (1.5 mmol), LiCl·H2O (4 mmol) in 2 ml DMSO was heated at 165 °C for about 18 hours. A mixture of racemic trans- and cis-isomers 1 and 4 were obtained and their separation was effected by column chromatography.

Identical spectra as for the nitriles 1 recovered from the biotransformations were obtained.

**cis-2,2-Dimethyl-3-phenylcyclopropanecarbonitrile (4a):** oil; 1H NMR (300Hz, CDCl₃) 7.33-7.38 (m, 5H, Ar-H) 2.43 (d, J = 8.7 Hz, 1H, CH), 1.71 (d, J = 8.7 Hz, 1H, CH), 1.39 (s, 3H, CH₃), 1.19 (s, 3H, CH₃); IR (KBr) 2234 cm⁻¹; MS (EI) m/z 171 (M⁺, 73%), 156 (83), 144 (8), 129 (100), 115 (21), 105 (29).

**cis-2,2-Dimethyl-3-(4-fluorophenyl)cyclopropanecarbonitrile (4b):** oil; 1H NMR (300Hz, CDCl₃) 7.01-7.32 (m, 4H, Ar-H) 2.36 (d, J = 8.6 Hz, 1H, CH), 1.69 (d, J = 8.9 Hz, 1H, CH), 1.36 (s, 3H, CH₃), 1.15 (s, 3H, CH₃); IR (KBr) 2235 cm⁻¹; MS (EI) m/z 189 (M⁺, 60%), 174 (100), 147 (90), 109 (23).

**cis-2,2-Dimethyl-3-(4-chlorophenyl)cyclopropanecarbonitrile (4c):** oil; 1H NMR (300Hz, CDCl₃) 7.33 (d, J = 8.5 Hz, 2H, Ar-H) 7.27 (d, J = 8.4 Hz, 2H, Ar-H) 2.35 (d, J = 8.7 Hz, 1H, CH), 1.70 (d, J = 8.7 Hz, 1H, CH), 1.36 (s, 3H, CH₃), 1.15 (s, 3H, CH₃); IR (KBr) 2236 cm⁻¹; MS (EI) m/z 207 (M⁺ + 2, 26), 205 (M⁺, 79%), 192 (33), 190 (100), 170 (88), 163 (57), 155 (32), 143 (45), 128 (53).

**cis-2,2-Dimethyl-3-(3-chlorophenyl)cyclopropanecarbonitrile (4d):** oil; 1H NMR (300Hz, CDCl₃) 7.27-7.31 (m, 4H, Ar-H) 2.37 (d, J = 8.7 Hz, 1H, CH), 1.72 (d, J = 8.7 Hz, 1H, CH), 1.37 (s, 3H, CH₃), 1.18 (s, 3H, CH₃); IR (KBr) 2235 cm⁻¹; MS (EI)
m/z 207 (M⁺ + 2, 19), 205 (M⁺, 57%), 192 (17), 190 (50), 170 (100), 163 (40), 155 (25), 143 (56).

cis-2,2-Dimethyl-3-(4-methoxyphenyl)cyclopropanecarbonitrile (4f): oil; ¹H NMR (300Hz, CDCl₃) δ 7.25 (d, J = 8.3 Hz, 2H, Ar-H) 6.89 (d, J = 8.3 Hz, 2H, Ar-H) 3.80 (s, 3H, CH₃O), 2.34 (d, J = 8.6 Hz, 1H, CH), 1.65 (d, J = 8.7 Hz, 1H, CH), 1.34 (s, 3H, CH₃), 1.15 (s, 3H, CH₃); IR (KBr) 2234 cm⁻¹; MS (EI) m/z 201 (M⁺, 56%), 186 (100), 171 (8).

cis-2,2-Dimethyl-3-(4-methylphenyl)cyclopropanecarbonitrile (4g): oil; ¹H NMR (300Hz, CDCl₃) δ 7.11-7.25 (m, 4H, Ar-H) 2.35 (d, J = 11.0 Hz, 2H, CH), 2.33 (s, 3H, CH₃), 1.64 (d, J = 11.4 Hz, 1H, CH), 1.34 (s, 3H, CH₃), 1.15 (s, 3H, CH₃); IR (KBr) 2234 cm⁻¹; MS (EI) m/z 185 (M⁺, 58%), 170 (100), 143 (58).

cis-2,2-Dimethyl-3-(2-methylphenyl)cyclopropanecarbonitrile (4h): mp 60-61°C; ¹H NMR (300Hz, CDCl₃) δ 7.19-7.50 (m, 4H, Ar-H), 2.32 (s, 3H, CH₃), 2.25 (d, J = 8.6 Hz, 1H, CH), 1.72 (d, J = 8.6 Hz, 1H, CH), 1.42 (s, 3H, CH₃), 1.12 (s, 3H, CH₃); IR (KBr) 2227 cm⁻¹; MS (EI) m/z 185 (M⁺, 62%), 170 (100), 155 (10), 143 (64), 128 (27), 115 (31).

General Method for the Preparation of trans-2,2-dimethyl-3-arylcyclopropanecarboxamides 2.⁸ Reaction of trans-2,2-dimethyl-3-arylcyclopropanecarbonitriles 1 (1 mmol) with potassium hydroxide (2 equ.) in tert-butyl alcohol (5 ml) under reflux afforded trans-2,2-dimethyl-3-arylcyclopropanecarboxamides 2 in 82-97% yield.
6. Preparation of Racemic Nitriles 5 and 8 and Amides 6 and 9.

A mixture of \textit{trans-} and \textit{cis-}chrysanthic acid was obtained in 93\% yield from the hydrolysis of commercially available ethyl chrysanthe mate with potassium hydroxide in alcohol. Repeated fractional crystallization of the crude mixture of \textit{trans-} and \textit{cis-}chrysanthic acids from ethyl acetate yielded pure \textit{cis-}chrysanthic acid (10a): mp 112-114\degree C (lit.\textsuperscript{2} mp 113-116\degree C), which was converted to \textit{cis-}amide (9a) by standard method in 80\% yield. \textit{cis-}Amide (9a): mp 91-92 \degree C (lit.\textsuperscript{2} mp 93\degree C).

Dehydration of \textit{cis-}amide to \textit{cis-}chrysanthic nitrile (8a) was accomplished in 74\% yield by the reaction with SOCl\textsubscript{2} in benzene and DMF at room temperature. In the same way, a mixture of \textit{trans-} and \textit{cis-}chrysanthic nitriles was obtained from a mixture of \textit{trans-} and \textit{cis-}chrysanthic acids. Reaction of the mixture of \textit{trans-} and \textit{cis-}chrysanthic nitriles with potassium hydroxide in tert-butyl alcohol\textsuperscript{8} afforded pure \textit{trans-}chrysanthic amide (6a) in 69\% yield, mp 125-126\degree C (lit.\textsuperscript{9} mp123-124\degree C). Dehydration of \textit{trans-}amide (6a) to \textit{trans-}chrysanthic nitrile (5a) was accomplished in 89\% yield by the reaction with \textit{p-}toluenesulfonyl chloride in pyridine at room temperature.\textsuperscript{9}

\textit{(+/-)-trans-2,2-Dimethyl-3-(2',2'-dimethylvinyl)cyclopropanecarbonitrile} (5a): oil; \textsuperscript{1}H NMR (CDCl\textsubscript{3}) \textsuperscript{\textdelta} 4.82 (d, \textit{J} = 7.6 Hz, 1H, vinyl-H), 1.88 (dd, \textit{J} = 5.8, 6.4 Hz, 1H, CH), 1.73 (s, 6H, 2CH\textsubscript{3}), 1.35 (s, 3H, CH\textsubscript{3}), 1.13 (s, 3H, CH\textsubscript{3}), 1.04 (d, \textit{J} = 5.1 Hz, 1H, CH); \textsuperscript{13}C NMR (300Hz, CDCl\textsubscript{3}) \textsuperscript{\textdelta} 137.8, 120.6, 119.1, 32.7, 25.6, 23.6, 20.2, 18.6, 17.8; IR (KBr) 2234 cm\textsuperscript{-1}; MS (EI) \textit{m/z} 149 (M\textsuperscript{+}, 45\%), 134 (100), 119 (31), 107 (57), 91 (26), 79 (26), 67 (17), 53 (17), 41 (37).
(+/-)-cis-2,2-Dimethyl-3-(2',2'-dimethylvinyl)cyclopropanecarbonitrile (8a): oil; 
$^1$H NMR (300Hz, CDCl$_3$) δ 5.01 (d, $J$ = 7.4 Hz, 1H, vinyl-H), 1.80 (dd, $J$ = 7.4, 8.6 Hz, 1H, CH), 1.78 (s, 3H, CH$_3$), 1.72 (s, 3H, CH$_3$), 1.44 (d, $J$ = 8.6 Hz, 1H, CH), 1.20 (s, 3H, CH$_3$), 1.19 (s, 3H, CH$_3$); $^{13}$C NMR (CDCl$_3$) δ 138.3, 119.1, 117.1, 29.3, 26.5, 25.6, 24.9, 18.7, 17.2, 16.7; IR (KBr) 2232 cm$^{-1}$, 1450, 1381; MS (EI) m/z 149 (M$^+$, 45%), 148 (17), 134 (100), 119 (37), 107 (65), 91 (33), 79 (29), 67 (24).

(+/-)-trans-2,2-Dimethyl-3-(2',2'-dimethylvinyl)cyclopropanecarboxamide (6a): 
mp 125-126 °C (lit.$^9$ mp123-124 °C).

(+/-)-cis-2,2-Dimethyl-3-(2',2'-dimethylvinyl)cyclopropanecarboxamide (9a): mp 91-92 °C (lit.$^2$ mp 93°C).

Racemic amides have the identical spectra as that of optically active amides and acids obtained from the biotransformations.

Hydrolysis of commercially available methyl 3-(2,2-dichlorovinyl)-2,2-dimethyl-(1-cyclopanecarboxylate) with potassium hydroxide in alcohol afforded a mixture of trans- and cis-2,2-dimethyl-3-(2',2'-dichlorovinyl)cyclopropanecarboxylic acids (94% yield), which was converted to amide (83% yield) by standard method. Pure trans-amide (6b) and cis-amide (9b) were obtained by column chromatography. Dehydration of trans- or cis-amide to trans-2,2-dimethyl-3-(2',2'-dichlorovinyl)cyclopropanecarbonitrile (5b) or cis-2,2-dimethyl-3-(2,2-dichlorovinyl)cyclopropanecarbonitrile (8b) was
accomplished in 85% and 90% yield by reaction with SOCl₂ in benzene and DMF at room temperature, respectively.

(+/-)-trans-2,2-Dimethyl-3-(2',2'-dichlorovinyl)cyclopropanecarbonitrile (5b):
mp 51-52°C; \(^1\)H NMR (300Hz, CDCl₃) δ 5.58 (d, J = 8.4 Hz, 1H, vinyl-H), 2.10 (dd, J = 5.3, 8.1 Hz, 1H, CH), 1.43 (s, 3H, CH₃), 1.33 (d, J = 5.2 Hz, 1H, CH), 1.22 (s, 3H, CH₃); \(^13\)C NMR (CDCl₃) δ 124.5, 124.2, 118.8, 32.6, 26.1, 23.0, 20.4, 18.0; IR (KBr) 3057, 2228, 1625 cm⁻¹; MS (El) m/z 193 (M⁺ + 4, 5), 191 (M⁺ + 2, 28), 189 (M⁺, 43%), 178 (5), 176 (31), 174 (50), 156 (31), 154 (100). Anal. Calcd. for C₈H₉Cl₂N: C, 50.55; H, 4.77; N, 7.37. Found: C, 50.78; H, 4.82; N, 7.50.

(+/-)-cis-2,2-Dimethyl-3-(2',2'-dichlorovinyl)cyclopropanecarbonitrile (8b): oil;
\(^1\)H NMR (300Hz, CDCl₃) δ 5.75 (d, J = 8.3 Hz, 1H, vinyl-H), 2.00 (dd, J = 8.3, 8.3 Hz, 1H, CH), 1.66 (d, J = 8.3 Hz, 1H, CH), 1.27 (s, 3H, CH₃), 1.25 (s, 3H, CH₃); \(^13\)C NMR (CDCl₃) δ 124.1, 123.3, 117.8, 29.9, 25.9, 25.8, 17.4, 17.1; IR (KBr) 3041, 2236, 1618 cm⁻¹; MS (El) m/z 193 (M⁺ + 4, 6), 191 (M⁺ + 2, 38), 189 (M⁺, 57%), 178 (6), 176 (38), 174 (58), 156 (33), 154 (100). Anal. Calcd. for C₈H₉Cl₂N: C, 50.55; H, 4.77; N, 7.37. Found: C, 50.54; H, 4.65; N, 7.28.

(+/-)-trans-2,2-Dimethyl-3-(2',2'-dichlorovinyl)cyclopropanecarboxamide (6b):
mp 98-99°C.

(+/-)-cis-2,2-Dimethyl-3-(2',2'-dichlorovinyl)cyclopropanecarboxamide (9b): mp 75-76°C.
Racemic amides have the identical spectra as that of optically active amides and acids obtained from the biotransformations.

Reference


