PPh₃-Catalyzed Synthesis of Dicyano-2-Methylenebut-3-Enoates as Efficient Dienes in Catalytic Asymmetric Inverse-Electron-Demand Diels-Alder Reaction

Xianxing Jiang, a,b Dan Fu, a Xiaomei Shi, a Shoulei Wang, a and Rui Wang *a,b

a Key Laboratory of Preclinical Study for New Drugs of Gansu Province, State Key Laboratory of Applied Organic Chemistry, Institute of Biochemistry and Molecular Biology, Lanzhou University, Lanzhou, China
b State Key Laboratory for Oxo Synthesis and Selective Oxidation, Lanzhou Institute of Chemical Physics, Chinese Academy of Sciences, Lanzhou 730000, China.

E-mail: wangrui@lzu.edu.cn

Supporting information

Contents
1.0 General methods S2
2.0 General procedure synthesis of dicyano-2-methylenebut-3-enoates S2
3.0 General procedure for PPh₃-catalyzed addition/asymmetric IEDDAR sequence S2
4.0 Characterization data S3
5.0 References S20
6.0 X-Ray structure of 5i S21
7.0 Copies of HPLC spectra of racemic/chiral products S22
8.0 Copies of NMR spectra of products S41
1.0 General Methods: All reactions were carried out under an argon atmosphere condition unless otherwise noted and solvents were dried according to established procedures. Reactions were monitored by thin layer chromatography (TLC), column chromatography purifications were carried out using silica gel GF254. Proton nuclear magnetic resonance (1H NMR) spectra were recorded on Brucker 300 MHz spectrometer in CDCl3 unless otherwise noted and carbon nuclear magnetic resonance (13C NMR) spectra were recorded on Brucker 300 MHz spectrometer in CDCl3 using tetramethylsilane (TMS) as internal standard unless otherwise noted. Data are presented as follows: chemical shift, integration, multiplicity (br = broad, s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, cm = complex multiplet) and coupling constant in Hertz (Hz). Infrared (IR) spectra were recorded on a FT-IR spectrometer. Optical rotations were recorded on a Perkin-Elmer 341 polarimeter. HR-MS was measured with an APEX II 47e mass spectrometer. Melting points were measured on an XT-4 melting point apparatus and were uncorrected. The ee values determination was carried out using chiral high-performance liquid chromatography (HPLC) with Daicel Chiracel chiral columns on Waters with a 2996 UV-detector and the dr values determined by 300 Hz 1H NMR.

Materials: The catalysts were synthesized according to the literature procedures.1

2.0 General procedure for synthesis of dicyano-2-methylenebut-3-enoates

\[
\begin{align*}
1 & \quad \text{(2.0 mmol)} & 2 & \quad \text{(2.4 mmol)} \\
\text{NC}_2\text{CN} & + \quad \text{CO}_2\text{R}^1 & \xrightarrow{\text{PPh}_3(20 \text{ mol} \%) \quad \text{tol, } 75 \degree \text{C}} & \quad \text{NC}_2\text{CN} \\
\text{R} & \quad \text{H} & \quad \text{CO}_2\text{R}^1 & \quad \text{R} \\
\end{align*}
\]

Arylidenedemalononitrile (2.0 mmol), PPh3 (20.0 mol%) were added to toluene (25 mL) in three-necked flask. The mixture was stirred at 75 °C under Argon. To this reaction mixture the solution of alkyl propiolate (2.4 mmol) in toluene (40 mL) was slowly added within 3 hours. Once the addition was finished, the reaction mixture was cooled down to room temperature. Then the mixture was directly subjected to flash column chromatography on silica gel (petroleum ether/ethyl acetate = 15:1) to give the products.

3.0 General procedure for the PPh3-catalyzed addition/asymmetric IEDDAR sequence

[Diagram of reaction scheme]

1. PPh3 (20 mol%) tol, 75 °C
2. Cata (10 mol%) PhCO2H(10 mol%) Tol, rt, 6 h

1 (0.3 mmol) 2 (0.36 mmol) 3 (0.4-0.5 mmol)

\[
\begin{align*}
1 & \quad \text{(0.3 mmol)} & 2 & \quad \text{(0.36 mmol)} & 3 & \quad \text{(0.4-0.5 mmol)} \\
\text{NC}_2\text{CN} & + \quad \text{CO}_2\text{R}^1 & \text{CHO} & \xrightarrow{\text{1. PPh}_3(20 \text{ mol} \%) \quad \text{tol, } 75 \degree \text{C}} & \quad \text{R'}\text{CO}_2\text{CH} \\
\text{R} & \quad \text{H} & \quad \text{R}^2 & \quad \text{R'} & \quad \text{R}^2 \\
\end{align*}
\]
Arylidenemalononitrile (0.3 mmol), PPh₃ (20.0 mol%) were added to toluene (3 mL) in three-necked flask. The mixture was stirred at 75 °C under Argon. To this reaction mixture the solution of alkyl propiolate (0.36 mmol) in toluene (6 mL) was slowly added within 1.5 hours. The solution was stirred at room temperature for 1 h, and then was subjected to flash column chromatography on silica gel (petroleum ether/ethyl acetate = 15:1), affording the crude products were directly dissolved in a stirred solution of catalyst (10 mol %), and benzoic acid (10 mol %) in dry toluene (1.2 mL). Then alkyl aldehyde (0.4-0.5 mmol) was added. The solution was stirred at room temperature for a specified reaction time. After the reaction was completed (monitored by TLC), the resulting mixture was concentrated under reduced pressure and the residue was purified through column chromatography on silica gel (petroleum ether/ethyl acetate = 7:1) to give the optical pure products. The enantiomeric purity of the major diastereomer was determined by using HPLC.

4.0 Characterization data

**Ethyl 4,4-dicyano-3-(4-methoxyphenyl)-2-methylenebut-3-enoate: 3a**

![Structure of 3a](image)

**¹H NMR** (300 MHz, CDCl₃): δ 7.63(d, J = 9.0 Hz, 2 H), 6.99(d, J = 8.7 Hz, 2 H), 6.88(s, 1 H), 6.14(s, 1 H), 4.13-4.20(dd, J = 7.2 Hz, 14.4 Hz, 2 H), 3.88(s, 3 H), 1.16(t, J = 7.2 Hz, 3 H);

**¹³C NMR** (75 MHz, CDCl₃): δ 169.3, 163.6, 163.1, 138.1, 134.5, 131.3, 126.0, 114.6, 113.6, 113.2, 81.9, 62.1, 55.7, 13.9.

**IR**: ν 2982, 2227, 1725, 1603, 1511, 1462, 1424, 1370, 1308, 1268, 1179, 1025, 838, 812, 665 cm⁻¹.

**HRMS-ESI** (m/z): calcd for C₁₆H₁₄N₂O₃⁺NH₄⁺:300.1343; found: 300.1341, 0.7ppm.

**Ethyl 4,4-dicyano-2-methylene-3-phenylbut-3-enoate: 3b**

![Structure of 3b](image)

**¹H NMR** (300 MHz, CDCl₃): δ 7.47-7.58(m, 5 H), 6.88(s, 1 H), 6.18(s, 1 H), 4.09-4.16(dd, J = 7.2 Hz, 14.1 Hz, 2 H), 1.10(t, J =6.9 Hz, 3 H);

**¹³C NMR** (75 MHz, CDCl₃): δ 170.6, 162.9, 137.9, 134.9, 133.9, 132.9, 129.1, 128.8, 112.8,112.7, 85.0, 62.1, 13.8.
IR: ν 2986, 2231, 1733, 1570, 1556, 1470, 1371, 1257, 1185, 1022, 911, 863, 810, 777, 701, 589 cm⁻¹.

**HRMS-ESI** (m/z): calcd for C₁₅H₁₂N₂O₂⁺NH₄⁺: 270.1237; found: 270.1231, 2.2ppm.

**Ethyl 4,4-dicyano-2-methylene-3-(naphthalen-1-yl)but-3-enolate: 3c**

![Image of molecule](image)

**¹H NMR** (300 MHz, CDCl₃): δ 8.02(d, J = 8.1 Hz, 1 H), 7.90-7.93(m, 1 H), 7.79-7.82(m, 1 H), 7.47-7.60(m, 4 H), 6.74(s, 1 H), 6.05(s, 1 H), 4.22-4.29(dd, J = 7.2 Hz, 14.4 Hz, 2 H), 1.19(t, J = 6.9 Hz, 3 H); **¹³C NMR** (75 MHz, CDCl₃): δ 170.3, 163.3, 139.0, 135.4, 133.8, 132.4, 132.3, 129.8, 128.9, 127.8, 127.0, 124.8, 112.1, 112.0, 89.1, 62.4, 13.9.

IR: ν 2985, 2231, 1727, 1556, 1467, 1370, 1343, 1248, 1159, 1091, 1021, 864, 777, 738 cm⁻¹.

**HRMS-ESI** (m/z): calcd for C₁₉H₁₄N₂O₂⁺NH₄⁺: 320.1394; found: 320.1401, 2.2ppm.

**Ethyl 4,4-dicyano-2-methylene-3-p-tolylbut-3-enolate: 3d**

![Image of molecule](image)

**¹H NMR** (300 MHz, CDCl₃): δ 7.50(d, J = 8.4 Hz, 2 H), 7.30(d, J = 8.1 Hz, 2 H), 6.89(s, 1 H), 6.17(s, 1 H), 4.12-4.19(dd, J = 7.2 Hz, 14.1 Hz, 2 H), 2.42(s, 3 H), 1.14(t, J = 7.2 Hz, 3 H); **¹³C NMR** (75 MHz, CDCl₃): δ 170.4, 163.1, 144.2, 138.0, 134.7, 130.4, 129.9, 128.9, 113.1, 112.9, 83.9, 62.1, 21.7, 13.8.

IR: ν 2985, 2228, 1729, 1608, 1550, 1448, 1410, 1258, 1184, 1022, 863, 820, 743, 666, 612 cm⁻¹.

**HRMS-ESI** (m/z): calcd for C₁₆H₁₄N₂O₂⁺NH₄⁺: 284.1394; found: 284.1401, 2.5ppm.

**Ethyl 4,4-dicyano-3-(3-methoxyphenyl)-2-methylenebut-3-enolate: 3e**

![Image of molecule](image)

**¹H NMR** (300 MHz, CDCl₃): δ 7.36-7.42(m, 1 H), 7.08-7.13(m, 3 H), 6.88(s, 1 H), 6.18(s, 1 H), 4.12-4.19(dd, J = 7.2 Hz, 14.1 Hz, 2 H), 3.84(s, 3 H), 1.14(t, J = 7.2 Hz, 3 H); **¹³C NMR** (75 MHz, CDCl₃): δ 170.4, 162.9, 159.8, 137.9, 135.0, 134.7, 130.3, 121.2, 118.8, 113.8, 112.8, 112.6, 85.1,
62.1, 55.6, 13.8.

IR: ν 2983, 2230, 1728, 1561, 1428, 1329, 1268, 1235, 1183, 1095, 1020, 865, 791, 704, 562 cm⁻¹.

HRMS-ESI (m/z): calcd for C₁₆H₁₄N₂O₃⁺NH₄⁺:300.1343; found: 300.1347, 1.3ppm.

**Ethyl 4,4-dicyano-2-methylene-3-m-tolylbut-3-enoate: 3f**

![Structure of 3f]

**¹H NMR** (300 MHz, CDCl₃): δ 7.35-7.37 (m, 4 H), 6.88 (s, 1 H), 6.17 (s, 1 H), 4.12-4.19 (dd, J = 7.2 Hz, 14.4 Hz, 2 H), 2.40 (s, 3 H), 1.13 (t, J = 7.2 Hz, 3 H); **¹³C NMR** (75 MHz, CDCl₃): δ 170.8, 163.0, 139.1, 138.0, 134.6, 133.9, 133.7, 129.2, 129.0, 126.0, 112.8, 112.7, 84.8, 62.1, 21.3, 13.8.

IR: ν 2985, 2230, 1730, 1559, 1449, 1371, 1262, 1216, 1183, 1098, 1021, 864, 793, 706, 592 cm⁻¹.

HRMS-ESI (m/z): calcd for C₁₆H₁₄N₂O₂⁺NH₄⁺:284.1394; found: 284.1388, 2.1ppm.

**Ethyl 4,4-dicyano-2-methylene-3-o-tolylbut-3-enoate: 3g**

![Structure of 3g]

**¹H NMR** (300 MHz, CDCl₃): δ 7.18-7.43 (m, 4 H), 6.76 (s, 1 H), 6.04 (s, 1 H), 4.21-4.28 (dd, J = 7.2 Hz, 14.4 Hz, 2 H), 2.35 (s, 3 H), 1.25 (t, J = 7.2 Hz, 3 H); **¹³C NMR** (75 MHz, CDCl₃): δ 171.4, 163.1, 138.5, 136.3, 135.3, 134.3, 131.5, 128.6, 126.2, 112.2, 111.9, 88.6, 62.3, 19.8, 13.9.

IR: ν 2985, 2232, 1729, 1560, 1454, 1391, 1252, 1158, 1115, 1022, 863, 767, 676, 593 cm⁻¹.

HRMS-ESI (m/z): calcd for C₁₆H₁₄N₂O₂⁺NH₄⁺:284.1394; found: 284.1400, 2.1ppm.

**Ethyl 3-(4-bromophenyl)-4,4-dicyano-2-methylenebut-3-enoate: 3h**

![Structure of 3h]

**¹H NMR** (300 MHz, CDCl₃): δ 7.65 (d, J = 8.7 Hz, 2 H), 7.45 (d, J = 8.7 Hz, 2 H), 6.91 (s, 1 H), 6.22 (s, 1 H), 4.12-4.19 (dd, J = 7.2 Hz, 14.1 Hz, 2 H), 1.15 (t, J = 7.2 Hz, 3 H); **¹³C NMR** (75 MHz, CDCl₃): δ 169.3, 162.7, 137.5, 135.3, 132.7, 132.5, 130.2, 127.9, 112.5, 112.4, 85.5, 62.3, 13.8.
IR: ν 2924, 2854, 2231, 1729, 1331, 1253, 1184, 1074, 1014, 904, 830, 729 cm⁻¹.

HRMS-ESI (m/z): calcd for C₁₅H₁₁BrN₂O₂⁺NH₄⁺: 348.0342; found: 348.0339, 0.9ppm.

Ethyl 3-(4-chlorophenyl)-4,4-dicyano-2-methylenebut-3-enoate: 3i

\[
\begin{align*}
\text{Cl} & \quad \text{COOEt} \\
\end{align*}
\]

\(^1\text{H NMR}\) (300 MHz, CDCl₃): δ 7.45-7.54 (dd, \(J = 8.7\) Hz, 18.0 Hz, 4 H), 6.90 (s, 1 H), 6.22 (s, 1 H), 4.12-4.19 (dd, \(J = 7.2\) Hz, 14.1 Hz, 2 H), 1.15 (t, \(J = 7.2\) Hz, 3 H); \(^{13}\text{C NMR}\) (75 MHz, CDCl₃): δ 169.1, 162.7, 139.3, 137.6, 135.2, 132.3, 130.1, 129.5, 112.6, 112.4, 85.5, 62.2, 13.8.

IR: ν 2985, 2231, 1729, 1590, 1490, 1410, 1254, 1184, 1096, 1018, 910, 834, 736, 650, 585 cm⁻¹.

HRMS-ESI (m/z): calcd for C₁₅H₁₁ClN₂O₂⁺NH₄⁺: 304.0847; found: 304.0841, 2.0ppm.

Ethyl 4,4-dicyano-3-(4-fluorophenyl)-2-methylenebut-3-enoate: 3j

\[
\begin{align*}
\text{F} & \quad \text{COOEt} \\
\end{align*}
\]

\(^1\text{H NMR}\) (300 MHz, CDCl₃): δ 7.58-7.63 (m, 2 H), 7.16-7.22 (m, 2 H), 6.91 (s, 1 H), 6.21 (s, 1 H), 4.13-4.20 (dd, \(J = 7.2\) Hz, 14.4 Hz, 2 H), 1.15 (t, \(J = 6.9\) Hz, 3 H); \(^{13}\text{C NMR}\) (75 MHz, CDCl₃): δ 169.2, 166.9, 163.5, 162.8, 158.4, 137.8, 135.0, 133.5, 133.4, 131.4, 131.3, 130.0, 117.4, 117.1, 116.8, 116.5, 112.7, 112.5, 85.0, 62.2, 13.8.

IR: ν 2986, 2231, 1729, 1599, 15081, 1472, 1410, 1245, 1163, 1106, 1020, 843, 749, 668, 528 cm⁻¹.

HRMS-ESI (m/z): calcd for C₁₅H₁₁FN₂O₂⁺NH₄⁺: 288.1143; found: 288.1148, 1.7ppm.

Ethyl 4,4-dicyano-2-methylene-3-(4-(trifluoromethyl)phenyl)but-3-enoate: 3k

\[
\begin{align*}
\text{F}_3\text{C} & \quad \text{COOEt} \\
\end{align*}
\]

\(^1\text{H NMR}\) (300 MHz, CDCl₃): δ 7.78 (d, \(J = 8.1\) Hz, 2 H), 7.68 (d, \(J = 8.4\) Hz, 2 H), 6.95 (s, 1 H), 6.27 (s, 1 H), 4.13-4.20 (dd, \(J = 7.2\) Hz, 14.4 Hz, 2 H), 1.14 (t, \(J = 7.2\) Hz, 3 H); \(^{13}\text{C NMR}\) (75 MHz, CDCl₃): δ 169.0, 162.5, 137.4, 137.2, 135.4, 129.0, 126.2, 126.1, 112.0, 111.9, 87.3, 62.4,
13.8.

**IR**: ν 2988, 2234, 1732, 1564, 1449, 1410, 1326, 1257, 1132, 1069, 1019, 845, 698, 645, 599 cm\(^{-1}\).

**HRMS-ESI** (m/z): calcd for C\(_{16}\)H\(_{11}\)F\(_3\)N\(_2\)O\(_2\)+NH\(_4\)^+: 338.1111; found: 338.1103, 2.4 ppm.

**Ethyl 3-(3-bromophenyl)-4,4-dicyano-2-methylenebut-3-enoate: 3l**

![Chemical Structure](image)

\(\text{Br} \)

**\(^1\)H NMR** (300 MHz, CDCl\(_3\)): δ 7.35-7.72 (m, 4 H), 6.92 (s, 1 H), 6.23 (s, 1 H), 4.13-4.20 (dd, \(J = 7.2\) Hz, 14.1 Hz, 2 H), 1.16 (t, \(J = 6.9\) Hz, 3 H); **\(^{13}\)C NMR** (75 MHz, CDCl\(_3\)): δ 168.9, 162.6, 137.4, 135.7, 135.6, 135.4, 131.3, 130.7, 127.3, 123.2, 112.2, 112.1, 86.5, 62.3, 13.8.

**IR**: ν 2924, 2853, 2232, 1729, 1559, 1470, 1407, 1249, 1183, 1075, 1021, 883, 792, 735, 688 cm\(^{-1}\).

**HRMS-ESI** (m/z): calcd for C\(_{15}\)H\(_{11}\)BrN\(_2\)O\(_2\)+NH\(_4\)^+: 348.0342; found: 348.0336, 2.1 ppm.

**Ethyl 3-(3-chlorophenyl)-4,4-dicyano-2-methylenebut-3-enoate: 3m**

![Chemical Structure](image)

\(\text{Cl} \)

**\(^1\)H NMR** (300 MHz, CDCl\(_3\)): δ 7.42-7.55 (m, 4 H), 6.92 (s, 1 H), 6.22 (s, 1 H), 4.13-4.20 (dd, \(J = 7.2\) Hz, 14.4 Hz, 2 H), 1.15 (t, \(J = 7.2\) Hz, 3 H); **\(^{13}\)C NMR** (75 MHz, CDCl\(_3\)): δ 169.0, 162.6, 137.4, 135.5, 135.3, 132.6, 130.5, 128.5, 126.9, 112.2, 86.5, 62.3, 13.8.

**IR**: ν 2924, 2232, 1730, 1560, 1472, 1411, 1250, 1184, 1100, 1021, 883, 794, 752, 692, 593 cm\(^{-1}\).

**HRMS-ESI** (m/z): calcd for C\(_{15}\)H\(_{11}\)ClN\(_2\)O\(_2\)+NH\(_4\)^+: 304.0847; found: 304.0854, 2.3 ppm.

**Ethyl 4,4-dicyano-3-(2-fluorophenyl)-2-methylenebut-3-enoate: 3n**

![Chemical Structure](image)

**\(^1\)H NMR** (300 MHz, CDCl\(_3\)): δ 7.51-7.58 (m, 1 H), 7.33-7.39 (ddd, \(J = 1.8\) Hz, 7.5 Hz, 1 H), 7.18-7.29 (m, 2 H), 6.86 (s, 1 H), 6.22 (s, 1 H), 4.15-4.22 (dd, \(J = 7.2\) Hz, 14.4 Hz, 2 H), 1.17 (t, \(J = 7.2\) Hz, 3 H); **\(^{13}\)C NMR** (75 MHz, CDCl\(_3\)): δ 165.4, 162.5, 160.9, 157.5, 137.5, 134.9, 134.3,
130.0, 124.7, 122.7, 117.0, 116.7, 111.8, 89.1, 62.2, 13.8.

**IR**: ν 2924, 2234, 1730, 1612, 1581, 1450, 1371, 1254, 1184, 1108, 1021, 911, 811, 766, 675 cm⁻¹.

**HRMS-ESI (m/z)**: calcd for C₁₅H₁₁FN₂O₂⁺Na⁺: 293.0697; found: 293.0700, 1.0ppm.

**Ethyl 4,4-dicyano-3-(furan-2-yl)-2-methylenebut-3-enoate: 3o**

![Structure diagram]

**1H NMR** (300 MHz, CDCl₃): δ 7.79 (d, J = 1.5 Hz, 1 H), 7.25 (d, J = 3.6 Hz, 1 H), 6.89(s, 1 H), 6.69-6.70(q, J = 1.5 Hz, 1 H), 6.12(s, 1 H), 4.24-4.31(dd, J = 7.2 Hz, 14.1 Hz, 2 H), 1.27(t, J = 7.2 Hz, 3 H); **13C NMR** (75 MHz, CDCl₃): δ 162.8, 153.0, 149.1, 148.7, 134.9, 134.3, 122.6, 114.3, 113.1, 113.0, 78.2, 62.3, 14.0.

**IR**: ν 3134, 2985, 2227, 1726, 1570, 1457, 1395, 1266, 1182, 1091, 1032, 852, 769, 668, 586 cm⁻¹.

**HRMS-ESI (m/z)**: calcd for C₁₃H₁₀N₂O₃⁺NH₄⁺: 260.1030; found: 260.1034, 1.5ppm.

**Ethyl 4,4-dicyano-2-methylene-3-(thiophen-2-yl)but-3-enoate: 3p**

![Structure diagram]

**1H NMR** (300 MHz, CDCl₃): δ 7.85-7.91(m, 2 H), 7.26-7.29(m, 1 H), 6.90(s, 1 H), 6.13(s, 1 H), 4.23-4.30(dd, J = 7.2 Hz, 14.4 Hz, 2 H), 1.25(t, J = 6.9 Hz, 3 H); **13C NMR** (75 MHz, CDCl₃): δ 162.8, 151.5, 138.7, 137.4, 136.4, 135.7, 134.1, 129.5, 113.6, 113.1, 79.3, 62.3, 14.0.

**IR**: ν 3108, 2985, 2225, 1725, 1537, 1410, 1322, 1257, 1156, 1064, 1021, 861, 730, 611, 570 cm⁻¹.

**HRMS-ESI (m/z)**: calcd for C₁₃H₁₀N₂O₂S⁺NH₄⁺: 276.0801; found: 276.0802, 0.4ppm.

**Methyl 4,4-dicyano-3-(4-methoxyphenyl)-2-methylenebut-3-enoate: 3q**

![Structure diagram]

**1H NMR** (300 MHz, CDCl₃): δ 7.64(d, J = 9.0 Hz, 2 H), 6.99(d, J = 9.0 Hz, 2 H), 6.89(s, 1 H),
6.13 (s, 1 H), 3.88(s, 3 H), 3.74(s, 3 H); $^{13}$C NMR (75 MHz, CDCl$_3$): δ 169.0, 163.7, 137.8, 134.8, 131.4, 125.9, 115.1, 114.7, 113.5, 113.2, 82.1, 55.7, 53.0.

IR: ν 2955, 2219, 1730, 1604, 1512, 1436, 1258, 1180, 1122, 1028, 837, 784, 740, 664 cm$^{-1}$.

HRMS-ESI (m/z): calcd for C$_{15}$H$_{12}$N$_2$O$_3$+Na$: 291.0740; found: 291.0737, 1.0ppm.

Methyl 3-(4-bromophenyl)-4,4-dicyano-2-methylenebut-3-enoate: 3r

![Methyl 3-(4-bromophenyl)-4,4-dicyano-2-methylenebut-3-enoate](image)

$^1$H NMR (300 MHz, CDCl$_3$): δ 7.66(d, J = 8.7Hz, 2 H), 7.46(d, J = 8.4Hz, 2 H), 6.92(s, 1 H), 6.21(s, 1 H), 3.73(s, 3 H); $^{13}$C NMR (75 MHz, CDCl$_3$): δ 169.0, 163.2, 137.2, 135.5, 133.1, 132.6, 131.8, 130.2, 112.5, 85.7, 53.1.

IR: ν 2923, 2229, 1729, 1580, 1437, 1401, 1338, 1253, 1158, 1073, 1007, 827, 726, 611 cm$^{-1}$.

HRMS-ESI (m/z): calcd for C$_{14}$H$_{9}$BrN$_2$O$_2$+NH$_4$+: 334.0186; found: 334.0177, 2.7ppm.

(4R,5S)-ethyl 3,3-dicyano-4-hydroxy-5-isopropyl-2-(4-methoxyphenyl)cyclohex-1-enecarboxylate: 5a

![ethyl 3,3-dicyano-4-hydroxy-5-isopropyl-2-(4-methoxyphenyl)cyclohex-1-enecarboxylate](image)

Colorless solid, [α]$_D ^{20}$ = -9 ($c$=1.0, CHCl$_3$); mp 123 °C. $^1$H NMR (300 MHz, CDCl$_3$): δ 7.26-7.29(dd, J = 2.1 Hz, 6.6 Hz, 2 H), 6.91-6.93(dd, J = 1.8 Hz, 6.6 Hz, 2 H), 4.11-4.17(dd, J = 6.3 Hz, 1 H), 3.83-3.95(dd, J = 6.9 Hz, 14.1 Hz, 2 H), 3.88-3.95(dd, J = 6.9 Hz, 14.1 Hz, 2 H), 3.25(d, J = 6.9 Hz, 1 H), 2.52-2.61(dd, J = 6.0 Hz, 5.7 Hz, 1 H), 2.34-2.44(m, 2 H), 2.09-2.20(m, 1 H), 1.03(d, J = 6.9 Hz, 3 H), 0.87-0.94(m, 6.o H); $^{13}$C NMR (75 MHz, CDCl$_3$): δ 167.5, 160.3, 136.4, 130.1, 129.9, 127.4, 114.2, 114.0, 113.0, 73.7, 61.4, 55.3, 48.5, 40.4, 26.3, 25.7, 20.0, 15.2, 13.6.

IR: ν 3462, 2963, 2253, 1716, 1663, 1608, 1512, 1465, 1371, 1290, 1252, 1179, 1107, 1027, 913, 833, 734 cm$^{-1}$.

HRMS-ESI (m/z): calcd for C$_{21}$H$_{24}$N$_2$O$_4$+H$: 369.1809; found: 369.1820, 3.0ppm.

Major diastereomer: ee was determined by HPLC analysis (Chiraleel OD-H, i-PrOH/ Hexane = 5/95, 1.0 mL/min, 217 nm.) Retention time: t$_{major}$ =11.043 min, t$_{minor}$ =20.611 min, ee = 97%.
(4S,5S)-ethyl 3,3-dicyano-4-hydroxy-5-isopropyl-2-phenylcyclohex-1-enecarboxylate: 5b

\[
\begin{align*}
\text{EtOOC} & \text{CN} \\
\text{OH} & \\
\end{align*}
\]

Colorless crystal, \([\alpha]_D^{20} = -24 \ (c=1.0, \ \text{CHCl}_3)\); mp 156 °C. \(^1\text{H} \text{NMR} \ (300 \text{ MHz, CDCl}_3): \delta \ 7.33-7.41(\text{m, 5 H}), 4.14-4.20(\text{dd, } J = 6.9 \text{ Hz, 11.4 Hz, 1 H}), 3.85-3.92(\text{dd, } J = 7.2 \text{ Hz, 14.1 Hz, 2 H}), 2.99(\text{d, } J = 4.8 \text{ Hz, 1 H}), 2.56-2.64(\text{dd, } J = 6.0 \text{ Hz, 5.7 Hz, 1 H}), 2.36-2.47(\text{m, 2 H}), 2.12-2.23(\text{m, 1 H}), 1.05(\text{d, } J = 6.9 \text{ Hz, 3 H}), 0.96(\text{d, } J = 6.9 \text{ Hz, 3 H}), 0.81(\text{t, } J = 7.2 \text{ Hz, 3 H}); \(^{13}\text{C} \text{NMR} \ (75 \text{ MHz, CDCl}_3): \delta 167.2, 136.4, 135.2, 130.4, 129.4, 128.7, 128.6, 114.0, 112.8, 73.8, 61.4, 48.3, 40.4, 26.3, 25.7, 20.0, 15.3, 13.4.
\]

\textbf{IR}: \nu 3463, 2966, 2254, 1714, 1662, 1467, 1371, 1281, 1259, 1106, 1020, 765, 705 \text{ cm}^{-1}.

\textbf{HRMS-ESI} (m/z): calcd for C\textsubscript{20}H\textsubscript{22}N\textsubscript{2}O\textsubscript{3}+NH\textsubscript{4}\textsuperscript{+}:356.1969; found: 356.1979, 2.8ppm.

\textbf{Major diastereomer}: ee was determined by HPLC analysis (Chiralcel OD-H, \textit{i}-PrOH/ Hexane = 5/95, 1.0 mL/min, 213 nm.) Retention time: \(t_{\text{major}} = 7.337 \text{ min, } t_{\text{minor}} = 10.553 \text{ min, } \text{ee} = 97\%\).

(4S,5S)-ethyl 3,3-dicyano-4-hydroxy-5-isopropyl-2-(naphthalen-1-yl)cyclohex-1-enecarboxylate: 5c

\[
\begin{align*}
\text{EtOOC} & \text{CN} \\
\text{OH} & \\
\end{align*}
\]

White solid, \([\alpha]_D^{20} = -13 \ (c=1.0, \ \text{CHCl}_3)\); mp 131 °C. \(^1\text{H} \text{NMR} \ (300 \text{ MHz, CDCl}_3): \delta 8.01(\text{d, } J = 8.1 \text{ Hz, 1 H}), 7.84-7.89(\text{dd, } J = 5.1 \text{ Hz, 12.6 Hz, 2 H}), 7.43-7.55(\text{m, 4 H}), 4.23-4.29(\text{dd, } J = 6.6 \text{ Hz, 10.8 Hz, 1 H}), 3.59-3.63(\text{dd, } J = 2.4 \text{ Hz, 7.2 Hz, 2 H}), 3.24(\text{d, } J = 6.9 \text{ Hz, 1 H}), 2.80-2.88(\text{dd, } J = 5.7 \text{ Hz, 5.4 Hz, 1 H}), 2.31-2.53(\text{m, 3 H}), 1.09(\text{d, } J = 7.2 \text{ Hz, 3 H}), 0.96(\text{d, } J = 6.6 \text{ Hz, 3 H}), 0.33(\text{t, } J = 7.2 \text{ Hz, 3 H}); \(^{13}\text{C} \text{NMR} \ (75 \text{ MHz, CDCl}_3): \delta 166.7, 138.6, 133.5, 132.2, 131.4, 129.8, 128.4, 128.3, 126.7, 126.4, 125.4, 124.7, 114.1, 112.7, 74.4, 61.2, 48.8, 40.5, 26.4, 25.9, 20.1, 15.4, 12.8.
\]

\textbf{IR}: \nu 3463, 3059, 2964, 2255, 1712, 1655, 1508, 1467, 1371, 1261, 1138, 1094, 1019, 912, 778, 734 \text{ cm}^{-1}.

\textbf{HRMS-ESI} (m/z): calcd for C\textsubscript{24}H\textsubscript{24}N\textsubscript{2}O\textsubscript{3}+NH\textsubscript{4}\textsuperscript{+}:406.2125; found: 406.2130, 1.2ppm.
Major diastereomer: ee was determined by HPLC analysis (Chiralcel AS-H, \( i\)-PrOH/ Hexane = 5/95, 1.0 mL/min, 221 nm.) Retention time: \( t_{\text{major}} = 20.644 \text{ min} \), ee > 99%.

\( \text{(4S,5S)-ethyl 3,3-dicyano-4-hydroxy-5-isopropyl-2-p-tolylcyclohex-1-enecarboxylate: 5d} \)

\[
\text{Colorless crystal, } \left[ \alpha \right]_{20}^{D} = -12 (c=1.0, \ \text{CHCl}_3); \ \text{mp } 154 ^\circ\text{C.} \]

\[ ^1\text{H NMR} (300 \text{ MHz, CDCl}_3): \delta \]
\[
7.18-7.25 (m, 4 \text{ H}), 4.12-4.17 (dd, \ J = 3.6 \text{ Hz, } 11.1 \text{ Hz, } 1 \text{ H}), 3.87-3.94 (dd, \ J = 7.2 \text{ Hz, } 14.1 \text{ Hz, } 2 \text{ H}), 3.21 (d, \ J = 5.4 \text{ Hz, } 1 \text{ H}), 2.53-2.61 (dd, \ J = 6.0 \text{ Hz, } 5.7 \text{ Hz, } 1 \text{ H}), 2.35-2.45 (m, 5 \text{ H}), 2.10-2.21 (m, 1 \text{ H}), 1.03 (d, \ J = 6.9 \text{ Hz, } 3 \text{ H}), 0.94 (d, \ J = 6.9 \text{ Hz, } 3 \text{ H}), 0.86 (t, \ J = 6.9 \text{ Hz, } 3 \text{ H}); \]

\[ ^{13}\text{C NMR} (75 \text{ MHz, CDCl}_3): \delta \]
\[
167.4, 139.3, 136.2, 132.2, 130.4, 129.3, 128.5, 114.1, 112.9, 73.7, 61.4, 48.4, 40.4, 26.3, 25.7, 21.3, 20.0, 15.2, 13.4. \]

\[ \text{IR: } \nu 3430, 2968, 2249, 1718, 1666, 1510, 1464, 1394, 1370, 1279, 1255, 1108, 1055, 1017, 911, 821, 727 \text{ cm}^{-1}. \]

\[ \text{HRMS-ESI (m/z): calcd for C}_{21}\text{H}_{24}\text{N}_2\text{O}_3\text{+NH}_4^+: 370.2125; found: 370.2128, 0.8ppm.} \]

Major diastereomer: ee was determined by HPLC analysis (Chiralcel OD-H, \( i\)-PrOH/ Hexane = 5/95, 1.0 mL/min, 220 nm.) Retention time: \( t_{\text{major}} = 7.002 \text{ min} \), ee > 99%.

\( \text{(4S,5S)-ethyl 3,3-dicyano-4-hydroxy-5-isopropyl-2-(3-methoxyphenyl)cyclohex-1-enecarboxylate: 5e} \)

\[
\text{Colorless solid, } \left[ \alpha \right]_{20}^{D} = -9 (c=1.0, \ \text{CHCl}_3); \ \text{mp } 112 ^\circ\text{C.} \]

\[ ^1\text{H NMR} (300 \text{ MHz, CDCl}_3): \delta \]
\[
7.27-7.34 (dd, \ J = 8.1 \text{ Hz, } 15.9 \text{ Hz, } 1 \text{ H}), 6.89-6.97 (m, 3 \text{ H}), 4.12-4.17 (dd, \ J = 5.4 \text{ Hz, } 11.1 \text{ Hz, } 1 \text{ H}), 3.88-3.95 (dd, \ J = 6.9 \text{ Hz, } 14.1 \text{ Hz, } 2 \text{ H}), 3.81 (s, 3 \text{ H}), 3.27-3.29 (d, \ J = 6.6 \text{ Hz, } 1 \text{ H}), 2.54-2.62 (dd, \ J = 6.0 \text{ Hz, } 6.0 \text{ Hz, } 1 \text{ H}), 2.35-2.46 (m, 2 \text{ H}), 2.11-2.21 (m, 1 \text{ H}), 1.03 (d, \ J = 6.9 \text{ Hz, } 3 \text{ H}), 0.84-0.94 (m, 6 \text{ H}); \]

\[ ^{13}\text{C NMR} (75 \text{ MHz, CDCl}_3): \delta \]
\[
167.3, 159.5, 136.4, 130.1, 129.8, 121.0, 115.3, 114.1, 113.9, 113.0, 73.7, 61.5, 55.3, 48.1, 40.4, 26.3, 25.7, 20.0, 15.2, 13.4. \]

\[ \text{IR: } \nu 3463, 2963, 2254, 1716, 1657, 1581, 1466, 1427, 1371, 1287, 1261, 1209, 1104, 1031, 913, 821, 727 \text{ cm}^{-1}. \]
HRMS-ESI (m/z): calcd for C_{21}H_{24}N_{2}O_{4}+NH_{4}^{+}: 386.2074; found: 386.2072, 0.5ppm.

Major diastereomer: ee was determined by HPLC analysis (Chiralcel OD-H, i-PrOH/ Hexane = 5/95, 1.0 mL/min, 208 nm.) Retention time: t_{major} =11.019 min, ee > 99%.

(4S,5S)-ethyl 3,3-dicyano-4-hydroxy-5-isopropyl-2-m-tolylcyclohex-1-enecarboxylate: 5f

Colorless crystal, [\alpha]_{D}^{20} = -16 (c=1.0, CHCl_3); mp 128 °C. \[^1H\text{ NMR}\] (300 MHz, CDCl_3): \(\delta\) 7.28-7.32(m, 1 H), 7.12-7.26(m, 3 H), 4.60-4.62(d, \(J = 5.4\text{ Hz}\), 0.6 H), 4.12-4.18(dd, \(J = 6.6\text{ Hz}\), 1 H), 2.37-2.70(m, 5.5 H), 2.15-2.22(m, 0.5 H), 1.78-1.84(m, 1 H), 1.02-1.08(m, 5 H), 0.93-0.96(d, \(J = 6.9\text{ Hz}\), 1 H), 0.81-0.86(dt, \(J = 1.5\text{ Hz}\), 6.9 Hz, 3 H); \[^{13}C\text{ NMR}\] (75 MHz, CDCl_3): \(\delta\) 167.5, 138.2, 136.2, 135.8, 135.2, 129.9, 129.2, 128.4, 125.7, 113.5, 113.2, 73.8, 70.6, 61.2, 48.2, 40.5, 29.1, 26.6, 25.7, 21.4, 20.3, 20.0, 15.3, 13.4.

IR: \(\nu\) 3463, 2963, 2252, 1716, 1656, 1604, 1257, 1186, 1102, 1019, 714 cm\(^{-1}\).

HRMS-ESI (m/z): calcd for C_{21}H_{24}N_{2}O_{3}+NH_{4}^{+}: 370.2125; found: 370.2122, 0.8ppm.

Major diastereomer: ee was determined by HPLC analysis (Chiralcel AD-H, i-PrOH/ Hexane = 5/95, 1.0 mL/min, 215 nm.) Retention time: t_{major} =8.545 min, t_{minor} =9.853 min, ee = 96%.

(4S,5S)-ethyl 3,3-dicyano-4-hydroxy-5-isopropyl-2-o-tolylcyclohex-1-enecarboxylate: 5g

White solid, [\alpha]_{D}^{20} = -17 (c=1.0, CHCl_3); mp 134 °C. \[^1H\text{ NMR}\] (300 MHz, CDCl_3): \(\delta\) 7.21-2.28(m, 4 H), 4.61(d, \(J = 4.8\text{ Hz}\), 1 H), 3.84-3.91(m, 2 H), 3.35-3.39(m, 1 H), 2.19-2.82 (cm, 6 H), 1.80-1.82(m, 1 H), 1.03-1.05(m, 5 H), 0.91-0.94(m, 1 H), 0.76-0.84(m, 3 H); \[^{13}C\text{ NMR}\] (75 MHz, CDCl_3): \(\delta\) 167.0, 137.2, 136.4, 135.2, 130.3, 129.2, 129.0, 128.5, 127.5, 125.8, 113.4, 113.3, 73.5, 70.3, 61.2, 46.5, 40.4, 29.2, 26.6, 20.3, 19.5, 15.3, 13.3.

IR: \(\nu\) 3467, 2965, 1714, 1655, 1583, 1463, 1371, 1280, 1258, 1231, 1108, 1034, 758, 730
HRMS-ESI (m/z): calcd for C_{21}H_{24}N_{2}O_{3}^+NH_{4}^+: 370.2125; found: 370.2119, 1.6 ppm.

Major diastereomer: ee was determined by HPLC analysis (Chiralcel AD-H, i-PrOH/Hexane = 5/95, 1.0 mL/min, 215 nm.) Retention time: t_{minor} = 7.451 min, t_{major} = 8.200 min, ee = 97%.

(4S,5S)-ethyl 2-(4-bromophenyl)-3,3-dicyano-4-hydroxy-5-isopropylcyclohex-1-enecarboxylate: 5h

\[
\begin{array}{c}
\text{Br} \\
\text{EtOCOOC} \\
\text{OH}
\end{array}
\]

Colorless crystal, [\alpha]_{D}^{20} = -6 (c=1.0, CHCl_3); mp 151 °C. \textbf{^1}H NMR (300 MHz, CDCl_3): \delta 7.55-7.58 (dd, J = 2.1 Hz, 6.6 Hz, 2 H), 7.21-7.24 (dd, J = 1.8 Hz, 6.6 Hz, 2 H), 4.11-4.17 (dd, J = 6.9 Hz, 11.4 Hz, 1 H), 3.89-3.96 (dd, J = 6.9 Hz, 14.1 Hz, 2 H), 3.25 (d, J = 6.9 Hz, 1 H), 2.56-2.64 (dd, J = 5.7 Hz, 5.7 Hz, 1 H), 2.35-2.45 (m, 2 H), 2.09-2.20 (m, 1 H), 1.04 (d, J = 6.9 Hz, 3 H), 0.88-0.94 (m, 6 H); \textbf{^13}C NMR (75 MHz, CDCl_3): \delta 166.8, 137.1, 134.0, 131.9, 130.4, 129.4, 123.9, 113.9, 112.7, 73.7, 61.7, 48.1, 40.4, 26.3, 25.6, 20.0, 15.2, 13.5.

IR: \nu 3465, 2964, 2255, 1717, 1657, 1587, 1487, 1392, 1371, 1257, 1105, 1072, 1012, 912, 825, 733 cm\(^{-1}\).

HRMS-ESI (m/z): calcd for C_{20}H_{21}BrN_{2}O_{3}^+NH_{4}^+: 434.1074; found: 434.1072, 0.5 ppm.

Major diastereomer: ee was determined by HPLC analysis (Chiralecel OD-H, i-PrOH/Hexane = 5/95, 1.0 mL/min, 216 nm.) Retention time: t_{major} = 7.164 min, t_{minor} = 10.085 min, ee = 95%.

(4S,5S)-ethyl 2-(4-chlorophenyl)-3,3-dicyano-4-hydroxy-5-isopropylcyclohex-1-enecarboxylate: 5i

\[
\begin{array}{c}
\text{Cl} \\
\text{EtOCOOC} \\
\text{OH}
\end{array}
\]

Colorless crystal, [\alpha]_{D}^{20} = -10 (c=1.0, CHCl_3); mp 140 °C. \textbf{^1}H NMR (300 MHz, CDCl_3): \delta 7.38-7.42 (m, 2 H), 7.26-7.31 (m, 2 H), 4.12-4.18 (dd, J = 5.4 Hz, 11.4 Hz, 1 H), 3.89-3.96 (dd, J = 7.2 Hz, 14.4 Hz, 2 H), 3.19 (d, J = 6.3 Hz, 1 H), 2.35-2.66 (m, 3 H), 2.10-2.20 (m, 1 H), 1.04 (d, J = 7.2 Hz, 3 H), 0.87-0.94 (m, 6 H); \textbf{^13}C NMR (75 MHz, CDCl_3): \delta 166.9, 137.1, 135.7, 133.6, 130.2,
129.3, 129.0, 113.9, 112.7, 73.7, 61.7, 48.1, 40.4, 26.3, 25.6, 20.0, 15.2, 13.5.

**IR:** ν 3463, 2963, 2927, 2255, 1717, 1655, 1593, 1491, 1467, 1371, 1257, 1094, 1015, 912, 828, 732 cm\(^{-1}\).

**HRMS-ESI** \((m/z)\): calcd for C\(_{20}\)H\(_{21}\)ClN\(_2\)O\(_3\)+NH\(_4^+\): 390.1579; found: 390.1573, 1.5ppm.

**Major diastereomer:** ee was determined by HPLC analysis (Chiralcel OD-H, \(i\)-PrOH/Hexane = 5/95, 1.0 mL/min, 220 nm.) Retention time: \(t_{\text{major}}\) = 6.651 min, \(t_{\text{minor}}\) = 8.576 min, ee = 97%.

\((4S,5S)\)-ethyl 3,3-dicyano-2-(4-fluorophenyl)-4-hydroxy-5-isopropylcyclohex-1-enecarboxylate: 5j

\[
\begin{align*}
\text{Colorless crystal, } [\alpha]_{D}^{20} & = -14 \ (c=1.0, \text{CHCl}_3); \text{ mp } 140 \degree C. \\
\text{H NMR} \ (300 \text{ MHz, CDCl}_3): \delta 7.30-7.36 (m, 2 H), 7.07-7.14 (m, 2 H), 4.62 (d, } J = 5.7 \text{ Hz, 0.4 H), 4.11-4.18 (dd, } J = 6.9 \text{ Hz, 11.4 Hz, 2 H), 2.34-2.71 (m, 2.5 H), 2.11-2.20 (m, 0.5 H), 1.75-1.85 (m, 1 H), 1.02-1.06 (m, 4 H), 0.86-0.94 (m, 5 H); \\
\text{C NMR} \ (75 \text{ MHz, CDCl}_3): \delta 167.2, 167.0, 137.2, 131.8, 131.7, 130.9, 130.8, 129.3, 127.8, 115.9, 115.6, 114.0, 112.7, 73.7, 70.3, 61.4, 48.3, 46.1, 40.4, 29.0, 26.6, 26.3, 25.6, 20.3, 20.0, 15.2, 13.5. \\
\text{IR: } \nu 3466, 2965, 2256, 1716, 1655, 1602, 1509, 1470, 1372, 1234, 1161, 1101, 1016, 913, 837, 734 \text{ cm}^{-1}. \\
\text{HRMS-ESI} \ (m/z): \text{ calcd for C}_{20}\text{H}_{21}\text{FN}_{2}\text{O}_{3}+\text{NH}_{4}^+: 374.1874; \text{ found: 374.1865, 2.4ppm.}
\end{align*}
\]

**Major diastereomer:** ee was determined by HPLC analysis (Chiralcel OD-H, \(i\)-PrOH/Hexane = 5/95, 1.0 mL/min, 220 nm.) Retention time: \(t_{\text{major}}\) = 7.030 min, \(t_{\text{minor}}\) = 9.108 min, ee = 93%.

\((4S,5S)\)-ethyl 3,3-dicyano-4-hydroxy-5-isopropyl-2-(4-(trifluoromethyl)phenyl)cyclohex-1-enecarboxylate: 5k

\[
\begin{align*}
\text{White solid, } [\alpha]_{D}^{20} & = -14 \ (c=1.0, \text{CHCl}_3); \text{ mp } 140 \degree C. \\
\text{H NMR} \ (300 \text{ MHz, CDCl}_3): \delta 7.71 (d, } J = 8.1 \text{ Hz, 2 H), 7.50 (d, } J = 8.1 \text{ Hz, 2 H), 4.15-4.21 (dd, } J = 6.9 \text{ Hz, 11.4 Hz, 1 H), 3.87-3.94 (dd, } J =
\end{align*}
\]
6.9 Hz, 14.1 Hz, 2 H), 3.16(d, J = 6.9 Hz, 1 H), 2.60-2.69(dd, J = 5.7 Hz, 5.7 Hz, 1 H), 2.36-2.48(m, 2 H), 2.12-2.23(m, 1 H), 1.05(d, J = 6.9 Hz, 3 H), 0.96(d, J = 6.9 Hz, 3 H), 0.82(t, J = 7.2 Hz, 3 H); \textsuperscript{13}C NMR (75 MHz, CDCl\textsubscript{3}): \text{\delta} 166.5, 138.8, 137.4, 129.5, 129.4, 125.6, 125.5, 113.7, 112.5, 73.8, 61.7, 47.9, 40.4, 26.4, 25.7, 20.0, 15.2, 13.3.

IR: \nu 3462, 2965, 2255, 1718, 1656, 1371, 1326, 1256, 1169, 1131, 1069, 1018, 838, 736 cm\textsuperscript{-1}.

HRMS-ESI (m/z): calcd for C\textsubscript{21}H\textsubscript{21}F\textsubscript{3}N\textsubscript{2}O\textsubscript{3}+NH\textsubscript{4}\textsuperscript{+}: 424.1843; found: 424.1847, 0.9ppm.

Major diastereomer: ee was determined by HPLC analysis (Chiralcel OD-H, \textit{i}-PrOH/ Hexane = 5/95, 0.5 mL/min, 215 nm.) Retention time: t\textsubscript{major} = 12.259 min, ee >99%.

(4S,5S)-ethyl 2-(3-bromophenyl)-3,3-dicyano-4-hydroxy-5-isopropylcyclohex-1-enecarboxylate: 5l

![Chemical Structure](image)

Pale yellow solid, [\alpha]\textsuperscript{20}D = -11 \degree (c=1.0, CHCl\textsubscript{3}); mp 134 °C. \textsuperscript{1}H NMR (300 MHz, CDCl\textsubscript{3}): \text{\delta} 7.54-7.58(m, 1 H), 7.48-7.49(m, 1 H), 7.29-7.32(m, 2 H), 4.63-4.64(d, J = 5.4 Hz, 1 H), 3.91-3.98(dd, J = 6.9 Hz, 14.1 Hz, 2 H), 2.85(t, J = 5.4 Hz, 1 H), 2.38-2.73(m, 2.5 H), 2.13-2.22(m, 0.5 H), 1.77-1.86(m, 1 H), 0.87-1.08(m, 9 H); \textsuperscript{13}C NMR (75 MHz, CDCl\textsubscript{3}): \text{\delta} 166.8, 137.4, 132.5, 132.3, 131.8, 130.1, 129.0, 127.4, 122.5, 113.1, 112.5, 77.4, 77.0, 76.6, 73.8, 61.4, 47.9, 40.4, 29.1, 26.6, 25.7, 20.3, 15.3, 13.5.

IR: \nu 3463, 2964, 2254, 1716, 1654, 1561, 1471, 1371, 1282, 1258, 1137, 1074, 788, 733, 704, 664 cm\textsuperscript{-1}.

HRMS-ESI (m/z): calcd for C\textsubscript{20}H\textsubscript{21}BrN\textsubscript{2}O\textsubscript{3}+NH\textsubscript{4}\textsuperscript{+}: 434.1071; found: 434.1060, 2.5ppm.

Major diastereomer: ee was determined by HPLC analysis (Chiralcel OD-H, \textit{i}-PrOH/ Hexane = 5/95, 0.5 mL/min, 223 nm.) Retention time: t\textsubscript{major} = 14.406 min, t\textsubscript{minor} = 19.203 min, ee = 96%.

(4S,5S)-ethyl 2-(3-chlorophenyl)-3,3-dicyano-4-hydroxy-5-isopropylcyclohex-1-enecarboxylate: 5m

![Chemical Structure](image)
White solid, [α]_D^20 = -15 (c=1.0, CHCl₃); mp 105 °C. \(^1\)H NMR (300 MHz, CDCl₃): δ 7.23-7.39(m, 4 H), 4.62(br, 1 H), 3.90-3.97(dd, J = 6.9 Hz, 14.1 Hz, 2 H), 3.22(s, 1 H), 2.65-2.72(m, 2.5 H), 2.13-2.21(m, 0.5 H), 1.76-1.83(m, 1 H), 1.02-1.07(m, 4 H), 0.86-0.95(m, 5 H); \(^13\)C NMR (75 MHz, CDCl₃): δ 167.0, 137.5, 134.4, 129.9, 129.6, 129.4, 129.0, 127.5, 127.0, 113.2, 113.0, 73.7, 70.4, 61.5, 47.9, 40.5, 29.1, 26.6, 20.3, 15.2, 13.5.

IR: ν 3461, 2962, 2928, 2250, 1719, 1655, 1565, 1471, 1371, 1283, 1259, 1136, 1087, 1017, 789, 706 cm⁻¹.

HRMS-ESI (m/z): calcld for C₂₀H₂₁ClN₂O₃⁺NH₄⁺:390.1579; found: 390.1571, 2.1ppm.

Major diastereomer: ee was determined by HPLC analysis (Chiralcel OD-H, i-PrOH/ Hexane = 5/95, 0.5 mL/min, 213 nm.) Retention time: t_major =14.118 min, ee >99%.

(4S,5S)-ethyl 3,3-dicyano-2-(2-fluorophenyl)-4-hydroxy-5-isopropylcyclohex-1-enecarboxylate: 5n

White solid, [α]_D^20 = -40 (c=1.0, CHCl₃); mp 134 °C. \(^1\)H NMR (300 MHz, CDCl₃): δ 7.38-7.44(m, 2 H), 7.11-7.24(m, 2 H), 4.63(d, J = 6.0 Hz, 0.4 H), 4.14-4.20(dd, J = 6.9 Hz, 11.4 Hz, 0.6 H), 3.90-3.97(dd, J = 7.2Hz, 14.4 Hz, 2 H), 3.29-3.39(dd, J = 6.9 Hz, 6.0 Hz, 1 H), 2.64-2.79(m, 1 H), 2.35-2.55(m, 1.5 H), 2.14-2.23(m, 0.5 H), 1.81-1.85(m, 1 H), 1.02-1.06(m, 4 H), 0.85-0.94(m, 5 H); \(^13\)C NMR (75 MHz, CDCl₃): δ 166.2, 158.0, 131.5, 131.4, 131.3, 124.4, 115.9, 115.6, 70.4, 61.6, 48.3, 40.4, 29.1, 26.3, 25.7, 20.3, 20.2, 20.0, 15.2, 13.4.

IR: ν 3468, 2966, 2254, 1715, 1657, 1613, 1490, 1448, 1371, 1261, 1136, 1104, 1021, 808, 763 cm⁻¹.

HRMS-ESI (m/z): calcld for C₂₀H₂₁FN₂O₃⁺NH₄⁺:374.1874; found: 374.1871, 0.3ppm.

Major diastereomer: ee was determined by HPLC analysis (Chiralcel OD-H, i-PrOH/ Hexane = 5/95, 1.0 mL/min, 213 nm.) Retention time: t_major =9.269 min, t_minor =11.573 min, ee =97%.

(4S,5S)-ethyl 3,3-dicyano-2-(furan-2-yl)-4-hydroxy-5-isopropylcyclohex-1-enecarboxylate: 5o
Colorless solid, $[\alpha]^2_D = -23$ ($c=1.0$, CHCl$_3$); mp 114 °C. $^1$H NMR (300 MHz, CDCl$_3$): $\delta$ 7.47(d, $J = 1.2$ Hz, 1 H), 6.69-6.73(dd, $J = 3.6$ Hz, 9.0 Hz, 1 H), 6.46-6.49(m, 1 H), 4.62(d, $J = 4.2$ Hz, 1 H), 4.20-4.25(dd, $J = 6.0$ Hz, 6.9 Hz, 2 H), 3.49-3.57(dd, $J = 7.2$ Hz, 5.7 Hz, 1 H), 2.34-2.64(m, 2.5 H), 2.09-2.11(m, 0.5 H), 1.69-1.84(m, 1 H), 1.19-1.24(dt, $J = 1.8$ Hz, 6.9 Hz, 3 H), 0.98-1.04(m, 5 H), 0.88(d, $J = 6.9$ Hz, 1 H); $^{13}$C NMR (75 MHz, CDCl$_3$): $\delta$ 168.5, 147.5, 143.6, 135.9, 135.1, 116.8, 113.5, 112.9, 111.6, 111.2, 73.9, 70.5, 61.9, 44.6, 40.5, 28.9, 27.1, 20.2, 14.0.

**IR:** $\nu$ 3466, 3154, 2966, 2256, 1723, 1652, 1472, 1371, 1284, 1250, 1162, 1020, 911, 743, 591 cm$^{-1}$.

**HRMS-ESI** ($m/z$): calcd for C$_{18}$H$_{20}$N$_2$O$_4$+NH$_4^+$:346.1761; found: 346.1750, 2.9ppm.

**Major diastereomer:** ee was determined by HPLC analysis (Chiralcel OD-H, $i$-PrOH/ Hexane = 5/95, 1.0 mL/min, 275 nm.) Retention time: $t_{major} = 12.100$ min, ee>99%.

(4S,5S)-ethyl 3,3-dicyano-4-hydroxy-5-isopropyl-2-(thiophen-2-yl)cyclohex-1-enecarboxylate:

Pale yellow solid, $[\alpha]^2_D = +35$ ($c=1.0$, CHCl$_3$); mp 153 °C. $^1$H NMR (300 MHz, CDCl$_3$): $\delta$ 7.42-7.44(dd, $J = 1.2$ Hz, 5.1 Hz, 1 H), 7.18-7.20(dd, $J = 0.9$ Hz, 3.3 Hz, 1 H), 7.05-7.08(dd, $J = 3.6$ Hz, 5.1 Hz, 1 H), 4.12-4.18(dd, $J = 6.9$ Hz, 11.4 Hz, 1 H), 3.98-4.05(dd, $J = 7.2$ Hz, 14.1 Hz, 2 H), 3.26(d, $J = 6.9$ Hz, 1 H), 2.54-2.62(dd, $J = 6.0$ Hz, 5.7 Hz, 1 H), 2.35-2.45(m, 2 H), 2.09-2.19(m, 1 H), 0.99-1.03(m, 6 H), 0.93(d, $J = 6.9$ Hz, 3 H); $^{13}$C NMR (75 MHz, CDCl$_3$): $\delta$ 167.3, 139.3, 134.7, 129.1, 127.9, 127.3, 123.3, 114.1, 112.7, 73.6, 61.8, 48.6, 40.3, 26.7, 25.6, 20.0, 15.2, 13.6.

**IR:** $\nu$ 3471, 3108, 2965, 2254, 1725, 1650, 1464, 1435, 1370, 1260, 1196, 1095, 1016, 855, 713 cm$^{-1}$.

**HRMS-ESI** ($m/z$): calcd for C$_{18}$H$_{20}$N$_2$O$_3$S+NH$_4^+$:362.1533; found: 362.1537, 1.1ppm.

**Major diastereomer:** ee was determined by HPLC analysis (Chiralcel OD-H, $i$-PrOH/ Hexane =
(4S,5R)-ethyl 3,3-dicyano-5-ethyl-4-hydroxy-2-(4-methoxyphenyl)cyclohex-1-enecarboxylate:

5q

White solid, $[\alpha]_{D}^{20} = -21 \ (c=1.0, \text{CHCl}_3)$; mp 102 °C. $^1$H NMR (300 MHz, CDCl$_3$): $\delta$ 7.25-7.31 (m, 2 H), 6.90-6.95 (m, 2 H), 4.02-4.07 (dd, $J = 2.7 \text{ Hz}, 3.3 \text{ Hz}, 1 \text{ H}$), 3.89-3.96 (dd, $J = 7.2 \text{ Hz}, 14.4 \text{ Hz}, 2 \text{ H}$), 3.83 (s, 3 H), 3.18 (br, 1 H), 2.75-2.83 (dd, $J = 5.4 \text{ Hz}, 5.7 \text{ Hz}, 1 \text{ H}$), 2.25-2.33 (m, 1 H), 1.96-2.13 (m, 2 H), 1.31-1.41(m, 1 H), 0.99-1.04 (m, 3 H), 0.90 (t, $J = 7.2 \text{ Hz}, 3 \text{ H}$); $^{13}$C NMR (75 MHz, CDCl$_3$): $\delta$ 167.4, 160.3, 136.0, 130.3, 130.1, 127.4, 114.0, 112.9, 75.1, 61.4, 55.3, 48.1, 37.1, 31.6, 23.5, 13.6, 10.1.

IR: $\nu$ 3463, 2969, 2253, 1716, 1656, 1608, 1180, 1105, 1028, 832, 735 cm$^{-1}$.

HRMS-ESI ($m/z$): calcd for C$_{20}$H$_{22}$N$_2$O$_4$+NH$_4^+$: 372.1918; found: 372.1928, 2.7ppm.

Major diastereomer: ee was determined by HPLC analysis (Chiralcel OD-H, $i$-PrOH/ Hexane = 5/95, 1.0 mL/min, 216 nm.) Retention time: $t_{\text{major}} = 13.859 \text{ min}, t_{\text{minor}} = 22.268 \text{ min}$, ee = 92%.

(4S,5S)-ethyl 3,3-dicyano-4-hydroxy-2-(4-methoxyphenyl)-5-phenylcyclohex-1-enecarboxylate: 5r

White solid, $[\alpha]_{D}^{20} = -7 \ (c=1.0, \text{CHCl}_3)$; mp 154 °C. $^1$H NMR (300 MHz, CDCl$_3$): $\delta$ 7.33-7.43 (m, 7 H), 6.94-6.97 (dd, $J = 1.8 \text{ Hz}, 6.6 \text{ Hz}, 2 \text{ H}$), 4.52 (d, $J = 11.1 \text{ Hz}, 1 \text{ H}$), 3.89-3.96 (dd, $J = 7.2 \text{ Hz}, 14.1 \text{ Hz}, 2 \text{ H}$), 3.84 (s, 3 H), 3.27-3.37 (m, 1 H), 2.79-3.00 (m, 2 H), 2.46 (br, 1 H), 0.91 (t, $J = 7.2 \text{ Hz}, 3 \text{ H}$); $^{13}$C NMR (75 MHz, CDCl$_3$): $\delta$ 166.8, 160.4, 137.1, 135.8, 130.8, 130.2, 129.6, 128.6, 128.1, 127.1, 114.0, 113.5, 112.5, 74.4, 61.5, 55.3, 47.3, 44.0, 34.6, 13.6.

IR: $\nu$ 3452, 2954, 2841, 2255, 1723, 1655, 1607, 1512, 1436, 1289, 1252, 1181, 1114, 1029, 912, 830, 733, 702 cm$^{-1}$.

HRMS-ESI ($m/z$): calcd for C$_{24}$H$_{22}$N$_2$O$_4$+NH$_4^+$: 420.1918; found: 420.1909, 2.1ppm.
**Major diastereomer**: ee was determined by HPLC analysis (Chiralcel OJ-H, i-PrOH/ Hexane = 5/95, 1.0 mL/min, 222 nm.) Retention time: t\text{major} = 13.101 min, ee > 99%.

\(4S,5S\)-methyl 3,3-dicyano-4-hydroxy-5-isopropyl-2-(4-methoxyphenyl)cyclohex-1-enecarboxylate: 5s

![Image]

Colorless solid, \([\alpha]\)\text{D} = -6 (c=1.0, CHCl\text{3}); mp 130 °C. \(\text{\textsuperscript{1}H NMR}\) (300 MHz, CDCl\text{3}): δ 7.24-7.29(m, 2 H), 6.90-6.94(m, 2 H), 4.60(s, 1 H), 3.83(s, 3 H), 3.48(s, 3 H), 3.14(br, 1 H), 2.34-2.68(m, 2.5 H), 1.72-1.85(m, 1.5 H), 1.01-1.06(m, 6 H); \(\text{\textsuperscript{13}C NMR}\) (75 MHz, CDCl\text{3}): δ 168.1, 160.1, 136.2, 129.9, 128.7, 127.9, 114.0, 113.5, 73.7, 70.5, 55.2, 52.2, 46.2, 40.5, 29.0, 26.7, 20.3, 15.2.

IR: v 3468, 2962, 2255, 1721, 1654, 1512, 1437, 1370, 1324, 1253, 1181, 1030, 972, 913, 831, 734 cm\(^{-1}\).

HRMS-ESI (m/z): calcd for C\textsubscript{20}H\textsubscript{22}N\textsubscript{2}O\textsubscript{4}+H\textsuperscript{+}: 355.1652; found: 355.1646, 1.7ppm.

**Major diastereomer**: ee was determined by HPLC analysis (Chiralcel OD-H, i-PrOH/ Hexane = 5/95, 1.0 mL/min, 224 nm.) Retention time: t\text{major} = 11.699 min, t\text{minor} = 25.162 min, ee = 93%.

\(4S,5S\)-methyl 2-(4-bromophenyl)-3,3-dicyano-4-hydroxy-5-isopropylcyclohex-1-enecarboxylate: 5t

![Image]

Colorless solid, \([\alpha]\)\text{D} = -8 (c=1.0, CHCl\text{3}); mp 141 °C. \(\text{\textsuperscript{1}H NMR}\) (300 MHz, CDCl\text{3}): δ 7.54-7.58(m, 2 H), 7.19-7.24(m, 2 H), 4.16(d, \(J = 11.1\) Hz, 1 H), 3.49(s, 3 H), 3.05(br, 1 H), 2.35-2.64(m, 3 H), 2.10-2.21(m, 1 H), 1.04(d, \(J = 7.2\) Hz, 3 H), 0.95(d, \(J = 6.9\) Hz, 3 H); \(\text{\textsuperscript{13}C NMR}\) (75 MHz, CDCl\text{3}): δ 167.1, 136.7, 133.9, 132.0, 130.1, 129.8, 124.0, 113.8, 112.6, 73.7, 52.4, 48.0, 40.3, 26.4, 25.6, 20.0, 15.2.

IR: v 3467, 2961, 2255, 1724, 1654, 1587, 1487, 1435, 1393, 1256, 1107, 1071, 1010, 911, 818, 731 cm\(^{-1}\).
**HRMS-ESI** (m/z): calcd for C_{19}H_{19}BrN_{2}O_{3}+H^{+}: 403.0652; found: 403.0642, 2.5ppm.

**Major diastereomer**: ee was determined by HPLC analysis (Chiralcel OD-H, i-PrOH/Hexane = 5/95, 1.0 mL/min, 218 nm.) Retention time: t_{major} = 7.921 min, t_{minor} = 12.481 min, ee = 96%.

5.0 References.

6.0 X-Ray structure of 5i

(4S,5S)-ethyl 2-(4-chlorophenyl)-3,3-dicyano-4-hydroxy-5-isopropylcyclohex-1-enecarboxylate: 5i (CCDC 825720).
7.0. Copies of HPLC spectra of racemic/chiral products

(4S,5S)-ethyl 3,3-dicyano-4-hydroxy-5-isopropyl-2-(4-methoxyphenyl)cyclohex-1-enecarboxylate: 5a

![Chemical structure of 5a]

<table>
<thead>
<tr>
<th>Entry</th>
<th>Retention Time</th>
<th>Area (%)</th>
<th>Int Type</th>
<th>Peak Type</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>10.530</td>
<td>50.35</td>
<td>bb</td>
<td>Unknown</td>
</tr>
<tr>
<td>2</td>
<td>19.102</td>
<td>49.65</td>
<td>bb</td>
<td>Unknown</td>
</tr>
</tbody>
</table>

![HPLC spectrum of 5a]

<table>
<thead>
<tr>
<th>Entry</th>
<th>Retention Time</th>
<th>Area (%)</th>
<th>Int Type</th>
<th>Peak Type</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>11.043</td>
<td>98.34</td>
<td>bb</td>
<td>Unknown</td>
</tr>
<tr>
<td>2</td>
<td>20.611</td>
<td>1.66</td>
<td>bb</td>
<td>Unknown</td>
</tr>
</tbody>
</table>
(4S,5S)-ethyl 3,3-dicyano-4-hydroxy-5-isopropyl-2-phenylcyclohex-1-enecarboxylate: 5b

![Chemical Structure]

<table>
<thead>
<tr>
<th>Entry</th>
<th>Retention Time</th>
<th>Area (%)</th>
<th>Int Type</th>
<th>Peak Type</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>7.510</td>
<td>50.82</td>
<td>bb</td>
<td>Unknown</td>
</tr>
<tr>
<td>2</td>
<td>10.590</td>
<td>49.18</td>
<td>bb</td>
<td>Unknown</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Entry</th>
<th>Retention Time</th>
<th>Area (%)</th>
<th>Int Type</th>
<th>Peak Type</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>7.337</td>
<td>98.41</td>
<td>bb</td>
<td>Unknown</td>
</tr>
<tr>
<td>2</td>
<td>10.553</td>
<td>1.59</td>
<td>bb</td>
<td>Unknown</td>
</tr>
</tbody>
</table>
(4S,5S)-ethyl 3,3-dicyano-4-hydroxy-5-isopropyl-2-(naphthalen-1-yl)cyclohex-1-enecarboxylate: 5c

![Chemical Structure]

<table>
<thead>
<tr>
<th>Entry</th>
<th>Retention Time</th>
<th>Area (%)</th>
<th>Int Type</th>
<th>Peak Type</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>18.983</td>
<td>54.89</td>
<td>bb</td>
<td>Unknown</td>
</tr>
<tr>
<td>2</td>
<td>44.088</td>
<td>45.11</td>
<td>bb</td>
<td>Unknown</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Entry</th>
<th>Retention Time</th>
<th>Area (%)</th>
<th>Int Type</th>
<th>Peak Type</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>20.644</td>
<td>100.00</td>
<td>bb</td>
<td>Unknown</td>
</tr>
<tr>
<td>2</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
(4S,5S)-ethyl 3,3-dicyano-4-hydroxy-5-isopropyl-2-p-tolylcyclohex-1-enecarboxylate: 5d

<table>
<thead>
<tr>
<th>Entry</th>
<th>Retention Time</th>
<th>Area (%)</th>
<th>Int Type</th>
<th>Peak Type</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>7.322</td>
<td>50.65</td>
<td>bb</td>
<td>Unknown</td>
</tr>
<tr>
<td>2</td>
<td>13.980</td>
<td>49.35</td>
<td>bb</td>
<td>Unknown</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Entry</th>
<th>Retention Time</th>
<th>Area (%)</th>
<th>Int Type</th>
<th>Peak Type</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>7.002</td>
<td>100.00</td>
<td>bb</td>
<td>Unknown</td>
</tr>
<tr>
<td>2</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
(4S,5S)-ethyl 3,3-dicyano-4-hydroxy-5-isopropyl-2-(3-methoxyphenyl)cyclohex-1-enecarboxylate: 5e

![Chemical Structure](image)

<table>
<thead>
<tr>
<th>Entry</th>
<th>Retention Time</th>
<th>Area (%)</th>
<th>Int Type</th>
<th>Peak Type</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>11.041</td>
<td>48.69</td>
<td>bb</td>
<td>Unknown</td>
</tr>
<tr>
<td>2</td>
<td>12.681</td>
<td>51.31</td>
<td>bb</td>
<td>Unknown</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Entry</th>
<th>Retention Time</th>
<th>Area (%)</th>
<th>Int Type</th>
<th>Peak Type</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>11.019</td>
<td>100.00</td>
<td>bb</td>
<td>Unknown</td>
</tr>
<tr>
<td>2</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
(4S,5S)-ethyl 3,3-dicyano-4-hydroxy-5-isopropyl-2-m-tolyclohex-1-ene carboxylate: 5f

![Chemical Structure](image)

<table>
<thead>
<tr>
<th>Entry</th>
<th>Retention Time</th>
<th>Area (%)</th>
<th>Int Type</th>
<th>Peak Type</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>8.574</td>
<td>64.51</td>
<td>bb</td>
<td>Unknown</td>
</tr>
<tr>
<td>2</td>
<td>9.867</td>
<td>35.49</td>
<td>bb</td>
<td>Unknown</td>
</tr>
</tbody>
</table>

![Retention Time Graph](image)

<table>
<thead>
<tr>
<th>Entry</th>
<th>Retention Time</th>
<th>Area (%)</th>
<th>Int Type</th>
<th>Peak Type</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>8.545</td>
<td>98.15</td>
<td>bb</td>
<td>Unknown</td>
</tr>
<tr>
<td>2</td>
<td>9.853</td>
<td>1.85</td>
<td>bb</td>
<td>Unknown</td>
</tr>
</tbody>
</table>
(4S,5S)-ethyl 3,3-dicyano-4-hydroxy-5-isopropyl-2-o-tolyloctahex-1-enecarboxylate: 5g

<table>
<thead>
<tr>
<th>Entry</th>
<th>Retention Time</th>
<th>Area (%)</th>
<th>Int Type</th>
<th>Peak Type</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>7.403</td>
<td>51.93</td>
<td>bb</td>
<td>Unknown</td>
</tr>
<tr>
<td>2</td>
<td>8.023</td>
<td>48.07</td>
<td>bb</td>
<td>Unknown</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Entry</th>
<th>Retention Time</th>
<th>Area (%)</th>
<th>Int Type</th>
<th>Peak Type</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>7.451</td>
<td>1.38</td>
<td>bb</td>
<td>Unknown</td>
</tr>
<tr>
<td>2</td>
<td>8.200</td>
<td>98.62</td>
<td>bb</td>
<td>Unknown</td>
</tr>
</tbody>
</table>
(4S,5S)-ethyl 2-(4-bromophenyl)-3,3-dicyano-4-hydroxy-5-isopropylcyclohex-1-enecarboxylate: 5h

![Chemical Structure](image)

<table>
<thead>
<tr>
<th>Entry</th>
<th>Retention Time</th>
<th>Area (%)</th>
<th>Int Type</th>
<th>Peak Type</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>7.252</td>
<td>53.86</td>
<td>bb</td>
<td>Unknown</td>
</tr>
<tr>
<td>2</td>
<td>10.064</td>
<td>46.14</td>
<td>bb</td>
<td>Unknown</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Entry</th>
<th>Retention Time</th>
<th>Area (%)</th>
<th>Int Type</th>
<th>Peak Type</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>7.164</td>
<td>97.37</td>
<td>bb</td>
<td>Unknown</td>
</tr>
<tr>
<td>2</td>
<td>10.085</td>
<td>2.63</td>
<td>bb</td>
<td>Unknown</td>
</tr>
</tbody>
</table>
(45S,55S)-ethyl 2-(4-chlorophenyl)-3,3-dicyano-4-hydroxy-5-isopropylcyclohex-1-enecarboxylate: 5i

![Chemical Structure](image)

<table>
<thead>
<tr>
<th>Entry</th>
<th>Retention Time</th>
<th>Area (%)</th>
<th>Int Type</th>
<th>Peak Type</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>6.811</td>
<td>48.44</td>
<td>bb</td>
<td>Unknown</td>
</tr>
<tr>
<td>2</td>
<td>8.863</td>
<td>51.56</td>
<td>bb</td>
<td>Unknown</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Entry</th>
<th>Retention Time</th>
<th>Area (%)</th>
<th>Int Type</th>
<th>Peak Type</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>6.651</td>
<td>98.65</td>
<td>bb</td>
<td>Unknown</td>
</tr>
<tr>
<td>2</td>
<td>8.576</td>
<td>1.35</td>
<td>bb</td>
<td>Unknown</td>
</tr>
</tbody>
</table>
(4S,5S)-ethyl 3,3-dicyano-2-(4-fluorophenyl)-4-hydroxy-5-isopropyl cyclohex-1-ene carboxylate: 5j

![Chemical Structure](image)

<table>
<thead>
<tr>
<th>Entry</th>
<th>Retention Time</th>
<th>Area (%)</th>
<th>Int Type</th>
<th>Peak Type</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>7.045</td>
<td>47.62</td>
<td>bb</td>
<td>Unknown</td>
</tr>
<tr>
<td>2</td>
<td>9.013</td>
<td>52.38</td>
<td>bb</td>
<td>Unknown</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Entry</th>
<th>Retention Time</th>
<th>Area (%)</th>
<th>Int Type</th>
<th>Peak Type</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>7.030</td>
<td>96.43</td>
<td>bb</td>
<td>Unknown</td>
</tr>
<tr>
<td>2</td>
<td>9.108</td>
<td>3.57</td>
<td>bb</td>
<td>Unknown</td>
</tr>
</tbody>
</table>
(4S,5S)-ethyl 3,3-dicyano-4-hydroxy-5-isopropyl-2-(4-(trifluoromethyl)phenyl)cyclohex-1-enecarboxylate: 5k

![Chemical Structure](image)

<table>
<thead>
<tr>
<th>Entry</th>
<th>Retention Time</th>
<th>Area (%)</th>
<th>Int Type</th>
<th>Peak Type</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>12.418</td>
<td>50.58</td>
<td>bb</td>
<td>Unknown</td>
</tr>
<tr>
<td>2</td>
<td>15.254</td>
<td>49.42</td>
<td>bb</td>
<td>Unknown</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Entry</th>
<th>Retention Time</th>
<th>Area (%)</th>
<th>Int Type</th>
<th>Peak Type</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>12.259</td>
<td>100.00</td>
<td>bb</td>
<td>Unknown</td>
</tr>
<tr>
<td>2</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Electronic Supplementary Material (ESI) for Chemical Communications
This journal is © The Royal Society of Chemistry 2011
(4S,5S)-ethyl 2-(3-bromophenyl)-3,3-dicyano-4-hydroxy-5-isopropylcyclohex-1-ene carboxylate: **5l**

![Chemical Structure](image)

<table>
<thead>
<tr>
<th>Entry</th>
<th>Retention Time</th>
<th>Area (%)</th>
<th>Int Type</th>
<th>Peak Type</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>14.802</td>
<td>50.42</td>
<td>bb</td>
<td>Unknown</td>
</tr>
<tr>
<td>2</td>
<td>19.444</td>
<td>49.58</td>
<td>bb</td>
<td>Unknown</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Entry</th>
<th>Retention Time</th>
<th>Area (%)</th>
<th>Int Type</th>
<th>Peak Type</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>14.406</td>
<td>98.22</td>
<td>bb</td>
<td>Unknown</td>
</tr>
<tr>
<td>2</td>
<td>19.203</td>
<td>1.78</td>
<td>bb</td>
<td>Unknown</td>
</tr>
</tbody>
</table>
(4S,5S)-ethyl 2-(3-chlorophenyl)-3,3-dicyano-4-hydroxy-5-isopropylcyclohex-1-enecarboxylate: 5m

<table>
<thead>
<tr>
<th>Entry</th>
<th>Retention Time</th>
<th>Area (%)</th>
<th>Int Type</th>
<th>Peak Type</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>14.308</td>
<td>50.21</td>
<td>bb</td>
<td>Unknown</td>
</tr>
<tr>
<td>2</td>
<td>18.589</td>
<td>49.79</td>
<td>bb</td>
<td>Unknown</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Entry</th>
<th>Retention Time</th>
<th>Area (%)</th>
<th>Int Type</th>
<th>Peak Type</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>14.118</td>
<td>100.00</td>
<td>bb</td>
<td>Unknown</td>
</tr>
<tr>
<td>2</td>
<td>16.580</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
(4S,5S)-ethyl 3,3-dicyano-2-(2-fluorophenyl)-4-hydroxy-5-isopropylcyclohex-1-enecarboxylate: 5n

<table>
<thead>
<tr>
<th>Entry</th>
<th>Retention Time</th>
<th>Area (%)</th>
<th>Int Type</th>
<th>Peak Type</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>9.388</td>
<td>49.67</td>
<td>bb</td>
<td>Unknown</td>
</tr>
<tr>
<td>2</td>
<td>11.597</td>
<td>50.33</td>
<td>bb</td>
<td>Unknown</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Entry</th>
<th>Retention Time</th>
<th>Area (%)</th>
<th>Int Type</th>
<th>Peak Type</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>9.269</td>
<td>98.69</td>
<td>bb</td>
<td>Unknown</td>
</tr>
<tr>
<td>2</td>
<td>11.573</td>
<td>1.31</td>
<td>bb</td>
<td>Unknown</td>
</tr>
</tbody>
</table>
(4S,5S)-ethyl 3,3-dicyano-2-(furan-2-yl)-4-hydroxy-5-isopropylcyclohex-1-enecarboxylate: 5o

<table>
<thead>
<tr>
<th>Entry</th>
<th>Retention Time</th>
<th>Area (%)</th>
<th>Int Type</th>
<th>Peak Type</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>12.080</td>
<td>50.00</td>
<td>bb</td>
<td>Unknown</td>
</tr>
<tr>
<td>2</td>
<td>26.603</td>
<td>50.00</td>
<td>bb</td>
<td>Unknown</td>
</tr>
</tbody>
</table>

Entry | Retention Time | Area (%) | Int Type | Peak Type |
<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>12.100</td>
<td>100.00</td>
<td>bb</td>
<td>Unknown</td>
</tr>
<tr>
<td>2</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
(4S,5S)-ethyl 3,3-dicyano-4-hydroxy-5-isopropyl-2-(thiophen-2-yl)cyclohex-1-enecarboxylate:

5p

<table>
<thead>
<tr>
<th>Entry</th>
<th>Retention Time</th>
<th>Area (%)</th>
<th>Int Type</th>
<th>Peak Type</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>9.893</td>
<td>50.07</td>
<td>bb</td>
<td>Unknown</td>
</tr>
<tr>
<td>2</td>
<td>18.243</td>
<td>49.93</td>
<td>bb</td>
<td>Unknown</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Entry</th>
<th>Retention Time</th>
<th>Area (%)</th>
<th>Int Type</th>
<th>Peak Type</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>9.735</td>
<td>98.66</td>
<td>bb</td>
<td>Unknown</td>
</tr>
<tr>
<td>2</td>
<td>18.197</td>
<td>1.34</td>
<td>bb</td>
<td>Unknown</td>
</tr>
</tbody>
</table>
(4S,5R)-ethyl 3,3-dicyano-5-ethyl-4-hydroxy-2-(4-methoxyphenyl)cyclohex-1-enecarboxylate:

5q

<table>
<thead>
<tr>
<th>Entry</th>
<th>Retention Time</th>
<th>Area (%)</th>
<th>Int Type</th>
<th>Peak Type</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>15.535</td>
<td>49.61</td>
<td>bb</td>
<td>Unknown</td>
</tr>
<tr>
<td>2</td>
<td>24.063</td>
<td>50.39</td>
<td>bb</td>
<td>Unknown</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Entry</th>
<th>Retention Time</th>
<th>Area (%)</th>
<th>Int Type</th>
<th>Peak Type</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>13.859</td>
<td>95.98</td>
<td>bb</td>
<td>Unknown</td>
</tr>
<tr>
<td>2</td>
<td>22.268</td>
<td>4.02</td>
<td>bb</td>
<td>Unknown</td>
</tr>
</tbody>
</table>
(4S,5S)-methyl 3,3-dicyano-4-hydroxy-5-isopropyl-2-(4-methoxyphenyl)cyclohex-1-enecarboxylate: 5s

![Structure of 5s]

<table>
<thead>
<tr>
<th>Entry</th>
<th>Retention Time</th>
<th>Area (%)</th>
<th>Int Type</th>
<th>Peak Type</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>10.974</td>
<td>50.53</td>
<td>bb</td>
<td>Unknown</td>
</tr>
<tr>
<td>2</td>
<td>22.695</td>
<td>49.47</td>
<td>bb</td>
<td>Unknown</td>
</tr>
</tbody>
</table>

![Graph of retention times and peak areas]

<table>
<thead>
<tr>
<th>Entry</th>
<th>Retention Time</th>
<th>Area (%)</th>
<th>Int Type</th>
<th>Peak Type</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>11.699</td>
<td>96.51</td>
<td>bb</td>
<td>Unknown</td>
</tr>
<tr>
<td>2</td>
<td>25.162</td>
<td>3.49</td>
<td>bb</td>
<td>Unknown</td>
</tr>
</tbody>
</table>
(4S,5S)-methyl 2-(4-bromophenyl)-3,3-dicyano-4-hydroxy-5-isopropylcyclohex-1-enecarboxylate: 5t

<table>
<thead>
<tr>
<th>Entry</th>
<th>Retention Time</th>
<th>Area (%)</th>
<th>Int Type</th>
<th>Peak Type</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>7.576</td>
<td>50.50</td>
<td>bb</td>
<td>Unknown</td>
</tr>
<tr>
<td>2</td>
<td>12.010</td>
<td>49.50</td>
<td>bb</td>
<td>Unknown</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Entry</th>
<th>Retention Time</th>
<th>Area (%)</th>
<th>Int Type</th>
<th>Peak Type</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>7.921</td>
<td>97.89</td>
<td>bb</td>
<td>Unknown</td>
</tr>
<tr>
<td>2</td>
<td>12.481</td>
<td>2.11</td>
<td>bb</td>
<td>Unknown</td>
</tr>
</tbody>
</table>
8.0 Copies of NMR spectra of products

Ethyl 4,4-dicyano-3-(4-methoxyphenyl)-2-methylenebut-3-enoate: 3a

![NMR spectrum of Ethyl 4,4-dicyano-3-(4-methoxyphenyl)-2-methylenebut-3-enoate: 3a]
Ethyl 4,4-dicyano-2-methylene-3-phenylbut-3-enoate: 3b
Ethyl 4,4-dicyano-2-methylene-3-(naphthalen-1-yl)but-3-enoate: 3c
Ethyl 4,4-dicyano-2-methylene-3-p-tolylbut-3-enoate: 3d
Ethyl 4,4-dicyano-3-(3-methoxyphenyl)-2-methylenebut-3-enoate: 3e
Ethyl 4,4-dicyano-2-methylene-3-m-tolylbut-3-enoate: 3f
Ethyl 4,4-dicyano-2-methylene-3-o-tolylbut-3-enoate: 3g
Ethyl 3-(4-chlorophenyl)-4,4-dicyano-2-methylenebut-3-enoate: 3i

\[
\begin{align*}
\text{NC} & \quad \text{CN} \\
\text{Cl} & \quad \text{COOEt}
\end{align*}
\]
Ethyl 4,4-dicyano-3-(4-fluorophenyl)-2-methylenebut-3-enoate: 3j
Ethyl 4,4-dicyano-2-methylene-3-(4-(trifluoromethyl)phenyl)but-3-enoate: 3k
Ethyl 3-(3-bromophenyl)-4,4-dicyano-2-methylenebut-3-enoate: 3\textit{l}
Ethyl 3-(3-chlorophenyl)-4,4-dicyano-2-methylenebut-3-enoate: 3m
Ethyl 4,4-dicyano-3-(2-fluorophenyl)-2-methylenebut-3-enoate: 3n
Ethyl 4,4-dicyano-3-(furan-2-yl)-2-methylenecbut-3-enoate: 3o
Ethyl 4,4-dicyano-2-methylene-3-(thiophen-2-yl)but-3-enoate: 3p
Methyl 4,4-dicyano-3-(4-methoxyphenyl)-2-methylenebut-3-enoate: 3q
Methyl 3-(4-bromophenyl)-4,4-dicyano-2-methylenebut-3-enoate: 3r
(4S,5S)-ethyl 3,3-dicyano-4-hydroxy-5-isopropyl-2-(4-methoxyphenyl)cyclohex-1-enecarboxylate: 5a
(4S,5S)-ethyl 3,3-dicyano-4-hydroxy-5-isopropyl-2-phenylcyclohex-1-enecarboxylate: 5b
(4S,5S)-ethyl 3,3-dicyano-4-hydroxy-5-isopropyl-2-(naphthalen-1-yl)cyclohex-1-enecarboxylate: 5c

Electronic Supplementary Material (ESI) for Chemical Communications
This journal is © The Royal Society of Chemistry 2011
(4S,5S)-ethyl 3,3-dicyano-4-hydroxy-5-isopropyl-2-p-tolylcyclohex-1-enecarboxylate: 5d
(4S,5S)-ethyl 3,3-dicyano-4-hydroxy-5-isopropyl-2-(3-methoxyphenyl)cyclohex-1-enecarboxylate: 5e
(4S,5S)-ethyl 3,3-dicyano-4-hydroxy-5-isopropyl-2-m-tolylcyclohex-1-ene carboxylate: 5f
(4S,5S)-ethyl 3,3-dicyano-4-hydroxy-5-isopropyl-2-o-tolylcyclohex-1-enecarboxylate: 5g
(4S,5S)-ethyl 2-(4-bromophenyl)-3,3-dicyano-4-hydroxy-5-isopropylcyclohex-1-enecarboxylate: 5h
(4S,5S)-ethyl 2-(4-chlorophenyl)-3,3-dicyano-4-hydroxy-5-isopropylcyclohex-1-enecarboxylate: 5i
(4S,5S)-ethyl 3,3-dicyano-2-(4-fluorophenyl)-4-hydroxy-5-isopropylcyclohex-1-enecarboxylate: 5j
(4S,5S)-ethyl 3,3-dicyano-4-hydroxy-5-isopropyl-2-(4-(trifluoromethyl)phenyl)cyclohex-1-enecarboxylate: 5k

Electronic Supplementary Material (ESI) for Chemical Communications
This journal is © The Royal Society of Chemistry 2011
(4S,5S)-ethyl 2-(3-bromophenyl)-3,3-dicyano-4-hydroxy-5-isopropylcyclohex-1-enecarboxylate: 5l
(4S,5S)-ethyl 2-(3-chlorophenyl)-3,3-dicyano-4-hydroxy-5-isopropylcyclohex-1-ene carboxylate: 5m
(4S,5S)-ethyl 3,3-dicyano-2-(2-fluorophenyl)-4-hydroxy-5-isopropylcyclohex-1-enecarboxylate: 5n
(4S,5S)-ethyl 3,3-dicyano-2-(furan-2-yl)-4-hydroxy-5-isopropylcyclohex-1-enecarboxylate: 5o
(4S,5S)-ethyl 3,3-dicyano-4-hydroxy-5-isopropyl-2-(thiophen-2-yl)cyclohex-1-enecarboxylate:

5p
(4S,5R)-ethyl 3,3-dicyano-5-ethyl-4-hydroxy-2-(4-methoxyphenyl)cyclohex-1-enecarboxylate:

5q

![Chemical Structure](image-url)
(4S,5S)-ethyl 3,3-dicyano-4-hydroxy-2-(4-methoxyphenyl)-5-phenylcyclohex-1-enecarboxylate: 5R
(4S,5S)-methyl 3,3-dicyano-4-hydroxy-5-isopropyl-2-(4-methoxyphenyl)cyclohex-1-enecarboxylate: 5s
(4S,5S)-methyl 2-(4-bromophenyl)-3,3-dicyano-4-hydroxy-5-isopropylcyclohex-1-ene carboxylate: 5t