Supporting Information

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Highly Enantioselective Synthesis of N,N-Dialkylbenzamides with Aryl-Carbonyl Axial Chirality by Rhodium-Catalyzed [2 + 2 + 2] Cycloaddition

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I. General

Anhydrous CH$_2$Cl$_2$ (No. 27,099-7) was obtained from Aldrich and used as received. Solvents for the synthesis of substrates were dried over Molecular Sieves 4A (Wako) prior to use. All reagents were obtained from commercial sources and used as received. All reactions were carried out under an atmosphere of argon or nitrogen in oven-dried glassware with magnetic stirring. Diynes 1a,$^{[1]}$ 1b,$^{[2]}$ 1c,$^{[2]}$ and 1d$^{[2]}$ were reported in the literatures.

II. Synthesis of Alkynylamides

**General procedure for synthesis of alkynylamides [4-Methoxy-4-methylpent-2-ynoic acid diisopropylamide (2a)]:** To a solution of diisopropylcarbamoyl chloride (973 mg, 5.94 mmol) and 3-methyl-1-butyn-3-ol (550 mg, 6.54 mmol) in Et$_3$N (18 mL) were added PdCl$_2$(PPh$_3$)$_2$ (125.2 g, 0.178 mmol), PPh$_3$ (155.9 mg, 0.594 mmol), and CuI (113.2 mg, 0.594 mmol) in this order at RT. The mixture was stirred at 90 °C for 2 h. The resulting mixture was filtered, concentrated, and purified by silica gel chromatography (hexane/EtOAc = 5:1–2:1), which furnished 4-hydroxy-4-methylpent-2-ynoic acid diisopropylamide (1.013 g, 4.79 mmol, 81% yield) as a pale yellow solid.

To a stirred suspension of NaH (55% in paraffin liquid, 233 mg, 5.33 mmol) in THF (9 mL) was added a THF (13 mL) solution of 4-hydroxy-4-methylpent-2-ynoic acid diisopropylamide (931 mg, 4.41 mmol) and iodomethane (0.55 ml, 8.8 mmol) at 0 °C, and the resulting mixture was stirred at RT for 2 h. The reaction was quenched with water and extracted twice with EtOAc. The organic layer was washed with brine, dried over Na$_2$SO$_4$, and concentrated. The crude product was purified by silica gel column chromatography (hexane/EtOAc = 10:1−5:1) to afford 2a (816 mg, 3.62 mmol, 82% yield) as a colorless solid.

![Chemical structure of 2a](image)

Colorless solid; Mp 28–30 °C; IR (neat) 2973, 2937, 2826, 2239, 2218, 1632, 1620, 1445, 1335 cm$^{-1}$; $^1$H NMR (CDCl$_3$, 300 MHz) $\delta$ 4.60–4.40 (m, 1H), 3.78–3.50 (m, 1H), 3.37 (s, 3H), 1.50 (s, 6H), 1.37 (d, $J = 6.9$ Hz, 6H), 1.25 (d, $J = 6.6$ Hz, 6H); $^{13}$C NMR (CDCl$_3$, 75 MHz) $\delta$ 153.1, 90.7, 78.5, 70.5, 52.0, 50.3, 45.6, 27.7, 20.9, 20.0; HRMS (EI) calcd for C$_{13}$H$_{23}$NO$_2$ [M]$^+$ 225.1729, found 225.1715.

**4-Methoxy-4-methylpent-2-ynoic acid diethylamide (2b).**

![Chemical structure of 2b](image)
Pale yellow oil; IR (neat) 2983, 2937, 2227, 1633, 1427, 1278, 1075 cm\(^{-1}\); \(^1\)H NMR (CDCl\(_3\), 300 MHz) \(\delta 3.56 (q, J = 7.2\) Hz, 2H), 3.42 (q, \(J = 7.2\) Hz, 2H), 3.38 (s, 3H), 1.50 (s, 6H), 1.22 (t, \(J = 7.2\) Hz, 3H), 1.14 (t, \(J = 7.2\) Hz, 3H); \(^1^3\)C NMR (CDCl\(_3\), 75 MHz) \(\delta 153.4, 91.3, 77.3, 70.5, 52.0, 43.5, 39.2, 27.7, 14.3, 12.7\); HRMS (El) calcd for C\(_{13}\)H\(_{19}\)NO\(_2\) [M\(^+\)] 197.1416, found 197.1367.

4-Methoxy-4-methylpent-2-ynoic acid dimethylamide (2c).

Pale yellow greasy solid; IR (neat) 2986, 2936, 2827, 2225, 1637, 1395, 1074 cm\(^{-1}\); \(^1\)H NMR (CDCl\(_3\), 300 MHz) \(\delta 3.37 (s, 3H), 3.20 (s, 3H), 2.97 (s, 3H), 1.50 (s, 6H); \(^1^3\)C NMR (CDCl\(_3\), 75 MHz) \(\delta 154.1, 92.6, 76.5, 70.5, 52.1, 38.3, 34.1, 27.7\); HRMS (El) calcd for C\(_8\)H\(_{12}\)NO \([\text{M–O\text{Me}}]^{+}\) 138.0919, found 138.0895.

4-Methoxy-4-methyl-1-piperidin-1-ylpent-2-yn-1-one (2d).

Pale yellow oil; IR (neat) 2985, 2938, 2858, 2225, 1632, 1433, 1267, 1074 cm\(^{-1}\); \(^1\)H NMR (CDCl\(_3\), 300 MHz) \(\delta 3.73–3.62 (m, 2H), 3.62–3.50 (m, 2H), 3.37 (s, 3H), 1.72–1.42 (m, 6H), 1.50 (s, 6H); \(^1^3\)C NMR (CDCl\(_3\), 75 MHz) \(\delta 152.4, 92.6, 76.9, 70.6, 52.1, 48.1, 42.3, 27.7, 26.3, 25.3, 24.4\); HRMS (El) calcd for C\(_{12}\)H\(_{19}\)NO \([\text{M}]^{+}\) 209.1416, found 209.1374.

4,4-Dimethylpent-2-ynoic acid diisopropylamide (2e).

Pale yellow solid; mp 56.4–57.0 °C; IR (KBr) 2969, 2932, 2254, 2220, 1628, 1616, 1338 cm\(^{-1}\); \(^1\)H NMR (CDCl\(_3\), 300 MHz) \(\delta 4.60–4.32 (m, 1H), 3.83–3.50 (m, 1H), 1.34 (d, \(J = 6.6\) Hz, 6H), 1.27 (s, 9H), 1.25 (d, \(J = 6.6\) Hz, 6H); \(^1^3\)C NMR (CDCl\(_3\), 75 MHz) \(\delta 153.9, 98.0, 74.2, 49.8, 45.4, 30.1, 27.6, 20.9, 20.1\); HRMS (El) calcd for C\(_{13}\)H\(_{23}\)NO \([\text{M}]^{+}\) 209.1780, found 209.1729.
4-Methylpent-2-yonoic acid diisopropylamide (2f).

Pale yellow solid; Mp 37.9–39.4 °C; IR (KBr) 2972, 2934, 2873, 2224, 1626, 1445, 1334 cm⁻¹; ¹H NMR (CDCl₃, 300 MHz) δ 4.61–4.33 (m, 1H), 3.79–3.49 (m, 1H), 2.68 (sept, J = 6.9 Hz, 1H), 1.33 (d, J = 6.6 Hz, 6H), 1.22 (d, J = 6.0 Hz, 6H), 1.20 (d, J = 6.9 Hz, 6H); ¹³C NMR (CDCl₃, 75 MHz) δ 153.8, 95.7, 74.7, 50.0, 45.4, 22.0, 20.9, 20.6, 20.0; HRMS (EI) calcd for C₁₂H₂₁NO [M⁺] 195.1623, found 195.1576.

Hept-2-yonoic acid diisopropylamide (2g).

Pale yellow oil; IR (neat) 2967, 2934, 2873, 2230, 1626, 1436, 1371, 1330 cm⁻¹; ¹H NMR (CDCl₃, 300 MHz) δ 4.68-4.39 (m, 1H), 3.79–3.37 (m, 1H), 2.33 (t, J = 7.2 Hz, 2H), 1.62-1.29 (m, 4H), 1.35 (d, J = 6.9 Hz, 6H), 1.23 (d, J = 6.9 Hz, 6H), 0.91 (t, J = 7.2 Hz, 3H); ¹³C NMR (CDCl₃, 75 MHz) δ 153.8, 91.1, 75.5, 50.1, 45.4, 29.8, 22.0, 20.9, 20.1, 18.6, 13.5; HRMS (EI) calcd for C₁₂H₂₀NO [M–Me⁺] 194.1545, found 194.1546.

3-o-Tolylpropynoic acid diisopropylamide (2h).

Colorless solid; Mp 41.5–42.3 °C; IR (KBr) 2972, 2934, 2208, 1622, 1439, 1335 cm⁻¹; ¹H NMR (CDCl₃, 300 MHz) δ 7.55–7.46 (m, 1H), 7.35–7.11 (m, 3H), 4.82–4.60 (m, 1H), 3.78–3.50 (m, 1H), 2.47 (s, 3H), 1.43 (d, J = 6.9 Hz, 6H), 1.29 (d, J = 6.9 Hz, 6H); ¹³C NMR (CDCl₃, 75 MHz) δ 153.7, 141.1, 132.7, 129.7, 129.6, 125.7, 120.8, 87.4, 86.9, 50.6, 45.7, 21.0, 20.6, 20.2; HRMS (EI) calcd for C₁₅H₁₈NO [M–Me⁺] 228.1388, found 228.1361.

3-(2-Bromophenyl)propynoic acid diisopropylamide (2i).
Colorless solid; Mp 89.0–90.1 °C; IR (KBr) 2974, 2931, 2214, 1619, 1470, 1438, 1335 cm\(^{-1}\); \(^1\)H NMR (CDCl\(_3\), 300 MHz) \(\delta\) 7.66–7.55 (m, 2H), 7.38–7.19 (m, 2H), 5.05–4.73 (m, 1H), 3.81–3.45 (m, 1H), 1.43 (d, \(J = 6.9\) Hz, 6H), 1.29 (d, \(J = 6.9\) Hz, 6H); \(^13\)C NMR (CDCl\(_3\), 75 MHz) \(\delta\) 153.3, 134.6, 132.5, 130.8, 127.2, 126.0, 123.4, 86.9, 86.2, 50.8, 45.9, 21.0, 20.1; HRMS (EI) calcd for C\(_{15}\)H\(_{18}\)NOBr \([M+]\) 307.0572, found 307.0551.

III. Synthesis of Axially Chiral Benzamides

**General procedure for Rh-catalyzed \([2 + 2 + 2]\) cycloaddition (Table 2, entry 1):** A CH\(_2\)Cl\(_2\) (0.5 mL) solution of (S)-Segphos (4.6 mg, 0.0075 mmol) was added to a CH\(_2\)Cl\(_2\) (0.5 mL) solution of [Rh(cod)]BF\(_4\) (3.0 mg, 0.0075 mmol) at RT, and the mixture was stirred for 5 min. The resulting solution was stirred under H\(_2\) (1 atm) at RT for 1 h, concentrated to dryness, and dissolved in CH\(_2\)Cl\(_2\) (0.5 mL). To this solution was added a CH\(_2\)Cl\(_2\) (0.5 mL) solution of 2a (37.2 mg, 0.165 mmol). Then a CH\(_2\)Cl\(_2\) (1.0 mL) solution of 1a (58.3 mg, 0.15 mmol) was added dropwise over 5 min at RT. The solution was stirred at RT for 1 h. The resulting solution was concentrated and purified by silica gel chromatography (hexane/EtOAc = 5:1–2:1), which furnished (–)-3aa (85.1 mg, 0.139 mmol, 92% yield, >99% ee) as a pale yellow oil.

(–)-5-Diisopropylcarbamoyl-6-(1-methoxy-1-methylethyl)-4,7-dimethylindan-2,2-dicarboxylic acid dibenzyl ester [(–)-3aa].

Pale yellow oil; [\(\alpha\)]\(^{25}\)_D \(-9.81^\circ\) (CHCl\(_3\), c 4.00, >99% ee); IR (neat) 2974, 2933, 1732, 1436, 1232, 1164, 1060 cm\(^{-1}\); \(^1\)H NMR (CDCl\(_3\), 300 MHz) \(\delta\) 7.41–7.14 (m, 10H), 5.16 (d, \(J = 13.5\) Hz, 2H), 5.12 (d, \(J = 13.5\) Hz, 2H), 3.68–3.38 (m, 6H), 3.08 (s, 3H), 2.41 (s, 3H), 2.14 (s, 3H), 1.67 (s, 3H), 1.63 (s, 3H), 1.59 (d, \(J = 6.9\) Hz, 3H), 1.54 (d, \(J = 6.9\) Hz, 3H), 1.14 (d, \(J = 6.3\) Hz, 3H), 0.97 (d, \(J = 6.3\) Hz, 3H); \(^13\)C NMR (CDCl\(_3\), 75 MHz) \(\delta\) 171.9, 171.7, 171.3, 140.5, 138.8, 138.0, 136.7, 135.4, 135.3, 130.6, 128.50, 128.49, 128.3, 128.2, 128.0, 127.8, 127.2, 79.2, 67.4, 67.3, 59.0, 50.4, 49.4, 45.9, 41.0, 40.1, 27.8, 27.4, 20.3, 20.2, 20.1, 20.0, 19.0, 16.8; HRMS (ESI) calcd for C\(_{38}\)H\(_{47}\)NO\(_6\)Na \([M+Na]^+\) 636.3301, found 636.3262; CHIRALPAK AD,
hexane/2-PrOH = 90:10, 1 mL/min, retention times: 8.58 min (major isomer) and 13.0 min (minor isomer).

(-)-5-Diethylcarbamoyl-6-(1-methoxy-1-methylethyl)-4,7-dimethylindan-2,2-dicarboxylic acid dibenzyl ester [(-)-3ab].

Pale yellow oil; [α]$_{25}^{D}$ $-$4.19° (CHCl$_3$, c 3.76, >99% ee); IR (neat) 2974, 2934, 1732, 1624, 1456, 1232, 1165, 1073 cm$^{-1}$; $^1$H NMR (CDCl$_3$, 300 MHz) δ 7.38–7.16 (m, 10H), 5.16 (d, $J$ = 12.6 Hz, 2H), 5.12 (d, $J$ = 12.6 Hz, 2H), 3.76–3.34 (m, 6H), 3.27–2.95 (m, 2H), 3.08 (s, 3H), 2.38 (s, 3H), 2.07 (s, 3H), 1.60 (s, 3H), 1.58 (s, 3H), 1.26 (t, $J$ = 7.2 Hz, 3H), 1.06 (t, $J$ = 7.2 Hz, 3H); $^{13}$C NMR (CDCl$_3$, 75 MHz) δ 172.2, 171.6, 171.2, 140.7, 139.7, 137.9, 135.5, 135.3, 135.2, 130.4, 128.5, 128.2, 128.0, 127.8, 127.0, 79.1, 67.4, 67.3, 59.0, 49.1, 43.1, 40.9, 40.0, 38.1, 27.6, 26.4, 18.8, 16.2, 12.7, 12.4; HRMS (FAB) calcd for C$_{35}$H$_{40}$NO$_5$ [M–OMe]$^+$ 554.2906, found 554.2938; CHIRALPAK AD, hexane/2-PrOH = 80:20, 1 mL/min, retention times: 6.50 min (major isomer) and 8.58 min (minor isomer).

(+)-5-Dimethylcarbamoyl-6-(1-methoxy-1-methylethyl)-4,7-dimethylindan-2,2-dicarboxylic acid dibenzyl ester [(+)-3ac].

Pale yellow oil; [α]$_{25}^{D}$ +0.829° (CHCl$_3$, c 3.97, >99% ee); IR (neat) 2933, 1733, 1633, 1498, 1456, 1389, 1236, 1165, 1073 cm$^{-1}$; $^1$H NMR (CDCl$_3$, 300 MHz) δ 7.40–7.14 (m, 10H), 5.14 (s, 4H), 3.70–3.44 (m, 4H), 3.09 (s, 3H), 3.05 (s, 3H), 2.78 (s, 3H), 2.37 (s, 3H), 2.03 (s, 3H), 1.59 (s, 3H), 1.57 (s, 3H); $^{13}$C NMR (CDCl$_3$, 75 MHz) δ 173.0, 171.6, 171.2, 140.7, 139.7, 137.6, 135.3, 135.0, 134.0, 128.5, 128.0, 127.8, 127.0, 79.1, 67.4, 67.3, 59.0, 49.1, 43.1, 40.9, 40.0, 38.1, 27.6, 26.4, 18.8, 16.2, 12.7, 12.4; HRMS (ESI) calcd for C$_{34}$H$_{39}$NO$_6$Na [M+Na]$^+$ 580.2675, found 580.2655; CHIRALPAK AD-H, hexane/2-PrOH = 90:10, 1 mL/min, retention times: 16.0 min (major isomer) and 19.2 min (minor isomer).

(-)-5-(1-Methoxy-1-methylethyl)-4,7-dimethyl-6-(piperidine-1-carbonyl)indan-2,2-dicarboxylic acid dibenzyl ester [(-)-3].
rboxylic acid dibenzyl ester [(-)-3ad].

Pale yellow oil; [α]$_{D}^{25}$ = -0.225° (CHCl$_3$, c 3.60, >99 % ee); IR (neat) 2937, 2854, 1733, 1628, 1440 cm$^{-1}$; $^1$H NMR (CDCl$_3$, 300 MHz) δ 7.35–7.18 (m, 10H), 5.16 (d, J = 12.6 Hz, 2H), 5.12 (d, J = 12.6 Hz, 2H), 4.16–3.98 (m, 1H), 3.75–3.44 (m, 4H), 3.36–2.88 (m, 3H), 3.09 (s, 3H), 2.37 (s, 3H), 2.09 (s, 3H), 1.82–1.35 (m, 6H), 1.59 (s, 3H), 1.58 (s, 3H); $^{13}$C NMR (CDCl$_3$, 75 MHz) δ 171.7, 171.5, 171.2, 140.7, 139.9, 137.7, 135.4, 135.31, 135.29, 130.4, 128.5, 128.2, 128.0, 127.9, 126.9, 79.1, 67.43, 67.36, 59.0, 49.4, 47.6, 41.5, 40.9, 40.0, 27.5, 26.4, 25.5, 25.1, 24.5, 18.8, 16.3; HRMS (ESI) calcd for C$_{37}$H$_{43}$NO$_6$Na [M+Na]$^+$ 620.2988, found 620.2990; CHIRALPAK AD, hexane/2-PrOH = 90:10, 1 mL/min, retention times: 15.8 min (major isomer) and 22.2 min (minor isomer).

(–)-5-tert-Butyl-6-diisopropylcarbamoyl-4,7-dimethyl-indan-2,2-dicarboxylic acid dibenzyl ester [(-)-3ae].

Colorless solid; Mp 33.1–33.9 °C; [α]$_{D}^{25}$ = -11.4° (CHCl$_3$, c 3.91, >99 % ee); IR (neat) 2965, 1735, 1626, 1232 cm$^{-1}$; $^1$H NMR (CDCl$_3$, 300 MHz) δ 7.38–7.16 (m, 10H), 5.16 (d, J = 12.6 Hz, 1H), 5.13 (s, 2H), 5.11 (d, J = 12.6 Hz, 1H), 3.65–3.42 (m, 6H), 2.39 (s, 3H), 2.13 (s, 3H), 1.60 (d, J = 6.9 Hz, 3H), 1.52 (d, J = 6.9 Hz, 3H), 1.51 (s, 9H), 1.16 (d, J = 6.6 Hz, 3H), 0.91 (d, J = 6.6 Hz, 3H); $^{13}$C NMR (CDCl$_3$, 75 MHz) δ 172.4, 171.7, 171.3, 142.3, 140.7, 136.9, 136.0, 135.40, 135.35, 130.9, 128.50, 128.49, 128.3, 128.2, 128.0, 127.8, 127.2, 67.4, 67.3, 59.1, 50.3, 46.0, 41.2, 40.1, 37.5, 32.4, 21.1, 20.4, 20.2, 19.6, 19.2, 16.9; HRMS (FAB) calcd for C$_{38}$H$_{48}$NO$_5$ [M+H]$^+$ 598.3532, found 598.3564; CHIRALPAK AD, hexane/2-PrOH = 90:10, 1.0 mL/min, retention times: 8.10 min (major isomer), 11.9 min (minor isomer).

(+)-5-Diisopropylcarbamoyl-6-isopropyl-4,7-dimethylindan-2,2-dicarboxylic acid dibenzyl ester [(+)3af].
Colorless solid; Mp 31.5–32.4 °C; $[\alpha]_D^{25} +1.91^\circ$ (CHCl$_3$, c 3.92, >99 % ee); IR (neat) 2964, 1734, 1626, 1233, 1159 cm$^{-1}$; $^1$H NMR (CDCl$_3$, 300 MHz) $\delta$ 7.39–7.16 (m, 10H), 5.16 (d, $J = 12.9$ Hz, 2H), 5.11 (d, $J = 12.9$ Hz, 2H), 3.69 (sept, $J = 6.6$ Hz, 1H), 3.64–3.39 (m, 5H), 3.07 (sept, $J = 6.6$ Hz, 3H), 1.36 (d, $J = 6.6$ Hz, 3H), 1.30 (d, $J = 6.6$ Hz, 3H), 1.09 (d, $J = 6.6$ Hz, 3H), 1.07 (d, $J = 6.6$ Hz, 3H); $^{13}$C NMR (CDCl$_3$, 75 MHz) $\delta$ 171.8, 171.3, 170.9, 140.1, 139.7, 137.6, 136.6, 135.34, 135.32, 129.7, 128.5, 128.0, 127.8, 125.9, 67.4, 67.3, 59.2, 50.4, 45.7, 40.4, 39.8, 31.8, 21.68, 21.65, 20.9, 20.7, 20.3, 17.3, 16.3; HRMS (FAB) calcd for C$_{37}$H$_{46}$NO$_5$ [M+H]$^+$ 584.3376, found 584.3354; CHIRALPAK AD, hexane/2-PrOH = 90:10, 1.0 mL/min, retention times: 9.88 min (major isomer) and 12.9 min (minor isomer).

(+)-5-n-Butyl-6-diisopropylcarbamoyl-4,7-dimethylindan-2,2-dicarboxylic acid dibenzyl ester [(+)-3ag].

Colorless solid; Mp 77.3–78.6 °C; $[\alpha]_D^{25} +9.77^\circ$ (CHCl$_3$, c 3.29, >99 % ee); IR (neat) 2964, 2936, 2871, 1734, 1626, 1237, 1158 cm$^{-1}$; $^1$H NMR (CDCl$_3$, 300 MHz) $\delta$ 7.40–7.15 (m, 10H), 5.17 (d, $J = 13.2$ Hz, 1H), 5.14 (s, 2H), 5.12 (d, $J = 13.2$ Hz, 1H), 3.72–3.39 (m, 6H), 2.62–2.33 (m, 2H), 2.16 (s, 3H), 2.12 (s, 3H), 1.60 (d, $J = 6.6$ Hz, 6H), 1.48–1.30 (m, 4H), 1.07 (d, $J = 6.6$ Hz, 6H), 0.92 (t, $J = 7.2$ Hz, 3H); $^{13}$C NMR (CDCl$_3$, 75 MHz) $\delta$ 171.8, 171.3, 170.4, 138.4, 137.2, 136.4, 135.6, 135.4, 135.3, 129.5, 128.5, 128.0, 127.8, 125.9, 67.4, 67.3, 59.4, 50.6, 45.6, 40.3, 39.8, 32.4, 30.9, 23.3, 21.0, 20.8, 20.4, 20.3, 16.1, 15.4, 13.8; HRMS (FAB) calcd for C$_{38}$H$_{48}$NO$_5$ [M+H]$^+$ 598.3532, found 598.3581; CHIRALPAK AD-H, hexane/2-PrOH = 90:10, 1.0 mL/min, retention times: 14.2 min (minor isomer) and 16.4 min (major isomer).

(–)-6-(1-Methoxy-1-methylethyl)-4,7-dimethyl-2-(toluene-4-sulfonyl)-2,3-dihydro-1H-is oindole-5-carboxylic acid diisopropylamide [(–)-3ba].
Pale yellow solid; Mp 78.1–78.8 °C; [α]$_{25}^D$ -2.05° (CHCl$_3$, c 2.57, >99% ee); IR (neat) 2974, 2932, 1438, 1348, 1326, 1165 cm$^{-1}$; $^1$H NMR (CDCl$_3$, 300 MHz) δ 7.78 (d, $J = 8.1$ Hz, 2H), 7.33 (d, $J = 8.1$ Hz, 2H), 4.75–4.55 (m, 2H), 4.55–4.35 (m, 2H), 3.62–3.36 (m, 2H), 3.06 (s, 3H), 2.41 (s, 3H), 2.34 (s, 3H), 2.10 (s, 3H), 1.62 (s, 3H), 1.59 (s, 3H), 1.56 (d, $J = 6.6$ Hz, 3H), 1.52 (d, $J = 6.6$ Hz, 3H), 1.13 (d, $J = 6.6$ Hz, 3H), 0.98 (d, $J = 6.6$ Hz, 3H); $^{13}$C NMR (CDCl$_3$, 75 MHz) δ 171.0, 143.7, 140.1, 137.4, 136.9, 134.5, 133.7, 129.8, 129.5, 127.5, 126.4, 79.1, 54.5, 53.8, 50.6, 49.3, 46.0, 27.3, 27.2, 21.5, 20.2, 20.1, 19.9, 18.8, 16.5; HRMS (ESI) calcd for C$_{28}$H$_{40}$N$_2$O$_4$SNa [M+Na]$^+$ 523.2607, found 523.2622; CHIRALPAK AD, hexane/2-ProOH = 90:10, 0.6 mL/min, retention times: 28.1 min (major isomer) and 30.2 min (minor isomer).

\begin{align*}
(-)-6-(1-Methoxy-1-methylethyl)-4,7-dimethyl-1,3-dihydroisobenzofuran-5-carboxylic acid diisopropylamide [(−)-3ca].
\end{align*}

Colorless solid; Mp 100.5–101.6 °C; [α]$_{25}^D$ -16.6° (CHCl$_3$, c 2.05, >99% ee); IR (neat) 2975, 2932, 1627, 1437, 1330, 1069, 752 cm$^{-1}$; $^1$H NMR (CDCl$_3$, 300 MHz) δ 5.21–4.93 (m, 4H), 3.61 (sept, $J = 6.6$ Hz, 1H), 3.51 (sept, $J = 6.6$ Hz, 1H), 3.11 (s, 3H), 2.83 (s, 3H), 2.14 (s, 3H), 1.68 (s, 3H), 1.64 (s, 3H), 1.59 (d, $J = 6.6$ Hz, 3H), 1.55 (d, $J = 6.6$ Hz, 3H), 1.16 (d, $J = 6.6$ Hz, 3H), 1.02 (d, $J = 6.6$ Hz, 3H); $^{13}$C NMR (CDCl$_3$, 75 MHz) δ 171.4, 139.8, 139.4, 137.2, 137.1, 128.3, 125.0, 79.2, 74.7, 74.2, 50.5, 49.5, 46.0, 27.6, 27.4, 20.30, 20.26, 20.1, 19.0, 16.7; HRMS (ESI) calcd for C$_{21}$H$_{33}$NO$_3$Na [M+Na]$^+$ 370.2358, found 370.2333; CHIRALPAK AD-H, hexane/2-ProOH = 90:10, 1.0 mL/min, retention times: 5.28 min (major isomer) and 8.57 min (minor isomer).

6-(1-Methoxy-1-methylethyl)-2-(toluene-4-sulfonyl)-2,3-dihydro-1H-isoinole-5-carboxylic acid diisopropylamide (3da).
Colorless solid; Mp 67.0–67.7 °C; IR (neat) 2974, 2933, 1628, 1442, 1329, 1165 cm\(^{-1}\); \(^1\)H NMR (CDCl\(_3\), 300 MHz) \(\delta\) 7.75 (d, \(J = 8.1\) Hz, 2H), 7.31 (d, \(J = 8.1\) Hz, 2H), 7.26 (s, 1H), 6.82 (s, 1H), 4.74–4.42 (m, 4H), 3.59 (sept, \(J = 6.6\) Hz, 1H), 3.43 (sept, \(J = 6.6\) Hz, 1H), 1.52 (d, \(J = 6.6\) Hz, 3H), 1.52 (s, 3H), 1.50 (d, \(J = 6.6\) Hz, 3H), 1.50 (s, 3H), 1.10 (d, \(J = 6.6\) Hz, 3H), 1.03 (d, \(J = 6.6\) Hz, 3H); \(^{13}\)C NMR (CDCl\(_3\), 75 MHz) \(\delta\) 171.4, 144.3, 143.7, 136.0, 136.4, 134.5, 133.4, 129.8, 127.5, 120.9, 120.4, 77.6, 53.6, 53.3, 50.7, 49.6, 45.3, 27.4, 26.3, 21.5, 20.3, 20.18, 20.16, 19.6; HRMS (ESI) calcd for C\(_{24}\)H\(_{36}\)N\(_2\)O\(_4\)SNa [M+Na]\(^+\) 495.2294, found 495.2299.

\((-\))-4,7-Dimethyl-6-\(o\)-tolyl-1,3-dihydroisobenzofuran-5-carboxylic acid diisopropylamide [\((-\)-3ch)].

Colorless solid; Mp 144.0–144.8 °C; \([\alpha]\)\(^{25}\) \(_{D}\) –7.69° (CHCl\(_3\), \(c\) 1.15, >99 % ee); IR (neat) 2962, 2877, 1621, 1442, 1368, 1339 cm\(^{-1}\); \(^1\)H NMR (CDCl\(_3\), 300 MHz) \(\delta\) 7.45–7.33 (m, 1H), 7.29–7.10 (m, 3H), 5.28–4.99 (m, 4H), 3.58 (sept, \(J = 6.6\) Hz, 1H), 3.17 (sept, \(J = 6.6\) Hz, 1H), 2.19 (s, 3H), 2.09 (s, 3H), 1.89 (s, 3H), 1.48 (d, \(J = 6.6\) Hz, 3H), 1.00 (d, \(J = 6.6\) Hz, 3H), 0.96 (d, \(J = 6.6\) Hz, 3H), 0.61 (d, \(J = 6.6\) Hz, 3H); \(^{13}\)C NMR (CDCl\(_3\), 75 MHz) \(\delta\) 168.9, 138.1, 137.5, 137.3, 137.1, 135.9, 135.7, 131.9, 129.3, 127.6, 127.4, 125.5, 124.6, 74.02, 73.96, 50.2, 45.4, 21.2, 20.4, 20.3, 19.7, 19.5, 16.22, 16.2; HRMS (FAB) calcd for C\(_{24}\)H\(_{36}\)NO\(_2\) [M+H]\(^+\) 366.2433, found 366.2452; CHIRALPAK AD-H, hexane/2-PrOH = 90:10, 1.0 mL/min, retention times: 6.03 min (major isomer), and 8.05 min (minor isomer).

\((S,S)-(\cdash)-6-(2-Bromophenyl)-4,7-dimethyl-1,3-dihydroisobenzofuran-5-carboxylic acid diisopropylamide [(S,S)-(\cdash)-3ci].

(S,S)-(\cdash)-6-(2-Bromophenyl)-4,7-dimethyl-1,3-dihydroisobenzofuran-5-carboxylic acid diisopropylamide [(S,S)-(\cdash)-3ci].
Colorless solid; Mp 131.8–132.5 °C; $[\alpha]_{D}^{25} = -25.9^\circ$ (CHCl$_3$, c 1.42, >99 % ee); IR (neat) 2967, 2931, 1624, 1441, 1340 cm$^{-1}$; $^1$H NMR (CDCl$_3$, 300 MHz) $\delta$ 7.59 (dd, $J = 7.5, 1.2$ Hz, 1H), 7.52 (dd, $J = 7.5, 1.8$ Hz, 1H), 7.33 (dt, $J = 7.5, 1.2$ Hz, 1H), 7.19 (dt, $J = 7.5, 1.8$ Hz, 1H), 5.27–5.04 (m, 4H), 3.76 (sept, $J = 6.6$ Hz, 1H), 3.22 (sept, $J = 6.6$ Hz, 1H), 2.19 (s, 3H), 1.98 (s, 3H), 1.48 (d, $J = 6.6$ Hz, 3H), 1.02 (d, $J = 6.6$ Hz, 3H), 0.98 (d, $J = 6.6$ Hz, 3H), 0.74 (d, $J = 6.6$ Hz, 3H); $^{13}$C NMR (CDCl$_3$, 75 MHz) $\delta$ 168.7, 138.5, 138.4, 137.9, 137.5, 135.1, 133.7, 132.1, 129.0, 128.1, 127.2, 125.0, 124.4, 74.1, 74.0, 50.4, 45.6, 21.13, 21.09, 20.3, 19.8, 16.6, 16.2; HRMS (ESI) calcd for C$_{23}$H$_{28}$BrNO$_2$Na [M+Na]$^+$ 452.1201, found 452.1200; CHIRALPAK AD-H, hexane/2-PrOH = 95:5, 1.0 mL/min, retention times: 10.3 min (major isomer) and 14.5 min (minor isomer).

IV. References
