Synthesis of 1,3-Dihydrobenzo[c]furans from *Ortho*- Lithiated Aryloxiranes

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SUPPORTING INFORMATION

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General. Tetrahydrofuran (THF) was freshly distilled under a nitrogen atmosphere over sodium/benzophenone ketyl. Petroleum ether refers to the 40-60 °C boiling fraction. For the ^1H and ^{13}C NMR spectra (^1H NMR 300, 400, 500 MHz; ^{13}C NMR 75.4, 100 MHz, 125 MHz), CDCl_3 was used as the solvent. GC-MS spectrometry analyses were performed on a gas chromatograph (dimethylsilicon capillary column, 30 m, 0.25 mm i.d., flow 1 mL/min, oven temperature 70 °C (2 min), rate 20 °C/min, plateau 280 °C) equipped with a mass selective detector operating at 70 eV (EI). Optical rotation was performed on purified **3a** and measured with a polarimeter using a cell of 1 dm path length at 20 °C; the concentration (c) is expressed in g/100 mL. Melting points were uncorrected. Analytical thin layer chromatography (TLC) was carried out on precoated 0.25 mm thick plates of Kieselgel 60 F254; visualization was accomplished by UV light (254 nm) or by spraying with a solution of 5 % (w/v) ammonium molybdate and 0.2 % (w/v) cerium(III) sulfate in 100 ml 17.6 % (w/v) aq. sulphuric acid and heating to 200 °C for some time until blue spots appear. All reactions involving air-sensitive reagents were performed under nitrogen in oven-dried glassware using syringe-septum cap technique. Enantiomeric purity assay for compound (+)-**3a** was carried out with both racemic and optically active substrates using ^1H NMR (500 MHz, CCl_4 with CDCl_3 as external standard) in the presence of the Chiral Solvating Agent (CSA) (*R*)-(-)-2,2,2-trifluoro-1-(9-anthryl)ethanol,¹ (CSA/**3a** molar ratio = 2/1). Oxiranes **1a-d**² were prepared according to the reported procedure. *o*-Bromo *trans*-stilbene oxide (*S,S*)-**1a** (ee = 99%) was obtained by preparative HPLC separation of the racemic mixture (Chiralcel OD-H, column 256 × 4.6 mm × ID; flow: 1 ml/min; eluent: *n*-hexane/IPA 90/10 – 95/5). Oxirane **1e** was prepared from the corresponding *ortho*-bromo-*cis*-stilbene³ by oxidation with mCPBA in CH_2Cl_2 .⁴

¹ Parker, D. *Chem. Rev.* **1991**, *91*, 1441–1457.

² Akguen, E.; Glinski, M. B.; Dhawan, K. L.; Durst, T. *J. Org. Chem.* **1981**, *46*, 2730–2734.

³ Dunne, E. C.; Coyne, E. J.; Crowley, P. B.; Gilheany D. G. *Tetrahedron Lett.* **2002**, *43*, 2449-2453.

⁴ Efange, S. M. N.; Kamath, A. P.; Khare, A. B.; Kung, M.; Mach, R. H.; Parsons, S. M. *J. Med. Chem.* **1997**, *40*, 3905–3914

(2*R*^{*},3*S*^{*})-2-(2-Bromophenyl)-3-phenyloxirane (1e): colourless oil, 70%, dr > 98/2. ¹H NMR (500 MHz) δ 4.42 (d, *J* = 4.3 Hz, 1 H), 4.49 (d, *J* = 4.3 Hz, 1 H), 7.00–7.04 (m, 1 H), 7.13–7.23 (m, 6 H), 7.34–7.43 (m, 2 H); ¹³C NMR (125 MHz) δ 59.5, 60.6, 122.1, 126.6, 127.55, 127.6, 128.9, 129.1, 131.7, 133.9, 134.0; GC-MS (70 eV) *m/z* (%) 276 (*M*⁺+2, 18), 274 (*M*⁺, 19), 247 (24), 245 (34), 195 (53), 185 (39), 183 (39), 178 (41), 165 (93), 89 (100); FT-IR (film, cm⁻¹) 3062, 2967, 1697, 1473, 1439, 1249, 1183, 1024, 899, 750, 698.

Phenyl[2-(3-phenyloxiranyl)phenyl]methanol (2d): colourless oil, inseparable mixture of diastereoisomers, 72% overall yield, dr 2/1. ¹H NMR (500 MHz) δ 2.66 (br s, exchanges with D₂O, 1 H minor + 1 H major), 3.41 (d, *J* = 1.9 Hz, 1 H major), 3.62 (d, *J* = 1.9 Hz, 1 H minor), 4.02 (d, *J* = 1.9 Hz, 1 H major), 4.07 (d, *J* = 1.9 Hz, 1 H minor), 5.95 (s, 1 H minor), 6.01 (s, 1 H major), 7.07–7.65 (m, 14 H major + 14 H minor); ¹³C NMR (125 MHz) δ 60.5, 60.6, 62.3, 63.1, 72.9, 73.00 124.3, 125.1, 125.5, 125.6, 126.0, 126.2, 126.9, 127.1, 127.3, 127.7, 127.90, 127.96, 128.0, 128.20, 128.28, 128.3, 128.4, 128.5, 128.7, 129.3, 134.4, 135.1, 136.5, 136.7, 141.1, 141.2, 142.2, 142.5; GC-MS (70 eV) *m/z* (%) major: 284 (*M*⁺ - H₂O, 14), 196 (91), 195 (100), 178 (86), 105 (22), 77 (26); GC-MS (70 eV) *m/z* (%) minor: 284 (*M*⁺ - H₂O, 12), 196 (43), 195 (100), 178 (79), 105 (26), 77 (31); FT-IR (film, cm⁻¹): 3424, 3063, 3032, 2923, 1494, 1454, 1181, 1025, 910.

(3*R,1'*S**)-3-Hydroxybenzyl-1,3-dihydrobenzo[c]furan-1-spiro-1'-cyclohexane (3b):** colourless oil, 67%, dr > 98/2. ^1H NMR (500 MHz) δ 1.62–1.86 (m, 10 H), 2.58 (br s, exchanges with D_2O , 1 H), 5.09 (d, $J = 3.8$ Hz, 1 H), 5.47 (d, $J = 3.8$ Hz, 1 H), 6.80–6.83 (m, 1 H), 7.20–7.24 (m, 2 H), 7.29–7.39 (m, 6 H); ^{13}C NMR (125 MHz) δ 22.1, 22.3, 27.0, 37.9, 38.1, 75.1, 85.3, 86.5, 120.6, 123.0, 124.5, 126.5, 127.4, 128.0, 128.2, 136.8, 139.5, 148.0; GC-MS (70 eV) m/z (%) 276 ($\text{M}^+ - \text{H}_2\text{O}$), 187 (100), 169 (32), 141 (20), 77 (11); FT-IR (film, cm^{-1}): 3428, 3032, 2927, 1459, 1365, 1042, 856, 751, 702. Anal. Cald for $\text{C}_{20}\text{H}_{22}\text{O}_2$: C, 81.60; H, 7.53. Found: C, 81.34; H, 7.66.

(1*R,1'*S**)-(3,3-Dimethyl-1,3-dihydrobenzo[c]furan-1-yl)-*p*-tolylmethanol (3c):** white solid, mp 83–84 °C (hexane), 69%, dr > 98/2. ^1H NMR (500 MHz) δ 1.47 (s, 3 H), 1.53 (s, 3 H), 1.68 (s, exchanges with D_2O , 1 H), 2.38 (s, 3 H), 5.02 (d, $J = 4.2$ Hz, 1 H), 5.48 (d, $J = 4.2$ Hz, 1 H), 6.69–6.71 (m, 1 H), 7.08–7.19 (m, 4 H), 7.25–7.31 (m, 3 H); ^{13}C NMR (125 MHz) δ 21.1, 29.2, 29.4, 75.1, 85.40, 85.45, 120.3, 123.0, 126.4, 126.9, 128.0, 128.8, 136.6, 136.8, 137.0, 147.9; GC-MS (70 eV) m/z (%) 268 (M^+ , 1), 250 (44), 235 (98), 147 (100), 129 (37), 119 (48), 105 (30); FT-IR (film, cm^{-1}): 3439, 3027,

2972, 2924, 1610, 1456, 1361, 1288, 1154, 1041, 761. Anal. Calcd for C₁₈H₂₀O₂: C 80.56 %; H 7.51 %.

Found: C 80.24 %; H 7.15 %

(1*R,1'*S**,3'*R*) and (1*R**,1'*S**,3'*S*)-(3-*tert*-Butyl-1,3-dihydrobenzo[*c*]furan-1-yl)phenylmethanol**

(3e): white solid, mp 104–106 °C (Et₂O), inseparable mixture of diastereoisomers, 65% overall yield, dr 1/1. ¹H NMR (500 MHz) δ 1.03 (s, 18 H), 2.03 (br s, exchanges with D₂O, 1 H), 2.30 (br s, exchanges with D₂O, 1 H), 4.14 (d, *J* = 8.5 Hz, 1 H), 4.58 (d, *J* = 8.5 Hz, 1 H), 4.76 (s, 1 H), 4.86 (d, *J* = 2.4 Hz, 1 H), 4.98 (d, *J* = 6.1 Hz, 1 H), 5.28 (dd, *J* = 6.1, 2.4 Hz, 1 H), 7.12 (d, *J* = 7.9 Hz, 1 H), 7.19–7.27 (m, 5 H), 7.32–7.44 (m, 8 H), 7.50–7.53 (m, 3 H), 7.68 (d, *J* = 7.3 Hz, 1 H); ¹³C NMR (125 MHz) δ 26.3, 26.4, 35.5, 37.9, 71.0, 76.1, 80.1, 84.7, 85.3, 91.1, 122.6, 123.3, 123.9, 125.9, 126.6, 126.7, 127.3, 127.6, 127.8, 128.4, 128.5, 130.0, 132.4, 134.2, 139.6, 140.3, 141.0, 141.4; GC-MS (70 eV) *m/z* (%) 282 (M⁺, 1), 264 (9), 207 (21), 175 (100), 157 (34), 142 (14), 119 (20), 77 (12); FT-IR (film, cm⁻¹): 3452, 3042, 2956, 1589, 1477, 1201, 1010, 860. Anal. Calcd for C₁₉H₂₂O₂: C, 80.82; H, 7.85. Found: C, 80.60; H, 8.11.

Phenyl(3-phenyl-3-propyl-1,3-dihydrobenzo[c]furan-1-yl)methanol (3f): dr 2/1. (**1*R**,1'*S**,3'*R****): white solid, mp 111-112 °C (hexane), 49%, *R_f* 0.3 (EP/AcOEt 8/2): ¹H NMR (500 MHz) δ 0.89 (t, *J* = 7.4 Hz, 3 H), 1.28–1.41 (m, 2 H), 1.89 (ddd, *J* = 14.1, 11.8, 4.5 Hz, 1 H), 2.24 (ddd, *J* = 14.1, 11.7, 4.9 Hz, 1 H), 2.59 (br s, exchanges with D₂O, 1 H), 5.24 (d, *J* = 4.1 Hz, 1 H), 5.55 (d, *J* = 4.1 Hz, 1 H), 6.66 (d, *J* = 7.6 Hz, 1 H), 7.08–7.12 (m, 1 H), 7.17–7.40 (m, 8 H), 7.46–7.49 (m, 4 H); ¹³C NMR (125 MHz) δ 14.6, 17.8, 44.5, 75.3, 85.6, 90.8, 121.9, 123.2, 125.3, 126.7, 127.0, 127.5, 127.8, 128.2, 128.4, 137.7, 139.9, 145.4, 146.3; GC-MS (70 eV) *m/z* (%) 326 (*M*⁺ – H₂O, 2), 237 (100), 195 (31), 165 (26), 131 (19), 91 (15); FT-IR (film, cm⁻¹): 3440, 3063, 3031, 2958, 1600, 1457, 1264, 1195, 1020, 909, 735, 700. Anal. Calcd. for C₂₄H₂₄O₂: C, 83.69; H, 7.02. Found: C, 83.30; H, 6.86. (**1*R**,1'*S**,3'*S****): white solid, mp 110-111 °C (hexane), 26%, *R_f* 0.4 (EP/AcOEt 8/2): ¹H NMR (500 MHz) δ 0.81 (t, *J* = 7.4 Hz, 3 H), 1.24–1.35 (m, 2 H), 1.86 (br s, exchanges with D₂O, 1 H), 1.98 (ddd, *J* = 14.0, 12.0, 4.4 Hz, 1 H), 2.17 (ddd, *J* = 14.1, 11.8, 4.4 Hz, 1 H), 5.01 (d, *J* = 4.4 Hz, 1 H), 5.52 (d, *J* = 4.4 Hz, 1 H), 6.52 (d, *J* = 7.6 Hz, 1 H), 7.10–7.14 (m, 1 H), 7.25–7.37 (m, 10 H), 7.53–7.55 (m, 2 H); ¹³C NMR (125 MHz) δ 14.1, 17.5, 45.6, 75.2, 87.4, 91.6, 122.8, 123.3, 125.5, 126.5, 127.2, 127.3, 127.5, 127.9, 128.2, 128.4, 138.2, 139.4, 144.1, 145.7; GC-MS (70 eV) *m/z* (%) 326 (*M*⁺ – H₂O, 4), 237 (100), 195 (42), 165 (33), 131 (18), 91 (12); FT-IR (film, cm⁻¹): 3424, 3030, 2958, 1599, 1447, 1262, 1019, 759, 702. Anal. Calcd. for C₂₄H₂₄O₂: C, 83.69; H, 7.02. Found: C, 83.32; H, 6.95.

(3-Styryl-1,3-dihydrobenzo[c]furan-1-yl)-*p*-tolylmethanol (3g): dr 1/1. (**1*R**,1'*S**,3'*R****): white solid, mp 152-153 °C (Et₂O), 34%, ¹H NMR (500 MHz) δ 2.10 (br s, exchanges with D₂O, 1 H), 2.39 (s, 3 H), 4.49 (d, *J* = 9.2 Hz, 1 H), 4.86 (d, *J* = 9.2 Hz, 1 H), 5.57 (d, *J* = 8.3 Hz, 1 H), 6.35 (dd, *J* = 15.9, 8.3 Hz,

1 H), 6.84 (d, $J = 15.9$ Hz, 1 H), 7.18–7.47 (m, 12 H), 7.68 (d, $J = 7.9$ Hz, 1 H); ^{13}C NMR (125 MHz) δ 21.2, 70.5, 80.0, 81.5 125.2, 126.0, 126.7, 127.30, 127.31, 127.9, 128.5, 128.7, 129.3, 134.1, 136.1, 136.5, 137.0, 138.2; GC-MS (70 eV) m/z (%) 342 (M^+ , 2), 324 (46), 295 (40), 222 (51). 205 (63), 202 (60), 131 (49), 118 (100), 105 (77), 77 (62); FT-IR (film, cm^{-1}): 3419, 3028, 2922, 1494, 1450, 1271, 1062, 750, 695. Anal. Calcd. for $\text{C}_{24}\text{H}_{22}\text{O}_2$: C, 84.18; H, 6.48. Found: C, 84.11; H, 6.36.

(1*R,1'*S**,3'*S**)**: white solid, mp 150-152 °C (Et_2O), 34% ^1H NMR (500 MHz) δ 2.07 (br s, exchanges with D_2O , 1 H), 2.39 (s, 3 H), 4.74 (d, $J = 8.2$ Hz, 1 H), 4.82 (d, $J = 8.2$ Hz, 1 H), 5.35 (d, $J = 7.0$ Hz, 1 H), 6.42 (dd, $J = 15.9, 7.0$ Hz, 1 H), 6.63 (d, $J = 15.9$ Hz, 1 H), 7.13–7.51 (m, 13 H); ^{13}C NMR (125 MHz) δ 21.1, 70.0, 80.6, 81.4 125.9, 126.3, 126.6, 126.7, 127.5, 127.8, 127.9, 128.7, 128.9, 133.4, 136.4, 136.5, 136.7, 138.2; GC-MS (70 eV) m/z (%) 342 (M^+ , 3), 324 (41), 222 (33). 205 (49), 202 (47), 131 (100), 118 (93), 105 (37), 91 (82); FT-IR (film, cm^{-1}): 3417, 3026, 2923, 1601, 1450, 1266, 1059, 1020, 750, 697. Anal. Calcd. for $\text{C}_{24}\text{H}_{22}\text{O}_2$: C, 84.18; H, 6.48. Found: C, 83.92; H, 6.16.

(3-Phenyl-3-styryl-1,3-dihydrobenzo[c]furan-1-yl)-*p*-tolyl-methanol (3h): overall yield 73% dr 1/1.

(1*R,1'*S**,3'*S**)**: oil, R_f 0.3 (EP/AcOEt 8/2). ^1H NMR (400 MHz) δ 2.19 (d, $J = 2.9$ Hz, exchanges with D_2O , 1 H), 2.38 (s, 3 H), 5.11–5.12 (m, 1 H), 5.60 (d, $J = 4.0$ Hz, 1 H), 6.58 (d, $J = 15.7$ Hz, 1 H), 6.64 (d, $J = 15.7$ Hz, 1 H), 6.67 (d, $J = 7.7$ Hz, 1 H), 7.16–7.47 (m, 17 H); ^{13}C NMR (100 MHz) δ 21.2, 74.7, 86.6, 91.0, 123.2, 123.4, 126.4, 126.7, 127.3, 127.5, 127.6, 127.97, 128.01, 128.4, 128.5, 128.6, 128.9, 132.7, 136.1, 136.5, 137.1, 138.0, 143.4, 143.8; MS (ESI) m/z 441 [$\text{M} + \text{Na}$] $^+$; FT-IR (film, cm^{-1}): 3565, 3445, 2921, 1599, 1447, 1266, 1017, 971, 748, 697.

(1*R,1'*S**,3'*R**)**: oil, R_f 0.2 (EP/AcOEt 8/2). ^1H

NMR (500 MHz) δ 2.34 (s, 3 H), 2.45 (br s, exchanges with D₂O, 1 H), 5.19 (br d, J = 4.2 Hz, 1 H), 5.68 (d, J = 4.4 Hz, 1 H), 6.57 (d, J = 16.1 Hz, 1 H), 6.67 (d, J = 7.7 Hz, 1 H), 6.72 (d, J = 16.1 Hz, 1 H), 7.16–7.45 (m, 17 H); ¹³C NMR (100 MHz) δ 21.1, 75.0, 87.0, 90.9, 123.2, 123.4, 126.1, 126.4, 126.8, 127.50, 127.51, 127.9, 128.1, 128.3, 128.6, 128.9, 130.7, 133.3, 136.1, 136.3, 137.2, 137.6, 143.8, 144.4; MS (ESI) m/z 441 [M + Na]⁺; FT-IR (film, cm⁻¹): 3557, 3444, 2922, 1599, 1447, 1178, 1018, 969, 749, 697.

(3,3-Dimethyl-1,3-dihydrobenzo[c]furan-1-yl)methanol (3i): colourless oil, 56%. ¹H NMR (500 MHz) δ 1.48 (s, 3 H), 1.57 (s, 3 H), 2.56 (br s, exchanges with D₂O, 1 H), 3.76 (dd, ² J = 11.7 Hz, ³ J = 5.8 Hz, 1 H), 3.93 (dd, ² J = 11.7 Hz, ³ J = 2.9 Hz, 1 H), 5.29 (dd, J = 5.8, 2.9 Hz, 1 H), 7.11–7.32 (m, 4 H); ¹³C NMR (125 MHz) δ 29.0, 29.7, 65.8, 82.3, 85.6, 120.1, 121.2, 127.4, 128.0, 137.5, 147.4; GC-MS (70 eV) m/z (%) 178 (M⁺, 1), 147 (100), 129 (46), 91 (13), 43 (10); FT-IR (film, cm⁻¹): 3418, 3022, 2971, 2924, 1455, 1361, 1037, 896, 761.

(1R*,1'S*)-1-(3,3-Dimethyl-1,3-dihydrobenzo[c]furan-1-yl)ethanol (3j): colourless oil, 67%, dr > 98/2. ¹H NMR (500 MHz) δ 1.17 (d, J = 6.5 Hz, 3 H), 1.44 (s, 3 H), 1.53 (s, 3 H), 2.57 (br s, exchanges with D₂O, 1 H), 3.98 (dq, J = 6.5, 4.3 Hz, 1 H), 5.17 (d, J = 4.3 Hz, 1 H), 7.08 (d, J = 7.3 Hz, 1 H), 7.21–7.28 (m, 3 H); ¹³C NMR (125 MHz) δ 17.8, 29.0, 29.3, 70.3, 85.2, 85.3, 120.5, 121.9, 127.2,

127.8, 138.1, 147.4; GC-MS (70 eV) m/z (%) 147 ($M^+ - CH_3CHOH$, 100), 129 (48), 91 (11), 43 (7); FT-IR (film, cm^{-1}): 3419, 3027, 2972, 2927, 1455, 1377, 1081, 1034, 760.

(3-Phenyl-1,3-dihydrobenzo[c]furan-1-yl)methanol (3k): dr 58/42. (**1R***,**3R***): colourless oil, 37%, R_f 0.3 (EP/AcOEt 8/2). ^1H NMR (500 MHz) δ 2.08 (br s, exchanges with D_2O , 1 H), 3.91 (dd, $^2J = 12.0$ Hz, $^3J = 5.4$ Hz, 1 H), 4.04 (dd, $^2J = 12.0$ Hz, $^3J = 3.1$ Hz, 1 H), 5.38 (br dd, $J = 5.4, 3.1$ Hz, 1 H), 6.16 (br s, 1 H), 6.99 (d, $J = 7.6$ Hz, 1 H), 7.24–7.37 (m, 8 H); ^{13}C NMR (125 MHz) δ 65.4, 84.1, 85.7, 121.0, 122.6, 127.7, 127.9, 128.2, 128.4, 128.6, 138.7, 141.4, 142.6; GC-MS (70 eV) m/z (%) 226 ($\text{M}^+ - 2$), 195 (100), 165 (29), 115 (6); FT-IR (film, cm^{-1}): 3446, 1597, 1449, 1360, 1268, 1073, 961, 931, 762, 709. (**1R***,**3S***): colourless oil, 33%, R_f 0.2 (EP/AcOEt 8/2): ^1H NMR (500 MHz) δ 2.27 (br s, exchanges with D_2O , 1 H), 3.82 (dd, $^2J = 11.7$ Hz, $^3J = 6.1$ Hz, 1 H), 3.96 (dd, $^2J = 11.7$ Hz, $^3J = 3.1$ Hz, 1 H), 5.55–5.58 (m, 1 H), 6.25 (d, $J = 2.5$ Hz, 1 H), 7.05 (d, $J = 7.8$ Hz, 1 H), 7.24–7.35 (m, 8 H); ^{13}C NMR (125 MHz) δ 65.8, 84.7, 85.7, 121.3, 122.4, 126.8, 127.9, 128.2, 128.3, 128.6, 138.0, 141.9, 142.5; GC-MS (70 eV) m/z (%) 226 ($\text{M}^+ - 2$), 195 (100), 165 (29), 115 (6); FT-IR (film, cm^{-1}): 3357, 1596, 1450, 1359, 1265, 1025, 930, 760, 698.

1-(3-Phenyl-1,3-dihydrobenzo[c]furan-1-yl)ethanol (3l): dr 1/1. (**1R***,**1'S***,**3'R***): colourless oil, 37%, R_f 0.3 (EP/AcOEt 8/2). ^1H NMR (500 MHz) δ 1.29 (d, $J = 6.7$ Hz, 3 H), 2.03 (br s, exchanges with D_2O , 1 H), 4.11 (br s, 1 H), 5.22 (br dd, $J = 4.3, 2.2$ Hz, 1 H), 6.11 (d, $J = 2.2$ Hz, 1 H), 6.98 (d, $J = 6.6$ Hz, 1

H) 7.26–7.37 (m, 8 H); ^{13}C NMR (125 MHz) δ 18.4, 70.3, 85.4, 86.8, 122.0, 122.5, 127.6, 127.7, 127.9, 128.4, 128.5, 139.5, 141.2, 142.5; GC-MS (70 eV) m/z (%) 240 (M^+ , 2), 195 (100), 165 (27), 152 (9), 115 (6); FT-IR (film, cm^{-1}): 3417, 3063, 2975, 2917, 1597, 1449, 1282, 1115, 930, 762, 701.

(1R*,1'S*,3'S*): colourless oil, 36% R_f 0.2: ^1H NMR (500 MHz) δ 1.22 (d, $J = 6.7$ Hz, 3 H), 1.98 (br s, exchanges with D_2O , 1 H), 4.08 (br s, 1 H), 5.45 (dd, $J = 3.3, 2.7$ Hz, 1 H), 6.22 (d, $J = 2.7$ Hz, 1 H), 7.01 (d, $J = 6.6$ Hz, 1 H) 7.23–7.34 (m, 8 H); ^{13}C NMR (125 MHz) δ 17.9, 71.2, 86.4, 87.7, 121.9, 122.5, 126.9, 127.7, 128.1, 128.2, 128.6, 138.4, 142.3, 142.7; GC-MS (70 eV) m/z (%) 240 (M^+ , 3), 195 (100), 165 (32), 152 (7), 115 (4); FT-IR (film, cm^{-1}): 3447, 3026, 2974, 2918, 2850, 1599, 1455, 1382, 1279, 1119, 753, 700.

(1R*,3R) and (1R*,3S)-(3-tert-Butyl-1,3-dihydrobenzo[c]furan-1-yl)methanol (3m): colourless oil, inseparable mixture of diastereoisomers, 60% overall yield, dr 1/1. ^1H NMR (500 MHz) δ 0.93 (s, 9 H), 1.00 (s, 9 H), 2.51 (br s, exchanges with D_2O , 2 H), 3.67 (dd, $^2J = 11.7$ Hz, $^3J = 5.5$ Hz, 1 H), 3.78 (dd, $^2J = 11.5$ Hz, $^3J = 7.1$ Hz, 1 H), 3.88 (dd, $^2J = 11.5$ Hz, $^3J = 3.1$ Hz, 1 H), 3.93 (dd, $^2J = 11.7$ Hz, $^3J = 3.5$ Hz, 1 H), 4.92–4.94 (m, 2 H), 5.17–5.20 (m, 1 H), 5.29–5.32 (m, 1 H), 7.15–7.33 (m, 8 H); ^{13}C NMR (125 MHz) δ 25.5, 26.1, 35.3, 37.0, 65.9, 66.0, 82.8, 84.1, 91.5, 91.8, 121.0, 121.2, 122.9, 123.1, 127.4, 127.52, 127.54, 127.6, 139.6, 139.8, 140.6, 140.8; GC-MS (70 eV) m/z (%), diastereoisomer with $t_R = 8.47$ min: 175 ($\text{M}^+ - \text{CH}_2\text{OH}$, 71), 149 (100), 131 (74), 103 (32), 77 (12); diastereoisomer with $t_R = 8.66$ min: 175 ($\text{M}^+ - \text{CH}_2\text{OH}$, 68), 149 (100), 131 (76), 103 (41), 77 (15); FT-IR (film, cm^{-1}): 3417, 3043, 2955, 2868, 1478, 1459, 1362, 1046, 748.

(1*R,1'*S**,3'*R*) and (1*R**,1'*S**,3'*S*)-1-(3-*tert*-Butyl-1,3-dihydrobenzo[c]furan-1-yl)ethanol (3n):** colourless oil, inseparable mixture of diastereoisomers, 65% overall yield, dr 77/23. ¹H NMR (500 MHz) δ 0.93 (s, 9 H minor), 1.00 (s, 9 H major), 1.04 (d, *J* = 6.5 Hz, 3 H minor), 1.36 (d, *J* = 6.4 Hz, 3 H major), 2.22 (br s, exchanges with D₂O, 1 H major + 1 H minor), 3.89–3.98 (m, 1 H major + 1 H minor), 4.83–4.86 (m, 2 H major), 4.93 (d, *J* = 2.8 Hz, 1 H minor), 5.25 (dd like t, *J* = 2.8 Hz, 1 H minor), 7.13–7.27 (m, 3 H major + 3 H minor), 7.34–7.37 (m, 1 H major + 1 H minor); ¹³C NMR (125 MHz) δ 17.1, 19.9, 25.6, 26.2, 35.5, 37.0, 71.0, 71.1, 85.5, 86.8, 91.1, 92.0, 121.6, 122.5, 122.7, 123.0, 123.3, 127.2, 127.3, 127.4, 139.9, 140.7, 140.8, 141.4; GC-MS (70 eV) *m/z* (%), Minor: 220 (*M*⁺, 1), 175 (100), 157 (67), 145 (52), 119 (48), 91 (32); Major: 220 (*M*⁺, 2), 175 (100), 157 (73), 145 (61), 119 (44), 91 (38); FT-IR (film, cm⁻¹): 3417, 2955, 1478, 1459, 1392, 1362, 1083, 1046, 748.

(1*R,3*R**) and (1*R**,3*S**)-(3-Phenyl-3-propyl-1,3-dihydrobenzo[c]furan-1-yl)methanol (3o):** inseparable mixture of diastereoisomers, colourless oil, 60%, dr 77/23. ¹H NMR (500 MHz) δ 0.90 (t, *J* = 7.4 Hz, 3 H major), 0.92 (t, *J* = 7.5 Hz, 3 H minor), 1.11–1.44 (m, 2 H major + 2 H minor), 2.01–2.28 (m, 1 H major + 1 H minor), 3.75 (dd, ²*J* = 11.7 Hz, ³*J* = 6.3 Hz, 1 H major), 3.89–3.93 (m, 2 H major + 2 H minor), 4.09 (dd, ²*J* = 11.6 Hz, ³*J* = 3.2 Hz, 1 H minor), 5.35 (dd, *J* = 5.8, 3.3 Hz, 1 H minor), 5.44 (dd, *J* = 6.3, 3.5 Hz, 1 H major), 7.17–7.42 (m, 7 H major + 7 H minor), 7.55–7.61 (m, 2 H major + 2 H

mior); ^{13}C NMR (125 MHz) δ 14.2, 14.3, 17.4, 17.6, 44.3, 44.8, 65.4, 65.9, 82.3, 83.9, 90.9, 91.4, 121.2, 121.3, 121.9, 122.6, 124.9, 125.2, 126.7, 127.0, 127.6, 127.7, 127.9, 128.0, 128.1, 128.2, 138.4, 138.6, 144.4, 145.2, 145.3, 145.8; MS (ESI) m/z 291 $[\text{M} + \text{Na}]^+$; FT-IR (film, cm^{-1}): 3418, 3030, 2958, 1456, 1122, 1035, 753, 700.

(1*R,1'*S**,3'*R**) and (1*R**,1'*S**,3'*S**)-1-(3-Phenyl-3-propyl-1,3-dihydrobenzo[c]furan-1-yl)ethanol**

(3p): inseparable mixture of diastereoisomers, 65% overall yield, dr: 1/1. ^1H NMR (500 MHz) δ 0.87 (t, $J = 7.3$ Hz, 3 H), 0.92 (t, $J = 7.3$ Hz, 3 H), 1.25 (d, $J = 6.4$ Hz, 3 H), 1.34 (d, $J = 6.3$ Hz, 3 H), 1.33–1.41 (m, 4 H), 2.01–2.33 (m, 4 H), 3.88–3.93 (m, 1 H), 4.12–4.17 (m, 1 H), 5.18 (d, $J = 5.1$ Hz, 1 H), 5.21 (d, $J = 4.5$ Hz, 1 H), 7.20–7.40 (m, 14 H), 7.53–7.59 (m, 4 H); ^{13}C NMR (125 MHz) δ 14.1, 14.3, 17.4, 17.5, 18.5, 18.6, 18.8, 18.9, 70.4, 70.5, 85.1, 86.8, 90.3, 91.3, 121.7, 122.0, 122.5, 122.8, 124.9, 125.4, 126.6, 126.9, 127.5, 127.6, 127.7, 127.8, 128.1, 128.2, 139.1, 139.6, 143.9, 145.3, 145.6, 145.7; GC-MS (70 eV) m/z (%) diastereoisomer with $t_R = 11.58$ min: 282 (M^+ , 1), 237 (100), 219 (18), 195 (39), 194 (36), 165 (38), 91 (26); diastereoisomer with $t_R = 11.62$ min: 282 (M^+ , 1), 237 (100), 219 (16), 195 (27), 194 (29), 165 (27), 91 (20); FT-IR (film, cm^{-1}): 3418, 2959, 1599, 1494, 1377, 1038, 954, 880, 752, 700.

Figure S1. Ortep view of (±)-**3a**

(1R*, 1'R*)-3q