Supplementary Material (ESI) for Organic and Biomolecular Chemistry

Supporting Information for:

Synthesis of densely functionalised arenes using [2+2+2] cycloaddition reactions

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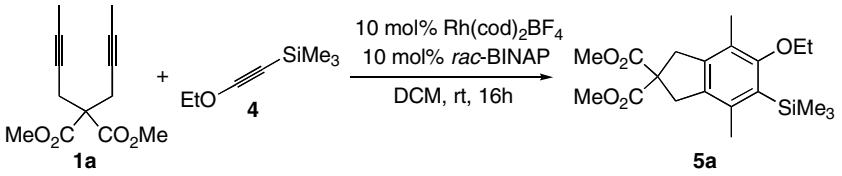
General. ^{1}H NMR spectra were recorded on Bruker Ultrashield 500 MHz or Varian XL 300 MHz spectrometers. Chemical shifts are reported in ppm from tetramethylsilane with the solvent resonance as the internal standard ($CDCl_3$: 7.26 ppm). Data are reported as follows: chemical shift, integration, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, br = broad, m = multiplet), and coupling constants (Hz). ^{13}C NMR was recorded on a Bruker 400 MHz (100 MHz) spectrometer with complete proton decoupling. Chemical shifts are reported in ppm from tetramethylsilane with the solvent as the internal standard ($CDCl_3$: 77.0 ppm). Mass spectrometry (*m*/*z*) was performed on a Fisons VG Trio 2000 (EI)/(CI) or a Concept IS (HRMS) spectrometer, with only molecular ions reported. Infrared (IR) spectra were obtained on an ATi Genesis Series FTIR, with υ_{max} in cm^{-1}. Bands are characterised as broad (br), strong (s), medium (m) and weak (w).

Flash chromatography was performed on Merck silica gel 60H (40-63 m, 230-300 mesh). Thin layer chromatography (TLC) was performed on aluminium backed plates pre-coated with silica (0.2 mm, Merck DC-alufolien Kieselgel 60). Visualisation was achieved by UV or by dipping in phosphomolybdic acid solution, followed by heating.

All reactions were conducted under an inert atmosphere of nitrogen unless otherwise stated. Compounds **1a**,[1] **1b**,[2] **1c**,[3] **1d**,[4] **1e**,[5] **1g**,[6] **1h**,[7] **2a**,[8] **2b**[8] and **4**[9] were prepared according to the literature methods and displayed similar spectroscopic properties. 2-Propynylbenzene **6a** was purchased from Aldrich, while derivatives **6b**,[10] **6c**[11] and **6d**[12] were synthesised and displayed similar spectroscopic properties to the literature data. Bis(cyclooctadiene) rhodium(I) tetrafluoroborate and *rac*-BINAP were purchased from Strem. All other reagents were purchased from Aldrich Chemical Companies and used directly.

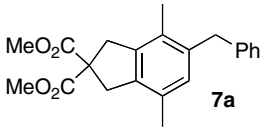
Representative procedure for [2+2+2] cycloaddition reaction: Synthesis of Dimethyl 5-Ethoxy-4,7-dimethyl-6-(trimethylsilyl)-1H-indene-2,2(3H)-dicarboxylate ***5a****.*



Rac-BINAP (13 mg, 0.021 mmol, 10 mol%), $Rh(cod)_2BF_4$ (8.5 mg, 0.021 mmol, 10 mol%), and DCM (1 ml) were added to a 10 ml glass vial and stirred for 5 min. The N_2 atmosphere was replaced with H_2, using a balloon of H_2, and the mixture stirred for 1h. The resulting deep red solution was concentrated to dryness. A solution of **1a** (50 mg, 0.21 mmol, 1 equiv.) and **4** (30 mg, 0.21 mmol, 1 equiv.) in DCM (2 ml) was added via cannula to the catalyst residue and the mixture stirred for 16h at room temperature. The mixture was concentrated under vacuum and the residue purified by flash chromatography (19:1 petrol/EtOAc) to provide a colourless solid (31mg, 39%).

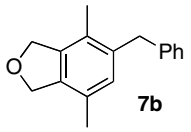
M.p. 90-92 ^{o}C. IR (neat): 2952 (w), 2924 (w), 1737 (s), 1436 (m), 1281 (m), 1248 (m) 1161 (m), 1118 (m) 1060 (w) cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$): δ 0.40 (9H, s), 1.43 (3H, *t*, J= 7.0 Hz), 2.17 (3H, s), 2.32 (3H, s), 3.56 (2H, s), 3.58 (2H, s), 3.73 (2H, q, *J* = 7.0 Hz), 3.80 (6H, s). ^{13}C NMR (125.8 MHz, $CDCl_3$): δ 3.0, 13.3, 15.6, 20.5, 40.4, 40.5, 53.3, 59.5, 70.1, 123.9, 129.5, 134.8, 137.6, 142.1, 162.9, 172.7. HRMS (E.I.) *m/z* calcd for $C_{20}H_{31}O_5Si$: 379.1935. Found: 379.1942.

Data for Dimethyl 5-Benzyl-4,7-dimethyl-1H-indene-2,2(3H)-dicarboxylate ***7a****:*



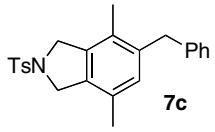
IR (neat): 3025 (w), 2952 (m), 2919 (w), 1736 (s), 1452 (m), 1433 (m), 1281 (m), 1249 (s), 1197 (m), 1162 (m), 1061 (m) cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ 2.16 (3H, s), 2.25 (3H, s), 3.60 (2H, s), 3.62 (2H, s), 3.82 (6H, s), 4.00 (2H, s), 6.85 (1H, s), 7.10-7.35 (5H, m). ^{13}C NMR (125.8 MHz, $CDCl_3$): δ 15.6, 18.7, 39.1, 39.6, 40.2, 53.0, 59.5, 125.8, 128.4, 128.6, 129.4, 130.2, 130.6, 136.6, 137.7, 139.2, 140.8, 172.5. HRMS (E.I.) *m/z* cald for $C_{22}H_{25}O_4$: 353.1747. Found: 353.1759.

Data for 5-Benzyl-4,7-dimethyl-1,3-dihydroisobenzofuran ***7b****:*



M.p. 68-70 ^{o}C. IR (neat): 3024 (m), 2917 (m), 2846 (s), 1762 (m), 1601 (m), 1493 (s), 1452 (s), 1365 (m), 1068 (m), 1049 (m), 1029 (m) 907 (s) cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ 2.13 (3H, s), 2.25 (3H, s), 4.04 (2H, s), 5.17 (4H, s), 6.93 (1H, s), 7.15-7.40 (5H, m). ^{13}C NMR (125.8 MHz, $CDCl_3$): δ 15.6, 18.4, 38.8, 73.8, 73.9, 126.0, 127.0, 128.3, 128.4, 128.6, 130.5, 135.9, 138.2, 138.6, 140.6. MS (E.I.) *m/z* cald for $C_{17}H_{19}O$: 239. Found: 239.

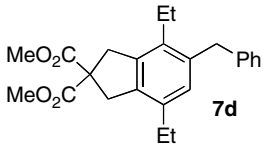
*Data for 5-Benzyl-4,7-dimethyl-2-tosylisoindoline **7c**:*



7c

M.p. 75-77 °C. IR (neat): 3025 (w), 2920 (m), 2853 (w), 1493 (w), 1452 (w), 1346 (m), 1165 (s), 1099 (m), 1062 (w) cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ 2.02 (3H, s), 2.13 (3H, s), 2.41 (3H, s), 3.91 (2H, s), 4.56 (4H, s), 6.83 (1H, s), 7.03-7.09 (2H, m), 7.13-7.28 (3H, m), 7.32 (2H, d, *J* = 8.2 Hz), 7.78 (2H, d, *J* = 8.3 Hz). ^{13}C NMR (125.8 MHz, $CDCl_3$): δ 15.4, 18.3, 21.5, 38.9, 53.3, 53.8, 126.0, 127.6, 128.3, 128.4, 128.5, 129.6, 129.8, 130.8, 133.1, 133.9, 135.7, 138.7, 140.2, 143.6. HRMS (E.I.) *m/z* cald for $C_{24}H_{25}NO_2S$: 392.1679. Found: 392.1679.

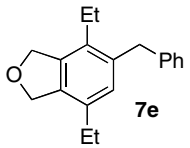
*Data for Dimethyl 5-Benzyl-4,7-diethyl-1H-indene-2,2(3H)-dicarboxylate **7d**:*



7d

IR (neat): 3060 (w), 3025 (m), 2962 (s), 2931 (s), 2872 (s), 1737 (s), 1601 (m), 1452 (s), 1434 (s), 1255 (s), 1197 (s), 1163 (s), 1078 (m) cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ 0.79 (3H, t, *J* = 7.6 Hz), 0.96 (3H, t, *J* = 7.6 Hz), 2.29-2.37 (4H, m), 3.35 (2H, s), 3.37 (2H, s), 3.55 (6H, s), 3.77 (2H, s), 6.59 (1H, s), 6.92 (2H, d, *J* = 7.1 Hz), 6.97 (1H, d, *J* = 7.3 Hz), 7.05 (2H, t, *J* = 7.5 Hz). ^{13}C NMR (125.8 MHz, $CDCl_3$): δ 14.0, 14.4, 23.1, 26.1, 38.5, 39.0, 39.4, 53.0, 60.0, 125.8, 127.5, 128.3, 128.9, 129.1, 135.8, 136.3, 137.0, 138.9, 141.5, 172.4. HRMS (E.I.) *m/z* cald for $C_{24}H_{29}O_4$: 381.2060. Found: 381.2052.

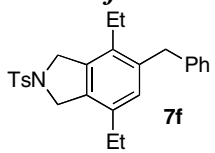
*Data for 5-Benzyl-4,7-diethyl-1,3-dihydroisobenzofuran **7e**:*



7e

M.p. 81-83 °C. IR (neat): 3025 (m), 2959 (s), 2931 (s), 2871 (s), 1761 (m), 1601 (m), 1494 (s), 1452 (s), 1050 (m), 952 (m) cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ 1.03 (3H, t, *J* = 7.5 Hz), 1.20 (3H, t, *J* = 7.8 Hz), 2.52 (4H, q, *J* = 7.5 Hz), 4.06 (2H, s), 5.16 (4H, s), 6.92 (1H, s), 7.10-7.35 (5H, m). ^{13}C NMR (125.8 MHz, $CDCl_3$): δ 13.8, 14.3, 24.7, 26.1, 38.1, 70.9, 73.2, 111.5, 127.5, 128.8, 129.4, 134.4, 134.8, 135.6, 137.5, 138.3, 141.3. MS (E.I.) *m/z* cald for $C_{26}H_{30}NO_2S$: 420. Found: 420.

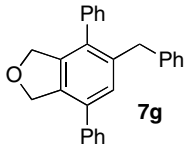
*Data for 5-Benzyl-4,7-diethyl-2-tosylisoindoline **7f**:*



7f

M.p. 98-100 °C. IR (neat): 3026 (m), 2966 (s), 2931 (s), 2872 (s), 1765 (w), 1734 (w), 1598 (s), 1494 (s), 1452 (s), 1347 (s), 1176 (s), 1099 (s) cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ 0.97 (3H, t, *J* = 7.6 Hz), 1.14 (3H, t, *J* = 7.6 Hz), 2.42 (3H, s), 2.42-2.49 (4H, m), 3.97 (2H, m), 4.60 (2H, s), 4.62 (2H, s), 6.86 (1H, s), 7.08 (2H, d, *J* = 7.7 Hz), 7.15-7.20 (1H, m), 7.23-7.28 (2H, m), 7.33 (2H, d, *J* = 8.0 Hz), 7.80 (2H, d, *J* = 8.0 Hz). ^{13}C NMR (125.8 MHz, $CDCl_3$): δ 14.0, 14.2, 21.5, 23.2, 25.8, 38.2, 52.9, 53.1, 126.0, 127.6, 128.4, 128.5, 129.7, 129.8, 132.8, 133.8, 134.7, 135.3, 136.0, 138.2, 140.9, 143.6. HRMS (E.I.) *m/z* cald for $C_{26}H_{30}O_2NS$: 420.1992. Found: 420.2006.

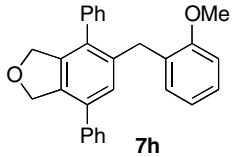
Data for 5-Benzyl-4,7-diphenyl-1,3-dihydroisobenzofuran ***7g****:*



7g

IR (neat): 3058 (w), 3025 (w), 2905 (w), 2849 (w), 1711 (m), 1493 (m), 1468 (m), 1363 (m), 1074 (m), 1054 (m), 907 (m) cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ 3.93 (2H, s), 4.91 (2H, s), 5.29 (2H, s), 7.00 (2H, d, *J* = 7.0 Hz), 7.18-7.20 (4H, m), 7.28 (1H, s), 7.35-7.48 (9H, m). ^{13}C NMR (125.8 MHz, $CDCl_3$): δ 38.6, 73.8, 74.0, 125.9, 127.4, 127.5, 127.9, 128.1, 128.3, 128.5, 128.7, 128.8 (x2), 129.7, 135.0 (x2), 138.7, 138.8, 139.6, 140.0, 141.2. HRMS (E.I.) *m/z* calcd for $C_{27}H_{22}O$: 362.1665. Found: 362.1657.

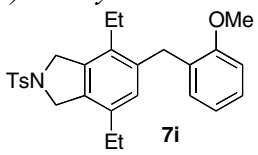
Data for 5-(2-Methoxybenzyl)-4,7-diphenyl-1,3-dihydroisobenzofuran ***7h****:*



7h

IR (neat): 3058 (m), 3026 (m), 2937 (m), 2835 (m), 1600 (m), 1587 (m), 1491 (s), 1465 (s), 1439 (m), 1244 (s), 1106 (m), 1052 (s), 1030 (m), 909 (s) cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ 3.74 (3H, s), 3.91 (2H, s), 4.93 (2H, s), 5.29 (2H, s), 6.55-6.80 (4H, m), 7.25-7.45 (10H, m). ^{13}C NMR (125.8 MHz, $CDCl_3$): δ 32.5, 55.2, 73.8, 74.1, 110.2, 120.4, 127.2, 127.3, 127.4, 127.5, 127.8, 127.9, 128.1, 128.3, 128.4, 128.7, 128.8, 129.1, 129.4, 129.6, 130.3, 134.7, 134.8, 138.6, 139.0, 139.4, 140.2, 157.2. HRMS (E.I.) *m/z* cald for $C_{28}H_{24}O_2$: 392.1771. Found: 392.1759.

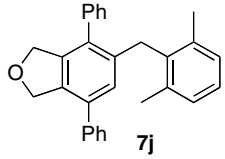
Data for 4,7-Diethyl-5-(2-methoxybenzyl)-2-tosylisoindoline ***7i****:*



7i

M.p. 138-140 °C. IR (neat): 2964 (m), 1932 (w), 2871 (w), 1598 (m), 1491 (m) 1347 (m), 1242 (m), 1164 (s), 1100 (m), 1057 (m) cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ 1.00 (3H, t, *J* = 7.6 Hz), 1.10 (3H, t, *J* = 7.6 Hz), 2.38-2.48 (4H, m), 3.82 (3H, s), 3.91 (2H, s), 4.57 (2H, s), 4.61 (2H, s), 6.74-6.87 (4H, m), 7.14-7.20 (1H, m), 7.32 (2H, d, *J* = 8.0 Hz), 7.78 (2H, d, *J* = 8.0 Hz). ^{13}C NMR (125.8 MHz, $CDCl_3$): δ 14.1, 14.2, 21.5, 23.1, 25.8, 31.8, 53.0, 53.2, 55.3, 110.1, 120.4, 127.3, 127.6, 129.2, 129.5, 129.7, 129.8, 132.5, 133.8, 134.8, 135.0, 135.8, 138.0, 143.6, 157.1. HRMS (E.I.) *m/z* cald for $C_{27}H_{32}NO_3S$: 450.2097. Found: 450.2099.

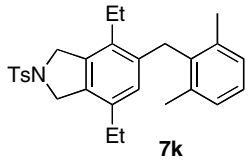
Data for 5-(2,6-Dimethylbenzyl)-4,7-diphenyl-1,3-dihydroisobenzofuran ***7j****:*



7j

M.p. 140-142 °C. IR (neat): 3059 (m), 3024 (m), 2943 (m), 2855 (m), 1601 (m), 1467 (s), 1448 (m) (s), 1055 (s), 909 (s) cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ 2.18 (6H, s), 3.80 (2H, s), 4.92 (2H, s), 5.23 (2H, s), 6.66 (1H, s), 6.94-7.52 (13H, m). ^{13}C NMR (125.8 MHz, $CDCl_3$): δ 20.2, 32.9, 73.7, 74.0, 126.3, 127.2, 127.3, 127.6, 127.8, 128.0, 128.2, 128.5, 128.6, 128.8, 129.1, 129.3, 131.7, 134.7, 134.8, 134.9, 136.9, 137.0, 137.5, 139.0, 139.3, 140.1. HRMS (E.I.) *m/z* cald for $C_{29}H_{25}O$: 389.1900. Found: 391.1900.

*Data for 5-(2,6-Dimethylbenzyl)-4,7-diethyl-2-tosylisoindoline 7**k**:*



7k

M.p. 165-167 ^{o}C. IR (neat): 3022 (w), 2964 (m), 2931 (w), 1465 (m), 1348 (m), 1164 (s), 1099 (m), 1062 (w) cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$): δ 0.93 (3H, t, *J* = 7.6 Hz), 1.19 (3H, t, *J* = 7.6 Hz), 2.14 (6H, s), 2.27 (2H, t, *J* = 7.6 Hz), 2.41 (3H, s), 2.64 (2H, t, *J* = 7.6 Hz), 3.93 (2H, s), 4.55 (2H, s), 4.65 (2H, s), 6.19 (1H, s), 7.04-7.13 (3H, m), 7.32 (2H, d, *J* = 8.1 Hz), 7.79 (2H, d, *J* = 8.1 Hz). ^{13}C NMR (125.8 MHz, $CDCl_3$): δ 13.5, 14.3, 20.0, 21.5, 23.1, 25.8, 31.2, 52.8, 53.1, 125.7, 126.4, 127.6, 128.1, 129.8, 132.2, 133.8, 134.2, 134.9, 136.1, 136.4, 136.9, 137.2, 143.6. HRMS (E.I.) *m/z* cald for $C_{28}H_{34}NO_2S$: 448.2305. Found: 448.2312.

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