Electronic supporting information

Pd-catalyzed cascade reactions involving skipped dienes: from double carbopalladation to remote C–C cleavage

Hamid Azizollahi,[a,b] Vaibhav P. Mehta,*[a,c] and José-Antonio García-López*[a]

a. Grupo de Química Organometálica, Departamento de Química Inorgánica, Universidad de Murcia, Murcia 30100, Spain. E-mail: joangalo@um.es

b. Department of Chemistry, Faculty of Science, Ferdowsi University of Mashhad, 91775-1436, Mashhad, Iran.

c. Department of Chemistry, Marwadi University, Rajkot - Morbi Highway, Gauridad, Rajkot, Gujarat 360003 (India). E-mail: mehtavp.13@gmail.com

Table of contents

- General Remarks S2
- Chart of starting materials S2
- Synthetic procedures and characterization of the starting materials S3
- Optimization table for the synthesis of compounds 2a and 3a S10
- General procedure C for synthesis of [4,5]-spirocycles 2a-n S11
- General procedure D for synthesis of compounds 3a-j S16
- Synthesis of [4,5]-spirocycles 6 and 7 S20
- Isolation of intermediate 4a and mechanistic experiments S21
- References S24
- ¹H- and ¹³C-NMR spectra S25
General Remarks

Nuclear Magnetic Resonance (NMR) spectra were recorded on a 400 or 300 MHz Bruker NMR spectrometers in CDCl₃ at 298 K (unless stated otherwise). All chemical shift values are reported in parts per million (ppm) relative to the solvent signal and were determined in CDCl₃, with coupling constant (J) values reported in Hz. All spectra were referenced to CDCl₃ the residual solvent peak CHCl₃ (δ = 7.26 ppm) for ¹H NMR and the CDCl₃ solvent peak (δ = 77.16 ppm) for ¹³C{¹H} NMR. The notation of signals is: Proton: δ chemical shift in ppm (number of protons, multiplicity, J value(s), proton assignment). Carbon: δ chemical shift in ppm (carbon assignment). Fluorine: δ chemical shift in ppm (Fluorine assignment). Splitting patterns are assigned s = singlet, bd = broad doublet, d = doublet, td = triplet of doublet, dt = doublet of triplet, t = triplet, q = quartet, br= broad signal. IR spectra were recorded on a PerkinElmer Spectrum 65 spectrometer using the ATR technique (attenuated total reflection) on bulk material, and data are quoted in wavenumbers (cm⁻¹). Reagents were either purchased directly from commercial suppliers or prepared according to literature procedures. Unless otherwise noted, yields refer to isolated material on the basis of product purity (≥95%) by ¹H-NMR following silica gel chromatography. TLC plates Alugram® Sil G/UV254. Detection under UV light at 254 nm. Chromatography: Separations were carried out on Silica gel (Sigma Aldrich, 40-63 µ, 60 Å).

Chart of starting materials
Synthesis of starting materials.

General procedure A for the synthesis of compounds 1a-q.

The starting 1,4-diene alcohol (2-methylenepent-4-en-1-ol) was prepared from propargyl alcohol and allylmagnesium bromide following a reported method in the literature.\cite{1}

Procedure A. Starting materials 1 were prepared according to a procedure previously reported in the literature.\cite{2} A solution of diisopropylazodicarboxylate (1 ml, 7.5 mmol, 1.5 eq) in dry THF (10 ml) was slowly added to a stirred solution of triphenylphosphine (2 g, 7.5 mmol, 1.5 eq) under a nitrogen atmosphere, followed by the corresponding 2-bromophenol derivatives (5 mmol, 1 eq) and 2-methylenepent-4-en-1-ol (0.49 g, 5 mmol), in THF (20 ml) at 0 ºC. The resulting mixture was stirred at room temperature overnight. After completion of the reaction, the reaction mixture was concentrated to approx. 5 ml and n-hexane (25 ml) was added. The resulting suspension was filtered and the solid was washed with n-hexane. The filtrate was evaporated to dryness and the crude was directly subjected to flash column chromatography using n-hexane as eluent to afford the pure products.

**Compound 1a.** Prepared according to procedure A from 2-bromophenol on a 10 mmol scale to afford the compound 1a as a colorless oil in 78% yield (1.97 g, 7.79 mmol). Rf (n-hexane) = 0.47. $^1$H NMR (300 MHz, CDCl$_3$) $\delta = 7.52$ (dd, $J = 7.8$, 1.6 Hz, 1 H), 7.21 (m, 1 H), 6.87 – 6.78 (m, 2 H), 5.92 – 5.79 (m, 1 H), 5.28 – 5.00 (m, 4 H), 4.50 (s, 2 H), 2.93 (d, $J = 6.9$ Hz, 2 H). $^{13}$C NMR (75 MHz, CDCl$_3$) $\delta =$ 154.83 (s, C$_{q}$), 142.40 (s, C$_{q}$), 135.17 (s, CH), 133.25 (s, CH), 128.25 (s, CH), 121.83 (s, CH), 116.95 (s, CH$_2$), 113.32 (s, CH), 113.18 (s, CH$_2$), 112.17 (s, C$_{q}$), 71.02 (s, CH$_2$), 37.55 (s, CH$_2$). IR (cm$^{-1}$): 1584, 1477, 1441, 1275, 1244, 1050, 1031, 913, 743. HR-MS (+APCI) m/z calcd for C$_{12}$H$_{14}$BrO [M+H]$^+$ 253.0223, found 253.0214.

**Compound 1b.** Prepared according to procedure A from 2-iodophenol on a 10 mmol scale to afford the compound 1b as a colorless oil in 73% yield (2.19 g, 7.3 mmol). Rf (n-hexane) = 0.51. $^1$H NMR (300 MHz, CDCl$_3$) $\delta = 7.77$ (dd, $J = 7.8$, 1.6 Hz, 1 H)
Compound 1c. Prepared according to procedure A from phenol on a 8 mmol scale to afford the compound 1c as a colorless oil in 55% yield (0.77 g, 4.4 mmol). Rf (n-hexane) = 0.48. $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ = 7.29 – 7.21 (m, 2 H), 6.96 – 6.87 (m, 3 H), 5.84 (m, 1 H), 5.24 – 4.97 (m, 4 H), 4.43 (s, 2 H), 2.88 (d, $J$ = 6.8 Hz, 2 H). $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ = 158.69 (s, C$_q$), 143.18 (s, C$_q$), 135.30 (s, CH), 129.32 (s, CH), 120.75 (s, CH), 116.79 (s, CH$_2$), 114.72 (s, CH$_2$), 112.95 (s, CH), 70.26 (s, CH$_2$), 37.61 (s, CH$_2$). IR (cm$^{-1}$): 1568, 1470, 1441, 1275, 1244, 1030, 740. HR-MS (+APCI) m/z calcd for C$_{12}$H$_{14}$O [M+H]$^+$ 271.0128, found 271.0116.

Compound 1d. Prepared according to procedure A from 2-bromo-4-fluorophenol on a 10 mmol scale to afford the compound 1d as a colorless oil in 69% yield (1.87 g, 6.9 mmol). Rf (n-hexane) = 0.46. $^1$H NMR (300 MHz, CDCl$_3$) $\delta$ = 7.28 (dd, $J$ = 7.8, 3.0 Hz, 1 H), 6.96 – 6.90 (m, 1 H), 6.80 (dd, $J$ = 9.1, 4.8 Hz, 1 H), 5.92 – 5.78 (m, 1 H), 5.27 – 5.03 (m, 4 H), 4.46 (s, 2 H), 2.92 (d, $J$ = 6.8, 2 H). $^{13}$C NMR (75 MHz, CDCl$_3$) $\delta$ = 156.59 (d, $J$ = 242.9 Hz, C$_q$), 151.56 (d, $J$ = 2.8 Hz, C$_q$), 142.37 (s, C$_q$), 135.13 (s, CH), 120.34 (d, $J$ = 25.7 Hz, CH), 116.97 (s, CH$_2$), 114.47 (d, $J$ = 22.7 Hz, CH), 113.92 (d, $J$ = 8.3 Hz, CH), 113.41 (s, CH$_2$), 112.33 (d, $J$ = 9.8 Hz, C$_q$), 71.86 (s, CH$_2$), 37.53 (s, CH$_2$). $^{19}$F NMR (282 MHz, CDCl$_3$) $\delta$ = -121.54 (s). IR (cm$^{-1}$): 1485, 1257, 1188, 1038, 912, 859, 784. HR-MS (+APCI) m/z calcd for C$_{12}$H$_{13}$BrFO [M+H]$^+$ 271.0128, found 271.0116.

Compound 1e. Prepared according to procedure A from 2-bromo-4-chlorophenol on a 9.64 mmol scale to afford the compound 1e as a colorless oil in 72% yield (1.99 g, 6.94 mmol). Rf (n-hexane) = 0.52. $^1$H NMR (300 MHz, CDCl$_3$) $\delta$ = 7.50 (d, $J$ = 2.5 Hz, 1 H), 7.20 - 7.10 (m, 1 H), 6.74 (d, $J$ = 8.8 Hz, 1 H), 5.87 – 5.78 (m, 1 H), 5.26 – 5.00 (m, 4 H), 4.45 (s, 2 H), 2.90 (d, $J$ = 7.2 Hz, 2 H). $^{13}$C NMR (75 MHz, CDCl$_3$) $\delta$ = 153.69 (s, C$_q$), 142.01 (s, C$_q$), 134.98 (s, CH), 132.68 (s, CH), 128.01 (s, CH), 125.94 (s, C$_q$), 117.02 (s, CH$_2$), 113.87 (s, CH), 113.43 (s, CH$_2$), 112.63 (s, C$_q$), 71.33 (s, CH$_2$),
37.45 (s, CH$_2$). IR (cm$^{-1}$): 1475, 1286, 1263, 1246, 1046, 913, 868, 800, 733. HR-MS (+APCI) m/z calcd for C$_{12}$H$_9$BrClO [M+H]$^+$ 286.9833, found 286.9820.

**Compound 1f.** Prepared according to procedure A from 3-bromo-4-hydroxybenzonitrile on a 10 mmol scale to afford the compound 1f as a colorless oil in 71% yield (1.97 g, 7.1 mmol). Rf (n-hexane/EtOAc, 10:1) = 0.58. $^1$H NMR (300 MHz, CDCl$_3$) $\delta$ = 7.81 (d, $J$ = 2.0 Hz, 1 H), 7.56 (dd, $J$ = 8.6, 2.0 Hz, 1 H), 6.92 (d, $J$ = 8.6 Hz, 1 H), 5.91–5.77 (m, 1 H), 5.29–5.06 (m, 4 H), 4.59 (s, 2 H), 2.92 (d, $J$ = 6.9 Hz, 2 H). $^{13}$C NMR (75 MHz, CDCl$_3$) $\delta$ = 158.33 (s, C$_q$), 141.21 (s, C$_q$), 136.53 (s, CH), 134.66 (s, CH), 132.82 (s, CH), 117.59 (s, C$_q$), 117.23 (s, CH$_2$), 113.97 (s, CH$_2$), 113.02 (s, CH), 112.56 (s, C$_q$), 105.04 (s, C$_q$), 71.28 (s, CH$_2$), 37.35 (s, CH$_2$). IR (cm$^{-1}$): 2227, 1596, 1490, 1294, 1265, 1194, 1051, 995, 913, 813. HR-MS (+APCI) m/z calcd for C$_{13}$H$_{13}$BrNO [M+H]$^+$ 278.0175, found 278.0179.

**Compound 1g.** Prepared according to procedure A from 2-bromo-4-(trifluoromethyl)phenol on a 4 mmol scale to afford the compound 1g as a colorless oil in 69% yield (0.89 g, 2.76 mmol). Rf (n-hexane) = 0.73. $^1$H NMR (300 MHz, CDCl$_3$) $\delta$ = 7.72 (dd, $J$ = 2.2, 0.8 Hz, 1 H), 7.44 – 7.40 (m, 1 H), 6.83 (dd, $J$ = 8.7, 0.9 Hz, 1 H), 5.61–5.78 (m, 1 H), 5.26 – 4.89 (m, 4 H), 4.49 (s, 2 H), 2.97 – 2.71 (d, $J$ = 6.9 Hz, 2 H). $^{13}$C NMR (75 MHz, CDCl$_3$) $\delta$ = 157.46 (s, C$_q$), 141.75 (s, C$_q$), 134.95 (s, CH), 130.56 (q, $J$ = 3.7 Hz, CH), 125.73 (q, $J$ = 3.7 Hz, CH), 124.02 (q, $J_{CF}$ = 32.9, C$_q$), 123.22 (q, $J_{CF}$ = 272.4, C$_q$), 117.24 (s, CH), 113.83 (s, CH$_2$), 112.69 (s, CH$_2$), 112.33 (s, C$_q$), 71.32 (s, CH$_2$), 37.54 (s, CH$_2$). $^{19}$F NMR (282 MHz, CDCl$_3$) $\delta$ = -61.71 (s). IR (cm$^{-1}$): 1609, 1501, 1406, 1322, 1268, 1120, 1079, 1049, 913, 813. HR-MS (+APCI) m/z calcd for C$_{13}$H$_{13}$BrF$_3$O [M+H]$^+$ 321.0096, found 321.0102.

**Compound 1h.** Prepared according to procedure A from 2-bromo-4-methylphenol on a 16 mmol scale to afford the compound 1h as a colorless oil in 65% yield (2.77 g, 10.4 mmol). Rf (n-hexane) = 0.48. $^1$H NMR (300 MHz, CDCl$_3$) $\delta$ = 7.33 (dd, $J$ = 2.2, 0.8 Hz, 1 H), 7.02 – 6.94 (m, 1 H), 6.74 (d, $J$ = 8.3 Hz, 1 H), 5.91–5.78 (m, 1 H), 5.26 – 5.01 (m, 4 H), 4.46 (s, 2 H), 2.91 (d, $J$ = 6.9, 2 H), 2.23 (s, 3 H). $^{13}$C NMR (75 MHz, CDCl$_3$) $\delta$ = 152.76 (s, C$_q$), 142.65 (s, C$_q$), 135.24 (s, CH), 133.64 (s, CH), 131.51 (s, C$_q$), 128.64 (s, CH), 116.83 (s, CH$_2$), 113.39 (s, CH), 113.06 (s, CH$_2$), 111.92 (s, C$_q$), 71.28 (s, CH$_2$), 37.54 (s, CH$_2$), 20.08 (s, CH$_3$) IR (cm$^{-1}$): 1493, 1284, 1250, 1048, 995, 910, 868, 801, 670. HR-MS (+APCI) m/z calcd for C$_{13}$H$_{16}$BrO [M+H]$^+$ 267.0379, found 267.0373.
Compound 1i. Prepared according to procedure A from 2-bromo-4-methoxyphenol on a 5 mmol scale to afford the compound 1i as a colorless oil in 71% yield (1.00 g, 3.55 mmol). Rf (n-hexane/EtOAc, 10:1) = 0.51. $^1$H NMR (300 MHz, CDCl$_3$) $\delta$ = 7.11 (dd, $J = 2.8$, 0.5 Hz, 1 H), 6.88 – 6.67 (m, 2 H), 5.86 (m, 1 H), 5.36 – 4.95 (m, 4 H), 4.62 – 4.16 (m, 2 H), 3.74 (s, 3 H), 2.94 (d, $J = 6.5$, 2 H). $^{13}$C NMR (75 MHz, CDCl$_3$) $\delta$ = 154.18 (s, C$_q$), 149.35 (s, C$_q$), 142.86 (s, C$_q$), 135.32 (s, CH), 118.83 (s, CH), 116.86 (s, CH$_2$), 114.79 (s, CH), 113.61 (s, CH), 113.21 (s, CH$_2$), 112.78 (s, C$_q$), 72.16 (s, CH$_2$), 55.83 (s, CH$_3$), 37.59 (s, CH$_2$). IR (cm$^{-1}$): 1491, 1459, 1438, 1271, 1210, 1037, 912, 779, 735. HR-MS (+APCI) m/z calcd for C$_{13}$H$_{15}$BrO$_2$ [M+H]$^+$ 283.0328, found 283.0331.

Compound 1j. Prepared according to procedure A from 2-bromo-4,6-di-tert-butylphenol on a 3 mmol scale to afford the compound 1j as a colorless oil in 65% yield (0.71 g, 1.95 mmol). Rf (n-hexane) = 0.72. $^1$H NMR (300 MHz, CDCl$_3$) $\delta$ = 7.41 (d, $J = 2.4$, 1 H), 7.29 (d, $J = 2.4$, 1 H), 5.95 – 5.81 (m, 1 H), 5.38 – 4.97 (m, 4 H), 4.51 (s, 2 H), 2.93 (d, $J = 6.8$, 2 H), 1.39 (s, 9 H), 1.28 (s, 9 H). $^{13}$C NMR (75 MHz, CDCl$_3$) $\delta$ = 152.33 (s, C$_q$), 147.24 (s, C$_q$), 144.24 (s, C$_q$), 143.29 (s, C$_q$), 135.64 (s, CH), 128.89 (s, CH), 123.70 (s, CH), 117.83 (s, C$_q$), 116.57 (s, CH$_2$), 111.93 (s, CH$_2$), 74.37 (s, CH$_2$), 37.87 (s, CH$_2$), 35.76 (s, C$_q$), 34.53 (s, C$_q$), 31.37 (s, CH$_3$), 30.90 (CH$_3$). IR (cm$^{-1}$): 1490, 1282, 1251, 1048, 995, 905, 868, 673. HR-MS (+APCI) m/z calcd for C$_{20}$H$_{30}$BrO [M+H]$^+$ 365.1475, found 365.1482.

Compound 1k. Prepared according to procedure A from 2-bromo-5-fluorophenol on a 10 mmol scale to afford the compound 1k as a colorless oil in 65% yield (1.76 g, 6.5 mmol). Rf (n-hexane) = 0.65. $^1$H NMR (300 MHz, CDCl$_3$) $\delta$ = 7.36 (dd, $J = 8.6$, 6.2 Hz, 1 H), 6.59 – 6.40 (m, 2 H), 5.82 – 5.66 (m, 1 H), 5.18 – 4.95 (m, 4 H), 4.38 (s, 2 H), 2.82 (d, $J = 6.9$, 2 H). $^{13}$C NMR (75 MHz, CDCl$_3$) $\delta$ = 162.49 (d, $J_{CF} = 246.2$ Hz, C$_q$), 155.72 (d, $J_{CF} = 10.1$ Hz, C$_q$), 141.80 (s, C$_q$), 134.97 (s, CH), 133.38 (d, $J_{CF} = 9.7$ Hz, CH), 117.12 (s, CH$_2$), 113.57 (s, CH$_2$), 108.42 (d, $J = 22.6$ Hz, CH), 106.35 (d, $J_{CF} = 3.7$ Hz, C$_q$), 101.55 (d, $J_{CF} = 26.8$ Hz, CH), 71.19 (s, CH$_2$), 37.49 (s, CH$_2$). $^{19}$F NMR (282 MHz, CDCl$_3$) $\delta$ = -111.82 (s). IR (cm$^{-1}$): 1604, 1581, 1481, 1420, 1290, 1280, 1164, 1110, 1040, 913, 829, 794. HR-MS (+APCI) m/z calcd for C$_{12}$H$_{13}$BrFO [M+H]$^+$ 271.0128, found 271.0116.
**Compound 1l.** Prepared according to procedure A from 2-bromo-5-methoxyphenol on a 2.95 mmol scale to afford the compound 1l as a colorless oil in 72% yield (0.62 g, 2.12 mmol). Rf (n-hexane/EtOAc, 20:1) = 0.53. $^1$H NMR (300 MHz, CDCl$_3$) $\delta$ = 7.40 (d, $J$ = 8.7 Hz, 1 H), 6.50 – 6.33 (m, 2 H), 5.90 – 5.79 (m, 1 H), 5.27 – 5.03 (m, 4 H), 4.49 (s, 2 H), 3.77 (s, 3 H), 2.94 (d, $J$ = 6.9 Hz, 2 H). $^{13}$C NMR (75 MHz, CDCl$_3$) $\delta$ = 159.95 (s, C$_q$), 155.51 (s, C$_q$), 142.34 (s, C$_q$), 135.19 (s, CH), 133.06 (s, CH), 116.99 (s, CH$_2$), 113.27 (s, CH$_2$), 106.16 (s, CH), 102.95 (s, C$_q$), 101.14 (s, CH), 71.06 (s, CH$_2$), 55.48 (s, CH$_3$), 37.57 (s, CH$_2$). IR (cm$^{-1}$): 1584, 1485, 1305, 1201, 1166, 1061, 830, 819, 785. HR-MS (+APCI) m/z calcd for C$_{13}$H$_{16}$BrO$_2$ [M+H]$^+$ 283.0328, found 283.0329.

**Compound 1m.** Prepared according to procedure A from methyl 4-bromo-3-hydroxybenzoate on a 4.2 mmol scale to afford the compound 1m as a colorless oil in 67% yield (0.87 g, 2.81 mmol). Rf (n-hexane/EtOAc, 10:1) = 0.75. $^1$H NMR (300 MHz, CDCl$_3$) $\delta$ = 7.60 (d, $J$ = 8.1 Hz, 1 H), 7.53 – 7.46 (m, 2 H), 5.93 – 5.80 (m, 1 H), 5.36 – 5.03 (m, 4 H), 4.58 (s, 2 H), 3.90 (s, 3 H), 2.94 (d, $J$ = 6.9 Hz, 2 H). $^{13}$C NMR (75 MHz, CDCl$_3$) $\delta$ = 166.25 (s, C$_q$), 154.84 (s, C$_q$), 142.00 (s, C$_q$), 135.06 (s, CH), 133.22 (s, CH), 130.34 (s, C$_q$), 122.84 (s, CH), 117.92 (s, C$_q$), 117.04 (s, C$_q$), 113.68 (s, CH), 113.57 (s, CH$_2$), 71.16 (s, CH$_2$), 52.25 (s, CH$_3$), 37.55 (s, CH$_2$). IR (cm$^{-1}$): 1719, 1576, 1433, 1411, 1287, 1233, 1104, 909, 757. HR-MS (+APCI) m/z calcd for C$_{14}$H$_{16}$BrO$_3$ [M+H]$^+$ 311.0277, found 311.0264.

**Compound 1n.** Prepared according to procedure A from methyl 2-bromopyridin-3-ol on a 3 mmol scale to afford the compound 1n as a light yellow oil in 62% yield (0.47 g, 1.86 mmol). The crude reaction mixture was purified by flash chromatography column (hexane/EtOAc, gradient from 0 to 50 % EtOAc). Rf (n-hexane/EtOAc, 10:1)= 0.44. $^1$H NMR (300 MHz, CDCl$_3$) $\delta$ = 7.97 (dd, $J$ = 4.5, 1.7 Hz, 1 H), 7.19 (m, 1 H), 7.12 (dd, $J$ = 8.1, 1.7 Hz, 1 H), 5.91– 5.78 (m, 1 H), 5.27 – 5.07 (m, 4 H), 4.55 (s, 2 H), 2.93 (d, $J$ = 6.9 Hz, 2 H). $^{13}$C NMR (75 MHz, CDCl$_3$) $\delta$ = 151.84 (s, C$_q$), 141.54 (s, C$_q$), 141.24 (s, CH), 134.82 (s, CH), 132.97 (s, C$_q$), 123.19 (s, CH), 119.89 (s, CH), 117.16 (s, CH$_2$), 113.88 (s, CH$_2$), 71.14 (s, CH$_2$), 37.40 (s, CH$_2$). IR (cm$^{-1}$): 1562, 1448, 1411, 1287, 1200, 1074, 1052, 994, 914, 793, 725. HR-MS (+ESI) m/z calcd for C$_{11}$H$_{13}$BrNO [M+H]$^+$ 254.0175, found 254.0177.
**Compound 1o.** Prepared according to procedure A from 3-bromonaphthalen-2-ol on a 2.5 mmol scale to afford the compound 1o as a yellow oil in 60% yield (0.45 g, 1.5 mmol). Rf (n-hexane) = 0.5. $^1$H NMR (300 MHz, CDCl$_3$) δ = 8.04 (s, 1 H), 7.74 – 7.61 (m, 2 H), 7.38 (m, 2 H), 7.12 (s, 1 H), 5.94 – 5.82 (m, 1 H), 5.42 – 5.03 (m, 4 H), 4.61 (s, 2 H), 2.99 (d, $J = 6.9$, 2 H). $^{13}$C NMR (75 MHz, CDCl$_3$) δ = 152.42 (s, C$_q$), 142.32 (s, C$_q$), 135.24 (s, CH), 133.36 (s, C$_q$), 132.19 (s, CH), 129.37 (s, C$_q$), 126.66 (s, CH), 126.58 (s, CH), 126.54 (s, CH), 124.44 (s, CH), 117.04 (s, CH$_2$), 113.77 (s, C$_q$), 113.31 (s, CH$_2$), 107.79 (s, CH), 71.03 (s, CH$_2$), 37.68. IR (cm$^{-1}$): 1590, 1496, 1450, 1326, 1248, 1213, 1180, 1031, 1018, 909, 859, 800, 743. HR-MS (+APCI) m/z calcd for C$_{16}$H$_{16}$BrO [M+H]$^+$ 303.0379, found 303.0375.

**Compound 1p.** Prepared according to procedure A from 2-bromonaphthalen-1-ol on a 2.5 mmol scale to afford the compound 1p as a colorless oil in 59% yield (0.44 g, 1.47 mmol). Rf (n-hexane) = 0.48. $^1$H NMR (300 MHz, CDCl$_3$) δ = 8.12 – 8.04 (m, 1 H), 7.73 (m, 1 H), 7.56 – 7.37 (m, 4 H), 5.96 – 5.87 (m, 1 H), 5.43 – 5.05 (m, 4 H), 4.47 (s, 2 H), 3.05 (d, $J = 6.8$ Hz, 2 H). $^{13}$C NMR (75 MHz, CDCl$_3$) δ = 151.88 (s, C$_q$), 143.34 (s, C$_q$), 135.42 (s, CH), 133.81 (s, C$_q$), 129.94 (s, CH), 129.11 (s, C$_q$), 127.90 (s, CH), 126.62 (s, CH), 126.42 (s, CH), 125.16 (s, CH), 121.94 (s, CH), 116.81 (s, CH$_2$), 113.45 (s, CH$_2$), 112.89 (s, C$_q$), 75.86 (s, CH$_2$), 37.78 (s, CH$_2$). IR (cm$^{-1}$): 1583, 1572, 1500, 1350, 1257, 1201, 1124, 1065, 911, 801, 780, 741. HR-MS (+APCI) m/z calcd for C$_{16}$H$_{16}$BrO [M+H]$^+$ 303.0379, found 303.0384.

**Compound 1q.** Prepared according to procedure A from 2-bromo phenol on a 5 mmol scale and 2-methylenehex-5-en-1-ol to afford the compound 1q as a colorless oil in 65 yield (0.87 g, 3.25 mmol). Rf (n-hexane) = 0.56. $^1$H NMR (300 MHz, CDCl$_3$) δ = 7.53 (dd, $J = 7.8$, 1.5 Hz, 1 H), 7.28 – 7.17 (m, 1 H), 6.92 – 6.76 (m, 2 H), 5.96 – 5.76 (m, 1 H), 5.28 – 4.95 (m, 4 H), 4.52 (s, 2 H), 2.29 (m, 4 H). $^{13}$C NMR (75 MHz, CDCl$_3$) δ = 154.98 (s, C$_q$), 143.52 (s, C$_q$), 137.99 (s, CH), 133.33 (s, CH), 128.27 (s, CH), 121.88 (s, CH), 114.89 (s, CH$_2$), 113.42 (s, CH), 112.60 (s, CH$_2$), 112.28 (s, C$_q$), 71.64 (s, CH$_2$), 32.34 (s, CH$_2$), 31.77 (s, CH$_2$). IR (cm$^{-1}$): 1585, 1476, 1442, 1278, 1245, 1050, 1030, 906, 745, 666. HR-MS (+APCI) m/z calcd for C$_{13}$H$_{16}$BrO [M+H]$^+$ 267.0379, found 267.0373.
Procedure B for the synthesis of compound 1r.

Procedure B. To a stirred solution of N-(2-bromophenyl)-4-methylbenzenesulfonamide (1.2 mmol, 1 equiv) and $K_2CO_3$ (2 equiv) in MeCN (15 ml) was added 2-(bromomethyl)penta-1,4-diene (1 equiv), prepared according to the reported procedure,\textsuperscript{[1]} under a nitrogen atmosphere. The resulting mixture was refluxed for 16 h. After completion of the reaction as checked by TLC, the reaction mixture was filtered and the filtrate was evaporated to dryness. The crude was directly subjected to flash column chromatography using n-hexane/ethyl acetate as eluent to afford the compound 1r.

Compound 1r. Light yellow oil. 67% yield (0.33 g, 0.80 mmol). The crude reaction mixture was purified by flash column chromatography (hexane/EtOAc, gradient from 0 to 35 % EtOAc). Rf (n-hexane/EtOAc, 20:1) = 0.23. $^1$HNMR (300 MHz, CDCl$_3$) $\delta$ = 7.63 – 7.54 (m, 3 H), 7.30 – 7.21 (m, 3 H), 7.19 – 7.05 (m, 2 H), 5.79 – 5.67 (m, 1 H), 5.11 – 4.98 (m, 2 H), 4.85 – 4.65 (m, 2 H), 4.36 – 3.97 (m, 2 H), 2.95 – 2.85 (d, $J$ = 6.1, 2 H), 2.42 (s, 3 H). $^{13}$C NMR (75 MHz, CDCl$_3$) $\delta$ = 143.58 (s, C$_q$), 141.96 (s, C$_a$), 137.63 (s, C$_a$), 136.11 (s, C$_q$), 135.20 (s, CH), 133.94 (s, CH), 131.81 (s, CH), 129.53 (s, CH), 129.39 (s, CH), 127.90 (s, CH), 127.66 (s, CH), 125.45 (s, C$_q$), 116.82 (s, CH$_2$), 116.11 (s, CH$_2$), 55.50 (s, CH$_2$), 37.80 (s, CH$_2$), 21.50 (s, CH$_3$). IR (cm$^{-1}$): 1596, 1471, 1352, 1167, 1090, 1047, 911, 859, 813, 783, 715, 660. HR-MS (+ESI) m/z calcd for C$_{19}$H$_{21}$BrNO$_2$S [M+H]$^+$ 406.0471, found 406.0472.
## Optimization table for the cascade reaction leading to 2a and 3a.\[^a\]

<table>
<thead>
<tr>
<th>Pd source loading (mol%)</th>
<th>Ligand (mol%)</th>
<th>Base (equiv)</th>
<th>Solvent/ T (°C)</th>
<th>Time (h)</th>
<th>Yield% (2a+3a)[^b]</th>
<th>Ratio 2a:3a [^c]</th>
<th>observations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pd(OAc)(_2) (10)</td>
<td>PPh(_3) (20)</td>
<td>Cs(_2)CO(_3) 1.5</td>
<td>DMF 80</td>
<td>16</td>
<td>-</td>
<td></td>
<td>complex mixture</td>
</tr>
<tr>
<td>Pd(OAc)(_2) (10)</td>
<td>PPh(_3) (20)</td>
<td>Cs(_2)CO(_3) 1.5</td>
<td>THF 80</td>
<td>16</td>
<td>-</td>
<td></td>
<td>complex mixture</td>
</tr>
<tr>
<td>Pd(OAc)(_2) (10)</td>
<td>PPh(_3) (20)</td>
<td>Cs(_2)CO(_3) 1.5</td>
<td>CH(_3)CN 80</td>
<td>16</td>
<td>20 (1:3)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pd(OAc)(_2) (10)</td>
<td>PPh(_3) (20)</td>
<td>Cs(_2)CO(_3) 1.5</td>
<td>HFIP 80</td>
<td>16</td>
<td>-</td>
<td></td>
<td>complex mixture</td>
</tr>
<tr>
<td>Pd(OAc)(_2) (10)</td>
<td>PPh(_3) (20)</td>
<td>Cs(_2)CO(_3) 1.5</td>
<td>Toluene 80</td>
<td>16</td>
<td>72 (1:2)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pd(OAc)(_2) (2.5)</td>
<td>PPh(_3) (5)</td>
<td>Cs(_2)CO(_3) 1.5</td>
<td>Toluene 80</td>
<td>16</td>
<td>45 (1:3)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pd(OAc)(_2) (10)</td>
<td>Xantphos (20)</td>
<td>Cs(_2)CO(_3) 1.5</td>
<td>Toluene 80</td>
<td>16</td>
<td>52 (1:10)</td>
<td></td>
<td>intermediate A detected</td>
</tr>
<tr>
<td>Pd(OAc)(_2) (10)</td>
<td>DPPF (20)</td>
<td>Cs(_2)CO(_3) 1.5</td>
<td>Toluene 80</td>
<td>16</td>
<td>62 (traces:1)</td>
<td></td>
<td>intermediate A detected</td>
</tr>
<tr>
<td>Pd(OAc)(_2) (10)</td>
<td>Johnphos (20)</td>
<td>Cs(_2)CO(_3) 1.5</td>
<td>Toluene 80</td>
<td>16</td>
<td>-</td>
<td></td>
<td>unreacted starting material</td>
</tr>
<tr>
<td>Pd(OAc)(_2) (10)</td>
<td>IMes-HCl (20)</td>
<td>Cs(_2)CO(_3) 1.5</td>
<td>Toluene 80</td>
<td>16</td>
<td>46 (6:1)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pd(OAc)(_2) (10)</td>
<td>Xantphos (20)</td>
<td>K(_2)CO(_3) 1.5</td>
<td>Toluene 80</td>
<td>16</td>
<td>35 (1:8)</td>
<td></td>
<td>intermediate A detected</td>
</tr>
<tr>
<td>Pd(OAc)(_2) (10)</td>
<td>Xantphos (20)</td>
<td>Et(_3)N 1.5</td>
<td>Toluene 80</td>
<td>16</td>
<td>10</td>
<td></td>
<td>30% intermediate A</td>
</tr>
<tr>
<td>Pd(OAc)(_2) (10)</td>
<td>Xantphos (20)</td>
<td>Cs(_2)CO(_3) 1.5</td>
<td>Toluene 80</td>
<td>1</td>
<td>traces</td>
<td>80% intermediate A</td>
<td></td>
</tr>
<tr>
<td>Pd(OAc)(_2) (5)</td>
<td>Xantphos (10)</td>
<td>Cs(_2)CO(_3) 1.5</td>
<td>1,4-Dioxane 80</td>
<td>16</td>
<td>65 (1:10)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pd(OAc)(_2) (10)</td>
<td>P(Cy)(_3) (20)</td>
<td>Cs(_2)CO(_3) 1.5</td>
<td>Toluene 80</td>
<td>16</td>
<td>90 (78)[^d]</td>
<td></td>
<td>70% intermediate A</td>
</tr>
<tr>
<td>Pd(OAc)(_2) (10)</td>
<td>P(Cy)(_3) (20)</td>
<td>Cs(_2)CO(_3) 1.5</td>
<td>Toluene 80</td>
<td>1</td>
<td>traces</td>
<td>85% intermediate A</td>
<td></td>
</tr>
<tr>
<td>Pd(OAc)(_2) (10)</td>
<td>DPEphos (20)</td>
<td>Cs(_2)CO(_3) 1.5</td>
<td>Toluene 80</td>
<td>16</td>
<td>74 (66)[^d]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pd(OAc)(_2) (5)</td>
<td>DPPH (10)</td>
<td>Cs(_2)CO(_3) 1.5</td>
<td>Toluene 80</td>
<td>1</td>
<td>-</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pd(OAc)(_2) (5)</td>
<td>DPEphos (10)</td>
<td>Cs(_2)CO(_3) 1.5</td>
<td>Toluene 80</td>
<td>1</td>
<td>10% (traces:1)</td>
<td></td>
<td>mainly unreacted starting material</td>
</tr>
<tr>
<td>Pd(OAc)(_2) (5)</td>
<td>P(Cy)(_3) (10)</td>
<td>K(_2)CO(_3) 1.5</td>
<td>Toluene 80</td>
<td>6</td>
<td>25 (1:traces)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

\[^a\] The optimized conditions for the synthesis of 2a and 3a are summarized in this table. The reaction conditions, including the Pd source, ligand, base, solvent, and temperature, are listed along with the time required and the yield of the product.

\[^b\] The yield of the product is expressed as a percentage of 2a and 3a combined.

\[^c\] The ratio of 2a to 3a is given in parentheses.

\[^d\] The values in parentheses represent additional details or conditions related to the reaction.
General procedure C for synthesis of [4,5]-spirocycles 2a-n.

Procedure C. A solution of the corresponding compounds 1a-p (0.5 mmol) in dry toluene (4 mL) under N₂ atmosphere was added to a mixture of Pd(OAc)₂ (11 mg, 10 mol%), PCy₃ (28 mg, 20 mol%) and Cs₂CO₃ (245 mg, 1.5 equiv) in a Schlenk tube under N₂ atmosphere. The reaction mixture was stirred at 120 °C for 16 hours. The resulting suspension was filtered through a Celite pad. The filtrate was evaporated to dryness and the crude was directly subjected to flash column chromatography using n-hexane/ethyl acetate as eluent to afford the pure products 2a-n.
**Compound 2a** Prepared according to the procedure C from compound 1a on a 0.3 mmol scale to afford the compound 2a as a yellow oil in 78% yield (40 mg, 0.23 mmol). Rf (n-hexane) = 0.2. $^1$H NMR (400 MHz, CDCl$_3$) $\delta = 7.35$ (ddd, $J = 7.4$, 1.4, 0.6 Hz, 1 H), 7.14 (ddd, $J = 8.0$, 7.4, 1.4 Hz, 1 H), 6.91 (td, $J = 7.4$, 1.0 Hz, 1 H), 6.78 (dt, $J = 8.0$, 0.8 Hz, 1 H), 4.96-4.93 (m, 2 H), 4.56 (s, 2 H), 3.13-3.01 (m, 2 H), 3.01-2.91 (m, 2 H). $^{13}$C NMR (75 MHz, CDCl$_3$) $\delta = 159.44$ (s, C$_q$), 142.80 (s, C$_q$), 134.32 (s, C$_q$), 128.32 (s, CH), 122.19 (s, CH), 120.88 (s, CH), 109.31 (s, CH), 107.49 (s, CH$_2$), 83.49 (s, CH$_2$), 45.53 (s, CH$_2$), 43.11 (s, C$_q$). IR (cm$^{-1}$): 1599, 1478, 1461, 1263, 1230, 1215, 971, 882, 828, 748, 740. HR-MS (+APCI) m/z calcd for C$_{12}$H$_{13}$O [M+H]$^+$ 173.0961, found 173.0969.

**Compound 2b** Prepared according to the procedure C from compound 1d on a 0.5 mmol scale to afford the compound 2b as a colorless oil in 71% yield (66 mg, 0.35 mmol). Rf (n-hexane) = 0.3. $^1$H NMR (400 MHz, CDCl$_3$) $\delta = 7.03$ (dd, $J = 7.9$, 2.7 Hz, 1 H), 6.80 (td, $J = 8.8$, 2.7 Hz, 1 H), 6.67 (dd, $J = 8.6$, 4.0 Hz, 1 H), 4.96-4.94 (m, 2 H), 4.56 (s, 2 H), 3.07-2.93 (m, 4 H). $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta = 157.87$ (d, $J = 237.4$ Hz, C$_q$), 155.37 (s, C$_q$), 142.10 (s, C$_q$), 135.79 (d, $J = 8.2$ Hz, C$_q$), 114.49 (d, $J = 24.2$ Hz, CH), 109.49 (d, $J = 8.5$ Hz, CH), 109.27 (d, $J = 24.7$ Hz, CH), 107.86 (s, CH$_2$), 83.89 (s, CH$_2$), 45.33 (s, CH$_2$), 43.52 (s, C$_q$). $^{19}$F NMR (188 MHz, CDCl$_3$) $\delta = -124.09$ (s). IR (cm$^{-1}$): 1483, 1462, 1257, 1170, 973, 880, 863, 807, 778, 737, 713. HR-MS (+APCI) m/z calcd for C$_{12}$H$_{12}$FO [M+H]$^+$ 191.0867, found 191.0872.

**Compound 2c** Prepared according to the procedure C from compound 1e on a 0.5 mmol scale to afford the compound 2c as a light yellow oil in 63% yield (65 mg, 0.31 mmol). Rf (n-hexane) = 0.32. $^1$H NMR (400 MHz, CDCl$_3$) $\delta = 7.30$ (dd, $J = 2.2$, 0.4 Hz, 1 H), 7.09 (dd, $J = 8.5$, 2.3 Hz, 1 H), 6.69 (dd, $J = 8.4$, 0.4 Hz, 1 H), 4.97-4.96 (m, 2 H), 4.58 (s, 2 H), 3.08-2.93 (m, 4 H). $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta = 158.12$ (s, C$_q$), 141.96 (s, C$_q$), 136.37 (s, C$_q$), 128.20 (s, CH), 125.51 (s, C$_q$), 122.43 (s, CH), 110.33 (s, CH), 108.01 (s, CH$_2$), 83.92 (s, CH$_2$), 45.46 (s, CH$_2$), 43.27 (s, C$_q$). IR (cm$^{-1}$): 1476, 1460, 1261, 1164, 1071, 969, 908, 878, 809, 731, 676. HR-MS (+APCI) m/z calcd for C$_{12}$H$_{12}$ClO [M+H]$^+$ 207.0571, found 207.0508.
Compound 2d Prepared according to the procedure C from compound 1f on a 0.5 mmol scale to afford the compound 2d as a colorless oil in 53% yield (51 mg, 0.26 mmol). Rf (n-hexane/EtOAc, 10:1) = 0.50. 1H NMR (300 MHz, CDCl3) δ = 7.63 (dd, J = 1.8, 0.5 Hz, 1 H), 7.48 – 7.45 (m, 1 H), 6.82 (dd, J = 8.3, 0.5 Hz, 1 H), 5.01 – 4.96 (m, 2 H), 4.66 (s, 2 H), 3.03 (t, J = 2.4 Hz, 4 H). 13C NMR (75 MHz, CDCl3) δ = 163.08 (s, Cq), 141.14 (s, Cq), 136.24 (s, Cq), 133.71 (s, CH), 126.46 (s, CH), 119.47 (s, Cq), 110.34 (s, CH), 108.46 (s, CH2), 84.27 (s, CH2), 45.75 (s, CH2), 42.71 (s, Cq), 30.89 (s, Cq).

Compound 2e Prepared according to the procedure C from compound 1g on a 0.5 mmol scale to afford the compound 2e as a colorless oil in 75% yield (89 mg, 0.37 mmol). Rf (n-hexane) = 0.40. 1H NMR (400 MHz, CDCl3) δ = 7.58 (dt, J = 1.9, 0.7 Hz, 1 H), 7.43 – 7.40 (m, 1 H), 6.87 – 6.77 (m, 1 H), 4.99 – 4.97 (m, 2 H), 4.64 (s, 2 H), 3.13 – 2.96 (m, 4 H). 13C NMR (100 MHz, CDCl3) δ = 162.13 (s, Cq), 141.69 (s, Cq), 135.31 (s, Cq), 124.55 (q, J = 32.1 Hz, Cq), 123.37 (q, J = 271.05 Hz, Cq), 119.64 (q, J = 3.7 Hz, CH), 109.38 (s, CH), 108.21 (s, CH2), 84.26 (s, CH2), 45.61 (s, CH2), 42.81 (s, Cq). 19F NMR (188 MHz, CDCl3) δ = -161.41 (s).

Compound 2f Prepared according to the procedure C from compound 1h on a 1 mmol scale to afford the compound 2f as a light yellow oil in 54% yield (100 mg, 0.54 mmol). Rf (n-hexane) = 0.25. 1H NMR (400 MHz, CDCl3) δ = 7.15 (dt, J = 2.0, 0.7 Hz, 1 H), 6.95 – 6.92 (m, 1 H), 6.67 (d, J = 8.1 Hz, 1 H), 4.95 – 4.92 (m, 2 H), 4.54 (s, 2 H), 3.09 – 3.00 (m, 2 H), 3.00 – 2.90 (m, 2 H), 2.31 (s, CH3). 13C NMR (75 MHz, CDCl3) δ = 157.45 (s, Cq), 142.96 (s, Cq), 134.33 (s, Cq), 130.26 (s, Cq), 128.75 (s, CH), 122.70 (s, CH), 108.88 (s, CH), 107.44 (s, CH2), 83.67 (s, CH2), 45.45 (s, CH2), 43.22 (s, Cq), 20.86 (s, CH3). IR (cm⁻¹): 1489, 1266, 1230, 1209, 1197, 970, 875, 807, 737. HR-MS (+APCI) m/z calcd for C13H12F3O [M+H]⁺ 241.0835, found 241.0846.

Compound 2g Prepared according to the procedure C from compound 1i on a 0.2 mmol scale to afford the compound 2g as a light yellow oil in 67% yield (27 mg, 0.13 mmol). Rf (n-hexane/EtOAc, 20:1) = 0.40. 1H NMR (300 MHz, CDCl3) δ =
6.92 (m, 1 H), 6.68 (m, 2 H), 4.94 (m, 2 H), 4.54 (s, 2 H), 3.78 (s, 3 H), 3.21 – 2.83 (m, 4 H). $^{13}$C NMR (75 MHz, CDCl$_3$) δ = 154.57 (s, C$_q$), 153.58 (s, C$_q$), 142.67 (s, C$_q$), 135.31 (s, C$_q$), 113.29 (s, CH), 109.27 (s, CH), 108.36 (s, CH), 107.59 (s, CH$_2$), 83.70 (s, CH$_2$), 56.06 (s, CH$_3$), 45.24 (s, CH$_2$), 43.61 (s, C$_q$).

IR (cm$^{-1}$): 1487, 1466, 1201, 1176, 1039, 1024, 974, 880, 802.

HR-MS (+APCI) m/z calcd for C$_{13}$H$_{15}$O$_2$ [M+H]$^+$ 203.1067, found 203.1062.

Compound 2h Prepared according to the procedure C from compound 1j on a 0.3 mmol scale to afford the compound 2f as an orange oil in 65% yield (55 mg, 0.2 mmol). Rf (n-hexane) = 0.28. $^1$H NMR (300 MHz, CDCl$_3$) δ = 7.22 (d, J = 2.1 Hz, 1 H), 7.14 (d, J = 2.1 Hz, 1 H), 4.95 – 4.92 (m, 2 H), 4.55 (s, 2 H), 3.17 – 3.03 (m, 2 H), 3.00 – 2.87 (m, 2 H), 1.36 (s, 9 H), 1.32 (s, 9 H).

$^{13}$C NMR (75 MHz, CDCl$_3$) δ = 155.35 (s, C$_q$), 143.49 (s, C$_q$), 143.47 (s, C$_q$), 134.01 (s, C$_q$), 131.90 (s, C$_q$), 122.32 (s, CH), 116.49 (s, CH), 107.29 (s, CH$_2$), 83.34 (s, CH$_2$), 45.62 (s, CH$_2$), 43.07 (s, C$_q$), 34.60 (s, C$_q$), 34.28 (s, C$_q$), 31.83 (s, CH$_3$), 29.40 (s, CH$_3$). IR (cm$^{-1}$): 1480, 1411, 1361, 1271, 1246, 1155, 980, 875, 818, 761. HR-MS (+APCI) m/z calcd for C$_{20}$H$_{29}$O $[\text{M+H}]^+$ 285.2213, found 285.2199.

Compound 2i Prepared according to the procedure C from compound 1k on a 1 mmol scale to afford the compound 2i as a colorless oil in 68% yield (129 mg, 0.68 mmol). Rf (n-hexane) = 0.32. $^1$H NMR (400 MHz, CDCl$_3$) δ = 7.30 – 7.19 (m, 1 H), 6.65 – 6.55 (m, 1 H), 6.49 (dt, J = 9.5, 1.7 Hz, 1 H), 4.94 (m, 2 H), 4.60 (s, 2 H), 3.09 – 2.90 (m, 4 H). $^{13}$C NMR (100 MHz, CDCl$_3$) δ = 163.27 (d, J = 243.3 Hz, C$_q$), 160.60 (d, J = 13.0 Hz, C$_q$), 142.4 (s, C$_q$), 130.10 (d, J = 2.5 Hz, C$_q$), 122.46 (d, J = 10.7 Hz, CH), 107.67 (s, CH$_2$), 107.45 (d, J = 23.0 Hz, CH), 97.76 (d, J = 26.5 Hz, CH), 84.61 (s, CH$_2$), 45.63 (s, CH$_2$), 42.61(s, C$_q$). $^{19}$F NMR (188 MHz, CDCl$_3$) δ = -114.38 (s). IR (cm$^{-1}$): 1611, 1493, 1438, 1331, 1263, 1129, 1092, 980, 883, 838, 796, 736. HR-MS (+APCI) m/z calcd for C$_{12}$H$_{12}$FO $[\text{M+H}]^+$ 191.0867, found 191.0872.

Compound 2j Prepared according to the procedure C from compound 1l on a 0.3 mmol scale to afford the compound 2j as a light yellow oil in 72% yield (44 mg, 0.22 mmol). Rf (n-hexane/EtOAc, 20:1) = 0.49. $^1$H NMR (400 MHz, CDCl$_3$) δ = 7.22 (d, J = 8.3 Hz, 1 H), 6.47 (dd, J = 8.2, 2.3 Hz, 1 H), 6.37 (d, J = 2.3 Hz, 1 H), 4.94 – 4.91 (m, 2 H), 4.57 (s, 2 H), 3.77 (s, 3 H), 3.08 – 2.99 (m, 2 H), 2.99 – 2.90 (m, 2 H). $^{13}$C NMR (100 MHz, CDCl$_3$) δ = 160.79 (s, C$_q$), 160.58 (s, C$_q$), 142.97 (s,
Compound 2k Prepared according to the procedure C from compound 1m on a 1 mmol scale to afford the compound 2k as a light yellow solid in 71% yield (164 mg, 0.71 mmol). Rf (n-hexane/EtOAc, 20:1) = 0.34. $^1$H NMR (400 MHz, CDCl$_3$) δ = 7.64 (dd, J = 7.8, 1.4 Hz, 1 H), 7.42 – 7.36 (m, 2 H), 4.98 – 4.96 (m, 2 H), 4.61 (s, 2 H), 3.89 (s, 3 H), 3.12 – 2.96 (m, 4 H). $^{13}$C NMR (100 MHz, CDCl$_3$) δ = 166.80 (s, C$q$), 159.53 (s, C$q$), 141.99 (s, C$q$), 139.85 (s, C$q$), 130.51 (s, C$q$), 122.97 (s, CH), 121.82 (s, CH), 110.16 (s, CH), 107.94 (s, CH$_2$), 83.68 (s, CH$_2$), 52.07 (s, CH$_3$), 43.03 (s, C$q$). IR (cm$^{-1}$): 1715, 1590, 1435, 1280, 1249, 1208, 1081, 988, 881, 763, 733, 702. HR-MS (+APCI) m/z calcd for C$_{13}$H$_{15}$O$_2$ [M+H]$^+$ 203.1067, found 203.1068.

Compound 2l Prepared according to the procedure C from compound 1n on a 1 mmol scale to afford the compound 2l as a light yellow oil in 78% yield (135 mg, 0.78 mmol). Rf (n-hexane/EtOAc, 20:1) = 0.21. $^1$H NMR (200 MHz, CDCl$_3$) δ = 8.15 (dd, J = 3.8, 2.4 Hz, 1 H), 7.05 – 7.00 (m, 2 H), 4.98 – 4.93 (m, 2 H), 4.68 (s, 2 H), 3.43 – 3.22 (m, 2 H), 3.04 – 2.80 (m, 2 H). $^{13}$C NMR (100 MHz, CDCl$_3$) δ = 154.85 (s, C$q$), 153.00 (s, C$q$), 142.29 (s, C$q$), 141.76 (s, CH), 122.45 (s, CH), 115.54 (s, CH), 107.82 (s, CH$_2$), 83.34 (s, CH$_2$), 43.81 (s, CH$_2$), 42.40 (s, C$q$). IR (cm$^{-1}$): 1603, 1576, 1426, 1271, 1159, 1106, 951, 877, 791, 763, 688. HR-MS (+ESI) m/z calcd for C$_{11}$H$_{12}$NO [M+H]$^+$ 174.0913, found 174.0911.

Compound 2m Prepared according to the procedure C from compound 1o on a 0.33 mmol scale to afford the compound 2m as a light yellow oil in 57% yield (41 mg, 0.18 mmol). Rf (n-hexane) = 0.20. $^1$H NMR (400 MHz, CDCl$_3$) δ = 7.80 – 7.72 (m, 2 H), 7.69 – 7.66 (m, 1 H), 7.38 – 7.34 (m, 1 H), 7.30 – 7.26 (m, 1 H), 7.08 (s, 1 H), 5.01 – 4.99 (m, 2 H), 4.62 (s, 2 H), 3.19 – 3.11 (m, 2 H), 3.11 – 3.01 (m, 2 H). $^{13}$C NMR (100 MHz, CDCl$_3$) δ = 158.37 (s, C$q$), 142.52 (s, C$q$), 137.44 (s, C$q$), 134.60 (s, C$q$), 129.85 (s, C$q$), 127.74 (s, CH), 126.80 (s, CH), 125.82 (s, CH), 123.27 (s, CH), 120.84 (s, CH), 107.88 (s, CH$_2$), 103.62 (s, CH), 83.67 (s, CH$_2$), 45.68 (s, CH$_2$), 42.70 (s, C$q$). IR
(cm⁻¹): 1636, 1470, 1449, 1402, 1238, 1145, 1105, 1007, 962, 881, 865, 838, 745. HR-MS (+APCI) m/z calcd for C₁₆H₁₅O [M+H]⁺ 223.1117, found 223.1117.

**Compound 2n.** Prepared according to the procedure C (heating the reaction mixture at 105 °C) from compound 1p on a 0.5 mmol scale to afford the compound 2n as a colorless oil in 56% yield (62 mg, 0.28 mmol). Rf (n-hexane) = 0.30. ¹H NMR data for the (400 MHz, CDCl₃) δ = 7.98 – 7.95 (m, 1 H), 7.84 – 7.82 (m, 1 H), 7.52 – 7.43 (m, 4 H), 5.00 – 4.98 (m, 2 H), 3.19 – 3.14 (m, 2 H), 3.07 – 3.03 (m, 2 H). ¹³C NMR (100 MHz, CDCl₃) δ = 154.75 (s, C.q), 143.0 (s, C.q), 134.16 (s, C.q), 127.88 (s, CH), 127.02 (s, C.q), 125.80 (s, CH), 125.45 (s, CH), 121.42 (s, CH), 120.91 (s, CH), 120.40 (s, C.q), 120.12 (s, CH), 107.49 (s, CH₂), 84.32 (s, CH₂), 45.67 (s, CH₂), 44.14 (s, C.q). IR (cm⁻¹): 1575, 1517, 1468, 1439, 1399, 1376, 1259, 1062, 957, 876, 803, 746. HR-MS (+APCI) m/z calcd for C₁₆H₁₅O [M+H]⁺ 223.1117, found 223.1114.

**General procedure D for synthesis of compounds 3a-k.**

![Scheme](image)

Procedure D. A solution of the corresponding compounds 1a-m (0.5 mmol) in dry toluene (4 mL) under N₂ atmosphere was added to a mixture of Pd(OAc)₂ (11 mg, 10 mol%), DPEphos (54 mg, 20 mol%) and Cs₂CO₃ (245 mg, 1.5 equiv) in a Schlenk tube under N₂ atmosphere. The reaction mixture was stirred at 80 °C for 16 hours. The resulting suspension was filtered through a Celite pad. The filtrate was evaporated to dryness and the crude was directly subjected to flash column chromatography using n-hexane/ethyl acetate as eluent to afford the pure products 3a-k.

**Compound 3a.** Prepared according to the procedure D from compound 1a on a 0.2 mmol scale (0.1 M solution) to afford the compound 3a as a colorless oil in 66% yield (22 mg, 0.13 mmol). Rf (n-hexane) = 0.30. ¹H NMR (300 MHz, CDCl₃) δ = 7.54 – 7.51 (m, 1 H), 7.46 – 7.43 (m, 1 H), 7.38 (t, J = 1.2, 1 H), 7.30 – 7.19 (m, 2 H), 5.66 – 5.62 (m, 2 H), 3.43 – 3.40 (m, 2 H), 1.76 – 1.74 (m, 3 H). ¹³C NMR (75 MHz, CDCl₃) δ = 155.1 (s, C.q), 144.0 (s, C.q), 134.2 (s, C.q), 128.0 (s, CH), 127.8 (s, CH), 127.5 (s, CH), 121.5 (s, CH), 120.9 (s, CH), 120.4 (s, C.q), 120.1 (s, CH), 107.4 (s, CH₂), 84.3 (s, CH₂), 45.7 (s, CH₂), 44.1 (s, C.q). IR (cm⁻¹): 1575, 1517, 1468, 1439, 1399, 1376, 1259, 1062, 957, 876, 803, 746. HR-MS (+APCI) m/z calcd for C₁₆H₁₅O [M+H]⁺ 223.1117, found 223.1114.
MHz, CDCl$_3$ $\delta$ = 155.49 (s, C$_q$), 141.23 (s, CH), 128.15 (s, C$_q$), 127.02 (s, CH), 125.65 (s, CH), 124.12 (s, CH), 122.20 (s, CH), 119.61 (s, CH), 119.39 (s, C$_q$), 111.39 (s, CH), 21.41 (s, CH$_2$), 12.81 (s, CH$_3$). IR (cm$^{-1}$): 1611, 1482, 1465, 1455, 1233, 1094, 1070, 749. HR-MS (+APCI) m/z calcd for C$_{12}$H$_{12}$O [M]$^+$ 172.0882, found 172.0814.

**Compound 3b.** Prepared according to the procedure D from compound 1d on a 0.33 mmol scale to afford the compound 3b as a light yellow oil in 53% yield (33 mg, 0.17 mmol). Rf (n-hexane) = 0.51. $^1$H NMR (300 MHz, CDCl$_3$) $\delta$ = 7.42 (t, $J$ = 1.3 Hz, 1 H), 7.37 (ddd, $J$ = 8.9, 4.1, 0.5 Hz, 1 H), 7.17 (ddd, $J$ = 8.6, 2.7, 0.5 Hz, 1 H), 6.99 (tdd, $J$ = 9.1, 2.7, 0.5 Hz, 1 H), 5.73–5.55 (m, 2 H), 3.42–3.35 (m, 2 H), 1.79–1.74 (m, 3 H). $^{13}$C NMR (75 MHz, CDCl$_3$) $\delta$ = 159.08 (d, $J$ = 242.9 Hz, C$_q$), 151.68 (s, C$_q$), 143.03 (s, CH), 126.57 (s, CH), 128.96 (d, $J$ = 10.2 Hz, C$_q$), 125.99 (s, CH), 119.68 (d, $J$ = 3.9 Hz, C$_q$), 112.017 (d, $J$ = 4.9 Hz, CH), 111.78 (d, $J$ = 21.7 Hz, CH), 105.25 (d, $J$ = 24.8 Hz, CH), 21.36 (s, CH$_2$), 12.84 (s, CH$_3$). $^{19}$F NMR (282 MHz, CDCl$_3$) $\delta$ = -121.49 (s). IR (cm$^{-1}$): 1480, 1449, 1264, 1162, 814, 733, 704. HR-MS (+APCI) m/z calcd for C$_{12}$H$_{12}$FO [M+H]$^+$ 191.0867, found 191.0872.

**Compound 3c.** Prepared according to the procedure D from compound 1e on a 0.5 mmol scale to afford the compound 3c as a colorless oil in 62% yield (64 mg, 0.31 mmol). Rf (n-hexane) = 0.50. $^1$H NMR (300 MHz, CDCl$_3$) $\delta$ = 7.49 (dd, $J$ = 2.1, 0.6 Hz, 1 H), 7.40 (t, $J$ = 1.3 Hz, 1 H), 7.37 (dd, $J$ = 8.7, 0.6 Hz, 1 H), 7.26–7.20 (m, 1 H), 5.73–5.54 (m, 2 H), 3.41–3.35 (m, 3 H). $^{13}$C NMR (75 MHz, CDCl$_3$) $\delta$ = 153.83 (s, C$_q$), 142.63 (s, CH), 128.96 (d, $J$ = 10.2 Hz, C$_q$), 125.99 (s, CH), 119.38 (s, CH), 112.38 (s, CH), 21.26 (s, CH$_2$), 12.87 (s, CH$_3$). IR (cm$^{-1}$): 1489, 1450, 1263, 1185, 1086, 800, 734, 700. HR-MS (+APCI) m/z calcd for C$_{12}$H$_{12}$ClO [M+H]$^+$ 207.0571, found 207.0504.

**Compound 3d.** Prepared according to the procedure D from compound 1f on a 0.5 mmol scale to afford the compound 3d as a light yellow oil in 57% yield (56 mg, 0.28 mmol). Rf (n-hexane/EtOAc, 20:1) = 0.38. $^1$H NMR (300 MHz, CDCl$_3$) $\delta$ = 7.88 (dd, $J$ = 1.6, 0.8 Hz, 1 H), 7.61–7.50 (m, 3 H), 5.78–5.54 (m, 2 H), 3.43 (m, 2 H), 1.77 (m, 3 H). $^{13}$C NMR (75 MHz, CDCl$_3$) $\delta$ = 157.16 (s, C$_q$), 143.38 (s, CH), 128.86 (s, C$_q$), 127.89 (s, CH), 126.61 (s, CH), 125.94 (s, CH), 124.99 (s, CH), 119.60 (s, C$_q$), 112.60 (s, CH), 106.15 (s, C$_q$), 30.95 (s, C$_q$), 21.14 (s, CH$_2$), 12.84 (s, CH$_3$). IR (cm$^{-1}$): 1611, 1482, 1465, 1455, 1233, 1094, 1070, 749. HR-MS (+APCI) m/z calcd for C$_{12}$H$_{12}$O [M]$^+$ 172.0882, found 172.0814.
Compound 3e. Prepared according to the procedure D from compound 1h on a 2 mmol scale to afford the compound 3e as a colorless oil in 76% yield (283 mg, 1.52 mmol). Rf (n-hexane) = 0.4. $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ = 7.36 – 7.34 (m, 1 H), 7.33 – 7.30 (m, 2 H), 7.09 (dd, J = 8.4, 1.8 Hz, 1 H), 5.72 – 5.57 (m, 2 H), 3.39 (m, 2 H), 2.45 (s, 3 H), 1.81 – 1.72 (m, 3 H). $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ = 153.84 (s, C$_q$), 141.36 (s, CH), 131.62 (s, C$_q$), 128.16 (s, C$_q$), 127.07 (s, CH), 125.59 (s, CH), 125.35 (s, CH), 119.40 (s, C$_q$), 119.08 (s, CH), 110.88 (s, CH), 21.41 (s, CH$_2$), 21.39 (s, CH$_3$), 12.86 (s, CH$_3$). IR (cm$^{-1}$): 1621, 1486, 1369, 1265, 1228, 1217, 1206, 813, 755, 703. HR-MS (+APCI) m/z calcd for C$_{13}$H$_{12}$NO [M+H]$^+$ 198.0913, found 198.0906.

Compound 3f. Prepared according to the procedure D from compound 1i on a 0.2 mmol scale to afford the compound 3f as a yellow oil in 66% yield (27 mg, 0.13 mmol). Rf (n-hexane/EtOAc, 20:1) = 0.58. $^1$H NMR (300 MHz, CDCl$_3$) $\delta$ = 7.39 – 7.35 (m, 1 H), 7.33 (d, J = 0.5 Hz, 1 H), 6.97 (d, J = 2.6 Hz, 1 H), 6.89 (ddd, J = 8.9, 2.7, 0.5 Hz, 1 H), 5.74 – 5.56 (m, 2 H), 3.85 (s, 3 H), 3.43 – 3.36 (m, 2 H), 1.77 (m, 3 H). $^{13}$C NMR (75 MHz, CDCl$_3$) $\delta$ = 155.62 (s, C$_q$), 150.42 (s, C$_q$), 142.13 (s, CH), 128.63 (s, C$_q$), 126.92 (s, CH), 125.67 (s, CH), 119.40 (s, C$_q$), 112.68 (s, CH), 111.81 (s, CH), 102.21 (s, CH), 55.92 (s, CH$_3$), 21.45 (s, CH$_2$), 12.86 (s, CH$_3$). IR (cm$^{-1}$): 1625, 1485, 1430, 1290, 1219, 1080, 1024, 933, 789, 734. HR-MS (+APCI) m/z calcd for C$_{13}$H$_{15}$O$_2$ [M+H]$^+$ 203.1067, found 203.1072.

Compound 3g. Prepared according to the procedure D from compound 1j on a 0.3 mmol scale to afford the compound 3g as a light yellow oil in 58% yield (49 mg, 0.17 mmol). Rf (n-hexane) = 0.41. $^1$H NMR (300 MHz, CDCl$_3$) $\delta$ = 7.38 – 7.35 (m, 2 H), 7.27 – 7.24 (m, 1 H), 5.72 – 5.57 (m, 2 H), 3.43 – 3.38 (m, 2 H), 1.77 (m, 3 H), 1.49 (s, 9 H), 1.38 (s, 9 H). $^{13}$C NMR (75 MHz, CDCl$_3$) $\delta$ = 152.00 (s, C$_q$), 145.04 (s, C$_q$), 140.46 (s, CH), 134.04 (s, C$_q$), 128.08 (s, C$_q$), 127.33 (s, CH), 125.35 (s, CH), 119.08 (s, C$_q$), 118.83 (s, CH), 113.35 (s, CH), 34.88 (s, C$_q$), 34.45 (s, C$_q$), 31.95 (s, CH$_3$), 29.92 (s, CH$_3$), 21.50 (s, CH$_2$), 12.83
Compound 3h. Prepared according to the procedure D from compound 1k on a 0.5 mmol scale to afford the compound 3h as a colorless oil in 57% yield (54 mg, 0.28 mmol). Rf (n-hexane) = 0.49. ¹H NMR (300 MHz, CDCl₃) δ = 7.43 (dd, J = 8.5, 5.4 Hz, 1 H), 7.38 (t, J = 1.3 Hz, 1 H), 7.17 (dd, J = 9.1, 2.3, 1 H), 7.02 – 6.96 (m, 1 H), 5.70 – 5.58 (m, 2 H), 3.41 – 3.38 (m, 2 H), 1.77 – 1.74 (m, 3 H). ¹³C NMR (75 MHz, CDCl₃) δ = 156.51 (d, J = 242.9 Hz, C₈), 150.78 (s, C₈), 142.13 (s, CH), 128.13 (s, CH₂), 125.99 (s, CH), 125.68 (d, J = 10.2 Hz, C₈), 121.52 (s, C₈), 119.69 (s, CH), 119.23 (s, C₈), 111.23 (s, CH), 104.22 (d, J = 24.8 Hz, CH), 20.46 (s, CH₂), 11.94 (s, CH₃). IR (cm⁻¹): 1605, 1491, 1436, 1278, 1263, 1234, 1133, 1039, 963, 833, 736. HR-MS (+APCI) m/z calcd for \(C_{20}H_{29}O\) [M+H]⁺ 285.2213, found 285.2208.

Compound 3i. Prepared according to the procedure D from compound 1l on a 0.35 mmol scale to afford the compound 3i as a yellow oil in 60% yield (42 mg, 0.21 mmol). Rf(n-hexane/EtOAc, 20:1) = 0.60. ¹H NMR (300 MHz, CDCl₃) δ = 7.39 (d, J = 8.4 Hz, 1 H), 7.30 (s, 1 H), 6.99 (d, J = 2.3 Hz, 1 H), 6.87 (dd, J = 8.5, 2.2 Hz, 1 H), 5.71 – 5.55 (m, 2 H), 3.85 (s, 3 H), 3.43 – 3.35 (m, 2 H), 1.76 (m, 3 H). ¹³C NMR (75 MHz, CDCl₃) δ = 157.92 (s, C₈), 156.40 (s, C₈), 140.30 (s, CH), 127.07 (s, CH), 125.56 (s, CH), 121.52 (s, C₈), 119.69 (s, CH), 119.23 (s, C₈), 111.23 (s, CH), 95.96 (s, CH), 55.70 (s, CH₃), 21.44 (s, CH₂), 12.85 (s, CH₃). IR (cm⁻¹): 1627, 1491, 1439, 1288, 1219, 1141, 1080, 1024, 933, 802, 736. HR-MS (+APCI) m/z calcd for \(C_{13}H_{15}O_2\) [M+H]⁺ 203.1067, found 203.1068.

Compound 3j. Prepared according to the procedure D from compound 1m on a 1 mmol scale to afford the compound 3j as a light yellow oil in 61% yield (140 mg, 0.61 mmol). Rf(n-hexane/EtOAc, 20:1) = 0.42. ¹H NMR (300 MHz, CDCl₃) δ = 8.15 (dd, J = 1.4, 0.7 Hz, 1 H), 7.95 (dd, J = 8.2, 1.4 Hz, 1 H), 7.61 – 7.48 (m, 2 H), 5.76 – 5.54 (m, 2 H), 3.94 (s, 3 H), 3.48 – 3.38 (m, 2 H), 1.82 – 1.71 (m, 3 H). ¹³C NMR (75 MHz, CDCl₃) δ = 167.32 (s, C₈), 154.88 (s, C₈), 144.24 (s, CH), 132.36 (s, C₈), 126.43 (s, CH), 126.17 (s, C₈), 126.11 (s, CH), 123.65 (s, CH), 119.71 (s, C₈), 119.27 (s, CH), 113.06 (s, CH), 52.16 (s, CH₃), 21.27 (s, CH₂), 12.87 (s, CH₃). IR (cm⁻¹): 1717, 1627, 1491, 1439, 1288, 1219, 1141, 1080, 1024, 933, 802, 736. HR-MS (+APCI) m/z calcd for \(C_{13}H_{15}O_2\) [M+H]⁺ 203.1067, found 203.1068.
1435, 1285, 1228, 1095, 980, 892, 759, 744. HR-MS (+APCI) m/z calcd for C_{14}H_{15}O_{3} [M+H]^+ 231.1016, found 231.1006.

**Synthesis of [4,5]-spirocycles 6 and 7.**

![Reaction Scheme]

**Compound 6.** Prepared according to the procedure D from compound 1r on a 0.2 mmol scale to afford the compound 6 as a colorless oil in 54% yield (35 mg, 0.10 mmol). Rf (n-hexane/EtOAc, 20:1) = 0.25. $^1$H NMR (300 MHz, CDCl$_3$) $\delta = 7.70 - 7.59$ (m, 3 H), 7.32 – 7.16 (m, 4 H), 7.05 (td, $J = 7.5$, 1.0 Hz, 1 H), 4.87 (m, 2 H), 3.94 (s, 2 H), 2.72 (m, 4 H), 2.36 (s, 3 H). $^{13}$C NMR (75 MHz, CDCl$_3$) $\delta = 144.03$ (s, C$_q$), 142.02 (s, C$_q$), 141.18 (s, C$_q$), 139.01 (s, C$_q$), 133.82 (s, C$_q$), 129.55 (s, CH), 128.15 (s, CH), 127.25 (s, CH), 124.38 (s, CH), 122.14 (s, CH), 114.92 (s, CH), 107.75 (s, CH$_2$), 62.60 (s, CH$_2$), 45.35 (s, CH$_2$), 41.43 (s, C$_q$), 21.47 (s, CH$_3$). IR (cm$^{-1}$): 1595, 1474, 1456, 1353, 1248, 1163, 1093, 1033, 888, 819, 766, 681, 655. HR-MS (+ESI) m/z calcd for C$_{19}$H$_{20}$NO$_2$S [M+H]$^+$ 326.1209, found 326.1211.

**Compound 7.** Prepared according to the procedure D from compound 1q on a 0.4 mmol scale to afford the compound 7 as a light yellow oil in 76% yield (56 mg, 0.30 mmol). Rf (n-hexane) = 0.20. $^1$H NMR (300 MHz, CDCl$_3$) $\delta = 7.13$ (m, 2 H), 6.88 (td, $J = 7.4$, 1.0 Hz, 1 H), 6.80 (dd, $J = 8.3$, 1.0 Hz, 1 H), 4.96 (m, 2 H), 4.32 (s, 2 H), 2.71 – 2.52 (m, 2 H), 2.52 – 2.34 (m, 2 H), 2.13 – 1.89 (m, 2 H). $^{13}$C NMR (75 MHz, CDCl$_3$) $\delta = 159.73$ (s, C$_q$), 149.92 (s, C$_q$), 133.75 (s, C$_q$), 128.17 (s, CH), 122.58 (s, CH), 120.62 (s, CH), 109.54 (s, CH), 107.09 (s, CH$_2$), 83.04 (s, CH$_2$), 52.51 (s, C$_q$), 46.12 (s, CH$_2$), 39.19 (s, CH$_2$), 31.34 (s, CH$_2$). IR (cm$^{-1}$): 1597, 1477, 1458, 1216, 1100, 1017, 963, 880, 831, 745. HR-MS (+APCI) m/z calcd for C$_{13}$H$_{15}$O [M+H]$^+$ 187.1117, found 187.1117.
Isolation of intermediate 4a and mechanistic experiments

Isomerization of compound 1a to intermediate 4a.

A solution of compound 1a (50 mg, 0.2 mmol) in dry toluene (3 mL) under N\textsubscript{2} atmosphere was added to a mixture of Pd(OAc\textsubscript{2}) (2.2 mg, 5 mol%), DPE-Phos (11 mg, 10 mol%) and Cs\textsubscript{2}CO\textsubscript{3} (98 mg, 1.5 equiv) in a Schlenk tube under N\textsubscript{2} atmosphere. The tube was sealed and the reaction mixture was stirred at 80 °C for 1 hour. The resulting suspension was filtered through a Celite pad. The filtrate was evaporated to dryness and the crude was directly subjected to flash column chromatography using n-hexane as eluent to afford the intermediate 4a as a colorless oil in 59% isolated yield (28 mg, 0.11 mmol). The isomerization of the starting material 1a also proceeded when using 10 mol% of Pd(dba\textsubscript{2}) instead of Pd(OAc\textsubscript{2}) as the catalyst, affording a 90% NMR yield.

Data for intermediate 4a: Rf (n-hexane) = 0.47. \textsuperscript{1}H NMR (300 MHz, CDCl\textsubscript{3}) \(\delta = 7.99 \text{ (dd, } J = 4.5, 1.7 \text{ Hz, } 1 \text{ H}), 7.20 \text{ (dd, } J = 8.1, 4.5 \text{ Hz, } 1 \text{ H}), 7.13 \text{ (dd, } J = 8.1, 1.7 \text{ Hz, } 1 \text{ H}), 6.19 - 6.10 \text{ (m, } 2 \text{ H}), 5.92 - 5.77 \text{ (m, } 1 \text{ H}), 5.27 \text{ (s, } 1 \text{ H}), 5.17 \text{ (dd, } J = 1.5, 0.8 \text{ Hz, } 1 \text{ H}), 4.78 \text{ (s, } 2 \text{ H}), 1.83 - 1.80 \text{ (m, } 3 \text{ H}). \textsuperscript{13}C NMR (75 MHz, CDCl\textsubscript{3}) \(\delta = 151.93 \text{ (s, } C_\text{q}), 141.45 \text{ (s, } CH), 139.44 \text{ (s, } C_\text{q}), 133.17 \text{ (s, } C_\text{q}), 130.13 \text{ (s, } CH), 126.58 \text{ (s, } CH), 123.22 \text{ (s, } CH), 120.26 \text{ (s, } CH), 115.37 \text{ (s, } CH), 69.05 \text{ (s, } CH_2), 18.57 \text{ (s, } CH_3)). \text{IR (cm}^{-1})\): 1584, 1477, 1442, 1273, 1240, 1048, 1030, 742, 663. HR-MS (+APCI) m/z calcd for C\textsubscript{12}H\textsubscript{14}BrO [M+H]\textsuperscript{+} 253.0222, found 253.0227.
Isomerization of compound 1c to 1,3-diene 4c.

**Isomerization via Pd(0).** A solution of compound 1c (35 mg, 0.2 mmol) in dry toluene (3 mL) under N₂ atmosphere was added to a mixture of Pd(dba)₂ (12 mg, 10 mol%), DPE-Phos (21 mg, 20 mol%) and Cs₂CO₃ (98 mg, 1.5 equiv) in a Schlenk tube under N₂ atmosphere. The tube was sealed and the reaction mixture was stirred at 80 °C for 16 h. The resulting suspension was filtered through a Celite pad. The filtrate was evaporated to dryness. The ¹H-NMR spectrum of the crude mixture showed 70% of unreacted starting material plus a mixture of unidentified compounds.

**Isomerization via Pd–H generation.** A solution of compound 1c (52 mg, 0.3 mmol) in dry toluene (3 mL) under N₂ atmosphere was added to a mixture of Pd(dba)₂ (17 mg, 10 mol%), PPh₃ (16 mg, 20 mol%) and PhCOOH (7 mg, 20 mol%) in a Schlenk tube under N₂ atmosphere. The tube was sealed and the reaction mixture was stirred at 80 °C for 6 h. The resulting suspension was filtered through a Celite pad. The filtrate was evaporated to dryness. The ¹H-NMR spectrum of the crude mixture nearly full conversion of the starting material into 1,3-diene 4c. The crude mixture was subjected to flash column chromatography using n-hexane as eluent to afford the diene 4c as a colorless oil in 57% isolated yield (30 mg, 0.17 mmol).

**Data for 1,3-diene 4c:** Colorless oil. 57% yield (30 mg, 0.17 mmol). Rf (n-hexane) = 0.50. ¹H NMR (400 MHz, CDCl₃) δ = 7.31 – 7.24 (m, 2 H), 7.00 – 6.90 (m, 3 H), 6.16 (dq, J = 15.9, 1.8 Hz, 2 H), 5.82 (dq, J = 16.0, 6.7 Hz, 1 H), 5.22 (s, 1 H), 5.13 (dd, J = 1.6, 0.8 Hz, 1 H), 4.66 (s, 1 H), 1.80 (dd, J = 6.7, 1.7 Hz, 3 H). ¹³C NMR (100 MHz, CDCl₃) δ = 158.68 (s, C₉), 140.95 (s, C₉), 130.67 (s, CH),
129.39 (s, CH), 126.28 (s, CH), 120.82 (s, CH), 115.29 (s, CH₂), 114.74 (s, CH), 68.13 (s, CH₂), 18.56 (s, CH₃). IR (cm⁻¹): 1598, 1493, 1235, 1170, 1031, 1011, 752, 690. HR-MS (+APCI) m/z calcd for C₁₂H₁₅O [M+H]+ 175.1117, found 175.1112.

**Reaction of 3-methylene-2,3-dihydrobenzofuran with a mixture of cis-/trans-1-bromopropene.**

A Schlenk tube was charged with Pd(OAc)₂ (10 mg, 0.044 mmol, 10 mol%), DPE-Phos (46 mg, 0.085 mmol, 20 mol%) and Cs₂CO₃ (210 mg, 0.65 mmol, 1.5 equiv) and 3-methylene-2,3-dihydrobenzofuran (57 mg, 0.432 mmol, 1 equiv) (prepared according to a previously reported procedure).[3] The tube was set under nitrogen atmosphere and dry toluene (3 mL) and cis-/trans-1-bromopropene (88 µL, 1 mmol, 2.4 equiv) were added. The tube was sealed and heated at 100 ºC for 16 h. The resulting suspension was filtered through a Celite pad. The filtrate was evaporated to dryness. The ¹H-NMR spectrum of the crude mixture showed 20% NMR yield of the benzofurane derivative 3a.
Cyclization of intermediate 4a with catalytic amount of Pd(OAc)$_2$ and PCy$_3$.

A solution of compound 4a (25 mg, 0.1 mmol, 1 equiv) in dry toluene (3 mL) under N$_2$ atmosphere was added to a mixture of Pd(OAc)$_2$ (2.5 mg, 10 mol%), PCy$_3$ (6 mg, 20 mol%) and Cs$_2$CO$_3$ (49 mg, 1.5 equiv) in a Schlenk tube under N$_2$ atmosphere. The tube was sealed and the reaction mixture was stirred at 80 °C for 16 hour. The resulting suspension was filtered through a Celite pad. The filtrate was evaporated to dryness. The $^1$H-NMR spectrum of the crude mixture showed the formation of the benzofuran derivative 3a in 65% NMR yield.

References


$^1$H NMR spectrum of compound 1a

$^{13}$C NMR spectrum of compound 1a
$^1$H NMR spectrum of compound 1b

$^{13}$C NMR spectrum of compound 1b
$^1$H NMR spectrum of compound 1c

\[ \text{Chemical Structure} \]

$^{13}$C NMR spectrum of compound 1c

\[ \text{Chemical Structure} \]
$^1$H NMR spectrum of compound 1d

13C NMR spectrum of compound 1d
$^{19}$F NMR spectrum of compound 1d
$^{1}H$ NMR spectrum of compound 1e

$^{13}C$ NMR spectrum of compound 1e
$^1$H NMR spectrum of compound 1f

$^{13}$C NMR spectrum of compound 1f
$^1$H NMR spectrum of compound 1g

$^{13}$C NMR spectrum of compound 1g
$^{19}$F NMR spectrum of compound 1g
$^1$H NMR spectrum of compound 1h

$^{13}$C NMR spectrum of compound 1h
$^1$H NMR spectrum of compound 1i

$^{13}$C NMR spectrum of compound 1i
$^1$H NMR spectrum of compound 1j

$^{13}$C NMR spectrum of compound 1j
$^1$H NMR spectrum of compound 1k

$^{13}$C NMR spectrum of compound 1k
$^{19}$F NMR spectrum of compound $1k$
$^1$H NMR spectrum of compound 11

$^{13}$C NMR spectrum of compound 11
$^1$H NMR spectrum of compound 1m

$^{13}$C NMR spectrum of compound 1m
\(^1\text{H NMR spectrum of compound 1o}\)

\(^{13}\text{C NMR spectrum of compound 1o}\)
$^1$H NMR spectrum of compound 1p

$^{13}$C NMR spectrum of compound 1p
$^1$H NMR spectrum of compound 1q

$^{13}$C NMR spectrum of compound 1q
$^1$H NMR spectrum of compound 1r

$^{13}$C NMR spectrum of compound 1r
$^1$H NMR spectrum of intermediate 4a

$^{13}$C NMR spectrum of intermediate 4a
$^1$H NMR spectrum of 4c

$^{13}$C NMR spectrum of 4c
$^1$H NMR spectrum of compound 2a

$^{13}$C NMR spectrum of compound 2a
$^1$H NMR spectrum of compound 2b

$^{13}$C NMR spectrum of compound 2b
$^{19}$F NMR spectrum of compound 2b
$^1$H NMR spectrum of compound 2c

$^{13}$C NMR spectrum of compound 2c
$^1$H NMR spectrum of compound 2d

$^{13}$C NMR spectrum of compound 2d
$^1$H NMR spectrum of compound 2e

$^{13}$C NMR spectrum of compound 2e
$^{19}$F NMR spectrum of compound 2e
$^1$H NMR spectrum of compound 2f

$^{13}$C NMR spectrum of compound 2f
$^1$H NMR spectrum of compound 2g

$^{13}$C NMR spectrum of compound 2g
$^1$H NMR spectrum of compound 2h

$^{13}$C NMR spectrum of compound 2h
$^1$H NMR spectrum of compound 2i

$^{13}$C NMR spectrum of compound 2i
$^{19}$F NMR spectrum of compound 21
$^1$H NMR spectrum of compound 2j

$^{13}$C NMR spectrum of compound 2j
$^1$H NMR spectrum of compound 2k

$^{13}$C NMR spectrum of compound 2k
$^1$H NMR spectrum of compound 2l

$^{13}$C NMR spectrum of compound 2l
$^1$H NMR spectrum of compound 2m

$^{13}$C NMR spectrum of compound 2m
$^{1}H$ NMR spectrum of compound 2n

$^{13}C$ NMR spectrum of compound 2n
$^1$H NMR spectrum of compound 3a

$^{13}$C NMR spectrum of compound 3a
$^1$H NMR spectrum of compound 3b

$^{13}$C NMR spectrum of compound 3b
$^{19}$F NMR spectrum of compound 3b
$^1$H NMR spectrum of compound 3c

$^{13}$C NMR spectrum of compound 3c
$^1$H NMR spectrum of compound 3d

$^{13}$C NMR spectrum of compound 3d
$^1$H NMR spectrum of compound 3e

$^{13}$C NMR spectrum of compound 3e
$^{1}$H NMR spectrum of compound 3f

$^{13}$C NMR spectrum of compound 3f
$^1$H NMR spectrum of compound 3g

$^{13}$C NMR spectrum of compound 3g
$^1$H NMR spectrum of compound 3h

$^{13}$C NMR spectrum of compound 3h
$^1$H NMR spectrum of compound 3i

$^{13}$C NMR spectrum of compound 3i
$^1$H NMR spectrum of compound 3j

$^{13}$C NMR spectrum of compound 3j
$^1$H NMR spectrum of compound 6

$^{13}$C NMR spectrum of compound 6
$^1$H NMR spectrum of compound 7

$^{13}$C NMR spectrum of compound 7