A Facile Synthesis of 1,1′-Spirobi(3*H*,3′*H*)isobenzofurans

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Abstract: The synthesis of a series of aryl 5,5-spiroketals containing a 1,1′-spirobi(3*H*,3′*H*)isobenzofuran ring system is reported. The key step involves addition of an aryllithium derived from a protected bromobenzyl alcohol to a phthalide; this is followed by deprotection of the benzyl alcohol and acid-catalysed cyclisation.

Key words: spiro compounds, ketals, phthalides, lithium compounds, heterocycles

The synthesis of spiroketals[1] has attracted considerable attention from the synthetic community due to the presence of this heterocyclic motif in many bioactive natural products including polyether antibiotics, marine and plant toxins, insect pheromones, antiparasitic agents, and antineoplastic agents. In contrast to the numerous reports on the synthesis of aliphatic spiroketals, the synthesis of benzannelated spiroketals has received less attention, despite their presence in a number of bioactive natural products. Our recent research has focused on the synthesis of aryl spiroketals related to the rubromycin family of antibiotics (Figure 1),[2] and has been prompted by the report that β-rubromycin (**1**) and γ-rubromycin that contain an aryl spiroketal ring exhibit potent inhibition of human telomerase,[3] with IC_{50} values of 3 μM, and are active against the reverse transcriptase of human immunodeficiency virus 1.[4] The fact that α-rubromycin, which lacks this aryl spiroacetal moiety, exhibits substantially decreased inhibitory potency towards telomerase (IC_{50} > 200 μM) suggests that this spiroacetal system plays an essential role in the observed inhibition of telomerase.

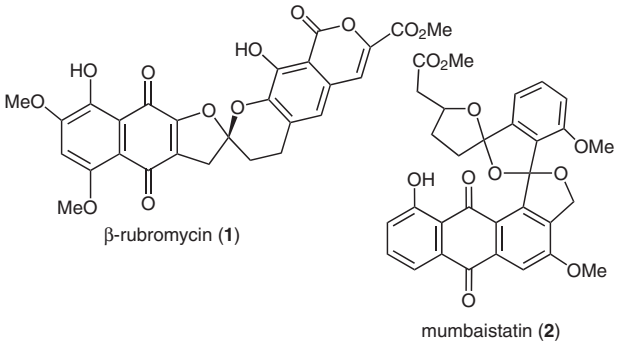
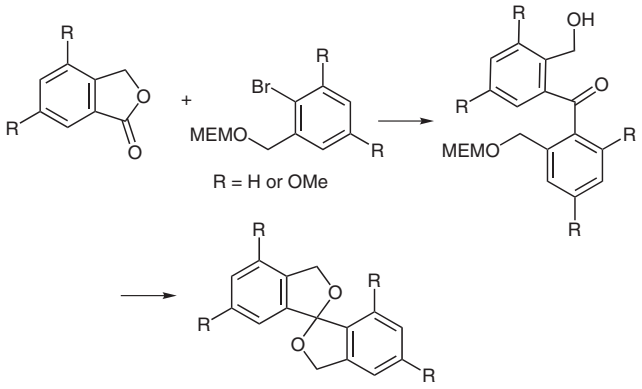


Figure 1

Several syntheses of 5,6-bisbenzannelated spiroketals related to the rubromycins have been reported. Notably, Danishefsky et al.[5] used Mitsunobu conditions to effect spirocyclisation of a keto lactol precursor as an elegant method to prepare the spiroketal unit of heliquinomycinone. Other synthetic approaches to 5,6-bisbenzannelated spiroketals include the use of a Nef-type reaction,[6] a hetero-Diels–Alder cycloaddition,[7] a [3+2] nitrile oxide/olefin cycloaddition,[8] a [3+2] cycloaddition between an enol ether and a zwitterion,[9] and addition of a lithiated methoxyallene to an aryl aldehyde/Heck reaction strategy.[10]

Our efforts in this area have focused on the use of a Sonogashira/acetylide coupling strategy to prepare several 5,6-aryl spiroketals[11] related to γ-rubromycin and a series of homologous 6,6-aryl spiroketals.[12] The work reported herein was prompted by the opportunity to investigate new benzannelated spiroketals for telomerase inhibitory activity; for this we synthesised a series of aryl 5,5-spiroketals containing a 1,1′-spirobi(3*H*,3′*H*)isobenzofuran skeleton that is present in the trimethyl derivative of mumbaistaton (**2**) (Figure 1), an inhibitor of glucose-6-phosphate translocase.[13]

To date, few syntheses of 1,1′-spirobi(3*H*,3′*H*)isobenzofurans have been reported. The simplest reported[14] preparation of this heterocyclic motif involved bromination of a 2,2′-dimethylbenzophenone followed by treatment with potassium hydroxide; however, this method is limited to the synthesis of symmetrical spiroketals. We herein report the synthesis of a series of 1,1′-spirobi(3*H*,3′*H*)isobenzofurans by addition of an aryllithium derived from a protected bromobenzyl alcohol to a phthalide, followed by acid-catalysed cyclisation (Scheme 1).



Scheme 1

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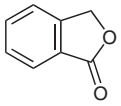
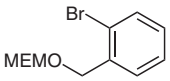
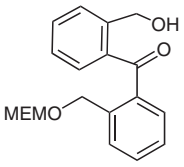
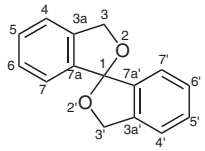
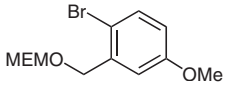
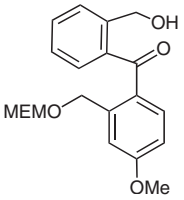
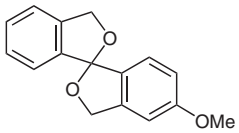
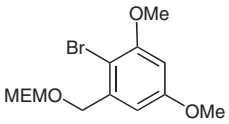
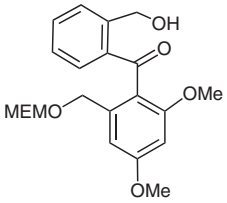
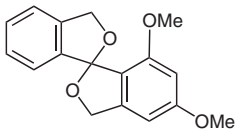
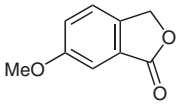
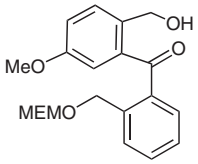
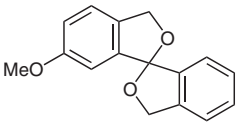
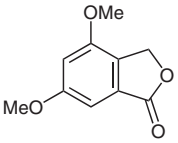
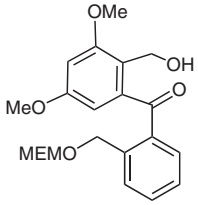
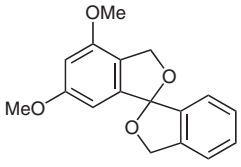
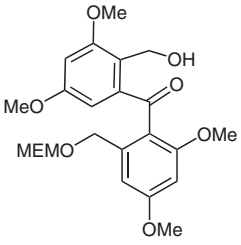
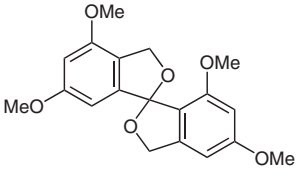
Epsztajn et al.[15] previously reported the reaction of phthalides with aryllithiums generated from aryl bromides by halogen–metal exchange. In this case, the phthalan addition products were not isolated, but underwent acid-catalysed elimination to form isobenzofurans, which next participated in hetero-Diels–Alder addition. We therefore envisaged that addition of an aryllithium bearing a suitably acid-labile protected hydroxymethyl substituent at the *ortho* position would undergo an addition reaction with a phthalide (Scheme 1). The adducts thus formed would then undergo acid-catalysed deprotection and cyclisation to afford aryl 5,5-spiroketals (Scheme 1). Initial experimentation established that the (2-methoxyethoxy)methyl protecting group was the ideal choice for effecting concomitant deprotection and cyclisation; thus, phthalides **3**, **4**, and **5** and aryl bromides **6**, **7**, and **8** were

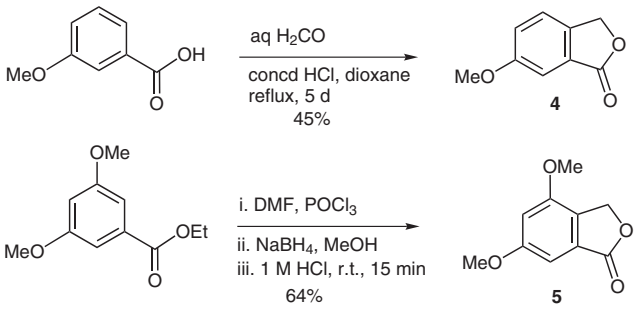
Table 1 Preparation of Spiroketals

Entry	Phthalide	Aryl bromide	Adduct[a]	Spiroketal[b]
1	 **3**	 **6**	 **9** (92%)	 **15** (53%, method A)
2	**3**	 **7**	 **10** (51%)	 **16** (51%, method A)
3	**3**	 **8**	 **11** (41%)	 **17** (55%, method A)
4	 **4**	**6**	 **12** (40%)	 **18** (48%, method B)
5	 **5**	**6**	 **13** (35%)	 **19** (44%, method B)
6	**5**	**8**	 **14** (32%)	 **20** (40%, method B)

[a] Reagents and conditions: bromide **6**, **7**, or **8**, *n*-BuLi, THF, –78 °C, 5 min, then LiBr (0.5 equiv), then phthalide **3**, **4**, or **5**, –78 °C, 0.5 h.
[b] Reagents and conditions: Method A: TMSBr (4.1 equiv), CH_2Cl_2, 4-Å MS, 0 °C, 0.5 h; Method B: $NaHSO_4{\cdot}SiO_2$ (1.3 equiv), CH_2Cl_2, r.t., 6 h.

obtained to demonstrate the generality of this procedure (Table 1).

Phthalide **4** was prepared by treatment of 3-methoxybenzoic acid with aqueous formaldehyde and concentrated hydrochloric acid in 1,4-dioxane under reflux for five days (Scheme 2).[16,17] Phthalide **5** was prepared by Vilsmeier–Haack formylation of ethyl 3,5-dimethoxybenzoate, followed by reduction of the formyl group, and subsequent cyclisation in the presence one molar hydrochloric acid (Scheme 2).[18] Aryl bromides **6**, **7**, and **8** were readily prepared by conversion of the corresponding benzylic alcohols into the (2-methoxyethoxy)methyl ethers by use of (2-methoxyethoxy)methyl chloride and *N*,*N*-diisopropylethylamine in dichloromethane.



Scheme 2

With phthalides **3**, **4**, and **5** and aryl bromides **6**, **7**, and **8** in hand, our attention turned to their union to provide keto alcohols **9**–**14** (Table 1). Lithium–halide exchange of bromide **6** was carried out by use of *n*-butyllithium in tetrahydrofuran at –78 °C; addition of phthalide **3** followed, and the mixture was stirred for three hours. Keto alcohol **9** formed as the single major product in 85% yield after purification by flash chromatography. The yield of the reaction was further improved to 92% by use of lithium bromide as additive,[19,20] whereas the use of tetramethylethylenediamine and hexamethylphosphoramide did not result in any improvement in yield.

Keto alcohols **10**–**14** were similarly prepared by the addition of the aryllithium derived from the appropriate bromide **6**, **7**, or **8** to phthalide **3**, **4**, or **5** (Table 1). In these cases, however, the presence of additional methoxy groups on either the aryl bromide or the phthalide component resulted in a significantly lower yield of the desired adducts.

The final step was investigated with several reagents to effect both deprotection of the (2-methoxyethoxy)methyl group and spirocyclisation. Use of trimethylsilyl bromide in dichloromethane in the presence of 4-Å molecular sieves at 0 °C (method A) or the heterogeneous catalyst sodium hydrogen sulfate on silica ($NaHSO_4 \cdot SiO_2$)[21] (method B) proved the optimum methods to effect formation of the desired spiroketals **15**–**20** from the corresponding keto alcohols **9**–**14** (Table 1).

The symmetrical nature of the parent spiroketal **15** could be established from its ^{1}H NMR spectrum. The 3-H_A and 3′-H_A protons appeared as a doublet at δ_H = 5.15 (J = 12.7 Hz) and the 3-H_B and 3′-H_B resonances gave a doublet at δ_H = 5.32 (J = 12.7 Hz). The ^{13}C NMR spectrum exhibited a characteristic spiroketal carbon at δ_C = 119.6.

The unsymmetrical aryl 5,5-spiroketal **16** was prepared by deprotection and cyclisation of adduct **10** in the presence of trimethylsilyl bromide (4.1 equiv) in dichloromethane and 4-Å molecular sieves at 0 °C. In this case, the 3-H_A and 3-H_B resonances appeared as two doublets at δ_H = 5.09 and 5.27 (J = 12.7 Hz), respectively, in the ^{1}H NMR spectrum, whilst 3′-H_A and 3′-H_B resonated as doublets at δ_H = 5.12 and 5.29 (J = 12.6 Hz), respectively. The ^{13}C NMR spectrum exhibited a characteristic spiroketal carbon at δ_C = 119.5. The ^{1}H and ^{13}C NMR data for spiroketals **16**–**20** were similar.

In conclusion, novel aryl spiroketals **15**–**20** were synthesised by addition of an aryllithium to a phthalide followed by acid-catalysed cyclisation. Whilst the yields obtained were moderate, the scope of this concise synthetic methodology has been successfully applied to the synthesis of several unsymmetrical aryl spiroketals with varying oxygenation patterns.

All reactions were carried out under a N_2 atmosphere, and oven-dried glassware and standard syringe and septum techniques were used, unless otherwise stated. THF was distilled from Na/benzophenone under N_2. CH_2Cl_2 was distilled from CaH_2 under N_2. Flash chromatography was performed on silica gel (Riedel-de Häen or Merck, 0.032–0.063 mm). Analytical TLC was performed with 0.20-mm silica gel 60 aluminum-backed plates and analysed with 365-nm UV irradiation followed by staining with either alkaline permanganate or vanillin/H_2SO_4 soln. HRMS was carried out with the use of EI, CI, and FAB techniques on a VG70-SE spectrometer operating at a nominal accelerating voltage of 70 eV and a nominal resolution of 5000–10000, as appropriate. NMR spectra were recorded on either a Bruker DRX300 [300 MHz (^{1}H), 75 MHz (^{13}C)] or a Bruker DRX400 [400 MHz (^{1}H), 100 MHz (^{13}C)] spectrometer. ^{1}H NMR chemical shifts are reported in ppm relative to TMS as internal standard. ^{13}C NMR chemical shifts are reported in ppm relative to TMS, with the solvent as an internal indicator ($CDCl_3$: δ = 77.0). Melting points were determined on a Kofler hot-stage apparatus and are uncorrected.

1-Bromo-2-{[(2-methoxyethoxy)methoxy]methyl}benzene (6)

DIPEA (2.0 mL, 11.5 mmol) was added to a soln of 2-bromobenzyl alcohol (1.00 g, 5.38 mmol) in anhyd CH_2Cl_2 (10.0 mL) at 0 °C under N_2. MEMCl (1.0 mL, 8.76 mmol) was added dropwise and the mixture was stirred at 0 °C for 1 h. It was then allowed to warm to r.t. and stirred for 8 h. The mixture was diluted with CH_2Cl_2 (10 mL), washed with sat. $NaHCO_3$ (2 × 20 mL) and brine (2 × 20 mL), and then dried ($MgSO_4$). The solvents were removed under reduced pressure and the crude product was purified by flash chromatography (silica gel, hexane–EtOAc, 9:1).

Yield: 1.36 g (92%); colourless oil.

IR (film): 2927, 2884, 1569, 1470, 1442, 1201, 1172, 1109, 1056, 1041, 1026, 752 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.38 (s, 3 H, 8′-H), 3.55–3.57 (m, 2 H, 6′-H), 3.74–3.76 (m, 2 H, 5′-H), 4.67 (s, 2 H, 1′-H), 4.84 (s, 2 H, 3′-H), 7.13 (ddd, J = 7.7, 7.7, 1.5 Hz, 1 H, 5-H), 7.29 (ddd, J = 7.7, 7.7, 0.9 Hz, 1 H, 4-H), 7.46 (dd, J = 7.7, 1.5 Hz, 1 H, 3-H), 7.52 (dd, J = 7.7, 0.9 Hz, 1 H, 6-H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 59.0 (CH_3, C-8′), 67.0 (CH_2, C-5′), 69.0 (CH_2, C-1′), 71.7 (CH_2, C-6′), 95.2 (CH_2, C-3′), 122.9 (C, C-1), 127.3 (CH, C-4), 129.0 (CH, C-5), 129.3 (CH, C-3), 132.5 (CH, C-6), 137.3 (C, C-2).

MS (EI, 70 eV): *m*/*z* (%) = 277 (0.02) [^{81}BrM + H$^+$], 275 (0.02) [^{79}BrM + H$^+$], 200 (22), 198 (22), 171 (97), 169 (100), 119 (31), 89 (81), 59 (48), 45 (71).

HRMS (EI): *m*/*z* [M + H$^+$] calcd for $C_{11}H_{15}{}^{79}BrO_3$: 275.0283; found: 275.0289; calcd for $C_{11}H_{15}{}^{81}BrO_3$: 277.0262; found: 277.0266.

1-Bromo-4-methoxy-2-{[(2-methoxyethoxy)methoxy]methyl}benzene (7)

Compound **7** was prepared as described above for **6**, from DIPEA (1.3 mL, 1.46 mmol), 2-bromo-5-methoxybenzyl alcohol[22] (750 mg, 3.46 mmol), and MEMCl (0.7 mL, 6.13 mmol).

Yield: 862 mg (82%); colourless oil.

IR (film): 2933, 2886, 1574, 1473, 1112, 1046, 1020, 854 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.39 (s, 3 H, 8′-H), 3.56–3.58 (m, 2 H, 6′-H), 3.75–3.77 (m, 2 H, 5′-H), 3.79 (s, 3 H, 4-OMe), 4.63 (s, 2 H, 1′-H), 4.85 (s, 2 H, 3′-H), 6.70 (dd, *J* = 8.7, 3.1 Hz, 1 H, 5-H), 7.04 (d, *J* = 3.1 Hz, 1 H, 3-H), 7.40 (d, *J* = 8.7 Hz, 1 H, 6-H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 55.5 (CH_3, OMe), 59.0 (CH_3, C-8′), 67.1 (CH_2, C-5′), 69.0 (CH_2, C-1′), 71.7 (CH_2, C-6′), 95.3 (CH_2, C-3′), 112.9 (C, C-1), 114.6 (CH, C-5), 114.7 (CH, C-3), 133.1 (CH, C-6), 138.3 (C, C-2), 159.0 (C, C-4).

MS (EI, 70 eV): *m*/*z* (%) = 306 (10) [^{81}BrM$^+$], 304 (10) [^{79}BrM$^+$], 201 (87), 199 (100), 149 (34), 121 (31), 89 (38), 59 (41), 45 (48).

HRMS (EI): *m*/*z* [M + H$^+$] calcd for $C_{12}H_{17}{}^{79}BrO_4$: 304.0310; found: 304.0315; calcd for $C_{12}H_{17}{}^{81}BrO_4$: 306.0290; found: 306.0289.

2-Bromo-1,5-dimethoxy-3-{[(2-methoxyethoxy)methoxy]methyl}benzene (8)

Compound **8** was prepared as described above for **6**, from DIPEA (0.75 mL, 4.31 mmol), 2-bromo-3,5-dimethoxybenzyl alcohol,[23] and MEMCl (0.35 mL, 3.07 mmol).

Yield: 489 mg (72%); colourless solid; mp 41–43 °C.

IR (film): 2951, 1594, 1369, 1331, 1117, 1099, 1074, 1052, 1023, 834 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.34 (s, 3 H, 8′-H), 3.52–3.54 (m, 2 H, 6′-H), 3.71–3.73 (m, 2 H, 5′-H), 3.76 (s, 3 H, 5-OMe), 3.80 (s, 3 H, 1-OMe), 4.62 (s, 2 H, 1′-H), 4.81 (s, 2 H, 3′-H), 6.37 (d, *J* = 2.7 Hz, 1 H, 6-H), 6.64 (d, *J* = 2.7 Hz, 1 H, 4-H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 55.3 (CH_3, OMe), 56.1 (CH_3, OMe), 58.8 (CH_3, C-8′), 66.9 (CH_2, C-5′), 69.0 (CH_2, C-1′), 71.6 (CH_2, C-6′), 95.1 (CH_2, C-3′), 98.6 (CH, C-6), 102.4 (C, C-2), 104.9 (CH, C-4), 139.1 (C, C-3), 156.3 (C, C-1), 159.6 (C, C-5).

MS (EI, 70 eV): *m*/*z* (%) = 336 (25) [^{81}BrM$^+$], 334 (25) [^{79}BrM$^+$], 232 (78), 231 (85), 230 (79), 229 (81), 151 (100), 135 (39), 59 (36), 45 (31).

HRMS (EI): *m*/*z* [M + H$^+$] calcd for $C_{13}H_{19}{}^{79}BrO_5$: 334.0416; found: 334.0416; calcd for $C_{13}H_{19}{}^{81}BrO_5$: 336.0395; found: 336.0404.

[2-(Hydroxymethyl)phenyl](2-{[(2-methoxyethoxy)methoxy]methyl}phenyl)methanone (9)

A 1.6 M soln of *n*-BuLi in hexane (0.65 mL, 1.04 mmol) was added to a soln of **6** (252 mg, 1.03 mmol) in anhyd THF (2 mL), and the mixture was stirred at –78 °C under N_2 for 5 min. A soln of LiBr (45 mg, 0.52 mmol) in anhyd THF (1 mL) was added dropwise. Then a soln of **3** (140 mg, 1.04 mmol) in anhyd THF (2 mL) was added dropwise. The mixture was stirred for 30 min at –78 °C, and then the reaction was quenched slowly with H_2O (5 mL) and the mixture was warmed to r.t. The aqueous layer was separated and then extracted with CH_2Cl_2 (2 × 10 mL). The organic layers were combined, washed with H_2O (10 mL) and brine (10 mL), and dried ($MgSO_4$). The solvents were removed under reduced pressure and the crude product was purified by flash chromatography (silica gel, hexane–EtOAc, 4:1).

Yield: 280 mg (92%); colourless oil.

IR (film): 3447, 2930, 2885, 1659, 1599, 1573, 1448, 1300, 1262, 1200, 1171, 1111, 1043, 929, 768, 736, 641 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.34 (s, 3 H, 8‴-H), 3.46–3.49 (m, 2 H, 6‴-H), 3.60–3.62 (m, 2 H, 5‴-H), 3.90 (t, *J* = 7.0 Hz, 1 H, CH_2OH), 4.63 (s, 2 H, 3‴-H), 4.68 (d, *J* = 7.0 Hz, 2 H, CH_2OH), 4.71 (s, 2 H, 1‴-H), 7.29–7.32 (m, 1 H, 5′-H), 7.33–7.35 (m, 2 H, 5″-H, 6″-H), 7.36–7.38 (m, 1 H, 4′-H), 7.49–7.52 (m, 1 H, 4″-H), 7.52–7.54 (m, 2 H, 3′-H, 6′-H), 7.55–7.57 (m, 1 H, 3″-H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 58.9 (CH_3, C-8‴), 64.2 (CH_2, CH_2OH), 66.9 (CH_2, C-5‴), 67.3 (CH_2, C-1‴), 71.6 (CH_2, C-6‴), 95.0 (CH_2, C-3‴), 127.2 (CH, C-5″), 127.3 (CH, C-5′), 128.8 (CH, C-3″), 130.1 (CH, C-6″), 130.4 (CH, C-3′), 131.3 (CH, C-4″), 131.9 (CH, C-4′), 132.5 (CH, C-6′), 137.6 (C, C-1′), 138.0 (C, C-1″), 138.2 (C, C-2″), 142.2 (C, C-2′), 200.9 (C, C-1).

MS (EI, 70 eV): *m*/*z* (%) = 313 (10) [M + H$^+$ – H_2O], 253 (19), 223 (45), 195 (18), 179 (16), 165 (21), 152 (16), 120 (16), 105 (16), 89 (74).

HRMS–FAB: *m*/*z* [M + H$^+$ – H_2O] calcd for $C_{19}H_{22}O_5$: 313.1440; found: 313.1440.

[2-(Hydroxymethyl)phenyl](4-methoxy-2-{[(2-methoxyethoxy)methoxy]methyl}phenyl)methanone (10)

Compound **10** was prepared as described above for **9**: 1.6 M *n*-BuLi in hexane (0.65 mL, 1.04 mmol) and **7** (313 mg, 1.03 mmol) in anhyd THF (2 mL) were combined at –78 °C under N_2, and LiBr (45 mg, 0.52 mmol) and **3** (142 mg, 1.06 mmol) were added in anhyd THF (2 mL).

Yield: 189 mg (51%); colourless oil.

IR (film): 3466, 2932, 2884, 1650, 1606, 1239, 1119, 1047 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.37 (s, 3 H, 8‴-H), 3.52–3.55 (m, 2 H, 6‴-H), 3.69–3.72 (m, 2 H, 5‴-H), 3.88 (s, 3 H, 4″-OMe), 4.61 (s, 2 H, CH_2OH), 4.77 (s, 2 H, 3‴-H), 4.88 (s, 2 H, 1‴-H), 6.78 (dd, *J* = 8.6, 2.6 Hz, 1 H, 5″-H), 7.23 (d, *J* = 2.6 Hz, 1 H, 3″-H), 7.32–7.34 (m, 1 H, 5′-H), 7.35–7.36 (m, 1 H, 6′-H), 7.36 (d, *J* = 8.6 Hz, 1 H, 6″-H), 7.51–7.52 (m, 2 H, 3′-H and 4′-H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 55.4 (CH_3, OMe), 58.9 (CH_3, C-8‴), 64.2 (CH_2, CH_2OH), 67.0 (CH_2, C-5‴), 67.5 (CH_2, C-1‴), 71.6 (CH_2, C-6‴), 95.2 (CH_2, C-3‴), 111.5 (CH, C-5″), 113.9 (CH, C-3″), 127.1 (CH, C-5′), 129.2 (C, C-1″), 130.4 (CH, C-3′), 131.0 (CH, C-6′), 131.8 (CH, C-4′), 134.1 (CH, C-6″), 138.8 (C, C-2′), 141.6 (C, C-1′), 142.7 (C, C-2″), 162.5 (C, C-4″), 199.6 (C, C-1).

MS (EI, 70 eV): *m*/*z* (%) = 343 (100) [M + H$^+$ – H_2O], 253 (44), 237 (32), 225 (12), 209 (14), 165 (13), 149 (11), 89 (35).

HRMS–FAB: *m*/*z* [M + H$^+$ – H_2O] calcd for $C_{20}H_{24}O_6$: 343.1546; found: 343.1543.

(2,4-Dimethoxy-6-{[(2-methoxyethoxy)methoxy]methyl}phenyl)[2-(hydroxymethyl)phenyl]methanone (11)

Compound **11** was prepared as described above for **9**: 1.6 M *n*-BuLi in hexane (0.5 mL, 0.80 mmol) and **8** (253 mg, 0.75 mmol) in anhyd THF (2 mL) were combined at –78 °C under N_2, and LiBr (35 mg, 0.40 mmol) and **3** (108 mg, 0.80 mmol) were added in anhyd THF (2 mL).

Yield: 117 mg (41%); colourless oil.

IR (film): 3458, 2930, 1655, 1602, 1143, 1041 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.33 (s, 3 H, 8″-H), 3.44–3.47 (m, 2 H, 6″-H), 3.54–3.56 (m, 2 H, 5″-H), 3.58 (s, 3 H, 2′-OMe), 3.86 (s, 3 H, 4′-OMe), 4.07 (t, *J* = 6.4 Hz, 1 H, CH_2OH), 4.52 (s, 2 H, 1″-H), 4.60 (s, 2 H, 3″-H), 4.76 (d, *J* = 6.4 Hz, 2 H, CH_2OH), 6.43 (d, *J* = 2.2 Hz, 1 H, 3′-H), 6.65 (d, *J* = 2.2 Hz, 1 H, 5′-H), 7.23–7.29 (m, 1 H, 5‴-H), 7.41–7.44 (m, 1 H, 6‴-H), 7.48–7.50 (m, 2 H, 3‴-H and 4‴-H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 55.4 (CH_3, OMe), 55.7 (CH_3, OMe), 58.9 (CH_3, C-8″), 64.7 (CH_2, CH_2OH), 66.91 (CH_2, C-5″), 66.94 (CH_2, C-1″), 71.6 (CH_2, C-6″), 94.9 (CH_2, C-3″), 98.1 (CH, C-3′), 105.2 (CH, C-5′), 121.5 (C, C-1′), 127.4 (CH, C-5‴), 130.4 (CH, C-3‴), 131.8 (CH, C-6‴), 132.5 (CH, C-4‴), 138.7 (C, C-1‴), 139.1 (C, C-6′), 141.7 (C, C-2‴), 158.8 (C, C-2′), 161.9 (C, C-4′), 200.3 (C, C-1).

MS (EI, 70 eV): *m*/*z* (%) = 391 (8%) [M + H$^+$], 373 (9), 285 (23), 255 (9), 152 (9), 124 (10).

HRMS–FAB: *m*/*z* [M + H$^+$] calcd for $C_{21}H_{26}O_7$: 391.1757; found: 391.1771.

[2-(Hydroxymethyl)-5-methoxyphenyl](2-{[(2-methoxyethoxy)methoxy]methyl}phenyl)methanone (12)

Compound **12** was prepared as described above for **9**: 1.6 M *n*-BuLi in hexane (0.30 mL, 0.48 mmol) and **6** (129 mg, 0.47 mmol) were combined in anhyd THF (2 mL) at –78 °C under N_2, and LiBr (22 mg, 0.25 mmol) and **4**[16,17] (82 mg, 0.50 mmol) were added in anhyd THF (2 mL).

Yield: 67 mg (40%); colourless oil.

IR (film): 3433, 2930, 1657, 1110, 1043 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.34 (s, 3 H, 8‴-H), 3.47–3.50 (m, 2 H, 6‴-H), 3.61–3.64 (m, 2 H, 5‴-H), 3.73 (s, 3 H, 5′-OMe), 4.58 (d, *J* = 3.7 Hz, 2 H, CH_2OH), 4.65 (s, 2 H, 3‴-H), 4.74 (s, 2 H, 1‴-H), 6.88 (d, *J* = 2.7 Hz, 1 H, 6′-H), 7.03 (dd, *J* = 8.4, 2.7 Hz, 1 H, 4′-H), 7.33 (ddd, *J* = 7.3, 7.3, 1.4 Hz, 1 H, 5″-H), 7.37 (dd, *J* = 7.3, 1.9 Hz, 1 H, 6″-H), 7.43 (d, *J* = 8.4 Hz, 1 H, 3′-H), 7.51 (ddd, *J* = 7.3, 7.3, 1.9 Hz, 1 H, 4″-H), 7.57 (d, 1 H, *J* = 7.3 Hz, 3″-H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 55.5 (CH_3, C-8‴), 59.0 (CH_3, OMe), 63.8 (CH_2, CH_2OH), 67.0 (CH_2, C-5‴), 67.4 (CH_2, C-1‴), 71.7 (CH_2, C-6‴), 95.2 (CH_2, C-3‴), 117.0 (CH, C-4′), 117.8 (CH, C-6′), 127.2 (CH, C-5″), 128.9 (CH, C-3″), 130.3 (CH, C-6″), 131.5 (CH, C-4″), 132.1 (CH, C-3′), 134.4 (C, C-2′), 137.8 (C, C-1″), 138.5 (C, C-2″), 139.2 (C, C-1′), 158.5 (C, C-5′), 200.7 (C, C-1).

MS (EI, 70 eV): *m*/*z* (%) = 342 (4) [M$^+$ – H_2O], 252 (73), 239 (38), 224 (62), 221 (53), 181 (30), 165 (30), 89 (39), 59 (100), 45 (39).

HRMS (EI): *m*/*z* [M – H_2O]$^+$ calcd for $C_{20}H_{24}O_6$: 342.1459; found: 342.1459.

[2-(Hydroxymethyl)-3,5-dimethoxyphenyl](2-{[(2-methoxyethoxy)methoxy]methyl}phenyl)methanone (13)

Compound **13** was prepared as described above for **9**: 1.6 M *n*-BuLi in hexane (0.25 mL, 0.40 mmol) and **6** (102 mg, 0.37 mmol) were combined in anhyd THF (2 mL) at –78 °C under N_2, and LiBr (17 mg, 0.20 mmol) and **5**[18] (55 mg, 0.28 mmol) were added in anhyd THF (1 mL).

Yield: 39 mg (35%); colourless oil.

IR (film): 3467, 2935, 1665, 1149, 1047 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 3.28 (1 H, br s, CH_2OH), 3.34 (s, 3 H, 8‴-H), 3.48–3.51 (m, 2 H, 6‴-H), 3.64–3.67 (m, 2 H, 5‴-H), 3.70 (s, 3 H, 5′-OMe), 3.87 (s, 3 H, 3′-OMe), 4.60 (s, 2 H, CH_2OH), 4.71 (s, 2 H, 3‴-H), 4.82 (s, 2 H, 1‴-H), 6.39 (d, *J* = 2.4 Hz, 1 H, 6′-H), 6.61 (d, *J* = 2.4 Hz, 1 H, 4′-H), 7.30 (ddd, *J* = 7.6, 7.5, 0.9 Hz, 1 H, 5″-H), 7.40 (dd, *J* = 7.6, 1.4 Hz, 1 H, 6″-H), 7.50 (ddd, *J* = 7.5, 7.5, 1.4 Hz, 1 H, 4″-H), 7.60 (d, *J* = 7.5 Hz, 1 H, 3″-H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 55.5 (CH_3, OMe), 55.98 (CH_3, OMe), 56.00 (CH_2, CH_2OH), 58.9 (CH_3, C-8‴), 67.0 (CH_2, C-5‴), 67.5 (CH_2, C-1‴), 71.7 (CH_2, C-6‴), 95.2 (CH_2, C-3‴), 101.4 (CH, C-4′), 106.5 (CH, C-6′), 122.6 (C, C-2′), 127.1 (CH, C-5″), 128.7 (CH, C-3″), 131.1 (CH, C-6″), 131.9 (CH, C-4″), 137.1 (C, C-1″), 139.1 (C, C-2″), 141.3 (C, C-1′), 159.2 (C, C-3′), 159.4 (C, C-5′), 200.3 (C, C-1).

MS (EI, 70 eV): *m*/*z* (%) = 372 (18) [M$^+$ – H_2O], 296 (26), 284 (55), 268 (31), 255 (40), 253 (34), 239 (46), 165 (23), 152 (19), 59 (19), 45 (100).

HRMS (EI): *m*/*z* [M – H_2O]$^+$ calcd for $C_{21}H_{26}O_7$: 372.1573; found: 372.1568.

(2,4-Dimethoxy-6-{[(2-methoxyethoxy)methoxy]methyl}phenyl)[2-(hydroxymethyl)-3,5-dimethoxyphenyl]methanone (14)

Compound **14** was prepared as described above for **9**: 1.6 M *n*-BuLi in hexane (0.15 mL, 0.24 mmol) and **8** (80 mg, 0.24 mmol) were combined in anhyd THF (2 mL) at –78 °C under N_2, and LiBr (10 mg, 0.20 mmol) and **5** (48 mg, 0.25 mmol) were added in anhyd THF (1 mL).

Yield: 34 mg (32%); colourless oil.

IR (film): 3432, 2924, 1647, 1152, 1039 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 3.33 (s, 3 H, 8″-H), 3.46–3.49 (m, 2 H, 6″-H), 3.57 (s, 3 H, 2′-OMe), 3.59–3.62 (m, 2 H, 5″-H), 3.67 (s, 3 H, 5‴-OMe), 3.85 (s, 3 H, 4′-OMe), 3.87 (s, 3 H, 3‴-OMe), 4.55 (s, 2 H, 1″-H), 4.64 (s, 2 H, 3″-H), 4.71 (s, 2 H, CH_2OH), 6.39 (d, *J* = 2.1 Hz, 1 H, 3′-H), 6.47 (d, *J* = 2.4 Hz, 1 H, 6‴-H), 6.59 (d, *J* = 2.4 Hz, 1 H, 4‴-H), 6.64 (d, *J* = 2.1 Hz, 1 H, 5′-H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 55.4 (CH_3, OMe), 55.5 (CH_3, OMe), 55.6 (CH_2, CH_2OH), 55.9 (CH_3, OMe), 56.1 (CH_3, OMe), 58.9 (CH_3, C-8″), 67.0 (CH_2, C-1″ and C-5″), 71.7 (CH_2, C-6″), 95.0 (CH_2, C-3″), 98.2 (CH, C-3′), 101.5 (CH, C-4‴), 105.4 (CH, C-5′), 106.9 (CH, C-6‴), 121.5 (C, C-1′), 122.4 (C, C-2‴), 139.6 (C, C-6′), 142.7 (C, C-1‴), 159.1 (C, C-3‴), 159.3 (C, C-2′), 159.4 (C, C-5‴), 162.1 (C, C-4′), 199.9 (C, C-1).

MS (EI, 70 eV): *m*/*z* (%) = 432 (20) [M$^+$ – H_2O], 372 (15), 359 (38), 342 (100), 329 (15), 315 (42), 311 (52), 299 (35), 284 (18), 269 (13), 193 (47), 164 (36), 151 (34), 89 (16), 59 (47), 45 (35).

HRMS (EI): *m*/*z* [M – H_2O]$^+$ calcd for $C_{23}H_{30}O_9$: 432.1784; found: 432.1776.

1,1′-Spirobi(3*H*,3′*H*)isobenzofuran (15)

TMSBr (0.20 mL, 1.51 mmol) was added dropwise to a mixture of **9** (110 mg, 0.37 mmol) in anhyd CH_2Cl_2 (5 mL) containing 4-Å MS, and the mixture was stirred at 0 °C under N_2 for 30 min. The reaction was quenched with sat. $NaHCO_3$ (10 mL) and the mixture was extracted with Et_2O (2 × 10 mL). The organic layers were combined, washed with H_2O (10 mL), and dried ($MgSO_4$). The solvents were removed under reduced pressure and the crude product was purified by flash chromatography (silica gel, hexane–EtOAc, 9:1, then 4:1).

Yield: 40 mg (53%); yellow solid; mp 96–98 °C.

IR (film): 2913, 2865, 1609, 1459, 1361, 1309, 1262, 1030, 1010, 926 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 5.15 (d, *J* = 12.7 Hz, 2 H, 3-H_A, 3′-H_A), 5.32 (d, *J* = 12.7 Hz, 2 H, 3-H_B, 3′-H_B), 7.09 (d, *J* = 7.7 Hz, 2 H, 7-H, 7′-H), 7.31 (dd, *J* = 7.7, 7.6 Hz, 2 H, 6-H, 6′-H), 7.34 (d, *J* = 7.5 Hz, 2 H, 4-H, 4′-H), 7.41 (ddd, *J* = 7.6, 7.5, 0.9 Hz, 2 H, 5-H, 5′-H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 71.6 (CH_2, C-3, C-3′), 119.6 (C, C-1), 120.9 (CH, C-4, C-4′), 123.3 (CH, C-7, C-7′), 128.0 (CH, C-6, C-6′), 129.3 (CH, C-5, C-5′), 139.3 (C, C-7a, C-7a′), 140.1 (C, C-3a, C-3a′).

MS (EI, 70 eV): *m*/*z* (%) = 224 (100) [M]$^+$, 206 (10), 195 (45), 177 (13), 165 (45), 90 (19), 89 (18).

HRMS (EI): *m*/*z* [M]$^+$ calcd for $C_{15}H_{12}O_2$: 224.0837; found: 224.0831.

5-Methoxy-1,1′-spirobi(3*H*,3′*H*)isobenzofuran (16)

Compound **16** was prepared as described above for **15**, from TMS-Br (0.3 mL, 2.2 mmol) and **10** (190 mg, 0.53 mmol) in anhyd CH_2Cl_2 (2 mL) containing 4-Å MS.

Yield: 69 mg (51%); colourless solid; mp 129–131 °C.

IR (film): 2927, 2863, 1612, 1496, 1462, 1272, 1039, 1024, 1015 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.84 (s, 3 H, 5-OMe), 5.09 (d, *J* = 12.7 Hz, 1 H, 3-H_A), 5.12 (d, *J* = 12.6 Hz, 1 H, 3′-H_A), 5.27 (d, *J* = 12.7 Hz, 1 H, 3-H_B), 5.29 (d, *J* = 12.6 Hz, 1 H, 3′-H_B), 6.83 (s, 1 H, 4-H), 6.84 (d, *J* = 8.4 Hz, 1 H, 6-H), 6.99 (d, *J* = 8.4 Hz, 1 H, 7-H), 7.08 (d, *J* = 7.2 Hz, 1 H, 7′-H), 7.29 (d, *J* = 7.2 Hz, 1 H, 4′-H), 7.32 (dd, *J* = 7.2, 7.2 Hz, 1 H, 6′-H), 7.39 (ddd, *J* = 7.2, 7.2, 0.9 Hz, 1 H, 5′-H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 55.6 (CH_3, OMe), 71.4 (CH_2, C-3, C-3′), 105.5 (CH, C-4), 114.7 (CH, C-6), 119.5 (C, C-1), 120.9 (CH, C-6′), 123.3 (CH, C-7′), 124.3 (CH, C-7), 128.0 (CH, C-4′), 129.2 (CH, C-5′), 131.6 (C, C-7a), 139.4 (C, C-3a′), 140.1 (C, C-7a′), 142.1 (C, C-3a), 161.0 (C, C-5).

MS (EI, 70 eV): *m*/*z* (%) = 254 (100) [M]$^+$, 225 (38), 210 (12), 194 (15), 181 (17), 165 (21), 152 (19), 149 (12), 77 (12).

HRMS (EI): *m*/*z* [M]$^+$ calcd for $C_{16}H_{14}O_3$: 254.0943; found: 254.0936.

5,7-Dimethoxy-1,1′-spirobi(3*H*,3′*H*)isobenzofuran (17)

Compound **17** was prepared as described above for **15**, from TMS-Br (0.10 mL, 0.75 mmol) and **11** (55 mg, 0.14 mmol) in anhyd CH_2Cl_2 (5 mL) containing 4-Å MS.

Yield: 22 mg (55%); colourless solid; mp 148–150 °C.

IR (film): 2867, 1606, 1343, 1149, 1092, 1026 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.55 (s, 3 H, 7-OMe), 3.83 (s, 3 H, 5-OMe), 5.10 (d, *J* = 12.6 Hz, 1 H, 3-H_A), 5.16 (d, *J* = 12.3 Hz, 1 H, 3′-H_A), 5.26 (d, *J* = 12.6 Hz, 1 H, 3-H_B), 5.29 (d, *J* = 12.3 Hz, 1 H, 3′-H_B), 6.32 (d, *J* = 1.6 Hz, 1 H, 6-H), 6.40 (d, *J* = 1.6 Hz, 1 H, 4-H), 7.10 (d, *J* = 7.4 Hz, 1 H, 7′-H), 7.28 (dd, *J* = 7.4, 7.1 Hz, 1 H, 6′-H), 7.29 (d, *J* = 7.4 Hz, 1 H, 4′-H), 7.36 (dd, *J* = 7.4, 7.1 Hz, 1 H, 5′-H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 55.4 (CH_3, OMe), 55.6 (CH_3, OMe), 71.7 (CH_2, C-3′), 71.9 (CH_2, C-3), 96.3 (CH, C-4), 98.4 (CH, C-6), 119.3 (C, C-1), 119.4 (C, C-7a), 120.7 (CH, C-4′), 122.6 (CH, C-7′), 127.6 (CH, C-6′), 128.7 (CH, C-5′), 139.4 (C, C-3a′), 139.6 (C, C-7a′), 143.3 (C, C-3a), 156.3 (C, C-7), 163.0 (C, C-5).

MS (EI, 70 eV): *m*/*z* (%) = 284 (100) [M]$^+$, 283 (70), 255 (52), 253 (65), 224 (15).

HRMS (EI): *m*/*z* [M]$^+$ calcd for $C_{17}H_{16}O_4$: 284.1049; found: 284.1041.

6-Methoxy-1,1′-spirobi(3*H*,3′*H*)isobenzofuran (18)

Activated $NaHSO_4{\cdot}SiO_2$[24] (ca. 14 mg, 0.078 mmol) was added to **12** (24 mg, 0.067 mmol) in anhyd CH_2Cl_2 (2 mL) under N_2, and the mixture was stirred at r.t. for 6 h. The catalyst was removed by filtration and washed with CH_2Cl_2 (2 × 5 mL). The solvents were removed under reduced pressure and the crude product was purified by flash chromatography (silica gel, hexane–EtOAc, 9:1, then 4:1).

Yield: 7 mg (48%); colourless oil.

IR (film): 2921, 2860, 1497, 1360, 1238, 1027 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.73 (s, 3 H, 6-OMe), 5.09 (d, *J* = 12.1 Hz, 1 H, 3-H_A), 5.15 (d, *J* = 12.7 Hz, 1 H, 3′-H_A), 5.25 (d, *J* = 12.1 Hz, 1 H, 3-H_B), 5.31 (d, *J* = 12.7 Hz, 1 H, 3′-H_B), 6.56 (d, *J* = 2.3 Hz, 1 H, 7-H), 6.96 (dd, *J* = 8.5, 2.3 Hz, 1 H, 5-H), 7.10 (d, *J* = 7.5 Hz, 1 H, 7′-H), 7.22 (d, *J* = 8.5 Hz, 1 H, 4-H), 7.32 (dd, *J* = 7.5, 7.4 Hz, 1 H, 6′-H), 7.34 (d, *J* = 7.4 Hz, 1 H, 4′-H), 7.41 (ddd, *J* = 7.4, 7.4, 0.9 Hz, 1 H, 5′-H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 55.5 (CH_3, OMe), 71.4 (CH_2, C-3), 71.6 (CH_2, C-3′), 107.2 (CH, C-7), 116.8 (CH, C-5), 119.6 (C, C-1), 120.9 (CH, C-4′), 121.7 (CH, C-4), 123.4 (CH, C-7′), 128.1 (CH, C-6′), 129.3 (CH, C-5′), 132.1 (C, C-3a), 139.2 (C, C-7a′), 140.1 (C, C-3a′), 140.6 (C, C-7a), 160.0 (C, C-6).

MS (EI, 70 eV): *m*/*z* (%) = 254 (100) [M]$^+$, 225 (58), 209 (22), 194 (21), 165 (24), 152 (19), 120 (39).

HRMS (EI): *m*/*z* [M]$^+$ calcd for $C_{16}H_{14}O_3$: 254.0943; found: 254.0939.

4,6-Dimethoxy-1,1′-spirobi(3*H*,3′*H*)isobenzofuran (19)

Compound **19** was prepared as described above for **18**, from activated $NaHSO_4{\cdot}SiO_2$ (ca. 28 mg, 0.16 mmol) and **13** (25 mg, 0.064 mmol) in anhyd CH_2Cl_2 (1 mL).

Yield: 8 mg (44%); colourless solid; mp 124–126 °C (from hexane).

IR (film): 2920, 1614, 1499, 1337, 1150, 1030 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.70 (s, 3 H, 6-OMe), 3.84 (s, 3 H, 4-OMe), 5.08 (d, *J* = 12.2 Hz, 1 H, 3-H_A), 5.14 (d, *J* = 12.7 Hz, 1 H, 3′-H_A), 5.20 (d, *J* = 12.2 Hz, 1 H, 3-H_B), 5.31 (d, *J* = 12.7 Hz, 1 H, 3′-H_B), 6.14 (d, *J* = 1.9 Hz, 1 H, 7-H), 6.45 (d, *J* = 1.9 Hz, 1 H, 5-H), 7.11 (d, *J* = 7.4 Hz, 1 H, 7′-H), 7.31 (dd, *J* = 7.4, 7.4 Hz, 1 H, 6′-H), 7.33 (d, *J* = 7.4 Hz, 1 H, 4′-H), 7.41 (ddd, *J* = 7.4, 7.4, 0.9 Hz, 1 H, 5′-H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 55.4 (CH_3, 4-OMe), 55.6 (CH_3, 6-OMe), 70.0 (CH_2, C-3), 71.6 (CH_2, C-3′), 98.0 (CH, C-7), 99.8 (CH, C-5), 120.0 (C, C-1), 120.8 (C, C-3a), 120.9 (CH, C-4′), 123.4 (CH, C-7′), 128.0 (CH, C-6′), 129.3 (CH, C-5′), 139.1 (C, C-7a′), 140.0 (C, C-3a′), 141.4 (C, C-7a), 154.4 (C, C-4), 162.0 (C, C-6).

MS (EI, 70 eV): *m*/*z* (%) = 284 (100) [M]$^+$, 255 (67), 253 (23), 239 (19), 224 (20), 152 (13), 150 (40), 90 (12), 77 (13).

HRMS (EI): *m*/*z* [M]$^+$ calcd for $C_{17}H_{16}O_4$: 284.1049; found: 284.1046.

4,5′,6,7′-Tetramethoxy-1,1′-spirobi(3*H*,3′*H*)isobenzofuran (20)

Compound **20** was prepared as described above for **18**, from activated $NaHSO_4{\cdot}SiO_2$ (ca. 10 mg, 0.056 mmol) and **14** (7 mg, 0.016 mmol) in anhyd CH_2Cl_2 (1 mL).

Yield: 2 mg (40%); colourless solid; mp 136–137 °C (from hexane).

IR (film): 2923, 1610, 1154, 1025 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.58 (s, 3 H, 7′-OMe), 3.72 (s, 3 H, 6-OMe), 3.82 (s, 3 H, 5′-OMe), 3.83 (s, 3 H, 4-OMe), 5.06 (d, *J* = 11.9 Hz, 1 H, 3-H_A), 5.08 (d, *J* = 12.8 Hz, 1 H, 3′-H_A), 5.18 (d, *J* = 11.9 Hz, 1 H, 3-H_B), 5.23 (d, *J* = 12.8 Hz, 1 H, 3′-H_B), 6.16 (d, *J* = 1.9 Hz, 1 H, 7-H), 6.32 (d, *J* = 1.7 Hz, 1 H, 4′-H), 6.39 (d, *J* = 1.7 Hz, 1 H, 6′-H), 6.41 (d, *J* = 1.9 Hz, 1 H, 5-H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 55.4 (CH_3, OMe), 55.5 (CH_3, OMe), 55.61 (CH_3, OMe), 55.63 (CH_3, OMe), 70.0 (CH_2, C-3), 71.9 (CH_2, C-3′), 96.4 (CH, C-6′), 97.7 (CH, C-7), 98.4 (CH, C-4′), 99.4 (CH, C-5), 119.2 (C, C-7a′), 119.7 (C, C-1), 120.2 (C, C-3a), 142.0 (C, C-7a), 143.4 (C, C-3a′), 154.2 (C, C-4), 156.5 (C, C-7′), 161.6 (C, C-6), 163.1 (C, C-5′).

MS (EI, 70 eV): *m*/*z* (%) = 344 (100) [M]$^+$, 315 (96), 299 (13), 284 (13), 193 (11), 150 (60), 77 (14), 69 (13), 57 (17), 43 (18).

HRMS (EI): *m*/*z* [M]$^+$ calcd for $C_{19}H_{20}O_6$: 344.1258; found: 344.1260.

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