# A Facile Synthesis of Aryl Spirodioxines Based on a 3*H*,3′*H*-2,2′-Spirobi(benzo[*b*][1,4]dioxine) Skeleton

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**Abstract:** The synthesis of a series of 6,6-bisbenzannulated spiroketals containing a 3*H*,3′*H*-2,2′-spirobi(benzo[*b*][1,4]dioxine) ring system is reported. The key step involves addition of a monobenzyl-protected catechol to the epoxide unit of a glycidol bearing a benzyl-protected catechol. The resultant alcohol adduct is oxidized to a ketone that then undergoes hydrogenation and acid-catalyzed cyclization to produce the desired spirodioxines.

**Key words:** bisbenzannulated spiroketals, benzyl ether, catechol, epoxide, spirodioxines

Spiroketals are present in many bioactive natural products of medicinal and environmental importance including insect pheromones, pesticides, antitumor agents and toxins;[1] they are therefore attractive synthetic targets for organic chemists. Although many syntheses of aliphatic spiroketals have been reported,[2] the synthesis of aromatic spiroketals is less common. The rubromycins (Figure 1) are a family of quinone antibiotics isolated from a strain of *Streptomyces* species that exhibit activity against Gram-positive bacteria.[3,4] β-Rubromycin (**2**) and γ-rubromycin (**3**) inhibit human telomerase ($IC_{50}$ 3.06 ± 0.85 μM and 2.64 ± 0.09 μM, respectively) and they also inhibit the reverse transcriptase of the moloney murine leukaemia virus and human immunodeficiency virus type 1.[3] β-Rubromycin (**2**) and γ-rubromycin (**3**) contain a 5,6-spiroketal moiety which in turn is linked to a hydroxynaphthoquinone chromophore and an isocoumarin moiety.[5] α-Rubromycin (**1**), derived from ring opening of the spiroketal core of β-rubromycin (**2**), exhibited much lower inhibition of telomerase ($IC_{50}$ > 200 μM). The absence of a spiroketal moiety in α-rubromycin (**1**) suggested that the spiroketal unit is an essential structural element for inhibition of telomerase.[3] Structurally related to the rubromycins are purpuromycin (**4**),[6] a potential topical agent for vaginal infections,[7] heliquinomycin (**5**),[8] an inhibitor of DNA helicase and griseorhodins C (**6**)[9] and G (**7**). All these compounds can act as bioreductive alkylating agents as postulated by Moore.[10]

To date several syntheses of 5,6-bisbenzannulated spiroketals related to the rubromycins have been reported. de Koning and co-workers[11] reported the synthesis of a 5,6-bisbenzannulated spiroketal via a Henry condensation between an aryl-containing nitroalkane and an aryl-containing aldehyde to afford a nitroolefin which underwent a Nef reaction mediated by Pearlman's catalyst to unmask the carbonyl group and induce the spiroketalization step.

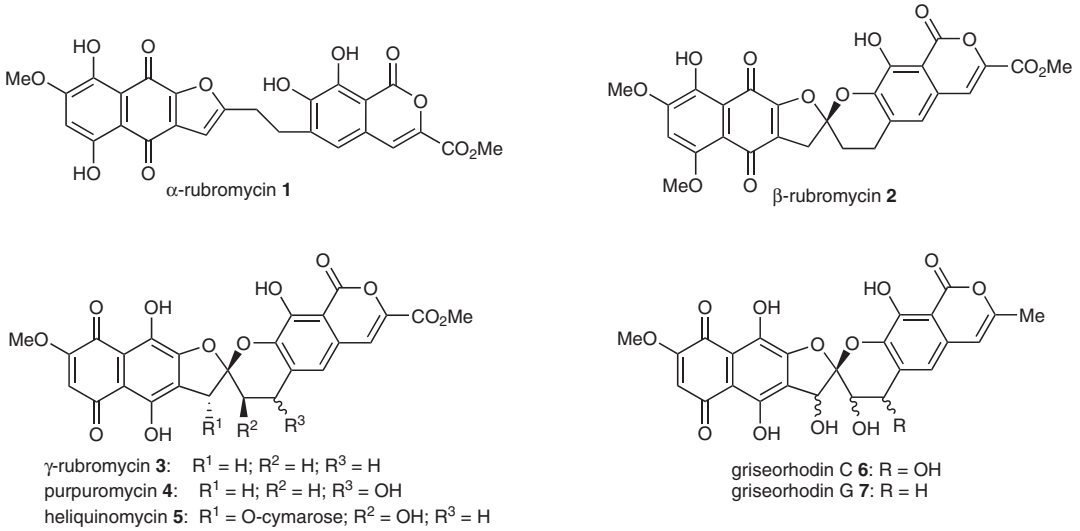


**Figure 1** The rubromycin family of antibiotics

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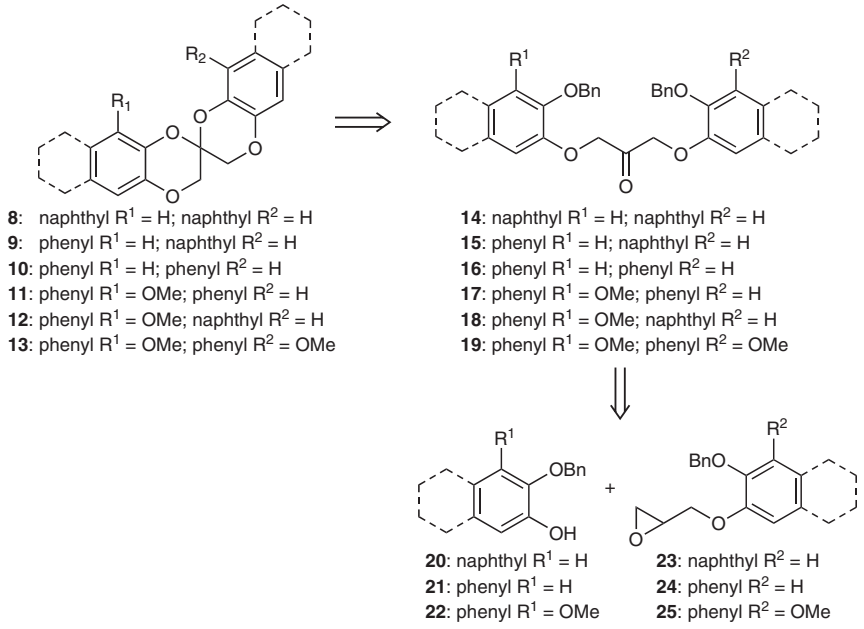
Danishefsky et al.[12] reported the total synthesis of heliquinomycinone, the aglycone of heliquinomycin (**5**), in which the 5,6-bisbenzannulated spiroketal moiety was synthesized from a lactol precursor under Mitsunobu conditions. The lactol precursor itself was assembled via addition of a lithiated naphthofuran to an aryl acetaldehyde. Other approaches for the syntheses of 5,6-bisbenzannulated spiroketals reported include use of a hetero-Diels–Alder cycloaddition between an *o*-quinone methide and an aryl-containing enol ether,[13] a [3+2] cycloaddition between an aryl-containing enol ether and a zwitterion,[14] a [3+2] cycloaddition between an aryl-containing nitroalkane and an aryl-containing olefin,[15] and Heck coupling of an aryl iodide with an aryl-containing enone with the enone being prepared via addition of a lithiated methoxyallene to a functionalized aryl aldehyde.[16]

Our research group has reported the synthesis of a series of 5,6-bisbenzannulated[17] and 6,6-bisbenzannulated[18] spiroketals related to γ-rubromycin (**3**) via acid-catalyzed spiroketalization of dihydroxyketones which in turn were assembled from the addition of lithiated aryl acetylenes to aryl aldehydes. As part of our synthetic program directed towards the synthesis of aryl spiroketal-containing scaffolds we have now extended this research to the synthesis of a series of 6,6-bisbenzannulated spiroketals that contain additional oxygen atoms, namely the 3*H*,3′*H*-2,2′-spirobi(benzo[*b*][1,4]dioxine) ring system. It was envisaged that these compounds could be used to probe the effect that introduction of additional heteroatoms might have on telomerase inhibition. Although the synthesis of 1,4,7,10-tetraoxaspiro[5.5]undecanes (aliphatic dioxa-6,6-spiroketals) have been reported,[19] the synthesis of 3*H*,3′*H*-2,2′-spirobi(benzo[*b*][1,4]dioxines) has not been reported. We therefore herein describe the synthesis of six novel aryl spirodioxines based on the 3*H*,3′*H*-2,2′-spirobi(benzo[*b*][1,4]dioxine) framework.

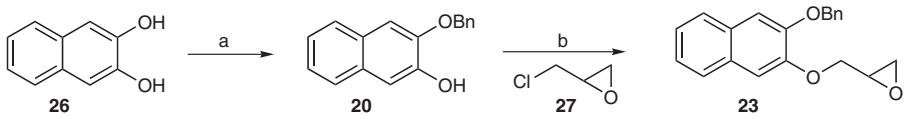
It was envisaged that 1,4-dioxine aryl spiroketals **8**–**13** could be readily assembled from protected diphenolic ketones **14**–**19**, each of which is available via the addition of an appropriate naphthol **20** or phenol **21** or **22** to an appropriate epoxide **23**–**25** (Scheme 1).

Naphthol **20** was prepared from 2,3-dihydroxynaphthalene **26** as reported by Weber et al.[20] (Scheme 2). Reaction of naphthol **20** with epichlorohydrin (**27**) and sodium hydroxide as base in the presence of benzyltriethylammonium chloride in tetrahydrofuran–water (1:1) at room temperature afforded epoxide intermediate **23**.

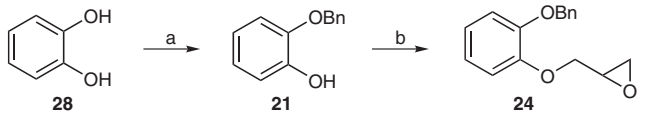
Phenol **21** was available by reaction of catechol (**28**) with benzyl bromide using sodium hydroxide in methanol at 100 °C (Scheme 3). Alkylation of phenol **21** with epichlorohydrin (**27**) in tetrahydrofuran–water (1.4:1) afforded epoxide **24**.




**Scheme 1**




**Scheme 2** *Reagents and conditions*: a) $NaHCO_3$, BnBr, DMF, 100 °C, 17 h, 33%; b) NaOH, **27**, $BnEt_3NCl$, THF–$H_2O$, 1:1, r.t., 17 h, 96%.

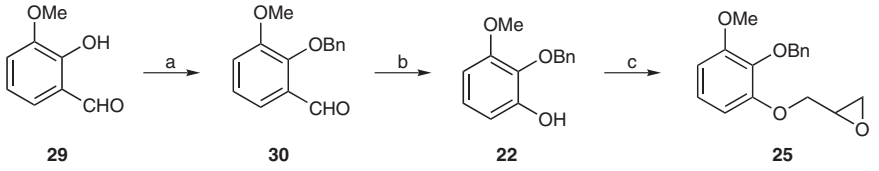



**Scheme 3** *Reagents and conditions*: a) NaOH, BnBr, MeOH, 100 °C, 22 h, 28%; b) NaOH, **27**, $BnEt_3NCl$, THF–$H_2O$, 1.4:1, r.t., 20 h, 95%.

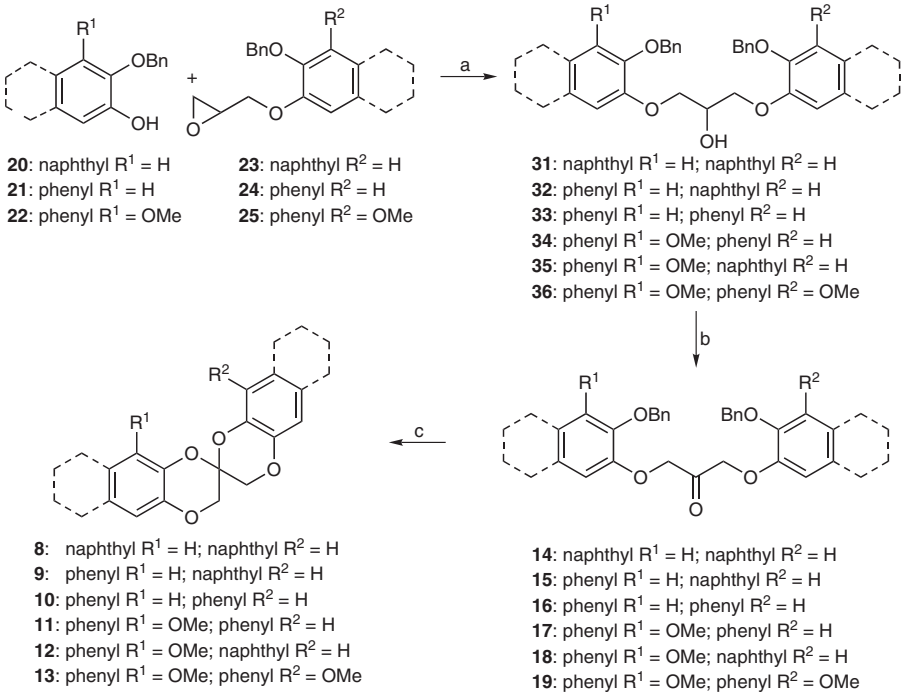
Phenol **22** was prepared in three steps from *o*-vanillin (**29**) (Scheme 4). Benzylation of *o*-vanillin (**29**) using the procedure reported by Lin et al.[21] afforded benzyl ether **30**. Baeyer–Villiger oxidation of the formyl group using *m*-chloroperoxybenzoic acid with *p*-toluenesulfonic acid as catalyst[22] followed by hydrolysis of the formate with potassium hydroxide[23] afforded phenol **22**. Phenol **22** was then similarly reacted with epichlorohydrin (**27**) to afford epoxide **25**.

With the key epoxide intermediates in hand, attention was turned to ring opening of these epoxides with the appropriate phenol or naphthol to afford alcohols **31**–**36**. This step was smoothly effected in good yield using potassium carbonate as base under reflux in acetone. Subsequent oxidation of the alcohols **31**–**36** to the corresponding ketones **14**–**19** was conducted using Dess–Martin periodinane[24] or tetra-*n*-propylammonium perruthenate. Finally hydrogenolysis of the benzyl ethers and subsequent acid-catalyzed cyclization using *p*-toluenesulfonic acid afforded spiroketals **8**–**13** (Scheme 5).

Initial attention focused on the synthesis of symmetrical spiroketal **8** from ketone **14**. Ketone **14** underwent hydrogenation over 10% palladium on activated carbon in ethanol at room temperature to afford hemiketal intermediate **37**. Evidence for the formation of hemiketal **37** was established from the crude $^1$H NMR spectrum that established two broad singlets assigned to two hydroxyl groups and a mass spectrum that established a molecular ion at $m/z$ = 374. A model study to effect the efficient cyclization of hemiketal **37** to spiroketal **8** was initiated using several acids and different reaction conditions (Table 1). Gentle reflux using *p*-toluenesulfonic acid in dichloromethane provided the optimum yield of spiroketal **8**. Both the $^1$H and $^{13}$C NMR spectra recorded for spiroketal **8** supported




**Scheme 4** *Reagents and conditions*: a) $K_2CO_3$, BnBr, THF, 75 °C, 15 h, 89%; b) *i*: MCPBA, *p*-TsOH, $CH_2Cl_2$, r.t., 3 h, *ii*: KOH, MeOH, r.t., 100 min, 53%; c) NaOH, **27**, $BnEt_3NCl$, THF–$H_2O$, 1.2:1, r.t., 23 h, 87%.




**20**: naphthyl $R^1$ = H
**21**: phenyl $R^1$ = H
**22**: phenyl $R^1$ = OMe

**23**: naphthyl $R^2$ = H
**24**: phenyl $R^2$ = H
**25**: phenyl $R^2$ = OMe

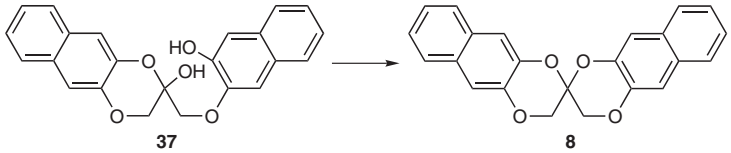
**31**: naphthyl $R^1$ = H; naphthyl $R^2$ = H
**32**: phenyl $R^1$ = H; naphthyl $R^2$ = H
**33**: phenyl $R^1$ = H; phenyl $R^2$ = H
**34**: phenyl $R^1$ = OMe; phenyl $R^2$ = H
**35**: phenyl $R^1$ = OMe; naphthyl $R^2$ = H
**36**: phenyl $R^1$ = OMe; phenyl $R^2$ = OMe

**8**: naphthyl $R^1$ = H; naphthyl $R^2$ = H
**9**: phenyl $R^1$ = H; naphthyl $R^2$ = H
**10**: phenyl $R^1$ = H; phenyl $R^2$ = H
**11**: phenyl $R^1$ = OMe; phenyl $R^2$ = H
**12**: phenyl $R^1$ = OMe; naphthyl $R^2$ = H
**13**: phenyl $R^1$ = OMe; phenyl $R^2$ = OMe

**14**: naphthyl $R^1$ = H; naphthyl $R^2$ = H
**15**: phenyl $R^1$ = H; naphthyl $R^2$ = H
**16**: phenyl $R^1$ = H; phenyl $R^2$ = H
**17**: phenyl $R^1$ = OMe; phenyl $R^2$ = H
**18**: phenyl $R^1$ = OMe; naphthyl $R^2$ = H
**19**: phenyl $R^1$ = OMe; phenyl $R^2$ = OMe

**Scheme 5** *Reagents and conditions*: a) $K_2CO_3$, acetone, reflux, **31**, 82%; **32**, 99%; **33**, 89%; **34**, 97%; **35**, 86%; **36**, 90%; b) DMP, $CH_2Cl_2$, r.t., 2–3 h, **14**, 68%; **15**, 60%; **19**, 92%, or TPAP, NMO, 4 Å MS, $CH_2Cl_2$, r.t., 1.5–2 h, **16**, 79%; **17**, 86%; **18**, 65%; c) *i*: $H_2$, 10% Pd/C, EtOAc (EtOH for **14**), r.t., 5.5–34.5 h, *ii*: *p*-TsOH, $CH_2Cl_2$, 50 °C, 4–7.2 h, **8**, 56%; **9**, 63%; **10**, 85%; **11**, 72%; **12**, 66%; **13**, 43% (EtOAc as solvent).

**Table 1** Cyclization of Hemiketal **37** to Spiroketal **8**




**37** **8**

| Entry | Acid | Solvent | Conditions | Yield (%) of spiroketal **8** |
|---|---|---|---|---|
| 1 | CSA | EtOH | 90 °C, 1 h then 100 °C, 69 h | 25 |
| 2 | concd HCl | EtOAc | 70 °C, 1 h then 100 °C, 5 h | no reaction |
| 3 | CSA | EtOH | 85 °C, 21 h | 31 |
| 4 | TFA | $CH_2Cl_2$ | 70 °C, 6 h then 90 °C, 19 h | 43 |
| 5 | $InCl_3$ | $CH_2Cl_2$ | r.t., 3 d | no reaction |
| 6 | $InCl_3$ | $CH_2Cl_2$ | 50 °C, 24 h | 48 |
| 7 | *p*-TsOH | $CH_2Cl_2$ | 50 °C, 7.2 h | 56 |

the formation of a symmetrical structure. 3-$H_A$ and 3′-$H_A$ resonated as a doublet at $\delta_H = 4.23$ ($J = 11.4$ Hz) and 3-$H_B$ and 3′-$H_B$ resonated as a doublet at $\delta_H = 4.41$ ($J = 11.4$ Hz). The characteristic spiro carbon resonated at $\delta_C = 91.6$ in the $^{13}C$ NMR spectrum.

Spiroketals **9**–**12** were synthesized from ketones **15**–**18** in a similar fashion to spiroketal **8**. Hydrogenation of ketones **15**–**18** over 10% palladium on activated carbon in ethyl acetate at room temperature followed by subsequent cyclization of the resultant hemiketal intermediates using *p*-toluenesulfonic acid in dichloromethane provided spiroketals **9**–**12** in moderate yields. For the synthesis of spiroketal **13**, the spiroketalization step was performed using ethyl acetate as the solvent due to the insolubility of the hemiketal intermediate in dichloromethane. Decomposition of spiroketal **13** readily took place thus necessitating rapid purification by flash chromatography.

For symmetrical spiroketals **8**, **10** and **13**, both the $^1H$ and $^{13}C$ NMR data provided clear evidence for the symmetrical nature of these products. For each of the three products, both protons from each methylene group resonated as an AB system (two doublets where each doublet exhibited a *J* value of 11.3–11.4 Hz) in the respective $^1H$ NMR spectra. In the case of unsymmetrical spiroketals **9**, **11** and **12**, the protons from the two methylene groups resonated as two separate AB systems (four doublets with each doublet exhibiting a *J* value of 11.3–11.4 Hz). For all six spiroketals **8**–**13**, a characteristic spiro carbon resonated at $\delta_C = 91.3$–$91.6$ in the $^{13}C$ NMR spectra.

In conclusion the synthesis of the novel 1,4-dioxine aryl spiroketals **8**–**13** has been achieved. Whilst the yields of the spiroketals thus obtained were moderate the simplicity of the procedure, and the novelty of the spiroketal scaffolds thus prepared, provides novel aromatic heterocyclic motifs to investigate further as DNA binding agents.

Melting points were determined on a Kofler hot-stage apparatus and are uncorrected. All glassware was flame or oven-dried under $N_2$ before use. THF was dried over Na/benzophenone and distilled under $N_2$. $CH_2Cl_2$ was distilled from $CaH_2$ under $N_2$. Analytical reagent grade acetone, DMF, EtOH and MeOH were used without further purification. Product purification by flash chromatography was performed using Merck 0.0063–0.10 mm silica gel with the solvent systems specified in the experimental procedures. TLC was performed on silica precoated aluminum plates (Merck Kieselgel 60 $F_{254}$) and visualized by UV irradiation and by staining with vanillin in methanolic $H_2SO_4$, mostain [a Mo(VI)-containing stain] or anisaldehyde. IR spectra were recorded using a Perkin-Elmer Spectrum 1000 FT-IR spectrometer as thin films between NaCl plates. Absorption peaks are expressed in wave numbers ($cm^{-1}$) and were measured between 450 and 4000 $cm^{-1}$. The strength of each absorption peak is expressed by the abbreviations: s = strong, m = medium, w = weak and br = broad. NMR spectra were recorded on either a Bruker DRX300 spectrometer operating at 300 MHz for $^1H$ nuclei and 75 MHz for $^{13}C$ nuclei or on a Bruker DRX400 spectrometer operating at 400 MHz for $^1H$ nuclei and 100 MHz for $^{13}C$ nuclei. $^1H$ NMR data is reported as chemical shift in ppm downfield from TMS as the internal standard, multiplicity, *J* in Hz, relative integral and assignment. $^{13}C$ NMR data is reported as chemical shift in ppm with reference to the residual $CDCl_3$ peak at $\delta = 77.0$, multiplicity with respect to proton (deduced from DEPT experiments) and assignment. All assignments were made using the $^1H$ and $^{13}C$ NMR survey spectra along with DEPT 135, DEPT 90, COSY, HSQC and HMBC spectra where required. Low-resolution mass spectra were recorded with a VG70-SE mass spectrometer operating at a nominal accelerating voltage of 70 eV. High-resolution mass spectra (HRMS) were recorded using a VG70-SE spectrometer operating at nominal resolution of 5000 to 10000 as appropriate. Fragmentation was induced using EI or FAB. FAB mass spectra were obtained using *m*-nitrobenzyl alcohol as the matrix. Major and significant fragments are quoted in the form x (y), where x is the mass-to-charge ratio and y is the percentage abundance relative to the base peak.

**3-(Benzyloxy)naphthalen-2-ol (20)[20,25]**

$NaHCO_3$ (5.30 g, 63 mmol) was added to a solution of 2,3-dihydroxynaphthalene (**26**; 10.1 g, 63 mmol) in DMF (30 mL) and the mixture stirred for 1 h at 100 °C under $N_2$. BnBr (8.54 mL, 72

mmol) was added dropwise over 25 min then the mixture heated with stirring at 100 °C under $N_2$ for 17 h, then cooled to r.t. The solvent was removed at reduced pressure and the resultant residue partitioned between $H_2O$ (50 mL) and $CH_2Cl_2$ (50 mL). The aqueous layer was separated then extracted with $CH_2Cl_2$ (2 × 50 mL). The organic layers were combined, washed with brine (2 × 35 mL) and dried ($MgSO_4$). The solvent was removed at reduced pressure and the crude product purified by column chromatography (silica gel, hexane–$Et_2O$, 5:1); yield: 5.21 g (33%); colorless solid; mp 94.5–96.0 °C (Lit.[20] mp 95–96 °C).

$^1$H NMR (400 MHz, $CDCl_3$): δ = 5.09 (s, 2 H, OC$H_2$Ph), 5.97 (s, 1 H, OH), 7.12 (s, 1 H, 4-H), 7.25–7.39 (m, 8 H, 1-H, 6-H, 7-H and $C_6H_5$), 7.60–7.62 (m, 2 H, 5-H and 8-H).

The $^1$H NMR data were similar to those reported in the literature.[25]

$^{13}$C NMR (100 MHz, $CDCl_3$): δ = 70.8 ($CH_2$, O$CH_2$Ph), 107.0 (CH, C-4), 109.5 (CH, C-1), 123.8 (CH, C-6 or C-7), 124.4 (CH, C-6 or C-7), 126.3 (CH, C-8), 126.5 (CH, C-5), 127.9 (CH, C-2′ and C-6′), 128.4 (CH, C-4′), 128.7 (CH, C-3′ and C-5′), 128.8 (C, C-4a), 129.7 (C, C-8a), 135.8 (C, C-1′), 145.7 (C, C-2), 146.4 (C, C-3).

**2-{[3-(Benzyloxy)naphthalen-2-yloxy]methyl}oxirane (23)**

NaOH (286 mg, 7.2 mmol), $BnEt_3NCl$ (300 mg, 1.3 mmol) and $H_2O$ (5 mL) were added to a solution of naphthol **20** (400 mg, 1.6 mmol) in anhyd THF (5 mL) at r.t. Epichlorohydrin (**27**; 1.25 mL, 16.0 mmol) was added dropwise. The mixture was stirred at r.t. under $N_2$ for 17 h after which $H_2O$ (20 mL) and EtOAc (20 mL) were added. The aqueous layer was separated and then extracted with EtOAc (2 × 25 mL). The organic layers were combined, washed with $H_2O$ (20 mL), brine (20 mL) and dried ($Na_2SO_4$). The solvents were removed at reduced pressure and the crude product purified by column chromatography (silica gel, hexane–EtOAc, 4:1); yield: 468 mg (96%); yellow oil which solidified as a pale cream-colored solid upon standing; mp 80.0–81.5 °C.

IR (film): 3059, 3032, 3003, 2925, 2871, 1509, 1485, 1258, 1172, 1115 cm$^{-1}$.

$^1$H NMR (300 MHz, $CDCl_3$): δ = 2.78 (dd, $J$ = 5.0, 2.6 Hz, 1 H, OC$H_A$H$_B$ epoxide), 2.87 (dd, $J$ = 4.9, 4.2 Hz, 1 H, OCH$_A$$H_B$ epoxide), 3.38–3.43 (m, 1 H, CHO epoxide), 4.10 (dd, $J$ = 11.2, 5.4 Hz, 1 H, OC$H_A$H$_B$), 4.33 (dd, $J$ = 11.2, 3.2 Hz, 1 H, OCH$_A$$H_B$), 5.20 (s, 2 H, OC$H_2$Ph), 7.17 (s, 2 H, 1′-H and 4′-H), 7.27–7.40 (m, 5 H, 3″-H, 4″-H, 5″-H, 6′-H and 7′-H), 7.48 (d, $J$ = 7.2 Hz, 2 H, 2″-H and 6″-H), 7.59–7.67 (m, 2 H, 5′-H and 8′-H).

$^{13}$C NMR (75 MHz, $CDCl_3$): δ = 44.7 ($CH_2$, $CH_2$ epoxide), 50.1 (CH, CHO epoxide), 69.6 ($CH_2$, $OCH_2$), 70.7 ($CH_2$, O$CH_2$Ph), 109.0 (CH, C-1′ or C-4′), 109.1 (CH, C-1′ or C-4′), 124.2 (CH, C-6′ or C-7′), 124.3 (CH, C-6′ or C-7′), 126.3 (CH, C-5′ or C-8′), 126.3 (CH, C-5′or C-8′), 127.2 (CH, C-2″ and C-6″), 127.8 (CH, C-4″), 128.5 (CH, C-3″ and C-5″), 129.2 (C, C-4′a or C-8′a), 129.5 (C, C-4′a or C-8′a), 136.8 (C, C-1″), 148.8 (C, C-2′ and C-3′).

MS (EI, 70 eV): $m/z$ (%) = 306 (26, [M]$^+$), 247 (0.5), 215 (1), 198 (2), 185 (4.5), 171 (3.5), 131 (5), 115 (2.5), 102 (4), 91 (100), 77 (2), 65 (5.5), 39 (2).

HRMS (EI): $m/z$ [M]$^+$ calcd for $C_{20}H_{18}O_3$: 306.1256; found: 306.1254.

**1,3-Bis[3-(benzyloxy)naphthalen-2-yloxy]propan-2-ol (31)**

$K_2CO_3$ (83 mg, 0.60 mmol) was added to a solution of naphthol **20** (100 mg, 0.40 mmol) in acetone (3 mL) at r.t. and the mixture refluxed for 15 min at 40 °C under $N_2$. A solution of epoxide **23** (135 mg, 0.44 mmol) in acetone (6 mL) was added and the mixture refluxed at 45 °C under $N_2$ for 1 h, and then at 80 °C for 3 h. Excess $K_2CO_3$ (545 mg, 3.94 mmol) was added and the mixture refluxed at 100 °C under $N_2$ for 19 h. The solvent was removed at reduced pressure and the resultant residue partitioned between $H_2O$ (30 mL) and $CH_2Cl_2$ (30 mL). The aqueous layer was separated then neutralized to pH 7 with solid $KH_2PO_4$ and extracted with $CH_2Cl_2$ (2 × 30 mL). The organic layers were combined and dried ($Na_2SO_4$). The solvent was removed at reduced pressure and the crude product purified by column chromatography (silica gel, hexane–EtOAc, 4:1); yield: 181 mg (82%); colorless solid; mp 144–146 °C.

IR (film): 3412, 3062, 2933, 1508, 1484, 1256 cm$^{-1}$.

$^1$H NMR (300 MHz, $CDCl_3$): δ = 3.32 (br s, 1 H, OH), 4.22–4.34 (m, 4 H, 2 × $OCH_2$), 4.44–4.51 (m, 1 H, C$H$OH), 5.11 (s, 4 H, OC$H_2$Ph), 7.13 (s, 2 H, 1′-H or 4′-H), 7.15 (s, 2 H, 1′-H or 4′-H), 7.22–7.32 (m, 10 H, 3″-H, 4″-H, 5″-H, 6′-H and 7′-H), 7.41–7.43 (m, 4 H, 2″-H and 6″-H), 7.57–7.62 (m, 4 H, 5′-H and 8′-H).

$^{13}$C NMR (75 MHz, $CDCl_3$): δ = 68.5 (CH, CHOH), 70.1 ($CH_2$, $OCH_2$), 70.6 ($CH_2$, O$CH_2$Ph), 108.9 (CH, C-1′ or C-4′), 109.3 (CH, C-1′ or C-4′), 124.2 (CH, C-6′ or C-7′), 124.3 (CH, C-6′ or C-7′), 126.3 (CH, C-5′ or C-8′), 126.4 (CH, C-5′ or C-8′), 127.2 (CH, C-2″ and C-6″), 127.9 (CH, C-4″), 128.5 (CH, C-3″ and C-5″), 129.3 (C, C-4′a or C-8′a), 129.5 (C, C-4′a or C-8′a), 136.7 (C, C-1″), 148.8 (C, C-2′ or C-3′), 148.9 (C, C-2′ or C-3′).

MS (FAB, 70 eV): $m/z$ (%) = 557 (3, [M + H]$^+$), 556 (3, [M]$^+$), 443 (0.5), 341 (1.5), 165 (4.5), 149 (9), 120 (12), 115 (5.5), 91 (34), 89 (21).

HRMS-FAB: $m/z$ [M]$^+$ calcd for $C_{37}H_{32}O_5$: 556.2250; found: 556.2246.

**1,3-Bis[3-(benzyloxy)naphthalen-2-yloxy]propan-2-one (14)**

Dess–Martin periodinane[24] (DMP, 113 mg, 0.31 mmol) was added to a solution of alcohol **31** (116 mg, 0.21 mmol) in anhyd $CH_2Cl_2$ (4 mL) at r.t. The mixture was stirred at r.t. for 2.2 h after which time the reaction was quenched with sat. $NaHCO_3$ (10 mL), and EtOAc (6 mL) was added. The aqueous layer was separated and extracted with EtOAc (2 × 10 mL). The organic layers were combined, dried ($MgSO_4$) and the solvents removed at reduced pressure. The crude product was purified by flash chromatography (silica gel, hexane–EtOAc, 5:1, then 2:1); yield: 79 mg (68%); cream-colored solid; mp 166–167.5 °C.

IR (film): 3063, 3033, 2927, 1733, 1508, 1483, 1375, 1253, 1175, 1115, 1046 cm$^{-1}$.

$^1$H NMR (400 MHz, $CDCl_3$): δ = 5.08 (s, 4 H, $OCH_2$), 5.23 (s, 4 H, OC$H_2$Ph), 7.06 (s, 2 H, 1′-H), 7.22 (s, 2 H, 4′-H), 7.28–7.35 (m, 10 H, 3″-H, 4″-H, 5″-H, 6′-H and 7′-H), 7.49 (d, $J$ = 7.1 Hz, 4 H, 2″-H and 6″-H), 7.53–7.55 (m, 2 H, 8′-H), 7.66 (d, $J$ = 7.6 Hz, 2 H, 5′-H).

$^{13}$C NMR (100 MHz, $CDCl_3$): δ = 70.7 ($CH_2$, O$CH_2$Ph), 72.7 ($CH_2$, $OCH_2$), 109.2 (CH, C-4′), 109.6 (CH, C-1′), 124.5 (CH, C-7′), 124.8 (CH, C-6′), 126.4 (CH, C-5′ or C-8′), 126.6 (CH, C-5′ or C-8′), 127.2 (CH, C-2″ and C-6″), 128.0 (CH, C-4″), 128.6 (CH, C-3″ and C-5″), 128.9 (C, C-8′a), 129.9 (C, C-4′a), 136.6 (C, C-1″), 147.9 (C, C-2′), 148.7 (C, C-3′), 202.2 (C, C=O).

MS (EI, 70 eV): $m/z$ (%) = 554 (1.5, [M]$^+$), 536 (1), 340 (1), 304 (2), 288 (3), 261 (1.5), 250 (11), 215 (1), 197 (1.5), 171 (2), 149 (1), 115 (2.5), 102 (2.5), 91 (100), 77 (4), 65 (6.5), 57 (5), 44 (4.5).

HRMS (EI): $m/z$ [M]$^+$ calcd for $C_{37}H_{30}O_5$: 554.2093; found: 554.2095.

**3*H*,3′*H*-2,2′-Spirobi(naphtho[2,3-*b*][1,4]dioxine) (8)**

10% Pd/C (60 mg, 0.56 mmol) was added to a solution of ketone **14** (84 mg, 0.15 mmol) in abs EtOH (2 mL) at r.t. The reaction was stirred under $H_2$ for 15.5 h after which time the catalyst was removed by filtration through Celite and washed with EtOAc (5 × 2 mL). The solvents were removed at reduced pressure and the resultant residue immediately redissolved in abs EtOH (2 mL). 10% Pd/C (60 mg, 0.56 mmol) was added and the mixture stirred under $H_2$

for 19 h. The catalyst was removed by filtration through Celite and washed with EtOAc (5 × 2 mL). The solvents were removed at reduced pressure and the crude intermediate immediately dissolved in anhyd $CH_2Cl_2$ (5 mL). *p*-TsOH·$H_2O$ (350 mg, 1.84 mmol) was added to this solution and the mixture heated under reflux at 50 °C under $N_2$ for 7.2 h, then cooled to r.t. $H_2O$ (7 mL), and $CH_2Cl_2$ (2 mL) were added to the mixture. The aqueous layer was separated then extracted with $CH_2Cl_2$ (2 × 7 mL) and EtOAc (5 mL). The organic layers were combined and dried ($MgSO_4$). The solvents were removed at reduced pressure and the crude product purified by column chromatography (silica gel, hexane–EtOAc, 16:1); yield: 30 mg (56%); colorless solid; mp 229–230 °C.

IR (film): 3061, 2928, 1512, 1472, 1365, 1261, 1167, 1125 $cm^{-1}$.

$^1H$ NMR (300 MHz, $CDCl_3$): δ = 4.23 (d, *J* = 11.4 Hz, 2 H, 3-$H_A$ and 3′-$H_A$), 4.41 (d, *J* = 11.4 Hz, 2 H, 3-$H_B$ and 3′-$H_B$), 7.27–7.36 (m, 6 H, 7-H, 7′-H, 8-H, 8′-H, 10-H and 10′-H), 7.40 (s, 2 H, 5-H and 5′-H), 7.59–7.62 (m, 2 H, 9-H and 9′-H), 7.68–7.71 (m, 2 H, 6-H and 6′-H).

$^{13}C$ NMR (75 MHz, $CDCl_3$): δ = 66.0 ($CH_2$, C-3 and C-3′), 91.6 (C, C-2), 112.7 (CH, C-5 and C-5′), 113.6 (CH, C-10 and C-10′), 124.6 (CH, C-7 and C-7′ or C-8 and C-8′), 124.8 (CH, C-7 and C-7′ or C-8 and C-8′), 126.6 (CH, C-6 and C-6′ or C-9 and C-9′), 126.7 (CH, C-6 and C-6′ or C-9 and C-9′), 129.8 (C, C-5a and C-5′a or C-9a and C-9′a), 130.0 (C, C-5a and C-5′a or C-9a and C-9′a), 140.6 (C, C-10a and C-10′a), 142.4 (C, C-4a and C-4′a).

MS (EI, 70 eV): *m*/*z* (%) = 356 (6.5, $[M]^+$), 287 (1.5), 197 (100), 178 (13), 171 (8), 149 (9.5), 141 (27.5), 127 (5.5), 115 (4), 102 (15), 91 (4.5), 71 (11), 57 (8), 41 (12.5).

HRMS (EI): *m*/*z* $[M]^+$ calcd for $C_{23}H_{16}O_4$: 356.1049; found: 356.1045.

### 2-(Benzyloxy)phenol (21)[26]

NaOH (4.1 g, 102 mmol) was added to a solution of catechol **28** (10.2 g, 93 mmol) in MeOH (30 mL) at r.t. The mixture was heated with a heat gun until most of the phenoxide salt had formed (indicated by the formation of a solid precipitate on the bottom of the flask). BnBr (12.10 mL, 102 mmol) was then added dropwise and the mixture was refluxed at 100 °C under $N_2$ for 22 h and then cooled to r.t. The solvent was removed at reduced pressure and the resultant residue partitioned between $H_2O$ (50 mL) and $CH_2Cl_2$ (50 mL). The aqueous layer was separated then extracted with $CH_2Cl_2$ (2 × 50 mL). The organic layers were combined and dried ($MgSO_4$). The solvent was removed at reduced pressure and the crude product purified by column chromatography (silica gel, hexane–$Et_2O$, 6:1) to afford the pure phenol **21** (1.89 g) as a yellow oil and a mixture of the phenol **21** contaminated with a by-product. 6 M NaOH (15 mL) was slowly added to a solution of the impure material in $Et_2O$ (10 mL) at r.t. The resultant solid was collected, washed with EtOAc (3 × 30 mL), filtered again, then taken up in $H_2O$ (40 mL), acidified to pH 0 using concd $H_2SO_4$ (18 M) and extracted with $CH_2Cl_2$ (4 × 40 mL). The organic layers were combined, dried ($MgSO_4$) and the solvents removed at reduced pressure; yield: 5.3 g (28%); pale orange oil.

$^1H$ NMR (300 MHz, $CDCl_3$): δ = 4.93 (s, 2 H, OC$H_2$Ph), 5.76 (s, 1 H, OH), 6.71–6.84 (m, 3 H, 3-H, 4-H and 5-H), 6.90–6.94 (m, 1 H, 6-H), 7.24–7.31 (m, 5 H, $C_6H_5$).

The $^1H$ NMR data were similar to that reported in the literature.[26]

$^{13}C$ NMR (75 MHz, $CDCl_3$): δ = 70.8 ($CH_2$, O*C*$H_2$Ph), 112.2 (CH, C-3 or C-5), 114.7 (CH, C-6), 119.9 (CH, C-4), 121.7 (CH, C-3 or C-5), 127.6 (CH, C-2′ and C-6′), 128.1 (CH, C-4′), 128.5 (CH, C-3′ and C-5′), 136.3 (C, C-1′), 145.7 (C, C-1), 145.8 (C, C-2).

### 2-{[2-(Benzyloxy)phenoxy]methyl}oxirane (24)[27]

Epoxide **24** was prepared as described above for epoxide **23**, from reaction of NaOH (2.7 g, 68 mmol), $BnEt_3NCl$ (3.1 g, 14 mmol) and epichlorohydrin (**27**; 13.3 mL, 169 mmol) with phenol **21** (3.4 g, 17 mmol) in anhyd THF (7 mL) and $H_2O$ (5 mL) at r.t. for 20 h; yield: 4.1 g (95%); pale yellow oil.

$^1H$ NMR (300 MHz, $CDCl_3$): δ = 2.66 (dd, *J* = 5.0, 2.7 Hz, 1 H, OC$H_A$$H_B$ epoxide), 2.77 (dd, *J* = 4.9, 4.2 Hz, 1 H, OC$H_A$$H_B$ epoxide), 3.27–3.32 (m, 1 H, CHO epoxide), 3.96 (dd, *J* = 11.3, 5.5 Hz, 1 H, OC$H_A$$H_B$), 4.20 (dd, *J* = 11.3, 3.3 Hz, 1 H, OC$H_A$$H_B$), 5.07 (s, 2 H, OC$H_2$Ph), 6.85–6.93 (m, 4 H, 3′-H, 4′-H, 5′-H and 6′-H), 7.23–7.35 (m, 3 H, 3″-H, 4″-H and 5″-H), 7.40–7.43 (m, 2 H, 2″-H and 6″-H). The $^1H$ NMR data were in similar agreement with the literature.[27]

$^{13}C$ NMR (75 MHz, $CDCl_3$): δ = 44.4 ($CH_2$, $CH_2$ epoxide), 50.0 (CH, CHO epoxide), 70.1 ($CH_2$, $OCH_2$), 71.0 ($CH_2$, O*C*$H_2$Ph), 114.9, 115.1, 121.4, 121.9 (CH, C-3′, C-4′, C-5′ and C-6′), 127.1 (CH, C-2″ and C-6″), 127.6 (CH, C-4″), 128.2 (CH, C-3″ and C-5″), 137.1 (C, C-1″), 148.7 (C, C-1′), 148.8 (C, C-2′).

### 1-[3-(Benzyloxy)naphthalen-2-yloxy]-3-[2-(benzyloxy)phenoxy]propan-2-ol (32)

Alcohol **32** was prepared as described above for alcohol **31**, from reaction of $K_2CO_3$ (311 mg, 2.3 mmol) and epoxide **23** (459 mg, 1.5 mmol) in acetone (3 mL) with phenol **21** (300 mg, 1.5 mmol) in acetone (3 mL) at 85 °C for 7 h then at 120 °C for 60 h; yield: 757 mg (99%); colorless oil that solidified upon standing; mp 74.5–75.5 °C.

IR (film): 3485, 3064, 3033, 2928, 1505, 1485, 1454, 1406, 1379, 1256, 1171, 1116, 1021 $cm^{-1}$.

$^1H$ NMR (300 MHz, $CDCl_3$): δ = 3.18 (br s, 1 H, OH), 4.18–4.32 (m, 4 H, 2 × $OCH_2$), 4.38–4.45 (m, 1 H, C*H*OH), 5.06 (s, 2 H, C-2‴–OC$H_2$Ph), 5.17 (s, 2 H, C-3′–OC$H_2$Ph), 6.84–6.96 (m, 4 H, 3‴-H, 4‴-H, 5‴-H and 6‴-H), 7.16 (s, 1 H, 1′-H or 4′-H), 7.17 (s, 1 H, 1′-H or 4′-H), 7.21–7.37 (m, 8 H, 3″-H, 3⁗-H, 4″-H, 4⁗-H, 5″-H, 5⁗-H, 6′-H and 7′-H), 7.38–7.41 (m, 2 H, 2⁗-H and 6⁗-H), 7.44–7.47 (m, 2 H, 2″-H and 6″-H), 7.60–7.64 (m, 2 H, 5′-H and 8′-H).

$^{13}C$ NMR (75 MHz, $CDCl_3$): δ = 68.6 (CH, CHOH), 70.1 ($CH_2$, $OCH_2$), 70.6 ($CH_2$, C-3′–O*C*$H_2$Ph), 71.0 ($CH_2$, $OCH_2$), 71.2 ($CH_2$, C-2‴–O*C*$H_2$Ph), 108.9 (CH, C-1′ or C-4′), 109.3 (CH, C-1′ or C-4′), 114.8 (CH, C-3‴ or C-5‴), 115.7 (CH, C-3‴ or C-5‴), 121.7 (CH, C-4‴ or C-6‴), 122.1 (CH, C-4‴ or C-6‴), 124.3 (CH, C-6′ or C-7′), 124.4 (CH, C-6′ or C-7′), 126.3 (CH, C-5′ or C-8′), 126.4 (CH, C-5′ or C-8′), 127.2 (CH, C-2″ and C-6″), 127.3 (CH, C-2⁗ and C-6⁗), 127.9 (CH, C-4″ or C-4⁗), 127.9 (CH, C-4″ or C-4⁗), 128.5 (CH, C-3″ and C-5″ or C-3⁗ and C-5⁗), 128.5 (CH, C-3″ and C-5″ or C-3⁗ and C-5⁗), 129.3 (C, C-4′a or C-8′a), 129.5 (C, C-4′a or C-8′a), 136.8 (C, C-1″), 137.0 (C, C-1⁗), 148.8 (C, C-1‴ or C-2′), 148.9 (C, C-1‴ or C-2′), 148.9 (C, C-3′), 149.1 (C, C-2‴).

MS (EI, 70 eV): *m*/*z* (%) = 506 (17, $[M]^+$), 488 (0.5), 416 (1), 398 (1), 340 (2.5), 306 (2), 289 (1), 250 (7), 229 (1), 216 (1.5), 199 (3), 181 (2.5), 171 (2), 160 (2.5), 149 (2), 131 (2), 115 (2), 102 (1), 91 (100), 65 (5.5), 57 (2.5), 41 (3).

HRMS (EI): *m*/*z* $[M]^+$ calcd for $C_{33}H_{30}O_5$: 506.2093; found: 506.2097.

### 1-[3-(Benzyloxy)naphthalen-2-yloxy]-3-[2-(benzyloxy)phenoxy]propan-2-one (15)

Ketone **15** was prepared as described above for ketone **14**, from reaction of DMP (338 mg, 0.80 mmol) with alcohol **32** (269 mg, 0.53 mmol) in anhyd $CH_2Cl_2$ (2 mL) at r.t. for 3 h; yield: 161 mg (60%); yellow oil that solidified upon standing; mp 105–106 °C.

IR (film): 3065, 3034, 2925, 1745, 1503, 1483, 1258, 1117 $cm^{-1}$.

$^1$H NMR (300 MHz, $CDCl_3$): δ = 4.98 (s, 2 H, $OCH_2$), 4.98 (s, 2 H, $OCH_2$), 5.09 (s, 2 H, C-2‴–O*C*$H_2$Ph), 5.22 (s, 2 H, C-3′–O*C*$H_2$Ph), 6.83–6.90 (m, 2 H, 3‴-H and 5‴-H), 6.94–6.96 (m, 2 H, 4‴-H and 6‴-H), 7.02 (s, 1 H, 1′-H), 7.21 (s, 1 H, 4′-H), 7.22–7.35 (m, 8 H, 3″-H, 3⁗-H, 4″-H, 4⁗-H, 5″-H, 5⁗-H, 6′-H and 7′-H), 7.40–7.43 (m, 2 H, 2⁗-H and 6⁗-H), 7.47–7.50 (m, 2 H, 2″-H and 6″-H), 7.57–7.60 (m, 1 H, 8′-H), 7.64–7.67 (m, 1 H, 5′-H).

$^{13}$C NMR (75 MHz, $CDCl_3$): δ = 70.6 ($CH_2$, C-3′–O*C*$H_2$Ph), 71.0 ($CH_2$, C-2‴–O*C*$H_2$Ph), 72.6 ($CH_2$, $OCH_2$), 73.4 ($CH_2$, $OCH_2$), 109.4 (CH, C-4′), 109.3 (CH, C-1′), 114.7 (CH, C-4‴ or C-6‴), 115.6 (CH, C-3‴ or C-5‴), 121.5 (CH, C-3‴ or C-5‴), 122.8 (CH, C-4‴ or C-6‴), 124.4 (CH, C-6′ or C-7′), 124.7 (CH, C-6′ or C-7′), 126.3 (CH, C-5′), 126.5 (CH, C-8′), 127.2 (CH, C-2″ and C-6″), 127.3 (CH, C-2⁗ and C-6⁗), 127.9 (CH, C-4″ or C-4⁗), 127.9 (CH, C-4″ or Ph C-4⁗), 128.5 (CH, C-3″ and C-5″ or C-3⁗ and C-5⁗), 128.6 (CH, C-3″ and C-5″ or C-3⁗ and C-5⁗), 128.9 (C, C-8′a), 129.8 (C, C-4′a), 136.6 (C, C-1″), 136.8 (C, C-1⁗), 147.8 (C, C-1‴ or C-2′), 147.8 (C, C-1‴ or C-2′), 148.6 (C, C-3′), 148.9 (C, C-2‴), 202.6 (C, C=O).

MS (EI, 70 eV): *m*/*z* (%) = 504 (1, $[M]^+$), 396 (< 0.5), 368 (< 0.5), 304 (1), 288 (1), 250 (3), 200 (4), 171 (2.5), 121 (2.5), 91 (100), 65 (7.5), 39 (3.5).

HRMS (EI): *m*/*z* $[M]^+$ calcd for $C_{33}H_{28}O_5$: 504.1937; found: 504.1932.

### 3*H*,3′*H*-Spiro(benzo[*b*][1,4]dioxine-2,2′-naphtho[2,3-*b*][1,4]dioxine) (9)

Spiroketal **9** was prepared as described above for spiroketal **8**, from reaction of 10% Pd/C (130 mg, 1.22 mmol) with ketone **15** (113 mg, 0.22 mmol) in anhyd EtOAc (4 mL) at r.t. under $H_2$ for 23 h, followed by subsequent reaction of *p*-TsOH·$H_2O$ (260 mg, 1.37 mmol) with hemiketal intermediate in anhyd $CH_2Cl_2$ (2 mL) at 50 °C for 6 h; yield: 46 mg (63%); colorless solid; mp 155.5–156.5 °C.

IR (film): 2927, 2855, 1511, 1496, 1472, 1276, 1261, 1126 $cm^{-1}$.

$^1$H NMR (300 MHz, $CDCl_3$): δ = 4.12 (d, *J* = 11.3 Hz, 1 H, 3-$H_A$), 4.18 (d, *J* = 11.4 Hz, 1 H, 3′-$H_A$), 4.32 (d, *J* = 11.3 Hz, 1 H, 3-$H_B$), 4.34 (d, *J* = 11.4 Hz, 1 H, 3′-$H_B$), 6.88–6.96 (m, 3 H, 5-H, 7-H and 6-H or 8-H), 6.99–7.02 (m, 1 H, 6-H or 8-H), 7.28–7.36 (m, 3 H, 7′-H, 8′-H and 10′-H), 7.38 (s, 1 H, 5′-H), 7.61–7.64 (m, 1 H, 6′-H or 9′-H), 7.67–7.70 (m, 1 H, 6′-H or 9′-H).

$^{13}$C NMR (75 MHz, $CDCl_3$): δ = 65.8 ($CH_2$, C-3), 65.9 ($CH_2$, C-3′), 91.5 (C, C-2), 112.7 (CH, C-5′), 113.6 (CH, C-10′), 117.2, 117.7, 122.5, 122.6 (CH, C-5, C-6, C-7 and C-8), 124.6 (CH, C-7′ or C-8′), 124.8 (CH, C-7′ or C-8′), 126.6 (CH, C-6′ or C-9′), 126.7 (CH, C-6′ or C-9′), 129.8 (C, C-5′a or C-9′a), 129.9 (C, C-5′a or C-9′a), 140.5 (C, C-8a), 140.7 (C, C-10′a), 142.3 (C, C-4′a), 142.4 (C, C-4a).

MS (EI, 70 eV): *m*/*z* (%) = 306 (38, $[M]^+$), 197 (41), 171 (2), 153 (3), 147 (100), 141 (3.5), 127 (2.5), 121 (4.5), 102 (7.5), 91 (4), 57 (4), 52 (5), 39 (3).

HRMS (EI): *m*/*z* $[M]^+$ calcd for $C_{19}H_{14}O_4$: 306.0892; found: 306.0889.

### 1,3-Bis[2-(benzyloxy)phenoxy]propan-2-ol (33)[28]

Alcohol **33** was prepared as described above for alcohol **31**, from reaction of $K_2CO_3$ (414 mg, 3.0 mmol) and epoxide **24** (387 mg, 1.5 mmol) in acetone (3 mL) with phenol **21** (300 mg, 1.5 mmol) in acetone (3 mL) at 95 °C for 5 h then at 110 °C for 39 h; yield: 611 mg (89%); pale yellow oil that solidified upon standing; mp 54–55 °C.

IR (film): 3479, 3063, 3032, 2930, 2872, 1592, 1504, 1454, 1381, 1256, 1211, 1124, 1024 $cm^{-1}$.

$^1$H NMR (300 MHz, $CDCl_3$): δ = 3.17 (d, *J* = 4.9 Hz, 1 H, OH), 4.13–4.20 (m, 4 H, 2 × $OCH_2$), 4.28–4.35 (m, 1 H, C*H*OH), 5.06 (s, 4 H, O*C*$H_2$Ph), 6.87–6.95 (m, 8 H, 3′-H, 4′-H, 5′-H and 6′-H), 7.24–7.35 (m, 6 H, 3″-H, 4″-H and 5″-H), 7.38–7.42 (m, 4 H, 2″-H and 6″-H).

$^{13}$C NMR (75 MHz, $CDCl_3$): δ = 68.6 (CH, CHOH), 70.9 ($CH_2$, $OCH_2$), 71.2 ($CH_2$, O*C*$H_2$Ph), 114.8, 115.6, 121.7, 122.1 (CH, C-3′, C-4′, C-5′ and C-6′), 127.3 (CH, C-2″ and C-6″), 127.8 (CH, C-4″), 128.5 (CH, C-3″ and C-5″), 137.1 (C, C-1″), 148.8 (C, C-1′), 149.1 (C, C-2′).

No $^1$H NMR or $^{13}$C NMR data were reported in the literature.

MS (EI, 70 eV): *m*/*z* (%) = 456 (9, $[M]^+$), 366 (1.5), 348 (< 0.5), 304 (< 0.5), 290 (2), 256 (3), 212 (0.5), 199 (4), 181 (2.5), 166 (1), 149 (5), 121 (4), 110 (3.5), 91 (100), 77 (3), 65 (8), 55 (4.5), 41 (6).

HRMS (EI): *m*/*z* $[M]^+$ calcd for $C_{29}H_{28}O_5$: 456.1937; found: 456.1939.

### 1,3-Bis[2-(benzyloxy)phenoxy]propan-2-one (16)[29]

Activated 4Å MS (30 mg), NMO (114 mg, 0.97 mmol) and TPAP (36 mg, 0.10 mmol) were added to a solution of alcohol **33** (222 mg, 0.49 mmol) in anhyd $CH_2Cl_2$ (1 mL) at r.t. The mixture was stirred at r.t. for 1.5 h after which the catalyst was removed by filtration through silica gel and washed with EtOAc (5 × 1.5 mL). The solvent was removed at reduced pressure and the crude product purified by column chromatography (silica gel, hexane–$Et_2O$, 1.5:1); yield: 175 mg (79%); colorless solid; mp 94–96 °C.

IR (film): 3064, 3033, 2923, 1744, 1593, 1505, 1454, 1381, 1258, 1212, 1125, 1047, 1024 $cm^{-1}$.

$^1$H NMR (300 MHz, $CDCl_3$): δ = 4.90 (s, 4 H, $OCH_2$), 5.09 (s, 4 H, O*C*$H_2$Ph), 6.80–6.91 (m, 4 H, 3′-H, 4′-H, 5′-H or 6′-H), 6.93–6.95 (m, 4 H, 3′-H, 4′-H, 5′-H or 6′-H), 7.26–7.34 (m, 6 H, 3″-H, 4″-H and 5″-H), 7.39–7.43 (m, 4 H, 2″-H and 6″-H).

$^{13}$C NMR (75 MHz, $CDCl_3$): δ = 71.1 ($CH_2$, O*C*$H_2$Ph), 73.4 ($CH_2$, $OCH_2$), 114.8, 115.6, 121.5, 122.8 (CH, C-3′, C-4′, C-5′ and C-6′), 127.3 (CH, C-2″ and C-6″), 127.9 (CH, C-4″), 128.5 (CH, C-3″ and C-5″), 136.9 (C, C-1″), 147.9 (C, C-1′), 149.0 (C, C-2′), 203.0 (C, C=O).

No $^1$H NMR or $^{13}$C NMR data were reported in the literature.

MS (EI, 70 eV): *m*/*z* (%) = 454 (4, $[M]^+$), 411 (< 0.5), 364 (< 0.5), 346 (1), 327 (1), 254 (2), 237 (6), 200 (2), 181 (3), 177 (1.5), 165 (2), 147 (6), 135 (1), 121 (5), 91 (100), 77 (1.5), 65 (6), 57 (1.5), 52 (2), 39 (2.5).

HRMS (EI): *m*/*z* $[M]^+$ calcd for $C_{29}H_{26}O_5$: 454.1780; found: 454.1776.

### 3*H*,3′*H*-2,2′-Spirobi(benzo[*b*][1,4]dioxine) (10)

Spiroketal **10** was prepared as described above for spiroketal **8**, from reaction of 10% Pd/C (29 mg, 0.27 mmol) with ketone **16** (69 mg, 0.15 mmol) in anhyd EtOAc (1.5 mL) at r.t. under $H_2$ for 5.5 h, followed by subsequent reaction of *p*-TsOH·$H_2O$ (60 mg, 0.32 mmol) with hemiketal intermediate in anhyd $CH_2Cl_2$ (1 mL) at 50 °C for 4 h; yield: 33 mg (85%); colorless solid; mp 136–137.5 °C.

IR (film): 3046, 2922, 2871, 2852, 1598, 1494, 1463, 1262, 1222, 1126, 1098, 1063, 1035 $cm^{-1}$.

$^1$H NMR (300 MHz, $CDCl_3$): δ = 4.08 (d, *J* = 11.3 Hz, 2 H, 3-$H_A$ and 3′-$H_A$), 4.25 (d, *J* = 11.3 Hz, 2 H, 3-$H_B$ and 3′-$H_B$), 6.86–7.00 (m, 8 H, 5-H, 5′-H, 6-H, 6′-H, 7-H, 7′-H, 8-H and 8′-H).

$^{13}$C NMR (75 MHz, $CDCl_3$): δ = 65.7 ($CH_2$, C-3 and C-3′), 91.3 (C, C-2), 117.1, 117.7, 122.4, 122.5 (CH, C-5, C-5′, C-6, C-6′, C-7, C-7′, C-8 and C-8′), 140.6 (C, C-8a and C-8′a), 142.3 (C, C-4a and C-4′a).

MS (EI, 70 eV): *m*/*z* (%) = 256 (29, $[M]^+$), 147 (100), 128 (1), 121 (6), 109 (2), 91 (4), 79 (6), 57 (2), 38 (11), 36 (4).

HRMS (EI): *m/z* $[M]^+$ calcd for $C_{15}H_{12}O_4$: 256.0736; found: $M^+$, 256.0734.

**2-(Benzyloxy)-3-methoxybenzaldehyde (30)[21]**

$K_2CO_3$ (6.8 g, 49 mmol) and BnBr (5.45 mL, 46 mmol) were added to a solution of *o*-vanillin (**29**; 5.3 g, 35 mmol) in anhyd THF (12 mL) at r.t. The mixture was refluxed at 75 °C under $N_2$ for 15 h. The solvent was removed at reduced pressure and the resultant residue partitioned between $H_2O$ (60 mL) and $CH_2Cl_2$ (50 mL). The aqueous layer was separated then extracted with $CH_2Cl_2$ (4 × 30 mL). The organic layers were combined and dried ($MgSO_4$). The solvent was removed at reduced pressure and the crude product purified by column chromatography (silica gel, hexane–$Et_2O$, 4:1); yield: 7.6 g (89%); pale yellow oil.

IR (film): 3067, 3033, 2940, 2874, 2840, 1691, 1584, 1481, 1455, 1440, 1391, 1371, 1266, 1250, 1216, 1183, 1068 $cm^{-1}$.

$^1H$ NMR (400 MHz, $CDCl_3$): δ = 3.84 (s, 3 H, $OCH_3$), 5.13 (s, 2 H, $OCH_2Ph$), 7.03–7.11 (m, 2 H, 4-H and 5-H), 7.25–7.36 (m, 6 H, 6-H and $C_6H_5$), 10.23 (d, *J* = 0.8 Hz, 1 H, CHO).

$^{13}C$ NMR (100 MHz, $CDCl_3$): δ = 55.7 ($CH_3$, $OCH_3$), 75.9 ($CH_2$, $OCH_2Ph$), 117.7 (CH, C-4), 118.5 (CH, C-6), 123.9 (CH, C-5), 128.1 (CH, C-4′), 128.2 (CH, C-2′ and C-6′ or C-3′ and C-5′), 128.3 (CH, C-2′ and C-6′ or C-3′ and C-5′), 129.9 (C, C-1), 136.2 (C, C-1′), 150.7 (C, C-2), 152.7 (C, C-3), 189.7 (CH, CHO).

MS (EI, 70 eV): *m/z* (%) = 242 (5, $[M]^+$), 213 (5), 150 (7), 122 (2), 108 (2), 91 (100), 80 (1), 65 (9.5), 51 (3.5), 39 (4).

HRMS (EI): *m/z* $[M]^+$ calcd for $C_{15}H_{14}O_3$: 242.0943; found: 242.0942.

IR, $^1H$ and $^{13}C$ NMR and MS data were in agreement with that reported in the literature.[21]

**2-(Benzyloxy)-3-methoxyphenol (22)[23]**

*p*-TsOH·$H_2O$ (38 mg, 0.20 mmol) was added to a solution of aldehyde **30** (0.96 g, 3.96 mmol) in anhyd $CH_2Cl_2$ (5 mL) at r.t. and the reaction flask was cooled to 0 °C. MCPBA (1.368 g, 7.92 mmol) was added at 0 °C and the mixture stirred at r.t. for 3 h. The reaction was quenched with aq sat. $Na_2S_2O_3$ (15 mL) and $CH_2Cl_2$ (10 mL) was added. The aqueous layer was separated then extracted with $CH_2Cl_2$ (15 mL) and EtOAc (10 mL). The organic layers were combined and dried ($MgSO_4$). The solvents were removed at reduced pressure and the crude ester intermediate immediately dissolved in MeOH (15 mL). KOH (0.476 g, 8.48 mmol) was added to this solution and the mixture stirred at r.t. for 20 min then additional KOH (0.5 g, 8.91 mmol) was added. The mixture was stirred at r.t. for 1 h after which further KOH (0.6 g, 10.69 mmol) was added and the mixture stirred for 20 min. The solvent was removed at reduced pressure and the resultant residue was partitioned between $H_2O$ (50 mL) and $Et_2O$ (30 mL). The aqueous layer was separated then acidified to pH 0 with concd HCl (36%) and extracted with $CH_2Cl_2$ (1 × 50 mL, then 4 × 25 mL). The $CH_2Cl_2$ layers were combined and dried ($MgSO_4$). The solvent was removed at reduced pressure and the crude product purified by column chromatography (silica gel, hexane–$Et_2O$, 3:1) to afford the pure phenol **22** (417 mg) and a mixture of phenol **22** contaminated with a by-product. The impure material was partitioned between $Et_2O$ (15 mL) and aq sat. $NaHCO_3$ (25 mL). The organic layer was separated then washed with aq sat. $NaHCO_3$ (3 × 25 mL) and dried ($MgSO_4$). The solvent was removed at reduced pressure to give phenol **22**; yield: 486 mg (53%); tan oil.

IR (film): 3514, 3062, 3031, 2942, 2838, 1598, 1495, 1479, 1455, 1379, 1268, 1220, 1171, 1090 $cm^{-1}$.

$^1H$ NMR (400 MHz, $CDCl_3$): δ = 3.81 (s, 3 H, $OCH_3$), 5.03 (s, 2 H, $OCH_2Ph$), 5.70 (s, 1 H, OH), 6.44 (dd, *J* = 8.4, 1.3 Hz, 1 H, 4-H), 6.54 (dd, *J* = 8.2, 1.5 Hz, 1 H, 6-H), 6.88 (t, *J* = 8.3 Hz, 1 H, 5-H), 7.29–7.38 (m, 5 H, $C_6H_5$).

$^{13}C$ NMR (100 MHz, $CDCl_3$): δ = 55.7 ($CH_3$, $OCH_3$), 75.1 ($CH_2$, $OCH_2Ph$), 103.9 (CH, C-4), 108.0 (CH, C-6), 124.0 (CH, C-5), 128.3 (CH, C-4′), 128.3 (CH, C-2′ and C-6′), 128.5 (CH, C-3′ and C-5′), 134.3 (C, C-2), 137.1 (C, C-1′), 149.6 (C, C-1), 152.5 (C, C-3).

IR, $^1H$ and $^{13}C$ NMR data were in agreement with those reported in the literature.[23]

**2-{[2-(Benzyloxy)-3-methoxyphenoxy]methyl}oxirane (25)[30]**

Epoxide **25** was prepared as described above for epoxide **23**, from reaction of NaOH (79 mg, 1.97 mmol), $BnEt_3NCl$ (119 mg, 0.52 mmol) and epichlorohydrin (**27**; 0.51 mL, 6.56 mmol) with phenol **22** (151 mg, 0.66 mmol) in anhyd THF (3.5 mL) and $H_2O$ (3 mL) at r.t. for 23 h; yield: 163 mg (87%); pale yellow oil.

IR (film): 3065, 3033, 3005, 2938, 2839, 1476, 1110 $cm^{-1}$.

$^1H$ NMR (300 MHz, $CDCl_3$): δ = 2.65 (dd, *J* = 5.0, 2.6 Hz, 1 H, $OCH_AH_B$ epoxide), 2.78 (dd, *J* = 4.9, 4.2 Hz, 1 H, $OCH_AH_B$ epoxide), 3.23–3.29 (m, 1 H, CHO epoxide), 3.77 (s, 3 H, $OCH_3$), 3.90 (dd, *J* = 11.2, 5.6 Hz, 1 H, $OCH_AH_B$), 4.16 (dd, *J* = 11.2, 3.2 Hz, 1 H, $OCH_AH_B$), 5.01 (s, 2 H, $OCH_2Ph$), 6.54 (dd, *J* = 8.3, 1.3 Hz, 1 H, 4′-H or 6′-H), 6.56 (dd, *J* = 8.4, 1.2 Hz, 1 H, 4′-H or 6′-H), 6.92 (t, *J* = 8.4 Hz, 1 H, 5′-H), 7.23–7.35 (m, 3 H, 3″-H, 4″-H and 5″-H), 7.47–7.51 (m, 2 H, 2″-H and 6″-H).

$^{13}C$ NMR (75 MHz, $CDCl_3$): δ = 44.3 ($CH_2$, $CH_2$ epoxide), 49.9 (CH, CHO epoxide), 55.8 ($CH_3$, $OCH_3$), 69.9 ($CH_2$, $OCH_2$), 74.8 ($CH_2$, $OCH_2Ph$), 105.9 (CH, C-4′ or C-6′), 107.2 (CH, C-4′ or C-6′), 123.5 (CH, C-5′), 127.5 (CH, C-4″), 127.9 (CH, C-3″ and C-5″), 128.2 (CH, C-2″ and C-6″), 137.6 (C, C-2′), 137.7 (C, C-1″), 152.5 (C, C-1′), 153.7 (C, C-3′).

No $^1H$ NMR or $^{13}C$ NMR data were reported in the literature.

MS (EI, 70 eV): *m/z* (%) = 286 (25, $[M]^+$), 195 (4), 178 (2), 165 (6), 151 (4), 139 (12), 117 (2), 111 (4), 91 (100), 77 (2), 65 (10), 57 (18), 45 (3), 39 (7).

HRMS (EI): *m/z* $[M]^+$ calcd for $C_{17}H_{18}O_4$: 286.1205; found: 286.1204.

**1-[2-(Benzyloxy)-3-methoxyphenoxy]-3-[2-(benzyloxy)phenoxy]propan-2-ol (34)**

Alcohol **34** was prepared as described above for alcohol **31**, from reaction of $K_2CO_3$ (121 mg, 0.88 mmol) and epoxide **24** (116 mg, 0.45 mmol) in acetone (3.5 mL) with phenol **22** (101 mg, 0.44 mmol) in acetone (0.5 mL) at 105 °C for 22.5 h; yield: 206 mg (97%); pale yellow oil.

IR (film): 3466, 3064, 3032, 2935, 1595, 1500, 1477, 1453, 1376, 1298, 1255, 1214, 1111, 1022 $cm^{-1}$.

$^1H$ NMR (400 MHz, $CDCl_3$): δ = 3.11 (d, *J* = 4.8 Hz, 1 H, OH), 3.79 (s, 3 H, $OCH_3$), 4.06–4.13 (m, 4 H, 2 × $OCH_2$), 4.22–4.26 (m, 1 H, CHOH), 4.97 (s, 2 H, C-2′–$OCH_2Ph$), 5.04 (s, 2 H, C-2‴–$OCH_2Ph$), 6.53 (dd, *J* = 8.4, 1.2 Hz, 1 H, 4′-H or 6′-H), 6.57 (dd, *J* = 8.4, 1.2 Hz, 1 H, 4′-H or 6′-H), 6.86–6.95 (m, 5 H, 5′-H, 3‴-H, 4‴-H, 5‴-H and 6‴-H), 7.22–7.33 (m, 6 H, 3″-H, 3⁗-H, 4″-H, 4⁗-H, 5″-H, 5⁗-H), 7.38–7.40 (m, 2 H, 2⁗-H and 6⁗-H), 7.43–7.45 (m, 2 H, 2″-H and 6″-H).

$^{13}C$ NMR (100 MHz, $CDCl_3$): δ = 56.0 ($CH_3$, $OCH_3$), 68.5 (CH, CHOH), 70.3 ($CH_2$, $OCH_2$), 70.7 ($CH_2$, $OCH_2$), 71.1 ($CH_2$, C-2‴–$OCH_2Ph$), 75.0 ($CH_2$, C-2′–$OCH_2Ph$), 105.9 (CH, C-4′ or C-6′), 107.3 (CH, C-4′ or C-6′), 114.7, 115.5, 121.6, 122.0 (CH, C-3‴, C-4‴, C-5‴ and C-6‴), 123.8 (CH, C-5′), 127.2 (CH, C-2⁗ and C-6⁗), 127.7 (CH, C-4″ or Ph C-4⁗), 127.8 (CH, C-4″ or C-4⁗), 128.1 (CH, C-2″ and C-6″), 128.1 (CH, C-3″ and C-5″ or C-3⁗ and C-5⁗), 128.4 (CH, C-3″ and C-5″ or C-3⁗ and C-5⁗), 137.0 (C, C-1⁗), 137.7 (C, C-2′), 137.8 (C, C-1″), 148.7 (C, C-1‴), 149.0 (C, C-2‴), 152.6 (C, C-1′), 153.8 (C, C-3′).

MS (EI, 70 eV): *m/z* (%) = 486 (14, $[M]^+$), 395 (1), 378 (1), 320 (1), 290 (2.5), 256 (1.5), 230 (4), 199 (3.5), 179 (4.5), 165 (2), 149 (4), 139 (4.5), 121 (3), 91 (100), 65 (5.5), 57 (6), 55 (4), 43 (4.5).

HRMS (EI): *m/z* $[M]^+$ calcd for $C_{30}H_{30}O_6$: 486.2042; found: 486.2039.

**1-[2-(Benzyloxy)-3-methoxyphenoxy]-3-[2-(benzyloxy)phenoxy]propan-2-one (17)**

Ketone **17** was prepared as described above for ketone **16**, from reaction of TPAP (30 mg, 0.085 mmol) and NMO (102 mg, 0.867 mmol) with alcohol **34** (211 mg, 0.434 mmol) in anhyd $CH_2Cl_2$ (1 mL) containing activated 4 Å MS (100 mg) at r.t. for 2 h; yield: 180 mg (86%); colorless solid; mp 73–75 °C.

IR (film): 3066, 3033, 2937, 1744, 1595, 1499, 1476, 1454, 1377, 1257, 1117 $cm^{-1}$.

$^1H$ NMR (300 MHz, $CDCl_3$): δ = 3.81 (s, 3 H, $OCH_3$), 4.81 (s, 2 H, C-3‴–$OCH_2$), 4.84 (s, 2 H, C-1′–$OCH_2$), 5.03 (s, 2 H, C-2′–O*C*$H_2$Ph), 5.08 (s, 2 H, C-2‴–O*C*$H_2$Ph), 6.41 (dd, *J* = 8.4, 1.2 Hz, 1 H, 4′-H or 6′-H), 6.61 (dd, *J* = 8.4, 1.1 Hz, 1 H, 4′-H or 6′-H), 6.79–6.98 (m, 5 H, 5′-H, 3‴-H, 4‴-H, 5‴-H and 6‴-H), 7.21–7.34 (m, 6 H, 3″-H, 3⁗-H, 4″-H, 4⁗-H, 5″-H and 5⁗-H), 7.40–7.42 (m, 2 H, 2⁗-H and 6⁗-H), 7.46–7.48 (m, 2 H, 2″-H and 6″-H).

$^{13}C$ NMR (75 MHz, $CDCl_3$): δ = 56.1 ($CH_3$, $OCH_3$), 71.0 ($CH_2$, C-2‴–O*C*$H_2$Ph), 72.9 ($CH_2$, C-1), 73.4 ($CH_2$, C-3), 75.0 ($CH_2$, C-2′–O*C*$H_2$Ph), 106.6 (CH, C-4′ or C-6′), 107.3 (CH, C-4′ or C-6′), 114.7, 115.7, 121.5, 122.8 (CH, C-3‴, C-4‴, C-5‴ and C-6‴), 123.8 (CH, C-5′), 127.3 (CH, C-2⁗ and C-6⁗), 127.8 (CH, C-4″), 127.9 (CH, C-4⁗), 128.1 (CH, C-3″ and C-5″ or C-3⁗ and C-5⁗), 128.4 (CH, C-2″ and C-6″), 128.5 (CH, C-3″ and C-5″ or C-3⁗ and C-5⁗), 136.8 (C, C-1⁗), 137.7 (C, C-1″), 137.7 (C, C-2′), 147.8 (C, C-1‴), 149.0 (C, C-2‴), 151.9 (C, C-1′), 154.1 (C, C-3′), 202.6 (C, C=O).

MS (EI, 70 eV): *m/z* (%) = 484 (2.5, $[M]^+$), 376 (1), 345 (2), 327 (3), 285 (1.5), 267 (2), 255 (1), 237 (6.5), 213 (1.5), 195 (3), 181 (4), 177 (3.5), 151 (3), 147 (5), 135 (4.5), 121 (2.5), 91 (100), 60 (6.5), 44 (3).

HRMS (EI): *m/z* $[M]^+$ calcd for $C_{30}H_{28}O_6$: 484.1886; found: 484.1877.

**8-Methoxy-3*H*,3′*H*-2,2′-spirobi(benzo[*b*][1,4]dioxine) (11)**

Spiroketal **11** was prepared as described above for spiroketal **8**, from reaction of 10% Pd/C (25 mg, 0.23 mmol) with ketone **17** (54 mg, 0.11 mmol) in anhyd EtOAc (1 mL) at r.t. under $H_2$ for 7 h, followed by subsequent reaction of *p*-TsOH·$H_2O$ (27 mg, 0.14 mmol) with hemiketal intermediate in anhyd $CH_2Cl_2$ (1 mL) at 50 °C for 4 h; yield: 23 mg (72%); colorless solid; mp 134.5–135.5 °C.

IR (film): 3043, 2925, 2852, 1494, 1478, 1270, 1256, 1214, 1124, 1108, 1093 $cm^{-1}$.

$^1H$ NMR (400 MHz, $CDCl_3$): δ = 3.80 (s, 3 H, $OCH_3$), 4.09 (d, *J* = 11.3 Hz, 1 H, 3-$H_A$), 4.16 (d, *J* = 11.3 Hz, 1 H, 3′-$H_A$), 4.24 (d, *J* = 11.3 Hz, 1 H, 3-$H_B$), 4.26 (d, *J* = 11.3 Hz, 1 H, 3′-$H_B$), 6.55 (dd, *J* = 8.2, 1.2 Hz, 1 H, 5-H or 7-H), 6.63 (dd, *J* = 8.4, 1.4 Hz, 1 H, 5-H or 7-H), 6.86 (t, *J* = 8.3 Hz, 1 H, 6-H), 6.87–6.99 (m, 4 H, 5′-H, 6′-H, 7′-H and 8′-H).

$^{13}C$ NMR (100 MHz, $CDCl_3$): δ = 56.3 ($CH_3$, $OCH_3$), 65.4 ($CH_2$, C-3), 65.5 ($CH_2$, C-3′), 91.4 (C, C-2), 105.6 (CH, C-5 or C-7), 109.7 (CH, C-5 or C-7), 117.2 (CH, C-5′ or C-6′ or C-7′ or C-8′), 117.7 (CH, C-5′ or C-6′ or C-7′ or C-8′), 121.4 (CH, C-6), 122.3 (CH, C-5′ or C-6′ or C-7′ or C-8′), 122.4 (CH, C-5′ or C-6′ or C-7′ or C-8′), 130.7 (C, C-8a), 140.9 (C, C-8′a), 142.1 (C, C-4′a), 143.1 (C, C-4a), 149.2 (C, C-8).

MS (EI, 70 eV): *m/z* (%) = 286 (28.5, $[M]^+$), 177 (24), 147 (100), 121 (5), 107 (3), 95 (6.5), 91 (5), 80 (4.5), 77 (4.5), 65 (2), 57 (4), 52 (7), 39 (11).

HRMS (EI): *m/z* $[M]^+$ calcd for $C_{16}H_{14}O_5$: 286.0841; found: 286.0844.

**1-[2-(Benzyloxy)-3-methoxyphenoxy]-3-[3-(benzyloxy)naphthalen-2-yloxy]propan-2-ol (35)**

Alcohol **35** was prepared as described above for alcohol **31**, from reaction of $K_2CO_3$ (65 mg, 0.47 mmol) and epoxide **23** (72 mg, 0.24 mmol) in acetone (5 mL) with phenol **22** (54 mg, 0.24 mmol) in acetone (3 mL) at 110 °C for 38 h; yield: 108 mg (86%); viscous yellow oil.

IR (film): 3462, 3062, 3032, 2938, 1599, 1508, 1477, 1256, 1173, 1112 $cm^{-1}$.

$^1H$ NMR (300 MHz, $CDCl_3$): δ = 3.13 (d, *J* = 4.6 Hz, 1 H, OH), 3.79 (s, 3 H, $OCH_3$), 4.12–4.22 (m, 4 H, 2 × $OCH_2$), 4.29–4.33 (m, 1 H, C*H*OH), 4.98 (s, 2 H, C-2′–O*C*$H_2$Ph), 5.13 (s, 2 H, C-3‴–O*C*$H_2$Ph), 6.54 (dd, *J* = 8.3, 1.2 Hz, 1 H, 4′-H or 6′-H), 6.56 (dd, *J* = 8.4, 1.1 Hz, 1 H, 4′-H or 6′-H), 6.92 (t, *J* = 8.4 Hz, 1 H, 5′-H), 7.10 (s, 1 H, 1‴-H), 7.15 (s, 1 H, 4‴-H), 7.20–7.35 (m, 8 H, 3″-H, 3⁗-H, 4″-H, 4⁗-H, 5″-H, 5⁗-H, 6‴-H and 7‴-H), 7.41–7.45 (m, 4 H, 2″-H, 2⁗-H, 6″-H and 6⁗-H), 7.58–7.63 (m, 2 H, 5‴-H and 8‴-H).

$^{13}C$ NMR (75 MHz, $CDCl_3$): δ = 56.0 ($CH_3$, $OCH_3$), 68.5 (CH, CHOH), 69.8 ($CH_2$, C-3), 70.3 ($CH_2$, C-1), 70.5 ($CH_2$, C-3‴–O*C*$H_2$Ph), 75.1 ($CH_2$, C-2′–O*C*$H_2$Ph), 106.0 (CH, C-4′ or C-6′), 107.4 (CH, C-4′ or C-6′), 108.8 (CH, C-4‴), 109.2 (CH, C-1‴), 123.8 (CH, C-5′), 124.2 (CH, C-6‴ or C-7‴), 124.3 (CH, C-6‴ or C-7‴), 126.3 (CH, C-5‴ or C-8‴), 126.4 (CH, C-5‴ or C-8‴), 127.2 (CH, C-2⁗ and C-6⁗), 127.7 (CH, C-4″ or C-4⁗), 127.8 (CH, C-4″ or C-4⁗), 128.0 (CH, C-2″ and C-6″), 128.1 (CH, C-3″ and C-5″ or C-3⁗ and C-5⁗), 128.5 (CH, C-3″ and C-5″ or C-3⁗ and C-5⁗), 129.2 (C, C-8‴a), 129.4 (C, C-4‴a), 136.7 (C, C-1⁗), 137.7 (C, C-1″), 137.8 (C, C-2′), 148.7 (C, C-2‴), 148.8 (C, C-3‴), 152.6 (C, C-1′), 153.8 (C, C-3′).

MS (EI, 70 eV): *m/z* (%) = 536 (12, $[M]^+$), 518 (0.5), 446 (1), 428 (0.5), 396 (0.5), 340 (4) 306 (2), 286 (1), 250 (3.5), 229 (2.5), 199 (4), 171 (3), 160 (3.5), 139 (2.5), 131 (3), 115 (2.5), 91 (100), 65 (7), 39 (4).

HRMS (EI): *m/z* $[M]^+$ calcd for $C_{34}H_{32}O_6$: 536.2199; found: 536.2203.

**1-[2-(Benzyloxy)-3-methoxyphenoxy]-3-[3-(benzyloxy)naphthalen-2-yloxy]propan-2-one (18)**

Ketone **18** was prepared as described above for ketone **16**, from reaction of TPAP (20 mg, 0.057 mmol) and NMO (47 mg, 0.403 mmol) with alcohol **35** (108 mg, 0.201 mmol) in anhyd $CH_2Cl_2$ (1.5 mL) containing activated 4Å MS (20 mg) at r.t. for 1.5 h; yield: 70 mg (65%); pale yellow oil that solidified as a cream-colored solid upon standing; mp 101–102 °C.

IR (film): 3065, 3033, 2936, 1745, 1476, 1258, 1177, 1114 $cm^{-1}$.

$^1H$ NMR (300 MHz, $CDCl_3$): δ = 3.82 (s, 3 H, $OCH_3$), 4.89 (s, 2 H, C-2‴–$OCH_2$), 4.90 (s, 2 H, C-1′–$OCH_2$), 5.05 (s, 2 H, C-2′–O*C*$H_2$Ph), 5.20 (s, 2 H, C-3‴–O*C*$H_2$Ph), 6.43 (dd, *J* = 8.4, 1.1 Hz, 1 H, 4′-H or 6′-H), 6.62 (dd, *J* = 8.4, 1.0 Hz, 1 H, 4′-H or 6′-H), 6.91 (t, *J* = 8.4 Hz, 1 H, 5′-H), 7.02 (s, 1 H, 1‴-H), 7.20 (s, 1 H, 4‴-H), 7.22–7.37 (m, 8 H, 3″-H, 3⁗-H, 4″-H, 4⁗-H, 5″-H, 5⁗-H, 6‴-H and 7‴-H), 7.46–7.49 (m, 4 H, 2″-H, 2⁗-H, 6″-H and 6⁗-H), 7.58–7.66 (m, 2 H, 5‴-H and 8‴-H).

$^{13}C$ NMR (75 MHz, $CDCl_3$): δ = 56.1 ($CH_3$, $OCH_3$), 70.6 ($CH_2$, C-3‴–O*C*$H_2$Ph), 72.6 ($CH_2$, $OCH_2$), 72.9 ($CH_2$, $OCH_2$), 75.1 ($CH_2$, C-2′–O*C*$H_2$Ph), 106.7 (CH, C-4′ or C-6′), 107.3 (CH, C-4′ or C-6′), 109.1 (CH, C-4‴), 109.5 (CH, C-1‴), 123.8 (CH, C-5′), 124.4 (CH, C-6‴ or C-7‴), 124.7 (CH, C-6‴ or C-7‴), 126.3 (CH, C-5‴),

126.5 (CH, C-8‴), 127.3 (CH, C-2‴′ and C-6‴′), 127.8 (CH, C-4″ or C-4‴′), 127.9 (CH, C-4′ or C-4‴′), 128.2 (CH, C-3″ and C-5″ or C-3‴′ and C-5‴′), 128.4 (CH, C-2′ and C-6′), 128.6 (CH, C-3′ and C-5′ or C-3‴′ and C-5‴′), 128.9 (C, C-8‴a), 129.8 (C, C-4‴a), 136.6 (C, C-1‴′), 137.7 (C, C-1′), 137.8 (C, C-2′), 147.8 (C, C-2‴′), 148.7 (C, C-3‴′), 151.9 (C, C-1′), 154.1 (C, C-3′), 202.2 (C, C=O).

MS (EI, 70 eV): *m*/*z* (%) = 534 (2, $[M]^+$), 516 (0.5), 443 (0.5), 426 (1.5), 394 (0.5), 377 (1), 304 (2), 287 (4.5), 267 (1.5), 250 (3), 230 (3.5), 197 (3), 177 (2), 171 (2), 151 (2), 115 (2), 102 (1.5), 91 (100), 65 (6), 51 (2), 39 (4).

HRMS (EI): *m*/*z* $[M]^+$ calcd for $C_{34}H_{30}O_6$: 534.2042; found: 534.2045.

**8-Methoxy-3*H*,3′*H*-spiro[benzo[*b*][1,4]dioxine-2,2′-naphtho[2,3-*b*][1,4]dioxine] (12)**

Spiroketal **12** was prepared as described above for spiroketal **8**, from reaction of 10% Pd/C (30 mg, 0.28 mmol) with ketone **18** (70 mg, 0.13 mmol) in anhyd EtOAc (1.5 mL) at r.t. under $H_2$ for 28 h, followed by subsequent reaction of *p*-TsOH·$H_2O$ (60 mg, 0.32 mmol) with hemiketal intermediate in anhyd $CH_2Cl_2$ (1.5 mL) at 50 °C for 6 h; yield: 29 mg (66%); colorless solid; mp 195–196 °C.

IR (film): 3057, 2924, 2850, 1510, 1498, 1473, 1365, 1270, 1256, 1214, 1167, 1123, 1110, 1090 $cm^{-1}$.

$^1H$ NMR (300 MHz, $CDCl_3$): δ = 3.76 (s, 3 H, $OCH_3$), 4.13 (d, *J* = 11.3 Hz, 1 H, 3-$H_A$), 4.24 (d, *J* = 11.4 Hz, 1 H, 3′-$H_A$), 4.31 (d, *J* = 11.3 Hz, 1 H, 3-$H_B$), 4.37 (d, *J* = 11.4 Hz, 1 H, 3′-$H_B$), 6.54 (dd, *J* = 8.3, 1.4 Hz, 1 H, 5-H or 7-H), 6.65 (dd, *J* = 8.4, 1.4 Hz, 1 H, 5-H or 7-H), 6.87 (t, *J* = 8.3 Hz, 1 H, 6-H), 7.28–7.36 (m, 3 H, 7′-H, 8′-H and 10′-H), 7.38 (s, 1 H, 5′-H), 7.62–7.70 (m, 2 H, 6′-H and 9′-H).

$^{13}C$ NMR (75 MHz, $CDCl_3$): δ = 56.2 ($CH_3$, $OCH_3$), 65.6 ($CH_2$, C-3), 65.8 ($CH_2$, C-3′), 91.5 (C, C-2), 105.6 (CH, C-5 or C-7), 109.7 (CH, C-5 or C-7), 112.8 (CH, C-5′), 113.5 (CH, C-10′), 121.5 (CH, C-6), 124.6 (CH, C-7′ or C-8′), 124.7 (CH, C-7′ or C-8′), 126.6 (CH, C-6′ or C-9′), 126.7 (CH, C-6′ or C-9′), 129.8 (C, C-5′a and C-9′a), 130.6 (C, C-8a), 141.0 (C, C-10′a), 142.3 (C, C-4′a), 143.1 (C, C-4a), 149.3 (C, C-8).

MS (EI, 70 eV): *m*/*z* (%) = 336 (33, $[M]^+$), 197 (100), 177 (47.5), 168 (4), 151 (2), 141 (5), 127 (3), 114 (3.5), 102 (8.5), 95 (6), 75 (3), 65 (2), 48 (4), 36 (3).

HRMS (EI): *m*/*z* $[M]^+$ calcd for $C_{20}H_{16}O_5$: 336.0998; found: 336.0992.

**1,3-Bis[2-(benzyloxy)-3-methoxyphenoxy]propan-2-ol (36)**

Alcohol **36** was prepared as described above for alcohol **31**, from reaction of $K_2CO_3$ (54 mg, 0.39 mmol) and epoxide **25** (75 mg, 0.26 mmol) in acetone (3 mL) with phenol **22** (60 mg, 0.26 mmol) in acetone (1.5 mL) at 105 °C for 21 h; yield: 121 mg (90%); viscous yellow oil.

IR (film): 3456, 3032, 2939, 2839, 1598, 1477, 1374, 1298, 1255, 1110 $cm^{-1}$.

$^1H$ NMR (300 MHz, $CDCl_3$): δ = 3.01 (br s, 1 H, OH), 3.80 (s, 6 H, $OCH_3$), 4.03–4.06 (m, 4 H, 2 × $OCH_2$), 4.14–4.21 (m, 1 H, C*H*OH), 4.97 (s, 4 H, O*C*$H_2$Ph), 6.50 (dd, *J* = 8.4, 1.2 Hz, 2 H, 4′-H or 6′-H), 6.57 (dd, *J* = 8.4, 1.2 Hz, 2 H, 4′-H or 6′-H), 6.92 (t, *J* = 8.3 Hz, 2 H, 5′-H), 7.21–7.32 (m, 6 H, 3″-H, 4″-H and 5″-H), 7.42–7.45 (m, 4 H, 2″-H and 6″-H).

$^{13}C$ NMR (75 MHz, $CDCl_3$): δ = 56.0 ($CH_3$, $OCH_3$), 68.5 (CH, CHOH), 70.2 ($CH_2$, $OCH_2$), 75.0 ($CH_2$, O*C*$H_2$Ph), 105.9 (CH, C-4′ or C-6′), 107.3 (CH, C-4′ or C-6′), 123.8 (CH, C-5′), 127.7 (CH, C-4″), 128.1 (CH, C-3″ and C-5″), 128.1 (CH, C-2″ and C-6″), 137.6 (C, C-2′), 137.8 (C, C-1″), 152.6 (C, C-1′), 153.7 (C, C-3′).

MS (EI, 70 eV): *m*/*z* (%) = 516 (14.5, $[M]^+$), 498 (1), 426 (3), 408 (1.5), 376 (0.5), 320 (4), 286 (4), 269 (1.5), 241 (1), 229 (7.5), 213 (1), 197 (3), 179 (8), 165 (3), 151 (5), 139 (7), 125 (3), 107 (3), 91 (100), 65 (8.5), 51 (3), 39 (6).

HRMS (EI): *m*/*z* $[M]^+$ calcd for $C_{31}H_{32}O_7$: 516.2148; found: 516.2150.

**1,3-Bis[2-(benzyloxy)-3-methoxyphenoxy]propan-2-one (19)**

Ketone **19** was prepared as described above for ketone **14**, from reaction of DMP (149 mg, 0.35 mmol) with alcohol **36** (121 mg, 0.23 mmol) in anhyd $CH_2Cl_2$ (2 mL) at r.t. for 2 h; yield: 111 mg (92%); colorless oil that solidified upon standing; mp 97.5–99.0 °C.

IR (film): 2939, 2839, 1744, 1597, 1492, 1475, 1375, 1300, 1257, 1115 $cm^{-1}$.

$^1H$ NMR (300 MHz, $CDCl_3$): δ = 3.81 (s, 6 H, $OCH_3$), 4.75 (s, 4 H, $OCH_2$), 5.03 (s, 4 H, O*C*$H_2$Ph), 6.36 (dd, *J* = 8.4, 1.2 Hz, 2 H, 4′-H or 6′-H), 6.61 (dd, *J* = 8.4, 1.2 Hz, 2 H, 4′-H or 6′-H), 6.91 (t, *J* = 8.3 Hz, 2 H, 5′-H), 7.22–7.32 (m, 6 H, 3″-H, 4″-H and 5″-H), 7.46–7.49 (m, 4 H, 2″-H and 6″-H).

$^{13}C$ NMR (75 MHz, $CDCl_3$): δ = 56.0 ($CH_3$, $OCH_3$), 72.9 ($CH_2$, $OCH_2$), 75.0 ($CH_2$, O*C*$H_2$Ph), 106.6 (CH, C-4′ or C-6′), 107.4 (CH, C-4′ or C-6′), 123.7 (CH, C-5′), 127.8 (CH, C-4″), 128.1 (CH, C-3″ and C-5″), 128.3 (CH, C-2″ and C-6″), 137.6 (C, C-2′), 137.7 (C, C-1″), 151.8 (C, C-1′), 154.0 (C, C-3′), 202.2 (C, C=O).

MS (EI, 70 eV): *m*/*z* (%) = 514 (1, $[M]^+$), 496 (0.5), 423 (1), 406 (3), 375 (2), 357 (1), 316 (1.5), 285 (2.5), 267 (8), 241 (1), 230 (2.5), 213 (2), 195 (4.5), 181 (5), 177 (12), 165 (3), 151 (8.5), 139 (2.5), 107 (2.5), 95 (6), 91 (100), 65 (7), 39 (5).

HRMS (EI): *m*/*z* $[M]^+$ calcd for $C_{31}H_{30}O_7$: 514.1992; found: 514.1991.

**8,8′-Dimethoxy-3*H*,3′*H*-2,2′-spirobi(benzo[*b*][1,4]dioxine) (13)**

Spiroketal **13** was prepared as described above for spiroketal **8**, from reaction of 10% Pd/C (30 mg, 0.28 mmol) with ketone **19** (61 mg, 0.12 mmol) in anhyd EtOAc (2 mL) at r.t. under $H_2$ for 24 h, followed by subsequent reaction of *p*-TsOH·$H_2O$ (60 mg, 0.32 mmol) with hemiketal intermediate in anhyd EtOAc (2 mL) at 100 °C for 6.2 h; yield: 16 mg (43%); colorless solid; mp 215.5–217.0 °C.

IR (film): 2956, 2922, 2850, 1495, 1479, 1285, 1252, 1215, 1111, 1073 $cm^{-1}$.

$^1H$ NMR (400 MHz, $CDCl_3$): δ = 3.79 (s, 6 H, $OCH_3$), 4.13 (d, *J* = 11.3 Hz, 2 H, 3-$H_A$ and 3′-$H_A$), 4.26 (d, *J* = 11.3 Hz, 2 H, 3-$H_B$ and 3′-$H_B$), 6.54 (dd, *J* = 8.2, 1.3 Hz, 2 H, 5-H and 5′-H or 7-H and 7′-H), 6.63 (dd, *J* = 8.3, 1.3 Hz, 2 H, 5-H and 5′-H or 7-H and 7′-H), 6.85 (t, *J* = 8.3 Hz, 2 H, 6-H and 6′-H).

$^{13}C$ NMR (100 MHz, $CDCl_3$): δ = 56.3 ($CH_3$, $OCH_3$), 65.3 ($CH_2$, C-3 and C-3′), 91.6 (C, C-2), 105.6 (CH, C-5 and C-5′ or C-7 and C-7′), 109.8 (CH, C-5 and C-5′ or C-7 and C-7′), 121.2 (CH, C-6 and C-6′), 131.0 (C, C-8a and C-8′a), 143.0 (C, C-4a and C-4′a), 149.2 (C, C-8 and C-8′).

MS (FAB, 70 eV): *m*/*z* (%) = 317 (3, $[M + H]^+$), 316 (3.5, $[M]^+$), 273 (7.5), 258 (4), 242 (4.5), 177 (8.5), 165 (6.5), 152 (10.5), 124 (12), 120 (14), 115 (6.5), 89 (24.5).

HRMS-FAB: *m*/*z* $[M]^+$ calcd for $C_{17}H_{16}O_6$: 316.0947; found: 316.0949.

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