Synthesis of *trans*- and *cis*-14-Phenylsulfonyl-1,7,9-trioxadispiro[5.1.5.3]hexadecane[1]

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The synthesis of the *trans*- and *cis*-isomers **1a** and **1b** of 14-phenylsulfonyl-1,7,9-trioxadispiro-[5.1.5.3]hexadecane *via* the addition of an α-sulfonyl carbanion to δ-valerolactone followed by acid-catalysed cyclization is described. Reductive removal of the sulfone group using Raney nickel afforded the parent bis-spiroacetals **9a** and **9b** together with the spiroacetal alcohol **10** which underwent oxidative cyclization to the parent bis-spiroacetals **9a** and **9b** upon treatment with iodobenzene diacetate and iodine.

Considerable interest has been aroused in the synthesis of spiroacetals[2] as these ring systems frequently appear as subunits in many naturally occurring biologically active compounds such as the polyether antibiotics, marine and plant toxins, insect pheromones, and the antiparasitic agents—the avermectins and milbemycins. In contrast to their bicyclic analogues the tricyclic bis-spiroacetals have generated comparatively little interest to date.

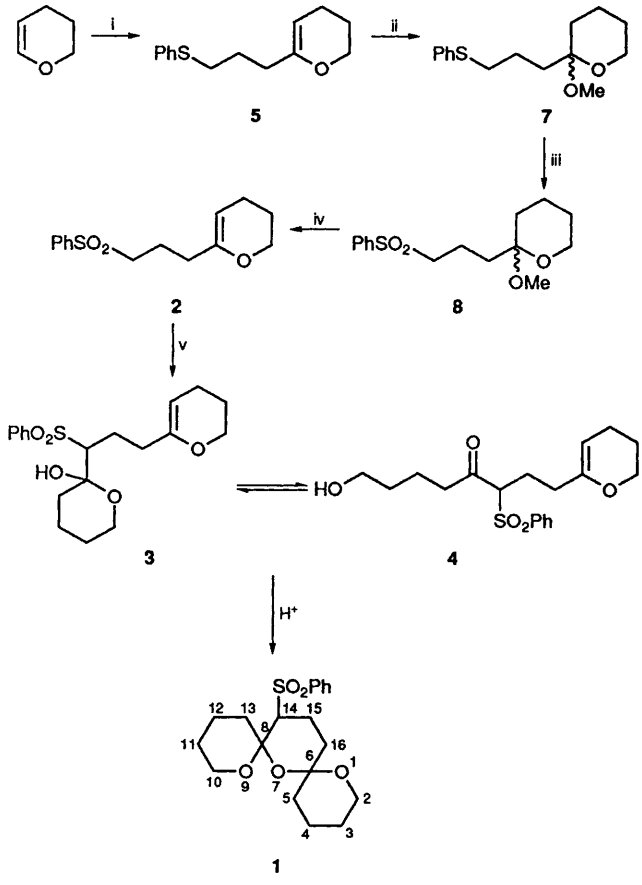
Examples of the preparation of bis-spiroacetals include the construction of the 1,6,8-trioxadispiro[4.1.4.2]tridec-13-ene[3] and 1,6,8-trioxadispiro[4.1.4.3]tetradecane[4] ring systems *via* an electrolytic alkoxylation and a Norrish type II reaction, respectively. In addition, synthetic studies directed towards the synthesis of the polyether antibiotics salinomycin and narasin provide examples of the preparation of the 1,6,8-trioxadispiro-[4.1.5.3]pentadec-13-ene ring system.[5] Our work in this area led to the synthesis of the bis-spiroacetal moiety of *epi*-17-deoxy-(O-8)-salinomycin *via* a Barton type reaction of a hydroxyspiroacetal.[6] We now wish to report[1] the full details of the synthesis of the *trans*- and *cis*-isomers, **1a** and **1b**, of 14-phenylsulfonyl-1,7,9-trioxadispiro[5.1.5.3]hexadecane which is homologous to the bis-spiroacetal ring system present in salinomycin. The incorporation of a phenylsulfonyl group at C-14 conferred crystallinity on the bis-spiroacetal ring system allowing determination of the stereochemistry using X-ray crystallography.

The synthesis of the bis-spiroacetal **1** followed from earlier work[7] on the synthesis of simpler bicyclic spiroacetals *via* the addition of α-sulfonyl carbanions to lactones. In the present work, addition of the α-sulfonyl carbanion generated from the sulfone **2**, to δ-valerolactone (Scheme 1) afforded a mixture of the keto alcohol **4** and the lactol **3** which then underwent smooth acid-catalysed cyclization to the desired molecule.

The key sulfonyl dihydropyran **2** was prepared by oxidation of the corresponding sulfide **5** obtained in 65% yield upon lithiation of 3,4-dihydropyran using butyllithium (1.0 equiv.) in tetrahydrofuran at 55 °C for 2.5 h followed by the addition of the bromide **6**. Oxidation of the sulfide **5** to the sulfone **2** could only be effected in 17% yield using sodium perborate in 50% methanolic potassium hydroxide at 60 °C. Other reagents, *e.g.* tetrabutylammonium oxone and oxone gave similarly disappointing yields.

The low yield in the oxidation of the sulfide **5** to the sulfone **2** was attributed to the high reactivity of the double bond. It was therefore decided to mask the double bond as a methoxy acetal. Thus, the sulfide **5** was converted into the methoxy acetal **7** upon treatment with Amberlite IR 120 resin in methanol at room temperature overnight. Formation of the methoxy acetal **7** also facilitated removal of the unchanged bromide **6** by flash chromatography due to the greater polarity difference between the bromide **6** and the methoxy acetal **7** compared to the dihydropyran **5**. Oxidation of the sulfide **7** to the sulfone **8** was then achieved using sodium perborate in methanolic potassium hydroxide in 72% yield.

With the synthesis of the methoxy sulfonyl acetal **8** completed, attention focused on the synthesis of the



Scheme 1 *Reagents and conditions:* i, BuLi (1.0 equiv.), 55 °C, 2.5 h, $Br(CH_2)_3SPh$ **6** 65%; ii, Amberlite IR 120 resin, MeOH, room temp., 16 h, 50%; iii, $NaBO_3{\cdot}4H_2O$, KOH, MeOH, 5 h, 60 °C, 72%; iv, then Amberlite IR 120 resin, toluene, reflux, 3 h, 55%; v, BuLi (2.0 equiv.), −78 °C, 0.25 h, δ-valerolactone, THF, then camphorsulfonic acid (cat.), CH_2Cl_2, 57%

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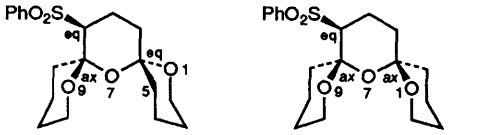


trans-**1a** — 3 anomeric effects

cis-**1b** — 4 anomeric effects; dipole–dipole interactions unfavourable

Fig. 1

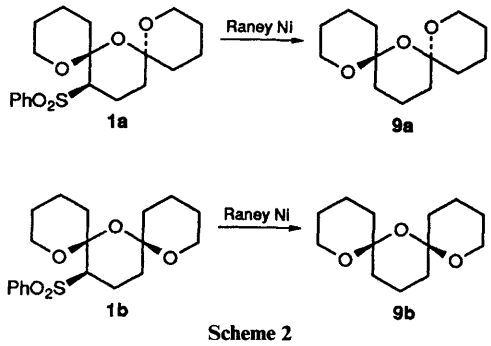
bis-spiroacetal **1** *via* reaction of the α-sulfonyl carbanion derived from **8** with δ-valerolactone followed by acid-catalysed cyclization. Despite many attempts to effect this reaction by varying the temperature, adding co-solvents and changing the dilution, the anion of methoxy sulfonyl acetal **8** failed to condense with δ-valerolactone. This was thought to be attributed to the formation of a stable chelate with the methoxy group.

Disappointed with the use of the methoxy sulfonyl acetal **8** in the condensation reaction, it was therefore decided to eliminate the methoxy acetal group to a double bond. In this way the methoxy acetal functionality served as a latent double bond and provided an indirect way of producing the sulfonyl dihydropyran **2** which could not be prepared in good yield *via* oxidation of the phenylthio dihydropyran **5**. Hence treatment of the methoxy sulfonyl acetal **8** with Amberlite IR 120 resin in toluene under reflux using a Dean and Stark apparatus for 3–4 h afforded the required dihydropyran **2** in 55% yield.

Finally condensation of the α-sulfonyl carbanion generated from the sulfone **2** using butyllithium (2 equiv.) at −78 °C for 0.25 h followed by the addition of δ-valerolactone at the same temperature afforded an equilibrium mixture of the open-chain keto alcohol **4** and the cyclic hemiacetal **3**. This mixture was then treated directly with camphorsulfonic acid (catalytic quantity) in dichloromethane at room temperature overnight to afford two stereoisomers of the bis-spiroacetal **1**.

The stereochemistry of the less polar isomer isolated in 28% yield after purification by flash chromatography, was determined by X-ray crystallography[1] as the *trans*-isomer **1a**. The conformation adopted (Fig. 1) was found to be that in which the oxygen of one of the terminal rings occupied an axial position whilst the oxygen atom of the other terminal ring occupied a pseudoequatorial position relative to the oxygen atom of the central ring. The central ring adopted a skew boat conformation thereby relieving the steric interactions between the oxygen atom (O-9) and the methylene group at C-5. In this conformation the carbon–oxygen bonds of the terminal rings are *anti* to one another thereby avoiding any unfavourable dipole–dipole interactions; the molecule exhibits three anomeric effects. This conformation is consistent with that observed for the analogous 1,6,8-trioxadispiro[4.1.4.3]tetradecane ring system.[4]

The stereochemistry of the more polar isomer isolated in 29% yield after purification by flash chromatography was also determined by X-ray crystallography[8] as the *cis*-isomer **1b** (Fig. 1) where the oxygen atoms of the two terminal rings occupy axial positions on the central ring allowing maximum stabilization by the anomeric effect. The two terminal rings have chair conformations, but the central ring is flexible showing two-fold disorder between a boat conformation (the major conformer, with an occupancy of 0.65) and a chair conformation (the minor conformer, with an occupancy of 0.35). The cavity created by this particular array of C–O bonds makes this compound an interesting model for examining the ionophoric capability of bis-spiroacetals.

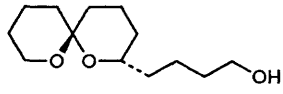


Scheme 2

Synthesis of the parent bis-spiroacetal required removal of the phenylsulfonyl group. Thus, reduction of the less polar sulfone **1a** using W-2 Raney nickel in ethanol afforded the less polar parent spiroacetal **9a** albeit in 10% yield whilst the more polar sulfone **1b** gave the more polar spiroacetal **9b** also in 10% yield. In both cases, however, the major product formed in this reduction step was the spiroacetal alcohol **10** in which hydrogenolysis of the C–O bond of one of the terminal rings had occurred in addition to reduction of the phenylsulfonyl group.

Attempts to minimize the formation of the fragmentation product **10** using other reducing agents such as Mg/MeOH, Bu_3SnH/AIBN, Al/Hg or Na/Hg were also unsuccessful. In these cases only a very low yield of the desired spiroacetals **9** were obtained and in several instances the spiroacetal alcohol **10** was formed but in much lower yield than when using Raney nickel.

Whilst it was disappointing that removal of the phenylsulfonyl group afforded mainly the spiroacetal alcohol **10**, nevertheless, subsequent oxidative cyclization afforded bis-spiroacetal **9**. Irradiation of a mixture of the alcohol **10**, iodobenzene diacetate (1 equiv.) and iodine (0.5 equiv.) in cyclohexane for 1 h gave a 1:1 mixture of the parent bis-spiroacetals **9a**, **9b** in 76% yield that were separated by flash chromatography.



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The synthetic sequence described herein provides an efficient entry to the bis-spiroacetal ring system **9** *via* the condensation of an α-sulfonyl carbanion with δ-valerolactone[7] followed by an oxidative cyclization using iodobenzene diacetate and iodine.[6] Moreover, the stereochemistry of the *cis*-bis-spiroacetals **1a** and **9a** is similar to that present in the polyether antibiotics salinomycin and narasin.

Experimental

M.p.s were determined on a Kofler hot-stage apparatus and are uncorrected. IR spectra were recorded on a Bio-Rad FTS 40V spectrophotometer as Nujol mulls or thin films between sodium chloride discs. ^{1}H NMR spectra were recorded at 270 MHz in $CDCl_3$ using tetramethylsilane as internal standard on a JEOL GX270 spectrometer. ^{13}C NMR spectra were recorded at 67.8 MHz on a JEOL GX270 spectrometer. All *J* values are given in Hz. Mass spectra and accurate mass measurements were recorded on a VG70-250S double focussing magnetic sector mass spectrometer with an ionization potential of 70 eV. Microanalyses were performed by the microanalytical laboratory, University of Otago.

3-*Bromopropyl Phenyl Sulfide* **6**.—3-Bromopropyl phenyl sulfide **6** was prepared from 1,3-dibromopropane and thiophenol following the procedure of Bakuzis *et al.*[9] as a colourless liquid, b.p. 85–88 °C/0.2 mmHg (lit.,[9] b.p. 117–120 °C/1.5 mmHg).

6-(3-*Phenylthiopropyl*)-3,4-*dihydro*-2H-*pyran* **5**.—To a stirred solution of 3,4-dihydro-2*H*-pyran (4.2 g, 50 mmol) in dry tetrahydrofuran (THF) (20 cm^3) cooled to 0 °C in an ice bath under nitrogen was added butyllithium (31 cm^3 of a 1.5 mol dm^{-3} solution in hexane, 50 mmol). The reaction mixture was heated at 55 °C for 2.5 h and a solution of 3-bromopropyl phenyl sulfide **6** (5.5 g, 24 mmol) in dry THF (20 cm^3) was added. The resulting mixture was heated at 55 °C for 2 h then quenched with water (15 cm^3). After extraction with diethyl ether (3 × 50 cm^3) the ethereal layer was washed with water (20 cm^3) and dried over sodium sulfate. The solvent was removed under reduced pressure and the residue purified by flash chromatography using hexane–diethyl ether (95:5) as eluent to afford the *title compound* **5** (5.34 g, 65%) as an unstable colourless oil (Found: M^+, 234.1070. $C_{14}H_{18}OS$ requires *M*, 234.1072); δ_H(270 MHz; $CDCl_3$) 1.44–2.15 (8 H, m, 4 × CH_2), 2.92 (2 H, t, *J* 8.5, CH_2S), 3.95 (2 H, t, *J* 6, CH_2O), 4.49 (1 H, t, *J* 4, HC=C) and 7.10–7.37 (5 H, m, Ar-H); δ_C(67.8 MHz; $CDCl_3$) 20.2, 22.4, 26.4, 32.7, 33.3 (t, C-3, C-4, C-1′, C-2′, C-3′), 66.1 (t, C-2), 96.1 (d, C-5), 125.8 (d, C-4″), 128.8, 128.9 (d, C-2″ and C-3″) 136.0 (s, C-1″) and 151.0 (s, C-6); *m*/*z* 234 (M^+, 31), 137 (C_8H_9S, 12), 136 (C_8H_8S, 100), 135 (C_8H_7S, 20) and 98 ($C_6H_{10}O$, 30).

2-*Methoxy*-2-(3-*phenylthiopropyl*)*tetrahydropyran* **7**.—The crude product **5**, prepared using the procedure described above, was dissolved in methanol (30 cm^3) and treated with Amberlite IR-120 resin at room temperature overnight. After removal of the resin by filtration, the solvent was removed at reduced pressure to give an oil that was purified by flash chromatography using hexane–diethyl ether (95:5) as eluent to give the *title methoxyacetal* **7** (3.20 g, 50%) as a colourless oil (Found: M − CH_3OH, 234.1078. $C_{14}H_{18}OS$ requires *M* − CH_3OH, 234.1074); ν_{max}(thin film)/cm^{-1} 2950s (CH) and 1580m (C=C); δ_H(270 MHz; $CDCl_3$) 1.33–1.89 (10 H, m, 5 × CH_2), 2.84–3.09 (2 H, m, CH_2S), 3.15 (3 H, s, OCH_3), 3.58–3.65 (2 H, m, CH_2O) and 7.13–7.35 (5 H, m, Ar-H); δ_C(67.8 MHz; $CDCl_3$) 18.6, 23.0, 25.1 (t, C-4, C-5, C-2′), 32.7, 33.9 (t, C-3, C-1′), 35.4 (t, C-3′), 47.4 (q, OCH_3), 61.3 (t, C-6), 98.7 (s, C-2), 125.8 (d, C-4″), 128.8, 129.1 (d, C-2″, C-3″) and 136.6 (s, C-1″); *m*/*z* 234 (M − CH_3OH, 21%) and 109 (C_7H_9O, 5). In subsequent experiments methoxyacetal **7** was used directly in the perborate oxidation reaction without purification.

2-*Methoxy*-2-(3-*phenylsulfonylpropyl*)*tetrahydropyran* **8**.—To a suspension of sodium perborate tetrahydrate (2.90 g, 19 mmol) in 1:1 methanol–aqueous potassium hydroxide solution with pH 11–12 (100 cm^3) was added 2-methoxy-2-(3-phenylthiopropyl)tetrahydropyran **7** (1.0 g, 3.8 mmol) in methanol (20 cm^3). The reaction mixture was then stirred at 60 °C for 5 h. After cooling, the methanol was removed under reduced pressure and the mixture extracted with ethyl acetate (3 × 50 cm^3). The ethyl acetate layer was washed with water (40 cm^3) and dried over anhydrous sodium sulfate. Removal of the solvent on a rotary evaporator afforded a colourless oil which upon purification by flash chromatography using hexane–ethyl acetate (1:1) as eluent yielded the *title compound* **8** (802 mg, 72%) as a colourless oil (Found: M − OCH_3, 267.1055. $C_{14}H_{19}O_3S$ requires *M* − OCH_3, 267.1047); ν_{max}(thin film)/cm^{-1} 2950s (CH), 1315s and 1150s (SO_2); δ_H(60 MHz; $CDCl_3$) 1.20–2.00 (10 H, m, 5 × CH_2), 2.90–3.30 (2 H, m, CH_2SO_2), 3.10 (3 H, s, OCH_3) 3.38–3.68 (2 H, m, CH_2O) and 7.43–8.05 (5 H, m, Ar-H); *m*/*z* 267 (M − OCH_3, 9%), 266 (M − CH_3OH, 6), 211 (M − CH_3OH − C_4H_7, 18), 125 (M − CH_3OH − $C_6H_5O_2S$, 16), 124 ($C_8H_{12}O$, 100), 109 (C_7H_9O, 13) and 96 (C_6H_8O, 23).

6-(3-*Phenylsulfonylpropyl*)-3,4-*dihydro*-2H-*pyran* **2**.—A solution of methoxyacetal **8** (802 mg, 2.7 mmol) dissolved in toluene (60 cm^3) was treated with Amberlite IR-120 resin and heated under reflux (Dean and Stark) for 3 h. The solution was quickly filtered and triethylamine (1 cm^3) added. After washing with potassium hydroxide solution (2 × 40 cm^3, pH 11–12) the organic layer was dried over anhydrous sodium sulfate. After removal of the solvent at reduced pressure the resultant yellow oil was purified by flash chromatography using hexane–ethyl acetate (1:1) as eluent affording the *title compound* **2** (440 mg, 55%) as colourless prisms, m.p. 93–95 °C (Found: C, 63.1; H, 6.8; S, 11.9. $C_{14}H_{18}O_3S$ requires C, 63.1; H, 6.8; S, 12.0%); ν_{max}(Nujol)/cm^{-1} 1310s, 1150s (SO_2), 1240m and 1080m (C=C); δ_H(270 MHz; $CDCl_3$) 1.63–2.04 (8 H, m, 4 × CH_2), 3.11 (2 H, t, *J* 7.0, CH_2SO_2), 3.89 (2 H, t, *J* 5.1, CH_2O), 4.44 (1 H, t, *J* 3.7, HC=C), 7.54–7.67 (3 H, m, 3″-H and 4″-H) and 7.89–7.93 (2 H, d, 2″-H); δ_C(67.8 MHz; $CDCl_3$) 20.1, 20.2, 22.3 (t, C-3, C-4, C-2′), 32.6 (t, C-1′), 55.4 (t, C-3′), 66.1 (t, C-2), 97.0 (d, C-5), 128.1 (d, C-3″), 129.3 (d, C-2″), 133.6 (d, C-4″), 139.1 (s, C-1″) and 152.0 (s, C-6); *m*/*z* 266 (M^+, 32%), 211 (M − C_4H_7, 6), 125 (M − $C_6H_5O_2S$, 27), 124 ($C_8H_{12}O$, 100), 109 (C_7H_9O, 18) and 96 (C_6H_8O, 40).

14-*Phenylsulfonyl*-1,7,9-*trioxadispiro*[5.1.5.3]*hexadecane* **1a**, **1b**.—To a solution of dihydropyran **2** (200 mg, 0.75 mmol) in dry THF (5 cm^3), cooled to −78 °C, under nitrogen, was added butyllithium (1.02 cm^3 of a 1.5 mol dm^{-3} solution in hexane, 1.5 mmol). After stirring at −78 °C for 0.25 h a solution of δ-valerolactone (150 mg, 1.50 mmol) in dry THF (1 cm^3) was added and stirring continued for a further 30 min at this temperature. The reaction mixture was then quenched by the addition of saturated aqueous sodium dihydrogen phosphate (5 cm^3) and extracted with diethyl ether (2 × 40 cm^3). After washing the ether layer with water (5 cm^3) and drying over anhydrous sodium sulfate, the solvent was removed at reduced pressure to give a yellow oil. This oil was redissolved in dichloromethane (10 cm^3), a catalytic amount of camphorsulfonic acid was added and the solution stirred at room temperature for 24 h. Purification using hexane–ethyl acetate (9:1) as eluent yielded: (i) the *title compound* **1a** (74 mg, 28%) R_f 0.78 (2:1 hexane–ethyl acetate) as colourless crystalline prisms, m.p. 116–117 °C (from hexane–diethyl ether) (Found: C, 62.6; H, 7.3; S, 8.6. $C_{19}H_{26}O_5S$ requires C, 62.3; H, 7.15; S, 8.75%); ν_{max}(Nujol)/cm^{-1} 1315s and 1140s (SO_2); δ_H(270 MHz; $CDCl_3$) 1.37–1.95 (15 H, m, 7 × CH_2 and 13eq-H), 2.66 (1 H, ddd, $J_{13ax,12ax}$ 13.2, $J_{13ax,13eq}$ 13.2, $J_{13ax,12eq}$ 4.4, 13ax-H), 3.52–3.91 (5 H, m, 2 × CH_2O and CHS), 7.48–7.64 (3 H, m, 3′-H and 4′-H) and 7.91 (2 H, d, $J_{2',3'}$ 7.7, 2′-H); δ_C(67.8 MHz; $CDCl_3$) 17.5, 18.6, 18.9 (t, C-4, C-12, C-15), 24.8, 25.2 (t, C-3, C-11), 31.4, 34.7, 35.6 (t, C-5, C-13, C-16), 61.4, 61.6 (t, C-2, C-10), 66.1 (d, C-14), 95.8, 96.2 (s, C-6, C-8), 128.5 (d, C-3′), 129.5 (d, C-2′), 133.3 (d, C-4′) and 139.2 (s, C-1′); *m*/*z* 366 (M^+, 12%), 225 (M − $C_6H_5O_2S$, 81), 125 ($C_8H_{12}O$, 38), 111 ($C_7H_{11}O$, 46) and 98 ($C_6H_{10}O$, 100); (ii) the *title compound* **1b** (86 mg, 29%), R_f 0.72 (2:1 hexane–ethyl acetate) as colourless needles, m.p. 104.5–105.5 °C (from hexane–diethyl ether) (Found: C, 62.5; H, 7.1; S, 8.6. $C_{19}H_{26}O_5S$ requires C, 62.3; H, 7.15; S, 8.75%); δ_H(270 MHz; $CDCl_3$) 1.41–1.97 (14 H, m, 6 × CH_2, 13eq-H and 15eq-H), 2.17–2.23 (1 H, m, 15ax-H), 2.66 (1 H, ddd, $J_{13ax,13eq}$ 13.0, $J_{13ax,12ax}$ 13.0, $J_{13ax,12eq}$ 4.4, 13ax-H), 3.14 (1 H, dd, $J_{14ax,15ax}$ 8.6, $J_{14ax,15eq}$ 5.7, 14ax-H), 3.57–3.60 (2 H, m, 2eq-H and 10eq-H), 3.83–3.97 (2 H, m, 2ax-H and 10ax-H), 7.47–7.62 (3 H, m, 3′-H and 4′-H) and 7.89 (2 H, m, 2′-H); δ_C(67.8

MHz; $CDCl_3$) 18.0, 18.8, 18.9 (t, C-4, C-12, C-15), 24.6, 25.3 (t, C-3, C-11), 33.5, 35.0, 36.7 (t, C-5, C-13, C-16), 62.1, 62.4 (t, C-2, C-10), 95.9, 96.2 (s, C-6, C-8), 128.3 (d, C-3′), 130.0 (d, C-2′), 133.1 (d, C-4′) and 139.4 (s, C-1′).

Reduction of Sulfone-bis-spiroacetal **1a** *Using W-2 Raney Nickel.*—To a solution of 14-phenylsulfonyl-1,7,9-trioxadispiro-[5.1.5.3]hexadecane **1a** (100 mg, 0.27 mmol) dissolved in ethanol (45 cm^3) was added W-2 Raney nickel (0.50 g) and the mixture heated under reflux for 1 h. The suspension was then filtered and the solvent removed under reduced pressure to give a colourless oil which was purified by flash chromatography using hexane–ethyl acetate (2:1) as eluent to give: (i) *bis-spiroacetal* **9a** (6.1 mg, 10%) as a colourless oil (Found: M^+, 226.1581. $C_{13}H_{24}O_3$ requires *M*, 226.1569); δ_H(270 MHz; $CDCl_3$) 1.03–2.06 (18 H, m, 9 × CH_2), 3.54–3.67 (2 H, m, 2eq-H and 10eq-H) and 3.86–4.02 (2 H, m, 2ax-H and 10ax-H); δ_C(67.8 MHz; $CDCl_3$) 14.0 (t, C-15), 19.2 (t, C-4, C-12), 25.5 (t, C-3, C-11), 33.6, 36.3 (t, C-5, C-13, C-14, C-16), 61.4 (t, C-2, C-10) and 96.6 (s, C-6, C-8); *m/z* 226 (M^+, 25%), 208 (M − H_2O, 99) and 137 ($C_9H_{13}O$, 100); (ii) 4-(1,7-*dioxaspiro*-[5.5]*undecan*-2-*yl*)*butan*-1-*ol* **10** (40.4 mg, 65%) as a colourless oil (Found: M^+, 228.1725. $C_{13}H_{24}O_3$ requires *M*, 228.1726); δ_H(270 MHz; $CDCl_3$) 1.08–1.74 (16 H, m, 7 × CH_2, 4′eq-H and 10′eq-H), 1.74–1.96 (2 H, m, 4′ax-H and 10′ax-H) and 3.58–3.70 (5 H, m, CH_2O, CHO and CH_2OH); δ_C(67.8 MHz; $CDCl_3$) 18.6, 18.8 (t, C-4′, C-10′), 22.0, 25.4 (t, C-3′, C-9′), 29.7, 31.2, 32.9, 35.9, 36.1 (t, C-2, C-3, C-4, C-5′, C-11′), 60.4 (t, C-8′), 62.9 (t, C-1), 69.0 (d, C-2′) and 95.5 (s, C-6′); *m/z* 228 (M^+, 9%), 155 (M − C_4H_9O, 93) and 100 ($C_5H_8O_2$, 25).

Reduction of Sulfone-bis-spiroacetal **1b** *Using W-2 Raney Nickel.*—Using the procedure described above for the reduction of sulfone bis-spiroacetal **1a**, sulfone bis-spiroacetal **1b** was reduced using W-2 Raney nickel to give: (i) *bis-spiroacetal* **9b** (6.0 mg, 10%) as a colourless oil (Found: M^+, 226.1579. $C_{13}H_{22}O_3$ requires *M*, 226.1569); δ_H(270 MHz; $CDCl_3$) 1.32–1.73 (15 H, m, 6 × CH_2, 4eq-H, 12eq-H and 15eq-H), 1.78–2.00 (3 H, m, 4ax-H, 12ax-H and 15ax-H), 3.57–3.72 (2 H, m, 2eq-H and 10eq-H) and 4.02–4.15 (2 H, m, 2ax-H and 10ax-H); δ_C(67.8 MHz; $CDCl_3$) 14.1 (t, C-15), 19.1 (t, C-4, C-12), 25.5 (t, C-3, C-11), 34.8, 37.7 (t, C-5, C-13, C-14, C-16), 62.0 (t, C-2, C-10) and 96.2 (s, C-6, C-8); *m/z* 226 (M^+, 25%), 208 (M − H_2O, 99) and 137 ($C_9H_{13}O$, 100); (ii) 4-(1,7-dioxaspiro-[5.5]undecan-2-yl)butan-1-ol (37.7 mg, 61%) as a colourless oil for which spectroscopic data (^1H NMR, ^{13}C NMR, MS) were in agreement with that reported above.

1,7,9-*Trioxadispiro*[5.1.5.3]*hexadecane* **9a**, **9b**.—To a solution of 4-(1,7-dioxaspiro[5.5]undecan-2-yl)butan-1-ol **10** (30 mg, 0.13 mmol) in cyclohexane (30 cm^3) was added iodobenzene diacetate (40 mg, 0.13 mmol) and iodine (16 mg, 0.06 mmol). After irradiating for 1 h at room temperature with a 275 W lamp, the reaction mixture was poured into diethyl ether (50 cm^3), washed with 10% aqueous sodium thiosulfate solution (20 cm^3), water (10 cm^3) and dried over sodium sulfate. Removal of the solvent at reduced pressure afforded an oil that was purified by flash chromatography using hexane–diethyl ether (9:1) as eluent to give: (i) 1,7,9-trioxadispiro-[5.1.5.3]hexadecane **9a** (11.3 mg, 38%) as a colourless oil for which spectroscopic data (^1H NMR, ^{13}C NMR, MS) were in agreement with that reported above (ii) 1,7,9-trioxadispiro-[5.1.5.3]hexadecane **9b** (11.3 mg, 38%) as a colourless oil for which spectroscopic data (^1H NMR, ^{13}C NMR, MS) were in agreement with that reported above.

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Paper 3/06017I
Received 8*th October* 1993
Accepted 17*th October* 1993