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A new synthesis of spiroketals via sulfonyl-substituted dihydropyrans

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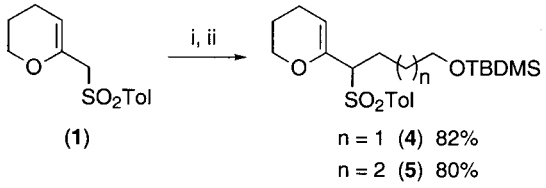
Abstract—6,6- and 6,5-Spiroketals were prepared in good overall yields by alkylation and epoxide-opening reactions of 3,4-dihydro-6-[(*para*-toluenesulfonyl)methyl]-2*H*-pyran (**1**) and subsequent acid catalysed cyclisation. The diastereoselectivity of the cyclisations was determined by a combination of 2D-NMR spectroscopy and X-ray crystallography. Attempted preparation of a 7,6-spiroketal using the same methodology was unsuccessful. © 2001 Elsevier Science Ltd. All rights reserved.

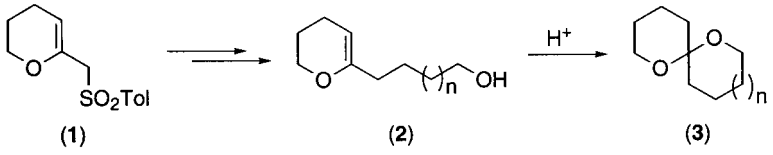
Spiroketals are found in a wide variety of natural products, from the simple spiroketals used as pheromones by a large number of insect species[1–3] to more complex molecules such as okadaic acid[4] and the spongistatins/altohyrtins,[5] and this diversity has led to significant interest in the development of methods for the synthesis of spiroketals.[6] Our recent work on the preparation[7] and reactions[8,9] of sulfonyl-substituted cyclic enol ethers suggested a versatile method for the synthesis of spiroketals (Scheme 1), with 3,4-dihydro-6-[(*para*-toluenesulfonyl)methyl]-2*H*-pyran (**1**) being elaborated to an alkoxy-substituted dihydropyran (**2**) followed by acid catalysed cyclisation to give the corresponding spiroketal (**3**). A number of similar approaches have been reported previously, with a variety of methods being used to prepare the intermediate alkoxy-substituted dihydropyrans.[10–14]

We initially investigated the synthesis of spiroketals via alkylation of the starting heterocycle (**1**), as previous work in this laboratory[8] had shown that this compound could be alkylated in good yield and excellent regioselectivity with a variety of alkylating agents. The alkylating agents required for the proposed spiroketal synthesis, 3-(*t*-butyldimethylsilyloxy)-1-iodopropane and 4-(*t*-butyldimethylsilyloxy)-1-iodobutane, were prepared from propane-1,3-diol and tetrahydrofuran respectively using standard methods.[15–17] Alkylation of the dihydropyran (**1**) with these ω-(silyloxy)alkyl iodides under the conditions described in our previous report[8] gave the corresponding ω-(silyloxy)alkyl dihydropyrans (**4**) and (**5**) in good yields (Scheme 2).

Deprotection of the 4-(silyloxy)butyl dihydropyran (**4**) and subsequent cyclisation were effected in a single pot by treatment with hydrochloric acid in aqueous THF (Scheme 3). The 6,6-spiroketal (**7**) was obtained in excellent yield as a 7.8:1 mixture of diastereoisomers. The ^{1}H NMR spectrum of the mixture showed a full set of signals corresponding to the major isomer, but most of the signals due to the minor



Scheme 2. *Reagents and conditions*: (i) *n*-BuLi, THF, −78°C, 0°C, 15 min. (ii) HMPA, ω-(silyloxy)alkyl iodide, −78°C→rt, 5 h.



Scheme 1.

Keywords: oxygen heterocycles; spiro compounds; stereochemistry; sulfones.

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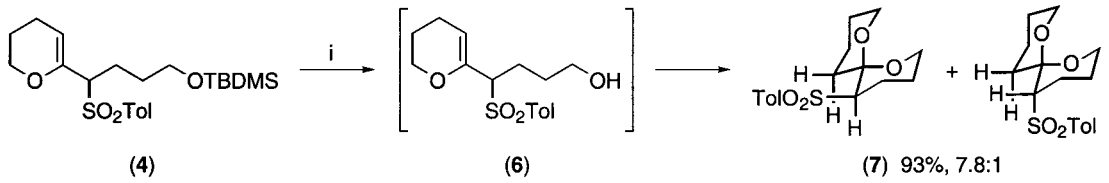
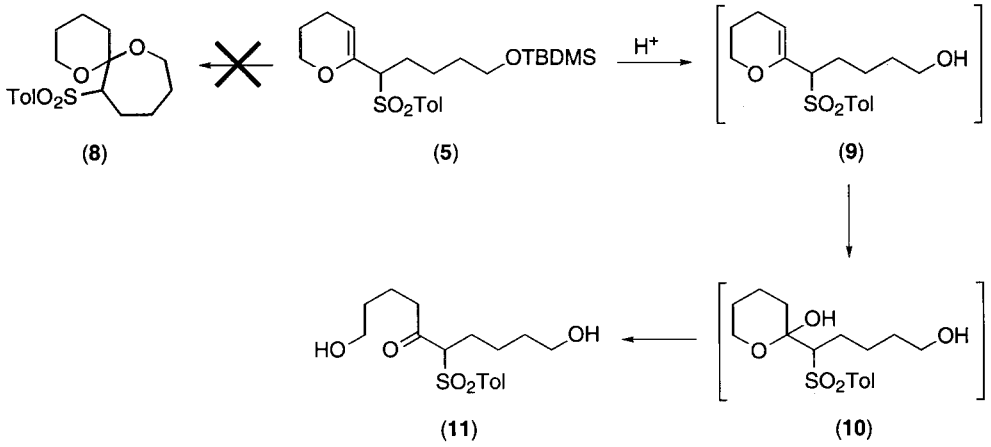


(4) (6) (7) 93%, 7.8:1

Scheme 3. *Reagents and conditions*: (i) HCl, aq. THF, rt, 27 h.

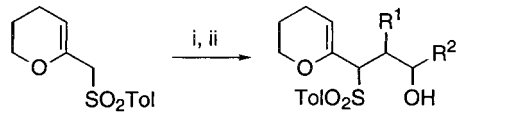


Scheme 4.

isomer were obscured by those of the major isomer. One signal that could be clearly distinguished for both isomers was the α-sulfonyl proton signal, which appeared at 3.04 (dd, $J_{ax,ax}$=12.8 Hz, $J_{ax,eq}$=4.2 Hz) ppm for the major isomer and 3.15 (t, $J_{eq,ax}$=4.9 Hz, $J_{eq,eq}$=4.9 Hz) ppm for the minor isomer. The observed coupling constants indicate that this proton is axial in the major isomer and equatorial in the minor isomer. On the basis of this analysis, and the known preference of spiroketals for a diaxial C–O conformation with axial substituents,[6,18] the major and minor isomers were assigned the ($5R^*$,$6S^*$) and ($5R^*$,$6R^*$) configurations respectively.

Under the same conditions the 5-(silyloxy)pentyl dihydropyran (**5**) did not give the expected 7,6-spiroketal (**8**). Instead, a dihydroxy ketone (**11**) resulting from ring opening of the intermediate hydroxyalkyl dihydropyran (**9**) was isolated in 95% yield (Scheme 4). The dihydroxy ketone (**11**) was also isolated as the sole product when the reaction was carried out under reflux rather than at room temperature. The failure of this reaction is surprising given the successful preparation of a 7,6-spiroketal by Nakamura et al. under similar conditions.[19] The reaction was also attempted under anhydrous conditions, using a catalytic amount of camphorsulfonic acid in dry dichloromethane, however no deprotection occurred and the starting material was recovered unchanged.

In order to extend the scope of this methodology for the synthesis of spiroketals, reactions of the sulfonyl-substituted dihydropyran (**1**) with epoxides were examined. Thus, treatment of the lithiosulfone derivative of the dihydropyran (**1**) with cyclohexene oxide or propylene oxide in the presence of HMPA and boron trifluoride gave the corresponding γ-hydroxy sulfones (**12**) and (**13**) in 71%[20] and 66% yields respectively (Scheme 5). In both cases the products were isolated as 1:1 mixtures of diastereoisomers.



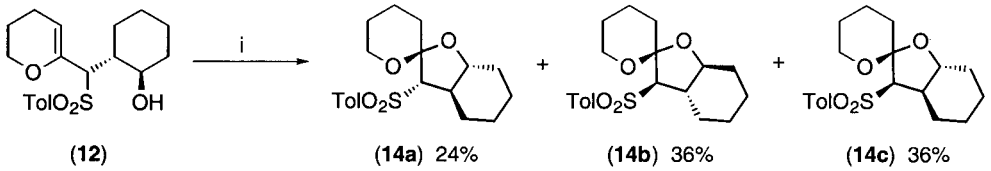
(1)

R^1, R^2 = -$(CH_2)_4$- (**12**) 71%

R^1 = H, R^2 = Me (**13**) 66%

Scheme 5. *Reagents and conditions*: (i) *n*-BuLi, THF, −78°C, 0°C 15 min. (ii) HMPA, $BF_3{\cdot}OEt_2$, epoxide, −78°C→rt, 5 h.

Subsequent treatment of the cyclohexene oxide adduct (**12**) with hydrochloric acid in aqueous THF gave the corresponding 6,5-spiroketal (**14**) as a mixture of diastereoisomers in 96% overall yield (Scheme 6). Three isomers were separated by flash chromatography. (It is interesting



(12) (14a) 24% (14b) 36% (14c) 36%

Scheme 6. *Reagents and conditions*: (i) HCl aq. THF, rt, 72 h.

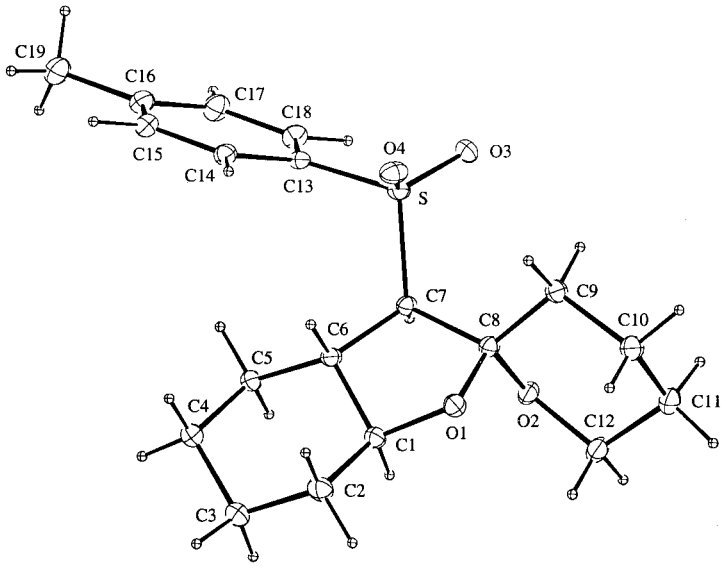


Figure 1. Structural diagram for (**14a**).[21]

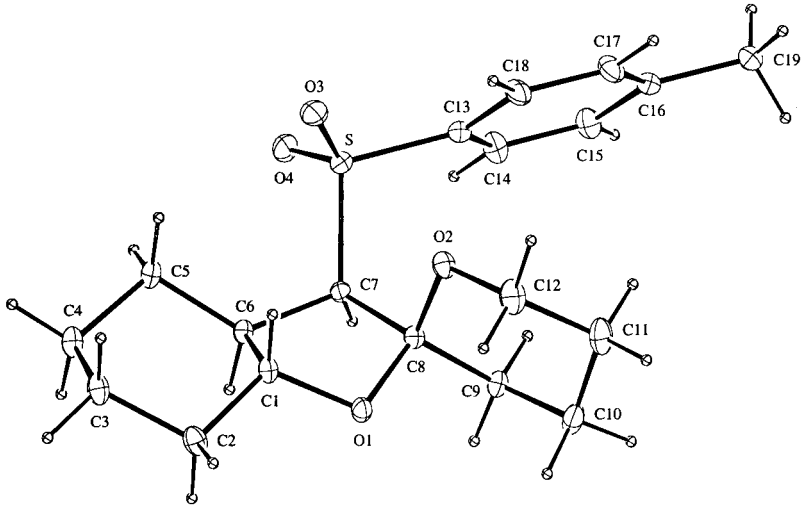
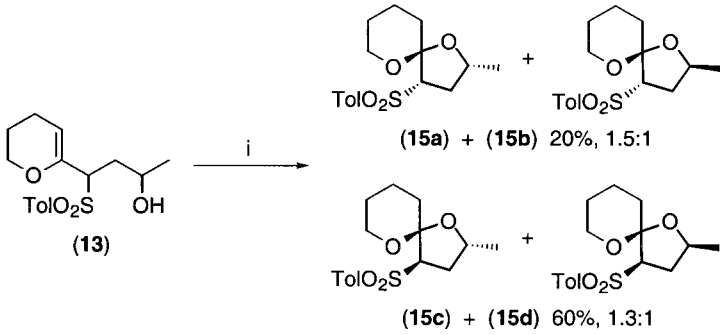


Figure 2. Structural diagram for (**14c**).[21]

to note that the fourth possible diastereoisomer was not formed, although it is not clear why this should be the case.) The relative stereochemistry shown in Scheme 6 for each structure was assigned on the basis of NOESY correlations and confirmed by single crystal X-ray diffraction of (**14a**) and (**14c**) (Figs. 1 and 2).

The propylene oxide adduct (**13**) was also cyclised under acidic conditions to give the corresponding 6,5-spiroketal (**15**) as a mixture of diastereoisomers in 80% overall yield (Scheme 7). In contrast with the previous example, all four diastereoisomers were formed, but they could not be completely separated by flash chromatography. Instead,



Scheme 7. *Reagents and conditions*: (i) HCl, aq. THF, rt, 72 h.

two pairs of isomers were obtained. The relative stereochemistry of each isomer was assigned on the basis of NOESY correlations. Within each pair the stereochemistry of the sulfone relative to the spiro carbon was the same, while the relative stereochemistry of the methyl substituent varied.

In conclusion, we have shown that 6,6- and 6,5-spiroketals can be prepared in good overall yields from 3,4-dihydro-6-[(*para*-toluenesulfonyl)methyl]-2*H*-pyran (**1**) by a two step alkylation/cyclisation or epoxide-opening/cyclisation procedure. Moderate to good diastereoselectivity was observed in the cyclisation reactions, with the α-sulfonyl stereocentre exerting a greater influence on the relative stereochemistry than the C2 stereocentre in the 5,6-spiroketals. This suggests that it may be possible to use the sulfone as a removable directing group in a stereoselective synthesis of spiroketals.

1. Experimental

1.1. General

^{1}H NMR spectra were recorded as deuterochloroform solutions on a Bruker AC300F (300 MHz), DMX300 (300 MHz), or DMX600 (600 MHz) spectrometer. Chemical shifts are measured in parts per million (δ, ppm) downfield from tetramethylsilane (TMS) relative to chloroform (δ_H=7.26 ppm) as an internal reference. Coupling constants (*J*) are reported in hertz (Hz). Multiplicities are designated as follows: singlet (s), doublet (d), triplet (t), quartet (q), multiplet (m), and broad (br). ^{13}C NMR spectra were recorded as deuterochloroform solutions on a Bruker AC300F (75.5 MHz), DMX300 (75.5 MHz), or DMX600 (150.9 MHz) spectrometer and are proton decoupled. Chemical shifts are reported in parts per million downfield from TMS relative to the central peak of the deuterochloroform triplet (δ_C=77.04 ppm). In assignments of spectra, Ar refers to quaternary aromatic carbons and ArCH refers to aromatic carbons bearing one hydrogen. Infrared spectra were obtained on a Perkin–Elmer 298 infrared spectrophotometer either as thin films of liquids or paraffin mulls of solids. Absorptions of medium or strong intensity are reported in cm^{-1}. Mass spectra, in electron ionisation mode, were obtained on a VG Quattro mass spectrometer at 70 eV ionising potential and with an ion source temperature of 210°C. Melting points were determined on a Reichert melting point apparatus and are uncorrected. Elemental analyses were performed by the School of Chemistry Microanalysis Service, UNSW, or the Research School of Chemistry Microanalysis Service, ANU.

Flash chromatography[22] was carried out using Merck Kieselgel 60 (230–400 mesh; No. 9385), using distilled solvents. Reagents and solvents were purified by standard procedures. Dry acetone refers to AR grade reagent distilled from anhydrous calcium sulfate and stored over 4 Å molecular sieves. *n*-Butyllithium was titrated by the method of Suffert.[23] Dry dichloromethane refers to AR grade reagent pre-dried over calcium chloride, stored over calcium hydride, and distilled freshly when required. Hexamethylphosphoric triamide (HMPA) was distilled under reduced pressure from calcium hydride and stored over 4 Å molecular sieves. Light petroleum refers to a hydrocarbon fraction boiling in the range 60–80°C. Dry pyridine refers to AR grade reagent distilled from potassium hydroxide and stored over fresh potassium hydroxide. Sodium iodide was heated gently under vacuum (~0.5 mmHg) until no further evolution of gas was evident. Dry tetrahydrofuran refers to AR grade reagent treated with sodium sulfite for the removal of peroxides, pre-dried over potassium hydroxide, heated at reflux over calcium hydride then distilled, stored over sodium metal and benzophenone, and distilled freshly when required. All other reagents were used without further purification.

3-(*t*-Butyldimethylsilyloxy)propan-1-ol,[15] 3-(*t*-butyldimethylsilyloxy)-1-iodopropane,[16] and 4-(*t*-butyldimethylsilyloxy)-1-iodobutane[17] were prepared according to standard literature procedures.

1.1.1. 3,4-Dihydro-6-[4′-(*t*-butyldimethylsilyloxy)-1′-(*para*-toluenesulfonyl)-1′-butyl]-2*H*-pyran (4). A solution of 3,4-dihydro-6-[(*para*-toluenesulfonyl)methyl]-2*H*-pyran (**1**) (1.00 g, 4.0 mmol) in dry tetrahydrofuran (60 mL) was placed under an argon atmosphere and cooled to −78°C. *n*-Butyllithium (1.36 M in hexanes, 2.7 mL, 3.67 mmol) was added dropwise then the temperature was allowed to rise to 0°C. After 15 min the solution was cooled to −78°C and HMPA (0.70 mL, d 1.030, 0.72 g, 4 mmol), followed by 3-(*t*-butyldimethylsilyloxy)-1-iodopropane (1.12 g, 3.7 mmol), was added. The solution was allowed to warm to room temperature over a period of 5 h. The reaction was quenched with brine (80 mL) then the mixture was separated and the aqueous layer was extracted with diethyl ether (3×60 mL). The combined organic extracts were washed with brine (200 mL) then dried over magnesium sulfate and the solvent removed under reduced pressure. Flash column chromatography (10% ethyl acetate/light petroleum) of the crude product gave the *title compound* (**4**) as colourless needles (1.36 g, 80%), mp 44–46°C. (Found: C, 62.1%; H, 8.2%. $C_{22}H_{36}O_4SSi$ requires C, 62.2%; H, 8.5%). ν_{max} (paraffin) 1665, 1600, 1390, 1360, 1310, 1300, 1290, 1250, 1230, 1205, 1180, 1140, 1105, 1100, 1080, 1060, 1005, 975, 910, 830, 810, 775, 705, 660, 610 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.01 (s, 6H, Si(CH_3)$_2$), 0.85 (s, 9H, C(CH_3)$_3$), 1.41–1.76 (m, 4H, H3+H3′), 1.79–2.09 (m, 4H, H2′+H4), 2.42 (s, 3H, $ArCH_3$), 3.46 (dd, *J*=11.7, 3.9 Hz, 1H, H1′), 3.58 (t, *J*=6.4 Hz, 2H, H4′), 3.73 (ddd, *J*=10.6, 6.5, 3.8 Hz, 1H, H2a), 3.83 (ddd, *J*=10.6, 6.5, 3.7 Hz, 1H, H2b), 4.70 (t, *J*=3.8 Hz, 1H, H5), 7.29 (d, *J*=8.5 Hz, 2H, ArH), 7.73 (d, *J*=8.5 Hz, 2H, ArH). ^{13}C NMR (75.5 MHz, $CDCl_3$) δ −5.4 (Si(CH_3)$_2$), 18.3 (C(CH$_3$)$_3$), 20.4 (C4), 21.6 ($ArCH_3$), 21.8 (C3), 22.2 (C3′), 25.9 (C(CH_3)$_3$), 29.8 (C2′), 62.5 (C4′), 66.3 (C2), 70.8 (C1′), 104.4 (C5), 129.2 (ArCH), 129.3 (ArCH), 135.2 (Ar), 144.2 (Ar or C6), 146.0 (Ar or C6). *m/z* 425 (M+H, 21%), 367 (M−Bu^t, 16), 269 (M−TolSO$_2$, 100), 137 (M−TolSO$_2$−Bu^{t}Me$_2$SiOH, 50), 91 (Tol, 43), 57 (Bu^t, 50).

1.1.2. 3,4-Dihydro-6-[5′-(*t*-butyldimethylsilyloxy)-1′-(*para*-toluenesulfonyl)-1′-pentyl]-2*H*-pyran (5). The product was prepared from 3,4-dihydro-6-[(*para*-toluenesulfonyl)methyl]-2*H*-pyran (**1**) (1.00 g, 4.0 mmol) and 3-(*t*-butyldimethylsilyloxy)-1-iodopropane (1.12 g, 3.7 mmol)

as described for 3,4-dihydro-6-[4′-(*t*-butyldimethylsilyloxy)-1′-(*para*-toluenesulfonyl)-1′-butyl]-2*H*-pyran (**4**). Flash column chromatography (10% ethyl acetate/light petroleum) of the crude product gave the *title compound* (**5**) as colourless needles (1.44 g, 82%), mp 56–58°C. (Found: C, 62.9%; H, 8.5%. $C_{23}H_{38}O_4SSi$ requires C, 63.0%; H, 8.7%). ν_{max} (paraffin) 1665, 1595, 1460, 1380, 1340, 1305, 1300, 1290, 1250, 1240, 1140, 1105, 1095, 1080, 1060, 980, 925, 840, 830, 820, 770, 710, 700, 655, 640, 630, 605 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$) δ 0.01 (s, 6H, $Si(CH_3)_2$), 0.86 (s, 9H, $C(CH_3)_3$), 1.20–1.34 (m, 1H, H3′a), 1.37–1.56 (m, 3H, H3+H3′b), 1.61–1.73 (m, 2H, H4′), 1.79–2.04 (m, 4H, H2′+H4), 2.43 (s, 3H, $ArCH_3$), 3.42 (dd, J=11.7, 3.9 Hz, 1H, H1′), 3.56 (t, J=6.2 Hz, 2H, H5′), 3.71 (ddd, J=10.5, 6.4, 4.0 Hz, 1H, H2a), 3.81 (ddd, J=10.5, 6.6, 3.9 Hz, 1H, H2b), 4.67 (t, J=3.8 Hz, 1H, H5), 7.29 (d, J=8.2 Hz, 2H, ArH), 7.73 (d, J=8.2 Hz, 2H, ArH). ^{13}C NMR (75.5 MHz, $CDCl_3$) δ −5.3 ($Si(CH_3)_2$), 18.3 ($C(CH_3)_3$), 20.4 (C4), 21.6 ($ArCH_3$), 21.8 (C3), 23.2 (C4′), 25.1 (C3′), 25.9 ($C(CH_3)_3$), 32.3 (C2′), 62.7 (C5′), 66.3 (C2), 71.2 (C1′), 104.3 (C5), 129.1 (ArCH), 129.3 (ArCH), 135.2 (Ar), 144.2 (Ar or C6), 146.1 (Ar or C6). *m/z* 439 (M+H, <1%), 225 (M−$TolSO_2$−Bu^{t}H, 14), 151 (M−$TolSO_2$−Bu^{t}Me$_2$SiOH, 100).

1.1.3. 5-(*para*-Toluenesulfonyl)-1,7-dioxaspiro[5.5]-undecane (7). To a solution of 3,4-dihydro-6-[4′-(*t*-butyldimethylsilyloxy)-1′-(*para*-toluenesulfonyl)-1′-butyl]-2*H*-pyran (**4**) (0.25 g, 0.59 mmol) in tetrahydrofuran (10 mL) and water (2.5 mL) under an argon atmosphere was added conc. hydrochloric acid (0.5 mL). After 27 h the reaction was quenched with saturated aqueous sodium hydrogen carbonate (5 mL) then the mixture was extracted with diethyl ether (2×10 mL). The combined organic extracts were dried over magnesium sulfate and the solvent removed under reduced pressure. Flash column chromatography (15% ethyl acetate/light petroleum) of the crude product gave the *title compound* (**7**) as colourless needles (0.17 g, 7.8:1 mixture of the (5R^*,6S^*) and (5R^*,6R^*) diastereoisomers by comparison of the α-sulfonyl proton signals at 3.04 (major) and 3.15 (minor) ppm in the ^1H NMR spectrum, 93%), mp 124–126°C. (Found: C, 61.8%; H, 6.9%. $C_{16}H_{22}O_4S$ requires C, 61.9%; H, 7.1%). ν_{max} (paraffin) 1340, 1315, 1305, 1285, 1270, 1255, 1235, 1195, 1185, 1170, 1140, 1095, 1090, 1065, 1050, 1040, 980, 960, 815, 800, 720, 710, 690, 670, 615 cm^{-1}. ^1H NMR (600 MHz, $CDCl_3$, major isomer only) δ 1.46–1.50 (m, 1H, H9a), 1.56–1.70 (m, 5H, H3a+H3b+H9b+H10a+H11a), 1.75–1.86 (m, 2H, H4a+H10b), 2.00 (dddd, J=12.5, 7.7, 3.8, 1.4 Hz, 1H, H4b), 2.88 (td, J=13.4, 4.6 Hz, 1H, H11b), 3.04 (dd, J=12.8, 4.2 Hz, 1H, H5), 3.58–3.63 (m, 4H, H2+H8), 7.30 (d, J=8.2 Hz, 2H, ArH), 7.74 (d, J=8.2 Hz, 2H, ArH). Assignment was determined with the aid of COSY and HSQC experiments. ^{13}C NMR (150.9 MHz, $CDCl_3$, major isomer only) δ 18.4 (C10), 21.6 ($ArCH_3$), 22.1 (C4), 24.7 (C9), 25.3 (C3), 32.6 (C11), 59.0 (C2), 60.9 (C8), 69.3 (C5), 95.6 (C6), 129.0 (ArCH), 129.9 (ArCH), 135.9 (Ar), 144.1 (Ar). Assignment was determined with the aid of HSQC and HMBC experiments. *m/z* 310 (M, 6%), 210 (M−SO_2−2×H_2O, 57), 155 (M−$TolSO_2$, 90), 91 (Tol, 75).

1.1.4. Attempted preparation of 11-(*para*-toluenesulfonyl)-1,7-dioxaspiro[5.6]dodecane (8). *Method A:* Treatment of 3,4-dihydro-6-[5′-(*t*-butyldimethylsilyloxy)-1′-(*para*-toluenesulfonyl)-1′-pentyl]-2*H*-pyran (**5**) (0.50 g, 1.14 mmol) with conc. hydrochloric acid in aqueous tetrahydrofuran as described for 5-(*para*-toluenesulfonyl)-1,7-dioxaspiro[5.5]-undecane (**7**) did not give the desired product.

Workup as described above gave *1,10-dihydroxy-6-(para-toluenesulfonyl)-5-decanone* (**11**) (0.37 g, 95%) as a colourless oil. The crude product was spectroscopically pure, and was characterised without further purification. (Found: C, 62.5%; H, 7.7%. $C_{17}H_{26}O_5S$–(0.9×H_2O) requires C, 62.6%; H, 7.5%). ν_{max} (film) 3430(br), 2940, 2880, 1720, 1600, 1440, 1400, 1300, 1210, 1185, 1140, 1075, 810, 725, 705, 680, 660, 610 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$) δ 1.22–1.33 (m, 2H, H8), 1.42–1.61 (m, 6H, H2+H9+2×OH), 1.63–1.73 (m, 2H, H3), 1.83–1.93 (m, 2H, H7), 2.46 (s, 3H, $ArCH_3$), 2.63 (dt, J=18.3, 6.8 Hz, 1H, H4a), 2.93 (dt, J=18.3, 7.1 Hz, 1H, H4b), 3.57 (t, J=5.8 Hz, 2H, H1 or H10), 3.64 (t, J=5.7 Hz, 2H, H1 or H10), 4.09 (dd, J=8.8, 5.8 Hz, 1H, H6), 7.35 (d, J=8.2 Hz, 2H, ArH), 7.64 (d, J=8.2 Hz, 2H, ArH). Assignment was determined with the aid of COSY and HSQC experiments. ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 19.5 (C3), 23.2 (C8), 25.6 ($ArCH_3$), 26.9 (C7), 31.6 (C2), 32.0 (C9), 44.7 (C4), 61.8 (C1 or C10), 62.2 (C1 or C10), 75.0 (C6), 129.4 (ArCH), 129.8 (ArCH), 133.4 (Ar), 145.5 (Ar), 202.8 (C5). Assignment was determined with the aid of HSQC and HMBC experiments. *m/z* 324 (M−H_2O, 8%), 169 (M−H_2O−$TolSO_2$, 41), 155 ($TolSO_2$, 15), 91 (Tol, 100).

Method B: 3,4-Dihydro-6-[5′-(*t*-butyldimethylsilyloxy)-1′-(*para*-toluenesulfonyl)-1′-pentyl]-2*H*-pyran (**5**) (0.25 g, 0.57 mmol) was treated with conc. hydrochloric acid in aqueous tetrahydrofuran as described for 5-(*para*-toluenesulfonyl)-1,7-dioxaspiro[5.5]undecane (**7**), with the exception that the reaction mixture was heated under reflux overnight. Examination of the ^1H NMR spectrum of the crude product showed only 1,10-dihydroxy-6-(*para*-toluenesulfonyl)-5-decanone (**11**).

Method C: To a stirred solution of 3,4-dihydro-6-[5′-(*t*-butyldimethylsilyloxy)-1′-(*para*-toluenesulfonyl)-1′-pentyl]-2*H*-pyran (**5**) (0.25 g, 0.57 mmol) in dry dichloromethane (50 mL) under an argon atmosphere was added camphorsulfonic acid (0.15 g, 0.63 mmol). After 18 h, ^1H NMR showed only starting material.

1.1.5. 3,4-Dihydro-6-[(2′-hydroxycyclohexyl)-(*para*-toluenesulfonyl)methyl]-2*H*-pyran (12). A solution of 3,4-dihydro-6-[(*para*-toluenesulfonyl)methyl]-2*H*-pyran (**1**) (1.00 g, 4.0 mmol) in dry tetrahydrofuran (60 mL) was placed under an argon atmosphere and cooled to −78°C. *n*-Butyllithium (2.34 M in hexanes, 1.6 mL, 3.74 mmol) was added dropwise then the temperature was allowed to rise to 0°C. After 15 min the solution was cooled to −78°C and HMPA (0.70 mL, d 1.030, 0.72 g, 4.0 mmol), was added dropwise, followed by cyclohexene oxide (0.40 mL, d 0.970, 0.39 g, 4.0 mmol) which was added all at once, then boron trifluoride etherate complex (0.50 mL, d 1.154, 0.58 g, 4.0 mmol). The solution was allowed to warm to room temperature over a period of 5 h then the reaction

was quenched with brine (80 mL). The mixture was separated and the aqueous layer was washed with diethyl ether (3×60 mL). The combined organic extracts were washed with brine (200 mL) then dried over magnesium sulfate and the solvent removed under reduced pressure. Flash column chromatography (30% ethyl acetate/light petroleum) of the crude product gave the *title compound* (**12**) as colourless prisms (1.00 g, 1:1 mixture of diastereoisomers by comparison of the vinyl proton signals at 4.55 and 4.82 ppm in the ^{1}H NMR spectrum, 71%), mp 95–97°C. (Found: C, 65.0%; H, 7.3%. $C_{19}H_{26}O_4S$ requires C, 65.1%; H, 7.5%). ν_{max} (paraffin) 3500(br), 1660, 1600, 1345, 1320, 1300, 1285, 1255, 1230, 1215, 1160, 1140, 1110, 1080, 1070, 1050, 1020, 920, 805, 800, 780, 770, 710, 700, 655, 635, 625, 615 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.18–1.52 (m, 2×H3′a+2×H4′a+2×H5′a+2×H6′a), 1.59–1.77 (m, 4× H4+2×H4′b+2×H5′b+1×H6′b), 1.80–1.93 (m, 4×H3+ 1×OH), 1.97–2.06 (m, 2×H3′b+1×OH), 2.17–2.32 (m, 2×H1′+1×H6′b), 2.41 (s, 1×$ArCH_3$), 2.42 (s, 1×$ArCH_3$), 3.25–3.35 (m, 1×H2′), 5.53 (dd, J=2.7, 0.8 Hz, 1×$CHSO_2$), 3.58–3.67 (m, 1×H2′), 3.79–3.92 (m, 4×H2), 4.09 (d, J=3.0 Hz, 1×$CHSO_2$), 4.55 (t, J=3.9 Hz, 1×H5), 4.82 (t, J=3.9 Hz, 1×H5), 7.28 (d, J=8.3 Hz, 2×ArH), 7.29 (d, J=8.2 Hz, 2×ArH), 7.75 (d, J=8.3 Hz, 2×ArH), 7.75 (d, J=8.2 Hz, 2×ArH). Assignment was determined with the aid of an HSQC experiment. ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 20.3 (2×C3), 21.4 (1×C4), 21.6 (2×$ArCH_3$), 21.7 (1×C4), 24.2 (1×C4′ or C5′), 24.8 (1×C4′ or C5′), 25.4 (1×C4′ or C5′), 25.6 (1×C4′ or C5′), 27.2 (1×C6′), 31.0 (1×C6′), 34.5 (1×C3′), 35.8 (1×C3′), 44.3 (1×C1′), 45.0 (1×C1′), 66.2 (1×C2), 66.4 (1×C2), 69.3 (1× $CHSO_2$), 70.9 (1×C2′), 71.2 (1×C2′), 74.9 (1×$CHSO_2$), 105.2 (1×C5), 105.5 (1×C5), 128.9 (1×ArCH), 129.0 (1× ArCH), 129.1 (1×ArCH), 129.2 (1×ArCH), 135.6 (1×Ar), 136.2 (1×Ar), 144.1 (1×Ar or C6), 144.4 (1×Ar or C6), 145.4 (1×Ar or C6), 145.8 (1×Ar or C6). m/z 351 (M+H, 34%), 333 (M−OH, 17), 195 (M−$TolSO_2$, 100), 177 (M− $TolSO_2$−H_2O, 48), 91 (Tol, 24).

1.1.6. 3,4-Dihydro-6-[3′-hydroxy-1′-(*para*-toluenesulfonyl)-1′-butyl]-2*H*-pyran (13). The product was prepared from 3,4-dihydro-6-[(*para*-toluenesulfonyl)-methyl]-2*H*-pyran (**1**) (1.00 g, 4.0 mmol) and propylene oxide (0.28 mL, d 0.830, 0.23 g, 4.0 mmol) as described for 3,4-dihydro-6-[(2′-hydroxycyclohexyl)-(*para*-toluenesulfonyl)-methyl]-2*H*-pyran (**12**). Flash column chromatography (30% ethyl acetate/light petroleum) of the crude product gave the *title compound* (**13**) as a colourless oil (0.82 g, 1:1 mixture of diastereoisomers by comparison of the vinyl proton signals at 4.67 and 4.69 ppm in the ^{1}H NMR spectrum, 66%). (Found: C, 61.9%; H, 7.0%. $C_{16}H_{22}O_4S$ requires C, 61.9%; H, 7.1%). ν_{max} (film) 3400(br), 2920, 2880, 1660, 1595, 1440, 1380, 1355, 1335, 1310, 1300, 1290, 1250, 1220, 1200, 1160, 1140, 1120, 1090, 1060, 1040, 1020, 815, 800, 705, 655 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.19 (d, J=6.2 Hz, 3×H4′), 1.23 (d, J=6.2 Hz, 3×H4′), 1.57–1.73 (m, 4×H3), 1.85–1.96 (m, 4×H4), 1.98–2.06 (m, 2×H2′a), 2.19 (dd, J=5.9, 5.2 Hz, 1×H2′b), 2.24 (dd, J=6.0, 5.3 Hz, 1×H2′b), 2.42 (s, 2×$ArCH_3$), 3.64–3.86 (m, 4×H2+2×H1′+2×OH), 3.99–4.14 (m, 2×H3′), 4.67 (t, J=4.0 Hz, 1×H5), 4.69 (t, J=4.0 Hz, 1×H5), 7.30 (d, J=8.1 Hz, 4×ArH), 7.72 (d, J=8.3 Hz, 2×ArH), 7.73 (d, J= 8.3 Hz, 2×ArH). ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 20.3 (1× C3), 20.4 (1×C3), 21.6 (2×$ArCH_3$+1×C4), 21.8 (1×C4), 23.1 (1×C4′), 24.2 (1×C4′), 34.4 (1×C2′), 35.3 (1×C2′), 65.0 (1×C1′), 65.8 (1×C1′), 66.3 (1×C2), 66.4 (1×C2), 68.2 (2×C3′), 104.2 (1×C5), 105.0 (1×C5), 129.2 (2× ArH), 129.2 (1×ArH), 129.3 (1×ArH), 134.8 (1×Ar), 135.0 (1×Ar), 144.3 (1×Ar or C6), 144.5 (1×Ar or C6), 145.8 (1×Ar or C6), 146.9 (1×Ar or C6). m/z 310 (M, <1%), 155 (M−$TolSO_2$, 17), 91 (Tol, 31).

1.1.7. Decahydro-3-(*para*-toluenesulfonyl)spiro[benzofuran-2(3*H*),2′-[2*H*]pyran] (14). To a stirred solution of 3,4-dihydro-6-[(2′-hydroxycyclohexyl)-(*para*-toluenesulfonyl)methyl]-2*H*-pyran (**12**) (0.25 g, 0.71 mmol) in tetrahydrofuran (10 mL) and water (2.5 mL) under an argon atmosphere was added conc. hydrochloric acid (0.5 mL). After three days the reaction mixture was poured into saturated aqueous sodium bicarbonate (5 mL) then extracted with diethyl ether (2×10 mL). The combined organic extracts were dried over magnesium sulfate and the solvent was removed under reduced pressure to give the *title compound* (**14**) as a mixture of diastereoisomers.

Flash column chromatography (10% ethyl acetate/light petroleum) of the crude product gave first (2R^*,3R^*,3aS^*,7aS^*)-decahydro-3-(*para*-toluenesulfonyl)spiro[benzofuran-2(3*H*),2′-[2*H*]pyran] (**14a**) as colourless prisms (0.06 g, 24%), mp 154–157°C. (Found: C, 64.9%; H, 7.5%. $C_{19}H_{26}O_4S$ requires C, 65.1%; H, 7.5%). ν_{max} (paraffin) 1355, 1305, 1295, 1280, 1230, 1205, 1180, 1145, 1080, 1070, 1045, 1030, 970, 935, 900, 890, 880, 810, 750, 700, 650, 635 cm^{-1}. ^{1}H NMR (600 MHz, $CDCl_3$) δ 0.84 (dtd, J=12.8, 11.8, 3.7 Hz, 1H, H4ax), 0.87–0.94 (m, 1H, H4eq), 1.04 (dtt, J=13.5, 12.8, 4.1 Hz, 1H, H5ax), 1.20 (dtt, J=14.2, 13.1, 4.0 Hz, 1H, H6ax), 1.42 (dtd, J=12.9, 11.5, 4.0 Hz, 1H, H7ax), 1.46–1.53 (m, 2H, H5eq+H5′a), 1.63 (qdd, J=13.1, 5.0, 3.9 Hz, 1H, H5′b), 1.69–1.73 (m, 1H, H4′a), 1.78–1.84 (m, 2H, H3a+H6eq), 1.86 (qt, J=13.3, 3.9 Hz, 1H, H4′b), 2.09–2.15 (m, 2H, H7eq+H3′a), 2.34 (td, J=13.3, 4.6 Hz, 1H, H3′b), 2.45 (s, 3H, $ArCH_3$), 3.36 (d, J=10.9 Hz, 1H, H3), 3.38 (ddd, J=11.4, 10.2, 3.7 Hz, 1H, H7a), 3.62 (ddt, J=11.2, 5.0, 1.6 Hz, 1H, H6′a), 3.88 (ddd, J=12.9, 10.9, 2.3 Hz, 1H, H6′b), 7.35 (d, J=8.2 Hz, 2H, ArH), 7.76 (d, J=8.2 Hz, 2H, ArH). Assignment was determined with the aid of COSY and HSQC experiments. ^{13}C NMR (150.9 MHz, $CDCl_3$) δ 19.6 (C4′), 22.1 ($ArCH_3$), 24.3 (C6), 25.4 (C5′), 25.7 (C5), 28.5 (C4), 31.1 (C7), 31.8 (C3′), 48.4 (C3a), 63.0 (C6′), 77.2 (C3), 79.8 (C7a), 106.7 (C2), 128.6 (ArCH), 130.2 (ArCH), 138.1 (Ar), 145.1 (Ar). Assignment was determined with the aid of HSQC and HMBC experiments. m/z 351 (M+H, <1%), 195 (M−$TolSO_2$, 100), 155 ($TolSO_2$, 17), 91 (Tol, 44).

Further elution gave (2R^*,3S^*,3aR^*,7aR^*)-decahydro-3-(*para*-toluenesulfonyl)spiro[benzofuran-2(3*H*),2′-[2*H*]pyran] (**14b**) as colourless needles (0.09 g, 36%), mp 157–160°C. A satisfactory elemental analysis could not be obtained. (Found: C, 64.4%; H, 7.3%. $C_{19}H_{26}O_4S$ requires C, 65.1%; H, 7.5%). ν_{max} (paraffin) 1595, 1460, 1440, 1360, 1290, 1280, 1250, 1210, 1200, 1190, 1150, 1140, 1120, 1110, 1080, 1070, 1045, 1030, 1015, 970, 950, 930, 915, 900, 880, 830, 810, 750, 705, 680, 635, 610 cm^{-1}. ^{1}H NMR

(600 MHz, $CDCl_3$) δ 1.15–1.28 (m, 3H, H4ax+H5ax+H6ax), 1.35–1.43 (m, 3H, H7ax+H5′), 1.46–1.48 (m, 1H, H3′a), 1.54–1.57 (m, 1H, H4′a), 1.70–1.75 (m, 3H, H5eq+H3′b+H4′b), 1.79–1.82 (m, 1H, H6eq), 2.02–2.10 (m, 2H, H3a+H7eq), 2.26–2.29 (m, 1H, H4eq), 2.45 (s, 3H, $ArCH_3$), 3.10 (d, J=12.0 Hz, 1H, H3), 3.26 (ddd, J=11.2, 10.3, 3.9 Hz, 1H, H7a), 3.60 (m, 1H, H6′a), 3.78 (dd, J=15.5, 11.2 Hz, 1H, H6′b), 7.31 (d, J=8.2 Hz, 2H, ArH), 7.79 (d, J=8.2 Hz, 2H, ArH). Assignment was determined with the aid of COSY and HSQC experiments. ^{13}C NMR (150.9 MHz, $CDCl_3$) δ 19.9 (C4′), 22.1 ($ArCH_3$), 24.4 (C6), 24.8 (C5′), 25.5 (C5), 28.5 (C4), 32.0 (C7), 34.4 (C3′), 45.3 (C3a), 62.2 (C6′), 76.4 (C3), 82.0 (C7a), 103.8 (C2), 129.4 (ArCH), 130.3 (ArCH), 137.2 (Ar), 144.7 (Ar). Assignment was determined with the aid of HSQC and HMBC experiments. m/z 350 (M, <1%), 195 (M−$TolSO_2$, 100), 155 ($TolSO_2$, 13), 91 (Tol, 53).

Further elution gave (2*R**, 3*S**, 3a*S**, 7a*S**)-decahydro-3-(*para*-toluenesulfonyl)spiro[benzofuran-2(3*H*),2′-[2*H*]pyran] (**14c**) as colourless needles (0.09 g, 36%), mp 140–143°C. (Found: C, 64.8%; H, 7.2%. $C_{19}H_{26}O_4S$ requires C, 65.1%; H, 7.5%). ν_{max} (paraffin) 1595, 1440, 1355, 1340, 1315, 1305, 1290, 1270, 1250, 1205, 1145, 1135, 1080, 1070, 1045, 1030, 970, 945, 910, 895, 815, 805, 730, 710, 680, 620 cm^{-1}. ^{1}H NMR (600 MHz, $CDCl_3$) δ 0.91–1.03 (m, 2H, H3′a+H5′a), 1.15 (qt, J=12.9, 3.8 Hz, 1H, H5ax), 1.27–1.39 (m, 4H, H6ax+H7ax+H4′a+H5′b), 1.45–1.49 (m, 1H, H3′b), 1.65 (qt, J=13.4, 3.8 Hz, 1H, H4′b), 1.81–1.86 (m, 2H, H5eq and H6eq), 1.90 (dtd, J=12.6, 10.5, 3.2 Hz, 1H, H3a), 2.06 (qd, J=12.8, 3.6 Hz, 1H, H4ax), 2.14–2.18 (m, 1H, H7eq), 2.27–2.32 (m, 1H, H4eq), 2.45 (s, 3H, $ArCH_3$), 3.57 (d, J=10.2 Hz, 1H, H3), 3.61 (ddt, J=11.3, 4.9, 1.8 Hz, 1H, H6′a), 3.82 (ddd, J=13.1, 11.3, 2.5 Hz, 1H, H6′b), 3.85 (td, J_{av} 11.2, 3.9 Hz, 1H, H7a), 7.31 (d, J=8.2 Hz, 2H, ArH), 7.80 (d, J=8.2 Hz, 2H, ArH). Assignment was determined with the aid of COSY and HSQC experiments. ^{13}C NMR (150.9 MHz, $CDCl_3$) δ 19.7 (C4′), 22.0 ($ArCH_3$), 24.3 (C6), 24.7 (C5′), 26.3 (C4), 26.7 (C5), 31.6 (C7), 35.4 (C3′), 48.7 (C3a), 62.0 (C6′), 74.2 (C3), 80.6 (C7a), 104.4 (C2), 129.2 (ArCH), 129.7 (ArCH), 139.3 (Ar), 144.3 (Ar). Assignment was determined with the aid of HSQC and HMBC experiments. m/z 350 (M, 1%), 195 (M−$TolSO_2$, 100), 177 (M−$TolSO_2$−H_2O, 25), 155 ($TolSO_2$, 17), 91 (Tol, 63).

1.1.8. Crystallography data for (2*R,3*R**,3a*S**,7a*S**)-decahydro-3-(*para*-toluenesulfonyl)-spiro[benzofuran-2(3*H*),2′-[2*H*]pyran] (14a).** *Crystal data:* $C_{19}H_{26}O_4S$, M 350.5, orthorhombic, space group Pbca, a=10.935(6), b=18.613(6), c=17.608(7) Å, V=3584(3) Å^3, D_c=1.30 g cm^{-3}, Z=8, μMo=1.90 cm^{-1}. Sample was an irregular fragment ca 0.1 mm radius, $2\theta_{max}$=50°. The number of reflections was 1534 considered observed out of 3145 unique data. Final residuals R, R_w were 0.042, 0.058 for the observed data. Full details have been deposited at the Cambridge Crystallographic Data Centre.

1.1.9. Crystallography data for (2*R,3*S**,3a*S**,7a*S**)-decahydro-3-(*para*-toluenesulfonyl)-spiro[benzofuran-2(3*H*), 2′-[2*H*]pyran] (14c).** *Crystal data:* $C_{19}H_{26}O_4S$, M 350.5, monoclinic, space group $P2_1/c$, a=8.200(5), b=11.328(3), c=19.805(13) Å, β=104.87(3)°, V=1778(2) Å^3, D_c=1.31 g cm^{-3}, Z=4, μMo=1.92 cm^{-1}. Sample was an irregular fragment ca 0.1 mm radius, $2\theta_{max}$=46°. The number of reflections was 1570 considered observed out of 2413 unique data, with R_{merge}=0.010. Final residuals R, R_w were 0.040, 0.055 for the observed data. Full details have been deposited at the Cambridge Crystallographic Data Centre.

1.1.10. 2-Methyl-4-(*para*-toluenesulfonyl)-1,6-dioxaspiro[4.5]decane (15). Treatment of 3,4-dihydro-6-[3′-hydroxy-1′-(*para*-toluenesulfonyl)-1′-butyl]-2*H*-pyran (**13**) (0.25 g, 0.81 mmol) with conc. hydrochloric acid as described for decahydro-3-(*para*-toluenesulfonyl)spiro-[benzofuran-2(3*H*),2′-[2*H*]pyran] (**14**) gave the *title compound* (**15**) as a mixture of diastereoisomers.

Flash column chromatography (10% ethyl acetate/light petroleum) of the crude product gave first a mixture of (2*R**,4*S**,5*S**)-2-methyl-4-(*para*-toluenesulfonyl)-1,6-dioxaspiro[4.5]decane (**15a**) and (2*R**,4*R**,5*R**)-2-methyl-4-(*para*-toluenesulfonyl)-1,6-dioxaspiro[4.5]decane (**15b**) as colourless prisms (0.05 g, 1.5:1 by comparison of the α-sulfonyl proton signals at 3.65 (major) and 3.68 (minor) ppm in the ^{1}H NMR spectrum, 20%), mp 106–109°C. (Found: C, 61.5%; H, 7.1%. $C_{16}H_{22}O_4S$ requires C, 61.9%; H, 7.1%). ν_{max} (paraffin) 1360, 1315, 1300, 1285, 1265, 1255, 1240, 1230, 1200, 1185, 1140, 1110, 1070, 1060, 1040, 985, 945, 880, 810, 730, 705, 680, 660, 645, 615 cm^{-1}. ^{1}H NMR (600 MHz, $CDCl_3$) δ 1.28 (d, J=6.3 Hz, 3H(minor), 1×RCH_3), 1.33 (d, J=6.1 Hz, 3H(major), 1×RCH_3), 1.47–1.52 (m, 1H(major)+1H(minor), 2×H8a), 1.56–1.68 (m, 1H(major)+1H(minor), 2×H8b), 1.69–1.74 (m, 1H(major)+1H(minor), 2×H9a), 1.82 (ddd, J=13.0, 8.9, 7.6 Hz, 1H(major), 1×H3a), 1.84–1.90 (m, 1H(major)+1H(minor), 2×H9b), 2.00–2.05 (m, 2H (minor), 1×H3a+1×H10a), 2.07 (ddd, J=13.0, 8.9, 5.9 Hz, 1H(major), 1×H3b), 2.16–2.25 (m, 2H(major)+1H(minor), 1×H10a+2×H10b), 2.32 (ddd, J=13.8, 7.1, 2.5 Hz, 1H(minor), 1×H3b), 2.44 (s, 3H(major), 1×$ArCH_3$), 2.45 (s, 3H(minor), 1×$ArCH_3$), 3.56–3.59 (m, 1H(major)+1H(minor), 2×H7a), 3.65 (dd, J=8.9, 7.6 Hz, 1H(major), 1×H4), 3.68 (ddd, J=8.5, 2.5, 0.6 Hz, 1H(minor), 1×H4), 3.82 (ddd, J=12.7, 11.2, 2.6 Hz, 1H(major), 1×H7b), 3.92 (ddd, J=12.4, 11.3, 2.7 Hz, 1H(minor), 1×H7b), 4.08 (d of quintets, J=8.9, 6.0 Hz, 1H(major), 1×H2), 4.50 (quintet of dd, J_{av}=6.7, 1.6, 0.7 Hz, 1H(minor), 1×H2), 7.34 (d, J=8.5 Hz, 2H(major), ArH), 7.36 (d, J=8.4 Hz, 2H(minor), ArH), 7.76 (d, J=8.5 Hz, 2H(major), ArH), 7.78 (d, J=8.4 Hz, 2H(minor), ArH). Assignment was determined with the aid of COSY and HSQC experiments. ^{13}C NMR (150.9 MHz, $CDCl_3$) δ 19.8 (C9(major)), 20.0 (C9minor)), 20.3 (RCH_3(major)), 22.0 ($ArCH_3$(major+minor)), 23.4 (RCH_3 (minor)), 25.4 (C8(major)), 25.5 (C8(minor)), 31.4 (C10(major)), 31.9 (C10(minor)), 34.9 (C3(minor)), 36.3 (C3(major)), 62.2 (C7(major+minor)), 72.1 (C2(major)), 72.8 (C4(minor)), 72.9 (C4(major)), 75.5 (C2(minor)), 106.3 (C5(major)), 106.5 (C5(minor)), 128.7 (ArCH(major)), 128.8 (ArCH(minor)), 130.2 (ArCH(major)), 130.3 (ArCH (minor)), 136.8 (Ar(minor)), 137.4 (Ar(major)), 145.0 (Ar (major)), 145.1 (Ar(minor)). Assignment was determined with the aid of HSQC and HMBC experiments. m/z 310 (M, 3%), 256 (M−3×H_2O, 11), 155 (M−$TolSO_2$, 83), 91 (Tol, 96).

Further elution gave a mixture of (2*R**,4*R**,5*S**)-2-methyl-4-(*para*-toluenesulfonyl)-1,6-dioxaspiro-[4.5]decane (**15c**) and (2*R**,4*S**,5*R**)-2-methyl-4-(*para*-toluenesulfonyl)-1,6-dioxaspiro[4.5]decane (**15d**) as colourless needles (0.15 g, 1.3:1 by comparison of the α-sulfonyl proton signals at 3.34 (minor) and 3.38 (major) ppm in the ^{1}H NMR spectrum, 60%), mp 144–146°C. (Found: C, 61.7%; H, 7.1%. $C_{16}H_{22}O_4S$ requires C, 61.9%; H, 7.1%). ν_{max} (paraffin) 1595, 1450, 1360, 1320, 1290, 1285, 1265, 1240, 1205, 1195, 1150, 1140, 1120, 1085, 1070, 1040, 1015, 970, 945, 900, 890, 870, 810, 730, 705, 670, 630 cm^{-1}. ^{1}H NMR (600 MHz, $CDCl_3$) δ 1.21 (d, *J*=6.2 Hz, 3H(major), 1×RCH_3), 1.28 (d, *J*=6.2 Hz, 3H(minor), 1×RCH_3), 1.44–1.65 (m, 4H(major)+4H(minor), 2×H8, 2×H9a+2×H10a), 1.71–1.77 (m, 1H(major)+1H(minor), 2×H9b), 1.80 (ddd, *J*=12.7, 10.4, 5.9 Hz, 1H(major), 1×H3a), 2.02 (td, *J*=13.3, 4.8 Hz, 1H(major), 1×H10b), 2.12 (td, *J*=13.3, 4.8 Hz, 1H(minor), 1×H10b), 2.21 (td, *J*=12.1, 8.7 Hz, 1H(minor), 1×H3a), 2.34 (ddd, *J*=12.0, 7.7, 6.7 Hz, 1H(minor), 1×H3b), 2.44 (s, 3H(major)+3H(minor), 2×$ArCH_3$), 2.64 (ddd, *J*=12.7, 8.8, 8.0 Hz, 1H(major), 1×H3b), 3.34 (dd, *J*=12.2, 7.7 Hz, 1H(minor), 1×H4), 3.38 (dd, *J*=10.4, 8.8 Hz, 1H(major), 1×H4), 3.62–3.66 (m, 1H(major)+1H(minor), 2×H7a), 3.73 (ddd, *J*=12.6, 11.1, 2.6 Hz, 1H(major), 1×H7b), 3.81 (ddd, *J*=12.7, 11.1, 2.5 Hz, 1H(minor), 1×H7b), 4.18 (d of quintets, *J*=8.7, 6.3 Hz, 1H(minor), 1×H2), 4.24 (d of quintets, *J*=8.1, 6.2 Hz, 1H(major), 1×H2), 7.32 (d(br), J_{av}=8.6 Hz, 2H(major)+2H(minor), ArH), 7.79 (d, *J*=8.3 Hz, 2H(minor), ArH), 7.80 (d, *J*=8.4 Hz, 2H(major), ArH). Assignment was determined with the aid of COSY and HSQC experiments. ^{13}C NMR (150.9 MHz, $CDCl_3$) δ 20.2 (C9(major+minor)), 21.7 (RCH_3(major)), 22.1 ($ArCH_3$(major+minor)), 23.5 (RCH_3(minor)), 25.0 (C8(major)), 25.2 (C8(minor)), 32.8 (C10(major)), 33.1 (C10(minor)), 33.8 (C3(major)), 34.3 (C3(minor)), 61.6 (C7(major+minor)), 71.1 (C4(major)), 71.9 (C2(major)), 72.0 (C4(minor)), 74.1 (C2(minor)), 104.3 (C5(minor)), 104.9 (C5(major)), 129.7 (ArCH(major+minor)), 129.9 (ArCH(major+minor)), 137.0 (Ar(minor)), 137.2 (Ar(major)), 144.8 (Ar(minor)), 144.9 (Ar(major)). Assignment was determined with the aid of HSQC and HMBC experiments. *m/z* 310 (M, 1%), 155 (M−$TolSO_2$, 44), 91 (Tol, 100).

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References

1. Franke, W.; Heeman, V.; Gerken, B.; Renwick, J. A. A.; Vite, J. P. *Naturwissenschaften* **1977**, *64*, 590–591.
2. Perkins, M. V.; Kitching, W.; König, W. A.; Drew, R. A. I. *J. Chem. Soc., Perkin Trans. 1* **1990**, 2501–2506.
3. Baker, R.; Herbert, R.; Howse, P. E.; Jones, O. T.; Franke, W.; Reith, W. *J. Chem. Soc., Chem. Commun.* **1980**, 52–53.
4. Tachibana, K.; Scheuer, P. J.; Tsukitani, Y.; Eugen, D. V.; Clardy, J.; Gopichand, Y.; Schmitz, F. J. *J. Am. Chem. Soc.* **1981**, *103*, 2469–2471.
5. For a review of the naming, synthesis, and structure determination of these compounds, see: Pietruszka, J. *Angew. Chem., Int. Ed. Engl.* **1998**, *37*, 2629–2636.
6. Vaillancourt, V.; Pratt, N. E.; Perron, F.; Albizati, K. F. In *The Total Synthesis of Natural Products*, ApSimon, J., Ed.; Wiley-Interscience: New York, 1992; 8, pp 533–691.
7. Edwards, G. L.; Muldoon, C. A.; Sinclair, D. J. *Tetrahedron* **1996**, *52*, 7779–7788.
8. Edwards, G. L.; Sinclair, D. J.; Wasiowych, C. D. *Synlett* **1997**, 1285–1286.
9. Edwards, G. L.; Sinclair, D. J. *Tetrahedron Lett.* **1999**, *40*, 3933–3934.
10. Kocienski, P.; Yeates, C. *Tetrahedron Lett.* **1983**, *24*, 3905–3906.
11. Ley, S. V.; Lygo, B. *Tetrahedron Lett.* **1984**, *25*, 113–116.
12. Ley, S. V.; Lygo, B.; Wonnacott, A. *Tetrahedron Lett.* **1985**, *26*, 535–538.
13. Ley, S. V.; Lygo, B.; Sternfeld, F.; Wonnacott, A. *Tetrahedron* **1986**, *42*, 4333–4342.
14. Greck, C.; Grice, P.; Ley, S. V.; Wonnacott, A. *Tetrahedron Lett.* **1986**, *27*, 5277–5280.
15. McDougal, P. G.; Rico, J. G.; Oh, Y.-I.; Condon, B. D. *J. Org. Chem.* **1986**, *51*, 3388–3390.
16. Nicolaou, K. C.; Papahatjis, D. P.; Claremon, D. A.; Magolda, R. L.; Dolle, R. E. *J. Org. Chem.* **1985**, *50*, 1440–1456.
17. Nyström, J.-E.; McCanna, T. D.; Helquist, P.; Amouroux, R. *Synthesis* **1988**, 56–58.
18. Deslongchamps, P. *Stereoelectronic Effects in Organic Chemistry*; Pergamon: Oxford, 1983, pp 4–53.
19. Nakamura, K.; Kitayama, T.; Inoue, Y.; Ohno, A. *Tetrahedron* **1990**, *46*, 7471–7481.
20. In the absence of boron trifluoride, the yield of the cyclohexene oxide adduct dropped to 19%.
21. Both structural diagrams use crystallographic numbering systems, which differ from the numbering system used in the text.
22. Still, W. C.; Kahn, M.; Mitra, A. *J. Org. Chem.* **1978**, *43*, 2923–2925.
23. Suffert, J. *J. Org. Chem.* **1989**, *54*, 509–510.