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Allylic Functionalization of the 1,7-Dioxaspiro[5.5]-undec-4-ene and 1,6,8-Trioxadispiro[4.1.5.3]-pentadec-13-ene Ring Systems.

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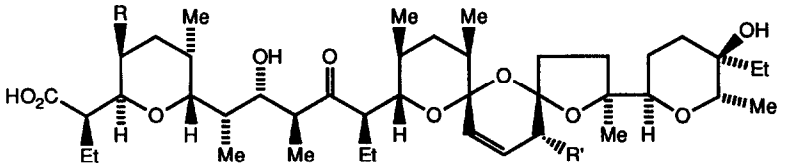
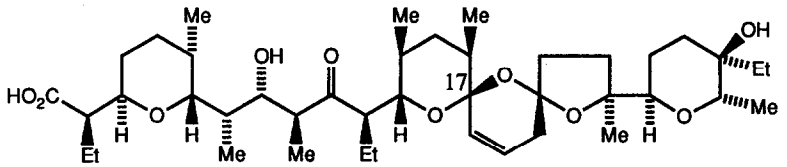
Abstract: Allylic bromination of the bicyclic spiroacetals **5, 6** and **7** gave predominantly the axial bromides **15, 21** and **23** which underwent S_N2 displacement to the equatorial alcohols **17, 22** and **25** respectively, using potassium superoxide and 18-crown-6 in THF/DMSO (10:1). Allylic bromination of the *cis*-bis-spiroacetal **26** gave predominantly the rearranged allylic bromide **29** which afforded alcohols **30** and **31** resulting from both S_N2' and S_N2 displacement upon treatment with potassium superoxide. Bromination of the *trans*-bis-spiroacetal **27** afforded a complex mixture from which only the non-rearranged bromide **34** could be isolated. This bromide **34** afforded the axial alcohol **37** upon treatment with potassium superoxide.

INTRODUCTION

The polyether antibiotics salinomycin **1**[1] and narasin A **2**[2] exhibit antimicrobial activity against gram-positive bacteria, mycobacteria and yeast. Moreover, they have adopted an important role in veterinary medicine as growth promotants for ruminants and in the treatment of coccidial infections in poultry. We have recently prepared[3] the *bis*-spiroacetal moiety of *epi*-17-deoxy-(*O*-8)-salinomycin **3** [namely *bis*-spiroacetal **4**]. In order to extend this methodology to the synthesis of salinomycin and narasin A a mild method for introduction of an hydroxyl group at the allylic position of the unsaturated spiroacetal ring was required.



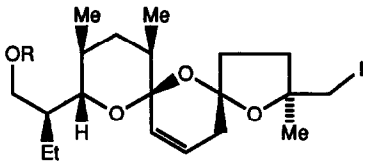
Salinomycin **1** : R=H R'=OH
Narasin A **2** : R=Me R'=OH



epi-17-Deoxy-(*O*-8)-salinomycin **3**

Whilst Deslongchamps *et al*[4] have successfully used the classical reagent, selenium dioxide, to oxidize the allylic position of a bicyclic spiroacetal this reagent proved ineffective for tricyclic spiroacetals due to the lability of the *bis*-spiro ring. An alternative strategy[5,6] utilising the oxidative rearrangement of a 2-furyl ketone to an unsaturated spiroacetal containing a carbonyl group at the allylic position gave the wrong stereochemistry upon reduction to the alcohol *(vide infra)*. In view of the numerous methods available to

synthesize unsaturated spiroacetals[7] it was decided to investigate the introduction of an allylic hydroxyl group *via* allylic bromination followed by nucleophilic displacement of the bromide using potassium superoxide.



4 : R=Si^{t}BuPh$_2$

RESULTS AND DISCUSSION

In order to study the stereochemical outcome of the intended allylic bromination, a series of bicyclic spiroacetals was prepared (Scheme 1) with no substituent at C-2, **6**, a methyl group at C-2, **5**, and two methyl groups at C-2, **7**. Thus, addition of the acetylide anion derived from the protected acetylenes **9-11** to δ-valerolactone **8** followed by treatment with acidic methanol provided the methoxyacetals **12-14** in 74-76% overall yield. Partial hydrogenation of the acetylenes **12-14** to the *cis*-alkenes over Lindlar catalyst followed by acid catalysed cyclization using a catalytic quantity of pyridinium *p*-toluenesulphonate (PPTS) in dichloromethane afforded the spiroacetals **5-7** in 50-80% yield. In this thermodynamically controlled cyclization step the most stable conformation of the spiroacetals was formed in which each ring oxygen is axial to the adjacent ring thereby gaining stability from the anomeric effect.

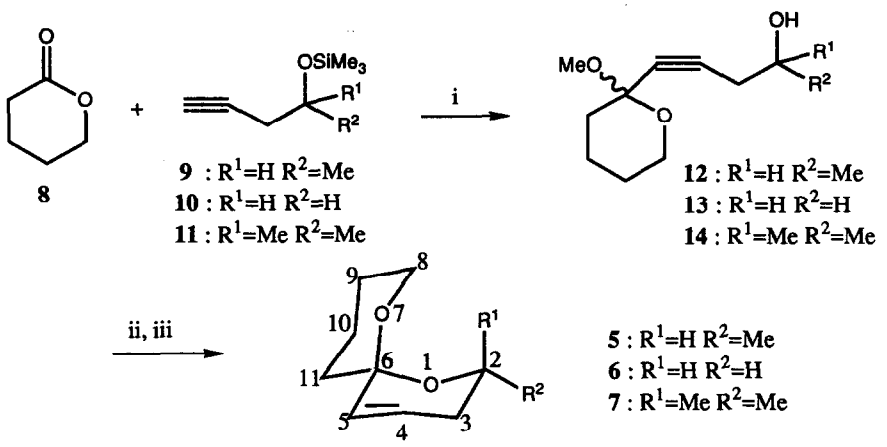
Having synthesized the required spiroacetals **5-7** the allylic bromination was investigated. Initial work was carried out on the monomethyl spiroacetal **5** because the presence of the methyl group at C-2 simplified the ^{1}H n.m.r. spectra of the allylic bromides and allowed ready assignment of the stereochemistry at C-3.

Treatment of spiroacetal **5** with N-bromosuccinimide (NBS) (1.0 equiv.) in carbon tetrachloride at reflux for 3 h. afforded bromides **15** and **16** in 51% and 25% yield respectively after purification by flash chromatography (Table). The major bromide was assigned as the axial bromide **15** and the minor bromide as the equatorial bromide **16** using ^{1}H n.m.r. spectroscopy.

In the ^{1}H n.m.r. spectrum for the axial bromide **15** the vinylic proton, 5-H resonated at δ 5.65 as a doublet, $J_{4,5}$ 9.9 Hz whilst the other vinylic proton, 4-H, resonated at δ 6.14 as a double doublet with $J_{4,5}$ 9.9 and $J_{3eq,4}$ 5.5 Hz. The allylic proton 3_{eq}-H, resonated as a double doublet at δ 4.35 with $J_{3eq,4}$ 5.5 and $J_{2ax,3eq}$ 2.2 Hz. The small magnitude of this latter coupling constant was consistent with the bromine atom at C-3 occupying an axial position.

In the ^{1}H n.m.r. spectrum for the equatorial bromide **16** the vinylic proton 5-H resonated as a double doublet at δ 5.61 with coupling constants, $J_{4,5}$ 10.0 and $J_{3ax,5}$ 1.8 Hz. The vinylic proton, 4-H also resonated as a double doublet at δ 5.97 with coupling constants $J_{4,5}$ 10.0 and $J_{3ax,4}$ 1.8 Hz. The allylic proton 3_{ax}-H, in this case resonated at δ 4.23 as a double double doublet, $J_{3ax,4}$ 1.8, $J_{3ax,5}$ 1.8 and $J_{2ax,3ax}$ 9.9 Hz. This latter large coupling constant established that the protons at C-2 and C-3 were 1,2-diaxial, thus confirming the assignment of both the methyl group at C-2 and the bromine atom at C-3 to be occupying equatorial positions.

The preferential formation of the axial bromide **15** over the equatorial bromide **16** (2:1) reflects the greater stability of the axial allylic radical over the equatorial allylic radical. Observation of coupling between the methine proton at C-2 and the allylic proton clearly established that allylic rearrangement had not taken place as such coupling would not be observed in the rearranged bromide.



Scheme 1. *Reagents* : (i) ^{n}BuLi, -78°C, THF, 0.75 h., then (**8**) 0.75 h., then MeOH, amberlite resin, room temp., 12 h., 74-76 % ; (ii) H_2, Lindlar, hexane / ethyl acetate ; (iii) CH_2Cl_2, PPTS, room temp. 0.5 h., 64-80 % .

The major axial bromide **15** underwent S_N2 displacement to the equatorial alcohol **17** upon treatment with potassium superoxide and 18-crown-6 in THF : DMSO (10:1) in 85% yield whilst the minor equatorial bromide **16** afforded the axial alcohol **18** in 87% yield. Assignment of the stereochemistry of the isomeric alcohols **17** and **18** was made using ^{1}H n.m.r. spectroscopy. Thus, the axial alcohol **18** exhibited the same coupling pattern in the vinylic region as the axial bromide **15** with 5-H resonating as a doublet at δ 5.75, $J_{4,5}$ 9.9 Hz and 4-H resonating at δ 6.08 as a double doublet, $J_{4,5}$ 9.9 and $J_{3eq,4}$ 1.8 Hz.

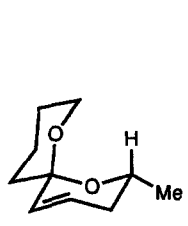
Conversion of the alcohols **17, 18** to their acetate derivatives **19, 20** also confirmed assignment of stereochemistry at C-3. The allylic proton 3-H in the axial acetate **20** resonated as a double doublet at δ 4.93 $J_{3,4}$ 5.3 Hz and $J_{3eq,2ax}$ 2.6 Hz, whilst this same proton in the equatorial acetate **19** resonated as a double double doublet at δ 5.01, $J_{2ax,3ax}$ 9.1, $J_{3ax,4}$ 1.5, and $J_{3ax,5}$ 1.5 Hz. The larger coupling constant observed for this isomer established that the protons at C-2 and C-3 were 1,2-diaxial hence the methyl and hydroxyl groups were equatorial.

Treatment of the unsubstituted spiroacetal **6** with NBS using the same conditions used for the monomethyl spiroacetal **5** afforded the axial bromide **21** in 54% yield. The ^{1}H n.m.r. spectrum for this bromide **21** resembled both the monomethyl axial bromide **15** and the alcohol **18** in the vinylic region. The corresponding equatorial bromide was not isolated, however, t.l.c. analysis of the reaction mixture did reveal the presence of a minor component similar in R_f to axial bromide **21.** Isolation of this component and subsequent ^{1}H n.m.r. analysis suggested the presense of both the equatorial bromide and a diene. Attempts to separate these compounds were unsuccessful.

Conversion of the axial bromide **21** to the equatorial alcohol **22** proceeded in 84% yield. The ^{1}H n.m.r. spectrum in the vinylic region of alcohol **22** was analogous to both the monomethyl equatorial bromide **16** and alcohol **17**, thus establishing that an S_N2 displacement had occurred as was observed in the monomethyl series.

Focusing next on the dimethyl series, spiroacetal **7** was treated with NBS affording the bromides **23** and **24** in 48% and 24% yield respectively. The ^{1}H n.m.r. spectra for both bromides had the same type of coupling pattern in the vinylic region as the axial bromides **15** and **21** suggesting the bromine atom occupied an axial position in both isomers. The mass spectra for the isomeric bromides provided evidence for assignment of the major bromide as the non-rearranged axial bromide **23** and the minor isomer as the

Table. Allylic Functionalization of the 1,7-Dioxaspiro[5.5]undec-4-ene Ring System.



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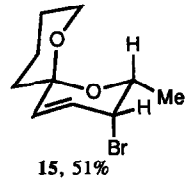
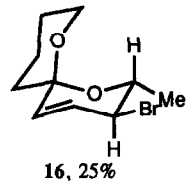
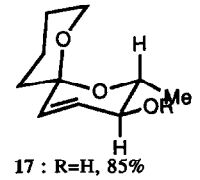


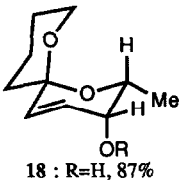
15, 51%



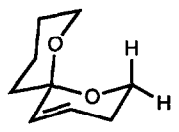
16, 25%



17 : R=H, 85%
19 : R=Ac



18 : R=H, 87%
20 : R=Ac



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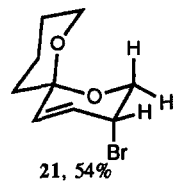
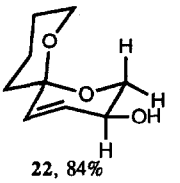
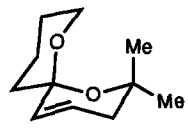


21, 54%



22, 84%



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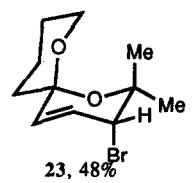
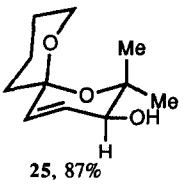
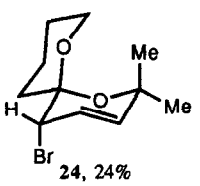


23, 48%



25, 87%

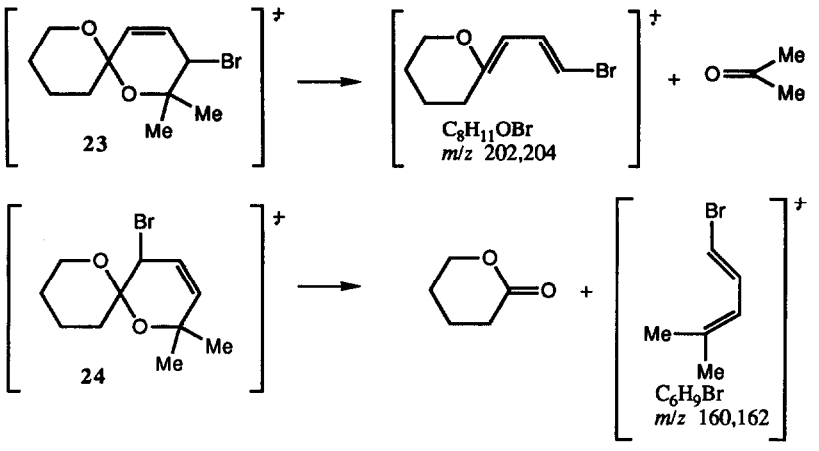


24, 24%

rearranged axial bromide **24**. Thus, bromide **23** underwent a characteristic retro-Diels-Alder fragmentation giving ions at *m/z* 202,204 whilst bromide **24** underwent a retro-Diels-Alder fragmentation giving ions at *m/z* 160,162 (Scheme 2).

The non-rearranged bromide **23** was treated with potassium superoxide yielding the equatorial alcohol **25**. The ^{1}H n.m.r. spectrum of this alcohol **25** resembled the spectra of the equatorial alcohols **22** and **17** in the vinylic region. This observation together with the characteristic retro-Diels-Alder fragmentation at *m/z* 140 established that the hydroxyl group was attached to C-3 and that S_N2' displacement to the rearranged alcohol had not taken place.

Having successfully effected an indirect allylic oxidation of the bicyclic unsaturated spiroacetals, a logical extension of this work was to apply these same reactions to the tricylic bis-spiroacetals **26** and **27**. The methodology so developed might then be applied to the conversion of *epi*-17-deoxy-(*O*-8)-salinomycin **3** into salinomycin **1**.



Scheme 2

Heating a solution of *cis*-bis-spiroacetal **26** with a slight excess of NBS resulted in formation of two diastereomeric bromides **28** and **29** in 23% and 42% yield respectively (Scheme 3). Both products exhibited similar ^{1}H n.m.r. spectra and the assignment of regiochemistry was made on the basis of the fragmentation pattern in the mass spectrum of each. Thus, the mass spectrum of **28** exhibited peaks at *m/z* 202,204 arising from a retro-Diels-Alder fragmentation of the unsaturated *bis*-spiroacetal substituted at C-15 whereas the other bromide **29** exhibited peaks at *m/z* 216,218 consistent with a retro-Diels-Alder fragmentation of an allylic bromide substituted at C-13.

Treatment of the major *cis*-bromide **29** with potassium superoxide and 18-crown-6 in dimethyl sulphoxide afforded an inseparable mixture of the alcohols **30** and **31**.(1.5 :1) in 65% yield which were then separated by flash chromatography upon conversion to their acetate derivatives **32** and **33**. Once again mass spectrometry confirmed the regiochemistry at the two acetates. Thus, acetate **32** exhibited characteristic retro-Diels-Alder fragmentations at *m/z* 182 and 140 whereas acetate **33** exhibited retro-Diels-Alder fragmentations at *m/z* 196 and 154.

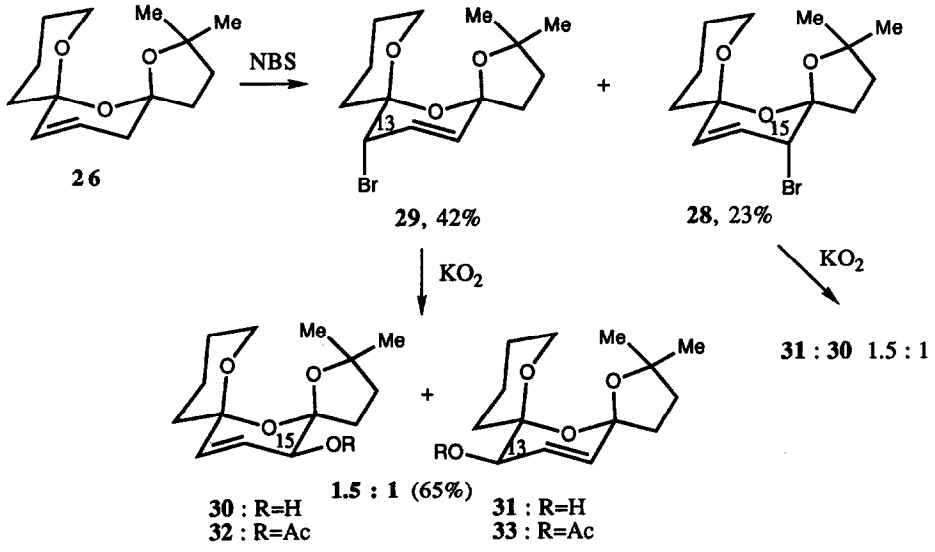
The ^{1}H n.m.r. data for acetate **32** was in agreement with that reported by Kocienski *et al* [5,9] for the same product prepared by reduction of the ketone further confirming that the acetoxy group in this isomer was attached to C-15. The CHOAc protons for the isomeric acetates **32** and **33** resonated at similar chemical shifts (δ 4.89 for **33** and δ 4.86 for **32**) implying that the orientation of these protons on their respective ring systems was the same. If the relative orientations differed then the resulting 1,2-*syn* relationship of one CHOAc proton with a C-O bond of a neighbouring ring would cause a significant deshielding effect. This relative deshielding effect has been observed by Kocienski *et al*[5] in the course of their work on this ring system.

The minor *cis*-bromide **28** was also treated with potassium superoxide and 18-crown-6 in dimethyl sulphoxide to afford an inseparable mixture of the alcohols **30** and **31** in 61% yield. In this case the 13-hydroxybis-spiroacetal **31** predominated over the 15-hydroxybis-spiroacetal **30** by 1.5:1. Once again, conversion to the acetate derivatives **32** and **33** allowed separation of the individual isomers.

The experimental results outlined above indicate that displacement of the bromides **28** and **29** occurs *via* S_N2 and S_N2' processes. Moreover, the S_N2' process in both cases was favoured and proceeded in an *anti* fashion[10].

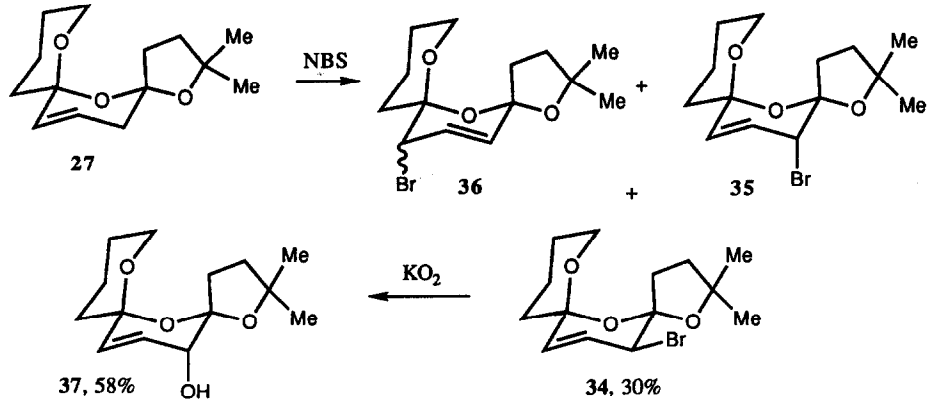
Allylic bromination of the *trans*-bis-spiroacetal **27** afforded two components by t.l.c. (Scheme 4). After purification by flash chromatography and subsequent ^{1}H n.m.r. analysis the first fraction was found to be the unrearranged allylic bromide **34** (30%). The second fraction, however, was found to be a complex mixture

comprising starting material **27**, and the bromides **35** and **36**. Since these products could not be isolated individually further experimentation with this fraction was not pursued. Displacement of the bromide **34**, however, with potassium superoxide in dimethyl sulphoxide using 18-crown-6 afforded alcohol **37** in 58% yield. The stereochemistry of this displacement product was confirmed by comparison of its ^{1}H n.m.r. spectrum with that reported by Kocienski *et al.*[5,9].



Scheme 3

In summary, an hydroxyl group has been introduced at the allylic position, C-15, of the 1,6,8-trioxadispiro[4.1.5.3]pentadec-13-enes **26** and **27** *via* allylic bromination. However, the feasibility of this methodology is complicated by a variety of regiochemical and stereochemical outcomes. Nevertheless, alcohol **30** does have the same stereochemistry as that present in salinomycin **1** and narasin A **2**.



Scheme 4

EXPERIMENTAL

General Methods.

Melting points were determined on a Kofler hot stage apparatus and are uncorrected. Infrared (IR) spectra were obtained using a BIO-RAD FTS-7 or a BIO-RAD FTS-40 spectrometer. ^{1}H NMR spectra were obtained at 270 MHz using a JEOL GX270 spectrometer or at 60 MHz using a Hitachi R-1200 spectrometer. Chemical shifts are given in parts per million downfield shift from tetramethylsilane as internal reference. ^{13}C NMR spectra were obtained at 67.8 MHz using a JEOL GX270 spectrometer. Mass spectra were recorded using a Varian VG70-250S double focusing magnetic sector mass spectrometer with an ionisation potential of 70 eV. Elemental analyses were performed at the microanalytical laboratory, University of Otago, Dunedin. Merck Kieselgel 60 (230-400 mesh) was used for flash chromatography. All solvents and reagents were purified and dried if necessary before use. 3-Butyn-1-ol and 4-pentyn-2-ol were purchased from the Aldrich Chemical Company. *Bis*-spiroacetals **26** and **27** were prepared as previously reported[11].

Preparation of trimethylsilyl ethers.

General procedure. Chlorotrimethylsilane (2.14g, 19.6 mmol) was added to a mixture of the appropriate alcohol (19.6 mmol) and dry triethylamine (5.45 ml, 39.2 mmol) in dry tetrahydrofuran (100 ml) at room temperature under nitrogen. The reaction mixture was stirred at room temperature for 16 h. whereupon a white precipitate formed. Water (10 ml) was added and the reaction mixture extracted with diethyl ether (3 x 60 ml). The ethereal extract was washed with water (40 ml) and dried over magnesium sulphate. Removal of solvent at reduced pressure afforded a pale yellow oil which was purified by flash chromatography using 4:1 hexane : ethyl acetate as eluant to give the desired trimethylsilyl ether.

2-Trimethylsilyloxy-4-pentyne (9). Prepared from 4-pentyn-2-ol (1.65 g, 19.6 mmol) as a colourless oil (2.05 g, 67%), b.p. 135-40°C / 760 mm Hg; δ_H (60 MHz; $CDCl_3$) 0.33 (9H, s, $SiMe_3$), 1.46 (3H, d, *J* 6 Hz, Me), 2.02 (1H, t, *J* 3 Hz, HC≡C), 2.28-2.48 (2H, m, CH_2) and 4.07 (1H, m, *J* 6 Hz, CHO).

1-Trimethylsilyloxy-3-butyne (10). Prepared from 3-butyn-1-ol (1.37 g, 19.6 mmol) as a pale yellow oil (2.06 g, 74%); δ_H (60 MHz; $CDCl_3$) 0.33 (9H, s, $SiMe_3$), 1.72 (1H, *J* 2 Hz, HC≡C), 3.26 (2H, dt, *J* 3, *J* 7 Hz, $CH_2C{\equiv}C$) and 3.57 (2H, *J* 7 Hz, CH_2OSi).

2-Methyl-2-trimethylsilyloxy-4-pentyne (11). Prepared from 2-methyl-4-pentyn-2-ol[12] (1.92 g, 19.6 mmol) as a pale yellow oil (1.67 g, 55%); δ_H (60 MHz; $CDCl_3$) 0.33 (9H, s, $SiMe_3$), 1.24 (6H, s, 2 x Me), 1.75 (1 H, t, *J* 3 Hz, HC≡C) and 2.26 (2H, d, *J* 3 Hz, $CH_2C{\equiv}C$).

Preparation of Methoxyacetals.

General procedure: A solution of n-butyllithium (4.28 ml, 6.85 mmol) was added to a solution of the appropriate trimethylsilyl ether (6.23 mmol) in dry tetrahydrofuran (950 ml) at -78°C under a nitrogen atmosphere. The resulting solution was stirred for 0.75 h. and a solution of δ-valerolactone (7.48 mmol) in tetrahydrofuran (10 ml) was added. After a further 0.75 h. the reaction mixture was quenched with ammonium chloride (5 ml) and allowed to warm to room temperature. After extraction with diethyl ether (2 x 50 ml) the combined ether extracts were washed with water (30 ml) and dried over magnesium sulphate. Removal of the solvent under reduced pressure yielded an oil which was dissolved in methanol (40 ml) and stirred for 12 h. with Amberlite resin. The reaction mixture was then filtered into a flask containing triethylamine (3 drops) and the solvent was removed at reduced pressure to give an oil, which was purified by flash chromatography, using 4 : 1 hexane : ethyl acetate as eluant. Methoxyacetals **12, 13, 14** were unstable therefore elemental analysis was not obtained.

1-(Tetrahydro-2-methoxypyran-2-yl)-1-pentyn-4-ol (12). Prepared from 2-trimethylsilyloxy-4-pentyne (**9**) (972 mg, 6.23 mmol) and δ-valerolactone (**8**) (749 mg, 7.48 mmol) as a colourless oil (987 mg, 80%); υ_{max} (thin film) 3422 (s, OH) and 2214 cm^{-1} (C≡C); δ_H (60 MHz; $CDCl_3$) 1.30 (3H, d, *J* 7 Hz, Me), 1.43-2.19 (6H, m, 3 x CH_2), 2.49 (2H, d, *J* 6 Hz, $CH_2C{\equiv}C$), 3.50 (3H, s, OMe) and 3.64-4.32 (3H, m, CH_2O

and CHOH); *m/z* 183 (M-Me, 5%), 167 (M-OMe, 74), 122 (M-OMe-C_2H_5O, 100) and 67 (72).

1-Tetrahydro-2-methoxypyran-2-yl)-1-butyn-4-ol (13). Prepared from 1-trimethylsilyloxy-3-butyne (**10**) (885 mg, 6.23 mmol) and δ-valerolactone (**8**) (749 mg, 7.48 mmol) as an oil (848 mg, 74%); υ_{max} (thin film) 3400 (br s, OH) and 2220 cm^{-1} (w, C≡C); δ_H (60 MHz; $CDCl_3$) 1.31-1.98 (6H, m, 3 x CH_2), 2.20-2.61 (2H, m, $CH_2C{\equiv}C$), 3.15-3.98 (4H, m, CH_2O and CH_2OH) and 3.60 (3H, s, OMe); *m/z* 153 (M-OMe, 100), 115 (61), 101 (54), 97 (47) and 55 (28).

4-Methyl-1-(tetrahydro-2-methoxypyran-2-yl)-1-pentyn-4-ol (14). Prepared from 2-methyl-2-trimethylsilyloxy-4-pentyne (**11**) (1.06 g, 6.23 mmol) and δ-valerolactone (**8**) (749 mg, 7.48 mmol) as an oil (1.01 g, 76%); υ_{max} (thin film) 3430 (s, OH) and 2230 cm^{-1} (C≡C); δ_H (60 MHz; $CDCl_3$) 1.32 (6H, s, 2 x Me), 1.61-2.18 (6H, m, 3 x CH_2), 2.14-2.68 (2H, m, $CH_2C{\equiv}C$), 3.48 (3H, s, OMe) and 3.50-4.33 (2H, m, CH_2O); *m/z* 212 (M^+, 0.2%), 197 (M-Me, 5), 181 (M-OMe, 100), 122 (C_8H_8O, 86) and 59 (92).

Preparation of Spiroacetals.

General Procedure: A solution of the appropriate methoxyacetal (5.33 mmol) in 4 : 1 hexane : ethyl acetate (30 ml) was stirred with Lindlar catalyst and potassium carbonate (150 mg) for 16h. under a balloon of hydrogen. The reaction mixture was then filtered and the solvent removed at reduced pressure to afford a colourless oil. The oil was dissolved in dichloromethane (20 ml), pyridinium *p*-toluenesulphonate (10 mg) was added and the reaction mixture was left to stand for 1h. Evaporation of the dichloromethane followed by purification of the residue by flash chromatography using 9 : 1 hexane : diethyl ether as eluant afforded the desired spiroacetal.

2-Methyl-1,7-dioxaspiro[5.5]undec-4-ene (5). Prepared from methoxyacetal (**12**) (1.06 g, 5.33 mmol) as a colourless oil (573 mg, 64%); (Found: C, 71.1; H, 9.6. $C_{10}H_{16}O_2$ requires C, 71.4; H, 9.6%); δ_H (270 MHz; $CDCl_3$) 1.26 (3H, d, *J* 6.6 Hz, Me) 1.53-1.95 (8H, m, 4 x CH_2), 3.57-3.64 (1H, m, 8_{eq}-H), 3.85 (1H, ddd, $J_{8ax,8eq}$ 11.6, $J_{8ax,9ax}$ 2.9 Hz, $J_{8ax,9eq}$ 2.9 Hz, 8_{ax}-H) 3.98-4.06 (1H, m CHMe), 5.62 (1H, ddd, $J_{4,5}$ 10.3, $J_{3,5}$ 1.5, $J_{3',5}$ 2.6 Hz, 5-H) and 5.86-5.92 (1H, m, 4-H); δ_C (67.8 MHz; $CDCl_3$) 18.5, 25.1, 32.3 (t, C9, C10, C11), 21.3 (q, Me), 34.9 (t, C3), 60.7 (t, C8), 63.1 (d, C2), 94.0 (s, C6), 127.9 (d, C5) and 130.4 (d, C4); *m/z* 168 (M^+, 52%), 140 ($C_8H_{12}O_2$, 62), 110 (83) and 98 (100).

1,7-Dioxaspiro[5.5]undec-4-ene (6). Prepared from methoxyacetal (**13**) (981 mg, 5.33 mmol) as a colourless oil (657 mg, 80%); δ_H (270 MHz; $CDCl_3$) 1.40-1.96 (7H, m, 3 x CH_2 and 3-H) 2.12-2.37 (1H, m, 3'-H), 3.50-3.99 (4H, m, 2 x OCH_2), 5.62 (1H, ddd, $J_{4,5}$ 10.3, $J_{3,5}$ 1.5 Hz, $J_{3',5}$ 2.9 Hz, 5-H) and 5.91-5.97 (1H, m, 4-H); δ_C (67.8 MHz; $CDCl_3$) 18.6, 24.7, 25.0 (t, C9, C10, or C11), 34.8 (t, C3), 57.7 (t, C2), 60.8 (t, C8), 92.8 (s, C6), 127.7 (d, C5) and 130.6 (d, C4). These ^1H n.m.r data are in agreement with that reported previously[13] for spiroacetal (**6**).

2,2-Dimethyl-1,7-dioxaspiro[5.5]undec-4-ene (7). Prepared from methoxyacetal (**14**) (1.13 g, 5.33 mmol) as a colourless oil (485 mg, 50%); (Found: C, 72.4; H, 9.9. $C_{11}H_{18}O_2$ requires C, 72.5; H, 9.9%); δ_H (270 MHz; $CDCl_3$) 1.28 (3H, s, Me), 1.32 (3H, s, Me), 1.51-1.68 (6H, m, 3 x CH_2), 1.85-1.94 (1H, m, 3-H), 2.03-2.13 (1H, m, 3'-H), 3.54-3.59 (1H, m 8_{eq}-H), 3.96 (1H, ddd, $J_{8ax,8eq}$ 11.0, $J_{8ax,9ax}$ 11.0, $J_{8ax,9eq}$ 2.9 Hz, 8_{ax}-H), 5.65 (1H, ddd, $J_{4,5}$ 10.3, $J_{3,5}$ 1.5, $J_{3',5}$ 2.9 Hz, 5-H) and 5.80-5.86 (1H, m, 4-H); δ_C (67.8 MHz; $CDCl_3$) 18.7, 25.4, 36.3, 37.3 (t, C9, C10, C11, or C3), 26.0, 31.0 (q, 2 x Me), 60.7 (t, C8), 70.4 (s, C2), 93.4 (s, C6), 125.3 (d, 5) and 129.7 (d, C4); *m/z* 182 (M^+, 19%), 127 ($C_8H_{12}O$, 39) and 98 ($C_6H_{10}O$, 100).

Preparation of Bromospiroacetals.

General Procedure. N-Bromosuccinimide (356 mg, 2.0 mmol) was added to a solution of the appropriate spiroacetal (2.0 mmol) in carbon tetrachloride containing anhydrous potassium carbonate (50 mg). The resulting reaction mixture was heated under reflux for 3h., allowed to cool and filtered. Evaporation of the filtrate at reduced pressure afforded a pale yellow oil which was purified by flash chromatography using

9:1 hexane : diethyl ether as eluant yielding the desired bromospiroacetal. The allylic bromides were unstable therefore elemental analyses are not reported.

3-Bromo-2-methyl-1,7-dioxaspiro[5.5]undec-4-ene (15), (16). Prepared from spiroacetal (**5**) (336 mg, 2.0 mmol) and *N*-bromosuccinimide (356 mg, 2.0 mmol). Purification by flash chromatography using 9:1 hexane : diethyl ether as eluant gave *bromospiroacetal (15)* as colourless needles (230 mg, 51%) m.p 82-83 °C; δ_H (270 HMz; $CDCl_3$) 1.37 (3H, d, $J_{2,Me}$ 6.2 Hz, Me), 1.55-2.10 (6H, m, 3 x CH_2), 3.61-3.64 (1H, m, 8_{eq}-H), 3.83 (1H, ddd, $J_{8ax,8eq}$ 11.4, $J_{8ax,9ax}$ 11.4, $J_{8ax,9eq}$ 3.3 Hz, 8_{ax}-H), 4.03 (1H, dq, $J_{2ax,3eq}$ 2.2, $J_{2,Me}$ 6.2 Hz, 2_{ax}-H), 4.35 (1H, dd, $J_{3eq,4}$ 5.5, $J_{2ax,3eq}$ 2.2 Hz, 3_{eq}-H), 5.65 (1H, d, $J_{4,5}$ 9.9 Hz, 5-H) and 6.14 (1H, dd, $J_{4,5}$ 9.9, $J_{3eq,4}$ 5.5 Hz, 4-H); δ_C (67.8 MHz; $CDCl_3$) 18.2, 24.9, 34.4 (t, C9, C10, or C11), 20.4 (q, Me), 50.2 (d, C3), 61.3 (t, C8), 64.7 (d, C2), 94.3 (s, C6), 129.1 (d, C5) and 131.6 (d, C4); *m/z* 202,204 ($C_8H_{11}OBr$, 16%) and 167 (M-Br, 100) and *bromospiroacetal* (**16**) as a colourless oil (113 mg, 25%); δ_H (270 MHz; $CDCl_3$) 1.42 (3H, d, $J_{2,Me}$ 6.2 Hz, Me), 1.20-1.90 (6H, m, 3 x CH_2) 3.59-3.82 (2H, m, 8_{ax}-H, 8_{eq}-H), 4.09-4.18 (1H, m, 2_{ax}-H), 4.23 (1H, ddd, $J_{2ax,3ax}$ 9.9, $J_{3ax,4}$ 1.8, $J_{3ax,5}$ 1.8 Hz, 3_{ax}-H), 5.61 (1H, dd, $J_{4,5}$ 10.0, $J_{3ax,5}$ 1.8 Hz, 5-H) and 5.97 (1H, dd, $J_{4,5}$ 10.0, $J_{3ax,4}$ 1.8 Hz, 4-H); *m/z* 202,204 ($C_8H_{11}OBr$, 12%) and 167 (M-Br, 100)

3-Bromo-1,7-dioxaspiro[5.5]undec-4-ene (21). Prepared from spiroacetal (**6**) (302 mg, 2.00 mmol) and *N*-bromosuccinimide (356 mg, 2.00 mmol) as a colourless oil (252 mg, 54%); δ_H (270 MHz; $CDCl_3$) 1.42-1.98 (6H, m, 3 x CH_2), 3.60-3.98 (2H, m, 8_{ax}-H, 8_{eq}-H), 4.00 (1H, ddd, $J_{2ax,2eq}$ 13.2, $J_{2eq,3eq}$ 1.1 $J_{2eq,4}$ 1.5 Hz, 2_{eq}-H), 4.31 (1H, dd, $J_{2ax,2eq}$ 13.2, $J_{2ax,3eq}$ 2.9 Hz, 2_{ax}-H) 4.48 (1H, dd, $J_{3eq,4}$ 5.5, $J_{2ax,3eq}$ 2.9 Hz, 3_{eq}-H), 5.69 (1H, d, $J_{4,5}$ 9.9 Hz, 5-H) and 6.08 (1H, ddd, $J_{4,5}$ 9.9, $J_{4,3eq}$ 5.5, $J_{4,2eq}$ 1.5 Hz, 4-H); δ_C (67.8 MHz; $CDCl_3$) 18.3, 24.8, 34.3 (t, C9, C10, or C11), 42.3 (d, C3), 61.3 (t, C8), 64.1 (t, C2), 92.8 (s, C6), 128.1 (d, C5) and 132.4 (d, C4); *m/z* 153 (M-Br, 100%) and 101 ($C_5H_9O_2$, 68).

3-Bromo-2,2-dimethyl-1,7-dioxaspiro[5.5]undec-4-ene (23) and 5-Bromo-2,2-dimethyl-1,7-dioxaspiro[5.5]undec-3-ene (24). Prepared from spiroacetal (**7**) and *N*-bromosuccinimide (356 mg 2.00 mmol). Purification by flash chromatography using 9:1 hexane : diethyl ether gave *bromospiroacetal (23)* (260 mg, 48%) as a colourless oil; (Found: M-H, 259.0331. $C_{11}H_{16}O_2{}^{79}Br$ requires M-H, 259.0368); δ_H (270 MHz; $CDCl_3$) 1.46 (3H, s, Me), 1.47 (3H, s, Me), 1.38-2.01 (6H, m, 3 x CH_2), 3.57-3.62 (1H, m, 8_{eq}-H) 3.96 (1H, ddd, $J_{8ax,\ 8eq}$ 11.4, $J_{8ax,9ax}$ 11.4, $J_{8ax,9eq}$ 3.7 Hz, 8_{ax}-H), 4.34 (1H, d, $J_{3,4}$ 5.9 Hz, 3-H), 5.67 (1H, d, $J_{4,5}$ 9.9 Hz, 5-H) and 6.13 (1H, dd, $J_{4,5}$ 9.9, $J_{3,4}$ 5.9 Hz, 4-H); δ_C (67.8 MHz; CCl_4) 18.3, 25.0, 35.8 (t, C9, C10, or C11), 25.7, 30.6 (q, 2 x Me), 53.1 (d, C-3), 60.5 (t, C-8), 72.1 (s, C-2), 93.5 (s, C-6), 127.1 (d, C-5) and 130.7 (d, C-4); *m/z* 259,261 (M-H, 9%), 245,247 (M-Me, 7), 202,204 ($C_8H_{11}OBr$, 22) and 181 (M-Br, 100) and *bromospiroacetal (24)* (135 mg, 24%) as a colourless oil; (Found: M-H, 259.0334. $C_{11}H_{16}O_2{}^{79}Br$ requires M-H, 259.0368); δ_H (270 MHz; $CDCl_3$) 1.35 (3H, s, Me), 1.36 (3H, s, Me), 1.39-1.63 (5H, m, 9_{ax}-H, 9_{eq}-H, 10_{ax}-H, 10_{eq}-H, 11_{ax}-H), 2.26 (1H, ddd, $J_{11ax,11eq}$ 13.6, $J_{11eq,10eq}$ 3.1, $J_{11eq,10ax}$ 3.1 Hz, 11_{eq}-H), 3.60-3.65 (1H, m, 8_{eq}-H), 3.86 (1H, ddd, $J_{8eq,8ax}$ 11.0, $J_{8ax,9ax}$ 11.0, $J_{8ax,9eq}$ 4.0 Hz, 8_{ax}-H), 4.33 (1H, d, $J_{4,5}$ 5.9 Hz, 5-H), 5.75 (1H, d, $J_{3,4}$ 10.3 Hz, 3-H) and 5.99 (1H, dd, $J_{3,4}$ 10.3, $J_{4,5}$ 5.9 Hz, 4-H); δ_C (67.8 MHz; $CDCl_3$) 19.3, 25.0, 35.9, (t, C-9, C-10, or C-11), 29.2, 29.4, (q, 2 x Me), 49.0 (d, C-5), 62.5 (t, C-8) 72.7 (s, C-2), 95.7 (s, C-6), 121.9 (d, C-3), 135.9 (d, C-4); *m/z* 259, 261 (M-H 12%), 245,247 (M-Me, 22), 181 (M-Br, 72) and 162, 160, (C_6H_9Br, 100).

Preparation of Hydroxyspiroacetals.

General Procedure. Potassium superoxide (256 mg, 3.60 mmol) and 18-crown-6 (238 mg, 0.90 mmol) were added to a solution of the appropriate bromospiroacetal (0.90 mmol) in tetrahydrofuran (20 ml) and dimethylsulphoxide (1 ml). The reaction mixture was stirred for 3h. and then extracted with diethyl ether. The ether layer was then washed with water, dried over magnesium sulphate and the solvent removed under reduced pressure to produce a colourless oil which was purified by flash chromatography using 9:1 pentane : diethyl ether.

trans-3-Hydroxy-2-methyl-1,7-dioxaspiro[5.5]undec-4-ene (17). Prepared from *cis*-bromospiroacetal (**15**) as colourless prisms (139 mg, 85%) m.p. 77-8°C; (Found: C, 65.3; H, 8.6. $C_{10}H_{16}O_3$ requires: C, 65.2; H, 8.8%); υ_{max} (Nujol) 3449 (OH), 2943 (CH) and 1074 cm^{-1} (C-O); δ_H (270 MHz; $CDCl_3$) 1.37 (3H, d, $J_{2,Me}$ 6.2 Hz, Me), 1.40-2.02 (6H, m, 3 x CH_2), 3.61-3.86 (4H, m, 2_{ax}-H, 3_{ax}-H, 8_{ax}-H, 8_{eq}-H), 5.63 (1H, dd, $J_{4,5}$ 9.9, $J_{3ax,5}$ 1.8 Hz, 5-H) and 5.83 (1H, dd, $J_{4,5}$ 9.9, $J_{3ax,4}$ 1.8 Hz, 4-H); δ_C (67.8 MHz; $CDCl_3$) 18.0, 25.0, 34.5 (t, C-9, C-10 or C-11), 29.7 (q, Me), 61.4 (t, C-8), 68.7, 70.0 (d, C-2, C-3), 93.8 (s, C-6), 131.4 (d, C-5) and 132.3 (d, C-4); *m/z* 184 (M^+, 1%), 167 (M-H_2O, 7) and 140 ($C_8H_{12}O_2$, 100). Alcohol (**17**) was converted to its acetate derivative (**19**) using acetic anhydride/triethylamine/dimethylaminopyridine (cat.) in dichloromethane as a colourless oil, δ_H (270 MHz; $CDCl_3$) 1.24 (3H, d, *J* 6.6 Hz, Me), 1.45-1.96 (6H, m, 3 x CH_2), 2.07 (3H, s, $COCH_3$), 3.59-3.96 (1H, m, 8_{eq}-H), 3.80 (1H, ddd, $J_{8ax,8eq}$ 11.0, $J_{8ax,9ax}$ 11.0, $J_{8ax,9eq}$ 2.9 Hz, 8_{ax}-H), 3.93-3.99 (1H, m, 2_{ax}-H), 5.01 (1H, ddd, $J_{2ax,3ax}$ 9.1, $J_{3ax,4}$ 1.5, $J_{3ax,5}$ 1.5 Hz, 3_{ax}-H), 5.67 (1H, dd, $J_{4,5}$ 10.3, $J_{3ax,5}$ 1.5 Hz, 5-H) and 5.75 (1H, dd, $J_{4,5}$ 10.3, $J_{3ax,4}$ 1.5 Hz, 4-H); *m/z* 167 (M-$OCOCH_3$, 13%) and 140 ($C_8H_{12}O_2$, 100).

cis-3-Hydroxy-2-methyl-1,7-dioxaspiro[5.5]undec-4-ene (18). Prepared from *trans*-bromospiroacetal (**16**) as colourless needles (142 mg, 87%) m.p. 74-76°C ; (Found: C, 65.2; H, 8.6. $C_{10}H_{16}O_3$ requires: C, 65.2; H, 8.8%); υ_{max} (Nujol) 3552 (OH), 2960 (CH) and 1078 cm^{-1} (C-O); δ_H (270 MHz; $CDCl_3$), 1.31 (3H, d, $J_{2,Me}$ 6.6 Hz, Me), 1.53-2.02 (6H, m, 3 x CH_2), 3.57-3.66 (2H, m, 3_{eq}-H, 8_{eq}-H), 3.81 (1H, ddd, $J_{8ax,8eq}$ 11.4, $J_{8ax,9ax}$ 11.4, $J_{8ax,9eq}$ 3.3 Hz, 8_{ax}-H), 4.09 (1H, dq, $J_{2ax,3eq}$ 2.2, $J_{2,Me}$ 6.6 Hz, 2_{ax}-H), 5.75 (1H, d, $J_{4,5}$ 9.9 Hz, 5-H) and 6.08 (1H, dd, $J_{4,5}$ 9.9, $J_{3eq,4}$ 5.5 Hz, 4-H); δ_C (67.8 MHz; $CDCl_3$) 18.3, 24.9, 34.8 (t, C-9, C-10, or C-11), 29.7 (q, Me), 61.4 (t, C-8), 66.5, 76.5 (d, C-2, C-3), 94.0 (s, C-6), 129.3 (d, C-5) and 133.2 (d, C-4); *m/z* 184 (M^+, 1%) and 140 (M-C_2H_4, 100). Alcohol (**18**) was converted to its acetate derivative (**20**) using acetic anhydride/triethylamine/dimethylaminopyridine (cat.) in dichloromethane as a colourless oil; δ_H (270 MHz; $CDCl_3$) 1.26 (3H, d, *J* 6.6 Hz, Me), 1.49-1.99 (6H, m, 3 x CH_2), 2.11 (3H, s, $COCH_3$), 3.62-3.69 (1H, m, 8_{eq}-H), 3.74-3.88 (1H, m, 8_{ax}-H), 4.22 (1H, dq, $J_{2,Me}$ 6.6, $J_{2ax,3eq}$ 2.6 Hz, 2_{ax}-H), 4.93 (1H, dd, $J_{3eq,4}$ 5.3, $J_{2ax,3eq}$ 2.6 Hz, 3_{eq}-H), 5.88 (1H, d, $J_{4,5}$ 9.9 Hz, 5-H) and 5.99 (1H, dd, $J_{4,5}$ 9.9, $J_{3eq,4}$ 5.3 Hz, 4-H); *m/z* 182 (M-C_2H_4O, 16%), 167 (M-$OCOCH_3$, 10) and 140 ($C_8H_{12}O_2$, 100).

1,7-Dioxaspiro[5.5]undec-4-en-3-ol (22). Prepared from bromospiroacetal (**21**) as a colourless oil (128 mg, 84%); (Found: C, 63.3; H, 8.1, $C_9H_{14}O_3$ requires C, 63.5; H, 8.3%); δ_H (270 MHz; $CDCl_3$) 1.15-1.90 (6H, m, 3 x CH_2), 3.52-3.82 (4H, m, 2 x CH_2O), 4.02-4.18 (1H, m, 3-H), 5.53 (1H, dd, $J_{4,5}$ 10.3, $J_{3,5}$ 1.8 Hz, 5-H) and 5.72 (1H, d, $J_{4,5}$ 10.3 Hz, 4-H); δ_C (67.8 MHz; C_6D_6) 18.5, 25.3, 34.9 (t, C-9, C-10, or C-11), 61.3, (t, C-8), 63.5 (d, C-3) 63.6 (t, C-2), 93.4 (s, C-6), 131.9 (d, C-5) and 132.7 (d, C-4); *m/z* 170 (M^+, 0.3%) and 140 ($C_8H_{12}O_2$, 100).

2,2-Dimethyl-1,7-dioxaspiro[5.5]undec-4-en-3-ol (25): Prepared from bromospiroacetal (**23**) as a colourless oil (155 mg, 87%); (Found: M^+, 198.1256. $C_{11}H_{18}O_3$ requires M^+, 198.1308); δ_H (270 MHz; C_6D_6) 1.30 (3H, s, Me), 1.40 (3H, s, Me), 1.15-1.63 (5H, m 9_{ax}-H, 9_{eq}-H, 10_{eq}-H, 11_{ax}-H, 11_{eq}-H), 1.85-2.07 (1H, m, 10_{ax}-H), 3.46-3.58 (1H, m, 8_{eq}-H), 3.83 (1H, br.s, OH), 3.95 (1H, ddd, $J_{8ax,8eq}$ 11.0, $J_{8ax,9ax}$ 11.0, $J_{8ax,9eq}$ 2.6 Hz, 8_{ax}-H), 5.50 (1H, dd, $J_{4,5}$ 10.3, $J_{3,5}$ 1.6 Hz, 5-H) and 5.62 (1H, dd, $J_{4,5}$ 10.3, $J_{3,4}$ 2.2 Hz, 4-H); *m/z* 198 (M^+, 1%), 181 (M-H_2O, 5), 140 ($C_8H_{12}O_2$, 100) and 98 ($C_6H_{10}O$, 35).

Preparation of Bromobis-spiroacetals.

cis-13-Bromo-2,2-dimethyl-1,6,8-trioxadispiro[4.1.5.3]pentadec-14-ene (29) and cis-15-bromo-2,2-dimethyl-1,6,8-trioxadispiro[4.1.5.3]pentadec-13-ene (28): Potassium carbonate (83 mg, 0.6 mmol) and *N*-bromosuccinimide (35 mg, 0.2 mmol) were suspended in a solution of *cis*-bis-spiroacetal (**26**)[11] (36 mg, 0.15 mmol) in carbon tetrachloride (3 ml) under nitrogen. The mixture was heated under reflux for 5.5 h. then poured into ether (30 ml). The ether extract was washed with water (10 ml), brine (10 ml) and dried over potassium carbonate. The solvent was evaporated under reduced pressure and the residue purified by flash chromatography using 9 : 1 hexane : ethyl acetate as eluant to give *cis-13-bromobis-spiroacetal* (**29**) (20

mg, 42%) as colourless prisms m.p. 62-63°C (Found: M^+, 318.0655 and 316.0673. $C_{14}H_{21}O_3Br$ requires M^+, 318.0654 and 316.0674); δ_H (270 MHz; $CDCl_3$) 1.22 (3H, s, Me), 1.48 (2H, s, Me), 1.37-2.26 (10H, m, 5 x CH_2), 3.64 (1H, m, 9_{eq}-H), 4.18 (1H, ddd, $J_{9ax,9eq}$ 11.7, $J_{9ax,8ax}$ 11.7 and $J_{9ax,8eq}$ 3.8 Hz, 9_{ax}-H), 4.27 (1H, d, J 5.9 Hz, CHBr), 5.68 (1H, d, J 9.9 Hz, 15-H) and 6.10 (1H, dd, $J_{14,15}$ 9.9 and $J_{14,13}$ 5.9 Hz, 14-H); *m/z* 318 (M^+, 30%), 316 (M^+, 30), 237 (M-Br, 100), 218 ($C_9H_{13}OBr$, 35) and 216 ($C_9H_{13}OBr$, 34) and *cis-15-bromobis-spiroacetal (28)* (11 mg, 23%) as a colourless oil (Found: M^+, 318.0655 and 316.0673. $C_{14}H_{21}O_3Br$ requires M^+, 318.0654 and 316.0674); δ_H (270 MHz; $CDCl_3$) 1.17 (3H, s, Me), 1.38 (3H, s, Me), 1.47-2.15 (8H, m, 3-H, 4-H, and 4 x CH_2), 3.65 (1H, m, 9_{eq}-H), 4.05 (1H, ddd, $J_{9ax,9eq}$ 11.4, $J_{9ax,8ax}$ 11.4, $J_{9ax,8eq}$ 3.2 Hz, 9_{ax}-H), 4.29 (1H, d, J 5.9 Hz, CHBr), 5.81 (1H, d, J 9.9 Hz, 13-H) and 6.13 (1H, dd, $J_{14,13}$ 9.9 and $J_{14,15}$ 5.9 Hz, 14-H); *m/z* 318, 316 (M^+, 32%), 237 (M-Br, 100), 204 ($C_8H_{11}OBr$, 32) and 202 ($C_8H_{11}OBr$, 31).

trans-15-Bromo-2,2-dimethyl-1,6,8-trioxadispiro[4.1.5.3]pentadec-13-ene (34). Potassium carbonate (47 mg, 0.35 mmol) and *N*-bromosuccinimide (15 mg, 0.1 mmol) were suspended in a solution of *trans*-bis-spiroacetal (**27**) (20 mg, 0.085 mmol) in carbon tetrachloride (2 ml) under nitrogen and the mixture heated under gentle reflux for 8 h. The solution was diluted with ether (30 ml). The ether extract was washed with water (10 ml), brine (10 ml) and dried over potassium carbonate. The solvent was removed under reduced pressure and the residue purified by flash chromatography using 9:1 hexane : ethyl acetate as eluant to afford *trans-15-bromobis-spiroacetal* (**34**) (8 mg, 30%) as a colourless oil (Found: M^+, 318.0662 and 316.0663. $C_{14}H_{21}O_3Br$ requires M^+, 318.0654 and 316.0674); δ_H (270 MHz; $CDCl_3$) 1.26 (3H, s, Me), 1.43 (3H, s, Me), 1.45-2.42 (9H, m, 3-H, 3-H', 4-H' and 3x CH_2), 2.54 (1H, ddd, $J_{4,4}$ 13.4, $J_{4,3}$ 7.8 and $J_{4,3}$ 3.8 Hz, 4-H), 3.74 (1H, m, 9_{eq}-H), 4.02 (1H, ddd, $J_{9ax,9eq}$ 11.0, $J_{9ax,10ax}$ 11.0 and $J_{9ax,10eq}$ 3.8 Hz, 9_{ax}-H), 4.55 (1H, dd $J_{15,14}$ 3.5 and $J_{15,13}$ 1.7 Hz, CHBr), 5.62 (1H, dd, $J_{13,14}$ 10.1 and $J_{13,15}$ 1.7 Hz, 13-H) and 6.03 (1H, dd, $J_{14,13}$ 10.1 and $J_{14,15}$ 3.5 Hz, 14-H); *m/z* 318, 316 (M^+, 38%), 237 (M-Br, 100), 204 ($C_8H_{11}OBr$, 69) and 202 ($C_8H_{11}OBr$, 74).

Preparation of Hydroxybis-spiroacetals.

cis-2,2-Dimethyl-13-hydroxy-1,6,8-trioxadispiro[4.1.5.3]pentadec-14-ene (31) and cis-2,2-dimethyl-15-hydroxy-1,6,8-trioxadispiro[4.1.5.3]pentadec-13-ene (30). A solution of 18-crown-6 (16 mg, 0.06 mmol) and *cis*-13-bromobis-spiroacetal (**29**) (18 mg, 0.06 mmol) in dry dimethylsulphoxide (1 ml) was stirred with potassium superoxide (15 mg, 0.2 mmol) for 8 h. under nitrogen. Water (1 ml) was added and the mixture extracted with ether (30 ml). The ether extract was washed with water (2 x 10 ml), brine (10 ml) and dried over potassium carbonate. The solvent was evaporated at reduced pressure and the residue purified by flash chromatography, using 1:2 hexane : ethyl acetate as eluant to give an inseparable mixture of *cis-15-hydroxybis-spiroacetal (30)* [5,9] and *cis-13-hydroxybis-spiroacetal (31)* (*) in the ratio of 1.5:1 and in the form of a colourless oil (11 mg, 65%) (Found: M^+, 254.9525. $C_{14}H_{22}O_4$ requires M^+, 254.9518); δ_H (270 MHz; $CDCl_3$) 1.17 (3H, s, 2-Me), 1.23 (3H, s, 2-Me*), 1.40 (3H, s, 2-Me), 1.48 (3H, s, 2-Me*), 1.46-2.18 (19H, m, 3-H, 3-H', 3-H*, 3-H'*, 4-H', 4-H*, 4-H'*, 3 x CH_2 and 3 x CH_2*), 2.27-2.40 (1H, m, 4-H), 3.57-3.66 (4H, m, 2 x CHOH and 2 x 9_{eq}-H), 4.05 (1H, ddd $J_{9ax,9eq}$ 11.5, $J_{9ax,8ax}$ 11.5 and $J_{9ax,8eq}$ 3.2 Hz, 9_{ax}-H), 4.19 (1H, ddd, $J_{9ax,9eq}$ 11.5, $J_{9ax,8ax}$ 11.5, $J_{9ax,8eq}$ 3.2 Hz, 9_{ax}-H*), 5.78 (1H, d, J 10.1 Hz, 15-H*), 5.88 (1H, d, J 10.1 Hz, 13-H), 6.08 (1H, dd, $J_{14,15}$ 10.1 and $J_{14,13}$ 5.8 Hz, 14-H*) and 6.11 (1H, dd, $J_{14,13}$ 10.1 and $J_{14,15}$ 5.5 Hz, 14-H); *m/z* 254 (M^+, 4%), 236 (M-H_2O, 8), 154 ($C_9H_{14}O_2$, 98) and 140 ($C_9H_{14}O_2$, 100). Repetition of the above procedure using the corresponding *cis*-15-bromobis-spiroacetal (**28**) afforded the same alcohols (**30**) and (**31**) in the ratio 1 : 1.5.

13-Acetoxy-2,2-dimethyl-1,6,8-trioxadispiro[4.1.5.3]pentadec-14-ene (33) and 15-Acetoxy-2,2-dimethyl-1,6,8-trioxadispiro[4.1.5.3]pentadec-13-ene (32). A solution of the mixture of alcohols (**30**) and (**31**), triethylamine (20 mg), acetic anhydride (20 mg) and a catalytic quantity of dimethylaminopyridine in dichloromethane (2 ml) was stirred at room temperature for 2h. The solution was diluted with ether (20 ml). The ether extract was washed with water (5 ml) and dried over potassium carbonate. The solvent was

removed under reduced pressure to afford a separable mixture of the acetates and which were purified by flash chromatography using 4 : 1 hexane : ethyl acetate as eluant to afford the less polar *cis-13-acetoxybis-spiroacetal (33)* as a colourless oil (Found: M^+, 296.1588. $C_{16}H_{24}O_5$ requires M^+, 296.1624); δ_H (270 MHz; $CDCl_3$) 1.23 (3H, s, 2-Me), 1.48 (3H, s, 2-Me), 1.24-2.15 (10H, m, 5 x CH_2), 2.05 (3H, s, OAc), 3.62 (1H, m, 9_{eq}-H), 4.18 (1H, m, 9_{ax}-H), 4.89 (1H, d, *J* 5.7 Hz, CHOAc), 5.87 (1H, d, *J* 10.1 Hz, 15-H) and 5.99 (1H, dd, $J_{14,15}$ 10.1 Hz and $J_{14,13}$ 5.7 Hz, 14-H); *m/z* 296 (M^+, 3%), 254 (M-AcOH, 7), 196 ($C_{11}H_{16}O_3$, 38) and 154 ($C_9H_{14}O_2$, 100) and *cis-15-acetoxybis-spiroacetal (32)*[5,9] as a colourless oil (Found: M+, 296.1613. $C_{16}H_{24}O_5$ requires M^+, 296.1624); δ_H (270 MHz; $CDCl_3$) 1.18 (3H, s, 2-Me), 1.40 (3H, s, 2-Me), 1.48-2.17 (10H, m, 5 x CH_2), 2.07 (3H, s, OAc), 3.65 (1H, m, 9_{eq}-H), 4.04 (1H, ddd, $J_{9ax,9eq}$ 11.5, $J_{9ax,8ax}$ 11.5 and $J_{9ax,8eq}$ 3.1 Hz, 9_{ax}-H), 4.86 (1H, d, *J* 5.5 Hz, CHOAc), 5.97 (1H, d *J* 10.1 Hz, 13-H) and 6.05 (1H, dd, *J* $_{14,13}$ 10.1 and $J_{14,15}$ 5.5 Hz, 14-H); *m/z* 296 (M^+, 3%), 254 (M-Ac, 23), 236 (M-AcOH, 15), 182 ($C_{10}H_{14}O_3$, 10) and 140 ($C_8H_{12}O_4$, 100).

trans-2,2-Dimethyl-15-hydroxy-1,6,8-trioxadispiro[4.1.5.3]pentadec-13-ene (**37**). A solution of 18-crown-6 (10 mg, 0.04 mmol) and *trans*-15-bromobis-spiroacetal (**34**) (12 mg, 0.04 mmol) in dry dimethylsulphoxide (1 ml) was stirred with potassium superoxide (24 mg. 0.2 mmol) for 8 h. under nitrogen. Water (1 ml) was added and the mixture extracted with ether (30 ml). The ether extract was washed with water (3 x 10 ml) brine (10 ml), and dried over potassium carbonate. The solvent was evaporated at reduced pressure and the residue purified by flash chromatography, using 1:2 hexane : ethyl acetate as eluant to give *trans-15-hydroxybis-spiroacetal (37)*[5,9] as a colourless oil (6 mg, 65%) (Found: M^+, 254.9525. $C_{14}H_{22}O_4$ requires M^+, 254.9518); δ_H (270 MHz; $CDCl_3$) 1.25 (3H, s, Me), 1.48 (3H, s, Me), 1.45-2.23 (9H, m, 3-H, 3-H', 4-H', and 3 x CH_2), 2.41 (1H, ddd, $J_{4,4}$ 13.0, $J_{4,3}$ 7.4 and 3.1 Hz, 4-H), 3.70 (1H, m, 9_{eq}-H), 4.01 (1H, m, 9_{ax}-H), 4.15 (1H, ddd $J_{15,OH}$ 4.9, $J_{15,14}$ 2.4 and $J_{15,13}$ 2.4 Hz, CHOH), 5.62 (1H, dd, $J_{13,14}$ 10.1 and $J_{13,15}$ 2.4 Hz, 13-H) and 5.88 (1H, dd, $J_{14,13}$ 10.1 and $J_{14,15}$ 2.4 Hz, 14-H); *m/z* 254 (M^+, 5%), 236 (M-H_2O, 10) and 140 ($C_9H_{14}O_2$, 100).

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REFERENCES AND NOTES

1. Kinashi, H.; Otake, N.; Yonehara, H.; Sato, S.; Saito, Y. *Tetrahedron Lett.*, **1973**, *49*, 4955.
2. Berg, D. H.; Hamill, R. L. *J. Antibiot.*, **1978**, *38*, 1.
3. Brimble, M. A.; Williams, G. M. *J. Org. Chem.*, submitted for publication.
4. Bernet, B.; Bishop, P. M.; Caron, M.; Kawamata, T.; Roy, B. L.; Ruest, L.; Sauve, G.; Soucy, P.; Deslongchamps, P. *Can. J. Chem.*, **1985**, *63*, 2810.
5. Kocienski, P.; Fall, Y.; Whitby, R. *J. Chem. Soc., Perkin Trans. I*, **1989**, 841
6. Perron, F.; Albizati, K. F. *J. Org. Chem.*, **1989**, *54*, 2044.
7. For reviews see: (a) Perron F.; Albizati, K. F. *Chem. Rev.*, **1989**, *89*, 1617. (b) Boivin, T. L. B. *Tetrahedron*, **1987**, *43*, 3309.
8. Preliminary communication see: Brimble, M. A.; Edmonds, M. K.; Williams, G. M. *Tetrahedron Lett.* **1990**, *31*, 7509.
9. We thank Professor Kocienski for kindly providing the appropriate n.m.r. spectra.
10. Both *syn* and *anti* S_N2' displacements can occur depending on the nature of the nucleophile and the leaving group. See: Stork, G.; Kreft, A. F. *J. Am. Chem. Soc*, **1979**, *99*, 3850; Oritani, T., Overton, K. H. *J. Chem. Soc., Chem. Commun.*, **1978**, 454; Chapleo, C. B.; Finch, M. A. W.; Roberts, S. M.; Woolley, G. T.; Newton, R. F.; Selby, D. W. *J. Chem. Soc., Perkin Trans. I*, **1980**, 1847.
11. Brimble, M. A.; Williams, G. M.; Baker, R. *J. Chem. Soc., Perkin Trans. I.*, **1991**, 2221.
12. Moreau, J. L.; Gaudemar, M. *Bull. Soc. Chem. Fr.*, **1970**, 2175.
13. Smith, A. B.; Thompson, A. S. *J. Org. Chem.*, **1984**, *49*, 1469.