Synthesis of 5-Hydroxy-1,7-dioxaspiro[5.5]undec-3-en-2-ones from 2-Benzenesulfonyltetrahydropyrans and 5-Hydroxybutenolides: X-Ray Crystal Structure Determination for (5*RS*,6*SR*)-5-Acetoxy-4-methoxy-3-methyl-1,7-dioxaspiro[5.5]undec-3-en-2-one

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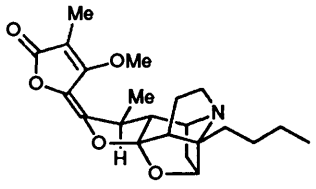
5-Hydroxy-1,7-dioxaspiro[5.5]undec-3-en-2-ones are obtained from reactions between 2-lithiated 2-benzenesulfonyltetrahydropyrans and 5-hydroxybutenolides. The structure of (5*RS*,6*SR*)-5-acetoxy-4-methoxy-3-methyl-1,7-dioxaspiro[5.5]undec-3-en-2-one **16** was confirmed by X-ray crystallography. Addition of 5-lithiated 2,3-dihydrofuran and 6-lithiated 3,4-dihydro-2*H*-pyran to the hydroxybutenolide **12** gave the butenolides **30** and **31**. Hydrolysis of **31** gave **33**, which on dehydration returned **31** rather the conjugated isomer **32**.

Stemofoline **1** is an insectical alkaloid which has not yet been synthesised.[1,2] One structural feature of stemofoline of interest is the 5-(alkoxyalkylidene)butenolide fragment **2**. We here report some investigations into possible approaches to 5-(alkoxyalkylidene)butenolides which may be applicable to the synthesis of stemofoline and related compounds.



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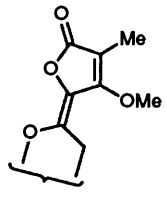

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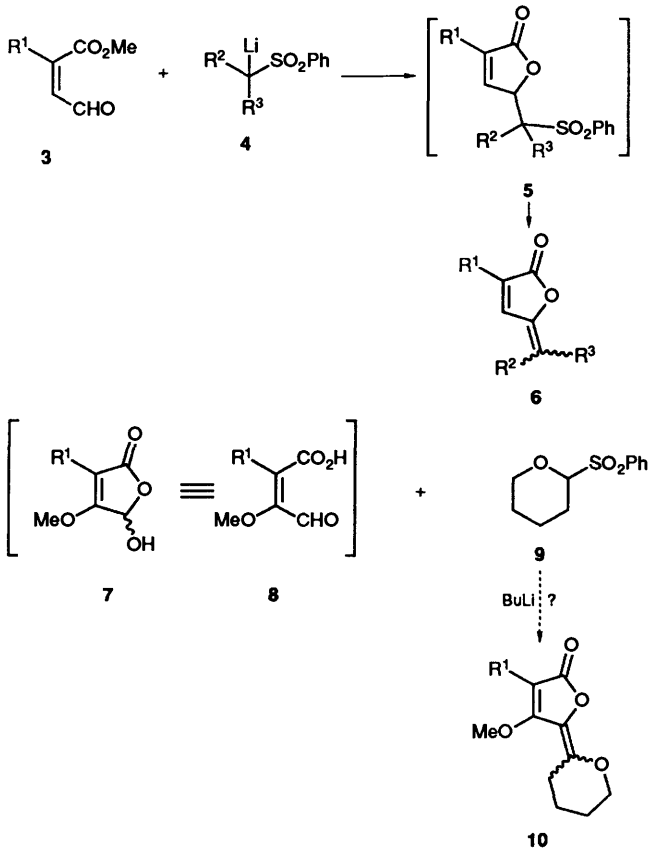
Deprotonation of α-benzenesulfonyl ethers using butyllithium or lithium diisopropylamide (LDA) generates the corresponding organometallic species which react with a wide range of electrophiles.[3,4] Subsequent elimination of sulfinate often occurs spontaneously on warming the reaction mixture to room temperature and gives the corresponding enol ether.[5] Enol ethers so obtained from cyclic α-sulfonyl ethers have been used for the synthesis of spiroacetals, including spiroacetal fragments of complex natural products.[6,7] Alternatively, the benzenesulfonyl substituent can be displaced by oxygen[8] and carbon[9] nucleophiles, leading to the synthesis of acetals and α-substituted ethers. α-Substituted amines have similarly been prepared from α-sulfonyl amines.[10]

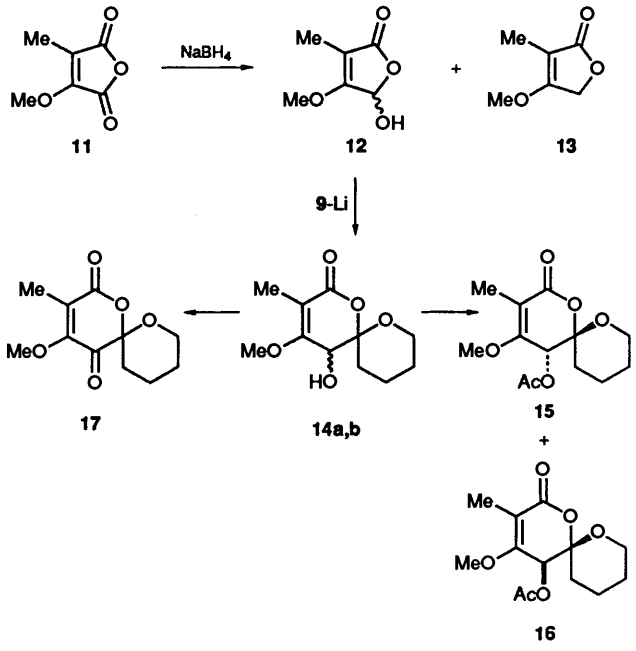
α-Lithiated sulfones **4** react with (*Z*)-formyl esters **3** to give 5-alkylidenebutenolides **6** *via* elimination of benzene sulfinate from the intermediate lactones **5**.[11] By analogy with this work, it was decided to investigate the synthesis of 5-(alkoxyalkylidene)butenolides **10** from cyclic α-sulfonyl ethers **9** and 5-hydroxybutenolides **7**.

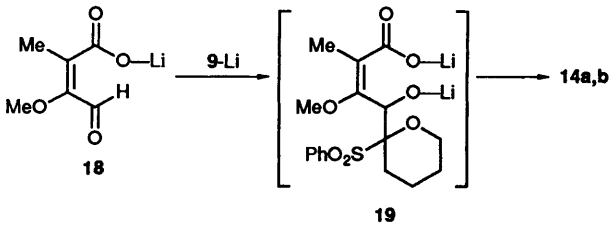


3 **4** **5** **6** **7** **8** **9** **10**

Results and Discussion

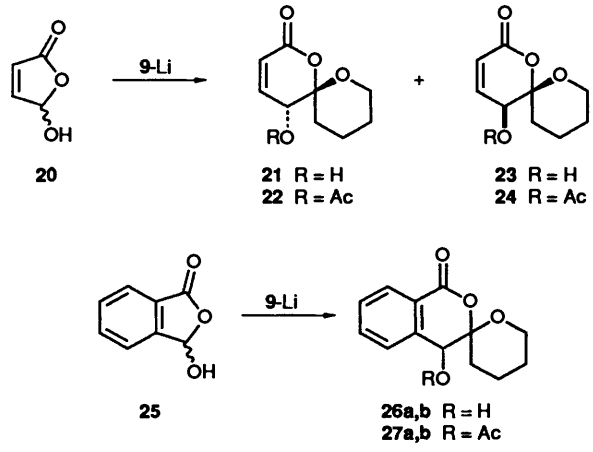
The hydroxybutenolide **12** was prepared by reduction of the anhydride **11** using sodium borohydride.[12] In our hands, this reduction was accompanied by the formation of small amounts of the lactone **13** (*ca.* 10%) as a side-product, but the required hydroxybutenolide could be isolated by extraction into aqueous sodium hydrogen carbonate and re-extraction back into ether after acidification. Deprotonation of the α-benzenesulfonyltetrahydropyran **9**[5] using butyllithium gave the corresponding α-lithiated sulfone which was added to the hydroxybutenolide **12** at −78 °C. A mixture of two products was isolated but the spectroscopic data obtained for the mixture were inconsistent with the expected 5-alkylidenebutenolides, *e.g.* the IR spectrum showed a strong O–H absorption at 3400 cm^{-1}. The mixture of products was acetylated and the acetates separated. The structure of the major, more polar, acetate was established by X-ray crystallography as the spiroacetal **16**, see Fig. 1. The other acetate was identified as the epimer **15**, and the products of the reaction between the hydroxybutenolide **12** and the lithiated α-benzenesulfonyl ether **9**, as the epimeric





alcohols **14**. Oxidation of this mixture of alcohols gave the ketone **17**.

The formation of the 5-hydroxyspiroacetals **14** is consistent with decomposition of the intermediate hydroxybutenolide adduct **19** *via* an intramolecular displacement of benzenesulfinate by the carboxylate. This decomposition occurs at a rate which is similar to the rate of formation of the adduct. Attempts to trap the intermediate **19**, *e.g.* by low temperature quench with acid, were unsuccessful.



This synthesis of spiroacetals was briefly explored using the hydroxybutenolides **20**[13] and **25** which gave the hydroxyspiroacetals **21** and **23** (70%), and **26a**, **b** (82%), respectively. The isomeric hydroxyspiroacetals could only be partially separated by flash chromatography, and were characterised as their acetates **22** and **24**, and **27a**, **b**.

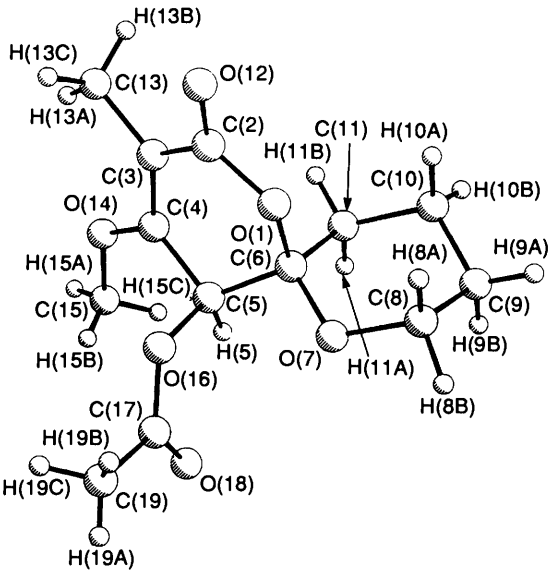
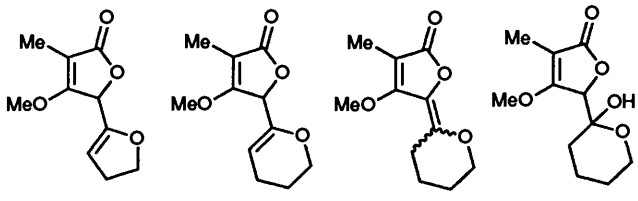


Fig. 1 Projection of the spiroacetal **16** as determined by X-ray crystallography showing the crystallographic numbering scheme used

As an alternative route to the 5-(alkoxyalkylidene)butenolides **10**, reactions of α-lithiated cyclic ethers and the anhydride **11**[12] and 5-hydroxybutenolide **12**[14] were investigated. Treatment of 2-tributylstannyltetrahydrofuran **28**[15] with butyllithium, followed by the addition of **11** or **12** did not give any identifiable products, although the expected adduct **29** was obtained, as a mixture of diastereoisomers, with benzaldehyde. However, treatment of 2,3-dihydrofuran or 3,4-dihydro-2*H*-pyran with *tert*-butyllithium followed by the addition of the hydroxybutenolide **12** gave the butenolides **30** and **31**. Attempts to isomerize **31** into its conjugated isomer **32** were unsuccessful,



and hydrolysis gave the hemiacetal **33** which on dehydration returned the non-conjugated compound **31** rather than its conjugated isomer **32**. Alternative approaches to the conjugated compound **32** are under investigation.

Structural and Conformational Aspects of the Spiroacetals.— The structure of the more polar 5-acetoxyspiroacetal prepared from hydroxybutenolide **12** was established as **16** by X-ray diffraction. The conformation of this spiroacetal as determined by the X-ray study, see Fig. 1, is unusual in that the oxygen of the tetrahydropyran ring is pseudoequatorial with respect to the lactone ring and not axial as would be expected on the basis of the anomeric effect.[16] Moreover the acetoxy substituent is axial rather than equatorial. Clearly this conformation must be more stable than that in which the acetoxy group is equatorial and the

tetrahydropyran oxygen axial. This may be due to the presence of the methoxy substituent at the 4-position which would have severe electronic and steric interactions with the 5-acetoxy group if the latter were in the equatorial position. This effect would appear to be dominant over the anomeric effect in this system. The X-ray structure of the isomeric spiroacetal **15** was not determined, but it is likely that the acetoxy substituent remains in the axial position to avoid the unfavourable interactions with the 4-methoxy substituent, but that in this case the tetrahydropyran oxygen is in the pseudoaxial position favoured on the basis of the anomeric effect.

The structures of the spiroacetals **22** and **24** were assigned on the basis of their NMR spectra. For the more polar acetate, 5-H shows only a very small vicinal coupling, *ca.* 2 Hz, with 4-H and an allylic coupling, also *ca.* 2 Hz, with 3-H, and would therefore appear to be axial. For the less polar acetate, 5-H is equatorial as indicated by the larger (6 Hz) vicinal coupling with 4-H, and the lack of an observable allylic coupling with 3-H. Thus for these spiroacetals which lack a substituent at 4-C, the 5-acetoxy substituent can be either axial or equatorial. If it is assumed that the tetrahydropyran oxygens in these isomers are axial in accordance with the anomeric effect, it follows that the less polar isomer is **22** and that the more polar isomer is **24**.

Molecular modelling studies were supportive of these configurational and conformational assignments. Fig. 2 shows the minimum energy conformations of the spiroacetal acetates **15**/**16** and **22**/**24**. These were found using the program MacroModel[17] (version 3.1x), using Monte Carlo-type conformational searching and the MM2 forcefield for energy minimisation. For both **15** and **16** the acetoxy substituent is axial and this preference dominates over the anomeric effect when the two are opposed. For **22** and **24**, the anomeric effect is dominant and the acetoxy group adopts either the axial or equatorial position depending upon the relative stereochemistry of the two chiral centres.

Experimental

All non-aqueous reactions were performed under an atmosphere of dry argon or nitrogen. ^{1}H NMR spectra were recorded on Bruker AC 300 and Varian Gemini 200 spectrometers. IR spectra were measured on a Perkin-Elmer 1710FT spectrometer as evaporated films. Mass spectra were recorded on Kratos MS20 and MS25 spectrometers using either electron impact (EI) or chemical ionisation (CI) modes. Melting points were determined on a Kofler block, and are uncorrected. All solvents were dried and distilled before use. Light petroleum refers to the fraction which distills at 40–60 °C, and ether to diethyl ether. Flash chromatography was carried out using May and Baker Sorbsil C60 40–60 μm.

Hydroxybutenolide **12** was prepared by reduction of the anhydride **11** using sodium borohydride. Extraction of the crude product into aqueous sodium hydrogen carbonate and re-extraction into ether after acidification gave the hydroxybutenolide **12** as a white crystalline solid, m.p. 93–95 °C (lit.,[12] 93 °C).

5-Acetoxy-4-methoxy-3-methyl-1,7-dioxaspiro[5.5]undec-3-en-2-one **15** *and* **16**.—Butyllithium (1.92 mmol) was added to a stirred solution of the sulfone **9**[5] (400 mg, 1.77 mmol) in THF (10 cm^3) at −78 °C. After 0.5 h a solution of the hydroxybutenolide **10**[12] (115 mg, 0.80 mmol) in THF (5 cm^3) was added, and the reaction mixture was stirred at −78 °C for 4 h before being quenched with saturated aqueous ammonium chloride (10 cm^3) and allowed to warm to room temperature. The aqueous phase was separated, extracted with ethyl acetate, dried ($MgSO_4$) and concentrated under reduced pressure. Chromatography of the residue [light petroleum–ether (3:2)] afforded the alcohols **14a**, **b** (115 mg, 63%) which could be partially separated by HPLC (Found: M$^+$, 228.0991. $C_{11}H_{16}O_5$ requires *M*, 228.0998); λ_{max}(MeOH)/nm 250. The more polar isomer **14a** was eluted first; ν_{max}/cm^{-1} 3415, 1703, 1654, 1051 and 986; δ_H(300 MHz; $CDCl_3$) 1.50–2.10 (7 H, m), 1.82 (3 H, s, 3-Me), 3.86 and 4.10 (each 1 H, m, 8-H), 3.96 (3 H, s, OMe) and 4.30 (1 H, s, 5-H); *m*/*z* (CI, NH_3) 246 (M$^+$ + 18, 38%), 229 (100), 118 (25) and 102 (66). The less polar isomer **14b** was eluted second; δ_H(300 MHz; $CDCl_3$) 1.47–2.10 (6 H, m), 1.79 (3 H, s, 3-Me), 2.25 (1 H, m), 3.70 and 3.90 (each 1 H, m, 8-H), 3.95 (3 H, s, OMe) and 4.09 (1 H, s, 5-H).

To a stirred solution of the spiroacetals **14a**, **b** (114 mg, 0.50 mmol) in dry ether (4 cm^3) was added a catalytic amount of DMAP, acetic anhydride (0.20 g, 1.96 mmol) and triethylamine (0.51 g, 5.05 mmol). The reaction mixture was stirred at ambient temperature for 3 h, quenched with water (5 cm^3), and the aqueous phase was separated and extracted with ethyl acetate. The combined organic phase was dried ($MgSO_4$) and concentrated under reduced pressure. Chromatography of the residue [light petroleum–ether (3:1)] separated the *acetates*; the less polar isomer, **15** (39 mg, 29%), m.p. 94–95 °C (Found: M$^+$, 270.1103. $C_{13}H_{18}O_6$ requires *M*, 270.1103); ν_{max}/cm^{-1} 1752, 1719, 1662, 1248, 1213, 1048 and 949; δ_H(300 MHz; $CDCl_3$) 1.43–1.77 (4 H, m), 1.84–2.08 (2 H, m,), 1.86 (3 H, s, 3-Me), 2.15 (3 H, s, $COCH_3$), 3.68–3.77 and 3.91 (each 1 H, m, 8-H), 3.76 (3 H, s, OMe) and 5.64 (1 H, m, 5-H); *m*/*z* (CI, NH_3) 288 (M$^+$ + 18, 1%), 272 (14), 271 (100), 213 (31) and 211 (19); the more polar isomer, **16** (50 mg, 37%), m.p. 120–122 °C; (Found: C, 57.7; H, 6.8. $C_{13}H_{18}O_6$ requires C, 57.8; H, 6.7%); ν_{max}/cm^{-1} 1754, 1711, 1658, 1220, 1094 and 982; δ_H(300 MHz; $CDCl_3$) 1.53–1.76 (4 H, m), 1.85–2.01 (2 H, m), 1.87 (3 H, s, 3-Me), 2.18 (3 H, s, $COCH_3$), 3.76 (3 H, s, OMe), 3.84 and 4.10 (each 1 H, m, 8-H) and 5.73 (1 H, s, 5-H); *m*/*z* (CI, NH_3) 288 (M$^+$ + 18, 1%), 272 (15), 271 (100), 213 (74), 211 (30) and 169 (16.4).

4-Methoxy-3-methyl-1,7-dioxaspiro[5.5]undec-3-ene-2,5-dione **17**.—Dimethyl sulfoxide (39 mm^3, 0.55 mmol) was added dropwise to a solution of oxalyl chloride (18 mm^3, 0.21 mmol) in dichloromethane (0.5 cm^3) at −50 °C. The mixture was stirred for 2 min, a solution of spiroacetals **14a**, **b** (41 mg, 0.18 mmol) in dichloromethane (3 cm^3) was added dropwise, and the reaction mixture stirred at −50 °C for 25 min before being quenched by the addition of triethylamine (0.5 cm^3). The reaction mixture was warmed to ambient temperature and concentrated under reduced pressure. The resulting oil was dissolved in water and extracted with ethyl acetate, and the combined organic phase dried ($MgSO_4$) and concentrated under reduced pressure. Chromatography of the residue [light petroleum–ether (2:1)], gave the *title compound* **17** as a yellow oil (24 mg, 59%) (Found: M$^+$, 226.0834. $C_{11}H_{14}O_5$ requires *M*, 226.0841); ν_{max}/cm^{-1} 1712, 1628, 1330 and 985; δ_H(300 MHz; $CDCl_3$) 1.65–1.90 (4 H, m), 1.96–2.13 (1 H, m), 2.08 (3 H, s, 3-Me), 2.21 (1 H, td, *J* 13, 5), 3.88 and 4.12 (each 1 H, m, 8-H) and 4.03 (3 H, s, OMe); *m*/*z* (CI, NH_3) 244 (M$^+$ + 18, 12%), 228 (12), and 227 (100).

5-Acetoxy-1,7-dioxaspiro[5.5]undec-3-en-2-ones **22** *and* **24**.—Following the procedure outlined above, the hydroxybutenolide **20**[13] (60 mg, 0.60 mmol) and sulfone **9** (305 mg, 1.35 mmol) gave the alcohols **21** and **23** (77 mg, 70%) one isomer of which could be partially separated by chromatography [light petroleum–ether (2:1)]; **23** (22 mg) [Found: (M + NH_4)$^+$, 202.1081. $C_9H_{16}NO_4$ requires *M*, 202.1079]; ν_{max}/cm^{-1} 3439, 1724, 1114, 970 and 949; δ_H(300 MHz; $CDCl_3$) 1.55–2.12 (6 H, m), 2.46 (1 H, d, *J* 11, OH), 3.81 and 3.97 (each 1 H, m, 8-H), 4.27 (1 H, dt, *J* 11, 2, 5-H), 5.97 (1 H, dd, *J* 10, 2, 3-H) and 6.64 (1 H, dd, *J* 10, 2, 4-H); *m*/*z* (CI, NH_3) 202 (M$^+$ + 18, 67%), 186 (8) and 185 (100).

Acetylation of the spiroacetals **21** and **23** (16 mg, 0.09 mmol)

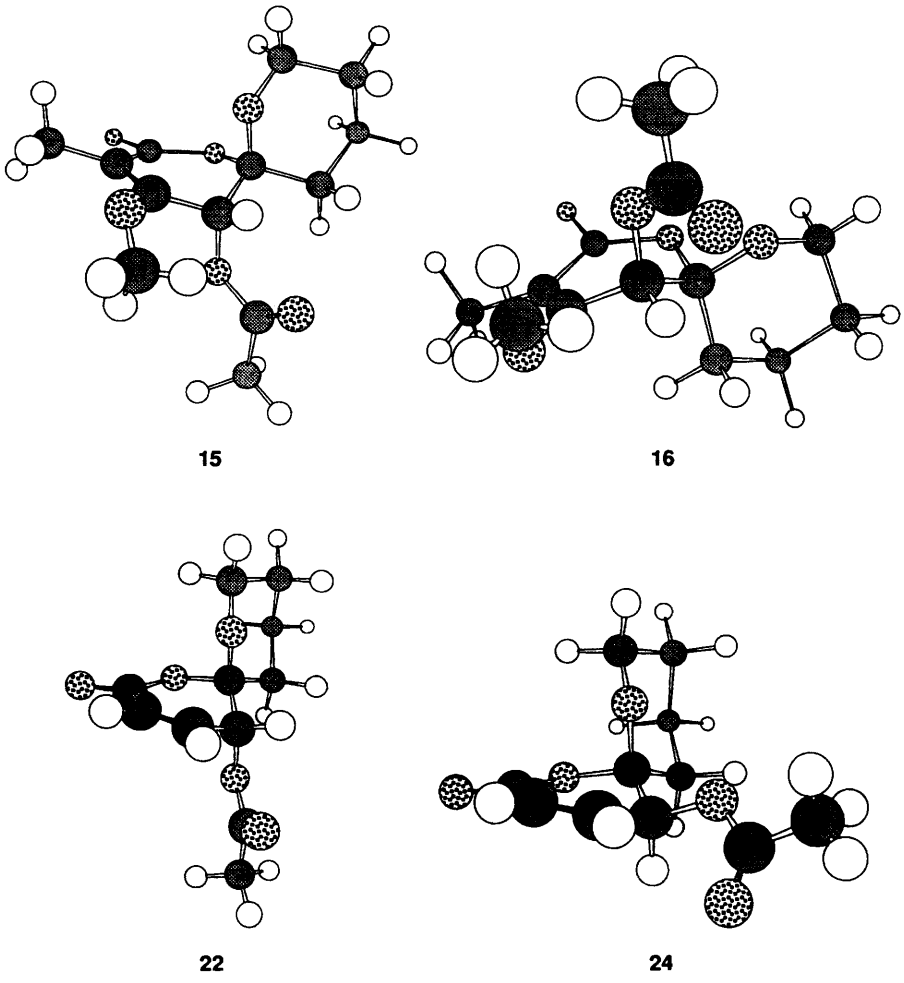


Fig. 2 Projections of the lowest energy conformations of spiroacetals **15/16** and **22/24** predicted on the basis of molecular modelling calculations

was carried out as described above to give the *title acetates* (77%); the less polar isomer **22** (9 mg) [Found: $(M + H)^+$, 227.0921. $C_{11}H_{15}O_5$ requires *M*, 227.0919]; ν_{max}/cm^{-1} 1735, 1218 and 1025; δ_H(300 MHz; $CDCl_3$) 1.44–1.78 (4 H, m) 1.91–2.15 (2 H, m), 2.11 (3 H, s, $COCH_3$), 3.75 and 3.95 (each 1 H, m, 8-H), 5.14 (1 H, d, *J* 6, 5-H), 6.19 (1 H, d, *J* 10, 3-H) and 6.81 (1 H, dd, *J* 10, 6, 4-H); *m/z* (CI, NH_3) 244 (M^+ + 18, 2%), 227 (68), 184 (20.0) and 169 (100); the more polar isomer **24** (6 mg) [Found: $(M + H)^+$, 227.0908. $C_{11}H_{15}O_5$ requires *M*, 227.0919]; ν_{max}/cm^{-1} 1735 and 1231; δ_H(300 MHz; $CDCl_3$) 1.54–1.77 (4 H, m), 1.87 and 1.96–2.15 (each 1 H, m), 2.22 (3 H, s, $COCH_3$), 3.85 and 3.99 (each 1 H, m, 8-H), 5.62 (1 H, t, *J* 2, 5-H), 6.07 (1 H, dd, *J* 10, 2, 3-H) and 6.54 (1 H, dd, *J* 10, 2, 4-H); *m/z* (CI, NH_3) 244 (M^+ + 18, 4%), 228 (18), 227 (100) and 169 (73.4).

4-*Acetoxy*-3,4,3′,4′,5′,6′-*hexahydrospiro*[2-*benzopyran*-3,2′-*pyran*]-1-*one* **27a**, **b**.—Following the procedure outlined above, the hydroxybutenolide **25** (140 mg, 0.93 mmol) and sulfone **9** (460 mg, 2.04 mmol) gave the alcohols **26a**, **b** (82%) which were partially separated by chromatography [light petroleum–ether (2:1)]; the less polar isomer **26a** (101 mg) (Found: M^+, 234.0896. $C_{13}H_{14}O_4$ requires *M*, 234.0892); ν_{max}/cm^{-1} 3438, 1729, 1607, 1460, 1079, 976 and 718; δ_H(300 MHz; $CDCl_3$) 1.57–2.26 (7 H, m), 3.70 and 3.96 (each 1 H, m, 8-H), 4.75 (1 H, s, 5-H), 7.45 (1 H, m, ArH), 7.60–7.75 (2 H, m, ArH) and 8.06 (1 H, d, *J* 8, ArH); *m/z* (CI, NH_3) 252 (M^+ + 18, 14%), 236 (11), 235 (100), 234 (19), 217 (17); the more polar isomer **26b** (77 mg) (Found: M^+, 234.0892. $C_{13}H_{14}O_4$ requires *M*, 234.0892); ν_{max}/cm^{-1} 3421, 1708, 1074, 1051, 985 and 940; δ_H(300 MHz; $CDCl_3$) 1.60–2.26 (7 H, m), 3.71 and 3.99 (each 1 H, m, 8-H), 4.58 (1 H, s, 5-H), 7.46–7.53 (2 H, m, ArH), 7.65 (1 H, td, *J* 8, 1, ArH) and 8.12 (1 H, dd, *J* 8, 1, ArH); *m/z* (CI, NH_3) 252 (M^+ + 18, 51%), 236 (10) and 235 (100).

Acetylation of the spiroacetals **26a**, **b** (80 mg, 0.34 mmol) gave the *title acetates* (87%); the less polar isomer **27a** (43 mg) [Found: $(M + H)^+$, 277.1076. $C_{15}H_{17}O_5$ requires *M*, 277.1076]; ν_{max}(film)/cm^{-1} 1735, 1606, 1462, 1220, 1072 and 1042; δ_H(300 MHz; $CDCl_3$) 1.54–1.84 (4 H, m), 1.97–2.16 (1 H, m), 2.05 (3 H, s, $COCH_3$), 2.22 (1 H, m), 3.67 and 3.91 (each 1 H, m, 8-H), 5.83 (1 H, s, 5-H), 7.48–7.64 (3 H, m, ArH) and 8.14 (1 H, m, ArH); *m/z* (CI, NH_3) 294 (M^+ + 18, 4%), 278 (16), 2.77 (100), 234 (14) and 219 (51); the more polar isomer **27b** (39 mg) [Found: $(M + H)^+$, 277.1073. $C_{15}H_{17}O_5$ requires *M*, 277.1076]; ν_{max}(film)/cm^{-1} 1735, 1607, 1460, 1222, 1070 and 1047; δ_H(300 MHz; $CDCl_3$) 1.59–1.81 (4 H, m), 1.92 (1 H, m), 2.00–2.13 (1 H, m), 2.32 (3 H, s, $COCH_3$), 3.76 and 3.99 (each 1 H, m, 8-H), 6.22 (1 H, s, 5-H), 7.25 (1 H, d, *J* 7.5, ArH), 7.46 (1 H, t, *J* 7.5, ArH), 7.62 (1 H, dt, *J* 7.5, 1, ArH) and 8.1 (1 H, dd, *J* 7.5, 1, ArH); *m/z* (CI, NH_3) 294 (M^+ + 18, 6%), 278 (16), 277 (100), 234 (21), 219 (69) and 217 (33).

2-(α-*Hydroxybenzyl*)*tetrahydrofuran* **29**.—Butyllithium (0.34 mmol) was added to a stirred solution of stannane **28**[15] (110 mg, 0.30 mmol) in THF (2 cm^3) at −78 °C. After 15 min, benzaldehyde (58.4 mg, 0.55 mmol) was added, followed, after 45 min at −78 °C, by saturated aqueous ammonium chloride (2 cm^3), and the mixture was allowed to warm to ambient temperature. The mixture was extracted with ether and the combined organic layer was dried ($MgSO_4$) and concentrated

Table 1 Positional parameters for spiroacetal **16**

Atom	*x*	*y*	*z*
O(1)	0.0434(2)	−0.6772(1)	0.1587(1)
O(7)	−0.0308(2)	−0.8352(1)	0.0779(1)
O(12)	0.1629(2)	−0.5307(1)	0.2381(2)
O(14)	0.2017(2)	−0.8063(1)	0.4615(1)
O(16)	0.2681(2)	−0.8548(1)	0.2635(1)
O(18)	0.2145(3)	−1.0252(2)	0.2461(2)
C(2)	0.1241(3)	−0.6186(2)	0.2492(2)
C(3)	0.1624(3)	−0.6629(2)	0.3538(2)
C(4)	0.1542(3)	−0.7659(2)	0.3626(2)
C(5)	0.1051(3)	−0.8340(2)	0.2664(2)
C(6)	−0.0236(3)	−0.7790(2)	0.1641(2)
C(8)	−0.1586(4)	−0.7992(3)	−0.0289(2)
C(9)	−0.3401(4)	−0.7952(2)	−0.0413(2)
C(10)	−0.3408(4)	−0.7283(2)	0.0475(2)
C(11)	−0.2036(3)	−0.7676(2)	0.1579(2)
C(13)	0.2216(4)	−0.5906(2)	0.4476(3)
C(15)	0.1872(7)	−0.9132(3)	0.4756(3)
C(17)	0.3052(3)	−0.9530(2)	0.2515(2)
C(19)	0.4735(4)	−0.9582(4)	0.2462(3)
H(5)	0.056(3)	−0.899(2)	0.269(2)
H(8A)	−0.126(3)	−0.731(2)	−0.037(2)
H(8B)	−0.147(3)	−0.854(2)	−0.080(2)
H(9A)	−0.413(4)	−0.767(2)	−0.115(2)
H(9B)	−0.377(4)	−0.865(2)	−0.035(2)
H(10A)	−0.311(3)	−0.651(2)	0.039(2)
H(10B)	−0.450(4)	−0.732(2)	0.046(2)
H(11A)	−0.234(3)	−0.838(2)	0.170(2)
H(11B)	−0.196(3)	−0.720(2)	0.217(2)
H(13A)	0.240(6)	−0.624(4)	0.509(4)
H(13B)	0.144(4)	−0.530(3)	0.429(3)
H(13C)	0.336(5)	−0.565(3)	0.468(3)
H(15A)	0.205(4)	−0.926(2)	0.549(3)
H(15B)	0.263(6)	−0.942(3)	0.461(3)
H(15C)	0.070(7)	−0.942(3)	0.426(4)
H(19A)	0.495(5)	−1.022(3)	0.237(3)
H(19B)	0.491(5)	−0.905(3)	0.208(4)
H(19C)	0.568(6)	−0.946(3)	0.316(4)

Table 2 Intramolecular distances (Å) involving the non-hydrogen atoms for spiroacetal **16** [a]

O(1)–C(2))	1.353(3)	C2)–C(3)	1.460(3)
O(1)–C(6)	1.454(2)	C(3)–C(4)	1.342(3)
O(7)–C(6)	1.388(3)	C(3)–C(13)	1.492(4)
O(7))–C(8)	1.451(3)	C(4)–C(5)	1.495(3)
O(12)–C(2)	1.216(3)	C(5)–C(6)	1.511(3)
O(14)–C(4)	1.352(3)	C(6)–C(11)	1.526(3)
O(14)–C(15)	1.409(4)	C(8)–C(9)	1.496(4)
O(16)–C(5)	1.454(3)	C(9)–C(10)	1.520(4)
O(16)–C(17)	1.341(3)	C(10)–C(11)	1.521(4)
O(18)–C(17)	1.198(3)	C(17)–C(19)	1.494(4)

[a] Estimated standard deviations in the least significant figure are given in parentheses.

under reduced pressure. Chromatography of the residue [light petroleum–ether (5:2)] afforded the title compound **29**[15] as an inseparable 1:1 mixture of diastereoisomers (28 mg, 52%); ν_{max}/cm^{-1} 3425, 3030, 1061 and 702; δ_H(300 MHz; $CDCl_3$) 1.56–1.97 (4 H, m), 2.20–2.55 (1 H, br s, OH), 3.77–4.13 (3 H, m), 4.46 (0.5 H, d, *J* 6, 7-H), 4.94 (0.5 H, d, *J* 3, 7-H) and 7.25–7.44 (5 H, m, ArH); *m/z* (CI, NH_3) 196 (M^+ + 18, 24), 178 (6), 162 (11) and 161 (100).

4-(4,5-*Dihydro*-2-*furyl*)-3-*methoxy*-2-*methylbut*-2-*en*-4-*olide* **30**.—*tert*-Butyllithium (1.3 mmol) was added dropwise to a stirred solution of 2,3-dihydrofuran (86 mg, 1.23 mmol) at −78 °C. The flask was transferred to an ice bath and stirred at 0 °C for 1 h, then re-cooled to −78 °C. A solution of the hydroxybutenolide **12** (80 mg, 0.56 mmol) cooled to −78 °C was added and the reaction was stirred at this temperature for 1 h, then allowed to warm to −10 °C over 2 h. The reaction was quenched with saturated aqueous ammonium chloride (5 cm^3), extracted with ethyl acetate, dried ($MgSO_4$) and concentrated under reduced pressure. Chromatography of the residue [light petroleum–ether (1:1)] yielded the *title compound* **30** as a white solid (87 mg, 80%), m.p. 114–117 °C (Found: C, 61.1; H, 6.4%; M^+, 196.0733. $C_{10}H_{12}O_4$ requires C, 61.2; H, 6.2%; *M*, 196.0736); ν_{max}/cm^{-1} 1738, 1661, 1337, 1090 and 1036; δ_H(300 MHz; C_6D_6) 1.64 (3 H, d, *J* 1, 3-Me), 2.12 (2 H, m, 4′-H_2), 3.12 (3 H, s, OMe), 3.95 (2 H, m, 5′-H_2), 4.77 (1 H, t, *J* 2.5, 3′-H) and 4.82 (1 H, d, *J* 1, 5-H); *m/z* (EI) 197 (M^+ + 1, 56%), 196 (22) and 128 (100).

4-(5,6-*Dihydro*-4H-*pyran*-2-*yl*)-3-*methoxy*-2-*methylbut*-2-*en*-4-*olide* **31**.—Using the procedure outlined above, 3,4-dihydro-2*H*-pyran (200 mg, 2.38 mmol) and the hydroxybutenolide **12** (130 mg, 0.90 mmol) gave the *title compound* **31** as a white solid (166 mg, 88%), m.p. 139–141 °C (Found: C, 62.8; H, 7.0%; M^+, 210.0900. $C_{11}H_{14}O_4$ requires C, 62.9; H, 6.7%; *M*, 210.0892); ν_{max}/cm^{-1} 1736, 1664, 1338, 1089 and 1030; δ_H(300 MHz; C_6D_6) 1.30 and 1.64 (each 2 H, m, 4′- and 5′-H_2), 1.77 (3 H, d, *J* 1.5, 3-Me), 3.25 (3 H, s, OMe), 3.54 (1 H, m, 6′-H_{ax}), 3.66 (1 H, m, 6′-H_{eq}), 4.57 (1 H, q, *J* 1.5, 5-H) and 4.68 (1 H, t, *J* 4, 3′-H); *m/z* (CI, NH_3) 228 (M^+ + 18, 5%), 212 (12) and 211 (100).

4-(2-*Hydroxy*-3,4,5,6-*tetrahydro*-2H-*pyran*-2-*yl*)-3-*methoxy*-2-*methylbut*-2-*en*-4-*olide* **33**.—Toluene-*p*-sulfonic acid monohydrate (50 mg, 0.26 mmol) was added to a stirred solution of butenolide **31** (28 mg, 0.13 mmol) in dichloromethane (3 cm^3) at ambient temperature. The mixture was stirred for 20 h and quenched with solid potassium carbonate. After 10 min, the reaction was filtered through Celite and concentrated under reduced pressure. Chromatography of the residue [light petroleum–ether (1:2)] yielded the *title compound* **33**, a mixture of diastereoisomers, as a pale yellow oil (12 mg, 40%) [Found: M^+ + H, 229.1077. $C_{11}H_{16}O_5$ requires *M*, 229.1076]; ν_{max}/cm^{-1} 3451, 1751 and 1662; δ_H(300 MHz; $CDCl_3$) 1.48–1.91 (6 H, m), 2.03 (1 H, d, *J* 1, 3-Me of minor isomer), 2.05 (2 H, d, *J* 1, 3-Me of major isomer), 3.59–3.79 and 3.85–3.95 (each 1 H, m), 4.14 (1 H, s, OMe of minor isomer), 4.17 (2 H, s, OMe of major isomer) and 4.43 (1 H, narrow m, 5-H); *m/z* (CI, NH_3) 246 (M^+ + 18, 17), 229 (31) and 211 (100).

Crystal Data for Compound **16**.—$C_{13}H_{18}O_6$, *M* = 270.28, colourless needles, crystal size 0.1 × 0.15 × 0.6 mm, monoclinic, *a* = 8.6498(8), *b* = 12.928(1), *c* = 14.0394(9) Å, β = 118.467(5)°, *U* = 1380.1(4) Å, space group $P2_1/c$(14), *Z* = 4, *D* = 1.301 g/cm^3, graphite monochromated Cu-Kα radiation from a 12 kW rotating anode generator, λ = 1.541 78 Å, μ(Cu-Kα) = 8.30 cm^{-1}, *F*(000) = 576.

Measurements were made on a Rigaku AFC5R diffractometer at 295 K, lattice parameters from the setting angles of 24 reflections in the range 77.4 < 2θ < 79.0°; ω–2θ scans, maximum 2θ = 120.2°, scan width (1.31 + 0.30 tan θ)° and scan speed 32.0°/min (in omega); weak reflections [$I < 10.0\ \sigma(I)$] rescanned (maximum of two rescans); 2329 reflections were collected, 2171 unique (R_{int} = 0.018), with 1751 considered observed [$I > 3.00\ \sigma(I)$]; intensities of three standard reflections measured after every 150 reflections did not change significantly; empirical absorption correction based on azimuthal scans of three reflections was applied, resulting in transmission factors ranging from 0.94 to 1.00; Lorentz and polarisation corrections applied.

The structure was solved by direct methods using the programs SHELXS[18] and DIRDIFF.[19] The non-hydrogen atoms were refined anisotropically. Hydrogen atoms were found in successive difference Fourier maps, and refined

Table 3 Intramolecular bond angles (°) involving the non-hydrogen atoms for spiroacetal **16**[a]

C(2)–O(1)–C(6))	119.8(2)	C(4)–C(5)–C(6))	110.1(2)
C(6)–O(7)–C(8)	115.4(2)	O(1)–C(6)–O(7)	106.4(2)
C(4)–O(14)–C(15)	121.3(2)	O(1)–C(6)–C(5)	110.2(2)
C(5)–O(16)–C(17)	118.2(2)	O(1)–C(6)–C(11)	109.3(2)
O(1)–C(2)–O(12)	117.0(2)	O(7)–C(6)–C(5)	106.8(2)
O(1)–C(2)–C(3)	119.6(2)	O(7)–C(6)–C(11)	112.4(2)
O(12)–C(2)–C(3)	123.5(2)	C(5)–C(6)–C(11)	111.7(2)
C(2)–C(3)–C(4)	119.0(2)	O(7)–C(8)–C(9)	111.9(2)
C(2)–C(3)–C(13)	117.4(2)	C(8)–C(9)–C(10)	109.8(2)
C(4)–C(3)–C(13)	123.4(2)	C(9)–C(10)–C(11)	109.9(2)
O(14)–C(4)–C(3)	118.4(2)	C(6)–C(11)–C(10)	111.7(2)
O(14)–C(4)–C(5)	121.1(2)	O(16)–C(17)–O(18)	123.8(2)
C(3)–C(4)–C(5)	120.4(2)	O(16)–C(17)–C(19)	110.3(3)
O(16)–C(5)–C(4)	105.8(2)	O(18)–C(17)–C(19)	125.9(3)
O(16)–C(5)–C(6)	110.2(2)		

[a] Estimated standard deviations in the least significant figure are given in parentheses.

isotropically. Full-matrix least squares of 244 parameters minimised the function $Ew(|F_o| - |F_c|)$.[2] The weighting scheme was based on counting statistics. Final $R = 0.051$, $R_w = 0.062$, maximum shift/error = 0.37 and the standard deviation of an observation of unit weight, $S = 2.44$. The maximum and minimum peaks on the final difference Fourier map corresponded to 0.27 and -0.21 $e^-/Å^3$, respectively. Neutral atom scattering factors were used,[20] anomalous dispersion effects were included in Fcalc;[21] the values for $\Delta f'$ and $\Delta f''$ were those of Cromer.[22] All calculations were performed using the TEXSAN[23] crystallographic software package of Molecular Structure Corporation. Atomic coordinates are given in Table 1, bond lengths in Table 2, and bond angles in Table 3.*

* Supplementary material (see Instructions for Authors, 1993, section 5.6.3, January issue) is available on request from the Cambridge Crystallographic Data Centre.

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