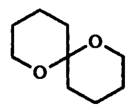
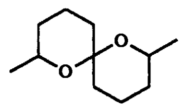
Syntheses of 2-ethyl-8-methyl-1,7-dioxaspiro[5.5]undecanols

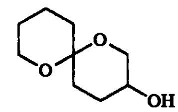
Mark F. Jacobs, Bill D. Suthers, Achim Hübener and William Kitching *
Department of Chemistry, The University of Queensland, Brisbane, Queensland 4072, Australia

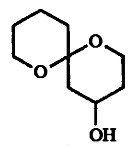
Synthetic approaches to ring- and side-chain hydroxy derivatives of the 2-ethyl-8-methyl-1,7-dioxaspiro-[5.5]undecane system **8** are described. Alkylation reactions of diethyl 3-oxopentanedioate, pentane-2,4-dione and acetone *N,N*-dimethylhydrazone have been employed. Appropriate choices of enantiomeric iodides in the alkylation sequences, sometimes followed by asymmetric dihydroxylation of derived hydroxyenones, have permitted access to key enantiomers of these alcohols, which have been fully characterised by ^{1}H and ^{13}C NMR spectroscopy, gas chromatographic–mass spectrometric methods, and chiral gas chromatography.

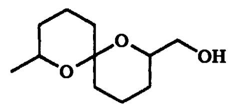
In previous publications[1–3] we have described the synthesis of a range of spiroacetals, many of which were components of insect secretions and emissions, particularly from Australasian fruit-fly species.[4,5] These unbranched, predominantly odd-carbon-numbered spiroacetals, *e.g.* **1** and **2**, were sometimes accompanied by low levels of hydroxy derivatives, *e.g.* **3** and **7**, whose structures and stereochemistry have been established in certain cases by chromatographic comparisons with synthesized samples.[1,6] Although less abundant than the odd-carbon-numbered examples, we have reported[7,8] that even-carbon-numbered spiroacetals, *e.g.* 2-ethyl-8-methyl-1,7-dioxaspiro-[5.5]undecane **8**, also occur in fruit-fly secretions, and we have established the absolute configuration of compound **8** in the case of *Bactrocera nigrotibialus*.[3] Examination of the gas chromatographic–mass spectrometric data of secretions in which compound **8** occurred indicated[9] low levels of hydroxy derivatives of compound **8**, *e.g.* **9** and **10**, as might have been expected on the pattern of occurrence of other hydroxy spiroacetals in insect species.[1,10] Clarification of the nature and stereochemistry of the suspected natural 2-ethyl-8-methyl-1,7-dioxaspiro[5.5]undecanols required regio- and stereo-selective syntheses of these alcohols for chromatographic and mass-spectrometric comparisons. The work described in the present report concerns spiroacetals **9**–**17** shown below.

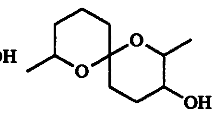

1

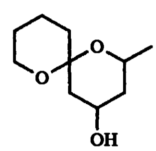

2

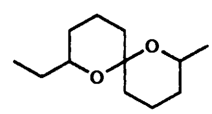

3

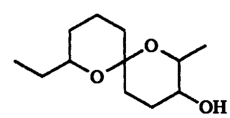

4

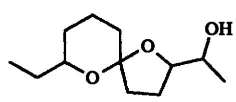

5

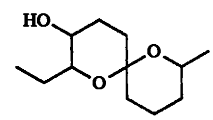

6

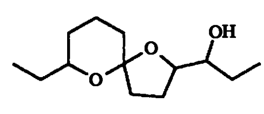

7

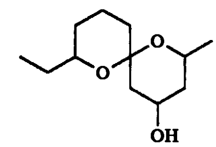

8

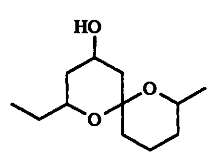

9

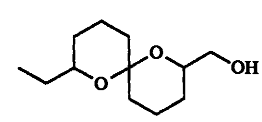

10

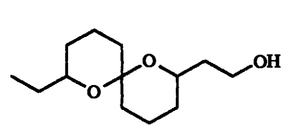

11

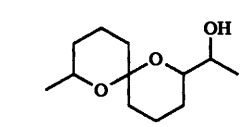

12


13


14


15

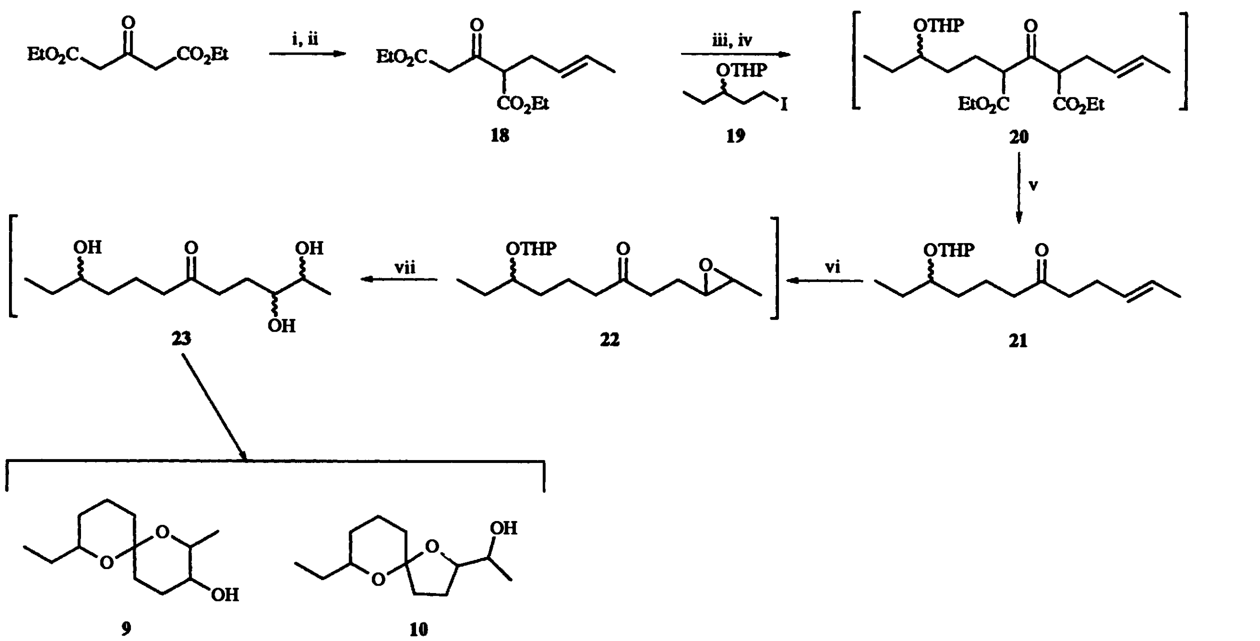

16


17

Results and discussion

The stereo- and regio-chemical possibilities in the 2,8-dimethyl-1,7-dioxaspiro[5.5]undecane system **2** carrying a hydroxy group at various positions have been outlined in detail elsewhere.[1] The present work addresses system **8** in which there are nine methyl or methylene sites for hydroxylation compared with four for system **2**, when one diastereoisomeric arrangement of the ring systems is considered.[1] Guidance from the mass spectral behaviour of natural components suspected to be hydroxy derivatives of compound **8**[9] indicated the possible occurrence of alcohols **9**, **11**, **13** and **14**, and these as the (*trans*/*trans*)-ring configured systems,† were chosen for synthesis. However, as before,[1,3] certain of the (*trans,cis*)-diastereoisomers were also obtained. The general approaches employed here are based closely on those described previously.[1] For completeness, certain stereoisomers of systems **15**–**17** were also synthesized, using asymmetric dihydroxylation as a key step.

† *cis* and *trans* are used to define the 1,3-stereochemical relationship between alkyl and oxygen on a tetrahydropyran ring, and have previously been referred to as *Z* and *E*. This practice in spiroacetal chemistry, and other ring systems for that matter, is convenient, but strictly speaking, incorrect. See, for examples, references 3, 5.



Scheme 1 *Reagents:* i, $Mg(OEt)_2$, EtOH; ii, $MeCH{=}CHCH_2Br$; iii, NaH, 18-crown-6; iv, **19**; v, 15% NaOH; vi, MCPBA; vii, AcOH–THF–water

8-Ethyl-2-methyl-1,7-dioxaspiro[5.5]undecan-3-ol 9

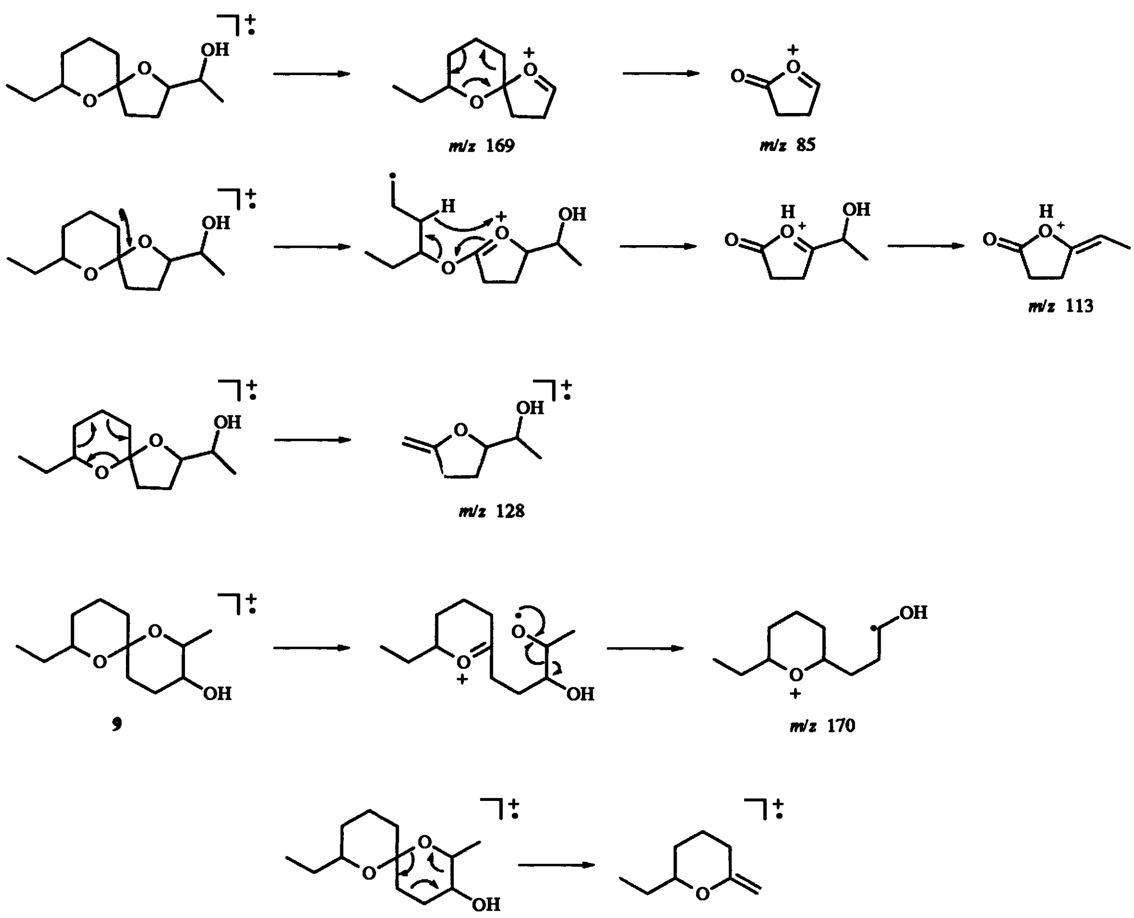
The approach employed utilised sequential alkylation of diethyl 3-oxopentanedioate[1,11] as developed previously[1] for the synthesis of compound **6**, and the steps involved in the acquisition of racemic product **9** are shown in Scheme 1.

The monoanion of the magnesium chelate[7] of diethyl 3-oxopentanedioate was alkylated with but-2-enyl bromide to produce compound **18** which was then alkylated with 1-iodo-3-(tetrahydropyran-2-yloxy)pentane **19** which was easily derived from methyl 3-oxopentanoate by standard procedures. Dialkylated derivative **20** was not isolated but experienced decarboxylative hyrolysis when treated with 15% aq. NaOH and refluxed for two days to provide enone **21**. Acidic work-up conditions were avoided to preserve the tetrahydropyranyloxy group, and chromatographic purification was not attempted as cyclisation and formation of a dihydropyran can intervene.[1,12] The crude product **21** was epoxidised with *m*-chloroperbenzoic acid (MCPBA) in dichloromethane to yield epoxide **22** which was not isolated but was subjected to hydrolysis and concurrent deprotection, and cyclisation (presumably *via* triol **23**) to a mixture of spiroacetals of systems **9** and **10**, in ~95% overall yield. GC–MS analysis indicated the presence of seven diastereoisomeric spiroacetals with one of system **9** (37%) and one of system **10** (37%) predominating. Isomers of compound **10** were readily characterised[1] by the ion at *m/z* 169, corresponding to M – $CH(OH)CH_3$, and isomers of **9** by prominent ions at *m/z* 170 and 126, as explained in Scheme 2.[13]

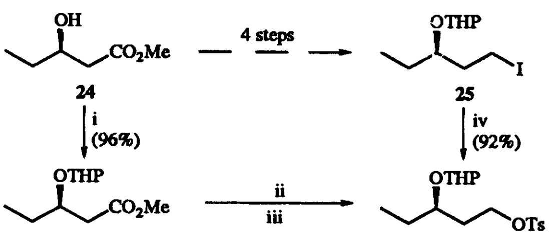
Following flash distillation, the components were separated by HPLC and their spectroscopic properties were identical with those of the enantiomers acquired using optically active iodide **25** in the synthesis summarised in Scheme 1. The racemic alcohols were utilised in chiral GC analyses in conjunction with the enantiomerically enriched samples now described.

(*R*)-Iodide **25**, previously[14] acquired from (*S*)-malic acid, was obtained from (*R*)-3-hydroxypentanoate[15] **24** as shown below (Scheme 3), and its use achieved the installation of (*R*)-chirality at C-10 in enone **21** (Scheme 1), and at C-8 in the target spiroacetal. However, epoxidation of ene **21** creates two additional chiral centres (in racemic form), as C-10 is too remote to cause significant asymmetric induction. The but-2-enyl bromide used was a 6:1 mixture of *E* and *Z* isomers, and thus a predominance of epoxides with like descriptors (for the epoxide carbons) is formed. S_N2-hydrolytic opening of the epoxides thus leads to diols with opposite configurations (from *E*) and like configurations (from *Z*), and removal of the tetrahydropyran (THP) group affords ketotriol **23** for which there are four stereoisomers, all with (*R*)-C-10. Spirocyclisation provides an additional chiral centre with the possibility of eight stereoisomers for each of the [5.5] and [4.5] ring systems, but the relative amounts are controlled by anomeric and steric effects.[1] Seven isomers were detected by GC–MS, and, as described above, two greatly predominated (36.5% and 38.5%), with the remaining minor components each constituting between 3% and 7% of the mixture. Isomers were identified in general by their mass spectral behaviour, as discussed above, and separated by high-performance liquid chromatography (HPLC). Of the two major isomers, that one with a shorter retention time (GC–MS) on a non-polar column was identified as the (*trans,trans,trans*) isomer **26** (Fig. 1) by analysis of the ^1H, ^{13}C and 2D NMR spectra. The signal at δ 3.06 was shown to arise from 3-H and exhibited two axial–axial and one axial–equatorial coupling, confirming the equatorial nature of 3-OH. Full discussion of the assignment of the spectra is presented elsewhere.[16]

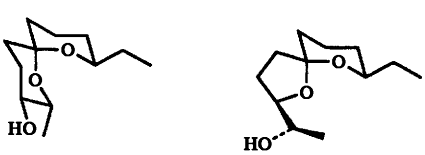
The other major isomer (38.5%), which eluted prior to the equatorial alcohol under HPLC conditions (silica; hexane–ethyl acetate), was an isomer of compound **10** on the basis of its mass spectrum. Stereochemical considerations and the expected incorporation of a *trans*-configured tetrahydropyran system led to the (*cis,trans*)-isomer **27** (Fig. 1). Complete NMR assignments were made and were consistent with this arrangement. A full discussion of the stereoisomeric interconversions available to isomers **26** and **27** is presented elsewhere.[16] A very minor isomer was also isolated and considered to be the C-3 epimer of compound **26** (*i.e.*, axial alcohol) on the basis of the signal at δ 3.75 for 2-H, which showed a small coupling (2.0 Hz) to 3-H, placing the latter in an equatorial environment, and thus the hydroxy group as axial. (Limited ^1H NMR data are summarised in the Experimental section.) Identification of the remaining minor components was not pursued as the fractions consisted of isomeric mixtures probably associated with simple epimerisation at the spirocentre, and the interconvertibility of the [5.5]undecane and [4.5]decane systems. Characterisation of these minor isomers was limited to GC–MS analysis and is reported in the



Scheme 2



Scheme 3 *Reagents:* i, DHP, PPTS, CH_2Cl_2; ii, $LiAlH_4$, Et_2O; iii, TsCl, pyridine; iv, NaI, acetone



(2*R*, 3*S*, 6*S*, 8*R*)
26

(2*R*, 5*S*, 7*R*, 11*S*)
27

Fig. 1

Experimental section. The optical purity of alcohols **26** and **27** was >99.5% enantiomeric excess (ee) by GC analysis (β-cyclodextrin column).

2-Ethyl-8-methyl-1,7-dioxaspiro[5.5]undecan-3-ol 11

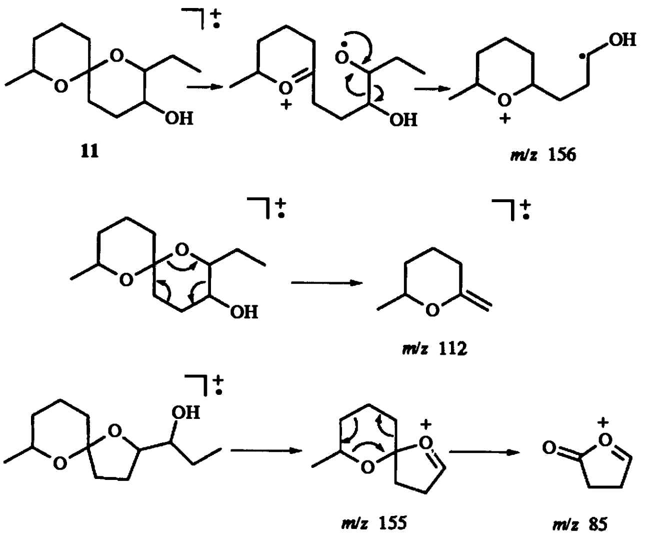
Alcohol **11** and the corresponding [4.5]decane isomer **12** were acquired by alkylation of diethyl 3-oxopentanedioate, as already detailed in Scheme 1 for alcohols **9** and **10**. In the present case, however, (*E*)-pent-3-enyl bromide and the chiral iodide 1-iodo-3-(tetrahydropyran-2-yloxy)butane [1,17,18] were employed. Use of essentially pure (*E*)-bromide ensured the formation of epoxides with like-configurations at adjacent carbons, and therefore unlike configurations of the resulting diols. Spirocyclisation gave a mixture of five isomeric spiroacetals (GC–MS analysis) of which two incorporated the [5.5]undecane system as in structure **11** (*m*/*z* 112, see Scheme 4) with the remaining three characterised by the base peak at *m*/*z* 155, indicating loss of the hydroxypropyl side-chain, appropriate for isomers of compound **12**.

HPLC separation (silica column) provided the two major isomers (37% and 40%), with the former being identified as compound **28** by analysis of its ^1H NMR spectrum, with the aid of 2D NMR techniques (see Fig. 2). In particular, the signal for 2-H^{ax} at δ_H 3.34 was identified by its coupling to the methylene protons (δ_H 1.49 and 2.00) on C-12 and to the low-field signal (δ_H 3.13) assigned to 3-H^{ax}.

This latter signal exhibited two axial–axial couplings and one smaller axial–equatorial coupling, and thus the hydroxy group was equatorial. A full discussion of the assignments is presented elsewhere.[16] The other major isomer isolated was contaminated (10%) with an isomeric component, with both exhibiting GC–MS behaviour typical of the [4.5]decane system, consistent with ^{13}C NMR resonances at δ_C ~ 106, typical of spirocarbon resonances in such systems. The *trans*-configured tetrahydropyran ring was supported by the low-field position of the resonance for 7-H^{ax} (δ_H 3.95) and for 9-H^{ax} (δ_H 1.85) ascribable to their 1,3-diaxial relationship with oxygen. This isomer is concluded to have structure **29**, with the minor contaminating isomer likely to be isomer **30**.[16]

8-Ethyl-2-methyl-1,7-dioxaspiro[5.5]undecan-4-ols 13

The 4-hydroxy isomers **13** and **14** have not been identified from natural sources, but synthesis was undertaken to facilitate comparisons with other monohydroxy spiroacetals, and to



Scheme 4

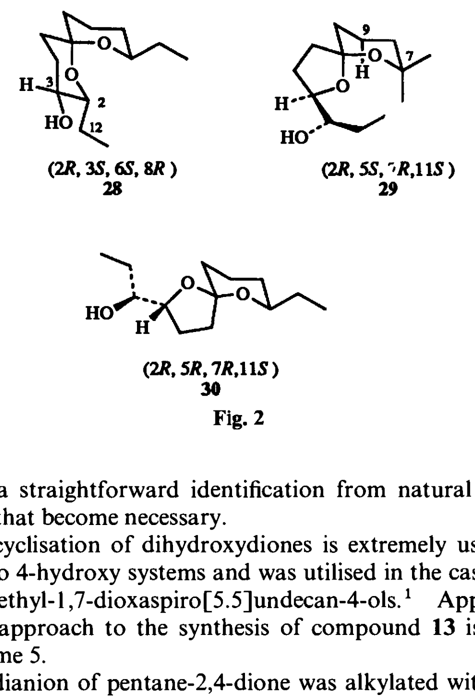
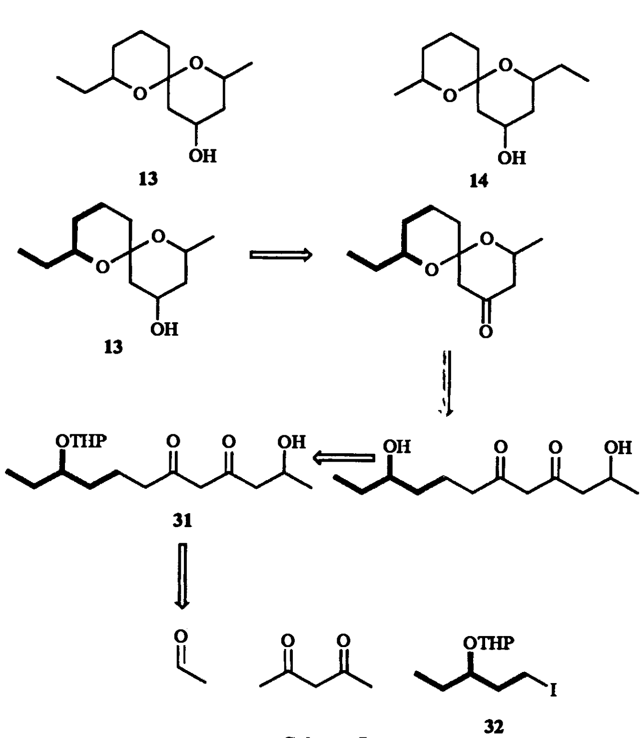


Fig. 2

enable a straightforward identification from natural sources should that become necessary.

The cyclisation of dihydroxydiones is extremely useful for access to 4-hydroxy systems and was utilised in the case of the 2,8-dimethyl-1,7-dioxaspiro[5.5]undecan-4-ols.[1] Application of this approach to the synthesis of compound **13** is shown in Scheme 5.

The dianion of pentane-2,4-dione was alkylated with chiral iodide **32** (as the racemate) to afford dione **33** which was isolated, and the reformed dianion was alkylated with acetaldehyde to provide dione **31**. Deprotection and cyclisation was effected in an HOAc–tetrahydrofuran (THF)–water (4:2:1) system to afford four isomeric spiroketones (GC–MS) with $M^+ = 212$ and characteristic ions at *m/z* 129, 126 and 111. This is



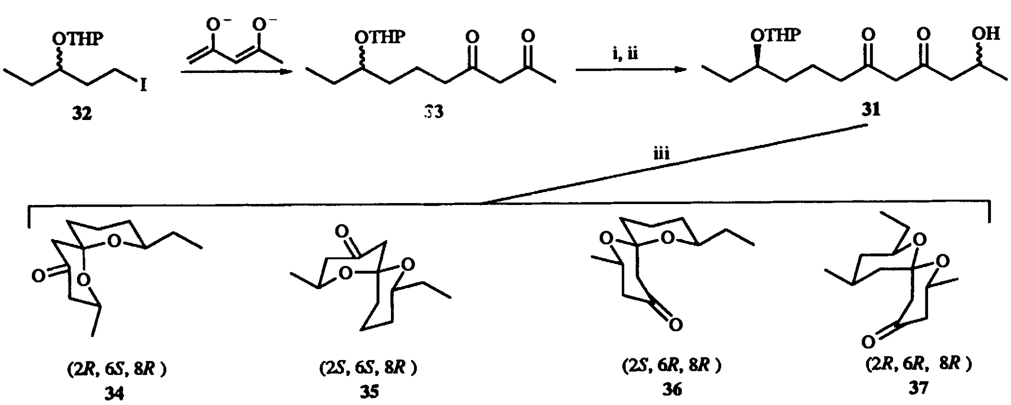
Scheme 5

summarised in Scheme 6, where one enantiomer of each of the racemic ketones **34**–**37** is drawn.

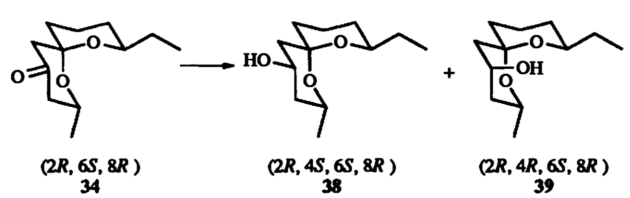
The major component (72%) was presumed to be the (*trans,trans*)-diastereoisomer **34** whilst two components in comparable amounts (13.6 and 13.1%) were thought to be the (*cis,trans*)- (**35**) and (*trans,cis*)- (**36**) isomers. A very minor component (1%), of longer retention time, had a very similar mass spectrum and was considered to be the least stable (*cis,cis*)-isomer[2] (**37**). Preparative HPLC (silica column) permitted acquisition of the isomers **34**–**36** (see Scheme 6) which were fully characterised by ^1H, ^{13}C and 2D NMR techniques. A full discussion of the NMR spectra is given elsewhere.[16]

Reduction of the individual isomers described above provided epimeric mixtures of the corresponding axial and equatorial alcohols, each of which exhibited molecular ions ($M^+ = 214$) and characteristic ions at *m/z* 131, 129, 128, 126 and 113. The racemic (*trans,trans*)-spiroketone **34** afforded a 58:42 mixture of equatorial isomer **38** and the axial epimer **39**, which could be separated by preparative gas chromatography (Scheme 7).

The stereochemistry of the ring systems and the orientations of the hydroxy groups were established by the usual NMR methods. For example, the axial epimer **39** exhibited signals for 2-H^{ax}, 8-H^{ax} and 4-H^{eq} at δ_H 4.10, 3.44 and δ_H 4.05,



Scheme 6 *Reagents:* i, LDA (2 mol equiv.); ii, acetaldehyde; iii, AcOH–THF–water



Scheme 7 *Reagents:* $LiAlH_4$, Et_2O

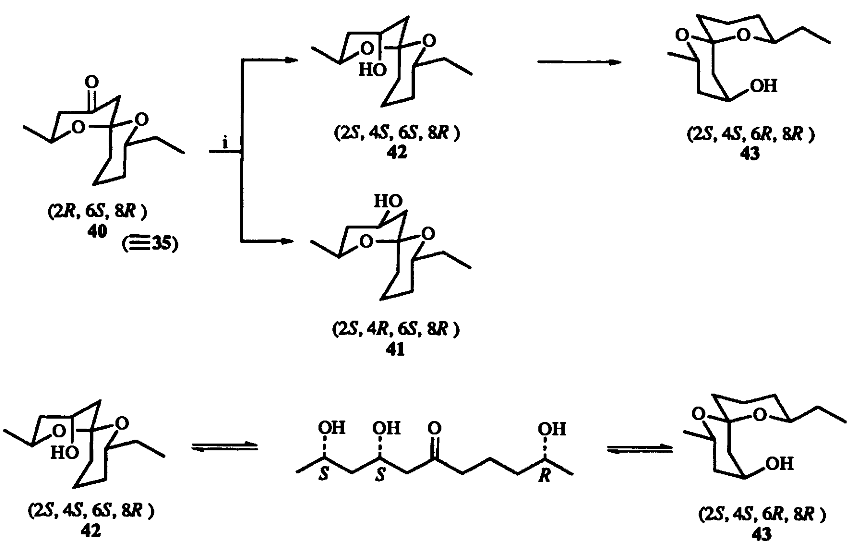
respectively, and 4-H^{eq} showed coupling to the hydroxy proton (δ_H 4.27), indicative of intramolecular H-bonding of this proton to the oxygen of the second ring.[19,20] This coupling (10.0 Hz) indicated a dihedral angle of ~ 155°, according to the modified Karplus equation.[21] The corresponding axial epimer of (*trans,trans*)-2,8-dimethyl-1,7-dioxaspiro[5.5]undecan-4-ol also exhibits such hydrogen bonding[1] and this phenomenon has been reported in 8-methyl-2-phenyl-1,7-dioxaspiro[5.5]-undecan-4-ol systems as well.[20,22] The second isomer was identified as the equatorial alcohol **38** (Scheme 7) on the basis of the coupling constants to 4-H (δ_H 4.12) and the spectral data are given in Tables 3 and 4.

In principle, the (*cis,trans*)- and (*trans,cis*)-spiroketones should constitute 50% of the total ketone product, but these isomers were less stable under the gas chromatographic conditions employed, and were obtained in modest yields only. The (*cis,trans*)-ketone **35**, was reduced with $LiAlH_4$ in diethyl ether and yielded four alcohols presumed to be epimeric alcohols of the (*cis,trans*) and (*trans,cis*) ring systems, the ability of which to interconvert (presumably through the ketotriols) has been emphasised previously.[23] Low levels of the epimeric (*trans,trans*)-spiro-alcohols were also present, but this was attributed to slight contamination with the (*trans,trans*)-ketone initially. Attempted purification of this alcohol mixture by preparative gas chromatography resulted in dehydration to produce olefinic spiroacetals, which are discussed elsewhere.[16] The alcohol mixture obtained from $LiAlH_4$ reduction of (*trans,cis*) ketone **36** consisted of three isomeric alcohols, but, again, attempted separation by preparative gas chromatography led to extensive dehydration. The NMR spectra of these alcohols were assigned to the axial and equatorial alcohols of the (*cis,trans*) and (*trans*,cis) systems, on the basis of complete NMR analyses of the alcohols obtained from the enatioselective route, which is now described.

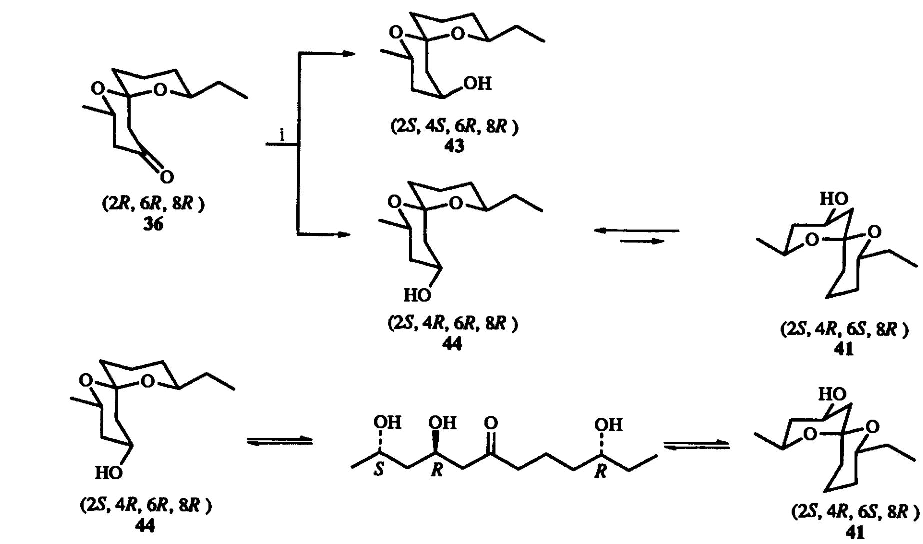
Enantioselective synthesis of 8-ethyl-2-methyl-1,7-dioxaspiro-[5.5]undecan-4-ols 13

Repetition of the sequence in Scheme 6 above with iodide **25**, the (*R*)-enantiomer of iodide **32**, provided the enantiomers of the desired equatorial and axial alcohols **38** and **39**, respectively. The ee of these alcohols was established as >99.5% by examination of their trifluoroacetate derivatives on a Lipodex A GC column. Reduction of the (2*S*,6*S*,8*R*) enantiomer **40** (≡**35**) of the (*cis,trans*)-ketone produced a mixture of two alcohols which were characterised by ^1H, ^{13}C and 2D NMR spectroscopy. The major alcohol (77%) was shown to be the equatorial alcohol **41** (see Scheme 8), with 2-H^{ax} (δ_H 3.19) and 8-H^{ax} (δ_H 4.01) exhibiting the expected coupling patterns, with 8-H^{ax} residing in the *trans*-configured ring on the basis of its deshielded position resulting from the 1,3-diaxial interaction with oxygen.[2,23] The remaining signal in the CH–O region (4-H) exhibited a coupling pattern requiring this proton to be axial and thus the hydroxy group was equatorial. The ^1H and ^{13}C chemical shifts are assembled in Tables 3 and 4. The structure of the minor isomer was more difficult to determine but it was tentatively assigned (*trans,cis*) ring stereochemistry, with 2-H^{ax} at lowest field (δ_H 4.23) and 8-H^{ax} at higher field (δ_H 3.15). The 4-H coupling pattern closely resembled a 'ddddd' pattern (J 10 and 4 × 5 Hz couplings) which would indicate coupling to OH (J 10 Hz) and an equatorial orientation for 4-H. Hydroxy-group coupling has been observed in this work for the axial alcohol **39** and, on this basis, the minor isomer would be (*trans,cis*)-**43** as such coupling is not possible in (*cis,trans*)-**42**. This conclusion requires ring opening, with the initially formed axial alcohol **42** converting into the apparently more stable alternative axial alcohol **43** *via* the ketotriol (Scheme 8).

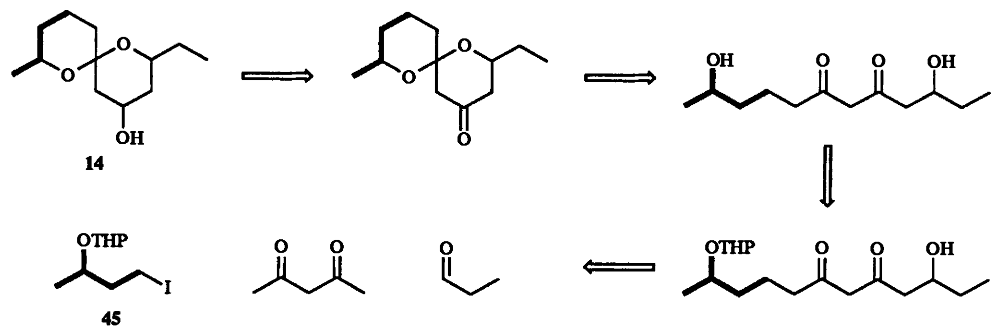
Reduction of the (2*S*,6*R*,8*R*)-spiroketone **36** with $LiAlH_4$ provided three alcohols, with the major one being the (*trans*,*cis*)-equatorial alcohol **44** (70%), along with some of the (*cis,trans*)-equatorial alcohol **41** (11%) and a third isomer thought to be the axial (*trans,cis*)-alcohol **43**. Material was limited and HPLC separation was not attempted, but ^1H, ^{13}C and 2D NMR spectra were obtained for the mixture. Ring stereochemistry was assigned to the predominant isomer on the basis of the chemical shifts of 2-H^{ax} (δ_H 4.23) and 8-H^{ax} (δ_H 3.15), and the minor equatorial alcohol **41** may have arisen through the ring opening–closing sequence shown in Scheme 9.



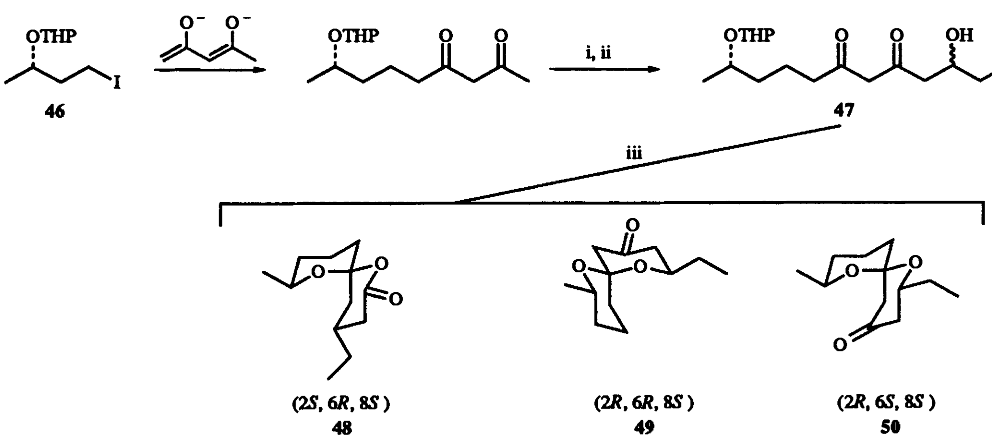
Scheme 8 *Reagent:* i, $LiAlH_4$



Scheme 9 *Reagent:* i, $LiAlH_4$



Scheme 10



Scheme 11 *Reagents:* i, LDA (2 mol equiv.); ii, propanal; iii, AcOH–THF–water

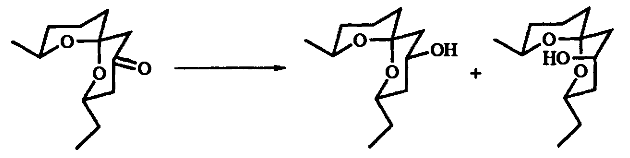
2-Ethyl-8-methyl-1,7-dioxaspiro[5.5]undecan-4-ols 14

As shown in Scheme 10, sequential alkylation of pentane-2,4-dione with 1-iodo-3-(tetrahydropyran-2-yloxy)butane **45** and propanal would provide the required dihydroxydione, the precursor of the 2-ethyl-8-methyl-1,7-dioxaspiro[5.5]undecan-4-one system. The availability of chiral iodide **45** in both enantiomeric forms allows access to enantiomers of the ketones, and by reduction, the alcohols.

In the event, (*S*)-1-iodo-3-(tetrahydropyran-2-yloxy)butane **46** was employed in the first alkylation, and the dianion formed from this product was treated with propanal, to provide hydroxy dione **47**, as shown in Scheme 11. The protected dihydroxy dione **47** was not purified (to avoid formation of a dihydropyran moiety) but was subjected to deprotection and cyclisation, with HOAc–THF to produce a mixture of three diastereoisomeric ketones (Scheme 11). All three exhibited an apparent molecular ion at *m*/*z* 212 and prominent ions at *m*/*z* 143, 142, 140 and 115, characteristic of the spiroacetal moiety. Although, in principle, the (*cis*,*trans*)- and (*trans*,*cis*)-spiroketones should constitute 50% of the ketone mixture (if no induction occurred during the alkylation step with propanal), preparative HPLC yielded the (*trans*,*trans*)-ketone **48** as the major component (88%) [slightly contaminated with the (*cis*,*trans*)-ketone **49**], and a minor amount of the pure (*trans*,*cis*)-ketone **50**.

(*trans*,*trans*)-Ketone **48** was fully characterised by NMR methods, and 2-H^{ax} and 8-H^{ax} were located at δ_H 3.62 and 3.54, respectively, and exhibited the expected coupling patterns. The ^1H and ^{13}C NMR spectra were fully assigned and are listed in Tables 1 and 2. A very minor component, shown to be the (*cis*,*trans*)-ketone **49**, contaminated ketone **48**, and from the downfield position of 8-H^{ax} relative to that of 2-H^{ax} [2,23] the ring stereochemistry was established at (*cis,trans*). This was confirmed also by the low-field position of 10-H^{ax}. Some of the ^{13}C signals for this isomer were located, *viz.* δ_C 203.0 (C=O), 99.02 (C-6) and 64.85 and 70.81 (C-2 and C-8), but full assignment of the higher-field part of the spectrum was not possible. The structure of the other minor isomer was established as the (*trans,cis*)-ketone **50**, on the basis of the low-field position (δ_H 4.26) of 2-H^{ax}, indicating operation of a 1,3-diaxial interaction with oxygen, whereas 8-H^{ax} was at higher field (δ_H 3.47). The data for the assigned ^1H and ^{13}C NMR spectra are presented in Tables 1 and 2.

Reduction of the spiroketone **48** with $LiAlH_4$ afforded the epimeric alcohols **51** and **52**, with the equatorial isomer predominating (54:46), as shown in Scheme 12.



(2*S*, 6*R*, 8*S*) **48** — (2*S*, 4*R*, 6*R*, 8*S*) **51** + (2*S*, 4*S*, 6*R*, 8*S*) **52**

Scheme 12 *Reagents:* $LiAlH_4$, Et_2O

Preparative gas chromatography afforded pure samples of the alcohols for NMR examination. The first eluting isomer was the axial epimer **52** which exhibited the usual coupling patterns for 2-H^{ax} (δ_H 3.84) and 8-H^{ax} (δ_H 3.67), whilst 4-H (δ_H 4.06) coupled to the hydroxy proton (*J* 9.5 Hz), indicative of its H-bonding to oxygen of the neighbouring ring. Thus the hydroxy group is axial, and the full assignments of the ^1H and ^{13}C NMR spectra are shown in Tables 3 and 4. The remaining isomer was the equatorial alcohol **51**, with 2-H^{ax} (δ_H 3.40) and 8-H^{ax} (δ_H 3.65) located by their characteristic coupling patterns, and similar considerations required the OH group to be equatorial. The NMR assignments are shown in Tables 3 and 4. The starting (*S*)-iodide **46** (~80% ee) yielded predominantly the enantiomers shown in Scheme 12, which, as expected, were of ~80% ee as determined by chiral GC analyses.

Table 1 ^{13}C NMR chemical shifts for diastereoisomers of 2,8-dialkyl (methyl, ethyl)-1,7-dioxaspiro[5.5]undecan-4-ones (C_6D_6)

Carbon	34	48	36	35	50	49
2	64.95	69.79	66.22	67.63	70.89	70.81 [a]
3	48.41	46.72	48.80	46.61	46.68	
4	203.52	203.83	203.87	204.58	204.05	203.05
5	51.69	52.00	46.05	50.75	47.36	
6	99.19	99.12	100.44	98.52	100.31	99.02
8	71.35	66.23	74.61	71.56	69.38	64.85 [a]
9	30.18	32.21	30.23	30.55	31.88	
10	19.24	19.33	19.55	18.85	18.86	
11	34.83	34.59	35.74	34.14	45.44	
12 Me/CH_2	21.67	29.29	21.89	22.40	29.37	
13 Me/CH_2	29.23	10.03	29.36	29.39	9.58	
14 Me	10.05	21.73	10.14	10.28	21.79	

[a] Interchangeable.

Side-chain hydroxy derivatives of 2-ethyl-8-methyl-1,7-dioxaspiro[5.5]undecane

Acquisition of enantiomers of systems **15–17** was based on alkylation of acetone *N,N*-dimethylhydrazone,[3,8] followed in

Table 2 ^1H NMR chemical shifts for diastereoisomers of 2,8-dialkyl (methyl, ethyl)-1,7-dioxaspiro[5.5]undecan-4-ones (C_6D_6)

Proton	34	48	36	35	50	49
2-H^{ax}	3.88	3.62	4.49	3.65	4.26	3.31
3-H^{ax}	1.79	1.80	1.83	2.30	1.85	2.20
3-H^{eq}	2.17	2.19	2.15	2.03	2.22	2.05
5-H^{ax}	1.97	1.97	1.84	2.43	1.87	2.48
5-H^{eq}	2.38	2.42	2.84	2.26	2.79	2.32
8-H^{ax}	3.27	3.54	3.18	3.77	3.47	4.06
9-H^{ax}	0.96	0.96	0.94	0.97	0.96	
9-H^{eq}	1.25	1.45	1.11	1.30	1.04–1.16	
10-H^{ax}	1.84	1.82	1.10	1.75	1.04–1.16	1.67
10-H^{eq}	1.33	1.31	1.34	1.30	1.37–1.46	
11-H^{ax}	1.10	1.08	1.61	1.05	1.60	
11-H^{eq}	1.55	1.53	1.49	1.50	1.37–1.46	
12 Me/CH_2	1.03	1.20/1.40	1.02	1.01	1.28/1.47	
13 Me/CH_2	1.26/1.40	0.83	1.23–1.5	1.2–1.43	0.77	0.81
14 Me	0.81	1.00	0.85	0.82	1.03	1.02

Table 3 ^{13}C NMR chemical shifts for 2,8-dialkyl (methyl, ethyl)-1,7-dioxaspiro[5.5]undecan-3- and -4-ols (C_6D_6)

Carbon	Parent	3-OH^{eq} 26	3-OH^{eq} 28	4-OH^{eq} 38	4-OH^{ax} 39	4-OH^{eq} 41	4-OH^{eq} 51	4-OH^{ax} 52
2	70.30	70.00	74.76	64.21	60.32	66.41	69.31	65.32
3	31.32	72.55	70.65	43.10	40.42	47.72	41.19	38.60
4	19.30 [a]	28.81	28.91	64.59	65.30	65.31	64.62	65.27
5	35.75 [b]	36.02	35.79	45.40	40.53	45.44	45.60	40.86
6	95.87	95.26	95.21	97.72	98.50	98.09	97.67	98.39
8	65.17	70.61	65.49	70.51	71.59	71.39	65.37	66.15
9	33.28	31.07	33.11	31.04	30.65	30.92	33.00	32.54
10	19.43 [a]	19.43	19.66	19.28	18.71	18.74	19.42	18.85
11	35.98 [b]	35.04	34.90	35.57	35.41	30.92	35.37	35.12
12 Me/CH_2	29.76	18.48	25.36	21.70	21.72	22.27	29.29	29.29
13 Me/CH_2	10.51	29.62	10.37	29.58	29.19	29.64	10.48	10.33
14 Me	22.20	10.41	22.06	10.42	10.36	10.06	22.07	21.84

[a,b] Interchangeable.

Table 4 ^{1}H NMR chemical shifts for 2,8-dialkyl (methyl, ethyl)-1,7-dioxaspiro[5.5]undecan-3- and -4-ols (C_6D_6)

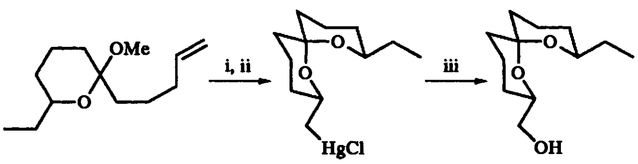
Hydrogen	Parent	3-OH^{eq} **26**	3-OH^{eq} **28**	4-OH^{eq} **38**	4-OH^{ax} **39**	4-OH^{eq} **41**	4-OH^{eq} **51**	4-OH^{ax} **52**
2-H^{ax}	3.51	3.58	3.34	3.67	4.10	3.19	3.40	3.84
3-H^{ax}	1.11	3.06	3.13	1.10	1.20	1.20	1.10	1.22
3-H^{eq}	1.36–1.46	OH	OH	1.74	1.80	1.56–1.72	1.74	1.80
4-H^{ax}	2.03^a	1.91	1.93	4.12	OH	3.66	4.13	OH
4-H^{eq}	1.36–1.46	1.58	1.58	OH	4.05	OH	OH	4.06
5-H^{ax}	1.31^b	1.39	1.36	1.24	1.30	1.56–1.72	1.23	1.31
5-H^{eq}	1.64	1.68	1.68	2.00	1.80	1.93	2.03	1.83
8-H^{ax}	3.78	3.45	3.73	3.39	3.44	4.01	3.65	3.67
9-H^{ax}	1.11	1.07	1.07	1.06	1.00	1.08	1.06	0.96
9-H^{eq}	1.36–1.46	1.36	1.36	1.33	1.25	1.27–1.45	1.3–1.4	1.22
10-H^{ax}	2.05^a	1.96	1.93	1.96	1.90	1.63	1.95	1.87
10-H^{eq}	1.36–1.46	1.40	1.36	1.37	1.30	1.27–1.45	1.3–1.4	1.21
11-H^{ax}	1.32^b	1.27	1.26	1.29	1.21	1.08	1.29	1.19
11-H^{eq}	1.64	1.55	1.52	1.62	1.47	1.56–1.72	1.60	1.45
12 Me/CH_2	1.5–1.59	1.34	2.00/1.49	1.15	1.15	1.13	1.36/1.53	1.37/1.52
13 Me/CH_2	1.00	1.35/1.52	1.10	1.26–1.53	1.16–1.34	1.27–1.45/1.52	0.95	0.96
14 Me	1.17	0.96	1.12	0.92	0.83	0.88	1.09	0.93

^{a,b} Interchangeable.

the main by application of asymmetric dihydroxylation (AD) methodology[24] to furnish 1,2-diols, which on cyclisation furnished the desired spiroketals bearing the hydroxy-substituted side-chain.

(8-Ethyl-1,7-dioxaspiro[5.5]undecan-2-yl)methanol 15

The racemic (*trans,trans*)-diastereoisomer of this system has been described previously[7,25] and was acquired by oxidative demercuriation as shown in Scheme 13.



Scheme 13 *Reagents and conditions:* i, $Hg(OAc)_2$, H_3O^+; ii, NaCl; iii, O_2, $HCONMe_2$, $NaBH_4$, 0 °C

In the present work acetone *N,N*-dimethylhydrazone was sequentially alkylated with (*R*)-iodide **25** and but-3-enyl bromide to provide protected hydroxy enone **53**. Reversible oxymercuriation cyclisation, as discussed previously,[3] led to the (*trans,trans*)-mercurial, which on oxidative demercuriation[25] provided [(*trans,trans*)-(8-ethyl-1,7-dioxaspiro[5.5]-undecan-2-yl)]methanol, necessarily as the (2*S*,6*S*,8*R*)-enantiomer **54** (Scheme 14).

Oxidative demercuriation provided the alcohol in moderate yield only (~50%),[7,25] and a more efficient procedure from enone **53** to stereoisomers of compound **15** was sought. Asymmetric dihydroxylation[24] was attractive as it could provide selectively the (*trans,trans*) or the (*trans,cis*) (*cis,trans*) arrangements of structure **15**. Based on the results of Sharpless,[24] it was anticipated that reaction of enone **53** with 'AD-α-mix' should provide predominantly the (*trans,trans*)-diastereoisomer as the (2*S*,6*S*,8*R*)-enantiomer **54** which was already available from the mercury-based chemistry shown in Scheme 14. This was indeed the case, as shown in Scheme 15, and use of 'AD-β-mix' provided a mixture mainly of the (*cis,trans*)- and (*trans,cis*)-diastereoisomers as the (2*R*,6*S*,8*R*)-**55** and (2*R*,6*R*,8*R*)-**56** enantiomers, respectively. The three diastereoisomers were separated by flash chromatography so that in spite of the ~70% ee in each of the AD reactions the contaminating minor isomer could be removed, although there were indications that the acetal centre was slightly labile on silica under some conditions.

1-(8-Methyl-1,7-dioxaspiro[5.5]undecan-2-yl)ethanol 17

Asymmetric dihydroxylation also provided access to spiroacetal system **17** as shown in Scheme 16. In the initial alkylation, use of (*R*)-1-iodo-3-(tetrahydropyran-2-yloxy)butane[1,23] **57** and (*E*)-pent-3-enyl bromide, followed by silica-induced removal of the hydrazone, provided protected hydroxy enone **58**, which was subjected to reaction with 'AD-α-mix' as shown in Scheme 16. Use of 'AD-β-mix' should provide stereoisomers **60** and **61**, as shown in Scheme 16 but this sequence was not conducted. The monoprotected keto triol was not isolated after the AD-reaction, but instead was treated with acid to effect deprotection and cyclisation to the spiroacetals. In this way, the (2*S*,6*S*,8*R*,12*S*)-isomer **59** was acquired, along with minor amounts of several other diastereoisomers.

2-(8-Methyl-1,7-dioxaspiro[5.5]undecan-2-yl]ethanol 16

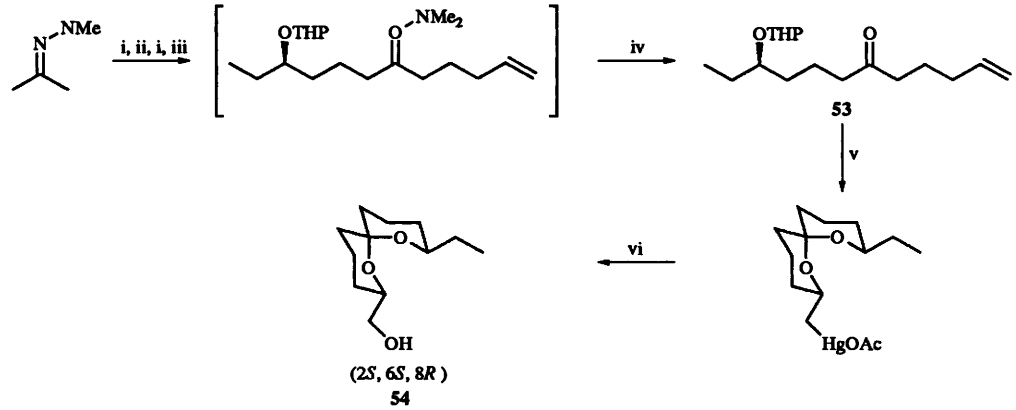
Sequential alkylation of acetone *N,N*-dimethylhydrazone was employed to access system **16**, and chirality control again was based on the use (*R*)-1-iodo-3-(tetrahydropyran-2-yloxy)butane **57**. The required formal 1,3-diol unit was introduced by use of acetonide **62**, which was acquired from diethyl 3-oxopentanedioate[26,27] as shown in Scheme 17. Deprotection and cylisation provided a mixture of diastereoisomers, and flash chromatography furnished pure (2*S*,6*S*,8*R*)-**63** but a mixture of the **64**–**65** pair.

The present work, when taken in conjunction with our previous reports,[1,6] essentially completes the syntheses of the alcohols shown in structures **1**–**17**, many in more than one diastereoisomeric form. We have not undertaken syntheses of the 2-ethyl-8-methyl-1,7-dioxaspiro[5.5]undecan-5-ols, or the 8-ethyl-2-methyl-1,7-dioxaspiro[5.5]undecan-6-ols, but adoption of our previous method[1] would provide these. However, there is no evidence that alcohols of these structural categories are insect components. With the availability of the currently described alcohols for which key spectroscopic data are located in the Tables, direct comparison with naturally occurring components will now be possible and should be reported in the near future.

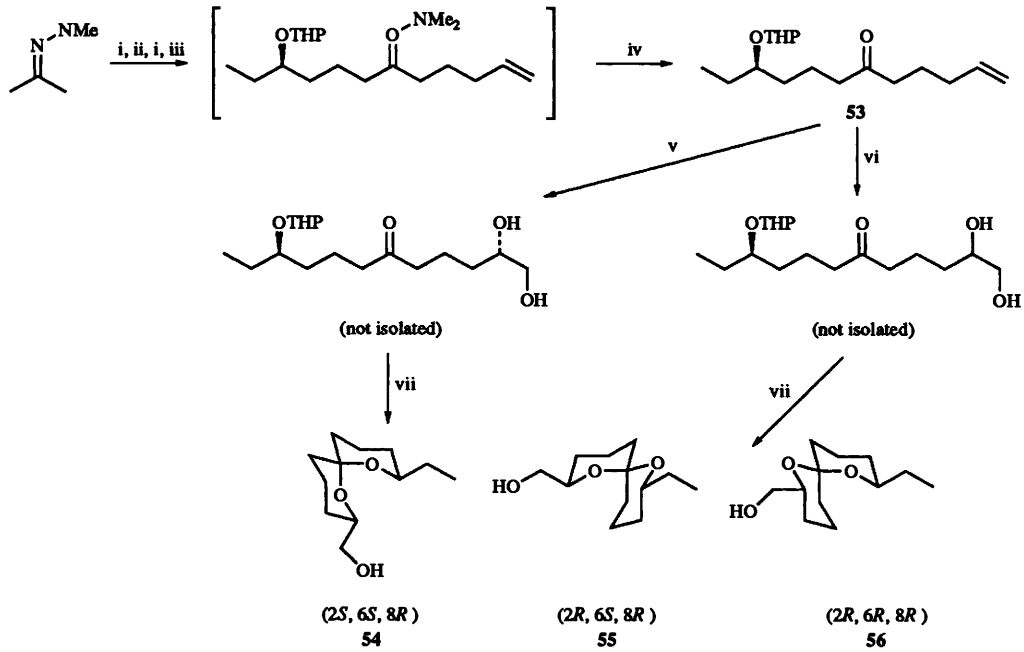
Experimental

Spectra

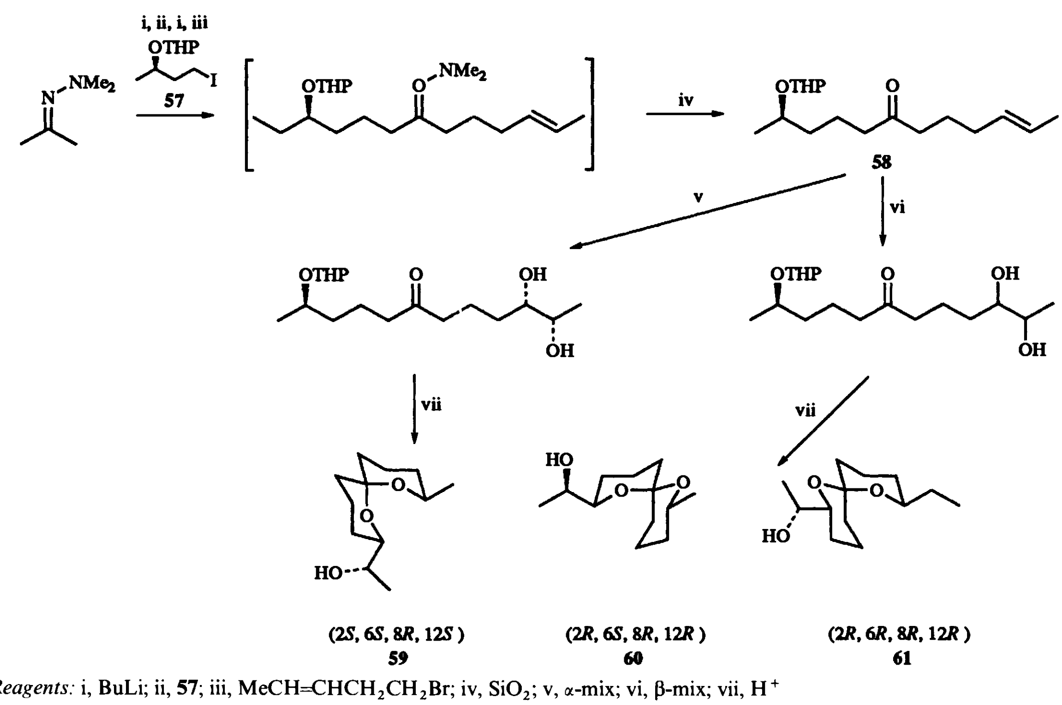
^{1}H NMR spectra were recorded at 400 MHz (FT mode) on a JEOL JNM-GX 400 spectrometer or at 500 MHz on a Bruker AMX-500 spectrometer. Deuteriochloroform or [$^2H_6$]benzene



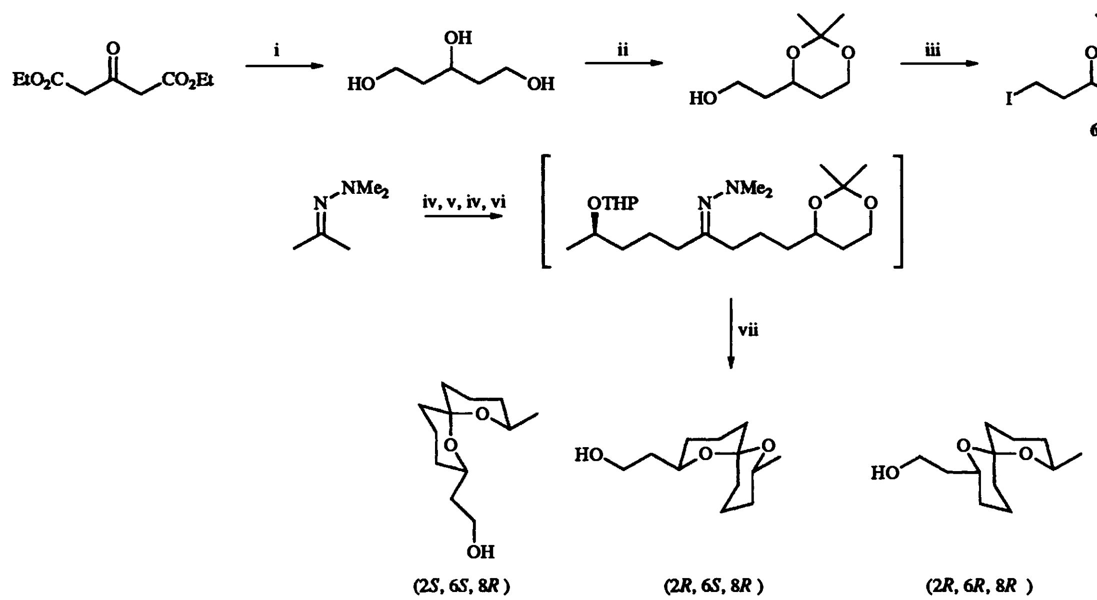
Scheme 14 *Reagents:* i, BuLi; ii, 25; iii, CH_2=$CHCH_2CH_2Br$; iv, SiO_2; v, $Hg(OAc)_2$, THF, H_3O^+; vi, O_2, $HCONMe_2$, $NaBH_4$



Scheme 15 *Reagents:* i, BuLi; ii, 25; iii, CH_2=$CHCH_2CH_2Br$; iv, SiO_2; v, α-mix; vi, β-mix; vii, H^+



Scheme 16 *Reagents:* i, BuLi; ii, 57; iii, MeCH=$CHCH_2CH_2Br$; iv, SiO_2; v, α-mix; vi, β-mix; vii, H^+



Scheme 17 *Reagents:* i, $LiAlH_4$; ii, $Me_2C(OMe)_2$, H^+; iii, PPh_3, I_2, imidazole; iv, BuLi; v, **57**; vi, **62**; vii, H^+

were employed as solvents, and chemical shifts (δ-values) are relative to internal tetramethylsilane (0.0 ppm), residual $CHCl_3$ (δ 7.24), or residual C_6D_5H (δ 7.15). ^{13}C NMR spectra were recorded on either a JEOL JNM-GX-400, Bruker AC200 or a Bruker AMX-500 spectrometer at 100, 25 or 125 MHz, respectively. Chemical shifts are referenced to the central peak of the triplet due to the solvent ($CDCl_3$, δ_C 77.00 or C_6D_6, δ_C 128.00). Two-dimensional NMR experiments were conducted on either the JEOL JNM-GX-400 or the Bruker AMX-500 spectrometer, using the supplied software. High-resolution mass spectra (sometimes on isomeric mixtures) were recorded on a Kratos MS-25RFA spectrometer. Preparative gas chromatography was performed using a Shimadzu gas chromatograph Model GC-9A equipped with OV101 and C-20M columns. Low-resolution mass spectra refer to combined GC–MS measurements recorded on a Hewlett-Packard 5970 Series GC–MS system, using a non-polar (BP5) column. Optical rotations were recorded using a Perkin-Elmer 241 MC polarimeter, and are reported in units of 10^{-1} deg cm^2 g^{-1}. Chiral gas chromatographic analyses were conducted using a Lipodex A 50m column (Macherey-Nagel) and a CP-cyclodextrin-2,3,6-M-19 50m column (Chrompack).

(R)-1-Iodo-3-(tetrahydropyran-2-yloxy)pentane 25

This iodide was acquired by the steps outlined in Scheme 3. Pyridinium toluene-*p*-sulfonate (PPTS) (0.4 g, 1.6 mmol) was added to a solution of methyl (*R*)-3-hydroxypentanoate (9.5 g, 72 mmol) (Sigma Chemicals) and dihydropyran (DHP) (8.2 g, 97.6 mmol) in dry CH_2Cl_2 (150 cm^3). The mixture was stirred for 3 h at room temperature, washed succcessively with 10% aq. Na_2CO_3 (3 × 50 cm^3) and water (2 × 50 cm^3), dried ($MgSO_4$), and concentrated under reduced pressure. Distillation (bp 96–98 °C; 0.3 mmHg) gave the desired protected ester as a clear oil (15.0 g, 96%); *m/z* 187 ($M^{\cdot+}$ − CH_2CH_3, 0.8%), 115 (43), 101 (38), 85 (100), 83 (36) and 73 (35); δ_C($CDCl_3$) (two diastereoisomers) dd 9.16, 9.60, 19.65, 19.76, 25.35, 25.39, 26.78, 28.38, 30.87, 31.00, 38.97, 40.32, 51.36, 51.41, 62.48, 62.70, 75.14, 75.25, 98.15, 98.50 and 172.16 (2 C); δ_H($CDCl_3$) (two diastereoisomers) 0.85 (3 H, t, *J* 7.45, Me), 0.90 (3 H, t, *J* 7.45, Me), 1.40–1.80 (18 H, m), 2.38–2.65 (4 H, m), 3.42 (2 H, m), 3.62 (3 H, s, CO_2Me), 3.62 (3 H, s, CO_2Me), 3.76–3.87 (2 H, m) and 4.63 (2 H, m, OCHO).

This ester (14.8 g, 68.5 mmol) was reduced with $LiAlH_4$ (1.95 g, 51.4 mmol) in the standard way, and distillation (bp 90–94 °C; 0.7 mmHg) yielded (*R*)-3-(tetrahydropyran-2-yloxy)-pentan-1-ol as a diastereoisomeric mixture (11.3 g, 88%); Isomer I: *m/z* 159 ($M^{\cdot+}$ − CH_2CH_3, 2%), 101 (20), 85 (100), 69 (65), 67 (16), 57 (24) and 56 (34). Isomer 2: *m/z* 159 (1%), 101 (20), 85 (100), 69 (60), 67 (17), 57 (20) and 56 (30); δ_C($CDCl_3$) (major diastereoisomer) 9.36, 20.21, 28.86, 30.96, 32.38, 34.60, 62.62, 66.60, 78.04 and 101.92; δ_H($CDCl_3$) 0.87 (t, *J* 7.45, Me, minor isomer), 0.90 (3 H, t, *J* 7.45, Me, major isomer), 1.45–1.84 (10 H, m), 2.37 (1 H, br s, OH), 3.46 (2 H, m), 3.60–3.92 (3 H, m), 4.47 (m, OCHO, minor isomer) and 4.68 (1 H, m, OCHO, major isomer).

(*R*)-3-(Tetrahydropyran-2-yloxy)-1-(toluene-*p*-sulfonyloxy)-pentane (17.34 g, 85%) was prepared from the above alcohol (11.2 g, 59.6 mmol) in the normal way and the crude tosyl ester (17.3 g, 50.6 mmol) was added to a solution of NaI (11.38 g, 75.9 mmol) and $NaHCO_3$ (6.38 g, 75.9 mmol) in dry acetone (180 cm^3) and the mixture was stirred for 20 h at room temp. The acetone was removed and the residue was diluted with toluene (100 cm^3) and water (100 cm^3). The aqueous layer was separated, and extracted with toluene (3 × 50 cm^3). The combined organic layers were washed successively with 10% aq. $Na_2S_2O_3$ (2 × 100 cm^3) and water (100 cm^3), dried ($MgSO_4$), and concentrated under reduced pressure to give crude iodide **25** (14.0 g). This crude product was used without purification and exhibited mass and ^1H and ^{13}C NMR spectra in agreement with those observed for the racemate **19** which was made from methyl 3-oxopentanoate by straightforward procedures and characterised as follows: *m/z* (GC–MS) 298 (M^+, 0.4%), 197 (9), 171 (4), 155 (8), 143 (8), 101 (11), 86 (6), 85 (100) (Found: M^+ + 1, 299.0516. Calc. for $C_{10}H_{20}IO_2$: *m/z* 299.0508); δ_C($CDCl_3$) (two diastereoisomers) 2.51, 3.19, 9.08, 9.57, 19.99, 20.12, 25.38, 25.40, 25.96, 27.60, 31.08, 31.15, 37.76, 39.05, 62.93, 63.14, 77.49, 78.93, 97.52 and 99.22; δ_H($CDCl_3$) (two diastereoisomers) 0.84 (3 H, t, *J* 7.45, Me), 0.89 (3 H, t, *J* 7.45, Me), 1.44–1.80 (16 H, m), 1.93–2.07 (4 H, m), 3.12–3.31 (4 H, m, CH_2I), 3.43–3.49 (2 H, m), 3.56–3.62 (2 H, m), 3.83–3.90 (2 H, m), 4.58 (1 H, dd, *J* 4.8 and OCHO) and 4.64 (1 H, dd, *J* 4.8 and 3, OCHO).

8-Ethyl-2-methyl-1,7-dioxaspiro[5.5]undecan-3-ols 9 and 1-(7-ethyl-1,6-dioxaspiro[4.5]decan-2-yl)ethanols 10

Diethyl 3-oxopentanedioate was sequentially alkylated with but-2-enyl bromide and (*R*)-1-iodo-3-(tetrahydropyran-2-yloxy)pentane **25** in the manner fully described elsewhere,[1,11] and outlined in Scheme 1 for the racemic iodide **19**. Hydrolysis–decarboxylation as detailed elsewhere[1] provided protected hydroxy enone (*R*)-**21** in 76% yield based on starting diethyl 3-oxopentanedioate [(M − THP + 1)$^+$, 198.1621. Calc. for $C_{12}H_{22}O_2$: *m/z* 198.1620]; δ_C($CDCl_3$; 500 Hz) (mixture of two diastereoisomers) 9.07, 9.85, 17.81 (2 C), 17.96, 19.23, 19.90, 20.01, 25.44 (2 C), 25.79, 26.72 (2 C), 27.58, 31.12 (2 C), 32.39, 33.68, 42.43, 42.48, 42.81, 42.84, 62.69, 62.86, 77.84, 77.94, 97.42, 97.86, 125.69, 125.76, 129.49, 129.58, 210.51 and 210.78; δ_H($CDCl_3$; 500 MHz) (mixture of two diastereoisomers) 0.82 (3 H, t, *J* 7.5, CH_2*Me*), 0.89 (3 H, t, *J* 7.5, CH_2*Me*), 1.37–2.81 (42 H, m), 3.4–3.55 (4 H, m), 3.85 (2 H, m), 4.57 (2 H, m) and 5.32–5.57 (4 H, m).

(*R*)-Enone **21** (2.9 g, 10.3 mmol) was dissolved in dry CH_2Cl_2 (150 cm^3) and MCPBA (2.33 g, 11.5 mmol) was added. The reaction mixture was stirred at room temperature, until reaction was complete (48 h), and was then worked up as described previously. The crude epoxides were dissolved in a mixed solvent of HOAc–THF–water (4:2:1; 50 cm^3) and the solution was stirred for 72 h at room temperature. The reaction mixture was diluted with diethyl ether, then saturated aq. $NaHCO_3$ and solid Na_2CO_3 were added until effervescence subsided. The organic layer was separated, dried ($MgSO_4$), and concentrated under reduced pressure to provide a mixture of spiroacetals (1.95 g, 88%). Flash chromatography on silica (70–230 mesh) and elution with ethyl acetate–hexane (1:5) gave a mixture of seven spiroacetals (GC–MS analysis) in the proportions 3.7:7.4:7.1:36.5:38.5:3.4:3.4 in order of elution on a non-polar column. Preparative HPLC provided the two major components in pure form for spectral analyses, but the minor isomers were obtained as mixtures. Isomer I (3.7%), of 1-(7-ethyl-1,6-dioxaspiro[4.5]decan-2-yl)ethanol: *m/z* 214 (M$^+$, 0%), 169 (83), 133 (17), 131 (24), 129 (17), 128 (35), 113 (62), 111 (17), 109 (16), 95 (27), 85 (100) and 83 (38); Isomer II (7.4%), of 1-(7-ethyl-1,6-dioxaspiro[4.5]decan-2-yl)ethanol: *m/z* 214 (M$^+$, 0%), 170 (15), 169 (83), 131 (36), 129 (17), 128 (37), 113 (47), 109 (17), 107 (16), 85 (100), 84 (16) and 83 (32); Isomer III (7.1%), possibly (2*R*,3*R*,6*S*,8*R*)-8-ethyl-2-methyl-1,7-dioxaspiro[5.5]undecan-3-ol (axial alcohol), *m/z* 214 (M$^+$, 0%), 170 (26), 128 (27), 126 (100), 113 (23), 97 (27), 85 (23), 84 (23), 83 (23) and 71 (25); δ_H(C_6D_6; 500 MHz) 0.93 (3 H, t, *J* 7.45, Me C-14), 1.17 (3 H, d, *J* 6, Me C-12), 3.30 (1 H, m, 3-H^{eq}), 3.38 (1 H, dddd, *J* 11.4, 7.8, 4.7 and 2.2, 8-H^{ax}) and 3.75 (1 H, qd, *J* 6.1 and 2, 2-H^{ax}); Isomer IV **26** (36.5%), (2R,3S,6S,8R)-8-*ethyl*-2-*methyl*-1,7-*dioxaspiro*[5.5]*undecan*-3-*ol* (equatorial alcohol), $[\alpha]_D^{24}$ +73.8 (*c* 1.634, pentane) (Found: C, 66.75; H, 10.67. $C_{12}H_{22}O_3$ requires C, 67.25; H, 10.35%); *m/z* 214 (M$^+$, 0%), 170 (29), 128 (22), 126 (100), 113 (16), 97 (17), 85 (17), 84 (22), 83 (22), 71 (14), 69 (11) and 68 (35); δ_C(C_6D_6) see Table 3; δ_H(C_6D_6; 500 MHz) 0.96 (3 H, t, *J* 7.45, Me C-14), 1.07 (1 H, tdd, *J* 13.07, 11.45 and 4.04, 9-H^{ax}), 1.27 (1 H, td, *J* 13.3 and 4.3, 11-H^{ax}), 1.32–1.43 [7 H, m, 5-H^{ax}, 9-H^{eq}, 10-H^{eq}, C-13 methylene proton, and including 1.34 (d, *J* 6.1, Me C-12)], 1.47–1.62 (3 H, m, 4-H^{eq}, 11-H^{eq} and C-13 methylene proton), 1.68 (1 H, ddd, *J* 13.26, 3.8 and 3, 5-H^{eq}), 1.91 [1 H, m, 4-H^{ax} (overlaps 10-H^{ax})], 1.96 (1 H, qt, *J* 13.18 and 4.1, 10-H^{ax}), 3.06 (1 H, m, 3-H^{ax}), 3.45 (1 H, dddd, *J* 11.4, 7.8, 4.7 and 2.2, 8-H^{ax}) and 3.58 (1 H, dq, *J* 9.0 and 6.1, 2-H^{ax}); Isomer V **27** (38.5%), 1-[(2*R*,5*S*,7*R*,11*S*)-7-ethyl-1,6-dioxaspiro[4.5]decan-2-yl]ethanol, $[\alpha]_D^{24}$ +77.6 (*c* 2.708, pentane); *m/z* 214 (M$^+$, 1%), 170 (14), 169 (96), 133 (13), 131 (31), 128 (38), 113 (56), 85 (100), 83 (31), 71 (22) and 69 (17) (Found: M$^+$, 214.1554. $C_{12}H_{22}O_3$ requires *M*, 214.1568); δ_H(C_6D_6) 0.89 (3 H, t, *J* 7.45, Me C-14), 1.03 (1 H, tdd, *J* 12.98, 11.00 and 3.95, 8-H^{ax}), 1.07 (3 H, d, *J* 6.4, Me C-12), 1.34 (2 H, m, 8-H^{eq} and one of the C-13 methylenes), 1.43–1.57 (6 H, m, 3- and 4-H, 9-H^{eq}, 10-H_2 and the other one of the C-13 methylenes), 1.86 (1 H, m, 9-H^{ax}), 1.98 (1 H, m, 4-H), 2.17 (1 H, m, 3-H), 2.70 (1 H, br s, OH), 3.72 (1 H, dddd, *J* 11.0, 7.2, 5.6 and 2.4, 7-H^{ax}), 3.91 (1 H, ddd, *J* 8.4, 6.6 and 3.4, 2-H^{ax}) and 4.03 (1 H, qd, *J* 6.62 and 3.65, 11-H); δ_C(C_6D_6) 9.98 (C-14), 18.90 (C-12), 20.51 (C-9), 22.98 (C-3), 29.57 (C-13), 30.16 (C-8), 34.42 (C-10), 39.48 (C-4), 68.90 (C-11), 72.43 (C-7), 85.85 (C-2) and 106.25 (C-5); Isomer VI (3.4%), of 1-(7-ethyl-1,6-dioxaspiro[4.5]decan-2-yl)ethanol, *m/z* 214 (M$^+$, 0%), 185 (19), 169 (96), 131 (27), 129 (28), 128 (33), 113 (47), 111 (20), 93 (27), 85 (100), 84 (21), 83 (43), 81 (22), 69 (36) and 67 (19); Isomer VII (3.4%), of 8-ethyl-2-methyl-1,7-dioxaspiro-[5.5]undecan-3-ol, *m/z* 214 (M$^+$, 0%), 185 (15), 170 (59), 169 (31), 130 (22), 129 (59), 126 (100), 113 (35), 111 (72), 97 (36), 95 (29), 93 (25), 84 (30), 93 (96), 69 (40) and 68 (45).

2-Ethyl-8-methyl-1,7-dioxaspiro[5.5]undecan-3-ols 11

(*E*)-Pent-2-en-1-ol was obtained from commercially available (*E*)-pent-2-enal by $LiAlH_4$ reduction in the normal way, and purified by distillation (bp 68–70 °C at 300 mmHg), δ_C($CDCl_3$) 13.30, 25.13, 63.68, 127.85 and 134.87; δ_H($CDCl_3$) 0.98 (3 H, t, Me), 1.82 (1 H, br s, OH), 2.05 (2 H, m, MeC*H*$_2$CH=), 4.07 (2 H, m, C*H*$_2$OH), 5.60 (1 H, m, C*H*=CHCH$_2$OH) and 5.74 (1 H, m, CH=C*H*CH$_2$OH).

(*E*)-1-Bromopent-2-ene. Bromine (17.18 g, 0.107 mol) as a solution in dry acetonitrile (25 cm^3) was added dropwise over a period of 0.5 h to a vigorously stirred solution of triphenylphosphine (28.14 g, 0.107 mol) in dry acetonitrile (150 cm^3) at 0 °C under nitrogen. A solution of (*E*)-pent-2-en-1-ol (7.7 g, 0.09 mol) in dry acetonitrile (20 cm^3) was added dropwise over a period of 20 min to this solution of triphenylphosphine dibromide. The mixture was stirred for 1 h at 0 °C and for a further 1 h at room temperature. Excess of triphenylphosphine dibromide was destroyed by the addition of methanol (8 cm^3) and the resulting mixture was extracted with pentane (8 × 100 cm^3). The acetonitrile layer was saturated with solid NaCl and extracted again with pentane (3 × 100 cm^3). The combined pentane layers were dried ($MgSO_4$), and concentrated under reduced pressure to give the crude bromide. Distillation (bp 53–55 °C; 30 mmHg) gave (*E*)-1-bromopent-2-ene (7.4 g, 55.5%), δ_C($CDCl_3$) 14.00, 25.08, 33.58, 125.36 and 138.04; δ_H($CDCl_3$) 0.85 (3 H, t, CH$_2$*Me*), 2.04 (2 H, m), 3.90 (2 H, d, CH_2Br) and 5.71 (2 H, m).

Diethyl 3-oxo-2-(pent-2-enyl)pentanedioate resulted from alkylation of diethyl 3-oxopentanedioate with (*E*)-1-bromopent-2-ene (1.62 g, 10.9 mmol) by utilising the procedure described above for compound **21**. Purification by flash chromatography on silica (70–230 mesh), and elution with diethyl ether–hexane (1:6), gave the desired enone as a clear oil (2.33 g, 87%), *m/z* 270 (M^{+}, 1%), 225 (M$^+$ − OCH_2CH_3, 26), 197 (23), 182 (21), 179 (37), 178 (45), 167 (67), 156 (33), 155 (94), 137 (25), 128 (20), 127 (44), 115 (24), 109 (100), 81 (68) and 79 (22); δ_C(C_6D_6) 13.51, 13.98 (2 C), 25.41, 31.01, 48.34, 58.96, 61.38, 61.47, 123.96, 136.63, 166.52, 168.70 and 197.27; δ_H($CDCl_3$) 0.88 (3 H, t, *J* 7.33, CH=CHCH$_2$*Me*), 1.21 (3 H, t, *J* 7.08, CO$_2$CH$_2$*Me*), 1.22 (3 H, t, *J* 7.08, CO$_2$CH$_2$*Me*), 1.92 (2 H, m, *J* 7, CH=CHC*H*$_2$Me), 2.50 (2 H, t, *J* 7.08, CHC*H*$_2$CH=), 3.4–3.6 (2 H, m, C*H*$_2$CO$_2$Et), 3.60 [1 H, t, *J* 7.33, COC*H*(CO$_2$Et)-CH$_2$], 4.13 (4 H, q, *J* 7.33, C*H*$_2$Me), 5.27 (1 H, dt, *J* 15.14, CH=) and 5.51 (1 H, dt, *J* 15.14 and 6.6, CH=).

2-(Tetrahydropyran-2-yloxy)dodec-9-en-6-one. The above mono-alkylated 3-oxoglutarate (2.71 g, 10.06 mmol) was treated with racemic 1-iodo-3-(tetrahydropyran-2-yloxy)butane (2.86 g, 10.06 mmol) in a manner already described to give the desired crude enone (2.41 g, 85%). Chromatographic purification was not attempted in order to avoid deprotection and formation of a dihydropyran as discussed earlier,[1] m/z 282 ($M^{\cdot+}$, 0%), 198 (16), 181 (38), 112 (30), 97 (26), 85 (100), 83 (38), 69 (47), 67 (22) (Found: M^+ − OTHP, 181.1578. $C_{12}H_{21}O$ requires m/z 181.1592); $\delta_C(CDCl_3)$ (two diastereoisomers) 13.76 (2 C), 19.04, 19.68, 19.80, 20.04, 20.07, 21.53, 25.47 (4 C), 31.19 (2 C), 36.01, 36.84, 42.62 (2 C), 42.75, 42.80, 62.59, 62.84, 70.72, 73.82, 95.73 98.83, 127.29, 127.35, 132.97, 133.03 and 210.76 (2 C); $\delta_H(CDCl_3)$ (two diastereoisomers) 0.91 (6 H, t, J 7.32, 2 × Me), 1.07 (3 H, d, J 5.86, Me of one diastereoisomer), 1.09–2.44 [35 H, m, including 1.16 (3 H, d, J 5.86, Me of one diastereoisomer)], 1.94 (4 H, m, J 6.5, C=CHCH_2Me), 3.41–3.86 (8 H, m, OCH) and 5.31–5.46 (m, CH=CH).

2-Ethyl-8-methyl-1,7-dioxaspiro[5.5]undecan-3-ol 11. By the procedure described earlier,[1] the above enone (2.2 g, 7.8 mmol) was treated with MCPBA (1.75 g, 8.7 mmol) to give the crude epoxide, which on treatment with the mixed solvent system glacial acetic acid–THF–water (4:2:1; 35 cm^3) for 60 h and the usual work-up yielded a crude mixture of spiroacetals. Flash chromatography on silica (70–230 mesh), and elution with EtOAc–hexane (1:5), provided a mixture of five spiroacetals (1.0 g, 60%) (by GC–MS analysis) in the proportions 4:2:17:37:40 (in order of elution on a non-polar column). The two major components were acquired in pure form by preparative HPLC, and these isomers were fully characterised. However, the minor components were obtained as mixtures, which were unsuitable for NMR examination, and their mass spectral data only are reported. Isomer I (4%), 1-(7-methyl-1,6-dioxaspiro[4.5]undecan-2-yl)propan-1-ol, m/z 214 (M^+, 0%), 156 (20), 155 (100), 145 (12), 128 (14), 127 (30), 115 (17), 99 (15), 95 (24), 85 (66), 84 (16), 83 (22), 81 (22) and 77 (19); Isomer II (2%), possibly (2*RS*,3*SR*,6*RS*,8*SR*)- or (2*RS*,3*SR*,6*SR*,8*SR*)-2-ethyl-8-methyl-1,7-dioxaspiro[5.5]undecan-3-ol (equatorial alcohol), m/z 214 (M^+, 0%), 156 (12), 155 (15), 142 (18), 127 (13), 112 (100), 97 (21), 85 (20), 84 (16), 83 (25) and 71 (21); Isomer III (17%), of 1-(7-methyl-1,6-dioxaspiro[4.5]decan-2-yl)propan-1-ol, m/z 214 ($M^{\cdot+}$, 0%), 170 (5), 156 (21), 155 (100), 142 (18), 127 (25), 115 (22), 112 (48), 99 (20), 97 (17), 95 (23), 85 (66), 84 (26), 83 (22) and 71 (22); $\delta_C(C_6D_6)$ 10.57 (C-14), 20.80, 22.32, 23.46, 26.22, 33.04, 33.23 and 38.37 (C-3, -4, -8, -9, -10, -12 and -14), 66.61, 73.67 and 81.07 (C-2, -7 and -11) and 106.29 (C-5); Isomer IV (37%) (2*RS*,3*SR*,6*SR*,8*RS*)-2-ethyl-8-methyl-1,7-dioxaspiro[5.5]undecan-3-ol **28** (equatorial alcohol) (120 mg), m/z 214 ($M^{\cdot+}$, 0%), 170 (2), 156 (16), 142 (8), 127 (7), 113 (9), 112 (100), 97 (4), 85 (11), 84 (18), 83 (18) and 69 (9) (Found: M^+, 214.1534. $C_{12}H_{22}O_3$ requires M, 214.1569); $\delta_C(C_6D_6)$ see Table 3; $\delta_H(C_6D_6)$ 1.07 (1 H, tdd, J 12.95, 11.23 and 4.15, 9-H^{ax}), 1.10 (3 H, t, J 7.33, Me C-13), 1.12 (3 H, d, J 6.1, Me C-14), 1.26 (1 H, td, J 13.18 and 4.4, 11-H^{ax}), 1.32–1.4 [3 H, m, including 1.36 (1 H, td, J 13.43 and 4.64, 5-H^{ax}), 5-H^{ax}, and 9- and 10-H^{eq})], 1.49 (1 H, m, C-12 methylene proton, overlaps with 11-H^{eq}), 1.52 (1 H, m, 11-H^{eq}), 1.58 (1 H, m 4-H^{eq}), 1.68 (1 H, ddd, J 13.18, 4.4 and 2.93, 5-H^{eq}), 1.93 (2 H, m, 4- and 10-H^{ax}), 2.00 (1 H, m, C-12 methylene proton, overlaps with 4- and 10-H^{ax}), 3.13 (1 H, ddd, J 11.23, 9.28 and 4.64, 3-H^{ax}), 3.34 (1 H, td, J 9.28 and 2.68, 2-H^{ax}) and 3.73 (1 H, dqd, J 11.23, 6.35 and 2.2, 8-H^{ax}); Isomer V (40%) (2*RS*,5*SR*,7*RS*,11*SR*)-1-(7-methyl-1,6-dioxaspiro[4.5]decan-2-yl)propan-1-ol **29** (190 mg), m/z 214 ($M^{\cdot+}$, 0%), 185 (3), 170 (5), 156 (15), 155 (100), 145 (12), 142 (15), 127 (19), 99 (10), 95 (13), 85 (50) and 83 (10) (Found: M^+, 214.1593. $C_{12}H_{22}O_3$ requires M, 214.1569); $\delta_C(C_6D_6)$ 10.78 (C-13), 20.64 (C-9), 22.01 (C-14), 22.51 (C-4 or -3), 26.53 (C-12), 32.75 (C-8), 33.81 (C-10), 39.48 (C-3 or -4), 67.46 (C-7), 74.38 (C-11), 84.84 (C-2) and 106.19 (C-5); $\delta_H(C_6D_6)$ 1.02 (1 H, m, 8-H^{ax}, overlaps with Me C-13 and Me C-14), 1.03 (3 H, t, J 7.45, Me C-13), 1.07 (3 H, d, J 6.35, Me C-14), 1.28 (1 H, dm, J 11.96, 8-H^{eq}, partial overlap with C-12 methylene protons), 1.30–1.57 (7 H, m, 3- and 4-H, 9-H^{eq}, 10-H_2, C-12 methylene protons), 1.85 (1 H, qt, J 12.94 and 4.15, 9-H^{ax}), 1.97 (1 H, dd, J 10.94 and 8.79, 3- or 4-H), 2.20 (1 H, m, 4- or 3-H), 3.05 (1 H, br s, OH), 3.82 (1 H, m, CHO of C-11), 3.95 (1 H, dqd, J 11.23, 6.35 and 2.2, 7-H^{ax}) and 4.05 (1 H, td, J 7.6 and 2.93, 2-H^{ax}).

Enantioselective synthesis of 2-ethyl-8-methyl-1,7-dioxaspiro-[5.5]undecan-3-ols

Use of (*R*)-1-iodo-3-(tetrahydropyran-2-yloxy)butane in the above sequence provided the enantiomers of the five spiroacetals described above. Their mass spectra were identical with those exhibited by the racemates. Preparative HPLC again cleanly provided the two major components, **28** (0.115 g) and **29** (0.15 g), whose ^1H and ^{13}C NMR spectra were identical with those reported for the racemates. (2*R*,3*S*,6*S*,8*R*)-**28**, $[\alpha]_D^{24}$ +74.6 (c 1.068, pentane). (2*R*,5*S*,7*R*,11*S*)-**29** $[\alpha]_D^{24}$ +45.0 (c 1.737, pentane).

8-Ethyl-2-methyl-1,7-dioxaspiro[5.5]undecan-4-ols 13

Synthesis of racemic 8-ethyl-2-methyl-1,7-dioxaspiro[5.5]-undecan-4-ols. 8-(*Tetrahydropyran-2-yloxy*)*decane*-2,4-*dione* **33**.—The dianion of pentane-2,4-dione (0.176 g, 1.76 mmol) was generated at −15 °C in dry THF in the normal way[1,20] and a solution of racemic iodide **32** (0.524 g, 1.76 mmol) in dry THF (5 cm^3) was added dropwise. The solution was allowed to warm to 0 °C over a period of 1 h and was then stirred at this temperature for a further 3 h. Standard work-up provided an orange oil, which on flash chromatography on silica (70–230 mesh) and elution with CH_2Cl_2–hexane (2:3 increasing to 3:1), gave the dione **33** (0.19 g, 40%) as a mixture of diastereoisomers. Isomer 1: m/z 185 (2%), 169 (18), 167 (4), 157 (4), 111 (10), 100 (8), 86 (5), 85 (100), 83 (10), 69 (6) and 67 (10); Isomer 2: m/z 185 (2%), 169 (20), 167 (2), 157 (3), 111 (8), 100 (6), 86 (6), 85 (100), 83 (10), 69 (6) and 67 (11) [Found: $(M + 1)^+$, 271.1914. $C_{15}H_{26}O_4$ + H requires m/z, 271.1909]; $\delta_C(CDCl_3)$ (enol form only) 9.12, 9.86, 19.93, 20.08, 21.17, 21.76, 24.93, 24.99, 25.49, 25.93, 27.60, 27.63, 31.19, 32.22, 32.45, 33.76, 38.16, 38.28, 62.72, 62.93, 77.77, 77.84, 97.90, 97.95, 99.74, 99.77, 191.42, 191.55, 193.83 and 193.93; $\delta_H(CDCl_3)$ 0.83 (3 H, t, J 7.45, Me), 0.89 (3 H, t, J 7.45, Me), 1.44–1.81 (24 H, m), 2.013 (3 H, s, Ac), 2.016 (3 H, s, Ac), 2.20 (2 H, t, J 7.56, CH_2CO), 2.24 (2 H, t, J 7.56, CH_2CO), 3.44 (2 H, m), 3.53 (2 H, m), 3.88 (2 H, m), 4.60 (2 H, m), 5.45 (1 H, s, HOC=C*H*CO, enol form) and 5.47 (1 H, s, HOC=C*H*C, enol form).

2-*Hydroxy*-10-(*tetrahydropyran*-2-*yloxy*)*dodecane*-4,6-*dione* **31**.—A solution of dione **33** (10.34 g, 38.3 mmol) in dry THF (50 cm^3) was added dropwise to a stirred solution of lithium diisopropylamide [from diisopropylamine (8.19 g, 81.1 mmol) and BuLi (2.5 mol dm^{-3} solution in hexane; 32.35 cm^3, 81.1 mmol) at 0 °C in dry THF (100 cm^3) at −78 °C under nitrogen. The resulting dark red solution was stirred at −78 °C for 2 h and was then treated with acetaldehyde (2.16 cm^3, 38.3 mmol). The solution was allowed to warm to 0 °C over a period of 3 h and was then poured into saturated aq. NH_4Cl (100 cm^3) and extracted with diethyl ether (3 × 100 cm^3). The combined organic layers were dried ($MgSO_4$), and concentrated under reduced pressure to yield the crude dione **31** (5.3 g, 55%), as a mixture of diastereoisomers. This product was used in the next step without purification: m/z (one diastereoisomer only) 213 (6%), 195 (8), 153 (25), 129 (10), 111 (26), 99 (10), 97 (11), 87 (20), 85 (100), 84 (27), 83 (23) and 71 (13).

8-*Ethyl*-2-*methyl*-1,7-*dioxaspiro*[5.5]*undecan*-4-*one* **34–37**.—The crude dione **31** (5.2 g) was stirred for 48 h in a mixture of glacial acetic acid (50 cm^3), THF (25 cm^3) and water (12.5 cm^3). Diethyl ether (50 cm^3) was added, and the vigorously stirred mixture was carefully treated with saturated aq. $NaHCO_3$ (20 cm^3) and then with solid Na_2CO_3. The ether layer was separated and after being combined with further ether extracts (3 × 50 cm^3) of the aqueous phase, was washed with saturated aq. NaCl (2 × 50 cm^3), dried ($MgSO_4$), and concentrated under reduced pressure. The residue was initially purified by distillation (bp 82–86 °C; 2 mmHg) followed by flash chromatography on silica (70–230 mesh), and elution with CH_2Cl_2–hexane (1:4 increasing to 4:1), to give a mixture of four spiroketones (by GC–MS analysis) in the proportions 72.2:13.6:13.1:1.1. Preparative HPLC provided only three isomers: compounds **34** (0.156 g), **35** (0.027 g) and **36** (0.056 g). HRMS (EI) (Found: M^+, 212.1410. $C_{12}H_{20}O_3$ requires *M*, 212.1412). Isomer I: (72.2%) (2RS,6SR,8RS)-8-*ethyl*-2-*methyl*-1,7-*dioxaspiro*[5.5]*undecan*-4-*one* **34**, *m/z* 212 ($M^{\cdot+}$, 11%), 183 (13), 154 (8), 129 (9), 127 (11), 126 (100), 113 (18), 111 (53), 99 (33), 98 (13), 97 (11), 87 (35), 85 (21), 84 (55), 83 (30) and 71 (21) (Found: M^+, 212.1410. $C_{12}H_{20}O_3$ requires *M*, 212.1412); $\delta_C(C_6D_6)$ see Table 1; $\delta_H(C_6D_6)$ 0.81 (3 H, t, *J* 7.45, Me C-14), 0.96 (1 H, tdd, *J* 13.19, 11.47 and 3.91, 9-H^{ax}), 1.03 (1 H, d, *J* 6.10, Me C-12), 1.10 (1 H, td, *J* 13.43 and 4.64, 11-H^{ax}), 1.25 (2 H, m, 9-H^{eq} and C-13 methylene proton), 1.35 (2 H, m, 10-H^{eq} and C-13 methylene proton), 1.55 (1 H, dm, *J* 13.19, 11-H^{eq}), 1.79 (1 H, dd, *J* 14.16 and 11.48, 3-H^{ax} overlapping with 10-H^{ax}), 1.84 (1 H, qt, *J* 13.43 and 4.15, 10-H^{ax}), 1.97 (1 H, d, *J* 14.16, 5-H^{ax}), 2.17 (1 H, ddd, *J* 14.16, 2.93 and 1.96,[a] 3-H^{eq}), 2.38 (1 H, dd, *J* 14.16 and 1.96,[a] 5-H^{eq}), 3.27 (1 H, dddd, *J* 11.5, 7.8, 4.9 and 2.2, 8-H^{ax}) and 3.88 (1 H, dtd, *J* 11.48, 6.1 and 2.93, 2-H^{ax}).[a] W-coupling; Isomer II: (13.6%) (2*RS*,6*RS*,8*SR*)-8-ethyl-2-methyl-1,7-dioxaspiro[5.5]undecan-4-one **35**, *m/z* 212 (M^+, 3%), 183 (7), 154 (3), 129 (100), 126 (34), 113 (7), 111 (57), 99 (21), 98 (7), 97 (6), 87 (58), 85 (8), 84 (28), 83 (16) and 71 (17); $\delta_C(C_6D_6)$ see Table 1; $\delta_H(C_6D_6)$ 0.82 (3 H, t, *J* 7.45, Me C-14), 0.97 (1 H, qd, *J* 13 and 4, 9-H^{ax}), 1.01 (3 H, d, *J* 6.1, Me C-12), 1.05 (1 H, td, *J* 13.3 and 4.4, 11-H^{ax}), 1.20–1.43 (4 H, m, C-13 methylene protons, 9- and 10-H^{eq}), 1.50 (1 H, dm, *J* 13.2, 11-H^{eq}), 1.75 (1 H, qt, *J* 13.68 and 3.91, 10-H^{ax}), 2.03 (1 H, ddd, *J* 16.36, 3.17 and 0.49,[b] 3-H^{eq}), 2.26 (1 H, dd, *J* 15.63 and 0.49,[b] 5-H^{eq}, overlapping with 3-H^{ax}), 2.30 (1 H, ddd, *J* 16.36, 11.72 and 0.49,[a] 3-H^{ax}, overlapping with 5-H^{eq}), 2.43 (1 H, dd, *J* 15.63 and 0.49,[a] 5-H^{ax}), 3.65 (1 H, dqd, *J* 11.72, 6.1 and 3.17, 2-H^{ax}) and 3.77 (1 H, dddd, *J* 11.55, 7.75, 4.88 and 2.2, 8-H^{ax}) [a] 1,3-diaxial coupling, [b] W-coupling); Isomer III (13.1%) (2*RS*,6*SR*,8*SR*)-8-ethyl-2-methyl-1,7-dioxaspiro[5.5]undecan-4-one **36**, *m/z* 212 ($M^{\cdot+}$, 22%), 183 (23), 154 (1), 129 (67), 126 (34), 113 (10), 111 (78), 110 (18), 99 (45), 98 (5), 97 (8), 87 (19), 85 (35), 84 (60), 83 (83), 82 (10), 71 (23), 69 (68), 55 (79) and 41 (100); $\delta_C(C_6D_6)$ see Table 1; $\delta_H(C_6D_6)$ 0.85 (3 H, t, *J* 7.45, Me C-14), 0.94 (1 H, qd, *J* 11 and 4.1, 9-H^{ax}), 1.02 (3 H, d, *J* 6.3, Me C-12), 1.04–1.14 (2 H, m, 10-H^{ax} and 9-H^{eq}), 1.23–1.49 (3 H, m, C-13 methylene protons and 10-H^{eq}), 1.49 (1 H, m, 11-H^{eq}), 1.61 (1 H, td, *J* 12.7 and 4.64, 11-H^{ax}), 1.81 (1 H, dd, *J* 13.92 and 11.0, 3-H^{ax}, overlapping with 5-H^{ax}), 1.84 (1 H, d, *J* 13.92, 5-H^{ax}, overlapping with 3-H^{ax}), 2.15 (1 H, ddd, *J* 13.92, 2.93 and 1.95,[a] 3-H^{eq}), 2.84 (1 H, dd, *J* 13.92 and 1.95,[a] 5-H^{eq}), 3.18 (1 H, dddd, *J* 11.5, 8.2, 6.0 and 2.7, 8-H^{ax}) and 4.49 (1 H, dqd, *J* 11.0, 6.1 and 2.93, 2-H^{ax}).[a] W-coupling; Isomer IV (1.1%), tentatively assigned from GC–MS data as (2*RS*,6*RS*,8*RS*)-8-ethyl-2-methyl-1,7-dioxaspiro[5.5]undecan-4-one **37**, *m/z* 212 (M^+, 21%), 198 (11), 153 (19), 129 (68), 126 (27), 111 (27), 97 (52), 87 (31), 84 (96), 83 (38), 69 (82), 68 (24), 55 (54), 43 (82) and 41 (100).

8-*Ethyl*-2-*methyl*-1,7-*dioxaspiro*[5.5]*undecan*-4-*ols* **38** *and* **39**.—A solution of the spiroketone **34** (0.5 g, 2.35 mmol) in dry diethyl ether (20 cm^3) was added dropwise to a stirred, cooled (0 °C) suspension of $LiAlH_4$ (0.09 g, 2.35 mmol) in dry diethyl ether (40 cm^3) under nitrogen. After being stirred for 2.5 h at room temperature, the solution was cooled (0 °C) and excess of $LiAlH_4$ was destroyed by addition of water (1 cm^3), 10% aq. NaOH (1 cm^3) and water (5 cm^3). The mixture was stirred for 40 min after which the precipitate was removed by filtration through Celite and rinsed sequentially with diethyl ether and THF. The organic phase was washed with saturated aq. NaCl (50 cm^3), dried ($MgSO_4$), and concentrated under reduced pressure to give a mixture of two isomeric alcohols in the ratio 42:58 (GC–MS; in order of elution on a non-polar GC column) (0.32 g, 64%). These alcohols were separated by preparative gas chromatography. HRMS (EI) (Found: M^+, 214.1569, $C_{12}H_{22}O_3$ requires M, 214.1569). Isomer I (42%) (2*RS*,4*RS*,6*SR*,8*RS*)-2-ethyl-8-methyl-1,7-dioxaspiro[5.5]undecan-4-ol **39** (axial alcohol), *m/z* 214 ($M^{\cdot+}$, 2%), 167 (13), 156 (10), 131 (82), 129 (44), 128 (67), 126 (17), 123 (13), 113 (71), 111 (21), 110 (13), 99 (17), 97 (12), 95 (14), 89 (26), 86 (13), 84 (10), 83 (27), 71 (77), 69 (27), 68 (37), 67 (17), 55 (50) and 43 (100) (Found: M^+, 214.1569. $C_{12}H_{22}O_3$ requires *M*, 214.1569); $\delta_C(C_6D_6)$ see Table 3; $\delta_H(C_6D_6)$ 0.83 (3 H, t, *J* 7.45, Me C-14), 1.00 (1 H, tdd, *J* 12.94, 11.72 and 3.66, 9-H^{ax}), 1.15 (3 H, d, *J* 6.11, Me C-12), 1.16–1.34 (7 H, m, C-13 methylene protons, 3-H^{ax}, 11-H^{ax}, 9-H^{eq}, 5-H^{ax} and 10-H^{eq}), 1.47 (1 H, dm, *J* 13.18, 11-H^{eq}), 1.80 (2 H, dm, *J* 12, 3-H^{eq} overlapping with 5-H^{eq}), 1.90 (1 H, qt, *J* 13.18 and 4.03, 10-H^{ax}), 3.44 (1 H, dddd, *J* 11.1, 8.0, 4.8 and 2.2, 8-H^{ax}), 4.05 (1 H, m, 4-H^{eq}), 4.10 (1 H, dqd, *J* 11.95, 6.11 and 1.96, 2-H^{ax}, partial overlap with 4-H^{eq}) and 4.27 (1 H, d, *J* 10.01, OH); Isomer II (2*RS*,4*SR*,6*SR*,8*RS*)-8-ethyl-2-methyl-1,7-dioxaspiro[5.2]undecan-4-ol **38** (equatorial alcohol), *m/z* 214 (M^+, 2%), 167 (15), 156 (13), 131 (99), 130 (24), 129 (37), 128 (83), 126 (33), 123 (12), 113 (55), 111 (22), 99 (23), 97 (16), 89 (46), 86 (23), 84 (15), 83 (26), 71 (81), 69 (30), 68 (42), 67 (18), 55 (54) and 43 (100); $\delta_C(C_6D_6)$ see Table 3; $\delta_H(C_6D_6)$ 0.92 (3 H, t, *J* 7.33, Me C-14), 1.06 (1 H, tdd, *J* 12.7, 11.23 and 4.15, 9-H^{ax}), 1.10 (1 H, q, *J* 12, 3-H^{ax}), 1.15 (3 H, d, *J* 6.34, Me C-12), 1.24 (1 H, dd, *J* 12.5 and 12.0, 5-H^{ax}), 1.24–1.53 (5 H, m, 11-H^{ax}, 9- and 10-H^{eq}, and C-13 methylene protons), 1.62 (1 H, dm, *J* 12.94, 11-H^{eq}), 1.74 (1 H, dm, *J* 12.2, 3-H^{eq}), 1.96 (1 H, qt, *J* 13.18 and 3.91, 10-H^{ax}), 2.00 (1 H, m, 5-H^{eq}), 3.39 (1 H, dddd, *J* 11.2, 8.3, 4.4 and 2.2, 8-H^{ax}), 3.67 (1 H, dqd, *J* 11.48, 6.34 and 1.96, 2-H^{ax}) and 4.12 (1 H, ddt, *J* 15.8, 11.23 and 4.88, 4-H^{ax}).

The spiroketone **35** (50 mg, 0.25 mmol) was reduced with $LiAlH_4$ as described for isomer **34**. A mixture of six isomeric alcohols in the proportions 3:4:4:65:6:18 (GC–MS: in order of elution on a non-polar column) was obtained. The two earlier eluting alcohols (3 and 4%) were identified (by their GC–MS spectra) as the axial and equatorial alcohols, **39** and **38** respectively, and their formation was due to a slight contamination with spiroketone **34** in the starting material. The four remaining alcohols were assigned as follows. Isomer I (4%), tentatively assigned as (2*RS*,4*RS*,6*SR*,8*SR*)-8-ethyl-2-methyl-1,7- dioxaspiro[5.5]undecan-4-ol **43** (axial alcohol), *m/z* 214 (M^+, 1%), 185 (11), 131 (73), 129 (100), 128 (47), 113 (52), 97 (47), 89 (27), 83 (39) and 71 (50); Isomer II (65%), tentatively assigned as (2*RS*,4*RS*,6*RS*,8*SR*)-8-ethyl-2-methyl-1,7-dioxaspiro[5.5]-undecan-4-ol **41** (equatorial alcohol), *m/z* 214 (M^+, 1%), 131 (98), 113 (71), 89 (91), 71 (100) and 55 (42); Isomer III (6%), tentatively assigned as (2*RS*,4*SR*,6*SR*,8*SR*)-8-ethyl-2-methyl-1,7-dioxaspiro[5.5]undecan-4-ol **44** (equatorial alcohol), *m/z* 214 (M^+, 0.4%), 129 (100), 128 (39), 99 (19), 83 (50), 71 (36), 69 (35) and 68 (24); Isomer IV (18%), tentatively assigned as (2*RS*,4*RS*,6*RS*,8*SR*)-8-ethyl-2-methyl-1,7-dioxaspiro[5.5]-undecan-4-ol **42** (axial alcohol), *m/z* 214 (1.2%), 131 (100), 130 (18), 128 (30), 113 (69), 89 (35), 71 (86) and 68 (22). Attempted preparative GC separation of the isomeric alcohols resulted in dehydration to unsaturated spiroacetal products. A mixture of the resultant alkenes was characterised[16] and is reported for an isomeric system (see later).

The spiroketone **36** (40 mg, 0.19 mmol) was reduced with $LiAlH_4$ to provide a mixture of three isomeric alcohols in the proportions 25:14:16 (GC–MS: in order of elution on a non-polar column). Isomer I (25%) exhibited the same mass spectrum as isomer I obtained on reduction of the spiroketone **40** (≡**35**). Isomer II (14%) exhibited the same mass spectrum as isomer II obtained on reduction of the spiroketone **40** (≡**35**), and isomer III (61%) exhibited the same mass spectrum as isomer III obtained on reduction of the spiroketone **40** (≡**35**). Attempted separation of these stereoisomers by preparative GC resulted in formation of an unsaturated system. Isomer I, *m/z* 196 (M^+, 4%), 123 (13), 113 (100), 110 (17), 95 (40) and 67 (17); isomer II, *m/z* 196 (7%), 167 (57), 123 (92), 113 (100), 110 (90), 95 (59), 69 (23), 68 (29), 67 (36) and 66 (42); $\delta_C(C_6D_6)$ (mixture of two isomers) 10.19, 10.54, 19.25, 19.29, 21.48, 21.55, 29.67, 29.82, 30.14, 30.68, 31.48, 32.92, 33.50, 35.51, 63.96, 66.88, 71.30, 74.23, 95.12, 95.20, 125.04, 126.96, 128.35 and 131.94; $\delta_H(C_6D_6)$ (mixture of two isomers) 0.92 (3 H, t, *J* 7.3, Me C-14), 0.93 (3 H, t, *J* 7.3, Me C-14), 1.11–1.85 [24 H, m, including 1.17 (3 H, d, *J* 6.1, Me C-12) and 1.23 (3 H, d, *J* 6.1, Me C-12')], 1.95 (2 H, qt, *J* 13.43 and 3.91, 10-H_2), 3.40 (1 H, ddd, *J* 11, 8 and 6, 8-H^{ax} or -H^{eq}), 3.81 (1 H, dqd, *J* 9.59, 6.35 and 4.64, 2-H^{ax} or -H^{eq}), 4.04 (1 H, dddd, *J* 11.23, 8, 6 and 2, 8-H^{eq} or -H^{ax}), 4.44 (1 H, dqd, *J* 9.5, 6.35 and 3.9, 2-H^{eq} or -H^{ax}), 5.59 (1 H, dt, *J* 10.01 and 4.15, C*H*=CH), 5.70 (1 H, ddd, *J* 10.25, 5.37 and 1.96, C*H*=CH), 5.72 (1 H, dt, *J* 10.25 and 2.2, C*H*=CH, overlaps with previous signal) and 6.03 (1 H, ddd, *J* 10.01, 2.68 and 1.46, C*H*=CH).

Enantioselective synthesis of 8-ethyl-2-methyl-1,7-dioxaspiro[5.5]undecan-4-ols

Optically active 8-ethyl-2-methyl-1,7-dioxaspiro[5.5]undecan-4-ones. Use of (*R*)-iodide **25** in the procedure outlined above resulted in the formation of three spiroketones in the proportions 78:11:11. Preparative HPLC provided (2*R*,6*S*,8*R*)-**34**, (0.99 g), (2*S*,6*S*,8*R*)-**35** (0.12 g) and (2*S*,6*R*,8*R*)-**36** (0.15 g), which displayed mass, ^{1}H and ^{13}C NMR spctra identical with those of their racemates. (2*R*,6*S*,8*R*)-**34**, $[\alpha]_D^{23}$ +91.5 (*c* 1.835, pentane); (2*S*,6*S*,8*R*)-**35**, $[\alpha]_D^{20}$ +152.0 (*c* 1.693, pentane); (2*S*,6*R*,8*R*)-**33**, $[\alpha]_D^{20}$ −3.0 (*c* 1.599, pentane).

Optically active 8-ethyl-2-methyl-1,7-dioxaspiro[5.5]undecan-4-ols. Reduction of (2*R*,6*S*,8*R*)-**34** (0.6 g, 2.8 mmol) with $LiAlH_4$ (0.054 g, 1.4 mmol) was conducted as described for the racemate to yield the epimeric alcohols **38** and **39** in the ratio 60:40 (GC–MS). Preparative GC provided samples of each alcohol which exhibited mass, ^{1}H and ^{13}C NMR spectra in agreement with those described for the racemates. (2*R*,4*R*,6*S*,8*R*)-**39** (173 mg), $[\alpha]_D$ +77.2 (*c* 1.381, pentane); (2*R*,4*S*,6*S*,8*R*)-**38** (300 mg), $[\alpha]_D$ +79.0 (*c* 1607, pentane). Reduction of ketone (2*S*,6*S*,8*R*)-**40** (≡**35**) (71 mg, 0.33 mmol) with $LiAlH_4$ (6.4 mg, 0.17 mmol) as described previously gave a mixture of two isomeric spiroalcohols (55 mg, 76%) in the ratio 23:77 (GC–MS: in order of elution on a non-polar column). The following spectral data were acquired using this mixture, as earlier attempts to isolate the individual alcohols resulted in dehydration; $[\alpha]_D^{20}$ +52.3 (*c* 2.9, pentane). Isomer I (23%) (2*S*,4*S*,6*R*,8*R*)-8-ethyl-2-methyl-1,7-dioxaspiro[5.5]undecan-4-ol **43** (axial alcohol), *m/z* 214 (M^+, 0%), 185 (12), 167 (20), 131 (30), 129 (100), 128 (42), 123 (24), 113 (51), 111 (61), 110 (25), 99 (21), 97 (22), 84 (17), 83 (60), 71 (37), 69 (34), 68 (36) and 67 (26); $\delta_C(C_6D_6$; 125 MHz) 10.13 (C-14), 19.25 (C-10), 22.06 (C-12), 29.70, 31.05 and 35.64 (C-9, -11 and -13), 40.14 and 45.22, (C-3 and -5), 62.34 (C-2), 67.38 (C-4), 70.99 (C-8) and 98.14 (C-6); $\delta_H(C_6D_6$; 500 MHz) 0.89 (3 H, t, *J* 7.5, Me C-14), 1.24 (3 H, d, *J* 6.1, Me C-12), 3.84 (1 H, dtd, *J* 12, 6 and 2.5, 8-H^{ax}), 4.08 (1 H, ddddd, *J* 10, 5, 5, 5 and 5, 4-H^{eq}) and 4.15 (1 H, m, 2-H^{ax}); isomer II (77%) (2*S*,4*R*,6*S*,8*R*)-8-ethyl-2-methyl-1,7-dioxaspiro[5.5]undecan-4-ol **41** (equatorial alcohol), *m/z* 214 (M^+, 0%), 167 (8), 131 (90), 130 (20), 129 (29), 128 (17), 126 (26), 113 (71), 111 (23), 95 (29), 89 (84), 83 (18), 71 (95), 69 (31), 68 (42), and 43 (100); $\delta_C(C_6D_6$; 125 MHz) 10.06 (C-14), 18.74 (C-10), 22.27 (C-12), 29.64 (C-13), 30.92 (C-9 and -11), 42.72 (C-3), 45.44 (C-5), 65.31 (C-4), 66.41 (C-2), 71.39 (C-8) and 98.09 (C-6); $\delta_H(C_6D_6$; 500 MHz) 0.88 (3 H, t, *J* 7.5, Me C-14), 1.08 (2 H, m, 9- and 11-H^{ax}), 1.13 (3 H, d, *J* 6.1, Me C-12), 1.20 (1 H, m, 3-H^{ax}), 1.27–1.45 (3 H, m, 9- and 10-H^{eq} and on of the C-13 methylene protons), 1.52 (1 H, m, one of C-13 methylene protons), 1.56–1.72 [4 H, m, including 1.63 (1 H, qt, *J* 13.2 and 3.8, 10-H^{ax}), 3- and 11-H^{eq}, and 5-H^{ax}], 1.93 (1 H, dm, *J* 12.66, 5-H^{eq}), 3.19 (1 H, dqd, *J* 11.23, 6.1 and 2.54, 2-H^{ax}), 3.66 (1 H, tt, *J* 9.85 and 5.04, 4-H^{ax}) and 4.01 (1 H, dtd, *J ca.* 12.0, 6.1 and 2.45, 8-H^{ax}). Reaction of (2*S*,6*R*,8*S*)-**36** (0.041 g, 0.2 mmol) with $LiAlH_4$ (3.8 mg, 0.1 mmol) as described previously, gave a mixture of three isomeric spiroalcohols [0.032 g, 77%) in the proportions 19:11:70 (GC–MS) in order of elution on a non-polar column]. $[\alpha]_D^{23}$ −22.2 (*c* 2.54, pentane). Isomer I (19%) (2*S*,4*S*,6*R*,8*R*)-8-ethyl-2-methyl-1,7-dioxaspiro[5.5]undecan-4-ol **43** (axial alcohol). GC–MS spectrum identical with that of isomer **43** described above. Isomer II (11%) (2*S*,4*R*,6*S*,8*R*)-8-ethyl-2-methyl-1,7-dioxaspiro[5.5]undecan-4-ol **41** (equatorial alcohol) had a GC–MS spectrum identical with that of isomer II obtained above (compound **41**). Isomer III (70%) (2*S*,4*R*,6*R*,8*R*)-8-ethyl-2-methyl-1,7-dioxaspiro[5.5]undecan-4-ol (**44**) (equatorial alcohol), *m/z* 214 (M^+, 0%), 185 (8), 167 (21), 129 (100), 128 (31), 126 (17), 113 (21), 111 (53), 99 (16), 83 (50), 71 (47), 69 (37), 68 (38) and 67 (17); $\delta_C(C_6D_6$; 125 MHz) (major isomer) 10.57 (C-14), 19.92 (C-10), 21.89 (C-12), 29.62 (C-13), 30.77 (C-9), 36.34 (C-11), 38.71 (C-5), 43.67 (C-3), 64.49 (C-4), 65.01 (C-2), 74.10 (C-8) and 98.88 (C-6); δ_C(minor isomer) 10.08, 18.75, 22.29, 29.71, 30.93, 42.69, 45.35, 65.30, 66.40, 71.38 and 98.08; δ_C(minor isomer) 10.13, 19.25, 22.05, 29.71, 31.07, 35.62, 40.14, 45.22, 62.35, 67.38 and 70.98; $\delta_H(C_6D_6$; 500 MHz) 0.90 (3 H, t, *J* 7.44, Me C-14), 0.97 (1 H, t, *J* 12.7, 5-H^{ax}), 1.05 (1 H, m, 9-H^{ax}), 1.11 (1 H, m, 3-H^{ax}), 1.15 (3 H, d, *J* 6.2, Me C-12), 1.21 (1 H, m, 9-H^{eq}), 1.25–1.39 (2 H, m, 10-H^{ax} and one of the C-13 methylene protons), 1.47 (1 H, m, 10-H^{eq}, overlapping with a C-13 methylene proton), 1.50 (1 H, m, one of the C-13 methylene protons), 1.57 (1 H, dt, *J* 12.82 and 4.1, 11-H^{eq}), 1.67 (1 H, td, *J* 12.82 and 4.1, 11-H^{ax}), 1.74 (1 H, m, 3-H^{eq}), 2.46 (1 H, dm, *J* 12.8, 5-H^{eq}), 3.15 (1 H, m, 8-H^{ax}), 3.87 (1 H, tt, *J* 11.00 and 4.5, 4-H^{eq}) and 4.23 (1 H, dqd, *J* 11.8, 6.2 and 2.2, 2-H^{ax}).

2-Ethyl-8-methyl-1,7-dioxaspiro[5.5]undecan-4-ols 14

3-Hydroxy-11-(tetrahydropyran-2-yloxy)dodecane-5,7-dione 47. The dione resulting from alkylation of the dianion of pentane-2,4-dione with (*S*)-1-iodo-3-(tetrahydropyran-2-yloxy)butane **46** (2.31 g, 9.03 mmol) was dissolved in dry THF (10 cm^3) and treated with lithium diisopropylamide in the manner already described. The resulting dark red solution was stirred at −78 °C for 2 h and treated with propanal (0.63 g, 10.8 mmol). The usual work-up gave dione **47** (3.06 g) as a mixture of diastereoisomers. This product was used without further purification, *m/z* 213 (7%), 212 (22), 211 (35), 195 (36), 153 (33), 140 (43), 139 (63), 127 (21), 113 (28), 97 (27), 85 (100), 83 (24), 69 (78) and 67 (22).

2-Ethyl-8-methyl-1,7-dioxaspiro[5.5]undecan-4-one. The crude dione **47** (3.0 g) was stirred for 72 h in a mixture of glacial acetic acid (20 cm^3), THF (10 cm^3) and water (5 cm^3) at 40–45 °C. Work-up in the described way gave an orange oil (2.23 g), which was purified by flash chromatography on silica (70–230 mesh) and eluted with CH_2Cl_2–hexane (1:4 increasing to 4:1). A mixture of three spiroketones in the proportions 87:7.8:5.2 was obtained (0.22 g, 17% from the iodide) (GC–MS). Preparative HPLC (silica column; elution with 20% diethyl ether–hexane) gave the isomers **48** and **50**. The isomer **49** was not isolated in pure form and was presumed to have decomposed or isomerised on the column. Both products **48** and **50** were contaminated with compound **49**, enabling characteristic signals in the ^{1}H and ^{13}C NMR spectra to be assigned for this isomer. Isomer I (87%) (2*S*,6*R*,8*S*)-2-ethyl-8-methyl-1,7-dioxaspiro-[5.5]undecan-4-one **48**, $[\alpha]_D^{23}$ −67.5 (*c* 10.4, pentane); *m/z* 212 (M^+, 20%), 183 (13), 143 (100), 140 (64), 139 (44), 125 (38), 115 (63), 113 (31), 112 (72), 98 (42), 97 (46), 84 (30), 83 (71), 82

Table 5 ^{13}C NMR chemical shifts for side-chain-hydroxylated 2,8-dialkyl (methyl, ethyl)-1,7-dioxaspiro[5.5]undecanes (C_6D_6)

Carbon	**54**	**59**	**63**
2	70.08	73.20	69.85
3	26.91	33.15[a]	32.86
4	18.68	19.34[b]	19.47
5	35.96	36.01[c]	35.23
6	95.81	96.35	96.21
8	70.47	65.42	65.50
9	31.05	25.26[a]	31.46
10	19.27	18.70[b]	18.91
11	35.65	35.42[c]	35.23
12 Me/OCH_2	66.45	70.08	38.63
13 Me/CH_2	29.66	18.80	61.50
14 Me	10.45	22.11	22.12

[a,b,c] Interchangeable.

Table 6 ^1H NMR chemical shifts for side-chain-hydroxylated 2,8-dialkyl (methyl, ethyl)-1,7-dioxaspiro[5.5]undecanes (C_6D_6)

Hydrogen	**54**	**59**	**63**
2-H^{ax}	3.75	3.5	3.69–3.77
3-H^{ax}	1.13		1.04
3-H^{eq}	1.23		1.26
4-H^{ax}	1.96	1.98[a]	1.81
4-H^{eq}	1.36		1.37
5-H^{ax}	1.26		1.23
5-H^{eq}	1.59		1.57
8-H^{ax}	3.48	3.65–3.8	3.69–3.77
9-H^{ax}	1.07		1.06
9-H^{eq}	1.34		1.36
10-H^{ax}	1.82	1.85[a]	1.96
10-H^{eq}	1.37		1.37
11-H^{ax}	1.29		1.23
11-H^{eq}	1.56		1.48
12 Me/CH_2	3.48	3.65–3.8	1.65/1.40
13 Me/CH_2	1.50/1.37	1.15	3.69–3.77
14 Me	0.98	1.14	1.14

[a] Interchangeable.

(34), 70 (24) and 69 (68) (Found: M^+, 212.1417. $C_{12}H_{20}O_3$ requires *M* 212.1412); $\delta_C(C_6D_6)$ see Table 1; $\delta_H(C_6D_6)$ 0.83 (3 H, t, *J* 7.45, Me C-13), 0.96 (1 H, tdd, *J* 13.18, 11.48 and 3.91, 9-H^{ax}), 1.00 (3 H, d, *J* 6.35 Me C-14), 1.08 (1 H, td, *J* 13.3 and 4.64, 11-H^{ax}), 1.2–1.47 [4 H, m, C-12 methylene protons, 10-H^{eq} (dd, δ 1.31) and 9-H^{eq} (dd, δ 1.45)], 1.53 (1 H, dm, *J* 13.18, 11-H^{eq}), 1.82 (1 H, qt, *J* 13.3 and 4.15, 10-H^{ax}), 1.80 (1 H, ddd, *J* 14.16, 11.72 and 0.74,[a] 3-H^{ax}), 1.97 (1 H, dd, *J* 14.41 and 0.74,[a] 5-H^{ax}), 2.19 (1 H, ddd, *J* 14.16, 2.93 and 1.95,[b] 3-H^{eq}), 2.42 (1 H, dd, *J* 14.41 and 1.95,[b] 5-H^{eq}), 3.54 (1 H, dqd, *J* 11.48, 6.35 and 2.2, 8-H^{ax}) and 3.62 (1 H, dddd, *J* 11.38, 7.91, 4.39 and 2.93, 2-H^{ax}). [a] 1,3-Diaxial coupling, [b] W-coupling; isomer II (7.8%) (2*R*,6*R*,8*S*)-2-ethyl-8-methyl-1,7-dioxaspiro[5.5]undecan-4-one **49**; *m/z* 212 ($M^{\cdot+}$, 4%), 183 (9), 143 (100), 139 (23), 125 (37), 113 (13), 112 (14), 97 (17), 87 (27), 83 (62) and 69 (26); $\delta_C(C_6D_6)$ (*inter alia*) see Table 1; $\delta_H(C_6D_6)$ 0.81 (3 H, t, *J* 7.45, Me C-13), 1.02 (3 H, d, *J* 6.1, Me C-14), 1.67 (1 H, qt, *J* 13.4 and 4.2, 10-H^{ax}), 2.05 (1 H, ddd, *J* 15.8, 3.17 and 0.74, 3-H^{eq}), 2.20 (1 H, dd, *J* 15.8 and 11.5, 3-H^{ax}, overlapped with 3-H^{eq} of *trans*, *trans*-isomer), 2.32 (1 H, dd, *J* 15.4 and 0.74,[b] 5-H^{eq}), 2.48 (1 H, dd, *J* 15.4 and 0.5, 5-H^{ax}), 3.31 (1 H, dddd, *J* 11.5, 7.7, 4.4 and 2.9, 2-H^{ax}) and 4.06 (1 H, dqd, *J* 11.4, 6.1 and 2.2, 8-H^{ax}); isomer III (5.2%) (2*R*,6*S*,8*S*)-2-ethyl-8-methyl-1,7-dioxaspiro[5.5]-undecan-4-one **50**, *m/z* 212 (M^+, 9%), 143 (10), 140 (15), 139 (11), 115 (100), 112 (14), 98 (33), 97 (59), 83 (26), 73 (15), 70 (17) and 69 (42); $\delta_C(C_6D_6)$ see Table 1; $\delta_H(C_6D_6)$ 0.77 (3 H, t, *J* 7.45, Me C-13), 0.96 (1 H, m, 9-H^{ax}), 1.03 (3 H, d, *J* 6.1, Me C-14), 1.04–1.16 (2 H, m, 9-H^{eq} and 10-H^{ax}), 1.28 (1 H, m, C-12 methylene proton), 1.37–1.46 (2 H, m, 10- and 11-H^{eq}), 1.47 (1 H, m, C-12 methylene proton), 1.60 (1 H, td, *J* 12.94 and 4.39 11-H^{ax}), 1.85 (1 H, dd, *J* 13.91 and 11.4, 3-H^{ax}), 1.87 (1 H, dd, *J* 13.91 and 0.74, 5-H^{ax}), 2.22 (1 H, ddd, *J* 13.91, 2.93 and 1.96,[b] 3-H^{eq}), 2.79 (1 H, dd, *J* 13.91 and 1.96,[b] 5-H^{eq}), 3.47 (1 H, dqd, *J* 9.28, 6.35 and 3.17, 8-H^{ax}), 4.26 (1 H, dddd, *J* 11.4, 6.67, 5.61 and 2.93, 2-H^{ax}). [b] W-coupling.

2-Ethyl-8-methyl-1,7-dioxaspiro[5.5]undecan-4-ols 51 and 52

Reduction of ketone (2*S*,6*R*,8*S*)-**48** (0.22 g, 1.03 mmol) with $LiAlH_4$ afforded the epimeric axial and equatorial alcohols, **52** and **51**, in the ratio 46:54 (GC–MS). Preparative HPLC (silica column) and elution with EtOAc–hexane (1:4) gave the individual *isomers* **52** (30 mg) and **51** (38 mg). HRMS (EI) (Found: M^+, 214.1604. $C_{12}H_{22}O_3$ requires M, 214.1569). Isomer I (46%) (2S,4S,8S)-2-*ethyl*-8-*methyl*-1,7-*dioxaspiro*[5.5]*undecan*-4-*ol* **52** (axial alcohol), $[\alpha]_D^{23}$ −60.0 (*c* 0.911, pentane); *m/z* 214 ($M^{\cdot+}$, 3%), 167 (11), 145 (41), 142 (36), 127 (75), 115 (78), 114 (21), 112 (36), 109 (23), 97 (44), 85 (38), 81 (23), 71 (28), 69 (42) and 43 (100) (Found: M^+, 214.1604. $C_{12}H_{22}O_3$ requires *M*, 214.1569); $\delta_C(C_6D_6)$ see Table 3; $\delta_H(C_6D_6)$ 0.93 (3 H, d, *J* 6.35, Me C-14), 0.96 (3 H, t, *J* 7.5, Me C-13), 0.96 (1 H, tdd, *J* 13.43, 11.48 and 4.15, 9-H^{ax} overlapping with Me C-13 and Me C-12), 1.19 (1 H, td, *J* 13.43 and 4.64, 11-H^{ax}), 1.22 (3 H, m, 3-H^{ax}, and 9- and 10-H^{eq}), 1.31 (1 H, dd, *J* 13.91 and 3.66, 5-H^{ax}), 1.37 (1 H, m, C-12 methylene proton), 1.45 (1 H, dm, *J* 13.43, 11-H^{eq}), 1.52 (1 H, m, C-12 methylene proton), 1.80 (1 H, dm, *J* 11.72, 3-H^{eq}), 1.83 (1 H, dm, *J* 14, 5-H^{eq}), 1.87 (1 H, qt, *J* 13.19 and 4.15, 10-H^{ax}), 3.67 (1 H, dqd, *J* 11.48, 6.35 and 2.2, 8-H^{ax}), 3.84 (1 H, dddd, *J* 11.8, 8, 4.4 and 2.2, 2-H^{ax}), 4.06 (1 H, m, 4-H^{eq}) and 4.32 (1 H, br d, *J* 9.52, OH); isomer II (54%) (2S,4R,6R,8S)-2-*ethyl*-8-*methyl*-1,7-*dioxaspiro*[5.5]*undecan*-4-*ol* **51** (equatorial alcohol), $[\alpha]_D^{23}$ −57.9 (*c* 0.411, pentane); *m/z* 214 ($M^{\cdot+}$, 3%), 167 (27), 145 (36), 142 (46), 127 (56), 115 (47), 112 (42), 109 (21), 97 (35), 85 (46), 81 (19), 71 (28), 69 (33) and 43 (100); $\delta_C(C_6D_6)$ see Table 3; $\delta_H(C_6D_6)$ 0.95 (3 H, t, *J* 7.33, Me C-13), 1.06 (1 H, tdd, *J* 12.94, 11.23 and 4.15, 9-H^{ax}), 1.09 (3 H, d, *J* 6.35, Me C-14), 1.10 (1 H, q, *J* 11.7, 3-H^{ax}), 1.23 (1 H, t, *J* 11.6, 5-H^{ax}), 1.29 (1 H, td, *J* 13.18 and 4.4, 11-H^{ax}), 1.30–1.41 (3 H, m, 9- and 10-H^{eq}, and one of the C-12 methylene protons), 1.53 (1 H, m, one of the C-12 methylene protons), 1.60 (1 H, dm, *J* 12.7, 11-H^{eq}), 1.74 (1 H, ddt, *J* 11.96, 4.64 and 2.2,[a] 3-H^{eq}), 1.95 (1 H, qt, *J* 13.18 and 4.15, 10-H^{ax}), 2.03 (1 H, ddd, *J* 11.23, 4.4 and 2.2,[a] 5-H^{eq}), 3.40 (1 H, dddd, *J* 11.4, 8.13, 4.64 and 2.2, 2-H^{ax}), 3.65 (1 H, dqd, *J* 11.23, 6.35 and 2.2, 8-H^{ax}) and 4.13 (1 H, tt, *J* 11.23 and 4.64, 4-H^{ax}). [a] W-coupling.

(*R*)-10-(Tetrahydropyran-2-yloxy)dodec-1-en-6-one 53

Acetone *N*,*N*-dimethylhydrazone (0.4 g, 4 mmol) was sequentially alkylated with iodide **25** and 4-bromobut-1-ene using the known procedure[3,8] by employing butyllithium as base. After work-up the crude hydrazone was cleaved by passage through a silica column [(20:1) hexane–diethyl ether] to provide the ketone **53** (400 mg, 35%), *m/z* 198 (0.7%), 197 (1.1), 181 (16), 97 (12) and 85 (100); $\delta_C(CDCl_3)$ (2 diastereoisomers) 9.10, 9.85, 19.94, 19.99, 20.05, 22.78, 22.80, 22.99, 25.87, 27.63, 31.17, 31.18, 32.49, 33.07, 33.09, 33.77, 41.80, 41.84, 42.87, 42.89, 62.71, 62.89, 77.04, 77.89, 97.51, 97.91, 115.09, 115.14, 137.95, 138.00, 210.81 and 211.10; $\delta_H(CDCl_3)$ 0.82 (3 H, t, *J* 7.4, Me), 0.89 (3 H, t, *J* 7.4, Me), 1.35–1.85 (26 H, m), 2.01 (4 H, q, *J* 7.2), 2.38 (10 H, qd, *J* 7.3 and 2.8), 3.39–3.65 (4 H, m), 3.85–3.95 (2 H, m), 4.55–4.65 (2 H, m), 4.88–5.04 (4 H, m) and 5.66–5.79 (2 H, m).

{(2*S*,6*S*,8*R*)-8-Ethyl-1,7-dioxaspiro[5.5]undecan-2-yl}-methanol 54

From oxymercuriation–oxidative demercuriation. Ketone **53** (50 mg, 0.2 mmol) was oxymercuriated as described previously[3] and the crude chloromercurial was subjected to oxidative demercuriation.[24] The resulting oil was purified by flash chromatography [SiO_2; (20:1–10:1–5:1) hexane–diethyl ether] to provide spiroketal **54** (50%) along with the reduced product 2-ethyl-8-methyl-1,7-dioxaspiro[5.5]undecane. Compound **54** was identical with the product from the AD reaction of enone **53**.

From asymmetric dihydroxylation. Ketone **53** (115 mg, 0.41 mmol) was dissolved in water–Bu^{t}OH (5 cm^3; 1:1) and commercial AD-mix-α (580 mg) and methanesulfonamide (40 mg) added. After being stirred for 6 days at 0 °C the reaction mixture was diluted with water and the usual work-up gave the monoprotected keto triol. After dissolution of the monoprotected keto triol in THF (10 cm^3), 1 mol dm^{-3} HCl (1 cm^3) was added and the reaction mixture was stirred overnight. The usual work-up gave the crude alcohol **54**, and purification by flash chromatography on silica gel [hexane–diethyl ether (5:1)] yielded pure alcohol (2*S*,6*S*,8*R*)-**54** (27 mg, 30%); *m*/*z* (EI) 214 (M^+, 15%), 185 (14), 184 (13), 183 (100), 156 (22), 131 (74), 130 (34), 129 (92), 128 (95), 126 (20), 113 (90), 111 (48), 99 (58), 97 (59) and 95 (10) (Found: M^+, 214.1577; C, 64.8; H, 10.2. $C_{12}H_{22}O_3$ requires *M*, 214.1569; C, 67.3; H, 10.3%); $[\alpha]_D^{25}$ +75.3 (*c* 0.868, pentane); $\delta_C(C_6D_6)$ see Table 5; $\delta_H(C_6D_6)$ 0.99 (3 H, t, *J* 7.4, 14-H_3), 1.00–1.43 (9 H, m), 1.45–1.63 (3 H, m), 1.82 (2 H, m, 4-H^{ax} + OH), 3.48 (2 H, m, 12-H + 8-H^{ax}) and 3.72 (m, 2-H^{ax}).

{(2*R*,6*S*,8*R*)}-55 and {(2*R*,6*R*,8*R*)-8-Ethyl-1,7-dioxaspiro[5.5]-undecane-2-yl}methanol 56

In the manner just described for the preparation of alcohol **54**, ketone **53** (216 mg, 0.77 mmol) was treated with AD-mix-β. Purification of the crude spiroketal by flash chromatography [(7:1) hexane–diethyl ether] yielded title compound **55** and **56** with ~10% cross-contamination. (2*R*,6*S*,8*R*)-**55** (27.4 mg, 6%), *m*/*z* (EI) 214 (M^+, 5%), 185 (6), 184 (7), 183 (54), 139 (12), 131 (61), 130 (22), 129 (28), 128 (20), 113 (100), 111 (19), 99 (28), 97 (18), 95 (14) and 85 (30) (Found: M^+, 214.1570; C, 63.5; H, 10.5. $C_{12}H_{22}O_3$ requires *M*, 214.1569; C, 67.3; H, 10.3%); $[\alpha]_D^{25}$ +27.5 (*c* 0.739, pentane); $\delta_C(C_6D_6)$ 9.95 (C-14), 18.72 (C-10), 18.96 (C-4), 26.53 (C-3), 29.70 (C-13), 30.32 (C-11), 30.90 (C-9), 36.61 (C-5), 66.35 (C-12), 71.30 (C-8), 73.39 (C-2) and 97.18 (C-6); $\delta_H(C_6D_6)$ 0.92 (3 H, t, *J* 7.52, 14-H_3), 0.94–1.15 (3 H, m), 1.15–1.30 (2 H, m) and 1.30–1.70 (m, 8-H^{ax}).

(2*R*,6*R*,8*R*)-**56** (24.5 mg, 14%), *m*/*z* (EI) 214 (M^+, 7%), 185 (14), 183 (27), 139 (6), 131 (16), 130 (12), 129 (100), 128 (29), 121 (8), 113 (22), 112 (6), 111 (61), 99 (21), 97 (16) and 85 (11) (Found: M^+, 214.1566; C, 66.6; H, 10.5. Calc. for $C_{12}H_{22}O_3$: M, 214.1569; C, 67.3; H, 10.3%); $[\alpha]_D^{25}$ −20.9 (*c* 0.688, pentane); $\delta_C(C_6D_6)$ 10.62 (C-14), 18.17 (C-4), 20.04 (C-10), 27.17 (C-3), 29.03 (C-5), 29.75 (C-13), 30.99 (C-9), 36.42 (C-11), 66.43 (C-12), 70.88 (C-2), 73.95 (C-8) and 97.32 (C-6); $\delta_H(C_6D_6)$ 0.89–0.98 (2 H, m), 1.04–1.14 (6 H, m), 1.41–1.65 (5 H, m), 1.93 (m, 5-H^{eq}), 3.02 (m, 8-H^{ax}), 3.46–3.55 (2 H, m, 12-H_2) and 4.24 (m, 2-H^{ax}).

4-(2-Iodoethyl)-2,2-dimethyl-1,3-dioxane 62

Diethyl 3-oxopentanedioate was reduced with $LiAlH_4$ in the reported manner[26] to provide pentane-1,3,5-triol. The triol was converted into the 1,3-*O*-isopropylidene derivative by stirring it in acetone containing dimethoxypropane and a catalytic amount of PPTS. 2-(2,2-Dimethyl-1,3-dioxan-4-yl)ethanol was purified by flash chromatography; $\delta_C(CDCl_3)$ 19.17, 29.89, 30.92, 38.18, 59.75, 60.47, 68.88 and 98.30; $\delta_H(CDCl_3)$ 1.32 (d, *J* 0.5, Me), 1.42 (d, *J* 0.5, Me), 1.39–1.46 (7 H, m), 1.59–1.72 (3 H, m), 3.55–3.85 (4 H, m), 3.93 (1 H, td, *J* 13 and 4) and 4.05–4.14 (1 H, m). Conversion into the iodide was achieved by the standard procedure using iodine, triphenylphosphine and imidazole in toluene. Purification by flash chromatography [(10:1) hexane–diethyl ether] provided iodide **62** in 60% yield, *m*/*z* (EI) 255 (63%), 195 (31), 155 (4), 128 (6), 127 (8) 68 (19), 67 (60) and 43 (100); $\delta_H(CDCl_3)$ 1.30 (d, *J* 1.6, Me), 1.41 (d, *J* 1.6, Me), 1.27–1.45 (1 H, m), 1.57 (1 H, m), 1.76–1.95 (2 H, m), 3.14–3.27 (2 H, m), 3.73–3.83 (1 H, m) and 3.86–3.99 (2 H, m).

2-(8-Methyl-1,7-dioxaspiro[5.5]undecan-2-yl)ethanols 63–65

Acetone *N*,*N*-dimethylhydrazone (110 mg, 1.1 mmol) in THF (15 cm^3) was sequentially alkylated with (*R*)-1-iodo-3-(tetrahydropyran-2-yloxy)butane **57** (312 mg, 1.1 mmol) and iodide **62** (230 mg, 0.85 mmol). The reaction mixture was quenched with 10% HCl (10 cm^3) and stirred overnight. Standard work-up gave a yellow oil, which on flash chromatography on silica gel [(2:1) hexane–diethyl ether] provided three diastereoisomers **63** (16.8 mg) and **64**/**65** (7.7 mg) as a mixture. Isomer I (2*S*,6*S*,8*R*)-**63**: *m*/*z* (EI) 214 (M^+, 6.3%), 170 (12), 153 (12), 145 (19), 142 (20), 140 (16), 127 (42), 125 (11), 115 (100), 114 (23), 113 (20), 112 (60), 109 (17), 101 (22), 99 (12), 97 (36), 85 (26), 83 (22), 81 (22) and 71 (34) (Found: M^+, 214.1565. $C_{12}H_{22}O_3$ requires *M*, 214.1569); $\delta_C(C_6D_6)$ see Table 5; $\delta_H(C_6D_6)$ 1.00–1.18 (3 H, m), 1.13 (d, *J* 6.3, Me), 1.18–1.41 (7 H, m), 1.48 (1 H, m), 1.57 (1 H, m), 1.65 (1 H, m), 1.81 (1 H, m), 1.96 (1 H, m) and 3.69–3.77 (4 H, m); Isomers II **64** and III **65**; $\delta_C(C_6D_6$; two isomers) 18.63, 18.80, 19.24, 20.07, 22.12, 22.36, 28.37, 30.11, 31.37, 31.61, 32.31, 33.27, 36.28, 36.58, 38.85, 38.96, 61.14, 61.17, 66.54, 68.63, 70.26, 72.57, 97.15 and 97.82; δ_H(two isomers) 0.83–1.74 [44 H, m, including doublets at 1.09 (*J* 6.2) and 1.13 (*J* 6.2), 2 × Me], 1.80–1.90 (1 H, m), 1.90–1.98 (1 H, m), 2.27 (br s), 2.60 (br s), 3.23–3.37 (2 H, m), 3.62–3.81 (4 H, m), 4.09–4.19 (1 H, m) and 4.23–4.32 (1 H, m).

(*R*)-2-(Tetrahydropyran-2-yloxy)dodec-10-en-6-one 58

Acetone *N*,*N*-dimethylhydrazone (0.3 g, 3 mmol) was sequentially alkylated with iodide **57** (852 mg, 3 mmol) and (*E*)-5-bromopent-2-ene by using the above described procedure employing butyllithium as base. After work-up the crude hydrazone was cleaved by passage through a silica column [(20:1) hexane–diethyl ether], and the obtained crude ketone **58** (400 mg, 50%) was used without further purification.

2-{(2*S*,6*S*,8*R*,12*S*)-(8-Methyl-1,7-dioxaspiro[5.5]undecan-2-yl}ethanol 59

By using the procedure described for the reaction of ketone **53**, crude ketone **58** (240 mg, 1 mmol) was treated with AD-mix-α. Purification of the crude spiroketal by flash chromatography on silica gel [(7:1) hexane–diethyl ether] yielded the spiroketal (80 mg) and smaller amounts of three other diastereoisomers (Found: M^+, 214.1570. $C_{12}H_{22}O_3$ requires *M*, 214.1569), $[\alpha]_D^{25}$ +33.3 (*c* 1.266, pentane); $\delta_C(C_6D_6)$ see Table 5; δ_H 1.0–1.15 (2 H, m), 1.14 (d, *J* 6.5, Me C-14), 1.15 (d, *J* 6.5, Me C-13), 1.20–1.65 (8 H, m), 1.80–2.05 (2 H, m, 4- and 10-H^{ax}), 1.90 (br s, OH), 3.50 (ddd, *J* 2.4, 4.8 and 11.6, 2-H) and 3.65–3.80 (2 H, m, 8- and 12-H).

Acknowledgements

We are indebted to the Australian Research Council for support of this work.

References

1 M. V. Perkins, M. F. Jacobs, W. Kitching, P. J. Cassidy, J. A. Lewis and R. A. I. Drew, *J. Org. Chem.*, 1992, **57**, 3365.
2 W. Kitching, J. A. Lewis, M. V. Perkins, R. A. I. Drew, C. J. Moore, W. Francke, W. A. König and V. Schurig, *J. Org. Chem.*, 1989, **54**, 3893.
3 M. V. Perkins, W. Kitching, W. A. König and R. A. I. Drew, *J. Chem. Soc., Perkin Trans. 1*, 1990, 2501.
4 S. Krohn, M. T. Fletcher, W. Kitching, R. A. I. Drew, C. J. Moore and W. Francke, *J. Chem. Ecol.*, 1991, **17**, 485.

5 M. T. Fletcher, J. A. Wells, M. F. Jacobs, S. Krohn, W. Kitching, R. A. I. Drew, C. J. Moore and W. Francke, *J. Chem. Soc., Perkin Trans. 1*, 1992, 2827.
6 M. T. Fletcher, M. F. Jacobs, W. Kitching, S. Krohn, R. A. I. Drew, G. E. Haniotakis and W. Francke, *J. Chem. Soc., Chem. Commun.*, 1992, 1457.
7 M. V. Perkins, M. T. Fletcher, W. Kitching, R. A. I. Drew and C. J. Moore, *J. Chem. Ecol.*, 1990, **16**, 2475.
8 M. V. Perkins, W. Kitching, R. A. I. Drew, C. J. Moore and W. A. König, *J. Chem. Soc., Perkin Trans. 1*, 1990, 1111.
9 Unpublished observations of Dr Sabine Krohn.
10 R. Baker and R. H. Herbert, *J. Chem. Soc., Perkin Trans. 1*, 1987, 1123, and references therein.
11 Y. Naoshima, H. Ike, T. Ogawa, T. Nakayama and H. Kondo, *Agric. Biol. Chem.*, 1984, **48**, 2151.
12 J. A. Lewis, Ph.D. Dissertation, Characterization and Synthesis of Dacine Fruit Fly Phenomones, The University of Queensland, 1987.
13 See, for example, W. Francke and W. Reith, *Liebigs Ann. Chem.*, 1979, 1; W. Francke, G. Hindorf and W. Reith, *Naturwissenschaften*, 1979, **66**, 619.
14 K. Mori and M. Ikunaka, *Tetrahedron*, 1984, **40**, 3471.
15 Available from the Sigma Chemical Co. See also K. Mori, *Tetrahedron*, 1989, **45**, 3233.
16 M. F. Jacobs, Ph.D. Dissertation, The University of Queensland, 1992.
17 D. Seebach and M. Züger, *Helv. Chim. Acta*, 1982, **65**, 495.
18 K. Mori and H. Watanabe, *Tetrahedron*, 1984, **40**, 299.
19 F. G. Cocu, G. Wolczunowicz, L. Bors and Th. Posternak, *Helv. Chim. Acta*, 1970, **53**, 1511.
20 M. A. Doherty, S. V. Ley, B. Lygo and D. J. Williams, *J. Chem. Soc., Perkin Trans. 1*, 1984, 1371.
21 R. J. R. Fraser, M. Kanfuran, P. Morand and G. Govil, *Can. J. Chem.*, 1969, **47**, 404.
22 M. V. Perkins, Ph.D. Dissertation, The University of Queensland, 1991.
23 K. Mori and H. Watanabe, *Tetrahedron*, 1986, **42**, 295.
24 K. B. Sharpless, W. Amberg, Y. L. Bennani, G. A. Crispano, J. Harting, K. Jeung, H. Kwong, K. Morikawa, Z. Wang, D. Xu and X. Zhang, *J. Org. Chem.*, 1992, **57**, 2768.
25 J. J. De Voss, J. F. Jamie, J. T. Blanchfield, M. T. Fletcher, M. G. O'Shea and W. Kitching, *Tetrahedron*, 1991, **47**, 1985. See also W. Kitching, J. A. Lewis, M. T. Fletcher, J. J. De Voss, R. A. I. Drew and C. J. Moore, *J. Chem. Soc., Chem. Commun.*, 1986, 855.
26 M. Viscontini and C. Ebnother, *Helv. Chem. Acta*, 1951, **13**, 116.
27 P. J. Garegg and B. Samuelsson, *J. Chem. Soc., Perkin Trans. 1*, 1980, 2866.

Paper 4/05438E
Received 6th *September* 1994
Accepted 6th *December* 1994