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MERCURY(II)-MEDIATED ROUTES TO SOME SIDE-CHAIN FUNCTIONALISED 1,7-DIOXASPIRO[5 5]UNDECANES APPLICATIONS OF LUCHE-BARBIER CHEMOSELECTIVE ADDITION TO KETOALDEHYDES[1]

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ABSTRACT The ketoaldehyde, 5-oxo-9-decenal (4) undergoes chemoselective addition to the aldehyde with either allyl or propargyl bromide under Luche-Barbier conditions Oxymercuration-cyclisation of the resulting hydroxyketones, followed by reductive or oxidative demercuration, provides functionalised spiroacetals, some of which are of insect origin

INTRODUCTION In connection with the suspected presence of spiroacetals in the rectal gland secretions of certain Australasian fruit-fly species,[2-5] methods have been developed for the acquisition of a number of alkyl-substituted 1,7-dioxaspiro[5 5]undecanes and also 1,6-dioxaspiro[4 5]decanes, which occur in a range of insect orders Some of the present work was prompted by the presence of a very minor component (apparent M = 226) thought to be either (1) or (2), in the rectal gland secretion of *B latifrons*[1] The possible presence of (2) was of interest, as methylketones are uncommon components of sex pheromones, and oxygenation of simple insect-derived alkyl-substituted spiroacetals appears to be confined to hydroxylation [3,7-9] Acquisition of (1) and (2), which was necessary for comparisons with the gc-ms behaviour of the natural component (~1% of the volatiles of the secretion),[10] and a route to (2) and other spiroacetals, is described herein The characterisation of (1) has been reported elsewhere [11]

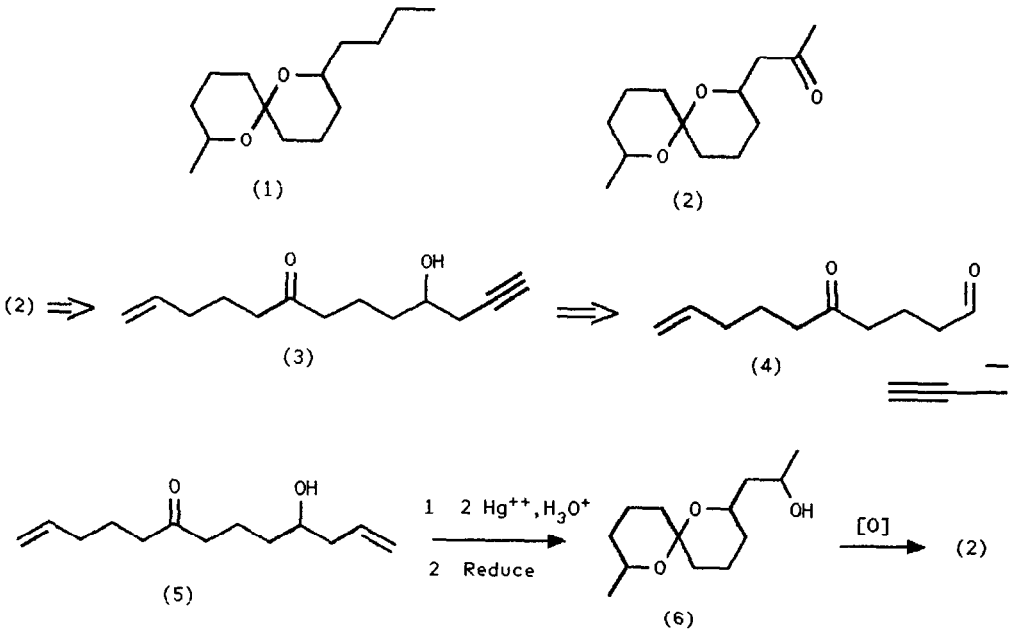
RESULTS AND DISCUSSION One approach to the synthesis of (2) was based on the hydroxymercuration-cyclisation[1,3] of a suitable hydroxyenone, with the added prospect that the above conditions would suffice for the hydrolysis of an installed propynyl function as in (3), and thus provide the 2-oxopropyl side chain This route would require the chemoselective addition of the 1-propynyl group to the appropriate ketoaldehyde (4), with a minimum of propynyl-1,2-propadienyl rearrangement This is summarised in Scheme 1 Alternatively chemoselective allylation of the ketoaldehyde (4) could be employed, and the resulting hydroxydienone (5) would experience both oxymercuration-cyclisation and normal oxymercuration under the standard conditions Reductive demercuration[1,3] would then provide (6), which could be oxidised to (2) This procedure avoids the possible problem of propynyl-allenyl rearrangement during the planned addition of the "propargyl" organometallic to the ketoaldehyde (4) (Scheme 1)

Dehydration ($KHSO_4$) of the tertiary alcohol (formed by addition of pent-4-enylmagnesium

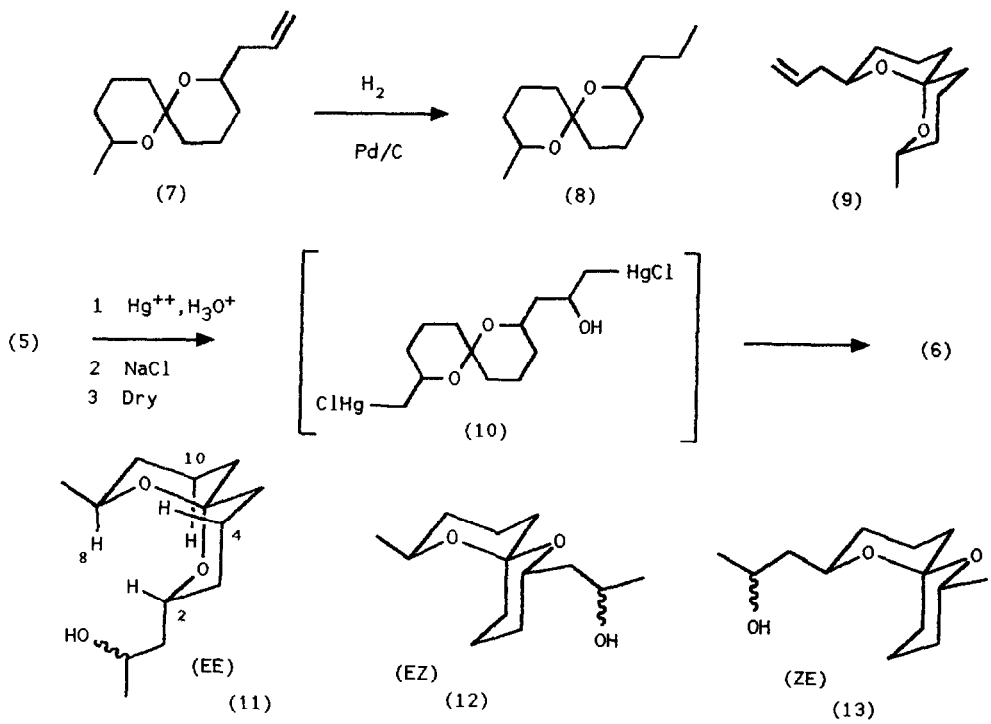
bromide to cyclopentanone) in the manner described elsewhere[12] provided a mixture of dienes (*ca* 4 1) with the desired 1-(pent-4'-enyl)cyclopentene predominating Regioselective epoxidation (m-chloroperbenzoic acid) furnished the 1-alkenyl-1,2-epoxycyclopentane which underwent smooth oxidative cleavage with periodate in ether, to provide (73%) the ketoaldehyde, 5-oxo-9-decenal (4), which has been fully described elsewhere [12]

Allylation of (4) was now required to proceed chemoselectively at the aldehyde The reports of Luche[13] that aldehydes and ketones experience smooth Barbier-type reaction with allyl bromide and zinc in aqueous medium (THF-saturated aqueous NH_4Cl) were attractive, especially since two ketoaldehydes were demonstrated to exhibit high chemoselectivity in this process This C-C bond forming reaction, remarkable for its efficiency in saturated aqueous NH_4Cl, has been further developed by other workers [14] (In this context, it should be noted that enantioselective allylation of aldehydes, utilising a titanium (IV) carbohydrate complex can be conducted at -74°C, at which temperature ketones are unreactive)[15] Thus treatment of ketoaldehyde (4) with allylbromide in the prescribed fashion led to homoallyl alcohol (5) (~70%) as anticipated on the basis of Luche's reports [13] Alcohol (5) was characterised by its i r (3360 and 1710 cm^{-1}), ^1H (δ 3 62, m, CHOH) and ^{13}C nmr spectra The mass spectrum lacked a molecular ion (M^+ = 210), but exhibited ions corresponding to M^+-H_2O (m/z 192) and $M^+-C_3H_5$ (m/z 169) Oxymercuration of the crude hydroxydienone (5) with two equivalents of $Hg(OAc)_2$ in THF-H_3O^+ was carried out, and demercuration with $NaBH_4$ under basic-biphasic conditions conducted as described previously [1,3] GC-MS examination indicated the formation of one major (*ca* 80%) and two minor diastereomers of the 2,8-dialkyl-1,7-dioxaspiro[5 5]undecane system,[16] but the very low intensity or absence of the m/z 45 ion ($CH_3\overset{+}{C}H=OH$), suggested that the prop-2-enyl side chain (as in (7) was present rather than the secondary alcohol Preliminary nmr spectra supported this, and hydrogenation (H_2, 1 atm, Pd/C) provided three isomers (gc-ms) of 2-n-propyl-8-methyl-1,7-dioxaspiro[5 5]undecane, (8), on the basis of the mass spectra (M^+ = 212(9 5)) and excellent correspondence with published[17] mass spectra of this system (Scheme 2) The major isomer from the demercuration was purified by preparative gas chromatography and shown by ^1H and ^{13}C nmr spectra to be (E,E)-2-(2'-propenyl)-8-methyl-1,7-dioxaspiro[5 5]undecane (9), on the basis of comparisons of the spectra with those of other spiroacetals[3,18] and the method of formation which involves reversible oxymercuration-cyclisation [3,6] This procedure would be anticipated to provide predominantly the anomerically stabilised (E,E) diastereomer

The formation of (9) indicates considerable deoxymercuration accompanies the reduction (with $NaBH_4$) of intermediate bismercurial (10), and this problem has been encountered previously [1,19] Although the use of tributyltinhydride for this reduction has certain drawbacks, mainly involving the complete removal of tin residues, deoxymercuration does appear to be minimised Consequently, the bismercurial, as the chloride (10) was dried, but not characterised, and treated with Bu_3SnH in benzene in the normal way GC-MS examination of the treated solution indicated the formation of the target alcohol (6) as a diastereomeric mixture, on the basis of a strong m/z 45 ion ($CH_3\overset{+}{C}HOH$) and



Scheme 1

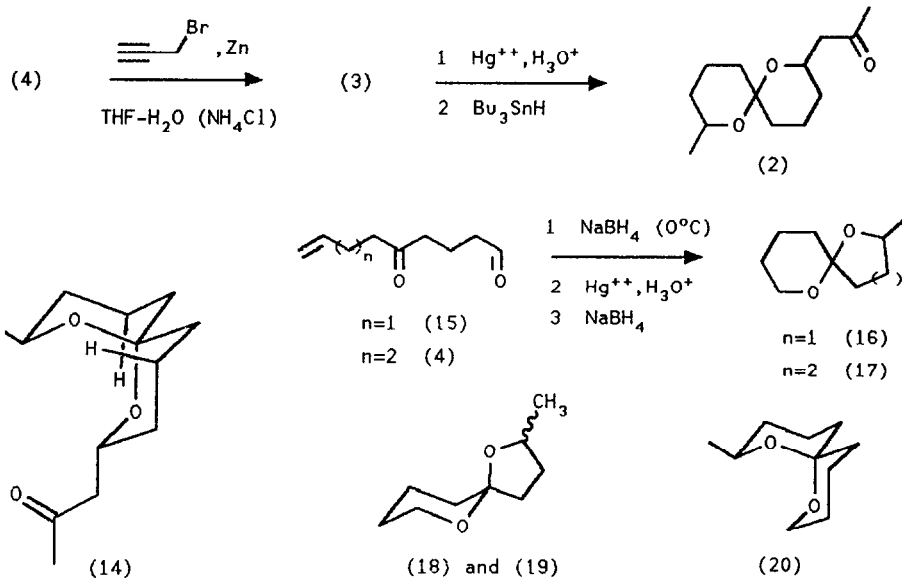


Scheme 2

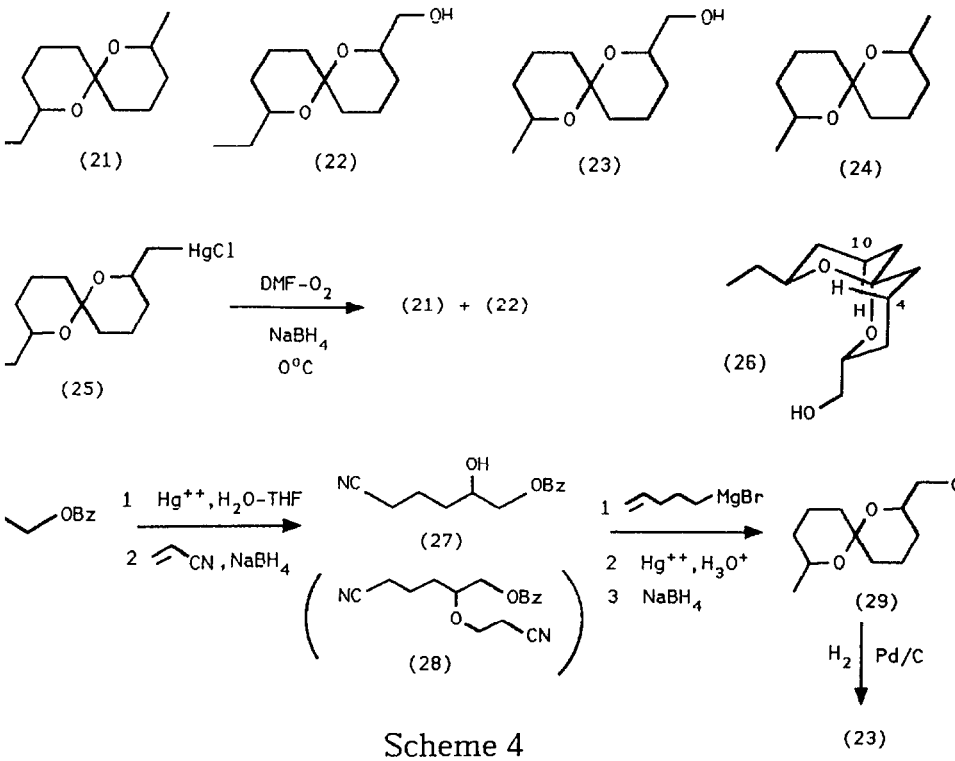
expected spiroacetal fragmentation pattern [16] (Scheme 2) Preparative gas–chromatography allowed separation of some of the isomers and two fractions were characterised The first consisted of two diastereomers and the ^{1}H and ^{13}C nmr spectra demonstrated each incorporated the (E,E) ring skeleton, but were epimeric in the hydroxypropyl side chain, as in (11) The (E,E) arrangement was confirmed[18,20] by the relatively low field resonances (δ 1 8– δ 2 0) for H_{4ax} and H_{10ax}, attributable to deshielding 1,3–diaxial interactions with oxygen The chemical shifts for H_2 and H_8 (see 11) (δ 3 8) are in close agreement with the shifts for authentic (E,E)–2,8–dimethyl–1,7–dioxaspiro[5 5]–undecane [3,18] The mass spectrum of (11) exhibits a weak (or absent) M^+ (m/z 228) peak, but the ion at m/z 169 (M^+–(CH_2–CH(OH)–CH_3)) is prominent as are those attributable to spiroacetal fragmentation (m/z 115 (100) and 112 (59 0)) and CH_3–$CH{=}\overset{+}{O}H$ (m/z 45)

The epimeric pairs (about the C2' hydroxyl) of the EZ (12) and ZE (13) ring systems were also isolated, albeit as minor products of the cyclisation With the side–chain epimers in each, there is a mixture of four diastereomers and these comprised the four–component mixture In the mass spectrum, weak M^+ (m/z 228, <1%), m/z 213 (M^+–CH_3, 1%) and m/z 169 (M^+–(CH_2–CH(OH)CH_3)), were in evidence as well as a strong m/z 45 (46), not present in the propenyl derivative (7) For this four–component mixture, forty–five of the expected fifty–two ^{13}C nmr signals were resolved, with those for the spirocarbons at δ 98 43, 98 07, 97 46 and 97 13 most diagnostic The ^{1}H chemical shift range for H_2 and H_8 in these isomers (δ 3 6–4 35) confirmed the (E,Z)/(Z,E) nature of the spiroacetal ring skeleton

With the availability of (6), ketone (2) should have been easily accessible through oxidation However, although the reaction appeared to proceed readily with PCC, purification proved tedious and a more direct route to (2) was desired Treatment of ketoaldehyde (4) with propargyl bromide and zinc, under Barbier–Luche conditions[13] led efficiently to essentially one component (gc–ms), which, while lacking a molecular ion (M^+ = 208), did exhibit ions at m/z 190 (M–H_2O, 1 2), 169 (M^+–C_3H_3, 2 5) and the dehydration–McClafferty ion at m/z 136 (8 0) corresponding to $C_9H_{12}O^+$ The ^{13}C spectrum provided the expected thirteen signals, with CHOH at δ 70 80 and C=O at δ 211 03 In the ^{1}H nmr spectrum, CHOH resonated at δ 3 83 (q, J ~7 Hz) In the i r spectrum, a terminal alkyne ν_{C-H} appeared at 3260 cm^{-1} However there was no spectroscopic evidence for significant levels of the rearranged propa–1,2–dienyl moiety , which does form in a bismuth–based version of the Barbier reaction with propargyl bromide [21] The described hydroxyenynone (3) was then subjected to the $Hg(OAc)_2$–H_3O^+–THF regimen for oxymercuration–cyclisation with the added duty of effecting hydrolysis of the terminal alkyne to the methylketone Analysis of the product oil (gc–ms) indicated the presence of three diastereomers of the required 2–(2'–oxopropyl)–8–methyl–1,7–dioxaspiro[5 5]undecane (2) (63%, 9% and 9% of the mixture) The low resolution mass spectrum of the major isomer exhibited a weak molecular ion (M^+, 226, <1%) and an ion m/z 169 (2%) corresponding to M^+–($CH_2C(O)CH_3$), together with prominent ions at m/z 115, 112 and 97 associated with the spiroacetal moiety Ions at m/z 43(100) and 58(8 7) were strongly indicative of the methylketone



Scheme 3



Scheme 4

The major isomer of (2) was obtained in pure form (preparative gas chromatography) and completely characterised by high field ^{1}H and ^{13}C nmr spectra, and on the basis of its spectra and mode of formation was assigned the (E,E) relative configuration (14) In the ^{1}H spectrum, H_{4ax} and H_{10ax} (see 14) which appear as quartets of triplets, are located at δ 1 9 and δ 1 75, requiring both to experience 1,3-diaxial interactions with oxygen The ^{13}C shifts are in harmony with those for other (E,E)-2,8-dialkyl-1,7-dioxaspiro[5 5]undecanes (Scheme 3)

The availability[12] of ketoaldehydes (4) and (15) (the latter from initial addition of but-3-enylmagnesium bromide to cyclopentanone) also permitted the straightforward acquisition of 2-methyl-1,7-dioxaspiro[5 5]undecane (17) and 2-methyl-1,6- dioxaspiro[4 5]decane (16) Thus careful reduction of the ketoaldehydes (4) and (15) with $NaBH_4$ at 0° C provided the unsaturated ketoalcohols which were not characterised, but immediately subjected to the oxymercuration-cyclisation-reduction regimen to provide (16) and (17) which exhibited spectral properties identical with those reported [4,16(b)] In the case of (16), two isomers were formed[4] (*ca* 2 1) (18 and 19), in contrast to (17) for which the (E,E) isomer only (20) was observed (Scheme 3)

"Oxidative demercuration"[22] has found a number of applications in synthesis and these have recently been reviewed [23] In the present context, to test for the possible presence of a hydroxylated derivative (M = 214) of the even carbon numbered spiroacetal, 2-ethyl-8-methyl-1,7-dioxaspiro[5 5]undecane (M = 198) (21) in a *Bactrocera spp*, it was decided to synthesise 8-ethyl-1,7-dioxaspiro[5 5]undecan-2-ylmethanol (22) for comparative purposes It was already known[3] that 8-methyl-1,7-dioxaspiro[5 5]undecan-2-ylmethanol (23) co-occurs with 2,8-dimethyl-1,7-dioxaspiro[5 5]undecane (24) in *B cucumis* (Scheme 4)

2-(Chloromercurimethyl)-8-ethyl-1,7-dioxaspiro[5 5]undecane (25) was available and had been demonstrated[5] to be the (E,E) diastereomer Reductive demercuration cleanly gave (21) [5] In contrast, treatment of (25), dissolved in oxygen-saturated N,N-dimethylformamide (DMF) at 0° C, with $NaBH_4$ resulted in rapid demercuration and gc-ms examination of the product oil showed that in addition to (21) (~50%) another component (~50%), with an apparent M^+ at m/z 214 (5 4) was formed This was thought to be (22) as indicated by ions at m/z 185 ($M^+-C_2H_5$) and 183 (42 4, M^+-CH_2-OH), together with the anticipated spiroacetal fragmentation ions This component was separated (preparative gas chromatography) and its high-field ^{13}C and ^{1}H nmr spectra established it to be a diastereomer of (22), and specifically the (E,E) isomer (26) The ^{13}C spectrum (twelve lines) could be largely assigned by comparisons with the spectra of authentic (E,E) isomers of (21) and (23) In the 400 MHz ^{1}H nmr spectrum, H_{4ax} and H_{10ax} (each a quartet of triplets) appear at δ 1 8-1 95, and these chemical shifts require each of H_{4ax} and H_{10ax} to experience a 1,3-diaxial interaction with oxygen, as present in (26) (Scheme 4) The position (δ 3 5 - δ 3 8) and appearance of the H_{2ax} and H_{8ax} resonances also require an (E,E) configured spiro-bicyclic system This illustration of the use of oxidative demercuration in synthesis of hydroxy-substituted spiroacetals[1] is capable of considerable development, although attempts to utilise other oxidants for the C-Hg bond e g

m-CPBA were not encouraging In syntheses utilising oxidative demercuration, the reduction product is also formed, and generally constitutes 30-50% of the product [23] In some cases, this level of reduction may be unacceptably high, although the reduced compound is easily separated from the desired alcohol

A mercurial-based free radical route to hydroxy-spiroacetal (23) has been developed and is based on free radical addition to acrylonitrile as developed largely by Giese and his collaborators [24] Allyl alcohol was protected (as the benzyl ether), hydroxymercurated in the normal way and the crude product was reduced with $NaBH_4$ in the presence of excess acrylonitrile[11] to provide a two component mixture (Scheme 4) The expected 1-benzyloxy-2-hydroxy-6-hexane-nitrile (27), and the other, a di-addition product (28), were separated by preparative HPLC Given the difficulty of generating oxygen centred radicals from a hydroxyl group under these conditions,[24] it is likely that (28) arises from acrylonitrile acting as an acceptor for addition in both a radical (carbon) and ionic (oxygen) sense Treatment of (27) with two equivalents of 4-pentenylmagnesium bromide in the described manner provided the addition product (74%) as an oil which was not characterised but subjected to hydroxymercuration in the normal way[3] and reduced with $NaBH_4$ to provide (29) as a colourless oil (73%) Hydrogenolysis (H_2, 1 atm, Pd/C) afforded the deprotected product, (23), which exhibited gas chromatographic and mass spectral data identical with those of an authentic sample [3,8,25]

The organomercury-based syntheses described in this report are capable of extension to provide other derivatives of the 1,7-dioxaspiro[5 5]undecane and 1,6-dioxaspiro[4 5]decane systems, which are important constituents of glandular secretions of a wide range of insect types

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EXPERIMENTAL SECTION

Combined gas chromatography-mass spectrometry was conducted with a Hewlett-Packard model 5992B instrument fitted with OV1 or BP5 capillary columns, whereas gas chromatographic analyses were performed using a Hewlett-Packard 5710A gas chromatograph with OV1 or BP5 capillary columns, or a Varian 3700 gas chromatograph with a OV101 capillary column Preparative gas chromatography was performed with a Shimadzu gas chromatograph Model GC-9A equipped with OV101 and C-20M columns Mass spectra refer to gc-ms data, except for accurate mass measurements which were conducted on a Kratos mass spectrometer ^1H nmr spectra were recorded at 400 MHz in the FT mode on a JEOL JNM-GX400 spectrometer Chemical shifts were referenced to internal tetramethylsilane (0 00 ppm) or residual $CHCl_3$ (7 24 ppm) ^{13}C nmr spectra were recorded at 25 05 or 100 MHz and chemical shifts were referenced to the central peak of the solvent ($CDCl_3$) signal at 77 00 ppm

5-Oxo-9-decenal (*4*) was obtained as described in detail elsewhere starting from cyclopentanone [12]

10-Hydroxy-1,12-tridecadien-6-one (*5*) Allyl bromide (0 13 g, 1 1 mmol), zinc (0 07 g, 1 1 mmol) and ketoaldehyde (4) (0 2 g, ~90% pure, 1 0 mmol) were stirred in saturated aqueous ammonium chloride (5 ml) and tetrahydrofuran (1 ml) for about thirty minutes The mixture was extracted into ether and this layer was washed thoroughly with water, dried ($MgSO_4$) and evaporated to yield a yellow oil (~0 2 g, 63%) This was found by gc–ms to be predominantly (5) along with some of the cyclic hemi-ketal *Ir* (*neat, cm*$^{-1}$) 3360 (br, s, O–H), 3070 (w, =CH) 2930 (br, m, C–H), 1710 (s, C=0), 1060 (br, m, C=0) ^{1}*H nmr* ($CDCl_3$) δ 5 78 (2H, m, =CH), 5 17–4 90 (4H, m, = CH_2), 3 62 (1H, m, 0–CH), 2 53–1 99 (8H, m, CH_2, on which was superimposed a singlet from –OH), 1 88–1 10 (6H, m) ^{13}*C nmr* 211 20, 137 90, 134 68, 117 98, 115 114, 70 18, 42 51, 41 84, 36 08, 33 03, 22 74, 19 67, 18 32 *Mass spectrum* 210 (M^+,0), 192 (M–18, 1 6), 151 (6 2), 169 (M–41,1 3), 138 (5 6), 97 (28 5), 81 (14 2), 80 (14 5), 79 (14 0), 69 (12 6), 67 (19 0), 55 (62 5), 53 (18 3), 43 (29 0), 41 (100)

10-Hydroxytrideca-1-en-12-yn-6-one (*3*) was acquired from ketoaldehyde (4) and propargyl bromide in the manner just described for obtaining (5) The ^{13}C nmr spectrum of the total product indicated essentially one component, other than residual solvent (ether, THF) and a little unreacted propargyl bromide *IR* (neat, cm^{-1}) 3350 (br, m, OH), 3260 (w, ≡CH), 3050, 2910, 1710 (s, C=0), 1630 (m, C=C), 1060 ^{1}*H nmr* 5 78 (1H, m, = CH), 4 98 (2H, m, =CH_2), 3 74 (1H, m, CHOH), 2 48–2 29 (5H, m, CH_2 and ≡CH), 2 06 (2H, m, CH_2) (OH superimposed), 1 80–1 32 (8H, m) ^{13}*C nmr* 211 03, 137 90, 115 20, 80 74, 70 80, 69 45, 42 37, 41 87, 35 52, 33 06, 27 33, 22 77, 19 83 *Mass Spectrum* 208 (M^+,0), 190 (M–18, 1 2), 169 (2 5), 151 (3 1), 149 (4 0), 136 (8 0), 133 (5 6), 125 (8 2), 108 (19 5), 99 (11 8), 97 (39 5), 94 (13 8), 93 (20 9), 79 (27 1), 77 (15 2), 71 (17 2), 69 (34 7), 55 (93 8), 53 (15 9), 43 (45 5), 41 (100)

2-(2'-Hydroxypropyl)-8-methyl-1,7-dioxaspiro[5 5]undecane (*6*) *and 2-(2'-propenyl)-8-methyl-1,7-dioxaspiro[5 5]undecane* (*7*) Hydroxydienone (5) was subjected to the standard hydroxymercuration–cyclisation–reduction routine (with $NaBH_4$) that has been described in detail elsewhere [3,6] Standard work-up and gc–ms examination of the crude total product indicated the presence of three isomers of (7) (40%, 4% and 3% of the mixture), with a low level of the alcohol (6) The crude product was taken and hydrogenated (H_2, 1 atm, Pd/C) to provide three isomers of *2-n-propyl-8-methyl-1,7-dioxaspiro[5 5]undecane* (*8*), on the basis of their mass spectra which were in excellent agreement with published spectra [17] *Mass spectrum of* (*8*) 212 (M^+, 9 5), 169 (15 7), 143 (31 2), 142 (16 4), 140 (41 0), 125 (51 1), 115 (97 2), 114 (26 8), 113 (11 7), 112 (83 6), 109 (11 2), 99 (17 2), 97 (69 0), 83 (27 2), 82 (21 9), 81 (10 5), 71 (27 0), 70 (13 6), 69 (35 6), 67 (19 3) The major isomer of (7) was purified by preparative gas chromatography and fully characterised as (9) *Mass spectrum of* (*9*) 210 (M^+, 1 8), 169 (32 4), 141 (23 4), 140 (22 1), 133 (7 9), 125 (18 7), 123 (30 5), 115 (100), 112 (44 7), 99 (22 1), 97 (94 0), 95 (19 0), 83 (13 8), 81 (33 0), 80 (20 6), 79 (18 4), 71 (31 7), 69 (35 4), 67 (22 2), 55 (79 3), 43 (75 4), 42 (44 1), 41 (100)

^1H *nmr* δ 1 03 (3H, d, J ~6 5 Hz, CH_3), 1 03–1 6 (10H, m), δ 1 8 (2H, m), 2 07 (1H, m), 2 09 (1H, m), 3 5 (1H, m), 3 62 (1H, m), 4 97 (2H, m), 5.83 (1H, m) ^{13}C *nmr* 135 64, 116 20, 96 12, 68 81, 65 09, 40 87, 35 42, 32 28, 32 87, 30 85, 21 86, 18 92, 18 83 *Accurate mass* Calcd for $C_{13}H_{22}O_2$ = 210 1619 Observed = 210 1622

Treatment of the hydroxymercuration product of (5) with excess aqueous NaCl, filtration and drying provided a solid, presumably (10), which was not characterised, but reduced with Bu_3SnH in benzene GC–MS examination revealed that alkene (7) was a minor product, and that diastereomers of (6) were formed

(E,E)-2-(2'-hydroxypropyl)-8-methyl-1,7-dioxaspiro[5 5]undecane (11) Preparative gas chromatography provided (11) which was the major diastereomer formed in the above sequence ((11 is a mixture of two diastereomers each having an (E,E) ring skeleton, but epimeric at carbon-2 in the hydroxypropyl group) ^1H *nmr* δ 3 6–4 12 (3H, m, CHO), 1 25–1 92 (ring H), 1 08 and 1 14 (3H, d, J ~6 7 Hz, CH_3's of major isomer), 1 09 and 1 11 (3H, d, J ~6 7 Hz, CH_3's of minor isomer) ^{13}C *nmr* (Major isomer) 96 37, 68 49, 65 59, 65 53, 43 45, 35 34, 35 09, 31 53, 30 45, 23 63, 21 80, 19 14, 18 66 (Minor isomer) 96 48, 71 29, 67 19, 64 98, 44 21, 35 40, 34 56, 32 59, 32 30, 23 37, 21 85, 18 96, 18 32 *Mass spectrum* 228 (M^+,0), 169 (4 7), 159 (4 7), 141 (21 6), 140 (15 2), 128 (4 6), 125 (10 5), 123 (17 3), 115 (100), 114 (17 3), 113 (11 1), 112 (59 0), 99 (15 9), 98 (10 7), 97 (40 5), 96 (8 8), 95 (16 3), 84 (12 0), 83 (13 7), 81 (18 2), 71 (18 3), 69 (28 3), 58 (14 6), 55 (52 0), 45 (32 2)

(E,Z) and (Z,E)-2-(2'-hydroxypropyl)-8-methyl-1,7-dioxaspiro[5 5]undecanes (12) and (13) were obtained as a mixture, with two isomers of each epimeric at C-2' in the hydroxypropyl group ^1H *nmr* was quite complex with a cluster of CH_3 doublets (J ~6 5 Hz) δ 1 05–1 2 (6H), 1 00–2 00 (ring H + OH), 3 6–4 35 (3H, m, CHO) ^{13}C *nmr* of the fifty-two signals required forty-five were resolved 98 43, 98 07, 97 46, 97 13 (spiro c's), 74 63, 71 30, 70 03, 68 77, 68 69, 68 35, 68 08, 67 19, 67 08, 66 65, 64 79, 64 67 (*C*-O), 44 64, 44 55, 44 24, 43 30, 32 99, 32 74, 32 18, 32 03, 31 34, 31 46 30 88, 30 34, 29 76, 29 49, 27 67, 23 80, 23 45, 23 37, 23 21, 22 14, 20 21, 19 92, 19 25, 19 06, 18 98, 18 41, 18 32, 18 22, 18 03 *Mass spectrum* 228 (M^+, <1), 213 ($M-CH_3$, <1), 169 (11 4), 159 (17 5), 158 (14 7), 141 (56 6), 140 (25 4), 125 (14 2), 123 (49 0), 115 (100), 114 (18 3), 113 (9 5), 112 (35 5), 99 (22 2), 98 (11 3), 97 (50 3), 95 (24 0), 83 (10 5), 81 (27 4), 73 (10 6), 71 (19 4), 69 (36 0), 45 (46 1)

2-(2'-Oxopropyl)-8-methyl-1,7-dioxaspiro[5 5]undecane (2) Crude (3) (~100 mg, 0 26 mmol) was dissolved in tetrahydrofuran 1% aqueous $HClO_4$ (1 1, 2 ml) and mercuric acetate (0 18 g, 0 57 mmol) was added After stirring for *ca* 5 hours, the mixture was cooled in ice, and dichloromethane (2 ml), benzyltriethylammonium chloride (0 30 g, 1 mmol), and sodium borohydride (0 20 g, 0 53 mmol) were added The mixture stirred (*ca* 5 min) and worked up in the normal way to provide an oil (~0 07 g) GC–MS analysis indicated that the oil consisted of three diastereomers of (2) (63%, 9%, 9%) Preparative gas chromatography provided the major isomer in pure form (14)

(E,E)-(2'-Oxopropyl)-8-methyl-1,7-dioxaspiro[5 5]undecane (14) I r 1712 (C=O) ^1H *nmr* 1 12

(3H, d, J = 6 4 Hz, CH_3), 2 19 (3H, s, CH_3CO), 1 1–2 0 (series of m, ring H), 2 35 and 2 63 (2H, "AB" part of ABX, J = 14 6, 4 1, 8 7 Hz, CH_2CO), 3 67 (1H, m, CHO), 4 05 (1H, m, CHO) ^{13}C *nmr* 207 93, 96 18, 66 30, 65 32, 49 89, 35 26, 35 17, 32 68, 31 73, 31 08, 21 83, 18 95, 18 61 *Mass spectrum* 226 (M^+, <1), 208 (3 4), 182 (1 1), 169 (2 0), 157 (4 8), 139 (6 6), 125 (6 1), 115 (27 7), 113 (7 8), 112 (39 4), 97 (39 7), 96 (18 2), 84 (9 4), 69 (17 1), 58 (8 7), 55 (26 8), 43 (100), 41 (30 4) *Accurate mass* Calcd for $C_{13}H_{22}O_3$ = 226 1569 Observed = 226 1573

2-Methyl-1,6-dioxaspiro[4 5]decane (16) was obtained as a mixture of the two isomers (18) and (19) by selective reduction of unsaturated ketoaldehyde (15) to yield the unsaturated hydroxyketone which was not isolated but immediately subjected to hydroxymercuration–cyclisation reduction in the reported way to provide (18) and (19) Spiroacetals (18) and (19) were characterised by their mass spectra which were in excellent agreement with those described [4,16] *Mass spectrum* 156 (M, 5 5), 141 (4 7), 128 (5 4), 112 (12 1), 111 (11 3), 101 (100), 100 (37 8), 98 (44), 85 (11 6), 83 (52 9), 59 (10 4), 57 (19 7), 56 (40 4), 55 (62 4)

2-Methyl-1,7-dioxaspiro[5 5]undecane (17) was produced essentially as (*E,E*) diastereomer (20), starting with ketoaldehyde (4), and using the procedure just described for acquiring spiroacetal (16) ^1H *nmr* 1 13 (3H, d, J ~6 3 Hz, CH_3), 1 1–1 65 (m, ring protons), 1 75–1 9 (2H, m, $1H_{4ax}$, H_{10ax}), 3 5–3 76 (3H, CHO) ^{13}C *nmr* 18 59, 18 91, 21 82, 25 43, 32 70, 35 09, 35 85, 60 28, 65 15, 95 60 *Mass spectrum* [26] 170 (M^+, 13 6), 155 (13 5), 126 (12 2), 125 (8 5), 115 (27 2), 114 (13 0), 112 (36 6), 111 (17 8), 101 (86 9), 100 (17 8), 98 (100), 97 (23), 83 (41 9), 69 (28), 55 (53) *Accurate mass* Calcd for $C_{10}H_{18}O_2$ = 170 1308 Observed = 170 1307

(E,E)-8-Ethyl-1,7-dioxaspiro[5 5]undecan-2-ylmethanol (26) Mercurial (25), fully described elsewhere,[5] was dissolved in oxygen-saturated DMF (0 05 g, 1 15 mmol in 30 ml) (~0° C) and to this solution was added dropwise a solution of $NaBH_4$ (66 mg in 30 ml of DMF) After *ca* thirty minutes, ether was added and the solution filtered through Celite (to remove mercury) The solution was concentrated and gc–ms examination showed the presence of two products (*ca* 50 50), with one being the known[3,4] *2-ethyl-8-methyl-1,7-dioxaspiro[5 5]undecane* (21), and the other exhibiting a mass spectrum appropriate for (22) This component was separated by preparative gas chromatography and shown to be the (E,E) diastereomer (26) ^1H *nmr* δ 0 96 (3H, t, J = 7 3 Hz, CH_3), 1 1–1 65 (9H, m), 1 8–2 15 (m, 3H including OH), 3 43–3 8 (series of m, 4H, CHO) ^{13}C *nmr* 10 29, 18 24, 18 94, 26 63, 29 26, 30 80, 35 33, 35 65, 66 37, 69 52, 70 53, 95 85 *Mass spectrum* 214 (M^+, 5 4), 185 (3 6, $M-C_2H_5$), 183 (42 4, $M-CH_2OH$), 156 (9 1), 139 (14 9), 131 (43 0), 130 (25 8), 129 (58 6), 128 (53 7), 126 (11 5), 121 (11 3), 113 (57 6), 111 (35 3), 99 (37 6), 97 (38 7), 95 (17 8), 87 (11 8), 85 (13 2), 84 (10 6), 83 (30 8), 81 (12 2), 71 (40 9), 70 (33 6), 69 (32 5), 68 (21 6), 67 (42 1), 58 (12 1), 57 (33 1), 55 (80 8), 53 (12 1), 43 (65 5), 42 (27 1), 41 (100)

8-Methyl-1,7-dioxaspiro[5 5]undecan-2-ylmethanol (23) 3-Benzyloxy-1- propene (from allyl alcohol and benzylbromide) was oxymercurated in the normal manner and reduced ($NaBH_4$) in

the presence of excess acrylonitrile The crude product (2 55 g) was purified by Kugelrohr distillation (165°C, (oven), 1 mm) and then filtration through silica gel (Kieselgel 60, 70–230 mesh) with dichloromethane to give the product as a mixture of two components (1 94 g, 44%) The required compound (27) was contaminated with the O–diaddition product (28), but these were separated by HPLC (silica with 3 2 hexane ethyl acetate) (27) ^1H *nmr* 7 32 (5H, m, Ar–*H*), 4 52 (2H, s, ArCH_2), 3 78 (1H, m, C*H*OH), 3 47 and 3 32 (2H, "AB" part of ABX pattern, J = 9 40, 3 22, 7 52 Hz), 2 49 (1H, br d, J = 3 Hz, OH), 2 37 (2H, m), 1 53–1 81 (4H, m) ^{13}C *nmr* 17 05, 21 71, 31 72, 69 50, 73 40, 74 25, 119 55, 127 74 (2C), 127 87, 128 47 (2C), 137 70 *Mass spectrum* 219 (M^+, 13 2), 107 (17 8), 105 (6 3), 98 (27 8), 93 (6 2), 92 (66 1), 91 (100), 65 (14 4), 55 (16 4), 54 (10 3) *Accurate mass* Calcd for $C_{13}H_{17}NO_2$ = 219 1265 Observed = 219 1259 The additional product (28) was also characterized (28) ^1H *nmr* 7 24 (5H, m, Ar*H*), 4 45 (2H, s, ArCH_2), 3 5–3 8 (3H, m), 3 41 (2H, dd), 2 48 (2H, m), 2 29 (2H, m), 1 68 (2H, m), 1 49 (2H, m) ^{13}C *nmr* 16 97, 19 14, 21 22, 30 60, 64 79, 72 43, 73 27, 78 44, 117 92, 119 42, 127 49(2C), 127 61, 128 28(2C), 137 71 *Mass spectrum* 272 (M^+, 0), 107 (14 8), 106 (95 3), 105 (96 4), 91 (13 2), 78 (19 1), 77 (100), 74 (9 6), 51 (48 4), 50 (27 7) *Accurate mass* Calcd for $C_{16}H_{20}N_2O_2$ + H = 273 1608 Observed = 273 1603

Nitrile (27) (0 849, 0 38 mmol) in anhydrous THF (5 ml) was added dropwise to a solution of pent–4–enylmagnesium bromide prepared from magnesium (0 037 g, 1 53 mmol) and pent–4–enylbromide (0 274 g, 1 82 mmol) in anhydrous THF (5 ml) This reaction mixture was refluxed for twelve hours and then poured into saturated NH_4Cl solution (10 ml) which was extracted with ether The combined extracts were dried ($MgSO_4$) and evaporated to give an oil (0 84 g, 74%) which was dissolved in THF and 1% aqueous $HClO_4$ (10 ml, 1 1) and treated with mercuric acetate (0 11 g, 0 35 mmol, 1 2 equiv) After stirring for two hours, the solution was demercurated with $NaBH_4$ in the normal way, and then filtered (Celite) and extracted with ether A colourless oil was obtained (0 061 g, 73%) which showed ^1H nmr and low resolution mass spectra corresponding to spiroacetal (29) ^1H *nmr* 7 35 (5H, m, Ar*H*), 4 56 (2H, s, $ArCH_2$) 3 75 (2H, m), 3 49 (1H, m), 3 47 (1H, m), 1 91 (2H, m), 1 59 (5H, m), 1 2–1 45 (5H, m), 1 13 (3H, d, J = 6 2, CH_3) *Mass spectrum* 290 (M^+, 0), 169 ($M-CH_2OCH_2C_6H_5$, 13 6), 125 (8 9), 115 (7 2), 112 (12 3), 91 (100), 77 (12 3), 55 (27 4), 43 (28 3), 41 (32 2) Compound (29) (0 061 g, 0 21 mmol) was dissolved in distilled methanol (5 ml) to which was added 5% Pd/C (0 010 g) This solution was stirred under hydrogen (1 atm) for one hour before filtration through Celite The methanol was removed (reduced pressure) to yield the title spiroacetal (23) (0 035 g, 72%) which displayed a mass spectrum and gc behaviour identical with those of an authentic sample [3,18,25] *Mass spectrum* 200 (M^+, 7 0), 169 (M^+-CH_2-OH, 21 7), 131 (28 1), 130 (17 5), 128 (18 8), 125 (25 4), 115 (51 9), 112 (23 9), 97 (67 8), 71 (44 4), 43 (87 9), 41 (100)

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