Novel synthesis of degradation products of carotenoids, megastigmatrienone analogues and blumenol-A

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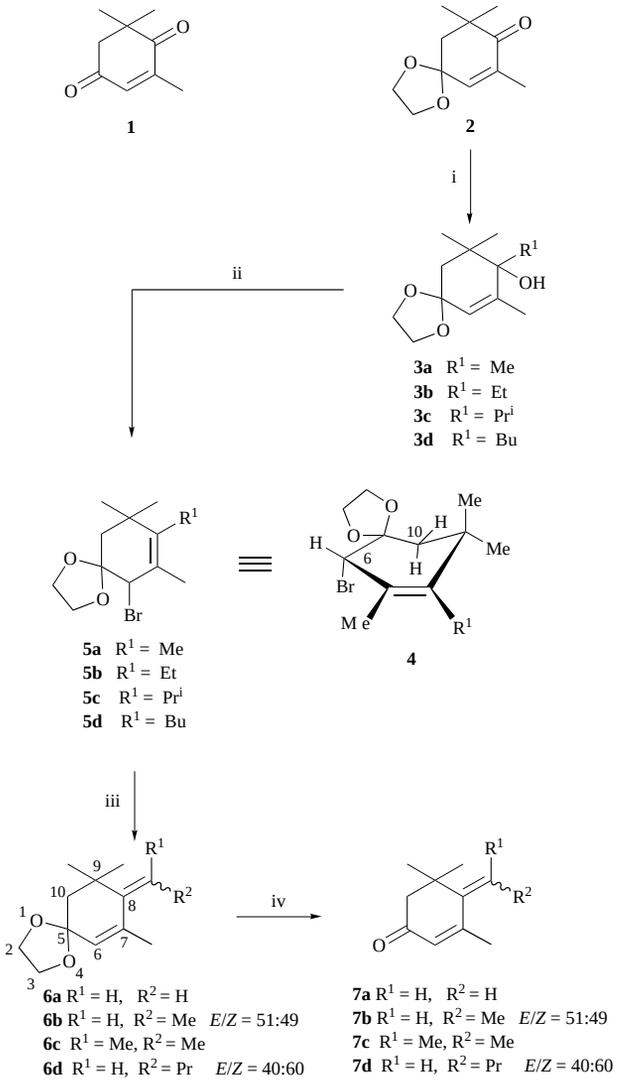
Synthesis of 4-alkylidene-3,5,5-trimethylcyclohex-2-enones 7 has been achieved utilising 1,4-conjugate dehydrobromination of allylic bromides 5 as a key step. This chemical transformation is applied to the synthesis of degradation products of carotenoids: megastigmatrienones 7e/1–4, 4-methylene-3,5,5-trimethylcyclohex-2-enone 7a, 4-(3-hydroxybutylidene)-3,5,5-trimethylcyclohex-2-enone 9, 1,3,7,7-tetramethyl-2-oxabicyclo[4.4.0]dec-5-en-9-one 10a–b and 3,4,7,8-tetrahydro-4,4,7-trimethylnaphthalen-2(6*H*)-one 15. A novel photoisomerisation of 4-[(*Z*)-3-acetoxybut-2-enyl]-4-hydroxy-3,5,5-trimethylcyclohex-2-enone 19 to 4-[(*E*)-3-acetoxybut-2-enyl]-4-hydroxy-3,5,5-trimethylcyclohex-2-enone 20 enables us to synthesise blumenol-A 21.

A large number of C_{13} degradation products of carotenoids have been isolated from various essential oils, black tea, and tobaccos. They are considered to be produced biogenetically by oxidative cleavage of conjugated double bonds of cyclic carotenoids;[1] for example lutein which is well-known as a colouring substance. Most C_{13} compounds commonly possess a carbonyl function at the C-3 position in the trimethylcyclohexane ring. Although they usually exist as minor flavour and fragrance components in essential oils, their importance has been well recognised. Megastigmatrienones **7e**/**1–4**, the C_{13} degradation product of carotenoids possessing a 4-alkylidene-3,5,5-trimethylcyclohex-2-enone skeleton, and blumenol-A **21** are known as key tobacco flavouring components.[2]

We report here a general and efficient synthesis of 4-alkylidene-3,5,5-trimethylcyclohex-2-enones **7**[3] utilising 1,4-conjugate dehydrobromination of the allylic bromides **5** and its application to the synthesis of degradation products, *i.e.* megastigmatrienones **7e**/**1–4**,[4–7] 4-methylene-3,5,5-trimethylcyclohex-2-enones **7a**,[8,9] 4-(3-hydroxybutylidene)-3,5,5-trimethylcyclohex-2-enone **9**,[10] 1,3,7,7-tetramethyl-2-oxabicyclo[4.4.0]dec-5-en-9-one **10a–b**[11,21] and 3,4,7,8-tetrahydro-4,4,7-trimethylnaphthalen-2(6*H*)-one **15**.[12] The synthesis of blumenol-A **21**[13] by photoisomerisation of the (*Z*)-olefin to the (*E*)-olefin is also reported.

Results and discussion

3,5,5-Trimethylcyclohex-2-ene-1,4-dione (oxophorone) **1** has been frequently used as the starting material in the synthesis of cyclic carotenoids[14] and flavouring components.[6,15,16] Recently, we have reported the practical preparation of oxophorone **1** from 3,5,5-trimethylcyclohex-3-enone by transition metal complex-catalysed molecular oxygen oxidation.[17] In the present study, we employed oxophorone **1** as the common starting material. Reactions of several alkyllithium compounds with keto acetal **2**, readily obtainable from oxophorone **1** according to the procedure by Shibagaki *et al.*,[16] afforded cyclohexenols **3** (42–92%) (Scheme 1). Bromination of the cyclohexenols **3** with phosphorus tribromide (PBr_3) in pyridine and toluene proceeded by displacement of the hydroxy group with a bromine atom together with a double-bond migration to give the allylic bromides **5**. Of these, the cyclohexenol **3a** provided a mixture of the allylic bromide **5a** and the dehydrobromination product the dienone **6a** in a 1:1 ratio as the result of an S_N2' reaction pathway. The stereochemistry of the allylic bromides **5** was determined from ^{1}H NMR analysis, *i.e.* the equatorial methine proton (δ 4.3, d, J 3 Hz) at the C-6 position couples to the equatorial proton at the C-10 position in a W coupling fashion. The axial proton at the C-10 position appeared at lower field than the equatorial one ($\Delta\delta = 0.9$ ppm) owing to the 1,3-diaxial relationship with the bromine atom. The bromides **5** were subjected to subsequent dehydrobromination without further purification because of their instability to heat. Although numerous methodologies to achieve dehydrobromination have been reported, little is known about 1,4-conjugate dehydrobromination.[18] Attempted dehydrobromination of the allylic bromides **5** with potassium *tert*-butoxide in dimethyl sulfoxide (DMSO) or triethylamine failed. However, the 1,4-conjugate dehydrobromination was accomplished upon treatment with a stoichiometric amount of 1,8-diazabicyclo[4.3.0]undec-7-ene (DBU) in refluxing toluene for 5 h, thus affording the dienes **6** (49–60%). Under the same reaction conditions, the bromide **5c** behaved exceptionally and was recovered unchanged. The desired diene **6c** was, however, obtained (20% yield), when the bromide **5c** was heated at 120 °C for 2 h. Both the stereostructures and the ratio of the dienes **6b** and **6d** were confirmed by inspection of their ^{1}H NMR spectra. Aasen *et al.* reported[4] that for megastigmatrienone **7e**/**1**, which possesses a (4*Z*)-double bond, the *gem*-dimethyl and the vinylmethyl signals appear at higher field by 0.16 ppm and at lower field by 0.21 ppm, respectively, than those for the (4*E*)-isomer **7e**/**4** (Scheme 2). This fact was useful for assignment of stereochemistry to the dienes **6b** and **6d**, the ratios for the geometrical isomers of which are shown in Scheme 1. Hydrolysis of the dienes **6** with aqueous hydrochloric acid in THF provided the dienones **7** (81–92%); compounds **7a** and **7e** are natural products.[5,8] Compound **7a** was used as an intermediate for a diterpenoid synthesis.[9] Since we had succeeded in constructing an extended α,β,γ,δ-unsaturated ketone system by use of a novel 1,4-conjugate dehydrobromination, we next focused our attention on the synthesis of C_{13} degradation products of carotenoids.



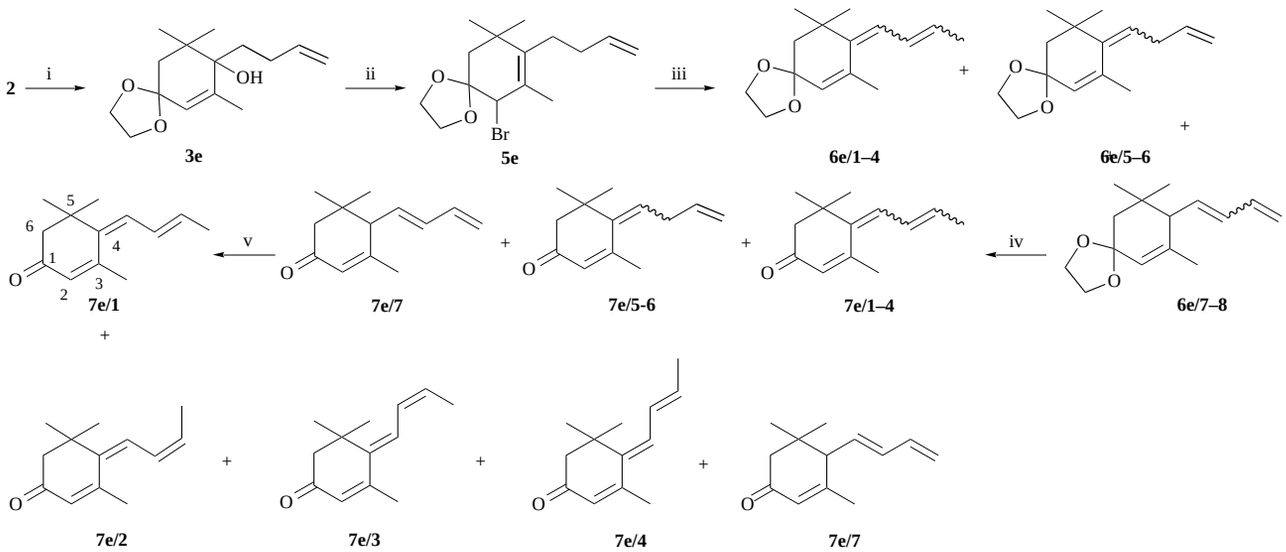
Scheme 1 *Reagents and conditions:* i, R^1Cl or R^1Br, Li, THF; ii, PBr_3, pyridine, toluene, −10 °C, 1 h; iii, DBU, toluene, reflux, 5 h; iv, aq. HCl, THF, 25 °C

Reaction of the keto acetal **2** with but-1-enyllithium prepared from lithium metal and 4-bromobut-1-ene afforded the cyclohexenol **3e** (80%), which was then converted into the allylic bromide **5e** with PBr_3. Treatment of **5e** with DBU in refluxing toluene afforded a mixture of deconjugated trienes **6e**/**5**–**8** and fully conjugated trienes **6e**/**1–4** in 60% yield. Presumably, the trienes **6e**/**5**–**6** are the initial products, and the trienes **6e**/**1**–**4** and **6e**/**7**–**8** could be formed from **6e**/**5**–**6** by DBU-catalysed migration of the terminal and exocyclic double bonds, respectively. The mixture of trienes **6e** was deprotected with aqueous hydrochloric acid in THF, to give a mixture of the trienones **7e** (82%). Both trienes **6e** and enones **7e** were obtainable as a mixture of geometrical isomers, as a result of the double bonds in the side chain, which we were unable to separate by silica gel chromatography; thus we used capillary gas chromatography to separate the isomers and determine the product ratios. The geometrical stereostructures present, however, remained uncharacterized (see Experimental section). The geometry of the trienones **7e** were confirmed by GC–FT/IR–MS, wherein the absorption bands at 910 and 990 cm^{-1} were assigned to the terminal allylic olefin and the α,β,γ,δ-unsaturated ketone, respectively. When a mixture of the trienones **7e** was heated in refluxing xylene in the presence of a catalytic amount of DBU for 4 h, an equilibrium of double bond isomers was attained and gave a mixture of megastigmatrienones **7e**/**1**–**4**[4–7] and **7e**/**7**[4] in 86% yield. These five isomers, all of which occur in nature, were detected by capillary gas chromatography, and isolated by repeated silica gel chromatography (Scheme 2). The spectral data (IR and ^{1}H NMR) for **7e**/**1**–**4** and **7e**/**7** were identical with those described in the literature.[4]

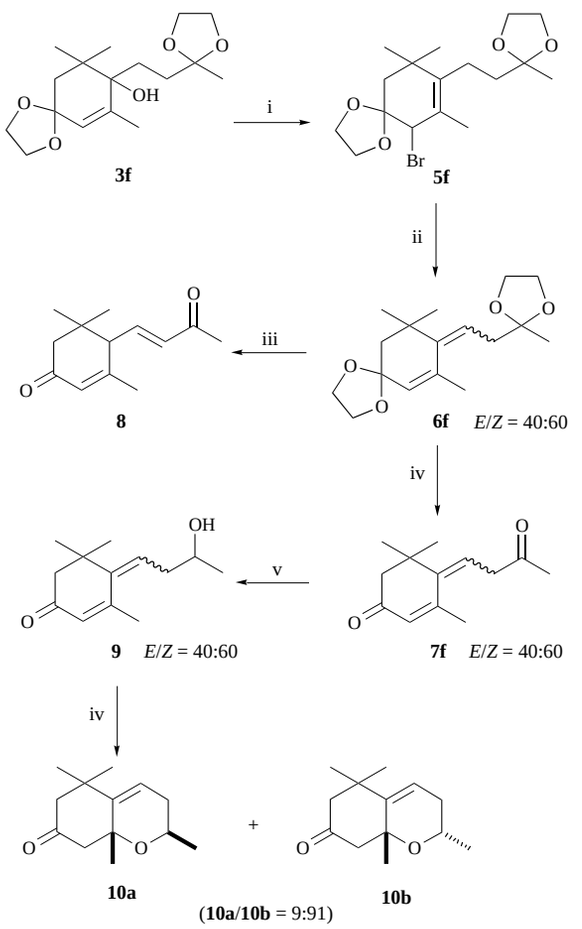
Treatment of the diacetal **3f**, readily obtainable from **2** by the published procedure,[16] with PBr_3 under our standard conditions afforded the allylic bromide **5f**, which was transformed into the dienes **6f** (49%) with DBU in refluxing toluene. Treatment of the diene **6f** with aqueous hydrochloric acid in THF at room temperature gave 3-oxo-α-ionone **8**[20] as the major product as a result of hydrolysis of the acetal groups and concomitant olefin migration of the initial product, the diketone **7f**. The diketone **7f** was obtained in 70% yield by treatment of the diene **6f** with silica gel impregnated with aqueous 37% H_2SO_4 in CH_2Cl_2 at room temperature. Chemoselective reduction of the diketone **7f** with zinc borohydride [$Zn(BH_4)_2$] provided the ketol **9**[10] (69%). Finally, treatment of the compound **9** with NaH afforded a diastereoisomeric mixture (a 1:9 ratio) of the bicyclic compounds **10a**–**b**[21] (48%). The compounds, **9** and **10a,b**, are natural products isolated from essential oil[22] and tobaccos[11] (Scheme 3).

Starting with the cyclohexenol **3a** an alternative synthesis of the dienone **7a** was carried out. Deprotection of **3a** provided hydroxy ketone **11a** (Scheme 4), bromination of which followed by dehydrobromination under our standard reaction conditions, afforded the dienone **7a** (27%). Alternatively, treatment of **11a** with PBr_3 and DBU in chloroform at room temperature for 2 h resulted in its one-pot conversion into **7a** (59%). Unfortunately, attempted conversion of other hydroxy ketones, derived from **3b**–**d** and aqueous hydrochloric acid, into the corresponding enones **7b**–**d** using the above PBr_3–DBU–$CHCl_3$ reagent failed; such reactions gave only a complex mixture of products. However, it is noteworthy that this one-pot bromination—dehydrobromination was successful in the synthesis of the tetrahydronaphthalenone **15**, a compound isolated from tobacco, and known as a key flavouring component.[12] An earlier synthesis of this was reported, but with less satisfactory results in terms of product purity.[12] Our synthesis started from hydroxy diketone **12**,[16] obtained from hydrolysis of the diacetal **3f**, in which an intramolecular vinylogous aldol condensation followed by dehydration afforded the hydroxy dienone **13** (70%). Regioselective hydrogenation of the γ,δ-olefin of **13** using 5% Pd–C in methanol in the presence of a catalytic amount of KOH gave the hydroxy enone **14** (78%) which, upon treatment with PBr_3 and DBU in $CHCl_3$, provided tetrahydronaphthalenone **15** (69%).

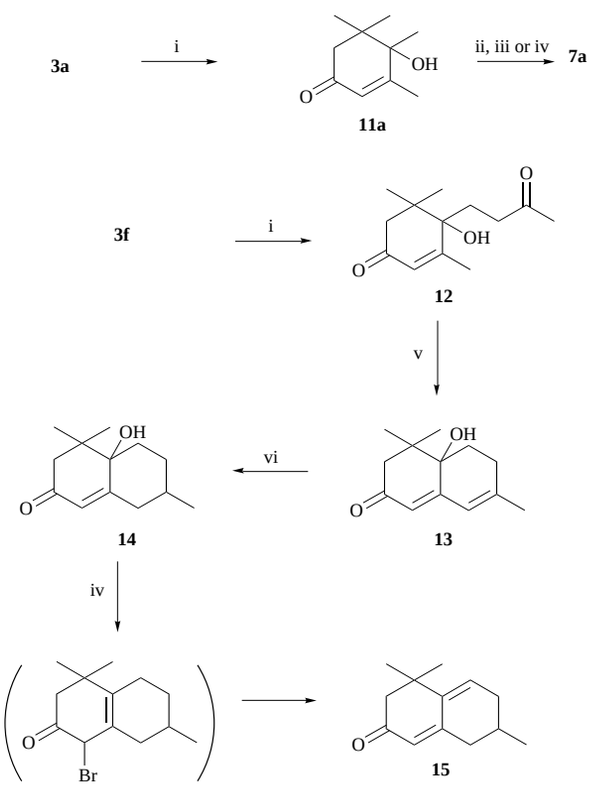
Finally, we turned our attention to the synthesis of blumenol-A **21**.[13] This natural product was isolated as a minor component from several natural sources,[19,23] and is well-known as both an endogeneous regulator of stomatal aperture[24] and a flavouring component[2] of tobacco. In this study the acetylenic alcohol **16**, obtainable from the keto acetal **2** by a published procedure,[6,21] was adopted as the starting material (Scheme 5). After acetylation (92%) of **16**, stereoselective hydrogenation of the resulting acetylene **17** to the (*Z*)-olefin **18** was accomplished in 70% yield using the Lindlar catalyst under a hydrogen atmosphere. Hydrolysis of **18** provided the (*Z*)-olefinic ketone **19** (84%). Attempted isomerisation of the (*Z*)-olefinic ketone **19** to the (*E*)-olefinic ketone **20** using toluene-*p*-sulfinic acid[25] and Pt–Al_2O_3[26] gave a mixture of products, from which the desired (*E*)-olefinic ketone **20** was absent. However, when a methanolic solution of **19** was irradiated with a mercury high-pressure immersion lamp (100 W) through a Pyrex filter at 20 °C for 4.5 h, the (*E*)-olefinic ketone **20** was isolated (75%) along with the rearranged product **22**[27] (12%). It is noteworthy that the present photoisomerisation in the absence of a sensitizer gave a high proportion of (*E*)-olefinic ketone **20** (**20**/**19** = 97:3). Compound **20** was transformed into blumenol-A **21** (85%) upon treatment with NaOMe in methanol and $CHCl_3$. The photochemical isomerisation of **19**



Scheme 2 *Reagents and conditions:* i, 4-bromobut-1-ene, Li, THF, room temperature; ii, PBr_3, pyridine, toluene, −10 °C, 1 h; iii, DBU, toluene, reflux, 5 h; iv, aq. HCl, THF, 25 °C; v, DBU, xylene, reflux, 4 h



Scheme 3 *Reagents and conditions:* i, PBr_3, pyridine, toluene, −10 °C, 1 h; ii, DBU, toluene, reflux, 5 h; iii, aq. HCl, THF, 25 °C; iv, 37% H_2SO_4 on silica gel, CH_2Cl_2, 25 °C, 2.5 h; v, $Zn(BH_4)_2$, THF, diethylene glycol dimethyl ether; vi, NaH, benzene, room temperature, 40 h



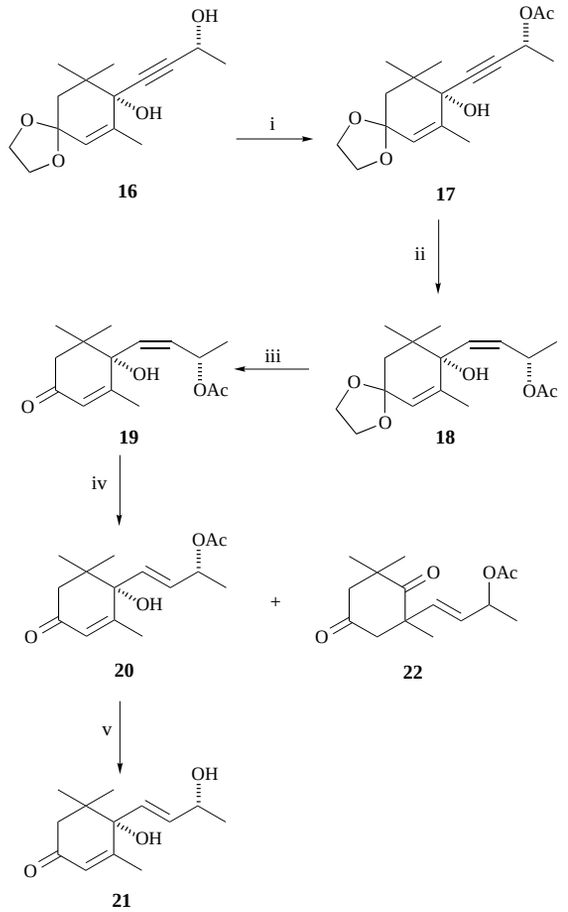
Scheme 4 *Reagents and conditions:* i, HCl, THF, room temperature; ii, PBr_3, pyridine, toluene, −10 °C, 1 h; iii, DBU, toluene, reflux, 5 h; iv, PBr_3, DBU, $CHCl_3$, 25 °C, 2 h; v, NaOH, MeOH; vi, H_2, Pd–C, KOH, MeOH

to **20** and formation of **22** is believed to occur *via* a cyclopropylmethyl radical intermediate (see Scheme 6).

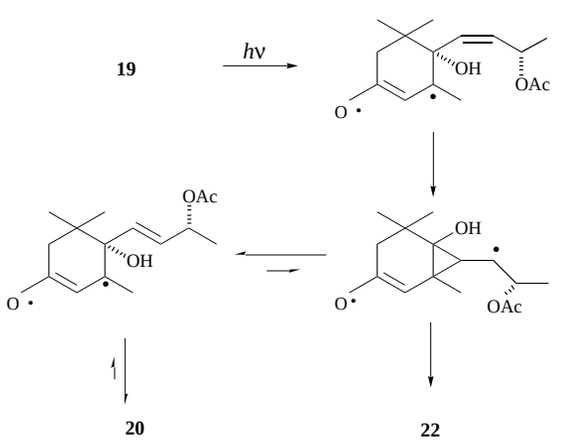
In summary, we have induced 1,4-conjugate dehydrobromination of allylic bromides **5** with DBU to afford 4-alkylidene-3,5,5-trimethylcyclohex-2-enones **7**. This preparative method was applied to the synthesis of several C_{13} degradation products of carotenoids, megastigmatrienones **7e**/**1**–**4**, 4-(3-hydroxybutylidene)-3,5,5-trimethylcyclohex-2-enone **9**, 1,3,7,7-tetramethyl-2-oxabicyclo[4.4.0]dec-5-en-9-one **10a**–**b**, and 3,4,7,8-tetrahydro-4,4,7-trimethylnaphthalen-2(6*H*)-one **15**. Photoisomerisation of the (*Z*)-olefin to the (*E*)-olefin was successfully applied to the synthesis of blumenol-A from the acetylenic alcohol **16**.

Experimental

All mps were determined with a Mettler FP62 hot-stage apparatus and are uncorrected. IR spectra were recorded on a



Scheme 5 *Reagents and conditions:* i, Ac_2O, pyridine, 12 h; ii, H_2, Lindlar cat., 20 °C; iii, aq. HCl, THF, room temperature, 5 h; iv, *hν*, MeOH, 20 °C, 4.5 h; v, NaOMe, MeOH, $CHCl_3$, room temperature, 6 h



Scheme 6

JASCO FT/IR-7000 spectrophotometer and a Hewlett Packard 59970 Chem. Station. ^{1}H NMR spectra were recorded on JEOL LA-400 (400 MHz), Varian (300 MHz), Varian (100 MHz) and Hitachi R-24B (60 MHz) spectrometers. *J* Values are given in Hz. Mass spectra were run on a Hewlett Packard 5992B, Hitachi M-80B with a Hitachi MO101 data system, and Hitachi M-4100 with a Hewlett Packard A 4032A data system, with or without a capillary gas chromatographic column. Capillary gas chromatographic analyses were carried out on Shimadzu GC-7A and Hewlett Packard 5890 series II instrument. THF, pyridine, chloroform, benzene, and toluene were used after drying with 4Å molecular sieves, 80–100 mesh. Extracts obtained on aqueous work-up of the reaction mixtures were washed with brine and dried (Na_2SO_4), unless otherwise stated. Identification of the synthetic known compounds and natural products synthesised in the present study was carried out by comparison of their spectral data with those reported in the literature.

7,8,9,9-Tetramethyl-1,4-dioxaspiro[4.5]dec-6-en-8-ol 3a[3]

Into a mixture of the keto acetal **2** (10.0 g, 51.0 mmol) and lithium metal (0.89 g, 128 mmol) in THF (80 cm^3) was bubbled methyl chloride at 10–15 °C until disappearance of the lithium metal; stirring was then continued for 1 h at room temperature. The reaction mixture was quenched by the addition of ice-cold aqueous NH_4Cl after which it was extracted with ethyl acetate. The combined extracts were washed with brine, dried (K_2CO_3) and evaporated. The crystalline residue was recrystallised from hexane to afford the title compound **3a** (9.90 g, 92%), mp 97–98 °C (lit.,[3] 94 °C); ν_{max}(KBr)/cm^{-1} 3500 (OH) and 1675 (C=C); δ_H(60 MHz) 0.98 (3 H, s, 9-Me), 1.04 (3 H, s, 9-Me), 1.22 (3 H, s, 8-Me), 1.44 (1 H, s, OH), 1.76 (2 H, s, 10-H_2),1.80 (3 H, d, *J* 2, 7-Me), 3.89 (4 H, s, OCH_2CH_2O), and 5.30 (1 H, br s, 6-H); *m/z* 197 (M^+ − Me, 12%), 156 (100), 126 (39), 113 (33), 112 (34), 111 (41), 87 (66), 69 (34), 43 (97) and 41 (36).

Representative procedure for the preparation of cyclohexenols 3b–d from the keto acetal 2

8-Ethyl-7,9,9-trimethyl-1,4-dioxaspiro[4.5]dec-6-en-8-ol 3b.[3] To a stirred mixture of small pieces of lithium metal (1.05 g, 151 mmol) in THF (80 cm^3) was added dropwise a solution of ethyl bromide (7.89 g, 72.4 mmol) and the keto acetal **2** (10.0 mg, 51.0 mmol) in THF (10 cm^3) under nitrogen at room temperature. Stirring was continued for 3 h after which the reaction mixture was quenched by addition to it of ice-cold aqueous NH_4Cl and then extracted with ethyl acetate. Evaporation of the extract left crystals which were recrystallised from hexane to give the title compound **3b** (8.44 g, 73%), mp 79–80 °C; ν_{max}(KBr)/cm^{-1} 3475 (OH), 2980 (C–H), 1660 (C=C) and 1090(C–O); δ_H(60 MHz) 0.93 (3 H, t, *J* 8, CH_2*Me*), 0.99 (3 H, s, 9-Me), 1.08 (3 H, s, 9-Me), 1.41 (1 H, s, OH), 1.80 (3 H, d, *J* 2, 7-Me), 1.56–2.25 (4 H, m), 3.92 (4 H, s, OCH_2CH_2O) and 5.40 (1 H, m, 6-H).

8-Isopropyl-7,9,9-trimethyl-1,4-dioxaspiro[4.5]dec-6-en-8-ol 3c. The reaction of lithium metal (1.76 g, 254 mmol) in THF (121 cm^3) with isopropyl bromide (15.0 g, 122 mmol) and the keto acetal **2** (16.79 mg, 85.7 mmol) in THF (16 cm^3) followed by purification of the crude product by chromatography on silica gel with ethyl acetate–hexane (1:4) gave the title compound **3c** (8.13 g, 42%), mp 45–47 °C; ν_{max}(KBr)/cm^{-1} 3459 (OH), 2952 (CH), 1657 (C=C) and 1084 (C–O); δ_H(60 MHz) 1.05 (6 H, d, *J* 9, 2 × CH*Me*), 1.01 (3 H, s, 9-Me), 1.08 (3 H, s, 9-Me), 1.49 (1 H, s, OH), 1.63 [1 H, d (of AB q), *J* 15, 10-H], 1.80 (3 H, d, *J* 2, 7-Me), 2.18 [1 H, d (of AB q), *J* 15, 10-H], 3.92 (4 H, m, OCH_2CH_2O) and 5.42 (1 H, m, 6-H); *m/z* 240 (M^+, 0.1%), 197 (100), 153 (25), 125 (25), 111 (28), 73 (41) and 43 (52) (Found: M^+, 240.1737. $C_{14}H_{24}O_3$ requires *M*, 240.1724).

8-Butyl-7,9,9-trimethyl-1,4-dioxaspiro[4.5]dec-6-en-8-ol 3d.[3] The reaction of lithium metal (1.05 g, 151 mmol) in THF (80 cm^3) with butyl chloride (6.70 g, 72.4 mmol) and the keto acetal **2** (10.0 mg, 51 mmol) in THF (10 cm^3) afforded the known title compound **3d** (10.20 g, 79%), mp 46–47 °C; ν_{max}(KBr)/cm^{-1} 3503 (OH), 2952 (C–H), 1665 (C=C) and 1095 (C–O); δ_H(60 MHz) 0.98 (3 H, s, 9-Me), 1.06 (3 H, s, 9-Me), 1.80 (3 H, d, *J* 2, 7-Me), 0.95–2.25 (12 H, m), 3.92 (4 H, s, OCH_2CH_2O) and 5.36 (1 H, m, 6-H).

General procedure for the preparation of the allylic bromides 5a–d from cyclohexenols 3a–d

To a stirred solution of each of the cyclohexenols **3a–d** (2.21 mmol) and pyridine (1.1 cm^3) in toluene (5 cm^3) was added dropwise a solution of PBr_3 (712 mg, 2.63 mmol) in toluene (1.7 cm^3) under nitrogen at −10 °C, and stirring was continued for 1 h. Each reaction mixture was then quenched by addition of aqueous K_2CO_3 and extracted with toluene. The combined

extracts were washed with brine, dried ($MgSO_4$) and evaporated below 35 °C to give the crude products. These were subjected to the next reaction without further purification because of their instability to heat.

6-Bromo-7,8,9,9-tetramethyl-1,4-dioxaspiro[4.5]dec-7-ene 5a. The reaction of **3a** with PBr_3 afforded a mixture (390 mg) of the title compound **5a** and diene **6a** in a ratio of 1:1 (from ^{1}H NMR). The title compound **5a**; ν_{max}(film)/cm^{-1} 2970 (OH) and 1640 (C=C); δ_H(60 MHz) 1.08 (3 H, s, 9-Me), 1.19 (3 H, s, 9-Me), 1.57 [1 H, dd (of AB q), *J* 14, 3, 10-H], 1.67 (3 H, s, 8-Me),1.80 (3 H, d, *J* 2, 7-Me), 2.43 [1 H, d (of AB q), *J* 14, 10-H], 4.00 (4 H, s, OCH_2CH_2O) and 4.30 (1 H, br s, 6-H).

6-Bromo-8-ethyl-7,9,9-trimethyl-1,4-dioxaspiro[4.5]dec-7-ene 5b. Semicrystals (78%); ν_{max}(film)/cm^{-1} 2960 (CH), 1639 (C=C) and 1082 (C–O); δ_H(60 MHz) 1.02 (3 H, t, *J* 8, CH_2*Me*), 1.01 (3 H, s, 9-Me), 1.18 (3 H, s, 9-Me), 1.53 [1 H, dd (of AB q), *J* 14, 3, 10-H], 1.84 (3 H, s, 7-Me), 1.98 (2 H, q, *J* 8, C*H*$_2$Me), 2.45 [1 H, d (of AB q), *J* 14, 10-H], 4.01 (4 H, s, OCH_2CH_2O) and 4.29 (1 H, d, *J* 3, 6-H).

6-Bromo-8-isopropyl-7,9,9-trimethyl-1,4-dioxaspiro[4.5]dec-7-ene 5c. Semicrystals (70%); ν_{max}(film)/cm^{-1} 2950 (C–H), 1635 (C=C) and 1096 (C–O); δ_H(60 MHz) 1.01 (3 H, s, 9-Me), 1.20 (3 H, s, 9-Me), 1.16 (3 H, d, *J* 7, CH*Me*), 1.18 (3 H, d, *J* 7, CH*Me*), 1.52 [1 H, dd (of AB q), *J* 14, 3, 10-H], 1.91 (3 H, s, 7-Me), 2.44 [1 H, d (of AB q), *J* 14, 10-H], 3.99 (4 H, s, OCH_2CH_2O) and 4.20 (1 H, d, *J* 3, 6-H).

6-Bromo-8-butyl-7,9,9-trimethyl-1,4-dioxaspiro[4.5]dec-7-ene 5d. Semicrystals (73%); ν_{max}(film)/cm^{-1} 2950 (CH), 1638 (C=C) and 1095 (C–O); δ_H(60 MHz) 0.80–2.15 (9 H, m), 1.09 (3 H, s, 9-Me), 1.17 (3 H, s, 9-Me), 1.50 [1 H, dd (of AB q), *J* 14, 3, 10-H], 2.42 [1 H, d (of AB q), *J* 14, 10-H], 4.00 (4 H, s, OCH_2-CH_2O) and 4.28 (1 H, d, *J* 3, 6-H).

General procedure for preparation of the dienes 6a–d from the allylic bromides 5a–d

To a solution of each of the allylic bromides **5a**–**d** in toluene (5 cm^3) was added DBU (337 mg, 2.21 mmol) under nitrogen at room temperature. The reaction mixture was refluxed for 5 h, and after being cooled to room temperature was quenched with water, and extracted with toluene. The combined extracts were washed with brine, dried ($MgSO_4$), and evaporated to give the crude product. This was chromatographed on silica gel with ethyl acetate–hexane (1:5) as an eluent to give the dienes **6a**–**d**.

7,9,9-Trimethyl-8-methylene-1,4-dioxaspiro[4.5]dec-6-ene 6a. The reaction of a mixture (380 mg) of the allylic bromide **5a** and the diene **6a** with DBU afforded the title compound **6a** (246 mg, 59% from **3b**); ν_{max}(film)/cm^{-1} 2975 (CH), 1610 (C=C) and 1225 (C–O); δ_H(60 MHz) 1.15 (6 H, s, 2 × 9-Me), 1.78 (2 H, s, 10-H$_2$), 1.83 (3 H, d, *J* 2, 7-Me), 3.89 (4 H, s, OCH_2CH_2O), 5.04 (2 H, m, C=C*H*$_2$) and 5.46 (1 H, br s, 6-H); *m/z* 194 (M$^+$, 55%), 179 (100), 149 (30), 138 (31), 119 (43), 107 (55), 91 (39) and 77 (20) (Found: M$^+$, 194.1351. $C_{12}H_{18}O_2$ requires *M*, 194.1306).

(*E*)- and (*Z*)-8-Ethylidene-7,9,9-trimethyl-1,4–dioxaspiro[4.5]-dec-6-ene 6b. The reaction of the allylic bromide **5b** (485 mg) with DBU (337 mg, 2.21 mmol) afforded the title compound **6b** (269 mg, 60% from **3b**), which was analysed by capillary GC (Methyl Silicone, 50 m, 70–200 °C, 5 °C min^{-1}) and shown to be a mixture of isomers, *E*/*Z* = 49:51. The title compound (*E*)-**6b**; ν_{max}(vapour phase)/cm^{-1} 2958 (CH), 1638 (C=C) and 1100 (C–O); *m/z* 208 (M$^+$, 49%), 193 (100), 163 (28), 149 (24), 133 (31), 121 (83), 105 (27), 91 (34) and 77 (27) (Found: M$^+$, 208.1406. $C_{13}H_{20}O_2$ requires *M*, 208.1462). The title compound (*Z*)-**6b**; ν_{max}(vapour phase)/cm^{-1} 2965 (C–H), 1648 (C=C), 1616 (C=C) and 1099 (C–O); *m/z* 208 (M$^+$, 47%), 193 (100), 163 (25), 149 (24), 133 (28), 121 (83), 105 (28), 91 (35) and 77 (28); (*E*)/(*Z*) = 51:49; δ_H(60 MHz) 1.10–1.31 (6 H, s, 2 × 9-Me), 1.73–1.95 (5 H, m), 1.82–2.03 (3 H, d, *J* 2, 7-Me), 3.95 (4 H, s, OCH_2CH_2O) and 5.31–5.81 (2 H, m, 2 × C=C*H*) (Found: M$^+$, 208.1426. $C_{13}H_{20}O_2$ requires *M*, 208.1462).

8-Isopropylidene-7,9,9-trimethyl-1,4-dioxaspiro[4.5]dec-6-ene 6c. The reaction of **5c** (452 mg) with DBU (337 mg, 2.21 mmol) for 2 h, followed by extraction of the product with ethyl acetate, afforded the title compound **6c** (96 mg, 20% from **3c**); ν_{max}(film)/cm^{-1} 2940 (CH), 1630 (C=C) and 1090; δ_H(60 MHz) 1.28 (6 H, s, 2 × 9-Me), 1.73 (3 H, s, =CMe), 1.82 (2 H, s, 10-H$_2$), 1.88 (3 H, s, =CMe), 1.94 (3 H, d, *J* 2, 7-Me), 3.95 (4 H, s, OCH_2CH_2O) and 5.53 (1 H, br s, 6-H); *m/z* 222 (M$^+$, 42%), 207 (50), 179 (13), 150 (45), 135 (100), 126 (73), 91 (36), 77 (20) and 41 (38) (Found: M$^+$ − Me, 222.1629. $C_{14}H_{22}O_2$ requires *M* − Me, 222.1618).

(*E*)- and (*Z*)-8-Butylidene-7,9,9-trimethyl-1,4-dioxaspiro-[4.5]dec-6-ene 6d. The reaction of **5d** (498 mg) with DBU afforded the title compound **6d** (285 mg, 56% from **3d**) which was analysed by capillary GC (Methyl Silicone, 50 m, 70–200 °C, 5 °C min^{-1}) and shown to be a mixture of isomers *E*/*Z* = 40:60. The title compound (*E*)-**6d**; ν_{max}(vapour phase)/cm^{-1} 2967 (CH), 1638 (C=C) and 1101 (C–O); *m/z* 236 (M$^+$, 73%), 221 (100), 193 (42), 149 (60), 135 (96), 126 (54), 121 (82), 107 (53), 105 (42), 93 (52), 91 (68) and 77 (45) (Found: M$^+$, 236.1731. $C_{15}H_{24}O_2$ requires *M*, 236.1775). The title compound (*Z*)-**6d**; ν_{max}(vapour phase)/cm^{-1} 2967 (CH), 1646 (C=C), 1616 (C=C) and 1100 (C–O); *m/z* 236 (M$^+$, 73%), 221 (100), 193 (43), 149 (55), 135 (93), 126 (50), 121 (78), 107 (50), 105 (41), 93 (52), 91 (68) and 77 (45) (Found: M$^+$, 236.1731. $C_{15}H_{24}O_2$ requires *M*, 236.1775); (*E*)/(*Z*) = 40:60; δ_H(60 MHz) 1.12–1.31 (6 H, s, 2 × 9-Me), 0.81–2.50 (9 H, m), 1.87–2.04 (3 H, d, *J* 2, 7-Me), 3.97 (4 H, s, OCH_2CH_2O) and 5.25–5.71 (2 H, m, 2 × C=C*H*).

Representative procedure for the preparation of the dienones 7a–d from the dienes 6a–d

4-Methylene-3,5,5-trimethylcyclohex-2-enone 7a.[3,9] A mixture of **6a** (232 mg, 1.2 mmol) and aqueous HCl (1 mol dm^{-3}; 0.89 cm^3, 0.89 mmol) in THF (2.3 cm^3) was stirred for 5 h at room temperature and then extracted with ethyl acetate. The combined extracts were washed with aqueous $NaHCO_3$ and brine, dried ($MgSO_4$) and evaporated. The crude product was chromatographed on silica gel with ethyl acetate–hexane (1:2) as an eluent to give the title natural product **7a** (165 mg, 92%); ν_{max}(film)/cm^{-1} 2990 (CH), 1675 (C=O) and 1590 (C=C); δ_H(60 MHz) 1.20 (6 H, s, 2 × 5-Me), 2.08 (3 H, d, *J* 1, 3-Me), 2.35 (2 H, s, 6-H$_2$), 5.39 (1 H, d, *J* 1, C=CH*H*), 5.46 (1 H, s, C=C*H*H) and 5.92 (2 H, br s, 2-H); *m/z* 150 (M$^+$, 53%), 135 (26), 108 (45), 107 (100), 91 (39), 66 (37) and 39 (28).

(*E*)- and (*Z*)-4-Ethylidene-3,5,5-trimethylcyclohex-2-enone 7b.[3] The reaction of the diene **6b** (*E*/*Z* = 49:51; 146 mg, 0.70 mmol) in THF (2.3 cm^3) with hydrochloric acid (0.89 cm^3, 0.89 mmol) afforded the known title compound **7b** (106 mg, 92%) which was analysed by capillary GC (Methyl Silicone, 50 m, 70–200 °C, 5 °C min^{-1}) and shown to contain a mixture of isomers *E*/*Z* = 49:51. (*E*)-**7b** and (*Z*)-**7b** were separated by repeated chromatography on silica gel. (*E*)-**7b**; ν_{max}(film)/cm^{-1} 2960 (CH), 1665 (C=O), 1610 (C=C) and 1590 (C=C); δ_H(60 MHz) 1.32 (6 H, s, 2 × 5-Me), 1.94–2.08 (6 H, m), 2.35 (2 H, s, 6-H$_2$), 5.90 (1 H, br s, 2-H) and 6.18 (1 H, q, *J* 8, C=C*H*Me); *m/z* 164 (M$^+$, 79%), 149 (46), 122 (71), 121 (100), 105 (31), 93 (34), 91 (33), 80 (45), 79 (43), 77 (38) and 39 (40). (*Z*)-**7b**; ν_{max}(film)/cm^{-1} 2960 (CH), 1660 (C=O), 1630 (C=C) and 1580 (C=C); δ_H(60 MHz) 1.18 (6 H, s, 2 × 5-Me), 1.92 (3 H, d, *J* 8, C=CH*Me*), 2.23 (2 H, s, 6-H$_2$), 2.26 (3 H, d, *J* 2, 3-Me), 5.85 (1 H, dq, *J* 8, 2, C=C*H*Me) and 5.90 (1 H, br s, 2-H); *m/z* 164 (M$^+$, 73%), 149 (56), 122 (48), 121 (100), 105 (29), 93 (26), 91 (32), 80 (38), 79 (41), 77 (33) and 39 (38).

4-Isopropylidene-3,5,5-trimethylcyclohex-2-enone (isoxylitone) 7c.[28] The reaction of **6c** (87 mg, 0.39 mmol) in THF (2.5 cm^3) with hydrochloric acid (0.97 cm^3, 0.97 mmol) afforded the known title product **7c** (59 mg, 85%); ν_{max}(film)/cm^{-1} 2950 (CH), 1660 (C=O), 1620 (C=C) and 1595 (C=C); δ_H(60 MHz) 1.31 (6 H, s, 2 × 5-Me), 1.84 (3 H, s, C=CMe*Me*), 2.00 (3 H, s, C=*CMe*Me), 2.17 (3 H, d, *J* 1, 3-Me), 2.29 (2 H, s, 6-H$_2$) and 5.90 (1 H, br s, 2-H).

(*E*)- and (*Z*)-4-Butylidene-3,5,5-trimethylcyclohex-2-enone 7d.[3] The reaction of **6d** (*E*/*Z* = 40:60, 154 mg, 0.65 mmol) in THF (2.5 cm^3) with hydrochloric acid (0.97 cm^3, 0.97 mmol) afforded the known title compound **7d** (101 mg, 81%) which was analysed by capillary GC (Methyl Silicone, 50 m, 70–200 °C, 5 °C min^{-1}), and shown to be a mixture of isomers, *E*/*Z* = 40:60. (*E*)-**7d** and (*Z*)-**7d** were separated by repeated chromatography on silica gel. (*E*)-**7d**; ν_{max}(film)/cm^{-1} 2950 (CH), 1665 (C=O), 1610 (C=C) and 1590 (C=C); δ_H(60 MHz) 0.8–1.70 (5 H, m), 1.30 (6 H, s, 2 × 5-Me), 1.94–2.08 (6 H, m), 2.08 (3 H, d, *J* 1, 3-Me), 2.33 (2 H, s, 6-H_2), 2.20–2.60 (2 H, m, C=CH-CH_2), 5.91 (1 H, br s, 2-H) and 5.98 (1 H, t, *J* 7, C=C*H*); *m/z* 192 (M^+, 96%), 150 (64), 149 (87), 135 (89), 121 (94), 108 (100), 107 (77), 93 (65), 91 (59), 79 (50), 77 (51) and 41 (56). (*Z*)-**7d**; ν_{max}(film)/cm^{-1} 2960 (C−H), 1660 (C=O), 1630 (C=C) and 1580 (C=C); δ_H(60 MHz) 0.8–1.72 (5 H, m), 1.18 (6 H, s, 2 × 5-Me), 2.21 (3 H, d, *J* 2, 3-Me), 2.28 (2 H, s, 6-H_2), 2.10–2.50 (2 H, m, C=CH-CH_2), 5.68 (1 H, dt, *J* 8, 2, C=CH) and 5.91 (1 H, br s, 2-H); *m/z* 192 (M^+, 95%), 150 (63), 149 (88), 135 (91), 121 (96), 108 (100), 107 (79), 93 (67), 91 (57), 79 (52), 77 (51) and 41 (54).

8-(But-3-enyl)-7,9,9-trimethyl-1,4-dioxaspiro[4.5]dec-6-en-8-ol 3e. According to the procedure described for the preparation of **3a**, the reaction of lithium metal (1.46 g, 210 mmol) in THF (67 cm^3) with 4-bromobut-1-ene (13.6 g, 100 mmol) and the keto acetal **2** (15.0 g, 57.8 mmol) in THF (25 cm^3) and subsequent chromatography of the oily residue on silica gel with ethyl acetate–hexane (1:4) provided the title compound **3e** (11.7g, 80%); ν_{max}(film)/cm^{-1} 3510 (OH), 2960 (CH), 1665 (C=C), 1639 (C=C), 1090 (C−O), 990 (C=C), 910 (C=C) and 830 (C=C); δ_H(60 MHz) 1.00 (3 H, s, 9-Me), 1.07 (3 H, s, 9-Me), 1.51 (1 H, s, OH), 1.80 (3 H, d, *J* 2, 7-Me), 1.51–2.25 (6 H, m), 3.93 (4 H, m, OCH_2CH_2O), 4.85–5.20 (2 H, m, CH=CH_2), 5.39 (1 H, m, 6-H) and 5.81 (1 H, m, C*H*=CH_2); *m/z* 252 (M^+, 0.7%), 197 (100), 155 (56), 125 (19), 111 (29), 87 (28) and 43 (27) (Found: M^+ − Me, 237.1478. $C_{14}H_{21}O_3$ requires *M* − Me, 237.1488).

6-Bromo-8-but-3-enyl-7,9,9-trimethyl-1,4-dioxaspiro[4.5]dec-7-ene 5e. According to the procedure described for the preparation of **5**, the reaction of **3e** (569 mg, 2.21 mmol) with PBr_3 (712 mg, 2.63 mmol) afforded the title compound **5e** (554 mg, 80% from **3e**); ν_{max}(film)/cm^{-1} 2950 (CH), 1633 (C=C), 1095 (C−O), 980 (C=C) and 910 (C=C); δ_H(60 MHz) 1.08 (3 H, s, 9-Me), 1.17 (3 H, s, 9-Me), 1.53 [1 H, dd (of AB q), *J* 14, 3, 10-H], 1.81 (3 H, s, 7-H), 2.05–2.23 (4 H, m), 2.41 [1 H, d (of AB q), *J* 14, 10-H], 3.97 (4 H, s, OCH_2CH_2O), 4.25 (1 H, d, *J* 2, 6-H), 4.82–5.25 (2 H, m, CH=CH_2) and 5.80 (1 H, m, C*H*=CH_2). Compound **5e** was subjected to the next reaction without purification, because of its instability to heat.

(*E*)- and (*Z*)-8-[(*E*)- and (*Z*)-But-2-enylidene]-7,9,9-trimethyl-1,4-dioxaspiro[4.5]dec-6-ene 6e/1–4, (*E*)- and (*Z*)-8-(but-3-enylidene)-7,9,9-trimethyl-1,4-dioxaspiro[4.5]dec-6-ene 6e/5–6 and 8-[(*E*) and (*Z*)-buta-1,3-dienyl]-7,9,9-trimethyl-1,4-dioxaspiro-[4.5]dec-6-ene 6e/7–8

According to the procedure described for the preparation of **6a–d**, the reaction of **5e** (541 mg) with DBU (337 mg, 2.21 mmol) afforded a mixture of the trienes **6e** (303 mg, 60% from **3e**) which was analysed by capillary GC (Methyl Silicone, 50 m, 70–200 °C, 5 °C min^{-1}), and shown to contain the conjugated trienes **6e/1–4**, deconjugated trienes **6e/5–6** and deconjugated trienes **6e/7–8** in a ratio of 21:26:53.

The conjugated trienes **6e/1–4** were further analysed by capillary GC, and shown to be a mixture of geometrical isomers **6e**/**Isomer-1**, **6e**/**Isomer-2**, **6e**/**Isomer-3**, and **6e**/**Isomer-4** in a ratio of 8:33:13:46. **6e**/**Isomer-1**; ν_{max}(vapour phase)/cm^{-1} 2965 (CH), 1649 (C=C) and 1098 (C−O); *m/z* 234 (M^+, 83%), 219 (35), 162 (71), 147 (100), 133 (52), 119 (52), 105 (56), 91 (78), 77 (46) and 41 (53) (Found: M^+, 234.1606. $C_{15}H_{22}O_2$ requires *M*, 234.1618). **6e**/**Isomer-2**; ν_{max}(vapour phase)/cm^{-1} 2965 (CH), 1647 (C=C), 1620 (C=C) and 1096 (C−O); *m/z* 234 (M^+, 83%), 219 (41), 162 (89), 147 (100), 133 (45), 119 (55), 105 (68), 91 (93), 77 (64) and 41 (80) (Found: M^+, 234.1617. $C_{15}H_{22}O_2$ requires *M*, 234.1618). **6e**/**Isomer-3**; ν_{max}(vapour phase)/cm^{-1} 2966 (CH), 1628 (C=C) and 1099 (C−O); *m/z* 234 (M^+, 88%), 219 (37), 162 (72), 147 (100), 133 (50), 119 (54), 105 (54), 91 (83), 77 (59) and 41 (58) (Found: M^+, 234.1663. $C_{15}H_{22}O_2$ requires *M*, 234.1618). **6e**/**Isomer-4**; ν_{max}(vapour phase)/cm^{-1} 2966 (CH), 1630 (C=C) and 1099 (C−O); *m/z* 234 (M^+, 62%), 219 (25), 162 (50), 147 (100), 133 (33), 119 (32), 105 (40), 91 (90), 77 (35) and 41 (43) (Found: M^+, 234.1655. $C_{15}H_{22}O_2$ requires *M*, 234.1618).

The mixture of unconjugated trienes **6e/5–6** was further analysed by capillary GC, and shown to contain the geometrical isomers **6e**/**Isomer-5** and **6e**/**Isomer-6** in a ratio of 81:19. **6e**/**Isomer-5**; ν_{max}(vapour phase)/cm^{-1} 2967 (CH), 1860 (C−*C*=*C*H_2), 1640 (C=C), 1096 (C−O), 976 (C−*C*=*C*H_2) and 920 (C−*C*=*C*H_2); *m/z* 234 (M^+, 42%), 219 (66), 193 (38), 178 (30), 163 (33), 149 (38), 133 (52), 119 (58), 105 (73), 93 (53), 91 (100), 77 (48), 65 (14), 53 (27) and 41 (37) (Found: M^+, 234.1651. $C_{15}H_{22}O_2$ requires *M*, 234.1618). **6e**/**Isomer-6**; ν_{max}(vapour phase)/cm^{-1} 3088 (CH), 2964 (CH), 1860 (C−*C*=*C*H_2), 1630 (C=C), 1100 (C−O), 976 (C−*C*=*C*H_2) and 920 (C−*C*=*C*H_2); *m/z* 234 (M^+, 46%), 219 (66), 193 (45), 178 (39), 163 (34), 149 (23), 133 (39), 119 (52), 105 (65), 93 (53), 91 (100), 77 (59), 65 (10), 53 (30) and 41 (44) (Found: M^+, 234.1642. $C_{15}H_{22}O_2$ requires *M*, 234.1618).

The mixture of conjugated trienes **6e/7–8** was further analysed by capillary GC, and shown to contain a mixture of geometrical isomers **6e**/**Isomer-7** and **6e**/**Isomer-8** in a ratio of 63:35. **6e**/**Isomer-7**; ν_{max}(vapour phase)/cm^{-1} 3094 (CH), 2929 (CH), 1804 (C=C−*C*=*C*H_2), 1636 (C=C), 1598 (C=C), 1099 (C−O), 1000 (C=C−*C*=*C*H_2) and 920 (C=C−*C*=*C*H_2); *m/z* 234 (M^+, 5%), 148 (26), 133 (100), 120 (20), 105 (25) and 91 (24) (Found: M^+, 234.1603. $C_{15}H_{22}O_2$ requires *M*, 234.1618). **6e**/**Isomer-8**; ν_{max}(vapour phase)/cm^{-1} 3094 (CH), 2964 (CH), 1808 (C=C−*C*=*C*H_2), 1677 (C=C), 1648 (C=C), 1602 (C=C), 1093 (C−O), 1002 (C=C−*C*=*C*H_2) and 903 (C=C−*C*=*C*H_2); *m/z* 234 (M^+, 10%), 178 (100), 163 (80), 148 (33), 133 (53), 105 (24), 91 (74), 77 (19) and 41 (24) (Found: M^+, 234.1603. $C_{15}H_{22}O_2$ requires *M*, 234.1618).

Megastigmatrienones;[4] **(*Z*)-4-[(*E*)-but-2-enylidene]-3,5,5-trimethylcyclohex-2-enone 7e/1, (*Z*)-4-[(*Z*)-but-2-enylidene]-3,5,5-trimethylcyclohex-2-enone 7e/2, (*E*)-4-[(*Z*)-but-2-enylidene]-3,5,5-trimethylcyclohex-2-enone 7e/3, (*E*)-4-[(*E*)-but-2-enylidene]-3,5,5-trimethylcyclohex-2-enone 7e/4, 4-[(*E*)-buta-1,3-dienyl]-3,5,5-trimethylcyclohex-2-enone 7e/7, and (*E*)- and (*Z*)-4-(but-3-enylidene)-3,5,5-trimethylcyclohex-2-enone 7e/5–6**

According to the procedure described for the preparation of compounds **7a–d**, the reaction of the trienes **6e** (143 mg, 0.61 mmol) with hydrochloric acid (0.97 cm^3, 0.97 mmol) afforded, in THF (2.5 cm^3), a mixture of the trienones **7e** (95 mg, 82%) which was analysed by capillary GC (Methyl Silicone, 50 m, 70–200 °C, 5 °C min^{-1}), and shown to contain the trienones **7e/1–4** (megastigmatrienone), **7e/5–6** and **7e/7** (megastigmatrienone) in a ratio of 51:25:24.

The mixture of conjugated trienes **7e/5–6** was further analysed by capillary GC, and shown to contain the geometrical isomers **7e**/**Isomer-5** and **7e**/**Isomer-6** in a ratio of 81:19. **7e**/**Isomer-5**; ν_{max}(vapour phase)/cm^{-1} 2972 (CH), 1691 (C=O), 1638 (C=C), 1591 (C=C), 991 (C−*C*=*C*H_2) and 918 (C−*C*=*C*H_2); *m/z* 190 (M^+, 15%), 136 (97), 134 (75), 108 (80), 105 (45), 93 (97), 91 (100), 77 (55) and 39 (62) (Found: M^+, 190.1314. $C_{13}H_{18}O$ requires *M*, 190.1356). **7e**/**Isomer-6**; ν_{max}(vapour phase)/cm^{-1} 2969 (CH), 1694 (C=O), 1640 (C=C), 1603 (C=C), 993 (C−*C*=*C*H_2) and 918 (C−*C*=*C*H_2); *m/z* 190 (M^+, 14%), 136 (92), 134 (84), 108 (66), 105 (45), 93 (95), 91 (100), 77 (56) and 39 (58) (Found: M^+, 190.1340. $C_{13}H_{18}O$ requires *M*, 190.1356).

Preparation of the megastigmatrienones 7e/1–4 and 7e/7 by isomerisation with base

A solution of the trienones **7e/1–4**, **7e/5–6** and **7e/7** (51:25:24) (101 mg, 0.53 mmol) and DBU (18 mg, 0.12 mmol) in xylene (2.5 cm^3) was refluxed for 4 h under nitrogen. The reaction mixture was washed successively with aqueous hydrochloric acid and brine, dried ($MgSO_4$) and evaporated. The oily residue was chromatographed on silica gel with ethyl acetate–hexane (1:4) as eluent to afford the trienones **7e** (87 mg, 86%) which were analysed by capillary GC (Methyl Silicone, 50 m, 70–200 °C, 5 °C min^{-1}), and shown to be a mixture of the megastigmatrienones **7e/1**, **7e/2**, **7e/3**, **7e/4** and **7e/7** in a ratio of 10:40:9:34:7. The five isomers were separated by repeated column chromatography on silica gel. **7e/1**; ν_{max}(film)/cm^{-1} 2971 (CH), 1690 (C=O) and 1604 (C=C); δ_H(300 MHz) 1.12 (6 H, s, 2 × 5-Me), 1.73 (3 H, dd, *J* 6.8, 1.5, C=C−Me), 2.20 (3 H, d, *J* 1.2, 3-Me), 2.22 (2 H, s, 6-H_2), 5.83 (2 H, m, 2-H and C=C*H*Me), 6.18 (1 H, d, *J* 11.3, C=C*H*−CH=C) and 6.46 (1 H, ddd, *J* 15.2, 11.3, 1.5, C*H*=C−Me); *m/z* 190 (M^+, 63%), 175 (50), 148 (62), 147 (75), 133 (68), 119 (58), 105 (58), 91 (100), 77 (71), 65 (30), 55 (26), 41 (79) and 39 (70). **7e/2**; ν_{max}(film)/cm^{-1} 2971 (CH), 1690 (C=O) and 1603 (C=C); δ_H(300 MHz) 1.15 (6 H, s, 2 × 5-Me), 1.76 (3 H, dd, *J* 7.2, 1.6, C=C−Me), 2.18 (3 H, s, 3-Me), 2.24 (2 H, s, 6-H_2), 5.67 (1 H, dq, *J* 10.7, 7.2, C=C*H*−Me), 5.85 (1 H, s, 2-H), 6.35 (1 H, ddd, *J* 11.3, 10.7, 1.7, C*H*=C−Me) and 6.46 (1 H, d, *J* 11.3, C=C*H*−CH=C); *m/z* 190 (M^+, 80%), 175 (51), 148 (63), 147 (72), 133 (78), 119 (63), 105 (68), 91 (100), 77 (62), 65 (46), 55 (47), 41 (63) and 39 (73). **7e/3**; ν_{max}(film)/cm^{-1} 2971 (CH), 1693 (C=O) and 1594 (C=C); δ_H(300 MHz) 1.21 (6 H, s, 2 × 5-Me), 1.73 (3 H, dd, *J* 7.3, 1.6, C=C−Me), 2.00 (3 H, s, 3-Me), 2.23 (2 H, s, 6-H_2), 5.73 (1 H, dq, *J* 10.7, 7.3, C=C*H*−Me), 5.79 (1 H, s, 2-H), 6.55 (1 H, ddd, *J* 12.4, 10.7, 1.6, C*H*=C−Me) and 6.68 (1 H, d, *J* 12.4, C=C*H*−CH=C); *m/z* 190 (M^+, 83%), 175 (51), 148 (46), 147 (51), 133 (83), 119 (71), 105 (88), 91 (100), 77 (91), 65 (55), 55 (34), 41 (76) and 39 (85). **7e/4**; ν_{max}(film)/cm^{-1} 2969 (C−H), 1692 (C=O) and 1593 (C=C); δ_H(300 MHz) 1.23 (6 H, s, 2 × 5-Me), 1.77 (3 H, dd, *J* 6.9, 1.5, C=C−Me), 1.96 (3 H, s, 3-Me), 2.23 (2 H, s, 6-H_2), 5.78 (1 H, s, 2-H), 5.85 (1 H, m, C=C*H*−Me), 6.36 (1 H, d, *J* 11.6, C=C*H*−CH=C) and 6.64 (1 H, ddd, *J* 14.6, 11.6, 1.5, C*H*=C−Me); *m/z* 190 (M^+, 63%), 175 (54), 148 (55), 147 (71), 133 (63), 119 (51), 105 (55), 91 (100), 77 (51), 65 (33), 55 (33), 41 (76) and 39 (54). **7e/7**; ν_{max}(vapour phase)/cm^{-1} 2969 (CH), 1817 (C=C−*C*=*C*H_2), 1695 (C=O), 1635 (C=C), 1000 (C−C=CH_2), 960 [(*E*, C=C)] and 908 (C−*C*=*C*H_2); δ_H(300 MHz) 0.86 (3 H, s, 5-Me), 0.93 (3 H, s, 5-Me), 1.80 (3 H, s, 3-Me), 1.97 [1 H, d (of AB q), *J* 16.7, 6-H], 2.25 [1 H, d (of AB q), *J* 16.7, 6-H], 2.46 (1 H, d, *J* 9.4, 4-H), 4.97 (1 H, d, *J* 9.9, C=C*H*H), 5.08 (1 H, d, *J* 16.9, C=C*H*H), 5.47 (1 H, dd, *J* 14.9, 9.5, CH−C*H*=C), 5.79 (1 H, s, 2-H), 6.06 (1 H, m, CH=C*H*−CH=CH_2) and 6.21 (1 H, m, C*H*−CH_2); *m/z* 190 (M^+, 8%), 134 (94), 119 (40), 105 (26), 91 (100), 77 (21) and 39 (28).

6-Bromo-8-(3,3-ethylenedioxybutyl)-7,9,9-trimethyl-1,4-dioxaspiro[4.5]dec-7-ene 5f

According to Method II of the general procedure, the reaction of **3f** (690 mg, 2.21mmol) with PBr_3 (712 mg, 2.63 mmol) afforded the title compound **5f** (613 mg, 74%); ν_{max}(film)/cm^{-1} 2975 (CH), 1639 (C=C) and 1095 (C−O); δ_H(60 MHz) 1.07 (3 H, s, 9-Me), 1.10 (3 H, s, 9-Me), 1.22 (3 H, s, C-Me), 1.76 (3 H, s, 7-Me), 1.45–2.22 (5 H, m), 2.32 [1 H, d (of AB q), *J* 14, 10-H], 3.81 (4 H, s, OCH_2CH_2O), 3.86 (4 H, s, OCH_2CH_2O) and 4.28 (1 H, d, *J* 3, 6-H). Compound **5f** was subjected to the next reaction without purification, because of its instability to heat.

(*E*) and (*Z*)-8-(3,3-Ethylenedioxybutylidene)-7,9,9-trimethyl-1,4-dioxaspiro[4.5]dec–6-ene 6f

According to the procedure described for the preparation of **6a–d**, the reaction of **5f** (595 mg) with DBU (337 mg, 2.21 mmol) afforded the diene **6f** (309 mg, 49% from **3f**) which was analysed by capillary GC (Methyl Silicone, 50 m, 70–200 °C, 5 °C min^{-1}) and shown to contain a mixture of (*E*)-**6f**/(*Z*)-**6f** = 38:62. (*E*)-**6f** and (*Z*)-**6f** were separated by repeated chromatography on silica gel. (*E*)-**6f**; ν_{max}(film)/cm^{-1} 2950 (CH), 1640 (C=C) and 1130 (C−O); δ_H(60 MHz) 1.30 (6 H, s, 2 × 9-Me), 1.33 (3 H, s, C−Me), 1.78 (2 H, s, 10-H_2), 1.88 (3 H, d, *J* 1, 7-Me), 2.70 (2 H, d, *J* 7, C=C−CH_2), 3.93 (8 H, s, 2 × OCH_2CH_2O), 5.51 (1 H, s, 6-H) and 5.69 (1 H, t, *J* 7, C=C*H*−CH_2); *m/z* (CI) 295 (MH^+, 100%), 251 (92), 233 (8), 209 (71) and 165 (38) (Found: M^+ − Me, 279.1538. $C_{16}H_{23}O_4$ requires *M* − Me, 279.1594). (*Z*)-**6f**; ν_{max}(film)/cm^{-1} 2980 (CH), 1640 (C=C), 1620 (C=C) and 1100 (C−O); δ_H(60 MHz) 1.13 (6 H, s, 2 × 9-Me), 1.31 (3 H, s, C-Me), 1.79 (2 H, s, 10-H_2), 2.03 (3 H, d, *J* 1, 7-Me), 2.59 (2 H, d, *J* 7, C=C−CH_2), 3.93 (8 H, s, 2 × OCH_2CH_2O) and 5.30–5.80 (2 H, m, 2 × C=CH); *m/z* (CI) 295 (MH^+, 100%), 251 (46), 233 (73), 209 (41) and 165 (14) (Found: M^+ − Me, 279.1626. $C_{16}H_{23}O_4$ requires *M* − Me, 279.1594).

(*E*)-4-(4-Oxo-2,6,6-trimethylcyclohex-2-enyl)but-3-en-2-one (3-oxo-α-ionone) 8[20]

According to the procedure described for the preparation of **7a–d**, the reaction of **6f** (353 mg, 1.2mmol; *E*:*Z* = 40:60) with hydrochloric acid (1 mol dm^{-3} solution; 1.17 cm^3, 1.17 mmol) in THF (3.0 cm^3) afforded the title natural product **8** (161 mg, 65%); ν_{max}(film)/cm^{-1} 2960 (CH), 1670 (C=O), 1379, 1265 and 995; δ_H(60 MHz) 1.02 (3 H, s, 6-Me), 1.08 (3 H, s, 6-Me), 1.90 (3 H, d, *J* 1, 2-Me), 2.05–2.25 (2 H, s, 5-H_2), 2.27 (3 H, s, COMe), 2.75 (1 H, d, *J* 9, 1-H), 5.93 (1 H, br s, 3-H), 6.13 (1 H, d, *J* 16, C=CHCO) and 6.72 (1 H, dd, *J* 16, 9, C−C*H*=CH); *m/z* 206 (M^+, 1%), 150 (17), 108 (100), 91 (12), 77 (18), 55 (8) and 43 (97). The spectra (IR, ^{1}H NMR, mass) of **8** were identical with those of an authentic sample.[20]

(*E*)- and (*Z*)-4-(3-Hydroxybutylidene)-3,5,5-trimethylcyclohex-2-enone 9[10]

A mixture of **6f** (2.41 g, 8.2 mmol; *E*:*Z* = 40:60) and 37% aq. H_2SO_4 impregnated silica gel (9.7 g) in CH_2Cl_2 (16 cm^3) was stirred at room temperature for 2.5 h and then filtered through a pad of Celite 545. The filtrate was washed successively with aqueous $NaHCO_3$ and brine, dried ($MgSO_4$) and evaporated to afford (*E*)- and (*Z*)-4-(3-oxobutylidene)-3,5,5-trimethylcyclohex-2-enone **7f** (1.69 g, 70%), which was analysed by GC (Silicone OV-17, 0.8 m, 185 °C), and shown to contain a mixture of *E*/*Z* isomers in a ratio of 40:60. (*E*)-**7f**; ν_{max}(vapour phase)/cm^{-1} 2971 (CH), 1736 (C=O), 1694 (C=O) and 1618 (C=C); *m/z* 206 (M^+, 8%), 164 (37), 149 (63), 121 (13), 105 (9), 91 (10), 77 (12) and 43 (100). (*Z*)-**7f**; ν_{max}(vapour phase)/cm^{-1} 2972 (CH), 1734 (C=O), 1692 (C=O) and 1620 (C=C); *m/z* 206 (M^+, 9%), 164 (42), 149 (78), 121 (8), 105 (10), 91 (12), 77 (13) and 43 (100). (*E*)/(*Z*) = 40:60; δ_H(60 MHz) 1.29–1.21 (6 H, s, 5-Me), 1.12–1.31 (3 H, d, *J* 1, 3-Me), 2.21–2.25 (3 H, s, COMe), 1.36 (2 H, s, 6-H_2), 3.45–3.59 (2 H, d, *J* 7, C=CH−CH_2), 5.91 (1 H, br s, 2-H) and 5.85–6.46 (1 H, m, C=C*H*−CH_2). To a stirred solution of **7f** (1.26 g, 6.1 mmol; *E*:*Z* = 40:60) in THF (15 cm^3) was added dropwise a solution of $Zn(BH_4)_2$ in diethylene glycol dimethyl ether[29] (2.04 mmol dm^{-3}; 7.9 cm^3, 3.87 mmol) at 5 °C, and stirring was continued for 3 h. The reaction mixture was quenched by addition of ice–water and then extracted with ethyl acetate. Removal of the solvent from the mixture left an oil which was chromatographed on silica gel with ethyl acetate–hexane (1:1) as eluent to afford the natural product **9** (875 mg, 69%), which was analysed by GC (Silicone OV-17, 0.8 m, 185 °C), and shown to be an isomeric mixture (*E*/*Z* = 40:60). The isomers (*E*)-**9** and (*Z*)-**9** were isolated by preparative GC (FFAP, 2 m, 200 °C). (*E*)-**9**; ν_{max}(film)/cm^{-1} 3480 (OH), 1650 (C=O), 1610 (C=C) and 1590 (C=C); δ_H(60 MHz) 1.25 [3 H, d, *J* 6, C(OH)*Me*], 1.28 (6 H, s, 2 × 5-Me), 2.08 (3 H, d, *J* 1, 3-Me), 2.34 (2 H, s, 6-H_2), 2.50–2.70 (2 H, m, C=CH−CH_2), 3.90 (1 H, m, C*H*OH), 5.90 (1 H, br s, 2-H) and 6.11 (1 H, t, *J* 6, C=C*H*−

CH_2); *m/z* 208 (M^+, 3%), 164 (50), 149 (100), 136 (5), 121 (21), 105 (13), 91 (15), 77 (14) and 45 (93). (*Z*)-**9**; ν_{max}(film)/cm^{-1} 3430 (OH), 1660 (C=O) and 1580 (C=C); δ_H(60 MHz) 1.18 (6 H, s, 2 × 5-Me), 1.35 [3 H, d, *J* 6, C(OH)*Me*], 2.21 (3 H, d, *J* 1, 3-Me), 2.29 (2 H, s, 6-H_2), 2.50–2.70 (2 H, m, C=CH−CH_2), 3.90 (1 H, m, C*H*OH), 5.66 (1 H, dt, *J* 6, 1, C=C*H*−CH_2) and 5.90 (1 H, br s, 2-H); *m/z* 208 (M^+, 1%), 164 (54), 149 (100), 136 (5), 121 (19), 105 (13), 91 (15), 77 (15) and 45 (80).

(2*R**,8a*R**)- and (2*R**,8a*S**)-2,3,5,6,8,8a-Hexahydro-2,5,5,8a-tetramethyl-7*H*-1-benzopyran-7-one 10a,b[21]

To sodium hydride (50%; 630 mg, 13.0 mmol), washed three times with benzene, was added dropwise at 0 °C a solution of **9** (*E* : *Z* = 40 : 60; 905 mg, 4.35 mmol) in benzene (9.0 cm^3). The resulting slurry was stirred at room temperature under nitrogen for 40 h after which it was poured into ice–water and extracted with ethyl acetate. Concentration of the extract left an oily residue which was chromatographed on silica gel with ethyl acetate–hexane (1 : 2) to afford the title natural product **10a**,**b** [434 mg, 48%; mp 47–48 °C (lit.,[11] 42–45 °C)]. The compound **10a**,**b** was analysed by capillary GC (FFAP, 50 m, 70–200 °C, 5 °C min^{-1}), and shown to be a mixture of two diastereoisomers in a ratio of 9 : 91. **10a**; ν_{max}(vapour phase)/cm^{-1} 2995 (CH), 1720 (C=O) and 1115 (C−O); *m/z* 208 (M^+, 30%), 194 (11), 193 (100), 151 (45), 124 (43), 109 (67), 107 (61), 91 (27), 43 (99) and 41 (39). **10b**; ν_{max}(vapour phase)/cm^{-1} 2997 (CH), 1718 (C=O) and 1120 (C−O); δ_H(60 MHz) 1.12 (3 H, s, 5-Me), 1.21 (3 H, s, 5-Me), 1.24 (3 H, d, *J* 6, 2-Me), 1.48 (3 H, s, 8a-Me), 1.90–2.20 (2 H, m, 3-H_2), 2.35 (2 H, s, 6-H_2), 2.58 (2 H, s, 8-H_2), 3.95 (1 H, m, 2-H) and 5.76 (1 H, dd, *J* 4, 4, 4-H); *m/z* 208 (M^+, 0.1%), 194 (2), 193 (100), 151 (15), 124 (34), 109 (70), 107 (33), 91 (19), 43 (53) and 41 (26).

4-Hydroxy-3,4,5,5-tetramethylcyclohex-2-enone 11a

To a stirred solution of **3a** (3.00 g, 14.2 mmol) in THF (15 cm^3) was added aqueous HCl (1 mol dm^{-3} solution; 5.0 cm^3, 5.0 mmol), and stirring was continued for 5 min at room temperature. The product was extracted with ethyl acetate. The extract was washed successively with aqueous $NaHCO_3$ and brine, dried ($MgSO_4$) and evaporated. The crystalline residue was recrystallised from ethyl acetate–hexane (1 : 10) to afford the title compound **11a** (1.90 g, 80%); ν_{max}(film)/cm^{-1} 3400 (OH), 2980 (CH), 1665 (C=O) and 1145 (C−O); δ_H(60 MHz) 1.07 (6 H, s, 2 × 5-Me), 1.38 (3 H, s, 4-Me), 1.80 (1 H, s, OH), 2.00 (3 H, d, *J* 1, 3-Me), 2.35 (2 H, s, 6-H_2) and 5.80 (1 H, br s, 2-H); *m/z* 168 (M^+, 0.8%), 125 (14), 112 (94), 84 (28), 69 (100) and 43 (45).

One-pot synthesis of 4-methylene-3,5,5-trimethylcyclohex-2-enone 7a

To a solution of **11a** (371 mg, 2.21 mmol) and DBU (1.00 g, 6.63 mmol) in chloroform (5 cm^3) was added dropwise a solution of PBr_3 (500 mg, 1.85 mmol) in chloroform (1.7 cm^3) under nitrogen at −5 °C. After the reaction mixture had been stirred for 2 h at room temperature, it was quenched with aqueous HCl and extracted with diethyl ether. The extract was washed successively with brine and aqueous $NaHCO_3$, dried ($MgSO_4$) and evaporated. The oily residue was chromatographed on silica gel with ethyl acetate–hexane (1 : 2) as eluent to afford the title compound **7a** (196 mg, 59%), whose IR and ^{1}H NMR spectra were identical with those mentioned above.

4a-Hydroxy-2,3,4,4a,5,6-hexa-4,5,6-hydro-4,4,7-trimethylnaphthalen-2-one 13

To a solution of NaOH (3.53 g, 88.3 mmol) in methanol (75 cm^3) was added the dione **12** (10.4 g, 48.6 mmol), prepared from the diacetal **3f** according to the published procedure,[16] in methanol (39 cm^3) and the reaction mixture was stirred at room temperature for 7 h. It was then neutralised with aqueous HCl and concentrated. The product was extracted with ethyl acetate and the extract was concentrated. The crystalline residue was recrystallised from ethyl acetate–hexane (1 : 10) to afford the title compound **13** (7.01 g, 70%); mp 95–96 °C (Found: C, 75.6; H, 8.9. $C_{13}H_{18}O_2$ requires C, 75.7; H, 8.8%); ν_{max}(KBr)/cm^{-1} 3400 (OH), 2980 (CH), 1660 (C=O) and 1630 (C=C); δ_H(60 MHz) 0.98 (3 H, s, 4-Me), 1.10 (3 H, s, 4-Me), 1.60–2.10 (2 H, m, 5-H_2), 1.96 (3 H, br s, 7-Me), 2.10–2.40 (3 H, m), 2.90 [1 H, d (of AB q), *J* 15, 3-H], 5.61 (1 H, br s, C=CH) and 6.00 (1 H, br s, C=CH); *m/z* 206 (M^+, 15%), 198 (20), 173 (10), 145 (20), 141 (15), 132 (100), 122 (44), 108 (54), 79 (88), 77 (36) and 43 (48).

4a-Hydroxy-3,4,5,6,7,8-hexahydro-4,4,7-trimethylnaphthalen-2-one 14

To a solution of KOH (26 mg, 0.5 mmol) in methanol (71 cm^3) were added the hydroxy dienone **13** (3.16 g, 15.2 mmol) and 5% Pd–C (190 mg). The resulting mixture was stirred under a hydrogen atmosphere at room temperature, until 1 equivalent of hydrogen had been absorbed. The catalyst was then filtered off and the filtrate was evaporated. The crystalline residue was recrystallised from ethyl acetate–hexane (1 : 10) to afford the title compound **14** (2.47 g, 78%), mp 114–115 °C (Found: C, 74.8; H, 9.7. $C_{13}H_{20}O_2$ requires C, 75.0; H, 9.7%); ν_{max}(KBr)/cm^{-1} 3450 (OH), 2980 (CH), 1675 (C=O) and 1625 (C=C); δ_H(60 MHz) 1.04 (3 H, s, 4-Me), 1.08 (3 H, s, 4-Me), 1.40 (3 H, d, *J* 7, 7-Me), 1.30–3.10 (10 H, m) and 5.78 (1 H, br s, C=CH); *m/z* 208 (M^+, 5%), 180 (7), 166 (28), 152 (100), 123 (23), 110 (49), 81 (46), 68 (18), 67 (17), 55 (23), 43 (21), 41 (48) and 39 (33).

2,3,4,6,7,8-Hexahydro-4,4,7-trimethylnaphthalen-2-one 15[12]

To a stirred solution of **14** (1.87 g, 89.9 mmol) and DBU (4.41g, 29.0 mmol) in chloroform (23 cm^3) was added dropwise a solution of PBr_3 (3.20 mg, 11.8 mmol) in chloroform (15 cm^3) under nitrogen at −5 °C. After being stirred for an additional 4 h at room temperature the reaction mixture was quenched, by addition of aqueous HCl, and then extracted with diethyl ether. The extract was washed successively with brine and aqueous $NaHCO_3$, dried ($MgSO_4$) and evaporated. The oily residue was chromatographed on silica gel with ethyl acetate–hexane (1 : 7) as eluent to afford the title natural product **15** (1.18 g, 69%); ν_{max}(film)/cm^{-1} 2975 (CH), 1670 (C=O), 1635 (C=C) and 1595 (C=C); δ_H(60 MHz) 0.99 (3 H, d, *J* 6, 7-Me), 1.05 (3 H, s, 4-Me), 1.16 (3 H, s, 4-Me), 1.50–2.15 (5 H, m), 2.29 (2 H, s, 3-H_2), 5.58 (1 H, s, 1-H) and 5.59 (1 H, m, 5-H); *m/z* 190 (M^+, 92%), 175 (47), 161 (19), 147 (83), 134 (100), 119 (63), 105 (50), 91 (63), 77 (29), 67 (16), 55 (21) and 41 (37).

(8*R**)-8-[(*S**)-3-Acetoxybut-1-ynyl]-8-hydroxy-7,9,9-trimethyl-1,4-dioxaspiro[4.5]dec-6-ene 17

To a solution of **16**[6,21] (6.00 g, 22.6 mmol) in pyridine (100 cm^3) was added acetic anhydride (50 cm^3), and stirring was continued at room temperature for 12 h. The reaction mixture was then poured into ice–water and extracted with ethyl acetate. Evaporation of the extract left an oily residue which was chromatographed on silica gel with ethyl acetate–hexane (1 : 2) to afford the title compound **17** (6.37 g, 92%); ν_{max}(film)/cm^{-1} 3464 (OH), 2974 (CH), 1744 (C=O), 1671 (C=C) and 1096 (C−O); δ_H(100 MHz) 1.08 (3 H, s, 9-Me), 1.12 (3 H, s, 9-Me), 1.47 [3 H, d, *J* 7, CH(OAc)*Me*], 1.88 (3 H, s, 7-Me), 1.92 (2 H, s, 10-H_2), 2.06 (3 H, s, OCOMe), 2.45 (1 H, br s, OH), 3.93 (4 H, s, OCH_2CH_2O), 5.36 (1 H, br s, 6-H) and 5.45 (1 H, q, *J* 7, C*H*OAc); *m/z* 308 (M^+, 0.2%), 252 (43), 192 (25), 164 (17), 162 (15), 92 (20) and 43 (100) (Found: M^+ − COMe, 265.1397. $C_{15}H_{21}O_4$ requires *M* − COMe, 265.1408).

(8*R**)-8-[(*S**,*Z*)-3-Acetoxybut-1-enyl]-8-hydroxy-7,9,9-trimethyl-1,4-dioxaspiro[4.5]dec-6-ene 18

A solution of **17** (6.3 g, 20.5 mmol) in ethyl acetate (75 cm^3) was hydrogenated in the presence of Lindlar catalyst (1 g; containing 5% Pd−C) at 20 °C, until 1 equivalent of hydrogen had been absorbed. The oily residue was filtered off and the filtrate was

evaporated. The crude product was chromatographed on silica gel with ethyl acetate–hexane (1:2) to give the title compound **18** (4.45 g, 70%); ν_{max}(film)/cm^{-1} 3430 (OH), 2980 (CH), 1710 (C=O), 1668 (C=C) and 1095 (C–O); δ_H(100 MHz) 1.03 (3 H, s, 9-Me), 1.08 (3 H, s, 9-Me), 1.30 [3 H, d, *J* 6, CH(OAc)*Me*], 1.73 (3 H, d, *J* 1, 7-Me), 1.80 (2 H, s, 10-H_2), 2.03 (3 H, s, OCOMe), 3.80–3.95 (4 H, s, OCH_2CH_2O), 4.78 (1 H, s, OH), 5.32–5.52 (2 H, m, CH=CH), 5.31 (1 H, d, *J* 1, 6-H) and 6.15 (1 H, m, C*H*OAc); *m/z* 310 (M^+, 0.3%), 250 (22), 240 (10), 194 (100), 179 (36), 164 (63), 149 (40), 109 (15), 87 (39) and 43 (77) (Found: $M^+ - CH_3CO_2H$, 250.1615. $C_{15}H_{22}O_3$ requires $M - CH_3CO_2H$, 250.1568).

(8*R)-4-[(*S**,*Z*)-3-Acetoxybut-1-enyl]-4-hydroxy-3,5,5-trimethylcyclohex-2-enone 19**

A solution of **18** (5.00 g, 16.1 mmol) and aqueous HCl (1 mol dm^{-3} solution; 25 cm^3, 25 mmol) in THF (25 cm^3) was stirred at room temperature for 5 h, and then extracted with ethyl acetate. Concentration of the extract left a crystalline residue which was recrystallised from ethyl acetate–hexane (1:3) to afford the title compound **19** (3.60 g, 84%), mp 149–150 °C (Found: C, 67.6; H, 8.3. $C_{15}H_{22}O_4$ requires C, 67.5; H, 8.4%); ν_{max}(KBr)/cm^{-1} 3520 (OH), 2970 (CH), 1715 (C=O), 1670 (C=O), 1662 (C=C) and 1260 (C–O); δ_H(100 MHz) 1.03 (3 H, s, 5-Me), 1.08 (3 H, s, 5-Me), 1.35 [3 H, d, *J* 6, CH(OAc)*Me*], 1.96 (3 H, d, *J* 1, 3-Me), 2.07 (3 H, s, OCOMe), 2.30 (2 H, s, 6-H_2), 5.38–5.65 (2 H, m), 5.83 (1 H, d, *J* 1, 2-H) and 6.15 (1 H, qd, *J* 6, 2, C*H*OAc); *m/z* 266 (M^+, 0.1%), 210 (11), 205 (8), 151 (37), 150 (95), 135 (55), 124 (32), 122 (96), 79 (37) and 43 (100).

(8*R)-4-Hydroxy-4-[(*S**, *E*)-3-hydroxybut-1-enyl]-3,5,5-trimethylcyclohex-2-enone (Blumenol-A) 21** [19,23]

A stirred solution of **19** (105 mg, 0.39 mmol) in methanol (3 cm^3) was irradiated with a mercury high-pressure lamp (100 W) at 20 °C for 4.5 h, and was then concentrated. The residue, showing a mixture of **19** and two products in a ratio of 3:83:14 by capillary GC (FFS, 50 m, 240 °C), was chromatographed on silica gel with ethyl acetate–hexane (1:3–1:1) to afford the rearranged known product, 6-[(*E*)-3-acetoxybut-1-enyl]-2,6,6-trimethylcyclohexane-1,4-dione **22** (13 mg, 12%) and the (*E*)-olefinic ketone, (8*R**)-4-[(*S**,*E*)-3-acetoxybut-1-enyl]-4-hydroxy-3,5,5-trimethylcyclohex-2-enone **20** (79 mg, 75%), along with a small amount of **19**. **22**; ν_{max}(film)/cm^{-1} 2980 (CH), 1720 (C=O), 1240 (C–O) and 980 (C=C); δ_H(400 MHz) 1.14 (3 H, s, 2-Me), 1.18 (3 H, s, 2-Me), 1.24 (3 H, s, 6-Me), 1.26 [3 H, d, *J* 7, CH(OH)*Me*], 2.02 (3 H, s, OCOMe), 2.43 [1 H, d (of AB q), *J* 17, COCH], 2.60 [1 H, d (of AB q), *J* 19, COCH], 2.81 [1 H, d (of AB q), *J* 19, COCH], 2.82 [1 H, d (of AB q), *J* 17, COCH], 5.26 (1 H, dq, *J* 16, 7, C*H*OAc) and 5.44 (1 H, dd, *J* 16, 7, CH=C*H*–CH) and 5.68 (1 H, d, *J* 16, C*H*=CH–CH). **20**; ν_{max}(film)/cm^{-1} 3480 (OH), 1740 (C=O), 1660 (C=O), 1240 (C–O) and 975 (C=C); δ_H(100 MHz) 0.99 (3 H, s, 5-Me), 1.07 (3 H, s, 5-Me), 1.32 [3 H, d, *J* 6, CH(OAc)*Me*], 1.88 (3 H, d, *J* 1, 3-Me), 1.95 (1 H, br s, OH), 2.04 (3 H, s, OCOMe), 2.20 [1 H, d (of AB q), *J* 17, 6-H], 2.48 [1 H, d (of AB q), *J* 17, 6-H], 5.39 (1 H, qd, *J* 6, 2, C*H*OAc), 5.75–5.85 (2 H, m, CH=CH) and 5.91 (1 H, d, *J* 1, 2-H); *m/z* 266 (M^+, 0.2%), 206 (15), 151 (33), 150 (85), 135 (32), 124 (74), 122 (67), 79 (34) and 43 (100). To a solution of **20** (500 mg, 1.88 mmol) in methanol (20 cm^3) and chloroform (40 cm^3) was added NaOMe (1 mol dm^{-3} methanol solution; 6 cm^3, 6 mmol), and stirring was continued at room temperature for 6 h. The oily residue obtained upon evaporation was extracted with ethyl acetate. Evaporation of the extract left a residue which was chromatographed on silica gel with ethyl acetate–hexane (2:1) to afford the title natural product **21** (358 mg, 85%), mp 125–126 °C (lit.,[18] 116–118 °C); ν_{max}(KBr)/cm^{-1} 3380 (OH), 1670 (C=O), 1618 (C=C), 1128 (C–O) and 975 (C=C); δ_H(400 MHz) 1.02 (3 H, s, 5-Me), 1.08 (3 H, s, 5-Me), 1.30 [3 H, d, *J* 6.5, CH(OH)*Me*], 1.90 (3 H, s, 3-Me), 2.08 (1 H, br s, OH), 2.15 (2 H, br s, OH), 2.23 [1 H, d (of AB q), *J* 17.1, 6-H], 2.45 [1 H, d (of AB q), *J* 17.1, 6-H], 4.41 [1 H, dq, *J* 6.1, 5.9, C*H*(OH)Me], 5.78 [1 H, d, *J* 15.6, C*H*=CH(OH)Me], 5.85 [1 H, dd, *J* 15.6, 5.9, CH=C*H*(OH)Me] and 5.90 (1 H, s, 1-H); *m/z* 206 ($M^+ - H_2O$, 3%), 150 (14), 124 (100), 79 (24) and 43 (37).

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