Total synthesis of milbemycin E: development of a procedure for the introduction of the 3,4-double bond and synthesis of the C(1)–C(10) fragment

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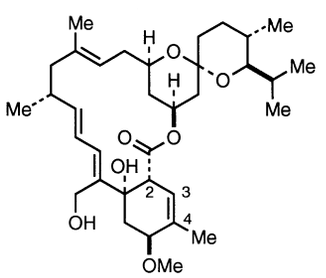
Dehydration of the 5-hydroxycyclohexanecarboxylate 13 gives the exocyclic alkene 14 rather than its endocyclic isomer. However, the 3,4-double bond can be introduced into precursors of milbemycin E 1 using oxidative elimination of phenylselanyl ketones. The hydroxycyclohexanones 6 and 31 have been converted into the phenylselanyl ketones 19 and 37, which on oxidative elimination followed by stereoselective reduction give the 3-methylcyclohex-2-enecarboxylates 23 and 40 together with only 10–15% of the exocyclic alkenes 24 and 42. Interestingly, if the oxidative elimination is carried out on the alcohol 25, the 5-methylenecyclohexanecarboxylate 24 is the major product. Conversion of 40 into its benzoate, and oxidation of the furan ring using singlet oxygen, gives the hydroxybutenolide 43 ready for incorporation into a milbemycin synthesis. To test the compatibilty of the cyclohexene double bond with the proposed Wittig reaction, the alcohol 40 has been converted into the *tert*-butyldimethylsilyl ether 44 and the furan oxidised to give the hydroxybutenolide 45. Condensation with an excess of (2-methylpropylidene)triphenylphosphorane gives the Wittig product which has been isolated as its methyl ester and isomerised using a trace of iodine into the (*Z*,*E*)-diene 47.

A convergent synthesis of milbemycin E **1** has been proposed based on the Wittig reaction between the phosphonium salt **2** and the hydroxybutenolide **3** (P = Me) as the key step.[1,2] The preceding paper reports the details of a synthesis of phosphonium salt **2**.[3] We now describe a synthesis of the hydroxybutenolide **3** (P = $SiMe_2Bu^t$), and an investigation into its participation in Wittig condensations.[4]



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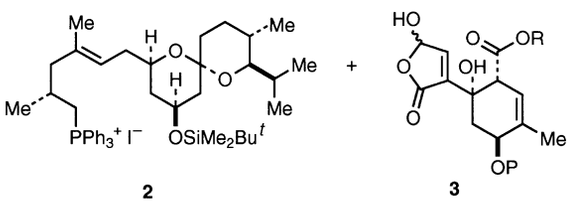
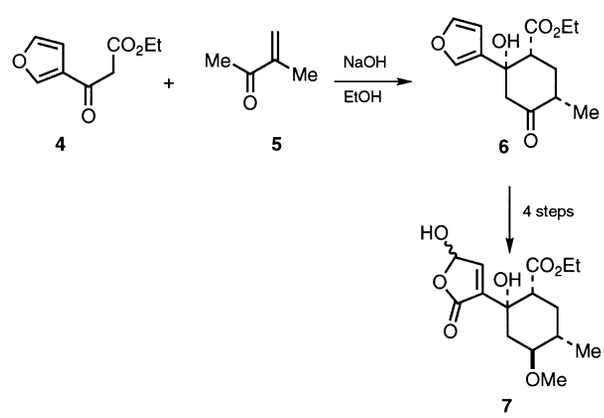


2 **3**

The hydroxybutenolide **7**, which differs from the required hydroxybutenolide **3** (P = Me) in lacking the milbemycin 3,4-double bond, has been used in preliminary investigations carried out to evaluate the viability of this approach to milbemycins and avermectins.[1] This double bond is important for biological activity and has a tendency to migrate to the 2,3-position.[5] Moreover, deconjugation is complicated by the formation of the alternative epimer at C(2).[6] Therefore it was necessary to develop a procedure for the regioselective introduction of the 3,4-double bond, and to show that migration into conjugation with the carboxy group at C(1) did not take place under the basic conditions required for the Wittig reaction. The hydroxybutenolide **7** had been obtained from the 2-furyl-2-hydroxy-4-oxocyclohexanecarboxylate **6** which, in turn, had been prepared from the keto ester **4** and 3-methylbut-3-en-2-one **5**.[1] It was decided to use the hydroxy-4-oxocyclohexanecarboxylate **6** as the starting material for the synthesis of the hydroxybutenolide **3**.



4 **5** **6** **7**

Results and discussion

Initial studies were directed towards the introduction of the double bond by dehydration of a tertiary alcohol. The hydroxycyclohexanecarboxylate **6**[1] was reduced using lithium tri-*sec*-butylborohydride to the 2,4-*cis*-diol **8**, addition of hydride

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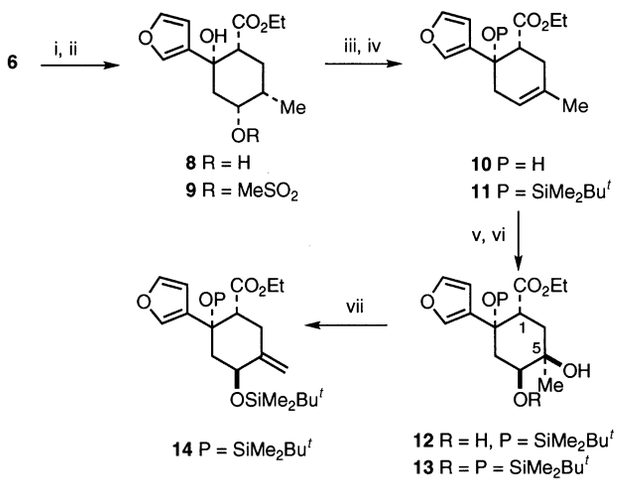


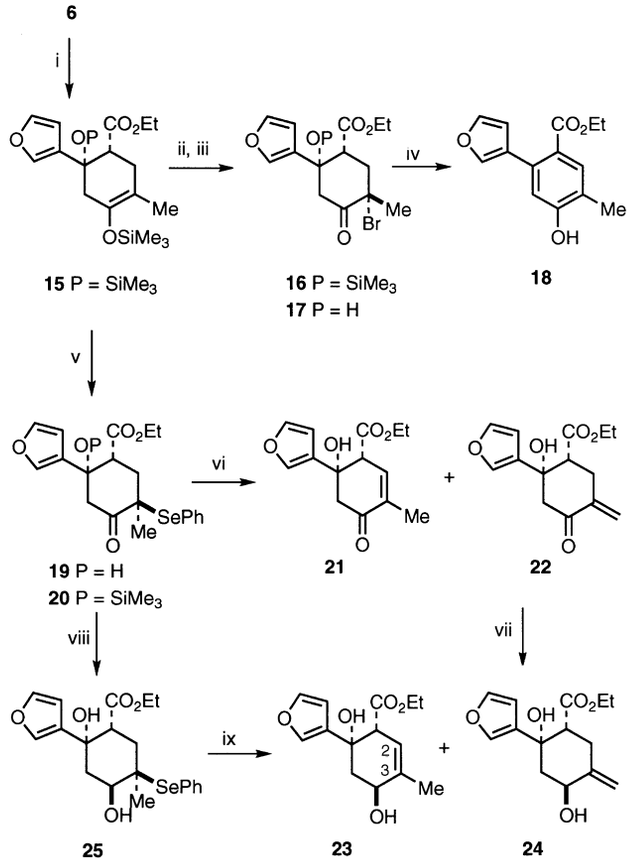
Scheme 1 *Reagents:* i, lithium tri-*sec*-butylborohydride; ii, methanesulfonyl chloride, pyridine; iii, 8-diazabicyclo[5.4.0]undec-7-ene, tetrahydrofuran, heat under reflux (53% from **8**); iv, *tert*-butyldimethylsilyl trifluoromethanesulfonate, 2,6-lutidine (100%); v, osmium tetraoxide, pyridine, then sodium hydrogen sulfite (91%); vi, *tert*-butyldimethylsilyl trifluoromethanesulfonate, 2,6-lutidine (90%); vii, methanesulfonyl chloride, triethylamine, dichloromethane (65%)

taking place on the less hindered face of the ketone (Scheme 1).[1] Treatment of this diol with methanesulfonyl chloride in pyridine gave the methanesulfonate **9** which was converted into the 6-hydroxycyclohex-3-enecarboxylate **10** using 8-diazabicyclo-[5.4.0]undec-7-ene in tetrahydrofuran heated under reflux. Protection of the tertiary alcohol as its *tert*-butyldimethylsilyl ether **11** was carried out using *tert*-butyldimethylsilyl trifluoromethanesulfonate, and the alkene was hydroxylated using osmium tetraoxide to give the *cis*-diol **12**.[7] Stereochemistry was assigned to this diol on the basis of addition of the osmium tetraoxide to the less hindered face of the alkene, and was confirmed by ^{1}H NOE studies on the bis-*tert*-butyldimethylsilyl ether **13**, no NOE effect being observed between the hydrogen at C(1) and the methyl group at C(5).

Attempts to dehydrate the alcohol **13** to the required 3-methylcyclohex-3-enecarboxylate gave only the isomeric 5-methylenecyclohexanecarboxylate **14**, *e.g.* methanesulfonyl chloride and triethylamine in dichloromethane gave the methylenecyclohexanecarboxylate **14** in 65% yield after chromatography. Preliminary studies into the isomerisation of the methylenecyclohexanecarboxylate into the 3-methylcyclohex-3-enecarboxylate were not encouraging, and although this rearrangement has been achieved by other workers,[8] it was decided to investigate an alternative procedure for the direct introduction of what is to become the 3,4-double bond.

The hydroxycyclohexanone **6** was converted regioselectively into the enol trimethylsilyl ether **15** by treatment with trimethylsilyl trifluoromethanesulfonate and triethylamine in carbon tetrachloride,[9] the formation of the silyl enol ether being accompanied by silylation of the tertiary hydroxy group (Scheme 2). The direct conversion of this enol ether into the corresponding cyclohexenone using palladium acetate and benzoquinone[10] or palladium acetate and diallyl carbonate,[11] gave only complex mixtures of products. Treatment with *N*-bromosuccinimide in tetrahydrofuran[12] gave the bromo ketone **16** in excellent yield with the configuration of the bromo ketone being established by NOE difference studies, but attempts to effect elimination of hydrogen bromide using either pyridine[13] or lithium carbonate and lithium bromide in dimethylformamide,[14] gave the phenol **18** as the only isolable product.

It was decided to investigate the oxidative elimination of a selenide to introduce the required double bond under non-basic conditions.[15,16] Treatment of the enol ether **15** with phenyl-



Scheme 2 *Reagents:* i, trimethylsilyl trifluoromethanesulfonate, triethylamine (100%); ii, *N*-bromosuccinimide, tetrahydrofuran (58%); iii, tetrabutylammonium fluoride (48%); iv, lithium bromide, lithium carbonate, *N*,*N*-dimethylformamide (42%); v, phenylselenenyl chloride, tetrabutylammonium fluoride (**19**, 84%; **20**, 12%); vi, 30% hydrogen peroxide, dichloromethane, 0 °C; vii, sodium triacetoxyborohydride, acetic acid (**23**, 61%; **24**, 9% from **19**); viii, sodium triacetoxyborohydride, acetic acid (83%); ix, 30% hydrogen peroxide, sodium hydrogen carbonate, dichloromethane, then add to carbon tetrachloride heated under reflux, 1 min (**23**, 9%; **24**, 70%)

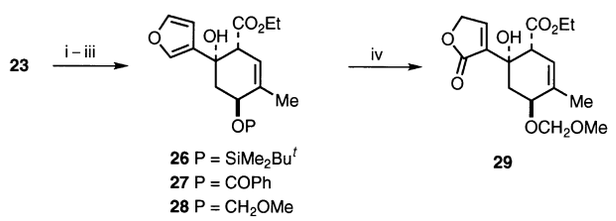
selenenyl chloride in the presence of tetrabutylammonium fluoride gave the phenylselanyl ketone **19** in which the phenylselanyl substituent had been introduced both stereo- and regioselectively and the tertiary alcohol had been desilylated, together with a small amount of the phenylselanyl ketone **20** in which the tertiary alcohol was still protected as its trimethylsilyl ether. Oxidative elimination was carried out by stirring a solution of the phenylselanyl ketone **19** in dichloromethane with aqueous hydrogen peroxide at 0 °C[17] and gave a mixture of the methylcyclohexenecarboxylate **21** and the isomeric 5-methylenecyclohexanecarboxylate **22**, ratio 85:15. Because it was thought that compound **21** would be unstable with respect to dehydration and tautomerism to the phenol **18**, no attempt was made to purify or separate these unsaturated ketones. Instead the mixture was immediately reduced using sodium triacetoxyborohydride[18] to give a mixture of the 4,6-dihydroxy-3-methylcyclohex-2-enecarboxylate **23** and the 2,4-dihydroxy-5-methylenecyclohexanecarboxylate **24** which were separated by flash chromatography and isolated in yields of 61% and 9%, respectively. These products were identified on the basis of spectroscopic data. For example, the ^{1}H NMR spectrum of the 4,6-dihydroxy-3-methylcyclohex-2-enecarboxylate **23** displayed a multiplet at δ 5.29 and a broadened singlet at δ 1.82 which were assigned to the vinylic proton at C(2) and the 3-CH_3 substituent respectively. The stereochemistry of the hydroxy group at C(4) followed from delivery of the triacetoxyborohydride reducing agent by the C(6)-hydroxy group.[18] The alcohol **23** was converted into its *tert*-butyldimethylsilyl ether **26**, its benzoate

27 and its methoxymethyl ether **28** ready for further manipulation.

To see whether the overall process would be more efficient if the sequence of oxidative elimination followed by reduction was reversed, the phenylselanyl ketone **19** was reduced with sodium triacetoxyborohydride to the alcohol **25**. Not surprisingly, oxidative elimination of the phenylselanyl substituent from the phenylselanyl alcohol was slower than from the phenylselanyl ketone **19**. However, when the oxidation was carried out using a mixture of aqueous hydrogen peroxide followed by brief heating in carbon tetrachloride under reflux to effect the elimination, a good yield of the alkenes **23** and **24** was obtained, but the regioselectivity had been reversed and the exocyclic alkene **24** was the major product, ratio **23**:**24** = 11:89.

The synthesis of the methylcyclohexenediol **23** had achieved the initial objective of this phase of our work, namely the introduction of what is to become the 3,4-double bond into precursors of the C(1)–C(10) fragment of a milbemycin. However, it remained to convert the furan ring of **23** into a hydroxybutenolide before the crucial Wittig reaction could be investigated. In the synthesis of the hydroxybutenolide **7** from the furan **6**,[1] this had been achieved by bromine oxidation and hydrolysis of the furan to a butenolide followed by free-radical bromination and hydrolysis to give the hydroxybutenolide. It was thought that these reactions would be incompatible with the presence of the cyclohexene double bond, but nevertheless it was decided to investigate them, albeit briefly.

Oxidation of the methoxymethyl ether **28** using bromine in methanol[1] gave a mixture of compounds which was hydrolysed directly using aqueous hydrogen chloride to give a modest yield of the butenolide **29**, identified from spectroscopic data (Scheme 3).[19,20] The regioselectivity of this oxidation of furan



Scheme 3 *Reagents:* i, *tert*-butyldimethylsilyl chloride, imidazole, *N*,*N*-dimethylformamide (62%); ii, benzoyl chloride, triethylamine, dichloromethane (60%); iii, chloromethyl methyl ether, diisopropylethylamine, dichloromethane (70%); iv, bromine, sodium acetate, methanol, then aqueous hydrogen chloride, tetrahydrofuran (26% from **28**)

28 has precedent,[1] and may be due to participation of the tertiary alcohol in the hydrolysis step. However, attempts at the free-radical bromination of the butenolide **29** using *N*-bromosuccinimide[1] gave complex mixtures of products which could not be separated or identified.

The hydroxybutenolide fragment would be incompatible with the methods used to introduce the 3,4-double bond; complications could arise, for example, during the phenylselanation of the ketone. Since it now appeared that the double bond was incompatible with the chemistry used to introduce the hydroxybutenolide, it was necessary to find an alternative procedure for this transformaton.

The oxidation of 2-trimethylsilylfurans using singlet oxygen has been reported as a regiospecific synthesis of hydroxybutenolides.[21] If this reaction could be carried out in the presence of the double bond, then it should give access to the hydroxybutenolide **3**. It was decided to investigate this possibility.

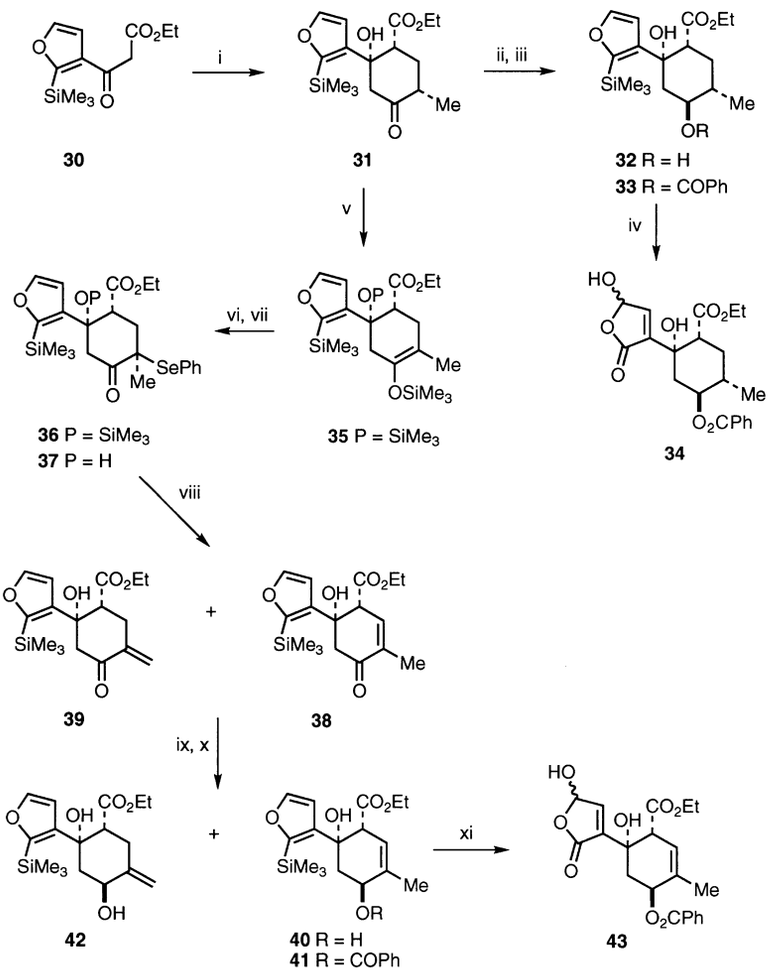
The Robinson reaction between ethyl 3-(2-trimethylsilyl-3-furyl)-3-oxopropanoate **30** and 3-methylbut-3-en-2-one **5** was carried out using sodium hydroxide in ethanol and gave the hydroxycyclohexanone **31** (58%) (Scheme 4).[1] Reduction using sodium triacetoxyborohydride gave the cyclohexanediol **32** which was converted into its monobenzoate **33**. Oxidation by bubbling oxygen through a solution in dichloromethane containing a catalytic amount of tetraphenylporphyrin at −78 °C gave the hydroxybutenolide **34**, as a mixture of epimers, identified by comparison of its spectroscopic data with those of other hydroxybutenolides prepared earlier.

Having shown that the oxidation of the silylated furans could be used to prepare hydroxybutenolides of the type required for our work, it was necessary to show that this chemistry could be carried out in the presence of what is to become the 3,4-double bond. The hydroxycyclohexanone **31** was converted into its trimethylsilyl enol ether **35** using trimethylsilyl trifluoromethanesulfonate and triethylamine. This procedure again gave the more substituted enol ether **35** and was accompanied by trimethylsilylation of the tertiary hydroxy group. Attempts to convert this enol ether into the phenylselanyl ketone **37** using phenylselenenyl chloride and tetrabutylammonium fluoride, following the procedure that had been used for the synthesis of **19**, were complicated by competing desilylation of the silylated furan. However, it was found that phenylselanation of the enol ether could be carried out by treatment with phenylselenenyl chloride alone which gave the phenylselanyl ketone **36** in which the tertiary alcohol was still silylated. Treatment with tetrabutylammonium fluoride in a separate step was not complicated by desilylation of the furan and gave the hydroxy phenylselanyl ketone **37**. Oxidative elimination of the phenylselanyl substituent was carried out using an excess of hydrogen peroxide and reduction of the mixture of the resultant unsaturated ketones **38** and **39** using sodium triacetoxyborohydride gave the methylcyclohexenediol **40** and the methylenecyclohexanediol **42**, ratio *ca*. 80:20. The exact ratio of the endo- and exo-cyclic alkenes obtained from this reaction was dependent upon the scale, better selectivity in favour of the required endo-isomer **40** being obtained for smaller scale reactions. Nevertheless yields of the methylcyclohexenediol **40** of 50–60% based on the phenylselanyl ketone **37** were obtained on the multi-gram scale. Benzoylation of the methylcyclohexenediol **40** gave the monobenzoate **41** which was oxidised using singlet oxygen following the procedure outlined above to give the hydroxybutenolide **43** as a mixture of epimers.

The structures of intermediates in this synthesis were assigned on the basis of spectroscopic data and precedent. The chiral centres at C(1) and C(2) [C(6) in unsaturated compounds] had been introduced during the preparation of the cyclohexanone **6**[1] and that at C(4) follows from the triacetoxyborohydride reduction.[18] The position of the double bond in **40** was confirmed by the ^{1}H NMR data with a singlet δ 1.92 (3 H), and a narrow multiplet at δ 5.38 (1 H), assigned to the 3-CH_3 group and H(2), respectively. At no stage in this work was there any evidence for migration of the double bond or for the equilibration of epimers, *e.g.* at C(1).‡ It would appear that the double bond had not interfered with the oxidation of the trimethylsilylfuran using singlet oxygen. It was now necessary to check the compatibility of this double bond with the Wittig reaction before attempting to complete a synthesis of milbemycin E **1**.

The 3-methylcyclohex-2-enediol **40** was converted into its

‡ The structure of the dihydroxycyclohexenecarboxylate **40** was checked by X-ray diffraction (O. S. Mills). Fig. 1 shows a projection of this ester which is consistent with the assigned structure (the ester **40** was racemic; the figure actually shows a projection of the enantiomer of **40** as depicted in the reaction schemes). *Crystal data:* $C_{17}H_{26}O_5Si$. M_r = 338.29, tetragonal, space group $I4_1/a$, Z = 16. At T = 293 K, a = 28.297(4), c = 9.536(1) Å, V = 7636(2) Å^3, λ(Mo-Kα) = 0.710 69 Å, D_x = 1.18 g cm^{-3}, μ = 1.48 cm^{-1}. Colourless needles, crystal dimensions 0.15 × 0.15 × 0.2 mm. Reflection intensities were collected on a CAD4 diffractometer using the θ–2θ scan method. Index limits were $0 \le h(k) \le 31$ and $-10 \le l = 0$. The structure was solved by direct methods (MULTAN[24]) and difference Fourier series. The structure was refined by our own full-matrix least-squares programme and converged to a final R = 10.1% for 2399 reflections, $|F| > 3\sigma(|F|)$, for 208 parameters (anisotropic thermal parameters for non-H atoms).



Scheme 4 *Reagents:* i, 3-methylbut-3-en-2-one **5**, sodium hydroxide, ethanol (58%); ii, sodium triacetoxyborohydride, acetic acid (81%); iii, benzoyl chloride, triethylamine, 4-dimethylaminopyridine, dichloromethane (60%); iv, oxygen, tetraphenylporphyrin, dichloromethane, *hν* (40%); v, trimethylsilyl trifluoromethanesulfonate, triethylamine, carbon tetrachloride (85%); vi, phenylselenenyl chloride, tetrahydrofuran (82%); vii, tetrabutylammonium fluoride, tetrahydrofuran (93%); viii, 30% aqueous hydrogen peroxide, dichloromethane, room temperature; ix, sodium triacetoxyborohydride, acetic acid (**40**, 57%; **42**, 17%; from **37**); x, benzoyl chloride, triethylamine, 4-dimethylaminopyridine, dichloromethane (60%); xi, oxygen, tetraphenylporphyrin, dichloromethane, *hν* (39%)

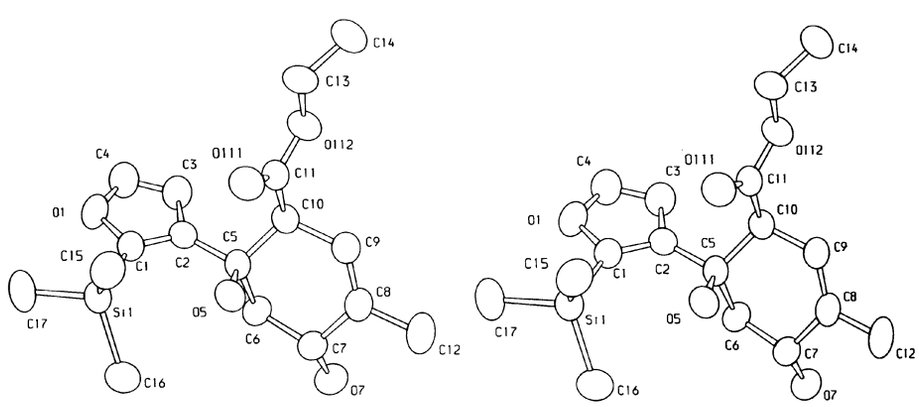
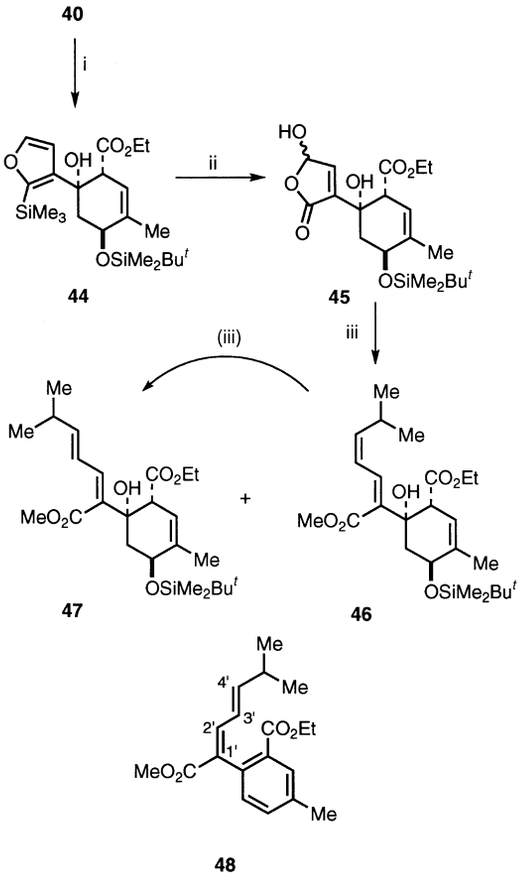


Fig. 1 Projection of the molecular structure of the ester **40** showing the crystallographic numbering system used

tert-butyldimethylsilyl monoether **44** which on oxidation using singlet oxygen gave the hydroxybutenolide **45** (Scheme 5). This was condensed with an excess of (2-methylpropylidene)triphenylphosphorane and the crude product mixture treated with diazomethane to give a mixture of the (*Z*,*Z*)- and (*Z*,*E*)-dienes **46** and **47**. This mixture of dienes was not separated. Rather it was stirred in benzene containing a trace of iodine, in daylight, to effect clean isomerisation of the (*Z*,*Z*)-isomer **46** into the (*Z*,*E*)-isomer **47** which was isolated in overall yields of *ca.* 60% based on the hydroxybutenolide **45**. No migration of the cyclohexene double bond was observed during this Wittig reaction providing the reaction was quenched below 0 °C. However, if the reaction mixture was allowed to warm to room temperature before being worked up, then a mixture of products was obtained in which the six-membered ring had aromatised. After treatment of this mixture with a catalytic amount of iodine, the major product isolated was provisionally identified as the (*E*,*E*)-isomer **48** from spectroscopic data. In particular, the 3′,4′-^{1}H coupling constant of 15 Hz was consistent with *E*-geometry across this double bond. The 1′,2′-double bond was assigned the *E*-stereochemistry from the unusually low chemical shift of the 3′-proton (δ 7.38). By keeping the temperature



Scheme 5 *Reagents:* i, *tert*-butyldimethylsilyl chloride, imidazole, *N*,*N*-dimethylformamide (85%); ii, oxygen, dichloromethane, tetraphenylporphyrin, *hν* (99%); iii, 3 mol equiv. 2-methylpropylidene(triphenyl)phosphorane, tetrahydrofuran, −78 °C to 0 °C then saturated aqueous ammonium chloride; diazomethane in ether; 5 mol% iodine, benzene (59% of **47** based on **45**)

of the reaction below −10 °C, aromatisation of the six-membered ring was avoided.

The work reported in this paper has provided hydroxybutenolides for incorportion into a synthesis of milbemycin E **1**. In particular, a procedure has been developed for the regioselective introduction of the 3,4-double bond, and the presence of this double bond has been found to be compatible with the Wittig reaction it is proposed to use in the final stages of the synthesis. One interesting aspect of the chemistry reported in this paper is the effect of the substituent at C(4) on the regioselectivity of the oxidative elimination of the phenyl selenide. The phenylselanyl ketones gave more of the endocyclic alkenes, whereas exocyclic alkenes were preferred if the ketones were reduced to the corresponding alcohols prior to the oxidative elimination step. The origin of this reversal in regioselectivity was not examined. It may be that conformational factors are involved if the six-membered ring has to adopt a boat conformation for the *syn*-elimination to take place. In particular, the hydroxy group in the hydroxy selenide would be forced into a hindered position in the preferred conformation for the oxidative elimination.[4] Alternatively, dipolar effects may be involved.[22] The following paper reports the completion of a synthesis of milbemycin E **1** using phosphonium salt **2** and hydroxybutenolide **3** (P = Me).[23]

Experimental

General experimental details are reported in the first paper in this series.[1]

Ethyl (1*RS*,6*SR*)-6-*tert*-butyldimethylsilyloxy-6-(3-furyl)-3-methylcyclohex-3-enecarboxylate 11

tert-Butyldimethylsilyl trifluoromethanesulfonate (0.48 cm^3, 1.8 mmol) was added dropwise to a stirred solution of ethyl (1*RS*,6*SR*)-6-(3-furyl)-6-hydroxy-3-methylcyclohex-3-enecarboxylate **10** (300 mg, 1.2 mmol)[1] and 2,6-lutidine (2,6-dimethylpyridine) (0.35 cm^3, 3.0 mmol) in dichloromethane (9.0 cm^3) at 0 °C. The mixture was stirred for 18 h at room temperature before the addition of water (5.0 cm^3). The two phases were separated and the aqueous phase extracted with ether (3 × 10 cm^3). The combined organic extracts were dried (Na_2SO_4) and concentrated under reduced pressure. Chromatography of the residue using light petroleum–ethyl acetate gave the *title compound* **11** (437 mg, 100%); ν_{max}/cm^{-1} 2860, 1730, 1260, 1186, 1095, 1075, 1040, 875 and 840; δ_H −0.17 and −0.03 (each 3 H, s, $SiCH_3$), 0.89 [9 H, s, $SiC(CH_3)_3$], 1.21 (3 H, t, *J* 7, $CO_2CH_2CH_3$), 1.65 (3 H, br s, 3-CH_3), 1.92 (1 H, dd, *J* 17, 6, 2-H), 2.30 (1 H, dd, *J* 17, 6, 2-H′), 2.57 and 2.77 (each 1 H, br d, *J* 17, 5-H), 2.85 (1 H, t, *J* 6, 1-H), 4.06 (2 H, m, $CO_2CH_2CH_3$), 5.40 (1 H, narrow m, 4-H), 6.40 (1 H, br s, 4′-H) and 7.30 (2 H, m, 2′-H and 5′-H); *m/z* (CI) 307 (M^+ − 57, 50%) and 233 (100).

Ethyl (1*RS*,2*SR*,4*SR*,5*RS*)-2-*tert*-butyldimethylsilyloxy-4,5-dihydroxy-2-(3-furyl)-5-methylcyclohexanecarboxylate 12

Osmium tetraoxide (500 mg, 1.97 mmol) in pyridine (10 cm^3) was added dropwise to a stirred solution of the 3-methylcyclohexenecarboxylate **11** (650 mg, 1.79 mmol) in pyridine (15 cm^3) at −30 °C. After 15 min, aqueous sodium hydrogen sulfite (0.6 M; 15 cm^3) and pyridine (2.5 cm^3) were added to the reaction, and the resulting mixture was allowed to warm to room temperature with stirring over 30 min. After extraction with chloroform (5 × 20 cm^3), the organic extracts were washed with aqueous hydrogen chloride (1 M; 2 × 20 cm^3) and brine (20 cm^3) and dried (Na_2SO_4). Concentration under reduced pressure gave a residue which was chromatographed using light petroleum–ethyl acetate (2:1) as eluent to give the *title compound* **12** (651 mg, 91%) as white needles, mp 112–113 °C (from ether) (Found: C, 60.0; H, 8.8. $C_{20}H_{34}O_6Si$ requires C, 60.3; H, 8.6%); ν_{max}/cm^{-1} 3620, 3570, 3460, 2860, 1730, 1260, 1170, 1095, 1030, 980 and 835; δ_H −0.19 and 0.06 (each 3 H, s, $SiCH_3$), 0.95 [9 H, s, $SiC(CH_3)_3$], 1.16 (3 H, t, *J* 7, $CO_2CH_2CH_3$), 1.34 (3 H, s, 5-CH_3), 1.77 (1 H, dd, *J* 14, 3.5, 6-H), 2.07 (1 H, br s, OH), 2.20 (3 H, m, 3-H_2 and 6-H′), 2.80 (1 H, dd, *J* 13, 3.5, 1-H), 3.87 (1 H, dd, *J* 10, 6, 4-H), 4.05 (2 H, m, $CO_2CH_2CH_3$), 6.30 (1 H, br s, 4′-H) and 7.31 (2 H, br s, 2′-H and 5′-H); *m/z* (CI) 383 (M^+ − 15, 10%), 341 (100) and 249 (80).

Ethyl (1*RS*,2*SR*,4*SR*,5*RS*)-2,4-bis(*tert*-butyldimethylsilyloxy)-2-(3-furyl)-5-hydroxy-5-methylcyclohexanecarboxylate 13

tert-Butyldimethylsilyl trifluoromethanesulfonate (0.250 cm^3, 1.1 mmol) was added dropwise to the diol **12** (290 mg, 0.73 mmol) in dichloromethane (10 cm^3) at 0 °C. Water (4 cm^3) was added, the layers were separated and the aqueous phase was extracted with ether (3 × 8 cm^3). The organic extracts were dried (Na_2SO_4) and concentrated under reduced pressure. Chromatography of the residue using light petroleum–ether (5:1) as eluent, gave the *title compound* **13** (336 mg, 90%) (Found: C, 60.6; H, 10.0. $C_{26}H_{48}O_6Si_2$ requires C, 60.9; H, 9.4%); ν_{max}/cm^{-1} 3570, 2860, 1740, 1255, 1180, 1090, 990, 890, 840 and 780; δ_H −0.14, 0.04, 0.11 and 0.13 (each 3 H, s, $SiCH_3$), 0.92 and 0.95 [each 9 H, s, $SiC(CH_3)_3$], 1.17 (3 H, t, *J* 7, $CO_2CH_2CH_3$), 1.22 (3 H, s, 5-CH_3), 1.85 (1 H, dd, *J* 13, 3, 6-H), 2.18 (3 H, m, 3-H_2 and 6-H′), 2.39 (1 H, br s, OH), 2.88 (1 H, dd, *J* 13, 3, 1-H), 3.96 (1 H, dd, *J* 11, 5, 4-H), 4.06 (2 H, m, $CO_2CH_2CH_3$), 6.32 (1 H, br s, 4′-H) and 7.34 (2 H, m, 2′-H and 5′-H); *m/z* (CI) 455 (M^+ − 57, 65%) and 363 (100).

Ethyl (1*RS*,2*SR*,4*SR*)-2,4-bis(*tert*-butyldimethylsilyloxy)-2-(3-furyl)-5-methylenecyclohexanecarboxylate 14

Methanesulfonyl chloride (0.192 cm^3, 2.5 mmol) was added dropwise to the alcohol **13** (640 mg, 1.25 mmol) and triethylamine (0.695 cm^3, 5.0 mmol) in dichloromethane (20 cm^3) at −15 °C. After 2 h, water (5 cm^3) and ether (20 cm^3) were added.

The layers were separated and the aqueous phase was extracted with ether (3 × 20 cm^3). The organic extracts were dried ($MgSO_4$) and concentrated under reduced pressure. Chromatography of the residue using light petroleum–ether (20:1) as eluent gave the *title compound* **14** (403 mg, 65%), mp 68–70 °C (from pentane) (Found: C, 63.5; H, 9.5. $C_{26}H_{46}O_5Si_2$ requires C, 63.1; H, 9.4%); ν_{max}/cm^{-1} 2860, 1730, 1470, 1460, 1255, 1110, 1030, 897, 875 and 840; δ_H −0.13 and 0.06 (each 3 H, s, $SiCH_3$), 0.11 (6 H, s, $SiCH_3$), 0.94 and 0.96 [each 9 H, s, $SiC(CH_3)_3$], 1.20 (3 H, t, *J* 7, $CO_2CH_2CH_3$), 1.83 (1 H, dd, *J* 13, 11, 3-H), 2.45 (3 H, m, 1-H, 3-H′ and 6-H), 2.86 (1 H, m, 6-H′), 4.08 (2 H, m, $CO_2CH_2CH_3$), 4.57 (1 H, m, 4-H), 4.84 and 5.06 (each 1 H, br s, vinylic H), 6.36 (1 H, br s, 4′-H) and 7.33 (2 H, m, 2′-H and 5′-H); *m/z* (EI) 479 (M^+ − 15, 10%), 437 (100) and 363 (30).

Ethyl (1*RS*,6*SR*)-4,6-bis(trimethylsilyloxy)-6-(3-furyl)-3-methylcyclohex-3-enecarboxylate 15

Trimethylsilyl trifluoromethanesulfonate (3.63 cm^3, 18.8 mmol) was added dropwise to a stirred solution containing the cyclohexanone **6** (2 g, 7.52 mmol) and triethylamine (3.15 cm^3, 22.6 mmol) in carbon tetrachloride (40 cm^3) at 0 °C. After warming to room temperature, the mixture was stirred for 2 days, water (15 cm^3) was added, the two phases were separated and the aqueous phase was extracted with ether (3 × 20 cm^3). The organic extracts were dried (Na_2SO_4) and concentrated under reduced pressure. Chromatography of the residue using light petroleum–ethyl acetate (20:1) as eluent gave the *title compound* **15** (3.08 g, 99.7%); ν_{max}/cm^{-1} 1740, 1260, 1180 and 830 cm^{-1}; δ_H 0.00 and 0.24 [each 9 H, s, $Si(CH_3)_3$], 1.23 (3 H, t, *J* 7, $CO_2CH_2CH_3$), 1.51 (3 H, br s, 3-CH_3), 1.91 (1 H, m, 2-H), 2.16 (1 H, m, 2-H′), 2.53 (1 H, br d, *J* 16, 5-H), 2.9 (2 H, m, 1-H and 5-H′), 4.11 (2 H, m, $CO_2CH_2CH_3$), 6.39 (1 H, br s, 4′-H) and 7.30 (2 H, m, 2′-H and 5′-H); *m/z* (CI) 411 (M^+ + 1, 1.5%) and 321 (100).

Ethyl (1*RS*,2*SR*,5*SR*)-5-bromo-2-(3-furyl)-5-methyl-4-oxo-2-trimethylsilyloxycyclohexanecarboxylate 16

N-Bromosuccinimide (215 mg, 1.2 mmol) in tetrahydrofuran (10 cm^3) was added slowly at 0 °C to the enol trimethylsilyl ether **15** (500 mg, 1.2 mmol) in tetrahydrofuran (10 cm^3). The mixture was stirred for 20 min before the addition of ether (20 cm^3) and water (5 cm^3). The aqueous phase was extracted with ether (3 × 15 cm^3), and the combined organic extracts dried ($MgSO_4$) and concentrated under reduced pressure. Chromatography of the residue using light petroleum–ethyl acetate (20:1) as eluent gave the *title compound* **16** (298 mg, 58%); ν_{max}/cm^{-1} 1730, 1385, 1260, 1180, 1100, 1055, 1000, 880, 860 and 850; δ_H 0.00 [9 H, s, $Si(CH_3)_3$], 1.12 (3 H, t, *J* 7.5, $CO_2CH_2CH_3$), 1.87 (3 H, br s, 5-CH_3), 2.35 (1 H, dd, *J* 15, 4, 6-H), 2.68 (1 H, dd, *J* 15, 12, 6-H′), 2.75 (1 H, d, *J* 16, 3-H), 3.21 (1 H, dd, *J* 12, 4, 1-H), 3.65 (1 H, d, *J* 16, 3-H′), 4.02 (2 H, m, $CO_2CH_2CH_3$), 6.27 (1 H, m, 4′-H), 7.37 (2 H, m, 2′-H and 5′-H); *m/z* (CI) 418 and 416 (M^+ + 1, each 1%) and 249 (100).

Ethyl (1*RS*,2*SR*,5*SR*)-5-bromo-2-(3-furyl)-2-hydroxy-5-methyl-4-oxocyclohexanecarboxylate 17

Tetrabutylammonium fluoride (1 M in tetrahydrofuran; 0.528 cm^3, 0.528 mmol) was added dropwise to the trimethylsilyl ether **16** (200 mg, 0.48 mmol) in tetrahydrofuran (5 cm^3) at room temperature. After 5 min, ether (25 cm^3) and water (10 cm^3) were added. The layers were separated and the aqueous phase was extracted with ether (3 × 20 cm^3). The organic extracts were dried ($MgSO_4$) and concentrated under reduced pressure. Chromatography of the residue using light petroleum–ethyl acetate (20:1) as eluent gave the *title compound* **17** (80 mg, 48%); ν_{max}/cm^{-1} 3480, 3150, 1725, 1380, 1190, 1040, 975, 915, 880 and 735; δ_H 1.14 (3 H, t, *J* 7, $CO_2CH_2CH_3$), 1.48 (3 H, s, 5-CH_3), 2.20 (1 H, dd, *J* 13, 4, 6-H), 2.37 (1 H, t, *J* 13, 6-H′), 2.75 (2 H, m, 3-H_2), 3.20 (1 H, dd, *J* 13, 4, 1-H), 4.08 (2 H, m, $CO_2CH_2CH_3$), 4.37 (1 H, br s, OH), 6.33 (1 H, br, 4′-H) and 7.35 (2 H, m, 2′-H and 5′-H); *m/z* (EI) 312, 314 (9%).

Ethyl 2-(3-furyl)-4-hydroxy-5-methylbenzoate 18

Lithium bromide (186 mg) and lithium carbonate (117 mg) were added to a solution of the hydroxycyclohexanone **17** (100 mg, 0.24 mmol) in dimethylformamide (3 cm^3). The mixture was heated under reflux for 16 h before pouring into water (5 cm^3). The mixture was extracted with ether (5 × 10 cm^3) and the organic phases were dried (Na_2SO_4) and concentrated under reduced pressure. Chromatography of the residue using light petroleum–ethyl acetate (5:1) as eluent gave the *title compound* **18** (25 mg, 42%); ν_{max}/cm^{-1} 3600, 3380, 1700, 1620, 1580, 1370, 1330, 1280, 1165, 1115, 1025, 915 and 880; δ_H 1.24 (3 H, t, *J* 7, $CO_2CH_2CH_3$), 2.27 (3 H, s, 5-CH_3), 4.21 (2 H, q, *J* 7, $CO_2CH_2CH_3$), 5.85 (1 H, br s, OH), 6.42 (1 H, m, 4′-H), 6.72 (1 H, s, 6-H), 7.38 and 7.43 (each 1 H, m, 2′-H and 5′-H) and 7.65 (1 H, s, 3-H); *m/z* (CI) 247 (M^+ + 1, 100%).

Ethyl (1*RS*,2*SR*,5*RS*)-2-(3-furyl)-2-hydroxy-5-methyl-4-oxo-5-phenylselanylcyclohexanecarboxylate 19

Tetrabutylammonium fluoride (1 M in tetrahydrofuran; 28.5 cm^3, 28.5 mmol) was diluted with tetrahydrofuran (25 cm^3) and stirred with activated molecular sieves for 20 h at room temperature. After cooling to 0 °C, phenylselenenyl chloride (3.29 g, 17 mmol) and the enol trimethylsilyl ether **15** (4.69 g, 11 mmol) in tetrahydrofuran (20 cm^3) were added dropwise over 5 min. The mixture was stirred for 25 min at 0 °C before the addition of water (25 cm^3) and extraction of the aqueous phase with ether (4 × 20 cm^3). The organic extracts were dried ($MgSO_4$) and concentrated under reduced pressure. Chromatography of the residue using gradient elution, with light petroleum–ethyl acetate (25:1 to 6:1) as eluent, gave two products. The less polar product was identified as *ethyl* (1RS,2SR,5RS)-2-(3-*furyl*)-5-*methyl*-4-*oxo*-5-*phenylselanyl*-2-*trimethylsilyloxycyclohexanecarboxylate* **20** (682 mg, 12%) (Found: C, 56.1; H, 6.1. $C_{23}H_{30}O_5SeSi$ requires C, 56.0; H, 6.1%); ν_{max}/cm^{-1} 1740, 1700, 1440, 1380, 1250, 1170, 1115, 1095, 1050, 1035, 1020, 995, 875, 860, 845 and 740; δ_H 0.01 [9 H, s, $Si(CH_3)_3$], 1.14 (3 H, t, *J* 7, $CO_2CH_2CH_3$), 1.46 (3 H, s, 5-CH_3), 2.18 (1 H, dd, *J* 15, 3.5, 6-H), 2.76 (2 H, m, 3-H and 6-H′), 3.25 (1 H, dd, *J* 13, 3.5, 1-H), 3.88 (1 H, d, *J* 15, 3-H′), 4.03 (2 H, m, $CO_2CH_2CH_3$), 6.32 (1 H, br s, 4′-H) and 7.31–7.48 (7 H, m, aromatic H, 2′-H and 5′-H); *m/z* (EI) 494 (M^+, 1%) and 379 (M^+ − 15, 1.5). The more polar product was identified as the *title compound* **19** (4.06 g, 84%), mp 93–94 °C (from ether) (Found: C, 57.3; H, 5.3. $C_{20}H_{22}O_5Se$ requires C, 57.0; H, 5.3%); ν_{max}/cm^{-1} 3490, 1705, 1440, 1380, 1185, 1165, 1030 and 880; δ_H 1.17 (3 H, t, *J* 7, $CO_2CH_2CH_3$), 1.47 (3 H, s, 5-CH_3), 2.29 (1 H, dd, *J* 14.5, 4, 6-H), 2.58 (2 H, m, 3-H and 6-H′), 3.65 (2 H, m, 1-H and 3-H′), 4.09 (2 H, m, $CO_2CH_2CH_3$), 4.19 (1 H, d, *J* 3, OH), 6.41 (1 H, br s, 4′-H) and 7.27–7.50 (7 H, m, aromatic H, 2′-H and 5′-H); *m/z* (CI) 405 (M^+ − 17, 60%), 403 (M^+ − 17, 30) and 249 (100).

Ethyl (1*RS*,4*SR*,6*SR*)-4,6-dihydroxy-6-(3-furyl)-3-methylcyclohex-2-enecarboxylate 23

Hydrogen peroxide (30% w/w in water; 1.08 cm^3, 9.5 mmol) was added to a rapidly stirred solution of the keto selenide **19** (400 mg, 0.95 mmol) in dichloromethane (20 cm^3) at 0 °C. After 15 min, the mixture was diluted with dichloromethane (20 cm^3) and washed with water (2 × 10 cm^3), dried (Na_2SO_4) and concentrated under reduced pressure. The residue was added to sodium triacetoxyborohydride in acetic acid (0.53 M; 3.6 cm^3) at room temperature and the mixture stirred for 1 h at room temperature. The mixture was concentrated under reduced pressure, diluted with ether (20 cm^3) and washed with aqueous sodium hydrogen carbonate (2 × 5 cm^3) and brine (5 cm^3). The organic layer was dried ($MgSO_4$) and concentrated under reduced pressure. Chromatography of the residue using light petroleum–ethyl acetate (2:1) as eluent gave two products. The less polar was identified as *ethyl* (1RS,2SR,4SR)-2,4-*dihydroxy*-2-(3-*furyl*)-5-*methylenecyclohexanecarboxylate* **24** (23 mg, 9%)

(Found: C, 62.9; H, 7.1. $C_{14}H_{18}O_5$ requires C, 63.1; H, 6.8%); ν_{max}/cm^{-1} 3470, 1710, 1380, 1185, 1165, 1030, 915, 875 and 735; δ_H 1.15 (3 H, t, *J* 7, $CO_2CH_2CH_3$), 1.50 (1 H, ddd, *J* 13, 12, 2, 3-H), 2.07 (1 H, br s, 4-OH), 2.38 (1 H, dd, *J* 13, 5, 3-H′), 2.55 (1 H, m), 2.75 (2 H, m), 4.06 (2 H, m, $CO_2CH_2CH_3$), 4.52 (1 H, d, *J* 2, 2-OH), 4.61 (1 H, m, 4-H), 4.93 and 5.1 (each 1 H, br s, vinylic H), 6.30 (1 H, br s, 4′-H) and 7.32 (2 H, br s, 2′-H and 5′-H); *m/z* (EI) 266 (M^+, 6%), 248 (6) and 203 (6). The more polar was identified as the *title compound* **23** (153 mg, 61%) (Found: C, 63.2; H, 7.0. $C_{14}H_{18}O_5$ requires C, 63.1; H, 6.8%); ν_{max}/cm^{-1} 3440, 1710, 1190, 1165, 1020, 915, 880 and 725; δ_H 1.18 (3 H, t, *J* 7, $CO_2CH_2CH_3$), 1.73 (1 H, ddd, *J* 13, 9, 2, 5-H), 1.82 (3 H, br s, 3-CH_3), 2.41 (1 H, dd, *J* 13, 5, 5-H′), 2.66 (1 H, br s, 4-OH), 3.46 (1 H, m, 1-H), 4.10 (2 H, q, *J* 7, $CO_2CH_2CH_3$), 4.46 (1 H, m, 4-H), 4.69 (1 H, d, *J* 2, 6-OH), 5.29 (1 H, m, 2-H), 6.32 (1 H, m, 4′-H) and 7.33 (2 H, m, 2′-H and 5′-H); *m/z* (EI) 266 (M^+, 3%) and 248 (8).

Ethyl (1*RS*,2*SR*,4*SR*,5*RS*)-2,4-dihydroxy-2-(3-furyl)-5-methyl-5-phenylselanylcyclohexanecarboxylate 25

Sodium triacetoxyborohydride in glacial acetic acid (0.53 M; 3.0 cm^3) was added to the phenylseleno ketone **19** (295 mg, 0.70 mmol) and the mixture stirred at room temperature for 1 h. After concentration under reduced pressure, the residue was dissolved in ether (15 cm^3), and washed with aqueous sodium hydrogen carbonate (2 × 5 cm^3) and brine (5 cm^3), then dried ($MgSO_4$). Concentration under reduced pressure gave a residue which was chromatographed using light petroleum–ethyl acetate (5:1) as eluent to give the *title compound* **25** (247 mg, 83%), mp 144–145 °C (from ether) (Found: C, 56.8; H, 5.7. $C_{20}H_{24}O_5Se$ requires C, 56.75; H, 5.7%); ν_{max}/cm^{-1} 3610, 3490, 3010, 1710, 1380, 1190, 1060, 1030 and 975; δ_H 1.17 (3 H, t, *J* 7, $CO_2CH_2CH_3$), 1.47 (3 H, s, 5-CH_3), 1.79 (1 H, dd, *J* 14, 4, 6-H), 1.95 (2 H, m, 3-H and 6-H′), 2.10 (1 H, br s, 4-OH), 2.16 (1 H, dd, *J* 14, 5, 3-H′), 3.45 (1 H, dd, *J* 13, 4, 1-H), 3.90 (1 H, m, 4-H), 4.05 (2 H, q, *J* 7, $CO_2CH_2CH_3$), 4.46 (1 H, d, *J* 3, 2-OH), 6.41 (1 H, m, 4′-H), 7.37 (5 H, m, 2′-H, 5′-H and aromatic H) and 7.70 (2 H, m, aromatic H); *m/z* (EI) 424 (M^+, 1.8%), 422 (M^+, 1.5) and 249 (100).

Ethyl (1*RS*,2*SR*,4*SR*)-2,4-dihydroxy-2-(3-furyl)-5-methylene-cyclohexanecarboxylate 24

Hydrogen peroxide (30% w/w in water; 6.28 cm^3, 55 mmol) and aqueous sodium hydrogen carbonate (5 cm^3) were added to a rapidly stirred solution of the phenylselanylcyclohexanecarboxylate **25** (1.47 g, 5.5 mmol) in dichloromethane (25 cm^3) at 0 °C. The mixture was rapidly stirred for 2 h, then syringed into carbon tetrachloride (40 cm^3) which was being heated under reflux. After 1 min, the mixture was cooled, washed with aqueous sodium hydrogen carbonate (2 × 20 cm^3) and dried ($MgSO_4$). Concentration under reduced pressure gave a residue which was chromatographed using gradient elution with light petroleum–ethyl acetate (3:1 to 2:1) as eluent to give the 4-methylenecyclohexanecarboxylate **24** (644 mg, 70%) and the 3-methylcyclohexenecarboxylate **23** (86 mg, 9%) which had spectroscopic data identical with those obtained previously.

Ethyl (1*RS*,4*SR*,6*SR*)-4-*tert*-butyldimethylsilyloxy-6-(3-furyl)-6-hydroxy-3-methylcyclohex-2-enecarboxylate 26

tert-Butyldimethylsilyl chloride (118 mg, 0.78 mmol) was added to a solution of imidazole (81 mg, 1.2 mmol) and the dihydroxycyclohexenecarboxylate **23** (160 mg, 0.60 mmol) in dimethylformamide (3 cm^3), and the mixture stirred for 18 h before the addition of ether (10 cm^3) and water (5 cm^3). The aqueous phase was extracted with ether (3 × 10 cm^3) and the organic extracts were washed with water (5 cm^3) and brine (5 cm^3). After drying ($MgSO_4$), concentration under reduced pressure of the organic extracts gave a residue which was chromatographed using light petroleum–ethyl acetate (10:1) as eluent to give the *title compound* **26** (142 mg, 62%), mp 110–112 °C (from ether); ν_{max}/cm^{-1} 3620, 3480, 1710, 1380, 1185, 1030, 880 and 725; δ_H 0.10 and 0.13 (each 3 H, s, $SiCH_3$), 0.90 [9 H, s, $SiC(CH_3)_3$], 1.12 (3 H, t, *J* 7, $CO_2CH_2CH_3$), 1.74 (1 H, m, 5-H), 1.80 (3 H, br s, 3-CH_3), 2.32 (1 H, dd, *J* 12.5, 5-H′), 3.48 (1 H, m, 1-H), 4.12 (2 H, q, *J* 7, $CO_2CH_2CH_3$), 4.55 (1 H, m, 4-H), 4.69 (1 H, d, *J* 2, 6-OH), 5.28 (1 H, m, 2-H), 6.33 (1 H, br s, 4′-H) and 6.35 (2 H, m, 2′-H and 5′-H); *m/z* (CI), 380 (M^+, 3%), 363 (40) and 231 (100).

Ethyl (1*RS*,4*SR*,6*SR*)-4-benzoyloxy-6-(3-furyl)-6-hydroxy-3-methylcyclohex-2-enecarboxylate 27

Benzoyl chloride (0.1 cm^3, 0.9 mmol) was added dropwise to a solution of triethylamine (0.17 cm^3, 1.2 mmol) and the dihydroxycyclohexenecarboxylate **23** (160 mg, 0.6 mmol) in dichloromethane (2.5 cm^3) at 0 °C. The reaction was allowed to warm to room temperature, stirred for 7 h and diluted by the addition of dichloromethane (15 cm^3). The organic phase was washed with water (3 cm^3), aqueous hydrogen chloride (1 M; 3 cm^3) and water (3 cm^3) and dried ($MgSO_4$). Concentration under reduced pressure gave a residue which was chromatographed using light petroleum–ethyl acetate (6:1) as eluent to give the *title compound* **27** (133 mg, 60%) recrystallised as needles, mp 105–106 °C (from ether) (Found: C, 68.0; H, 6.0. $C_{21}H_{22}O_7$ requires C, 68.1; H, 6.0%); ν_{max}/cm^{-1} 3470, 1710, 1450, 1370, 1305, 1265, 1170, 1110, 1070, 1020, 960, 870 and 850; δ_H 1.16 (3 H, t, *J* 7, $CO_2CH_2CH_3$), 1.77 (3 H, s, 3-CH_3), 1.90 (1 H, dd, *J* 13, 10, 5-H), 2.62 (1 H, dd, *J* 13, 6, 5-H′), 3.56 (1 H, m, 1-H), 4.09 (2 H, q, *J* 7, $CO_2CH_2CH_3$), 4.53 (1 H, br s, 6-OH), 5.46 (1 H, m, 2-H), 5.91 (1 H, m, 4-H), 6.32 (1 H, br s, 4′-H), 7.27–7.97 (7 H, m, 2′-H, 5′-H and aromatic H); *m/z* (CI) 388 (M^+ + 18, 45%) and 353 (100).

Ethyl (1*RS*,4*SR*,6*SR*)-6-(3-furyl)-6-hydroxy-4-methoxymethoxy-3-methylcyclohex-2-enecarboxylate 28

Chloromethyl methyl ether (0.2 cm^3, 2.59 mmol) was added dropwise to a solution of diisopropylethylamine (0.6 cm^3, 3.46 mmol) and the dihydroxycyclohexenecarboxylate **23** (460 mg, 1.73 mmol) in dichloromethane (7 cm^3) at 0 °C. The mixture was heated under reflux for 17 h before being cooled to room temperature and diluted with dichloromethane (30 cm^3). The solution was washed with hydrochloric acid (1 M; 2 × 5 cm^3), water (5 cm^3) and brine (5 cm^3) and dried ($MgSO_4$). Concentration under reduced pressure and chromatography with gradient elution using light petroleum–ethyl acetate (6:1 to 4:1) as eluent gave the *title compound* **28** (375 mg, 70%); ν_{max}/cm^{-1} 3480, 3110, 1710, 1370, 1340, 1190, 1165, 1150, 1100, 1045 and 1030; δ_H 1.21 (3 H, t, *J* 7, $CO_2CH_2CH_3$), 1.78 (1 H, m, 5-H), 2.52 (1 H, dd, *J* 12, 5, 5-H′), 3.38 (3 H, s, OCH_3), 3.50 (1 H, m, 1-H), 4.13 (2 H, q, *J* 7, $CO_2CH_2CH_3$), 4.44 (1 H, m, 4-H), 4.61 (1 H, d, *J* 2, 6-OH), 4.67 and 4.75 (each 1 H, d, *J* 7.5, $CHHOCH_3$), 5.35 (1 H, m, 2-H), 6.35 (1 H, br s, 4′-H) and 7.35 (2 H, m, 2′-H and 5′-H); *m/z* (EI) 310 (M^+, 1%) and 248 (25).

Ethyl (1*RS*,4*SR*,6*SR*)-6-(2-oxo-1-oxacyclopent-3-en-3-yl)-6-hydroxy-4-methoxymethoxy-3-methylcyclohex-2-enecarboxylate 29

Bromine (0.1 M in methanol; 3.0 cm^3) was added slowly to the methoxymethyl ether **28** (93 mg, 0.302 mmol) and sodium acetate (82 mg) in methanol (5 cm^3) at 0 °C. The mixture was warmed to room temperature and stirred for 10 min. Concentration under reduced pressure gave a residue which was dissolved in ether (25 cm^3) and the solution washed with aqueous sodium hydrogen carbonate (2 × 15 cm^3) and dried (K_2CO_3). Concentration under reduced pressure gave a residue which was dissolved in tetrahydrofuran (3 cm^3) and aqueous hydrogen chloride (3 M; 1 cm^3) was added at room temperature. After 0.5 h, the mixture was diluted with ether (30 cm^3) and washed with aqueous sodium hydrogen carbonate (2 × 5 cm^3) and water (5 cm^3) and dried ($MgSO_4$). Concentration under reduced pressure and chromatography using ethyl acetate–light petroleum

(2:1) as eluent gave the *title compound* **29** (22 mg, 26%) (Found: C, 58.9; H, 7.2. $C_{16}H_{22}O_7$ requires C, 58.9; H, 6.8%); ν_{max}/cm^{-1} 3470, 3005, 1750, 1710, 1450, 1370, 1350, 1195, 1150, 1100, 1040 and 1025; δ_H 1.24 (3 H, t, *J* 7, $CO_2CH_2CH_3$), 1.83 (3 H, br s, 3-CH_3), 2.22 (2 H, m, 5-H_2), 3.37 (3 H, s, OCH_3), 3.40 (1 H, m, 1-H), 4.13 (2 H, m, $CO_2CH_2CH_3$), 4.37 (1 H, m, 4-H), 4.57 (1 H, br s, 6-OH), 4.66 and 4.72 (each 1 H, d, *J* 7, $CHHOCH_3$), 4.80 (2 H, br s, 5′-H_2), 5.40 (1 H, m, 2-H) and 7.52 (1 H, br s, 4′-H); *m/z* (CI) 344 (M^+ + 18, 20%), 265 (60) and 201 (100).

Ethyl (1*RS*,2*SR*,4*SR*,5*SR*)-4-benzoyloxy-2-hydroxy-5-methyl-2-(2-trimethylsilyl-3-furyl)cyclohexanecarboxylate 33

Triethylamine (0.385 g, 3.8 mmol) and a catalytic amount of 4-dimethylaminopyridine were added to the dihydroxycyclohexanecarboxylate **32**[1] (1.0 g, 2.93 mmol) in dichloromethane (25 cm^3) at room temperature. The solution was cooled to 0 °C and benzoyl chloride (0.44 g, 3.22 mmol) was added. The reaction mixture was allowed to attain ambient temperature and stirred for 24 h before being washed with aqueous hydrogen chloride (3 M; 25 cm^3), saturated aqueous sodium hydrogen carbonate (25 cm^3) and brine (25 cm^3). The organic phase was dried ($MgSO_4$) and concentrated under reduced pressure. Chromatography of the residue using light petroleum–ethyl acetate (10:1) as eluent gave the *title compound* **33** (0.78 g, 60%); ν_{max}/cm^{-1} 3460, 3070, 1785, 1720, 1605, 1587, 1565, 1270, 1185, 1100, 1030, 890 and 845; δ_H 0.35 [9 H, s, $Si(CH_3)_3$], 1.1 (3 H, d, *J* 7, 5-CH_3), 1.14 (3 H, t, *J* 7, OCH_2CH_3), 1.60 (1 H, td, *J* 15, 2.5, 3-H), 1.95 (3 H, m), 2.43 (1 H, dd, *J* 15, 5, 3-H′), 2.97 (1 H, dd, *J* 12.5, 7.5, 1-H), 4.05 (2 H, m, OCH_2CH_3), 4.48 (1 H, d, *J* 2, 2-OH), 5.27 (1 H, td, *J* 15, 5, 4-H), 6.23 (1 H, d, *J* 2, 4′-H), 7.4–8.1 (6 H, m); *m/z* (CI) 444 (M^+, 4%), 429 (10), 305 (70) and 233 (100).

Ethyl (1*RS*,2*SR*,5*SR*)-4-benzoyloxy-2-hydroxy-2-[(5-hydroxy-2-oxo-1-oxacyclopent-3-en-3-yl)]-5-methylcyclohexanecarboxylate 34

Oxygen was bubbled (15 cm^3 min^{-1}) through a solution of the 2-trimethylsilylfuran **33** (180 mg, 0.405 mmol) and a catalytic amount of tetraphenylporphyrin in dichloromethane (75 cm^3) at −78 °C for 5 min with simultaneous irradiation with white light using a 500 W lamp. The reaction mixture was allowed to attain ambient temperature and was concentrated under reduced pressure. Chromatography of the residue using light petroleum–ethyl acetate (1:1) gave the *title compound* **34** (65 mg, 40%); ν_{max}/cm^{-1} 3460, 1760, 1710, 1600, 1580, 1276, 1115, 1100, 1020, 930 and 718; δ_H 1.05 (3 H, d, *J* 5, 5-CH_3), 1.25 (3 H, t, *J* 7, OCH_2CH_3), 2.0 (5 H, m), 3.36 (1 H, dd, *J* 12, 2, 1-H), 4.08 (2 H, q, *J* 7, OCH_2CH_3), 4.55 (1 H, br s, 2-OH), 5.08 (1 H, m, 4-H), 6.13 (1 H, br s, 5′-H), 7.27 (1 H, br s, 4′-H) and 7.42–8.05 (5 H, m, aromatic H); *m/z* (CI) 422 (M^+ + 18, 60%), 406 (40), 378 (20), 322 (35), 258 (35) and 200 (100).

Ethyl (1*RS*,6*SR*)-4,6-bis(trimethylsilyloxy)-3-methyl-6-(2-trimethylsilyl-3-furyl)cyclohex-3-enylcarboxylate 35

Following the procedure outlined above for the synthesis of the enol trimethylsilyl ether **15**, the hydroxycyclohexanone **31** (2.2 g, 6.5 mmol) gave, after chromatography using light petroleum–ethyl acetate (20:1) as eluent, the *title compound* **35** (2.68 g; 85%); ν_{max}/cm^{-1} 1730, 1695, 1250, 1170, 1140, 1075, 1064, 918, 900 and 835; δ_H 0.00 [9 H, s, 6-$OSi(CH_3)_3$], 0.27 [9 H, s, 4-$OSi(CH_3)_3$], 0.39 [9 H, s, 2′-$Si(CH_3)_3$], 1.24 (3 H, t, *J* 7, OCH_2CH_3), 1.48 (3 H, br s, 3-CH_3), 1.84 (1 H, dd, *J* 15, 5, 2-H), 2.05 (1 H, d, *J* 15, 2-H′), 2.58 and 3.00 (each 1 H, d, *J* 15, 5-H), 3.08 (1 H, dd, *J* 7, 2, 1-H), 4.1 (2 H, m, OCH_2CH_3), 6.29 (1 H, d, *J* 2, 4′-H) and 7.43 (1 H, d, *J* 2, 5′-H); *m/z* (CI) 483 (M^+ + 1, 10%) and 393 (100).

Ethyl (1*RS*,2*SR*,5*RS*)-5-methyl-4-oxo-5-phenylselanyl-2-trimethylsilyloxy-2-(2-trimethylsilyl-3-furyl)cyclohexanecarboxylate 36

Phenylselenenyl chloride (5.2 g, 27 mmol) was added to the enol trimethylsilyl ether **35** (13 g, 27 mmol) in tetrahydrofuran (450 cm^3) at 0 °C. The reaction mixture was stirred at 0 °C for 1 h and quenched with saturated aqueous ammonium chloride (100 cm^3). After the addition of ether (200 cm^3), the organic phase was washed with water (100 cm^3) and the combined aqueous phases extracted with ether (3 × 100 cm^3). The combined organic extracts were washed with brine (2 × 100 cm^3), dried (Na_2SO_4) and concentrated under reduced pressure. Chromatography of the residue using light petroleum–ethyl acetate (40:1) as eluent gave the *title compound* **36** (12.5 g; 82%), mp 92–94 °C (from light petroleum–ethyl acetate) (Found: C, 54.9; H, 6.95. $C_{26}H_{38}O_5Si_2Se$ requires C, 55.2; H, 6.75%); ν_{max}/cm^{-1} 1737, 1704, 1252, 1177, 1117, 1010 and 843; δ_H 0.02 [9 H, s, 2-$OSi(CH_3)_3$], 0.4 [9 H, s, 2′-$Si(CH_3)_3$], 1.07 (3 H, t, *J* 7, OCH_2CH_3), 1.49 (3 H, s, 5-CH_3), 2.13 (1 H, dd, *J* 15, 5, 6-H), 2.77 (1 H, d, *J* 15, 3-H), 2.80 (1 H, t, *J* 15, 6-H), 3.15 (1 H, dd, *J* 15, 5, 1-H), 3.9 (2 H, m, OCH_2CH_3), 4.08 (1 H, d, *J* 15, 3-H), 6.33 (1 H, d, *J* 2, 4′-H), 7.50 (1 H, d, *J* 2, 5′-H) and 7.4 (5 H, m, aromatic H); *m/z* (CI) 566 (M^+, 5%), 549 (20) and 477 (100).

Ethyl (1*RS*,2*SR*,5*RS*)-2-hydroxy-5-methyl-4-oxo-5-phenylselanyl-2-(2-trimethylsilyl-3-furyl)cyclohexanecarboxylate 37

Tetrabutylammonium fluoride (1 M in tetrahydrofuran; 22.7 cm^3), previously dried over 4 Å molecular sieves, was added to the trimethylsilyl ether **36** (12.8 g, 22.7 mmol) in tetrahydrofuran (380 cm^3) at −78 °C. The reaction mixture was stirred at −78 °C for 3 h and quenched with saturated aqueous ammonium chloride (100 cm^3). Ether (100 cm^3) was added, the reaction mixture washed with water (100 cm^3) and the combined aqueous phases washed with ether (3 × 100 cm^3). The ether extracts were washed with brine (2 × 100 cm^3), dried (Na_2SO_4) and concentrated under reduced pressure. Chromatography of the residue, on base washed silica, using light petroleum–ethyl acetate (20:1) gave the *title compound* **37** (10.4 g, 93%), mp 94–96 °C (from light petroleum–ethyl acetate) (Found: C, 56.1; H, 6.25. $C_{23}H_{30}O_5SeSi$ requires C, 55.95; H, 6.15%); ν_{max}/cm^{-1} 3470, 1705, 1375, 1250, 1185, 1100 and 840; δ_H 0.32 [9 H, s, $Si(CH_3)_3$], 1.15 (3 H, t, *J* 7, OCH_2CH_3), 1.48 (3 H, s, 5-CH_3), 2.28 (1 H, dd, *J* 15, 5, 6-H), 2.55 (2 H, overlapping dd, *J* 15, 14, 6-H′ and d, *J* 15, 3-H), 3.49 (1 H, dd, *J* 15, 3, 3-H), 3.66 (1 H, dd, *J* 15, 5, 1-H), 4.08 (2 H, m, OCH_2CH_3), 4.30 (1 H, d, *J* 3, 2-OH), 6.33 (1 H, d, *J* 2, 4′-H), 7.38 (5 H, m, aromatic H) and 7.55 (1 H, d, *J* 2, 5′-H); *m/z* (EI) 494 (M^+, 20%) and 337 (50).

Ethyl (1*RS*,4*SR*,6*SR*)-4,6-dihydroxy-3-methyl-6-(2-trimethylsilyl-3-furyl)cyclohex-2-enecarboxylate 40

Hydrogen peroxide (30% w/w in water; 20.3 cm^3) was added to the keto selenide **37** (8.9 g, 18 mmol) in dichloromethane (254 cm^3) at 0 °C. The reaction mixture was stirred for 0.5 h at room temperature and washed with water (2 × 100 cm^3) and brine (100 cm^3). The organic phase was dried (Na_2SO_4) and concentrated under reduced pressure, and the residue dried by azeotropic distillation of benzene (3 × 50 cm^3) to give the methylcyclohexenone **38** together with its methylenecyclohexanone isomer **39** which were used immediately without purification; δ_H(methylcyclohexenone **38**) 0.32 [9 H, s, $Si(CH_3)_3$], 1.18 (3 H, t, *J* 7, OCH_2CH_3), 1.90 (3 H, m, 3-CH_3), 2.65 and 2.85 (each 1 H, d, *J* 16, 5-H), 3.92 (1 H, t, *J* 2, 1-H), 4.17 (2 H, m, OCH_2CH_3), 4.45 (1 H, br s, OH), 6.22 (1 H, d, *J* 2, 4′-H), 6.42 (1 H, m, 2-H) and 7.52 (1 H, d, *J* 2, 5′-H); *m/z* (CI) 354 (M^+ + 18, 20%), 337 (10), 319 (40) and 247 (100).

To the methylcyclohexenone **38** was added a solution of sodium triacetoxyborohydride, which had been prepared by portionwise addition of sodium borohydride (2.8 g, 73.6 mmol) to rapidly stirred anhydrous acetic acid (240 cm^3) while maintaining the temperature of the acetic acid below 20 °C, and the solution was stirred at room temperature for 3 h. The solvent was removed under reduced pressure, the residue dissolved in ether (150 cm^3) and the solution washed with saturated aqueous sodium hydrogen carbonate (3 × 100 cm^3). The aqueous phase

was extracted with ether (3 × 100 cm^3) and the combined organic phases washed with brine (200 cm^3), dried ($MgSO_4$) and concentrated under reduced pressure. Chromatography of the residue using light petroleum–ethyl acetate (12–4:1) as eluent, gave two products. The less polar compound was identified as the 5-methylenecyclohexanecarboxylate **42** (1.05 g, 17%); δ_H 0.35 [9 H, s, $Si(CH_3)_3$], 1.10 (3 H, t, *J* 7, OCH_2CH_3), 1.49 (1 H, td, *J* 12, 3, 3-H_{ax}), 2.34 (1 H, dd, *J* 12, 6, 3-H_{eq}), 2.54 (1 H, dd, *J* 12, 3, 6-H_{eq}), 2.76 (1 H, t, *J* 12, 6-H_{ax}), 2.88 (1 H, dd, *J* 12, 3, 1-H), 4.05 (2 H, m, OCH_2CH_3), 4.50 (1 H, d, *J* 2, 2-OH), 4.62 (1 H, m, 4-H), 5.92 and 6.08 (each 1 H, br s, vinylic H), 6.13 (1 H, d, *J* 2, 4′-H) and 7.47 (1 H, d, *J* 2, 5′-H).

The more polar product was identified as the *title compound* **40** (3.45 g, 57%), mp 90–91 °C (from light petroleum–ethyl acetate) (Found: C, 60.3; H, 7.9. $C_{17}H_{26}O_5Si$ requires C, 60.3; H, 7.75%); ν_{max}/cm^{-1} 3450, 1700, 1370, 1330, 1310, 1240, 1180, 1080, 1005 and 835; δ_H 0.33 [9 H, s, $Si(CH_3)_3$], 1.17 (3 H, t, *J* 7, OCH_2CH_3), 1.52 (1 H, d, *J* 6, 4-OH), 1.75 (1 H, m, 5-H), 1.92 (3 H, br s, 3-CH_3), 2.38 (1 H, dd, *J* 15, 5, 5-H′), 3.60 (1 H, m, 1-H), 4.08 (2 H, m, OCH_2CH_3), 4.53 (1 H, m, 4-H), 4.63 (1 H, d, *J* 2, 6-OH), 5.38 (1 H, m, 2-H), 6.20 (1 H, d, *J* 2, 4′-H), 7.55 (1 H, d, *J* 2, 5′-H); *m/z* (EI) 338 (M^+, 1%), 321 (6) and 320 (5).

Ethyl (1*RS*,4*SR*,6*SR*)-4-benzoyloxy-6-hydroxy-3-methyl-6-(2-trimethylsilyl-3-furyl)cyclohex-2-enecarboxylate 41

Triethylamine (35 mg, 0.35 mmol) and a trace of 4-dimethylaminopyridine were added to the dihydroxycyclohexenecarboxylate **40** (90 mg, 0.27 mmol) in dichloromethane (2.5 cm^3). The solution was cooled to 0 °C, benzoyl chloride (41 mg, 2.97 mmol) was added and the reaction mixture was allowed to attain ambient temperature and stirred for 24 h. Dichloromethane (10 cm^3) was added and the reaction mixture washed with aqueous sodium hydrogen carbonate (10 cm^3) and water (2 × 10 cm^3). The organic phase was dried (Na_2SO_4) and concentrated under reduced pressure. Chromatography of the residue on base washed silica, using light petroleum–ethyl acetate (10:1) as eluent, gave the *title compound* **41** (68 mg, 60%); ν_{max}/cm^{-1} 1715, 1314, 1270, 1190, 1110, 1096, 1025 and 844; δ_H 0.37 [9 H, s, $Si(CH_3)_3$], 1.20 (3 H, t, *J* 7, OCH_2CH_3), 1.87 (3 H, br s, 3-CH_3), 1.90 (1 H, m, 5-H), 2.60 (1 H, dd, *J* 10, 5, 5-H′), 3.73 (1 H, m, 1-H), 4.15 (2 H, q, *J* 7, OCH_2CH_3), 4.67 (1 H, d, *J* 2, 6-OH), 5.55 (1 H, m, 2-H), 6.01 (1 H, m, 4-H), 6.21 (1 H, d, *J* 2, 4′-H), 7.38–8.10 (5 H, m, aromatic H) and 7.55 (1 H, d, *J* 2, 5′-H); *m/z* (CI), 460 ($M^+ + NH_4$, 25%) 420 (60) and 303 (100).

Ethyl (1*RS*,4*SR*,6*SR*)-4-benzoyloxy-6-hydroxy-6-(5-hydroxy-2-oxo-1-oxacyclopent-3-en-3-yl)-3-methylcyclohex-2-enecarboxylate 43

Following the procedure outlined above for the synthesis of the hydroxybutenolide **34**, the 2-trimethylsilylfuran **41** (42 mg, 0.095 mmol) gave, after chromatography on base washed silica using light petroleum–ethyl acetate (1:1) eluent, the *title compound* **43** (15 mg, 39%) as a mixture of epimers, mp 92–94 °C (from carbon tetrachloride); ν_{max}/cm^{-1} 1767, 1717, 1602, 1270, 1194, 1177, 1112, 1070 and 1026; δ_H 1.27 (3 H, t, *J* 7, OCH_2CH_3), 1.83 (3 H, br s, 3-CH_3), 2.33 (2 H, m, 5-H_2), 4.13 (3 H, m, OCH_2CH_3 and 1-H), 4.45 (0.5 H, d, *J* 2, 6-OH), 4.60 (0.5 H, d, *J* 2, 6-OH), 5.55 (1 H, br s, 2-H), 5.87 (1 H, m, 4-H), 6.10 (1 H, m, 5′-H), 7.28 (1 H, m, 4′-H) and 7.36–8.10 (5 H, m, aromatic H); *m/z* (CI) 460 (M^+ + 18, 25%), 420 (60) and 303 (100).

Ethyl (1*RS*,4*SR*,6*SR*)-4-*tert*-butyldimethylsilyloxy-6-hydroxy-3-methyl-6-(2-trimethylsilyl-3-furyl)cyclohex-2-enecarboxylate 44

tert-Butyldimethylsilyl chloride (470 mg, 3.1 mmol) was added to a solution of the diol **40** (880 mg, 2.6 mmol) and imidazole (443 mg, 6.5 mmol) in *N*,*N*-dimethylformamide (16 cm^3) at 0 °C and the mixture stirred for 16 h at ambient temperature before being diluted with ether (50 cm^3) and washed with water (2 × 25 cm^3). The aqueous phase was extracted with ether (3 × 30 cm^3) and the organic extracts washed with brine (100 cm^3) and dried ($MgSO_4$). Concentration under reduced pressure and chromatography of the residue using light petroleum–ether (40:1) as eluent gave the *title compound* **44** (1.0 g, 85%) as a white crystalline solid, mp 87–88 °C (Found: C, 60.85; H, 9.35. $C_{23}H_{40}O_5Si_2$ requires C, 61.0; H, 8.9%); ν_{max}/cm^{-1} 3450, 1710, 1250, 1195, 1090, 1015, 890 and 840; δ_H 0.1 and 0.12 (each 3 H, s, $OSiCH_3$), 0.33 [9 H, s, $Si(CH_3)_3$], 0.90 [9 H, s, $SiC(CH_3)_3$], 1.18 (3 H, t, *J* 7, CH_2CH_3), 1.75 (1 H, m, 5-H), 1.84 (3 H, br s, 3-CH_3), 2.25 (1 H, m, 5-H′), 3.63 (1 H, m, 1-H), 4.11 (2 H, q, *J* 7, CH_2CH_3), 4.6 (1 H, m, 4-H), 4.77 (1 H, d, *J* 2, 6-OH), 5.33 (1 H, m, 2-H), 6.2 (1 H, d, *J* 2, 4′-H) and 7.53 (1 H, d, *J* 2, 5′-H); *m/z* (CI) 452 (M^+, 2%) and 435 (100).

Ethyl (1*RS*,4*SR*,6*SR*)-4-*tert*-butyldimethylsilyloxy-6-hydroxy-6-(5-hydroxy-2-oxo-1-oxacyclopent-3-en-3-yl)-3-methylcyclohex-2-enecarboxylate 45

Following the procedure outlined above for the synthesis of the hydroxybutenolide **34**, the 2-trimethylsilylfuran **44** (100 mg, 0.22 mmol) gave, after irradiation for 15 min, the *title compound* **45** (91 mg, *ca*. 100%) which was used without further purification; ν_{max}/cm^{-1} 3350br, 1750, 1710, 1210 and 910; δ_H 0.1 [6 H, s, $Si(CH_3)_2$], 0.88 [9 H, s, $SiC(CH_3)_3$], 1.25 (3 H, m, CH_2CH_3), 1.75 (3 H, br s, 3-CH_3), 2.23 (2 H, m, 5-H_2), 4.02 (1 H, m, 1-H), 4.2 (2 H, m, CH_2CH_3), 4.5 (1 H, m, 4-H), 4.55 (1 H, d, *J* 2, 6-OH), 5.10 (1 H, br s, 5′-OH), 5.3 (1 H, m, 2-H), 6.07 (1 H, m, 5′-H) and 7.18 (1 H, m, 4′-H).

Ethyl 2-[(1*E*,3*E*)-1-methoxycarbonyl-5-methylhexa-1,3-dien-1-yl]-5-methylbenzoate 48

Butyllithium (1 M in hexane; 0.9 cm^3, 0.9 mmol) was added to (2-methylpropyl)triphenylphosphonium bromide (307 mg, 0.77 mmol) suspended in tetrahydrofuran (8 cm^3) at 0 °C and the solution stirred for 0.5 h before cooling to −78 °C. The hydroxybutenolide **45** (91 mg, 0.22 mmol) in tetrahydrofuran (2.5 cm^3) was added *via* a cannula and the solution stirred for 0.5 h at −78 °C, warmed to ambient temperature and stirred for a further 0.5 h. The reaction mixture was quenched with saturated aqueous ammonium chloride (3 cm^3) and the aqueous phase extracted with ether (3 × 10 cm^3). The organic extracts were washed with brine (10 cm^3), dried ($MgSO_4$) and concentrated under reduced pressure. The residue was suspended in ether (5 cm^3), and a solution of diazomethane in ether added, until the yellow colour persisted. The excess of diazomethane was quenched by the addition of acetic acid (0.5 cm^3) and the solution concentrated under reduced pressure. Chromatography of the residue using light petroleum–ether (10:1) as eluent gave a mixture of dienyl esters, ratio 2:1, which was dissolved in benzene (2 cm^3), iodine (0.05 mmol) was added, and the reaction stirred for 24 h. The solution was diluted with ether (5 cm^3) and washed with saturated aqueous sodium thiosulfate (5 cm^3), brine (5 cm^3), dried ($MgSO_4$) and concentrated under reduced pressure. Chromatography using light petroleum–ether (10:1) as eluent gave the *title compound* **48** (30 mg, 43%); ν_{max}/cm^{-1} 1710, 1630, 1590, 1290, 1250, 1190, 1160, 1080, 980 and 905; δ_H 1.08 [6 H, d, *J* 7, $CH(CH_3)_2$], 1.33 (3 H, t, *J* 7, CH_2CH_3), 2.41 (3 H, s, 5-CH_3), 2.5 (1 H, m, 5′-H), 3.66 (3 H, s, CO_2CH_3), 4.25 (2 H, q, *J* 7, CH_2CH_3), 6.02 (1 H, dd, *J* 15, 7, 4′-H), 6.53 (1 H, d, *J* 11, 2′-H), 7.18 (1 H, d, *J* 7, 3-H), 7.33 (1 H, dd, *J* 7, 1.5, 4-H), 7.38 (1 H, ddd, *J* 15, 11, 2, 3′-H) and 7.78 (1 H, m, 6-H); *m/z* (EI) 316 (M^+, 8%), 273 (36), 247 (73) and 219 (75).

Ethyl (1*RS*,4*SR*,6*SR*)-4-*tert*-butyldimethylsilyloxy-6-hydroxy-6-[(1*Z*,3*E*)-1-methoxycarbonyl-5-methylhexa-1,3-dien-1-yl]-3-methylcyclohex-2-enecarboxylate 47

Butyllithium (1 M in hexane; 0.82 cm^3, 0.82 mmol) was added to (2-methylpropyl)triphenylphosphonium bromide (275 mg, 0.68 mmol) in tetrahydrofuran (8 cm^3) at 0 °C, and the solution

stirred for 0.5 h before cooling to −78 °C. The hydroxybutenolide **45** (91 mg, 0.22 mmol) in tetrahydrofuran (2.5 cm^3) was added *via* a cannula and the reaction mixture was warmed to 0 °C over 0.5 h and quenched by the addition of saturated aqueous ammonium chloride (3 cm^3). The aqueous phase was extracted with ether (3 × 10 cm^3) and the organic extracts were washed with brine (10 cm^3), dried ($MgSO_4$) and concentrated under reduced pressure. Following the procedure outlined for the synthesis of the dienyl ester **48**, this product was esterified using diazomethane and isomerised by treatment with iodine to give, after chromatography using light petroleum–ether (10:1) as eluent, the *title compound* **47** (61 mg, 59%); ν_{max}/cm^{-1} 3430, 1708, 1370, 1330, 1250, 1190, 1070, 905 and 835; δ_H 0.09 and 0.11 (each 3 H, s, $SiCH_3$), 0.9 [9 H, s, $SiC(CH_3)_3$], 1.03 [6 H, d, *J* 6.5, $CH(CH_3)_2$], 1.24 (3 H, t, *J* 7, CH_2CH_3), 1.78 (3 H, br s, 3-CH_3), 2.0 (1 H, ddd, *J* 13, 9.5, 2.5, 5-H), 2.11 (1 H, dd, *J* 13, 6, 5-H′), 2.40 (1 H, m, 5′-H), 3.80 (3 H, s, CO_2CH_3), 3.83 (1 H, m, 1-H), 4.17 (2 H, q, *J* 7, $CO_2CH_2CH_3$), 4.49 (1 H, m, 4-H), 4.59 (1 H, d, *J* 2, 6-OH), 5.26 (1 H, m, 2-H), 5.95 (1 H, dd, *J* 15, 7, 4′-H), 6.39 (1 H, ddd, *J* 15, 11, 1.5, 3′-H) and 6.75 (1 H, d, *J* 11, 2′-H); *m/z* (EI) 467 (M^+ + 1, 1%), 450 (10), 410 (31) and 285 (85).

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