Studies in iridoid synthesis. Chemoselective transformations of *cis*-1,2,4,6-tetrahydrophthalic anhydride†

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Received 22nd October 2007, Accepted 20th November 2007
First published as an Advance Article on the web 20th December 2007
DOI: 10.1039/b716256a

In the course of synthetic studies towards the development of diastereoselective routes to secoiridoid aglycones, *cis*-1,2,4,6-tetrahydrophthalic anhydride was transformed into the corresponding lactone *cis*-3a,4,7,7a-tetrahydro-3*H*-isobenzofuran-1-one, which served as a key precursor for a variety of chemoselective synthetic manipulations. Unsuccessful formylation of an ester intermediate resulted in a (*E*/*Z*) mixture of vinyl alcohols which were protected as acetates and as a single *p*-methoxybenzyl (PMB) ether (*E*) isomer. Dihydroxylation of the cyclohexene motif using OsO_4 led to the unexpected deprotection of the PMB ether. On the other hand, successful formylation of a suitably silyl protected lactonised intermediate was achieved using *tert*-butoxybis(dimethylamino)methane, or Bredereck's reagent. Tetrabutylammonium fluoride (TBAF) deprotection of a methoxyethoxymethyl (MEM)-ether intermediate serendipitously afforded an approximately 1 : 1 mixture of pyrano-pyranones, which are products of a seldom encountered intramolecular Michael addition, using an oxygen donor, to the terminus of an α,β-unsaturated system, followed by β-elimination of the MEM moiety.

Introduction

The secoiridoid aglycone fragment **1** (Fig. 1, R = H) is also the aglycone of more frequently reported secoiridoids, including sweroside (Fig. 1, R = glucose).[1] Early synthetic studies towards secoiridoids in racemic form have included a base-mediated Grob-type fragmentation,[2] and a [2 + 2] photocycloaddition[3] as key reactions. Most published syntheses of complex secoiridoids rely on an advanced secoiridoid precursor as a starting point. This is exemplified by the syntheses of bakankosin[4] and hunterioside,[5] which were both derived from the natural product secologanin.

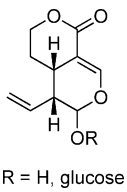

Fig. 1 Structures of secoiridoid aglycone **1** and sweroside **2**.

The susceptibility of the hemiacetal in sweroside aglycone **1** (Fig. 1, R = H) to epimerisation to give the thermodynamically favoured *trans*-isomer has frequently been reported, particularly upon de- and re-glycosidation.[3,6–8] This precluded the use of readily available sweroside or secologanin as starting materials. Thus, in view of the aforementioned, we sought an alternative synthetic approach to sweroside aglycone **1**.

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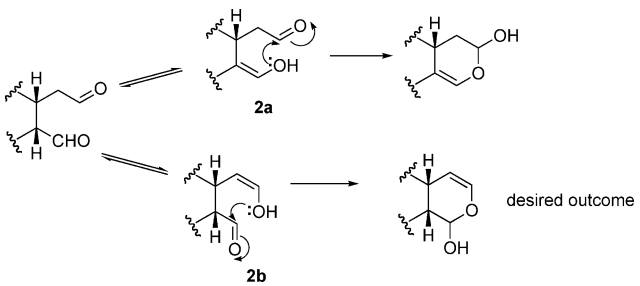
† Electronic supplementary information (ESI) available: Experimental details and characterisation data. See DOI: 10.1039/b716256a

In a major departure from previous synthesis,[3] dismantling of the acetal was the first disconnection chosen. Because of the labile nature of the hemiacetal, glycosidation must take place immediately after closure to the dihydropyranose system, as such protecting the hemiacetal. Prior to planning a route, the following constraints were identified:

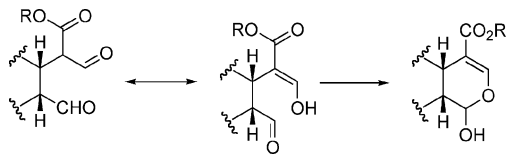
(i) The carboxyl moiety should be in place prior to attempted closure of the dihydropyranoid ring. As shown in Scheme 1, enolisation of either one of the formyl (**2a** or **2b**) moieties results in the formation of two different hemiacetals, one of which compromises a chiral centre.



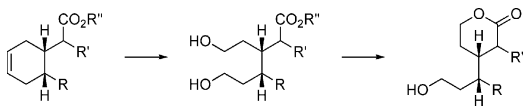
Scheme 1 Competing formation of two possible hemiacetals.

Formation of the desired hemiacetal would be facilitated if **2a** were present as its enol tautomer. Conjugation of the carboxyl C=O bond with the enol C=C bond should provide stabilisation of this enol tautomer and ensure its existence in preference to the aldehyde form, Scheme 2.

(ii) Chemodifferentiation of the hydroxyethyl moieties formed after oxidative cleavage of the cyclohexene motif would be facilitated if the carboxyl was in place prior to diol formation. δ-Lactone formation would thus provide the required chemodifferentiation step, Scheme 3.



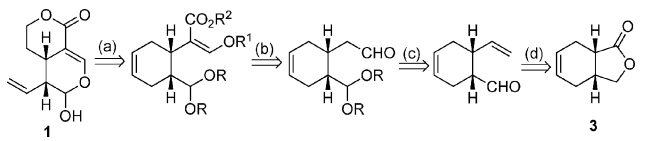
Scheme 2 Formation of desired hemiacetal *via* conjugation of a carbonyl group with an enol double bond.



Scheme 3 Chemodifferentiation of hydroxyethyl moieties *via* lactone formation.

(iii) In order to accommodate analogue synthesis, dihydropyran ring closure and acetal protection should be the last steps in the synthesis.

A retrosynthetic scheme observing the foregoing requirements was devised and is outlined in Scheme 4. Transformation (a) consists of a series of functional group interconversions involving elimination, a coupled oxidative endocyclic double bond cleavage–termini reduction followed by lactonisation and deprotection of the enolic and acetal moieties with concomitant ring closure. An enolate-mediated process is reflected in the C–C bond formation step (b), so utilising the carbonyl functionality available at this point. The aldehyde would be protected as an enol ether after the homologation process. Transformation (c) comprises firstly, acetal formation, followed by regioselective functionalisation of the exocyclic olefin to install the requisite carbonyl group. For process (d), opening of the heterocyclic moiety



Scheme 4 Retrosynthetic plan for the racemic synthesis of sweroside aglycone.

is required first, to allow access to both termini. Homologative olefination and oxidation of the 'northern' and 'southern' termini respectively complete this step.

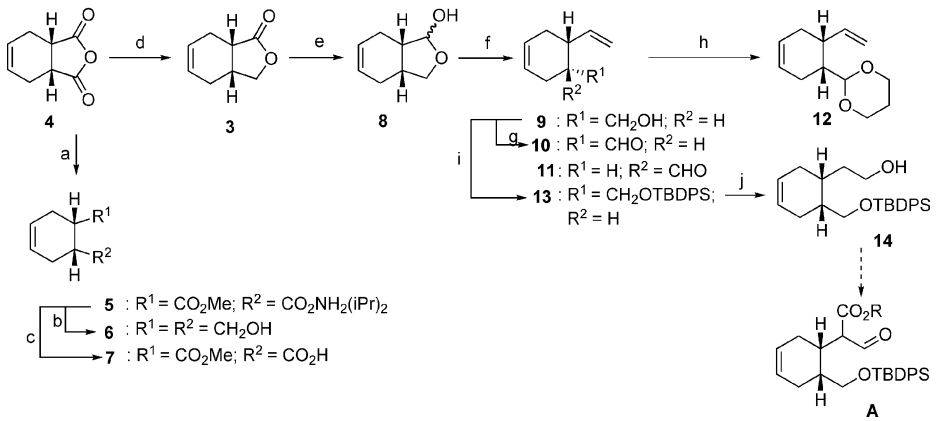
Results and discussion

The synthesis of the required starting lactone **3** *via* reduction of a mixed anhydride or acid chloride was largely unsuccessful. Methanolysis of *cis*-1,2,4,6-tetrahydrophthalic anhydride, **4** in the presence of diisopropylamine provided the novel salt **5**. Following a procedure described by Zwanenberg *et al.*,[9] the salt was treated with isobutyl chloroformate to give a mixed anhydride. Filtration followed by reduction with sodium borohydride ($NaBH_4$) using the conditions described led largely to the diol **6**, the product of over-reduction, Scheme 5.

The methyl half ester of **4** was produced by simple methanolysis and, more efficiently, by acidifying an aqueous solution of **5** followed by extraction of **7**, Scheme 5.

Selective borohydride reduction of **7** *via* acid chloride formation was accompanied by over-reduction in spite of stoichiometric and temperature control. The simplest reduction proved to be a literature procedure[10] in which the anhydride was directly reduced with $NaBH_4$ in cold *N*,*N*-dimethylformamide (DMF) to give the lactone as a single product, which could be purified by vacuum distillation, Scheme 5.

The next step was to conduct homologation studies on lactone **3**. Both stepwise[11] and one pot procedures[12] have been described for the diisobutylaluminium hydride (DIBAH) reduction of **3** to the corresponding lactol followed by a Wittig reaction with a methylphosphorane to give the homologated olefin. This procedure was selected because, in addition to one-carbon homologation, it provided a ring opened intermediate in which the cyclohexenyl substituents were clearly chemodifferentiated. The hydroxyl group in the Wittig product would be accessible for oxidation to the required aldehyde level. The olefin is ideally primed for further functionalisation since it is monosubstituted. It is thus chemodifferentiated from the endocyclic double bond as well as providing an opportunity for regioselective hydroboration.



Scheme 5 *Reagents and conditions*: (a) $HN(iPr)_2$, MeOH, 85%; (b) (i) isobutylOCOCl, CH_2Cl_2, 0–25 °C then filter; (ii) $NaBH_4$, CH_2Cl_2–H_2O, 0 °C; (c) 1 M HCl; (d) $NaBH_4$, DMF, 0 °C, 78%; (e) (i) DIBAH (1.5 mol. equiv., slow addition), toluene, −78 °C, 72%, (ii) DIBAH (1.1 mol. equiv., fast addition), toluene, −78 °C, 92%; (f) $Ph_3P^+CH_3I^-$, *n*BuLi, THF, 0–25 °C, 89% (g) (i) PCC–alumina, CH_2Cl_2 (0.58 M), (ii) PCC–alumina, CH_2Cl_2 (0.04 M), (iii) $(COCl)_2$, DMSO, CH_2Cl_2, −78 °C, then Et_3N, −78–25 °C, (iv) TPAP, NMO, 4 Å mol. sieve, CH_2Cl_2; (h) propane-1,3-diol, $HC(OCH_3)_3$, *p*TsOH, 23% (over 2 steps); (i) TBDPSCl, imidazole, DMF, 99%; (j) 9-BBN, THF, then 1 M NaOH, H_2O_2, 99%.

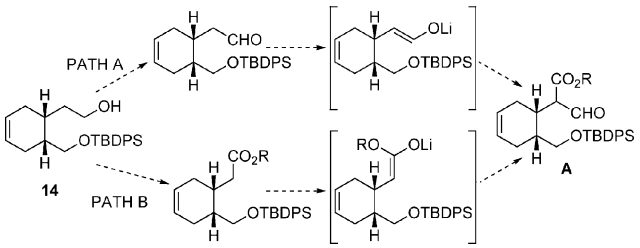
In the event, the reduction procedure was found to be less selective than that described and reduction of the product lactol to diol **6** was observed prior to complete consumption of starting lactone. The reaction of **3** with 1.5 equivalents of DIBAH showed complete consumption of starting material and a 3 : 1 distribution of products **8** and **6**, Scheme 5. It was later noted that very fast addition of DIBAH to a rapidly stirring solution of **3** minimised over-reduction and stoichiometric hydride could be used to give **8** in 92% yield.

The synthesis of **10** was most efficiently achieved when two discrete steps were used, as opposed to the one-pot procedure. The oxidation of the exposed hydroxyl group using chromium trioxide–pyridine has been reported,[11] but in a poor yield (55%). This oxidation proved to be problematic for two reasons; (i) the epimerisable nature of the bridgehead position α to the aldehyde carbonyl in the product and (ii) the volatile nature of the aldehyde. Epimerisation was noted in the oxidation with pyridinium chlorochromate (PCC)–alumina where a mixture of inseparable products, **10** and **11** was recovered in proportions that varied from 9 : 1 to 4 : 6 depending on the reaction conditions, Scheme 5. Swern oxidation[13] as well as oxidation with tetrapropylammonium perruthenate (TPAP)[14] provided only the desired *cis* diastereomer **10**. In all cases the recovery of this compound was less than 50%. This was assumed to be due to evaporation of the aldehyde during isolation. One of the work-up procedures recommended for the TPAP oxidation[14] is a non-aqueous procedure involving flash chromatography of the reaction mixture to give the aldehyde. This protocol was followed using dichloromethane as the elution solvent to give a solution of the aldehyde in dichloromethane, which provided the reaction medium for the protection of **10** as an acetal, thus minimising the handling and losses due to evaporation. Cyclic acetal formation was achieved, but the recovery of the dioxanyl derivative **12** was only 23% over the two steps.

In order to eliminate the losses caused by handling **10**, the synthetic plan was altered. The conversion of the alcohol into the desired aldehyde oxidation state was delayed until later in the synthesis when the intermediates were expected to be less volatile. The hydroxyl group in **9** was thus silylated as a *tert*-butyldiphenylsilyl (TBDPS) ether to give **13**. Hydroboration–oxidation using 9-borabicyclononane (9-BBN–H_2O_2) provided a single product showing the expected chemo- and regioselectivity, **14**, Scheme 5.

The selection of the oxidation level into which the hydroxyl group in **14** should be converted was dependent on the second one-carbon homologation strategy to be applied. Oxidation to an aldehyde followed by base-mediated enolate formation and carboxylation of the enolate would give the desired intermediate **A** [Scheme 6 Path A]. Similarly, oxidation to an acid followed by ester formation, deprotonation and formylation of the enolate would lead to the same intermediate [Scheme 6 Path B].

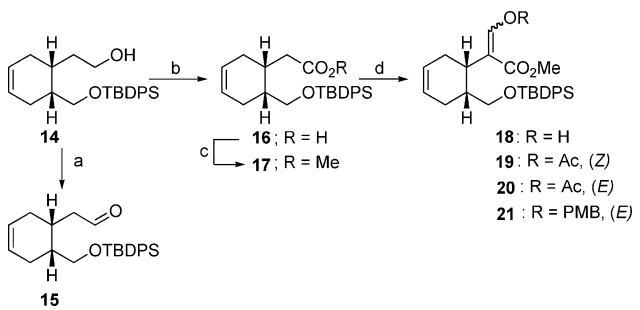
The selection of Path A as the first option attempted was made firstly, because the aldehyde should be accessible in a single step using mild oxidative conditions and secondly, to avoid complications that could arise from the ambident nature of enolate anions. The oxidation of **14** using Dess–Martin periodinane,[15] to aldehyde **15** proceeded as expected. Treatment of **15** with lithium diisopropylamide (LDA) followed by methyl cyanoformate gave a complex mixture of products. When the enolate was treated with



Scheme 6 Enolate-mediated routes to **A**.

methyl chloroformate or carbon dioxide, mixtures dominated by unreacted starting material were produced. A carboxylation using the *in situ* formation of a magnesium carbonate species similar to the Stiles reagent (magnesium methyl carbonate)[16] also gave unsatisfactory results.

The alternative homologation sequence (Path B, Scheme 6) was thus attempted. The ester was prepared by a Jones oxidation of **14** to give acid **16**. The reaction was performed at low temperature (−16 °C) to preclude any silyl deprotection under the strongly acidic conditions. The acid was converted into its methyl ester **17** that was successfully formylated by enolate formation with LDA followed by treatment with ethyl formate to deliver enolic tautomers **18** (Scheme 7).



Scheme 7 *Reagents and conditions*: (a) periodinane, CH_2Cl_2, 92%; (b) 8 M CrO_3, acetone, −16 °C, 80%; (c) MeI, K_2CO_3, DMF, 0–25 °C, 89%; (d) (i) LDA, HCO_2Et, THF, −78– −40 °C, 92% (**18**); (ii) Ac_2O, pyr, DMAP, CH_2Cl_2, 92% (**19**/**20**, *E*,*Z*) or NaH, PMBCl, DMF, 92% (**21**).

The overlapping spectra were too complex to be fully assigned and **18** was thus derivatised to allow characterisation. The enol acetates **19** and **20** were formed under standard acetylation conditions, Scheme 7. The assignment of **19** and **20** as the *Z* and *E* geometrical isomers respectively was made on the basis of NOE difference NMR experiments.

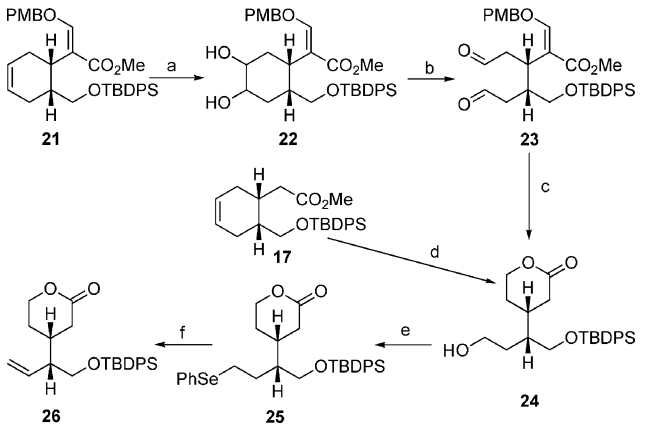
To avoid the cumbersome task of characterising two isomers in further steps in the synthesis, an attempt to enhance the *E*-selectivity of the protection reaction was made by forming the more sterically demanding *p*-methoxybenzyl (PMB) ether **21**. The PMB ether was also selected because of the variety of conditions that could be applied if selective deprotection was required.[17] A single isomer was isolated in good yield.

Oxidative cleavage

In comparing **21** to the required 'skeleton of functionality' described earlier, it can be noted that the carbon framework was in place and only the oxidation states at the olefin termini and the alcohol required alteration. Although two olefinic moieties

are present in **21**, it was hoped that the enolic olefin would be less susceptible to oxidative cleavage due to the presence of electron withdrawing functionality in the carboxy substituent.

The stoichiometric reaction of **21** with osmium tetroxide (OsO_4) in pyridine furnished equal quantities of the glycol **22** and *p*-methoxybenzyl alcohol (Scheme 8), which indicated that unexpected deprotection of the vinyl alcohol had occurred. Other reaction products were detected using TLC but these were extremely polar and were not isolated.



Scheme 8 *Reagents and conditions*: (a) OsO_4, pyr, 43%; (b) $Pb(OAc)_4$, toluene, 45% (**23**); (c) $NaBH_4$, MeOH, 35%; (d) O_3, CH_2Cl_2, −78 °C, then $BH_3{\cdot}Me_2S$, 25 °C, 67%; (e) PhSeCN, nBu$_3$P, THF, 87%; (f) $NaIO_4$, MeOH–H_2O, then Et_3N–benzene, reflux, 89%.

Since literature precedence indicates that PMB ethers are stable to OsO_4 dihydroxylation conditions,[18] the unexpected deprotection could be rationalised by invoking the interaction of OsO_4 with the enolic double bond to give a cyclic osmate ester, which, upon hydrolysis would be expected to give the deprotection result in addition to dihydroxylating the species.

The glycol **22** was successfully cleaved with lead tetraacetate in toluene. The product was extremely unstable and seemingly decomposed during isolation and chromatography resulting in a poor yield of 45%, Scheme 8. The dihydroxylation step was not investigated further due to the undesirable outcome of the glycol cleavage experiment described above.

Ozonolysis of **21** followed by $NaBH_4$ reduction of the ozonide resulted in a complex mixture of products. This result, as well as the lack of stability demonstrated by the glycol cleavage product, required that the synthetic route that had been designed around the existing literature precedent be altered. The oxidative cleavage was thus attempted prior to the second homologation step, *i.e.* on **17**.

Ozonolysis of **17** followed by a reductive work-up of the ozonide with sodium borohydride was attempted, but again, a complex mixture of products was observed by TLC. Ozonolysis of **17** followed by the addition of dimethyl sulfide furnished a single product (by TLC). Flippin *et al.*[19] have developed a procedure for the reduction of ozonides to alcohols using borane–dimethyl sulfide complex. Employed at room temperature, this reagent is tolerant to ester functionality. On the ozonide of **17**, yields of **24** improved, but could only be optimised at 67% (Scheme 8). In each case, a mixture of decomposition products accompanied **24** in the crude reaction extract.

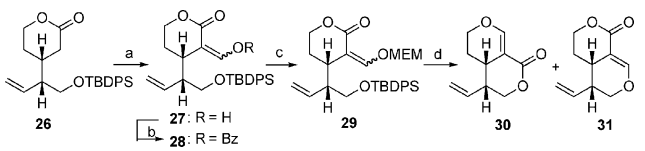
Pyrolytic *syn*-elimination

Reaction of **24** with phenyl selenocyanate using Grieco conditions[20] afforded the primary selenide **25**. Treatment of this with H_2O_2 followed by warming gave a 60% yield of the elimination product **26**.[21] Under neutral or acidic conditions, the phenyl seleninic acid formed from this reaction reacts with olefins to yield β-hydroxy selenides.[22] On the other hand, the use of $NaIO_4$ delivered a superior (87%) yield. Following $NaIO_4$ promoted formation of the selenoxide, the latter was subjected to heating in the presence of triethylamine and benzene and the pyrolytic elimination was optimised at 89%, Scheme 8.

Attempts to introduce the *o*-nitrophenylselenium onto **24** in order to accelerate elimination[23] resulted in incomplete reaction and the recovery of the diaryldiselenide along with the desired product. Alteration of the reaction conditions (concentration, rate of addition, order of reagent addition and stoichiometry) did not improve the recovery and a significant proportion of starting material was isolated after each reaction.

One-carbon homologation revisited

The enolate-mediated formylation reaction that had been delayed until after successful oxidative cleavage could now be employed. The protocol that was used to formylate the ester **17** (LDA–ethyl formate, Scheme 7) was applied to the lactone **26**. Although formylation was achieved, a minimum of 50% starting material was recovered from each reaction. Increased ratios of reagents, increased reaction times and increased reaction temperatures did not improve this reactivity. *tert*-Butoxybis(dimethylamino)methane, or Bredereck's reagent, is used to introduce one-carbon units to a wide variety of compound classes bearing CH- or CH_2-acidic positions.[24] Bredereck's reagent offers a mild and neutral introduction of enamine or aldehyde functionality and has been successfully employed during a solid phase synthesis of 5-aminopyrazoles.[25] The primary reaction product is an enamine, which may be hydrolysed upon work-up to give formyl functionality. Treatment of **26** with neat Bredereck's reagent at 80 °C produced a single product (by TLC) which was treated with cold HCl–methanol to give the formyl product **27** (Scheme 9). The NMR spectra were again complicated by the presence of tautomers. Benzoylation of **27** provided a single enol benzoate **28**.



Scheme 9 *Reagents and conditions*: (a) Bredereck's reagent, 80 °C, 85%; (b) BzCl, pyr, 75% (c) MEMCl, EtN(iPr)$_2$, CH_2Cl_2, 79%; (d) TBAF, THF, 0–25 °C.

The designated connectivities on **28** were confirmed using COSY and HSQC spectra. The assignment of **28** as the *E*-isomer was made on the basis of the chemical shift of the vinyl proton. In this case, **28** was formed diastereoselectively, and no comparative chemical shift data were available. These data were however available for the analogous tetrahydropyranones.[26] The chemical shift of the vinyl proton on the *E*-isomer (δ 8.64) was similar to that in **28** (δ 8.48) whilst that on the *Z*-isomer (δ 7.79)

was not in this range. It was thus possible to assign the *E* geometry to **28**.

Approaches to chemoselective differentiation

The robust nature of TBDPS as a protecting group for alcohols proved to be a problem in the required deprotection step. Treatment of **28** with tetrabutylammonium fluoride (TBAF) in THF at 25 °C was slow and multiple products were formed. The alternative fluoride source routinely used for silyl deprotections, hydrogen fluoride (HF), was also unreactive and concentrated mixtures were required to achieve deprotection, which was again accompanied by decomposition. Since the strongly basic (TBAF) and acidic (HF) conditions could induce hydrolysis of the benzoate ester as well as desilylation, the ester was replaced with an ether protecting group in an attempt to achieve selectivity during the TBAF deprotection. Reaction of **27** with methoxyethoxymethyl chloride and diisopropylamine furnished the MEM ether **29**, Scheme 9. The TBAF deprotection afforded an approximately 1 : 1 mixture of pyrano-pyranones **30** and **31**, which were partially separable and multiple chromatographic steps furnished analytical samples of each, Scheme 9.

These unexpected products were the result of Michael addition of a free hydroxyl group to the terminus of the α,β-unsaturated system, followed by β-elimination of the methoxyethoxymethyl moiety. In the case of **31** the Michael donor was the hydroxyl group revealed by the deprotection step. For the formation of **30**, however, the deprotected hydroxyl group had successfully competed for δ-lactone formation, leaving the newly released alcohol to perform the Michael reaction sequence, Scheme 9. The intramolecular Michael reaction using an oxygen donor is frequently used in the synthesis of oxygen heterocycles.[27] The ring closure observed here, in which β-elimination to give a dihydropyran was facilitated by the presence of a leaving group on the Michael acceptor, has seldom been exploited. In a literature example where the α,β-unsaturated system and the nucleophilic oxygen were suitably tethered, this reaction has been used during a novel approach to dihydropyranones.[28]

The assignments were finally confirmed by long range couplings observed in HMQC spectra for the samples. In both spectra, a cross peak corresponding to 3-bond coupling between C-6 and 8-H was observed as shown in Fig. 2. These couplings are only possible if the pyran and pyranone rings are arranged as shown.

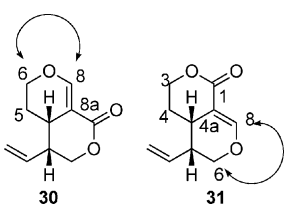
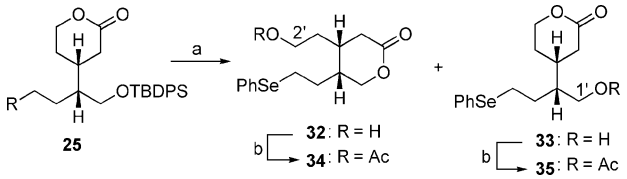


Fig. 2 Observed long range couplings in **30** and **31**.

Whilst the unwanted Michael reactivity could be avoided by protecting the formyl group as an acetal, the equilibration between the two possible δ-lactones would be more difficult to control. To ascertain whether this equilibration was restricted to the system described above, **25** was subjected to TBAF deprotection conditions. The result was a 69% yield of an inseparable mixture of alcohols **32** and **33**. The mixture was acetylated using acetic anhydride and DMAP in pyridine, to give the acetylated products, **34** and **35**, which were partially separable (Scheme 10). The similarity of the spectroscopic data for these compounds once again indicated that they were isomers. Although all the NMR signals were assigned using COSY and HSQC spectra, the two δ-lactones could not be distinguished. HMBC provided the necessary information when cross peaks signifying 4 bond couplings between the acetate methyl protons and C-2′ in **34**, and C-1′ in **35** were detected.



Scheme 10 *Reagents and conditions*: (a) TBAF, THF, 0 °C, 69%; (b) Ac_2O, DMAP, pyr.

In conclusion, the studies undertaken delivered products which are structurally similar to the target sweroside aglycone and led to the unravelling of a seldom encountered intramolecular Michael addition, using an oxygen donor, to the terminus of an α,β-unsaturated system, followed by β-elimination to deliver pyrano-pyranones.

Experimental

(4*R**,5*R**)-4-(1,3-Dioxan-2-yl)-5-vinylcyclohexene (12)

Tetrapropylammonium perruthenate (17 mg, 0.05 mmol), *N*-methylmorpholine-*N*-oxide (826 mg, 7.06 mmol) and powdered 4 Å molecular sieves (1.2 g) were added to **9** (650 mg, 4.71 mmol) in dichloromethane (10 cm^3) at 25 °C under nitrogen. After 2.5 h the reaction mixture was loaded directly onto a silica column (70 g) and eluted under pressure with dichloromethane. Product fractions were collected and pooled to give a 200 cm^3 solution in dichloromethane to which trimethyl orthoformate (2.6 cm^3, 23.6 mmol), propane-1,3-diol (4.0 cm^3, 55.7 mmol) and toluene-*p*-sulfonic acid (60 mg, 0.32 mmol) were added and the resulting mixture was stirred for 40 h. Aqueous saturated sodium hydrogen carbonate was added and the resulting mixture was extracted with dichloromethane. The combined organic phase was dried ($MgSO_4$) and the solvent was removed under reduced pressure to give an oily product (1.03 g). Chromatography on silica gel (70 g) using ethyl acetate–hexane (1 : 9) as eluent yielded the *vinyl acetal* **12** (210 mg, 23%) as an oil, δ_H (300 MHz, $CDCl_3$) 1.28–1.36 (1H, m, 5′-H_A) 1.71–2.19 (5H, m, 3-H_2, 4-H, 5′-H_B and 6-H_A), 2.25–2.37 (1H, m, 6-H_B), 2.69–2.77 (1H, m, 5-H), 3.68 (1H, dd, *J* 12.2 and 2.4 Hz, 4′-H_A or 6′-H_A), 3.73 (1H, dd, *J* 12.2 and 2.5 Hz, 4′-H_A or 6′-H_A), 4.05–4.16 (2H, m, 4′-H_B and 6′-H_B), 4.27 (1H, d, *J* 7.7 Hz, 2′-H), 5.02 (1H, dd, *J* 10.5 and 2.3 Hz, 2″-H_A), 5.06 (1H, dd, *J* 17.1, 2.3 and 0.9 Hz, 2″-H_B), 5.57–5.70 (2H, m, 1-H and 2-H) and 5.86 (1H, ddd, *J* 17.1, 10.5 and 8.9 Hz, 1″-H); δ_C (75 MHz, $CDCl_3$) 23.9 (C-3), 26.3 (C-5′), 31.3 (C-6), 36.6 (C-5), 41.9 (C-4), 66.6 and 66.8 (C-4′ and C-6′), 104.1 (C-2′), 115.3 (C-2″), 125.3 and 126.3 (C-1 and C-2) and 139.1 (C-1″); (Found: M^+, 194.1322. Calc. for $C_{12}H_{18}O_2$: *M*, 194.1307).

(4*R,5*R**)-4-*tert*-Butyldiphenylsilanyloxymethyl-5-vinylcyclohexene (13)**

Alcohol **9** (1.10 g, 8.0 mmol) in dry *N*,*N*-dimethylformamide (15 cm^3) and *tert*-butyldiphenylsilyl chloride (2.3 cm^3, 8.8 mmol) were added sequentially to a stirred solution of imidazole (0.65 g, 9.6 mmol) in dry *N*,*N*-dimethylformamide (20 cm^3). The reaction was stirred at 25 °C for 16 h after which it was diluted with diethyl ether (100 cm^3) and washed with water. The organic phase was dried ($MgSO_4$) and the solvent was removed under reduced pressure. The residue was chromatographed on silica gel (100 g) using ethyl acetate–hexane (1 : 9) as eluent to give the *silyl ether* **13** (2.97 g, 99%) as an oil, δ_H (400 MHz, $CDCl_3$) 1.07 [9H, s, $C(CH_3)_3$], 1.78–1.91 (1H, m, 3-H_A), 1.92–2.03 (1H, m, 6-H_A), 2.02–2.21 (2H, m, 3-H_B and 4-H), 2.26–2.40 (1H, m, 6-H_B), 2.65–2.79 (1H, m, 5-H), 3.53 (1H, dd, *J* 9.9 and 6.8 Hz, 1′-H_A), 3.59 (1H, dd, *J* 9.9 and 7.2 Hz, 1′-H_B), 4.99 (1H, dd, *J* 10.3 and 2.1 Hz, 2″-H_A), 5.05 (1H, ddd, *J* 17.2, 2.1 and 1.1 Hz, 2″-H_B), 5.61–5.72 (2H, m, 1-H and 2-H), 5.79 (1H, ddd, *J* 17.2, 10.3 and 8.3 Hz, 1″-H), 7.35–7.48 (6H, m, Ar-H) and 7.66–7.78 (4H, m, Ar-H); δ_C (100 MHz, $CDCl_3$) 19.2 [$C(CH_3)_3$] 25.4 (C-3), 26.8 [$C(CH_3)_3$], 30.3 (C-6), 37.6 (C-5), 39.3 (C-4), 65.4 (C-1′), 115.1 (C-2″), 125.4 and 125.8 (C-1 and C-2), 127.5, 129.4(3) and 129.4(4), 134.0(2) and 134.0(5), 135.5(2) and 135.5(5) (Ar-C‡) and 138.8 (C-1″); (Found: M^+, 376.2208. Calc. for $C_{25}H_{32}OSi$: *M*, 376.2220).

(4*R,5*R**)-4-*tert*-Butyldiphenylsilanyloxymethyl-5-(1-hydroxyethyl)cyclohexene (14)**

9-Borabicyclo[3.3.1]nonane (0.65 g, 5.3 mmol) was added to a stirred solution of **13** (1.00 g, 2.7 mmol) in tetrahydrofuran (50 cm^3). After 2 h of stirring at 25 °C, 1 M NaOH (25 cm^3) was slowly added, followed by 30% hydrogen peroxide (10 cm^3) and the resulting mixture was stirred for 14 h. The mixture was diluted with water (100 cm^3) and extracted with ethyl acetate. The extract was dried ($MgSO_4$), and the solvent was removed under reduced pressure. The residue (3.01 g) was adsorbed onto silica gel (6 g) and chromatographed on silica (150 g) using ethyl acetate–toluene (1 : 9) as eluent to yield the *alcohol* **14** (1.04 g, 99%) as an oil, $\nu_{max}(CHCl_3)/cm^{-1}$ 3620 (OH); δ_H (400 MHz, $CDCl_3$) 1.08 [9H, s, $C(CH_3)_3$], 1.38–1.54 (2H, m, 1″-H_2), 1.78–1.87 (1H, m, 6-H_A), 1.92–2.10 (5H, m, 3-H_2, 4-H, 5-H and 6-H_B), 3.50–3.70 (4H, m, 1′-H_2 and 2″-H_2), 5.57–5.70 (2H, m, 1-H and 2-H), 7.38–7.48 (6H, m, Ar-H) and 7.67–7.73 (4H, m Ar-H); δ_C (100 MHz, $CDCl_3$) 19.2 [$C(CH_3)_3$], 26.2 (C-3), 26.9 [$C(CH_3)_3$], 29.5 (C-6), 30.2 (C-5), 32.7 (C-1″), 38.7 (C-4), 61.6 (C-2″), 64.2 (C-1′), 125.5 and 125.8 (C-1 and C-2), 127.5(9) and 127.6(0), 129.5(3) and 129.5(5), 133.8(4) and 133.8(7), 135.5(6) and 135.5(8) (Ar-C); (Found: M^+, 394.2333. Calc. for $C_{25}H_{34}O_2Si$: *M*, 394.2325).

(4*R,5*R**)-4-*tert*-Butyldiphenylsilanyloxymethyl-5-formylmethylcyclohexene (15)**

Dess–Martin periodinane (1.30 g, 3.07 mmol) was added to a solution of **14** (1.00 g, 2.54 mmol) in dichloromethane (50 cm^3). The mixture was stirred for 2.5 h at 25 °C after which it was diluted with ether (100 cm^3), washed with 0.1 M sodium thiosulfate, sodium hydrogen carbonate (sat.) and water. The organic phase was dried ($MgSO_4$) and the solvent was removed under reduced pressure to give an oil (1.23 g). Chromatography on silica gel (100 g) using ethyl acetate–hexane (1 : 9) as eluent afforded the *aldehyde* **15** (920 mg, 92%) as an oil, $\nu_{max}(CHCl_3)/cm^{-1}$ 1721 (CO); δ_H (400 MHz, $CDCl_3$) 1.07 [9H, s, $C(CH_3)_3$], 1.72–1.86 (2H, m, 3-H_A and 6-H_A), 2.00–2.12 (2H, m, 3-H_B and 4-H), 2.15–2.26 (1H, m, 6-H_B), 2.25–2.40 (2H, m, 1″-H_2), 2.55–2.68 (1H, br. s, 5-H), 3.55 (1H, dd, *J* 10.4 and 7.3 Hz, 1′-H_A), 3.61 (1H, dd, *J* 10.4 and 6.3 Hz, 1′-H_B), 5.52–5.70 (2H, m, 1-H and 2-H), 7.35–7.44 (6H, m, Ar-H), 7.62–7.67 (4H, m Ar-H) and 9.71 (1H, dd, *J* 2.4 and 1.6 Hz, 2″-H); δ_C (100 MHz, $CDCl_3$) 19.2 [$C(CH_3)_3$], 25.6 (C-3), 26.8 [$C(CH_3)_3$], 27.5 (C-5), 29.8 (C-6), 38.5 (C-4), 43.5 (C-1″), 64.6 (C-1′), 124.9 and 125.6 (C-1 and C-2), 127.6(1) and 127.6(4), 129.5(9) and 129.6(4), 133.6, 135.5(0) and 135.5(5) (Ar-C) and 202.8 (C-2″); (Found: M^+, 392.2177. Calc. for $C_{25}H_{32}O_2Si$: *M*, 392.2169).

(1*R,6*R**)-(6-*tert*-Butyldiphenylsilanyloxymethylcyclohex-3-en-1-yl)acetic acid (16)**

An excess of 8 M CrO_3 was added to a stirred solution of **14** (715 mg, 1.81 mmol) in acetone (30 cm^3) at −30 °C. The solution was left at −16 °C for 14 h, after which the excess reagent was consumed by the addition of propan-2-ol (10 cm^3). The solution was diluted with ether (100 cm^3) and washed with water (2 × 100 cm^3). The organic phase was dried ($MgSO_4$) and the solvent was removed under reduced pressure to give an oil (760 mg). Chromatography on silica gel (60 g) using ethyl acetate–hexane (1 : 9) as eluent afforded the *acid* **16** (591 mg, 80%), $\nu_{max}(CHCl_3)/cm^{-1}$ 3512 (OH), 1706 (C=O); δ_H (400 MHz, $CDCl_3$) 1.07 [9H, s, $C(CH_3)_3$], 1.78–1.96 (2H, m, 3-H_A and 6-H_A), 2.02–2.14 (2H, m, 3-H_B and 4-H), 2.16–2.21 (1H, m, 6-H_B), 2.23 (1H, dd, *J* 15.4 and 10.3 Hz, 1″-H_A), 2.33 (1H, dd, *J* 15.5 and 4.2 Hz, 1″-H_B), 2.48–2.57 (1H, m, 5-H), 3.58 (2H, d, *J* 6.4 Hz, 1′-H_2), 5.54–5.70 (2H, m, 1-H and 2-H), 7.36–7.42 (6H, m, Ar-H) and 7.64–7.70 (4H, m Ar-H); δ_C (100 MHz, $CDCl_3$) 19.2 [$C(CH_3)_3$], 25.8 (C-3), 26.8 [$C(CH_3)_3$], 29.6 (C-6), 30.1 (C-5), 34.0 (C-1″), 38.5 (C-4), 64.7 (C-1′), 125.0 and 125.6 (C-1 and C-2), 127.5(9) and 127.6(1), 129.5(4) and 129.6(0), 133.6(0) and 133.6(6), 135.5(1) and 135.5(6) (Ar-C) and 179.4 (C-2″); (Found: M^+, 408.2124. Calc. for $C_{25}H_{32}O_3Si$: *M*, 408.2120).

Methyl (1*R,6*R**)-(6-*tert*-butyldiphenylsilanyloxymethylcyclohex-3-en-1-yl)acetate (17)**

Potassium carbonate (182 mg, 1.32 mmol) and iodomethane (0.11 cm^3, 1.76 mmol) were added to a solution of acid **16** (360 mg, 0.88 mmol) in *N*,*N*-dimethylformamide (10 cm^3) at 0 °C. The solution was stirred at 0 °C for 30 min and allowed to warm to 25 °C over 1 h. Dichloromethane (50 cm^3) was added and the resulting mixture was washed with water and brine, dried ($MgSO_4$) and the solvent was removed under reduced pressure to give an oil (1.50 g). Chromatography on silica gel (100 g) using ethyl acetate–hexane (1 : 19) as eluent afforded the *ester* **17** (330 mg, 89%) as an oil, $\nu_{max}(CHCl_3)/cm^{-1}$ 1730 (CO); δ_H (400 MHz, $CDCl_3$) 1.06 [9H, s, $C(CH_3)_3$], 1.78–1.92 (2H, m, 3-H_A and 6-H_A), 2.02–2.14 (2H, m, 3-H_B and 4-H), 2.14–2.22 (1H, m, 6-H_B), 2.20 (1H, dd, *J* 15.3 and 10.2 Hz, 1″-H_A), 2.28 (1H, dd, *J* 15.3 and 4.3 Hz, 1″-H_B),

‡ The diastereotopic nature of the two phenyl substituents of TBDPS is reflected by the duplication of signals. Where these have been resolved, the relevant figures for both signals have been included.

2.45–2.54 (1H, m, 5-H), 3.57 (1H, dd, *J* 10.4 and 6.8 Hz, 1′-H_A), 3.60 (1H, dd, *J* 10.4 and 6.7 Hz, 1′-H_B), 3.65 (3H, s, CO_2CH_3), 5.52–5.68 (2H, m, 1-H and 2-H), 7.35–7.49 (6H, m, Ar-H) and 7.64–7.70 (4H, m Ar-H); δ_C (100 MHz, $CDCl_3$) 19.2 [$C(CH_3)_3$], 25.9 (C-3), 26.8 [$C(CH_3)_3$], 29.7 (C-6), 30.4 (C-5), 34.1 (C-1″), 38.7 (C-4), 51.4 (CO_2CH_3), 64.7 (C-1′), 125.1 and 125.6 (C-1 and C-2), 127.6, 129.5(2) and 129.5(5), 133.7(0) and 133.7(4), 135.5(2) and 135.5(6) (Ar-C) and 173.9 (C-2″); (Found: M^+, 422.2268. Calc. for $C_{26}H_{34}O_3Si$: *M*, 422.2275).

Formylation of ester 17

n-Butyllithium (2.5 M solution in hexane, 0.48 cm^3) was added to a stirred solution of diisopropylamine (0.17 cm^3, 1.20 mmol) in tetrahydrofuran (3 cm^3) at −78 °C. After 30 min stirring at −78 °C, a solution of **17** (422 mg, 1.00 mmol) in tetrahydrofuran (3 cm^3) was added and the resulting solution was stirred for 60 min. Ethyl formate (0.12 cm^3, 1.53 mmol) was added and the solution was warmed over 60 min to −40 °C, where the temperature was maintained for a further 60 min. The reaction was acidified with 5% H_3PO_4 and the volatile media were removed *in vacuo.* The resulting mixture was extracted with diethyl ether and the organic phase was washed with brine and dried ($MgSO_4$). Removal of the solvent under reduced pressure gave a residue (497 mg) which was further purified by chromatography on silica gel (50 g) using ethyl acetate–hexane (1 : 19) as eluent to yield **18** (415 mg, 92%) as an inseparable mixture of the geometrical isomers methyl (1′*S**,2*E*,6′*R**)- and methyl (1′*S**,2*Z*,6′*R**)-3-hydroxy-2-(6-*tert*-butyldiphenylsilanyloxymethylcyclohex-3-en-1-yl)acrylate.

Acetylation of the formylation mixture 18

Acetic anhydride (0.23 cm^3, 2.4 mml), pyridine (0.04 cm^3, 0.5 mmol) and 4-dimethylaminopyridine (20 mg, 0.16 mmol) were added to a solution of **18** (110 mg, 0.24 mmol) in dichloromethane (5 cm^3). The resulting solution was stirred for 15 h at 25 °C. Water (5 cm^3) was added and the mixture was stirred for 20 min. The organic phase was washed with water followed by cold 1 M HCl, dried ($MgSO_4$) and the solvent was removed under reduced pressure to yield the acetylated mixture (120 mg). Chromatography on silica gel (15 g) using ethyl acetate–hexane (1 : 9) as eluent yielded *methyl (1′S*,2Z,6′R*)-3-acetoxy-2-(6-tert-butyldiphenylsilanyloxymethylcyclohex-3-en-1-yl)acrylate* **19** (33 mg, 28%) as an oil, $\nu_{max}(CHCl_3)/cm^{-1}$ 1719 and 1761 (CO); δ_H (400 MHz, $CDCl_3$) 1.03 [9H, s, $C(CH_3)_3$], 2.03–2.15 (4H, m, 2′-H_A, 5′-H_2 and 6′-H), 2.15 (3H, s, 3-OCOCH_3), 2.17–2.27 (1H, m, 2′-H_B), 3.08–3.14 (1H, m, 1′-H), 3.48 (1H, dd, *J* 10.1 and 7.8 Hz, 1″-H_A), 3.61 (1H, dd, *J* 10.1 and 6.0 Hz, 1″-H_B), 3.68 (3H, s, 1-OCH_3), 5.61–5.72 (2H, m, 3′-H and 4′-H), 7.29 (1H, d, *J* 1.5 Hz, 3-H), 7.33–7.44 (6H, m, Ar-H) and 7.59–7.66 (4H, m Ar-H); δ_C (100 MHz, $CDCl_3$) 19.2 [$C(CH_3)_3$], 20.6 (3-OCOCH_3), 25.9 (C-5′), 26.8 [$C(CH_3)_3$], 28.1 (C-2′), 34.0 (C-1′), 38.3 (C-6′), 51.7 (1-OCH_3), 63.8 (C-1″), 119.5 (C-2), 125.5 and 126.1 (C-3′ and C-4′), 127.5, 129.4(0) and 129.4(3), 133.8, 135.5 (Ar-C), 137.7 (C-3), 167.1 and 167.3 (C-1 and 3-O*C*OCH$_3$); (Found: M^+, 492.2317. Calc. for $C_{29}H_{36}O_5Si$: *M*, 492.2323).

Further elution afforded *methyl (1′S*,2E,6′R*)-3-acetoxy-2-(6-tert-butyldiphenylsilanyloxymethylcyclohex-3-en-1-yl)acrylate* **20** (77 mg, 64%), $\nu_{max}(CHCl_3)/cm^{-1}$ 1711 and 1771 (CO); δ_H (200 MHz, $CDCl_3$) 1.02 [9H, s, $C(CH_3)_3$], 1.89 (3H, s, $COCH_3$), 2.00–2.70 (5H, m, 2′-H_2, 5′-H_2 and 6′-H), 3.15 (1H, ddd, *J* 11.8, 5.5 and 3.3 Hz, 1′-H), 3.50–3.70 (2H, m, 1″-H_2), 3.68 (3H, s, 1-OCH_3), 5.52–5.73 (2H, m, 3′-H and 4′-H), 7.30–7.47 (6H, m, Ar-H), 7.54–7.65 (4H, m Ar-H) and 8.12 (1H, s, 3-H); (Found: M^+, 492.2330. Calc. for $C_{29}H_{36}O_5Si$: *M*, 492.2323).

Methyl (1′*S**,2*E*,6′*R**)-2-(6-*tert*-butyldiphenylsilanyloxymethylcyclohex-3-en-1-yl)-3-*p*-methoxybenzyloxyacrylate (21)

n-Butyllithium (10 M solution in hexane, 0.14 cm^3, 1.40 mmol) was added to a stirred solution of diisopropylamine (0.20 cm^3, 1.41 mmol) in tetrahydrofuran (4 cm^3) at −78 °C. After 30 min stirring at −78 °C, a solution of **17** (500 mg, 1.18 mmol) in tetrahydrofuran (4 cm^3) was added and the resulting solution was stirred for 60 min. Ethyl formate (0.14 cm^3, 1.78 mmol) was added and the solution was warmed over 60 min to −40 °C, where the temperature was maintained for a further 60 min. The reaction was acidified with 5% H_3PO_4 and the volatile media were removed *in vacuo.* The resulting mixture was extracted with diethyl ether and the organic extract was washed with brine and dried ($MgSO_4$). Removal of the solvent under reduced pressure gave an oil (730 mg) which was dissolved in dry dimethylformamide (20 cm^3). Sodium hydride (60% dispersion in oil, 40 mg, 1.00 mmol) was added and the mixture was stirred at 25 °C for 60 min, after which *p*-methoxybenzyl chloride (0.36 cm^3, 2.65 mmol) was added. After 4 h stirring, the reaction mixture was diluted with dichloromethane, washed with water and dried ($MgSO_4$). Removal of the solvent under reduced pressure gave a residue (1.073 g) which was chromatographed on silica gel (100 g) using ethyl acetate–hexane (1 : 9) as eluent to yield the *aryl enol* **21** (620 mg, 92%) as an oil, $\nu_{max}(CHCl_3)/cm^{-1}$ 1699 (CO); δ_H (400 MHz, $CDCl_3$) 1.02 [9H, s, $C(CH_3)_3$], 1.72–1.82 (1H, m, 2′-H_A), 2.03–2.11 (1H, m, 6′-H), 2.19–2.30 (1H, m, 5′-H_A), 2.43–2.53 (1H, m, 5′-H_B), 2.60–2.72 (1H, m, 2′-H_B), 3.07 (1H, ddd, *J* 12.6, 5.4 and 3.3 Hz, 1′-H), 3.63 (3H, s, 1-OCH_3), 3.64–3.78 (2H, m, 1″-H_2), 3.77 (3H, s, Ar–OCH_3), 4.52 (1H, d, *J* 11.7 Hz, Ar–CH_A–O), 4.58 (1H, d, *J* 11.7 Hz, Ar–CH_B–O), 5.52–5.68 (2H, m, 3′-H and 4′-H), 6.70–6.75 (2H, m, PMB Ar-H), 6.95–7.02 (2H, m, PMB Ar-H), 7.22–7.45 (7H, m, 3-H and TPS Ar-H) and 7.56–7.65 (4H, m TPS Ar-H); δ_C (100 MHz, $CDCl_3$) 19.3 [$C(CH_3)_3$], 24.8 (C-2′), 27.0 [$C(CH_3)_3$], 27.6 (C-5′), 34.4 (C-1′), 40.0 (C-6′), 51.5 (1-OCH_3), 55.5 (Ar–OCH_3), 63.1 (C-1″), 75.8 (Ar–CH_2–O), 112.7 (C-2), 114.6 (PMB Ar-C), 125.2, 127.8 (C-3′ and C-4′), 127.7 and 129.8 (PMB Ar-C), 128.0(8) and 128.1(6), 129.9(7) and 129.9(9), 135.0(2) and 135.1(3), 136.3(2) and 136.4(0) (TPS Ar-C), 159.0 (C-3), 160.5 (PMB Ar-C) and 170.0 (C-1); (Found: M^+, 570.2780. Calc. for $C_{35}H_{42}O_5Si$: *M*, 570.2791).

Methyl (2*E*,1′*S**,2′*R**)-2-(2-*tert*-butyldiphenylsilanyloxymethyl-4ξ-5ξ-dihydroxycyclohexan-1-yl)-3-*p*-methoxybenzyloxyacrylate (22)

Osmium tetroxide (152 mg, 0.60 mmol) was added to a stirred solution of **21** (285 mg, 0.5 mmol) in dry pyridine (10 cm^3) and the solution was stirred at 25 °C for 60 min. Saturated aqueous sodium metabisulfite was added and the solution was stirred for 2 h, after which it was acidified with 1 M HCl and extracted with ethyl acetate. The extract was dried ($MgSO_4$), and the solvent was

removed to give a solid residue (300 mg). Chromatography on silica gel (50 g) using ethyl acetate–hexane (1 : 1) as eluent afforded the *cyclohexanediol* **22** (130 mg, 43%), mp 141–142 °C (from toluene); $\nu_{max}(CHCl_3)/cm^{-1}$ 3611 (OH); δ_H (400 MHz, $CDCl_3$) 1.02 [9H, s, $C(CH_3)_3$], 1.60 (1H, br. s, OH), 1.61 (1H, dt, *J* 14.3 and 2 × 4.1 Hz, 6′-H_A), 1.75 (1H, td, *J* 2 × 13.1 and 4.5 Hz, 3′-H_A), 2.07 (1H, br. s, OH), 2.08–2.17 (2H, m, 2′-H and 3′-H_B), 2.22 (1H, td, *J* 2 × 14.3 and 2.7 Hz, 6′-H_B), 3.28 (1H, dt, *J* 9.9 and 2 × 4.1 Hz, 1′-H), 3.50–3.61 (2H, m, 1″-H_A and 4′-H), 3.61 (3H, s, 1-OCH_3), 3.67 (1H, t, *J* 2 × 10.3 Hz, 1″-H_B), 3.78 (3H, s, Ar–OCH_3), 3.88–3.92 (1H, m, 5′-H), 4.65 (2H, s, Ar–CH_2–O), 6.72–6.78 (2H, m, PMB Ar-H), 7.00–7.06 (2H, m, PMB Ar-H), 7.28–7.45 (7H, m, 3-H and TPS Ar-H) and 7.56–7.65 (4H, m TPS Ar-H); δ_C (100 MHz, $CDCl_3$) 19.2 [*C*$(CH_3)_3$], 26.9 [C(*C*$H_3)_3$], 29.2 (C-3′), 29.7 (C-1′), 30.4 (C-6′), 40.5 (C-2′), 51.2 (1-OCH_3), 55.3 (Ar–OCH_3), 62.1 (C-1″), 67.4 (C-4′), 69.4 (C-5′), 75.5 (Ar–CH_2–O), 111.2 (C-2), 114.0, 127.8 and 129.2 (PMB Ar-C), 127.4(9) and 127.5(6), 129.4 (7) and 129.5(1), 133.9(6) and 134.1(1), 135.6 (TPS Ar-C), 158.5 (C-3), 160.0 (PMB Ar-C) and 168.9 (C-1); (Found: C, 69.2; H, 7.4%, $M^+ - C_4H_9$, 547.2133. Calc. for $C_{35}H_{44}O_7Si$: C, 69.5; H, 7.4%, $C_{31}H_{35}O_7Si$: *M*, 547.2143).

Methyl (2*E*,3*S**,4*R**)-4-*tert*-butyldiphenylsilanyloxymethyl-3-formylmethyl-2-*p*-methoxybenzyloxymethylene-6-oxohexanoate (23)

Lead tetraacetate (150 mg, 0.34 mmol) was added over a 30 min period to a stirred solution of **22** (160 mg, 0.26 mmol) in toluene (5 cm^3). The solution was stirred at 25 °C for a further 30 min, after which ethylene glycol (2 drops) was added and the solution was stirred for 10 min. The resulting mixture was filtered through Celite and the solvent was removed to give an oily residue (200 mg). Chromatography on silica gel (20 g) using ethyl acetate–hexane (1 : 9) as eluent afforded the unstable *dialdehyde* **23** (70 mg, 45%) as an oil, $\nu_{max}(CHCl_3)/cm^{-1}$ 1722 (CO); δ_H (400 MHz, $CDCl_3$) 1.04 [9H, s, $C(CH_3)_3$], 2.28 (1H, ddd, *J* 17.0, 4.3 and 2.1 Hz, 5-H_A), 2.34 (1H, ddd, *J* 16.2, 4.3 and 1.3 Hz, 1″-H_A), 2.45 (1H, ddd, *J* 17.0, 8.2 and 2.1 Hz, 5-H_B), 2.52–2.62 (1H, m, 4-H), 2.70 (1H, ddd, *J* 16.2, 10.6 and 3.3 Hz, 1″-H_B), 3.43–3.52 (1H, m, 3-H), 3.58 (1H, dd, *J* 5.3 and 10.8 Hz, 1‴-H_A), 3.66 (3H, s, 1-OCH_3), 3.70 (1H, dd, *J* 10.8 and 3.2 Hz, 1‴-H_B), 3.81 (3H, s, Ar-OCH_3), 4.91 (2H, s, Ar-CH_2–O), 6.86–6.96 (2H, m, PMB Ar-H), 7.20–7.24 (2H, m, PMB Ar-H), 7.35–7.46 (6H, m, TPS Ar-H), 7.51 (1H, s, 1′-H), 7.58–7.70 (4H, m TPS Ar-H), 9.43 (1H, dd, *J* 3.3 and 1.3 Hz, 2″-H) and 9.55 (1H, t, *J* 2 × 2.1 Hz, 6-H); δ_C (100 MHz, $CDCl_3$) 19.2 [*C*$(CH_3)_3$], 26.8 [C(*C*$H_3)_3$], 30.7 (C-3), 38.0 (C-4), 44.6 (C-1″), 44.8 (C-5), 51.3 (1-OCH_3), 55.3 (Ar–OCH_3), 64.1 (C-1‴), 75.5 (Ar–CH_2–O), 110.1 (C-2), 114.2, 127.5 and 129.6 (PMB Ar-C), 127.7(2) and 127.7(5), 129.7(8) and 129.8(4), 133.0, 135.5(9) and 135.6(3) (TPS Ar-C), 159.3 (C-2′), 160.0 (PMB Ar-C), 167.7 (C-1), 202.0 (C-2″) and 202.3 (C-6); (Found: M^+ 602.2678. Calc. for $C_{35}H_{42}O_7Si$: *M*, 602.2689).

(2′*R**,4*R**)-4-(1-*tert*-Butyldiphenylsilanyloxy-4-hydroxybutan-2-yl)tetrahydropyran-2-one (24)

Ozone was bubbled through a solution of **17** (200 mg, 0.47 mmol) in dichloromethane (10 cm^3) at −78 °C until a faint blue colour appeared. Nitrogen was bubbled through the solution for 10 min and borane–dimethylsulfide complex (1.0 M solution in dichloromethane, 1.9 cm^3) was added. The solution was warmed to 25 °C and stirred for 18 h. The reaction was acidified with 1 M HCl (0.5 cm^3) and the solution was stirred vigorously for 2 h. Solid sodium carbonate was added until the pH of the aqueous portion reached 10. Magnesium sulfate was added to dry the solution and the mixture was filtered through a sintered glass funnel and rinsed with dichloromethane. The filtrate and rinsings were combined and the solvent was removed under reduced pressure to give a crude product (210 mg). Chromatography on silica gel (25 g) using ethyl acetate–hexane (3 : 2) as eluent yielded the *lactone* **24** (135 mg, 67%) as an oil, $\nu_{max}(CHCl_3)/cm^{-1}$ 1731 (CO); δ_H (400 MHz, $CDCl_3$) 1.06 [9H, s, $C(CH_3)_3$], 1.46–1.68 (4H, m, 5-H_A, 3′-H_2 and 2′-H), 1.68–1.77 (1H, m, 5-H_B), 1.85 (1H, br. s, OH), 2.07–2.25 (2H, m, 3-H_A and 4-H), 2.59 (1H, ddd, *J* 16.7, 5.5 and 1.8 Hz, 3-H_B), 3.54–3.66 (4H, m, 1′-H_2 and 4′-H_2), 4.13 (1H, td, *J* 2 × 11.3 and 3.6 Hz, 6-H_A), 4.31 (1H, ddd, *J* 11.3, 4.9 and 3.6 Hz, 6-H_B), 7.34–7.50 (6H, m, Ar-H) and 7.58–7.67 (4H, m Ar-H); δ_C (100 MHz, $CDCl_3$) 19.2 [*C*$(CH_3)_3$], 26.5 (C-5), 26.9 [C(*C*$H_3)_3$], 31.2 (C-3′), 32.8 (C-4), 33.9 (C-3), 41.8 (C-2′), 60.7 and 63.7 (C-1′ and C-4′), 68.6 (C-6), 127.7(3) and 127.8(1), 130.0, 132.9(2) and 132.9(8), 135.5(6) and 135.5(9) (Ar-C) and 171.5 (C-2); (Found: M^+, 426.2216. Calc. for $C_{25}H_{34}O_4Si$: *M*, 426.2224).

(2′*R**,4*R**)-4-(1-*tert*-Butyldiphenylsilanyloxy-4-phenylselanylbutan-2-yl)tetrahydropyran-2-one (25)

Phenylselenocyanate (538 mg, 2.95 mmol) in tetrahydrofuran (5 cm^3) and tri-*n*-butylphosphine (0.98 cm^3, 3.94 mmol) were added sequentially to a stirred solution of **24** (840 mg, 1.97 mmol) in tetrahydrofuran (15 cm^3). The resulting solution was stirred at 25 °C for 30 min, after which the solvent was removed under reduced pressure to give a crude mixture which was chromatographed directly on silica gel (60 g) using ethyl acetate–hexane (2 : 3) as eluent to yield *phenyl selenide* **25** (970 mg, 87%) as an oil, $\nu_{max}(CHCl_3)/cm^{-1}$ 1730 (CO); δ_H (400 MHz, $CDCl_3$) 1.03 [9H, s, $C(CH_3)_3$], 1.42–1.79 (5H, m, 5-H_2, 3′-H_2 and 2′-H), 2.06–2.21 (2H, m, 3-H_A and 4-H), 2.51–2.58 (1H, m, 3-H_B), 2.65 (1H, ddd, *J* 12.1, 8.5 and 7.3 Hz, 4′-H_A), 2.84 (1H, ddd, *J* 12.1, 8.8 and 5.2 Hz, 4′-H_B), 3.58 (1H, dd, *J* 10.9 and 5.0 Hz, 1′-H_A), 3.62 (1H, dd, *J* 10.9 and 4.2 Hz, 1′-H_B), 4.06–4.14 (1H, m, 6-H_A), 4.29 (1H, ddd, *J* 11.3, 4.7 and 3.8 Hz, 6-H_B), 7.15–7.25 (4H, m, Ar-H), 7.32–7.45 (7H, m, Ar-H) and 7.55–7.66 (4H, m, Ar-H); δ_C (100 MHz, $CDCl_3$) 19.2 [*C*$(CH_3)_3$], 25.6 (C-5), 26.6 (C-3′), 27.0 [C(*C*$H_3)_3$], 28.1 (C-4′), 32.7 (C-4), 34.1 (C-3), 44.6 (C-2′), 62.6 (C-1′), 68.7 (C-6), 127.8(3) and 127.8(4), 129.9(2) and 129.9(5), 133.1(1) and 133.1(8), 135.6(0) and 135.6(2) (TPS Ar-C), 127.1, 129.1, 129.8 and 132.8 (PhSe Ar-C) and 171.3 (C-2); (Found: $M^+ - C_4H_9$, 509.1032. Calc. for $C_{27}H_{29}O_3{}^{80}SeSi$: *M*, 509.1043).

(2′*R**,4*R**)-4-(1-*tert*-Butyldiphenylsilanyloxybut-3-en-2-yl)tetrahydropyran-2-one (26)

Water (30 cm^3) and sodium periodate (2.40 g, 11.2 mmol) were added to a stirred solution of **25** (1.10 g, 1.95 mmol) in methanol (100 cm^3). The resulting mixture was stirred at 25 °C for 20 min, poured into dichloromethane, washed with brine (200 cm^3) and dried ($MgSO_4$). The solvent was evaporated to give the selenoxide (1.20 g) which was dissolved in benzene–triethylamine (1 : 1)

(100 cm^3), refluxed for 10 min, and cooled. The solution was poured into an aqueous saturated sodium hydrogen carbonate solution (300 cm^3), extracted with diethyl ether and the organic extract dried ($MgSO_4$). The solvent was removed under reduced pressure to give an oil (1.01 g) which was purified by flash chromatography on silica gel (40 g) using ethyl acetate–hexane (1 : 9) as eluent to give the *olefin* **26** (707 mg, 89%) as an oil, $\nu_{max}(CHCl_3)/cm^{-1}$ 1732 (CO); δ_H (400 MHz, $CDCl_3$) 1.04 [9H, s, $C(CH_3)_3$], 1.48–1.58 (1H, m, 5-H_A), 1.77–1.85 (1H, m, 5-H_B), 2.02–2.12 (1H, m, 2′-H), 2.17 (1H, dd, *J* 16.6 and 10.7 Hz, 3-H_A), 2.20–2.31 (1H, m, 4-H), 2.57 (1H, ddd, *J* 16.6, 5.3 and 1.7 Hz, 3-H_B), 3.65 (1H, dd, *J* 10.3 and 5.6 Hz, 1′-H_A), 3.69 (1H, dd, *J* 10.3 and 5.1 Hz, 1′-H_B), 4.17 (1H, td, *J* 2 × 11.2 and 3.7 Hz, 6-H_A), 4.32 (1H, ddd, *J* 11.2, 4.7 and 4.2 Hz, 6-H_B), 5.05 (1H, dd, *J* 17.2 and 1.8 Hz, 4′-H_A), 5.14 (1H, dd, *J* 10.3 and 1.8 Hz, 4′-H_B), 5.66 (1H, ddd, *J* 17.2, 10.3 and 9.2 Hz, 3′-H), 7.35–7.49 (6H, m, Ar-H) and 7.59–7.65 (4H, m, Ar-H); δ_C (100 MHz, $CDCl_3$) 19.3 [*C*$(CH_3)_3$], 26.9 [C(*C*$H_3)_3$], 27.1 (C-5), 31.4 (C-4), 33.7 (C-3), 51.0 (C-2′), 64.5 (C-1′), 68.4 (C-6), 118.5 (C-4′), 127.8, 129.8, 133.3, 135.5(8) and 135.6(1) (Ar-C), 136.0 (C-3′) and 171.6 (C-2); (Found: $M^+ - C_4H_9$, 351.1415. Calc. for $C_{21}H_{23}O_3Si$: *M*, 351.1414).

(2′*R,4*S**)-4-(1-*tert*-Butyldiphenylsilanyloxybut-3-en-2-yl)-3-formyltetrahydropyran-2-one (27)**

tert-Butoxybis(dimethylamino)methane (2.58 cm^3, 12.5 mmol) was added to a flask containing lactone **26** (512 mg, 1.25 mmol) fitted with a condenser and N_2 inlet. The resulting mixture was stirred for 15 h at 82 °C. The solution was cooled and poured into a rapidly stirring solution of methanol (50 cm^3) and 3 M HCl (12 cm^3). The mixture was warmed to 25 °C with stirring and the volatile media were removed under reduced pressure. The residue was extracted with ethyl acetate, the organic extract was dried ($MgSO_4$) and the solvent was removed *in vacuo* to give a solid residue (606 mg). The material was chromatographed on silica gel (40 g) using ethyl acetate–hexane (1 : 4) as eluent to give the *formyl lactone* **27** (462 mg, 85%), mp 109–112 °C (from ethyl acetate–hexane), $\nu_{max}(CHCl_3)/cm^{-1}$ 1658 and 1702 (CO); (Found: C, 71.5; H, 7.4%, $M^+ - C_4H_9$, 379.1363. Calc. for $C_{26}H_{32}O_4Si$: C, 72.2; H, 7.3%, *M*, 379.1369).

(2′*R,3*E*,4*S**)-4-(1-*tert*-Butyldiphenylsilyanyloxybut-3-en-2-yl)-3-benzoyloxymethylenetetrahydropyran-2-one (28)**

Lactone **26** (300 mg, 0.74 mmol) was formylated as described above. The unpurified formyl lactone **27** (423 mg) was dissolved in dry pyridine (5 cm^3). Benzoyl chloride (0.2 cm^3, 240 mg, 1.72 mmol) was added and the solution was stirred at 25 °C for 30 min. The pyridine was removed under reduced pressure by azeotrope formation with toluene (3 × 30 cm^3). The resulting material was dissolved in dichloromethane, washed with brine and the aqueous phase extracted with dichloromethane. The organic extract was dried ($MgSO_4$) to give the benzoylated product (492 mg) which was purified by chromatography on silica gel (70 g) using ethyl acetate–hexane (1 : 9) to elute excess benzoyl chloride followed by elution with ethyl acetate–hexane (2 : 3) to yield the *enol benzoate* **28** (298 mg, 75% over 2 steps), $\nu_{max}(CHCl_3)/cm^{-1}$ 1713 and 1749 (CO); δ_H (400 MHz, $CDCl_3$) 1.08 [9H, s, $C(CH_3)_3$], 1.89–2.10 (2H, m, 5-H_2), 2.36–2.47 (1H, m, 2″-H), 3.47 (1H, dd, *J* 13.1 and 5.9 Hz, 4-H), 3.77 (1H, dd, *J* 10.4 and 5.3 Hz, 1″-H_A), 3.82 (1H, dd, *J* 10.4 and 4.6 Hz, 1″-H_B), 4.15–4.23 (1H, m, 6-H_A), 4.33–4.41 (1H, ddd, *J* 11.7, 9.2 and 3.9 Hz, 6-H_B), 5.00–5.07 (2H, m, 4″-H_2), 5.94 (1H, ddd, *J* 16.9, 10.4 and 9.2 Hz, 3″-H), 7.30–8.12 (15H, m, Ar-H) and 8.48 (1H, d, *J* 1.1 Hz, 1′-H); δ_C (100 MHz, $CDCl_3$) 19.5 [*C*$(CH_3)_3$], 25.6 (C-5), 27.1 [C(*C*$H_3)_3$], 33.1 (C-4), 49.6 (C-2″), 65.2 (C-1″), 66.1 (C-6), 115.6 (C-3), 118.0 (C-4″), 127.9(8) and 128.1(4), 127.9, 129.1, 130.0(2) and 130.0(9), 130.4, 133.4(5) and 133.5(1), 134.5, 135.8(1) (Ar-C), 136.0 (C-3″), 145.3 (C-1′), 162.2 (Ar-C=O) and 166.5 (C-2); (Found: $M^+ - C_4H_9$, 483.1633. Calc. for $C_{21}H_{23}O_3Si - C_4H_9$: *M*, 483.1628).

(2′*R,4*S**)-4-(1-*tert*-Butyldiphenylsilyanyloxybut-3-en-2-yl)-3-methoxyethoxymethoxymethylenetetrahydropyran-2-one (29)**

Formyl lactone **27** (220 mg, 0.50 mmol) was dissolved in dry dichloromethane (10 cm^3). Methoxyethoxymethyl chloride (0.07 cm^3, 76 mg, 0.61 mmol) was added, followed by diisopropylethylamine (0.11 cm^3, 82 mg, 0.63 mmol). The mixture was stirred at 25 °C for 16 h, after which water (10 cm^3) was added and the aqueous phase was extracted with dichloromethane. The organic phase was dried ($MgSO_4$) and the solvent was removed under reduced pressure to give an oil (272 mg). Chromatography on silica gel (25 g) using ethyl acetate–hexane (3 : 7) as eluent, furnished the *enol ether* **29** (207 mg, 79%) as an oil, $\nu_{max}(CHCl_3)/cm^{-1}$ 1698 (CO); δ_H (400 MHz, $CDCl_3$) 1.05 [9H, s, $C(CH_3)_3$], 1.78–1.88 (1H, m, 5-H_A), 1.89–2.00 (1H, m, 5-H_B), 2.38–2.48 (1H, m, 2″-H), 3.17 (1H, dd, *J* 12.1 and 6.1 Hz, 4-H), 3.35 (3H, s, OCH_3), 3.46–3.57 and 3.62–3.67 (4H, m, O*C*H_2*C*H_2O), 3.67 (1H, dd, *J* 10.3 and 5.9 Hz, 1″-H_A), 3.72 (1H, dd, *J* 10.3 and 5.1 Hz, 1″-H_B), 4.05–4.15 (1H, m, 6-H_A), 4.32 (1H, ddd, *J* 11.3, 9.2 and 3.7 Hz, 6-H_B), 4.95–5.06 (4H, m, 4″-H_2 and OCH_2O), 5.69–5.81 (1H, m, 3″-H), 7.34–7.45 (6H, m, Ar-H), 7.56 (1H, s, 1′-H) and 7.61–7.67 (4H, m, Ar-H); δ_C (100 MHz, $CDCl_3$) 19.3 [*C*$(CH_3)_3$], 25.9 (C-5), 26.8 [C(*C*$H_3)_3$], 32.1 (C-4), 49.8 (C-2″), 59.1 (OCH_3), 65.5 (C-6), 65.7 (C-1″), 68.5 and 71.3 (O*C*H_2*C*H_2O), 97.1 (OCH_2O), 109.3 (C-3), 117.1 (C-4″), 127.6(4) and 127.6(7), 129.7, 133.5(4) and 133.6(1), 135.6 (Ar-C), 137.9 (C-3″), 155.9 (C-1′) and 167.7 (C-2); (Found: $M^+ - C_4H_9$, 467.1889. Calc. for $C_{21}H_{23}O_3Si - C_4H_9$: *M*, 467.1890).

Deprotection of silyl ether 29

Tetrabutylammonium fluoride (1 M in THF, 0.62 cm^3, 0.62 mmol) was added to a stirred solution of **29** (524 mg, 0.31 mmol) in tetrahydrofuran (5 cm^3) at 0 °C. The solution was warmed to 25 °C. After stirring for 16 h, the reaction was complete (TLC). Water (10 cm^3) was added and the mixture was extracted with ethyl acetate. The organic extract was dried ($MgSO_4$) and the solvent was removed under reduced pressure to give a crude mixture (168 mg). Chromatography on silica gel (20 g) using ethyl acetate–hexane (2 : 3) as eluent yielded *(4R*,4aS*)-4-vinyl-4,4a,5,6-tetrahydro-3H-pyrano[3,4-c]pyran-1-one* **30** (12 mg, 22%) as an oil, $\nu_{max}(CHCl_3)/cm^{-1}$ 1708 (CO) and 1611 (C=C conj.); δ_H (300 MHz, $CDCl_3$) 1.60–1.89 (2H, m, 5-H_2), 2.52–2.59 (1H, m, 4-H), 2.80–2.89 (1H, m, 4a-H), 3.97–4.08 (1H, m, 6-H_A), 4.30–4.40 (1H, m, and 6-H_B), 4.33 (1H, dd, *J* 11.1 and 2.5 Hz, 3-H_A), 4.44 (1H, dd, *J* 11.1 and 2.0 Hz, 3-H_B), 5.22–5.30 (2H, m, 2′-H_2), 5.73–5.88 (1H, m, 1′-H) and 7.73–7.76 (1H, br. d, 8-H); δ_C (75 MHz, $CDCl_3$) 24.9 (C-5), 33.2 (C-4a), 40.5 (C-4), 66.8 (C-6), 72.7 (C-3), 102.4

(C-8a), 119.4 (C-2′), 132.7 (C-1′), 157.9 (C-8) and 165.4 (C-1); (Found: M^+, 180.0790. Calc. for $C_{10}H_{12}O_3$: *M*, 180.0786), followed by mixed fractions (25 mg, 44%) which were combined and re-chromatographed on silica gel (10 g) using ethyl acetate–hexane (3 : 7). Partial separation gave further **30** (5 mg) followed by mixed fractions (5 mg) and *(4aS*,5R*)-5-vinyl-4,4a,5,6-tetrahydro-3H-pyrano[3,4-c]pyran-1-one* **31** (14 mg), $\nu_{max}(CHCl_3)/cm^{-1}$ 1703 (CO) and 1612 (C=C conj.); δ_H (300 MHz, $CDCl_3$) 1.58–1.83 (2H, m, 4-H_2), 2.55–2.63 (1H, m, 5-H), 2.85 (1H, dtd, *J* 11.8, 2 × 5.3 and 2.4 Hz, 4a-H), 4.13–4.32 (3H, m, 3-H_A and 6-H_2), 4.41 (1H, ddd, *J* 11.3, 4.4 and 2.4 Hz, 3-H_B), 5.20–5.30 (2H, m, 2′-H_2), 5.74 (1H, ddd, *J* 9.3, 10.3 and 17.0 Hz, 1′-H) and 7.73–7.76 (1H, br. d, 8-H); δ_C (75 MHz, $CDCl_3$) 26.4 (C-4), 33.1 (C-4a), 38.9 (C-5), 67.7 (C-3), 71.8 (C-6), 102.5 (C-8a), 118.7 (C-1′), 133.2 (C-2′), 156.2 (C-8) and 166.0 (C-1); (Found M^+, 180.0785. Calc. for $C_{10}H_{12}O_3$: *M*, 180.0786).

Deprotection of silyl ether 25

Tetrabutylammonium fluoride (1.0 M solution in THF, 2.0 cm^3, 2.0 mmol) was added to a stirred solution of silyl ether **25** (565 mg, 1.00 mmol) in 10 cm^3 tetrahydrofuran at 0 °C. After 90 min, water (10 cm^3) was added and the resulting mixture was extracted with ethyl acetate, dried ($MgSO_4$) and the solvent was removed under reduced pressure to give a residue (603 mg). Chromatography on silica gel (50 g) using ethyl acetate–hexane (3 : 2) as eluent yielded an inseparable mixture of alcohols **32** and **33** (224 mg, 69%). The mixture (220 mg, 0.67 mmol) in pyridine (10 cm^3) was treated with acetic anhydride (0.32 cm^3, 3.36 mmol) and dimethylaminopyridine (20 mg, 0.16 mmol) and then stirred at 25 °C for 16 h. Toluene was added (30 cm^3) and the mixture was concentrated under reduced pressure (3×), resulting in an oil (320 mg) which was chromatographed on silica gel (30 g) using ethyl acetate–hexane (3 : 7) as eluent to give *(4R*,5R*)-4-acetoxyethyl-5-phenylselanylethyl-3,4,5,6-tetrahydropyran-2-one* **34** (36 mg, 14%) $\nu_{max}(CHCl_3)/cm^{-1}$ 1732 (CO); δ_H (300 MHz, $CDCl_3$) 1.44–1.54 (1H, m, 1′-H_A), 1.60–1.75 (3H, m, 1′-H_B, 1″-H_2), 2.03 (3H, s, CO_2CH_3), 2.06–2.22 (2H, m, 4-H, 5-H), 2.32 (1H, dd, *J* 18.1 and 8.5 Hz, 3-H_A), 2.60 (1H, dd, *J* 18.1 and 6.2 Hz, 3-H_B), 2.85 (1H, dt, *J* 12.4 and 2 × 7.6 Hz, 2″-H_A), 3.03 (1H, ddd, *J* 12.4, 7.6 and 5.9 Hz, 2″-H_B), 4.00–4.12 (2H, m, 2′-H_2), 4.25 (2H, d, *J* 4.8 Hz, 6-H_2), 7.23–7.29 (3H, m, Ar-H) and 7.44–7.51 (2H, m, Ar-H); δ_C (75 MHz, $CDCl_3$) 20.9 (CO_2CH_3), 24.9 (C-1″), 25.0 (C-2″), 29.4 (C-1′), 31.8 (C-4), 34.1 (C-3), 35.2 (C-5), 61.6 (C-2′), 70.8 (C-6), 127.3, 129.2 and 132.8 (Ar-C), 169.7 (CO_2CH_3) and 170.8 (C-2); (Found: M^+, 370.0667. Calc. for $C_{17}H_{22}O_4{}^{80}Se$: *M*, 370.0683) followed by mixed fractions (97 mg, 39%) and *(2′R*,4R*)-3-(1′-acetoxy-4-phenylselanylbut-2-yl)pentan-5-olide* **35** (25 mg, 10%) as an oil, $\nu_{max}(CHCl_3)/cm^{-1}$ 1735 (CO); δ_H (300 MHz, $CDCl_3$) 1.58 (1H, dtd, *J* 14.0, 2 × 10.7 and 4.9 Hz, 5-H_A), 1.67–1.93 (4H, m, 2′-H, 3′-H_2 and 5-H_B), 2.03 (3H, s, CO_2CH_3), 2.00–2.14 (1H, m, 4-H), 2.23 (1H, dd, *J* 17.0 and 11.0 Hz, 3-H_A), 2.59 (1H, ddd, *J* 17.0, 6.0 and 1.8 Hz, 3-H_B), 2.84 (1H, dt, *J* 2 × 7.8 and 12.3 Hz, 4′-H_A), 3.00 (1H, ddd, *J* 12.3, 6.9 and 5.4 Hz, 4′-H_B), 4.07 (1H, d, *J* 4.9, 1′-H_2), 4.18 (1H, td, *J* 2 × 11.4 and 3.6 Hz, 6-H_A), 4.37 (1H, ddd, *J* 11.4, 4.9 and 3.6 Hz, 6-H_B), 7.23–7.38 (3H, m, Ar-H) and 7.44–7.52 (2H, m, Ar-H); δ_C (75 MHz, $CDCl_3$) 20.8 (CO_2CH_3), 25.2 (C-4′), 26.3 (C-5), 28.4 (C-3′), 32.9 (C-4), 33.8 (C-3), 41.5 (C-2′), 63.4 (C-1′), 68.3 (C-6), 127.3, 129.2, 129.4 and 133.0 (Ar-C) and 170.1 and 170.1 (C-2 and CO_2CH_3); (Found: M^+, 370.0665. Calc. for $C_{17}H_{22}O_4{}^{80}Se$: *M*, 370.0683).

Acknowledgements

We thank the South African National Research Foundation for financial support.

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