Synthesis of 2,5-dihydrofurans *via* alkylidene carbene insertion reactions

Louise F. Walker,[a] Ahmed Bourghida,[a] Stephen Connolly[b] and Martin Wills*[a]

[a] *Department of Chemistry, University of Warwick, Coventry, UK CV4 7AL*
[b] *Medicinal Chemistry, AstraZeneca R&D Charnwood, Bakewell Road, Loughborough, Leicestershire, UK LE11 5RH*

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The insertion reaction of alkylidene carbenes is demonstrated to be an effective method for the synthesis of 2,5-dihydrofuran ring systems. The best results have been obtained on substrates containing electron-withdrawing substituents, which appear less prone to the competing rearrangement reaction. This insight has led to the development of a new method for the synthesis of the core structure of the squalestatin–zaragozic acid natural products.

Introduction

Alkylidene carbenes **1** represent a class of valuable synthetic intermediates which have been employed in a number of total syntheses of challenging natural products.[1–17] The formation of these reactive species may be achieved by a number of methods,[2–17] including treatment of vinyl halides with a strong base,[2–5] nucleophilic addition to alkynyliodonium salts,[6] and by the reaction of a carbonyl compound with diazomethylphosphonate[7,8] or lithio(trimethylsilyl)diazomethane (LTDM).[9–13] Although carbenes **1** (R = H, R′ = alkyl) undergo rapid rearrangement to alkynes,[18] substrates lacking a hydrogen atom adjacent to the carbene are known to participate in insertion reactions with appropriate functional groups. Intramolecular trapping of the carbene with hydroxy or amino groups provides a convenient method for the synthesis of heterocycles,[2,9,14,15] and insertion of the carbenes into proximal C–H bonds provides a convenient method for the synthesis of cyclopentenes,[4,6,7,10,16,17] or heterocyclic products.[5,8,10,13,17] In our studies on the total synthesis of neohalicholactone, a 2,5-dihydrofuran side product was obtained *via* the insertion of a vinylidene carbene generated from a 1,1-dibromoalkene.[19]

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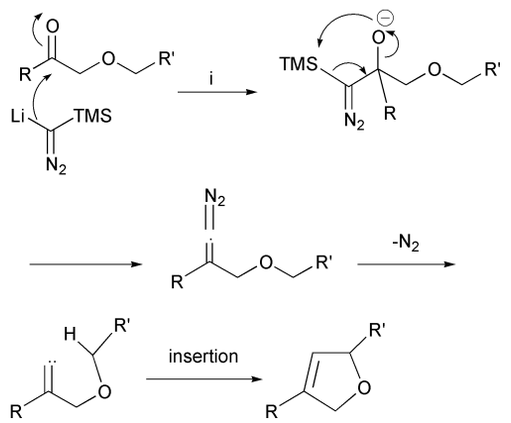
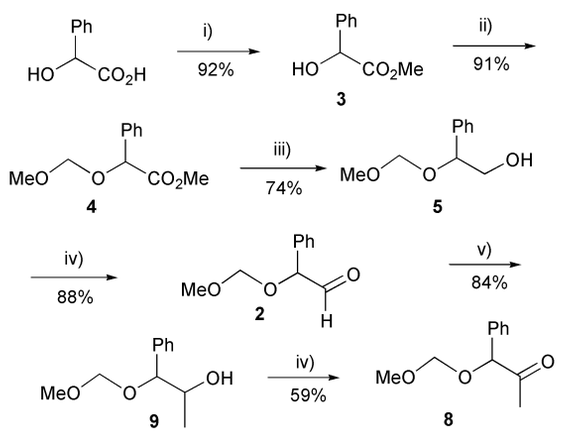
Intrigued by this latter result, we chose to pursue a systematic investigation into the scope and limitations of alkylidene insertion reactions as a method for 2,5-dihydrofuran synthesis. Throughout our work we chose to use the commercially available reagent (trimethylsilyl)diazomethane (TMSDM),[9–13] lithiation of which with *n*BuLi generates the active reagent LTDM. The proposed mechanism for the generation of an alkylidene carbene by the reaction of lithiated TMSDM and a carbonyl compound is shown in Scheme 1. It was also our intention to study the diastereoselectivity of the reaction with respect to 2,5-disubstituted-2,5-dihydrofurans and examine the nature of the stereochemical induction. We also wished to explore the application of this methodology in natural product synthesis.

The first 2,5-dihydrofuran precursor we selected for study was the aldehyde **2** which, on reaction with LTDM, would yield an alkylidene carbene. The two heteroatoms adjacent to the



Scheme 1 *Reagents and conditions*: i) TMSDM, *n*BuLi, DME–hexane.

C(5)–H bond would be expected to increase the rate of insertion.[11b,20,21] Generally, electron donating groups activate C–H bonds towards insertion and electron withdrawing groups deactivate. Aldehyde **2** was synthesised from (±)-mandelic acid † (Scheme 2). The methyl ester of mandelic acid **3** was prepared under standard esterification conditions then protected with a



Scheme 2 *Reagents and conditions*: i) AcCl, MeOH. ii) $(MeO)_2CH_2$, P_2O_5, $CHCl_3$. iii) $LiAlH_4$, Et_2O, reflux, iv) DMSO, ClCOCOCl, NEt_3, DCM. v) MeMgBr, THF, rt, overnight.

† The IUPAC name for mandelic acid is phenylglycolic acid.

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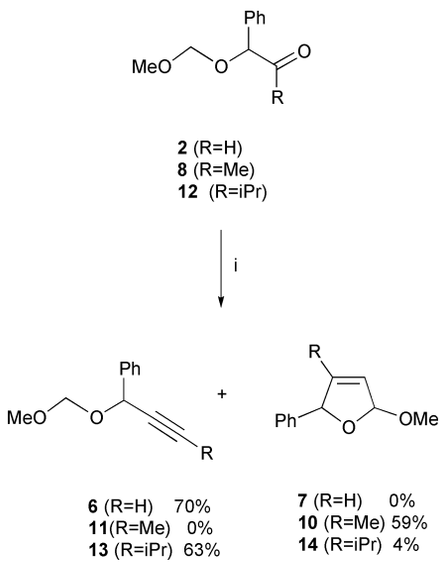
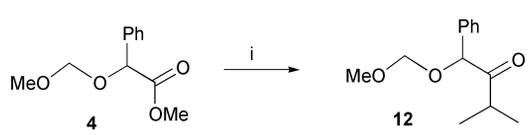
methoxymethyl (MOM) protecting group using dimethoxymethane and catalytic phosphorus pentaoxide in chloroform.[22] Reduction of the ester **4** with lithium aluminium hydride followed by Swern oxidation led to the generation of 2-phenyl-2-methoxymethoxyethanal **2**. Aldehyde **2** was treated with LTDM and an alkyne **6** was obtained as the exclusive product in good yield as the result of a 1,2-hydrogen shift (Scheme 3) with no evidence of the corresponding 2,5-dihydrofuran **7**. It was therefore clear that hydrogen migration was always likely to outpace any attempted insertion reaction in an aldehyde-derived system. The methyl ketone **8** was therefore synthesised from aldehyde **2** by a Grignard reaction with methylmagnesium bromide and oxidation of the resulting alcohol **9** (Scheme 2). Treatment of **7** with LTDM resulted in the formation of 2,5-dihydrofuran **10** by a C(5)–H insertion reaction, which appeared to be a single diastereoisomer by ^{1}H NMR (Scheme 3). There was no evidence of formation of the corresponding alkyne **11**



Scheme 3 *Reagents and conditions*: i) TMSDM, *n*BuLi, DME–hexane.

In order to facilitate a shorter synthesis of analogues of ketone **8** we examined the direct conversion of a methyl ester to ketones *via* a Weinreb amide intermediate. We elected to use the method reported by Williams and co-workers in which a Grignard reagent is employed as both the base and the organometallic reagent.[23] A combination of bases and Grignard reagents were experimented with but only one combination proved successful in our hands; the use of isopropylmagnesium chloride as both the base and Grignard reagent (Scheme 4).



Scheme 4 *Reagents and conditions*: i) PrMgBr, Me(MeO)NH·HCl, THF.

This resulted in the formation of an isopropyl ketone **12** which on treatment with LTDM gave a mixture of products, the major (63%) being alkyne **13**, the product of an 1,2-alkyl shift and the minor (*ca.* 4%) being the desired 2,5-dihydrofuran **14**, formed as a single diastereoisomer (Scheme 3).

If we consider the later two results in terms of the electron donating nature of the β-alkyl substituents, we can see that the methyl group is electron donating but does not migrate whereas the greater electron donating ability of the isopropyl group resulted in its migration (Fig. 1). Therefore, it might be expected that an electron withdrawing group in the β-position to the carbene might prevent migration. To test this speculation a series of ketones which had electron withdrawing α-alkoxy-substituents were synthesised. These were prepared by a variety of methods.

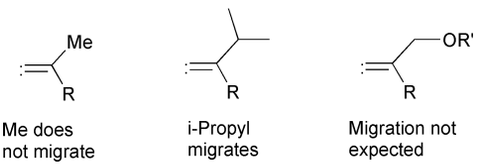
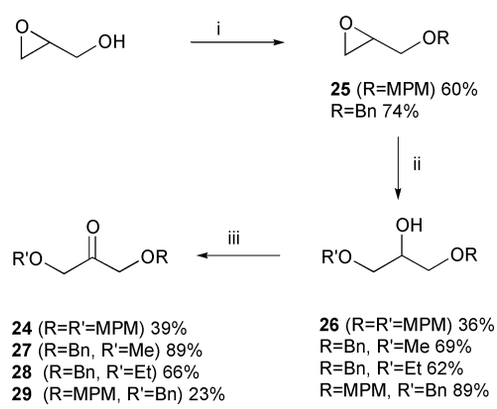
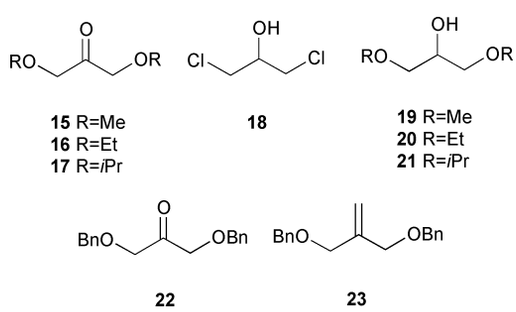


Fig. 1 Electron-donating nature of β-substituents.

Symmetrical ketones **15**–**17** were formed by reaction of 1,3-dichloropropan-2-ol **18** and the appropriate sodium alkoxide followed by oxidation of the corresponding alcohols **19**–**21** by PCC oxidation.[24a] The synthesis of 1,3-bis(benzyloxy)propan-2-one **22** was achieved by reaction of 3-chloro-2-chloromethyl-prop-1-ene with sodium benzyl oxide followed by ozonolysis of the double bond in the product **23** to give the ketone. 1,3-Bis(*p*-methoxyphenylmethoxy)propan-2-one **24** was synthesised from (±)-glycidol (Scheme 5). The alcohol was deprotonated and reacted with *p*-methoxybenzyl chloride. Epoxide **25** was then opened with *p*-methoxybenzyl alcohol in the presence of catalytic lithium perchlorate.[24b] Finally oxidation of this alcohol **26** by PCC gave the desired ketone **24**. The same method was employed for the synthesis of a series of unsymmetrical ketones **27**–**29** (Scheme 5). The results of insertion reactions on these compounds would provide evidence of the relative rates of insertion into different C(5)–H bonds adjacent to benzyl, methyl, ethyl and *p*-methoxyphenylmethyl (MPM). One final ketone **30** was synthesised by deprotonation of cyclopentanol with sodium hydride and subsequent reaction with 3-bromo-2-methylpropene in DMF. The double bond of the resulting alkene was then ozonolised to give ketone **30**.



Scheme 5 *Reagents and conditions*: i) NaH, RX, DMF, ii) $LiClO_4$, R′OH, MeCN, reflux, iii) PCC, ClCOCOCl, NEt_3, DCM.



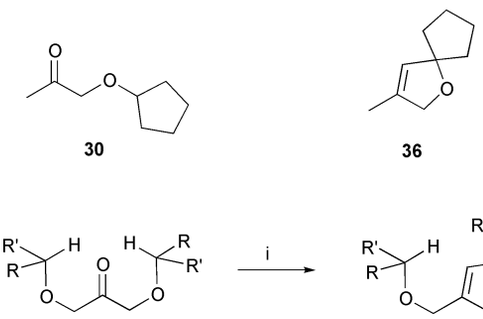
Each symmetrical ketone was then treated with LTDM at −78 °C and allowed to warm to rt over 4 h (Scheme 6 and Table 1). The reaction of 1,3-dimethoxy- **15** and 1,3-diisopropoxypropan-2-one **17** with LTDM resulted in poor yields of insertion products **31** and **35**. In the case of diisoprop-

Table 1 Alkylidene carbene insertion reactions

Substrate	R	R′	Product	Yield (%)
15	H	H	**31**	14
16	H	Me	**32**	55
22	H	Ph	**33**	70
24	H	*p*-(MeO)C_6H_4	**34**	61
17	Me	Me	**35**	27

Table 2 Alkylidene carbene insertion reactions of unsymmetrical ketones

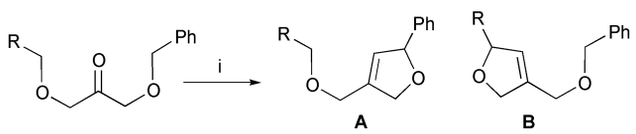
Substrate	R	Ratio A : B	Yield (%)
27	H	1 : 2	34
28	Me	5 : 3	52
29	*p*-(MeO)C_6H_4	1 : 1	32



Scheme 6 *Reagents and conditions*: i) TMSDM, *n*BuLi, DME–hexane.

oxypropan-2-one, starting material was also recovered from the reaction indicating that the reaction did not reach completion in 4 h. Ketones **16**, **22** and **24** all gave good yields of 2,5-dihydrofuran products **32**–**34**. The presence of an adjacent aromatic group appears to result in activation of the C(5)–H bond in the same way as the α oxygen.[21] On reaction with LTDM a spiro-2,5-dihydrofuran **36** was formed from ketone **30** in 57% yield.

There was generally little selectivity between the different C(5)–H bonds in the unsymmetrical ketones examined (Scheme 7, Table 2). Although yields of products were poor, which limits



Scheme 7 *Reagents and conditions*: i) TMSDM, *n*BuLi, DME–hexane.

the validity of the data, there appears to be a potential order of insertion preference of methoxy > OBn = OMPM > ethoxy. However, other factors may be significantly more important to the regioselectivity. Indeed an observation by Taber[17b] indicates that the environment of the activating group may be of less significance than the method employed to prepare the carbene.

Insertion products **10** and **14** may possess *trans* or *cis* relative stereochemistry. In the two examples described so far both products appeared to be formed as single diastereoisomers. For 2-methoxy-4-methyl-5-phenyl-2,5-dihydrofuran (**10**) we have tentatively assigned this to be *cis*, based on a consideration of the likely transition states that have been postulated (Fig. 2),[6a,11b] to predict the diastereoselective outcome of such reactions. 2,5-Dihydrofuran **14** was formed along with the alkyne **13**. This 2,5-dihydrofuran was also obtained as a single diastereoisomer to which we also tentatively assign the same relative stereochemistry. We followed these results with one further example to investigate the diastereoselectivity of the reaction. Pyruvaldehyde dibenzyl acetal was prepared by reacting the corresponding dimethyl acetal with benzyl alcohol in the presence of

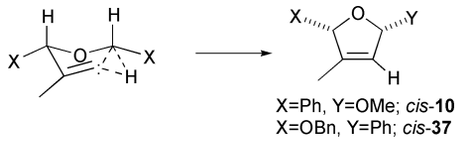
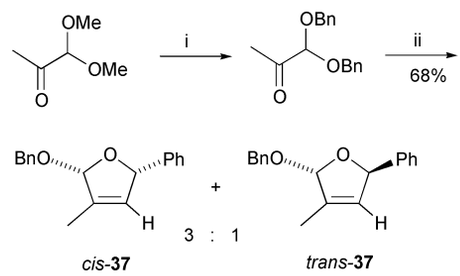


Fig. 2 Proposed mode of formation of **10** and **37**.

catalytic PTSA. Upon reaction with LTDM, this ketone gave 2,5-dihydrofuran **37** as a 3 : 1 mixture of diastereoisomers of which the major isomer was predicted to be the *cis*-isomer (Scheme 8) by considering the predicted transition state for its formation, *i.e.* bearing pseudo-equatorial substituents (Fig. 3).



Scheme 8 *Reagents and conditions*: i) BnOH, PTSA, toluene, reflux. ii) TMSDM, *n*BuLi, DME–hexane.

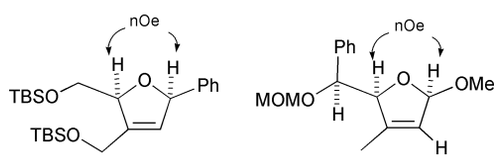
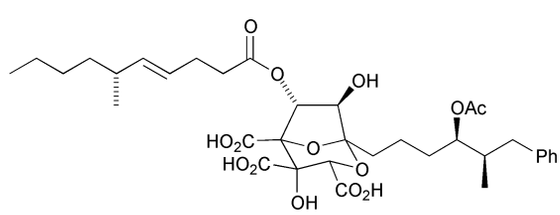


Fig. 3 Compounds related to **10**, **14** and **37** demonstrated to be *cis*-by NOE measurements.

The measurement of nuclear Overhauser effects (NOE) provides a means for the assignment of relative stereochemistry in compounds of rigid structure, such as heterocycles. Although NOE studies were not carried out during the course of this study on compounds **10**, **14** and **37** due to the lack of a suitable facility, two closely related compounds, illustrated in Fig. 3, have been made in our group *via* identical insertion reactions. In both cases analysis exhibited a strong NOE between the protons at the 2 and 5 positions of the dihydrofuran ring.[25] This suggests a *cis*-relationship between these protons in the illustrated compounds and, by analogy, in the rings of compounds **10**, **14** and **37**.

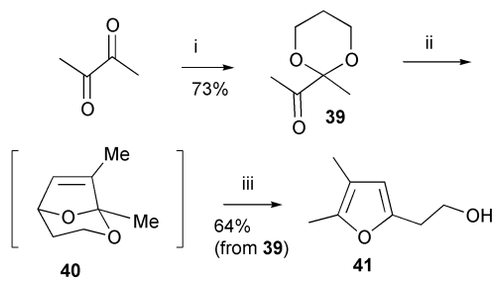


The squalestatin–zaragozic acid class of natural products (*e.g.* zaragozic acid C **38**) have been a subject of great interest to synthetic organic chemists on account of their biological activity and complex structure.[26] Though their synthesis has been realised by a number of groups, each synthesis utilises an acid catalysed ketalisation reaction in order to close the bicyclic core. We set out to synthesise the bicylic core by an alkylidene carbene C(5)–H insertion reaction (Scheme 9). We envisioned construction of the six-membered ketal followed by generation of an alkylidene carbene that would insert into the C(3)– or C(3′)–H axial bond to give the five-membered ring of the bicyclic core.

Whilst devising a model system for the key cyclisation step, we considered that a methyl group at the C(1) position would be

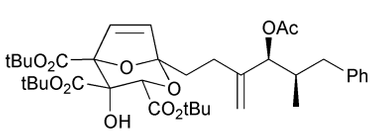
Scheme 9 Proposed synthetic approach to squalestatins–zaragozic acid core.

required to force the less bulky sp^2 ketone into the axial position where it would readily insert into the corresponding axial C(3)– or C(3′)–H bond. The synthesis of ketal **39** was achieved by heating butane-2,3-dione with propane-1,3-diol and PTSA (Scheme 10). This ketone was then treated with LTDM under



Scheme 10 *Reagents and conditions*: i) propane-1,3-diol, PTSA, toluene, 90 °C. ii) TMSDM, *n*BuLi, DME–hexane. iii) silica gel or alumina.

the standard conditions described above. ^{1}H NMR analysis of the crude product from this reaction showed that the insertion reaction had indeed been successful and the bicyclic product **40** had been formed exclusively. Unfortunately, attempted purification of this product by column chromatography on silica gel or alumina resulted in rearrangement to give a furan **41** which was isolated in good yield. The rearrangement is likely to proceed *via* an acid-catalysed opening of the six-membered ring followed loss of a proton from C(5) resulting in aromatisation to the furan. This type of rearrangement has been observed before by a team at GlaxoSmithKline.[27] When a squalestatin analogue **42** was treated with acid, it underwent ring opening with elimination, yielding furan **43**.



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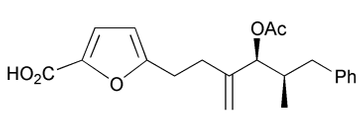

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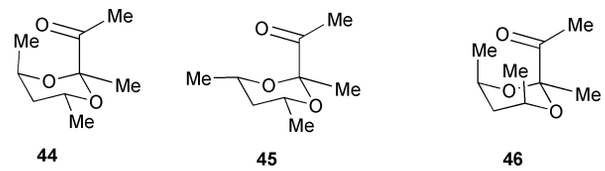
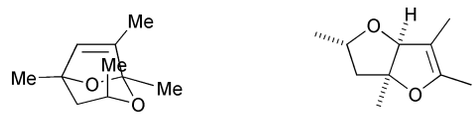
A further set of ketals were synthesised by the independent reactions of (*R*,*R*)-(−)-pentane-2,4-diol and *meso*-pentane-2,4-diol with butane-2,3-dione and PTSA. This resulted in the preparation of three ketals **44**–**46**. The relative stereochemistry in the ketals **45** (40%) and **46** (15%) prepared from *meso*-pentane-2,4-diol was assigned following reaction with LTDM as only **45** would be predicted to be able to form the desired product by alkylidene carbene insertion into the axial C(5)–H bond.

Each ketal in turn was then treated with LTDM. The ketal **44** gave the expected insertion product **47** in a crude form but attempted purification by column chromatography resulted in rearrangement, not to the furan, but to the fused bicyclic

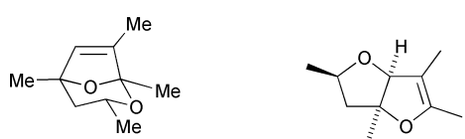


44 **45** **46**

product **48**. In this case this is almost certainly because there is no group that may be eliminated from the C(5) position resulting in aromatisation. The exact structure of the bicyclic product obtained was confirmed by a 3-bond correlation NMR study. As expected, ketal **46**, bearing axial methyl groups at C(3) and C(3′), gave no insertion product. Ketal **45** was treated with LTDM, and once again the crude NMR spectrum showed that the reaction had given the insertion product **49**. Upon purification by column chromatography a rearrangement had taken place leading to **50** (45% overall yield), analogous to that observed with ketal **44**. In the case of this ketal there is no diaxial interaction between the C(3) methyl and the five-membered ring but despite this the rearrangement still proceeded.



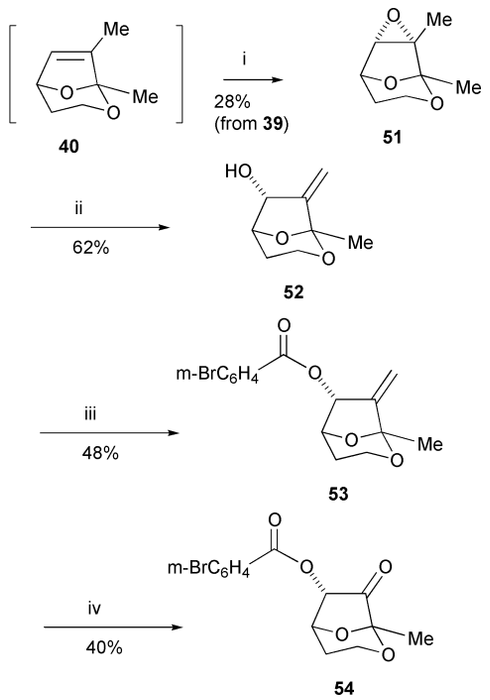
47 **48**



49 **50**

As all attempts to abate the rearrangement process by placing groups at the C(3) and C(3′) positions of the ketal had failed, we next chose to carry through the crude insertion products to the next step of the sequence toward the squalestatin–zaragozic acid core. The insertion reaction proceeded well so our next tasks were to convert the methyl and double bond groups into the required ester and alcohol groups with appropriate stereochemistry. We achieved this by epoxidation of the double bond, ring opening of the epoxide and esterification of the alcohol followed by simple ozonolysis of the double bond and reduction of the ketone product (Scheme 11). This sequence was carried out on the simplest crude bicyclic core **40** with the first step, epoxidation, first using MCPBA (*m*-chloroperbenzoic acid). Unfortunately no desired product was obtained in the reaction, and furan **41** was obtained as the major product. Using dimethyldioxirane,[28] a neutral epoxidising reagent, the epoxidation reaction was successful but the product **51** was formed in low yield. It is also interesting to note that only one product was formed in this reaction which we believe was probably due to attack from the less hindered *exo* face giving the relative stereochemistry required at the C(6) position. The next step in this sequence was ring opening of the epoxide with base. LDA failed to give any of the desired product therefore the use of dilithiated (1*S*,2*R*)-norephedrine was investigated. This particular base was chosen as it has been used effectively in the enantioselective rearrangement of epoxides to allylic alcohols.[29] In the event, the rearrangement of epoxide **51**[30] proceeded smoothly in reasonable yield to give the racemic allylic alcohol **52** (Scheme 11).

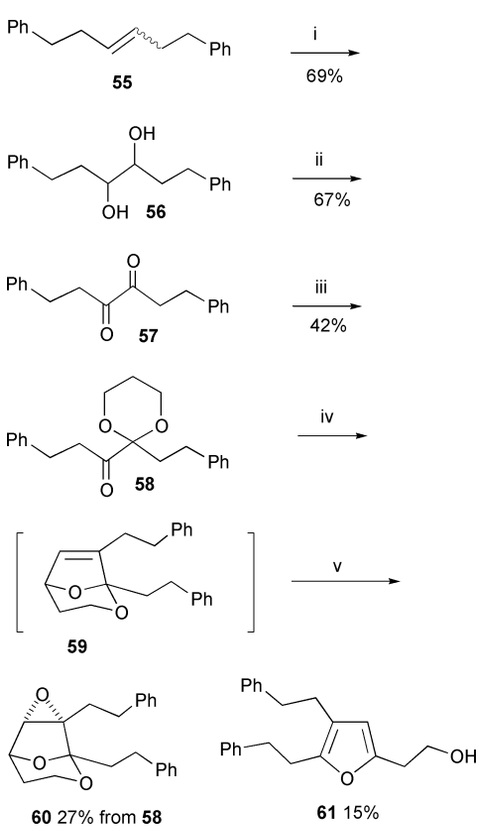
The next two steps were a simple coupling between the alcohol and 3-bromobenzoic acid with DCC and DMAP[31] and ozonolysis of the double bond to give ketone **54**. 3-Bromobenzoic acid was used to form the ester **53** (48% yield) as it was hoped this would lead to a crystalline compound suitable for X-ray analysis. This would establish without doubt the relative



Scheme 11 *Reagents and conditions*: i) dimethyldioxirane, acetone. ii) (1*R*, 2*S*)-Norephedrine, *n*-BuLi, THF, PhH. iii) DCC, DMAP, *m*-$BrC_6H_4CO_2H$, DCM. iv) Ozone, DCM, Me_2S.

stereochemistry at C(6). Unfortunately neither the alkene nor the ketone **54** (formed from **53** in 40% yield) were solids.

We also investigated the synthesis of a more complex intermediate for the squalestatin–zaragozic acid synthesis (Scheme 12). This was designed to facilitate the incorporation of a more complex chain at the ketal of the bicyclic product; an essential requirement for the total synthesis. However a disadvantage



Scheme 12 *Reagents and conditions*: i) NMO, OsO_4, $MeSO_2NH_2$, acetone–H_2O. ii) ClCOCOCl, DMSO, Et_3N, DCM. iii) Propane-1,3-diol, PTSA, toluene, reflux, 15 h. iv) TMSDM, *n*-BuLi, DME–hexanes. v) Dimethyldioxirane, acetone.

with this route is the potentially wasteful removal of the resulting chain at C(7) in the bicyclic core after the insertion reaction has been performed. In this step half of the original ketone is cleaved in the ozonolysis which, in a more complex analogue would lead to the loss of a chain of considerable complexity. However this route will hopefully demonstrate that the insertion reaction will still occur predominantly into the C(5)–H of the ketal and not into the C(1) side chain.

The starting material for this synthesis was 3-phenylpropyl-(triphenyl)phosphonium bromide which was used in a Wittig reaction with hydrocinnamaldehyde to give alkene **55**. This alkene was reacted with catalytic osmium tetraoxide in a dihydroxylation[32] and then the resulting diol **56** oxidised by a Swern oxidation to give 1,6-diphenylhexane-3,4-dione **57**. Ketal formation proceeded cleanly to give the desired ketal **58**, which was treated with LTDM. The insertion reaction proceeded with exclusive insertion into the desired C(5)–H bond yielding the crude bicyclic core **59** which was directly epoxidised to **60** using dimethyldioxirane. This reaction also resulted in the formation of some furan **61**, which is as a result of the starting material rearranging as we have seen before. With the epoxide **60** in hand an attempt to deprotonate and ring open the epoxide was carried out using lithiated (1*S*,2*R*)-norephedrine. However we did not obtain any of the desired product in the reaction and no starting material was retrieved.

In summary we have demonstrated that the insertion reactions of alkylidene carbenes with proximal C–H bonds represent a valuable method for the formation of heterocyclic systems. We are currently extending our investigations to more complex systems, including carbohydrates, and these results will be reported in due course.

Experimental

All reactions were carried out in vacuum-flame-dried or oven-dried glassware under nitrogen unless otherwise stated. Reagents were obtained from commercial sources and were either used directly or purified by standard methods. THF and diethyl ether were freshly distilled from sodium using benzophenone as an indicator; DCM from calcium hydride; toluene from sodium. DMF, DMSO and acetonitrile were distilled from calcium hydride under reduced pressure and DME was distilled from calcium hydride. All the above purifications were carried out under nitrogen. Petroleum ether refers to that fraction which boils in the range 40–60 °C.

The reactions were monitored by TLC using aluminium backed silica gel 60 (F_{254}) plates, pre-coated with a layer of silica (Merck), and these were visualised with UV (λ = 254 nm) and then phosphomolybdic acid solution, potassium permanganate solution or 2,4-dinitrophenylhydrazine solution. All organic layers were concentrated by rotary evaporation on a Büchi rotary evaporator, the final traces of solvents being removed on a static oil pump (2 mmHg). Column chromatography was carried out on silica gel 60 (40–63 μm).

Melting points were measured on a Stuart Scientific SMP1 instrument and are uncorrected. Infrared spectra (IR) were recorded on a Perkin–Elmer 1310 FTIR spectrometer for samples between sodium chloride plates with peak intensities specified as strong (s), medium (m), weak (w) and broad (br). Optical rotations were measured on a Perkin-Elmer 241 polarimeter (sodium D line) at ambient temperature with a 1 cm rotation cell. $[\alpha]_D$ values are reported in 10^{-1} deg cm^2 g^{-1}. Nuclear magnetic resonance spectra (NMR) were recorded on a Bruker AC 250 MHz, Bruker ARX-400, Bruker 300 MHz or Bruker 500 MHz spectrometer. The chemical shift values are quoted in ppm and these are relative to the standard tetramethylsilane (TMS) for ^{1}H NMR and to the centre line of the chloroform triplet δ 77.0 for ^{13}C NMR. The peak multiplicities are specified as singlet (s), doublet (d), double-doublet (dd), triplet (t), quartet (q) or septet (sept) and coupling constants

(J) quoted in Hz. Mass spectra (MS) were obtained with a Kratos analytical MS80 RFAO spectrometer and high resolution determinations were obtained from the EPSRC Mass Spectrometry Service Centre, Swansea. Elemental analyses were performed with a Carlo Erba 1106 elemental analyser.

Determination of enantiomeric excesses by HPLC analysis was achieved using a Waters 501 HPLC pump, Waters 486 tuneable absorbance detector, Waters 746 data module and a Chiralcel OD column.

General experimental for the generation of alkylidene carbenes

TMSDM (trimethylsilyldiazomethane, 2.0 mmol, 2.0 M in hexanes) was stirred in DME (3 ml) at −78 °C and to this *n*-butyllithium (1.0 mmol, 2.5 M in hexanes) was added dropwise. Once the addition was complete the reaction was stirred for 20 min and allowed to warm until a clear solution was observed (−10 °C). The reaction was cooled to −60 °C and the ketone (1.0 mmol) in DME (3 ml) was added slowly. Once the addition was complete the reaction was stirred, allowed to come to rt over 4 h and quenched by the addition of water (5 ml). The reaction was extracted with ethyl acetate (3 × 5 ml), the combined organic layers were dried over sodium sulfate and filtered, and the solvent removed by rotary evaporation. Purification by column chromatography followed or use of crude product in the next step.

Preparation of (±)-methyl phenylglycolate 3

Methanol (50 ml) was stirred at 0 °C and to this, acetyl chloride (3.0 ml, 42 mmol) was added dropwise. Once the addition was complete, the cooling bath was removed and the reaction was stirred at rt for 30 min. The reaction was cooled once more to 0 °C, as was a solution of (±)-mandelic acid (5.0 g, 33 mmol) in methanol (6 ml). The 0.84 M solution of acetyl chloride–methanol was added to the mandelic acid and the reaction stirred overnight at rt. The solvent was removed by rotary evaporation and the product was obtained as a white solid (5.1 g, 92%), mp 57–58.5 °C (lit.,[33] 58 °C) with no further purification required. R_f 0.70 (10% ethyl acetate–petroleum ether); δ_H($CDCl_3$, 250.1 MHz) 7.44–7.26 (5H, m, aryl CH), 5.28 (1H, d, J 5.8, CH), 3.76 (3H, s, CH_3), 3.52 (1H, d, J 5.8, OH); δ_C($CDCl_3$, 62.9 MHz) 174.1 (CO_2R), 138.2 (aryl C_i), 128.6 (aryl C_m), 128.5 (aryl C_p), 126.6 (aryl C_o), 72.8 (CH), 53.0 (CH_3); *m*/*z* (CI) 184 ([M + NH_4]$^+$, 100%), 166 ([M]$^+$, 38), 149 ([M − OH]$^+$, 28), 124 (7), 107 ([M − CO_2Me]$^+$, 33), 94 (9), 79 (22).

Preparation of methyl 2-(methoxymethoxy)-2-phenylethanoate 4

Methyl mandelate **3** (4.0 g, 24 mmol) and dimethoxymethane (130 ml, 1.60 mol) were stirred vigorously in chloroform (130 ml) at 0 °C. To this solution, phosphorus pentaoxide (70 g, 0.49 mol) was added and the reaction stirred for 2 h at rt. The reaction was quenched at 0 °C with saturated sodium carbonate solution (100 ml) and the chloroform removed by rotary evaporation. The aqueous layer was extracted with diethyl ether (4 × 120 ml), the combined organic layers were dried over magnesium sulfate and filtered, and the solvent removed. Purification by column chomatography eluting with 7% ethyl acetate–petroleum ether gave the product as a colourless oil (4.57 g, 91%). Found: C 62.74% H 6.72%, $C_{11}H_{14}O_4$ requires C 62.86% H 6.67%. R_f 0.55 (20% ethyl acetate–petroleum ether); ν_{max}(neat)/cm^{-1} 2954 (m), 2894 (m), 1753 (s), 1714 (m); δ_H($CDCl_3$, 250.1 MHz) 7.48–7.28 (5H, m, aryl CH), 5.18 (1H, s, CH), 4.74 (1H, d, J_{AB} 6.8, MeOCHH′O), 4.68 (1H, d, J_{AB} 6.8, MeOCHH′O), 3.69 (3H, s, CO_2CH_3), 3.37 (3H, s, OCH_3); δ_C($CDCl_3$, 62.9 MHz) 170.8 (CO_2Me), 135.8 (aryl C_i), 128.4 (aryl C_p), 128.3 (aryl C_m), 127.1 (aryl C_o), 94.7 (MeOCH$_2$O), 76.3 (CH), 55.5 (OCH_3), 51.9 (CO_2CH_3); *m*/*z* (CI) 228 ([M + NH_4]$^+$, 15%), 211 ([M + H]$^+$, 9), 179 ([M − OMe]$^+$, 88), 166 (18), 151 ([M − CO_2Me]$^+$, 50), 124 (45), 105 (15), 94 (10), 77 ([Ph]$^+$, 6), 62 (9), 45 ([$MeOCH_2$]$^+$, 100).

Preparation of 2-(methoxymethoxy)-2-phenylethanol 5

Lithium aluminium hydride (3.0 g, 80 mmol) was stirred in diethyl ether (50 ml) at 0 °C and to this suspension methyl 2-(methoxymethoxy)-2-phenylethanoate **4** (2.76 g, 13.1 mmol) in diethyl ether (15 ml) was added dropwise over 30 min. The reaction was refluxed for 3 h and cooled, after which water (3 ml), 15% sodium hydroxide solution (3 ml) and further water (9 ml) were added. The solid was filtered off and the solvent removed by evaporation. Purification by column chromatography eluting with 10–25% ethyl acetate–petroleum ether gave the product as a colourless oil (1.77 g, 74%). R_f 0.45 (20% ethyl acetate–petroleum ether); ν_{max}(neat)/cm^{-1} 3434 (s), 3029 (w), 2932 (s), 2888 (s), 1736 (w); δ_H($CDCl_3$, 250.1 MHz) 7.37–7.22 (5H, m, aryl CH), 4.72–4.67 (1H, dd, J 4.0 and 8.0, CH), 4.61 (2H, s, OCH_2O), 3.73 (1H, dd, J_{AB} 11.9 and J_{AX} 8.0, CHH′OH), 3.64 (1H, dd, J_{AB} 11.9 and J_{BX} 4.0, CHH′OH), 3.35 (3H, s, OCH_3), 3.26 (1H, s, OH); δ_C($CDCl_3$, 62.9 MHz) 138.6 (aryl C_i), 128.4 (aryl C_m), 128.0 (aryl C_p), 127.0 (aryl C_o), 94.8 (MeOCH$_2$O), 79.9 (CH), 67.1 (CH_2OH), 55.5 (CH_3); *m*/*z* (CI) 200 ([M + NH_4]$^+$, 100%), 182 ([M]$^+$, 9), 170 (56), 156 (21), 151 ([M − MeO]$^+$, 51), 138 (35), 124 (20), 45 ([$MeOCH_2$]$^+$, 52); Found: 200.1287, [$C_{10}O_{14}O_3$ + NH_4]$^+$ requires 200.1287.

Preparation of 2-(methoxymethoxy)-2-phenylethanal 2

Oxalyl chloride (0.66 ml, 1.32 mmol) was stirred in DCM (2.5 ml) at −78 °C and to this DMSO (0.19 ml, 2.64 mmol) in DCM (3 ml) was added over 5 min. The reaction was stirred for a further 15 min before the addition of 2-(methoxymethoxy)-2-phenylethanol **5** (0.15 g, 0.80 mmol) in DCM (3 ml). Once again the reaction was stirred for 15 min after which time triethylamine (0.76 ml, 5.50 mmol) was added and the cooling bath removed. After 30 min stirring at rt and the addition of water (5 ml), the aqueous layer was extracted with DCM (4 × 10 ml). The combined organic layers were dried over sodium sulfate, filtered and the solvent removed. Purification of the residue by column chromatography eluting with 10% ethyl acetate–petroleum ether gave the product as a colourless oil (0.13 g, 88%). R_f 0.43 (20% ethyl acetate–petroleum ether); ν_{max}(neat)/cm^{-1} 3028 (w), 2943 (m), 2886 (m), 1738 (s); δ_H($CDCl_3$, 250.1 MHz) 9.61 (1H, d, J 7.8, CHO), 7.42–7.28 (5H, m, aryl CH), 5.04 (1H, d, J 7.8, CH), 4.78 (1H, d, J_{AB} 6.7, OCHH′O), 4.75 (1H, d, J_{AB} 6.7, OCHH′O), 3.42 (3H, s, CH_3); δ_C($CDCl_3$, 62.9 MHz) 197.8 (C=O), 133.5 (aryl C_i), 129.0 (aryl C_m), 128.9 (aryl C_p), 127.6 (aryl C_o), 95.1 (MeOCH$_2$O), 83.1 (CH), 55.9 (CH_3O). The aldehyde was prone to rapid oxidation and was not fully characterised but used directly in the next step.

Preparation of 3-(methoxymethoxy)-3-phenylpropyne 6

TMSDM (1.5 ml, 3.1 mmol) was lithiated with *n*-butyllithium (1.2 ml, 3.0 mmol) and this reacted with 2-(methoxymethoxy)-2-phenylethanal **2** (0.13 g, 0.72 mmol) in DME (5 ml) under the standard conditions described. Purification by column chromatography eluting with 5% ethyl acetate–petroleum ether gave the product as a pale yellow oil (0.09 g, 70%). R_f 0.68 (20% ethyl acetate–petroleum ether); ν_{max}(neat)/cm^{-1} 3288 (m), 3033 (w), 2953 (m), 2890 (m); δ_H($CDCl_3$, 250.1 MHz) 7.56–7.34 (5H, m, aryl CH), 5.43–5.42 (1H, m, PhCH), 5.03 (1H, d, J 6.7, MeCHH′O), 4.66 (1H, d, J 6.7, MeOCHH′O), 3.44 (3H, s, CH_3O), 2.63 (1H, d, J 2.1, CCH); δ_C($CDCl_3$, 62.9 MHz) 137.9 (aryl C_i), 128.6 (aryl C), 127.4 (aryl C), 93.8 (MeOCH$_2$O), 81.3 (PhCH), 75.3 (PhCHCCH), 67.0 (PhCHCCH), 55.8 (CH_3O); *m*/*z* (CI) 194 ([M + NH_4]$^+$, 12%), 164 (10), 144 (41), 132 (75), 115 ([M − $MeOCH_2O$]$^+$, 89), 89 (10), 63 (9), 45 ([$MeOCH_2$]$^+$, 49), 18 (100); Found: 194.1181, [$C_{11}H_{12}O_2$ + NH_4]$^+$ requires 194.1181.

Preparation of 1-(methoxymethoxy)-1-phenylpropan-2-ol 9

2-(Methoxymethoxy)-2-phenylethanal **2** (0.5 g, 2.8 mmol) was stirred in THF (20 ml) at −78 °C and to this solution methylmagnesium bromide (2.4 ml, 3.3 mmol) was added. The cooling bath was removed once the addition was complete and the reaction was stirred at rt overnight. The reaction was quenched by the addition of saturated ammonium chloride solution (25 ml) and extracted with diethyl ether (3 × 30 ml). The combined organic extracts were dried over magnesium sulfate and filtered, and the solvent removed by rotary evaporation. The crude residue was purified by column chromatography eluting with 10–20% ethyl acetate–petroleum ether. The product was obtained as a mixture of diastereoisomers in a ratio of 3 : 1 and as a colourless oil (0.46 g, 84%). R_f 0.17 (15% ethyl acetate–petroleum ether); ν_{max}(neat)/cm^{-1} 3447 (br), 3029 (w), 2934 (m), 2888 (m); δ_H($CDCl_3$, 250.1 MHz) 7.38–7.26 (5H$_{maj}$ + 5H$_{min}$, m, aryl C*H*), 4.60 (1H$_{min}$, d, J_{AB} 6.8, MeOC*H*H′O), 4.57 (1H$_{min}$, d, J_{AB} 6.8, MeOCH*H*′O), 4.56 (2H$_{maj}$, s, MeOCH_2O), 4.51 (1H$_{min}$, d, *J* 4.9, PhC*H*), 4.31 (1H$_{maj}$, d, *J* 7.9, PhC*H*), 4.00–3.85 (1H$_{min}$ + 1H$_{maj}$, m, MeC*H*OH), 3.39 (3H$_{min}$, s, CH_3O), 3.38 (3H$_{maj}$, s, CH_3O), 3.11 (1H$_{maj}$, br s, O*H*), 2.40 (1H$_{min}$, br d, *J* 4.9, O*H*), 1.15 (3H$_{min}$, d, *J* 6.4, CH_3CH), 1.00 (3H$_{maj}$, d, *J* 6.4, CH_3CH); δ_C($CDCl_3$, 62.9 MHz) 138.3 (aryl C_i)1C$_{maj}$, 138.0 (aryl C_i)1C$_{min}$, 126.3 (aryl C_m)2C$_{maj}$, 128.1 (aryl C_m)2C$_{min}$, 128.0 (aryl C_p)1C$_{maj}$, 127.7 (aryl C_p)1C$_{min}$, 126.6 (aryl C_o)2C$_{maj}$ + 2C$_{min}$, 94.6 (*C*H$_2$)1C$_{min}$, 94.2 (*C*H$_2$)1C$_{maj}$, 83.7 (Ph*C*H)1C$_{maj}$, 82.2 (Ph*C*H)1C$_{min}$, 70.9 (Me*C*HOH)1C$_{maj}$, 70.5 (Me*C*HOH)1C$_{min}$, 55.6 (*C*H$_3$O)1C$_{maj}$ + 1C$_{min}$, 18.2 (*C*H$_3$CH)1C$_{maj}$ + 1C$_{min}$; *m*/*z* (CI) 214 ([M + NH$_4$]$^+$, 100%), 198 (29), 184 (37), 170 (17), 152 ([M − MeOCH]$^+$, 65), 135 ([M − MeOCH$_2$O]$^+$, 12), 120 (16), 105 ([M − PhCH$_2$]$^+$, 19), 91 ([PhCH$_2$]$^+$, 13), 52 (41), 47 (24); Found: 214.1443, [$C_{11}H_{16}O_3$ + NH$_4$]$^+$ requires 214.1443.

Preparation of 1-(methoxymethoxy)-1-phenylpropan-2-one 8

Oxalyl chloride (1.41 ml, 2.82 mmol) was stirred at −78 °C in DCM (6 ml) and to this solution DMSO (0.40 ml, 5.64 mmol) was added in DCM (6 ml). The reaction was stirred for 20 min before the addition of 1-(methoxymethoxy)-1-phenylpropan-2-ol **9** (0.46 g, 2.35 mmol) in DCM (6 ml). Once more the reaction was stirred for 20 min and then triethylamine (1.60 ml, 11.8 mmol) was added. The cooling bath was removed and the reaction stirred for 30 min at rt. The reaction was quenched by the addition of water (25 ml) and extracted with DCM (3 × 25 ml). The combined organic extracts were dried over magnesium sulfate and filtered, and the solvent removed. Purification of the residue by column chromatography eluting with 7% ethyl acetate–petroleum ether gave the product as a colourless oil (0.27 g, 59%). R_f 0.47 (20% ethyl acetate–petroleum ether); ν_{max}(neat)/cm^{-1} 3059 (m), 2948 (m), 2824 (w), 1722 (s); δ_H($CDCl_3$, 250.1 MHz) 7.43–7.27 (5H, m, aryl C*H*), 5.10 (1H, s, PhC*H*), 4.70 (1H, d, *J* 6.7, MeOC*H*H′O), 4.66 (1H, d, *J* 6.7, MeOCH*H*′O), 3.38 (3H, s, CH_3O), 2.13 (3H, s, CH_3C); δ_C($CDCl_3$, 62.9 MHz) 205.7 (*C*=O), 135.6 (aryl C_i), 128.8 (aryl C_m), 128.6 (aryl C_p), 127.4 (aryl C_o), 94.7 (O*C*H$_2$O), 83.4 (Ph*C*H), 55.9 (O*C*H$_3$), 25.7 (*C*H$_3$C); *m*/*z* (CI) 212 ([M + NH$_4$]$^+$, 67%), 180 (8), 168 (22), 163 ([M − MeO]$^+$, 100), 152 (13), 122 (7), 105 (19), 94 (11), 78 (8), 58 (12), 52 (42), 44 (15); Found: 212.1287, [$C_{11}H_{14}O_3$ + NH$_4$]$^+$ requires 212.12867.

Preparation of 2-methoxy-4-methyl-5-phenyl-2,5-dihydrofuran 10

TMSDM (1.13 ml, 2.26 mmol) was lithiated with *n*-butyllithium (0.90 ml, 2.26 mmol) and reacted with 1-(methoxymethoxy)-1-phenylpropan-2-one (0.11 g, 0.57 mmol) in DME (4 ml) under the standard conditions described. Purification by column chromatography eluting with 5% ethyl acetate–petroleum ether gave the product as an apparent single diastereoisomer as a pale yellow oil (60 mg, 59%). R_f 0.68 (20% ethyl acetate–petroleum ether); ν_{max}(neat)/cm^{-1} 3063 (m), 3030 (m), 2981 (s), 2891 (s), 2825 (m), 1648 (w); δ_H($CDCl_3$, 250.1 MHz) 7.45–7.17 (5H, m, aryl C*H*), 5.92–5.88 (1H, dq, *J* 3.8 and 1.2, C=C*H*), 5.61–5.57 (2H, m, PhC*H* and MeOC*H*), 3.45 (3H, s, CH_3O), 1.60 (3H, dd, *J* 1.5 and 1.2, CH_3C=CH); δ_C($CDCl_3$, 62.9 MHz) 145.5 (Me*C*=CH), 139.4 (aryl C_i), 128.6 (aryl C_m), 128.2 (aryl C_p), 127.0 (aryl C_o), 120.9 (C=*C*H), 109.3 (MeO*C*H), 89.5 (Ph*C*H), 54.6 (*C*H$_3$O), 12.4 (*C*H$_3$C=CH); *m*/*z* (EI) 190 ([M]$^+$, 15%), 159 ([M − MeO]$^+$, 60), 129 (56), 91 (64), 57 (17), 51 (23), 45 (100); Found: 190.0994, [$C_{12}H_{14}O_2$]$^+$ requires 190.0994.

Preparation of 1-(methoxymethoxy)-3-methyl-1-phenylbutan-2-one 12

N,O-Dimethylhydroxylamine hydrogen chloride (70 mg, 0.74 mmol) was stirred as a slurry in THF (0.95 ml) at −20 °C and to this solution isopropylmagnesium chloride (0.72 ml, 1.4 mmol, 2 M in THF) was added dropwise. Methyl 2-(methoxymethoxy)-2-phenylethanoate **4** (0.10 g, 0.48 mmol) was then added and the reaction stirred for 30 min. The reaction was quenched by the addition of dilute ammonium chloride solution (5 ml) and extracted with diethyl ether (4 × 6 ml). The combined organic extracts were dried over magnesium sulfate and filtered, and the solvent removed by rotary evaporation. Purification by column chromatography eluting with 10% ethyl acetate–petroleum ether gave the product as a pale yellow oil (0.06 g, 53%). R_f 0.39 (20% ethyl acetate–petroleum ether); ν_{max}(neat)/cm^{-1} 3062 (w), 3030 (w), 2970 (s), 2933 (m), 2890 (m), 2824 (w), 1726 (s); δ_H($CDCl_3$, 250.1 MHz) 7.38–7.35 (5H, m, aryl C*H*), 5.26 (1H, s, PhC*H*), 4.67 (1H, d, J_{AB} 7.3, MeOC*H*H′O), 4.65 (1H, d, J_{AB} 7.3, MeOCH*H*′O), 3.36 (3H, s, CH_3O), 2.85 [1H, sept, *J* 6.8, (CH$_3$)$_2$C*H*], 1.06 [3H, d, *J* 6.8, CH_3C(H)CH′$_3$], 0.94 [3H, d, *J* 6.8, CH$_3$C(H)C*H*′$_3$]; δ_C($CDCl_3$, 62.9 MHz) 211.0 (*C*=O), 135.5 (aryl C_i), 128.8 (aryl C_p), 128.7 (aryl C_m), 128.0 (aryl C_o), 94.6 (O*C*H$_2$O), 81.6 (Ph*C*H), 55.8 (O*C*H$_3$), 36.7 [(CH$_3$)$_2$*C*H], 19.1 [*C*H$_3$(Me)CH], 18.8 [Me(*C*H$_3$)CH]; *m*/*z* (CI) 240 ([M + NH$_4$]$^+$, 100%), 223 ([M + H]$^+$, 12), 191 ([M − MeO]$^+$, 100), 180 (45); Found: 223.1329, [$C_{13}H_{18}O_3$ + H]$^+$ requires 223.1334.

Preparation of 1-(methoxymethoxy)-4-methyl-1-phenylpent-2-yne 13 and 4-isopropyl-2-methoxy-5-phenyl-2,5-dihydrofuran 14

TMSDM (0.45 ml, 0.90 mmol) was lithiated with *n*-butyllithium (0.53 ml, 0.90 mmol) and reacted with 1-(methoxymethoxy)-3-methyl-1-phenylbutan-2-one **12** (50 mg, 0.22 mmol) in DME (3 ml) under the standard conditions described. Purification by column chromatography eluting with 5% ethyl acetate–petroleum ether gave the products **13** : **14** as an inseparable mixture in a ratio of 16 : 1 in the form of a pale yellow oil (0.03 g, 67%). R_f 0.60 (20% ethyl acetate–petroleum ether); δ_H($CDCl_3$, 250.1 MHz) 7.41–7.22 (5H$_{maj}$ + 5H$_{min}$, m, aryl C*H*), 5.94–5.91 (1H$_{min}$, m, C=C*H*), 5.79–5.75 (1H$_{min}$, m, MeOC*H*), 5.59–5.56 (1H$_{min}$, m, PhC*H*), 5.59–5.56 (1H$_{maj}$, m, PhC*H*), 5.12 (1H$_{maj}$, d, *J* 6.2, MeOC*H*H′), 4.78 (1H$_{maj}$, d, *J* 6.2, MeOCH*H*′), 3.46 (3H$_{min}$, s, CH_3O), 3.35 (3H$_{maj}$, s, CH_3O), 2.18–1.95 [1H$_{maj}$ + 1H$_{min}$, m, (CH$_3$)$_2$C*H*], 1.02 (3H$_{maj}$, t, *J* 6.9, CH_3CHCH′$_3$), 0.85 (3H$_{maj}$, d, *J* 6.3, CH$_3$CHC*H*′$_3$), 0.80 [6H$_{min}$, dd, J 5.2 and 2.5, (C*H*$_3$)$_2$CH].

Preparation of 1,3-dimethoxypropan-2-ol 19 [34]

Methanol (100 ml) was stirred at 0 °C and to this pieces of sodium metal (0.60 g, 26.1 mmol) were added over 1 h. Once all the sodium was consumed 1,3-dichloropropan-2-ol **18** (1.00 ml, 10.5 mmol) was added and the cooling bath removed. The reaction was stirred at rt for 1.5 h and the sodium chloride removed by filtration. Water (100 ml) was added to the reaction and the aqueous methanol layer extracted with diethyl ether (3 × 100 ml). The combined organic layers were dried over

magnesium sulfate and filtered, and the solvent removed. The crude residue was purified by column chromatography eluting with 8–20% methanol-DCM and the product obtained as a colourless oil (0.62 g, 49%). R_f 0.18 (60% ethyl acetate–petroleum ether); ν_{max}(neat)/cm^{-1} 3426 (br), 2982 (m), 2892 (s), 2822 (m); δ_H($CDCl_3$, 250.1 MHz) 4.00–3.94 (1H, m, C*H*OH), 3.50–3.38 (4H, m, OCH_2CHCH_2O), 3.39 (6H, s, OCH_3), 2.72 (1H, br s, O*H*); δ_C($CDCl_3$, 62.9 MHz) 73.5 (O*C*H$_2$), 68.6 (*C*H), 58.5 (O*C*H$_3$); *m*/*z* (CI) 138 ([M + NH_4]$^+$, 39%), 121 ([M + H]$^+$, 13), 106 (30), 91 (42), 74 (100), 58 (54); Found: 138.1134, [$C_5H_{12}O_3$ + NH_4]$^+$ requires 138.1130.

Preparation of 1,3-dimethoxypropan-2-one 15[35]

Sodium acetate (0.82 g, 10.0 mmol), silica (2.16 g) and 1,3-dimethoxypropan-2-ol **19** (0.60 g, 5.0 mmol) were stirred at 0 °C in DCM (25 ml). PCC (2.16 g, 10.0 mmol) was added in portions over 5 min and the reaction stirred for a further 10 min. The cooling bath was removed and the reaction stirred at rt overnight. The reaction was filtered through silica, the silica washed with DCM (3 × 30 ml) and the solvent removed from the combined filtrate and washings. Purification of the residue by column chromatography eluting with 40% ethyl acetate–petroleum ether gave the product as a colourless oil (0.21 g, 36%). R_f 0.36 (40% ethyl acetate–petroleum ether); ν_{max}(neat)/cm^{-1} 2999 (m), 2940 (m), 2835 (m), 1731 (s); δ_H($CDCl_3$, 250.1 MHz) 4.19 [4H, s, OCH_2C(=O)CH_2O], 3.42 (6H, s, CH_3O); δ_C($CDCl_3$, 62.9 MHz) 205.1 (*C*=O), 75.3 (O*C*H$_2$C*C*H$_2$O), 58.7 (*C*H$_3$O); *m*/*z* (CI) 136 ([M + NH_4]$^+$, 100%), 106 (24), 77 (32), 74 (30), 58 (29); Found: 136.0975, [$C_5H_{10}O_3$ + NH_4]$^+$ requires 136.0974.

Preparation of 3-methoxymethyl-2,5-dihydrofuran 31[36]

TMSDM (1.27 ml, 2.54 mmol) was lithiated with *n*-butyllithium (1.01 ml, 2.54 mmol) and reacted with 1,3-dimethoxypropan-2-one **15** (0.15 g, 1.27 mmol) in DME (10 ml) under the standard conditions described. Purification by column chromatography eluting with 0–5% ethyl acetate–petroleum ether gave the product as a pale yellow oil (0.02 g, 14%). R_f 0.70 (20% ethyl acetate–petroleum ether); ν_{max}(neat)/cm^{-1} 2859 (m), 2928 (m); δ_H($CDCl_3$, 250.1 MHz) 4.66–4.70 (5H, m, furan CH_2 and C*H*), 3.55–3.59 (2H, m, MeOCH_2), 3.35 (3H, s, CH_3O); δ_C($CDCl_3$, 62.9 MHz) 155.8 (R_2*C*=CH), 129.6 (O*C*H$_2$C=CH), 120.5 (R_2C=*C*H), 115.3 (O*C*H$_2$CH=CR_2), 59.3 (MeO*C*H$_2$), 14.1 (*C*H$_3$O).

Preparation of 1,3-diethoxypropan-2-ol 20[34]

Ethanol (200 ml) was stirred at rt and to this sodium (3.50 g, 152 mmol) was added in portions with occasional cooling. Once addition of the sodium was completed the reaction was stirred for a further 30 min and then 1,3-dichloropropan-2-ol **18** (5.00 ml, 52.4 mmol) was added. The reaction was stirred overnight and then water (150 ml) was added. The majority of the ethanol was removed and then the aqueous layer was extracted with diethyl ether (3 × 150 ml). The combined organic layers were dried over magnesium sulfate and filtered, and the solvent removed. Purification of the residue by column chromatography eluting with 60% ethyl acetate–petroleum ether gave the product as a colourless oil (4.57 g, 59%). R_f 0.51 (70% ethyl acetate–petroleum ether); ν_{max}(neat)/cm^{-1} 3446 (br), 2973 (m), 2868 (m); δ_H($CDCl_3$, 250.1 MHz) 3.98–3.91 (1H, br m, C*H*OH), 3.52 (4H, q, *J* 7.0, MeCH_2), 3.50 [2H, dd, J_{AB} 9.7 and J_{AX} 3.7, OC*H*H′CH(OH)C*H*H′O], 3.45 [2H, dd, J_{AB} 9.7 and J_{BX} 6.4, OCH*H*′CH(OH)CH*H*′O], 2.76 (1H, br d, *J* 2.4, CHO*H*), 1.21 (6H, t, *J* 7.0, CH_3CH$_2$O); δ_C($CDCl_3$, 62.9 MHz) 77.6 (O*C*H$_2$CH*C*H$_2$O), 69.3 (*C*HOH), 66.6 (Me*C*H$_2$O), 14.9 (*C*H$_3$CH$_2$O); *m*/*z* (CI) 166 ([M + NH_4]$^+$, 48%), 149 ([M + H]$^+$, 100), 103 ([M − OCH_2CH_3]$^+$, 13), 87 (72), 59 ([$CH_3CH_2OCH_2$]$^+$, 65); Found: 149.1178, [$C_7H_{16}O_3$ + H]$^+$ requires 149.1178.

Preparation of 1,3-diethoxypropan-2-one 16[37]

1,3-Diethoxypropan-2-ol **20** (4.00 g, 27 mmol) was stirred in DCM (150 ml) at rt with silica (11.7 g) and sodium acetate (4.5 g, 54 mmol). To this PCC (11.7 g, 54.0 mmol) was added in portions over 20 min and the reaction stirred overnight at rt. The reaction was filtered through silica and the silica washed with DCM (3 × 100 ml). The solvent was removed by rotary evaporation, the crude residue purified by column chromatography eluting with 20% ethyl acetate–petroleum ether and the product obtained as a colourless oil (2.43 g, 62%). R_f 0.41 (40% ethyl acetate–petroleum ether); ν_{max}(neat)/cm^{-1} 2978 (m), 2851 (m), 1730 (s); δ_H($CDCl_3$, 250.1 MHz) 4.23 [4H, s, CH_2-C(=O)CH_2], 3.56 (4H, q, *J* 7.0, CH_3CH_2O), 1.25 (6H, t, *J* 7.0, CH_3CH$_2$O); δ_C($CDCl_3$, 62.9 MHz) 206.4 (*C*=O), 74.3 [O*C*H$_2$-C(=O)*C*H$_2$O], 67.2 (Me*C*H$_2$O), 14.9 (*C*H$_3$); *m*/*z* (CI) 164 ([M + NH_4]$^+$, 76%), 149 (71), 147 ([M + H]$^+$, 55), 103 (23), 87 ([M − $EtOCH_2$]$^+$, 12), 59 ([$EtOCH_2$]$^+$, 100), 47 (22); Found: 164.1287, [$C_7H_{14}O_3$ + NH_4]$^+$ requires 164.1286.

Preparation of 4-ethoxymethyl-2-methyl-2,5-dihydrofuran 32

TMSDM (1.20 ml, 2.40 mmol) was lithiated with *n*-butyllithium (0.95 ml, 2.40 mmol) and reacted with 1,3-diethoxypropan-2-one **16** (0.18 g, 1.20 mmol) in DME (10 ml) under the standard conditions described. Purification by column chromatography eluting with 0–5% ethyl acetate–petroleum ether gave the product as a pale yellow oil (0.09 g, 55%). R_f 0.65 (20% ethyl acetate–petroleum ether); ν_{max}(neat)/cm^{-1} 2976 (m), 2931 (m), 2871 (m), 1654 (w); δ_H($CDCl_3$, 250.1 MHz) 5.67–5.64 (1H, m, C=C*H*), 4.98–4.91 (1H, m, MeC*H*), 4.70–4.52 (2H, m, OCH_2C=CH), 4.06 (2H, d, *J* 0.9, OCH_2OEt), 3.48 (2H, q, *J* 7.0, MeCH_2O), 1.25 (3H, d, *J* 6.4, CH_3CH), 1.20 (3H, t, *J* 7.0, CH_3CH$_2$O); δ_C($CDCl_3$, 62.9 MHz) 137.6 (*C*=CH), 127.3 (C=*C*H), 82.3 (Me*C*H), 74.9 (furan *C*H$_2$), 66.0 (EtO*C*H$_2$), 65.9 (Me*C*H$_2$O), 21.7 (*C*H$_3$CH), 15.1 (*C*H$_3$CH$_2$O).

Preparation of 1,3-diisopropoxypropan-2-ol 21

Isopropyl alcohol (125 ml) was stirred at rt and to this pieces of sodium (2.80 g, 122 mmol) were added over a period of 8 h. Once all the sodium was consumed 1,3-dichloropropan-2-ol **18** (4.0 ml, 42 mmol) was added and the reaction stirred overnight at rt. Water (100 ml) was added to the reaction which was then extracted with diethyl ether (3 × 100 ml). The combined organic extracts were dried over magnesium sulfate and filtered, and the solvent evaporated off. Purification of the residue by column chromatography eluting with 20% ethyl acetate–petroleum ether gave the product as a colourless oil (4.14 g, 56%). R_f 0.46 (20% ethyl acetate–petroleum ether); ν_{max}(neat)/cm^{-1} 3440 (br), 2983 (m), 2862 (m), 1650 (w); δ_H($CDCl_3$, 250.1 MHz) 3.83–3.90 (1H, m, C*H*OH), 3.60 [2H, sept, *J* 6.1, C*H*(CH_3)$_2$], 3.49 (2H, dd, J_{AB} 9.6 and J_{AX} 4.8, OC*H*H′CHC*H*H′O), 3.43 (2H, dd, J_{AB} 9.6 and J_{BX} 6.1, OCH*H*′CHCH*H*′O), 2.78 (1H, br d, *J* 4.4, O*H*), 1.16 [12H, d, *J* 6.1, (CH_3)$_2$CH]; δ_C($CDCl_3$, 62.9 MHz) 71.9 [(CH_3)$_2$*C*HO], 69.6 (O*C*H$_2$CH*C*H$_2$O), 69.1 (*C*HOH), 21.8 (*C*H$_3$); *m*/*z* (CI) 194 ([M + NH_4]$^+$, 8%), 177 ([M + H]$^+$, 100), 135 (47), 117 ([M − (CH_3)$_2$CHO]$^+$, 6), 100 (14), 85 (11), 73 {[(CH_3)$_2$CHOCH_2]$^+$, 30}, 43 {[(CH_3)$_2$C*H*]$^+$, 12}; Found: 194.1752, [$C_9H_{20}O_3$ + NH_4]$^+$ requires 194.1756.

Preparation of 1,3-diisopropoxypropan-2-one 17

Silica (3.7 g), sodium acetate (1.40 g, 17.0 mmol) and 1,3-diisopropoxypropan-2-ol **21** (1.50 g, 8.51 mmol) were stirred at 0 °C in DCM (30 ml) and to this PCC (3.70 g, 17.0 mmol) was added in portions over 10 min. Once the addition was complete the cooling bath was removed and the reaction stirred overnight at rt. The reaction was filtered through silica, the silica washed with DCM (3 × 50 ml) and the solvent removed by rotary evaporation. Purification of the residue by column chromato-

graphy eluting with 10% ethyl acetate–petroleum ether gave the product as a colourless oil (0.89 g, 55%). R_f 0.55 (20% ethyl acetate–petroleum ether); ν_{max}(neat)/cm^{-1} 2974 (s), 2933 (m), 2877 (m), 1738 (s); δ_H($CDCl_3$, 250.1 MHz) 4.23 [4H, s, CH_2-C(=O)CH_2], 3.63 [2H, sept, J 6.1, $(CH_3)_2CHO$], 1.20 [12H, d, J 6.1, $(CH_3)_2CH$]; δ_C($CDCl_3$, 62.9 MHz) 207.0 (C=O), 72.7 (Me_2CH), 72.2 [OCH_2C(=O)CH_2O], 21.7 (CH_3); m/z (CI) 192 ([M + NH_4]$^+$, 100%), 175 ([M + H]$^+$, 88), 150 (25), 136 (96), 117 (22), 101 {[M − $(CH_3)_2CH$]$^+$, 64}, 58 (22), 47 (30); Found: 192.1560, [$C_9H_{18}O_3$ + NH_4]$^+$ requires 192.1560.

Preparation of 4-isopropoxymethyl-2,2-dimethyl-2,5-dihydrofuran 35

TMSDM (1.10 ml, 2.20 mmol) was lithiated with *n*-butyllithium (0.88 ml, 2.20 mmol) and reacted with 1,3-diisopropoxypropan-2-one **17** (0.19 g, 1.10 mmol) in DME (4 ml) under the standard conditions described. Purification by column chromatography eluting with 5% ethyl acetate–petroleum ether gave the product as a pale yellow oil (0.05 g, 27%). R_f 0.54 (20% ethyl acetate–petroleum ether); ν_{max}(neat)/cm^{-1} 2973 (s), 2932 (m), 2872 (m), 2247 (w); δ_H($CDCl_3$, 250.1 MHz) 5.50–5.48 (1H, m, C=CH), 4.49–4.47 (2H, m, CH=CCH_2O), 3.93–3.91 [2H, m, $(CH_3)_2CHOCH_2C$], 3.52–3.46 [1H, m, $(CH_3)_2CH$], 1.18 (6H, s, CH_3CCH_3), 1.03 (3H, d, J 6.1, CH_3CH), 1.00 (3H, d, J 6.1, CH_3CH); δ_C($CDCl_3$, 62.9 MHz) 136.7 (R_3C=CH), 130.7 (R_3C=CH), 87.9 [$R_2C(CH_3)_2$], 74.0 (furan$C$H$_2$), 72.5 [CH-$(CH_3)_2$], 64.7 (PrOCH$_2$O), 27.7 (CH_3CCH_3), 22.0 [CH_3(Me)-CH], 21.9 [Me(CH_3)CH].

Preparation of 1,1-bis(benzyloxymethyl)ethylene 23

Sodium hydride (4.00 g, 0.10 mol) was stirred in DMF (200 ml) at 0 °C and to this benzyl alcohol (10.4 ml, 0.10 mol) was added dropwise. Once the addition was complete the reaction was stirred for 20 min, the cooling bath was removed and stirring continued for a further h at rt. 3-Chloro-2-chloromethylprop-1-ene (4.8 ml, 40 mmol) was added and the reaction stirred overnight. Saturated ammonium chloride solution (150 ml) was added to quench the reaction and then the aqueous mixture was extracted with ethyl acetate (4 × 200 ml). The combined organic layers were dried over magnesium sulfate, filtered and concentrated. Purification of the residue by column chromatography eluting with 10–20% ethyl acetate–petroleum ether gave the product as a colourless oil (10.4 g, 97%). Found: C 80.62% H 7.82%, $C_{18}H_{20}O_2$ requires C 80.60% H 7.46%. R_f 0.58 (30% ethyl acetate–petroleum ether); ν_{max}(neat)/cm^{-1} 3087 (m), 3030 (m), 2926 (s), 2858 (s); δ_H($CDCl_3$, 299.9 MHz) 7.37–7.25 (10H, m, aryl CH), 5.26 (2H, d, J 0.9, CH_2=CR_2), 4.52 (4H, s, PhCH_2), 4.07 [4H, d, J 0.9, OCH_2C(=CH_2)CH_2O]; δ_C($CDCl_3$, 75.4 MHz) 142.6 (CH_2=CR_2), 138.2 (aryl C_i), 128.3 (aryl C_m), 127.6 (aryl C_o), 127.5 (aryl C_p), 114.3 (CH_2=CR_2), 72.2 (CH_2), 70.9 (CH_2); m/z (CI) 286 ([M + NH_4]$^+$, 36%), 269 ([M + H]$^+$, 59), 233 (53), 198 (26), 177 ([M − $PhCH_2$]$^+$, 57), 131 (48), 108 (67), 91 ([$PhCH_2$]$^+$, 100), 65 (33).

Preparation of 1,3-bis(benzyloxy)propan-2-one 22

1,1-Bis(benzyloxymethyl)ethylene **23** (3.12 g, 11.6 mmol) was stirred in DCM (40 ml) at −60 °C. An empty trap followed by a trap containing a solution of 5% potassium iodide in 50% acetic acid–water were connected to the outlet. Ozone was passed through the reaction mixture for 35 min by which time the solution appeared pale blue. Oxygen was bubbled through the solution for 10 min followed by nitrogen for 20 min. Triphenylphosphine (4.60 g, 17.5 mmol) was added and the cooling bath removed. The reaction was stirred overnight, the solvent removed and purified by column chromatography eluting with 10–25% ethyl acetate–petroleum ether yielding the product as a white solid (3.02 g, 96%). R_f 0.25 (20% ethyl acetate–petroleum ether); ν_{max}(neat)/cm^{-1} 3087 (w), 3063 (m), 3031 (m), 2936 (m), 2876 (m), 1727 (s); δ_H($CDCl_3$, 299.9 MHz) 7.42–7.28 (10H, m, aryl CH), 4.57 (4H, s, PhCH_2O), 4.24 [4H, s, OCH_2C(O)-CH_2O]; δ_C($CDCl_3$, 75.4 MHz) 205.6 (C=O), 137.0 (aryl C_i), 128.5 (aryl C_m), 128.0 (aryl C_o), 127.9 (aryl C_p), 73.6 (CH_2), 73.5 (CH_2); m/z (CI) 288 ([M + NH_4]$^+$, 100%), 182 (29), 108 (41), 91 ([$PhCH_2$]$^+$, 22); Found: 288.1590, [$C_{17}H_{18}O_3$ + NH_4]$^+$ requires 288.1600.

Preparation of 4-(benzyloxymethyl)-2-phenyl-2,5-dihydrofuran 33

TMSDM (1.85 ml, 3.70 mmol) was lithiated with *n*-butyllithium (1.48 ml, 3.70 mmol) and reacted with 1,3-bis(benzyloxy)propan-2-one **22** (0.50 g, 1.90 mmol) in DME (12 ml) under the standard conditions described. Purification by column chromatography eluting with 0.5% ethyl acetate–petroleum ether gave the product as a pale yellow oil (0.36 g, 70%). R_f 0.41 (20% ethyl acetate–petroleum ether); ν_{max}(neat)/cm^{-1} 3062 (w), 3028 (w), 2853 (m); δ_H($CDCl_3$, 250.1 MHz) 7.35–7.21 (10H, m, aryl CH), 5.84–5.79 (2H, m, PhCH and CH=C), 4.92–4.84 (1H, m, OCHH′), 4.81–4.73 (1H, m, OCHH′), 4.53 (2H, s, PhCH_2O), 4.16–4.20 (2H, m, BnO-CHH′); δ_C($CDCl_3$, 62.9 MHz) 141.9 (C=CH), 138.1 (aryl C_i), 137.8 (aryl C_i), 128.4 (aryl C_m), 127.8 (aryl C_p), 127.7 (aryl C_o), 127.6 (aryl C_p), 126.3 (aryl C_o), 88.2 (PhCH), 75.8 (furan CH_2), 72.4 (PhCH$_2$), 65.5 (BnOCH$_2$C=C); m/z (CI) 266 ([M]$^+$, 9), 58 (48), 145 (13), 122 (33), 115 (17), 105 (100), 91 ([$PhCH_2$]$^+$, 100), 77 ([Ph]$^+$, 90), 69 (15), 65 (27), 51 (62), 43 (12); Found: 266.1307, [$C_{18}H_{18}O_2$]$^+$ requires 266.13068.

Preparation of (±)-2-(*p*-methoxyphenylmethoxymethyl)oxirane 25 (R = MPM)

Sodium hydride (0.84 g, 21 mmol) was stirred in DMF (30 ml) at 0 °C and to this (±)-glycidol (1.13 ml, 17.0 mmol) was added dropwise. The cooling bath was removed once the addition was complete and the reaction stirred for 1 h at rt. The reaction was cooled to 0 °C once more and *p*-methoxybenzyl chloride (2.6 ml, 19 mmol) and tetrabutylammonium iodide (0.24 g, 0.87 mmol, 5%) added. The reaction was stirred for 3 days at rt, quenched with saturated ammonium chloride solution (50 ml) and extracted with diethyl ether (2 × 100 ml). The combined organic layers were washed with water (5 × 100 ml), dried over magnesium sulfate and filtered, and the solvent removed. Purification of the residue by column chromatography eluting with 10–20% ethyl acetate–petroleum ether gave the product as a colourless oil (1.97 g, 60%). R_f 0.56 (20% ethyl acetate–petroleum ether); ν_{max}(neat)/cm^{-1} 3000 (m), 2934 (m), 2862 (m) 2838 (m); δ_H($CDCl_3$, 250.1 MHz) 7.30–7.24 (2H, m, aryl CH β to COMe), 6.91–6.85 (2H, m, aryl CH α to COMe), 4.51 (2H, dd, J_{AB} 11.3, aryl CH_2O), 3.80 (3H, s, CH_3O), 3.72 (1H, dd, J_{AB} 11.3 and J_{AX} 3.0, aryl OCHH′), 3.41 (1H, dd, J_{AB} 11.3 and J_{BX} 5.8, aryl OCHH′), 3.20–3.14 (1H, m, CH), 2.79 (1H, dd, J_{AB} 5.1 and J_{AX} 4.2, RCHCHH′), 2.60 (1H, dd, J_{AB} 5.1 and J_{BX} 2.9, RCHCHH′); δ_C($CDCl_3$, 62.9 MHz) 159.1 (aryl C_iOMe), 129.8 (aryl CCH$_2$O), 129.3 (aryl CH β to COMe), 113.6 (aryl CH α to COMe), 72.8 (aryl CH$_2$O), 70.4 (CH_2OCH_2Ar), 55.1 (OCH$_3$), 50.7 (CH), 44.2 (OCH$_2$CH); m/z (EI) 194 ([M]$^+$, 100%), 163 ([M − OMe]$^+$, 6), 122 (69), 78 (22); Found: 194.0950, [$C_{11}H_{14}O_3$]$^+$ requires 194.0943.

Preparation of 1,3-bis(*p*-methoxyphenylmethoxy)propan-2-ol 26 (R = R′ = MPM)

(±)-2-(*p*-Methoxyphenylmethoxymethyl)oxirane **25** (R = MPM) (0.5 g, 2.6 mmol) was stirred in acetonitrile (7 ml) with *p*-methoxybenzyl alcohol (0.39 ml, 3.10 mmol). Lithium perchlorate (0.55 g, 5.20 mmol) was added and the reaction heated at 95 °C overnight. Water (15 ml) was added to the cooled reaction, which was then extracted with diethyl ether (3 × 15 ml). The combined organic layers were dried over

magnesium sulfate and filtered, and the solvent removed by evaporation. The residue was purified by column chromatography eluting with 0–40% ethyl acetate–petroleum ether to give the product as a colourless oil (0.26 g, 36%). R_f 0.27 (20% ethyl acetate–petroleum ether); ν_{max}(neat)/cm^{-1} 3438 (br), 3003 (w), 2926 (m), 2855 (w); δ_H($CDCl_3$, 250.1 MHz) 7.25–7.29 (4H, m, aryl C*H* β to COMe), 6.85–6.89 (4H, m, aryl C*H* α to COMe), 4.47 (4H, s, aryl CH_2O), 4.02–3.94 (1H, m, OCH$_2$C*H*-CH$_2$O), 3.80 (6H, s, CH_3O), 3.51 (2H, dd, J_{AB} 9.6 and J_{AX} 4.7, OC*H*H′CHC*H*H′O), 3.48 (2H, dd, J_{AB} 9.6 and J_{BX} 6.1, OCH-*H*′CHCH*H*′O), 2.28 (1H, s, CHO*H*); δ_C($CDCl_3$, 62.9 MHz) 159.2 (aryl C_iOMe), 130.0 (aryl C_iC), 129.4 (aryl *C*H β to COMe), 113.8 (aryl *C*H α to COMe), 73.1 (aryl*C*H$_2$O), 71.0 (O*C*H$_2$CH*C*H$_2$O), 69.6 (*C*HOH), 55.2 (O*C*H$_3$); *m*/*z* (CI) 350 ([M + NH$_4$]$^+$, 4%), 211 ([M − MeOC$_6$H$_4$CH$_2$]$^+$, 4), 154 (19), 138 (32), 136 (20), 121 ([MeOC$_6$H$_4$CH$_2$]$^+$, 100); Found: 350.1962, [$C_{19}H_{24}O_5$ + NH$_4$]$^+$ requires 350.1967.

Preparation of 1,3-bis(*p*-methoxyphenylmethoxy)propan-2-one 24

1,3-Bis(*p*-methoxyphenylmethoxy)propan-2-ol **26** (R = R′ = MPM) (0.36 g, 1.1 mmol), silica (0.5 g) and sodium acetate (0.18 g, 2.2 mmol) were stirred in DCM (10 ml) at 0 °C. To this solution PCC (0.5 g, 2.2 mmol) was added and after 30 min the cooling bath was removed. The reaction was stirred overnight and filtered through silica. The silica was washed with DCM (3 × 20 ml) and the solvent removed by evaporation. After purification of the residue by column chromatography eluting with 20–30% ethyl acetate–petroleum ether the product was obtained as a colourless oil (0.14 g, 39%) which was a white solid at −18 °C. R_f 0.35 (20% ethyl acetate–petroleum ether); ν_{max}(neat)/cm^{-1} 3002 (w), 2936 (m), 2837 (m), 1732 (s); δ_H($CDCl_3$, 250.1 MHz) 7.28–7.22 (4H, m, aryl C*H* α to COMe), 6.90–6.95 (4H, m, aryl C*H* β to COMe), 4.49 (4H, s, aryl CH_2O), 4.19 [4H, s, OCH_2C(=O)CH_2O], 3.80 (6H, s, CH_3O); δ_C($CDCl_3$, 62.9 MHz) 205.8 (*C*=O), 159.3 (aryl C_iOMe), 129.5 (aryl C_iC), 128.8 (aryl *C*H β to COMe), 113.7 (aryl *C*H α to COMe), 73.0 (*C*H$_2$), 72.9 (*C*H$_2$), 55.1 (O*C*H$_3$); *m*/*z* (EI) 330 ([M]$^+$, 4%), 267 (54), 241 (16), 209 ([M − MeOC$_6$H$_4$CH$_2$]$^+$, 76), 195 (57), 149 (17), 137 ([MeOC$_6$H$_4$CH$_2$O]$^+$, 76), 121 ([MeOC$_6$H$_4$CH$_2$]$^+$, 100), 109 (38), 91 (52), 78 (72), 65 (32), 51 (42), 39 (29); Found: 330.1439, [$C_{19}H_{22}O_5$]$^+$ requires 330.1467.

Preparation of 2-(*p*-methoxyphenyl)-4-(*p*-methoxyphenylmethoxymethyl)-2,5-dihydrofuran 34

TMSDM (0.43 ml, 0.86 mmol) was lithiated with *n*-butyllithium (0.38 ml, 0.86 mmol) and reacted with 1,3-bis(*p*-methoxyphenylmethoxy)propan-2-one **24** (0.14 g, 0.43 mmol) in DME (5 ml) under the standard conditions described. Purification by column chromatography eluting with 5% ethyl acetate–petroleum ether gave the product as a pale yellow oil (0.09 g, 61%); mp 38.5–39.0 °C; R_f 0.23 (20% ethyl acetate–petroleum ether); ν_{max}(hexachlorobuta-1,3-diene)/cm^{-1} >3000 (w), 2997 (w), 2951 (m), 2835 (m), 1652 (w); δ_H($CDCl_3$, 250.1 MHz) 7.28–7.20 (4H, m, aryl C*H* β COMe), 6.92–6.84 (4H, m, aryl C*H* α to COMe), 5.78–5.75 (2H, m, ArC*H*O and R$_2$C=C*H*), 4.88–4.79 (1H, dm, OC*H*H′C=CH), 4.76–4.68 (1H, dm, OCH*H*′C=CH), 4.48 (2H, s, ArCH_2O), 4.18 (2H, m, ArCH$_2$OCH_2), 3.80 (3H, s, OCH_3), 3.79 (3H, s, OCH_3); δ_C($CDCl_3$, 62.9 MHz) 159.3 (aryl C_iOMe), 159.2 (aryl C_iOMe), 138.1 (aryl C_iC), 133.8 (aryl C_iC), 129.7 (R$_2$*C*=CH), 129.2 (aryl *C*H β to COMe), 127.7 (aryl *C*H β to COMe), 126.2 (C=*C*H), 113.7 (aryl *C*H α to COMe), 87.7 (Ar*C*H), 75.5 (furan *C*H$_2$), 72.0 (Ar*C*H$_2$O), 65.1 (ArCH$_2$-OCH_2C=C), 55.1 (OCH_3); *m*/*z* (CI) 327 ([M + H]$^+$, 4%), 188 (7), 159 (4), 135 (22), 121 ([MeOC$_6$H$_4$CH$_2$]$^+$, 100), 115 (24), 108 (4), 91 (9), 78 (6), 58 (4); Found: 327.1596, [$C_{20}H_{22}O_4$ + H]$^+$ requires 327.1596.

Preparation of (±)-2-benzyloxymethyloxirane 25 (R = Bn)

Sodium hydride (1.05 g, 43.7 mmol) was stirred in THF (25 ml) at 0 °C and to this (±)-glycidol (2.42 ml, 36.0 mmol) was added slowly over 10 min. The reaction was stirred at rt for 1 h before cooling once more to 0 °C. Benzyl bromide (5.20 ml, 43.7 mmol) was added and the reaction stirred overnight at rt. The reaction was quenched by the addition of saturated ammonium chloride solution (30 ml) and extracted with diethyl ether (3 × 30 ml). The organic layers were combined, dried over magnesium sulfate and filtered, and the solvent removed by rotary evaporation. Purification of the residue by column chromatography eluting with 5% ethyl acetate–petroleum ether gave the product as a colourless oil (4.44 g, 74%). Found: C 72.69% H 7.24%, $C_{10}H_{12}O_2$ requires C 73.17% H 7.32%. R_f 0.58 (20% ethyl acetate–petroleum ether); ν_{max}(neat)/cm^{-1} 3060 (w), 3029 (w), 2997 (w), 2861 (m); δ_H($CDCl_3$, 250.1 MHz) 7.37–7.25 (5H, m, aryl C*H*), 4.60 (1H, d, J_{AB} 11.9, PhC*H*H′O), 4.56 (1H, d, J_{AB} 11.9, PhCH*H*′O), 3.76 (1H, dd, J_{AB} 11.3 and J_{AX} 3.1, BnOC*H*H′), 3.43 (1H, dd, J_{AB} 11.3 and J_{AX} 5.9, BnOCH*H*′), 3.22–3.16 (1H, m, C*H*), 2.79 (1H, dd, J_{AB} 4.9 and J_{AX} 4.1, CHC*H*H′), 2.61 (1H, dd, J_{AB} 4.9 and J_{AX} 2.8, CHCH*H*′); δ_C($CDCl_3$, 62.9 MHz) 137.8 (aryl C_i), 128.4 (aryl C_m), 127.7 (aryl C_{o+p}), 73.2 (Ph*C*H$_2$O), 70.8 (BnO*C*H$_2$), 50.8 (*C*H), 44.2 (O*C*H$_2$CH); *m*/*z* (EI) 164 ([M]$^+$, 23%), 107 ([PhCH$_2$O]$^+$, 92), 91 ([PhCH$_2$]$^+$, 100), 84 (34), 79 (70), 65 (55), 57 ([epoxideCH$_2$]$^+$, 32), 51 (32), 43 (47).

Preparation of 1-benzyloxy-3-methoxypropan-2-ol 26 (R = Bn, R′ = Me)

2-Benzyloxymethyloxirane **25** (R = Bn) (1.5 g, 9.2 mmol) was stirred in methanol (40 ml) at rt and to this solution lithium perchlorate (1.95 g, 18.3 mmol) was added and the reaction refluxed for 3 days. After cooling to rt the reaction was quenched by the addition of water (40 ml) and extracted with diethyl ether (3 × 40 ml). The combined organic layers were dried over magnesium sulfate and filtered, and the solvent evaporated off. Purification of the residue by column chromatography eluting with 5–10% ethyl acetate–petroleum ether gave the product as a colourless oil (1.25 g, 69%). R_f 0.30 (20% ethyl acetate–petroleum ether); ν_{max}(neat)/cm^{-1} 3429 (br), 3062 (w), 3029 (w), 2894 (m); δ_H($CDCl_3$, 250.1 MHz) 7.35–7.28 (5H, m, aryl C*H*), 4.56 (2H, s, PhCH_2), 4.01–3.97 (1H, m, C*H*), 3.59–3.41 [4H, m, CH_2CH(OH)CH_2], 3.37 (3H, s, CH_3O), 2.67 (1H, br s, O*H*); δ_C($CDCl_3$, 62.9 MHz) 137.9 (aryl C_i), 128.4 (aryl C_m), 127.7 (aryl C_{o+p}), 73.7 (*C*H$_2$OMe), 73.4 (O*C*H$_2$Ph), 71.3 (*C*H$_2$OBn), 69.4 (*C*HOH), 59.1 (O*C*H$_3$); *m*/*z* (EI) 196 ([M]$^+$, 36%), 107 (73), 91 ([PhCH$_2$]$^+$, 100), 72 ([MeOCH$_2$-HCHCH$_2$]$^+$, 81), 65 (63), 58 ([MeOCH$_2$CH]$^+$, 21), 51 (29), 45 ([MeOCH$_2$]$^+$, 81); Found: 196.1100, [$C_{11}H_{16}O_3$]$^+$ requires 196.10995.

Preparation of 1-benzyloxy-3-methoxypropan-2-one 27

Oxalyl chloride (1.80 ml, 2.47 mmol) was stirred at −78 °C in DCM (3 ml) and to this DMSO (0.35 ml, 4.94 mmol) in DCM (3 ml) was added dropwise. The reaction was stirred for 20 min before the addition of 1-benzyloxy-3-methoxypropan-2-ol **26** (R = Bn, R′ = Me) (0.40 g, 1.90 mmol) in DCM (3 ml). Once more the reaction was stirred for 20 min and then triethylamine (1.43 ml, 10.3 mmol) was added and the cooling bath removed. The reaction was stirred for 40 min at rt and then quenched by the addition of water (12 ml). The layers were separated and the aqueous layer extracted with DCM (3 × 10 ml). The combined organic layers were dried over magnesium sulfate and filtered, and the solvent removed. The product was isolated by column chromatography eluting with 10% ethyl acetate–petroleum ether as a colourless oil (0.37 g, 89%). R_f 0.56 (20% ethyl acetate–petroleum ether); ν_{max}(neat)/cm^{-1} 3062 (w), 3029 (w), 2974 (m), 2894 (m), 1730 (s); δ_H($CDCl_3$, 250.1 MHz) 7.38–7.29

(5H, m, aryl C*H*), 4.59 (2H, s, PhCH_2), 4.22 (2H, s, BnOCH_2), 4.21 (2H, s, MeOCH_2), 3.40 (3H, s, CH_3O); δ_C($CDCl_3$, 62.9 MHz) 205.6 (*C*=O), 136.9 (aryl C_i), 128.5 (aryl C_m), 128.0 (aryl C_p), 127.9 (aryl C_o), 76.1 (Ph*C*H_2O), 73.5 [CH_2C(O)*C*H_2], 73.4 [*C*H_2C(O)CH_2], 59.4 (*C*H_3O); *m*/*z* (CI) 212 ([M + NH_4]$^+$, 14%), 122 (5), 108 (43), 91 ([PhCH_2]$^+$, 100), 78 (15), 65 (4), 58 (7), 51 (4), 45 ([MeOCH_2]$^+$, 19); Found: 212.1282, [$C_{11}H_{14}O_3$ + NH_4]$^+$ requires 212.1287.

Preparation of 4-(methoxymethyl)-2-phenyl- (A) and 3-(benzyloxymethyl)-2,5-dihydrofurans (B) from 27

TMSDM (1.03 ml, 2.06 mmol) was lithiated with *n*-butyllithium (0.82 ml, 2.06 mmol) and reacted with 1-benzyloxy-3-methoxypropan-2-one (0.20 g, 1.03 mmol) in DME (8 ml) under the standard conditions described. Purification by column chromatography eluting with 5% ethyl acetate–petroleum ether gave the products as an inseparable mixture in a 2 : 1 ratio (0.07 g, 34%) in the form of a yellow oil. R_f 0.45 (20% ethyl acetate–petroleum ether); ν_{max}(neat)/cm^{-1} 3029 (w), 2923 (m), 2851 (m); δ_H($CDCl_3$, 250.1 MHz) 7.36–7.18 (5H_{min} + 5H_{maj}, m, aryl C*H*), 5.85–5.77 (1H_{min} + 2H_{maj}, m, C=C*H* and C=C*HCH*Ph), 4.90–4.72 (2H_{maj}, m, CH_2OCH), 4.71–4.63 (4H_{min}, m, CH_2OCH_2), 4.52 (2H_{min}, s, PhCH_2), 4.14–4.13 (2H_{min}, m, BnOCH_2), 4.11–4.10 (2H_{maj}, m, MeOCH_2), 3.38 (3H_{maj}, s, CH_3O); δ_C($CDCl_3$, 62.9 MHz) 141.8 (*C*=CH)1C_{min}, 137.9 (*C*=CH)1C_{maj}, 137.8 (aryl C_i)1C_{min}, 137.4 (aryl C_i)1C_{maj}, 129.5 (aryl C_p)1C_{maj}, 128.5 (aryl C_m)2C_{maj}, 128.4 (aryl C_m)2C_{min}, 127.8 (aryl C_p)1C_{min}, 127.7 (aryl C_o)2C_{min}, 126.3 (aryl C_o)2C_{maj}, 122.8 (C=CH)1C_{maj}, 120.2 (C=CH)1C_{min}, 88.2 (Ph*C*H)1C_{maj}, 75.8 (furan *C*H_2), 75.7 (furan *C*H_2), 75.5 (furan *C*H_2), 72.3 (Ph*C*H_2)1C_{min}, 68.0 (MeO*C*H_2C=C)1C_{maj}, 65.5 (BnO*C*H_2C=C)1C_{min}, 58.3 (O*C*H_3)1C_{maj}; *m*/*z* (CI) 208 ([M + NH_4]$^+$, 41%), 191 ([M + H]$^+$, 100), 173 (17), 159 (39), 141 (17), 129 (18), 117 (16), 105 (91), 91 ([PhCH_2]$^+$, 86), 84 (30), 65 (18), 45 ([MeOCH_2]$^+$, 45); Found: 191.1072, [$C_{12}H_{14}O_2$ + H]$^+$ requires 191.1072.

Preparation of 1-benzyloxy-3-ethoxypropan-2-ol 26 (R = Bn, R′ = Et)

2-Benzyloxymethyloxirane **25** (R = Bn) (1.5 g, 9.2 mmol) was stirred in ethanol (40 ml) at rt and lithium perchlorate (1.95 g, 18.3 mmol) added. The reaction was refluxed for 3 days, quenched by the addition of water (50 ml) at rt and extracted with diethyl ether (3 × 50 ml). The combined organic layers were dried over magnesium sulfate, filtered and concentrated. Purification of the residue by column chromatography eluting with 10% ethyl acetate–petroleum ether gave the product as a colourless oil (1.2 g, 62%). R_f 0.41 (20% ethyl acetate–petroleum ether); ν_{max}(neat)/cm^{-1} 3443 (br), 3062 (w), 3029 (w), 2974 (m), 2865 (s); δ_H($CDCl_3$, 250.1 MHz) 7.36–7.28 (5H, m, aryl C*H*), 4.56 (2H, s, PhCH_2O), 4.04–3.94 (1H, m, C*H*), 3.59–3.42 [6H, m, MeCH_2OCH_2CH(OH)CH_2], 2.62 (1H, d, *J* 4.3, O*H*), 1.20 (3H, t, *J* 7.0, CH_3CH_2O); δ_C($CDCl_3$, 62.9 MHz) 137.9 (aryl C_i), 128.4 (aryl C_m), 127.7 (aryl C_o), 73.4 (Ph*C*H_2O), 71.6 (EtO*C*H_2), 71.3 (BnO*C*H_2), 69.5 (*C*HOH), 66.8 (Me*C*H_2O), 15.1 (*C*H_3); *m*/*z* (EI) 210 ([M]$^+$, 36%), 164 (36), 107 ([PhCH_2O]$^+$, 67), 91 ([PhCH_2]$^+$, 100), 61 (79), 43 (56); Found: 210.1256, [$C_{12}H_{18}O_3$]$^+$ requires 210.1256.

Preparation of 1-benzyloxy-3-ethoxypropan-2-one 28

Oxalyl chloride (1.70 ml, 2.47 mmol) was stirred in DCM (3 ml) at −78 °C and DMSO (0.35 ml, 4.94 mmol) in DCM (3 ml) was added dropwise. The reaction was stirred for 20 min and then 1-benzyloxy-3-ethoxypropan-2-ol **26** (R = Bn, R′ = Et) (0.40 g, 1.90 mmol) in DCM (3 ml) was added. Once more the reaction was stirred for 20 min, triethylamine (1.43 ml, 10.3 mmol) added and the cooling bath removed. The reaction was stirred for 40 min at rt, quenched by the addition of water (12 ml) and extracted with DCM (3 × 10 ml). The combined organic layers were dried over magnesium sulfate and filtered, and the solvent removed. Purification of the residue by column chromatography eluting with 10% ethyl acetate–petroleum ether gave the product as a colourless oil (0.26 g, 66%). R_f 0.65 (20% ethyl acetate–petroleum ether); ν_{max}(neat)/cm^{-1} 3071 (m), 3030 (m), 2976 (m), 2914 (m), 1732 (s); δ_H($CDCl_3$, 250.1 MHz) 7.40–7.30 (5H, m, aryl C*H*), 4.59 (2H, s, PhCH_2), 4.24 (2H, s, BnOCH_2C), 4.23 (2H, s, EtOCH_2C), 3.53 (2H, q, *J* 7.0, MeCH_2O), 1.23 (3H, t, *J* 7.0, CH_3CH_2O); δ_C($CDCl_3$, 62.9 MHz) 206.0 (*C*=O), 137.0 (aryl C_i), 128.5 (aryl C_m), 128.0 (aryl C_p), 127.8 (aryl C_o), 74.3 (Ph*C*H_2O), 73.5 [*C*H_2C(O)CH_2], 73.4 [CH_2C(O)*C*H_2], 67.2 (Me*C*H_2O), 14.9 (*C*H_3); *m*/*z* (CI) 226 ([M + NH_4]$^+$, 50%), 195 (18), 184 (33), 195 (50), 138 (14), 120 (27), 108 (85), 91 ([PhCH_2]$^+$, 100), 76 (46), 65 (23), 59 ([EtOCH_2]$^+$, 78), 47 (68); Found: 226.1443, [$C_{12}H_{16}O_3$ + NH_4]$^+$ requires 226.1443.

Preparation of 4-ethoxymethyl-2-phenyl- (A) and 4-(benzyloxymethyl)-2-methyl-2,5-dihydrofuran (B) from 28

TMSDM (2.00 ml, 4.00 mmol) was lithiated with *n*-butyllithium (1.6 ml, 4.0 mmol) and reacted with 1-benzyloxy-3-ethoxypropan-2-one (0.26 g, 1.26 mmol) in DME (6 ml) under the standard conditions described. Purification by column chromatography eluting with 1–10% ethyl acetate–petroleum ether gave the products as an inseparable mixture in a 5 : 3 ratio (0.14 g, 52%) in the form of a pale yellow oil. R_f 0.52 (20% ethyl acetate–petroleum ether); ν_{max}(neat)/cm^{-1} 3036 (w), 3000 (w), 2956 (m), 2931 (m), 2837 (m); δ_H($CDCl_3$, 250.1 MHz) 7.71–7.16 (5H_{maj} + 5H_{min}, m, aryl C*H*), 5.85–5.76 (2H_{min}, m, PhC*HCH*=C), 5.73–.69 (1H_{maj}, m, C=C*H*), 5.08–4.95 (1H_{maj}, m, MeC*H*), 4.92–4.72 (2H_{min}, m, OCH_2C=CH), 4.76–4.57 (2H_{maj}, m, CH_2C=CH), 4.51–4.55 (2H_{maj}, m, PhCH_2), 4.17 (2H_{min}, s, EtOCH_2), 4.12 (2H_{maj}, s, BnOCH_2), 3.53 (2H_{min}, q, *J* 7.0, MeCH_2O), 1.28 (3H_{maj}, d, *J* 6.4, CH_3CH), 1.25 (3H_{min}, t, *J* 7.0, CH_3CH_2O); δ_C($CDCl_3$, 62.9 MHz) 137.7 (aryl C_i)1C_{min}, 137.3 (aryl C_i)1C_{maj}, 129.6 (aryl *C*), 128.4 (aryl *C*), 127.8 (aryl *C*), 127.7 (aryl *C*), 126.3 (aryl *C*), 88.2 (Ph*C*H)1C_{min}, 82.4 (Me*C*H)1C_{maj}, 75.9 (furan *C*H_2)1C_{min}, 74.9 (furan *C*H_2)1C_{maj}, 72.4 (Ph *C*H_2)1C_{maj}, 66.0 (EtO*C*H_2C=CH and Me*C*H_2O)2C_{min}, 65.6 (BnO*C*H_2C=CH)1C_{maj}, 22.7 (*C*H_3CH)1C_{maj}, 15.1 (*C*H_3-CH_2O)1C_{min}; *m*/*z* (CI) 222 ([M + NH_4]$^+$, 77%), 205 ([M + H]$^+$, 84), 187 (53), 159 ([M − EtO]$^+$, 70), 113 ([M − Bn]$^+$, 58), 105 (74), 95 (67), 91 ([PhCH_2]$^+$, 100), 85 (35), 81 (43), 59 ([EtOCH_2]$^+$, 43), 41 (35); Found: 205.1229, [$C_{13}H_{16}O_2$ + NH_4]$^+$ requires 205.1228.

Preparation of 1-benzyloxy-3-(*p*-methoxybenzyloxy)propan-2-ol 26 (R = MPM, R′ = Bn)

2-(*p*-Methoxybenzyloxymethyl)oxirane **25** (R = MPM) (1.00 g, 5.16 mmol) was stirred in benzyl alcohol (8 ml, excess) at rt and to this lithium perchlorate (1.09 g, 10.3 mmol) was added. The reaction was stirred at 60 °C for 4 days, water (20 ml) added and the mixture extracted with ethyl acetate (3 × 30 ml). The combined organic layers were dried over magnesium sulfate and filtered, and the solvent removed by rotary evaporation. Purification of the residue by column chromatography eluting with 10–40% ethyl acetate–petroleum ether gave the product as a colourless oil (1.38 g, 89%). R_f 0.14 (20% ethyl acetate–petroleum ether); ν_{max}(neat)/cm^{-1} 3442 (br), 3062 (w), 3002 (w), 2907 (s), 2861 (s); δ_H($CDCl_3$, 250.1 MHz) 7.37–7.28 (5H, m, phenyl C*H*), 7.27–7.21 (2H, m, aryl C*H* β to COMe), 6.90–6.84 (2H, m, aryl C*H* α to COMe), 5.54 (2H, s, MeOC_6H_4CH_2), 4.47 (2H, s, PhCH_2), 4.04–3.96 (1H, m, C*H*OH), 3.79 (3H, s, OCH_3), 3.58–3.45 (4H, m, OCH_2CHCH_2O), 2.57 (1H, br s, CHO*H*); δ_C($CDCl_3$, 62.9 MHz) 159.2 (aryl C_iOMe), 137.9 (phenyl C_iC), 130.0 (aryl C_iC), 129.3 (aryl *C*H β to COMe), 128.4 (phenyl C_m), 127.7 (phenyl $C_{p\,+\,o}$), 113.8 (aryl *C*H α to COMe), 73.4 (Ph*C*H_2O), 73.0 (Ar*C*H_2O), 71.3 (BnO*C*H_2), 70.9 (ArO*C*H_2), 69.5, (*C*H) 55.2 (*C*H_3O); *m*/*z* (EI) 302 ([M]$^+$, 7%), 21 ([M −

$PhCH_2]^+$, 70), 181 ([M − $MeOC_6H_4CH_2]^+$, 60), 137 ([MeO-$C_6H_4CH_2O]^+$, 86), 121 ([$MeOC_6H_4CH_2]^+$, 100), 91 ([$PhCH_2]^+$, 92), 77 ([Ph]$^+$, 67), 65 (62), 51 (58); Found: 302.1527, [$C_{18}H_{22}O_4]^+$ requires 302.1518.

Preparation of 1-benzyloxy-3-(*p*-methoxybenzyloxy)propan-2-one 29

1-Benzyloxy-3-(*p*-methoxybenzyloxy)propan-2-ol **26** (R = MPM, R′ = Bn) (1.00 g, 3.31 mmol), silica (1.43 g) and sodium acetate (0.54 g, 6.62 mmol) were stirred in DCM (20 ml) at 0 °C. PCC (1.43 g, 6.62 mmol) was added in portions over 10 min and cooling was maintained for a further 20 min. The reaction was stirred for 48 h at rt and then filtered through silica. The silica was washed with DCM (2 × 50 ml) and the solvent removed from the combined filtrate and washings by rotary evaporation. Purification of the residue by column chromatography eluting with 5–20% ethyl acetate–petroleum ether gave the product as a colourless oil (0.28 g, 28%). R_f 0.32 (20% ethyl acetate–petroleum ether); ν_{max}(neat)/cm^{-1} 3063 (w), 3031 (w), 3004 (w), 2935 (m), 2864 (m), 2837 (m), 1735 (s); δ_H($CDCl_3$, 250.1 MHz) 7.39–7.30 (5H, m, phenyl C*H*), 7.28–7.22 (2H, m, aryl C*H* β to COMe), 6.91–6.85 (2H, m, aryl C*H* α to COMe), 4.56 (2H, s, ArCH_2O), 4.49 (2H, s, PhCH_2O), 4.23 [2H, s, ROCH_2C(=O)CH_2OR′], 4.20 [2H, s, ROCH_2C(=O)CH_2OR′], 3.79 (3H, s, CH_3O); δ_C($CDCl_3$, 62.9 MHz) 205.8 (*C*=O), 159.4 (aryl C_iOMe), 136.9 (phenyl C_i), 129.6 (aryl C_i), 128.5 (aryl *C* β to COMe), 127.9 (phenyl C_p), 128.9 (phenyl C_m), 128.0 (phenyl C_o), 113.8 (aryl *C*H α to COMe), 73.5 (CH_2), 73.4 (CH_2), 73.2 (CH_2), 73.1 (CH_2), 55.2 (CH_3O); *m*/*z* (CI) 318 ([M + $NH_4]^+$, 41), 138 (35), 121 ([$MeOC_6H_4CH_2]^+$, 100); Found: 318.1712, [$C_{18}H_{20}O_4$ + $NH_4]^+$ requires 318.1705.

Preparation of 4-(*p*-methoxybenzyloxymethyl)-2-phenyl- (A) and 4-(benzyloxymethyl)-2-(*p*-methoxyphenyl)-2,5-dihydrofuran (B) from 29

TMSDM (0.83 ml, 1.67 mmol) was lithiated with *n*-butyllithium (0.67 ml, 1.67 mmol) and reacted with 1-benzyloxy-3-(*p*-methoxybenzyloxy)propan-2-one **29** (0.25 g, 0.83 mmol) in DME (4 ml) under the standard conditions described. Purification by column chromatography eluting with 5% ethyl acetate–petroleum ether gave the products as an inseparable mixture in a ratio of 1 : 1 as a pale yellow oil (0.08 g, 32%). R_f 0.52 (20% ethyl acetate–petroleum ether); ν_{max}(neat)/cm^{-1} 3062 (w), 3030 (w), 3003 (w), 2850 (m); δ_H($CDCl_3$, 250.1 MHz) 7.38–7.20 ($7H_A$ + $7H_B$, m, aryl C*H*), 6.91–6.85 ($2H_A$ + $2H_B$, m, aryl C*H* α to COMe), 5.84–5.77 ($2H_A$ + $2H_B$, m, 4 × C*H*), 4.88–4.71 ($2H_A$ + $2H_B$, m, furan CH_2), 4.56 ($2H_A$, s, ArCH_2O), 4.48 ($2H_B$, s, PhCH_2O), 4.22–4.20 (2H, m, ArCH_2OCH_2), 4.18–4.16 (2H, m, ArCH_2OCH_2), 3.80 (3H, s, OCH_3), 3.79 (3H, s, OCH_3); δ_C($CDCl_3$, 62.9 MHz) 159.3 (aryl C_iOMe)$1C_A$ + $1C_B$, 138.2 (R_2C=CH)$1C_A$ + $1C_B$, 134.0 (aryl C_i)$1C_A$ + $1C_B$, 129.4 (aryl *C*H β to COMe), 128.5 (aryl *C*), 127.8 (aryl *C*), 127.7 (C=*C*H), 126.4 (C=*C*H), 126.3 (aryl *C*), 113.8 (aryl *C*H α to COMe)$1C_A$ + $1C_B$, 88.2 (Ph*C*H)$1C_A$, 87.8 (Ar*C*H)$1C_B$, 75.9 (furan CH_2)$1C_A$, 75.6 (furan CH_2)$1C_B$, 72.4 (PhCH_2)$1C_B$, 72.1 (ArCH_2)$1C_A$, 65.5 (BnOCH_2C=C)$1C_B$, 65.2 (ArCH_2OCH_2-C=C)$1C_A$, 55.2 (OCH_3)$1C_A$ + $1C_B$; *m*/*z* (EI) 296 ([M]$^+$, 32%), 173 (23), 158 (68), 145 (23), 135 (96), 121 ([$MeOC_6H_4CH_2]^+$, 100), 91 ([$PhCH_2]^+$, 95), 84 (72), 77 ([Ph]$^+$, 74), 65 (24), 51 (24), 43 (30); Found: 296.1412, [$C_{19}H_{20}O_3]^+$ requires 296.1213.

Preparation of 1-cyclopentyloxy-2-methylpropene

Sodium hydride (3.0 g, 74 mmol) was stirred in DMF (100 ml) at 0 °C and to this cyclopentanol (6.7 ml, 74 mmol) was added carefully over 10 min. The cooling bath was removed once the addition was completed and the reaction stirred for 1 h at rt. 3-Bromo-2-methylpropene (6.62 g, 49.0 mmol) was then added dropwise and the reaction stirred overnight at rt. The reaction was quenched by the addition of saturated ammonium chloride solution (150 ml), extracted with ethyl acetate (3 × 150 ml) and the combined organic layers were washed with water (4 × 150 ml), dried over magnesium sulfate, filtered and concentrated. Purification of the residue by column chromatography eluting with 5–10% ethyl acetate–hexane gave the product as a colourless oil (3.87 g, 56%). R_f 0.78 (30% ethyl acetate–petroleum ether). Found: C 77.40% H 11.41%, $C_9H_{16}O$ requires C 77.14% H 11.43%. ν_{max}(neat)/cm^{-1} 2959 (s), 2915 (s), 1454 (m); δ_H ($CDCl_3$, 299.9 MHz) 4.97–4.95 (1H, m, C=C*H*H′), 4.87–4.85 (1H, m, C=CH*H*′), 3.95–3.88 (1H, m, CH_2CHCH_2), 3.83 (2H, s, OCH_2C=CH_2), 1.77–1.59 [6H, m, $OCHCH_2$(C*H*-H′)$_2CH_2$], 1.73 (3H, s, CH_3), 1.55–1.49 [2H, m, OCH_2(CH-*H*′)$_2CH_2$]; δ_C($CDCl_3$, 75.4 MHz) 142.9 (CH_3C=C), 111.4 (CH_2=C), 80.6 (*C*H), 72.6 (CCH_2O), 32.2 (CH_3C), 23.5 ($OCHCH_2CH_2CH_2CH_2$), 19.6 ($OCHCH_2CH_2CH_2CH_2$).

Preparation of 1-cyclopentyloxypropan-2-one 30

1-Cyclopentyloxy-2-methylpropene (1.50 g, 10.7 mmol) was stirred in DCM (20 ml) at −60 °C. An empty trap followed by a trap containing a solution of 5% potassium iodide in 50% acetic acid–water were connected to the outlet and then ozone bubbled through the reaction for 30 min. Air and nitrogen were bubbled through for a further 30 min each and then triphenylphosphine (4.22 g, 16.1 mmol) was added. The cooling bath was removed and the reaction stirred overnight at rt. The solvent was removed by evaporation and purification of the residue by column chromatography eluting with 10% ethyl acetate–petroleum ether gave the product as a colourless oil (1.36 g, 90%). R_f 0.44 (30% ethyl acetate–petroleum ether); ν_{max}(neat)/cm^{-1} 2957 (s), 2871 (m), 1719 (s) C=O; δ_H($CDCl_3$, 299.9 MHz) 3.98 [2H, s, MeC(=O)CH_2O], 3.97–3.91 (1H, m, C*H*), 2.17 (3H, s, CH_3C=O), 1.78–1.65 [6H, m, $CHCH_2$(C*H*H′)$_2CH_2$], 1.60–1.52 [2H, m, $CHCH_2$(CH*H*′)$_2CH_2$]; δ_C($CDCl_3$, 75.4 MHz) 207.8 (*C*=O), 82.3 (O*C*H), 74.6 (C*C*H_2O), 31.2 (CH_3C=O), 26.4 ($OCH_2CH_2CH_2CH_2$), 23.4 ($OCH_2CH_2CH_2CH_2$); *m*/*z* (EI) 160 ([M + $NH_4]^+$, 73%), 143 ([M + H]$^+$, 78), 116 (73), 99 ([M − CH_3C=O]$^+$, 82), 85 ([M − CH_3C=$OCH_2]^+$, 77), 75 (84), 69 ([CH_3C=$OCH_2O]^+$, 98), 58 (100); Found: 160.1338, [$C_8H_{14}O_2$ + $NH_4]^+$ requires 160.13375.

Preparation of 3-methyl-1-oxaspiro[4.4]non-3-ene 36

TMSDM (6.0 ml, 12 mmol) was lithiated with *n*-butyllithium (4.8 ml, 12 mmol) and reacted with 1-cyclopentyloxypropan-2-one **30** (0.85 g, 6.00 mmol) in DME (20 ml) under the standard conditions described. Purification by column chromatography eluting with 0.5% ethyl acetate–petroleum ether gave the product as a pale yellow oil (0.47 g, 57%). R_f 0.62 (15% ethyl acetate–hexane); ν_{max}(neat)/cm^{-1} 3074 (w), 2961 (m), 2874 (m); δ_H($CDCl_3$, 299.9 MHz) 5.36–5.32 (1H, m, C=C*H*), 4.44 (2H, dd, *J* 1.0, OCH_2C=C), 1.80–1.72 (4H, m, $CCH_2CH_2CH_2CH_2$), 1.73 (3H, dd, *J* 1.0, CH_3C=C), 1.68–1.59 (4H, m, CCH_2-$CH_2CH_2CH_2$); δ_C($CDCl_3$, 75.4 MHz) 134.8 (CH_3C=C), 127.1 (*C*H=C), 98.6 (OCR_3), 76.6 (OCH_2C=C), 38.4 (CCH_2-$CH_2CH_2CH_2$), 24.3 ($CCH_2CH_2CH_2CH_2$), 12.3 (CH_3C=C); *m*/*z* (EI) 138 ([M]$^+$, 31%), 123 ([M − $CH_3]^+$, 49), 95 (93), 81 (92), 79 (61), 67 (71), 55 (100), 53 (62); Found: 138.1045, [$C_9H_{14}O]^+$ requires 138.10447.

Preparation of pyruvaldehyde dibenzyl acetal

Pyruvaldehyde dimethyl acetal (4.0 ml, 33 mmol) was stirred in benzyl alcohol (20 ml) and PTSA (0.63 g, 3.3 mmol) added. The reaction was heated at 80 °C for 20 h and then cooled to rt. Water (50 ml) and DCM (60 ml) were added and then the aqueous layer extracted with DCM (3 × 60 ml). The organic layers were combined, dried over magnesium sulfate and filtered, and the solvent removed by rotary evaporation. Purification of the residue by column chromatography eluting with

5% ethyl acetate–petroleum ether gave the product as a colourless oil (2.92 g, 33%). R_f 0.76 (20% ethyl acetate–petroleum ether); ν_{max}(neat)/cm^{-1} 3061 (m), 3029 (m), 2934 (m), 2874 (m), 1729 (s); δ_H($CDCl_3$, 250.1 MHz) 7.34–7.30 (10H, m, aryl C*H*), 4.73 (1H, s, C*H*), 4.67 (2H, d, J_{AB} 11.8, PhC*H*H′O), 4.59 (2H, d, J_{AB} 11.8, PhCH*H*′O), 2.24 (3H, s, CH_3); δ_C($CDCl_3$, 62.9 MHz) 203.8 (*C*=O), 136.8 (aryl C_i), 128.5 (aryl C_m), 128.0 (aryl C_{o+p}), 100.9 (*C*H), 69.2 (Ph*C*H_2O), 25.0 (CH_3); *m*/*z* (CI) 288 ([M + NH_4]$^+$, 83%), 212 (49), 181 (12), 108 (86), 91 ([$PhCH_2$]$^+$, 100); Found: 288.1600, [$C_{17}H_{18}O_3$ + NH_4]$^+$ requires 288.1600.

Preparation of 2-(benzyloxy)-3-methyl-5-phenyl-2,5-dihydrofuran 37

TMSDM (3.70 ml, 7.41 mmol) was lithiated with *n*-butyllithium (2.90 ml, 7.41 mmol) and reacted with pyruvaldehyde dibenzyl acetal (1.00 g, 3.70 mmol) in DME (30 ml) under the standard conditions described. Purification by column chromatography eluting with 10% ethyl acetate–petroleum ether gave the products as an inseparable mixture in a 3 : 1 ratio (0.67 g, 68%) in the form of a pale yellow oil. R_f 0.47 (20% ethyl acetate–petroleum ether); ν_{max}(neat)/cm^{-1} 3061 (m), 3028 (m), 2934 (m), 2869 (m); δ_H($CDCl_3$, 250.1 MHz) 7.42–7.23 ($10H_{maj}$ + $10H_{min}$, m, aryl C*H*), 5.92 ($1H_{min}$, d, *J* 4.0, C=C*H*), 5.88–5.85 ($1H_{min}$, m, PhC*H*), 5.82–5.80 ($1H_{min}$, m, BnOC*H*), 5.77–5.74 ($2H_{maj}$, m, C*H*), 5.68–5.66 ($1H_{maj}$, m, C*H*), 4.86 ($1H_{maj}$, d, *J* 11.9, PhC*H*H′O), 4.81 ($1H_{min}$, d, *J* 11.9, PhC*H*H′O), 4.65 ($1H_{min}$, d, *J* 11.9, PhCH*H*′O), 4.63 ($1H_{maj}$, d, *J* 11.9, PhCH*H*′O), 1.84–1.82 ($3H_{min}$, m, CH_3), 1.82–1.80 ($3H_{maj}$, m, CH_3); δ_C($CDCl_3$, 62.9 MHz) 141.1 (aryl *C*), 138.3 (aryl *C*), 135.7 (aryl *C*), 135.2 (aryl *C*)$1C_{maj}$, 128.7–126.5 (aryl *C*)10_{maj} + 10_{min}, 109.6 (BnO*C*H)$1C_{min}$, 109.4 (BnO*C*H)$1C_{maj}$, 87.3 (Ph*C*H)$1C_{maj}$, 86.9 (Ph*C*H)$1C_{min}$, 69.5 (Ph*C*H_2)$1C_{maj}$ + $1C_{min}$, 11.9 (CH_3C=CH)$1C_{maj}$ + $1C_{min}$; *m*/*z* (CI) 281 ([M + NH_4 − H]$^+$, 13%), 265 ([M + H − H_2]$^+$, 27), 249 (17), 205 (10), 188 (33), 175 ([M − Bn]$^+$, 60), 159 ([M − BnO]$^+$, 100), 147 (50); Found: 265.1229, [$C_{18}H_{18}O_2$ + H − H_2]$^+$ requires 265.1229.

Preparation of 1,3-dioxane-2-carbaldehyde

Pyruvaldehyde dimethyl acetal (2.00 ml, 16.0 mmol) and propane-1,3-diol (1.40 ml, 19.2 mmol) were stirred in toluene (5 ml) and PTSA (0.15 g, 0.80 mmol) was added. The reaction was heated at 80 °C for 5 h and, after cooling, the solvent was removed by rotary evaporation. Purification of the residue by column chromatography eluting with 5% ethyl acetate–petroleum ether gave the product as a colourless oil (1.05 g, 51%). R_f 0.54 (20% ethyl acetate–petroleum ether); ν_{max}(neat)/cm^{-1} 2962 (m), 2868 (m), 1733 (s); δ_H($CDCl_3$, 250.1 MHz) 4.76 (1H, s, CH), 4.25–4.18 (2H, m, $OCH_aH_eCH_2$), 3.91–3.81 (2H, m, $OCH_aH_eCH_2$), 2.23 (3H, s, CH_3), 2.26–2.14 (1H, m, $OCH_2CH_aH_e$), 1.48–1.39 (1H, m, $OCH_2CH_aH_e$); δ_C($CDCl_3$, 62.9 MHz) 201.8 (*C*=O), 100.3 (*C*H), 66.9 (*C*H_2O), 25.5 (CH_3), 24.8 (OCH_2CH_2).

Preparation of 2-acetyl-2-methyl-1,3-dioxane 39

Butane-2,3-dione (5.1 ml, 58 mmol) was stirred in toluene (100 ml) and propane-1,3-diol (4.2 ml, 58 mmol) and PTSA (0.55 g, 2.90 mmol) were added. The reaction was heated at 90 °C for 16 h and cooled to rt. The solvent and excess butane-2,3-dione were removed by rotary evaporation and the crude residue was purified by column chromatography eluting with 20% ethyl acetate–hexane. The product was obtained as a colourless oil (6.1 g, 73%). R_f 0.61 (20% ethyl acetate–petroleum ether); ν_{max}(neat)/cm^{-1} 2969 (s), 2886 (m), 1728 (s); δ_H($CDCl_3$, 299.9 MHz) 4.02–3.95 (2H, m, $OCH_aH_eCH_2CH_aH_eO$), 3.82–3.73 (2H, m, $OCH_aH_eCH_2CH_aH_eO$), 2.25 [3H, s, C(=O)CH_3], 2.12–1.96 (1H, m, $OCH_2CH_aH_eCH_2O$), 1.46–1.38 (1H, m, $OCH_2CH_aH_eCH_2O$), 1.41 (3H, s, CH_3CR_3); δ_C($CDCl_3$, 75.4 MHz) 208.2 (*C*=O), 100.8 (*C*R_4), 62.6 (O*C*H_2), 25.0 (CH_3), 24.9 (OCH_2CH_2), 24.0 (R_3CCH_3); *m*/*z* (CI) 162 ([M + NH_4]$^+$, 87%), 145 ([M + H]$^+$, 100), 111 (16), 101 ([M − CH_3C=O]$^+$, 78), 86 (24), 58 (16), 44 (27); Found: 162.1130, [$C_9H_{14}O$ + NH_4]$^+$ requires 162.1130.

Preparation of 1,7-dimethyl-2,8-dioxabicyclo[3.2.1]oct-6-ene 40 and rearrangement to 5-(2-hydroxyethyl)-2,3-dimethylfuran 41

TMSDM (13.0 ml, 27.8 mmol) was lithiated with *n*-butyllithium (11.1 ml, 27.8 mmol) and reacted with 2-acetyl-2-methyl-1,3-dioxane **39** (2.00 g, 13.9 mmol) in DME (30 ml) under the standard conditions described. The crude residue was carried through without further purification as an orange oil (2.24 g). δ_H($CDCl_3$, 299.9 MHz) 6.07–6.06 (1H, m, *H*C=CMe), 4.64 (1H, br d, *J* 0.6, *H*CR_3), 3.91 (1H, td, *J* 4.4 and 11.3, $OCH_aH_eCH_2$), 3.82 (1H, ddd, *J* 4.6, 0.8 and 11.3, $OCH_aH_eCH_2$), 2.32–2.21 (1H, m, $OCH_2CH_aH_e$), 1.80 (3H, t, *J* 1.1, C=CCH_3), 1.45 (3H, s, CH_3CR_3), 1.25–1.23 and 1.21–1.16 (1H, m, $OCH_2CH_aH_e$); δ_C($CDCl_3$, 100.6 MHz) 138.9 (C=*C*Me), 128.6 (C=*C*H), 109.3 (R_4C), 78.4 (H*C*R_3), 61.8 (O*C*H_2CH_2), 29.4 (OCH_2CH_2), 22.6 (C=*C*H_3), 13.0 (CH_3).

Attempted purification of this compound by column chromatography eluting with 20% ethyl acetate–hexane resulted in a rearrangement product, **41**, obtained as a pale orange oil (0.62 g, 64%). R_f 0.35 (20% ethyl acetate–petroleum ether); ν_{max}(neat)/cm^{-1} 3402 (br), 2954 (s), 2912 (m), 1761 (m), 1261 (m); δ_H($CDCl_3$, 400.0 MHz) 5.88 (1H, s, C*H*), 3.83 (2H, t, *J* 6.1, CH_2OH), 2.86 (2H, t, *J* 6.1, CH_2CH_2OH), 2.17 (3H, s, CH_3OC), 1.90 (3H, s, CH_3C=CO), 1.66 (1H, br s, O*H*); δ_C($CDCl_3$, 100.6 MHz) 149.6 (O*C*CH_2CH_2OH), 146.3 (O*C*Me), 114.5 (OC=*C*Me), 109.9 (C=*C*H), 61.3 (CH_2CH_2OH), 31.6 (OC*C*H_2-CH_2OH), 11.3 (CH_3CO), 9.9 (CH_3C=CO); *m*/*z* (EI) 140 ([M]$^+$, 70%), 109 ([M − CH_2OH]$^+$, 100), 95 ([M − CH_2CH_2OH]$^+$, 17), 79 (35), 73 (46), 65 ([M − 2CH_3 and CH_2CH_2OH]$^+$, 36); Found: 141.0917, [$C_8H_{12}O_2$ + H]$^+$ requires 141.0916.

Preparation of 2-acetyl-2,4,4,6-tetramethyl-1,3-dioxane

Butane-2,3-dione (2.6 ml, 29 mmol) was stirred in DCM (50 ml) with 2-methylpentane-2,4-diol and PTSA (1.38 g, 7.30 mmol) and refluxed for 20 h. The reaction was cooled to rt, after which the solvent and excess butane-2,3-dione were removed by rotary evaporation. Purification of the residue by column chromatography eluting with 15% ethyl acetate–petroleum ether gave the product as a colourless oil (1.02 g, 19%). R_f 0.62 (20% ethyl acetate–petroleum ether); ν_{max}(neat)/cm^{-1} 2976 (s), 1736 (s); δ_H($CDCl_3$, 299.9 MHz) 4.16–4.09 (1H, m, CH_e), 2.24 [3H, s, C(=O)CH_3], 1.57 (1H, dd, J_{AB} 13.5 and J_{AX} 3.3, $CHCH_aH_e$), 1.47 (1H, dd, J_{AB} 13.5 and J_{BX} 11.5, $CHCH_aH_e$), 1.46 [3H, s, MeC(=O)CCH_3], 1.36 [3H, s, $R_2C(CH_3)CH_3'$], 1.31 (3H, d, *J* 11.5, CH_3CH), 1.31 [3H, s, $R_2C(CH_3)CH_3'$]; δ_C($CDCl_3$, 75.4 MHz) 206.6 (*C*=O), 98.9 [MeC(=O)*C*R_2], 72.1 [$R_2C(CH_3)_2$], 62.8 (*C*H), 43.2 (CH_2), 32.2 [C(=O)*C*H_3], 28.3 [MeC(=O)-C*C*H_3], 23.4–22.0–20.9 (CH_3); *m*/*z* (CI) 204 ([M + NH_4]$^+$, 29%), 187 ([M + H]$^+$, 46), 169 (12), 143 ([M − CH_3C=O]$^+$, 80), 131 (67), 118 (12), 104 (45), 83 (100), 55 (66), 43 ([CH_3C=O]$^+$, 86); Found: 187.1334, [$C_{10}H_{18}O_3$ + H]$^+$ requires 187.1334.

Preparation of (4*R*,6*R*)-1-(2,4,6-trimethyl-1,3-dioxan-2-yl)-ethanone 44

Butane-2,3-dione (0.25 ml, 2.90 mmol), (*R*,*R*)-(−)-pentane-2,4-diol and PTSA (0.4 g, 0.2 mmol) were stirred in toluene (10 ml) and refluxed for 2 h. The reaction was allowed to cool to rt and the solvent and excess butane-2,3-dione were removed by rotary evaporation. Purification of the residue by column chromatography eluting with 10% ethyl acetate–hexane gave the product as a colourless oil (0.23 g, 70%). R_f 0.53 (40% ethyl acetate–hexane); ν_{max}(neat)/cm^{-1} 2975 (s), 2934 (s), 1732 (s); δ_H($CDCl_3$, 299.9 MHz) 4.15–4.08 [1H, m, OCH_a(Me)CH_2-CH_e(Me)O], 3.91–3.84 [1H, m, OCH_a(Me)CH_2CH_e(Me)O],

2.25 (3H, s, CH_3CC=O), 1.71–1.62 [1H, m, OCH(Me)CH_aH_e], 1.59–1.50 [1H, m, OCH(Me)CH_aH_e], 1.38 [3H, s, MeC(=O)-CCH_3], 1.25 (3H, d, *J* 2.3, CH_3CHCH$_2$CHMe), 1.23 (3H, d, *J* 2.3, MeCHCH$_2$CHCH_3); δ_C($CDCl_3$, 75.4 MHz) 208.2 (*C*=O), 100.5 (*C*R$_4$), 65.0 (*C*H), 64.5 (*C*′H), 39.3 (CH_2), 25.0 (CH_3-C=O), 22.6 [MeC(=O)CCH_3], 21.6 (CH_3CH), 21.1 (*C*′H_3CH); *m*/*z* (CI) 190 ([M + NH_4]$^+$, 32%), 173 ([M + H]$^+$, 100), 155 ([M − OH]$^+$, 5), 129 ([M − MeC=O]$^+$, 94), 104 (33), 86 {[M − MeC(=O)C(–O)Me]$^+$ or [MeC(=O)C(–O)Me]$^+$, 55}, 69 (63), 60 (11), 43 ([MeC=O]$^+$, 42); Found: 173.1178, [$C_9H_{16}O_3$ + H]$^+$ requires 173.11778.

Preparation of 1,3,5,7-tetramethyl-2,8-dioxabicyclo[3.2.1]oct-6-ene 47 and rearrangement to 1,3,4,7-tetramethyl-2,6-dioxabicyclo[3.3.0]oct-3-ene 48

TMSDM (1.10 ml, 2.20 mmol) was lithiated with *n*-butyllithium (0.90 ml, 2.20 mmol) and reacted with (4*R*,6*R*)-2-acetyl-2,4,6-trimethyl-1,3-dioxane **44** (0.19 g, 1.10 mmol) in DME (12 ml) under the standard conditions described. The crude residue was obtained as an orange oil (0.23 g). δ_H($CDCl_3$, 299.9 MHz) 5.71 (1H, q, *J* 1.6, MeC=C*H*), 4.29–4.18 (1H, m, MeCH_e), 2.18 (1H, dd, J_{AB} 13.0 and J_{AX} 8.6, CHCH$_a$$H_e$), 1.78 (3H, d, *J* 1.6, CH_3C=CH), 1.43 (3H, s, CH_3CR$_3$), 1.43–1.42 and 1.38–1.37 (1H, m, CHCH_aH$_e$) 1.35 (3H, s, CH_3CR$_3$), 1.28 (3H, d, *J* 7.1, CH_3CH); δ_C($CDCl_3$, 75.4 MHz) 142.4 (Me*C*=C), 133.1 (MeC=*C*H), 107.1 [Me*C*(OR)$_2$R], 82.0 [Me*C*(OR)R$_2$], 67.9 (Me*C*H), 37.0 (CH_2), 24.4 (CH_3CH), 23.7 [CH_3C(OR)$_2$R], 21.6 [CH_3C(OR)R$_2$], 12.0 (CH_3C=C). Attempted purification of this compound by column chromatography eluting with 20% ethyl acetate–hexane resulted in a rearrangement product **48** obtained as a pale orange oil (50 mg, 29%). R_f 0.71 (40% ethyl acetate–hexane); ν_{max}(neat)/cm^{-1} 2970 (m), 2911 (m), 2838 (w); δ_H($CDCl_3$, 500.1 MHz) 4.58 (1H, s, OC*H*CCH$_3$), 3.88 (1H, ddq, *J* 11.1, 4.8 and 6.0, C*H*CH$_2$), 2.15 (1H, dd, J_{AB} 12.9 and J_{AX} 4.2, CHCH$_a$$H_e$), 1.75 [3H, s, C$H_3$C(OR)=C], 1.62 (3H, s, C$H_3$C=C–OR), 1.46 (1H, dd, J_{AB} 12.9 and J_{AX} 11.1, CHCH_aH$_e$), 1.43 (3H, s, CH_3CR$_3$), 1.25 (3H, d, *J* 6.0, CH_3CH); δ_C($CDCl_3$, 75.4 MHz) 151.5 [Me*C*=C(Me)–O], 101.8 [MeC=*C*(Me)–O], 94.2 (Me-C*C*H), 90.7 (R$_4$*C*), 72.3 (Me*C*H), 48.4 (*C*H$_2$), 23.6 (*C*H$_3$CR$_3$), 19.1 (*C*H$_3$CH), 11.5 [MeC=C(*C*H$_3$)OR], 9.7 [*C*H$_3$C=C(Me)-OR]; *m*/*z* (CI) 169 ([M + H]$^+$, 33%), 152 ([M − CH_3]$^+$, 11), 151 ([M − CH_4]$^+$, 100); Found: 169.1229, [$C_{10}H_{16}O_2$ + H]$^+$ requires 169.1229.

Preparation of 2-acetyl-2,4,6-trimethyl-1,3-dioxane 45 and 46

Butane-2,3-dione (1.01 ml, 11.5 mmol), *meso*-pentane-2,4-diol (0.8 g, 7.7 mmol) and PTSA (0.15 g, 0.77 mmol) were refluxed in toluene (20 ml) for 5 h. The reaction was cooled to rt, after which the solvent and excess butane-2,3-dione were removed by rotary evaporation. Purification of the residue by column chromatography eluting with 5–10% ethyl acetate–hexane gave the products as colourless oils (0.20 g, 15% and 0.53 g, 40%). The major product **45** gave the following data: R_f 0.46 (40% ethyl acetate–hexane); ν_{max}(neat)/cm^{-1} 2975 (s), 2937 (m), 1728 (s); δ_H($CDCl_3$, 299.9 MHz) 3.79–3.68 (2H, m, MeCH_aCH$_2$-CH_aMe), 2.22 [3H, s, C(=O)CH_3], 1.47 (1H, dt, J_{AB} 13.3 and J_{AX} 2.5, CHCH$_a$$H_e$CH), 1.42 (3H, s, R$_3CCH_3$), 1.24 (1H, dd, *J* 11.2, CHCH_aH$_e$CH), 1.23 (6H, d, *J* 6.0, CH_3CHCH$_2$CH-CH_3); δ_C($CDCl_3$, 75.4 MHz) 208.8 (*C*=O), 101.7 [Me*C*(OR)$_2$C], 68.5 (*C*H), 39.4 (*C*H$_2$), 25.2 [*C*H$_3$C(OR)$_2$C], 25.1 (*C*H$_3$C=O), 21.7 (*C*H$_3$CH); *m*/*z* (CI) 190 ([M + NH_4]$^+$, 21%), 173 ([M + H]$^+$, 100), 155 ([M − OH]$^+$, 21), 129 ([M − MeCO]$^+$, 87), 101 (15), 86 {[MeCH(O)CH$_2$CHMe]$^+$ or [MeC(=O)C(O)Me]$^+$, 15}, 69 (22), 43 ([MeC=O]$^+$, 27); Found: 173.1178, [$C_9H_{16}O_2$ + H]$^+$ requires 173.1178.

Data for the minor product **46**: R_f 0.53 (40% ethyl acetate–petroleum ether); ν_{max}(neat)/cm^{-1} 2976 (s), 2915 (m), 1737 (s); δ_H($CDCl_3$, 299.9 MHz) 4.05 (2H, ddd, *J* 2.5, 6.1 and 5.5, MeCH_eCH$_2$CH_eMe), 2.26 (3H, s, CH_3C=O), 1.58 (1H, dt, J_{AB} 13.0 and J_{AX} 2.5, CHCH$_a$$H_e$CH), 1.49 (3H, s, C$H_3CR_3$), 1.31–1.19 (1H, m, CHC$H_aH_e$CH), 1.21 (6H, d, *J* 6.2, CH_3CHCH$_2$-CHCH_3); δ_C($CDCl_3$, 75.4 MHz) 204.8 (*C*=O), 99.2 [Me*C*-(OR)$_2$C], 65.8 (Me*C*HO), 40.5 (*C*H$_2$), 23.2 (*C*H$_3$C=O), 22.0 (*C*H$_3$CR$_3$), 15.2 (*C*H$_3$CH); *m*/*z* (CI) 173.2 ([M + H]$^+$, 100%); Found: 173.1178, [$C_9H_{18}O_3$ + H]$^+$ requires 173.1178.

Preparation of 1,3,5,7-tetramethyl-2,8-dioxabicyclo[3.2.1]oct-6-ene 49 and rearrangement to 1,3,4,7-tetramethyl-2,6-dioxabicyclo[3.3.0]oct-3-ene 50

TMSDM (1.74 ml, 3.49 mmol) was lithiated with *n*-butyllithium (1.40 ml, 3.49 mmol) and reacted with 2-acetyl-2,4,6-trimethyl-1,3-dioxane **45** (0.30 g, 1.74 mmol) in DME (16 ml) under the standard conditions described. The crude residue was obtained as an orange oil (0.36 g). δ_H($CDCl_3$, 299.9 MHz) 5.80 (1H, q, *J* 1.5, C=CH), 3.82–3.70 (1H, m, MeCH_aCH$_2$), 1.75 (3H, d, *J* 1.6, CH_3C=CH), 1.54–1.42 (1H, m, CHCH$_a$$H_e$C), 1.47 [3H, s, C$H_3$C(OR)$_2$C], 1.32 [3H, s, C$H_3$C(OR)R$_2$], 1.26–1.15 (1H, m, CHC$H_aH_e$C), 1.19 (3H, d, *J* 6.3, CH_3CH); δ_C($CDCl_3$, 100.6 MHz) 140.6 (Me*C*=C), 133.6 (MeC=*C*H), 110.5 [Me*C*(OR)$_2$R], 84.9 [Me*C*(OR)R$_2$], 69.0 (Me*C*H), 44.2 (*C*H$_2$), 25.5 (*C*H$_3$CH), 24.2 [*C*H$_3$C(OR)$_2$R], 23.7 [*C*H$_3$C(OR)R$_2$], 13.9 (*C*H$_3$C=C). Attempted purification of this compound by column chromatography eluting with 20% ethyl acetate–hexane resulted in a rearrangement product **50** obtained as a pale orange oil (0.14 g, 45%). R_f 0.64 (30% ethyl acetate–petroleum ether); ν_{max}(neat)/cm^{-1} 2973 (m), 2908 (m), 2838 (w); δ_H($CDCl_3$, 299.9 MHz) 4.37 (1H, br s, OC*H*CCH$_3$), 3.97–3.86 (1H, m, MeCH_aCH$_2$), 2.14 (1H, dd, J_{AB} 12.6 and J_{AX} 5.3, CHCH$_a$$H_e$), 1.84 (1H, dd, J_{AB} 12.6 and J_{AX} 9.3, CHCH_aH$_e$), 1.74 (3H, t, *J* 0.9, OCCH_3), 1.68 (3H, d, *J* 0.9, OC=CCH_3), 1.37 (3H, s, R$_3$CCH_3), 1.27 (3H, d, *J* 6.2, CHCH_3); δ_C($CDCl_3$, 75.4 MHz) 152.5 [Me*C*=C(Me)O], 106.1 [MeC=*C*(Me)O], 96.6 (R$_4$*C*), 75.9 (Me*C*H), 50.8 (*C*H$_2$), 26.1 (*C*H$_3$CR$_3$), 22.3 (*C*H$_3$CH), 14.0 [MeC=C(*C*H$_3$)O], 12.0 [MeC=C(*C*H$_3$)O]; *m*/*z* (CI) 169 ([M + H]$^+$, 62%), 152 ([M − CH_3]$^+$, 3), 151 ([M − CH_4]$^+$, 100); Found: 169.1229, [$C_{10}H_{16}O_2$ + H]$^+$ requires 169.1229.

Preparation of 1,8-dimethyl-2,7,9-trioxatricyclo[3.3.1.0^{6,8}]-nonane 51

Freshly prepared dimethyldioxirane solution[8b] (140 ml) was added directly to a stirred solution of 1,7-dimethyl-2,8-dioxabicyclo[3.2.1]oct-6-ene **40** (1.00 g, 7.14 mmol) in acetone (20 ml) cooled at −78 °C. The reaction was allowed to come to rt overnight and then concentrated. The crude residue was purified by column chromatography eluting with 25–30% ethyl acetate–petroleum ether and the product **51** was obtained as a colourless oil (0.32 g, 28%). R_f 0.45 (20% ethyl acetate–petroleum ether); ν_{max}(neat)/cm^{-1} 2966 (s), 2879 (m), 2838 (m); δ_H($CDCl_3$, 299.9 MHz) 4.27 (1H, d, *J* 3.9, CH$_2$C*H*), 4.06 (1H, ddd, J_{AB} 12.0, J_{AX} 7.2 and $J_{AX'}$ 0.7, OCH$_a$$H_e$), 3.85 (1H, dd, J_{AB} 12.0 and J_{AX} 4.8, OCH_aH$_e$), 3.52 (1H, s, epoxide C*H*), 2.40–2.30 (1H, m, OCH$_2$CH$_a$$H_e$), 1.58 (3H, s, C$H_3$ β to epoxide), 1.48–1.42 (1H, m, OCH$_2$CH_aH$_e$), 1.36 (3H, s, CH_3 α to epoxide); δ_C($CDCl_3$, 75.4 MHz) 102.4 (R$_4$*C* α to 2O's), 71.2 (CH$_2$*C*H), 59.8 (O*C*H$_2$), 58.8 (CH$_2$CH*C*HO), 58.4 (R$_4$*C* of epoxide), 25.5 (*C*H$_2$CH$_2$O), 17.9 (R$_3$*C*CH$_3$), 10.6 (CHC*C*H$_3$); *m*/*z* (CI) 174 ([M + NH_4]$^+$, 2%), 157 ([M + H]$^+$, 100), 96 (10), 81 (16); Found: 157.0865, [$C_8H_{12}O_3$ + H]$^+$ requires 157.08647.

Preparation of 6-hydroxy-1-methyl-7-methylene-2,8-dioxabicyclo[3.2.1]octane 52

(1*S*,2*R*)-Norephedrine (0.66 g, 4.36 mmol) was stirred in THF (13 ml) and benzene (20 ml) at 0 °C and to this solution *n*-butyllithium (3.49 ml, 8.72 mmol) was added slowly over 5 min. The cooling bath was removed after a further 5 min and the reaction stirred at rt for 30 min. The cooling bath was replaced and 1,8-dimethyl-2,7,9-trioxatricyclo[3.3.1.0^{6,8}]nonane

51 (0.20 g, 1.28 mmol) was added in THF (7 ml). The reaction was then stirred overnight at rt, quenched by the addition of methanol (13 ml) and filtered through Celite. The solvent was removed by rotary evaporation and purification of the residue by column chromatography eluting with 2% methanol–DCM gave the product as a pale yellow oil (0.12 g, 62%). R_f 0.22 (10% methanol–dichloromethane); ν_{max}(hexachlorobuta-1,3-diene)/cm^{-1} 3426 (br), 2966 (m); δ_H($CDCl_3$, 250.1 MHz) 5.63 (1H, d, *J* 1.3, C=C*H*H′), 5.40 (1H, d, *J* 1.3, C=CH*H*′), 4.47 (1H, t, *J* 1.2, C*H*OH), 4.31–4.29 (1H, m, CH_2CH), 3.86–3.69 (2H, m, OCH_aH_e), 2.31–2.16 (1H, m, $OCH_2CH_aH_e$), 1.57 (3H, s, CH_3), 1.43–1.41 and 1.38–1.35 (1H, m, $OCH_2CH_aH_e$); δ_C($CDCl_3$, 62.9 MHz) 153.6 (R_2C=CH_2), 112.4 (C=CH_2), 104.3 (MeCR_3), 80.9 [*C*H(OH)], 74.9 (CH_2CH), 60.1 (CH_2CH_2O), 27.5 (CH_2-CH_2O), 22.3 (CH_3); *m*/*z* (EI) 157 ([M]$^+$, 100%), 137 ([M − OH]$^+$, 41), 126 (27), 112 (29), 97 (42); Found: 157.0865, $[C_8H_{12}O_3]^+$ requires 157.08647.

Preparation of 6-(3-bromobenzoyloxy)-1-methyl-7-methylene-2,8-dioxabicyclo[3.2.1]octane 53

6-Hydroxy-1-methyl-7-methylene-2,8-dioxabicyclo[3.2.1]octane **52** (0.10 g, 0.64 mmol) was stirred in DCM (20 ml) at 0 °C with 3-bromobenzoic acid (0.39 g, 1.92 mmol) and DMAP (0.07 g, 0.58 mmol). To this solution DCC (0.15 g, 0.71 mmol) was added. The cooling bath was removed after 10 min and the reaction stirred for 24 h at rt. The dicyclohexylurea was removed by suction filtration and the filtrate washed with 0.5 M hydrochloric acid (50 ml) and saturated sodium hydrogen carbonate solution (50 ml). The organic layer was dried over magnesium sulfate and filtered, and the solvent removed by rotary evaporation. Purification by column chromatography eluting with 50% ethyl acetate–petroleum ether gave the product as a colourless oil (0.11 g, 48%). R_f 0.30 (20% ethyl acetate–petroleum ether); ν_{max}(neat)/cm^{-1} 3054 (w), 2969 (m), 2870 (w), 1719 (s); δ_H($CDCl_3$, 250.1 MHz) 8.17 (1H, t, *J* 1.5, aryl CH α to Br and CO_2R), 7.98 (1H, dt, *J* 1.5 and 7.9, aryl CH α to CO_2R), 7.70 (1H, dq, *J* 0.9 and 7.9, β to Br), 7.33 (1H, t, *J* 7.9, β to Br and CO_2R), 5.78 (1H, t, *J* 1.22, C=C*H*H′), 5.73 (1H, d, *J* 1.2, C=CH*H*′), 5.50 (1H, d, *J* 1.5, RCO_2CH), 4.50–4.48 (1H, m, RCO_2CHCH), 3.92–3.87 (2H, m, CH_aH_eO), 2.38–2.23 (1H, m, $CH_aH_eCH_2O$), 1.62 (3H, s, CH_3), 1.60–1.52 (1H, m, $CH_aH_eCH_2O$); δ_C($CDCl_3$, 62.9 MHz) 165.2 (ArCO_2R), 148.9 (CH_2=CR_2), 136.1 (BrC*C*HCH), 132.5 (BrC*C*HCCO_2), 131.5 (*C*CO_2R), 129.8 (ArCH*C*HCH), 128.2 (*C*HCO_2H), 122.3 (*C*Br), 114.6 (C=CH_2), 104.4 (MeCR_3), 78.2 (*C*HC=CH_2), 76.8 (O*C*H), 60.0 (CH_2CH_2O), 27.4 (CH_2CH_2O), 22.0 (CH_3); *m*/*z* (CI) 358 ([M + NH_4, ^{81}Br]$^+$, 2%), 356 ([M + NH_4, ^{79}Br]$^+$, 2), 341 ([M + H, ^{81}Br]$^+$, 4), 339 ([M + H, ^{79}Br]$^+$, 4), 158 (6), 156 (46), 141 (68), 139 (100); Found: 338.0154, $[C_{15}H_{15}{}^{79}BrO_4]^+$ requires 338.0154.

Preparation of 6-(3-bromobenzoyloxy)-1-methyl-2,8-dioxabicyclo[3.2.1]octan-7-one 54

1-Methyl-6-(3-bromobenzoyloxy)-7-methylene-2,8-dioxabicyclo[3.2.1]octane **53** (73 mg, 0.22 mmol) was stirred in DCM (10 ml) at −60 °C and ozone was bubbled through the solution. The reaction was warmed to ~0 °C to effect solution of the alkene and the reaction continued for 30 min. Dimethyl sulfide (30 µl, 0.32 mmol) was added, the cooling bath removed and the reaction stirred overnight. The solvent was removed under reduced pressure. Purification by column chromatography eluting with 20–60% ethyl acetate–petroleum ether gave the product as a colourless oil (30 mg, 40%). R_f 0.30 (20% ethyl acetate–petroleum ether); ν_{max}(neat)/cm^{-1} 3066 (w), 2961 (w), 2866 (w), 1780 (m), 1730 (s); δ_H($CDCl_3$, 250.1 MHz) 8.17 (1H, t, *J* 1.8, aryl C*H* α to Br and CO_2R), 7.98 (1H, dq, *J* 1.0 and 7.0, aryl C*H* α to CO_2R), 7.74 (1H, dq, *J* 1.0 and 7.9, aryl C*H* β to Br), 7.34 (1H, t, *J* 7.9, aryl C*H* β to Br and CO_2R), 5.23 (1H, s, RCO_2CH), 4.65 (1H, d, *J* 4.0, RCO_2CHCH), 4.10 (1H, dd, J_{AB} 12.8, J_{AX} 7.9 and $J_{AX'}$ 1.0, OCH_aH_e), 3.98 (1H, dd, J_{AB} 12.8 and J_{AX} 3.7, OCH_aH_e), 2.67–2.51 (1H, m, $OCH_2CH_aH_e$), 2.05 (3H, s, CH_3CR_3), 1.87–1.84 and 1.82–1.79 (1H, m, OCH_2-CH_aH_e); δ_C($CDCl_3$, 100.6 MHz) 206.8 (*C*=O), 164.5 (Ar*C*O_2R), 136.6 (aryl *C*H α to CBr), 132.8 (aryl *C*H α to CBr and CCO_2R), 130.4 (aryl*C*CCO_2R), 130.0 (aryl *C*H β to CBr and CCO_2R), 128.5 (aryl *C*H α to CCO_2R), 122.5 (aryl *C*Br), 99.2 (Me*C*R_3), 76.7 (O*C*H), 72.4 (*C*HC=O), 61.3 (O*C*H_2), 27.7 (OCH_2CH_2), 18.7 (CH_3); *m*/*z* (CI) 343 ([MH, ^{81}Br]$^+$, 47%), 341 ([MH, ^{79}Br]$^+$, 46), 263 (37), 252 (15), 185 ([M − BrC_6H_4]$^+$, 16), 176 (100), 160 (41), 159 (79), 143 (50), 122 (22), 114 (18), 105 (22), 52 (25), 44 (21); Found: 341.0024, $[C_{14}H_{13}{}^{79}BrO_5 + H]^+$ requires 341.0025.

Preparation of 1,6-diphenylhex-3-ene 55 [38]

3-Phenylpropyl(triphenyl)phosphonium bromide (10.0 g, 21.7 mmol) was stirred in THF (50 ml) at 0 °C and *n*-butyllithium (8.67 ml, 21.7 mmol) was added dropwise. Once addition was complete the reaction was stirred for 30 min at rt and dihydrocinnamaldehyde (3.43 ml, 26.0 mmol) in THF (50 ml) was added. The reaction was stirred for 3 h, quenched by the addition of water (80 ml) and extracted with diethyl ether (3 × 100 ml). The combined organic layers were dried over magnesium sulfate, filtered and concentrated. Purification of the residue by column chromatography eluting with 10% ethyl acetate–petroleum ether gave the product as an inseparable mixture of isomers in a ratio of 4 : 1 in the form of a colourless oil (3.68 g, 72%). R_f 0.66 (20% ethyl acetate–petroleum ether); ν_{max}(neat)/cm^{-1} 3081 (w), 3059 (m), 3023 (s), 2921 (s), 2852 (m); δ_H($CDCl_3$, 250.1 MHz) 7.30–7.13 ($10H_{maj}$ + $10H_{min}$, m, aryl C*H*), 5.49–5.45 ($2H_{min}$, m, RC*H*=C*H*R), 5.44–5.39 ($2H_{maj}$, m, RC*H*=C*H*R), 2.68–2.62 ($4H_{min}$, m, PhCH_2), 2.60–2.53 ($4H_{maj}$, m, PhCH_2), 2.33–2.25 ($4H_{maj}$ + $4H_{min}$, m, CH_2C=CCH_2); δ_C($CDCl_3$, 62.9 MHz) 141.9 (aryl C_i)$2C_{maj}$, 141.5 (aryl C_i)$2C_{min}$, 130.0 (*C*H=*C*H)$2C_{min}$, 129.3 (*C*H=*C*H)$2C_{maj}$, 128.3 (aryl *C*)-$4C_{maj}$ + $4C_{min}$, 128.1 (aryl *C*)$4C_{maj}$ + $4C_{min}$, 125.6 (aryl C_p)-$2C_{maj}$, 125.2 (aryl C_p)$2C_{min}$, 35.9 (Ph*C*H_2)$2C_{min}$, 35.7 (Ph*C*H_2)-$2C_{maj}$, 34.3 (*C*H_2C=C*C*H_2)$2C_{min}$, 29.0 (*C*H_2C=C*C*H_2)$2C_{maj}$; *m*/*z* (EI) 236 ([M]$^+$, 50%), 145 ([M − Bn]$^+$, 56), 131 ([M − $PhCH_2CH_2$]$^+$, 42), 117 (61), 104 (49), 91 ([$PhCH_2$]$^+$, 100), 77 ([Ph]$^+$, 25), 65 (55), 51 (24), 41 (28); Found: 236.1565, $[C_{18}H_{18}]^+$ requires 236.1565.

Preparation of 1,6-diphenylhexane-3,4-diol 56

N-Methylmorpholine *N*-oxide (1.54 g, 13.1 mmol) was stirred in water (16 ml) and acetone (8.0 ml) and to this mixture 1,6-diphenylhex-3-ene **55** (2.82 g, 12.0 mmol) and osmium tetraoxide (0.03 ml, 0.12 mmol) were added. Methanesulfonamide (1.14 g, 12.0 mmol) was added to the reaction, which was then heated at 60 °C for 2 days. After cooling to rt sodium hydrosulfite (0.20 g) was added followed by a slurry of Florisil (2 g) in water (10 ml). The reaction was stirred for 10 min and filtered through Florisil. The Florisil was washed with acetone which was then neutralised (pH 7) with 6 M sulfuric acid. The acetone was removed and the pH of the resulting aqueous solution adjusted to pH 2. The acidic aqueous layer was extracted with DCM (4 × 50 ml), the combined organic layers were dried over magnesium sulfate and filtered, and the solvent removed by rotary evaporation. Purification of the residue by column chromatography eluting with 20–50% ethyl acetate–petroleum ether gave the major product as white crystals (2.24 g, 69%) after recrystallisation from hexane. Mp 132–135 °C; R_f 0.32 (60% ethyl acetate–petroleum ether); ν_{max}(Nujol mull)/cm^{-1} 3236 (m), 3026 (m), 2922 (s), 2854 (s); δ_H(DMSO, 250.1 MHz) 7.30–7.11 (10H, m, aryl C*H*), 4.20 [2H, br s, CH(O*H*)CH-(O*H*)], 3.29–3.21 (2H, br m, C*H*OHC*H*OH), 2.85–2.73 (2H, m, PhC*H*H′), 2.61–2.52 (2H, m, PhCH*H*′), 1.92–1.81 (2H, m, CHC*H*H′), 1.63–1.48 (2H, m, CHCH*H*′); δ_C(DMSO, 62.9 MHz) 142.9 (aryl C_i), 128.4 (aryl *C*), 128.3 (aryl *C*), 125.6 (aryl

C_p), 73.3 (*C*HOH), 35.1 (Ph*C*H$_2$), 31.8 (PhCH$_2$*C*H$_2$CH); *m*/*z* (CI) 288 ([M + NH$_4$]$^+$, 15%), 253 ([M − OH]$^+$, 50), 235 (56), 208 (32), 145 (18), 130 (70), 117 (92), 104 (61), 91 ([PhCH$_2$]$^+$, 100), 78 (24), 65 (39); Found: 288.1964, [C$_{18}$H$_{22}$O$_2$ + NH$_4$]$^+$ requires 288.19635.

Preparation of 1,6-diphenylhexane-3,4-dione 57 [39]

Oxalyl chloride (4.0 ml, 8.0 mmol) was stirred at −78 °C in DCM (20 ml) and to this DMSO (1.13 ml, 16.0 mmol) in DCM (20 ml) was added dropwise over 5 min and the reaction stirred for a further 20 min. 1,6-Diphenylhexane-3,4-diol **56** (0.90 g, 3.33 mmol) in DCM (30 ml) was then added slowly over 10 min. Once the addition was complete the reaction was stirred for 20 min and then triethylamine (4.63 ml, 33.3 mmol) was added and the cooling bath removed. The reaction was left to come to rt over 30 min, then quenched by the addition of water (100 ml) and extracted with DCM (3 × 100 ml). The organic layers were combined, dried over magnesium sulfate and filtered, and the solvent removed by rotary evaporation. The crude residue was purified by column chromatography eluting with 10% ethyl acetate–petroleum ether and the product isolated as bright yellow crystals (0.60 g, 67%). Found: C 80.91% H 6.81%, C$_{18}$H$_{18}$O$_2$ requires C 81.20% H 6.77%; mp 91–92.5 °C; R_f 0.60 (40% ethyl acetate–petroleum ether); ν_{max}(Nujol mull)/cm^{-1} 2923 (s), 2853 (s), 1706 (m); δ_H(CDCl$_3$, 250.1 MHz) 7.30–7.14 (10H, m, aryl C*H*), 3.08–3.02 (4H, m, C*H*$_2$C=O), 2.94–2.84 (4H, m, PhC*H*$_2$); δ_C(CDCl$_3$, 62.9 MHz) 198.5 (*C*=O), 140.2 (aryl C_i), 128.4 (aryl *C*), 128.2 (aryl *C*), 126.2 (aryl C_p), 37.5 (Ph*C*H$_2$), 28.0 (*C*H$_2$C=O); *m*/*z* (EI) 266 ([M]$^+$, 70%), 224 (19), 175 ([M − PhCH$_2$]$^+$, 19), 133 ([PhCH$_2$CH$_2$C=O]$^+$, 81), 105 ([PhCH$_2$CH$_2$]$^+$, 100), 91 ([PhCH$_2$]$^+$, 95), 83 (33), 77 ([Ph]$^+$, 69), 65 (52), 55 (16), 51 (48), 43 (37).

Data for minor product where mono-oxidation resulted in the formation of 1,6-diphenyl-4-hydroxyhexan-3-one, which was obtained as a pale yellow oil (0.23 g, 26%). R_f 0.45 (40% ethyl acetate–petroleum ether); ν_{max}(neat)/cm^{-1} 3471 (br m), 3085 (w), 3062 (w), 3027 (m), 2927 (m), 2862 (w), 1711 (s); δ_H(CDCl$_3$, 250.1 MHz) 7.30–7.12 (10H, m, aryl C*H*), 4.09 (1H, t, *J* 4.2, C*H*OH), 3.33 (1H, br s, O*H*), 2.93–2.84 (2H, m, C*H*$_2$-C=O), 2.78–2.61 (4H, m, PhC*H*$_2$), 2.14–2.00 (1H, m, PhC*H*-H′CHOH), 1.83–1.68 (1H, m, PhCH*H*′CHOH); δ_C(CDCl$_3$, 62.9 MHz) 210.2 (*C*=O), 139.9 (aryl C_i), 139.4 (aryl C_i), 127.5 (aryl *C*), 127.3 (aryl *C*), 125.3 (aryl C_p), 125.1 (aryl C_p), 74.7 (*C*HOH), 38.5 (Ph*C*H$_2$CH$_2$C=O), 34.4 (Ph*C*H$_2$CH$_2$CH), 30.0 (PhCH$_2$*C*H$_2$CH), 28.4 (PhCH$_2$*C*H$_2$C=O); *m*/*z* (CI) 286 ([M + NH$_4$]$^+$, 69%), 269 ([M + H]$^+$, 64), 251 ([M − OH]$^+$, 47), 233 (58), 181 (48), 164 (82), 134 (69), 117 (61), 105 ([PhCH$_2$CH$_2$]$^+$, 79), 91 ([PhCH$_2$]$^+$, 100), 78 (50), 65 (72); Found: 286.1807, [C$_{18}$H$_{20}$O$_2$ + NH$_4$]$^+$ requires 286.1807.

Preparation of 2-(2-phenylethyl)-2-(3-phenylpropanoyl)-1,3-dioxane 58

1,6-Diphenylhexane-3,4-dione **57** (1.00 g, 3.76 mmol) was stirred in toluene (50 ml) with propane-1,3-diol (0.27 ml, 3.76 mmol) and PTSA (0.18 g, 0.94 mmol) and the reaction refluxed overnight. The reaction was cooled, after which water (50 ml) was added and the layers separated. The aqueous layer was extracted with ethyl acetate (2 × 50 ml) and the organic layers were combined, dried over magnesium sulfate, filtered and concentrated. Purification of the residue by column chromatography eluting with 5% ethyl acetate–petroleum ether gave the product as a yellow oil (0.52 g, 42%). R_f 0.43 (20% ethyl acetate–petroleum ether); ν_{max}(neat)/cm^{-1} 3060 (w), 3024 (w), 2962 (m), 2926 (m), 1723 (s); δ_H (250.1 MHz, CDCl$_3$) 7.30–7.07 (10H, m, aryl C*H*), 3.99–3.91 (2H, m, OCH$_a$*H*$_e$CH$_2$CH$_a$*H*$_e$), 3.73–3.63 (2H, m, OC*H*$_a$H$_e$CH$_2$C*H*$_a$H$_e$O), 2.89–2.93 (4H, m, PhC*H*$_2$), 2.63–2.57 (2H, m, C*H*$_2$C=O), 2.11–1.92 (1H, m, OCH$_2$CH$_a$*H*$_e$), 1.90–1.83 (2H, m, C*H*$_2$CR$_3$), 1.38–1.36 and 1.32–1.30 (1H, dm, OCH$_2$C*H*$_a$H$_e$); δ_C (62.9 MHz, CDCl$_3$) 209.2 (*C*=O), 141.4 (aryl C_i), 140.9 (aryl C_i), 128.4 (aryl *C*), 128.3 (aryl *C*), 128.2 (aryl *C*), 126.1 (aryl C_p), 125.8 (aryl C_p), 101.9 (R$_4$*C*), 62.5 (O*C*H$_2$), 39.2 (Ph*C*H$_2$), 38.8 (Ph*C*H$_2$), 29.4 (*C*H$_2$CR$_3$), 28.2 (*C*H$_2$C=O), 24.9 (OCH$_2$*C*H$_2$CH$_2$O); *m*/*z* (CI) 342 ([M + NH$_4$]$^+$, 100%), 325 ([M + H]$^+$, 27), 266 (10), 249 (14), 191 ([M − PhCH$_2$CH$_2$C=O]$^+$, 73), 91 ([PhCH$_2$]$^+$, 7); Found: 342.2084, [C$_{21}$H$_{24}$O$_3$ + NH$_4$]$^+$ requires 342.2069.

Preparation of 1,7-bis(2-phenylethyl)-2,8-dioxabicyclo[3.2.1]oct-6-ene 59

TMSDM (1.54 ml, 3.09 mmol) was lithiated with *n*-butyllithium (1.23 ml, 3.09 mmol) and reacted with 2-(2-phenylethyl)-2-(3-phenylpropanoyl)-1,3-dioxane **58** (0.50 g, 1.54 mmol) in DME (15 ml) under the standard conditions described. The crude residue was carried through without further purification as an orange oil (0.84 g). δ_H(CDCl$_3$, 250.1 MHz) 7.32–7.13 (10H, m, aryl C*H*), 6.17 (1H, q, *J* 1.8, C=C*H*), 4.73–4.77 (1H, m, C*H*CH$_2$CH$_2$O), 3.94–3.78 (2H, m, OC*H*$_a$-*H*$_e$CH$_2$), 2.96–2.88 (2H, m, PhC*H*$_2$CH$_2$C=C), 2.84 (1H, dd, *J* 5.2 and 12.2, PhC*H*H′), 2.60 (1H, ddd, *J* 5.2, 12.2 and 14.0, PhCH*H*′), 2.46–2.37 (2H, m, PhCH$_2$C*HH*C=C), 2.34–2.22 (1H, m, OCH$_2$CH$_a$*H*$_e$), 2.14 (1H, ddd, *J* 5.5, 12.2 and 14.0, Ph-CH$_2$C*H*H′CR$_3$), 1.96 (1H, ddd, *J* 5.2, 12.2 and 14.0, PhCH$_2$-CH*H*′CR$_3$), 1.27–1.26 and 1.22–1.20 (1H, m, OCH$_2$C*H*$_a$H$_e$). This compound was used in the next step without further purification due its instability to silica gel and alumina.

Preparation of 1,8-bis(2-phenylethyl)-2,7,9-trioxatricyclo-[3.3.1.0^{6,8}]nonane 60 and 5-(2-hydroxyethyl)-2,3-bis(2-phenylethyl)furan 61

At −78 °C, a solution of freshly prepared dimethyldioxirane solution (140 ml) was added to a stirred solution of 1,7-bis(2-phenylethyl)-2,8-dioxabicyclo[3.2.1]oct-6-ene **59** (0.78 g, ~1.54 mmol) in acetone (15 ml). The reaction was stirred and allowed to warm to rt overnight. The solvent was removed by rotary evaporation and purification of the residue by column chromatography gave two products of which one was the desired product as a colourless oil (0.14 g, 27%). The other was a result of rearranged starting material, 2,3-bis(2-phenylethyl)-5-(2-hydroxyethyl)furan, as a pale yellow oil (74 mg, 15%).

Epoxide **60**: R_f 0.55 (60% ethyl acetate–petroleum ether); ν_{max}(neat)/cm^{-1} 3061 (w), 3026 (w), 2957 (m), 2873 (w); δ_H(CDCl$_3$, 250.1 MHz) 7.33–7.09 (10H, m, aryl C*H*), 4.34 (1H, d, *J* 3.4, OCH$_2$CH$_2$C*H*), 4.00 (1H, td, J_{AB} 11.9 and J_{AX} 4.6, OCH$_a$*H*$_e$CH$_2$), 3.85 (1H, dd, J_{AB} 11.9 and J_{BX} 7.4, OC*H*$_a$H$_e$-CH$_2$), 3.62 (1H, s, epoxide C*H*), 2.86–2.73 (3H, m, PhC*H*$_2$ and PhC*H*H′), 2.67–2.55 (1H, m, PhCH*H*′), 2.48–2.26 (3H, m, PhCH$_2$C*H*$_2$ and OCH$_2$CH$_a$*H*$_e$), 2.01–1.94 (2H, m, PhCH$_2$-C*HH*), 1.44–1.37 (1H, m, OCH$_2$C*H*$_a$H$_e$); δ_C(CDCl$_3$, 62.9 MHz) 141.9 (aryl C_i), 140.9 (aryl C_i), 128.4 (aryl *C*), 128.2 (aryl *C*), 128.1 (aryl *C*), 126.1 (aryl C_p), 125.7 (aryl C_p), 103.2 (R$_4$*C*), 71.2 (*C*HCH$_2$CH$_2$O), 61.2 (epoxide R$_4$*C*), 59.7 (*C*H$_2$O), 56.2 (epoxide *C*H), 34.6 (Ph*C*H$_2$), 30.2 (Ph*C*H$_2$), 28.6 (PhCH$_2$-*C*H$_2$CR$_3$), 25.5 (OCH$_2$*C*H$_2$), 25.2 (PhCH$_2$*C*H$_2$–epoxide); *m*/*z* (CI) 354 ([M + NH$_4$]$^+$, 31%), 337 ([M + H]$^+$, 100), 186 (15); Found: 337.1817, [C$_{22}$H$_{24}$O$_3$ + H]$^+$ requires 337.1804.

Furan **61**: R_f 0.27 (60% ethyl acetate–petroleum ether); δ_{max}(neat)/cm^{-1} 3410 (br), 3084 (w), 3060 (w), 3026 (m), 2934 (m); δ_H(CDCl$_3$, 250.1 MHz) 7.32–7.12 (10H, m, aryl C*H*), 5.99 (1H, t, *J* 1.2, C*H*), 3.85 (2H, t, *J* 6.4, C*H*$_2$OH), 3.05 (2H, dd, *J* 9.1 and 7.0, PhC*H*$_2$CH$_2$CO), 2.85–2.68 (6H, m, C*H*$_2$CH$_2$-OH, PhC*H*$_2$CH$_2$C=CO and BnC*H*$_2$CO), 2.52–2.46 (2H, m, BnC*H*$_2$C=CO); δ_C(CDCl$_3$, 62.9 MHz) 149.9 (O*C*CH$_2$CH$_2$OH), 149.0 (O*C*CH$_2$Bn), 141.7 (aryl C_i), 141.3 (aryl C_i), 126.1 (aryl *C*), 125.8 (aryl *C*), 125.7 (aryl *C*), 125.6 (aryl *C*), 117.2 (C=*C*CH$_2$Bn), 108.2 (*C*H), 61.0 (*C*H$_2$OH), 36.5 (Ph*C*H$_2$CH$_2$-CO), 34.8 (Ph*C*H$_2$CH$_2$C=CO), 31.5 (C*C*H$_2$CH$_2$OH), 27.9 (Bn*C*H$_2$CO), 26.7 (Bn*C*H$_2$C=CO).

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