Diastereoselective SmI_2 mediated cascade radical cyclisations of methylenecyclopropane derivatives—syntheses of paeonilactone B and 6-*epi*-paeonilactone A

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The SmI_2 mediated cascade cyclisations of several methylenecyclopropyl ketones have been examined and found to proceed with high diastereoselectivity, which is critically dependent on the presence of HMPA in the reaction. In one case the radical species at the end of the cascade sequence underwent an unexpected and highly stereoselective dimerisation. The cascade methodology has been applied to a short synthesis of (±)-paeonilactone B and of (±)-6-*epi*-paeonilactone A.

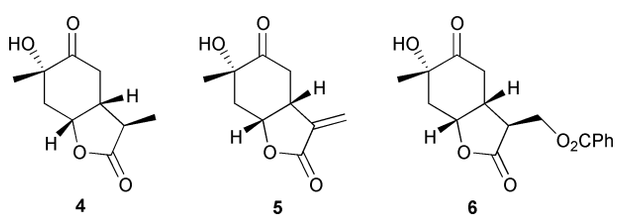
Cascade radical cyclisation reactions have proved to be very popular as a synthetic strategy as they allow the construction of several C–C bonds in one step and can provide elegant synthetic routes to complex polycyclic compounds and natural products.[1] Cascade reactions, initiated in particular by the versatile lanthanide reagent SmI_2,[2] have also been a focus of recent attention. The versatility of SmI_2 is emphasised by the fact that it can be used to generate both carbon centred radicals and carbanions (by a further one-electron reduction of the radical species) and several cascade sequences utilising combinations of both of these aspects have been described.[3] Cascade processes, initiated by SmI_2, and using exclusively radical intermediates[4] are, however, complicated—and potentially limited—by the fact that each radical intermediate can undergo competitive reduction to the corresponding organosamarium species, which may then effectively terminate the intended cascade sequence. The rate constant for reduction of a primary alkyl radical to give an organosamarium species in THF has been estimated as 5×10^5–7×10^6 M^{-1} s^{-1} (depending on HMPA concentration).[5] Thus with SmI_2 solutions of 0.1 M, a radical cyclisation will need to have a rate constant $\geq 5 \times 10^4$ s^{-1} to compete effectively with the alternative reduction pathway.

In previous work we have developed radical cascade sequences involving methylenecyclopropane derivatives, which have provided novel routes to a range of bicyclic[6] and spirocyclic compounds.[7] The key step in these cascade sequences has been the 5-*exo* cyclisation of a methylenecyclopropylpropyl radical **1**, followed by rapid '*endo*' opening of the resulting cyclopropylmethyl radical **2** to give methylenecyclohexyl radicals **3** which can then be used in further bond-forming steps (Scheme 1).

Scheme 1

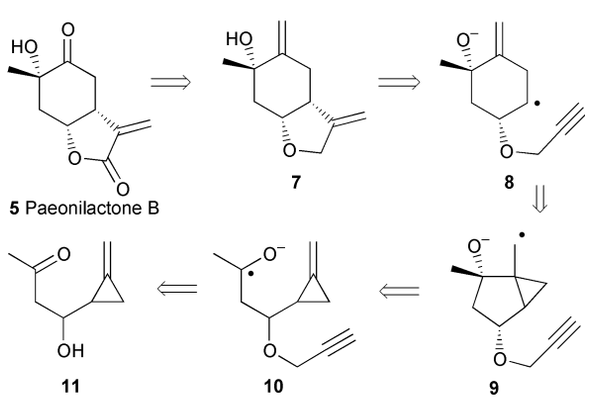
In order to extend the scope of this chemistry we chose to investigate the 5-*exo* cyclisation of methylenecyclopropyl ketyl radicals, and in particular sought to use this chemistry for the synthesis of the paeonilactone family of natural products. In so doing we wished to explore the potential for using SmI_2 in such cyclisations and particularly to investigate whether it could be used to mediate radical cascade sequences efficiently. In this paper we wish to report full details of this study which has led to short syntheses of paeonilactone B and 6-*epi*-paeonilactone A, as well as uncovering an unusual stereoselective dimerisation at the end of a radical cascade sequence.[8]

The paeonilactones A (**4**), B (**5**) and C (**6**) are all constituents



of the paeony root (the root of *Paeonia albiflora* Pallas) which has been used extensively in Chinese and Japanese medicines for the treatment of pain.[9] Apart from their analgesic properties, the high density of stereocentres and oxygen functionality around the cyclohexane nucleus has made the paeonilactone family challenging synthetic targets.[10]

A retrosynthetic analysis of paeonilactone B (Scheme 2)

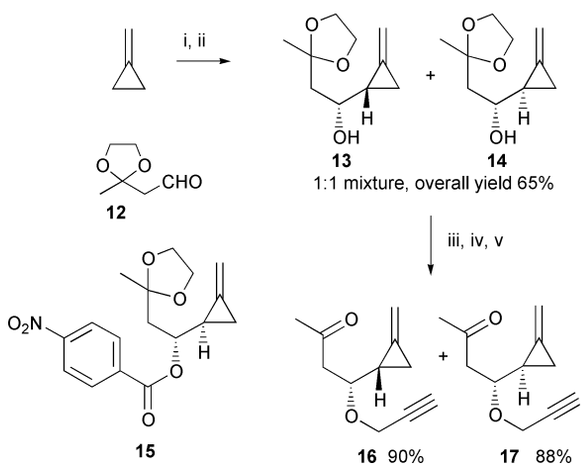


Scheme 2

suggested that the *cis*-fused bicyclic methylenecyclohexane **7** could be prepared by a 5-*exo* cyclisation of methylenecyclohexyl radical **8** onto a pendant alkyne, and **8** could, in

turn, arise from cyclisation of ketyl radical **10** onto a methylenecyclopropane unit with subsequent '*endo*' ring opening of **9**. Whether such a sequence would prove to be diastereoselective and provide the correct relative stereochemistry of the tertiary alcohol required for the natural product was one of the key aspects of the proposed investigation.

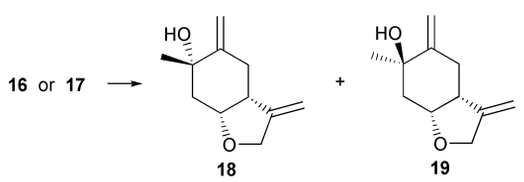
The synthesis of paeonilactone B began with addition of lithiated methylenecyclopropane[11] to aldehyde **12**, to produce the desired alcohols as a readily separable mixture of diastereoisomers **13** and **14** (Scheme 3). The relative stereochemistry for



Scheme 3 *Reagents and conditions*: (i) BuLi, THF, −78 °C; (ii) **12**; (iii) NaH, DMPU, THF; (iv) $HC{\equiv}CCH_2Br$; (v) TsOH, acetone, H_2O.

the two diastereoisomers was established by X-ray crystallographic structure analysis of the *p*-nitrobenzoate ester **15** derived from alcohol **14**.[12] Alkylation of the alcohols gave the corresponding propargyl ethers,‡ and subsequent ketal deprotection provided the two diastereomeric cyclisation precursors, **16** and **17** respectively, in essentially quantitative yield.

Treatment of ketone **16** with SmI_2, under standard conditions[13] (slow addition of **16** to 2.2 equiv. SmI_2, Bu^tOH, HMPA, THF, 0 °C) gave the desired bicyclic products as a readily separable mixture of diastereoisomers, **18** and **19**, in 57% and 6% isolated yields respectively (ratio **18**:**19**, 10:1 by analysis of the ^1H NMR of the crude reaction mixture) (Scheme 4). In contrast, treatment of diastereoisomeric ketone



Conditions:	Yield	Ratio 18:19
16, SmI_2, Bu^tOH, HMPA, THF, 0ºC	63%	10 : 1
16, SmI_2, Bu^tOH, DMPU, THF, 0ºC	40%	1.5 : 1
16, SmI_2, Bu^tOH, THF, 0ºC	~20%	1 : 1.3
17, SmI_2, Bu^tOH, HMPA, THF, 0ºC	79%	<1 : 30
17, SmI_2, Bu^tOH, DMPU, THF, 0ºC	62%	<1 : 30
17, SmI_2, Bu^tOH, THF, 0ºC	0%	

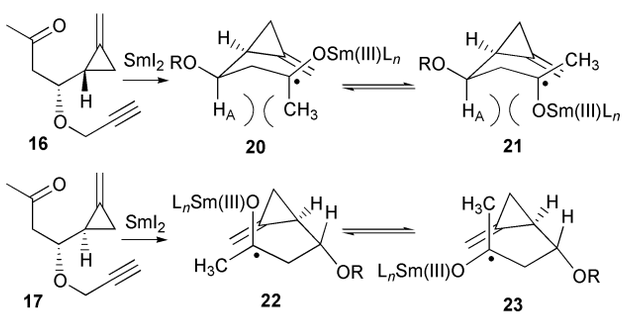
Scheme 4

17 with SmI_2, under identical conditions, gave the bicyclic product **19** in 79% isolated yield, and only a trace of the diastereoisomer **18** (ratio **19**:**18**, >30:1).

The stereochemistry of **18** was ultimately confirmed by the successful conversion to the natural product paeonilactone B (*vide infra*), but the stereochemistry of both **18** and **19** was at this stage assigned on the basis of NOE studies and on the known preference for the cyclisation of cycloalkyl radicals onto tethered alkenes and alkynes to give *cis*-fused bicyclic systems.[14]

In order to rationalise the observed diastereoselectivity we repeated the cyclisations under identical conditions, but replacing HMPA with the less effective chelator DMPU.[15] These cyclisation reactions gave the bicyclic products with reduced overall yields and required a larger excess of SmI_2 (~6 equiv.) for consumption of starting material (Scheme 4). Notably, for the cyclisation of **16**, the diastereoselectivity was reduced (ratio **18**:**19**, 1.5:1), whereas for the cyclisation of **17** the diastereoselectivity was seemingly unaffected (ratio **19**:**18**, >30:1). In the absence of either DMPU or HMPA the cyclisation was, as expected, a poor reaction. Thus **16** gave an overall yield of ~20% of **18** and **19**, but with a reversal of stereoselectivity (ratio **18**:**19**, 1:1.3), while cyclisation of **17**, under these conditions, yielded none of the desired bicyclic compounds.

The selectivity observed for the cyclisation of **16** in favour of **18**, in the presence of HMPA, in which the tertiary alcohol and ether oxygen are *cis* in the bicyclic product, might be the consequence of chelation control from the weakly basic propargylic ether oxygen to the samarium(III) bound to the ketyl radical. However, the decrease in selectivity for the cyclisation of **16** as HMPA is replaced by the weaker chelator DMPU, and reversal of selectivity when neither is present (leaving the even less effective chelator, THF, as the available samarium ligand), effectively rules out this possibility. It seems probable that the first step of the cyclisation of **16**, which effectively sets the relative stereochemistry of the product, proceeds through a chair-like transition state, allowing the propargyl ether substituent to adopt a pseudo-equatorial position (Scheme 5).



Scheme 5

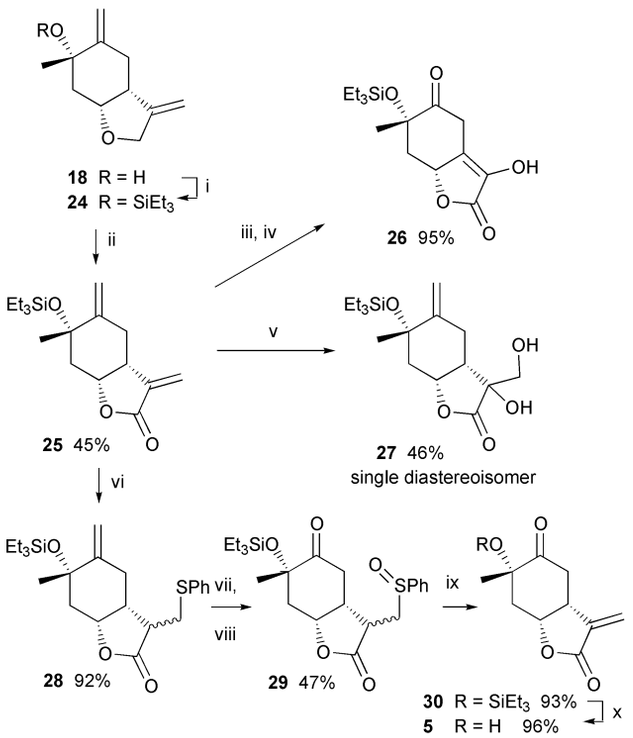
As a consequence of the bond angles of the methylenecyclopropyl group, the alkene appears to be essentially staggered between the ketyl radical oxygen and the ketyl methyl group. Thus the preference for conformer **20** over **21** may largely result from the preference for the bulky OSm(III)$(HMPA)_n$ moiety to also adopt a pseudo-equatorial position and avoid a 1,3 diaxial interaction with H_A. Replacement of HMPA with DMPU may effectively reduce the steric bulk of the OSm(III)L_n moiety,[15] leading to a lower selectivity for conformer **20**. In the absence of either HMPA or DMPU the ketyl methyl becomes sterically dominant, leading to a reversal in selectivity.

In contrast, the first step of the cyclisation of **17** may well proceed through a boat-like transition state, since a chair-like transition state would force the propargyl ether substituent into a severely hindered axial orientation. In the boat-like transition state the alkene now appears to be largely eclipsed with either the ketyl methyl group (**22**) or the ketyl radical oxygen (**23**). Conformer **22** may now be preferred over **23** since it alleviates the electronic repulsion between the ketyl oxygen functionality and the alkene π-system,[16] and this preference is unaffected by replacing HMPA with DMPU.

Completion of the synthesis of paeonilactone B **5** firstly required protection of the tertiary allylic alcohol of **18** as the

‡ Propargyl = prop-2-ynyl.

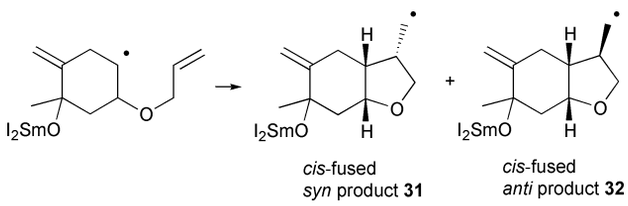
triethylsilyl ether **24**,[17] followed by oxidation of the allyl ether to the desired α-methylene lactone **25** using CrO_3 and pyridine (Scheme 6).[18] The selective oxidation of the ostensibly more



Scheme 6 *Reagents and conditions*: (i) Et_3SiOTf, Et_3N, CH_2Cl_2, 0 °C; (ii) CrO_3, pyridine, CH_2Cl_2, rt; (iii) O_3, EtOH, −110 °C; (iv) Me_2S; (v) OsO_4, THF, H_2O or cat. $K_2OsO_4{\cdot}2H_2O$, K_2CO_3, $K_3Fe(CN)_6$, Bu^{t}OH, H_2O; (vi) PhSH, Et_3N, CH_2Cl_2; (vii) O_3, MeOH, −78 °C; (viii) Me_2S; (ix) CCl_4, reflux; (x) HF·pyridine, THF.

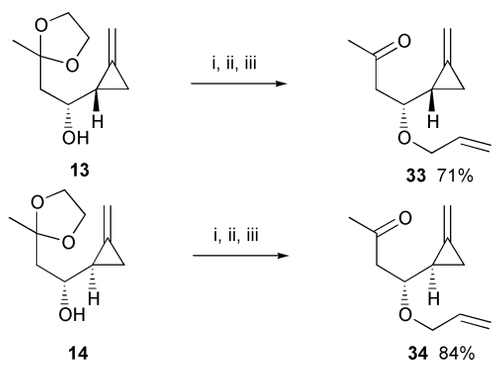
electrophilic cyclohexyl alkene of **25** proved to be impossible, with both alkenes reacting rapidly with ozone at −110 °C in EtOH to give **26** in almost quantitative yield. Even more frustratingly, treatment of **25** with OsO_4 led to **27** with dihydroxylation of just the α-methylene lactone, presumably due to steric congestion around the cyclohexyl alkene. Instead, base mediated Michael addition of thiophenol to **25** gave the thioether **28**, which was then successfully ozonolysed to give the desired ketone, with concomitant oxidation of the thioether to the corresponding sulfoxide **29**. Thermal elimination of phenylsulfenic acid[19] then reinstalled the α-methylene lactone and deprotection of the resulting silyl ether **30** was successfully achieved using pyridine·HF[20] to give (±)-paeonilactone B **5**, whose structure was confirmed by comparison of NMR and IR spectroscopic data to those reported previously for the natural paeonilactone.[9]

The SmI_2 mediated cascade reaction of methylenecyclopropyl ketone **16** thus provides a short route to paeonilactone B, and proceeds with high diastereoselectivity which is critically dependent on the presence of HMPA. Clearly a synthesis of paeonilactone A **4** could be achieved by a stereoselective reduction of the exocyclic alkene of paeonilactone B, but having established that the SmI_2 mediated cascade reaction of propargyl ether **16** proceeds with high diastereoselectivity to give the bicyclic ether **18** it was of interest to see if the cascade methodology could be extended to the cyclisation of the corresponding allyl ethers which might, in principle, install the methyl substituent for paeonilactone A directly. The stereochemical outcome of the cyclisation of cyclohexyl radicals onto a pendant butenyl (or allyloxy) residue has been investigated in some detail. Studies by RajanBabu[21] and Beckwith and Page[22] indicate that if the cyclisation proceeds with the butenyl sidechain in an equatorial orientation (relative to the pseudo-chair cyclohexane) then the *cis*-fused 7-*syn* product **31** will be the preferred product whereas if the cyclisation proceeds with the butenyl sidechain in an axial orientation then the *cis*-fused 7-*anti* product **32** will be preferred (Scheme 7).



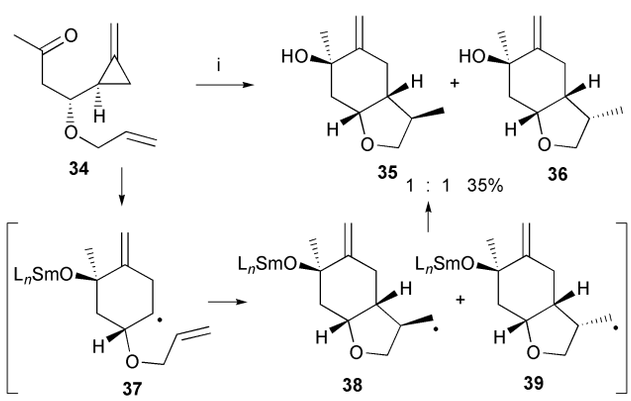
Scheme 7

The diastereomeric allyl ethers **33** and **34** were prepared in analogous fashion to the corresponding propargyl ethers, by alkylation of the separated alcohols **13** and **14** with allyl bromide, and subsequent ketal deprotection (Scheme 8).



Scheme 8 *Reagents and conditions*: (i) NaH, DMPU, THF; (ii) allyl bromide; (iii) TsOH, acetone, H_2O.

Treatment of allyl ether **34** with SmI_2, as before in the presence of HMPA, gave a 1:1 mixture of diastereoisomeric bicycles, **35** and **36** in 35% isolated yield[23] (Scheme 9). A slightly



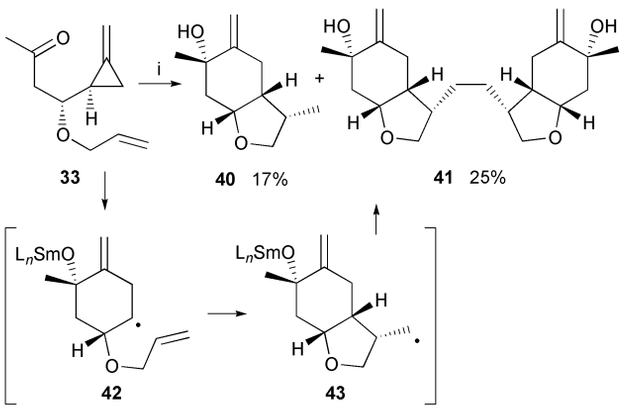
Scheme 9 *Reagents and conditions*: (i) SmI_2, Bu^{t}OH, HMPA, THF, 0 °C.

improved yield (40%) of the same 1:1 mixture was obtained by carrying out the reaction at −78 °C. No other bicyclic products could be isolated from these reactions (nor could they be detected in the ^1H or ^{13}C NMR spectra of the crude reaction mixture).

The stereochemical outcome of this cyclisation is readily rationalised in terms of the model presented above (Scheme 5) for the cyclisation of the analogous propargyl ether **17**. Thus the cyclisation of the initially formed ketyl radical may proceed *via* a boat-like transition state to give methylenecyclohexyl radical **37**, as essentially a single diastereoisomer, which then cyclises to give a 1:1 mixture of alkyl radicals **38** and **39**, which in turn are reduced to the organosamarium and quenched by

Bu^{t}OH. Replacement of HMPA with DMPU in the reaction (0 °C) led to a lower yield (20%) of bicyclic products, but with no change to the diastereoselectivity, again mirroring the results observed with the corresponding propargyl ether **17**. Thus it seems that cyclisation of cyclohexyl radical **37**, under the conditions used here, gives no stereoselectivity at the newly formed chiral centre. The lower yields of the cascade process in comparison to the analogous propargyl ethers were also disappointing and indeed somewhat surprising since the rate constant for cyclisation of the hex-5-enyl radical is greater than the corresponding rate constant for cyclisation of the hex-5-ynyl radical[24] and thus one might anticipate that cyclisation of **37** (or **42**) would be more efficient than cyclisation of **8**. Since no identifiable byproducts were isolated from these cyclisations it is not possible to speculate on the reasons for the relatively low yields in the allyl ether cyclisations.

Cyclisation of **33** in the presence of HMPA, on the other hand, gave a single diastereomeric bicycle **40** in just 17% isolated yield, but accompanied by a 25% yield of a dimeric product **41**, as a single diastereoisomer,[25] with the same relative stereochemistry for the bicyclic portion as for **40** (Scheme 10).

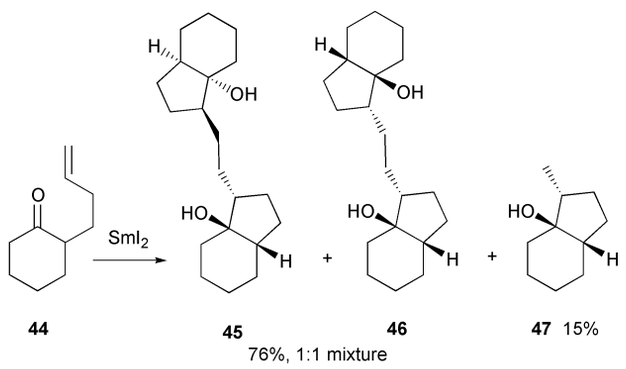


Scheme 10 *Reagents and conditions*: (i) SmI_2, Bu^{t}OH, HMPA, THF, 0 °C.

Again, no other bicyclic or dimeric products could be isolated from the reaction (nor could they be detected in the ^{1}H or ^{13}C NMR spectra of the crude reaction mixture) and again the stereochemical outcome of this cyclisation is readily rationalised in terms of the model presented previously for the cyclisation of the analogous propargyl ether **16**. Thus the cyclisation of the initially formed ketyl radical may proceed *via* a chair-like transition state to give methylenecyclohexyl radical **42**, as essentially a single diastereoisomer. Radical **42** then cyclises to give exclusively alkyl radical **43** which is either reduced to the organosamarium and quenched to give **40**, or dimerises to give **41**. The sequence therefore appears to be highly stereoselective, although it does not give the desired stereochemistry for the natural product paeonilactone A.

As before with the analogous propargyl ether **16**, replacement of HMPA with DMPU in the cyclisation led to a loss of stereoselectivity in the first steps of the cascade, and thus to the formation of both methylenecyclohexyl radicals **37** and **42**, which in turn gave a mixture of all three bicyclic products **35**, **36** and **40**, but no dimeric products were detected, indicating that the presence of HMPA is essential for the formation of **41**.

The formation of dimer **41** was quite unexpected since it is formed under conditions of relatively high SmI_2 concentration where rapid reduction of the primary radical **43** and quenching would be expected, as observed for intermediates **38** and **39**. In a further experiment we treated a 1:1 mixture of starting allyl ethers **33** and **34** with SmI_2, under the same conditions as before, with HMPA, and obtained a mixture of all three bicyclic products **35**, **36** and **40** and the single dimeric product **41**. Thus, under conditions that generate all three primary radicals **38**, **39** and **43**, it is only **43** which dimerises. Even more remarkably, the dimerisation occurs only between opposite enantiomers of **43**, to give the dimer as a *meso* isomer, and none of the 'homo' coupling of identical enantiomers is observed! Dimerisation (Wurtz coupling) of organosamariums such as benzylsamarium diiodide are well known[2] and recently a non-stereoselective dimerisation of a samarium-derived glucosyl radical has been described.[26] However the only example of dimerisation at the end of a radical cyclisation sequence that we are aware of, was reported by Molander and McKie *et al*.[15] in which cyclisation of **44** led to a mixture of diastereomeric dimers **45** and **46**, under conditions of relatively low SmI_2 concentration (Scheme 11).



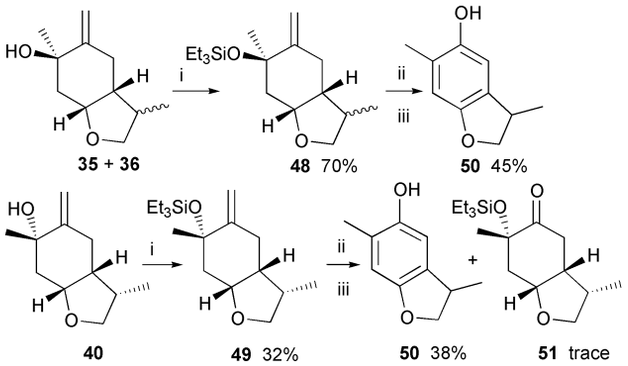
Scheme 11

The dimerisation was not observed when higher concentrations of SmI_2 (as in our work described here) were used.

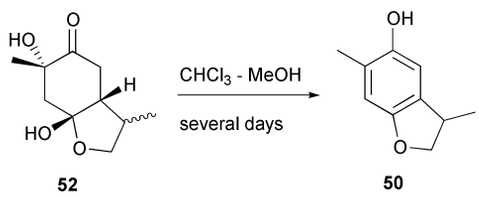
Clearly radical intermediate **43** is more stable than any of the other radical intermediates formed in the cyclisation sequence, and we believe this can be explained most readily by the fact that this intermediate has both the OSm(III) and the alkyl radical on the *endo* face of the bicyclic structure, allowing stabilisation of the radical by interaction with the samarium(III). This would effectively 'protect' the radical from further reduction by SmI_2, allowing build up of the radical species and eventual dimerisation. The exclusive formation of the *meso* dimer is harder to rationalise. The dimerisation may involve formation of a diradical intermediate from two monomers **43** (*e.g.* bridging of two ketyl oxygens with two samariums) followed by radical coupling to give the dimeric product. For the formation of such an intermediate, approach of identical enantiomers to each other may be impeded relative to the approach of opposite enantiomers. Alternatively, the structure of the *rac* diradical intermediate, if formed, may not readily allow coupling of the two alkyl radicals and may be slowly quenched to give **40**, or it may equilibrate with a *meso* diradical intermediate whose structure does allow radical coupling.

Although the cyclisations of the allyl ethers failed to provide the correct stereochemistry for paeonilactone A, the conversion of the bicyclic ethers **35**, **36** and **40** to diastereoisomers of the natural product was none-the-less investigated. The diastereomeric mixture of alcohols **35** and **36** was converted to the corresponding mixture of triethylsilyl ethers **48** in 70% yield, whereas the single diastereomeric alcohol **40** was converted to triethylsilyl ether **49** in only 32% yield, reflecting the difficulty of protecting an alcohol on the *endo* face of a *cis*-fused bicyclic system (Scheme 12).

Ozonolysis of triethylsilyl ethers **48** did not produce the desired cyclohexanone, but gave instead the dihydrobenzofuran **50** in 45% yield (Scheme 12). Similarly ozonolysis of triethylsilyl ether **49** gave dihydrobenzofuran **50** in 38% yield accompanied by a small amount of the desired cyclohexanone **51**. The dihydrobenzofuran **50** has previously been isolated as the major product from the decomposition of the paeony root metabolite **52**, when the latter was stored as a solution in $CHCl_3$–MeOH



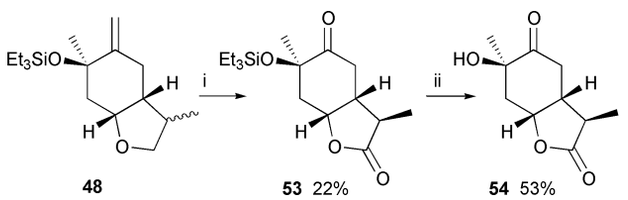
Scheme 12 *Reagents and conditions*: (i) Et_3SiOTf, Et_3N, CH_2Cl_2, 0 °C; (ii) O_3, MeOH, −60 °C; (iii) Me_2S.



Scheme 13

for several days (Scheme 13).[27] Ozonolysis of the silyl ethers **48** and **49** presumably leads to an intermediate related to **52**, which subsequently aromatises by enolisation and elimination.

As an alternative to ozonolysis, oxidation of the silyl ethers using RuO_4 was attempted. Disappointingly, treatment of silyl ether **49** under these conditions led only to decomposition of the starting material and recovery of Et_3SiOH. Oxidation of silyl ethers **48** using RuO_4 did, however, lead to concomitant oxidation of both the cyclohexyl alkene and the tetrahydrofuran ring to give the bicyclic lactone **53**, as a single diastereoisomer in 22% yield and this was successfully deprotected to give (±)-6-*epi*-paeonilactone A **54** (Scheme 14). Presumably **53**



Scheme 14 *Reagents and conditions*: (i) $RuCl_3{\cdot}H_2O$, $NaIO_4$, H_2O, CCl_4; (ii) HF·pyridine, THF.

is produced as a single diastereoisomer because only the corresponding diastereoisomer of the silyl ether **48** is successfully oxidised, or because the chiral centre α to the newly formed lactone is epimerised under the reaction conditions.

In summary, the SmI_2 cyclisation of methylenecyclopropyl ketones has been investigated in detail. Efficient cascade processes have been produced indicating that the radical intermediates are sufficiently long-lived in the presence of excess SmI_2 to allow the cascade sequence to be realised. In addition, the cascade sequences we have investigated are highly stereoselective, although the selectivity is heavily influenced by the precise reaction conditions, and specifically by the use of HMPA as an additive.[28] The efficiency and stereoselectivity of these cascade processes have allowed them to be used in short syntheses of (±)-paeonilactone B and of (±)-6-*epi*-paeonilactone A.

Experimental

General procedures

All reactions requiring anhydrous conditions were conducted in flame dried glassware under a static, inert atmosphere unless otherwise stated. THF and toluene were distilled from sodium benzophenone ketyl,[29] CH_2Cl_2 was distilled from calcium hydride, and petrol was distilled and the fraction boiling between 40 and 60 °C was used. All other solvents were of commercial grade and were used without further purification. Thin layer chromatography was performed on plastic backed sheets (Camlab) coated with silica gel (SiO_2: 0.25 mm). Flash column chromatography was performed on Sorbil C_{60}, 40–60 mesh silica.

Infra-red spectra were recorded on a Perkin-Elmer 1600 series FT-IR spectrometer. Proton NMR spectra were obtained at 270 MHz on a JEOL GX 270, at 300 MHz on a Bruker AC 300, and at 360 MHz on a Bruker Aspect 3000 spectrometer. Spectra were referenced with respect to the residual solvent peak for the deuterated solvent concerned. ^{13}C NMR spectra were obtained at 75 MHz on a Bruker AC 300. COSY spectra and ^1H–^{13}C correlation spectra were measured on a Bruker AC 300, and NOE data were recorded on the Bruker Aspect 3000 spectrometer, or obtained courtesy of Zeneca Agrochemicals, Bracknell. Mass spectra were obtained on a VG analytical 70–250-SE normal geometry double focusing mass spectrometer. All EI data were acquired at 70 eV, with the source temperature at 200 °C and with an accelerating voltage of 6 kV. All CI data were obtained using ammonia reagent gas, the source temperature being 200 °C and with an emission current of 0.5 mA. All ES spectra were recorded on a Micromass Platform quadrupole mass analyser with an electrospray ion source.

Methylenecyclopropane was prepared according to the method of Binger and co-workers[30] and was handled using the experimental methods described by Thomas[11a] Sternberg and Binger.[11b] 2-(2-Methyldioxolan-2-yl)ethanal **12** was prepared in three steps from ethyl acetoacetate according to the method of Kelly *et al.*[31]

(1*R*)-2-(2-Methyl-1,3-dioxolan-2-yl)-1-[(1*S*)-2-methylenecyclopropyl]ethanol 13 and (1*R*)-2-(2-methyl-1,3-dioxolan-2-yl)-1-[(1*R*)-2-methylenecyclopropyl]ethanol 14

^{n}BuLi (28 ml of 2.5 M solution in hexane, 0.070 mol) was added to a solution of methylenecyclopropane (5 ml, 0.074 mol) in THF (100 ml) at −30 °C. The temperature was allowed to warm to 0 °C over 1 h and maintained at 0 °C for 1 h, then raised to room temperature for 10 min before cooling to −78 °C. Aldehyde **12** (8.39 g, 0.063 mol) in THF (50 ml) at −78 °C was added *via* cannula to the solution over 10 min. The reaction mixture was allowed to warm to −20 °C and the reaction quenched with aq. NH_4Cl (10 ml of a pH 7 buffered solution). The aqueous layer was extracted with Et_2O (3 × 150 ml) and the organic layer dried over $MgSO_4$. The crude reaction mixture was concentrated *in vacuo* and purified by flash column chromatography eluting with petrol, gradually increasing the polarity to 30% Et_2O–petrol, to give alcohols **13** and **14** as a colourless oil (7.54 g, 65%) and as a 1:1 mixture of diastereoisomers. The diastereoisomers (2 g) were separated by flash column chromatography, eluting with petrol, gradually increasing the polarity to 30% Et_2O–petrol to give **13** (503 mg), $R_f = 0.50$ (70% EtOAc–petrol); ν_{max} (liq. film)/cm^{-1} 3475, 2980, 1379; δ_H (300 MHz, $CDCl_3$) 5.55 (1H, br s, C=CH_AH$_B$), 5.43 (1H, br s, C=CH$_A$$H_B$), 4.02 (4H, br s, O(C$H_2$)$_2$O), 3.55 (1H, ddd, $J = 2$, 7, 10 Hz, C*H*OH), 3.25 (1H, br s, OH), 2.10 (1H, dd, $J = 2$, 15 Hz, CH_AH$_B$CHOH), 1.91 (1H, dd, $J = 10$, 15 Hz, CH$_A$$H_B$CHOH), 1.62 (1H, m, cyclopropyl CH), 1.38 (3H, s, CH_3), 1.24 (1H, tt, $J = 2$, 9 Hz, cyclopropyl CH), 0.98 (1H, m, cyclopropyl C*H*); δ_C (75 MHz, $CDCl_3$) 133.6, 110.1, 103.8 (2), 70.4 (1), 64.7 (2), 64.2 (2), 44.1 (2), 24.1 (3), 21.2 (1), 6.7 (2); *m*/*z* (CI+) 185 $[M + H]^+$ (5%), 167 $[M - OH]^+$ (10%). HRMS $C_{10}H_{17}O_3$ $[M + H]^+$ requires 185.1178, found 185.1177.

A 1:1 mixture of both diasteroisomers (737 mg).

And **14** (509 mg), $R_f = 0.48$ (70% EtOAc–petrol); ν_{max} (liq.

film)/cm^{-1} 3475, 2982, 1380; δ_H (300 MHz, $CDCl_3$) 5.42 (2H, s with fine coupling, C=CH_2), 4.01 (4H, br s, O(CH_2)$_2$O), 3.65 (1H, s, OH), 3.41 (1H, dt, J = 4, 8 Hz, C*H*OH), 2.00–1.92 (2H, m, CH_2CHOH), 1.58 (1H, m, cyclopropyl CH), 1.37–1.27 (1H, m, cyclopropyl CH), 1.36 (3H, s, CH_3), 1.12 (1H, m, cyclopropyl CH); δ_C (75 MHz, $CDCl_3$) 132.8, 110.3, 104.1 (2), 71.2 (1), 64.9 (2), 64.4 (2), 44.9 (2), 24.2 (3), 21.9 (1), 8.6 (2); *m/z* (CI+) 185 [M + H]$^+$ (8%), 167 [M − OH]$^+$ (10%) (Found: C, 64.87; H, 8.87. $C_{10}H_{16}O_3$ requires C, 65.19; H, 8.75%).

(±)-(1*R*)-2-(2-Methyl-1,3-dioxolan-2-yl)-1-[(1*R*)-2-methylenecyclopropyl]ethyl 4-nitrobenzoate 15

p-Nitrobenzoyl chloride (590 mg, 3.2 mmol) was added to a solution of alcohol **14** (64 mg, 0.35 mmol) and pyridine (0.5 ml, 6 mmol) in CH_2Cl_2 (2 ml). The reaction mixture was stirred at room temperature for 48 h under N_2. The reaction mixture was washed with a saturated solution of $CuSO_4$ (2 ml) and the aqueous layer extracted with CH_2Cl_2 (3 × 2 ml). The combined organic phase was dried over $MgSO_4$, concentrated *in vacuo* and purified by flash column chromatography, eluting with hexane, gradually increasing the polarity to 50% EtOAc–hexane to give ester **15** as a yellowish crystalline solid (104 mg, 90%) which was recrystallised from ethanol–water, R_f = 0.68 (70% EtOAc–hexane); ν_{max} (liq. film)/cm^{-1} 2985, 2886, 1722, 1607, 1527, 1349; δ_H (300 MHz, $CDCl_3$) 8.30 (2H, d, J = 8 Hz, ArH), 8.21 (2H, d, J = 8 Hz, ArH), 5.50 (1H, s with fine splitting, C=CH_AH$_B$), 5.45 (1H, s with fine splitting, C=CH$_A$$H_B$), 5.08 (1H, dt, J = 2, 9 Hz, CHO), 3.98–3.80 (4H, m, O(CH_2)$_2$O), 2.35 (1H, dd, J = 9, 15 Hz, CH_AH$_B$CHO), 2.09 (1H, dd, J = 2, 15 Hz, CH$_A$$H_B$CHO), 1.85 (1H, m, cyclopropyl C*H*), 1.45–1.25 (2H, m, cyclopropyl CH), 1.35 (3H, s, CH_3); δ_C (75 MHz, $CDCl_3$) 164.6, 150.6, 136.4, 131.8, 131.0 (1), 123.7 (1), 108.7, 105.1 (2), 73.9 (1), 64.6 (2), 64.5 (2), 43.2 (2), 24.5 (3), 20.5 (1), 8.9 (2); *m/z* (CI) 334 [M + H]$^+$ (10%), 351 [M + NH_4]$^+$ (5%); X-ray crystal structure was obtained and is published elsewhere.[12]

(±)-(4*R*)-4-[(1*S*)-2-Methylenecyclopropyl]-4-(prop-2-ynyloxy)-butan-2-one 16

Alcohol **13** (301 mg, 1.63 mmol) in THF (1.5 ml) was added to NaH (60% dispersion in oil, 151 mg, 3.78 mmol) in THF (3 ml) under Ar and the reaction mixture was stirred for 20 min. DMPU (460 µl, 3.8 mmol) was added and the reaction mixture stirred for 10 min. Propargyl bromide (80% solution in toluene, 695 µl, 6.25 mmol) was added and the reaction mixture stirred overnight. The reaction was quenched with aq. NH_4Cl (3 ml of a sat. solution) and the aqueous phase extracted with Et_2O (3 × 10 ml). The combined organic phase was dried over $MgSO_4$, concentrated *in vacuo* and purified by flash column chromatography, eluting with petrol, and gradually increasing the polarity to 40% Et_2O–petrol to give the propargyl ether as a pale yellow oil (332 mg, 91%), R_f = 0.59 (50% Et_2O–petrol); ν_{max} (liq. film)/cm^{-1} 2985, 2105, 1445, 1380; δ_H (300 MHz, $CDCl_3$) 5.48 (2H, m, C=CH_2), 4.35 (1H, dd, J = 2, 15 Hz, CH_ACH$_B$-C≡C), 4.24 (1H, dd, J = 2, 15 Hz, CH$_A$CH_BC≡C), 3.95 (4H, m, O(CH_2)$_2$O), 3.20 (1H, dt, J = 3, 8 Hz, C*H*OCH_2), 2.40 (1H, t, J = 2 Hz, C≡CH), 2.05 (1H, dd, J = 8, 15 Hz, CH_ACH$_B$CHO), 1.98 (1H, dd, J = 3, 15 Hz, CH$_A$CH_BCHO), 1.60 (1H, m, cyclopropyl CH), 1.40 (3H, s, CH_3), 1.25 (1H, m, cyclopropyl CH), 0.85 (1H, m, cyclopropyl C*H*); δ_C (75 MHz, $CDCl_3$) 134.4, 109.3, 104.6 (2), 80.4, 76.8 (1), 74.2 (1), 64.7 (2), 64.6 (2), 55.9 (2), 44.1 (2), 24.5 (3), 20.3 (1), 6.7 (2); *m/z* (CI) 223 [M + H]$^+$ (18%), 240 [M + NH_4]$^+$ (7%); HRMS $C_{13}H_{19}O_3$ [M + H]$^+$ requires 223.1334, found 223.1319.

The propargyl ether (305 mg, 1.37 mmol) and *p*-TsOH (310 mg, 1.63 mmol) in wet acetone (60 ml of 10% water in acetone) was stirred for 24 h at room temperature. The reaction mixture was concentrated *in vacuo* and Et_2O (50 ml) was added. The mixture was washed with aq. $NaHCO_3$ (25 ml). The aqueous layer was extracted with Et_2O (3 × 25 ml), and the combined aqueous phases were dried over $MgSO_4$ and concentrated *in vacuo* to give ketone **16** as a colourless oil (245 mg, 99%), R_f = 0.45 (50% Et_2O–petrol); ν_{max} (liq. film)/cm^{-1} 2991, 2105, 1718, 1359; δ_H (300 MHz, $CDCl_3$) 5.49 (2H, s, C=CH_2), 4.33 (1H, dd, J = 2, 16 Hz, CH_AH$_B$C≡C), 4.20 (1H, dd, J = 2, 16 Hz, CH$_A$$H_B$C≡C), 3.59 (1H, dt, J = 4, 8 Hz, C*H*OCH_2), 2.81 (1H, dd, J = 8, 16 Hz, CH_AH$_B$CHO), 2.65 (1H, dd, J = 4, 16 Hz, CH$_A$$H_B$CHO), 2.42 (1H, t, J = 2 Hz, C≡CH), 2.20 (3H, s, CH_3), 1.55 (1H, m, cyclopropyl CH), 1.20 (1H, m, cyclopropyl CH), 0.90 (1H, m, cyclopropyl CH); δ_C (75 MHz, $CDCl_3$) 206.9, 133.2, 105.1 (2), 80.0, 76.7 (1), 74.4 (1), 56.5 (2), 48.8 (2), 31.1 (3), 19.1 (1), 6.57 (2); *m/z* (CI+) 179 [M + H]$^+$ (100%), 196 [M + NH_4]$^+$ (100%); HRMS $C_{11}H_{15}O_2$ [M + H]$^+$ requires 179.1072, found 179.1076.

(±)-(4*R*)-4-[(1*R*)-2-Methylenecyclopropyl]-4-(prop-2-ynyloxy)-butan-2-one 17

Using an identical procedure to that used for the preparation of ketone **16**, alcohol **14** (298 mg, 1.62 mmol) was first alkylated with propargyl bromide to give the propargyl ether as a pale yellow oil (316 mg, 88%), R_f = 0.55 (50% Et_2O–petrol); ν_{max} (liq. film)/cm^{-1} 2985, 2100, 1445, 1380; δ_H (300 MHz, $CDCl_3$) 5.46 (2H, br s, C=CH_2), 4.38 (2H, br s, CH_2C≡C), 3.95 (4H, m, O(CH_2)$_2$O), 3.35 (1H, dt, J = 2, 9 Hz, C*H*OCH_2), 2.41 (1H, t, J = 1 Hz, C≡CH), 2.05 (1H, dd, J = 9, 15 Hz, CH_AH$_B$CHO), 1.90 (1H, dd, J = 2, 15 Hz, CH$_A$$H_B$CHO), 1.55 (1H, m, cyclopropyl C*H*), 1.40 (1H, m, cyclopropyl C*H*), 1.38 (3H, s, CH_3), 1.22 (1H, m, cyclopropyl CH); δ_C (75 MHz, $CDCl_3$) 131.2, 109.1, 104.5 (2), 80.1, 76.6 (1), 74.2 (1), 64.6 (2), 64.3 (2), 55.7 (2), 44.3 (2), 24.5 (3), 19.4 (1), 9.9 (2); *m/z* (CI): 223 [M + H]$^+$ (9%), 240 [M + NH_4]$^+$ (4%); HRMS $C_{13}H_{19}O_3$ [M + H]$^+$ requires 223.1334, found 223.1344.

The propargyl ether (292 mg, 1.32 mmol) was deprotected to give ketone **17** as a colourless oil (234 mg, 100%), R_f = 0.51 (50% Et_2O–petrol); ν_{max} (liq. film)/cm^{-1} 2990, 2105, 1718, 1365; δ_H (300 MHz, $CDCl_3$) 5.47 (1H, s with fine splitting, C=CH_A-H$_B$), 5.42 (1H, s with fine splitting, C=CH$_A$$H_B$), 4.34 (2H, br s, CH_2C≡C), 3.59 (1H, dt, J = 4, 8 Hz, C*H*OCH_2), 2.82 (1H, dd, J = 8, 15 Hz, CH_AH$_B$CHO), 2.55 (1H, dd, J = 4, 15 Hz, CH$_A$-H_BCHO), 2.43 (1H, t, J = 1 Hz, C≡CH), 2.19 (3H, s, CH_3), 1.55 (1H, m, cyclopropyl CH), 1.45 (1H, m, cyclopropyl CH), 1.20 (1H, m, cyclopropyl CH); δ_C (75 MHz, $CDCl_3$) 206.8, 130.6, 105.2 (2), 79.9, 76.7 (1), 74.6 (1), 56.5 (2), 49.7 (2), 30.9 (3), 18.8 (1), 10.05 (2); *m/z* (CI+) 179 [M + H]$^+$ (100%), 196 [M + NH_4]$^+$ (100%); HRMS $C_{11}H_{15}O_2$ [M + H]$^+$ requires 179.1072, found 179.1080.

General procedure for samarium iodide mediated cyclisations—cyclisation of ketones 16 and 17 to give bicyclic alcohols 18 and 19

HMPA or DMPU (see text) (30 mmol) was added to a freshly prepared solution of SmI_2 (3.1 mmol, 0.15 M solution) in THF to give a purple solution, which was cooled to 0 °C. Methylenecyclopropyl ketone (1.4 mmol) and ^{t}BuOH (0.21 g, 2.8 mmol) in THF (30 ml) were added over 90 min and the reaction mixture were allowed to warm to room temperature. The crude mixture was washed with aq. citric acid (2.5 g in 50 ml water) and extracted with 1:1 EtOAc–petrol (4 × 50 ml). The combined organic phase was washed with brine (50 ml) then water (50 ml), dried over $MgSO_4$ and concentrated *in vacuo.* The crude reaction mixture was purified by flash column chromatography, eluting with petrol, and gradually increasing the polarity to 50% Et_2O–petrol to give the desired bicyclic alcohols.

Using this procedure (see text) alcohol **18** was isolated as a colourless oil, R_f = 0.14 (50% Et_2O–petrol); ν_{max} (liq. film)/cm^{-1} 3420, 2935, 2860, 1670, 1650, 1449, 1365; δ_H (500 MHz, $CDCl_3$) 5.01 (1H, br s, CH_AH$_B$=C), 4.98–4.90 (2H, m, CH_2=C), 4.84 (1H, br s, CH$_A$$H_B$=C), 4.44 (1H, d with fine splitting, J = 14 Hz,

$OCH_ACH_BC{=}CH_2$), 4.35–4.25 (2H, m, $OCH_AH_BC{=}CH_2$ and CH_2CHO), 2.75 (1H, m, $CHC{=}CH_2$), 2.60 (1H, dd, $J = 7$, 14 Hz, $CHCH_AH_BC{=}CH_2$), 2.33 (1H, dd, $J = 8$, 14 Hz, $CHCH_AH_BC{=}CH_2$), 1.85 (2H, m, CH_2CHO), 1.72 (1H, br s, OH), 1.43 (3H, s, CH_3); δ_C (75 MHz, $CDCl_3$) 150.9, 150.8, 107.9 (2), 104.2 (2), 78.0 (1), 72.14, 69.9 (2), 44.6 (1), 33.6 (2), 30.5 (2), 28.8 (3); *m/z* (CI+) 163 $[M - H_2O]^+$ (100%), 180 $[M]^+$ (100%); HRMS $C_{11}H_{16}O_2$ $[M]^+$ requires 180.1150, found 180.1150.

Alcohol **19** was isolated as a colourless oil, $R_f = 0.44$ (50% Et_2O–petrol); ν_{max} (liq. film)/cm^{-1} 3420, 3080, 2925, 2860, 1670, 1645, 1440, 1370; δ_H (500 MHz, $CDCl_3$) 5.00 (2H, s, $CH_2{=}C$), 4.93 (1H, br s, $CH_AH_B{=}C$), 4.83 (1H, br s, $CH_AH_B{=}C$), 4.51 (1H, d with fine splitting, $J = 14$ Hz, $OCH_AH_BC{=}CH_2$), 4.23 (1H, d with fine splitting, $J = 14$ Hz, $OCH_AH_BC{=}CH_2$), 4.16 (1H, m, CH_2CHO), 3.75 (1H, br s, OH), 2.73 (1H, br q, $J = 7$ Hz, $CHC{=}CH_2$), 2.44 (1H, dd, $J = 7$, 14 Hz, $CHCH_AH_BC{=}CH_2$), 2.31 (1H, dd, $J = 7$, 14 Hz, $CHCH_AH_BC{=}CH_2$), 2.21 (1H, dd, $J = 3$, 15 Hz, CH_AH_BCHO), 1.79 (1H, dd, $J = 3$, 15 Hz, CH_AH_BCHO), 1.34 (3H, s, CH_3); δ_C (75 MHz, $CDCl_3$) 152.0, 151.0, 108.7 (2), 104.5 (2), 79.3 (1), 70.9, 70.5 (2), 45.2 (1), 41.0 (2), 34.3 (2), 27.1 (3); *m/z* (CI+) 163 $[M - H_2O]^+$ (100%), 180 $[M]^+$ (50%), 181 $[M + H]^+$ (10%); HRMS $C_{11}H_{17}O_2$ $[M + H]^+$ requires 181.1228, found 181.1219.

(±)-(3a*R*,6*S*,7a*R*)-6-Methyl-3,5-dimethyleneperhydrobenzo[*b*]-furan-6-yl triethylsilyl ether 24

Alcohol **18** (353 mg, 1.97 mmol) and triethylamine (700 µl, 2 mmol) in CH_2Cl_2 (8 ml) were stirred at 0 °C under a flow of N_2. Triethylsilyl trifluoromethanesulfonate (600 µl, 2.6 mmol) was added and the reaction mixture stirred at 0 °C for 1 h, and allowed to warm to room temperature. The reaction mixture was washed with $NaHCO_3$ (1 ml) and extracted with CH_2Cl_2 (3 × 3 ml), and the combined organic phases were dried over $MgSO_4$ and concentrated *in vacuo*. The crude reaction mixture was purified by column chromatography, eluting with petrol, gradually increasing the polarity to 20% Et_2O–petrol to give triethylsilyl ether **24** as a brownish oil (180 mg, 75%), $R_f = 0.73$ (30% Et_2O–petrol); ν_{max} (liq. film)/cm^{-1} 2954, 2876, 1670, 1645, 1460, 1370; δ_H (300 MHz, $CDCl_3$) 5.12 (1H, s, $C{=}CH_AH_B$), 5.01 (1H, s with fine splitting, $C{=}CH_CH_D$), 4.94 (1H, s with fine splitting, $C{=}CH_CH_D$), 4.76 (1H, s with fine splitting, $C{=}CH_AH_B$), 4.37 (2H, br s, $OCH_2C{=}CH_2$), 4.33 (1H, dt, $J = 9$, 6 Hz, CH_2CHO), 2.80 (1H, m, $CHC{=}CH_2$), 2.65 (1H, dd, $J = 5$, 15 Hz, $CHCH_AH_BC{=}CH_2$), 2.49 (1H, dd, $J = 7$, 15 Hz, $CHCH_AH_BC{=}CH_2$), 1.88 (1H, dd, $J = 6$, 13 Hz, CH_AH_BCHO), 1.70 (1H, dd, $J = 9$, 13 Hz, $CHCH_AH_BCHO$), 1.35 (3H, s, CH_3), 0.96 (9H, t, $J = 7$ Hz, $(CH_3CH_2)_3Si$), 0.61 (6H, q, $J = 7$ Hz, $(CH_3CH_2)_3Si$); δ_C (75 MHz, $CDCl_3$) 149.8, 149.3, 108.7, (2), 104.3 (2), 77.8 (1), 74.2, 69.6 (2), 43.3 (1), 43.1 (2), 31.4 (2), 27.7 (3), 6.9 (3), 6.7 (2); *m/z* (APCI+) 295.3 $[M + H]^+$ (100%) (Found: C, 68.99; H, 10.20. $C_{17}H_{30}O_2Si$ requires C, 69.33; H, 10.30%).

(±)-(3a*R*,6*S*,7a*R*)-6-Methyl-3,5-dimethylene-6-(triethylsilyloxy)-perhydrobenzo[*b*]furan-2-one 25

Using a modification of the method of Brocksom,[18] chromium trioxide (1.7 g, 17 mmol) and pyridine (1.7 ml, 21 mmol) in CH_2Cl_2 (17 ml) were stirred vigorously for 10 min at 0 °C under Ar. Triethylsilyl ether **24** (180 mg, 0.61 mmol) in CH_2Cl_2 (2 ml) was added, and the suspension was allowed to stir for 4 h. The CH_2Cl_2 was decanted from the solid, and the solid dissolved in $NaHCO_3$ (250 ml) and extracted with CH_2Cl_2 (3 × 200 ml). The combined organic phases were dried over $MgSO_4$ and concentrated *in vacuo*. The crude reaction mixture was purified by column chromatography, eluting with petrol, gradually increasing the polarity with Et_2O to give lactone **25** as a clear oil (85 mg, 45%), $R_f = 0.52$ (50% Et_2O–petrol); ν_{max} (liq. film)/cm^{-1} 2957, 2878, 1760, 1665, 1651, 1456; δ_H (300 MHz, $CDCl_3$) 6.25 (1H, d, $J = 3$ Hz, $H_AH_BC{=}CCO_2$), 5.58 (1H, d, $J = 3$ Hz, $H_AH_BC{=}CCO_2$), 5.13 (1H, s, $CH_2C{=}CH_AH_B$), 4.86 (1H, s, $CH_2C{=}CH_AH_B$), 4.66 (1H, q, $J = 7$ Hz, $CHCHO$), 3.15 (1H, m, $CHCHO$), 2.65 (1H, dd, $J = 6$, 14 Hz, $CH_AH_BC{=}CH_2$), 2.50 (1H, dd, $J = 7$, 14 Hz, $CH_AH_BC{=}CH_2$), 2.08 (1H, dd, $J = 5$, 13 Hz, CH_AH_BCHO), 1.90 (1H, dd, $J = 8$, 13 Hz, CH_AH_BCHO), 1.38 (3H, s, CH_3), 0.76 (9H, t, $J = 7$ Hz, $(CH_3CH_2)_3Si$), 0.38 (6H, q, $J = 7$ Hz, $(CH_3CH_2)_3Si$); δ_C (75 MHz, $CDCl_3$) 170.3, 148.4, 138.5, 121.3 (2), 110.0 (2), 76.3 (1), 73.0, 44.4 (2), 40.3 (1), 32.6 (2), 27.7 (3), 7.2 (3), 6.8 (2); *m/z* (EI+) 309 $[M + H]^+$ (15%); HRMS $C_{17}H_{29}O_3Si$ $[M + H]^+$ requires 309.1886, found 309.1883.

(±)-(3a*R*,6*S*,7a*R*)-6-Methyl-3-methylene-6-(triethylsilyloxy)-perhydrobenzo[*b*]furan-2,5-dione 30

Lactone **25** (31 mg, 0.10 mmol), thiophenol (20 µl, 0.2 mmol) and triethylamine (28 µl, 0.2 mmol) in CH_2Cl_2 (1 ml) were stirred at room temperature under Ar for 4 h. The reaction was concentrated *in vacuo* and purified by column chromatography, eluting with petrol, gradually increasing the polarity to 80% Et_2O–petrol to give thioethers **28** as a brown oil and as a mixture of diastereoisomers (37 mg, 93%), $R_f = 0.77$ (60% Et_2O–petrol). Ozone was bubbled through a stirred solution of the thioethers **28** (28 mg, 0.067 mmol) in MeOH (1.5 ml) at −78 °C until the solution turned deep blue. The reaction mixture was purged with oxygen followed by N_2 and dimethylsulfide (1 ml) was added. The reaction mixture was allowed to warm to room temperature and was filtered through a silica plug and concentrated *in vacuo*. The resulting sulfoxide **29** was refluxed in CCl_4 (2.5 ml) for 24 h. The reaction mixture was washed with $NaHCO_3$, water and concentrated *in vacuo* to give triethylsilyl-protected paeonilactone B **30** (13 mg, 40%), $R_f = 0.85$ (70% Et_2O–petrol); ν_{max} (liq. film)/cm^{-1} 2957, 2875, 1730, 1670, 1414; δ_H (300 MHz, $CDCl_3$) 6.30 (1H, d, $J = 2$ Hz, $C{=}CH_AH_B$), 5.64 (1H, d, $J = 2$ Hz, $C{=}CH_AH_B$), 4.84 (1H, dt, $J = 7$, 5 Hz, $CHCHO$), 3.55 (1H, q, $J = 7$ Hz, $CHCHO$), 2.88 (1H, dd, $J = 7$, 15 Hz, $CH_AH_BC{=}O$), 2.66 (1H, dd, $J = 7$, 15 Hz, $CH_AH_BC{=}O$), 2.35 (1H, dd, $J = 5$, 14 Hz, CH_AH_BCHO), 2.23 (1H, dd, $J = 5$, 14 Hz, CH_AH_BCHO), 1.36 (3H, s, CH_3), 0.92 (9 H, t, $J = 7$ Hz, $Si(CH_2CH_3)_3$), 0.60 (6H, q, $J = 7$ Hz, $Si(CH_2CH_3)_3$); δ_C (75 MHz, $CDCl_3$) 207.9, 179.0, 138.4, 122.4 (2), 75.2, 74.0 (1), 42.6 (1), 38.7 (2), 38.6 (2), 24.6 (3), 7.1 (3), 6.4 (2); *m/z* (FAB) 281 $[M - CH_2CH_3]^+$ (100%), 311 $[M + H]^+$ (25%); HRMS-FAB $C_{16}H_{27}O_4Si$ $[M + H]^+$ requires 311.1678, found 311.1654.

(±)-Paeonilactone B 5

HF·pyridine (40 µl) was added to silyl ether **30** (5.0 mg, 0.016 mmol) in THF (1 ml) at room temperature under argon and stirred overnight. The reaction was quenched with water (1 ml) and the aqueous layer extracted with EtOAc (3 × 2 ml), dried over $MgSO_4$ and concentrated *in vacuo*. The reaction mixture was purified by flash column chromatography eluting with CH_2Cl_2, and gradually increasing the polarity to 0.5% MeOH–petrol to give (±)-paeonilactone B **5** as a colourless oil (3.1 mg, 96%), $R_f = 0.09$ (1% MeOH–CH_2Cl_2); δ_H (360 MHz, $CDCl_3$) 6.39 (1H, d, $J = 3$ Hz, $H_AH_BC{=}C$), 5.70 (1H, d, $J = 3$ Hz, $H_AH_BC{=}C$), 5.01 (1H, ddd, $J = 6$, 8, 9 Hz, $CHCHO$), 3.69 (1H, m, $CHCHO$), 3.39 (1H, s, O*H*), 2.97 (1H, dd, $J = 8$, 16 Hz, $CH_AH_BC{=}O$), 2.81 (1H, dd, $J = 4$, 16 Hz, $CH_AH_BC{=}O$), 2.55 (1H, dd, $J = 6$, 14 Hz, CH_AH_BCHO), 1.98 (1H, dd, $J = 9$, 14 Hz, CH_AH_BCHO), 1.42 (3H, s, CH_3); δ_C (125 MHz, $CDCl_3$) 209.9, 168.8, 136.5, 123.2 (2), 73.9, 73.2 (1), 41.6 (2), 39.5 (1), 36.8 (2), 25.1 (3).

NMR data agrees with those previously reported.[9]

(±)-(4*R*)-4-[(1*S*)-2-Methylenecyclopropyl]-4-(prop-2-enyloxy)-butan-2-one 33

Alcohol **13** (1.35 g, 7.3 mmol) in THF (7 ml) was added to a suspension of NaH (60% dispersion in oil, 0.72 g, 0.018 mol) in THF (13 ml) at room temperature, under N_2 and stirred for 10

min. DMPU (2.1 ml, 0.028 mol) was added and the reaction mixture stirred for a further 10 min, followed by the addition of allyl bromide (2.4 ml, 0.028 mol); the reaction mixture was stirred for 12 hours. The reaction mixture was washed with aq. NH_4Cl (5 ml) and extracted with Et_2O (3 × 5 ml), dried over $MgSO_4$, concentrated *in vacuo* and purified by column chromatography, eluting with petrol, gradually increasing the polarity to 50% EtOAc–petrol to give the allyl ether as a yellowish oil (1.24 g, 76%), $R_f = 0.69$ (50% Et_2O–petrol); ν_{max} (liq. film)/cm^{-1} 2984, 2878, 1646, 1424, 1377; δ_H (300 MHz, $CDCl_3$) 5.95 (1H, ddt, $J = 11$, 17, 5 Hz, $H_2C{=}CH$), 5.45 (2H, br s, $H_2C{=}C$), 5.29 (1H, br d, $J = 17$ Hz, $CH_AH_B{=}CH$), 5.16 (1H, br d, $J = 11$ Hz, $CH_AH_B{=}CH$), 4.28 (1H, dd, $J = 5$, 12 Hz, $OCH_AH_BCH{=}CH_2$), 4.10–3.85 (5H, m, $OCH_AH_BCH{=}CH_2$ and $O(CH_2)_2O$), 3.08 (1H, dt, $J = 3$, 8 Hz, $CHOCH_2$), 2.05 (1H, dd, $J = 8$, 14 Hz, $CH_AH_BCHOCH_2$), 1.95 (1H, dd, $J = 3$, 14 Hz, $CH_AH_B{-}CHOCH_2$), 1.58 (1H, m, cyclopropyl CH), 1.40 (3H, s, CH_3), 1.25 (1H, m, cyclopropyl CH), 0.85 (1H, m, cyclopropyl CH); δ_C (75 MHz, $CDCl_3$) 135.3 (1), 134.9, 116.5 (2), 109.4, 104.3 (2), 78.7 (1), 70.0 (2), 64.5 (2), 44.0 (2), 24.6 (3), 20.9 (1), 6.8 (2); *m/z* (CI) 225 $[M + H]^+$ (12%); HRMS $C_{13}H_{21}O_3$ $[M + H]^+$ requires 225.1491, found 225.1487.

The ketal (335 mg, 1.5 mmol) was deprotected using identical conditions to those for the preparation of ketone **16**, and gave ketone **33** as a yellowish oil (248 mg, 93%), $R_f = 0.56$ (50% Et_2O–petrol); ν_{max} (liq. film)/cm^{-1} 2925, 2865, 1719, 1665, 1423, 1357; δ_H (300 MHz, $CDCl_3$) 5.88 (1H, m, $H_2C{=}CH$), 5.47 (2H, br s, $H_2C{=}C$), 5.25 (1H, br d, $J = 17$ Hz, $CH_AH_B{=}CH$), 5.15 (1H, br d, $J = 10$ Hz, $CH_AH_B{=}CH$), 4.22 (1H, dd, $J = 5$, 12 Hz, CH_AH_BO), 3.94 (1H, dd, $J = 6$, 12 Hz, CH_AH_BO), 3.45 (1H, dt, $J = 4$, 8 Hz, CHO), 2.82 (1H, dd, $J = 8$, 16 Hz, CH_AH_BCHO), 2.60 (1H, dd, $J = 4$, 16 Hz, CH_AH_BCHO), 2.17 (3H, s, CH_3), 1.60 (1H, m, cyclopropyl CH), 1.17 (1H, m, cyclopropyl CH), 0.90 (1H, m, cyclopropyl CH); δ_C (75 MHz, $CDCl_3$) 207.4, 135.0 (1), 133.8, 116.9 (2), 104.8 (2), 77.9 (1), 70.4 (2), 48.8 (2), 31.3 (3), 19.7 (1), 6.6 (2); *m/z* (ES+) 178.7 $[M]^+$ (10%), 202.9 $[M + Na]^+$ (30%), 219.9 $[M + K]^+$ (100%); HRMS $C_{11}H_{17}O_2$ $[M + H]^+$ requires 181.1229, found 181.1228.

(±)-(4*R*)-4-[(1*R*)-2-Methylenecyclopropyl]-4-(prop-2-enyloxy)-butan-2-one 34

Using an identical procedure to that used for the preparation of ketone **33**, alcohol **14** (1.35 g, 7.3 mmol) was first alkylated with allyl bromide to give the allyl ether as a yellowish oil (1.71 g, 99%), $R_f = 0.68$ (50% Et_2O–petrol); ν_{max} (liq. film)/cm^{-1} 2990, 2878, 1645, 1431; δ_H (300 MHz, $CDCl_3$) 5.92 (1H, ddt, $J = 10$, 17, 5 Hz, $H_2C{=}CH$), 5.45 (2H, m, $H_2C{=}C$), 5.28 (1H, br d, $J = 17$ Hz, $CH_AH_B{=}CH$), 5.15 (1H, br d, $J = 10$ Hz, $CH_AH_B{=}CH$), 4.30 (1H, dd, $J = 5$, 12 Hz, $OCH_AH_BCH{=}CH_2$), 4.02 (1H, dd, $J = 5$, 12 Hz, $OCH_AH_BCH{=}CH_2$), 4.00–3.85 (4H, m, $O(CH_2)_2O$), 3.12 (1H, dt, $J = 2$, 8 Hz, $CHOCH_2$), 2.05 (1H, dd, $J = 8$, 14 Hz, $CH_AH_BCHOCH_2$), 1.85 (1H, dd, $J = 2$, 14 Hz, $CH_AH_BCHOCH_2$), 1.60 (1H, m, cyclopropyl CH), 1.41 (1H, m, cyclopropyl CH), 1.40 (3H, s, CH_3), 1.12 (1H, m, cyclopropyl CH); δ_C (75 MHz, $CDCl_3$) 135.5 (1), 132.1, 116.5 (2), 109.3, 104.3 (2), 78.5 (1), 70.2 (2), 64.5 (2), 64.4 (2), 44.4 (2), 24.7 (3), 20.4 (1), 10.1 (2); *m/z* (CI) 225 $[M + H]^+$ (12%); HRMS $C_{13}H_{21}O_3$ $[M + H]^+$ requires 225.1491, found 225.1455.

The ketal (435 mg, 1.94 mmol) was deprotected to give ketone **34** as a colourless oil (293 mg, 84%), $R_f = 0.29$ (50% Et_2O–petrol); ν_{max} (liq. film)/cm^{-1} 2925, 1720, 1665, 1426, 1360; δ_H (300 MHz, $CDCl_3$) 5.88 (1H, m, $H_2C{=}CH$), 5.50 (1H, s, $CH_AH_B{=}C$), 5.44 (1H, s, $CH_AH_B{=}C$), 5.25 (1H, br d, $J = 17$ Hz, $H_AH_BC{=}CH$), 5.15 (1H, br d, $J = 10$ Hz, $H_AH_BC{=}CH$), 4.24 (1H, dd, $J = 5$, 12 Hz, OCH_AH_B), 4.03 (1H, dd, $J = 6$, 12 Hz, OCH_AH_B), 3.43 (1H, dt, $J = 4$, 8 Hz, CHO), 2.85 (1H, dd, $J = 8$, 15 Hz, CH_AH_BCHO), 2.52 (1H, dd, $J = 4$, 15 Hz, $CH_AH_B{-}CHO$), 2.17 (3H, s, CH_3), 1.57 (1H, m, cyclopropyl CH), 1.42 (1H, m, cyclopropyl CH), 1.12 (1H, m, cyclopropyl CH); δ_C (75 MHz, $CDCl_3$) 207.1, 135.1 (1), 131.2, 116.9 (2), 104.9 (2), 77.9 (1), 70.6 (2), 49.6 (2), 31.2 (3), 19.6 (1), 10.0 (2); *m/z* (ES+) 202.9 $[M + Na]^+$ (30%), 219.9 $[M + K]^+$ (80%); HRMS $C_{11}H_{17}O_2$ $[M + H]^+$ requires 181.1229, found 181.1227.

SmI_2 mediated cyclisations of ketones 33 and 34

Ketones **33** and **34** were cyclised, in the presence of DMPU or HMPA, according to the general procedure described above. Using this procedure (see text) alcohols **35** and **36** were isolated as a 1:1 mixture of diastereoisomers and as a colourless oil, $R_f = 0.18$ (50% Et_2O–petrol); ν_{max} (liq. film)/cm^{-1} 3476, 2970, 2932, 2875, 1649, 1457, 1135; δ_H (300 MHz, $CDCl_3$) 5.04 (0.5 H, s with fine coupling, $C{=}CH_AH_B$ (**35**)), 5.00 (0.5 H, s with fine coupling, $C{=}CH_AH_B$ (**36**)), 4.82 (1H, s with fine splitting, $C{=}CH_AH_B$), 4.27 (1 H, dt, $J = 7$, 6 Hz, $CHOCH_2$ (**36**)), 4.12 (1 H, m, $CHOCH_2$ (**35**)), 4.08 (0.5 H, dd, $J = 7$, 8 Hz, OCH_AH_B (**36**)), 3.95 (0.5 H, t, $J = 8$ Hz, OCH_AH_B (**35**)), 3.48 (0.5 H, dd, $J = 8$, 10 Hz, OCH_AH_B (**35**)), 3.33 (0.5 H, dd, $J = 7$, 9 Hz, OCH_AH_B (**36**)), 2.55–1.58 (6H, m, $CH_2CH(O)CHCH_2$), 1.42 (1.5 H, s, CH_3COH (**35**)), 1.39 (1.5 H, s, CH_3COH (**36**)), 1.01 (1.5 H, d, $J = 7$ Hz, CH_3CH (**36**)), 0.99 (1.5 H, d, $J = 7$ Hz, CH_3CH (**35**)); δ_C (75 MHz, $CDCl_3$) 153.5, 151.5, 108.2 (2), 106.3 (2), 79.7 (1), 77.4, 76.5 (1), 74.2 (2), 72.4 (2), 72.1, 46.9 (1), 43.9 (2), 43.8 (1), 43.1 (2), 37.6 (1), 37.4 (1), 33.2 (2), 29.9 (2), 29.0 (3), 28.9 (3), 17.2 (3), 12.1 (3); *m/z* (EI+) 182 $[M]^+$ (10%); HRMS $C_{11}H_{18}O_2$ $[M]^+$ requires 182.1307, found 182.1306.

Alcohol **40** was isolated as a colourless oil, $R_f = 0.30$ (50% Et_2O–petrol); ν_{max} (liq. film)/cm^{-1} 3470, 2932, 2875, 1650, 1457, 1381; δ_H (300 MHz, $CDCl_3$) 4.91 (1H, s, $C{=}CH_AH_B$), 4.84 (1H, s, $C{=}CH_AH_B$), 4.38 (1H, s, OH), 4.13 (1H, m, $CHOCH_2$), 3.99 (1H, t, $J = 8$ Hz, OCH_AH_B), 3.58 (1H, dd, $J = 8$, 10 Hz, OCH_AH_B), 2.55 (1H, m, $CHCH_3$), 2.43 (1H, m, CHCHO), 2.26 (1H, dd, $J = 3$, 15 Hz, CH_AH_BCHO), 2.12–2.02 (2 H, m $CH_2C{=}CH_2$), 1.68 (1H, dd, $J = 3$, 15 Hz, CH_AH_BCHO), 1.35 (3H, s, CH_3COH), 1.05 (3H, d, $J = 8$ Hz, CH_3CH); δ_C (75 MHz, $CDCl_3$) 151.6, 107.9 (2), 80.3 (1), 72.4 (2), 70.9, 43.7 (1), 41.5 (2), 38.0 (1), 27.8 (2), 26.3 (3), 11.9 (3); *m/z* (EI+) 182 $[M]^+$ (8%); HRMS $C_{11}H_{18}O_2$ $[M]^+$ requires 182.1307, found 182.1298.

Dimeric alcohol **41** was isolated as a white solid, mp 188–190 °C, $R_f = 0.18$ (50% Et_2O–petrol); δ_H (300 MHz, $CDCl_3$) 4.92 (2H, s, $C{=}CH_AH_B$), 4.86 (2H, s, $C{=}CH_AH_B$), 4.35 (2H, s, OH), 4.13 (2H, br s, $CHOCH_2$), 4.03 (2H, t, $J = 9$ Hz, OCH_AH_B), 3.65 (2H, t, $J = 9$ Hz, OCH_AH_B), 2.55–2.39 (4H, m, $CH_AH_BC{=}CH_2$ + $CHCH_2O$), 2.28 (2H, dd, $J = 15$, 2 Hz, CH_AH_BCHO), 2.23–2.00 (4H, m, $CH_AH_BC{=}CH_2$, $CHCHCH_2O$), 1.70 (2H, dd, $J = 15$, 2 Hz, CH_AH_BCHO), 1.43 (4H, m, $(CH_2)_2$), 1.40 (6H, s, CH_3); δ_C (75 MHz, $CDCl_3$) 151.2, 108.2 (2), 80.2 (1), 71.4 (2), 70.8, 44.2 (1), 42.3 (1), 41.5 (2), 27.7 (2), 27.0 (2), 26.3 (3); *m/z* (CI+) 327 $[M - 2H_2O]^+$ (50%), 344 $[M - H_2O]^+$ (10%).

X-Ray crystal structure was obtained and is published elsewhere.[25]

(±)-(3*S*,3a*R*,6*S*,7a*R*)-3,6-Dimethyl-5-methyleneperhydrobenzo-[*b*]furan-6-yl triethylsilyl ether 49

Alcohol **40** (94 mg, 0.51 mmol) and TEA (2 ml, 15 mmol) in CH_2Cl_2 (4 ml) were stirred at 0 °C under a flow of N_2 and triethylsilyl trifluoromethanesulfonate (3 ml, 9.7 mmol) was added. The reaction mixture was stirred at 0 °C for 1 h and allowed to warm to room temperature. The reaction mixture was washed with aq. $NaHCO_3$ (5 ml) and extracted with CH_2Cl_2 (3 × 5 ml), dried over $MgSO_4$ and concentrated *in vacuo*. The crude reaction mixture was purified by column chromatography, eluting with petrol, gradually increasing the polarity to 2% EtOAc–petrol to give silyl ether **49** as an oil (49 mg, 32%), $R_f = 0.68$ (30% Et_2O–petrol); ν_{max} (liq. film)/cm^{-1} 2955, 2876, 1650, 1459, 1414, 1379; δ_H (300 MHz, $CDCl_3$) 4.92 (1H, s, $C{=}CH_AH_B$), 4.82 (1H, s, $C{=}CH_AH_B$), 4.06 (1H, q, $J = 5$, Hz, $CHOCH_2$), 3.89 (1H, t, $J = 8$ Hz, OCH_AH_B), 3.47 (1H, dd, $J = 8$, 10 Hz, OCH_AH_B), 2.51–2.38 (2H, m, $CHCH_3$ +

C*H*CHCH$_3$), 2.16 (1H, dd, J = 4, 14 Hz, CH_AH$_B$CHO), 2.05 (1H, dd, J = 5, 12 Hz, CH_AH$_B$C=CH$_2$), 2.00 (1H, dd, J = 5, 12 Hz, CH$_A$$H_B$C=CH$_2$), 1.67 (1H, dd, J = 5, 14 Hz, CH$_A$$H_B$CHO), 1.36 (3H, s, C$H_3$COH), 0.99 (3H, d, J = 7 Hz, CHCH_3), 0.94 (9H, t, J = 8 Hz, (CH_3CH$_2$)$_3$), 0.58 (6H, q, J = 8 Hz, (CH$_3$-CH_2)$_3$); δ_C (75 MHz, CDCl$_3$) 153.3, 107.8 (2), 78.1 (1), 72.7, 72.4 (2), 44.2 (2), 43.5 (1), 37.7 (1), 28.66 (2), 28.63 (3), 12.1 (3), 7.1 (3), 6.6 (2); *m*/*z* (CI+) 267 [M − Et]$^+$ (100%), 296 [M]$^+$ (5%); HRMS $C_{17}H_{32}O_2Si$ [M]$^+$ requires 296.2171, found 296.2120.

(±)-(3a*R*,6*R*,7a*R*)-3,6-Dimethyl-5-methyleneperhydrobenzo[*b*]-furan-6-yl (triethylsilyl) ether 48

A 1 : 1 mixture of alcohols **35** and **36** (330 mg, 1.81 mmol) was silylated using identical conditions to those for the silylation of alcohol **40** to give a 1 : 1 mixture of the silyl ethers **48** as an oil (381 mg, 70%), R_f = 0.83 (30% Et$_2$O–petrol); ν_{max} (liq. film)/cm^{-1} 2955, 2875, 1650, 1471, 1384; δ_H (300 MHz, CDCl$_3$) 5.11 (0.5 H, s, C=CH_AH$_B$), 4.91 (0.5 H, s, C=CH_AH$_B$), 4.76 (0.5 H, s, C=CH$_A$$H_B$), 4.74 (0.5 H, s, C=CH$_A$$H_B$), 4.36 (0.5 H, dt, J = 8, 6 Hz, C*H*OCH$_2$), 4.10 (0.5 H, m, C*H*OCH$_2$), 4.05 (0.5 H, t, J = 8 Hz, OCH_AH$_B$), 3.94 (0.5 H, t, J = 8 Hz, OCH_AH$_B$), 3.46 (0.5 H, t, J = 8 Hz, OCH$_A$$H_B$), 3.34 (0.5 H, J = 8 Hz, OCH$_A$$H_B$), 2.82–1.75 (6H, m, CH$_2$CH(O)CHCH$_2$), 1.44 (1.5 H, s, C$H_3$COH), 1.39 (1.5 H, s, C$H_3$COH), 1.05–0.90 (12H, m, (CH_3CH$_2$)$_3$ + CHCH_3), 0.65–0.55 (6H, m, (CH$_3$CH_2)$_3$); δ_C (75 MHz, CDCl$_3$) 153.0, 150.8, 107.9 (2), 106.9 (2), 79.9 (1), 77.0 (1), 74.9, 74.4, 74.3 (2), 72.4 (2), 46.7 (1), 44.8 (2), 44.7 (2), 43.9 (1), 37.6 (1), 35.7 (1), 31.9 (2), 29.7 (2), 29.4 (3), 27.7 (3), 16.5 (3), 12.1 (3), 7.3 (3), 7.2 (3), 7.1 (2), 6.8 (2); *m*/*z* (CI+) 267 [M − Et]$^+$ (100%), 296 [M]$^+$ (30%); HRMS $C_{17}H_{32}O_2Si$ [M]$^+$ requires 296.2171, found 296.2151.

5-Hydroxy-3,6-dimethyl-2,3-dihydrobenzofuran 50

Ozone was bubbled through a stirred solution of silyl ethers **48** (116 mg, 0.38 mmol) in MeOH (10 ml) at −60 °C, until the solution turned deep blue (20 min). The reaction mixture was purged with oxygen then N_2, dimethyl sulfide (6 ml, 0.082 mmol) was added and the reaction mixture allowed to warm to room temperature and concentrated *in vacuo*. The crude reaction mixture was purified by column chromatography, eluting with petrol, gradually increasing the polarity to 20% EtOAc–petrol to give dihydrobenzofuran **50** as a white solid (28 mg, 45%), R_f = 0.35 (30% EtOAc–petrol); δ_H (300 MHz, CDCl$_3$) 6.63 (1H, s, Ar*H*), 6.58 (1H, s, Ar*H*), 4.64 (1H, dd, J = 8, 9 Hz, OCH_AH$_B$), 4.45 (1H, s, O*H*), 4.03 (1H, dd, J = 8, 9 Hz, OCH$_A$$H_B$), 3.48 (1H, apparent sextet, J = 7.5 Hz, C*H*CH$_3$), 2.21 (3H, s, CH_3), 1.30 (3H, d, J = 7 Hz, CH_3); δ_C (75 MHz, CDCl$_3$) 153.7, 147.7, 130.6, 123.1, 111.2 (1), 110.9 (1), 78.8 (2), 36.9 (1), 19.4 (3), 16.3 (3); *m*/*z* (EI+) 164 [M]$^+$ (100%). Data agree with those previously reported.[27]

(±)-(3*R*,3a*R*,6*R*,7a*R*)-3,6-Dimethyl-6-(triethylsilyloxy)perhydrobenzo[*b*]furan-2,5-dione 53

Ruthenium(III) chloride hydrate (50 mg, 0.24 mmol) was added to a biphasic suspension of NaIO$_4$ (0.6 g, 2.8 mmol) in CCl$_4$ (25 ml) and H$_2$O (25 ml). Silyl ethers **48** (65 mg, 0.22 mmol) were added and the reaction mixture was allowed to stir overnight. The reaction mixture was washed with H$_2$O (10 ml) and the aqueous layer extracted with CH$_2$Cl$_2$ (3 × 30 ml), dried over MgSO$_4$ and concentrated *in vacuo*. The crude reaction mixture was purified by column chromatography, eluting with CH$_2$Cl$_2$, gradually increasing the polarity to MeOH to give **53** (15 mg, 22%) as a clear oil, R_f = 0.38 (30% EtOAc–petrol); ν_{max} (liq. film)/cm^{-1} 2956, 2877, 1780, 1728, 1458, 1419, 1376; δ_H (300 MHz, CDCl$_3$) 5.03 (1H, dt, J = 10, 7 Hz, CHO), 3.28 (1H, dd, J = 8, 15 Hz, CH_AH$_B$C=O), 2.73 (1H, m, C*H*CH$_3$), 2.57 (1H, dd, J = 6, 14 Hz, CH_AH$_B$CHO), 2.35 (1H, dd, J = 2, 15 Hz, CH$_A$$H_B$C=O), 2.31 (1H, m, C*H*CHCH$_3$), 1.63 (1H, dd, J = 10, 14 Hz, CH$_A$$H_B$CHO), 1.34 (3H, s, CH$_3$CO), 1.26 (3H, d, J = 7 Hz, CHCH_3), 0.98 (9H, t, J = 8 Hz, (CH_3CH$_2$)$_3$), 0.66 (6H, q, J = 7 Hz, (CH$_3$CH_2)$_3$); δ_C (75 MHz, CDCl$_3$) 208.9, 178.1, 75.5, 74.2 (1), 44.2 (1), 43.6 (2), 37.9 (1), 35.9 (2), 22.9 (3), 13.4 (3), 7.1 (3), 6.6 (2); *m*/*z* (CI+) 255 [M − (CH$_2$CH$_3$)$_2$]$^+$ (25%), 283 [M − CH$_2$CH$_3$]$^+$ (100%), 313 [M + H]$^+$ (10%); HRMS $C_{16}H_{29}O_4Si$ [M + H]$^+$ requires 313.1835, found 313.1823.

(±)-6-*epi*-Paeonilactone A 54

HF·pyridine (40 µl) was added to silyl ether **53** (10 mg, 0.032 mmol) in THF (2 ml) at room temperature under argon and the reaction was stirred for 6 hours. The reaction was quenched with water (1 ml) and the aqueous layer extracted with EtOAc (3 × 2 ml), dried over MgSO$_4$ and concentrated *in vacuo*. The crude reaction mixture was purified by flash column chromatography, eluting with Et$_2$O, to give 6-*epi*-paeonilactone A **54** as a colourless oil (3.0 mg, 53%), R_f = 0.24 (1% Et$_2$O); δ_H (360 MHz, CDCl$_3$) 4.86 (1H, dt, J = 5, 6 Hz, CHO), 3.10 (1H, br s, OH), 2.84 (1H, dd, J = 7, 14 Hz, CH_AH$_B$C=O), 2.64 (1H, m, C*H*CHCH$_3$), 2.53 (1H, dd, J = 9, 14 Hz, CH$_A$$H_B$C=O), 2.48 (1H, dq, J = 5, 7 Hz, C*H*CH$_3$), 2.39 (1H, dd, J = 6, 15 Hz, CH_AH$_B$COH), 2.31 (1H, dd, J = 5, 15 Hz, CH$_A$$H_B$COH), 1.43 (3H, s, CH$_3$), 1.33 (3H, d, J = 7 Hz, CHCH$_3$); δ_C (75 MHz, CDCl$_3$) 207.5, 170.4, 74.4 (1), 74.1, 44.5 (1), 42.5 (1), 42.0 (2), 38.0 (2), 26.2 (3), 14.4 (3); *m*/*z* (CI+) 181 [M − OH]$^+$ (15%), 199 [M + H]$^+$ (60%), 216 [M + NH$_4$]$^+$ (5%); HRMS $C_{10}H_{15}O_4$ [M + H]$^+$ requires 199.0970, found 199.0976.

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