Mechanism and applications of lithium amide-induced asymmetric rearrangements of 4-substituted and 4,4-disubstituted cyclopentene oxides to cyclopentenols

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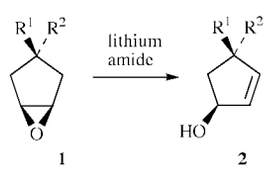
The preparation and lithium amide-induced rearrangements of 1,2-dideuterated 4-substituted cyclopentene oxides **11** and **19** are described, providing insight into the deprotonation mechanisms operating in such systems. Highly enantioselective syntheses of 4-substituted *cis*-4-hydroxymethylcyclopent-2-en-1-ols **32a–c** are described. Also described are asymmetric syntheses of prostaglandin precursor **40** and (+)-iridomyrmecin (**48**) *via* highly enantioselective rearrangement of the epoxide **3** and subsequent Ireland–Claisen rearrangement.

Base-induced rearrangements of epoxides,[1] particularly enantioselective rearrangements of achiral epoxides,[2] are attracting increasing interest. In particular, the chiral base-induced rearrangements of 4-substituted cyclopentene oxides **1** to cyclopentenols **2** have been intensively examined [eqn. (1)].[2] In

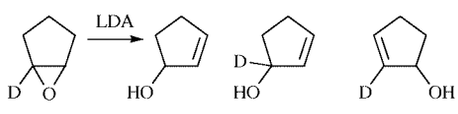


1 2 (1)

this paper we detail the synthesis and rearrangement chemistry of 1,2-dideuterium-labelled 4-substituted cyclopentene oxides, which allow the rearrangement mechanism to be examined.[3] Also described is the asymmetric rearrangement of 4,4-disubstituted cyclopentene oxides, which give additional mechanistic information and provides a method for the enantioselective synthesis of quaternary carbon-containing cyclopentenols.[4] Further applications of the cyclopentene oxide–cyclopentenol asymmetric rearrangement are also demonstrated in syntheses of a key prostaglandin precursor and the insecticidal iridoid (+)-iridomyrmecin.[5] ‡

A deuterium labelling study reported by Thummel and Rickborn in 1970 established that a *syn* β-elimination process operated in the rearrangements of 4-*tert*-butylcyclohexene oxides to cyclohexenols using $LiNEt_2$ in ether–hexane,[6] and this has led to the adoption of a cyclic *syn* β-elimination mechanism involving coordination of the base with the epoxide oxygen to aid in explanations for asymmetric induction in cyclopentene oxide systems with chiral lithium amides.[2] Morgan and Gajewski recently reported a deuterium labelling study with cyclohexene oxide which confirmed a β-elimination mechanism for this ring system.[7] However, their results with cyclopentene oxide indicated that cyclopentenol was formed *via* α-elimination using LDA in ether or benzene [eqn. (2)].

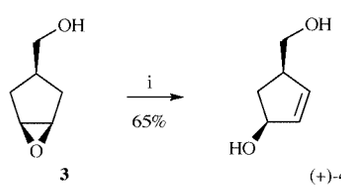
A knowledge of the mechanisms of base-induced rearrangements of epoxides is essential for understanding asymmetric induction processes (and the rational design of new



(2)

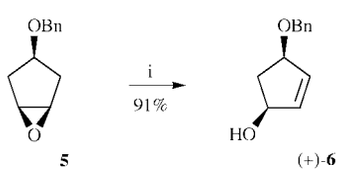
	α only	α or β	β only
benzene	0.23	0.77	—
ether	0.29	0.71	—
HMPA	—	0.50	0.50

chiral bases) in this area. Our study focused on an examination of the mechanism(s) by which lithium amides react with epoxides **3** and **5** to generate the synthetically useful[2] cyclopentenols **4** and **6** (Schemes 1 and 2). In particular, we were



3 (+)-**4**

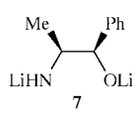
Scheme 1 *Reagents and conditions*: i, Bu^nLi (6 equiv.), (1*R*,2*S*)-norephedrine (3 equiv.), C_6H_6–THF (3:2), 0 °C to 25 °C, 12 h.



5 (+)-**6**

Scheme 2 *Reagents and conditions*: i, Bu^nLi (6 equiv.), (1*R*,2*S*)-norephedrine (3 equiv.), THF −78 °C to 0 °C, 16 h.

interested in the mode of action of dilithiated (1*R*,2*S*)-norephedrine **7**, originally found by Milne and Murphy to give



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cyclopentenol **6** from epoxide **5** in up to 86% ee,[8] and found by ourselves to give the cyclopentenol (+)-**4** from epoxide **3**

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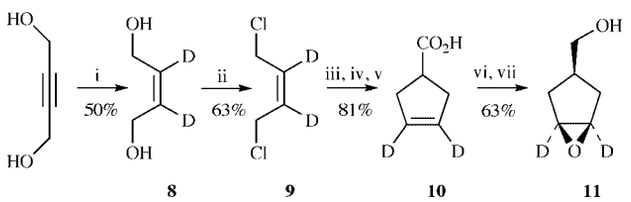
‡ The IUPAC name for iridomyrmecin is hexahydro-4,7-dimethylcyclopenta[*c*]pyran-3(1*H*)-one.

in >95% ee.[9] During the course of our studies we repeated the rearrangement of epoxide **5** using dilithiated (1*R*,2*S*)-norephedrine **7**, since comparison of our results[9] with Milne and Murphy's original report[8] indicated that opposite senses of asymmetric induction had occurred for epoxides **3** and **5**. However, we found that PCC oxidation[10] of the resultant alcohol (+)-**6** from epoxide **5** gave (4*R*)-4-benzyloxycyclopent-2-en-1-one {$[\alpha]_D^{23}$ +21.9 (*c* 0.9 in $CHCl_3$), lit.[11] $[\alpha]_D^{16}$ +42 (*c* 0.9 in $CHCl_3$)}. These results therefore indicate that the predominant sense of asymmetric induction indicated in Milne and Murphy's work[8] should be reversed; the corrected predominant sense of asymmetric induction is shown in Scheme 2.[12]

The acid **10** was considered to be a potentially common precursor to both of the corresponding dideuterated epoxides (**11** and **19**) of epoxides **3** and **5**, and was prepared from *cis*-2,3-dideuteriobut-2-ene-1,4-diol (**8**)[13] following well-established chemistry in the unlabelled series. Thus, the diol **8** was converted into the dichloride **9** (63%) using thionyl chloride and pyridine according to the procedure of Bobbitt and coworkers.[14] The acid **10** was obtained (81%) from the dichloride **9** following the optimised procedure of Deprés and Greene.[15] Subsequent reduction[16] of the acid **10** followed by hydroxy-directed epoxidation[9] gave the epoxide **11** (63%, Scheme 3).[17]

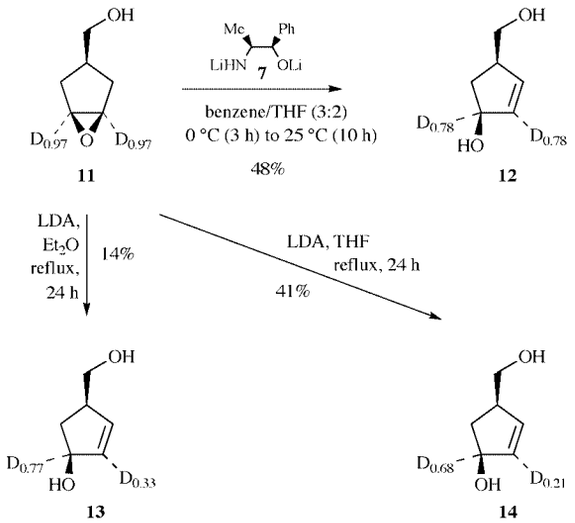


Scheme 3 *Reagents and conditions*: i, D_2 (1 atm.), Lindlar catalyst, py, 40 °C, 120 h; ii, $SOCl_2$, cat. py, −40 °C to 25 °C, 16 h; iii, $(MeO_2C)_2CH_2$, LiH, DMF, 25 °C, 72 h; iv, KOH, 80% aq. EtOH, 25 °C, 18 h; v, 180 °C, 4 h; vi, $LiAlH_4$, Et_2O, 18 h, 25 °C, 12 h; vii, Bu^tOOH, cat. $VO(acac)_2$, CH_2Cl_2, 25 °C, 24 h.

In accord with our earlier work[9] the epoxide **11** (97% deuterium labelled, by ^{1}H-NMR analysis of ring methylenes at δ 1.98 and residual epoxide methines at δ 3.49) smoothly rearranged using dilithiated (1*R*,2*S*)-norephedrine **7** (3 equiv.) to give the alcohol **12** (Scheme 4). Analysis of the ^{1}H-NMR spectrum of alcohol **12** indicated a clean β-elimination mechanism. The partial loss of deuterium at both labelled positions in alcohol **12** also indicates some reversible deprotonation at the α-position (reversible α-deprotonations have been observed in other deuterium labelling studies with epoxides and lithium amides).[1] Identical deuterium levels at the vinylic and allylic positions in alcohol **12** suggest no detectable enantioselectivity in this reversible α-deprotonation process [8% ee was observed in the rearrangement of *exo*-norbornene§ oxide to nortricyclanol using dilithiated (1*R*,2*S*)-norephedrine].[18] Reaction of epoxide **11** with LDA (3 equiv.) in ether was noticeably slower than in the nondeuterated case, and required heating at reflux to give alcohol **13** in poor yield. Significant, but not complete reduction of deuterium at the vinylic position in alcohol **13** is consistent with rearrangement due to a mixture of α- and β-deprotonation; a similar result, but higher yielding, was observed from epoxide **11** and LDA (3 equiv.) in THF which gave alcohol **14** (Scheme 4). In ether, the isolated yield of alcohol **13** does not strictly rule out mainly β-deprotonation operating in combination with a secondary deuterium isotope effect; the result in THF is more convincing in that some of alcohol **14** arises *via* α-deprotonation.

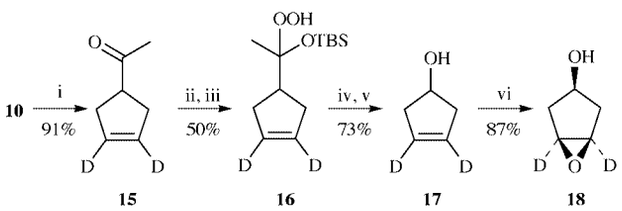
In order to examine the mechanism of the lithium amide-induced rearrangements of the epoxide **5** using dideuterated epoxide **19**, the preparation of the precursor epoxyalcohol **18**

§ The IUPAC name for norbornane is bicyclo[2.2.1]heptane.



Scheme 4

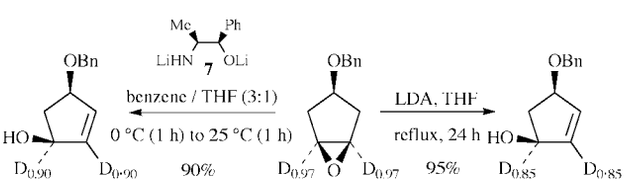
from the ketone **15** (derived from the acid **10**, Scheme 5) was initially attempted *via* a one-pot epoxidation–Baeyer–Villiger protocol. However, all attempts to achieve this resulted in either no reaction, or only conversion to the corresponding epoxyketone, which was also separately unreactive to a variety of Baeyer–Villiger reaction conditions;[19] this lack of reactivity may be due to the electron withdrawing effect of the epoxide functional group. The desired transformation of ketone **15** into epoxyalcohol **18** was successfully carried out in a stepwise manner (Scheme 5). Proceeding *via* the α-silyloxyhydroperoxide **16**[20] is noteworthy in that this sequence achieves the equivalent of a Baeyer–Villiger reaction on the (unstrained) keto group in the presence of the double bond.



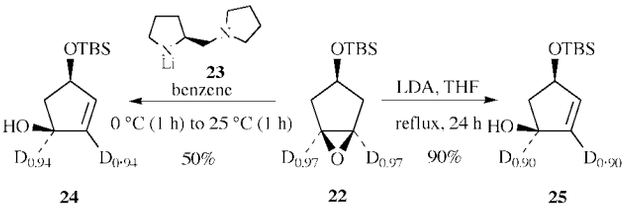
Scheme 5 *Reagents and conditions*: i, MeLi (2 equiv.), Et_2O, 0 °C to 25 °C, 4 h; ii, LDA, TBDMSOTf, THF, HMPA, −78 °C to 0 °C, 1 h; iii, H_2O_2 (2 M in Et_2O), Et_2O, cat. TFA, 25 °C, 14 h; iv, $(Bz)_2O$, DMAP, hexane, 25 °C, 4 h, then reflux, 4 h; v, K_2CO_3, MeOH, 4 h; vi, MCPBA, CH_2Cl_2, 0 °C, 2 h.

The epoxide **19** (easily prepared from **18**)[8] on treatment with dilithiated (1*R*,2*S*)-norephedrine **7** (3 equiv.) gave the alcohol **20**.[21] The ^{1}H-NMR spectrum of alcohol **20** indicated a clean β-elimination process (Scheme 6). β-Elimination was also observed using the epoxide **22** (prepared from **18**)[10] with lithium (*S*)-2-[(pyrrolidin-1-yl)methyl]pyrrolidinide **23**[10] (1.5 equiv.) in benzene, which gave alcohol **24** (Scheme 7). Reaction of epoxides **19** and **22** with LDA (3 equiv.) in THF (−70 °C, 3 h) gave similarly deuterated alcohols **21** and **25**.

The mode of reactivity (α- or β-deprotonation) of an epoxide with a base is significantly influenced by the conformations



Scheme 6

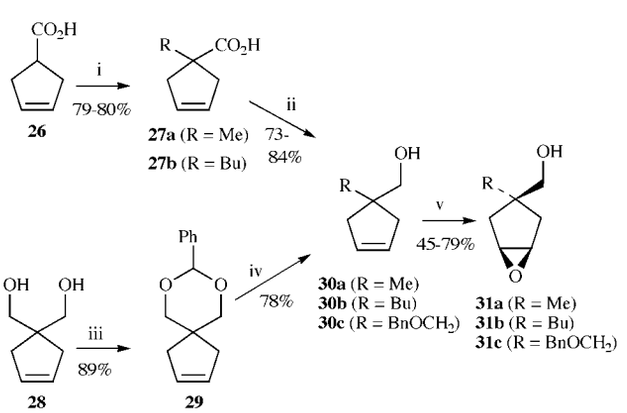


Scheme 7

accessible to the epoxide under the reaction conditions.[1] Calculations indicate that cyclopentene oxide does not easily adopt a conformation suitable for *syn* β-elimination.[7] Our study shows that *cis* 4-substituted cyclopentene oxides such as **3** and **5** generally rearrange to allylic alcohols *via* a β-elimination mechanism (although our results with LDA and dideuterated epoxide **11** suggest that the nature of the base also influences the site of deprotonation). A possible explanation for the switch in mechanistic pathway followed for epoxides **3** and **5** compared with cyclopentene oxide is that the 4-substituent in the former cases results in the 'chair cyclohexane' conformation being favoured (with a suitable geometry for *syn* β-elimination), rather than the 'boat cyclohexane' conformation favoured for cyclopentene oxide. Coordination of the base to both oxygen atoms in epoxides **3** and **5**[10] may also encourage β-elimination.

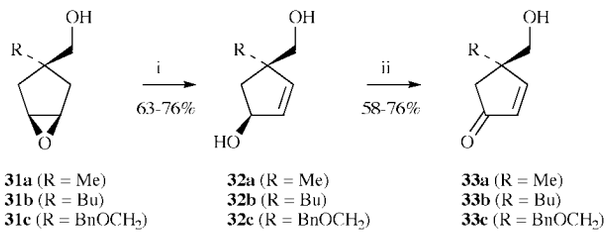
Our above observations do not distinguish between *syn* or *anti* β-deprotonation mechanisms, although a *syn* process would be anticipated on the basis of Thummel and Rickborn's results with 4-*tert*-butylcyclohexene oxides (*vide supra*). To probe this aspect we examined the effect of additional *trans*-substituents on the rearrangement of cyclopentene oxides **1** [eqn. (1), $R^1 = CH_2OH$, $R^2 \neq H$]. If a *syn* β-deprotonation were to operate *trans*-substituents were predicted not to disrupt substantially the transition state aggregate for rearrangement, and hence the ee, from that which operated with the original epoxide **3** (Scheme 1). Aside from the mechanistic information obtained, this study would also develop methodology for the asymmetric synthesis of quaternary carbon-containing materials, itself an area of considerable research interest.[22]

In order to examine this chemistry readily available cyclopent-3-enecarboxylic acid **26**[15] (*cf.* Scheme 3) and cyclopent-3-ene-1,1-dimethanol **28**[23] were first converted into the alcohols **30a–c** using standard procedures (Scheme 8), followed by hydroxyl-directed epoxidation under our previously reported conditions[9] to give the representative epoxy alcohols **31a–c**. Analysis of the ^{1}H-NMR spectra of the crude epoxy alcohols **31a–c** indicated that, in each case, only a single isomer was produced. *cis*-Relative stereochemistry between the hydroxymethyl and epoxide groups were assigned by analogy with our earlier work.[9]



Scheme 8 *Reagents and conditions*: i, LDA (2 equiv.), RI, THF, 0 °C, 15 h; ii, $LiAlH_4$, Et_2O, 0 °C, 3 h; iii, PhCHO, cat. PTSA, toluene, reflux, 14 h; iv, DIBAL-H, toluene, 0 °C, 14 h; v, Bu^{t}OOH, cat. $VO(acac)_2$, CH_2Cl_2, 25 °C, 24 h.

Pleasingly, the epoxy alcohols **31a–c** smoothly rearranged using dilithiated (1*R*,2*S*)-norephedrine **7** to give the *cis*-diols **32a–c** (Scheme 9). The *cis*-diols **32a–c** are potentially useful intermediates in the synthesis of carbocyclic nucleoside analogues related to the anti-HIV agent carbovir[9,24] and diol **32a** also has potential utility in the synthesis of the antifungal antibiotic viridenomycin.[25] Selective oxidation of the allylic hydroxy[26] of *cis*-diols **32a–c** gave the hydroxy enones **33a–c**. Chiral HPLC analysis of the 2,4-dinitrobenzoate derivatives of the hydroxy enones **33a–c** indicated that high asymmetric induction had been maintained in the rearrangements of the epoxy alcohols **31a–c** [R = Me (99% ee), Bu (96% ee), $BnOCH_2$ (89% ee)], compared with that observed with epoxide **3**.[9]



Scheme 9 *Reagents and conditions*: i, (1*R*,2*S*)-norephedrine (3 equiv.), BuLi (6 equiv.), 3:2 benzene–THF, 0 °C to 25 °C, 12 h; ii, PDC, 2% AcOH in EtOAc, 25 °C, 1.5 h.

The absolute stereochemistry of the major enantiomer of the diol **32b** is as shown in Scheme 9, and was determined *via* the corresponding hydroxy enone **33b** after 3,5-dinitrobenzoate derivatisation, ketalisation [(−)-(2*R*,3*R*)-2,3-bis(TMSO)-butane, cat. TMSOTf],[27] and subsequent X-ray crystallographic analysis of the resultant ketal **34** (Fig. 1). The sense of asymmetric induction parallels that observed in our earlier study (Scheme 1).[9] The absolute stereochemistry induced in the diols **32a**,**c** was assigned by analogy with diol **32b**.

Although alcohols **4** and **32** are of demonstrated[9] and potential[24] utility in the preparation of carbocyclic nucleosides, we sought to demonstrate further their utility in synthesis. Here we detail the conversion of alcohol **4** by [3,3] sigmatropic rearrangement to functionalised 1,2-dialkylcyclopent-3-enes with control of relative and absolute stereochemistry and, specifically, to prostaglandin precursor **40** and (+)-iridomyrmecin (**48**).[5]

For the purposes of merging with previous prostaglandin syntheses,[28] the diol (−)-**4** [readily available from epoxide **3**

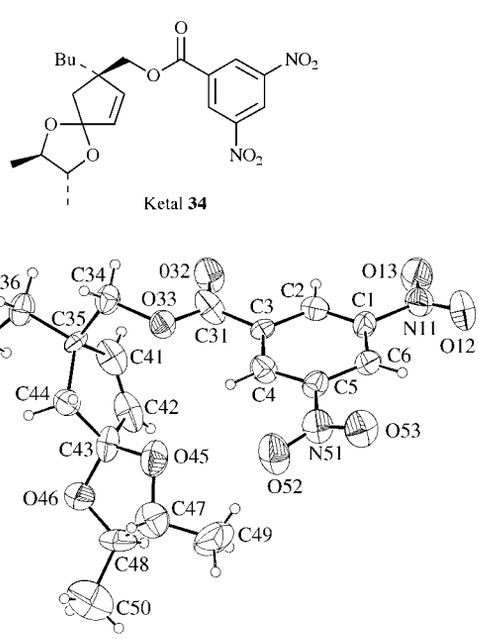
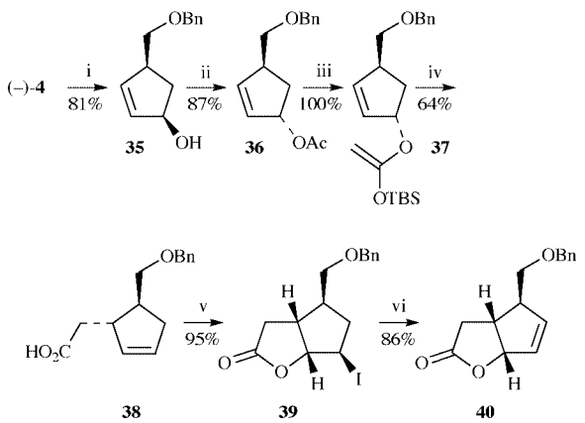


Fig. 1 Molecular structure of ketal **34** (thermal ellipsoids are at the 30% level).

using dilithiated (1*S*,2*R*)-norephedrine *ent*-**7**][9] was first monoprotected[29] as its benzyl ether **35** (81%, Scheme 10). Benzyl ether **35** was then acetylated under Mitsunobu conditions,[30] which gave the *trans*-acetate **36** (87%) along with the chromatographically separable regioisomeric (from S_N2' reaction) *trans*-acetate (10%); formation of the latter was minimised at −10 °C. After some experimentation, conditions were found which reproducibly allowed conversion of the *trans*-acetate **36** to acid **38**. Thus, silylation of acetate **36** using Raucher and Schindele's general procedure[31] gave complete conversion to the silyl ketene acetal **37** which was directly heated in xylenes at 190 °C in a sealed tube[32] to give, on basic work-up, the acid **38** (64%). Iodolactonisation of the acid **38** (95%) and subsequent elimination of HI from the iodolactone **39** using DBU gave the lactone **40**[33] {86% [37% overall from diol (−)-**4**], $[\alpha]_D^{20}$ +195.3 (*c* 1.0 in $CHCl_3$), lit.[33a] $[\alpha]_D^{28}$ +205.3 (*c* 1 in $CHCl_3$)}. Lactone **40** has been converted to PGA_2 and thence to all the primary prostaglandins,[28] and has also been used in the synthesis of tylonolide hemiacetal.[33c] The present asymmetric synthesis of lactone **40** compares with the original resolution- and subsequent chiral auxiliary-based approaches,[28] and more recent enantioselective developments.[34]

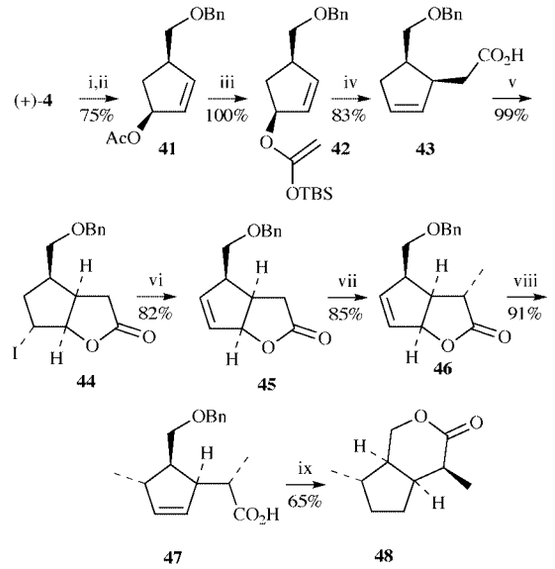


Scheme 10 *Reagents and conditions*: i, NaH (1.15 equiv.), BnBr, DMF, −60 °C (3 h) to 25 °C (14 h); ii, AcOH (4 equiv.), PPh_3 (4 equiv.), DEAD. (2 equiv.), Et_2O, −10 °C (3 h) to 25 °C (14 h); iii, LDA (1.4 equiv.), TBDMSCl (1.3 equiv.), HMPA, THF, −78 °C (35 min) to 25 °C (20 min); iv, xylenes, 190 °C (sealed tube), 18 h, then aq. NaOH, THF, 2 h; v, I_2 (3 equiv.), $NaHCO_3$ (30 equiv.), MeCN, 25 °C, 24 h; vi, DBU, THF, reflux, 3 h.

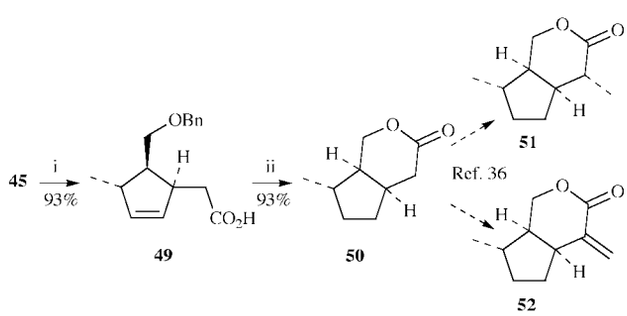
The synthesis of (+)-iridomyrmecin (**48**) from diol (+)-**4** proceeded initially along similar lines to that described above, but without the requirement for inversion during acetylation (Scheme 11). Lactone **45** (as the racemate) has previously been converted into (±)-iridomyrmecin (**48**) in three steps.[35,36] This work was followed with slight modifications to the first two steps. Thus, in our hands, methylation of the lactone **45** (85%) required HMPA as an additive and subsequent S_N2' ring-opening of **46** was best effected using methodology developed by Curran and co-workers,[37] to give the acid **47** (91%). Treatment of the acid **47** with Pd/C in EtOH under H_2[35] gave (+)-iridomyrmecin (**48**) {65% [26% overall from (+)-**4**], $[\alpha]_D^{20}$ +199.1 (*c* 0.22 in CCl_4), lit.[38] $[\alpha]_D^{17}$ +205 (*c* 0.223 in CCl_4)}.

The present enantioselective synthesis of iridomyrmecin (**48**) compares with previous asymmetric syntheses using substrates from the 'chiral pool' and chiral auxiliary-based approaches.[36] Lactone **50** is available *via* methyl cupration of lactone **45**, which constitutes formal syntheses of the iridoids (−)-isoiridomyrmecin (**51**) and (+)-teucriumlactone (**52**) (Scheme 12).[39]

In summary, deuterium labelling studies have been used to establish that the lithium amide-induced desymmetrising rearrangements of 4-substituted cyclopentene oxides to cyclopentenols generally proceed by a β-elimination mechanism.



Scheme 11 *Reagents and conditions*: i, as i in Scheme 10; ii, Ac_2O, py, $CHCl_3$, 25 °C, 3 h; iii–vi as iii–vi in Scheme 10; vii, LDA (1.25 equiv.), HMPA (1.1 equiv.), MeI (4.5 equiv.), THF, −78 °C, 5 h; viii, MeMgBr (2 equiv.), CuBr·Me_2S (1.8 equiv.), Me_2S, THF, −25 °C, 5 h; ix, H_2 (1 atm.), 10% Pd/C, EtOH, 25 °C, 48 h.



Scheme 12 *Reagents and conditions*: i, ii, as viii, ix in Scheme 11.

Enantioselective rearrangement of achiral 4,4-disubstituted cyclopentene oxides has been shown to provide quaternary carbon-containing cyclopentenols in good ee and indicates that the β-elimination is a *syn* process. Finally, the utility of cyclopentenols obtained by epoxide rearrangement have been further demonstrated in enantioselective syntheses of a prostaglandin intermediate and iridoids.

Experimental

General details

All reactions requiring anhydrous conditions were conducted in flame-dried apparatus under an atmosphere of argon. Syringes and needles for the transfer of reagents were dried at 140 °C and allowed to cool in a desiccator over P_2O_5 before use. Ethers were distilled from sodium benzophenone ketyl; (chlorinated) hydrocarbons, and amines from CaH_2. DMF was dried ($MgSO_4$ unless stated otherwise) and then distilled under reduced pressure. Internal reaction temperatures are reported unless stated otherwise. Reactions were monitored by TLC using commercially available glass-backed plates, pre-coated with a 0.25 mm layer of SiO_2 containing a fluorescent indicator (Merck). Column chromatography was carried out on Kieselgel 60 (40–63 μm). Light petroleum refers to the fraction with bp 40–60 °C. $[\alpha]_D$ Values are given in 10^{-1} deg cm^2 g^{-1}. IR spectra were recorded as thin films unless stated otherwise. Peak intensities are specified as strong (s), medium (m) or weak (w). ^1H and ^{13}C NMR spectra were recorded in $CDCl_3$ unless stated otherwise with Varian Gemini 200, Bruker AC200, Bruker

WM250, Bruker WH300, JEOL EX400, Bruker AM500 or Bruker AMX500 spectrometers. Chemical shifts are reported relative to $CHCl_3$ [δ_H 7.26, δ_C(central line of t) 77.0]. Coupling constants (J) are given in Hz. Chiral stationary phase HPLC was performed using a Daicel Chiralpak AD column (4.6 mm × 250 mm) on a Gilson system with 712 Controller Software and a 118 UV/VIS detector set at 254 nm unless stated otherwise. Retention times for major ($t_R$mj) and minor ($t_R$mn) enantiomers are given in min. Chiral GC was performed using a 50m GTA column (Chiraldex BAS technical, injection temperature 250 °C, detector temperature 300 °C, column temperature 100 °C, carrier gas H_2 at 100 KPa).

1-([3,4-$^2H_2$]Cyclopent-3-en-1-yl)ethanone 15

MeLi (1.6 mol dm^{-3} in Et_2O; 12.8 cm^3, 20.5 mmol) was added over a period of 15 min to a vigorously stirred solution of acid **10** (1.0 g, 8.8 mmol, 97% dideuterium labelled by ^{1}H NMR analysis of ring methylenes at δ 2.67 and residual =CHs at δ 5.63) in Et_2O (20 cm^3) at 0 °C. On formation of a heavy white precipitate the reaction was warmed to room temperature and allowed to stir for 4 h. The reaction was then cooled to 0 °C and H_2O (5 cm^3) carefully added. After 15 min the organic layer was separated, washed with H_2O (5 × 10 cm^3), dried ($MgSO_4$) and evaporated under reduced pressure (without external heating) to give *ketone* **15**[40] (0.90 g, 91%); R_f 0.46 (50% Et_2O in light petroleum); ν_{max}/cm^{-1} 2859w, 2361w, 1710s, 1397m, 1364m, 1275m, 1207m and 838s; δ_H(200 MHz) 5.66 (0.06H, s, 2 × CH=), 3.23 (1H, quint, J 7, CHC=O), 2.60 (4H, d, J 7, 2 × CH_2) and 2.18 (3H, s, Me); δ_C(50 MHz) 209.4 (C=O), 128.0 (m, 2 × CD=), 49.1 (*C*HC=O), 34.1 (2 × CH_2) and 27.5 (Me); *m*/*z* (EI) 112 (M$^+$, 52%), 111 (17), 97 (48), 96 (17), 68 (86) and 67 (62) (Found: M$^+$, 112.0857. $C_7D_2H_8O$ requires M, 112.0857).

1-(*tert*-Butyldimethylsilyloxy)-1-([3,4-$^2H_2$]cyclopent-3-en-1-yl)-ethyl hydroperoxide 16

BuLi (1.6 mol dm^{-3} in hexanes; 32.4 cm^3, 51.8 mmol) was added to a solution of diisopropylamine (7.65 cm^3, 53.6 mmol) in THF (50 cm^3) at 0 °C. After 5 min HMPA (8.8 cm^3) was added and the reaction cooled to −78 °C. After 15 min ketone **15** (4.00 g, 35.7 mmol) in THF (100 cm^3) was added and the reaction maintained at −78 °C for 20 min. TBDMSOTf (10.7 g, 40.48 mmol) in THF (10 cm^3) was added and the reaction allowed to warm to room temperature. After 1 h the reaction was partitioned between pentane (100 cm^3) and aq. NaOH (0.1 mol dm^{-3}; 100 cm^3) The organic layer was separated and the aq. layer extracted with pentane (2 × 100 cm^3). The combined organic solutions were washed with aq. NaOH (0.1 mol dm^{-3}; 2 × 50 cm^3), H_2O (50 cm^3), dried (Na_2SO_4) and evaporated under reduced pressure to give a yellow oil, the *silyl enol ether* (8.0 g, 99%); R_f 0.80 (20% Et_2O in light petroleum); ν_{max}/cm^{-1} 3401w, 2929s, 2857s, 1658m, 1620m, 1471m, 1463m, 1362s, 1292m, 1254m, 1174m, 1031m and 1004s; δ_H(200 MHz) 5.67 (0.06H, s, 2 × CH=), 4.09 (1H, d, J 2, C*H*H=), 3.97 (1H, d, J 2, CH*H*=), 2.97 (1H, m, C*H*C=CH_2), 2.46 (4H, m, 2 × CH_2), 0.96 (9H, s, 3 × Me) and 0.19 (6H, s, 2 × Me); δ_C(50 MHz) 162.1 (C, quat.), 129.8 (m, 2 × CD=), 87.7 (CH_2=), 44.0 (*C*HC=), 36.5 (2 × CH_2), 25.5 (3 × Me), 23.1 (C, quat. Si) and −5.0 (2 × Me); *m*/*z* (CI, NH_3) 227 (M + H$^+$, 20%), 133 (12), 132 (96), 130 (13) and 102 (100) (Found: M + H$^+$, 227.1800. $C_{13}D_2H_{23}OSi$ requires M, 227.1800).

A solution of H_2O_2 [2 mol dm^{-3} in Et_2O, prepared from a mixture of H_2O_2 in H_2O (30% w/v, 339 cm^3, 1 mol dm^{-3}) and Et_2O (120 cm^3) then dried ($MgSO_4$) and filtered; 82.7 cm^3, 165 mmol] was added carefully to a solution of the above silyl enol ether (7.5 g, 33 mmol) and TFA (0.0127 cm^3, 1.66 mmol) in Et_2O (70 cm^3) at 0 °C. The reaction was then allowed to warm to room temperature. After 14 h the reaction was partitioned between pentane (100 cm^3) and saturated aq. $NaHCO_3$ (50 cm^3). The organic layer was separated and the aq. layer extracted with pentane (3 × 50 cm^3). The combined organic extracts were washed with brine (2 × 50 cm^3), dried (Na_2SO_4) and the solvent carefully removed under reduced pressure without external heating. Purification of the residue by column chromatography (20% Et_2O in pentane) gave a colourless oil, *α-silyloxyhydroperoxide* **16** (4.38 g, 51%, 98% based on recovered ketone **15**, 1.74 g); R_f 0.62 (20% Et_2O in light petroleum); ν_{max}/cm^{-1} 3350m, 2954s, 2886s, 1472m, 1463s, 1253s, 1173s, 1155s, 1133s, 1110s and 1006m; δ_H(200 MHz) 7.46 (1H, br s, OOH), 5.65 (0.06H, s, 2 × CH=), 2.76 (1H, quint, J 5, C*H*COOH), 2.43–2.20 (4H, m, 2 × CH_2), 1.37 (3H, s, Me), 0.91 (9H, s, 3 × Me) and 0.21 (6H, s, 2 × Me); δ_C(125 MHz) 129.8 (m, 2 × CD=), 107.8 (C, quat.), 44.8 (*C*HCOOH), 34.6 (CH_2), 34.3 (CH_2), 25.6 (3 × Me), 18.0 (CSi, quat.), 0.8 (Me) and −3.2 (2 × Me); *m*/*z* (EI) 244 (15%), 243 (22), 227 (20), 193 (15), 192 (100), 162 (23), 146 (54), 132 (42), 129 (75), 128 (41) and 102 (57).

[3,4-$^2H_2$]Cyclopent-3-en-1-ol 17

DMAP (1.29 g, 10.56 mmol) was added slowly to a stirred solution of α-silyloxyhydroperoxide **16** (2.30 g, 8.83 mmol) and Bz_2O (2.39 g, 10.6 mmol) in hexane (10 cm^3) at −20 °C. The reaction was allowed to warm to room temperature and stirred for 4 h then heated to reflux. After a further 4 h the reaction was cooled to room temperature and filtered through Celite (5 g), washed with saturated aq. NH_4Cl (2 × 10 cm^3) and brine (2 × 10 cm^3), dried ($MgSO_4$) and evaporated under reduced pressure. The residue was dissolved in MeOH (10 cm^3) and stirred vigorously with K_2CO_3 (1 g) for 4 h. The reaction was then filtered and evaporated under reduced pressure without external heating. Purification of the residue by column chromatography (20% Et_2O in pentane) gave a colourless oil, *alcohol* **17**[41] (0.560 g, 73%); R_f 0.10 (20% Et_2O in pentane); ν_{max}/cm^{-1} 3338s, 3055m, 2929s, 2848s, 1442m, 1074m and 1038s; δ_H(200 MHz) 5.72 (0.06H, m, 2 × CH=), 4.53 (1H, quint, J 5, C*H*OH), 2.65 (2H, dd, J 4 and 8, 2 × C*H*H), 2.29 (2H, dd, J 4 and 8, 2 × CH*H*) and 1.60 (1H, br s, OH); δ_C(50 MHz) 128.5 (m, 2 × CD=), 71.3 (CHOH) and 42.3 (2 × CH_2); *m*/*z* (EI) 86 (M$^+$, 57%), 85 (50), 58 (42), 57 (100) and 56 (47) (Found: M, 86.0701. $C_5D_2H_6O$ requires M, 86.0701).

(1α,3α,5α)-[1,5-$^2H_2$]-Oxabicyclo[3.1.0]hexan-3-ol 18

MCPBA (55% w/w in H_2O; 0.801 g, 2.55 mmol) was added portion-wise to a stirred solution of alcohol **17** (0.200 g, 2.32 mmol) in CH_2Cl_2 (6 cm^3) at 0 °C. The reaction was stirred at 0 °C for 1 h then allowed to warm to room temperature and stirred for a further 1 h. Excess $Ca(OH)_2$ was then added and the reaction was filtered and evaporated under reduced pressure. Purification of the residue by column chromatography (50% Et_2O in pentane) gave a colourless oil, *epoxyalcohol* **18**[42] (0.206 g, 87%, 97% deuterium labelled by ^{1}H-NMR analysis of ring methylenes at δ 2.33–2.02 and residual CHOs at δ 3.58); R_f 0.40 (Et_2O); ν_{max}/cm^{-1} 3436s, 2960m, 2926m, 1632m, 1413m, 1357m, 1304m, 1190m and 1067s; δ_H(200 MHz) 4.02 (1H, quint, J 3, C*H*OH), 3.58 (0.06H, s, 2 × CHO) and 2.33–2.02 (4H, m, 2 × CH_2); δ_C(50 MHz) 69.3 (CHOH), 57.4 (m, 2 × CDO) and 37.4 (2 × CH_2); *m*/*z* (EI) 86 (5%), 84 (12), 82 (6), 69 (16), 68 (48) and 43 (100).

(1α,3α,5α)-[1,5-$^2H_2$]-3-Benzyloxy-6-oxabicyclo[3.1.0]hexane 19

Sodium hydride (27.3 mg, 1.14 mmol) was added to a stirred solution of epoxyalcohol **18** (80 mg, 0.784 mmol) in THF (2 cm^3) at 0 °C. After 15 min BnBr (112 μl, 0.941 mmol) was added and the reaction stirred at 0 °C for 1 h. The reaction was then allowed to warm to room temperature and stirred for a further 1 h. MeOH (2 cm^3) was added and after 15 min evaporated under reduced pressure. The residue was taken up in Et_2O (5 cm^3) and washed with H_2O (2 × 5 cm^3), brine (2 × 5 cm^3),

dried ($MgSO_4$) and evaporated under reduced pressure. Purification of the residue by column chromatography (50% Et_2O in pentane) gave a colourless oil, *epoxide* **19**[43] (138.5 mg, 92%); R_f 0.25 (50% Et_2O in pentane); ν_{max}/cm^{-1} 3064m, 2923s, 2861s, 1496m, 1364s, 1349s, 1096s, 1064s and 1028m; δ_H(200 MHz) 7.39–7.19 (5H, m, 5 × Ar), 4.42 (2H, s, CH_2Ar), 4.00 (1H, quint, *J* 7, C*H*OH), 3.47 (0.06H, s, 2 × CHO), 2.14 (1H, d, *J* 15, C*H*H) and 1.89 (1H, d, *J* 15, CH*H*); δ_C(125 MHz) 138.7 (Ar, quat.), 128.5 (2 × Ar), 127.9 (2 × Ar), 127.6 (Ar), 77.3 (CH_2Ar), 70.8 (CHOBn), 57.6 (m, 2 × CDO) and 34.8 (2 × CH_2); *m*/*z* (CI, NH_3) 210 (M + NH_4^+, 100%), 209 (15), 194 (31), 193 (M + H^+, 14) and 120 (22) (Found: M + H^+, 193.119. $C_{12}D_2H_{13}O_2$ requires *M*, 193.1189).

1-Butylcyclopent-3-enecarboxylic acid 27b

BuLi (2.5 mol dm^{-3} in hexanes; 15.0 cm^3, 37.5 mmol) was added dropwise to a stirred solution of diisopropylamine (5.5 cm^3, 39 mmol) in THF (10 cm^3) at 0 °C. After 15 min a solution of cyclopent-3-enecarboxylic acid **26**[15] (2.0 g, 18 mmol) in THF (5 cm^3) was added dropwise, at 0 °C. After a further 15 min BuI (2.0 cm^3, 18 mmol) was added in one portion. The reaction mixture was allowed to warm to room temperature overnight. The reaction was made acidic by dropwise addition of aq. HCl (2 mol dm^{-3}, *ca.* 10 cm^3) and then extracted with Et_2O (2 × 20 cm^3). The combined ethereal extracts were washed with aq. HCl (2 mol dm^{-3}; 3 × 20 cm^3), H_2O (2 × 20 cm^3) and brine (2 × 20 cm^3), dried ($MgSO_4$) and concentrated under reduced pressure. Purification of the residue by column chromatography (50% Et_2O in light petroleum) gave a colourless oil, *acid* **27b** (2.40 g, 79%); R_f 0.39 (40% Et_2O in light petroleum); ν_{max}/cm^{-1} 3080s, 2660m, 1718w and 1620w; δ_H(400 MHz) 5.68–5.63 (2H, m, 2 × CH=), 2.94 (2H, dd, *J* 10 and 7, 2 × CH*H*), 2.26 (2H, dd, *J* 10 and 7, 2 × CH*H*), 1.72–1.66 (2H, m, CH_2), 1.38–1.24 (4H, m, 2 × CH_2) and 0.91 (3H, t, *J* 7, Me); δ_C(100 MHz) 185.2 (C=O, quat), 128.9 (2 × CH=), 52.4 (C, quat.), 45.5 (2 × CH_2), 39.4 (CH_2), 27.7 (CH_2), 24.2 (CH_2) and 13.8 (Me); *m*/*z* (EI) 168 (M^+, 11%), 123 (98), 111 (67), 81 (51), 79 (56) and 67 (100) (Found: M^+, 168.1150. $C_{10}H_{16}O_2$ requires *M*, 168.1150).

8-Phenyl-7,9-dioxaspiro[4.5]dec-2-ene 29

A solution of cyclopent-3-ene-1,1-dimethanol **28**[23] (0.500 g, 3.9 mmol), benzaldehyde (3.65 cm^3, 35.9 mmol) and PTSA (10 mg) in toluene (15 cm^3) was heated at reflux in a Dean–Stark apparatus. After 14 h the reaction was cooled to room temperature, washed with saturated aq. $NaHCO_3$ (2 × 10 cm^3) and brine (2 × 10 cm^3), dried ($MgSO_4$) and evaporated under reduced pressure. Purification of the residue by column chromatography (10% Et_2O in light petroleum) gave a white solid, *acetal* **29** (0.748 g, 89%); R_f 0.45 (50% Et_2O in light petroleum); mp 57–59 °C (from Et_2O) (Found: C, 65.70; H, 9.38. $C_{14}H_{16}O_2$ requires C, 65.59; H, 9.44%); ν_{max}/cm^{-1}(CH_2Cl_2) 3434s, 3054s, 3035s, 1643s, 1500s, 1451s and 1025s; δ_H(400 MHz) 7.35–7.28 (5H, m, Ar), 5.76–5.68 (1H, m, CH=), 5.65–5.61 (1H, m, CH=), 5.50 (1H, s, C*H*Ph), 3.98 (2H, d, *J* 16, 2 × CH*H*O), 3.79 (2H, d, *J* 16, 2 × C*H*HO), 2.72 (2H, d, *J* 4, CH_2) and 2.00 (2H, d, *J* 4, CH_2); δ_C(100 MHz) 138.4 (Ar, quat.), 129.8 (CH=), 128.8 (CH=), 128.3 (2 × Ar), 127.5 (Ar), 126.1 (2 × Ar), 101.6 (*C*HPh), 76.2 (2 × CH_2O), 41.9 (CH_2), 40.8 (C, quat.) and 38.3 (CH_2).

1-Methylcyclopent-3-ene-1-methanol 30a

A solution of 1-methylcyclopent-3-ene-1-carboxylic acid **27a**[44] (0.50 g, 3.97 mmol) in Et_2O (5 cm^3) was added dropwise to a stirred solution of $LiAlH_4$ (0.24 g, 6.35 mmol) in Et_2O (15 cm^3) at 0 °C. After 3 h H_2O (0.24 cm^3), aq. NaOH (0.1 mol dm^{-3}; 0.24 cm^3) and H_2O (0.72 cm^3) were successively added to the reaction at 0 °C. The resulting mixture was filtered and the residue washed with Et_2O (2 × 10 cm^3). The combined organic layers were washed with aq. NaOH (0.1 mol dm^{-3}; 2 × 10 cm^3), brine (2 × 10 cm^3), dried ($MgSO_4$) and evaporated under reduced pressure to give a colourless oil, *alcohol* **30a** (0.37 g, 84%); R_f 0.35 (20% Et_2O in light petroleum); ν_{max}/cm^{-1} 3347s, 2927s, 1628w, 1354m and 1044s; δ_H(400 MHz) 6.53–6.44 (2H, m, 2 × CH=), 4.26 (2H, s, CH_2O), 3.23 (2H, dd, *J* 10 and 7, 2 × CH*H*), 2.99 (2H, dd, *J* 10 and 7, 2 × C*H*H) and 2.02 (3H, s, Me); δ_C(100 MHz) 129.0 (2 × CH=), 70.9 (CH_2O), 43.0 (2 × CH_2), 42.8 (C, quat.) and 24.8 (Me); *m*/*z* (EI) 112 (M^+, 12%), 97 (39), 93 (37), 81 (45), 69 (52) and 67 (26) (Found: M^+, 112.0888. $C_7H_{12}O$ requires *M*, 112.0888).

1-Butylcyclopent-3-ene-1-methanol 30b

Following the procedure for the preparation of alcohol **30a**, but using acid **27b** (2.0 g, 11.9 mmol) and $LiAlH_4$ (0.65 g, 17.2 mmol) gave a colourless oil, *alcohol* **30b** (1.33 g, 73%); R_f 0.42 (50% Et_2O in light petroleum); ν_{max}/cm^{-1} 3343s, 2924s, 1622w, 1349s and 1048s; δ_H(400 MHz) 5.63–5.56 (2H, m, 2 × CH=), 3.46 (1H, d, *J* 5, CH*H*O), 3.42 (1H, d, *J* 5, C*H*HO), 2.37–2.31 (4H, m, 2 × allylic CH_2), 1.52–1.16 (6H, m, 3 × CH_2) and 1.22 (3H, t, *J* 7, Me); δ_C(100 MHz) 129.0 (2 × CH=), 68.9 (CH_2O), 45.8 (C, quat.), 41.1 (2 × allylic CH_2), 37.2 (CH_2), 26.8 (CH_2), 23.4 (CH_2) and 14.0 (Me); *m*/*z* (EI) 154 (M^+, 5%), 123 (43), 81 (33), 80 (52), 77 (30) and 67 (41) (Found: M^+, 154.1358. $C_{10}H_{18}O$ requires *M*, 154.1358).

1-Benzyloxymethylcyclopent-3-ene-1-methanol 30c

A solution of DIBAL-H (1.0 mol dm^{-3} in toluene; 5.77 cm^3, 5.77 mmol) was added dropwise to a stirred solution of acetal **29** (0.500 g, 2.31 mmol) in toluene (10 cm^3) at 0 °C. After 14 h MeOH (2 cm^3) was added at 0 °C, followed by aq. NaOH (0.1 mol dm^{-3}; 2 cm^3). The organic layer was separated and washed with brine (2 × 5 cm^3), dried ($MgSO_4$) and evaporated under reduced pressure. Purification of the residue by column chromatography (50% Et_2O in light petroleum) gave a colourless oil, *alcohol* **30c** (0.390 g, 78%); R_f 0.13 (25% Et_2O in light petroleum); ν_{max}/cm^{-1} 3430s, 3053s, 2849s, 1621m, 1498s, 1455s and 1030s; δ_H(400 MHz) 7.40–7.28 (5H, m, Ar), 5.58 (2H, s, 2 × CH=), 4.54 (1H, d, *J* 7, CH*H*Ph), 4.50 (1H, d, *J* 7, C*H*HPh), 3.63 (1H, d, *J* 6.5, CH*H*OH), 3.59 (1H, d, *J* 6.5, C*H*HOH), 3.48 (2H, s, CH_2OBn), 2.45–2.35 (1H, br s, OH), 2.24 (2H, d, *J* 6, 2 × CH*H*) and 2.17 (2H, d, *J* 6, 2 × C*H*H); δ_C(100 MHz) 138.0 (Ar, quat.), 128.8 (2 × CH=), 128.4 (2 × Ar), 127.7 (Ar), 127.5 (2 × Ar), 77.8 (*C*H_2Ph), 73.5 (*C*H_2OBn), 69.8 (CH_2OH), 47.0 (C, quat.) and 39.0 (2 × CH_2); *m*/*z* (CI, NH_3) 236 (M + NH_4^+, 46%) and 219 (M + H^+, 100) (Found: M + H^+, 219.1385. $C_{14}H_{19}O_2$ requires *M*, 219.1385).

(1α,3α,5α)-3-Methyl-6-oxabicyclo[3.1.0]hexane-3-methanol 31a

tert-Butyl hydroperoxide[9] (6.9 mol dm^{-3} in CH_2Cl_2; 1.84 cm^3, 12.8 mmol) was added dropwise to a stirred solution of alcohol **30a** (0.70 g, 6.2 mmol) and vanadyl acetylacetonate (*ca.* 20 mg) in CH_2Cl_2 (10 cm^3) at room temperature. After 24 h aq. sodium sulfite (15% w/v; 10 cm^3) was added and the reaction mixture stirred until tested negative for oxidant by acidified starch–iodine paper (*ca.* 1 h). The reaction was filtered and the filtrate washed with brine (2 × 10 cm^3), dried ($MgSO_4$) and concentrated under reduced pressure. Purification of the residue by column chromatography (Et_2O) gave a colourless oil, *epoxy alcohol* **31a** (0.59 g, 74%); R_f 0.44 (Et_2O); ν_{max}/cm^{-1} 3389s, 2917s, 1043s and 837s; δ_H(400 MHz) 3.54 (2H, s, CH_2O), 3.30–3.25 (2H, d, *J* 3, 2 × CHO), 2.27 (2H, d, *J* 10, 2 × CH*H*), 1.60 (2H, d, *J* 10, 2 × C*H*H) and 1.38 (3H, s, Me); δ_C(100 MHz) 71.2 (CH_2OH), 58.9 (2 × CHO), 53.1 (C, quat.), 38.4 (2 × CH_2) and 26.0 (Me); *m*/*z* (EI) 129 (M + H^+, 25%), 111 (47), 97 (58) and 81 (100) (Found: M + H^+, 129.0916. $C_7H_{13}O_2$ requires *M*, 129.0916).

(1α,3α,5α)-3-Butyl-6-oxabicyclo[3.1.0]hexane-3-methanol 31b

Following the procedure for the preparation of epoxy alcohol **31a**, but using alcohol **30b** (1.00 g, 6.5 mmol) and *tert*-butyl hydroperoxide (6.9 mol dm^{-3} in CH_2Cl_2; 1.88 cm^3, 13.0 mmol) gave, after purification by column chromatography (50% Et_2O in light petroleum) a colourless oil, *epoxy alcohol* **31b** (0.87 g, 79%); R_f 0.35 (50% Et_2O in light petroleum); ν_{max}/cm^{-1} 3420m, 2954s, 1051s and 868m; δ_H(400 MHz) 3.55 (1H, d, *J* 5, CH*H*O), 3.51 (1H, d, *J* 5, C*H*HO), 3.47–3.38 (2H, m, 2 × CHO), 2.15 (2H, d, *J* 10, 2 × CH*H*), 1.72 (2H, d, *J* 10, 2 × C*H*H), 1.45–1.10 (6H, m, 3 × CH_2) and 0.92 (3H, t, *J* 7, Me); δ_C(100 MHz) 69.2 (CH_2O), 58.8 (2 × CHO), 45.1 (C, quat.), 39.3 (2 × CH_2), 37.1 (CH_2), 26.8 (CH_2), 23.1 (CH_2) and 13.8 (Me); *m*/*z* (EI) 170 (M^+, 24%), 111 (44), 97 (43) and 81 (100) (Found: M^+, 170.1307. $C_{10}H_{18}O_2$ requires *M*, 170.1307).

(1α,3α,5α)-3-Benzyloxymethyl-6-oxabicyclo[3.1.0]hexane-3-methanol 31c

Following the procedure for the preparation of epoxy alcohol **31a**, but using alcohol **30c** (0.30 g, 1.38 mmol) and *tert*-butyl hydroperoxide (6.9 mol dm^{-3} in CH_2Cl_2; 0.40 cm^3, 2.76 mmol) gave, after purification by column chromatography (35% Et_2O in light petroleum) a colourless oil, *epoxy alcohol* **31c** (143 mg, 45%); R_f 0.63 (Et_2O); ν_{max}/cm^{-1} 3430s, 3082s, 2849s, 2659m, 1715m and 1619w; δ_H(400 MHz) 7.37–7.28 (5H, m, Ar), 4.52 (1H, d, *J* 7, CH*H*Ph), 4.48 (1H, d, *J* 7, C*H*HPh), 3.51 (1H, d, *J* 6.5, CH*H*OH), 3.49 (1H, d, *J* 6.5, C*H*HOH), 3.41 (2H, s, 2 × CHO), 3.29 (2H, s, CH_2OBn), 2.06 (2H, d, *J* 15, 2 × CH*H*) and 1.76 (2H, d, *J* 15, 2 × C*H*H); δ_C(100 MHz) 137.9 (Ar, quat.), 128.4 (2 × Ar), 127.7 (Ar), 127.6 (2 × Ar), 76.6 (*C*H_2Ph or *C*H_2OBn), 73.4 (*C*H_2Ph or *C*H_2OBn), 69.5 (CH_2OH), 58.9 (2 × CHO), 46.5 (C, quat.) and 34.4 (2 × CH_2); *m*/*z* (CI, NH_3) 249 (M + NH_4^+, 70%), 235 (M + H^+, 44), 217 (15), 160 (15), 144 (48) and 127 (100) (Found: M + H^+, 235.1334. $C_{14}H_{19}O_3$ requires *M*, 235.1334).

(1*S*,4*R*)-4-Hydroxymethyl-4-methylcyclopent-2-en-1-ol 32a

BuLi (2.5 mol dm^{-3} in hexanes; 1.84 cm^3, 4.60 mmol) was added dropwise to a stirred solution of (1*R*,2*S*)-norephedrine (0.36 g, 2.34 mmol) in benzene (12 cm^3) and THF (8 cm^3) at 0 °C. After 30 min a solution of epoxy alcohol **31a** (0.10 g, 0.78 mmol) in THF (2 cm^3) was added dropwise to the reaction mixture over a period of 15 min. The solution was then allowed to warm to room temperature overnight. MeOH (10 cm^3) was added and the solution filtered through Celite and evaporated under reduced pressure. The residue was adsorbed onto silica (1.0 g) and purified by column chromatography (30% EtOAc in Et_2O) to give a pale yellow oil, *cis-diol* **32a** (63 mg, 63%); R_f 0.32 (30% EtOAc in Et_2O); $[\alpha]_D^{20}$ −24.7 (*c* 6.03 in $CHCl_3$); ν_{max}/cm^{-1} 3310s, 2952s, 1669w, 1358m and 1042s; δ_H(400 MHz) 5.97 (1H, dd, *J* 7 and 2, CH=), 5.66 (1H, d, *J* 7, CH=), 4.72 (1H, ddd, *J* 7, 2 and 2, CHO), 3.49 (1H, d, *J* 7, CH*H*O), 3.45 (1H, d, *J* 7, C*H*HO), 2.93–2.45 (1H, br s, OH), 2.40–2.09 (1H, br s, OH), 1.92 (1H, dd, *J* 14 and 2, CH*H*), 1.75 (1H, dd, *J* 14 and 7, C*H*H) and 1.04 (3H, s, Me); δ_C(100 MHz) 140.7 (CH=), 133.9 (CH=), 75.9 (CHO), 67.7 (CH_2O), 50.1 (C, quat.), 45.0 (CH_2) and 23.1 (Me); *m*/*z* (EI) 129 (M + H^+, 12%), 111 (33), 97 (26), 80 (100) and 79 (43) [Found: M + H^+ (Self protonated), 129.0916. $C_7H_{13}O_2$ requires *M*, 129.0916].

(1*S*,4*R*)-4-Butyl-4-hydroxymethylcyclopent-2-en-1-ol 32b

Following the procedure for the preparation of diol **32a**, but using epoxy alcohol **31b** (0.30 g, 1.76 mmol), BuLi (2.5 mol dm^{-3} in hexanes; 4.2 cm^3, 10.5 mmol) and (1*R*,2*S*)-norephedrine (0.80 g, 5.28 mmol) gave, after purification by column chromatography (30% EtOAc in Et_2O) a pale yellow oil, *cis-diol* **32b** (203 mg, 67%); R_f 0.38 (30% EtOAc in Et_2O); $[\alpha]_D^{20} = -28.9$ (*c* 6.08 in $CHCl_3$); ν_{max}/cm^{-1} 3331s, 2927s, 1620w, 1380m and 1037s; δ_H(400 MHz) 5.96 (1H, dd, *J* 5 and 2, CH=), 5.62 (1H, d, *J* 5, CH=), 4.68 (1H, ddd, *J* 5, 2 and 2, CHO), 3.47 (1H, d, *J* 8, CH*H*O), 3.43 (1H, d, *J* 8, C*H*HO), 3.30–2.92 (1H, br s, OH), 2.89–2.15 (1H, br s, OH), 1.95 (1H, dd, *J* 12 and 2, CH*H*), 1.64 (1H, dd, *J* 12 and 5, C*H*H), 1.40–1.10 (6H, m, 3 × CH_2) and 0.87 (3H, t, *J* 7, Me); δ_C(100 MHz) 139.6 (CH=), 133.9 (CH=), 75.7 (CHO), 66.7 (CH_2O), 53.9 (C, quat.), 42.1 (CH_2), 36.1 (CH_2), 26.5 (CH_2), 23.3 (CH_2) and 13.9 (Me); *m*/*z* (CI, NH_3) 188 (M + NH_4^+, 12%), 170 (32), 139 (47), 122 (86), 83 (49), 80 (100) and 79 (98) [Found: (M + NH_4^+), 188.1651. $C_{10}H_{22}NO_2$ requires *M*, 188.1651].

(1*S*,4*S*)-4-Benzyloxymethyl-4-hydroxymethylcyclopent-2-en-1-ol 32c

Following the procedure for the preparation of diol **32a**, but using epoxy alcohol **31c** (0.10 g, 0.43 mmol), BuLi (2.2 mol dm^{-3} in hexanes; 1.18 cm^3, 2.60 mmol) and (1*R*,2*S*)-norephedrine (0.196 g, 1.29 mmol) gave, after purification by column chromatography (30% EtOAc in Et_2O) a pale yellow oil, *cis-diol* **32c** (76 mg, 76%); R_f 0.21 (Et_2O); $[\alpha]_D^{20}$ −77.0 (*c* 6.1 in $CHCl_3$); ν_{max}/cm^{-1} 3353s, 3061s, 3032s, 2928s, 2859s, 1665m, 1455s, 1364s and 1096s; δ_H(400 MHz) 7.37–7.28 (5H, m, Ar), 5.99 (1H, dd, *J* 5 and 2, CH=), 5.81 (1H, d, *J* 5, CH=), 4.66 (1H, dd, *J* 5 and 2, CHO), 4.51 (1H, d, *J* 7, CH*H*Ph), 4.49 (1H, d, *J* 7, C*H*HPh), 3.64 (1H, d, *J* 11, C*H*HOH), 3.58 (1H, d, *J* 11, CH*H*OH), 3.36 (1H, d, *J* 11, C*H*HOCH_2), 3.32 (1H, d, *J* 11, CH*H*OCH_2), 2.03 (1H, dd, *J* 14 and 5, C*H*H) and 1.67 (1H, d, *J* 14, CH*H*); δ_C(100 MHz) 138.5 (Ar, quat.), 136.7 (CH=), 135.7 (CH=), 128.4 (2 × Ar), 128.0 (Ar), 127.7 (2 × Ar), 75.6 (*C*H_2Ph), 73.4 (*C*H_2OBn), 66.2 (CH_2OH), 57.5 (CHOH), 55.3 (C, quat.) and 40.9 (CH_2); *m*/*z* (CI, NH_3) 252 (M + NH_4^+, 12%), 234 (M^+, 35), 217 (15), 108 (12) and 96 (15) (Found: M + NH_4^+, 252.1600. $C_{14}H_{22}NO_3$ requires *M*, 252.1600).

(4*R*)-4-Hydroxymethyl-4-methylcyclopent-2-en-1-one 33a

PDC (293 mg, 0.78 mmol) was added in one portion to a stirred solution of *cis*-diol **32a** (100 mg, 0.78 mmol) in EtOAc (10 cm^3) and AcOH (0.2 cm^3) at room temperature. After 1.5 h Et_2O (10 cm^3) was added, the reaction filtered and the residue washed with Et_2O (2 × 10 cm^3). The volatile solvents were evaporated under reduced pressure and the remaining AcOH removed by azeotropic distillation with toluene (5 cm^3). Purification of the residue by column chromatography (75% EtOAc in hexane) gave a colourless oil, *hydroxy enone* **33a** (69 mg, 70%). R_f 0.32 (30% EtOAc in Et_2O); $[\alpha]_D^{20}$ +97.0 (*c* 1.0 in $CHCl_3$); ν_{max}/cm^{-1} 3423s, 2933s, 2861s, 1712s, 1678s and 1583m; δ_H(400 MHz) 7.40 (1H, d, *J* 5.5, CH=), 6.08 (1H, d, *J* 5.5, CH=), 3.55 (1H, d, *J* 10, CH*H*O), 3.50 (1H, d, *J* 10, C*H*HO), 2.38 (1H, d, *J* 18.5, C*H*H), 2.03 (1H, d, *J* 18.5, CH*H*) and 1.02 (3H, s, Me); δ_C(100 MHz) 208.4 (C=O), 169.4 (CH=), 133.9 (CH=), 69.0 (CH_2O), 45.1 (CH_2) and 22.5 (Me); *m*/*z* (EI) 126 (M^+, 28%), 111 (22), 95 (100), 81 (31), 67 (100) and 41 (75) (Found: M^+, 126.0681. $C_7H_{10}O_2$ requires *M*, 126.0681). The ee of the 2,4-dinitrobenzoate derivative was determined to be 99% by HPLC (75:25 EtOH–hexane, 1 cm^3 min^{-1}), $t_R$mj, 19.2; $t_R$mn, 36.4.

(4*R*)-4-Butyl-4-hydroxymethylcyclopent-2-en-1-one 33b

Following the procedure for the preparation of hydroxy enone **33a**, but using *cis*-diol **32b** (180 mg, 1.06 mmol) and PDC (398 mg, 1.06 mmol) gave, after purification by column chromatography (75% EtOAc in hexane) a colourless oil, *hydroxy enone* **33b** (103 mg, 58%); R_f 0.36 (25% EtOAc in Et_2O); $[\alpha]_D^{20}$ +109 (*c* 1.0 in $CHCl_3$); ν_{max}/cm^{-1} 3423s, 2930s, 2860s, 1710s, 1678s and 1586m; δ_H(400 MHz) 7.46 (1H, d, *J* 6, CH=), 6.17 (1H, d, *J* 6, CH=), 3.68 (1H, d, *J* 10, CH*H*O), 3.60 (1H, d, *J* 10, C*H*HO), 2.28 (1H, d, *J* 18, CH*H*), 2.22 (1H, d, *J* 18, C*H*H), 1.60–1.10 (6H, m, 3 × CH_2) and 0.89 (3H, t, *J* 7, Me); δ_C(100 MHz) 209.8 (C=O), 169.3 (CH=), 134.3 (CH=), 67.8 (CH_2O), 51.0 (C, quat.),

42.9 (CH_2), 34.7 (CH_2), 26.5 (CH_2), 23.2 (CH_2) and 13.9 (Me); *m/z* (EI) 168 (M^+, 12%), 138 (68) and 95 (100) (Found: M^+, 168.1142. $C_{10}H_{16}O_2$ requires *M*, 168.1150). The ee of the 2,4-dinitrobenzoate derivative was determined to be 96% by HPLC (75:25 EtOH–hexane, 1 cm^3 min^{-1}), $t_R$mj, 49.2; $t_R$mn, 16.4.

(4*S*)-4-Benzyloxymethyl-4-hydroxymethylcyclopent-2-en-1-one 33c

Following the procedure for the preparation of hydroxy enone **33a**, but using *cis*-diol **32c** (100 mg, 0.43 mmol) and PDC (161 mg, 0.43 mmol) gave, after purification by column chromatography (75% EtOAc in hexane) a colourless oil, *hydroxy enone* **33c** (76 mg, 76%); R_f 0.21 (Et_2O); $[\alpha]_D^{20}$ −38.0 (*c* 0.10 in $CHCl_3$); ν_{max}/cm^{-1} 3422s, 3030s, 2917s, 2850s, 1711s, 1678s and 1586m; δ_H(400 MHz) 7.65 (1H, d, *J* 5.5, CH=), 7.38–7.29 (5H, m, Ar), 6.23 (1H, d, *J* 5.5, CH=), 4.53 (2H, s, CH_2Ph), 3.77 (1H, d, *J* 7, C*H*HOBn), 3.68 (1H, d, *J* 7, CH*H*OBn), 3.58 (1H, d, *J* 7, C*H*HOH), 3.52 (1H, d, *J* 7, CH*H*OH), 2.31 (1H, d, *J* 15, CH*H*), 2.18 (1H, d, *J* 15, C*H*H); δ_C(100 MHz) 208.2 (C=O), 165.9 (CH=), 137.4 (Ar, quat.), 135.2 (CH=), 128.6 (2 × Ar), 128.0 (Ar), 127.6 (2 × Ar), 74.2 (*C*H_2Ph or *C*H_2OBn), 73.6 (*C*H_2Ph or *C*H_2OBn), 67.2 (CH_2OH), 51.7 (C, quat.) and 41.7 (CH_2); *m/z* (EI) 232 (M^+, 19%), 202 (13) and 91 (100) (Found: M^+, 232.1120. $C_{14}H_{16}O_3$ requires *M*, 232.1099). The ee of the 2,4-dinitrobenzoate derivative was determined to be 89% by HPLC (90:10 EtOH–hexane, 1 cm^3 min^{-1}), $t_R$mj, 9.3; $t_R$mn, 8.1.

Preparation of crystalline (2*R*,3*R*,8*R*)-2,3-dimethyl-7-butyl-1,4-dioxaspiro[4.4]non-8-en-7-ylmethyl 3,5-dinitrobenzoate 34

A solution of hydroxy enone **33b** (30 mg, 0.18 mmol), 3,5-dinitrobenzoyl chloride (62 mg, 0.27 mmol) and Et_3N (37 µl, 0.27 mmol) in CH_2Cl_2 (10 cm^3) was stirred at room temperature. After 14 h CH_2Cl_2 (10 cm^3) was added and the reaction mixture washed with saturated aq. $NaHCO_3$ (2 × 10 cm^3), brine (2 × 10 cm^3), dried ($MgSO_4$) and evaporated under reduced pressure. Purification of the residue by column chromatography (75% Et_2O in light petroleum) gave a colourless oil, *dinitrobenzoate* **34** (58 mg, 89%); R_f 0.55 (75% Et_2O in light petroleum); $[\alpha]_D^{20}$ +47.0 (*c* 1.0 in $CHCl_3$); ν_{max}/cm^{-1} 3105m, 2935m, 2862m, 1736s, 1721s, 1716s, 1590m, 1561m, 1465s, 1276s and 1077m; δ_H(400 MHz) 9.25–9.21 (1H, m, Ar), 9.10–9.02 (2H, m, Ar), 7.51 (1H, d, *J* 6, CH=), 6.26 (1H, d, *J* 6, CH=), 4.55 (1H, d, *J* 11, CH*H*O), 4.43 (1H, d, *J* 11, C*H*HO), 2.44 (1H, d, *J* 18, CH*H*), 2.36 (1H, d, *J* 18, C*H*H), 1.78–1.64 (2H, m, CH_2), 1.43–1.24 (4H, m, 2 × CH_2) and 0.83 (3H, t, *J* 7, Me); δ_C(100 MHz) 207.5 (C=O), 166.7 (CH=), 162.3 (OC=O), 148.8 (Ar, quat.), 134.8 (CH=), 133.2 (2 × Ar, quat.), 129.3 (2 × Ar), 122.7 (Ar), 70.2 (CH_2O), 49.1 (C, quat.), 43.2 (*C*H_2C=O), 35.3 (CH_2), 26.4 (CH_2), 23.1 (CH_2) and 13.8 (Me); *m/z* (EI) 363 (M + H^+, 27%), 332 (44), 290 (34), 195 (100), 149 (68), 137 (81), 109 (32) and 95 (83) (Found: M + H^+, 363.1192. $C_{17}H_{19}N_2O_7$ requires *M*, 363.1192).

TMSOTf (25 µl, 0.14 mmol) was added to a stirred solution of the above dinitrobenzoate (50 mg, 0.14 mmol) and (2*R*,3*R*)-2,3-bis(trimethylsilyloxy)butane (50 mg, 0.21 mmol) in CH_2Cl_2 (3 cm^3) at −78 °C and the reaction was then allowed to warm to 0 °C. After 6 h the reaction was recooled to −78 °C, pyridine (50 µl) was then added and the mixture was allowed to warm to ambient temperature. The reaction mixture was evaporated under reduced pressure and the residue purified by column chromatography (10% Et_2O in light petroleum) to give a white solid, *ketal* **34** (38 mg, 63%); R_f 0.71 (50% Et_2O in light petroleum); mp 84–86 °C (from MeOH); $[\alpha]_D^{20}$ +65 (*c* 1.0 in $CHCl_3$); ν_{max}/cm^{-1} 3085w, 3030m, 2930m, 2856m, 2239m, 1736m, 1549m, 1497m, 1456s, 1342m and 1257s; δ_H(400 MHz) 9.20–9.15 (3H, m, Ar), 5.77 (1H, d, *J* 6, CH=), 5.71 (1H, d, *J* 6, CH=), 4.36 (1H, d, *J* 11, CH*H*O), 4.28 (1H, d, *J* 11, C*H*HO), 3.55–3.50 (2H, m, 2 × CH), 2.11 (1H, d, *J* 8, CH*H*), 2.03 (1H, d, *J* 8, C*H*H), 1.53–1.42 (4H, m, 2 × CH_2), 1.38–1.00 (8H, m, 2 × Me and CH_2) and 0.83 (3H, t, *J* 7, Me); *m/z* (CI, NH_3) 435 (M + H^+, 100%), 405 (30), 333 (14), 223 (100) and 209 (29) (Found: C, 58.1; H, 6.0; N, 6.45. $C_{21}H_{26}N_2O_8$ requires C, 58.1; H, 6.0; N, 6.45%).

X-Ray structure determination of (2*R*,3*R*,8*R*)-2,3-dimethyl-7-butyl-1,4-dioxaspiro[4.4]non-8-en-7-ylmethyl 3,5-dinitrobenzoate 34

$C_{21}H_{26}N_2O_8$, $M = 434.44$. Monoclinic, $a = 37.76$ (2), $b = 5.740$ (6), $c = 10.910$ (7) Å, $\beta = 98.240$ (10)°, $V = 2340$ (3) $Å^3$, space group *C*2, $Z = 4$, $D_c = 1.233$ mg m^{-3}, *F*(000) 920, independent reflections 1363 [*R*(int) = 0.0215], Final *R* indices [$I > 2\sigma(I)$], $R_1 = 0.0732$, $wR_2 = 0.0923$, *R* indices (all data) $R_1 = 0.1831$, $wR_2 = 0.2048$. Data were collected with Mo-Kα radiation using an MAR research Image Plate System. The crystal was positioned at 75 mm from the image plate. 95 Frames were measured at 2° intervals with a counting time of 2 min. Data analysis was carried out with the XDS program.[45] The space group was confirmed as *C*2 by the successful structure determination using direct methods with the SHELX-86 program.[46] The non-hydrogen atoms were refined with anisotropic thermal parameters. The hydrogen atoms were included in geometric positions and refined with isotropic parameters equivalent to 1.2× that of the atoms to which they were bonded. The structure was then refined using SHELXL-93.[47] The largest peak and hole in the final difference Fourier map were 0.285 and −0.361 e $Å^{-3}$. CCDC reference number 207/377. See http://www.rsc.org/suppdata/p1/1999/3579 for crystallographic files in .cif format.

(1*R*)-*cis*-4-Benzyloxymethylcyclopent-2-en-1-ol 35

A solution of *cis*-diol (−)-**4**[9] [0.500 g, 4.99 mmol, ⩾99% ee by chiral GC analysis of the bistrifluoroacetate derivative (prepared by evaporation of a solution of TFAA and the diol in CH_2Cl_2), $t_R$mj 7.04 min, $t_R$mn 7.18 min] in DMF (3.5 cm^3) was added dropwise to a stirred suspension of NaH [dry, 95% (0.145 g, 5.74 mmol)] in DMF (10 cm^3) at 0 °C. After 15 min the reaction was cooled to −60 °C and BnBr (0.61 cm^3, 5.10 mmol) in DMF (3.5 cm^3) added dropwise. After 3 h the reaction was allowed to warm to room temperature over 14 h and the reaction was then cooled to 0 °C and MeOH (15 cm^3) added. The reaction mixture was evaporated under reduced pressure and the residue dissolved in Et_2O (50 cm^3) and washed with saturated aq. $CuSO_4$ (3 × 5 cm^3). The organic layer was dried ($MgSO_4$) and evaporated under reduced pressure. Purification of the residue by column chromatography (50% Et_2O in light petroleum) gave a colourless oil, *benzyl ether* **35** (0.818 g, 81%); R_f 0.48 (50% Et_2O in light petroleum); $[\alpha]_D^{20}$ −43.1 (*c* 1.0 in $CHCl_3$); ν_{max}/cm^{-1} 3401s, 2858s, 1716m, 1363s, 1309m, 1258m, 1207m and 1094s; δ_H(200 MHz) 7.40–7.27 (5H, m, Ar), 5.86–5.83 (1H, m, CH=), 5.73 (1H, dd, *J* 5.5 and 2, CH=), 4.65–4.59 (1H, m, C*H*OH), 4.43 (2H, s, CH_2Ph), 3.48 (1H, d, *J* 4, C*H*HO), 3.46 (1H, d, *J* 4, CH*H*O), 2.86 (1H, m, C*H*CH_2O), 2.75–2.62 (1H, br s, OH), 2.33 (1H, ddd, *J* 8, 8 and 7, C*H*H) and 1.56 (1H, dd, *J* 8 and 8, CH*H*); δ_C(50 MHz) 138.3 (Ar, quat.), 136.9 (CH=), 134.3 (CH=), 128.3 (2 × Ar), 127.6 (3 × Ar), 77.0 (CHOH), 73.9 (CH_2Ph), 73.0 (CH_2O), 44.9 (*C*HCH_2OBn) and 37.4 (CH_2); *m/z* (CI, NH_3) 205 (M + H^+, 100%) and 222 (M + NH_4^+, 47) (Found: M + NH_4^+, 222.1494. $C_{13}H_{20}NO_2$ requires *M*, 222.1494).

(1*S*)-*trans*-4-Benzyloxymethylcyclopent-2-en-1-yl acetate 36

DEAD (203 µl, 1.29 mmol) in Et_2O (0.5 cm^3) was added dropwise to a stirred solution of benzyl ether **35** (0.135 g, 0.661 mmol), Ph_3P (0.692 g, 2.64 mmol) and AcOH (76 µl, 2.66 mmol) in Et_2O (3.0 cm^3) at −10 °C. The reaction was maintained at −10 °C for 3 h then allowed to warm to 25 °C. After

14 h the reaction was filtered through Celite and washed with Et_2O (3 × 5 cm^3). The combined filtrates were evaporated under reduced pressure. Purification of the residue by column chromatography (30% Et_2O in light petroleum) gave a colourless oil, *acetate* **36** (141 mg, 87%); R_f 0.43 (25% Et_2O in light petroleum); $[\alpha]_D^{20}$ −150.8 (*c* 1.0 in $CHCl_3$); ν_{max}/cm^{-1} 3060m, 2921s, 2851m, 2349m, 2240m, 1739m, 1727m, 1659m, 1612m and 1360m; δ_H(200 MHz) 7.42–7.27 (5H, m, Ar), 6.18 (1H, dd, *J* 8 and 4, CH=), 5.92–5.88 (1H, m, CH=), 5.73 (1H, m, C*H*OAc), 4.54 (2H, s, CH_2Ph), 3.37 (2H, s, CH_2OBn), 3.26–3.20 (1H, m, C*H*CH_2OBn) and 2.10–1.94 (5H, m, CH_2 and Me); δ_C(50 MHz) 171.4 (C=O), 139.6 (CH=), 138.5 (Ar, quat.), 130.7 (CH=), 128.6 (2 × Ar), 127.8 (3 × Ar), 80.0 (OCH), 73.6 (CH_2Ph), 73.2 (CH_2O), 45.0 (*C*HCH_2O), 33.9 (CH_2) and 21.2 (Me); *m*/*z* (CI, NH_3) 247 (M + H^+, 5%), 204 (55), 187 (100), 108 (18) and 96 (50) (Found: M + H^+, 247.1334. $C_{15}H_{19}O_3$ requires *M*, 247.1334).

[(1*S*)-*trans*-1-(4-Benzyloxymethylcyclopent-2-en-1-yloxy)-ethenyloxy] *tert*-butyldimethylsilane 37

BuLi (2.38 mol dm^{-3} in hexanes; 0.247 cm^3, 0.589 mmol) was added dropwise to a stirred solution of diisopropylamine (85 µl, 0.603 mmol) in THF (0.5 cm^3) at 0 °C. After 5 min HMPA (0.1 cm^3) was added and the reaction cooled to −78 °C. After 10 min a solution of acetate **36** (0.100 g, 0.406 mmol) in THF (1.0 cm^3) was added dropwise and the reaction maintained at −78 °C for a further 20 min. A solution of TBDMSCl (80 mg, 0.532 mmol) in THF (0.1 cm^3) was added and the reaction maintained at −78 °C for 5 min before warming to room temperature. After 20 min ice-cold pentane (10 cm^3) and aq. NaOH (0.1 mol dm^{-3}, 10 cm^3) were added. The aq. layer was separated and extracted with pentane (2 × 10 cm^3). The combined pentane extracts were washed with aq. NaOH (0.1 mol dm^{-3}; 2 × 10 cm^3), H_2O (10 cm^3) and aq. NaOH (0.1 mol dm^{-3}; 10 cm^3), dried (Na_2SO_4) and the solvent evaporated to give a yellow oil, *silyl ketene acetal* **37** (0.147 g, 100%); $[\alpha]_D^{20}$ +9.0 (*c* 1.0 in $CHCl_3$); ν_{max}/cm^{-1} 3056s, 2926s, 1704s, 1496m, 1454s, 1408s, 1362s, 1273m, 1161s, 1103s, 1028s, 936m, 735s and 698s; δ_H(200 MHz) 7.37–7.28 (5H, m, Ar), 6.20 (1H, dd, *J* 4 and 2, CH=), 5.89 (1H, ddd, *J* 4, 4 and 2, CH=), 5.08–5.00 (1H, m, CHOCOSi), 4.54 (2H, s, CH_2Ph), 3.45 (2H, d, *J* 7, CH_2OBn), 3.29 (1H, d, *J* 2, CH=), 3.27–3.19 (1H, m, C*H*CH_2O), 3.12 (1H, d, *J* 2, CH=), 2.18–1.87 (2H, m, CH_2), 0.93 (9H, s, Bu^t) and 0.17 (6H, s, 2 × Me); δ_C(50 MHz) 160.7 (C, quat.), 138.9 (CH=), 138.6 (Ar, quat.), 130.7 (CH=), 128.6 (2 × Ar), 127.8 (3 × Ar), 82.2 (CHO), 73.7 (CH_2Ph), 73.2 (CH_2O), 61.7 (CH_2=COSi), 45.0 (*C*HCH_2O), 33.8 (CH_2), 25.6 (Bu^t), 18.0 (C, quat. Si) and −4.6 (2 × Me); *m*/*z* (CI, NH_3) 361 (M + H^+, 17%), 332 (12), 316 (24), 315 (100), 289 (20), 269 (20), 264 (8) and 247 (36) (Found: M + H^+, 361.2199. $C_{21}H_{33}O_3Si$ requires *M*, 361.2199).

(1*S*)-*trans*-(5-Benzyloxymethylcyclopent-2-en-1-yl)acetic acid 38

A solution of silyl ketene acetal **37** (0.100 g, 0.28 mmol) in dry xylenes (5 cm^3) was heated in a sealed tube to 190 °C for 18 h. After cooling to ambient temperature the solvent was removed under reduced pressure and the residue dissolved in THF (5 cm^3). Aq. NaOH (2 mol dm^{-3}, 5 cm^3) was added and the reaction stirred vigorously for 2 h. Pentane was then added (5 cm^3) and the mixture extracted with aq. NaOH (2 mol dm^{-3}, 3 × 5 cm^3) [benzyl ether *trans*-**35** (185 mg, 33%) was isolated from the organic layer]. The combined aq. layers were acidified with HCl (6 mol dm^{-3}, 10 cm^3) and extracted with Et_2O (3 × 5 cm^3). The combined organic layers from this last stage were dried (Na_2SO_4) and evaporated under reduced pressure to give a pale yellow oil, *acid* **38** (0.044 g, 64%); R_f 0.65 (Et_2O); $[\alpha]_D^{20}$ +39.4 (*c* 1.0 in $CHCl_3$); ν_{max}/cm^{-1} 3056m, 2925s, 2855s, 2339, 2316, 1734s, 1700s, 1102s and 1029s; δ_H(200 MHz) 7.36–7.28 (5H, m, Ar), 5.74–5.64 (2H, m, 2 × CH=), 4.54 (2H, s, CH_2Ph), 3.53–3.39 (2H, m, CH_2OBn), 2.90–2.86 (1H, m, C*H*CH_2OBn) and 2.61–2.11 (5H, m, C*H*CH_2CO_2H, CHC*H*$_2CO_2H$ and CH_2); δ_C(50 MHz) 178.5 (C=O), 138.4 (Ar, quat.), 132.6 (CH=), 130.4 (CH=), 128.3 (2 × Ar), 127.6 (2 × Ar), 127.5 (Ar), 73.8 (CH_2Ph), 73.0 (CH_2O), 45.3 (*C*HCH$_2$C=O), 43.3 (*C*HCH_2O), 39.9 (CH_2C=O) and 35.6 (CH_2); *m*/*z* (CI, NH_3) 264 (M + NH_4^+, 72%), 248 (13), 247 (M + H^+, 100), 246 (M, 4), 229 (15), 204 (14) and 187 (28) (Found: M + H^+, 247.1334. $C_{15}H_{19}O_3$ requires *M*, 247.1334).

(3a*R*,4*S*,6*R*,6a*R*)-4-Benzyloxymethyl-6-iodohexahydrocyclopenta[*b*]furan-2-one 39

I_2 (0.309 g, 1.218 mmol) was added to a stirred solution of $NaHCO_3$ (1.023 g, 12.18 mmol) and acid **38** (0.100 g, 0.406 mmol) in MeCN (2.5 cm^3) at room temperature. The solution was stirred in the dark for 24 h then diluted with Et_2O (10 cm^3), washed with saturated aq. sodium thiosulfate (2 × 5 cm^3), H_2O (2 × 5 cm^3), dried ($MgSO_4$) and evaporated under reduced pressure to give *iodolactone* **39** (0.143 g, 95%); R_f 0.19 (30% Et_2O in light petroleum); $[\alpha]_D^{20}$ −40.9 (*c* 1.0 in $CHCl_3$); ν_{max}/cm^{-1} 3062m, 3030m, 2920s, 2855s, 2251w, 1783s, 1496m, 1454s, 1414m, 1366s, 1302s, 1274m, 1164s, 1104s, 1028s, 1002 and 944m; δ_H(200 MHz) 7.40–7.29 (5H, m, Ar), 5.12 (1H, dd, *J* 4 and 7, CHI), 4.52 (2H, s, CH_2Ph), 4.24–4.16 (1H, m, CHOC=O), 3.59–2.53 (2H, m, CH_2OBn), 2.86–2.47 (4H, m, C*H*CH_2OBn, CH_2C=O and C*H*CH_2C=O) and 2.12–2.00 (2H, m, CH_2); δ_C (50 MHz) 177.0 (C=O), 137.9 (Ar, quat.), 128.7 (3 × Ar), 128.0 (2 × Ar), 92.5 (CHI), 73.4 (CH_2Ph), 68.8 (CH_2O), 39.8 (*C*HOC=O), 38.2 (CH_2C=O), 37.4 (*C*HCH_2O), 29.7 (*C*HCH_2C=O) and 27.8 (CH_2); *m*/*z* (CI, NH_3) 372 (M^+, 18%), 227 (29), 181 (27), 92 (55) and 91 (100) (Found: M^+, 372.0222. $C_{15}H_{17}IO_3$ requires *M*, 372.0222).

(3a*R*,4*S*,6a*S*)-4-Benzyloxymethyl-3,3a,4,6a-tetrahydrocyclopenta[*b*]furan-2-one 40

DBU (36.3 µl, 0.243 mmol) was added dropwise to a stirred solution of iodolactone **39** (90 mg, 0.242 mmol) in THF (3.0 cm^3) at room temperature. The reaction was heated to reflux for 3 h, then cooled to room temperature and the solvent evaporated under reduced pressure. Pentane (3.0 cm^3) and H_2O (3.0 cm^3) were added to the residue and the aq. layer separated and extracted with pentane (2 × 3.0 cm^3). The combined organic layers were dried and the solvent evaporated under reduced pressure to give *lactone* **40** (0.051 g, 86%); R_f 0.46 (75% Et_2O in light petroleum); $[\alpha]_D^{20}$ +195.3 (*c* 1.0 in $CHCl_3$) {lit.[33a] $[\alpha]_D^{28}$ +205.3 (*c* 1 in $CHCl_3$), lit.[33b] $[\alpha]_D^{27}$ +205.7 (*c* 0.7 in $CHCl_3$), lit.[33c] $[\alpha]_D$ +204.8 (*c* 0.71 in $CHCl_3$)}; ν_{max}/cm^{-1} 3063m, 3030m, 2926s, 2856s, 1779s, 1454s, 1416m, 1363s, 1158s, 1096s, 1053s, 1028s and 856m; δ_H(200 MHz) 7.30–7.20 (5H, m, Ar), 5.99–5.82 (2H, m, 2 × CH=), 5.37 (1H, m, CHOC=O), 4.44 (2H, s, CH_2Ph), 3.39 (1H, dd, *J* 10 and 5, C*H*CH_2C=O), 3.26 (1H, dd, *J* 10 and 6, C*H*CH_2OBn), 2.79 (2H, m, CH_2OBn), 2.66 (1H, dd, *J* 17 and 12, CH*H*C=O) and 2.20 (1H, dd, *J* 17 and 5, C*H*HC=O).

(1*S*)-*cis*-4-Benzyloxymethylcyclopent-2-en-1-yl acetate 41

Following the procedure for the preparation of benzyl ether **35**, but using *cis*-diol (+)-**4**[9] (0.50 g, 4.99 mmol, ⩾99% ee by chiral GC analysis of the bistrifluoroacetate derivative) NaH [dry, 95% (0.145 g, 5.74 mmol)] and BnBr (0.605 cm^3, 5.09 mmol) gave a colourless oil, (1*S*)-*cis*-4-benzyloxymethylcyclopent-2-en-1-ol (0.785 g, 77%); $[\alpha]_D^{20}$ +42.3 (*c* 1.23 in $CHCl_3$).

A solution of Ac_2O (111 µl, 1.17 mmol) in $CHCl_3$ (1 cm^3) was added dropwise to the above benzyl ether (0.200 g, 0.979 mmol) and pyridine (94 µl, 1.17 mmol) in $CHCl_3$ (2.0 cm^3) at room temperature. After 3 h MeOH was added (5 cm^3) and the reaction stirred for 30 min. The solvent was evaporated under reduced pressure and the residue purified by column chromatography (25% Et_2O in light petroleum) to give a colourless oil,

acetate **41** [0.236 g, 98%, 75% from *cis*-diol (+)-**4**]; R_f 0.44 (25% Et_2O in light petroleum); $[\alpha]_D^{20}$ −0.3 (*c* 1.03 in $CHCl_3$); ν_{max}/cm^{-1} 3065m, 3031m, 2937s, 2857s, 2252w, 1732s, 1496m, 1454s, 1364s, 1243s, 1088s, 1020s, 910s, 734s and 699s; δ_H(200 MHz) 7.42–7.27 (5H, m, Ar), 6.20 (1H, d, *J* 8, CH=), 5.89 (1H, m, CH=), 5.67–5.63 (1H, m, C*H*OAc), 4.58 (2H, s, CH_2Ph), 3.45 (2H, m, CH_2OBn), 2.94 (1H, m, C*H*H), 2.52 (1H, m, CH*H*) and 2.05 (3H, s, Me); δ_C(50 MHz) 171.0 (C=O), 138.6 (Ar, quat.), 138.3 (CH=), 130.7 (CH=), 128.5 (2 × Ar), 127.7 (3 × Ar), 79.5 (OCH), 74.0 (CH_2Ph), 73.0 (CH_2O), 44.8 (*C*HCH_2O), 33.5 (CH_2) and 21.0 (Me); *m*/*z* (CI, NH_3) 264 (M + NH_4^+, 21%), 247 (M + H^+, 5), 204 (57), 188 (12), 187 (100) and 96 (10) (Found: M + H^+, 247.1334. $C_{15}H_{19}O_3$ requires *M,* 247.1334).

[(1*S*)-*cis*-1-(4-Benzyloxymethylcyclopent-2-en-1-yloxy)-ethenyloxy]*tert*-butyldimethylsilane 42

Following the procedure for the preparation of silyl ketene acetal **37**, but using BuLi (2.50 mol dm^{-3} in hexanes; 0.236 cm^3, 0.589 mmol), diisopropylamine (85 µl, 0.605 mmol), acetate **41** (0.100 g, 0.406 mmol), and TBDMSCl (80 mg, 0.532 mmol) gave a yellow oil, *silyl ketene acetal* **42** (0.146 g, 100%); $[\alpha]_D^{20}$ +17.8 (*c* 1.0 in $CHCl_3$); ν_{max}/cm^{-1} 3065m, 3031m, 2930s, 2886s, 2858s, 1736m, 1650s, 1473m, 1362m, 1340m, 1269s, 1091m, 1050m, 1003m, 938m, 828m and 786m; δ_H(200 MHz) 7.36–7.27 (5H, m, Ar), 6.06 (1H, d, *J* 6, CH=), 5.91–5.88 (1H, m, CH=), 5.00–4.96 (1H, m, CHOCOSi), 4.53 (2H, s, CH_2Ph), 3.45–3.42 (2H, m, CH_2OBn), 3.30 (1H, d, *J* 2, CH=), 3.13 (1H, d, *J* 2, CH=), 2.93–2.90 (1H, m, C*H*CH_2OBn), 2.46–2.44 (1H, m, C*H*H), 1.69–1.65 (1H, m, CH*H*), 0.95 (9H, s, Bu^t) and 0.18 (6H, s, 2 × Me); δ_C(50 MHz) 160.3 (COSi, quat.), 138.2 (Ar, quat.), 137.3 (CH=), 130.4 (CH=), 128.1 (2 × Ar), 127.4 (3 × Ar), 81.6 (OCH), 74.2 (CH_2Ph), 72.9 (CH_2O), 61.4 (*C*H_2=COSi), 44.4 (*C*HCH_2O), 33.2 (CH_2), 25.2 (Bu^t), 17.6 (CSi, quat.) and −4.2 (2 × Me); *m*/*z* (CI, NH_3) 361 (M + H^+, 17%), 332 (12), 316 (24), 315 (100), 289 (20), 266 (20), 264 (68) and 247 (36) (Found: M + H^+, 361.2199. $C_{21}H_{33}O_3Si$ requires *M*, 361.2199).

(1*S*)-*cis*-(5-Benzyloxymethylcyclopent-2-en-1-yl)acetic acid 43

Following the procedure for the preparation of acid **38**, but using silyl ketene acetal **42** (0.730 g, 2.03 mmol) gave a yellow oil, *acid* **43** (0.415 g, 83%); R_f 0.68 (Et_2O); $[\alpha]_D^{20}$ +77.6 (*c* 1.02 in $CHCl_3$); ν_{max}/cm^{-1} 3060s, 2927s, 2854s, 2317w, 1708s, 1496s, 1453m, 1411m, 1365m, 1266m, 1210m, 1095m, 1028m, 934m, 838w, 734m and 698s; δ_H(200 MHz) 7.36–7.28 (5H, m, Ar), 5.78–5.74 (2H, m, 2 × CH=), 4.52 (2H, s, CH_2Ph), 3.56–3.42 (2H, m, CH_2OBn), 3.29–3.14 (1H, m, C*H*CH_2OBn) and 2.82–2.04 (5H, m, C*H*CH_2CO_2H, CHC*H*$_2CO_2H$ and CH_2); δ_C(50 MHz) 179.6 (C=O), 138.4 (Ar, quat.), 134.0 (CH=), 130.6 (CH=), 128.6 (3 × Ar), 127.9 (2 × Ar), 73.1 (CH_2Ph), 70.7 (CH_2O), 42.3 (*C*HCH_2C=O), 40.0 (*C*HCH_2O), 34.9 (*C*H_2C=O) and 34.6 (CH_2); *m*/*z* (CI, NH_3) 264 (M + NH_4^+, 4%), 247 (M + H^+, 7), 220 (7), 201 (10), 158 (14), 156 (23), 108 (28) and 106 (100) (Found: M + H^+, 247.1334. $C_{15}H_{19}O_3$ requires *M*, 247.1334).

(3a*R*,4*R*,6*R*,6a*S*)-4-Benzyloxymethyl-6-iodohexahydrocyclopenta[*b*]furan-2-one 44

Following the procedure for the preparation of iodolactone **39**, but using acid **43** (0.220 g, 0.89 mmol), I_2 (0.680 g, 2.68 mmol), and $NaHCO_3$ (2.25 g, 26.79 mmol) gave a colourless oil, *iodolactone* **44** (0.328 g, 99%); R_f 0.36 (50% Et_2O in light petroleum); $[\alpha]_D^{20}$ +7.3 (*c* 1.0 in $CHCl_3$); ν_{max}/cm^{-1} 3062w, 3030m, 2920s, 2855s, 2251w, 1783s, 1496m, 1454s, 1414m, 1366s, 1302s, 1274m, 1164s, 1104s, 1028s, 1002m and 944m; δ_H(200 MHz) 7.42–7.28 (5H, m, Ar), 5.23 (1H, m, *J* 6, CHI), 4.52 (3H, app. s, CH_2Ph and CHOC=O), 3.63–3.43 (2H, m, CH_2OBn), 3.30–3.19 (1H, m, C*H*CH_2C=O), 3.05–2.98 (1H, m, C*H*CH_2OBn), 2.64 (2H, d, *J* 6, CH_2C=O) and 2.16–1.87 (2H, m, CH_2); δ_C(50 MHz) 175.9 (C=O), 138.3 (Ar, quat.), 128.4 (3 × Ar), 127.7 (2 × Ar), 92.2 (CHI), 74.4 (CH_2Ph), 71.1 (CH_2O), 43.2 (CH_2C=O), 41.1 (*C*HOC=O), 40.7 (*C*HCH_2O), 32.7 (*C*HCH_2-C=O) and 28.8 (CH_2); *m*/*z* (CI, NH_3) 390 (M + NH_4^+, 17%), 373 (M + H^+, 5), 264 (58), 247 (32), 158 (70), 156 (42), 108 (26) and 106 (100) (Found: M + H^+, 373.0301. $C_{15}H_{18}IO_3$ requires *M,* 373.0301).

(3a*R*,4*R*,6a*S*)-4-Benzyloxymethyl-3,3a,4,6a-tetrahydrocyclopenta[*b*]furan-2-one 45

Following the procedure for the preparation of lactone **40**, but using iodolactone **44** (345 mg, 0.926 mmol) and DBU (139 µl, 0.931 mmol) gave a colourless oil, *lactone* **45**[35] (185 mg, 82%); R_f 0.46 (33% light petroleum in Et_2O); $[\alpha]_D^{20}$ +24.8 (*c* 1.0 in $CHCl_3$); ν_{max}/cm^{-1} 3031m, 2926s, 2857s, 1770s, 1704m, 1674m, 1626m, 1496m, 1454s, 1413m, 1365s, 1171s, 1095s, 1020s, 973m, 912m, 739s and 699s; δ_H(200 MHz) 7.30–7.20 (5H, m, Ar), 5.86–5.82 (2H, m, 2 × CH=), 5.34–5.27 (1H, m, CHOC=O), 4.42 (2H, s, CH_2Ph), 3.63–2.94 (4H, m, CH_2OBn and CH_2-C=O) and 2.57–2.16 (2H, m, C*H*CH_2OBn and C*H*CH_2C=O); δ_C(50 MHz) 177.0 (C=O), 137.9 (CH=), 136.8 (Ar, quat.), 129.9 (CH=), 128.7 (2 × Ar), 128.1 (3 × Ar), 88.8 (*C*HOC=O), 73.4 (CH_2Ph), 69.5 (CH_2O), 65.8 (*C*H_2C=O), 47.1 (*C*HCH_2C=O) and 38.1 (*C*HCH_2O).

(3*S*,3a*S*,4*R*,6a*S*)-4-Benzyloxymethyl-3,3a,4,6a-tetrahydro-3-methylcyclopenta[*b*]furan-2-one 46

BuLi (2.50 mol dm^{-3} in hexanes; 529 µl, 1.322 mmol) was added dropwise to a stirred solution of diisopropylamine (192 µl, 1.370 mmol) in THF (3.5 cm^3) at −78 °C. After 30 min lactone **45** (0.275 g, 1.13 mmol) in HMPA (211 µl) and THF (1.75 cm^3) was added over 5 min at −78 °C. After 2 h MeI (319 µl, 5.116 mmol) was added dropwise and the reaction maintained at −78 °C for a further 2 h. Saturated aq. NH_4Cl (5 cm^3) was added and the reaction warmed to room temperature. The aq. layer was separated and extracted with Et_2O (2 × 10 cm^3). The combined organic layers were washed with brine (2 × 10 cm^3), dried ($MgSO_4$) and evaporated under reduced pressure. Purification of the residue by column chromatography (25% Et_2O in light petroleum) gave a colourless oil, *methylated lactone* **46**[35] (249 mg, 85%); R_f 0.63 (66% Et_2O in light petroleum); $[\alpha]_D^{20}$ +10.2 (*c* 0.57 in $CHCl_3$); ν_{max}/cm^{-1} 3064s, 3031s, 2859s, 1716m, 1674m, 1622m, 1496m, 1455s, 1362s, 1200s, 1075s, 1020s, 921m, 793s, 742s and 698s; δ_H (200 MHz) 7.36–7.27 (5H, m, Ar), 5.92–5.90 (2H, m, 2 × CH=), 5.40 (1H, dd, *J* 8 and 2, CHOC=O), 4.54 (1H, d, *J* 2, C*H*HPh), 4.50 (1H, d, *J* 2, CH*H*Ph), 3.65–3.45 (2H, m, CH_2OBn), 3.29–3.14 (1H, m, C*H*MeC=O), 2.89 (1H, dd, *J* 8 and 7, C*H*CH_2OBn), 2.62–2.60 (1H, m, C*H*CHMe) and 1.20 (3H, d, *J* 7, Me); δ_C(50 MHz) 180.0 (C=O), 137.6 (Ar, quat.), 136.7 (CH=), 130.0 (CH=), 128.4 (2 × Ar), 127.9 (3 × Ar), 86.5 (*C*HOC=O), 73.5 (CH_2Ph), 69.4 (CH_2O), 47.3 (*C*HCHC=O), 47.1 (*C*HCH_2OBn), 39.8 [*C*H(Me)C=O] and 16.4 (Me).

(2*S*)-2-[(1*S*,4*S*,5*R*)-5-Benzyloxymethyl-4-methylcyclopent-2-en-1-yl]propanoic acid 47

MeMgBr (3.0 mol dm^{-3} in Et_2O; 755 µl, 2.265 mmol) was added dropwise to a stirred solution of CuBr·Me_2S[48] (0.432 g, 2.10 mmol) in THF (3.0 cm^3) and Me_2S (1.82 cm^3) at −25 °C (regulated by the addition of CO_2(s) to acetone). After 1 h methylated lactone **46** (0.300 g, 1.161 mmol) in THF (0.85 cm^3) was added over a period of 2 min at −25 °C. After 5 h the reaction was warmed to room temperature, poured onto aq. NaOH (2.0 mol dm^{-3}, 5 cm^3) and the reaction stirred for a further 2 h. HCl (1.0 mol dm^{-3}, ~10 cm^3) was added to the reaction and the aq. layer extracted with Et_2O (3 × 10 cm^3). The

combined organic layers were washed with H_2O (5 cm^3), brine (2 × 5 cm^3), dried ($MgSO_4$) and evaporated under reduced pressure to give a colourless oil, *acid* **47**[35] (289 mg, 91%); R_f 0.58 (66% Et_2O in light petroleum); $[\alpha]_D^{20}$ +109.9 (*c* 0.80 in $CHCl_3$); ν_{max}/cm^{-1} 3060s, 2927s, 2854s, 2317w, 1708s, 1496s, 1454m, 1411m, 1365m, 1266m, 1210m, 1096m, 1028m, 934m, 838w, 734m and 698s; δ_H(200 MHz) 7.36–7.28 (5H, m, Ar), 5.70 (1H, app. d, *J* 6, CH=), 5.67 (1H, app. d, *J* 6, CH=), 4.58 (2H, s, CH_2Ph), 3.81–3.59 (2H, m, CH_2OBn), 2.94–2.92 (1H, m, C*H*MeC=O), 2.72–2.68 (1H, m, C*H*CH_2OBn), 2.17–2.14 (1H, m, C*H*CHMe), 1.21 (3H, d, *J* 6.5, Me) and 1.03 (1H, d, *J* 6.5, C*H*Me); δ_C(50 MHz) 181.0 (C=O), 138.5 (Ar, quat.), 136.7 (CH=), 130.0 (CH=), 128.3 (2 × Ar), 127.5 (3 × Ar), 75.1 (CH_2Ph), 73.1 (CH_2O), 50.7 (*C*HC=O), 49.9 (*C*HCHC=O), 45.0 (*C*HCH_2OBn), 43.4 (*C*HMe), 20.4 [*C*H(Me)C=O] and 14.5 (Me).

(+)-Iridomyrmecin 48

H_2 was added to a twice evacuated, vigorously stirred suspension of 10% palladium on carbon (*ca.* 65 mg) and acid **47** (0.250 g, 0.911 mmol) in EtOH (5 cm^3) at room temperature. After 48 h the reaction was filtered through a plug of silica and evaporated under reduced pressure. Purification of the residue by column chromatography (66% Et_2O in hexane) gave a white solid, (+)-iridomyrmecin **48** (99 mg, 65%); R_f 0.68 (66% Et_2O in hexane); mp 58–59 °C (pentane) (lit.[38] 59–60 °C); $[\alpha]_D^{20}$ +199.1 (*c* 0.22 in CCl_4), lit.[38] $[\alpha]_D^{17}$ +205 (*c* 0.223 in CCl_4); δ_H(200 MHz) 4.26 (1H, dd, *J* 12 and 3, CH*H*CO), 4.16 (1H, d, *J* 12, C*H*HCO), 2.75–2.50 (2H, m, C*H*CH_2O and C*H*(Me)-C=O), 1.90–1.70 (4H, m, C*H*CHMe, CHCH_2 and C*H*Me), 1.14 (3H, d, *J* 6.5, Me), 1.04 (3H, d, *J* 6.5, Me) and 1.30–0.90 (2H, m, CH_2).

(1*R*,4*R*,5*S*)-(5-Benzyloxymethyl-4-methylcyclopent-2-en-1-yl)acetic acid 49

Following the procedure for the preparation of acid **47**, but using lactone **45** (0.70 g, 2.87 mmol), MeMgBr (3.0 mol dm^{-3} in Et_2O; 1.76 cm^3, 5.28 mmol) and CuBr·Me_2S (1.01 g, 4.91 mmol) gave a colourless oil, *acid* **49** (0.690 g, 93%); R_f 0.59 (75% Et_2O in light petroleum); $[\alpha]_D^{20}$ +134.1 (*c* 1.00 in EtOH); ν_{max}/cm^{-1} 3060s, 2927s, 2854s, 2317w, 1708s, 1497s, 1454m, 1412m, 1365m, 1266m, 1210m, 1096m, 1028m, 934m, 838w, 734m and 698s; δ_H(200 MHz) 7.36–7.28 (5H, m, Ar), 5.70 (1H, d, *J* 6, CH=), 5.67 (1H, d, *J* 6, CH=), 4.58 (2H, s, CH_2Ph), 3.81–3.73 (1H, m, C*H*HC=O), 3.57–3.51 (2H, m, CH_2OBn), 3.33–3.17 (1H, m, C*H*HC=O), 2.69–2.39 (1H, m, C*H*CH_2OBn), 2.18 (1H, m, C*H*Me) and 1.08 (3H, d, *J* 6.5, Me); δ_C(50 MHz: d_6-acetone) 174.8 (C=O), 139.0 (Ar, quat.), 136.3 (CH=), 132.9 (CH=), 128.4 (2 × Ar), 127.7 (2 × Ar), 127.6 (1 × Ar), 72.7 (CH_2Ph), 69.7 (CH_2O), 48.8 (*C*HCH_2C=O), 45.0 (*C*H_2C=O), 43.0 (*C*HCH_2-OBn), 41.4 (*C*HMe) and 19.2 (Me); *m*/*z* (EI) 260 (M^+, 4%), 247 (7), 220 (12), 201 (11), 158 (15), 156 (20), 108 (35) and 106 (100) (Found: M^+, 260.1412. $C_{16}H_{20}O_3$ requires *M,* 260.1412).

(4a*R*,7*S*,7a*R*)-Hexahydro-7-methylcyclopenta[*c*]pyran-3-one 50

Following the procedure for the preparation of iridomyrmecin **48**, but using acid **49** (0.600 g, 2.31 mmol) gave a white solid, *lactone* **50**[49] (0.330 g, 93%); R_f 0.73 (75% Et_2O in light petroleum); mp 42–43 °C (pentane); [lit.[49a] (racemate) 40.5–42 °C; lit.[50] 55–56 °C]; $[\alpha]_D^{20}$ +90.2 (*c* 1.00 in $CHCl_3$), {lit.[50] $[\alpha]_D$ +97, lit.[39b] (enantiomer) $[\alpha]_D^{25}$ −92 (*c* 1.00 in $CHCl_3$)}; ν_{max}/cm^{-1} 3060s, 2927s, 2854s, 2317w, 1708s, 1496s, 1454m, 1411m, 1365m, 1266m, 1210m, 1095m, 1028m, 934m, 838w, 734m and 698s; δ_H(200 MHz) 4.27 (1H, dd, *J* 11.5 and 4.5, CH*H*OC=O), 4.11 (1H, dd, *J* 11.5 and 4.5, C*H*HOC=O), 2.65–2.55 (2H, m, C*H*HC=O and C*H*CH_2C=O), 2.37–2.33 (1H, m, CH*H*C=O), 2.02–1.99 (1H, m, C*H*H), 1.90–1.75 (3H, m, CH*H*, C*H*Me and C*H*CHMe), 1.3–1.1 (2H, m, CH_2) and 1.06 (3H, d, *J* 6.5, Me).

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