Studies towards the total synthesis of lycoposerramine A. Synthesis of a model for the tetracyclic core†

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Lycoposerramine A (**1**) is a pentacyclic alkaloid isolated in 2001 by Takayama and co-workers. A concise synthesis of a model compound **8** for the tetracyclic core of this natural product is described. Key steps include the desymmetrising free-radical cyclisation of compound **7** to give compound **18** and spirocyclisation of compound **26** to give compound **8**. Earlier approaches using a novel high-yielding stereoselective anionic cyclisation of a cyclohexa-1,4-diene are also reported.

Introduction

Lycoposerramine A[1] (**1**) (Fig. 1) is a pentacyclic alkaloid isolated in 2001 by Takayama and co-workers. It belongs to the fawcettimine class of lycopodium alkaloids,[2] and contains a 6–5 carbobicyclic core bridged by a pyrrolidine ring. Additionally, there is a fused azonane ring present in all compounds of this class, while lycoposerramine A is unique among natural products in that it possesses an oxadiazolidine ring, this being fused to the pyrrolidine. The dense array of functionality and stereochemistry of this pentacyclic core presents a significant challenge for organic chemists, and there have been no synthetic approaches reported to date. Takayama and co-workers have reported the conversion of serratinine into lycoposerramine B.[3] The only other synthetic work on this structural group[4] of lycoposerramine alkaloids is a recent report from ourselves[5] of the synthesis of the tricyclic core of lycoposerramine S (**2**),[6] a simpler natural product which lacks the oxadiazolidinone ring. The parent compound in this class, fawcettimine (**3**), was first prepared by Inubushi in 1979,[7] although Heathcock's 1986 synthesis is regarded as a defining achievement in this area.[8] The first enantioselective total synthesis of this compound was reported recently,[9] along with a further formal total synthesis.[10] The cores of fawcettimine and serratinine have also been prepared.[11] These targets are structurally related to magellanine and paniculatine, which have been synthesised a number of times.[12]

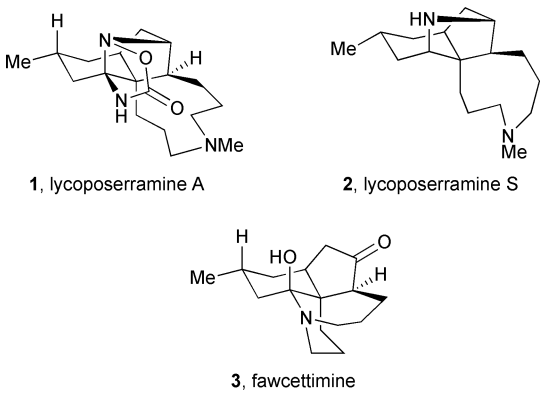
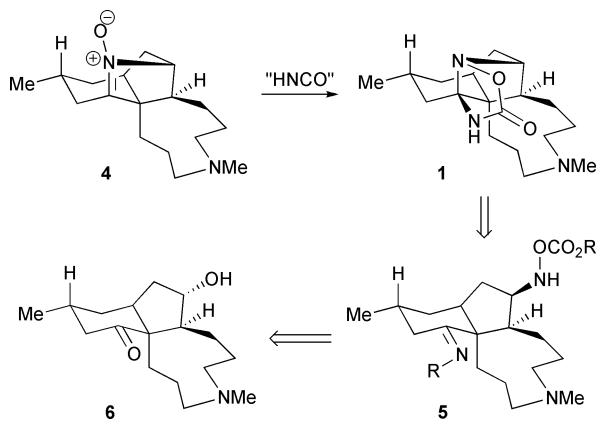


Fig. 1 Fawcettimine and lycoposerramine alkaloids.

Discussion

Lycoposerramine A presents a number of significant synthetic challenges. We chose to install the quaternary stereogenic centre in the carbobicyclic core by diastereoselective cyclisation of a cyclohexa-1,4-diene precursor,[13,14] so that the quaternary centre is formed indirectly, with no bond formation at this carbon. The unusual oxadiazolidinone ring is spirocyclic to the cyclohexane ring and attached to the cyclopentane ring. This means that the conventional method for the preparation of this heterocycle, the cycloaddition of a nitrone with an isocyanate, is not possible, since the nitrone **4** would be extremely strained (anti-Bredt) (Scheme 1). We therefore elected to attempt formation of this heterocycle by addition of a hydroxylamine carbonate onto a suitably-disposed imine (**5** → **1**). This imine would be derived from ketone **6**, which will be available by desymmetrisation of a cyclohexa-1,4-diene precursor. We now report the successful realisation of studies culminating in the synthesis of tetracyclic model compound **8** from cyclohexadiene **7** (Scheme 2).



Scheme 1 Proposed synthetic approach to lycoposerramine A.

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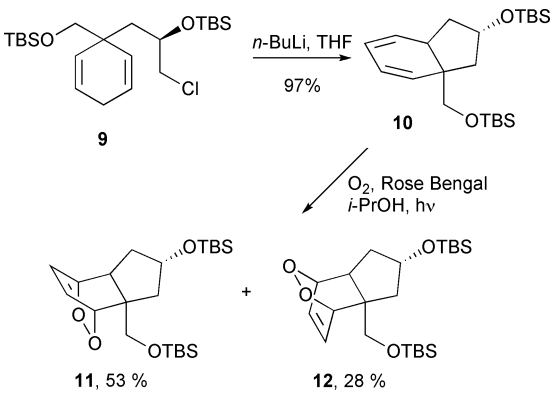
† Electronic supplementary information (ESI) available: Copies of NMR spectra for compounds **7**, **8**, **10–16** and **18–26**. See DOI: 10.1039/b909860g

Scheme 2 Summary of the present work.

Approach 1 – Anionic cyclisation

We have previously utilised compounds related to **7** in electrophile-initiated cyclisations[15] and free-radical cyclisations.[5] Cyclohexa-1,4-dienes can be deprotonated by butyllithium,[16] although amine additives are generally required. We were therefore slightly surprised to find that treatment of diene **9** with *n*-butyllithium in THF gave 1,3-diene **10** as a single diastereoisomer in near-quantitative yield (Scheme 3). There is precedent for such mild deprotonation reactions in the work of Landais.[17] Although the stereochemistry of the product **10** could not be proven spectroscopically, there seems little doubt given the conformational bias observed in our earlier studies. This was followed by oxygenation of the diene to give a separable mixture of endoperoxides **11** and **12**.[18]

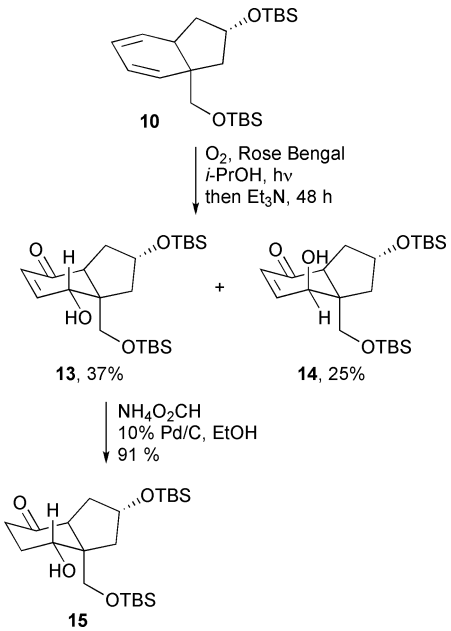


Scheme 3 Anionic cyclisation and photooxygenation from compound **9**.

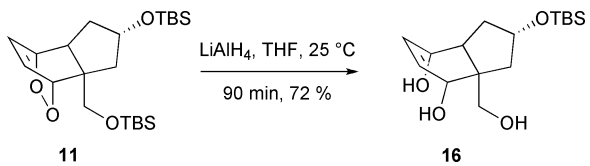
Rather than routinely isolate these endoperoxides, compound **10** was subjected to a two-step procedure involving the above oxygenation followed immediately by Kornblum–de la Mare rearrangement. The major isomer from this sequence, **13**, could be hydrogenated to provide hydroxyketone **15** (Scheme 4).

A range of conditions was evaluated in attempts to deoxygenate the ketone groups present in either of these compounds. These included the Huang–Minlon-modified Wolff–Kishner reduction, tosylhydrazone formation and reduction ($LiAlH_4$ or $NaBH_4$) and dithiane formation/reduction. Only in the latter case was any success observed. Reaction of compound **13** with ethanedithiol/Me_2AlCl followed by reduction (Raney Ni, EtOH) gave a low yield of a compound which appeared to derive from removal of the ketone group and alkene double-bond. However, this result could not be optimised above 20% yield, and so was abandoned.

The reduction of endoperoxide **11** was investigated next. Using $LiAlH_4$, this also resulted in serendipitous deprotection of the primary silyl ether (Scheme 5). Compound **16** was then protected as a benzylidene acetal, presumably tethering the primary and proximal secondary alcohols. However, we were unable to unambiguously prove this. This lack of clear proof,



Scheme 4 Kornblum–de la Mare rearrangement from compound **10**.

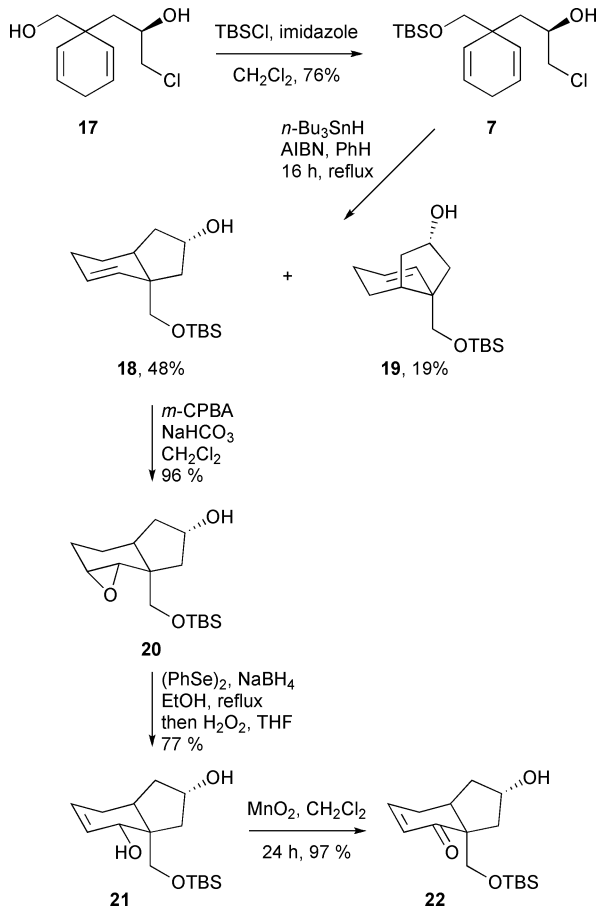


Scheme 5 Reduction of compound **11**.

coupled with additional steps required to elaborate this compound (deoxygenation of the alcohol, selective cleavage of the benzylidene protecting group to the primary benzyl ether and oxidation of the secondary alcohol) meant that the synthesis was becoming unwieldy, and so this line of attack was abandoned in favour of a route featuring free-radical cyclisation[19] as the key step.

Approach 2 – Radical cyclisation

We have previously reported that compound **9** undergoes free-radical cyclisation with good stereoselectivity (5:1) but in low yield.[5] The free-secondary alcohol cyclises with lower stereoselectivity; however, the overall yields are higher, and an additional deprotection step will not be needed, so this route is actually preferable. Monoprotection of diol **17**[15] was followed by cyclisation (slow addition of Bu_3SnH and AIBN as solutions in benzene over 10 h by syringe pump) resulted in the formation of a separable mixture of compounds **18** and **19** (Scheme 6). Epoxidation of the major isomer **18** with *m*-CPBA produced a 7:1 mixture of epoxide diastereoisomers. We assume that stereoisomer **20** is favored as a result of epoxidation taking place selectively on the convex face, although the bulk of the CH_2OTBS group makes this slightly ambiguous. The epoxide was then ring-opened by the phenylselenenyl anion; selenoxide elimination then gave allylic alcohol **21**.[20] Oxidation finally delivered the required enone **22**.[21] Although compound **20** has been drawn in a conformation to resemble that of the natural product target **1**, one would expect ring-opening in this conformation to take place at the position closest to ring-fusion according to the Fürst–Plattner



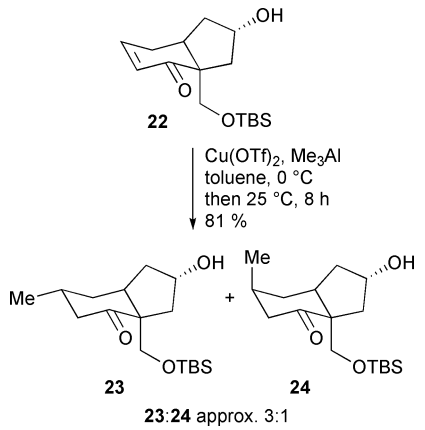
Scheme 6 Synthesis of enone **22**.

rule.[22] We have recently observed apparent violations of the Fürst–Plattner rule in the opening of structurally-related epoxides which were characterized crystallographically[23], so that the present regioselectivity could be attributed to steric hindrance from the cyclopentane ring, or be an indication that the reaction is not taking place *via* the conformation shown. We were unable to determine the epoxide or carbinol stereochemistry in compounds **20** and **21** respectively, and this information is lost in the oxidation to compound **22**.

Conjugate addition to enone **22** was accomplished using trimethylaluminium and copper triflate in toluene, giving a 3:1 mixture favouring the desired stereoisomer **23** in 81% yield (Scheme 7). The stereochemical assignment of the methyl group was confirmed by subsequent formation of compound **8** (*vide infra*). Unfortunately, compounds **23** and **24** were inseparable in our hands, so that the mixture of isomers was carried through the subsequent steps. Other conditions were evaluated in this transformation, including $MeCu(CN)Li.BF_3$ in THF, which gave a 3:2 mixture favouring diastereoisomer **24**.[24]

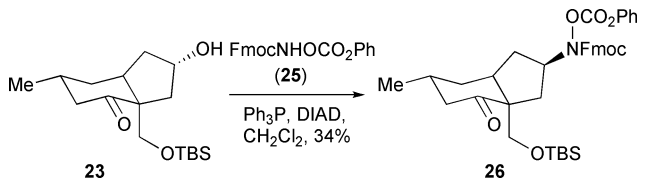
Approach to the oxadiazolidinone ring

With key intermediate **23** now in hand, we turned our attention to construction of the oxadiazolidinone ring system. We envisaged introduction of the hydroxylamine[25] moiety using a Mitsunobu reaction.[26] Since this reaction is incompatible with imines, this would define the order of steps required. Reaction of compound



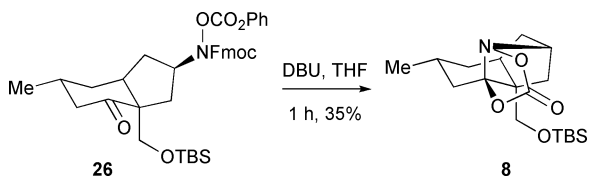
Scheme 7 Conjugate addition to enone **22**.

23 with $FMocNHOCO_2Ph$ (**25**) gave compound **26**, albeit in modest yield (Scheme 8). This compound gave extremely broad NMR spectra. While the data are not reported in the experimental section, copies of spectra are provided as ESI†.



Scheme 8 Mitsunobu reaction to form compound **26**.

A number of methods for imine formation were attempted using this compound. All were uniformly unsuccessful. We therefore demonstrated the viability of dioxazolidinone formation by deprotection of compound **26** with DBU in THF. Under these conditions, removal of the FMoc group led to cyclisation onto the carbonyl; a second cyclisation with loss of phenol then furnished the heterocycle **8** (Scheme 9). At this point, the stereochemistry of the methyl group was confirmed by measurement of the coupling constants of one of the adjacent CH_2 protons at 1.24 ppm. This particular proton has couplings of 14.1 Hz (geminal) and 12.4 Hz (vicinal, to an adjacent axial hydrogen) and 3.8 Hz (to the ring junction hydrogen). Therefore, the methyl group is equatorial.



Scheme 9 Spirocyclisation to form compound **8**.

Conclusions

An efficient approach to the carbobicyclic core **23** of lycoposerramine A (**1**) has been developed. Formation of the oxadiazolidinone ring is a significant challenge, since it requires introduction of two sensitive functional groups, imine and hydroxylamine, simultaneously. However, in model studies, we have shown that the cyclisation of a hydroxylamine nitrogen onto a carbon–heteroatom

double-bond, followed by attack of the heteroatom onto the carbonate carbonyl group, is a viable strategy for the formation of this heterocycle. This work therefore represents the first synthetic approach to lycoposerramine A.

Experimental section

tert-Butyl-(((2*RS*,3a*SR*,7a*SR*)-2-(*tert*-butyldimethylsilyloxy)-2,3,3a,7a-tetrahydro-1*H*-inden-3a-yl)methoxy)dimethylsilane (10)

Chloride **9**[5] (7.6 g, 17.7 mmol) was dissolved in THF (50 mL) and cooled to −78 °C. Following the dropwise addition of 1.6 M BuLi (12.1 mL, 19.4 mmol, 1.1 equiv.), the cooling bath was removed and the reaction allowed to warm to room temperature. After stirring for a further 1 h, 2 M HCl (50 mL) was added, the organic layer was separated and the aqueous phase extracted with Et_2O (2× 20 mL). The combined organic extracts were dried over Na_2SO_4 and concentrated *in vacuo* to give the *title compound* (6.75 g, 97%) as a pale yellow oil (Found: MO_2H^+, 427.2729. $C_{22}H_{43}O_4Si_2$ requires M, 427.2700); ν_{max} (CH_2Cl_2) 2942, 2855, 1472, 1255, 1098, 836 and 774 cm^{-1}; δ_H (500 MHz; $CDCl_3$) 5.78-5.74 (1 H, m, one of alkene CH), 5.74-5.71 (2 H, m, 2 × alkene CH), 5.43 (1 H, d, *J* 9.5, one of alkene CH), 4.12 (1 H, app. tt, *J* 5.5, 3.8, CHOTBS), 3.46 (1 H, d, *J* 9.2, one of CH_2O), 3.34 (1 H, d, *J* 9.2, one of CH_2O), 2.66 - 2.60 (1 H, m, ring junction CH), 1.97-1.90 (2 H, m, one of CCH_2CHO and one of CHCH_2CHO), 1.67 (1 H, dd, *J* 13.6, 5.5, one of CCH_2CHO), 1.59 (1 H, ddd, *J* 12.4, 10.2, 5.5, one of CHCH_2CHO), 0.87 (18 H, s, $SiC(CH_3)_3$), 0.04 (6 H, s, 2 × $SiCH_3$), 0.01 (3 H, s, $SiCH_3$) and 0.01 (3 H, s, $SiCH_3$); δ_C (125 MHz; $CDCl_3$) 132.4 (CH), 129.9 (CH), 120.8 (CH), 120.3 (CH), 70.4 (CH), 69.6 (CH_2), 46.3 (CH_2), 46.0 (C), 44.3 (CH_2), 37.8 (CH), 25.9 (CH_3), 25.9 (CH_3), 18.3 (C), 18.1 (C), −4.7 (CH_3), −4.8 (CH_3) and −5.4 (CH_3); *m*/*z* (TOF ES+) 427 (MO_2H^+, 100%) and 428 (10).

Endoperoxides 11 and 12

A solution of diene **10** (2.67 g, 6.7 mmol) and Rose Bengal (cat., approx 100 mg) in *i*-PrOH (50 mL) was cooled to approx 15 °C by flowing water through the outer jacket of a cold finger condenser. A steady stream of O_2 was then bubbled through the solution while it was irradiated using a 500 W halogen lamp from a distance of approximately 10 cm for 18 h. The solvent was removed *in vacuo*, with the minimum heat possible, and the residue purified by chromatography on silica (1–2% Et_2O in petroleum ether) giving the major isomer **11** (1.53 g, 53%) and minor isomer **12** (0.81 g, 28%), both pale yellow oils.

Data for compound 11. Pale yellow oil (1.53 g, 53%) (Found: MH^+, 427.2719. $C_{22}H_{43}O_4Si_2$ requires 427.2700); ν_{max} (CH_2Cl_2) 2955, 2856, 1636, 1472, 1361, 1254, 1071, 836 and 774 cm^{-1}; δ_H (500 MHz; $CDCl_3$) 6.65 (1 H, ddd, *J* 7.9, 6.1, 1.5, one of alkene CH), 6.52 (1 H, ddd, *J* 7.9, 6.1, 1.5, one of alkene CH), 4.73 (1 H, app. dt, *J* 6.1, 1.5, CCHO), 4.61 (1 H, app. ddt, *J* 6.1, 4.4, 1.5, CHC*H*O), 4.20 (1 H, app. tt, *J* 4.4, 1.8, CHOTBS), 3.88 (1 H, dd, *J* 8.9, 1.3, one of CH_2O), 3.81 (1 H, d, *J* 8.9, one of CH_2O), 2.18 (1 H, app. td, *J* 8.4, 4.4, ring junction CH), 2.03 (1 H, dt, *J* 13.8, 1.8, one of CCH_2CHO), 1.82 (1 H, ddt, *J* 13.3, 8.4, 1.8, one of CHCH_2CHO), 1.19 (1 H, ddd, *J* 13.3, 8.4, 4.4, one of CHCH_2CHO), 1.14 (1 H, dd, *J* 13.8, 4.4, one of CCH_2CHO), 0.89 (9 H, s, $SiC(CH_3)_3$), 0.87 (9 H, s, $SiC(CH_3)_3$), 0.05 (6 H, s, 2 × $SiCH_3$), 0.02 (3 H, s, $SiCH_3$) and 0.02 (3 H, s, $SiCH_3$); δ_C (125 MHz; $CDCl_3$) 133.1 (CH), 131.3 (CH), 74.3 (CH), 74.0 (CH), 73.6 (CH), 66.7 (CH_2), 49.1 (C), 41.9 (CH), 41.1 (CH_2), 39.9 (CH_2), 25.9 (CH_3), 25.9 (CH_3), 18.3 (C), 18.0 (C), −4.8 (CH_3), −4.9 (CH_3), −5.3 (CH_3) and −5.4 (CH_3); *m*/*z* (TOF ES+) 427 (MH^+, 100%) and 295 (10).

Data for compound 12. Pale yellow oil (0.81 g, 28%) (Found: MH^+, 427.2730. $C_{22}H_{43}O_4Si_2$ requires 427.2700); ν_{max} (CH_2Cl_2) 2942, 2856, 1466, 1361, 1255, 1094, 836 and 775 cm^{-1}; δ_H (400 MHz; $CDCl_3$) 6.63-6.60 (2 H, m, 2 × alkene CH), 4.64-4.58 (1 H, m, CHOTBS), 4.54-4.49 (1 H, m, one of HC=CHC*H*O), 4.35-4.31 (1 H, m, one of HC=CHC*H*O), 3.64 (1 H, d, *J* 9.3, one of CH_2O), 3.23 (1 H, d, *J* 9.3, one of CH_2O), 2.19 (1 H, dd, *J* 13.3, 4.8, one of CCH_2CHO), 2.12 (1 H, ddd, *J* 13.1, 7.1, 4.8, one of CHCH_2CHO), 1.86 (1 H, ddd, *J* 13.3, 3.0, 2.0, one of CCH_2CHO), 1.77 (1 H, dddd, *J* 13.1, 8.6, 3.0, 2.0, one of CHCH_2CHO), 1.61 (1 H, ddd, *J* 8.6, 7.1, 2.0, ring junction CH), 0.88 (9 H, s, $SiC(CH_3)_3$), 0.87 (9 H, s, $SiC(CH_3)_3$), 0.06 (6 H, s, 2 × $SiCH_3$), 0.01 (3 H, s, $SiCH_3$) and 0.00 (3 H, s, $SiCH_3$); δ_C (125 MHz; $CDCl_3$) 132.1 (CH), 131.3 (CH), 76.4 (CH), 76.2 (CH), 74.6 (CH), 70.2 (CH_2), 48.1 (C), 39.2 (CH), 38.9 (CH_2), 37.0 (CH_2), 25.9 (CH_3), 25.8 (CH_3), 18.1 (C), 18.1 (C), −4.7 (CH_3), −4.8 (CH_3), −5.4 (CH_3) and −5.6 (CH_3); *m*/*z* (TOF ES+) 427 (MH^+, 100%) and 295 (10).

(2*RS*,3a*RS*,7*SR*,7a*SR*)-2-(*tert*-Butyldimethylsilyloxy)-7a-((*tert*-butyldimethylsilyloxy)methyl)-7-hydroxy-3,3a,7,7a-tetrahydro-1*H*-inden-4(2*H*)-one (13) and (2*RS*,3a*RS*,7*RS*,7a*SR*)-2-(*tert*-butyldimethylsilyloxy)-7a-((*tert*-butyldimethylsilyloxy)-methyl)-7-hydroxy-3,3a,7,7a-tetrahydro-1*H*-inden-4(2*H*)-one (14)

Oxidation of diene **10** (3.80 g, 9.6 mmol) was conducted as described above, after 18 h irradiation the lamp and oxygen supply were removed and Et_3N (10 mL) added. After stirring for a further 48 h the solvent was removed *in vacuo* and the residue chromatographed on silica (5–10% EtOAc in petroleum ether) to give the *title compounds* **13** (1.51 g, 37%) as a light yellow oil, followed by **14** (1.03 g, 25%) as a yellow oil.

Data for compound 13. Light yellow oil (1.51 g, 37%) (Found: MH^+, 427.2701. $C_{22}H_{43}O_4Si_2$ requires M, 427.2700); ν_{max} (CH_2Cl_2) 3448, 2943, 2857, 1666, 1472, 1256, 1083, 837 and 776 cm^{-1}; δ_H (400 MHz; $CDCl_3$) 6.95 (1 H, dd, *J* 10.2, 2.2, *H*C=CHC=O), 5.95 (1 H, dd, *J* 10.2, 1.9, CH=C*H*C=O), 4.67 (1 H, d, *J* 7.4, OH), 4.33–4.38 (1 H, app. tt, *J* 5.7, 2.3, CHOTBS), 4.37-4.33 (1 H, app. tt, *J* 7.4, 2.2, C*H*OH), 4.09 (1 H, d, *J* 10.0, one of CH_2O), 3.61 (1 H, d, *J* 10.0, one of CH_2O), 2.66 (1 H, dd, *J* 11.3, 8.1, ring junction CH), 2.38 (1 H, dd, *J* 14.4, 6.2, one of CCH_2CHOTBS), 2.08-1.94 (2 H, m, two of CHCH_2CHOTBS), 1.72 (1 H, app. broad d, *J* 14.4, one of CCH_2CHOTBS), 0.89 (9 H, s, $SiC(CH_3)_3$), 0.87 (9 H, s, $SiC(CH_3)_3$), 0.09 (3 H, s, $SiCH_3$), 0.07 (3 H, s, $SiCH_3$) and 0.04 (6 H, s, 2 × $SiCH_3$); δ_C (125 MHz; $CDCl_3$) 199.4 (C=O), 152.9 (CH), 127.3 (CH), 72.7 (CH), 71.9 (CH), 69.6 (CH_2), 51.8 (C), 51.0 (CH), 45.1 (CH_2), 38.7 (CH_2), 25.8 (CH_3), 25.7 (CH_3), 18.0 (C), 18.0 (C), −4.8 (CH_3), −4.8 (CH_3) and −5.5 (CH_3), −5.7 (CH_3); *m*/*z* (TOF ES+) 427 (MH^+, 10%), 336 (77), 295 (62), 277 (100) and 163 (11).

Data for compound 14. Yellow oil (1.03 g, 25%) (Found: MH^+, 427.2729. $C_{22}H_{43}O_4Si_2$ requires M, 427.2700); ν_{max} (CH_2Cl_2) 3449, 2943, 2857, 1675, 1471, 1362, 1256 and 1085 cm^{-1}; δ_H (400 MHz; $CDCl_3$) 6.74 (1 H, dd, *J* 10.3, 1.9, C*H*=CHC=O), 5.95 (1 H, dd, *J* 10.3, 2.4, CH=C*H*C=O), 4.81 (1 H, app. q, *J* 2.2, C*H*OH), 4.28-4.22 (1 H, m, CHOTBS), 3.93 (1 H, d, *J* 9.4, one of CH_2O), 3.74 (1 H, d, *J* 9.4, one of CH_2O), 3.43 (1 H, d, *J* 3.0, OH), 2.62 (1 H, ddd, *J* 13.8, 7.1, 2.3, one of CHCH_2CHO), 2.45 (1 H, app. broad d, *J* 8.4, ring junction CH), 2.02 (1 H, dd, *J* 14.5, 8.1, one of CCH_2CHO), 1.88 (1 H, ddd, *J* 13.8, 8.4, 5.7, one of CHCH_2CHO), 1.75 (1 H, app. broad d, *J* 14.5, one of CCH_2CHO), 0.92 (9 H, s, $SiC(CH_3)_3$), 0.86 (9 H, s, $SiC(CH_3)_3$), 0.11 (6 H, s, $SiCH_3$) and 0.01 (6 H, s, $SiCH_3$); δ_C (125 MHz; $CDCl_3$) 199.5 (C), 151.3 (CH), 127.2 (CH), 71.5 (CH), 70.7 (CH), 70.1 (CH_2), 52.6 (C), 49.8 (CH), 39.8 (CH_2), 38.0 (CH_2), 25.9 (CH_3), 18.2 (C), 18.0 (C), –4.8 (CH_3), –4.9 (CH_3), –5.5 (CH_3) and –5.6 (CH_3); *m*/*z* (TOF ES+) 428 (9), 427 (MH^+, 100%) and 295 (11).

(2*SR*,3a*RS*,7*SR*,7a*SR*)-2-(*tert*-Butyldimethylsilyloxy)-3a-((*tert*-butyldimethylsilyloxy)methyl)-7-hydroxyhexahydro-1*H*-inden-4(2*H*)-one (15)

10% Pd/C (100 mg) and ammonium formate (560 mg, 8.9 mmol) were added to a solution of enone **13** (377 mg, 0.88 mmol) in EtOH (10 mL). This was heated to reflux for 2 h, allowed to cool and filtered through a pad of silica, washing with Et_2O. The filtrate was concentrated *in vacuo* and the residue partitioned between Et_2O (20 mL) and brine (20 mL). The organic layer was separated and the aqueous phase extracted with Et_2O (2 × 10 mL). The combined organic extracts were dried over Na_2SO_4 and concentrated *in vacuo* to yield the *title compound* (341 mg, 91%) as a pale yellow oil (Found: MH^+, 429.2870. $C_{22}H_{45}O_4Si_2$ requires M, 429.2856); ν_{max} (CH_2Cl_2) 3446, 2942, 2857, 1706, 1472, 1362, 1255, 1075, 837 and 776 cm^{-1}; δ_H (400 MHz; $CDCl_3$) 4.53 (1 H, broad s, OH), 4.35-4.29 (1 H, m, CHOTBS), 4.00 (1 H, d, *J* 10.1, one of CH_2O), 3.91–3.85 (1 H, m, C*H*OH), 3.77 (1 H, d, *J* 10.1, one of CH_2O), 2.77 (1 H, app. t, *J* 7.7, ring junction CH), 2.67 (1 H, ddd, *J* 16.5, 10.1, 7.2, one of CH_2C=O), 2.29 (1 H, ddd, *J* 16.5, 6.3, 4.1, one of CH_2C=O), 2.23 (1 H, ddd, *J* 13.2, 7.7, 5.4, one of CHCH_2CHOTBS), 2.13-1.92 (2 H, m, CH_2CHOH), 1.83-1.75 (1 H, m, one of CHCH_2CHOTBS), 1.75 (1 H, dd, *J* 14.3, 6.0, one of CCH_2CHOTBS), 1.51 (1 H, app. broad d, *J* 14.3, one of CCH_2CHOTBS), 0.90 (9 H, s, $SiC(CH_3)_3$), 0.86 (9 H, s, $SiC(CH_3)_3$), 0.10 (3 H, s, one of $SiCH_3$), 0.10 (3 H, s, one of $SiCH_3$), 0.03 (3 H, s, one of $SiCH_3$) and 0.03 (3 H, s, one of $SiCH_3$); δ_C (100 MHz; $CDCl_3$) 213.3 (C), 72.8 (CH), 72.0 (CH), 69.6 (CH_2), 52.8 (C), 51.8 (CH), 43.4 (CH_2), 38.1 (CH_2), 34.0 (CH_2), 27.5 (CH_2), 25.8 (CH_3), 25.7 (CH_3), 18.0 (C), 17.9 (C), –4.8 (CH_3), –5.0 (CH_3) and –5.7 (CH_3); *m*/*z* (TOF ES^+) 429 (MH^+, 35%), 338 (100), 320 (5), 297 (28) and 279 (5).

(2*RS*,3a*SR*,4*SR*,7*RS*,7a*RS*)-2-(*tert*-Butyldimethylsilyloxy)-3a-(hydroxymethyl)-2,3,3a,4,7,7a-hexahydro-1*H*-indene-4,7-diol (16)

To a solution of peroxide **11** (379 mg, 0.89 mmol) in THF (10 mL) was added a 1 M solution of $LiAlH_4$ in THF (2.0 mL, 2.0 mmol, 2.2 equiv.). After stirring for 90 min the reaction was quenched with 2 M NaOH, dried over Na_2SO_4 and filtered. The solvent was removed *in vacuo* and the residue crystallised from Et_2O and petroleum ether to give the *title compound* (191 mg, 72%) as a colourless solid, m.p. 84–87 °C (Found: MH^+, 315.1996. $C_{16}H_{31}O_4Si$ requires 315.1992); ν_{max} (CH_2Cl_2) 3406, 2924, 2856, 1458, 1260, 1089, 1022, 800 and 750 cm^{-1}; δ_H (400 MHz; $CDCl_3$) 6.07 (1 H, dd, *J* 9.8, 3.7, one of alkene CH), 6.00 (1 H, app. ddt, *J* 9.8, 4.9, 1.1, one of alkene CH), 4.29-4.23 (1 H, m, CHOTBS), 4.08 (1 H, app. broad s, one of HC=CHC*H*O), 4.00-3.92 (2 H, m, one of HC=CHC*H*O and one of CH_2O), 3.69 (1 H, app. broad d, *J* 10.9, one of CH_2O), 3.09 (1 H, broad s, OH), 3.01 (1 H, broad d, *J* 5.3, OH), 2.85 (1 H, d, *J* 8.2, OH), 2.41 (1 H, ddd, *J* 11.8, 7.9, 2.0, ring junction CH), 1.89 (1 H, app. ddt, *J* 13.4, 7.9, 1.5, one of CHCH_2CHO), 1.86 (1 H, dd, *J* 13.8, 5.9, one of CCH_2CHO), 1.58-1.49 (2 H, m, one of CHCH_2CHO and one of CCH_2CHO), 0.87 (9 H, s, $SiC(CH_3)_3$) and 0.04 (6 H, s, 2 × $SiCH_3$); δ_C (125 MHz; $CDCl_3$) 134.2 (CH), 130.5 (CH), 71.3 (CH), 70.5 (CH), 69.1 (CH_2), 66.2 (CH), 48.7 (C), 47.9 (CH), 45.5 (CH_2), 41.0 (CH_2), 25.8 (CH_3), 18.0 (C), –4.8 (CH_3) and –4.8 (CH_3); *m*/*z* (TOF ES+) 315 (MH^+, 29%), 183 (4) and 165 (100).

(*RS*)-1-(1-((*tert*-Butyldimethylsilyloxy)methyl)cyclohexa-2,5-dienyl)-3-chloropropan-2-ol (7)

Imidazole (2.53 g, 40 mmol, 2.2 equiv.) and TBDMSCl (2.72 g, 18 mmol, 1.0 equiv.) were added to a solution of diol **17**[15] (3.65 g, 18 mmol) in CH_2Cl_2 (30 mL). After stirring for 1 h, saturated aqueous NH_4Cl (30 mL) was added and the organic phase separated. The aqueous layer was extracted with CH_2Cl_2 (2 × 10 mL), the combined organic phases were dried over Na_2SO_4 and the residue purified by chromatography on silica (10% Et_2O in petroleum ether) to give the *title compound* (4.35 g, 76%) as a colourless oil (Found: MH^+, 317.1710. $C_{16}H_{30}O_2SiCl$ requires M, 317.1724); ν_{max} (neat) 3426, 2942, 2855, 1471, 1409, 1361, 1255, 1107, 940, 837, 776, 723 and 698 cm^{-1}; δ_H (500 MHz; $CDCl_3$) 5.91-5.82 (2 H, m, 2 × alkene CH), 5.70 (1 H, app. dq, *J* 10.2, 2.0, alkene CH), 5.48 (1 H, app. dq, *J* 10.2, 2.0, alkene CH), 3.98-3.92 (1 H, m, C*H*OH), 3.53 (1 H, dd, *J* 11.0, 4.4, one of CH_2Cl), 3.48 (1 H, dd, *J* 11.0, 4.4, one of CH_2Cl), 3.41 (1 H, d, *J* 9.5, one of CH_2O), 3.40 (1 H, d, *J* 9.5, one of CH_2O), 2.99 (1 H, d, *J* 2.9, OH), 2.69-2.66 (2 H, m, CH=CH-CH_2), 1.76-1.69 (2 H, m, CH_2CHOH), 0.89 (9 H, s, $SiC(CH_3)_3$) and 0.03 (6 H, s, $Si(CH_3)_2$); δ_C (125 MHz; $CDCl_3$) 130.1 (CH), 130.0 (CH), 126.2 (CH), 125.6 (CH), 71.3 (CH_2), 69.2 (CH), 50.2 (CH_2), 42.5 (CH_2), 40.9 (C), 26.7 (CH_2), 25.9 (CH_3), 18.3 (C) and –5.4 (CH_3); *m*/*z* (TOF ES+) 319 (5), 317 (MH^+, 21%), 187 (9) and 185 (100).

(2*RS*,3a*RS*,7a*RS*)-7a-((*tert*-Butyldimethylsilyloxy)methyl)-2,3,3a,4,5,7a-hexahydro-1*H*-inden-2-ol (18) and (2*SR*,3a*RS*,7a*RS*)-7a-((*tert*-butyldimethylsilyloxy)methyl)-2,3,3a,4,5,7a-hexahydro-1*H*-inden-2-ol (19)

Chloride **7** (2.265 g, 7.16 mmol) was dissolved in benzene (30 mL) and the solution heated to reflux. AIBN (235 mg, 1.43 mmol, 0.2 equiv.) and Bu_3SnH (2.3 mL, 8.59 mmol, 1.2 equiv.), each in 5 mL benzene, were added over 10 h by syringe pump. After a further 6 h at reflux the solvent was removed *in vacuo* and the residue chromatographed on silica containing approximately 10% w/w NaF (7–10% EtOAc in petroleum ether) affording compound **18** (960 mg, 48%) followed by compound **19** (385 mg, 19%), both as colourless oils.

Data for compound 18. Colourless oil (960 mg, 48%) (Found: MH^+, 283.2091. $C_{16}H_{31}O_2Si$ requires M, 283.2093); ν_{max} (neat) 3369, 2930, 2851, 1652, 1470, 1253, 1096, 838, 756, 709 and 677 cm^{-1}; δ_H (500 MHz; $CDCl_3$) 5.70 (1 H, ddd, *J* 10.0, 5.4, 2.4, CH_2CH=CH), 5.36 (1 H, app. broad d, *J* 10.0, CH_2CH=C*H*), 4.14-4.09 (1 H, m, C*H*OH), 3.39 (1 H, d, *J* 9.5, one of CH_2O), 3.38 (1 H, d, *J* 9.5, one of CH_2O), 3.14 (1 H, d, *J* 9.0, OH), 2.41 (1 H, app. ddt, *J* 11.4, 7.5, 4.1, ring junction CH), 2.02-1.93 (1 H, m, one of CH_2CH=CH), 1.88 (1 H, dqd, *J* 17.6, 4.7, 1.2, one of CH_2CH=CH), 1.84 (1 H, dt, *J* 14.1, 1.7), 1.75-1.56 (5 H, m), 0.92 (9 H, s, $SiC(CH_3)_3$) and 0.09 (6 H, s, $Si(CH_3)_2$); δ_C (125 MHz; $CDCl_3$) 132.3 (CH), 126.6 (CH), 71.1 (CH), 68.4 (CH_2), 45.7 (CH_2), 45.7 (C), 39.7 (CH_2), 26.0 (CH_3), 22.1 (CH_2), 20.5 (CH_2), 18.4 (C), −5.5 (CH_3) and −5.5 (CH_3); *m*/*z* (TOF ES+) 283 (MH^+, 92%), 189 (17) and 133 (100).

Data for compound 19. Colourless oil (385 mg, 19%) (Found: MH^+, 283.2090. $C_{16}H_{31}O_2Si$ requires M, 283.2093); ν_{max} (neat) 3336, 2927, 2856, 1652, 1472, 1255, 1093, 837, 774, 705 and 668 cm^{-1}; δ_H (500 MHz; $CDCl_3$) 5.76 (1 H, ddd, *J* 10.0, 5.0, 2.5, CH_2CH=CH), 5.55 - 5.50 (1 H, m, CH_2CH=C*H*), 4.21 (1 H, app. tdd, *J* 7.0, 5.4, 4.3, C*H*OH), 3.34 (1 H, d, *J* 9.7, one of CH_2O), 3.32 (1 H, d, *J* 9.7, one of CH_2O), 2.20-2.02 (4 H, m, $CHCH_2CHOH$, one of CCH_2CHOH and one of CH_2CH=CH), 1.95 (1 H, app. dtdd, *J* 18.0, 5.0, 2.9, 1.6, one of CH_2CH=CH), 1.68-1.50 (3 H, m, CH_2CH_2CH=CH and ring junction CH), 1.45 (1 H, dd, *J* 13.4, 4.3, one of CCH_2CHOH), 0.88 (9 H, s, $SiC(CH_3)_3$), 0.02 (3 H, s, one of $Si(CH_3)_2$) and 0.02 (3 H, s, one of $Si(CH_3)_2$); δ_C (125 MHz; $CDCl_3$) 133.5 (CH), 127.4 (CH), 72.4 (CH), 68.2 (CH_2), 46.6 (C), 44.4 (CH_2), 39.7 (CH_2), 36.4 (CH), 25.9 (CH_3), 22.2 (CH_2), 20.7 (CH_2), 18.3 (C), −5.5 (CH_3) and -5.5 (CH_3); *m*/*z* (TOF ES+) 324 (MH^+.CH_3CN, 15%), 284 (19), 283 (MH+, 100%) and 265 (12).

(1a*SR*,3a*RS*,5*RS*,6a*SR*,6b*RS*)-6a-((*tert*-Butyldimethylsilyloxy)-methyl)octahydro-1a*H*-indeno[4,5-*b*]oxiren-5-ol (20)

$NaHCO_3$ (0.84 g, 10 mmol, 1.5 equiv.) and *m*-CPBA (77%, 2.24 g, 10 mmol, 1.5 equiv.) were added to a solution of alkene **18** (1.88 g, 6.67 mmol) in CH_2Cl_2 (40 mL). After stirring for 3 h the reaction was quenched by the addition of saturated aqueous solutions of $Na_2S_2O_3$ (30 mL) and $NaHCO_3$ (10 mL). Stirring was continued for 10 min, the organic layer was separated and the aqueous phase extracted with CH_2Cl_2 (2 × 15 mL). The combined organic extracts were dried over Na_2SO_4 and concentrated *in vacuo.* The residue was filtered through a column of silica with Et_2O to give the *title compound* as the major component of an approx. 7:1 mixture of epoxide diastereoisomers (1.90 g, 96%) as a colourless oil (Found: MH^+, 299.2043. $C_{16}H_{31}O_3Si$ requires M, 299.2042); ν_{max} (CH_2Cl_2) 3438, 2932, 2856, 1471, 1256, 1083, 1063, 838 and 779 cm^{-1}; δ_H (500 MHz; $CDCl_3$) 4.13 (1 H, app. broad t, *J* 3.8, C*H*OH), 3.66 (1 H, d, *J* 9.5, one of CH_2O), 3.61 (1 H, d, *J* 9.5, one of CH_2O), 3.17 (1 H, app. broad t, *J* 3.3, CCHC*H*), 2.75 (1 H, dd, *J* 4.1, 0.7, CC*H*CH), 2.19 (1 H, app. tdd, *J* 13.1, 6.7, 4.6, ring junction CH), 1.94 (1 H, app. ddt, *J* 13.1, 4.6, 2.3, one of $CHCHCH_2$), 1.85 (1 H, dd, *J* 14.4, 2.7, one of CCH_2CHOH), 1.84 (1 H, app. tdd, *J* 13.1, 4.6, 0.7, one of $CHCHCH_2$), 1.78 (1 H, dd, *J* 14.4, 4.6, one of CCH_2CHOH), 1.74 (1 H, app. tt, *J* 13.1, 4.6, one of $CCHCH_2CH_2$), 1.62 (1 H, ddd, *J* 13.1, 6.7, 2.2, one of $CHCH_2CHOH$), 1.52 (1 H, app. td, *J* 13.1, 3.5, one of $CHCH_2CHOH$), 1.27 (1 H, app. ddt, *J* 13.1, 4.6, 2.3, one of $CCHCH_2CH_2$), 0.92 (9 H, s, $SiC(CH_3)_3$), 0.14 (3 H, s, one of $Si(CH_3)_2$) and 0.13 (3 H, s, one of $Si(CH_3)_2$); δ_C (100 MHz; $CDCl_3$) 71.8 (CH), 67.3 (CH_2), 56.0 (CH), 51.3 (CH), 44.1 (CH_2), 43.1 (C), 40.1 (CH_2), 32.3 (CH), 25.9 (CH_3), 19.2 (CH_2), 18.4 (C), 16.9 (CH_2), −5.6 (CH_3) and −5.6 (CH_3); *m*/*z* (TOF ES+) 299 (MH^+, 100%), 281 (19), 167 (47) and 149 (21).

(2*RS*,3a*SR*,4*SR*,7a*RS*)-3a-((*tert*-Butyldimethylsilyloxy)methyl)-2,3,3a,4,7,7a-hexahydro-1*H*-indene-2,4-diol (21)

$NaBH_4$ (291 mg, 7.66 mmol, 1.2 equiv.) was added in small portions to a suspension of $(PhSe)_2$ (1.20 g, 3.83 mmol, 0.6 equiv.) in EtOH (30 mL). After the evolution of hydrogen had subsided a solution of epoxide **20** (1.90 g, 6.38 mmol) in EtOH (10 mL) was added to the light yellow solution. This was refluxed overnight, the solvent removed *in vacuo* and the residue dissolved in THF (30 mL). H_2O_2 (5 mL, 49 mmol, 30% aqueous solution) was added in one portion and the mixture warmed carefully in an oil bath until a vigorous exothermic reaction set in. The oil bath was quickly removed until the reaction began to subside, at which point it was replaced in order to maintain reflux for a further 1 h. The resulting clear, homogeneous solution was allowed to cool and washed with brine (30 mL). The aqueous phase was extracted with Et_2O (2 × 20 mL) and the combined organic layers washed with $Na_2S_2O_3$ (30 mL), dried over Na_2SO_4 and concentrated *in vacuo.* The residue was purified by chromatography on silica (25–50% EtOAc in petroleum ether) to give the *title compound* (1.46 g, 77%) as a colourless waxy solid, m.p. 87–94 °C (Found: MH^+, 299.2047. $C_{16}H_{31}O_3Si$ requires M, 299.2042); ν_{max} (CH_2Cl_2) 3394, 2934, 1648, 1435 and 1049 cm^{-1}; δ_H (400 MHz; $CDCl_3$) 5.85 (1 H, app. broad d, *J* 9.9, one of alkene CH), 5.70 (1 H, app. dtd, *J* 9.9, 4.6, 2.0, one of alkene CH), 4.44-4.39 (1 H, app. tdd, *J* 6.2, 2.8, 1.7, CH_2CHOH), 3.96 (1 H, app. broad s, CHC*H*OH), 3.93 (1 H, d, *J* 9.7, one of CH_2O), 3.48 (1 H, d, *J* 9.7, one of CH_2O), 2.38 (1 H, dd, *J* 14.2, 6.2, one of CCH_2CHOH), 2.27 (1 H, ddd, *J* 17.1, 7.4, 4.6, one of CH_2CH=CH), 2.05 (1 H, app. dtd, *J* 11.7, 7.4, 4.2, ring junction CH), 1.84 (1 H, app. ddt, *J* 13.5, 7.4, 1.4, one of $CHCH_2CHOH$), 1.79 (1 H, ddd, *J* 17.1, 4.2, 2.0, one of CH_2CH=CH), 1.68 (1 H, ddd, *J* 14.2, 2.8, 1.4, one of CCH_2CHOH), 1.63 (1 H, ddd, *J* 13.5, 11.7, 6.2, one of $CHCH_2CHOH$) 0.90 (9 H, s, $SiC(CH_3)_3$), 0.09 (3 H, s, one of $Si(CH_3)_2$) and 0.08 (3 H, s, one of $Si(CH_3)_2$); δ_C (100 MHz; $CDCl_3$) 132.2 (CH), 125.9 (CH), 73.1 (CH), 71.5 (CH), 69.2 (CH_2), 49.3 (C), 44.5 (CH_2), 43.0 (CH_2), 37.4 (CH), 26.8 (CH_2), 25.8 (CH_3), 18.1 (C) and −5.7 (CH_3); *m*/*z* (TOF ES+) 300 (8), 299 (MH^+, 100%).

(2*RS*,3a*SR*,7a*RS*)-3a-((*tert*-Butyldimethylsilyloxy)methyl)-2-hydroxy-3,3a,7,7a-tetrahydro-1*H*-inden-4(2*H*)-one (22)

MnO_2 (4.25 g, 49 mmol, 10 equiv.) was added to a solution of alcohol **21** (1.46 g, 4.9 mmol) in CH_2Cl_2 (40 mL). The resulting suspension was stirred for 24 h then filtered through a pad of silica, washing well with EtOAc. Concentration of the filtrate *in vacuo* gave the *title compound* (1.40 g, 97%) as a pale yellow oil (Found: MH^+, 297.1880. $C_{16}H_{29}O_3Si$ requires M, 297.1886); ν_{max} (CH_2Cl_2) 3410, 2929, 2856, 1657, 1471, 1393, 1253, 1089, 839 and 777 cm^{-1}; δ_H (400 MHz; $CDCl_3$) 6.84 (1 H, dddd, *J* 10.1, 5.7, 2.4, 1.3, *H*C=CHC=O), 6.04 (1 H, ddd, *J* 10.1, 2.8, 1.2, HC=C*H*C=O), 4.23-4.18 (1 H, m, C*H*OH), 3.82 (1 H, d, *J* 9.3,

one of CH_2O), 3.60 (1 H, d, *J* 9.3, one of CH_2O), 2.85 (1 H, app. dt, *J* 12.3, 7.0, ring junction CH), 2.78 (1 H, ddt, *J* 19.1, 7.0, 2.8, one of C=CHCH_2) 2.47 (1 H, dd, *J* 14.7, 6.3, one of CCH_2CHOH), 2.33 (1 H, app. broad dd, *J* 19.1, 5.7, one of C=CHCH_2), 1.83 (1 H, app. ddt, *J* 13.3, 7.0, 1.7, one of CHCH_2CHOH), 1.75 (1 H, ddd, *J* 13.3, 12.3, 5.2, one of CHCH_2CHOH), 1.62 (1 H, dt, *J* 14.7, 2.1, one of CCH_2CHOH), 0.85 (9 H, s, SiC$(CH_3)_3$), 0.03 (3 H, s, one of Si$(CH_3)_2$) and 0.00 (3 H, s, one of Si$(CH_3)_2$); δ_C (100 MHz; $CDCl_3$) 202.5 (C), 148.3 (CH), 129.3 (CH), 70.7 (CH), 68.8 (CH_2), 56.9 (C), 43.6 (CH_2), 42.3 (CH_2), 37.4 (CH), 26.9 (CH_2), 25.8 (CH_3), 18.2 (C), −5.7 (CH_3) and −5.7 (CH_3); *m*/*z* (TOF ES+) 297 (MH^+, 100%).

(2*RS*,3a*SR*,6*SR*,7a*RS*)-3a-((*tert*-Butyldimethylsilyloxy)methyl)-2-hydroxy-6-methylhexahydro-1*H*-inden-4(2*H*)-one (23) and (2*RS*,3a*SR*,6*RS*,7a*RS*)-3a-((*tert*-butyldimethylsilyloxy)methyl)-2-hydroxy-6-methylhexahydro-1*H*-inden-4(2*H*)-one (24)

Copper(II) triflate (29 mg, 0.08 mmol, 0.1 equiv.) was added to a solution of enone **22** (235 mg, 0.79 mmol) in toluene (10 mL) and the resulting suspension was cooled to 0 °C. A 2 M solution of Me_3Al in hexanes (1.2 mL, 2.37 mmol, 3 equiv.) was added dropwise, the cooling bath was removed and the reaction stirred for 8 h before quenching carefully with saturated aqueous $NaHCO_3$ (20 mL). This was all filtered through a pad of silica, washing with Et_2O, and the organic layer separated. The aqueous phase was extracted with Et_2O (2 × 20 mL) and the combined organic layers were dried over Na_2SO_4 and concentrated *in vacuo*. The residue was purified by chromatography on silica (20–25% EtOAc in hexane) to give the *title compounds*, **23** and **24**, approx. 3:1, as a pale yellow oil (200 mg, 81%); ν_{max} (CH_2Cl_2) 3388, 2952, 1694, 1455, 1344 and 1041 cm^{-1}; δ_H (400 MHz; $CDCl_3$) 4.21-4.16 (1 H, m, C*H*OH), 3.68 (1 H, d, *J* 9.2, one of CH_2O), 3.62 (1 H, d, *J* 9.2, one of CH_2O), 2.79-2.75 (1 H, m, ring junction CH), 2.55 (1 H, dd, *J* 14.8, 5.8, one of CCH_2CHOH), 2.38 (1 H, app. ddd, *J* 14.6, 3.5, 1.9, one of CH_2C=O), 2.10 (1 H, dd, *J* 14.6, 12.6, one of CH_2C=O), 2.05-1.90 (1 H, m, MeCH), 1.79-1.66 (3 H, m, one of CHCH_2CHOH and MeCHCH_2CH), 1.60 (1 H, app. td, *J* 13.2, 4.8, one of CHCH_2CHOH), 1.51 (1 H, app. dt, *J* 14.8, 2.1, one of CCH_2CHOH), 1.00 (3 H, d, *J* 6.4, Me), 0.89 (9 H, s, SiC$(CH_3)_3$), 0.06 (3 H, s, one of Si$(CH_3)_2$) and 0.04 (3 H, s, one of Si$(CH_3)_2$).

(9*H*-Fluoren-9-yl)methyl phenoxycarbonyloxycarbamate (25)

Phenyl chloroformate (0.12 mL, 0.93 mmol, 1.0 equiv.) was added dropwise to a vigorously stirred biphasic mixture of FmocNHOH[27] (238 mg, 0.93 mmol) in EtOAc (20 mL) and saturated aqueous $NaHCO_3$ (20 mL) at 0 °C. After 30 min the cooling bath was removed and the stirring continued overnight. The organic phase was separated, the aqueous phase extracted with EtOAc (2 × 10 mL) and the combined organic phases dried over Na_2SO_4. Removal of the solvent *in vacuo* gave a semi-solid residue which was purified by chromatography on silica (CH_2Cl_2) to afford the *title compound* (221 mg, 63%) as a colourless solid. Recrystallisation from toluene/hexane gave an analytical sample, m.p. 104–107 °C (Found: M + NH_4^+, 393.1467. $C_{22}H_{21}N_2O_5$ requires M, 393.1450); ν_{max} (CH_2Cl_2) 3280, 3066, 2956, 2897, 1804, 1741, 1593, 1487, 1476, 1450, 1216, 1120, 1032, 961, 759, 741 and 688 cm^{-1}; δ_H (500 MHz; $CDCl_3$) 8.13 (1 H, s, NH), 7.77 (2 H, d, *J* 7.5, aromatic CH), 7.61 (2 H, d, *J* 7.5, aromatic CH), 7.39 (4 H, m, aromatic CH), 7.34-7.27 (3 H, m, aromatic CH), 7.25-7.21 (2 H, m, aromatic CH) 4.55 (2 H, d, *J* 7.1, CHCH_2O) and 4.29 (1 H, t, *J* 7.1, C*H*CH$_2$O); δ_C (125 MHz; $CDCl_3$) 156.2 (C), 153.9 (C), 150.8 (C), 143.1 (2 × C), 141.3 (2 × C), 129.7 (2 × CH), 128.0 (2 × CH), 127.2 (2 × CH), 126.7 (CH), 125.0 (2 × CH), 120.5 (2 × CH), 120.1 (2 × CH), 68.8 (CH_2) and 46.8 (CH); *m*/*z* (TOF ES+) 394 (25), 393 (M + NH_4^+, 100%), 338 (9) and 191 (12).

(9*H*-Fluoren-9-yl)methyl (2*SR*,3a*SR*,6*SR*,7a*RS*)-3a-((*tert*-butyldimethylsilyloxy)methyl)-6-methyl-4-oxooctahydro-1*H*-inden-2-yl(phenoxycarbonyloxy)carbamate (26)

Triphenylphosphine (255 mg, 0.97 mmol, 1.7 equiv.) and FmocNHOCO$_2$Ph (**25**) (365 mg, 0.97 mmol, 1.7 equiv.) were added to a stirred solution of alcohol **23** (177 mg, 0.57 mmol) in CH_2Cl_2 (10 mL). DIAD (0.19 mL, 0.97 mmol, 1.7 equiv.) was added dropwise and stirring continued for 30 min. Removal of the volatiles *in vacuo* gave a residue which was purified by chromatography on silica (10% EtOAc in petroleum ether) to give the *title compound* (130 mg, 34%) as a colourless, viscous oil; ν_{max} (CH_2Cl_2) 3066, 2955, 2857, 1808, 1732, 1714, 1593, 1494, 1454, 1394, 1209, 1104, 840 and 742 cm^{-1}. Copies of ^{1}H and ^{13}C NMR spectra provided as ESI†.

Carbonate 8

To a solution of ketone **26** (32 mg, 0.05 mmol) in THF (2 mL) was added DBU (0.02 mL, 0.13 mmol, 2.8 equiv.). After stirring for 1 h, the solution was concentrated *in vacuo* and the residue chromatographed on silica (5–10% EtOAc in petroleum ether). The *title compound* (6 mg, 35%) was obtained as a colourless oil (Found: MH^+, 354.2125. $C_{18}H_{32}NO_4Si$ requires M, 354.2101); ν_{max} (CH_2Cl_2) 2928, 2855, 1808, 1704, 1471, 1257, 1097, 838 and 777 cm^{-1}; δ_H (400 MHz; $CDCl_3$) 3.86 (1 H, d, *J* 10.5, one of CH_2O), 3.78 (1 H, d, *J* 10.5, one of CH_2O), 3.73-3.70 (1 H, app. broad d, *J* 3.6, CHN), 2.37 (1 H, app. dq, *J* 11.8, 3.8, ring junction CH), 2.04-1.96 (3 H, m, CHMe, one of CCH_2CHN and one of MeCHCH_2C), 1.94 (1 H, ddd, *J* 13.6, 11.8, 4.1, one of CHCH_2CHN), 1.64 (1 H, d, *J* 11.8, one of CCH_2CHN), 1.54 (1 H, app. t, *J* 13.5 one of MeCHCH_2C), 1.48 (1 H, app. broad d, *J* 14.1, one of MeCHCH_2CH), 1.40 (1 H, app. dt, *J* 13.6, 3.8, one of CHCH_2CHN), 1.24 (1 H, ddd, *J* 14.1, 12.4, 3.8, one of MeCHCH_2CH), 0.98 (3 H, d, *J* 6.3, CH_3), 0.89 (9 H, s, SiC$(CH_3)_3$) and 0.06 (6 H, s, Si$(CH_3)_2$); δ_C (100 MHz; $CDCl_3$) 154.1 (C), 106.6 (C), 65.4 (CH), 60.0 (CH_2), 54.0 (C), 37.7 (CH_2), 37.0 (CH_2), 34.2 (CH), 32.2 (CH_2), 30.8 (CH_2), 25.8 (CH_3), 23.5 (CH), 21.3 (CH_3), 18.2 (C), −5.6 (CH_3) and −5.6 (CH_3); *m*/*z* (TOF ES$^+$) 395 (MH^+. CH_3CN, 100%), 354 (MH^+, 15), 338 (5), 310 (9), 262 (10), 234 (7) and 191 (3).

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