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Stereoselective synthesis of polyfunctionalised hydroxylated cyclopentanes from dihydroxylated 2-cyclopentenone derivatives

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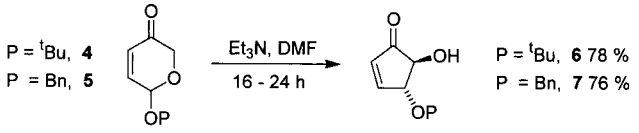
Abstract—Dihydroxylated cyclopentenones can be readily synthesised via a base mediated isomerisation reaction. These species and their derivatives can be used to provide a wide range of synthetically useful intermediates by participation in a variety of stereoselective transformations. These include: nucleophilic and conjugate addition, intermolecular cycloaddition, intramolecular free-radical cyclisation and palladium mediated coupling reactions.

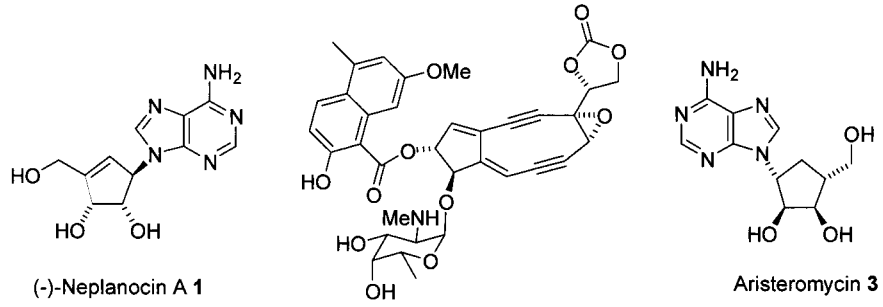
1. Introduction

The preparation of cyclopentanoid containing compounds has attracted considerable attention from synthetic chemists and there are a large number of biologically important targets which incorporate this motif within their overall structure (e.g. Scheme 1).[1] As part of our general interest in this area, and a particular need in our dienediyne programme for general methods, we have devised a convenient preparative approach to cyclopentenone **6** from pyranone **4** under base mediated conditions (Scheme 2).[2]

Compounds such as **6** and **7** have great potential as high-value intermediates for synthetic chemistry. The availability of the two (differentiated) hydroxyl groups and the enone, alongside the inherent pseudo-symmetry should provide the appropriate molecular features required to ensure that a variety of stereoselective manipulations can be effected (Fig. 1). The purpose of this paper is to demonstrate that in general it is possible to effect classes of transformations



Scheme 2. Base mediated isomerisation of pyranones **4** and **5** affording cyclopentenones **6** and **7**.



Scheme 1. Biologically important molecules possessing the cyclopentanol ring.

Keywords: cyclopentenones; coupling reactions; Diels–Alder reactions; radical cyclisations; Grignard reactions; conjugate addition.
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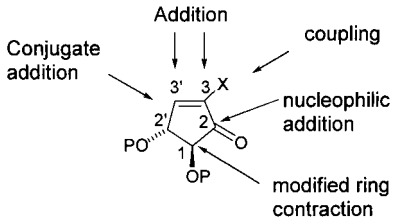


Figure 1. Pseudosymmetric dihydroxylated cyclopentenones.

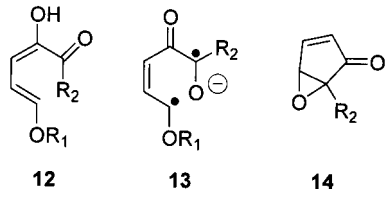
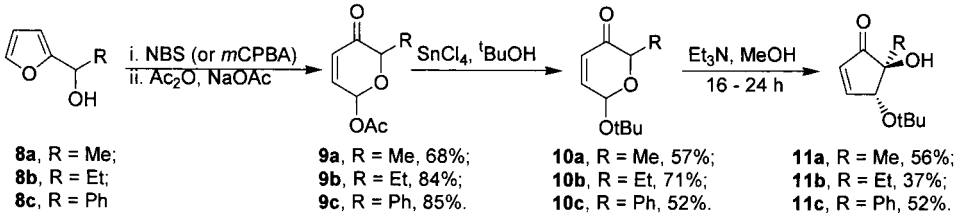


Figure 2. Possible intermediates in the base mediated isomerisation reaction of pyranones.



Scheme 3. Preparation of C-1 functionalised cyclopentenones from substituted furfuryl alcohols.

as highlighted in Fig. 1. All the transformations described are highly (stereo)selective and deliver functionalised cyclopentane derivatives in good yields.

2. Results and discussion

2.1. C-1 Position

Whilst it would clearly be possible to manipulate **6** in order to prepare C-1 substituted compounds, access to such compounds can be achieved via a modification of the ring contraction methodology. Thus, we have found that the pyranone to cyclopentenone rearrangement process can be extended as shown in Scheme 3. Using a combination of standard procedures and methodology previously described[3] we were able to prepare pyranones **10a–c** which undergo ring contraction to give the cyclopentenones **11a–c** as the sole products as confirmed by X-ray crystallography.[4]

The mechanism for this transformation may involve one of the following three pathways:

- Cyclisation of intermediate **12** formed by electrocyclic ring opening of an enol derived from **10**.
- 1,2-Wittig rearrangement invoking biradical **13**.[5]
- Cyclisation to give epoxide **14** followed by nucleophilic ring opening[6] (Fig. 2).

In our opinion, the least likely of the three possibilities is the pathway involving intermediate epoxide **14** due to the success of the isomerisation reaction in methanol.

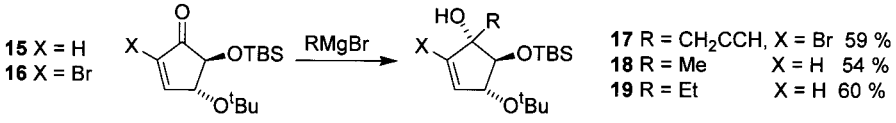
2.2. C-2 Position

We have previously described a number of simple 1,2-addition processes to cyclopentenones using carbon nucleophiles, most notably in our work in the dienediyne area.[7] Thus, for example, it is possible to perform a stereoselective addition of a Grignard reagent to cyclopentenones of the form **15** and **16** to give the resulting products as single diastereoisomers. Stereochemical assignments are made by analogy with **18**, which was characterised by X-ray crystallography. Further, no loss of reactivity or stereoselectivity is witnessed when a sterically demanding bromine atom is introduced α to the reacting centre (Scheme 4).

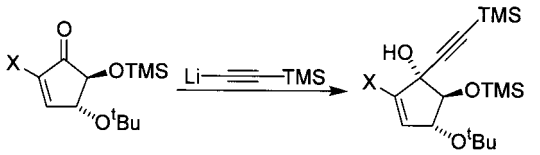
During our investigations it was noted that the corresponding Grignard reaction using bromo acetylenes proceeded in poor yield (<40%). Further investigations identified that simple 1,2-additions using alkynyl lithium species proceeded in good yield providing the corresponding propargyl alcohols as single diastereoisomers (Scheme 5).

Selective incorporation of fluorine into organic compounds remains of great interest to both academic and industrial chemists. The highly reactive nature of compounds containing fluorine has provided an impetus for the development of a plethora of new reagents that can be utilised to incorporate fluorine into organic molecules. In the electrophilic fluorination reagents class, DAST has been shown to be particularly useful for selective fluorination of both carbonyls and especially alcohols.[8]

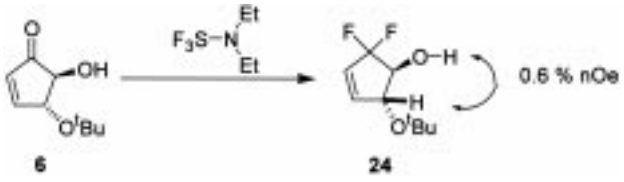
It is evident that there are two reactive sites at which fluorination by DAST might occur within the parent cyclopentenone **6** and as such one would assume that a mixture



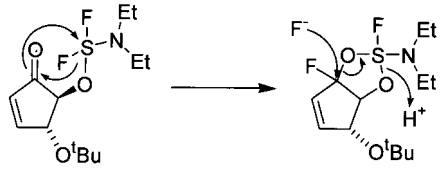
Scheme 4. *Conditions*: −78°C, Et_2O, 2 h.



Scheme 5. *Conditions*: −78°C, THF, 30 min, **20** or **21**, 3 h.



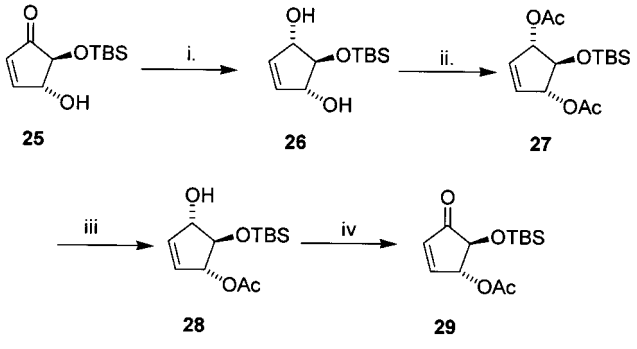
Scheme 6. Selective difluorination of an enone using DAST.



Scheme 7. Possible mechanism for the fluorination of cyclopentenone **24**.

of fluorinated products could be obtained. Reactions of the enone **6** with excess DAST yielded a sole product, which was identified as the 2,2-difluorinated cyclopentene **24** in quantitative yield. The structure was determined by a range of ^{1}H and ^{19}F NMR experiments (Scheme 6).

A possible mechanism for this transformation is shown in Scheme 7. Initial reaction with DAST occurs at the alcohol site. This enables attack of the fluoride ion at the carbonyl position forming a five-membered sulfur-containing ring. The ring is broken by attack of a further fluoride ion at the 2-position liberating the 2,2-difluorinated cyclopentenol **24**. We believe that the close proximity of the alcohol and carbonyl functionalities facilitates this reaction. Fluorination is not observed with related compounds incorporating a free OH at C-4.



Scheme 8. *Reagents and conditions*: (i) $NaBH_4$, $CeCl_3$, MeOH, 0°C, 2 h, 80%; (ii) Ac_2O, Pyr, DMAP, DCM, 0°C–rt, 2 h, 87%; (iii) lipase Amano AK, 30°C, 68 h, 91%; (iv) Dess–Martin periodinane, rt, 2 h, 80%.

In a more general sense it is most noteworthy that very high levels of stereocontrol can be realised in the simple ketone reduction under Luche conditions.[9] Thus, cyclopentenone **25** can undergo reduction with excellent levels of selectivity to give *meso* **26** from which **27** can be easily derived. The symmetrical nature of this species clearly renders the C-2 and C-2′ positions equivalent. Perhaps of greater value however is the ability to provide an enantioselective synthesis of **29** from **27**. In good agreement with the work of Hirama,[10] we found that bis-acetate **27** undergoes desymmetrisation using lipase (Amano AK) in 91% yield (>90% ee). Simple oxidation of the resulting alcohol **28** using Dess–Martin conditions yields enantiomerically pure **29** (30% overall yield from **25**). We believe that this methodology provides an adequate preparative asymmetric synthesis of enantiomerically pure dihydroxylated cyclopentenones such as **29**, and we are exploiting its applicability for the preparation of multi-gram quantities of **29** and congeners (Scheme 8).

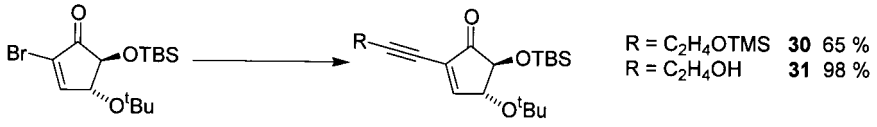
2.3. C-3 Position

We have been able to affect C3-functionalisation of enone **6** via the vinyl bromide **16** which undergoes a palladium catalysed Sonogashira coupling (Scheme 9).[11] Previous work suggests that the vinyl iodide would be required for complete conversion and that yields can be severely reduced when vinyl bromides are utilised.[12] In the event we decided to attempt coupling reactions using the easily prepared vinyl bromide **16**. Using standard Sonogashira coupling conditions[13] we were able to afford substituted enynes in moderate to good yield.

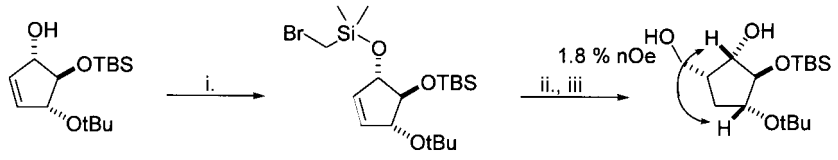
It is interesting to note that the rate of addition of the acetylene to the reaction mixture had a profound effect on the yield of the reaction. Optimisation studies identified that slow addition of the acetylene over a 3 h period prevented dimerisation of the alkyne.

An alternative approach to C-3 functionalisation can be achieved using a radical cyclisation reaction (Scheme 10).

We have utilised a stereoselective hydro-hydroxymethylation protocol using a radical cyclisation to afford 1,3-diol **34** via a 5-*exo* mode of cyclisation from alcohol **32**. This reaction proceeds through an intramolecular radical cyclisation using the temporary connectivity of a silicon linkage to afford selectivity.[14] Silyl ether **33** was prepared by treatment of allylic alcohol **32** with bromomethylchlorodimethylsilane in the presence of a base. Submission of **33** to

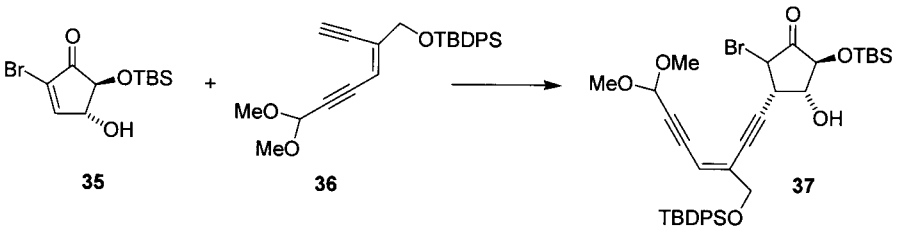


Scheme 9. *Reagents and conditions*: CuI (9%), $(PPh_3)_2PdCl_2$ (4%), *N,N*-diisopropylamine (10 equiv.), THF, 50°C, HCCR.



32 33 34

Scheme 10. *Reagents and conditions*: (i) $BrCH_2Si(CH_3)_2Cl$, DCM, 0°C, $^iPr_2NH$, 64%; (ii) TBTH, AIBN, Δ; (iii) KF, K_2CO_3, MeOH, H_2O_2, 76%.



35 36 37

Scheme 11. *Reagents and conditions*: *n*-BuLi, THF, 0°C, −78°C, 30 min, then Et_2AlCl, rt, 1 h, then **35**, 85%.

standard radical cyclisation conditions (AIBN, benzene, TBTH) followed by Tamao–Fleming oxidation gave **34** in 76% yield. A *cis*-vicinal relationship between the hydroxy group and the newly introduced hydroxymethyl group is observed. This *cis* relationship occurs due to the restrictions upon cyclisation to form a five-membered siloxane ring. This demonstrates the feasibility of using a radical addition approach for the introduction of a hydroxymethyl group onto a polyhydroxylated template. This is noteworthy as this motif is often found in cyclopentane containing natural products.

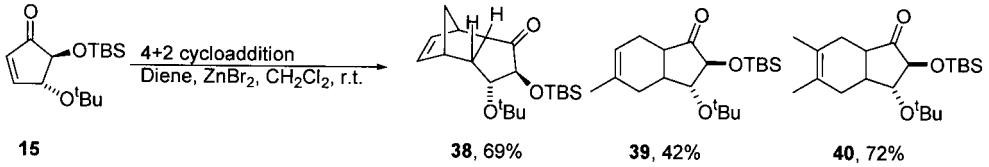
2.4. C-3 and C-3′ Positions

Our work in the dienediyne area has demonstrated that stereoselective conjugate addition of alkynes is possible as highlighted in Scheme 11. This reaction makes use of the neighbouring hydroxyl group, which has been shown to be a requirement for this type of reaction, presumably offering an intramolecular delivery pathway. Previously, we have described the conjugate addition of a highly functionalised enediyne to cyclopentenone **35**.[15] Recently, we have extended this methodology to include functionalised enones (i.e. X=Br) which undergo conjugate addition reactions yielding brominated C3-functionalised cyclopentanones of the form **37** (85%). Whilst we have not yet had occasion to carry out an extensive investigation these results suggest that this approach could be extended to a range of both simple and complex nucleophiles and would follow a predictable pathway.

An alternative method for introducing additional groups onto the cyclopentenone template is to use the enone in a cycloaddition reaction. The cyclopentenone **15**, possessing an electron deficient double bond is ideally suited for a Diels–Alder reaction. Reactions of this nature lead to highly functionalised bicyclic compounds. Using simple dienes, such as cyclopentadiene (with cyclopentenone **15**) we have observed a stereoselective *endo*-cycloaddition, which has been confirmed by crystallography. The reaction proceeds slowly, often taking up to 6 days to proceed to completion in the presence of a catalytic amount of zinc chloride. However, although the yields are acceptable, attempts to make improvements by use of stoichiometric amounts of Lewis acid results in decomposition of the highly sensitive cyclopentenone **15**. Further investigations have been carried out using various electron rich dienes, but at present this transformation seems to be limited to simple dienes such as isoprene, 2,3-dimethylbutadiene and cyclopentadiene yielding bicyclic and tricyclic compounds of the nature **38**, **39** and **40** (Scheme 12).

In summary, we have shown the following new features involving dihydroxylated cyclopentenones:

- Base mediated ring contraction methodology can be extended to give C-5 substituted cyclopentenones.
- Carbon and hydride nucleophiles undergo stereoselective ketone and/or conjugate addition.
- Intramolecular radical cyclisations can be used for the introduction of a hydroxymethyl group present in many natural products.
- Ketone difluorination allows the introduction of an important synthetic motif.



15 38, 69% 39, 42% 40, 72%

Scheme 12. Cycloaddition reactions.

- Enone component can participate in 4+2 cycloadditions.
- Asymmetric synthesis of dihydroxylated cyclopentenones is possible.

This work amply illustrates that dihydroxylated cyclopentenones can participate in a wide range of selective transformations and can serve as versatile synthetic intermediates for compounds containing polyhydroxylated cyclopentane frameworks.

3. Experimental

3.1. General

All glassware was oven or flame dried prior to use. All reagents and solvents were purchased from commercial sources and used as supplied or purified using standard methods. Preparations were performed under an inert atmosphere unless stated otherwise. ^{1}H NMR spectra were recorded on a Bruker spectrometer at 300 MHz operating at ambient probe temperature. Coupling constants were measured in Hertz. ^{13}C NMR spectra were recorded at 75 MHz in $CDCl_3$ using residual $CHCl_3$ as internal reference. Infra red spectra were recorded on a Perkin–Elmer 1710 FTIR spectrometer as thin films, solutions or KBr discs. Mass spectra were recorded on a Kratos MS25 spectrometer. Analytical thin layer chromatography was carried out using SIL G/UV$_{254}$ plates and visualised using standard procedures. Melting points are uncorrected. Crystal structures for **38**–**40**, **11a**–**c** and **18** have been deposited with the CCDB (cf: 154513–154519, respectively). Literature protocols were used for the preparation of compounds **8**–**10**.[2–4]

3.2. General method A for the base mediated isomerisation

To a stirred solution of the pyranone (1 equiv.) in methanol (5 mL mmol^{-1}) was added triethylamine (5 equiv.) dropwise. The reaction was heated to 60°C until TLC analysis showed complete consumption of the pyranone (24–48 h). Purification was achieved by chromatography on silica gel with petrol/ethyl acetate (5:1 v/v) as the eluent.

3.2.1. 4-*tert*-Butoxy-5-methyl-5-hydroxy-cyclopent-2-enone (11a). The general method A was employed for the preparation of **11a**. The quantities of reagents used were as follows: 6-*tert*-butoxy-2-methyl-2*H*-pyran-3-one **10a** (604 mg, 3.3 mmol), triethylamine (2.3 mL, 16.4 mmol). The title compound **11a** was isolated as a white solid (338 mg, 56%). Mp 81.3–82.1°C; ν_{max} 3417, 3092, 2981, 1710 cm^{-1}; δ_H (300 MHz, $CDCl_3$) 1.16 (3H, s), 1.23 (9H, s), 3.20 (1H, br s), 4.55 (1H, d, J=1.9 Hz), 6.15 (1H, d, J=6.1 Hz), 7.24 (1H, dd, J=6.1, 1.9 Hz); δ_C (75 MHz, $CDCl_3$) 22.0, 28.6, 75.4, 78.3, 80.7, 130.9, 163.2, 209.3; HRMS $[M]^+$ found 184.1099, requires for $C_{10}H_{16}O_3$ 184.1099.

3.2.2. 4-*tert*-Butoxy-5-ethyl-5-hydroxy-cyclopent-2-enone (11b). The general method A was employed for the preparation of **11b**. The quantities of reagents used were as follows: 6-*tert*-butoxy-2-ethyl-2*H*-pyran-3-one **10b** (213 mg, 1.1 mmol), triethylamine (0.75 mL, 5.4 mmol). The title compound **11b** was isolated as a white solid (78 mg, 37%). Mp 73.2–74.1°C; ν_{max} 3452, 2977, 1716 cm^{-1}; δ_H (300 MHz, $CDCl_3$) 0.78 (3H, t, J=3.5 Hz), 1.22 (9H, s), 1.45–1.75 (2H, m), 3.33 (1H, br s), 4.54 (1H, d, J=1.8 Hz), 6.17 (1H, d, J=6.1 Hz), 7.26 (1H, dd, J=6.1, 1.8 Hz); δ_C (75 MHz, $CDCl_3$) 8.2, 28.6, 28.7, 75.4, 78.5, 83.7, 131.5, 163.2, 208.2; HRMS $(M+H)^+$ found 199.1334, requires for $C_{11}H_{19}O_3$ 199.1334.

3.2.3. 4-*tert*-Butoxy-5-hydroxy-5-phenyl-cyclopent-2-enone (11c). The general method A was employed for the preparation of **11c**. The quantities of reagents used were as follows 6-*tert*-butoxy-2-phenyl-2*H*-pyran-3-one **10c** (110 mg, 0.45 mmol), triethylamine (0.31 mL, 2.2 mmol). The title compound **11c** was isolated as a brown oil (57 mg, 52%). ν_{max} 3452, 2977, 1716, 1592, 735, 699 cm^{-1}; δ_H (300 MHz, $CDCl_3$) 0.96 (9H, s), 3.15 (1H, br s), 4.76 (1H, t, J=1.8 Hz), 6.43 (1H, dd, J=1.8, 6.0 Hz), 7.18–7.24 (5H, m), 7.52 (1H, dd, J=2.1, 6.0 Hz); δ_C (75 MHz, $CDCl_3$) 22.2, 73.4, 77.7, 84.7, 124.6, 125.6, 125.8, 130.8, 136.6, 163.0, 206.4; *m/z* 247 $(M+H)^+$; HRMS $[M+H]^+$ found 247.1333, requires for $C_{15}H_{19}O_3$ 247.1334.

3.3. General method B for the addition of a nucleophile to a carbonyl

The Grignard reagent (1.2 equiv. as a 3 M solution in diethyl ether) was slowly added to a cooled (−84°C) solution of *trans*-4-*tert*-butoxy-5-*tert*-butyldimethylsilyloxy-cyclopenten-1-one **15** (1 equiv.) in diethyl ether (7 mL mmol^{-1}). Stirring was continued at −84°C for 2 h before the reaction was quenched with saturated $NaHCO_3$ (3 mL), washed with water (2×3 mL) and brine (3 mL), dried ($MgSO_4$), filtered and concentrated in vacuo. Purification was achieved by chromatography on silica gel with petrol/ethyl acetate (7:1 v/v) as the eluent.

3.3.1. 1-Methyl-*trans*-4-*tert*-butoxy-5-*tert*-butyldimethylsilylcyclopent-2-en-1-ol (18). The general method B was employed for the preparation of **18**. The quantities of reagents used were as follows: methyl magnesium bromide (0.28 mL, 0.84 mmol), *trans*-4-*tert*-butoxy-5-*tert*-butyldimethylsilyloxy-cyclopenten-1-one **15** (200 mg, 0.7 mmol). The title compound **18** isolated as a pale yellow oil (113 mg, 54%). ν_{max} 3452, 2930, 1600, 1265, 939 cm^{-1}; δ_H (300 MHz; $CDCl_3$) 0.14 (6H, s), 0.94 (9H, s), 1.22 (9H, s), 1.25 (3H, s), 1.72 (1H, br s), 3.85 (1H, d, J=5.4 Hz), 4.15 (1H, d, J=5.4 Hz), 5.66 (1H, dd, J=6.3, 1.3 Hz), 5.77 (1H, dd, J=6.3, 1.1 Hz); δ_C (75 MHz, $CDCl_3$) −4.3, −4.1, 18.0, 21.7, 25.8, 28.4, 73.8, 79.6, 80.2, 88.5, 132.6, 138.0; *m/z* 283 $[M-OH]^+$; HRMS $[M-OH]^+$ found 283.2093, requires for $C_{16}H_{31}O_2Si$ 283.2093.

3.3.2. 1-Ethyl-*trans*-4-*tert*-butoxy-5-*tert*-butyldimethylsilylcyclopent-2-en-1-ol (19). The general method B was employed for the preparation of **19**. The quantities of reagents used were as follows: ethyl magnesium bromide (0.28 mL, 0.84 mmol), *trans*-4-*tert*-butoxy-5-*tert*-butyldimethylsilyloxy-cyclopenten-1-one **15** (200 mg, 0.7 mmol). The title compound **19** isolated as a pale yellow oil (132 mg, 60%). ν_{max} 3585, 2887, 1635, 1266, 976 cm^{-1}; δ_H (300 MHz; $CDCl_3$) 0.13 (3H, s), 0.14 (3H, s), 0.93 (9H,

s), 1.22 (9H, s), 1.22–1.24 (3H, m), 1.57–1.63 (3H, m), 3.89 (1H, d, J=5.6 Hz), 4.17 (1H, d, J=5.6 Hz), 5.73–5.77 (2H, m); δ_C (75 MHz, $CDCl_3$) −4.4, −4.1, 8.1, 18.0, 25.9, 28.5, 29.6, 73.7, 79.6, 83.0, 88.9, 133.8, 135.9; m/z 297 $[M-OH]^+$; HRMS $[M]^+$, found 314.2277, requires for $C_{17}H_{34}O_3Si$ 314.2277.

3.3.3. 2-Bromo-*trans*-4-*tert*-butoxy-1-(2-propynyl)-5-*tert*-butyldimethylsilyloxy-cyclopent-2-en-1-ol (17). To magnesium turnings (1.02 g, 42.5 mmol) and mercuric chloride in diethyl ether (15 mL g^{-1}) was added propargyl bromide (1 mL) and one iodine crystal. Gentle heat was applied to the reaction vessel and upon reaction initiation the remaining propargyl bromide (2.8 mL, 42.2 mmol) was added slowly. The reaction mixture was left until complete consumption of the magnesium had occurred (30 min). The Grignard reagent was cooled to −78°C whereupon a solution of 2-bromo-*trans*-4-*tert*-butoxy-5-*tert*-butyldimethylsilyloxycyclopenten-1-one **16** (9.3 g, 25.6 mmol) in diethyl ether (2.5 mL $mmol^{-1}$) was added over a 20 min period. The cooling bath was removed and stirring was continued for a further 3 h. The reaction was quenched at reduced temperature (0°C) with saturated ammonium chloride solution (20 mL). The organic layer was washed with water (2×20 mL), dried ($MgSO_4$), filtered and concentrated in vacuo to yield a yellow oil. The oil was purified by chromatography on silica gel with petrol/ethyl acetate (3:1 v/v) as the eluent to yield the title compound as a light grey solid (mp 116–118°C). (6.1 g, 59%); ν_{max} 3422, 3311, 2959, 1618, 1254, 994, 742 cm^{-1}; δ_H (300 MHz, $CDCl_3$) 0.15 (3H, s), 0.16 (3H, s), 0.96 (9H, s), 1.21 (9H, s), 2.00 (1H, t, J=2.5 Hz), 2.35 (1H, br s), 2.52 (1H, dd, J=16.5, 2.5 Hz), 2.58 (1H, dd, J=16.5, 2.5 Hz), 4.04 (1H, d, J=5.4 Hz), 4.32 (1H, dd, J=5.4, 1.2 Hz), 6.04 (1H, d, J=1.2 Hz); δ_C (75 MHz, $CDCl_3$) −4.5, −4.2, 17.9, 25.6, 25.8, 28.3, 71.1, 74.2, 78.0, 79.2, 81.8, 85.9, 128.1, 134.7; m/z 404 $[M+H]^+$; HRMS $[M-C_4H_9, OH]^+$, found 329.0572, requires for $C_{14}H_{22}O_2BrSi$ 329.0572.

3.3.4. 2-Bromo-4-*tert*-butyl-1-trimethylsilylethynyl-5-trimethylsilyloxy-cyclopent-2-enol (23). To a solution of trimethylsilylacetylene (184 mg, 1.9 mmol) in THF (2 mL) cooled to −78°C was added *n*BuLi (0.82 mL of a 2.3 M solution in hexanes, 1.9 mmol) dropwise. After 30 min a solution of enone **21** (500 mg, 1.6 mmol) in THF (3 mL) was added to the lithium acetylide solution and stirring was continued for a further 3 h at reduced temperature −78°C. The reaction was allowed to warm to ambient temperature before being quenched with sodium bicarbonate solution (10 mL). The reaction mixture was diluted with ethyl acetate (50 mL) and washed with saturated ammonium chloride solution (10 mL). The organic portion was dried ($MgSO_4$), filtered and concentrated in vacuo. The resulting oil was purified by chromatography on silica gel with petrol/ethyl acetate (7:1 v/v) as the eluent yielding the title compound as a yellow oil. (460 mg, 68%). ν_{max} 3446, 2168, 1158, 1110, 844, 761 cm^{-1}; δ_H (300 MHz, $CDCl_3$) 0.00 (18H, s), 1.02 (9H, s), 2.35 (1H, s), 3.80 (1H, d, J=5.0 Hz), 4.03 (1H, dd, J=1.3, 5.0 Hz), 5.73 (1H, d, J=1.3 Hz); δ_C (75 MHz, $CDCl_3$) 0.0, 0.2, 28.0, 60.1, 74.1, 77.9, 79.2, 86.6, 93.0, 101.3, 126.8, 134.4; m/z (FAB) 419 $[M]^+$; HRMS $[M+NH_4]^+$ found 436.1341, requires for $C_{17}H_{34}O_3BrNSi_2$ 436.1339.

3.3.5. 4-*tert*-Butoxy-1-trimethylsilylethynyl-5-trimethylsilyloxy-cyclopent-2-enol (22). To a solution of trimethylsilylacetylene (487 mg, 4.9 mmol), in THF (10 mL) cooled to −78°C was added *n*BuLi (2 mL of a 2.5 M solution in hexanes, 4.9 mmol) dropwise. After 30 min a solution of *trans*-4-butoxy-5-trimethylsiloxy-cyclopenten-1-one **20** (1 g, 4 mmol), in THF (6 mL) was added to the lithium acetylide solution and stirring was continued for a further 3 h at reduced temperature. The reaction was allowed to warm to ambient temperature before being quenched with sodium bicarbonate solution (10 mL). The reaction mixture was diluted with ethyl acetate (50 mL) and washed with saturated ammonium chloride solution (10 mL). The organic portion was dried ($MgSO_4$), filtered and concentrated in vacuo to give an orange oil. The oil was purified by chromatography on silica gel with petrol/ethyl acetate (7:1 v/v) as the eluent. (860 mg, 62%). ν_{max} 3436, 2163, 887 cm^{-1}; δ_H (300 MHz, $CDCl_3$) 0.01 (18H, s), 1.04 (9H, s), 2.08 (1H, s), 3.74 (1H, d, J=4.5 Hz), 3.94 (1H, dd, J=6.4, 4.5 Hz), 5.79 (2H, d, J=6.4 Hz); δ_C (75 MHz, $CDCl_3$) 0.0, 0.3, 28.0, 73.7, 78.0, 79.2, 87.8, 92.1, 103.1, 134.1, 134.7; m/z (ES) 358 $[M+NH_4]^+$; HRMS $[M+NH_4]^+$ found 358.2235, requires for $C_{17}H_{36}O_3NSi_2$ 358.2234.

3.3.6. 5-*tert*-Butoxy-2,2-difluoro-cyclopent-3-enol (24). To a solution of 5-*tert*-butyl-4-hydroxycyclopent-2-one **6** (200 mg, 1.2 mmol) in DCM (4 mL) cooled to −78°C was added diethylaminosulfur trifluoride (948 mg, 5.9 mmol). The reaction was slowly allowed to warm to an ambient temperature over 4 h and stirring was continued for a further 24 h. The reaction mixture was poured onto basic alumina, washed with water (5 mL), dried (Na_2SO_4), filtered and concentrated in vacuo. Purification was achieved by chromatography on silica gel with petrol/ethyl acetate (10:1 v/v) as the eluent, yielding the title compound as colourless crystals (mp 68–70°C), (224 mg, 98%). ν_{max} (neat) 3387, 1395, 1367, 1207, 1187, 774, 759 cm^{-1}; δ_H (500 MHz, $CDCl_3$) 1.21 (9H, s), 2.39 (1H, br s), 4.08 (1H, ddd, J=4.5, 9.0, 13.0 Hz), 4.43 (1H, dddd, J=1.5, 3.2, 4.5, 9.0 Hz), 5.86 (1H, ddd, J=1.5, 1.5, 6.4 Hz), 6.09 (1H, dddd, J=0.7, 1.5, 1.5, 6.4 Hz); δ_F (282 MHz, $CDCl_3$) −106.35 (ddd, J=255.4, 8.1, 3.2 Hz), −95.72 (dddd, J=255.4, 13.0, 7.5, 1.5 Hz); δ_C (75 MHz, $CDCl_3$) 28.2, 75.2, 78.4 (dd, J=1.5, 7.0 Hz), 80.9 (t, J=23.0 Hz), 125.9 (dd, J=248.2, 241.6 Hz), 126.9 (dd, J=22.5, 30.6 Hz), 143.9 (dd, J=8.0, 11.0 Hz); m/z (EI) 192 $[M]^+$; HRMS $[M+NH_4]^+$ found 210.1303, requires for $C_9H_{18}O_2FN$ 210.1306.

3.3.7. *meso-trans*, *trans*-3,5-Dihydroxy-4-*tert*-butyldimethylsilyloxy-cyclopentene (26). To a solution of **25** (132 mg, 0.58 mmol) in methanol (3 mL) at 0°C was added $CeCl_3 \cdot 7H_2O$ (0.29 g, 0.78 mmol) followed by $NaBH_4$ (30 mg, 0.9 mmol) portionwise. The reaction was stirred at 0°C for 2 h then quenched with saturated aqueous NH_4Cl solution (5 mL), extracted with ethyl acetate (5×5 mL), washed with brine (10 mL), dried over magnesium sulphate, filtered and concentrated in vacuo. Column chromatography in 30% EtOAc/petrol resulted in a white crystalline solid (mp 105–106°C), (107 mg, 80%). ν_{max} 3446, 3054, 2361 cm^{-1}; δ_H (300 MHz, $CDCl_3$) 0.01 (6H, s), 0.77 (9H, s), 1.79–1.81 (2H, m,), 3.78 (1H, t, J=4.1 Hz), 4.28 (2H, d, J=4.1 Hz), 5.70 (2H, s); δ_C (75 MHz, $CDCl_3$) −4.1, 18.5, 26.2, 81.7, 90.9, 134.4;

HRMS $[M+NH_4]^+$ found 248.1682, requires for $C_{11}H_{26}NO_3Si$ 248.1682.

3.3.8. ±4-*tert*-Butoxy-5-(*tert*-butyldimethylsilyloxy)cyclopent-2-enol (32). The above method was utilised for the preparation of **32**. The quantities of reagents used were as follows: **15** (1.8 g, 6.3 mmol), MeOH (25 mL), $CeCl_3{\cdot}7H_2O$ (2.8 g, 7.6 mmol), $NaBH_4$ (287.7 mg, 7.6 mmol). The title compound was isolated as a white solid (1.3 g, 78%), (de 95%). ν_{max} 3054, 2987 cm^{-1}; δ_H (300 MHz, $CDCl_3$) 0.12 (3H, s), 0.15 (3H, s), 0.91 (9H, s), 1.21 (9H, s), 1.98 (1H, br s), 3.88 (1H, t, J=4.1 Hz), 4.26 (1H, d, J=3.4 Hz), 5.30 (1H, br s), 5.75 (2H, dd, J=6.4, 7.6 Hz); δ_C (75 MHz, $CDCl_3$) −4.3, 18.0, 25.8, 28.5, 74.0, 80.6, 80.7, 88.9, 133.2, 134.8; HRMS (EI^+) $[M+Na]^+$ found 309.1858, requires for $C_{15}H_{30}O_3SiNa$ 309.1862.

3.3.9. *meso-trans*, *trans*-3,5-Diacetoxy-4-*tert*-butyldimethylsiloxy-cyclopentene (27). To a solution of **26** (143 mg, 0.621 mmol) in DCM (5 mL) was added DMAP (26 mg, 0.212 mmol). The solution was cooled to 0°C and acetic anhydride (0.13 mL, 1.37 mmol) was added with stirring, followed by pyridine (0.11 mL, 1.37 mmol) dropwise. The resulting clear solution was stirred at 0°C for 15 min, then allowed to warm to room temperature and stirred for a further 75 min. The reaction was quenched with saturated $NaHCO_3$ solution (5 mL), extracted with ethyl acetate (3×5 mL), washed with 1N HCl (10 mL), followed by brine (10 mL), dried over $MgSO_4$, filtered and concentrated in vacuo. Column chromatography on silica gel eluting with 5% EtOAc/petrol to 10% EtOAc/petrol resulted in a colourless liquid (170 mg, 87%). ν_{max} 2932, 1745, 1026 cm^{-1}; δ_H (300 MHz, $CDCl_3$) 0.00 (6H, s), 0.81 (9H, s), 2.02 (6H, s), 4.27 (1H, t, J=4.5 Hz), 5.32 (2H, d, J=4.5 Hz), 5.84 (2H, s); δ_C (75 MHz, $CDCl_3$) −4.6, 18.3, 21.4, 26.1, 82.7, 83.0, 132.8, 170.8; HRMS $[M+NH_4]^+$ found 332.1894, requires for $C_{15}H_{30}NO_5Si$ 332.1893.

3.3.10. *trans*, *trans*-3-Acetoxy-5-hydroxy-4-*tert*-butyldimethylsiloxy-cyclopentene (28). To a stirred suspension of **27** (92 mg, 0.29 mmol) in 1 M pH 7 phosphate buffer (5 mL) was added lipase Amano AK (65 mg). The mixture was heated at ca. 30°C for 68 h, allowed to cool to room temperature then extracted with ethyl acetate (5×5 mL). The organic extracts were combined, washed with water (15 mL), dried over magnesium sulphate and concentrated in vacuo. Column chromatography eluting with 20% EtOAc/petrol resulted in a colourless oil (72 mg, 91%); $[\alpha]^{30}_D$=+61.5° (c 1.00, $CHCl_3$); ν_{max} 3415, 2360, 1641, 1025 cm^{-1}; δ_H (300 MHz, $CDCl_3$) 0.00 (3H, s), 0.03 (3H, s), 0.81 (9H, s), 1.75 (1H, d, J=7.2 Hz), 1.98 (3H, s), 4.04 (1H, t, J=3.8 Hz), 4.39 (1H, br s), 5.23 (1H, br s), 5.72 (1H, br d, J=6.0 Hz), 5.83 (1H, br d, J=6.0 Hz); δ_C (75 MHz, $CDCl_3$) −4.6, 16.7, 19.7, 24.4, 79.5, 81.6, 84.8, 129.3, 134.3, 169.4; HRMS found 273.1526 $[M+H]^+$, required for $C_{13}H_{25}O_4Si$ 273.1522.

3.3.11. (+)-(4*S*, 5*R*)-*trans*-4-*tert*-Butoxy-5-hydroxy-2-cyclopenten-1-one (29). To a stirred solution of **28** (40 mg, 0.15 mmol) in DCM (3 mL) was added Dess–Martin periodinane (100 mg, 0.24 mmol). The solution was stirred at room temperature for 2 h. The reaction was quenched with sodium thiosulphate solution (3 mL), extracted with ethyl acetate (3×5 mL), dried ($MgSO_4$) and concentrated in vacuo. Column chromatography eluting with 30% EtOAc/petrol resulted in a colourless oil (32 mg, 80%). $[\alpha]^{27}_D$=+150.6° (c 1.02, $CHCl_3$); ν_{max} 2930, 1742, 1033 cm^{-1}; δ_H (300 MHz, $CDCl_3$) 0.00 (3H, s), 0.04 (3H, s), 0.79 (9H, s), 2.01 (3H, s), 4.15 (1H, d, J=2.6 Hz), 5.54 (1H, br s), 6.17 (1H, d, J=6.0 Hz), 7.23 (1H, dd, J=1.7, 6.0 Hz); δ_C (75 MHz, $CDCl_3$) −3.6, −3.0, 18.1, 22.5, 27.6, 80.0, 80.4, 135.8, 157.1, 171.9, 203.2; HRMS found $[M+H]^+$ 271.1371, required for $C_{13}H_{23}O_4Si$ 271.1365.

3.4. General method C for the Sonogashira coupling reaction

To a solution of vinyl bromide **16** (1 equiv.), in THF (8 mL $mmol^{-1}$) was added *N*,*N*-diisopropylamine (6 equiv.), CuI (9 mol%) and $(PPh_3)_2PdCl_2$ (4 mol%). The reaction mixture was heated to 50°C, whereupon a solution of the acetylene (1 equiv.) in THF (8 mL $mmol^{-1}$) was added dropwise over a 3 h period. The resultant mixture was stirred at 50°C until the reaction was seen to have gone to completion (ca. 1 h). The mixture was allowed to cool to room temperature and quenched with saturated NH_4Cl solution (5 mL). The aqueous layer was extracted with ether (3×5 mL), dried ($MgSO_4$), filtered and concentrated in vacuo. Purification was achieved by chromatography on silica gel with petrol/ether (3:1 v/v) as the eluent.

3.4.1. *trans*-4-*tert*-Butoxy-5-(*tert*-butyldimethylsilyloxy)-2-(4-trimethylsilyloxy-1-butynyl)-cyclopent-2-en-1-one (30). The general method C was employed for the preparation of **30**. The quantities of reagents used were as follows: **16** (137 mg, 0.38 mmol), *N*,*N*-diisopropylamine (0.31 mL, 2.2 mmol), CuI (7 mg, 0.034 mmol), $(PPh_3)_2PdCl_2$ (11 mg, 0.015 mmol), but-3-ynyloxy-trimethylsilane (54 mg, 0.38 mmol). **30** isolated as a yellow oil (105 mg, 65%). ν_{max} 2959, 2931, 2887, 2236, 1739, 1585, 1473, 1068, 840, 782 cm^{-1}; δ_H (300 MHz, $CDCl_3$) 0.06 (9H, s), 0.15 (3H, s), 0.20 (3H, s), 0.93 (9H, s), 1.28 (9H, s), 2.68 (2H, t, J=6.2 Hz), 3.79 (2H, t, J=6.2 Hz), 4.16 (1H, d, J=2.5 Hz), 4.53 (1H, d, J=2.5 Hz), 7.23 (1H, d, J=2.5 Hz); δ_C (75 MHz, $CDCl_3$) −4.7, −3.8, 2.4, 18.8, 24.4, 26.2, 28.8, 29.5, 61.1, 72.8, 75.5, 80.6, 81.6, 95.7, 128.1, 159.5, 200.6; HRMS found $[M-CH_3]^+$ 409.2230, required for $C_{21}H_{37}O_4Si_2$ 409.2230.

3.4.2. *trans*-4-*tert*-Butoxy-5-(*tert*-butyldimethylsilyloxy)-2-(4-hydroxy-1-butynyl)-cyclopent-2-en-1-one (31). The general method C was employed for the preparation of **31**. The quantities of reagents used were as follows: **16** (75 mg, 0.21 mmol), *N*,*N*-diisopropylamine (0.15 mL, 1.1 mmol), CuI (3.2 mg, 0.016 mmol), $(PPh_3)_2PdCl_2$ (5.2 mg, 0.0075 mmol), 3-butyn-1-ol (0.016 mL, 0.21 mmol). **31** isolated as a yellow oil (70 mg, 98%). ν_{max} 3426, 2362, 1372, 1084, 839, 781 cm^{-1}; δ_H (300 MHz, $CDCl_3$) 0.14 (3H, s), 0.19 (3H, s), 0.93 (9H, s), 1.29 (9H, s), 2.10 (1H, s), 2.68 (2H, t, J=6.0 Hz), 3.79 (2H, t, J=6.0 Hz), 4.16 (1H, d, J=2.9 Hz), 4.54 (1H, s), 7.23 (1H, s); δ_C (75 MHz, $CDCl_3$) −4.7, −3.8, 18.8, 24.5, 26.2, 28.8, 61.2, 75.6, 76.2, 81.6, 95.7, 128.5, 159.5, 199.0; HRMS found $[M+H]^+$ 353.2148, required for $C_{19}H_{33}O_4Si$ 353.2148.

3.4.3. ±3-(Bromomethyl-dimethylsilyloxy)-5-*tert*-butoxy-4-(*tert*-butyldimethylsilyloxy)-cyclopentene (33). To a stirred solution of cyclopentenol **32** (1.0811 g, 3.78 mmol) in DCM (50 mL) cooled to 0°C was added bromomethyldimethylsilyl chloride (1.03 mL, 7.56 mmol). To the resulting solution was added *N*,*N*-diisopropylamine (1.32 mL, 7.56 mmol) and stirring was continued for 1 h at 0°C. The reaction was quenched with saturated NH_4Cl solution and extracted into ethyl acetate (3×30 mL). The organic extracts were washed with brine, dried over $MgSO_4$, filtered and concentrated in vacuo. Purification on silica gel with petrol/ethyl acetate (6:1 v/v) as the eluent yielded the title compound as a colourless oil. (1.055 g, 64%). ν_{max} 3054, 2985 cm^{-1}; δ_H (300 MHz, $CDCl_3$) 0.10 (3H, s), 0.11 (3H, s), 0.28 (3H, s), 0.29 (3H, s), 0.91 (9H, s), 1.21 (9H, s), 2.47 (2H, s), 3.92 (1H, t, *J*=5.2 Hz), 4.21 (1H, dd, *J*=3.9, 1.1 Hz), 4.45 (1H, dd, *J*=3.9, 1.1 Hz), 5.69 (2H, d, *J*=5.7 Hz); δ_C (75 MHz, $CDCl_3$) −2.6, −2.3, 16.4, 17.9, 25.9, 28.5, 73.7, 76.6, 80.3, 88.6, 132.6, 134.4; HRMS (EI^+) found $[M+H]^+$ 437.1540, required for $C_{18}H_{38}O_3Si_2Br$ 437.1543.

3.4.4. 3-*tert*-Butoxy-2-(*tert*-butyldimethylsilyloxy)-5-hydroxymethylcyclopentanol (34). To a solution of bromomethylsilyl ether **33** (880.4 mg, 2.0 mmol) in degassed benzene (200 mL) set to reflux (80°C) was added a solution of AIBN (35 mg, 0.2 mmol) and tributyl tin hydride (0.7 mL, 2.6 mmol) in benzene (20 mL) at a rate of 20 mL h^{-1}. Upon addition the reaction was refluxed for 2 h, after which the solvent was removed in vaccuo. To the resulting residue was added MeOH (16 mL), THF (16 mL), K_2CO_3 (334.9 mg, 2.4 mmol) and KF (258.1 mg, 4.4 mmol). To the stirring suspension was added a solution of H_2O_2 (15 mL, 27.5 wt%) and stirring was continued for a further 2 h at 60°C. The reaction was quenched with brine (30 mL) and extracted into ethyl acetate (5×30 mL). The combined organic extracts were dried over $MgSO_4$, filtered and concentrated in vaccuo. Purification was achieved by chromatography on silica gel with petrol/ethyl acetate (2:1 v/v) as the eluent. The title compound was isolated as a yellow oil (482.6 mg, 76%). ν_{max} 3468, 2976 cm^{-1}; δ_H (300 MHz, $CDCl_3$) 0.02 (6H, s), 0.86 (9H, s), 1.17 (9H, s), 1.24 (1H, s), 1.36–1.44 (1H, m), 2.07–2.17 (1H, m), 2.38–2.45 (1H, m), 3.28 (1H, br s), 3.72–3.80 (3H, m), 3.85–3.86 (1H, m), 3.95–3.96 (1H, m); δ_C (75 MHz, $CDCl_3$) −4.2, 18.3, 26.1, 28.7, 34.2, 42.2, 63.7, 74.8, 77.7, 79.9, 83.1; HRMS (ES^+) found $[M+H]^+$ 319.2303, required for $C_{16}H_{35}O_4Si$ 319.2304.

3.4.5. 2-Bromo-5-(*tert*-butyldimethylsilyloxy)-3-[3-(*tert*-butyldiphenylsilyloxymethyl)-7,7-dimethoxy-hept-3-ene-1,5-diynyl]-4-hydroxy-cyclopentanone (37). To a solution of (2-ethynyl-6,6-dimethoxy-hex-2-en-4-ynyloxy)-*tert*-butyldiphenyl-silane **36** (88 mg, 0.21 mmol) in THF (1 mL) was added *n*BuLi (0.093 mL of a 2.5 M solution in hexanes, 0.23 mmol) at −78°C. After 40 min diethylaluminium chloride (0.253 mL of a 1 M solution in THF, 0.253 mmol) was added and the reaction was left to warm to room temperature over 1 h. The acetylide solution was added via canula to a solution of **35** (30 mg, 0.1 mmol) in THF (1 mL) at −45°C. The reaction was quenched after 3 h with Rochelle's salt (5 mL), extracted with ethyl acetate (3×10 mL), washed with brine (10 mL), dried over $MgSO_4$, filtered and concentrated in vacuo. Purification was achieved by chromatography on silica gel by eluting with petrol/ether (20:1 v/v) to give **37** as a yellow oil (10 mg, 85%). ν_{max} 3417, 3053, 2978, 2873, 1770, 1383 cm^{-1}; δ_H (300 MHz, $CDCl_3$) 0.00 (3H, s), 0.02 (3H, s), 0.75 (9H, s), 0.95 (9H, s), 2.92 (1H, d, *J*=4.0 Hz), 3.28 (6H, s), 3.50 (1H, dd, *J*=4.0, 9.0 Hz), 3.93 (1H, s), 4.05–4.07 (1H, m), 4.14 (2H, s), 4.31 (1H, d, *J*=9.0 Hz), 5.21 (1H, s), 7.51–7.54 (4H, m), 6.18 (1H, s), 7.26–7.33 (6H, m),; δ_C (75 MHz, $CDCl_3$) −0.5, −0.4, 18.6, 19.7, 26.0, 27.2, 44.3, 47.4, 53.2, 65.3, 75.1, 76.5, 83.0, 84.1, 91.5, 93.3, 93.9, 113.4, 128.3, 130.4, 133.0, 135.8, 136.3, 206.1; *m*/*z* $(EI)^+$ 695 $[M-OMe]^+$, 669 $[M-{}^tBu]^+$; HRMS (EI^+) found $[M+NH_4]^+$ 742.2588, required for $C_{37}H_{53}O_6Si_2BrN$ 742.2595.

3.5. Diels–Alder reactions

3.5.1. 3-*tert*-Butoxy-2-(*tert*-butyldimethylsilyloxy)-2,3,3a,4,7,7a-hexahydro-4,7-methano-inden-1-one (38). To a stirring solution of cyclopentenone **15** (0.293 g, 1.03 mmol) in benzene (5 mL) cooled to −78°C was added freshly distilled cyclopentadiene (0.85 mL, 10.3 mmol). The reaction was slowly allowed to warm to 0°C, where $ZnCl_2$ (14.1 mg, 0.1 mmol) was added. Stirring was continued at an ambient temperature for 22 h. The reaction was quenched with $NaHCO_3$ solution (15 mL) and extracted into diethyl ether (3×20 mL). The organic extracts were washed with brine (20 mL), dried over $MgSO_4$, filtered and concentrated in vacuo. Purification on silica gel with petrol/ethyl acetate (4:1 v/v) as the eluent yielded the title compound as a white crystalline solid. Yield (0.249 g, 69%). Mp 92.2–93.8°C; ν_{max} 2977, 1746 cm^{-1}; δ_H (300 MHz, $CDCl_3$) 0.00 (3H, s), 0.06 (3H, s), 0.86 (9H, s), 1.21 (9H, s), 1.41 (2H, dd, *J*=8.0, 5.0 Hz), 2.84–2.93 (2H, m), 3.14 (2H, s), 3.84 (1H, d, *J*=9.0 Hz), 3.93–3.99 (1H, m), 5.93 (1H, dd, *J*=5.0, 3.0 Hz), 6.40 (1H, dd, *J*=5.0, 3.0 Hz); δ_C (75 MHz, $CDCl_3$) −4.7, −4.2, 18.8, 26.1, 29.0, 46.0, 46.1, 48.0, 51.8, 53.7, 73.9, 75.4, 82.6, 134.9, 139.4; HRMS (ES^+) found $[M+NH_4]^+$ 368.2625, required for $C_{20}H_{38}O_3SiN$ 368.2621; X-ray: *endo* exclusively.

3.5.2. 3-*tert*-Butoxy-2-(*tert*-butyldimethylsilyloxy)-5-methyl-2,3,3a,4,7,7a-hexahydro-4,7-methano-inden-1-one (39). To a stirring solution of cyclopentenone **15** (0.297 g, 1.05 mmol) in benzene (5 mL) was added $ZnCl_2$ (71.3 mg, 0.52 mmol) and freshly distilled isoprene (1.0 mL, 10.5 mmol). The reaction was stirred for 6 days and concentrated in vacuo to yield a brown oil. Purification on silica gel with petrol/ethyl acetate (6:1 v/v) as the eluent yielded the title compound as a colourless oil. Yield (0.265 g, 72%). ν_{max} 2984, 1741 cm^{-1}; δ_H (300 MHz, $CDCl_3$) 0.10 (3H, s), 0.13 (3H, s), 0.90 (9H, s), 1.26 (9H, s), 1.65 (3H, s), 1.82–2.18 (3H, m), 2.36–2.58 (3H, m), 3.85 (1H, d, *J*=9.0 Hz), 4.06 (1H, dd, *J*=9.0. 6.0 Hz), 5.34 (1H, s); δ_C (75 MHz, $CDCl_3$) −4.5, −4.0, 18.8, 22.6, 24.4, 26.1, 27.2, 29.1, 34.3, 45.2, 74.4, 77.8, 78.4, 119.7, 113.4, 215.1; HRMS (ES^+) found $[M+NH_4]^+$ 370.2777, required for $C_{20}H_{40}O_3SiN$ 370.2771; X-ray: *endo* exclusively.

3.5.3. 3-*tert*-Butoxy-2-(*tert*-butyldimethylsilyloxy)-5,6-dimethyl-2,3,3a,4,7,7a-hexahydro-4,7-methano-inden-1-one (40). To a stirring solution of cyclopentenone **15**

(0.285 g, 1.0 mmol) in benzene (5 mL) was added $ZnCl_2$ (68.2 mg, 0.52 mmol) and freshly distilled 2,3-dimethylbutadiene (1.1 mL, 10.0 mmol). The reaction was stirred for 6 days and concentrated in vacuo to yield a brown oil. Purification on silica gel with petrol/ethyl acetate (6:1 v/v) as the eluent yielded the title compound as a colourless oil. (0.155 g, 42%). ν_{max} 2985, 1741 cm^{-1}; δ_H (300 MHz, $CDCl_3$) 0.09 (3H, s), 0.13 (3H, s), 0.90 (9H, s), 1.25 (9H, s), 1.59 (3H, s), 1.62 (3H, s), 1.98 (2H, d, J=6.0 Hz), 2.09 (1H, d, J=18.0 Hz), 2.36 (1H, d, J=18.0 Hz), 2.43–2.50 (2H, m), 3.84 (1H, d, J=9.0 Hz), 4.01–4.06 (1H, m); δ_C (75 MHz, $CDCl_3$) −4.5, −4.1, 18.8, 19.4, 19.8, 26.1, 29.1, 29.2, 34.8, 46.3, 74.4, 78.8, 78.7, 125.0, 125.5, 215.4; HRMS (ES^+) found $[M+NH_4]^+$ 384.2931, required for $C_{21}H_{42}O_3SiN$ 384.2934; X-ray: *endo* exclusively.

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