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Synthesis of the Northern hemisphere of the briaranes

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ABSTRACT

A highly functionalized fragment corresponding to the Northern hemisphere of the briaranes has been synthesized employing a sulfonyl diene Diels–Alder reaction, oxidative desulfonylation, Eschenmoser rearrangement and Keck radical allylation.

1. Introduction

A review published in 1999 reported 299 natural products in the briarane family, isolated from marine organisms from a variety of locations around the world including the coast of Taiwan, the Caribbean Sea and the Ligurian Sea.[1] Since then, numerous additions to the family have been made, bringing the total to well over 300.[2] The briarane skeleton is characterized by a six-membered ring fused to a ten-membered ring and often with a butenolide or derivative attached to the latter, as in brianthein W (Fig. 1). The basic skeleton always includes unsaturation and bears various methyl groups, especially one at the C1 quaternary centre, hydroxy groups and, sometimes ether linkages including epoxides, and halogen atoms.

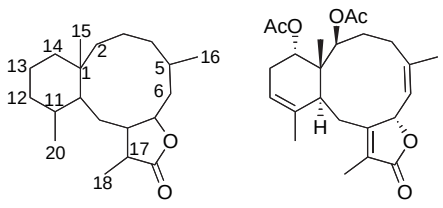

Figure 1. The briarane skeleton and brianthein W.

Various members of the family, as well as analogues,[3] have been screened for biological activity, and a range of properties has been reported. Despite this combination of structural challenge and biological activity, there has been little synthetic work reported for this family of compounds.[4] We wish to report an approach to what might be termed the briarane Northern hemisphere, in racemic form: C1 to C6 and the cyclohexane moiety.

2. Results and discussion

A challenge anticipated early was the quaternary centre at C1. We planned to employ a sigmatropic rearrangement to install this quaternary centre, starting from an allylic alcohol. This led us to a crotonate Diels–Alder reaction as the method for formation of the six-membered ring. Crotonate derivatives are often reluctant dienophiles and, therefore, we sought a robust functionalized diene that would permit conversion to the desired allylic alcohol after the cycloaddition. Bäckvall has reported the use of sulfonyl dienes even in reactions with electron poor dienophiles.[5] As various methods are available for subsequent desulfonylation,[6] this route was selected. The required sulfonyl diene **3** was synthesized from crotyl chloride (*E*/*Z* mixture) (Scheme 1). This was converted to a crotyl sulfone **1** by reaction with toluene sulfinic acid sodium salt under van Leusen's phase transfer conditions.[7] Deprotonation with *n*-butyl lithium and quenching with paraformaldehyde gave the alcohol **2**, which was dehydrated in one pot by treatment with mesyl chloride and excess triethylamine to give the sulfonyl diene **3** as a single geometrical isomer. Diene **3** is unstable, undergoing a Diels–Alder dimerisation if stored in its pure form, as has also

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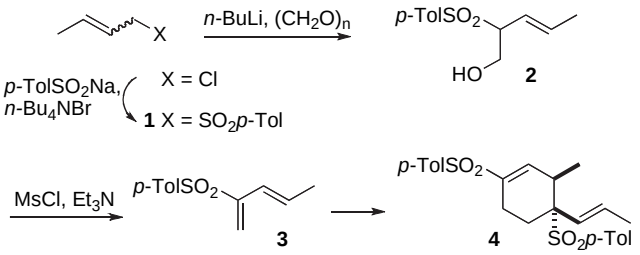
been observed for related esters and nitriles.[8] Thus, sulfonyl diene **3** was handled as a solution in dichloromethane and stored at −80 °C.



Scheme 1. Sulfonyl diene synthesis and dimerisation.

The dimer **4** proved to be crystalline, and the structure was confirmed by X-ray crystallography (Fig. 2).[9]

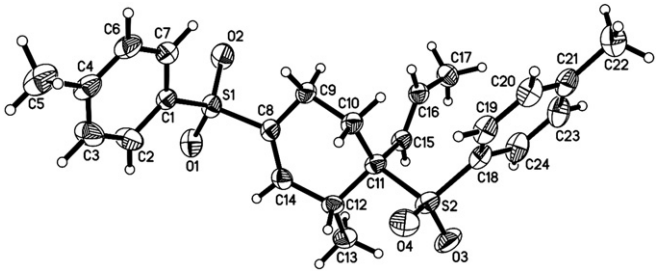
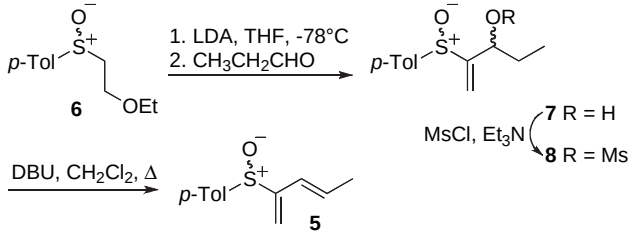


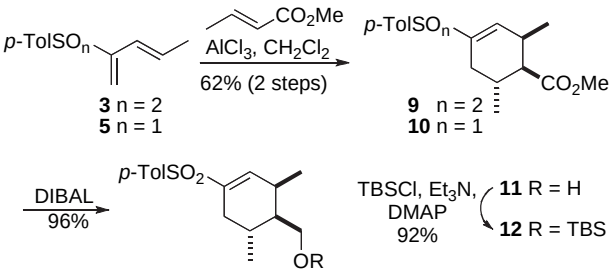
Figure 2. diene dimer **4**.

The corresponding sulfoxide **5** was also prepared, but by a modification of the method of Maignan (Scheme 2).[10] The 2-ethoxyethylsulfoxide **6** (prepared from the readily available vinyl sulfoxide[11]) was deprotonated with LDA and the resulting anion was quenched with propionaldehyde. Dehydration of the resulting alcohol **7** to give the diene was effected in two steps: formation of mesylate **8** and elimination with DBU. In contrast to sulfone **3**, sulfoxide **5** did not dimerise during isolation or storage.



Scheme 2. Sulfinyl diene synthesis.

While sulfonyl diene **3** undergoes cycloaddition with methyl acrylate quite rapidly giving the expected cycloadduct in 4 h using aluminium trichloride as a Lewis acid catalyst,[12] the reaction with methyl crotonate is sluggish, requiring 7 days in dichloromethane at reflux. Despite the harsh reaction conditions, the Diels–Alder adduct **9** was isolated in 62% yield over two steps, as a single (racemic) stereoisomer, accompanied by a small amount (5% yield) of dimer **4** (Scheme 3). The Diels–Alder reaction of the corresponding sulfoxide **5**, proved to be even slower and resulted in the formation of an inseparable mixture of stereoisomers due to the chiral centre at sulfur. The approach using the sulfoxide was not, therefore, pursued further. Reduction of the ester group of sulfone **9** with DIBAL yielded the primary alcohol **11**. Crystals of this alcohol suitable for X-ray analysis were obtained, allowing confirmation of the structure (Fig. 3). The stereochemistry was, as anticipated, in accordance with the Alder cis-*endo* rule. The free alcohol was then protected as its TBS ether **12**.



Scheme 3. Sulfonyl and sulfinyl diene Diels–Alder reactions.

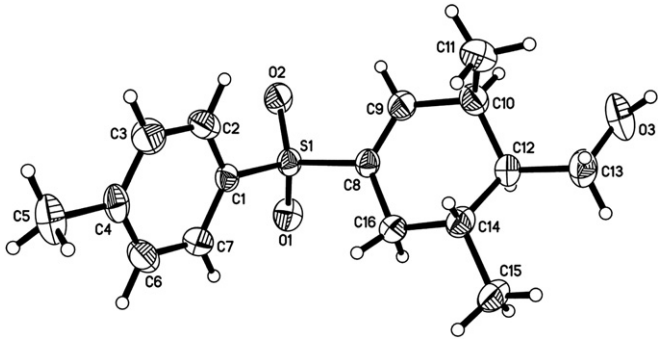
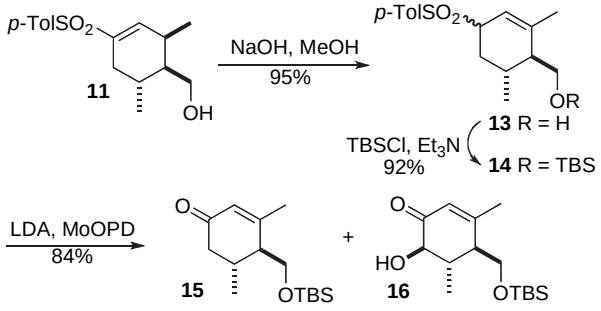


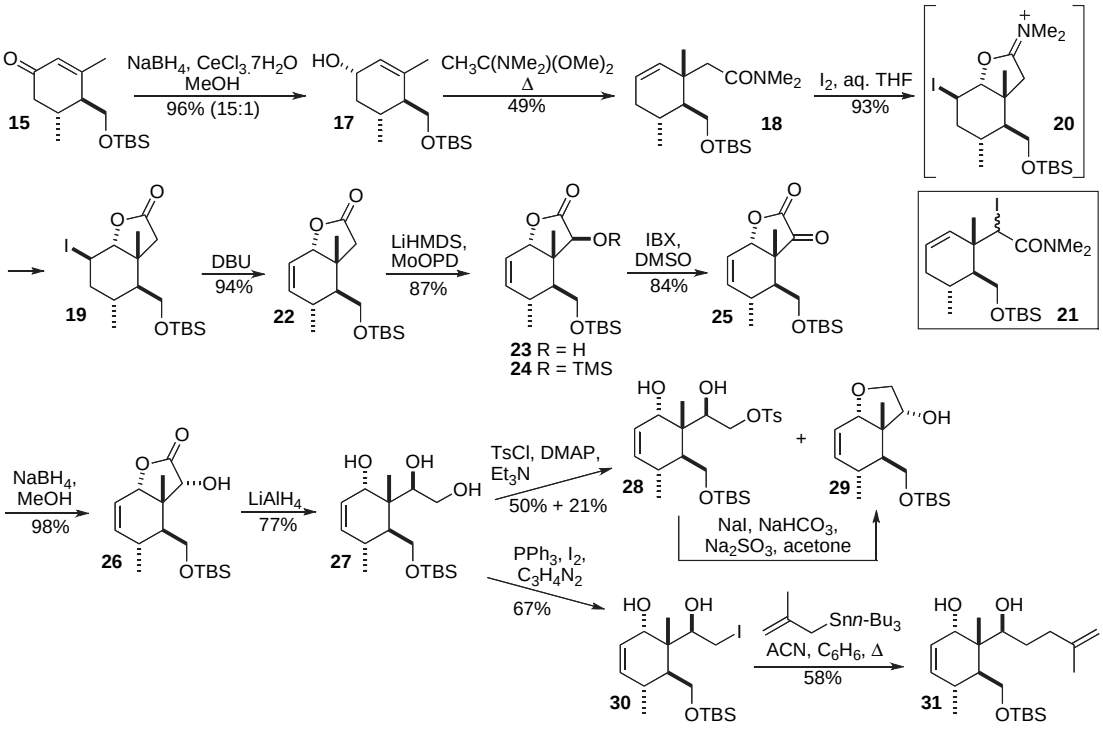
Figure 3. alcohol **11**.

Oxidative desulfonylation of the vinyl sulfone **12** proved to be troublesome (Scheme 4). Attempts at either electrophilic epoxidation (mcpba) or nucleophilic (Weitz–Scheffer) epoxidation[13] (*t*-BuOOLi or H_2O_2, NaOH) failed, as did attempts to oxidize the double bond using osmium tetroxide under either Upjohn[14] or Tsuji[15] conditions. Attempts at γ-deprotonation with either LDA or *n*-BuLi were, likewise, fruitless. During epoxidation studies, it was noticed that prolonged treatment of alcohol **11** with sodium hydroxide in hot methanol resulted in isomerisation of the double bond, cleanly giving the β,γ-unsaturated sulfone **13** as a mixture of diastereoisomers. The identity of the major isomer could not be determined due to overlapping ^{1}H NMR signals. After silylation of the free alcohol, oxidative desulfonylation[16] could be achieved by treatment with an excess of LDA and MoOPD ($MoO_5 \cdot Py \cdot DMPU$)[17] to give cyclohexenone **15**. To obtain an optimum yield of cyclohexenone **15**, it was necessary to limit the reaction time. An extended reaction time resulted in significant over-oxidation, yielding some of the α-hydroxylated enone **16** as a single stereoisomer.[18] The observation of a 12.3 Hz coupling constant between the α and β-protons indicated that the new hydroxyl group was equatorial, corresponding to approach of the MoOPD reagent to the face opposite the methyl group.



Scheme 4. Oxidative desulfonylation.

Cyclohexenone **15** was reduced with sodium borohydride to give the equatorial alcohol **17** (15:1 ratio of diastereoisomers)



Scheme 5. Completion of the synthesis of the Northern hemisphere fragment.

(Scheme 5). Addition of cerium trichloride[19] was unnecessary in obtaining exclusive 1,2-addition, but a slight improvement in the stereoselectivity was found when this additive was employed. Several methods were tried for introducing the briarane C1 quaternary centre by a [3,3]-sigmatropic rearrangement.[20] Use of Johnson's modification of the Claisen rearrangement[21] (triethyl orthoacetate and propionic acid at reflux) gave none of the desired product, neither did conversion of the alcohol to its acetate ester, followed by attempted Ireland–Claisen rearrangement. Treatment of **17** with ethyl vinyl ether and mercuric acetate,[22] followed by heating did give some of the rearranged aldehyde by ^{1}H NMR, but this material could not be isolated. Attempts to obtain the same aldehyde by the method of Mandai,[23] involving oxa-Michael addition of **17** to an aryl vinyl sulfoxide, were similarly unsuccessful.[24] Finally, employing Eschenmoser's variation of the Claisen rearrangement,[25] heating with dimethylacetamide dimethyl acetal in xylene at reflux, gave the desired rearranged amide **18** in modest but useable yield (Scheme 5).[26] This reaction was most effectively carried out in a microwave. The difficulty in achieving this transformation can be attributed to the equatorial disposition of the alcohol. While amides are less susceptible to nucleophilic attack than other carboxyl derivatives, they are more susceptible to electrophilic attack. Amide **18** was, therefore, subjected to cycloiodination[27] to give iodolactone **19** as a single isomer. Curiously, if the reaction was quenched and worked up as soon as TLC indicated disappearance of the starting material, then a low yield of iodolactone **19** was obtained, accompanied by unreacted starting material **18**. On prolonged reaction, however, an almost quantitative yield of iodolactone **19** could be obtained. We attribute this to fast iodocyclisation, but slow hydrolysis of intermediate **20**, with the iodocyclisation reversing under the work up conditions. A minor by-product of the cycloiodination was assigned structure **21**. This by-product was obtained as a single diastereoisomer, although it was not possible to determine which one.[28] Elimination of the iodine from lactone **19** was achieved by heating with DBU in THF. An X-ray structure of the elimination product **22** was obtained (Fig. 4). This compound represents a highly functionalized intermediate for the briarane ready for further manipulation to introduce different cyclohexane substitution patterns.

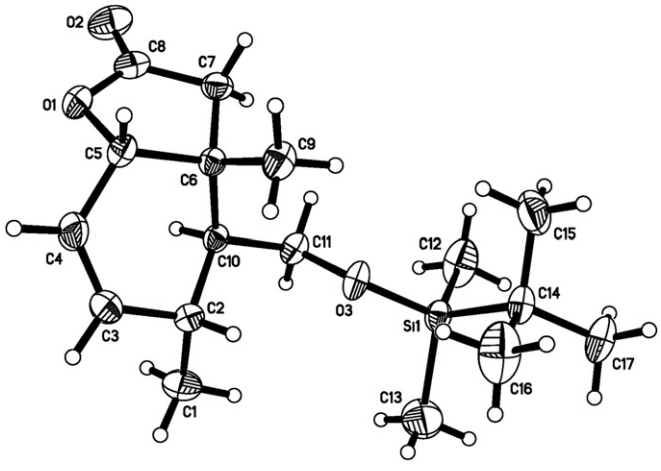


Figure 4. lactone **22**.

Nevertheless, introduction of the remaining portion of the Northern hemisphere required further elaboration of lactone **22**. At this point, we opted to introduce the briarane C2 hydroxyl group. Attempts to do this using LDA and MoOPD led to recovery of starting material. Reasoning that the bulk of LDA was preventing removal of the crowded proton α to the lactone carbonyl, we turned to other bases. The use of an excess of LiHMDS, followed by MoOPD gave an excellent yield of the α-hydroxylated lactone **23** as a single stereoisomer. Interestingly, use of KHMDS gave only a modest yield

of the desired α-hydroxylated lactone **23**, accompanied by a small amount of the TMS ether **24**,[29] presumably due to the hexamethyldisilylamine by-product acting as a silylating agent for the reactive potassium alkoxide.

Inspection of molecular models, supported by NOE studies, indicated that hydroxylation occurred on the convex face of the enolate of **22**, *syn* to the methyl group. This is opposite to the stereochemistry required for the natural products. The hydroxyl group was inverted by oxidation to the ketolactone **25** with an excess of IBX,[30] followed by sodium borohydride reduction, giving alcohol **26**, diastereoisomeric with **23**. This reduction was completely stereoselective. Further reduction with lithium aluminium hydride yielded triol **27**. In order to introduce the remaining Northern hemisphere carbon atoms, we attempted to convert the primary alcohol group of triol **27** into a leaving group. Tosylation proceeded in modest yield and was accompanied by *in situ* formation of the tetrahydrofuran **29**.[31] Attempts at a Finkelstein reaction of tosylate **28** (sodium iodide, sodium bicarbonate and sodium sulfite) resulted in the formation of additional amounts of this tetrahydrofuran and none of the desired iodide. The desired iodide **30** could, however, be obtained directly from the triol **27** by treatment with iodine and triphenylphosphine in the presence of imidazole,[32] although a small amount of the tetrahydrofuran **29** was also obtained. The key difference between the two iodination methods appears to be the reaction temperature. With iodide **30** in hand, the remainder of the Northern hemisphere was installed by free radical Keck allylation[33] using methallyltri-*n*-butyltin in the presence of 1,1′-azobis(cyclohexanecarbonitrile) (ACN) as initiator, giving a highly functionalised Northern hemisphere fragment **31**. During the free radical methallylation, no intramolecular attack on the cyclohexene double bond was noted, presumably due to the equatorial disposition of the radical containing side-chain.

3. Conclusion

We have completed a viable route to the Northern hemisphere to give a highly functionalized intermediate. Studies on the installation of a butenolide, and closure of the ten-membered ring are in progress.

4. Experimental

4.1. General procedures

All reactions were carried out under a nitrogen atmosphere using oven-dried glassware (120 °C), which was cooled under vacuum. All commercially obtained reagents were used as received. Analytical TLC was carried out on precoated plates (silica gel 60, F_{254}). Column chromatography was performed with silica gel 60 (230–400 mesh). ^{1}H NMR spectra were recorded in $CDCl_3$ at 300 or 400 MHz; chemical shifts are expressed in parts per million relative to an internal standard. Peaks are assigned by consideration of chemical shift values and coupling patterns. Melting points are uncorrected. Infrared spectra were recorded as Nujol mulls or neat.

*4.1.1. 1-(p-Tolylsulfonyl)-but-2-ene (**1**).* Crotyl chloride (7.86 mL, 80.1 mmol, *E*/*Z* mixture) was added to a suspension of sodium *p*-toluenesulfinate (15.77 g, 88.2 mmol) and tetra-*n*-butyl ammonium bromide (1.29 g, 4.0 mmol) in 1,2-dimethoxyethane (70 mL). The mixture was heated at reflux for 30 min, then cooled to room temperature, diluted with water (20 mL) and extracted with Et_2O (50 mL×3). The combined organic layers were washed with water and brine and dried over anhydrous $MgSO_4$. After removal of solvent under reduced pressure, the residue was purified by column chromatography (SiO_2, 25% EtOAc in hexanes) to give *sulfone* **1** (14.41 g, 68.53 mmol, 86%) as a colourless solid (72:28 mixture of *E* and *Z* isomers); mp 32–34 °C; R_f=0.26 (25% ethyl acetate/hexane); ν_{max}/cm^{-1} 1666, 1597, 1433, 1396, 1315, 1300, 1143, 1087, 968, 929, 815, 723, 624; δ_H (400 MHz; $CDCl_3$) 7.86 (d, 2H, *J*=8.1 Hz, Ar–H, cis and trans), 7.29 (d, 2H, *J*=8.1 Hz, Ar–H, cis and trans), 5.77 (dq, 1H, *J*=10.8, 7.0 Hz, C*H*CH$_3$, cis), 5.52 (dq, 1H, *J*=15.3, 6.4 Hz, C*H*CH$_3$, trans), 5.36 (dtq, 1H, *J*=15.3, 7.3, 1.5 Hz, C*H*=CHCH$_3$, cis and trans), 3.79 (d, 2H, *J*=7.9 Hz, SO_2CH_2, cis), 3.67 (d, 2H, *J*=7.3 Hz, SO_2CH_2, trans), 2.39 (s, 3H, CH_3, cis and trans), 1.62 (app.d, 3H, *J*=6.4 Hz, CH_3, trans), 1.31 (app.d, 3H, *J*=7.0 Hz, CH_3, cis); δ_C (100 MHz; $CDCl_3$) 144.6, 136.3, 135.6, 129.6 (2C), 128.4 (2C), 117.1, 60.1, 21.6, 18.1; *m*/*z*, 211 (M+H$^+$, 100%), 210, 195; HRMS found 211.0785 (M+H$^+$, $C_{11}H_{14}O_2S$ requires 211.0793).

*4.1.2. 2-(p-Tolylsulfonyl)pent-3-en-1-ol (**2**).* *n*-BuLi (21.8 mL of a 1.6 M solution in hexanes, 32.7 mmol) was added over 5 min to a suspension of sulfones **1** (4.91 g, 23.4 mmol) and paraformaldehyde (1.40 g, 46.7 mmol) in THF (70 mL) at −78 °C under nitrogen. After stirring at this temperature for 1 h, the temperature was allow to rise to −25 °C over a period of 5 h. The reaction mixture was quenched with saturated aq NH_4Cl (30 mL) and extracted with Et_2O (50 mL×3). The combined organic layers were washed with water and brine and dried over anhydrous $MgSO_4$. After removal of solvent under reduced pressure, the residue was purified by column chromatography (SiO_2, 50% EtOAc in hexanes) to give *sulfonyl alcohols* **2** (3.60 g, 14.98 mmol, 64%) as a colourless oil (64:36 mixture of *E* and *Z* isomers); R_f=0.25 (50% ethyl acetate/hexane); ν_{max}/cm^{-1} 3458, 3030, 2920, 1643, 1597, 1494, 1444, 1300, 1141, 966, 815, 709; δ_H (400 MHz; $CDCl_3$) 7.73 (d, 2H, *J*=8.2 Hz, Ar–H, cis), 7.70 (d, 2H, *J*=8.2 Hz, Ar–H, trans), 7.34 (d, 2H, *J*=8.2 Hz, Ar–H, cis and trans), 5.81 (dq, 1H, *J*=10.8, 7.0 Hz, C*H*CH$_3$, cis), 5.54 (dq, 1H, *J*=15.3, 6.5 Hz, C*H*CH$_3$, trans), 5.53–5.10 (m, 1H, C*H*=CHCH$_3$, cis and trans), 4.30–3.60 (m, 2H, C*H*$_2$OH, cis and trans), 2.98 (dt, 1H, *J*=4.6, 3.1 Hz, SO_2CH_2, cis), 2.88 (dt, 1H, *J*=5.6, 2.1 Hz, SO_2CH_2, trans), 2.45 (s, 3H, CH_3, cis and trans), 1.66 (dd, 3H, *J*=6.5, 1.4 Hz, CH_3, trans), 1.31 (dd, 3H, *J*=7.0, 1.7 Hz, CH_3, trans); δ_C (100 MHz; $CDCl_3$) 145.1, 136.1, 134.1, 129.7, 129.6, 129.1 (2C), 119.1, 70.4, 60.9, 21.7, 18.3; *m*/*z*, 263 (M+Na$^+$, 100%) 258; HRMS found 263.0713 (M+Na$^+$, $C_{12}H_{16}O_3S$ requires 263.0718).

*4.1.3. 2-(p-Tolylsulfonyl)penta-1,3-diene (**3**).* Triethylamine (4.0 mL, 28.6 mmol) and methanesulfonyl chloride (2.2 mL, 28.6 mmol) were added dropwise and sequentially to a solution of alcohol **2** (3.43 g, 14.3 mmol) in dichloromethane (42 mL) at 0 °C under nitrogen. The reaction mixture was stirred at 0 °C for 30 min, then allowed to warm slowly to room temperature and stirred for an additional for 4 h. The reaction mixture was diluted with H_2O (30 mL) and extracted with CH_2Cl_2 (100 mL×2). The combined organic layers were washed with water and brine and dried over anhydrous $MgSO_4$. The solution of *diene* **3** was stored at (−78 °C) or used directly in the next step without concentration or isolation; R_f=0.33 (25% ethyl acetate/hexane); δ_H (400 MHz; $CDCl_3$) 7.72 (app.d, 2H, *J*=7.9 Hz, Ar–H), 7.32 (app.d, 2H, *J*=7.9 Hz, Ar–H), 6.17 (br s, 1H, C=C*H*H), 6.13 (dq, 1H, *J*=15.8, 6.5 Hz, CH=C*H*CH$_3$), 6.01 (app.d, 1H, *J*=15.8 Hz, C*H*=CHCH$_3$), 5.83 (br s, 1H, C=CH*H*), 2.42 (s, 3H, Ar–CH$_3$), 1.74 (d, 3H, *J*=6.5 Hz, CH_3); δ_C (75 MHz; $CDCl_3$) 148.4, 144.4, 136.4, 133.5, 129.7 (3C), 128.0, 121.9, 121.3, 21.5, 18.5.

*4.1.4. 2-(p-Tolylsulfinyl)pent-1-en-3-ol (**7**).* A solution of 1-(2-ethoxyethylsulfinyl)-4-methylbenzene **6** (2.76 g, 13 mmol) in THF (25 mL) was added dropwise at −78 °C to a solution of lithium diisopropylamide (LDA) under nitrogen [prepared by reacting diisopropylamine (5.85 mL, 32.5 mmol) in THF (32 mL) with *n*-BuLi (17.9 mL of a 1.6 M solution in hexane, 28.6 mmol) at −78 °C for 30 min]. After stirring at −78 °C for 1 h, propionaldehyde (1.12 mL, 15.6 mmol) was added. The mixture was stirred at −78 °C for 3 h,

and then quenched with saturated NH_4Cl (30 mL). The mixture was diluted with water (50 mL) and extracted with Et_2O (30 mL×3). The combined organic layers were washed with water and brine and dried over anhydrous $MgSO_4$. After removal of solvent under reduced pressure, the residue was purified by column chromatography (SiO_2, 50% EtOAc in hexanes) to give *sulfoxide* **7** (0.81 g, 3.64 mmol, 28% yield) as a colourless oil; R_f=0.17 (50% ethyl acetate/hexane); ν_{max}/cm^{-1} 3003, 2872, 1643, 1633, 1492, 1377, 1354, 1215, 1107, 1085, 1041, 806, 754; δ_H (500 MHz; $CDCl_3$) 7.55 (d, 2H, *J*=8.1 Hz, Ar–H, minor), 7.52 (d, 2H, *J*=8.1 Hz, Ar–H, major), 7.31 (d, 2H, *J*=8.1 Hz, Ar–H, major), 7.27 (d, 2H, *J*=8.1 Hz, Ar–H, minor), 6.07 (s, 1H, C=C*H*H, minor), 6.06 (s, 1H, C=C*H*H, major), 5.85 (s, 1H, C=CH*H*, major), 5.84 (s, 1H, C=CH*H*, minor), 4.15–4.03 (m, 1H, C*H*OH, major and minor), 2.41 (s, 3H, CH_3, major), 2.40 (s, 3H, CH_3, minor), 1.75–1.46 (m, 2H, CH_2CH$_3$, major and minor), 0.86 (t, 3H, *J*=7.4 Hz, CH_3, minor), 0.80 (t, 3H, *J*=7.4 Hz, CH_3, major); δ_C (100 MHz; $CDCl_3$) 156.9 (minor), 156.1 (major), 142.0 (major), 141.9 (minor), 139.7 (minor), 138.9 (major), 130.1 (2C) (major), 130.0 (2C) (minor), 125.5 (2C) (minor), 125.2 (2C) (major), 117.5 (major), 117.3 (minor), 70.7 (minor), 69.7 (major), 29.4 (minor), 28.4 (major), 21.5 (major and minor), 9.7 (minor), 9.5 (major); *m*/*z*, 225 (M+H$^+$, 100%), 208, 207, 206, 189, 163, 157, 141, 139, 131; HRMS found 225.0945 (M+H$^+$, $C_{12}H_{17}O_2S$ requires 225.0949).

*4.1.5. 2-(p-Tolylsulfinyl)pent-1-en-3-yl methanesulfonate (**8**).* A solution of methanesulfonyl chloride (0.37 mL, 4.81 mmol) in CH_2Cl_2 (1 mL) was added to a solution of sulfoxide **7** (0.83 g, 3.70 mmol) and triethylamine (0.67 mL, 4.81 mmol) in CH_2Cl_2 (18.5 mL) at 0 °C under nitrogen. The reaction mixture was allowed to warm slowly to room temperature and stirred for 16 h. The mixture was diluted with NH_4Cl (10 mL) and water (10 mL), and extracted with Et_2O (3×25 mL). The combined organic layers were washed with water and brine and dried over anhydrous $MgSO_4$. After removal of solvent under reduced pressure, the residue was purified by column chromatography (SiO_2, 50% EtOAc in hexanes) to give mesylate **8** (1.11 g, 3.67 mmol, 99% yield) as a yellow oil; R_f=0.37 (50% ethyl acetate/hexane); ν_{max}/cm^{-1} 3024, 2976, 2937, 1629, 1595, 1492, 1454, 1352, 1174, 1080, 1047, 914, 850, 812; δ_H (300 MHz; $CDCl_3$) 7.55 (d, 2H, *J*=8.1 Hz, Ar–H, minor), 7.51 (d, 2H, *J*=8.1 Hz, Ar–H, major), 7.32 (d, 2H, *J*=8.1 Hz, Ar–H, major and minor), 6.32 (d, 1H, *J*=0.9 Hz, C=C*H*H, minor), 6.27 (d, 1H, *J*=0.9 Hz, C=C*H*H, major), 6.03 (d, 1H, *J*=0.9 Hz, C=CH_2, major and minor), 5.02–4.85 (m, 1H, CH–OMs, major and minor), 2.89 (s, 3H, CH_3, major), 2.60 (s, 3H, CH_3, minor), 2.40 (s, 3H, CH_3, major and minor), 1.92–1.68 (m, 1H, C*H*HCH$_3$, major), 1.63–1.31 (m, 3H, C*H*HCH$_3$, minor and CH*H*CH$_3$, major and minor), 0.85 (t, 3H, *J*=7.3 Hz, CH_3, major), 0.85 (t, 3H, *J*=7.3 Hz, CH_3, minor); δ_C (75 MHz; $CDCl_3$) 152.6 (major), 152.4 (minor), 142.64 (major), 142.59 (minor), 138.7 (minor), 138.1 (major), 130.3 (2C) (major), 130.2 (2C) (minor), 125.6 (2C) (minor), 125.1 (2C) (major), 120.71 (major), 120.67 (minor), 78.8 (minor), 77.4 (major), 38.4 (major), 38.3 (minor), 29.4 (major), 29.0 (minor), 21.5 (major and minor), 9.4 (minor), 9.0 (major); *m*/*z*, 303 (M+H$^+$, 100%), 302, 300, 295, 291; HRMS found 303.0724 (M+H$^+$, $C_{13}H_{19}O_4S_2$ requires 303.0725).

*4.1.6. (E)-1-Methyl-4-(penta-1,3-dien-2-ylsulfinyl)benzene (**5**).* DBU (1.94 mL, 13.0 mmol) was added slowly to a solution of mesylate **8** (1.96 g, 6.5 mmol) in CH_2Cl_2 (32.5 mL) under nitrogen. The mixture was heated at reflux for 2 h, then diluted with saturated aq NH_4Cl (10 mL) and extracted with Et_2O (3×25 mL). The combined organic layers were washed with water and brine and dried over anhydrous $MgSO_4$. After removal of solvent under reduced pressure, the residue was purified by column chromatography (SiO_2, 50% EtOAc in hexanes) to give *dienyl sulfoxide* **5** (0.86 g, 4.2 mmol, 64%) as a yellow solid; mp 59–60 °C; R_f=0.54 (50% ethyl acetate/hexane); ν_{max}/cm^{-1} 3020, 2992, 2850, 1643, 1595, 1492, 1446, 1398, 1377, 1303, 1178, 1082, 1051, 960, 912, 810; δ_H (300 MHz; $CDCl_3$) 7.52 (d, 2H, *J*=8.1 Hz, Ar–H), 7.25 (d, 2H, *J*=8.1 Hz, Ar–H), 6.10–5.80 (m, 3H, C=CH_2 and CH=C*H*CH$_3$), 5.69 (s, 1H, C*H*=CHCH$_3$), 2.36 (s, 3H, CH_3), 1.68 (d, 3H, *J*=5.5 Hz, CH_3); δ_C (75 MHz; $CDCl_3$) 151.1, 141.8, 140.2, 131.4, 129.9 (2C), 125.6, 123.5 (2C), 114.9, 21.4, 18.7; *m*/*z*, 207 (M+H$^+$, 100%), 189, 186, 183, 171, 165, 159, 157, 149, 143; HRMS found 207.0840 (M+H$^+$, $C_{12}H_{15}OS$ requires 207.0844).

4.1.7. (1R,2R*,6S*)-Methyl 2,6-dimethyl-4-tosylcyclohex-3-enecarboxylate (**9**).* $AlCl_3$ (9.53 g, 71.5 mmol), CH_2Cl_2 (70 mL) and methyl crotonate (7.6 mL, 71.5 mmol) were stirred under nitrogen until a homogeneous solution was formed. A solution of dienyl sulfone **3** (14.3 mmol) in CH_2Cl_2 (125 mL) was added over 5 min. The mixture was heated at reflux for 7 days, then cooled to 0 °C, quenched with sat NH_4Cl (50 mL) and extracted with CH_2Cl_2 (50 mL×3). The combined organic layers were washed with water and brine and dried over anhydrous $MgSO_4$. After removal of solvent under reduced pressure, the residue was purified by column chromatography (SiO_2, 25% EtOAc in hexanes) to give *cyclohexenyl sulfone* **9** (2.86 g, 8.86 mmol, 62%) as a colourless solid and *dimer* **4** (0.33 g, 0.74 mmol, 5%) as a colourless solid. Cyclohexenyl sulfone **9**: mp 95–96 °C; R_f=0.26 (25% ethyl acetate/hexane); ν_{max}/cm^{-1} 2954, 2931, 1732, 1651, 1597, 1454, 1435, 1371, 1300, 1220, 1145, 1089, 1010, 906, 815, 665; δ_H (500 MHz; $CDCl_3$) 7.70 (d, 2H, *J*=8.2 Hz, Ar–H), 7.31 (d, 2H, *J*=8.2 Hz, Ar–H), 6.92 (app.d, 1H, *J*=3.9 Hz, SO_2C=C*H*), 3.64 (s, 3H, OCH_3), 2.85–2.74 (m, 1H, C=CHC*H*CH$_3$), 2.42 (s, 3H, CH_3), 2.35 (app.t, 1H, *J*=6.1 Hz, C*H*CO$_2$CH$_3$), 2.33 (app.d, 1H, *J*=5.6 Hz, SO_2CC*H*H), 2.10–1.93 (m, 1H, CH$_2$C*H*CH$_3$), 1.73 (dddd, 1H, *J*=16.8, 9.6, 2.1, 2.1 Hz, SO_2CCH*H*), 0.98 (d, 3H, *J*=7.3 Hz, CH_3), 0.96 (d, 3H, *J*=6.5 Hz, CH_3); δ_C (75 MHz; $CDCl_3$) 173.3, 144.3, 140.4, 138.3, 136.1, 129.8 (2C), 128.0 (2C), 51.4, 49.2, 31.9, 30.3, 25.5, 21.6, 19.6, 16.1; *m*/*z*, 345 (M+Na$^+$, 100%) 323, 281, 139. Anal. Calcd for $C_{17}H_{22}O_4S$: C, 63.33; H, 6.88. Found: C, 63.12; H, 6.98.

4.1.8. (1S,2S*,6R*)-Methyl 2,6-dimethyl-4-(p-tolylsulfinyl) cyclohex-3-enecarboxylate (**10**).* $AlCl_3$ (2.21 g, 16.6 mmol), CH_2Cl_2 (32 mL) and methyl crotonate (3.5 mL, 33.2 mmol) were mixed and stirred under nitrogen until a homogeneous solution formed. A solution of dienyl sulfoxide **5** (0.69 g, 3.3 mmol) in CH_2Cl_2 (6.6 mL) was added and the mixture was heated at reflux for 10 days. The reaction was cooled to 0 °C, quenched with saturated aq NH_4Cl (30 mL) and extracted with CH_2Cl_2 (50 mL×3). The combined organic layers were washed with water and brine and dried over anhydrous $MgSO_4$. After removal of solvent under reduced pressure, the residue was purified by column chromatography (SiO_2, 50% EtOAc in hexanes) to give cyclohexenyl sulfoxide **10** (0.57 g, 1.85 mmol, 56%) as a colourless oil (3:1 mixture of two diastereoisomers); R_f=0.38 (50% ethyl acetate/hexane); ν_{max}/cm^{-1} 2956, 2927, 2874, 1733, 1453, 1433, 1216, 1158, 1082, 1044, 1014, 809, 620; δ_H (300 MHz; $CDCl_3$) 7.27 (d, 2H, *J*=8.0 Hz, Ar–H, major and minor), 7.10 (d, 2H, *J*=8.0 Hz, Ar–H, major and minor), 6.39 (app.s, 1H, SO_2C=C*H*, major and minor), 3.47 (s, 3H, OCH_3, minor), 3.46 (s, 3H, OCH_3, major), 2.72–2.50 (m, 1H, C=CHC*H*CH$_3$, major and minor), 2.25 (dd, 1H, *J*=10.1, 5.8 Hz, C*H*CO$_2$CH$_3$, major and minor), 2.21 (s, 3H, CO$_2$CH$_3$, major and minor), 1.93–1.66 (m, 2H, CH$_2$C*H*CH$_3$ and SO_2CC*H*H, major and minor), 1.42 (ddd, 1H, SO_2CCH*H*, major and minor), 0.84 (d, 3H, *J*=6.6 Hz, CH_3, minor), 0.82 (d, 3H, *J*=6.7 Hz, CH_3, major), 0.75 (d, 3H, *J*=6.7 Hz, CH_3, major), 0.74 (d, 3H, *J*=6.6 Hz, CH_3, minor); δ_C (75 MHz; $CDCl_3$) 173.54 (major), 173.48 (minor), 141.5 (major and minor), 141.4 (major and minor), 139.2 (major and minor), 136.5 (minor), 135.4 (major), 129.9 (2C) (major), 129.8 (2C) (minor), 125.0 (2C) (major), 124.8 (2C) (minor), 51.3 (major and minor), 50.4 (minor), 50.0 (major), 32.5 (minor), 32.0 (major), 27.9 (major), 26.8 (minor), 25.8 (major), 25.4 (minor), 21.4 (major and minor), 19.7 (major), 19.6 (minor), 16.6 (major), 16.5 (minor); *m*/*z*, 307

($M+H^+$, 100%), 306, 299, 295, 289, 284; HRMS found 307.1363 ($M+H^+$, $C_{17}H_{23}O_3S$ requires 307.1368).

4.1.9. ((1R,2R*,6S*)-2,6-Dimethyl-4-tosylcyclohex-3-enyl)methanol (**11**).* A solution of DIBAL in toluene (65.6 mL of a 1 M solution, 65.6 mmol) was added over 30 min to a solution of cyclohexenyl sulfone **9** (5.74 g, 18.7 mmol) in dry CH_2Cl_2 (95 mL) at −78 °C under nitrogen. The mixture was stirred for a further 3 h at −78 °C, then the reaction was quenched with a solution of Rochelle's salt (1.2 M aq potassium sodium tartrate, 50 mL). The viscous mixture was stirred vigorously for 1 h, allowed to stand until two clear phases formed. The reaction mixture was extracted with CH_2Cl_2 (3×50 mL). The combined organic layers were washed with water and brine and dried over anhydrous $MgSO_4$. After removal of solvent under reduced pressure, the residue was purified by column chromatography (SiO_2, 50% EtOAc in hexanes) to give *alcohol* **11** (5.30 g, 18.0 mmol, 96%) as a colourless solid; mp 104–105 °C; R_f=0.25 (50% ethyl acetate/hexane); ν_{max}/cm^{-1} 3441, 1643, 1595, 1300, 1286, 1273, 1149, 1105, 1082, 1004, 806, 669, 623; δ_H (400 MHz; $CDCl_3$) 7.70 (d, 2H, *J*=8.1 Hz, Ar–H), 7.30 (d, 2H, *J*=8.1 Hz, Ar–H), 6.94 (app.d, 1H, *J*=4.1 Hz, SO_2C=C*H*), 3.68 (dd, 1H, *J*=10.1, 6.1 Hz, C*H*HOH), 3.51 (dd, 1H, *J*=10.1, 10.1 Hz, CH*H*OH), 2.80–2.66 (m, 1H, C=CHC*H*CH_3), 2.42 (s, 3H, CH_3), 2.27 (app.d, 1H, *J*=12.2 Hz, SO_2CC*H*H), 1.85–1.67 (m, 2H, SO_2CCH*H* and CH_2C*H*CH_3), 1.63–1.46 (m, 1H, C*H*CH_2OH), 1.01 (d, 3H, *J*=7.3 Hz, CH_3), 0.87 (d, 3H, *J*=6.2 Hz, CH_3); δ_C (100 MHz; $CDCl_3$) 144.1, 142.4, 138.0, 136.3, 129.8 (2C), 127.9 (2C), 61.7, 43.6, 30.8, 30.7, 26.0, 21.6, 18.7, 14.5; *m*/*z*, 295 ($M+H^+$, 100%), 280, 279, 260, 255, 238, 204, 180, 167, 163, 150. Anal. Calcd for $C_{16}H_{22}O_3S$: C, 65.27; H, 7.53. Found: C, 65.33; H, 7.58.

4.1.10. t-Butyl(((1S,2S*,6R*)-2,6-dimethyl-4-tosylcyclohex-3-enyl)-methoxy) dimethylsilane (**12**).* A solution of *t*-butyldimethylsilyl chloride (0.42 g, 2.77 mmol) in THF (8 mL) was added dropwise to a solution of alcohol **11** (0.54 g, 1.85 mmol), 4-(dimethylamino)-pyridine (45.0 mg, 0.37 mmol) and triethylamine (0.36 mL, 2.59 mmol) in THF (9.0 mL) at 0 °C under nitrogen. The reaction mixture was stirred at 0 °C for 30 min, then allowed to warm up slowly to room temperature and stirred for an additional 20 h. The reaction mixture was quenched with NH_4Cl (15 mL) and extracted with Et_2O (20 mL×3). The combined organic layers were washed with water and brine and dried over anhydrous $MgSO_4$. The solvent was removed under reduced pressure, and the residue was purified by column chromatography (SiO_2, 25% EtOAc in hexanes) to give *silyl ether* **12** (0.69 g, 1.68 mmol, 91%) as a colourless solid; mp 70–72 °C; R_f=0.44 (25% ethyl acetate/hexane); ν_{max}/cm^{-1} 1641, 1597, 1467, 1454, 1377, 1300, 1290, 1149, 1112, 1083, 885, 837, 813, 775, 667, 619; δ_H (500 MHz; $CDCl_3$) 7.71 (d, 2H, *J*=8.1 Hz, Ar–H), 7.31 (d, 2H, *J*=8.1 Hz, Ar–H), 6.45 (app.d, 1H, *J*=4.3 Hz, SO_2C=C*H*), 3.58 (dd, 1H, J=9.9, 6.0 Hz, C*H*HOTBS), 3.45 (dd, 1H, *J*=9.9, 9.9 Hz, CH*H*OTBS), 2.75–2.63 (m, 1H, C=CHC*H*CH_3), 2.42 (s, 3H, Ar–CH_3), 2.26 (app.d, 1H, J=12.3 Hz, SO_2CC*H*H), 1.82–1.66 (m, 2H, SO_2CCH*H* and CH_2C*H*CH_3), 1.58–1.46 (m, 1H, C*H*CH_2OTBS), 0.99 (d, 3H, J=7.3 Hz, CH_3), 0.86 (d, 3H, J=8.6 Hz, CH_3), 0.85 (s, 9H, SiC$(CH_3)_3$), 0.00 (s, 3H, $SiCH_3$), 0.01 (s, 3H, $SiCH_3$); δ_C (100 MHz; $CDCl_3$) 144.0, 142.7, 138.0, 136.5, 129.7 (2C), 128.0 (2C), 61.8, 43.7, 31.1, 31.0, 25.82 (3C), 25.77, 21.6, 18.6, 18.1, 14.5, −5.4, −5.5; *m*/*z*; 431 ($M+Na^+$, 100%), 409, 389, 357, 339, 335, 279, 254, 233, 222, 206, 166, 140; HRMS found 431.2054 ($M+Na^+$, $C_{22}H_{36}O_3SSiNa$ requires 431.2052).

4.1.11. ((1R,6S*)-2,6-Dimethyl-4-tosylcyclohex-2-enyl)methanol (**13**).* Sodium hydroxide (2.27 g, 56.77 mmol) was added to a solution of alcohol **11** (2.39 g, 8.1 mmol) in MeOH (40 mL). The mixture was heated at reflux for 7 h, then cooled to room temperature, neutralised with 2 M HCl and extracted with CH_2Cl_2 (50 mL×3). The combined organic layers were washed with water and brine and dried over anhydrous $MgSO_4$. After removal of solvent under reduced pressure, the residue was purified by column chromatography (SiO_2, 50% EtOAc in hexanes) to give *cyclohexenyl sulfone* **13** (2.28 g, 7.74 mmol, 95%) as a yellow oil; R_f=0.25 (50% ethyl acetate/hexane); ν_{max}/cm^{-1} 3435, 3419, 3020, 2958, 1637, 1597, 1448, 1379, 1286, 1217, 1143, 1085, 754, 665; δ_H (400 MHz; $CDCl_3$) 7.66 (d, 2H, *J*=8.2 Hz, Ar–H), 7.28 (d, 2H, *J*=8.2 Hz, Ar–H), 5.53 (br s, 1H, C*H*=CCH_3), 3.66 (br s, 1H, SO_2C*H*), 3.53 (dd, 1H, *J*=11.1, 3.2 Hz, C*H*HOH), 3.33 (dd, 1H, *J*=11.1, 6.8 Hz, CH*H*OH), 2.38 (s, 3H, CH_3), 2.25 (br s, 1H, OH), 2.22–2.14 (m, 1H, C*H*CH_3), 1.92 (ddd, 1H, *J*=13.4, 8.0, 4.4 Hz, SO_2CHC*H*H), 1.77 (br s, 1H, C*H*CH_2OH), 1.72 (s, 3H, CH_3), 1.52 (ddd, 1H, *J*=13.4, 6.7, 6.7 Hz, SO_2CHCH*H*), 0.86 (d, 3H, *J*=6.9 Hz, CH_3); δ_C (100 MHz; $CDCl_3$) 144.7, 141.9, 134.3, 129.6 (2C), 129.0 (2C), 115.0, 62.7, 60.7, 48.5, 26.7, 26.1, 23.0, 21.6, 19.6; *m*/*z*, 317 ($M+Na^+$, 100%), 295, 157; HRMS found 317.1183 ($M+Na^+$, $C_{16}H_{22}O_3SNa$ requires 317.1187).

4.1.12. t-Butyl(((1R,6S*)-2,6-dimethyl-4-tosylcyclohex-2-enyl)methoxy) dimethylsilane (**14**).* A solution of *t*-butyldimethylsilyl chloride (0.81 g, 5.4 mmol) in THF (6.7 mL) was added dropwise to a solution of alcohol **13** (0.66 g, 2.2 mmol), triethylamine (0.48 mL, 3.34 mmol) and 4-(dimethylamino)pyridine (0.03 g, 0.22 mmol) in THF (6.7 mL) at 0 °C. The mixture was allowed to warm slowly to room temperature and stirred for an additional 20 h. The reaction mixture was quenched with saturated aq NH_4Cl (15 mL) and extracted with Et_2O (25 mL×3). The combined organic layers were washed with water and brine and dried over anhydrous $MgSO_4$. After removal of solvent under reduced pressure, the residue was purified by column chromatography (SiO_2, 25% EtOAc in hexanes) to give *silyl ether* **14** (0.84 g, 2.06 mmol, 92%) as a colourless solid; mp 62–64 °C; R_f=0.44 (25% ethyl acetate/hexane); ν_{max}/cm^{-1} 1286, 1255, 1220, 1126, 1083, 879, 837, 812, 773, 673, 599, 574, 557, 511; δ_H (500 MHz; $CDCl_3$) 7.71 (d, 2H, *J*=8.1 Hz, Ar–H, minor), 7.68 (d, 2H, *J*=8.1 Hz, Ar–H, major), 7.31 (d, 2H, *J*=8.1 Hz, Ar–H, minor), 7.30 (d, 2H, *J*=8.1 Hz, Ar–H, major), 5.64 (br s, 1H, C*H*=CCH_3, minor), 5.58 (br s, 1H, C*H*=CCH_3, major), 3.74 (dd, 1H, *J*=11.3, 2.7 Hz, SO_2CH, major), 3.62 (dd, 1H, *J*=10.4, 2.7 Hz, SO_2CH, minor), 3.39 (dd, 1H, *J*=9.9, 4.4 Hz, C*H*HOTBS, major and minor), 2.85 (dd, 1H, *J*=9.9, 9.9 Hz, CH*H*OTBS, major and minor), 2.41 (s, 3H, CH_3, minor), 2.40 (s, 3H, CH_3, major), 2.23–2.12 (m, 1H, C*H*CH_3, major and minor), 1.83–1.50 (m, 3H, SO_2C*H* and SO_2CHC*H*$_2$, major and minor), 1.72 (s, 3H, CH_3, major and minor), 0.95 (d, 3H, *J*=6.6 Hz, CH_3, minor), 0.85 (d, 3H, *J*=7.1 Hz, CH_3, major), 0.82 (s, 9H, SiC$(CH_3)_3$, major), 0.80 (s, 9H, SiC$(CH_3)_3$, minor), −0.03 (s, 6H, Si$(CH_3)_2$, minor), −0.06 (s, 6H, Si$(CH_3)_2$, major); δ_C (100 MHz; $CDCl_3$) 144.4, 141.0, 133.8, 129.6, 129.4 (2C), 129.1, 114.4, 64.0, 60.6, 48.5, 28.5, 25.9 (2C), 25.8, 24.1, 23.7, 21.6, 18.6, 18.2, −5.4, −5.5; *m*/*z*, 431 ($M+Na^+$, 100%), 409, 271, 209; HRMS found 431.2048 ($M+Na^+$, $C_{22}H_{36}O_3SSiNa$ requires 431.2052).

4.1.13. (4R,5S*)-4-((t-Butyldimethylsilyloxy)methyl)-3,5-dimethylcyclohex-2-enone (**15**).* A solution of lithium diisopropylamide [prepared by reacting diisopropylamine (5.05 mL, 28.0 mmol) in THF (50 mL) with *n*-BuLi (1.6 M in hexane, 17.5 mL, 28.0 mmol) at −78 °C for 30 min] was added dropwise to a suspension of sulfone **14** (1.91 g, 4.67 mmol) and MoOPD (6.72 g, 17.5 mmol) in THF (55 mL) at −78 °C under nitrogen. The mixture was stirred at −78 °C for 3 h, then quenched with 2 M HCl (30 mL), and extracted with Et_2O (3×75 mL). The combined organic layers were washed with water and brine and dried over anhydrous $MgSO_4$. After removal of solvent under reduced pressure, the residue was purified by column chromatography (SiO_2, 25% EtOAc in hexanes) to give *enone* **15** (1.06 g, 3.94 mmol, 84%) as a colourless oil; R_f=0.43 (25% ethyl acetate/hexane); ν_{max}/cm^{-1} 2954, 2927, 1647, 1629, 1460, 1438, 1375, 1300, 1251, 1105, 1004, 991, 835, 775; δ_H (500 MHz; $CDCl_3$) 5.91 (s, 1H, C=CH), 3.80 (app.d, 1H, *J*=1.3 Hz, C*H*HOTBS), 3.79 (app.d, 1H, *J*=2.5 Hz, CH*H*OTBS), 2.60 (dd, 1H, *J*=16.9, 5.1 Hz,

COC*H*H), 2.48–2.35 (m, 1H, C*H*CH$_3$), 2.17–2.06 (m, 2H, COCH*H* and C*H*CH$_2$OTBS), 1.99 (s, 3H, CH$_3$), 1.05 (d, 3H, *J*=7.0 Hz, CH$_3$), 0.87 (s, 9H, SiC(CH$_3$)$_3$), 0.052 (s, 3H, SiCH$_3$), 0.050 (s, 3H, SiCH$_3$); δ_C (125 MHz; $CDCl_3$) 199.2, 161.1, 127.8, 62.7, 49.8, 41.9, 30.2, 25.8 (3C), 23.5, 20.0, 18.2, −5.49, −5.52; *m*/*z*, 269 (M+H$^+$, 100%), 268, 239, 223, 185, 137, 107; HRMS found 269.1934. (M+H$^+$, $C_{15}H_{29}O_2Si$ requires 269.1937).

4.1.14. (4R,5S*)-4-((t-Butyldimethylsilyloxy)methyl)-3,5-dimethylcyclohex-2-enol (**17**).* Sodium borohydride (0.67 g, 17.75 mmol) was added portionwise to a solution of $CeCl_3 \cdot 7H_2O$ (1.98 g, 5.33 mmol) and enone **15** (0.95 g, 3.55 mmol) in methanol (50 mL) at −78 °C under nitrogen. The temperature was allowed to increase slowly to −40 °C. Stirring was continued at this temperature for an additional 15 h. The reaction mixture was then quenched with saturated aq NH_4Cl solution (20 mL). HCl (aq, 2 M) was added until the reaction mixture became clear, and it was extracted with Et_2O (3×75 mL). The combined organic layers were washed with water and brine and dried over anhydrous $MgSO_4$. After removal of solvent under reduced pressure, the residue was purified by column chromatography (SiO_2, 25% EtOAc in hexanes) to give *alcohol* **17** (0.87 g, 3.23 mmol, 91%) as a colourless oil (95:5 mixture of diastereoisomers); R_f=0.25 (25% ethyl acetate/hexane); ν_{max}/cm^{-1} 3348, 3331, 2954, 2927, 2856, 1718, 1664, 1469, 1462, 1384, 1361, 1253, 1112, 1095, 1029, 987, 875, 837, 773; δ_H (300 MHz; $CDCl_3$) 5.51 (s, 1H, C=CH), 4.18 (br s, 1H C*H*OH), 3.71 (dd, 1H, *J*=6.1, 2.3 Hz, C*H*HOTBS), 3.65 (dd, 1H, *J*=6.1, 1.9 Hz, CH*H*OTBS), 2.02–1.94 (m, 1H, C*H*HCHCH$_3$), 1.91–1.80 (m, 1H, CHCH$_3$), 1.72 (s, 3H, CH$_3$), 1.68 (br d, 1H, *J*=3.9 Hz, C*H*CH$_2$OTBS), 1.40 (br s, 1H, OH), 1.28–1.18 (m, 1H, CH*H*CHCH$_3$), 1.03 (d, 3H, *J*=4.0 Hz, CH$_3$), 0.86 (s, 9H, SiC(CH$_3$)$_3$), 0.02 (s, 6H, Si(CH$_3$)$_2$); δ_C (125 MHz; $CDCl_3$) 137.0, 128.5, 67.3, 61.1, 49.2, 40.5, 27.8, 25.8 (3C), 21.5, 20.5, 18.2, −5.5 (2C); *m*/*z*, 293 (M+Na$^+$, 100%), 269, 253, 251, 247, 239, 236, 228, 222, 217, 212, 207, 192; HRMS found 293.1917 (M+Na$^+$, $C_{15}H_{30}O_2SiNa$ requires 293.1913).

4.1.15. 2-((1R,5S*,6R*)-6-((t-Butyldimethylsilyloxy)methyl)-1,5-dimethylcyclohex-2-enyl)-N,N-dimethylacetamide (**18**).* Allylic alcohol **17** (3.93 g, 14.5 mmol) and *N*,*N*-dimethylacetamide dimethyl acetal (4.25 mL, 29.07 mmol) were heated by microwave irradiation employing 150 °C, 150 W and a pressure of 150 psi for 1 h. The volatiles were evaporated and the residue was purified by column chromatography (SiO_2, 25% EtOAc in hexanes) to give *amide* **18** (2.28 g, 6.73 mmol, 46%, 49% conversion from dr96:4) as a colourless solid; mp 65–67 °C; R_f=0.30 (25% ethyl acetate/hexane); ν_{max}/cm^{-1} 1653, 1620, 1307, 1253, 1193, 1105, 1058, 991, 862, 837, 773, 719; δ_H (500 MHz; $CDCl_3$) 5.61 (ddd, 1H, *J*=10.0, 5.2, 1.5 Hz, C*H*=CH), 5.53 (d, 1H, *J*=10.0 Hz, CH=C*H*), 3.83 (dd, 1H, *J*=10.8, 3.5 Hz, C*H*HOTBS), 3.77 (dd, 1H, *J*=10.8, 5.5 Hz, CH*H*OTBS), 3.04 (s, 3H, NCH$_3$), 2.95 (s, 3H, NCH$_3$), 2.54 (s, 2H, C*H*$_2$N(CH$_3$)$_3$), 2.10–1.95 (m, 1H, CH=CHC*H*H), 1.88–1.73 (m, 2H, CH=CHCH*H* and C*H*CH$_3$), 1.72–1.63 (m, 1H, C*H*CH$_2$OTBS), 1.10 (s, 3H, CH$_3$), 1.01 (d, 3H, *J*=6.0 Hz, CH$_3$), 0.91 (s, 9H, SiC(CH$_3$)$_3$), 0.073 (s, 3H, SiCH$_3$), 0.069 (s, 3H, SiCH$_3$); δ_C (75 MHz; $CDCl_3$) 171.7, 136.1, 124.3, 61.6, 48.9, 43.5, 39.1, 38.3, 35.4, 35.1, 27.3, 25.9 (3C), 23.9, 19.8, 18.1, −5.6, −5.7; *m*/*z*, 340 (M+H$^+$, 100%), 328, 317, 295, 279, 264, 246, 237, 223, 209, 208, 195, 181; HRMS found 340.2675 (M+H$^+$, $C_{19}H_{38}NO_2Si$ requires 340.2672).

4.1.16. (3aS,4R*,5S*,7S*,7aS*)-4-((t-Butyldimethylsilyloxy)methyl)-7-iodo-3a,5-dimethylhexahydrobenzofuran-2(3H)-one (**19**).* Iodine (1.22 g, 4.81 mmol) was added to a solution of amide **18** (0.82 g, 2.40 mmol) in THF–H_2O (9.6 mL: 9.6 mL) at 0 °C. The mixture was allowed to warm slowly to room temperature and stirred for an additional 30 h, then the reaction was quenched with saturated aq $Na_2S_2O_3$ solution until the mixture became colourless. The mixture was extracted with Et_2O (3×20 mL), and the combined organic layers were washed with water and brine and dried over anhydrous $MgSO_4$. After removal of solvent under reduced pressure, the residue was purified by column chromatography (SiO_2, 25% EtOAc in hexanes) to give *iodide* **19** (0.98 g, 2.23 mmol, 93%) as a colourless solid and *iodide* **21** (0.01 g, 0.02 mmol, 1%) as a yellow oil. *Iodide* **19**: mp 77–79 °C; R_f=0.57 (25% ethyl acetate/hexane); ν_{max}/cm^{-1} 3020, 2954, 2927, 1784, 1637, 1462, 1388, 1327, 1257, 1215, 1195, 1143, 1097, 993, 837, 756; δ_H (500 MHz; $CDCl_3$) 4.66 (d, 1H, *J*=2.8 Hz, CHI), 4.53 (s, 1H, CHO), 3.81 (dd, 1H, *J*=10.6, 3.7 Hz, C*H*HOTBS), 3.67 (dd, 1H, *J*=10.6, 7.6 Hz, CH*H*OTBS), 2.97 (d, 1H, *J*=7.2 Hz, C*H*HCO), 2.37 (d, 1H, *J*=7.2 Hz, CH*H*CO), 2.08–1.93 (m, 2H, CHCH$_3$ and CHIC*H*H), 1.92–1.77 (m, 1H, CHICH*H*), 1.50 (s, 3H, CH$_3$), 1.41–1.27 (m, 1H, C*H*CH$_2$OTBS), 1.02 (d, 3H, *J*=6.3 Hz, CH$_3$), 0.92 (s, 9H, SiC(CH$_3$)$_3$), 0.08 (s, 6H, Si(CH$_3$)$_2$); δ_C (75 MHz; $CDCl_3$) 174.6, 88.6, 61.6, 47.1, 45.4, 42.7, 39.7, 26.1, 25.9 (3C), 22.1, 21.9, 19.3, 18.1, −5.6, −5.8; *m*/*z*, 461 (M+Na$^+$, 100%), 439, 414, 413, 403, 393, 344, 330, 275, 257, 223, 209, 180; HRMS found 461.0990 (M+Na$^+$, $C_{17}H_{31}O_3SiINa$ requires 461.0985).

4.1.17. (3aS,4R*,5S*,7aR*)-4-((t-Butyldimethylsilyloxy)methyl)-3a,5-dimethyl-3,3a,4,5-tetrahydrobenzofuran-2(7aH)-one (**22**).* DBU (0.92 mL, 6.2 mmol) was added to a solution of iodide **19** (0.68 g, 1.55 mmol) in THF (7.8 mL) under nitrogen. The mixture was heated at reflux for 2 h, then the reaction was quenched with saturated aq NH_4Cl (5 mL) and extracted with Et_2O (3×10 mL). The combined organic layers were washed with water and brine and dried over anhydrous $MgSO_4$. After removal of solvent under reduced pressure, the residue was purified by column chromatography (SiO_2, 25% EtOAc in hexanes) to give *cyclohexene* **22** (0.45 g, 1.45 mmol, 94%) as a colourless solid; mp 97–98 °C; R_f=0.49 (25% ethyl acetate/hexane); ν_{max}/cm^{-1} 2956, 2927, 2881, 2854, 1762, 1745, 1460, 1384, 1249, 1222, 1197, 1170, 1126, 993, 833, 773; δ_H (400 MHz; $CDCl_3$) 5.91 (d, 1H, *J*=10.0 Hz, C*H*=CH), 5.79 (ddd, 1H, *J*=10.0, 4.6, 2.5 Hz, CH=C*H*), 4.28 (d, 1H, *J*=4.6 Hz, CHO), 3.79 (dd, 1H, *J*=11.3, 3.3 Hz, C*H*HOTBS), 3.75 (dd, 1H, *J*=11.3, 5.5 Hz, CH*H*OTBS), 2.96 (d, 1H, *J*=17.4 Hz, C*H*HCO), 2.39 (d, 1H, *J*=17.4 Hz, CH*H*CO), 2.32–2.18 (m, 1H, C*H*CH$_3$), 1.37–1.23 (m, 1H, C*H*CH$_2$OTBS), 1.11 (s, 3H, CH$_3$), 1.10 (d, 3H, *J*=6.0 Hz, CH$_3$), 0.89 (s, 9H, SiC(CH$_3$)$_3$), 0.06 (s, 6H, Si(CH$_3$)$_2$); δ_C (100 MHz; $CDCl_3$) 176.0, 141.0, 119.3, 82.5, 61.1, 44.3, 43.0, 41.2, 29.1, 25.8 (3C), 19.4, 18.9, 18.1, −5.6, −5.7; *m*/*z*, 333 (M+Na$^+$, 100%), 311, 310, 295, 276, 231, 223, 210, 187, 177, 159, 150; HRMS found 333.1853 (M+Na$^+$, $C_{17}H_{30}O_3SiNa$ requires 333.1862).

4.1.18. (3S,3aR*,4R*,5S*,7aR*)-4-((t-Butyldimethylsilyloxy)methyl)-3-hydroxy-3a,5-dimethyl-3,3a,4,5-tetrahydrobenzofuran-2(7aH)-one (**23**).* Lithium bis(trimethylsilyl)amide (1.32 mL of a 1 M solution in THF, 1.32 mmol) was added to a suspension of lactone **22** (0.20 g, 0.66 mmol) and MoOPD (0.50 g, 1.32 mmol) in THF (6.5 mL) at −78 °C under nitrogen. The mixture was allowed to warm slowly to −40 °C and stirring was continued for 30 min at this temperature. The mixture was allowed to warm to −10 °C and stirring was continued for 18 h at this temperature. The mixture was quenched with saturated aq NH_4Cl solution, and extracted with Et_2O (3×20 mL). The combined organic layers were washed with water and brine and dried over anhydrous $MgSO_4$. After removal of solvent under reduced pressure, the residue was purified by column chromatography (SiO_2, 25% EtOAc in hexanes) to give *hydroxylactone* **23** (0.17 g, 0.52 mmol, 79%) as a colourless solid; mp 96–98 °C; R_f=0.59 (50% ethyl acetate/hexane); ν_{max}/cm^{-1} 3400, 2954, 2929, 1759, 1666, 1512, 1462, 1359, 1251, 1215, 1116, 991, 835, 752; δ_H (500 MHz; $CDCl_3$) 5.86 (dd, 1H, *J*=10.1, 2.0 Hz, C*H*=CH), 5.72 (ddd, 1H, *J*=10.1, 2.9, 2.9 Hz, CH=C*H*), 4.62 (app.s, 1H, CHOCO), 4.44 (d, 1H, *J*=3.5 Hz, C*H*OH), 3.81 (dd, 1H, *J*=10.5, 3.5 Hz, C*H*HOTBS), 3.66 (dd, 1H, *J*=10.5, 4.5 Hz, CH*H*OTBS), 2.72 (d, 1H, *J*=3.5 Hz, CHO*H*), 2.37–2.22 (m, 1H, C*H*CH$_3$), 1.49 (app.q, 1H, *J*=4.5 Hz, C*H*CH$_2$OTBS), 1.17 (d, 3H, *J*=7.4 Hz, CH$_3$), 1.12 (s, 3H, CH$_3$), 0.87 (s, 9H, SiC(CH$_3$)$_3$), 0.05 (s, 3H, SiCH$_3$), 0.04 (s, 3H, SiCH$_3$); δ_C (100 MHz; $CDCl_3$) 176.6,

138.3, 120.6, 81.0, 74.3, 63.7, 43.9, 43.7, 31.6, 25.8 (3C), 21.0, 18.1, 14.8, −5.6, −5.7; *m*/*z*, 349 (M+Na^+, 100%), 327, 323, 311, 280, 251, 240, 224, 195, 177, 159, 149, 131; HRMS found 349.1810 (M+Na^+, $C_{17}H_{30}O_4SiNa$ requires 349.1811).

4.1.19. (3aS,4R*,5S*,7aR*)-4-((t-Butyldimethylsilyloxy)methyl)-3a,5-dimethyl-4,5-dihydrobenzofuran-2,3(3aH,7aH)-dione (**25**).* 2-Iodoxybenzoic acid (0.18 g, 0.63 mmol) was added to a solution of hydroxylactone **23** (17.9 mg, 0.055 mmol) in DMSO (1 mL) at room temperature. The mixture was stirred at room temperature for 4 days, then the reaction mixture was diluted with saturated $NaHCO_3$ solution (10 mL), and extracted with Et_2O (3×15 mL). The combined organic layers were washed with water and brine and dried over anhydrous $MgSO_4$. After removal of solvent under reduced pressure, the residue was purified by column chromatography (SiO_2, 25% EtOAc in hexanes) to give *ketone* **25** (15.0 mg, 0.046 mmol, 84%) as a colourless solid; mp 74–75 °C; R_f=0.61 (25% ethyl acetate/hexane); ν_{max}/cm^{-1} 2955, 2929, 2884, 2857, 1787, 1461, 1249, 1110, 990, 952, 909, 832, 775, 675; δ_H (300 MHz; $CDCl_3$) 6.06 (dd, 1H, *J*=10.1, 1.5 Hz, C*H*═CH), 5.90 (ddd, 1H, *J*=10.1, 4.3, 2.5 Hz, CH═C*H*), 4.59 (d, 1H, *J*=4.3 Hz, CHOCO), 3.69 (dd, 1H, *J*=11.3, 3.5 Hz, C*H*HOTBS), 3.65 (dd, 1H, *J*=11.3, 3.0 Hz, CH*H*OTBS), 2.60–2.40 (m, 1H, C*H*CH_3), 1.43 (ddd, 1H, *J*=9.3, 3.5, 3.3 Hz, C*H*CH_2OTBS), 1.24 (s, 3H, CH_3), 1.13 (d, 3H, *J*=7.1 Hz, CHC*H*$_3$), 0.88 (s, 9H, $SiC(CH_3)_3$), 0.08 (s, 3H, $SiCH_3$), 0.04 (s, 3H, $SiCH_3$); δ_C (125 MHz; $CDCl_3$) 197.9, 160.8, 142.1, 119.0, 79.2, 58.7, 48.3, 41.1, 28.5, 25.8 (3C), 19.0, 18.1, 13.7, −5.7, −5.8; *m*/*z*, 347 (M+Na^+, 100%), 325, 324, 311, 306, 298, 280, 278, 266, 261, 257, 242, 238; HRMS found 347.1651 (M+Na^+, $C_{17}H_{28}O_4SiNa$ requires 347.1655).

4.1.20. (3R,3aS*,4S*,5R*,7aS*)-4-((t-Butyldimethylsilyloxy)methyl)-3-hydroxy-3a,5-dimethyl-3,3a,4,5-tetrahydrobenzofuran-2(7aH)-one (**26**).* Sodium borohydride (93 mg, 2.46 mmol) was added portionwise to a solution of ketone **25** (0.16 g, 0.49 mmol) in methanol (5 mL) at −78 °C. The temperature was allowed to rise gradually to 0 °C and the mixture was stirred at this temperature for an additional 2 h, then quenched with saturated aq NH_4Cl solution, and extracted with Et_2O (3×20 mL). The combined organic layers were washed with water and brine and dried over anhydrous $MgSO_4$. After removal of solvent under reduced pressure, the residue was purified by column chromatography (SiO_2, 25% EtOAc in hexanes) to give *hydroxylactone* **26** (0.16 g, 0.48 mmol, 98%) as a colourless solid; mp 92–94 °C; R_f=0.26 (50% ethyl acetate/hexane); ν_{max}/cm^{-1} 3381, 3305, 3018, 2956, 2929, 2883, 2856, 1774, 1462, 1255, 1215, 1141, 958, 835, 756; δ_H (300 MHz; $CDCl_3$) 5.91 (dd, 1H, *J*=9.9, 1.9 Hz, C*H*═CH), 5.81 (ddd, 1H, *J*=9.9, 5.1, 2.3 Hz, CH═C*H*), 5.73 (app.d, 1H, *J*=10.0 Hz, OH), 4.23–4.12 (m, 2H, C*H*OCO and C*H*OH), 3.82 (dd, 1H, *J*=11.3, 1.8 Hz, C*H*HOTBS), 3.74 (dd, 1H, *J*=11.3, 7.7 Hz, CH*H*OTBS), 2.05–1.87 (m, 1H, C*H*CH_3), 1.42 (ddd, 1H, *J*=10.0, 7.7, 1.8 Hz, C*H*CH_2OTBS), 1.15 (s, 3H, CH_3), 1.13 (d, 3H, *J*=7.0 Hz, CH_3), 0.91 (s, 9H, $SiC(CH_3)_3$), 0.11 (s, 6H, $Si(CH_3)_2$); δ_C (125 MHz; $CDCl_3$) 175.6, 141.0, 118.9, 79.4, 77.1, 61.0, 45.2, 44.4, 29.7, 25.7 (3C), 19.9, 18.1, 15.9, −5.4, −5.6; *m*/*z*, 349 (M+Na^+, 100%), 326, 311, 279, 274, 256, 240, 220, 213, 200, 180, 177; HRMS 349.1814 (M+Na^+, $C_{17}H_{30}O_4SiNa$ requires 349.1811).

4.1.21. (R)-1-((1R*,2S*,5R*,6S*)-6-((t-Butyldimethylsilyloxy)methyl)-2-hydroxy-1,5-dimethylcyclohex-3-enyl)ethane-1,2-diol (**27**).* A solution of hydroxylactone **26** (30.8 mg, 0.09 mmol) in THF (1 mL) was slowly added to a suspension of $LiAlH_4$ (10.7 mg, 0.28 mmol) in THF (0.5 mL) at 80 °C under nitrogen. After heating at reflux for 2 h, the reaction mixture was cooled to 0 °C, and quenched with saturated aq NH_4Cl (3 mL) and water (5 mL) and stirred for an additional 5 min. The insoluble materials were removed by filtration through Celite, washing with THF, and the filtrate was extracted with Et_2O (3×10 mL). The combined organic layers were washed with water and brine and dried over anhydrous $MgSO_4$. After removal of solvent under reduced pressure, the residue was purified by column chromatography (SiO_2, 50% EtOAc in hexanes) to give *triol* **27** as a colourless solid (23.9 mg, 0.07 mmol, 77%); mp 118–120 °C; R_f=0.21 (50% ethyl acetate/hexane); ν_{max}/cm^{-1} 3368, 2955, 2928, 2884, 2857, 1461, 1253, 1103, 1066, 1026, 995, 864, 834, 774; δ_H (300 MHz; $CDCl_3$) 5.73 (ddd, 1H, *J*=9.8, 5.4, 1.8 Hz, C*H*═CH), 5.65 (dd, 1H, *J*=9.8, 1.9 Hz, CH═C*H*), 4.58 (app.d, 1H, *J*=5.1 Hz, C*H*OH-CH_2OH), 4.12 (br s, 1H, OH), 3.97–3.65 (m, 6H, C*H*$_2$OH, C*H*$_2$OTBS, C*H*OH, OH), 2.47 (br s, 1H, OH), 2.10–1.87 (m, 2H, C*H*CH_3, C*H*CH_2OTBS), 1.14 (d, 3H, *J*=6.5 Hz, CHC*H*$_3$), 0.90 (s, 9H, $SiC(CH_3)_3$), 0.76 (s, 3H, CH_3), 0.111 (s, 3H, $SiCH_3$), 0.106 (s, 3H, $SiCH_3$); δ_C (125 MHz; $CDCl_3$) 136.3, 125.8, 78.3, 71.3, 62.3, 61.2, 42.4, 40.8, 30.6, 25.8 (3C), 19.6, 18.1, 16.3, −5.58, −5.63; *m*/*z*, 353 (M+Na^+, 100%), 314, 313, 306, 299, 294; HRMS 353.2129 (M+Na^+, $C_{17}H_{34}O_4SiNa$ requires 353.2124).

4.1.22. (R)-2-((1R*,2S*,5R*,6S*)-6-((t-Butyldimethylsilyloxy)methyl)-2-hydroxy-1,5-dimethyl-cyclohex-3-enyl)-2-hydroxyethyl 4-methylbenzenesulfonate (**28**).* Triethylamine (0.04 mL, 0.31 mmol) was added to a solution of triol **27** (92.5 mg, 0.28 mmol), 4-(dimethylamino)pyridine (7 mg, 0.06 mmol) and *p*-TsCl (80 mg, 0.42 mmol) in CH_2Cl_2 (2.8 mL) at 0 °C under nitrogen. The reaction mixture was allowed to warm slowly to room temperature (5 h). The mixture was diluted with saturated aq NH_4Cl (5 mL) and water (10 mL), and extracted with CH_2Cl_2 (3×10 mL). The combined organic layers were washed with water and brine and dried over anhydrous Na_2SO_4. After removal of solvent under reduced pressure, the residue was purified by column chromatography (SiO_2, 25% EtOAc in hexanes) to give *tosylate* **28** as a colourless oil (67.8 mg, 50%) and *tetrahydrofuran* **29** (18.8 mg, 21%) as a colourless solid. *Tosylate* **28**: R_f=0.57 (25% ethyl acetate/hexane); ν_{max}/cm^{-1} 3369, 2962, 2926, 2879, 1457, 1357, 1174, 1033, 1009, 970, 814, 682, 665, 553; δ_H (500 MHz; $CDCl_3$) 7.81 (d, 2H, *J*=8.2 Hz, Ar–H), 7.33 (d, 2H, *J*=8.2 Hz, Ar–H), 5.76–5.60 (m, 2H, C*H*═C*H*), 4.46 (dd, 1H, *J*=10.6, 2.1 Hz, C*H*HOTs), 4.28 (dd, 1H, *J*=10.6, 8.1 Hz, CH*H*OTs), 3.96 (dd, 1H, *J*=8.1, 2.1 Hz, C*H*OHCH$_2$OTs), 3.77 (app.d, 1H, *J*=10.8 Hz, C*H*HOTBS), 3.73 (app.d, 1H, *J*=5.2 Hz, CH═CHC*H*OH), 3.69 (dd, 1H, *J*=10.8, 6.6 Hz, CH*H*OTBS), 2.44 (s, 3H, Ar–CH_3), 2.08–1.88 (m, 2H, C*H*CH_3 and C*H*CH_2OTBS), 1.11 (d, 3H, *J*=6.4 Hz, CHC*H*$_3$), 0.89 (s, 9H, $SiC(CH_3)_3$), 0.77 (s, 3H, CH_3), 0.09 (s, 6H, $Si(CH_3)_2$); δ_C (75 MHz; $CDCl_3$), 144.7, 138.7, 134.3, 129.9 (2C), 127.7 (2C), 121.2, 86.5, 79.7, 71.6, 61.6, 47.1, 44.8, 30.5, 25.8 (3C), 21.7, 19.6, 18.1, 12.1, −5.5, −5.6; *m*/*z*, 507 (M+Na^+, 100%), 485; HRMS 507.2223 (M+Na^+, $C_{24}H_{40}O_6SiSNa$ requires 507.2213).

4.1.23. (1S,4R*,5S*,6R*)-5-((t-Butyldimethylsilyloxy)methyl)–1-hydroxy-2-iodoethyl)-4,6-dimethylcyclohex-2-enol (**30**).* Imidazole (15 mg, 0.21 mmol) followed by a solution of triphenylphosphine (19 mg, 0.07 mmol) in CH_2Cl_2 was slowly added to a solution of triol **27** (21.2 mg, 0.064 mmol) in CH_2Cl_2 (0.5 mL) at −30 °C under nitrogen. A solution of iodine (18 mg, 0.07 mmol) in CH_2Cl_2 (0.5 mL) was added dropwise to the stirred reaction mixture. The mixture was stirred at this temperature for 2 h, then quenched with saturated aq $Na_2S_2O_3$ (5 mL) and extracted with CH_2Cl_2 (3×10 mL). The combined organic layers were washed with water and brine and dried over anhydrous $Na_2S_2O_4$. After removal of solvent under reduced pressure, the residue was purified by column chromatography (SiO_2, 25% EtOAc in hexanes) to give *iodide* **30** (18.9 mg, 0.043 mmol, 67%) as a colourless oil and *tetrahydrofuran* **29** (3.1 mg, 0.01 mmol, 15%) as a colourless solid. *Iodide* **30**: R_f=0.27 (25% ethyl acetate/hexane); ν_{max}/cm^{-1} 3387, 2922, 2851, 1448, 1416, 1374, 1259, 1092, 1031, 987, 892, 838, 578, 553; δ_H (300 MHz; $CDCl_3$) 5.75 (ddd, 1H, *J*=9.8, 5.4, 2.0 Hz, C*H*═CH), 5.71 (dd, 1H, *J*=9.8, 2.0 Hz, CH═C*H*), 4.68 (br s, 1H, OH), 4.45 (br s, 1H, OH), 4.05 (dd, 1H, *J*=9.5, 4.5 Hz, C*H*HI), 3.96 (dd, 1H, *J*=8.2, 4.5 Hz, C*H*HOTBS), 3.84–3.56 (m,

4H, *CH*OH, *CH*OHCH$_2$I, CH*H*I and CH*H*OTBS), 1.90–1.79 (m, 1H, *CH*CH$_2$OTBS), 1.72 (app.d, 1H, *J*=7.1 Hz, *CH*CH$_3$), 1.13 (d, 3H, *J*=7.1 Hz, CHC*H*$_3$), 0.92 (s, 9H, SiC(CH$_3$)$_3$), 0.82 (s, 3H, CH$_3$), 0.11 (s, 6H, Si(CH$_3$)$_2$); δ_C (125 MHz; CDCl$_3$) 137.8, 116.2, 75.3, 70.3, 63.0, 47.4, 42.1, 30.6, 29.7, 25.9 (3C), 19.9, 18.2, 12.0, −5.3, −5.4; *m*/*z*, 441 (M+H$^+$, 100%), 428, 427, 390, 312, 294, 277, 251, 212, 180, 162, 146; HRMS 441.1326 (M+H$^+$, $C_{17}H_{34}O_3SiI$ requires 441.1322).

4.1.24. (1S,4R*,5S*,6S*)-5-((t-Butyldimethylsilyloxy)methyl)-6-((S*)-1-hydroxy-4-methylpent-4-enyl)-4,6-dimethylcyclohex-2-enol (**31**).* Methallyltri-*n*-butyltin (0.42 g, 0.12 mmol) was added to a solution of **30** (13.2 mg, 0.30 mmol) and 1,1′-azobis(cyclohexanecarbonitrile) (3.0 mg, 0.009 mmol) in benzene (1 mL) at room temperature under nitrogen. The mixture was heated at reflux for 6 h, then allowed to cool to room temperature. DBU (0.2 mL) was added and the mixture was stirred for an additional 1 h, then diluted with water (10 mL) and extracted with CH_2Cl_2 (3×10 mL). The combined organic layers were washed with water and brine and dried over anhydrous $NaSO_4$. After removal of solvent under reduced pressure, the residue was purified by column chromatography (SiO_2, 10% EtOAc in hexanes) to give *alkene* **31** (6.4 mg, 0.017 mmol, 58%) as a colourless oil; R_f=0.46 (25% ethyl acetate/hexane); ν_{max}/cm^{-1} 3397, 2956, 2929, 2884, 2857, 1729, 1649, 1461, 1253, 1102, 1072, 993, 862, 832, 774; δ_H (300 MHz; CDCl$_3$) 5.79 (ddd, 1H, *J*=9.8, 5.5, 2.0 Hz, *CH*=CH), 5.63 (dd, 1H, *J*=9.8, 2.2 Hz, CH=C*H*), 4.72 (br s, 2H, CH=C*H*H and OH), 4.71 (s, 1H, C=C*H*H), 4.41 (d, 1H, *J*=4.4 Hz, OH), 3.99 (d, 1H, *J*=5.5 Hz, CH=CHC*H*OH), 3.73 (dd, 1H, *J*=10.6, 1.7 Hz, *CH*HOTBS), 3.70–3.53 (m, 2H, CC*H*OH and CH*H*OTBS), 2.39 (ddd, 1H, *J*=14.4, 7.1, 7.1 Hz, CHOHCH$_2$C*H*H), 2.18–2.02 (m, 2H, CHOHCH$_2$CH*H* and CHOHC*H*HCH$_2$), 1.93–1.77 (m, 3H, C*H*CH$_3$, CHOHCH*H*CH$_2$ and C*H*CH$_2$OTBS), 1.74 (s, 3H, CH$_3$), 1.15 (d, 3H, *J*=6.8 Hz, CH$_3$), 0.91 (s, 9H, SiC(CH$_3$)$_3$), 0.68 (s, 3H, CH$_3$), 0.11 (s, 3H, Si(CH$_3$)), 0.10 (s, 3H, Si(CH$_3$)); δ_C (100 MHz; CDCl$_3$) 145.8, 135.8, 126.5, 110.3, 76.9, 70.8, 61.7, 42.8, 41.7, 35.2, 31.2, 27.7, 25.9 (3C), 22.6, 19.8, 18.2, 16.1, –5.6 (2C); *m*/*z*, 391 (M+Na$^+$, 100%), 368, 352, 351, 330, 314, 279, 278, 238, 218, 216, 198, 178; HRMS 391.2653 (M+Na$^+$, $C_{21}H_{40}O_3SiNa$ requires 391.2644).

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29. Data for TMS ether **24**: mp 47–49 °C; R_f=0.64 (25% ethyl acetate/hexane); ν_{max}/cm^{-1} 2956, 2929, 2883, 2856, 1778, 1660, 1512, 1462, 1404, 1359, 1251, 1228, 1097, 989, 939, 837, 775; δ_H (500 MHz; CDCl$_3$) 5.87 (dd, 1H, *J*=10.0, 2.2 Hz, *CH*=CH), 5.76 (ddd, 1H, *J*=10.0, 4.6, 2.4 Hz, CH=C*H*), 4.54 (d, 1H, *J*=4.6 Hz, CHOCO), 4.35 (s, 1H, *CH*OTMS), 3.74 (d, 2H, *J*=4.0 Hz, C*H*$_2$OTBS), 2.35–2.22 (m, 1H, *CH*CH$_3$), 1.17 (dt, 1H, *J*=8.9, 4.0 Hz, *CH*CH$_2$OTBS), 1.06 (d, 3H, *J*=7.2 Hz, CH$_3$), 1.00 (s, 3H, CH$_3$), 0.89 (s, 9H, SiC(CH$_3$)$_3$), 0.19 (s, 9H, Si(CH$_3$)$_3$), 0.06 (s, 3H, SiCH$_3$), 0.05 (s, 3H, SiCH$_3$); δ_C (125 MHz; CDCl$_3$) 175.2, 140.2, 119.5, 80.3, 75.3, 62.0, 44.7, 42.9, 30.1, 25.8 (3C), 19.9, 18.1, 12.5, 0.07 (3C), −5.5, −5.6; *m*/*z*, 421 (M+Na$^+$, 100%), 399, 391, 349, 327, 267, 249, 221, 195, 177, 159, 146, 131; HRMS found 421.2207 (M+Na$^+$, $C_{20}H_{38}O_4Si_2Na$ requires 421.2206).
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31. None of the alternative epoxide product could be detected. Data for tetrahydrofuran **29**: mp 63–65 °C; R_f=0.36 (25% ethyl acetate/hexane); ν_{max}/cm^{-1} 3408, 2954, 2928, 2880, 2857, 1461, 1252, 1097, 1074, 1037, 1004, 985, 833, 774; δ_H (500 MHz; CDCl$_3$) 5.84 (ddd, 1H, *J*=10.0, 3.5, 2.6 Hz, *CH*=CH), 5.65 (d, 1H, *J*=10.0 Hz, CH=C*H*), 4.45 (dd, 1H, *J*=4.5, 1.6 Hz, OH), 3.96 (dt, 1H, *J*=4.5, 4.5 Hz, *CH*OH), 3.93–3.86 (m, 2H, OC*H*H and C*H*HOTBS), 3.81 (ddd, 1H, *J*=9.4, 4.5, 1.6 Hz, OCH*H*), 3.65–3.52 (m, 2H, *CH*OCH$_2$, CH*H*OTBS), 1.93 (dd, 1H, *J*=10.3, 3.9 Hz, *CH*CH$_2$OTBS), 1.90–1.82 (m, 1H, *CH*CH$_3$), 1.09 (d, 3H, *J*=6.7 Hz, CH$_3$), 0.97 (s, 3H, CH$_3$), 0.93 (s, 9H, SiC(CH$_3$)$_3$), 0.13 (s, 6H, Si(CH$_3$)$_2$); δ_C (125 MHz; CDCl$_3$) 136.6, 123.9, 83.3, 81.1, 72.7, 62.8, 45.7, 41.2, 29.7, 25.8 (3C), 20.3, 18.6, 18.1, −5.6, −5.7; *m*/*z*, 313 (M+H$^+$, 100%), 312, 292, 262, 251, 227, 198, 180, 162; HRMS 313.2200 (M+H$^+$, $C_{17}H_{33}O_3Si$ requires 313.2199).
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