Tetrahedron 66 (2010) 6340-6348

Contents lists available at ScienceDirect

Tetrahedron

journal homepage: www.elsevier.com/locate/tet

Synthesis of the Northern hemisphere of the briaranes

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ARTICLE INFO

ABSTRACT

Article history: Received 22 January 2010 Received in revised form 15 March 2010 Accepted 1 April 2010 Available online 8 April 2010

Keywords: Diels-Alder Sulfone Oxidation Allylation Cyclolactonisation

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.

> OAc 20

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 highly functionalized fragment corresponding to the Northern hemisphere of the briaranes has been

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 nbutyl 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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synthesized employing a sulfonyl diene Diels-Alder reaction, oxidative desulfonylation, Eschenmoser rearrangement and Keck radical allylation.

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^{0040-4020/\$ -} see front matter © 2010 Elsevier Ltd. All rights reserved. doi:10.1016/j.tet.2010.04.003

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 2ethoxyethylsulfoxide **6** (prepared from the readily available vinyl sulfoxide¹¹) 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) epoxidation¹³ (t-BuOOLi or H₂O₂, NaOH) failed, as did attempts to oxidize the double bond using osmium tetroxide under either Upjohn¹⁴ or Tsuji¹⁵ 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 ¹H NMR signals. After silylation of the free alcohol, oxidative desulfonylation¹⁶ could be achieved by treatment with an excess of LDA and MoOPD (MoO₅·Py·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 trichloride¹⁹ 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 rearrangement²¹ (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 ¹H 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 cycloiodination²⁷ 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 hexame-thyldisilylamine 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**. *svn* 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 allylation³³ 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). ¹H NMR spectra were recorded in CDCl₃ 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 Et₂O (50 mL×3). The combined organic layers were washed with water and brine and dried over anhydrous MgSO₄. After removal of solvent under reduced pressure, the residue was purified by column chromatography (SiO₂, 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; $\delta_{\rm H}$ (400 MHz; CDCl₃) 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, CHCH₃, cis), 5.52 (dq, 1H, *J*=15.3, 6.4 Hz, CHCH₃, trans), 5.36 (dtq, 1H, *J*=15.3, 7.3, 1.5 Hz, CH=CHCH₃, cis and trans), 3.79 (d, 2H, *J*=7.9 Hz, SO₂CH₂, cis), 3.67 (d, 2H, *J*=7.3 Hz, SO₂CH₂, trans), 1.31 (app.d, 3H, *J*=7.0 Hz, CH₃, cis); $\delta_{\rm C}$ (100 MHz; CDCl₃) 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_{111H4}O₂S 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 $-25 \degree C$ over a period of 5 h. The reaction mixture was quenched with saturated aq NH₄Cl (30 mL) and extracted with Et_2O (50 mL \times 3). The combined organic layers were washed with water and brine and dried over anhydrous MgSO₄. After removal of solvent under reduced pressure, the residue was purified by column chromatography (SiO₂, 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); *v*_{max}/cm⁻¹ 3458, 3030, 2920, 1643, 1597, 1494, 1444, 1300. 1141, 966, 815, 709; $\delta_{\rm H}$ (400 MHz; CDCl₃) 7.73 (d, 2H, *J*=8.2 Hz, Ar– H, cis), 7.70 (d, 2H, I=8.2 Hz, Ar-H, trans), 7.34 (d, 2H, I=8.2 Hz, Ar-H, cis and trans), 5.81 (dq, 1H, *J*=10.8, 7.0 Hz, CHCH₃, cis), 5.54 (dq, 1H, J=15.3, 6.5 Hz, CHCH₃, trans), 5.53-5.10 (m, 1H, CH=CHCH₃, cis and trans), 4.30-3.60 (m, 2H, CH₂OH, cis and trans), 2.98 (dt, 1H, J=4.6, 3.1 Hz, SO₂CH₂, cis), 2.88 (dt, 1H, J=5.6, 2.1 Hz, SO₂CH₂, trans), 2.45 (s, 3H, CH₃, cis and trans), 1.66 (dd, 3H, J=6.5, 1.4 Hz, CH₃, trans), 1.31 (dd, 3H, *J*=7.0, 1.7 Hz, CH₃, trans); δ_C (100 MHz; CDCl₃) 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⁺, C₁₂H₁₆O₃S 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 H₂O (30 mL) and extracted with CH₂Cl₂ (100 mL×2). The combined organic layers were washed with water and brine and dried over anhydrous MgSO₄. 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; CDCl₃) 7.72 (app.d, 2H, *I*=7.9 Hz, Ar-H), 7.32 (app.d, 2H, *I*=7.9 Hz, Ar-H), 6.17 (br s, 1H, C=CHH), 6.13 (dq, 1H, J=15.8, 6.5 Hz, CH=CHCH₃), 6.01 (app.d, 1H, J=15.8 Hz, CH=CHCH₃), 5.83 (br s, 1H, C=CHH), 2.42 (s, 3H, Ar-CH₃), 1.74 (d, 3H, J=6.5 Hz, CH₃); δ_{C} (75 MHz; CDCl₃) 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-(2ethoxyethylsulfinyl)-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 guenched with saturated NH₄Cl (30 mL). The mixture was diluted with water (50 mL) and extracted with Et₂O (30 mL \times 3). The combined organic layers were washed with water and brine and dried over anhydrous MgSO₄. After removal of solvent under reduced pressure, the residue was purified by column chromatography (SiO₂, 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); v_{max}/cm⁻¹ 3003, 2872, 1643, 1633, 1492, 1377, 1354. 1215, 1107, 1085, 1041, 806, 754; δ_H (500 MHz; CDCl₃) 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=CHH, minor), 6.06 (s, 1H, C=CHH, major), 5.85 (s, 1H, C=CHH, major), 5.84 (s, 1H, C=CHH, minor), 4.15-4.03 (m, 1H, CHOH, major and minor), 2.41 (s, 3H, CH₃, major), 2.40 (s, 3H, CH₃, minor), 1.75–1.46 (m, 2H, CH₂CH₃, major and minor), 0.86 (t, 3H, J=7.4 Hz, CH₃, minor), 0.80 (t, 3H, J=7.4 Hz, CH₃, major); δ_{C} (100 MHz; CDCl₃) 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⁺, C₁₂H₁₇O₂S 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 CH₂Cl₂ (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 CH₂Cl₂ (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 NH₄Cl (10 mL) and water (10 mL), and extracted with Et₂O (3×25 mL). The combined organic layers were washed with water and brine and dried over anhydrous MgSO₄. After removal of solvent under reduced pressure, the residue was purified by column chromatography (SiO₂, 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); *v*_{max}/cm⁻¹ 3024, 2976, 2937, 1629, 1595, 1492, 1454, 1352, 1174, 1080, 1047, 914, 850, 812; $\delta_{\rm H}$ (300 MHz; CDCl₃) 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=CHH, minor), 6.27 (d, 1H, J=0.9 Hz, C=CHH, major), 6.03 (d, 1H, J=0.9 Hz, C=CH₂, major and minor), 5.02–4.85 (m, 1H, CH-OMs, major and minor), 2.89 (s, 3H, CH₃, major), 2.60 (s, 3H, CH₃, minor), 2.40 (s, 3H, CH₃, major and minor), 1.92–1.68 (m, 1H, CHHCH₃, major), 1.63–1.31 (m, 3H, CHHCH₃, minor and CHHCH₃, major and minor), 0.85 (t, 3H, J=7.3 Hz, CH₃, major), 0.85 (t, 3H, J=7.3 Hz, CH₃, minor); δ_C (75 MHz; CDCl₃) 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+, C₁₃H₁₉O₄S₂ 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 CH₂Cl₂ (32.5 mL) under nitrogen. The mixture was heated at reflux for 2 h, then diluted with saturated aq NH₄Cl (10 mL) and extracted with Et₂O (3×25 mL). The combined organic layers were washed with water and brine and dried over anhydrous MgSO₄. After removal of solvent under reduced pressure, the residue was purified by column chromatography (SiO₂, 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; $\delta_{\rm H}$ (300 MHz; CDCl₃) 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=CH₂ and CH=CHCH₃), 5.69 (s, 1H, CH=CHCH₃), 2.36 (s, 3H, CH₃), 1.68 (d, 3H, *J*=5.5 Hz, CH₃); $\delta_{\rm C}$ (75 MHz; CDCl₃) 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⁺, C₁₂H₁₅OS requires 207.0844).

4.1.7. (1R*,2R*,6S*)-Methyl 2,6-dimethyl-4-tosylcyclohex-3-enecarboxylate (9). AlCl₃ (9.53 g, 71.5 mmol), CH₂Cl₂ (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 CH₂Cl₂ (125 mL) was added over 5 min. The mixture was heated at reflux for 7 days, then cooled to 0 °C, quenched with sat NH₄Cl (50 mL) and extracted with CH₂Cl₂ (50 mL×3). The combined organic layers were washed with water and brine and dried over anhydrous MgSO₄. After removal of solvent under reduced pressure, the residue was purified by column chromatography (SiO₂, 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; $\delta_{\rm H}$ (500 MHz; CDCl₃) 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, SO₂C=CH), 3.64 (s, 3H, OCH₃), 2.85-2.74 (m, 1H, C=CHCHCH₃), 2.42 (s, 3H, CH₃), 2.35 (app.t, 1H, *I*=6.1 Hz, CHCO₂CH₃), 2.33 (app.d, 1H, *J*=5.6 Hz, SO₂CCHH), 2.10–1.93 (m, 1H, CH₂CHCH₃), 1.73 (dddd, 1H, J=16.8, 9.6, 2.1, 2.1 Hz, SO₂CCHH), 0.98 (d, 3H, I=7.3 Hz, CH₃), 0.96 (d, 3H, I=6.5 Hz, CH₃); δ_{C} (75 MHz; CDCl3) 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 C17H22O4S: 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). AlCl₃ (2.21 g, 16.6 mmol), CH₂Cl₂ (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 CH₂Cl₂ (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 NH₄Cl (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 MgSO₄. After removal of solvent under reduced pressure, the residue was purified by column chromatography (SiO₂, 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); *v*_{max}/cm⁻¹ 2956, 2927, 2874, 1733, 1453, 1433, 1216, 1158, 1082, 1044, 1014, 809, 620; $\delta_{\rm H}$ (300 MHz; CDCl₃) 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, SO₂C=CH, major and minor), 3.47 (s, 3H, OCH₃, minor), 3.46 (s, 3H, OCH₃, major), 2.72-2.50 (m, 1H, C=CHCHCH₃, major and minor), 2.25 (dd, 1H, J=10.1, 5.8 Hz, CHCO₂CH₃, major and minor), 2.21 (s, 3H, CO₂CH₃, major and minor), 1.93–1.66 (m, 2H, CH₂CHCH₃ and SO₂CCHH, major and minor), 1.42 (ddd, 1H, SO₂CCHH, major and minor), 0.84 (d, 3H, J=6.6 Hz, CH₃, minor), 0.82 (d, 3H, J=6.7 Hz, CH₃, major), 0.75 (d, 3H, *J*=6.7 Hz, CH₃, major), 0.74 (d, 3H, *J*=6.6 Hz, CH₃, minor); $\delta_{\rm C}$ (75 MHz; CDCl₃) 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 cyclohexenvl sulfone 9 (5.74 g, 18.7 mmol) in dry CH₂Cl₂ (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 CH₂Cl₂ (3×50 mL). The combined organic layers were washed with water and brine and dried over anhydrous MgSO₄. After removal of solvent under reduced pressure, the residue was purified by column chromatography (SiO₂, 50% EtOAc in hexanes) to give alcohol 11 (5.30 g, 18.0 mmol, 96%) as a colourless solid; mp 104-105 °C; $R_{\rm f}$ =0.25 (50% ethyl acetate/hexane); $v_{\rm max}$ /cm⁻¹ 3441, 1643, 1595, 1300, 1286, 1273, 1149, 1105, 1082, 1004, 806, 669, 623; $\delta_{\rm H}$ (400 MHz; CDCl₃) 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, SO₂C=CH), 3.68 (dd, 1H, J=10.1, 6.1 Hz, CHHOH), 3.51 (dd, 1H, J=10.1, 10.1 Hz, CHHOH), 2.80-2.66 (m, 1H, C=CHCHCH₃), 2.42 (s, 3H, CH₃), 2.27 (app.d, 1H, J=12.2 Hz, SO₂CCHH), 1.85-1.67 (m, 2H, SO₂CCHH and CH₂CHCH₃), 1.63-1.46 (m, 1H, CHCH₂OH), 1.01 (d, 3H, J=7.3 Hz, CH₃), 0.87 (d, 3H, J=6.2 Hz, CH₃); δ_C (100 MHz; CDCl₃) 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 C₁₆H₂₂O₃S: 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 NH₄Cl (15 mL) and extracted with Et_2O (20 mL×3). The combined organic layers were washed with water and brine and dried over anhydrous MgSO₄. The solvent was removed under reduced pressure, and the residue was purified by column chromatography (SiO₂, 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); v_{max}/cm^{-1} 1641, 1597, 1467, 1454, 1377, 1300, 1290, 1149, 1112, 1083, 885, 837, 813, 775, 667, 619; δ_H (500 MHz; CDCl₃) 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, SO₂C=CH), 3.58 (dd, 1H, J=9.9, 6.0 Hz, CHHOTBS), 3.45 (dd, 1H, J=9.9, 9.9 Hz, CHHOTBS), 2.75-2.63 (m, 1H, C=CHCHCH₃), 2.42 (s, 3H, Ar-CH₃), 2.26 (app.d, 1H, J=12.3 Hz, SO₂CCHH), 1.82–1.66 (m, 2H, SO₂CCHH and CH₂CHCH₃), 1.58-1.46 (m, 1H, CHCH₂OTBS), 0.99 (d, 3H, J=7.3 Hz, CH₃), 0.86 (d, 3H, J=8.6 Hz, CH₃), 0.85 (s, 9H, SiC(CH₃)₃), 0.00 (s, 3H, SiCH₃), 0.01 (s, 3H, SiCH₃); δ_C (100 MHz; CDCl₃) 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⁺, C₂₂H₃₆O₃SSiNa 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 CH₂Cl₂ (50 mL×3). The combined organic layers were washed with water and brine and dried over anhydrous MgSO₄. After removal of solvent under

reduced pressure, the residue was purified by column chromatography (SiO₂, 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; $\delta_{\rm H}$ (400 MHz; CDCl₃) 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, CH=CCH₃), 3.66 (br s, 1H, SO₂CH), 3.53 (dd, 1H, *J*=11.1, 3.2 Hz, CHHOH), 3.33 (dd, 1H, *J*=11.1, 6.8 Hz, CHHOH), 2.38 (s, 3H, CH₃), 2.25 (br s, 1H, OH), 2.22–2.14 (m, 1H, CHCH₃), 1.92 (ddd, 1H, *J*=13.4, 8.0, 4.4 Hz, SO₂CHCHH), 1.77 (br s, 1H, CHCH₂OH), 1.72 (s, 3H, CH₃), 1.52 (ddd, 1H, *J*=13.4, 6.7, 6.7 Hz, SO₂CHCHH), 0.86 (d, 3H, *J*=6.9 Hz, CH₃); $\delta_{\rm C}$ (100 MHz; CDCl₃) 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⁺, C₁₆H₂₂O₃SNa 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 NH₄Cl (15 mL) and extracted with Et₂O (25 mL×3). The combined organic layers were washed with water and brine and dried over anhydrous MgSO₄. After removal of solvent under reduced pressure, the residue was purified by column chromatography (SiO₂, 25% EtOAc in hexanes) to give silvl 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; $\delta_{\rm H}$ (500 MHz; CDCl₃) 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, CH=CCH₃, minor), 5.58 (br s, 1H, CH=CCH₃, major), 3.74 (dd, 1H, J=11.3, 2.7 Hz, SO₂CH, major), 3.62 (dd, 1H, J=10.4, 2.7 Hz, SO₂CH, minor), 3.39 (dd, 1H, J=9.9, 4.4 Hz, CHHOTBS, major and minor), 2.85 (dd, 1H, J=9.9, 9.9 Hz, CHHOTBS, major and minor), 2.41 (s, 3H, CH₃, minor), 2.40 (s, 3H, CH₃, major), 2.23-2.12 (m, 1H, CHCH₃, major and minor), 1.83-1.50 (m, 3H, SO₂CH and SO₂CHCH₂, major and minor), 1.72 (s, 3H, CH₃, major and minor), 0.95 (d, 3H, *J*=6.6 Hz, CH₃, minor), 0.85 (d, 3H, J=7.1 Hz, CH₃, major), 0.82 (s, 9H, SiC(CH₃)₃, major), 0.80 (s, 9H, SiC(CH₃)₃, minor), -0.03 (s, 6H, Si(CH₃)₂, minor), -0.06 (s, 6H, Si(CH₃)₂, major); δ_C (100 MHz; CDCl₃) 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⁺, C₂₂H₃₆O₃SSiNa 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 MgSO₄. After removal of solvent under reduced pressure, the residue was purified by column chromatography (SiO2, 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); v_{max}/cm⁻¹ 2954, 2927, 1647, 1629, 1460, 1438, 1375, 1300, 1251, 1105, 1004, 991, 835, 775; $\delta_{\rm H}$ (500 MHz; CDCl₃) 5.91 (s, 1H, C=CH), 3.80 (app.d, 1H, J=1.3 Hz, CHHOTBS), 3.79 (app.d, 1H, J=2.5 Hz, CHHOTBS), 2.60 (dd, 1H, J=16.9, 5.1 Hz,

COCHH), 2.48–2.35 (m, 1H, CHCH₃), 2.17–2.06 (m, 2H, COCHH and CHCH₂OTBS), 1.99 (s, 3H, CH₃), 1.05 (d, 3H, *J*=7.0 Hz, CH₃), 0.87 (s, 9H, SiC(CH₃)₃), 0.052 (s, 3H, SiCH₃), 0.050 (s, 3H, SiCH₃); $\delta_{\rm C}$ (125 MHz; CDCl₃) 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⁺, C₁₅H₂₉O₂Si 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 CeCl₃·7H₂O (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 NH₄Cl solution (20 mL). HCl (aq, 2 M) was added until the reaction mixture became clear, and it was extracted with Et₂O $(3 \times 75 \text{ mL})$. The combined organic layers were washed with water and brine and dried over anhydrous MgSO₄. After removal of solvent under reduced pressure, the residue was purified by column chromatography (SiO₂, 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); v_{max}/cm^{-1} 3348, 3331, 2954, 2927, 2856, 1718, 1664, 1469, 1462, 1384, 1361, 1253, 1112, 1095, 1029, 987, 875, 837, 773; $\delta_{\rm H}$ (300 MHz; CDCl₃) 5.51 (s, 1H, C=CH), 4.18 (br s, 1H CHOH), 3.71 (dd, 1H, J=6.1, 2.3 Hz, CHHOTBS), 3.65 (dd, 1H, J=6.1, 1.9 Hz, CHHOTBS), 2.02-1.94 (m, 1H, CHHCHCH₃), 1.91–1.80 (m, 1H, CHCH₃), 1.72 (s, 3H, CH₃), 1.68 (br d, 1H, J=3.9 Hz, CHCH₂OTBS), 1.40 (br s, 1H, OH), 1.28–1.18 (m, 1H, CHHCHCH₃), 1.03 (d, 3H, *I*=4.0 Hz, CH₃), 0.86 (s, 9H, SiC(CH₃)₃), 0.02 (s, 6H, Si(CH₃)₂); δ_C (125 MHz; CDCl₃) 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⁺, C₁₅H₃₀O₂SiNa 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 (SiO₂, 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); $v_{\rm max}/{\rm cm}^{-1}$ 1653, 1620, 1307, 1253, 1193, 1105, 1058, 991, 862, 837, 773, 719; $\delta_{\rm H}$ (500 MHz; CDCl₃) 5.61 (ddd, 1H, *J*=10.0, 5.2, 1.5 Hz, CH=CH), 5.53 (d, 1H, J=10.0 Hz, CH=CH), 3.83 (dd, 1H, J=10.8, 3.5 Hz, CHHOTBS), 3.77 (dd, 1H, J=10.8, 5.5 Hz, CHHOTBS), 3.04 (s, 3H, NCH₃), 2.95 (s, 3H, NCH₃), 2.54 (s, 2H, CH₂N(CH₃)₃), 2.10-1.95 (m, 1H, CH=CHCHH), 1.88-1.73 (m, 2H, CH=CHCHH and CHCH₃), 1.72-1.63 (m, 1H, CHCH₂OTBS), 1.10 (s, 3H, CH₃), 1.01 (d, 3H, *I*=6.0 Hz, CH₃), 0.91 (s, 9H, SiC(CH₃)₃), 0.073 (s, 3H, SiCH₃), 0.069 (s, 3H, SiCH₃); δ_C (75 MHz; CDCl₃) 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⁺, C₁₉H₃₈NO₂Si requires 340.2672).

4.1.16. $(3aS^*,4R^*,5S^*,7S^*,7aS^*)-4-((t-Butyldimethylsilyloxy)methyl)-7-iodo-3a,5-dimethylhexahydrobenzofuran-2(3H)-one (19). Iodine (1.22 g, 4.81 mmol) was added to a solution of amide 18 (0.82 g, 2.40 mmol) in THF-H₂O (9.6 mL: 9.6 mL) at 0 °C. The mixture was allowed to warm slowly to room temperature and stirred for an additional 30 h, then the reaction was quenched with saturated aq Na₂S₂O₃ solution until the mixture became colourless. The mixture was extracted with Et₂O (3×20 mL), and the combined organic$

layers were washed with water and brine and dried over anhydrous MgSO₄. After removal of solvent under reduced pressure, the residue was purified by column chromatography (SiO₂, 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; $\delta_{\rm H}$ (500 MHz; CDCl₃) 4.66 (d, 1H, *J*=2.8 Hz, CHI), 4.53 (s, 1H, CHO), 3.81 (dd, 1H, *J*=10.6, 3.7 Hz, CHHOTBS), 3.67 (dd, 1H, *J*=10.6, 7.6 Hz, CHHOTBS), 2.97 (d, 1H, *J*=7.2 Hz, CHHCO), 2.37 (d, 1H, J=7.2 Hz, CHHCO), 2.08-1.93 (m, 2H, CHCH₃ and CHICHH), 1.92-1.77 (m, 1H, CHICHH), 1.50 (s, 3H, CH₃), 1.41-1.27 (m, 1H, CHCH₂OTBS), 1.02 (d, 3H, J=6.3 Hz, CH₃), 0.92 (s, 9H, SiC(CH₃)₃), 0.08 (s, 6H, Si(CH₃)₂); δ_C (75 MHz; CDCl₃) 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⁺, C₁₇H₃₁O₃SilNa requires 461.0985).

4.1.17. (3aS*,4R*,5S*,7aR*)-4-((t-Butyldimethylsilyloxy)methyl)-3a,5dimethyl-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 guenched with saturated aq NH₄Cl (5 mL) and extracted with Et_2O (3×10 mL). The combined organic layers were washed with water and brine and dried over anhydrous MgSO₄. After removal of solvent under reduced pressure, the residue was purified by column chromatography (SiO₂, 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); $\nu_{\rm max}/{\rm cm}^{-1}$ 2956, 2927, 2881, 2854, 1762, 1745, 1460, 1384, 1249, 1222, 1197, 1170, 1126, 993, 833, 773; $\delta_{\rm H}$ (400 MHz; CDCl₃) 5.91 (d, 1H, *J*=10.0 Hz, CH=CH), 5.79 (ddd, 1H, *J*=10.0, 4.6, 2.5 Hz, CH=CH), 4.28 (d, 1H, J=4.6 Hz, CHO), 3.79 (dd, 1H, J=11.3, 3.3 Hz, CHHOTBS), 3.75 (dd, 1H, J=11.3, 5.5 Hz, CHHOTBS), 2.96 (d, 1H, J=17.4 Hz, CHHCO), 2.39 (d, 1H, J=17.4 Hz, CHHCO), 2.32–2.18 (m, 1H, CHCH₃), 1.37–1.23 (m, 1H, CHCH₂OTBS), 1.11 (s, 3H, CH₃), 1.10 (d, 3H, J=6.0 Hz, CH₃), 0.89 (s, 9H, SiC(CH₃)₃), 0.06 (s, 6H, Si(CH₃)₂); δ_{C} (100 MHz; CDCl₃) 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⁺, C₁₇H₃₀O₃SiNa requires 333.1862).

4.1.18. (3*S**,3*aR**,4*R**,5*S**,7*aR**)-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 guenched with saturated aq NH₄Cl solution, and extracted with Et₂O (3×20 mL). The combined organic layers were washed with water and brine and dried over anhydrous MgSO₄. After removal of solvent under reduced pressure, the residue was purified by column chromatography (SiO₂, 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; $\delta_{\rm H}$ (500 MHz; CDCl₃) 5.86 (dd, 1H, *J*=10.1, 2.0 Hz, CH=CH), 5.72 (ddd, 1H, J=10.1, 2.9, 2.9 Hz, CH=CH), 4.62 (app.s, 1H, CHOCO), 4.44 (d, 1H, J=3.5 Hz, CHOH), 3.81 (dd, 1H, J=10.5, 3.5 Hz, CHHOTBS), 3.66 (dd, 1H, J=10.5, 4.5 Hz, CHHOTBS), 2.72 (d, 1H, J=3.5 Hz, CHOH), 2.37–2.22 (m, 1H, CHCH₃), 1.49 (app.q, 1H, *J*=4.5 Hz, CHCH₂OTBS), 1.17 (d, 3H, J=7.4 Hz, CH₃), 1.12 (s, 3H, CH₃), 0.87 (s, 9H, SiC(CH₃)₃), 0.05 (s, 3H, SiCH₃), 0.04 (s, 3H, SiCH₃); δ_{C} (100 MHz; CDCl₃) 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⁺, C₁₇H₃₀O₄SiNa requires 349.1811).

4.1.19. (3aS*,4R*,5S*,7aR*)-4-((t-Butyldimethylsilyloxy)methyl)-3a,5dimethyl-4,5-dihydrobenzofuran-2,3(3aH,7aH)-dione (25). 2-Iodoxvbenzoic 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 NaHCO₃ solution (10 mL), and extracted with Et₂O (3×15 mL). The combined organic layers were washed with water and brine and dried over anhydrous MgSO₄. After removal of solvent under reduced pressure, the residue was purified by column chromatography (SiO₂, 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); *v*_{max}/cm⁻¹ 2955, 2929, 2884, 2857, 1787, 1461, 1249, 1110, 990, 952, 909, 832, 775, 675; $\delta_{\rm H}$ (300 MHz; CDCl₃) 6.06 (dd, 1H, J=10.1, 1.5 Hz, CH=CH), 5.90 (ddd, 1H, J=10.1, 4.3, 2.5 Hz, CH=CH), 4.59 (d, 1H, J=4.3 Hz, CHOCO), 3.69 (dd, 1H, J=11.3, 3.5 Hz, CHHOTBS), 3.65 (dd, 1H, J=11.3, 3.0 Hz, CHHOTBS), 2.60-2.40 (m, 1H, CHCH₃), 1.43 (ddd, 1H, J=9.3, 3.5, 3.3 Hz, CHCH₂OTBS), 1.24 (s, 3H, CH₃), 1.13 (d, 3H, J=7.1 Hz, CHCH₃), 0.88 (s, 9H, SiC(CH₃)₃), 0.08 (s, 3H, SiCH₃), 0.04 (s, 3H, SiCH₃); δ_C (125 MHz; CDCl₃) 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⁺, C₁₇H₂₈O₄SiNa 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 $-78 \degree$ 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 NH₄Cl solution, and extracted with Et_2O (3×20 mL). The combined organic layers were washed with water and brine and dried over anhydrous MgSO₄. After removal of solvent under reduced pressure, the residue was purified by column chromatography (SiO₂, 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); v_{max}/cm^{-1} 3381, 3305, 3018, 2956, 2929, 2883, 2856, 1774, 1462, 1255, 1215, 1141, 958, 835, 756; $\delta_{\rm H}$ (300 MHz; CDCl₃) 5.91 (dd, 1H, *J*=9.9, 1.9 Hz, CH=CH), 5.81 (ddd, 1H, J=9.9, 5.1, 2.3 Hz, CH=CH), 5.73 (app.d, 1H, J=10.0 Hz, OH), 4.23-4.12 (m, 2H, CHOCO and CHOH), 3.82 (dd, 1H, J=11.3, 1.8 Hz, CHHOTBS), 3.74 (dd, 1H, J=11.3, 7.7 Hz, CHHOTBS), 2.05-1.87 (m, 1H, CHCH₃), 1.42 (ddd, 1H, J=10.0, 7.7, 1.8 Hz, CHCH₂OTBS), 1.15 (s, 3H, CH₃), 1.13 (d, 3H, *J*=7.0 Hz, CH₃), 0.91 (s, 9H, SiC(CH₃)₃), 0.11 (s, 6H, Si(CH₃)₂); δ_{C} (125 MHz; CDCl₃) 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⁺, C₁₇H₃₀O₄SiNa requires 349.1811).

4.1.21. (R^*)-1-((1 R^* ,2 S^* ,5 R^* ,6 S^*)-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 LiAlH₄ (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 NH₄Cl (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 Et₂O (3×10 mL). The combined organic layers were washed with water and brine and dried over anhydrous MgSO₄. After removal of solvent under reduced pressure, the residue was purified by column chromatography (SiO₂, 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); *v*_{max}/cm⁻¹ 3368, 2955, 2928, 2884, 2857, 1461, 1253, 1103, 1066, 1026, 995, 864, 834, 774; $\delta_{\rm H}$ (300 MHz; CDCl₃) 5.73 (ddd, 1H, *I*=9.8, 5.4, 1.8 Hz, CH=CH), 5.65 (dd, 1H, *I*=9.8, 1.9 Hz, CH=CH), 4.58 (app.d, 1H, *I*=5.1 Hz, CHOH-CH₂OH), 4.12 (br s, 1H, OH), 3.97-3.65 (m, 6H, CH₂OH, CH₂OTBS, CHOH, OH), 2.47 (br s, 1H, OH), 2.10-1.87 (m, 2H, CHCH₃, CHCH₂OTBS), 1.14 (d, 3H, *J*=6.5 Hz, CHCH₃), 0.90 (s, 9H, SiC(CH₃)₃), 0.76 (s, 3H, CH₃), 0.111 (s, 3H, SiCH₃), 0.106 (s, 3H, SiCH₃); δ_{C} (125 MHz; CDCl₃) 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⁺, C₁₇H₃₄O₄SiNa requires 353.2124).

4.1.22. (*R**)-2-((1*R**,2*S**,5*R**,6*S**)-6-((*t*-Butyldimethylsilyloxy) methyl)-2-hydroxy-1,5-dimethyl-cyclohex-3-enyl)-2-hydroxyethyl 4methylbenzenesulfonate (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 CH₂Cl₂ (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 NH₄Cl (5 mL) and water (10 mL), and extracted with CH₂Cl₂ (3×10 mL). The combined organic layers were washed with water and brine and dried over anhydrous Na₂SO₄. After removal of solvent under reduced pressure, the residue was purified by column chromatography (SiO₂, 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; CDCl₃) 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, CH=CH), 4.46 (dd, 1H, J=10.6, 2.1 Hz, CHHOTs), 4.28 (dd, 1H, J=10.6, 8.1 Hz, CHHOTs), 3.96 (dd, 1H, J=8.1, 2.1 Hz, CHOHCH₂OTs), 3.77 (app.d, 1H, J=10.8 Hz, CHHOTBS), 3.73 (app.d, 1H, J=5.2 Hz, CH=CHCHOH), 3.69 (dd, 1H, J=10.8, 6.6 Hz, CHHOTBS), 2.44 (s, 3H, Ar-CH₃), 2.08–1.88 (m, 2H, CHCH₃ and CHCH₂OTBS), 1.11 (d, 3H, J=6.4 Hz, CHCH₃), 0.89 (s, 9H, SiC(CH₃)₃), 0.77 (s, 3H, CH₃), 0.09 (s, 6H, Si(CH₃)₂); δ_C (75 MHz; CDCl₃), 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⁺, C₂₄H₄₀O₆SiSNa 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 CH₂Cl₂ was slowly added to a solution of triol 27 (21.2 mg, 0.064 mmol) in CH₂Cl₂ (0.5 mL) at -30 °C under nitrogen. A solution of iodine (18 mg, 0.07 mmol) in CH₂Cl₂ (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 Na₂S₂O₃ (5 mL) and extracted with CH₂Cl₂ (3×10 mL). The combined organic layers were washed with water and brine and dried over anhydrous Na₂S₂O₄. After removal of solvent under reduced pressure, the residue was purified by column chromatography (SiO₂, 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); v_{max}/cm⁻¹ 3387, 2922, 2851, 1448, 1416, 1374, 1259, 1092, 1031, 987, 892, 838, 578, 553; $\delta_{\rm H}$ (300 MHz; CDCl₃) 5.75 (ddd, 1H, J=9.8, 5.4, 2.0 Hz, CH=CH), 5.71 (dd, 1H, J=9.8, 2.0 Hz, CH=CH), 4.68 (br s, 1H, OH), 4.45 (br s, 1H, OH), 4.05 (dd, 1H, J=9.5, 4.5 Hz, CHHI), 3.96 (dd, 1H, J=8.2, 4.5 Hz, CHHOTBS), 3.84-3.56 (m, 4H, CHOH, CHOHCH₂I, CHHI and CHHOTBS), 1.90–1.79 (m, 1H, CHCH₂OTBS), 1.72 (app.d, 1H, *J*=7.1 Hz, CHCH₃), 1.13 (d, 3H, *J*=7.1 Hz, CHCH₃), 0.92 (s, 9H, SiC(CH₃)₃), 0.82 (s, 3H, CH₃), 0.11 (s, 6H, Si(CH₃)₂); $\delta_{\rm C}$ (125 MHz; CDCl₃) 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⁺, C₁₇H₃₄O₃Sil 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 NaSO₄. After removal of solvent under reduced pressure, the residue was purified by column chromatography (SiO₂, 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); *v*_{max}/cm⁻¹ 3397, 2956, 2929, 2884, 2857, 1729, 1649, 1461, 1253, 1102, 1072, 993, 862, 832, 774; $\delta_{\rm H}$ (300 MHz; CDCl₃) 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=CH), 4.72 (br s, 2H, CH=CHH and OH), 4.71 (s, 1H, C=CHH), 4.41 (d, 1H, *I*=4.4 Hz, OH), 3.99 (d, 1H, *I*=5.5 Hz, CH=CHCHOH), 3.73 (dd, 1H, *I*=10.6, 1.7 Hz, CHHOTBS), 3.70–3.53 (m, 2H, CCHOH and CHHOTBS), 2.39 (ddd, 1H, *I*=14.4, 7.1, 7.1 Hz, CHOHCH₂CHH), 2.18–2.02 (m, 2H, CHOHCH2CHH and CHOHCHHCH2), 1.93-1.77 (m, 3H, CHCH3, CHOHCHHCH₂ and CHCH₂OTBS), 1.74 (s, 3H, CH₃), 1.15 (d, 3H, *I*=6.8 Hz, CH₃), 0.91 (s, 9H, SiC(CH₃)₃), 0.68 (s, 3H, CH₃), 0.11 (s, 3H, Si(CH₃)), 0.10 (s, 3H, Si(CH₃)); δ_C (100 MHz; CDCl₃) 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⁺, C₂₁H₄₀O₃SiNa requires 391.2644).

Acknowledgements

We thank Nanyang Technological University and the Singapore Ministry of Education Academic Research Fund Tier 2 (grant T206B1220RS) for support of this work. XK thanks NTU for a URECA scholarship.

References and notes

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- 9. Other data for dimer 4: mp 142–143 °C; $R_{\rm j}$ =0.13 (25% ethyl acetate/hexane); $\nu_{\rm max}/{\rm cm}^{-1}$ 1645, 1595, 1288, 1151, 1139, 1091, 970, 800, 707, 655, 594; $\delta_{\rm H}$ (300 MHz; CDCl₃) 7.66 (d, 2H, J=8.2 Hz, Ar–H), 7.54 (d, 2H, J=8.2 Hz, Ar–H), 7.26 (app.t, 4H, J=7.9 Hz, Ar–H), 6.74 (app.d, 1H, J=2.4 Hz, SO₂C=CH), 5.51 (dd, 1H, J=16.0, 1.3 Hz, CH=CHCH₃), 5.30 (dq, 1H, J=16.0, 6.3 Hz, CH=CHCH₃), 3.35–3.15 (m, 1H, CHCH₃), 2.38 (s, 6H, CH₃ (2C)), 2.28–2.00 (m, 2H, SO₂CCH₂), 1.97–1.78 (m, 2H, SO₂CCH₂CH₂), 1.61 (dd, 3H, J=6.3, 1.3 Hz, CH=CHCH₃), 1.39 (d, J=7.4 Hz, CH₃); $\delta_{\rm C}$ (75 MHz; CDCl₃) 144.9, 144.3, 1411, 1377, 135.8, 133.2, 131.9, 130.6, 129. 7 (2C), 129.1 (2C), 127.9 (2C), 121.9 (2C), 67.8, 33.8, 25.6, 21.59, 21.56, 20.5, 18.5, 120.2 (20.2

16.8; $m/z,\,467~(M+Na^+,\,100\%)$ 445, 413, 391, 363, 287, 205, 167, 149, 131. Anal. Calcd for $C_{24}H_{28}O_4S_2;$ C, 64.38; H, 6.53. Found: C, 64.72; H, 6.54.

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- 18. Data for hydroxyketone **16**: mp 47–48 °C; R_{f} =0.34 (25% ethyl acetate/hexane); ν_{max}/cm^{-1} 3479, 2957, 2928, 2887, 2856, 1657, 1461, 1376, 1251, 1085, 986, 882, 833, 772, 681; $\delta_{\rm H}$ (500 MHz; CDCl₃) 6.03 (s, 1H, C=CH), 3.99 (dd, 1H, *J*=10.6, 2. 0 Hz, CHHOTBS), 3.81 (dd, 1H, *J*=10.6, 1.8 Hz, CHHOTBS), 3.81 (dr s, 1H, OH), 3. 80 (d, 1H, *J*=12.3 Hz, CHOH), 2.18–2.08 (m, 2H, CHCH₃ and CHCH₂OTBS), 2.04 (s, 3H, CH₃), 1.23 (d, 3H, *J*=6.0 Hz, CH₃), 0.84 (s, 9H, SiC(CH₃)₃), 0.05 (s, 3H, SiCH₃), 0.04 (s, 3H, SiCH₃); $\delta_{\rm C}$ (125 MHz; CDCl₃) 199.2, 164.6, 125.4, 76.7, 59.3, 49.4, 37.9, 25.7 (3C), 22.1, 18.1, 15.7, -5.6, -5.7; *m*/z, 285 (M+H⁺, 100%), 284, 270, 269, 266, 255, 237, 231, 206, 171, 155, 151; HRMS found 285.1887. (M+H⁺, C₁₅H₂₉O₃Si requires 285.1886).
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 Some of the acetate of compound **17** could also be isolated from the reaction
- 26. Some of the acetate of compound **17** could also be isolated from the reaction mixture: R_f =0.37 (25% ethyl acetate/hexane); ν_{max}/cm^{-1} 2954, 2927, 2856, 1735, 1469, 1462, 1373, 1242, 1114, 1099, 1026, 873, 837, 775; $\delta_{\rm H}$ (500 MHz; CDCl₃) 5.47 (s, 1H, CH=C), 5.29 (br s, 1H, CHOCO), 3.69 (app.d, 2H, *J*=3.1, Hz, CH₂OTBS), 2.10–2.20 (m, 1H, CHHCHCH₃), 2.05 (s, 3H, OCOCH₃), 2.10–1.90 (m, 1H, CHCHCH₃), 1.76 (br s, 4H, CHCH₂OTBS and CH=CCH₃), 1.43–1.31 (m, 1H, CHHCHCH₃), 1.04 (d, 3H, *J*=6.7 Hz, CH₃), 0.88 (s, 9H, SiC(CH₃)₂), 0.04 (s, 6H, Si(CH₃)₂); $\delta_{\rm C}$ (100 MHz; CDCl₃) 170.9, 1389, 123.7, 69.9, 61.3, 49.0, 35.3, 27.4, 25. 8 (3C), 21.8, 21.5, 20.20 (M+Na⁺, C₁/H₃2₀/3SiNa requires 335.2018).
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- 28. Data for iodide **21**: R_f =0.55 (25% ethyl acetate/hexane); ν_{max}/cm^{-1} 3018, 2954, 2929, 1782, 1643, 1462, 1388, 1257, 1215, 1097, 989, 837, 748, 665; $\delta_{\rm H}$ (500 MHz; CDCl₃) 5.79 (app.d, 1H, *J*=10.2 Hz, *CH*=CH), 5.68–5.57 (m, 1H, *CH*=CH), 5.20 (s, 1H, CHI), 3.76 (dd, 1H, *J*=10.8, 3.6 Hz, *CH*HOTBS), 3.64 (dd, 1H, *J*=10.8, 6.3 Hz, CHHOTBS), 3.02 (s, 3H, NCH₃), 2.89 (s, 3H, NCH₃), 1.97 (dt, 1H, *J*=168, 4.3 Hz, CH=CHCHH), 1.83 (dt, 1H, *J*=10.6, 2.3 Hz, CHCH₃), 1.81–1.65 (m, 2H, CH=CHCHH and CHCH₂OTBS), 1.12 (s, 3H, CH₃), 0.95 (d, 3H, *J*=6.0 Hz, CH₃), 0.88 (s, 9H, SiC(CH₃)₃), 0.054 (s, 3H, SiCH₃), 0.052 (s, 3H, SiCH₃); $\delta_{\rm C}$ (100 MHz; CDCl₃) 169.8, 136.1, 123.6, 62.3, 44.9, 41.2, 38.2, 38.1, 36.5, 34.6, 29.0, 26.0 (3C), 25.8, 19.8, 18.4, -5.4, -5.5; *m/z*, 466 (M+H⁺, 100%), 414, 413, 392, 391, 341, 340, 311, 279, 257, 205, 180, 149; HRMS found 466.1628 (M+H⁺, Cl₉H₃₇NO₂Sil requires 466.1638).
- 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; CDCl₃) 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=CH), 4.54 (d, 1H, *J*=4.6 Hz, CHOCO), 4.35 (s, 1H, CHOTMS), 3.74 (d, 2H, *J*=4.0 Hz, CH₂OTBS), 2.35–2.22 (m, 1H, CHCH₃), 1.17 (dt, 1H, *J*=8.9, 4.0 Hz, CHC₄OTBS), 1.06 (d, 3H, *J*=7.2 Hz, CH₃), 1.00 (s, 3H, CH₃), 0.89 (s, 9H, SiC(CH₃)₃), 0.19 (s, 9H, SiC(CH₃)₃), 0.06 (s, 3H, SiCH₃), 0.05 (s, 3H, SiCH₃); δ_C (125 MHz; CDCl₃) 175.2, 140.2, 119.5, 80.3, 75.3, 62.0, 44.7, 42.9, 30.1, 25.8 (3C), 19.9, 181, 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⁺, C₂₀H₃₈O₄Si₂Na requires 421.2206).
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