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SmI_2-mediated dialdehyde 'radical then aldol' cyclization cascades: a feasibility study

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ABSTRACT

Dialdehydes undergo 'radical then aldol' cyclization cascades upon treatment with SmI_2, generating four contiguous stereocenters with high diastereocontrol. The scope of the process has been explored and the cascade has been extended to also include lactone reduction.

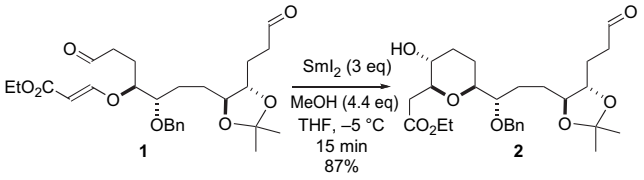
1. Introduction

Since its introduction to the synthetic community by Kagan, samarium(II) iodide (SmI_2) has become one of the most important reducing agents in organic synthesis.[1] The versatile, single electron-transfer reagent has been used to mediate many processes ranging from functional group interconversions to complex carbon–carbon bond-forming sequences.[1] In particular, cyclization reactions mediated by the reagent have met many synthetic challenges in natural product synthesis.[1f] In this context, we have introduced several stereoselective cyclizations using the lanthanide reagent in recent years.[2–6] Of the many reducing agents available to the synthetic chemist, SmI_2 is the one reagent able to orchestrate powerful sequential processes.[1a] The development of sequential reactions in which a number of transformations convert simple starting materials to complex products, using a single reagent, in a single synthetic operation, is one of the most important goals of the synthetic chemist.

Here we report in full our feasibility studies on the development of a dialdehyde cyclization cascade mediated by SmI_2 in which the aldehyde groups undergo stereoselective reaction in a programmed sequence to give complex products.[7]

2. Results and discussion

In 2002 Takahashi and Nakata described a synthesis of mucocin that involved the SmI_2-mediated, aldehyde–alkene cyclization of dialdehyde **1** to give **2** as the key step in their approach (Scheme 1).[8]



Scheme 1. Takahashi and Nakata's SmI_2-mediated cyclization en route to mucocin.

Carbonyl-alkene cyclizations using SmI_2 are believed to proceed by reduction of the aldehyde to the ketyl radical anion followed by addition to the alkene.[1,9] The transformation of **1** to **2** is therefore remarkable as only one aldehyde is reduced by the reagent. The authors observed that the use of excess SmI_2 or prolonged reaction times led to reduction of the second aldehyde and the formation of complex product mixtures. Intrigued by this result, we speculated that a new class of sequential cyclization mediated by SmI_2 might be possible using *dialdehyde* substrates: one aldehyde acts as a radical precursor while the other remains unreactive until late in the sequence when it behaves as an electrophile. We envisaged several classes of dialdehyde cascade from which we selected to study the feasibility of the sequence using substrates **3**. We proposed that aldehyde group 1 would react first through a facile 5-*exo*-*trig* radical cyclization while aldehyde group 2 waits in line. After radical cyclization, aldehyde group 2, in samarium enolates **4**,[10] would undergo aldol cyclization to form tricyclic systems **5** (Scheme 2).

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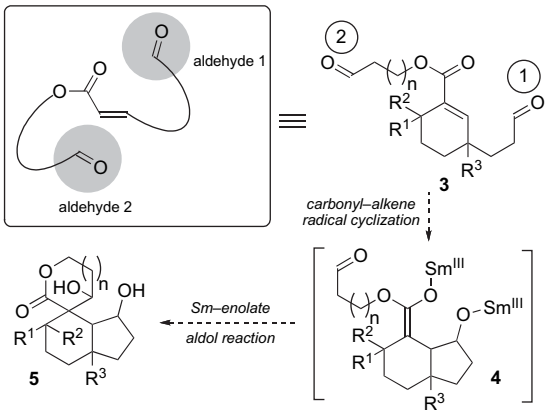
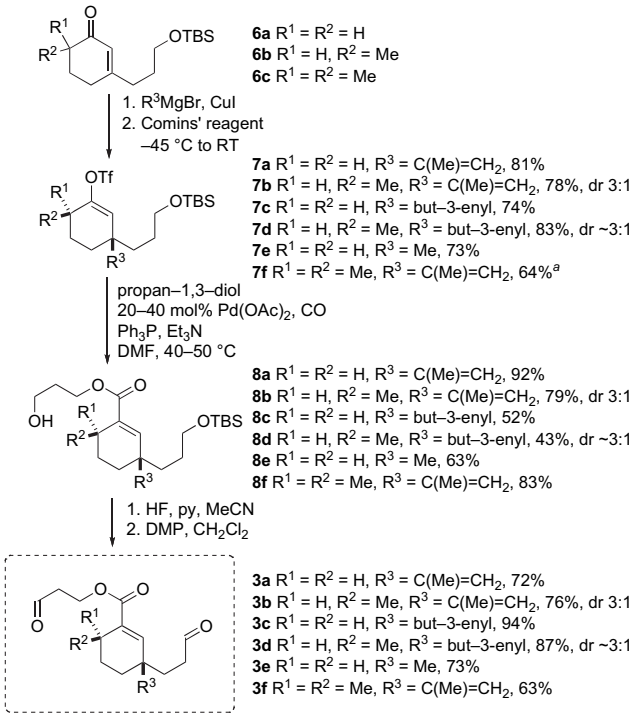


Scheme 2. Proposed sequential dialdehyde cyclizations mediated by SmI_2.

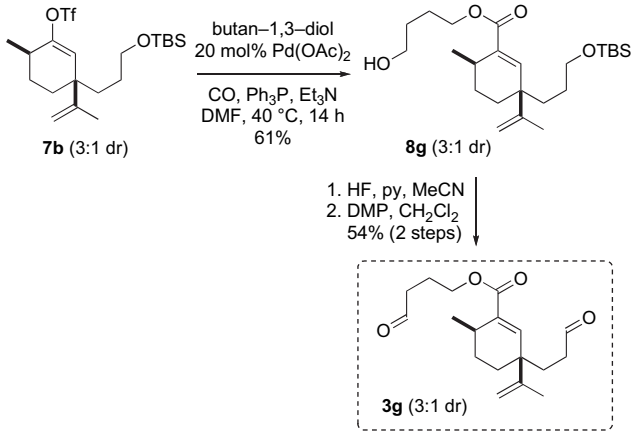
Although an example of a ketyl-olefin cyclization/*inter*molecular aldol sequence has been reported by Enholm,[11] to our knowledge, no intramolecular variants have been reported presumably as both aldehydes in the starting material would be expected to react with SmI_2 to give complex product mixtures. If successful, we anticipated that the sequential cyclizations of **3**, in which four contiguous stereocenters, including one quaternary stereocenter, are generated, would occur with high diastereocontrol.

We began by preparing a range of dialdehyde substrates **3** (n=1) by a modification of our previously reported route to related substrates.[6] Addition of an organocopper to cyclohexanones **6a–c** gave vinyl triflates **7a–f** after trapping of the intermediate enolates with Comins' reagent *N*-(5-chloro-2-pyridyl)bis(trifluoromethanesulfonimide).[12] Organocopper addition to cyclohexenone **6b** gave **7b** and **7d** as a 3:1 mixture of diastereoisomers. Palladium-catalyzed carbonylation in the presence of propan-1,3-diol gave esters **8a–f** in moderate to good yield. Deprotection and oxidation using the Dess–Martin periodinane[13] gave dialdehydes **3a–3f** (Scheme 3).



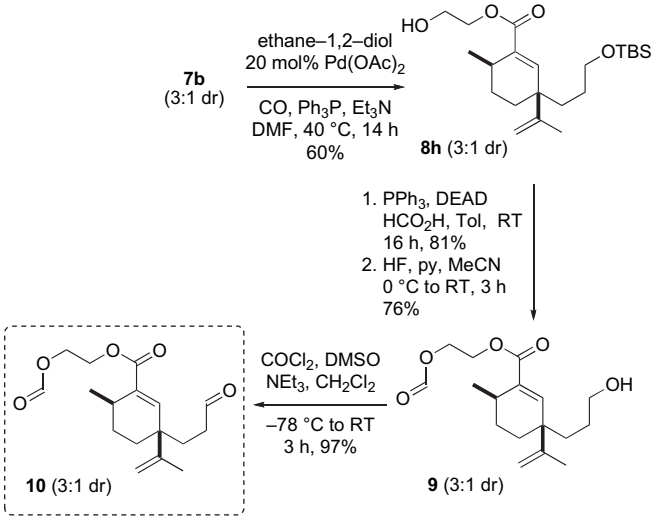
Scheme 3. Synthesis of dialdehyde cyclization substrates **3a–3f** (n=1). [a] **7f** was formed by cuprate addition (82%), followed by triflate formation in a separate step (LDA; Comins' reagent, 78%). Comins' reagent: *N*-(5-chloro-2-pyridyl)bis(trifluoromethanesulfonimide).

We have also prepared dialdehyde substrate **3g** (n=2) to investigate the feasibility of forming a seven-membered lactone ring in the second stage of the cascade (Scheme 4). Vinyl triflate **7b** underwent palladium-catalyzed carbonylation in the presence of butan-1,4-diol to give ester **8g** in 61%. Deprotection and oxidation gave dialdehyde **3g** in 54% yield (two steps).



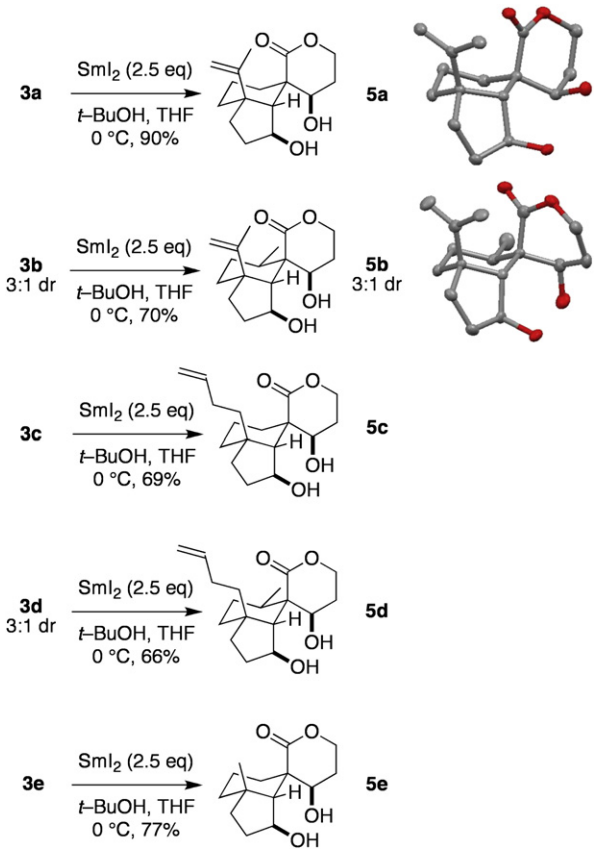
Scheme 4. Synthesis of dialdehyde cyclization substrate **3g** (n=2).

Finally, we prepared formate **10** to investigate the possibility of trapping the Sm-enolate intermediate with a formate ester in a 'radical then Dieckman' cyclization cascade (Scheme 5). Palladium-catalyzed carbonylation of **7b** in the presence of ethane-1,2-diol gave ester **8h**. Mitsunobu reaction with formic acid was used to introduce the formate group[14] and deprotection of the silyl ether gave **9**. Finally, a Swern oxidation[15] gave formate-aldehyde **10** in excellent yield (Scheme 5).



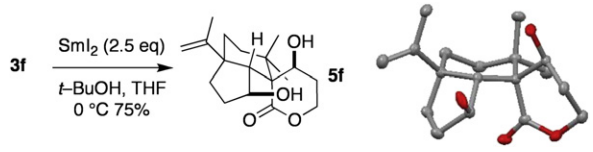
Scheme 5. Synthesis of 'dialdehyde' cyclization substrate **10**.

With dialdehydes **3a–3f** in hand we investigated the proposed cyclization sequence. Pleasingly, upon treatment with SmI_2, dialdehydes **3a–3e** underwent double cyclization to give tricyclic products **5a–5e** in good yield and with excellent control in the construction of four stereocenters (Scheme 6).[16] The cyclization of **3b** and **3d**, 3:1 mixture of diastereoisomers, led to **5b** and **5d** as similar diastereoisomeric mixtures that were readily separated by chromatography. The structure of **5a** and **5b** was confirmed by X-ray crystallography (Scheme 6).[7]



Scheme 6. Sequential dialdehyde cyclizations mediated by SmI_2.

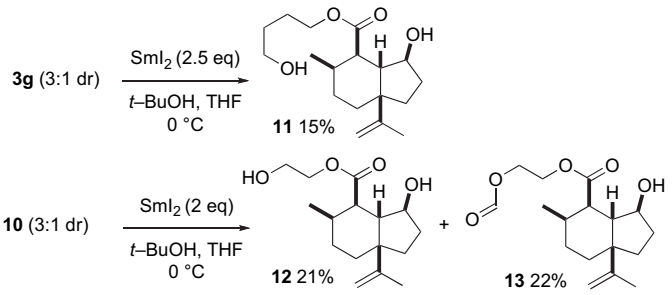
Interestingly, the sequential cyclization of **3f** containing a *gem*-dimethyl group gave **5f** containing the opposite configuration at the quaternary stereocenter constructed during the aldol stage of the cascade (Scheme 7). The structure of **5f** was confirmed by X-ray crystallographic analysis.[7] We have previously observed a similar switch in diastereoselectivity in the protonation of an analogous Sm(III)-enolate.[6] It is likely that this switch is evidence of a different conformation for the intermediate Sm-enolate where the most accessible face is now the top face.



Scheme 7. Sequential cyclization of dialdehyde **3f** mediated by SmI_2.

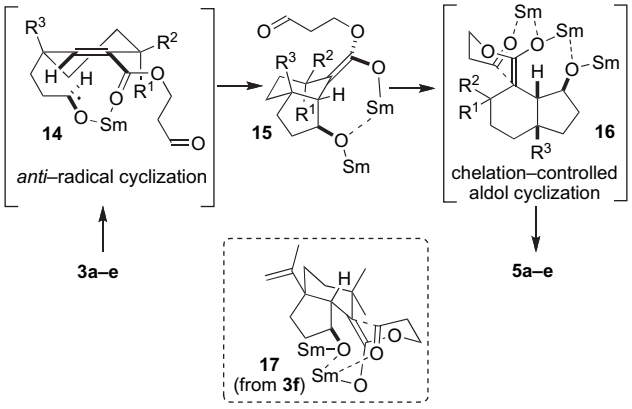
Unfortunately, attempts to form a larger lactone ring in the second stage of the cyclization were unsuccessful: treatment of **3g** with SmI_2 gave a complex mixture from which **11** was isolated in 15% yield (Scheme 8). Similarly, attempts to carry out a 'radical then Dieckman' cascade using substrate **10** were unsuccessful: alcohol **12** and formate **13** were the major products isolated in a combined yield of 43% (Scheme 8). Presumably, substrates **3g** and **10** fail to undergo the second stage of the cascade as protonation of the Sm-enolate intermediate is faster than cyclization to form a seven-membered ring.

We believe that the highly diastereoselective cascade reactions begin with an *anti*-selective ketyl-olefin cyclization through transition structure **14** to give samarium enolates **15**.[10] Chelation to Sm(III) leads to selective enolate formation and subsequently to diastereoselective aldol cyclization through six-membered transition structure **16** on the most open bottom face of enolates **15**



Scheme 8. Unsuccessful cyclizations of **3g** and **10**.

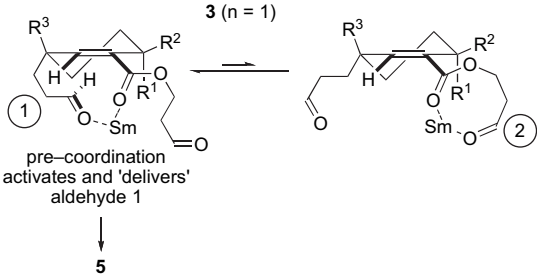
(Scheme 9). Substrate **3f** is an exception and the aldol cyclization proceeds through attack on the top face of a Sm(III)-enolate **17** in a different conformation (also Scheme 9).



Scheme 9. Origin of diastereoselectivity in the dialdehyde cyclization sequence.

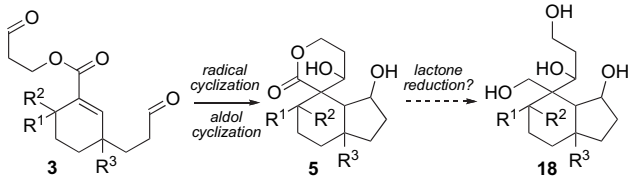
It is interesting to speculate on the origin of the apparent selectivity for one aldehyde over the other in our studies, and in the reduction reported by Takahashi and Nakata.[8] Provided the cascade begins with the addition of a ketyl radical anion to the alkene,[9] we believe that there are two possible explanations for the apparent difference in reactivity of the two aldehydes.

1) It is thought that the reduction of carbonyl groups with SmI_2 is reversible, with the ketyl radical anion being drained from the equilibrium by cyclization.[17] As only aldehyde group 1 in **3** is able to undergo facile cyclization, that aldehyde is seen to react in the presence of the other.
2) It is well appreciated that pre-coordination of Lewis acidic samarium to the carbonyl and unsaturated ester components in ketyl-olefin cyclizations is important for promoting reaction and controlling the diastereoselectivity of such additions.[18] Pre-coordination of samarium to the aldehyde and ester carbonyl groups may increase the reactivity of the proximal aldehyde group 1 leading to its selective reduction over the remote aldehyde (Scheme 10).



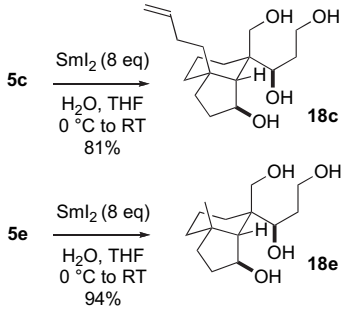
Scheme 10. Pre-coordination as a possible origin of selectivity.

Finally, we have studied the feasibility of extending the cascade to include reduction of the lactone ring in the products (Scheme 11). We have recently reported the first reductions of some simple aliphatic esters and lactones using SmI_2 with water as a cosolvent.[19,20] The reduction of lactones using SmI_2–H_2O is particularly selective in that only six-membered lactones are reduced in the presence of other lactones and esters.[19] We have proposed that anomeric stabilization of the radical anion formed by electron transfer from Sm(II) to the lactone carbonyl is crucial for the success of the reductions and therefore, the conformation of the radical-anion intermediates (and the lactone starting materials) is important.



Scheme 11. Extending the dialdehyde cyclization cascade.

We began by studying the final, lactone reduction stage of the extended sequence. Treatment of spirocyclic lactones **5c** and **5e** with SmI_2–H_2O gave the expected tetraols **18c** and **18e** in good yield (Scheme 12).

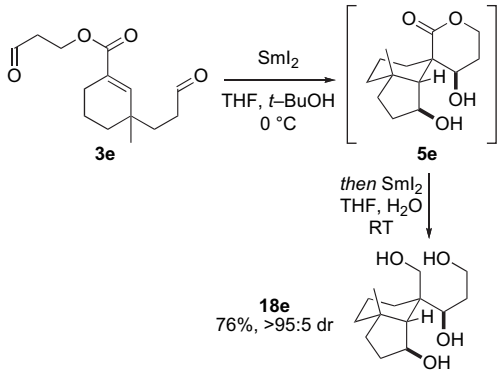


Scheme 12. Lactone reduction using SmI_2–H_2O.

Interestingly, attempted reduction of spirocyclic lactones **5b**, **5d** and **5f** returned only starting material. We believe the conformation of the lactone ring in **5b**, **5d** and **5f** renders the lactone carbonyl unreactive to SmI_2–H_2O. This hypothesis is supported in part by X-ray crystallographic data (Schemes 6 and 7): the chair conformation of the lactone rings in **5c** and **5e** facilitates reduction to give axial radical anions stabilized by the anomeric effect,[19] whereas the distorted chair conformation of the lactone ring in **5b** or the boat conformation in **5f** renders the lactone carbonyl unreceptive to electron transfer.[19]

We next investigated the extended cascade reaction. Although attempts to carry out a one-pot sequence using SmI_2–H_2O were unsuccessful,[21] successive one-pot treatment of **3e** with SmI_2 in THF/*t*-BuOH and SmI_2–H_2O gave **18e** in 76% yield (Scheme 13).

In summary, we have shown the feasibility of SmI_2-mediated, dialdehyde, 'radical then aldol' cyclization cascades in which one aldehyde is reduced while the other waits in line. In the cascade reactions studied here, two rings and four contiguous stereocenters are generated with high diastereocontrol. We have also identified some current limitations of the approach. We believe the cascade reaction of dialdehydes constitutes a new class of SmI_2-mediated sequence.[1a] Finally, we have shown the feasibility of extending the cascade sequence to include lactone reduction. These studies provide a further illustration of the remarkable selectivity possible in the reduction of lactones with SmI_2–H_2O and raise the possibility of using conformational change to 'switch on' reactivity in SmI_2-mediated chemistry.



Scheme 13. One-pot, additive-controlled dialdehyde reaction cascade.

3. Experimental

3.1. General methods and procedures

All reactions were carried out under an inert nitrogen atmosphere unless otherwise stated. Glassware for inert atmosphere reactions was oven-dried and cooled under a flow of nitrogen. Tetrahydrofuran (THF) was distilled over sodium wire and benzophenone, CH_2Cl_2, toluene and triethylamine were distilled over calcium hydride and dimethyl formamide (DMF) was dried over activated molecular sieves. All other solvents and reagents were purchased from commercial sources and used as supplied. ^1H NMR spectra were recorded on a 300, 400 or 500 MHz spectrometer; ^{13}C NMR spectra were recorded on a 75, 100 or 125 MHz spectrometer. All chemical shift values are reported in parts per million, with coupling constants in hertz. The notation of signals is: δ_H chemical shift in ppm (number of protons, multiplicity, *J* value(s), proton assignment). δ_C chemical shift in ppm (carbon assignment). If assignment is ambiguous, for example in the case of overlapping aromatic signals, a range of shifts is reported. Routine TLC analysis was carried out on aluminium sheets coated with silica gel 60 F254, 0.2 mm thickness. Solvent systems were petroleum ether 40–60/ethyl acetate. Plates were viewed with a 254 nm ultraviolet lamp and dipped in aqueous potassium permanganate, *p*-anisaldehyde or DNP. Flash column chromatography was carried out on 40–63 μm, 60A silica gel. Low-resolution mass and high-resolution mass spectra were obtained using electron impact ionisation (EI) and chemical ionisation (CI) techniques, or positive and/or negative electrospray ionisation (ES). Melting points were measured on a variable heater apparatus and are uncorrected. IR spectra were recorded on a FTIR spectrometer as evaporated films (from CH_2Cl_2) or neat, using sodium chloride windows.

3.2. General procedure 1. Formation of vinyl triflates 7a–f

To a stirred suspension of copper(I) iodide in THF at −45 °C was added a solution of the Grignard reagent over 30 min. After stirring for a further 30 min, a solution of the α,β-unsaturated ketone **6a–c** in THF was added dropwise. The reaction was stirred at −45 °C until the disappearance of the α,β-unsaturated ketone was observed by TLC analysis of the reaction mixture, this generally occurred after approximately 1 h. A solution of Comins' reagent in THF was added and the reaction was allowed to warm to room temperature and stirred until completion as judged by TLC analysis. The reaction was quenched by the addition of aqueous saturated NH_4Cl and the aqueous phase was extracted with Et_2O (×3). The combined organic fractions were dried (Na_2SO_4) and concentrated in vacuo. The crude vinyl triflate was purified by chromatography on silica gel.

3.2.1. 3-(3-(tert-Butyldimethylsilyloxy)propyl)-3-(prop-1-en-2-yl)-cyclohex-1-enyl trifluoromethanesulfonate ***7a****.* General procedure 1

using isopropenyl magnesium bromide in THF (0.50 M, 16.0 mL, 8.00 mmol), copper(I) iodide (1.52 g, 8.00 mmol) in THF (8 mL), 3-(3-(*tert*-butyldimethylsilyloxy)propyl)cyclohex-2-enone[6] **6a** (1.07 g, 3.99 mmol) in THF (4 mL) and Comins' reagent (3.46 g, 8.81 mmol) in THF (9 mL) after 24 h gave **7a** (1.44 g, 3.25 mmol, 81%) as a colourless oil. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 0.05 (6H, s, Si(CH_3)$_2$), 0.90 (9H, s, C(CH_3)$_3$), 1.22–1.53 (4H, m, CH_2), 1.55–1.80 (4H, m, CH_2), 1.70 (3H, m, H_2C=CCH_3), 2.27 (2H, m, CH_2COS), 3.58 (2H, m, CH_2CH_2O), 4.70 (1H, dd, J=0.7, 1.6 Hz, C=CH_2), 4.94 (1H, t, J=1.5 Hz, C=CH_2), 5.73 (1H, s, *H*C=COS). ^{13}C NMR ($CDCl_3$, 75 MHz) δ −5.3 (Si(CH_3)$_2$), 18.3 (*C*(CH_3)$_3$), 18.7 (H_2C=C*C*H$_3$), 19.0 (CH_2CH_2COS), 25.9 (SiC(*C*H$_3$)$_3$), 27.3 (CH_2CH_2O), 27.9 (CH_2COS), 31.6 (C*C*H$_2$(CH$_2$)$_2$COS), 35.1 (C*C*H$_2$(CH$_2$)$_2$O), 45.3 (*C*), 63.2 (CH_2O), 114.6 (H_2*C*=C), 124.3 (H*C*=COS), 147.8 (HC=*C*OS), 149.2 (*C*=CH$_2$). CF_3 not observed. ν_{max} (thin film/cm^{-1}): 2952 (s), 2891 (m), 2859 (s), 1686 (m), 1637 (m), 1418 (s), 1248 (s), 1209 (s). MS (ES$^+$) *m*/*z* (%): 443 (10, M+H), 460 (14, M+NH$_4$), 465 (100, M+Na). HRMS: calcd for C_{19} (M+H): 443.1894. Found: 443.1897.

3.2.2. rac-(3R,6R)-3-(3-(tert-Butyldimethylsilyloxy)propyl)-6-methyl-3-(prop-1-en-2-yl)cyclohex-1-enyl trifluoromethanesulfonate ***7b***. For the preparation of **7b**, see Ref. 6.

3.2.3. 3-(But-3-enyl)-3-(3-(tert-butyldimethylsilyloxy)propyl)-cyclohex-1-enyl trifluoromethanesulfonate ***7c***. General procedure 1 using butenyl magnesium bromide in THF (0.52 M, 20.0 mL, 10.4 mmol), copper(I) iodide (2.06 g, 10.6 mmol) in THF (36 mL), 3-(3-(*tert*-butyldimethylsilyloxy)propyl)cyclohex-2-enone[6] **6a** (1.12 g, 4.16 mmol) in THF (10 mL) and Comins' reagent (3.26 g, 8.32 mmol) in THF (6 mL) after 12 h gave **7c** (1.40 g, 3.07 mol, 74%) as a pale yellow oil. ^{1}H NMR ($CDCl_3$, 500 MHz) δ 0.06 (6H, s, Si(CH_3)$_2$); 0.90 (9H, s, C(CH_3)$_3$), 1.38–1.53 (8H, m, CH_2), 1.83–1.77 (2H, m, CH_2CH_2COS), 2.02 (2H, q, J=8.3 Hz, CH_2CH=CH$_2$), 2.28 (2H, t, J=6.3 Hz, CH_2COS), 3.59 (2H, t, J=6.3 Hz, CH_2O), 4.95 (1H, dd, J=10.1, 1.8 Hz, *cis* CH_2=CH), 5.02 (1H, dd, J=17.2, 1.8 Hz, *trans* CH_2=CH), 5.54 (1H, s, *H*C=COS), 5.79 (1H, ddt, J=17.1, 10.1, 6.7 Hz, *C*H=CH$_2$). ^{13}C NMR ($CDCl_3$, 125 MHz) δ −5.4 (Si(CH_3)$_2$), 18.3 (*C*(CH_3)$_3$), 19.3 (CH_2CH_2COS), 25.9 (C(*C*H$_3$)$_3$), 27.1 (CH_2), 27.5 (CH_2COS), 28.1 (CH_2CH=CH$_2$), 31.1 (CH_2), 35.3 (CH_2), 38.2 (CH_2), 38.5 (*C*), 63.3 (CH_2O), 114.5 (H_2*C*=CH), 126.1 (*C*H=COS), 138.6 (*C*H=CH$_2$), 148.9 (C=COS). CF_3 not observed. ν_{max} (thin film/cm^{-1}): 2938 m (s), 1419 (s), 1142 (m), 1004 (w), 836 (w). MS (ES$^+$) *m*/*z* (%): 474 (100, M+NH$_4$); Calcd for C_{20}H (M+H): 457.2050. Found: 457.2045.

3.2.4. rac-(3S,6R)-3-(But-3-enyl)-3-(3-(tert-butyldimethylsilyloxy)-propyl)-6-methylcyclohex-1-enyl trifluoromethanesulfonate ***7d***. General procedure 1 using butenyl magnesium bromide in THF (0.50 M, 17.7 mL, 8.85 mmol), copper(I) iodide (1.76 g, 9.20 mmol) in THF (25 mL), 3-(3-(*tert*-butyldimethylsilyloxy)propyl)-6-methylcyclohex-2-enone[6] **6b** (1.00 g, 3.54 mmol) in THF (10 mL) and Comins' reagent (2.78 g, 7.08 mmol) in THF (6 mL) after 12 h gave **7d** (1.39 g, 2.95 mmol, 83%; dr 3:1) as a pale yellow oil. ^{1}H NMR ($CDCl_3$, 500 MHz) δ 0.05 (s, Si(CH_3)$_2$, minor diastereoisomer), 0.06 (6H, s, Si(CH_3)$_2$), 0.90 (9H, s, C(CH_3)$_3$), 1.14 (3H, d, J=7.0 Hz, CH*C*H$_3$), 1.32–1.47 (9H, m, CH_2), 1.85–1.94 (1H, m, 1H from CH_2CHCH$_3$), 1.94–2.01 (2H, m, CH_2CH=CH$_2$), 2.44 (1H, sextet, J=6.5 Hz, *CH*CH$_3$), 3.59 (2H, t, J=5.8 Hz, CH_2O), 4.95 (dd, J=10.1, 1.8 Hz, *cis* CH_2=CH, minor diastereoisomer), 4.96 (1H, dd, J=10.1, 1.8 Hz, *cis* CH_2=CH), 5.02 (dd, J=17.1, 1.8 Hz, *trans* CH_2=CH, minor diastereoisomer), 5.03 (1H, dd, J=17.1, 1.8 Hz, *trans* CH_2=CH), 5.49 (1H, s, *H*C=COS), 5.80 (1H, ddt, J=17.2, 10.4, 6.70 Hz, *C*H=CH$_2$). ^{13}C NMR ($CDCl_3$, 125 MHz,) δ −5.3 (Si(CH_3)$_2$), 17.8 (CH*C*H$_3$), 18.3 (*C*(CH_3)$_3$), 25.9 (C(CH_3)$_3$), 27.1 (CH_2CH_2O), 28.0 (CH_2CHCH$_3$), 28.3 (CH_2CH=CH$_2$), 29.2 (CH_2CH_2CHCH$_3$), 32.3 (*C*HCH$_3$), 35.3 (CH_2(CH$_2$)$_2$O), 38.3 (CH_2CH_2CHCH$_3$), 38.8 (*C*), 63.4 (CH_2O), 114.5 (H_2*C*=CH), 118.5 (q, J=319.7 Hz, *C*F$_3$), 125.8 (H*C*=COS), 138.6 (*C*H=CH$_2$), 152.8 (HC=*C*OS). ν_{max} (thin film/cm^{-1}): 2935 (m), 1416 (s), 1143 (m), 1004 (w), 835 (w). MS (EI$^+$) *m*/*z* (%): 471 (100, M+H); Calcd for C_{21}H: 470.2128. Found: 470.2131.

3.2.5. 3-(3-(tert-Butyldimethylsilyloxy)propyl)-3-methylcyclohex-1-enyl trifluoromethanesulfonate ***7e***. General procedure 1 using MeMgBr in Et_2O (3.00 M, 3.10 mL, 9.32 mmol), copper(I) iodide (1.78 g, 9.32 mmol) in THF (36 mL), 3-(3-(*tert*-butyldimethylsilyloxy)-propyl)cyclohex-2-enone[6] **6a** (1.00 g, 3.72 mmol) in THF (10 mL) and Comins' reagent (2.92 g, 7.43 mmol) in THF (6 mL) after 12 h gave **7e** (1.13 g, 2.71 mmol, 73%) as a pale yellow oil. ^{1}H NMR ($CDCl_3$, 500 MHz) δ 0.05 (6H, s, Si(CH_3)$_2$), 0.90 (9H, s, C(CH_3)$_3$), 1.04 (3H, s, C*C*H$_3$), 1.31–1.43 (3H, m, *CH*$_2$(CH$_2$)$_2$O, 1H from *CH*$_2$(CH$_2$)$_2$COS), 1.43–1.59 (3H, m, *CH*$_2$CH$_2$O, 1H from *CH*$_2$(CH$_2$)$_2$COS), 1.73–1.87 (2H, m, *CH*$_2$CH$_2$COS), 2.22–2.33 (2H, m, *CH*$_2$COS), 3.59 (2H, t, J=6.3 Hz, *CH*$_2$O), 5.51 (1H, s, *CH*=COS). ^{13}C NMR ($CDCl_3$, 125 MHz) δ −5.3 (Si(*C*H$_3$)$_2$), 18.3 (*C*(CH$_3$)$_3$), 19.5 (*C*H$_2$CH$_2$COS), 25.9 (C(*C*H$_3$)$_3$), 26.7 (*C*CH$_3$), 27.4 (*C*H$_2$CH$_2$O), 27.6 (*C*H$_2$COS), 33.4 (*C*H$_2$CH$_2$CH$_2$COS), 35.6 (*C*), 38.2 (*C*H$_2$(CH$_2$)$_2$O), 63.5 (*C*H$_2$O), 127.1 (*C*H=COS), 148.5 (CH=*C*OS), CF_3 not observed. ν_{max} (thin film/cm^{-1}): 2915 (w), 2857 (w), 1418 (m), 1361 (m), 1247 (m), 1208 (m), 1143 (m), 1099 (w). MS (ES$^+$) *m*/*z* (%): 325 (34), 417 (54, M+H), 434 (100, M+NH$_4$), 439 (31, M+Na). HRMS: Calcd for $C_{17}H_{35}O_4NF_3SSi$ (M+NH$_4$): 434.2003. Found: 434.2004.

3.2.6. 3-(3-(tert-Butyldimethylsilyloxy)propyl)-6,6-dimethyl-3-(prop-1-en-2-yl)cyclohex-1-enyl trifluoromethanesulfonate ***7f***. To a stirred suspension of copper(I) iodide (926 mg, 4.86 mmol) in THF (5.00 mL) at −45 °C was added a solution of isopropenyl magnesium bromide (0.50 M, 9.73 mL, 4.86 mmol) in THF over 30 min. After stirring for a further 30 min, a solution of 3-(3-(*tert*-butyldimethylsilyloxy)-propyl)-6,6-dimethylcyclohex-2-enone[6] **6c** (721 mg, 2.43 mmol) in THF (2.50 mL) was added dropwise. The reaction was stirred at −45 °C for 1 h before the reaction was quenched by the addition of aqueous saturated NH_4Cl (10 mL) and upon warming to ambient temperature the aqueous phase was extracted with Et_2O (20 mL×3). The combined organic fractions were dried (Na_2SO_4) and concentrated in vacuo. The crude product was subsequently purified by chromatography on silica gel to give 5-(3-(*tert*-butyldimethylsilyloxy)-propyl)-2,2-dimethyl-5-(prop-1-en-2-yl)cyclohexanone (678 mg, 2.00 mmol, 82%) as a colourless oil. ^{1}H NMR ($CDCl_3$, 400 MHz) δ 0.03 (6H, s, Si(CH_3)$_2$), 0.88 (9H, s, C(CH_3)$_3$), 1.05 (3H, s, C(C*H*$_3$)$_2$), 1.11 (3H, s, C(C*H*$_3$)$_2$), 1.18–1.39 (4H, m, CH_2), 1.50–1.60 (2H, m, CH_2), 1.64 (3H, s, H_2C=CCH_3), 1.68–1.87 (2H, m, CH_2), 2.29 (1H, d, J=14.6 Hz, C(O)CH_2), 2.61 (1H, dd, J=14.6, 2.3 Hz, C(O)CH_2), 3.44–3.62 (2H, m, CH_2O), 4.69 (1H, s, C=CH_2), 4.91 (1H, s, C=CH_2). ^{13}C NMR ($CDCl_3$, 100 MHz) δ −5.3 (Si(CH_3)$_2$), 18.4 (*C*(CH$_3$)$_3$), 18.9 (H_2C=C*C*H$_3$), 25.4 (C(*C*H$_3$)$_2$), 25.8 (C(*C*H$_3$)$_2$), 26.0 (C(*C*H$_3$)$_3$), 27.0 (CH_2), 30.7 (CH_2), 34.8 (CH_2), 35.8 (CH_2), 44.2 (*C*), 47.0 (C(O)CH_2), 47.4 (C(O)*C*(CH$_3$)$_2$), 63.3 (*C*H$_2$O), 114.2 (C=*C*H$_2$), 147.4 (*C*=CH$_2$), 216.1 (*C*=O). ν_{max} (thin film/cm^{-1}): 2936 (s), 2859 (m), 1706 (s, C=O), 1637 (w), 1462 (m), 1385 (w), 1255 (m), 1201 (w), 1101 (s). MS (ES$^+$) *m*/*z* (%): 247 (50, (M-SiMe$_2$*t*-Bu)+Na), 339 (5, M+H), 361 (100, M+Na). HRMS: calcd for $C_{20}H_{38}O_2NaSi$ (M+Na): 361.2533. Found: 361.2525. To a stirred solution of diisopropylamine (0.32 mL, 2.26 mmol) in THF (2.00 mL) at −78 °C was added a solution of *n*-butyllithium in hexanes (2.15 M, 1.05 mL, 2.26 mmol). After stirring for 20 min, a solution of 5-(3-(*tert*-butyldimethylsilyloxy)propyl)-2,2-dimethyl-5-(prop-1-en-2-yl)cyclohexanone (638 mg, 1.88 mmol) in THF (2.00 mL) was added dropwise. After 1 h, a solution of Comins' reagent (1.48 g, 3.77 mmol) in THF (4 mL) was added and the reaction was stirred for 2 h at −78 °C before being allowed to warm to 0 °C and stirred for 1 h. The reaction was quenched with water (10 mL) and the aqueous phase was extracted with Et_2O (10 mL×3). The combined organic fractions were washed with ice cold aqueous NaOH (0.1 M, 5 mL×2) before being dried (Na_2SO_4) and concentrated in vacuo. Purification by chromatography on silica gel gave **7f** (691 mg, 1.47 mmol, 78%) as a colourless oil. ^{1}H NMR ($CDCl_3$, 400 MHz) δ 0.05 (6H, s, Si(CH_3)$_2$), 0.90 (9H, s,

C(CH_3)$_3$), 1.12 (3H, s, C(CH_3)$_2$), 1.14 (3H, s, C(CH_3)$_2$), 1.31–1.55 (6H, m, CH_2), 1.57–1.69 (2H, m, CH_2), 1.71 (3H, s, H_2C=CCH_3), 3.52–3.65 (2H, m, CH_2O), 4.75 (1H, s, C=CH_2), 4.93 (1H, s, C=CH_2), 5.60 (1H, s, HC=COS). ^{13}C NMR ($CDCl_3$, 100 MHz) δ −5.3 (Si(CH_3)$_2$), 18.3 (C(CH)$_3$), 18.7 (H_2C=CCCH_3), 25.6 (C(CH_3)$_2$), 25.9 (C(CH_3)$_3$), 26.4 (C(CH_3)$_2$), 27.3 (CH_2), 28.7 (CH_2), 35.0 (CH_2), 35.2 (CH_2), 35.3 (C(CH$_3$)$_2$), 46.3 (C), 63.2 (CH_2O), 114.6 (C=CH_2), 122.1 (HC=COS), 147.7 (C=CH_2), 155.6 (HC=COS). CF_3 not observed. ν_{max} (thin film/cm^{-1}): 2932 (s), 2891 (m), 2863 (s), 1670 (w), 1634 (w), 1463 (w), 1414 (s), 1366 (w), 1248 (m). MS (ES$^+$) m/z (%): 471 (10, M+H), 493 (100, M+Na). HRMS: calcd for $C_{21}H_{37}O_4F_3NaSSi$ (M+Na): 493.2026. Found: 493.2035.

3.3. General procedure 2. Carbonylative coupling of vinyl triflates 7a–f with a diol to give 8a–8h

Carbon monoxide gas was bubbled through a suspension of the vinyl triflate (1 equiv), palladium acetate (0.2 or 0.4 equiv), triphenylphosphine (0.4 or 0.8 equiv), diol (40 equiv) and triethylamine (2 equiv) in DMF for 30 min. The reaction was then heated at 40 or 50 °C under an atmosphere of carbon monoxide until the disappearance of the vinyl triflate was observed by TLC analysis. Upon cooling, the reaction was quenched with water and extracted with Et_2O (×3). The combined organic extracts were dried (Na_2SO_4) and concentrated in vacuo. The crude products were purified by chromatography on silica gel.

3.3.1. 3-Hydroxypropyl 3-(3-(tert-butyldimethylsilyloxy)propyl)-3-(prop-1-en-2-yl)cyclohex-1-enecarboxylate ***8a****.* General procedure 2 using 3-(3-(*tert*-butyldimethylsilyloxy)propyl)-3-(prop-1-en-2-yl)-cyclohex-1-enyl trifluoromethanesulfonate **7a** (868 mg, 1.96 mmol), palladium acetate (88.0 mg, 0.392 mmol), triphenylphosphine (206 mg, 0.784 mmol), propan-1,3-diol (5.67 mL, 78.4 mmol) and triethylamine (0.547 mL, 3.92 mmol) in DMF (10 mL) at 40 °C gave, after 24 h, **8a** (717 mg, 1.81 mmol, 92%) as a yellow oil. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 0.05 (6H, s, Si(CH_3)$_2$), 0.89 (9H, s, C(CH_3)$_3$), 1.15–1.80 (8H, m, CH_2), 1.72 (3H, m, H_2C=CCH_3), 1.92 (2H, quintet, J=6.0 Hz, $OCH_2CH_2CH_2O$), 2.06–2.35 (2H, m, CH_2C=CH), 3.58 (2H, m, CH), 3.71 (2H, t, J=5.8 Hz, CH_2OH), 4.32 (2H, t, J=5.8 Hz, CH_2OC(O)), 4.58 (1H, dd, J=0.8, 1.7 Hz, C=CH_2), 4.90 (1H, t, J=1.5 Hz, C=CH_2), 6.95 (1H, s, C(O)C=CHC). ^{13}C NMR ($CDCl_3$, 100 MHz) δ −5.3 (Si(CH_3)$_2$), 18.4 (C(CH$_3$)$_3$), 18.6 (CH_2), 18.8 (H_2C=CCH$_3$), 24.8 (CH_2), 26.0 (C(CH_3)$_3$), 27.4 (CH_2), 31.8 (CH_2), 31.9 (CH_2), 34.9 (CH_2), 44.6 (C), 59.3 (CH_2OH), 61.2 (CH_2OC(O)), 63.4 (CH_2OSi), 114.1 (H_2C=C), 129.7 (HC=CC(O)), 145.3 (HC=CC(O)), 148.4 (H_2C=C), 167.9 (C=O). ν_{max} (thin film/cm^{-1}): 3411 (br), 2950 (s), 2892 (m), 2858 (s), 1713 (s, C=O), 1643 (w), 1470 (w), 1389 (w), 1257 (s), 1098 (s). MS (ES$^+$) m/z (%): 397 (10, M+H), 414 (15, M+NH_4), 419 (100, M+Na). HRMS: calcd for $C_{22}H_{41}O_4Si$ (M+H): 397.2769. Found: 397.2764.

3.3.2. rac-(3R,6R)-3-Hydroxypropyl 3-(3-(tert-butyldimethylsilyloxy)-propyl)-6-methyl-3-(prop-1-en-2-yl)cyclohex-1-enecarboxylate ***8b****.* General procedure 2 using *rac*-(3*R*,6*R*)-3-(3-(*tert*-butyldimethylsilyloxy)propyl)-6-methyl-3-(prop-1-en-2-yl)cyclohex-1-enyl trifluoromethanesulfonate **7b**[6] (301 mg, 0.659 mmol, dr 3:1), palladium acetate (30.0 mg, 0.132 mmol), triphenylphosphine (69.0 mg, 0.264 mmol), propan-1,3-diol (1.43 mL, 19.8 mmol) and triethylamine (0.184 mL, 1.32 mmol) in DMF (3 mL) at 40 °C, after 16 h, gave **8b** (214 mg, 0.521 mmol, 79%, dr 3:1) as a yellow oil. ^{1}H NMR ($CDCl_3$, 500 MHz, major diastereoisomer) δ 0.04 (6H, s, Si(CH_3)$_2$), 0.89 (9H, s, C(CH_3)$_3$), 1.04 (3H, d, J=6.6 Hz, CHCH_3), 1.33–1.81 (8H, m, CH_2), 1.73 (3H, s, H_2C=CCH_3), 1.92 (2H, quintet, J=6.1 Hz, $OCH_2CH_2CH_2O$), 2.06 (1H, br s, OH), 2.54–2.72 (1H, m, CHCH$_3$), 3.50–3.65 (2H, m, CH), 3.71 (2H, br s, CH), 4.33 (2H, t, J=6.0 Hz, CH_2OC(O)), 4.65 (1H, s, C=CH_2), 4.87 (1H, s, C=CH_2), 6.89 (1H, s, C(O)C=CHC). ^{13}C NMR ($CDCl_3$, 125 MHz, major diastereoisomer) δ −5.3 (Si(CH_3)$_2$), 18.3 (C(CH$_3$)$_3$), 19.0 (H_2C=CCH$_3$), 20.1 (CHCH$_3$), 26.0 (C(CH_3)$_3$), 27.3 (CH_2), 27.4 (CH_2), 29.1 (CHCH$_3$), 30.2 (CH_2), 32.0 (CH_2CH_2OH), 34.5 (CH_2), 44.6 (C), 59.2 (CH_2OH), 61.0 (C(O)OCH_2), 63.4 (CH_2OSi), 113.0 (H_2C=C), 134.8 (C(O)C=CH), 144.7 (C(O)C=CH), 149.0 (H_2C=C), 168.2 (C=O). ^{1}H NMR ($CDCl_3$, 500 MHz, minor diastereoisomer) δ 0.05 (6H, s, Si(CH_3)$_2$), 0.90 (9H, s, C(CH_3)$_3$), 1.07 (3H, d, J=6.9 Hz, CHCH_3), 1.33–1.81 (8H, m, CH_2), 1.72 (3H, s, H_2C=CCH_3), 1.92 (2H, quintet, J=6.1 Hz, $OCH_2CH_2CH_2O$), 2.06 (1H, br s, OH), 2.54–2.72 (1H, m, CHCH$_3$), 3.50–3.65 (2H, m, CH), 3.71 (2H, br s, CH), 4.33 (2H, t, J=6.0 Hz, CH_2OC(O)), 4.53 (1H, s, C=CH_2), 4.89 (1H, s, C=CH_2), 6.86 (1H, s, C(O)C=CHC). ^{13}C NMR ($CDCl_3$, 125 MHz, minor diastereoisomer) δ −5.3 (Si(CH_3)$_2$), 18.3 (C(CH$_3$)$_3$), 18.8 (CHCH$_3$), 19.8 (H_2C=CCH$_3$), 26.0 (SiC(CH_3)$_3$), 26.5 (CH_2), 27.5 (CH_2), 28.1 (CHCH$_3$), 30.2 (CH_2), 32.0 (CH_2CH_2OH), 35.0 (CH_2), 44.9 (C), 59.2 (CH_2OH), 61.0 (C(O)OCH_2), 63.4 (CH_2OSi), 114.3 (H_2C=C), 134.7 (C(O)C=CH), 145.0 (C(O)C=CH), 147.9 (H_2C=C), 167.9 (C=O). ν_{max} (thin film/cm^{-1}): 3468 (br), 2931 (m), 2858 (w), 1705 (m, C=O), 1458 (w), 1377 (w), 1249 (s), 1097 (m). MS (ES$^+$) m/z (%): 433 (100, M+Na). HRMS: calcd for $C_{23}H_{46}O_4NSi$ (M+NH_4): 428.3191. Found: 428.3193.

3.3.3. 3-Hydroxypropyl 3-(but-3-enyl)-3-(3-(tert-butyldimethylsilyloxy)propyl)cyclohex-1-enecarboxylate ***8c****.* General procedure 2 using 3-(but-3-enyl)-3-(3-(*tert*-butyldimethylsilyloxy)propyl)-cyclohex-1-enyl trifluoromethanesulfonate **7c** (230 mg, 0.504 mmol), palladium acetate (23.0 mg, 0.101 mmol), triphenylphosphine (53.0 mg, 0.201 mmol), propan-1,3-diol (1.46 mL, 20.1 mmol) and triethylamine (0.140 mL, 1.01 mmol) in DMF (1.7 mL) at 40 °C gave, after 12 h, **8c** (107 mg, 0.261 mmol, 52%) as a yellow oil. ^{1}H NMR ($CDCl_3$, 500 MHz) δ 0.04 (6H, s, Si(CH_3)$_2$), 0.89 (9H, s, C(CH_3)$_3$), 1.36–1.51 (8H, m, CH_2), 1.62–1.67 (2H, m, CH_2CH_2CC(O)), 1.91 (2H, quintet, J=6.0 Hz, $OCH_2CH_2CH_2O$), 1.97–2.04 (2H, m, CH_2CH=CH_2), 2.20 (2H, t, J=6.0 Hz, CH_2CC=O), 3.57 (2H, t, J=6.0 Hz, CH_2OSi), 3.70 (2H, t, J=6.0 Hz, CH_2OH), 4.30 (2H, t, J=6.0 Hz, CH_2OC(O)), 4.93 (1H, d, J=10.1 Hz CH=CH_2 *cis*), 5.00 (1H, d, J=17.1 Hz, CH=CH_2 *trans*), 5.78 (1H, ddt, J=17.7, 10.1, 6.5 Hz, CH=CH$_2$), 6.74 (1H, s, C(O)C=CHC). ^{13}C NMR (125 MHz, $CDCl_3$) δ −5.64 (Si(CH_3)$_2$), 18.4 (C(CH$_3$)$_3$), 18.9 (CH_2CH_2CC(O)), 24.3 (CH_2CC(O)), 26.0 (C(CH_3)$_3$), 27.2 (CH_2), 28.2 (CH_2CH=CH_2), 31.4 (CH_2), 31.9 (CH_2CH_2OH), 35.1 (CH_2), 37.7 (C), 38.4 (CH_2), 59.2 (CH_2OH), 61.2 (CH_2OC(O)), 63.6 (CH_2OSi), 114.3 (CH_2=CH), 129.3 (HC=CC(O)), 139.0 (CH=CH$_2$), 147.4 (HC=CC(O)), 168.1 (C=O). ν_{max} (thin film/cm^{-1}): 3427 (s), 2932 (s), 2857 (s), 1712 (s, C=O), 1641 (w), 1460 (w), 1389 (w), 1268 (s), 1098 (s), 1055 (m), 972 (w), 911 (w), 836 (s), 776 (m). MS (ES$^+$) m/z (%): 433 (100, M+Na). HRMS: Calcd for $C_{23}H$ (M+Na): 433.2745. Found: 433.2741.

3.3.4. rac-(3S,6R)-3-Hydroxypropyl 3-(but-3-enyl)-3-(3-(tert-butyldimethylsilyloxy)propyl)-6-methylcyclohex-1-enecarboxylate ***8d****.* General procedure 2 using *rac*-(3*S*,6*R*)-3-(but-3-enyl)-3-(3-(*tert*-butyldimethylsilyloxy)propyl)-6-methylcyclohex-1-enyl trifluoromethanesulfonate **7d** (1.59 g, 3.38 mmol, dr 3:1), palladium acetate (152 mg, 0.676 mmol), triphenylphosphine (354 mg, 1.35 mmol), propan-1,3-diol (9.70 mL, 135 mmol) and triethylamine (0.942 mL, 6.76 mmol) in DMF (11.2 mL) at 40 °C, after 12 h, gave **8d** (618 mg, 1.46 mmol, 43%, dr 3:1) as a yellow oil. ^{1}H NMR ($CDCl_3$, 500 MHz) δ 0.04 (6H, s, Si(CH_3)$_2$), 0.88 (9H, s, C(CH_3)$_3$), 1.02 (3H, d, J=6.8 Hz, CH_3), 1.04 (d, J=6.8 Hz, CH_3 (minor diastereoisomer)), 1.24–1.62 (9H, m, CH_2), 1.72–1.81 (1H, m, 1H from CH_2CHCH$_3$), 1.88–1.97 (2H, m, CH_2CH_2OH), 1.98–2.08 (2H, m, CH_2CH=CH_2), 2.60–2.61 (1H, m, CHCH$_3$), 3.53–3.60 (2H, m, CH_2OSi), 3.70 (2H, t, J=6.0 Hz, CH_2OH), 4.26–4.35 (2H, m, CH_2OC(O)), 4.92 (dd, J=10.1, 1.8 Hz CH=CH_2 *cis*, minor diastereoisomer), 4.93 (1H, dd, J=10.1, 1.8 Hz CH=CH_2 *cis*), 4.99 (dd, J=16.9, 1.8 Hz, CH=CH_2 *trans*, minor diastereoisomer), 5.01 (1H, dd, J=16.9, 1.8 Hz, CH=CH_2 *trans*), 5.80 (1H, ddt J=16.9, 10.3, 6.6 Hz, CH=CH$_2$), 6.66 (1H, s, C(O)C=CHC). ^{13}C NMR (125 MHz, $CDCl_3$) δ −5.6 (Si(CH_3)$_2$), 18.0 (C(CH$_3$)$_3$), 19.7 (CHCH$_3$), 25.6 (C(CH_3)$_3$), 26.2 (CH_2), 26.7 (CH_2), 26.9 (CH_2), 27.6 (CHCH$_3$), 28.0 (CH_2), 31.6

(CH_2CH_2OH), 34.7 (CH_2), 37.6 (C), 38.0 (CH_2), 58.8 (CH_2OH), 60.7 ($C(O)OCH_2$), 63.3 (CH_2OSi), 114.0 ($H_2C{=}CH$), 134.0 ($C(O)C{=}CH$), 138.6 ($H_2C{=}CH$), 146.7 ($C(O)C{=}CH$), 167.6 ($C{=}O$). ν_{max} (thin film/cm^{-1}): 3434 (s), 2928 (s), 2857 (s), 1712 (s, C=O), 1640 (w), 1472 (w), 1388 (w), 1361 (w), 1255 (s), 1060 (m), 1005 (w), 939 (w), 910 (w), 836 (s), 813 (w), 775 (m). MS (ES^+) m/z (%): 425 (100, M+H). HRMS: Calcd for $C_{24}H$ (M+H): 425.3082. Found: 425.3078.

3.3.5. 3-Hydroxypropyl 3-(3-(tert-butyldimethylsilyloxy)propyl)-3-methylcyclohex-1-enecarboxylate ***8e***. General procedure 2 using 3-(3-(*tert*-butyldimethylsilyloxy)propyl)-3-methylcyclohex-1-enyl trifluoromethanesulfonate **7e** (1.00 g, 2.40 mmol), palladium acetate (108 mg, 0.481 mmol), triphenylphosphine (252 mg, 0.961 mmol), propan-1,3-diol (6.94 mL, 96.0 mmol) and triethylamine (0.669 mL, 4.80 mmol) in DMF (8 mL) at 40 °C after 12 h gave **8e** (564 mg, 1.52 mmol, 63%) as a brown oil. ^{1}H NMR ($CDCl_3$, 500 MHz) δ 0.03 (6H, s, $Si(CH_3)_2$), 0.88 (9H, s, $C(CH_3)_3$), 0.99 (3H, s, CCH_3), 1.41–1.29 (3H, m, $CH_2(CH_2)_2OSi$, 1H from CH_2CH_2OSi), 1.42–1.54 (3H, m, $CH_2(CH_2)_2CC(O)$, 1H from CH_2CH_2OSi), 1.56–1.70 (2H, m, $CH_2CH_2C(O)$), 1.89 (2H, quintet, J=6.3 Hz, $OCH_2CH_2CH_2O$), 2.12 (1H, dt, J=19.7, 7.8 Hz, 1H from $CH_2CC(O)$), 2.24 (1H, dt, J=17.6, 5.6 Hz, 1H from $CH_2CC(O)$), 3.56 (2H, t, J=6.3 Hz, CH_2OSi), 3.68 (2H, t, J=6.1 Hz, CH_2OH), 4.27 (2H, t, J=6.1 Hz, $CH_2OC(O)$), 6.69 (1H, s, $C(O)C{=}CHC$). ^{13}C NMR (125 MHz, $CDCl_3$) δ −5.64 ($Si(CH_3)_2$), 18.0 ($C(CH_3)_3$), 18.6 ($CH_2CH_2CC(O)$), 24.0 ($CH_2CC{=}O$), 25.6 ($C(CH_3)_3$), 26.1 (CH_3), 27.1 ($CH_2CH_2CH_2CC(O)$), 31.5 (CH_2CH_2OH), 33.2 (CH_2CH_2OSi), 34.7 (C), 37.6 ($CH_2(CH_2)_2OSi$), 58.8 (CH_2OH), 60.8 ($CH_2OC(O)$), 63.3 (CH_2OSi), 128.1 ($HC{=}CC(O)$), 148.0 ($HC{=}CC(O)$), 167.8 ($C{=}O$). ν_{max} (thin film/cm^{-1}): 3453 (s), 2933 (s), 2894 (s), 1713 (s, C=O), 1644 (m), 1471 (m), 1463 (m), 1389 (m), 1360 (w), 1274 (s), 1154 (w), 1099 (s), 1056 (m), 1005 (w), 938 (w), 836 (s), 775 (s). MS (EI^+) m/z (%): 393 (100, M+Na). HRMS: Calcd for $C_{20}H$ (M+H): 371.2612. Found: 371.2613.

3.3.6. 3-Hydroxypropyl 3-(3-(tert-butyldimethylsilyloxy)propyl)-6,6-dimethyl-3-(prop-1-en-2-yl)cyclohex-1-enecarboxylate ***8f***. General procedure 2 using 3-(3-(*tert*-butyldimethylsilyloxy)-propyl)-6,6-dimethyl-3-(prop-1-en-2-yl)cyclohex-1-enyl trifluoromethanesulfonate **7f** (691 mg, 1.47 mmol), palladium acetate (132 mg, 0.587 mmol), triphenylphosphine (308 mg, 1.18 mmol), propan-1,3-diol (4.20 mL, 58.7 mmol) and triethylamine (0.409 mL, 2.94 mmol) in DMF (7.5 mL) at 50 °C, after 5 days, gave **8f** (517 mg, 1.22 mmol, 83%) as a yellow oil. ^{1}H NMR ($CDCl_3$, 400 MHz) δ 0.04 (6H, s, $Si(CH_3)_2$), 0.89 (9H, s, $C(CH_3)_3$), 1.15 (3H, s, $C(CH_3)_2$), 1.22 (3H, s, $C(CH_3)_2$), 1.29–1.68 (8H, m, CH_2), 1.71 (3H, s, $H_2C{=}CCH_3$), 1.91 (2H, quintet, J=6.1 Hz, $OCH_2CH_2CH_2O$), 2.17 (1H, br s, OH), 3.50–3.64 (2H, m, CH), 3.70 (2H, t, J=6.1 Hz, CH), 4.30 (2H, m, $CH_2OC(O)$), 4.59 (1H, s, $C{=}CH_2$), 4.88 (1H, s, $C{=}CH_2$), 6.74 (1H, s, $C(O)C{=}CHC$). ^{13}C NMR ($CDCl_3$, 100 MHz) δ −5.3 ($Si(CH_3)_2$), 18.4 ($C(CH_3)_3$), 18.8 ($H_2C{=}CCH_3$), 26.0 ($C(CH_3)_3$), 27.3 ($C(CH_3)_2$), 27.5 (CH_2), 28.2 ($C(CH_3)_2$), 28.3 (CH_2), 32.0 (CH_2), 33.4 ($C(CH_3)_2$), 34.8 (CH_2), 36.5 (CH_2), 45.0 (C), 59.2 (CH_2OH), 60.7 ($C(O)OCH_2$), 63.4 (CH_2OSi), 113.9 ($H_2C{=}C$), 137.8 ($C(O)C{=}CH$), 144.5 ($C(O)C{=}CH$), 148.3 ($H_2C{=}C$), 168.0 ($C{=}O$). ν_{max} (thin film/cm^{-1}): 3440 (br), 2948 (s), 2839 (s), 2735 (w), 1714 (s, C=O), 1633 (m), 1461 (m), 1388 (m), 1361 (m), 1327 (w), 1253 (s), 1100 (s). MS (ES^+) m/z (%): 425 (20, M+H), 447 (100, M+Na). HRMS: calcd for $C_{24}H_{45}O_4Si$ (M+H): 425.3082. Found: 425.3082.

3.3.7. rac-(3R,6R)-4-Hydroxybutyl 3-(3-(tert-butyldimethylsilyloxy)-propyl)-6-methyl-3-(prop-1-en-2-yl)cyclohex-1-enecarboxylate ***8g***. General procedure 2 using *rac*-(3*R*,6*R*)-3-(3-(*tert*-butyldimethylsilyloxy)propyl)-6-methyl-3-(prop-1-en-2-yl)cyclohex-1-enyl trifluoromethanesulfonate **7b**[6] (502 mg, 1.10 mmol, dr 3:1), palladium acetate (49.0 mg, 0.220 mmol), triphenylphosphine (115 mg, 0.440 mmol), 1,4-butanediol (2.92 mL, 33.0 mmol) and triethylamine (0.306 mL, 2.20 mmol) in DMF (6 mL) at 40 °C, after 14 h, gave **8g** (285 mg, 0.671 mmol, 61%, dr 3:1) as a yellow oil. ^{1}H NMR ($CDCl_3$, 500 MHz, major diastereoisomer) δ 0.03 (6H, s, $Si(CH_3)$), 0.87 (9H, s, $C(CH_3)_3$), 1.03 (3H, d, J=6.9 Hz, $CHCH_3$), 1.32–1.82 (12H, m, CH_2), 1.71 (3H, s, $H_2C{=}CCH_3$), 2.51–2.70 (1H, m, $CHCH_3$), 3.48–3.63 (2H, m, CH_2OSi), 3.68 (2H, t, J=6.3 Hz, CH_2OH), 4.10–4.24 (2H, m, $CH_2OC(O)$), 4.65 (1H, s, $C{=}CH_2$), 4.85 (1H, s, $C{=}CH_2$), 6.86 (1H, s, $C(O)C{=}CHC$). ^{13}C NMR ($CDCl_3$, 125 MHz, major diastereoisomer) δ −5.3 ($Si(CH_3)_2$), 18.4 ($C(CH_3)_3$), 19.0 ($H_2C{=}CCH_3$), 20.1 ($CHCH_3$), 25.2 (CH_2), 26.0 ($C(CH_3)_3$), 27.3 (CH_2), 27.4 (CH_2), 29.1 (CH_2), 29.3 (CH_2), 30.2 (CH_2), 34.5 ($CHCH_3$), 44.5 (C), 62.4 (CH_2OH), 63.5 ($C(O)OCH_2$), 64.1 (CH_2OSi), 113.0 ($H_2C{=}C$), 135.0 ($C(O)C{=}CH$), 144.3 ($C(O)C{=}CH$), 149.0 ($H_2C{=}C$), 167.8 ($C{=}O$). ^{1}H NMR ($CDCl_3$, 500 MHz, minor diastereoisomer) δ 0.04 (6H, s, $Si(CH_3)$), 0.88 (9H, s, $C(CH_3)_3$), 1.06 (3H, d, J=6.9 Hz, $CHCH_3$), 1.32–1.82 (12H, m, CH_2), 1.70 (3H, s, $H_2C{=}CCH_3$), 2.51–2.70 (1H, m, $CHCH_3$), 3.48–3.63 (2H, m, CH_2OSi), 3.68 (2H, t, J=6.3 Hz, CH_2OH), 4.10–4.24 (2H, m, $CH_2OC(O)$), 4.52 (1H, s, $C{=}CH_2$), 4.87 (1H, s, $C{=}CH_2$), 6.83 (1H, s, $C(O)C{=}CHC$). ^{13}C NMR ($CDCl_3$, 125 MHz, minor diastereoisomer) δ −5.3 ($Si(CH_3)$), 18.4 ($C(CH_3)_3$), 18.8 ($H_2C{=}CCH_3$), 19.9 ($CHCH_3$), 25.1 (CH_2), 26.0 ($C(CH_3)_3$), 26.5 (CH_2), 27.4 (CH_2), 27.5 (CH_2), 28.1 (CH_2), 29.3 (CH_2), 35.0 ($CHCH_3$), 44.8 (C), 62.0 (CH_2OH), 63.3 ($C(O)OCH_2$), 64.1 (CH_2OSi), 114.3 ($C{=}CH_2$), 134.9 ($C(O)C{=}CH$), 144.5 ($C(O)C{=}CH$), 147.9 ($C{=}CH_2$), 167.5 ($C{=}O$). ν_{max} (thin film/cm^{-1}): 3468 (br), 2931 (m), 2858 (w), 1705 (m, C=O), 1458 (w), 1377 (w), 1249 (s), 1097 (m). MS (ES^+) m/z (%): 433 (100, M+Na). HRMS: calcd for $C_{23}H_{46}O_4NSi$ ($M+NH_4$): 428.3191. Found: 428.3193.

3.3.8. rac-(3R,6R)-2-hydroxyethyl 3-(3-(tert-butyldimethylsilyloxy)-propyl)-6-methyl-3-(prop-1-en-2-yl)cyclohex-1-enecarboxylate ***8h***. General procedure 2 using *rac*-(3*R*,6*R*)-3-(3-(*tert*-butyldimethylsilyloxy)propyl)-6-methyl-3-(prop-1-en-2-yl)cyclohex-1-enyl trifluoromethanesulfonate **7b**[6] (1.08 g, 2.37 mmol, dr 3:1), palladium acetate (106 mg, 0.473 mmol), triphenylphosphine (249 mg, 0.946 mmol), ethane-1,2-diol (3.97 mL, 71.0 mmol) and triethylamine (0.659 mL, 4.73 mmol) in DMF (12 mL) at 40 °C, after 14 h, gave **8h** (564 mg, 1.42 mmol, 60%, dr 3:1) as a yellow oil. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 0.04 (6H, s, $Si(CH_3)_2$), 0.05 (s, $Si(CH_3)_2$, minor diastereoisomer), 0.88 (9H, s, $C(CH_3)_3$), 0.89 (s, $C(CH_3)_3$, minor diastereoisomer), 1.05 (3H, d, J=6.8 Hz, $CHCH_3$), 1.08 (d, J=7.9 Hz, $CHCH_3$, minor diastereoisomer), 1.31–181 (8H, m, CH_2), 1.73 (3H, s, $H{=}CCH_3$), 2.18 (1H, br s, OH), 2.55–2.72 (1H, m, $CHCH_3$), 3.48–3.65 (2H, m, CH_2OSi), 3.81–3.93 (2H, m, CH_2OH), 4.26–4.34 (2H, m, $CH_2OC(O)$), 4.54 (s, $C{=}CH_2$, minor diastereoisomer), 4.65 (1H, s, $C{=}CH_2$), 4.87 (1H, s, $C{=}CH_2$), 4.89 (s, $C{=}CH_2$, minor diastereoisomer), 6.89 (s, $C(O)C{=}CHC$, diastereoisomer minor), 6.92 (1H, s, $C(O)C{=}CHC$). ^{13}C NMR ($CDCl_3$, 75 MHz) δ −5.3 ($Si(CH_3)_2$), 18.4 ($C(CH_3)_3$), 18.8 ($H_2C{=}CCH_3$, minor diastereoisomer), 19.0 ($H_2C{=}CCH_3$), 19.9 ($CHCH_3$, minor diastereoisomer), 20.1 ($CHCH_3$), 26.0 ($C(CH_3)_3$), 26.5 (CH_2, minor diastereoisomer), 27.3 (CH_2), 27.5 (CH_2), 28.2 ($CHCH_3$, minor diastereoisomer), 29.1 ($CHCH_3$), 30.2 (CH_2), 34.5 (CH_2), 35.1 (CH_2, minor diastereoisomer), 44.7 (C), 45.0 (C, minor diastereoisomer), 61.6 (CH_2OH), 63.4 ($C(O)OCH_2$), 66.2 (CH_2OSi), 113.1 ($H_2C{=}C$), 114.4 ($H_2C{=}C$, minor diastereoisomer), 134.7 ($C(O)C{=}CH$), 145.1 ($C(O)C{=}CH$), 145.3 ($C(O)C{=}CH$, minor diastereoisomer), 147.9 ($H_2C{=}C$, minor diastereoisomer), 149.0 ($H_2C{=}C$), 168.2 ($C{=}O$). ν_{max} (thin film/cm^{-1}): 3435 (br), 3083 (w), 2858 (s), 2729 (w), 1714 (s, C=O), 1636 (m), 1462 (m), 1385 (m), 1334 (w), 1253 (s), 1099 (s). MS (ES^+) m/z (%): 397 (5, M+H), 414 (10, $M+NH_4$), 419 (100, M+Na). HRMS: calcd for $C_{22}H_{44}O_4NSi$ ($M+NH_4$): 414.3034. Found: 414.3033.

3.4. General procedure 3. Formation of diols by HF-mediated TBDMS ether cleavage

To a solution of silyl ethers **8a–g** (1 equiv) in a 2:1 mixture of acetonitrile and pyridine at 0 °C was added dropwise aqueous

60% HF (10–25 equiv). The reaction was then stirred at room temperature until the starting alcohol had been consumed (TLC analysis). The reaction was quenched by dropwise addition of aqueous saturated $NaHCO_3$. Once effervescence had subsided, the mixture was extracted with Et_2O (×3). The combined organic extracts were washed with aqueous saturated $CuSO_4$ (×2), brine (×2) and then dried (Na_2SO_4). Concentration in vacuo gave the diols, which in some cases needed to be purified by chromatography on silica gel.

3.4.1. 3-Hydroxypropyl 3-(3-hydroxypropyl)-3-(prop-1-en-2-yl)-cyclohex-1-enecarboxylate. General procedure 3 using 3-hydroxypropyl 3-(3-(*tert*-butyldimethylsilyloxy)propyl)-3-(prop-1-en-2-yl) cyclohex-1-enecarboxylate **8a** (400 mg, 1.01 mmol), aqueous 60% HF (0.340 mL, 10.1 mmol), pyridine (2 mL) and MeCN (4 mL), after 4 h, gave 3-hydroxypropyl 3-(3-hydroxypropyl)-3-(prop-1-en-2-yl)cyclohex-1-enecarboxylate (278 mg, 0.985 mmol, 98%) as a colourless oil. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.25–1.81 (8H, m, CH_2), 1.71 (3H, m, H_2C=CCH_3), 1.91 (2H, quintet, *J*=6.1 Hz, $OCH_2CH_2CH_2O$), 2.05–2.20 (1H, m, 1H from CH_2C=CH), 2.24–2.33 (1H, m, 1H from CH_2C=CH), 2.41 (1H, br s, OH), 3.61 (2H, t, *J*=4.9 Hz, $C(CH_2)_2CH_2O$), 3.70 (2H, t, *J*=6.0 Hz, $O(CH_2)_2CH_2O$), 4.30 (2H, t, *J*=6.1 Hz, $CH_2OC(O)$), 4.57 (1H, dd, *J*=0.8, 1.7 Hz, C=CH_2), 4.90 (1H, t, *J*=1.4 Hz, C=CH_2), 6.94 (1H, s, C(O)C=CHC). ^{13}C NMR ($CDCl_3$, 75 MHz) *δ* 18.6 (CH_2), 18.9 (H_2C=CCH_3), 24.8 (CH_2), 27.4 (CH_2), 31.8 (CH_2), 31.9 (CH_2), 34.8 (CH_2), 44.6 (*C*), 59.4 ($O(CH_2)_2CH_2O$), 61.4 ($C(O)OCH_2$), 63.2 ($C(CH_2)_2CH_2O$), 114.2 (C=CH_2), 129.9 (HC=*C*C(O)), 145.0 (*C*=CH_2), 148.3 (HC=CC(O)), 168.0 (*C*=O). ν_{max} (thin film/cm^{-1}): 3353 (br), 2937 (s), 2864 (m), 1710 (s, C=O), 1637 (w), 1452 (w), 1377 (w), 1254 (s), 1109 (w), 1054 (m). MS (ES$^+$) *m*/*z* (%): 283 (8, M+H), 305 (100, M+Na). HRMS: calcd for $C_{16}H_{26}O_4Na$ (M+Na): 305.1723. Found: 305.1730.

3.4.2. rac-(3R,6R)-3-Hydroxypropyl 3-(3-hydroxypropyl)-6-methyl-3-(prop-1-en-2-yl)cyclohex-1-enecarboxylate. General procedure 3 using *rac*-(3*R*,6*R*)-3-hydroxypropyl 3-(3-(*tert*-butyldimethylsilyloxy)propyl)-6-methyl-3-(prop-1-en-2-yl)cyclohex-1-enecarboxylate **8b** (1.20 g, 2.92 mmol, dr 3:1), aqueous 60% HF (2.44 mL, 73.3 mmol), pyridine (10 mL) and MeCN (20 mL), after 24 h, gave *rac*-(3*R*,6*R*)-3-hydroxypropyl 3-(3-hydroxypropyl)-6-methyl-3-(prop-1-en-2-yl)cyclohex-1-enecarboxylate (835 mg, 2.82 mmol, 96%, dr 3:1) as a yellow oil. ^{1}H NMR ($CDCl_3$, 300 MHz, major diastereoisomer) *δ* 1.03 (3H, d, *J*=6.8 Hz, CHCH_3), 1.18–1.86 (8H, m, CH_2), 1.72 (3H, s, H_2C=CCH_3), 1.91 (2H, quintet, *J*=6.0 Hz, $OCH_2CH_2CH_2O$), 2.50–2.71 (1H, m, *C*HCH$_3$), 3.59 (2H, t, *J*=5.2 Hz, $C(CH_2)_2CH_2O$), 3.70 (2H, t, *J*=6.0 Hz, $O(CH_2)_2CH_2O$), 4.31 (2H, t, *J*=6.0 Hz, $CH_2OC(O)$), 4.65 (1H, s, C=CH_2), 4.86 (1H, s, C=CH_2), 6.88 (1H, s, C(O)C=C*H*). ^{13}C NMR ($CDCl_3$, 75 MHz, major diastereoisomer) *δ* 19.1 (H_2C=CCH$_3$), 20.1 (CHCH$_3$), 27.3 (CH_2), 27.4 (CH_2), 29.1 (CHCH$_3$), 30.3 (CH_2), 31.9 (CH_2), 34.5 ($OCH_2CH_2CH_2O$), 44.6 (*C*), 59.3 ($O(CH_2)_2CH_2O$), 61.3 ($C(O)OCH_2$), 63.2 ($C(CH_2)_2CH_2O$), 113.2 (H_2C=C), 135.0 (C(O)*C*=CH), 144.5 (C(O)C=*C*H), 148.8 (H_2C=*C*), 168.1 (*C*=O). ^{1}H NMR ($CDCl_3$, 300 MHz, minor diastereomer) *δ* 1.04 (3H, d, *J*=6.6 Hz, CHCH_3), 1.18–1.86 (8H, m, CH_2), 1.71 (3H, s, H_2C=CCH_3), 1.91 (2H, quintet, *J*=6.0 Hz, OCH_2CH_2-CH_2O), 2.50–2.71 (1H, m, *C*HCH$_3$), 3.59 (2H, t, *J*=5.2 Hz, $C(CH_2)_2CH_2O$), 3.70 (2H, t, *J*=6.0 Hz, $O(CH_2)_2CH_2O$), 4.31 (2H, t, *J*=6.0 Hz, $CH_2OC(O)$), 4.52 (1H, s, C=CH_2), 4.88 (1H, s, C=CH_2), 6.84 (1H, s, C(O)C=C*H*). ^{13}C NMR ($CDCl_3$, 75 MHz, minor diastereoisomer) *δ* 18.8 (H_2C=CCH$_3$), 19.8 (CHCH$_3$), 26.0 (CH_2), 26.4 (CH_2), 27.5 (CH_2), 28.1 (CHCH$_3$), 29.7 (CH_2), 34.9 ($OCH_2CH_2CH_2O$), 44.9 (*C*), 59.3 ($O(CH_2)_2CH_2O$), 61.2 ($C(O)OCH_2$), 63.2 ($C(CH_2)_2CH_2O$), 114.5 (H_2C=C), 134.9 (C(O)*C*=CH), 144.7 (C(O)C=*C*H), 147.8 (H_2C=*C*), 167.8 (*C*=O). ν_{max} (thin film/cm^{-1}): 3351 (br), 2939 (s), 1701 (s, C=O), 1450 (w), 1247 (m), 1057 (m). MS (ES$^+$) *m*/*z* (%): 319 (100, M+Na). HRMS: calcd for $C_{17}H_{32}ON$ (M+NH_4): 314.2326. Found: 314.2326.

3.4.3. 3-Hydroxypropyl 3-(but-3-enyl)-3-(3-hydroxypropyl)cyclohex-1-enecarboxylate. General procedure 3 using 3-hydroxypropyl 3-(but-3-enyl)-3-(3-(*tert*-butyldimethylsilyloxy)propyl)cyclohex-1-enecarboxylate **8c** (200 mg, 0.487 mmol), aqueous 60% HF (0.160 mL, 4.90 mmol), pyridine (2.5 mL) and MeCN (5.00 mL), after 12 h, gave 3-hydroxypropyl 3-(but-3-enyl)-3-(3-hydroxypropyl)-cyclohex-1-enecarboxylate (141 mg, 0.476 mmol, 98%) as a yellow oil. ^{1}H NMR ($CDCl_3$, 500 MHz) *δ* 1.39–1.56 (8H, m, CH_2), 1.66 (2H, quintet, *J*=6.1 Hz, CH_2CH$_2$CC(O)), 1.91 (2H, quintet, *J*=6.1 Hz, $OCH_2CH_2CH_2O$), 2.01 (2H, q, *J*=5.3 Hz, CH_2CH=CH$_2$), 2.21 (2H, t, *J*=6.0 Hz, CH_2CC(O)), 3.62 (2H, t, *J*=6.1 Hz, $C(CH_2)_2$), 3.71 (2H, t, *J*=6.1 Hz, $O(CH_2)_2CH_2O$), 4.30 (2H, t, *J*=6.0 Hz, $CH_2OC(O)$), 4.94 (1H, dd, *J*=10.1, 1.8 Hz CH=CH_2 *cis*), 5.01 (1H, dd, *J*=17.1, 1.8 Hz, CH=CH_2 *trans*), 5.79 (1H, ddt, *J*=17.1, 10,1, 6.6 Hz, C*H*=CH$_2$), 6.74 (1H, s, C(O)C=C*H*). ^{13}C NMR (125 MHz, $CDCl_3$) *δ* 19.1 (CH$_2$CH$_2$CC(O)), 24.6 (CH_2CC(O)), 27.4 (CH_2), 28.5 (CH$_2$CH=CH$_2$), 31.6 (CH_2), 32.1 (C(O)OCH$_2$CH$_2$), 35.5 (CH_2), 38.0 (*C*), 38.7 (CH_2), 59.5 ($O(CH_2)_2CH_2O$), 61.6 ($C(O)OCH_2$), 63.6 ($C(CH_2)_2CH_2O$), 114.7 (CH_2=CH), 129.8 (HC=*C*C(O)), 139.1 (*C*H=CH$_2$), 147.4 (HC=CC(O)), 168.3 (*C*=O). ν_{max} (thin film/cm^{-1}): 3362 (br), 2936 (s), 2862 (m), 1709 (s, C=O), 1640 (m), 1454 (w), 1394 (w), 1271 (s), 1265 (s), 1084 (m), 1056 (s), 910 (m), 751 (w). MS (EI$^+$) *m*/*z* (%): 319 (100, M+Na). HRMS: Calcd for $C_{17}H$ (M+Na): 319.1880. Found: 319.1881.

3.4.4. rac-(3S,6R)-3-Hydroxypropyl 3-(but-3-enyl)-3-(3-hydroxypropyl)-6-methylcyclohex-1-enecarboxylate. General procedure 3 using *rac*-(3*S*,6*R*)-3-hydroxypropyl 3-(but-3-enyl)-3-(3-(*tert*-butyldimethylsilyloxy)propyl)-6-methylcyclohex-1-enecarboxylate **8d** (111 mg, 0.261 mmol, dr 3:1), aqueous 60% HF (90.0 μL, 2.60 mmol), pyridine (1.3 mL) and MeCN (2.6 mL), after 12 h, gave *rac*-(3*S*,6*R*)-3-hydroxypropyl 3-(but-3-enyl)-3-(3-hydroxypropyl)-6-methylcyclohex-1-enecarboxylate (78.0 mg, 0.251 mmol, 96%, dr 3:1) as a yellow oil. ^{1}H NMR ($CDCl_3$, 500 MHz) *δ* 1.06 (d, *J*=6.9 Hz, CH_3, minor diastereoisomer), 1.07 (3H, d, *J*=7.3 Hz, CH_3), 1.30–1.60 (8H, m, CH_2), 1.71–1.77 (2H, m, CH_2CHCH$_3$), 1.88 (2H, quintet, *J*=6.0 Hz, CH_2CH$_2$OC(O)), 2.00 (2H, q, *J*=5.7 Hz, CH_2CH=CH$_2$), 2.60–2.64 (1H, m, *C*HCH$_3$), 3.57 (2H, t, *J*=6.6 Hz, $C(CH_2)_2CH_2O$), 3.67 (2H, t, *J*=6.0 Hz, $O(CH_2)_2CH_2O$), 4.26–4.31 (2H, m, CH_2OC(O)), 4.89 (dd, *J*=10.1, 1.6 Hz, CH=CH_2 *cis*, minor diastereoisomer), 4.91 (1H, dd, *J*=10.1, 1.6 Hz, CH=CH_2 *cis*), 4.96 (dd, *J*=17.4, 1.6 Hz, CH=CH_2 *trans* minor diastereoisomer), 4.98 (1H, dd, *J*=17.1, 1.6 Hz, CH=CH_2 *trans*), 5.76 (1H, ddt, *J*=17.1, 10,1, 6.3 Hz, C*H*=CH$_2$), 6.67 (1H, s, C(O)C=C*H*C). ^{13}C NMR ($CDCl_3$, 125 MHz) *δ* 20.0 (CHCH$_3$), 26.5 (CH_2CHCH$_3$), 26.8 (CH_2), 27.0 (CH_2), 27.9 (CHCH$_3$), 28.3 (CH_2CH=CH$_2$), 31.8 ($OCH_2CH_2CH_2O$), 35.5 (CH_2), 38.0 (*C*), 38.4 (CH_2), 59.0 ($O(CH_2)_2CH_2O$), 61.2 ($C(O)OCH_2$), 63.2 ($C(CH_2)_2CH_2O$), 114.4 (CH_2=CH), 134.5 (HC=*C*C(O)), 138.8 (*C*H=CH$_2$), 146.8 (HC=CC(O)), 167.9 (*C*=O). ν_{max} (thin film/cm^{-1}): 3356 (br), 3075 (w), 2934 (s), 2869 (m), 1709 (s, C=O), 1639 (m), 1452 (m), 1394 (w), 1363 (w), 1335 (w), 1257 (s), 1119 (w), 1059 (s), 910 (m), 769 (w). MS (ES$^+$) *m*/*z* (%): 333 (100, M+Na). HRMS: Calcd for $C_{18}H$ (M+Na): 333.2036. Found: 333.2038.

3.4.5. 3-Hydroxypropyl 3-(3-hydroxypropyl)-3-methylcyclohex-1-enecarboxylate. General procedure 3 using 3-hydroxypropyl 3-(3-(*tert*-butyldimethylsilyloxy)propyl)-3-methylcyclohex-1-enecarboxylate **8e** (560 mg, 1.51 mmol), aqueous 60% HF (0.510 mL, 15.2 mmol), pyridine (7.5 mL) and MeCN (15 mL), after 12 h, gave 3-hydroxypropyl 3-(3-hydroxypropyl)-3-methylcyclohex-1-enecarboxylate (380 mg, 1.48 mmol, 98%) as a colourless oil. ^{1}H NMR ($CDCl_3$, 500 MHz) *δ* 1.04 (3H, s, CH_3), 1.92 (2H, quintet, *J*=5.8 Hz,

$CH_2CH_2OC(O)$), 1.35–1.75 (8H, m, CH_2), 2.25 (1H, td, J=5.6, 1.5 Hz, 1H from $CH_2CC(O)$), 2.29 (1H, td, J=5.5, 1.8 Hz, 1H from $CH_2CC(O)$), 3.64 (2H, t, J=6.3 Hz, $C(CH_2)_2CH_2OH$), 3.71 (2H, t, J=6.0 Hz, $O(CH_2)_2CH_2OH$), 4.31 (2H, t, J=6.0 Hz, $CH_2OC(O)$), 6.71 (1H, s, C(O)C=CHC). ^{13}C NMR (125 MHz, $CDCl_3$) δ 19.0 (CH_2), 24.3 ($CH_2CC(O)$), 26.5 (CH_3), 27.3 (CH_2), 31.8 ($OCH_2CH_2CH_2O$), 33.6 (CH_2), 35.1 (C), 38.0 (CH_2), 59.1 ($O(CH_2)_2CH_2O$), 61.3 ($C(O)OCH_2$), 63.2 ($C(CH_2)_2CH_2O$), 128.7 (HC=CC(O)), 148.2 (HC=CC(O)), 168.2 (C=O). ν_{max} (thin film/cm^{-1}): 3370 (br), 2929 (s), 2863 (m), 1709 (s, C=O), 1683 (s), 1273 (s), 1243 (s), 1084 (m), 1049 (s), 918 (w). MS (ES$^+$) m/z (%): 279 (100, M+Na). HRMS: calcd for $C_{14}H_{24}O_4Na$ (M+Na): 279.1572. Found: 279.1570.

3.4.6. 3-Hydroxypropyl 3-(3-hydroxypropyl)-6,6-dimethyl-3-(prop-1-en-2-yl)cyclohex-1-enecarboxylate. General procedure 3 using 3-hydroxypropyl 3-(3-(*tert*-butyldimethylsilyloxy)propyl)-6,6-dimethyl-3-(prop-1-en-2-yl)cyclohex-1-enecarboxylate **8f** (517 mg, 1.22 mmol), aqueous 60% HF (0.400 mL, 12.2 mmol), pyridine (5 mL) and MeCN (10 mL), after 12 h, gave 3-hydroxypropyl 3-(3-hydroxypropyl)-6,6-dimethyl-3-(prop-1-en-2-yl)cyclohex-1-enecarboxylate (360 mg, 1.16 mmol, 95%) as a colourless oil. ^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.17 (3H, s, CCH_3), 1.23 (3H, s, CCH_3), 1.31–1.70 (8H, m, CH_2), 1.72 (3H, s, $H_2C=CCH_3$), 1.92 (2H, quintet, J=6.1 Hz, $OCH_2CH_2CH_2O$), 2.10 (1H, br s, OH), 3.59–3.67 (2H, m, $C(CH_2)$), 3.72 (2H, t, J=5.9 Hz, $O(CH_2)$), 4.31 (2H, t, J=6.1 Hz, $CH_2OC(O)$), 4.61 (1H, s, C=CH_2), 4.90 (1H, s, C=CH_2), 6.75 (1H, s, C(O)C=CHC). ^{13}C NMR ($CDCl_3$, 75 MHz) δ 18.9 ($H_2C=CCH_3$), 27.3 ($C(CH_3)_2$), 27.5 (CH_2), 28.2 ($C(CH_3)_2$), 28.3 (CH_2), 31.9 (CH_2), 33.4 ($C(CH_3)_2$), 34.8 (CH_2), 36.7 (CH_2), 45.0 (C), 59.4 ($O(CH_2)_2CH_2O$), 61.0 ($C(O)OCH_2$), 63.3 ($C(CH_2)_2CH_2O$), 114.0 ($H_2C=C$), 138.1 (C(O)C=CH), 144.3 (C(O)C=CH), 148.1 ($H_2C=C$), 167.9 (C=O). ν_{max} (thin film/cm^{-1}): 3302 (br), 2948 (m), 2864 (m), 1715 (s, C=O), 1620 (w), 1540 (w), 1455 (w), 1251 (m). MS (ES$^+$) m/z (%): 328 (60, M+NH_4), 333 (100, M+Na). HRMS: calcd for $C_{18}H_{30}O_4Na$ (M+Na): 333.2036. Found: 333.2047.

3.4.7. rac-(3R,6R)-4-Hydroxybutyl 3-(3-hydroxypropyl)-6-methyl-3-(prop-1-en-2-yl)cyclohex-1-enecarboxylate. General procedure 3 using *rac*-(3*R*,6*R*)-4-hydroxybutyl 3-(3-(*tert*-butyldimethylsilyloxy)propyl)-6-methyl-3-(prop-1-en-2-yl)cyclohex-1-enecarboxylate **8g** (280 mg, 0.659 mmol, dr 3:1), aqueous 60% HF (0.659 mL, 19.8 mmol), pyridine (5 mL) and MeCN (10 mL), after 12 h, gave *rac*-(3*R*,6*R*)-4-hydroxybutyl 3-(3-hydroxypropyl)-6-methyl-3-(prop-1-en-2-yl)cyclohex-1-enecarboxylate (166 mg, 0.534 mmol, 81%, dr 3:1) as a colourless oil. ^{1}H NMR ($CDCl_3$, 300 MHz, major diastereoisomer) δ 1.05 (3H, d, J=6.8 Hz, CHCH), 1.20–1.90 (12H, m, CH_2), 1.73 (3H, s, $H_2C=CCH_3$), 2.53–2.74 (1H, m, $CHCH_3$), 3.49–3.67 (2H, m, $C(CH_2)_2CH_2O$), 3.70 (2H, t, J=6.3 Hz, $O(CH_2)_3CH_2O$), 4.08–4.30 (2H, m, $CH_2OC(O)$), 4.67 (1H, s, C=CH_2), 4.88 (1H, s, C=CH_2), 6.89 (1H, s, C(O)C=CHC). ^{13}C NMR ($CDCl_3$, 75 MHz, major diastereoisomer) δ 19.1 ($H_2C=CCH_3$), 20.1 ($CHCH_3$), 25.2 (CH_2), 27.4 (CH_2), 27.5 (CH_2), 29.1 ($CHCH_3$), 29.4 (CH_2), 30.3 (CH_2), 34.5 (CH_2), 44.6 (C), 62.5 ($O(CH_2)_3CH_2O$), 63.3 ($C(O)OCH_2$), 64.1 ($C(CH_2)_2CH_2O$), 113.2 ($H_2C=C$), 135.3 (C(O)C=CH), 144.0 (C(O)C=CH), 148.9 ($H_2C=C$), 167.7 (C=O). ^{1}H NMR ($CDCl_3$, 300 MHz, minor diastereoisomer) δ 1.07 (3H, d, J=6.2 Hz, CHCH), 1.20–1.90 (12H, m, CH_2), 1.72 (3H, s, $H_2C=CCH_3$), 2.53–2.74 (1H, m, $CHCH_3$), 3.49–3.67 (2H, m, $C(CH_2)_2CH_2O$), 3.70 (2H, t, J=6.3 Hz, $O(CH_2)_3CH_2O$), 4.08–4.30 (2H, m, $CH_2OC(O)$), 4.55 (1H, s, C=CH_2), 4.90 (1H, s, C=CH_2), 6.84 (1H, s, C(O)C=CHC). ^{13}C NMR ($CDCl_3$, 75 MHz, minor diastereoisomer) δ 18.9 ($H_2C=CCH_3$), 19.8 ($CHCH_3$), 26.0 (CH_2), 26.4 (CH_2), 27.5 (CH_2), 27.5 (CH_2), 28.1 ($CHCH_3$), 29.4 (CH_2), 34.9 (CH_2), 44.9 (C), 62.5 ($O(CH_2)_3CH_2O$), 63.3 ($C(O)OCH_2$), 64.2 ($C(CH_2)_2CH_2O$), 114.4 ($H_2C=C$), 135.2 (C(O)C=CH), 144.3 (C(O)C=CH), 147.8 ($H_2C=C$), 167.4 (C=O). ν_{max} (thin film/cm^{-1}): 3401 (br), 2941 (s), 2868 (m), 1703 (s), 1636 (m), 1452 (m), 1377 (w), 1254 (s). MS (ES$^+$) m/z (%): 311 (90, M+H), 333 (100, M+Na). HRMS: calcd for $C_{18}H_{30}O_4Na$ (M+Na): 333.2036. Found: 333.2052.

3.5. General procedure 4. Oxidation of diols to dialdehydes 3a–g using the Dess–Martin periodinane (DMP)

DMP (3 equiv) was added to a solution of the diol (1 equiv) in CH_2Cl_2 and the reaction was stirred until complete (TLC analysis). The reaction was quenched with aqueous saturated $NaHCO_3$ and extracted with Et_2O (×3). The combined organic extracts were dried (Na_2SO_4) and concentrated in vacuo before purification by rapid chromatography through a short plug of silica gel.

*3.5.1. 3-Oxopropyl 3-(3-oxopropyl)-3-(prop-1-en-2-yl)cyclohex-1-enecarboxylate **3a**.* General procedure 4 using 3-hydroxypropyl 3-(3-hydroxypropyl)-3-(prop-1-en-2-yl)cyclohex-1-enecarboxylate (441 mg, 1.56 mmol), DMP (1.99 g, 4.69 mmol) and CH_2Cl_2 (15 mL), after 5 h, gave **3a** (316 mg, 1.14 mmol, 73%) as a colourless oil. ^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.23–1.35 (1H, m, CH), 1.43–1.55 (1H, m, CH_2), 1.58–1.88 (3H, m, CH_2), 1.68 (3H, m, $H_2C=CCH_3$), 1.80–1.90 (1H, m, CH_2), 2.05–2.17 (1H, $CH_2C=CH$), 2.18–2.39 (2H, m, CCH_2CH_2CHO and $CH_2C=CH$), 2.41–2.52 (1H, m, CCH_2CH_2CHO), 2.80 (2H, td, J=6.1 Hz, J=1.6 Hz, OCH_2CH_2CHO), 4.46 (2H, t, J=6.2 Hz, $CH_2CH_2OC(O)$), 4.59 (1H, s, C=CH_2), 4.92 (1H, t, J=1.3 Hz, C=CH_2), 6.80 (1H, s, C(O)C=CHC), 9.75 (1H, t, J=1.4 Hz, $C(CH_2)_2CHO$), 9.79 (1H, t, J=1.6 Hz, $O(CH_2)_2CHO$). ^{13}C NMR ($CDCl_3$, 75 MHz) δ 18.4 (CH_2), 18.8 ($H_2C=CCH_3$), 24.7 (CH_2), 30.0 (CH_2), 31.6 (CH_2), 39.1 (CCH_2CH_2CHO), 42.8 (OCH_2CH_2CHO), 44.1 (C), 58.1 ($C(O)OCH_2$), 114.9 ($H_2C=C$), 130.4 (CH=CC(O)), 143.9 ($H_2C=C$), 147.4 (CH=CC(O)), 167.0 ($C(O)OCH_2$), 199.5 (CHO), 201.8 (CHO). ν_{max} (thin film/cm^{-1}): 2934 (s), 2869 (m), 1721 (br s, C=O), 1642 (w), 1455 (w), 1382 (w), 1274 (s). MS (ES$^+$) m/z (%): 301 (100, M+Na). HRMS: calcd for $C_{16}H_{22}O_4Na$: 301.1410. Found: 301.1401.

*3.5.2. rac-(3R,6R)-3-Oxopropyl 6-methyl-3-(3-oxopropyl)-3-(prop-1-en-2-yl)cyclohex-1-enecarboxylate **3b**.* General procedure 4 using *rac*-(3*R*,6*R*)-3-hydroxypropyl 3-(3-hydroxypropyl)-6-methyl-3-(prop-1-en-2-yl)cyclohex-1-enecarboxylate (200 mg, 0.675 mmol, dr 3:1), DMP (859 mg, 2.02 mmol) and CH_2Cl_2 (6.8 mL), after 4 h, gave **3b** (155 mg, 0.530 mmol, 79%, dr 3:1) as a colourless oil. ^{1}H NMR ($CDCl_3$, 300 MHz, major diastereoisomer) δ 0.99 (3H, d, J=7.0 Hz, $CHCH_3$), 1.17–1.49 (2H, m, CH_2), 1.57–1.93 (4H, s, CH_2), 1.67 (3H, s, $H_2C=CCH_3$), 2.19–2.64 (3H, m, $CHCH_3$, CH_2), 2.79 (2H, td, J=6.1, 1.4 Hz, OCH_2CH_2CHO), 4.35–4.54 (2H, m, $CH_2OC(O)$), 4.64 (1H, s, C=CH_2), 4.88 (1H, s, C=CH_2), 6.73 (1H, s, C(O)C=CHC), 9.73 (1H, br s, $C(CH_2)_2CHO$), 9.79 (1H, t, J=1.5 Hz, $O(CH_2)_2CHO$). ^{13}C NMR ($CDCl_3$, 75 MHz, major diastereoisomer) δ 19.0 ($H_2C=CCH_3$), 20.0 ($CHCH_3$), 27.1 (CH_2), 29.0 ($CHCH_3$), 29.7 (CH_2), 30.0 (CH_2), 39.1 (CCH_2CH_2CHO), 42.8 (OCH_2CH_2CHO), 44.1 (C), 58.0 ($C(O)OCH_2$), 113.9 ($H_2C=C$), 135.5 (CH=CC(O)), 143.4 (CH=CC(O)), 147.9 ($H_2C=C$), 167.2 ($C(O)OCH_2$), 199.4 (CHO), 201.8 (CHO). ^{1}H NMR ($CDCl_3$, 300 MHz, minor diastereoisomer) δ 1.02 (3H, d, J=7.9 Hz, $CHCH_3$), 1.17–1.49 (2H, m, CH_2), 1.57–1.93 (4H, s, CH_2), 1.67 (3H, s, $H_2C=CCH_3$), 2.19–2.64 (3H, m, $CHCH_3$, CH_2), 2.79 (2H, td, J=6.1, 1.4 Hz, OCH_2CH_2CHO), 4.35–4.54 (2H, m, $CH_2OC(O)$), 4.53 (1H, s, C=CH_2), 4.90 (1H, s, C=CH_2), 6.70 (1H, s, C(O)C=CHC), 9.75 (1H, br s, $C(CH_2)_2CHO$), 9.79 (1H, t, J=1.5 Hz, $O(CH_2)_2CHO$). ^{13}C NMR ($CDCl_3$, 75 MHz, minor diastereoisomer) δ 18.8 ($H_2C=CCH_3$), 19.7 ($CHCH_3$), 25.9 (CH_2), 26.4 (CH_2), 28.0 ($CHCH_3$), 30.2 (CH_2), 39.2 (CCH_2CH_2CHO), 42.8 (OCH_2CH_2CHO), 44.5 (C), 58.0 ($C(O)OCH_2$), 115.2 ($H_2C=C$), 135.4 (CH=CC(O)), 143.7 (CH=CC(O)), 146.9 ($H_2C=C$), 166.8 ($C(O)OCH_2$), 199.4 (CHO), 201.8 (CHO). ν_{max} (thin

film/cm^{-1}): 2934 (m), 1707 (s, C=O), 1451 (w), 1246 (m), 1039 (w). MS (ES$^+$) *m*/*z* (%): 310 (50, M+NH_4), 315 (100, M+Na). HRMS: calcd for $C_{17}H_{28}O_4N$ (M+NH_4): 310.2013. Found: 310.2010.

3.5.3. 3-Oxopropyl 3-(but-3-enyl)-3-(3-oxopropyl)cyclohex-1-enecarboxylate ***3c***. General procedure 4 using 3-hydroxypropyl 3-(but-3-enyl)-3-(3-hydroxypropyl)cyclohex-1-enecarboxylate (35.0 mg, 0.118 mmol), DMP (150 mg, 0.354 mmol) and CH_2Cl_2 (1.2 mL), after 4 h, gave **3c** (33.0 mg, 0.113 mmol, 96%) as a colourless oil. ^{1}H NMR ($CDCl_3$, 500 MHz) δ 1.37–1.52 (4H, m, CH_2), 1.66 (2H, quintet, *J*=6.1 Hz, CH_2CH$_2$CC(O)), 1.71 (2H, ddd, *J*=9.5, 6.5, 2.8 Hz, CCH_2CH$_2$CHO), 1.97–2.04 (2H, m, CH_2CH=CH$_2$), 2.17–221 (2H, m, CH_2CC(O)), 2.35–2.47 (2H, m, CCH$_2$CH_2CHO), 2.82 (2H, td, *J*=6.1, 1.7 Hz, CH_2CH$_2$OC(O)), 4.48 (2H, t, *J*=6.0 Hz, CH_2OC(O)), 4.95 (1H, dd, *J*=10.3, 1.7 Hz, *cis* CH=CH_2), 5.01 (1H, dd, *J*=17.2, 1.7 Hz, *trans* CH=CH_2), 5.77 (1H, ddt, *J*=17.2, 10.3, 6.4 Hz, CH=CH$_2$), 6.64 (1H, s, C(O)C=CH), 9.77 (1H, s, CHO), 9.81 (1H, s, CHO). ^{13}C NMR ($CDCl_3$, 125 MHz) δ 18.7 (*C*H$_2$CH$_2$CC(O)), 24.1 (*C*H$_2$(CH$_2$)$_2$CC(O)), 28.1 (*C*H$_2$CH=CH$_2$), 30.8 (CCH$_2$CH$_2$CHO), 31.1 (*C*H$_2$), 37.5 (*C*), 38.5 (*C*H$_2$), 39.0 (CCH$_2$*C*H$_2$CHO), 42.8 (OCH$_2$CH$_2$CHO), 58.1 (C(O)O*C*H$_2$), 114.7 (*C*H$_2$=CH), 130.3 (CH=*C*C(O)), 138.4 (CH$_2$=*C*H), 146.0 (*C*H=CC(O)), 167.0 (*C*(O)OCH$_2$), 199.6 (*C*HO), 202.0 (*C*HO). ν_{max} (thin film/cm^{-1}): 2933 (m), 2854 (w), 1717 (s, C=O), 1711 (s, C=O), 1642 (m), 1456 (w), 1389 (w), 1243 (s). MS (ES$^+$) *m*/*z* (%): 379 (100), 374 (20). Mass ion not observed.

3.5.4. rac-(3S,6R)-3-Oxopropyl 3-(but-3-enyl)-6-methyl-3-(3-oxopropyl)cyclohex-1-enecarboxylate ***3d***. General procedure 4 using *rac*-(3*S*,6*R*)-3-hydroxypropyl 3-(but-3-enyl)-3-(3-hydroxypropyl)-6-methylcyclohex-1-enecarboxylate (67.0 mg, 0.216 mmol, dr 3:1), DMP (275 mg, 0.647 mmol) and CH_2Cl_2 (2.2 mL), after 4 h, gave **3d** (60.0 mg, 0.196 mmol, 91%, dr 3:1) as a colourless oil. ^{1}H NMR ($CDCl_3$, 500 MHz) δ 1.03 (3H, d, *J*=6.8 Hz, CH_3), 1.04 (d, *J*=7.1 Hz, CH_3, minor diastereoisomer), 1.31–1.49 (4H, m, CH_2), 1.58–1.76 (4H, m, CH_2), 1.88–2.07 (2H, m, CH_2CH=CH$_2$), 2.42 (2H, td, *J*=8.1, 1.8 Hz, CCH$_2$CH_2CHO), 2.61–2.65 (1H, m, CHCH$_3$), 2.81 (2H, td, *J*=6.0, 1.8 Hz, OCH$_2$CH_2CHO), 4.53–4.41 (2H, m, CH_2OC(O)), 4.94 (1H, dd, *J*=10.1, 1.5 Hz, *cis* CH_2=CH), 5.00 (1H, dd, *J*=17.1, 1.8 Hz, *trans* CH_2=CH), 5.70–5.82 (1H, m, CH=CH$_2$), 6.55 (1H, s, C(O)C=CH), 9.75 (1H, t, *J*=1.8 Hz, CHO), 9.81 (1H, t, *J*=1.8 Hz, CHO). ^{13}C NMR ($CDCl_3$, 125 MHz) δ 20.0 (CH*C*H$_3$), 26.5 (*C*H$_2$), 26.9 (*C*H$_2$), 27.9 (*C*HCH$_3$), 28.3 (*C*H$_2$CH=CH$_2$), 30.7 (*C*H$_2$), 37.6 (*C*), 38.4 (*C*H$_2$), 38.9 (CCH$_2$CH$_2$CHO), 42.8 (OCH$_2$*C*H$_2$CHO), 58.0 (C(O)O*C*H$_2$), 114.7 (*C*H$_2$=CH), 135.3 (CH=*C*C(O)), 138.4 (CH$_2$=*C*H), 145.6 (*C*H=CC(O)), 166.9 (*C*(O)OCH$_2$), 199.5 (*C*HO), 201.9 (*C*HO). ν_{max} (thin film/cm^{-1}): 2928 (m), 2849 (w), 1716 (s, C=O), 1708 (s, C=O), 1451 (w), 1249 (m), 1118 (w), 1058 (m), 1046 (m), 908 (w). MS (ES$^+$) *m*/*z* (%): 307 (100, M+H). HRMS: Calcd for $C_{18}H_{27}O_4$ (M+H): 307.1904. Found: 307.1900.

3.5.5. 3-Oxopropyl 3-methyl-3-(3-oxopropyl)cyclohex-1-enecarboxylate ***3e***. General procedure 4 using 3-hydroxypropyl 3-(3-hydroxypropyl)-3-methylcyclohex-1-enecarboxylate (93.0 mg, 0.363 mmol), DMP (462 mg, 1.09 mmol) and CH_2Cl_2 (3.6 mL), after 4 h, gave **3e** (68.0 mg, 0.270 mmol, 74%) as a colourless oil. ^{1}H NMR ($CDCl_3$, 500 MHz) δ 1.01 (3H, s, CH_3), 1.38–1.42 (2H, m, CH_2(CH$_2$)$_2$CC(O)), 1.57–1.63 (2H, m, CH_2CH$_2$CC(O)), 1.67 (2H, t, *J*=8.1 Hz, CCH_2CH$_2$CHO), 2.07–2.14 (1H, m, 1H from CH_2CC(O)), 2.24 (1H, dt, *J*=17.1, 4.8 Hz, 1H from CH_2CC(O)), 2.35–2.48 (2H, m, CCH$_2$CH_2CHO), 2.80 (2H, td, *J*=6.2, 1.9 Hz, OCH$_2$CH_2CHO), 4.46 (2H, t, *J*=6.0 Hz, CH_2OC(O)), 6.61 (1H, s, C(O)C=CHC), 9.76 (1H, s, CHO), 9.80 (1H, s, CHO). ^{13}C NMR ($CDCl_3$, 125 MHz) δ 18.8 (*C*H$_2$CH$_2$CC(O)), 24.2 (*C*H$_2$CC(O)), 26.4 (*C*H$_3$), 33.4 (*C*H$_2$(CH$_2$)$_2$CC(O)), 33.5 (C*C*H$_2$CH$_2$CHO), 34.9 (*C*), 39.1 (CCH$_2$*C*H$_2$CHO), 42.8 (OCH$_2$*C*H$_2$CHO), 58.0 (C(O)O*C*H$_2$), 129.3 (C(O)*C*=CH), 146.8 (C(O)C=*C*H), 167.2 (*C*(O)OCH$_2$), 199.6 (*C*HO), 202.1 (*C*HO). ν_{max} (thin film/cm^{-1}): 2935 (m), 2858 (w), 2725 (w), 1717 (s, C=O), 1710 (s, C=O), 1645 (w), 1458 (w), 1384 (w), 1268 (m), 1241 (s), 1083 (m). Mass spectra for this compound were not informative.

3.5.6. 3-Oxopropyl 6,6-dimethyl-3-(3-oxopropyl)-3-(prop-1-en-2-yl)cyclohex-1-enecarboxylate ***3f***. General procedure 4 using 3-hydroxypropyl 3-(3-hydroxypropyl)-6,6-dimethyl-3-(prop-1-en-2-yl)cyclohex-1-enecarboxylate (237 mg, 0.763 mmol), DMP (972 mg, 2.29 mmol) and CH_2Cl_2 (7.5 mL), after 6 h, gave **3f** (154 mg, 0.503 mmol, 66%) as a colourless oil. ^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.14 (3H, s, CCH_3), 1.20 (3H, s, CCH_3), 1.32–1.57 (4H, m, CH_2), 1.67–1.76 (1H, m, CCH_2CH$_2$CHO), 1.70 (3H, s, H$_2$C=CCH_3), 1.80–1.93 (1H, m, CCH_2CH$_2$CHO), 2.29–2.41 (1H, m, CCH$_2$CH_2CHO), 2.42–2.55 (1H, m, CCH$_2$CH_2CHO), 2.83 (2H, td, *J*=6.1, 1.5 Hz, OCH$_2$CH_2CHO), 4.48 (2H, t, *J*=6.2 Hz, CH_2OC(O)), 4.62 (1H, s, C=CH_2), 4.93 (1H, s, C=CH_2), 6.62 (1H, s, C(O)C=CHC), 9.78 (1H, s, C(CH$_2$)$_2$), 9.83 (1H, t, *J*=1.5 Hz, O(CH$_2$)$_2$). ^{13}C NMR ($CDCl_3$, 100 MHz) δ 18.8 (H$_2$C=C*C*H$_3$), 27.2 (C(*C*H$_3$)$_2$), 28.1 (C(*C*H$_3$)$_2$), 28.2 (*C*H$_2$), 30.0 (*C*H$_2$), 33.4 (*C*(CH$_3$)$_2$), 36.3 (*C*H$_2$), 39.2 (CCH$_2$CH$_2$CHO), 42.8 (OCH$_2$CH$_2$CHO), 44.5 (*C*), 57.8 (C(O)OCH$_2$), 114.8 (H$_2$*C*=C), 138.5 (CH=*C*C(O)), 143.3 (*C*H=CC(O)), 147.2 (H$_2$C=*C*), 167.0 (*C*(O)OCH$_2$), 200.0 (*C*HO), 202.0 (*C*HO). ν_{max} (thin film/cm^{-1}): 2952 (m), 1712 (s, C=O), 1634 (w), 1454 (w), 1388 (w), 1255 (m). Mass spectra for this compound were not informative.

3.5.7. rac-(3R,6R)-4-Oxobutyl 6-methyl-3-(3-oxopropyl)-3-(prop-1-en-2-yl)cyclohex-1-enecarboxylate ***3g***. General procedure 4 using *rac*-(3*R*,6*R*)-4-hydroxybutyl 3-(3-hydroxypropyl)-6-methyl-3-(prop-1-en-2-yl)cyclohex-1-enecarboxylate (160 mg, 0.515 mmol, dr 3:1), DMP (656 mg, 1.55 mmol) and CH_2Cl_2 (6.8 mL), after 4 h, gave **3g** (105 mg, 0.343 mmol, 67%, dr 3:1) as a colourless oil. ^{1}H NMR ($CDCl_3$, 300 MHz, major diastereoisomer) δ 1.02 (3H, d, *J*=6.8 Hz, CH*C*H$_3$), 1.21–1.94 (6H, m, CH_2), 1.70 (3H, s, H$_2$C=CCH_3), 2.03 (2H, quintet, *J*=6.8 Hz, OCH$_2$CH_2CH$_2$CHO), 2.25–2.76 (5H, m, CH_2C(O) and CHCH$_3$), 4.17 (2H, t, *J*=6.3 Hz, CH_2OC(O)), 4.68 (1H, s, C=CH_2), 4.90 (1H, s, C=CH_2), 6.75 (1H, s, C(O)C=CHC), 9.76 (1H, br s, CHO), 9.80 (1H, br s, CHO). ^{13}C NMR ($CDCl_3$, 75 MHz, major diastereoisomer) δ 19.0 (H$_2$C=C*C*H$_3$), 20.0 (CH*C*H$_3$), 21.5 (*C*H$_2$), 27.2 (*C*H$_2$), 29.0 (*C*HCH$_3$), 29.7 (*C*H$_2$), 30.1 (*C*H$_2$), 39.1 (CCH$_2$CH$_2$CHO), 40.7 (O(CH$_2$)$_2$CH$_2$CHO), 44.1 (*C*), 63.5 (C(O)OCH$_2$), 113.8 (H$_2$*C*=C), 135.7 (CH=*C*C(O)), 143.0 (*C*H=CC(O)), 148.0 (H$_2$C=*C*), 167.3 (*C*(O)OCH$_2$), 201.3 (*C*HO), 201.9 (*C*HO). ^{1}H NMR ($CDCl_3$, 300 MHz, minor diastereoisomer) δ 1.05 (3H, d, *J*=8.3 Hz, CH*C*H$_3$), 1.21–1.94 (10H, m, CH_2 and H$_2$C=CCH_3), 2.03 (2H, quin, *J*=6.8 Hz, OCH$_2$CH_2CH$_2$CHO), 2.25–2.76 (4H, m, CH_2C(O) and CHCH$_3$), 4.17 (2H, t, *J*=6.3 Hz, CH$_2$CH_2OC(O)), 4.57 (1H, s, C=CH_2), 4.93 (1H, s, C=CH_2), 6.71 (1H, s, C(O)C=CHC), 9.76 (1H, br s, CHO), 9.78 (1H, br s, CHO). ^{13}C NMR ($CDCl_3$, 75 MHz, minor diastereoisomer) δ 18.8 (H$_2$C=C*C*H$_3$), 19.8 (CH*C*H$_3$), 22.2 (*C*H$_2$), 26.4 (*C*H$_2$), 28.0 (*C*HCH$_3$), 30.0 (*C*H$_2$), 30.2 (*C*H$_2$), 39.2 (CCH$_2$CH$_2$CHO), 40.7 (O(CH$_2$)$_2$CH$_2$CHO), 44.5 (*C*), 63.4 (C(O)OCH$_2$), 115.1 (H$_2$*C*=C), 135.6 (CH=*C*C(O)), 143.3 (*C*H=CC(O)), 147.0 (H$_2$C=*C*), 167.0 (*C*(O)OCH$_2$), 201.5 (*C*HO), 201.9 (*C*HO). ν_{max} (thin film/cm^{-1}): 2934 (m), 2951 (m), 2873 (m), 1728 (s, C=O). 1422 (w), 1259 (m). MS (ES$^+$) *m*/*z* (%): 307 (10, M+H), 324 (100, M+NH_4), 329 (50, M+Na). HRMS: calcd for $C_{18}H_{26}O_4Na$ (M+Na): 329.1723. Found: 329.1720.

3.5.8. Formation of rac-(3R,6R)-2-(formyloxy)ethyl 3-(3-hydroxypropyl)-6-methyl-3-(prop-1-en-2-yl)cyclohex-1-enecarboxylate ***9***. To solution of *rac*-(3*R*,6*R*)-2-hydroxyethyl 3-(3-(*tert*-butyldimethylsilyloxy)propyl)-6-methyl-3-(prop-1-en-2-yl)cyclohex-1-enecarboxylate **8h** (350 mg, 0.882 mmol, dr 3:1), diethyl azodicarboxylate (0.280 mL, 1.76 mmol) and PPh_3 (463 mg, 1.76 mmol) in toluene (15 mL) was added formic acid (68.0 μL, 1.76 mmol) at 23 °C. The mixture was then stirred for 16 h before

concentration in vacuo and purification by chromatography on silica gel to give *rac*-(3*R*,6*R*)-2-(formyloxy)ethyl 3-(3-(*tert*-butyldimethylsilyloxy)propyl)-6-methyl-3-(prop-1-en-2-yl)cyclohex-1-enecarboxylate (302 mg, 0.711 mmol, 81%, dr 3:1) as a yellow oil that was used in the next step without further purification. To a solution of *rac*-(3*R*,6*R*)-2-(formyloxy)ethyl 3-(3-(*tert*-butyldimethylsilyloxy)-propyl)-6-methyl-3-(prop-1-en-2-yl)cyclohex-1-enecarboxylate (302 mg, 0.711 mmol, dr 3:1) in pyridine (5 mL) and MeCN (10 mL) at 0 °C was added dropwise aqueous 60% HF (0.710 mL, 21.3 mmol). After 3 h, the reaction was quenched with the dropwise addition of an excess of aqueous saturated $NaHCO_3$ (20 mL). After the effervescence had subsided, the mixture was extracted with Et_2O (20 mL×3). The combined organic extracts were washed with aqueous saturated $CuSO_4$ (10 mL×2) and then with brine (10 mL×2) before being dried (Na_2SO_4). Concentration in vacuo and purification by chromatography on silica gel gave **9** (169 mg, 0.544 mmol, 76%, dr 3:1) as a colourless oil. ^{1}H NMR ($CDCl_3$, 500 MHz) δ 1.04 (3H, d, J=6.6 Hz, CHCH_3), 1.06 (d, J=6.9 Hz, CHCH_3, minor diastereoisomer), 1.21–1.83 (8H, m, CH_2), 1.71 (s, H_2C=CCH_3, minor diastereoisomer), 1.72 (3H, s, H_2C=CCH_3), 1.91 (1H, br s, OH), 2.55–2.69 (1H, m, CHCH$_3$), 3.53–3.68 (2H, m, CH_2OH), 4.27–4.48 (4H, m, CH_2OC(O)), 4.53 (s, C=CH_2, minor diastereoisomer), 4.65 (1H, s, C=CH_2), 4.87 (1H, s, C=CH_2), 4.89 (s, C=CH_2, minor diastereoisomer), 6.87 (s, C(O)C=CH, minor diastereoisomer), 6.91 (1H, s, C(O)C=CH), 8.10 (1H, s, OCHO). ^{13}C NMR ($CDCl_3$, 75 MHz) δ 18.8 (H_2C=CCH$_3$, minor diastereoisomer), 19.1 (H_2C=CCH$_3$), 19.7 (CHCH_3, minor diastereoisomer), 20.0 (CHCH_3), 25.9 (CH_2, minor diastereoisomer), 26.3 (CH_2, minor diastereoisomer), 27.3 (CH_2), 27.4 (CH_2), 27.4 (CH_2, minor diastereoisomer), 28.0 (CHCH$_3$, minor diastereoisomer), 29.1 (CHCH$_3$), 30.2 (CH_2), 34.4 (CH_2), 34.9 (CH_2, minor diastereoisomer), 44.6 (*C*), 44.9 (*C*, minor diastereoisomer), 61.6 (C(O)OCH_2, minor diastereoisomer), 61.7 (C(O)OCH_2), 61.8 (C(O)OCH_2), 61.8 (C(O)OCH_2, minor diastereoisomer), 63.3 (CH_2OH), 113.2 (H_2C=C), 114.5 (H_2C=C, minor diastereoisomer), 134.5 (H_2C=C, minor diastereoisomer), 134.6 (H_2C=C), 145.1 (C(O)C=CH), 145.3 (C(O)C=CH, minor diastereoisomer), 147.7 (C=CH, minor diastereoisomer), 148.7 (C=CH), 160.8 (OCHO), 167.0 (C(O)CH$_2$, minor diastereoisomer), 167.3 (C(O)CH$_2$). ν_{max} (thin film/cm^{-1}): 3421 (br), 2920 (w), 2848 (w), 1718 (m, C=O), 1647 (m), 1538 (w), 1438 (w), 1321 (w), 1253 (w). MS (ES$^+$) *m*/*z* (%): 328 (20, M+NH$_4$), 333, (100, M+Na). HRMS: calcd for $C_{17}H_{30}O_5N$ (M+NH$_4$): 328.2118. Found: 328.2117.

3.5.9. Formation of rac-(3R,6R)-2-(formyloxy)ethyl 6-methyl-3-(3-oxopropyl)-3-(prop-1-en-2-yl)cyclohex-1-enecarboxylate ***10***. To a solution of oxalyl chloride (45.0 μL, 0.534 mmol) in CH_2Cl_2 (1 mL) at −78 °C was dropwise added DMSO (63.0 μL, 0.889 mmol). After 20 min, *rac*-(3*R*,6*R*)-2-(formyloxy)ethyl 3-(3-hydroxypropyl)-6-methyl-3-(prop-1-en-2-yl)cyclohex-1-enecarboxylate **9** (138 mg, 0.445 mmol, dr 3:1) in CH_2Cl_2 (1 mL) was dropwise added and the mixture stirred for 45 min before triethylamine (0.245 mL, 1.76 mmol) was added and the reaction allowed to warm to 23 °C. Upon warming, the reaction was stirred for 3 h before quenching with aqueous saturated $NaHCO_3$ (10 mL) and extracted with Et_2O (5 mL×3). After drying (Na_2SO_4) and concentration in vacuo, **10** (133 mg, 0.431 mmol, 97%, dr 3:1) was isolated as a yellow oil that was used without further purification. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.04 (3H, d, J=7.0 Hz, CHCH_3), 1.06 (d, J=7.5 Hz, CHCH_3, minor diastereoisomer), 1.20–1.50 (2H, m, CH_2), 1.54–1.93 (4H, m, CH_2), 1.71 (3H, s, H_2C=CCH_3), 2.27–2.53 (2H, m, CH_2CHO), 2.55–2.70 (1H, m, CHCH$_3$), 4.25–4.47 (4H, m, CH_2O), 4.58 (s, C=CH_2, minor diastereoisomer), 4.69 (1H, s, C=CH_2), 4.91 (1H, s, C=CH_2), 6.78 (s, *H*C=CC(O), minor diastereoisomer), 6.81 (1H, s, *H*C=CC(O)), 8.09 (1H, s, OCHO), 9.76 (1H, t, J=1.2 Hz, CH$_2$CHO), 9.79 (t, J=1.3 Hz, CH$_2$CHO, minor diastereoisomer). ν_{max} (thin film/cm^{-1}): 2938 (s), 2873 (w), 1732 (s, C=O), 1738 (s, C=O), 1699 (s, C=O), 1694 (s, C=O), 1634 (m), 1455 (m), 1377 (w), 1253 (s), 1179 (w).

3.6. General procedure 5. Samarium(II) iodide-mediated cascade cyclization of dialdehydes 3a–f

SmI_2 in THF (0.1 M, 2.5 equiv) was added to degassed *t*-BuOH and the resulting solution was stirred under a nitrogen atmosphere for 20 min before being cooled to 0 °C (ice bath). After cooling, the dialdehyde **3a**–**f** (1 equiv) was added dropwise as a solution in THF and the reaction was stirred for 30 min before the excess SmI_2 was quenched by allowing air to reach the reaction. Once the solution was yellow, an aqueous saturated solution of K/Na tartrate was added and the crude reaction mixture was extracted with Et_2O (×3). The combined organic fractions were washed with water and brine, dried (Na_2SO_4) and concentrated in vacuo. The crude products were purified by chromatography on silica gel.

3.6.1. Spirocycle ***5a***. General procedure 5 using 3-oxopropyl 3-(3-oxopropyl)-3-(prop-1-en-2-yl)cyclohex-1-enecarboxylate **3a** (77.0 mg, 0.277 mmol) in THF (2.00 mL), SmI_2 (0.1 M in THF, 6.92 mL, 0.692 mmol) and *t*-BuOH (1.8 mL) gave **5a** (70.0 mg, 0.250 mmol, 90%, dr>95:5) as a colourless solid. Mp 191 °C (CH_2Cl_2/hexanes). ^{1}H NMR (DMSO-d_6, 400 MHz) δ 1.04–1.18 (2H, m, CH_2), 1.28–1.40 (1H, m, CH_2), 1.41–1.56 (3H, m, CH_2), 1.58–1.69 (1H, m, CH_2), 1.70–1.84 (2H, m, CH_2), 1.76 (3H, s, CH_3), 1.84–1.98 (1H, m, CH_2), 2.01–2.14 (1H, m, CH_2), 2.14–2.28 (1H, m, CH_2), 2.42 (1H, d, J=7.8 Hz, CCHOHCH$_2$), 3.98 (1H, m, CH$_2$CHOH), 4.23 (1H, m, 1H from CH_2OC(O)), 4.33 (2H, m, CHCHOH and 1H from CH_2OC(O)), 4.57 (2H, s, C=CH_2), 5.56 (1H, d, J=4.0 Hz, OH), 5.75 (1H, d, J=4.3 Hz, OH). ^{13}C NMR (DMSO-d_6, 100 MHz) δ 18.4 (CH_2), 19.9 (H_2C=CCH$_3$), 25.5 (CH_2), 28.7 (CH_2), 29.7 (CH_2), 31.4 (CH_2), 37.9 (CH_2), 49.2 (*C*), 49.7 (*C*), 50.0 (CCHCHOH), 65.0 (CH_2OC(O)), 71.0 (CCHOH), 72.9 (CHCHOH), 107.2 (C=CH_2), 150.0 (*C*=CH$_2$), 173.9 (*C*=O). ν_{max} (thin film/cm^{-1}): 3335 (br), 2924 (s), 2862 (m), 2849 (m), 1715 (s), 1632 (w), 1451 (w), 1257 (m). MS (ES$^+$) *m*/*z* (%): 303 (100, M+Na), 281 (42, M+H). HRMS: calcd for $C_{16}H_{24}O_4Na$ (M+Na): 303.1567. Found: 303.1566.

3.6.2. Spirocycle ***5b***. General procedure 5 using *rac*-(3*R*,6*R*)-3-oxopropyl 6-methyl-3-(3-oxopropyl)-3-(prop-1-en-2-yl)cyclohex-1-enecarboxylate **3b** (140 mg, 0.479 mmol, dr 3:1) in THF (2 mL), SmI_2 (0.1 M in THF, 12.0 mL, 1.20 mmol) and *t*-BuOH (2.80 mL) gave a major spirocycle **5b** (74 mg, 0.251 mol, 52%, dr>95:5) and a minor spirocycle (26 mg, 88.3 μmol, 18%, dr>95:5). Major spirocycle **5b** isolated as yellow solid. Mp 170 °C (CH_2Cl_2/hexanes). ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.05 (3H, d, J=6.6 Hz, CHCH_3), 1.22–1.47 (4H, m, CH_2), 1.63 (1H, m, CH_2), 1.74 (3H, s, H_2C=CCH_3), 1.81–1.97 (2H, m, CH_2), 2.10–2.37 (2H, m, CH_2), 2.46 (1H, m, CHCH$_3$), 2.56 (1H, d, J=8.5 Hz, CHCHOH), 2.59–2.77 (1H, m, CH_2), 4.08–4.29 (2H, m, CCHOHCH$_2$ and 1H from CH$_2$CH_2OC(O)), 4.43 (1H, ddd, J=11.9, 8.0, 4.4 Hz, CH$_2$CH_2OC(O)), 4.90–4.66 (3H, m, C=CH_2 and CHCHOHCH$_2$). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 14.2 (CHCH_3), 16.0 (H_2C=CCH_3), 27.0 (CH_2), 28.5 (CH_2), 29.4 (CH_2), 30.1 (CHCH$_3$), 30.8 (CH_2), 38.6 (CH_2), 48.7 (CCHCHOH), 50.6 (CCHCHOH), 53.1 (CC(O)), 64.5 (CH_2OC(O)), 69.0 (CCHOH), 73.5 (CHCHOH), 110.4 (C=CH_2), 147.7 (*C*=CH$_2$), 171.6 (*C*=O). ν_{max} (thin film/cm^{-1}): 3311 (br), 2935, (m), 1706 (s, C=O), 1263 (w), 1065 (m). MS (ES$^+$) *m*/*z* (%): 295 (5, M+H), 317 (100, M+Na). HRMS: calcd for $C_{17}H_{27}O_4$ (M+H): 295.1904. Found: 295.1902. Minor spirocycle isolated as a yellow gum. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.02 (3H, d, J=7.0 Hz, CHCH_3), 1.19–2.37 (11H, m, CH_2 and CHCH$_3$), 1.91 (3H, s, H_2C=CCH_3), 2.80 (1H, d, J=6.8 Hz, CHCHOH), 4.09–4.21 (1H, m, CCHOHCH$_2$), 4.36 (1H, dt, J=11.6, 5.9 Hz, CH$_2$CH_2OC(O)), 4.41–4.50 (1H, m, CHCHOHCH$_2$), 4.51–4.63 (1H, m, CH$_2$CH_2OC(O)), 4.81–4.90 (1H, m, C=CH_2), 5.00 (1H, s, C=CH_2). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 18.8 (CHCH$_3$), 20.2 (H_2C=CCH$_3$), 27.3 (CH_2), 27.7 (CH_2), 28.1 (CH_2), 32.1 (CHCH$_3$), 32.7

(CH_2), 37.8 (CH_2), 49.6 (*C*CHCHOH), 51.0 (CCHCHOH), 54.8 (*C*C(O)), 65.4 ($CH_2OC(O)$), 70.3 (*C*CHOH), 76.4 (CH*C*HOH), 109.4 (C=*C*H_2), 152.7 (*C*=CH_2), 174.2 (*C*=O). ν_{max} (thin film/cm^{-1}): 3311 (br), 2935, (m), 1706 (s, C=O), 1263 (w), 1065 (m). MS (ES^+) *m*/*z* (%): 295 (7, M+H), 317 (100, M+Na). HRMS: calcd for $C_{17}H_{30}O_4$ (M+NH_4): 312.2169. Found: 312.2163.

3.6.3. Spirocycle ***5c****.* General procedure 5 using 3-oxopropyl 3-(but-3-enyl)-3-(3-oxopropyl)cyclohex-1-enecarboxylate **3c** (33.0 mg, 0.113 mmol) in THF (1 mL), SmI_2 (0.1 M in THF, 2.82 mL, 0.282 mmol) and *t*-BuOH (0.760 mL) gave **5c** (23.0 mg, 78.1 μmol, 69%, dr>95:5) as a colourless oil. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.05–1.12 (1H, m, 1H from CH_2), 1.30–1.38 (4H, m, 1H from 3×CH_2, 1H from CCH_2CH_2CH=CH_2), 1.49–1.54 (2H, m, 1H from CCH_2CH_2CHOH, 1H from CH_2), 1.71–1.74 (1H, m, 1H from CCH_2CH_2CHOH), 1.79–1.82 (1H, m, 1H from CCH_2CH_2CHOH), 1.83–1.89 (4H, m, CCH_2CH_2CH=CH_2, 1H from CCH_2CH_2CH=CH_2, 1H from $CH_2CH_2OC(O)$), 2.08–2.13 (2H, m, 1H from CCH_2CH_2CHOH, 1H from CH_2), 2.19 (1H, d, *J*=8.6 Hz, CC*H*CHOH), 2.36 (1H, dddd, *J*=14.3, 11.0, 7.7, 3.5 Hz, 1H from $CH_2CH_2OC(O)$), 4.07 (1H, t, *J*=4.3 Hz, CC*H*OH), 4.28–4.37 (2H, m, 1H from CH_2OC(O), CCHC*H*OH), 4.52 (1H, td, *J*=11.1, 5.8 Hz, 1H from CH_2OC(O)), 4.85 (1H, dd, *J*=10.1, 2.2 Hz, *cis* CH=CH_2), 4.97 (1H, dd, *J*=17.1, 2.2 Hz, *trans* CH=CH_2), 5.82 (1H, ddt, *J*=17.1, 10.4, 6.6 Hz, C*H*=CH_2). ^{13}C NMR ($CDCl_3$, 125 MHz) δ 18.6 (CH_2), 26.1 (CH_2CH_2OC=O), 29.1 (CH_2), 29.2 (CH_2), 31.8 (CH_2), 32.4 (CCH_2CH_2CHOH), 35.6 (CH_2CH=CH_2), 38.4 (CCH_2CH_2CHOH), 44.6 (*C*CHOH), 50.6 (CCH_2CH_2CH=CH_2), 51.7 (*C*C=O), 66.0 (CH_2OC=O), 72.7 (CCHOH), 75.3 (CCHCHOH), 113.8 (HC=CH_2), 139.9 (HC=CH_2), 176.0 (*C*=O). ν_{max} (thin film/cm^{-1}): 3402 (br), 2938 (s), 2864 (m), 1718 (s, C=O), 1639 (w), 1458 (m), 1399 (w), 1259 (w), 1152 (m), 1052 (m), 908 (w). MS (ES^+) *m*/*z* (%): 317 (100, M+Na). HRMS: Calcd for $C_{17}H_{26}O_4Na$ (M+Na): 317.1723. Found: 317.1715.

3.6.4. Spirocycle ***5d****.* General procedure 5 using *rac*-(3*S*,6*R*)-3-oxopropyl 3-(but-3-enyl)-6-methyl-3-(3-oxopropyl)cyclohex-1-enecarboxylate **3d** (50.0 mg, 0.163 mmol, dr 3:1) in THF (1 mL), SmI_2 (0.1 M in THF, 4.08 mL, 0.408 mmol) and *t*-BuOH (1.02 mL) gave a major spirocycle **5d** (33.0 mg, 0.106 mmol, 66%, dr>95:5) as a colourless oil. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.10 (3H, d, *J*=6.8 Hz, CH_3), 1.22–1.32 (2H, m, 1H from CH_2CHCH_3, 1H from CH_2), 1.40–1.47 (2H, m, 1H from CH_2, 1H from CCH_2CH_2CHOH), 1.50–1.68 (2H, m, 1H from CH_2, 1H from CCH_2CH_2CHOH), 1.70–1.80 (1H, m, 1H from CH_2CHCH_3), 1.86–1.98 (4H, m, CH_2CH=CH_2, CCH_2CH_2CHOH), 2.13 (1H, d, *J*=8.8 Hz, CC*H*CHOH), 2.17–2.25 (2H, m, 1H from $CH_2CH_2OC(O)$, C*H*CH_3), 2.30–2.41 (1H, m, 1H from CH_2), 2.58–2.68 (1H, m, 1H from $CH_2CH_2OC(O)$), 4.15–4.27 (2H, m, 1H from $CH_2OC(O)$, CC*H*OH), 4.47 (1H, ddd, *J*=11.7, 8.1, 4.9 Hz, 1H from $CH_2OC(O)$), 4.73 (1H, td, *J*=9.1, 6.3 Hz, CHC*H*OH), 4.90 (1H, dd, *J*=10.1, 2.0 Hz, *cis* CH_2=CH), 4.99 (1H, dd, *J*=17.1, 2.0 Hz, *trans* CH_2=CH), 5.78 (1H, ddt, *J*=17.1, 10.1, 6.5 Hz, CH_2=C*H*). ^{13}C NMR ($CDCl_3$, 125 MHz) δ 15.6 (CH*C*H_3), 26.6 (CH_2), 27.5 ($CH_2CH_2OC(O)$), 28.1 (CH_2), 28.8 (CH_2CH=CH_2), 29.7 ($CHCH_3$), 30.9 (CH_2), 35.0 (CH_2CHCH_3), 35.9 (CH_2CH_2CHOH), 45.1 (*C*CHOH), 51.7 (*C*HCHOH), 52.9 (*C*C(O)), 64.4 ($CH_2OC(O)$), 68.7 (*C*CHOH), 73.3 (CCHC*H*OH), 113.6 (CH=CH_2), 138.7 (C*H*=CH_2), 173.5 (*C*=O). ν_{max} (thin film/cm^{-1}): 3381 (br), 2933 (s), 2868 (m), 1711 (s, C=O), 1640 (w), 1253 (w), 1175 (m), 1064 (m), 909 (m), 733 (w). MS (ES^+) *m*/*z* (%): 331 (100, M+Na). HRMS: Calcd for $C_{18}H_{28}O_4Na$ (M+Na): 331.1880. Found: 331.1882.

3.6.5. Spirocycle ***5e****.* General procedure 5 using 3-oxopropyl 3-methyl-3-(3-oxopropyl)cyclohex-1-enecarboxylate **3e** (50.0 mg, 0.198 mmol) in THF (1.50 mL), SmI_2 (0.1 M in THF, 4.95 mL, 0.495 mmol) and *t*-BuOH (1 mL) gave **5e** (39.0 mg, 0.153 mmol, 77%, dr>95:5) as a colourless oil. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.03–1.037 (1H, m, 1H from CH_2), 1.18–1.21 (1H, m, 1H from CH_2), 1.23 (3H, s, CH_3), 1.28–1.29 (1H, m, 1H from CH_2), 1.39–1.54 (4H, m, 1H from CCH_2CH_2CHOH, 1H from CCH_2CH_2CHOH, CH_2), 1.71–1.76 (1H, m, 1H from CCH_2CH_2CHOH), 1.83–1.91 (2H, m, 1H from $CH_2CH_2OC(O)$, 1H from CH_2), 2.08–2.15 (2H, m, CC*H*CHOH, 1H from CCH_2CH_2CHOH), 2.24–2.33 (1H, m, 1H, from $CH_2CH_2OC(O)$), 4.08 (1H, t, *J*=3.9 Hz, CC*H*OH), 4.29–4.36 (2H, m, 1H from C$H_2OC(O)$, CHC*H*OH), 4.59 (1H, td, *J*=11.0, 5.9 Hz, 1H from C$H_2OC(O)$). ^{13}C NMR ($CDCl_3$, 125 MHz) δ 19.0 (CH_2), 26.0 ($CH_2CH_2OC(O)$), 28.5 (CH_2), 28.9 (CH_3), 32.2 (CCH_2CH_2CHOH), 33.1 (CH_2), 40.4 (CCH_2CH_2CHOH), 41.8 (*C*CHCHOH), 50.6 (*C*C(O)), 53.8 (*C*CHCHOH), 66.2 ($CH_2OC(O)$), 72.8 (CCHOH), 75.6 (CHCHOH), 176.1 (*C*=O). ν_{max} (thin film/cm^{-1}): 3397 (br), 2929 (s), 2859 (m), 1723 (s, C=O), 1460 (m), 1265 (w), 1158 (m), 1078 (w), 1006 (w). MS (ES^+) *m*/*z* (%): 277 (100, M+Na). HRMS: Calcd for $C_{14}H_{22}O_4Na$ (M+Na): 277.1410. Found: 277.1404.

3.6.6. Spirocycle ***5f****.* General procedure 5 using 3-oxopropyl 6,6-dimethyl-3-(3-oxopropyl)-3-(prop-1-en-2-yl)cyclohex-1-enecarboxylate **3f** (28.0 mg, 91.4 μmol) in THF (2 mL), SmI_2 (0.1 M in THF, 2.28 mL, 0.228 mmol) and *t*-BuOH (0.900 mL) gave spirocycle **5f** (21.0 mg, 68.1 μmol, 75%, dr>95:5) as a light yellow solid. Mp 159–160 °C (CH_2Cl_2/hexanes). ^{1}H NMR ($CDCl_3$, 400 MHz) δ 0.96 (1H, m, CH_2), 1.00 (3H, s, C(CH_3)$_2$), 1.04 (3H, s, C(C)$_2$), 1.26 (1H, m, CH_2), 1.35–1.48 (2H, m, CH_2), 1.52–1.67 (1H, m, CH_2), 1.74–1.82 (1H, m, CH_2), 1.88 (3H, s, H_2C=CCH_3), 1.98–2.25 (2H, m, CH_2), 2.33 (1H, dddd, *J*=13.7, 8.2, 5.1, 3.3 Hz, CHOHCH_2CH_2O), 2.57 (1H, td, *J*=12.7, 7.8 Hz, CH_2), 2.76 (1H, br s, C*H*CHOH), 3.58 (1H, br s, OH), 4.15 (1H, ddd, *J*=8.1, 5.9, 2.1 Hz, CHC*H*OH), 4.23 (1H, dd, *J*=7.7, 3.2 Hz, CC*H*OH), 4.32 (1H, dt, *J*=11.4, 5.6 Hz, C$H_2OC(O)$), 4.59 (1H, ddd, *J*=11.4, 7.9, 5.0 Hz, C$H_2OC(O)$), 4.92 (1H, s, C=CH_2), 5.07 (1H, s, C=CH_2). ^{13}C NMR ($CDCl_3$, 100 MHz) δ 20.1 (H_2C=C*C*H_3), 23.5 (C(*C*H_3)$_2$), 28.7 (CH_2), 29.3 (C(*C*H_3)$_2$), 29.2 (CH_2), 33.9 (CH_2), 34.0 (two signals, CH_2), 36.0 (*C*(CH$_3$)$_2$), 49.2 (CCHCHOH), 50.7 (CCHCHOH), 59.7 (*C*(C(O))), 65.3 ($CH_2OC(O)$), 71.9 (CCHOH), 82.0 (CHCHOH), 110.0 (C=CH_2), 153.8 (*C*=CH_2), 173.3 (*C*=O). ν_{max} (thin film/cm^{-1}): 3389 (br), 2953 (s), 2925 (s), 2858 (m), 1715 (s, C=O), 1631 (w), 1459 (w), 1108 (w). MS (ES^+) *m*/*z* (%): 326 (10, M+NH_4), 331 (100, M+Na). HRMS: calcd for $C_{18}H_{28}O_4Na$ (M+Na): 331.1880. Found: 331.1879.

3.6.7. Attempted cascade cyclization of rac-(3R,6R)-4-oxobutyl 6-methyl-3-(3-oxopropyl)-3-(prop-1-en-2-yl)cyclohex-1-enecarboxylate ***3g****.* SmI_2 (0.1 M in THF, 5.30 mL, 0.530 mmol) was added to degassed *t*-BuOH (1.46 mL) and the resulting complex was stirred under a nitrogen atmosphere for 20 min before being cooled to 0 °C (ice bath). After cooling, *rac*-(3*R*,6*R*)-4-oxobutyl 6-methyl-3-(3-oxopropyl)-3-(prop-1-en-2-yl)cyclohex-1-enecarboxylate **3g** (65.0 mg, 0.212 mmol, dr 3:1) was added dropwise as a solution in THF (2 mL) and the reaction was stirred for 30 min before the excess SmI_2 was quenched by allowing air to reach the reaction. Once the solution was yellow, an aqueous saturated solution of K/Na tartrate (10 mL) was added and the crude reaction mixture was extracted with Et_2O (10 mL×3). The combined organic fractions were washed with water (5 mL) and brine (5 mL), dried (Na_2SO_4) and concentrated in vacuo. The crude products were purified by chromatography on silica gel to give **11** (10.0 mg, 32.2 μmol, 15%) as colourless oil. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 0.90 (3H, d, *J*=7.2 Hz, CHCH_3), 1.15–1.36 (2H, m, CH_2), 1.40–1.84 (8H, m, CH_2), 1.86 (3H, s, H_2C=CCH_3), 1.89 (s, H_2C=CCH_3, minor diastereoisomer), 2.03–2.27 (2H, m, CH_2), 2.27–2.37 (1H, m, C*H*C(O)), 2.45 (d, *J*=10.7 Hz, C*H*CHOH minor diastereoisomer), 2.55 (1H, d, *J*=10.7 Hz, C*H*CHOH), 3.69 (2H, t, *J*=6.1 Hz, CH_2OH), 3.81–3.93 (1H, m, CHC*H*OH), 4.03–4.33 (2H, m, C$H_2OC(O)$), 4.89–4.98 (1H, m, C=CH_2), 4.99–5.12 (1H, m, C=CH_2). ^{13}C NMR ($CDCl_3$, 75 MHz) δ 13.8 (CH*C*H_3), 19.1 (H_2C=C*C*H_3), 19.3 (H_2C=C*C*H_3, minor diastereoisomer), 24.1 (CH_2), 24.3 (CH_2, minor diastereoisomer),

26.5 (CH_2), 27.3 (CH_2), 28.2 (CH_2), 28.4 (CH_2, minor diastereoisomer), 28.7 (CH_2, minor diastereoisomer), 29.0 ($CHCH_3$), 30.8 (CH_2), 30.9 (CH_2), 31.9 (CH_2, minor diastereoisomer), 32.2 (CH_2, minor diastereoisomer), 45.7 (CHCHCHOH), 46.2 (CHCHCHOH), 48.2 (*C*), 48.9 (minor diastereoisomer), 51.2 (minor diastereoisomer), 51.3 (minor diastereoisomer), 61.2 (CH_2OH), 63.2 ($CH_2OC(O)$), 77.7 (CHCHOH, minor diastereoisomer), 78.8 (CHCHOH), 109.6 (C=CH_2), 109.8 (C=CH_2, minor diastereoisomer), 150.3 (*C*=CH_2), 151.6 (*C*=CH_2, minor diastereoisomer), 174.0 (*C*=O), 174.6 (*C*=O, minor diastereoisomer). MS (ES^+) *m*/*z* (%): 311 (18, M+H), 328 (10, M+NH_4), 333 (100, M+Na).

*3.6.8. Attempted cascade cyclization of rac-(3R,6R)-2-(formyloxy)ethyl 6-methyl-3-(3-oxopropyl)-3-(prop-1-en-2-yl)cyclohex-1-enecarboxylate **10**.* SmI_2 (0.1 M in THF, 3.65 mL, 0.365 mmol) was added to degassed *t*-BuOH (1.13 mL) and the resulting complex was stirred under a nitrogen atmosphere for 20 min before being cooled to 0 °C (ice bath). After cooling, *rac*-(3*R*,6*R*)-2-(formyloxy)ethyl 6-methyl-3-(3-oxopropyl)-3-(prop-1-en-2-yl)cyclohex-1-enecarboxylate **10** (45.0 mg, 0.146 mmol, dr 3:1) was added dropwise as a solution in THF (2 mL) and the reaction was stirred for 30 min before the excess SmI_2 was quenched by allowing air to reach the reaction. Once the solution was yellow, a saturated aqueous solution of K/Na tartrate (10 mL) was added and the crude reaction mixture was extracted with Et_2O (10 mL×3). The combined organic fractions were washed with water (5 mL) and brine (5 mL), dried (Na_2SO_4) and concentrated in vacuo. The crude products were purified by chromatography on silica gel to give **12** (9.00 mg, 31.9 μmol, 21%) and **13** (10.0 mg, 32.2 μmol, 22%). *rac*-(3*S*,3a*S*,4*R*,5*R*,7a*R*)-2-Hydroxyethyl 3-hydroxy-5-methyl-7a-(prop-1-en-2-yl)-octahydro-1*H*-indene-4-carboxylate **12** was isolated as colourless oil. ^1H NMR ($CDCl_3$, 300 MHz) δ 0.92 (3H, d, *J*=7.0 Hz, CHCH_3), 1.18–1.96 (7H, m, CH_2), 1.85 (3H, s, H_2C=CCH_3), 2.02–2.30 (2H, m, $CHCH_3$ and CH_2), 2.40 (1H, dd, *J*=10.7, 4.5 Hz, CHC(O)), 2.61 (1H, d, *J*=10.9 Hz, C(O)CH-CHOH), 3.68–3.93 (3H, m, CH_2OH and CHOH), 4.04–4.18 (1H, m, $CH_2OC(O)$), 4.26–4.43 (1H, m, $CH_2OC(O)$), 4.94 (1H, s, C=CH_2), 5.04 (1H, s, C=CH_2). ^{13}C NMR ($CDCl_3$, 75 MHz) δ 14.7 ($CHCH_3$), 20.0 (H_2C=CCH_3), 20.4 (H_2C=CCH_3, minor diastereoisomer), 27.6 (CH_2), 28.5 (CH_2), 29.3 (CH_2, minor diastereoisomer), 30.2 ($CHCH_3$), 30.9 (CH_2, minor diastereoisomer), 31.9 (CH_2, minor diastereoisomer), 32.0 (CH_2), 32.3 (CH_2), 32.6 ($CHCH_3$, minor diastereoisomer), 33.0 (CH_2, minor diastereoisomer), 46.5 (CHOHCHCH), 47.8 (CHCHCH), 49.1 (*C*), 49.6 (*C*, minor diastereoisomer), 52.1 (*C*H, minor diastereoisomer), 52.6 (*C*H, minor diastereoisomer), 61.0 ($CH_2OC(O)$), 61.1 ($CH_2OC(O)$, minor diastereoisomer), 66.0 (CH_2OH), 79.2 (CHOH, minor diastereoisomer), 79.9 (CHOH), 110.6 (C=CH_2), 110.8 (C=CH_2, minor diastereoisomer), 151.4 (*C*=CH_2), 152.0 (*C*=CH_2, minor diastereoisomer), 175.0 (*C*=O), 175.9 (*C*=O, minor diastereoisomer). ν_{max} (thin film/cm^{-1}): 3401 (br), 3085 (w), 2955 (s), 1730 (s, C=O), 1635 (m), 1454 (m), 1384 (w), 1248 (w), 1217 (w), 1171 (w). MS (ES^+) *m*/*z* (%): 265 (25, [M+H]−H_2O), 283 (10, M+H), 300 (35, M+NH_4), 305 (100, M+Na). HRMS: calcd for $C_{16}H_{26}O_4Na$ (M+Na): 305.1729. Found: 305.1715. *rac*-(3*S*,3a*S*,4*R*,5*R*,7a*R*)-2-(Formyloxy)ethyl 3-hydroxy-5-methyl-7a-(prop-1-en-2-yl)-octahydro-1*H*-indene-4-carboxylate **13** isolated as colourless oil. ^1H NMR ($CDCl_3$, 300 MHz) δ 0.90 (3H, d, *J*=7.2 Hz, CHC*H*), 1.03–1.12 (1H, m, C*H*CH_3), 1.16–2.00 (6H, m, CH_2), 1.87 (3H, m, H_2C=CCH_3), 2.00–2.29 (2H, m, CH_2), 2.35–2.43 (1H, m, C*H*C=O), 2.50–2.59 (1H, m, CHC*H*CHOH), 3.87 (1H, br s, C*H*OH), 4.25–4.52 (4H, m, $CH_2OC(O)$), 4.80–5.13 (2H, m, C=CH_2), 8.09 (1H, s, OC*H*O). ^{13}C NMR ($CDCl_3$, 75 MHz) δ 14.9 (CH*C*H), 20.3 (H_2C=CCH_3), 27.4 (CH_2), 28.5 (CH_2), 29.9 ($CHCH_3$), 31.9 (CH_2), 32.2 (CH_2), 46.8 (CHCHCH or CHCHCHOH), 46.9 (CHCHCH or CHCHCHOH), 49.1 (*C*), 61.6 ($CH_2OC(O)$), 61.8 ($CH_2OC(O)$), 79.6 (CHOH), 110.7 (C=CH_2), 151.1 (*C*=CH_2), 160.6 (OCHO), 174.6 (*C*(O)). ν_{max} (thin film/cm^{-1}): 2996 (m), 2955 (m), 2873 (w), 1723 (s), 1460 (w), 1442, (w), 1251 (w), 1168 (m). MS (ES^+) *m*/*z* (%): 328 (40, M+NH_4), 333 (100, M+Na). HRMS: calcd for $C_{17}H_{26}O_5Na$ (M+Na): 333.1678. Found: 333.1661.

*3.6.9. Reduction of spirocyclic lactone 5c with SmI_2–H_2O to give rac-(1R)-1-[(3S,3aR,4S,7aS)-3-hydroxy-4-(hydroxymethyl)-7a-(but-3-en-1-yl)octahydro-1H-inden-4-yl]propane-1,3-diol **18c**.* Degassed, distilled water (1.15 mL) was added to a solution of SmI_2 in THF (0.1 M, 4.60 mL, 0.460 mmol) and stirred under nitrogen until the solution turned a dark red. Degassed spirocycle **5c** (17 mg, 57.7 μmol) was added as a solution in THF (0.700 mL) and the reaction was stirred for 18 h until the solution had decolourised. An aqueous saturated solution of K/Na tartrate (10 mL) was added and the mixture was extracted with EtOAc (5×15 mL). The combined organic fractions were washed with water (2×15 mL) and brine (15 mL), dried (Na_2SO_4) and concentrated in vacuo. The crude products were purified by chromatography on silica gel to give **18c** (14.0 mg, 46.9 μmol, 81%) as a colourless oil. ^1H NMR ($CDCl_3$, 400 MHz) δ 1.15–1.42 (4H, m, CH_2), 1.57–1.75 (7H, m, 1H from CH_2CH$_2$OH, 1H from CCH_2CH$_2$CHOH, 1H from CH_2, 1H from CCH$_2$CH_2CH=CH$_2$, CH_2), 1.87–1.97 (2H, m, 1H from CH_2CH$_2$OH, 1H from CH_2), 2.02–2.11 (1H, m, 1H from CCH$_2$CH_2CH=CH$_2$), 2.17–2.23 (2H, m, 1H from CCH$_2$CH_2CHOH, 1H from CCH$_2$CH_2CH=CH$_2$), 2.37 (1H, d, *J*=7.3 Hz, CC*H*CHOH), 3.77 (1H, d, *J*=11.4 Hz, 1H from CCH_2OH), 3.83–3.96 (4H, m, 1H from CCH_2OH, CC*H*OH, CH$_2$CH_2OH), 4.51 (1H, td, *J*=8.6, 2.8 Hz, CCHC*H*OH), 4.93 (1H, dd, *J*=10.1, 2.0 Hz, *cis* CH=CH_2), 5.03 (1H, dd, *J*=17.1, 2.0 Hz, *trans* CH=CH_2), 5.84 (1H, ddt, *J*=17.1, 10.1, 6.7 Hz, C*H*=CH$_2$). ^{13}C NMR ($CDCl_3$, 125 MHz) δ 18.1 (CH_2), 27.8 (CH_2), 28.9 (CH_2CH=CH$_2$), 29.7 (CH_2), 31.6 (CH_2CH_2OH), 31.8 (CH_2), 36.9 (CH_2), 38.2 (CH_2), 41.4 (*C*), 44.8 (*C*), 50.8 (CCHCHOH), 62.8 (CH_2CH_2OH), 65.6 (CCH_2OH), 74.6 (CCHCHOH), 81.3 (CCHOH), 114.1 (HC=CH_2), 139.5 (HC=CH_2). ν_{max} (thin film/cm^{-1}): 3324 (br OH), 2923 (s), 2855 (m), 1721 (w), 1640 (w), 1554 (m), 1434 (m), 1361 (w), 1233 (w), 1049 (m), 908 (w). MS (ES^+) *m*/*z* (%): 321 (100, M+Na). HRMS: calcd for $C_{17}H_{30}O_4Na$ (M+Na): 321.2042. Found: 321.2051.

*3.6.10. Reduction of spirocyclic lactone **5e** with SmI_2–H_2O to give rac-(1R)-1-[(3S,3aR,4S,7aS)-3-hydroxy-4-(hydroxymethyl)-7a-methyl-octahydro-1H-inden-4-yl]propane-1,3-diol **18e**.* Degassed, distilled water (1.73 mL) was added to a solution of SmI_2 in THF (0.1 M, 6.90 mL, 0.690 mmol) and stirred under nitrogen until the solution turned a dark red. Degassed spirocycle **5e** (22 mg, 86.5 μmol) was added as a solution in THF (1 mL) and the reaction was stirred for 18 h until the solution had decolourised. An aqueous saturated solution of K/Na tartrate (10 mL) was added and the mixture was extracted with EtOAc (5×15 mL). The combined organic fractions were washed with water (2×15 mL) and brine (15 mL), dried (Na_2SO_4) and concentrated in vacuo. The crude products were purified by chromatography on silica gel to give **18e** (21.0 mg, 81.3 μmol, 94%) as a colourless oil. ^1H NMR ($CDCl_3$, 400 MHz) δ 1.15–1.30 (4H, m, CH_2), 1.26 (3H, s, CH_3), 1.40–1.46 (3H, m, 1H from CCH_2CH$_2$CHOH, CH_2), 1.55–1.62 (1H, m, 1H from CCH$_2$CH_2CHOH), 1.68–1.74 (1H, m, 1H from CHOHCH_2CH$_2$OH), 1.86–1.92 (2H, m, 1H from CCH_2CH$_2$CHOH, 1H from CHOHCH_2-CH$_2$OH), 2.17–2.23 (1H, m, 1H from CCH$_2$CH_2CHOH), 2.31 (1H, d, *J*=7.8 Hz, CC*H*CHOH), 3.78 (1H, d, *J*=11.6 Hz, 1H from CCH_2OH), 3.83–3.96 (4H, m, 1H from CCH_2OH, CC*H*OH, CH$_2$CH_2OH), 4.48 (1H, td, *J*=8.8, 2.5 Hz, CCHC*H*OH). ^{13}C NMR ($CDCl_3$, 125 MHz) δ 18.4 (CH_2), 26.9 (CH_3), 27.6 (CH_2), 29.7 (CH_2), 31.5 (CH_2CH_2OH), 31.7 (CCH_2CH_2CHOH), 41.3 (CCH_2CH_2CHOH), 41.4 (*C*), 41.6 (*C*), 52.3 (CCHCHOH), 62.7 (CH_2CH_2OH), 65.1 (CCH_2OH), 74.7 (CCHCHOH), 81.2 (CCHOH). ν_{max} (thin film/cm^{-1}): 3327 (br O–H), 2929 (s), 2858 (m), 2365 (w), 2341 (w), 1458 (w), 1052 (s). MS (ES^+) *m*/*z* (%): 281

(100, M+Na). HRMS: Calcd for $C_{14}H_{26}O_4Na$ (M+Na): 281.1729. Found: 281.1724.

*3.6.11. SmI_2-mediated, dialdehyde cyclization cascade–lactone reduction to give **18e** from **3e**.* SmI_2 (0.1 M in THF, 3.70 mL, 0.370 mmol) was added to degassed *t*-BuOH (0.73 mL) and the resulting complex was stirred under a nitrogen atmosphere for 20 min before being cooled to 0 °C (ice bath). After cooling, 3-oxopropyl 3-methyl-3-(3-oxopropyl)cyclohex-1-enecarboxylate **3e** (37.0 mg, 0.147 mmol) was added dropwise as a solution in THF (1.50 mL) and the reaction was stirred for 30 min. The ice bath was removed and a solution of SmI_2 (0.1 M in THF, 12.1 mL, 1.21 mmol) and degassed, distilled water (3.02 mL) was added. The reaction was stirred for 18 h until the solution had decolourised. An aqueous saturated solution of K/Na tartrate (10 mL) was added and the mixture was extracted with EtOAc (5×15 mL). The combined organic fractions were washed with water (2×15 mL) and brine (15 mL), dried (Na_2SO_4) and concentrated in vacuo. The crude products were purified by chromatography on silica gel to give **18e** (29.0 mg, 0.112 mmol, 76%) as a colourless oil.

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21. Treatment of **3e** with SmI_2–H_2O appeared to give products resulting from radical cyclization but not aldol cyclization. This is presumably due to rapid protonation of the intermediate samarium enolate by H_2O, thus preventing aldol cyclization. The second aldehyde is then reduced by the reagent system.