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Studies towards the total synthesis of solanoeclepin A: synthesis and potato cyst nematode hatching activity of analogues containing the tetracyclic left-hand substructure †

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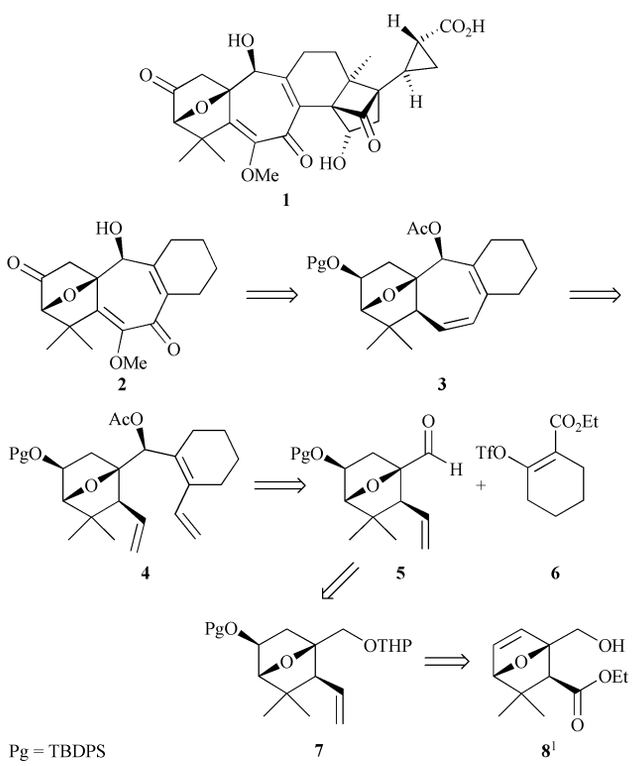
In our studies towards the total synthesis of solanoeclepin A, a natural hatching agent of potato cyst nematodes, three analogues containing the tetracyclic left-handed substructure have been synthesised. First, the synthesis of the parent tetracycle **2** in enantiopure form is reported. Key steps are (1) chromium-mediated coupling of aldehyde **5** (see preceding paper in this issue) and vinyl triflate **6** to furnish an α,β-unsaturated lactone, which was transformed into triene **4** in six-steps, (2) ring-closing metathesis of **4** to tetracycle **3** and (3) oxidative functionalisation of the least substituted double bond of **3** to provide the fully functionalised tetracyclic left-handed substructure of solanoeclepin A. The methodology developed was successfully applied in the synthesis of two more elaborate solanoeclepin A analogues **9** and **11**. Both compounds, prepared as mixtures of diastereomers, showed promising biological activity in hatching activity tests.

Introduction

As described in the preceding paper[1] our synthetic strategy to prepare the tetracyclic left-handed substructure **2** of solanoeclepin A (**1**)[2] by using a McMurry coupling as the key step failed. In this paper we present an alternative and successful approach for the construction of the highly functionalised seven-membered ring by using an olefin metathesis process to provide **3**. Target compound **2** was expected to be accessible *via* oxidative functionalisation of the least substituted double bond of diene **3**, the latter being the product of a ring-closing metathesis (RCM)[3] reaction of divinyl compound **4**. As described in the previous paper[1] a convergent approach can be used to construct **4**. To this end, aldehyde **5**, which in this case contains a vinyl functionality, and vinyl triflate‡ **6** have to be coupled. It was expected that aldehyde **5** would be readily available from compound **7**, which should arise from the well known hydroxy ester **8** reported in the previous paper (Scheme 1).[1]

To gain a better insight into the structure–activity relationships (SAR) of the natural product, the second part of this paper reports the syntheses and biological activity of two more elaborate model compounds **9** and **11** (Scheme 2). As was concluded from SAR studies of glycinoeclepin A,[4] the hatching agent of the soybean cyst nematode, a carboxylic acid group is essential for hatching activity. For this reason it was decided that solanoeclepin A analogues **9** and **11** should contain this moiety properly attached to the tetracyclic left-handed substructure. It was speculated that a cyclopropane ring[5] could also be important for the hatching activity.

In order to gain rapid access to these analogues a non-diastereoselective approach was chosen. Testing mixtures of diastereomers would give a positive result even if only one of the isomers were active. Once activity is found in one of the mixtures, efforts can be made to elucidate the structure of the active diastereomer. Therefore, compounds **9** and **11** were synthesised by coupling enantiopure aldehyde **5** with racemic vinyl triflates **10** and **12**, respectively.



Scheme 1

† Electronic supplementary information (ESI) available: further experimental details. See http://www.rsc.org/suppdata/p1/b2/b202020n/
‡ The IUPAC name for triflate is trifluoromethanesulfonate.

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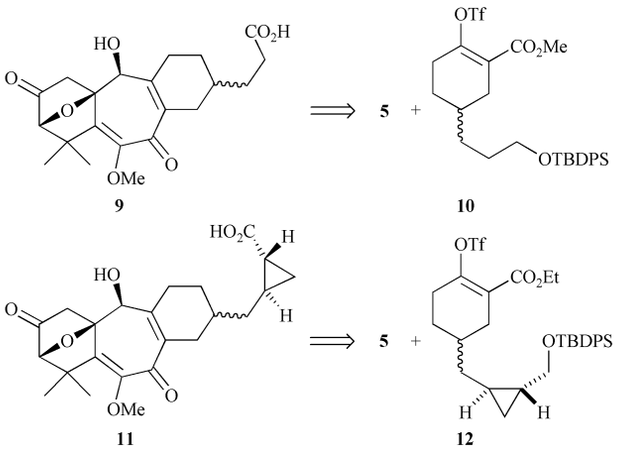
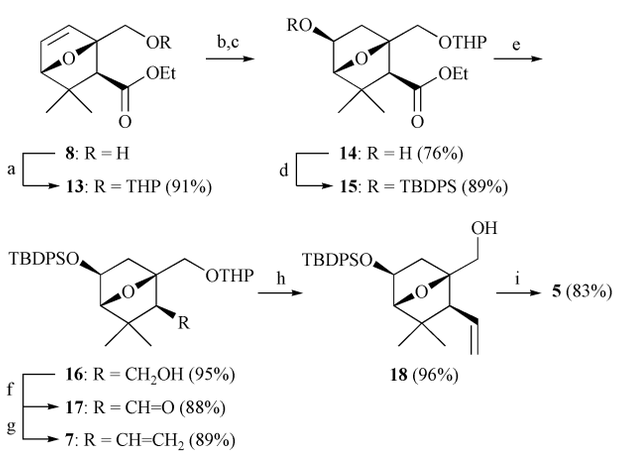


Scheme 2

Results and discussion

Preparation of aldehyde 5

The first step in the synthesis of aldehyde **5** was THP protection of the enantiopure hydroxy ester **8**[1] to provide **13** (Scheme 3).



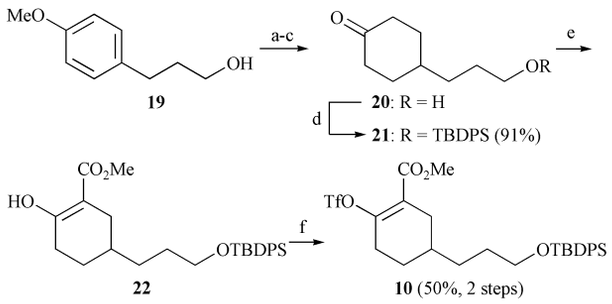
Scheme 3 *Reagents and conditions*: a, DHP, *p*-TsOH, CH_2Cl_2; b, disiamylborane, THF, −20 °C; c, NaOH, H_2O_2; d, TBDPSCl, imidazole, DMF; e, $LiAlH_4$, THF; f, TPAP, NMO, acetone; g, $Ph_3P{=}CH_2$, THF; h, HOAc, THF, H_2O; i, SO_3·pyridine, DMSO, Et_3N, CH_2Cl_2.

Hydroboration[6] of **13** by using disiamyl §borane furnished, after oxidative workup, alcohol **14** as the major product in a 76% yield (89 : 11 regioselectivity). After protection of the secondary hydroxy group of **14** as a TBDPS ether to give **15**, the ester function of **15** was readily reduced to the primary alcohol **16**. TPAP–NMO oxidation[7] then gave aldehyde **17** in high yield. Subsequent Wittig olefination afforded **7**. To prepare the required aldehyde the tetrahydropyranyl group was cleaved and the resulting alcohol **18** was oxidised by applying a sulfur trioxide, pyridine–DMSO oxidation.[8] The developed sequence was used to synthesise aldehyde **5** in enantiopure form ($[a]_D^{22}$ +19.2 10^{-1} × deg cm^2 g^{-1} (*c* = 1.06, $CHCl_3$)) in batches of 20 g in 11% overall yield from furfural.

Synthesis of vinyl triflate 10

Vinyl triflate **10** was synthesised as shown in Scheme 4. Commercially available 3-(4-methoxyphenyl)propan-1-ol (**19**) was converted to hydroxyketone **20** by a literature procedure.[9] The hydroxy group of **20** was protected as silyl ether **21**. Subsequent acylation with methyl cyanoformate[10] led to **22** which exists completely in the enol form according to ^{1}H NMR in $CDCl_3$.

§ The IUPAC name for disiamyl is 1,2-dimethylprop-1-yl.

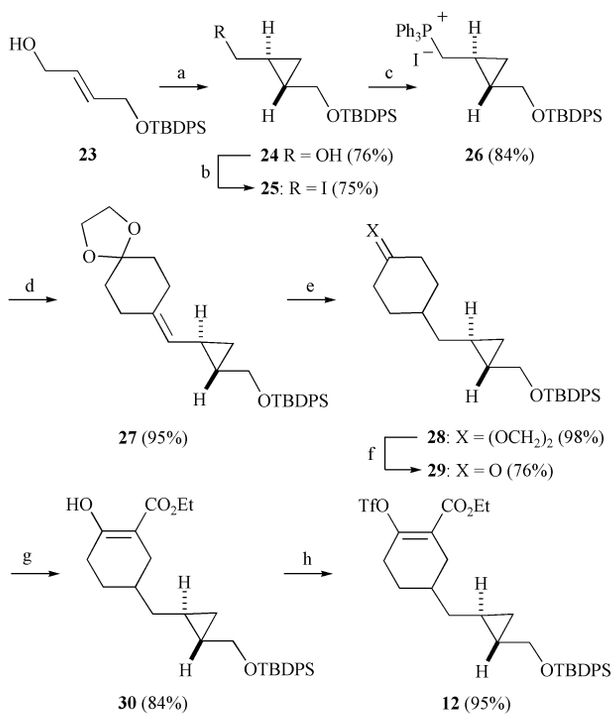


Scheme 4 *Reagents and conditions*: a, Na, NH_3, *t*-BuOH–THF 1 : 1, −33 °C; b, HCl (aq); c, Pd/C–H_2, EtOAc; d, TBDPSCl, imidazole, DMF; e, LDA, THF, −78 °C; then HMPT, $NCCO_2Me$, −78 °C, 10 min; f, NaH, $(CF_3SO_2)_2NPh$, THF, 0 °C ⟶ rt.

Finally, reaction with *N*-phenyltrifluoromethanesulfonimide[11] yielded vinyl triflate **10**.

Synthesis of vinyl triflate 12

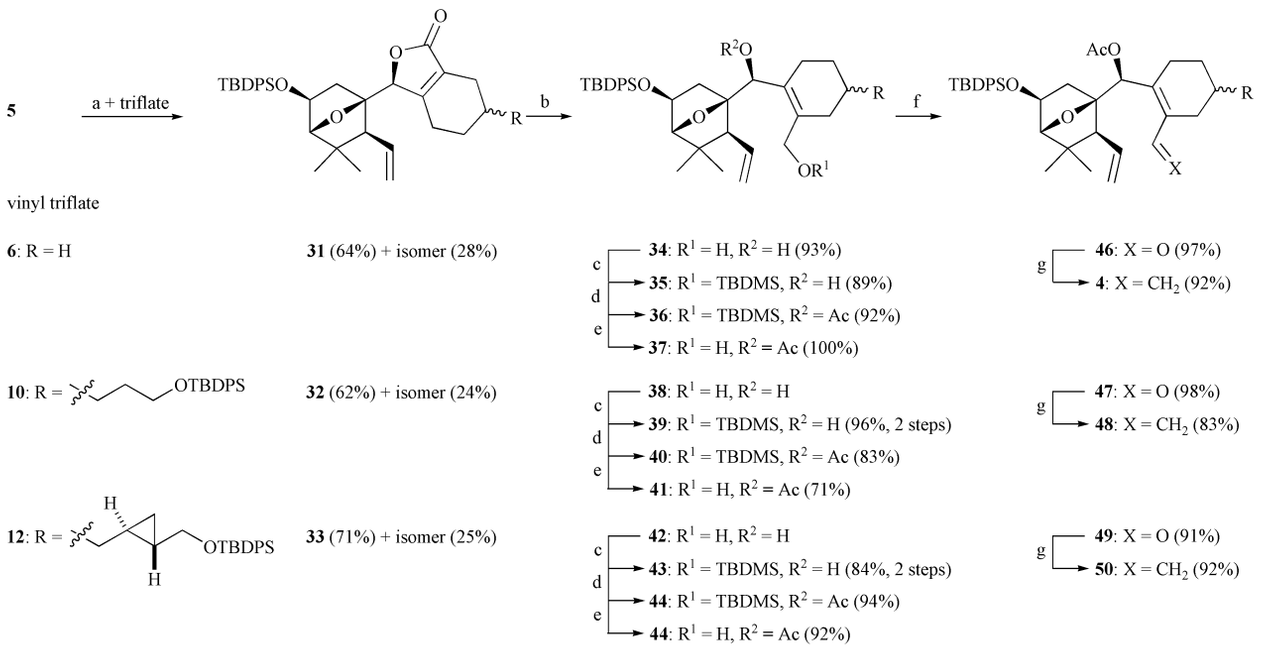
(*E*)-Alkene **23**[12] was expected to be a good precursor for a Simmons–Smith cyclopropanation, which could lead to a *trans*-disubstituted cyclopropane (Scheme 5). Treatment of allylic



Scheme 5 *Reagents and conditions*: a, $Zn(CH_2I)_2$·DME, CH_2Cl_2, rt, 18 h; b, I_2, PPh_3, imidazole, toluene, acetonitrile (2 : 1); c, PPh_3, toluene, reflux; d, KO*t*-Bu, toluene, 70 °C, 30 min, then cyclohexane-1,4-dione monoethylene ketal, 70 °C, 6 h; e, PtO_2 (cat.), H_2, EtOAc, 40 min; f, *p*-TsOH (cat.), acetone, 40 °C; g, LDA, THF, −78 °C; then HMPT, $NCCO_2Et$, −78 °C; h, NaH, $(CF_3SO_2)_2NPh$, THF, 0 °C ⟶ rt.

alcohol **23** with a $Zn(CH_2I)_2$·DME complex[13] resulted in a clean cyclopropanation reaction on a 37 mol scale to provide the *trans*-cyclopropane **24** as a racemate. It is well-known that this process can also be carried out in an enantioselective fashion.[14]

The hydroxy group of **24** was then replaced by iodide.[15] Treatment of iodide **25** with triphenylphosphine in refluxing toluene gave phosphonium salt **26**. For the Wittig reaction with cyclohexane-1,4-dione monoethylene acetal the reaction conditions appeared to be crucial for a successful transformation.[16] Ylide formation by using potassium *tert*-butoxide at 70 °C was followed, after 30 min, by addition of the ketone. Alkene **27** was obtained in almost quantitative yield after 6 h. Clean hydrogen-



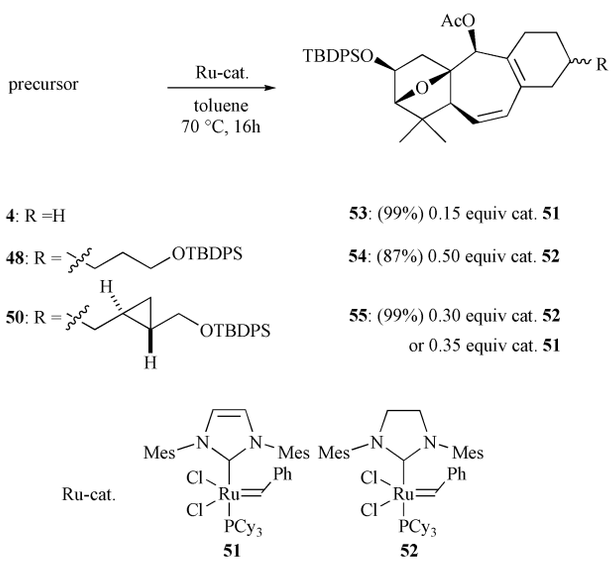
Scheme 6 *Reagents and conditions*: a, $CrCl_2$, $NiCl_2$ (cat.), DMF, 50 °C, 18 h; b, $LiAlH_4$, Et_2O, rt, 30 min; c, TBDMSCl, imidazole, DMF; d, Ac_2O, pyridine, CH_2Cl_2; e, CSA (cat.), MeOH, 0 °C; f, TPAP, NMO, acetone; g, $Ph_3P{=}CH_2$, THF, 0 °C.

ation of the double bond was accomplished using a platinum catalyst with careful monitoring of the reaction by ^1H NMR. Because the cyclopropane ring was prone to hydrogenolysis the reaction was stopped after 30 min. Hydrolysis of the acetal in **28** was followed by introduction of the ester group by using Mander's procedure.[10] Triflation[11] of **30** afforded vinyl triflate **12** as a close to equimolar mixture of four diastereoisomers in 11 steps and 25% overall yield from (*E*)-but-2-ene-1,4-diol.

Seven-membered ring formation

The chromium-mediated coupling[17] of aldehyde **5** and vinyl triflate **6** afforded the α,β-unsaturated lactone **31** (Scheme 6). Under the reaction conditions a mixture of diastereomers (69 : 31) was found. The chromium-mediated couplings of aldehyde **5** and vinyl triflates **10** and **12** gave lactones **32** and **33**, respectively, in a similar yield and diastereoselectivity. At this point the α,β-unsaturated lactone **31** had to be converted into RCM precursor **4**. A highly efficient six-step procedure was developed to accomplish this transformation. The sequence started with a lithium aluminium hydride reduction of the lactone. The resulting primary hydroxy group of **34** was protected as a TBDMS ether (**35**) and the secondary hydroxy group was then protected as an acetate to give compound **36**. Subsequently the allylic hydroxy group was selectively deprotected by a catalytic amount of camphorsulfonic acid (CSA) to afford alcohol **37**. The latter was oxidised using TPAP–NMO to give aldehyde **46**, which in crude form was subjected to a Wittig olefination resulting in RCM precursor **4** in a good overall yield of 67% over six steps. The use of this protocol for the transformation of **32** and **33** resulted in a six-step route to **48** and **50** in overall yields of 46% and 61%, respectively.

When triene **4** was subjected to a catalytic amount of Grubbs' catalyst[18] the cyclisation appeared to be extremely slow. In fact one equiv. of this catalyst in hot toluene was required to get a full conversion of the starting material. This problem could be solved by using second generation ruthenium-based catalysts **51**[19] or **52**[20] (Scheme 7). Gratifyingly, only 15 mol% of the unsaturated imidazolin-2-yl catalyst (**51**) in hot toluene effected quantitative ring closure of triene **4** after 16 h. Precursors **48** and **50** were somewhat more difficult to cyclise. Eventually, treatment of these precursors with the ruthenium catalysts demonstrated that the seven-membered

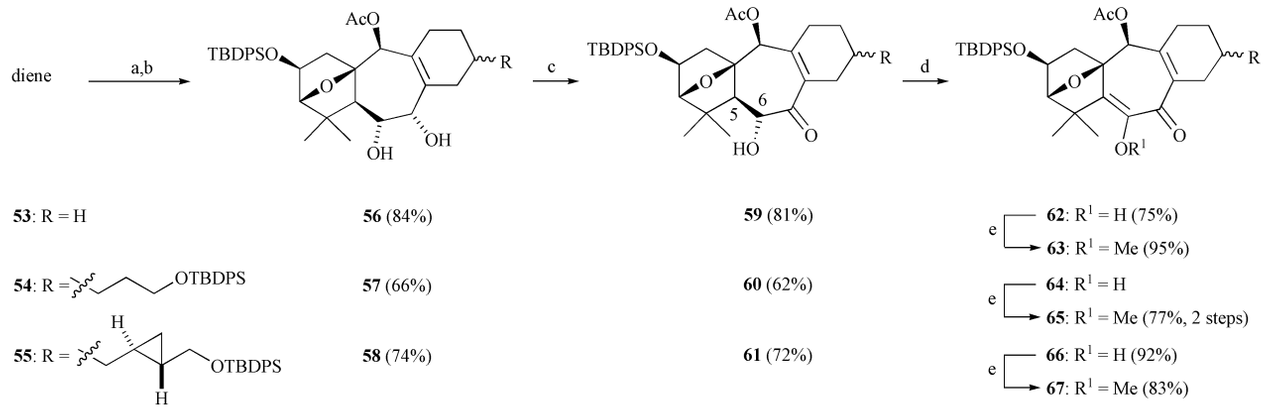


Scheme 7

ring can be efficiently constructed *via* RCM furnishing **54** and **55** in excellent yields.

Introduction of the oxygen substituents

Having the dienes **53**–**55** available, the least-substituted double bond needed to be functionalised with oxygen substituents. The first attempt at this involved the introduction of a 1,2-diketone in one step using $KMnO_4$ in acetic anhydride.[21] This reagent mixture led to complete cleavage of the C=C bond resulting in a diacid. It was then decided to introduce the 1,2-diketone *via* a milder three-step procedure. First the least hindered double bond was dihydroxylated (Scheme 8). Remarkably, catalytic osmium tetraoxide in the presence of stoichiometric *N*-methylmorpholine *N*-oxide appeared to be fully inactive. It is well-known that the reactivity of osmium tetraoxide can be increased by the addition of tertiary amines.[22] Recent studies on the mechanistic details of amine-accelerated dihydroxylation with osmium tetraoxide by Corey and coworkers[23] suggested that a 2 : 1 complex of DMAP and osmium tetraoxide could be effective for this transformation. In fact, this reagent caused smooth and selective dihydroxylation of the least hindered



Scheme 8 *Reagents and conditions*: a, OsO_4 (1 equiv.), DMAP (2 equiv.), *t*-BuOH–H_2O (1 : 1), rt, 30 min; b, Na_2SO_3; c, Dess–Martin periodinane, CH_2Cl_2 −20 °C ⟶ rt; d, $Cu(OAc)_2$, MeOH, reflux; e, Ag_2O, MeI, DMF.

double bond. The parent system **53** gave a 78 : 22 diastereomeric mixture of *cis*-diols **56**. RCM products **54** and **55** were also readily dihydroxylated, but the ratio of *cis*-diols could not be determined due to the complexity of the isomer mixtures.

The next step was the oxidation of both hydroxy groups. Direct double oxidation of the mixture of **56** to the 1,2-diketone by using DMSO-based reagents did not lead to any isolable products. The use of manganese dioxide or TPAP as the oxidant was also unsuccessful. These reagents caused a rapid oxidative cleavage of the C–C bond to give a dialdehyde in an almost quantitative yield.[24]

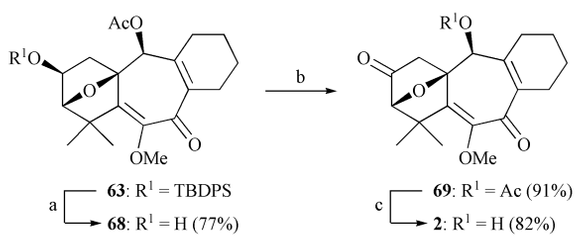
Faced with these disappointing results, it became obvious that simultaneous oxidation of both hydroxy groups to arrive at the diketone was not possible. Fortunately, it appeared feasible to oxidise the hydroxy groups separately. In analogy with literature reports,[25] the more reactive allylic hydroxy group of **56**–**58** could be oxidised with Fétizon's reagent[26] to give α-hydroxyketones **59**, **60** and **61**, respectively. It was then found that the α-hydroxyketones could be obtained even more efficiently from the diols by using 1 equiv. of the Dess–Martin periodinane,[27] if the reaction was carefully monitored to prevent over-oxidation. The α-hydroxyketones were obtained as single isomers, presumably by equilibration of H-6 under the reaction conditions. In these isomers H-5 and H-6 have a *trans*-configuration (J = 12 Hz) to allow intramolecular hydrogen bond formation between the hydroxy group and the ketone.

The last step to the diketone was the oxidation of the second hydroxy group. To prevent C–C bond cleavage as observed in previous oxidative methods, an alternative oxidative agent was used. It is known that α-hydroxyketones can be oxidised to α-diketones by using cupric acetate.[28] Even though to the best of our knowledge cupric acetate has never been used for the synthesis of seven-membered ring 1,2-diketones, this reagent was investigated. Gratifyingly, treatment of the hydroxyketones (**59**–**61**) with cupric acetate in refluxing methanol resulted in the desired 1,2-diketones, which existed completely in the enol form according to NMR data. Because these enols proved to be rather unstable they were directly methylated. The significantly more stable methyl enol ethers **63**, **65** and **67** were obtained in excellent yields.

Completion of the synthesis

To complete the synthesis of the tetracyclic left-handed substructure **2** the silyl ether in **63** was cleaved (Scheme 9). Subsequent oxidation of the liberated hydroxy group and removal of the acetate group of **69** resulted in the desired product (**2**), which was a stable crystalline compound (mp 173 °C) with a high optical rotation ($[\alpha]_D^{24}$ +495 × 10^{-1} deg cm^2 g^{-1} (c = 0.6, $CHCl_3$)).

Upon recrystallisation of **2** colourless crystals were obtained, which appeared suitable for X-ray crystal structure determination. The X-ray analysis proved the structure of **2**, including the orientation of the hydroxy group which was introduced *via* the chromium-mediated coupling (Fig. 1).



Scheme 9 *Reagents and conditions*: a, HF·pyridine, THF, 0 °C; b, TPAP, NMO, acetone; c, K_2CO_3, MeOH.

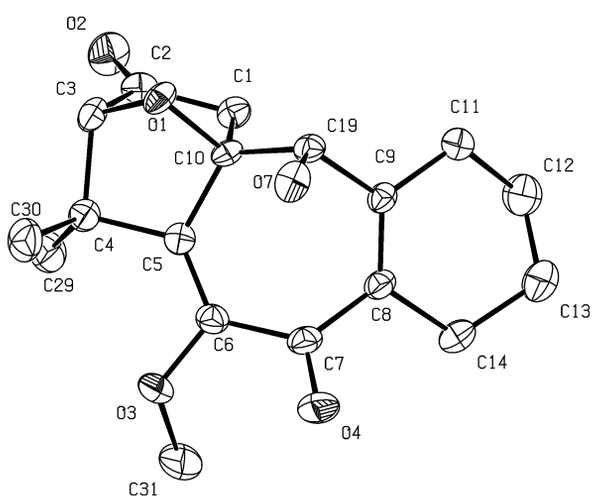
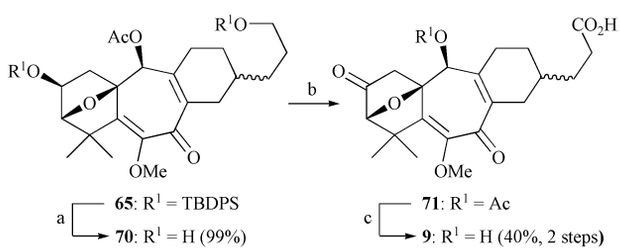


Fig. 1 ORTEP plot of the crystal structure of 2.

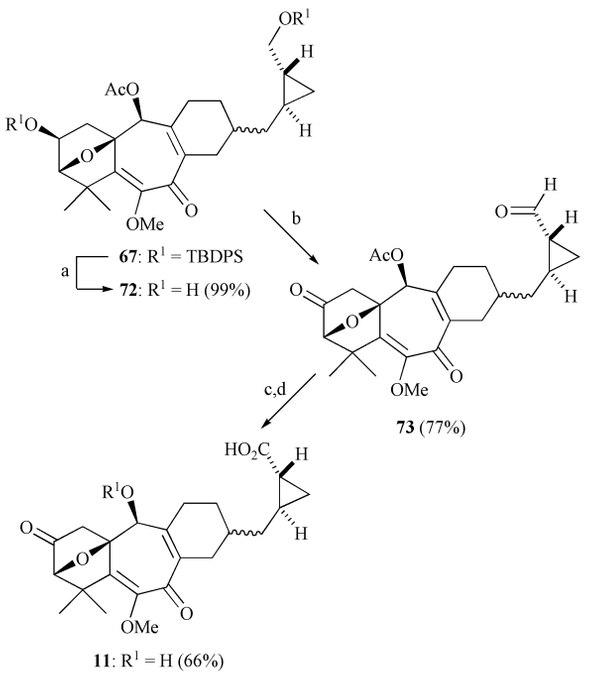
In the last few steps of the synthesis of the solanoeclepin A analogue, **9**, the two silyl ethers of **65** were hydrolysed using TBAF, which was made slightly acidic by the addition of acetic acid (Scheme 10). Diol **70** was subsequently oxidised to keto



Scheme 10 *Reagents and conditions*: a, TBAF, HOAc, THF, rt, 16 h; b, TPAP, NMO, acetone; c, K_2CO_3, MeOH.

acid **71**. Surprisingly, the TPAP oxidation did not stop at the aldehyde stage but went on to give the corresponding acid. Methanolysis of the acetate resulted in the desired compound **9** as a 1 : 1 mixture of two enantiopure diastereomers. Reversed phase thin layer chromatography afforded the pure diastereomeric mixture.

To complete the synthesis of analogue **11** a comparable approach was used. After removal of the silyl ethers from **67** the resulting diol **72** was treated with TPAP–NMO (Scheme 11). In this case the oxidation stopped at the aldehyde stage and



Scheme 11 *Reagents and conditions*: a, TBAF, HOAc, THF, rt, 16 h; b, TPAP, NMO, acetone; c, $NaClO_2$, 2-methylbut-2-ene, NaH_2PO_4, *t*-BuOH–H_2O (1 : 1); d, K_2CO_3, MeOH.

compound **73** was isolated. Oxidation of the aldehyde moiety to the acid group was accomplished by using a buffered solution of sodium chlorite.[29] Methanolysis of the acetate then gave **11**, which was isolated as an approximately equimolar mixture of four enantiopure isomers. Reversed phase thin layer chromatography afforded the purified diastereomeric mixture of **11**.

Hatching activity tests

The solanoeclepin A model compounds **2**, **9** and **11**, prepared as described in this paper, were tested for their biological activity as hatching agents of potato cyst nematodes. As a reference substance so-called Potato Root Diffuse (PRD) containing natural hatching material was used. PRD is obtained by collecting the extract of young, two to ten weeks old, potato plants.

In the hatching activity tests[30] potato cyst nematode (PCN) eggs (*ca.* 300 eggs in 4 mL of water at pH = 4) were subjected to the new compounds in a range of concentrations. These PCN eggs were isolated from their protective cyst to increase their biological response towards the hatching agent. The various testing samples were obtained by diluting the following stock solutions (*N* (relative concentration) = 1): 125 mg L^{-1} of compound **2**, 250 mg $L^{-1}$of compound **9** and 500 mg L^{-1} of compound **11**, 2, 10, 20 and 100 times.

After 10 days (the optimum hatching time[30]) the number of PCN hatched was estimated (Fig. 2). In the *in vivo* tests two of the synthesised solanoeclepin A analogues **9** and **11** showed promising hatching activity. The hatching activity curves for these compounds are similar to the one of PRD (with the exception of the highest concentration of compound **9**). It can

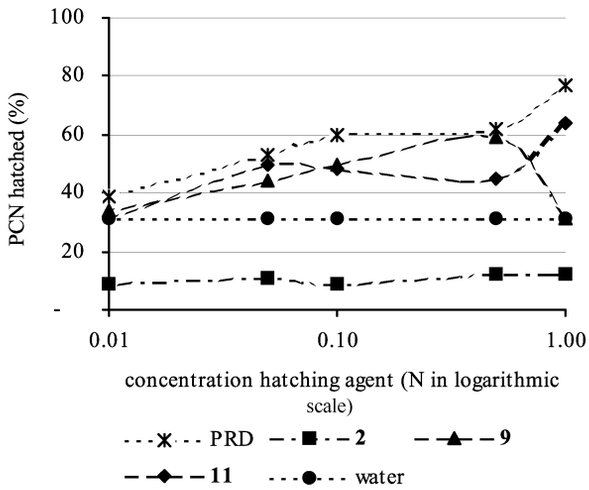


Fig. 2 PCN hatching activity tests.

be concluded that a carboxylic acid function tethered to compound **2**, which itself is devoid of any hatching activity, results in biologically active compounds. The role of the length and the structure of this tether must await further studies.

These results will direct future design and syntheses of new potentially biologically active solanoeclepin A model compounds. Eventually, this approach might lead to synthetically well accessible and biologically active solanoeclepin A analogues, which could lead to an environmentally benign method to control PCN.

Conclusion

The syntheses of three solanoeclepin A model compounds containing the tetracyclic left-handed substructure have been reported. In a convergent approach these analogues were assembled *via* a chromium-mediated coupling of aldehyde **5** with vinyl triflates **6**, **10** and **12**. The seven-membered ring was constructed by using a ruthenium catalysed ring-closing metathesis reaction. Oxidative functionalisation of the least hindered double bond eventually led to the desired compounds. The synthetic approach presented augurs well for a successful completion of the total synthesis of the natural product as soon as a properly functionalised vinyl triflate becomes available. Two of the model compounds showed good hatching activity, which is promising for the development of environmentally benign methods to control potato cyst nematodes.

Experimental[1]

(1*R*,2*S*,4*S*)-3,3-Dimethyl-1-[(2*R**)-tetrahydropyran-2-yloxymethyl]-7-oxabicyclo[2.2.1]hept-5-ene-2-carboxylic acid ethyl ester (13)

To a solution of crude alcohol **8**[1] (6.3 g, 20.2 mmol) in CH_2Cl_2 (150 mL) was added 3,4-dihydro-2*H*-pyran (4.6 mL, 51 mmol, 2.5 equiv.) and a catalytic amount of *p*-TsOH·H_2O (38 mg, 0.20 mmol, 1 mol%). The reaction mixture was stirred at rt for 16 h. Then the reaction mixture was quenched by adding saturated aqueous $NaHCO_3$ (250 mL) and extracted with CH_2Cl_2 (3 × 250 mL). The combined organic layers were washed with brine and subsequently dried over Na_2SO_4 and the solvent was removed *in vacuo*. Column chromatography (petroleum ether–EtOAc (8 : 2)) furnished the protected alcohol **13** (5.71 g, 18.4 mmol, 91%) as a colourless oil as a mixture of diastereomers; R_f = 0.64 (petroleum ether–EtOAc (3 : 7)); IR 2945, 1737, 1032; ^{1}H NMR (500 MHz) δ 6.48–6.45 (2H, m), 4.69 (0.5H, m), 4.59 (0.5H, m), 4.37 (1H, m), 4.25–4.12 (3H, m), 4.06–4.01 (1H, m), 3.88–3.81 (1H, m) 3.53–3.51 (1H, m), 2.25 (1H, m), 1.81–1.50 (6H, m), 1.28 (3H, m), 1.12 (3H, s), 1.06 (3H, s); ^{13}C NMR

(125 MHz) δ 171.8, 137.3, 136.9, 135.4, 135.3, 99.3, 98.9, 90.4, 89.7, 87.0, 86.9, 65.6, 65.6, 62.0, 62.0, 60.0, 59.8, 55.8, 55.2, 44.4, 44.1, 30.3, 30.3, 26.3, 26.2, 25.3, 25.3, 24.9, 24.8, 19.2, 19.2, 14.4, 14.3; HRMS (FAB) [M + H^+] calcd for $C_{17}H_{27}O_5$: 311.1859, found: 311.1851.

(1*R*,2*S*,4*R*,5*S*)-5-Hydroxy-3,3-dimethyl-1-[(2*R)-tetrahydropyran-2-yloxymethyl]-7-oxabicyclo[2.2.1]heptane-2-carboxylic acid ethyl ester (14)**

A solution of 2-methylbut-2-ene (33.5 mL of a 2.0 M solution in THF, 67 mmol, 2 equiv.) in THF (30.2 mL) was cooled to 0 °C and a borane–methyl sulfide complex (3.20 mL, 34.0 mmol) was added dropwise. The reaction mixture was allowed to warm to rt and was stirred for 4 h giving a 0.5 M solution of disiamylborane in THF.

A solution of alkene **13** (4.54 g, 14.6 mmol) in THF (10 mL) was cooled to −60 °C. To this solution was added disiamylborane (44 mL of a 0.5 M solution in THF, 22.0 mmol, 1.5 equiv.) and the colourless reaction mixture was stirred at −20 °C for 16 h. The reaction was allowed to warm to 0 °C and NaOH (32 mL of a 3.0 M solution, 96 mmol, 6.5 equiv.) was carefully added, followed by H_2O_2 (14 mL of a 35 wt% solution in water, 144 mmol, 10 equiv.). After stirring the reaction mixture for 3 h, saturated aqueous NH_4Cl (40 mL) was added and the aqueous layer was extracted with EtOAc (3 × 75 mL). The combined organic layers were washed with brine and subsequently dried over Na_2SO_4 and the solvent was removed *in vacuo*. Column chromatography (petroleum ether–EtOAc (2 : 8)) afforded alcohol **14** (3.59 g, 10.9 mmol, 76%) as a colourless oil as a 1 : 1 mixture of diastereomers (and its other regioisomer (378 mg, 1.15 mmol, 8%) as a 1 : 1 mixture of diastereomers, as a colourless oil); R_f = 0.27 (R_f regioisomer = 0.46)(petroleum ether–EtOAc (3 : 7)); IR 3447 (br), 2954, 1737, 1140, 1029; ^{1}H NMR (400 MHz) δ (0.5H, m), 4.54 (0.5H, m), 4.31 (1H, m), 4.17–4.08 (3H, m), 4.00 (1H, dd, J = 9.7, 7.1 Hz), 3.88–3.82 (1.5H, m), 3.78–3.73 (0.5H, m), 3.54–3.47 (1H, m), 2.33 (0.5H, s), 2.32 (0.5H, s), 2.20 (0.5H, dd, J = 13.8, 7.0 Hz), 2.09–2.00 (1H, m) 1.95 (0.5H, br s), 1.85 (0.5H, d, J = 13.8 Hz), 1.79–1.42 (6H, m), 1.28–1.23 (3H, m), 1.19 (1.5H, s), 1.19 (1.5H, s), 1.05 (3H, s); ^{13}C NMR (100 MHz) δ 170.8, 170.5, 99.6, 98.9, 91.9, 91.9, 87.5, 87.2, 71.3, 71.2, 67.9, 66.4, 62.3, 62.0, 60.4, 60.0, 59.9, 59.6, 47.0, 45.5, 43.2, 43.0, 30.5, 30.4, 25.4, 25.3, 25.2, 25.1, 19.3, 19.2, 14.4, 14.2; HRMS (FAB) [M + H^+] calcd for $C_{17}H_{29}O_6$: 329.1964, found: 329.1960.

(1*R*,2*S*,4*R*,5*S*)-5-(*tert*-Butyldiphenylsilyloxy)-3,3-dimethyl-1-[(2*R)-tetrahydropyran-2-yloxymethyl]-7-oxabicyclo[2.2.1]-heptane-2-carboxylic acid ethyl ester (15)**

To a solution of alcohol **14** (3.65 g, 11.1 mmol) in CH_2Cl_2 (150 mL) was added TBDPSCl (6.37 mL, 24.5 mmol, 2.2 equiv.) and imidazole (2.50 g, 36.7 mmol, 3.3 equiv.). The reaction mixture was stirred for 16 h at rt. Then the reaction mixture was poured into water (100 mL) and after separation of the organic layer the aqueous layer was extracted with EtOAc (2 × 200 mL). The combined organic layers were washed with brine and subsequently dried over Na_2SO_4 and the solvent was removed *in vacuo*. Column chromatography (petroleum ether–Et_2O (9 : 1)) afforded the protected alcohol **15** (5.59 g, 9.88 mmol, 89%) as a colourless oil, as a 1 : 1 mixture of diastereomers; R_f = 0.76 (petroleum ether–Et_2O (1 : 1)); IR 2946, 1740, 1113, 1071, 1032; ^{1}H NMR (500 MHz) δ 7.70–7.64 (4H, m), 7.45–7.36 (6H, m), 4.74 (0.5H, m), 4.51 (0.5H, m), 4.39–4.35 (1H, m), 4.14–3.99 (4H, m), 3.88–3.84 (0.5H, m), 3.80–3.75 (0.5H, m), 3.65 (0.5H, s), 3.64 (0.5H, s), 3.63–3.51 (1H, m), 2.16 (0.5H, s), 2.15 (0.5H, s), 2.11 (0.5H, dd, J = 12.9, 6.8 Hz), 2.00 (0.5H, d, J = 12.4 Hz), 1.89 (0.5H, dd, J = 12.9, 6.8 Hz), 1.80–1.71 (2H, m), 1.64–1.44 (4.5H, m), 1.22 (1.5H, t, J = 7.0 Hz), 1.21 (1.5H, t, J = 7.0 Hz), 1.07 (4.5H, s), 1.06 (4.5H, s), 0.88 (1.5H, s), 0.87 (1.5H, s), 0.76 (1.5H, s), 0.74 (1.5H, s); ^{13}C NMR (125 MHz) δ 171.0, 170.6, 135.7, 135.6, 134.0, 134.0, 133.8, 133.8, 129.6, 129.6, 127.6, 99.2, 98.9, 91.7, 91.6, 87.3, 86.6, 72.0, 71.9, 68.3, 66.8, 62.1, 61.9, 59.8, 59.7, 59.6, 59.1, 47.9, 45.9, 43.2, 42.8, 30.5, 30.4, 26.8, 25.4, 25.3, 25.1, 25.1, 24.5, 24.5, 19.3, 19.2, 19.0, 14.3, 14.2; HRMS (FAB) [M + H^+] calcd for $C_{33}H_{47}O_6Si$: 567.3142, found: 567.3123.

(1*R*,2*R*,4*R*,5*S*)-5-{(*tert*-Butyldiphenylsilyloxy)-3,3-dimethyl-1-[(2*R)-tetrahydropyran-2-yloxymethyl]-7-oxabicyclo[2.2.1]-heptan-2-yl}methanol (16)**

A solution of ester **15** (5.6 g, 9.9 mmol) in Et_2O (80 mL) was cooled to −78 °C and lithium aluminium hydride (14.8 mL of a 1.0 M solution in Et_2O, 14.8 mmol, 1.5 equiv.) was added dropwise. The reaction mixture was allowed to warm to rt and was stirred for 15 min. Then the mixture was quenched by adding EtOAc followed by saturated aqueous Na_2SO_4 (0.5 mL) and was dried over Na_2SO_4 and filtered to remove any solids. Evaporation of the solvent gave alcohol **16** (5.0 g, 9.4 mmol, 95%) as a colourless oil, as a 1 : 1 mixture of diastereomers; R_f = 0.14 (petroleum ether–Et_2O (1 : 1)); IR 3474 (br), 3071, 2942, 1113, 1068, 1033; ^{1}H NMR (400 MHz) δ 7.73–7.63 (4H, m), 7.44–7.35 (6H, m), 4.69–4.65 (1H, m), 4.38–4.37 (1H, m), 4.20 (0.5H, d, J = 10.6 Hz), 4.14 (0.5H, d, J = 10.1 Hz), 3.90–3.83 (1.5H, m), 3.74–3.52 (1.5H, m), 3.48–3.41 (2H, m), 3.39–3.31 (1H, m), 2.03 (1H, m), 2.01–1.94 (1.5H, m), 1.79–1.72 (3H, m), 1.63–1.39 (4.5H, m), 1.06 (4.5H, s), 1.06 (4.5H, s), 0.81 (3H, s), 0.65 (3H, s); ^{13}C NMR (100 MHz) δ 135.7, 135.7, 134.1, 134.0, 133.9, 129.6, 129.6, 127.6, 99.6, 99.4, 92.4, 92.3, 86.7, 86.4, 72.2, 72.0, 68.1, 67.5, 63.1, 62.9, 60.1, 60.0, 56.4, 48.2, 47.5, 41.3, 41.2, 30.5, 30.4, 26.8, 25.1, 24.6, 24.5, 22.9, 22.8, 19.7, 19.6, 19.0; HRMS (FAB) [M + H^+] calcd for $C_{31}H_{45}O_5Si$: 525.3036, found: 525.3022.

(1*R*,2*S*,4*R*,5*S*)-5-(*tert*-Butyldiphenylsilyloxy)-3,3-dimethyl-1-[(2*R)-tetrahydropyran-2-yloxymethyl]-7-oxabicyclo[2.2.1]-heptane-2-carbaldehyde (17)**

To a solution of alcohol **16** (4.8 g, 9.2 mmol) in acetone (40 mL) were added NMO (1.6 g, 13.7 mmol, 1.6 equiv.) and TPAP (40 mg, 0.11 mmol, 1.2 mol%). The reaction mixture was stirred for 2 h and filtered over a thin pad of silica, followed by exhaustive rinsing with EtOAc. Evaporation of the solvents and column chromatography (petroleum ether–Et_2O (4 : 1)) afforded aldehyde **17** (4.2 g, 8.1 mmol, 88%) as a colourless oil, as a 1 : 1 mixture of diastereomers; R_f = 0.48 (petroleum ether–Et_2O (1 : 1)); IR 2939, 2858, 1713, 1111, 1068; ^{1}H NMR (400 MHz) δ 9.63 (0.5H, d, J = 6.2 Hz), 9.60 (0.5H, d, J = 6.2 Hz), 7.68 (2H, d, J = 7.8 Hz), 7.63 (2H, d, J = 7.8 Hz), 7.46–7.36 (6H, m), 4.69 (0.5H, m), 4.63 (0.5H, m), 4.35 (1H, dd, J = 6.6, 2.0 Hz), 4.09 (0.5H, d, J = 11.4 Hz), 4.02 (0.5H, d, J = 11.4 Hz), 3.82–3.62 (3H, m), 3.58–3.49 (1H, m), 1.92 (0.5H, dd, J = 13.0, 6.9 Hz), 1.89–1.49 (8.5H, m), 1.07 (9H, s), 1.02 (1.5H, s), 1.02 (1.5H, s), 0.69 (1.5H, s), 0.68 (1.5H, s); ^{13}C NMR (100 MHz) δ 203.5, 135.8, 135.7, 133.9, 133.7, 129.8, 129.7, 127.7, 98.8, 98.7, 91.9, 89.2, 89.0, 72.2, 71.7, 67.2, 66.4, 65.9, 65.7, 61.7, 61.4, 46.0, 45.2, 44.4, 44.3, 30.0, 30.0, 25.3, 25.3, 25.1, 25.0, 24.9, 19.0, 18.8, 18.6.

(1*R*,2*S*,4*R*,5*S*)-*tert*-Butyl{6,6-dimethyl-4-[(2*R)-tetrahydropyran-2-yloxymethyl]-5-vinyl-7-oxabicyclo[2.2.1]heptan-2-yloxy}diphenylsilane (7)**

A solution of methyltriphenylphosphonium bromide (7.52 g, 21.1 mmol, 2.55 equiv.) in THF (200 mL) was cooled to 0 °C and *n*-BuLi (12.8 mL of a 1.6 M solution in hexanes, 20.5 mmol, 2.5 equiv.) was added. The yellow suspension was stirred at 0 °C for 1 h and then aldehyde **17** (4.31 g, 8.25 mmol) in THF (50 mL) was added *via* a double tipped needle. The reaction mixture was allowed to warm to rt and stirring was continued for 2 h. The reaction was then quenched by adding acetone

(colour changed from yellow to white). The reaction mixture was diluted with Et_2O (200 mL) and was washed with water (200 mL). After separation of the organic layer the aqueous layer was extracted with Et_2O (2 × 200 mL). The combined organic layers were washed with brine and subsequently dried over Na_2SO_4 and the solvent was removed *in vacuo*. Column chromatography (petroleum ether–EtOAc (9 : 1)) afforded protected alcohol **7** (3.82 g, 7.34 mmol, 89%) as a colourless oil, as a mixture of diastereomers; $R_f = 0.64$ (petroleum ether–Et_2O (1 : 1)); IR 3071, 2943, 2860, 1113, 1070; ^{1}H NMR (500 MHz) δ 7.71–7.67 (4H, m), 7.45–7.37 (6H, m), 5.70–5.59 (1H, m), 4.97–4.94 (1H, m), 4.85–4.80 (1.5H, m), 4.59 (0.5H, m), 4.40 (1H, m), 3.97–3.92 (1H, m), 3.85–3.81 (0.5H, m), 3.76–3.74 (0.5H, m), 3.69–3.61 (2H, m), 3.54–3.50 (1H, m), 2.12 (0.5H, d, J = 13.0 Hz), 1.95–1.44 (8.5H, m), 1.08 (4.5H, s), 1.08 (4.5H, s), 0.81 (1.5H, s), 0.80 (1.5H, s), 0.66 (1.5H, s), 0.64 (1.5H, s); ^{13}C NMR (125 MHz) δ 136.4, 135.8, 135.8, 135.7, 135.7, 134.3, 134.3, 134.1, 134.1, 129.6, 129.5, 127.6, 127.6, 116.6, 116.2, 98.8, 98.6, 91.9, 91.8, 88.4, 87.7, 72.4, 72.3, 67.2, 65.7, 62.0, 61.5, 61.4, 60.7, 45.3, 43.7, 42.7, 42.7, 30.5, 30.4, 26.9, 26.8, 25.6, 25.5, 25.1, 25.0, 24.5, 24.4, 19.2, 19.0, 18.9); HRMS (FAB) [M + H$^+$] calcd for $C_{32}H_{45}O_4Si$: 521.3087, found: 521.3050.

(+)-(1*R*,2*S*,4*R*,5*S*)-[5-(*tert*-Butyldiphenylsilyloxy)-3,3-dimethyl-2-vinyl-7-oxabicyclo[2.2.1]heptan-1-yl]methanol (18)

Protected alcohol **7** (1.9 g, 3.7 mmol) was dissolved in a mixture of HOAc–THF–water (4 : 2 : 1 v/v/v) (35 mL) and heated at 60 °C for 16 h. Evaporation of the solvents and column chromatography (petroleum ether–Et_2O (4 : 1)) afforded alcohol **18** (1.5 g, 3.4 mmol, 96%) as a colourless oil; $R_f = 0.43$ (petroleum ether–Et_2O (1 : 1)); $[\alpha]_D^{20}$ +18.9 (c = 1.02, $CHCl_3$); IR 3459 (br), 3071, 2958, 1112, 1077; ^{1}H NMR (400 MHz) δ 7.69–7.58 (4H, m), 7.42–7.33 (6H, m), 5.67 (1H, ddd, J = 17.0, 10.4, 10.3 Hz), 4.99 (1H, dd, J = 10.0, 2.1 Hz), 4.87 (1H, dd, J = 16.9, 2.0 Hz), 4.39 (1H, dd, J = 6.8, 2.2 Hz), 3.84 (1H, d, J = 12.3 Hz), 3.64 (1H, s), 3.59 (1H, d, J = 12.3 Hz), 1.99 (1H, d, J = 12.7 Hz), 1.87 (1H, br s), 1.82 (1H, dd, J = 12.8, 6.9 Hz), 1.74 (1H, d, J = 10.7 Hz), 1.07 (9H, s), 0.80 (3H, s), 0.61 (3H, s); ^{13}C NMR (100 MHz) δ 135.9, 135.8, 135.7, 134.1, 133.9, 129.7, 129.6, 127.6, 116.9), 92.0, 88.9, 72.5, 62.4, 60.4, 44.3, 43.2, 26.9, 24.9, 24.3, 19.0; HRMS (EI) calcd for $C_{27}H_{36}O_3Si$: 436.2434, found: 436.2433.

(+)-(1*R*,2*S*,4*R*,5*S*)-5-(*tert*-Butyldiphenylsilyloxy)-3,3-dimethyl-2-vinyl-7-oxabicyclo[2.2.1]heptanecarbaldehyde (5)

To a solution of alcohol **18** (1.0 g, 2.3 mmol) in CH_2Cl_2 (10 mL) was added DMSO (2.6 mL, 36.6 mmol, excess) and triethylamine (1.8 mL, 12.9 mmol, 6 equiv.) followed by SO_3·pyridine (1.2 g, 7.5 mmol, 3 equiv.). The orange reaction mixture was stirred at rt for 3 h. Then the reaction mixture was diluted by adding Et_2O (30 mL) and quenched with saturated aqueous NH_4Cl (30 mL). After separation of the organic layer the aqueous layer was extracted with Et_2O (2 × 30 mL). The combined organic layers were washed with brine and subsequently dried over Na_2SO_4 and the solvent was removed *in vacuo*. Column chromatography (petroleum ether–Et_2O (4 : 1)) afforded aldehyde **5** (829 mg, 1.9 mmol, 83%) as a light yellow oil; $R_f = 0.52$ (petroleum ether–Et_2O (1 : 1)); $[\alpha]_D^{22}$ +19.2 (c = 1.06, $CHCl_3$); IR 3072, 2961, 2858, 1732, 1111, 1068; ^{1}H NMR (400 MHz) δ 9.84 (1H, s), 7.68 (2H, d, J = 6.4 Hz), 7.62 (2H, d, J = 6.5 Hz), 7.46–7.37 (6H, m), 5.54 (1H, ddd, J = 17.0, 10.4, 10.3 Hz), 5.02 (1H, dd, J = 10.1, 1.8 Hz), 4.90 (1H, dd, J = 16.9, 1.6 Hz), 4.39 (1H, dd, J = 6.8, 2.2 Hz), 3.77 (1H, s), 2.13–2.02 (2H, m), 1.80 (1H, d, J = 12.8 Hz), 1.06 (9H, s), 0.84 (3H, s), 0.62 (3H, s); ^{13}C NMR (100 MHz) δ 203.2, 138.7, 138.6, 137.8, 137.6, 136.7, 136.5, 132.8, 132.8, 132.5, 130.7, 130.5, 121.0, 95.4, 95.2, 74.2, 64.5, 46.7, 45.9, 29.8, 27.9, 27.1, 22.0; HRMS (FAB) [M + H$^+$] calcd for $C_{27}H_{35}O_3Si$: 435.2355, found: 435.2339.

4-[3-(*tert*-Butyldiphenylsilyloxy)propyl]cyclohexanone (21)

To a solution of ketone **20** (13 g, 83 mmol, prepared according to the literature[9]) in DMF (70 mL) were added imidazole (11.3 g, 166 mmol, 2 equiv.) and TBDPSCl (22.8 g, 83 mmol, 1 equiv.). After stirring the solution at rt for 16 h, the mixture was poured into water (150 mL). After separation of the organic layer the aqueous layer was extracted with EtOAc (3 × 50 mL). The combined organic layers were washed with brine and dried over Na_2SO_4. Evaporation of the solvent and column chromatography (petroleum ether–EtOAc (4 : 1)) afforded ketone **21** (30 g, 76 mmol, 91%) as a colourless oil; $R_f = 0.22$ (petroleum ether–EtOAc (9 : 1)); IR 2931, 2858, 1716, 1428, 1111; ^{1}H NMR (400 MHz) δ 7.67–7.65 (4H, m), 7.45–7.36 (6H, m), 3.67 (2H, t, J = 6.4 Hz), 2.38–2.23 (4H, m), 2.04–1.97 (2H, m), 1.67–1.58 (3H, m), 1.41–1.32 (4H, m), 1.05 (9H, s); ^{13}C NMR (100 MHz) δ 212.3, 135.5, 133.9, 129.5, 127.5, 63.8, 40.7, 35.5, 32.6, 31.5, 30.0, 26.7, 19.0.

rac-5-[3-(*tert*-Butyldiphenylsilyloxy)propyl]-2-hydroxycyclohex-1-enecarboxylic acid methyl ester (22)

A solution of ketone **21** (7.47 g, 19 mmol) in THF (15 mL) was cooled to −78 °C. To this solution was added LDA (21.0 mL of a 1.0 M solution in THF, 21.0 mmol, 1.1 equiv.) and the reaction mixture was allowed to warm to 0 °C in *ca.* 1 h. After cooling the reaction mixture to −78 °C, HMPT (3.4 mL, 28.5 mmol, 1.5 equiv.) was added followed by methyl cyanoformate (2.51 mL, 28.5 mmol, 1.5 equiv.) and stirring was continued at −78 °C for 10 min. The reaction was quenched by pouring it into water. After separation of the organic layer the aqueous layer was extracted with Et_2O (3 × 30 mL). The combined organic layers were washed with brine and subsequently dried over Na_2SO_4. Evaporation of the solvent and column chromatography (petroleum ether–Et_2O (9 : 1)) afforded ester **22** (9.2 g). The crude product was used in the next step; R_f = 0.42 (petroleum ether–EtOAc (9 : 1)); IR 3071, 2931, 2857, 1659, 1616, 1214, 1119; ^{1}H NMR (400 MHz) δ 12.14 (1H, s), 7.69–7.66 (4H, m), 7.43–7.36 (6H, m), 3.76 (3H, s), 3.67 (2H, t, J = 6.4 Hz), 2.42–2.37 (1H, m), 2.30–2.05 (2H, m), 1.86–1.73 (2H, m), 1.65–1.52 (3H, m), 1.51–1.42 (3H, m), 1.06 (9H, s); ^{13}C NMR (100 MHz) δ 176.1, 172.9, 172.8, 135.0, 134.0, 133.9, 132.0, 130.8, 129.8, 129.5, 129.4, 127.5, 96.9, 63.9, 63.7, 51.2, 35.0, 32.9, 33.2, 30.0, 28.8, 27.9, 27.8, 26.8, 19.1; HRMS (FAB) [M + H$^+$] calcd for $C_{27}H_{37}O_4Si$: 453.2461, found: 453.2468.

rac-5-[3-(*tert*-Butyldiphenylsilyloxy)propyl]-2-trifluoromethylsulfonyloxycyclohex-1-enecarboxylic acid methyl ester (10)

A solution of β-ketoester **22** (9.2 g) in THF (50 mL) was cooled to 0 °C. To this solution was carefully added NaH (0.85 g of a 60% dispersion in mineral oil, 21 mmol, 1.1 equiv.) and stirring was continued for 30 min. Then *N*-phenyltrifluoromethanesulfonimide (3.8 g, 21 mmol, 1.1 equiv.) was added in one portion and the reaction mixture was allowed to warm to rt in *ca.* 90 min. Then the reaction mixture was carefully poured into saturated aqueous $NaHCO_3$ (40 mL) and after separation of the organic layer, the aqueous layer was extracted with Et_2O (3 × 30 mL). The combined organic layers were washed with brine and subsequently dried over Na_2SO_4. Evaporation of the solvent and column chromatography (petroleum ether–EtOAc (4 : 1)) purification afforded vinyl triflate **10** 23 (5.5 g, 9.4 mmol, 50% over 2 steps) as a colourless oil; R_f = 0.42 (petroleum ether–EtOAc (9 : 1)); IR 3072, 2931, 2858, 1730, 1426, 1211; ^{1}H NMR (400 MHz) δ 7.69–7.64 (4H, m), 7.46–7.35 (6H, m), 3.81 (3H, s), 3.68 (2H, t, J = 6.4 Hz), 2.64–2.63 (1H, m), 2.60–2.41 (2H, m), 2.08–2.00 (1H, m), 1.87–1.83 (1H, m), 1.64–1.53 (3H, m), 1.42–1.22 (3H, m), 1.06 (9H, s); ^{13}C NMR (100 MHz) δ 164.9, 151.6, 135.5, 133.8, 129.5, 127.6, 122.1, 118.5 (q, J = 317 Hz), 63.7, 52.0, 32.2, 31.9, 31.2, 29.7, 28.3, 28.0, 26.8, 19.1; HRMS (FAB) [M + H$^+$] calcd for $C_{28}H_{36}F_3O_6SSi$: 585.1954, found: 585.1928.

(*R,*R**)-[2-(*tert*-Butyldiphenylsilyloxymethyl)cyclopropyl]-methanol (24)**

A solution of 1,2-dimethoxyethane (10.4 mL, 100 mmol, 3 equiv.) in CH_2Cl_2 (250 mL) was cooled to −15 °C. To this solution was added Et_2Zn (100 mL of a 1.0 M solution in hexanes, 100 mmol, 3 equiv.) and after 10 min CH_2I_2 (16.2 mL, 200 mmol, 6 equiv.) was added dropwise at such a rate as to keep the temperature below −10 °C (approximately 30 min). The clear solution was stirred at −20 °C for 30 min and allylic alcohol **23** (12.2 g, 37 mmol)[12] in CH_2Cl_2 (60 mL) was added dropwise. The reaction mixture was stirred at rt for 18 h and was then carefully poured into saturated aqueous $NaHCO_3$ (200 mL). After separation of the organic layer the aqueous layer was extracted with EtOAc (3 × 150 mL). The combined organic layers were washed with brine and subsequently dried over Na_2SO_4. Evaporation of the solvent and column chromatography (petroleum ether–Et_2O (3 : 1 ⟶ 1 : 1)) afforded cyclopropane **24** (9.6 g, 28 mmol, 76%) as a colourless oil; R_f = 0.61 (Et_2O); IR 3310 (br), 3070, 2959, 2859, 1112, 1076; ^{1}H NMR (400 MHz) δ 7.68–7.65 (4H, m), 7.43–7.36 (6H, m), 3.69 (1H, dd, J = 10.8, 5.4 Hz), 3.47–3.41 (3H, m), 1.37 (1H, br s), 1.05 (9H, s), 0.97–0.94 (2H, m), 0.46–0.39 (2H, m); ^{13}C NMR (100 MHz) δ 135.6, 133.8, 129.6, 127.6, 66.5, 66.4, 26.9, 19.3, 19.2, 19.2, 7.7; HRMS (FAB) [M + H^+] calcd for $C_{21}H_{29}O_2Si$: 341.1937, found: 341.1933.

(*R,*R**)-*tert*-Butyl[(2-iodomethylcyclopropyl)methoxy]-diphenylsilane (25)**

A solution of cyclopropane **24** (9.4 g, 28 mmol) in dry toluene (150 mL) and acetonitrile (75 mL) was cooled to 0 °C. To this solution was added triphenylphosphine (10.7 g, 41 mmol, 1.5 equiv.) and stirring was continued at 0 °C for 10 min. Then imidazole (7.6 g, 112 mmol, 4 equiv.) was added. After stirring at 0 °C for 15 min, iodine (10.7 g, 42 mmol, 1.5 equiv.) was added in portions of *ca.* 0.5 g in approximately 45 min. The yellow–brown solution was stirred at 0 °C for 30 min. Then the reaction mixture was poured into saturated aqueous $Na_2S_2O_3$. After separation of the organic layer the aqueous layer was extracted with Et_2O (2 × 200 mL). The combined organic layers were washed with brine and subsequently dried over Na_2SO_4 and the solvent was removed *in vacuo*. Column chromatography (petroleum ether–Et_2O (4 : 1)) afforded iodide **25** (9.5 g, 21 mmol, 75%) as a colourless oil; R_f = 0.73 (petroleum ether–Et_2O (2 : 1)); IR 3064, 2932, 2855, 1105, 1072; ^{1}H NMR (400 MHz) δ 7.68–7.66 (4H, m), 7.43–7.36 (6H, m), 3.63 (1H, dd, J = 10.8, 5.5 Hz), 3.49 (1H, dd, J = 10.8, 6.1 Hz), 3.13 (2H, dd, J = 7.7, 3.4 Hz), 1.24–1.18 (1H, m), 1.05 (9H, s), 1.04–0.99 (1H, m), 0.74–0.72 (1H, m), 0.46–0.43 (1H, m); ^{13}C NMR (100 MHz) δ 135.5, 133.7, 133.6, 129.6, 127.5, 65.6, 26.8, 26.7, 21.0, 19.2, 15.2, 12.5; HRMS (FAB) [M + H^+] calcd for $C_{21}H_{28}IOSi$: 451.0954, found: 451.0946.

(*R,*R**)-[2-(*tert*-Butyldiphenylsilyloxymethyl)cyclopropyl-methyl]triphenylphosphonium iodide (26)**

To a solution of iodide **25** (9.1 g, 20.4 mmol) in toluene (100 mL) was added triphenylphosphine (5.8 g, 22 mmol, 1.1 equiv.). The colourless solution was stirred at 100 °C and after 16 h a white product precipitated. The precipitate was collected by filtration and was rinsed with cold toluene. Recrystallisation of the product from hot toluene afforded phosphonium salt **26** (12.2 g, 17.1 mmol, 84%) as a white amorphous solid. Mp 205–206 °C; ^{1}H NMR (400 MHz, CD_3OD) δ 7.88–7.66 (15H, m), 7.56–7.51 (4H, m), 7.46–7.35 (6H, m), 3.60–3.32 (4H, m), 1.06–1.00 (2H, m), 0.95 (9H, s), 0.69–0.64 (1H, m), 0.51–0.47 (1H, m).

(*R,*S**)-*tert*-Butyl[2-(1,4-dioxaspiro[4.5]decan-8-ylidene-methyl)cyclopropylmethoxy]diphenylsilane (27)**

A white suspension of phosphonium salt **26** (11.36 g, 16 mmol, 1.1 equiv.) in toluene (80 mL) was heated to 70 °C. To this suspension was added KO*t*-Bu (15.0 mL of a 1.0 M solution in THF, 15 mmol, 1.0 equiv.) and stirring was continued at 70 °C for 30 min. To the brown solution was added cyclohexane-1,4-dione monoethylene ketal (2.30 g, 14.7 mmol) and the reaction mixture was stirred at 70 °C for 6 h. Then the reaction mixture was poured into water (150 mL) and after separation of the organic layer the aqueous layer was extracted with Et_2O (3 × 150 mL). The combined organic layers were washed with brine and subsequently dried over Na_2SO_4. Evaporation of the solvent and column chromatography (petroleum ether–Et_2O (9 : 1)) afforded alkene **27** (6.53 g, 14.1 mmol, 95%) as a colourless oil; R_f = 0.58 (petroleum ether–Et_2O (1 : 1)); IR 3071, 2954, 1117, 1078; ^{1}H NMR (500 MHz) δ 7.68–7.65 (4H, m), 7.44–7.35 (6H, m), 4.61 (1H, d, J = 9.0 Hz), 3.97 (4H, s), 3.65 (1H, dd, J = 10.7, 5.8 Hz), 3.55 (1H, dd, J = 10.7, 6.3 Hz), 2.38 (2H, t, J = 6.2 Hz), 2.20 (2H, t, J = 6.2 Hz), 1.69–1.65 (4H, m), 1.39–1.34 (1H, m), 1.04 (9H, s), 0.91–0.85 (1H, m), 0.63–0.59 (1H, m), 0.47–0.42 (1H, m); ^{13}C NMR (125 MHz) δ 135.6, 135.6, 134.7, 129.5, 127.6, 127.6, 127.5, 125.6, 109.0, 66.7, 64.2, 36.1, 35.3, 33.2, 26.8, 25.5, 22.6, 19.2, 15.3, 11.6; HRMS (FAB) [M + H^+] calcd for $C_{29}H_{39}O_3Si$: 463.2668, found: 463.2677.

(*R,*R**)-*tert*-Butyl[2-(1,4-dioxaspiro[4.5]decan-8-ylmethyl)-cyclopropylmethoxy]diphenylsilane (28)**

To a solution of alkene **27** (6.49 g, 14.0 mmol) in EtOAc was added PtO_2 (80 mg, 0.35 mmol, 2.5 mol%). The reaction mixture was stirred under a hydrogen atmosphere (1 atm) for 40 min. Filtration over a thin pad of Celite® and evaporation of the solvent gave acetal **28** (6.41 g, 13.8 mmol, 98%) as a colourless oil; R_f = 0.57 (petroleum ether–Et_2O (1 : 1)); IR 3070, 2933, 2859, 1109; ^{1}H NMR (400 MHz) δ 7.68–7.65 (4H, m), 7.42–7.35 (6H, m), 3.94 (4H, s), 3.67 (1H, dd, J = 10.7, 5.7 Hz), 3.36 (1H, dd, J = 10.7, 7.2 Hz), 1.91–1.70 (4H, m), 1.55–1.49 (3H, m), 1.46–1.34 (1H, m), 1.32–1.14 (3H, m), 1.04 (9H, s), 0.79–0.74 (1H, m), 0.58–0.52 (1H, m), 0.29–0.22 (1H, m), 0.19–0.16 (1H, m); ^{13}C NMR (100 MHz) δ 135.6, 134.8, 134.1, 134.0, 129.5, 127.6, 127.5, 109.2, 67.7, 64.2, 64.1, 40.5, 37.1, 34.5, 30.3, 30.1, 26.8, 21.0, 19.2, 15.4, 9.5; HRMS (FAB) [M + H^+] calcd for $C_{29}H_{41}O_3Si$: 465.2825, found: 465.2810.

(*R,*R**)-4-[2-(*tert*-Butyldiphenylsilyloxymethyl)cyclopropyl-methyl]cyclohexanone (29)**

To a solution of acetonide **28** (6.39 g, 13.8 mmol) in acetone (150 mL) was added *p*-TsOH (100 mg, 0.52 mmol, 4 mol%). The reaction mixture was stirred at 40 °C for 7 h and then saturated aqueous $NaHCO_3$ was added to the reaction mixture. The aqueous layer was extracted with Et_2O (3 × 150 mL). The combined organic layers were washed with brine and subsequently dried over Na_2SO_4. Evaporation of the solvent and column chromatography (petroleum ether–Et_2O (6 : 1)) afforded ketone **29** (4.41 g, 10.5 mmol, 76%) as a colourless oil; R_f = 0.42 (petroleum ether–Et_2O (2 : 1)); IR 3070, 2931, 2858, 1715, 1110, 1064; ^{1}H NMR (400 MHz) δ 7.68–7.65 (4H, m), 7.44–7.35 (6H, m), 3.74 (1H, dd, J = 10.7, 5.4 Hz), 3.34 (1H, dd, J = 10.7, 7.4 Hz), 2.37–2.27 (4H, m), 2.23–2.18 (1H, m), 2.12–2.08 (1H, m), 1.83–1.76 (1H, m), 1.45–1.36 (4H, m), 1.05 (9H, s), 0.83–0.81 (1H, m), 0.59–0.57 (1H, m), 0.33–0.29 (1H, m), 0.23–0.19 (1H, m); ^{13}C NMR (100 MHz) δ 212.4, 135.5, 134.0, 133.9, 129.5, 127.6 (Ar), 67.6, 40.9, 40.8, 39.7, 36.9, 32.8, 32.5, 26.8, 21.1, 19.2, 15.3, 9.4; HRMS (FAB) [M + H^+] calcd for $C_{27}H_{37}O_2Si$: 421.2563, found: 421.2574.

5-[2-(*tert*-Butyldiphenylsilyloxymethyl)-(*R,*R**)-cyclopropyl-methyl]-2-hydroxycyclohex-1-enecarboxylic acid ethyl ester (30)**

Following the same procedure as described for the preparation of **22**, ketone **29** (2.4 g, 5.7 mmol) was converted to β-ketoester

30 (2.4 g, 4.8 mmol, 84%). Column chromatography (petroleum ether–Et_2O (9 : 1)) afforded β-ketoester **30** as an equimolar mixture of two diastereomers as a colourless oil; R_f = 0.76 (petroleum ether–Et_2O (1 : 1)); IR 3070, 2931, 2858, 1651, 1615, 1216, 1111; ^{1}H NMR (400 MHz) δ 12.2 (0.5H, s), 12.2 (0.5H, s), 7.68–7.65 (4H, m), 7.43–7.35 (6H, m), 4.21–4.15 (2H, m), 3.74 (0.5H, dd, J = 10.7, 5.5 Hz), 3.65 (0.5H, dd, J = 10.7, 5.8 Hz), 3.47 (0.5H, dd, J = 10.8, 6.6 Hz), 3.33 (0.5H, dd, J = 10.6, 7.4 Hz), 2.45–2.42 (1H, m), 2.28 (2H, m), 1.99–1.82 (2H, m), 1.70–1.61 (1H, m), 1.47–1.43 (1H, m), 1.33–1.19 (5H, m), 1.05 (4.5H, s), 1.04 (4.5H, s), 0.99–0.79 (1H, m), 0.62–0.60 (1H, m), 0.35–0.28 (1H, m), 0.22–0.19 (1H, m); ^{13}C NMR (100 MHz) δ 172.6, 171.8, 171.6, 135.7, 135.5, 134.0, 133.9, 133.8, 129.5, 129.4, 127.4, 97.1, 97.1, 67.6, 67.2, 60.0, 40.0, 39.8, 34.4, 34.1, 28.9, 28.8, 28.7, 27.6, 27.5, 26.8, 26.7, 21.1, 20.7, 19.1, 19.1, 15.1, 14.6, 14.2, 9.7, 9.2; HRMS (FAB) [M + H^+] calcd for $C_{30}H_{43}O_4Si$: 493.2774, found: 493.2792.

5-[2-(*tert*-Butyldiphenylsilyloxymethyl)-(*R**,*R**)-cyclopropylmethyl]-2-trifluoromethylsulfonyloxycyclohex-1-enecarboxylic acid ethyl ester (12)

Following the same procedure as described for the preparation of **10**, β-ketoester **30** (2.4 g, 4.9 mmol) was converted to vinyl triflate **12**. Column chromatography (petroleum ether–Et_2O (9 : 1)) afforded vinyl triflate **12** (2.9 g, 4.7 mmol, 95%) as an equimolar mixture of two diastereomers as a colourless oil; R_f = 0.67 (petroleum ether–Et_2O (2 : 1)); IR 3073, 2934, 2859, 1729, 1415, 1208; ^{1}H NMR (400 MHz) δ 7.67–7.65 (4H, m, Ar–H), 7.44–7.35 (6H, m), 4.26 (2H, q, 7.1 Hz), 3.74 (0.5H, dd, J = 10.7, 5.4 Hz), 3.68 (0.5H, dd, J = 10.7, 5.5 Hz), 3.40 (0.5H, dd, J = 10.7, 6.9 Hz), 3.32 (0.5H, dd, J = 10.7, 7.5 Hz), 2.68–2.60 (1H, m), 2.46–2.32 (2H, m), 2.17–2.05 (1.5H, m), 1.98–1.92 (0.5H, m), 1.71–1.56 (1H, m), 1.48–1.17 (6H, m), 1.04 (4.5H, s), 1.03 (4.5H, s), 0.95–0.77 (1H, m), 0.59–0.53 (1H, m), 0.36–0.28 (1H, m), 0.23–0.18 (1H, m); ^{13}C NMR (100 MHz) δ 164.5, 151.2, 151.1, 135.5, 135.3, 133.8, 133.8, 131.9, 131.8, 129.5, 129.5, 127.5, 122.6, 122.5, 118.3 (q, J = 317 Hz), 67.5, 67.1, 61.3, 39.0, 38.9, 33.2, 32.9, 32.4, 32.1, 28.3, 28.2, 27.9, 27.8, 26.7, 26.6, 21.0, 20.7, 19.2, 14.9, 14.4, 13.8, 9.5, 9.1; HRMS (FAB) [M + H^+] calcd for $C_{31}H_{40}F_3O_6SSi$: 625.2267, found: 625.2267.

(+)-(3*S*)-3-[(1*R*,2*S*,4*R*,5*S*)-5-(*tert*-Butyldiphenylsilyloxy)-3,3-dimethyl-2-vinyl-7-oxabicyclo[2.2.1]heptan-1-yl]-4,5,6,7-tetrahydroisobenzofuran-1(3*H*)-one (31)

To a solution of aldehyde **5** (280 mg, 0.65 mmol) in DMF (10 mL) was added vinyl triflate **6** (419 mg, 1.38 mmol, 2.1 equiv.) followed by $CrCl_2$ (320 mg, 2.61 mmol, 4 equiv.) and $NiCl_2$ (2.4 mg, 18.5 μmol, *ca.* 1 mol%). The resulting green reaction mixture was stirred at 50 °C for 18 h. After cooling the mixture to 0 °C it was quenched by adding saturated aqueous NH_4Cl (3 mL) followed by water (15 mL). The aqueous mixture was extracted with EtOAc (3 × 20 mL). The combined organic layers were washed with brine and subsequently dried over Na_2SO_4 and the solvent was removed *in vacuo*. Column chromatography (petroleum ether–Et_2O (9 : 1)) afforded diastereomeric lactone **31** (223 mg, 0.41 mmol, 64%) and its isomer (104 mg, 0.19 mmol, 28%) as colourless viscous oils; R_f = 0.51 (R_f isomer = 0.32) (petroleum ether–Et_2O (1 : 1)); $[a]_D^{21}$ +47.9 (c = 0.99, $CHCl_3$); IR 3071, 2933, 2857, 1760, 1111, 1010; ^{1}H NMR (400 MHz) δ 7.65 (2H, d, J = 7.9 Hz), 7.55 (2H, d, J = 7.9 Hz), 7.46–7.31 (6H, m), 5.67 (1H, ddd, J = 17.0, 10.4, 10.3 Hz), 5.13 (1H, dd, J = 10.1, 1.9 Hz), 5.07–5.03 (2H, m), 4.31 (1H, d, J = 5.9 Hz), 3.58 (1H, s), 2.87–2.80 (1H, m), 2.38–2.22 (3H, m), 2.00 (1H, d, J = 10.6 Hz), 1.77–1.63 (6H, m), 1.05 (9H, s), 0.78 (3H, s), 0.65 (3H, s); ^{13}C NMR (100 MHz) δ 160.9, 135.7, 135.6, 134.8, 133.9, 133.4, 129.8, 128.1, 127.8, 127.7, 118.7, 92.2, 88.0, 80.9, 71.5, 61.6, 42.3, 40.9, 26.8, 25.5, 24.8, 24.6, 21.7, 21.6, 20.2, 18.3; HRMS (FAB) [M + H^+] calcd for $C_{34}H_{43}O_4Si$: 543.2931, found: 543.2931.

(+)-(*S*)-[(1*R*,2*S*,4*R*,5*S*)-5-(*tert*-Butyldiphenylsilyloxy)-3,3-dimethyl-2-vinyl-7-oxabicyclo[2.2.1]heptan-1-yl](2-hydroxymethylcyclohex-1-enyl)methanol (34)

To a solution of lactone **31** (330 mg, 0.61 mmol) in Et_2O (4 mL) was rapidly added lithium aluminium hydride (1.0 mL of a 1.0 M solution in Et_2O, 1 mmol, 1.7 equiv.) in one portion at rt. The reaction mixture was stirred for 30 min and then quenched by adding EtOAc and few drops of saturated aqueous Na_2SO_4. The reaction mixture was dried over Na_2SO_4 and filtration and evaporation of the solvent gave diol **34** (314 mg, 0.57 mmol, 93%) as a colourless viscous oil; R_f = 0.28 (petroleum ether–Et_2O (1 : 3)); $[a]_D^{19}$ = +15.2 (c = 2.03, $CHCl_3$); IR 3420 (br), 3071, 2929, 2857, 1113; ^{1}H NMR (400 MHz) δ 7.64–7.61 (4H, m), 7.43–7.36 (6H, m), 5.94 (1H, ddd, J = 16.9, 10.4, 10.3 Hz), 5.19 (1H, dd, J = 10.1, 2.1 Hz), 5.08 (1H, s), 5.07 (1H, dd, J = 17.0, 2.0 Hz), 4.38 (1H, d, J = 11.2 Hz), 4.32 (1H, dd, J = 6.5, 1.5 Hz), 3.63 (1H, s), 3.60–3.52 (1H, m), 3.41–3.28 (1H, br s), 2.61–2.52 (1H, m), 2.31–2.10 (2H, m), 2.08–1.99 (2H, m), 1.93 (1H, d, J = 10.1 Hz), 1.89 (1H, dd, J = 13.5, 7.3 Hz), 1.69–1.60 (4H, m), 1.05 (9H, s), 0.81 (3H, s), 0.67 (3H, s); ^{13}C NMR (100 MHz) δ 136.5, 136.3, 135.8, 135.7, 134.0, 133.8, 132.7, 129.7, 129.7, 127.7, 116.6, 91.4, 90.6, 72.8, 69.8, 63.1, 62.0, 44.2, 43.4, 29.7, 28.9, 26.9, 26.3, 25.0, 24.3, 22.6, 19.0; HRMS (FAB) [M + Na^+] calcd for $C_{34}H_{46}NaO_4Si$: 569.3063, found: 569.3080.

(+)-(*S*)-[2-(*tert*-Butyldimethylsilyloxymethyl)cyclohex-1-enyl]-[(1*R*,2*S*,4*R*,5*S*)-5-(*tert*-butyldiphenylsilyloxy)-3,3-dimethyl-2-vinyl-7-oxabicyclo[2.2.1]heptan-1-yl]methanol (35)

To a solution of diol **34** (312 mg, 0.55 mmol) in DMF (8 mL) were added imidazole (112 mg, 1.65 mmol, 3 equiv.) and TBDMSCl (166 mg, 1.10 mmol, 2 equiv.). The reaction mixture was stirred at rt for 16 h and then poured in water (25 mL). The aqueous layer was extracted with EtOAc (3 × 25 mL) and the combined organic layers were washed with brine and subsequently dried over Na_2SO_4. After evaporation of the solvent and column chromatography purification (petroleum ether–Et_2O (9 : 1)) alcohol **35** (323 mg, 0.48 mmol, 89%) was obtained as a colourless oil. Alcohol **35** could be used crude in the next reaction; R_f = 0.63 (petroleum ether–Et_2O (1 : 1)); $[a]_D^{19}$ +6.14 (c = 1.32, $CHCl_3$); IR 3471 (br), 3071, 2930, 2857, 1095; ^{1}H NMR (400 MHz) δ 7.69–7.63 (4H, m), 7.45–7.36 (6H, m), 5.66 (1H, ddd, J = 17.0, 10.4, 10.3 Hz), 5.01 (1H, dd, J = 10.0, 2.1 Hz), 4.83 (1H, dd, J = 16.9, 2.1), 4.37 (1H, dd, J = 6.7, 1.7 Hz), 3.96–3.93 (2H, m), 3.73–3.69 (1H, m), 3.52 (1H, s), 2.40 (1H, br s), 2.04 (1H, d, J = 12.7 Hz), 1.92–1.86 (1H, m), 1.77–1.59 (5H, m,), 1.41–1.32 (4H, m), 1.06 (9H, s), 0.91 (9H, s), 0.75 (3H, s), 0.60 (3H, s), 0.07 (6H, s); ^{13}C NMR (100 MHz) δ 136.3, 135.8, 135.8, 134.2, 134.0, 129.6, 129.6, 127.6, 116.6, 92.5, 90.7, 72.6, 72.4, 61.1, 61.0, 43.6, 41.5, 27.6, 26.9, 26.6, 26.1, 25.1, 24.3, 21.1, 20.6, 18.9, 18.3, −5.34, −5.35.

(+)-(*S*)-Acetic acid [2-(*tert*-butyldimethylsilyloxymethyl)-cyclohex-1-enyl][(1*R*,2*S*,4*R*,5*S*)-5-*tert*-butyldiphenylsilyloxy)-3,3-dimethyl-2-vinyl-7-oxabicyclo[2.2.1]heptan-1-yl]methyl ester (36)

To a solution of alcohol **35** (387 mg, 0.59 mmol) in CH_2Cl_2 (2 mL) was added acetic anhydride (0.5 mL, 5.3 mmol, 10 equiv.) and pyridine (200 μL, 2.5 mmol, 5 equiv.) and stirring was continued at rt for 16 h. To get full conversion the reaction mixture was stirred at 50 °C for 3 h. Then the mixture was poured into saturated aqueous $NaHCO_3$ (50 mL) and extracted with EtOAc (3 × 20 mL). The combined organic layers were washed with brine and subsequently dried over Na_2SO_4. Evaporation of the solvent gave acetate **36** (377 mg, 0.54 mmol, 92%) as an oil. Acetate **36** was used crude in the next reaction; R_f = 0.66 (petroleum ether–Et_2O (1 : 1)); $[a]_D^{20}$ +15.5 (c = 1.25, $CHCl_3$); IR 3072, 2931, 2857, 1747, 1234, 1113; ^{1}H NMR (400 MHz)

δ 7.66–7.61 (4H, m), 7.42–7.35 (6H, m), 5.74 (1H, s), 5.65 (1H, ddd, J = 16.9, 10.4, 10.2 Hz), 4.96 (1H, dd, J = 10.0, 2.3 Hz), 4.79 (1H, dd, J = 16.9, 2.2 Hz), 4.47 (1H, d, J = 12.9 Hz), 4.33 (1H, dd, J = 6.5, 1.7 Hz), 4.13 (1H, d, J = 12.9 Hz), 3.54 (1H, s), 2.40–2.31 (1H, m), 2.17–1.99 (3H, m), 1.94 (3H, s), 1.87–1.81 (2H, m), 1.72 (1H, d, J = 12.6 Hz), 1.59–1.53 (4H, m), 1.04 (9H, s), 0.92 (9H, s), 0.75 (3H, s), 0.63 (3H, s), 0.11 (3H, s), 0.10 (3H, s); HRMS (FAB) [M + H^+] calcd for $C_{42}H_{63}O_5Si_2$: 703.4214, found: 703.4210.

(*S*)-Acetic acid [(1*R*,2*S*,4*R*,5*S*)-5-*tert*-butyldiphenylsilyloxy)-3,3-dimethyl-2-vinyl-7-oxabicyclo[2.2.1]heptan-1-yl](2-hydroxymethylcyclohex-1-enyl)methyl ester (37)

A solution of protected alcohol **36** (428 mg, 0.61 mmol) in MeOH (20 mL) was cooled to 0 °C. To this solution were added a few crystals of CSA and stirring was continued at 0 °C for 2 h. Then saturated aqueous $NaHCO_3$ (3 mL) was added to quench the reaction followed by water (15 mL). The aqueous layer was extracted with EtOAc (3 × 20 mL). The combined organic layers were washed with brine and subsequently dried over Na_2SO_4 and the solvent was removed *in vacuo*. Crude allylic alcohol **37** (364 mg, 0.62 mmol, 100%) was obtained as a colourless oil; R_f = 0.18 (petroleum ether–Et_2O (1 : 1)); IR 3505 (br), 3070, 2930, 2856, 1743, 1234, 1113, 1019; ^{1}H NMR (400 MHz) δ 7.64–7.61 (4H, m), 7.44–7.37 (6H, m), 5.98 (1H, s), 5.67 (1H, ddd, J = 16.9, 10.4, 10.3 Hz), 4.98 (1H, dd, J = 10.1, 2.3 Hz), 4.80 (1H, dd, J = 16.9, 2.2 Hz), 4.44 (1H, d, J = 11.5 Hz), 4.34 (1H, dd, J = 6.6, 1.5 Hz), 3.68 (1H, d, J = 11.6 Hz), 3.64 (1H, s), 2.58–2.51 (1H, m), 2.09–1.97 (3H, m), 1.94 (3H, s), 1.91 (1H, dd, J = 12.9, 6.6 Hz), 1.87 (1H, d, J = 10.6 Hz), 1.72 (1H, d, J = 12.9 Hz), 1.64–1.52 (4H, m), 1.05 (9H, s), 0.78 (3H, s), 0.66 (3H, s); ^{13}C NMR (100 MHz) δ 169.5, 137.5, 136.0, 135.7, 135.7, 133.8, 129.8, 129.7, 129.4, 127.7, 127.7, 116.6, 91.7, 89.1, 71.7, 71.6, 62.8, 61.4, 43.3, 42.4, 29.1, 26.7, 26.1, 25.5, 24.7, 22.5, 22.5, 20.6, 18.9; HRMS (FAB) [M + Na^+] calcd for $C_{36}H_{48}NaO_5Si$: 611.3169, found: 611.3168.

(−)-(*S*)-Acetic acid [(1*R*,2*S*,4*R*,5*S*)-5-*tert*-butyldiphenylsilyloxy)-3,3-dimethyl-2-vinyl-7-oxabicyclo[2.2.1]heptan-1-yl]-(2-formylcyclohex-1-enyl)methyl ester (46)

To a solution of allylic alcohol **37** (367 mg, 0.62 mmol) in acetone (20 mL) were added NMO (110 mg, 0.94 mmol, 1.5 equiv.) and TPAP (6.6 mg, 18 μmol, 3 mol%). The dark mixture was stirred for 2 h and filtered over a thin pad of silica followed by exhaustive rinsing with EtOAc. Evaporation of the solvent gave aldehyde **46** (353 mg, 0.60 mmol, 97%) as an oil; R_f = 0.68 (petroleum ether–Et_2O (1 : 1)); $[\alpha]_D^{20}$ −35.5 (c = 1.75, $CHCl_3$); IR 3071, 2935, 2859, 1750, 1672, 1228, 1111; ^{1}H NMR (500 MHz) δ 10.18 (1H, s), 7.66–7.58 (4H, m, Ar–H), 7.44–7.36 (6H, m), 6.23 (1H, s), 5.65 (1H, ddd, J = 16.9, 10.5, 10.0 Hz), 5.01 (1H, dd, J = 10.0, 1.7 Hz), 4.84 (1H, dd, J = 16.9, 2.0 Hz), 4.35 (1H, d, J = 6.6 Hz), 3.54 (1H, s), 2.37–2.18 (4H, m), 1.99 (3H, s), 1.95 (1H, dd, J = 12.7, 6.6 Hz), 1.87 (1H, d, J = 10.7 Hz), 1.66–1.59 (5H, m), 1.02 (9H, s), 0.74 (3H, s), 0.63 (3H, s); ^{13}C NMR (125 MHz) δ 191.3, 169.4, 151.3, 136.6, 135.7, 135.6, 133.9, 133.8, 129.7, 129.7, 127.7, 127.6, 117.1, 91.3, 88.2, 71.6, 71.5, 61.5, 43.7, 42.8, 28.3, 26.7, 25.1, 24.5, 22.7, 21.9, 21.3, 20.5, 19.0 ($C(CH_3)_3$); HRMS (FAB) [M + H^+] calcd for $C_{36}H_{47}O_5Si$: 587.3193, found: 587.3179.

(+)-(*S*)-Acetic acid [(1*R*,2*S*,4*R*,5*S*)-5-(*tert*-butyldiphenylsilyloxy)-3,3-dimethyl-2-vinyl-7-oxabicyclo[2.2.1]heptan-1-yl]-(2-vinylcyclohex-1-enyl)methyl ester (4)

To a suspension of methyltriphenylphosphonium bromide (860 mg, 1.90 mmol, 2.1 equiv.) in THF (15 mL) at 0 °C was added dropwise *n*-BuLi (1.13 mL of a 1.6 M solution in hexanes, 1.80 mmol, 2.0 equiv.). The yellow suspension was stirred at 0 °C for 1 h and aldehyde **46** (530 mg, 0.90 mmol) in THF (10 mL) was added *via* a double tipped needle. The reaction mixture was stirred for 45 min and then quenched by adding saturated aqueous $NaHCO_3$. The aqueous layer was extracted with EtOAc (3 × 30 mL). The combined organic layers were washed with brine and subsequently dried over Na_2SO_4 and the solvent was removed *in vacuo*. Column chromatography (petroleum ether–Et_2O (9 : 1)) afforded triene **4** (483 mg, 0.83 mmol, 92%) as an oil; R_f = 0.76 (petroleum ether–Et_2O (1 : 1)); $[\alpha]_D^{21}$ +8.51 (c = 2.1, $CHCl_3$); IR 3072, 2932, 2858, 1747, 1234, 1113, 1027; ^{1}H NMR (400 MHz) δ 7.66–7.60 (4H, m), 7.42–7.34 (6H, m), 7.03 (1H, dd, J = 17.3, 11.1 Hz), 5.85 (1H, s), 5.70 (1H, ddd, J = 16.9, 10.3, 10.3 Hz), 5.21 (1H, d, J = 17.2 Hz), 5.03 (1H, d, J = 11.1 Hz), 4.97 (1H, dd, J = 10.1, 2.3 Hz), 4.80 (1H, dd, J = 16.9, 2.2 Hz), 4.33 (1H, dd, J = 6.0, 2.2 Hz), 3.63 (1H, s), 2.32–2.18 (4H, m), 1.95 (3H, s), 1.85–1.83 (3H, m), 1.65–1.54 (4H, m), 1.02 (9H, s), 0.78 (3H, s), 0.66 (3H, s); ^{13}C NMR (100 MHz) δ 169.3, 136.6, 135.7, 135.7, 134.3, 134.1, 132.7, 132.3, 129.6, 129.6, 127.6, 127.6, 116.2, 111.7, 91.4, 89.8, 73.5, 71.8, 62.0, 44.3, 42.6, 28.3, 26.8, 25.5, 25.3, 24.7, 22.5, 22.4, 20.7, 19.0; HRMS (FAB) [M + H^+] calcd for $C_{37}H_{49}O_4Si$: 585.3400, found: 585.3400.

(+)-(2*S*,3*R*,5*S*,10*R*,19*S*)-Diene 53

A solution of triene **4** (300 mg, 513 μmol) in toluene (70 mL, 7.3 mM) was thoroughly degassed with argon. Then catalyst **51** (64 mg, 75 μmol, 15 mol%) was added and the brown reaction mixture was stirred at 70 °C for 16 h. After cooling to rt the solvent was removed *in vacuo*. Column chromatography (petroleum ether–Et_2O (9 : 1)) afforded diene **53** (283 mg, 509 μmol, 99%) as an oil; R_f = 0.75 (petroleum ether–Et_2O (1 : 1)); $[\alpha]_D^{22}$ +78.0 (c = 0.79, MeOH); IR 2941, 2860, 1740, 1240, 1108; ^{1}H NMR (500 MHz) δ 7.68–7.60 (4H, m), 7.43–7.38 (6H, m), 5.70 (1H, d, J = 11.7 Hz), 5.50 (2H, m), 4.44 (1H, m), 3.62 (1H, s), 2.47–2.42 (1H, m), 2.05 (3H, s), 1.98–1.90 (3H, m), 1,87 (1H, d, J = 7.0 Hz), 1.67–1.49 (6H, m), 1.05 (9H, s), 0.67 (6H, s); HRMS (FAB) [M + H^+] calcd for $C_{35}H_{45}O_4Si$: 557.3087, found: 557.3095.

(2*S*,3*R*,5*R*,6*S*,7*R*,10*R*,19*S*)- and (2*S*,3*R*,5*R*,6*R*,7*S*,10*R*,19*S*)-Diol 56

To a vigorously stirred solution of diene **53** (162 mg, 291 μmol) in *tert*-butanol (7 mL) was added DMAP (71.2 mg, 580 μmol, 2 equiv.). Then OsO_4 (7.4 mL of a 1 wt% solution in water (291 μmol, 1 equiv.)) was added in one portion to the reaction mixture. The reaction mixture turned brown immediately and stirring was continued for 30 min. Then Na_2SO_3 (189 mg, 1.50 mmol, 5 equiv.) was added in one portion. After stirring for 30 min, the reaction mixture was filtered over a thin pad of silica to remove the solids and rinsed with MeOH (30 mL). Evaporation of the solvents *in vacuo* and column chromatography (petroleum ether–Et_2O (1 : 3)) afforded a 78 : 22 mixture of *cis*-diols **56** (145 mg, 246 μmol, 84%) as a white solid; R_f = 0.05 (petroleum ether–Et_2O (1 : 1)); IR (KBr) 3436 (br), 3184, 2932, 1737, 1603, 1240, 1111; ^{1}H NMR (500 MHz) δ 7.66 (2H, d, J = 7.8 Hz), 7.62 (2H, d, J = 7.8 Hz), 7.44–7.35 (6H, m), 5.76 (0.2H, s), 5.46–5.41 (0.7H, m), 5.41–5.30 (0.6H, m), 4.55–4.48 (1H, m), 4.42–4.40 (0.8H, dd, J = 6.8, 2.9 Hz), 4.33–4.32 (0.2H, dd, J = 4.4, 2.9 Hz), 4.10 (1H, s), 3.70 (0.2H, s), 3.58 (0.8H, s), 2.48–2.40 (0.7H, m), 2.34–2.31 (0.8H, m), 2.20 (1H, s), 2.07–2.01 (5.5H, m), 1.99–1.90 (2H, m), 1.89–1.80 (1H, m), 1.73–1.43 (4H, m), 1.16 (3H, s), 1.04 (9H, s), 0.69 (3H, s); HRMS (FAB) [M + H^+] calculated for $C_{35}H_{47}O_6Si$: 591.3142, found: 591.3142.

(+)-(2*S*,3*R*,5*S*,6*R*,10*R*,19*S*)-α-Hydroxyketone 59

To a solution of the mixture of *cis*-diols **56** (37.8 mg, 64.0 μmol) in CH_2Cl_2 (2 mL) at −20 °C was added Dess–Martin reagent (35 mg, 83 μmol, 1.3 equiv.). The reaction mixture was allowed

to warm to rt in 1 h and was stirred for another 2 h. The reaction was quenched by adding saturated aqueous $NaHCO_3$ (3 mL) and saturated aqueous Na_2SO_3 (3 mL). The aqueous layer was extracted with CH_2Cl_2 (3 × 10 mL). The combined organic layers were washed with brine and subsequently dried over Na_2SO_4 and the solvent was removed *in vacuo*. Column chromatography (petroleum ether–Et_2O (3 : 1)) afforded α-hydroxyketone **59** (31.1 mg, 52 μmol, 81%) as a white solid $[\alpha]_D^{22}$ +11.8 (*c* = 0.91, $CHCl_3$); R_f = 0.54 (petroleum ether–Et_2O (1 : 1)); IR 3458, 2937, 1746, 1645,1232, 1079; ^{1}H NMR (400 MHz) δ 7.66 (2H, d, *J* = 7.7 Hz), 7.62 (2H, d, *J* = 7.7 Hz), 7.46–7.37 (6H, m), 5.30 (1H, s), 4.77 (1H, dd, *J* = 12.2, 1.8 Hz), 4.46 (1H, dd, *J* = 6.9, 3.1 Hz), 3.72 (1H, d, *J* = 1.8 Hz), 3.67 (1H, s), 2.82–2.70 (1H, m), 2.58–2.49 (1H, m), 2.30–2.20 (1H, m), 2.04 (3H, s), 2.03–1.96 (1H, m), 1.86 (1H, dd, *J* = 11.2, 6.9 Hz), 1.80–1.45 (6H, m), 1.19 (3H, s), 1.06 (9H, s), 0.66 (3H, s); ^{13}C NMR (125 MHz) δ 203.3, 169.6, 150.5, 135.8, 135.7, 134.7, 133.6, 133.6, 129.9, 129.8, 127.7, 127.7, 93.4, 85.4, 76.7, 73.8, 72.4, 54.3, 49.0, 43.2, 32.7, 26.9, 25.4, 23.7, 22.4, 21.9, 21.5, 21.1, 19.0; HRMS (FAB) [M + H^+] calcd for $C_{35}H_{45}O_6Si$: 589.2985, found: 589.2966.

(+)-(2*S*,3*R*,10*R*,19*S*)-Enol ketone 62

To a solution of α-hydroxyketone **59** (23.4 mg, 39.8 μmol) in MeOH (2 mL) was added cupric acetate monohydrate (31.2 mg, 172 μmol, 4.3 equiv.). The blue mixture was stirred at 60 °C for 6 h. Then the green mixture was cooled to rt and quenched with water (10 mL) followed by extraction with CH_2Cl_2 (3 × 10 mL). The combined organic layers were washed with brine and subsequently dried over Na_2SO_4 and the solvent was removed *in vacuo*. Column chromatography (petroleum ether–Et_2O (4 : 1)) afforded enol ketone **62** (17.4 mg, 29.7 μmol, 75%) as a white solid; R_f = 0.61 (petroleum ether–Et_2O (1 : 1)); $[\alpha]_D^{23}$ +122.6 (*c* = 1.6, $CHCl_3$); IR 3385, 2934, 1742, 1604, 1236, 1078; ^{1}H NMR (500 MHz) δ 7.68 (2H, d, *J* = 6.6 Hz), 7.63 (2H, d, *J* = 6.6 Hz), 7.46–7.38 (6H, m), 6.45 (1H, s), 5.24 (1H, s), 4.43 (1H, dd, *J* = 6.8, 2.7 Hz), 3.74 (1H, s), 2.76–2.64 (2H, m), 2.26–2.22 (1H, m), 1.98 (3H, s), 1.97–1.91 (1H, m), 1.78–1.75 (1H, m), 1.70–1.57 (5H, m), 1.19 (3H, s), 1.08 (9H, s), 0.84 (3H, s); ^{13}C NMR (125 MHz, C_6D_6) δ 188.7, 170.6, 146.3, 141.1, 136.9, 136.9, 134.8, 134.8, 134.5, 130.9, 130.9, 129.2, 129.0, 92.7, 87.9, 75.9, 73.7, 46.5, 45.6, 33.2, 27.8, 27.5, 24.4, 22.8, 22.5, 20.8, 20.5, 20.0; HRMS (FAB) [M + H^+] calcd for $C_{35}H_{43}O_6Si$: 587.2829, found: 587.2822.

(+)-(2*S*,3*R*,10*R*,19*S*)-Methyl enol ether 63

To a solution of enol ketone **62** (17.2 mg, 29.3 μmol) in DMF (0.5 mL) was added iodomethane (200 μL, 3.2 mmol, 109 equiv.) and Ag_2O (80 mg, 346 μmol, 12 equiv.) and the resulting gray suspension was stirred at rt for 16 h. Then the reaction mixture was filtered over a thin pad of Celite® and the filtrate was washed with Et_2O (20 mL). Evaporation and column chromatography (petroleum ether–Et_2O (3 : 1)) afforded methyl enol ether **63** (16.8 mg, 28.0 μmol, 95%) as an oil; R_f = 0.52 (petroleum ether–Et_2O (1 : 1)); $[\alpha]_D^{22}$ +152.6 (*c* = 1.1, $CHCl_3$); IR 2935, 1743, 1642, 1236, 1080; ^{1}H NMR (500 MHz) δ 7.74 (2H, d, *J* = 6.6 Hz), 7.64 (2H, d, *J* = 6.6 Hz), 7.47–7.39 (6H, m), 5.13 (1H, s), 4.39 (1H, dd, *J* = 6.8, 2.4 Hz), 3.69 (1H, s), 3.48 (3H, s), 2.68–2.59 (2H, m), 2.15–2.11 (1H, m), 1.95 (3H, s), 1.84–1.80 (2H, m), 1.77–1.65 (5H, m), 1.18 (3H, s), 1.08 (9H, m), 0.81 (3H, s); ^{13}C NMR (125 MHz) δ 190.6, 170.3, 146.7, 145.7, 139.5, 137.8, 135.8, 135.7, 133.7, 133.6, 129.9, 129.8, 127.8, 127.8, 91.7, 86.5, 75.0, 71.6, 59.4, 46.0, 44.2, 31.1, 26.9, 26.3, 24.3, 21.9, 21.7, 21.0, 20.8, 19.0; HRMS (FAB) [M + H^+] calcd for $C_{36}H_{45}O_6Si$: 601.2985, found: 601.3024.

(+)-(2*S*,3*R*,10*R*,19*S*)-Alcohol 68

A solution of protected alcohol **63** (26.3 mg, 43.8 μmol) in THF (3 mL) was cooled to 0 °C. Then HF·pyridine (70% HF–30% pyridine, 0.2 mL) was added and the reaction mixture was allowed to warm to rt. After stirring the mixture at rt for 3 h, the reaction was carefully quenched with saturated aqueous $NaHCO_3$ (3 mL) and extracted with CH_2Cl_2 (3 × 5 mL). The combined organic layers were washed with brine and subsequently dried over Na_2SO_4 and the solvent was removed *in vacuo*. Column chromatography (petroleum ether–Et_2O (1 : 1 ⟶ 1 : 9)) afforded alcohol **68** (12.3 mg, 34.0 μmol, 77%) as a white solid; R_f = 0.23 (Et_2O); $[\alpha]_D^{22}$ +227.3 (*c* = 1.1, $CHCl_3$); IR 3470 (br), 2935, 1743, 1645, 1237; ^{1}H NMR (500 MHz) δ 5.17 (1H, s), 4.39 (1H, dd, *J* = 6.9, 1.7 Hz), 3.91 (1H, s), 3.59 (3H, s), 2.67–2.61 (2H, m), 2.24–2.18 (2H, m), 1.98 (3H, s), 1.91–1.87 (1H, m), 1.79–1.61 (5H, m), 1.36 (3H, s), 1.29 (3H, s); ^{13}C NMR (125 MHz) δ 190.5, 170.3, 146.6, 145.6, 138.7, 138.6, 91.9, 86.9, 74.7, 70.8, 59.5, 45.9, 44.7, 31.3, 26.3, 24.4, 21.9, 21.7, 21.5, 20.8; HRMS (FAB) [M + H^+] calcd for $C_{20}H_{27}O_6$: 363.1808, found: 363.1825.

(+)-(3*R*,10*R*,19*S*)-Ketone 69

To a solution of alcohol **68** (11.4 mg, 31.5 μmol) in acetone (3 mL) were added NMO (8.8 mg, 75.2 μmol, 2.4 equiv.) and a catalytic amount of TPAP. The dark mixture was stirred for 30 min and the reaction mixture was filtered over a thin pad of silica followed by exhaustive rinsing with EtOAc. The solvent was removed *in vacuo*. Column chromatography (pentane–Et_2O (4 : 1)) afforded ketone **69** (10.4 mg, 28.8 mmol, 91%) as an oil; R_f = 0.42 (petroleum ether–Et_2O (1 : 1)); $[\alpha]_D^{22}$ +423 (*c* = 1.3, $CHCl_3$); IR 2935, 1769, 1746, 1643, 1233; ^{1}H NMR (500 MHz) δ 5.23 (1H, s), 3.88 (1H, s), 3.62 (3H, s), 2.67–2.62 (2H, m), 2.48 (1H, d, *J* = 16.8 Hz), 2.22 (1H, d, *J* = 16.6 Hz), 2.18–2.14 (1H, m), 2.01 (3H, s), 1.92–1.88 (1H, m), 1.71–1.57 (4H, m), 1.44 (3H, s), 1.29 (3H, s); ^{13}C NMR (125 MHz) δ 207.3, 189.9, 170.1, 147.0, 144.0, 139.0, 138.5, 88.8, 86.8, 74.0, 59.6, 46.4, 44.6, 31.3, 26.4, 23.5, 21.8, 21.6, 20.9, 20.7; HRMS (FAB) [M + H^+] calcd for $C_{20}H_{25}O_6$: 361.1651, found: 361.1648.

(+)-(3*R*,10*R*,19*S*)-Ketone 2

To a solution of ketone **69** (8.0 mg, 22 μmol) in MeOH (2 mL) was added K_2CO_3 (7.5 mg, 54 μmol, 2.5 equiv.). The reaction mixture was stirred at rt for 1 h. Then the reaction mixture was poured into saturated aqueous $NaHCO_3$ and extracted with CH_2Cl_2 (3 × 5 mL). The combined organic layers were washed with brine and subsequently dried over Na_2SO_4 and the solvent was removed *in vacuo*. Column chromatography (pentane–Et_2O (2 : 3)) afforded alcohol **2** (5.8 mg, 18 μmol, 82%) as a white solid which was recrystallised from pentane–Et_2O to give colourless crystals; R_f = 0.24 (petroleum ether–Et_2O (1 : 3)); mp 172.5–173.5 °C; $[\alpha]_D^{24}$ + 495 (*c* = 0.6, $CHCl_3$); IR 3474 (br), 2935, 1767, 1642; ^{1}H NMR (500 MHz) δ 4.26 (1H, s), 3.88 (1H, s), 3.63 (3H, s), 2.70–2.65 (1H, m), 2.52–2.46 (1H, m), 2.37 (1H, d, *J* = 16.8 Hz), 2.32 (1H, br s), 2.19 (1H, d, *J* = 16.8 Hz), 2.17–2.13 (1H, m), 1.98–1.91 (1H, m), 1.73–1.61 (4H, m), 1.45 (3H, s), 1.23 (3H, s); ^{13}C NMR (125 MHz) δ 207.9, 189.2, 147.3, 142.5, 140.2, 138.3, 89.2, 88.9, 74.4, 59.8, 46.5, 44.3, 32.1, 26.3, 23.6, 22.0, 21.7, 21.1; HRMS (FAB) [M + H^+] calcd for $C_{18}H_{23}O_5$: 319.1546, found: 319.1548.

Crystallographic data for **2**:¶ $C_{18}H_{22}O_5$, M_r = 318.3643, orthorhombic, $P2_12_12_1$, *a* = 7.8483(9), *b* = 8.1518(10), *c* = 24.541(5) Å, *V* = 1570.1(4) Å^3, *Z* = 4, D_x = 1.35 g cm^{-3}, λ(Cu-Kα) = 1.5418 Å, μ(Cu-Kα) = 8.0 cm^{-1}, *F*(000) = 680, 243 K, final *R* = 0.044 for 1829 observed reflections.

(2*S*,3*R*,10*R*,13*R*,19*S*)- and (2*S*,3*R*,10*R*,13*S*,19*S*)-Diol 70

To a solution of methyl enol ether **65** (see supplementary information) (21 mg, 24 μmol) in THF (1 mL) was added

¶ CCDC reference number 149470. See http://www.rsc.org/suppdata/p1/b2/b202020n/ for crystallographic files in .cif or other electronic format.

HOAc (1 drop) followed by tetrabutylammonium fluoride (160 μL of a 1 M solution in THF, 160 μmol, 6 equiv.) and the reaction mixture was stirred at rt for 16 h. Evaporation and purification by column chromatography (Et_2O → EtOAc) afforded diol **70** (9.5 mg, 23 μmol, 99%) as a 1 : 1 mixture of two diastereomers as a colourless oil; R_f = 0.11 (EtOAc); IR 3417 (br), 2928, 1740, 1633, 1238, 1030; ^{1}H NMR (400 MHz) δ 5.19 (0.5H, s), 5.16 (0.5H, s), 4.38 (1H, d, J = 5.3 Hz), 3.90 (1H, s), 3.64–3.62 (2H, m), 3.60 (1.5H, s), 3.56 (1.5H, s), 2.71–2.61 (1H, m), 2.37–2.10 (3H, m), 1.98 (1.5H, s), 1.96 (1.5H, s), 1.81–1.73 (2H, m), 1.68–1.52 (3H, m), 1.49–1.36 (4H, m), 1.35 (1.5H, s), 1.35 (1.5H, s), 1.22 (3H, s); HRMS (FAB) [M + H^+] calcd for $C_{23}H_{33}O_7$: 421.2226, found: 421.2233.

(3*R*,10*R*,13*R*,19*S*)- and (3*R*,10*R*,13*S*,19*S*)-Acid 9

To a solution of diol **70** (9.5 mg, 23 μmol) in acetone (1 mL) were added NMO (9.8 mg, 84 μmol, 3.6 equiv.) and tetrapropylammonium perruthenate (2.8 mg, 7.6 μmol, 0.3 equiv.). The reaction mixture was stirred at rt for 16 h. The reaction mixture was filtered over a thin pad of silica and rinsed with EtOAc–HOAc (1000 : 1). Evaporation of the solvent gave acid **71**. Then the crude acid was dissolved in MeOH (0.5 mL) and K_2CO_3 (400 μL of a 0.1 M solution in MeOH, 40 μmol, 1.7 equiv.) was added. The reaction mixture was stirred at rt for 3 h. Filtration over a thin pad of silica and evaporation of the solvent gave solanoeclepin A analogue **9** as a 1 : 1 mixture of two diastereomers, which were purified by reversed phase thin layer chromatography (Merck RP-18 F_{254s}) R_f = 0.53 (H_2O–MeCN (1 : 1)) to give the pure product (3.5 mg, 9.0 μmol, 40%); IR 3445 (br), 2932, 1771, 1698, 1632; ^{1}H NMR (400 MHz, CD_3OD) δ 4.24 (0.5H, s), 4.22 (0.5H, s), 3.87 (1H, s), 3.59 (1.5H, s), 3.56 (1.5H, s), 2.52–2.45 (2H, m), 2.31–2.10 (6H, m), 1.69–1.53 (5H, m), 1.43 (3H, s), 1.26 (3H, s); ^{13}C NMR (125 MHz) δ 207.1 (C-2), 189.1, 188.9 (C-7), 176.4 (C-21), 147.3, 147.0, 140.9, 139.9, 139.8, 139.7, 137.4, 137.3, 89.2, 89.1, 88.8, 88.7, 74.3, 64.8, 46.6, 46.5, 44.4, 43.9, 35.2, 34.9, 33.4, 33.2, 33.2, 32.5, 32.3, 29.3, 29.2, 28.1, 27.7, 23.6, 21.6, 21.1; HRMS (FAB) [M + H^+] calcd for $C_{21}H_{27}O_7$: 391.1757, found: 391.1725.

(2*S*,3*R*,10*R*,13*R*,19*S*,20*R*,22*R*)-, (2*S*,3*R*,10*R*,13*R*,19*S*,20*S*,-22*S*)-, (2*S*,3*R*,10*R*,13*S*,19*S*,20*R*,22*R*)- and (2*S*,3*R*,10*R*,13*S*,-19*S*,20*S*,22*S*)-Diol 72

Following the same procedure as described for the preparation of **70**, the TBDPS groups of enol ketone **67** (18 mg, 20 μmol were removed. Column chromatography (Et_2O → EtOAc) afforded diol **72** (9.1 mg, 20 μmol, 99%) as a as an equimolar mixture of four diastereomers as a colourless oil; R_f = 0.13 (EtOAc); IR 3520 (br), 2964, 2856, 1739, 1720, 1633, 1238, 1065; ^{1}H NMR (400 MHz) δ 5.19–5.16 (1H, m), 4.40–4.38 (1H, m), 3.60 (1H, s), 3.59 (1.5H, s), 3.57 (1.5H, s), 3.48–3.43 (2H, m), 2.71–2.62 (1H, m), 2.37–2.10 (4H, m), 2.04 (1.5H, s), 1.98 (1.5H, s), 1.86–1.46 (7H, m), 1.25 (3H, s), 1.22 (1.5H, s), 1.21 (1.5H, s), 0.89–0.83 (1H, m), 0.67–0.65 (1H, m), 0.41–0.39 (1H, m), 0.2–0.30 (1H, m); HRMS (EI) calcd for $C_{25}H_{34}O_7$: 446.2305, found: 446.2300.

(3*R*,10*R*,13*R*,19*S*,20*R*,22*R*)-, (3*R*,10*R*,13*R*,19*S*,20*S*,22*S*)-, (3*R*,10*R*,13*S*,19*S*,20*R*,22*R*)- and (3*R*,10*R*,13*S*,19*S*,20*S*,22*S*)-Aldehyde 73

To a solution of diol **72** (9.1 mg, 20 μmol) in acetone (1 mL) were added NMO (5 mg, 42 μmol, 2.1 equiv.) and tetrapropylammonium perruthenate (3.1 mg, 8.5 μmol, 0.4 equiv.). The reaction mixture was stirred at rt for 6 h and filtered over a thin pad of silica followed by exhaustive rinsing with EtOAc. Evaporation of the solvent afforded aldehyde **73** (6.5 mg, 15 μmol, 77%) as an equimolar mixture of four diastereomers as a white solid; IR 2932, 1769, 1744, 1704, 16.43, 1233; ^{1}H NMR (400 MHz) δ 9.09 (0.25H, d, J = 5.2 Hz), 9.07 (0.25H, d, J = 5.2 Hz), 9.03 (0.25H, d, J = 5.4 Hz), 9.02 (0.25H, d, J = 5.4 Hz), 5.26 (0.25H, s), 5.25 (0.25H, s), 5.21 (0.5H, s), 3.88 (1H, s), 3.64 (0.75H, s), 3.62 (0.75H, s), 3.61 (1.5H, s), 2.95–2.90 (0.5H, m), 2.75–2.63 (1H, m), 2.47 (1H, d, J = 16.7 Hz), 2.32–2.03 (4H, m), 2.01 (1.5H, s), 2.00 (1.5H, s), 1.99–1.81 (1.5H, m), 1.69–1.47 (4H, m), 1.45 (1.5H, s), 1.44 (1.5H, s), 1.30 (1.5H, s), 1.29 (1.5H, s), 0.95–0.79 (3H, m); ^{13}C NMR (100 MHz) δ 207.1, 207.0, 200.8, 200.7, 189.9, 189.3, 170.2, 147.1, 147.0, 144.6, 144.5, 139.4, 139.3, 138.2, 138.1, 88.8, 86.9, 86.5, 73.8, 73.6, 59.7, 59.6, 46.5, 46.4, 44.7, 44.4, 39.0, 38.9, 38.8, 38.7, 33.1, 33.0, 33.0, 32.1, 32.0, 31.5, 30.5, 30.4, 30.4, 30.3, 27.8, 27.6, 26.9, 23.5, 21.0, 20.9, 20.7, 20.6, 20.4, 20.2, 15.3, 15.1, 15.0; HRMS (FAB) [M + H^+] calcd for $C_{25}H_{31}O_7$: 443.2070, found: 443.2069.

(3*R*,10*R*,13*R*,19*S*,20*R*,22*R*)-, (3*R*,10*R*,13*R*,19*S*,20*S*,22*S*)-, (3*R*,10*R*,13*S*,19*S*,20*R*,22*R*)- and (3*R*,10*R*,13*S*,19*S*,20*S*,22*S*)-Acid 11

To a solution of aldehyde **73** (6.5 mg, 15 μmol) in *tert*-butanol (0.1 mL) and 2-methyl-2-butene (0.1 mL) was added a solution of $NaClO_2$ (8.0 mg, 88 μmol, 5.9 equiv.) and NaH_2PO_4 (8.1 mg, 68 μmol, 4.5 equiv.) in H_2O (0.1 mL). This reaction mixture was stirred at rt for 2 h and then filtered over a thin pad of silica. Evaporation of the solvent gave the crude acid (HRMS (FAB) [M + H^+] calcd for $C_{25}H_{31}O_8$: 459.2019, found: 459.2032). The crude acid was dissolved in MeOH (0.5 mL). To this solution was added K_2CO_3 (400 μL of a 0.1 M solution in MeOH, 40 μmol, 2.6 equiv.) and stirring was continued at rt for 3 h. Filtration over a thin pad of silica and evaporation gave crude acid **11**, which was further purified by reversed phase thin layer chromatography (Merck RP-18 F_{254s}) to give solanoeclepin A analogue **11** (4.3 mg, 10 μmol, 66%) as an equimolar mixture of four diastereomers as a white solid; R_f = 0.53 (H_2O–MeCN (1 : 1)). IR 3395 (br), 2932, 1766, 1693, 1632; ^{1}H NMR (500 MHz) δ 4.30 (0.25H, s), 4.29 (0.25H, s), 4.28 (0.5H, s), 3.88 (1H, s), 3.66 (0.75H, s), 3.65 (0.75H, s), 3.62 (1.5H, s), 2.98–2.96 (0.5H, m), 2.57–2.53 (1.5H, m), 2.36 (1H, d, J = 16.9 Hz), 2.36–2.14 (3H, m), 1.90–1.82 (2H, m), 1.69–1.52 (3H, m), 1.45 (3H, s), 1.39–1.63 (2H, m), 1.29 (1.5H, s), 1.26 (1.5H, s), 0.89–0.80 (2H, m); ^{13}C NMR (125 MHz) δ 207.7, 189.0, 188.8, 178.7, 147.4, 147.2, 140.8, 139.8, 139.8, 137.5, 137.1, 89.3, 89.0, 88.9, 74.2, 73.8, 65.4, 46.6, 46.5, 44.4, 44.0, 39.4, 39.2, 33.5, 33.4, 33.1, 33.0, 33.0, 32.9, 32.5, 32.0, 28.1, 27.7, 23.6, 21.6, 21.5, 21.1, 20.1, 16.3; HRMS (FAB) [M + H^+] calcd for $C_{23}H_{29}O_7$: 417.1913, found: 417.1917.

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