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Synthesis of the Tricyclic Core of Solanoeclepin A through Intramolecular [2+2] Photocycloaddition of an Allene Butenolide

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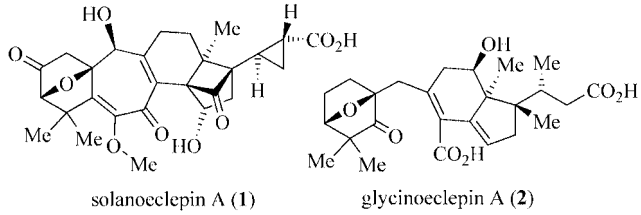
Studies are reported towards the synthesis of solanoeclepin A (**1**), the hatching agent of potato cyst nematodes. Two approaches are investigated to access the tricyclic core including the intricate bicyclo[2.1.1]hexanone moiety. The first approach is based on the intramolecular [2+2] photocycloaddition of dioxenone butenolide **10** and is shown to be less practical due to the limited synthetic utility of the photoproduct **11**. The second approach uses as the key step the intramolecular [2+2] photocycloaddition reaction of allene butenolide **39**. This latter photosubstrate is prepared through silver-mediated coupling of silyloxyfuran **9** and allenic bromide **34**. A five-step sequence starting with the Baylis–Hillman reaction between benzyl butadienolate and paraformaldehyde leads to bromide **34**. The crucial photocycloaddition of **39** proceeds with excellent regioselectivity and produces the adduct **40** in good yield. This methylenecyclobutane-containing product **40** is deemed to contain the appropriate functionalities for future studies towards the natural product as is indicated through a model study leading to cyclobutanone **25**.

Introduction

Solanoeclepin A (**1**, Figure 1) is the most active natural hatching agent of potato cyst nematodes (PCN) showing activity at nanomolar concentration.[1] Its structure was finally elucidated in 1992 by X-ray analysis after a long period of intensive studies through the joint efforts of a number of Dutch research organizations.[2] The similarities between solanoeclepin A and glycinoeclepin A (**2**), the hatching agent of soybean cyst nematodes, are quite interesting although the latter shows no stimulus for the potato cyst nematode. The total synthesis[3–5] and some studies on the structure-activity relationship of glycinoeclepin A have been published.[6,7]



solanoeclepin A (**1**) glycinoeclepin A (**2**)

Figure 1. Natural hatching agents of cyst nematodes.

The great interest in the structure of the PCN hatching agent results from the need to develop an environmentally benign way to combat the nematodes, which cause serious losses in potato production. The unavailability of the natural product in useful quantities from natural sources and the unique structure render solanoeclepin A a challenging synthetic target. Moreover, the synthetic work will provide information on structure-activity relationships, which could lead to simpler analogs of solanoeclepin A possessing sufficient hatching activity for PCN.[8]

Our synthetic approach to solanoeclepin A is based on the eventual chromium-mediated[9] coupling of aldehyde **3** with enol triflate **4** and subsequent closure of the seven-membered ring (Scheme 1). We recently published[10] the synthesis of aldehyde **3** in enantiopure form and the proof of principle for the formation of the seven-membered ring so that the next goal was the preparation of the tetracyclic substructure **4**. For the construction of this cyclobutane-containing tricyclic core of solanoeclepin A, we planned to make use of an intramolecular [2+2] photocycloadditon.[11] This full paper presents our recent progress with regard to the synthesis of **4**, which has resulted in an expedient route to **5**, containing the intricate bicyclo[2.1.1]cyclohexane moiety. The key step is an intramolecular [2+2] photocycloaddition of a butenolide with either a dioxenone as in **6** or an allene as in **7**.

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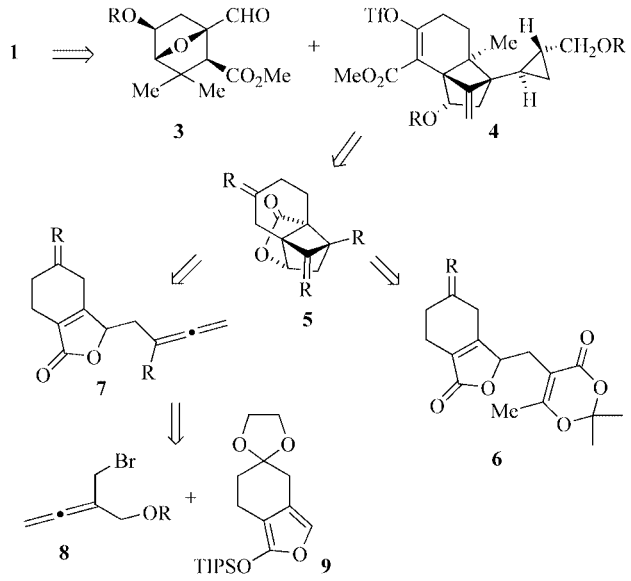
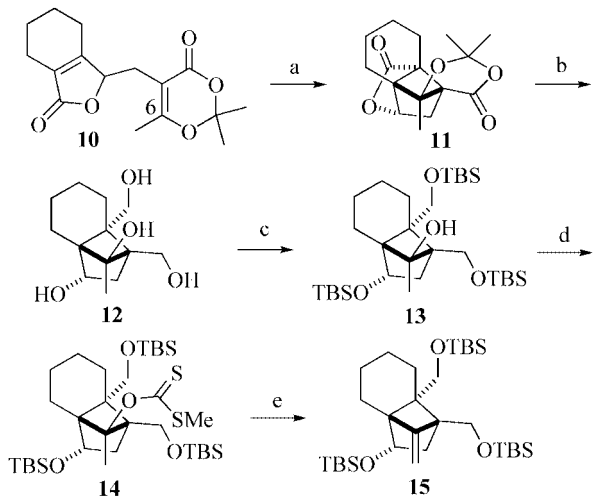


Scheme 1. Retrosynthesis of solanoeclepin A (arbitrary protective groups indicated as R).



Scheme 2. Reaction conditions: (a) *hv*, 300 nm, MeCN/acetone (9:1, v/v); (b) $LiAlH_4$ (5 equiv.), room temp., 52% (2 steps); (c) TBSOTf, 2,6-lutidine, 83%; (d) KHMDS, –78 oC, 1 h; then CS_2, –10 °C, 2 h; then MeI, room temp., 1 h, 60%; (e) xylene, reflux, 1 h, 60%.

Results and Discussion

First Approach: [2+2] Photocycloaddition of a Dioxenone

The dioxenone structure has proved to be a versatile and efficient building block in synthetic photochemistry allowing elegant cyclobutane ring formation via [2+2]cycloaddition.[12] In previous studies in our laboratory[13] it has been discovered that acetone sensitized irradiation of dioxenone **10** produced the bicyclo[2.1.1]cyclohexane skeleton **11** in a very high yield (Scheme 2). In this process the lactone connection appeared essential to obtain the desired crossed regioselectivity.[13] While the convenient access to **11** was encouraging, the well-known sensitivity of this structure to cyclobutane fragmentation limited its synthetic possibilities. The most obvious way to remove the danger of De Mayo fragmentation[12b] was exhaustive reduction. Thus, $LiAlH_4$ reduction of the cycloadduct **11** gave the tetrahydroxytricyclic system **12** in moderate overall yield (52%) from **10**.[13ab]

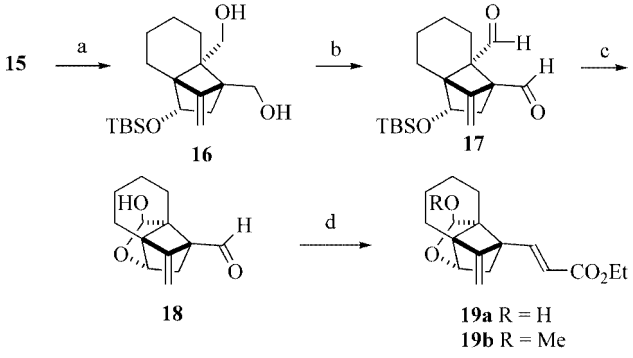
Several studies were then directed at distinguishing the different hydroxy groups by subsequent chemoselective protection, but this appeared difficult.[13a] The most selective reaction found was the simultaneous silylation of the primary and secondary hydroxyls which provided the tertiary alcohol **13** in good yield. An extensive investigation was also devoted to the utility of the dioxenone butenolide corresponding to **10** but lacking the C6 methyl group. In that series of compounds the synthesis of the photochemistry precursor was much more difficult and selectivity in hydroxy group distinction was no better.[13d]

We then decided to turn the presence of the methyl group to our advantage and considered the elimination of the tertiary hydroxy group to the corresponding exocyclic alkene via pyrolysis of the derived xanthate.[14] The conversion of this exocyclic methylene into the carbonyl in a later phase of the synthesis should be possible via ozonolysis[15] or an alternative oxidative cleavage procedure. In other words, the double bond could then function as an appropriate protective group for the four-membered ring ketone moiety.

Alcohol **13** was thus treated with potassium hexamethyldisilazide (KHMDS) at –78 °C for 1 h followed by the successive addition of carbon disulfide and methyl iodide. In this way, the desired xanthate **14** was successfully isolated in 60% yield. Xanthate **14** turned out to be reasonably stable and could be purified by column chromatography despite the fact that tertiary xanthates have been rarely characterized due to their usual instability towards elimination to give olefins or rearrangement to give *S*-alkyl dithiocarbonates.[16] The stability of **14** is obviously associated with its cyclobutane nature preventing formation of a tertiary carbocation. Interestingly, elimination can only occur in an exocyclic fashion as the two adjacent cyclobutane carbons are quaternary. Indeed, upon heating at reflux in xylene for 1 h, pyrolysis of **14** smoothly took place furnishing alkene **15** in 60% yield. The formation of the exocyclic methylene moiety of **15** is clearly apparent by the presence of two singlets at δ = 4.72 and 4.34 ppm in its ^1H NMR spectrum. Unfortunately, our attempts to transform the double bond of **15** into a cyclobutanone moiety via ozonolysis at this stage were unsuccessful (vide infra).

We then further investigated the feasibility of chemoselective reactions on the three protected hydroxy groups in order to deprotect the two rather similar primary alcohols of olefin **15**. Treatment of **15** with 10 mol-% of CSA in a mixture of CH_2Cl_2 and MeOH at 0 °C led to the formation of diol **16** in a yield of 67% (Scheme 3).[17] Upon oxidation of the two primary alcohols using the Dess–Martin periodinane reagent,[18] dialdehyde **17** was obtained and used for the next step without purification. Interestingly, treatment of **17** with TBAF effected liberation of the secondary hydroxy group which subsequently cyclized onto the

nearby aldehyde moiety to form lactol **18** in reasonable yield as a single diastereomer. The relative stereochemistry at the lactol stereocenter is unknown. Lactol **18** was then treated with an excess (ca. 6 equiv.) of the potassium salt of triethyl phosphonoacetate to give the desired unsaturated ester **19a** in 83% yield. Protection of the lactol led to cyclic methyl acetal **19b** as a 3:1 mixture of acetal stereoisomers. At this point the earlier developed chemistry to introduce the cyclopropane ring could be applied.[13c] In the meantime, however, we realized that the synthetic route was becoming lengthy and felt the urge to invent a more direct approach.



Scheme 3. Reaction conditions: (a) CSA (cat), CH_2Cl_2/MeOH, (9:1 v/v), 67%; (b) Dess–Martin periodinane, CH_2Cl_2, room temp.; (c) TBAF, THF, 60% (2 steps); (d) triethyl phosphonoacetate, KHMDS, THF, 0 °C, 83%; then $CH(OMe)_3$, CH_2Cl_2, 87%.

Second Approach: [2+2] Photocycloaddition of Allene Butenolides

As shown in Scheme 1, compound **5** contains the tricyclic core of fragment **4** with the exocyclic methylene group as a possible protective group for the ketone moiety. In the above approach the double bond was introduced through a four step sequence from dioxenone **6**. We envisioned that the structural motif of olefin **5** might be assembled in a single step by using an intramolecular [2+2] photocycloaddition of butenolide **7**. This photochemistry precursor would preserve the advantage of the lactone function, while the allene moiety was anticipated to remedy the problems associated with the dioxenone functionality. The substituted allene butenolide **7** should be conveniently accessible based on the coupling procedure developed by Jefford[19] between the substituted allenic bromide **8** and silyloxyfuran **9**.

Photocycloaddition of an Allene Butenolide Model System. When we began our study of allenes of type **7**, there was one literature example of an intramolecular [2+2] photocycloaddition of an α,β-unsaturated γ-lactone with an allene at the γ-position. Coates et al. reported in 1982 the photochemistry of the homologous system and observed only rather low regioselectivity (Figure 2),[20] namely only 16% of the crossed adduct from reaction of the internal double bond of the allene, while 40% of straight product was obtained (33% reaction of the internal and 7% reaction of the terminal allene double bond).

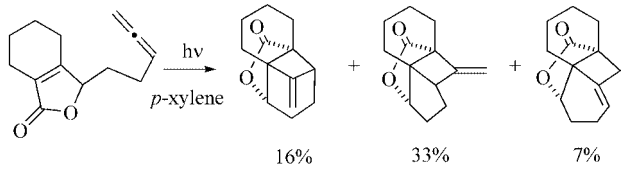
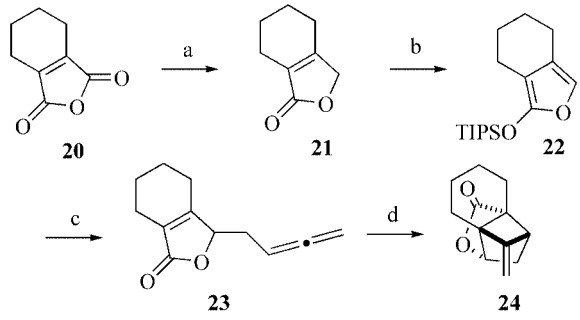


Figure 2. Allene butenolide photocycloaddition precedent by Coates (ref.[20]).

In order to examine the utility of allenes of type **7** having a two-carbon linkage between allene and butenolide double bonds, we synthesized allene **23** as a model system starting from the commercially available cyclic anhydride **20** (Scheme 4).[21] The known butenolide **21**[22] was readily converted into silyl dienolate **22** and then treated with 1-bromo-2,3-butadiene[23] in the presence of silver trifluoroacetate at low temperature to provide the desired photosubstrate **23** in 64% from **21**. We were very pleased with this coupling result as the Jefford coupling procedure[19] was not known for allyl bromides of the allenic type.



Scheme 4. Reaction conditions: (a) $NaBH_4$, THF, 60%; (b) TIPSOTf, iPr_2NEt, CH_2Cl_2; (c) $CH_2=C=CHCH_2Br$, $AgOCOCF_3$, CH_2Cl_2, –78 °C, 64% (2 steps); (d) *hv* (300 nm), MeCN/acetone (9:1 v/v), 5 h, 70%.

The key [2+2] photocycloaddition of allene **23** was carried out in a 9:1 v/v acetonitrile acetone solution in a quartz vessel (Rayonet RPR-3000 Å lamps) and was found to proceed remarkably well leading to the single product **24** as a crystalline solid (m.p. 125–127 °C) in 70% yield. The structure of **24** was proven by X-ray analysis.[21] The exclusive formation of **24** emphasizes the great preference for five-membered ring formation in intramolecular [2+2]-photocycloaddition (the so-called rule of five).[24] The selectivity difference with the allene studied by Coates (Figure 2)[20] may be explained by the fact that five-membered ring formation in the case of **23** leads to an allylic radical intermediate, whereas five-membered ring formation from Coates's substrate gives a much less stable vinyl radical, so that other cyclization modes can compete (see Figure 3).

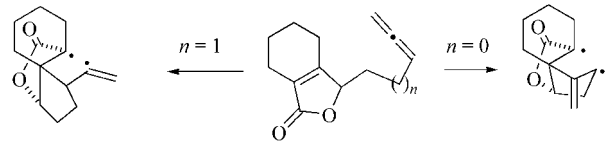
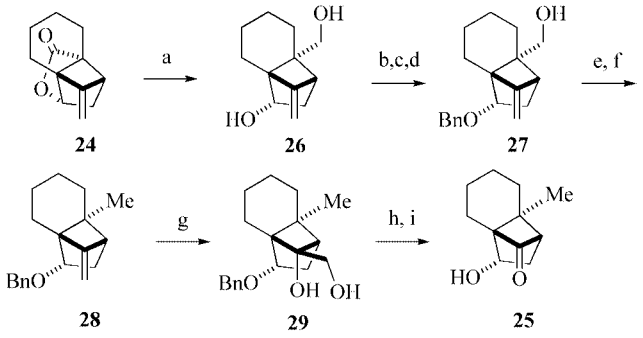


Figure 3. Diradical intermediates in the intramolecular photocycloaddition.

Further chemistry of **24** was then investigated in order to reach the model cyclobutanone **25**. To that end, the lactone function of **24** was reduced to diol **26** in good yield using $LiAlH_4$ (Scheme 5). We planned to generate the angular methyl group by reductive removal of a sulfonate. Thus, a protection–deprotection sequence then produced the primary alcohol **27** in good yield.[25] Tosylation of **27** followed by reduction with sodium triethylborohydride[26] gave **28** in good yield. Cleavage of the alkene in **28** through ozonolysis appeared not possible. Osmium-mediated dihydroxylation was only productive with stoichiometric amounts of osmium tetroxide in a pyridine/water mixture at 65 °C.[27] In this way a single diol **29** was obtained. From ^{1}H NMR NOE measurements it was clear that the dihydroxylation had taken place from the more open *endo* face of the alkene. Removal of the benzyl protective group by hydrogenolysis followed by oxidative cleavage of the diol with sodium periodate furnished the desired cyclobutanone **25** in acceptable overall yield as a crystalline solid (m.p. 103–106 °C, IR $\tilde{\nu}$ = 1798 and 1766 cm^{-1}). The structure was confirmed by X-ray analysis.[21] Interestingly, this rather strained β-hydroxy ketone appeared to be quite stable, although its stability in aqueous medium at different pH values was not studied.[28]

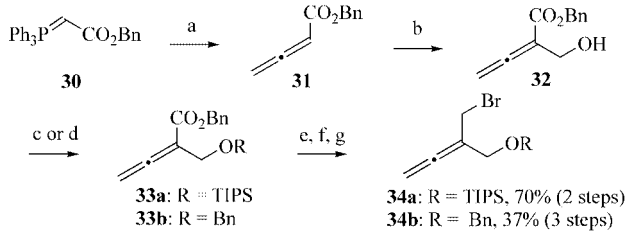


Scheme 5. Reaction conditions: (a) $LiAlH_4$, THF, 74%; (b) TBSCl, imidazole, DMF; (c) BnBr, NaH, THF, Bu_4NI (cat), 90% (2 steps) (d) CSA (cat), MeOH/CH_2Cl_2 (9:1, v/v), 84%; (e) TsCl, pyridine; (f) $LiBHEt_3$, THF, 66% (two steps); (g) OsO4 (1.5 equiv.), pyridine water, 65 °C, 60% (73% conv.); (h) H2 (1 atm), 10% Pd/C, ethanol, 65%; (i) $NaIO_4$, acetone/water, 67%.

Compound **25** contains the key structural features of the core of solanoeclepin A. However, the ultimate natural product requires one hydrogen atom of the cyclobutanone ring in **25** to be replaced by a cyclopropanecarboxylic acid function. In addition, the vinyl triflate moiety, the functionality for connecting fragments **3** and **4** of solanoeclepin A (Scheme 1) needs to be installed on the six-membered ring. The synthesis of the key intermediate **5** therefore requires the preparation of the functionalized coupling components, i.e. allenic bromide **8** and silyloxyfuran **9**.

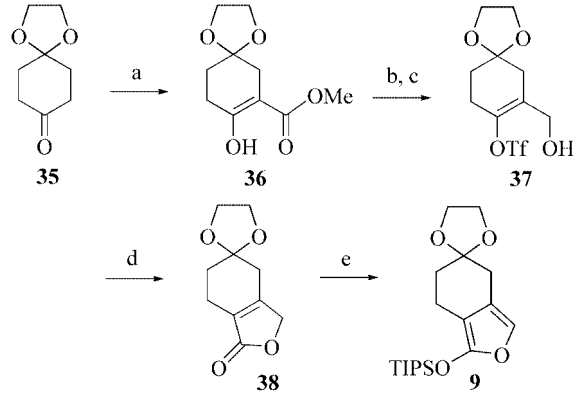
Allenic Bromide 8. The key step of the synthesis of this allene is the well-known Baylis–Hillman reaction[29] of ethyl butanedienoate (**31**), although formaldehyde had not yet been reported as an electrophile in this type of DABCO-catalyzed reaction.[30] Treatment of commercially available triphenylphosphorane **30** with acetyl chloride in the presence of Et_3N furnished α-allenic ester **31** in good yield (Scheme 7).[31] The Baylis–Hillman reaction was initially carried out by using an aqueous solution of formaldehyde, generated in situ from paraformaldehyde and aqueous phosphoric acid,[32] but this procedure was not successful. The use of an excess of dry paraformaldehyde and 20 mol-% of DABCO in THF turned out to be much better. The temperature and the reaction time were found to seriously influence the yield of the Baylis–Hillman reaction of allene **31**. The reaction was best started at –10 °C and continued at about 18 °C for 1.5 h. These optimized conditions resulted in a clean mixture of product **32** (60%) and the starting allene **31** (28%), which could easily be separated by column chromatography.

The hydroxy group of allene **32** was then protected either as a triisopropylsilyl ether or as a benzyl ether.[33] Reduction of the ester moiety using DIBAL-H[34] followed by mesylation and substitution of the resulting alcohol gave the corresponding allenic bromide **34a**,**b** in moderate yield over three steps. The modest yield of this sequence is probably due to the low efficiency of the reduction step which appeared to be greatly dependent upon the temperature, the reaction time and the amount of DIBAL-H used (Scheme 6).



Scheme 6. Reaction conditions: (a) MeCOCl, Et_3N, CH_2Cl_2, 82%; (b) DABCO (cat), $(CH_2O)_n$, THF, 60% (28% of **31**); (c) TIPSOTf, Et_3N, 79%; (d) $PhCH_2OC(NH)CCl_3$, TMSOTf (cat), 67%; (e) DIBAL-H, CH_2Cl_2, –78 °C; (f) MsCl, Et_3N; (g) LiBr, acetone.

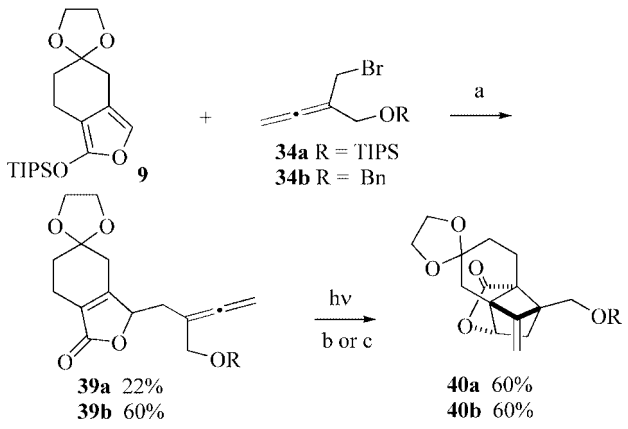
Preparation of Silyloxyfuran 9. With the required allenic bromide **34** in our hands, we turned to the preparation of its eventual coupling partner, silyloxyfuran **9**. Starting from the commercially available monoethylene acetal of 1,4-



Scheme 7. Reaction conditions: (a) $(MeO)_2CO$, NaH, KH, 90%; (b) iPr_2NEt, Tf_2O; (c) DIBAL, –78 °C to room temp.; (d) $Pd(PPh_3)_4$, CO, LiCl, Et_3N, MeCN, reflux, 85% (3 steps); (e) TIPSOTf, iPr_2NEt, 0 °C to room temp., 20 h.

cyclohexanedione (**35**), butenolide **38** was synthesized through a four-step sequence as depicted in Scheme 7. Methoxycarbonylation of **35** was achieved in 90% yield with dimethyl carbonate by using sodium hydride in conjunction with potassium hydride.[35] The enol **36** was subsequently converted into its triflate upon treatment with Hünig's base and triflic anhydride followed by reduction of the ester moiety with DIBAL-H to give the allylic alcohol **37**. Palladium-catalyzed carbonylation of the vinyl triflate furnished butenolide **38** in 85% overall yield as a crystalline solid (m.p. 100–104 °C). Exposure of **38** to TIPS-OTf and Hünig's base[36] in CH_2Cl_2 yielded the desired silyloxyfuran **9** as an oil which was used for the next step without further purification.

Substituted Allene Butenolides and Photocyclization. The coupling reaction between silyloxyfuran **9** and bromides **34a**,**b** was then carried out. Treatment of a mixture of **34a** and **9** in CH_2Cl_2 at –78 °C with silver trifluoroacetate led to the desired allene butenolide **39a** in 22% yield (Scheme 8). This low yield is could be due to the instability of the silyl ether group under the Lewis acidic conditions. This explanation was confirmed when we found that a satisfactory 60% yield of **39b** was obtained from the coupling reaction of **9** with benzyl-protected bromide **34b**.



Scheme 8. Reaction conditions: (a) $AgOCOCF_3$, CH_2Cl_2, –78 °C to room temp.; (b) for **39a**: MeCN/acetone (9:1 v/v); (c) for **39b**: benzene/acetone (9:1 v/v).

The key photocycloaddition of **39** was then investigated. Acetone-sensitized irradiation of butenolide **39a** at 300 nm for 1 h in acetonitrile/acetone, 9:1, as the solvent resulted in the desired crossed cycloadduct **40a** in good yield. In contrast, irradiation of **39b** under the same conditions led to **40b** in only low yield along with extensive decomposition of the starting material. Further investigation of the photocycloaddition reaction of **39b** revealed that it proceeded best in a 9:1 mixture of benzene and acetone as the solvent. Under such optimized conditions the photocycloadduct **40b** was isolated in 60% yield as a stable colourless oil (IR $\tilde{\nu}$ = 1770 cm^{-1}). The ^1H NMR spectrum of the cycloadduct **40b** shows two singlets at δ = 4.78 and 4.76 ppm which clearly corresponds to the exocyclic methylene moiety as observed previously with the model **24**. The ease of the cycloaddition leading to three quaternary centres in a highly compact setting is noteworthy.

This account of our progress towards the synthesis of solanoeclepin A ends here. The photocycloadducts **40a** and **40b** are believed to contain appropriate functionalities for further elaboration towards the right-hand substructure **4** of the natural product (Scheme 1). Application of the chemistry developed previously for the model **24** to the photocycloadduct **40a** or **40b** should provide the angular methyl and the cyclobutanone functions. The protected primary alcohol should serve as a handle for incorporating a cyclopropanecarboxylic acid moiety at a later phase of the synthesis. The critical installation of the vinyl triflate from the ketone could eventually accomplish the right hand substructure **4**, a projected key intermediate in the eventual synthesis of solanoeclepin A.

Conclusions

The compact tricyclic core of solanoeclepin A (**1**), containing the strained bicyclo[2.1.1]hexanone moiety, was prepared by using as the key step an intramolecular [2+2] photocycloaddition reaction of an allene butenolide. This synthetic strategy has efficiently produced the expedient intermediate **40** in eight steps (longest linear sequence) from ylide **30**. Further studies are underway along the lines described above and the results thereof will be reported in due course.

Experimental Section

General Information: All reactions involving oxygen or moisture sensitive compounds were carried out under dry nitrogen. THF and Et_2O were distilled from sodium/benzophenone and CH_2Cl_2 was distilled from CaH_2. DMF and toluene were distilled from CaH_2 and stored over 4 Å molecular sieves. Triethylamine was stored over KOH pellets. DMSO was dried and stored over 4 Å molecular sieves. Flash column chromatography was performed using Acros silica gel (0.030–0.075 mm). Petroleum ether (PE, 60/80) used for chromatography was distilled prior to use. TLC analyses were performed on Merck F-254 silica gel plates. The R_f values given pertain to the solvent system used for the chromatographic purification. IR spectra were measured using a Bruker IFS 28 FT-spectrophotometer and wavelengths ($\tilde{\nu}$) are reported in cm^{-1}. ^1H NMR spectra were recorded on a Bruker AC 200 (200 MHz), a Bruker ARX 400 (400 MHz) and Varian Inova (500 MHz). The latter machines were also used for ^{13}C NMR spectra (50, 100 and 125 MHz, respectively). Unless otherwise indicated, $CDCl_3$ was used as the solvent. Chemical shifts are given in ppm (δ) relative to an internal standard of chloroform (δ =7.26 ppm for ^1H NMR and 77.0 for ^{13}C NMR). Mass spectra and accurate mass determinations were performed on a JEOL JMS SX/SX102A, coupled to a JEOL MS-MP7000 data system. Elemental analyses were performed by Dornis u. Kolbe, Mikroanalytisches Laboratorium, Mülheim an der Ruhr, Germany.

3-(*tert*-Butyldimethylsilanoxy)-1,7a-bis(*tert*-butyldimethylsilanoxymethyl)-8-methyloctahydro-1,3a-methanoinden-8-ol (13): To a solution of tetrahydroxy compound **12**[13b] (40 mg, 0.17 mmol) in CH_2Cl_2 (1 mL) was added dropwise at 0 °C, TBDMSOTf (195 μL,

0.85 mmol) and 2,6-lutidine (200 μL, 1.7 mmol). The resulting mixture was stirred at 0 °C for 1 h. The reaction was quenched by addition of saturated aqueous $NaHCO_3$ (1 mL). The combined organic layers were washed with brine, dried with $MgSO_4$ and concentrated in vacuo. Purification by chromatography (EtOAc/PE = 1:40) afforded **13** (80 mg, 83%) as a colourless oil. R_f = 0.19. IR ($CHCl_3$): $\tilde{\nu}$ = 2958, 2929, 2856, 1467, 1254, 1214, 1059 cm^{-1}. ^1H NMR: δ = 4.50 (dd, J = 10.6, 2.4 Hz, 1 H), 4.04 (d, J = 10.7 Hz, 1 H), 3.83 (dd, J = 7.5, 2.5 Hz, 1 H), 3.80 (d, J = 10.7 Hz, 1 H), 3.25 (d, J = 10.6 Hz, 1 H), 2.88 (s, 1 H), 2.86–2.77 (m, 1 H), 2.00 (dd, J = 12.3, 7.5 Hz, 1 H), 2.00–1.87 (m, 2 H), 1.64–1.59 (m, 2 H), 1.48–1.43 (m, 2 H), 1.48–1.43 (m, 2 H), 1.37–1.18 (m, 2 H), 1.13 (s, 3 H), 0.88 (s, 27 H), 0.04 (s, 3 H), 0.04 (s, 3 H), 0.03 (s, 3 H), 0.02 (s, 3 H), 0.00 (s, 3 H), –0.01 (s, 3 H). ^{13}C NMR: δ = 85.0, 73.1, 63.6, 62.7, 57.7, 55.8, 50.6, 37.8, 27.3, 26.0, 25.9, 25.8, 22.0, 21.7, 21.1, 20.8, 18.24, 18.1, 18.0, –4.7, –5.1, –5.3, –5.5, –5.6, –5.7. HRMS (FAB) calcd. for $C_{31}H_{65}O_4Si_3$ [MH^+] 585.4191, found 585.4079.

Xanthate 14: To a solution of alcohol **13** (900 mg, 1.54 mmol) in freshly distilled THF (15 mL) at –78 °C was added dropwise KHMDS in THF (0.5 M in toluene, 6 mL, 2 equiv.). The resulting mixture was stirred at –78 °C for 1 h and then carbon disulfide was added (0.5 mL, 5 equiv.). The reaction mixture was then warmed up to –10 °C and stirred for an additional 2 h. Methyl iodide (0.5 mL, 5 equiv.) was added and the reaction mixture was warmed to room temp. and stirred for 1.5 h. The reaction was quenched by saturated aqueous NH_4Cl (15 mL). The layers were separated and the aqueous phase was extracted with diethyl ether (3 × 15 mL). The combined organic layers were washed with brine (50 mL), dried with $MgSO_4$ and concentrated in vacuo. Purification by chromatography (3% Et_3N in PE) afforded the xanthate **14** (623 mg, 60%) as a colourless oil. R_f = 0.4. IR ($CHCl_3$): $\tilde{\nu}$ = 2928, 2855, 1471, 1234, 1064 cm^{-1}. ^1H NMR: δ = 4.48 (dd, J = 2, J = 11 Hz, 1 H), 3.95 (d, J = 11 Hz, 1 H), 3.89 (dd, J = 3, J = 7 Hz, 1 H), 3.82 (d, J = 11 Hz, 1 H), 3.28 (d, J = 11 Hz, 1 H), 2.54 (s, 3 H), 2.4 (dd, J = 7, J = 13 Hz, 1 H), 2.17–2.11 (m, 1 H), 1.97–1.75 (m, 1 H), 1.76–1.72 (m, 4 H), 1.69–1.20 (m, 6 H), 0.89–0.87 (m, 27 H), 0.18–0.00 (m, 18 H). ^{13}C NMR: δ = 212.3, 99.1, 71.6, 62.4, 61.4, 59.5, 58.5, 50.2, 36.8, 25.73, 25.71, 25.5, 25.2, 21.57, 21.50, 20.2, 19.5, 17.98, 17.91, 17.8, 17.7, –4.9, –5.1, –5.3, –5.4, –5.6, –5.7. HRMS (FAB) calcd. for $C_{33}H_{67}O_4S_2Si_3$ [MH^+] 675.3789, found 675.3787.

Methylenecyclobutane 15: A solution of the xanthate **14** (224 mg, 0.33 mmol) in xylene (5 mL) was added dropwise to boiling xylene (5 mL) and the resulting mixture was refluxed for 1.5 h and concentrated in vacuo. Purification by chromatography (5% Et_3N in PE) afforded alkene **15** (60%) as a colourless oil. R_f = 0.43. IR ($CHCl_3$): $\tilde{\nu}$ = 2930, 2857, 1471, 1255, 1066 cm^{-1}. ^1H NMR: δ = 4.72 (s, 1 H), 4.35 (d, J = 12 Hz, 1 H), 4.34 (s, 1 H), 3.85 (dd, J = 2, J = 7 Hz, 1 H), 3.79–3.73 (m, 2 H), 3.38 (d, J = 11 Hz, 1 H), 2.28 (dd, J = 7, J = 11 Hz, 1 H), 1.93 (d, J = 13 Hz, 1 H), 1.63 (d, J = 2, J = 11 Hz, 1 H), 1.50–1.10 (m, 7 H), 0.89 (s, 9 H), 0.88 (s, 9 H), 0.87 (s, 9 H), 0.04 (s, 6 H), 0.01 (s, 6 H), 0.00 (s, 6 H). ^{13}C NMR: δ = 157.4, 93.3, 73.2, 61.2, 61.0, 60.6, 59.5, 47.1, 38.4, 25.7, 25.6, 25.5, 25.3, 21.8, 21.2, 20.4, 18.0, 17.9, 17.7, –4.9, –5.2, –5.5, –5.7, –5.81, –5.88. HRMS (FAB) calcd. for $C_{31}H_{63}O_3Si_3$ [MH^+] 567.4085, found 567.4097.

Diol 16: To a solution of olefin **15** (260 mg, 0.459 mmol) in CH_2Cl_2/MeOH (8 mL, 9:1, v/v) at 0 °C was added CSA (13.5 mg, 0.11 equiv.). The reaction mixture was warmed to room temp. and stirred for 4 h. The reaction was quenched by addition of saturated aqueous $NaHCO_3$ (10 mL). The layers were separated and the aqueous phase was extracted with diethyl ether (3 × 10 mL). The combined organic layers were washed with brine (40 mL), dried with $MgSO_4$ and concentrated in vacuo. Purification by chromatography (PE/EtOAc = 2:1) afforded the diol **16** (67%) as a colourless oil (R_f = 0.26). IR ($CHCl_3$): $\tilde{\nu}$ = 3300, 2932, 1118, 1042 cm^{-1}. ^1H NMR: δ = 4.39 (s, 1 H), 4.37 (d, J = 11 Hz, 1 H) 4.36 (s, 1 H), 3.94 (dd, J = 2.5, J = 7 Hz, 1 H), 3.69 (d, J = 11 Hz, 1 H), 3.57 (d, J = 11 Hz, 1 H), 3.49 (d, J = 11 Hz, 1 H), 2.14 (d, J = 11 Hz, 1 H), 2.12–1.94 (m, 2 H), 1.61–1.41 (m, 6 H), 1.25–1.20 (m, 1 H) 0.88 (s, 9 H), 0.04 (s, 3 H), 0.02 (s, 3 H). ^{13}C NMR: δ = 155.7, 93.2, 72.9, 61.8, 60.8, 58.6, 58.2, 47.0, 39.2, 25.5, 24.8, 21.5, 21.1, 20.5, 17.8, –4.98, –5.27. HRMS (FAB) calcd. for $C_{19}H_{35}O_3Si$ [MH^+] 339.2355, found 339.2344.

Lactol 18: To a stirred solution of Dess–Martin periodinane (Aldrich) (0.4 g, 3 equiv.) in CH_2Cl_2 (2 mL) at room temp. was added solution of diol **16** (100 mg, 0.295 mmol) in CH_2Cl_2 (2 mL). The reaction mixture was stirred at room temp. for 1 h and diethyl ether (5 mL) was added. The suspended mixture was poured into 1.3 M aqueous NaOH (7 mL) and the aqueous layer was extracted with diethyl ether (3 × 10 mL). The combined organic layers were washed with brine (40 mL), dried with $MgSO_4$ and concentrated in vacuo to afford crude dialdehyde **17** that was used for the next step without purification. ^1H NMR: 9.9 (s, 1 H), 9.8 (s, 1 H), 4.9 (s, 1 H), 4.6 (s, 1 H), 4 (d, J = 4 Hz, 1 H), 2.3–1.2 (m, 8 H), 0.9 (s, 9 H), 0.1 (s, 6 H).

To a solution of crude dialdehyde **17** in THF (3 mL) at 0 °C was added TBAF (1 M in THF) (0.5 mL, 2 equiv.). The resulting mixture was warmed to room temp. and stirred for 1 h. The reaction was quenched by addition of saturated aqueous $NaHCO_3$ (5 mL). The layers were separated and the aqueous phase was extracted with diethyl ether (3 × 5 mL). The combined organic layers were washed with brine (20 mL), dried with $MgSO_4$ and concentrated in vacuo. Purification by chromatography (PE/EtOAc = 1:1) afforded lactol **18** (38 mg, 60% over two steps) as a colourless oil and as a single diastereoisomer (R_f = 0.3). IR ($CHCl_3$): $\tilde{\nu}$ = 3401, 2931, 2861, 1710, 800 cm^{-1}. ^1H NMR: δ = 9.85 (s, 1 H), 5.53 (d, J = 4 Hz, 1 H), 4.97 (s, 1 H), 4.64 (s, 1 H), 4.31 (d, J = 4 Hz, 1 H), 3.49 (d, J = 4 Hz, 1 H), 2.51 (d, J = 11 Hz, 1 H), 2.08 (dd, J = 4, J = 11 Hz, 1 H), 2.06–1.05 (m, 8 H). ^{13}C NMR: δ = 200.5, 149.8, 99.4, 96.5, 81.4, 65.3, 64.2, 60.1, 37.8, 21.1, 20.8, 20.6, 19.2.

Lactol Ester 19a: To a solution of triethyl phosphonoacetate (43.4 μL, 1.2 equiv.) in THF (3 mL) was added KHMDS (0.5 M in toluene) (1.3 mL, 1.2 equiv.) at 0 °C. The reaction mixture was stirred at 0 °C for 1 h and the solution of lactol **18** (40 mg, 0.18 mmol) in THF (3 mL) was added dropwise. The resulting mixture was stirred for 30 min and warmed to room temp. Saturated aqueous NH_4Cl (10 mL) was added and the mixture was stirred for 15 min. The layers were separated and the aqueous phase was extracted with diethyl ether (3 × 10 mL). The combined organic layers were washed with brine (30 mL), dried with $MgSO_4$ and concentrated in vacuo. Purification by chromatography (PE/EtOAc = 1.5:1) afforded ester **56** (43.3 mg, 83%) (R_f = 0.32). IR ($CHCl_3$): $\tilde{\nu}$ = 3394, 2938, 1706, 1650 cm^{-1}. ^1H NMR: δ = 7.04 (d, J = 16 Hz, 1 H), 6.02 (d, J = 16 Hz, 1 H), 5.52 (s, 1 H), 4.68 (s, 1 H), 4.51 (s, 1 H), 4.27 (d, J = 4.5 Hz, 1 H), 4.18 (q, J = 7 Hz, 2 H), 3.50–3.30 (br., 1 H), 2.34 (d, J = 11 Hz, 1 H), 1.96 (dd, J = 5, J = 11 Hz, 1 H), 1.87–1.77 (m, 2 H), 1.62–1.25 (m, 5 H), 1.28 (t, J = 7 Hz, 3 H), 1.25–1.06 (m, 1 H). ^{13}C NMR: δ = 166.4, 153.3, 143.0, 122.8, 100.0, 94.3, 81.9, 64.1, 60.1, 58.7, 58.5, 39.8, 20.8, 20.6, 20.5, 19.2, 14.0.

Protected Lactol 19b: To a solution of the lactol **19a** (175 mg, 0.6 mmol) in CH_2Cl_2 (10 mL) was added at room temp. trimethyl

orthoformate (0.8 mL, 12 equiv.) and PPTS (45 mg, 0.3 equiv.). The reaction mixture was stirred at room temp. overnight. The reaction was quenched by saturated aqueous $NaHCO_3$ (10 mL). The layers were separated and the aqueous phase was extracted with diethyl ether (3 × 10 mL). The combined organic layers were washed with brine (40 mL), dried with $MgSO_4$ and concentrated in vacuo. Purification by chromatography (PE/EtOAc = 4:1) afforded the product **62** (157 mg, 87%, 3:1 mixture of two diasteroisomers) as a colourless oil (R_f = 0.43). IR ($CHCl_3$): $\tilde{\nu}$ = 2923, 1710, 1650 cm^{-1}. ^1H NMR (major): δ = 6.99 (d, J = 16 Hz, 1 H), 5.97 (d, J = 16 Hz, 1 H), 5.00 (s, 1 H), 4.68 (s, 1 H), 4.51 (s, 1 H), 4.25 (d, J = 4.6 Hz, 1 H), 4.19 (q, J = 7 Hz, 2 H), 3.41 (s, 3 H), 2.24 (d, J = 11 Hz, 1 H), 1.92–1.84 (m, 2 H), 1.75 (d, J = 11 Hz, 2 H), 1.61–1.32 (m, 4 H), 1.29 (t, J = 7 Hz, 3 H), 1.11–0.89 (m, 1 H).

4,5,6,7-Tetrahydro-3*H*-isobenzofuran-1-one (21): To a stirred suspension of $NaBH_4$ (950 mg, 25.1 mmol) in THF (70 mL) at 0 °C was added dropwise over 2 h a solution of 3,4,5,6-tetrahydrophthalic anhydride **20** (3.8 g, 25.0 mmol) in THF (100 mL). The reaction mixture was stirred at 0 °C for 1 h and at room temp. for another 1 h. The reaction mixture was cooled to 0 °C and acidified with 2 M HCl (until pH 3). The layers were separated and the aqueous phase was extracted with CH_2Cl_2 (2 × 100 mL). The combined organic layers were washed with saturated aqueous $NaHCO_3$ (300 mL) and brine (300 mL), dried with $MgSO_4$ and concentrated in vacuo. Purification by chromatography (PE/EtOAc = 2:1) afforded **21** (2.13 g, 15.4 mmol, 60%) as a colourless solid, m.p. 56–57 °C (ref.[22] m.p. 53–54 °C). IR ($CHCl_3$): $\tilde{\nu}$ = 1735, 1678 cm^{-1}. ^1H NMR: δ = 4.67 (br. s, 2 H), 2.30 (m, 2 H), 2.22 (m, 2 H), 1.75 (m, 4 H). ^{13}C NMR: δ = 174.1, 160.9, 126.0, 71.8, 23.3, 21.3, 21.2, 19.7.

Triisopropyl-(4,5,6,7-tetrahydroisobenzofuran-1-yloxy)silane (22): To a stirred solution of lactone **21** (100 mg, 0.72 mmol) in CH_2Cl_2 (2 mL) at 0 °C was added dropwise triisopropylsilyl triflate (250 μL, 285 mg, 0.93 mmol) and diisopropylethylamine (251 μL, 186 mg, 1.44 mmol). The reaction mixture was warmed to room temp. and stirred overnight. The reaction was quenched with ice-cold saturated aqueous NH_4Cl (2 mL). The layers were separated and the aqueous phase was extracted with diethyl ether (3 × 10 mL). The combined organic layers were washed with brine (30 mL), dried with MgSO4, and concentrated in vacuo to afford **22** as a colourless oil, which was used for the next step without further purification. ^1H NMR: δ = 6.55 (s, 1 H), 2.46 (m, 2 H), 2.34 (m, 2 H), 1.63 (m, 4 H), 1.21 (m, 3 H), 1.07 (m, 18 H).

3-(Buta-2,3-dienyl)-4,5,6,7-tetrahydro-3*H*-isobenzofuran-1-one (23): To a solution of the crude silyloxyfuran **22** and 1-bromobuta-2,3-diene[23] (144 mg, 1.08 mmol, 1.5 equiv.) in CH_2Cl_2 (25 mL) at –78 °C was added silver trifluoroacetate (240 mg, 1.09 mmol). The reaction mixture was stirred at –78 °C for 20 min and then at –20 °C for 3 h and at room temp. overnight. The mixture was filtered through Celite® and the filtrate was concentrated in vacuo. Purification by chromatography (PE/EtOAc = 4:1) afforded **23** (85 mg, 0.45 mmol, 62% from **21**) as a slightly yellow oil (R_f = 0.17). IR (neat): $\tilde{\nu}$ = 2941, 2947, 1957, 1747, 1681 cm^{-1}. ^1H NMR: δ = 5.00 (m, 1 H), 4.88 (m, 1 H), 4.70 (m, 2 H), 2.58 (m, 1 H), 2.31 (m, 1 H), 2.22 (m, 4 H), 1.74 (m, 4 H). ^{13}C NMR: δ = 209.3, 173.2, 162.7, 127.2, 83.2, 81.6, 75.2, 31.1, 23.1, 21.4 (2 C), 19.7. HRMS (FAB) calcd. for $C_{12}H_{15}O_2$ [MH^+] 191.1072, found 191.1076.

General Procedure A for the Intramolecular [2+2] Photocycloadditions: The photoreaction was carried out in an air-cooled quartz vessel in a Rayonet photoreactorvessel with Rayonet RPR 300 nm lamps. A solution of the substrate in the indicated solvent was degassed by bubbling argon through for 30 min. The solution was kept under argon and irradiated for the time indicated. The reaction was followed by monitoring the UV absorption of the starting material on TLC. When complete conversion was observed, the solvent was removed in vacuo.

Photocycloaddition Product 24: According to the general procedure A, solution of allene **23** (85 mg, 0.45 mmol) in acetonitrile/acetone (0.05 M, 9:1 v/v) was irradiated (300 nm) for 5 h to give **24** (60 mg, 0.32 mmol, 70%) as colourless crystals after column chromatography (PE/EtOAc = 4:1), R_f = 0.40, m.p. 125–127 °C. IR ($CHCl_3$): $\tilde{\nu}$ = 2941, 1763, 1215 cm^{-1}. ^1H NMR: δ = 4.76 (s, 1 H), 4.61 (d, J = 3.9 Hz, 1 H), 4.56 (s, 1 H), 2.94 (s, 1 H), 2.17 (br. d, J = 13.8 Hz, 1 H), 2.10 (dd, J = 12.0, 4.1 Hz, 1 H), 1.87 (br. d, J = 15 Hz, 1 H), 1.73 (dd, J = 12.0, 2.3 Hz, 1 H), 1.62–1.45 (m, 4 H), 1.35 (m, 1 H), 0.96 (m, 1 H). ^{13}C NMR: δ = 175.6, 150.8, 96.0, 79.6, 66.0, 53.9, 48.4, 36.6, 21.7, 21.1, 20.1, 19.3. Elemental analysis: calcd. for $C_{12}H_{14}O_2$, C 75.76, H 7.42; found C 75.65, H 7.40. The crystal structure of this compound was published elsewhere.[21]

7a-Hydroxymethyl-8-methyleneoctahydro-1,3a-methanoinden-3-ol (26): To a 1 M solution of $LiAlH_4$ in THF (6.5 mL, 5 equiv.) at room temp. was added a solution of lactone **24** (250 mg, 1.315 mmol) in THF (5 mL). The resulting mixture was stirred at room temp. for 30 min and carefully quenched with EtOAc. Saturated aqueous Na_2SO_4 (10 drops) was then added and the mixture was stirred for 1 h. After addition of more solid Na_2SO_4 the mixture was filtered through Celite® and concentrated in vacuo. Purification by chromatography (EtOAc) afforded diol **26** as a colourless solid (189 mg, 74%). R_f = 0.30, m.p. 110–114 °C. IR (neat): $\tilde{\nu}$ = 3397, 2934, 1690 cm^{-1}. ^1H NMR (methanol): δ = 4.53 (s, 1 H), 4.35 (s, 1 H), 4.23 (dd, J = 11.9, 1.8 Hz, 1 H), 3.88 (dd, J = 7.6, 2.6 Hz, 1 H), 3.46 (d, J = 11.9 Hz, 1 H), 2.65 (s, 1 H), 2.10 (ddd, J = 11.8, 7.8, 1.7 Hz, 1 H), 2.03 (br. d, J = 13.4 Hz, 1 H), 1.89–1.85 (m, 1 H), 1.67–1.50 (m, 6 H), 1.30–1.26 (m, 1 H). ^{13}C NMR (methanol): δ = 158.0, 94.5, 73.3, 63.5, 60.3, 51.3, 47.1, 36.6, 28.8, 23.0, 22.8, 21.6.

7a-(*tert*-Butyldimethylsilanyloxymethyl)-8-methyleneoctahydro-1,3a-methanoinden-3-ol: To a stirred solution of diol **26** (158 mg, 0.81 mmol) in DMF (5 mL) at room temp. was added *tert*-butyldimethylsilyl chloride (182 mg, 1.5 equiv.) and imidazole (386 mg, 7 equiv.). The reaction mixture was stirred for 5 h and diluted with EtOAc (10 mL). The organic phase was washed with 2% aqueous solution of citric acid (10 mL), water (10 mL), and brine (10 mL), dried with $MgSO_4$ and concentrated in vacuo to provide 273 mg (0.88 mmol) crude silyl-protected alcohol as a colourless oil. The crude silyl ether was used for the next step without further purification. IR (neat): $\tilde{\nu}$ = 3400, 2930, 1684 (w), 1254, 1080 cm^{-1}. ^1H NMR: δ = 4.51 (s, 1 H), 4.34 (s, 1 H), 3.94–3.80 (m, 2 H), 3.74 (d, J = 10.9 Hz, 1 H), 3.12 (d, J = 6.8 Hz, 1 H), 2.61 (s, 1 H), 2.14 (ddd, J = 12.0, 7.6, 1.6 Hz, 1 H), 1.86–1.72 (m, 3 H), 1.67–1.48 (m, 5 H), 1.35–1.27 (m, 1 H), 0.90 (s, 9 H), 0.07 (s, 3 H), 0.06 (s, 3 H). ^{13}C NMR: δ = 156.2, 93.7, 72.6, 63.8, 62.4, 50.4, 45.1, 36.5, 30.8, 25.7, 21.9, 21.5, 20.7, 18.0, –5.6, –5.8.

(3-Benzyloxy-8-methylenehexahydro1,3a-methanoinden-7a-ylmethoxy)-*tert*-butyldimethylsilane: To a solution of the above crude alcohol (273 mg, 0.88 mmol) in THF (5 mL) at room temp. was added benzyl bromide (0.2 mL, 288 mg, 1.68 mmol), and sodium hydride (60 wt.% dispersion in mineral oil, 80 mg, 2 equiv.). The resulting mixture was stirred at room temp. for 30 min. Tetra-*n*-butylammonium iodide (cat) was added and stirring was continued overnight. The reaction was quenched with ice water. The layers were separated and the aqueous phase extracted with diethyl ether (3 × 10 mL). The combined organic layers were washed with brine (30 mL), dried with $MgSO_4$ and concentrated in vacuo to afford

the fully protected compound as a colourless oil after chromatographic purification (290 mg, 0.73 mmol, 90% from **26**). IR (neat): $\tilde{\nu}$ = 2929, 1684 cm^{-1} (w), 1077 cm^{-1}. ^1H NMR: δ = 7.35–7.24 (m, 5 H), 4.56 (d, J = 12.2 Hz, 1 H), 4.52 (s, 1 H), 4.46 (d, J = 12.2 Hz, 1 H), 4.34 (s, 1 H), 4.23 (dd, J = 10.8, 1.7 Hz, 1 H), 3.69 (dd, J = 7.3, 2.7 Hz, 1 H), 3.47 (d, J = 10.8 Hz, 1 H), 2.68 (s, 1 H), 2.09–2.00 (m, 2 H), 1.87 (dd, J = 11.5, 1.9 Hz, 1 H), 1.64–1.46 (m, 6 H), 1.25–1.20 (m, 1 H), 0.88 (s, 9 H), 0.02 (s, 6 H). ^{13}C NMR (200 MHz): δ = 156.2, 139.0, 128.2 (2 C), 127.23, 127.18 (2 C), 94.0, 79.8, 72.1, 61.4, 59.7, 49.9, 46.2, 33.7, 26.9, 26.0, 21.9, 21.7, 21.1, 18.3, –5.31, –5.33.

(3-Benzyloxy-8-methylenehexahydro-1,3a-methanoinden-7a-yl)methanol (27): To a stirred solution of the above silyl ether (312 mg, 0.78 mmol) in CH_2Cl_2/MeOH (9:1 v/v, 5 mL) at room temp. was added camphorsulphonic acid (60 mg, 0.3 equiv.). The reaction mixture was stirred at room temp. for 3 h and quenched with saturated aqueous $NaHCO_3$ (5 mL). The layers were separated and the aqueous phase extracted with EtOAc (3 × 5 mL). The combined organic layers were washed with brine (20 mL), dried with $MgSO_4$, and concentrated in vacuo to give alcohol **27** as a slightly yellow oil (185 mg, 0.65 mmol, 84%) after chromatography (hexane/EtOAc = 3:1). R_f = 0.26. IR (neat): $\tilde{\nu}$ = 3370, 2930, 1687, 1452 cm^{-1}. ^1H NMR: δ = 7.34–7.26 (m, 5 H), 4.63 (d, J = 11.9 Hz, 1 H), 4.55 (s, 1 H), 4.48 (d, J = 11.9 Hz, 1 H), 4.37 (s, 1 H), 3.93 (d, J = 11.9 Hz, 1 H), 3.81–3.76 (m, 2 H), 2.66 (s, 1 H), 2.11 (br. s, 1 H), 2.05 (ddd, J = 11.9, 7.1, 1.6 Hz, 1 H), 1.97 (br. d, J = 11 Hz, 1 H), 1.90–1.48 (m, 8 H). ^{13}C NMR: δ = 155.3, 138.1, 128.2 (2 C), 127.4, 127.2 (2 C), 94.2, 79.5, 71.2, 63.7, 61.8, 49.8, 45.6, 33.6, 30.8, 21.8, 21.5, 21.2.

(3-Benzyloxy-8-methylenehexahydro-1,3a-methanoinden-7a-yl)methyl *p*-Toluenesulfonate: To a stirred solution of alcohol **27** (227 mg, 0.80 mmol) in pyridine (4 mL) at room temp. was added *p*-toluenesulfonyl chloride (306 mg, 1.60 mmol). The reaction mixture was stirred overnight and quenched with ice-cold 3% aqueous citric acid (10 mL). The layers were separated and the aqueous phase extracted with EtOAc (3 × 10 mL). The combined organic layers were washed with water (30 mL), brine (30 mL), dried with $MgSO_4$, and concentrated in vacuo to afford the crude tosylate as a colourless oil (341 mg, 0.78 mmol), that was used for the next step without further purification. IR ($CHCl_3$): $\tilde{\nu}$ = 2939, 1696, 1598, 1452, 1356, 1175 cm^{-1}. ^1H NMR: δ = 7.73 (d, J = 8.3 Hz, 2 H), 7.37–7.21 (m, 7 H), 4.77 (dd, J = 10.5, 1.9 Hz, 1 H), 4.58 (s, 1 H), 4.42 (d, J = 12.0 Hz, 1 H), 4.38 (s, 1 H), 4.32 (d, J = 12.0 Hz, 1 H), 3.92 (d, J = 10.5 Hz, 1 H), 3.64 (dd, J = 7.3, 2.5 Hz, 1 H), 2.71 (s, 1 H), 2.41 (s, 3 H), 1.98–1.90 (m, 2 H), 1.67–1.41 (m, 7 H), 1.06–1.00 (m, 1 H). ^{13}C NMR: δ = 154.4, 144.2, 138.3, 132.8, 129.5 (2 C), 128.1 (2 C), 127.8 (2 C), 127.2, 126.9 (2 C), 95.3, 78.8, 70.7, 68.7, 62.2, 49.7, 44.0, 33.0, 26.8, 21.4, 21.3, 21.0, 20.6. HRMS (FAB) calcd. for $C_{26}H_{31}O_4S$ [MH^+] 439.1943, found 439.1945.

3-Benzyloxy-7a-methyl-8-methyleneoctahydro-1,3a-methanoindene (28): Lithium triethyl borohydride (1 M in THF, 3 mL, 4 equiv.) was added to a solution of the above tosylate in THF (10 mL) at 0 °C. The reaction mixture was brought to reflux for 1 h and then cooled to 0 °C. The reaction was quenched with ice/water and the layers were separated. The aqueous layer was extracted with diethyl ether (3 × 10 mL). The combined organic layers were washed with 3 N aqueous NaOH (10 mL) and 30% aqueous H_2O_2 (10 mL), water (30 mL), brine (30 mL), dried with $MgSO_4$, and concentrated in vacuo to provide **28** (142 mg, 0.53 mmol, 66% from **27**) as a colourless oil after chromatography (hexane/EtOAc = 20:1). R_f = 0.50. IR (neat): $\tilde{\nu}$ = 2931, 2857, 2860, 1686, 1455, 1355, 867 cm^{-1}. ^1H NMR: δ = 7.36–7.24 (m, 5 H), 4.58 (d, J = 12.3 Hz, 1 H), 4.49 (s, 1 H), 4.47 (d, J = 12.3 Hz, 1 H), 4.33 (s, 1 H), 3.69 (dd, J = 7.3, 2.8 Hz, 1 H), 2.51 (s, 1 H), 2.02 (ddd, J = 11.4, 7.3, 1.6 Hz, 1 H), 1.91–1.81 (m, 2 H), 1.66–1.42 (m, 6 H), 1.28–1.20 (m, 1 H), 1.16 (s, 3 H). ^{13}C NMR: δ = 157.0, 139.1, 128.0 (2 C), 127.0, 126.9 (2 C), 93.7, 79.8, 71.0, 61.0, 51.8, 41.2, 34.1, 33.8, 22.2, 21.8, 20.6, 16.4. HRMS (FAB) calcd. for $C_{19}H_{25}O$ [MH^+] 269.1905, found 269.1908.

3-Benzyloxy-8-hydroxymethyl-7a-methyloctahydro-1,3a-methanoinden-8-ol (29): To a stirred solution of **28** (113 mg, 0.42 mmol) in pyridine/water (1:1, v/v, 5 mL) at room temp. was added OsO_4 (161 mg, 0.63 mmol, 1.5 equiv.). The reaction mixture was heated to 65 °C, stirred for 6 h at this temperature and then cooled to room temp. Saturated aqueous $NaHSO_3$ (10 mL) and solid Na_2SO_3 (50 mg) were added and the resulting mixture was stirred for 30 min. The layers were separated and the aqueous phase was extracted with EtOAc (3 × 10 mL). The combined organic layers were washed with saturated aqueous $NaHSO_3$ (30 mL), water (30 mL), brine (30 mL), dried with $MgSO_4$, and concentrated in vacuo to afford the crude product. Chromatographic purification (hexanes/EtOAc = 1:1) gave residual starting material (26.0 mg, 0.097 mmol) and diol **29** (55.6 mg, 0.18 mmol, 60% yield, based on 73% conversion) as a colourless oil. R_f = 0.37. IR (neat): $\tilde{\nu}$ = 3400, 2926, 1453, 1274, 1073 cm^{-1}. ^1H NMR: δ = 7.36–7.23 (m, 5 H), 4.62 (d, J = 12.3 Hz, 1 H), 4.50 (d, J = 12.3 Hz, 1 H), 4.38 (br. d, J = 11 Hz, 1 H), 4.25 (br. d, J = 11 Hz, 1 H), 4.15 (dd, J = 7.1, 2.2 Hz, 1 H), 3.15 (s, 1 H), 2.29 (s, 1 H), 2.24–2.11 (m, 1 H), 2.08–2.07 (m, 1 H), 1.92–1.91 (m, 2 H), 1.67–1.60 (m, 4 H), 1.46–1.32 (m, 3 H), 1.20 (s, 3 H). ^{13}C NMR: δ = 139.3, 128.0 (2 C), 126.9 (3 C), 81.0, 80.8, 71.5, 67.8, 58.3, 48.3, 38.7, 33.0, 32.4, 22.0, 21.7, 21.2, 20.4.

8-Hydroxymethyl-7a-methyloctahydro-1,3a-methanoindene-3,8-diol: A mixture of benzyl ether **29** (48 mg, 0.159 mmol) and pre-equilibrated 10% Pd/C (40 mg) in ethanol (2 mL) was treated with hydrogen at room temp. and atmospheric pressure for 30 min. The mixture was filtered and the filtrate was evaporated to yield the desired triol (22 mg, 0.104 mmol, 65%) as a colourless oil after chromatographic purification (EtOAc). R_f = 0.30. IR (neat): $\tilde{\nu}$ = 3400, 2932, 1058 cm^{-1}. ^1H NMR (CD_3OD): δ = 4.36–4.32 (m, 1 H), 4.33 (d, J = 11.5 Hz, 1 H), 4.1 (d, J = 11.5 Hz, 1 H), 2.3–2.27 (m, 2 H), 2.24 (s, 1 H), 1.7 (dd, J = 1, J = 11 Hz, 1 H), 1.66–1.4 (m, 7 H), 1.16 (s, 3 H). ^{13}C NMR: δ = 81.0, 73.9, 67.8, 58.0, 48.4, 38.6, 34.6, 33.2, 22.0, 21.35, 21.31, 19.9.

3-Hydroxy-7a-methyloctahydro-1,3a-methanoinden-8-one (25): To a stirred solution of the above triol (22 mg, 0.104 mmol) in acetone/water (1:1, v/v, 2 mL) at 0 °C was added $NaIO_4$ (45 mg, 2 equiv.). The resulting mixture was warmed up to room temp. and stirred for 30 min. Most of the acetone was evaporated in vacuo. The residue was dissolved in EtOAc (5 mL) and the organic phase washed with brine (5 mL) and concentrated in vacuo to provide cyclobutanone **25** as a colourless solid after chromatography purification (hexanes/EtOAc = 4:1). R_f = 0.10. Recrystallization (diisopropyl ether) gave colourless crystals (12 mg, 0.067 mmol, 64%), m.p. 103–106 °C. IR (neat): $\tilde{\nu}$ = 3430, 2938, 1798, 1766 cm^{-1}. ^1H NMR: δ = 4.08 (dd, J = 7.8, 2.8 Hz, 1 H), 2.63 (s, 1 H), 2.28 (ddd, J = 12.7, 7.8, 1.5 Hz, 1 H), 2.00 (ddd, J = 12.7, 3.0, 1.6 Hz, 1 H), 1.87 (br. s, 1 H), 1.8–1.2 (m, 8 H), 1.31 (s, 3 H). ^{13}C NMR: δ = 202.8, 70.0, 67.9, 61.0, 36.1, 35.3, 32.4, 22.2, 21.3, 18.8, 14.2. The crystal structure of this compound was published elsewhere.[21]

Benzyl Buta-2,3-dienoate (31):[31] Benzyl (triphenylphosphoranylidene)acetate (50.42 g, 123 mmol) was dissolved in CH_2Cl_2 (400 mL) in a three-necked, round-bottomed flask under nitrogen. The solution was stirred at room temp. as solution of Et_3N (12.42 g, 1 equiv.) in CH_2Cl_2 (100 mL) was added dropwise

(10 min). After 10 min, CH_3COCl (9.66 g, 1 equiv.) in CH_2Cl_2 (100 mL) was added dropwise over a period of 20 min. Stirring was continued for an additional 30 min, after which the clear, yellow mixture was evaporated on a rotary evaporator at reduced pressure. A portion of PE (800 mL) was added to the residue and the slurry was allowed to stand for 2 h while it was shaken periodically to facilitate solidification. The precipitate was removed by filtration and the filter was washed with PE (2 × 50 mL). The filtrates were combined and the solvent was evaporated. Purification by chromatography (PE/EtOAc = 4:1) afforded the desired product (17.46 g, 82%) as a colourless oil. R_f = 0.43. IR ($CHCl_3$): $\tilde{\nu}$ = 1969, 1716, 1259, 1155, 855 cm^{-1}. ^1H NMR: δ = 7.37–7.31 (m, 5 H), 5.68 (t, J = 6.5 Hz, 1 H), 5.23 (d, J = 6.5 Hz, 2 H), 5.19 (s, 2 H). ^{13}C NMR: δ = 215.8, 165.2, 135.7, 128.3, 128.0, 127.9, 87.6, 79.2, 66.3.

Benzyl 2-(Hydroxymethyl)buta-2,3-dienoate (32): To a suspension of paraformaldehyde (95%, 535 mg, 5 equiv.) (pre-dried under vacuum at 50 °C for 30 min) in THF (10 mL) at –10 °C was added dropwise a solution of DABCO (pre-dried under vacuum for 30 min, 76 mg, 0.2 equiv.) in THF (5 mL) followed by a solution of allenic ester **31** (590 mg, 3.39 mmol) in THF (5 mL). The reaction mixture was warmed to 18 °C and stirred for 1.5 h. The reaction was quenched by saturated aqueous NH_4Cl (10 mL). The layers were separated and the aqueous phase was extracted with ethyl acetate (3 × 10 mL). The combined organic layers were washed with brine (30 mL), dried with $MgSO_4$ and concentrated in vacuo. Purification by chromatography (PE/EtOAc = 1.5:1) afforded the desired product **32** (416 mg, 60%) as slightly brown oil along with the starting allene **31** (28%). R_f = 0.25. IR ($CHCl_3$): $\tilde{\nu}$ = 3407, 1966, 1708, 1262, 1027, 854 cm^{-1}. ^1H NMR: δ = 7.35–7.25 (m, 5 H), 5.26 (s, 2 H), 5.22 (s, 2 H), 4.34 (s, 2 H), 2.50 (s, br. s, 1 H). ^{13}C NMR: δ = 213.0, 166.4, 135.5, 128.3, 128.0, 127.7, 99.5, 79.8, 66.5, 60.7.

Benzyl 2-(Triisopropylsilanyloxymethyl)buta-2,3-dienoate (33a): To a solution of allenyl methyl alcohol **32** (350 mg, 1.71 mmol) in CH_2Cl_2 (20 mL) at 0 °C was added TIPSOTf (0.7 mL, 1.5 equiv.) followed by Et_3N (260 mg, 1.5 equiv.). The reaction mixture was stirred 0 °C for 1 h. The reaction was quenched by saturated aqueous $NaHCO_3$ (20 mL). The layers were separated and the aqueous phase was extracted with diethyl ether (3 × 20 mL). The combined organic layers were washed with brine (60 mL), dried with $MgSO_4$ and concentrated in vacuo. Purification by chromatography (PE/EtOAc = 15:1) afforded the desired product (484 mg, 79%) as a colourless oil (R_f = 0.3). IR (neat): $\tilde{\nu}$ = 2943, 2865, 1969, 1712, 1258, 1064 cm^{-1}. ^1H NMR: δ = 7.35–7.29 (m, 5 H), 5.26 (t, J = 3 Hz, 2 H), 5.20 (s, 2 H), 4.47 (t, J = 3 Hz, 2 H), 1.25–1.01 (m, 21 H). ^{13}C NMR: δ = 213.5, 165.6, 135.8, 128.2, 127.8, 127.6, 101.4, 80.6, 66.2, 59.7, 17.7, 11.7.

2-[(Triisopropylsilyloxy)methyl]buta-2,3-dien-1-ol: To a stirred solution of allenic ester **33a** (214 mg, 0.59 mmol) in dried toluene (8 mL) at –78 °C was added DIBAL-H (1.5 M in toluene) (1.2 mL, 3 equiv.). The reaction mixture was stirred at –78 °C for 1 h and carefully quenched with EtOAc at 0 °C. Saturated aqueous solution of Na_2SO_4 (0.5 mL) was added and the resulting mixture was stirred for 1 h. After adding solid Na_2SO_4, the mixture was filtered through Celite® and the filtrate was concentrated in vacuo. Purification by chromatography (PE/EtOAc = 5:1) afforded the title compound (91.5 mg, 61%) as a colourless oil (R_f = 0.26). IR ($CHCl_3$): $\tilde{\nu}$ = 3396, 2943, 2866, 1961 cm^{-1}. ^1H NMR: δ = 4.86–4.84 (m, 2 H), 4.40–4.39 (m, 2 H), 4.27–4.24 (m, 2 H), 2.32 (t, J = 6 Hz, 1 H), 1.31–1.01 (m, 21 H). ^{13}C NMR (benzene): δ = 206.1, 104.53, 77.37, 64.2, 62.78, 18.0, 12.8.

[2-(Bromomethyl)buta-2,3-dienyloxy]triisopropylsilane (34a): To a solution of MsCl (1.54 mL, 1.5 equiv.) in CH_2Cl_2 (30 mL) at 0 °C was added a solution of 2-[(triisopropylsilyloxy)methyl]buta-2,3-dien-1-ol (3.345 g, 13.06 mmol) in CH_2Cl_2 (8 mL) followed by Et_3N (2.73 mL, 1.5 equiv.). The reaction mixture was warmed to room temp. and stirred for 30 min. CH_2Cl_2 (10 mL) was added and the organic phase was washed with water (30 mL), brine (30 mL), dried with $MgSO_4$ and concentrated in vacuo to afford the crude mesylate which was used for the next step without purification. ^1H NMR: δ = 4.95 (t, J = 2 Hz, 2 H), 4.83 (t, J = 1.8 Hz, 2 H), 4.33 (t, J = 2 Hz, 2 H), 3.02 (s, 3 H), 1.14–1.03 (m, 21 H).

To a stirred solution of LiBr (4.46 g, 4 equiv.) in acetone (20 mL) at 0 °C was added a solution of the above crude mesylate in acetone (20 mL). The reaction mixture was stirred at room temp. for 30 min then water was added. The aqueous layer was extracted with CH_2Cl_2 (3 × 20 mL) and the combined organic layers were washed with brine (60 mL), dried with $MgSO_4$ and concentrated in vacuo to give allenyl methyl bromide **34a** (2.91 g, 70% two steps) as a colourless oil after purification (PE/EtOAc = 2:1). R_f = 0.6. IR (neat): $\tilde{\nu}$ = 2943, 2866, 1955 cm^{-1}. ^1H NMR (benzene): δ = 4.51–4.49 (m, 2 H), 4.35 (t, J = 2.4 Hz, 2 H), 3.97–3.96 (m, 2 H), 1.10–1.01 (m, 21 H). ^{13}C NMR (benzene): δ = 207.3, 102.8, 77.7, 62.6, 31.8, 18.8, 12.9.

Butenolide 38: To a stirred solution of β-keto ester **36**[35] (8.56 g, 40 mmol) in CH_2Cl_2 (100 mL) at –78 °C was added dropwise DIPEA (35 mL, 5 equiv.) and triflic anhydride (8.1 mL, 1.2 equiv.). The reaction mixture was warmed to room temp. for 4 h, and then stirred for 18 h. The reaction mixture was washed with ice water (100 mL), 10% aqueous solution of citric acid (2 × 100 mL), dried with $MgSO_4$ and concentrated in vacuo. The residue was dissolved in EtOAc and filtered through silica and solvent was evaporated to afford the crude vinyl triflate (14.45 g) as a yellow oil which was used for the next step without purification. ^1H NMR: δ = 4.05–3.96 (m, 4 H), 3.80 (s, 3 H), 2.67–2.62 (m, 4 H), 1.90 (t, J = 6.4 Hz, 2 H).

To a stirred solution of the crude triflate (3.46 g) in THF (75 mL) at –78 °C was added DIBAL-H (1.5 M in toluene, 15.3 mL, 2.3 equiv.) over 40 min. The resulting mixture was stirred at –78 °C for 2 h and warmed to room temp. Saturated aqueous Na_2SO_4 was then added at 0 °C. After stirring for 1 h at room temp., solid Na_2SO_4 was added. The mixture was stirred for 2 days at room temp. and filtered through Celite® and concentrated in vacuo to afford the crude alcohol **37** (3.06 g, 96%) which was used for the next step without further purification. ^1H NMR: δ = 4.19 (s, 2 H), 4.02–3.97 (m, 4 H), 2.60–2.50 (m, 4 H), 1.90 (t, J = 6.4 Hz, 2 H).

CO was bubbled through a solution of the crude **37** (3.06 g), $Pd(PPh_3)_4$ (25.55 mg, 5 mol-%) and LiCl (20 mg, 5 mol-%) in MeCN (30 mL) for 20 min. To this solution was added Et_3N (2.7 mL) and the resulting mixture was refluxed for 7 h under an atmosphere of CO (1 bar, balloon). After cooling to room temp., the reaction mixture was filtered through Celite® and concentrated in vacuo. The residue was purified by flash chromatography (PE/EtOAc = 1:1) affording the desired butenolide **38** (1.59 g, 86%) from **36** as white crystals (R_f = 0.17). M.p. 100–104 °C. IR ($CHCl_3$): $\tilde{\nu}$ = 2935, 1755, 1682 cm^{-1}. ^1H NMR: δ = 4.67 (t, J = 2.6 Hz, 2 H), 4.02 (s, 4 H), 2.56 (s, 2 H), 2.48–2.42 (m, 2 H), 1.87 (t, J = 6.4 Hz, 2 H). ^{13}C NMR: δ = 173.0, 158.5, 126.0, 107.6 (2 C), 71.1, 64.7, 34.5, 30.7, 18.9. HRMS (EI) calcd. for $C_{10}H_{12}O_4$ 196.0736, found 196.0733.

Silyloxyfuran 9: To a stirred solution of lactone **38** (70 mg, 0.35 mmol) in CH_2Cl_2 (5 mL) at 0 °C was added dropwise triisopropylsilyl triflate (0.15 mL, 1.3 equiv.) and diisopropylethylamine (0.1 mL, 2 equiv.). The reaction mixture was warmed to room temp. and stirred overnight. The reaction was quenched with ice-

cold saturated aqueous NH_4Cl (5 mL). The layers were separated and the aqueous phase was extracted with diethyl ether (3 × 10 mL). The combined organic layers were washed with brine (30 mL), dried with $MgSO_4$, and concentrated in vacuo to afford **9** as a colourless oil, which was used for the next step without further purification. ^1H NMR: δ = 6.58 (s, 1 H), 4.02–3.99 (m, 4 H), 2.69 (s, 2 H), 2.54 (t, J = 6.6 Hz, 2 H), 1.83 (t, J = 6.6 Hz, 2 H), 1.31–1.17 (m, 3 H), 1.08 (s, 6 H), 1.06 (s, 6 H), 1.04 (s, 6 H).

General Procedure B for the Jefford Coupling Reaction: A mixture of silver trifluoroacetate (1.2 equiv.), molecular sieves (4 Å) and the allenic bromide **34** (1.2 equiv.) in CH_2Cl_2 (0.3 M) was stirred for 10 min at –78 °C before adding a solution of furanolate **9** (1 equiv.) in CH_2Cl_2 (0.3 M). The resulting mixture was stirred at –78 °C for 20 min and at –20 °C for additional 2 h and then at room temp. overnight. The reaction mixture was filtered through Celite® and solvent evaporated in vacuo. The coupling product was purified by column chromatography.

TIPS-Substituted Allenyl Butenolide 39a: According to procedure B, allene bromide **34a** (1.3 g, 1.5 equiv.) gave butenolide **39a** (260 mg, 22%). IR (neat): $\tilde{\nu}$ = 2944, 2867, 1960, 1758 cm^{-1}. ^1H NMR: δ = 5.01–4.98 (m, 2 H), 4.83–4.75 (m, 2 H), 4.23 (qt, J = 12, J = 2.5 Hz, 2 H), 4.00 (br. s, 4 H), 2.60–2.34 (m, 6 H), 1.86–1.77 (m, 2 H), 1.13–0.87 (m, 21 H). ^{13}C NMR (in benzene): δ = 172.2, 160.9, 127.6, 108.7, 99.6, 80.8, 77.6 (not seen in $CDCl_3$), 65.4, 65.19, 65.18, 53.9, 53.2, 32.4, 31.4, 20.0, 18.8, 12.9.

Photocycloadduct 40a: According to procedure A, butenolide **39a** (260 mg, 0.599 mmol) in acetonitrile/acetone (9:1, v/v, 30 mL) was irradiated for 15 min which gave **40a** (155 mg, 60%) as a colourless oil after purification (PE/EtOAc = 4:1). R_f = 0.23. IR ($CHCl_3$): $\tilde{\nu}$ = 2944, 2865, 1779, 1111 cm^{-1}. ^1H NMR: 4.77 (s, 2 H), 4.63 (d, J = 4 Hz, 1 H), 3.96–3.85 (m, 6 H), 2.16–2.10 (m, 2 H), 2.03 (dd, J = 14, J = 1.6 Hz, 1 H), 1.91–1.8 (m, 3 H), 1.65–1.61 (m, 1 H), 1.42 (td, J = 4, J = 14 Hz, 1 H), 1.10–0.99 (m, 21 H). ^{13}C NMR: 174.5, 151.6, 108.4, 96.6, 79.8, 65.1, 64.4, 63.8, 59.1, 59.0, 54.5, 38.7, 30.8, 29.1, 17.7, 17.3, 11.6.

Benzyl 2-(Benzyloxymethyl)buta-2,3-dienoate (33b): To a solution of allenyl methyl alcohol **32** (364 mg, 1.78 mmol) in CH_2Cl_2 (15 mL) at 0 °C was added benzyl trichloroacetimidate (0.34 mL, 1 equiv.) followed by TMSOTf (64 μL, 0.2 equiv.). The reaction mixture was warmed to room temp. and stirred overnight. Solvent was then evaporated under reduced pressure. PE/Et_2O (6:1) (20 mL) was added to the residue and the slurry was filtered through a plug of silica gel to remove the formed trichloroacetamide. The silica gel was washed with PE/Et_2O (6:1) (3 × 10 mL). The combined organic layers were washed with saturated aqueous $NaHCO_3$ (30 mL), brine (30 mL), dried with $MgSO_4$ and concentrated in vacuo. Purification by chromatography (PE/EtOAc = 5:1) afforded the desired product **33b** (312 mg, 60%) as a colourless oil (R_f = 0.3). IR (neat): $\tilde{\nu}$ = 1965, 1708, 1260, 1070 cm^{-1}. ^1H NMR: δ = 7.39–7.27 (m, 10 H), 5.27 (t, J = 2 Hz, 2 H), 5.22 (s, 2 H), 4.57 (s, 2 H), 4.28 (t, J = 2 Hz, 2 H).

2-(Benzyloxymethyl)buta-2,3-dien-1-ol: To a stirred solution of allenyl ester **33b** (1.6 g, 5.44 mmol) in dried CH_2Cl_2 (60 mL) at –78 °C was added DIBAL-H (1.5 M in toluene) (11 mL, 3 equiv.). The reaction mixture was stirred at –78 °C for 2 h and carefully quenched with EtOAc at 0 °C. Saturated aqueous Na_2SO_4 (0.5 mL) was added and the resulting mixture was stirred for 1 h. After adding solid Na_2SO_4, the mixture was filtered through Celite® and the filtrate was concentrated in vacuo. Purification by chromatography (PE/EtOAc = 2:1) afforded a mixture of the desired 2-benzyloxymethyl-buta-2,3-dien-1-ol contaminated with benzyl alcohol (803 mg) as a colourless oil (R_f = 0.23) which was used for the next step without further purification. IR (neat): $\tilde{\nu}$ = 3357, 1957, 1072, 1018 cm^{-1}. ^1H NMR: δ = 7.50–7.25 (m, 5 H), 4.95–4.80 (m, 2 H), 4.54 (s, 2 H), 4.25 (br., 2 H), 4.20–4.10 (m, 2 H).

[2-(Bromomethyl)buta-2,3-dienyloxymethyl]benzene (34b): To a solution of MsCl (0.5 mL, 1.5 equiv.) in CH_2Cl_2 (30 mL) at 0 °C was added a solution of the above mixture of 2-(benzyloxymethyl) buta-2,3-dien-1-ol and benzyl alcohol (803 mg) in CH_2Cl_2 (15 mL) followed by Et_3N (0.9 mL, 1.5 equiv.). The reaction mixture was stirred at 0 °C for 30 min CH_2Cl_2 (10 mL) was added and the organic phase was washed with water, brine (30 mL), dried with $MgSO_4$ and concentrated in vacuo to afford the crude mesylate (1.24 g) which was used for the next step without purification. To a stirred solution of LiBr (432 mg, 4 equiv.) in acetone (10 mL) at 0 °C was added a solution of the crude mesylate (1.24 g) in acetone (10 mL). The reaction mixture was stirred at room temp. for 30 min then water was added. The aqueous layer was extracted with CH_2Cl_2 and the combined organic layers were washed with brine (20 mL), dried with $MgSO_4$ and concentrated in vacuo to give allenyl methyl bromide **34b** (516 mg, 37% from **33b**) as a colourless oil after purification (PE and then PE/EtOAc = 7:1). R_f = 0.43. IR ($CHCl_3$): $\tilde{\nu}$ = 2857, 1951, 1207, 1071 cm^{-1}. ^1H NMR: δ = 7.35–7.27 (m, 5 H), 4.90 (t, J = 2 Hz, 2 H), 4.53 (s, 2 H), 4.18 (t, J = 2 Hz, 2 H), 4.10 (t, J = 2 Hz, 2 H). ^{13}C NMR: δ = 207.5, 137.6, 128.2, 127.6, 127.5, 98.6, 76.9, 72.0, 67.6, 31.3. HRMS (FAB) calcd. for $C_{12}H_{14}BrO$ [MH$^+$] 253.0228, found 253.0228.

Benzyl-Substituted Allenyl Butenolide 39b: According to procedure B, allenyl methyl bromide **34b** gave the coupling product **39b** after purification by chromatography (PE/EtOAc = 1:1) (R_f = 0.28). IR (neat): $\tilde{\nu}$ = 2888, 1957, 1752, 1063 cm^{-1}. ^1H NMR: δ = 7.35–7.26 (m, 5 H), 4.96 (br. s, 1 H), 4.86–4.80 (m, 2 H), 4.49 (s, 2 H), 4.08–4.00 (m, 2 H), 3.99–3.95 (br. s, 4 H), 2.58–2.50 (m, 2 H), 2.46–2.36 (m, 3 H), 2.35–2.29 (m, 1 H), 1.84–1.78 (m, 2 H). ^{13}C NMR: δ = 207.1, 172.0, 160.9, 137.7, 128.2, 127.6, 127.5, 126.2, 107.5, 95.2, 80.3, 70.2, 71.6, 70.9, 64.5, 34.2, 31.9, 30.4, 18.7. HRMS (FAB) calcd. for $C_{22}H_{25}O_5$ [MH$^+$] 369.1702, found 396.1698.

Photocycloaddition Product 40b: According to procedure A, solution of allene **39b** in benzene/acetone (9:1, v/v) was irradiated (300 nm) for 1 h to give **39b**. Purification by chromatography (PE/EtOAc = 2:1) afforded the cyclized adduct (R_f = 0.28). IR ($CHCl_3$): $\tilde{\nu}$ = 2949, 2880, 1770, 1111 cm^{-1}. ^1H NMR: δ = 7.35–7.27 (m, 5 H), 4.78 (s, 1 H), 4.76 (s, 1 H), 4.65 (d, J = 4 Hz, 1 H), 4.48 (s, 2 H), 3.96–3.83 (m, 4 H), 3.67 (d, J = 10.5 Hz, 1 H), 3.62 (d, J = 10.5 Hz, 1 H), 2.17–2.02 (m, 3 H), 1.91–1.80 (m, 3 H), 1.65–1.60 (m, 1 H), 1.4 (td, J = 4, J = 14 Hz, 1 H). ^{13}C NMR: δ = 174.6, 151.3, 137.7, 128.2, 127.4, 127.2, 108.3, 96.8, 79.9, 73.0, 65.4, 65.2, 64.4, 63.8, 57.3, 54.9, 39.0, 30.8, 29.1, 17.4. HRMS (FAB) calcd. for $C_{22}H_{25}O_5$ [MH$^+$] 369.1702, found 369.1703.

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[1] J. G. Mulder, P. Diepenhorst, P. Plieger, I. E. M. Brüggemann-Rotgans, PCT Int. Appl. WO 93/02,083 (*Chem. Abstr.* **1993**, *118*, 185844z).

[2] H. Schenk, R. A. J. Driessen, R. de Gelder, K. Goubitz, H. Nieboer, I. E. M. Brüggemann-Rotgans, P. Diepenhorst, *Croat. Chem. Acta* **1999**, *72*, 593.

[3] A. Murai, N. Tanimoto, N. Sakamoto, T. Masamune, *J. Am. Chem. Soc.* **1988**, *110*, 1985.
[4] a) K. Mori, H. Watanabe, *Pure Appl. Chem.* **1989**, *61*, 543; b) H. Watanabe, K. Mori, *J. Chem. Soc., Perkin Trans. 1* **1991**, 2919.
[5] a) E. J. Corey, I. N. Houpis, *J. Am. Chem. Soc.* **1990**, *112*, 8997; b) E. J. Corey, B. Hong, *J. Am. Chem. Soc.* **1994**, *116*, 3149.
[6] A. Murai, M. Ohkita, T. Honda, K. Hoshi, N. Tanimoto, S. Araki, A. Fukuzawa, *Chem. Lett.* **1992**, 2103.
[7] a) G. A. Kraus, B. Johnston, A. Kongsjahju, G. L. Tylka, *J. Agric. Food Chem.* **1994**, *42*, 1839; b) G. A. Kraus, P. K. Choudhury, *Eur. J. Org. Chem.* **2004**, 2193.
[8] Another approach towards the oxabicyclo[2.2.1]heptane segment of solanoeclepin A has been published very recently: M. Isobe, S. Tojo, *Synthesis* **2005**, 1237.
[9] a) A. Fürstner, *Chem. Rev.* **1998**, *98*, 991; b) K. Takai, M. Tagashira, T. Kuroda, K. Ishima, K. Utimoto, H. Nozaki, *J. Am. Chem. Soc.* **1986**, *108*, 6048; c) P. Knochel, C. J. Rao, *Tetrahedron* **1993**, *49*, 29.
[10] a) J. C. J. Benningshof, R. H. Blaauw, A. E. van Ginkel, J. H. van Maarseveen, F. P. J. T. Rutjes, H. Hiemstra, *J. Chem. Soc., Perkin Trans. 1* **2002**, 1693; b) J. C. J. Benningshof, M. Ijsselstijn, S. R. Wallner, A. L. Koster, R. H. Blaauw, A. E. van Ginkel, J.-F. Brière, J. H. van Maarseveen, F. P. J. T. Rutjes, H. Hiemstra, *J. Chem. Soc., Perkin Trans. 1* **2002**, 1701; c) J. C. J. Benningshof, R. H. Blaauw, A. E. van Ginkel, F. P. J. T. Rutjes, J. Fraanje, K. Goubitz, H. Schenk, H. Hiemstra, *Chem. Commun.* **2000**, 1465.
[11] The most direct approach to the bicyclo[2.1.1]hexanone skeleton of **4** would be an intramolecular ketene olefin cycloaddition, but this strategy was not viable in view of literature precedent: B. B. Snider, R. A. H. F. Hui, *J. Org. Chem.* **1985**, *50*, 5167.
[12] a) C. Kaneko, M. Sato, J. Sakaki, Y. Abe, *J. Heterocycl. Chem.* **1990**, *27*, 25; b) J. D. Winkler, C. Mazur Bowen, F. Liotta, *Chem. Rev.* **1995**, *95*, 2003; c) N. Haddad, I. Rukhman, Z. Abramovich, *J. Org. Chem.* **1997**, *62*, 7629; d) J. D. Winkler, E. M. Doherty, *J. Am. Chem. Soc.* **1999**, *121*, 7425.
[13] a) R. H. Blaauw, J.-F. Brière, R. de Jong, J. C. J. Benningshof, A. E. van Ginkel, F. P. J. T. Rutjes, J. Fraanje, K. Goubitz, H. Schenk, H. Hiemstra, *Chem. Commun.* **2000**, 1463; b) R. H. Blaauw, J.-F. Brière, R. de Jong, J. C. J. Benningshof, A. E. van Ginkel, J. Fraanje, K. Goubitz, H. Schenk, F. P. J. T. Rutjes, H. Hiemstra, *J. Org. Chem.* **2001**, *66*, 233; c) J.-F. Brière, R. H. Blaauw, J. C. J. Benningshof, A. E. van Ginkel, J. H. van Maarseveen, H. Hiemstra, *Eur. J. Org. Chem.* **2001**, 2371; d) R. H. Blaauw, J. C. J. Benningshof, A. E. van Ginkel, J. H. van Maarseveen, H. Hiemstra, *J. Chem. Soc., Perkin Trans. 1* **2001**, 2250.
[14] a) L. A. Chugaev, *Ber. Dtsch. Chem. Ges.* **1899**, *32*, 3332; b) M. B. Smith, J. March, *Advanced Organic Chemistry*, 5th ed., Wiley, New York, **2001**, p. 1330; c) C. H. DePuy, R. W. King, *Chem. Rev.* **1960**, *60*, 431.
[15] a) L. Fitjer, U. Quabeck, *Synthesis* **1987**, 299; b) P. S. Bailey, *Chem. Rev.* **1958**, *58*, 925.
[16] D. H. R. Barton, S. I. Parekh, C.-L. Tse, *Tetrahedron Lett.* **1993**, *34*, 2733.
[17] K. C. Nicolaou, K. R. Reddy, G. Skokotas, F. Sato, X.-Y. Xiao, *J. Am. Chem. Soc.* **1992**, *114*, 7935.
[18] a) D. B. Dess, J. C. Martin, *J. Am. Chem. Soc.* **1991**, *113*, 7277; b) D. B. Dess, J. C. Martin, *J. Org. Chem.* **1983**, *48*, 4155.
[19] a) C. W. Jefford, A. W. Sledeski, J. Boukouvalas, *Helv. Chim. Acta* **1989**, *72*, 1362; b) C. W. Jefford, A. W. Sledeski, J.-C. Rossier, J. Boukouvalas, *Tetrahedron Lett.* **1990**, *31*, 5741.
[20] R. Coates, P. D. Senter, W. Baker, *J. Org. Chem.* **1982**, *47*, 3597.
[21] For a preliminary account of this work, see B. T. B. Hue, J. Dijkink, S. Kuiper, K. K. Larson, F. S. Guziec Jr., K. Goubitz, J. Fraanje, H. Schenk, J. H. van Maarseveen, H. Hiemstra, *Org. Biomol. Chem.* **2003**, *1*, 4364.
[22] D. Butina, F. Sondheimer, *Synthesis* **1980**, 543.
[23] a) W. J. Bailey, C. R. Pfeifer, *J. Org. Chem.* **1955**, *20*, 1337; b) J. Pornet, B. Randrianoelina, L. Miginiac, *J. Organomet. Chem.* **1979**, *174*, 1.
[24] a) R. Srinivasan, K. H. Carlough, *J. Am. Chem. Soc.* **1968**, *89*, 4932; b) R. S. H. Liu, G. S. Hammond, *J. Am. Chem. Soc.* **1967**, *89*, 4936.
[25] Attempted direct synthesis of the monotosylate from **26** by using tosyl chloride in pyridine followed by reduction failed, probably because of the proximity of the secondary alcohol causing formation of a cyclic ether. See ref.[13d].
[26] S. Krishnamurthy, H. C. Brown, *J. Org. Chem.* **1976**, *41*, 3064.
[27] T. Honda, H. Takada, S. Miki, M. Tsubuki, *Tetrahedron Lett.* **1993**, *34*, 8275.
[28] The reported instability of the natural product in basic medium may be associated with the β-hydroxy ketone moiety.
[29] a) D. Basavaiah, P. D. Rao, R. S. Hyma, *Tetrahedron* **1996**, *52*, 8001; b) S. E. Drewes, G. H. P. Roos, *Tetrahedron* **1988**, *44*, 4653.
[30] S. Tsuboi, H. Kuroda, S. Takatsuka, T. Fukawa, T. Sakai, M. Utaka, *J. Org. Chem.* **1993**, *58*, 5952.
[31] R. W. Lange, H.-J. Hansen, *Org. Synth.* **1984**, *62*, 202.
[32] R. Bittman, H.-S. Byun, K. C. Reddy, *Tetrahedron Lett.* **1994**, *35*, 1371.
[33] U. Groth, P. Eckenberg, T. Huhn, N. Richter, C. Schmeck, *Tetrahedron* **1993**, *49*, 1619.
[34] S. Ma, N. Jiao, S. Zhao, H. Hou, *J. Org. Chem.* **2002**, *67*, 2837.
[35] a) J.-F. Lavallee, C. Spino, R. Ruel, K. T. Hogan, P. Deslongchamps, *Can. J. Chem.* **1992**, *70*, 1406; b) G. T. Crisp, A. G. Meyer, *J. Org. Chem.* **1992**, *57*, 6972.
[36] a) S. F. Martin, K. J. Barr, D. W. Smith, S. K. Bur, *J. Am. Chem. Soc.* **1999**, *121*, 6990; b) J. Boukouvalas, N. Lachance, *Synlett* **1998**, 31.

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