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PAPER

Unprecedented influence of remote substituents on reactivity and stereoselectivity in Cu(I)-catalysed [2 + 2] photocycloaddition. An approach towards the synthesis of tricycloclavulone†

Sujit Mondal, Ram Naresh Yadav and Subrata Ghosh*

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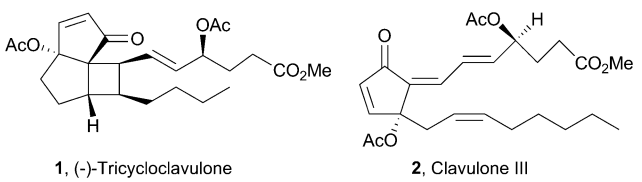
Cu(I)-catalysed [2 + 2] photocycloaddition of 1,6-dienes embedded in a furano sugar is described in connection to a synthetic approach to an abnormal marine prostanoid tricycloclavulone. An unprecedented influence of remote substituents on the reactivity and stereoselectivity of the photocycloaddition reaction has been uncovered during this investigation. While an alkene substituent inhibits cycloaddition through steric effects, a substituent having a hydroxyl or alkoxy group at the same location facilitates cycloaddition exclusively from its own side. This investigation has led to the synthesis of a functionalised 5,4-fused core unit of tricycloclavulone.

Introduction

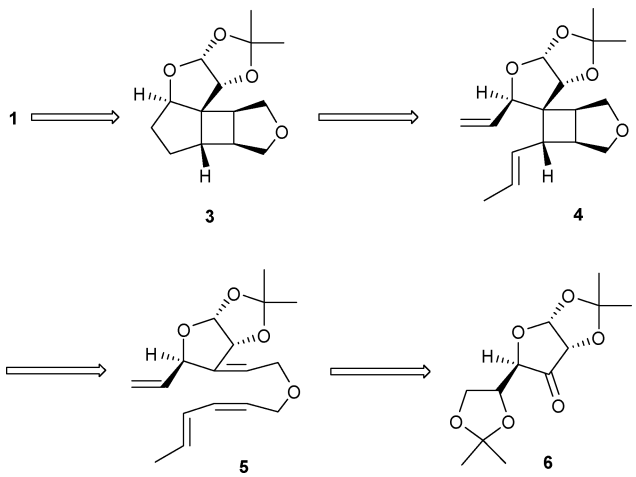
Tricycloclavulone **1** is an unusual marine prostanoid that was isolated from Okinawan soft coral *Clavularia viridis* by Iguchi and coworkers (Fig. 1).[1] This abnormal prostanoid is constituted of a tricyclo[5.3.0.0^{1,4}]decane skeleton having a highly functionalised angularly fused 5,5,4-ring system. The relative stereochemistry of the chiral centres of tricycloclavulone was established by the analysis of spectroscopic data. Subsequently, this group reported its total synthesis and established its absolute stereochemistry.[2] Tricycloclavulone is believed to be derived from clavulone III **2**, one of the large number of marine prostanoids that possess a wide range of bioactivities.[3] While no bioactivity has been reported for **1**, considering its possible genesis, tricyclcoclavulone or its analogues might exhibit bioactivity. The potential bioactivity along with its structural novelty elicited considerable interest[2,4] for synthesis of tricycloclavulone. As part of our continued interest[5] in the synthesis and application[6] of cyclobutane derivatives in organic synthesis, we initiated a program for development of a flexible route for synthesis of **1** and its analogues.



1, (-)-Tricycloclavulone **2**, Clavulone III

Fig. 1 Marine prostanoids.

Retrosynthetically, we envisaged that **1** could in principle be obtained from the tetracycle **3** (Scheme 1). While the sugar residue in **3** could be employed to construct the cyclopentenone, the tetrahydrofuran ring in **3** could be opened up to provide the substituents on the cyclobutane ring. Compound **3** could be obtained through a ring closing metathesis (RCM)[7]-reduction protocol from the diene **4**. The cyclobutane derivative **4** could in principle be obtained from a Cu(I)-catalysed[8] [2 + 2] photocycloaddition of the teraene **5** which could easily be synthesised from the sugar derivative **6**. Herein we report the results of our investigation based on this synthetic plan. During this investigation we have demonstrated an unprecedented influence of remote substituents on the efficiency and stereochemical outcome in a Cu(I)-catalysed [2 + 2] photocycloaddition reaction.



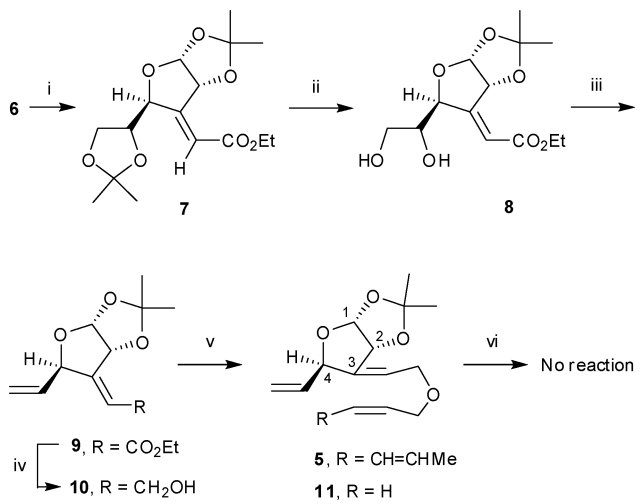
Scheme 1 Retrosynthesis.

Department of Organic Chemistry, Indian Association for the Cultivation of Science, Jadavpur, Kolkata, 700 032, India. E-mail: ocsg@iacs.res.in; Fax: +91 33 2473 2805; Tel: +91 33 2473 4971

† Electronic supplementary information (ESI) available: NMR spectra of all new compounds and 2D NMR and NOE spectra for **27**. See DOI: 10.1039/c1ob05233k

Results and discussion

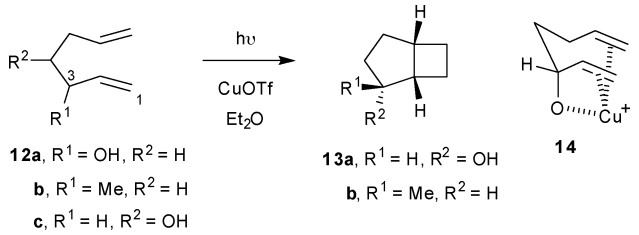
The investigation was initiated with the synthesis of the tetraene **5** from the known 3-keto sugar **6**[9] (Scheme 2). Horner–Wadsworth–Emmons olefination of the ketone **6** afforded the α,β-unsaturated ester **7**[10] along with its *E*-isomer in high yield in *ca.* 4 : 1 ratio. The pure *Z*-isomer was obtained in 67% yield as the major product by column chromatography. The labile 5,6-di-*O*-isopropylidene group of **7** was selectively deprotected with 75% aqueous acetic acid to provide the diol **8** in 88% yield. Following the known protocol,[11] the diol **8** was transformed to the diene **9** in 80% yield on treatment of its dimesylate derivative with NaI in DMF. Reduction of the ester **9** with DIBALH gave the allyl alcohol **10** in 96% yield. Treatment of the allyl alcohol **10** with sodium hydride followed by sorbyl bromide provided the tetraene **5** in 85% yield.



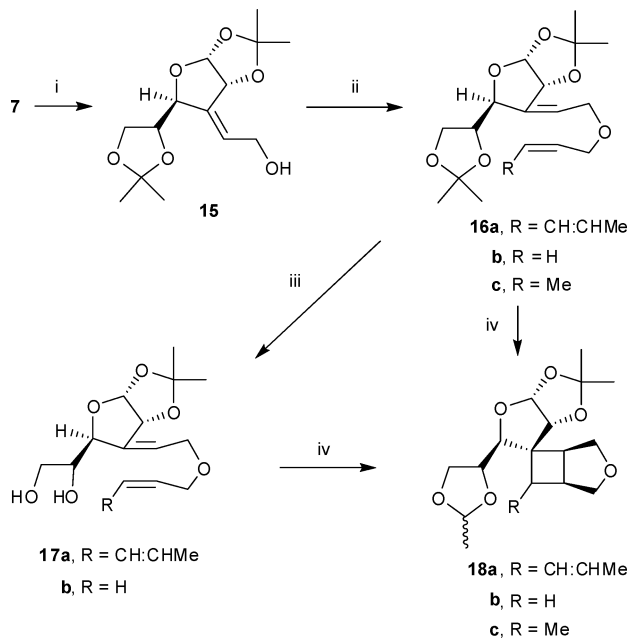
Scheme 2 Preparation of substrates **5** and **11**. Reagents and conditions: (i) $(EtO)_2P(O)CH_2CO_2Et$, NaH, THF, 0 °C, 0.5 h, 85% (1 : 4 *E*/*Z* separable mixture); (ii) AcOH–H_2O (3 : 1), rt, 12 h, 88%; (iii) (a) MsCl, Et_3N, DMAP (cat.), CH_2Cl_2, 0 °C→rt, 2 h; (b) NaI, DMF, 100 °C, 4 h, 80% two steps; (iv) DIBALH, CH_2Cl_2, –78 °C, 0.5 h, 96%; (v) NaH, THF–HMPA, reflux, sorbyl bromide for **5**, 85%; and allyl bromide for **11**, 90%; (vi) *hν*, Et_2O, CuOTf (20 mol%), 6–12 h, no reaction.

Based on the mode of addition[12] of nucleophiles to the ketone **6**, it was expected that photocycloaddition of **5** would take place from the face opposite to the acetonide moiety to produce **4**. Surprisingly, when a solution of this tetraene in diethyl ether was irradiated in the presence of the Cu(I) complex $(CuOTf)_2{\cdot}C_6H_6$ as catalyst for more than 12 h under a positive pressure of Ar, the compound **5** remained unchanged. We thought that the propenyl chain at the alkene terminus in **5** (R = CH═CHMe) increased the steric bulk during cycloaddition. Thus, the structurally simple triene **11** was chosen. The triene **11** was prepared from the alcohol **10** on reaction of its sodium salt with allyl bromide. However, the triene **11** also failed to undergo photocycloaddition under the same reaction conditions. An examination of the structure of the tetraene **5** and the triene **11** reveals that cycloaddition from the α-face is blocked by the 1,2-di-*O*-isopropylidine unit. However, cycloaddition from the β-face might also be blocked by the C-4 vinyl unit. This probably explains the inertness of the tetraene **5** and the triene **11** to undergo intramolecular cycloaddition to produce the corresponding cyclobutane derivatives.

Substituents at the C_3 position of 1,6-dienes have a profound influence on the reactivity and stereochemical outcome during Cu(I)-catalysed [2 + 2] photocycloaddition.[13] It has been demonstrated that the dienol **12a** undergoes smooth photocycloaddition to produce **13a** as the major product, while **12b** produces **13b** as the major product. The formation of **13a** has been attributed to the involvement of the Cu(I) complex **14** in which both the olefinic units and the hydroxyl group are co-ordinated to Cu. The formation of **13b** from **12b** has been attributed to the steric effect of the Me group. Furthermore, it has also been shown that a remote hydroxyl group as in **12c** makes the cycloaddition non-stereoselective.



With this background we decided to carry out photocycloaddition of the triene **17a** and the diene **17b** (Scheme 3). Although **17a** and **17b** lack hydroxyl groups at allylic positions, they do have hydroxyl groups at a remote location. The triene **17a** was prepared in the following way. Reduction of the unsaturated ester **7** with DIBALH led to the alcohol **15**.[10b] Compound **15** was transformed to the triene **16a** on treating its sodium alkoxide with sorbyl bromide. Treatment of **16a** with 75% aqueous acetic acid afforded the diol **17a**. In a similar fashion the diene **17b** was prepared in overall excellent yield.



Scheme 3 Synthesis and [2 + 2] photocycloaddition of substrates **16a–c** and **17a**, **b**. Reagents and conditions: (i) DIBALH, CH_2Cl_2, –78 °C, 0.5 h, 96%; (ii) NaH, THF–HMPA, reflux, sorbyl bromide for **16a**, 85%; allyl bromide for **16b**, 90% and methallyl bromide for **16c**, 85%; (iii) AcOH–H_2O (3 : 1), rt, 10 h, 75–80%; (iv) *hν*, Et_2O, CuOTf (15–20 mol%), 4–4.5 h, 60–70%.

Amazingly, the triene **17a** and the diene **17b** in diethyl ether underwent smooth photocycloaddition when irradiated in the presence of CuOTf (cat.) to produce the cyclobutane derivatives **18a** and **18b** in 60% and 65% isolated yields, respectively, in only 3–4 h.[14] Even the dienes **16a–c**, each of which having a bulky acetonide moiety at C-4, underwent smooth cycloaddition to produce adducts **18a–c** in moderate to good yields. Structures of the photoadducts were determined through analysis of the NMR spectral data. The stereochemical outcome of the cycloaddition reaction was established by analogy to the formation of the cyclobutane derivative **27** from cycloaddition of the structurally analogous diene **25** (*vide infra*). Smooth reaction of the compounds **16a–c** and **17a**, **b** compared to the inertness of the corresponding deoxy analogues **5** and **11** towards photocycloaddition suggests that the remote oxygen functionality present in them plays a significant role in facilitating photocycloaddition. It may be noted that during cycloaddition, the vicinal diol of **17a**, **b** and the 5,6-acetonide of **16a–c** have been transformed to the acetal of acetaldehyde.[14]

The facile reactivity of the dienes towards photocycloaddition may possibly be attributed to the involvement of the tri-co-ordinated Cu(I) complex **19** and **20** for the substrates **17a**, **b** and **16a–c**, respectively (Fig. 2). Involvement of the complex **21** (R = OH), arising from participation of the C_6-hydroxyl group, may also be invoked for facile cycloaddition of **17a**, **b**. The involvement of these complexes can also explain the stereochemical outcome observed during photocycloaddition to form the cyclobutane derivatives **18a–c** arising through cycloaddition from the side of the C-4 substituents (β-face).

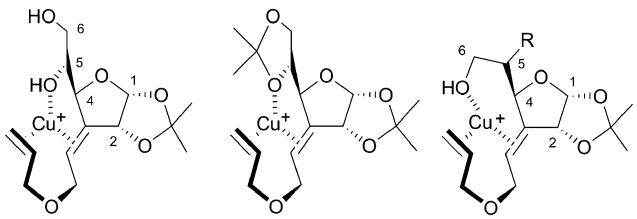
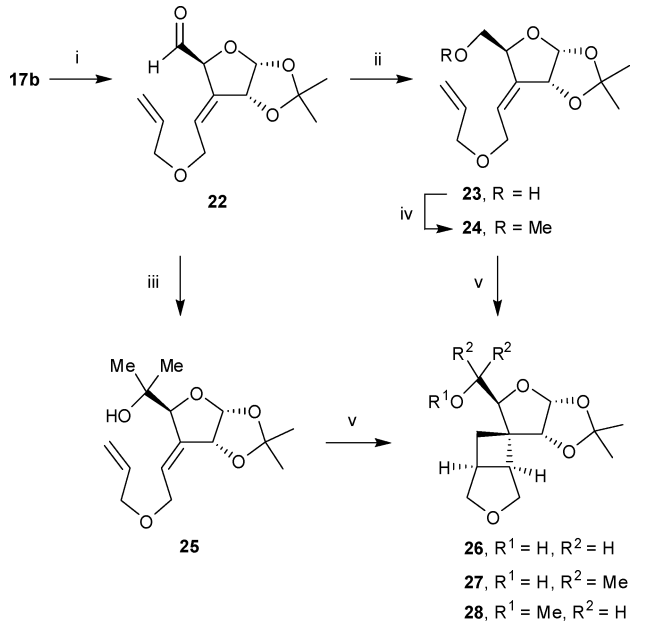


Fig. 2 Tri-co-ordinated Cu(I) complexes.

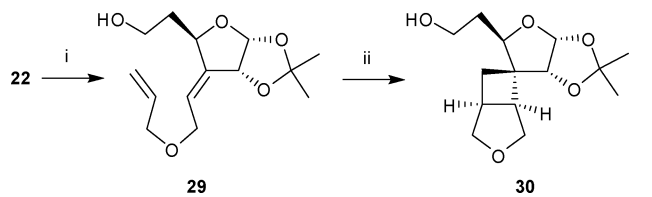
To demonstrate that the C_5-hydroxyl group participates in chelation during the photocycloaddition reaction, the diene **23** was chosen. The diene **23** was prepared from periodate cleavage of the diol **17b**, followed by reduction of the resulting aldehyde **22** (Scheme 4). An ethereal solution of the diene **23** in the presence of CuOTf, under identical reaction conditions, led to smooth cycloaddition and produced the cyclobutane derivative **26** in 85% yield. To demonstrate that it is the electronic effect that is more important in bringing about photocycloaddition, the diene **25** was chosen. The diene **25** was prepared from the aldehyde **22** in three steps (addition of MeMgBr, oxidation of the resulting alcohol with Dess–Martin periodinane (DMP) and finally addition of MeMgBr to the resulting methyl ketone) in overall 70% yield. In the diene **25**, the β-face is blocked by a bulky substituent (*gem*-dimethyl) containing a hydroxyl group. When the diene **25** was irradiated under the same reaction conditions, photocycloaddition was completed in only 2 h and the cyclobutane derivative **27** was obtained in 82% yield.



Scheme 4 Synthesis and photocycloaddition of substrates **23**, **24** and **25**. Reagents and conditions: (i) $NaIO_4$, $THF–H_2O$, 2 h, 90%; (ii) $NaBH_4$, MeOH, −30 °C, 1 h, 85%; (iii) (a) MeMgBr, Et_2O, −50 °C, 30 min; (b) DMP, CH_2Cl_2, rt, 2 h; (c) MeMgBr, Et_2O, 0 °C, 1 h, 70% in three steps; (iv) NaH, THF–HMPA, MeI, 90%; (v) *hν*, Et_2O, CuOTf (10 mol%), 2 h, 85% for **26**, 82% for **27** and 80% for **28**.

A free hydroxyl group is not necessarily required for directing photocycloaddition through a Cu(I) complex such as **19**. An alkyl ether can also facilitate cycloaddition through a Cu(I) complex analogous to **20**. Thus, the methyl ether analogue **24**, prepared from **23** on methylation (NaH–MeI), underwent smooth photocycloaddition under identical reaction conditions to produce the adduct **28** in 80% yield.

To determine whether a C_6-hydroxyl group can facilitate and direct photocycloaddition through a complex like **21** (R = H), the diene **29** was chosen. The compound **29** was prepared from the aldehyde **22** in a three step sequence in 45% overall yield as delineated in Scheme 5. When an ethereal solution of the diene **29** was irradiated under the same reaction conditions, the photoadduct **30** was obtained in 65% yield. This established that Cu(I) catalysed photocycloaddition of the dienes **17a**, **b** may proceed through either complex **19** or **21**.



Scheme 5 Synthesis and photocycloaddition of substrate **29**. Reagents and conditions: (i) (a) $Ph_3PCH_2OCH_3Cl$, KHMDS, THF, 0 °C; (b) 5% HCl, THF, 0 °C→rt, 15 min; (c) $NaBH_4$, MeOH, 0 °C, 45% three steps; (ii) *hν*, Et_2O, CuOTf (10 mol%), 3 h, 65%.

That addition took place from the β-face was established from determination of the structure of the adduct **27** by analysis of its NMR spectral data. Stereochemical assignment is based on 2D NMR spectroscopy (HSQC, NOESY) and NOE (Fig. 3).

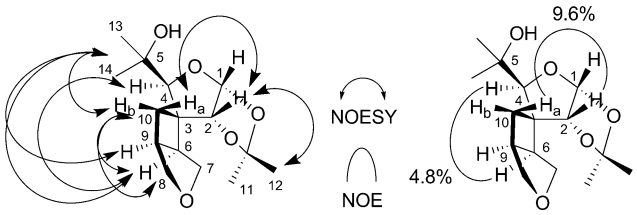
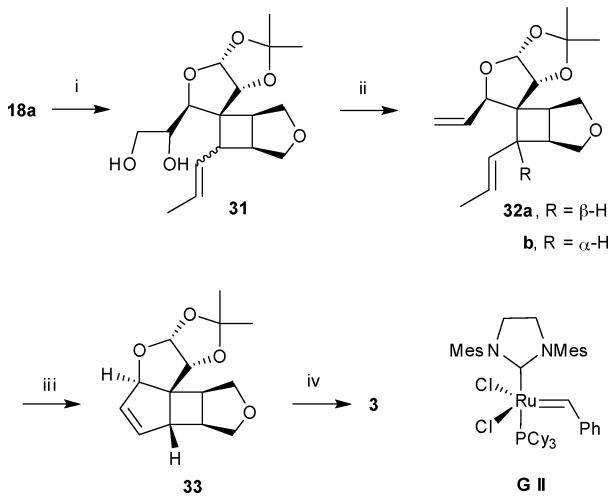


Fig. 3 Significant NOESY and NOE correlations in **27**.

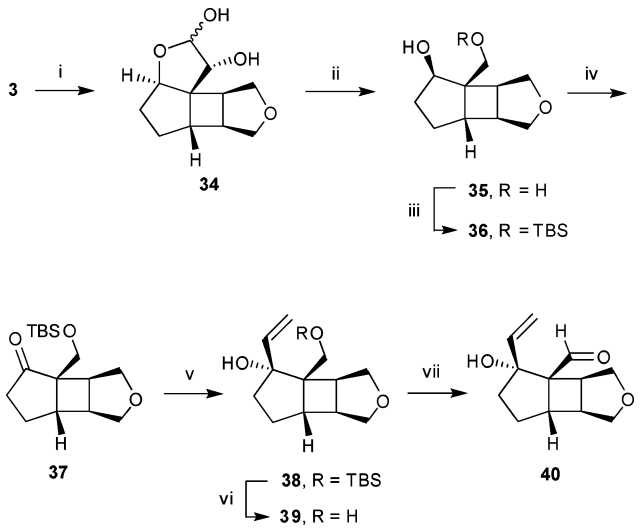
Strong correlations between C_2–H, C_{10}–H_a and C_4–H, C_6–H in the NOESY spectrum clearly established the structure. This assignment is further corroborated by strong NOE between C_2–H and C_{10}–H_a (9.6%) and C_4–H and C_6–H (4.8%). Successful addition of the diene **25** to the cyclobutane derivative **27** clearly demonstrates that electronic effects can override the steric effects.

After successfully preparing the cyclobutane derivative **18a**, we next focused our attention on its elaboration to tricycloclavulone as delineated in Scheme 6. The labile 5,6-acetal moiety of **18a** was deprotected oxidatively with DDQ to afford the corresponding diol **31** as a mixture of two diastereomers (*ca.* 2.2 : 1). The diol **31** was then converted to the diene **32**, in overall excellent yield, on treatment of the corresponding dimesylate with NaI. The diene **32**, when treated with Grubbs' 2nd generation catalyst (G-II), underwent smooth ring closure to produce the tetracycle **33** in 65% yield. During the RCM reaction the major isomer **32a** underwent cyclisation, leaving the minor isomer **32b** intact. Catalytic hydrogenation of the cyclopentene **33** afforded the desired tetracycle **3** in 94% yield.



Scheme 6 Preparation of tetracycle **3**. Reagents and conditions: (i) DDQ (0.1 eqv.), CH_3CN–H_2O (9 : 1), 60 °C, 4 h, 80%; (i) (a) MsCl, Et_3N, DMAP (cat), CH_2Cl_2, quantitative; (b) NaI, DMF, 100 °C, 4 h, 80%; (iii) 8 mol% Grubbs' II, toluene, 100 °C, 4 h, 65% (96% based on the recovery of starting material as **32b**); (iv) H_2, Pd–C, MeOH, 94%.

After successful accomplishment of the linear 5,4-fused ring system, we focused our attention on converting the sugar residue to a cyclopentenone ring. Treatment of **3** with 10% H_2SO_4 accomplished deketalisation to produce the diol **34** as an epimeric mixture in 87% yield. The compound **34** was then treated with $NaIO_4$ and the resulting aldehyde was reduced with lithium aluminium hydride to afford the diol **35** in 80% overall yield (Scheme 7).

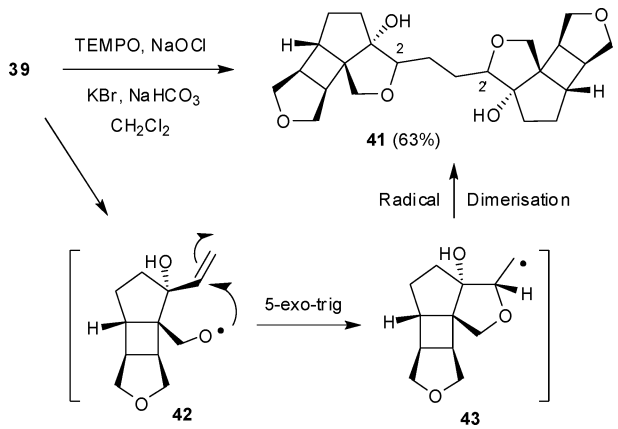


Scheme 7 Synthesis of aldehyde **40**. Reagents and conditions: (i) 10% H_2SO_4, THF, reflux, 5 h, 87%; (ii) (a) $NaIO_4$, THF–H_2O, 0 °C; (b) LAH, Et_2O, 0 °C, 80% two steps; (iii) TBSCl, Et_3N, DMAP (cat), CH_2Cl_2, 90%; (iv) DMP, CH_2Cl_2, 0 °C→rt, 30 min, 90%; (v) tetravinyl tin, *n*-BuLi, THF, $CeCl_3$, −78→−30 °C, 0.5 h, 50%; (vi) TBAF, THF, 0 °C, 1 h, 90%; (vii) DMP, CH_2Cl_2, 0 °C, 24%.

The selective protection of the primary alcohol of the diol **35** as silyl ether with TBSCl and the subsequent oxidation of the secondary alcohol in **36** with DMP, provided the cyclopentanone **37** in overall excellent yield. Addition of freshly prepared vinyl lithium in the presence of anhydrous $CeCl_3$ in THF at −78 °C produced the allyl alcohol **38** in 50% yield. The silyl ether in **38** was then deprotected using TBAF to obtain the diol **39**. Oxidation of the primary alcohol in **39** with DMP provided the aldehyde **40** in poor yield (24%).

In an attempt to increase the yield of the aldehyde **40**, oxidation of **39** was carried out with TEMPO. The desired aldehyde **40** was not obtained at all. Rather a white solid, m.p. 135–136 °C, characterised as the C-2 symmetric dimeric compound **41**, was isolated exclusively in 63% yield (Scheme 8). Probably during oxidation, the intermediate oxy-radical[15] **42** underwent facile intramolecular 5-*exo*-*trig* mode addition to the vinyl group followed by dimerisation of the resulting species **43**, leading to the formation of the compound **41**. The structure of the dimer **41** was established through analysis of its ^1H, ^{13}C, DEPT and HRMS data. Isolation of **41** established that a vinyl group added to **37** from the side of the hydroxy-methyl group to produce **38**. Stereochemical assignment at C-2 of **41** could not be made with the available data.

We thought that a three-step sequence involving addition of vinyl magnesium bromide to **40**, oxidation of the resulting allyl alcohol and RCM of the resulting dienone would provide the cyclopentenone unit present in **1**. However, addition of vinyl magnesium bromide or vinyl lithium to the highly crowded aldehyde unit in **40** or its silyl ether failed.



Scheme 8 Formation of the dimer **41**.

Conclusion

Cu(I)-catalysed [2 + 2] photocycloaddition of 1,6-dienes embedded in a furano sugar has been investigated in connection to a synthetic approach to the marine prostanoid tricycloclavulone. During this investigation it has been demonstrated that remote substituents greatly influence the reactivity and stereochemical outcome of the photocycloaddition reaction. While a remote alkene inhibits cycloaddition, a hydroxy-alkyl substituent facilitates stereoselective cycloaddition from its own face. Although total synthesis of **1** could not be achieved, this investigation has led to the synthesis of a tricyclic system having the 5,4-fused core unit of **1** functionalised at all the required positions with the correct stereochemistry.

Experimental section

General

Nuclear magnetic resonance (NMR) spectra were recorded on a Bruker-Avance DPX_{300} (^1H, 300 MHz; ^{13}C, 75 MHz) spectrometer or a Bruker-Avance DPX_{500} (^1H, 500 MHz; ^{13}C, 125 MHz) spectrometer using residual chloroform (^1H, 7.26 ppm) and $CDCl_3$ (^{13}C, 77.15 ppm) as an internal standard. The chemical shifts are expressed in parts per million (δ) downfield from Me_4Si. The standard abbreviations s, d, t, q and m refer to singlet, doublet, triplet, quartet and multiplet respectively. The coupling constant (J), whenever discernible, has been reported in Hertz (Hz). ^{13}C peak assignment is based on DEPT experiments. Infrared (IR) spectra were recorded on a Shimadzu FTIR-8300 spectrometer. Spectra were calibrated against polystyrene absorption at 1601 cm^{-1}. Solid samples were recorded as KBr discs and liquids as thin film in between NaCl plates. High resolution mass spectra (HRMS) were recorded in a QTOF I (quadrupole-hexapole-TOF) mass spectrometer with an orthogonal Z-spray-electrospray interface on Micro (YA-263) mass spectrometer (Manchester, UK). Optical rotations were measured using a Jasco P-1020 digital polarimeter and $[\alpha]_D$ values are given in units of 10^{-1} deg cm^2 g^{-1}. All reactions were monitored by TLC using Merck precoated silica gel plates. Petroleum ether refers to the fraction with b.p. 60–80 °C. A usual work up of the reaction mixture consists of extraction with diethyl ether, washing with brine, drying over Na_2SO_4, and removal of the solvent in vacuo. Melting points were taken in open capillaries in a sulfuric acid bath and are uncorrected. Column chromatography was carried out with silica gel (60–120 mesh).

(*Z*)-ethyl 2-((3a*R*,5*S*,6a*R*)-5-((*R*)-2,2-dimethyl-1,3-dioxolan-4-yl)-2,2-dimethylfuro[2,3-*d*][1,3]dioxol-6(3a*H*,5*H*,6a*H*)-ylidene)acetate 7

Triethyl phosphonoacetate (3.4 mL, 17.2 mmol) was added dropwise to a stirred suspension of NaH (750 mg, 18.8 mmol, 60% in oil) in THF (40 mL) in a 100 mL two-necked round bottom flask equipped with an Ar-balloon at 0 °C. As the evolution of hydrogen gas ceased (15 min), a solution of the ketone **5** (3.5 g, 13.6 mmol) in THF (15 mL) was added to the reaction mixture at the same temperature. The reaction mixture was then stirred for another 20 min at 0 °C. It was then quenched with saturated aqueous NH_4Cl solution. After being diluted with diethyl ether, the reaction mixture was washed with brine, dried over anhydrous Na_2SO_4. Evaporation of the solvent, followed by column chromatography (diethyl ether : petroleum ether, 1 : 12) gave the *Z*-ester **7** (3.0 g, 67%) along with the *E*-ester (0.82 g, 18%). Both the isomers were characterised on comparison of their NMR, IR, HRMS and optical rotation data with the reported compounds.[9]

(*Z*)-ethyl 2-((3a*R*,5*S*,6a*R*)-5-((*R*)-1,2-dihydroxyethyl)-2,2-dimethylfuro[2,3-*d*][1,3]dioxol-6(3a*H*,5*H*,6a*H*)-ylidene)acetate 8

Ester **7** (2 g) was treated with 80% aqueous acetic acid (12 mL) for 12 h at rt. On completion of the deprotection (TLC), excess acetic acid was removed under vacuum. Column chromatography of the residual mass with 1 : 1 ethyl acetate : petroleum ether as the eluent gave the diol **8** (1.52 g, 88%) as a viscous oil. $[\alpha]_D^{29}$ 126.8 (*c* 4.15, $CHCl_3$); ν_{max}/cm^{-1} 3418, 2990, 2941, 1715, 1649, 1375, 1219, 1028; ^1H NMR (300 MHz, $CDCl_3$) δ 6.30 (1H, br s), 5.86 (1H, d, J = 4.1 Hz), 5.74 (1H, d, J = 3.5 Hz), 4.80 (1H, d, J = 6.1 Hz), 4.22 (2H, q, J = 7.0 Hz), 3.77 (1H, br s), 3.74–3.70 (2H, m), 2.24 (2H, br s), 1.49 (3H, s), 1.41 (3H, s), 1.30 (3H, t, J = 7.0 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 165.3 (CO), 155.8 (C), 117.5 (CH), 112.8 (C), 104.8 (OOCH), 80.0 (OCH), 78.4 (OCH), 73.6 (OCH), 63.3 (OCH_2), 60.8 (OCH_2), 27.3 (CH_3), 27.1 (CH_3), 14.1 (CH_3); HRMS (ESI) m/z calcd for $C_{13}H_{20}O_7Na$ $(M+Na)^+$, 311.1107; found 311.1104.

(*Z*)-ethyl 2-((3a*R*,5*R*,6a*R*)-2,2-dimethyl-5-vinylfuro[2,3-*d*][1,3]dioxol-6(3a*H*,5*H*,6a*H*)-ylidene)acetate 9

A solution of the diol **8** (600 mg, 2.08 mmol) in dichloromethane (20 mL) at 0 °C under Ar atmosphere was treated with triethyl amine (1.52 mL, 10.41 mmol), DMAP (25 mg, cat.) and mesyl chloride (0.52 mL, 6.3 mmol). After the reaction was complete (3 h, TLC) it was quenched with the addition of water. The residual mass obtained after usual work up was directly used for the next step. NaI (460 mg, 3.01 mmol) was added to a solution of the dimesylate (900 mg, 2.03 mmol) in dry DMF (30 mL). The reaction mixture was heated at 100 °C for 4 h with stirring. After removing the solvent under vacuum, the reaction mixture was diluted with the addition of diethyl ether and washed with saturated $Na_2S_2O_3$ solution doped with $NaHCO_3$. After usual work up the residual mass thus obtained was purified through column chromatography, using 1 : 9 ether : petroleum ether as the eluent, to provide the diene-ester **9** (420 mg, 80%) as a light yellow oil. $[\alpha]_D^{28}$ 115.5 (*c* 6.2,

$CHCl_3$); ν_{max}/cm^{-1} 2986, 2938, 1724, 1684, 1647, 1373, 1217, 1028; ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.89 (1H, d, J = 3.9 Hz), 5.73–5.68 (2H, m), 5.67–5.59 (1H, m), 5.40 (1H, d, J = 2.0 Hz), 5.36 (1H, d, J = 3.6 Hz), 5.12 (1H, d, J = 7.3 Hz), 4.20 (2H, q, J = 7.1 Hz), 1.51 (3H, s), 1.39 (3H, s), 1.27 (3H, t, J = 7.1 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 165.1 (CO), 156.8 (C), 133.8 (CH), 121.0 (CH_2), 117.3 (CH), 112.6 (C), 104.8 (OOCH), 81.2 (OCH), 77.3 (OCH), 60.8 (OCH_2), 27.2 (CH_3), 26.9 (CH_3), 14.2 (CH_3); HRMS (ESI) m/z calcd for $C_{13}H_{18}O_5Na$ (M+Na)$^+$, 277.1052; found 277.1053.

(*Z*)-2-((3a*R*,5*R*,6a*R*)-2,2-dimethyl-5-vinylfuro[2,3-*d*][1,3]dioxol-6(3a*H*,5*H*,6a*H*)-ylidene)ethanol 10

To a solution of the ester **9** (500 mg, 1.97 mmol) in dry dichloromethane (20 mL) at −78 °C was added DIBALH (16.5 mL, 4.2 mmol, 20 wt% in toluene), and was stirred for 30 min at the same temperature. After the reaction was complete (TLC) it was quenched with the addition of 30% Rochelle salt (33 mL) solution and was stirred vigorously at rt for 1 h. After usual work up, the solvent was evaporated in a rotary evaporator, followed by column chromatography of the crude mass over silica gel using 1 : 1 ethyl acetate : petroleum ether as the eluent, to afford the alcohol **10** (480 mg, 96%) as a light yellow viscous oil. $[\alpha]_D^{26}$ 50.3 (c 1.4, $CHCl_3$); ν_{max}/cm^{-1} 3368, 1643, 1445, 1377, 1125, 1051; ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.86 (1H, d, J = 4.2 Hz), 5.70–5.58 (2H, m), 5.35–5.29 (2H, m), 5.17 (1H, d, J = 4.1 Hz), 5.02 (1H, d, J = 7.0 Hz), 4.30 (2H, dd, J = 1.0, 6.2 Hz), 2.33 (1H, br s), 1.49 (3H, s), 1.35 (3H, s); ^{13}C NMR (75 MHz, $CDCl_3$) δ 141.5 (C), 135.1 (CH), 127.1 (CH), 119.7 (CH_2), 112.1 (C), 104.7 (OOCH), 81.4 (OCH), 77.5 (OCH), 60.1 (OCH_2), 27.3 (CH_3), 27.1 (CH_3); HRMS (ESI) m/z, calcd for $C_{11}H_{16}O_4Na$ (M+Na)$^+$, 235.0946; found 235.0952.

General experimental procedure for synthesis of ethers (5, 11 and 16a–c)

The general procedure is illustrated by the synthesis of **5**:

(3a*R*,5*R*,6*Z*,6a*R*)-6-(2-(hexa-2,4-dienyloxy)ethylidene)-2,2-dimethyl-5-vinyltetrahydrofuro[2,3-*d*][1,3]dioxole 5

To a stirred suspension of NaH (160 mg, 4.0 mmol, 60 wt% in paraffin oil) in THF (15 mL) under Ar-atmosphere was added the alcohol **10** (400 mg, 1.89 mmol) in THF (5 mL), and was refluxed for 1 h. HMPA (1 mL) followed by sorbyl bromide (335 mg, 2.11 mmol) was then added to the reaction mixture and stirred for another 2 h. After being cooled in an ice bath, the reaction was quenched with the addition of saturated NH_4Cl solution (3 mL). The crude compound obtained after usual work up was filtered through a silica gel column to afford the sorbyl ether **5** (468 mg, 85%) as a light yellow oil. $[\alpha]_D^{27}$ 150.6 (c 5.66, $CHCl_3$); ν_{max}/cm^{-1} 2986, 2936, 2855, 1456, 1373, 1217, 1049; ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.24–6.17 (1H, m), 6.10–6.01 (1H, m), 5.87 (1H, d, J = 4.0 Hz), 5.76–5.58 (4H, m), 5.37–5.31 (2H, m), 5.10 (1H, d, J = 3.6 Hz), 5.03 (1H, d, J = 7.2 Hz), 4.24–4.09 (2H, m), 4.02–4.00 (2H, m), 1.76 (3H, d, J = 6.6 Hz), 1.51 (3H, s), 1.37 (3H, s); ^{13}C NMR (75 MHz, $CDCl_3$) δ 141.8 (C), 135.0 (CH), 133.8 (CH), 130.8 (CH), 130.4 (CH), 126.4 (CH), 125.0 (CH), 119.9 (CH_2), 112.1 (C), 104.8 (OOCH), 81.3 (OCH), 77.6 (OCH), 71.1 (OCH_2), 66.8 (OCH_2), 27.3 (CH_3), 27.1 (CH_3), 18.2 (CH_3); HRMS (ESI) m/z calcd for $C_{17}H_{24}O_4Na$ (M+Na)$^+$, 315.1572; found 315.1571.

(3a*R*,5*R*,6a*R*,*Z*)-6-(2-(allyloxy)ethylidene)-2,2-dimethyl-5-vinyltetrahydrofuro[2,3-*d*][1,3]dioxole 11

Following the above procedure for sorbylation of the alcohol **10**, sodium alkoxide of alcohol **10** (300 mg, 1.42 mmol) in THF (20 mL) was treated with allyl bromide (180 mg, 1.50 mmol) to afford, after column chromatography, the allyl ether **11** (340 mg, 90%) as a light yellow oil. $[\alpha]_D^{27}$ 79.6 (c 0.63, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.96–5.88 (1H, m), 5.87 (1H, d, J = 4.1 Hz), 5.70–5.64 (1H, m), 5.60–5.57 (1H, m), 5.37–5.31 (2H, m), 5.27–5.04 (4H, m), 4.22–4.15 (2H, m), 4.16–4.00 (2H, m), 1.51 (3H, s), 1.38 (3H, s); ^{13}C NMR (75 MHz, $CDCl_3$) δ 141.9 (C), 135.1 (CH), 134.7 (CH), 125.0 (CH), 119.8 (CH_2), 117.5 (CH_2), 112.2 (C), 104.8 (OOCH), 81.4 (OCH), 77.7 (OCH), 71.7 (OCH_2), 67.2 (OCH_2), 27.35 (CH_3), 27.2 (CH_3); HRMS (ESI) m/z calcd for $C_{14}H_{20}O_4K$ (M+K)$^+$, 291.0999; found 291.0999.

(3a*R*,5*S*,6*Z*,6a*R*)-5-((*R*)-2,2-dimethyl-1,3-dioxolan-4-yl)-6-(2-(hexa-2,4-dienyloxy)ethylidene)-2,2-dimethyltetrahydrofuro[2,3-*d*][1,3]dioxole 16a

Following the procedure for sorbylation of the alcohol **10**, sodio-salt of the alcohol **15** (400 mg, 1.39 mmol) in THF (25 mL) was treated with sorbyl bromide (250 mg, 1.57 mmol) to afford, after column chromatography, the sorbyl ether **16a** (435 mg, 85%) as a light yellow oil. $[\alpha]_D^{26}$ 98.0 (c 3.03, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.25–6.16 (1H, m), 6.09–6.01 (2H, m), 5.80 (1H, d, J = 4.2 Hz), 5.76–5.58 (2H, m), 5.01 (1H, d, J = 4.1 Hz), 4.61 (1H, br s), 4.22–4.13 (2H, m), 4.07–4.00 (4H, m), 3.94–3.89 (1H, m), 1.74 (3H, d, J = 6.6 Hz), 1.46 (3H, s), 1.41 (3H, s), 1.35 (3H, s), 1.33 (3H, s); ^{13}C NMR (75 MHz, $CDCl_3$) δ 140.5 (C), 133.8 (CH), 130.9 (CH), 130.4 (CH), 126.5 (CH), 126.0 (CH), 112.5 (C), 110.0 (C), 105.0 (OOCH), 79.9 (OCH), 78.7 (OCH), 77.6 (OCH), 71.1 (OCH_2), 67.1 (OCH_2), 66.9 (OCH_2), 27.5 (CH_3), 27.4 (CH_3), 26.7 (CH_3), 25.5 (CH_3), 18.2 (CH_3); HRMS (ESI) m/z calcd for $C_{20}H_{30}O_6Na$ (M+Na)$^+$, 389.1940; found, 389.1941.

(3a*R*,5*S*,6a*R*,*Z*)-6-(2-(allyloxy)ethylidene)-5-((*R*)-2,2-dimethyl-1,3-dioxolan-4-yl)-2,2-dimethyltetrahydrofuro[2,3-*d*][1,3]dioxole 16b

Following a procedure similar to the allyllation of the alcohol **10**, the sodio-salt of the allyl alcohol **15** (500 mg, 1.74 mmol) in THF (25 mL) was treated with allyl bromide (250 mg, 2.09 mmol) under reflux to obtain, after column chromatography, the allyl ether **16b** (512 mg, 90%) as a light yellow oil. $[\alpha]_D^{27}$ 131.8 (c 4.1, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.06–6.00 (1H, dd, J = 5.7, 7.3 Hz), 5.94–5.88 (1H, m), 5.80 (1H, d, J = 4.0 Hz), 5.29 (1H, dd, J = 1.0, 17.5 Hz), 5.19 (1H, d, J = 10.0 Hz), 5.10 (1H, d, J = 4.0 Hz), 4.61 (1H, d, J = 5.0 Hz), 4.24–4.14 (2H, m), 4.06–3.97 (4H, m), 3.95–3.89 (1H, m), 1.46 (3H, s), 1.41 (3H, s), 1.35 (3H, s), 1.33 (3H, s); ^{13}C NMR (125 MHz, $CDCl_3$) δ 140.6 (C), 134.7 (CH), 125.9 (CH), 117.4 (CH_2), 112.5 (C), 110.0 (C), 105.0 (OOCH), 80.0 (OCH), 78.7 (OCH), 77.6 (OCH), 71.6 (OCH_2), 67.4 (OCH_2), 66.9 (OCH_2), 27.5 (CH_3), 27.4 (CH_3), 26.7 (CH_3), 25.6 (CH_3); HRMS (ESI) m/z calcd for $C_{17}H_{26}O_6Na$ (M+Na)$^+$, 349.1627; found, 349.1627.

(*R*)-1-((3a*R*,5*S*,6*Z*,6a*R*)-6-(2-(hexa-2,4-dienyloxy)ethylidene)-2,2-dimethyltetrahydrofuro[2,3-*d*][1,3]dioxol-5-yl)ethane-1,2-diol 17a

Following the procedure for selective deprotection of the 5,6-acetonide group of compound **7**, the labile acetonide of the sorbyl ether **16a** (700 mg, 1.91 mmol) was deprotected with 80% aqueous acetic acid (10 mL) to afford the diol **17a** (435 mg, 70%) as a viscous liquid. $[\alpha]_D^{27}$ 131.3 (*c* 2.8, $CHCl_3$); ν_{max}/cm^{-1} 3478, 2988, 2938, 1641, 1435, 1373, 1213, 1017; ^1H NMR (300 MHz, $CDCl_3$) δ 6.24–5.88 (3H, m), 5.82 (1H, d, J = 4.3 Hz), 5.76–5.56 (2H, m), 5.11 (1H, d, J = 4.0 Hz), 4.71 (1H, br s), 4.21–4.15 (2H, m), 4.13–4.00 (3H, m), 3.67 (2H, br s), 2.97 (2H, br s), 1.74 (3H, d, J = 6.6 Hz), 1.43 (3H, s), 1.36 (3H, s); ^{13}C NMR (75 MHz, $CDCl_3$) δ 140.4 (C), 134.0 (CH), 130.8 (CH), 130.6 (CH), 126.2 (CH), 125.5 (CH), 112.7 (C), 105.0 (OOCH), 81.0 (OCH), 78.8 (OCH), 73.9 (OCH), 71.2 (OCH_2), 67.1 (OCH_2), 63.3 (OCH_2), 27.5 (CH_3), 27.4 (CH_3), 18.2 (CH_3); HRMS (ESI) m/z calcd for $C_{17}H_{26}O_6Na$ $(M+Na)^+$, 349.1627; found, 349.1624.

(*R*)-1-((3a*R*,5*S*,6a*R*,*Z*)-6-(2-(allyloxy)ethylidene)-2,2-dimethyltetrahydrofuro[2,3-*d*][1,3]dioxol-5-yl)ethane-1,2-diol 17b

Acid catalysed selective deprotection of 5,6-acetonide of the allyl ether **16b** (850 mg, 2.61 mmol) was carried out following the similar protocol described earlier with 75% aqueous acetic acid (8 mL) to afford, after column chromatography, the diol **17b** (560 mg, 75%) as a colourless viscous oil. $[\alpha]_D^{28}$ 138.7 (*c* 4.1, $CHCl_3$); ν_{max}/cm^{-1} 3412, 2986, 2936, 2870, 1645, 1454, 1373, 1213, 1028 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 5.94–5.78 (2H, m), 5.81 (1H, d, J = 4.0 Hz), 5.26 (1H, d, J = 17.2 Hz), 5.18 (1H, d, J = 10.3 Hz), 5.09 (1H, br s), 4.69 (1H, br s), 4.21–4.12 (2H, m), 4.03–3.97 (2H, m), 3.99 (1H, d, J = 5.6 Hz), 3.65 (2H, br s), 3.24 (2H, br s), 1.41 (3H, s), 1.34 (3H, s); ^{13}C NMR (75 MHz, $CDCl_3$) δ 140.5 (C), 134.5 (CH), 125.3 (CH), 117.7 (CH_2), 112.6 (C), 105.0 (OOCH), 81.0 (OCH), 78.9 (OCH), 74.0 (OCH), 71.8 (OCH_2), 67.3 (OCH_2), 63.2 (OCH_2), 27.5 (CH_3), 27.4 (CH_3); HRMS (ESI) m/z calcd for $C_{14}H_{22}O_6Na$ $(M+Na)^+$, 309.1314; found, 309.1314.

General experimental procedure for photochemical reaction

The general procedure is illustrated by the synthesis of the cyclobutane **18b**:

(1*S*,3a′*R*,5*S*,5′*S*,6*R*,6a′*R*)-2′,2′-dimethyl-5′-(2-methyl-1,3-dioxolan-4-yl)dihydro-3a′*H*-3-oxaspiro[bicyclo[3.2.0]heptane-6,6′-furo[2,3-*d*][1,3]dioxole] 18b

A solution of the diol **17b** (500 mg, 1.74 mmol) in dry diethyl ether (dried by distillation over Na-benzophenone under Ar atmosphere) (120 mL) was poured into a pyrex cell. The ethereal solution was then degassed by bubbling Ar gas through it for 30 min. Freshly prepared $(CuOTf)_2{\cdot}C_6H_6$ (76 mg, 0.26 mmol) was added to the reaction mixture. The reaction mixture was then irradiated internally under a positive pressure of Ar with a Hanovia 450 W medium pressure mercury vapour lamp through a water cooled quartz immersion well for about 4 h. After completion (TLC), the reaction mixture was poured into ice cold ammonia solution (10 mL, 35%) in a separatory funnel. After thorough shaking, the blue coloured aqueous layer was separated. The organic layer was washed with brine, dried over anhydrous Na_2SO_4 and finally evaporation of the solvent *in vacuo*, which afforded an oil. The crude mass was then purified through column chromatography over silica-gel using petroleum ether : diethyl ether (9 : 1) as the eluent, to provide the cyclobutane derivative **18b** (mixture of two diastereoismers, *ca.* 2 : 1) (354 mg, 65%) as a light yellow oil. $[\alpha]_D^{26}$ 89.8 (*c* 1.77, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$) (mixture of two diastereoismers, *ca.* 2 : 1) δ 5.55 (1H, d, J = 3.9 Hz), 5.53 (1H, d, J = 3.3 Hz), 5.17 (1H, q, J = 4.8 Hz), 5.05 (1H, q, J = 4.8 Hz), 4.55 (2H, t, J = 3.2 Hz), 4.45 (2H, d, J = 9.9 Hz), 4.30–4.13 (2H, m), 4.08–3.94 (4H, m), 3.91–3.77 (5H, m), 3.48–3.38 (5H, m), 3.02–2.90 (4H, m), 2.29–2.19 (2H, m), 1.48 (6H, s), 1.41 (3H, d, J = 4.8 Hz), 1.38 (3H, d, J = 4.8 Hz), 1.29 (6H, s); ^{13}C NMR (75 MHz, $CDCl_3$) (mixture of two diastereomers) δ 112.4, 112.3, 103.8, 103.6, 102.4, 102.1, 86.2, 85.9, 82.6, 81.0, 74.8, 73.8, 73.7, 73.6, 70.8, 70.7, 70.2, 69.6, 48.6, 48.5, 41.6, 41.3, 35.1 (2CH), 28.1, 28.0, 27.1, 27.0, 26.6, 26.5, 20.2, 20.1; HRMS (ESI) m/z calcd for $C_{16}H_{24}O_6Na$ $(M+Na)^+$, 335.1471; found, 335.1472.

(1*S*,3a′*R*,5*S*,5′*S*,6*R*,6a′*R*)-2′,2′-dimethyl-5′-(2-methyl-1,3-dioxolan-4-yl)-7-(prop-1-enyl)dihydro-3a′*H*-3-oxaspiro[bicyclo[3.2.0]heptane-6,6′-furo[2,3-*d*][1,3]dioxole] 18a

(350 mg, 65%) from 500 mg (1.53 mmol) of **17a** and (460 mg, 60%) from 800 mg (2.21 mmol) of **16a**. $[\alpha]_D^{26}$ 23.4 (*c* 3.8, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$) (for major two diastereomers) δ 5.67–5.55 (2H, m), 5.11 (1H, d, J = 4.4 Hz), 5.59 (1H, d, J = 3.4 Hz), 5.48–5.34 (2H, m), 5.15 (1H, q, J = 4.7 Hz), 5.00 (1H, q, J = 4.8 Hz), 4.67–4.54 (2H, m), 4.45 (1H, d, J = 3.3 Hz), 4.43 (1H, d, J = 10.5 Hz), 4.35 (1H, d, J = 10.0 Hz), 4.23–4.17 (1H, m), 3.95–3.82 (5H, m), 3.77–3.65 (3H, m), 3.50–3.45 (2H, m), 3.42–3.37 (2H, m), 3,05–32.99 (2H, m), 2.93–2.83 (3H, m), 2.54–2.52 (1H, m), 1.66–1.63 (3H, td, J = 1.6, 6.3 Hz), 1.55–1.53 (3H, dd, J = 1.5, 6.8 Hz) 1.45 (6H, s), 1.40 (3H, d, J = 4.8 Hz), 1.34 (3H, d, J = 4.8 Hz), 1.29 (3H, s), 1.28 (3H, s); ^{13}C NMR (75 MHz, $CDCl_3$) δ 130.1 (CH), 129.8 (CH), 126.3 (CH), 125.0 (CH), 112.2 (C), 112.1 (C), 103.7 (CH), 103.5 (CH), 102.2 (CH), 101.8 (CH), 87.6 (CH), 87.3 (CH), 83.9 (CH), 83.1 (CH), 74.6 (CH), 73.8 (CH), 72.6 (CH_2), 72.3 (CH_2), 71.0 (CH_2), 70.6 (CH_2), 70.4 (CH_2), 70.3 (CH_2), 53.3 (C), 53.4 (C), 46.4 (CH), 46.0 (CH), 43.4 (CH), 41.3 (CH), 38.9 (CH), 38.6 (CH), 27.1 (CH_3), 27.0 (CH_3), 26.6 (CH_3), 26.5 (CH_3), 20.3 (CH_3), 20.1 (CH_3), 18.0 ($2CH_3$); HRMS (ESI) m/z calcd for $C_{19}H_{28}O_6K$ $(M+K)^+$, 391.1523; found, 391.1527.

((1*S*,3a′*R*,5*S*,5′*S*,6*R*,6a′*R*)-2′,2′-dimethyldihydro-3a′*H*-3-oxaspiro[bicyclo[3.2.0]heptane-6,6′-furo[2,3-*d*][1,3]dioxole]-5′-yl)methanol 26

(127 mg, 85%) from 150 mg (0.58 mmol) of **23**. $[\alpha]_D^{23}$ 73.6 (*c* 2.1, $CHCl_3$); ν_{max}/cm^{-1} 3435, 2980, 2934, 2857, 1373, 1217, 1074, 1036; ^1H NMR (300 MHz, $CDCl_3$) δ 5.62 (1H, d, J = 3.3 Hz), 4.49 (1H, d, J = 3.3 Hz), 4.44 (1H, d, J = 9.9 Hz), 4.08 (1H, dd, J = 3.9, 6.3 Hz), 3.94–3.91 (2H, m), 3.76 (1H, d, J = 9.2 Hz), 3.41 (1H, dd, J = 5.2, 10.2 Hz), 3.37 (1H, dd, J = 4.5, 9.3 Hz), 2.77–2.70 (2H, m), 2.43 (1H. br s), 2.16 (1H, ddd, J = 2.4, 8.4, 12.8 Hz), 1.45 (3H, s), 1.31 (1H, d, J = 5.3 Hz), 1.27 (3H, s); ^{13}C NMR (75 MHz, $CDCl_3$) δ 112.3 (C), 103.8 (OOCH), 85.7 (OCH), 82.7 (OCH), 73.6 (OCH_2), 70.7 (OCH_2), 61.8 (OCH_2), 47.7 (C), 40.5 (CH),

34.9 (CH), 27.9 (CH_2), 26.9 (CH_3), 26.5 (CH_3); HRMS (ESI) *m/z* calcd for $C_{13}H_{20}O_5Na$ $(M+Na)^+$, 279.1208; found, 279.1208.

2-((1*S*,3a′*R*,5*S*,5′*S*,6*R*,6a′*R*)-2′,2′-dimethyldihydro-3a′*H*-3-oxaspiro[bicyclo[3.2.0]heptane-6,6′-furo[2,3-*d*][1,3]dioxole]-5′-yl)propan-2-ol 27

(122 mg, 82%) from 150 mg (0.52 mmol) of **25**. $[\alpha]_D^{24}$ 77.5 (*c* 2.82, $CHCl_3$); ν_{max}/cm^{-1} 3460, 2979, 2934, 2853, 1373, 1219, 1099, 1034; ^1H NMR (500 MHz, $CDCl_3$) δ 5.59 (1H, d, J = 3.0 Hz), 4.60 (1H, d, J = 3.0 Hz), 4.53 (1H, d, J = 10.0 Hz), 3.80 (1H, d, J = 9.5 Hz), 3.77 (1H, s), 3.45 (1H, dd, J = 5.0, 9.0 Hz), 3.33 (1H, dd, J = 5.5, 10.0 Hz), 3.17 (1H, dd, J = 9.7, 12.4 Hz), 2.93 (1H, dd, J = 7.5, 13.0), 2.91–2.87 (1H, m), 2.25 (1H. br s), 1.50 (3H, s), 1.46 (3H, s), 1.35 (3H, s), 1.32 (3H, s), 1.21– 1.19 (1H, m); ^{13}C NMR (125 MHz, $CDCl_3$) δ 112.3 (C), 102.3 (OOCH), 87.3 (OCH), 85.9 (OCH), 74.1 (OCH_2), 71.5 (C), 71.0 (OCH_2), 48.5 (C), 42.3 (CH), 34.9 (CH), 28.3 (CH_2), 27.4 (CH_3), 26.9 ($2CH_3$), 24.7 (CH_3); HRMS (ESI) *m/z* calcd for $C_{15}H_{24}O_5Na$ $(M+Na)^+$, 307.1521; found, 307.1522.

(1*S*,3a′*R*,5*S*,5′*S*,6*R*,6a′*R*)-5′-(methoxymethyl)-2′,2′-dimethyldihydro-3a′H-3-oxaspiro[bicyclo[3.2.0]heptane-6,6′-furo[2,3-*d*][1,3]dioxole] 28

(110 mg, 79%) from 140 mg (0.52 mmol) of **24**. $[\alpha]_D^{23}$ 98.4 (*c* 1.88, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$) δ 5.62 (1H, d, J = 3.1 Hz), 4.50 (1H, d, J = 3.1 Hz), 4.46 (1H, d, J = 9.9 Hz), 4.15 (1H, t, J = 5.3 Hz), 3.77 (1H, d, J = 8.1 Hz), 3.76 (1H, s), 3.66 (1H, dd, J = 6.6, 9.8 Hz), 3.43 (3H, s), 3.40–3.37 (1H, m), 2.79–2.77 (2H, m), 2.14–2.06 (1H, m), 1.47 (3H, s), 1.29 (3H, s), 1.33–1.24 (1H, m); ^{13}C NMR (75 MHz, $CDCl_3$) δ 112.2 (C), 103.9 (OOCH), 85.5 (OCH), 80.6 (OCH), 73.7 (OCH_2), 71.8 (OCH_2), 70.7 (OCH_2), 59.5 (OCH_3), 48.0 (C), 40.7 (CH), 35.1 (CH), 28.0 (CH_2), 27.0 (CH_3), 26.6 (CH_3); HRMS (ESI) *m/z* calcd for $C_{14}H_{22}O_5Na$ $(M+Na)^+$, 293.1365; found, 293.1366.

2-((1*S*,3a′*R*,5*S*,5′*R*,6*R*,6a′*R*)-2′,2′-dimethyldihydro-3a′*H*-3-oxaspiro[bicyclo[3.2.0]heptane-6,6′-furo[2,3-*d*][1,3]dioxole]-5′-yl)ethanol 30

(26 mg, 65%) from 40 mg (0.15 mmol) of **29**. $[\alpha]_D^{26}$ 29.78 (*c* 0.54, $CHCl_3$); ^1H NMR (500 MHz, $CDCl_3$) δ 5.62 (1H, d, J = 3.5 Hz), 4.51 (1H, d, J = 3.0 Hz), 4.47 (1H, d, J = 10.0 Hz), 4.11 (1H, t, J = 6.5 Hz), 3.94–3.85 (2H, m), 3.82 (1H, d, J = 11.0 Hz), 3.49–3.39 (2H, m), 2.80–2.74 (1H, m), 2.60 (1H, t, J = 6.7 Hz), 2.14 (1H, dd, J = 11.3, 12.4 Hz), 1.93 (2H, dd, J = 6.0, 11.4 Hz), 1.79 (1H, br s), 1.33 (1H, dd, J = 5.0, 11.5 Hz), 1.48 (3H, s), 1.25 (3H, s); ^{13}C NMR (125 MHz, $CDCl_3$) δ 112.2 (C), 103.9 (OOCH), 85.1 (OCH), 81.3 (OCH), 73.7 (OCH_2), 70.7 (OCH_2), 61.8 (OCH_2), 48.8 (C), 40.3 (CH), 34.9 (CH), 31.1 (CH_2), 27.9 (CH_2), 26.9 (CH_3), 26.5 (CH_3); HRMS (ESI) *m/z* calcd for $C_{14}H_{22}O_5Na$ $(M+Na)^+$, 293.1365; found, 293.1363.

((3a*R*,5*S*,6a*R*,*Z*)-6-(2-(allyloxy)ethylidene)-2,2-dimethyltetrahydrofuro[2,3-*d*][1,3]dioxol-5-yl)methanol 23

The diol **17b** (400 mg, 1.39 mmol) in THF–H_2O (2 : 1) (12 mL) at 0 °C was treated with $NaIO_4$ (448 mg, 2.1 mmol) at 0 °C for 30 min. Workup of the reaction mixture was done as usual to afford the aldehyde **22** (318 mg, 90%). The aldehyde **22** (300 mg, 1.18 mmol) in MeOH (6 mL) at −30 °C was immediately treated with $NaBH_4$ (45 mg, 1.18 mmol) to afford, after column chromatography, the alcohol **23** (257 mg, 85%) as a colourless oil $[\alpha]_D^{22}$ 207.5 (*c* 2.1, $CHCl_3$); ν_{max}/cm^{-1} 3444, 2988, 2936, 2866, 1647, 1456, 1373, 1242, 1053, 1017; ^1H NMR (300 MHz, $CDCl_3$) δ 6.00–5.80 (1H, m), 5.87 (1H, d, J = 4.2 Hz), 5.67 (1H, dt, J = 1.7, 5.4 Hz), 5.29 (1H, dd, J = 1.4, 17.2 Hz), 5.21 (1H, dd, J = 1.4, 10.4 Hz), 5.10 (1H, d, J = 4.1 Hz), 4.79 (1H, d, J = 1.4 Hz), 4.27–4.13 (2H, m), 3.99 (2H, dd, J = 1.1, 5.6 Hz), 3.81 (1H, dd, J = 3.0, 12.0 Hz), 3.62 (1H, dd, J = 4.8, 12.0 Hz), 2.23 (1H, br s), 1.48 (3H, s), 1.36 (3H, s); ^{13}C NMR (75 MHz, $CDCl_3$) δ 139.6 (C), 134.5 (CH), 124.5 (CH), 117.5 (CH_2), 112.5 (C), 105.0 (OOCH), 80.7 (OCH), 78.7 (OCH), 71.6 (OCH_2), 67.2 (OCH_2), 64.0 (OCH_2), 27.5 ($2CH_3$); HRMS (ESI) *m/z* calcd for $C_{13}H_{20}O_5Na$ $(M+Na)^+$, 279.1208; found, 279.1207.

(3a*R*,5*S*,6a*R*,*Z*)-6-(2-(allyloxy)ethylidene)-5-(methoxymethyl)-2,2-dimethyltetrahydrofuro[2,3-*d*][1,3]dioxole 24

Following the procedure for synthesis of the ether **5**, the sodio-salt of the alcohol **23** (150 mg, 0.59 mmol) was treated with methyl iodide (0.08 ml, 1.25 mmol) to afford, after usual workup and column chromatography, the methyl ether **24** (142 mg, 90%) as a light yellow oil. $[\alpha]_D^{22}$ 160.0 (*c* 1.43, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$) δ 5.98–5.83 (1H, m), 5.86 (1H, d, J = 4.4 Hz), 5.69 (1H, dd, J = 5.7, 6.4 Hz), 5.28 (1H, d, J = 17.2 Hz), 5.18 (1H, d, J = 10.4 Hz), 5.08 (1H, d, J = 4.10 Hz), 4.82 (1H, br s), 4.27–4.13 (2H, m), 4.05–3.95 (2H, m), 3.57 (1H, dd, J = 3.5, 10.4 Hz), 3.44 (1H, dd, J = 5.2, 10.4 Hz), 3.36 (3H, s), 1.44 (3H, s), 1.36 (3H, s); ^{13}C NMR (75 MHz, $CDCl_3$) δ 140.5 (C), 134.6 (CH), 124.2 (CH), 117.4 (CH_2), 112.3 (C), 105.1 (OOCH), 79.0 (OCH), 78.6 (OCH), 74.6 (OCH_2), 71.5 (OCH_2), 67.2 (OCH_2), 59.5 (OCH_3), 27.5 ($2CH_3$); HRMS (ESI) *m/z* calcd for $C_{14}H_{22}O_5Na$ $(M+Na)^+$, 293.1365; found, 293.1366.

2-((3a*R*,5*S*,6a*R*,*Z*)-6-(2-(allyloxy)ethylidene)-2,2-dimethyltetrahydrofuro[2,3-*d*][1,3]dioxol-5-yl)propan-2-ol 25

The aldehyde **22** (350 mg, 1.38 mmol) in dry diethyl ether (15 mL) at −50 °C was treated with MeMgBr (prepared from the reaction of Mg (66 mg, 2.76 mmol) with MeI (0.17 mL, 2.25 mmol) in diethyl ether). The alcohol obtained in this way, without further purification, was dissolved in dichloromethane (15 mL) and was treated with DMP (643 mg, 1.51). After completion of the reaction (TLC), the reaction mixture was diluted with diethyl ether, washed with saturated $Na_2S_2O_3$ solution doped with $NaHCO_3$ and worked up as usual to afford the corresponding ketone. The methyl ketone, thus obtained, in Et_2O at 0 °C was treated with MeMgBr. The reaction mixture was quenched with addition of saturated aqueous NH_4Cl solution and was diluted with diethyl ether. The mixture was then allowed to settle and the clear solution was decanted, evaporated and purified by column chromatography to afford the tertiary alcohol **25** (270 mg, 70% in three steps) as a clear liquid. $[\alpha]_D^{24}$ 158.5 (*c* 0.76 $CHCl_3$); ν_{max}/cm^{-1} 3412, 2936, 2870, 1450, 1373, 1211, 1157, 1026; ^1H NMR (for major diastereomer) (300 MHz, $CDCl_3$) δ 6.00–5.83 (2H, m), 5.88 (1H, d, J = 4.1 Hz), 5.29 (1H, dd, J = 1.4, 17.2 Hz), 5.22 (1H, d, J = 10.4 Hz), 5.10 (1H, d, J = 3.7 Hz), 4.51 (1H, br s), 4.26 (1H, d, J = 6.2 Hz), 4.02–3.96 (3H, m), 2.04 (1H, br s), 1.42 (3H, s), 1.39 (3H, s), 1.20 (3H, s), 1.16 (3H, s); ^{13}C NMR (for major diastereomer) (75 MHz, $CDCl_3$) δ

140.2 (C), 134.8 (CH), 127.0 (CH), 117.4 (CH_2), 112.7 (C), 105.3 (OOCH), 88.3 (OCH), 80.1 (OCH), 73.2 (C), 71.6 (OCH_2), 67.7 (OCH_2), 27.9 (CH_3), 27.5 (CH_3), 25.7 (CH_3), 25.1 (CH_3); HRMS (ESI) calcd for $C_{15}H_{24}O_5Na$ $(M+Na)^+$, 307.1521; found, 307.1522.

2-((3a*R*,5*R*,6a*R*,*Z*)-6-(2-(allyloxy)ethylidene)-2,2-dimethyltetrahydrofuro[2,3-*d*][1,3]dioxol-5-yl)ethanol 29

KHMDS (8.4 mL, 0.5 M in toluene) was added dropwise into a suspension of (methoxymethyl)triphenylphosphonium chloride (1.7 g, 5.0 mmol) in THF (8 mL) at 0 °C. After stirring the reaction mixture for 15 min, a solution of the aldehyde **22** (420 mg, 1.67 mmol) in THF (5 mL) was added to it. Stirring was continued for 30 min at the same temperature. The reaction was quenched with water (3 mL) and worked up as usual. Column chromatography of the crude mass afforded a light yellow oil (235 mg, 51%) which was immediately treated with 5% HCl (0.5 mL) in THF (5 mL) to afford an aldehyde (145 mg, 65%). A solution of the aldehyde thus obtained in MeOH (2 mL) at 0 °C, was treated with $NaBH_4$ (21 mg, 0.54 mmol). The reaction mixture was quenched with 10% aqueous AcOH solution. MeOH was evaporated under vacuo. The reaction mixture was diluted with diethyl ether and worked up as usual to afford, after column chromatography, the alcohol **29** (100 mg, 69%) as a light yellow oil. $[\alpha]_D^{22}$ 72.0 (*c* 0.25, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.97–5.87 (1H, m), 5.85 (1H, d, J = 4.5 Hz), 5.62 (1H, dt, J = 2.0, 5.5 Hz), 5.31 (1H, qd, J = 1.5, 18.4 Hz), 5.18 (1H, dd, J = 2.0, 10.5 Hz), 5.10 (1H, d, J = 4.0 Hz), 4.86 (1H, d, J = 8.0 Hz), 4.24 (1H, dd, J = 7.7, 12.8 Hz), 4.16 (1H, qd, J = 5.7, 13.0 Hz), 4.02–4.00 (2H, m), 3.83 (2H, t, J = 6.3 Hz), 2.09–2.02 (1H, m), 1.79 (1H, br s), 1.77–1.70 (1H, m), 1.49 (3H, s), 1.37 (3H, s); ^{13}C NMR (125 MHz, $CDCl_3$) δ 142.6 (C), 134.6 (CH), 123.6 (CH), 117.6 (CH_2), 112.3 (C), 104.5 (OOCH), 78.4 (OCH), 78.0 (OCH), 71.7 (OCH_2), 67.2 (OCH_2), 60.5 (OCH_2), 35.8 (CH_2), 27.3 (CH_3), 27.2 (CH_3); HRMS (ESI) m/z calcd for $C_{14}H_{22}O_5Na$ $(M+Na)^+$, 293.1365; found, 293.1366.

(*R*)-1-((1*S*,3a′*R*,5*S*,5′*S*,6*R*,6a′*R*)-2′,2′-dimethyl-7-(prop-1-enyl)dihydro-3a′*H*-3-oxaspiro[bicyclo[3.2.0]heptane-6,6′-furo[2,3-*d*][1,3]dioxole]-5′-yl)ethane-1,2-diol 31

To a stirred solution of the cyclobutane derivative **18a** (400 mg, 1.23 mmol) in acetonitrile : water (9 : 1) (10 mL) was added 2,3-dichloro-5,6-dicyanobenzoquinone (DDQ) (28 mg, 0.13 mmol). After stirring the reaction mixture for 4 h at 60 °C, it was cooled in an ice bath. The reaction was then quenched with the slow addition of saturated $NaHCO_3$ solution (1.5 mL). Acetonitrile was first evaporated off in a rotary evaporator and the residual mass was diluted with water, extracted with ether, washed with brine and finally dried over anhydrous Na_2SO_4. Evaporation of the solvent under vacuo followed by column chromatography of the crude mass (1 : 1 ethyl acetate : petroleum ether) provided the diol **31** in *ca.* 2.1 : 1 diastereomeric mixture (295 mg, 80%) as a light yellow viscous liquid. ν_{max}/cm^{-1} 3412, 3381, 2984, 2934, 2857, 1441, 1373, 1217, 1168, 1018; ^{1}H NMR (300 MHz, $CDCl_3$) (for major diastereomer) δ 5.71–5.58 (1H, m), 5.61 (1H, d, J = 3.2 Hz), 5.50–5.27 (1H, m), 4.47 (1H, d, J = 3.3 Hz), 4.42–5.30 (2H, m), 3.94–3.90 (1H, m), 3.83–3.62 (3H, m), 3.50–3.33 (2H, m), 3.07–2.91 (2H, m), 2.68 (2H, br s), 2.54 (1H, m), 1.65 (3H, td, J = 1.6, 6.3 Hz), 1.46 (3H, s), 1.26 (3H, s); ^{13}C NMR (75 MHz, $CDCl_3$) (for major diastereomer) δ 129.9 (CH), 124.8 (CH), 112.0 (C), 103.2 (OOCH), 87.1 (OCH), 82.0 (OCH), 72.2 (OCH_2), 70.3 (OCH_2), 69.4 (OCH), 65.5 (OCH_2), 53.0 (C), 46.0 (CH), 41.1 (CH), 38.8 (CH), 26.8 (CH_3), 26.3 (CH_3), 13.7 (CH_3). HRMS (ESI) m/z calcd for $C_{17}H_{26}O_6Na$ $(M+Na)^+$, 349.1627; found 349.1627.

(1*S*,3a′*R*,5*S*,5′*R*,6*R*,6a′*R*)-2′,2′-dimethyl-7-(prop-1-enyl)-5′-vinyldihydro-3a′*H*-3-oxaspiro[bicyclo[3.2.0]heptane-6,6′-furo[2,3-*d*][1,3]dioxole] 32

A solution of the above diol **31** (500 mg, 1.53 mmol) in dichloromethane (20 mL) at 0 °C under Ar atmosphere was treated with triethyl amine (1.12 mL, 7.67 mmol), DMAP (20 mg, cat.) and methane sulfonyl chloride (0.38 mL, 4.6 mmol). After the reaction was complete (2 h, TLC) it was quenched by the addition of water. The crude product obtained after usual work up was directly used for the next step. A mixture of dimesylate (730 mg, 1.51 mmol) and NaI (340 mg, 2.27 mmol) in dry DMF (25 mL) was heated to 100 °C with stirring for 4 h. After removing the solvent under vacuum, the reaction mixture was diluted with addition of diethyl ether, quenched with saturated $Na_2S_2O_3$ solution doped with $NaHCO_3$. After usual work up the residual mass was purified through column chromatography using 1 : 8 diethyl ether : petroleum ether as the eluent to provide the diene **32** (350 mg, 80%), as a light yellow oil. $[\alpha]_D^{26}$ 22.1 (*c* 1.21, $CHCl_3$); ν_{max}/cm^{-1} 2984, 2936, 2855, 1454, 1373, 1217, 1165, 1088, 1028; ^{1}H NMR (300 MHz, $CDCl_3$) (for major diastereomer) δ 6.25–6.17 (1H, m), 5.70 (1H, d, J = 3.3 Hz), 5.62–5.60 (1H, m), 5.41–5.38 (1H, m), 5.35–5.24 (2H, m), 4.44 (1H, d, J = 3.3 Hz), 4.42 (1H, d, J = 7.2 Hz), 4.41–4.35 (1H, dd, J = 8.2, 10.5 Hz), 3.75 (1H, t, J = 10.4 Hz), 3.54 (1H, dd, J = 6.8, 9.3 Hz), 3.38 (1H, dd, J = 4.2, 9.2 Hz), 2.78–2.71 (1H, m), 2.68–2.48 (2H, m), 1.64 (3H, td, J = 1.6, 6.4 Hz), 1.48 (3H, s), 1.30 (3H, s); ^{13}C NMR (75 MHz, $CDCl_3$) (for major diastereomer) δ 134.1 (CH), 130.0 (CH), 125.9 (CH), 118.5 (CH_2), 112.0 (C), 103.9 (OOCH), 86.4 (OCH), 84.6 (OCH), 72.2 (OCH_2), 70.3 (OCH_2), 54.8 (C), 46.0 (CH), 41.5 (CH), 38.1 (CH), 26.9 (CH_3), 26.4 (CH_3), 13.7 (CH_3). HRMS (ESI) m/z calcd for $C_{17}H_{24}O_4Na$ $(M+Na)^+$, 315.1572; found 315.1574.

Synthesis of the unsaturated tetracyclic compound 33

To a solution of the diene **32** (200 mg, 0.68 mmol) in degassed dry toluene (50 mL) was added Grubbs' 2nd generation catalyst (47 mg, 0.055 mmol) and refluxed for 4 h. The solvent was evaporated off and the residual mass was chromatographed to provide the tetracycle **33** (111 mg, 65%) as a light yellow oil as a single diastereoisomer. $[\alpha]_D^{24}$ 62.3 (*c* 5.2, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.01 (1H, dd, J = 2.5, 5.5 Hz), 5.70 (1H, d, J = 5.5 Hz), 5.57 (1H, d, J = 2.9 Hz), 5.04 (1H, t, J = 2.1 Hz), 4.72 (1H, d, J = 9.7 Hz), 4.68 (1H, d, J = 2.8 Hz), 4.00 (1H, d, J = 9.5 Hz), 3.50 (1H, dd, J = 5.5, 9.5 Hz), 3.38 (1H, dd, J = 5.2, 9.7 Hz), 2.84 (1H, t, J = 7.0 Hz), 2.70 (1H, br s), 2.48–2.42 (2H, m), 1.51 (3H, s), 1.34 (3H, s); ^{13}C NMR (75 MHz, $CDCl_3$) δ 138.2 (CH), 131.9 (CH), 113.0 (C), 105.3 (OOCH), 92.9 (OCH), 83.9 (OCH), 73.5 (OCH_2), 71.1 (OCH_2), 54.3 (C), 51.6 (CH), 43.9 (CH), 41.3 (CH), 28.3 (CH_3), 27.2 (CH_3); HRMS (ESI) m/z calcd for $C_{14}H_{18}O_4Na$ $(M+Na)^+$, 273.1103; found 273.1106.

Synthesis of the saturated tetracycle 3

To a solution of the cyclopentene **33** (100 mg, 0.4 mmol) in methanol (5 mL) was added Pd/C (10 mg) and was stirred under a positive pressure of hydrogen for 6 h. The reaction mixture was filtered through an alumina bed and was concentrated to afford the saturated compound **3** (94 mg, 94%) as a colourless oil. $[\alpha]_D^{26}$ 81.4 (*c* 1.0, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$) δ 5.62 (1H, d, J = 3.5 Hz), 4.64 (1H, d, J = 3.5 Hz), 4.44 (1H, d, J = 10.1 Hz), 4.41 (1H, d, J = 3.0 Hz), 3.86 (1H, d, J = 9.2 Hz), 3.42 (1H, dd, J = 5.2, 9.6 Hz), 3.40 (1H, dd, J = 5.7, 10.0 Hz), 2.53 (1H, t, J = 6.8 Hz), 2.27–2.21 (1H, m), 2.05–1.94 (2H, m), 1.92–1.77 (2H, m), 1.56–1.50 (1H, m), 1.45 (3H, s), 1.27 (3H, s); ^{13}C NMR (75 MHz, $CDCl_3$) δ 112.0 (C), 105.6 (OOCH), 88.2 (OCH), 83.4 (OCH), 73.9 (OCH_2), 70.8 (OCH_2), 57.2 (C), 44.8 (CH), 40.0 (CH), 38.5 (CH), 30.9 (CH_2), 30.2 (CH_2), 27.4 (CH_3), 26.6 (CH_3). HRMS (ESI) m/z calcd for $C_{14}H_{20}O_4Na$ $(M+Na)^+$, 275.1259; found 275.1251.

Synthesis of the compound 34

Compound **3** (120 mg, 0.48 mmol) in THF (8 mL) was treated with 10% aqueous H_2SO_4 (1 mL) under reflux for 5 h. After completion of the reaction, it was quenched by saturated $NaHCO_3$ solution. Usual work up gave a crude mass that was then purified by column chromatography to afford the diol **34** (87 mg, 87%) as a viscous liquid. ^1H NMR (300 MHz, $CDCl_3$) (for mixture of two anomers) δ 5.22 (1H, br s), 5.13 (1H, d, J = 2.5 Hz), 4.53–4.45 (4H, d, J = 2.9 Hz), 4.18–4.07 (2H, m), 3.86 (2H, d, J = 9.2 Hz), 3.61 (4H, br s), 3.46–3.41 (4H, m), 2.58–2.54 (2H, m), 2.29–2.24 (2H, m), 2.06–1.90 (6H, m), 1.73 (2H, m), 1.60–1.54 (2H, m); ^{13}C NMR (75 MHz, $CDCl_3$) (for mixture of two anomers) δ 104.4 (OOCH), 99.0 (OOCH), 90.4 (OCH), 87.3 (OCH), 77.7 (OCH), 73.7 (OCH_2), 73.4 (OCH), 70.8 (OCH_2), 70.4 (OCH_2), 57.1 (C), 56.6 (C), 46.8 (CH), 45.5 (CH), 39.9 (CH), 39.7 (CH), 38.9 (CH), 38.5 (CH), 32.1 (CH_2), 30.0 (CH_2); HRMS (ESI) m/z calcd for $C_{11}H_{16}O_4Na$ $(M+Na)^+$, 235.0946; found 235.0944.

Synthesis of the compound 35

The diol **34** (80 mg, 0.38 mmol) in THF (8 mL) and water (3 mL) was cooled in an ice-bath and $NaIO_4$ (162 mg, 0.76 mmol) was added to the reaction mixture. After stirring for 1 h, it was worked up following the usual procedure to provide a crude mass that was used for the next step without further purification. The crude compound in diethyl ether (15 mL) was cooled to 0 °C and LAH (20 mg, 0.52 mmol) was added to it and allowed to stir for 20 min. It was then quenched by sequential addition of 0.02 mL H_2O, 0.02 ml 15% aq. NaOH solution and 0.06 mL H_2O. The clear ethereal solution obtained after decantation was concentrated and the crude residue was purified through column chromatography to afford the diol **35** (56 mg, 80%) as a viscous liquid. $[\alpha]_D^{26}$ 7.6 (*c* 0.41, $CHCl_3$); ν_{max}/cm^{-1} 3480, 2951, 2930, 2857, 1464, 1254, 1078; ^1H NMR (500 MHz, $CDCl_3$) δ 4.12 (1H, d, J = 9.5 Hz), 4.07 (1H, d, J = 4.5 Hz), 3.95 (1H, d, J = 11.0 Hz), 3.86 (1H, d, J = 9.1 Hz), 3.78 (1H, d, J = 11.0 Hz), 3.65 (1H, t, J = 5.4 Hz), 3.45 (1H, dd, J = 5.0, 9.3 Hz), 3.34 (1H, dd, J = 5.0, 10.0 Hz), 2.73 (1H, br s), 2.23–2.12 (3H, m), 1.97–1.89 (2H, m), 1.86–1.82 (1H, m), 1.56–152 (1H, m); ^{13}C NMR (125 MHz, $CDCl_3$) δ 79.8 (OCH), 73.7 (OCH_2), 69.6 (OCH_2), 60.4 (OCH_2), 51.7 (C), 43.6 (CH), 41.9 (CH), 40.1 (CH), 34.2 (CH_2), 30.5 (CH_2); HRMS (ESI) m/z calcd for $C_{10}H_{16}O_3Na$ $(M+Na)^+$, 207. 0997; found 207.0998.

Synthesis of the compound 36

To a solution of the diol **35** (55 mg, 0.30 mmol) in dichloromethane (5 mL) was added Et_3N (0.3 mL, 0.9 mmol), DMAP (cat) and TBSCl (54 mg, 0.36 mmol) and was stirred for 4 h at rt. After quenching by the addition of water, the reaction mixture was worked up to obtain a crude mass and the crude mass was chromatographed to afford the silyl ether **36** (80 mg, 90%) as a colourless oil. ^1H NMR (500 MHz, $CDCl_3$) δ 4.05 (1H, d, J = 5.5 Hz), 4.03 (1H, d, J = 10.0 Hz), 4.01 (1H, d, J = 10.0 Hz), 3.85 (1H, d, J = 9.0 Hz), 3.80 (1H, d, J = 10.5 Hz), 3.46 (1H, dd, J = 5.0, 9.0 Hz), 3.32 (1H, dd, J = 5.0, 10.0 Hz), 3.20 (1H, br s), 2.21–2.19 (1H, m), 2.10 (1H, m), 1.97–1.93 (1H, m), 1.90–1.86 (2H, m), 1.64–1.62 (1H, m), 1.55–1.51 (1H, m), 0.88 (9H, s), 0.10 (3H, s), 0.09 (3H, s); ^{13}C NMR (125 MHz, $CDCl_3$) δ 80.2 (OCH), 73.8 (OCH_2), 69.2 (OCH_2), 61.0 (OCH_2), 51.5 (C), 43.9 (CH), 42.0 (CH), 40.1 (CH), 33.4 (CH_2), 30.9 (CH_2), 25.9 ($3CH_3$), 18.1 (C), –5.3 (CH_3), –5.5 (CH_3).

Synthesis of the cyclopentanone 37

A solution of the cyclopentanol **36** (80 mg, 0.27 mmol) in dichloromethane (15 mL) was treated with DMP (137 mg, 0.32 mmol) and stirred for 30 min at rt. On completion (TLC), it was quenched by $Na_2S_2O_3$ solution doped with $NaHCO_3$ and was stirred vigorously. Usual workup of the reaction mixture afforded, after column chromatography, the cyclopentanone **37** (71 mg, 90%) as a colourless oil. $[\alpha]_D^{26}$ –96.9 (*c* 0.58, $CHCl_3$); ν_{max}/cm^{-1} 2953, 2857, 1738, 1254, 1086; ^1H NMR (300 MHz, $CDCl_3$) δ 3.94 (2H, t, J = 10.2 Hz), 3.82 (1H, d, J = 9.1 Hz), 3.72 (1H, d, J = 9.1 Hz), 3.43 (1H, dd, J = 4.8, 9.2 Hz), 3.30 (1H, dd, J = 5.8, 10.3 Hz), 2.69–2.46 (4H, m), 2.39–2.29 (1H, m), 2.06–1.97 (1H, m), 1.91–1.84 (1H, m), 0.80 (9H, s), –0.01 (3H, s), –0.03 (3H, s); ^{13}C NMR (75 MHz, $CDCl_3$) δ 223.2 (CO), 73.5 (OCH_2), 68.6 (OCH_2), 61.1 (OCH_2), 52.4 (C), 43.8 (CH), 41.2 (CH), 40.9 (CH), 37.2 (CH_2), 26.6 (CH_2), 25.8 ($3CH_3$), 18.1 (C), –5.4 (CH_3), –5.6 (CH_3); HRMS (ESI) m/z calcd for $C_{16}H_{28}O_3SiNa$ $(M+Na)^+$, 319.1705; found 319.1704.

Synthesis of the compound 38

To a solution of the ketone **37** (100 mg, 0.34 mmol) in THF (10 mL) was added anhydrous $CeCl_3$ (69 mg, 0.28 mmol) and stirred for 5 min at rt. Vinyl lithium (prepared from *n*-BuLi (1.8 mL, 1.2 mmol, 1.5 M in hexane) and tetravinyl tin (0.07 mL, 0.4 mmol)) was then added to the reaction mixture at –30 °C and stirred for 30 min. The reaction mixture was quenched with saturated aqueous NH_4Cl solution and was allowed to settle. The clear solution was decanted and evaporated in a rotary evaporator. The residue was chromatographically purified to afford the compound **38** (55 mg, 50%) as a light yellow oil. $[\alpha]_D^{26}$ 26.3 (*c* 0.66, $CHCl_3$); ^1H NMR (500 MHz, $CDCl_3$) δ 6.05 (1H, dd, J = 11.0, 17.0 Hz), 5.39 (1H, dd, J = 1.5, 16.8 Hz), 5.08 (1H, dd, J = 1.5, 11.0 Hz), 4.15 (1H, d, J = 10.0 Hz), 4.06 (1H, d, J = 10.0 Hz), 3.89 (1H, d, J = 9.5 Hz), 3.56 (1H, dd, J = 6.5, 9.5 Hz), 3.49 (1H, d, J = 10.0 Hz), 3.44 (1H, dd, J = 5.5, 10.0 Hz), 3.16 (1H, dd, J = 6.0, 7.8 Hz), 2.37–2.29 (2H, m), 1.82–1.70 (2H, m), 1. 26–1.51 (2H, m), 0.87 (9H, s), 0.06

(3H, s), 0.00 (3H, s); ^{13}C NMR (125 MHz, $CDCl_3$) δ 141.4 (CH), 111.7 (CH_2), 83.8 (C), 73.8 (OCH_2), 70.7 (OCH_2), 62.3 (OCH_2), 51.4 (C), 42.6 (CH), 41.9 (CH), 38.5 (CH), 37.4 (CH_2), 30.3 (CH_2), 26.1 ($3CH_3$), 18.2 (C), −5.5 (CH_3), −5.8 (CH_3); HRMS (ESI) *m/z* calcd for $C_{18}H_{32}O_3SiNa$ $(M+Na)^+$, 347.2018; found 347.2019.

Synthesis of the compound 39

The silyl ether **38** (50 mg, 0.15 mmol) in THF (5 mL) was treated with TBAF (0.2 mL, 1.0 M in THF) at 0 °C for 15 min. Usual work up followed by column chromatography afforded the diol **38** (32 mg, 98%) as a viscous liquid. $[\alpha]_D^{24}$ 22.1 (*c* 1.5, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.12 (1H, dd, *J* = 11.0, 16.7 Hz), 5.42 (1H, d, *J* = 16.7 Hz), 5.13 (1H, d, *J* = 11.0 Hz), 4.25 (1H, d, *J* = 10.0 Hz), 4.02 (1H, d, *J* = 11.0 Hz), 3.99–3.78 (2H, m), 3.57–3.53 (2H, m), 3.16 (1H, dd, *J* = 6.0, 7.5 Hz), 2.34–2.31 (2H, m), 2.30–2.25 (1H, m), 1.83–1.70 (2H, m), 1.56–1.52 (1H, m); ^{13}C NMR (125 MHz, $CDCl_3$) δ 141.8 (CH), 111.4 (CH_2), 83.8 (C), 73.8 (OCH_2), 70.8 (OCH_2), 61.8 (OCH_2), 51.9 (C), 42.9 (CH), 41.7 (CH), 38.2 ($2CH_2$), 30.1 (CH_2); HRMS (ESI) *m/z* calcd for $C_{12}H_{18}O_3Na$ $(M+Na)^+$, 233.1154; found 233.1156.

Synthesis of the aldehyde 40

Following the procedure of oxidation of the alcohol **36**, the compound **39** (30 mg, 0.14 mmol) in CH_2Cl_2 (5 mL) was oxidised with DMP (73 mg, 0.17 mmol) to afford the aldehyde **40** (7 mg, 24%). ν_{max}/cm^{-1} 3406, 2953, 2855, 1713, 1615, 1512, 1454; ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.84 (1H, s), 6.20 (1H, dd, *J* = 11.0, 17.5 Hz), 5.37 (1H, d, *J* = 17.5 Hz), 5.29 (1H, d, *J* = 11.0 Hz), 4.06 (1H, d, *J* = 4.5 Hz), 4.04 (1H, d, *J* = 4.0 Hz), 3.53 (1H, dd, *J* = 5.8, 9.3 Hz), 3.29 (1H, dd, *J* = 5.0, 10.5 Hz), 2.81 (1H, dd, *J* = 3.0, 7.0 Hz), 2.72 (1H, dd, *J* = 6.2, 7.2 Hz), 2.37–2.28 (2H, m), 2.25–2.18 (1H, m), 1.82 (1H, dd, *J* = 6.2, 12.8 Hz), 1.71 (1H, dd, *J* = 6.2, 12.5 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 205.2 (CHO), 138.5 (CH), 116.2 (CH_2), 85.3 (C), 74.2 (OCH_2), 69.6 (OCH_2), 62.4 (C), 43.2 (CH), 42.9 (CH), 40.5 ($2CH_2$), 30.2 (CH_2); HRMS (ESI) *m/z* calcd for $C_{12}H_{16}O_3Na$ $(M+Na)^+$, 231.0997; found 231.0997.

Oxidation of the alcohol 39 with TEMPO. Synthesis of dimer 41

To a solution of the diol **39** (35 mg, 0.17 mmol) in dichloromethane (2 mL) was added 2,2,6,6-tetramethylpiperidine-1-oxyl (TEMPO) (10 mg, 0.06 mmol), saturated $NaHCO_3$ solution (0.20 mL) and KBr (40 mg, 0.34 mmol). After cooling the reaction mixture at 0 °C, NaOCl solution (0.20 mL, 4% w/v) was added dropwise and stirred vigorously for 1 h. Usual work up of the reaction mixture followed by column chromatography of the residue over silica gel (5 : 2 petroleum ether : ether) afforded the dimer **41** as a white solid (22 mg, 63%). m.p. 135–136 °C. $[\alpha]_D^{26}$ 4.5 (*c* 1.8, $CHCl_3$); ν_{max}/cm^{-1} 3400, 2940, 2864, 1531; ^{1}H NMR (300 MHz, CDCl3) δ 3.94–3.88 (8H, m), 3.57 (2H, dd, *J* = 6.8, 10.2 Hz), 3.48–3.41 (4H, m), 2.97 (2H, t, *J* = 6.5 Hz), 2.41–2.36 (2H, m), 2.16–2.05 (6H, m), 1.95–1.82 (6H, m), 1.65 (2H, dd, *J* = 6.3, 13.3 Hz); ^{13}C NMR (C_2 symmetric dimer) (75 MHz, $CDCl_3$) δ 89.5 (C), 84.6 (OCH), 73.9 (OCH_2), 72.4 (OCH_2), 70.0 (OCH_2), 56.9 (C), 48.8 (CH), 40.6 (CH), 37.4 (CH), 35.4 (CH_2), 30.6 (CH_2), 28.9 (CH_2); HRMS (ESI) *m/z* calcd for $C_{24}H_{34}O_6Na$ (M+Na)+, 441.2251; found 441.2253.

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